

A new eremophilane sesquiterpene from *Senecio nemorensis*

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A new eremophilane sesquiterpene was isolated from the MeOH extract of the aerial parts of *Senecio nemorensis*. Its structure was established as 11-hydroxy-1 β -methoxy-8-oxoeremophila-6,9-dien-12-oic methyl ester by extensive application of spectroscopic methods, including IR, EI-MS, HR-ESI-MS, 1D and 2D NMR spectroscopy.

Keywords: compositae, *Senecio nemorensis*, sesquiterpene, eremophilane

Senecio species (Compositae) are a rich source of eremophilane sesquiterpenes.¹ However, the secondary metabolites of the same species distributed in different regions are always different. *Senecio nemorensis*, is a perennial plant, which is widely distributed in China. Earlier phytochemical investigation of whole plants of this species collected in northwest China have led to the isolation of a new and two known furanoeremophilane sesquiterpenes.² The same species collected in south China, gave³ three new highly oxygenated eremophilane-type sesquiterpenes and nine known compounds. With the aim of finding antibacterial sesquiterpenes and discovering the relationship between chemical constituents and ecological factors, we investigated the chemical constituents of the roots of this plant collected in east China, and isolated three new eremophilenolides.⁴ Subsequent studies of the aerial parts of *Senecio nemorensis* afforded a new eremophilane sesquiterpene **1** (Fig. 1). Its isolation and structural elucidation are reported here.

The methanol extract of the aerial parts of *Senecio nemorensis* which had been collected in east China, was partitioned with CHCl₃ and water. The CHCl₃ soluble fraction was separated by silica gel column chromatography with gradient elucidaion. Compound **1** was finally obtained after repeated silica gel column chromatographic and preparative thin layer chromatographic purification.

Compound **1** was obtained as colourless gum. Its IR spectrum exhibited intense absorption bands at 3427 (OH), 1754 (C=O), 1674 (C=O), and 1636 (C=C) cm⁻¹. The EI-MS spectrum showed the molecular ion at *m/z* 308. The HR-ESI-MS spectrum of this compound also showed the quasimolecular ion peak at *m/z* 309.1693 ([M + H]⁺), which established the molecular formula as C₁₇H₂₄O₅ ([M + H]⁺,

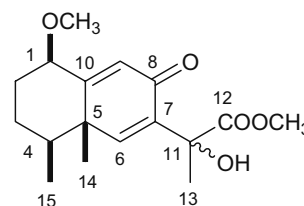


Fig. 1 The structure of compound **1**.

calcd. 309.1697) and indicated the presence of six degrees of unsaturation in **1**. In the ¹H NMR spectrum, there were typical signals for two methoxyl groups at δ_{H} 3.24 and 3.74 (s, 3H, respectively), three methyl groups at δ_{H} 1.61 (s, 3H), 1.32 (s, 3H) and 1.12 (d, *J* = 6.6 Hz, 3H), two trisubstituted alkene protons at δ_{H} 7.09 (br s, 1H) and 6.20 (s, 1H), as well as an oxygenated methenyl proton at δ_{H} 3.86 (br s, 1H) (Table 1). Apart from the carbon signals for two methoxyl groups, the ¹³C NMR spectrum of **1** showed the presence of 15 carbons, including a ketone carbonyl at δ_{C} 186.1, an ester carbonyl at δ_{C} 175.5, an oxygenated methine carbon at δ_{C} 82.4 and an oxygenated quaternary carbon at δ_{C} 73.6 (Table 1). Comparison of the data of ¹H and ¹³C NMR spectra with those of reported compounds,^{5,6,7} and considering the chemical shifts and coupling patterns of the signals of two alkene protons, together with the high field shift of the signal for the ketonic carbonyl suggested the main framework of **1** be an 8-oxoeremophila-6,9-diene. Detailed analysis of the HMBC correlations further confirmed the location of the substituents. In the HMBC spectrum (Fig. 2), the correlations between δ_{H} 6.20 (H-9)/ δ_{C} 82.4 (C-1) and δ_{H} 3.24 (–OCH₃)/ δ_{C} 82.4 (C-1) indicated that

Table 1 ¹H, ¹³C and DEPT data of compound **1** (CDCl₃, δ in ppm, TMS)^{a,b}

No.	δ_{H}	δ_{C}	DEPT
1	3.86 (br s)	82.4	CH
2	2.14 (m, 1H), 1.61 (m, 1H)	33.3	CH ₂
3	1.86 (m, 1H), 1.58 (m, 1H)	25.5	CH ₂
4	1.48 (m, 1H)	41.2	CH
5	–	44.2	C
6	7.09 (s, 1H)	152.5	CH
7	–	137.5	C
8	–	186.1	C
9	6.20 (s, 1H)	127.7	CH
10	–	164.4	C
11	–	73.6	C
12	–	175.5	C
13	1.61 (s, 3H)	23.0	CH ₃
14	1.32 (s, 3H)	17.2	CH ₃
15	1.12 (d, <i>J</i> = 6.6 Hz, 3H)	16.1	CH ₃
1-OCH ₃	3.24 (s, 3H)	52.8	CH ₃
12-OCH ₃	3.74 (s, 3H)	56.5	CH ₃

^aMeasured at 600 MHz for ¹H NMR and 150 MHz for ¹³C NMR.

^bAssigned by ¹H–¹H COSY and HMBC spectrum.

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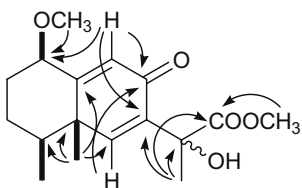


Fig. 2 The key HMBC correlations of **1**.

a methoxyl was attached to C-1. The correlations between $\delta_{\text{H}} 1.61$ (CH_3 -13)/ $\delta_{\text{C}} 73.6$ (C-11), $\delta_{\text{H}} 1.61$ (CH_3 -13)/ $\delta_{\text{C}} 137.5$ (C-7), $\delta_{\text{H}} 1.61$ (CH_3 -13)/ $\delta_{\text{C}} 175.5$ (C-12) and $\delta_{\text{H}} 3.74$ ($-\text{OCH}_3$)/ $\delta_{\text{C}} 175.5$ (C-12) suggested that a hydroxyl was attached to C-11 and a carboxyl at C-12 had formed a methyl ester.

In the NOESY spectrum, the correlations between CH_3 -14 and the methoxyl attached to C-1, and between CH_3 -14 and CH_3 -15 suggested that the methoxyl at C-1 and the two methyls were β -oriented. The configuration of C-11 was not determined because of the restricted amount of material. Based on these conclusions, compound **1** was identified as 11-hydroxy-1 β -methoxyl-8-oxoeremophila-6,9-dien-12-oic methyl ester.

Experimental

The IR spectrum was recorded with a Bruker Vertex 70 FT-IR spectrometer as a KBr disc. Optical rotation was measured on a Perkin-Elmer 341 polarimeter. ^1H , ^{13}C NMR (DEPT) and 2D NMR were recorded on Bruker AVANCE 600 spectrometer with TMS as internal reference. EI-MS and HR-ESI-MS spectra were obtained respectively on HP-5988A GC/MS and Bruker APEX II spectrometers using a direct insertion probe method. Silica gel (200–300 and 300–400 mesh) used for column chromatography (CC) and preparative TLC precoated plates were purchased from Qingdao Marine Chemical Factory in China. Spots were detected on TLC under UV light at 254 nm or by heating after spraying with 5% H_2SO_4 in $\text{C}_2\text{H}_5\text{OH}$.

Plant material

The aerial parts of *Senecio nemorensis* was collected from Kunyu Mountains, Weihai, P.R. China in September 2006, and identified by Hong Zhao, (Shandong University, Weihai). A voucher specimen (No. KY2006001) is deposited in the Laboratory of Botany, Marine College, Shandong University at Weihai.

Extraction and isolation

The powdered air-dried whole plants of *S. nemorensis* (5.8 Kg) were extracted with methanol three times at room temperature, each for 6 days. After concentration of the combined extracts under reduced pressure, the residue (386 g) was suspended in water and then extracted successively with hexane and CHCl_3 , respectively. The CHCl_3 soluble fraction (85 g) was chromatographed over a silica-gel column (200–300 mesh, 900 g) with an elution gradient of petroleum ether (b.p. 60–90°C) – acetone (20:1, 10:1, 5:1). Three fractions were collected according to their TLC analysis: 1–3. The main constituents of fraction 1 (petroleum ether–acetone 20:1, 18 g) were a volatile oil and β -sitosterol. Fraction 2 (petroleum ether–acetone 10:1, 22 g) was isolated by silica gel column chromatography using petroleum ether (b.p. 60–90°C) – acetone (15:1) as an eluent to yield five fractions: f_1 – f_4 . Fraction f_3 (670 mg) was further isolated by repeated silica gel column chromatography. It was finally purified by preparative TLC eluting with CHCl_3 –acetone (150:1) to yield compound **1** ($R_f = 0.37$, 6 mg). No interesting spot was found in Fraction 3 (petroleum ether–acetone 5:1, 19 g).

11-Hydroxy-1 β -methoxyl-8-oxoeremophila-6,9-dien-12-oic methyl ester (1): $\text{C}_{17}\text{H}_{24}\text{O}_5$, Colourless gum. $[\alpha]_{\text{D}}^{18} -42.8$ (c 0.4, CHCl_3). IR (KBr) $\nu_{\text{max}}/\text{cm}^{-1}$: 3427, 2923, 1754, 1674, 1636, 1471, 1259. EI-MS m/z (rel. int.): 308 (1), 261 (1), 258 (2), 249 (20), 217 (37), 199 (3), 193 (13), 175 (20), 163 (9), 145 (6), 115 (6), 99 (9), 91 (9), 77 (10), 71 (11), 59 (15), 53 (6), 43 (100). HR-ESI-MS: m/z : 309.1693 ($[\text{M} + \text{H}]^+$, $\text{C}_{17}\text{H}_{25}\text{O}_5$, calcd. 309.1697). ^1H , ^{13}C NMR and DEPT data see Table 1.

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