

Two New Eremophilenolides from *Cacalia pilgeriana*

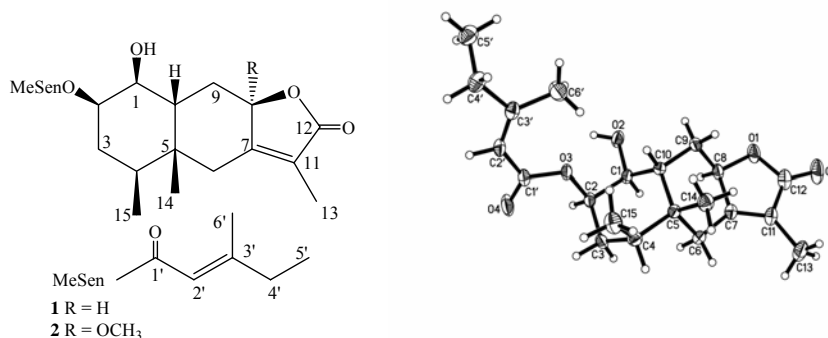
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Abstract: Two new eremophilenolides, 1 β -hydroxy-2 β -methylseneciocyloxyeremophil-7 (11)-en-8 β (12)-olide (**1**), 1 β -hydroxy-2 β -methylseneciocyloxy-8 α -methoxyeremophil-7 (11)-en-8 β (12)-olide (**2**), were isolated from the roots of *Cacalia pilgeriana*. Their structures were elucidated by spectroscopic methods and X-ray diffraction analysis.

Keywords: *Cacalia pilgeriana*, Compositae, eremophilenolide.

Phytochemically, the genus *Cacalia* was characterized by containing eremophilenolide sesquiterpenes¹⁻³. We previously reported two new *ent*-kaurenoids isolated from the roots of *Cacalia pilgeriana* (Diels) Ling⁴. Further study has provided two new eremophilenolides **1** and **2**.



Compound **1** was obtained as white prisms from acetone, m.p. 162-164°C, $[\alpha]_D^{21}$ -120 (c 0.6, CHCl₃). The molecular formula of **1** was determined as C₂₁H₃₀O₅ by HRESIMS [M+H]⁺ at *m/z* 363.2156 (calcd. 363.2166). Its IR absorptions indicated the presence of a hydroxyl group (3356 cm⁻¹) and an α , β -unsaturated γ -lactone unit (1745 cm⁻¹). The signals of δ_H 5.67 (tq, 1 H, *J* = 1.2, 1.2 Hz, H-2'), 2.18 (dq, 2 H, *J* = 1.2, 7.5 Hz, H-4'), 1.08 (t, 3H, *J* = 7.5 Hz, H-5'), 2.18 (d, 3H, *J* = 1.2 Hz, H-6') and δ_C 166.9 (s, C-1'), 113.8 (d, C-2'), 163.5 (s, C-3'), 33.7 (t, C-4'), 11.8 (q, C-5'), 18.8 (q, C-6') in its ¹H and ¹³C

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NMR spectra (**Table 1**) displayed the presence of a methylseneciocyloxy group⁵, which was also confirmed by the C₆H₁₀O₂ unit in the fragment ion peaks at *m/z* 248 [M-114 (C₆H₁₀O₂)]⁺ and 97 [(C₆H₁₀O₂)-OH]⁺ in its EIMS⁶. Except for six carbons of a methylseneciocyloxy group, the ¹³C NMR spectra of **1** showed 15 carbon signals for three methyls, three methylenes, five methylenes including three oxygenated carbons, four quaternary carbons including one carbonyl carbon and two olefinic carbons, indicating a sesquiterpene skeleton with an α , β -unsaturated γ -lactone unit and in agreement with an eremophil-7(11)-en-8(12)-olide¹⁻³ structure type. The ¹H-¹H COSY spectrum confirmed the presence of the fragment of CH₃ (15)-CH (4)-CH₂ (3)-CH (2)-CH (1)-CH (10)-CH₂ (9), and C-1, C-2 were oxygenated. The methylseneciocyloxy group was deduced to be located at C-2 by the cross-peak δ_{C-1} 166.9/ δ_{H-2} 5.21 in the HMBC spectrum. The relative stereochemistry of **1** was finally determined by the X-ray diffraction analysis. So compound **1** was identified as 1 β -hydroxy-2 β -methylseneciocyloxyeremophil-7 (11)-en-8 β (12)-olide.

Table 1 ¹H NMR (400 MHz), ¹³C NMR (100 MHz) data of **1** and **2** (CDCl₃, TMS, δ ppm)

No.	1 δ_H J (Hz)	2 δ_H J (Hz)	1 δ_C	2 δ_C
1	α 3.84 (dd, 3.6, 4.5)	α 4.18 (dd, 3.0, 7.2)	68.2 d	68.0 d
2	α 5.21 (d, 3.6)	α 5.20 (d, 3.0)	71.6 d	71.6 d
3	α 2.08 (m) β 1.98 (m)	2.01 (m)	31.1 t	31.1 t
4	α 1.61 (tq, 5.7, 6.9)	1.62 (tq, 3.9, 7.5)	36.9 d	37.3 d
5	-	-	40.5 s	41.3 s
6	α 2.64 (dd, 1.2, 14.4) β 2.20 (d, 14.4)	α 2.58 (dd, 1.2, 13.5) β 2.10 (d, 13.5)	28.5 t	31.3 t
7	-	-	161.8 s	157.8 s
8	α 4.92 (dd, 7.8, 9.6)	-	77.4 d	105.8 s
9	2.86 (ddd, 2.1, 6.0, 12.6) 1.42 (dt, 3.9, 12.6)	2.88 (d, 14.7) 1.73 (dd, 5.0, 14.7)	34.5 t	33.8 t
10	β 2.04 (m)	1.94 (dd, 5.0, 7.2)	38.4 d	38.5 d
11	-	-	122.3 s	126.5 s
12	-	-	174.8 s	171.6 s
13	1.80 (d, 1.2)	1.85 (d, 1.2)	8.0 q	8.1 q
14	0.88 (s)	0.88 (s)	24.3 q	23.7 q
15	1.12 (d, 6.9)	1.11 (d, 6.9)	18.1 q	18.6 q
1'	-	-	166.9 s	166.7 s
2'	5.67 (tq, 1.2, 1.2)	5.66 (tq, 1.2, 1.2)	113.8 d	114.0 d
3'	-	-	163.5 s	163.1 s
4'	2.18 (dq, 1.2, 7.5)	2.19 (dq, 1.2, 7.2)	33.7 t	33.7 t
5'	1.08 (t, 7.5)	1.08 (t, 7.2)	11.8 q	11.8 q
6'	2.18 (d, 1.2)	2.17 (d, 1.2)	18.8 q	18.8 q
MeO	-	3.21 (s)	-	50.2 q

Compound **2** was yielded as colorless needles from acetone, m.p. 138-140°C, [α]_D²⁴ -152 (*c* 3.8, CHCl₃). The molecular formula of **2** was determined as C₂₂H₃₂O₆ by HRESIMS [M+Na]⁺ at *m/z* 415.2082 (calcd. 415.2092). Its NMR spectra (**Table 1**) were extremely similar to those of **1** except the proton of C-8 was substituted by a methoxy group, which could be confirmed by the cross-peak δ_{C-8} 105.8/ δ_H 3.21 in the HMBC spectrum. The eremophilane derivatives isolated from the genus *Cacalia* and *Ligularia* were the *cis*-fused A/B ring system^{1-3,7,8}, so the proton of C-10 was in the

β -configuration. Furthermore, difference NOE spectrum of **2** showed that the H-2 signal had a clear enhancement (8.1%) irradiating H-1, but the H-10 signal had no change. Thus H-1 and H-2 were in the α -configuration and the substituents at C-1 and C-2 were in the β -configuration. Naya *et al.* reported that for 8α -methoxyeremophilenolide derivatives the C-15 doublet methyl is downfield from the C-14 singlet methyl and the chemical shifts are reversed in the 8β -series^{9, 10}. Compound **2** showed the presence of signals at δ_{H} 1.11 (d, $J = 6.9$ Hz, Me-15) and δ_{H} 0.88 (s, Me-14). Thus **2** was deduced as 1β -hydroxy- 2β -methylseneciolyoxy- 8α -methoxyeremophil-7 (11)-en- 8β (12)-olide.

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