

GUAIANOLIDES FROM *CENTAUREA MUSIMOMUM*

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Key Word Index—*Centaurea musimomum*; Compositae; sesquiterpene lactones; guaianolides.

Abstract—Two new guaianolides have been isolated from the aerial parts of *Centaurea musimomum*, 3-oxo-4 α -acetoxy-15-hydroxy-1 α H, 5 α H, 6 β H, 7 α H, 11 β H-guai-10(14)-ene-6,12-olide and 3-oxo-4 α -hydroxy-15-hydroxy-1 α H, 5 α H, 6 β H, 7 α H, 11 β H-guai-10(14)-ene-6,12-olide. The structures of the compounds were elucidated by NMR spectroscopy. © 1997 Elsevier Science Ltd. All rights reserved

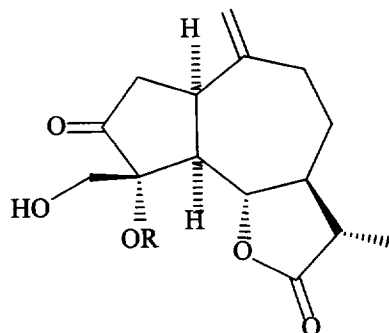
INTRODUCTION

In continuation of our study on *Centaurea* species found in Algeria [1–3], we isolated two new guaianolides from the methanol extract of the aerial parts of *Centaurea musimomum* collected in the region of Constantine (Algeria).

RESULTS AND DISCUSSION

The chloroform soluble part of the methanol extract from the aerial parts of *Centaurea musimomum* yielded two new guaianolides **1** and **2**. The IR spectra of these two compounds exhibited bands indicative of hydroxyl (3410 cm⁻¹), lactone carbonyl (1770 cm⁻¹), cyclopentanone (1730 cm⁻¹) and C=C double bond. In addition to the absorptions characterising these functions, the IR spectrum of **1** exhibited acetate bands (1720 and 1240 cm⁻¹). The UV spectra of both compounds exhibited end absorption at $\lambda_{\max}$ = 214 nm.

The ¹³C NMR spectrum of **1** (Table 1) confirmed the presence of three carbonyl groups by exhibiting three carbonyl signals at δ 219 (ketone), 176 (lactone) and 170 (ester). The chemical shift value of the lactonic carbonyl signal showed that the C-11/C-13 bond was saturated. Furthermore, a DEPT experiment showed two methyl, five methylene, and five methyne carbons and confirmed the presence of five quaternary carbons. These results, in addition to those obtained by EIMS and CIMS (NH₃) which, respectively, showed a [M]⁺ ion at m/z 322 and a [M + NH₄]⁺ ion at m/z 340, led to the formula C₁₇H₂₂O₆. The presence



	R
1	Ac
2	H

of fragments at m/z 262 (EIMS) and 263 (CIMS) suggested a C₂ ester side chain.

The ¹H NMR spectral data (Table 2) indicated that the side chain was an acetoxy group (δ 2.09) which was assigned to C-4. The spectrum also showed an AB system (δ 4.15, and 4.32, J = 11.7 Hz) which was attributed to CH₂-15, carrying a hydroxyl group while a doublet at δ 1.24 (J = 6.84 Hz) could be attributed to a methyl group on C-11. Assuming the usual β -orientation for the side chain at C-7, this methyl must be α because of the value of $J_{11,13}$ (10 Hz) and, therefore, H-6 must be β ($J_{6,7}$ = 10.3 Hz) [4–5]. The quartet of doublets at δ 1.44, (J = 12.7, 4.9) was attributed to H-8_{ax} because of the chemical shift which is in good

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Table 1. ^{13}C NMR data for compounds **1** and **2** [100.62 MHz, CDCl_3 for **1**, $\text{CDCl}_3 + 1$ drop CD_3OD for **2**, TMS as internal standard]

C	1	2
1	39.68	39.62
2	43.85	43.86
3	219	219.74
4	75.60	77.20
5	51.35	51.40
6	86.87	87.21
7	49.58	49.29
8	27.23	26.85
9	38.46	38.61
10	148.83	148.95
11	47.20	47.08
12	176.21	178.85
13	14.12	13.89
14	112.87	112.48
15	64.12	63.12
16	170.37	
17	20.67	

agreement with the literature data for similar guaianolides [6–12]. The methylene protons at (δ 4.48 and 4.99) were assigned to an exocyclic methylene at C-10. The presence of *W*-coupling (1.5 Hz) between H-5 and H-2 α showed that these protons were *cis*-oriented. The α -orientation of the acetoxy group at C-4 in **1** and of the C-4 hydroxy group in **2** could be inferred from the relative upfield shift of H-6 (δ H-6 = 3.77 for **1** and 4.17 for **2**) [13, 14]. These proton assignments were confirmed by ^1H - ^1H COSY, ^1H - ^{13}C COSY, DEPT and spin decoupling experiments.

The NMR spectrum of **2** is similar to that of **1** (Tables 1 and 2), the only difference being the disappearance of the acetyl group signal. Consequently,

the acetoxy group at C-4 in **1** is replaced by a hydroxy group in **2**.

EXPERIMENTAL

Centaurea musimomum was collected in the Souk-Ahras area in the East of Algeria in June 1992. It was identified by Dr Nadra Khalfallah and deposited in the herbarium of Research Unit of Chemistry, University of Constantine.

Extraction and isolation. Air dried powdered aerial parts (298 g) were soaked in MeOH (2 l). The MeOH extract was evapd and the residue dissolved in H_2O (115 ml). The soln was treated with $\text{Pb}(\text{OAc})_2$. After 3 min centrifugation, the mixture was filtered and the yellow-coloured filtrate extracted with CHCl_3 (3×45 ml) [15]. The extract was concd *in vacuo* at room temp, the residue weighing 11.2 g. A part of this residue (6.2 g) was separated by CC (silica gel 200–400 mesh) using solvent mixtures (CHCl_3 - Me_2CO) with increasing polarities. The frs were combined into nine crude ones. Only frs 3 (400 mg) and 8 (360 mg) were studied. Fr. 3 on rechromatography on silica gel using solvent mixtures (petrol-Et $_2\text{O}$ - Me_2CO) with increasing polarities gave **1** (148.2 mg) and fr. 8 on rechromatography on silica gel column with CHCl_3 -petrol-EtOAc, 1 : 1 : 1 gave **2** (33.2 mg).

3-Oxo-4 α -acetoxy-15-hydroxy-1 α H, 5 α H, 6 β H, 7 α H, 11 β H-guai-10(14)-ene-6,12-olide 1. Crystals, mp 143–144 $^\circ$, UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 214, IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3410 (OH), 1770 (γ -lactone), 1730 (cyclopentanone), 1720 and 1240 (OAc), 1640 (C=C). EIMS 70 eV, *m/z* (rel. int.): 322 [M] $^+$ (4.26), 304 [$\text{M} - \text{H}_2\text{O}$] $^+$ (0.52), 292 [$\text{M} - \text{CH}_2\text{O}$] (4.03), 262 [$\text{M} - \text{CH}_3\text{CO}_2\text{H}$] $^+$ (3.1), 250 (11), 105 (16.11), 93 (12.89), 91 (15.07), 81 (15.59), 79 (17.67), 69 (11.90), 43 [CH_3CO] $^+$ (100), 41 (31.70). CISM (NH_3), *m/z* (rel. int.): 340 [$\text{M} - \text{NH}_4$] $^+$ (100),

Table 2. ^1H NMR spectral data for compounds **1** and **2** [400 MHz, CDCl_3 for **1**, $\text{CDCl}_3 + 1$ drop CD_3OD for **2**; TMS as internal standard]

H	1	J(Hz)	2	J(Hz)
1 α	3.16 ddd	(<i>J</i> = 8.3, 7.8, 3.4 Hz)	3.09 ddd	(<i>J</i> = 8.38, 7.81, 3.66 Hz)
2 α	2.59 ddd	(<i>J</i> = 19, 3.4, 1.5 Hz)	2.52 ddd	(<i>J</i> = 19, 3.66, 1.24 Hz)
2 β	2.64 dd	(<i>J</i> = 19, 7.8 Hz)	2.56 dd	(<i>J</i> = 19, 7.81 Hz)
5 α	2.3 br t	(<i>J</i> = 8.3 Hz)	2.28 br t	(<i>J</i> = 8.38 Hz)
6 β	3.71 dd	(<i>J</i> = 10.3, 8.3 Hz)	4.15 dd	(<i>J</i> = 10.1, 8.38 Hz)
7 α	2.75 m		2.67 m	
8ax	1.44 qd	(<i>J</i> = 12.7, 4.9 Hz)	1.56 qd	(<i>J</i> = 12.73, 5 Hz)
8eq	2.28 m		2.22 m	
9ax	2.18 m		2.11 td	(<i>J</i> = 12.73, 5 Hz)
9eq	2.71 m		2.63 m	
11 β	2.40 dqd	(<i>J</i> = 10, 6.84, 1.5 Hz)	2.34 dqd	(<i>J</i> = 10.41, 6.88, 1.25 Hz)
13	1.24 d	(<i>J</i> = 6.84 Hz)	1.26 d	(<i>J</i> = 6.88 Hz)
14a	4.68 s		4.68 s	
14b	4.99 s		4.99 s	
15a	4.15 d	(<i>J</i> = 11.7 Hz)	3.77 d	(<i>J</i> = 11.26 Hz)
15b	4.32 d	(<i>J</i> = 11.7 Hz)	3.83 d	(<i>J</i> = 11.26 Hz)
17	2.09 s			

323 [MH]⁺ (7.13), 305 [MH – H₂O]⁺ (0.8), 263 [MH – CH₃CO₂H]⁺ (0.8); [α]_D²⁷ + 124–125° (CHCl₃; c 0.1).

3-*Oxo-4α-hydroxy-15-hydroxy-1αH*, 5*αH*, 6*βH*, 7*αH*, 11*βH*-*guai-10(14)-ene-6,12-olide* 2. Crystals, mp (154–155°); UV λ_{max}^{MeOH} nm: 214; IR ν_{max}^{KBr} cm^{–1}: 3400 (OH), 1770 (γ-lactone), 1730 (cyclopentanone), 1640 (C=C). EIMS 70 eV, *m/z* (rel. int.): 280 [M]⁺ (2), 262 [M – H₂O]⁺ (1.5), 252 [M – CO]⁺ (8.44), 250 [M – CH₂O]⁺ (42.22), 249 [M – CH₂OH]⁺ (4.89), 107 (29.33), 105 (37.33), 91 (35.11), 81 (43.110), 69 (37.33), 55 (44.89), 43 (34.67), 41 (100); CISM(NH₃), *m/z* (rel. int.): 298 [MNH₄]⁺ (100), 281 [MH]⁺ (9.05); [α]_D²⁷ + 145 (CHCl₃; c 0.04).

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