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SESQUITERPENE LACTONES FROM *CENTAUREA GLOMERATA*

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Key Word Index—*Centaurea glomerata*, Compositae, germacradienolides, sesquiterpene lactones, esters, arctigenin

Abstract—The investigation of the aerial parts of *Centaurea glomerata* afforded four new sesquiterpene lactones of the germacradienolide type and the lignan lactone arctigenin Their structures were elucidated by spectroscopic methods

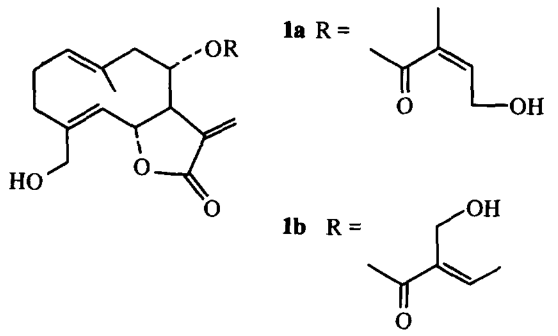
INTRODUCTION

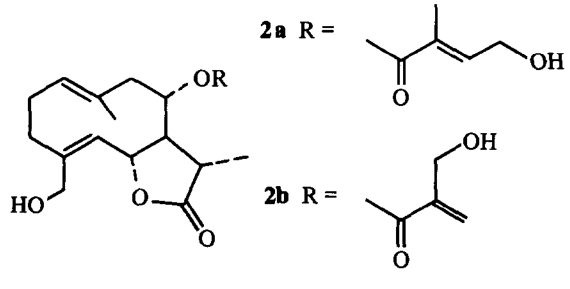
Centaurea species (compositae) contain a variety of sesquiterpene lactones of various types, many of which have been shown to be biologically active [1–20]

There is no information on the sesquiterpene lactones of *C glomerata* which is indigenous to Egypt A preliminary investigation of the flavonoid content resulted in identification of rutin, apigenin and luteolin 7-glucoside among other unidentified flavonoids [21]

RESULTS AND DISCUSSION

Column chromatography of the extract of the aerial parts of *Centaurea glomerata* Vahl gave a semi-solid mixture of sesquiterpene lactones in addition to the known lignan arctigenin [22] The mixture could be separated by HPLC into four new sesquiterpene lactone esters of the germacradienolide type (**1a**, **2a** and a mixture of **1b** and **2b**) All four compounds had similar IR and UV spectral data The IR spectrum exhibited several major absorption bands, including a band at 1760 cm^{-1} due to the presence of γ-lactone moiety, two bands at 1710 cm^{-1} and 1650 cm^{-1} indicating an unsaturated ester and a band at 3600 cm^{-1} due to a hydroxyl group They were identified as C-8 esters of the known sesquiterpene lactone salonitenolide [16, 17], compounds **2a** and **2b** were identified as 11,13-dihydrosalonitenolide esters The dihydro structure of compounds **2a** and **2b** was indicated by the methyl doublet at δ1 37 for the C-13 methyl group together with a double quartet at δ2 53 for H-11 and the change of chemical shift of H-7 to δ2 18 or 2 22 instead of 3 07 (Table 1) All compounds exhibited a prominent loss of the ester side chain from the molecular ion in the mass spectrum confirming the identity of the ester moiety The acid part of compounds **1a** and **2a** was found to be 1-hydroxy-3-methyl-2-butenoic acid (structural isomer of sarracinic acid) and compound **1b** to be a sarracinoyl moiety as previously found in *Liatris* species [23–25] and sarracine alkaloid [26] The acid part of compound **2b** was found to be a 2-hydroxy methyl acrylate moiety


1a R =
1b R =


2a R =
2b R =

Compound 1a

Colourless oil, identified as the 1-hydroxy-3-methyl-2-butenoic acid ester of the sesquiterpene lactone alcohol salonitenolide $C_{20}H_{26}O_6$, MS *m/z* 362 $[M]^+$ The ^{1}H NMR spectrum (Table 1) displayed two doublets at δ6 27 and 5 75 characteristic for a $=CH_2$ group conjugated with the lactone carboxyl Another broad doublet was observed at δ4 40 for $-CH_2OH$ of the acyl part and a broad singlet at 1 84 represented the methyl group of the acyl fraction attached to an olefinic bond. A triplet quartet was located at δ6 87 for the olefinic proton of the acyl radical The presence of the acid part in the ester was also confirmed from the mass spectral peak at *m/z* 246 126 $[M-RCOOH]^+$, calculated for $C_{15}H_{18}O_3$

Compound 2a

Identified as 11,13-dihydro compound **1a**, $C_{20}H_{28}O_6$,

Table 1 ^{1}H NMR spectral data of compounds **1a**, **2a**, **1b** and **2b** (400 MHz, $CDCl_3$, TMS as internal standard)

	1a	**2a**	**1b**	**2b**
H-1	4 99 *br dd*	4 96 *br dd*	4 99 *m*	
H-2	2 20 *m*	2 18 *m*	2 22 *m*	
H-2′				
H-3	2 58 *br d*	2 56 *br d*	2 59 *br d*	2 57 *br d*
H-3′	1 97 *ddd*	1 95 *m*		
H-5	4 83 *br d*	4 75 *br d*	4 83 *br d*	4 75 *br d*
H-6	5 10 *dd*	5 00 *dd*	5 10 *dd*	5 00 *m*
H-7	3 07 *dddd*	2 18 *m*	3 07 *dddd*	2 22 *m*
H-8	5 16 *br dd*	5 24 *ddd*	5 25 *m*	
H-9	2 58 *br d*	2 50 *br d*	2 59 *br d*	
H-9′	2 46 *dd*	2 41 *dd*	2 48 *br dd*	
H-11	—	2 53 *dq*	—	2 59 *m*
H-13	6 27 *d*	1 37 *d*	6 29 *d*	
H-13′	5 75 *d*		5 76 *d*	1 38 *d*
H-14	1 50 *br s*	1 48 *br s*	1 50 *br s*	
H-15	4 30 *d*	4 30 *dd*	4 32 *br d*	
H-15′	4 08 *d*	4 08 *dd*	4 11 *br d*	
	6 87 *tq*	6 85 *tq*	7 01 *q*	6 27 *br s*
OAc	4 40 *br d*	4 40 *br dd*	1 96 *d*	
	1 84 *br s*	1 87 *dq*	4 38 *br s*	4 38 *br s*

J (Hz) Compound **1a** 1,2 = 1,2′ = 5, 2,3′ = 6, 2′,3′ = 10, 3,3′ = 16, 5,6 = 6,7 = 9, 7,8 ~ 8, 7,13 = 3 5, 7,13′ = 3, 8,9′ = 11, 3′,4′ = 6, compound **2a** 1,2 = 11, 1,2′ = 5, 3,3′ = 15, 5,6 = 6,7 = 10, 7,8 = 9, 7,11 = 11, 8,9′ = 10, 9,9′ = 13, 11,13 = 7, compound **1b** 3,3′ = 15, 5,6 = 6,7 = 10; 7,8 = 9, 7,13 = 3 5, 7,15′ = 3, 8,9′ = 10, 9,9 = 14, OCOH, 3′,4′ = 7, compound **2b** 3,3′ = 15, 5,6 = 6,7 = 10, 7,8 ~ 9, 7,11 ~ 11

MS m/z 364 $[M]^+$ The dihydro-nature of compound **2a** was indicated by the ^{1}H NMR spectral data (Table 1) and also confirmed by mass spectral measurements m/z 248 141 $[M-RCOOH]^+$, calculated for $C_{15}H_{20}O_3$

Compound 1b

This is a structural isomer of compound **1a** It differed only in the nature of the sarracinoyl moiety This was confirmed by comparing its ^{1}H NMR spectrum with the reported ^{1}H NMR spectral data of sarracinic acid [23–26] The ^{1}H NMR spectrum showed a quartet at δ7 01 characteristic for an olefinic proton and a doublet at δ1 96 for the vinyl methyl group together with a broad singlet at δ4 38 for CH_2OH (Table 1)

Compound 2b

This compound had the same dihydro-nature of the sesquiterpene lactone alcohol as compound **2a** (^{1}H NMR and mass spectral data) The acid part was a 2-hydroxymethyl acrylate moiety This was indicated by a broad singlet at δ6 27 for $=CH_2$ and a signal at δ4 38 for CH_2OH in the ^{1}H NMR spectrum and a mass spectral ion at m/z 85 for RCO. From the above data compound **2b** is possibly 11,13-dihydro-onopordopicrin [27]

EXPERIMENTAL

The plant material of *Centaurea glomerata* Vahl was collected in early April 1982 near Alexandria, Egypt The plant was previously authenticated by the late Professor Dr V Tackholm, Faculty of Science, Cairo University A voucher specimen is deposited in the Department of Pharmacognosy, Faculty of Pharmacy, University of Alexandria

Fresh aerial parts (4 kg) were extracted with petrol–Et_2O (1 1) and solvents were removed under red pres The extract was suspended in 30% EtOH, filtered and the filtrate was extracted successively with 4 × 7 5 l petrol and 4 × 0 5 l $CHCl_3$ The $CHCl_3$ extract was dried and evaporated to give 2 g of residue The latter was fractionated by CC (silica gel) using petrol, $CHCl_3$ and MeOH with gradual increase in polarity Fractions eluted with petrol–$CHCl_3$ (4 6) (0 1 g) afforded the known lignan arctigenin [22] Fractions obtained with $CHCl_3$–MeOH (9 1) (0 2 g) gave a mixture of four sesquiterpene lactones with very close R_f values This mixture was separated by HPLC (RP 8, MeOH–H_2O, 3 2, flow rate 3 ml/min, *ca* 100 bar) to compounds **1a**, **2a**, **1b** and **2b**

Compound **1a** Colourless oil

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\mathrm{nm}}{+126 \quad +133 \quad +153 \quad +284}\ (c\ 0\ 92,\ CHCl_3)$$

IR $\nu^{CHCl_3}_{max}$ cm^{-1} 3600 (OH), 1760 (γ-lactone) 1710, 1650 MS m/z (rel int) 362 (0 5), $[M]^+$, 246 126, 228 (15) $[M-246-18]^+$, 119 (76), 99 (70), 71 (73), 55 (100)

Compound **2a** MS m/z (rel int) 364 (0 3) $[M]^+$, 248 141 $[M-116]^+$ (calculated for $C_{15}H_{20}O_3$ 248 141), 230 (5) $[248-H_2O]^+$, 121 (100), 99 (76), 71 (73)

Compound **1b** This is a structural isomer of compound **1a** with the same mass spectral data

Compound **2b** MS m/z (rel int) 350 (0 3) $[M]^+$, 248 142 (10) $[M-102]^+$ calculated for $C_{15}H_{20}O_3$, 230 (2) $[M-248-18]^+$

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