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GUAIANOLIDES FROM *CYNARA SIBTHORPIANA*

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Abstract—The aqueous extract of the leaves of *Cynara sibthorpiana* afforded a terpenoid alcohol vomifoliol (= blumenol A) and three guaianolide sesquiterpene lactones, namely the cytotoxic zaluzanin-C, solstitalin and a new guaianolide named as sibthorpine

Cynara sibthorpiana Boiss & Helder is a wild plant indigenous to Egypt [1] Up to the present time nothing has been reported about the chemistry of this species Meanwhile the medicinal effect of *Cynara scolymus* on liver and kidney functions [2] has attracted the attention of various workers Cynarin [3], cynarolide [4], cynaropicrin [5], groshemin [6] and dehydrocynaropicrin [7] are the main isolated compounds from *Cynara* species The aqueous extract of the leaves of *Cynara sibthorbiana* afforded a terpene alcohol and three guaianolides

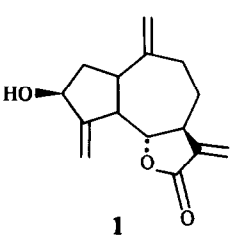
The guaianolide **1**, was identified as zaluzanin C [8, 9] and the terpene alcohol **2**, as vomifoliol (= blumenol A) [10–16] through the comparison of their ^{1}H NMR spectra with those of authentic materials Zaluzanin C was previously isolated from different *Zaluzania* species [8, 9] and it has a tumor-inhibitory activity against the P-388 lymphocytic leukemia [8, 9] Vomifoliol was previously isolated from several plants [10–16] However, this is the first report of the isolation of this compound from a *Cynara* species The ethyl acetate extract of the aqueous extract was chromatographed over a silica gel column The 5% methanol in chloroform fraction appeared as a single spot in different TLC systems, but ^{1}H NMR measurements indicated a mixture of two isomers **3** and **4** Therefore the whole fraction was acetylated The ^{1}H NMR spectrum of the acetyl derivative proved the presence of two isomers The acetylated mixture was rechromatographed by preparative TLC to afford compounds **5** and **6** Compound **5** was identified as solstitalin diacetate through its ^{1}H NMR spectrum and by comparing it with that of authentic material [17, 18]

Compound **6** is a diacetate derivative of a new guaianolide, and had $[M]^+$ at *m/z* at 364 1522 indicating the empirical formula $C_{19}H_{24}O_7$ Comparing the ^{1}H NMR spectra of the new compound and solstitalin we found that the stereochemistry at C-3 is different in the two compounds The ^{1}H NMR spectrum of solstitalin showed clearly the geminal coupling between the methylenic protons (H-15a and H-15b) and the H-3α (J = 2 Hz), while this coupling is absent in the case of the new compound In addition the spectra of the new compound showed a paramagnetic shift of H-3β (J = 12 Hz), H-15a (J = 7 Hz) and H-15b (J = 10 Hz) At the same time the C-3 acetate exhibited a diamagnetic shift (J = 4 5 Hz) All of the above data indicated that the stereochemistry at C-3 is different in the two lactones The new compound is the 3α-hydroxy epimer of solstitalin which is named sibthorpin

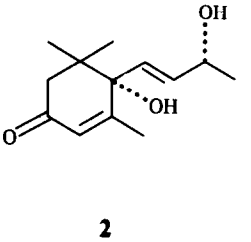
EXPERIMENTAL

The fresh leaves (1 kg) of *Cynara sibthorpiana* collected near Alexandria were minced and macerated with boiling water (2 l) for 1 hr The aq extract was filtered and extracted successively with $CHCl_3$ (6 l) and EtOAc (6 l)

The $CHCl_3$ extract (600 mg) was chromatographed on a silica gel column (30 g, 3 × 50 cm) with elution by $CHCl_3$, 1%, 2% and 3% MeOH in $CHCl_3$ (500 ml of each) The 3% MeOH in $CHCl_3$ fraction was further fractionated by preparative TLC (silica gel, Et_2O–petrol, 1 1) affording zaluzanin-C (**1**) [8, 9] as a crystalline compound mp 93–95° (lit mp 95–96°) and vomifoliol (**2**)



1



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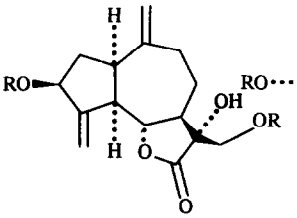
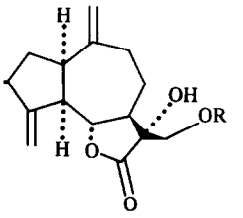


R
3 H
5 Ac



R
4 H
6 Ac

Table 1 ^{1}H NMR spectral data of compounds **5** and **6** (400 MHz, $CDCl_3$ and TMS as internal standards)

H-1	2 9 (overlapped with H-5)	3 065 (overlapped with H-5)
H-2α	2 5 (overlapped with H-7) *dddd*	2 24 *dddd*
H-2β	1 8 *dddd*	1 96 (overlapped with H-9β)
H-3	5 55 *ttt*	5 67 *t*
H-5	2 9 (overlapped with H-1)	3 065 (overlapped with H-1)
H-6	4 1 *t*	4 0 *t*
H-7	2 55 *m* (overlapped with H-2)	2 5 *dtd*
H-8α	2 25 *dddd*	2 15 *m*
H-8β	1 425 *dddd*	1 345 *dd*
H-9α	2 59 *tt*	2 59 *tt*
H-9β	1 98 *ddd*	1 98 (overlapped with H-2)
H-13	4 35 *d*	4 32 *d*
H-13′	4 08 *d*	4 085 *d*
H-14	4 95 *s*	4 945 *s*
H-14′	4 92 *s*	4 80 *s*
H-15	5 41 *t*	5 48 *d*
H-15′	5 31 *t*	5 41 *d*
11-OH	3 215 *s*	3 225 *s*
3-Ac	2 11 *s*	2 065 *s*
13-Ac	2 08 *s*	2 08 *s*

J (Hz), compound **6** 1, 2α = 2α, 3α = 7 5, 1, 2β = 16, 1, 5 = 9, 2β, 3α = 8 5, 2α, 3α = 7, 8α = 8α, 9α = 4 5, 3α, 15 = 3α, 15′ = 15, 15′ = 2, 5, 6 = 6, 7 = 10, 7, 8β = 8α, 9β = 8β, 9α = 13, 13′ = 12, 8β, 9β = 4 0, 2α, 2β = 8α, 8β = 9α, 9β = 12 5

(= blumenol A) [10–15] as a crystalline compound mp 114° (lit mp 115°)

The EtOAc extract was freed from solvent and extracted with $CHCl_3$ (300 ml), the $CHCl_3$ extract (1 g) was chromatographed on a silica gel column (50 g, 3 × 80 cm) with elution by $CHCl_3$ (600 ml), 3% and 5% MeOH in $CHCl_3$ (500 ml each) The 5% MeOH in $CHCl_3$ fraction was acetylated using the standard procedure and after evaporation rechromatographed by preparative TLC (silica gel, Et_2O–petrol, 1 1, two developments) affording **5**, colorless oil (R_f 0 41) and compound **6**, colorless oil (R_f 0 52), MS *m/z* (rel int) 364 1522 $[M]^+$ ($C_{19}H_{24}O_7$) (8 0), 322 $[M-C_2H_2O]^+$ (5 7), 304 $[M-AcOH]^+$ (10 0), 280 $[322-C_2H_2O]^+$ (14), 244 $[304-AcOH]^+$ (14 0), 226 $[244-H_2O]^+$ (15 0), 216 $[244-CO]^+$ (22), 198 $[226-CO$ and $216-H_2O]^+$, 175 (68), 159 (39) and 157 (100),

$$[\alpha]^{\lambda}_{240} = \frac{\begin{matrix}589 & 578 & 546 & 436\,\text{nm}\\ +141 & +153 & +165 & +270\end{matrix}}{} \quad (CHCl_3,\ c\ 0\,17)$$

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