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TWO GUAIANOLIDES FROM *CICHORIUM PUMILUM*

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Key Word Index—*Cichorium pumilum*, Compositae, sesquiterpene lactones, guaianolides

Abstract—The roots of *Cichorium pumilum* afforded two new guaianolides, 10β-hydroxyguaia-4,13-dien-6,12-olide and the corresponding 11β,13-dihydro derivative which could be separated only after transforming the methylene lactone into the corresponding pyrazoline The structures were elucidated by 400 MHz ^{1}H NMR spectroscopy The chemotaxonomic situation is discussed briefly

INTRODUCTION

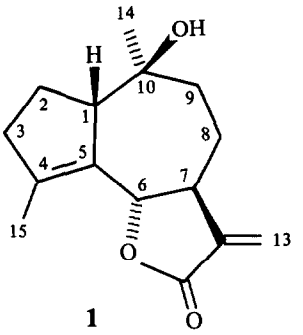
Some species of *Cichorium* [1] are widely cultivated but not much is known on the chemistry of this genus In addition to widespread triterpenes and phenolic compounds [2], some coumarins as cichorin [3] as well as the guaianolides lactucin [4] and lactucopicrin [5] have been reported We have investigated the roots of *Cichorium pumilum* Jacq (subsp of *C endiva* L [6]) From the leaves a flavone glucoside was reported [7], while the roots have not been studied so far The results will be discussed in this paper

Table 1 ^{1}H NMR spectral data of compounds **1–3** (400 MHz, TMS as internal standard)

	1	**2**		**3**	
	$CDCl_3$	$CDCl_3$	C_6D_6	$CDCl_3$	C_6D_6
H-1	3 55 *br dd*	3 53 *br dd*	3 24 *br d*	3 53 *br dd*	3 27 *br dd*
H-2	+	1 80 *dddd*	1 52 *dddd*	1 76 *m*	1 61 *dddd*
H-2′	+	+	1 37 *m*	+	1 39 *m*
H-3	+	2 08 *m*	1 96 *dddd*	2 18 *m*	1 95 *dddd*
H-3′	+		1 77 *dddd*		1 78 *dddd*
H-6	4 55 *dddq*	5 76 *dddq*	5 74 *dddq*	4 59 *dddq*	4 15 *dddq*
H-7	2 57 *ddddd*	2 28 *ddd*	1 64 *ddd*	+	1 39 *m*
H-8	+	1 69 *dddd*	1 43 *dddd*	+	
H-8′	+	1 50 *br d*	1 88 *br d*	+	1 90 *br d*
H-9	+	1 28 *ddd*	0 90 *ddd*	1 31 *m*	1 00 *m*
H-9′	+	+	0 85 *br d*	+	
H-11	–	–	–	2 26 *dq*	1 60 *dq*
H-13	6 15 *d*	4 69 *t*	4 23 *ddd*	1 26 *d*	1 05 *d*
H-13′	5 49 *d*		4 04 *ddd*		
H-14	1 12 *s*	1 19 *s*	0 95 *s*	1 13 *s*	1 02 *s*
H-15	1 88 *br s*	1 93 *br s*	2 01 *br s*	1 86 *br s*	2 01 *br s*
H-16	–	1 55 *ddd*	0 75 *ddd*	–	–
H-16′	—	2 21 *ddd*	1 83 *ddd*	–	–

+, Overlapping multiplets

J (Hz) Compound **1** 1, 2 = 10; 1, 2′ = 4, 3, 6 = 3′, 6 = 6, 15 ~ 1, 6, 7 = 10, 7, 8 = 11, 7, 8′ = 3, 7, 13 = 3 3, 7, 13′ = 3, compound **2** 1, 2 = 11 5, 1, 2′ ~ 2, 1, 9′ ~ 1, 2, 2′ = 12, 2, 3 = 11, 2, 3′ = 5, 3, 3′ = 16, 3, 6 = 3′, 6 = 6, 15 ~ 1, 6, 7 = 10, 7, 8 = 11 5, 7, 8′ = 3, 8, 8′ = 12, 8, 9 = 11, 8, 9′ = 4, 8′, 9 = 3, 9, 9′ = 12, 13, 13′ = 13, 13, 16 = 6, 13, 16′ = 9, 13′, 16 = 9 5, 13′, 16′ = 6, 16, 16′ = 17, compound **3** 1, 2 = 11, 1, 2′ = 3, 2, 2′ = 12, 2, 3 = 11, 2, 3′ = 5, 2′, 3 ~ 5, 2′, 3′ = 2, 3, 3′ = 16, 3, 6 = 3′, 6 = 6, 15 ~ 1, 6, 7 = 10, 7, 11 = 11 5, 8, 8′ = 12, 11, 13 = 7



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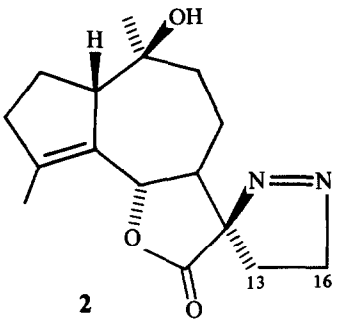

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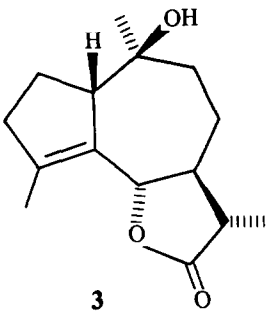

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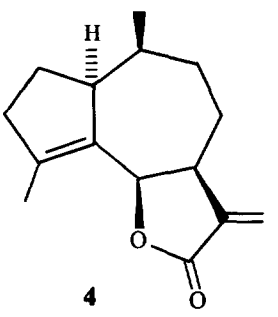

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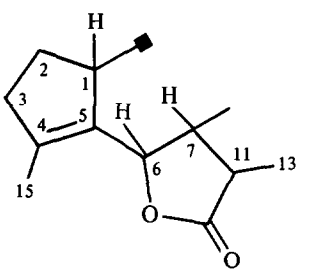

A

RESULTS AND DISCUSSION

The extract of the roots of flowering plants of *C pumilum* Jacq , collected in May 1982 south of Alexandria, was separated by column chromatography From the polar parts a mixture of two sesquiterpene lactones were obtained which could not be separated The ^{1}H NMR spectrum of the mixture, however, clearly showed that a methylene lactone and a 11,13-dihydro derivative were present (Table 1) Accordingly, addition of diazomethane transformed the methylene lactone to the corresponding pyrazoline which easily could be separated from the dihydro derivative

The molecular formula of the latter was $C_{15}H_{22}O_3$ Elimination of water (*m/z* 232) and a corresponding band in the IR spectrum showed that a γ-lactone with one hydroxyl group was present Accordingly, the molecular formula required a tricyclic compound as the ^{1}H NMR spectrum showed that a double bond must be present (δ1 86 *br s*, olefinic methyl) Spin decoupling allowed the assignment of all signals, only those of H-7–H-9 being overlapped multiplets The narrowly split doublet at δ4 15 (in deuteriobenzene) showed allylic couplings with the olefinic methyl and two further protons, both obviously being allylic ones, and a vicinal coupling with an overlapped signal at 1 39 The latter was further coupled with a double quartet at δ1 60 *dq*, its irradiation collapsed the methyl doublet at 1 05 to a singlet, and therefore was H-11 Further decouplings starting with the signals of the allylic protons led to the sequence A, indicating already the presence of a guaianolide.

As H-1 showed a *W*-coupling with the multiplet at 1 00 and as the unusual downfield shift of the H-1 signal needed to be explained a 10β-hydroxyl group had to be assumed if a model was considered, thus leading to the structure **3** The stereochemistry at C-6, C-7 and C-11 clearly followed from the couplings observed, while that at C-1 was deduced from the fact that diazomethane addition only took place from the β-face (see below) and from the *W*-coupling $J_{1,9}$

The methylene lactone most likely was the corresponding 11,13-dehydro derivative of **3** Though the lactone itself could not be obtained pure, the ^{1}H NMR spectral data (Table 1) of the corresponding pyrazoline clearly showed that the adduct was **2** and hence the natural compound was **1** Accordingly, the signals for **1**, which

could be seen in the mixture of **1** and **3**, nicely agreed with this proposal, though the signals of the methylene group were overlapping In the spectrum of **2**, especially in deuteriobenzene, all signals could be assigned by spin decoupling (Table 1) The downfield shift of H-6 clearly showed that a β-addition had taken place Inspection of models with a 1α- and a 1β-proton showed that this addition required a guaianolide with a 1β-proton All couplings observed also supported this assumption As **3** obviously was the dihydro derivative of **1** the proposed stereochemistry of **3** was further supported by that of **1**, which is related to osmitopsin [8] This lactone was erroneously described as its antipode It therefore differs in the stereochemistry at C-1, C-6 and C-10 and hence should be shown as **4** Since the guaianolide **1** without an oxygen function at C-10 is not known, we have named this lactone cichopumilide

The chemotaxonomic relevance of these guaianolides has to be studied further So far only lactucin and related lactones were reported from *Lactuca* species [9], a genus which also is placed with *Cichorium* in the *Cichorium* group of Jeffrey [1]

EXPERIMENTAL

The fresh roots (5 kg) (voucher deposited in the Dept of Pharmacognosy, University of Alexandria, Egypt) were chopped and extracted with Et_2O–petrol (1 1), and the extract was separated by CC (silica gel) With $CHCl_3$–petrol (1 1), 100 mg of the mixture of **1** and **3** (*ca* 5 3) could be obtained crystalline The mixture could not be separated by TLC in different solvent mixtures Addition of CH_2N_2 in Et_2O afforded the adduct **2** (R_f 0 15) which could be separated from **3** (R_f 0 7) by TLC (Et_2O–petrol, 3 1)

10β-*Hydroxycichopumilide* (**1**) Colourless crystalline compound, mp 137°, which could not be separated from **3**, MS *m/z* (rel int) 248 141 $[M]^+$ (11) ($C_{15}H_{20}O_3$) Pyrazoline **2** Colourless crystals, mp 165° (Et_2O), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1780 (γ-lactone), 1455, 1380, 1295, 1160, 1145, 990, MS *m/z* (rel int) 290 163 $[M]^+$ (12) ($C_{16}H_{22}N_2O_3$), 262 $[M-N_2]^+$ (50), 247 $[262-Me]^+$ (26), 246 $[M-CO_2]^+$ (30), 244 $[262-H_2O]^+$ (48), 229 $[244-Me]^+$ (38), 218 $[244-CO]^+$ (84), 205 (89), 177 (100)

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{+157 \quad +168 \quad +198 \quad +445} \ (CHCl_3,\ c\ 0\,32)$$

10β-*Hydroxy*-11β,13-*dihydrocichopumilide* (**3**) Colourless crystals, mp 176° (Et_2O), IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3595 (OH), 1770 (γ-lactone), 1460, 1380, 1180, 1160, 1145, 1035, 990, MS *m/z* (rel int) 250 157 $[M]^+$ (39) ($C_{15}H_{22}O_3$), 235 $[M-Me]^+$ (10), 232 $[M-H_2O]^+$ (24), 217 $[232-Me]^+$ (13), 206 $[M-CO_2]^+$ (100), 191 $[206-Me]^+$ (22)

$$[\alpha]_{24°}^{\lambda} = \frac{489 \quad 578 \quad 546 \quad 436\ nm}{+38 \quad +48 \quad +53 \quad +94} \ (CHCl_3,\ c\ 0\,1)$$

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