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SESQUITERPENE LACTONES FROM *SONCHUS MACROCARPUS*

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Key Word Index—*Sonchus macrocarpus*; Compositae; sesquiterpene lactones; eudesmanolides; guaianolides.

Abstract—Eight sesquiterpene lactones were isolated from the roots of *Sonchus macrocarpus*. The eudesmanolides 15-hydroxy-4β,15-dihydroreynosin and 15-hydroxy-4β,15,11β,13-tetrahydroreynosin were isolated for the first time.

INTRODUCTION

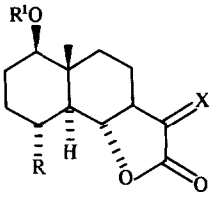
Species belonging to the genus *Sonchus* are known to contain sesquiterpene lactones mainly of the eudesmanolide type [1–3], in addition to the guaianolide jacquinelin [4]. Recently we have isolated from the aerial parts of *Sonchus macrocarpus* Boulos et Jeffrey two new eudesmanolides [5], sonchucarpolide (**1**) and its 11β,13-dihydro derivative (**2**). This paper examines the sesquiterpene fractions of the root extract.

RESULTS AND DISCUSSION

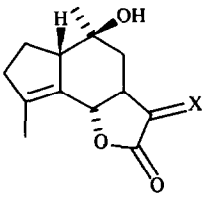
The extract of the roots of *Sonchus macrocarpus* afforded eight sesquiterpene lactones in addition to methyl-1β,6α,15-trihydroxy-4β,15-dihydrocostate (**11**). The isolated lactones include the eudesmanolides, sonchucarpolide (**1**) and its 11β,13-dihydro derivative (**2**) [5], reynosin (**7**) [6] and its 11β,13-dihydro derivative (**8**) [7]. The guaianolides 10β-hydroxycichopumilode (**9**) and its 11β,13-dihydroderivative (**10**) [8] were isolated for the first time from the genus *Sonchus*. Furthermore, two new eudesmanolides (**3** and **4**) were isolated.

The known lactones were identified by comparing the 400 MHz ^{1}H NMR and mass spectra with those of authentic materials. The structure of **3** followed from the molecular formula and from the ^{1}H NMR spectrum (Table 1) which showed that in addition to the methylene lactone moiety, a secondary and a primary hydroxy group were present. Accordingly, acetylation afforded the diacetate **5**. Spin decoupling with both **3** and **5** led to the proposed stereochemistry. Especially the couplings of H-5 required an equatorial orientation of the substituent at C-4 and the couplings of H-1 indicated a β-hydroxy group. The presence of a 6α,12-lactone followed from the couplings of H-6. All data of **4** and **6** indicated that these compounds are the corresponding 11,13-dihydro derivatives of **3** and **5** respectively. The α-orientation of the 11-methyl group was deduced from the relatively large coupling constant $J_{7,11}$. The structure of **4** was further established by correlation with **1** which by reduction with sodium borohydride was transformed to a diol identical with **4**.

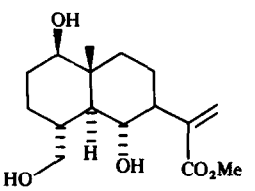
The ^{1}H NMR spectrum of **11** (Table 1), molecular formula $C_{16}H_{26}O_5$, was in part close to that of **3**. However, the signals of H-13 are now singlets. Together with the presence of the methoxy signal therefore a formal



1 R = CHO, R^1 = H, X = CH_2
2 R = CHO, R^1 = H, X = Me, H
3 R = CH_2OH, R^1 = H, X = CH_2
4 R = CH_2OH, R^1 = H, X = Me, H
5 R = CH_2OAc, R^1 = Ac, X = CH_2
6 R = CH_2OAc, R^1 = Ac, X = Me, H
7 R = Me, R^1 = H, X = CH_2
8 R = Me, R^1 = H, X = Me, H



X
9 CH_2
10 Me, H



11

Table 1. ^{1}H NMR spectra data of **3–6** and **11** (400 MHz, $CDCl_3$, TMS as internal standard)

	3	4	5	6	11
H-1	3.35 *dd*	3.35 *dd*	4.64 *dd*	4.61 *dd*	3.29 *dd*
H-4	1.80 *m*	1.79 *m*	1.97 *m*	1.97 *m*	1.60 *m*
H-5	1.5 *m*	1.44 *dd*		1.46 *dd*	1.08 *dd*
H-6	3.93 *dd*	3.94 *dd*	3.87 *dd*	3.89 *dd*	3.80 *dd*
H-7	2.52 *ddddd*	1.70 *m*	2.49 *ddddd*	1.50 *m*	2.49 *ddd*
H-9α	1.50 *m*	1.49 *ddd*			1.50 *m*
H-9β	2.10 *ddd*	2.07 *ddd*			1.96 *ddd*
H-11	—	2.28 *dq*	—	2.22 *dq*	—
H-13	6.10 *d*	1.21 *d*	6.07 *d*	1.18 *d*	6.30 *s*
H-13′	5.44 *d*		5.39 *d*		5.74 *s*
H-14	0.92 *s*	0.94 *s*	1.08 *s*	1.01 *s*	0.91 *s*
H-15	3.78 *dd*	3.77 *dd*	4.52 *dd*	4.52 *dd*	3.70 *dd*
H-15′	3.55 *dd*	3.57 *dd*	4.01 *dd*	3.93 *dd*	3.46 *dd*
OAc	—	—	2.06 s	2.05 s	—
			2.04 *s*	2.03 *s*	

J (Hz): Compounds **3** and **5**: 1, 2 = 12; 1, 2′ = 5; 4, 5 = 5, 6 = 6, 7 = 10; 4, 15 = 3.5; 4, 15′ = 8; 15, 15′ = 11.5; 7, 8 = 11; 7, 8′ = 7, 13 = 7, 13′ = 3; compounds **4** and **6**: 7, 11 = 12; 11, 13 = 7; compound **11**: 4, 5′ = 10; 4, 15 = 2; 4, 15′ = 5; 5, 6 = 6, 7 = 10; 7, 8 = 5; 7, 8′ = 13; 8, 9β = 8′, 9β = 3.5; 9α, 9β = 13; 15, 15′ = 11.

methynolysis product of **3** was most likely. The occurrence of 11,13-dihydro derivatives [5,9] of more widespread lactones in members of the tribe Lactuceae may be of chemotaxonomic relevance. However, our knowledge on the chemistry of this tribe is still very limited [9,10].

EXPERIMENTAL

Five kg of fresh roots (collected from Damanhor region near Alexandria in April 1982. Voucher specimen has been deposited in the herbarium of the Department of Pharmacognosy, Faculty of Pharmacy. Alexandria, Egypt) were extracted with Et_2O–petrol (2:1) and the resulting extract was separated by CC (silica gel) starting with petrol by adding increasing amounts of Et_2O and finally with Et_2O–MeOH (30:1). TLC (SiO_2 PF 254, Et_2O–petrol, 3:1, zones vizualized by UV light) of the less polar fractions gave 20 mg 10β-hydroxycichopumilode [2] and 10 mg of its 11β,13-dihydro derivative [2]. TLC of the next fraction (Et_2O, two developments) gave 15 mg reynosin (**7**) and 10 mg **1** and **2** (*ca* 3:2, increasing polarity). TLC of the most polar fractions (Et_2O–MeOH, 30:1) afforded a mixture of 6 mg **3**, **4** and **11** (*ca* 3:2:1), 10 mg dihydro reynosin (**8**). HPLC (RP 8, MeOH–H_2O, 11:9) of the mixture of **3**, **4** and **11** gave enriched fractions of each, but complete separation could not be achieved. Only **4** could be obtained crystalline while **3** and **11** were oils.

Sonchucarpolide (**1**) *and* 11β,13-*dihydrosonchucarpolide* (**2**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 2740, 1730 (CHO); MS *m/z* (rel. int.): 266.151 and 264.136 $[M]^+$ (2) ($C_{15}H_{22}O_4$ and $C_{15}H_{20}O_4$), 149 (59), 69 (88), 55 (100).

15-*Hydroxy*-4β,15-*dihydroreynosin* (**3**). Colourless oil, not free from **4**; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 266.153 $[M]^+$ (6) (calc. for $C_{15}H_{22}O_4$; 266.152). Acetylation (Ac_2O, 1 hr, 70°) gave **5**, still containing **6**, MS *m/z* (rel. int.): 290.152 $[M-HOAc]^+$ (10) (calc. for $C_{17}H_{22}O_4$; 290.152), 230 $[290-HOAc]^+$ (19), 55 (100).

15-*Hydroxy*-4β,15,11β,13-*tetrahydroreynosin* (**4**). Colourless crystals, not free from **3**, mp 185–187°; MS *m/z* (rel. int.): 268.167 $[M]^+$ (22) (calc. for $C_{15}H_{24}O_4$; 268.168). Acetylation afforded the diacetate **6**, still containing **5** (TLC, silica gel, Et_2O–petrol, 9:1); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1745, 1240 (OAc); MS *m/z* (rel. int.): 292.167 $[M-HOAc]^+$ (44) (calc. for $C_{17}H_{24}O_4$; 292.167), 264 $[292-CO]^+$ (41), 159 (62), 147 (65), 81 (79), 55 (100). Reaction of **6** with excess of diazomethane in Et_2O gave after TLC (Et_2O) **6**, free from **5**; ^{1}H NMR: see Table 1.

Preparation of **4**. To 2 mg **1** in ml MeOH 10 mg $NaBH_4$ were added. After 5 min dil H_2SO_4 was added. TLC (Et_2O) afforded 1 mg **4** which was homogeneous by TLC and ^{1}H NMR.

Reynosin (**7**). Colourless crystals mp 144°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH), 1752 (γ-lactone), 895 (exo methylene); MS *m/z* (rel. int.): 248 $[M]^+$ (10.5) ($C_{15}H_{20}O_3$) and 230 $[M-H_2O]^+$ (100).

11β,13-*Dihydroreynosin* (**8**). Colourless crystals mp 129°; MS *m/z* (rel. int.): 250.156 $[M]^+$ (5) ($C_{15}H_{22}O_3$) and 232 $[M-H_2O]^+$ (100).

10β-*Hydroxy-cichopumilode* (**9**). Mp 137°; MS *m/z* (rel. int.): 248.141 $[M]^+$ (11) ($C_{15}H_{20}O_3$).

10β-*Hydroxy*-11β,13-*dihydrocichopumilode* (**10**). Colourless crystals, mp 176°; 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).

Methyl-1β,6α,15-*trihydroxy*-4β,15-*dihydrocostate* (**11**). Colourless oil not free from **3**; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 298 $[M]^+$ (0.5), 280.167 $[M-H_2O]^+$ (22) (calc. for $C_{16}H_{24}O_4$; 280.168), 248 $[280-MeOH]^+$ (21), 218 $[248-CH_2O]^+$ (28), 57 (100).

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