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SESQUITERPENE LACTONE GLYCOSIDES FROM *CREPIS PYRENAICA*

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Key Word Index—*Crepis pyrenaica*; Asteraceae; Lactuceae; sesquiterpene lactone glycosides; guaianolides.

Abstract—From the roots of *Crepis pyrenaica*, seven guaianolide glycosides were isolated, including 8-epiisolippidiol-3-β-D-glucopyranoside and its 11,13-dehydro-derivative. Their structures were determined by spectroscopic methods.

INTRODUCTION

Plants of the tribe Lactuceae (Asteraceae) produce a variety of sesquiterpene lactone glycosides. Stimulated by our interest in the compounds of the genus *Crepis* we have investigated the hitherto unstudied *Crepis pyrenaica* (L.) W. Greuter and isolated seven closely related guaianolide glycosides, two of which (**3** and **4**) are characterized for the first time.

RESULTS AND DISCUSSION

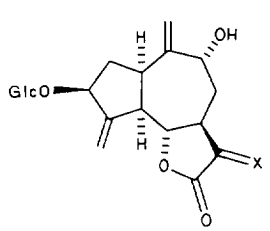
The ethanol extract of the fresh roots was chromatographed on a silica gel column to separate fractions eluting with $CHCl_3$–MeOH (9:1) which contained complex mixtures of compounds **1**–**7**. The fractions were subjected to HPLC giving the known 8-epidesacylcynaropicrin glucoside (**5**) [1] as the main constituent, its two esters, **6** and **7** [1], along with macrocliniside A (**1**) [2] and ixerin F (**2**) [3]. The glucosides, identified by direct comparison with authentic samples, were reported previously from *Crepis* species [1, 4–7].

In addition to **1**, **2** and **5**, more polar fractions of the original chromatography afforded two hydrogenated derivatives of **5**, namely 8-epiisolippidiol-3-β-D-glucopyranoside (**4**) and its 11,13-dehydro derivative (**3**).

The structures of **3** and **4** were deduced on spectral evidence, by comparison with each other, and with **5**. The ^1H NMR data of the cyclopentane ring protons of **3** were very similar to those of **4**, and allowed assignment of the same substituents and relative configurations for this part of the two compounds. A structural feature common to the seven-membered ring of **3** and **5** was also deduced. For comparison we have added the ^1H NMR for **5** to Table 1.

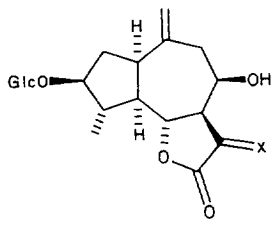
The above findings were supported by the electron impact-mass spectra of **3** and **4**, which showed diagnostically important fragment ion peaks at *m/z* 264, 246, 228 and at *m/z* 266, 248, 230, respectively, corresponding to the aglycone moieties and successive loss of two molecules of water. Moreover, the mass spectra of **3** and **4** were both characterized by the presence of peaks at *m/z* 166 and at *m/z* 168, respectively, due to C-1/C-10 and C-5/C-6 fissions of the aglycone skeletons.

The β-linkage of the glucose moiety in both **3** and **4** was deduced from the large coupling constant of the anomeric proton signal. The stereochemistry at all the



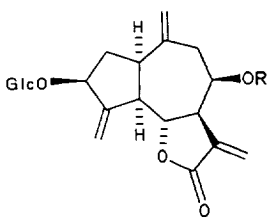
1 X = CH_2

2 X = H, α Me



3 X = CH_2

4 X = H, α Me

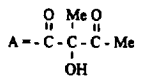


5 R = H

6 R = A

7 R = B

Glc = β - D - glucopyranoside



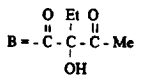


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Table 1. ^{1}H NMR data of compounds **3**, **4** and **5** (300 MHz, pyridine-d_5, TMS as int. standard, δ-values)

H	3	4	5
1	2.76 *br q* (9)	2.72 *br q* (9)	2.89 *br q* (9)
2	2.47 *dt* (13.2, 6.7)	2.46 *dt* (13.6, 6.7)	2.43 *dt* (14, 8)
2′	2.18 *dt* (13.2, 8.9)	2.13 *dt* (13.6, 9.1)	2.23 *dt* (14, 7)
3	3.89 *ddd* (8.9, 8.5, 6.7)	3.88 *ddd* (9.1, 8.5, 6.7)	4.84 *br t* (8)
4	2.27 *ddt* (9, 8.5, 6.6)	2.25 *ddt* (9, 8.5, 6.6)	
5	1.82 *br q* (9)	1.78 *br q* (9)	2.80 *br t* (9)
6	4.82 *dd* (10, 9)	4.53 *t* (10)	5.10 *t* (10)
7	2.97 *dddd* (10, 3.4, 3, 2.5)	2.02 *ddd* (11.6, 10, 2,5)	3.10 *dddd* (10, 3.5, 3.1, 2.5)
9	2.73 *dd* (13.2, 4.8)	2.76 *dd* (13.2, 4.9)	2.63 *dd* (13.3, 5.2)
9′	2.38 *dd* (13.2, 3.7)	2.29 *dd* (13.2, 3.3)	2.55 *dd* (13.3, 5.6)
11		3.18 *dt* (11.6, 7)	
13	6.47 *d* (3.4)	1.25 *d* (7)	6.50 *d* (3.5)
13′	5.67 *d* (3)		5.70 *d* (3.1)
14	5.16 *br s*	5.11 *br s*	5.19 *d* (1.6)
14′	5.07 *br s*	5.05 *br s*	5.00 *d* (1.6)
15	1.40 *d* (6.6)	1.40 *d* (6.6)	5.91 *d* (1.5)
15′			5.60 *d* (1.5)
Glucose protons			
1	4.92 *d* (7.8)	4.92 *d* (7.7)	5.05 *d* (7.8)
2	4.07 *br t* (8)	4.05 *br t* (8)	4.07 *br t* (8)
3	4.1–4.4 *m**	4.1–4.4 *m**	4.1–4.4 *m**
4			
5	3.97 *m*	3.98 *m*	3.97 *m*
6	4.41 *dd* (12, 5.4)	4.41 *dd* (12, 5.4)	4.40 *dd* (12, 5.4)
6′	4.57 *br d* (12)	4.56 *dd* (12, 2.2)	4.56 *br d* (12)

J values (parentheses) in Hz.
*Overlapped with H-8 signal.

chiral centres of the aglycones followed from the relevant values of the coupling constants, which were in good agreement with those of 8-epiisolippidiol [8] or 8-epidesacylcynaropicrin [9], whose structures have been confirmed by X-ray diffraction analyses [10, 11]. A glucoside of 8-epiisolippidiol was detected in *Crepis* species on the basis of hydrolytic studies [1, 5], but its spectral data were not recorded and the position of attachment of the sugar moiety was not determined.

EXPERIMENTAL

General procedure. Merck silica gel was used for CC (Art. 7754) and TLC (Art. 5553). Semiprep. HPLC was performed on a Delta-Pak C 18 cartridge column (particle size 15 μm, 25 × 100 mm) coupled to a UV photodiode array detector. The column was eluted with MeOH–H_2O (7:13) mixt. at flow rate 3 ml min^{-1}. Sesquiterpene lactone glycosides isolated previously in this laboratory [1, 4, 7] were used as authentic samples for comparing their physical and spectral data with those of the known compounds.

Plant material. Roots of *C. pyrenaica* were collected in August 1993 from plants growing in the Garden of Medicinal Plants of the Institute of Pharmacology, Polish Academy of Sciences, Kraków, where a voucher specimen was deposited.

Extraction and isolation of compounds. Fr. roots (326 g) were exhaustively extracted with EtOH at room temp. and the residue (39 g), obtained by removal of the solvent under vacuum, was chromatographed on a silica gel column, packed in hexane, using hexane–EtOAc (9:1 → 1:1) followed by $CHCl_3$–MeOH (19:1 → 4:1) gradient solvent systems. Elution of the column with the hexane–EtOAc gradient gave mainly mixts of widespread triterpenes and sterols which were not further sepd. Elution with $CHCl_3$–MeOH (9:1) afforded complex mixts of sesquiterpene lactone glycosides which were grouped according to their homogeneity. The relevant frs were purified by prep. TLC ($CHCl_3$–MeOH, 17:3, one or three developments) and further sepd by HPLC to give **1** (8 mg), **2** (9 mg), **3** (7 mg), **4** (6 mg), **5** (25 mg), **6** (5 mg), and **7** (5 mg), .

Compound **3**. Solid. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1760 (γ-lactone); EIMS (15 eV) *m/z* (rel. int. %): 426 $[M]^+$ (0.7), 264 $[M - 162]^+$ (0.9), 246 $[264 - 18]^+$ (1.0), 229 $[264 - 17 - 18]^+$ (1.0), 228 $[264 - 2 \times 18]^+$ (0.7), 166 $[C_9H_{10}O_3]^+$ (6.0), 98 (1.6), 96 (1.0), 61 (100), 43 (41.5); ^{1}H NMR: see Table 1.

Compound **4**. Solid. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1740 (γ-lactone); EIMS (15 eV) *m/z* (rel. int. %): 428 $[M]^+$ (0.5), 266 $[M - 162]^+$ (2.5), 249 $[266 - 17]^+$ (17.5), 248 $[266 - 18]^+$ (4.5), 231 $[266 - 17 - 18]^+$ (10.5), 230 $[266 - 2 \times 18]^+$ (2.6), 168 $[C_9H_{12}O_3]^+$ (25.9), 98 (6.2), 61 (88.5), 43 (100), ^{1}H NMR: see Table 1.

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