GROSULFEIMIN AND NEW RELATED GUAIANOLIDES FROM *CYNARA SCOLYMUS* L.

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Abstract: Three new guaianolides 11-H-13-methylsulfonylgrosheimin ***5*** (Grosulfeimin), 8-deoxy-11,13-dihydroxygrosheimin ***7*** and 8-deoxy-11-hydroxy-13-chlorogrosheimin ***8*** have been isolated from the leaves of *Cynara scolymus* L. Besides, 8-epigrosheimin ***9*** has been isolated for the first time from this source.

The structures were determined by spectroscopical methods and by chemical correlations.

Key words: *Cynara scolymus* L., sesquiterpene lactones, sulfonyl guaianolides, guaianolides.

INTRODUCTION

Stimulated by the growing interest in biologically active sesquiterpene lactones from Compositae, particularly in their cytotoxic activities [1-4], some investigations have been carried out on *Cynara scolymus* L. leading to the isolation and chemical elucidation of the following guaianolides: cynaropicrin ***1***, [3,5], 3-dehydrocynaropicrin ***2***, grosheimin ***3*** [3,6-10], cynarolyde [11] and cynarotriol ***4*** [12]. Moreover, some analytical procedures for the quantitative determination of these lactones in artichoke have been pointed out [13].

RESULTS AND DISCUSSION

In the course of our studies on the Italian flora [14-17] we have now isolated from the leaves of *Cynara scolymus* L. three new guaianolides, identified as 11-H-13-methylsulfonylgrosheimin ***5*** in the methanol extract, 8-deoxy-11-hydroxy-13-chlorogrosheimin ***8*** and 8-deoxy-11,13-dihydroxygrosheimin ***7*** in the chloroform

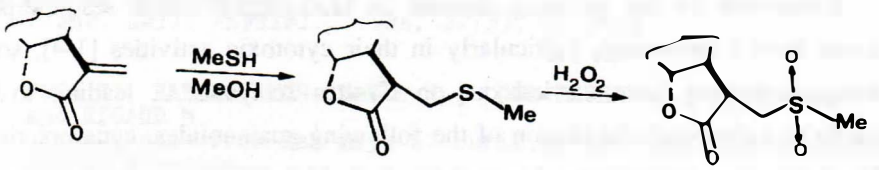
extract. The known 8-epigrosheimin ***9***, previously obtained from *Crepis virens* [17], was also isolated and characterized.

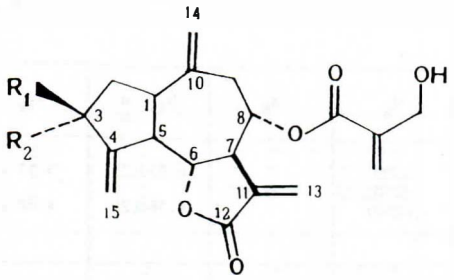
Compound ***5***, namely Grosulfeimin, is to be considered an unusual natural product, being known in the literature the sole case of the isolation of the methylsulfonylguaianolide Sulferalin from *Helenium autumnale* [18,19].

The structures of ***5***, ***7*** and ***8*** were determined on the basis of their elemental analysis, IR, MS, ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50.32 MHz) spectra. These were confirmed, for grosulfeimin ***5***, by chemical correlation with grosheimin ***3*** *via* 11-H-3-methylsulfidegrosheimin ***6*** (see scheme) and, for the compounds ***7*** and ***8***, by spectroscopical data of their parent compounds obtained by acetylation (***7a***, ***8a***) and by acetonylation (***7b***) (see tables 1 and 2).

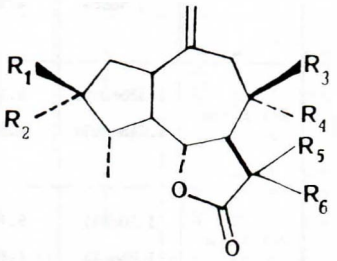
Identification of ***9*** was achieved by direct comparison of an authentical sample of 8-epigrosheimin from *Crepis virens* [17].

Repeated chromatographic separations of the $CHCl_3$-soluble extract (29.8 g) and of the MeOH-soluble extract (10.8 g) from the leaves of *Cynara scolymus* L. were carried out on silica gel columns by means of normal and/or flash-chromatography techniques using the eluents: $CHCl_3$ ---> $CHCl_3$/MeOH=70/30, and monitoring by TLC (silica gel plates), eluents: $CHCl_3$/MeOH=95/5 ---> 70/30, phosphomolibdic reagent and H_2SO_4 10% as spray detectors.





Compd.	R_1	R_2
1	OH	H
2	O	



Compd.	R_1	R_2	R_3	R_4	R_5	R_6
3	O		H	OH	$=CH_2$	
4	OH	H	H	H	OH	CH_2OH
4a	OAc	H	H	H	OAc	CH_2OAc
5	O		H	OH	H	$CH_2SO_2CH_3$
6	O		H	OH	H	CH_2SCH_3
7	O		H	H	OH	CH_2OH
7a	O		H	H	OAc	CH_2OAc
7b	O		H	H	$O\text{-}C(CH_3)_2\text{-}O$	
8	O		H	H	OH	CH_2Cl
8a	O		H	H	OAc	CH_2Cl
9	O		OH	H	$=CH_2$	

Table 1

Comp.	H_1	H_6	H_8	H_{13} a b	H_{14}	H_{15}	others*
3	3.19 d(8) d(8) d(2)	4.00 d(10) d(10)	3.92 m	6.31d(2) 6.38d(2)	5.11 s 4.87 s	1.17 d(8)	========
5	3.15 m	4.28 d(10) d(10)	4.10 m	3.89 d(4) 3.94 d(4)	5.04 s 4.86 s	1.12 d(7)	3.20 s ▲
6	3.20 m	4.30 d(10) d(10)	4.03 m	3.45 d(3) d(9) 3.69 d(3) d(9)	5.10 s 4.75 s	1.20 d(7)	2.15 s •
7	3.15 m	4.35 d(10) d(10)	2.1-2.2 m	3.58brs 3.58brs	4.98 s 4.70 s	1.18 d(7)	========
7a	3.25 m	4.15 d(10) d(10)	2.2-2.3 m	4.38brd(5) 4.44brd(5)	5.12 s 4.88 s	1.20 d(7)	2.05 s ϕ 2.12 s ϕ
7b	3.30 m	4.17 d(10) d(10)	2.1-2.2 m	3.30d(4) 3.26d(4)	5.10 s 4.87 s	1.22 d(8)	1.36 s ⊕ 1.59 s ⊕
8	3.25 m	4.20 d(10) d(10)	2.1-2.2 m	3.64brs 3.64brs	5.06 s 4.69 s	1.23 d(7)	==========
8a	3.30 m	4.18 d(9) d(9)	2.3-2.4 m	3.89brd(5) 3.78brd(5)	5.09 s 4.80 s	1.21 d(8)	2.08 s ϕ
9	3.25 m	4.57 d(10) d(10)	4.08 m	6.40 s 5.67 s	5.08 s 4.85 s	1.27 d(6)	==========

[1]H-NMR of compounds 5, 6, 7, 7a, 7b, 8, 8a, 9 at 200 MHz, comp. 3 at 400 MHz. Solvent $CDCl_3$. In parentheses coupling constants in Hz.

* -OAc(ϕ), $>(CH_3)_2$(⊕), $-SO_2CH_3$(▲), $-SCH_3$(▪).

Table 2

Comp.	3[18]	4a[12]	5	6	7	7a	8	8a	9
C-15	15.0 q	18.0 q	15.2 q	14.7 q	14.8 q	14.2 q	14.1 q	15.9 q	16.2 q
CH_3-S	======	======	======	19.7 q	======	======	======	======	======
$\underline{CH_3}$-CO	======	20.5 q 20.9 q 21.1 q	======	======	======	20.7 q 21.1 q	======	20.6 q	======
C-2,9	43.5 t 49.2 t	35.3 t 36.8 t	43.5 t 48.5 t	42.9 t 47.7 t	41.9 t 46.8 t	41.7 t 47.0 t	41.3 t 46.6 t	41.0 t 45.9 t	43.5 t 48.8 t
C-1,4,5,7	40.4 d 47.2 d 49.8 d 51.1 d	42.6 d 43.6 d 48.6 d 50.8 d	40.2 d 43.7 d 48.5 d 50.6 d	41.0 d 43.9 d 47.2 d 49.7 d	35.1 d 41.5 d 42.2 d 50.5 d	34.8 d 40.9 d 42.3 d 51.1 d	34.9 d 42.8 d 44.0 d 51.4 d	35.1 d 43.0 d 45.3 d 50.9 d	40.3 d 47.4 d 48.9 d 51.3 d
CH_3-SO_2	======	======	40.6 q	======	======	======	======	======	======
C-8	73.2 d	27.5 t	72.6 d	73.0 d	33.3 t	31.6 t	30.5 t	32.7 t	71.6 d

C-6	83.3 d	79.9 d	83.5 d	84.0 d	82.8 d	82.5 d	82.3 d	83.0 d	83.6 d
C-14	114.4 t	113.1 t	115.1 t	114.7 t	116.5 t	115.3 t	112.9 t	114.2 t	116.0 t
C-13	124.5 t	62.7 t	48.0 t	26.3 t	61.9 t	65.4 t	52.7 t	54.8 t	122.5 t
C-11	138.7 s	79.7 s	49.1 d	48.5 d	78.1 s	81.4 s	76.8 s	82.3 s	144.0 s
C-10	145.4 s	148.7 s	145.6 s	146.2 s	147.0 s	148.1 s	148.3 s	149.2 s	136.4 s
CH_3-CO	======	169.1 s 164.4 s 170.9 s	======	======	======	165.7 s 169.9 s	======	168.3 s	======
C-12	170.3 s	171.7 s	170.4 s	171.3 s	173.2 s	175.0 s	175.8 s	176.6 s	170.8 s
C-3	218.7 s	84.4 d	218.9 s	218.4 s	215.8 s	216.4 s	218.3 s	218.0 s	220.5 s

^{13}C-NMR (50.32) of compounds **4a**[12], **5**, **6**, **7**, **7a**, **8**, **8a**, **9** in $CDCl_3$, comp. **3**[18] in Pyr D_5.

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