Phytochemistry, Vol. 25, No. 7, pp. 1659–1662, 1986.
Printed in Great Britain.

0031-9422/86 $3.00 + 0.00
Pergamon Journals Ltd.

SESQUITERPENE LACTONES AND EUDESMANE DERIVATIVES FROM *ONOPORDON CARMANICUM*

A. RUSTAIYAN, B. AHMADI, J. JAKUPOVIC* and F. BOHLMANN*

Department of Chemistry, Shahid Beheshty University, Teheran, Iran; *Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany

(*Received* 27 *September* 1985)

Key Word Index—*Onopordon carmanicum*; Compositae; sesquiterpene lactones; germacranolide; eudesmanolide; elemane and eudesmane derivatives.

Abstract—The aerial parts of *Onopordon carmanicum* afforded in addition to onopordopicrin and two related esters the epoxide of onopordopicrin, a new elemane derivative, two eudesmanolides and two eudesmane derivatives which most likely are the precursors of the latter lactones. The structures were elucidated by highfield NMR spectroscopy.

INTRODUCTION

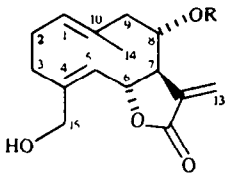
The genus *Onopordon* (Compositae, tribe Cynareae) is placed together with the large genera *Cousinia*, *Saussurea* and *Jurinea* in the subtribe Carduinae. Taxonomically this genus is closely related to *Cousinia*, while the position of *Jurinea* and *Saussurea* is uncertain [1]. So far from the genus *Onopordon* in addition to widespread compounds several C_{17}-acetylenes [2] and the germacranolide onopordopicrin [3–6] as well as closely related lactones [5, 6] have been reported. Similar 15-hydroxyl germacranolides with an 8α-acyloxy group have been isolated from *Jurinea* species. This type of sesquiterpene lactone seems to be characteristic for a group of genera in the Cynareae. They have been reported from *Centaurea*, *Arctium* and *Cnicus* species. However, lactones with the same substitution pattern with an additional hydroxyl group at C-14 are reported from *Dicoma* species (tribe Mutisieae) [7]. This type is present also in some *Jurinea* species [8]. From *Cousinia* species so far no lactones are reported. We have studied now a further *Onoportdon* species *O. carmanicum* (Bornm.) Bornm.

RESULTS AND DISCUSSION

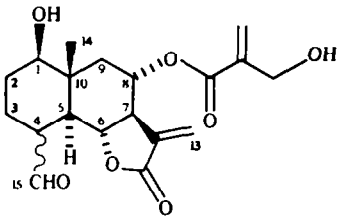
The polar fractions of the extract of the aerial parts of *O. carmanicum* gave as the main constituents onopordopicrin (3) [3] as well as a complex mixture of sesquiterpene lactones which could be separated by HPLC. In addition to the isobutyrate **1** [6] and the corresponding methacrylate **2** [6] the 4α,5β-epoxide of onopordopicrin (**9**), the epimeric aldehydes **4** and **5**, the epimeric methyl esters of the corresponding precursors **6** and **7** as well as the elemane **8** were isolated.

The structure of **5** could be deduced from the ^{1}H NMR spectrum (Table 1) where the signals could be assigned by spin decoupling. The four-fold doublet at δ2.81 was that of H-7 as irradiation at this point caused the lowfield doublets at δ6.14 and 5.57 (H-13) to collapse. Furthermore, the triplet at δ4.01 and the triplet of doublets at 5.31 were changed to a doublet and a double doublet respectively. Accordingly, these signals were those of H-6 and H-8. Further decouplings allowed assignment of the signals and H-9 and H-5. As the latter was coupled with a four-fold doublet (*dddd*) at δ2.45 (H-4) the sequence could be completed by the protons at C-1–C-4 and C-15. The signal of H-15 was a lowfield doublet at δ9.68 indicating the presence of an aldehyde group. The double doublet at 3.46 was due to the axial proton under the hydroxyl group at C-1 while the typical signals of a hydroxymethacrylate indicated the nature of the ester residue at C-8. The configurations at C-1 and C-4–C-8 followed from the couplings observed. Lactone **5** is related to the 8-desacyloxy derivative sonchucarpolide [9]. Accordingly, the ^{1}H NMR spectra are similar. The ^{1}H NMR spectrum (Table 1) of the isomeric lactone **4** was in part similar to that of **5**. However, in addition to differences in the chemical shifts the aldehyde signal was a broadened singlet at δ9.91. Spin decoupling indicated that the whole sequence was identical with that of **5**. However, the H-4 signal now was a broadened triplet at δ2.76 indicating that there could only be a very small coupling between H-4 and H-15. As the couplings $J_{4,5}$ and $J_{3,4}$ required an equatorial proton at C-4 the aldehyde group at this carbon was axial. The same situation is present in a eudesmane derivative isolated from a *Verbesina* species [10] where also no coupling was observed between H-4 and H-15. Thus compounds **4** and **5** were epimeric at C-4.

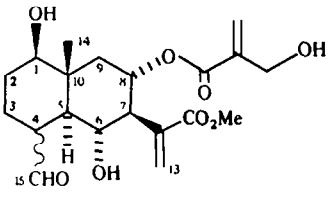
The spectra of compounds **6** and **7** were in part close to those of **4** and **5**. The difference between these compounds was again the stereochemistry at C-4 which was indicated by a singlet at δ9.93 for compound **7** and a doublet at 9.33 for isomer **6**. The methoxy singlets at δ3.73 and 3.77, respectively, as well as slightly broadened singlets for exomethylene protons indicated the presence of methyl esters of hydroxy acids formed by hydrolysis of the lactones **4** and **5**. Accordingly, triplets at δ3.93 and 4.41 respectively were due to the protons under the 6-hydroxyl group. In agreement with the proposed stereochemistry at



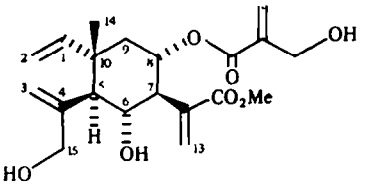
1 R = iBu
2 R = Meacr
3 R = 4OH·Meacr



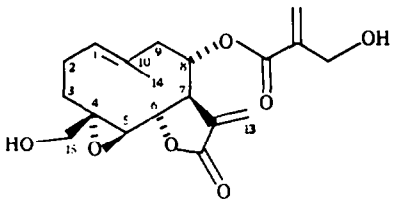
4 4αH
5 4βH



6 4αH
7 4βH



8



9

C-4 in the spectra of compounds **4** and **6** deshielding effect of the aldehyde group at the H-6 was observed. Compound **7** has been named carmanin.

The ^{1}H NMR spectrum of **8** (Table 1) was in part similar to those of compounds **6** and **7**. However, several typical lowfield signals clearly indicated the presence of an elemane derivative (5.68 *dd*, 4.95 *br d*, 4.91 *br d*, 5.37 *br s* and 5.01 *br s*). From a pair of doublets at δ4.03 and 3.90 the nature of the substituent at C-4 could be deduced. Compound **8**, which we have named elemacarmanin, is formed by a Cope reaction of the unknown methyl ester of the hydroxy acid corresponding to onopordopicrin.

The structure of **9** clearly followed from the ^{1}H NMR spectrum (Table 1) as all signals could be assigned by spin decoupling. As one of the protons at C-9 showed couplings with H-1 and H-2 the sequence could be determined directly. The chemical shift of H-5 (δ2.83 *d*) required the presence of an epoxide, the nature of the oxygen functions followed from the typical signals of a hydroxy methacrylate and a primary hydroxyl group which only could be due to H-15. Thus compound **4** was the 4α,5β-epoxide of onopordopicrin. Inspection of Dreiding models together with the observed coupling indicated that the preferred conformation of **9** was that was both C-14 and C-15 above the plane.

The chemistry of this *Onopordon* species again shows that onopordopicrin is characteristic for this genus. However, as compounds **4–9** were minor components investigations of further species are necessary to see whether these compounds are more widespread in this genus. The absence of gauianolides, which are widespread in the tribe Cynareae, may be of chemotaxonomic interest. Preliminary results on some *Cousinia* species have shown that guaianolides like aguerin A and B are present. This would not support the proposed close relationship of the latter genus with *Onopordon*. The chemistry of *Jurinea* species is more close to that of *Onopordon* though in *Jurinea* mainly 14,15-dihydroxygermacranolides have been isolated, but also a few guaianolides, which are also widespread in *Saussurea* species. Many more species of the whole subtribe have to be studied to obtain a more detailed picture.

Table 1. ^{1}H NMR spectral data of compounds 4–9 (400 MHz, $CDCl_3$, TMS as internal standard)

H	4	5	6	7	8	9
1	3.33 *dd*	3.46 *dd*	3.27 *dd*	3.30 *dd*	5.68 *dd*	5.34 *br dd*
2	1.71 *br d*	1.8–1.5 *m*	1.68 *m*	*	4.95 *br d*	2.43 *br dd*
2′	1.58 *dddd*		1.61 *m*		4.91 *br d*	2.23 *m*
3	2.41 *br dd*		2.34 *m*		5.37 *br s(cis)*	2.33 *m*
3′	1.45 *dddd*		1.41 *m*		5.01 *br s*	1.27 *ddd*
4	2.76 *br t*	2.45 *dddd*	2.91 *br t*	2.50 *m*	—	—
5	2.01 *dd*	1.91 *dd*	1.69 *dd*	1.88 *dd*	2.10 *d*	2.83 *d*
6	4.51 *t*	4.01 *t*	4.41 *t*	3.93 *t*	4.18 *t*	4.66 *dd*
7	2.85 *dddd*	2.81 *dddd*	2.67 *t*	2.56 *t*	2.70 *t*	3.25 *dddd*
8	5.36 *ddd*	5.31 *ddd*	4.31 *ddd*	5.34 *ddd*	5.41 *ddd*	4.64 *ddd*
9	2.47 *dd*	2.50 *dd*	2.33 *dd*	2.48 *dd*	1.90 *dd*	2.55 *dd*
9′	1.30 *br dd*	1.37 *dd*	1.23 *dd*	1.30 *dd*	1.60 *t*	2.49 *br d*
13	6.15 *d*	6.14 *d*	6.32 *br s*	6.27 *br s*	6.28 *br s*	6.32 *d*
13′	5.58 *d*	5.57 *d*	5.74 *br s*	5.68 *br s*	5.72 *br s*	5.72 *d*
14	0.90 *s*	1.06 *s*	0.90 *s*	1.00 *s*	1.16 *s*	1.82 *br s*
15	9.91 *br s*	9.68 *d*	9.93 *s*	9.33 *d*	4.03 *d* 3.90 *d*	3.85 *d* 3.67 *d*
OCOR	6.25 *br s*	6.29 *br s*	6.12 *br s*	6.12 *br s*	6.15 *br s*	6.25 *br s*
	5.91 *br s*	5.94 *br s*	5.77 *br s*	5.76 *br s*	5.78 *br s*	5.92 *br s*
	4.30 *br s*	4.36 *br s*	4.20 *br s*	4.18 *br s*	4.21 *br s*	4.28 *br s*
OMe	—	—	3.77 *s*	3.73 *s*	3.75 *s*	—

*Obscured multiplets.

J (Hz): compounds 4–7: 1,2 = 4; 1,2′ = 11; 2,2′ = 13; 2′,3 = 4; 2′,3′ = 13; 3,3′ = 13; 5,6 = 6,7 = 7,8 = 11; 8,9 = 4; 8,9′ = 12; 9,9′ = 13; compounds 4 and 6: 3′,4 = 4,5 = 5.5; compounds 4, 5, 8 and 9: 7,13 ~ 3; compounds 5 and 7: 3,4 ~ 3; 3′,4 = 4,5 = 11; 4,15 = 4; compound 8: 1,2c = 11, 1,2t = 17; 5,6 = 6,7 = 10; 7,8 = 8,9′ = 11; 8,9 = 4; 9,9′ = 15, 15′ = 13; compound 9: 1,2 = 4; 1,2′ = 12; 2,2′ = 13; 2,3′ = 5; 2′,3′ = 12; 3,3′ = 13; 5,6 = 9; 6,7 ~ 8; 7,8 ~ 6; 8,9 = 10; 8,9′ ~ 2; 9,9′ = 12.

EXPERIMENTAL

The air dried aerial parts (300 g, voucher deposited in the Herbarium of the Dept. of Botany, University of Iran) were extracted at room temp. with MeOH–Et_2O–petrol (1:1:1). The extract obtained was separated by CC (silica gel). The polar fractions (Et_2O to Et_2O–MeOH, 1:10) were further separated first by TLC (silica gel, PF 254) and further by HPLC (RP 8, *ca* 100 bar, flow rate *ca* 3 ml/min). The CC fraction obtained with Et_2O gave *ca* 15 mg 1 and 15 mg 2, the CC fractions with Et_2O–MeOH (50:1) and 1.2 g 3 and the fraction with Et_2O–MeOH (30:1) yielded a mixture of lactones which were separated first by medium pressure chromatography (silica gel, ϕ 60 μ, 3 bar, Et_2O to Et_2O–MeOH, 10:1). Fractions 15–22 gave further f33 and HPLC (MeOH–H_2O, 3:2) of fractions 34–39 afforded 2 mg 9 (R_t 8.4 min). HPLC of fractions 40–46 (MeOH–H_2O, 3:2) gave 30 mg 4 (R_t 6.0 min) and 25 mg 8 (R_t 8.0 min). HPLC of fractions 47–50 (MeOH–H_2O, 3:2) afforded 20 mg 6 (R_t 4.4 min), 50 mg 5 (R_t 5.3 min) and 10 mg 7 (R_t 5.6 min). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic materials.

8α-[4-Hydroxymethacryloyloxy]-4-epi-sonchucarpolide (4). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 2750 (CHO), 1770 (γ-lactone), 1720 (C=CCO_2R, CHO); CIMS *m/z* (rel. int.): 365 (8) $[M+1]^+$ ($C_{19}H_{24}O_7+1$), 347 (19) $[365-H_2O]^+$, 263 (51) $[365-RCO_2H]^+$, 101 (100); $[\alpha]_D = +124°$ ($CHCl_3$; *c* 0.15).

8α-[4-Hydroxymethacryloyloxy]-sonchucarpolide (5). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 2750 (CHO), 1770 (γ-lactone), 1725 (C=CCO_2R, CHO); CIMS: *m/z* (rel. int.): 365 (2) $[M+1]^+$ ($C_{19}H_{24}O_7+1$), 263 (48) $[365-RCO_2H]^+$; $[\alpha]_D = +151°$ ($CHCl_3$; *c* 0.12).

4-epi-Carmanin (6). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1715 (C=CCO_2R, CHO); CIMS *m/z* (rel. int.): 397 (3) $[M+1]^+$ ($C_{20}H_{28}O_8+1$), 379 (12) $[397-H_2O]^+$, 295 (100) $[397-RCO_2H]^+$; $[\alpha]_D = +56°$ ($CHCl_3$; *c* 0.1).

Carmanin (7). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1715 (C=CCO_2R, CHO); CIMS *m/z* (rel. int.): 397 (9) $[M+1]^+$ ($C_{20}H_{28}O_8+1$), 379 (32) $[397-H_2O]^+$, 295 (100) $[397-RCO_2H]^+$, 277 (72) $[295-H_2O]^+$.

Elemacarmanin (8). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3605 (OH), 1715, 1630 (C=CCO_2R); MS *m/z* (rel. int.): 380 (0.1) $[M]^+$ ($C_{20}H_{28}O_7$), 278.152 (3) $[M-RCO_2H]^+$ ($C_{16}H_{22}O_4$), 260 (4) $[278-H_2O]^+$, 85 (100) $[RCO]^+$; $[\alpha]_D = +29°$ ($CHCl_3$; *c* 0.26).

Onopordopicrin-4α,5β-epoxide (9). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3605 (OH), 1770 (γ-lactone), 1720 (C=CCO_2R); CIMS *m/z* (rel. int.): 365 (4) $[M+1]^+$ ($C_{19}H_{24}O_7+1$), 293 (7) $[365-RCO_2H]^+$, 263 (22) $[293-CH_2O]^+$, 245 (20) $[263-H_2O]^+$; $[\alpha]_D = +22°$ ($CHCl_3$; *c* 0.1).

Acknowledgement—A.R. thanks the Ministry of Culture and Higher Education of Iran for financial support.

REFERENCES

1. Dittrich, M. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds) p. 1010. Academic Press, London.

2. Bohlmann, F., Burhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*, p. 448. Academic Press, London.
3. Drozdz, B., Holub, M., Samek, Z., Herout, V. and Sorm, F. (1968) *Coll. Czech. Chem. Commun.* **33**, 1730.
4. Khafagy, S. M., Metwally, A. M. and Omar, A. A. (1977) *Pharmazie* **32**, 123.
5. Rustaiyan, A., Nazarians, L. and Bohlmann, F. (1979) *Phytochemistry* **18**, 879.
6. Rustaiyan, A., Nazarians, L. and Bohlmann, F. (1979) *Phytochemistry* **18**, 883.
7. Bohlmann, F., Singh, P. and Jakupovic, J. (1982) *Phytochemistry* **21**, 2029.
8. Suchy, M. (1969) *Coll. Czech. Chem. Commun.* **34**, 229.
9. Mahmoud, Z., El-Masry, S., Amer, M., Zieache, J. and Bohlmann, F. (1983) *Phytochemistry* **22**, 1390.
10. Bohlmann, F. and Lonitz, M. (1978) *Chem. Ber.* **111**, 254.