

SESQUITERPENE LACTONES FROM *PERITYLE EMORYI*

C. ZDERO, F. BOHLMANN and H. M. NIEMEYER*

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.; *Facultad de Ciencias, Universidad de Chile, Santiago, Chile

(Received 5 June 1989)

Key Word Index—*Perityle emoryi*; Compositae; sesquiterpene lactones; germacranolides; guaianolides; thymol derivatives.

Abstract—The extract of the aerial parts of *Perityle emoryi* gave, in addition to seven known sesquiterpene lactones, six new germacranolides and a guaianolide as well as a further thymol derivative together with several known ones and two labdanes. The structures were elucidated by high field $^1\text{H NMR}$ spectroscopy. The chemotaxonomic aspects are discussed briefly.

INTRODUCTION

The genus *Perityle* with about 50 species is distributed over southwestern U.S.A. and northern Mexico, only one species, *P. emoryi* Torr., is also present in South America. Traditionally, this genus was placed in the artificial tribe Helenieae. Most of the genera of the latter tribe have now been placed in the Heliantheae, although for *Perityle* its inclusion in Senecioneae is also discussed [1]. In a recent revision of the Heliantheae, it was placed in the subtribe Peritylinae in the tribe Heliantheae [2]. Only one species has been studied chemically [3]. The results already indicated that this genus is better placed in the Heliantheae. We have now studied a second species, *P. emoryi* Torr., from which only flavones found in several other *Perityle* species were isolated [4]. The results are discussed in this paper.

RESULTS AND DISCUSSION

The extract of the aerial parts of *P. emoryi* afforded caryophyllene, the flavone penduletin, the known germacranolides **1** [5], **2** [6], **3** [7], **6** [7], **7** [8] and **9** [9] as well as **4**, **5**, **8** and the epimeric esters **10** and **11** which could not be separated. Furthermore, the guaianolides **12** [3] and **13**, the *ent*-labdanes **20** and **21** [10], the thymol derivatives **14** [11], **15** [12], **17** [13], **18** [14] and **19** [15] as well as the unknown triol **16** were isolated. The structure of the latter followed from its $^1\text{H NMR}$ spectrum (see Experimental). As expected, the signals of H-9 and H-10 were somewhat complex as the molecule is not completely symmetrical. The mass spectrometric fragmentation of **16** also supports the structure. In addition to elimination of water, loss of a methoxy group (m/z 151) was observed. Again elimination of water leads to the base peak (m/z 133).

The structure of the lactone **4** also followed from its $^1\text{H NMR}$ spectrum (Table 1). While the signals of the lactone part were nearly identical with those of **2** and **3**, the nature of the ester side chain could be deduced from the typical signals of an α -[1,2-dihydroxy-ethyl]-acrylate present in cnicin [16].

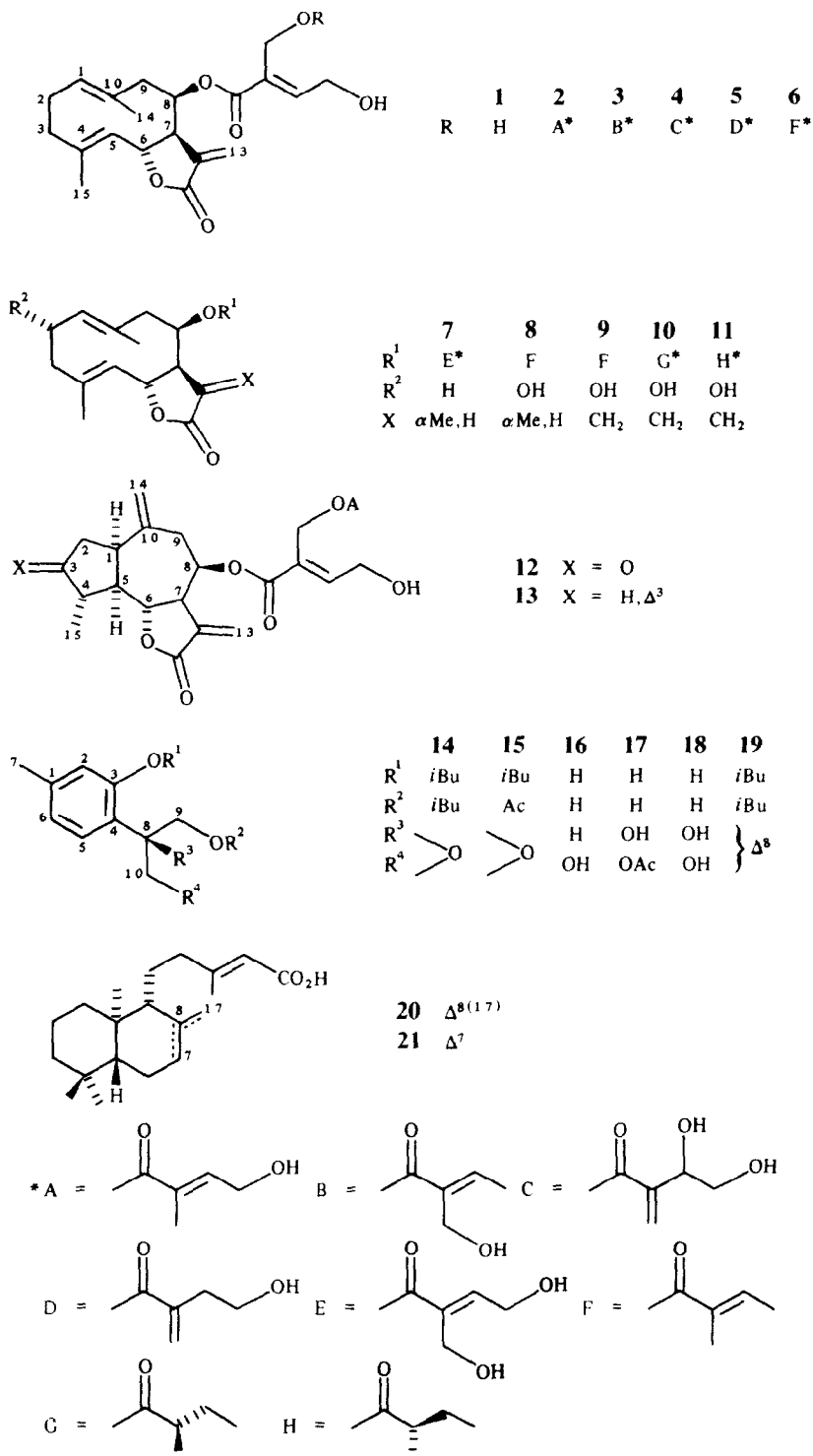
The $^1\text{H NMR}$ spectrum of **5** (Table 1) was very similar to those of **2–4**. However, the changed ester side chain clearly followed from the signals at δ 3.74, 3.70, 2.54 and 2.48 which were not first order. Spin decoupling indicated that the two lower field signals were allylically coupled with the exomethylene protons which showed broadened signals at δ 6.16 and 5.71 and vicinal couplings with the protons responsible for the signals at δ 2.54 and 2.48. Thus an α -[2-hydroxyethyl]-acrylate was present which seems to be very rare.

That **8** was a 11 β ,13-dihydrogermacrolide could be deduced from the $^1\text{H NMR}$ spectrum (Table 1) which was in part similar to that of **9**. However, a double quartet at δ 2.38 and a methyl doublet at δ 1.28 resembled the corresponding signals of **7**. The three-fold doublet at δ 4.75 required the presence of a 2 α -hydroxy group as followed from spin decoupling. Thus lactone **8** was the 11 β ,13-dihydro derivative of mollisorin A [9].

The $^1\text{H NMR}$ spectrum of the unseparable mixture of **10** and **11** (Table 1) was similar to that of **9**. However, the characteristic signals of a tiglate moiety were replaced by a double set of 2-methylbutyryloxy groups. Saturation of the signal at δ 2.34 collapsed the two doublets at δ 1.12 and 1.10 to singlets while saturation of the multiplets at δ 1.64 and 1.45 collapsed the triplets at δ 0.87 and 0.83 to doublets. Thus **10** and **11** were also dihydro derivatives of **9**, in which the tiglate double bond was hydrogenated from both sides affording the α -epimeric 2-methyl butyrates.

The structure of **13** followed from its $^1\text{H NMR}$ spectrum (Table 1) which was similar to that of the corresponding 24-desoxy derivative from a *Helogyne* species [17]. As expected, the vinylic methyl signal in the side chain was replaced by a pair of broadened doublets at δ 4.32 and 4.27.

The sesquiterpene lactone chemistry of *P. emoryi* is similar to that of *P. vaseyi* though the variations are more pronounced in the former species. Furthermore, no thymol derivatives were reported from *P. vaseyi*. However, the relevance of these compounds is limited as they are widespread in several tribes of the family. *Perityle* is



better placed in the Heliantheae as germacranolides are not reported from Senecioneae.

EXPERIMENTAL

The air-dried plant material (170 g) (collected in January 1989 in Northern Chile, voucher AH3, deposited in the Herbarium of the University of Chile, Santiago) was extracted at room temp.

with MeOH-Et₂O-petrol (1:1:1). The extract was defatted by treatment with MeOH and the soluble part was separated first by CC and TLC as reported previously [18]. Fr. 1 (Et₂O-petrol, 1:9) gave 15 mg caryophyllene, fr. 2 (Et₂O-petrol, 1:3) gave by TLC (Et₂O-petrol, 1:3) 30 mg neryl isobutyrate, 30 mg **19** and 20 mg **14**. Fr. 3 (Et₂O) gave by TLC (Et₂O-petrol, 1:1) 80 mg **14**, 80 mg **20**, 8 mg **21** and 20 mg **15**. Fr. 4 (Et₂O-MeOH, 9:1) afforded by HPLC (RP 8, flow rate 3 ml/min, ca 100 bar,

Table 1. $^1\text{H NMR}$ spectral data of **4**, **5**, **8**, **10**, **11** and **13** (CDCl_3 , 400 MHz, δ -values)

H	4	5	8	10	11	13
1	4.87 <i>br dd</i>	4.90 <i>br dd</i>	5.00 <i>br t</i>	4.99 <i>br t</i>		3.14 <i>dt</i>
2	+	+	4.75 <i>dt</i>	4.76 <i>dt</i>		{ 2.55 <i>m</i> 2.42 <i>br d</i>
3	+	+	{ 2.71 <i>dd</i> 2.11 <i>t</i>	{ 2.74 <i>dd</i> 2.12 <i>t</i>		5.58 <i>tq</i>
5	4.72 <i>br d</i>	4.77 <i>br d</i>	4.91 <i>br d</i>	4.98 <i>br d</i>		2.88 <i>br t</i>
6	5.07 <i>dd</i>	5.13 <i>dd</i>	5.03 <i>t</i>	5.06 <i>t</i>		4.51 <i>dd</i>
7	2.92 <i>br dt</i>	2.95 <i>br dt</i>	2.03 <i>ddd</i>	2.94 <i>br dt</i>		3.18 <i>dddd</i>
8	5.78 <i>br d</i>	5.85 <i>br d</i>	5.45 <i>br d</i>	5.77 <i>br d</i>		5.75 <i>dt</i>
9	2.82 <i>br dd</i>	2.85 <i>br dd</i>	2.85 <i>br dd</i>	2.78 <i>br dd</i>		2.59 <i>dd</i>
9'	2.33 <i>br d</i>	2.37 <i>br d</i>	2.23 <i>dd</i>	2.34 <i>br d</i>		2.50 <i>dd</i>
11	—	—	2.38 <i>dq</i>	—		—
13	6.19 <i>d</i>	6.28 <i>d</i>	{ 1.28 <i>d</i>	6.32 <i>d</i>	6.31 <i>d</i>	6.29 <i>d</i>
13'	5.56 <i>d</i>	5.60 <i>d</i>		6.60 <i>d</i>	5.59 <i>d</i>	5.62 <i>d</i>
14	1.43 <i>br s</i>	1.46 <i>br s</i>	1.53 <i>br s</i>	1.53 <i>br s</i>		5.02 <i>br s</i> 4.87 <i>br s</i>
15	1.77 <i>br s</i>	1.78 <i>br s</i>	1.78 <i>d</i>	1.80 <i>br s</i>		1.86 <i>br s</i>
2'	—	—	—	2.34 <i>dd q</i>		—
3'	7.13 <i>t</i>	7.10 <i>t</i>	6.89 <i>qq</i>	1.64 <i>m</i> 1.45 <i>m</i>		7.12 <i>t</i>
4'	{ 4.49 <i>dd</i> 4.43 <i>dd</i>	{ 4.54 <i>dd</i> 4.48 <i>dd</i>	1.84 <i>dq</i>	1.12 <i>d</i>	1.10 <i>d</i>	{ 4.55 <i>dd</i> 4.46 <i>d</i>
5'	{ 5.05 <i>d</i> 4.78 <i>d</i>	{ 5.00 <i>d</i> 4.94 <i>d</i>	1.86 <i>dq</i>	0.87 <i>t</i>	0.83 <i>t</i>	{ 5.01 <i>d</i> 4.79 <i>d</i>
3''	4.57 <i>dd</i>	{ 2.54* 2.48*	—	—		6.63 <i>tq</i>
4''	3.71 <i>dd</i> 3.42 <i>dd</i>	3.74* 3.70*	—	—		4.32 <i>br dd</i> 4.27 <i>br dd</i>
5''	6.21 <i>br s</i> 5.98 <i>br s</i>	6.16 <i>br s</i> 5.71 <i>br d</i>	—	—		—

† Overlapped multiplets.

* Not first order.

J [Hz]: compounds **4**, **5** and **8**: 5, 6 = 9.5; 6, 7 = 8.5; 7, 13 = 3.5; 7, 13' = 3; 8, 9 = 4; 9, 9' = 14; (compound **8**: 1, 2 = 2, 3 = 10; 2, 2' = 11; 2, 3' = 6) OOCOR 3', 4' = 6; 4₁, 4₂ = 15 (compound **4**: 3'', 4'' = 3; 3'', 4'' = 6; 4'', 4'' = 11; compound **5**: 3', 4' = 6; 4₁, 4₂ ~ 14; compound **8**: 3', 4' = 7; 3', 5' = 4'; 5' = 1.5); compounds **10** and **11**: 1, 2 = 2, 3 = 10; 2, 2' = 11; 2, 3 = 6; 5, 6 = 6, 7 = 9; 7, 13 = 3.5; 7, 13' = 3; 8, 9 = 4; OOCOR: 2', 3₁' = 2'; 3₂' = 2'; 5' = 3'; 4' = 7; compound **13**: 1, 2 = 1, 5 = 8; 1, 2' = 4; 2, 3 = 3, 15 ~ 2; 5, 6 = 9.5; 6, 7 = 8.5; 7, 8 = 7, 13 ~ 3; 8, 9 = 8, 9' = 4; 9, 9' = 13; OOCOR 3', 4' = 6; 5₁, 5₂ = 12; 3'', 4'' = 6; 3'', 5'' = 1.5.

MeOH-H₂O, 3:1) 5 mg penduletin (*R_f*, 3.6 min), 2 mg **6**, (*R_f*, 5.8 min) and four mixtures (4/1 *R_f*, 0.5 min, 4/2 *R_f*, 1.8 min, 4/3 *R_f*, 2.6 min and 4/4 *R_f*, 3.0 min). TLC of 4/1 (CHCl_3 -C₆H₆-Et₂O-MeOH, 6:6:6:1 = T1) gave 3 mg **17**, 7 mg **16** (*R_f* 0.37), 30 mg **12** and 20 mg **18**. TLC (T1) of 4/2 gave 10 mg **1** and 75 mg **4** (*R_f* 0.38). TLC (CHCl_3 -C₆H₆-Et₂O-MeOH, 10:10:10:1 = T2) of 4/3 afforded 3 mg **9**, 2 mg **2** and a mixture which gave by HPLC (MeOH-H₂O, 3:2) 1 mg **7** (*R_f*, 10.0 min), 3 mg **5** (*R_f*, 13.8 min) and 2 mg **3** (*R_f*, 14.6 min). TLC of 4/4 (T2) gave 3 mg **13** (*R_f* 0.40) and a mixture which afforded by HPLC (MeOH-H₂O, 3:2) 1 mg **8** (*R_f*, 12.3 min) and 1 mg **10/11** (*R_f*, 14.2 min).

8 β -[2-(1,2-dihydroxyethyl)acryloyloxy]-Germacra-1(10)E.4E., 11(13)-trien-12.6 α -olide (**4**). Gum, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1760 (γ -lactone), 1720 (C=CCO₂R); MS *m/z* (rel. int): 445.186 [M-CH₂O]⁺ (0.3) (calc. for C₂₄H₂₉O₈ 445.186), 230 [M-RCO₂H]⁺ (8), 227 [RCO]⁺ (7), 215 [230-Me]⁺ (7), 84 (100); [α]_D²⁵ +22 (CHCl₃; c 6.5).

8 β -[2-(2'-hydroxyethyl)-acryloyloxy]-Germacra-1(10)E.4E.11

(13)-trien-12.6 α -olide (**5**). Gum, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1765 (γ -lactone), 1725 (C=CCO₂R); MS *m/z* (rel. int): 230.131 [M-RCO₂H]⁺ (91) (calc. for C₁₅H₁₈O₂ 230.131), 215 (30), 99 [RCO]⁺ (83), 71 [99-CO]⁺ (45), 69 [99-CH₂O]⁺ (99), 68 [99-CH₂OH]⁺ (100).

2 α -Hydroxy-8 β -tigloyloxy-11 β ,13H-germacra-1(10)E.4E-dien-12.6 α -olide (**8**). Gum, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1770 (γ -lactone), 1710 (C=CCO₂R); MS *m/z* (rel. int): 348.194 [M]⁺ (0.3) (calc. for C₂₀H₂₈O₅ 348.194), 248 [M-RCO₂H]⁺, 233 [248-Me]⁺ (5), 83 [RCO]⁺ (100), 55 [83-CO]⁺ (68).

Epimeric 2 α -hydroxy-8 β -[2-methylbutyryloxy]-germacra-1(10)E.4E.11(13)-trien-12.6 α -olides (**10** and **11**). Gum, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1760 (γ -lactone), 1730 (CO₂R); MS *m/z* (rel. int): 348.194 [M]⁺ (calc. for C₂₀H₂₈O₅ 348.194), 246 [M-RCO₂H]⁺ (5), 231 [246-Me]⁺ (2), 85 [RCO]⁺ (44), 57 [85-CO]⁺ (100).

Ligustrin-[5-O-(4'-hydroxytigloyl)-4-hydroxy]-sarracinate (**13**). Gum, IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm⁻¹: 3600 (OH), 1760 (γ -lactone), 1720 (C=CCO₂H); MS *m/z* (rel. int): 458.194 [M]⁺ (3) (calc. for

$C_{25}H_{30}O_8$ 458.194), 440 $[M-H_2O]^+$ (2), 422 $[440-H_2O]^+$ (12), 228 $[M-RCO_2H]^+$ (42), 99 $[RCO]^+$ (80), 69 $[99-CH_2O]^+$ (100).

9,10-Dihydroxythymol (16). Oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1} : 3600, 3400 (OH); MS m/z (rel. int): 182.094 $[M]^+$ (31) (calc. for $C_{10}H_{14}O_3$ 182.094), 164 $[M-H_2O]^+$ (17), 151 $[M-CH_2OH]^+$ (48), 133 $[151-H_2O]^+$ (100), 105 $[133-CO]^+$ (74); 1H NMR ($CDCl_3$): δ 6.70 (*br s*, H-2), 6.91 (*d*, H-5, $J=8$ Hz), 6.66 (*br d*, H-6, $J=8$ Hz), 2.23 (*s*, H-7), 3.11 (*tt*, H-8, $J=7, 7$ Hz), 4.02 (A_2, A'_2 , X system, H-9 and H-10).

Acknowledgement—We thank the Volkswagen-Stiftung for financial support. We are indebted to Mrs C. Fernandez, Mrs A. Hoffmann and Mr M. Qúezada for help in plant collection.

REFERENCES

- Powell, A. M. and Turner, B. L. (1974) *Am. J. Botany* **61**, 87.
- Robinson, H. (1981) *Smithsonian Contrib. Botany* **51**, 80.
- Pfeil, R. M., Gage, D. A., Lee, E. F., Miski, M., Mabry, T. J. and Powell, A. M. (1987) *Phytochemistry* **26**, 195.
- Crins, W. J., Bohm, B. B., Powell, A. M. and Guppy, M. (1988) *Biochem. Syst. Ecol.* **16**, 273.
- Dolejs, L. and Herout, V. (1962) *Coll. Czech. Chem. Commun.* **27**, 2654.
- Miski, M., Gage, D. A. and Mabry, T. J. (1987) *Phytochemistry* **26**, 3277.
- Bohlmann, F., Zdero, C. and Turner, B. L. (1985) *Phytochemistry* **24**, 1263.
- Dominguez, X. A., Sanchez, H., Slim, J., Jakupovic, J., Chau-Thi, T. V. and Bohlmann, F. (1988) *Phytochemistry* **27**, 613.
- Ohno, N. and Mabry, T. J. (1979) *Phytochemistry* **18**, 1003.
- Bevan, C. W. L., Ekong, D. E. V. and Okugun, J. I. (1968) *J. Chem. Soc. C*, 1067.
- Bohlmann, F., Niedballa, U. and Schulz, J. (1969) *Chem. Ber.* **102**, 864.
- Bohlmann, F. and Zdero, C. (1979) *Chem. Ber.* **109**, 791.
- Bohlmann, F., Trinks, C., Jakupovic, J., King, R. M. and Robinson, H. (1984) *Planta Med.* **50**, 284.
- Delle Monache, G., Delle Monache, F., Becerra, J., Silva, M. and Menichini, F. (1984) *Phytochemistry* **23**, 1947.
- Bohlmann, F., Jakupovic, J. and Lonitz, M. (1977) *Chem. Ber.* **15**, 1309.
- Samek, Z., Holub, M., Herout, V. and Sorm, F. (1969) *Tetrahedron Letters* 2931.
- Zdero, C., Bohlmann, F. and Dillon, M. O. (1988) *Phytochemistry* **27**, 616.
- Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.