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SEVEN SESQUITERPENE LACTONES FROM *FERREYANTHUS* SPECIES

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Key Word Index—*Ferreyanthus fruticosus*; *F. rugosus*; Compositae; sesquiterpene lactones; germacranolides; linalol derivatives.

Abstract—The investigation of two *Ferreyanthus* species afforded seven germacranolides which have not been isolated previously. Two derivatives of linalol were also present. The structures were elucidated by spectroscopic methods. Chemotaxonomic relationships are briefly discussed.

INTRODUCTION

Ferreyanthus is a genus with seven species restricted to Peru and Ecuador. It is placed in the tribe Liabeae, previously part of the Senecioneae [1]. So far only one species has been studied chemically [2]. In addition to traces of polyacetylenes, a guaianolide was isolated, indicating that a separation of this group from the Senecioneae was supported by the chemistry. We now have studied two further species and the results are reported in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Ferreyanthus fruticosus* (Muschler) H. Robinson afforded, in addition to widespread triterpenes, the germacranolide **1** and an inseparable mixture of traces of hydroperoxides derived from it. The structure of **1** followed from the ^{1}H NMR spectrum (Table 1) which showed that a mixture of conformers was present. While at room temperature the signals were broadened, at $-20°$ spin decoupling allowed the assignment of most signals of three different conformers. The stereochemistry could be deduced from the coupling and chemical shifts, especially when compared to those of similar lactones like laurenobiolide, where a mixture of conformers was also observed [3]. However, because of overlapping, not all signals could be assigned to a single conformer. The concentrations of the three conformers were in the ratio of 4:3:2 and therefore not very different from that found in the case of laurenobiolide where an additional 6α-acetoxy group is present. If the couplings of H-8 of the three conformers were compared with those reported for laurenobiolide [3] the main conformer most likely was that with H-15 above and H-14 below the plane. As, however, the signals of H-1 and H-5 were in part overlapped, clear assignments by NOE were not possible.

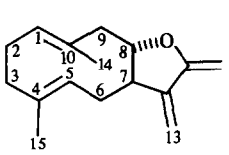
The aerial parts of *Ferreyanthus rugosus* (Ferreya) R. et B. also contain triterpenes, the linalol derivatives, **9** and **10**, the angelate **11** [4] and the germacranolides **2**–**7** as well as the eudesmanolide **8** [5]. The tiglate **4** and the corresponding isobutyrate **5** could not be separated. The structures clearly followed, however, from the ^{1}H NMR spectrum (Table 2) though again at room temperature the signals were broadened. At 60° most signals could be assigned by spin decoupling. The relative position of the oxygen functions also could be deduced from the ^{1}H NMR spectrum. As in similar cases a clear difference in the chemical shifts of the signals of the proton at the ester group bearing carbon was visible. As these protons were coupled with the H-9 protons, the ester groups were at C-8 and consequently 6,12-lactones were present. The stereochemistry followed from the couplings observed which agreed with those of similar compounds like artemorin [6]. The structures of **6** and **7**, which also could not be separated, clearly could be deduced by triphenylphosphine reduction of **4** and **5** respectively. The chemical shifts of **6** and **7** (Table 2) were slightly different from those of **4** and **5**.

Table 1. ^{1}H NMR spectral data of **1** (400 MHz, $CDCl_3$, $-20°$, TMS as internal standard)

H-1	4.98, 4.93, 4.95 *m*
H-5	5.11, 4.69, 5.09 *br d*
H-7	2.75, 2.75, 2.78 *m*
H-8	4.34, 4.15, 4.59 *ddd*
H-9	2.67, 2.41, 2.98 *br dd*
H-13	6.345, 6.30, 6.34 *d*
H-13'*	5.69, 5.64, 5.70 *d*
H-14†	1.57, 1.52, 1.59 *br s*
H-15†	1.59, 1.64, 1.67 *br s*

*Relative intensity 4:3:2.
†May be in part interchangeable.
J (Hz): 5, 6 ~ 10; 7, 8 = 4.5, 8 and 6; 7, 13 = 3.5; 7, 13' = 3; 8, 9α = 11, 10.5 and 11; 8, 9β = 2.5, 1 and 3.5; 9α, 9β = 14.

The presence of hydroperoxides were indicated by the typical low field signals around 8 ppm. Again a clear spectrum only was obtained at an elevated temperature. The same was true for that of **2** and **3**, which again could not be separated (Table 2). Spin decoupling allowed the assignment of most signals. The chemical shift of H-14 required a conformation, where the conjugated keto group was in an *s-trans*-conformation. The couplings



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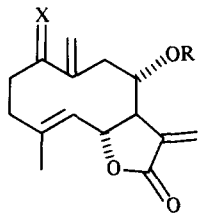
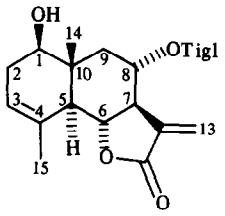


	2	3	4	5	6	7
X	=O		βOH, H		βOOH, H	
R	Tigl	iBu	Tigl	iBu	Tigl	iBu



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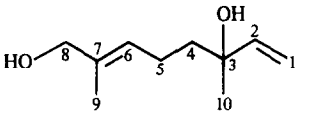

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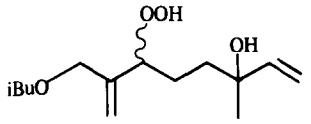

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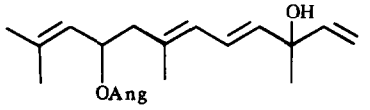

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observed agreed with the presence of a conformation with both C-14 and C-15 above the plane if models were inspected. Also the down field shift of the H-9α signal supported this assumption. Again the different ester groups caused a clear shift difference of the H-8 signals, while most of the other signals were influenced only very slightly (Table 2).

The structure of **9** followed from the ^{1}H NMR spectrum (see Experimental) which was similar to that of linalol. The presence of a 8-hydroxy group could be deduced from the broadened singlet at δ4.45 which replaced one of the methyl signals in the spectrum of linalol. Comparison of the chemical shifts with those of terpenoids with the same end group further indicated that the hydroxyl group could not be placed at C-9. In the mass spectrum no molecular ion could be observed even by chemical ionization. Though again no molecular ion could be observed in the mass spectrum the structure of **10** also followed from the ^{1}H NMR spectrum (see Experimental). All ^{1}H NMR signals could be assigned by spin decoupling. The relative position of the oxygen functions followed from the chemical shifts of H-6 and H-8. Obviously **10** was formed by esterification of **9** followed by attack of oxygen. The relative configuration at C-3 and C-6 could not be determined.

The constituents of the *Ferreyanthus* species investigated clearly showed that there is no relationship to the chemistry of other members of the tribe Senecioneae. So far only a few other species places in the Liabeae have been studied. Germacranolides, in part also oxygenated in similar ways, have been reported from *Liabum* [7] and *Munnozia* [8]. However, also guaianolides were isolated [2]. Many more species will have to be studied to get a clear picture of the chemotaxonomy of this tribe.

EXPERIMENTAL

The air dried aerial plant material was collected in January 1983 in Peru und extracted with MeOH–Et_2O–petrol, 1:1:1, at room temperature and worked-up in the usual fashion [9].

The polar CC-fractions (Et_2O and Et_2O–petrol, 1:1) of the extract 230 g of *Ferreyanthus fruticosus* (voucher RMK 9302) afforded by TLC (SiO_2 PF 254, detection by UV light and $KMnO_4$ spraying, Et_2O–C_6H_6–CH_2Cl_2, 1:6:6) 6.8 mg **1** (R_f 0.62).

The polar CC-fractions of 230 g of *F. rugosus* (voucher RMK 9220) were as follows: 1 (Et_2O–petrol, 1:3), 2 (Et_2O–petrol, 1:1) and 3 (Et_2O and Et_2O–MeOH, 10:1). TLC of the first fraction (Et_2O–petrol, 1:3) gave 5 mg **20** (R_f 0.52) and TLC of fraction 2 (Et_2O–C_6H_6–CH_2Cl_2, 1:5:5) afforded five zones: Repeated

Table 2. ^{1}H NMR spectral data of 2–7 (400 MHz, $CDCl_3$, TMS as internal standard)

	2*		3*	4†		5†	6‡		7‡
H-1	—		—		4.00 *br d*			4.15 *br d*	
H-2		2.94 *m*			2.01 *m*			2.09 *dddd*	
H-2′		2.72 *m*			1.90 *m*			1.90 *m*	
H-3		2.55 *m*			2.21 *m*			2.24 *m*	
H-3′		2.38 *ddd*							
H-5	5.13 *br d*		5.12 *br d*		5.32 *m*			5.33 *br d*	
H-6	4.60 *t*		4.58 *t*	4.49 *t*		4.47 *t*	4.46 *t*		4.44 *t*
H-7		3.06 *m*			3.41 *m*			3.28 *m*	
H-8	4.97 *br t*		4.85 *br t*	5.32 *m*		5.26 *m*		5.24 *br t*	
H-9	2.83 *dd*		2.78 *dd*		2.55 *br dd*			2.43 *br dd*	
H-9′		2.61 *br d*			2.40 *br d*			2.60 *m*	
H-13	6.20 *dd*		6.26 *dd*	6.19 *d*		6.21 *d*	6.20 *d*		6.22 *d*
H-13′	5.87 *d*		5.89 *d*	5.57 *d*		5.60 *d*	5.62 *d*		5.66 *d*
H-14		5.87 *d*			5.33 *br s*			5.49 *br d*	
H-14′					5.27 *br s*			5.28 *br s*	
H-15	1.80 *d*		1.79 *d*	1.78 *d*		1.77 *d*	1.72 *br s*		1.71 *br s*
OCOR	6.91 *qq*		2.55 *qq*	6.92 *qq*		2.61 *qq*	6.91 *qq*		2.60 *qq*
	1.83 *dq*		1.22 *d*	1.84 *dq*		1.21 *d*	1.84 *dq*		1.21 *d*
	1.88 *dq*		1.20 *d*	1.88 *dq*			1.88 *dq*		1.215 *d*

Signals indicated as *m* were unresolved or overlapped multiplets.
*60°.
†62°.
‡57°.
J (Hz): 5, 6 = 6, 7 = 7, 8 ~ 10; 5, 15 = 1.5; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 ~ 8; 8, 9′ ~ 1.5; 9, 9′ = 17; OAng: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ ~ 1.5; OiBu: 2′, 3′ = 2′, 4′ = 7; compounds **2** and **3**: 2, 3 = 5; 2, 3′ = 6; 3, 3′ = 12; 13, 13′ = 0.5; compounds **4**–**7**: 1, 2 = 2.5; 1, 2′ = 9; 2, 2′ = 13; 2, 3 = 4; 2, 3′ = 2.

TLC (each with Et_2O–petrol, 7:1) gave from the less polar zone 5 mg **11** (R_f 0.85) and 0.7 mg **8** (R_f 0.71), from the next one 2 mg **9** (R_f 0.48), from the third one 4 mg **4** and **5** (*ca* 4:1) (R_f 0.32), from the next one 3 mg **6** and **7** (*ca* 4:1) (R_f 0.28), from the fifth one 3 mg **2** and **3** (*ca* 5:1) (R_f 0.25) and from the last one 1.2 mg **8** (R_f 0.23). TLC of fraction 3 gave no definite compounds.

The pairs of esters (**2**/**3**, **4**/**5** and **6**/**7**) could not be separated by TLC in different solvent mixtures or by HPLC (reversed phase). They showed no additional signals in the 400 MHz ^{1}H NMR spectra.

Desacetoxylaurenobiolide (**1**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (γ-lactone), 1665, 1612, 1415, 1400, 1345, 1332, 1316, 1280, 1005, 960, 860; MS *m/z* (rel. int.): 232 $[M]^+$ (10) ($C_{15}H_{20}O_2$), 217 $[M-Me]^+$ (3), 204 $[M-CO]^+$ (3), 168 (35), 81 (30), 68 (100). CD (MeCN): ε_{260} −0.4.

8α-Tigloyloxy- and 8α-isobutyryloxyanhydroverlotorin (**2** *and* **3**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (γ-lactone), 1730 (COOR), 1710 (C=CCO$_2$R), 1692 (C=CC=O); MS *m/z* (rel. int.): 244.110 $[M-RCO_2H]^+$ (7) ($C_{15}H_{16}O_3$), 226 $[244-H_2O]^+$ (4), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (62); CI (isobutane): 345 $[M+1]^+$ (12), 333 $[M+1]^+$ (4), 245 $[345-RCO_2H]^+$ (100), 227 $[245-H_2O]^+$ (76), 101 $[RCO_2H+1]^+$ (18), 83 $[101-H_2O]^+$ (22). CD (MeCN): ε_{234} +6.0.

8α-Tigloyloxy- and 8α-isobutyryloxyartemorin (**4** *and* **5**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1765 (γ-lactone), 1725 (CO$_2$R), 1710 (C=CCO$_2$R); MS *m/z* (rel. int.): 246.126 $[M-RCO_2H]^+$ (1) ($C_{15}H_{18}O_3$), 228 $[246-H_2O]^+$ (14), 213 $[228-Me]^+$ (8), 83 $[C_4H_7CO]^+$ (88), 71 $[C_3H_7CO]^+$ (37), 55 $[83-CO]^+$ (100); CI (isobutane): 347 $[M+1]^+$ (9), 335 $[M+1]^+$ (2), 247 $[M+1-RCO_2H]^+$ (85), 229 $(247-H_2O]^+$ (100), 101 $[RCO_2H+1]^+$ (20) 83 $[101-H_2O]^+$ (18).

8α-Tigloyloxy- and 8-isobutyryloxy-1β-peroxycostunolide (**6** *and* **7**). Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3515 (OH), 1763 (γ-lactone), 1730 (CO$_2$R), 1705 (C=CCO$_2$R); MS *m/z* (rel. int.) (CI, isobutane): 363 $[M+1]^+$ (12), 351 $[M+1]^+$ (2), 101 $[RCO_2H+1]^+$ (100).

Reaction with triphenylphosphine in $CDCl_3$ at room temperature 20°, afforded a mixture of **4** and **5**, ^{1}H NMR spectrum identical with that of the natural alcohols.

8-Hydroxylinalol (**9**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1605 (C=C), 925 (CH=CH$_2$); MS (CI, isobutane): 153 $[M+1-H_2O]^+$ (33), 135 $[153-H_2O]^+$ (100); ^{1}H NMR ($CDCl_3$): δ5.22 (H-1t, *dd*, *J* = 17.5, 1.5 Hz), 5.07 (H-1c, *dd*, *J* = 11, 1.5 Hz), 5.91 (H-2, *dd*, *J* = 17.5, 11 Hz), 2.0 (H-4 and H-5, *m*), 5.46 (H-6, *br dd*, *J* = 11, 6 Hz), 4.45 (H-8, *br s*), 1.65 (H-9, *br s*), 1.30 (H-10, *s*).

8-Isobutyryloxy-6-peroxi-7(9)-dehydro-6,7-dihydrolinalol (**10**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3520 (OH), 1735 (CO$_2$R), 1610 (C=C); MS *m/z* (rel. int.): 187 $[M-OCOR]^+$ (1), 71 $[C_3H_7CO]^+$ (100); ^{1}H NMR ($CDCl_3$): δ5.21 (H-1t, *dd*, *J* = 17.5, 1 Hz), 5.07 (H-1c, *dd*, *J* = 11, 1 Hz), 5.87 (H-2, *dd*, *J* = 17.5, 11 Hz), 1.7–1.5 (H-4 and H-5, *m*), 4.42 (H-6, *br dd*, *J* = 6.5, 3 Hz), 4.80 (H-8, *br d*, *J* = 13 Hz), 4.49 (H-8′, *br d*, *J* = 13 Hz), 5.27 (H-9, *br s*), 5.24 (H-9′, *br s*), 1.28 (H-10, *s*), 9.24 (*br s*, OOH), 2.61 (H-2′, *qq*, *J* = 7, 7 Hz), 1.20 (H-3′$_1$, *d*, *J* = 7 Hz), 1.19 (H-3′$_2$, *d*, *J* = 7 Hz).

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