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HIGHLY OXYGENATED FUROEREMOPHILANE DERIVATIVES FROM *SENECIO ZOELLNERI*

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Key Word Index—*Senecio zoellneri*; Compositae; sesquiterpene lactones; oxygenated furoeremophilane derivatives; *seco*-furoeremophilanolides.

Abstract—The aerial parts of *Senecio zoellneri* afforded, in addition to known compounds, five oxygenated furoeremophilane derivatives and three *seco*-furoeremophilanolides, all of which are probably formed by oxidation of 3β-hydroxy-6β-acyloxyeuryopsin.

INTRODUCTION

Many species from the large genus *Senecio* have been investigated chemically. The most widespread compounds are furoeremophilanes and their derivatives. We have now studied the chemistry of *S. zoellneri* Martic. et Quez.

RESULTS AND DISCUSSION

The aerial parts of *S. zoellneri* afforded spathulenol, *p*-hydroxyacetophenone, tremetone, cinnamyl angelate, the furoeremophilone **10** and the highly oxygenated derivatives **2**–**9**.

The structure of cinnamyl angelate followed directly from its ^{1}H NMR spectrum. The ^{1}H NMR spectra of **5** and **6** (Table 1) differed only in the signals of the ester residues. Spin decoupling allowed the assignment of all signals. The sequences obtained indicated the presence of eremophilanolides with a 3β-hydroxy, a 6β-acyloxy and a 8α-methoxy group. The configuration at C-8 followed from the chemical shifts of the neighbouring protons which differed from the shifts of similar lactones with opposite configuration at C-8 [1, 2].

The ^{1}H NMR spectrum of **4** differed from that of **5** by the absence of the methoxy singlet. All data agree with the presence of the corresponding 8α-hydroxy derivative. The ^{1}H NMR spectra of **2** and **3** (Table 1) again differed only in the signals of the ester groups. In part the data were close to those of **5** and **6**. However, the signals of H-6, H-9 and H-13 differed markedly. The molecular formula of **2** is $C_{19}H_{26}O_6$ indicating that it is an isomer of **4**. The chemical shifts of H-13 in **2** and **3** required a methyl group on an oxygen-bearing carbon and singlets at δ5.30 and 5.25 agree with the presence of a 7,8,11,12-bis-epoxide. The configuration of the epoxides could not be determined. However, inspection of models and the proposed formation favours the α-orientation. A similar compound derived from a furocadinane has been isolated from a *Baccharis* species [3]. Most likely compounds **2** and **3** are formed via the endoperoxide **1**, the addition product of the corresponding furoeremophilane and singlet oxygen. The bis-epoxides **2** and **3** then could be transformed to the lactones of type **4** as shown in the Scheme.

The structures of the lactones **7** and **8** could be deduced from their ^{1}H NMR spectra (Table 1) which were similar to those of the corresponding 3-desacetoxy derivative of **8** [4]. The splitting of several ^{1}H NMR signals showed that both **7** and **8** are mixtures of C-8 epimers which could not be separated. As the relation was *ca* 1:2, the ^{1}H NMR signals were easily assigned. The couplings of H-3 indicated the proposed configuration at C-3, while that at C-6 was supported by biogenetic considerations as again these compounds are most likely derived from **4**.

The ^{1}H NMR spectrum of **9** (Table 1) differed markedly from those of **4**–**8**. The presence of a new exomethylene group followed from the signals at δ4.86 and 5.23, while signals at δ4.49 and 4.45 require the presence of two hydroxy groups. In agreement with all data structure **9** was proposed. The stereochemistry was confirmed by NOED [H-14 with H-15 (7%), H-13 (7%) and H-9′ (8%); H-13 with H-6 (5%); H-4 with H-3 (4%); OMe with H-8 (10%); H-1 with H-9 (8%) and H-3 with H-6 (8%)]. Lactone **9**, which we have named secosenzoellneride, is probably formed by fragmentation of the 9-hydroxy derivative of **4**.

EXPERIMENTAL

The air-dried plant material (448 g, voucher Niemeyer 8986, deposited in the Herbarium of the University of Chile, Santiago, collected in May 1989 in the Region de Tarapaca) was extracted with a mixt. of solvents comprising petrol, Et_2O and MeOH in equal amounts. The extract was freed from solvent, defatted by MeOH and subsequently separated by CC (silica gel) using petrol, Et_2O and MeOH with increasing polarity. The frs obtained from the column were later further separated and purified by repeated TLC and HPLC as reported previously [5] to give 10 mg **2** (HPLC: MeOH–H_2O, 3:2), 2 mg **3** (TLC1), 6 mg **4** (TLC2), 5 mg **5** (TLC2), 3 mg **6** (TLC2), 4 mg **7** (TLC1), 5 mg **8** (TLC1), 3 mg **9** (TLC1), 3 mg cinnamylangelate, 6 mg tremetone,

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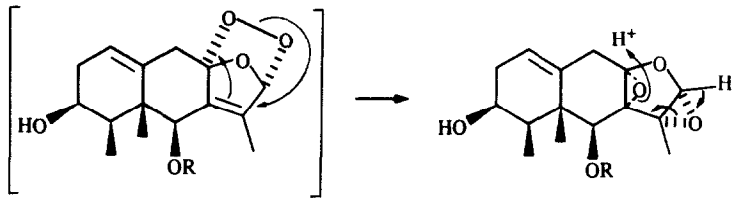
Table 1. ^{1}H NMR spectral data of compounds **2–9** (400 MHz, $CDCl_3$, δ-values)

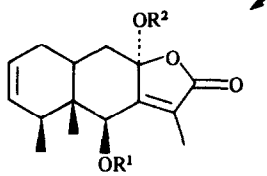
H	2	3	4	5	6	7		8		9
1	5.47 *br q*	5.50 *br q*	5.68 *m*	5.65 *ddd*	5.66 *ddd*	6.89	6.85 *dd*	6.89	6.84 *dd*	4.45 *br t*
2	2.53 *dddd*	2.55 *dddd*	2.30 *br dt*	2.30 *br dt*	2.30 *br dt*	2.87	2.83 *ddd*	2.90	2.85 *ddd*	1.99 *br d*
2′	2.21 *br dt*	2.22 *br dt*	2.15 *m*	2.16 *m*	2.16 *m*	2.40 *m*		2.40 *m*		1.73 *br dt*
3	3.95 *br d*	3.96 *br d*	4.08 *ddd*	4.01 *ddd*	4.02 *ddd*	5.42 *m*		5.45 *m*		4.47 *dt*
4	1.77 *dq*	1.82 *dq*	1.82 *dq*	1.85 *dq*	1.95 *m*	2.41	2.45 *dq*	2.40 *m*		2.28 *br q*
6	5.25 *s*	5.30 *s*	5.68 *q*	5.40 *q*	5.47 *d*	5.78	5.81 *s*	5.86	5.91 *s*	6.58 *s*
8	—	—	—	—	—	5.67 *br s*		5.69 *br s*		5.58 *br s*
9	2.92 *dd*	2.94 *dd*	2.74 *d*	2.78 *d*	2.79 *d*	9.29	9.36 *s*	9.30	9.36 *s*	5.23 *s*
9′	2.38 *d*	2.42 *d*	2.50 *ddd*	2.43 *ddd*	2.44 *ddd*					4.86 *d*
12	5.30 *s*	5.35 *s*	—	—	—	—	—	—	—	—
13	1.64 *s*	1.64 *s*	1.88 *d*	1.92 *d*	1.85 *d*	2.19	2.10 *s*	2.17	2.19 *s*	2.10 *s*
14	1.28 *s*	1.32 *s*	1.05 *s*	1.07 *s*	1.10 *s*	1.35	1.36 *s*	1.37	1.38 *s*	1.10 *s*
15	1.04 *d*	1.07 *d*	1.03 *d*	1.06 *d*	1.05 *d*	0.85	0.88 *s*			0.82 *d*
OCOR	2.62 *qq*	6.13 *qq*	2.74 *qq*	2.72 *qq*	6.30 *qq*	2.62 *qq*		6.16 *qq*		2.68 *qq*
	1.23 *d*	2.04 *dq*	1.29 *d*	1.30 *d*	2.08 *dq*	1.20	1.18 *d*	1.99 *dq*		1.25 *d*
	1.22 *d*	1.96 *dq*	1.25 *d*	1.26 *d*	2.01 *dq*	1.19	1.16 *d*	1.95	1.96 *dq*	1.20 *d*
						2.05 *s*	2.06 *s*(OAc)	2.05 *s*		
OMe	—	—	—	3.19 *s*	3.22 *s*	—	—	—	—	3.43 *s*

J [Hz]: Compounds **2** and **3**: 1,2 = 1,2′ = 1,9 ~ 3; 2,2′ = 18; 2,3 = 5; 3,4 = 2; 4,15 = 7; 9,9′ = 15; compounds **4–6**: 1,2 = 2,3 ~ 4.5; 1,2′ = 3; 1,9′ = 2′,9′ ~ 2; 2,2′ = 18; 2′,3 = 9; 3,4 = 2.5; 4,15 = 7; 6,13 = 1; 9,9′ = 13; compounds **7** and **8**: 1,2 = 3; 1,2′ = 4; 2,2′ = 20; 2,3 = 6; 3,4 = 2.5; 4,15 = 7; compound **9**: 1,2 = 1,2′ = 4; 1,9′ ~ 1; 2,2′ = 2′,3 = 12; 2,3 = 3,4 = 3.5; 4,15 = 7; OiBu: 2,3 = 2,4 = 7; OAng: 3,4 = 7; 3,5 = 4,5 = 1.5.

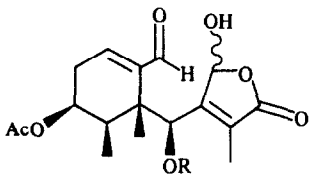


1

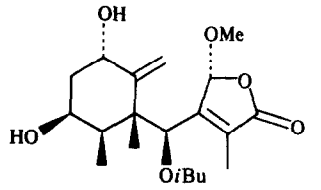
2 R = *i*Bu
3 R = Ang



4 R^1 = *i*Bu, R^2 = H
5 R^1 = *i*Bu, R^2 = Me
6 R^1 = Ang, R^2 = Me



7 R = *i*Bu
8 R = Ang



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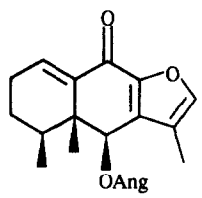

10

25 mg spathulenol and 50 mg *p*-hydroxyacetophenone. Known compounds were identified by comparing their spectral data with those of the reference compounds. TLC1: C_6H_6–CH_2Cl_2–Et_2O (1:1:2); TLC2: C_6H_6–CH_2Cl_2–Et_2O (3:3:4).

3β-Hydroxy-6β-isobutyryloxy-7,8,11,12-*bis-epoxyfuroeremophil*-1(10)-*ene* (**2**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3520 (OH), 1750 (CO_2R); MS *m/z* (rel. int.): 350.173 $[M]^+$ (3) (calc. for $C_{19}H_{26}O_6$: 350.173), 262 $[M-RCO_2H]^+$ (46), 205 $[262-C_3H_5O]^+$ (90), 120 (77), 71 $[RCO]^+$ (100).

3β-Hydroxy-6β-angeloyloxy-7,8,11,12-*bis-epoxyfuroeremophil*-1(10)-*ene* (**3**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 362.173 $[M]^+$ (1) (calc. for $C_{20}H_{26}O_6$: 362.173), 262 $[M-RCO_2H]^+$ (44), 205 (26), 120 (26), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (60).

3β,8α-Dihydroxy-6β-isobutyryloxyeremophil-1(10),7(11)-*dien*-12,8*β*-*olide* (**4**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (OH), 1750 (γ-lactone, CO_2R); MS *m/z* (rel. int.): 350 $[M]^+$ (0.5), 332.163 $[M-H_2O]^+$ (2) (calc. for $C_{19}H_{24}O_5$: 332.163), 244 $[332-RCO_2H]^+$ (42), 140 (90), 121 (52), 106 (62), 71 $[RCO]^+$ (100).

3β-Hydroxy-6β-isobutyryloxy-8α-methoxyeremophil-1(10), 7(11)-*dien*-12,8*β*-*olide* (**5**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1750 (CO_2R); MS *m/z* (rel. int.): 364.189 $[M]^+$ (1) (calc. for $C_{20}H_{28}O_6$: 364.189), 332 $[M-MeOH]^+$ (1.3), 276 $[M-RCO_2H]^+$ (23), 244 $[276-MeOH]^+$ (17), 121 (26), 71 $[RCO]^+$ (100).

3β-Hydroxy-6β-angeloyloxy-8α-methoxyeremophil-1(10),7(11)-*dien*-12,8*β*-*olide* (**6**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 376.189 $[M]^+$ (2.5) (calc. for $C_{21}H_{28}O_6$: 376.189), 344 $[M-MeOH]^+$ (2.5), 276 $[M-RCO_2H]^+$ (24), 244 $[276-MeOH]^+$ (18), 121 (35), 107 (42), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (47).

3β-Acetoxy-6β-isobutyryloxy-seco-*macrotolide* (**7**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 1700 (C=CCHO), 1790 (γ-lactone), 1740 (CO_2R); CIMS *m/z* (rel. int.): 279 $[M+1-RCO_2H$, ketene$]^+$ (1.5), 261 $[279-H_2O]^+$ (1), 221 (3), 203 (4), 133 (26), 73 (100).

3β-Acetoxy-6β-angeloyloxy-seco-*macrotolide* (**8**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 1700 (C=CCHO), 1790 (γ-lactone), 1745 (OAc), 1720 (C=CCO_2R); CIMS *m/z* (rel. int.): 343 $[M+1-HOAc, H_2O]^+$ (0.5), 279 $[M+1-RCO_2H$, ketene$]^+$ (2.5), 261 $[279-H_2O]^+$ (2.5), 203 (100).

seco-*Senzoellneride* (**9**). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1750 (γ-lactone, CO_2R); MS *m/z* (rel. int.): 382 $[M]^+$ (0.5), 364.189 $[M-H_2O]^+$ (1.7) (calc. for $C_{20}H_{28}O_6$: 364.189), 294 $[M-RCO_2H]^+$ (12), 276 $[294-H_2O]^+$ (12), 262 $[294-MeOH]^+$ (18), 244 $[262-H_2O]^+$ (17), 158 (51), 140 (100), 71 $[RCO]^+$ (82).

Cinnamylangelate. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (C=CCO_2R); MS *m/z* (rel. int.): 216.115 $[M]^+$ (**8**) (calc. for $C_{14}H_{16}O_2$: 216.115), 117 $[M-OAng]^+$ (40), 83 $[RCO]^+$ (100); ^1H NMR ($CDCl_3$): δ7.40 (*br d*, H-2, H-6), 7.33 (*br t*, H-3, H-5), 7.25 (*br t*, H-4), 6.18 (*dt*, H-7), 5.84 (*dt*, H-8), 4.81 (*dd*, H-9); OAng: 6.10 *qq*, 2.00 *dq*, 1.92 *dq*; *J* [Hz]: 2,3 = 3,4 ~ 8; 7,8 = 16; 7,9 = 1.5; 8,9 = 7; OAng: 3,4 = 7; 3,5 = 4,5 = 1.5.

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