Phytochemistry, 1980, Vol. 19, pp. 2681–2684. © Pergamon Press Ltd. Printed in England. 0031-9422/80/1201-2681 $02.00/0

EREMOPHILANE DERIVATIVES FROM *SENECIO* SPECIES*

FERDINAND BOHLMANN and JÜRGEN ZIESCHE

Institute for Organic Chemistry, Technical University Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, W. Germany

(*Received* 17 *March* 1980)

Key Word Index—*Senecio alatus*; *S. amplexicaulis*; Compositae; new hydroxyeremophilane; new furanoeremophilanes; new eremophilanolides.

Abstract—The investigation of two further *Senecio* species afforded two new furanoeremophilanes, four eremophilanolides and a new hydroxyeremophilane. The structures of two furanoeremophilane, isolated before, have been revised.

Though many *Senecio* species have been investigated chemically [1], nothing is known of the constituents of those growing in the Himalayan region. We have now investigated two of them. *Senecio amplexicaulis* Wall. afforded α- and β-farnesene (**1** and **2**), β-sesquiphellandrene (**3**), linalolacetate (**4**), a mixture of **5a–c**, high concentrations of the *p*-hydroxyacetophenone derivatives **9** [2], **10** [3] and **11** [4], as well as a previously unknown sesquiterpene alcohol, $C_{15}H_{26}O$. Careful NMR investigations of this alcohol, its acetate and of the two isomeric hydrocarbons obtained by treatment with thionylchloride/pyridine led to structure **12a**. The ^1H NMR- as well as the ^{13}C NMR data are fully in agreement with this structure (see Table 1). The presence of an eremophilane derivative clearly follows from the ^1H NMR data obtained after addition of $Eu(fod)_3$. The observed shifts of both methyl singlets and the splitting of the 6-H signals, only visible after addition of the shift reagent, strongly support the presence of a 5-methyl group. Though the ^1H NMR spectra of **12a**, **12b** and of the isomeric hydrocarbons **13** and **14** could be interpreted only in part, the proposed structures are reasonably certain. The stereochemistry of the ring fusion as a *trans*-decalin can be deduced only indirectly. The signal of 7-H in all compounds clearly indicates axial orientation of the isopropenyl group, which would be very unlikely in a *cis*-decalin derivative.

The roots of *S. alatus* Wall. also contain the mixture **5a–c**, small amounts of **6** [5], **7** [6] and **8** [7] as well as a complex mixture of eremophilane derivatives.

Table 1. ^1H NMR data of **12a**, **12b**, **13** and **14** ($CDCl_3$, TMS as internal standard)

	12a	$Eu(fod)_3$†	**12b**	**13**	**14***	**12a** (^{13}C)	
3α-H	2.06 *dddd*	3.08 *d(br)*	2.04 *d(br)*	2.28 *d(br)*	5.32 *br*	C-1 41.6 *t*‡	C-9 40.5 *t*‡
3β-H	1.33 *m*	2.04 *ddd*	1.35 *m*	2.00 *dd(br)*		C-2 22.8 *t*	C-10 39.5 *d*
6α-H	1.75 *m*	2.47 *d(br)*	1.77 *m*			C-3 43.4 *t*	C-11 146.9 *s*
6β-H		2.64 *d(br)*			1.85 *m*	C-4 72.0 *s*	C-12 110.9 *t*
7α-H	2.43 *br*	2.67 *br*	2.43 *br*	2.41 *br*	2.41 *br*	C-5 35.4 *s*	C-13 18.9 *q*
12-H	4.92 *dq*	4.95 *dq*	4.94 *dq*	4.90 *dq*	4.92 *dq*	C-6 23.6 *t*	C-14 22.4 *q*†
12'-H	4.87 *dq*	5.13 *s(br)*	4.91 *dq*	4.82 *s(br)*	4.85 *dq*	C-7 49.3 *d*	C-15 22.8 *q*†
13-H	1.75 *s(br)*	1.93 *s(br)*	1.77 *s(br)*	1.73 *s(br)*	1.76 *s(br)*	C-8 20.2 *t*	
14-H	0.93 *s*	1.27 *s*	0.98 *s*	0.76 *s*	0.86 *s*		
15-H	1.09 *s*	1.83 *s*	1.43 *s*	4.69 *ddd* 4.43 *ddd*	1.62 *ddd*		
OAc	—	—	1.95 *s*				

J (Hz): **12a/b**: 1α,3α = 2α,3α = 2β,3α ~ 1.5; 3α,3β = 13; 6α,6β = 13; 7,12 = 12,13 ~ 1.5; **13**: 2α,3β = 10; 3α,3β = 13; 3α,15 = 3β,15 = 15, 15' = 7, 12 = 12, 13 ~ 1.5; **14**: 2, 3 = 2, 15 = 7, 12 = 12, 13 ~ 1.5.

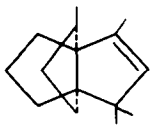
* 2β-H 2.00 *d(br)* (*J* = 15).

†‡ Perhaps interchangeable.

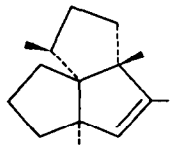
* Part 295 in the series "Naturally Occurring Terpene Derivatives"; for Part 294 see: Bohlmann, F., Ziesche, J., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 2675.

$Me(CH_2)_n CH=CH_2$ $n = 8,9,10$

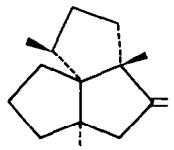
5a, b, c



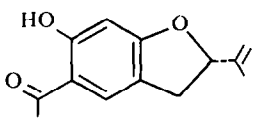
6



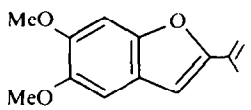
7



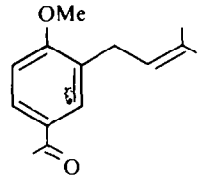
8



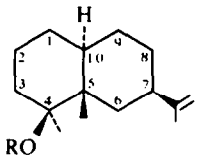
9



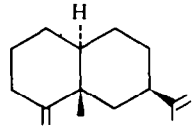
10



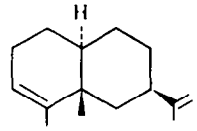
11



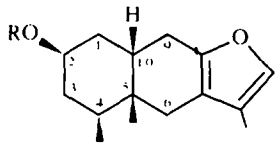
12a R = H
12b R = Ac



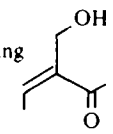
13



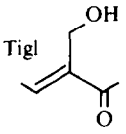
14

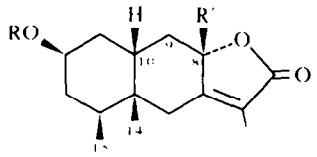


15 R = Ang
16 R =



17 R = Tigl
18 R =





R	Ang					Ang
R′	H	H	H	OH	OAc	OH
	19	**20**	**20a**	**21**	**21a**	**22**

The less polar fractions afforded two furanoeremophilanes, both being esters. The first one is an angelate and the second a 5-hydroxyangelate. Only at elevated temperature could well resolved ^{1}H NMR spectra be obtained (see Table 2). This is typical for *cis*-fused furanoeremophilanes. The spectra are very similar to those of two esters isolated earlier from *S. greyi* [8], which we assumed to be 3-tigloyl and 3-hydroxytigloyl derivatives. Careful double resonance experiments, however, clearly show that the structures of these esters must be revised. Irradiation of the 4-H signal in all compounds shows that this is not coupled to the proton on the carbon which bears the ester residues. Further decoupling experiments show that the esters are 2β. However, a 'steroid-conformation' must be assumed, in which the left ring is somewhat distorted, as the couplings of 2α-H and 4α-H are unusual (see Table 2). All data are in agreement with structures **15** and **16**, while the structures of those compounds isolated earlier [8] should be changed to **17** and **18**.

The more polar fractions contain two compounds, which obviously are oxidation products of **16**. Their ^{1}H NMR data (see Table 2) are in good agreement with structures **20** and **21**, both being transformed to the acetates **20a** and **21a** respectively. Again the 2β-position of the ester residue could be established by double resonance. The ^{1}H NMR spectra of both lactones are already sharp at room temperature; the couplings of 9-H in the spectrum of **21a** clearly indicate again a *cis*-ring fusion. **20** and **21** are most probably artefacts as within two weeks **15** and **16** are completely transformed to **19** and **20** respectively by air oxidation at room temperature. This again supports the structures of **15** and **16**.

The aerial parts also contain **5a–c**, **15**, **16**, **20** and **21** as well as two other lactones, which must have structures **19** and **22**. All ^{1}H NMR data are very similar to those of **20** and **21** respectively. Again these compounds may be artefacts. **19** has been isolated before [9]; it was first assumed to be a 3-angeloyloxy derivative but was revised to **1a** by synthesis of the corresponding alcohol [10]. The configuration at C-8, in **21** and **22** is not really established, but is that of similar lactones [11].

So far the constituents of these two *Senecio* species from the Himalayan region show no relationship to other species in the genus. Surely, more species have to be investigated to see where these taxa should be placed.

EXPERIMENTAL

The air dried plant material, collected in the Giharwal district of the Himalayan region was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by column chromatography (SiO_2) and further by TLC (SiO_2, GF 254). Known compounds were identified by comparison of the IR and ^{1}H NMR spectra with those of authentic material.

Senecio amplexicaulis. The whole plants (180 g) afforded 5 mg **1**, 5 mg **2**, 15 mg **3**, 100 mg **4**, 15 mg **5a–c**, 400 mg **9**, 800 mg **10**, 300 mg **11** and 200 mg **12a** (Et_2O–petrol, 1:3).

Senecio alatus. The roots (80 g) afforded 50 mg **5a–c**, 2 mg **6**, 2 mg **7** and 1 mg **8** (the latter three identified by GC/MS); 100 mg **15** (Et_2O–petrol, 1:10), 1.5 g **16** (Et_2O–petrol, 1:1), 10 mg **20** (Et_2O) and 10 mg **21** (Et_2O), while the aerial parts (80 g) gave 5 mg **5a–c**, 10 mg **15**, 20 mg **16**, 1 mg **19**, 5 mg **20**, 5 mg **21** and 4 mg **22** (Et_2O).

4-*Hydroxy*-10α-H-*eremophil*-11(12)*ene* (**12a**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1635, 890 (C=CH_2); MS: M$^+$ *m/e* (rel. int.) 222.198 (3) ($C_{15}H_{26}O$); 204 (100) (M – H_2O); 189 (93) (204 – Me); 161 (87) (189 – C_2H_4).

$$[\alpha]_{24} = \frac{589}{+12.4}\ \frac{578}{+12.9}\ \frac{546}{+14.7}\ \frac{436\,nm}{+23.7}\ (c = 3.4, CHCl_3).$$

Table 2. ^{1}H NMR data of **15**, **16**, **19**, **20a**, **21a** and **22**

	15 (C_6D_6, 77°)	**16** (C_6D_6, 77°)	**19** ($CDCl_3$)	**20a** ($CDCl_3$)	**21a** ($CDCl_3$)	**22** ($CDCl_3$)
1α-H			1.38 *ddd*	1.37 *ddd*	1.37 *ddd*	1.38 *ddd*
2α-H	5.19 *dddd*		4.94 *dddd*	4.98 *dddd*	4.93 *dddd*	4.91 *dddd*
4-H	1.60 *m*		1.66 *m*	1.65 *m*	1.65 *m*	1.65 *m*
6-H	2.45 *d*	2.43 *d*	2.92 *d*	2.93 *d*	2.86 *d*	2.79 *d*
6'-H	1.9 *m*		1.90 *m*	1.93 *d(br)*	1.9 *m*	1.9 *m*
8-H		—	4.62 *dd(br)*	4.62 *dd(br)*	—	—
9-H	2.58 *dd(br)*	2.57 *dd(br)*	2.29 *ddd*	2.30 *ddd*	2.51 *dd*	2.20 *dd*
9'-H	2.44 *dd(br)*			} 1.85 *m*	1.87 *dd*	
10-H					1.85 *m*	
12-H	7.04 *s(br)*		—	—	—	—
13-H	1.83 *d*	1.84 *d*	1.81 *s(br)*	1.82 *s(br)*	1.86 *d*	1.82 *d*
14-H	0.86 *s*	0.87 *s*	1.11 *s*	1.11 *s*	1.11 *s*	1.12 *s*
15-H	0.84 *d*	0.82 *d*	0.87 *d*	0.89 *d*	0.90 *d*	0.88 *d*
OCOR	5.79 *qq*	6.03 *tq*	6.02 *qq*	6.39 *tq*	6.40 *tq*	6.03 *qq*
	2.00 *dq*	1.99 *tq*	1.96 *dq*	2.08 *tq*	2.08 *tq*	1.95 *dq*
	1.91 *dq*	4.21 *s(br)*	1.86 *dq*	4.71 *s(br)*	4.72 *s(br)*	1.86 *dq*
OAc		—	—	2.06 *s*	2.06 *s*	3.09 *s(br)*
					2.07 *s*	(OH)

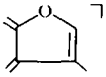
J (Hz): **15/16**: 1α, 2α = 2α, 3α ~ 3; 1β, 2α = 2α, 3β ~ 8–10; 4, 15 = 7; 6, 6' = 15; 9, 9' = 17; 9, 10 = 7; 12, 13 = 1; **19/20**: 1α, 2α = 2α, 3α = 5; 1β, 2α – 2α, 3β – 11; 3α, 4 = 5; 3β, 4 = 8; 4, 15 = 7; 6, 6' = 14; 8, 9 = 6.5; 8, 9' = 10; 8, 13 = 1.5; 9, 9' = 15; 9, 10 = 3.5; 9', 10 = 4.

To 10 mg **12a** in 0.1 ml dimethylaniline were added 50 mg AcCl. After 20 hr RT usual work-up afforded 8 mg **12b**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730, 1250 (OAc); 3090, 1640, 895 (C=CH_2); MS: M^+ *m/e* (rel. int.) 264 (1); 204 (94) (M − AcOH); 189 (100) (204 − Me).

To 20 mg **12a** in 1 ml pyridine 0.1 ml $SOCl_2$ were added (0). After 3 hr usual work-up afforded a mixture of **13** and **14** (2:1), which were separated by $AgNO_3$-coated TLC plates. **13**: Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3090, 1640, 895 (C=CH_2) MS: M^+ *m/e* (rel. int.) 204 (55) ($C_{15}H_{24}$); 189 (60) (M − Me); 161 (100) ($C_{12}H_{17}$); 147 (63) ($C_{11}H_{15}$); 133 (67) ($C_{10}H_{13}$); 119 (45) (C_9H_{11}); 105 (77) (C_8H_9); 93 (68) (C_7H_9); 91 (70) (C_7H_7); 79 (68) (C_6H_7); 67 (53) (C_5H_7). **14**: Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3090, 1650, 895 (C=CH_2); MS: M^+ *m/e* (rel. int.) 204 (18) ($C_{15}H_{24}$); 189 (10) (M − Me); 161 (100) ($C_{12}H_{17}$); 122 (85) (C_9H_{14}); 107 (53) (C_8H_{11}).

2β-Angeloyloxy-10β-H-furanoeremophilane (**15**). Colourless, unstable oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1715, 1650 (C=CCO_2R); MS: M^+ *m/e* (rel. int.) 316.204 (12) ($C_{20}H_{28}O_3$); 216 (38) (M − RCO_2H); 83 (100) ($C_4H_7CO^+$).

$$[\alpha]_{24}^{\lambda} = \frac{589}{-26.9}\ \frac{578}{-27.4}\ \frac{546\text{ nm}}{-31.0}\ (c = 1.4,\ CHCl_3).$$

2β-[5′-Hydroxyangeloyloxy]-10β-H-furanoeremophilane (**16**). Colourless, unstable oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH); 1720, 1655 (C=CCO_2R); MS: M^+ *m/e* (rel. int.) 332.199 (40) ($C_{20}H_{28}O_4$): 216 (25) (M − RCO_2H); 108 (100) ().

$$[\alpha]_{24}^{\lambda} = \frac{589}{-32.7}\ \frac{578}{-34.1}\ \frac{546}{-38.5}\ \frac{436\text{ nm}}{-63.4}\ (c = 3.48,\ CHCl_3).$$

2β-[5′-Hydroxyangeloyloxy]-10β-H-eremophilanolide (**20**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH); 1760 (lactone); 1720, 1650 (C=CCO_2R); MS: M^+ *m/e* (rel. int.) 348.194 (5) ($C_{20}H_{28}O_5$), 233 (100) (M − RCO_2); 232 (67) (M − RCO_2H); 99 (78) ($MeCH{=}C(CH_2OH)CO^+$).

10 mg **20** were acetylated with Ac_2O (1 hr, 70). Usual work-up afforded 10 mg **20a**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765 (lactone); 1750, 1250 (OAc), 1725, 1650 (C=CCO_2R); MS (CI, isobutane): 781 (2 × M + 1) (20), 391 (100) (M + 1).

$$[\alpha]_{24}^{\lambda} = \frac{589}{+16.2}\ \frac{578}{+17.7}\ \frac{546}{+20.9}\ \frac{436\text{ nm}}{+42.6}\ (c = 0.53,\ CHCl_3).$$

2β-[5′-Hydroxyangeloyloxy]-8β-hydroxy-10β-H-eremophilanolide (**21**). Colourless gum, which only was isolated as its diacetate **21a** (2 hr, 70°, Ac_2O), colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (lactone); 1770, 1745, 1240, 1220 (OAc); MS (CI, isobutane): 449 (8) (M + 1); 389 (100) (M + 1 − AcOH).

$$[\alpha]_{24}^{\lambda} = \frac{589}{+1.4}\ \frac{578}{+2.1}\ \frac{546}{+12.1}\ \frac{436\text{ nm}}{+62.9}\ (c = 0.14,\ CHCl_3).$$

2β-Angeloyloxy-8β-hydroxy-10β-H-eremophilanolide (**22**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1765 (lactone), 1715, 1650 (C=CCO_2R); MS (CI, isobutane): 349 (25) (M + 1), 245 (42) (M + 1 − RCO_2H); 218 (100).

$$[\alpha]_{24}^{\lambda} = \frac{589}{+9.6}\ \frac{578}{+9.8}\ \frac{546}{+11.6}\ \frac{436\text{ nm}}{+65.5}\ (c = 0.44,\ CHCl_3).$$

Acknowledgements We thank the Deutsche Forschungsgemeinschaft for financial support and Dr. R. Gupta, University of Delhi, for the plant material.

REFERENCES

1. Bohlmann, F., Zdero, C., Berger, D., Suwita, A., Mahanta, P. K. and Jeffrey, C. (1979) *Phytochemistry* **18**, 79.
2. Kamthory, B. and Robertson, A. (1939) *J. Chem. Soc.* 933.
3. Murae, T., Tanahashi, Y. and Takahashi, T. (1968) *Tetrahedron* **24**, 2177.
4. Bohlmann, F. and Grenz, B. (1970) *Chem. Ber.* **103**, 90.
5. Zalkow, L. H., Harris, R. N. VI. and Van Derveer, D. (1978) *Chem. Comm.* 420.
6. Zalkow, L. H., Harris, R. N. III., Van Derveer, D. and Bertrand, J. A. (1977) *Chem. Comm.* 456.
7. Bohlmann, F., Le Van, N., Van Cuong Pham, T., Schuster, A., Zabel, V. and Watson, W. H. (1979) *Phytochemistry* **18**, 1831.
8. Bohlmann, F., Ehlers, D. and Zdero, C. (1978) *Phytochemistry* **17**, 467.
9. Novotny, L., Jizba, J., Herout, V. and Sorm, F. (1962) *Coll. Czech. Chem. Comm.* **27**, 1393.
10. Kitahara, Y., Maeda, S., Ueno, M., Funamizu, M., Kato, T., Novotny, L., Herout, V. and Sorm, F. (1977) *Chem. Letters* 1031.
11. Moriyama, Y. and Takahashi, T. (1976) *Chem. Pharm. Bull.* **24**, 360.