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SESQUITERPENES FROM THREE *SENECIO* SPECIES*

FERDINAND BOHLMANN and JÜRGEN ZIESCHE

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

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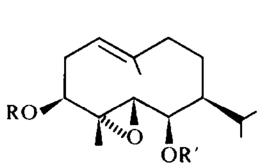
Key Word Index—*Senecio fulgens*; *S. crassissimus*; *S. nebrodensis*; Compositae; sesquiterpenes; new bisabolene derivatives; new norsesquiterpene; new β-caryophyllene alcohol derivative.

Abstract—Three succulent *Senecio* species afforded, in addition to known compounds, two further bisabolene derivatives, a norsesquiterpene and a diol related to β-caryophyllene alcohol, which, however, has a different stereochemistry. Structures were elucidated by spectroscopic methods and some chemical transformations. The chemotaxonomic relevance of the results is discussed briefly.

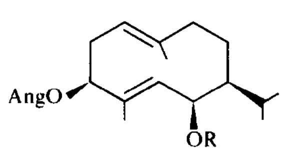
Investigation of several succulent *Senecio* species has shown that the widespread furanoeremophilanes are missing and that they are normally replaced by highly oxygenated sesquiterpenes with different carbon skeletons [1]. We now have investigated three further species. The roots of *Senecio crassissimus* Humb. afforded germacrene D, bicyclogermacrene, lupeone, the germacrene derivatives **1a** [2], **1b** [2], **3** [3] and **4** [2] as well as the *cis*-caryophyllene epoxide **5**, so far not isolated in nature, but already prepared from the *cis*-hydrocarbon [4]. The aerial parts contain germacrene D, bicyclogermacrene, aromadendrene, lupeol, its acetate, lupeone, β-amyrin acetate, β-amyrenone, glutin-5(6)-en-3β-ol, 28-oxo-β-amyrenone, the angelate **6** [3], the epoxides **1a**, **1b**, **2a** [3] and **2b** [2] and a diol, most probably **16**. The structure of the latter was supported by intensive ^{1}H NMR studies of the diol, of the corresponding mono- and diacetate (**17** and **18**) as well as those of the ketone **19** and the keto acetate **20**. Careful spin decoupling in different solvents also after addition of Eu(fod)$_3$ and ^{13}C NMR of **16** and **17** finally led to the proposed structures. Also comparisons of the ^{1}H- and ^{13}C-NMR data with those of β-caryophyllene alcohol (**21**) [5] were useful. The presence of a secondary and a tertiary hydroxyl is shown by the formation of a mono- and a diacetate as well by oxidation yielding a ketone, which further could be transformed to a keto acetate. The ^{1}H NMR data (see Table 1) could not be assigned completely. The deduced spin systems, however, are only in agreement with the proposed structures. The position of the secondary hydroxyl follows from the observed signals in the ^{1}H NMR spectrum of the ketone **19**. The neighbouring CH_2 group obviously has two adjacent hydrogens as shown by spin decoupling. The presence of the four-membered ring also could be established by spin decoupling. Irradiation of the typical three-fold doublet, also present in caryophyllene derivatives, collapses the double doublet at 1.83, which must be assigned to 10-H as this signal is strongly shifted after addition of Eu(fod)$_3$. The 9-H as well as the 7-H signals also showed strong shifts. This requires a *cis*-position of the 9-H and the OH-group. Also the different shifts of the C-11-methyl signals are in agreement with this stereochemistry as can be seen from models. The co-occurrence with **5** also supports this configuration. These further show that the six-membered ring is present in a boat form as the couplings of 5-H are very small. This conformation is favoured as in a chair C-6 and C-12 would be forced very near to each other. The presence of a CH_2-bridge (C-15) also follows from the ^{1}H NMR data (2.31 *d* and 1.61 *d*). For both signals strong Eu(fod)$_3$ induced shifts were observed. The relative orientation of the C-4 methyl group also follows from the Eu(fod)$_3$ induced shift. The only remaining hydrogens, whose signals could not be assigned clearly, can only be placed at C-2 and 3. The ^{13}C NMR data (see Table 2) support the proposed structures. The multiplicity requires a tricyclic compound with two secondary centres only except that of the hydroxyl bearing carbon. Therefore no other carbon skeleton seems to be possible. **16** is most probably formed by enzymatic opening of the epoxide ring of *cis*-caryophyllene epoxide (**5**), which would lead to the carbenium ion **22**. The latter easily could be transformed to **16**, which we have named senecrassane-5,8-diol. The 1,9-*trans* diol has already been prepared from caryophyllene [10].

The roots of *S. nebrodensis* L. afforded the eremophilane derivatives **12** and **13** [2]. A re-investigation of the ^{1}H NMR data in connection with the re-investigation of the stereochemistry of petasol [6] showed that the configuration at C-7 should change to 7β-H. Further α-zingiberene and the aldehyde **14** are present, which on reduction gave the alcohol **15**. The ^{1}H NMR data clearly show the close relationship to the known 2-hydroxy compound [7]. **14** is a further norsesquiterpene with the same carbon skeleton, which often is present in *Senecio* species [1, 2]; the absolute configuration was not determined. The aerial parts only gave β-farnesene, α-curcumene, β-selinene, selina-4,11-diene, **12**, **13** and high concentrations of 3-ethyl-*cis*-crotonic acid. The aerial parts of *S. fulgens* Nicholsen afforded germacrene D,

* Part 299 in the series "Naturally Occurring Terpene Derivatives". For Part 298 see Bohlmann, F., Jakupovic, J., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 109.



1a R = Ang, R′ = H
1b R = Ang, R′ = Ac
2a R = Sen, R′ = H
2b R = Tigl, R′ = H



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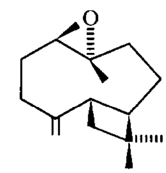
4 R = Ac



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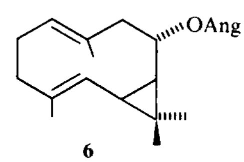

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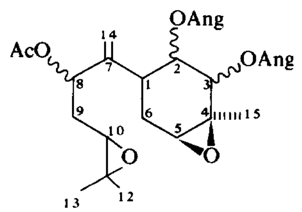
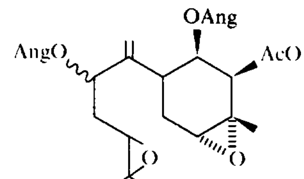


7 2α, 3α-H
8 2β, 3β-H



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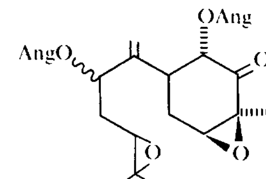

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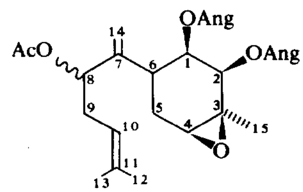

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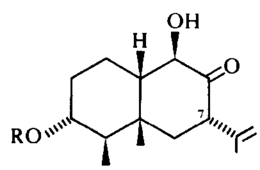
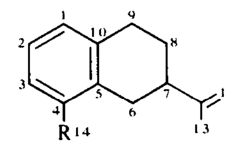
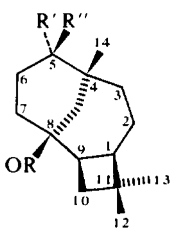


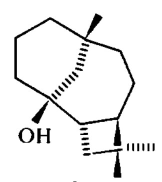
12 R = Ang
13 R = Sen



14 R = CHO
15 R = CH_2OH



	16	17	18	19	20
R	H	H	Ac	H	Ac
R′	H	H	H	= O	= O
R″	OH	OAc	OAc		



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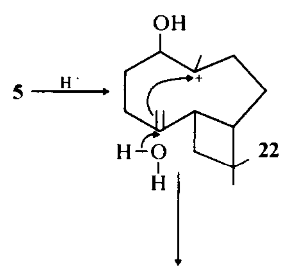

16

lupeone, friedelin and the bisepoxides **8** [8] and **9** [9], while the roots in addition to **7** and **8** contain the monoepoxide **11** and the ketone **10**, both not isolated before. **11** is obviously the precursor of **7**, the ^1H NMR data are very similar and therefore the relative positions of the ester groups were most probably the same. A stereo isomer of **10** was isolated before [8]. Careful inspection of the ^1H NMR spectra (see Table 3) showed that the stereochemistry of **10** is changed most probably only at C-3 and C-4. The observed couplings agree with the proposed relative configurations at C-1, C-4 and C-6, while the absolute configuration, however, is not established in all these compounds.

This investigation shows again that highly oxygenated sesquiterpenes are characteristic for this group of *Senecio* species. So far no taxonomic differentiation of the species, which contains different types of highly substituted sesquiterpenes, is possible.

EXPERIMENTAL

The fresh plant material grown from seeds was extracted with Et_2O–petrol (1:2) and the resulting extracts after treatment with MeOH (to remove long-chain saturated hydrocarbons) were first separated by column chromatography (SiO_2, act. grade II) and further by repeated TLC (SiO_2, GF 254). Known compounds were identified by comparing the IR and ^1H NMR spectra with those of authentic material.

Senecio crassissimus (*voucher* 78/1262). The roots (50 g) afforded 5 mg germacrene D, 5 mg bicyclogermacrene, 10 mg lupeone, 10 mg **1a**, 30 mg **1b**, 10 mg **3**, 5 mg **4** and 5 mg **5**, while the aerial parts (250 g) gave 1 mg germacrene D, 5 mg bicyclogermacrene, 2 mg aromadendrene, 60 mg **1a**, 100 mg **1b**, 5 mg **2a**, 10 mg **2b**, 10 mg **5**, 10 mg lupeol acetate, 10 mg lupeone, 5 mg **6**, 10 mg β-amyrin acetate, 5 mg β-amyrenone, 10 mg glutin-5(6)-en-3β-ol, 10 mg 2β-oxo-β-amyrenone and 10 mg **16** (Et_2O–petrol, 1:1).

Table 1. ^{1}H NMR data of **16–20** (270 MHz, $CDCl_3$, TMS as internal standard)

	16	**17**	+Eu(fod)$_3$	**18**	**19**	**20**
1-H	1.65 *ddd*					
5-H	3.33 *t* (*br*)	4.56 *t* (*br*)	7.91 *s* (*br*)	4.56 *t* (*br*)	—	—
6-H			3.90 *d* (*br*)	—	2.63 *ddd*	2.81 *ddd*
6′-H			3.30 *dd* (*br*)		2.37 *ddd*	2.37 *m*
7-H			4.93 *dd* (*br*)		2.00 *ddd*	
7′-H			3.78 *d* (*br*)		1.96 *ddd*	
9-H	2.49 *ddd*	2.50 *ddd*	4.52 *ddd*	3.31 *ddd*	2.69 *ddd*	3.28 *ddd*
10-H	1.76 *dd*		3.50 *dd*		1.83 *dd*	1.88 *dd*
10′-H			2.65 *m*			
12-H	0.94 *s*	0.95 *s*	1.27 *s*	0.94 *s*	1.01 *s*	0.98 *s*
13-H	1.19 *s*	1.20 *s*	1.47 *s*	1.18 *s*	1.24 *s*	1.21 *s*
14-H	1.01 *s*	0.92 *s*	2.18 *s*	0.94 *s*	1.10 *s*	1.01 *s*
15-H	1.85 *d*	1.92 *d*	4.23 *m*	2.02 *d*	2.31 *d*	2.38 *d*
15′-H	1.34 *dd*	1.38 *dd*	2.81 *d* (*br*)	1.48 *d*	1.61 *d*	
OAc	—	2.06 *s*	4.23 *s*	1.92 *s*	—	1.95 *s*
				2.09 *s*		

J (Hz): 1, 2 = 13; 1, 2′ = 3; 1, 9 = 10; 3, 15 = 1; 5, 6 ~ 2.5; 6, 6′ = 17; 6, 7 = 10; 6, 7′ = 6; 6′, 7 = 4.5; 6′, 7′ = 4.5; 7, 7′ = 14; 9, 10 = 10; 9, 10′ = 8; 10, 10′ = 11; 15, 15′ = 14.

Table 2. ^{13}C NMR data of **16**, **17** and **21** ($CDCl_3$, TMS as internal standard)

	16*	**17***	**21**	Δ†
C-1	41.7 *d*	41.6 *d*	39.6 *d*	1.37
C-2	22.1 *t*	22.0 *t*	21.9 *t*	0.86
C-3	34.5 *t*	34.4 *t*	37.5 *t*	0.80
C-4	37.6 *s*	36.3 *s*	34.9 *s*	0.89
C-5	74.2 *d*	75.8 *d*	36.7 *t*	0.80
C-6	35.8 *t*	35.9 *t*	20.8 *t*	1.07
C-7	27.2 *t*	29.8 *t*	38.6 *t*	2.86
C-8	72.6 *s*	72.4 *s*	70.8 *s*	7.30
C-9	49.1 *d*	49.0 *d*	44.7 *d*	1.45
C-10	38.5 *t*	39.3 *t*	34.5 *t*	1.58
C-11	34.0 *s*	34.0 *s*	34.7 *s*	1.12
C-12	30.1 *q*	29.8 *q*	33.3 *q*	0.37
C-13	24.5 *l*	24.4 *q*	30.5 *q*	0.36
C-14	27.2 *q*	28.7 *q*	20.8 *q*	0.49
C-15	36.5 *t*	36.6 *t*	48.8 *t*	2.46

* Assignments in part uncertain, some signals may be interchangeable.
† Δ values after addition of Yb(fod)$_3$.

Senecio nebrodensis (*voucher* 79/1399). The roots (200 g) afforded 5 mg α-zingiberene, 400 g **12**, 20 mg **13** and 2 mg **14** (Et_2O–petrol, 1:10), while the aerial parts (3 kg) gave 3.7 g 3-ethyl-*cis*-crotonic acid, 5 mg *β*-farnesene, 5 mg α-curcumene, 10 mg selina-4,11-diene, 5 mg *β*-selinene, 20 mg **12** and 5 mg **13**.

Senecio fulgens (*voucher* 79/1413). The roots (70 g) afforded 10 mg **7**, 40 mg **8**, 10 mg **10** (Et_2O–petrol, 1:1) and 1 mg **11** (Et_2O–petrol, 1:1), while the aerial parts (300 g) gave 3 mg germacrene D, 10 mg lupeone, 10 mg friedelin, 10 mg **7** and 20 mg **8**.

1α,8-*Diangeloyloxy*-3*β*,4*β*,10,11-*diepoxy-bisabol*-7(14)*en*-2-*one* (**10**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730, 1655 (C=CO_2R); 3100, 855 (C=CH_2); MS: M^+ *m/e* (rel. int.) 446.230 (22) ($C_{25}H_{34}O_7$); 375 (15) $(M - \underset{O}{Me_2C{-}CH})$; 346 (8) (M − AngOH); 246 (8) (346 − AngOH); 83 (100) ($C_4H_7CO^+$).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-65.9 \quad -78.6 \quad -76.7 \quad -119.8}\,(c = 0.95).$$

Table 3. ^{1}H NMR data of **10** and **11** (270 MHz, TMS as internal standard)

	10 (C_6D_6)	**11** ($CDCl_3$)
1-H	6.20 *d*	5.33 *dd* (*br*)
2-H	—	5.36 *d*
4-H	2.71 *d*	3.19 *d*
6-H	2.45 *dd* (*br*)	2.45 *dd* (*br*)
8-H	5.40 *dd*	5.16 *dd*
9-H	1.9 *m*	2.0 *m*
10-H	2.84 *dd*	5.04 *t* (*br*)
12-H	1.16 *s*	1.70 *s* (*br*)
13-H	1.16 *s*	1.64 *s* (*br*)
14-H	5.16 *s* (*br*)	5.20 *s* (*br*)
14'-H	4.92 *s* (*br*)	5.02 *s* (*br*)
15-H	1.24 *s*	1.32 *s*
OCOR	5.78, 5.74 *qq*	6.11, 6.06 *qq*
	2.04, 2.03 *dq*	2.01, 1.98 *dq*
	1.94, 190 *dq*	1.91, 1.89 *dq*

J (Hz): **10**: 1, 6 = 12; 4, 5 = 4; 5, 6 = 12; 5′, 6 = 7; 8, 9 = 4; 8, 9′ = 8; 9, 10 = 7; 9′, 10 = 5; **11**: 1, 2 = 1, 6 = 4; 4, 5 = 5; 5, 6 = 12; 5, 6′ = 7; 8, 9 = 6; 8, 9′ = 8; 9, 10 = 7; Ang: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.5.

8-*Acetoxy-1β,2β-diangeloyloxy-3β,4β-epoxy-bisobola-7(14), 10-diene* (**11**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1250 (OAc); 1720, 1655 (C=CCO$_2$R); MS: M$^+$ *m/e* (rel. int.) 474.262 (7) ($C_{27}H_{38}O_7$); 405 (7) (M − Me$_2$CH=CHCH$_2$); 374 (46) (M − AngOH); 314 (3) (374 − HOAc); 214 (1) (314 − AngOH); 83 (100) ($C_4H_7CO^+$).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-15.8 \quad -16.7 \quad -20.0 \quad -42.5} (c = 0.12).$$

2-*Desoxyliguhodgonal* (**14**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2730, 1700 (CHO); 2080, 1650, 900 (C=CH$_2$); MS: M$^+$ *m/e* (rel. int.) 200, 120 (100) ($C_{14}H_{16}O$); 185 (61) (M − Me); 157 (77) (185 − CO). ^{1}H NMR ($CDCl_3$): 10.27 *s* (CHO); 7.63 *dd* (3-H, *J* = 8, 1.5)″ 7.3 *m* (1,2-H); 8.42 *s* (*br*) and 4.80 *s* (*br*) (12-H); 3.52 *dd* (6-H, *J* = 18.5); 2.94 *m* (6′-H, 9-H); 184 *s* (*br*) (13-H). 2 mg **14** in 1 ml MeOH were reduced with 5 mg NaBH$_4$ (room temp. 15 min). TLC (Et$_2$O–petrol, 1:3) afforded 1 mg **15**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630 (OH); 1655, 905 (C=CH$_2$); MS: M$^+$ *m/e* (rel. int.) 202 (51); 184 (41) (M − H$_2$O); 169 (100) (184 − Me); ^{1}H NMR ($CDCl_3$): 7.21 *dd* (1-H); 7.13*dd* (2-H); 7.06 *d* (*br*) (3-H); 4.69 *s* (14-H); 4.80 *s* (*br*) (12-H); 2.96 *dd* (6-H); 2.62 *dd* (6′-H); 2.89 *m* (9-H); 2.37 *m* (7-H); 1.83 *dd* (13-H) [*J* (Hz) = 1, 2 = 2, 3 = 8; 1, 3 = 1.5; 6, 6′ = 17; 6, 7 = 5; 6′, 7 = 11; 12, 13 = 1].

Senecrassidiol (**16**). Colourless crystals, mp 93–96° (isopropopanol), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630, 3610 (OH); MS: M$^+$ *m/e* (rel. int.)—; 220.183 (3) ($C_{15}H_{24}O$, M − H$_2$O); 205 (8) (220 − Me); 187 (6) (205 − H$_2$O); 123 (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-10.9 \quad -11.7 \quad -13.9 \quad -26.1} (c = 0.23).$$

5 mg **16** in 0.5 ml Ac$_2$O were heated for 3 hr at 70°. TLC (Et$_2$O–petrol, 1:3) afforded 3 mg **17** and 2 mg **18**; **17**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); 1740, 1250 (OAc); MS: M$^+$ *m/e* (rel. int.)—; 262.193 (1) ($C_{17}H_{26}O_2$, M − H$_2$O); 220 (2) (M − HOAc); 123 (100); 43 (45) (MeCO$^+$).

18, colourless oil, MS: M$^+$ *m/e* 322 (0.2); 304 (0.2) (M − H$_2$O); 262 (5) (M − HOAc); 202 (29) (262 − HOAc); 187 (17) (202 − Me); 43 (100) (MeCO$^+$). 5 mg **16** in 1 ml CH$_2$Cl$_2$ were stirred 2 hr with 10 mg pyridinium chlorochromate. TLC (Et$_2$O–petrol, 1:3) afforded 4 mg **19**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); 1715 (CO); to 4 mg **19** in 0.1 ml dimethyl aniline and 0.1 ml AcCl were added. After 20 hr room temp. usual work-up afforded by TLC (Et$_2$O–petrol, 1:3) 4 mg **20**, colourless oil, MS: M$^+$ *m/e* (rel. int.) 278 (0.5); 260 (0.5) (M − H$_2$O); 218 (12) (M − HOAc); 162 (93); 136 (100).

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