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SANDARACOPIMARENE DERIVATIVES FROM *SENECIO SUBRUBRIFLORUS**

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Key Word Index—*Senecio subrubriflorus*; Compositae; diterpenes; sandaracopimarene derivatives; shikimic acid ester; bisabolene derivative.

Abstract—Several new sandaracopimarene derivatives were isolated from *Senecio subrubriflorus*. A triphenyl acetate of shikimic acid and a 4, 7-oxide of bisabolene were also present. The structures were elucidated by high field ^{1}H NMR spectroscopy. The chemistry of this species differs considerably from that of other *Senecio* species.

INTRODUCTION

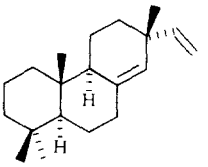
From the large genus *Senecio* more than 100 species have already been investigated chemically. As is apparent from several taxonomic studies [1], this genus is not uniform and a revision of the whole tribe is in progress [1]. We have now studied the constituents of a further species and the results are discussed in this paper.

RESULTS AND DISCUSSION

The roots of *Senecio subrubriflorus* O. Hoffm. afforded α-pinene, caryophyllene, bicyclogermacrene, bisabolene, the sandarocopimardienes **1** [2] and **2** [3], the acetates **4** and **5** [4], the diol **6** [4] and three further derivatives, the senecioates **7** and **9** and the tiglate **8**. The aerial parts gave germacrene D, bicyclogermacrene, curcumene, α-farnesene, eugenol, nerolidol, linolenic acid, the sandaracopimarene derivatives **3** [2], **4**, **5**, **7–10**, **11** [4] and **13** as well as the bisabolenoxide **15** and the triphenyl acetate of shikimic acid (**14a**). The structures of the diterpenes **7–10** were deduced from the ^{1}H NMR spectral data (Table 1), which were similar to those of **11** and the acetate of **12** [4], respectively. The relative position of the ester groups followed from the chemical shifts of H-11 and H-12, while the stereochemistry at C-11 and C-12 was deduced from the couplings $J_{9,11}$ and $J_{11,12}$. The axial orientation of the 8-hydroxyl and the 13-methyl groups followed from the chemical shift of the latter. Oxidation of **12** gave a ketone which was identical with **13**. Its structure, therefore, was also established. The absolute configuration of all diterpenes was probably the same and the optical rotation of **1** was identical to that reported for this diterpene [2]. Furthermore, **13** showed a positive Cotton effect, which also supported the proposed absolute configuration. The structure of **14a**, which was transformed to the ester **14b**, also followed from the spectral data. In the mass spectrum, however, no molecular ion was detected. The $[M - HO_2CCH_2Ph]^+$ peak (*m/z* 406) in the spectrum of **14b** agreed with $C_{24}H_{22}O_6$. Furthermore, a fragment at *m/z* 153 ($C_8H_9O_3$) corresponded to the expected ion formed by loss of phenylacetic acid, its acyloxy radical and phenyl ketene. The latter was most probably due to the *m/z* 118 peak, while the base peak was *m/z* 91 (C_7H_7). The fragment *m/z* 288 was formed by loss of the acid and of phenyl ketene. The presence of three phenyl acetic groups only followed from the integral of the ^{1}H NMR spectrum (Table 2) and the presence of three methylene groups, which gave rise to an AB quartet and two singlets in deuteriochloroform, while in deuteriobenzene two AB quartets were visible. Spin decoupling further allowed the assignment of all protons of the cyclohexene derivative, as homoallylic as well as allylic couplings were present. The couplings agreed with those reported for shikimic acid [5]. Accordingly, the stereochemistry was also solved. The structure of **15** followed from the molecular formula ($C_{15}H_{26}O$), the IR spectrum, which showed the absence of hydroxyl and carbonyl groups, and the ^{1}H NMR spectrum (Table 3). The Eu(fod)$_3$ induced shifts in particular supported the proposed structure, though even at 400 MHz many signals were overlapped multiplets. However, as the methyl singlets were shifted most and the nature of the side-chain clearly followed from the ^{1}H NMR spectrum, **15** seemed to be the most likely structure. This was supported by the ^{13}C NMR signals.

The chemistry of this *Senecio* species differs from those investigated previously. So far only one other species, *S. hypochoerideus* [6], has afforded a sandarocopimarene derivative. Further investigation may show whether more species contain these diterpenes, which so far have been isolated mainly from species belonging to the tribe Calenduleae.

*Part 433 in the series "Naturally Occurring Terpene Derivatives". For Part 432 see Bohlmann, F. and Singh, P. (1982) *Phytochemistry* **21** (in press).



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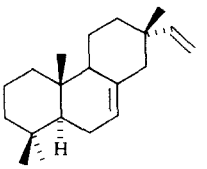

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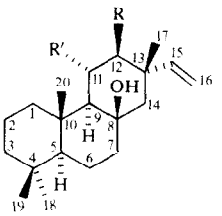
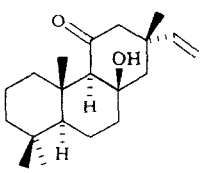


	3	4	5	6	7	8	9	10	11	12
R	H	OAc	OAc	OH	OH	OH	H	H	OH	H
R'	H	OH	H	OH	OSen	OTigl	OSen	OTigl	OAc	OH



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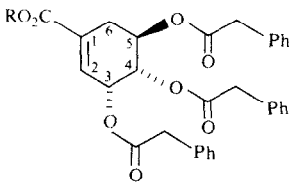
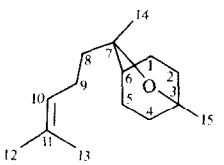


14a R = H

14b R = Me



15

EXPERIMENTAL

The air-dried plant material, collected in February 1981 in Transvaal (voucher 81/137 and 81/256, deposited in the Botanic Research Institute, Pretoria), was extracted with Et_2O–petrol (1:2) and the resulting extracts separated by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the ^1H NMR spectra with those of authentic material. The roots (200 g) afforded 50 mg α-pinene, 5 mg bicyclogermacrene, 5 mg bisabolene, 2 mg caryophyllene, 20 mg **1** [$[\alpha]_D = -16°$ ($CHCl_3$; *c* 1.7)] 5 mg **2**, 1 g **4**, 400 mg **5**, 50 mg **6**, 200 mg **7** (Et_2O–petrol, 1:1, several times), 50 mg **8** (same solvent), 300 mg **9** (Et_2O–petrol, 1:3), while the aerial parts (350 g) gave 20 mg germacrene D, 5 mg bicyclogermacrene, 3 mg curcumene, 5 mg α-farnesene, 4 mg eugenol, 30 mg nerolidol, 20 mg linolenic acid, 10 mg **3**, 25 mg **4**, 20 mg **5**, 3 mg **7**, 1 mg **8**, 30 mg **9**, 3 mg **10** (Et_2O–petrol, 1:3, several times), 20 mg **11**, 5 mg **13**, (Et_2O–petrol, 1:3), 10 mg **14a** (Et_2O–petrol, 3:1, several times) and 50 mg **15** (Et_2O–petrol, 1:20).

8β - Hydroxy - 11α - senecioyloxy - sandaracopimar - 15 - ene (**9**). Colourless crystals, mp 141°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1715, 1645 ($C{=}CCO_2R$), 3080, 915 ($CH{=}CH_2$); MS *m/z* (rel. int.): 388.298 $[M]^+$ (2) ($C_{25}H_{40}O_3$), 370 $[M-H_2O]^+$ (6), 288 $[M-RCO_2H]^+$ (15), 270 $[288-H_2O]^+$ (21), 255 $[270-Me]^+$ (12), 220 $[288-\text{isoprene}]^+$ (12), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (53);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ \text{nm}}{-45 \quad -46 \quad -54 \quad -93} \quad (CHCl_3;\ c = 0.21).$$

8β - Hydroxy - 11α - tiglinoyloxy - sandaracopimar - 15 - ene (**10**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1705, 1645 ($C{=}CCO_2R$), 3080, 915 ($CH{=}CH_2$); MS *m/z* (rel. int.): 388.298 $[M]^+$ ($C_{25}H_{40}O_3$) (1), 370 (6), 288 16), 270 (28), 255 (19), 220 (14), 83 (100), 55 88).

8β, 12β - Dihydroxy - 11α - senecioyloxy - sandaracopimar - 15 - ene (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590

Table 1. ^{1}H NMR spectral data of compounds **7–10** and **13** (400 MHz, $CDCl_3$, TMS as internal standard)

	7†		8†	9	10	13*
H-1α		1.05 *ddd*		1.05 *ddd*	1.04 *ddd*	1.13 *ddd*
H-1β		1.85 *ddd*		1.99 *ddd*	1.85 *ddd*	2.23 *ddd*
H-9	—		—	—	—	2.14 *br s*
H-11α	—		—	—	—	2.44 *br d*
H-11β	5.57 *dd*		5.58 *dd*	5.57 *ddd*	5.61 *ddd*	2.15 *dd*
H-15	5.82 *dd*		5.81 *dd*	5.74 *dd*	5.74 *dd*	5.78 *dd*
H-16*c*		4.99 *dd*		4.82 *dd*	4.82 *dd*	4.90 *d*
H-16*t*		5.01 *dd*		4.87 *dd*	4.85 *dd*	4.91 *d*
H-17		1.30 *s*		1.33 *s*	1.31 *s*	1.35 *s*
H-18		0.88 *s*		0.88 *s*	0.88 *s*	0.87 *s*
H-19		8.85 *s*		0.85 *s*	0.85 *s*	0.87 *s*
H-20	1.11 s		1.12 *s*	1.08 *s*	1.08 *s*	1.24 *s*
OAc	—		—	—	—	—
OCOR	5.61 *qq*		6.86 *qq*	5.60 *qq*	6.81 *qq*	—
	2.19 *d*		1.80 *dq*	2.19 *d*	1.79 *dq*	
	1.91 *d*		1.84 *dq*	1.89 *d*	1.82 *dq*	

*H-12α 2.44 *br d*, H-12β 2.15 *dd* (J = 12.5, 2 Hz); H-14 1.82 *d* and 1.68 *d* (J = 14, 2 Hz).

†H-12α 3.42 *br d*.

J (Hz): 1α, 1β = 13; 1α, 2α = 4; 1α, 2β = 12; 1β, 2α = 2; 1β, 2β = 4; 9, 11β = 10; 11β, 12α = 10; 11β, 12β = 4; 15, 16*c* = 10; 15, 16*t* = 17; 16*c*, 16*t* = 1; OSen: 2′, 4′ = 2′, 5′ = 1.3; OTigl: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.3.

Table 2. ^{1}H NMR spectral data of **14b** (400 MHz, TMS as internal standard)

	$CDCl_3$	+ Eu(fod)$_3$ Δ-values	C_6D_6
H-2	6.72 *ddd*	1.19	6.59 *ddd*
H-3	5.69 *br dd*	0.99	5.79 *br dd*
H-4	5.19 *dd*	1.10	5.30 *dd*
H-5	5.29 *ddd*	1.10	5.49 *ddd*
H-6α	2.35 *dddd*	1.13	2.23 *dddd*
H-6β	2.89 *dddd*	1.01	2.86 *dddd*
OMe	3.77 *s*	0.07	3.29 *s*
$OCOCH_2R$	2.51 *s*, 3.47 *s*	1.12, 0.46	3.24 *s* (2H)
	3.28 *d*		3.34 and 3.28 *d*
	(J = 14.5 Hz)	0.56	
	3.22 *d*		3.20 and 3.13 *d*
Ph	7.35–7.20 *m* (14H)	0.1	7.25–7.05 *m*
	7.13 *br d* (1H)	0.2	

J (Hz): 2, 3 = 4; 2, 6α = 2, 6β = 1.5; 3, 4 = 4; 3, 6α = 3, 6β ~ 1.5; 4, 5 = 8.5; 5, 6α = 6.5; 5, 6β = 5; 6α, 6β = 18.5.

(OH), 1700, 1645 (C=CCO$_2$R), 3080, 915 (CH=CH$_2$); MS *m/z* (rel. int.): 404 [M]$^+$ (0.1), 386.282 [M − H$_2$O]$^+$ ($C_{25}H_{38}O_3$) (2), 304 [M − RCO$_2$H]$^+$ (9), 286 [304–H$_2$O]$^+$ (11), 271 [286 − Me]$^+$ (7), 218 [286 − isoprene]$^+$ (37), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (61).

8β, 12β - *Dihydroxy* - 11α - *tiglinoyloxy* - *sandaracopimar* - 15 - *ene* (8). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1700, 1640 (C=CCO$_2$R), 3080, 915 (CH=CH$_2$); MS *m/z* (rel. int.): 404 [M]$^+$ (0.1), 386.282 [M − H$_2$O]$^+$ ($C_{25}H_{38}O_3$) (2), 304 (8), 286 (12), 271 (8), 218 (40), 83 (100).

8β - *Hydroxy* - *sandaracopimar* - 15 - *en* - 11 - *one* (13). Colourless crystals, mp 207°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1710 (C=O), 3080, 915 (CH=CH$_2$); MS *m/z* (rel. int.): 304.240 [M]$^+$ ($C_{20}H_{32}O_2$) (41), 286 [M − H$_2$O]$^+$ (19), 271 [286 − Me]$^+$

Table 3. ^1H and ^{13}C NMR spectral data of compound **15** (400 and 270 MHz respectively, TMS as internal standard)

	^1H NMR			^{13}C NMR	
	$CDCl_3$	Δ‡	C_6D_6		C_6D_6
H-1		0.12	1.38 *m*	C-1	23.0 *t**
H-2	1.51 *m*	0.24	1.95 *m*	C-2	32.2 *t*†
H-4	1.65 *m*	—	1.8–1.6 *m*	C-3	69.2 *s*
H-5		—	—	C-4	32.0 *t*†
H-6		—	—	C-5	23.2 *t**
H-8	1.98 *m*	0.13	2.12 *m*	C-6	31.1 *d*
H-9	1.91 *m*	0.14	2.03 *m*	C-7	75.3 *s*
H-10	5.13 *tqq*	0.04	5.29 *tqq*	C-8	42.3 *t*
H-12	1.61 *br s*	0.03	1.63 *br s*	C-9	23.8 *t*
H-13	1.68 *br s*	0.01	1.73 *br s*	C-10	125.7 *d*
H-14	1.05 *s*	0.31	1.15 *s*	C-11	130.7 *s*
H-15	1.23 *s*	0.28	1.29 *s*	C-12	17.6 *q*
				C-13	25.8 *q*
				C-14	25.8 *q*
				C-15	27.9 *q*

*†Signals with similar sign may be interchangeable.
‡Δ-Values after addition of $Eu(fod)_3$.
J (Hz): 9, 10 = 7; 10, 12 = 10, 13 = 1.3.

(17), 236 $[M-\text{isoprene}]^+$ (53), 221 $[236-Me]^+$ (14), 153 (100);

$$[\alpha]^{\lambda}_{24°} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+4 \quad +5 \quad +5 \quad +9} \quad (CHCl_3;\ c = 0.23).$$

CD (MeCN) $\Delta\epsilon_{307} + 0.25$. **12** (5 mg) in 2 ml CH_2Cl_2 was stirred for 6 hr with 20 mg pyridine dichromate. TLC (Et_2O–petrol, 1:3) afforded 3 mg **13**, identical with the natural compound.

Shikimic acid triphenylacetate (**14a**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600–2700, 1700 (CH_2H), 1750 (CO_2R); MS *m/z* (rel. int.): 392.128 $[M-RCO_2H]^+$ (1) ($C_{23}H_{20}O_6$), 274 $[392-PhCH{=}C{=}O]^+$ (1), 139 $[274-O_2CCH_2Ph]^+$ (42), 91 $[C_7H_7]^+$ (100). To 10 mg **14a** excess of CH_2N_2 in Et_2O was added. TLC (Et_2O–petrol, 1:1) afforded 8 mg **14b**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750 (CO_2R), 1730 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 406.142 $[M-RCO_2H]^+$ (10) ($C_{24}H_{22}O_6$), 374 $[406-MeOH]^+$ (0.2), 288 $[406-PhCH{=}C{=}O]^+$ (6), 153 $[288-O_2CCH_2Ph]^+$ (15), 118 $[PhCH{=}C{=}O]^+$ (38), 91 $[C_7H_7]^+$ (100);

$$[\alpha]^{\lambda}_{24°} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-81 \quad -85 \quad -98 \quad -176} \quad (CHCl_3;\ c\ 0.79).$$

3, 7 - *Oxidobisabol* - 10 - *ene* (**15**). Colourless oil, $bp_{0.1}$ 120°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1500, 1490, 1475, 1410, 1250, 1100, 1090, 1015; MS *m/z* (rel. int.): 222.198 $[M]^+$ (3) ($C_{15}H_{26}O$), 204 $[M-H_2O]^+$ (17), 139 $[M-CH_2CH_2CH{=}CMe_2]^+$ (100):

$$[\alpha]^{\lambda}_{24°} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-8.4 \quad -8.7 \quad -10.0 \quad -16.9} \quad (CHCl_3;\ c = 4.06).$$

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