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TWO TRICYCLIC SESQUITERPENES FROM *SENECIO ANTEUPHORBIUM* AND *URSINIA NANA**

FERDINAND BOHLMANN, JÜRGEN ZIESCHE and RAJINDER K. GUPTA

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, W. Germany

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Key Word Index—*Senecio anteuphorbium*; *Ursinia nana*; Compositae; sesquiterpenes; new carbon skeleton.

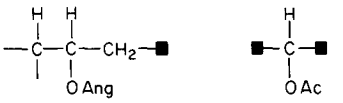
Abstract—The aerial parts of *Senecio anteuphorbium* afforded a new sesquiterpene diester, its structure being elucidated by extensive NMR investigations of the natural compound and of several derivatives. One of the derivatives was isolated from the roots of *Ursinia nana*. These two compounds together with 8α-hydroxy-presilphiperfolene, are the first derivatives of a new type of sesquiterpene, which is the precursor of a new group of tricyclic sesquiterpenes.

INTRODUCTION

During our earlier investigations of some succulent *Senecio* species, we studied the constituents of *S. anteuphorbium* [1]. The structure of one sesquiterpene could not then be elucidated. We have therefore isolated this compound again to establish its structure.

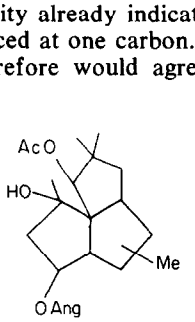
RESULTS AND DISCUSSION

From the aerial parts of *Senecio anteuphorbium* Sch. Bip., in addition to compounds reported previously [1], we have isolated a crystalline angelate, which further contained an hydroxy and an acetate group, as deduced from the IR and ^{1}H NMR spectrum (Table 1). In the mass spectrum, no molecular ion could be observed. However, the fragments obtained clearly showed that the molecular formula must be $C_{22}H_{34}O_5$. Elimination of acetic acid gave *m/z* 318 and of angelic acid *m/z* 278 followed by loss of acetic acid affording *m/z* 218, which by loss of water gave *m/z* 200. Since the ^{1}H NMR as well as the ^{13}C NMR spectrum indicated the absence of olefinic carbons in the sesquiterpene moiety, a tricyclic compound must be present. Partial hydrolysis gave a dihydroxy angelate, which on oxidation with pyridine chlorochromate yielded a ketone, which was identical with a compound isolated in minute amounts from the roots of *Ursinia nana*, together with other constituents [2]. Lithium aluminium hydride reduction gave a triol, while acetylation with acetyl chloride in the presence of dimethyl aniline led to a diacetate. The new acetate group was obviously tertiary, based on the ^{1}H NMR spectrum. The ^{1}H NMR spectrum of the natural compound showed, in addition to the signals of the acetate and angelate groups, three methyl singlets, one being narrowly split by a *W*-coupling, and a methyl doublet. Furthermore, two downfield signals could be visualized, a singlet at δ 4.61 and a threefold doublet at δ 5.50, which was coupled with a two-proton doublet at δ 1.98 and a multiplet at δ 1.56. Since in the spectrum of the diol the singlet was shifted upfield, the relative position of the ester group in the partial structures A and B could be assigned:

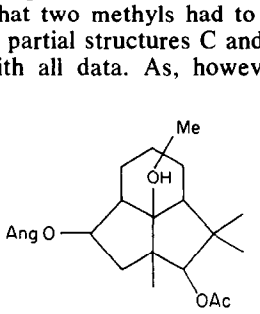


A B

Relatively little further information could be obtained from the ^{13}C NMR spectrum (Table 2). However, the carbon bearing the tertiary hydroxyl was at an extremely low field (δ 93.8), indicating it has a central position in the molecule. The presence of five doublets and three singlets still allowed the formulation of several structures, though the observed multiplicity already indicated that two methyls had to be placed at one carbon. The partial structures C and D therefore would agree with all data. As, however,



C



D

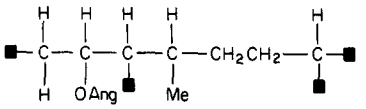
*Part 411 in the series "Naturally Occurring Terpene Derivatives". For Part 410 see Bohlmann, F. and Wegner, P. (1982) *Phytochemistry* **21**, 1175.

Table 1. ^{1}H NMR spectral data of compounds **2–6** (400 MHz, TMS as internal standard)

	2		**3**		**4**	**5**		**6**	
	$CDCl_3$	C_6D_6–$CDCl_3$	$CDCl_3$	C_6D_6	$CDCl_3$	$CDCl_3$	C_6D_6	$CDCl_3$	C_6D_6
H-1	1.56 m	1.56 dd	1.42 dd	1.23 dd		2.19 dd	2.44 dd	1.54 dd	1.24 dd
H-2	5.50 ddd	5.53 ddd	5.45 ddd	5.53 ddd	4.52 ddd	5.53 ddd	5.65 ddd	5.47 ddd	5.45 ddd
H-3α	1.98 d	1.98 dd	1.99 dd	1.95 dd	1.93 dd	2.01 d	2.12 dd	2.12 dd	2.03 dd
H-3β		2.07 ddq	2.26 ddd	2.47 ddd	2.05 ddd		2.21 ddd	2.26 ddd	2.50 ddd
H-5	4.61 s	4.52 s	3.35 s	3.37 d	3.35 d	4.49 s	4.53 s	—	—
H-7	1.88 dd	1.74 dd	1.78 dd	1.41 dd	1.69 dd	2.52 dd	2.57 dd	2.01 dd	1.59 dd
H-9	1.56 m	1.25 qddd	1.54 qddd	1.19 qddd	1.47 qddd			1.60 qddd	1.22 qddd
H-10α		1.42 dddd	1.68 dddd	1.35 dddd		1.62 dddd		1.79 dddd	1.40 dddd
H-10β		0.91 dddd	1.05 dddd	0.76 dddd		1.48 dddd		1.15 dddd	0.80 dddd
H-11α		0.99 dddd	1.32 dddd	0.93 dddd		1.40 dddd		1.57 dddd	1.13 dddd
H-11β		1.34 dddd	1.67 dddd	1.26 dddd		1.74 dddd		1.84 dddd	1.37 ddd
H-12	1.32 s	0.99 d	1.24 d	0.83 d	1.17 d	1.37 sbr	0.94 d	1.38 d	0.97 d
H-13	1.27 s	1.05 s	1.24 s	1.04 s	1.23 s	1.25 s	1.04 s	1.36 s	1.50 s
H-14	1.18 s	1.07 s	1.21 s	1.29 s	1.20 s	1.07 s	1.04 s	1.24 s	1.15 s
H-15	0.97 d	0.90 d	0.97 d	0.92 d	1.03 d	1.00 d	1.01 d	1.03 d	0.97 d
OCOR	6.02 qq	5.74 qq	6.05 qq	5.71 qq		6.05 qq	5.68 qq	6.06 qq	5.76 qq
	1.98 dq	1.93 dq	1.97 dq	1.98 dq	—	1.96 dq	1.94 dq	1.96 dq	1.98 dq
	1.89 dq	1.88 dq	1.87 dq	1.88 dq	—	1.85 dq	1.82 dq	1.86 dq	1.88 dq
OH	3.23 sbr	3.08 sbr	3.05 sbr	2.40 sbr	2.94 sbr	—	—	2.37 sbr	1.64 sbr
			3.55 d	3.29 d	3.54 d	—	—		
OAc	2.11 s	1.60 s	—	—	—	2.07 s	1.82 s	—	—
						2.00 s	1.70 s		

J (Hz): 1, 2 = 2.5; 1, 9 = 12; 2, 3α = 7; 2, 3β = 7; 3α, 3β = 11; 3β, 12 = 1; 7, 11α = 11; 7, 11β = 7; 9, 10α = 3; 9, 10β = 11; 9, 15 = 7; 10α, 10β = 13; 10α, 11α = 3; 10α, 11β = 2; 10β, 11α = 11; 10β, 11β = 3; 11α, 11β = 12.

seven asymmetric centres are present, X-ray analysis seems to be necessary. Unfortunately all attempts in this direction were unsuccessful, though two different groups have tried to solve the problem. We therefore again turned back to detailed NMR studies. At 400 MHz in a mixture of C_6D_6–$CDCl_3$ all signals were assigned by spin decoupling, which was further established with the complete assignment of the signals in the spectra of the diol, the diacetate and the corresponding ketone (Table 1). Starting with the proton under the angelate residue, spin decoupling led to the sequence **E**:

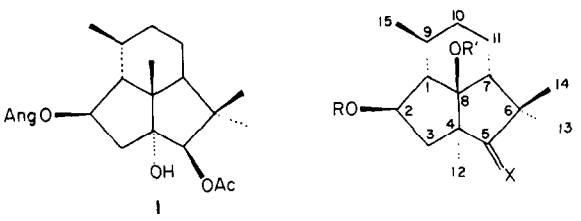


E

Together with the partial structure B, the already proposed dimethyl grouping and the last methyl, which also needed to be linked to carbon, all carbons were assigned. The only possible structures therefore were **1** and **2**. As, however, acetylation led to a clear downfield shift of the signals of H-1 and H-7, structure **1** was ruled out. Also, the ^{13}C NMR signal at δ 93.8 agreed much better with structure **2**. The stereochemistry of **2** was deduced from the couplings observed when a model was inspected. The small coupling $J_{1,2}$ required a β-orientation of the angelate residue, while the large coupling $J_{1,9}$ needed a 9β-methyl group. Also, the couplings of H-9, H-10 and H-11 agreed with the presence of a six-membered ring present in a chair conformation, $J_{7,11\alpha}$ being

Table 2. ^{13}C NMR signals of compounds **2** and **3** ($CDCl_3$, TMS as internal standard)

	2	Δ	3
C-1	55.7 d	0.63	57.2 d
C-2	83.5 d	0.89	84.2 d
C-3	39.4 t	0.99	38.4 t
C-4	58.1 s	0.95	57.9 s
C-5	87.4 d	1.59	86.9 d
C-6	51.2 s	0.79	51.6 s
C-7	53.1 d	0.53	53.0 d
C-8	93.8 s	0.56	95.5 s
C-9	33.9 d	0.27	33.9 d
C-10	35.5 t	0.32	35.6 t
C-11	26.3 t	0.24	26.1 t
C-12	21.4 q	0.24	21.3 q
C-13 } C-14 }	27.4 q	0.40	27.2 q
C-15	29.7 q	0.67	29.8 q
C-1'	167.5 s	1.76	167.8 s
C-2'	128.4 s	0.88	128.2 s
C-3'	136.8 d	0.40	137.3 d
C-4'	15.7 q	0.30	15.7 q
C-5'	20.6 q	0.47	20.5 q
OAc	169.6 s	4.41	—
	20.9 q	1.78	—



1

	2	3	4	5	6
R	Ang	Ang	H	Ang	Ang
R'	H	H	H	Ac	H
X	βOAc_1H	βOH_1H	H_2	βOAc_1H	=O

large. The β-orientation of the acetoxy group and the presence of a 4α-methyl could be assigned only indirectly. When the chemical shifts of H-12 in the spectra of **2** and **3** were compared, no drastic shift differences were observed, as would occur if the acetoxy group was α-orientated. If, however, the methyl group was β-orientated, the observed coupling $J_{1,2}$ would not agree with the angles shown in a model either with a β or with an α-angelate residue. The ^{13}C NMR spectra of **2** and **3** (Table 2) were also in agreement with the proposed structure. The observed shifts after addition of $Yb(fod)_3$ also supported the assignments. As the acetate carbonyl was most readily complexed by the shift reagent, the relative small shift of C-12 further supported the proposed β-orientation of the acetate group. As **2** has been transformed to **6**, the structure of the ketone isolated from *Ursinia nana* was also established. **2** is 5β-acetoxy-2β-angeloyloxy-8β-hydroxypresilphiperfolane and **6** is 2β-angeloyloxy-presilphiperfol-5-one, derivatives of the common precursor of several tricyclic sesquiterpenes [3], which have been isolated in the last four years.

EXPERIMENTAL

The fresh aerial parts (800 g) of *S. anteuphorbium* (grown from cuttings from Kew Gardens) were extracted with Et_2O–petrol, 1 : 2, and the resulting extract was separated by column chromatography (Si gel) and the fraction obtained with Et_2O–petrol, 1 : 1, was further separated by TLC (Si gel). Finally, 60 mg **2** were obtained, colourless crystals, mp 75–75.5° (isopropanol), IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3590 (OH), 1750, 1230 (OAc), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 318.219 $[M-HOAc]^+$ (0.05) ($C_{20}H_{30}O_3$), 300 $[318-H_2O]^+$ (0.3), 278 $[M-HOAng]^+$ (1.5), 260 $[278-H_2O]^+$ (4), 218 $[278-HOAc]^+$ (49), 203 $[218-Me]^+$ (11), 200 $[218-H_2O]^+$ (10), 185 $[200-Me]^+$ (8), 175 $[203-CO]^+$ (13), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (75).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 548 \quad 436 \text{ nm}}{+11.0 \quad +11.3 \quad +13.0 \quad +23.5} \quad (c = 0.63, CHCl_3).$$

To 20 mg **2** in 1 ml MeOH, 20 mg KOH in 0.1 ml H_2O were added. After 2 hr standing at room temp. TLC (Et_2O–petrol, 1:1) 15 mg **3** were obtained, colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600, 3380 (OH), 1710, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 336 $[M]^+$ (0.1), 318 $[M-H_2O]^+$ (0.1), 236 $[M-HOAng]^+$ (6), 218 $[236-H_2O]^+$ (58), 203 $[218-Me]^+$ (12), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (88). To 5 mg **2** in 1 ml Et_2O, 10 mg $LiAlH_4$ were added. After 5 min, dil. H_2SO_4 was added. TLC (Et_2O) afforded 3 mg **4**, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3620, 3380 (OH); MS (CI,

iso-butane) *m/z* (rel. int.). 255 $[M+1]^+$ (1), 237 $[255-H_2O]^+$ (3), 219 $[237-H_2O]^+$ (100), 201 $[219-H_2O]^+$ (10).

To 5 mg **2** in 0.1 ml dimethylaniline, 0.1 ml AcCl were added. After 5 days standing at room temp. TLC (Et_2O–petrol, 1:3) 5 mg **5** were obtained, colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1730, 1260, 1245 (OAc), 1710, 1650 ($C{=}CCO_2R$); MS (CI, *iso*-butane) *m/z* (rel. int.): 361 $[M+1-HOAc]^+$ (31), 301 $[361-HOAc]^+$ (37), 261 $[361-HOAng]^+$ (80), 219 $[261-ketene]^+$ (48), 201 $[261-HOAc]^+$ (100). 15 mg **3** in 2 ml CH_2Cl_2 were stirred for 12 hr with 20 mg pyridine chlorochromate. TLC (Et_2O–petrol, 1:3) afforded 10 mg **6**, which was identical with the ketone isolated from the roots (130 g) of *Ursinia nana* from the fraction with Et_2O–petrol, 1:3, (3 mg). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1750, 1235 (OAc), 1715, 1645 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 334.214 $[M]^+$ (0.5) ($C_{20}H_{30}O_4$), 234 $[M-HOAng]^+$ (25), 219 $[234-Me]^+$ (9), 191 $[219-CO]^+$ (22), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (95).

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