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FOUR GUAIANOLIDES, A EUDESMANOLIDE AND A GERMACRANOLIDE FROM *URSINIA SAXATILIS**

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Key Word Index—*Ursinia saxatilis*; Compositae; sesquiterpene lactones; guaianolides; eudesmanolide, germacranolide.

Abstract—An investigation of *Ursinia saxatilis* afforded in addition to known compounds a new eudesmanolide derived from ursialpinolide, a germacranolide related to haageanolide and four guaianolides. The structures were elucidated by spectroscopic methods and some chemical transformations, whilie the stereochemistry of the main constituent was established by X-ray analysis. The relationships of the new sesquiterpene lactones to those isolated before from *Ursinia* species and the chemotaxonomy are discussed briefly.

INTRODUCTION

The placement of the South African genus *Ursinia* has been in doubt for a long time. While Hoffmann[1] had placed it in the Arcoteae, more recently Merxmüller[2] suggested that this genus might be a very isolated member of the Anthemideae or might even merit subtribal rank of its own. Finally a new tribe Ursininae was proposed[3] on the basis of the Astereae type pollen grains, the broadly ovate anther-appendages and the large squamose scales of the pappus. The chemical constituents so far examined show close relationships to other woody South African genera[4], all so far placed in the Anthemideae. One of these genera, *Athanasia*, seems to be taxonomically close to *Pentzia*, which belongs to the Anthemideae. No indications so far are apparent from the chemical data of any relationship with the Arctoteae. We now have investigated *Ursinia saxatilis* N. E. Br. Again the typical furanosequiterpene **1** was present. Furthermore several sesquiterpene lactones were isolated, 6 of them for the first time.

RESULTS AND DISCUSSION

The aerial parts of *Ursinia saxatilis* afforded lupeol and its Δ-12,13 isomer, taraxasteryl acetate, the furanosesquiterpene **1**[4] and ursialpinolide (**2**)[4]. Furthermore 6 new sesquiterpene lactones were isolated, the eudesmanolide **3**, the germacranolide **7** and the guaianolides **8–11**. **3** obviously was closely related to **2**. The ^{1}H NMR spectral data therefore were close to those of **2** (Table 1). However, the H-3 signal was at somewhat lower fields and a singlet at 3.49 ppm indicated the presence of a methyl ether. Furthermore some signals were slightly shifted when compared to those of **2**. As, however, the general coupling pattern was identical in both lactones, a 3-methoxy-4-hydroxy derivative of **2** must be proposed. The stereochemistry at C-3 could not be deduced directly from the ^{1}H NMR spectrum of **3**. Acid catalysed methanolysis of **2**, however, afforded in addition to two isomeric lactones and an isomerized aromatic compound a OMe derivative, which was identical with the natural product. From the ^{1}H NMR spectra (Table 1) of the natural lactone and the reaction products the structures **3–6** could be proposed. In the spectrum of **3** the absence of an allylic coupling supported a 3β-methoxy group, if models were considered, while the similarity of the other signals with those of **4** indicated the presence of epimers. Consequently the third isomer most likely was **5**. The 1α-orientation of the methoxy group was supported by the downfield shift of the H-9α signal and the absence of an allylic coupling. The structure of **6** clearly followed from the presence of aromatic methyl signals. The formation of **3–6** could be explained, if protonation of the epoxide led to the ion **12**, which by attack of methanol at C-3 would lead to **3** and **4**, while addition at C-1 could be sterically influenced by the C-10 methyl group. Elimination would afford a dienyl cation, which could easily rearrange to **6**.

The ^{1}H NMR spectral data of the diacetate **7** (Table 2) showed that a *trans,trans*-germacranolide was present. Spin decoupling allowed the assignment of all signals. The stereochemistry at C-3, C-6 and C-9 was deduced from the couplings observed and by comparing the data with those of haageanolide acetate as well as with those of germacranolides with a 3β-acyloxy group. Obviously **7** was present in the usual preferred conformation with the methyls at C-4

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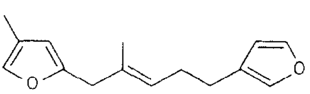
*Part 407 in the series "Naturally Occurring Terpene Derivatives". For Part 406 see Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 1155.

Table 1. ^{1}H NMR spectral data of compounds **3**–**6** (400 MHz, $CDCl_3$, TMS as internal standard)

	3	**4**	**4**(C_6D_6)	**5**	**6**
H-1	5.73 *d*	5.54 *s*	5.15 *d*	3.06 *d*	—
H-2	5.81 *dd*		5.39 *d*	5.97 *dd*	6.95 *s*
H-3	3.24 *d*	3.74 *s*	3.58 *dd*	5.73 *d*	
H-5	1.70 *dd*	1.67 *dd*	1.33 *brd*	2.00 *m*	—
H-6α	2.28 *brdd*	2.26 *brdd*	2.04 *brdd*		2.85 *m*
H-6α	1.40 *ddd*	1.35 *ddd*	1.15 *ddd*	1.4 *m*	
H-7	3.05 *ddddd*	3.12 *brddd*	2.29 *brddd*	2.99 *brddd*	3.43 *ddddd*
H-8	4.51 *ddd*	4.54 *brdd*	3.80 *brdd*	4.59 *brdd*	5.04 *ddd*
H-9α	1.60 *dd*	1.59 *dd*	1.00 *dd*	2.35 *dd*	3.09 *dd*
H-9β	2.16 *brd*	2.20 *brd*	1.80 *brd*	1.77 *dd*	2.86 *dd*
H-13	6.13 *d*	6.18 *brs*	6.18 *brs*	6.15 *brs*	6.22 *d*
H-13′	5.63 *d*	5.64 *brs*	5.00 *brs*	5.60 *bts*	5.49 *d*
H-14	1.08 *s*	1.10 *s*	0.92 *s*	0.98 *s*	2.27 *s*
H-15	1.14 *s*		0.98 *s*	1.12 *s*	2.23 *s*
OMe	3.49 *s*	3.51 *s*	3.23 *s*	3.41 *s*	—

J(Hz): Compounds **3** and **4**: 1, 2 = 9; 2, 3 = 4.5; 5, 6α = 1.5; 5, 6β = 12; 6α, 7 = 8; 6β, 7 = 12; 6α = 13; 7, 8 = 5; 7, 13 ~ 1; 8, 9α = 5; 8, 9β ~ 1; 9α, 9β = 15 (compound **4**: 1, 3 = 2; 2, 3 = 1.5); compound **5**: 1, 2 = 5; 2, 3 = 10; 6α, 7 = 5; 6β, 7 = 12; 7, 8 = 6; 8, 9α = 5; 8, 9β = 3; 9α, 9β = 15; compound **6**: 6α, 7 ~ 6; 6β, 7 = 11; 7, 8 = 5; 7, 13 = 2.7; 7, 13′ = 2.5; 8, 9α = 8.5; 8, 9β = 5; 9α, 9β = 15.5.



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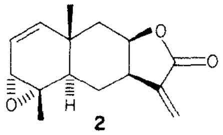

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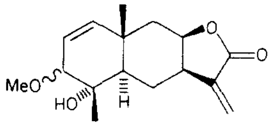
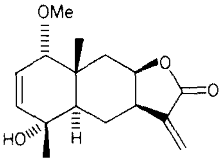


3 β-OMe

4 α-OMe



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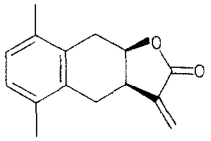

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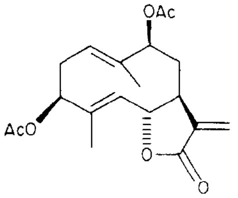

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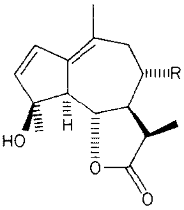
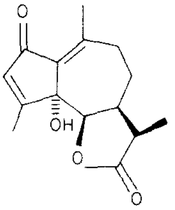


8 R=H

9 R=OMebu

10 R=OiVal



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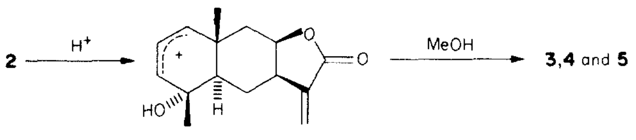

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and C-10 orientated parallel at the same side of the 10-membered ring. The ^{1}H NMR spectral data of the main constituent, the guaianolide **8** (Table 2) showed the presence of an olefinic methyl, a tertiary and a secondary one. The downfield shift of one of the olefinic signals further indicated a conjugated diene system, while the corresponding coupling indicated a double bond in a 5-membered ring. As the proton under the lactone oxygen was a double doublet with large couplings, the presence of a guaianolide was obvious. The methyl doublet indicated a 11, 13-dihydro lactone. The stereochemistry at C-11 followed from the coupling $J_{7,11}$, as lactones with a 11α-methyl group normally show couplings in the range of 10–12 Hz. The configuration at C-4 only could be proposed from the chemical shift of H-15, which seemed to be influenced by the lactone oxygen. Therefore the stereochemistry was established by X-ray analysis (see Fig. 1). The ^{1}H NMR spectral data of **9** and **10** (Table 2), which could not be separated clearly, showed that 8α-acyloxy derivatives of **8** were present. The nature of the ester residue followed from the typical ^{1}H NMR signals, while the stereochemistry at C-8 could be deduced from the couplings observed. The ^{1}H NMR spectrum of **11** (Table 2) clearly indicated the presence of a derivative of achillin[5]. From the missing coupling $J_{5,6}$ the position of the additional hydroxy group was deduced, its α-orientation followed from the downfield shift of the H-7 signal if compared with that in achillin, while the stereochemistry at C-6 and C-11 again was indicated

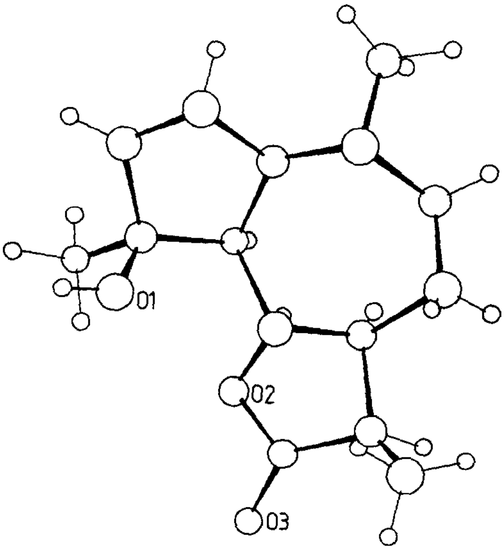


Fig. 1. Stereoscopic view of **8**.

Table 2. ^{1}H NMR spectral data of compounds **7–11** (400 MHz, $CDCl_3$, TMS as internal standard)

			8				
		7	$CDCl_3$	$CDCl_3$–C_6H_6 (1:1)	**9**	**10**	**11**
H-1		5.25 *brdd*	—	—	—		—
H-2	α	2.58 *ddd*	6.44 *d*	6.28 *d*	6.43 *d*		—
	β	2.35 *ddd*					
H-3		5.19 *dd*	5.86 *d*	5.78 *d*	5.90 *d*		6.15 *q*
H-5		4.82 *brd*	2.68 *brd*	2.42 *brd*	2.66 *brd*		—
H-6		4.58 *dd*	4.32 *dd*	4.12 *dd*	4.19 *dd*		4.46 *d*
H-7		2.70 *ddddd*	2.32 *dddd*	1.79 *dddd*	2.36 *m*		2.95 *dddd*
H-8	α	2.18 *dd*	1.76 *dddd*	1.25 *dddd*	4.76 *ddd*		1.84 *dddd*
	β	1.93 *ddd*	1.37 *dddd*	0.97 *dddd*			1.20 *dddd*
H-9		5.16 *dd*	2.23 *m*	1.89 *m*	α 2.36 *m*		3.02 *dd*
					β 1.5 *m*		2.05 *dd*
H-11		—	2.67 *dq*	2.30 *dq*	2.79 *dq*		2.84 *dq*
H-13		6.25 *d*	1.17 *d*	0.87 *d*	1.14 *d*		1.15 *d*
H-13′		5.58 *d*					
H-14		1.50 *brs*	1.86 *brs*	1.68 *brs*	1.90 *brs*		2.37 *s*
H-15		1.73 *brs*	1.54 *s*	1.45 *s*	1.53 *s*		2.10 *d*
OCOR		2.06 *s*	—	—	2.3 *m*	2.18 *d*	—
		2.11 *s*	—	—	1.58 *ddq*	2.12 *m*	
					1.43 *ddq*	0.97 *d*	
					0.92 *t*		
					1.14 *d*		

J(Hz): Compound **7**: 1, 2α = 4; 1, 2β = 12; 2α, 2β = 13; 2α, 3α = 5; 2β, 3α = 11; 5, 6 = 9; 6, 7 = 10; 7, 8α ~ 1; 7, 8β = 10; 7, 13 = 3.5; 7, 13′ = 3; 8α, 8β = 13; 8α, 9α = 3; 8β, 9α = 10; compounds **8–10**: 2, 3 = 5.5; 5, 6 = 10; 6, 7 = 10.5; 7, 8α = 2; 7, 8β = 12; 7, 11 = 11, 13 = 7.5; 8α, 8β = 14; 8α, 9α ~ 5; 8β, 9α ~ 10; (compounds **9** and **10**: 7, 8β = 8β, 9α = 11; 8β, 9β = 2.5); compound **11**: 3, 15 = 1.3; 6, 7 = 4; 7, 8α = 6; 7, 8β = 12; 7, 11 = 11, 13 = 7; 8α, 8β = 8α, 9α ~ 1; 8α, 9β = 8; 8β, 9α = 12; 8β, 9β ~ 1; 9α, 9β = 14.

by the corresponding couplings. These results on this species again support the placement of the genus *Ursinia* near to the woody South African species of the tribe Anthemideae, either as a subtribe of the latter or as a distinct tribe.

EXPERIMENTAL

The air dried plant material (voucher 81/118, deposited in the National Botanic Research Institute, Pretoria) was extracted with Et_2O-petrol (1:2), and the resulting extracts separated by CC (Si gel) and repeated TLC (Si gel). Known compounds were identified by comparing their ^1H NMR spectra with those of authentic compounds. The aerial parts (100 g) afforded 20 mg lupeol and its Δ-12,13 isomer, 15 mg taraxasteryl acetate, 10 mg **1** (Et_2O-MeOH-CH_2Cl_2, 5 : 1 : 45), while the roots (30 g) gave 60 mg **2**, 2 mg **7** and 1 mg **9** and **10** (Et_2O-C_6H_6-CH_2Cl_2, 2 : 2 : 9).

4α-Hydroxy-3α-methoxy-3,4-desoxo-ursialpinolide (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3575 (OH), 1780 (γ-lactone); MS *m/z* (rel int): 278.152 $[M]^+$ (4) ($C_{16}H_{22}O_4$), 248 $[M-CH_2O]^+$ (9), 230 $[248-H_2O]^+$ (22), 215 $[230-Me]^+$ (10), 72 $[C_4H_7O]^+$ (100).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{-137\quad -142\quad -164\quad -285}\ (c=0.2,\ CHCl_3)$$

(a) 15 mg **2** in 10 ml MeOH containing 0.03 ml H_2SO_4 after standing 50 min at room temp. was neutralized and extracted with Et_2O. TLC (Et_2O-CH_2Cl_2, 1 : 1) afforded 2 mg **3**, 2 mg **4** and 6 mg **5**.

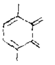
(b) 7 mg in 10 ml MeOH in the presence of 0.15 ml H_2SO_4 and warming for 3 min at 70° afforded after TLC (CH_2Cl_2) 1.3 mg **6**.

4: Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3610 (OH), 1775 (γ-lactone); MS *m/z* (rel int): 278.152 $[M]^+$ (4) ($C_{16}H_{22}O_4$), 246 $[M-MeOH]^+$ (1), 228 $[246-H_2O]^+$ (1), 71 $[C_4H_7O]^+$ (100).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{+185\quad +187\quad +194\quad +236}\ (c=0.2,\ CHCl_3)$$

5: Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel int): 278.152 $[M]^+$ (1) ($C_{16}H_{22}O_4$), 260 $[M-H_2O]^+$ (3), 246 $[M-MeOH]^+$ (1), 228 $[246-H_2O]^+$ (4), 213 $[228-Me]^+$ (3), 114 (100), 71 (50).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{+129\quad +154\quad +174\quad +323}\ (c=0.6,\ CHCl_3)$$

6: Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1780 (γ-lactone); MS *m/z* (rel int): 228.115 $[M]^+$ (70) ($C_{15}H_{16}O_2$), 200 $[M-CO]^+$ (10), 132 [ $]^+$ (100), 117 $[132-Me]^+$ (40).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{+49\quad +61\quad +68\quad +122}\ (c=0.13,\ CHCl_3)$$

3β-Acetoxyhaageanolide acetate (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1770 (γ-lactone), 1740, 1235 (OAc); MS *m/z* (rel int): 306 $[M-\text{ketene}]^+$ (0.1), 289.144 $[M-OAc]^+$ (23) ($C_{17}H_{21}O_4$), 247 $[306-OAc]^+$ (15), 229 $[289-HOAc]^+$ (15), 81 (100).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{+53\quad +59\quad +63\quad +122}\ (c=0.2,\ Et_2O)$$

Desacetoxymatricin (**8**). Colourless crystals, mp 154° (Et_2O), IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3590 (OH), 1790 (γ-lactone); MS *m/z* (rel int): 248.144 $[M]^+$ (48) ($C_{15}H_{20}O_3$), 233 $[M-Me]^+$ (100), 215 $[233-H_2O]^+$ (39), 187 $[213-CO]^+$ (38).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{+26\quad +29\quad +35\quad +72}\ (c=0.4,\ Et_2O)$$

X-ray analysis of **8**. Single crystals were orthorhombic, space group $P_{2_12_12_1}$ with $a = 14.1566$, $b = 10.388$ and $c = 9.042$ Å. The intensity data were measured on Syntex P2 diffractometer (CuK_α radiation). The structure was solved with MULTAN. Detailed results will be published elsewhere.

8α-(2-Methylbutyryloxy)- and isovaleryloxy)-desacetoxymatricin (**9** and **10**). Colourless gum, which could not be separated, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3560 (OH), 1795 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel int): 348 $[M]^+$ (0.1), 246.126 $[M-HO_2CR]^+$ (39) ($C_{15}H_{18}O_3$), 231 $[246-Me]^+$ (100), 228 $[246-H_2O]^+$ (10), 218 $[246-CO]^+$ (6), 201 $[218-OH]^+$ (9), 200 $[228-CO]^+$ (11), 185 $[200-Me]^+$ (20), 173 $[201-CO]^+$ (44). $[\alpha]_D$ positive.

5α-Hydroxy achillin (11). Colourless gum, IR ν_{max}^{CCl}, cm^{-1}: 3600 (OH), 1800 (γ-lactone), 1710 (C=CCO); MS: *m/z* (rel int): 262.121 $[M]^+$ (33), ($C_{15}H_{18}O_4$), 244 $[M-H_2O]^+$ (20), 218 $[M-CO_2]^+$ (61), 203 $[218-{}^{\cdot}Me]^+$ (25), 189 $(218-{}^{\cdot}CHO)^+$ (100).

$$[\alpha]_{24^\circ}^{\lambda}=\frac{589\quad 578\quad 546\quad 436\,\text{nm}}{-60\quad -68\quad -75\quad -85}\ (c=0.4,\ CHCl_3)$$

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