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GUAIANOLIDES AND FURANOSESQUITERPENES FROM *URSINIA NANA**

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Key Word Index—*Ursinia nana*; Compositae; sesquiterpene lactones; guaianolides; furanosesquiterpenes.

Abstract—The investigation of *Ursinia nana* afforded in addition to the typical known furanosesquiterpenes two new compounds, probably both derived from the main constituent. In addition hanphyllin and five new guaianolides were isolated. The structures were elucidated by spectroscopic methods.

INTRODUCTION

The South African genus *Ursinia* can be characterized by the occurrence of typical furanosesquiterpenes such as compounds **3** and **5** [1], which are often accompanied by different types of sesquiterpene lactones [1–3]. *Ursinia nana* DC. ssp. *leptophylla* Prass. also contains **3** and **5** together with several sesquiterpene lactones and two derivatives of **5**, most probably formed by oxidation of **5**.

RESULTS AND DISCUSSION

The aerial parts of *Ursinia nana* afforded bicyclogermacrene, stigmasterol, sitosterol, large amounts of 7-methoxycoumarin, nerolidol (**1**) and the 12-hydroxy derivative **2** [1], the furanosesquiterpenes **3** [4] and **5** [5], hanphyllin (**8**) [6], its isovalerate **9** [7], **16** [8] and several guaianolides in minor quantities. ^{1}H NMR studies finally led to the elucidation of structures **10**–**14** (Table 1). Compounds **10** and **11** could not be separated. However, the ^{1}H NMR spectrum clearly indicated that these lactones only differed in the nature of the ester group at C-8. The presence of guaianolides with a Δ^{2}-double bond could be deduced from the typical olefinic doublets at δ 6.32 and 5.95, while the 6,12-lactone followed from the signals H-5 through H-7, which could be assigned by spin decoupling. As $J_{5,6}$ and $J_{6,7}$ were both *ca* 10 Hz the stereochemistry at these centres was established. The α-orientation of the methyl at C-4 was proposed from the chemical shift of the signals of H-15 and H-6, which were close to those of a similar lactone from an *Athanasia* species, while the ^{1}H NMR spectrum of the 4-epimer from the same plant showed the expected downfield shifts of these signals [9]. Compounds **10** and **11** therefore most probably were 8α-acyl derivatives of 9-desacetoxy-4-epi-athamantolide. The ^{1}H NMR spectral data of **12** were similar to those of **10** and **11** (Table 1). However, the H-5 signal and the signals of the ester part were missing. The molecular formula showed that four oxygens were present and therefore an additional hydroxyl at C-5 was proposed. As the H-7 signal was shifted downfield, a 5α-hydroxyl was very likely. The signals of H-6 and H-15 were also shifted downfield if compared with those of **10**. Therefore, a 4α-methyl group was very probable. The ^{1}H NMR spectrum of **13** (Table 1), molecular formula $C_{15}H_{16}O_{3}$, showed broadened singlets at δ 5.44 and 5.18 which indicated the presence of an exomethylene group. Therefore an anhydro compound of **12** was very likely. Again the downfield shift of the H-7 signal required a 5α-orientation of the hydroxyl and its position was further supported by the absence of a H-5 signal. The H-2 and H-3 signals were shifted downfield in support of the proposed additional conjugation. Spin decoupling allowed the assignment of all signals. The lactone **14** was an isomer of **12**. The additional olefinic methyl group followed from the ^{1}H NMR spectrum (Table 1), indicating the presence of a Δ^{3}-double bond. The ^{1}H NMR signals at δ 4.93 and 5.78 must be those of H-2 and H-3, indicating a 2-hydroxy derivative. However, the stereochemistry at C-2 could not be established with certainty. As no hydrogen bond between possible C-3 and C-5 hydroxyl groups was revealed in the IR spectrum, a 2β-hydroxyl was more likely. Therefore compound **14** was 5α-hydroxy-9-desacetoxyanhydroathamantholide.

The roots afforded stigmasterol, sitosterol, **3**–**5**, **15** [10] and two derivatives of **5**, the furanes **6** and **7**. The ^{1}H NMR spectral data of **7** (Table 2) were in part nearly identical with those of **5**, indicating the same situation at C-1 through C-7. However, the IR spectrum showed that a γ-lactone was present. In the ^{1}H NMR spectrum two broadened doublets at δ 4.22 and 4.10 were sharpened on irradition of the H-6 signal, indicating an allylic position (H-8). The chemical shifts required an oxygen function at C-8 leading to the sequence **B**. As the olefinic signal at δ 5.87 was coupled with the olefinic methyl and a broadened

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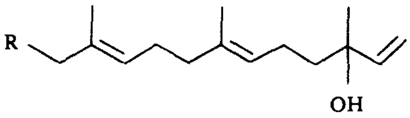
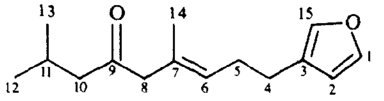
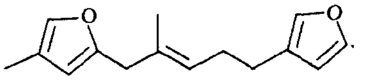
*Part 395 in the series "Naturally Occurring Terpene Derivatives". For Part 394 see Bohlmann, F., Jakupovic, J., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1103.



1 R = H
2 R = OH



3 Δ 10,11
4



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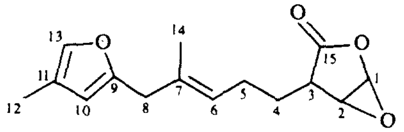

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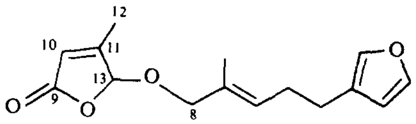

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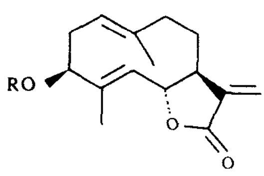
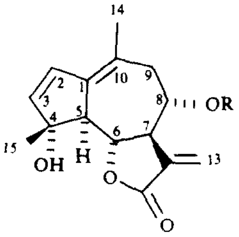
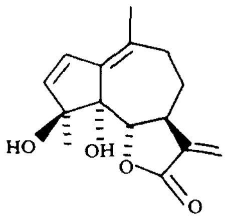


8 R = H
9 R = *i*Val



10 R = *i*Val
11 R = Me bu



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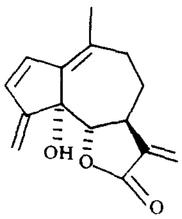

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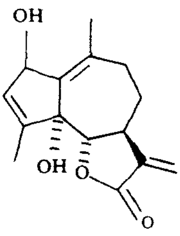

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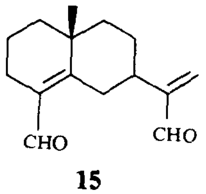

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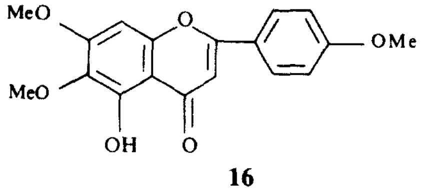

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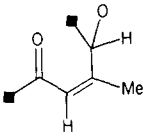
Table 1. ^{1}H NMR spectral data of compounds **10–14** (400 MHz, $CDCl_3$, TMS as int. standard)

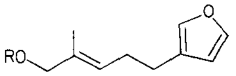
	10	**11**	**12**	**13**	**14**
H-2	6.32 *d*		6.53 *d*	6.53 *br d*	4.93 *br s*
H-3	5.95 *d*		5.86 *d*	6.31 *br d*	5.78 *br s*
H-5	3.03 *br d*		—	—	—
H-6	4.08 *dd*		4.55 *d*	3.80 *d*	3.83 *d*
H-7	3.14 *dddd*		3.47 *m*	3.71 *ddddd*	3.64 *ddddd*
H-8	5.01 *dd*		1.43 *m* 1.74 *m*	1.48 *m* 2.09 *m*	1.48 *m* 1.76 *m*
H-9	2.45 *m*		2.58 *br dd* 2.26 *br d*	2.90 *br dd* 2.17 *br d*	2.77 *br dd* 2.17 *m*
H-13	6.28 *d*		6.23 *d*	6.13 *d*	6.14 *d*
H-13'	5.83 *d*		5.50 *d*	5.40 *d*	5.40 *d*
H-14	1.86 *d*		1.91 *br s*	1.92 *br s*	2.01 *br s*
H-15	1.45 *s*		1.61 *s*	5.44 *br s* 5.18 *br s*	2.00 *br s*
OCOR	2.25 *br d*	2.40 *tq*	—	—	—
	2.05 *m*	1.75 *ddq*			
	1.01 *d*	1.50 *ddq*			
	1.00 *d*	0.95 *t*			
		1.22 *d*			

J(Hz): Compounds **10** and **11**: 2,3 = 5.5; 5,6 = 11; 6,7 = 7,8 = 10; 7,13 = 3.5; 7,13' = 3; 8,9 ~ 7; compound **12**: 2,3 = 6; 6,7 = 10.5; 7,8 = 10 and 3; 7,13 = 3.5; 7,13' = 3; 8,9 = 10; 9,9' = 14; compound **13**: 2,3 = 6; 6,7 = 7,8 = 10; 7,8 = 3; 7,13 = 3.5; 7,13' = 3; 8,8' = 12; 8',9 = 12; 9,9' = 13; compound **14**: 6,7 = 10; 7,8 = 10; 7,8' = 3; 7,13 = 3.5; 7,13' = 3; 8',9 = 12; 9,9' = 13.

singlet at δ 5.60 the partial structure **A** had to be assumed.



A



B

Combination with the sequence **B** therefore led to structure **7**. Also the mass spectral data supported this structure. While electron impact conditions showed no molecular ion, chemical ionization gave a $[M+1]^+$ ion, followed by loss of water and the base peak at *m*/*z* 149, obviously formed by loss of the lactone part together with the ether oxygen, probably generated by protonation of the latter. Though the lactone may be simply derived from the corresponding monoterpene, an oxidative rearrangement of **5** seems to be more likely. However, this would require a migration of the monoterpene part from C-9 to C-13. Perhaps an endoperoxide of **5** may be involved, though no clear mechanism of this rearrangement could be drawn. We have named compound **7** ursinanolide.

The furan **6** must be formed by oxidation of **5**, again most likely via the corresponding endoperoxide. The structure followed from the molecular formula and the ^{1}H NMR spectral data (Table 2). The position

Table 2. ^{1}H NMR spectral data of compounds **6** and **7** (400 MHz, $CDCl_3$, TMS as int. standard)

	6	**7**
H-1	5.58 *d*	7.34 *dd*
H-2	3.80 *dd*	6.27 *br s*
H-3	2.80 *ddd*	—
H-4	1.93 *m*	2.50 *br t*
H-4'	1.80 *m*	
H-5	2.31 *br dt*	2.33 *br dt*
H-6	5.26 *tq*	5.52 *br t*
H-8	3.26 *br s*	4.22 *br d* 4.10 *br d*
H-10	5.89 *br s*	5.87 *dq*
H-12	1.99 *d*	2.04 *d*
H-13	7.06 *dq*	5.60 *br s*
H-14	1.64 *br s*	1.66 *br s*
H-15	—	7.21 *dt*

J(Hz): Compound **6**: 1,2 = 2,3 = 2.5; 3,4 = 4.5; 3,4' = 10.5; 4,5 = 5,6 = 7; 6,8 = 6,14 = 1; 10,12 = 10,13 = 12,13 ~ 1; compound **7**: 1,2 = 1,15 = 1.5; 4,5 = 5,6 = 7; 4,15 = 1; 8,8' = 11; 10,12 = 10,13 = 1.5.

of the epoxide was deduced from the chemical shift of H-1 and the corresponding couplings. Spin decoupling allowed the assignment of the signals of H-2 and H-3. The observed coupling $J_{2,3}$ would agree with the proposed relative stereochemistry at C-2 and C-3, since models showed that a *trans*-relationship of H-2 and H-3 would have led to a smaller coupling. The signals of H-5 through H-14 were similar to those of **5**, indicating the same substitution and stereochemistry.

The chemistry of this *Ursinia* species again showed the close relationship of this genus to *Athanasia* were furanosesquiterpenes as well as similar guaianolides are frequent [9]. This clearly shows that this genus cannot be placed in the tribe Arctoteae, but the question whether *Ursinia* should be placed as a new tribe [11, 12] or should be combined with the woody South African genera of the tribe Anthemideae, perhaps in a subtribe of Anthemideae, still has to be decided.

EXPERIMENTAL

The air dried plant material, collected in February 1981 in Transvaal, voucher 81/35, deposited in the Botanical Research Institute, Pretoria, was extracted with Et_2O–petrol (1:2) and the resulting extracts were 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 aerial parts (225 g) afforded 50 mg bicyclogermacrene, 100 mg stigmasterol, 100 mg sitosterol, 500 mg 7-methoxycoumarin, 5 mg **1**, 10 mg **2**, 20 mg **3**, 200 mg **5**, 200 mg **8**, 50 mg **9**, 1 mg **10** and 1 mg **11** (Et_2O–petrol, 2:1, several times), 1 mg **12** (C_6H_6–CH_2Cl_2–Et_2O, 1:1:1), 1 mg **13** (Et_2O–petrol, 1:1), 1 mg **14** (Et_2O–petrol, 2:1) and 200 mg **16**. The roots (130 g) gave 50 mg stigmasterol, 50 mg sitosterol, 20 mg **3**, 1 mg **4**, 200 mg **5**, 1 mg **6** (Et_2O–petrol, 1:1), 1 mg **7** (C_6H_6–CH_2Cl_2, 1:1, several times) and 1 mg **15**.

1,2 - *Epoxy* - 1,2,3,15 - *tetrahydro* - 6 - *dehydrolasiosperm*-15-*one* (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1815 (y-lactone); MS *m/z* (rel. int.): 262.121 $[M]^+$ (3) ($C_{15}H_{18}O_4$), 149 $[C_{10}H_{13}O]^+$ (30), 57 (100). $[\alpha]_{365nm} = +14$ ($CHCl_3$; *c* 0.1).

Ursinanolide (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800, 1770 (γ-lactone); MS *m/z* (rel. int.): 165 $[M-A]^+$ (20), 149 $[C_{10}H_{13}O]^+$ (18), 97 $[A]^+$ (80), 81 [pyrylium]$^+$ (100). CIMS(*i*-butane): 263 $[M+1]^+$ (2), 245 $[263-H_2O]^+$ (18), 149 $[M-C_5H_5O_3]^+$ (100). A = 3-methylbutenolide.

8α-Isovaleryloxy- and (2-*methylbutyryloxy*)-9-*desacetoxy*-4-*epi*-*athamantholide* (**10** *and* **11**). Inseparable colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790 (lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 244.100 $[M-RCO_2H]^+$ (1), 226 $[244-H_2O]^+$ (6), 57 (100). $[\alpha]_D = +8$ ($CHCl_3$; *c* 0.1).

5*α*-*Hydroxy*-9-*desacetoxyathamantholide* (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790 (lactone); MS *m/z* (rel. int.): 262.120 $[M]^+$ (11) ($C_{15}H_{18}O_4$), 247 $[M-Me]^+$ (8) 234 $[M-CO]^+$ (11), 219 $[234-Me]^+$ (9), 57 (100). $[\alpha]_D = -8$ ($CHCl_3$; *c* 0.1).

9-*Desacetoxyanhydroathamantholide* (**13**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790 (lactone); MS *m/z* (rel. int.): 244.110 $[M]^+$ (75) ($C_{15}H_{16}O_3$), 226 $[M-H_2O]^+$ (58), 211 $[226-Me]^+$ (27), 198 $[226-CO]^+$ (83), 183 $[198-Me]^+$ (72), 91 (100). $[\alpha]_D = +4$ ($CHCl_3$; *c* 0.1).

2-*Hydroxy*-8-*desacetoxyzuurbergenin* (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775 (lactone); MS *m/z* (rel. int.): 262.121 $[M]^+$ (2) ($C_{15}H_{18}O_4$), 244 $[M-H_2O]^+$ (27), 226 $[244-H_2O]^+$ (18), 211 $[226-Me]^+$ (10), 198 $[226-CO]^+$ (22), 183 $[198-Me]^+$ (32), 91 (100).

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