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FURTHER GLAUCOLIDES FROM SOUTH AFRICAN *VERNONIA* SPECIES

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Key Word Index—*Vernonia oligocephala*; *V. sutherlandii*; *V. adoensis*; Compositae; sesquiterpene lactones.

Abstract—The investigation of three South African *Vernonia* species afforded minute amounts of five new glaucolides, two monoepoxides and three diepoxides. The structures were elucidated by ^{1}H NMR spectroscopy. The roots of *Vernonia sutherlandii* contain, in addition to vernonataloide, bergamotene and santalene, minute amounts of the corresponding acetoxy derivatives.

INTRODUCTION

In continuation of our investigation of South African *Vernonia* species, we have studied again *V. olicephala* and two further species, *V. sutherlandii* and *V. adoensis*. All three species afforded glaucolides. The structure elucidation is discussed in this paper.

RESULTS AND DISCUSSION

Since in our first investigation of *Vernonia oligocephala* (DC.) Sch. Bip. ex Walp. [1] only very little plant material was available, we decided to study this South African species again. The aerial parts afforded in addition to widespread compounds, minute amounts of three sesquiterpene lactones, 8α-(2-hydroxymethyl acryloyloxy)-hirsutinolide-13-*O*-acetate [1, 2] and the glaucolides **1** and **2**.

The structure of **1** clearly followed from the ^{1}H NMR spectral data (Table 1), which agreed closely with those of the corresponding methacrylate isolated from *Vernonia natalensis* [3]. The nature of the ester residue at C-8 followed from the characteristic ^{1}H NMR signals [2.83 *d*

Table 1. ^{1}H NMR spectral data of compounds **1–5** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	**2**	**3**	**4**	**5**
H-1	2.71 *br d*	—	6.07 *br s*	3.72 *ddd*	3.72 *ddd*
H-2		2.68 *m*	—	5.81 *dd*	5.80 *dd*
H-3			2.90 *d* 2.41 *d*	5.71 *dd*	5.69 *dd*
H-5	2.61 *d*	2.58 *d*	2.84 *d*	2.59 *d*	2.56 *d*
H-6	4.95 *d*	4.87 *d*	4.88 *d*	4.91 *d*	4.89 *d*
H-8	5.28 *d*	4.94 *dd*	5.09 *dd*	5.63 *br d*	5.58 *br d*
H-9	2.68 *d*	2.55 *ddd*	3.18 *ddd*	2.82 *dd*	2.79 *dd*
H-9′	2.03 *dd*	2.21 *ddd*	2.66 *dd*	1.83 *br d*	1.76 *br d*
H-10	—	2.96 *ddq*	—	—	—
H-13	5.00 *br d*	4.90 *ABq*	4.91 *s*	4.82 *d*	4.98 *dd*
H-13′	4.88 *br d*			4.76 *d*	4.74 *d*
H-14	1.53 *s*	1.18 *d*	1.85 *d*	3.76 *br d*	3.75 *br d**
H-14′				3.70 *br d*	3.68 *br dd**
H-15	1.58 *s*	1.63 *s*	1.67 *s*	1.77 *s*	1.75 *s*
OAc	2.11 *s*	2.09 *s*	2.12 *s*	2.05 *s*	2.10 *s*
OCOR	1.51 *s*	4.32 *br d*	1.52 *s*	2.00 *br s*	2.45 *tq*
	2.83 *d*	6.29 *br t*	2.80 *d*	6.26 *dq*	1.70 *ddq*
	3.12 *d*	5.99 *br t*	3.10 *d*	5.77 *dq*	1.49 *ddq*
					0.91 *t*
					1.22 *d*

* After addition of D_2O sharp doublets.

J (Hz): Compound **1**: 1, 2 = 10; 5, 6 = 8, 9′ = 9; 9, 9′ = 13, 13′ = 13; $3_1'$, $3_2'$ = 6; compound **2**: 5, 6 = 9; 8, 9 = 4; 8, 9′ = 3; 9, 10 = 11; 9′, 10 = 2.5; 9, 9′ = 15; 10, 14 = 7; compound **3**: 1, 9 = 2; 1, 14 = 1; 3, 3′ = 12; 5, 6 = 9.5; 8, 9 = 8, 9′ = 7; 9, 9′ = 14.5; compounds **4** and **5**: 1, 2 = 1, 3 = 1, 9 = 6, 13 ~ 1; 2, 3 = 12; 5, 6 = 9; 8, 9 = 8; 9, 9′ = 16; 14, 14′ = 12; 14′, OH = 6.

and 3.12*d* ($J = 6$ Hz), 1.51*s*]. The remaining signals showed only small differences in the chemical shifts.

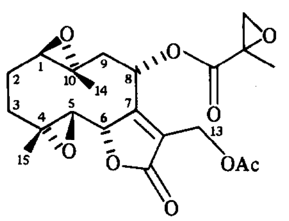
The ^{1}H NMR spectrum of **2** (Table 1) was close to that of the corresponding glaucolide A derivative with a methacrylate group at C-8, which was isolated from a *Stilpnophytum* species [4], and also to that of a 10-acetoxy derivative from an *Erlangea* species [5]. The nature of the ester group was easily deduced from the typical ^{1}H NMR signals. Hence **2** is stilpnotomentolide-8-*O*-[4-hydroxymethacrylate].

The aerial parts of *V. sutherlandii* Harv. afforded, in addition to widespread compounds, the glaucolide **1** and a second one, a derivative of glaucolide D [6], in which the oxygen function at C-2 is transformed to a keto group (**3**). The structure followed from the molecular formula and the ^{1}H NMR spectral data (Table 1). Spin decoupling in the usual way allowed the assignment of all signals which were in part close to those of glaucolide D. The changed situation at C-2 caused a downfield shift of the H-1 signal. Furthermore, the presence of a pair of doublets at δ 2.90 and 2.41 was obviously due to signals of a methylene group in an α-position to a keto group. As the chemical shifts of H-8 and H-13 were the same as in glaucolide D, the proposed relative position of the ester groups was very likely.

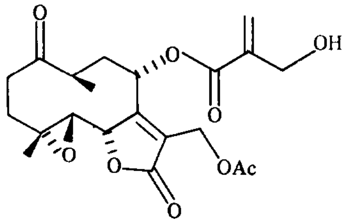
The roots afforded in addition to simple compounds minute amounts of vernonataloide [3], α-santalene and the corresponding 12-acetoxy derivatives **6** and **7**. The structures followed from the molecular formula and the ^{1}H NMR spectra (Table 2), which were very close to those of α-bergamotene and α-santalene. Comparison of the ^{1}H NMR spectrum of 13-acetoxy α-santalene with that of **7** further showed that these acetates only differed in the stereochemistry of the 10,11-double bond. As in similar cases, the chemical shifts of the signals of the olefinic proton and the methyl group differed in the expected way, while all other signals were nearly identical. The same conclusions led to the proposed stereochemistry of **6**. Again the signal of the olefinic methyl was at a slightly higher field and the H-10 signal was at δ 5.51. The signs of the optical rotations of **6** and **7** indicated that the acetates had the same absolute configuration as the hydrocarbons.

The aerial parts of *V. adoensis* Sch. Bip. ex Walp., which so far have only been investigated for flavanoids [7], afforded in addition to simple triterpenes minute amounts of the glaucolides **4** and **5**. Only by chemical ionizations could M + 1 ions be observed. The structures followed from the ^{1}H NMR spectra (Table 1). All signals were assigned by spin decoupling in the usual way. The nature of the ester groups at C-8 were easily deduced from the typical signals of a methacrylate and a 2-methyl butyrate, respectively.

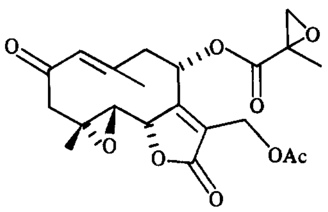
The presence of diepoxides in both lactones followed from the chemical shifts of the H-1 and H-5 doublets, while the position of the hydroxyl group was deduced from the downfield shift of H-9 when compared with the



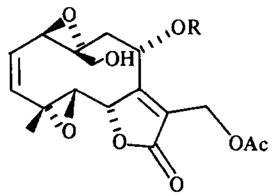
1



2

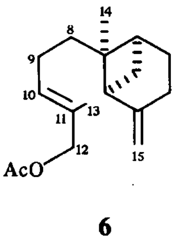


3



4 R = COC(Me)=CH$_2$

5 R = COCH(Me)Et



6

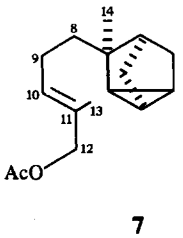


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Table 2. ^{1}H NMR spectral data of compounds **6** and **7** (400 MHz, CDCl$_3$, TMS as internal standard)

	6	**7**
H-1	2.53 *t*	1.58 *br s*
H-2	—	1.61 *d*
H-2′	—	1.07 *d*
H-3	2.58 *ddddd*	0.83 *br s*
H-3′	2.26 *br ddd*	—
H-4	1.84 *m*	0.83 *br s*
H-4′		—
H-5	2.04 *br ddd*	—
H-6	2.30 *ddd*	—
H-6′	1.44 *d*	—
H-7	—	1.58 *d*
H-7′	—	1.04 *d*
H-8	1.55 *m*	1.24 *m*
H-8′		1.17 *m*
H-9	2.04 *m*	1.98 *m*
H-9′		
H-10	5.51 *tq*	5.47 *tq*
H-12	4.47 *br s*	4.44 *br s*
H-12′		
H-13	1.68 *br s*	1.66 *br s*
H-14	0.72 *s*	0.99 *s*
H-15	4.57 *br dd*	0.83 *s*
H-15′	4.64 *br ddd*	
OAc	2.08 *s*	

J (Hz): Compound **6**: 1, 6 = 5.5; 3, 3′ = 13; 3, 4 $\sim$ 10; 3, 4′ = 3, 15 = 3, 15′ $\sim$ 2; 3′, 4 $\sim$ 2; 3′, 4′ $\sim$ 8; 3′, 15 = 3′, 15′ $\sim$ 1.5; 4, 5 = 5, 6 = 5, 6′ $\sim$ 7; 6, 6′ = 11; 9, 10 = 9′, 10 = 7; 10, 12 = 10, 13 $\sim$ 1; compound **7**: 2, 2′ = 7, 7′ = 11; 9, 10 = 9′, 10 = 7; 10, 12 = 10, 13 $\sim$ 1.

shift in the spectrum of **1**. Furthermore, no deshielding effect of H-6 was visible, which would be expected as the coupling $J_{5,6}$ indicated a *trans*-dihedral arrangement of H-5 and H-6.

The isolation of very minute amounts of glaucolides from further *Vernonia* species may be an indication that in those cases where no lactones have been detected a more careful re-investigation may be necessary, especially as the typical methylene lactone signals are missing in the ^{1}H NMR spectra, which in addition often show broad signals only due to the flexibility of these systems. Therefore the detection of minute amounts causes more difficulty, but in connection with the chemotaxonomy, the detection seems to be worthwhile. The results again show the similarity of the chemistry of the South American and South African *Vernonia* species.

EXPERIMENTAL

The air-dried plant material, collected in February 1981 in Transvaal, was extracted with Et$_2$O (12 hr, room temp.) and worked-up in the usual fashion. Vouchers have been deposited at the Herbarium of the Botanic Research Institute, Pretoria. The extract of the aerial parts (70 g) of *Vernonia oligocephala* (voucher 81/15) gave CC fractions as follows: 1 (100 ml, petrol), 2 (200 ml, Et$_2$O–petrol, 1:10 and 1:3) and 3 (200 ml, Et$_2$O–petrol, 1:1, Et$_2$O and Et$_2$O–MeOH, 10:1). TLC (always SiO$_2$ PF254, detection by UV 255 nm) of fraction 3 (CH$_2$Cl$_2$–C$_6$H$_6$–Et$_2$O, 1:1:1, 2 developments) gave *ca* 1 mg **1**, (R_f 0.45) 1 mg 8α-[2-hydroxymethylacryloyloxy]-hirsutinolide-13-*O*-acetate and 1 mg **2** (R_f 0.40). The extract of the aerial parts (90 g) of *Vernonia sutherlandii* (voucher 81/133) gave CC fractions as follows: 1 (50 ml, petrol), 2 (100 ml, Et$_2$O–petrol, 1:10 and 1:3), 3 (100 ml, Et$_2$O–petrol, 1:1 and Et$_2$O) and 4 (50 ml, Et$_2$O–MeOH, 10:1). TLC of fraction 4 (CH$_2$Cl$_2$–C$_6$H$_6$–Et$_2$O–MeOH, 2:2:2:1) gave *ca* 1 mg **1** (R_f 0.63) and 1 mg **3** (R_f 0.60).

The extract of the roots (40 g) gave CC fractions as follows: 1 (50 ml, petrol), 2 (100 ml, Et$_2$O–petrol, 1:10 and 1:3) and 3 (100 ml, Et$_2$O and Et$_2$O–MeOH, 10:1). TLC of fraction 1 (petrol) gave 15 mg of a mixture of α-bergamotene and α-santalene (*ca* 2:1), which was identified by GC/MS and by comparing the MS and ^{1}H NMR spectra with those of authentic samples, and 1 mg tridecapentainene. TLC of fraction 2 (Et$_2$O–petrol, 1:4) afforded *ca* 1 mg **6** (R_f 0.75) and 0.5 mg **7** (R_f 0.70), and TLC of fraction 3 (petrol–Et$_2$O–CHCl$_3$–C$_6$H$_6$, 8:1:1:1, 2 developments) gave *ca* 1 mg vernonataloide [3] (R_f 0.35). The CC fractions of the extract of the aerial parts (150 g) of *Vernonia adoensis* (voucher 81/90) were as follows: 1 (200 ml, petrol), 2 (100 ml, Et$_2$O–petrol, 1:10 and 1:3), 3 (100 ml, Et$_2$O–petrol, 1:1 and Et$_2$O). TLC of fraction 3 (Et$_2$O–CH$_2$Cl$_2$–C$_6$H$_6$, 1:1:1) gave 2 mg **4** (R_f 0.52) and 1 mg **5** (R_f 0.50). Due to the minute amounts, lactones **1**–**5** could not be induced to crystallize although they were homogeneous by TLC in different solvent mixtures (see above) and no impurities could be detected in the ^{1}H NMR spectra. Known compounds were identified by comparing all spectroscopic data, especially the 400 MHz ^{1}H NMR spectra with those of authentic material. Quantities were determined by weight.

17,18-Epoxyvernonataloide (**1**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (γ-lactone), 1745 (OAc, CO$_2$R); MS (CI, isobutane) *m/z* (rel. int.): 423 $[M+1]^+$ (11), 321 $[423-RCO_2H]^+$ (16), 261 $[321-HOAc]^+$ (100), 243 $[261-H_2O]^+$ (30), 99 $[RCO]^+$ (53).

Stilpnotomentolide-8-O-[4-hydroxymethacrylate] (**2**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1735 (CO$_2$R); MS *m/z* (rel. int.): 362.137 $[M-HOAc]^+$ (2) (C$_{19}$H$_{22}$O$_7$), 260 $[362-RCO_2H]^+$ (4), 55 (100).

2-Oxo-2-desacetoxyglaucolide D (**3**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone) 1740 (OAc, CO$_2$R), 1690 (C=CCO); MS *m/z* (rel. int.): 420.142 $[M]^+$ (2) (C$_{21}$H$_{24}$O$_9$), 402 $[M-H_2O]^+$ (1), 318 $[M-RCO_2H]^+$ (2), 300 $[402-RCO_2H]^+$ (1.5), 258 $[318-HOAc]^+$ (12), 240 $[300-HOAc]^+$ (20), 85 $[RCO]^+$ (15), 57 $[85-CO]^+$ (100).

14-Hydroxy-8-desacyl-2,3-dehydrovernonataloide-8-O-methacrylate (**4**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1745 (OAc), 1720 (C=CCO$_2$R); MS (CI, isobutane) *m/z* (rel. int.): 421 $[M+1]^+$ (21), 391 $[421-CH_2O]^+$ (25), 207 (100).

14-Hydroxy-8-desacyl-2,3-dehydrovernonataloide-8-O-[2-methyl butyrate] (**5**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1735 (OAc, CO$_2$R); MS (CI, isobutane) *m/z* (rel. int.): 437 $[M+1]^+$ (19), 335 $[437-RCO_2H]^+$ (10), 275 $[335-HOAc]^+$ (19), 257 $[275-H_2O]^+$ (14), 229 $[257-CO]^+$ (100).

12-Acetoxy-α-bergamotene (**6**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (OAc); MS *m/z* (rel. int.): 262.193 $[M]^+$ (2.5) (C$_{17}$H$_{26}$O$_2$), 202 $[M-HOAc]^+$ (8), 187 $[202-Me]^+$ (6), 159 (12), 133 (33), 119 (36), 107 (30), 93 (100), 91 (51), 79 (50), 67 (51), 55 (64).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-17 \quad -18 \quad -20 \quad -30} \ (\text{CHCl}_3;\ c\ 0.1).$$

12-Acetoxy-α-santalene (**7**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (OAc); MS *m/z* (rel. int.): 262.193 $[M]^+$ (1) (C$_{17}$H$_{26}$O$_2$), 202 $[M-HOAc]^+$ (17), 187 $[202-Me]^+$ (14), 159 (11), 121 (43), 119 (33), 107 (36), 105 (30), 94 (64), 93 (100), 91 (50), 79 (49), 77 (36), 67 (31), 55 (48), $[\alpha]_D \sim +14$ (CHCl$_3$; *c* 0.05).

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REFERENCES

1. Bohlmann, F., Brindöpke, G. and Rastogi, R. C. (1978) *Phytochemistry* **17**, 465.
2. Bohlmann, F., Jakupovic, J., Gupta, R. K., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 473 (there the change of the absolute configuration is proposed).
3. Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 2263.
4. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1045.
5. Bohlmann, F. and Czerson, H. (1978) *Phytochemistry* **17**, 1190.
6. Betkouski, M., Mabry, T. J., Taylor, I. F. and Watson, W. H. (1975) *Rev. Latinoam. Quim.* **6**, 191.
7. Mabry, T. J., Abdel-Baset, Z., Padolina, W. G. and Jones, S. B. (1975) *Biochem. Syst. Ecol.* **2**, 185.

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A HYDROXYGERMACRENE AND OTHER CONSTITUENTS FROM *PSEUDOBRICKELLIA BRASILIENSIS*[*]

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Key Word Index—*Pseudobrickellia brasiliensis*; Compositae; sesquiterpene; 4β-hydroxygermacra-1(10),5-diene; triterpenes; 11α-hydroxy-α-amyrin.

Abstract—*Pseudobrickellia brasiliensis* afforded, in addition to known compounds, a new germacradiene derivative and a hydroxy-α-amyrin.

The small genus *Pseudobrickellia* is placed in the subtribe Alomiinae (tribe Eupatorieae) [1]. So far nothing is known on the chemistry of this genus. The aerial parts of *P. brasiliensis* (Spreng.) K. et R. afforded lupeol and its Δ^{12} isomer, β-amyrin acetate, spathulenol, cadinene, cadinol, oplopanone (**1**) [2] and a further sesquiterpene alcohol. The structure of the latter followed from the ^{1}H NMR spectrum (Table 1) which was very close to that of **2** [3]. However, the chemical shifts of H-5 and H-6 had changed, the double doublet of H-6 now being at higher field. Nuclear Overhauser experiments showed by irradiation of the signal of H-15 a clear effect on the signals of H-3β and H-5. Inspection of models showed that obviously the preferred conformations were the same for both **2** and **3**, a chair-chair conformation with the 10-methyl and the 4-methyl (in **2**) or 4-hydroxyl group (in **3**) quasi-axial above the plane. This clearly followed from the couplings observed. Accordingly, the new sesquiterpene alcohol is the 4-epimer of **2** with a quasi-axial hydroxyl at C-4. Furthermore two isomeric triterpene diols were present

Table 1. ^{1}H NMR spectral data of compounds **2** and **3** (400 MHz, CDCl$_3$, TMS as internal standard)

	3	**2**	**2** (C$_6$D$_6$)
H-1	4.95 *d br*	4.95 *d br*	4.97 *d br*
H-2α	1.95 *d br*	1.96 *d br*	1.96 *m*
H-2β	2.50 *dddd*	2.51 *dddd*	2.67 *dddd*
H-3α	1.54 *m**	1.52 *m*	1.35 *m*
H-3β	1.64 *ddd*	1.65 *ddd*	1.50 *ddd*
H-5	5.25 *d*	5.17 *d*	5.06 *d*
H-6	5.17 *dd*	5.25 *dd*	5.30 *dd*
H-7	2.02 *m*	2.02 *m*	1.96 *m*
H-8	1.39 *m*	1.41 *m*	1.35 *m*
H-9	2.25 *m*	2.26 *m*	2.21 *m*
H-11	1.39 *m*	1.41 *m*	1.35 *m*
H-12	0.82 *d*	0.84 *d*	0.95 *d*
H-13	0.78 *d*	0.80 *d*	0.91 *d*
H-14	1.54 *s br*	1.55 *s br*	1.59 *dd*
H-15	1.19 *s*	1.21 *s*	1.12 *s*

*CDCl$_3$–C$_6$D$_6$, 2:1, H-3α 1.40 *ddd*.

J (Hz): 1, 2α ~ 2.5; 1, 2β = 11.5; 2α, 2β = 14; 2α, 3α ~ 3; 2α, 3β = 3.5; 2β, 3α = 11; 2β, 3β = 3.5; 3α, 3β = 14; 5, 6 = 16; 6, 7 = 9.3; 11, 12 = 11, 13 = 7.

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[*] Part 461 in the series "Naturally Occurring Terpene Derivatives". For part 460 see Greger, H., Zdero, C. and Bohlmann, F. (1983) *Phytochemistry* **21**, 2085.