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# HIRSUTINOLIDES FROM SOUTH AFRICAN *VERNONIA* SPECIES*

FERDINAND BOHLMANN, NEZHUN ATES (GOREN) and JASMIN JAKUPOVIC

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

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**Key Word Index**—*Vernonia glabra* var *glabra*; *V poskeana* var *poskeana*, *V poskeana* var *chlorolepis*, *V neocorymbosa*; Compositae, sesquiterpene lactones, hirsutinolides; sesquiterpene aldehydes

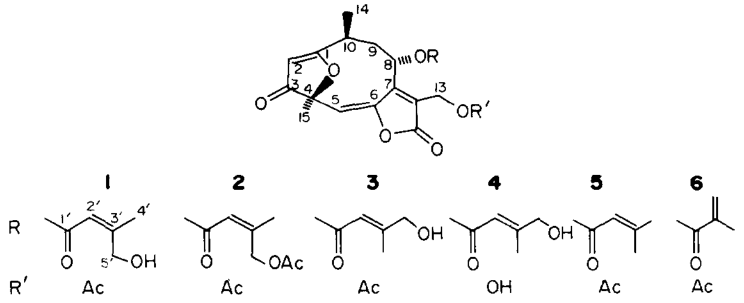
**Abstract**—The investigation of four South African *Vernonia* species afforded, in addition to known compounds, six ketohirsutinolides with different oxygen functions at C-8 and C-13, respectively. Furthermore, an eremantholide was present, which was the 16-epimer of a known compound and two sesquiterpene aldehydes were isolated.

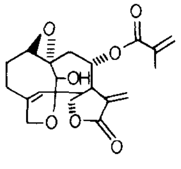
## INTRODUCTION

From the large genus *Vernonia*, with more than 1000 taxa, a considerable number of species have been investigated chemically. The most widespread compounds are highly oxygenated germacranolides [1]. While previous investigations indicated clear differences between the New World and Old World members [2], more recent studies show a closer relationship This is particularly indicated by the occurrence of the very typical glaucolides and hirsutinolides in both South American and South African *Vernonia* species [3, 4]. In continuation of our investigations of South African Compositae we have studied the constituents of four further *Vernonia* species. The results are discussed in this paper

## RESULTS AND DISCUSSION

The aerial parts of *Vernonia glabra* (Steetz) Vatke var *glabra* afforded squalene, germacrene A, α- and β-selinene, selina-4,11-diene, β-elemene, eremanthine (**10**), dehydrocostus lactone (**11**), 13-acetoxygeranyl linalol (**14**) [5], a mixture of the isomeric aldehydes, **18** [6], and two further aldehydes, the carbinol, **15**, and germacra-1(10),4,11(13)-





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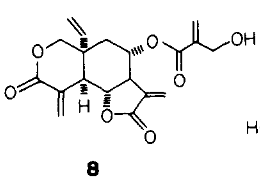

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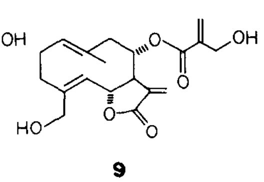

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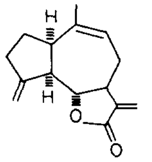

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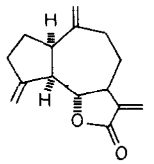

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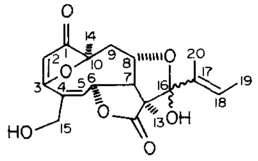

**12** 16β-OH
**13** 16α-OH

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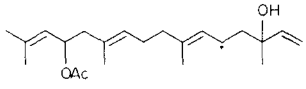
*Part 464 in the series "Naturally Occurring Terpene Derivatives". For Part 463 see Bohlmann, F, Wallmeyer, M, Jakupovic, J and Ziesche, J. (1983) *Phytochemistry* **22** (in press) trien-12-al (**19**) However, the latter could not be separated from **18** Heating of **19** afforded the β-elemen-12-al(**20**), which was purified after boranate reduction as the corresponding alcohol, **21** The structures of **20** and **21** followed from the molecular formula and the $^1$H NMR spectral data (Table 1). Also, the structure of **15** was deduced from the $^1$H NMR spectrum (Table 1) However, the stereochemistry at C-4 could not be assigned with certainty The chemical shift of H-14 indicated a β-orientation of the C-4-methyl group as an axial hydroxyl group at C-4 causes a considerable downfield shift of H-14 The root extract gave no characteristic compounds.



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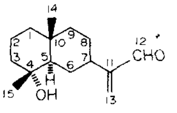
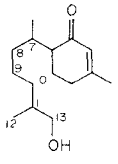
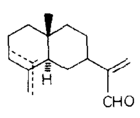


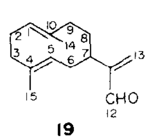
**15**



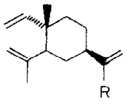
**16**
**17** Δ 10, 11



**18**



**19**



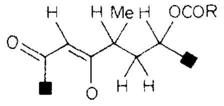
**20** R = CHO
**21** R = $CH_2OH$

Table 1 $^1$H NMR spectral data of compounds **18**, **20** and **21** (400 MHz, TMS as internal standard)

| | **20** ($C_6D_6$) | **21** ($CDCl_3$) | **18** ($CDCl_3$) |
|---|---|---|---|
| H-1 | 5 78 *dd* | 5 86 *dd* | -- |
| H-2 | 4 96 *dd* | 4 90 *dd* | -- |
| H-2′ | 4 95 *dd* | 4 89 *dd* | — |
| H-3 | 4 94 *dq* | 4 82 *dq* | — |
| H-3′ | 4 67 *dq* | 4 57 *dq* | - |
| H-5 | 1 96 *dd* | 1 91 *m* | -- |
| H-7 | 2 57 *dddd* | | 2 53 *dddd* |
| H-12 | 9 41 *s* | 4 12 *br s* | 9 52 *s* |
| H-13 | 5 69 *s* | 5 05 *dd* | 6 28 *s* |
| H-13′ | 5 30 *s* | 4 94 *dd* | 5 96 *s* |
| H-14 | 0 99 *s* | 0 89 *s* | 0 89 *s* |
| H-15 | 1 70 *dd* | 1 60 *dd* | 1 08 *s* |

*J*(Hz) 1, 2 = 17, 1, 2′ = 10, 2, 2′ = 1, 3, 3′ = 3, 15 = 1, 5, 6 = 13, 5, 6′ = 3 5, 6, 7 = 7, 8 = 12, 6′, 7 = 7, 8′ = 3, compound **21** 7, 13 = 13, 13′ ~ 1 5

The aerial parts of *Vernonia poskeana* Vatke et Hildebr var *poskeana* afforded germacrene D and the hirsutinolides, **3–6** $^1$H NMR spectra in deuteriochloroform were broadened as usual But at elevated temperatures in deuteriobenzene clear assignments of all signals were possible The spectra showed that these lactones differed only in the nature of the oxygen functions (Table 2). In the spectrum of **6** the presence of a methacrylate was obvious by the typical signals at δ 6 21, 5 35 and 1 87. The presence of an enol lactone followed from the singlet at 5 76 and the pair of doublets at 5 09 and 4 94 (H-13) and their chemical shifts indicated that an acetoxy group was at C-13 The presence of a furanone moiety followed from the intense IR band at 1600 cm$^{-1}$ and from the $^1$H NMR spectrum. A broadened singlet at 5 09 was coupled with a broadened double doublet quartet at 2 50, its irradiation led to the sequence **A** Therefore, the structure **6** was most likely



**A**

Table 2 $^1$H NMR spectral data of compounds **1–6** (400 MHz, $C_6D_6$, 70°, TMS as internal standard)

| | **1** | **2** | **3** | **4** | **5**($CDCl_3$) | **6** |
|---|---|---|---|---|---|---|
| H-2 | 5 11 *br s* | 5 15 *br s* | 5 28 *br s* | 5 14 *br s* | 5 62 *br s* | 5 09 *br s* |
| H-5 | 5 75 *s* | 5 78 *s* | 5 78 *s* | 5.76 *s* | 5 86 *s* | 5 76 *s* |
| H-8 | 6 33 *br d* | 6 33 *br d* | 6 35 *br d* | 6 35 *br d* | 6 5 *m* | 6 44 *br d* |
| H-9 | 2 26 *ddd* | 2 35 *ddd* | 2 50 *ddd* | 2 26 *ddd* | 2 74 *ddd* | 2 32 *ddd* |
| H-9′ | 1 25 *dd* | 1 35 *dd* | 1 46 *dd* | 1 35 *m* | 1 55 *m* | 1 26 *dd* |
| H-10 | 2 57 *br ddq* | 2 58 *br ddq* | 2 67 *br ddq* | 2.57 *br ddq* | 3 00 *m* | 2 50 *br ddq* |
| H-13 | 5 33 *br d* | 5.35 *br d* | 5 20 *br d* | 4 48 *d* | 5 59 *d* | 5 09 *d* |
| H-13′ | 5 15 *br d* | 5 20 *br d* | 5 11 *br d* | 4 40 *d* | 5 41 *d* | 4 94 *d* |
| H-14 | 0 78 *d* | 0 78 *d* | 0 88 *d* | 0 76 *d* | 1 20 *d* | 0 73 *d* |
| H-15 | 1 39 *s* | 1 39 *s* | 1 48 *s* | 1 38 *s* | 1 58 *s* | 1 35 *s* |
| H-2′ | 5 70 *tq* | 5.74 *tq* | 6 11 *tq* | 6 10 *tq* | 6 20 *br s* | 6 21 *dq**<br>5 35 *dq* |
| H-4′ | 1 64 *br s* | 1 64 *br s* | 3 61 *br s* | 3 58 *br s* | 1 87 *d* | 1 87 *dd* |
| H-5′ | 4 39 *br s* | 5 04 *d*<br>4.97 *d* | 2 05 *br s* | 1 93 *br s* | 2 11 *d* | — |
| OAc | 1 68 *s* | 1 68 *s*<br>1 72 *s* | 1 82 *s* | -- | 2 00 *s* | 1 87 *s* |

*H-3′ $J_{3',4'}$ = 1 and 1.5, $J_{3',3'}$ = 1, 2,
*J* (Hz) 2, 10 ~ 1, 8, 9 = 9, 9, 9′ = 15, 9, 10 = 5, 9′, 10 = 10.5; 10, 14 = 6 5, 13, 13′ = 13, 2′, 4′ = 2′, 5′ ~ 1

The stereochemistry at C-8 and C-10 followed from the couplings if a model was considered Compound **6** was related, therefore, to other hirsutinolides isolated from *Vernonia* species [3, 4], which had not been designated as furanones. The $^1H$ NMR spectrum of **5** was nearly identical with that of **6**, only the methacrylate was replaced by senecioate as was shown by the typical signals Also, the spectral data of **3** were close to those of **5** and **6**. As already shown by the IR spectrum this lactone had an additional hydroxy group The $^1H$ NMR spectral data showed that a 4-hydroxysenecioate was present, as was deduced from the typical signals of the ester moiety The position of the hydroxy group followed from the chemical shift of H-5′ Compound **4** was the corresponding 13-desacetyl derivative. Accordingly, the H-13 doublets were shifted upfield and the acetate methyl signal was missing, while the remaining signals were close to those in the spectrum of **3** The roots gave a small amount of a sesquiterpene lactone, its $^1H$ NMR spectrum was nearly identical with that of the known eremantholide, **12** [7] However, small shift differences, especially in that of the methyl groups may indicate a different stereochemistry at C-16 The same differences were visible in the spectra of the corresponding 15-*O*-acetates (Table 3) Also, the optical rotations were different As the stereochemistry at C-16 of several eremantholides are established, the new lactone (**13**) was most likely the 16α-hydroxy derivative of **12**

The aerial parts of *Vernonia poskeana* Vatke et Hildebr. var *chlorolepis* (Steetz) O Hoffm afforded germacrene D, squalene and also two hirsutinolides related to **3**–**6**. Accordingly, the $^1H$ NMR spectra (Table 2) were similar. The $^1H$ NMR spectrum of the main constituent, **2**, showed that the ester group at C-8 was 5-acetoxy senecioate as followed from the typical signals in deuteriobenzene at elevated temperature The stereochemistry of the $\Delta^{2'}$double bond was deduced from the chemical shift of the olefinic methyl signal (H-4′) Spin decoupling allowed the assignment of all signals. The $^1H$ NMR spectrum of the minor lactone showed that we were dealing with the corresponding 5′-desacetyl derivative, **1** Accordingly, the doublets of H-5′ were shifted upfield. The roots gave β-bergamotene and sitosterol

Table 3 $^1H$ NMR spectral data of compounds **12** and **13** and their 15-*O*-acetates (400 MHz, $CDCl_3$, TMS as internal standard)

| | 12 | 13 | 12 Ac | 13 Ac |
|---|---|---|---|---|
| H-2 | 5 70 *s* | 5 81 *s* | 5 70 *s* | 5 72 *s* |
| H-5 | 6 30 *dq* | 6 31 *dq* | 6 33 *dq* | 6 34 *dq* |
| H-6 | 5 02 *ddq* | 5 03 *ddq* | 5 03 *ddq* | 5 06 *ddq* |
| H-7 | 2.89 *dd* | 2 97 *dd* | 2 08 *dd* | 2.85 *dd* |
| H-8 | 4 15 *ddd* | 4.04 *ddd* | 4.25 *ddd* | 4 10 *ddd* |
| H-9 | 2 40 *dd* | 2 44 *dd* | 2.40 *dd* | 2 45 *dd* |
| H-9′ | 2 05 *dd* | 2.03 *dd* | 2 06 *dd* | 2 02 *dd* |
| H-13 | 1 12 *s* | 1 13 *s* | 1 14 *s* | 1 13 *s* |
| H-14 | 1 48 *s* | 1 45 *s* | 1 49 *s* | 1 45 *s* |
| H-15 | 4 39 *br s* | 4 39 *d*<br>4.34 *d* | 4 72 *br s* | 4 77 *br s* |
| H-18 | 5 94 *qq* | 5 92 *qq* | 5.94 *qq* | 5 92 *qq* |
| H-19 | 1 63 *dq* | 1 65 *dq* | 1 63 *dq* | 1.64 *dq* |
| H-20 | 1 75 *dq* | 1 76 *dq* | 1 75 *dq* | 1.76 *dq* |
| OAc | — | — | 2 11 *s* | 2.11 *s* |

*J* (Hz). 5, 6 = 2.5, 6, 7 = 7.5, 7, 8 = 4, 8, 9 = 2, 8, 9′ = 12; 9, 9′ = 14, 18, 19 = 7, 18, 20 = 19, 20 = 1

The aerial parts of *Vernonia neocorymbosa* Hilliard afforded squalene, vernolide (**7**) [8] and vernodalin (**8**) [9], while the roots contained the 13-hydroxybisabol-2-en-1-one **16** [10] and 13-hydroxybisabol-2,10-dien-1-one (**17**) as well as small amounts of onopordopicrin (**9**) [11]. The acetate of **17** was isolated previously [10]

The new results on some South African *Vernonia* species again show that the constituents of the South African *Vernonia* species are at least in part similar to those of the American species The hirsutinolides **1**–**6** are obviously closely related to glaucolide A

## EXPERIMENTAL

The air-dried plant material, collected in February 1981 in Transvaal, 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 their high field $^1H$ NMR spectra or by direct comparison with authentic material Vouchers were deposited in the Botanic Research Institute, Pretoria

Vernonia glabra (*voucher* 81/63) The aerial parts (175 g) afforded 3 mg α- and 3 mg β-selinene, 1 mg selina-4,11-diene, 1 3 mg β-elemene, 2 mg germacrene A, 2 mg squalene, 1 5 mg **10**, 2 mg **11**, 5 mg **14**, 3 mg **15** ($Et_2O$–petrol, 1 3), 4 mg of a mixture of the isomeric aldehydes, **18** and 4 mg **19** ($Et_2O$–petrol, 1 10), colourless oil, not free from **18** Heating in $C_6D_6$ at 125° for 30 min afforded 4 mg **20**, which was purified by TLC ($Et_2O$–petrol, 1 10) ($^1H$ NMR see Table 1), colourless oil, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ 2700, 1700 (C=CCHO), reduction with $NaBH_4$ in MeOH gave 2 mg **21** ($^1H$ NMR see Table 1)

*4α-Hydroxyeudesm-*11*-en-*12*-al* (**15**) Colourless oil, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ 3600 (OH), 2700, 1700 (CHO), MS *m/z* (rel int ) 236 178 $[M]^+$ (2) ($C_{15}H_{24}O_2$), 218 $[M-H_2O]^+$ (56), 203 $[218-Me]^+$ (32), 175 $[203-CO]^+$ (24), 71 (91), 55 (100)

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589\quad 578\quad 546\quad 436\,\text{nm}}{-7\quad -8\quad -9\quad -13}\,(CHCl_3,\ c\ 0\ 3)$$

Vernonia poskeana *var.* poskeana (*voucher* 18/197) The aerial parts (60 g) afforded 20 mg germacrene D and, by TLC ($Et_2O$, several times), of the polar fraction 6 7 mg **3**, 6 mg **4**, 1 5 mg **5** and 5 mg **6**, while the roots (20 g) gave 2.5 mg **13**, colourless gum, which could not be induced to crystallize Acetylation ($Ac_2O$, 1 hr, 70°) afforded the 15-*O*-acetate ($^1H$ NMR spectra see Table 3). $[\alpha]_D + 10°$ ($CHCl_3$, *c* 0 13) MS *m/z* (rel int ) 358 $[M-HOAc]^+$ (2), 258 $[358-C_5H_8O_2]^+$ (2), 83 $[C_4H_7CO]^+$ (100)

*8α-(4′-Hydroxysenecioyloxy)-3-oxo-1-desoxy-1,2-dehydro-hirsutinolide-*13-O*-acetate* (**3**) Colourless gum, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ 3600 (OH), 1780 (lactone), 1740 (OAc), 1730 ($C=CCO_2R$), 1600 (C=COR), MS *m/z* (rel int ) 316 095 $[M-RCO_2H]^+$ (15) ($C_{17}H_{16}O_6$), 274 $[316-\text{ketene}]^+$ (8), 257 $[316-OAc]^+$ (30), 99 $[C_4H_6(OH)CO]^+$ (100), 71 $[99-CO]^+$ (90)

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589\quad 578\quad 546\quad 436\,\text{nm}}{-203\quad -215\quad -258\quad -615}\,(CHCl_3,\ c\ 0\ 55)$$

*8α-(4′-Hydroxysenecioyloxy)-3-oxo-1-desoxy-1,2-dehydro-hirsutinolide* (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ 3600 (OH), 1780 (lactone), 1730 ($C=CCO_2R$, C=O), 1600 (C=COR), MS *m/z* (rel int ) 274 085 $[M-RCO_2H]^+$ (27) ($C_{15}H_{14}O_5$), 246 $[274-CO]^+$ (8), 231 $[246-Me]^+$ (20), 99 $[RCO]^+$ (78), 71 $[99-CO]^+$ (100)

*8α-Senecioyloxy-3-oxo-1-desoxy-*1, *2-dehydrohirsutinolide-*13-O*-acetate* (**5**) Colourless gum, IR $\nu_{max}^{CCl_4}$ $cm^{-1}$ 3600 (OH), 1780 (lactone), 1725 ($C=CCO_2R$, $C=O$), MS $m/z$ (rel int) 316 $[M-RCO_2H]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (85)

*8α-(2-Methylacryloyloxy)-3-oxo-1-desoxy-1,2-dehydrohirsutinolide-13-O-acetate* (**6**) Colourless gum, IR $\nu_{max}^{CCl_4}$ cm$^{-1}$ 1780 (lactone), 1745 (OAc), 1720 ($C=CCO_2R$, $C=O$), 1600 ($C=COR$), MS $m/z$ (rel int) 342 $[M-HOAc]^+$ (1), 316 095 $[M-RCO_2H]^+$ (21) ($C_{17}H_{16}O_6$), 257 $[316-OAc]^+$ (41), 69 $[C_3H_5CO]^+$ (100)

Vernonia poskeana *var* chlorolepis (*voucher* 81/270) The aerial parts (130 g) afforded 60 mg germacrene D, 60 mg squalene, 2 5 mg **1** ($Et_2O$) and 33 mg **2** ($Et_2O$), while the roots (220 g) gave 100 mg *β*-bergamotene and 10 mg sitosterol

*8α-(5′-Hydroxysenecioyloxy)-3-oxo-1-desoxy-1,2-dehydrohirsutinolide-13-O-acetate* (**1**) Colourless gum, IR $\nu_{max}^{CCl_4}$ cm$^{-1}$ 3600 (OH), 1770 (lactone), 1750 (OAc), 1720 ($C=CCO_2R$, $C=O$), 1600 ($C=COR$), MS $m/z$ (rel int) 316 $[M-RCO_2H]^+$ (0 5), 274 085 $[316-\text{ketene}]^+$ (28) ($C_{15}H_{14}O_5$), 99 $[RCO]^+$ (100)

*8α-(5′-Acetoxysenecioyloxy)-3-oxo-1-desoxy-1,2-dehydrohirsutinolide-13-O-acetate* (**2**) Colourless gum, IR $\nu_{max}^{CCl_4}$ cm$^{-1}$ 1780 (lactone), 1750 (OAc), 1720 ($C=CCO_2R$, $C=O$), 1600 ($C=COR$), MS $m/z$ (rel int) 316 095 $[M-RCO_2H]^+$ (32) ($C_{17}H_{16}O_6$), 274 $[316-\text{ketene}]^+$ (17), 257 $[316-OAc]^+$ (38), 99 $[RCO-\text{ketene}]^+$ (100)

Vernonia neocorymbosa (*voucher* 81/84) The aerial parts (250 g) afforded 100 mg squalene, 25 mg **7** and 1 3 mg **8**, while the roots gave 3 mg **9**, 3 mg **16** and 3 mg **17**, which was not obtained free from **16**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm$^{-1}$ 3630 (OH), 1670 ($C=CC=O$), MS $m/z$ (rel int) 236 $[M]^+$ (0 3), 218 $[M-H_2O]^+$ (4) ($C_{15}H_{22}O$), 137 $[C_9H_{13}O]^+$ (57), 110 $[C_7H_{10}O]^+$ (McLafferty) (100), 95 $[110-Me]^+$ (53), 82 $[110-CO]^+$ (43), $^1$H NMR ($C_6D_6$) 5 76 (*q*, H-2), 2 26 (*m*, H-4), 2 38 (*dddq*, H-7), 5 44 (*br t*, H-10), 1 90 (*br s*, H-12), 3 84 (*br s*, H-13), 1 35 (*d*, H-14), 2 03 (*br d*, H-15) ($J$ 2, 15 = 1 Hz, 6, 7 = 3 Hz, 7, 8 ~ 8 Hz, 7, 14 = 7 Hz, 9, 10 = 7 Hz)

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