Phytochemistry, 1980, Vol 19, pp 2669 2673. © Pergamon Press Ltd. Printed in England. 0031-9422/80/1201-2669 $02.00/0

SEVEN GUAIANOLIDES FROM THE TRIBE VERNONIEAE*

FERDINAND BOHLMANN,† CHRISTA ZDERO,† ROBERT M. KING‡ and HAROLD ROBINSON
† Institute for Organic Chemistry, Technical University Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, W. Germany; ‡ Smithsonian Institution, Washington, DC 20560, U.S.A.

(*Received* 28 *February* 1980)

Key Word Index—*Lychnophora blanchetii*; *Centratherum punctatum*; *Piptocarpha oblonga*; *Albertinia brasiliensis*; *Pseudostifftia kingii*; *Elephantopus hirtiflorus*; Compositae; sesquiterpene lactones; new guaianolides.

Abstract—Investigation of six species, all belonging to the Vernonieae, afforded in addition to known compounds seven new guaianolides five of them related to eremanthine, one of the lactones which may be typical of the tribe. The structures were elucidated by spectroscopic methods. Chemotaxonomic aspects are discussed briefly.

INTRODUCTION

So far only about 10 of the 70 genera of the large tribe Vernonieae have been investigated chemically [1]. We therefore have collected species in Brazil from the small genera *Lychnophora*, *Albertinia*, *Pseudostifftia*, the large genus *Piptocarpha*, all not studied before, *Centratherum punctatum*, from which the heliangolide centratherin has been isolated previously [2] and an additional *Elephantopus* species. In addition to known compounds, seven new guaianolides were isolated.

RESULTS AND DISCUSSION

The roots of *Lychnophora blanchetii* (Sch. Bip.) H. Robinson contain the widespread trideca-pentaynene (**1**) [3], eremanthine (**7**) [4], costunolide (**10**) and lupeyl acetate (**21**). The polar fractions afforded a complex mixture of additional sesquiterpene lactones. **16** (6α-angeloyloxy-goyazen sanolide) [5] could be separated from the other compounds only by TLC. HPLC, using a reversed phase system, allowed the nearly complete separation of three other lactones: **11** and **12** (8α-[2-methylacryloyloxy]- and tiglinoyloxy-cumambranolide) as well as **14** (8α-methylacryloyloxy]-estafiatin). The structures of **11** and **12** could easily be deduced from the spectral data. The ^{1}H NMR data are very similar to those of **13**, which we have isolated from an *Eremanthus* species [6] (see Table 1). The nature of the ester residues clearly follows from the corresponding signals, 2-methylacryloyl: 6.20 (*br. s*), 5.70 *dq* and 2.01 (*br. s*) and tiglinoyl: 6.95 (*br. q*), 1.85 (*br. d*) and 1.81 (*br. s*). Double resonance experiments establish the assignments of the other signals, which show only small shift differences, when compared with the chemical shifts of **13**. **12**, however, could not be separated completely from **14**. The structure of the latter also follows from the observed ^{1}H NMR data. Most of the signals are very similar to those of estafiatin [7]. The signals, which must be assigned to 7-, 8- and 13′-H, however, are changed typically. Irradiation at 3.24 ppm clearly shows that we are dealing with the signal of 7-H, as the 13-H doublets collapse to singlets, the double doublet at 4.12 to a doublet and the three-fold doublet at 5.09 to a doublet of doublets. The coupling constants for 8-H (5.09 *ddd*) further indicate an α-position of the methylacrylate. The aerial parts also contain **1**, **7** and **21** as well as lupeol (**22**) and 6α-[2-methylacryloyloxy]-goyazensanolide (**15**) [4].

The roots of *Centratherum punctatum* Cass. contain **1**, traces of tridec-1,11-dien-3,5,7,9-tetrayne (**2**) [3], **7** and **21** as well as two further isomeric sesquiterpene lactones, as follows from the molecular formula and the ^{1}H NMR data (see Table 1). The slightly less polar lactone obviously is 8α-isovaleryloxyeremanthine (**8**), while the more polar lactone is 8α-isovaleryloxydehydrocostuslactone (**9**). The structure of **8** could be deduced from the ^{1}H NMR data. Irradiation at the four-fold doublet at 3.23 ppm collapses the 13-H doublets to singlets and the doublet of doublets at 4.02 to a doublet, while the overlapping signals at 5.40 were altered. In C_6D_6, however, these two signals are separated clearly (5.30 *dd* and 5.44 *dq*). Irradiation of the 7-H signal shows that the former must be assigned to 8β-H, while the stereochemistry follows from the observed coupling $J_{7,8}$ = 10 Hz. The ^{1}H NMR spectrum of **8** is very similar to that of the corresponding senecioate [8]. The ^{1}H NMR spectrum of the second lactone (see Table 1) clearly indicates that a guaianolide of the dehydrocostuslactone-type must be present (six signals of methylene protons). Again the position of the ester residue follows from decoupling experiments (irradiation at 3.14 ppm, 7-H). Also the configurations at all centres could be established by decoupling. The ^{1}H NMR spectra of the corresponding senecioate [9] and the tiglate [10] are very similar, again establishing the proposed structure of **9**.

The aerial parts afforded **1**, germacrene D (**3**), bicyclogermacrene (**4**), humulene (**5**), caryophyllene (**6**), eremantholide A (**17**) [11] and **21**, while centratherin (2) was not observed, perhaps due to the limited amount of material.

The aerial parts of *Piptocarpha oblonga* (Gardn.) Baker afforded **3**, **21**, **22** as well as sakuranetin (**23**) [12],

---

* Part 289 in the series "Naturally Occurring Terpene Derivatives"; for Part 288 see: Bohlmann, F., Jakupovic, J., Robinson, H. and King, R. M. (1980) *Phytochemistry* **19**, 2769.

Table 1. ^{1}H NMR data for the sesquiterpene lactones **8**, **9**, **11**, **12**, **14**, **18** and **19**

	8	C_6D_6	**9**	**11**	**12**	**14**	**18**	**19**
1-H	2.93 *ddd*	2.41 *ddd*	2.97 *ddd*	2.61 *ddd*	2.60 *ddd*	3.03 *m*	2.88 *m*	2.89 *m*
2-H	2.08 *m*	1.57 *m*	2.2 *m*	2.26 *dd(br)*	2.25 *dd(br)*	2.06 *m*	2.00 *m*	2.49 *m*
2′-H	1.76 *m*	1.33 *m*		2.11 *dd(br)*	2.10 *dd(br)*	1.9 *m*	1.85 *m*	1.76 *m*
3-H	2.48 *m*	2.17 *m*	2.51 *m*	5.52 *s(br)*	5.52 *s(br)*	3.38 *s(br)*	2.49 *t(br)*	5.60 *dd(br)*
3′-H								
5-H	2.84 *dd(br)*	2.33 *dd(br)*	2.82 *dd(br)*	2.79 *dd(br)*	2.79 *dd(br)*	1.78 *dd*	2.88 *m*	2.89 *m*
6-H	4.02 *dd*	3.40 *dd*	4.02 *dd*	4.04 *dd*	4.04 *dd*	4.12 *dd*	2.24 *dd(br)* (α) 2.00 *m* (β)	2.22 *dd* 2.03 *m*
7-H	3.23 *dddd*	2.84 *dddd*	3.14 *dddd*	3.98 *dddd*	3.96 *dddd*	3.24 *dddd*	2.80 *dddd*	2.72 *dddd*
8-H	5.40 *m*	5.30 *dd(br)*	5.00 *ddd*	5.23 *ddd*	5.23 *dd(br)*	5.09 *ddd*	3.78 *ddd*	3.78 *ddd*
9-H	5.40 *m*	5.44 *dq*	2.71 *dd*	2.36 *dd*	2.36 *dd*	2.40 *m*	3.02 *dd*	3.05 *dd*
9′-H			2.27 *m*	1.91 *dd(br)*	1.93 *dd*		2.33 *dd*	2.33 *dd*
13-H	6.26 *d(br)*	6.32 *dd*	6.24 *d*	6.18 *d*	6.16 *d*	6.24 *d*	6.21 *d*	6.22 *d*
13′-H	5.69 *d(br)*	5.56 *dd*	5.65 *d*	5.50 *d*	5.49 *d*	5.62 *d*	5.52 *d*	5.51 *d*
14-H	1.83 *s(br)*	1.47 *s(br)*	5.06 *s(br)*	1.25 *s*	1.24 *s*	5.11 *d*	5.03 *s(br)*	5.09 *s(br)*
14′-H			4.94 *s(br)*			4.84 *d(br)*	4.91 *s(br)*	5.05 *s(br)*
15-H	5.2 *ddd*	5.33 *ddd*	5.30 *s(br)*	1.92 *s(br)*	1.93 *s(br)*	1.62 *s*	4.95 *ddd*	5.14 *dd*
15′-H	5.05 *ddd*	5.05 *ddd*	5.10 *s(br)*				4.81 *ddd*	5.02 *dd*
OCOR	2.27 *m*	2.06 *d(br)*	2.27 *m*	6.20 *s(br)*	6.95 *q(br)*	6.20 *s(br)*	—	2.27 *d(br)*
	2.17 *m*	2.17 *m*	2.17 *m*	5.70 *dq*	1.85 *d(br)*	5.69 *s(br)*		2.13 *m*
	1.00 *d*(6H)	0.91 *d*	1.02 *d*(6H)	2.01 *s(br)*	1.81 *s(br)*	2.00 *s(br)*		0.99 *d*
		0.90 *d*						

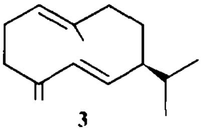
J (Hz): 7,13 = 3.5; 7,13′ = 3; **8**: 1,2 = 1,2′ = 1,5 ~ 7; 3,15 = 5,15 = 1.5; 5,6 = 6,7 = 9.8; 7,8 = 10; 8.9 = 3.5; 9,14 = 1.5; 13,13′ = 0.5; **9**: 1,2 = 1,2′ = 1.5 ~ 7; 5,6 = 10.5; 6,7 = 9; 7,8 = 9; 8.9 = 5; 8,9′ = 9; 9,9′ = 14; **11/12**: 1,2 = 9; 1,2′ = 10; 1,5 = 8; 2,2′ = 16; 5,6 = 6,7 = 9.5; 7,8 = 10; 8,9 = 5; 9,9′ = 16; **14**: 1,14 = 1.5; 5,6 = 11; 6,7 = 9; 7,8 = 9; 8,9 = 4; 8,9′ = 3; **18/19**: 2,3 ~ 8; 3,15 = 2; 5,6α = 5; 5,15 = 2; 6α,6β = 13; 6β,7 = 7,8 = 10; 8,9 = 5; 8,9′ = 11; 9,9′ = 12; (**19**: 2,3 = 7.5; 2′,3′ = 3′,4′ = 3′,5′ = 7).

$Me[C \equiv C]_5CH = CH_2$

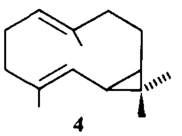
1

$MeCH = CH[C \equiv C]_4CH = CH_2$

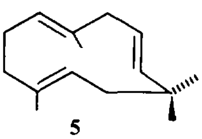
2



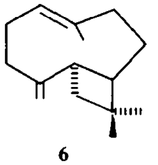
3



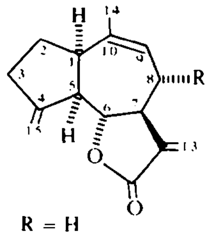
4



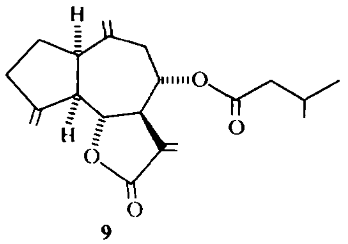
5



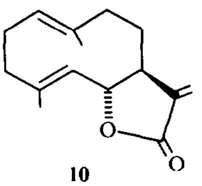
6



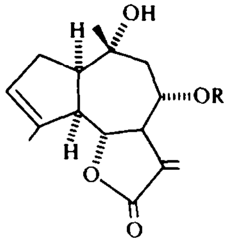
7 R = H
8 R = OCOCH$_2$CHMe$_2$

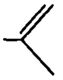


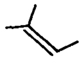
9



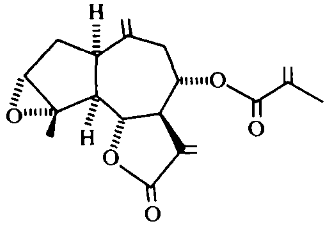
10



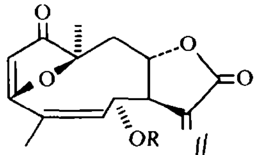
11 R = CO 

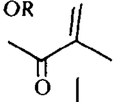
12 R = CO 

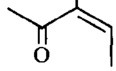
13 R = COCHMe$_2$

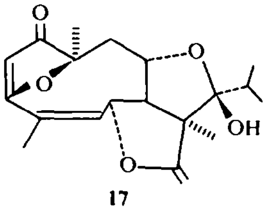


14

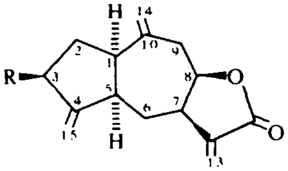


15 R = 

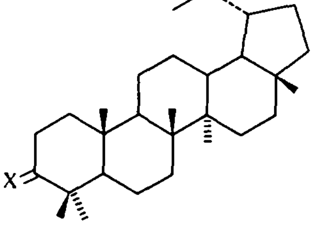
16 R = 



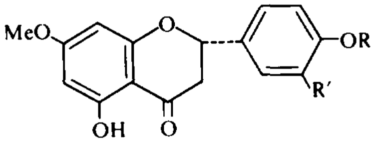
17



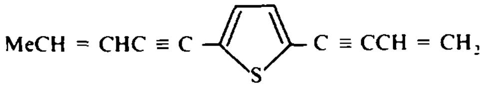
18 R = H
19 R = OCOCH$_2$CHMe$_2$



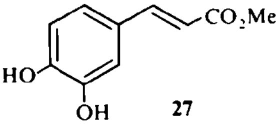
20 X = O
21 X = βOAc; H
22 X = βOH, H



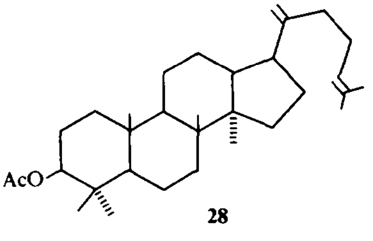
23 R = R' = H
24 R = Me, R' = H
25 R = H, R' = OMe



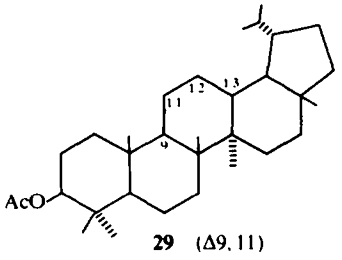
26



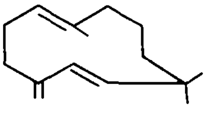
27



28



29 (Δ9, 11)
30 (Δ12, 13)



31

naringenin 7,4′-dimethyl ether (**24**) [13] and dimethyleriodictyol (**25**) [14], the first one in an unusually high concentration. The aerial parts of *Albertinia brasiliensis* Spreng. afforded only squalene, **21** and **22**.

The roots of *Elephantopus hirtiflorus* DC. afforded **1**, **2**, **21** and **22** and small amounts of two sesquiterpene lactones, most probably the guaianolides **18** and **19**. The structures were elucidated by their ^{1}H NMR data (see Table 1). The presence of 8,12-lactones clearly follows from the 8-H signal in the spectrum of **18**, being a three-fold doublet at 3.78 ppm (J = 10, 10, 5 Hz). Irradiation at the four-fold doublet at 2.80 collapses the signal at 3.78 to a double doublet, the methylene signals (13-H) to singlets and changes the overlapped signals at 2.0 ppm, which allows the assignments of 6β-, 7-, 8- and 13-H. No coupling is observed between 6α- and 7-H, which is in agreement with a model, the angle between these hydrogens being nearly 90°. Further decoupling experiments show that the broad multiplet at 2.88 ppm must be assigned to 1- and 5-H Irradiation of this signal shows couplings with 14- and 15-H as well as with the protons, which have resonances at 2.24 (6α-H, *dd*), 2.0 (2-H and 6β-H, *m*), 1.85 (2-H, *m*). Assignments for 2-H could be established by irradiation at 2.49 (3-H), which causes changes at 2.0 and 1.85 ppm and collapses the 15-H signals to doublets. Irradiation of the 8-H signal further allows the assignment of 9-H (3.02, *dd* and 2.33, *dd*). Inspection of models show that a *cis*- or a *trans*-lactone would agree with the observed couplings. A negative Cotton-effect at 250 nm, however, indicates a *cis*-7,12-lactone [15]. Furthermore the highfield position of the 8-H signal and the observed couplings may be an indication for a *cis*-fused 8,12-lactone [16]. A Dreiding model explains the relative chemical shifts of 9-H and the highfield shift of 8α-H, which seems to be shielded by the 10,14-double bond. The stereochemistry at C-1 and C-5 is not certain since the signals of 1- and 5-H are overlapped also in C_6D_6. Even addition of Eu(fod)$_3$ does not separate these signals. This, however, is only likely if **18** is a *cis*-annelated guaianolide as is usual in this tribe. The ^{1}H NMR data of **19** are very similar to those of **18**. The presence of a 3-isovaleryloxy group clearly follows from the observed changes in the ^{1}H NMR (see Table 1). The β-orientation is indicated by the chemical shift and the couplings of 3-H, which are nearly identical with those of zaluzanin C-esters [8]. We have named **18** elehirtanolide. The aerial parts only gave **21** and a small amount of unidentified triterpene acetates.

The roots of *Pseudostifftia kingii* H. Robins., which most probably belongs to the Vernonieae [17], contain **1**, **2**, **21**, **22**, **26** [3], **27** and **28**. The aerial parts gave **2**, **21**, **22**, **29** [18], **30** [18] and **31**. These constituents unfortunately are not very characteristic and therefore cannot support the taxonomy. The present results on species representing six different genera show again that guaianolides are widespread in the tribe Vernonieae. However, the overall picture still is very complicated. There are some groups where mainly furanone-heliangolides are present, but also in these cases especially eremanthine often co-occurs. In the genus *Vernonia*, glaucolides, however, are widespread, though here also groupings appear in which these lactones are replaced by other types. So far little is known about the systematic relationships within this large genus [19]. *Pseudostifftia* and *Piptocarpha* gave no lactones; botanically they are not very close to *Vernonia*. However, in all genera lupeol or its derivatives are present [17, 20]. Surely much more work needs to be done, both chemically and systematically.

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as internal standard; MS: 70 eV, direct inlet; optical rotation: $CHCl_3$. The air dried plant material (all collected in north-eastern Brazil) was extracted with Et_2O-petrol, 1:2 and the resulting extracts first separated by column chromatography (SiO_2, act. grade II) and further by repeated TLC (SiO_2, GF 254). The extracts of aerial parts first were treated with MeOH to remove long chain saturated hydrocarbons. Known compounds were identified by comparison of their IR and ^{1}H NMR spectra with those of authentic material.

Lychnophora blanchetii (*voucher RMK* 8151). The roots (100 g) afforded 0.2 mg **1**, 15 mg **7**, 5 mg **10**, 3 mg **11**, 2 mg **12** and 2 mg **14** (separated by HPLC, MeOH/H_2O 7:3, reversed phase) 2 mg **16** and 20 mg **21**, while the aerial parts (500 g) gave traces of **1**, 10 mg **7**, 50 mg **15**, 10 mg **21** and 10 mg **22**.

Centratherum punctatum (*voucher RMK* 8047). The roots (30 g) afforded 0.1 mg **1**, traces of **2**, 10 mg **7**, 15 mg **8** (Et_2O-petrol 1:3), 5 mg **9** (Et_2O-petrol 1:3) and 5 mg **21**, while the aerial parts (150 g) yielded traces of **1**, 10 mg **3**, 5 mg **4**, 3 mg **5**, 10 mg **6**, 1 mg **17** and 5 mg **21**.

Piptocarpha oblonga (*voucher RMK* 8020). The aerial parts (500 g) afforded 10 mg **3**, 200 mg **21**, 100 mg **22**, 3 mg **23**, 40 mg **24** and 30 mg **25**.

Albertinia brasiliensis (*voucher RMK* 7987). The aerial parts (480 g) afforded 50 mg **21**, 200 mg **22** and 20 mg squalene.

Elephantopus hirtiflorus (*voucher RMK* 8050). The roots (10 g) afforded 0.1 mg **1**, traces of **2**, 0.5 mg **18** (Et_2O-petrol 1:3), 1 mg **19** (Et_2O-petrol 1:1), 10 mg **21** and 10 mg **22**, while the aerial parts (75 g) gave 3 mg **21** and a mixture of triterpene acetates, which have not been identified.

Pseudostifftia kingii (*voucher RMK* 8084). The roots (95 g) afforded 0.1 mg **1**, 0.5 mg **2**, 20 mg **21**, 20 mg **22**, 0.5 mg **26**, 5 mg **27** and 5 mg **28**, while the aerial parts (750 g) gave 0.2 mg **2**, 20 mg **21**, 30 mg **22**, 5 mg **29**, 5 mg **30** and 10 mg **31**.

8α-*Isovaleryloxy-eremanthine* (**8**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R), 3100, 1660 ($C{=}CH_2$); MS: M^+ *m/e* (rel. int.): 330.147 (3) ($C_{20}H_{26}O_4$): 228 (37) ($M - RCO_2H$); 213 (15) (228 − Me); 200 (17) (228 − CO); 185 (14) (200 − Me); 85 (77) ($C_4H_9CO^+$); 57 (100) (85 − CO).

$$[\alpha]_{24}^{\lambda} = \frac{589}{+66.7}\;\frac{578}{+74.2}\;\frac{546}{+81.9}\;\frac{436}{+144.7}\;\frac{365\,\text{nm}}{+230.6}$$

(c = 0.36)

8α-*Isovaleryloxy-dehydrocostuslactone* (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); 3090, 1660, 1650, 910 ($C{=}CH_2$); MS M^+ *m/e* (rel. int.): 330.183 (1) ($C_{20}H_{26}O_4$); 228 (28) ($M - RCO_2H$); 213 (6) (228 − ˙Me); 85 (96) ($C_4H_9CO^+$); 57 (100) (85 − CO).

8α-[2-*Methylacryloyloxy*]-*cumambranolide* (**11**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH); 1777 (γ-lactone); 1723, 1640 ($C{=}CCH_2R$), 3050, 1665 ($C{=}CH_2$); MS: M^+ *m/e* (rel. int.): 332.163 (7) ($C_{19}H_{24}O_5$); 246 (22) ($M - RCO_2H$); 228 (31) (246 − H_2O); 69 (100) ($C_3H_5CO^+$).

8α-*Tiglinoyloxycumambranolide* (**12**). Colourless gum, not free from **14**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1780 (γ-lactone), 1720, 1640 ($C{=}CCO_2R$); MS: M^+ *m/e* (rel. int.): 346.178 (1) ($C_{20}H_{26}O_5$); 246 (6) ($M - RCO_2H$); 228 (10) (246 − H_2O); 213 (7) (228 − ˙Me); 83 (100) ($C_4H_7CO^+$).

8α-[2-*Methylacryloyloxy*]-*estafiatin* (**14**). Colourless gum, not free from **12**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1720, 1655 ($C{=}CCO_2R$); MS: M^+ *m/e* (rel. int.): 330.147 (1) ($C_{19}H_{22}O_5$); 244 (7) ($M - RCO_2H$); 69 (100) ($C_3H_5CO^+$).

Elehirtanolide (**18**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone); 3080, 1650, 859 ($C{=}CH_2$); MS: M^+ *m/e* (rel. int.): 230.131 (35) ($C_{15}H_{18}O_2$); 215 (12) (M − ˙Me); 202 (40) (M − CO); 91 (100) ($C_7H_7^+$); CD (MeCN). $\Delta\varepsilon_{250} \sim -1$; $\Delta\varepsilon_{215} \sim +5$

(due to the small amount available no exact values can be given).

3β-Isovaleryloxyelehirtanolide (**19**). Colourless oil. IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1785, 1665 (γ-lactone), 1740 (CO_2R); 3090, 1645, 910 ($C{=}CH_2$); MS: M$^+$ *m/e* (rel. int.): 330.183 (8) ($C_{20}H_{26}O_4$); 246 (7) (M − O=C=CHCHMe$_2$); 245 (6) (M − COR); 228 (15) (M − RCO_2H); 85 (100) ($C_4H_9CO^+$); 57 (91) (85 − CO).

Acknowledgements—We thank Dr. Scott A. Mori and Dr. P. Alvim, Centro de Pesquisas do Cacau at Itabuna, Bahia, Brazil, for their help during plant collection and the Deutsche Forschungsgemeinschaft for financial support.

REFERENCES

1. Harborne, J. B. and Williams, C. A. (1977) in *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L. eds.) p. 524. Academic Press, London.
2. Ohno, N., McCornick, S. and Mabry, T. J. (1979) *Phytochemistry* **18**, 681.
3. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, London.
4. Vichnewski, W., Sarti, S., Gilbert, B. and Herz, W. (1975) *Phytochemistry* **15**, 191.
5. Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1980) *Phytochemistry* **19**, 2381.
6. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, 2663.
7. Sanchez-Viesoa, F. and Romo, J. (1963) *Tetrahedron* **19**, 1285.
8. Bohlmann, F., Brindöpke, G. and Rastogi, R. C. (1978) *Phytochemistry* **17**, 475.
9. Bohlmann, F. and Zdero, C. (1977) *Phytochemistry* **16**, 778.
10. Bohlmann, F., Grenz, M. and Zdero, C. (1977) *Phytochemistry* **16**, 285.
11. Le Quesne, P. W., Le Very, S. B., Menachery, M. B., Brennan, T. F. and Raffauf, R. F. (1978) *J. Chem. Soc. Perkin Trans. I*: 1572.
12. Asahina, Y. (1908) *J. Pharm. Soc. Jpn.* **313**, 213.
13. Wollenweber, C. and Egger, K. (1971) *Z. Pflanzenphysiol.* **65**, 427.
14. Geissman, T. A. (1958) *Aust. J. Chem* **11**, 371.
15. Stöcklin, W., Waddell, T. G. and Geissman, T. A. (1970) *Tetrahedron* **26**, 2397.
16. Herz, W. and Santhanam, P. S. (1967) *J. Org. Chem.* **32**, 507.
17. Robinson, H. (1979) *Phytologia* **44**, 442.
18. Bohlmann, F. and Knoll, K.-H. (1978) *Phytochemistry* **17**, 599.
19. Jones, S. B. (1977) in *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L. eds.) p. 503. Academic Press, London.
20. Robinson, H. (1979) *Phytologia* **44**, 300.