Phytochemistry, Vol. 20, No. 9, pp. 2233–2237, 1981.
Printed in Great Britain.

0031-9422/81/092233-05 $02.00/0

HIRSUTINOLIDES FROM *VERNONIA* SPECIES*

FERDINAND BOHLMANN, LUTZ MÜLLER, RAJINDER K. GUPTA, ROBERT M. KING† and HAROLD ROBINSON†

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany; †Smithsonian Institution, Washington, DC 20560, U.S.A.

(*Received* 31 *December* 1980)

Key Word Index—*Vernonia* species; Compositae; sesquiterpene lactones; hirsutinolides; triterpenes.

Abstract—Out of the nineteen species of *Vernonia* studied, five contained highly oxygenated sesquiterpene lactones, while the rest contained predominantly triterpenes, especially lupane derivatives.

The chemistry of the large genus *Vernonia* has been studied by many authors [1,2]. Especially highly oxygenated germacranolides are widespread in this genus. However, there are several species which lack these types of compounds. We have now investigated 19 further species, mainly from Brazil; only five of them contained sesquiterpene lactones, while the rest predominantly contained triterpenes (Table 2), also very widespread in the genus. The aerial parts of *V. echitifolia* Mart. afforded **15–21**, sesamine (**2**) as well as the penta- and hexamethoxy compounds **3** and **4**. **3** seemed to be a new compound. Its structure followed from the ^{1}H NMR data and the molecular formula. The roots gave **1** [3], **2–4**, **5** [4] and traces of the dihydro derivative **6**, which had already been prepared from **5** [5]. The roots of *V. venosissima* Sch. Bip. ex Baker afforded **15–18**, **22–24**, **26** and two sesquiterpene lactones, the hirsutinolides **13a** and **14**. **13a** on heating with acetic anhydride afforded **14**. Consequently, the isovalerate residue had to be placed at C-1. The ^{1}H NMR data of **13a** (Table 1) were very similar to those of related hirsutinolides [6,7], therefore the stereochemistry must be the same. **14** had been prepared already by elimination of acetic acid from the corresponding acetate [7]. The spectral data consequently were identical. All the other species investigated gave only known compounds (Table 2). The overall picture with regard to the distribution of terpenes in the genus *Vernonia* is unchanged by this study. Thus while many species contain highly oxygenated sesquiterpene lactones, several afforded mainly triterpenes, especially lupane derivatives.

EXPERIMENTAL

The air-dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were treated with MeOH to remove long-chain hydrocarbons. The extracts then were separated by CC (Si gel) and TLC (Si gel). Known compounds were identified by comparison of their IR and ^{1}H NMR spectra with those of authentic materials.

5-Methoxyeudesmin (**3**). Colourless crystals, not free from **4**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2835, 2820 (OMe), 1590, 1510 (aromatic); MS *m/z* (rel. int.): 416.184 (M^+, 100) ($C_{23}H_{28}O_7$), 386 (416 − CH_2O, 71), 355 (386 − OMe, 8), 177 (90), 165 (93), 141 (75); ^{1}H NMR ($CDCl_3$): 3.12 (*m*, H-1, 5), 4.75 (*d*, H-2, J = 4 Hz), 4.77 (*d*, H-6, J = 4 Hz), 4.3 and 3.90 (*m*, H-4,8), 3.85, 3.88, 3.91 (*s*, OMe), 6.58 (*s*, 2-H, H-2′, 6′), 6.92 (*s* (*br*), H-2″), 6.85 (*d*, H-5″, J = 8 Hz), 6.88 (*dd*, H-6″, J = 8, 1.5 Hz).

11,13β-Dihydrodehydrozaluzanin C (**6**). Colourless, not completely pure gum, which could not be induced to crystallize,

Table 1. ^{1}H NMR spectral data of compounds **6**, **13a** and **14** (270 MHz, $CDCl_3$, TMS as internal standard)

	6	**13a** (C_6D_6, 77°)	**14**
H-2	2.66 *dd*	2.3 *m*	4.83 *dd*
H-3	2.54 *dd*		2.87 *dd*
	—		2.74 *dd*
H-5	—	5.74 *s*	5.89 *s*
H-6	3.94 *dd*	—	—
H-7	2.57 *m*	—	—
H-8	—	6.02 *dd* (*br*)	6.21 *d* (*br*)
H-9	2.0 *m*	2.7 *m*	2.64 *dd*
H-9′		2.1 *m*	1.98 *dd*
H-11	2.27 *dq*	—	—
H-13	1.20 *d*	5.09 *d*	5.04 *d*
H-13′		4.93 *d*	4.99 *d*
H-14	4.92 *s* (*br*)	1.67 *s*	1.67 *s*
H-14′	4.59 *s* (*br*)		
H-15	6.24 *d* (*br*)	1.43 *s*	1.42 *s*
H-15′	5.78 *d* (*br*)		
OCOR	—	0.81 *d*	—
		0.80 *d*	
		1.4 *m*	
		1.7 *m*	
OAc	—	1.86 *s*	2.10 *s*
		1.71 *s*	2.09 *s*

J (Hz): compound **6**: 1,2 = 8; 1,2′ = 2.5; 2,2′ = 18.5; 5,6 = 6,7 = 9; 5.15 = 5,15′ = 3; 7,11 = 12; 11,13 = 6.5; compound **13a**: 8,9 ~ 3; 13,13′ = 13; compound **14**: 2,3 = 2; 2,3′ = 3; 3,3′ = 15.5; 8,9 = 7; 8,9′ = 1; 8,9′ = 15; 13,13′ = 13.

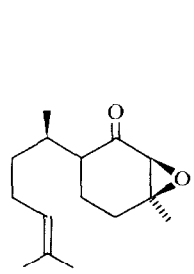
*Part 362 in the series "Naturally Occurring Terpene Derivatives". For Part 361 see Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 2029.

Table 2. Constituents of the *Vernonia* species examined

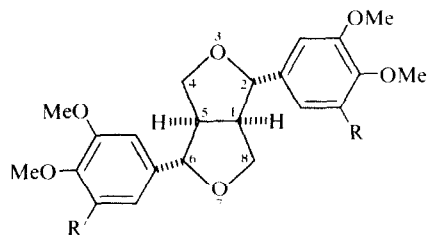
Species	Voucher	Roots		Aerial parts	
		Wt (g)	Constituents	Wt (g)	Constituents
V. alemeda H. Robins.	RMK 8208	20	20 mg **16**	600	100 mg **16**, 100 mg **18**, 60 mg **29**, 30 mg **30**, 30 mg **31**
V. condensata Baker	RMK 8013	—		930	50 mg **15**, 50 mg **17**
V. corizcea Less	RMK 8203	5	10 mg **15**, 10 mg **17**	50	10 mg **15**, 2 mg **17**, 10 mg **19**, 2 mg **29**, 5 mg **36**
V. echitifolia Mart.	RMK 8206	150	10 mg **1**, 2 mg **2**, 5 mg **3**, 5 mg **4**, 1 mg **5**, 1 mg **6**	1500	200 mg **2**, 200 mg **3**, 300 mg **4**, 100 mg **15**, 75 mg **16**, 50 mg **17**, 10 mg **18**, 150 mg **19**, 25 mg **20**, 2 mg **21**
V. farinosa Baker	RMK 8092	30	5 mg **15**, 15 mg **16**, 15 mg **18**, 5 mg **22**, 25 mg **23**	190	35 mg **19**, 20 mg **24**, 40 mg **25**
V. gigantea Trell. Branner et Cor.	LeVan 78/31	—		1000	160 mg **16**, 90 mg **17**, 100 mg **18**, 75 mg **37**
V. hagei H. Robins.	RMK 8059	40	100 mg **16**	200	50 mg **15**, 100 mg **16**, 10 mg **29**
V. holosericea Mart. ex DC	RMK 8091	10	100 mg **15**, 100 mg **17**, 50 mg **19**	100	50 mg **15**, 50 mg **16**
V. intermedia DC	78/1394	50	25 mg **5**, 1.5 mg **7**, 40 mg **8**, 25 mg **9**, 20 mg **10**, 3 mg **11**, 0.5 mg **38**	350	25 mg **16**, 25 mg **18**
V. kuntzei Hieron.	RMK 7640	30	2 mg **18**, 15 mg **39**	200	10 mg **13b**, 2 mg **13c**, 5 mg **19**, 10 mg **24**, 20 mg **29**, 2 mg **31**, 5 mg **35**, 10 mg **36**

V. laxa Gardn.	RMK 8105	40	50 mg **16**	100	50 mg **15**, 20 mg **16**, 20 mg **17**
V. mariana Mart.	RMK 8383	130	50 mg **15**, 10 mg **16**, 20 mg **17**, 75 mg **18**, 5 mg **20**, 50 mg **21**, 5 mg **24**, 2 mg **26**	330	25 mg **15**, 50 mg **16**, 10 mg **17**, 60 mg **18**, 5 mg **20**, 30 mg **21**, 10 mg **26**
V. missionis Gardn.	RMK 8383	600	10 mg **15**, 30 mg **16**, 5 mg **17**, 35 mg **18**, 2 mg **20**, 5 mg **21**, 5 mg **24**	440	100 mg **15**, 70 mg **16**, 5 mg **17**, 30 mg **18**, 70 mg **20**, 20 mg **21**
V. myrsinitis Ekman	RMK 8281	800	15 mg **15**, 40 mg **16**, 3 mg **17**, 45 mg **18**, 2 mg **20**	600	10 mg **19**, 30 mg **29**, 10 mg **30**, 5 mg **31**, 10 mg **35**
V. obtusata Less	RMK 8355	100	15 mg **15**, 60 mg **16**, 10 mg **17**, 30 mg **18**, 10 mg **21**, 5 mg **24**	200	10 mg **12**, 6 mg **15**, 40 mg **16**, 3 mg **17**, 40 mg **18**, 2 mg **24**, 10 mg **27**, 2 mg **28**, 30 mg **36**
V. regis H. Robins.	RMK 8158	135	100 mg **16**, 10 mg **32**, 10 mg **33**, 10 mg **34**	140	100 mg **15**, 50 mg **16**
V. teixeirae H. Robins.	RMK 8236	—		400	15 mg **15**, 50 mg **16**, 15 mg **17**, 100 mg **18**, 15 mg **20**, 50 mg **21**, 5 mg **27**, 10 mg **28**
V. tomentella Mart.	RMK 8392	500	20 mg **15**, 20 mg **29**, 10 mg **30**, 0.2 mg **38**	—	
V. venosissima Sch. Bip. ex Baker	RMK 8261	200	5 mg **13a**, 5 mg **14**, 4 mg **15**, 60 mg **16**, 2 mg **17**, 60 mg **18**, 3 mg **22**, 40 mg **23**, 2 mg **24**, 2 mg **26**	300	10 mg **13**, 20 mg **15**, 25 mg **16**, 5 mg **17**, 10 mg **18**, 5 mg **20**, 5 mg **21**, 2 mg **24**

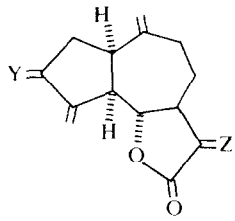
19 Squalene, **20** β-amyrin, **21** β-amyrin acetate, **22** taraxasterol, **23** taraxasteryl acetate, **24** stigmasterol, **25** oleonolic acid, **26** kaurenic acid, **27** 4-methoxycinnamic acid, **28** 3,4-dimethoxycinnamic acid, **29** germacrene D, **30** bicyclogermacrene, **31** α-humulene, **32** isocomene, **33** β-isocomene, **34** modhephene, **35** caryophyllene, **36** methyl linolenoate, **37** glaucolide A, **38** tridecapentaynene, **39** 2-[penta-1,3-diinyl]-5-but-3-en-1-ynyl thiophene.



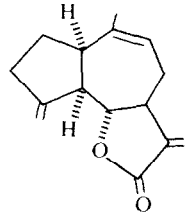
1



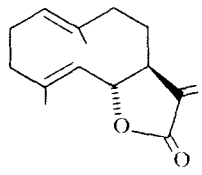
	2	3	4
R	H	OMe	OMe
R′	H	H	OMe



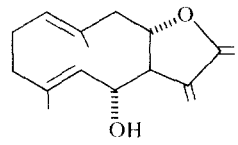
5 Z = CH_2, Y = O
6 Z = H, αMe, Y = O
7 Z = CH_2, Y = H_2
8 Z = CH_2, Y = αOSen, H
9 Z = CH_2, Y = αOH, H



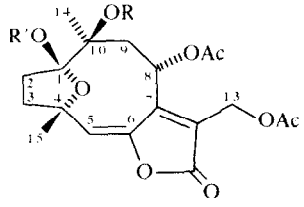
10



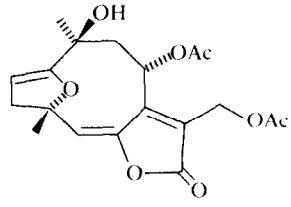
11



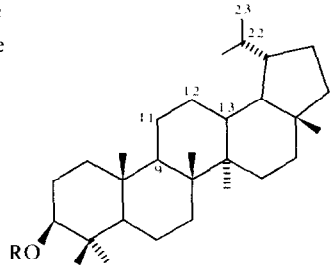
12



	13a	13b	13c
R	H	H	Ac
R′	iVal	H	Me



14



15 R = H, Δ22,23
16 R = Ac, Δ22,23
17 R = H, Δ12,13
18 R = Ac, Δ12,13

(lit. [5], mp 107°); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (γ-lactone), 1730 (C=O); MS *m/z* (rel. int.): 246.126 (M^+, 11) ($C_{15}H_{18}O_3$), 152 (M − C_6H_6O, 100); $[\alpha]_D$ positive ($CHCl_3$).

1(O)-*Acetyl-8α-acetoxy-10β-hydroxy-hirsutinolide* 1(O)-*isovalerate* (**13a**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560 (OH), 1770 (lactone), 1743 (OAc, CO_2R); UV λ_{max} = 286 nm (Et_2O); MS *m/z* (rel. int.): 480.200 (M^+, 1) ($C_{24}H_{32}O_{10}$), 420 (M − AcOH, 1), 360 (420 − AcOH, 2), 318 (420 − RCO_2H, 3), 276 (318 − ketene, 10), 258 (276 − H_2O, 7), 85 ($C_4H_9CO^+$, 38), 57 (85 − CO, 100);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 547 \quad 546 \quad 436\,nm}{-4 \quad -4 \quad -6 \quad -29} (c = 0.91,\ CHCl_3).$$

5 mg **13a** in 1 ml Ac_2O were heated 1 hr at 70°. TLC (Et_2O–petrol, 3:1) afforded 3 mg **14**.

8α-Acetoxy-10β-hydroxy-isohirsutinolide 13(O)-*acetate* (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1770 (lactone), 1747, 1230 (OAc); MS *m/z* (rel. int.): 318.110 (M − AcOH, 5) ($C_{17}H_{18}O_6$), 303 (318 − Me, 1), 290 (318 − CO, 8), 230 (290 − AcOH, 41), 57 (100);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+8 \quad +14 \quad +15 \quad +38} (c = 0.16,\ CHCl_3).$$

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

REFERENCES

1. Fischer, N. H., Olivier, R. J. and Fischer, H. D. (1979) *Fortschr. Chem. Org. Naturst.* **38**, 47.
2. Bohlmann, F., Jakupovic, J., Gupta, R. J., King, R. M. and Robinson, H. (1980) *Phytochemistry* **20**, 473.
3. Bohlmann, F., Zdero, C. and Schöneweiss, S. (1976) *Chem. Ber.* **109**, 3366.
4. Romo, J., Romo de Vivar, A. and Joseph-Nathan (1966) *Tetrahedron* **22**, 29.
5. Romo de Vivar, A., Cabrera, A., Ortega, A. and Romo, J. (1967) *Tetrahedron* **23**, 3903.
6. Bohlmann, F., Brindöpke, G. and Rastogi, R. C. (1978) *Phytochemistry* **17**, 475.
7. Bohlmann, F., Mahanta, P. K. and Dutta, L. N. (1979) *Phytochemistry* **18**, 289.