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THREE BOURBONENOLIDES AND OTHER SESQUITERPENE LACTONES FROM TWO *VERNONIA* SPECIES*

FERDINAND BOHLMANN, PAHUP SINGH, NALEEN BORTHAKUR 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 arkansana*; *V. profuga*; Compositae; Vernonieae; sesquiterpene lactones; bourbonenolides; guaianolides; glaucolides.

Abstract—A re-investigation of *V. arkansana* afforded several new sesquiterpene lactones, three bourbonenolides, obviously closely related to those isolated from this plant previously, a glaucolide and a methoxy derivative most probably formed by fragmentation of the corresponding bourbonenolide. From *V. profuga* in addition to known lactones a new guaianolide was isolated. The biogenetic relationships of the *Vernonia* sesquiterpene lactones are discussed briefly.

INTRODUCTION

From the large genus *Vernonia* many species have been investigated chemically. In addition to triterpenes, mainly of the lupane type [1], many highly oxygenated sesquiterpene lactones are present, especially germacranolides of the glaucolide type [1–3]. We now have investigated *Vernonia profuga* cf. L. and again some more material of *V. arkansana* DC. In addition to known sesquiterpene lactones several new ones were isolated, their structures being elucidated by spectroscopic methods.

RESULTS AND DISCUSSION

Vernonia arkansana has been investigated before [2, 4]. The investigation of some more material, however, gave several new compounds. The roots afforded costunolide and the known guaianolides **1**, **3**–**7** [3] and **8**, the hydroxy derivative of **6**. The structure clearly followed from the ^{1}H NMR data (Table 1), which were similar to those of **6**. The stereochemistry at C-8 was deduced from the couplings observed for H-8 and from the typical down-field shift of H-13′. The aerial parts gave lupeol, its acetate and the glaucolide marginatin (**10**) [4, 5] together with the corresponding methacrylate **11**, its structure also clearly following from the ^{1}H NMR data (Table 1), only the signals of the ester residue being different from those of **10**. Further lactones could be separated only with difficulty. Finally four compounds were obtained, three again only differing in the ester residues. The most polar was the diacetate **12**, while in two others one acetate group was replaced by a tiglate and a methacrylate residue, respectively (**13** and **14**). The structure of **12** could be deduced from the ^{1}H NMR data (Table 1), especially when compared with those of the bourbonenolides of type **16** isolated before [2]. However, the presence of an additional ester group and two doublets at 4.95 and 4.76 ppm as well as the absence of signals of exomethylene protons clearly showed that a modified glaucolide was present, which obviously was derived from bourbonene. Consequently, the signals of H-1–H-3, H-5, H-8 and H-9 showed a similar splitting pattern as the corresponding signals of **16** [2]. The H-8 signal, however, was shifted down-field due to the allylic nature of this proton, when compared with the chemical shift of H-8 in the spectrum of **16**. Also some other shifts and couplings were slightly changed. NOE showed that the stereochemistry at C-1, C-4 and C-5 was different from that of **16**. Irradiation of the H-1 signal caused a clear NOE of H-2, H-9α and H-15, while no effect for H-14 was observed. The stereochemical assignment was further supported by a hydrogen bond visible in the IR spectra of **12**–**14**. The ^{1}H NMR data of **13** and **14** corresponded to those of **12** (Table 1). However, in the spectra of **13** and **14** the H-8 signal was slightly shifted down-field, indicating that the unsaturated ester groups had to be placed at C-8 and not at C-13. Furthermore, an 13-acetoxy group is present in all sesquiterpene lactones of this type and therefore the proposed relative positions of the ester groups were very likely.

The ^{1}H NMR data of the last lactone agreed with the structure **15**. While only one ester residue was present, a methoxy group was introduced, most probably at C-10. From the signals of H-13 the presence of a methylene lactone was deduced. However, the absence of signals for H-6 and H-7 indicated a 6,7-double bond, its presence being supported by a down-field shifted doublet at 2.86 ppm, which was coupled with a broadened double doublet at 2.26 ppm. These signals probably were those of H-1 and H-5. All data therefore agreed best with the proposed structure, though the stereochemistry at C-4 and C-10 was only assigned by analogy to that of **12**–**14**. **15** could be formed by a fragmentation of **12** by attack of methanol at C-10 as shown in Scheme 1.

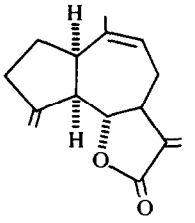
The roots of *Vernonia profuga* cf. L. afforded also **1**, **2**, **4**–**8** and a further guaianolide, the diol **9**. The structure

*Part 363 in the series "Naturally Occurring Terpene Derivatives". For Part 362 see Bohlmann, F., Müller, L., Gupta, R. K., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 2233.

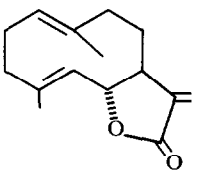
Table 1. ^{1}H NMR spectral data of compounds **8**, **9** and **11–15** ($CDCl_3$, 400 MHz, TMS as internal standard)

	8	**9**	**11**	**12**	**13**	**14**	**15**
H-1	3.20 *br ddd*	2.80 *br ddd*	5.08 *br dd*	3.36 *br dd*	2.38 *br dd*	2.39 *br dd*	2.26 *dd*
H-2α	2.61 *dd*	2.13 *ddd*		1.85 *m*	1.85 *m*	1.85 *m*	1.85 *m*
H-2β	2.50 *dd*	1.70 *ddd*					1.72 *m*
H-3	—	3.72 *ddd*		2.05 *m* 1.85 *m*	2.05 *m* 1.85 *m*	2.05 *m* 1.85 *m*	1.92 *m* 1.85 *m*
H-4	—	1.88 *ddq*	—	—	—	—	—
H-5	3.25 *dddd*	1.93 *ddd*	2.39 *d*	1.67 *d*	2.69 *d*	2.69 *d*	2.86 *d*
H-6	3.98 *dd*	3.93 *dd*	3.89 *d*	—	—	—	—
H-7	3.08 *dddd*	1.88 *ddd*	—	—	—	—	—
H-8	3.92 *m*	3.66 *ddd*	5.35 *m*	6.30 *br dd*	6.35 *br dd*	6.36 *br dd*	5.48 *dd*
H-9α	2.20 *br dd*	2.11 *br dd*		1.91 *dd*	1.94 *dd*	1.96 *dd*	1.43 *dd*
H-9β	2.31 *br dd*	2.72 *br dd*		2.55 *dd*	2.59 *dd*	2.59 *dd*	2.28 *dd*
H-11	—	2.52 *dq*	—	—	—	—	—
H-13	6.38 *d*	1.40 *d*	4.98 *br d*	4.95 *br d*	4.89 *br d*	4.91 *br d*	6.78 *br s*
H-13′	6.31 *d*		4.88 *d*	4.76 *d*	4.75 *d*	4.75 *d*	6.53 *br s*
H-14	5.03 *br s*	5.00 *br s*	1.74 *br s*	1.08 *br s*	1.09 *br s*	1.10 *br s*	1.00 *s*
H-14′	4.83 *br s*	5.03 *br s*					
H-15	6.27 *d*	1.18 *d*	1.42 *s*	1.22 *br s*	1.22 *br s*	1.24 *br s*	1.28 *s*
H-15′	5.88 *d*						
OCOR	—	—	5.67 *dq*	—	6.91 *qq*	5.69 *br s*	—
			6.12 *br s*	—	1.83 *dq*	6.16 *br s*	—
			1.92 *br s*	—	1.86 *dq*	1.98 *br s*	—
OAc			2.07 *s*	2.18 *s* 2.08 *s*	2.05 *s*	2.05 *s*	2.12 *s*
OH				2.95 *br s*	2.95 *br s*	2.95 *br s*	

J (Hz): compound **8**: 1,2α = 8; 1,2β = 5; 1,5 = 9; 2α,2β = 18; 5,6 = 6,7 = 7,8 = 9.5; 5,15 = 2.5; 7,13 = 3.5; 7,13′ = 3; 8,9α = 6; 8,9β = 7.5; 9α,9β = 13; compound **9**: 1,2α = 6; 1,2β = 10; 1,5 = 8; 2α,2β = 12; 2α,3 = 9; 3,4 = 6; 4,5 = 10; 5,6 = 6,7 = 7,8 = 10; 7,11 = 11; 8,9α = 10; 8,9β = 4; 9α,9β = 12; 11,13 = 7; compound **11**: 1,2 = 10; 1,2′ ~ 4; 5,6 = 9; 13,13′ = 13; compounds **12–14**: 1,2 = 1,5 = 7; 8,9α = 9; 8,9β = 7; 9α,9β = 13,13′ = 12.5; compound **15**: 1,2 = 1,2′ = 7.5; 1,5 = 7; 8,9α = 10.5; 8,9β = 7; 9α,9β = 13.



1



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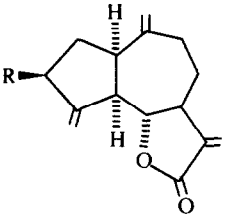
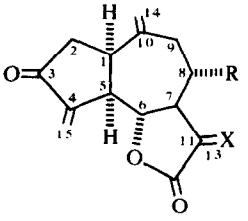
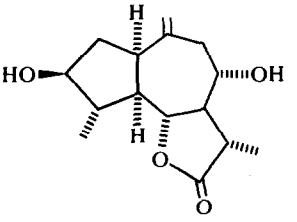


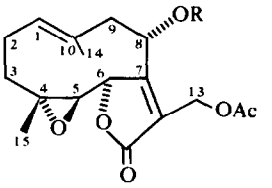
3 R = H
4 R = OSen
5 R = OH



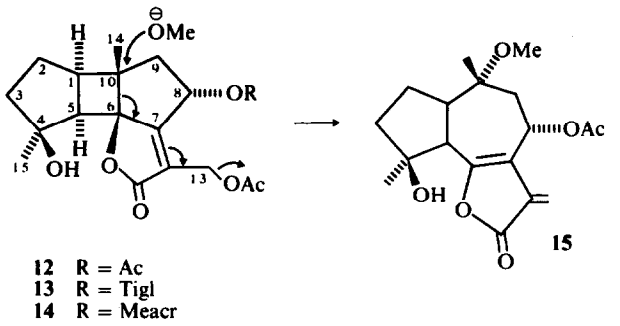
6 X = CH_2, R = H
7 X = H, αMe, R = OH
8 X = CH_2, R = OH



9

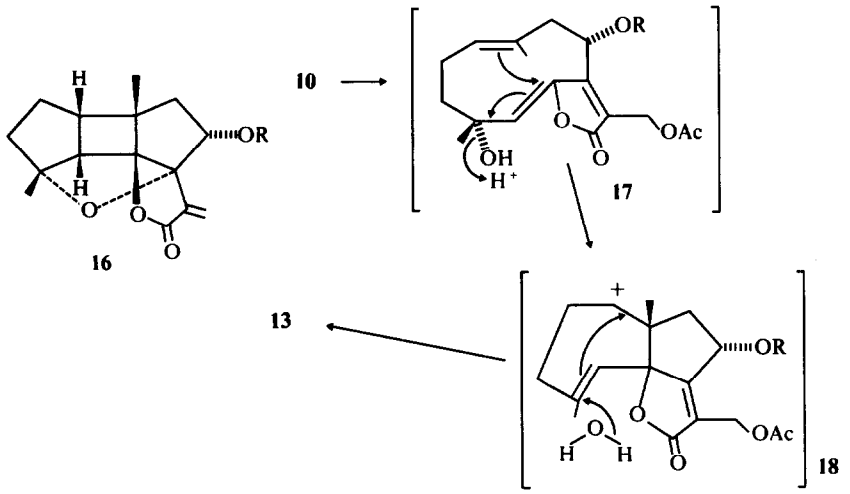


10 R = Tigl
11 R = Meacr



12 R = Ac
13 R = Tigl
14 R = Meacr

Scheme 1.



Scheme 2.

followed from the ^{1}H NMR data (Table 1) and spin decoupling. The couplings observed allowed the assignment of the stereochemistry at C-3, C-4, C-8 and C-11. **9** therefore is a tetrahydro derivative of **7**. The aerial parts gave lupeyl acetate and its Δ9,11 and Δ12,13 isomers, **10** and **13**.

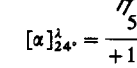
The isolation of **10–15** supports the proposed relationship of the bourbonenolides to the glaucolides of type **10**. A proton-catalysed opening of the epoxide ring in **10** would lead to **17**, which by further protonation could be transformed to **18**, perhaps the direct precursor of **13** (Scheme 2). **16** is probably formed from the 1,5 isomer of **13**, which would indicate two different ways of cyclization of **18**. A direct formation of **13** from **17** by a cycloaddition therefore seems to be less likely, as a different stereochemistry of the double bonds would be required for the formation of the bourbonenolides isolated.

EXPERIMENTAL

The fresh plant material, grown from seeds, was extracted with Et_2O–petrol, 1:2 and the resulting extracts were separated by CC (Si gel) and further by TLC (Si gel). Known compounds were identified by comparing the IR and ^{1}H NMR data with those of authentic material. Vouchers are deposited in the Institute of Organic Chemistry, Technical University of Berlin.

Vernonia arkansana (*voucher* 79/1500). The roots (300 g) afforded 5 mg **1**, 4 mg **2**, 3 mg **3**, 20 mg **4**, 5 mg **5**, 40 mg **6**, 3 mg **7** and 5 mg **8** (Et_2O–petrol, 3:1), while the aerial parts (1.5 kg) gave 20 mg lupeol, 25 mg lupeyl acetate, 15 mg **10**, 5 mg **11** (Et_2O–petrol, 3:1), 6 mg **12** (Et_2O–petrol, 3:1), 8 mg **13** (Et_2O–petrol, 3:1), 2 mg **14** (Et_2O–petrol, 3:1) and 1 mg **15** (Et_2O–petrol, 3:1).

Vernonia profuga (*voucher* 79/1464). The roots (1 kg) afforded 10 mg **1**, 19 mg **2**, 22 mg **4**, 28 mg **5**, 220 mg **6**, 6 mg **7**, 6 mg **8** and 15 mg **9**, while the aerial parts (5 kg) gave 20 mg lupeyl acetate, its Δ9,11 and Δ12,13 isomers (*ca* 2:1:2), 14 mg **10** and 6 mg **13**.

8α-Hydroxydehydrozaluzanin C (**8**). Colourless crystals, 191° (MeOH), IR ν_{max}^{KBr} cm^{-1}: 3440 (OH), 1760 (lactone), 1710 (C=CCO); MS *m/z* (rel. int.): 260.105 (M^+, 9) ($C_{15}H_{16}O_4$), 242 ($M - H_2O$, 33), 231 ($M - CHO$, 19), 166 ($M - C_6H_6O$(O= ), 100).

$$[\alpha]_{24°}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436\,\text{nm}\\ +118 & +124 & +147 & +293\end{matrix}}{} \quad (c = 0.3, CHCl_3).$$

8α-Hydroxy-4β,15,11β,13-tetrahydrozaluzanin C (**9**). Colourless crystals mp 159°, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3615 (OH), 1780 (lactone); MS *m/z* (rel. int.): 266 (M^+, 1.5), 248.141 ($M - H_2O$, 6) ($C_{15}H_{20}O_3$), 220 (248 – CO, 10), 205 (220 – Me, 6), 168 ($M - C_6H_{10}O$, 68), 55 ($C_4H_7^+$, 100).

8-Deacyl marginatin-methacrylate (**11**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (lactone), 1760 (OAc), 1725, 1650 (C=CCO$_2$R); MS *m/z* (rel. int.): 304 ($M - RCO_2H$, 0.5), 244.110 (304 – AcOH, 6) ($C_{15}H_{16}O_3$), 229 (244 – Me, 2), 216 (244 – CO, 7), 69 ($C_3H_5CO^+$, 100).

8α,13-*Diacetoxy-4β-hydroxy-bourbon-7(11)-en-6,12-olide* (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1790 (lactone), 1760 (OAc); MS *m/z* (rel. int.): 304 (M − AcOH, 0.5), 244.110 (304 − AcOH, 14), 226 (244 − H_2O, 6), 186 (244 − Me_2CO, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-38 \quad -41 \quad -49 \quad -100} \quad (c = 0.6, CHCl_3).$$

13-*Acetoxy-8α-tiglinoyloxy-4β-hydroxy-bourbon-7(11)-en-6,12-olide* (**13**). Colourless crystals, mp 143°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1780 (lactone), 1745 (OAc), 1720, 1645 (C=CCO_2R); MS *m/z* (rel int): 404 (M^+, 0.5), 344 (M − AcOH, 0.3), 244.110 (344 − RCO_2H, 10) ($C_{15}H_{16}O_3$), 226 (244 − H_2O, 2), 186 (244 − Me_2CO, 52), 83 ($C_4H_7CO^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-20 \quad -23 \quad -28 \quad -64} \quad (c = 0.8, CHCl_3).$$

13-*Acetoxy-8α-methacryloyloxy-4β-hydroxy-bourbon-7(11)-en-6,12-olide* (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1785 (lactone), 1750 (OAc), 1725, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 330 (M − AcOH, 0.2), 244.110 (330 − RCO_2H, 12) ($C_{15}H_{16}O_3$), 186 (244 − Me_2CO, 72), 69 ($C_3H_5CO^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-20 \quad -24 \quad -29 \quad -72} \quad (c = 0.2, CHCl_3).$$

8α-*Acetoxy-4α-hydroxy-10α-methoxy-guai-6,7,11(13)-diene-6,12-olide* (**15**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1780 (lactone), 1750 (OAc); MS *m/z* (rel. int.): 304 (M − MeOH, 0.5), 244.110 (304 − AcOH, 6) ($C_{15}H_{16}O_3$), 186 (244 − Me_2CO, 43), 57 ($C_4H_9^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+4 \quad +1 \quad -2 \quad -30} \quad (c = 0.1, CHCl_3).$$

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