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FOUR GUAIANOLIDES AND OTHER CONSTITUENTS FROM THREE *KAUNIA* SPECIES*

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Key Word Index—*Kaunia arbuscularis*; *K. saltensis*; *K. ignorata*; Compositae; Eupatorieae; sesquiterpene lactones; guaianolides; thymol derivatives.

Abstract—The investigation of three species of the new genus *Kaunia* afforded four new guaianolides and four thymol derivatives. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

Nothing is known on the chemistry of the new genus *Kaunia*, taxonomically related to the Ageratinae [1]. Though only a few genera of this subtribe have been investigated previously, the constituents of the *Kaunia* species may show whether there are relationships to other genera placed in this subtribe. All three species afforded thymol derivatives and two of them contained guaianolides similar to those isolated from *Stevia* species.

RESULTS AND DISCUSSION

The aerial parts of *Kaunia arbuscularis* (B. L. Robins) K. et R. afforded squalene, lupeol, stigmasterol, glutinol, α- and γ-curcumene, the guaianolides **2** [2], **7** [3], **8** [4], the germacranolides **11** [5] and **12** [6], the carbinol **14** [7], the thymol derivatives **15** [8] and **16** [9] as well as two further ones, the alcohols **20** and **21**, which, however, could not be separated. From the spectroscopic data (MS and ^{1}H NMR, Table 2) the structures could be deduced. The polar fractions afforded five further guaianolides, all closely related to **2** and **7**. Careful ^{1}H NMR studies led to the structures **1**, **4**, **6**, **9** and **10**. **6** could be separated from **1** only after transformation of **1** into the pyrazoline **3**. The ^{1}H NMR data (Table 1) of **1** showed, that a *trans*-6,12-guaianolide was present. Irradiation of the H-7 signal allowed the assignment of the signals of H-6, H-8 and H-13. Further spin decoupling of the signals of H-6 and H-8β led to the assignment of H-5 and H-9, respectively. The down-field shift of the H-5 signal required a position between two double bonds, thus indicating 1,10 and 3,4-double bonds. This was supported by the corresponding olefinic methyl signals (H-14 and H-15). Irradiation of the latter caused a sharpening of two broad doublets around 3 ppm, which therefore were those of H-2. Addition of diazomethane gave mainly the pyrazoline **3**, as could be deduced from the down-field shift of the H-6 signal (Table 1), while that of H-7 and H-5 was changed only very little. We have named **1** kauniolide.

The ^{1}H NMR data of **6** (Table 1) were very similar to those of **1**. However, the methylene signals of H-13 were replaced by a double quartet for H-11 and a doublet for H-13, indicating the presence of a 11,13-dihydro derivative of **1**. The coupling observed for $J_{11,13}$ showed the presence of an α-orientated methyl group, especially when compared with those in the spectra of **7** and **8**. The ^{1}H NMR data of the acetate **5**, obtained by acetylation of **4** showed that this lactone was the 2α-acetoxy derivative of 7-desoxyrupicolin B. The couplings of H-2 favoured the proposed stereochemistry at C-2, when models were inspected. The ^{1}H NMR data of **9** and **10** (Table 1), isolated in minute amounts as an inseparable mixture, also showed clearly that these lactones again differed at C-11 and C-13 only, one being a methylene lactone and the second the corresponding 11β,13-dihydro compound.

The ^{1}H NMR data further showed, when compared with those of **2** and **7**, respectively, that the 1,10-double bond is missing. The broadened H-14 signals were replaced by a sharp singlet at 1.6 ppm, indicating a 10-hydroxy group, its presence already being clear from the IR and MS data. Though the stereochemistry at C-10 could not be established rigorously the proposed one is plausible, since inspection of models showed that the proposed configuration would agree better with the chemical shifts of H-1 and H-14 than one in which these assignments are reversed. The aerial parts of *K. ignorata* (Hieron.) K. et R. afforded α-humulene, caryophyllene, bicyclogermacrene, β-selinene, the thymol derivatives **15**, **16**, **17**–**19** [**10**], **24** [11], **25** [12] and **26** [13] and the guaianolides **2** and **13**. The structure of the latter again could be deduced from the ^{1}H NMR data (Table 1). All signals were similar to those of corresponding guaianolides. The proposed 3α, 4α-epoxide was supported by the chemical shifts of H-5 of H-6, which also ruled out a β-epoxide structure, which should induce down-field shift of the H-6 signal. Also the ^{13}C NMR data (see Experimental) agreed with the proposed structures.

The aerial parts of *K. saltensis* (Hieron.) K. et R. afforded the thymol derivatives **24** and **28** as well as the unknown acetate **23** and the hydroxyketone **27**. Again the

*Part 358 in the series "Naturally Occurring Terpene Derivatives". For Part 357 see Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 2245.

Table 1. ^{1}H NMR spectral data of compounds **1**, **3**, **5**, **6**, **9**, **10** and **13** ($CDCl_3$, TMS as internal standard, 400 MHz)

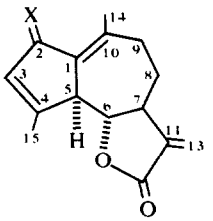
	1	**3**	**5**	**6**	**9**	**10**	**13**
H-1	—	—	3.40 *dd* (*br*)	—	2.72 *d*	2.70 *d*	—
H-2	3.00 *d* (*br*)	3.04 *d* (*br*)	5.61 *d* (*br*)	2.98 *d* (*br*)	—	—	—
H-2′	2.94 *d* (*br*)	2.96 *d* (*br*)		2.93 *d* (*br*)	—	—	—
H-3	5.53 *ddq*	5.58 *ddq*	5.68 *s* (*br*)	5.50 *ddq*	6.09 *dq*	6.05 *dq*	3.36 *s* (*br*)
H-5	3.40 *d* (*br*)	3.38 *d* (*br*)	2.72 *dd* (*br*)	3.30 *d* (*br*)	3.20 *dd* (*br*)	3.09 *dd* (*br*)	3.46 *d* (*br*)
H-6	3.64 *dd*	4.76 *dd*	4.23 *dd*	3.64 *dd*	4.39 *dd*	4.34 *dd*	3.66 *dd*
H-7	2.79 *ddddd*	2.42 *ddd*	2.86 *m*	1.85 *m*	2.7 *m*		2.86 *dddd*
H-8α	1.9 *m*	1.36 *m*	2.1 *m*	1.8 *m*			2.2 *m*
H-8β	1.37 *dddd*		1.55 *m*	1.29 *dddd*			1.45 *dddd*
H-9α	2.30 *dd* (*br*)	2.18 *m*	2.51 *ddd* (*br*)	2.2 *m*			2.47 *dd* (*br*)
H-9β	2.1 *m*	2.09 *ddd*	2.30 *m*	2.10 *ddd*			2.34 *dd*
H-11	—	—	—	2.19 *dq*			—
H-13	6.21 *d*	2.20 *ddd*	6.22 *d*	1.21 *d*	6.22 *d*	1.25 *d*	6.17 *d*
H-13′	5.48 *d*	1.52 *ddd*	5.50 *d*		5.53 *d*		5.43 *d*
H-14	1.71 *s* (*br*)	1.71 *ddd*	4.99 *s* (*br*) 4.97 *s* (*br*)	1.71 *s* (*br*)	1.61 *s*	1.60 *s*	2.34 *s* (*br*)
H-15	1.95 *s* (*br*)	1.98 *s* (*br*)	1.97 *s* (*br*)	1.90 *s* (*br*)	2.33 *s* (*br*)	2.30 *s* (*br*)	1.79 *s*
H-16	—	4.68 ABX_2	—	—	—	—	—

J (Hz): compound **1**, **3** and **6**: 2,2′ = 20; 2,3 = 3,15 ~ 1.5; 2,14 = 5,14 ~ 1.5; 5,6 = 6,7 = 10; 7,8α = 5; 7,8β = 10; 7,13 = 3.5; 7,13′ = 3; (compound **3**: 13,16 = 9; 13,16′ = 6.5; 13′,16 = 7; 13′,16′ = 9; 13,13′ = 13; compound **6**: 7,11 = 12; 8α,9β = 6, 8β,9β = 2; 9α,9β = 14; 11,13 = 7); compound **5**: 1,2 = 8; 1,5 = 10; 5,6 = 6,7 = 10; 7,13 = 3.5; 7,13′ = 3; 8α,9α = 5; 8β,9α = 9; 9α,9β = 14 (OAc 2.01 s); compounds **9**/**10**: 1,5 = 6.5; 3,5 = 3,15 ~ 1.5; 5,6 = 6,7 = 10; 7,13 = 3.5; 7,13′ = 3 (compound **10**: 11,13 = 7); compound **13**: 5,6 = 6,7 = 7,8β = 10; 7,13 = 3.5; 7,13′ = 3; 7α,8α = 3; 8α,8β = 13; 8α,9α = 2; 8α,9β = 11; 8β,9α = 11,8β,9β = 2.

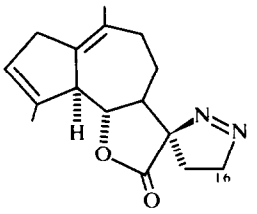
Table 2. ^{1}H NMR spectral data of compounds **20**, **21**, **23** and **27** ($CDCl_3$, TMS as internal standard, 400 MHz)

	20	**21**	**23**	**27**
H-2	6.75 *s* (*br*)	6.74 *s* (*br*)	6.84 *s* (*br*)	6.65 *dq*
H-3	—	—	—	4.35 ddq
H-4	—	—	—	1.96 *dddd*
H-5	7.02 *d*	7.01 *d*	7.20 *d*	2.46 *dd*
H-5′				2.11 *dd*
H-6	6.72 *d* (*br*)	6.96 *d* (*br*)	6.92 *d* (*br*)	—
H-7	2.31 *s*	2.29 *s*	5.06 *s* (*br*)	1.78 *dd*
H-8	—	3.23 *ddq*	3.31 *qq*	2.19 *dqq*
H-9	5.47 *s* (*br*)	1.32 *d*	1.20 *d*	0.96 *d*
H-9′	5.37 *d*			
H-10	4.40 *s* (*br*)	3.94 *dd* 3.73 *dd*		0.89 *d*
OAc(OMe)	—	—	2.10 *s* 3.84 *s*	—

J (Hz): compound **20**: 5,6 = 8; 9,10 = 1.5; compound **21**: 5,6 = 8; 8,9 = 7; 8,10 = 3.5; 8,10′ = 8; 10,10′ = 10; compound **23**: 5,6 = 8; 8,9 = 8,10 = 7; compound **27**: 2,3 = 2,7 = 1.5; 3,4 = 10; 4,5 = 3.5; 4,5′ = 13; 4,8 = 3.5; 5,5′ = 16; 8,9 = 8,10 = 7.



1 X = H_2 **2** X = O



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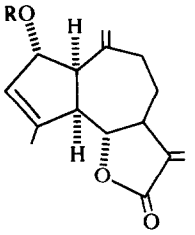
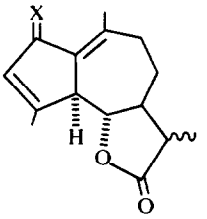
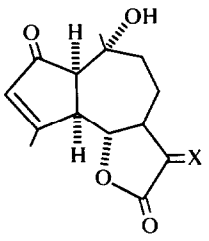


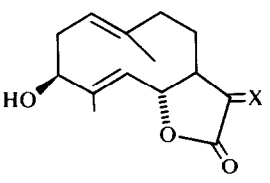
4 R = H **5** R = Ac



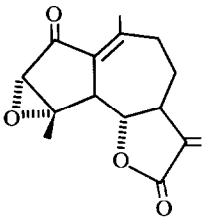
6 X = H_2, 11β-H
7 X = O, 11β-H
8 X = O, 11α-H



9 X = CH_2
10 X = H, α-Me



11 X = CH_2
12 X = H, α-Me



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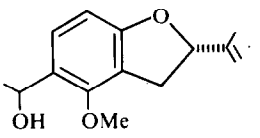

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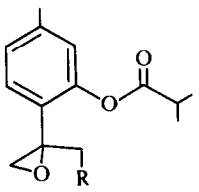
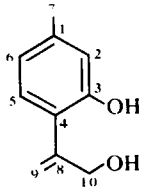
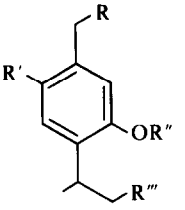


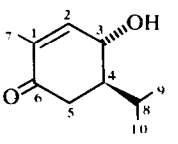
15 R = OAc
16 R = Oi Bu
17 R = OMebu
18 R = OH
19 R = H



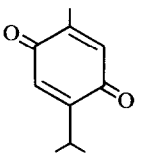
20
21 8, 9-H



	22	**23**	**24**	**25**	**26**
R	H	OAc	H	H	H
R′	H	H	OMe	OMe	OMe
R″	Me	Me	Me	OiBu	OiBu
R‴	H	H	H	OAc	



27



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structures could be deduced from the ^{1}H NMR data (Table 2). The spectrum of **23** allowed the assignment of the position of the methoxy group by comparing the chemical shifts with those of **22**, while the structure of **27** followed from the chemical shifts and the couplings observed. The small coupling $J_{2,3}$ and the large coupling $J_{3,4}$ required a *trans*-configuration at C-3 and C-4. **27** is probably an intermediate in the formation of thymol. The roots only afforded caryophyllene, dammaradienyl acetate and **22**. Though the chemistry of the three species investigated indicated large variations in thymol derivatives, the occurrence of closely related guaianolides may be of chemotaxonomic importance. The latter are also reported from *Guevaria* [14] and *Stevia* species [15–18]. However, so far insufficient data are available for final conclusions, especially since these guaianolides are widespread throughout the Compositae.

EXPERIMENTAL

The air-dried plant material was extracted with Et_2O–petrol, 1:2, and the resulting extracts were separated first by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the IR and ^{1}H NMR data with those of authentic material.

Kaunia arbuscularis (*B. L. Robins*) *K. et R.* (*voucher RMK* 7863). The aerial parts (1.2 kg) afforded 20 mg glutinol, 34 mg lupeol, 50 mg stigmasterol, 22 mg α- and 193 mg γ-curcumene, 40 mg squalene, 50 mg **1** (Et_2O–petrol, 1:1), 730 mg **2**, 20 mg **4** (Et_2O–petrol, 3:1), 40 mg **6** (Et_2O–petrol, 1:1), **6** could be isolated pure only after transformation of **1** into **3** by addition of CH_2N_2. 200 mg **7**, 160 mg **8**, 1 mg **9**, (Et_2O–petrol, 3:1), 2 mg **10** (Et_2O–petrol, 3:1), 9 mg **11**, 9 mg **12**, 7 mg **14** and 4 mg **20** and **21** (1:1) (Et_2O–petrol, 3:1).

Kaunia ignorata (*Hieron.*) *K. et R.* (*voucher RMK* 7631). The aerial parts (2 kg) afforded 50 mg α-humulene, 100 mg

caryophyllene, 50 mg bicyclogermacrene, 20 mg β-selinene, 80 mg **2**, 30 mg **13** (Et_2O–petrol, 3:1), 50 mg **15**, 20 mg **16**, 10 mg **17**, 10 mg **18**, 20 mg **19**, 50 mg **24**, 10 mg **25** and 10 mg **26**.

Kaunia saltensis (*Hieron.*) *K. et R.* (*voucher RMK* 7663). The aerial parts (120 g) afforded 200 mg **24**, 10 mg **23** (Et_2O–petrol, 1:10), 5 mg **27** (Et_2O–petrol, 1:1) and 5 mg **28**, while the roots (50 g) gave 2 mg caryophyllene, 10 mg dammaradienyl acetate and 10 mg **22**.

Kauniolide (**1**). Colourless gum, not completely free from **6** IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (γ-lactone); MS *m/z* (rel. int.): 230.146 (M^+, 100) ($C_{15}H_{18}O_2$), 215 (M − Me, 24), 202 (M − CO, 6), 187 (202 − Me, 12), 159 ($C_{12}H_{15}^+$, 87).

2α-Hydroxy-8-desoxyrupicolin B (**4**). Isolated as its acetate **5** (1 hr, Ac_2O, 70°), colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740, 1240 (OAc); MS *m/z* (rel. int.): 288.136 (M^+, 5) ($C_{17}H_{20}O_4$), 273 (M − Me, 1), 246 (M − ketene, 64), 228 (M − AcOH, 100), 213 (228 − Me, 12), 200 (228–CO, 9), 185 (200–Me, 11), 91 ($C_7H_7^+$, 51).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546\,nm}{-7.5 \quad -8.5 \quad -10.0} \quad (c = 0.3,\ CHCl_3).$$

11β,13-Dihydrokauniolide (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790 (γ-lactone), 835 (CH=C); MS *m/z* (rel. int.): 232.146 (M^+, 100) ($C_{15}H_{20}O_2$), 217 (M − Me, 22), 204 (M − CO, 3), 189 (204 − Me, 9), 159 ($C_{12}H_{15}^+$, 60).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546\,nm}{+14.3 \quad +14.5 \quad +16.9} \quad (c = 0.5,\ CHCl_3).$$

10α-Hydroxyarbiglovin and 11β,13-dihydroarbiglovin (**9** *and* **10**). Inseparable, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1785 (γ-lactone), 1700 (C=CCO); addition of CH_2N_2 in Et_2O afforded 1.5 mg **10**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1785 (γ-lactone), 1700 (C=CC=O); MS *m/z* (rel. int.): 264.136 (M^+, 10) ($C_{15}H_{20}O_4$), 249 (M − Me, 10), 246 (M − H_2O, 35), 231 (249 − H_2O, 4), 169 (M − C_6H_7O, 16), 151 (169 − H_2O, 11), 57 (100).

2-Oxoludartin (**13**). Colourless crystals, mp 182–183° (Et_2O–petrol); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780 (γ-lactone), 1725, 1640 (C=CC=O); MS *m/z* (rel. int.): 260.105 (M^+, 100) ($C_{15}H_{16}O_4$), 245 (M − Me, 24), 231 (M − CHO, 14), 203 (M − C_3H_5O, 41), 175 (203 − CO, 42); ^{13}C NMR ($CDCl_3$): (C-1–C-15): 131.1 *s*, 197.6 *s*, 63.1 *d*, 62.3 *s*, 54.1 *d*, 80.3 *d*, 50.4 *d*, 24.8 *t*, 37.3 *t*, 159.0 *s*, 138.5 *s*, 168.7 *s*, 118.4 *t*, 18.7 *q*, 22.8 *q*.

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-34 \quad -43 \quad -63 \quad -373} \quad (c = 1.4,\ CHCl_3).$$

10-Hydroxythymol and 8,9-dehydro-10-hydroxythymol (**20** *and* **21**). Inseparable, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1630 (C=C); MS *m/z* (rel. int.): 166.099 and 164.084 (M^+, 16 and 14) ($C_{10}H_{14}O_2$ and $C_{10}H_{12}O_2$), 135 (M–CH_2OH, 100).

7-Acetoxythymol methyl ether (**23**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1230 (OAc); MS *m/z* (rel. int.): 222.136 (M^+, 38) ($C_{13}H_{18}O_3$), 207 (M − Me, 100), 180 (M − ketene, 27), 151 (180 − CHO, 30).

3α-Hydroxycarvotagenone (**27**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1690 (C=CCO); MS *m/z* (rel. int.): 168.115 (M^+, 30) ($C_{10}H_{16}O_2$), 150 (M − H_2O, 8), 135 (150 − Me, 18), 126 (M − H_2C=CHMe, 48), 98 (M − H_2C=$CHCHMe_2$, 100, RDA), 70 (98 − CO, 53).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-53 \quad -54 \quad -62 \quad -110} \quad (c = 0.3,\ CHCl_3).$$

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