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FUROEUDESMANES AND OTHER CONSTITUENTS FROM REPRESENTATIVES OF THE *PLUCHEA* GROUP

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Key Word Index—*Epaltes gariepina, Laggera alata, Pechuel-Loeschea leibnitziae*; Compositae; sesquiterpenes; eudesmane derivatives; furoeudesmanes; guaianolides.

Abstract—An investigation of three species of the *Pluchea* group obtained from Namibia afforded five new furoeudesmane derivatives from *Epaltes gariepina*, two eudesmanes from *Laggera alata* and two guaianolides from *Pechuel-Loeschea leibnitziae*. The structures were elucidated by high field NMR techniques and the chemotaxonomy is discussed briefly.

INTRODUCTION

The *Pluchea* group (Compositae, tribe *Inulea*, subtribe Inulinae) is distributed over the warmer parts of both hemispheres [1]. While several representatives of the two large genera *Blumea* and *Pluchea* have been studied chemically, little is known concerning the *Epaltes*, *Laggera* and *Pechuel-Loeschea*. We therefore have studied one species from each of these genera which were collected in Namibia. The results are discussed in this paper.

RESULTS AND DISCUSSION

A sample of *Pechuel-Loeschea leibnitziae* (O. Kuntze) O. Hoffm. from Transvaal has been studied previously [2]. We have now investigated a sample from Namibia. The main constituents were the same but in addition to the guaianolide **1** [2], the acetates **2** and **3** were isolated. The structure of **2** followed from its ^{1}H NMR spectrum (Table 1). In deuteriobenzene all signals could be assigned by spin decoupling. Starting with the five-fold doublet at δ2.09 (H-7) the signals were assigned for H-6, H-8, and H-13. As the signal of H-6 showed homoallylic couplings with two further allylic protons the presence of a 12,8-guaianolide with a 1,5-double bond was very likely. The position of an acetoxy group at C-3 also followed from the results of spin decoupling. Two methyl doublets at δ0.74 and 0.87 were coupled with allylic protons which further supported the presence of a guaianolide. The stereochemistry was determined by NOE difference spectroscopy. Clear effects were observed between H-10, H-2α (4%) and H-9α (5%), between H-14, H-2β (4%) and H-8 (10%), between H-15, H-6β (3%), between H-7, H-6α (5%) and H-9α (3%), between H-4, H-3 (6%) and H-6 (6%), between H-8, H-14 (5%) and H-6β (4%) as well as between H-3 and H-4 (6%). These results required a β-orientation of both methyls and of the acetoxy group while the lactone possessed a *trans*-configuration.

Table 1. ^{1}H NMR spectral data of compounds **2** and **3** (400 MHz, C_6D_6, δ-values)

H	**2**	**3**
2α	2.29 *ddt*	1.83 *ddd*
2β	2.45 *br ddd*	1.58 *dt*
3	5.23 *ddd*	4.97 *dt*
4	2.65 *br dq*	2.75 *br dq*
6α	1.86 *br dd*	5.25 *br t*
6β	1.46 *br dd*	
7	2.09 *ddddd*	2.83 *ddddd*
8	3.68 *ddd*	3.54 *ddd*
9α	1.50 *dt*	1.44 *dt*
9β	1.95 *dt*	2.06 *dt*
10	2.00 *m*	1.44 *m*
13	6.14 *d*	6.19 *d*
13′	4.91 *d*	5.11 *d*
14	0.74 *d*	0.60 *d*
15	0.87 *d*	0.88 *d*
OAc	1.78 *s*	1.76 *s*

* H-1 2.11 *br t*.

J [Hz]: compound **2**: 2α, 2β = 15; 2α, 3 = 2β, 3 = 3, 4 = 7; 2α, 6β = 4; 2β, 6β = 4, 10 ~ 1.5; 4, 15 = 7; 6α, 6β = 16; 6α, 7 = 3.5; 6β, 7 = 12; 7, 8 = 10; 7, 13 = 3.5; 7, 13′ = 3; 8, 9β = 2.5; 8, 9α = 9α, 9β = 12; 9β, 10 = 3; 9α, 10 = 5; 10, 14 = 7; compound **3**: 1, 2α = 8.5; 1, 2β = 9; 1, 10 ~ 2; 1, 6 = 6, 7 ~ 3; 2α, 2β = 12.5; 2α, 3 = 6.5; 2β, 3 = 9; 3, 4 = 6.5; 4, 15 = 7; 7, 8 = 10; 7, 13 = 3.5; 7, 13′ = 3; 8, 9α = 9α, 9β = 12; 8, 9β = 9β, 10 = 2.5; 9α, 10 = 3; 10, 14 = 7.

The ^{1}H NMR spectrum of **3** (Table 1) differed from that of **2** especially by the replacement of the H-6 double doublets by a low field triplet at δ5.25. The assignment again clearly followed from the results of spin decoupling which also led to a complete sequence due to the allylic couplings. The stereochemistry again was deduced from the NOEs [H-4 with H-3 (4%), H-10 (4%), H-9α (4%) and H-7 (6%), H-14 with H-8 (7%) and H-2β (4%)]. Thus **2** and **3** only differed in the position of the double bonds.

It is probable that the desacetyl derivative of **2** and **3** is the precursor of the main constituent **1** which would be formed by oxidation and double bond migration.

From the genus *Laggera*, with 15 species present in Africa, Asia and Australia, results have been reported only on the Indian species, *L. aurita*. In addition to some thymol derivatives, laggerol, a bisabolene derivative, was isolated [3]. The extract of the aerial parts of *Laggera alata* (D. Don) Schultz-Bip. ex Olivier afforded the known cuauthemone derivatives **4** and **5** [4, 5] and the corresponding formate **6**, the coniferyl alcohol derivative **9** [7], the angelate **8** [4] and the dihydroxyeudesmene **7**. The structure of the latter followed from the molecular formula ($C_{15}H_{26}O_2$) and the ^{1}H NMR spectrum (Table 2). In deuteriobenzene all signals could be assigned by spin decoupling and the configurations at C-5, C-7 and C-8 followed from the couplings. Thus **7** was the desoxy derivative of longilobol which was isolated from an *Artemisia* species [6]. The structure of **6** clearly followed from the ^{1}H NMR data (Table 2) which were of course similar to those of **5**. The presence of the formate followed from the low field singlet at δ7.97 and the absence of the acetate methyl singlet as well as from the molecular formula and the fragment $[M-HCO_2H]^+$ in the mass spectrum. The extract of the aerial parts of *Epaltes gariepina* (DC) Steetz gave bicyclogermacrene, spathulenol, T-cadinol and the furoeudesmanes **10**–**14** which were extremely unstable.

The structure of **10**, molecular formula $C_{15}H_{22}O_3$, followed from its ^{1}H NMR spectum in deuteriobenzene (Table 2) which was in part similar to that of furoeremophilanes. The broadened signals of H-9 showed homoallylic couplings with H-6 and the signals at δ7.07 *br s* and 1.84 *d* are typical for β-methyl furans. However, spin decoupling showed that an eudesmane derivative was present with hydroxy groups at C-3 and C-4 and a furan moiety at C-7 and C-8. The stereochemistry followed from the couplings of H-3 and H-5 while the latter also indicated the presence of a *trans*-decalin systeme. The precursor of compound **10** is probably cuauthemone, the 3-desacyl derivative of **4** [4], which by allylic oxidation at C-12 followed by semi-acetal formation and elimination of water would lead to **10**.

The ^{1}H NMR spectra of **11**–**13** (Table 2) also had to be measured in deuteriobenzene as the signals could be assigned by spin decoupling only in this solvent. Also the compounds were not decomposed so rapidly in benzene as in chloroform. The typical signals of the ester residues showed that compound **11** was the 3-*O*-epoxyangelate of **10**, compound **12** the isovalerate and compound **13** the angelate. As in similar cases in the esters the H-6α signal was slightly shifted downfield and in compound **13** the H-3 signal was more deshielded as in **11** and **12**.

The ^{1}H NMR spectrum of **14** (Table 2) differed from that of **11** by the presence of a new low-field signal at δ5.29. Spin decoupling indicated that the latter was due to H-6 as shown by a small homoallylic coupling with H-9′ and a vicinal one with H-5 (2.04 *d*). The coupling of the latter required a 6β-hydroxy group and its nature was also supported by the molecular formula of **14**

Table 2. ^{1}H NMR spectral data of compounds of **6**, **7** and **10**–**14** (400 MHz, C_6D_6, δ-values)

H	**6*** ($CDCl_3$)	**7**	**10**	**11†**	**12‡**	**13§**	**14‖**
1α	1.51 *ddd*	1.16 *dt*	1.78 *dt*	1.55 *dt*	1.58 *dt*	1.57 *m*	1.64 *m*
1β	1.32 *br d*	1.36 *br d*	1.10 *dt*	1.10 *br d*	1.10 *dt*	1.09 *m*	1.15 *br d*
2α	2.01 *dddd*	1.51 *m*	1.58 *dq*	1.80 *br d*	1.77 *dq*	1.77 *br d*	1.78 *dddd*
2β	1.80 *dddd*		1.47 *ddt*	1.48 *ddt*	1.49 *ddt*	1.49 *ddt*	1.64 *m*
3	5.86 *dd*	1.93 *br dt* 2.27 *dddd*	3.41 *br t*	4.98 *dd*	4.96 *dd*	5.08 *dd*	4.93 *dd*
5	2.30 *m*	1.68 *br d*	1.88 *dd*	2.00 *dd*	2.00 *dd*	1.98 *dd*	2.04 *d*
6α	2.93 *br d*	1.51 *m*	2.70 *ddd*	2.85 *ddd*	2.80 *ddd*	2.87 *ddd*	5.29 *br d*
6β	2.30 *m*	1.04 *q*	2.20 *dddd*	2.23 *dddd*	2.19 *dddd*	2.24 *dddd*	
7	—	1.49 *m*	—	—	—	—	—
8	—	3.97 *dt*	—	—	—	—	—
9	2.30 *d*	1.31 *t*	2.43 *br d*	2.44 *br d*	2.42 *br d*	2.45 *br d*	2.29 *br d*
9′	2.23 *d*	1.77 *dd*	2.33 *br d*	2.35 *br d*	2.31 *br d*	2.36 *br d*	2.41 *d*
12	2.07 *br*	1.23 *s*	7.07 *br s*	7.08 *br s*	7.06 *br s*	7.07 *br s*	6.97 *q*
13	1.86 *br s*	1.20 *s*	1.89 *d*	1.87 *d*	1.84 *br s*	1.84 *d*	1.92 *d*
14	1.01 *s*	0.72 *s*	0.75 *s*	0.74 *s*	0.70 *s*	0.73 *s*	1.11 *s*
15	1.55 *s*	4.82 *q* 4.51 *q*	1.04 *s*	1.11 *s*	1.05 *s*	1.11 *s*	1.64 *s*

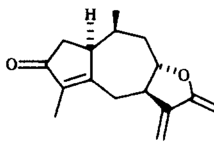
* OCOR: 3.06 *q*, 1.32 *d* ($J = 5.5$), 1.55 *s*; OCOH: 7.97 *s*;

† OCOR: 2.57 *q*, 1.20 *d*, 1.39 *s*;

‡ OCOR: 2.03 *d*, 2.10 *tqq*, 0.89 *d*, 0.88 *d* (J[Hz]: 2, 3 = 3, 4 = 3, 5 = 7); § OCOR: 5.71 *qq*, 1.99 *dq*, 1.78 *dq*.

‖ OCOR: 2.57 *q*, 1.27 *d*, 1.45 *s*;

J[Hz]: Compound **6**: 1α, 1β = 1α, 2β = 2α, 2β = 13; 1α, 2α = 1β, 2α = 1β, 2β = 2α, 3 ~ 3; 2β, 3 = 2; 6α, 6β = 14; 9, 9′ = 15; compound **7**: 1α, 1β = 1α, 2β = 2α, 2β = 3α, 3β = 5, 6β = 6α, 6β = 6β, 7 ~ 13; 1α, 2α = 4.5; 1β, 2α = 1β, 3β = 2β, 3β ~ 2; 3α, 15 = 3β, 15 = 3α, 15′ = 5, 15 = 5, 15′ ~ 1.5; 7, 8 = 8, 9α = 11; 8, 9β = 4.5; 9α, 9β = 12; compounds **10**–**14**: 1α, 1β = 1α, 2β = 2α, 2β = 13; 1α, 2α = 1β, 2β = 1β, 2α ~ 3.5; 2α, 3 = 2β, 3 ~ 2.5; 5, 6α = 4.5; 5, 6β = 11.5; 6α, 6β = 16; 6α, 9 = 6β, 9 = 1.5; 9, 9′ = 15; 9, 13 = 12, 13 ~ 1 (compound **14**: 5, 6 = 3).



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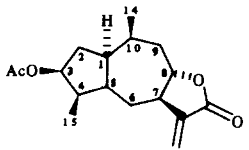
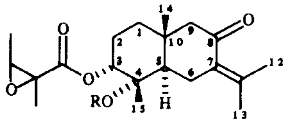
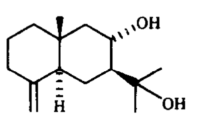


2 $\Delta^{1(5)}$
3 Δ^{5}



	4	**5**	**6**
R	H	Ac	CHO



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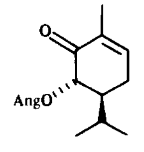

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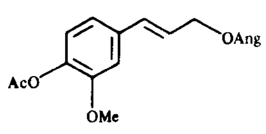

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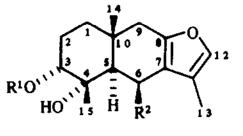

	10	**11**	**12**	**13**	**14**
R^1	H	Epang	*i*Val	Ang	Epang
R^2	H	H	H	H	OH

($C_{20}H_{28}O_6$) which indicated that compound **14** differed from **11** only by one additional oxygen. The unusual shift of H-6 must be due to the deshielding effects of the 4-hydroxy and 3-acyloxy groups. We have named the diol **10**, 3α-hydroxyfuroepaltol and the names for **11**–**14** are derived from this. Lactones isolated from *Pluchea rosea* [9] may be the oxidation products of the corresponding furoeudesmanes which, however, have not been isolated from that species.

The chemistry of representatives of the *Pluchea* group, which can be characterized by the pluriseriate, mostly filiform female florets [1], presents only in part a uniform picture. The South and Central American *Pluchea* species can be characterized by the occurrence of cuauthemone derivatives [10]. The same is true for South and Central American *Epaltes* [11], *Blumea* [12] and *Tessaria* species [10]. Several species from other parts of the World contain other constituents like thymol derivatives [12] which are widespread in the whole subtribe.

The genus *Laggera* was previously combined with *Blumea* [13] but later separated again [14]. The chemistry of *L. alata* supports its reclassification as it shows much more relationship to *Pluchea* than to *Blumea*. The compounds isolated from *Pechuel-Loeschea*, however, show no relationship to those of the *Pluchea* group but to those of the *Inula* group. As mentioned previously [1] the generic limits of the *Pluchea* group are especially weak. Accordingly, the placement of some species in distinct genera may be in part doubtful. Nevertheless, the overall picture of the chemistry of this group is helpful for the taxonomy of this difficult group.

EXPERIMENTAL

The air-dried plant material (collected in March 1988 in Namibia, vouchers deposited in the SW African Herbarium at Windhoek) was extracted with MeOH–Et_2O–petrol (1:1:1) and the extracts separated as reported previously [15]. The extract of the aerial parts (390 g) of *Pechuel-Loeschea leibnitziae* (voucher 88/111, collected near the Brandberg) gave by CC and TLC 200 mg thymohydroquinone dimethyl ether, 200 mg pechueloic acid, 300 mg 3-oxo-isocostic acid, 500 mg 5,4′-dihydroxy-6,7-dimethoxyflavone, 2 g **1**, 20 mg **2** (HPLC, MeOH–H_2O, 7:3, always RP 8, R_t 5.0 min) and 3 mg **3** (same conditions, R_t 5.5 min.

The extract of 150 g aerial parts of *Laggera alata* (voucher 88/73, collected near Otjiwarongo) gave by CC and TLC 10 mg **8**, 15 mg **9**, 30 mg **4**, 30 mg **5**, 2 mg **6** (HPLC, MeOH–H_2O, 7:3, R_t 4.7 min) and 10 mg **7** (same conditions, R_t 14.4 min).

The extract of 150 g aerial parts of *Epaltes gariepina* (collected near the road Grootfontain–Tsumeb, voucher 88/92) gave by CC four fractions (1: petrol, 2: Et_2O–petrol, 1:1; 3: Et_2O and 4: Et_2O–MeOH, 9:1). Fraction 1 gave 20 mg bicyclogermacrene, fraction 2 by HPLC (MeOH–H_2O, 4:1) 5 mg spathulenol, 50 mg cadinol-T and a mixture (R_t 4.8 min) which gave by TLC (Et_2O petrol, 1:1) 10 mg **13** (R_f 0.68) and 8 mg **12** (R_f 0.53). TLC of fraction 3 (Et_2O–petrol, 1:1) gave 200 mg **11** (R_f 0.45) and 90 mg **12** (R_f 0.63). HPLC (MeOH–H_2O, 3:2) of one-tenth of fraction 4 gave 150 mg **10** (R_t 12.9 min) and 10 mg **14** (R_t 9.8 min).

3β-Acetoxy-4α, 10αH-guaia-1(5) 11 (13)-dien-12,8α-olide (**2**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740, 1250 (OAc); MS *m/z* (rel.int.): 230.130 $[M-HOAc]^+$ (58) (calc. for $C_{15}H_{18}O_2$: 230.130), 215 (10), 187 (13), 120 (48), 105 (37), 94 (100); $[\alpha]_D^{24°}$ +7° ($CHCl_3$; *c* 1.04).

3β-Acetoxy-1α, 10αH -guaia-5, 11 (13)-dien-12, 8α-olide (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740, 1245 (OAc); MS *m/z* (rel int.) 290.152 $[M]^+$ (6) (calc. for $C_{17}H_{22}O_4$: 290.152), 248 (7), 230 (68), 215 (22), 187 (20), 129 (100), 94 (40), 91 (54).

3-O-[*2′,3′-epoxy-2′-methylbutyroyl*]*-Cuauthemon-O-formiate* (**6**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765 (CHO), 1740 (CO_2R), 1685 (C=CC=O); MS *m/z* (rel. int.): 378.204 $[M]^+$ (1) (calc. for $C_{21}H_{30}O_6$: 378.204), 350 $[M-CO]^+$ (5), 332 $[M-HCO_2H]^+$ (3), 216 $[232-RCO_2H]^+$ (100), 201 $[216-Me]^+$ (49), 162 (77), 147 (74), 105 (66), 93 (64), 91 (62).

5-Desoxylongilobol (**7**). Colourless crystals, mp 160°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3360 (OH), 1650 (C=C); MS *m/z* (rel.int.): 223.169 $[M-Me]^+$ (2) (calc. for $C_{14}H_{23}O_2$: 223.169), 205 $[223-H_2O]^+$ (4), 187 $[205-H_2O]^+$ (8), 162 (100), 147 (64), 106 (46), 105 (45) 93 (36), 91 (33); $[\alpha]_D^{24°}$ +73° ($CHCl_3$; *c* 0.20).

3α-Hydroxyfuroepaltol (**10**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560, 3440 (OH); MS *m/z* (rel. int.): 250.157 $[M]^+$ (66) (calc. for $C_{15}H_{22}O_3$: 250.157), 232 $[M-H_2O]^+$ (12), 207 $[M-CH_2CHO]^+$ (30), 149 (22), 108 $[A]^+$ (100).*

3α-[*2′,3′-epoxy-2′ methybutyryloxy*]*-Furoepaltol* (**11**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO_2R); MS *m/z* (rel. int.): 348.194 $[M]^+$ (100) (calc. for $C_{20}H_{28}O_5$: 348.194), 232 $[M-RCO_2H]^+$ (8), 214 (26), 199 (22), 149 (36), 108 $[A]^+$ (45).

3α-Isovaleryloxyfuroepaltol (**12**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1745 (CO_2R); MS *m/z* (rel. int.): 334.214 $[M]^+$ (44) (calc. for $C_{20}H_{30}O_4$: 334.214), 232 $[M-RCO_2H]^+$ (11), 214 (22), 199 (26), 177 (52), 161 (100), 119 (72), 105 (84), 93 (90), 91 (82).

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* A =

3α-Angeloyloxyfuroepaltol (**13**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1730, 1650 (C=CCO$_2$R); MS *m/z* (rel.int.): 332.199 $[M]^+$ (38) (calc. for $C_{20}H_{28}O_4$: 332.199), 314 (1), 232 (14), 214 (34), 199 (28), 162 (41), 161 (47), 147 (62), 108 $[A]^+$ (100); $[\alpha]_D^{22°}$ +23° (CHCl$_3$, *c* 0.44).

6β-Hydroxy-3α-[2′,3′-epoxy-2′-methylbutyryloxy]-furoepaltol (**14**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3460 (OH), 1745 (CO$_2$R); MS *m/z* (rel.int.): 364.189 $[M]^+$ (27) (calc. for $C_{20}H_{28}O_6$: 364.189), 346 (10), 250 $[M-RCO_2H]^+$ (100), 108 $[A]^+$ (83).

Compounds **10–14** were extremely unstable and they rapidly became red in air.

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