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4α,15-DIHYDROENCELIN AND RELATED SESQUITERPENE ACIDS FROM *PERYMENIUM FEATHERSTONEI*

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Key Word Index—*Perymenium featherstonei*; Compositae; sesquiterpenes; eudesmanolide; eudesmanoic acids.

Abstract—*Perymenium featherstonei* afforded, in addition to the known *ent*-kaurene derivative 4α,15-dihydroencelin, two closely related epimeric acids.

INTRODUCTION

So far only one species of the South and Central American genus *Perymenium* has been studied chemically [1]. As only *ent*-kaurene derivatives were isolated a further species, *P. featherstonei* Blake, collected in Peru, was investigated to see whether chemotaxonomic relationships to other genera of the subtribe Ecliptinae [2] exist. The results will be discussed in this paper.

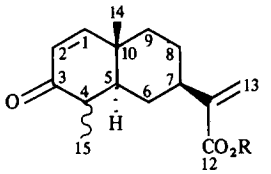
RESULTS AND DISCUSSION

The aerial parts of *Perymenium featherstonei* Blake afforded germacrene D, *ent*-kaurenic acid, its 15α-angeloyloxy derivative, *ent*-kauren-19-ol, 8-desoxysalonitenolide [3], two epimeric keto acids, the eudesmane derivatives **1a** and **2a**, as well as the eudesmanolide **3**. The structure of the latter followed from the molecular formula ($C_{15}H_{18}O_3$) and the ^{1}H NMR spectrum (Table 1). Spin decoupling allowed the assignment of all signals though the signals of H-6 and H-9 were overlapped in deuteriochloroform. Addition of deuteriobenzene shifted the signal of H-6β less than those of H-6α and H-9β. Therefore all sequences and couplings could be assigned. The configuration at C-4 followed from the coupling $J_{4,5}$. The couplings of H-8 showed that a *cis*-fused 8,12-lactone was present with the same conformation as alantolactone and related eudesmanolides. The position of the keto group and of the *cis*-double bond directly followed from the ^{1}H NMR spectrum. All data

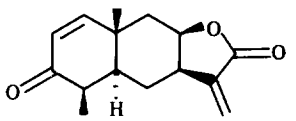
Table 1. ^{1}H NMR spectral data of compounds **1–3** (400 MHz, $CDCl_3$, TMS as internal standard)

	1a	**2a**	**1b**	**2b**	**1b** $CDCl_3$–C_6D_6	**2b** $CDCl_3$–C_6D_6	**3**	**3** $CDCl_3$–C_6D_6
H-1	6.80 *d*	6.73 *d*	6.78 *d*	6.72 *d*	6.54 *d*	6.40 *d*	6.76 *d*	6.34 *d*
H-2	5.89 *d*	5.87 *d*	5.87 *d*	5.85 *d*	5.81 *d*	5.75 *d*	5.89 *d*	5.71 *d*
H-4	2.46 *dq*	2.27 *dq*	2.45 *dq*	2.26 *dq*	2.34 *dq*	2.06 *dq*	2.49 *dq*	2.25 *dq*
H-5	2.15 *ddd*	1.72 *ddd*	2.15 *ddd*	1.71 *ddd*	1.95 *ddd*	1.49 *ddd*	2.08 *ddd*	1.63 *ddd*
H-6α	1.56 *br d*	1.8 *m*	1.51 *br d*	1.79 *br d*	1.36 *br d*	1.62 *br d*	1.67 *m*	1.20 *m*
H-6β	1.63 *ddd*	1.33 *ddd*	1.62 *ddd*	1.31 *ddd*	1.59 *ddd*	1.10 *ddd*		1.36 *ddd*
H-7	2.60 *dddd*	2.51 *ddddd*	2.60 *ddddd*	2.52 *ddddd*	2.50 *ddddd*	2.37 *ddddd*	3.07 *ddddd*	2.52 *ddddd*
H-8α	1.78 *br d*	1.8 *m*	1.74 *br d*	1.73 *br d*	1.63 *br d*	1.56 *br d*	4.58 *ddd*	4.11 *ddd*
H-8β	1.6 *m*		1.61 *m*	1.58 *dddd*	1.59 *dddd*	1.39 *dddd*		
H-9α	1.51 *ddd*	1.6 *m*	1.48 *ddd*	1.50 *ddd*	1.36 *m*	1.39 *ddd*	2.26 *dd*	1.88 *dd*
H-9β	1.6 *m*		1.58 *m*	1.67 *m*		1.24 *m*	1.65 *dd*	1.20 *m*
H-13	6.36 *s*	6.36 *s*	6.19 *d*	6.18 *d*	6.13 *d*	6.07 *d*	6.20 *d*	6.01 *d*
H-13′	5.73 *s*	5.71 *s*	5.60 *dd*	5.58 *dd*	5.44 *dd*	5.36 *dd*	5.65 *d*	5.29 *d*
H-14	1.20 *s*	1.11 *s*	1.19 *s*	1.10 *s*	1.02 *s*	0.86 *s*	1.25 *s*	0.97 *s*
H-15	1.13 *d*	1.12 *d*	1.19 *d*	1.11 *d*	1.03 *d*	1.01 *d*	1.12 *d*	0.90 *d*
OMe	—	—	3.77 *s*	3.77 *s*	3.63 *s*	3.55 *s*	—	—

J (Hz): Compounds **1a**/**1b** and **2a**/**2b**: 1, 2 = 10; 5, 6α = 3; 5, 6β = 12; 6α, 6β = 13; 6α, 7 = 4; 6β, 7 = 12; 7, 8α ~ 3; 7, 8β = 12; 8α, 8β = 13; 7, 13′ = 1; 8α, 9α ~ 3; 8α, 9β ~ 3; 8β, 9α ~ 10; 8β, 9β ~ 5; 9α, 9β = 13; 13, 13′ = 1; compounds **1a**/**1b**; 4, 5 = 6; 4, 15 = 8; compounds **2a**/**2b**: 4, 5 = 12.5; 4, 15 = 7; compound **3**: 1, 2 = 13; 4, 5 = 6; 4, 15 = 8; 5, 6α = 2.5; 5, 6β = 13; 6α, 6β = 13; 6α, 7 ~ 6; 6β, 7 = 11.5; 7, 8 = 5; 7, 13 = 1; 7, 13′ = 1; 8, 9α = 5; 8, 9β = 1.5; 9α, 9β = 15.



1a R = H, 4α H
1b R = Me, 4α H
2a R = H, 4β H
2b R = Me, 4β H



3

therefore only agree with the structure of 4α,15-dihydroencelin (**3**).

The structures of the acids **1a** and **2a**, which were transformed to the corresponding methyl esters **1b** and **2b**, also followed from the molecular formulae and the ^{1}H NMR spectral data (Table 1). All signals in the ^{1}H NMR spectra of **1b** could be assigned by spin decoupling starting with the five fold doublet at δ2.60, clearly the signal of H-7 which followed from decoupling of the H-13′ signal and of four other signals. The stereochemistry at C-4 again could be deduced from the corresponding coupling $J_{4,5}$ and that at C-7 was deduced from the presence of two large couplings ($J_{6\beta,7\alpha}$ and $J_{7\alpha,8\beta}$).

The ^{1}H NMR spectral data of **2b** differed only slightly from those of **1b**. A clear difference, however, was detectable between the chemical shifts of some protons. The coupling $J_{4,5}$ in the spectrum of **2b** required a *trans*-diaxial orientation of the protons at C-4 and C-5 thus indicating that **1a** and **2a** most likely were C-4 epimers which could be established by complete epimerization of **1a** to **2a**. The observed shift differences in the spectra of **1b** and **2b** probably required different conformations of the cyclohexenone ring in both epimers. Most likely **1b** adopts a boat-conformation to avoid a 1,3-diaxial orientation of the methyl groups at C-4 and C-10, while for **2b** a normal half chair conformation can be assumed.

The co-occurrence of **1a** and **3** may be an indication that 8,12-*cis*-eudesmanolides may be formed via the corresponding eudesmanoic acids rather than from 8,12-*cis*-germacranolides which seem to be rare.

The roots afforded the widespread trideca-3,5,7,9,11-pentayn-1-ene, germacrene *D*, *ent*-kaurenic acid, its 15α-angeloyloxy and isobutyryloxy derivatives and *ent*-kaurenol.

The isolation of the eudesmanolide **3** from a *Perymenium* species supports the placement of this genus in the Ecliptinae where eudesmanolides and *ent*-kaurenic acid derivatives are common (*Aspilia* [4], *Baltimora* [5], *Dimerostemma* [6], *Encelia* [7–9], *Steiractinia* [4], *Wedelia* [10], *Zexmenia* [11], *Zinnia* [12]). From a few genera costic acid derivatives were reported which may replace the eudesmanolides [13–15]. However, several other types of natural product are present in this somewhat diverse subtribe.

EXPERIMENTAL

The air dried plant material (voucher RMK 9025) was extracted with Et_2O–petrol, 1:2, and the resulting extracts were evaporated under vacuum. The extract of the aerial parts (300 g) gave CC fractions (silica gel) as follows: 1 (100 ml, petrol), 2 (200 ml, Et_2O–petrol, 1:10 and 1:3), 3 (100 ml, Et_2O–petrol, 1:1), 4 (200 ml, Et_2O and Et_2O–MeOH, 10:1). TLC (silica gel, PF 254, petrol) of fraction 1 gave 5 mg germacrene D (R_f 0.60; detection always by UV-light and $KMnO_4$ spray). TLC of 2 (Et_2O–petrol, 1:10) afforded 1 g *ent*-kaurenic acid (R_f 0.45), TLC of 3 (Et_2O–petrol, 1:1) gave 50 mg 15α-angeloyloxy-*ent*-kaurenic acid (R_f 0.63) and 100 mg *ent*-kauren-19-ol (R_f 0.38). Fraction 4 on repeated TLC (Et_2O–petrol, 3:1) afforded 10 mg **2a** (R_f 0.65), 20 mg **1a** (R_f 0.61) and a mixture of more polar compounds, which after TLC (C_6H_6–Et_2O–CH_2Cl_2, 1:1:1) gave 3 mg **3** (R_f 0.63) and *ca* 2 mg crude 8-desoxysalonitenolide which was purified by HPLC (RP 8, MeOH–H_2O 13:7, R_t 6:1 min.).

The extract of the roots (100 g) gave fractions as follows: 1 (50 ml, petrol), 2 (100 ml, Et_2O–petrol, 1:10 and 1:3), 3 (100 ml, Et_2O–petrol, 1:1) and 4 (100 ml Et_2O and Et_2O–MeOH, 10:1). TLC (silica gel PF 254) of fraction 1 (petrol) gave 5 mg germacrene D and *ca* 0.5 mg tridecapentayn-1-ene (estimated by UV-extinction). TLC of 2 (Et_2O–petrol, 1:10) gave 0.5 g *ent*-kaurenic acid (R_f 0.48), and TLC of 3 (Et_2O–petrol, 1:1) afforded 20 mg 15α-angelolyloxy- and 20 mg 15α-isobutyryloxy-*ent*-kaurenic acid (R_f 0.60) while fraction 4 gave no definite compounds. Known compounds were identified by comparing their 400 MHz ^{1}H NMR spectra with those of authentic material. Quantities were estimated by weight.

3-Oxo-1,2-dehydro-4α,15-dihydro costic acid (**1a**). Colourless oil; MS *m/z* (rel. int.): 248.141 $[M]^+$ (44) ($C_{15}H_{20}O_3$), 233 $[M-Me]^+$ (8), 230 $[M-H_2O]^+$ (16), 202 $[230-CO]^+$ (14), 95 $[C_7H_{11}]^+$ (90), 67 $[C_5H_7]^+$ (100). Addition of CH_2N_2 in Et_2O afforded the methyl ester **1b** (TLC, Et_2O–petrol, 1:3 R_f 0.48), colourless oil, $bp_{0.1}$ 125° (bath temp. short way dest.); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (C=CCO$_2$R), 1675, 1620 (C=CC=O); MS *m/z* (rel. int.): 262.157 $[M]^+$ (100) ($C_{16}H_{22}O_3$), 247 $[M-Me]^+$ (12), 230 $[M-MeOH]^+$ (44), 215 $[230-Me]^+$ (34), 202 $[230-CO]^+$ (56), 95 (79), 91 (89), 67 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-25 \quad -26 \quad -36 \quad -152} CHCl_3;\ c\ 1.34$$

To 10 mg **1a** in 1 ml tert.-butanol 5 mg potassium-tertbutylate was added. After 1 h, usual work-up afforded **2a**, identical with the natural acid, while nothing of the epimer was detectable.

3-Oxo-1,2-dehydro-4β,15-dihydro costic acid (**2a**). Colourless oil; MS *m/z* (rel. int.): 248.141 $[M]^+$ (36) ($C_{15}H_{20}O_3$), 233 $[M-Me]^+$ (8), 230 $[M-H_2O]^+$ (9), 202 $[230-CO]^+$ (14), 95 (50), 67 (58), 61 (100). Addition of CH_2N_2 in Et_2O gave the methyl ester **2b** (TLC, Et_2O–petrol, 1:3: R_f 0.45), colourless oil, $bp_{0.1}$ 125° (bath temp., short way dest.); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (C=CCO$_2$R), 1675, 1620 (C=CC=O); MS *m/z* (rel. int.): 262.157 $[M]^+$ (61) ($C_{16}H_{22}O_3$), 247 $[M-Me]^+$ (8), 230 $[M-MeOH]^+$ (41), 215 $[230-Me]^+$ (16), 202 $[230-CO]^+$ (31), 95 (77), 91 (78), 67 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-50 \quad -52 \quad -61 \quad -130} CHCl_3;\ c\ 0.63$$

4α,15-*Dihydroencelin* (3). Colourless crystals, mp 175° (Et_2O); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1760 (γ-lactone), 1670 (C=CC=O); MS *m/z* (rel. int.): 246.126 $[M]^+$ (21) ($C_{15}H_{18}O_3$), 231 $[M-Me]^+$ (3), 218 $[M-CO]^+$ (3), 97 (71), 95 (79), 69 (100), 55 (98).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{+14 \quad +14 \quad +20 \quad +53} CHCl_3;\ c\ 0.1$$

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2-ACETOXY-3α,4α-EPOXY-3,4-DIHYDROKAUNIOLIDE FROM *GROSVENORIA COELOCAULIS*

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Key Word Index—*Grosvenoria coelocaulis*; Compositae; sesquiterpene lactones; guaianolides.

Abstract—The aerial parts of *Grosvenoria coelocaulis* gave the known guaianolides dehydroleucodin, desacetoxymatricarin, kauniolide and a new one, 2β-acetoxy-3α,4α-epoxy-3,4-dihydrokauniolide.

Grosvenoria (Compositae, tribe Eupatorieae) is a small genus [1] ranging from central Ecuador into northern Peru, which is placed in the subtribe Critoniinae [2]. So far nothing is known on the chemistry of this genus. We have now investigated *Grosvenoria coelocaulis* (B. L. Robins.) K. et R. from northern Peru. The aerial parts afforded α-curcumene and α-zingiberene as well as the known guaianolides kauniolide (**1**) [3], dehydroleucodin [4], desacetoxymatricarin [5] together with a new one, $C_{17}H_{20}O_5$. The IR spectrum of the latter indicated the presence of a γ-lactone and an acetate group (1770, 1738, 1245 cm^{-1}). From the ^1H NMR spectrum (Table 1) the presence of 6α,12-methylene lactone could be deduced. A typical fourfold doublet at δ2.80 was due to the H-7 signal. Accordingly, its irradiation collapsed the H-13 doublets to singlets, the double doublet at δ3.63 to a doublet and changed the overlapped multiplet around 2.10 while a quartet at 1.33 collapsed to a triplet. Addition of deuteriobenzene allowed the assignment of all signals by spin decoupling. As H-2 showed a *W*-coupling with H-5 and an allylic coupling with H-14 the whole sequence leading to the structure **2** could be assigned. The chemical shifts of H-2 and H-3 in combination with the other data indicated a 2-acetoxy derivative of kauniolide where the 3,4-double bond was transformed to an epoxide. Inspection of a model showed that the small coupling $J_{2,3}$ required a *trans*-orientation of H-2 and H-3, while the chemical shift of H-15 obviously was influenced by the deshielding effect of the lactone oxygen at C-6. This, however, required a 4β-methyl group as the stereochemistry at C-5–C-7 clearly followed from the *trans*-diaxial couplings of H-5–H-7. Also the observed couplings of H-8 and H-9 nicely agreed with the angles which could be deduced from a model. Thus the new compound is 2β-