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THREE FURANOHELIANGOLIDES FROM *CALEA VILLOSA**

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Key Word Index—*Calea villosa*; Compositae; sesquiterpene lactones; germacranolides; heliangolides.

Abstract—*Calea villosa* afforded three new sesquiterpene lactones, two furanoheliangolides and an epoxygermacranolide, as well as several known compounds. The structures were elucidated by spectroscopic methods.

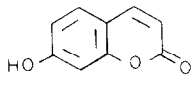
In continuation of our investigations of *Calea* species [1], we have studied the constituents of *Calea villosa* Sch. Bip. ex Baker. The roots afforded α-humulene, caryophyllene, β-sesquiphellandrene, the thymol derivatives **2–8**, the angelate **9** [2] and the furanoheliangolides **12** [3], **13** [4] and **15**. The latter also was present in the aerial parts, which further afforded germacrene D, α-humulene, caryophyllene, bicyclogermacrene, umbelliferone (**1**), nerolidol (**17**), the 13-hydroxy derivative **18** [5], the heliangolides **12–14** [3] and **16** as well as the epoxygermacranolides **10** [6, 7] and **11**. The structure of the latter followed from the molecular formula ($C_{25}H_{34}O_7$) and high field ^{1}H NMR spectroscopy (Table 1), which clearly showed that a germacranolide was present with two ester residues, an angelate and a 2-methylbutyrate. The nature of a third oxygen function followed from a double doublet at δ 2.73 and a singlet at 1.54, indicating a 1,10-epoxide as spin decoupling showed that the remaining low field signals were those of a germacranolide with ester functions at C-3 and C-8 and of a 6,12-lactone. The stereochemistry at C-8 followed from the small coupling $J_{7,8}$, while the couplings of H-3 indicated β-orientation of the second ester group, when compared with data of similar lactones. From the chemical shifts and the couplings of H-1 and H-5–H-7 the stereochemistry at the corresponding carbons was deduced. The relative position of the two ester groups was supported by biogenetic considerations since the other lactones (**12–16**) also were 8β-angeloyloxy derivatives. The chemical shifts of H-3 and H-8 agreed with this proposal as unsaturated ester groups always cause a slight downfield shift of the corresponding signal when compared with that of a saturated ester. The structure of **15**, which could be separated from **13** and **16** only with difficulty, followed from the similarity of the ^{1}H NMR spectrum (Table 1) to that of **14** [3]. The signal of the olefinic methyl at C-4 was replaced by a broadened doublet at δ 4.50 indicating a 15-hydroxy group. Accordingly the H-5 signal was shifted slightly downfield, when compared with the shift of H-5 in **14**. This assumption was further established by spin decoupling, which allowed assignment of all signals. The stereochemistry of **15** was obviously the same as that of **14**, for which an 11β,13-epoxide was tentatively proposed [3] only on the basis of Eu(fod)$_3$ induced shifts. This assignment still needs to be established. The structure

Table 1. ^{1}H NMR spectral data of compounds **11**, **15** and **16** (400 MHz, $CDCl_3$, TMS as internal standard)

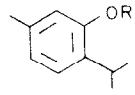
	11	**15**	**16**
H-1	2.73 *dd*	—	—
H-2α	1.52 *dd*	5.69 *s*	5.66 *s*
H-2β	2.44 *ddd*		
H-3	5.51 *dd*	—	—
H-5	5.49 *br d*	6.29 *dt*	6.30 *dt*
H-6	5.15 *dd*	5.33 *ddt*	5.22 *ddt*
H-7	2.93 *dddd*	3.85 *dd*	3.43 *dd*
H-8	5.74 *br d*	5.12 *ddd*	5.07 *ddt*
H-9α	2.85 *dd*	2.42 *dd*	2.52 *dd*
H-9β	1.32 *dd*	2.20 *dd*	2.35 *dd*
H-13	6.34 *d*	3.80 *d*	4.25 *d*
H-13′	5.60 *d*	3.86 *d*	3.90 *d*
H-14	1.54 *s*	1.45 *s*	1.46 *s*
H-15	1.86 *d*	4.50 *br d*	4.41 *br d*
OAng	6.16 *qq*	6.16 *qq*	6.14 *qq*
	2.00 *dq*	1.94 *dq*	1.93 *dq*
	1.89 *dq*	1.81 *dq*	1.80 *dq*
OCOR	2.60 *tq*	—	—
	1.70 *ddq*		
	1.40 *ddq*		
	1.15 *d*		
	0.90 *t*		

J (Hz): Compound **11**: 1,2α = 11; 1,2β = 2; 2α,2β = 13; 2α,3α = 11; 2β,3α = 6; 5,6 = 10; 6,7 = 9; 7,8 ~ 1; 7,13 = 3.5; 7,13′ = 3; 8,9α = 6; 8,9β = 1.5; 9α,9β = 15; compound **15** and **16**: 5,6 = 4; 5,15 = 2; 6,7 = 4.5; 6,15 ~ 1; 7,8 = 2; 8,9α = 4.5; 8,9β = 3; 9β = 15; 13,13′ = 4.5 (compound **16**: 13).

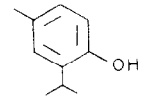
*Part 458 in the series "Naturally Occurring Terpene Derivatives". For Part 457 see Bohlmann, F., Grenz, M., Jakupovic, J., King, R. M. and Robinson, H. *Phytochemistry* (in press).



1



2 R = H
3 R = *i*Bu
4 R = *i*Val



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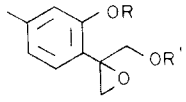
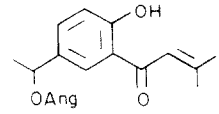


	6	7	8
R	*i*Bu	*i*Bu	*i*Bu
R'	MeBu	Ac	*i*Bu



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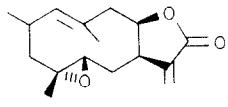

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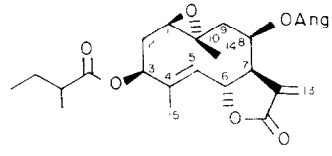
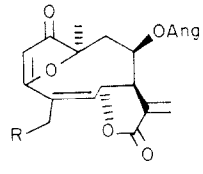
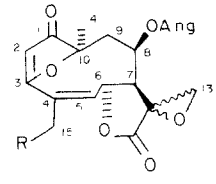


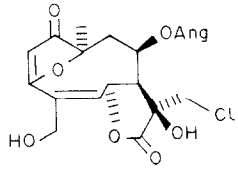
11



12 R = H
13 R = OH



14 R = H
15 R = OH



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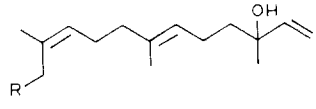

17 R = H
18 R = OH

of **16** could also be deduced easily from the ^{1}H NMR spectrum (Table 1), which again differed from that of the corresponding 15-desoxy compound [3] by the replacement of the signal of the olefinic methyl at C-4 by that of a hydroxymethylene group. All signals could be assigned by spin decoupling. Except for the high concentration of **1**, the chemistry of this species was very similar to that of previously investigated *Calea* species.

EXPERIMENTAL

The air-dried plant material, collected in Bahia, Brazil (voucher RMK 8640, deposited in the U.S. National Herbarium, Washington) 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). The roots (100 g) gave 10 mg α-humulene, 5 mg β-sesquiphellandrene, 20 mg caryophyllene, 20 mg **2**, 30 mg **3**, 10 mg **4**, 20 mg **5**, 200 mg **6**, 100 mg **7**, 50 mg **8**, 200 mg **9**, 5 mg **12**, 50 mg **13** (Et_2O, several times) and 20 mg **15** (same solvent), while the aerial parts (200 g) afforded 50 mg germacrene D, 100 mg α-humulene, 20 mg caryophyllene, 20 mg bicyclogermacrene, 500 mg **1**, 20 mg **10**, 10 mg **11** (CH_2Cl_2–C_6H_6–Et_2O, 1:1:1), 50 mg **12**, 100 mg **13**, 100 mg **14**, 20 mg **15** (Et_2O, several times), 10 mg **16** (same solvent), 200 mg **17** and 10 mg **18**. The known compounds were identified by comparing their ^{1}H NMR spectra, IR and MS with those of authentic compounds.

8β-Angeloxyloxy-3β-(2-methylbutyryloxy)-1β, 10α-epoxy-1,10H-costunolide (**11**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 446.230 [M]$^+$ (0.2) ($C_{25}H_{34}O_7$), 428 [M − H_2O]$^+$ (0.1), 346

$[M - AngOH]^+$ (0.6), 344 $[M - C_4H_9CO_2H]^+$ (0.9), 244 $[344 - AngOH]^+$ (5), 326 $[344 - H_2O]^+$ (1), 85 $[C_4H_9CO]^+$ (31), 83 $[C_4H_7CO]^+$ (100), 57 $[85 - CO]^+$ (68), 55 $[83 - CO]^+$ (52).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+10 \quad +17 \quad +19 \quad +38} (CHCl_3; c0.4).$$

11,13-*Epoxy*-11,13H-*budlein A* (**15**). Colourless crystals, mp 93°, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1800 (γ-lactone), 1720 (C=CCO), 1600 (C=C–OR); MS *m/z* (rel. int.): 390.132 $[M]^+$ (16), 291 $[M - OCOR]^+$ (2), 273 $[291 - H_2O]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (98); $[\alpha]_D = -27°$.

11β-*Hydroxy*-13-*chloro*-11,13H-*budlein A* (**16**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1780 (γ-lactone), 1720 ($C=CCO_2R$); MS *m/z* (rel. int.): 426.103 $[M]^+$ (5) ($C_{20}H_{23}O_8Cl$), 390 $[M - HCl]^+$ (10), 327 $[M - OCOR]^+$ (1), 291 $[327 - HCl]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (94).

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EREMOPHILENE AND GERMACRENE DERIVATIVES FROM *SENECIO GLANDULOSO-PILOSUS**

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Key Word Index—*Senecio glanduloso-pilosus*; Compositae; sesquiterpenes; eremophilene derivative; germacrene hydroperoxide.

Abstract—*Senecio glanduloso-pilosus* afforded in addition to known compounds a new eremophilene derivative and a hydroperoxide derived from germacrene D.

In a continuation of our investigation of *Senecio* species we have studied the constituents of *S. glanduloso-pilosus* Volkens et Muschler. The aerial parts afforded germacrene D, α-humulene, β-farnesene, 5'-angeloyloxysenspeciosone (**1**)[1] and the isomeric ester **2** as well as the hydroperoxide **6**. The structure of **2** followed from the molecular formula and the ^1H NMR spectral data (Table 1), which were similar to those of **1** and of the 7,11-isomer of **2**[1]. The nature of the ester residue clearly followed from the typical ^1H NMR signals. The three-fold doublet at δ 6.22 was coupled with one of the olefinic protons and with those of a neighbouring CH_2 group, which were also coupled with a methyl group (1.00*t*). The stereochemistry at C-7, C-9 and C-10 followed from the couplings $J_{6,7}$ and $J_{9,10}$, which were identical with those of the isomeric ester isolated previously[1]. Structures **1–5** represent the relative configurations, which are also probably the absolute ones as the configuration at C-7 is normally β. The structure of **6** was deduced from the spectral data. In the mass

*Part 438 in the series "Naturally Occurring Terpene Derivatives". For Part 437 see Bohlmann, F., Gupta, R. K. and Jakupovic, J., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 1665.