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FIVE EUDESMANOLIDES FROM *CALOSTEPHANE DIVARICATA**

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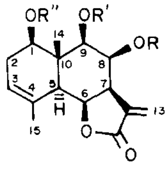
Key Word Index—*Calostephane divaricata*; Compositae; Inuleae; sesquiterpene lactones; eudesmanolides.

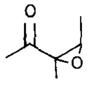
Abstract—The investigation of *Calostephane divaricata* afforded in addition to known compounds five new eudesmanolides, all being tri-substituted derivatives of 6-epi-α-cyclocostunolides. The structures were elucidated by highfield ^{1}H NMR spectroscopy. The relative positions of the oxygen functions could not be established with certainty. The observed shift differences agreed well with the proposed structures.

So far nothing is known on the chemistry of the small South African genus *Calostephane* (tribe Inuleae), which is placed in the subtribe Inulinae in the *Inula* group [1]. We now have studied the constituents of *C. divaricata* Benth. The roots only afforded β-farnesene, sitosterol and stigmasterol, while the aerial parts in addition to β-farnesene, α-humulene, taraxasterol, lupeol and their acetates gave a complex mixture of sesquiterpene lactones, which could only be separated with difficulty. Finally, five lactones were obtained, the eudesmanolides **1–5**. The ^{1}H NMR spectra (Table 1) showed that the compounds were trisubstituted 6, 12-lactones with two ester groups and one hydroxyl. The position of the functions clearly followed from spin decoupling. Starting with the 7-H signal the protons H-6, H-8 and H-13 could be assigned. Further decouplings led to the assignment of H-5 and H-9. As the H-5 signal showed allylic coupling with an olefinic proton which itself coupled with allylic protons which were coupled too with a downfield double doublet, the signals of H-3–H-1 could also be assigned. The chemical shift of H-6 indicated that it was the proton under the lactone oxygen, but the coupling $J_{6,7}$ was not in agreement with a 6,12-*trans*-eudesmanolide. The small coupling $J_{7,13}$ was an indication of a *cis*-lactone. This was supported by a positive Cotton effect [2]. Inspection of a model further showed that the coupling $J_{7,8}$ required a 8β-oxygen function, while the proton at C-1 was clearly α-orientated. The presence of a hydrogen bond, which followed from the IR spectra, required a 9β-oxygen function, while the small coupling $J_{8,9}$ also would agree with a 9α-function. This, however, would not explain the hydrogen bond and furthermore two axial oxygen functions probably would lead to a changed conformation of ring B. The relative position of the oxygen functions could be assigned by comparing the chemical shifts of H-1, H-8 and H-9. As usual the angelate residue caused a slightly greater downfield shift than the epoxy angelate as can be seen in the spectra of the isomers **1** and **3**, while the chemical shifts of H-8 and H-9 showed that ester groups were at C-8 and C-9. Similarly the relative position of the ester groups in **2** followed from the chemical shifts of H-1 and H-8 in the spectra of **2** and **5**. Therefore the position of the ester groups in all lactones seems to be clear. Due to the small amounts of material, no further attempts were possible to establish the proposed relative positions of the ester groups. **1–5** are derivatives of 6-epi-α-cyclocostunolide, which most probably has been isolated from a *Critonia* species [3]. The configuration at C-6 and C-7 of critonilide and isocritonilide, however, has to be changed. Further investigations may show whether these lactones are of chemotaxonomic importance. So far nothing is known on the chemistry of the genera which are closely related to *Calostephane*.



	1	2	3	4	5
R	Ang	Epang	Epang	Epang	Epang
R'	Epang*	H	Ang	Epang	H
R''	H	Ang	H	H	Epang

* Epang =



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*Part 425 in the series "Naturally Occurring Terpene Derivatives". For Part 424, see Bohlmann, F. and Borthakur, N. (1982) *Phytochemistry* **21**, 1160.

Table 1. ^{1}H NMR spectral data of compounds **1–5** (400 MHz, $CDCl_3$, TMS as int. standard)

	1	**2**	**3**	**4**	**5**
H-1	3.73 *dd br*	4.78 *dd br*	3.75 *dd br*	3.74 *m*	4.71 *dd br*
H-3	5.48 *s br*	5.44 *s br*	5.45 *s br*	5.47 *s br*	5.45 *s br*
H-5	2.63 *d br*	2.65 *d br*	2.65 *d br*	2.58 *d br*	2.58 *d br*
H-6	4.64 *dd*	4.59 *dd*	4.64 *dd*	4.63 *dd*	4.59 *dd*
H-7	3.73 *m*	3.73 *dddd*	3.75 *m*	3.74 *m*	3.72 *m*
H-8	5.24 *dd*	5.11 *dd*	5.14 *dd*	5.17 *dd*	5.16 *dd*
H-9	5.08 *d*	3.66 *s br*	5.18 *d*	5.05 *d*	3.72 *m*
H-13	6.40 *d*	6.32 *d*	6.34 *d*	6.40 *d*	6.37 *d*
H-13'	5.86 *d*	5.77 *d*	5.80 *d*	5.84 *d*	5.82 *d*
H-14	1.01 *s*	1.11 *s*	1.02 *s*	1.03 *s*	1.09 *s*
H-15	1.91 *s br*	1.90 *s br*	1.89 *s br*	1.90 *s br*	1.91 *s br*
OCOR	6.16 *qq*	6.12 *qq*	6.15 *qq*	3.05 *q*	3.03 *q*
	2.02 *dq*	1.97 *dq*	1.98 *dq*	1.33 *d*	1.30 *d*
	1.93 *dq*	1.79 *dq*	1.80 *dq*	1.45 *s*	1.44 *s*
	3.05 *q*	3.08 *q*	3.10 *q*	3.08 *q*	3.07 *q*
	1.35 *d*	1.32 *d*	1.40 *d*	1.38 *d*	1.31 *d*
	1.46 *s*	1.60 *s*	1.61 *s*	1.59 *s*	1.59 *s*

J (Hz): 1α, 2α = 6; 1α, 2β = 10; 5, 6 = 9.5; 6, 7 = 7; 7, 8 = 4; 7, 13 = 2; 7, 13' = 1.7; 8, 9 = 1.5; OAng: 3', 4' = 7; 3', 5' = 4', 5' = 1.3; OEpang: 3', 4' = 5.

EXPERIMENTAL

The air-dried plant material, collected in Transvaal, voucher 81/49, deposited in the Botanic Research Institute, Pretoria, was extracted with Et_2O–petrol, 1:2, and the extracts obtained were separated by CC (Si gel) and further by TLC (Si gel). Known compounds were identified by comparing the ^{1}H NMR spectra with those of authentic material. The roots (15 g) gave 30 mg β-farnesene, 3 mg sitosterol and 3 mg stigmasterol, while the aerial parts (100 g) afforded 10 mg β-farnesene, 5 mg α-humulene, 10 mg taraxasterol and 10 mg of its acetate, 5 mg lupeol and 10 mg of its acetate as well as a mixture of **1–5**, which after repeated TLC (Et_2O) afforded 6 mg **1**, 5 mg **2**, 6 mg **3**, 1 mg **4**, and 1 mg **5**.

8β-Angeloyloxy-1β-hydroxy-9β-[2, 3-epoxy-2-methylbutyryloxy]-6-epi-α-cyclocostunolide (**1**). Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3500 (OH), 1770 (γ-lactone), 1745 (CO_2R), 1710, 1650 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 460.210 $[M]^+$ (0.3) ($C_{25}H_{32}O_8$), 442 $[M-H_2O]^+$ (1), 360 $[M-AngOH]^+$ (0.5), 345 $[360-Me]^+$ (5), 244 $[360-RCO_2H]^+$ (10), 226 $[244-H_2O]^+$ (9), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (48).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-25 \quad -28 \quad -38 \quad -69} \quad (c = 0.5,\ CHCl_3).$$

CD(MeCN) $\Delta\epsilon_{255} = +0.55$.

1β-Angeloyloxy-9β-hydroxy-8β-[2, 3-epoxy-2-methylbutyryloxy]-6-epi-α-cyclocostunolide (**2**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3540 (OH), 1785 (γ-lactone), 1750 (CO_2R), 1725, 1650 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 460.210 $[M]^+$ (0.2) ($C_{25}H_{32}O_8$), 442 (0.3), 360 (0.3), 344 $[M-RCO_2H]^+$ (1), 244 $[344-AngOH]^+$ (11), 226 (14), 83 (100), 55 (47).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-79 \quad -85 \quad -98 \quad -171} \quad (c = 0.12,\ CHCl_3).$$

9β-Angeloyloxy-1β-hydroxy-[2, 3-epoxy-2-methylbutyryloxy]-6-epi-α-cyclocostunolide (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3530 (OH), 1785 (γ-lactone), 1740 (CO_2R), 1725, 1650 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 460.210 $[M]^+$ (0.2) ($C_{25}H_{32}O_8$), 442 (0.3), 361 $[M-OAng]^+$ (0.4), 360 (0.2), 344 (2), 342 (2), 244 (10), 83 (100), 55 (51).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-26 \quad -28 \quad -32 \quad -58} \quad (c = 0.5,\ CHCl_3).$$

1β-Hydroxy-8β, 9β-di-[2, 3-epoxy-2-methylbutyryloxy]-6-epi-α-cyclocostunolide (**4**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3560 (OH), 1785 (γ-lactone), 1745 (CO_2R); MS *m/z* (rel. int.): 360.157 $[M-RCO_2H]^+$ (9) ($C_{20}H_{24}O_6$), 244 $[360-RCO_2H]^+$ (23), 266 (31).

9β-Hydroxy-1β, 8β-di-[2, 3-epoxy-2-methylbutyryloxy]-6-epi-α-cyclocostunolide (**5**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3520 (OH), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 360.157 $[M-RCO_2H]^+$ (2) ($C_{20}H_{24}O_6$), 342 (2.5), 244 (60), 226 (62).

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