Phytochemistry, Vol. 21, No. 2, pp. 371–374, 1982.
Printed in Great Britain.

0031-9442/82/020371-04$03.00/0

THREE CADINENE DERIVATIVES AND A PROSTAGLANDIN-LIKE ACID FROM *CHROMOLAENA* SPECIES*

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(*Received* 26 *May* 1981)

Key Word Index—*Chromolaena chasleae*; *C. pseudoinsignis*; Compositae; Eupatorieae; sesquiterpenes; cadinene derivatives; prostaglandin-like acid.

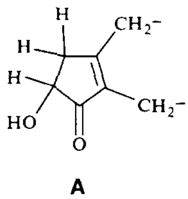
Abstract—An investigation of the aerial parts of *Chromolaena chasleae* afforded a prostaglandin-like acid, whose structure followed from the ¹H NMR spectral data and from the reaction with periodate, which afforded a hemiacetal. From a new *Chromolaena* species, three novel cadinene derivatives were isolated, which were closely related to those isolated previously from this genus.

Table 1. ¹H NMR spectral data of compounds **10**, **11** and **13** (400 MHz, $CDCl_3$, TMS as int. standard)

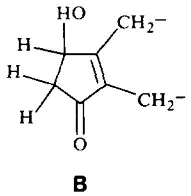
	10	**11**	**13**
H-2	2.26 *t*	2.32 *t*	2.31 *t*
H-3	1.59 *tt*	1.61 *tt*	1.60 *tt*
H-4–6	1.30 *m*	1.34 *m*	1.30 *m*
H-7	1.48 *m*	1.52 *m*	1.45 *ddt*
H-8	2.44 *br dt*	2.45 *dt*	2.26 *dt*
H-8′	2.35 *br dt*	2.33 *m*	2.23 *dt*
H-10	2.85 *dd*	2.82 *dd*	2.64 *dd*
H-10′	2.30 *dd*	2.40 *dd*	2.46 *dd*
H-11	4.18 *dd*	3.87 *dd*	5.66 *br ddd*
H-14	2.92 *dd*	2.94 *br d*	3.11 *br d*
H-14′	2.87 *dd*		
H-15	5.16 *dtt*	5.20 *dtt*	5.21 *dtt*
H-16	5.35 *dtt*	5.36 *dtt*	5.37 *dtt*
H-17	2.10 *br tq*	2.15 *br tq*	2.14 *dtq*
H-18	0.95 *t*	0.99 *t*	0.97 *t*
OH	3.3 *br s*		4.52 *br d*
OMe	3.64 *s*	3.67, 3.56 *s*	3.67 *s*

J (Hz): 2, 3 = 3, 4 = 7, 8 = 16, 17 = 17, 18 = 7.5; 8, 8′ = 15; 10, 10′ = 18; 10, 11 = 3.5; 10′, 11 = 5; 11, OH = 3.5; 14, 15 = 2; 14, 16 = 2; 15, 16 = 10.5; compound **10**: 14, 14′ = 15; 10, 11 = 7; 10′, 11 = 3; compound **13**: 2, 3 = 3, 4 = 7.

In continuation of our chemosystematic studies of the tribe Eupatorieae (Compositae) we now have investigated two further *Chromolaena* species. The aerial parts of *C. chasleae* (B. L. Robins.) K. et R. afforded germacrene D, squalene, the flavonoids **1** [1], **2** [2], **3** [3], **4** [4], **5** [2] and **6** [5] as well as the prostaglandin-like acids **7a** and **b** [6], **8** [6] and **9**. The structure of the new compound followed from the spectral data and from the results of the periodate reaction. **9** was transformed first by addition of diazomethane to the ester **10**. The ¹H NMR spectral data (Table 1) were in part similar to those of other esters of this type [6], indicating the presence of the side-chains $-(CH_2)_7CO_2Me$ and $-CH_2CH{=}CHEt$(*cis*). Double doublets at 4.18, 2.39 and 2.85 ppm obviously had to be assigned to partial structure **A** or **B**:



A



B

The sharpness of the downfield signal favoured the partial structure **A**. Reaction with periodate gave **13**, obviously formed from the expected acid aldehyde **12**. All signals in the spectra of **10** and **13** could be assigned by spin decoupling except those of H-4–H-6. As the chemical shifts of H-14 indicated the position of the keto group at C-12, the structure of the natural compound therefore was established. The reaction of **9** with diazomethane gave in addition to **10** small amounts of two further compounds, the methyl ether **11** and the pyrazoline derivative **14**. The latter must be formed through elimination of H_2O followed by 1,3-dipolar addition to the 10,11-double bond. The absolute configuration of the acid **9** could not be

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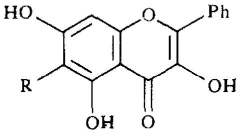
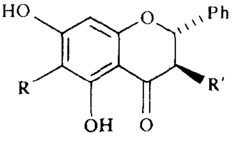
*Part 388 in the series "Naturally Occurring Terpene Derivatives". For Part 387 see Bohlmann, F. and Bapuji, M. (1982) *Phytochemistry* **21** (in press).

determined. The roots gave germacrene D, stigmasterol and sitosterol only.

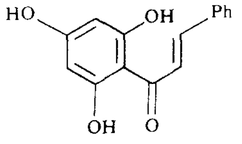
The roots of *Chromolaena pseudoinsignis* K. et R. afforded germacrene D, bisabolene, β-farnesene, 7-methoxycoumarin (**15**) and the furocadinenes **17–19** [7, 8] as well as three further cadinene derivatives, the keto diol **16** and the epimeric methyl ethers **20** and **21**, which could not be separated. The ^{1}H NMR spectral data (Table 2), however, allowed the assignment of most of the signals by spin decoupling. Starting with the H-5 signal whose assignment followed from the chemical shift, most of the signals of the epimers could be assigned. The relative stereochemistry at C-5, C-6, C-9 and C-10 followed from the couplings observed and the differences of the chemical shifts, if models were considered with different preferred conformations, with an axial 9-methyl in **20** and an equatorial one in **21**. Consequently deshielding effects



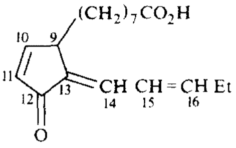
1 R = H
2 R = OMe



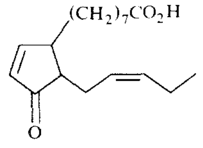
3 R = H, R′ = H
4 R = H, R′ = OH
5 R = OMe, R′ = OH



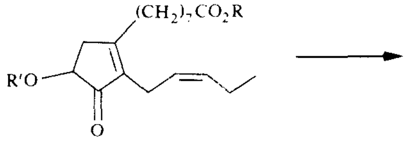
6



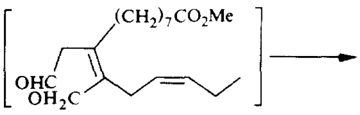
7a 13*Z*, 15*E*
7b 13*E*, 15*Z*



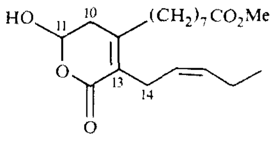
8



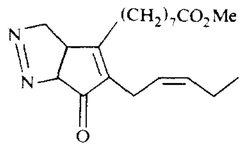
9 R = R′ = H
10 R = Me, R′ = H
11 R = R′ = Me



12



13



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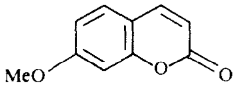
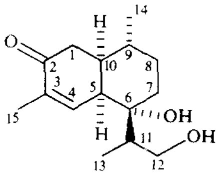
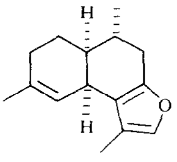


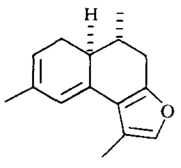
15



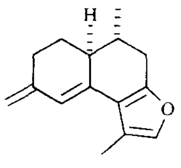
16



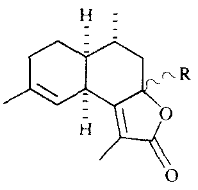
17



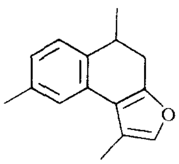
18



19



20 R = α OMe
21 R = β OMe



22

Table 2. ^1H NMR spectral data of compounds **16**, **20** and **21** (400 MHz, $CDCl_3$ TMS as int. standard)

	16	C_6D_6	**20**	**21**
H-1α	2.40 *dd*	2.14 *dd*	1.28 *m*	
H-1β	2.77 *dd*	2.86 *dd*	1.43 *m*	
H-4	6.37 *br s*	6.00 *br s*	5.05 *br s*	5.65 *br d*
H-5	2.95 *br*	2.70 *br*	3.58 *br dd*	3.28 *br dd*
H-7α	1.45 *m*	1.35 *m*	—	—
H-7β	1.13 *ddd*	0.78 *ddd*	—	—
H-8α	1.35 *dddd*	1.35 *m*	1.73 *dd*	1.27 *dd*
H-8β	1.80 *m*	1.65 *m*	2.19 *br d*	2.34 *dd*
H-9	1.48 *m*	1.35 *m*	1.87 *m*	2.01 *m*
H-10	2.33 *br d*	2.24 *br d*		
H-11	1.45 *m*	1.49 *m*	—	—
H-12	3.70 *dd*	3.13 *dd*	—	—
H-12′	4.11 *dd*	3.63 *dd*	—	—
H-13	1.20 *d*	1.07 *d*	1.90 *d*	1.88 *s*
H-14	0.88 *d*	0.85 *d*	1.21 *d*	0.94 *d*
H-15	1.77 *dd*	1.90 *dd*	1.73 *br s*	1.68 *br s*
OMe	—	—	3.16 *s*	3.12 *s*

J (Hz): Compound **16**: 1α, 1β = 16; 1α, 10 = 5; 1β, 10 = 2.5; 5, 10 ~ 5; 7α,, 7β = 13; 7β, 8α = 12; 7β, 8β = 4; 8α, 8β = 13; 8α, 9β = 12; 9β, 10α = 10; 9β, 14 = 7; 11, 12 = 3; 11, 12′ = 2.5; 11, 13 = 7; 12, 12′ = 11; compound **20**: 4, 5 ~ 4; 4, 15 = 5, 15 ~ 1.5; 5, 6 ~ 6; 8α, 8β = 13; 8α, 9β = 6; 8β, 9β ~ 1; 9β, 14 = 7; 5, 13 = 1.5; compound **21**: 4, 5 ~ 2; 4, 15 = 5, 15 ~ 1.5; 8α, 8β = 13; 8α, 9β = 13; 8β, 9β = 3.5.

of the methoxy group were different in both epimers, as in **20** H-5 and H-14 and in **21** H-4 were close to the oxygen of the methoxy group. Different stereochemistry at C-9 was less likely.

The structure of the diol **16** also followed from the ^1H NMR spectral data (Table 2). The position of the hydroxyl groups could be deduced from the multiplicity of the CH_2OH signals, while the position of the keto group followed from the downfield shift of the H-4 signal. The *cis*-relationship of H-5 and H-10 was deduced from the half-width of the H-5 signal, while the orientation of the C-9-methyl followed from the couplings of H-10, though again this signal was a broadened doublet. As, however, spin decoupling clearly showed that $J_{9,10}$ was about 10 Hz, the stereochemistry was established. As the H-5 signal obviously was shifted downfield by the 6-hydroxyl group, its α-orientation was most likely. The absolute configuration of **16**, **20** and **21**, however, was not determined. The aerial parts gave germacrene D, bisabolene, phytol, herniarin (**15**), **16**–**19** and **22** [9].

So far the results on the chemistry of *Chromolaena* species show that one species contained a sesquiterpene lactone [10] and that most of the others afforded cadinene derivatives [7–9, 11]. A third group may be characterized by unusual prostaglandin-like acids [6] and the absence of the former types of constituents. However, still more species have to be investigated to get a clear picture of this large genus.

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil, 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 their ^1H NMR spectra with those of authentic material.

Chromolaena chasleae (*voucher RMK* 8867, *deposited in the U.S. National Herbarium*). The roots (35 g) afforded 2 mg germacrene D, 3 mg stigmasterol and 2 mg sitosterol, while the aerial parts (340 g) gave 80 mg germacrene D, 200 mg squalene, 50 mg **1**, 80 mg **2**, 60 mg **3**, 15 mg **4**, 10 mg **5**, 1.5 mg **6**, 2 mg **7a**, 1 mg **7b**, 2 mg **8**, 35 mg **9** (Et_2O), which was purified as its methyl ester **10** (addition of CH_2N_2 in Et_2O). In addition to **10**, 2 mg **11** and 1 mg **14** were obtained after TLC (CH_2Cl_2–C_6H_6, 1 : 1).

5 - Hydroxy - 2[pent - 2c - enyl] - 3 - [(7 - carbomethoxy) - heptyl] - cyclopent - 2 - en - 1 - one (**10**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (OH), 1740 (CO_2R), 1705, 1630 (C=CC=O); MS *m/z* (rel. int.): 322.214 $[M]^+$ (8) ($C_{19}H_{30}O_4$), 304 $[M-H_2O]^+$ (22), 291 $[M-OMe]^+$ (14), 275 $[304-Et]^+$ (25), 253 $[M-CH_2CH{=}CHEt]^+$ (2), 165 $[M-(CH_2)_7CO_2Me]^+$ (47), 147 $[165-H_2O]^+$ (42), 55 $[C_4H_7]^+$ (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 549\ \text{nm}}{-15.5 \quad -15.7 \quad -18.7} \quad (\text{CHCL}_3;\ c,\ 1.2).$$

11: Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R), 1705 (C=CC=O); MS *m/z* (rel. int.): 336 $[M]^+$ (10), 306 $[M-CH_2O]^+$ (14), 305 $[M-OMe]^+$ (14), 304 $[M-MeOH]^+$ (14), 275 $[304-Et]^+$ (18), 55 (100).

14: Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745 (CO_2R), 1725 (C=CC=O); MS *m/z* (rel. int.): 346 $[M]^+$ (9), 318 $[M-N_2]^+$ (5), 289 $[318-Et]^+$ (10), 55 (100). To 12 mg **10** in 1 ml MeOH 30 mg $NaIO_4$ in 0.1 ml H_2O was added. After 2 hr water was added and the reaction product isolated with Et_2O. TLC (Et_2O-petrol, 3 : 1) afforded 8 mg **13**, colourless gum (^1H NMR data see Table 1).

Chromolaena pseudoinsignis (*voucher RMK* 8279, *deposited in the U.S. National Herbarium*). The roots (150 g) afforded 6 mg germacrene D, 5 mg bisabolene, 5 mg β-farnesene, 25 mg **15**, 3 mg **16** (Et_2O), 5 mg **17**, 1.5 mg **18**, 4 mg **19** and 3 mg of a mixture of **20** and **21** (*ca* 1:1), colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone); MS *m/z* (rel. int.): 262.157 $[M]^+$ (18) ($C_{16}H_{22}O_3$), 230 $[M-MeOH]^+$ (100), 231 $[M-OMe]^+$ (25), 215 $[230-Me]^+$ (14), 203 $[231-CO]^+$ (55), 174 $[203-CHO]^+$ (74).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589}{+80}\,\frac{578}{+82}\,\frac{546}{+95}\,\frac{436\text{ nm}}{+181}\ (CHCl_3;\ c,\ 0.22).$$

6α, *12-Dihydroxy-cadin-3-en-2-one* (**16**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3400 (OH), 1685 (C=CC=O); MS *m/z* (rel. int.): 252.173 $[M]^+$ (3) ($C_{15}H_{24}O_3$), 234 $[M-H_2O]^+$ (7), 219 $[234-Me]^+$ (4), 203 $[234-CH_2OH]^+$ (7), 175 $[203-CO]^+$ (22), 109 $[C_8H_{13}]^+$ (100). $[\alpha]_D$ +15.3 ($CHCl_3$; *c*, 0.6).

The aerial parts (120 g) gave 10 mg germacrene D, 10 mg bisabolene, 5 mg phytol, 80 mg **15**, 7 mg **16**, 3 mg **17**, 2 mg **18**, 4 mg **19** and 2 mg **22**.

Acknowledgements—We thank Drs. Scott A. Mori and P. Alvim, Herbario Centro de Pesquisas do Cacau at Itabanu, Bahia, Brazil, for their help during plant collection and the Deutsche Forschungsgemeinschaft for financial support.

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