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NEW LABDANE DERIVATIVES AND FURTHER CONSTITUENTS OF *BRICKELLIA SPECIES*[*]

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Key Word Index—*Brickellia* species; *Pleurocaronis pluriseta*; *Pseudokirsteniopsis perpetiolata*; Eupatorieae; Compositae; new labdane derivatives; new acetylenic compound; new acetophenone derivative.

Abstract—The investigation of several *Brickellia* species and two further related species afford besides known compounds four new labdane derivatives, a new acetylenic carbinol and a new dihydrobenzofuran derivative. The structures have been elucidated by spectroscopic methods. The chemotaxonomic aspects are discussed briefly.

INTRODUCTION

The large genus *Brickellia* has not been extensively investigated chemically. So far diterpenes [1], flavones [2], thymol derivatives [1] and several nerolidol derivatives [1, 3] have been isolated which may be characteristic for the genus. However the same types of compounds are present in other genera of the tribe *Eupatorieae* e.g. *Ageratina* [4], *Eupatorium* [5], *Hebeclinium* [6], *Heterocondylius* [6], *Peteravenia* [7] and *Radlkoferotomia* [8] (= *Carelia*). It therefore was of interest to investigate more species to determine whether these compounds are really characteristic or not.

RESULTS AND DISCUSSION

The roots of *Brickellia argyrolepis* contained the already known nerolidol derivatives **1** and **2**, while the aerial parts afforded a complex mixture of acids, which could not be separated completely. Only after esterification were the resulting esters isolated in pure state. The spectroscopic date showed that we were dealing with the labdane derivatives **3**, **5**, **7** and **9** (see Table 1). The ^{1}H-NMR data clearly showed that **3** and **7** were angelicates while **5** and **9** were tiglates. The configuration of the double bond in **3** and **5** followed from the chemical shift of the olefinic methyl group at C-13, while the axial orientation of the CH_2OR-group was shown by comparison of the NMR data with those of similar compounds [9]. Compounds **7** and **9** were the 13,14-dihydroderivatives. Therefore in the NMR spectra there was a doublet for the C-13-methyl and pairs of doublets for the 14-H. However, the configuration at C-13 and the absolute configurations of **3**, **5**, **7** and **9** have not been established.

The roots of *B. californica* contained the known nerolidol derivatives **11**, **12** and the dehydronerolidol **13** as shown by the NMR data together with a ketone identified as **14**. Acetylation and the observed shifts after addition of $Eu(fod)_3$ established the position of the substituents (see Table 2). The substitution pattern of **14**

Table 1. ^{1}H-NMR data of compounds **3–9**[*]

	3	**4**	**5**	**6**	**7**	**8**	**9**
7-H	*s*(*br*) 5.37	*s*(*br*) 5.38	*s*(*br*) 5.37	*s*(*br*) 5.38	*s*(*br*) 5.37	*s*(*br*) 5.37	*s*(*br*) 5.37
12-H	*ddd* 2.76	*m* 2.70	*ddd* 2.76	*m* 2.70			
12′-H	*ddd* 2.67		*ddd* 2.67				
14-H	*s*(*br*) 5.67	*s*(*br*) 5.46	*s*(*br*) 5.66	*s*(*br*) 5.63	*dd* 2.37	*dd* 2.31	*dd* 2.37
14′-H						*dd* 2.15	
16-H	*d* 1.94	*d* 1.96	*d* 1.93	*d* 1.90	*d* 1.00	*d* 0.95	*d* 1.00
17-H	(*sbr*) 1.74	*s*(*br*) 1.77	*s*(*br*) 1.74	*s*(*br*) 1.73	*s*(*br*) 1.67	*s*(*br*) 1.65	*s*(*br*) 1.67
18-H	*s* 0.98	*s* 0.98	*s* 0.97	*s* 0.98	*s* 0.99	*s* 0.98	*s* 0.99
19-H	*d* 4.39	*d* 4.40	*d* 4.40	*d* 4.37	*d* 4.40	*d* 4.39	*d* 4.36
19′-H	*d*(*br*) 4.00	*d*(*br*) 3.99	*d*(*br*) 3.99	*d*(*br*) 3.99	*d*(*br*) 4.00	*d*(*br*) 3.97	*d*(*br*) 4.00
20-H	*s* 0.77	*s* 0.77	*s* 0.76	*s* 0.77	*s* 0.79	*s* 0.77	*s* 0.78
OCOR	*qq* 6.06	*qq* 6.05	*qq* 6.84	*qq* 6.84	*qq* 6.06	*qq* 6.05	*qq* 6.84
	dq 2.00	*dq* 1.99	*d*(*br*) 1.78	*d*(*br*) 1.79	*dq* 2.00	*dq* 2.00	*d*(*br*) 1.80
	dq 1.88	*dq* 1.88	*s*(*br*) 1.82	*s*(*br*) 1.83	*dq* 1.90	*dq* 1.89	*s*(*br*) 1.84
OMe	—	*s* 3.67	—	*s* 3.67	—	*s* 3.67	—

J (Hz): 11, 12 = 11; 11′, 12 = 6; 12,12′ = 11; 14,16 = 1; 19,19′ = 11; **7–9**: 13,14 = 6; 13′,14′ = 8; 13,16 = 7; 14,14′ = 14; OCOR: 7 and 1.

[*] All spectra in $CDCl_3$ at 270 MHz, TMS as int. stand.

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[*] Part 136 in the series 'Naturally Occurring Terpene-Derivatives'; for part 135 see: Bohlmann, F. and Zdero, C. (1978) *Phytochemistry* in press.

Table 2. ^1H-NMR data of **14** and **15** ($CDCl_3$)

	14	**15**	Δ*
2-H	*dd* 5.05	*dd* 5.23	0.05
3-H	*ddd* 3.35	*ddd* 3.38	0.05
3'-H	*ddd* 3.05	*ddd* 3.08	0.06
4-H	*t* 6.81	*t* 6.90	0 20
6-H	*s* 7.07	*s* 7.18	0.36
11-H	*s*(*br*) 5.09	*s*(*br*) 5.11	0.02
11'-H	*s*(*br*) 4.93	*s*(*br*) 4.94	0.02
12-H	*s*(*br*) 1.76	*s*(*br*) 1.77	0 04
14-H	*s* 2.57	*s* 2.52	0.27
OAc	—	*s* 2.33	0.20

J(Hz): 2, 3 = 9; 2,3' = 17; 3,4 = 1.

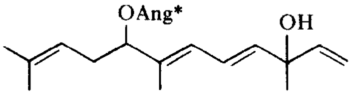
*Δ values after addition of about 0.1 equivalents of $Eu(fod)_3$

is unusual, normally in this type of compound the aceto group is at C-5.

The aerial parts of *B. coulteri* only yielded germacrene D (**16**) and no other characteristic compounds.

The roots of *B. cylindracea* again contained the nerolidol derivatives **1** and **2** together with a complex mixture of triterpenes which were not identified.

The roots of *B. laciniata* contained the nerolidol derivative **12** together with the acetylenic compound **17**. The nature of the chromophore clearly followed from the UV spectrum, while the position of the hydroxyl was shown by manganese dioxide oxidation to the corresponding ketone **18**. Furthermore the MS data were only in agreement with this assumption. However, **17** was a mixture of stereoisomers which could not be separated. **17** or similar compounds have not been isolated before



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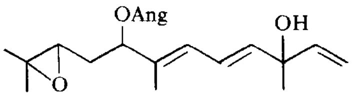

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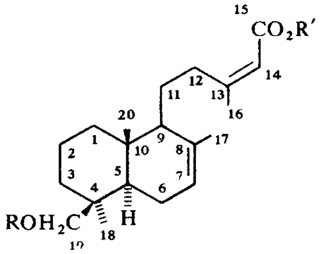
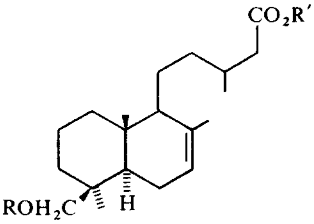
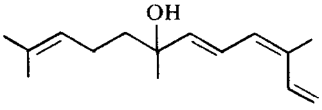


	3	**4**	**5**	**6**
R	Ang	Ang	Tigl	Tigl
R'	H	Me	H	Me



7	**8**	**9**	**10**
Ang	Ang	Tigl	Tigl
H	Me	H	Me



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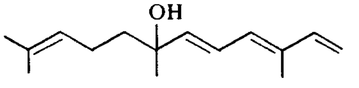

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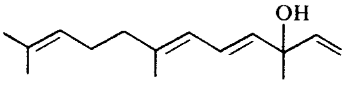

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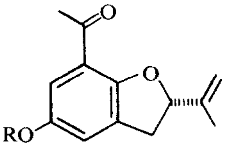
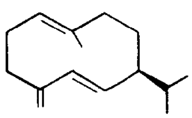


14· R = H **15**: R = Ac



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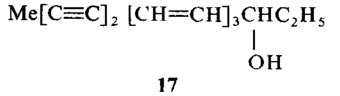
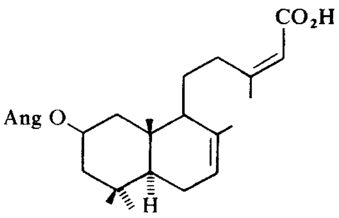


$$Me[C\equiv C]_2\,[CH{=}CH]_3\underset{\displaystyle OH}{\underset{|}{C}}HC_2H_5$$

17

$Me[C\equiv C]_2\,[CH{=}CH]_3COC_2H_5$

18



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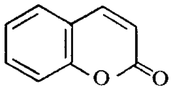

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* Ang = angeloyl, Tigl = tigloyl.

and it is the first acetylene found in *Brickellia* species.

The aerial parts of *Pleurocaronis pluriseta* contained the labdane derivative **19**. *Pleurocaronis* is closely related to *Brickellia* and it belongs, according to King et Robinson, to the *Alomiinae*. The same is true for *Pseudokirsteniopsis*. While the roots of *P. perpetiolata* did not afford any characteristic compounds, the aerial parts yielded **16**, coumarin (**20**) and no diterpenes.

In summary the nerolidol derivatives are widespread in the genus *Brickellia*, but the labdane derivatives may also be of chemotaxonomical interest.

EXPERIMENTAL

The air dried plant material was extracted with Et_2O–petrol (1 :2) and the resulting extracts were first separated by CC (Si gel, act. grade II) and then by TLC (Si gel, GF 254) using Et_2O–petrol-mixtures. Known compounds were identified by comparison of the NMR and IR spectra with those of authentic compounds.

Brickellia argyrolepis *B L. Robinson* (*voucher RMK 7230, collected in Guatemala*). 30 g roots afforded 50 mg **1** and 80 mg **2** and 180 g of aerial parts gave 50 mg **3**, 15 mg **5**, 30 mg **7** and 5 mg **9** (all Et_2O–petrol, 2 :1). The acids were esterified in Et_2O with CH_2N_2 and the resulting esters separated by TLC (Et_2O–petrol, 1 :3, several times).

Brickellia californica (*voucher 3177*). 200 g roots afforded 13 mg **14** (Et_2O–petrol, 1 :1). 30 mg **11**, 25 mg **12** and 25 mg **13** (Et_2O–petrol, 1 : 1, $AgNO_3$ Si gel TLC).

Brickellia coulteri *Gray* (*voucher RMK 20905*). 60 g aerial parts afforded 8 mg **16**.

Brickellia cylindracea (*voucher 3176*). 200 g roots yielded 320 mg **1** and 308 mg **2** together with a complex mixture of 60 mg triterpenes.

Brickellia laciniata (*voucher 3175*). 1 kg roots afford 70 mg **12** and 6 mg **17** (Et_2O–petrol, 1 : 3).

Pleurocaronis plurieta (*Gray*) *K. et R.* (*voucher 20904*). 55 g aerial parts afforded 9 mg **19**.

Pseudokirsteniopsis perpetiolata *K. et R.* (*voucher RMK 7319, collected in Guatemala*). 29 g of roots gave no characteristic compounds, while 59 g aerial parts yielded 5 mg **16** and 4 mg **20**.

19-Angeloyloxy-13,14-dehydrocativic acid (**3**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2400, (CO_2H); 1720, 1640 ($C{=}CCO_2R$). MS *m/e* (rel. int.): 402.277 (2) (calc. for $C_{26}H_{38}O_4$ 402.277), —$C_4H_7CO_2H$ 302 (36), $C_4H_7CO^+$ 83 (100). To 30 mg **3** in 2 ml Et_2O an excess of an ethereal CH_2N_2 soln was added. After 2 min the soln was evapd and the residue purified by TLC to give 30 mg **4**, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1650 ($C{=}CCO_2R$).

19-Tigloyloxy-13,14-dehydro cativic acid (**5**). Colourless oil, not free from **3**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2400, 1690 (CO_2H); 1720, 1640 ($C{=}CCO_2R$). 10 mg **5** was esterified as above. After TLC 8 mg **6** was obtained, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720, 1650 ($C{=}CCO_2R$). MS *m/e* (rel. int.): 416.291 (1) (calc. for $C_{26}H_{40}O_4$ 416.293), —$C_4H_7CO_2H$ 316 (13), 316 —$^{\cdot}CH_3$ 301 (4), 316—$^{\cdot}CH_2CH_2C(Me){=}CHCO_2Me$ 189 (69), $C_4H_7CO^+$ 83 (100)

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-22.8 \quad -23.6 \quad -26.8 \quad -50.4^\circ}\,(c = 0.5)$$

19-Angeloyloxycativic acid (**7**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2400, 1690, (CO_2H) 1720, 1645 ($C{=}CCO_2R$). After esterification **8** was obtained, colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R) 1715, 1650 ($C{=}CCO_2R$). MS *m/e* (rel. int.): 418.308 (5) (calc. for $C_{26}H_{42}O_4$ 418.308), —$C_4H_7CO_2H$ 318 (33), —$^{\cdot}CH_2O$ Ang 305 (30), 318 —$^{\cdot}CH_3$ 303 (12), 318 —$^{\cdot}CH_2CH(Me)CH_2Me$ 203 (51), 318 —$^{\cdot}CH_2CH_2CH(Me)\,CH_2CO_2Me$ 189 (92), $C_4H_7CO^+$ 83 (100).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-10 \quad -10.2 \quad -12.2 \quad -26.2^\circ}(c = 0.5)$$

19-Tigloyloxycativic acid (**9**). Colourless oil, not free from **7**, IR: 3500–2500, 1690 (CO_2H); 1720, 1645 ($C{=}CCO_2R$).

4,5-Dehydronerolidol (**13**). Colourless oil IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH); 960 (*trans* $CH{=}CH$). ^{1}H-NMR. δ Me *s*(*br*) 1.76, 1.68, 1.60, 1.40; olef. H, *t*(*br*) 5.08, *d*(*br*) 5.84 (J = 10), *dd* 6.47 (J = 10), *dd* 6.47 (J = 15, 10), *d* 5.68 (J = 15), *dd* 5.99 (J = 17, 10.5), *d*(*br*) 5.26 (J = 17), *d*(*br*) 5.07 (J = 10.5), $(CH_2)_2$ *s*(*br*) 2.09.

5-Hydroxy-7-acetyl-2α-isopropenyl-2,3-dihydrobenzofuran (**14**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: CO 1645; aromatic 1595. MS *m/e* (rel. int.): 218.094 (84) (calc. for $C_{13}H_{14}O_3$ 218.094); —$^{\cdot}CH_3$ 203 (100). 10 mg **14** was heated with 3 ml Ac_2O for 30 min at 70°. After evapn and TLC (Et_2O–petrol, 1 : 1) 8 mg **15** was obtained.

3-Hydroxy-tetradecatrien (*4,6,8*)-*diyn*-(*10, 12*) (**17**). Yellow oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: OH 3600, $C{\equiv}C$ 2150, $C{=}C$ 1640, 960. UV $\lambda_{max}^{Et_2O}$ nm: 356, 336, 321. MS *m/e* (rel. int.): 200.120 (100) (calc. for $C_{14}H_{16}O$ 200.120); —$^{\cdot}C_2H_5$ 171 (63). 3 mg **17** in 2 ml Et_2O were stirred with 50 mg MnO_2 for 1 hr. After TLC (Et_2O–petrol, 1 :10) 2 mg **18** was obtained, UV $\lambda_{max}^{Et_2O}$ nm: 360, 338, 318, 275, 263.

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