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FIVE GERMACRANOLIDES FROM *GOCHNATIA DISCOIDEA**

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Key Word Index—*Gochnatia discoidea*; *G. blanchetiana*; Compositae; Mutisieae; sesquiterpene lactones; new germacranolides.

Abstract—The investigation of two further *Gochnatia* species afforded five new germacranolides, all being 8,12-lactones. The structures were elucidated by intensive ^{1}H NMR studies and by some chemical transformations. The chemotaxonomic aspects are discussed briefly.

INTRODUCTION

So far only two species of the large genus *Gochnatia* (tribe Mutisieae, Compositae) have been investigated chemically. In addition to triterpenes [1, 2], only a guaianolide [2] was isolated. We now have studied the constituents of two further species; one only gave triterpenes, while the other contains several germacranolides, five being new. All compounds are 8,12-lactones, only one with a 1:10,4:5-*cis*-configuration of the double bonds.

RESULTS AND DISCUSSION

The roots of *Gochnatia discoidea* (Less.) Cabrera afforded squalene, lupeyl acetate, the isomeric acetates **2** and **3** as well as dammadienyl acetate, while the aerial parts in addition to squalene, lupeol, its acetate, **2**, **3** and euphol acetate contain a complex mixture of sesquiterpene lactones, which could only be separated by repeated TLC and partly only by HPLC. Finally seven lactones were isolated, all showing very uncharacteristic ^{1}H NMR spectra at RT. Two of them, however, are identical with artemisiifolin (**4**) and its acetate **5** [3]. At higher temperatures in deuterobenzene, the ^{1}H NMR data of three further lactones (see Table 1) are very similar in part to those of **5**. The spectrum of the main lactone at 120° displays signals typical for a 5-acetyl sarracinate (7.03 *q*, 1.63 *d*, 4.92 *s*(*br*) and 1.77 *s*). The presence of 8,12-lactone is indicated by the threefold broadened doublet at 3.86. Spin decoupling shows that the latter is coupled with double doublets at 2.72 and 1.85 and the fourfold doublet at 2.60. The latter is coupled with the methylene protons at C-13 as can be shown by irradiation at 2.60, which causes collapsing of the methylene double doublets to doublets and of the double doublet at 4.06 to a doublet. The latter is further coupled wih a broadened doublet at 4.79. These results only agree with the presence of the same sequence (C-5 through C-9) as in **5**. Together with the other data the only possible structure therefore is **6**. The ^{1}H NMR data of the two other lactones, again in C_6D_6 at 120°, are very similar to those of **6**. Only the ester residue at C-15 must be different. The corresponding NMR signals clearly indicate the presence of the esters **7** and **8** (see Table 1). Furthermore we have transformed **6** and **7** as well as **5** to the corresponding pyrazolines. While **6** and **7** yielded the β-adducts **11** and **12** only, **5** in addition to **10a** [3] also gave the α-adduct **10b**. Again the ^{1}H NMR data (see Table 1) established the structures. Spin decoupling allows the assignment of all signals and supports the proposed stereochemistry. In order to get clear spectra also at RT we have tried to oxidize the free hydroxyl in **6**. Oxidation with pyridinium dichromate [4, 5], however, afforded the epoxide **16**, its ^{1}H NMR spectrum being very similar to that of simsia lactone acetate [6], again supporting the proposed structure. A further lactone obviously is an isomer of **8**. While the signal of 6-H is shifted downfield, the 15-H doublets are at higher fields. Therefore the only possible structure for this lactone is **9**.

The last compound showed ^{1}H NMR signals (see Table 2) which were very different from those of **5**–**9**. The presence of a tiglate residue and of two hydroxy methylene group could easily be recognized. The signals of the methylene group being doublets, an allylic position must be assumed. Consequently manganese dioxide oxidation afforded a dialdehyde. The position of the signals of the aldehyde protons clearly indicate a *cis*, *cis*-configuration of the double bonds [7] as in the lactones isolated from *Acanthospermum hispidum* [8]. The typical upfield shift of the 8-H, however, can only be explained, if a 8,12-lactone is again present, which leads to structure **13**. The ^{1}H NMR data of the corresponding pyrazoline derivatives **15** and those of the dialdehyde **14** (see Table 2) support the proposed structure.

While the roots of *G. blanchetiana* (DC.) Cabrera gave no characteristic compounds, the aerial parts afforded again squalene, lupeol, its acetate, betulinic acid and dammarene diol together with further unidentified triterpenes, while no sequiterpene lactones could be detected.

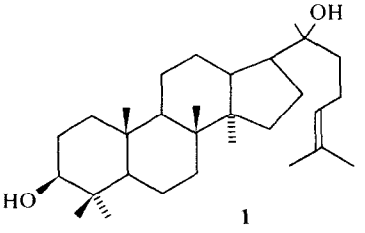
* Part 298 in the series "Naturally Occurring Terpene Derivatives"; for Part 297 see: Bohlmann, F., Grenz, M., Dhar, A. K. and Goodman, M. (1981) *Phytochemistry*, **20**, 105.

Table 1. ^{1}H NMR data of **6**–**12** and **16** (270 MHz, TMS as int. standard)

	6*	**7***	**8***	**9***	**10a**†	**10b**†	**11**	**12**	**16**‡
1-H	4.71 *dd(br)*	4.73 *dd(br)*	4.69 *dd(br)*	4.84 *dd(br)*	4.99 *dd(br)*	5.05 *dd(br)*	4.99 *dd(br)*	5.00 *d(br)*	4.83 *m*
2,3-H	2.2–2.0 *m*	2.2–2.0 *m*	2.15–2.0 *m*	2.2–1.9 *m*	2.5–1.8 *m*	2.5–1.85 *m*	2.5–1.85 *m*	2.5–1.85 *m*	2.5–2.0 *m*
5-H	4.79 *d(br)*	4.80 *d(br)*	4.77 *d(br)*	4.60 *d(br)*	4.82 *d(br)*	4.93 *d(br)*	4.83 *d(br)*	4.82 *d(br)*	2.21 *d*
6-H	4.06 *dd(br)*	4.05 *dd(br)*	4.04 *dd(br)*	5.57 *dd(br)*	4.57 *ddd(br)*	4.45 *ddd*	4.61 *ddd*	4.64 *dd(br)*	3.48 *ddd*
7-H	2.60 *dddd*	2.69 *dddd*	2.58 *dddd*	2.82 *dddd*	2.52 *dd*	3.39 *dd*	2.52 *dd*	2.52 *dd*	2.4 *m*
8-H	3.86 *ddd(br)*	3.87 *ddd(br)*	3.85 *m*	3.96 *m*	5.08 *dd(br)*	4.36 *ddd*	5.10 *ddd*	5.11 *ddd*	3.85 *ddd*
9α-H	2.72 *dd(br)*	2.73 *d(br)*	2.72 *dd(br)*	2.75 *d(br)*	3.08 *d(br)*	3.02 *d(br)*	3.08 *d(br)*	3.08 *d(br)*	2.5 *d(br)*
9β-H	1.85 *dd(br)*	1.85 *m*	1.83 *dd(br)*	1.95 *m*	2.49 *dd*	1.59 *dd*	2.50 *dd*	2.50 *dd*	1.60 *dd*
13-H	6.44 *dd*	6.44 *dd*	6.44 *dd*	6.38 *dd*	} 2.2–1.9 *m*	} 2.2–1.7 *m*	} 2.2–1.9 *m*	} 2.2–1.9 *m*	6.46 *dd*
13′-H	6.15 *dd*	6.15 *dd*	6.13 *dd*	5.79 *dd*					5.95 *dd*
14-H	1.32 *s(br)*	1.34 *s(br)*	1.31 *s(br)*	1.36 *s(br)*	1.38 *s(br)*	1.34 *s(br)*	1.38 *s(br)*	1.41 *s(br)*	1.34 *s(br)*
15-H	4.56 *s(br)*	4.55 *d(br)*	4.52 *d(br)*	3.91 *d(br)*	3.97 *d(br)*	4.02 *d(br)*	4.09 *d(br)*	4.15 *d(br)*	4.58 *d*
15′-H	4.75 *d(br)*	4.75 *d(br)*	4.75 *d(br)*	4.08 *d(br)*	4.94 *d(br)*	4.94 *d(br)*	5.03 *d(br)*	5.02 *d(br)*	4.78 *dd*§
R′CO	7.03 *q*‖	6.89 *q*‖	6.84 *t(br)*¶	6.85 *tq*¶	—	—	7.13 *q*‖	6.99 *q*‖	7.10 *q*‖
	1.63 *d*‖	1.58 *d*‖	3.96 *d(br)*¶	3.99 *dq*¶	—	—	1.94 *d*‖	1.92 *d*‖	1.56 *d*‖
	4.92 *s(br)*	4.29 *s(br)*	1.75 *d*	1.73 *dt*	—	—	4.81 AB*q*	4.33 *s(br)*	4.95 *s(br)*
OAc	1.77 *s*	—	—	—	2.03 *s*	2.05 *s*	2.03 *s*	—	1.75 *s*
16-H	—	—	—	—	4.86 *ddd*	4.82 *ddd*	4.89 *ddd*	4.88 *ddd*	—
16′-H	—	—	—	—	4.72 *ddd*	4.75 *ddd*	4.61 *ddd*	4.74 *ddd*	—

* C_6D_6, 120° sealed tube.
† $CDCl_3$ RT.
‡ C_6D_6, 80°.
§ OH 1.93 *d* (J = 2).
‖ J = 7.
¶ J = 6.

J (Hz): **6**–**9**: 1,2α = 1,2β = 7.5; 5,6 = 8; 6,7 = 9.5; 7,8 = 5.5; 7,13 = 2,7; 7,13′ = 2.5; 8,9α = 2; 8,9β = 13.5; 9α,9β = 13.5; 13,13′ = 1.5; 15,15′ = 12.5; **10**–**12**: 5,6 = 6,7 = 7,8 = 9.5; 8,9α = 1.5; 8,9β = 9.5; 9α,9β = 12.5; 13,16 = 5; 13,16′ = 9.5; 15,15′ = 11.5; 16,16′ = 18; **16**: 5,6 = 3; 6, OH = 2; 6,7 = 10; 7,8 = 4; 7,13 = 2.5; 7,13′ = 2; 8,9α = 4; 8,9β = 11.5; 9α,9β = 13.5; 13,13′ = 1.5; 15,15′ = 12.5.



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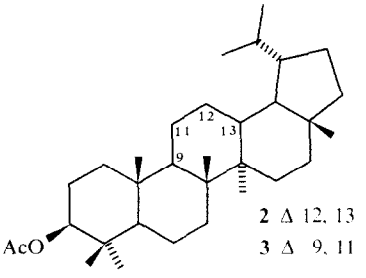
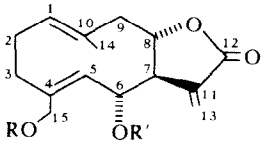
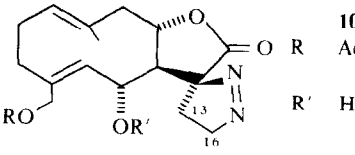


2 Δ 12, 13
3 Δ 9, 11

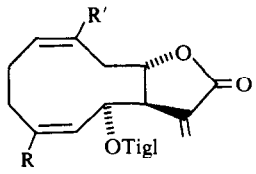


	4	**5**	**6**	**7**	**8**	**9**
R	H	Ac	CO–, OAc	CO–, OH	HO, CO–	H
R′	H	H	H	H	H	HO, CO–

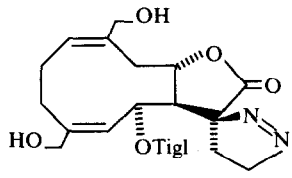


	10a	**10b***	**11**	**12**
R	Ac	Ac	CO–, OAc	CO–, OH
R′	H	H	H	H

* 11β-CH_2.



	13	14
R	CH_2OH	CHO
R′	CH_2OH	CHO



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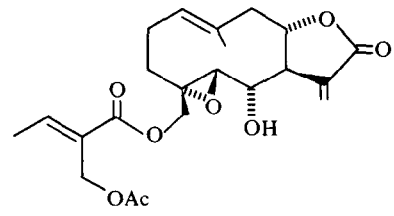

16

Table 2. ^{1}H NMR data of **13**, **14** and **15**

	13 (C_6D_6, 60°)	**14** ($CDCl_3$)	**15** ($CDCl_3$)
1-H	4.71 *dd*(*br*)	6.58 *dd*	5.13 *dd*
2-H	2.32 *m*		
2′-H	1.96 *m*		2.7–2.1 *m*
3-H	2.36 *m*		
3′-H	1.8 *m*		
5-H	4.54 *d*(*br*)	6.26 *dd*	4.89 *d*
6-H	4.89 *dd*	5.45 *dd*	6.00 *dd*
7-H	2.76 *dddd*		2.89 *dd*
8-H	5.34 *ddd*	5.1 *ddd*	5.68 *ddd*
9α-H	2.69 *d*(*br*)		2.60 *dd*
9β-H	2.23 *dd*		2.43 *dd*
13-H	6.41 *dd*	6.38 *d*(*br*)	2.7–2.1 *m*
13′-H	5.71 *d*(*br*)	5.76 *d*(*br*)	
14-H	3.69 *d*(*br*)	9.39 *s*	3.96 *d*(*br*)
14′-H	3.92 *d*(*br*)		4.27 *d*(*br*)
15-H	3.73 *d*(*br*)	9.48 *s*	4.04 *d*(*br*)
15′-H	3.98 *d*(*br*)		4.48 *d*(*br*)
RCO	6.85 *qq*	6.92 *qq*	6.63 *qq*
	1.49 *dq*	1.85 *dq*	1.83 *dq*
	1.78 *dq*	1.86 *s*(*br*)	1.80 *dq*
16-H	—	—	4.72 *ddd*
16′-H	—	—	4.57 *ddd*

J (Hz): 1,2 = 9; 1,2′ = 3.5; 5,6 = 6,7 = 7,8 = 10; 7,13 = 3; 7,13′ = 2.5; 8,9α = 2; 8,9β = 10; 9α,9β = 13.5; 14,14′ = 12.5; 15,15′ = 14; **15**: 13,16 = 5; 13,16′ = 9.5; 16,16′ = 18.

These results may be of chemotaxonomic importance. Very similar lactones were isolated from *Dicoma* species [9] belonging to the same subtribe Gochnatiinae [10]. From further genera belonging to this subtribe different sesquiterpene lactones were reported. A *Moquinia* species contains an eudesmanolide [11], *Cnicothamnus* species an eudesmanolide, a germacranolide, and a guaianolide [1], a *Wunderlichia* species a germacranolide [13], while the *Onoseris* species investigated so far [12] afforded 5-methylcoumarins and no sesquiterpene lactones, which also so far have not been isolated from the other three subtribes. Gochnatiinae is considered to be the most primitive subtribe in the Mutisieae [10]. So far this assumption is supported by the chemistry, since only the species of this subtribe show relationships to the Cynareae and the Vernonieae through the sesquiterpenes and, in the latter case, through the triterpenes.

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as int. standard; MS: 70 eV, direct inlet; optical rotation, $CHCl_3$. The air dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were first separated by column chromatography (SiO_2, act. grade II) and further by TLC (SiO_2, GF 254). **4**, **7** and **13** could be separated by HPLC (reversed phase, MeOH/H_2O 7:3) only. Known compounds were identified by comparing the IR- and ^{1}H NMR spectra with those of authentic compounds.

Gochnatia discoidea (*voucher RMK* 8125). The roots (13 g) afforded 10 mg squalene, 80 mg lupeyl acetate, 60 mg **2**, 10 mg **3**, and 50 mg dammadienyl acetate, while the aerial parts (350 g) gave 80 mg squalene, 200 g lupeol acetate, 30 mg euphol acetate, 20 mg **2**, 20 mg **3**, 60 mg lupeol, 20 mg **4**, 40 mg **5**, 50 mg **6** (Et_2O), 40 mg **7** (Et_2O), 15 mg **8** (Et_2O), 30 mg **9** (Et_2O) and 30 mg **13** (Et_2O).

Gochnatia blanchetiana (*voucher RMK* 8094). The roots (10 g) gave no characteristic compounds and the aerial parts (180 g) 200 mg squalene, 50 mg lupeol acetate, 100 mg lupeol, 30 mg betulinic acid, 10 mg dammarenediol and 1 g further unidentified triterpenes.

Artemisiifolin-15-O-*acetyl-sarracinate* (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); 1760 (γ-lactone), 1730 (CO_2R); MS: M$^+$ *m/e* 404 (0.5%) ($C_{22}H_{28}O_8$); 345.170 (1) ($C_{20}H_{25}O_5$, M − ·OAc); 246 (7) (M − RCO_2H); 228 (9) (246 − H_2O); 141 (68) ($MeCH{=}C(CH_2OH)CO^+$); 81 (100) (141 − AcOH). CD (MeCN): $\Delta\varepsilon_{251}$ − 1.46. To 10 mg **6** in 1 ml Et_2O excess of CH_2N_2 in Et_2O were added. After 15 sec the solution was evapd. TLC ($CHCl_3$/C_6H_6/MeOH 10:10) afforded 10 mg **11**, colourless gum, ^{1}H NMR see Table 1;

$$[\alpha]_{24°}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436\,\text{nm}\\ -100 & -106 & -128 & -312\end{matrix}}{} \quad (c = 0.9).$$

CD (Et_2O): $\Delta\varepsilon_{327}$ − 12.27; $\Delta\varepsilon_{217}$ + 20.3; 10 mg **6** in 2 ml CH_2Cl_2 were stirred 24 hr with 20 mg pyridinium dichromate. TLC (Et_2O) afforded 2 mg **16**, colourless gum. ^{1}H NMR see Table 1.

Artemisiifolin-15-O-*sarracinate* (**7**). Colourless gum, ^{1}H NMR see Table 1. 10 mg **7** were transformed to the pyrazoline **12** (see above), colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); 1775 (lactone); 1710, 1650 ($C{=}CO_2R$); MS: M$^+$ *m/e* 404.195 (1%) ($C_{21}H_{28}N_2O_6$); 376 (1) (M − N_2); 260 (7) (376 − RCO_2H); 242 (9) (260 − H_2O); 227 (6) (242 − Me); 99 (92) ($MeCH{=}CH(CH_2H)CO^+$); 81 (100) (99 − H_2O).

Artemisiifolin-15-O-[4-*hydroxytiglate*] (**8**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); 1735 (lactone); 1710, 1650 ($C{=}CCO_2R$); MS: M$^+$ *m/e* 362.173 (1%) ($C_{20}H_{26}O_6$); 345 (0.5) (M − OH); 246 (9) (M − RCO_2H); 228 (22) (246 − H_2O); 99 (75) ($HOCH_2CH{=}C(Me)CO^+$); 83 (100).

Artemisiifolin-6-O-[4-*hydroxytiglate*] (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); 1760 (γ-lactone); 1700, 1655 ($C{=}CCO_2R$); MS: M$^+$ *m/e* 362.173 (3%) ($C_{20}H_{26}O_6$); 246 (14) (M − RCO_2H); 228 (16) (246 − H_2O); 217 (29) (246 − ·CHO);

99 (100) ($HOCH_2CH{=}C(Me)CO^+$);

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-18 \quad -19.4 \quad -21.8 \quad -35} \quad (c = 1.0).$$

CD (MeCN): $\Delta\varepsilon_{258} - 0.36$.

14-*Hydroxy*-cis, cis-*artemisiifolin*-6-O-*tiglate* (**13**). Colourless gum, MS: M^+ *m/e* 358.142 (1%) ($C_{20}H_{22}O_6$); 258 (2) ($M - RCO_2H$); 240 (1) ($258 - H_2O$); 212 (2) ($240 - CO$); 183 ($212 - CHO$); 83 (100) ($C_4H_7CO^+$). ^{1}H NMR see Table 2. 5 mg **13** were transformed to the pyrazoline **15**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); 1770 (lactone); 1710, 1650 ($C{=}CCO_2R$); MS: M^+ *m/e* 404.195 (0.5%) ($C_{21}H_{28}N_2O_6$); 376 (0.5) ($M - N_2$); 276 (1) ($376 - RCO_2H$); 258 (3) ($276 - H_2O$); 83 (100) ($C_4H_7CO^+$).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+118 \quad +125 \quad +146 \quad +297} \quad (c = 0.2).$$

CD (Et_2O): $\Delta\varepsilon_{327} + 11.7$; $\Delta\varepsilon_{221} + 83.2$. 10 mg **13** in 1 ml Et_2O were stirred for 1 hr with 100 mg MnO_2. TLC (Et_2O–petrol 1:1) afforded 1 mg **14**, colourless gum, ^{1}H NMR see Table 1.

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