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LABDANE DERIVATIVES AND FLAVONES FROM *GUTIERREZIA DRACUNCULOIDES**

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Key Word Index—*Gutierrezia dracunculoides*; Compositae; new labdane derivatives: new flavones.

Abstract—An investigation of the aerial parts of *Gutierrezia dracunculoides* afforded, in addition to known compounds, three new labdane derivatives, all related to lambertianic acid, 17-hydroxy- and 17-acetoxylambertianic acid and 7α-hydroxylambertianic acid, two esterified and three highly oxygenated flavones, 5,7,4′-trihydroxy-3,3′-dimethoxyflavone-4′-*O*-[2-methylbutyrate] and isovalerate, 3′,5′-dihydroxy-3,5,6,7,8,4′-hexamethoxyflavone, 5,3′,5′-trihydroxy-3,6,7,8,4′-pentamethoxyflavone and 5,7,3′,5′-tetrahydroxy-3,6,8,4′-tetramethoxyflavone. The structures were elucidated by spectroscopic methods and a few chemical transformations.

INTRODUCTION

A few species of the American genus *Gutierrezia* (Compositae, tribe Astereae) have been investigated chemically and diterpenes [1, 2], triterpenes [2] and acetylenes [3] have been reported. *G. dracunculoides* (DC.) Blake contains the clerodane derivative gutierolide [1]. A re-investigation afforded three other diterpenes in high concentration as well as five new flavones.

RESULTS AND DISCUSSION

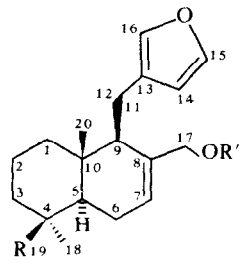
While the roots only gave shionone, the aerial parts afforded germacrene D, caryophyllene, α- and β-pinene, pinocarvol and myrtenol. The more polar fractions contained a complex mixture of diterpenic acids, fatty acids and flavones, which could only be separated with difficulty, especially as there was rapid decomposition of the diterpenic acids, which all contained a β-substituted furan ring, as deduced from the ^{1}H NMR spectrum of the crude mixture. The diterpenes could be purified only with loss of large amounts of material. The main constituent was the acid **5**; its structure followed from the ^{1}H NMR data (Table 1) and those of the acetate **6**. The axial orientation of the carboxyl group at C-4 was deduced from the typical position of the signal of the C-10 methyl,

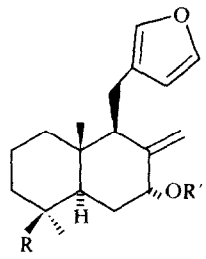
Table 1. ^{1}H NMR spectral data of compounds **1**–**6** (270 MHz, TMS as internal standard, $CDCl_3$)

	1	**2**	**3**	**4**	**5**	**6**
7-H	5.75 *d(br)*	5.78 *d(br)*	5.77 *d(br)*	5.78 *d(br)*	4.42 *dd(br)*	5.33 *dd*
12-H	2.73 *ddd*	2.57 *ddd*	2.57 *ddd*	2.73 *ddd*	2.53 *m*	2.52 *ddd*
12′-H	2.47 *m*	2.37 *m*	2.35 *m*	2.45 *m*	2.27 *m*	2.32 *m*
14-H	6.30 *s(br)*	6.27 *s(br)*	6.26 *s(br)*	6.29 *s(br)*	6.27 *s(br)*	6.27 *s(br)*
15-H	7.36 *s(br)*	6.36 *dd*	7.35 *dd*	7.35 *s(br)*	7.36 *dd*	7.36 *dd*
16-H	7.25 *s(br)*	7.22 *s(br)*	7.22 *s(br)*	7.24 *s(br)*	7.22 *s(br)*	7.18 *s(br)*
17-H	4.20 *d*	4.60 *d*	4.59 *d*	4.19 *d*	5.12 *s(br)*	5.22 *s(br)*
17′-H	4.03 *d*	4.50 *d*	4.49 *d*	4.01 *d*	4.74 *s(br)*	4.83 *s(br)*
18-H	1.24 *s*	1.23 *s*	1.22 *s*	0.87 *s*	1.14 *s*	1.13 *s*
19-H	—	—	—	3.38 *d*, 3.14 *d*	—	—
20-H	0.80 *s*	0.80 *s*	0.79 *s*	0.81 *s*	0.71 *s*	0.72 *s*
OAc	—	′2.07 *s*	2.07 *s*	—	—	2.06 *s*
OMe	—	—	3.65 *s*	—	—	3.63 *s*

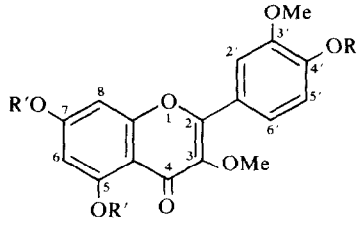
J (Hz): **1**–**3**: 6,7 = 4; 11,12 = 11; 11′,12 = 5; 12,12′ = 15; 14,15 = 15,16 ~ 1.5; 17,17′ = 12; **4**–**6**: 6,7 = 3; 11,12 = 10; 11′,12 = 5; 12,12′ = 14; 14,15 = 15,16 ~ 1.5.

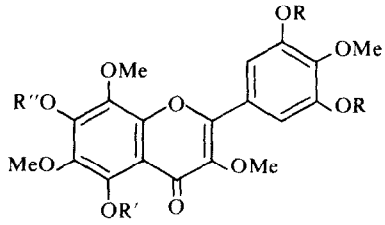
* Part 297 in the series "Naturally Occurring Terpene Derivatives". For Part 296 see Bohlmann, F., Jakupovic, J., Gupta, R. K., King, R. M. and Robinson, H. (1980) *Phytochemistry* **19**, (in press).





	1	2	3	4		5	6
R	CO_2H	CO_2H	CO_2Me	CH_2OH	R	CO_2H	CO_2Me
R′	H	Ac	Ac	H	R′	H	Ac





	7	8	9	10		11	12	13	14	15	16
R	Mebu	*i*-Val	Mebu	*i*-Val	R	H	H	H	Ac	Ac	Ac
R′	H	H	Ac	Ac	R′	Me	H	H	Me	Ac	Ac
					R″	Me	Me	H	Me	Me	Me

while the absolute configuration was assigned only from the optical rotation, which was positive for all compounds as in the case of lambertianic acid. The position of the hydroxyl group was deduced from the observed chemical shifts of 7-H and 17-H. The β-substituted furan displayed the typical ^{1}H NMR signals, while the other signals were very similar to those of related diterpenes [2]. The ^{1}H NMR data (Table 1) of two further acids clearly indicated the presence of isomeric alcohol **1** and its acetate **2**.

Together with **2**, two flavones were isolated, which could not be separated. The ^{1}H NMR data (Table 2) showed that both differed only in the ester moiety, one being a methylbutyrate and the other an isovalerate.

Table 2. ^{1}H NMR spectral data of compounds **7**–**16** (270 MHz, $CDCl_3$)

	7	8	9	10	11	12	13	14	15	16
6-H		6.24 *d*		7.32 *d*	—	—	—	—	—	—
8-H		6.34 *d*		6.83 *d*	—	—	—	—	—	—
2′-H	7.80 *d*		7.78 *d*	7.81 *d*	7.78 *d*	7.39 *s*	7.40 *s*	7.36 *s*	7.86 *s*	7.82 *s*	7.81 *s*
5′-H		7.06 *dd*		7.08 *dd*	—	—	—	—	—	—
6′-H		7.98 *dd*		8.03 *dd*	7.39 *s*	7.40 *s*	7.36 *s*	7.86 *s*	7.82 *s*	7.81 *s*
OMe		3.84 *s*		3.81 *s*	4.08 *s*	4.11 *s*	4.04 *s*	4.10 *s*	4.09 *s*	4.00 *s*
	3.91 *s*		3.90 *s*	3.92 *s*	4.03 *s*	4.03 *s*	4.00 *s*	3.98 *s*	4.00 *s*	3.92 *s*
					3.99 *s*	3.95 *s*	3.99 *s*	3.98 *s*	3.90 *s*	3.87 *s*
					3.96 *s*	3.95 *s*	3.89 *s*	3.95 *s*	3.88 *s*	3.85 *s*
					3.93 *s*	3.86 *s*	—	3.91 *s*	3.84 *s*	—
					3.82 *s*	—	—	3.90 *s*	—	—
OAc		—		2.47 *s*	—	—	—	2.39 *s*	2.49 *s*	2.50 *s*
				2.35 *s*	—	—	—	2.39 *s*	2.38 *s*	2.42 *s*
									2.38 *s*	2.38 *s*
										2.38 *s*
OH		12.57 *s*		—	6.29 *s*	12.24 *s*	12.50 *s*	—	—	—
						6.11 *s*				
OCOR	2.73 *tq**		2.52 *d**	2.72 *tq*	2.51 *d*	—	—	—	—	—
	1.90 *m*		2.34 *m*	1.88 *m*	2.34 *m*					
	1.65 *m*		1.11 *d**	1.65 *m*	1.11 *d*					
	1.08 *t**			1.08 *t*						
	1.35 *d**			1.35 *d*						

J (Hz): **7**–**10**: 6,8 = 2; 2′,5′ = 1.5; 5′,6′ = 9.
* *J* = 7.

Careful inspection of the ^{1}H NMR data and those of the corresponding diacetates led to the structures **7** and **8**. In particular, the shift differences in the spectra of **7**/**8** and **9**/**10** allowed the assignments of the three hydroxyl positions, while the position of the ester groups followed from the observed shift of 5′-H, indicating that no methoxy group was at C-4′, which would lead to an upfield shift.

In the most polar fractions three further flavones were present, and were identified as compounds **11**–**13**, all with the same substitution pattern. The position of the free hydroxyl again followed from the shift differences in the spectra of **11**–**13** and of the acetates **14**–**16**, as well as from the shifts of the UV maxima after addition of alkali or aluminium chloride. All three flavones seem to be unknown.

The isolation of **1**, **2** and **5** indicates again that labdane derivatives may be characteristic for the genus, as compounds closely related to these were isolated from *G. mandonii* and *G. lucida* [2]. However, two further species only afforded triterpenes [2]. Gutierolide was not isolated.

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as internal standard; IR: CCl_4; MS: 70 eV, direct inlet; optical rotation: $CHCl_3$. The air-dried plant material, collected in Oklahoma, was extracted with Et_2O–petrol (1:2). The resulting extracts were treated with MeOH to remove long-chain hydrocarbons and then separated first by CC (Si gel, act. grade II) and further by repeated TLC. The roots (180 g) afforded 20 mg shionone, while the aerial parts (1 kg) gave 55 mg germacrene D, 30 mg caryophyllene, 45 mg α- and β-pinene (1:1), 80 mg pinocarvol, 85 mg myrtenol, 5 g of unsaturated fatty acids, 15 mg **1** (Et_2O–petrol, 3:1), 200 mg **2** (Et_2O–petrol, 1:1) 2 g **5** (Et_2O), 30 mg **7** and **8** (Et_2O–petrol, 1:1), 300 mg **11** (Et_2O), 200 mg **12** (Et_2O) and 25 mg **13** (Et_2O).

17-Hydroxyisolambertianic acid (**1**). Colourless gum; MS *m/e* (rel. int.): 314 (M^+, 38), 299 (27) (M − $^{\cdot}$Me), 55 (100); purified as its acetate **2** (1 hr Ac_2O, 70°), colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3500–2500, 1695 (CO_2R), 1735, 1240 (OAc), 890 (furan); MS *m/e* (rel. int.): 374 (M^+, 0.2), 314.188 (19) ($C_{20}H_{26}O_3$, M − HOAc), 82 (100) (

A).

$$[\alpha]_{24°}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436\,\text{nm}\\ +11.5 & +11.9 & +13.6 & +22.4\end{matrix}}{} \quad (c = 1.0).$$

To 10 mg **2** in 2 ml Et_2O, 10 mg $LiAlH_4$ were added. After addition of dil H_2SO_4, the reaction product was separated by TLC (Et_2O) yielding 5 mg **4**, colourless gum; ^{1}H NMR spectrum see Table 1. Compound **2** on esterification with CH_2N_2 afforded **3**; ^{1}H NMR spectrum see Table 1.

7α-Hydroxylambertianic acid (**5**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 3500–2500, 1700 (CO_2H), 885 (furan); MS *m/e* (rel. int.): 332.199 (M^+, 7) ($C_{20}H_{28}O_4$), 314 (35) (M − H_2O), 82 (100) (**A**). 20 mg **5** were acetylated (Ac_2O, 1 hr 70°) and esterified with CH_2N_2 yielding 15 mg **6**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (CO_2R, OAc), 3090, 1655 (C=CH), 880 (furan); MS *m/e* (rel. int.): 388.225 (M^+, 1) ($C_{23}H_{32}O_5$), 328 (59) (M − HOAc), 269 (20) (328 − $^{\cdot}CO_2Me$), 82 (100) (**A**).

$$[\alpha]_{24°}^{\lambda} = \frac{\begin{matrix}589 & 578 & 546 & 436\,\text{nm}\\ +4.1 & +4.6 & +5.1 & +7.3\end{matrix}}{} \quad (c = 0.41).$$

5,7,4′-Trihydroxy-3,3′-dimethoxyflavone-4′-O-[2-methylisobutyrate and isovalerate (**7** *and* **8**). Yellow crystals, mp 156° (could not be separated); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1740 (CO_2R); UV λ_{max}^{MeOH} cm^{-1} nm: 340 (br), 268; +OH^- 374; MS *m/e* (rel. int.): 414.131 (M^+, 20) ($C_{22}H_{22}O_8$), 330.072 (75) ($C_{17}H_{14}O_7$, M − O=C=C(Me)Et), 57 (100) ($C_4H_9^+$). To 10 mg **7** and **8** in 1 ml CH_2Cl_2 and 0.1 ml Ac_2O, 10 mg 4-pyrrolidinopyridine [4] were added. After 20 hr the usual work-up afforded 10 mg **9** and **10**, also inseparable; MS *m/e* (rel. int.): 498.153 (M^+, 2) ($C_{26}H_{26}O_{10}$), 456 (4) (M − ketene), 372 (22) (456 − O=C-=C(Me)Et), 330 (17) (372 − ketene), 95 (100). 10 mg **7** and **8** on saponification (MeOH, KOH, 70°) afforded 2-methylbutyric acid and isovaleric acid (identified as its methyl esters by ^{1}H NMR and GC–MS).

3′,5′-Dihydroxy-3,5,6,7,8,4′-hexamethoxyflavone (**11**). Yellow crystals, mp 224°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3520 (OH) 1640, 1600 (flavone); UV λ_{max}^{MeOH} nm: 331, 258; +OAc^- 331; +$AlCl_3$ 331; MS *m/e* (rel. int.): 434.121 (M^+, 65) ($C_{21}H_{22}O_{10}$), 419 (100) (M − Me), 389 (7) (419 − CH_2O). 20 mg **11** were acetylated as above with Ac_2O–4-pyrrolidonopyridine. Usual work-up afforded 15 mg **14**; ^{1}H NMR spectrum see Table 2.

5,3′,5′-Trihydroxy-3,6,7,8,4′-pentamethoxyflavone (**12**). Yellow crystals, mp 189°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (OH), 1600 (flavone); UV λ_{max}^{MeOH} nm: 336, 270; +$AlCl_3$ 360; +OAc^- 334; MS *m/e* (rel. int.): 420.106 (M^+, 88) ($C_{20}H_{20}O_{10}$), 405 (100) (M − $^{\cdot}$Me). Acetylation (see above) afforded **15**; ^{1}H NMR spectrum see Table 2.

5,7,3′,5′-Tetrahydroxy-3,6,8,4′-tetramethoxyflavone (**13**). Yellow, amorphous powder, which could not be crystallized; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (OH), 1600 (flavone); UV λ_{max}^{MeOH} nm: 336 +OH^- 390; +$AlCl_3$ 360; MS *m/e* (rel. int.): 406.080 (M^+, 100) ($C_{19}H_{18}O_{10}$), 391 (95) (M–Me). Acetylation as above afforded **16**; ^{1}H NMR spectrum see Table 2.

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