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GUTIERREZIAL AND FURTHER DITERPENES FROM *GUTIERREZIA SAROTHRAE*

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Key Word Index—*Gutierrezia sarothrae*; Compositae; diterpenes; *ent*-labdane derivatives; new diterpene skeleton.

Abstract—The aerial parts of *Gutierrezia sarothrae* afforded in addition to polyalthic acid, daniellic acid and nivenolide, 14 new diterpenes, most of them closely related to polyalthic acid. One of these compounds has a new carbon skeleton. The structures were elucidated by spectroscopic methods and by some chemical transformations.

INTRODUCTION

Gutierrezia (Compositae, tribe Astereae) is a genus with about 20 species present only in North and South America [1, 2]. So far six species have been studied chemically. In addition to widespread compounds [3, 4], acetylenes [5] and labdane derivatives were isolated [4, 6, 7]. From the roots of *G. sarothrae* (Pursh.) Britt. et Rusby only baccharis oxide was isolated [7], while the essential oil of the aerial parts gave common mono- and sesquiterpenes [8]. We now have studied the aerial parts of *G. sarothrae* in more detail. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *G. sarothrae* afforded in addition to germacrene D, 1,10-epoxycaryophyllene and the C_{17}-acetylenic compound **22** [9], several diterpenes including the known compounds polyalthic acid (**1**) [10], daniellic acid (**2**) [11] and nivenolide (**16**) [12]. The structure of **1** was established by comparing the physical data with those reported in the literature and by rigorous ^{1}H NMR spectroscopy including NOE difference spectra. The latter allowed the assignment of the complete stereochemistry, while the absolute configuration followed from the optical rotation which agreed with that of polyalthic acid with known configuration [10]. The ^{1}H NMR data of **2** were close to those of **1**. However, the stereochemistry at C-4 clearly followed from the chemical shift of H-5. The latter is deshielded if the carboxy group is equatorial. Again the optical rotation indicated that an ent-labdane was present. The data of **16** also agreed with those reported in the literature [12] and the structure was further established by spin decoupling of the ^{1}H NMR spectrum.

The main constituent of this species was a hydroxy acid which was purified as its methyl ester. The spectral data indicated that **3a**, the methyl ester of 3α-hydroxy polyalthic acid was present (Table 1). The stereochemistry at C-3 followed from the couplings observed, while the equatorial carbomethoxy group led to the expected down field shift of the H-5 signal. Spin decoupling allowed the assignment of nearly all signals, though a few were overlapped multiplets. Furthermore, the structure was supported by the ^{13}C NMR spectrum (see Experimental), where the signals were assigned by selective hetero-decoupling.

The ^{1}H NMR spectral data of the methyl esters of **4**–**6** (Table 1) indicated the presence of esters of **3a**. The nature of the ester group at C-3 followed from the typical signals in the ^{1}H NMR spectra. The structures were further supported by the ^{13}C NMR spectrum of **5a** which agreed well with the proposed formula. The ^{1}H NMR spectrum of **7a** was close to that of **3a** (Table 2). However, the changed stereochemistry at C-4 led to an expected difference in the chemical shift of the H-5 signals, indicating that the compound was 3α-hydroxydaniellic acid.

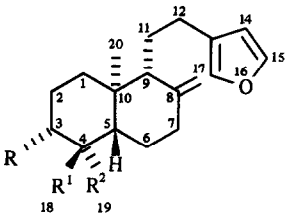
In the ^{1}H NMR spectrum of **8** (Table 2) the presence of a labdane with hydroxy groups at C-18 and 19 followed from the corresponding pairs of doublets around δ 4. Spin decoupling indicated the presence of W-couplings between H-3α and 19 and between H-18 and H-19′ which allowed a clear assignment of the signals.

The structure of the diol **9** followed from the ^{1}H NMR spectrum (Table 2) and was established by reduction of **3a** with lithium aluminium hydride which afforded a diol identical with the natural compound. Reduction of **7a** gave **10**, the ^{1}H NMR of which typically differing from that of **9**.

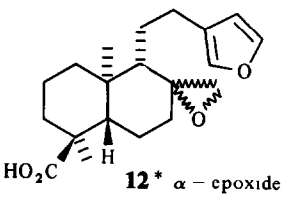
The structure of **11**, which was purified as its methyl ester **11a**, again could be easily deduced from the spectral data (Table 3). The relative position of the oxygen functions at C-4 followed from the chemical shift of H-5 and also from the presence of a W-coupling between H-3α and H-19.

The methyl esters of **12** and **13** differed in the ^{1}H NMR spectra (Table 2) by the presence of a W-coupling of H-17 in the spectrum of **13a**. Inspection of models showed that this required a 8β,17-epoxide. The remaining signals of **12a** and **13a** were close to those of **3a** though the H-7 signals were as expected, at higher fields. No pronounced differences were visible in the MS of **12a** and **13a**, only the relative intensities of the fragments differed slightly.

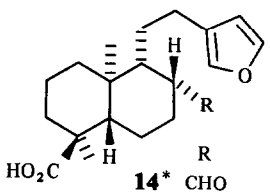
The structure of the aldehyde **14a** followed from its molecular formula ($C_{21}H_{20}O_4$), the characteristic signals in the ^{1}H NMR spectrum (Table 2), and from the product of



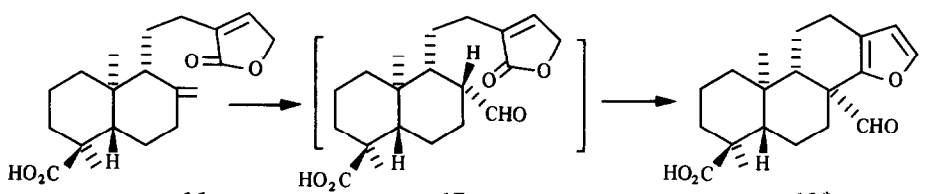
	1*	2*	3*	4*	5*	6*	7*	8	9	10	11*
R	H	H	OH	OAng	OMebu	OiBu	OH	H	OH	OH	H
R^1	CO_2H	Me	CO_2H	CO_2H	CO_2H	CO_2H	Me	CH_2OH	CH_2OH	Me	CO_2H
R^2	Me	CO_2H	Me	Me	Me	Me	CO_2H	CH_2OH	Me	CH_2OH	CH_2OH



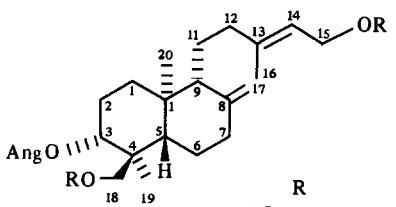
12* α – epoxide
13* β – epoxide



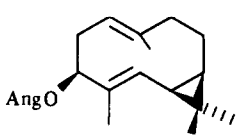
14* CHO
15* CH_2OH



16 **17** **18***



19 R = H
20 R = Ac



21

$H_2C{=}CH\ CH(OH)\ [C{\equiv}C]_2\ CH(OAc)\ CH{=}CH(CH_2)_5CH{=}CH_2$ **22**

* **1a** – **7a**, **11a** – **15a** and **18a** are the corrosponding methyl esters

boranate reduction, the alcohol **15a**. The stereochemistry at C-4 could be deduced by comparing the ^{1}H NMR spectrum with that of **3a**, while the configuration at C-8 followed from the chemical shift of H-7α and the couplings of H-8 which required an equatorial proton at C-8. The very small coupling $J_{8,17}$ indicated a restricted rotation of the 8,17-bond. The ^{1}H NMR data of the corresponding alcohol **15a** further supported the structure.

The methyl ester of **18** showed no molecular ion in the MS. The highest fragment obviously was formed by loss of formyl radical leading to *m/z* 315 ($C_{20}H_{27}O_3$). However, by chemical ionization a clear M + 1 peak could be observed [*m/z* 345 (100%)]. The ^{1}H NMR spectrum of **18a** (Table 2) clearly indicated the presence of a diterpene with only two furan protons (δ 7.25 *br s* and 6.22 *d*). These shifts showed that one of the α-furane protons were missing. Spin decoupling allowed the clear assignment of

Table 1. ^{1}H NMR spectral data of **3a–6a** and **18a** (400 MHz, $CDCl_3$, TMS as internal standard)

	3a	3a* C_6D_6	4a	5a	6a	6a ($CDCl_3$–C_6D_6)	18a†
H-1α		1.43 *m*‡	1.8 *m*‡	1.81 *ddd*	1.80 *ddd*	1.65 *ddd*	1.75 *m*
H-1β	1.21 *ddd*	0.97 *ddd*	1.31 *ddd*	1.32 *ddd*	1.31 *ddd*	1.19 *m*‡	1.06 *m*
H-3β	4.00 *dd*	4.02 *dd*	5.22 *dd*	5.14 *dd*	5.17 *dd*	5.18 *dd*	
H-5	1 79 *dd*	1.90 *dd*	1.9 *m*‡	1.91 *dd*	1.92 *dd*	1.90 *dd*	1.83 *dd*
H-6α	1.52 *dddd*	1.32 *dddd*	1.55 *dddd*	1.55 *dddd*	1.53 *dddd*	1.48 *dddd*	1.59 *m*
H-6β	1.19 *dddd*	1.52 *dddd*	1.15 *dddd*	1.15 *dddd*	1.16 *dddd*	1.16 *dddd*	1.17 *dddd*
H7α	2.36 *ddd*	2.31 *ddd*	2.36 *ddd*	2.36 *ddd*	2.36 *ddd*	2.30 *ddd*	2.89 *dddd*
H7β	1.99 *br ddd*	1.99 *br dddd*	2.01 *br ddd*	1.99 *br ddd*	2.00 *br ddd*	1.95 *br ddd*	1.35 *dddd*
H-11α							2.05 *m*
H-12	2.55 *br ddd*	2.55 *br ddd*	2.55 *br ddd*	2.55 *br ddd*	2.55 *br ddd*	2.49 *br ddd*	2.68 *ddd*
H-12′	2.24 *br ddd*	2.18 *br ddd*	2.27 *ddd*	2.24 *ddd*	2.25 *ddd*	2 18 *ddd*	2.52 *ddd*
H-14	6.25 *dd*	6.16 *dd*	6.25 *dd*	6.25 *dd*	6.25 *dd*	6.16 *dd*	6.22 *d*
H-15	7.35 *t*	7.21 *t*	7.36 *t*	7.36 *t*	7.36 *t*	7.25 *br s*	7.25 *br s*
H-16	7.18 *br s*	7.13 *br s*	7.19 *br s*	7.19 *br s*	7.19 *br s*	7.11 *br s*	
H-17	4.88 *br s*	4.90 *br s*	4 89 *br s*	4.89 *br s*	4.89 *br s*	4.85 *br s*	9.76 *d*
H-17′	4.59 *br s*	4.62 *br s*	4.60 *br s*	4.60 *br s*	4.60 *br s*	4.57 *br s*	
H-18	—	—	—	—	—	—	—
H-19	1.11 *s*	1.25 *s*	1.20 *s*	1.18 *s*	1.18 *s*	1.19 *s*	1.14 *s*
H-20	0.70 *s*	0.62 *s*	0.72 *s*	0.72 *s*	0.73 *s*	0.65 *s*	0.82 *s*
OMe	3.71 *s*	3.42 *s*	3.64 *s*	3.63 *s*	3.64 *s*	3.52 *s*	3.64 *s*
OCOR	—	—	6.00 *qq*	2.31 *tq*	2.46 *qq*	2.39 *qq*	
			1.92 *dq*	1.41 *m*	1.09 *d*	1.06 *d*	
			1.82 *dq*	1.02 *d*	1.09 *d*		
				0.83 *t*			

*H-2, 1.52–1.35 *m*; H-11, 1.57 *m*.

†H-9, 1.75 *m*.

‡Overlapped.

J (Hz): 1α, 1β = 1β, 2α = 14; 1α, 2α = 1α, 2β = 1β, 2β = 2β, 3 ~ 4; 2α, 3 = 11; 4, 6α = 12; 5, 6β = 2.5; 6α, 7α = 4; 6α, 6β = 6α, 7β = 12; 6β, 7α = 6β, 7β = 5; 7α, 7β = 13; 7α, 17 = 7β, 17 ~ 1; 11, 12 = 5; 11, 12′ = 8; 11′, 12 = 11′, 12′ = 7; 12, 12′ = 14; 12, 16 ~ 1; 14, 15 = 15, 16 ~ 1; compound **18a**: 1α, 1β = 1β, 2α = 10; 1β, 2β = 5; 5, 6α = 12.5; 6α, 6β = 13.5; 6α, 7α = 3; 6β, 7α = 3; 6β, 7β = 4; 6α, 7β = 13; 7β, 17 = 1.5; 11α, 12α = 6; 11α, 12β = 1.5; 11β, 12α = 10; 11β, 12α = 6.5; 12, 12′ = 17; 14, 15 = 2; OAng: 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1; OMebu: 2′, 3′ = 2′, 3′ = 3′, 4 = 7; OiBu: 2′, 3′ = 2′, 4′ = 7.

nearly all signals, only those of H-2, H-3 and H-11 were overlapping multiplets. The partial similarity of the spectrum with that of **1a** showed that the stereochemistry at C-1 to C-10 was identical in both compounds. A clear W-coupling of H-17 with H-7β showed that the doublet at δ 9.76 was due to the aldehyde proton at C-17. The axial orientation could be deduced from this coupling, while spin decoupling allowed the assignment of the remaining signals. The couplings of H-12 further showed that these protons were those of a cyclohexane ring. The down field shift of the H-7α signal indicated the α-orientation of the aldedhye group at C-8. The strong fragment *m/z* 315 [M −CHO] also supported the position of the aldehyde group. Most likely **18** was formed from **3** by transformation via **16** to give rise to the aldehyde **17**, probably via an 8,17-epoxide. Finally aldol condensation of **17** would give the aldehyde **18**, which we name gutierrezial. Compounds with an isomeric carbon skeleton and a C-18 to C-14 ring junction of the furan ring have been reported from sponges [13].

The structures of the angelate **19** easily could be deduced from the ^{1}H NMR spectrum and from that of the corresponding diacetate **20**, which was obtained by acetylation (Table 3). The relative position of the methylol group followed from the absence of a W-coupling between H-3β and the methylol doublets and from the chemical shifts of H-18. The stereochemistry of the Δ^{13} double bond was deduced from the chemical shift difference in the spectra of **19** and **20** and by comparison with similar labdanes.

As the absolute configuration of **1** and **2** was clear most likely all the diterpenes were *ent*-labdanes. The roots afforded baccharisoxide [14] **1**, **3** and the angelate **21** [15], which so far only was isolated from the tribe Senecioneae.

The results show again that labdane derivatives are common in *Gutierrezia* species while baccharisoxide is widespread in the genus *Baccharis*. The C_{17}-acetylene **22** so far only was isolated from species which also belong to the tribe Astereae. Further detailed investigations may show whether chemistry is able to show clear limits of *Gutierrezia*.

EXPERIMENTAL

Air dried aerial parts (650 g) (voucher RMK 9079, collected in Colorado) were extracted with Et_2O–petrol–MeOH, 1:1:1. The extract obtained was worked-up in the usual fashion [16]. The CC fractions were combined following the ^{1}H NMR spectra of the crude fractions I (petrol and Et_2O–petrol, 1:10), II (Et_2O–petrol, 1·3, 1:1 and 3.1) and III (Et_2O and Et_2O–MeOH, 10:1).

Re-CC of fraction I gave with petrol 50 mg germacrene D, with

Table 2. ^{1}H NMR spectral data of **7a**, **8–10**, and **11a–15a** (400 MHz, $CDCl_3$, TMS as internal standard)

	7a	**8**	**9**	**10**	**11a**	**12a**	**13a**	**14a***	**15a†**
H-1β	1.13 *ddd*	0.98 *ddd*	1.11 *ddd*	1.10 *ddd*	1.12 *ddd*	0.95 *ddd*	1.04 *dd*		1.3–1.7 *m*
H-3	3.10 *ddd*	0.99 *ddd*; 2.04 *br ddd*	3.64 *dd*	3.45 *dd*					
H-5	1.21 *dd*	1.27 *dd*	1.21 *dd*	1.16 *dd*	1.94 *dd*	1.86 *dd*	2.06 *dd*	1.74 *dd*	1.72 *m*
H-6α	2.03 *dddd*	1.37 *dddd*	1.41 *dddd*	1.27 *dddd*	1.51 *dddd*	1.75 *dddd*	1.97 *dddd*	1.47 *dddd*	1.3–1.7 *m*
H-6β		1.78 *br d*	1.54 *dddd*	1.80 *m*	1.81 *br d*	1.16 *dddd*			
H-7α	2.41 *ddd*	2.38 *ddd*	2.31 *ddd*	2.41 *ddd*	2.34 *ddd*	1.30 *ddd*	1.41 *ddd*	2.29 *ddd*	
H-7β	1.98 *m*	1.94 *br ddd*	1.97 *br ddd*	1.94 *br ddd*	1.94 *m*	1.97 *br ddd*	1.82 *br ddd*	1.36 *dddd*	
H-12	2.55 *br ddd*	2.54 *br ddd*	2.54 *br ddd*	2.54 *br ddd*	2.54 *br ddd*	2.36 *m*	2.51 *br ddd*	2.68 *br ddd*	2.54 *br ddd*
H-12′	2.23 *br ddd*	2.23 *br ddd*	2.22 *br ddd*	2.22 *br ddd*	2.24 *br ddd*	2.30 *m*	2.35 *br ddd*	2.45 *br ddd*	2.33 *br ddd*
H-14	6.25 *dd*	6.25 *dd*	6.24 *dd*	6.24 *dd*	6.25 *dd*	6.24 *br s*	6.25 *dd*	6.28 *dd*	6.27 *dd*
H-15	7.34 *t*	7.35 *t*	7 34 *t*	7 34 *t*	7.35 *t*	7.34 *t*	7.30 *t*	7.38 *t*	7.36 *t*
H-16	7.18 *br t*	7.19 *br t*	7.18 *br t*	7.18 *br t*	7.19 *br t*	7.20 *br s*	7 20 *br s*	7.24 *br t*	7.22 *br s*
H-17	4 90 *br s*	4.85 *br s*	4.87 *br s*	4.87 *br s*	4.86 *br s*	2.59 *d*	2.75 *dd*	10.0 *br s*	3.70 *br d*
H-17′	4.38 *br s*	4.57 *br s*	4.57 *br s*	4.57 *br s*	4.58 *br s*	2 35 *d*	2.53 *d*		3.58 *dd*
H-18	1.38 *s*	3.88 *d*	3.66 *d*	1 22 *s*	—	—	—	—	—
H-18′		3.39 *br d*	3.38 *d*		—	—	—	—	—
H-19	—	3.92 *d*	0.83 *s*	4.18 *d*	3.89 *br d*	1.19 *s*	1.20 *s*	1.12 *br s*	1.14 *s*
H-19′	—	3 70 *br d*		3.30 *br d*	3.74 *d*				
H-20	0.51 *s*	0.63 *s*	0.71 *s*	0.62 *s*	0.67 *s*	0.90 *s*		0.77 *s*	0.73 *s*
OMe	3.64 *s*	—	—	—	—	3.67 *s*	3.64 *s*	3.65 *s*	3.65 *s*
OH	3 26 *s*			2 76 *br s*; 2.45 *br s*					

*H-8, 2 54 *br t*; H-11, 1.64 *ddd*

†H-8, 1.95 *m*

J (Hz). 1α, 1β = 1β, 2α = 14; 5, 6α = 12; 5, 6β = 2.5; 6α, 7α ~ 4; 6α, 6β = 6α, 7β ~ 12; 6β, 7α ~ 1; 6β, 7β ~ 5; 7α, 7β ~ 13; 7α, 17 = 7β, 17 ~ 1; 11, 12 = 5; 11, 12′ = 8; 11′, 12 = 11′, 12′ ~ 7; 12, 12′ = 14; 12, 16 ~ 1, 14, 15 = 15, 16 ~ 1, compound **7a**: 2α, 3β = 10; 2β, 3β = 4; 3β, OH = 12; compound **8**: 2α, 3α = 2β, 3α = 2β, 3β = 4; 2α, 3β = 12; 3α, 3β = 14; 3α, 19 = 18, 19′ ~ 0.5; 18, 18′ = 19, 19′ = 11; compound **9**: 2α, 3 = 11.5; 2β, 3 = 5; 18, 18′ = 11; compound **10**: 19, 19′ = 11; compound **11a**: 3α, 19 = 0.5; 19, 19′ = 12; compound **12a**: 17, 17′ = 4; compound **13a**: 7β, 17 = 2; 17, 17′ = 4; compound **15a**: 8, 17 ~ 2; 8, 17′ = 17, 17′ = 10.

Table 3. ^{1}H NMR spectral data of **19** and **20** (400 MHz, $CDCl_3$, TMS as internal standard)

	19	**20**
H-3	5.00 *br dd*	4.91 *br dd*
H-7	2.39 *br d*	2 39 *br d*; 2 18 *br ddd*
H-12	2.16 *m*	2 0–1.8 *m*
H-14	5.39 *br t*	5.32 *br t*
H-15	4.14 *br d*	4.57 *br d*
H-16	1.68 *br s*	1 71 *br s*
H-17	4 85 *br s*	4.86 *br s*
H-17′	4.53 *br s*	4.53 *br s*
H-18	3 35 *br d*	3.88 *br d*
H-18′	2 97 *d*	3 72 *d*
H-19	0 75 *s*	0.84 *s*
H-20	0 68 *s*	0 76 *s*
OAng	6.01 *qq*	6 03 *qq*
	1 98 *dq*	1.96 *dq*
	1 89 *dq*	1.86 *dq*
OAc	—	2.07, 2.06 *s*

J (Hz): 2α, 3 = 12, 2β, 3 = 4.5, 3, 19 ~ 0 5, 7α, 7β = 13, 14, 15 = 7; 18, 18′ = 12; 3′, 4′ = 7, 3′, 5′ = 4′, 5′ = 1

Et_2O–petrol, 1 . 10, 2 mg caryophyllene 1,10-epoxide, 200 mg **1** and a mixture of **1** and **2**. After addition of CH_2N_2, TLC ($AgNO_3$ coated SiO_2, Et_2O–petrol, 1 : 20, detection with $KMnO_4$ spraying) gave 50 mg **2a** (R_f 0.45) and 20 mg **1a** (R_f 0.35). With Et_2O–petrol, 1 : 3, 1.5 g **1** were obtained. To the next CC fraction (Et_2O–petrol, 1 : 1) CH_2N_2 was added. TLC (Et_2O-petrol, 1 : 3) gave two zones. TLC (Et_2O–petrol, 1 : 10) of the first zone gave 30 mg **1a**, a mixture of **4a** and **5a** (R_f 0.60) and 150 mg **5a** (R_f 0.50), 15 mg of **5a** were purified by HPLC (MeOH–H_2O, 17 · 3, R_t 7.5 min, always RP 8, flow rate 330 *ca* 100 bar). The mixture of **4a** and **5a** afforded by TLC (Et_2O–petrol, 1 : 10) 20 mg **5a** and 2 mg **4a** (R_f 0.52). TLC (Et_2O–petrol, 1 · 10) of the polar TLC zone gave 30 mg **5a** and 6 mg of a mixture of **5a** and **6a** (*ca* 1 : 1). HPLC (RP 8, MEOH–H_2O, 17 : 3) gave 3 mg **6a** (R_t 5.8 min.). The next zone gave by TLC (Et_2O–petrol, 1 : 3) 8 mg crystalline **18a** (R_f 0.50). TLC (C_6H_6–$CHCl_3$, 3 · 1) of the mother liquor of **18a** gave 2 mg **13a** (R_f 0 44) and crude **14a** (R_f 0 40) which was purified by HPLC (RP 8, MeOH–H_2O, 4 : 1) affording 5 mg **14a** (R_t 4.8 min). The ^{1}H NMR spectrum of the next TLC zone showed the presence of **22**, **14a** and a further epoxide (*ca* 1 1 . 1) After addition of $NaBH_4$ **14a** was transformed to **15a** and was separated by TLC (Et_2O–petrol, 1 : 1). The less polar zone (R_f 0.68) still contained a mixture of **22** and the epoxide. After stirring with MnO_2 **22** was transformed to the corresponding ketone and TLC (Et_2O–petrol, 1 · 3) afforded 2 6 mg **12a** (R_f 0.45).

The second combined part of the CC (II) was esterified by

addition of CH_2N_2 affording 3.8 g of an ester mixture which was separated by medium pressure chromatography (130 g SiO_2 ϕ 30–60 μm with raising amounts of Et_2O, 25 ml fractions). Fractions 27–35 gave 200 mg **1a**, 39–41 a mixture of 20 mg **5a** and **4a** (*ca* 20:1), 42–44 30 mg **5a**, 45–47 a mixture of 10 mg **5a** and **6a** (*ca* 10:1), 48–53 a mixture of 10 mg **5a**, **6a**, **14a** and **18a** (*ca* 2:2.1:3), 60–62 60 mg **7a** (purified by TLC, Et_2O–petrol, 1:1, R_f 0.68), 66–68 100 mg **11a** (purified by TLC, Et_2O–petrol, 1:1, R_f 0.55), 78–80 1.5 g crude **3a** and 84–86 a mixture, which by TLC ($CHCl_3$–C_6H_6–Et_2O, 2:2:1) afforded 2 mg **16** (R_f 0.50) and 6 mg **19** (R_f 0.32) (fractions not mentioned did not contain definite compounds).

The last part (III) of the CC was combined with fractions 78–80, esterified and separated also by medium pressure CC (180 g SiO_2, 25 ml fractions). With Et_2O–petrol, 1:1, nothing of interest was obtained (fractions 1–11). Fractions 12–17 (Et_2O) gave 80 mg **11**, 18–23 nothing definite, 24–31 4 g **3a**, 32–34 (Et_2O) gave a mixture, which was separated further by TLC (Et_2O–petrol, 3:1). The least polar zone gave by TLC ($CHCl_3$–C_6H_6–Et_2O, 1:1:1, three developments) 10 mg **8a** (R_f 0.40). The more polar zone gave by HPLC (RP 8, MeOH–H_2O, 3·1) 10 mg **9** (R_t 8.5 min).

The extract of 220 g roots gave by CC and TLC (s.a.) 80 mg baccharis oxide [identified by comparing with authentic material, TLC (Et_2O–petrol, 1 20, R_f 0.68), ^1H NMR spectrum identical], 150 mg **1** and 80 mg **3**. Compounds **4a**–**7a**, **9** and **11a**–**14a** were oils. They showed no impurities in their 400 MHz ^1H NMR spectra and were homogeneous by TLC and HPLC (reversed phase).

3α-Hydroxypolyalthic acid (**3**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600–2700, 1700 (OH, CO_2H); ^1H NMR ($CDCl_3$): δ 4.02 *dd* (H-3), 2.37 *br d* (H-7α), 2.02 *ddd* (H-2β), 2.55 *br ddd* and 2.24 *br ddd* (H-12), 6.25 *br s* (H-14), 7.34 *t* (H-15), 7.19 *br s* (H-16), 4.89 and 4.60 *br s* (H-17), 1.19 *s* (H-19), 0.70 *s* (H-20) Methyl ester (**3a**) colourless crystals, mp 65° (Et_2O–petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}. 3600 (OH), 1720 (CO_2R), 3080, 1640, 900 (C=CH_2), 880 (furane); MS *m/z* (rel. int.): 346.214 $[M]^+$ (41) (calc. for $C_{21}H_{30}O_4$: 346.214), 328 $[M-H_2O]^+$ (10), 313 $[328-Me]^+$ (4), 287 $[M-CO_2Me]^+$ (6), 269 $[287-H_2O]^+$ (10), 187 $[269-C_5H_6O]^+$ (35), 81 $[C_5H_5O$, pyrrylium ion$]^+$ (100); ^{13}C NMR ($CDCl_3$) (C-1 to C-20). δ 36.6, 37.1, 75.5, 53.9, 50.3, 26.3, 37.6, 147.1, 55.5, 38.6, 24.2, 23.3, 125.3, 110.9, 142.7, 138.7, 107.3, 177.9, 10.6, 14.9, 52.1 (OMe) (multiplicity determined by DEPT spectroscopy, assignment by selective spin decoupling).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-33 \quad -33 \quad -36 \quad -59} \ (CHCl_3;\ c\ 0.48)$$

Methyl-3α-angeloyloxypolyalthoate (**4a**) Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730 (CO_2R, C=CCO_2R), 905 (C=CH_2), 880 (furane), MS *m/z* (rel. int.) 428.256 $[M]^+$ (14) (calc. for $C_{26}H_{36}O_5$: 428.256), 328 $[M-RCO_2H]^+$ (11), 269 $[328-CO_2Me]^+$ (7), 187 $[269-C_5H_8O]^+$ (24), 83 $[C_4H_7CO]^+$ (91), 81 $[C_5H_5O]^+$ (60), 55 $[83-CO]^+$ (100).

Methyl-3α-[2-methylbutyryloxy]-polyalthoate (**5a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO_2R), 3080, 1640, 900 (C=CH_2), 880 (furane); MS *m/z* (rel. int.) 430.272 $[M]^+$ (11) (calc. for $C_{26}H_{38}O_5$. 430.272), 328 $[M-RCO_2H]^+$ (22), 269 $[328-CO_2Me]^+$ (9), 187 $[269-C_5H_6O]^+$ (28), 85 $[C_4H_9CO]^+$ (37), 81 $[C_5H_5O]^+$ (51), 57 $[85-CO]^+$ (100); ^{13}C NMR ($CDCl_3$) (C-1 to C-20): δ 36.3, 26.7, 76.9, 52.2, 50.4, 26.1, 37.5, 146.9, 55.5, 38.6, 24.3, 23.3, 125.2, 110.8, 142.8, 138.7, 107.4, 176.5, 11.3, 14.9, OMe 52.1; OCOR: 175.5, 41.3, 23.7, 16.4, 11.8.

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-39 \quad -40 \quad -46 \quad -76} \ (CHCl_3,\ c\ 5.11).$$

Methyl-3α-isobutyryloxypolyalthoate (**6a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}. 1735 (CO_2R), 3080, 1640, 900 (C=CH_2), 880 (furane); MS *m/z* (rel. int.): 416.256 $[M]^+$ (42) (calc. for $C_{25}H_{36}O_5$: 416.256), 401 $[M-Me]^+$ (3), 328 $[M-RCO_2H]^+$ (24), 269 $[328-CO_2Me]^+$ (12), 187 $[269-C_5H_6O]^+$ (38), 81 $[C_5H_5O]^+$ (100), 71 $[C_3H_7CO]^+$ (69).

Methyl-3α-hydroxydaniellate (**7a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560, 1715 (OH, CO_2R hydrogen bonded), 3080, 1650, 905 (C=CH_2), 880 (furane); MS *m/z* (rel. int.): 346.214 $[M]^+$ (21) (calc. for $C_{21}H_{30}O_4$: 346.214), 328 $[M-H_2O]^+$ (3), 287 $[M-CO_2Me]^+$ (7), 269 $[287-H_2O]^+$ (10), 187 $[269-C_5H_6O]^+$ (18), 81 $[C_5H_5O]^+$ (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-41 \quad -43 \quad -49 \quad -81} \ (CHCl_3;\ c\ 1.17).$$

10 mg **7a** in 3 ml THF was heated 30 min with 10 mg $LiAlH_4$. After addition of dil H_2SO_4 the compound was extracted with Et_2O. After evaporation 5 mg colourless crystals were obtained from Et_2O–petrol, mp 134°; IR $\nu_{max}^{CHCl_3}$ cm^{-}: 3590 (OH), 3080, 1640, 900 (C=CH_2), 880 (furane); MS *m/z* (rel. int.): 318.219 $[M]^+$ (17) (calc. for $C_{20}H_{30}O_3$: 318.219), 300 $[M-H_2O]^+$ (10), 282 $[300-H_2O]^+$ (3), 269 $[300-CH_2OH]^+$ (10), 187 $[269-C_5H_6O]^+$ (10), 81 $[C_5H_5O]^+$ (100).

$$[\alpha]_{24}^{\lambda}{}^{\circ} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-32 \quad -33 \quad -37 \quad -60} \ (CHCl_3;\ c\ 0.38).$$

18-Hydroxydaniellol (**8**). Colourless crystals, mp 114° (Et_2O–petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3615 (OH), 3080, 1640, 900 (C=CH_2), 880 (furane); MS *m/z* (rel. int.): 318.219 $[M]^+$ (18) (calc. for $C_{20}H_{30}O_3$: 318.219), 300 $[M-H_2O]^+$ (9), 269 $[300-CH_2OH]^+$ (16), 187 $[269-C_5H_6O]^+$ (15), 81 $[C_5H_5O]^+$ (100)

$$[\alpha]_{24}^{\lambda}{}^{\circ} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-31 \quad -31 \quad -36 \quad -57} \ (CHCl_3;\ c\ 0.07).$$

3α,18-Dihydroxy-19-desoxydaniellol (**9**) Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}. 3620 (OH), 3080, 1650, 905 (C=CH_2), 880 (furane); MS *m/z* (rel. int.) 318.219 $[M]^+$ (38) (calc. for $C_{20}H_{30}O_3$. 318.219), 303 $[M-Me]^+$ (4), 300 $[M-H_2O]^+$ (8), 287 $[M-CH_2OH]^+$ (7), 285 $[303-H_2O]^+$ (4), 269 $[300-CH_2OH]^+$ (3), 81 $[C_5H_5O]^+$ (100)

$$[\alpha]_{24}^{\lambda}{}^{\circ} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-31 \quad -32 \quad -36 \quad -58} \ (CHCl_3,\ c\ 0.74).$$

10 mg **3a** in 3 ml THF afforded by reduction with $LiAlH_4$ (s.a.) 6 mg **9**, identical with the natural compound (^1H NMR, TLC, optical rotation).

Methyl-19-hydroxypolyalthoate (**11a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}. 3600 (OH), 1720 (CO_2R, hydrogen bonded), 3080, 1655, 905 (C=CH_2), 885 (furane); MS *m/z* (rel. int.) 346.214 $[M]^+$ (22) (calc. for $C_{21}H_{30}O_4$. 346.214), 328 $[M-H_2O]^+$ (10), 316 $[M-CH_2O]^+$ (2), 287 $[M-CO_2Me]^+$ (4), 269 $[287-H_2O]^+$ (5), 187 $[269-C_5H_6O]^+$ (12), 81 $[C_5H_5O]^+$ (100).

$$[\alpha]_{24}^{\lambda}{}^{\circ} = \frac{589 \quad 578 \quad 546\ nm}{-26 \quad -26 \quad -28} \ (CHCl_3,\ c\ 7.13).$$

Methyl-8α,17-epoxy-8,17-dihydropolyalthoate (**12a**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}. 1725 (CO_2R), 875 (furane), MS *m/z* (rel. int.). 346.214 $[M]^+$ (7) (calc. for $C_{21}H_{30}O_4$: 346.214), 328 $[M-H_2O]^+$ (6), 317 $[M-CHO]^+$ (6), 287 $[M-CO_2Me]^+$ (4), 269 $[287-H_2O]^+$ (4), 187 $[269-C_5H_6O]^+$ (22), 81 $[C_5H_5O]^+$ (100).

$$[\alpha]_{24}^{\lambda}{}^{\circ} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-19 \quad -19 \quad -23 \quad -40} \ (CHCl_3;\ c\ 0.26).$$

Methyl-8β,17-epoxy-8,17-dihydropolyalthoate (**13a**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725 (CO_2R), 875 (furane); MS *m/z*

(rel. int.): 346.214 $[M]^+$ (10) (calc. for $C_{21}H_{30}O_4$. 346.214), 328 $[M-H_2O]^+$ (7), 317 $[M-CHO]^+$ (10), 315 $[M-CH_2OH]^+$ (6), 287 $[M-CO_2Me]^+$ (5), 269 $[287-H_2O]^+$ (6), 187 $[269-C_5H_6O]^+$ (11), 81 $[C_5H_5O]^+$ (100).

$$[\alpha]_{24}^{\lambda\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-35 \quad -37 \quad -42 \quad -48} \text{ (CHCl}_3\text{, } c \text{ 0.06).}$$

Methyl-17-*oxo*-8β,17-dihydropolyalthoate (**14a**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2730, 1725 (CHO, CO_2R), 880 (furane); MS *m/z* (rel. int.): 346.214 $[M]^+$ (10) (calc. for $C_{21}H_{30}O_4$: 346 214), 328 $[M-H_2O]^+$ (4), 318 $[M-CO]^+$ (5), 287 $[M-CO_2Me]^+$ (8), 82 $[C_5H_6O]^+$ (100), 81 $[C_5H_5O]^+$ (58).

$$[\alpha]_{24}^{\lambda\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-48 \quad -49 \quad -57 \quad -109} \text{ (CHCl}_3\text{; } c \text{ 0 33)}$$

5 mg **14a** were reduced in MeOH with 10 mg $NaBH_4$ TLC (Et_2O–petrol, 1:1, R_f 0.32) afforded 3 mg **15a**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1725 (CO_2R), 875 (furane); MS *m/z* (rel. int.): 348.230 $[M]^+$ (1) (calc. for $C_{21}H_{32}O_4$: 348.230), 330 $[M-H_2O]^+$ (1), 289 $[M-CO_2Me]^+$ (1), 271 $[289-H_2O]^+$ (2), 189 $[271-C_5H_6O]^+$ (4), 82 $[C_5H_6O]^+$ (100), 81 $[C_5H_5O]^+$ (44)

Gutierrezial methyl ester (**18a**). Colourless crystals, mp 128° (petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 1720 (CHO, CO_2R); MS *m/z* (rel. int.): 315.196 $[M-CHO]^+$ (51) (calc. for $C_{20}H_{27}O_3$. 315.196), 255 $[315-HCO_2Me]^+$ (12), 181 (22), 147 (31), 121 $[C_9H_{13}]^+$ (100), CI (isobutane): 345 $[M+1]^+$ (100), 315 $[345-CH_2O]^+$ (7).

$$[\alpha]_{24}^{\lambda\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+427 \quad +463 \quad +548 \quad +1225} \text{ (CHCl}_3\text{; } c \text{ 0.06).}$$

3α-*Angeloyloxy*-15,18-*dihydroxy*-ent-*labda*-8(17),13E-*diene* (**19**) Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1700, 1645 (C=CCO_2R), 900 (C=CH_2), MS *m/z* (rel. int.): 304.240 $[M-RCO_2H]^+$ (4) (calc. for $C_{20}H_{32}O_2$: 304.240), 289 $[304-Me]^+$ (7), 273 $[304-CH_2OH]^+$ (8), 271 $[289-H_2O]^+$ (10), 259 $[289-CH_2O]^+$ (10), 256 $[271-Me]^+$ (10), 83 $[C_4H_7CO]^+$ (76), 55 $[83-CO]^+$ (100).

6 mg **19** in 0.1 ml Ac_2O were heated for 1 hr at 70°. TLC (Et_2O–petrol, 1.1) gave 4.5 mg **20** (R_f 0.75), colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}. 1740 (OAc), 1710, 1645 (C=CCO_2R), 900 (C=CH_2); MS *m/z* (rel. int.): 428 293 $[M-HOAc]^+$ (3) (calc. for $C_{27}H_{40}O_4$: 428 293), 413 $[428-Me]^+$ (2), 388 $[M-RCO_2H]^+$ (3), 373 $[388-Me]^+$ (2), 328 $[388-HOAc]^+$ (21), 313 $[328-Me]^+$ (11), 269 $[328-OAc]^+$ (12), 268 $[328-HOAc]^+$ (20), 253 $[268-Me]^+$ (20), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (98).

$$[\alpha]_{24}^{\lambda\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-60 \quad -61 \quad -70 \quad -118} \text{ (CHCl}_3\text{, } c \text{ 0.45).}$$

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