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SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM AUSTRALIAN *HELIPTERUM* SPECIES

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Key Word Index—*Helipterum* species; Compositae; sesquiterpene lactones; germacranolides; guaianolides; eudesmanolides; diterpenes, *ent*-beyerene derivatives; trixagol isomer; cembrol; bisabolene derivative; alkylated salicyclic acids.

Abstract—The investigation of 17 Australian *Helipterum* species afforded 32 new sesquiterpene lactones (four germacranolides, 22 guaianolides and six eudesmanolides), a bisabolene derivative, four *ent*-beyerene derivatives, cembrol, an isomer of trixagol and four alkylated salicyclic acids. The structures were elucidated by high field NMR techniques. Three South African species gave no characteristic compounds.

INTRODUCTION

Very little is known about the chemistry of the large genus *Helipterum* which is mainly distributed over Australia and South Africa. The delimitation from the related genus *Helichrysum* still is not solved [1]. In particular, the situation of the Australian members of both genera is in question [1].

Bentham [2] divided the genus into four sections, two of them being restricted to Australia. So far a few species have been analysed for acetylenes [3] and only from *Helipterum craspedioides* has the isolation of an *ent*-beyerene derivative been reported [4]. We have studied 17 Australian species and three South African species. The results of this study are discussed in this paper.

RESULTS AND DISCUSSION

The extract of the aerial parts of *Helipterum moschatum* (Cunn. ex DC) F. Muell. afforded 14,15-diacetoxycostunolide [5] and the guaianolides **4–23**. The ^{1}H NMR spectra (Table 1) of **4** was in part similar to that of zaluzanin C-acetate [6]. However, the H-5 signal was a broadened doublet indicating an additional substituent at C-1. The molecular formula ($C_{17}H_{20}O_5$) could only be deduced indirectly by the presence of two mass fragmentation ions formed by loss of water (*m/z* 286) and by loss of acetic acid (*m/z* 244). Comparison of the couplings and of the chemical shifts with those of zaluzanin C-acetate indicated an unchanged stereochemistry and the presence of a 1α-hydroxy group.

The ^{1}H NMR spectra of **5–9** were similar to that of **4**, only the signals of the acetate group being replaced by those of a propionate, an isobutyrate, a 2-methyl butyrate, an isovalerate or an angelate residue, respectively. As in other cases the 2-methyl butyrate **7** and the isovalerate **8** could not be separated.

The ^{1}H NMR spectra of **10–23** (Table 2) differed more markedly from those of **4–9**. In particular, the signals of the exomethylene protons at C-14 were replaced by pairs of doublets around δ 4.5. Furthermore, the H-5 signal was shifted downfield indicating a neighbouring sp^2 carbon. Spin decoupling allowed the assignment of all signals and the presence of homoallylic couplings between H-2 and H-9 led to a complete sequence which required the proposed structures. A broadened doublet for H-3 did not allow direct assignment of the configuration which, however, could be determined by NOE difference spectroscopy in the case of the diacetate **16** in deuteriobenzene. The clear effect between the acetate methyl and H-6 required a 3β-acetoxy group though the couplings of H-3 clearly differed from those of the lactones **4–9**. NOE's between H-5 and H-7 as well as between H-6 and H-8β established the remaining stereochemistry. The nature of the oxygen functions in the lactones **10–23** were deduced from the characteristic signals of the ester groups and the position of the hydroxy groups followed from the chemical shifts of H-3 and H-14. Lactones of the types **10–23** are not common. The 3-desoxy derivatives with a free hydroxy group at C-14, we have named helipterolide.

Very similar lactones were isolated from the aerial parts of *H. maryonii* S. Moore. In addition to 14,15-diacetoxycostunolide and aguerin A (**1**) [7], the helipterolides **10–12** and the additional 8α-acyloxy derivatives of zaluzanin C, **2** and **3**, were present. The structures of these two lactones followed from the ^{1}H NMR spectra which were similar to that of **1**. Again the nature of the ester groups at C-8 followed from the characteristic signals. As in similar cases the conjugated acid moiety in lactone **3** caused a downfield shift of H-8 and also of H-7 and H-9. As the data of **1** are not clear in the lit. [7], we have included its ^{1}H NMR signals in Table 1.

From the aerial parts of *H. propinquum* W. Fitzg., in addition to the flavone hispidulin, the germacranolides **24–27** were isolated. While the methacrylate **24** and the angelate **26** could be crystallized, the isobutyrate **25** and the senecioate **27** were gums not completely free from **24** and **26**, respectively. The ^{1}H NMR spectrum of **24** (Table 3) clearly showed that a germacranolide was present. Spin decoupling allowed the assignment of all signals. As

Table 1. [1]H NMR spectral data of compounds **1**–**9** (400 MHz, $CDCl_3$, δ-values)

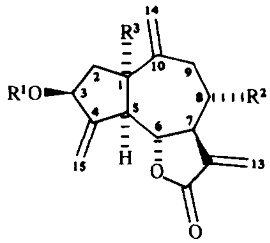
H	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
1	2.97 *dt*	2.96 *dt*	2.98 *dt*	—	—	—	—	—	—
2	2.23 *dt*	2.23 *m*	2.23 *m*	2.43 *br dd*	2.43 *br dd*	2.43 *br dd*	2.44 *br dd*	2.44 *br dd*	2.51 *br dd*
2′	1.72 *ddd*	1.72 *ddd*	1.74 *ddd*	2.19 *dd*	2.20 *dd*	2.18 *dd*	2.18 *dd*	2.18 *dd*	2.22 *dd*
3	4.56 *tt*	4.56 *tt*	4.57 *tt*	5.75 *tt*	5.76 *tt*	5.75 *tt*	5.76 *tt*	5.76 *tt*	5.82 *tt*
5	2.83 *br t*	2.82 *br t*	2.85 *br t*	2.78 *br d*	2.80 *br d*	2.80 *br d*	2.79 *br d*	2.79 *br d*	2.81 *br d*
6	4.23 *dd*	4.21 *dd*	4.24 *dd*	3.90 *t*	3.91 *t*	3.91 *t*	3.91 *t*	3.91 *t*	3.92 *t*
7	3.12 *tt*	3.10 *tt*	3.17 *tt*	3.02 *ddddd*	3.03 *ddddd*	3.05 *ddddd*	3.05 *m*	3.05 *m*	3.05 *m*
8	5.03 *ddd*	5.03 *ddd*	5.12 *ddd*	2.30 *m* 1.45 *m*	2.30 *m* 1.45 *m*	2.30 *m* 1.45 *m*	2.30 *m* 1.45 *m*	2.30 *m* 1.45 *m*	2.30 *m* 1.45 *m*
9	2.64 *dd*	2.66 *dd*	2.70 *dd*	2.60 *ddd*	2.62 *ddd*	2.63 *ddd*	2.63 *ddd*	2.63 *ddd*	2.63 *ddd*
9′	2.34 *dd*	2.34 *dd*	2.40 *dd*	2.30 *dd*	2.30 *m*	2.30 *m*	2.30 *m*	2.30 *m*	2.30 *m*
13	6.23 *d*	6.23 *d*	6.22 *d*	6.20 *d*	6.21 *d*	6.21 *d*	6.21 *d*	6.21 *d*	6.21 *d*
13′	5.61 *d*	5.62 *d*	5.61 *d*	5.48 *d*	5.49 *d*	5.49 *d*	5.49 *d*	5.49 *d*	5.49 *d*
14	5.13 *br s*	5.13 *br s*	5.13 *br s*	5.19 *br s*	5.19 *br s*	5.20 *br s*	5.20 *br s*	5.20 *br s*	5.19 *br s*
14′	4.91 *br s*	4.92 *br s*	4.94 *br s*	5.09 *br s*	5.09 *br s*	5.09 *br s*	5.09 *br s*	5.09 *br s*	5.09 *br s*
15	5.50 *t*	5.49 *t*	5.51 *t*	5.54 *t*	5.54 *t*	5.53 *t*	5.54 *t*	5.54 *t*	5.54 *t*
15′	5.36 *t*	5.36 *t*	5.36 *t*	5.40 *t*	5.39 *t*	5.36 *t*	5.37 *t*	5.38 *t*	5.42 *t*
OCOR	2.62 *qq*	2.26 *m* (2H)	6.20 *qq*	2.10 *s*	2.37 *q*	2.59 *qq*	2.40 *tq*	2.22 *m*	6.11 *qq*
	1.24 *d*	2.16 *m*	2.03 *dq*		1.17 *t*	1.20 *d*	1.70 *m*	2.18 *m*	2.00 *dq*
	1.22 *d*	1.00 *d* (6H)	1.93 *dq*			1.19 *d*	1.47 *m*	0.97 *d*	1.90 *dq*
							0.92 *t*		
							1.16 *d*		

J [Hz]: compounds **1**–**3**: 1,2 = 2,3 = 2′,3 = 7; 1,2′ = 11; 1,5 = 8; 2,2′ = 13; 3,15 = 5,15 = 1.5; 5,6 = 10; 6,7 = 7,8 = 9; 7,13 = 3.5; 7,13′ = 3; 8,9 = 5; 8,9′ = 3.5; 9,9′ = 14.5; compounds **4**–**9**: 2,2′ = 14; 2,3 = 8; 2′,3 = 7; 3,15 = 5,15 ~ 1.5; 5,6 = 6,7 = 10; 7,8 = 4; 7,8′ = 10; 7,13 = 3.5; 7,13′ = 3; 8,9 ~ 4; 8′,9 = 9,9′ ~ 12; OProp: 2′,3′ = 7.5; O*i*Bu: 2′,3′ = 7; OMeBu: 2′,5′ = 3′,4′ = 7; O*i*Val: 3′,4′ = 7; OAng: 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5.

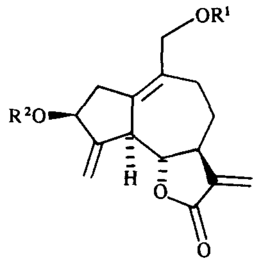
Table 2. [1]H NMR spectral data of **10**–**23**

H	**10**	**11**	**12**	**13**	**14**	**15**	**16**
2	2.73 *dq*	2.73 *dq*	2.74 *dq*	2.73 *br d*	2.73 *br d*	2.73 *br d*	2.75 *br s*
2′	2.59 *br dt*	2.60 *br dt*	2.60 *br dt*	2.61 *br d*	2.61 *br d*	2.61 *br d*	
3	4.54 *br d*	4.54 *br d*	4.54 *br d*	4.54 *br d*	4.54 *br d*	4.54 *br d*	5.51 *br d*
5	3.43 *br d*	3.43 *br d*	3.43 *br d*	3.43 *br d*	3.43 *br d*	3.43 *br d*	3.46 *br d*
6	3.88 *t*	3.88 *t*	3.88 *t*	3.87 *t*	3.87 *t*	3.87 *t*	3.73 *t*
7	2.78 *tq*	2.78 *tq*	2.78 *tq*	2.78 *tq*	2.78 *tq*	2.78 *tq*	2.79 *t*
8	2.16 *dddd*	2.15 *dddd*	2.15 *dddd*	2.15 *br d*	2.15 *br d*	2.15 *br d*	2.17 *dddd*
8′	1.42 *br q*	1.41 *br q*	1.42 *br q*	1.42 *br q*	1.42 *br q*	1.42 *br q*	1.40 *br q*
9	2.44 *ddd*	2.44 *ddd*	2.43 *ddd*	2.43 *br dd*	2.43 *br dd*	2.46 *br dd*	2.45 *ddd*
9′	2.26 *br t*	2.25 *br t*	2.24 *br t*	2.25 *br t*	2.25 *br t*	2.25 *br t*	2.26 *br t*
13	6.14 *d*	6.14 *d*	6.14 *d*	6.14 *d*	6.14 *d*	6.14 *d*	6.15 *d*
13′	5.41 *d*	5.41 *d*	5.41 *d*	5.41 *d*	5.41 *d*	5.41 *d*	5.42 *d*
14	4.61 *d*	4.62 *d*	4.59 *br s*	4.60 *br s*	4.60 *br s*	4.68 *d*	4.60 *d*
14′	4.54 *d*	4.56 *d*				4.61 *d*	4.50 *d*
15	5.39 *br s*	5.38 *br s*	5.38 *br s*	5.39 *br s*	5.39 *br s*	5.39 *br s*	5.52 *br s*
15′	5.31 *br s*	5.31 *br s*	5.30 *br s*	5.32 *br s*	5.32 *br s*	5.32 *br s*	5.44 *br s*
OAc	2.07 *s*	2.35 *q*	2.57 *qq*	2.40 *m*	2.21 *d* (2H)	6.21 *qq*	2.07 *s*
OCOR	—	1.15 *t*	1.18 *d*	1.68 *m*	2.15 *m*	1.99 *dq*	2.01 *s*
				1.47 *m*	0.97 *d*	1.89 *dq*	
				0.91 *t*			
				1.15 *d*			

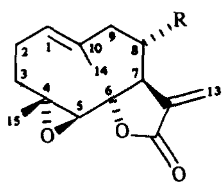
J [Hz]: 2,2′ = 17; 2,3 = 2,9 = 1.5; 2′,3 = 5; 2′,9 ~ 2; 5,6 = 6,7 = 10; 7,8 = 8,9 = 8,9′ ~ 3; 7,8′ = 8′,9 = 11; 7,13 = 3.5; 7,13′ = = 7; 3′,5′ = 4′,5′ = 1.5.



	1	2	3	4	5	6	7	8	9
R¹	H	H	H	Ac	Prop	*i*Bu	MeBu	*i*Val	Ang
R²	O*i*Bu	O*i*Val	OAng	H	H	H	H	H	H
R³	H	H	H	OH	OH	OH	OH	OH	OH



	10	11	12	13	14	15	16	17	18	19	20	21	22	23
R¹	Ac	Prop	*i*Bu	MeBu	*i*Val	Ang	Ac	Ac	Ac	Ac	Ac	Ac	Prop	*i*Bu
R²	H	H	H	H	H	H	Ac	Prop	*i*Bu	MeBu	*i*Val	Ang	Ac	Ac



	24	25	26	27	27a
R	OMeacr	O*i*Bu	OAng	OSen	H

($CDCl_3$, 400 MHz, δ-values)

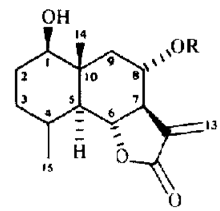
17	18	19	20	21	22	23
} 2.75 *br s*	} 2.73 *br s*	} 2.74 *br s*	} 2.74 *br s*	} 2.74 *br s*	2.77 *br d* 2.72 *br d*	} 2.76 *br s*
5.54 *br d*	5.54 *br d*	5.52 *br d*	5.52 *br d*	5.53 *br d*	5.52 *br d*	5.53 *br d*
3.46 *br d*	3.46 *br d*	3.46 *br d*	3.46 *br d*	3.46 *br d*	3.46 *br d*	3.46 *br d*
3.72 *t*	3.72 *t*	3.72 *t*	3.72 *t*	3.73 *t*	3.72 *t*	3.72 *t*
2.80 *tq*	2.80 *tq*	2.80 *tq*	2.80 *tq*	2.80 *tq*	2.80 *tq*	2.80 *tq*
2.17 *dddd*	2.17 *dddd*	2.17 *dddd*	2.17 *dddd*	2.17 *dddd*	2.17 *dddd*	2.18 *dddd*
1.39 *br q*	1.38 *br q*	1.39 *br q*	1.39 *br q*	1.39 *br q*	1.39 *br q*	1.39 *br q*
2.45 *ddd*	2.44 *ddd*	2.45 *ddd*	2.45 *ddd*	2.45 *ddd*	2.45 *ddd*	2.45 *ddd*
2.26 *br t*	2.27 *br t*	2.28 *br t*	2.28 *br t*	2.28 *br t*	2.25 *br t*	2.27 *br t*
6.15 *d*	6.15 *d*	6.15 *d*	6.16 *d*	6.15 *d*	6.15 *d*	6.15 *d*
5.42 *d*	5.42 *d*	5.42 *d*	5.42 *d*	5.42 *d*	5.42 *d*	5.42 *d*
4.61 *d*	4.61 *d*	4.60 *d*	4.60 *d*	4.61 *d*	4.61 *d*	4.61 *d*
4.50 *d*	4.50 *d*	4.51 *d*	4.51 *d*	4.51 *d*	4.51 *d*	4.51 *d*
5.52 *br s*	5.51 *br s*	5.52 *br s*	5. 52 *br s*	5.54 *br s*	5.52 *br s*	5.53 *br s*
5.44 *br s*	5.43 *br s*	5.44 *br s*	5.44 *br s*	5.47 *br s*	5.44 *br s*	5.44 *br s*
2.07 *s*	2.47 *qq*	2.32 *tq*	2.13 *d* (2H)	6.03 *qq*	2.01 *s*	2.56 *qq*
2.28 *q*	1.10 *d*	1.61 *m*	2.05 *m*	1.94 *dq*	2.35 *q*	1.18 *d*
1.09 *t*		1.45 *m*	0.91 *d*	1.81 *dq*	1.15 *t*	1.17 *d*
		0.86 *t*				
		1.09 *d*				

3; 8,8′ = 9,9′ = 13; OProp: 2′,3 = 7.5; O*i*Bu: 2′,3′ = 7; OMeBu: 2′,5′ = 3′,4′ = 7; O*i*Val: 3′,4′ = 7; OAng: 3′,4′

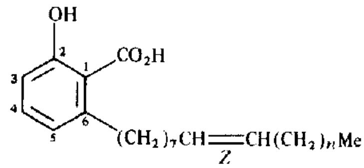
Table 3. ^{1}H NMR spectral data of compounds **24**–**27** ($CDCl_3$, 400 MHz, δ-values)

H	24	25	26	27
1	5.29 *br dd*	5.27 *br dd*	5.29 *br dd*	5.26 *br d*
2	2.42 *m*	2.42 *m*	2.43 *m*	2.43 *m*
2'	2.27 *br d*	2.27 *br d*	2.27 *br d*	2.26 *br d*
3	1.26 *m*	1.26 *m*	1.26 *m*	1.26 *m*
3'	2.18 *ddd*	2.18 *ddd*	2.18 *ddd*	2.17 *ddd*
5	2.65 *d*	2.64 *d*	2.65 *d*	2.65 *d*
6	4.32 *dd*	4.28 *dd*	4.36 *dd*	4.31 *dd*
7	3.28 *dddd*	3.27 *dddd*	3.27 *dddd*	3.26 *dddd*
8	4.58 *ddd*	4.48 *ddd*	4.57 *ddd*	4.57 *ddd*
9	2.57 *t*	2.51 *t*	2.55 *t*	2.55 *t*
9'	2.46 *br d*	2.40 *br d*	2.46 *br d*	2.46 *br d*
13	6.32 *d*	6.37 *d*	6.32 *d*	6.32 *d*
13'	5.69 *d*	5.74 *d*	5.65 *d*	5.72 *d*
14	1.82 *br s*	1.81 *br s*	1.82 *br s*	1.81 *br s*
15	1.28 *s*	1.27 *s*	1.29 *s*	1.28 *s*
OCOR	6.10 *br s*	2.47 *qq*	6.18 *qq*	5.64 *br s*
	5.62 *dq*	1.17 *d*	1.95 *dq*	2.11 *d*
	1.91 *br s*	1.12 *d*	1.87 *dq*	1.91 *d*

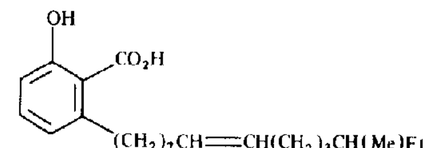
J [Hz]: 1,2 = 12; 1,2' = 4; 2,2' = 14; 2,3 = 6; 2',3' = 2; 3,3' = 13; 5,6 = 9; 7,8 = 7; 7,13 = 3.5; 7,13' = 3; 8,9 = 9,9' = 12; 8,9' = 1.5; OMeacr: 3,3' = 3',4 = 1; O*i*Bu: 2,3 = 2,4 = 3; OAng: 3,4 = 7; 3,5 = 4,5 = 1.5; OSen: 2,4 = 2,5 = 1.



	28	29	30	31	32	33	34	35
R	Ang	Ang	Ang	Tigl	Tigl	Tigl	*i*Bu	Ang
	$\Delta^{4(15)}$	Δ^3	Δ^4	$\Delta^{4(15)}$	Δ^3	Δ^4	$\Delta^{4(15)}$	4αOMe



36 n = 5
37 n = 7



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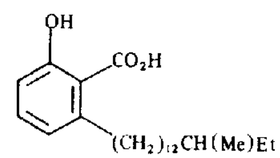

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36a–39a are the dimethoxy derivatives

irradiation of the signal at δ 3.28 collapsed the exomethylene doublets to singlets it was due to H-7. Accordingly, starting with the latter the whole sequence could be determined. The chemical shift of the H-5 doublet required an epoxide proton and inspection of a model showed that the couplings of H-8 required a 8α-methacryloyloxy group and a *trans*-diaxial orientation of the protons at C-5 and C-6. Thus a 4α,5β-epoxy derivative of costunolide was present. Accordingly, the ^{1}H NMR spectrum was similar to that of parthenolide (**27a**). The spectra of **25**–**27** (Table 3) showed that the corresponding isobutyrate, angelate and senecioate, respectively, were present. The ^{1}H NMR spectrum of deltoidin A, the 8-*epi* derivative of **26** [8], clearly differed from that of **26**.

The aerial parts of *H. roseum* (Hook.) Benth. afforded the eudesmanolides **28**–**35**. The ^{1}H NMR spectral data of **28** were identical with those of chapinolin which has been isolated during the preparation of this paper [9] and those of **32** indicated that we were dealing with beogradolide [10]. The ^{1}H NMR spectra of **31** and **34** (Table 4) were similar to those of reynosin [11] and **28** indicating that these lactones were the corresponding tiglate and isobutyrate, respectively.

The spectrum of **29** (Table 4) showed similarities to that of balchanin [12] and **32**. The signals of the ester residue indicated the presence of the corresponding angelate. The spectra of **28** and **29** clearly differed from those of the corresponding 8β-epimers [13].

The ^{1}H NMR spectrum of **30** (Table 4) showed that again a 8α-angeloxyloxy derivative was present. The absence of olefinic proton signals at C-3 or C-15 and the fact that H-6 was a broadened doublet indicated that we were dealing with a derivative of arbusculin B [14]. Spin decoupling showed that an equatorial hydroxy group was at C-1 and an equatorial angeloyloxy group at C-8. Thus **30** was 1β-hydroxy-8α-angeloxyoxyarbusculin B. The ^{1}H NMR spectrum of **33** (Table 4) showed that the corresponding 8α-tigloyloxy derivative was present.

The ^{1}H NMR spectrum of **35** (Table 4) indicated that this lactone was a 4-methoxyeudesmanolide with the same oxygen functions at C-1 and C-8 as in **28**–**30**. Due to the missing double bond in addition to the H-14 singlet at δ 1.11 a second one for H-15 at δ 1.30 was visible. The chemical shift of the latter indicated an axial orientation of the 4-methyl group if compared with the shifts of epimeric 4-hydroxyeudesmanolides [15].

The roots of *H. roseum* gave the bisabolene derivative **45**. The ^{1}H NMR spectrum (see Experimental) in deuteriobenzene could be completely assigned by spin decoupling. A broadened triplet at δ 5.65 (J = 3 Hz) and a three proton singlet at δ 1.70 required an axial orientated acetoxy group. Furthermore the typical signals of a prenyl side chain, broadened singlets for exomethylene protons and a pair of narrowly split doublets at δ 3.21 and 3.10 (J = 4 Hz) were visible. The latter signals were due to epoxide protons. Inspection of a model indicated that the observed very small coupling of the epoxide proton required a *cis*-orientation of H-1 and H-6. As the latter was axial orientated the relative configuration at the ring substituents was very likely. This was finally established by the observed NOE's. Thus clear effects were obtained between H-1 and H-6, between H-14, H-1 and H-6, between H-2 and H-15', as well as between H-15' and H-2. The relative configuration at C-6 and C-7 followed from a model and the mentioned NOE between H-14 and H-1.

Table 4. ^{1}H NMR spectral data of compounds **29–31** and **33–35** (400 MHz, $CDCl_3$, δ-values)

H	29	30	31	33	34	35*
1	3.67 *dd*	3.57 *dd*	3.53 *dd*	3.54 *dd*	3.53 *dd*	3.43 *dd*
3	5.35 *br s*	2.22 *br ddd*	2.13 *br dt*	2.22 *br ddd*	2.13 *br dt*	†
3′		2.05 *br d*	2.35 *ddd*	2.05 *br d*	2.35 *ddd*	†
5	2.38 *m*	—	2.23 *br d*	—	2.21 *br d*	1.94 *d*
6	4.06 *t*	4.66 *br d*	4.14 *t*	4.66 *br d*	4.12 *t*	4.16 *t*
7	2.86 *tt*	2.94 *tt*	2.91 *tt*	2.93 *tt*	2.87 *tt*	2.93 *tt*
8	5.34 *dt*	5.28 *dt*	5.21 *dt*	5.26 *dt*	5.21 *dt*	5.24 *dt*
9	2.52 *dd*	2.55 *dd*	2.53 *dd*	2.52 *dd*	2.48 *dd*	2.48 *dd*
9′	1.28 *dd*	1.32 *dd*	1.33 *dd*	1.30 *dd*	1.29 *t*	1.30 *t*
13	6.11 *d*	6.21 *d*	6.11 *d*	6.20 *d*	6.14 *d*	6.13 *d*
13′	5.53 *d*	5.64 *d*	5.53 *d*	5.63 *d*	5.54 *d*	5.53 *d*
14	0.95 *s*	1.18 *s*	0.90 *s*	1.18 *s*	0.87 *s*	1.11 *s*
15	1.85 *br s*	1.88 *br s*	5.03 *br s* 4.90 *br s*	1.88 *br s*	5.02 *br s* 4.89 *br s*	1.30 *s*
OCOR	6.15 *qq*	6.17 *qq*	6.90 *qq*	6.90 *qq*	2.59 *qq*	6.16 *qq*
	2.00 *dq*	2.01 *dq*	1.82 *br d*	1.82 *br s*	1.20 *d*	2.00 *dq*
	1.89 *dq*	1.90 *dq*	1.85 *br s*	1.85 *br s*	1.19 *d*	1.90 *dq*

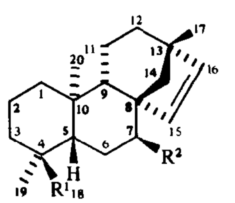
*OMe: 3.21 *s*; †obscured multiplets.

J [Hz]: 1,2 = 11; 1,2′ = 4; 6,7 = 7,8 = 11; 7,13 = 3; 8,9 = 4.5; 9,9′ = 8,9′ = 13; compounds **31** and **34**: 2,3 = 12; 2,3′ = 5; 3,3′ = 14; 5,6 = 11; compounds **30** and **33**: 2,3 = 2′,3 = 9; 3,3′ = 17.

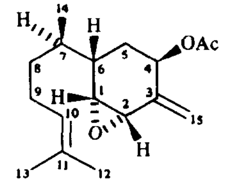
As the absolute configuration of bisabolone isolated from Compositae is established [16] the given one is most likely.

The aerial parts of *H. floribundum* DC gave costol acetate [17] and isovalerate [19], tulipinolide [20] 8α-acetoxydehydrocostus lactone [21] and the *ent*-beyerene derivatives erythroxylol A (**40**) [22] and **41–44** which were isolated as their methyl esters **41a–44a**. The ^{1}H NMR spectra of **42a** and **43a** (Table 5) indicated that we were dealing with the methyl esters of the 18-*O*-malonate and succinate of erythroxylol A. The ^{13}C NMR spectra supported this assumption (Table 6). The position of the oxygen function followed from the chemical shift of H-18 and the absence of a *W*-coupling which always can be observed in similar diterpenes with an axial CH_2OR group. Accordingly, the ^{1}H NMR spectrum of the epimeric succinate is different [23]. The ^{1}H NMR spectrum of **41a** (Table 5) showed that an 4-epimer of the known 19-oic acid [24] was present. Therefore the signals of the methyl groups at C-4 and C-10 were shifted in the expected way if compared with the corresponding epimers of kaurenic acid.

In the ^{1}H NMR spectrum of **44a** in deuteriobenzene (Table 5) nearly all signals could be assigned. Obviously, this compound was a derivative of **43a** as most signals were nearly identical. However, an additional triplet at δ 3.71 ($J = 2.5$ Hz) required a further oxygen function. As the chemical shifts of H-15 and H-16 were influenced a



	40	41	42	43	44
R^1	CH_2OH	CO_2H	$CH_2OCOCH_2CO_2H$	$CH_2OCOCH_2CH_2CO_2H$	$CH_2OCOCH_2CH_2CO_2H$
R^2	H	H	H	H	OH



45

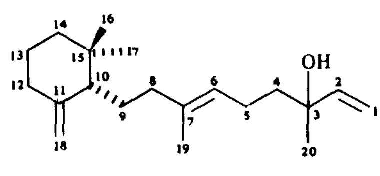


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Table 5. ^{1}H NMR spectral data of compounds **41a–44a** (400 MHz, $CDCl_3$, δ-values)

H	41a	42a	43a	44a (C_6D_6)
5	*	*	*	2.06 *dd*
6	*	*	*	1.46 *ddd*
7	*	*	*	3.71 *t*
14α	*	*	*	1.54 *d*
14β	*	*	*	1.76 *dd*
15	5.65 *br d*	5.67 *br d*	5.67 *br d*	5.50 *br d*
16	5.45 *br d*	5.45 *br d*	5.45 *br d*	5.53 *br d*
17	0.98 *s*	0.99 *s*	0.99 *s*	1.11 *s*
18	—	3.93 *d*	3.88 *d*	4.33 *d*
18′	—	3.72 *d*	3.67 *d*	3.42 *d*
19	1.16 *s*	0.84 *s*	0.83 *s*	0.72 *s*
20	0.76 *s*	0.78 *s*	0.77 *s*	0.76 *s*
OR	3.66 *s*	3.40 *s*	2.65 *m* (4H)	2.61 *ddd*
		3.76 *s*	3.70 *s*	2.26 *ddd*
				2.50 *ddd*
				2.32 *ddd*
				3.33 *s*

*Overlapped multiplets.

J [Hz]: Compound **41a**: 15,16 = 6; compounds **42a** and **43a**: 15,16 = 6; 18,18′ = 11; compound **44a**: 5,6 = 12; 5,6′ = 6,7 = 6′,7 = 2.5; 12β,14β = 2; 14α,14β = 10; 15,16 = 6; 18,18′ = 11; $OCOCH_2CH_2CO_2Me$: 2,2′ = 3,3′ = 13; 2,3 = 2′,3′ = 10; 2,3′ = 2′,3 ~ 4.

Table 6. ^{13}C NMR spectral data of compounds **40a** and **42a–44a** ($CDCl_3$, 100.6 MHz, δ-values)

C	40a	42a	43a	44a
1	38.8	38.6	38.6	38.8
2	18.0	17.6	17.7	18.3
3	35.4	35.8	35.8	36.3
4	37.6	49.9	49.7	37.5
5	49.1	49.8	49.9	47.0
6	19.9	20.0	20.1	28.3
7	37.0	36.8	36.1	72.9
8	48.6	48.8	48.8	44.0
9	52.8	52.8	52.8	47.0
10	37.1	37.1	37.1	36.4
11	20.3	20.0	20.1	20.2
12	33.2	33.1	33.1	33.3
13	43.6	43.6	43.6	44.0
14	61.2	61.1	61.1	57.5
15	135.0	135.1	135.1	134.1
16	136.0	136.5	136.5	137.4
17	24.9	24.9	24.9	25.2
18	72.3	74.0	73.4	72.3
19	17.7	17.6	17.6	18.0
20	15.6	15.5	15.5	15.2
OCOR		41.5	29.3 *t*	29.2 *t*
			29.0 *t*	28.9 *t*
		166.9 *s*	172.7 *s*	173.0 *s*
		166.5 *s*	172.2 *s*	172.4 *s*
		52.5 *q*	51.8 *q*	51.4 *q*

hydroxy group at C-12 or C-7 was indicated. A decision was possible by the observed NOE's. Irradiation of the singlet at δ 0.72 gave clear effects with the doublets at δ 4.33 and 3.42 while irradiation of the singlet at δ 0.76 gave a NOE with H-15 and H-6α. Thus H-19 and H-20 could be assigned. Further NOE's were present between H-17, H-14 and H-16 as well as between H-7 and H-15. Thus the presence of a 7β-hydroxy derivative of **43a** was settled. Also the ^{13}C NMR data agreed with this structure (Table 6).

The aerial parts of *H. sterilescens* F. Muell. afforded a mixture of acids which was separated as the di-*O*-methyl derivatives **36a–39a**. The structure of **36a** followed from the spectral data. From the ^{1}H NMR spectrum (Experimental) the presence of an alkylated salicyclic acid ester could be deduced by the typical signals and chemical shifts of the aromatic protons. Also the nature of the side chain followed from the ^{1}H NMR data and the ^{13}C NMR spectrum supported the proposed structure. In the mass spectrum the observed fragment at *m/z* 180 is almost certainly formed by a McLafferty fragmentation (A) while the base peak *m/z* 161 is best formulated as fragment **B** formed by cyclic loss of methanol followed by allylic cleavage of the side chain. The position of the double bond was determined by the mass spectrum of the epoxide which showed fragments at *m/z* 273 ($C_{17}H_{21}O_3$ $[M-MeOH]^+$, C_6H_{13}) and *m/z* 245 ($C_{16}H_{21}O_2$, $[273-CO]^+$). All data of **37a** were identical with those of **36a** except the molecular ion which indicated a heptadecenyl side chain. Again the position of the double bond was determined via the MS of the epoxide.

The ^{1}H NMR spectrum of **38a** differed from that of **36a** by the presence of an additional methyl doublet. Accordingly, the side chain was branched. Inspection of the ^{13}C NMR data indicated by the observed shifts of the methyl carbons a CH(Me)Et end group if compared with the shifts of authentic compounds [25]. The MS of the corresponding epoxide indicated the position of the double bond. The ^{1}H NMR spectrum of **39a** showed the absence of the double bond but again showed that a branched side chain was present. The ^{13}C NMR data indicated the same position of the methyl group as in **38a**. Most likely the acids **36** and **37** are acetogenins formed from precursors of unsaturated C_{24} and C_{26} acids while **38** and **39** are more unusual as in the biosynthesis the introduction of a methyl group has to be explained. As far as we know no similar natural compounds have been reported.

The aerial parts of *H. venustum* S. Moore gave γ-curcumene, nerolidol, cembrol and a further diterpene, the vinyl carbinol **46**. The structure followed from the ^{1}H NMR spectrum (Experimental) and the ^{13}C NMR data. Spin decoupling together with the observed NOE's allowed the assignment of most signals. Furthermore, the fragmentation pattern in the mass spectrum supported the structure. In particular, splitting of the 9,10-bond led to the fragment *m/z* 123. An isomer of **46** with a primary hydroxy group has been reported from a Scrophulariaceae [26]. Compound **46** we have named helipterol. As no authentic sample and no extensive NMR data of cembrol were available the structure was determined by its ^{1}H and ^{13}C NMR data including NOE's as well as by those of the corresponding hydrocarbon (−)cembrene obtained by treatment of the alcohol with traces of acid. The hydrocarbon obtained was enantiomeric to that reported from *Pinus armandi* [27].

The overall picture of the chemistry of the genus *Helipterum* shows that the Australian representatives differ from the South African ones particularly by the accumulation of sesquiterpene lactones. Furthermore, the proposed close relationships to *Helichrysum* are not clear as sesquiterpene lactones are very rare in this genus. However, diterpenes have been reported from a few species. In the subtribe Gnaphalinae *ent*-beyerene derivatives are reported from *Helichrysum*, *Helipterum* and *Myriocephalus*.

EXPERIMENTAL

The air-dried plant material was collected in Australia in August 1986 (vouchers deposited in the US National Herbarium, Washington) and in South Africa in September 1986 (vouchers deposited in the Compton Herbarium, Kirstenbosch, R.S.A.). The material was extracted, worked-up and the extracts separated as reported previously [28]. The conditions of final isolation are given together with the data of the new compounds (TLC: T1 = Et_2O–petrol, 1:1; T2 3:1; T3 1:19; T4 1:3; HPLC (RP 18, *ca* 100 bar, flow rate, 3 ml/min) HP1 = MeOH–H_2O 3:1; HP2 7:3; HP3 9:1).

Helipterum moschatum (collected in S Australia, voucher RMK 9617, 350 g material). TLC and HPLC gave 6 mg **4**, 1 mg **5**, 5 mg **6**, 3 mg **7–9**, 120 mg **10**, 5 mg **11**, 5 mg **12**, 2 mg **13** and **14**, 0.5 mg **15**, 100 mg **16**, 10 mg **17**, 15 mg **18**, 4 mg **19** and **20**, 0.5 mg **21**, 2 mg **22**, 3 mg **23** and 50 mg 14,15-diacetoxycostunolide.

Helipterum propinquum (collected in W Australia, voucher RMK 9576, 90 g material). TLC and HPLC gave 6 mg **24**, 2 mg **25**, 4 mg **26**, 2 mg **27** and 50 mg hispidulin.

Helipterum maryonii (collected in W Australia, voucher 9559, 75 g material). TLC and HPLC gave 3 mg **1**, 2 mg **2**, 3 mg **3**, 1 mg **10**, 25 mg **11**, 0.5 mg **12** and 1 mg 14,15-diacetoxycostunolide.

Helipterum floribundum (collected in S Australia, voucher RMK 9578, 280 g material). TLC and HPLC gave 3 mg costol isovalerate, 6 mg costol acetate, 10 mg tulipinolide, 6 mg 8-acetoxydehydrocostus lactone, 4 mg **40**, 5 mg **41**, 14 mg **42**, 18 mg **43** and 10 mg **44** (**41–44** isolated as their methyl esters **41a–44a**).

Helipterum roseum (collected in W Australia, voucher RMK 9533, 210 g of aerial parts). TLC and HPLC gave 20 mg **28**, 20 mg **29**, 10 mg **30**, 4 mg **31**, 3 mg **32**, 2 mg **33**, 1 mg **34** and 2 mg **35**. The extract of the roots (20 g) gave by CC and TLC 5 mg **45**.

Helipterum sterilescens (collected in W Australia, voucher RMK 9566, 200 g aerial parts). The polar CC fractions gave 100 mg of a mixture of acids which were transferred to the di-*O*-methyl derivatives by addition of CH_2N_2. TLC (Et_2O–petrol, 3:1) gave no separation. HPLC (MeOH–H_2O, 9:1) finally gave 3 mg **36a**, 1.5 mg **38a**, 1.5 mg **37a** and 2 mg **39a**.

Helipterum venustum (collected in W. Australia, voucher RMK 9557, 160 g aerial parts). CC and TLC afforded 20 mg γ-curcumene, 30 mg nerolidol and a mixture of diterpenes which were separated by HPLC (MeOH–H_2O, 9:1) affording 30 mg cembrol which was transformed to (−)-cembrene by standing in $CDCl_3$ with traces of acid ($[\alpha]_D^{24°} -210°$) and 5 mg **46**.

Constituents of further species see Table 7.

Table 7. Constituents of further *Helipterum* species

Name (voucher, collected)	Aerial parts (g)	Constituents
H. charsleyae F. Muell. (RMK 9570, W. Australia)	180	—
H. chlorocephalum (Turcz.) Benth. (RMK 9547, W. Australia)	180	10 mg **28**, 15 mg **29**, 5 mg **30**
H. corymbiflorum Schldl. (RMK 9631, SO Australia)	300	650 mg hispidulin, 1 g eupafolin [18]
H. hyalospermum F. Muell. ex Benth. (RMK 9511, W. Australia)	200	40 mg selina-4(15)-11-diene, 8 mg selina-3,11-diene, 200 mg nerolidol
H. manglessii (Lindley) F. Muell. ex Benth. (RMK 9534, W. Australia)	70	5 mg pinoresinol
H. spicatum (Steetz) F. Muell. ex Benth. (RMK 9543, W. Australia)	60	—
H. splendidum Hemsl. (RMK 9565, W. Australia)	95	2 mg **28**, 1 mg **29**, 1 mg **30**
H. strictum (Lindley) Benth. (RMK 9569, W. Australia)	200	500 mg **27a**
H. tenellum Turcz. (RMK 9595, W. Australia)	145	100 g luteolin, 75 mg 3′-*O*-methylluteolin, 30 mg 3β-methyl-4β-hydroxybutenolide
H. troedellii F. Muell. (RMK 9625, W. Australia)	140	—
H. gnaphaloides (L.) DC (86/228, South Africa, Hermanus)	230	10 mg *p*-hydroxyacetophenone, 4 mg 2,3-dihydroaromaticin
H. speciosissimun (L.) DC (86/211, South Africa, Table Mountain)	160	—
H. milleflorum (L.) Druce (86/115, South Africa, Table Mountain)	600	—

Zaluzanin C derivatives

8α-Isobutyryloxy (aguerin A) (**1**). Colourless crystals, mp 105°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3080, 1640, 865 ($C{=}CH_2$), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 332.163 $[M]^+$ (3) (calc. for $C_{19}H_{24}O_5$: 332.163), 244 $[M-RCO_2H]^+$ (13), 226 $[244-H_2O]^+$ (9), 71 $[RCO]^+$ (100); $[\alpha]_D^{24°}$ +85 ($CHCl_3$; *c* 0.25); HP 2, R_t 7.5 min.

8α-Isovaleryloxy and angeloyloxy (**2** and **3**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3080, 1640, 860 ($C{=}CH_2$), 1780 (γ-lactone), 1740 (CO_2R), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 and 344.163 $[M]^+$ (1.2 and 1.7) (calc. for $C_{20}H_{26}O_5$: 346.178; $C_{20}H_{24}O_5$: 344.163), 244 $[M-RCO_2H]^+$ (14), 226 (9), 85 $[C_4H_9CO]^+$ (14), 83 $[C_4H_7CO]^+$ (100); HP 2, R_t 11.5 min.

1α-Hydroxy-3-O-acetate (**4**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3090, 1640 ($C{=}CH_2$), 1780 (γ-lactone), 1745, 1240 (OAc); MS *m/z* (rel. int.): 286.121 $[M-H_2O]^+$ (1.5) (calc. for $C_{17}H_{18}O_4$: 286.121), 244 $[M-HOAc]^+$ (22), 226 (9), 94 (100); $[\alpha]_D^{24}$ +70 ($CHCl_3$; *c* 0.29); HP 1, R_t 1.5 min.

1α-Hydroxy-3-O-propionate (**5**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3080, 1640 ($C{=}CH_2$), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 244.110 $[M-RCO_2H]^+$ (15) (calc. for $C_{15}H_{16}O_3$: 244.110), 226 (21), 57 $[RCO]^+$ (100); HP 1, R_t 2.4 min.

1α-Hydroxy-3-O-isobutyrate (**6**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3590 (OH), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 244.110 $[M-RCO_2H]^+$ (38) (calc. for $C_{15}H_{16}O_3$: 244.110), 226 (12), 71 $[RCO]^+$ (100); HP 1, R_t 3.7 min.

1α-Hydroxy-3-O-2-methylbutyrate, isovalerate and angelate (**7–9**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1735 (CO_2R), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 328.167 and 326.152 $[M-H_2O]^+$ (0.4 and 0.5) (calc. for $C_{20}H_{24}O_4$: 328.167 and $C_{20}H_{22}O_4$: 326.152), 344 $[M-RCO_2H]^+$ (21), 226 (8), 85 $[C_4H_9CO]^+$ (41), 83 $[C_4H_7CO]^+$ (56), 57 $[85-CO]^+$ (100); HP 1, R_t 5.4 min.

Helipterolide derivatives

3β-Hydroxy-14-O-acetate (**10**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3080, 1645, 860 ($C{=}CH_2$), 1780 (γ-lactone), 1745, 1235 (OAc); MS *m/z* (rel. int.): 304.131 $[M]^+$ (1.5) (calc. for $C_{17}H_{20}O_5$: 304.131), 286 $[M-H_2O]^+$ (31), 244 $[M-HOAc]^+$ (84), 226 $[244-H_2O]^+$ (100), 91 (92); HP 2, R_t 2.5 min. Acetylation (Ac_2O, 1 hr, 70°) afforded **16**, identical with the natural product (^1H NMR and mp).

3β-Hydroxy-14-O-propionate (**11**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 300.136 $[M-H_2O]^+$ (8) (calc. for $C_{18}H_{20}O_4$: 300.136), 244 $[M-RCO_2H]^+$ (26), 226 $[244-H_2O]^+$ (31), 91 (26), 57 $[RCO]^+$ (100); $[\alpha]_D^{24°}$ −28 ($CHCl_3$; *c* 0.15); HP 2, R_t 4.3 min.

3β-Hydroxy-14-O-isobutyrate (**12**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 314.152 $[M-H_2O]^+$ (7) (calc. for $C_{19}H_{22}O_4$: 314.152), 244 $[M-RCO_2H]^+$ (24), 226 $[244-H_2O]^+$ (34), 71 $[RCO]^+$ (100); HP 1, R_t 3.5 min.

3β-Hydroxy-14-O-2-methylbutyrate, isovalerate and angelate (**13–15**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1735 (CO_2R), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 and 344.163 $[M]^+$ (0.3 and 0.1) (calc. for $C_{20}H_{26}O_5$: 346.178 and $C_{20}H_{24}O_5$: 344.163), 244 $[M-RCO_2H]^+$ (21), 226 (26), 85 $[C_4H_9CO]^+$ (46), 83 $[C_4H_7CO]^+$ (30), 57 $[85-CO]^+$ (100); HP 1, R_t 4.7 min.

3β-Acetoxy-14-O-acetate (**16**). Colourless crystals, mp 122°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1745, 1240 (OAc); MS *m/z* (rel. int.): 286.121 $[M-HOAc]^+$ (14) (calc. for $C_{17}H_{18}O_4$: 286.121), 226 $[286-HOAc]^+$ (100); $[\alpha]_D^{24°}$ −72 ($CHCl_3$; *c* 0.39); ^{13}C NMR (C_6D_6, 106.4 MHz, C-1–C-15): 141.0, 37.9, 82.0, 146.2, 53.1, 76.4, 51.6, 26.0, 30.5, 140.8, 132.0, 168.7, 117.8, 66.7, 116.3; OAc: 169.6, 170.0, 20.4, 20.8; HP 1, R_t 2.4 min.

3β-Propionyloxy-14-O-acetate (**17**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 300.136 $[M-HOAc]^+$ (1) (calc. for $C_{18}H_{20}O_4$: 300.136), 286 $[M-C_2H_5CO_2H]^+$ (18), 226 $[286-HOAc]^+$ (100), 57 $[RCO]^+$ (56); $[\alpha]_D^{24°}$ −66 ($CHCl_3$; *c* 0.81); HP 1, R_t 3.1 min.

3β-Isobutyryloxy-14-O-acetate (**18**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 314.152 $[M-HOAc]^+$ (0.1) (calc. for $C_{19}H_{22}O_4$: 314.152), 286 $[M-RCO_2H]^+$ (21), 226 $[286-HOAc]^+$ (100), 71 $[RCO]^+$ (21); $[\alpha]_D^{24°}$ −56 ($CHCl_3$; *c* 0.96); HP 1, R_t 4.5 min.

3β-2-Methylbutyryloxy, isovaleryloxy and angeloyloxy-14-O-acetate (**19–21**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775 (γ-lactone), 1745 (CO_2R); MS *m/z* (rel. int.): 286.121 $[M-RCO_2H]^+$ (11) (calc. for $C_{17}H_{18}O_4$: 286.121), 226 $[286-HOAc]^+$ (100), 85 $[C_4H_9CO]^+$ (24), 83 $[C_4H_7CO]^+$ (26), 57 $[85-CO]^+$ (98); HP 1, R_t 5.7 min.

3β-Acetoxy-14-O-propionate (**22**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 300.136 $[M-HOAc]^+$ (7) (calc. for $C_{18}H_{20}O_4$: 300.136), 286 $[M-C_2H_5CO_2H]^+$ (26), 226 $[286-HOAc]^+$ (100), 57 $[RCO]^+$ (66); HP 1, R_t 3.6 min.

3β-Acetoxy-14-O-isobutyrate (**23**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1740 (CO_2R); MS *m/z* (rel. int.): 314.152 $[M-HOAc]^+$ (6) (calc. for $C_{19}H_{22}O_4$: 314.152), 286 $[M-RCO_2H]^+$ (4), 226 $[286-HOAc]^+$ (100), 71 $[RCO]^+$ (39); HP 1, R_t 4.6 min.

8α-Methacryloyloxyparthenolide (**24**). Colourless crystals, mp. 138°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 332.162 $[M]^+$ (0.1) (calc. for $C_{19}H_{24}O_5$: 332.162), 246 $[M-RCO_2H]^+$ (21), 188 (30), 69 $[RCO]^+$ (100); $[\alpha]_D^{24°}$ −53 ($CHCl_3$; *c* 0.08), HP 3, R_t 3.3 min; TLC 1 (4 ×), R_f 0.40.

8α-Isobutyryloxyparthenolide (**25**). Colourless gum, not free from **24**; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1735 (CO_2R); MS *m/z* (rel. int.): 334.178 $[M]^+$ (0.1) (calc. for $C_{19}H_{26}O_5$: 334.178), 246 $[M-RCO_2H]^+$ (28), 71 (100); HP 3, R_t 3.3 min; TLC 1 (4 ×), R_f 0.45.

8α-Angeloyloxyparthenolide (**26**). Colourless crystals, mp 152°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1715, 1645 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.8) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (62), 188 (58), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (70); $[\alpha]_D^{24°}$ −52 ($CHCl_3$; *c* 0.2); HP 3, R_t 4.7 min; TLC 1 (4 ×), R_f 0.55).

8α-Senecioyloxyparthenolide (**27**). Colourless gum, not free from **26**; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.6) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (45), 83 $[RCO]^+$ (100); HP 3, R_t 4.7 min; TLC 1 (4 ×), R_f 0.55.

8α-Angeloyloxyreynosin (**28**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1785 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.3) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (10), 228 $[246-H_2O]^+$ (38), 83 $[RCO]^+$ (100); HP 3, R_t 2.9 min.; TLC 1 (6 ×), R_f 0.68.

8α-Angeloyloxybalchanin (**29**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1785 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.5) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (11), 228 $[246-H_2O]^+$ (40), 83 $[RCO]^+$ (100); $[\alpha]_D^{24°}$ +140 ($CHCl_3$; *c* 0.45); HP 3, R_t 3.7 min.

1β-Hydroxy-8α-angeloyloxyarbusculin B (**30**). Colourless crystals, mp 55°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1785 (γ-lactone), 1720 ($C{=}CCO_2R$); MS *m/z* (rel. int.): 346.178 $[M]^+$ (1.2) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (22), 228 $[246-H_2O]^+$ (28), 213 $[228-Me]^+$ (22), 202 $[246-CO_2]^+$ (100), 83

$[RCO]^+$ (92), 55 $[83-CO]^+$ (98); $[\alpha]_D^{24°}+144$ ($CHCl_3$; *c* 0.68); HP 3, R_t 4.4 min; TLC 1 (6 ×), R_f 0.75.

8α-*Tigloyloxyreynosin* (**31**). Colourless crystals, mp 78°; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1725 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.3) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (8), 228 $[246-H_2O]^+$ (20), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (76); $[\alpha]_D^{24°}+156$ ($CHCl_3$; *c* 0.31); HP 3, R_t 2.9 min; TLC 1 (6 ×), R_f 0.60.

1β-*Hydroxy*-8α-*tigloyloxyarbusculin B* (**33**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (1.3) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[M-RCO_2H]^+$ (19), 228 $[246-H_2O]^+$ (26), 213 $[228-Me]^+$ (17), 202 $[246-CO_2]^+$ (90), 83 $[RCO]^+$ (97), 55 $[83-CO]^+$ (100); $[\alpha]_D^{24°}+143$ ($CHCl_3$; *c* 0.1); HP 3, R_t 4.4 min; TLC 1 (6 ×), R_f 0.68.

8α-*Isobutyryloxyreynosin* (**34**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1740 (CO$_2$R); MS *m/z* (rel. int.): 334.178 $[M]^+$ (0.7) (calc. for $C_{19}H_{26}O_5$: 334.178), 246 $[M-RCO_2H]^+$ (38), 228 $[246-H_2O]^+$ (90), 213 $[228-Me]^+$ (26), 202 $[246-CO_2]^+$ (42), 71 $[RCO]^+$ (100); HP 3, R_t 2.0 min.; TLC 2, R_f 0.62.

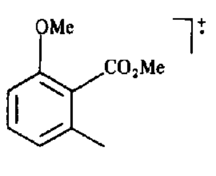
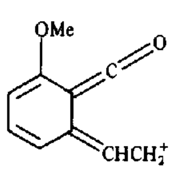
8α-*Angeloyloxy*-1β-*hydroxyarbusculin*-4-O-*methyl ether* (**35**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1715, 1640 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M-MeOH]^+$ (2) (calc. for $C_{20}H_{26}O_5$: 346.178), 246 $[346-RCO_2H]^+$ (4), 228 $[246-H_2O]^+$ (2), 188 (4), 115 (8), 85 (100), 83 $[RCO]^+$ (56), 55 $[83-CO]^+$ (43); HP 3, R_t 2.0 min; TLC 2, R_f 0.28.

6-[*Pentadec*-8′Z-*enyl*]-*salicyclic acid* (**36**). Isolated as its di-O-methyl derivative **36a**, colourless oil; MS *m/z* (rel. int.): 374.282 $[M]^+$ (12) (calc. for $C_{24}H_{38}O_3$: 374.282), 343 $[M-OMe]^+$ (25), 342 $[M-MeOH]^+$ (14), 180 $[A^*]^+$ (37), 161 $[B^*]^+$ (100); ^{1}H NMR (400 MHz, $CDCl_3$): δ6.76 (*d*, *J* = 8 Hz), 7.27 (*t*, *J* = 8, 8), 6.82 (*d*, *J* = 8) (aromatic), 2.53 (*br t*, *J* = 8) (PhCH$_2$), 2.00 (*m*), 5.35 (*m*) (CH$_2$CH=CHCH$_2$), 1.57 (*m*), 1.30 (*m*) $(CH_2)_n$, 0.89 (*t*, *J* = 6.5) (Me); ^{13}C NMR ($CDCl_3$, C-1–C-6): 123.5, 156.3, 108.4, 130.3, 121.5, 141.5; OMe: 55.9, 52.1; CH=CH: 130.0, 129.9; CH$_2$: 33.5, 31.8, 29.5, 29.4, 29.0, 22.7; Me: 14.1; HP3, R_t 7.5 min.

Epoxidation ($CHCl_3$, *m*-chloroperbenzoic acid, 1 hr, 20°) afforded the 8′,9′-epoxide; colourless oil; MS *m/z* (rel. int.): 390.277 $[M]^+$ (1.5) (calc. for $C_{24}H_{38}O_4$: 390.277), 358 $[M-MeOH]^+$ (12), 273.149 $[M-C_6H_{13}]^+$ (11), 245.154 $[273-CO]^+$ (11), 180 $[A]^+$ (40), 161 $[B]^+$ (100); ^{1}H NMR ($CDCl_3$, 400 MHz): as **36a**, except for replacement of the multiplet at δ5.35 by 2.90 and absence of the multiplet at δ2.00.

6-[*Heptadec*-8′Z-*enyl*]-*salicyclic acid* (**37**). Isolated as its di-O-methyl derivative **37a**; colourless oil; MS *m/z* (rel. int.): 402.313 $[M]^+$ (14) (calc. for $C_{26}H_{42}O_3$: 402.313), 371 $[M-OMe]^+$ (12), 370 $[M-MeOH]^+$ (8), 180 $[A]^+$ (42), 161 $[B]^+$ (100); ^{1}H NMR and ^{13}C NMR as those of **36a**. HP3, R_t 11.7 min. Epoxidation (s.a.) afforded the 8′,9′-epoxide which was characterized by its MS and its ^{1}H NMR (s.a.).

6-[13-*Methylpentadec*-8′Z-*enyl*]-*salicyclic acid* (**38**). Isolated as its di-O-methyl derivative **38a**; colourless oil; MS *m/z* (rel. int.): 388.298 $[M]^+$ (28) (calc. for $C_{25}H_{40}O_3$: 388.298), 357 $[M-OMe]^+$ (22), 356 $[M-MeOH]^+$ (14), 299 $[356-C_4H_9]^+$ (5), 180 $[A]^+$ (77), 161 $[B]^+$ (100); ^{1}H NMR ($CDCl_3$): as **36a**, except CHMe: 0.84 (*d*, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$): as **36a**, except 46.5 *d*, 19.2 *q* and 11.4 *q*. HP3, R_t 8.8 min. Epoxidation (s.a.) gave the 8′,9′-epoxide which was characterized by its MS and its ^{1}H NMR (s.a.).

A  B 

6-[13-*Methylpentadecyl*]-*salicyclic acid* (**39**). Isolated as its di-O-methyl derivative **39a**; colourless oil; MS *m/z* (rel. int.): 390.313 $[M]^+$ (58) (calc. for $C_{25}H_{42}O_3$: 390.313), 358 $[M-MeOH]^+$ (26), 180 $[A]^+$ (59), 161 $[B]^+$ (100); ^{1}H NMR ($CDCl_3$): as **36a**, except for absence of multiplets at δ2.00, 5.35 and presence of 0.84 (*d*, *J* = 6 Hz); ^{13}C NMR ($CDCl_3$): as **36a**, except for absence of 130.0, 129.9 *d* and presence of 46.8 *d*, 19.3 *q*, 11.4 *q*. HP3, R_t 12.7 min.

ent-*Beyer*-15-*en*-18-*oic acid* (**41**). Isolated as its methyl ester **41a**; colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730 (CO$_2$R); MS *m/z* (rel. int.): 316.240 $[M]^+$ (48), 301 $[M-Me]^+$ (6), 270 $[301-OMe]^+$ (12), 257 $[M-CO_2Me]^+$ (9), 135 (40), 87 (59), 74 (100), 55 (70); TLC 3, R_f 0.53.

18-*Hydroxy*-ent-*beyer*-15-*en-malonate* (**42**). Isolated as its methyl ester **42a**; colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (CO$_2$R); MS *m/z* (rel. int.): 388.261 $[M]^+$ (62) (calc. for $C_{24}H_{36}O_4$: 388.261), 270 $[M-RCO_2H]^+$ (34), 257 $[M-CH_2OCOR]^+$ (32), 148 (64), 135 (100), 134 (88), 105 (86); $[\alpha]_D^{24°}+9$ ($CHCl_3$; *c* 2.51); TLC 4 (5 ×), R_f 0.65.

18-*Hydroxy*-ent-*beyer*-15-*en-succinate* (**43**). Isolated as its methyl ester **43a**; colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745 (CO$_2$R); MS *m/z* (rel. int.): 402.277 $[M]^+$ (31) (calc. for $C_{25}H_{38}O_4$: 402.277), 308 $[M-C_7H_{10}]^+$ (17), 270 $[M-RCO_2H]^+$ (38), 257 $[M-CH_2OCOR]^+$ (30), 135 (72), 115 $[RCO]^+$ (61), 95 (74), 81 (92), 55 (100); TLC 4 (5 ×), R_f 0.58.

7β,18-*Dihydroxy*-ent-*beyer*-15-*en*-18-O-*succinate* (**44**). Isolated as its methyl ester **44a**; colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3550 (OH), 1740 (CO$_2$R); MS *m/z* (rel. int.): 418.272 $[M]^+$ (25) (calc. for $C_{25}H_{38}O_5$: 418.272), 400 $[M-H_2O]^+$ (14), 268 $[400-RCO_2H]^+$ (64), 255 $[400-CH_2OCOR]^+$ (66), 165 (70), 146 (95), 121 (100), 115 $[RCO]^+$ (39); $[\alpha]_D^{24°}+44$ ($CHCl_3$; *c* 1.0); TLC 2, R_f 0.55.

4β-*Acetoxy*-1α,2α-*epoxy-bisabola*-3(15),10-*diene* (**45**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1245 (OAc); MS *m/z* (rel. int.): 278 $[M]^+$ (0.15), 218.167 $[M-HOAc]^+$ (2.5) (calc. for $C_{15}H_{22}O$: 218.167), 200 $[218-H_2O]^+$ (3), 177 (6.5), 118 (100), 109 (64), 69 (93); ^{1}H NMR (400 MHz, C_6D_6): δ3.10 (*dt*, H-1), 3.21 (*dd*, H-2), 5.65 (*t*, H-4), 1.64 (*m*, H-5), 1.45 (*dt*, H-5′), 2.10 (*ddd*, H-6), 1.70 (*m*, H-7), 1.51 (*m*, H-8), 1.29 (*m*, H-8′), 2.09 (*m*, H-9), 2.01 (*br ddt*, H-9′), 5.23 (*tqq*, H-10), 1.74 (*br s*, H-12), 1.62 (*br s*, H-13), 1.00 (*d*, H-14), 5.58 and 5.32 (*br s*, H-15), 1.70 (*s*, OAc); *J* [Hz]: 1,2 = 4; 1,5 = 1,6 = 3.4 ~ 0.5; 4,5 = 4,5′ = 3.5; 5,5′ = 14; 5,6 = 10; 5′,6 = 4; 6,7 = 5; 8,9 = 9,10 = 7; 10,12 = 10,13 = 1.5; $[\alpha]_D^{24°}-33$ ($CHCl_3$; *c* 1.1); TLC 2, R_f 0.62.

Helipterol (**46**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 3080, 1640, 915 (CH=CH$_2$); MS *m/z* (rel. int.): 290.261 $[M]^+$ (0.15) (calc. for $C_{20}H_{34}O$: 290.261), 275 $[M-Me]^+$ (0.5), 272 $[M-H_2O]^+$ (4), 257 $[272-Me]^+$ (10), 123 $[C_9H_{15}]^+$ (32), 109 $[C_8H_{13}]^+$ (57), 95 (62), 81 (100), 69 (92); ^{1}H NMR (C_6D_6, 400 MHz): δ0.90 (*s*, H-17), 1.01 (*s*, H-16), 1.17 (*s*, H-20), 1.68 (*br s*, H-19), 5.26 (*dd*, H-1, *J* = 17, 1.5 Hz), 5.01 (*dd*, H-1′, *J* = 11, 1.5), 5.81 (*dd*, H-2, *J* = 17, 11), 5.34 (*br t*, H-6), 1.78 (*dd*, H-10), 4.93 and 4.75 (*br s*, H-18), 2.25 – 2.00 (*m*, H-5, H-5′, H-8, H-12, H-12′), 1.94 (*m*, H-8′), 1.68 (*m*, H-9), 1.63 – 1.40 (*m*, H-4, H-4′, H-9′, H-13, H-14, H-14′), 1.20 (*m*, H-13); ^{13}C NMR ($CDCl_3$, C-1–C-20): δ111.7 *t*, 145.1 *d*, 73.5 *s*, 42.1 *t*, 22.7 *t*, 123.8 *d*, 136.2 *s*, 32.8 *t*, 24.7 *t*, 53.6 *d*, 149.3 *s*, 36.3 *t*, 23.7 *t*, 38.2 *t*, 34.9 *t*, 27.9 *q*, 26.2 *q*, 108.8 *t*, 16.1 *q*, 28.4 *q*; $[\alpha]_D^{24°}+13$ ($CHCl_3$; *c* 0.31). HP3, R_t 12.7 min.

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