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NEW MELAMPOLIDES, KAURENE DERIVATIVES AND OTHER CONSTITUENTS FROM *ICHTHYOTHERE* SPECIES*

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Key Word Index—*Ichthyothere terminalis*; *I. ulei*; Compositae; sesquiterpene lactones; melampolides; *ent*-kaurane derivatives; seco-kaurene derivatives; *ent*-labdane derivatives; geranylnerol lactones; monoterpenes.

Abstract—The reinvestigation of *Ichthyothere terminalis* afforded, in addition to known compounds, two new melampolides, a hydroxy borneol, a pinene derivative, two *ent*-labdane derivatives, four derivatives of 9(11)-dihydro-*ent*-kaurenic acid, seven *ent*-kaurene derivatives and three seco-kaurenic acid derivatives, while *I. ulei* gave six diterpene lactones derived from geranylnerol and a new melampolide. The structures were elucidated by highfield ^{1}H NMR spectroscopy and some chemical transformations. The chemotaxonomy of the genus is discussed briefly.

INTRODUCTION

The South American genus *Ichthyothere* was placed by Hoffmann [1] in the subtribe Melampodinae; but was transferred to the Millerinae by Stuessy [2]. More recent taxonomic studies, however, showed [Robinson, H., unpublished work] that it should be retained in the Melampodinae. So far the chemistry is not helpful for a clear decision between these two possibilities as only kaurenic acid derivatives and two acetylenic compounds have been reported from this genus [3–5]. We have therefore reinvestigated two collections of *I. terminalis* and studied the constituents of *I. ulei*.

RESULTS AND DISCUSSION

The roots of *I. terminalis* (Spreng.) Malme afforded germacrene D, bicyclogermacrene, β-eudesmene, biformene, cyperene (**4**), ozic acid (**18**) [6], the kaurene derivatives **35–37**, **39**, **42** and **58** as well as an isomer of **58**, the hydroxy acetate **57**. The structure of **57** followed from the molecular formula and the ^{1}H NMR spectrum (see Experimental), which was close to that of 16-hydroxy-*ent*-kaurane. The position of the additional hydroxy group, which obviously was axially oriented, could not be established with certainty. Spin decoupling showed that the proton under the hydroxy group was coupled with a proton which itself had three further couplings. Therefore, the hydroxyl had to be placed at C-1 or C-3. From biogenetic considerations, a 3-hydroxy group would be more likely as the aerial parts afforded 3-oxygenated *ent*-kaurene derivatives, too. The aerial parts gave germacrene D, bicyclogermacrene, **18** and derivatives **19** and **20**, isolated as the methylesters **21** and **22**, 9,11-dehydro-*ent*-kaurenic acid (**23**) [7], its 12- and 15-hydroxy derivatives **30** [8] and **33** [9], the corresponding ketone **34** [9], *ent*-kaurenic acid (**37**), the grandifloric acid esters **39** and **40** [11], the hydroxy senecioate and tiglate **45** and **46** [11] as well as the further *ent*-kaurene derivatives **24**, **26**, **28**, **31**, **43**, **47**, **49**, **51**, **53** and **55**, which were separated as their methyl esters **25**, **27**, **29**, **32**, **44**, **48**, **50**, **52**, **54** and **56**. Furthermore, the monoterpene derivatives **1** and **2** were present as well as the melampolides **6** and **7**. The structure of **1** followed from the molecular formula, the ^{1}H NMR spectrum (Table 1) and spin decoupling, while the presence of a hydroxy ketone could be deduced from the IR spectrum. The presence of a pinene derivative followed from the typical signals of H-4–H-6 and the methyl singlets, while the position of the oxygen functions could be deduced from the chemical shifts if a model was inspected. The 3-keto group caused a downfield shift of H-4, while the β-orientation of the 1-hydroxyl was very likely as no downfield shift of H-5α was visible, as would be expected in the case of a 1α-hydroxy group. The structure of **2**, which was transformed to the diacetate **3**, followed from the ^{1}H NMR spectral data (Table 1), which were close to those of borneol and its acetate respectively. However, the signal of one methyl group was replaced by two downfield doublets. As the signal of H-4 was shifted downfield, one of the methyls at the bridge was oxygenated. Eu(fod)$_3$-induced shifts led to the proposed position of the hydroxymethylene group, as H-2 was much

*Part 440 in the series "Naturally Occurring Terpene Derivatives". For Part 439, see Bohlmann, F., Singh, P. and Jakupovic, J. (1982) *Phytochemistry* **21**, 2029.

Table 1. ^{1}H NMR spectral data of compounds **1–3** (400 MHz, $CDCl_3$, TMS as int. standard)

	1	2	3
H-2α	2.76 *d(br)*	—	
H-2β	2.60 *d*	4.07 *ddd*	4.94 *ddd*
H-3α	—	1.06 *dd*	1.06 *dd*
H-3β	—	2.29 *dddd*	2.37 *m*
H-4	2.62 *dd*	1.90 *dd*	1.92 *dd*
H-5α	1.98 *d*	1.30 *m*	1.3 *m*
H-5β	2.53 *dddd*	1.73 *m*	1.6 *m*
H-6α	2.11 *dd(br)*	1.98 *ddd*	2.0 *m*
H-6β	—	1.30 *m*	1.3 *m*
H-7	1.48 *s*	0.92 *s*	0.91 *s*
H-9	1.40 *s*	1.02 *s*	0.97 *s*
H-10	0.95 *s*	3.67 *d*	4.12 *d*
		3.47 *d*	3.97 *d*
OAc	—	—	2.06 *s*

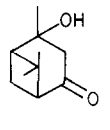
J (Hz): Compound **1**: 2α, 2β = 20; 2α, 5β = 1.5; 4, 5β = 4, 6 = 5.5; 5α, 5β = 11; 5β, 6 = 5.5; compound **2**: 2β, 3α = 3.5; 2β, 3β = 10; 2β, 6β = 1.5; 3α, 3β = 13.5; 3β, 4 = 4.5; 3β, 5β = 3.5; 4,5β = 4.5; 5α, 6α = 6α, 6β = 13; 5β, 6α = 4; 10, 10′ = 11; compound **3**: 2β, 3α = 3.5; 2β, 3β = 10; 2β, 6β = 1.5; 3α, 3β = 14; 3β, 4 = 4, 5β = 4.5; 10, 10′ = 11.

less shifted than H-10, and H-5β showed a pronounced shift. **2** has been prepared from bromocamphor [12]. The chemical shifts of the methyl singlet agreed with those of the synthetic material. **2** most probably was formed via limonene-8,9-epoxide, which also supported the proposed arrangement of the hydroxyl if a *trans*, anti, *trans*-concerted reaction was assumed. The structure of **6** was deduced from the ^{1}H NMR spectrum (Table 2) and spin decoupling. The data were closely related to those of longipilin acetate [13]. However, an additional downfield signal and a missing coupling of H-1 indicated a 2-hydroxy group, the orientation of which was deduced from the couplings observed assuming the usual conformation of melampolides. Surprisingly, an upfield shift of the H-9 signal was observed, which may be explained by a small change in the conformation leading to a reduced deshielding effect of the epoxide group. The ^{1}H NMR spectral data of **7** and those of the corresponding acetate **8** (Table 2) showed that again a melampolide was present, as in addition to the typical signals of a methylene lactone (δ 6.43 and 5.88 *d*) a downfield shifted doublet at δ 6.46 and a methoxy singlet were recognized. A 2,5-oxygen ring was indicated by a considerable downfield shift of the H-9 signal, consequently a 3,4-double bond was very

Table 2. ^{1}H NMR spectral data of compounds **6–9** (400 MHz, $CDCl_3$, TMS as int. standard)

	6	7	8	9
H-1	6.95 *d*	6.46 *d*	6.57 *d*	6.77 *dd*
H-2α	5.19 *ddd(br)*	—	—	2.80 *dddd*
H-2β	—	—	—	2.63 *m*
H-3α	2.52 *dd*	5.69 *dq*	5.84 *s(br)*	2.49 *ddd*
H-3β	1.46 *dd*			2.10 *dd(br)*
H-5	2.70 *d*	5.41 *ddq*	5.45 *d(br)*	4.92 *d(br)*
H-6β	4.25 *dd*	5.17*dd*	5.23 *dd*	5.09 *dd*
H-7α	2.99 *dddd*	2.87 *dddd*	2.86 *m*	2.63 *m*
H-8α	6.75 *dd*	6.29 *dd*	6.29 *dd*	6.79 *dd*
H-9β	5.55 *d*	6.85 *dd*	6.98 *dd*	5.35 *dd*
H-13	6.37 *d*	6.43 *d*	6.44 *d*	6.28 *d*
H-13′	5.93 *d*	5.88 *d*	5.90 *d*	5.83 *d*
H-14	—	—	—	9.47 *d*
H-15	1.70 *s*	1.78 *s(br)*	1.80 *dd*	2.04 *d*
OMe	3.85 *s*	3.83 *s*	3.84 *s*	—
OAc	2.03 *s*	1.97 *s*	1.96 *s*	
			2.07 *s*	1.94 *s*
	6.11 *qq*	6.07 *qq*	6.08 *qq*	
OAng	1.93 *dq*	1.91 *dq*	1.93 *dq*	—
	1.77 *dq*	1.80 *dq*	1.79 *dq*	
				6.16 *s(br)*
				5.87 *dt*
				4.67 *d(br)*
				4.71 *d(br)*

J (Hz): compound **6**: 1, 2α = 8; 2α, 3α = 3; 2α, 3β = 3α, 3β = 13.5; 5, 6β = 6β, 7α = 9.5; 7α, 8α = 1.5; 7α, 13 = 7α, 13′ = 3; 8α, 9β = 9; 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.5; compounds **7/8**: 1, 9β = 1; 3, 5 = 3, 15 = 5, 15 = 1.5; 5, 6β = 4.5; 6β, 7α = 7; 7α, 8α = 1.5; 7α, 13 = 3.5; 7α, 13′ = 3; 8α, 9β = 10.5; 3′, 4′ = 7; 3′, 5′ = 4′, 5′ = 1.5; compound **9**: 1, 2α = 10; 1, 2β = 7.5; 2α, 2β = 2α, 3β = 13.5; 2α, 3α = 2.5; 2β, 3α = 6; 3α, 3β = 12.0; 5, 6β = 6β, 7α = 10; 7α, 8α = 1.5; 7α, 13 = 7α, 13′ = 3; 8α, 9β = 8.5; 9β, 14 = 2; 5, 15 = 1.2; $3'_1$, $3'_2 = 3'_1$, 4′ = 1; $4'_1$, $4'_2 = 14$.



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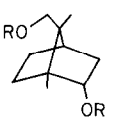

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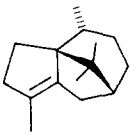
3 R=Ac



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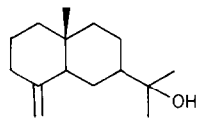

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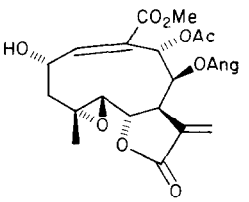

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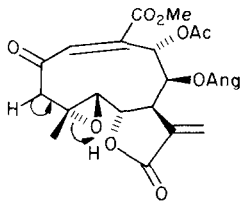
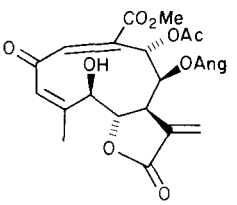


6a



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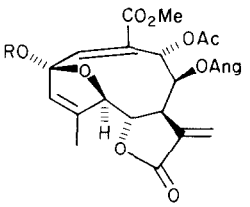
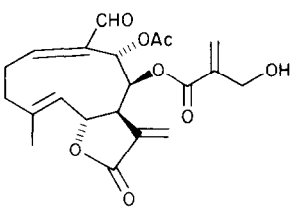


7 R=H
8 R=Ac



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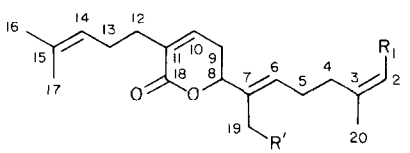
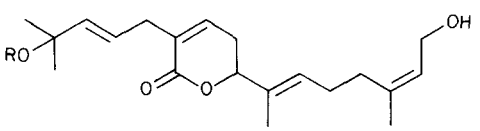
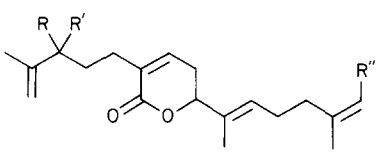


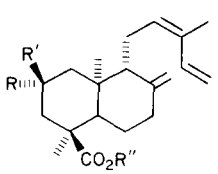
	10	11	12
R	CH_2OH	CHO	CH_2OH
R′	H	H	OAc



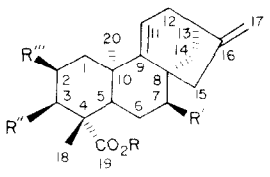
13 R=OH
14 R=H



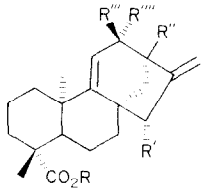
	15	16	17
R	OOH	OH	=O
R′	H	H	
R″	CH_2OH	CH_2OH	CHO



	18	19	20	21	22
R	H	OH	=O	OH	=O
R′	H	H		H	
R″	H	H	H	Me	Me



	23	24	25	26	27	28	29
R	H	H	Me	H	Me	H	Me
R′	H	OH	OH	H	H	H	H
R″	H	H	H	OH	OAc	H	H
R‴	H	H	H	H	H	OH	OH



	30	31	32	33	34
R	H	H	Me	H	H
R′	OH	H	H	H	H
R″	H	OH	OH	H	H
R‴	H	H	H	OH	} =O
R⁗	H	H	H	H	}

likely. Spin decoupling allowed the assignment of all signals. As **7** could be acetylated, a semi ketal was present. Consequently, in the spectrum of **8** no drastic shifts were observed. The stereochemistry at C-6–C-9 followed from the couplings, which were close to those of similar melampolides, while the nature of the ester groups followed from the typical ^{1}H NMR signals. The orientation of the ether ring followed from the chemical shift of H-9. **7** most probably was formed via the 2-dehydro compound **6a**, which could be transformed by proton attack to a 3,4-dehydro-5-hydroxy compound **6b**; its semi ketal would be **7**, which we have named ichthyotherminolide.

Table 3. ^{1}H NMR spectral data of compounds of **21** and **22** (400 MHz, $CDCl_3$, TMS as int. standard)

	21	**22**
H-1α	1.80 *ddd*	2.38 *d(br)*
H-1β	1.61 *dd*	2.52 *dd*
H-2β	4.34 *dddd*	—
H-3α	1.97 *ddd*	2.95 *d(br)*
H-3β	2.06 *dd*	2.27 *dd*
H-5β	2.03 *dd*	2.47 *dd*
H-6α	1.5 *m*	1.53 *dddd*
H-6β	1.4 *m*	1.42 *d(br)*
H-7α	2.25 *ddd*	2.41 *ddd*
H-7β	2.05 *m*	2.11 *ddd*
H-9β		2.06 *dd(br)*
H-11	2.32 *m* 2.15 *m*	2.27 *m*
H-12	5.29 *t(br)*	5.27 *t(br)*
H-14	6.79 *ddd*	6.73 *ddd*
H-15*c*	5.10 *ddd*	5.12 *ddd*
H-15*t*	5.19 *d(br)*	5.21 *d(br)*
H-16	1.78 *ddd*	1.78 *ddd*
H-17	4.88 *d*	4.92 *d*
H-17′	4.53 *d(br)*	4.58 *s(br)*
H-18	1.38 *s*	1.16 *s*
H-20	1.02 *s*	0.72 *s*
OMe	3.68 *s*	3.72 *s*

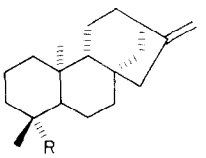
J (Hz): compound **21**: 1α, 1β = 14; 1α, 2β = 1β, 2β = 2β, 3α = 2β, 3β ~ 4; 1α, 3α = 1. 5; 3α, 3β = 14; 5β, 6α = 12; 5β, 6β = 3; 6α, 7α = 4.5; 6β, 7α = 2.5; 7α, 7β = 13; 11, 12 = 11′, 12 = 6.5; 11, 16 = 12, 14 = 12, 15*t* = 12, 15*c* = 12, 16 = 15*c*, 15*t* ~ 1; 17, 17′ = 1.5; compound **22**: 1α, 1β = 13; 1α, 3α = 2; 3α, 3β = 13; 5β, 6α = 6α, 6β = 6α, 7β = 12.5; 5β, 6β = 3; 6α, 7α = 4.5; 6β, 7α = 2.5; 6β, 7α = 2.5; 6β, 7β = 5; 7α, 7β = 13; 9, 11 = 4; 9, 11′ = 9; 11, 12 = 6.5; 11, 16 = 12, 14 = 12, 15*t* = 12, 15*c* = 12, 16 ~ 1; 14, 15*c* = 11; 14, 15*t* = 17; 15*c*, 15*t* = 1; 17, 17′ = 1.5.

The structure of **22** followed from the molecular formula and the ^{1}H NMR spectrum (Table 3), which was in part close to that of the methyl ester of **18** clearly indicating the presence of an ozic acid derivative. Spin decoupling showed that the double doublets at δ 2.52 and 2.27 were coupled with each other and geminal with two additional downfield shifted doublets at δ 2.38 and 2.95. Obviously these signals were those of H-1 and H-3. Accordingly, a keto group at C-2 was present. As followed from the IR spectrum, **21** had a hydroxyl group, while the molecular formula differed from that of **22** by two additional hydrogens. The ^{1}H NMR spectrum (Table 3) again was very similar to that of the ester of **18**. A quintet at δ 4.34 showed that an axial hydroxyl was present. As this signal was coupled with four neighbouring protons, the hydroxyl could only be placed at C-2. Accordingly, **21** was the dihydro derivative of **22**. The ^{1}H NMR spectrum of **25** (Table 4) showed that a hydroxy derivative of methyl-9,11-dehydro-*ent*-kaurenoate was present. The position of this group followed from the splitting of the signal of the proton under the hydroxyl, which indicated a position with two neighbours only. As one of the H-14 signals was shifted downfield the hydroxyl was placed at C-7. This was supported by spin decoupling which allowed the assignment of nearly all signals. Inspection of a model showed that the couplings observed required a twisted ring B, probably due to steric hindrance between the hydroxyl group and C-15. The ^{1}H NMR spectral data of **27** (Table 4), which was prepared from the corresponding acid **26** by esterification and acetylation, again showed that a derivative of **23** was present bearing an additional oxygen function. As in the case of **57**, this could only be placed axially orientated at C-1 or C-3, if the results of spin decoupling were considered. A clear decision again was not possible. As shown below, the co-occurrence of 3-

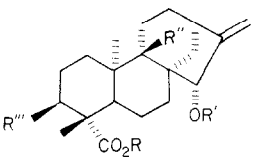
Table 4. ^{1}H NMR spectral data of compounds **25**, **27**, **29**, **32**, **44**, **48**, **50**, **52** and **54** (400 MHz, $CDCl_3$, TMS as int. standard)

	25	**27**	**29**	**32**	**44**	**48**	**50**	**52**	**54**
H-1	1.90 *d*(*br*)								
H-2	1.81 *ddddd* 1.49 *d*(*br*)	1.5 *m* 2.12 *m*	4.17 *dddd*						
H-3	2.17 *d*(*br*) 0.99 *ddd*	5.32 *dd*	2.27 *ddd* 1.00 *dd*	2.15 *d*(*br*) 1.00 *ddd*	2.15 *d*(*br*) 1.03 *ddd*	4.05 *s*(*br*)	4.05 *s*(*br*)	4.05 *s*(*br*)	2.17 *d*(*br*) 1.00 *ddd*
H-5	1.76 *dd*	1.95 *dd*		1.60 *dd*					
H-6	3.04 *ddd* 1.55 *ddd*	2.53 *ddd*(*br*) 1.77 *m*		2.47 *m* 1.85 *m*					
H-7	4.18 *dd*	1.3 *m* 2.1 *m*							
H-11	5.30 *dd*	5.25 *dd*	5.29 *dd*	5.33 *dd*					5.38 *dd*
H-12	2.44 *ddd* 2.01 *d*(*br*)	2.44 *ddd* 2.00 *d*(*br*)	2.42 *ddd* 1.99 *d*(*br*)	2.51 *dd* 2.21 *dd*					4.09 *s*(*br*)
H-13	2.81 *dd*	2.79 *s*(*br*)	2.77 *dd*(*br*)	—	2.74 *s*(*br*)	2.78 *s*(*br*)	2.78 *s*(*br*)	2.78 *s*(*br*)	
H-14	2.07 *dd*	1.62 *dd*	1.63 *dd*	1.68 *dd*	2.09 *d*(*br*)				1.75 *dd*
H-14′	1.34 *dd*	1.5 *m*	1.5 *m*	1.72 *dd*					1.65 *dd*
H-15	2.69 *ddd*	2.21 *ddd*	2.19 *ddd*	2.37 *ddd*	4.55 *s*(*br*)				2.00 *d*
H-15′	2.22 *d*(*br*)	2.64 *d*(*br*)	2.60 *d*(*br*)	2.63 *dddd*		5.96 *s*(*br*)	5.96 *s*(*br*)	6.00 *s*(*br*)	1.74 *d*
H-17	4.95 *s*(*br*)	4.95 *s*(*br*)	4.91 *s*(*br*)	5.14 *dd*(*br*)	5.23 *s*(*br*)	5.13 *s*(*br*)	5.15 *s*(*br*)	5.17 *s*(*br*)	2.92 *d*
H-17′	4.83 *s*(*br*)	4.84 *s*(*br*)	4.80 *s*(*br*)	4.87 *dd*(*br*)	5.10 *s*(*br*)	5.10 *s*(*br*)	5.10 *s*(*br*)	5.10 *s*(*br*)	2.78 *d*
H-18	1.18 *s*	1.17 *s*	1.26 *s*	1.18 *s*	1.21 *s*	1.28 *s*	1.28 *s*	1.28 *s*	1.18 *s*
H-20	0.89 *s*	0.95 *s*	0.95 *s*	0.94 *s*	0.99 *s*	0.99 *s*	0.99 *s*	0.99 *s*	0.99 *s*
OMe	3.66 *s*	3.68 *s*	3.66 *s*	3.66 *s*	3.65 *s*	3.65 *s*	3.65 *s*	0.65 *s*	3.66 *s*
OR						5.58 *dq*	6.83 *qq*	6.03 *qq*	
						2.19 *d*	1.83 *dq*	1.98 *dq*	
						1.90 *d*	1.79 *dq*	1.88 *dq*	

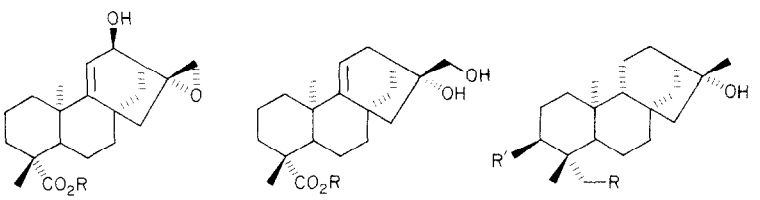
J (Hz) compounds **25**, **27** and **29**: 11, 12 = 4.5; 11, 12′ = 3; 12, 12′ = 16; 12, 13 = 2.5; 12′, 13 ~ 13, 14 = 5; 13, 14′ = 2.5; 14, 14′ = 10; 15, 15′ = 15; 15, 17 ~ 2; compound **25**: 1, 1′ = 2, 2′ = 13; 2, 3 ~ 3; 2, 3′ = 13; 2′, 3 ~ 3; 2′, 3′ = 3.5; 3, 3′ = 13; 5, 6 = 5, 6′ = 10; 6, 6′ = 13.5; 6, 7 = 6′, 7 = 9; compound **27**: 2, 3 = 2′, 3 = 2.5; 5, 6 = 10; 5, 6′ = 8; 6, 6′ = 13; 6, 7 = 10; 6′, 7 ~ 3; compound **29**: 1, 2 = 11; 1′, 2 = 4; 2, 3 = 4; 2, 3′ = 11; 3, 3′ = 12.5; compound **32**: 2, 3′ = 13; 2′, 3′ = 4; 3,3 = 13; 5,6 = 10; 5,6′ = 8; compounds **44** and **54**: 2′, 3 = 13; 2′, 3′ = 3.5; 3, 3′ = 13; compound **54**: 17, 17′ = 4.5; 11, 12 = 4; 11, 13 = 1; 13, 14 = 5; 13, 14′ = 2; 14, 14′ = 11.



35 R = CH_2OH
36 R = CHO
37 R = CO_2H



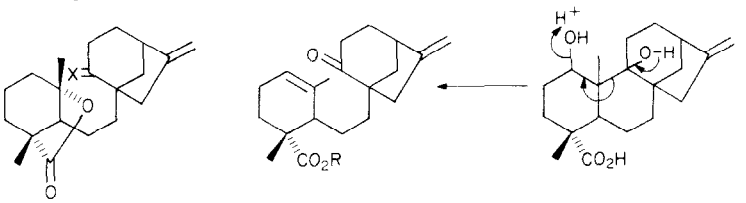
	38	39	40	41	42	43	44	45	46	47	48	49	50	50a	50b	51	52
R	H	H	H	H	H	H	Me	H	H	H	Me	H	Me	Me	Me	H	Me
R′	H	Sen	Tigl	Ang	*i*Val	H	H	Sen	Tigl	Sen	Sen	Tigl	Tigl	Tigl	Tigl	Ang	Ang
R″	H	H	H	H	H	OH	OH	OH	OH	OH	OH	OH	OH	OH	αOH	OH	OH
R‴	H	H	H	H	H	H	H	H	H	OH	OH	OH	OH	OAc	OH	OH	OH



53 R = H
54 R = Me

55 R = H
56 R = Me

57 R = H, R′ = OAc
58 R = OAc, R′ = H



59 X = O
60 X = H, β-OH
61 X = H, α-OH
62 X = H, β-OAc
63 X = H, α-OAc

64 R = H
65 R = Me

66

hydroxy-*ent*-kaurenic acid derivatives supported a 3-position. The molecular formula of **29** and the ^{1}H NMR spectrum (Table 4) indicated the presence of an isomer of **27**. As the signal of the proton under the hydroxy group was a fourfold doublet, the latter had to be placed at C-2, while the couplings required an equatorial orientation. Also, **32** was an isomer of **27** and **29**. The ^{1}H NMR spectrum (Table 4) showed no additional downfield signals. Accordingly, a tertiary alcohol was very likely. The absence of the typical H-13 signal clearly showed that a hydroxy group was at C-13. Spin decoupling allowed the assignment of most of the signals, which supported the proposed structures by the absence of couplings $J_{12,13}$ and $J_{13,14}$. The ^{1}H NMR spectral data of **44** clearly showed that it was the diol corresponding to the known esters **45** and **46**. Accordingly the H-15 signal was shifted upfield, while the other signals were nearly identical with those of **39–42**. The separation of the esters **48**, **50** and **52** caused difficulties, only **50** could be obtained pure. As followed from the ^{1}H NMR spectra (Table 4), they only differed in the nature of the ester group at C-15. From the typical signals, the presence of a senecioate, a tiglate and an angelate could be deduced. The spectra were close to those of **45** and **46**, indicating the same substitution except one additional hydroxy group. Spin decoupling showed that the corresponding proton under the hydroxy group was coupled with two hydrogens which were further coupled with two hydrogens. Accordingly, an axially orientated hydroxy group was at C-1 or C-3. If a 1-hydroxy derivative was present, an acetonide should be formed on treatment with acetone and acid. This reaction with **50**, however, led to **50b**, an isomer at C-9, as clearly followed from the differences in the ^{1}H NMR spectrum (see Experimental). As the deshielding effect of the 9β-OH group was missing, the H-15 signal was shifted upfield. Acetylation of **50**

Table 5. ^{1}H NMR spectral data of compounds **60–63** and **65** (400 MHz, $CDCl_3$ TMS as int. standard)

	60	61	62	63	65*
H-1					5.27 *s(br)*
H-9α	3.32 *dd*	—	4.82 *m*	—	—
H-9β	—	3.41 *s(br)*	—	4.82 *m*	—
H-13	2.57 *s(br)*	2.60 *dd(br)*	2.61 *s(br)*	2.63 *s(br)*	2.83 *s(br)*
H-15	2.40 *d(br)*	2.12 *dddd*	2.54 *d(br)*	2.18 *d(br)*	2.38 *d(br)*
H-15′	1.89 *d(br)*	2.07 *ddd*		2.09 *ddd*	2.28 *ddd(br)*
H17	4.81 *s(br)*	4.87 *s(br)*	4.82 *s(br)*	4.88 *s(br)*	5.03 *dd(br)*
H-17′	4.78 *s(br)*	4.81 *s(br)*	4.79 *s(br)*	4.82 *s(br)*	4.94 *s(br)*
H-18	1.20 *s*	1.20 *s*	1.16 *s*	1.14 *s*	1.16 *s*
H-20	1.42 *s*	1.42 *s*	1.38 *s*	1.36 *s*	1.76 *s(br)*
OAc	—	—	2.02 *s*	2.05 *s*	3.73 *s*

*H-11 2.24 (*dd, br*) and 2.38 (*m*).

J (Hz): compound **60**: 9α, 10α = 6; 10β = 10; 15, 15′ = 17; compound **61**: 12β, 13 = 13, 14β = 5; 14α, 15 = 15, 17 = 15, 17′ = 15′, 17 = 15′, 17′ = 2; 15, 15′ = 17; compound **65**: 11α, 11β = 16; 11α, 12α = 6; 15, 15′ = 16; 15′, 17 = 15′, 17′ = 2.

afforded **50a**. The observed upfield shift of H-18 (see Experimental) showed that the secondary hydroxy group was at C-3. The molecular formula and the ^{1}H NMR spectrum of **54** showed that an epoxide of **33** was present. The typical signals of the exomethylene protons were replaced by a pair of doublets at δ 2.92 and 2.78, while the other signals were close to those of **33**. The orientation of the epoxide group was deduced by comparison with other kauran epoxides with known configuration. In the ^{1}H NMR spectrum of **56** (see Experimental) the signals of the exomethylene protons were missing. The molecular formula clearly showed that two additional hydroxy groups were present, while the ^{1}H NMR spectrum indicated that a diol, formed via the epoxide of **23**, had to be proposed. Though the stereochemistry at C-16 could not be determined, the proposed one is very likely from biogenetic considerations as the diol surely was formed via an epoxide.

The investigation of a second collection of *I. terminalis* mainly gave the same compounds, but a few different ones were isolated (see Experimental). A prominent constituent of the aerial parts was the lactone **59** [14], which was accompanied with the epimeric alcohols **60** and **61**. The structure of **60** and **61** were established by reduction of **59**, which afforded the same mixture. The separation of **60** and **61** as well as of their acetates **62** and **63** was not possible. The ^{1}H NMR spectra, however, could be assigned from the mixtures (Table 5). The structure of **65**, obtained by esterification of the natural acid, also followed from the ^{1}H NMR spectrum (Table 5). Spin decoupling allowed the assignment of H-1–H-3 and H-20, while the remaining signals were nearly identical with those of **59**. The structure was further supported by the mass spectrum which showed in addition to the usual fragments (*m/z* 312 $[M-H_2O]^+$, 298 $[M-MeOH]^+$, 270 $[298-CO]^+$, 253 $[312-CO_2Me]^+$) a strong fragment *m/z* 163, obviously formed by splitting the 5,6-bond followed by elimination of methanol (*m/z* 121). **64** probably is formed by fragmentation of the so far unknown diol **66**. **64** we have named terminalic acid.

The aerial parts of *Ichthyothere ulei* Thunb. afforded germacrene D, bicyclogermacrene, α-humulene, squalene, *ent*-kaurenal (**36**), *ent*-kaurenic acid (**37**), and its derivatives **39–41**, **43**, **45** and **46** as well as the acanthospermal derivative **9** and the lactones **10** and **12–16**, all derived from geranylnerol. The structure of **9** followed from the ^{1}H NMR spectrum (Table 2), as all signals were close to those of acanthospermal A [15], except those of the ester part, which was easily deduced to be a hydroxymethacrylate. The structure of **10**, molecular formula $C_{20}H_{30}O_3$, followed from the ^{1}H NMR spectral data (Table 6) and from those of the corresponding aldehyde **11**, obtained by oxidation of **10**. Starting with the irradiation of the most downfield shifted signal at δ 6.55 the nature of a six membered lactone ring could be established, its presence already was supported by the IR spectrum. The position of this ring could be deduced by spin decoupling of **11**. Irradiation of the signal of the aldehyde proton collapsed the broadened doublet at δ 5.90 to a singlet. The corresponding proton was further coupled with a doublet at δ 2.00 and showed an allylic coupling with a pair of double triplets, which were coupled with a broadened doublet triplet at δ 2.33. Irradiation at δ 5.53 collapsed the latter to a triplet and sharpened the signal of the proton under the lactone oxygen. Thus the whole sequence of H-1–H-10 was established. Further decouplings allowed the assignment of all signals. The configuration of the 2,3-double bond followed from the chemical shift of H-20. Comparing the ^{1}H NMR spectral data of **12** with those of **10** (Table 6) showed that the C-7 methyl was transformed to an acetoxy methylene group. Accordingly, **12** was the 19-acetoxy derivative of **10**, which we have named ichthyouleolide. The hydroperoxide **13** gave no molecular ion, however, reaction with triphenylphosphine afforded the diol **14**, which also only showed a $[M-H_2O]^+$ peak in the mass spectrum. The ^{1}H NMR spectra of **13** and **14**, however, clearly showed that in addition to the lactone ring two oxygen functions were present. Again spin decoupling allowed the assignment of all signals. The position of the 13,14-double bond followed from the chemical shift of the broadened doublet at δ 3.07 and 3.02 respectively, while that of the hydroperoxide

Table 6. ^{1}H NMR spectral data of compounds **10–17** (400 MHz, $CDCl_3$, TMS as int. standard)

	10	**11**	**12**	**13**	**14**	**15**	**16**	**17**
H-1	4.11 *dq*	9.90 *d*	4.10 *d(br)*	4.11 *d(br)*	4.11 *d(br)*	4.11 *d(br)*	4.12 *d(br)*	9.90 *d*
H-2	5.45 *tq*	5.90 *d(br)*	5.48 *t(br)*	5.46 *tq*	5.45 *t(br)*	5.46 *t(br)*	5.47 *t(br)*	5.90 *d*
H-4	2.16 *m*	2.67 *dt*	2.17 *m*	2.16 *m*	2.16 *m*	2.17 *m*	2.17 *m*	2.66 *dt*
H-5		2.62 *dt*						2.64 *dt*
		2.33 *dt(br)*						2.33 *dt*
H-6	5.52 *tq(br)*	5.53 *t(br)*	5.89 *t(br)*	5.54 *tq(br)*	5.53 *t(br)*	5.53 *t(br)*	5.54 *t(br)*	5.52 *t(br)*
H-8	4.68 *dd(br)*	4.68 *dd(br)*	4.83 *dd(br)*	4.74 *dd(br)*	4.72 *dd*	4.73 *dd(br)*	4.73 *dd*	4.70 *dd*
H-9	5.52 *ddddd*	2.49 *ddddd*	2.55 *dd(br)*	2.57 *dddt*	2.55 *ddd*	2.54 *ddddd*	2.56 *ddddd*	2.50 *m*
H-9′	2.25 *ddd(br)*	2.22 *m*	2.3 *m*	2.30 *ddd(br)*	2.28 *ddd(br)*	2.28 *ddd(br)*	2.29 *ddd(br)*	2.25 *m*
H-10	6.55 *ddt*	6.55 *d(br)*	6.56 *d(br)*	6.61 *ddt*	6.56 *dd(br)*	6.60 *m*	6.64 *d(br)*	6.68 *dd*
H-12	2.38 *dt(br)*	2.38 *m*	2.37 *m*	3.07 *d(br)*	3.02 *d(br)*	2.44 *dt(br)*	2.35	2.40
H-12′	2.25 *dt(br)*	2.28 *m*	2.3 *m*			2.33 *dt(br)*	2.50 *m*	2.50 *m*
H-13	2.16 *m*	2.17 *dt*	2.17 *m*	5.74 *dt*	5.65 *dt*	1.76 *m*	1.76 *m*	2.96 *dt*
								2.94 *dt*
H-14	5.09 *tqq*	5.09 *tqq*	5.09 *t(br)*	5.64 *d*	5.71 *d*	4.33 *t*	4.08 *t(br)*	—
H-16	1.60 *s(br)*	1.60 *s(br)*	1.61 *s(br)*	1.36 *s*	1.32 *s*	1.76 *s(br)*	1.77 *s(br)*	1.87 *s(br)*
H-17	1.69 *s(br)*	1.69 *s(br)*	1.70 *s(br)*			5.02 *s(br)*	4.98 *s(br)*	5.99 *s(br)*
							4.87 *s(br)*	5.78 *s(br)*
H-19	1.71 *d(br)*	1.71 *s(br)*	4.75 *d*	1.72 *d*	1.71 *s(br)*	1.71 *s(br)*	1.73 *s(br)*	1.70 *s(br)*
			4.70 *d*					
H-20	1.75 *dt*	2.00 *d*	1.76 *d*	1.76 *d*	1.76 *s(br)*	1.76 *s(br)*	1.76 *s(br)*	1.99 *d*
OAc	—	—	2.07 *s*	—	—	—	—	—

J(Hz): 1, 2 = 5, 6 = 12, 13 = 12′, 13 = 13, 14 = 7; 1, 20 = 0.8; 2, 20 = 1.5; 6, 19 = 1.2; 9 = 12; 8, 9′ = 3.5; 9, 9′ = 18; 9, 10 = 9, 12 = 9, 12′ = 2; 9′, 10 = 6.5; 10, 12 = 10, 12′ = 1.5; 12, 12′ = 15; 14, 16 = 14, 17 = 1.4; compound **11**: 1, 2 = 7.5; 4, 4′ = 15; compounds **13** and **14**: 13, 14 = 16; compounds **15** and **16**: 13, 14 = 7; compound **17**: 1, 2 = 7.5; 4, 4′ = 15; 12, 13 = 7; 13, 13′ = 14.

group could be deduced from the shift differences observed for H-13, H-14, H-16 and H-17. As all the other signals were the same as those of **10**, identical structure and configuration were obvious. The spectral data of **15** and **16** showed that again a hydroperoxide and the corresponding alcohol were present. Oxidation of the latter afforded the keto aldehyde **17**, its ^{1}H NMR spectrum clearly showed that **16** was an isomer of **14** (Table 6) formed by allylic rearrangement. Accordingly, the signal of the olefinic methylene protons were shifted downfield in the spectrum of **17**. Again all signals in the spectra of **15–17** could be assigned by spin decoupling.

The overall picture of the chemistry of the genus *Ichthyothere* showed that a large variety of diterpenes is typical. The isolation of the melampolides supports the placement of this genus in the subtribe Melampodinae. So far these compounds have only been isolated from one *Siegesbeckia* species, placed in the Millerinae [3, 6, 7], while the other genera have no lactones of this type. However, the diterpenes from this genus are pimarane derivatives [16]. In the genus *Smallanthus*, also placed in the Melampodinae [3], melampolides and *ent*-kaurene derivatives are widespread [18–20]. The latter are present in large quantities in the subtribe Espeletiinae. Lactones derived from geranylgeraniol have been isolated from *Acanthospermum* [21], which also contains melampolides. Ichthyotherol [6] was not isolated. Probably it was destroyed as the *Ichthyothere* species are rather succulent in the field and quickly blacken on drying. However, this compound has been isolated from very different genera, in part belonging to other tribes. Therefore the reliability of a close relationship of *Ichthyothere* and *Clibadium* raises serious questions.

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil, was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated first by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the ^{1}H NMR spectra with those of authentic compounds. Probably several of the new compounds are crystalline, but due to the minute amounts no crystals were obtained.

Ichthyothere terminalis (*voucher RMK* 8630). The roots (40 g) afforded 50 mg germacrene D, 5 mg bicyclohermacrene, 5 mg β-eudesmene, 5 mg biformene, 20 mg cyperene (**4**), 20 mg **18**, 2 mg **35**, 10 mg **36**, 80 mg **36**, 10 mg **39**, 20 mg **42**, 20 mg **57** (Et_2O–petrol, 3:1) and 5 mg **58**, while the aerial parts (400 g) gave 200 mg germacrene D, 20 mg bicyclogermacrene, 2 mg **1** (Et_2O–petrol, 1:1), 15 mg **2** (AcOEt), 2 mg **6** (C_6H_6–CH_2Cl_2–Et_2O, 4:4:1), 5 mg **7** (same solvent), 50 mg **18**, 5 mg **19** and 5 mg **20**, which were converted to Me esters by addition of CH_2N_2 (sepn: Et_2O–petrol, 1:2), 500 mg **23**, 10 mg **24**, 5 mg **26**, 5 mg **28** and 5 mg **31** (separated as their Me esters **25**, **27**, **29** and **32**, Et_2O–petrol, 1:2), 5 mg **30**, 80 mg **33**, 40 mg **34**, 50 mg **37**, 10 mg **39**, 60 mg **40**, 50 mg **45**, 350 mg **47** and further acids, which after addition of CH_2N_2 afforded 5 mg **44**, 4 mg **48**, 15 mg **50**, 5 mg **52**, 10 mg **54** and 5 mg **56** (separated by repeated TLC: Et_2O–petrol, 4:1 and C_6H_6–CH_2Cl_2–Et_2O, 2:2:1).

Second collection (*voucher RMK* 8742). The roots (40 g) gave germacrene D, 7 mg bicyclogermacrene, 30 mg **35**, 100 mg **36**, 340 mg **37**, 15 mg **38** and 15 mg **39**, **40** and **42** (*ca* 1:1:1), while the aerial parts (100 g) afforded 400 mg germacrene D, 50 mg bicyclogermacrene, 100 mg **5**, 700 mg **23**, 10 mg **33**, 3 mg **34**, 100 mg **37**, 3 mg **38**, 100 mg **40**, 300 mg **59**, 6 mg **60**, 2 mg **61** and 10 mg **64** (isolated as its Me ester **65**) (**60**, **61** and **65** were separated by TLC using C_6H_6–CH_2Cl_2–Et_2O, 4:4:1).

Ichthyothere ulei (*voucher RMK* 8916). The aerial parts (160 g) gave 80 mg germacrene D, 30 mg bicyclogermacrene, 10 mg α-humulene, 20 mg squalene, 5 mg **9** (C_6H_6–Et_2O, 1:1), 7 mg **10** and 1 mg **12** (C_6H_6–Et_2O, 1:1), 3 mg **13**, 1 mg **14**, 3 mg **15**, 1 mg **16** (**13–16** separated with C_6H_6–Et_2O, 1:1), 10 mg **36**, 260 mg **37**, 100 mg **39–41** (*ca* 1:1:5), 5 mg **43**, 4 mg **45** and 15 mg **46**.

1-*Hydroxy-pinan*-3-*one* (**1**). Colourless oil, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3610 (OH), 1710 (C=O); MS *m/z* (rel. int.): 168.115 [M]$^+$ (8) ($C_{10}H_{16}O_2$), 150 [M–H_2O]$^+$ (9), 135 [150–Me]$^+$ (10), 110 [M–MeC(OH)CH_2]$^+$ (60), 95 [110–Me]$^+$ (100), 82 [110–CO]$^+$ (87).

10-*Hydroxyborneol* (**2**). Colourless crystals, mp 275° IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3640 (OH); MS *m/z* (rel. int.): 139 [M–CH_2OH]$^+$ (31), 121 [139–H_2O]$^+$ (32), 108 [139–CH_2OH]$^+$ (100). 5 mg **2** was heated 1 hr with 0.1 ml Ac_2O at 70° affording 5 mg **3**, MS *m/z* (rel. int.): 195.139 [M–OAc]$^+$ (54), 135 [195–HOAc]$^+$ (44), 57 (100).

2α-*Hydroxylongipilin acetate* (**6**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1785 (γ-lactone), 1740 (OAc), 1725 (C=CCO_2R); MS *m/z* (rel. int.): 346.116 [M–AngOH]$^+$ (3) ($C_{18}H_{20}O_8$), 83 [C_4H_7CO]$^+$ (100), 55 [83–CO]$^+$ (81).

Ichthyotherminolide (**7**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1790 (γ-lactone), 1740 (OAc), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 462 [M]$^+$ (0.2), 402.132 [M–HOAc]$^+$ (3) ($C_{21}H_{22}O_8$), 320 [402–O=C=C(Me)CH=CH_2]$^+$ (12), 302 [402–AngOH]$^+$ (4), 270 [302–MeOH]$^+$ (5), 242 [270–CO]$^+$ (6), 83 [C_4H_7CO]$^+$ (100), 55 [83–CO]$^+$ (62);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-25 \quad -30 \quad -34 \quad -61} \; (c = 0.3, CHCl_3).$$

5 mg **7** on heating with 0.1 ml Ac_2O at 70° (1 hr) afforded 5 mg **8**, colourless gum, ^{1}H NMR see Table 2.

8-*Desacylacanthospermal*[4-*hydroxymethacrylate*] (**9**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1785 (γ-lactone), 1740 (OAc), 1725 (C=CCO_2R, C=CCHO); MS *m/z* (rel. int.): 404.147 [M]$^+$ (0.3) ($C_{21}H_{24}O_8$), 344 [404–HOAc]$^+$ (3), 242 [344–RCO_2H]$^+$ (28), 85 [RCO]$^+$ (100), 57 [85–CO]$^+$ (28).

Ichthyouleolide (**10**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1730 (δ-lactone); MS *m/z* (rel. int.): 300.209 [M–H_2O]$^+$ (10) ($C_{20}H_{28}O_2$), 285 [300–Me]$^+$ (1.5), 231 [300–CH_2CH=CMe_2]$^+$ (17), 69 [C_5H_9]$^+$ (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-33.6 \quad -34.2 \quad -40.3 \quad -81.3} \; (c = 0.67, CHCl_3).$$

5 mg **10** were stirred with 50 mg MnO_2 for 4 hr, TLC (Et_2O–petrol, 1:2) afforded 3 mg **11**, colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1730 (δ-lactone), 2730, 1680 (C=CCHO); ^{1}H NMR see Table 6.

10-*Acetoxyichthyouleolide* (**12**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1730 (OAc, δ-lactone); MS (CI, isobutane) *m/z* (rel. int.): 359 [M + 1–H_2O]$^+$ (23), 299 [359–HOAc]$^+$ (100), 281 [299–H_2O]$^+$ (25).

15-*Peroxy*-13, 14t-*dehydro*-14, 15-*dihydroichthyouleolide* (**13**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3520 (OH), 1730 (δ-

lactone); MS *m/z* (rel. int.): 332 $[M-H_2O]^+$ (0.5), 317.212 $[M-O_2H]^+$ (1.5) ($C_{20}H_{29}O_3$), 298 $[332-H_2O_2]^+$ (3), 55 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{-8}\ \frac{578}{-8}\ \frac{546}{-13}\ \frac{436\text{ nm}}{-16}\ (c = 0.2, CHCl_3).$$

To 3 mg **13** in 0.5 ml $CDCl_3$ 10 mg triphenylphosphine was added. After 5 min the ^1H NMR spectrum was identical with **14**.

15-*Hydroxy*-13, 14t-*dehydro*-14, 15-*dihydroichthyouleolide* (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3610 (OH), 1730 (δ-lactone); MS *m/z* (rel. int.): 316.204 $[M-H_2O]^+$ (0.5) ($C_{20}H_{28}O_3$), 298 $[316-H_2O]^+$ (14), 229 $[298-CH_2CH{=}CMe_2]^+$ (20), 55 (100).

14-*Peroxy*-15, 17-*dehydro*-14, 15-*dihydroichthyouleolide* (**15**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3620, 3520 (OH), 1735 (δ-lactone); MS *m/z* (rel. int.): 350 $[M]^+$ (0.1), 332 $[M-H_2O]^+$ (0.3), 317.212 $[M-O_2H]^+$ (0.3), 314 $[332-H_2O]^+$ (0.5), 298 $[332-H_2O_2]^+$ (1), 229 $[298-CH_2CH{=}CMe_2]^+$ (15), 55 (100).

3 mg **15** were transformed to **16** by addition of triphenylphosphine.

14-*Hydroxy*-15, 17-*dehydro*-14, 15-*dihydroichthyouleolide* (**16**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1735 (δ-lactone); MS *m/z* (rel. int.): 316.204 $[M-H_2O]^+$ (1) ($C_{20}H_{28}O_3$), 298 $[316-H_2O]^+$ (3), 55 (100). 2 mg **16** on oxidation with MnO_2 in Et_2O (2 hr) afforded 1 mg **17**, colourless gum; ^1H NMR see Table 6.

2α-*Hydroxy*-12, 13Z-*ozic acid methylester* (**21**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1720, 1240 (equatorial CO_2R); MS *m/z* (rel. int.): 332.235 $[M]^+$ (5) ($C_{21}H_{32}O_3$), 314 $[M-H_2O]^+$ (4), 300 $[M-MeOH]^+$ (2), 285 $[300-Me]^+$ (2), 272 $[300-CO]^+$ (5), 55 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{-20}\ \frac{578}{-21}\ \frac{546}{-23}\ \frac{436\text{ nm}}{-47}\ (c = 0.1, CHCl_3).$$

2-*Oxo*-12, 13Z-*ozic acid methylester* (**22**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1730 (C=O), 1720 (CO_2R); MS *m/z* (rel. int.): 330.219 $[M]^+$ (26) ($C_{21}H_{30}O_3$), 299 $[M-OMe]^+$ (16), 271 $[M-CO_2Me]^+$ (10), 55 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{-11}\ \frac{578}{-11}\ \frac{546}{-12}\ \frac{436\text{ nm}}{-40}\ (c = 0.2, CHCl_3).$$

Methyl-7β-*hydroxy*-9(11)-*dehydro*-ent-*kaurenoate* (**25**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1730 (CO_2R); MS *m/z* (rel. int.): 330.220 $[M]^+$ (58), 315 $[M-Me]^+$ (26), 312 $[M-H_2O]^+$ (30), 271 $[M-CO_2Me]^+$ (16), 253 $[271-H_2O]^+$ (43), 162 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{+11.3}\ \frac{578}{+11.6}\ \frac{546}{+15.6}\ \frac{436\text{ nm}}{+32.0}\ (c = 0.3, CHCl_3).$$

Methyl-3β-*acetoxy*-9(11)-*dehydro*-ent-*kaurenoate* (**27**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1735 (OAc, CO_2R); MS *m/z* (rel. int.): 372.230 $[M]^+$ (18) ($C_{23}H_{32}O_4$), 357 $[M-Me]^+$ (10), 312 $[M-HOAc]^+$ (67), 297 $[312-Me]^+$ (100), 237 $[297-HCO_2Me]^+$ (71);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{+15}\ \frac{578}{+17}\ \frac{546}{+23}\ \frac{436\text{ nm}}{+44}\ (c = 0.1, CHCl_3).$$

Methyl-2β-*hydroxy*-9(11)-*dehydro*-ent-*kaurenoate* (**29**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1730 (CO_2R); MS *m/z* (rel. int.): 330.215 $[M]^+$ (25) ($C_{21}H_{30}O_3$), 315 $[M-Me]^+$ (26), 312 $[M-H_2O]^+$ (21), 297 $[312-Me]^+$ (14), 284 $[312-CO]^+$ (14), 271 $[M-CO_2Me]^+$ (12), 253 $[271-H_2O]^+$ (38), 237 $[297-HCO_2Me]^+$ (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{+6}\ \frac{578}{+7}\ \frac{546}{+12}\ \frac{436\text{ nm}}{+20}\ (c = 0.2, CHCl_3).$$

Methyl-13α-*hydroxy*-9(11)-*dehydro*-ent-*kaurenoate* (**32**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1725 (CO_2R); MS *m/z* (rel. int.): 330.215 $[M]^+$ (31) ($C_{21}H_{30}O_3$), 315 $[M-Me]^+$ (63), 271 $[M-CO_2Me]^+$ (19), 255 $[315-HCO_2Me]^+$ (75), 91 (100);

$$[\alpha]_{24°}^{\lambda} = \frac{589}{+7}\ \frac{578}{+8}\ \frac{546}{+12}\ \frac{436\text{ nm}}{+22}\ (c = 0.3, CHCl_3).$$

Methyl-9β-*hydroxygrandiflorate* (**44**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1720 (CO_2R); MS *m/z* (rel. int.): 348.230 $[M]^+$ (15) ($C_{21}H_{32}O_4$), 330 $[M-H_2O]^+$ (41), 312 $[330-H_2O]^+$ (15), 299 $[330-OMe]^+$ (12), 271 $[330-CO_2Me]^+$ (25), 253 $[271-H_2O]^+$ (15), 148 (100), 91 (78), 55 (84).

Methyl-3β,9β-*dihydroxy*-15α-*senecioyloxy and angeloyloxy*-ent-*kaurenoate* (**48** *and* **52**). Colourless gum, which could not be separated, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3500 (OH), 1730 (CO_2R), 1720, 1650 (C=CCO$_2$R); MS *m/z* (rel. int.): 446 $[M]^+$ (0.1), 346.214 $[M-RCO_2H]^+$ (3) ($C_{21}H_{28}O_4$), 328 $[346-H_2O]^+$ (8), 314 $[346-MeOH]^+$ (1), 269 $[328-CO_2Me]^+$ (5), 83 $[C_4H_7CO]^+$ (100).

Methyl-3β, 9β-*dihydroxy*-15α-*tiglinoyloxy*-ent-*kaurenoate* (**50**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3500 (OH), 1730 (CO_2R), 1720, 1650 (C=CCO$_2$R); MS *m/z* (rel. int.): 446 $[M]^+$ (0.1), 346.214 $[M-RCO_2H]^+$ (3) ($C_{21}H_{28}O_4$), 296 $[328-MeOH]^+$ (4), 286 $[346-HCO_2Me]^+$ (3), 268 $[296-CO]^+$ (4), 83 $[C_4H_7CO]^+$ (100). $[\alpha]_D - 21°$ ($c = 1.0$, $CHCl_3$).

5 mg **50** was heated for 1 hr with 0.1 ml Ac_2O. TLC (Et_2O–petrol, 3:1) afforded 3 mg **50a**, colourless gum, ^1H NMR ($CDCl_3$): 5.29 (*dd*, H-3, $J = 2.5, 2.5$), 1.14 (*s*, H-18), 0.99 (*s*, H-20) (other signals nearly identical with those of **50**).

To 5 mg in 1 ml Me_2CO 10 mg *p*-toluene sulfonic acid was added. After 12 hr TLC (Et_2O) afforded 3 mg **50b**, colourless gum; MS *m/z* (rel. int.): 428 $[M-H_2O]^+$ (0.5), 328 $[428-RCO_2H]^+$ (95), 310 $[328-H_2O]^+$ (52), 295 $[310-Me]^+$ (22), 269 $[328-CO_2Me]^+$ (44), 251 $[269-H_2O]^+$ (100); ^1H NMR ($CDCl_3$): 5.56 [*s* (*br*), H-15], 5.11 [*s* (*br*)] and [*s* (*br*)] (H-17), 1.26 (*s*, H-18), 1.13 (*s*, H-20) (other signals nearly identical with those of **50**).

Methyl-12β-*hydroxy*-16α, 17-*epoxy*-16, 17-*dihydro*-9(11)-*dehydro*-ent-*kaurenoate* (**54**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1720 (CO_2R); MS *m/z* (rel. int.): 346.214 $[M]^+$ (3) ($C_{21}H_{30}O_4$), 328 $[M-H_2O]^+$ (5), 300 $[328-CO]^+$ (3), 287 $[M-CO_2Me]^+$ (15), 269 $[287-H_2O]^+$ (15), 107 (93), 91 (100).

Methyl-16α, 17-*dihydroxy*-16, 17-*dihydro*-9(11)-*dehydro*-ent-*kaurenoate* (**56**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3400 (OH), 1730 (CO_2R); MS *m/z* (rel. int.): 348.230 $[M]^+$ (7) ($C_{21}H_{32}O_4$), 330 $[M-H_2O]^+$ (74), 315 $[330-Me]^+$ (68), 299 $[330-OMe]^+$ (30), 289 $[M-CO_2Me]^+$ (9), 271 $[289-H_2O]^+$ (32), 91 (88), 55 (100); ^1H NMR ($CDCl_3$): 2.25 [*d* (*br*), H-3], 1.01 (*ddd*, H-3', $J = 13, 13, 4$), 5.15 (*dd*, H-11, $J = 4, 1$), 3.65 *d* and 3.54 (*d*, H-17, $J = 11$), 1.17 (*s*, H-18), 0.91 (*s*, H-20), 3.65 (*s*, OMe).

3β-*Acetoxy*-16-*hydroxy*-ent-*kaurane* (**57**). Colourless crystals, mp 185°, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1740 (OAc); MS *m/z* (rel. int.): 348.266 $[M]^+$ (3) ($C_{22}H_{36}O_3$), 330 $[M-H_2O]^+$ (22), 288 [330–ketene]$^+$ (64), 270 $[330-HOAc]^+$ (88), 255 $[270-Me]^+$ (65), 230 $[288-CH_2C(OH)Me]^+$ (81), 215 $[230-Me]^+$ (48), 136 (94), 121 (100); ^1H NMR ($CDCl_3$): 1.91 (*dddd*,

H-2, J = 12, 13, 4.5, 2.5), 160 (*m*, H-2), 4.62 (*dd*, H-3, J = 2.5, 2.5), 1.83 [*d* (*br*), H-14, J = 13], 1.36 (*s*, H-17), 1.04 (*s*, H-18), 0.82 (*s*, H-19), 0.87 (*s*, H-20), 2.04 (*s*, OAc).

9α- and 9β-hydroxy-9-desoxo-wedelia-seco-kaurenolide (**60** *and* **61**). Colourless gum, which could not be separated, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 318.220 $[M]^+$ (61) ($C_{20}H_{30}O_3$), 300 $[M-H_2O]^+$ (53), 282 $[300-H_2O]^+$ (50), 274 $[M-CO_2]^+$ (12), 256 $[274-H_2O]^+$ (11), 163 (100), 146 (77), 123 (76), 109 (73), 91 (75), 81 (74), 67 (58), 55 (98). 15 mg **60** and **61** were heated for 2 hr with 1 ml Ac_2O at 70°. TLC afforded 12 mg **62** and **63**, which also could not be separated; ^1H NMR see Table 5. 25 mg **59** on reduction with $NaBH_4$ afforded 20 mg of a mixture of **60** and **61** (*ca* 3:1), which again could not be separated. The ^1H NMR spectrum was identical with that of the natural mixture.

Methyl terminaloate (**65**). Colourless gum, IR $\nu_{max}^{CCl_4}$, cm^{-1}: 1730 (CO_2R), 1720 (C=O); MS *m/z* (rel. int.): 330.220 $[M]^+$ (12) ($C_{21}H_{30}O_3$), 312 $[330-H_2O]^+$ (46), 270 $[M-HCO_2Me]^+$ (100), 253 $[312-CO_2Me]^+$ (44), 163 (82), 121 (91), 107 (93);

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+25 \quad +26 \quad +29 \quad +43} \quad (c = 0.7,\ CHCl_3).$$

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