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SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM *SCHISTOSTEPHIUM* SPECIES*

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Key Word Index—*Schistostephium artemisiifolium*; *S. crataegifolium*; *S. heptalobum*; *S. rotundifolium*; Compositae; Anthemideae; sesquiterpenes; sesquiterpene lactones; eudesmanolides; germacranolides; prostaglandin-like acid.

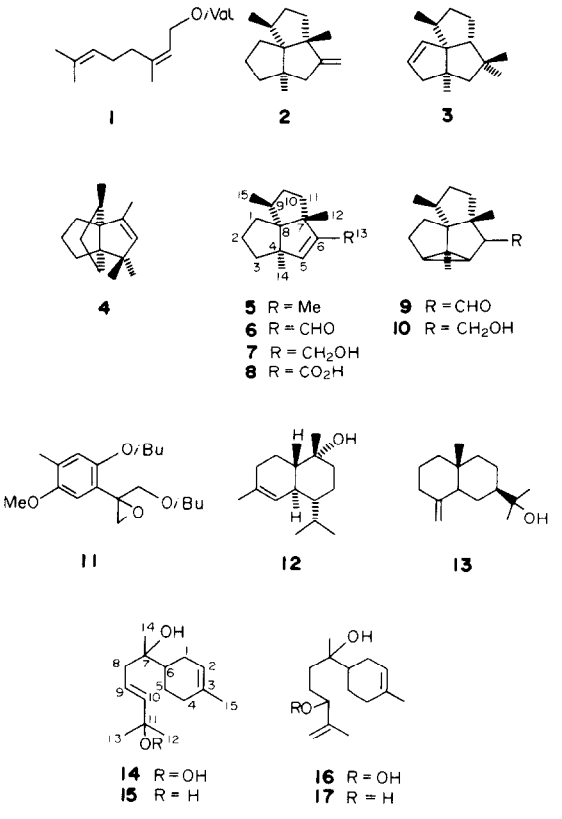
Abstract—From four *Schistostephium* species, in addition to known compounds, 43 new ones were isolated, three isocomene, two bisabolene, two eudesmane, two allo-himachalene and two nerolidol derivatives, two sesquiterpenes with a new carbon skeleton derived from isocomene, nine eudesmanolides, 20 6,12- and 8,12-germacranolides respectively, and a prostaglandin-like acid. The structures were elucidated by spectroscopic methods, especially high field ^{1}H NMR and some chemical transformations. The stereochemistry of some 8,12-germacranolides was established by partial synthesis which required revision of the previous assignments of the configuration of inunolide, its 4,5- and 1,10-epoxide, vernudifloride, simsiolide, 6-hydroxy-1,10-epoxyinunolide and perhaps also of tanachin. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

So far nothing is known on the chemistry of the South African composite genus *Schistostephium*, which is placed in tribe Anthemideae. Also, no taxonomic investigations are reported concerning relationships to other genera in the Anthemideae. We now have studied four species to see whether the chemistry shows indications of relationships to other South African genera of this tribe. The results are discussed in this paper.

RESULTS AND DISCUSSION

The roots of *Schistostephium artemisiifolium* Bak. afforded α-humulene, squalene, caryophyllen-1,10-epoxide, α-humulen-1,10-epoxide, β-isocomene (**2**) [1], silphinene (**3**) [2], modhephene (**4**) [3], isocomene (**5**) [4], dehydrofalcarinol (**25**) [5] and four substituted polycyclic sesquiterpenes, the isocomene derivatives, **6**–**8**, and the tetracyclic aldehyde, **9**. The structure of **6** was deduced from the molecular formula and the ^{1}H NMR spectrum (Table 1), which was close to that of **5**. Also, the ^{13}C NMR signals were in agreement with the proposed structure. In the ^{1}H NMR spectrum the H-5 signal was shifted downfield, while the chemical shifts of C-5, C-6 and C-13 in the ^{13}C NMR spectrum clearly indicated the presence of a conjugated aldehyde. Boranate reduction afforded the alcohol, **7**, whose ^{1}H NMR spectrum was identical with that of the natural compound. The ^{1}H NMR spectral data of **8** were close to those of **6**, but the signal of the aldehyde proton was missing. As already indicated by the molecular formula and the IR spectrum, the presence of the corresponding acid was obvious. The ^{1}H NMR spectral data of **9** and those of the corresponding alcohol, **10** (Table 2), obtained by reduction of **9**, together with the molecular formula indicated a tetracyclic sesquiterpene



* Part 462 in the series "Naturally Occurring Terpene Derivatives". For Part 461 see Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. *Phytochemistry* (in press).

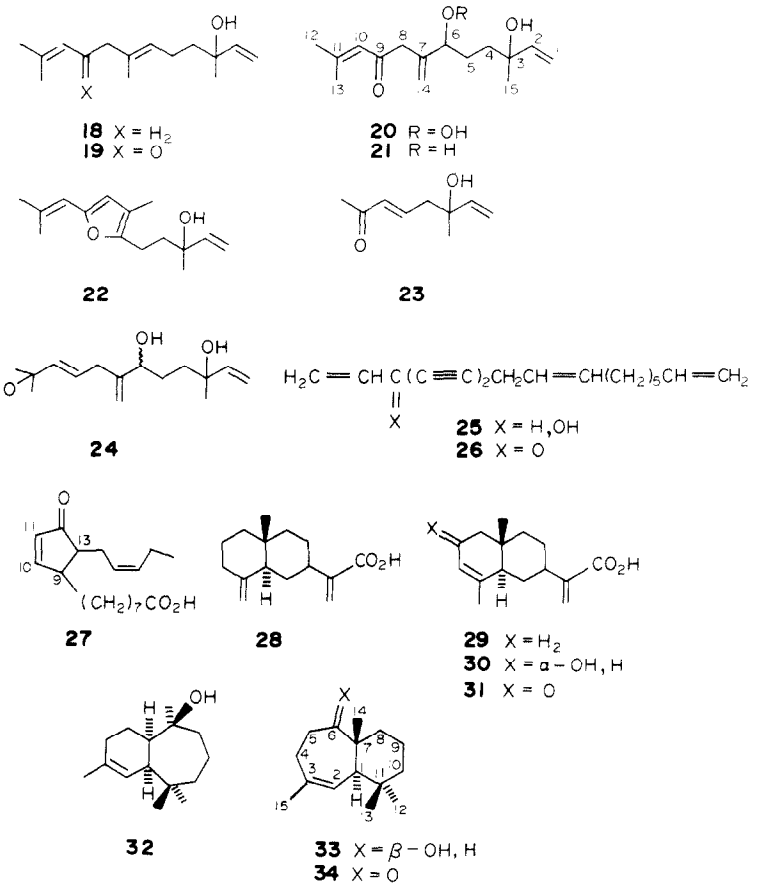


Table 1. ^{1}H NMR spectral data of compounds **6**–**8** (400 MHz, $CDCl_3$, TMS as internal standard) and ^{13}C NMR of **6**

	6	**7**	**8**	**6** ^{13}C NMR	
H-1α	1.16 *ddd*	—	1.18 *ddd*	C-1	24.3 *t*
H-1β	1.82 *m*	—	—	C-2	32.2 *t*
H-2α	1.75 *br dd*	—	1.72 *br dd*	C-3	42.2 t
H-2β	1.39 *dddd*	—	1.41 *ddd*	C-4	57.3 *s*
H-3α	1.54 *br ddd*	—	1.50 *ddd*	C-5	138.2 *d*
H-3β	1.82 *m*	—	1.82 *br dd*	C-6	149.8 *s*
H-5	6.34 *s*	5.18 *dd*	6.52 *s*	C-7	66.4 *s*
H-6	2.00 *ddq*	2.01 *ddq*	2.01 *ddq*	C-8	58.2 *s*
H-10α	1.48 *dddd*	—	1.53 *dddd*	C-9	39.3 *d*
H-10β	1.30 *dddd*	—	1.27 *dddd*	C-10	33.0 *t*
H-11α	1.82 *ddd*	—	1.91 *ddd*	C-11	38.2 *t*
H-11β	1.65 *ddd*	—	1.63 *ddd*	C.12	22.5 *q*
H-12	1.30 *s*	1.08 *s*	1.29 *s*	C-13	190.3 *d*
H-13	9.62 *s*	4.13 *d*	—	C-14	22.7 *q*
H-14	1.16 *s*	1.07 *s*	1.12 *s*	C-15	17.1 *q*
H-15	0.86 *d*	0.84 *d*	0.86 *d*		

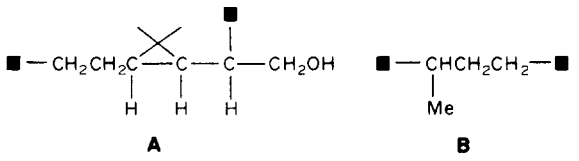
J (Hz): 1α, 1β = 2α, 2β = 3α, 3β = 10α, 10β = 11α, 11β ~ 12; 1α, 2α = 7; 1α, 2β = 12; 1β, 2β = 7; 2α, 3α = 7; 2α, 3β ~ 2; 2β, 3α = 7; 9, 10α = 9, 15 = 7; 9, 10β = 2; 10α, 11α = 6; 10α, 11β = 6; 10β, 11α = 3; 10β, 11β = 6; compound **7**: 5, 13 = 1.5.

Table 2. ^{1}H NMR spectral data of compounds **9** and **10** (400 MHz, TMS as internal standard)

		10	
	9 ($CDCl_3$)	C_6D_6	$CDCl_3$
H-1α	—	1.71 *d*	1.72 *dd*
H-1β	1.63 *m*	1.58 *br dd*	1.56 *m*
H-2α	1.91 *ddd*	1.86 *ddd*	1.85 *ddd*
H-2β	1.4 *m*	1.48 *dddd*	1.41 *dddd*
H-3	1.3 *m*	1.19 *ddd*	1.2 *m*
H-5	1.54 *br d*	0.94 *br d*	0.97 *br d*
H-6	2.30 *br s*	1.64 *br dd*	1.64 *br dd*
H-9	2.15 *ddq*	2.13 *ddq*	2.14 *ddq*
H-10α	2.05 *m*	2.00 *ddd*	2.01 *ddd*
H-10β	1.3 *m*	1.30 *ddd*	1.25 *m*
H-11α	1.63 *m*	1.60 *ddd*	1.56 *m*
H-11β	1.3 *m*	1.22 *dd*	1.25 *m*
H-12	1.16 *s*	1.40 *s*	1.25 *s*
H-13	9.71 *d*	3.62 *dd*	3.78 *dd*
H-13′		3.57 *dd*	3.67 *dd*
H-14	1.04 *s*	0.86 *s*	0.85 *s*
H-15	0.89 *d*	0.93 *d*	0.88 *d*

J (Hz): 1α, 1β = 12; 1α, 2β = 10; 2α, 2β = 12; 2α, 3α = 6.5; 2α, 5α = 5α, 6β ~ 1; 3α, 5α = 8; 6β, 13 = 5; 6β, 13′ = 8.5; 9α, 10α = 9; 9α, 10β = 7; 9α, 15 = 7; 10α, 10β = 12; 10α, 11α = 4; 10β, 11α = 10; 10β, 11β = 7; 11α, 11β = 12; 13, 13′ = 10; compound **9**: 6, 13 = 2.

since no double bond was present. In deuteriobenzene all signals in the spectrum of the alcohol, **10**, could be assigned by spin decoupling. Starting with the signal of the hydroxymethylene group sequence **A** could be established.



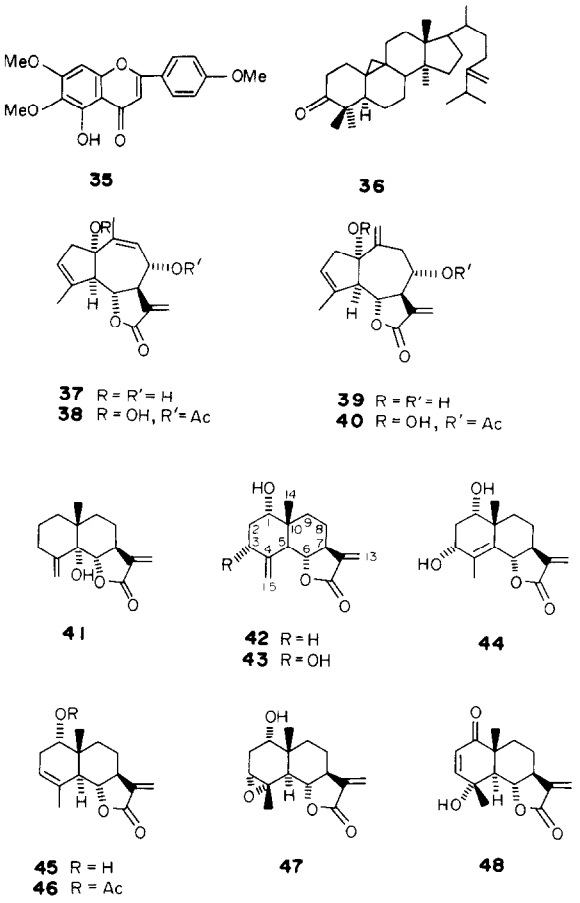
A **B**

Further decouplings led to sequence **B**. The combination with the two additional methyl groups, therefore, led to structure **10**. The stereochemistry at C-3, C-5 and C-6 was deduced from the couplings observed. Inspection of a model showed that the angle between H-5 and H-6 was nearly 90° if the hydroxymethylene group was α-orientated. The presence of a cyclopropane ring was deduced from the chemical shifts of H-3 and H-5 and the coupling $J_{3,5}$, while the shift differences of H-5 in the spectra of **9** and **10** supported the proposed arrangement of the oxygen function. Though the stereochemistry at C-7 and C-8 could not be established with certainty, the one which is proposed here is the most likely on biogenetic grounds. Compound **9**, which we have named 3,5-cycloisocomen-13-al, is clearly formed via **6**. The aerial parts afforded germacrene D, camphor, spathulenol, phytol, **7**, **10** and **11** [6].

The roots of *S. rotundifolium* (DC.) Fenzl. ex Harv. gave friedelin, nerol isovalerate (**1**), **5**, **25** and two eudesmanolides, reynosin (**49**) [7] as well as its 1-epimer, **42**. The structure of the latter was deduced from the ^{1}H NMR spectrum (Table 3) which was close to that of **49**. However, the couplings of H-1 indicated the presence of an axial hydroxyl group. The remaining signals were close to those of **49**. However, some chemical shifts were altered slightly, especially the H-3α and H-5α signals which were shifted downfield due to the deshielding effect of the 1α-hydroxy group. The aerial parts afforded germacrene D, caryophyllen-1,10-epoxide, rupicolin A (**37**) [8], the hydroperoxide, **38** [9], the isomeric lactones, **39** [8] and **40** [9], arbusculin (**41**) [10], **42** and **49**.

Several collections of two further species from different locations in Transvaal were examined. The aerial parts of *Schistostephium heptalobum* (DC.) Oliv. et Hiern., collected near Duevels Kloof, afforded germacrene D, bicyclogermacrene, squalene, chrysanthemone, caryophyllene epoxide, lupeol and its acetate, the eudesmanolides **43** [10], **44**, **45** [11], **46**, **47** [12] and **48** [12] as well as the germacranolides **58**, **59** [6], **60** [6], **63**, **64** [13] and **70**, while the roots gave germacrene D, caryophyllene, β-bisabolene, caryophyllen-1,10-epoxide, α-humulen-1,10-epoxide, lupeyl acetate, taraxasteryl acetate, stigmasterol, sitosterol, nerol isovalerate (**1**), **2**, **3**, cadinol (**12**), dehydrofalcarinone (**26**), cycloartenone (**36**), **45** and the germacranolide, **64**.

The aerial parts of a small collection near Lydenburg afforded germacrene D, 5-hydroxy-6,7,4'-trimethoxyflavone (**35**), the germacranolides **69** [14], **71** [15], **80** [16], **92** [16], **93** [16] and **96** [10], while the roots gave stigmasterol, sitosterol, **5**–**7**, β-eudesmol (**13**) and **26**. The structure of **44** was deduced from the molecular formula and the ^{1}H NMR spectrum (Table 3) which was in part



35 **36**

37 R = R' = H
38 R = OH, R' = Ac

39 R = R' = H
40 R = OH, R' = Ac

41

42 R = H
43 R = OH

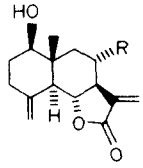
44

45 R = H
46 R = Ac

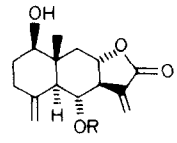
47 **48**

close to that of **43**. Spin decoupling allowed the assignment of all signals. The presence of a 4,5-double bond could be deduced from the H-6 signal which was coupled with a five-fold doublet (H-7), with the olefinic methyl and with a low field four-fold doublet, obviously the signal of H-3. The proposed stereochemistry agreed with the couplings. The ^{1}H NMR spectrum of **46** (Table 3) indicated that this lactone was simply the acetate of **45**. Accordingly, the H-1 signal was shifted downfield. Again the structure of **58** could be easily deduced from the ^{1}H NMR spectrum (Table 4) since it was very similar to that of the known ester, **60**. Obviously, only the ester group was replaced by an acetoxy group. Also, the structure of **63** was deduced from the ^{1}H NMR spectrum (Table 4) which was close to that of the known acetate, **64** [13]. The molecular formula of **70** differed from that of **58** by an additional oxygen. The ^{1}H NMR spectrum of **70** (Table 4) was also similar to that of **58**. However, the presence of a 1,10-epoxide was indicated by a double doublet at δ 3.09. Spin decoupling allowed the assignment of all signals, while the stereochemistry was deduced from the couplings observed. Compound **70**, therefore, was 9β-acetoxy-1,10-epoxycostunolide.

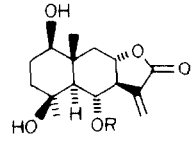
The aerial parts of *Schistostephium crataegifolium* (DC.) Fenzl. ex Harv., collected near Lydenburg, afforded germacrene D, bicyclogermacrene, lupeol, its acetate, the bisabolene derivatives **14** and **16**, the prostaglandin-like acid **27**, the flavone **35**, the eudesmanolides **50**–**52**, **53** [17] and **54**–**56** as well as the germacranolides **71** [15], **80** [16],



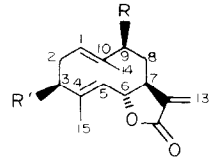
49 R = H
50 R = OAc



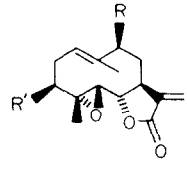
51 R = MeAcr
52 R = Sen
53 R = Ang



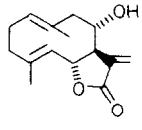
54 R = MeAcr
55 R = Sen
56 R = Ang



	57	58	59	60	61	62
R	H	OAc	OMeBu	O/Val	OH	OH
R′	OH	H	H	H	OAc	O/Bu



	63	64	65	66	67	68
R	OH	OAc	H	H	H	H
R′	H	H	OH	OAc	OMeBu	O/Val



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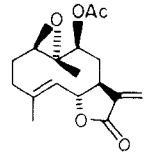
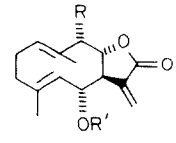
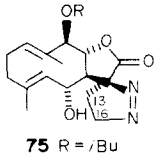


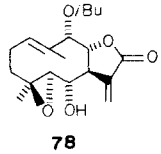
70



	71	72	73	74	74 a
R	H	O/Bu	OMeBu	O/Val	H
R′	H	H	H	H	Sen, 8-epi



75 R = /Bu
76 R = MeBu
77 R = /Val



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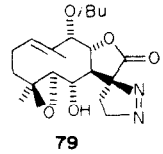

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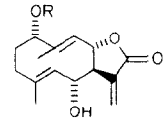
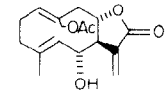


88 R = H
89 R = OH



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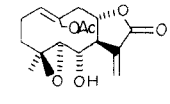

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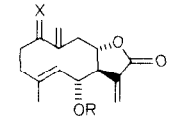
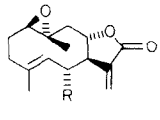
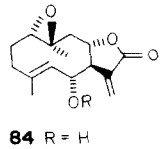


	92	93	94	95	96	97	98	99	100
R	H	H	H	H	H	MeAcr	MeAcr	MeAcr	MeAcr
X	α-OOH	β-OOH	α-OH	β-OH	O	α-OOH	β-OOH	α-OH	β-OH



80 R = OH
80 a R = OH, 8-epi
81 R = O Sen
82 R = OAng
83 R = OAc
83 a R = H
83 b R = H, 8-epi



84 R = H
85 R = Sen
86 R = Ang
87 R = Ac

81, **82** [18], **84** [16], **85**, **86**, **88** [16], **89** [16], **90**, **91**, **92–95** [16], **96** [10], **97** and **98**, while the roots gave germacrene D, bicyclogermacrene and dehydrofalcarinone (**26**). The aerial parts of the same species, collected near Zeerust, afforded germacrene D, bicyclogermacrene, α-pinene,

Table 3. ^{1}H NMR spectral data of compounds **42**, **44**, **46** and **50–56** (400 MHz, $CDCl_3$, TMS as internal standard)

	42	**44**	**46**	**50**	**51**	**52**	**53**	**54**	**55**	**56**
H-1	3.48 *dd*	3.58 *br d*	4.65 *ddd*	3.52 *ddd*	3.59 *br d*	3.58 *br d*	3.59 *br d*	3.49 *br d*	3.49 *br d*	3.50 *dd*
H-2α	—	2.20 *m*	2.43 *br dd*	1.84 *dddd*	1.90 *m*	1.91 *m*	1.92 *m*			
H-2β	—	2.11 *ddd*	2.09 *m*	1.55 *m*	1.55 *m*	1.55 *m*	1.55 *m*	1.45–	1.45–	1.45–
H-3α	2.56 *br dd*		5.30 *m*	2.10 *m*	2.05 *ddd*	2.05 *ddd*	2.04 *ddd*	1.80 *m*	1.80 *m*	1.80 *m*
H-3β	2.35 *br dd*	3.99 *dddd*		2.35 *ddd*	2.31 *ddd*	2.30 *ddd*	2.31 *ddd*			
H-5α	2.84 *br d*	—	2.71 *br d*	2.21 *br d*	2.24 *br d*	2.18 *br d*	2.21 *br d*	1.91 *d*	1.93 *d*	1.92 *d*
H-6β	4.01 *dd*	4.54 *ddq*	3.93 *dd*	4.11 *dd*	5.57 *dd*	5.53 *dd*	5.61 *dd*	5.76 *dd*	5.72 *dd*	5.81 *dd*
H-7α	2.56 *ddddd*	2.70 *ddddd*	2.53 *ddddd*	2.84 *dddd*	2.81 *dddd*	2.77 *dddd*	2.80 *dddd*	2.89 *dddd*	2.82 *dddd*	2.90 *br dd*
H-8α	2.0 *m*	2.20 *m*	2.05 *m*	—	—	—	—	—	—	—
H-8β	1.70 *dddd*	1.68 *dddd*	1.65 *m*	5.19 *ddd*	4.09 *ddd*	4.08 *ddd*	4.08 *ddd*	4.04 *ddd*	4.03 *ddd*	4.06 *ddd*
H-9α	2.15 *m*	2.35 *ddd*	2.05 *m*	2.50 *dd*	2.59 *dd*	2.57 *dd*	2.59 *dd*	2.55 *dd*	2.54 *dd*	2.56 *dd*
H-9β	1.38 *m*	1.42 *m*	1.40 *m*	1.39 *br dd*	1.55 *m*	1.55 *m*	1.55 *m*	1.5 *m*	1.5 *m*	1.50 *m*
H-13	6.08 *d*	6.18 *d*	6.08 *d*	6.15 *d*	6.11 *d*	6.12 *d*	6.12 *d*	6.09 *d*	6.09 *d*	6.10 *d*
H-13′	5.40 *d*	5.50 *d*	5.39 *d*	5.53 *d*	5.38 *d*	5.41 *d*	5.49 *d*	5.28 *d*	5.32 *d*	5.32 *d*
H-14	0.84 *s*	1.06 *s*	0.91 *s*	0.86 *s*	0.87 *s*	0.87 *s*	0.87 *s*	1.05 *s*	1.04 *s*	1.06 *s*
H-15	4.96 *ddd*	2.08 *d*	1.89 *br s*	5.00 *br s*	4.86 *br s*	4.87 *br s*	4.88 *br s*	1.27 *s*	1.26 *s*	1.30 *s*
H-15′	4.83 *ddd*			4.86 *br s*	4.60 *br s*	4.64 *br s*	4.64 *br s*			
OR	—	3.18 *d*	2.08 *s*	2.11 *s*	6.08 *br s*	5.63 *br s*	6.10 *qq*	6.16 *br s*	5.70 *qq*	6.24 *qq*
		2.54 *d*			5.59 *br s*	2.17 *br s*	1.93 *dq*	5.68 *br s*	2.23 *q*	2.04 *dq*
					1.90 *br s*	1.89 *br s*	1.82 *dq*	1.98 *dd*	1.95 *d*	1.92 *dq*

J (Hz): Compound **42**: 1, 2 = 2.5; 2α, 3α = 5; 3α, 3β = 15; 2α, 3β = 12; 3, 15 = 5, 15 = 1.3; 5, 6 = 6, 7 = 10.5; 7, 8α = 3; 7, 8β = 12; 8α, 8β = 13; compound **44**: 1β, 2α = 4; 1β, 2β = 2.5; 1β, OH = 7; 2α, 2β = 15; 2α, 3β = 2; 2β, 3β = 4.5; 3β, 6β = 1.5; 3β, OH = 6; 6β, 7α = 7α, 8β = 12; 6β, 15 = 1.5; 7α, 8α = 7α, 13 = 7α, 13′ = 3; 8α, 8β = 13; 8α, 9β = 4.5; 8β, 9α = 12.5; 8β, 9β = 5; 9α, 9β = 13; compound **46**: 1β, 2α = 5; 2α, 2β = 20; 5α, 6β = 12; 6β, 7α = 7α, 8β = 11; 7α, 8α = 7α, 13 = 7α, 13′ = 3; compound **50**: 1α, 2α = 1α, OH = 4.5; 1α, 2β = 12; 2α, 2β = 13; 2α, 3α = 5; 2α, 3β = 2; 2β, 3β = 5; 3α, 3β = 14; 5α, 6β = 6β, 7α = 7α, 8β = 11; 7α, 13 = 7α, 13′ = 3; 8β, 9α = 11.5; 8β, 9β = 4.5; 9α, 9β = 13; compounds **51–53**: 1α, 2β = 12; 2α, 3α = 5; 2α, 3β = 2; 2β, 3α = 3α, 3β = 13; 2β, 3β = 5; 5α, 6β = 6β, 7α = 7α, 8β = 8β, 9α = 10.5; 7α, 13 = 7α, 13′ = 3; 8β, 9β = 4; 9α, 9β = 12; compounds **54–56**: 1α, 2α = 1α, OH = 4.5; 1α, 2β = 10; 5α, 6β = 6β, 7α = 10; 7α, 8β = 8β, 9α = 12; 7α, 13 = 7α, 13′ = 3; 8β, 9β = 4; 9α, 9β = 11.5.

Table 4. ^{1}H NMR spectral data of compounds **58**, **61–63**, **65–68** and **70** (400 MHz, $CDCl_3$, TMS as internal standard)

	58	**61**	**62**	**63**	**65**	**66**	**67**	**68**	**70**
H-1	5.03 *br d*	5.27 *br d*	5.27 *br d*	5.62 *br d*	5.12 *br dd*	5.16 *br d*	5.17 *br d*	5.17 *br d*	3.09 *dd*
H-2α	2.2 *m*–	2.60 *m*	2.60 *m*	2.27 *br d*	2.4 *m*	2.62 *m*	2.59 *m*	2.59 *m*	2.13 *br d*
H-2β	2.35 *m*	2.35 *m*	2.34 *m*	2.49 *dddd*		2.38 *m*	2.36 *ddd*	2.36 *ddd*	1.51 *dddd*
H-3α	2.09 *m*	5.21 *dd*	5.21 *dd*	2.16 *ddd*	3.43 *br dd*	4.48 *dd*	4.51 *dd*	4.51 *dd*	2.43 *ddd*
H-3β	2.30 *m*	—	—	1.31 *dd*	—	—	—	—	2.25 *ddd*
H-5	4.74 *br d*	4.88 *br d*	4.88 *br d*	2.47 *d*	2.78 *d*	2.86 *d*	2.87 *d*	2.87 *d*	5.28 *br d*
H-6β	4.59 *dd*	4.56 *dd*	4.56 *dd*	3.85 *dd*	3.92 *dd*	3.89 *dd*	3.89 *dd*	3.89 *dd*	4.62 *dd*
H-7α	2.96 *ddddd*	3.07 *m*	3.08 *m*	3.39 *dddd*	2.73 *m*	2.75 *m*	2.75 *dddd*	2.75 *dddd*	2.92 *ddddd*
H-8α	2.38 *ddd*	2.35 *m*	2.34 *m*	2.37 *br dd*	2.15 *m*	2.16 *m*	2.15 *m*	2.15 *m*	2.51 *ddd*
H-8β	1.94 *ddd*	1.86 *ddd*	1.86 *ddd*	1.93 *br dd*	1.70 *m*	1.70 *m*	1.70 *m*	1.70 *m*	1.82 *br dd*
H-9α	5.34 *br d*	4.37 *br d*	4.37 *br d*	4.36 *br d*	2.40 *m*	2.38 *m*	2.39 *m*	2.39 *m*	5.32 *br d*
H-9β	—	—	—	—	2.15 *m*	2.16 *m*	2.15 *m*	2.15 *m*	—
H-13	6.27 *d*	6.28 *d*	6.28 *d*	6.32 *d*	6.35 *d*	6.36 *d*	6.35 *d*	6.35 *d*	6.27 *d*
H-13′	5.49 *d*	5.54 *d*	5.54 *d*	5.63 *d*	5.63 *d*	5.64 *d*	5.63 *d*	5.63 *d*	5.45 *d*
H-14	1.44 *br s*	1.44 *br s*	1.43 *br s*	1.71 *s*	1.73 *s*	1.73 *s*	1.74 *s*	1.74 *s*	1.16 *s*
H-15	1.72 *d*	1.70 *d*	1.71 *d*	1.29 *s*	1.32 *s*	1.37 *s*	1.37 *s*	1.36 *s*	1.83 *d*
OR	2.13 *s*	2.60 *qq*	2.11 *s*	—	—	2.11 *s*	2.41 *tq*	2.25 *d*	2.06 *s*
		1.18 *d*					1.70 *m*	2.16 *m*	
							1.51 *m*	0.96 *d*	
							1.15 *d*		
							0.90 *t*		

J (Hz): Compound **58**: 1, 2α = 5; 1, 2β = 11; 5, 6β = 10; 5, 15 = 1; 6β, 7α = 8.5; 7α, 8α = 1.5; 7α, 8β = 10; 7α, 13 = 3.7; 7α, 13′ = 3.2; 8α, 8β = 15.5; 8α, 9α = 6; 8β, 9α = 1.5; compounds **61** and **62**: 1, 2β = 12; 2α, 3α = 5.5; 2β, 3α = 11.5; 5, 6β = 10; 5, 15 = 1.5; 6β, 7α = 8.5; 7α, 8β = 10; 7α, 13 = 3.8; 7α, 13′ = 3.5; 8α, 8β = 15.5; 8α, 9α = 6.5; 8β, 9α = 1.5; compound **63**: 1, 2α = 3; 1, 2β = 11.5; 2α, 2β = 2β, 3α = 3α, 3β = 13; 2α, 3α = 5; 2α, 3β = 3; 2β, 3β = 4; 5, 6β = 10.5; 5, 15 = 1; 6β, 7α = 9; 7α, 8α = 1; 7α, 8β = 10; 7α, 13 = 3.7; 7α, 13′ = 3.2; 8α, 8β = 16; 8α, 9α = 7.5; compounds **65–68**: 1, 2α = 4.5; 1, 2β = 2α, 2β = 12.5; 2α, 3α = 6; 2β, 3α = 11.5; 5α, 6β = 6β, 7α = 7α, 8β = 8.5; 7α, 13 = 7α, 13′ = 3.5; compound **70**: 1, 2α = 3; 1, 2β = 11.5; 2α, 2β = 14; 2α, 3α = 5.5; 2α, 3β = 4.5; 2β, 3α = 13; 2β, 3β = 2.5; 5, 6β = 6β, 7α = 7α, 8β = 10; 5, 15 = 1.5; 7α, 8α = 1; 7α, 13 = 3.5; 7α, 13′ = 3; 8α, 8β = 16; 8α, 9α = 7.

borneol, bornyl acetate, the nerolidol derivatives **19** [19] and **20**, dehydrofalcarinol (**25**), the corresponding ketone, **26**, the germacranolides **61**, **62**, **72–74** and **78**. The aerial parts of a third sample, collected near Barberton, afforded germacrene D, bicyclogermacrene, the nerolidol derivatives **18**, **23** [20] and **24**, **27**, costic acid (**28**) and its derivatives **29** [21], **30** and **31**, himachalol (**32**), as well as the germacranolides **57** [22] and **65–68**, while the roots gave longifolene, β-santalene, **1**, **6**, **26**, **32** and the allohimachalene derivatives **33** and **34**.

The ^{1}H NMR spectra of **14** and **16** (Table 5), which could not be separated, indicated that they were bisabolol derivatives since the spectra were close to that of bisabolol. However, an additional oxygen function was indicated by the changed signals of the olefinic protons and by a multiplet at δ 4.31 in the spectrum of **16**. A broadened singlet at δ 7.98 could be that of a hydroperoxide. Indeed, addition of triphenylphosphine transformed the compounds to the diols **15** and **17**, which could now be separated. The ^{1}H NMR spectra of **15** and **17** (Table 5) allowed the assignment of the structures. While the signals of H-1–H-8, H-14 and H-15 were nearly identical with those of bisabolol, the remaining signals indicated the presence of the isomeric allyl alcohols **15** and **17** thus showing that the natural compounds were the hydroperoxides **14** and **16**, formed by attack of oxygen on bisabolol. The stereochemistry at C-7 and C-10, however, could not be determined.

The ketone **20** was obtained only in minute amounts. Again a low field ^{1}H NMR signal at δ 10.85 led to the

Table 5. ^{1}H NMR spectral data of compounds **14** **17** (400 MHz, $CDCl_3$, TMS as internal standard)

	14	**15**	**16**	**17**
H-2	5.37 *br s*	5.36 *br s*	5.37 *br s*	5.37 *br s*
H-8	—	2.25 *dd*	—	—
		2.18 *dd*		
H-9	5.80 *dt*	5.71 *m*	—	—
H-10	5.65 *br d*		4.31 *m*	4.06 *m*
H-12	1.32 *s*	1.33 *s*	5.02 *br s*	4.96 *br s*
H-12′				4.84 *br s*
H-13	—		1.73 *br s*	1.73 *br s*
H-14	1.09 *s*	1.09 *s*	1.10 *s*	1.10 *s*
H-15	1.63 *br s*	1.64 *br s*	1.63 *br s*	1.64 *br s*

J (Hz): Compound **14**: 8, 8′ = 14; 8, 9 = 8′, 9 = 7; 9, 10 = 16; compound **15**: 8, 8′ = 14; 7, 9 = 8′, 9 = 6.

supposition that a hydroperoxide might be present. Reaction with triphenylphosphine led to the keto diol **21** and the trisubstituted furan **22**. The ^{1}H NMR spectra (Table 6) could be fully assigned by spin decoupling. The senecioyl moiety in **20** and **21** clearly was indicated by the low field methyl signals and the broadened singlet at δ 6.15, while a pair of doublets near 3.25 showed the presence of a neighbouring allylic methylene group. Two

Table 6. ^{1}H NMR spectral data of compounds **20–22** and **24** (400 MHz, $CDCl_3$, TMS as internal standard)

	20	**21**	**22**	**24**
H-1*c*	5.04 *dd*	5.03 *br d*	5.08 *br d*	5.06 *dd*
H-1*t*	5.18 *dd*	5.19 *br d*	5.24 *br d*	5.21 *dd*
H-2	5.86 *dd*	5.86 *dd*	5.91 *dd*	5.89 *dd*
H-4	1.46 *m*	—	1.84 *m*	1.5 *m*
H-5	1.65 *m* 1.37 *m*	—	2.59 *m*	1.4–1.6 *m*
H-6	4.34 *dd*	4.11 *m*	—	4.10 *m*
H-8	3.28 *d* 3.21 *d*	3.29 *d* 3.20 *d*	5.93 *br s*	2.80 *dd* 2.73 *dd*
H-9	—	—	—	5.63 *dt*
H-10	6.15 *br s*	6.14 *br s*	5.95 *br s*	5.68 *d*
H-12	1.93 *br s*	1.89 *br s*	1.85 *br s*	1.31 *s*
H-13	2.17 *br s*	2.14 *br s*	1.92 *br s*	1.31 *s*
H-14	5.32 *br s* 5.07 *br s*	5.15 *br s* 4.91 *br s*	1.90 *br s*	5.05 *br s* 4.86 *br s*
H-15	1.25 *s*	1.25 *s*	1.29 *s*	1.28 *s*
OH	10.85 *s*	—	—	—

J (Hz): 1*c*, 1*t* = 1.5; 1*c*, 2 = 11; 1*t*, 2 = 17; compound **20**: 6, 8 = 7; 8, 8′ = 18; compound **21**: 8, 8′ = 16.5; compound **24**: 8, 8′ = 16.5; 8, 9 = 6; 9, 10 = 16.

Table 7. ^{1}H NMR spectral data of compound **27** (400 MHz, $CDCl_3$, TMS as internal standard)

H-2	2.35 *t*
H-8	1.71 *m*
H-8′	1.14 *m*
H-9	2.97 *m*
H-10	7.73 *dd*
H-11	6.18 *dd*
H-13	2.44 *ddd*
H-14	2.51 *ddd*
H-14′	2.14 *ddd*
H-15	5.36 *ddd*
H-16	5.42 *dt*
H-17	2.06 *dq*
H-18	0.96 *t*

J (Hz): 1, 2 = 7; 9, 10 = 2.8; 9, 11 = 2; 9, 13 = 9; 10, 11 = 6.2; 13, 14 = 5; 13, 14′ = 6; 14, 14′ = 15.5; 14, 15 = 6; 14′, 15 = 7; 15, 16 = 11; 16, 17 = 17, 18 = 7.

Table 8. ^{1}H NMR spectral data of compounds **30** and **31** (400 MHz, $CDCl_3$, TMS as internal standard)

	30	**31**
H-1α	1.25 *dd*	2.22 *br d*
H-1β	1.91 *ddd*	2.29 *d*
H-2β	4.32 *br dd*	—
H-3	5.40 *br s*	5.89 *br s*
H-5α	2.06 *br d*	2.47 *br d*
H-6α	1.86 *br ddd*	2.06 *br d*
H-6β	1.15 *ddd*	1.33 *ddd*
H-7α	2.52 *br dddd*	2.62 *br dddd*
H-8α	1.30 *m*	1.3–1.6 *m*
H-8β	1.57 *dddd*	
H-9α	1.35 *ddd*	
H-9β	1.51 *ddd*	
H-13	6.31 *br s*	6.36 *br s*
H-13′	5.68 *br s*	5.72 *br s*
H-14	0.83 *s*	0.92 *s*
H-15	1.64 *ddd*	1.90 *dd*

J (Hz): Compound **30**: 1α, 1β = 12; 1α, 2β = 10; 1β, 2β = 6; 1β, 3 = 1; 2β, 15 = 3, 15 = 5α, 15 = 1.5; 5α, 6β = 6α, 6β = 6β, 7α = 12.5; 5α, 6α = 6α, 7α = 7α, 8α = 3.5; 7α, 8β = 8α, 8β = 8β, 9α = 9α, 9β = 13; 8α, 9α = 4.5; 8β, 9β = 4; compound **31**: 1α, 1β = 16; 5α, 6β = 6α, 6β = 6β, 7α = 7α, 8β = 13; 3,15 = 5α, 15 = 1.5; 6α, 7α = 7α, 8α = 3.5.

broadened singlets near δ 5.1 and a low field signal at 4.24 and 4.11, respectively, showed the presence of a disubstituted vinyl group and an allylic oxygen function, while the second end group was deduced from the typical signals, thus leading to the proposed structures. The ^{1}H NMR spectrum of **22** further supported the structure of the hydroperoxide **20**. The furan most probably was formed by traces of acid present in chloroform.

The mass spectrum of **24** did not show the molecular ion, even by chemical ionization. However, the ^{1}H NMR spectrum (Table 6) indirectly showed that three hydroxy groups were present as three tertiary methyl signals were shifted down field and a multiplet at δ 4.10 was obviously due to a proton under a hydroxyl group. Again, spin decoupling allowed the assignment of all signals, only those of H-4 and H-5 being overlapping multiplets. Compound **24** was presumably formed by enzymatic oxidation of nerolidol.

The IR spectrum of **27** showed that an acid was present, while the molecular formula indicated the presence of an additional oxygen function. The ^{1}H NMR spectrum (Table 7) indicated the presence of a conjugated ketone by the low field double doublets at δ 7.73 and 6.18. Spin decoupling further showed that a three-fold doublet at δ 2.44 was coupled with three signals of allylic protons. The remaining signals indicated that that the prostaglandin-like acid **27** was the only possible structure which was similar to several other acids, isolated from *Calea* species [23].

The ^{1}H NMR spectra of **30** and **31** (Table 8) showed, in part, similarities to that of **29**. The presence of a conjugated ketone in the acid **30** was deduced from the broadened singlet at δ 5.89 which was coupled with an olefinic methyl group. A broadened doublet at δ 2.47 most likely was that of H-5. This could be established by spin decoupling. Starting with the typical signal of H-7 the sequence H-5–H-9 could be assigned. A pair of doublets around δ 2.2 were the signals of H-1 thus confirming the structure of **30**.

The ^{1}H NMR spectrum of **31** showed that the corresponding alcohol was present. Again all signals could be assigned by spin decoupling. The couplings of H-2

indicated an α-orientation of the hydroxy group if a model was considered.

The ^{1}H NMR spectra of **33** and **34** (Table 9) showed that allohimachalene derivatives were present as spin decoupling, allowed the assignment of all signals. Careful NOE investigation, however, showed that **33** was *trans*-fused. Especially in the observed NOE difference spectra, irradiation of both H-12 and H-13 showed a clear effect of H-2 which supported this assumption, if a model was inspected, as only in this configuration is H-2 located between H-12 and H-13, while in a *cis*-fused isomer in both possible conformers always only one methyl is near H-2. For allohimachalol a *cis*-ring fusion was reported following mechanistic considerations [24]. Unfortunately, no direct comparison was possible. Oxidation of **33** afforded **34**. Accordingly, the natural compounds had the same carbon skeleton and identical stereochemistry.

Table 9. ^{1}H NMR spectral data of compounds **33** and **34** (400 MHz, $CDCl_3$ TMS as internal standard)

	33	**34**
H-1α	1.65 *br d*	2.78 *br d*
H-2	5.27 *br d*	5.36 *br d*
H-4α	1.83 *dddd*	2.44 *br d*
H-4β	2.18 *br dd*	2.14 *m*
H-5α	1.36 *dddd*	3.46 *ddd*
H-5β	1.63 *m*	2.23 *ddd*
H-6β	3.19 *dd*	—
H-12	0.81 *s*	0.89 *s*
H-13	0.99 *s*	0.94 *s*
H-14	0.77 *s*	1.10 *s*
H-15	1.76 *br s*	1.67 *br s*

J (Hz): Compound **33**: 1α, 2 = 6; 2, 4α = 4α, 5α = 1.5; 4α, 4β = 14.5; 4α, 5β = 6.5; 4β, 5α = 12; 5α, 5β = 14; 5α, 6β = 11.5; 5β, 6β = 3.5; compound **34**: 1α, 2 = 6; 4α, 4β = 17.5; 4α, 5α = 7; 4α, 5β = 3.5; 4β, 5α = 5α, 5β = 12; 4β, 5β = 6.5.

The ^{1}H NMR spectrum of **50** (Table 3) showed similarities with that of reynosin (**49**). The presence of an additional oxygen function followed from a low field three-fold doublet at δ 5.19 and a methyl singlet at 2.11 indicating an acetoxy group. Spin decoupling showed that the corresponding proton under the acetoxy group was coupled with H-7 (four-fold doublet at 2.84) and with two double doublets which obviously had to be assigned to H-9, thus leading to the proposed structure. The proposed stereochemistry at C-5–C-8 agreed with the couplings observed, while the presence of a 6,12-lactone was deduced from the relative chemical shifts of H-6 and H-8. Accordingly, in the ^{1}H NMR spectra of **51** and **52** (Table 3) the shifts of H-6 and H-8 were reversed and were close to that of **53**. The nature of the ester groups was deduced from the typical ^{1}H NMR signals.

The ^{1}H NMR spectra of **54**–**56** (Table 3) showed that these lactones only differed in the nature of the ester groups which, due to the observed chemical shifts, were at C-6. The spectral data were close to those of **51**–**53**. However, the signals of the methylene protons in the spectra of the latter were replaced by a methyl singlet, whose chemical shift indicated that tertiary methyl carbinols were present. Accordingly, the H-3 signals were shifted upfield leading to unresolved multiplets overlapping with those of H-2. While the stereochemistry at C-1 and C-5–C-8 directly followed from the couplings, the β-orientation of the 4-hydroxy group was deduced from the observed downfield shift of H-14, if compared with that in **51**–**53**, and from the chemical shift of H-15 which better agreed with an equatorial methyl group. Probably tanapsin, isolated from a *Tanacetum* species [25], where no stereochemistry was assigned at C-4, may be identical with **56**, but no material was available for direct comparison.

The ^{1}H NMR spectra of **61** and **62** (Table 4) again showed that these lactones differed only in the nature of ester groups, one being an acetate and the second an isobutyrate. The presence of costunolide derivatives and the substitution pattern was obvious from the spectra too and was established by spin decoupling, which also showed that the free hydroxyl was at C-9. The stereochemistry at C-3 and C-9 was deduced from the corresponding couplings, especially if compared with those of known stereochemistry [22, 26, 27].

The structures of the epoxides **65**, **66** and the mixture of **67** and **68**, which could not be separated, followed from the ^{1}H NMR spectra (Table 4) which showed that they were 4,5-epoxygermacranolides differing only in the oxygen function at C-3. Compounds **66**–**68** were esters of **65** since this could be deduced from the downfield shift of the broadened double doublet at δ 3.43 in the spectra of **66**–**68**, while the nature of the ester groups could be recognized from the characteristic signals. The 3-position of the oxygen function was confirmed by the results of spin decoupling, while the stereochemistry at C-3–C-7 was deduced from the couplings observed.

The lactones **72**–**74** could be separated only in part. The ^{1}H NMR spectra of **72** and of the mixture of **73** and **74** (Table 10) indicated mixtures of conformers, but showed some similarities to the spectrum of **71**. Therefore, the presence of 8,12-lactones was very likely. Addition of diazomethane afforded the corresponding pyrazolines **75**–**77**. The clear ^{1}H NMR spectra allowed the assignment of most signals which indicated that they were derivatives of **71** [15], which had an additional oxygen function at C-9, whose nature followed from the corresponding ^{1}H NMR signals. The couplings of H-6–H-9 agreed with the proposed stereochemistry.

The ^{1}H NMR spectrum of **78** also indicated the presence of a mixture of conformers. Even the spectrum of the corresponding pyrazoline **79** (Table 10) was not very sharp but allowed the assignment of most signals by spin decoupling which led to the proposed structure. While the stereochemistry at C-6–C-9 could be deduced from the corresponding couplings, the presence of a β-epoxide only followed from careful inspection of the spectra of the various epoxides derived from **71** which were prepared by partial synthesis as the same problems arose with the stereochemistry of **80**–**82**, **84**–**86** and **91** (see below).

Epoxidation of **71** with one equivalent of *m*-chloroperbenzoic acid in the presence of sodium hydrogen carbonate afforded mainly **103**, small amounts of the isomer **111** and the diepoxides **104** and **106**. Epoxidation of the acetate of **71** afforded pyrethrosin (**83**) and **87** in nearly equal amounts as well as small quantities of **105** and **107**–**109**. The structures and stereochemistry of these epoxides were deduced from the ^{1}H NMR spectra (Table 11), by inspection of models and spin decoupling. The

Table 10. ^{1}H NMR spectral data of compounds **75–77**, **79** and **97–102** (400 MHz, TMS as internal standard)

	97 (C_6D_6, 70°)	**98** ($CDCl_3$)	**99** ($CDCl_3$, 57°)	**100** ($CDCl_3$, 57°)	**101** ($CDCl_3$)	**102** ($CDCl_3$)	**75** ($CDCl_3$)	**76** ($CDCl_3$)	**77** ($CDCl_3$)	**79** ($CDCl_3$, 57°)
H-1	3.87 *br dd*	4.15 *br d*	3.91 *br dd*	4.04 *m*	4.15 *m*	3.85 *m*	4.95 *br dd*	4.97 *br d*	4.97 *br d*	5.69 *br dd*
H-5	4.83 *br d*	5.18 *br d*	4.98 *br d*	5.11 *br d*	5.06 *br d*	5.05 *br d*	4.56 *br d*	4.57 *br d*	4.57 *br d*	2.41 *d*
H-6β	5.25 *dd*	5.43 *dd*	5.28 *br dd*	5.38 *dd*	5.56 *dd*	5.51 *dd*	4.49 *dd*	4.50 *dd*	4.50 *dd*	4.70 *dd*
H-7α	2.80 *m*	3.19 *m*	3.10 *m*	3.17 *m*	2.85 *m*	2.84 *dd*	3.01 *dd*	3.01 *dd*	3.01 *dd*	2.99 *dd*
H-8β	3.84 *m*	3.93 *br dd*	4.08 *m*	4.04 *m*	4.79 *ddd*	4.83 *br dd*	5.15 *br d*	5.14 *br d*	5.14 *br d*	4.91 *dd*
H-9α	2.08 *dd*	2.34 *br dd*	2.42 *dd*	2.31 *dd*	2.69 *dd*	2.39 *br dd*	—	—	—	—
H-9β	2.89 *br d*	3.15 *dddd*	2.99 *br d*	3.07 *br d*	2.94 *dddd*	3.24 *br d*	5.69 *br s*	5.73 *br s*	5.73 *br s*	5.50 *br s*
H-13	6.33 *dd*	6.29 *d*	6.32 *d*	6.26 *d*	—	—	2.14 *ddd*	2.14 *ddd*	2.14 *ddd*	2.22 *m*
H-13′	5.66 *dd*	5.78 *d*	5.81 *d*	5.73 *d*	—	—	1.94 *ddd*	1.94 *ddd*	1.94 *ddd*	1.74 *m*
H-14	4.90 *br s*	5.45 *dd*	5.17 *br s*	4.36 *br s*	5.16 *br d*	5.50 *br s*	} 1.57 *br s*	} 1.57 *br s*	} 1.57 *br s*	} 1.79 *br s*
H-14′	4.86 *br s*	5.38 *br d*	5.12 *br d*	5.16 *d*	5.14 *d*	5.28 *br d*				
H-15	1.54 *d*	1.74 *d*	1.80 *br s*	1.74 *d*	1.80 *d*	1.74 *d*	1.60 *br s*	1.60 *br s*	1.60 *br s*	1.46 *s*
H-16	—	—	—	—	5.11 *m*	4.68 *m*	4.85 *ddd*	4.85 *ddd*	4.85 *ddd*	4.86 *m*
H-16′	—	—	—	—	4.63 *m*	4.57 *m*	4.72 *ddd*	4.71 *ddd*	4.71 *ddd*	4.71 *m*
OR	6.06 *br s*	6.16 *br s*	6.12 *br s*	6.13 *br s*	5.93 *br s*	5.93 *br s*	2.69 *qq*	2.52 *tq*	0.96 *d*	2.60 *qq*
	5.27 *dq*	5.68 *dq*	5.61 *br s*	5.60 *dq*	5.55 *dq*	5.57 *br dq*	1.22 *d*	1.18 *d*	—	1.18 *d*
	1.84 *dd*	1.96 *dd*	1.95 *br s*	1.94 *dd*	1.85 *br s*	1.86 *dd*	1.21 *d*	0.90 *t*	—	—
OOH	7.75 *br s*	7.88 *s*	—	—	—	—	—	—	—	—

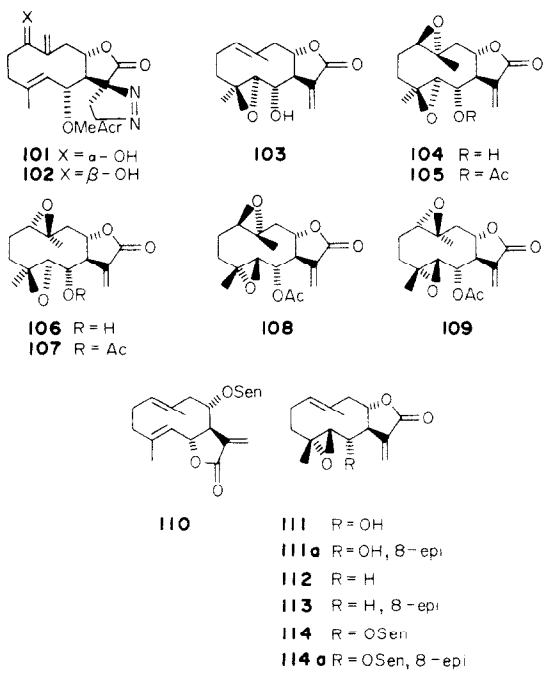
J (Hz): Compounds **75–77**: 1, 2α = 3; 1, 2β = 12; 5, 6β = 6β, 7α = 7α, 8β = 10; 13, 13′ = 12; 13, 16 = 6; 13, 16′ = 10; 13′, 16 = 10; 13′, 16′ = 6; 16, 16′ = 18.5; compound **79**: 1, 2 = 7; 5β, 6β = 3; 6β, 7α = 11.5; 7α, 8β = 7; 8β, 9β = 2; 13, 13′ = 12; 13, 16 = 13′, 16′ = 6; 13, 16′ = 13′, 16 = 10; 16, 16′ = 18; compound **97**: 1β, 2α = 10; 1β, 2β = 3.5; 5, 6β = 6β, 7α = 10; 5, 15 = 1; 8β, 9α = 10; 9α, 9β = 14; compound **98**: 1α, 2β = 11; 1α, 14 = 1.5; 5, 6β = 6β, 7α = 7α, 8β = 10; 7α, 13 = 7α, 13′ = 3; 8β, 9α = 7; 9α, 9β = 15; 9β, 14 = 9β, 14′ = 2; compound **99**: 1β, 2α = 10; 1β, 2β = 3; 5, 6β = 6β, 7α = 10; 8β, 9α = 10; 9α, 9β = 15; compound **100**: 5, 6β = 6β, 7α = 10; 5, 15 = 1; 7α, 13 = 7α, 13′ = 3; 8β, 9α = 7; 9α, 9β = 15; 9β, 14′ = 2; compound **101**: 5, 6β = 6β, 7α = 7α, 8β = 10; 5,15 = 1; 8β, 9α = 8; 8β, 9β = 9β, 14 = 9β, 14′ = 2; 9α, 9β = 16.5; compound **102**: 5, 6β = 6β, 7α = 7α, 8β = 10; 5,15 = 1; 8β, 9α = 6.5; 9α, 8β = 17; 9β, 14′ = 2.

Table 11. ^{1}H NMR spectral data of compounds **83**, **87** and **103–109** (400 MHz, $CDCl_3$, TMS as internal standard)

	83 (C_6D_6, 77°)	**87** (C_6D_6, 77°)	**103** (60°)	**104**	**105**	**106**	**107**	**108**	**109**
H-1	2.25 *d*	2.25 *br d*	5.37 *br t*	3.06 *dd*	3.08 *dd*	2.92 *br d*	2.92 *br d*	2.84 *br d*	3.08 *dd*
H-5	4.70 *br d*	4.88 *br d*	2.68 *d*	2.74 *d*	2.79 *d*	2.99 *d*	3.02 *d*	2.91 *d*	2.92 *d*
H-6	4.62 *dd*	4.62 *dd*	4.12 *dd*	4.20 *dd*	5.39 *dd*	4.13 *dd*	525 *dd*	4.89 *dd*	4.93 *dd*
H-7	2.52 *br d*	2.87 *br d*	2.88 *m*	2.91 *m*	3.10 *m*	3.01 *ddddd*	3.18 *ddddd*	3.10 *m*	3.28 *ddddd*
H-8	3.67 *dd*	3.84 *ddd*	4.44 *ddd*	4.48 *ddd*	4.58 *ddd*	4.59 *ddd*	4.66 *ddd*	4.23 *ddd*	4.24 *ddd*
H-9	2.52 *br d*	2.01 *dd*	2.86 *dd*	2.68 *dd*	2.68 *dd*	2.26 *dd*	2.28 *dd*	2.60 *d*	2.2 *m*
H-9′	1.19 *dd*	1.87 *dd*	2.03 *dd*	1.40 *dd*	1.38 *dd*	2.01 *dd*	1.99 *dd*	1.58 *dd*	
H-13	6.34 *dd*		6.44 *dd*	6.45 *dd*	6.41 *d*	6.47 *dd*	6.43 *d*	6.41 *d*	6.41 *d*
H-13′	5.59 *dd*	5.57 *dd*	6.15 *dd*	6.19 *dd*	5.83 *d*	6.11 *dd*	5.87 *d*	5.82 *d*	5.84 *d*
H-14	0.94 *s*	1.04 *s*	1.79 *br s*	1.38 *s*	1.39 *s*	1.48 *s*	1.48 *s*	1.41 *s*	1.48 *s*
H-15	1.48 *br s*	1.52 *br s*	1.63 *s*	1.70 *s*	1.62 *s*	1.56 *s*		1.46 *s*	1.57 *s*
OAc	1.69 *s*	1.67 *s*	—	—	2.10 *s*	—	2.08 *s*	2.10 *s*	2.13 *s*

J (Hz): Compound **83**: 1, 2 = 11; 5, 6 = 6, 7 = 10; 7, 8 = 6.5; 7, 13 = 7, 13′ = 3; 8, 9′ = 9; 9, 9′ = 14; 13, 13′ = 1.2; compound **87**: 1, 2 = 10; 5, 6 = 6, 7 = 10; 7, 8 = 8, 9 = 4; 7, 13 = 7, 13′ = 3; 8, 9′ = 11.5; 9, 9′ = 14; 13, 13′ = 1; compound **103**: 1, 2 = 8; 5, 6 = 3.5; 6, 7 = 11; 7, 8 = 8, 9 = 4; 7, 13 = 2.8; 7, 13′ = 2.2; 8, 9′ = 11.5; 9, 9′ = 13; 13, 13′ = 1.2; compounds **104** and **105**: 1, 2 = 9.5; 1, 2′ = 6; 5, 6 = 3; 6, 7 = 11.5; 7, 8 = 4; 7, 13 = 7, 13′ = 2.8; 8, 9 = 2; 8, 9′ = 12.5′; 9, 9′ = 13.5; 13, 13′ = 1; compounds **106** and **107**: 1, 2 = 11; 5, 6 = 3.5; 6, 7 = 11; 7, 8 = 2.5; 7, 13 = 7, 13′ = 2.2; 8, 9 = 5.5; 8, 9′ = 12; 9, 9′ = 14.5; 13, 13′ = 1; compound **108**: 1, 2 = 11; 5, 6 = 6, 7 = 10; 7, 8 = 3.5; 7, 13 = 2.5; 7, 13′ = 2; 8, 9′ = 10; 9, 9′ = 14; compound **109**: 1, 2 = 4; 1, 2′ = 9; 5, 6 = 9.5; 6, 7 = 11; 7, 8 = 8, 9 = 4; 7, 13 = 2.5; 7, 13′ = 2.2; 8, 9′ = 11.

observed couplings of H-8 agreed nicely with the expected ones. As the ^{1}H NMR spectrum of **71** clearly showed the presence of an 8,12-lactone, all epoxides obtained were 8,12-*trans*-lactones and differed only in the stereochemistry of the epoxides, which being derived from *trans* double bonds were all *trans* epoxides. Obviously, attack of the peracid was directed by the conformation of the substrate, by neighbouring group participation of the hydroxyl and by steric effects. Accordingly, **71** showed a preference for attack on the Δ^4-double bond. The main product, therefore, could be **103** or **111**. Inspection of models showed that the observed coupling $J_{5,6}$ agreed only with the stereochemistry of **103**, thus indicating that **71** mainly was attacked in a conformation where the 4-methyl group was below the plane. The ^{1}H NMR spectrum of **111** was identical with that of simsiolide (**111a**) [28]. The configuration of this substance, therefore, has to be revised. If the ^{1}H NMR spectral data of some further compounds, reported as *cis*-8,12-lactones, especially the H-8 signals, were compared with those obtained here, its was obvious that their structures also had to be revised. The structure and configuration at C-8 of the senecioate **74a** from *Vernonia nudiflora* [29] has to be changed to **110**, as the spectral data were close to those of **69** and its acetate. The 6-desoxy derivative of **111** was isolated from an *Inula* [6] and a *Telekia* species [30], also here the configuration at C-8 has to be changed from **113** to **112**. Two further lactones, which were isolated previously, have to be assigned as 8,12-*trans*-lactones, **80a** from a *Mikania* species [16] obviously has to be revised to **84** and a second from an *Inula* species (**83b**) [6] most probably is the 6-desoxy derivative **83a** as followed from the characteristic ^{1}H NMR signals of H-8.



In addition to **103** and **111**, the diepoxides **104** and **106** were obtained in minute amounts. These compounds obviously were formed by attack on the two possible conformers of **103**. The stereochemistry of these isomers followed from the inspection of models which showed that the observed signals and couplings agreed only with the proposed assignment (Table 11). Especially the couplings $J_{8,9}$ were characteristic and allowed a clear assignment. The stereochemistry of the epoxidation products of the acetate of **71** also could be deduced from the ^{1}H NMR spectra (Table 11). The spectrum of the monoepoxides **83** and **87** again differed typically in the couplings of H-9, thus allowing a clear assignment. As both isomers were obtained in nearly equal amounts, it is not surprising that further epoxidation afforded all four possible diepoxides. Their configurational assignment also was possible by the same typical ^{1}H NMR effects already observed in the spectra of the monoepoxides. As both **83** and **87** gave rise

to two diepoxides, two conformations of 1,10-monoepoxides obviously were attacked. The ^{1}H NMR spectral data of **83** were close to those of **80** [16], **81** and **82** [25], while those of **87** were similar to those of **85** and **86**. The nature of the different oxygen functions at C-6 could be deduced easily from the characteristic ^{1}H NMR signals. Perhaps **86** is identical with tanachin [32], but no material was available for direct comparison.

The ^{1}H NMR spectral data of **91** (Table 12) showed that this lactone was the 14-acetoxy derivative of **103** as all couplings were identical. The olefinic methyl signal was replaced by a pair of broadened doublets and an acetoxymethyl signal and the chemical shifts were somewhat different due to the deshielding effect of the acetoxy group.

From the results presented in this paper and the revisions proposed for compounds described earlier, it appears that all 8,12-germacranolides isolated so far probably have a *trans*-lactone function. The ^{1}H NMR spectra of 8,12-lactone epoxides with an α-orientated epoxymethyl indicate the presence of a mixture of conformers at room temperature, while those with β-methyl groups give clear spectra.

The ^{1}H NMR spectra of **97** and **98** as well as their reduction products **99** and **100** were close to those of **92**–**95**. The structures of these compounds have been established by a partial synthesis starting with **71** [Bohlmann, F. and Adler, A., unpublished]. The presence of a 6-*O*-methacrylate clearly followed from the corresponding ^{1}H NMR signals in the spectra of the pyrazolines **101** and **102** obtained from **99** and **100** (Table 10). Perhaps **94** or **95** may be identical with tanachin [32]. However, no material was available for direct comparison.

The collections of the variable species *S. heptalobum* and *S. crinegifolium* showed clear differences in the secondary metabolites isolated from them. Taxonomic investigations may be necessary to establish whether this is due to varieties or to differences in local conditions. The overall picture of the chemistry of *Schistostephium*, however, seems to be relatively clear. The nature of the lactones and the acetylenic compounds indicate a relationship to *Artemisia* from which similar compounds have been isolated although the high degree of variation is unusual in this genus. Further investigation may show whether derivatives **6**–**10** of isocomene are of chemotaxonomic importance.

EXPERIMENTAL

The air-dried plant material, collected in February 1981 in Transvaal, was extracted with Et_2O–petrol (1 : 2) and the resulting extracts were separated by CC (Si gel) and further by repeated TLC (Si gel) and in part by HPLC (reversed phase). It is probable that many of the new lactones are crystalline; however, due to the small amounts only gums were obtained. Known compounds were identified by comparing the high field ^{1}H NMR spectra with those of authentic material. In cases where no material was available, rigorous structure elucidation by using all spectroscopic methods was achieved and the data obtained were compared with those reported in the lit. Vouchers were deposited in the Herbarium of the Botanic Research Institute, Pretoria, South Africa.

Schistostephium artemisiifolium (*voucher* 81/72). The roots

Table 12. ^{1}H NMR spectral data of compounds **81**, **85**, **86**, **90** and **91** (400 MHz, TMS as internal standard)

	81 ($CDCl_3$)	**85** (C_6D_6, 80°)	**86** (C_6D_6, 80°)	**90** (C_6D_6, 115°)	**91** ($CDCl_3$, 57°)
H-1	2.68 *m*	2.28 *dd*	2.27 *dd*	4.82 *br t*	5.56 *br t*
H-2α	1.43 *m*	1.7 *m*	1.7 *m*	1.8 *m*–2.2 *m*	2.44 *m*
H-2β	1.55 *m*	1.25 *m*	1.25 *m*		
H-3α	2.34 *ddd*	1.95 *m*	1.95 *m*		1.25 *ddd*
H-3β	2.25 *ddd*	1.7 *m*	1.7 *m*	1.35 *m*	2.16 *ddd*
H-5	5.09 *br d*	4.99 *d*	4.96 *d*	4.61 *br d*	2.74 *d*
H-6	5.37 *dd*	5.29 *dd*	5.29 *dd*	3.74 *br m*	4.11 *dd*
H-7	3.04 *dddd*	2.98 *dddd*	2.98 *dddd*	2.72 *br m*	3.06 *dddd*
H-8	4.12 *dd*	4.49 *ddd*	4.48 *ddd*	3.82 *br m*	4.53 *ddd*
H-9α	2.04 *br dd*	2.03 *dd*	2.03 *dd*	2.78 *br dd*	2.95 *br dd*
H-9β	2.68 *m*	1.0 *m*	1.7 *m*	1.8–2.2 *m*	2.10 *br dd*
H-13	6.33 *d*	6.36 *dd*	6.35 *dd*	6.41 *dd*	6.43 *dd*
H-13′	5.90 *d*	5.75 *dd*	5.68 *dd*	5.95 *br s*	6.11 *dd*
H-14	1.28 *s*	1.09 *s*	1.09 *s*	4.42 *br s*	4.67 *br d* 4.60 *br d*
H-15	1.86 *br s*	1.59 *br s*	1.57 *br s*	1.35 *br s*	1.49 *s*
OR	5.66 *br s*	5.69 *br s*	5.80 *br q*	1.76 *s*	2.05 *s*
	2.16 *br s*	2.11 *d*	1.95 *dq*		2.18 OH *d*
	1.91 *br s*	1.54 *d*	1.85 *dq*		

J (Hz): Compound **81**: 2α, 3α = 6; 2α, 3β = 3; 2β, 3α = 3α, 3β = 13; 2β, 3β = 5; 5, 6β = 6β, 7α = 10; 7α, 13 = 3; 7α, 13′ = 2.5; 7α, 8β = 6; 8β, 9α = 8; 9α, 8β = 14; compounds **85** and **86**: 1α, 2α = 3; 1α, 2β = 10; 5, 6β = 6β, 7α = 10; 7α, 8α = 4; 7α, 13 = 3; 7α, 13′ = 2.5; 8α, 9α = 4; 8α, 9β = 11; 9α, 9β = 14; 13, 13′ = 1; compound **90**: 1, 2 = 8; 5, 6β = 9; 7, 13 = 2.8; 8α, 9α = 3.5; 9α, 9β = 14; 13, 13′ = 1.5; compound **91**: 1, 2 = 8; 2, 3 = 4; 2, 3′ = 10; 3, 3′ = 13; 5, 6β = 3.5; 6β, 7α = 10.5; 6β, OH = 1; 7α, 8α = 3.5; 7α, 13 = 2.5; 7α, 13′ = 2.2; 8α, 9α = 4.5; 8α, 9β = 12; 9α, 9β = 14; 14, 14′ = 12.

(40 g) afforded 2 mg α-humulene, 3 mg squalene, 5 mg caryophyllen-1,10-epoxide, 5 mg α-humulen-1,10-epoxide, 2 mg **2**, 2 mg **3**, 2 mg **4**, 3 mg **5**, 10 mg **6** (Et_2O–petrol, 1:10), 2 mg **7** (Et_2O–petrol, 1:3), **8** mg 8 (Et_2O–petrol, 1:3) and 5 mg **9** (Et_2O–petrol, 1:10), while the aerial parts (310 g) gave 30 mg germacrene D, 25 mg camphor, 5 mg spathulenol, 10 mg phytol, 5 mg **7**, 2 mg **10** (Et_2O–petrol, 1:3) and 5 mg **11**.

Schistostephium rotundifolium (*voucher* 81/148). The roots (10 g) gave 8 mg friedelin, 10 mg **1**, 10 mg **5**, 2 mg **25**, 2 mg **42** (Et_2O–petrol, 3:1) and 2 mg **49**, while the aerial parts (30 g) afforded 10 mg germacrene D, 5 mg caryophyllen-1,10-epoxide, 2 mg **37**, 2 mg **38**, 2 mg **39**, 3 mg **40**, 2 mg **41**, 8 mg **42** and 3 mg **49**.

Schistostephium heptalobum. (a) *Collected near Duevels Kloof, Transvaal* (*voucher* 81/83). The roots (70 g) gave 2 mg germacrene D, 3 mg caryophyllene, 10 mg β-bisabolene, 1 mg caryophyllen-1,10-epoxide, 1 mg α-humulen-1,10-epoxide, 3 mg lupeyl acetate, 2 mg taraxasteryl acetate, 2 mg stigmasterol, 2 mg sitosterol, 5 mg **1**, 1 mg **2**, 10 mg **3**, 3 mg **12**, 1 mg **26**, 4 mg **36**, 30 mg **45** and 5 mg **64**.

The aerial parts (190 g) afforded 10 mg squalene, 150 mg germacrene D, 50 mg bicyclogermacrene, 10 mg chrysanthemone, 2 mg caryophyllen-1,10-epoxide, 150 mg lupeol, 50 mg of its acetate, 5 mg **43**, 2 mg **44**, 300 mg **45**, 2 mg **46**, 5 mg **47**, 2 mg **48**, 10 mg **58**, 5 mg **59**, 5 mg **60**, 5 mg **63**, 60 mg **64** and 5 mg **70** (the lactones were separated by repeated TLC, CH_2Cl_2–C_6H_6–Et_2O, 1:1:1).

(b) *Collected near Lydenburg* (*voucher* 81/94). The roots (8 g) gave 5 mg stigmasterol, 5 mg sitosterol, 5 mg **5**, 1 mg **6**, 1 mg **7**, 5 mg **13** and 2 mg **26**, while the aerial parts (18 g) afforded 25 mg germacrene D, 2 mg **35** and a mixture of lactones, which were separated by repeated TLC (CH_2Cl_2–C_6H_6–Et_2O, 1:1:1) affording 10 mg **69**, 12 mg **71**, 3 mg **80**, 2 mg **92**, 2 mg **93** and 2 mg **96**.

Schistostephium crataegifolium. (a) *Collected near Lydenburg, Transvaal* (*voucher* 81/110). The aerial parts (80 g) gave 10 mg germacrene D, 5 mg bicyclogermacrene, 5 mg lupeol, 5 mg of its acetate, 1 mg **14** and 2 mg **16** (Et_2O), 2 mg **27** (Et_2O), 10 mg **35** and a complex mixture of lactones, which was separated first by TLC (Et_2O) and further by HPLC, MeOH–H_2O (13:7 and 3:2) affording 2 mg **50**, 2 mg **51**, 2 mg **52**, 4 mg **53**, 1 mg **54**, 1 mg **55**, 3 mg **56**, 1 mg **71**, 1 mg **80**, 1 mg **81**, 4 mg **82**, 1 mg **84**, 1 mg **85**, 3 mg **86**, 2 mg **88**, 1 mg **89**, 2 mg **90**, 5 mg **91**, 2 mg **92**, 2 mg **93**, 1 mg **94**, 1 mg **95**, 2 mg **96**, 1 mg **97** and 1 mg **98**. The roots (50 g) gave 2 mg germacrene D, 2 mg bicyclogermacrene and 1 mg **26**.

(b) *Collected near Zeerust, Transvaal* (*voucher* 81/195). The aerial parts (95 g) afforded 10 mg germacrene D, 2 mg bicyclogermacrene, 5 mg α-pinene, 5 mg borneol, 15 mg of its acetate, 5 mg **19**, 2 mg **20**, 1 mg **26**, 2 mg **61**, 3 mg **62**, 1 mg **72**, 1 mg **73**, 1 mg **74** and 2 mg **78** (polar compounds separated by TLC (Et_2O) and further by HPLC, MeOH–H_2O (13:7).

(c) *Collected near Barberton, Transvaal* (*voucher* 81/242). The roots (60 g) gave 5 mg longifolene, 5 mg β-santalene, 4 mg **1**, 2 mg **6**, 2 mg **26**, 5 mg **32**, 3 mg **33** (Et_2O–petrol, 1:3), 2 mg **34** ($AgNO_3$-coated Si gel, Et_2O–petrol, 1:6), while the aerial parts (200 g) afforded 5 mg germacrene D, 8 mg bicyclogermacrene, 5 mg **18**, 2 mg **23**, 1 mg **24** (Et_2O), 2 mg **27** (Et_2O), 1 mg **28**, 3 mg **29**, 1 mg **30** (Et_2O), 1 mg **31** (Et_2O), 3 mg **32** and a complex mixture of lactones which was separated by repeated TLC (CH_2Cl_2–Et_2O–C_6H_6, 2:3:1) affording 1 mg **57**, 4 mg **65**, 1 mg **66**, 1 mg **67** and 1 mg **68**.

α-Isocomen-13-al (**6**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2710, 1685 (C=CCHO); MS *m/z* (rel. int.): 218.167 $[M]^+$ (77) ($C_{15}H_{22}O$), 203 $[M-Me]^+$ (83), 189 $[M-CHO]^+$ (100), 176 $[M-C_3H_6]^+$ (97), 161 $[176-Me]^+$ (52).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-108 \quad -114 \quad -133 \quad -251} \ (CHCl_3;\ c\ 0.13).$$

Reduction with $LiAlH_4$ afforded **7**, identical with the natural product.

13-Hydroxy-α-isocomene (**7**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 220.183 $[M]^+$ (22) ($C_{15}H_{24}O$), 205 $[M-Me]^+$ (11), 202 $[M-H_2O]^+$ (5), 189 $[M-CH_2OH]^+$ (47), 178 $[M-C_3H_6]^+$ (100), 163 $[178-Me]^+$ (20).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-96 \quad -96 \quad -111 \quad -180} \ (CHCl_3;\ c\ 0.13).$$

α-Isocomen-13-acid (**8**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600–2600, 1690, 1640 (C=CCO_2H); MS *m/z* (rel. int.): 234.162 $[M]^+$ (78) ($C_{15}H_{22}O_2$), 219 $[M-Me]^+$ (20), 206 $[M-CO]^+$ (24), 192 $[M-C_3H_6]^+$ (100), 189 $[M-CO_2H]^+$ (38).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-49 \quad -51 \quad -59 \quad -105} \ (CHCl_3;\ c\ 0.67).$$

3,5-Cycloisocomen-13-al (**9**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 1725 (CHO); MS *m/z* (rel. int.): 218.167 $[M]^+$ (50) ($C_{15}H_{22}O$), 189 $[M-CHO]^+$ (100).

3,5-Cycloisocomen-13-ol (**10**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 220.183 $[M]^+$ (8) ($C_{15}H_{24}O$), 205 $[M-Me]^+$ (2), 136 $[205-C_5H_9]^+$ (100), 121 $[136-Me]^+$ (37); CI (isobutane): 221 $[M+1]^+$ (28), 203 $[221-H_2O]^+$ (100).

7-Hydroxy-11-peroxybisabol-2,9t-diene and 7-hydroxy-11-peroxybisabol-2,11-diene (**14 and 16**). Colourless oil, which could not be separated. After reduction with triphenylphosphine in $CDCl_3$ (5 min, 20°) TLC (Et_2O) afforded 1 mg **15** and 2 mg **17**, ^1H NMR see Table 5.

6-Peroxy-10-oxo-6,7-dihydro-7,14-dehydronerolidol (**20**). Colourless oil, which after reaction with triphenylphosphine in $CDCl_3$ (5 min, 20°) afforded 1 mg **21** (^1H NMR see Table 6) and 1 mg **22**, colourless oil, MS *m/z* (rel. int.): 234.162 $[M]^+$ (22) ($C_{15}H_{22}O_2$), 216 $[M-H_2O]^+$ (20), 201 $[216-Me]^+$ (18), 149 $[M-CH_2C(OH)(Me)CH{=}CH_2]^+$ (100).

6,11-Dihydroxy-6,7,10,11-tetrahydro-7,14,9,10-bisdehydronerolidol (**24**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 236 $[M-H_2O]^+$ (2), 218 $[236-H_2O]^+$ (3); CI (isobutane): 237 $[M+1-H_2O]^+$ (10), 219 $[237-H_2O]^+$ (100), 201 $[219-H_2O]^+$ (26).

4-[7-Carboxyheptyl(1)]-5-pent-2-en-yl(1)-cyclopent-2-en-1-one (**27**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2700, 1720 (CO_2H, C=C–C=O); MS *m/z* (rel. int.): 292.204 $[M]^+$ (42) ($C_{18}H_{28}O_3$), 274 $[M-H_2O]^+$ (10), 224 $[M-C_5H_8]^+$ (45) (McLafferty), 206 $[224-H_2O]^+$ (27), 177 $[206-CHO]^+$ (73), 149 $[177-CO]^+$ (79), 95 $[C_6H_7O]^+$ (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{+89 \quad +94 \quad +114 \quad +179} \ (CHCl_3;\ c\ 0.1).$$

2α-Hydroxyisocostic acid (**30**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600–2600, 1700 (C=CCO_2H, OH); MS *m/z* (rel. int.): 250.157 $[M]^+$ (28) ($C_{15}H_{22}O_3$), 235 $[M-Me]^+$ (100), 232 $[M-H_2O]^+$ (32), 217 $[235-H_2O]^+$ (82), 204 $[232-CO]^+$ (10), 189 $[204-Me]^+$ (24).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{+11 \quad +15 \quad +20 \quad +29} \ (CHCl_3;\ c\ 0.1).$$

2-Oxo-isocostic acid (**31**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600–2600, 1700 (C=CCO_2H, C=O); MS *m/z* (rel. int.): 248.141 $[M]^+$ (37) ($C_{15}H_{20}O_3$), 230 $[M-H_2O]^+$ (18), 95 $[C_7H_{11}]^+$ (100).

$$[\alpha]_{24}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{+31 \quad +36 \quad +43 \quad +66} \ (CHCl_3;\ c\ 0.08).$$

trans-*Allohimachalol* (**33**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 222.198 $[M]^+$ (22) ($C_{15}H_{26}O$), 204 $[M-H_2O]^+$ (34), 189 $[204-Me]^+$ (30), 119 (66), 107 (100), 93 (83), 81 (68), 69 (60), 55 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+13 \quad +18 \quad +22 \quad +33} (CHCl_3;\ c\ 0.3).$$

trans-*Allohimachalone* (**34**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1710 (C=O); MS *m/z* (rel. int.): 220.183 $[M]^+$ (81) ($C_{15}H_{24}O$), 205 $[M-Me]^+$ (27), 202 $[M-H_2O]^+$ (6), 177 $[205-CO]^+$ (28), 163 (35), 138 (76), 110 (82), 107 (100), 93 (68), 81 (75), 69 (92), 55 (86).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-54 \quad -57 \quad -73 \quad -133} (CHCl_3;\ c\ 0.2).$$

1-epi-*Reynosin* (**42**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone); MS *m/z* (rel. int.): 248.141 $[M]^+$ (4) ($C_{15}H_{20}O_3$), 230 $[M-H_2O]^+$ (100), 215 $[230-Me]^+$ (17), 202 $[230-CO]^+$ (12), 187 $[202-Me]^+$ (11).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+132 \quad +140 \quad +160 \quad +274} (CHCl_3;\ c\ 0.75).$$

1α,3α-*Dihydroxyarbusculin B* (**44**). Colourless gum, 3600 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 264.136 $[M]^+$ (32) ($C_{15}H_{20}O_4$), 246 $[M-H_2O]^+$ (42), 231 $[246-Me]^+$ (26), 213 $[231-H_2O]^+$ (27), 149 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+18 \quad +20 \quad +23 \quad +38} (CHCl_3;\ c\ 0.1).$$

Douglanin acetate (**46**). Colourless gum, 1780 (γ-lactone), 1735, 1240 (OAc); MS *m/z* (rel. int.): 230.131 $[M-HOAc]^+$ (100) ($C_{15}H_{18}O_2$), 215 $[230-Me]^+$ (28), 197 $[215-H_2O]^+$ (12), 169 $[197-CO]^+$ (13).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+80 \quad +84 \quad +98 \quad +171} (CHCl_3;\ c\ 0.2).$$

Dentatin A acetate (**50**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (1) ($C_{17}H_{22}O_5$), 288 $[M-H_2O]^+$ (4), 246 $[M-HOAc]^+$ (32), 228 $[246-H_2O]^+$ (100), 213 $[228-Me]^+$ (34), 200 $[228-CO]^+$ (30).

Desacylchrysanin-6-O-*methacrylate* (**51**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1725 (C=CCO$_2$R); MS *m/z* (rel. int.): 332.162 $[M]^+$ (0.2) ($C_{19}H_{24}O_5$), 317 $[M-Me]^+$ (0.2), 246 $[M-RCO_2H]^+$ (10), 228 $[246-H_2O]^+$ (30), 213 $[228-Me]^+$ (28), 69 $[C_3H_5CO]^+$ (100).

Desacylchrysanin-6-O-*senecioate* (**52**). Colourless gum, 3600 (OH), 1785 (γ-lactone), 1730 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.6) ($C_{20}H_{26}O_5$), 328 $[M-H_2O]^+$ (0.6), 246 $[M-RCO_2H]^+$ (9), 228 $[246-H_2O]^+$ (22), 213 $[228-Me]^+$ (15), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (47).

Desacyltanapsin-6-O-*methacrylate* (**54**). Colourless gum, 3620 (OH), 1780 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 246.125 $[M-RCO_2H]^+$ (5) ($C_{15}H_{18}O_3$), 69 $[C_3H_5CO]^+$ (100).

Desacyltanapsin-6-O-*senecioate* (**55**). Colourless gum, 3620 (OH), 1780 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.4) ($C_{20}H_{26}O_5$), 246 $[M-RCO_2H]^+$ (6), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (42).

'*Tanapsin*' (**56**). Colourless gum, 3620 (OH), 1780 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.3) ($C_{20}H_{26}O_5$), 246 $[M-RCO_2H]^+$ (7), 83 $[C_4H_7CO]^+$ (100).

Haageanolide acetate (**5**). Colourless gum, 1770 (γ-lactone) 1750, 1230 (OAc); MS *m/z* (rel. int.): 290.152 $[M]^+$ (3) ($C_{17}H_{22}O_4$), 230 $[M-HOAc]^+$ (100), 215 $[230-Me]^+$ (30), 202 $[230-CO]^+$ (14).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+76 \quad +81 \quad +91 \quad +170} (CHCl_3;\ c\ 0.2).$$

3β-*Acetoxy*-9β-*hydroxycostunolide* (**61**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1745 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (1) ($C_{17}H_{22}O_5$), 246 $[M-HOAc]^+$ (12), 231 $[246-Me]^+$ (6), 55 (100).

9β-*Hydroxy*-3β-*isobutyryloxycostunolide* (**62**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1740 (CO$_2$R); MS *m/z* (rel. int.): 334.178 $[M]^+$ (1) ($C_{19}H_{26}O_5$), 246 $[M-RCO_2H]^+$ (10), 228 $[246-H_2O]^+$ (6), 55 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+5 \quad +6 \quad +7 \quad +11} (CHCl_3;\ c\ 0.1).$$

9β-*Hydroxy*-4α,5β-*epoxycostunolide* (**63**). Colourless gum, 3600 (OH), 1780 (γ-lactone); MS *m/z* (rel. int.): 264.136 $[M]^+$ (16) ($C_{15}H_{20}O_4$), 246 $[M-H_2O]^+$ (5), 55 (100).

3β-*Hydróxy*-4α,5β-*epoxycostunolide* (**65**). Colourless gum, 3600 (OH), 1780 (γ-lactone); MS *m/z* (rel. int.): 264.136 $[M]^+$ (6) ($C_{15}H_{20}O_4$), 81 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-11 \quad -13 \quad -14 \quad -18} (CHCl_3;\ c\ 0.2).$$

3β-*Acetoxy*-4α,5β-*epoxycostunolide* (**66**). Colourless gum, 1780 (γ-lactone), 1745 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (1) ($C_{17}H_{22}O_5$), 246 $[M-HOAc]^+$ (32), 55 (100).

3β-*Isovaleryloxy- and* (2-*methylbutyryloxy*)-4α,5β-*epoxycostunolide*, **67** *and* **68**. Colourless gum, which could not be separated, 1780 (γ-lactone), 1730 (CO$_2$R); MS *m/z* (rel. int.): 348.194 $[M]^+$ (0.5) ($C_{20}H_{28}O_5$), 264 $[M-O=C=CHR]^+$ (15), 246 $[M-RCO_2H]^+$ (3), 85 $[C_4H_9CO]^+$ (62), 57 $[85-CO]^+$ (100).

1β,10α-*Epoxyhaageanolide acetate* (**70**). Colourless gum, 1780 (γ-lactone), 1750 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (3) ($C_{17}H_{22}O_5$), 264 $[M-ketene]^+$ (10), 246 $[M-HOAc]^+$ (4), 228 $[246-H_2O]^+$ (3), 218 $[246-CO]^+$ (9), 203 $[218-Me]^+$ (9), 81 (100).

9α-*Isobutyryloxydesacetyl laurenobiolide* (**72**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1735 (CO$_2$R); MS *m/z* (rel. int.): 334 $[M]^+$ (2), 246.125 $[M-RCO_2H]^+$ (4.5) ($C_{15}H_{18}O_3$), 228 $[246-H_2O]^+$ (4), 71 $[C_3H_7CO]^+$ (100). To 1 mg **72** in 1 ml Et_2O excess of CH_2N_2 was added. After 5 min the soln was evaporated and the residue was purified by TLC (Et_2O) affording 1 mg **75**, ^{1}H NMR see Table 10.

9α-*Isovaleryloxy- and* (2-*methylbutyryloxy*)-*desacetyl laurenobiolide* (**73** *and* **74**). Colourless gum, which could not be separated, 3600 (OH), 1780 (γ-lactone), 1735 (CO$_2$R); MS *m/z* (rel. int.): 348.194 $[M]^+$ (2) ($C_{20}H_{28}O_5$), 246 $[M-RCO_2H]^+$ (4), 85 $[C_4H_9CO]^+$, 57 $[85-CO]^+$ (100). The mixture was transformed to the pyrazolines **76** and **77** (see above), ^{1}H NMR spectra see Table 10.

9α-*Isobutyryloxy*-4β,5α-*epoxydesacetyl laurenobiolide* (**78**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1730 (CO$_2$R); MS *m/z* (rel. int.): 350 $[M]^+$ (0.1), 280.131 $[M-O=C=CMe_2]^+$ (0.6) ($C_{15}H_{20}O_5$), 262.121 $[M-RCO_2H]^+$ (1.4) ($C_{15}H_{18}O_4$), 244 $[262-H_2O]^+$ (1.5), 71 $[C_3H_7CO]^+$ (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+12 \quad +16 \quad +18 \quad +31} (CHCl_3;\ c\ 0.2).$$

Compound **78** was transformed to the pyrazoline **79** (see above), ^{1}H NMR see Table 10.

1β,10α-*Epoxydesacetyl laurenobiolide senecioate* (**81**). Colourless gum, 1780 (γ-lactone), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.3) ($C_{20}H_{26}O_5$), 246 $[M-RCO_2H]^+$ (1), 83 $[C_4H_7CO]^+$ (100).

1α,10β-*Epoxydesacetyl laurenobiolide senecioate and angelate* (**85** *and* **86**). Colourless gum, which could not be separated, 1775 (γ-lactone), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 346.178 $[M]^+$ (0.2) ($C_{20}H_{26}O_5$), 246 $[M-RCO_2H]^+$ (1), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (43).

14-*Acetoxydesacetyl laurenobiolide* (**90**). Colourless gum, 3600 (OH), 1770 (γ-lactone), 1750 (OAc); MS *m/z* (rel. int.): 306.147 $[M]^+$ (1) ($C_{17}H_{22}O_5$), 246 $[M-HOAc]^+$ (12), 228 $[246-H_2O]^+$ (30), 213 $[228-Me]^+$ (11), 55 (100).

14-*Acetoxy*-4β,5α-*epoxydesacetyl laurenobiolide* (**91**). Colourless gum, 3600 (OH), 1780 (γ-lactone), 1740 (OAc); MS *m/z* (rel. int.): 322.142 $[M]^+$ (1.5) ($C_{17}H_{22}O_6$), 280 $[M-ketene]^+$ (5), 262 $[M-HOAc]^+$ (2), 69 (100).

1α-*Peroxy*-1-*desoxytatridin B*-6-O-*methacrylate* (**97**). Colourless gum, 1775 (γ-lactone), 1725 (C=CCO_2R). Addition of triphenylphosphine in $CDCl_3$ gave **99**, which was transformed to the pyrazoline **101**, ^1H NMR see Table 10.

1β-*Peroxy*-1-*desoxytatridin B*-6-O-*methacrylate* (**98**) Colourless gum, 1775 (γ-lactone), 1725 (C=CCO_2R). Compound **98** was transformed by addition of triphenylphosphine to **100** and then by addition of CH_2N_2 to the pyrazoline, **102**, ^1H NMR see Table 10.

Preparation of **103**, **104**, **106** *and* **111**. 30 mg **71** in 3 ml CH_2Cl_2 was stirred for 5 min with 0.5 ml $NaHCO_3$ soln and 20 mg *m*-chloroperbenzoic acid. TLC (Et_2O) afforded 5 mg **71**, 20 mg **103**, 2 mg **104**, 2 mg **106** and 1 mg **111**, ^1H NMR spectra see Table 11. Compound **111** was identical with the natural lactone.

Preparation of **83**, **87**, **105** and **107**–**109**. 30 mg **71** was acetylated (Ac_2O, 1 hr, 70°) and the acetate were epoxidized as above. TLC (Et_2O) afforded 8 mg **83**, 8 mg **87**, 2 mg **105**, 2 mg **107**, 2 mg **108** and 2 mg **109**, ^1H NMR spectra see Table 11.

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