Phytochemistry, Vol. 20, No. 6, pp. 1323–1333, 1981.
Printed in Great Britain.

0031-9422/81/061323-11 $02.00/0

NEW TYPES OF SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM *TRICHOGONIA* SPECIES*

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(*Received* 8 *September* 1980)

Key Word Index—*Trichogonia grazielae*; *T. prancii*; *T. salviaefolia*; *T. scottmorii*; *T. villosa*; Compositae; Eupatorieae; sesquiterpene lactones; sesquiterpene dilactones; rearranged germacranolides; heliangolides; *p*-hydroxyacetophenones.

Abstract—The investigation of five *Trichogonia* species afforded seven new furanoheliangolides, three dilactones of a new type, four pairs of epimeric rearranged germacranolides, a new sesquiterpene acid and nine new *p*-hydroxyacetophenone derivatives, two of them of a new type with a furan ring. The structures were elucidated by spectroscopic methods and some chemical transformations. The structure of one of the dilactones was established by X-ray analysis. The biogenetic pathways and the chemotaxonomic importance of the new compounds are discussed.

INTRODUCTION

The mainly Brazilian genus *Trichogonia* (DC) Gardn. [1], earlier a section of *Kuhnia* [2], is placed in the *Gyptis* group (tribe Eupatorieae) [3]. No chemical investigations have been reported previously on these plants. In continuation of our chemosystematic studies of the tribe Eupatorieae, we have studied the constituents of five *Trichogonia* species to determine if the chemistry may give indications of the relationships in this diverse group.

RESULTS AND DISCUSSION

The aerial parts of *T. prancii* afforded a very complex mixture of sesquiterpene lactones, which could be only partly separated. The main constituents were the lactones **1a** and **4**, which could not be separated even by HPLC. The ^{1}H NMR spectrum of **1a** (Table 1) showed that a heliangolide with a furanone ring was present, which was further supported by the characteristic UV maximum and the IR bands. The nature of the ester residue also followed from the typical ^{1}H NMR signals, while the stereochemistry at C-6 through C-9 was deduced from the observed couplings. The relative position of the ester residue followed from the chemical shift of H-8, which was assigned by spin decoupling in the usual way. The presence of a 6,12-lactone was indicated by the similarity of the chemical shifts of H-5 through H-8 with those of known lactones of this type [4–6]. The stereochemistry at C-8 and C-9 was supported by the presence of a hydrogen bond between the 9-hydroxy and the 1-keto group, which followed from the IR band and the large H-9,OH-coupling.

Acetylation of **1a** and **4** using 4-pyrrolidinopyridine as a catalyst [7] afforded the acetates **2** and **5**, which were identical with two other lactones also present in the extract. Again a separation of these two lactones was not possible. The ^{1}H NMR data of **4** (Table 1) clearly showed that the 11,13-double bond in **1a** was epoxidized. All couplings were nearly the same as in the spectrum of **1a**. However, the orientation of the epoxide ring could not be assigned with certainty. Most probably a β-epoxide was present as H-6 seemed to be deshielded, if the chemical shifts were compared in the spectra of **1a** and **4**, while the signals of H-8 and H-9 were, as expected, at slightly higher fields in the spectrum of **4**. A further heliangolide was an isomer of **1a**, in which the relative positions of the methacrylate and the hydroxy group were interchanged. The ^{1}H NMR data (Table 1) and those of the acetate obtained by acetylation showed that the structure was **3a**. The free C-8 hydroxy group caused a considerable downfield shift of the H-6 signal, again supporting the proposed stereochemistry at these centres. Compounds **1a**, **2** and **3a** were derivatives of atripliciolide, which is the 8-desacyl-9-desoxy derivative of **1a** [6].

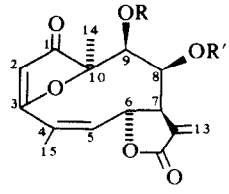
The structure elucidation of three further sesquiterpene lactones caused more difficulties. ^{1}H NMR spectroscopic investigations (Table 2) finally led to the structures **6**, **7** and **8a**. Mild acetylation of **6** afforded **7**, indicating identical stereochemistry at all centres in both compounds. Spin decoupling allowed the assignment of the signals of H-5 through H-9 in the usual way starting with irradiation of the H-7 signal. The chemical shifts of H-5 and H-6 obviously required an acceptor group at C-3, while a quartet at δ 5.01 and a doublet at 1.39 (3 H) could be explained, if a *seco*-germacranolide with a ten-membered lactone ring were present. Inspection of a model showed that H-6 should be strongly deshielded by the lactone oxygen, the C-10 hydroxy and the C-8 ester group. The observed couplings were in good agreement with the angles deduced from the model. We have given the name trichogoniolide to compound **6**.

* Part 332 in the series "Naturally Occurring Terpene Derivatives". For Part 331 see Bohlmann, F., Jakupovic, J., Dhar, A. K., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1081.

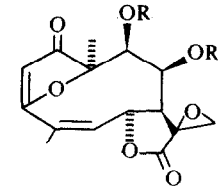
Table 1. ^{1}H NMR spectral data of compounds of **1a**, **1b**, **2**, **3a**, **3b**, **4**, **5** and **41** (400 MHz, TMS as internal standard, $CDCl_3$)

	1a	**1b**	**2**	**3a**	**3b**	**4**	**5**	**41**
H-2	5.64 *s*	5.63 *s*	5.64 *s*	5.61 *s*	5.67 *s*	5.65 *s*	5.63 *s*	5.60 *br.s*
H-5	5.97 *dq*	5.98 *dq*	6.00 *dq*	6.00 *dq*	6.02 *dq*	6.03 *dq*	6.06 *dq*	2.58 *ddd* 2.06 *br.d*
H-6	4.95 *ddq*	5.03 *ddq*	5.24 *ddq*	5.73 *ddq*	5.36 *ddq*	5.03 *ddq*	5.21 *ddq*	4.27 *ddd*
H-7	3.67 *dddd*	3.65 *dddd*	3.67 *dddd*	3.46 *dddd*	3.69 *dddd*	3.19 *dd*	3.26 *dd*	3.30 *m*
H-8	5.10 *dd*	5.18 *dd*	5.38 *dd*	4.16 *dd*	5.50 *dd*	4.98 *dd*	5.13 *dd*	5.30 *br.d*
H-9	4.19 *dd*	4.8 *dd*	5.33 *d*	5.28 *d*	5.30 *d*	3.98 *dd*	5.09 *d*	4.18 *dd*
H-13	6.36 *d*	6.39 *d*	6.40 *d*	6.37 *d*	6.44 *d*	3.47 *d*	3.42 *d*	6.40 *d*
H-13′	5.72 *d*	5.72 *d*	5.83 *d*	5.70 *d*	5.89 *d*	3.41 *d*	3.36 *d*	5.77 *d*
H-14	1.67 *s*	1.68 *s*	1.53 *s*	1.48 *s*	1.53 *s*	1.65 *s*	1.51 *s*	1.66 *s*
H-15	2.06 *dd*	2.07 *dd*	1.07 *dd*	2.05 *dd*	2.09 *dd*	2.09 *dd*	2.07 *dd*	1.40 *d*
OCOR	6.03 *dq*	6.17 *qq*	6.07 *dq*	6.45 *dq*	6.28 *dq*	6.12 *dq*	6.14 *dq*	6.16 *qq*
	5.68 *dq*	1.94 *dq*	5.63 *dq*	5.74 *dq*	5.72 *dq*	5.72 *dq*	5.73 *dq*	1.95 *dq*
	1.88 *dd*	1.85 *dq*	1.89 *dd*	2.02 *dd*	1.98 *dd*	1.89 *dd*	1.90 *dd*	1.85 *dq*
OAc	—	—	2.13 *s*	—	2.01 *s*	—	2.14 *s*	
OH	3.55 *d*	3.40 *d*	—		—	3.61 *d*	—	3.90 *d*

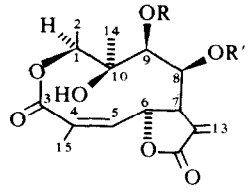
J (Hz): Compounds: **1**/**2**: 5,6 = 4; 5,15 = 1.7; 6,7 = 3.5; 6,15 = 1.7; 7,8 = 2; 7,13 = 3; 7,13′ = 2.7; 8,9 = 3; (**1**: 9,OH = 11.5); compounds **3a**/**3b**: 5,6 = 3.5; 5,15 = 1.8; 6,7 = 3.5; 6,15 = 1.8; 7,8 = 2; 7,13 = 3.5; 7,13′ = 3; 8,9 = 2.5; compounds **4**/**5**: 5,6 = 4; 5,15 = 1.7; 6,7 = 4; 6,15 = 1.7; 7,8 = 2; 8,9 = 2.5; 13,13′ = 4.5; OMeacr: $3'_1$, $3'_2$ = 3′, 4′ ~ 1; compound **41**: 4,5 = 7; 4,15 = 7; 5,5′ = 14; 5,6 = 11; 6,7 = 5; 7,8 ~ 0.5.



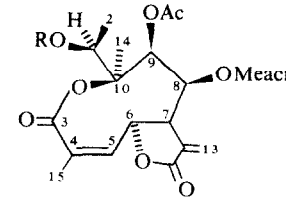
	1a	**1b**	**2**	**3a**	**3b**	**3c**
R	H	H	Ac	Meacr	Meacr	4′-AcAng
R′	Meacr	Ang	Meacr	H	Ac	H



	4	**5**
R	H	Ac
R′	Meacr	Meacr



	6	**7**
R	H	Ac
R′	Meacr	Meacr



8a R = H
8b R = Ac

The ^{1}H NMR data of **8a** (Table 2) showed that this lactone must be an isomer of **6**. The H-1 signal was a double quartet, its position already indicated a proton under a free hydroxy group. Irradiation of the doublet at δ 2.49 collapsed the signal at 3.98 to a quartet. The latter was coupled with the methyl doublet at 1.33. The presence of a nine-membered lactone was supported by the observed downfield shift of the 10-methyl signal. Acetylation afforded the diacetate **8b**, its ^{1}H NMR data further supported the proposed structure of **8a**, which we have named isotrichogoniolide-9-O-acetate. The stereochemistry at C-1 in **6**, **7** and **8a** could not be determined. X-ray analysis of **7** (Fig. 1) showed that the 1-methyl was β-orientated and therefore the same configuration was also very likely in **8a**. Most probably these lactones were formed by degradation of **1a** (Scheme 1). So far the only known *seco*-germacranolide is the diol pycnolide [8]. The aerial parts also contained germacrene D, bicyclogermacrene, α-humulene, taraxasterol and taraxasteryl acetate. The roots afforded bicyclogermacrene, α-humulene, lupeyl acetate and two further compounds with molecular formulae $C_{14}H_{12}O_3$ and $C_{16}H_{16}O_4$. The ^{1}H NMR data (Table 3) showed that these compounds must be very similar. The former had an aldehyde group which was replaced in the second compound by a CH_2OAc group. The signals of the aromatic protons indicated the presence of unsymmetrically trisubstituted benzene derivatives, one substituent being a vinyl group, which must be far away from the aldehyde group, as no considerable shift differences in the ^{1}H NMR spectra of the two compounds were observed, while the narrowly split downfield signal at δ 8.10 in the spectrum of the aldehyde was at higher field in the spectrum of the acetate. In the latter, this signal was further split to a double triplet indicating an allylic coupling with the CH_2OAc protons. The signal at 8.10 was coupled with a broadened singlet at 7.30, which was strongly shifted after addition of Eu(fod)$_3$. All data agreed most accurately with the structures **9** and **10a**. This assumption was confirmed by the catalytic hydrogenation of **10a**, which led to the alcohol **12a**, as could be deduced from the ^{1}H NMR data (Table 3). However, only in a mixture of $CDCl_3$–C_6D_6 were all the signals separated. Spin decoupling showed that the signal at δ 1.72 was

Table 2. ^{1}H NMR spectral data of compounds **6**, **7**, **8a** and **8b** (400 MHz, TMS as internal standard, $CDCl_3$)

	6	**7**	**7**(C_6D_6)	**8a**	**8b**
H-1	4.89 *q*	5.01 *q*	4.84 *q*	3.98 *dq*	5.19 *q*
H-2	1.51 *d*	1.39 *d*	1.13 *d*	1.33 *d*	1.38 *d*
H-5	6.29 *dq*	6.33 *dq*	6.03 *dq*	6.39 *dq*	6.42 *dq*
H-6	6.39 *ddq*	6.21 *ddq*	6.34 *ddq*	6.17 *ddq*	6.13 *ddq*
H-7	3.61 *dddd*	3.76 *dddd*	3.79 *dddd*	3.20 *dddd*	3.23 *dddd*
H-8	5.41 *dd*	5.49 *dd*	5.61 *dd*	5.59 *dd*	5.63 *dd*
H-9	4.26 *br.dd*	5.70 *d*	5.79 *d*	5.63 *d*	5.49 *d*
H-13	6.25 *d*	6.24 *d*	6.19 *d*	6.33 *d*	6.32 *d*
H-13′	5.71 *d*	5.69 *d*	5.22 *d*	5.68 *d*	5.67 *d*
H-14	1.46 *s*	1.43 *s*	0.96 *s*	1.75 *s*	1.83 *s*
H-15	1.94 *dd*	1.97 *dd*	1.75 *dd*	1.93 *dd*	1.94 *dd*
OMeacr	6.15 *dq*	6.03 *dq*	6.24 *dq*	6.00 *dq*	5.96 *dq*
	5.66 *dq*	5.58 *dq*	5.19 *dq*	5.58 *dq*	5.56 *dq*
	1.92 *dd*	1.86 *dd*	1.88 *dd*	1.85 *dd*	1.83 *br.s*
OAc	—	2.14 *s*	1.66 *s*	2.16 *s*	2.08 *s*
					1.98 *s*
OH		2.64 *br.s*		2.49 *d*	—

J (Hz): Compounds **6**/**7**: 1,2 = 6.5; 5,6 = 4; 5,15 = 1.7; 6,7 = 1.5; 6,15 = 1.7; 7,8 = 3.5; 7,13 = 2; 7,13′ = 1.7; 8,9 = 4; compounds **8a**/**8b**: 1,2 = 6.5; 5,6 = 2.5; 5,15 = 1.8; 6,7 = 2.5; 6,15 = 1.8; 7,8 = 4; 7,13 = 2.5; 7,13′ = 2; 8,9 = 5; OMeacr: $3'_1,3'_2 = 3',4' \sim 1$.

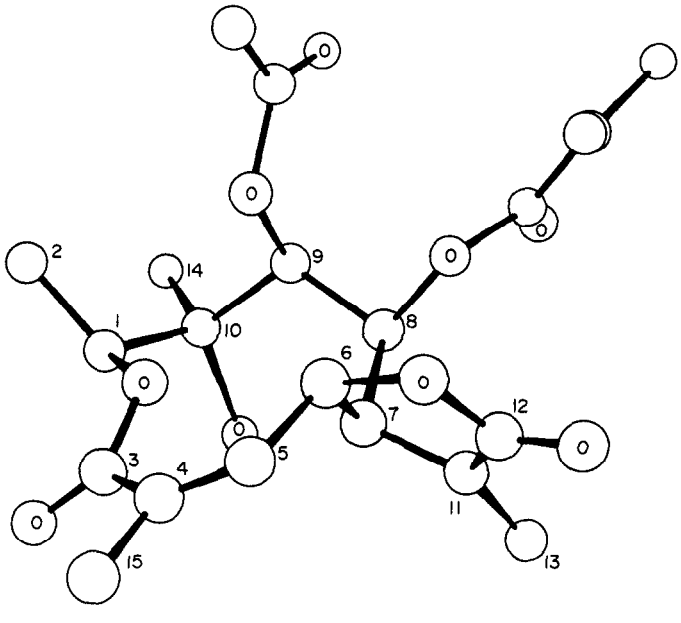
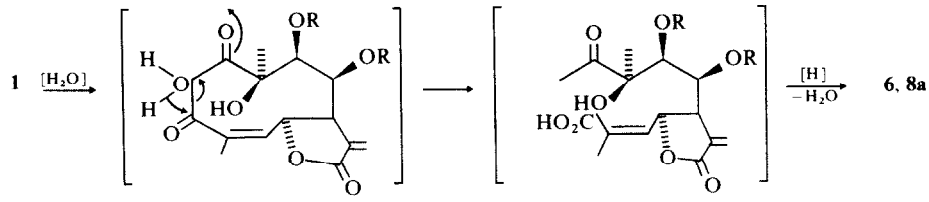


Fig. 1. Perspective drawing of compound **7**.



Scheme 1.

coupled with two groups of signals, which must be assigned to CH_2OAc and CH_2OH. The proton which coupled with these groups was further coupled with a multiplet at 1.56. Irradiation of the latter collapsed the triplet at 2.62 to a singlet, clearly indicating the sequence H-9 through H-13. Acetylation of **12a** afforded a symmetrical compound as could be seen from the ^1H NMR spectrum (Table 3). The formation of **12a** obviously included a hydrogenolysis of the intermediate **11** (Scheme 2). Sodium boronate reduction of **9** gave the alcohol **10b**, whose ^1H NMR data (Table 3) also supported the proposed structures. Compound **10a** is probably formed in the plant starting with the prenylated *p*-methoxyacetophenone **13** by oxidation and ring closure via **14** and **15** (Scheme 3).

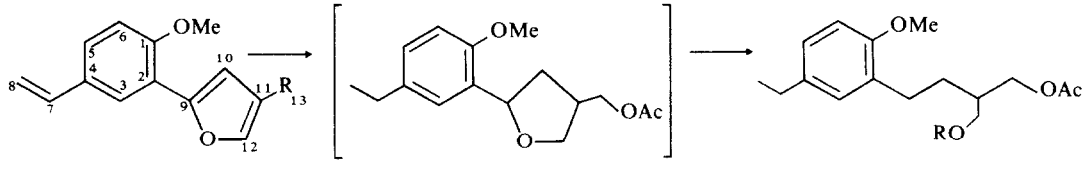
The roots of *T. grazielae* afforded germacrene D and again several *p*-hydroxyacetophenone derivatives, only one being known, the carbinol **21** [9]. The structures of six further compounds (**16**–**20** and **22**) followed from the ^1H NMR data (Table 4). From the spectrum of **16** the presence of a dimethyl allyl side-chain was obvious. Furthermore, the typical signals of an angelate could be seen, which had to be placed in a benzylic position, following from the corresponding quartet at δ 5.91. The ^1H NMR data of **17** were similar to those of the known 4-acetyl chromanone [10]. However, the acetyl group was

Table 3. ^1H NMR spectral data of compounds **9**, **10a**, **10b**, **12a** and **12b** (270 MHz, TMS as internal standard, $CDCl_3$)

	9	**Δ*(9)**	**10a**	**Δ*(10a)**	**10b**	**12a***	**12b**
H-3	7.91 *d*	0.05	7.89 *d*	0.02	7.90 *d*	6.92 *br.s*	6.95 *d*
H-5	7.37 *dd*	0.02	7.31 *dd*	0.01	7.31 *dd*	6.93 *br.d*	7.00 *dd*
H-6	6.95 *d*	0.02	6.98 *d*	0.01	6.92 *d*	6.63 *d*	6.76 *d*
H-7	6.72 *dd*	0.03	6.71 *dd*	0.01	6.71 *dd*	2.52 *q*	2.57 *q*
H-8*t*	5.70 *dd*	0.03	5.69 *dd*	0.02	5.70 *dd*	1.18 *t*	1.21 *t*
H-8*c*	5.21 *dd*	0.03	5.18 *dd*	0.02	5.18 *dd*		
H-9	—	—	—	—	—	2.62 *t*	2.65 *t*
H-10	7.30 *br.s*	0.33	6.98 *br.s*	0.12	7.01 *br.s*	1.56 *m*	1.66 *m*
H-11	—	—	—	—	—	1.72 *ddddt*	2.06 *m*
H-12 H-12′	8.10 *d*	0.11	7.89 *dt*	0.12	7.46 *dt*	3.39 *dd* 3.34 *dd*	4.14 *dd*
H-13 H-13′	9.98 *s*	0.35	5.02 *br.s*	0.40	4.62 *br.s*	4.15 *dd* 4.06 *dd*	4.10 *dd*
OAc	—	—	2.09 *s*	0.36	—	1.83 *s*	2.06 *s*
OMe	3.96 *s*	0.04	3.95 *s*	0.02	3.96 *s*	3.58 *s*	3.79 *s*

* 400 MHz, $CDCl_3$–C_6D_6(1:2).

J (Hz): Compounds **9**,**10a**/**b**: 3,5 = 2; 5,6 = 8.5; 7,8*t* = 17; 7,8*c* = 10; 8*t*,8*c* = 1; 10,12 = 12,13 ~ 1; compound **12a**: 5,6 = 8; 7,8 = 7.5; 9,10 = 8; 10,11 ~ 5; 11,12 = 4.5; 11,12′ = 6; 12,12′ = 11; 11,13 = 4.5; 11,13′ = 6; 13,13′ = 11; (**12b**: 11,12 = 11,13 = 5; 11,12′ = 11,13′ = 6).

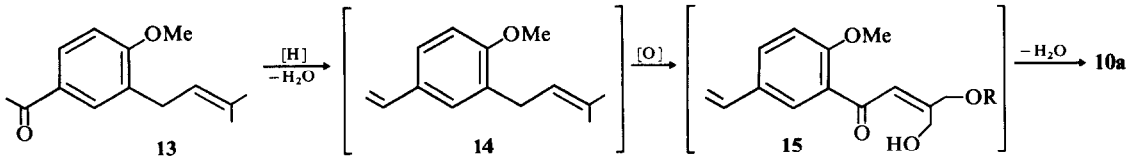


9 R = CHO
10a R = CH_2OAc
10b R = CH_2ON

11

12a R = H
12b R = Ac

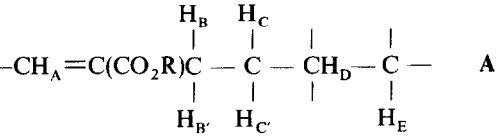
Scheme 2.



Scheme 3.

replaced by a vinyl group, as could be deduced from the typical signals. The substitution pattern clearly followed from the couplings and chemical shifts of the aromatic protons. The ^{1}H NMR data of **18a** showed that we were dealing with an *ortho*-hydroxyketone (12.81 *s*). All other signals were in full agreement with the structure proposed. The ^{1}H NMR data of **19** and **20** were similar, except for the signals of the ester residue. While **19** was obviously an angelate, the situation in **20** only became clear in C_6D_6 at 400 MHz. Due to the chiral centre at C-7, the protons of the CH_2OAc group were not equivalent and therefore two complex signals were observed which were poorly separated. Irradiation at 1.83 collapsed the signals at 5.91 to a triplet and those at 5.27 and 5.22 to doublets. The structure of **22** followed directly from the ^{1}H NMR data. The free 7-hydroxy group caused a pronounced upfield shift of H-7 compared with those in **19** and **20**. Compound **18a** is closely related to **10a**.

The aerial parts afforded germacrene D, α-humulene, aromadendrene, caryophyllene, herniarin, the *p*-hydroxyacetophenone derivative **13** and γ-muurolen-15-oic acid (**23a**), whose structure elucidation caused some difficulties. From the ^{1}H NMR spectrum of the corresponding methyl ester **23b** (Table 5), the presence of an *iso*-propyl group, a conjugated carboxyl group and a methylene group were deduced. The ^{13}C NMR spectrum (see Experimental) showed no quarternary saturated carbon signals and four tertiary ones. Together with the ^{1}H NMR data this was an indication of the presence of a cadinane or a guaiane derivative. Careful spin decoupling in different solvents, also after addition of Eu(fod)$_3$, led to the partial structure **A**.



A

The allylic position of H_B followed from the allylic coupling with H_A, while the presence of a neighbouring CH_2 group was deduced from the two observed vicinal couplings of $H_{B'}$. However, $H_{B'}$ only gave a broadened double doublet. Irradiation of the H_D signal showed in

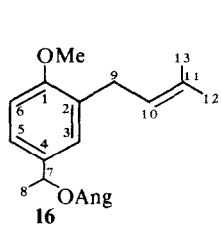
Table 4. ^{1}H NMR spectral data* of compounds **16**–**20** and **22** (270 MHz, TMS as int. stand., $CDCl_3$)

	16	**17**	**18a**	**18b**	**19**	**20**†	**22**
H-3	7.16 *d*	7.88 *d*	7.76 *d*	7.61 *d*	7.78 *d*	7.82 *d*	7.84 *d*
H-5	7.18 *dd*	7.57 *dd*	7.58 *dd*	7.46 *dd*	7.50 *dd*	7.29 *dd*	7.55 *dd*
H-6	6.80 *d*	6.91 *d*	6.97 *d*	6.91 *d*	6.98 *d*	7.07 *d*	6.93 *d*
H-7	5.91 *q*	6.66 *dd*	6.68 *dd*	6.67 *dd*	5.94 *q*	5.97 *q*	4.89 *q*
H-8	1.55 *d*	5.68 *d*	5.63 *d*	5.66 *d*	1.58 *d*	1.42 *d*	1.49 *d*
H-8′		5.21 *d*	5.19 *d*	5.18 *d*			
H-9	3.30 *br.d*	—	—	—	—	—	—
H-10	5.30 *br.t*	2.74 *s*	6.83 *qq*	6.62 *qq*	6.79 *qq*	6.68 *qq*	2.73 *s*
H-12	1.74 *br.s*	1.47 *s*	2.07 *d*	1.98 *d*	2.07 *d*	1.64 *d*	1.46 *s*
H-13	1.70 *br.s*		2.22 *d*	2.24 *d*	2.21 *d*	2.09 *d*	
OCOR	6.03 *qq*	—	—	—	6.08 *qq*	5.91 *tq*	—
	1.98 *dq*	—	—	—	1.98 *dq*	5.27 *ddq*	—
	1.90 *dq*	—	—	—	1.91 *dq*	5.21 *ddq*	—
				—		1.83 *dt*	—
OAc	—	—	—	—	—	1.76 *s*	—
OMe	3.81 *s*	—	—		—	—	—
OH	—	—	12.81 *s*		12.80 *s*	12.83 *s*	—

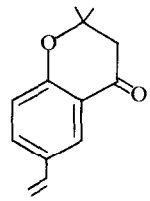
* 400 MHz, C_6D_6.

† Numbering as in **16**.

J (Hz): Compound **16**: 3,5 = 2; 5,6 = 8.5; 7,8 = 6.5; 9,10 = 7.5; compounds **17**/**18**: 7,8 = 17; 7,8′ = 10.5; compound **20**: 3′,4′ = 5; 3′,5′ = 1.5; $4'_1$,$4'_2$ = 12.



16



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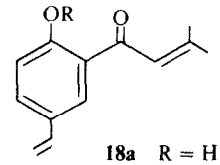
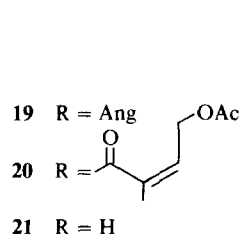
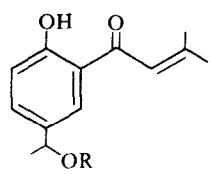
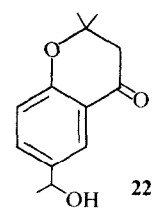


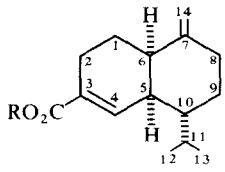
18a R = H
18b R = Me



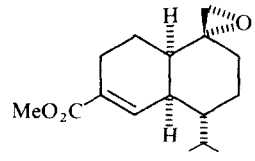




22



23a R = H
23b R = Me



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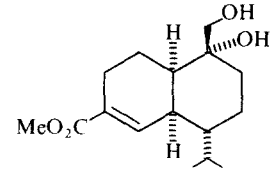

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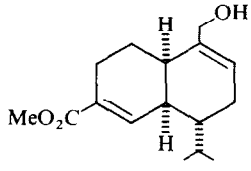

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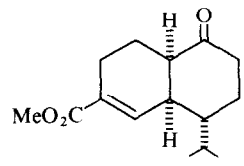
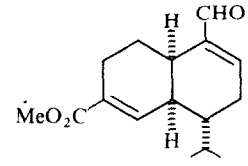


27



28

addition to the coupling J_{CD} that this proton was further coupled with a proton, which after addition of Eu(fod)$_3$ could be assigned clearly (H_E). The latter was further coupled with the olefinic proton (H_A). Therefore the presence of a six-membered ring was established. Further decoupling experiments showed that the *iso*-propyl group was located α to H_E. As H_D showed no additional coupling, an allylic position was very likely, in agreement with its chemical shift. This, however, led to the structure of a cadinene derivative. The observed couplings $J_{5,6}$ and $J_{5,10}$ required the assigned stereochemistry. As some signals, even at 400 MHz, were still overlapped, compound **23b** was degraded. Epoxidation gave, as expected, only one epoxide. Acid-catalysed hydrolysis led to the diol **25** and the elimination product **26**, its ^{1}H NMR spectrum and spin decoupling further supporting the proposed structure and stereochemistry of **23b**. The *cis* position of H-6 and the C-7 hydroxy group in the diol **25** followed from the direction of the elimination of water. As the signals of H-9 were still overlapped, the H-10 signal was not first order. However, spin decoupling established the proposed stereochemistry at C-5, C-6 and C-10. The diol **25** was further degraded to the corresponding ketone **27**, but its ^{1}H NMR spectrum was not very instructive as most signals were overlapped. Furthermore, compound **26** was transformed to the aldehyde **28**, which had ^{1}H NMR data in agreement with the proposed structure.

The aerial parts of *T. scottmorii* afforded germacrene D, γ-selinene (**29**) and the corresponding ketone **30**, the 4-hydroxygermacra-1(10),5-diene (**31**), the chromene **32**, taraxasteryl acetate and again a furanoheliangolide, the acetoxy angelate **3c** [11].

The aerial parts of *T. salviaefolia* afforded germacrene D, taraxasteryl acetate and a complex mixture of sesquiterpene lactones, all being of a new type. After repeated TLC four pairs of inseparable, epimeric hemiacetals were obtained, **36a** and **36b**, **37a** and **37b**, **38a** and **38b** and **39a** and **39b**. The main constituents were **37a** and **37b**, which on oxidation afforded a single compound, the dilactone **37c**. The ^{1}H NMR data of **37a/b** (Table 6) showed the presence of an acetate and an epoxyangelate residue, which must be placed at C-8 and C-9, as irradiation of the H-1 signal caused a sharpening of a doublet which was coupled with a second one. The H-13 signals were singlets, indicating a substituent at C-7. The ^{13}C NMR spectrum of the epimers indicated that only one quarternary carbon not bearing an oxygen function was present, while two downfield doublets at 105.4 and 108.7 respectively, indicated hemiacetal carbons. Inspection of models showed that the two epimers

Table 5. ^{1}H NMR spectral data of compounds **23b**, **24** and **26–28** (400 MHz, TMS as internal standard)

	23b							
	$CDCl_3$	C_6D_6	$+Eu(fod)_3$	**24**	**26** (C_6D_6)	Δ*(**26**)	**27** ($CDCl_3$)	**28** ($CDCl_3$)
H-1α	2.14 *m*	1.50 *m*	1.58 *m*		1.73 *m*	0.07		2.01 *br.d*
H-1β	1.95 *dddd*	1.82 *dddd*	1.97 *dddd*		1.42 *dddd*	0.09		1.40 *dddd*
H-2α	2.2 *m*	2.34 *m*	2.87 *br.ddd*		2.18 *br.ddd*	0.20		2.36 *m*
H-2β	2.5 *br.dd*	2.62 *br.dd*	3.25 *br.dd*		2.45 *br.ddd*	0.13		2.39 *br.d*
H-4	7.12 *ddd*	7.31 *br.d*	7.80 *br.d*	7.13 *br.d*	7.19 *ddd*	0.11	6.91 *ddd*	7.07 *br.d*
H-5	2.2 *m*	2.12 *m*	2.29 *ddd*		2.12 *ddd*	0.13		2.26 *ddd*
H-6	2.39 *br.ddd*	2.34 *m*	2.49 *ddd*		2.26 *br.ddd*	0.23	2.77 *ddd*	2.34 *m*
H-8	2.20 *m*	2.12 *m*	2.12 *m*		5.53 *br.dd*	0.30		6.83 *br.dd*
H-9α	1.54 *m*	1.40 *m*	1.55 *m*		1.73 *m*	0.18		2.36 *ddd*
H-9β	1.73 *dddd*	1.54 *m*						2.16 *br.dd*
H-10	1.10 *dddd*	1.03 *m*	1.05 *m*		1.32 *m*	0.19		1.67 *dddd*
H-11	2.0 *m*	1.95 *dqq*	2.10 *m*		1.89 *dqq*	0.06	2.04 *dqq*	2.01 *dqq*
H-12	0.93 *d*	0.84 *d*	0.88 *d*	0.94 *d*	0.77 *d*	0.04	1.04 *d*	0.96 *d*
H-13	0.86 *d*	0.73 *d*	0.78 *d*	0.91 *d*	0.72 *d*	0.05	0.97 *d*	0.93 *d*
H-14	4.70 *br.s*	4.75 *br.s*	4.79 *br.s*	2.64 *d*	3.91 *br.d*	0.55	—	9.42 *s*
H-14′	4.65 *dd*	4.73 *br.s*	4.76 *br.s*	2.63 *d*	3.80 *br.d*	0.55	—	
OMe	3.74 *s*	3.55 *s*	4.20 *s*	3.74 *s*	3.45 *s*	0.18	3.74 *s*	3.75 *s*

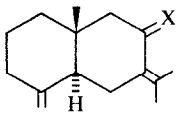
* Δ-values after addition of $Eu(fod)_3$.

J (Hz): Compound **23b**: 1α,1β = 13; 1α,2α = 6; 1α,6 = 12; 1β,2α = 12; 1β,2β = 6; 1β,6 = 12; 2α,4 = 2β,4 ~ 1.5; 4,5 = 5; 5,6 = 6; 5,10 = 12; 8α,9β = 8β,9β = 3.5; 8,14′ ~ 1.5; 9α,9β = 13; 9α,10 = 12; 9β,10 = 4; 10,11 = 12; 11,12 = 11,13 = 7; compound **26**: 1α,1β = 10; 1α,2α = 1α,2β = 4; 1β,2α = 10; 1β,2β = 5; 1β,6 = 10; 2α,2β = 17; 2α,4 = 2β,4 ~ 1.5; 4,5 = 5; 5,6 ~ 5; 5,10 = 10; 8,9 = 3.5; 8,14′ ~ 1.5; 10,11 ~ 10; 11,12 = 11,13 = 7; compound **28**: 1α,1β = 12; 1β,2α = 1β,6 = 12; 1β,2β = 5; 4,5 = 5; 5,6 = 6; 5,10 = 10; 8,9α = 5; 8,9β = 1.5; 9α,9β = 19; 9α,10 = 10; 9β,10 = 5; 10,11 = 10; 11,12 = 11,13 = 7.

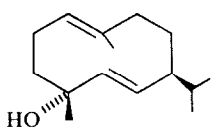
obviously differed in the stereochemistry at the hemiacetal carbon. In the case of the α-orientated hydroxyl (**37a**) H-1 was deshielded, while the β-hydroxy group (**37b**) deshielded the 4-methyl group. A smaller effect on the chemical shifts of H-8, H-9 and H-13 was observed. In the spectrum of the dilactone **37c** the expected shifts were obtained (Table 6). In particular, the downfield shift of the C-4 methyl signal supported the position of the new lactone carbonyl. The stereochemistry at C-6 was deduced from the chemical shift of H-6, which obviously was not much affected by the orientation of the 5-hydroxyl group, while a 6β-proton should be deshielded strongly by a 5β-hydroxy group. The observed $Eu(fod)_3$-induced shifts further supported the proposed stereochemistry. The ^{1}H NMR spectra of the three other pairs of epimers were similar to those of **37a/b**. The spectrum of the epimers **36a/b** showed that the epoxyangelate was replaced by an angelate residue. Compounds **38a/b** and **39a/b** obviously had a free 9-hydroxy group, as the broadened doublet (allylic coupling with H-1) was shifted to higher fields. This was the main argument for the relative position of the ester groups in **36a/b** and **37a/b**. A small shift difference for H-8 in the spectra of these two pairs further supported this assumption. We propose the name trichosalviolide for the parent compound of these lactones without oxygen functions at C-5, C-8 and C-9 (numbering as in a germacranolide). Most probably these lactones are formed as shown in Scheme 4 starting with the epoxide **33** which was formed by oxidation of costunolide. A Wagner–Meerwein rearrangement of the opened epoxide and subsequent attack of the aldehyde carbonyl at C-7, transformed to a cation by protonation of the hydroxyl, would lead to the natural compounds.

The roots afforded germacrene D, bicyclogermacrene and again several *p*-hydroxyacetophenone derivatives, the vinyl compounds **16**, **17** and **18a** as well as the phenols **19–21**. In addition to these compounds, the methyl ether of **18a** (**18b**) and the enol ether of **17** (**40**) were isolated. The structures followed from the mass spectra and the ^{1}H NMR data. In the ^{1}H NMR spectrum of **18b** some signals were shifted slightly, compared with those of **18a** (Table 4), while the ^{1}H NMR data of **40** (see Experimental) showed that no aromatic ketone was present. Consequently the signals of the aromatic protons were at higher fields. The position of the methoxy group followed from the chemical shift of the olefinic proton.

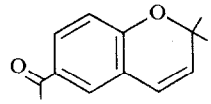
The roots of *T. villosa* afforded germacrene D, **18a**, **19**, **20** and **40**, while the aerial parts gave germacrene D, bicyclogermacrene, α-humulene, aromadendrene, taraxasteryl acetate, **18a** and the furanoheliangolides **1b** and **41**. The ^{1}H NMR data of **1b** were similar to those of **1a** (Table 1) except for the signals of the different ester residues. The ^{1}H NMR spectrum of **41** showed some similarity to that of **1b** (Table 1). The presence of a methyl doublet, however, and the signals of H-4 through H-6 and of H-15



29 X = H,H
30 X = O



31



32

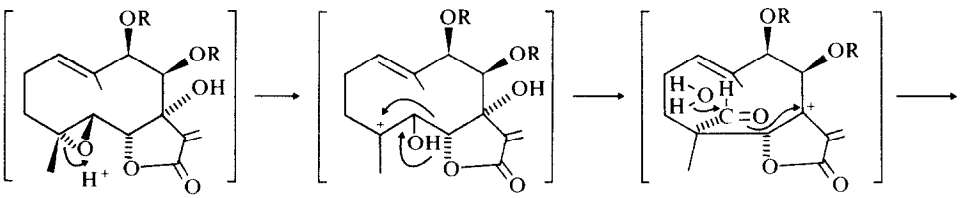
Table 6. ^{1}H NMR spectral data of compounds **36a/b–39a/b**

	$CDCl_3$, 400 MHz										
	36a	**36b**	**37a**	**37b**	Δ*		**37c**	**38a**	**38b**	**39a**	**39b**
H-1	6.01 *br.dd*	5.68 *br.dd*	6.03 *br.dd*	5.68 *br.dd*	0.29	0.21	5.52 *br.dd*	5.84 *br.d*	5.55 *br.d*	5.86 *br.d*	5.55 *br.d*
H-2	2.3 *m*		2.45 *m*								
H-2′	2.25 *ddd*		2.34 *br.d*				2.53 *m*	2.4–2.1 *m*		2.4–2.1 *m*	
H-3	1.65 *br.dd*		1.66 *br.dd*				2.42 *m*	1.68 *br.dd*		1.68 *m*	
H-3′	2.3 *m*		2.25 *ddd*				2.05 *m*				
H-5	4.93 *s*	5.39 *s*	4.93 *d*	5.39 *d*	0.23	0.25	—	4.93 *s*	5.38 *s*	4.92 *d*	5.38 *d*
H-6	4.92 *s*	4.87 *s*	4.92 *s*	4.88 *s*	0.35	0.35	5.11 *s*	4.93 *s*	4.88 *s*	4.92 *s*	4.88 *s*
H-8	5.69 *d*	5.73 *d*	5.66 *d*	5.71 *d*	0.77	0.77	5.73 *d*	5.60 *d*	5.63 *d*	5.63 *d*	5.67 *d*
H-9	4.79 *br.d*	6.75 *br.d*	6.80 *br.d*	5.77 *br.d*	0.78	0.76	5.95 *d*	4.85 *d*	4.80 *br.d*	4.83 *d*	4.79 *d*
H-13	6.45 *s*	6.40 *s*	6.42 *s*	6.37 *s*	0.29	0.31	6.61 *s*	6.46 *s*	6.40 *s*	6.43 *s*	6.37 *s*
H-13′	6.12 *s*	6.07 *s*	6.11 *s*	6.05 *s*	0.27	0.31	6.28 *s*	6.09 *s*	6.03 *s*	6.08 *s*	6.02 *s*
H-14	1.79 *br.s*	1.82 *br.s*	1.82 *br.s*	1.85 *br.s*	0.26	0.27	1.89 *br.s*	1.78 *br.s*	1.82 *br.s*	1.81 *br.s*	1.84 *br.s*
H-15	0.96 *s*	2.02 *s*	0.97 *s*	1.03 *s*	0.14	0.22	1.11 *s*	0.97 *s*	1.03 *s*	0.97 *s*	1.03 *s*
OAc	2.02 *s*	2.03 *s*	2.04 *s*	2.05 *s*	0.26	0.34	2.05 *s*	—	—	—	—
OCOR	6.07 *qq*		3.00 *q*†		0.46		3.03 *q*	6.14 *qq*		3.00 *q*	
	1.92 *dq*		1.19 *d*		0.47		1.22 *d*	1.97 *dq*		1.19 *d*	
	1.82 *dq*		1.95 *s*		0.32		1.53 *s*	1.82 *br.s*		1.53 *s*	
OH			3.65 *d*	2.66 *d*			—				

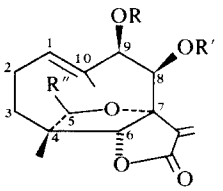
* Δ-values after addition of $Eu(fod)_3$.

† In C_6D_6: 2.66 and 2.64 *q*, 1.24 and 1.22 *d*, 1.47 and 1.45 *s*.

J (Hz): 1,2 = 12; 1,2′ = 3.5; 1,9 ~ 0.5; 2,3 ~ 2; 2′,3 = 8; 3,3′ = 14; 5,OH = 4.5 (compound **37b**: 2.5); 8,9 = 4; OAng: 3′,5′ = 7; 3′,5′ = 4′,5′ = 1.5; OEpang: 3′,4′ = 5.

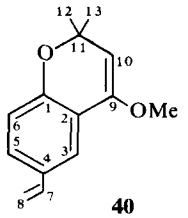


33 **34** **35**



	36a **36b**	**37a** **37b**	**37c**	**38a** **38b**	**39a** **39b**
R	Ac	Ac	Ac	H	H
R′	Ang	Epang	Epang	Ang	Epang
R″	α-OH β-OH	α-OH β-OH	=O	α-OH β-OH	α-OH β-OH

Scheme 4.



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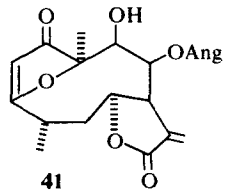

41

were typically changed indicating a hydrogenated 4,5-double bond. The stereochemistry at C-4 was probably the same as in zexbrevin [12], an 8-*O*-methacrylate.

The overall picture of the chemistry of the genus *Trichogonia* showed that *p*-hydroxyacetophenone derivatives are characteristic, especially those where the aceto group is transformed to a vinyl group. Furthermore, the occurrence of highly oxidized germacranolides and their transformation products seems to be typical. Furanoheliangolides have been isolated from this group so far only from *Conocliniopsis* [13]. Highly oxygenated sesquiterpene lactones are also present in *Lasiolaena* [14] and *Agrianthus* [15], while *p*-hydroxyacetophenone derivatives were isolated from a *Bahianthus* [16] and a *Campuloclinium* species (F. Bohlmann *et al.*, unpublished results). This taxonomically somewhat diverse group therefore seems also not to be very uniform chemically. However, so far not many genera have been investigated.

EXPERIMENTAL

The air-dried plant material was extracted with Et_2O–petrol (1:2) and the resulting extracts were first separated by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the IR and ^1H NMR spectra with those of authentic material.

Trichogonia prancii Barroso (voucher RMK 8274). The aerial parts (430 g) afforded 5 mg germacrene D, 5 mg bicyclogermacrene, 5 mg α-humulene, 100 mg taraxasterol and 80 mg taraxasteryl acetate, 30 mg **1a** (Et_2O–petrol, 1:3), 2 mg **2** (Et_2O–petrol, 3:1), 8 mg **3a** (Et_2O–petrol, 3:1), 25 mg **4** (Et_2O–petrol, 3:1), 5 mg **5** (Et_2O–petrol, 3:1), 5 mg **6** (Et_2O–petrol, 3:1), 15 mg **7** (Et_2O–petrol, 3:1) and 5 mg **8a** (Et_2O–petrol, 3:1). (**1**–**8a** were further purified by TLC using $CHCl_3$–Et_2O, 1:1.) The roots (260 g) yielded 4 mg α-humulene, 7 mg bicyclogermacrene, 10 mg lupeyl acetate, 20 mg **9** (Et_2O–petrol, 1:3) and 15 mg **10a** (Et_2O–petrol, 1:3).

Trichogonia grazielae K. et R. (voucher RMK 8271). The roots (150 g) afforded 2 mg germacrene D, 5 mg **16** (Et_2O–petrol, 1:10), 2 mg **17** (Et_2O–petrol, 1:10), 15 mg **18a** (Et_2O–petrol, 1:3), 15 mg **19** (Et_2O–petrol, 1:3), 60 mg **20** (Et_2O–petrol, 1:3), 2 mg **21** and 1 mg **22** (Et_2O–petrol, 3:1), while the aerial parts (200 g) gave 10 mg germacrene D, 10 mg α-humulene, 30 mg aromadendrene, 20 mg caryophyllene, 100 mg herniarin, 50 mg **13** and 400 mg **23a** (Et_2O–petrol, 1:3).

Trichogonia scottmorii K. et R. (voucher RMK 8018). The aerial parts (50 g) afforded 10 mg germacrene D, 10 mg taraxasteryl acetate, 50 mg **3c**, 10 mg **29**, 15 mg **30**, 10 mg **31** and 5 mg **32**.

Trichogonia salviaefolia Gardn. (voucher RMK 8183). The aerial parts (300 g) afforded 30 mg germacrene D, 50 mg taraxasteryl acetate, 1 g fatty acids, 15 mg **36a/b**, 100 mg **37a/b**, 5 mg **38a/b** and 10 mg **39a/b** (all purified by TLC, Et_2O–petrol, 3:1 and then $CHCl_3$–Et_2O, 1:1), while the roots (80 g) gave 10 mg germacrene D, 2 mg bicyclogermacrene, 2 mg **16**, 3 mg **17**, 30 mg **18a**, 2 mg **18b** (Et_2O–petrol, 1:3), 8 mg **19**, 60 mg **20**, 10 mg **21** and 2 mg **40** (Et_2O–petrol, 1:10).

Trichogonia villosa (DC) Sch. Bip. ex Baker (voucher RMK 8361). Roots (29 g) afforded 5 mg germacrene D, 30 mg **18a**, 5 mg **19**, 40 mg **20** and 3 mg **40**, while the aerial parts (60 g) gave 40 mg germacrene D, 5 mg bicyclogermacrene, 10 mg α-humulene, 3 mg aromadendrene, 50 mg taraxasteryl acetate, 5 mg **1b** (Et_2O–petrol, 3:1), 5 mg **18a** and 5 mg **41** (Et_2O–petrol, 3:1).

9β-Hydroxyatripliciolide-8-O-*methacrylate* (**1a**). Colourless gum, not separated from **4**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (hydrogen-bonded OH), 1783 (γ-lactone), 1730, 1650 (C=CCO_2R), 1705, 1595 (C=C–C=C–OR); MS *m/z* (rel. int.): 360. 121 (M^+, 11) ($C_{19}H_{20}O_7$), 342 (M − H_2O, 1), 274 (M − RCO_2H, 3), 69 ($C_3H_5CO^+$, 100). To 10 mg of a mixture of **1a** and **4** in 1 ml $CHCl_3$, 10 mg 4-pyrrolidinopyridine and 0.1 ml Ac_2O were added. After 12 hr, TLC (Et_2O–petrol, 3:1) afforded 10 mg of **2** and **5**, which could not be separated. Both compounds were identical (^1H NMR spectra) with the natural compounds.

9β-Hydroxyatripliciolide-8-O-*angelate* (**1b**). Colourless crystals, mp 75° (petrol); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3530 (OH), 1785 (γ-lactone), 1735, 1655 (C=CCO_2R), 1710, 1600 (O=C–C=C–OR); MS *m/z* (rel. int.): 374.137 (M^+, 10) ($C_{20}H_{22}O_7$), 356 (M − H_2O, 0.5), 274 (M − RCO_2H, 3), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 74).

9β-Acetoxyatripliciolide-8-O-*methacrylate* (**2**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1740 (OAc), 1715 (C=CCO_2R, C=O), 1595 (C=COR); MS *m/z* (rel. int.): 402. 131 (M^+, 16) ($C_{21}H_{22}O_8$), 360 (M − ketene, 5), 343 (M − OAc, 2), 274 (360 − RCO_2H, 5), 232 (274 − C_2H_2O, 18), 69 ($C_3H_5CO^+$, 100).

9β-Methacryloyloxyatripliciolide (**3a**). Colourless crystals, mp 164°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1785 (γ-lactone), 1720, 1650 (C=CCO_2R), 1720, 1605 (O=CC=COR); MS *m/z* (rel. int.): 360.121 (M^+, 12) ($C_{19}H_{20}O_7$), 274 (M − RCO_2H, 1), 256 (274 − H_2O, 1), 232 (274 − C_2H_2O, 17), 69 ($C_3H_5CO^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-82.5 \quad -87.5 \quad -101.0 \quad -199.5} \quad (c = 0.2,\ CHCl_3).$$

Compound **3a** (5 mg) was acetylated as above. TLC (Et_2O–petrol, 3:1) afforded 5 mg **3b**, colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (γ-lactone), 1730 (OAc, C=CCO_2R, C=O), 1610 (C=COR); MS *m/z* (rel. int.): 402.131 (M^+, 35) ($C_{21}H_{22}O_8$), 360 (M − ketene, 6), 342 (M − HOAc, 2), 300 (342 − C_2H_2O, 9), 274 (360 − RCO_2H, 4), 232 (274 − C_2H_2O, 19), 69 ($C_3H_5CO^+$, 100).

9β-Hydroxy-11β,13-epoxyatripliciolide-8-O-*methacrylate* (**4**). Colourless gum, not separated from **1**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3540 (hydrogen-bonded OH), 1805 (γ-lactone), 1730, 1650 (C=CCO_2R), 1705, 1595 (O=C–C=C–OR); MS *m/z* (rel. int.): 376.116 (M^+, 5) ($C_{19}H_{20}O_8$), 290 (M − RCO_2H, 1), 69 ($C_3H_5CO^+$, 100).

9β-Acetoxy-11β,13-epoxyatripliciolide-8-O-*methacrylate* (**5**). Colourless gum, not separated from **2**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1795 (γ-lactone), 1740 (OAc), 1715 (C=CCO_2R, C=O), 1590 (C=COR); MS *m/z* (rel. int.): 418.126 (M^+, 12) ($C_{21}H_{22}O_9$), 376

(M − ketene, 6), 291 (376 − $RCO_2^·$, 6), 69 ($C_3H_5CO^+$, 100).

Trichogoniolide (**6**). Colourless gum. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 1765 (γ-lactone), 1720 (C=CCO_2R, lactone), 1645, 1610 (C=C); MS *m/z* (rel. int.): 380.147 (M^+, 4) ($C_{19}H_{24}O_8$), 362 (M − H_2O, 1), 336 (M − CO_2, 1), 69 ($C_3H_5CO^+$, 100). Compound **6** (5 mg) was acetylated as above. TLC (Et_2O–petrol, 3:1) afforded 4 mg **7**, identical with the natural acetate.

Trichogoniolide-9-O-acetate (**7**). Colourless crystals, mp 215° (Et_2O). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3420 (OH), 1778 (γ-lactone), 1755(OAc), 1725 (C=CCO_2R, lactone), 1640, 1605 (C=C); MS *m/z* (rel. int.): 422.158 (M^+, 0.5) ($C_{21}H_{26}O_9$), 404.147 (M − H_2O, 1) ($C_{21}H_{24}O_8$), 380 (M − ketene, 0.5), 362 (M − HOAc, 1), 347 (362 − Me˙, 0.5), 336 (M − RCO_2H, 3), 294 (336 − ketene, 2), 276 (336 − HOAc, 4), 258 (276 − H_2O, 2), 69 ($C_3H_5CO^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,nm}{-246.2 \quad -256.5 \quad -293.9 \quad -520.1 \quad -857.2}$$

($c = 0.69$, $CHCl_3$).

Isotrichogoniolide-9-O-acetate (**8a**). Colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1735 (C=CCO_2R, lactone), 1640 (C=C); MS *m/z* (rel. int.): 422.158 (M^+, 0.5) ($C_{21}H_{26}O_9$), 404.147 (M − H_2O, 1) ($C_{21}H_{24}O_8$), 380 (M − ketene, 1), 362 (M − HOAc, 1), 344 (404 − HOAc, 0.5), 336 (M − RCO_2H, 4), 318 (336 − H_2O, 4), 276 (336 − HOAc, 4), 241 (276 − MeCHOH, 6), 232 (276 − CO_2, 7), 69 ($C_3H_5CO^+$, 100). Compound **8a** (5 mg) was acetylated as above. TLC (Et_2O) afforded 4 mg **8b**, colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1745 (OAc), 1720 (C=CCO_2R, lactone); MS *m/z* (rel. int.): 464 (M^+, 0.3), 404.147 (M − HOAc, 8) ($C_{21}H_{26}O_9$), 318 (404 − RCO_2H, 2), 69 ($C_3H_5CO^+$, 100).

2-[4′-*Formylfuryl*]-4-*vinylanisole* (**9**). Colourless crystals, mp 159° (petrol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2725, 1690 (furan aldehyde), 1630, 910 (CH=CH_2); MS *m/z* (rel. int.): 228.078 (M^+, 72) ($C_{14}H_{12}O_3$), 213 (M − Me, 6), 185.060 (213 − CO, 33) ($C_{12}H_9O_2$), 157.065 (185 − CO, 100) ($C_{11}H_9O$), 128.063 (157 − CHO, 97) ($C_{10}H_8$). To 5 mg **9** in 1 ml MeOH, 10 mg $NaBH_4$ was added. TLC (Et_2O–petrol, 1:1) afforded 3 mg **10b**, colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1635, 920 (CH=CH_2); MS *m/z* (rel. int.): 230 (M^+, 100), 215 (M − Me˙, 2), 201 (M − CHO˙, 3), 187 (215 − CO, 10).

2-[4′-*Acetoxymethylfuryl*]-4-*vinylanisole* (**10a**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745, 1260 (OAc), 1630, 910 (CH=CH_2); MS *m/z* (rel. int.): 272.155 (M^+, 100) ($C_{16}H_{16}O_4$), 230 (M − ketene, 16), 215 (230 − Me˙, 9), 201 (230 − CHO˙, 33), 187 (215 − CO, 18), 128 ($C_{10}H_8$, 11). Compound **10a** (8 mg) in 3 ml Et_2O was hydrogenated in the presence of palladium on $BaSO_4$ (1 hr). TLC (Et_2O–petrol, 1:1) afforded 6 mg **12a**, colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1740, 1250 (OAc); MS *m/z* (rel. int.): 280 (M^+, 28), 162 ($EtC_6H_3(OMe)CH{=}CH_2^+$, 70), 149 ($EtC_7H_5OMe^+$, 100), 119 (149 − CH_2O, 45). Compound **12a** (6 mg) was acetylated as above, yielding 6 mg **12b**. For ^1H NMR data see Table 2.

2-[3′,3′-*Dimethylallyl*]-4-[1-*angeloyloxyethyl*]-*anisole* (**16**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1715, 1655 (C=CCO_2R), 1615, 1505 (aromate); MS *m/z* (rel. int.): 302.188 (M^+, 19) ($C_{19}H_{26}O_3$), 203 (M − OAng˙, 100), 202 (M − AngOH, 28), 187 (202 − Me˙, 68), 83 ($C_4H_7CO^+$, 28).

2,2-*Dimethyl*-6-*vinylchroman*-4-*one* (**17**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1700, 1615 (PhCO), 1635, 915 (CH=CH_2); MS *m/z* (rel. int.): 202.099 (M^+, 56) ($C_{13}H_{14}O_2$), 187 (M − Me˙, 100), 146 (M − $Me_2C{=}CH_2$, 74), 118 (146 − CO, 20).

2-*Senecioyl*-4-*vinylphenol* (**18a**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2700, 1630 (hydrogen-bonded hydroxyketone), 1610, 915 (CH=CH_2); MS *m/z* (rel. int.): 202.099 (M^+, 11) ($C_{13}H_{14}O_2$), 187 (M − Me˙, 100), 147 (M − CH˙=CMe_2, 15).

2-*Senecioyl*-4-*vinylanisole* (**18b**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1655 (C=CCOPh), 1620, 1495 (aromate), 910 (CH=CH_2); MS *m/z* (rel. int.): 216.115 (M^+, 78) ($C_{14}H_{16}O_2$), 201 (M − Me˙, 100), 187 (M − CHO˙, 91).

2-*Senecioyl*-4-[1-*angeloyloxyethyl*]-*phenol* (**19**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500–2700, 1640 (hydrogen-bonded ketone), 1715 (C=CCO_2R); MS *m/z* (rel. int.): 302.152 (M^+, 8) ($C_{18}H_{22}O_4$), 287 (M − Me, 18), 203 (M − OAng, 28), 187 (287 − AngOH, 100), 147 (203 − CH=CMe_2, 52), 83 ($C_4H_7CO^+$, 21).

2-*Senecioyl*-4-[1-(4′-*acetoxyangeloyloxyethyl*-]-*phenol* (**20**). Yellow oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400–2600, 1645 (hydrogen-bonded ketone), 1747, 1225 (OAc), 1715 (C=CCO_2R); MS *m/z* (rel. int.): 360 (M^+, 0.2), 345.134 (M − Me˙, 6) ($C_{19}H_{21}O_6$), 203 (M − O_2CR˙, 55), 187 (345 − RCO_2H, 100), 147 (203 − CH_2=CMe_2, 32).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546\,nm}{+3.6 \quad +4.0 \quad +4.5} \quad (c = 6.0,\ CHCl_3).$$

2,2-*Dimethyl*-6-[1-*hydroxyethyl*]-*chroman*-4-*one* (**22**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630 (OH), 1705, 1625 (PhCO); MS *m/z* (rel. int.): 220.110 (M^+, 31) ($C_{13}H_{16}O_3$), 205 (M − Me˙, 88), 149 (205 − CH_2=CMe_2, 100).

γ-*Muurolen*-15-*oic acid* (**23a**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400–2500, 1692, 1645 (C=CCO_2H); MS *m/z* (rel. int.): 234.162 (M^+, 38) ($C_{15}H_{22}O_2$), 191 (M − C_3H_7˙, 100); ^{13}C NMR ($CDCl_3$) (C-1 through C-15): 24.7 *t*, 26.1 *t*, 129.4 *s*, 144, 7 *d*, 40.3 *d*, 42.3 *d*, 151.9 *s*, 31.2 *t*, 24.7 *t*, 33.8 *d*, 27.2 *d*, 21.4 *q*, 15.8 *q*, 107.8 *t*, 171.8 *s* (doublets and triplets assigned by partial decoupling). Addition of CH_2N_2 in Et_2O afforded **23b** (TLC, Et_2O–petrol, 1:10), colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3060, 900 (C=CH_2), 1720, 1645 (C=CCO_2R); MS *m/z* (rel. int.): 248.197 (M^+, 82) ($C_{16}H_{24}O_2$), 233 (M − Me˙, 5), 217 (M − OMe˙, 11) 205 (M − C_3H_7˙, 100), 189 (217 − CO, 22), 173 (205 − MeOH, 71), 145 (173 − CO, 70).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+28.1 \quad +19.2 \quad -22.9 \quad +50.0} \quad (c = 8.2,\ CHCl_3).$$

To 50 mg **23b** in 2 ml $CHCl_3$, 75 mg *m*-chlorperbenzoic acid was added. After 2 hr the reaction product (**24**), was isolated, colourless oil. Its ^1H NMR spectrum (Table 5) indicated that only one epoxide had been formed.

The crude epoxide (**24**) was warmed in MeOH–2 N H_2SO_4 (2:1) for 30 min at 70°, affording 15 mg **26** (TLC: Et_2O–petrol, 1:1) and 25 mg **25**, which was directly reacted with $NaIO_4$. TLC (Et_2O–petrol, 1:3) gave 12 mg **27**, colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1720 (C=CCO_2R, C=O); MS *m/z* (rel. int.): 250.157 (M^+, 100) ($C_{15}H_{22}O_3$), 219 (M − OMe˙, 60), 218 (M − MeOH, 91), 175 (218 − C_3H_7˙, 95). **26**: Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 264.172 (M^+, 6) ($C_{16}H_{24}O_3$), 246 (M − H_2O, 55), 233 (M − OMe˙, 32), 203 (246 − C_3H_7˙, 48), 134 (100). Compound **26** (10 mg) was stirred with 100 mg MnO_2 for 1 hr. TLC (Et_2O–petrol, 1:3) afforded 8 mg **28**, colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 1690 (CHO), 1720, 1645 (C=CCO_2R); MS *m/z* (rel. int.): 262.157 (M^+, 49), 244 (M − H_2O, 16), 230 (M − MeOH, 66), 219 (M − C_3H_7˙, 27), 202 (230 − CO, 15), 187 (230 − C_3H_7˙, 100), 159 (187 − CO, 63), 131 (159 − CO, 50), 91 ($C_7H_7^+$, 41).

9β-*Acetoxy*-8β-*angeloyloxy*-5α- *and* 5β-*hydroxytrichosalviolide* (**36a/b**). Colourless crystalline mixture, mp 144° (Et_2O–petrol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1773 (γ-lactone), 1750, 1237 (OAc), 1730 (CO_2R)m, 1660 (C=CH_2); MS *m/z* (rel. int.): 420.178 (M^+, 0.2) ($C_{22}H_{28}O_8$), 378 (M − ketene, 1), 360 (M − HOAc, 4), 278 (378 − AngOH, 6), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 42); CI (*iso*-butane): 421 (M + 1, 8), 403 (421 − H_2O, 13), 361 (421 − HOAc,

100), 303 (403 − AngOH, 58), 285 (303 − H_2O, 23), 261 (361 − AngOH, 20), 243 (261 − H_2O, 17), 83 ($C_4H_7CO^+$, 59).

9β-Acetoxy-8β-[2-methyl-2,3-epoxybutyryloxy]-5α and 5β-hydroxytrichosalviolide (**37a/b**). Colourless crystalline mixture, mp 224° (Et_2O). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1730 (OAc, CO_2R); MS *m/z* (rel. int.): 436.173 (M^+, 0.3) ($C_{22}H_{28}O_9$), 418 (M − H_2O, 1), 394 (M − ketene, 3), 376 (M − HOAc, 6), 358 (376 − H_2O, 1), 320 (M − RCO_2H, 4), 302 (320 − H_2O, 5), 278 (320 − ketene, 36), 260 (320 − HOAc, 37), 232 (260 − CO, 70), 99 (RCO^+, 30), 71 (99 − CO, 100); ^{13}C NMR ($CDCl_3$) (C-1 through C-15): 129.6 (129, 3), 30.9, 38.5, 47.9, (50.7), 105.4 (108.7), 84.2 (86.1), 87.7 (83.6), 76.4 (77.3), 76.5 (76.1), 130.7, 138.9 (140.2), 168.4, 128.0 (127.6), 19.1, 13.6 (13.2) (some signals may be interchangeable). Compounds **37a/b** (5 mg) in 2 ml $CHCl_3$ were stirred for 2 hr with 50 mg pyridine dichromate. TLC (Et_2O–$CHCl_3$, 1:2) afforded 3 mg **37c**, colourless crystals, mp 212° (Et_2O–petrol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1790, 1783 (γ-lactone), 1755 (OAc), 1730 (CO_2R); MS *m/z* (rel. int.): 434.158 (M^+, 6) ($C_{22}H_{26}O_9$), 392 (M − ketene, 10), 374 (M − HOAc, 6), 276 (392 − RCO_2H, 100), 258 (276 − H_2O, 20), 248 (276 − CO, 21), 230 (258 − CO, 26), 99 (RCO^+, 20), 71 (99 − CO, 81).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-5.6 \quad -8.9 \quad -8.9 \quad -11.1} (c = 0.1, CHCl_3).$$

8β-Angeloyloxy-5α- and 5β,9β-dihydroxytrichosalviolide (**38a/b**). Colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1730 (CO_2R); MS *m/z* (rel. int.): 378 (M^+, 0.1), 360.157 (M − H_2O, 0.5) ($C_{20}H_{24}O_6$), 278 (M − AngOH, 7), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 54).

8β-[2-Methyl-2,3-epoxybutyryloxy]-5α- and 5β,9β-dihydroxytrichosalviolide (**39a/b**). Colourless gum. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1665, 1620 (C=CCOPh), 910 ($CH=CH_2$); MS *m/z* (rel. int.): 376.152 (M − H_2O, 1), 278 (M − RCO_2H), 99 (RCO^+, 11), 71 (99 − H_2O, 100).

4-Methoxy-6-vinyl-2,3-dimethylchromene (**40**). Colourless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3070, 1630, 905 ($CH=CH_2$), 1650 (C=COR), 1600, 1490 (aromate); MS *m/z* (rel. int.): 216.115 (M^+, 14) ($C_{14}H_{16}O_2$), 186 (M − CH_2O, 7), 171 (186 − ·Me, 2); ^1H NMR ($CDCl_3$): 1.45 (*s*, H-12 and 13), 3.70 (*s*, OMe), 6.64 (*dd*, *J* = 17.5, 11 Hz, H-7), 5.62 (*dd*, *J* = 17.5, 1 Hz, H-8*t*), 5.11 (*dd*, *J* = 11, 1 Hz, H-8*c*), 7.47 (*d*, *J* = 2 Hz, H-3), 7.22 (*dd*, *J* = 8 Hz, H-5), 6.75 (*d*, *J* = 8 Hz, H-6), 4.64 (*s*, H-10).

8β-Angeloyloxy-9β-hydroxyzexbrevanolide (**41**). Colourless gum. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (C=CCO_2R) 1700 (C=CCO), 1600 (C=COR); MS *m/z* (rel. int.): 376.152 (M^+, 4) ($C_{20}H_{24}O_7$), 358 (M − H_2O, 0.5), 276 (M − AngOH, 0.5), 83 ($C_4H_7CO^+$, 100).

X-ray analysis of **7**. The compound crystallizes in the orthorhombic system, space group $P2_12_12_1$, with lattice constants $a = 21.214$ (5), $b = 12{,}110$ (3) and $c = 8.594$ (2) Å, $Z = 4$. Single crystal X-ray data were taken with a Syntex $P2_1$ diffractometer (monochromated MoK_α radiation), using a variable-speed ω-scan technique. 1538 unique reflections with $2\theta \leq 45°$ were measured, of which 1400 with intensities $I > 2\sigma_I$ were considered as observed. The structure was solved by direct methods (MULTAN). Full matrix isotropic refinement of all non-hydrogen atoms gave an *R*-value of 10%. Refinement is still in progress. Details of the X-ray structure determination will be published elsewhere. Fig. 1 shows a perspective drawing of the compound. For reasons of clarity, only the essential carbon atoms are labelled. (The radii of the spheres do not represent isotropic temperature factors, but are different according to perspective height.)

Acknowledgements—We thank Drs. Scott A. Mori and P. Alvim, Herbario Centro de Pesquisas do Cacau at Itabanu, Bahia, Brazil, for their help during plant collection and the Deutsche Forschungsgemeinschaft for financial support.

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