Phytochemistry, Vol. 20, No. 4, pp. 743–749, 1981.
Printed in Great Britain.

0031–9422/81/040743–07 $02.00/0

FOURTEEN HELIANGOLIDES FROM *CALEA* SPECIES*

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(*Revised received* 11 *August* 1980)

Key Word Index—*Calea pilosa*; *C. mortii*; Compositae; sesquiterpene lactones; new heliangolides; myrtenyl heliangolide; new chromene derivative; new dithienyl derivative.

Abstract—The investigation of two further *Calea* species afforded, in addition to known compounds, fourteen new heliangolides, most of them being 11,13-epoxides. One lactone is a new type, a heliangolide substituted with a monoterpene residue. Furthermore, a new chromene and a new dithienyl derivative were isolated. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The large genus *Calea* belongs to the Heliantheae (Compositae) and is placed in the subtribe Galinsoginae [1]. The chemical results so far available, however, indicate that some species only show relationships to *Galinsoga*, *Tridax* and *Jaegeria*, typical members of this subtribe. The latter three genera are characterized by the occurrence of special C_{17}-acetylenes [2], which are present in some *Calea* species [2, 3]. Most *Calea* species, however, contain sesquiterpene lactones, mainly heliangolides [4–6], which are not present in any of the other genera placed in this subtribe [1] that have been investigated (*Spilanthes*, *Selloa*). The present paper is concerned with the heliangolides of *Calea pilosa* Baker and *C. mortii* H. Robins. In addition to known lactones, fourteen new ones have been isolated, all with a furanone ring. Most of them are 11,13-epoxides and one is of a new type, a heliangolide substituted with pinene.

RESULTS AND DISCUSSION

The roots of *Calea pilosa* contain, in addition to caryophyllene, α-humulene, β-sesquiphellandrene, thymol methyl ether, thymohydroquinone dimethyl ether and squalene, the dehydrothymol derivatives **11** and **12** and minute amounts of the tricyclic hydrocarbons **1** [7], **2** [8], **3**–**5** [9] and **6** [10]. These hydrocarbons are present in nearly all tribes (F. Bohlmann *et al.*, unpublished work). The aerial parts contain squalene, α-humulene, caryophyllene epoxide, spathulenol (**10**), thymohydroquinone dimethyl ether and the dehydro compound **12**, nerolidol (**7**) and the hydroxy derivatives **8** [11] and **9** [12], phytol, β-amyrin and the dithienyl derivatives **18**, **19** [2] and **20** [2]. **18** has not been isolated before but its structure is easily deduced from spectral data (see Experimental). The aerial parts also contain a very complex mixture of sesquiterpene lactones, only three of which have known structures; the atripliciolides **22** and **26** [13], and calaxin (**23**) (the configuration at C-8 of **23** has been revised to 8α-H [14]). One of the lactones is obviously the angelate **21**, i.e. a 15-deoxybudlein A. Its ^{1}H NMR data are very similar to those of **22** and **23** (Table 1). Two other lactones have ^{1}H NMR spectra very similar to that of **26** (Table 2). These data clearly show that they differ only in the nature of the ester residue at C-8. Their structures therefore are **24** and **25**, i.e. 9α-hydroxyatripliciolide 8-*O*-angelate and -tiglate respectively. Three additional lactones were separated by HPLC. Careful inspection of the ^{1}H NMR data together with the molecular formulae showed that these lactones are probably **27**–**29**. Most of the ^{1}H NMR data (Table 1) are very similar to those of **21**–**23**. However, the typical signals for methylene lactone protons are replaced by two highfield doublets, which can only be assigned to epoxide protons. The configuration at C-11 cannot be assigned with certainty. The observed Eu(fod)$_3$ induced shifts may favour a β-epoxide. However, the situation is more clear in the case of the corresponding chlorohydrin (see below). Obviously the configuration at C-11 is the same in three other epoxides, which from the ^{1}H NMR data can be shown to have an additional 9α-hydroxy group (Table 2). Again these lactones differ from each other only in the nature of the ester residue at C-8. The data for **24**–**26** are very similar to those for **27**–**29**.

Two more lactones were isolated from the more polar fractions. They can be assigned structures **33a** and **35** on the basis of the ^{1}H NMR data (Tables 1 and 2). **33a** is transformed to the acetate **33b** by acetylation using 4-pyrrolidinopyridine [15] as a catalyst. The hydroxyl group has to be placed at C-11 as the 13-H doublets are only slightly shifted. The spectrum of **33b** indicates a β-orientated C-11-oxygen function, as the signals of 6- and 8-H are shifted downfield by the acetate group. Reaction of **27** with hydrogen chloride gives **33a** together with other products, which are most probably formed by addition to the 4,5-double bond and by attack of the chloride ion at C-11. The structure of **35** is easily deduced from ^{1}H NMR data (Table 2), which are very similar to those of **33a** and **30**,

* Part 301 in the series "Naturally Occurring Terpene Derivatives"; for part 300 see: Bohlmann, F., Ziesche, J., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 751.

Table 1. ^{1}H NMR data of **21**, **27**–**29**, **33a**, **33b** and **34** (270 MHz, TMS as int. standard, $CDCl_3$)

	21	**27**	Δ*	**28**	**29**	**33a**	**33b**	**34**
H-2	5.59 *s*	5.60 *s*	0.61	5.60 *s*	5.60 *s*	5.58 *s*	5.57 *s*	5.58 *s*
H-5	5.95 *dq*	6.01 *dq*	0.68	6.01 *dq*	6.02 *dq*	6.02 *dq*	6.09 *dq*	6.02 *dq*
H-6	5.35 *ddq*	5.30 *ddq*	0.59	5.23 *ddq*	5.24 *ddq*	5.21 *ddq*	5.51 *ddq*	5.14 *ddq*
H-7	3.71 *ddd*	3.31 *dd*	0.34	3.28 *dd*	3.28 *dd*	3.40 *dd*	3.56 *dd*	3.37 *dd*
H-8	5.14 *d*	5.14 *ddd*	0.58	5.05 *ddd*	5.06 *ddd*	5.12 *ddd*	5.47 *ddd*	6.03 *ddd*
H-9	2.53 *dd*	2.41 *dd*	0.77	2.42 *dd*	2.44 *dd*	2.53 *dd*	2.77 *dd*	2.51 *dd*
H-9′	2.30 *dd*	2.20 *dd*	0.57	2.18 *dd*	2.19 *dd*	2.39 *dd*	2.00 *dd*	2.34 *dd*
H-13	6.36 *d*	3.34 *d*	0.19	3.35 *d*	3.35 *d*	4.25 *d*	3.99 *d*	4.30 *d*
H-13′	5.70 *d*	3.30 *d*	0.18	3.28 *d*	3.29 *d*	3.90 *d*	3.82 *d*	3.90 *d*
H-14	1.49 *s*	1.47 *s*	0.46	1.47 *s*	1.47 *s*	1.47 *s*	1.41 *s*	1.48 *s*
H-15	2.08 *dd*	2.09 *dd*	0.20	2.09 *dd*	2.09 *dd*	2.08 *dd*	2.09 *dd*	2.08 *dd*
OCOR	6.13 *qq*	6.16 *dd*	0.20	6.82 *qq*	6.08 *s(br)*	6.14 *qq*	6.14 *qq*	6.81 *qq*
	1.94 *dq*	1.95 *dq*	0.05	1.81 *dq*	5.67 *s(br)*	1.95 *dq*	2.00 *dq*	1.81 *dq*
	1.80 *dq*	1.82 *dq*	0.21	1.76 *dq*	1.88 *s(br)*	1.81 *dq*	1.81 *dq*	1.75 *dq*

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

J(Hz): **21**, **27**–**29**: 5, 6 = 4; 5, 15 = 1.5; 6, 7 = 4; 6, 15 = 1.5; 7.8 ~ 2; 8,9 = 6; 8, 9′ = 3; 9, 9′ = 15; 13, 13′ = 4.5; **33**/**34**: 5, 6 = 4; 5, 15 = 1.5; 6, 7 = 6.5; 7, 8 = 2; 8, 9 = 4.5; 8, 9′ = 2.5; 9, 9′ = 15; 13, 13′ = 12; OAng/OTigl: 3″, 4″ = 7; 3″, 5″ = 4″, 5″ = 1.5.

indicating the presence of a 9α-hydroxyl group. An additional lactone present in minute amounts only is the costunolide derivative **36**. The ^{1}H NMR data (Table 3) show the presence of an acetate, an angelate and an epoxide group. Spin decoupling clearly shows the presence of a 1,10-epoxide group whilst the β-orientation of the ester groups on C-3 and C-8 follows from the observed couplings. The relative position of these groups is established by partial hydrolysis, which gives a monoester as can be seen from the ^{1}H NMR data (Table 3). The angelate group is still present whereas the acetate group is replaced by a hydroxyl group, which must be placed at C-3. As usual methanol adds to the 11,13-double bond. The structure of the hydrolyzed lactone therefore is **37** and consequently the structure of the natural compound is clarified.

Table 2. ^{1}H NMR data of **24**, **25**, **30**–**32** and **35** (270 MHz, TMS as int. standard, $CDCl_3$)

	24	**25**	**30**	**31**	**32**	**35**
H-2	5.61 *s*	5.62 *s*	5.62 *s*	5.62 *s*	5.62 *s*	5.57 *s*
H-5	5.99 *dq*		6.05 *dq*	6.05 *dq*	6.05 *dq*	6.01 *dq*
H-6	5.33 *ddq*	5.24 *ddq*	5.23 *dq*	5.15 *dq*	5.16 *dq*	5.30 *ddq*
H-7	3.91 *ddd*	3.89 *ddd*	3.41 *dd*	3.41 *dd*	3.41 *dd*	3.74 *dd*
H-8	5.12 *dd*	5.07 *dd*	5.05 *dd*	4.97 *dd*	4.98 *dd*	5.25 *dd*
H-9	4.11 *dd*	4.09 *dd*	4.01 *dd*	4.00 *dd*	4.03 *dd*	4.19 *d(br)*
H-13	6.37 *d*	6.35 *d*	3.37 *d*	3.37 *d*	3.39 *d*	4.01 *d*
H-13′	5.78 *d*	5.74 *d*	3.34 *d*	3.34 *d*	3.34 *d*	3.87 *d*
H-14	1.57 *s*	1.58 *s*	1.54 *s*	1.55 *s*	1.55 *s*	1.54 *s*
H-15	2.06 *dd*	2.07 *dd*	2.08 *dd*	2.07 *dd*	2.08 *dd*	2.10 *dd*
OCOR	6.19 *qq*	6.79 *qq*	6.19 *qq*	6.86 *qq*	6.12 *s(br)*	6.16 *qq*
	1.96 *dq*	1.81 *dq*	1.96 *dq*	1.83 *dq*	5.71 *s(br)*	1.96 *dq*
	1.84 *dq*	1.76 *dq*	1.84 *dq*	1.77 *dq*	1.89 *s(br)*	1.78 *dq*

J (Hz): 5, 6 = 3.5; 5, 15 = 1.7; 6, 7 = 4; 6, 15 = 1.7; 7, 8 = 1.5; 7, 13 = 3; 7,13′ = 2.5; 8, 9 = 5; 9 OH ~ 4: **30**–**32**: 13, 13′ = 4; **35**: 13, 13′ = 12.

Finally, there is the structure of a very unusual lactone. The ^{1}H NMR data are very similar in part to those of **27**; however, the olefinic methyl signal is replaced by a doublet and additional signals are present, which are very similar to those of α-pinene except the olefinic methyl signal, which is replaced by an allylic methylene multiplet, as is shown by spin decoupling. The molecular formula, $C_{30}H_{30}O_7$, a $C_{10}H_{15}$-fragment and the ^{1}H NMR data (Table 3) are in agreement only with a 4,5-dihydro derivative of **27**, which is substituted at C-5 with a myrtenyl group. The observed couplings of 4-, 5- and 6-H agree best with a β-orientation of the 4-methyl- and the myrtenyl-residue leading to the structure **38**. The 4β-orientation is supported by the absence of allylic coupling between 2- and 4-H, which can always be recognized in similar lactones with a 4α-methyl group. Also the 4-methyl signal shows an upfield shift due to the absence of the deshielding effect of the lactone oxygen found in lactones with an α-methyl group. Models show that in a lactone with a 4β-methyl the observed couplings $J_{4,5}$ and $J_{5,6}$ requires a β-orientation of the myrtenyl group. In the plant, **38** may be formed by addition of β-pinene to the activated 4,5-double bond of **33a** (see scheme). The names of the new lactones we have deduced from atripliciolide, which is the free alcohol of 9-deoxy **24**.

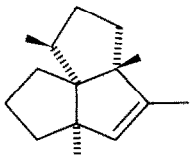
The roots of *C. morii* contain germacrene D, γ-humulene, the chromene derivatives **13** [16], **14** [16] and **15** [17] as well as the new chromene derivative **16**, the structure of which is easily deduced from the spectral data (see Experimental). The aerial parts contain germacrene D, bicyclogermacrene, 7-deoxyeuparin, 2,2-dimethyl-6-acetylchromene and the lactones **22**, **27**, **28**, **33a** and **38** as well as the tiglate **34**, the structure of which is established by comparison of the ^{1}H NMR data (Table 1) with those of **33a**. The co-occurrence of **36** and various furanoheliangolides is an indication that the latter type of lactone may be formed via **40** by hydrolysis of the epoxide of **39**, the 3-deacetyl derivative of **36**. Oxidation of **40** at C-1 would lead to **41**, the direct precursor of **21** (see scheme). The acetylation of the 3-hydroxyl group may be the reason for the isolation of a small amount of this intermediate. This proposal is supported by the fact that all known heliangolides have an oxygen function at C-3 or C-15, which after oxidation could facilitate the isomerisation of the 4,5-double bond.

The chemical results obtained on two further *Calea* species again support the view that most of the genus *Calea* needs to be transformed from the subtribe Galisoginae to the subtribe Neurolaeninae [18], while the rest of the *Calea* species, reestablished as the genus

Table 3. ^{1}H NMR data of **36**, **37** and **38** (270 MHz, TMS as int. standard, $CDCl_3$)

	36	**37**		**38**
H-1	2.83 *dd*	2.70 *dd*	H-2	5.60 *s(br)*
H-2α	1.56 *dd*		H-4	2.93 *dq*
H-2β	2.47 *ddd*		H-5	3.08 *ddt*
H-3α	5.51 *dd*	4.60 *dd(br)*	H-6	4.54 *dd*
H-5	5.51 *d(br)*	5.36 *d(br)*	H-7	2.82 *d(br)*
H-6	5.18 *dd*	5.14 *dd*	H-8	4.95 *ddd*
H-7	2.94 *ddd(br)*		H-9α	2.63 *dd*
H-8	5.76 *d(br)*	5.45 *d(br)*	H-9β	2.1 *m*
H-9α	2.86 *dd*	2.82 *dd*	H-13	3.25 *d*
H-9β	1.32 *dd*	1.3 *m*	H-13	3.22 *d*
H-13	6.34 *d*	3.77 *dd*	H-14	1.39 *s*
H-13′	5.62 *d*	3.63 *dd*	H-15	1.24 *d*
H-14	1.20 *s*	1.18 *s*	H-2′	5.35 *m*
H-15	1.86 *d*	1.88 *d*	H-5_1′	1.14 *d*
OCOR	6.16 *qq*	6.23 *qq*	H-5_2′	2.41 *dt*
	2.00 *dq*	2.06 *dq*	H-7′	2.1–2.3 *m*
	1.89 *dq*	1.96 *dq*	H-9′	0.86 *s*
OAc	2.12 *s*	—	H-10′	1.31 *s*
OMe	—	3.36 *s*		

J (Hz): **36**: 1,2α = 11; 1,2β = 2; 2α,2β = 13;2α,3α = 11; 2β,3α = 6; 5,6 = 10; 6,7 = 9; 7,8 ~ 1; 7,13 = 3.5; 7,13′ = 3; 8,9α = 6; 8,9β = 1.5; 9α,9β = 15.5; **37**: 11,13 = 3, 13,13′ = 10; **38**: 4,5 = 5; 4,15 = 7; 5,6 = 6.7 = 5; 5,7′ ~ 6; 8,9 = 5; 8,9′ = 3; 9,9′ = 15; 13,13′ = 4.5; 4′,5_2′ = 5_2′,6′ = 5; 5_1′,5_2′ = 9; OAng: 3,4 = 7; 3,4 = 7; 3,5 = 4,5 = 1.5.



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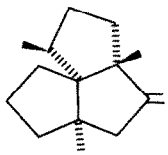

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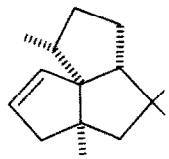

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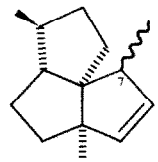
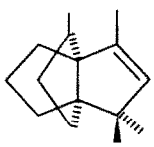


4 7αH
5 7βH



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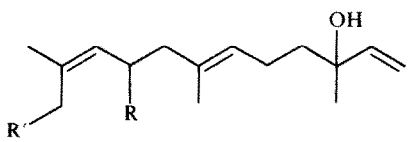
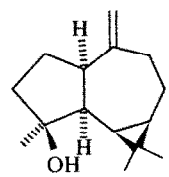


7 R = R′ = H
8 R = OH, R′ = H
9 R = H, R′ = OH



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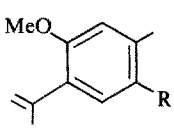

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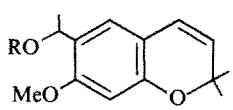
12 R = OMe



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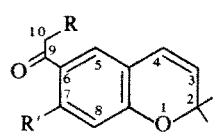
14 R = Ang



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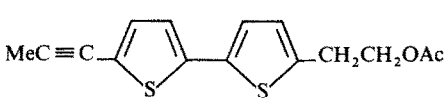
16 R = OAc, R′ = OMe
17 R = R′ = H



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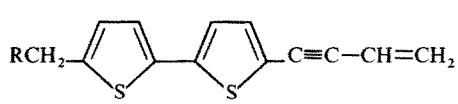

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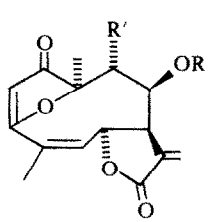
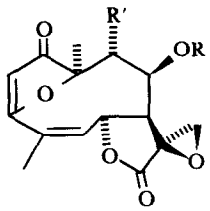
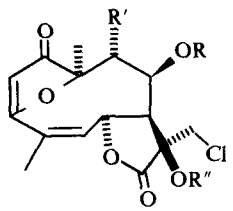
20 R = OAc



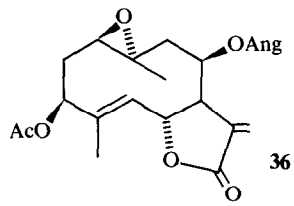
	21	**22**	**23**	**24**	**25**	**26**
R	Ang	Tigl	Meacr	Ang	Tigl	Meacr
R′	H	H	H	OH	OH	OH



	27	28	29	30	31	32
R	Ang	Tigl	Meacr	Ang	Tigl	Meacr
R′	H	H	H	OH	OH	OH



	33a	33b	34	35
R	Ang	Ang	Tigl	Ang
R′	H	H	H	OH
R″	H	Ac	H	H



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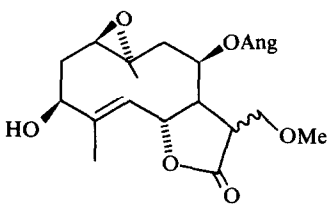

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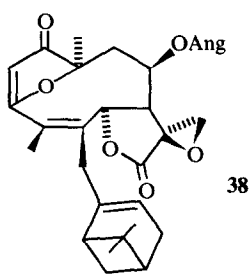

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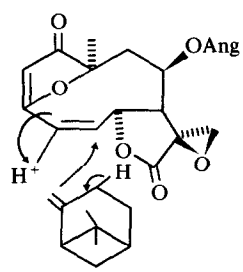
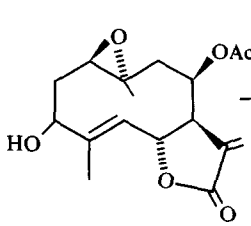


33a



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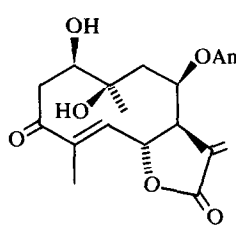
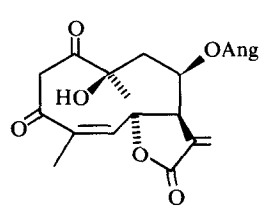


40



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Alloispermum [19], should be retained in the Galinsoginae [18]. Chemically the latter are characterized by the occurrence of dehydrofalcarinone and related compounds [2], which are present in *Galinsoga*, *Tridax*, *Schistocarpha*, *Bebbia* and *Jaegeria*.

EXPERIMENTAL

^{1}H NMR: 270 MHz, TMS as int. standard; MS: 70 eV, direct inlet; optical rotation, $CHCl_3$. The air-dried plant material, collected in north-eastern Brazil, was extracted with Et_2O–petrol (1:2). The resulting extracts were separated by column chromatography (SiO_2, act. grade II) followed by TLC (Si gel GF 254) and if necessary, by HPLC. Hydrocarbons were separated by GC and identified by GC/MS and ^{1}H NMR. Known compounds were identified by comparing the IR and ^{1}H NMR spectra with those of authentic compounds.

Calea pilosa (voucher RMK 8063). The roots (50 g) afforded 23 mg caryophyllene, 5 mg α-humulene, 3 mg β-sesquiphellandrene, 3 mg squalene, 2 mg thymol methyl ether, 52 mg thymohydroquinone dimethyl ether, 3 mg **11**, 210 mg **12** and **17** mg of a mixture of nearly equal parts of **1**–**6**. The aerial parts (400 g) afforded 5 mg α-humulene, 8 mg squalene, 30 mg caryophyllene epoxide, 12 mg **10**, 20 mg thymohydroquinone dimethyl ether, 250 mg **12**, 28 mg nerolidol, 2 mg **8**, 46 mg **9**, 15 mg phytol, 15 mg β-amyrin, 5 mg **18** (Et_2O–petrol, 1:10), 6 mg **19**, 36 mg **20**, 14 mg **21**, 7 mg **22**, 12 mg **23**, 53 mg **24**, 11 mg **25**, 25 mg **26**, 42 mg **27**, 7 mg **28**, 6 mg **29**, 44 mg **30**, 2 mg **31**, 1 mg **32**, 6 mg **33a**, 1 mg **35**, 3 mg **36** and 2 mg **38** (the lactones **21**–**35** were separated by TLC followed by reversed phase-HPLC, RP 18, MeOH–H_2O (1:1) (**21**–**23** and **27**–**29** MeOH–H_2O, 3:2).

Calea morii (voucher RMK 8097). The roots (15 g) afforded 1 mg germacrene D, 6 mg γ-humulene, 3 mg **13**, 2 mg **14**, 2 mg **15** and 1 mg **16** (Et_2O–petrol, 1:1), while the aerial parts (315 g) gave 20 mg bicyclogermacrene, 180 mg germacrene D, 3 mg **17**, 5 mg 7-desoxyeuparin, 8 mg **22**, 106 mg **27**, 80 mg **28**, 15 mg **33a**, 3 mg **34** and 8 mg **38**.

2,3-*Dimethyl*-6-[*acetoxy acetyl*]-7-*methoxy chromene* (**16**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1760 (OAc), 1690 (PhCO); MS *m/e* (rel. int.): 290.115 (M^+, 20) ($C_{16}H_{18}O_5$), 275 (M − Me), 217 (M − CH_2OAc, 100); ^{1}H NMR ($CDCl_3$): δ = 5.55 *d* (4-H), 7.67 *s* (5-H), 6.38 *s* (8-H), 5.18 *s* (10-H), 1.45 *s* (11, 12-H), 2.21 *s* (OAc), 3.91 *s* (OMe).

2-[2-*Acetoxyethyl*]-5-*prop*-1-*inyl*-*dithienyl* (**18**). Yellow oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1240 (OAc); UV (Et_2O) λ_{max} = 336 nm; MS *m/e* (rel. int.): 290.044 (M^+, 12) ($C_{15}H_{14}O_2S_2$), 230 (M − AcOH, 100), 217 (M − CH_2OAc, 35); ^{1}H NMR ($CDCl_3$) δ = 4.39 *t* (1-H, *J* = 6.5), 3.11 *td* (2-H, *J* = 6.5, 1), 6.75 *dt* (4-H, *J* = 3.5, 1), 6.93 *d* (5-H), 6.98 *d* (8-H, *J* = 3.5), 6.99 *brd* (9-H), 2.09 *brs* (13-H), 2.08 *s* (OAc).

Atripliciolide angelate (**21**). Colourless gum, not free from **27**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1720, 1650 (C=CCO_2R): MS M^+ = 258.142 ($C_{20}H_{22}O_6$).

9α-*Hydroxyatripliciolide*-8-O-*angelate* (**24**). Colourless gum; UV (Et_2O) λ_{max} = 259 nm; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1780 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO); MS *m/e* (rel. int.): 374.137 (M^+, 1) ($C_{20}H_{22}O_7$), 274 (M − AngOH, 4), 232 (274 − C_2H_2O, 17), 217 (232 − $^•$Me, 2), 83 ($C_4H_7CO^+$, 100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+3.5 \quad +4.8 \quad +8.1} \quad (c = 1.9).$$

9α-*Hydroxyatripliciolide*-8-O-*tiglate* (**25**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1770 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO), 1600 (C=COR); MS *m/e* (rel. int.); 374.137 (M^+, 1) ($C_{20}H_{22}O_7$), 274 (M − TiglOH, 1), 232 (274 − C_2H_2O, 12), 83 ($C_4H_7CO^+$, 100).

11,13-*Dihydro*-11,13-*epoxyatripliciolide angelate* (**27**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO), 1595 (C=COR); UV (Et_2O) λ_{max} = 260 nm; MS *m/e* (rel. int.): 374.137 (M^+, 17) ($C_{20}H_{22}O_7$), 275 (M − RCO_2, 2), 83 ($C_4H_7CO^+$, 100).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-62.3 \quad -64.6 \quad -71.1 \quad -84.5} \quad (c = 1.4).$$

To 10 mg **27** in 1 ml $CHCl_3$ was added 0.5 ml of a soln of HCl in $CHCl_3$. After 30 min at RT, the solution was shaken with $NaHCO_3$ soln. TLC (Et_2O) afforded 2 mg **33a** and two further compounds.

11,13-*Dihydro*-11-13-*epoxyatripliciolide tiglate* (**28**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO), 1595 (C=COR); MS *m/e* (rel. int.): 374.297 (M^+, 16) ($C_{20}H_{22}O_7$), 275 (M − $RCO_2^•$, 2), 83 ($C_4H_7CO^+$, 100).

11,13-*Dihydro*-11,13-*epoxyatripliciolide methacrylate* (**29**). Colourless gum, not free from **23**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800 (γ-lactone), 1720 and 1650 (C=CCO_2R, C=CCO), 1600 (C=COR); MS *m/e* (rel. int.): 360.121 (M^+, 4) ($C_{19}H_{20}O_7$), 275 (M − $RCO_2^•$, 5), 69 ($C_3H_5CO^+$, 100).

9α-*Hydroxy*-11,13-*dihydro*-11,13-*epoxyatripliciolide*-8-O-*angelate* (**30**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1795 (γ-lactone), 1720 and 1650 (C=CO_2R, C=CCO), 1595 (C=COR); MS *m/e* (rel. int.): 390.131 (M^+, 2) ($C_{20}H_{22}O_8$), 290 (M − RCO_2H, 3), 83 ($C_4H_7CO^+$, 100).

9α-*Hydroxy*-11,13-*dihydro*-11,13-*epoxyatripliciolide*-8-O-*tiglate* (**31**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1795 (γ-lactone), 1710 and 1650 (C=CCO_2R, C=CCO), 1595 (C=COR); MS *m/e* (rel. int.): 390.131 (M^+, 4) ($C_{20}H_{22}O_8$), 83 ($C_4H_7CO^+$, 100).

9α-*Hydroxy*-11,13-*dihydro*-11,13-*epoxyatripliciolide*-8-O-*methycrylate* (**32**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1795 (γ-lactone), 1710 and 1650 (CC=CCO_2R, C = CCO); MS *m/e* (rel. int.): 376,116 (M^+, 7) ($C_{19}H_{20}O_8$), 69 (C_3H_5CO, 100).

11-*Hydroxy*-13-*chloro*-11,13-*dihydroatripliciolide*-8-O-*angelate* (**33a**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1800 (γ-lactone), 1720 and 1650 (C=CCO_2R, C=CCO), 1600 (C=COR); MS *m/e* (rel. int.): 410, 113 (M^+, 10) ($C_{20}H_{23}O_7Cl$), 374 (M − HCl, 2), 311 (M − $RCO_2^•$, 1), 83 ($C_4H_7CO^+$, 200).

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546\,\text{nm}}{+7.0 \quad +7.8 \quad +10.6} \quad (c = 1.4).$$

To 10 mg **33a** in 1 ml $CHCl_3$ were added 20 mg 4-pyrrolidinopyridine and 0.1 ml Ac_2O. After 3 hr, the usual workup afforded after TLC (Et_2O–petrol, 3:1) 10 mg **33b**, colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1800 (γ-lactone), 1750 and 1230 (OAc), 1715 and 1655 (C = CCO_2R, C=CCO), 1600 (C=COR); MS *m/e* (rel. int.): 452 (M^+, 2) ($C_{22}H_{25}O_8Cl$), 392.102 ($C_{20}H_{21}O_6Cl$, M − AcOH, 16), 83 ($C_4H_7CO^+$, 100).

11-*Hydroxy*-13-*chloro*-11,13-*dihydroatripliciolide*-8-O-*tiglate* (**34**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3580 (OH), 1800 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO); MS *m/e* (rel. int.): 410.113 (M^+, 8) ($C_{20}H_{23}O_7Cl$), 83 ($C_4H_7CO^+$, 100).

9α,11-*Dihydroxy*-13-*chloro*-11,13-*dihydroatripliciolide*-8-O-*angelate* (**35**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1800 (γ-lactone), 1715 and 1650 (C=CCO_2R, C=CCO); MS *m/e* (rel. int.): 4.26.107 (M^+, 1) ($C_{20}H_{23}O_8Cl$), 391 (M − Cl, 0.5), 327 (M − RCO_1, 0.5), 83 ($C_4H_7CO^+$, 70), 55 (83 − CO, 100).

3β-*Acetoxy*-8β-*angeloyloxy*-1,10-*dihydro*-1α,10β-*epoxycostunolide* (**36**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750 and 1230 (OAc), 1725, 1650 (C=CCO_2R); MS (Cl, isobutane) *m/e* (rel. int.): 405 (M + 1, 42), 397 (M + 1 − H_2O), 345 (M + 1 − HOAc), 305 (M + 1 − AngOH, 55), 245

(305 − HOAc), 100), 227 (245 − H_2O, 35), 83 ($C_4H_7CO^+$, 50); MS (EI) *m/e* (rel. int.): 305 (M − AngOH, 0.5), 83 ($C_4H_7CO^+$, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+61.3 \quad +64.7 \quad +72.0 \quad +126.0} (c = 0.15).$$

To 5 mg **36** in 1 ml MeOH was added 0.1 ml 1M KOH. After 10 min, the usual workup and TLC (Et_2O–petrol, 3:1) afforded 3 mg **37**, colourless gum; MS (CI, isobutane) *m/e* (rel. int.): 395 (M + 1, 100), 295 (M + 1 − AngOH, 8), 83 ($C_4H_7CO^+$, 12).

5-*Myrtenyl*-4,5-11,13-*tetrahydro*-11,13-*epoxyatripliciolide*-8-O-*angelate* (**38**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1795 (γ-lactone), 1720 and 1645 (C=CCO_2R, C=CCO), 1595 (C=COR); MS *m/e* (rel. int.): 510.262 (M^+, 0.5) ($C_{30}H_{38}O_7$), 411 (M − RCO_2, 0.5), 135 ($C_{10}H_{15}$, 10), 83 ($C_4H_7CO^+$, 100); MS (CI, isobutane) *m/e* (rel. int.): 511 (M + 1, 100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{+73.3 \quad +76.7 \quad +93.3 \quad +218.7} (c = 0.15)$$

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.

REFERENCES

1. Stuessy, T. F. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds.) p. 638. Academic Press, London.
2. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally Occurring Acetylenes*. Academic Press, London.
3. Bohlmann, F. and Zdero, C. (1976) *Phytochemistry* **15,** 1177.
4. Bohlmann, F. and Zdero, C. (1977) *Phytochemistry* **16,** 1065.
5. Quijano, L., Romo de Vivar, A. and Rios, T. (1979) *Phytochemistry* **18,** 1745.
6. Bohlmann, F. and Jakupovic, J. (1979) *Phytochemistry* **18,** 119.
7. Zalkow, L. H., Harris, R. N., III, Van Derveer, D. and Bertrand, J. A. (1977) *J. Chem. Soc. Commun.* 456.
8. Bohlmann, F., Le Van, N., Cuong Pham, T. V., Jakupovic, J., Schuster, A., Zabel, V. and Watson, W. H. (1979) *Phytochemistry* **18,** 1831.
9. Bohlmann, F. and Jakupovic, J. (1980) *Phytochemistry* **19,** 259.
10. Zalkow, L. H., Harris, R. N. III and Van Derveer, D. (1978) *J. Chem. Soc. Commun.* 420.
11. Bohlmann, F. and Zdero, C. (1980) *Phytochemistry* **19,** 149.
12. Bohlmann, F. and Zdero, C. (1980) *Phytochemistry* **19,** 587.
13. Bohlmann, F., Mahanta, P. K., Natu, A. A., King, R. M. and Robinson, H. (1978) *Phytochemistry* **17,** 471.
14. Baruah, N. C., Sharma, R. P., Madhusudanan, K. P., Thyagarajan, G., Herz, W. and Murani, R. (1979) *J. Org. Chem.* **44,** 1831.
15. Höfle, G. and Steglich, W. (1972) *Synthesis* 619.
16. Bohlmann, F. and Grenz, M. (1977) *Chem. Ber.* **110,** 1327.
17. Anthonsen, T. (1969) *Acta Chem. Scand.* **23,** 3605.
18. Robinson, H., Bohlmann, F. and King, R. M. (1978) *Phytologia* **41,** 50.
19. Robinson, H. (1978) *Phytologia* **41,** 33.