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NEW GERMACRANOLIDES, GUAIANOLIDES AND REARRANGED GUAIANOLIDES FROM *LASIOLAENA SANTOSII**

FERDINAND BOHLMANN†, JASMIN JAKUPOVIC†, ROBERT M. KING‡ and HAROLD ROBINSON‡

† Institute for Organic Chemistry, Technical University Berlin, Strasse des 17. Juni 135, D-1000 Berlin 12, West Germany; ‡ Smithsonian Institution, Washington, DC 20560, U.S.A.

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Key Word Index—*Lasiolaena santosii*; Compositae; Eupatorieae; sesquiterpene lactones; germacranolides; guaianolides; rearranged guaianolides; eudesmane derivatives; diterpenes.

Abstract—The aerial parts of *L. santosii* afforded three new diterpenes, a phenylpropanol, three eudesmane derivatives, three germacranolides, seventeen guaianolides and four rearranged guaianolides of a, so far, unknown type. Furthermore, several known compounds were isolated. The structures of the new compounds, the separations of which caused difficulties, were elucidated by spectroscopic methods and by some chemical transformations. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

The small Brazilian genus *Lasiolaena* [1] (Compositae, tribe Eupatorieae) is placed in the *Gyptis* group [2], closest to the widely distributed *Conocliniopsis*, which also has the receptacle highly conical but glabrous and the pappus setae narrowed at the tip. *Agrianthus* and *Bahianthus* are related genera. From the latter the widely distributed euparin derivatives and kolavanes have been isolated [3], while *Agrianthus* contains highly oxygenated guaianolides [4], and *Conocliniopsis* contains heliangolides with a furanone ring [5]. *Conoclinium*, also placed in this group, gave several flavones only [6]. None of the remaining genera of this group has been studied chemically. We have now investigated *Lasiolaena santosii* K. et R. to see whether the chemistry showed further indications of relationships in this diverse group. The aerial parts of this plant were found to be extremely rich in sesquiterpene lactones, among them four lactones with a new type of rearranged carbon skeleton. Furthermore, some new diterpenes and eudesmane derivatives, as well as an unusual phenylpropanol ester, were isolated.

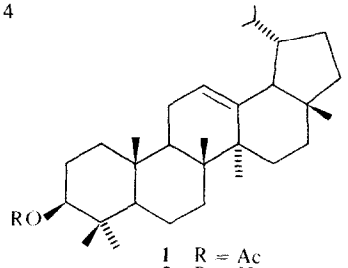
RESULTS AND DISCUSSION

The roots of *L. santosii* afforded squalene, dammadienone, dammadienol and its acetate, while the aerial parts, in addition to these compounds, contained germacrene D, caryophyllene epoxide, lupeol and its acetate, as well as the isomers **1**–**4** [7], the triacetate **5** [8] and a very complex mixture of polar compounds from which the germacranolides eupatolide (**13**) [9] and balchanolide (**14**) [10], the flavone **45** and thirty new compounds were isolated. The latter were made up of the *ent*-labdane derivative **6**, the geranyl geraniol derivatives **7** and **8**, the 7-epimeric methyl esters of 1β-hydroxycostic acid **10** and **11**, the eudesmanolide **12**, the germacranolides **15**–**17**, the rearranged guaianolides **21**–**24**, the guaianolides **25**–**27** and **29**–**41**, and the phenyl propanol derivative **43**. The latter is closely related to the corresponding dimethoxy compound isolated from a *Schkuhria* species [11]. However, in this case an unseparable mixture of four esters each with a different chain length was present. Acetylation under mild conditions afforded the diacetate **44**. The ^{1}H NMR data (see Experimental) were nearly identical with those of the known ester [11]. The position of the methoxy group was deduced from the observed shift differences of the aromatic protons in the spectra of **43** and **44**, while the position of the ester chain methyl group could not be determined. The structure of the diacetate **6** followed from the ^{1}H NMR data (Table 1), especially when the Eu(fod)$_3$-induced shifts were taken into consideration. The observed shifts of the C-4 and C-10 methyl signals were in agreement with an acetoxy group at C-3 and not at C-1, while the position of the hydroxyl at C-11 followed from the ^{1}H NMR data. The configuration at this centre, however, was not determined. All signals could be assigned, after the addition of Eu(fod)$_3$, by spin decoupling (Table 1).

The structure of **7** directly followed from the ^{1}H NMR spectrum (Table 1). The chemical shift of H-14, which could be assigned by spin decoupling, was obviously shifted downfield and was coupled with the methylene doublet at δ 3.15. Furthermore, the position of the secondary methyl group α to the keto group followed from the chemical shift of the corresponding methine proton (2.59 *tq*). Of the remaining two hydroxyls one had to be placed at C-1 and the second at C-19, as is the case with compounds with a hydroxyl at C-20 a pronounced shift of the 2-H signal was observed. The configuration at C-11 was not determined.

The third diterpene, the triol **8** was obviously closely related to **7**. To establish the positions of the hydroxyls, **8** was transformed to the dialdehyde **9** by partial oxidation

* Part 319 in the series "Naturally Occurring Terpene Derivatives". For Part 318 see Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1069.



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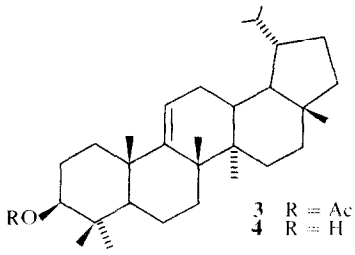
2 R = H



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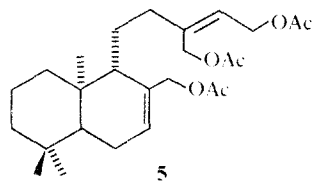

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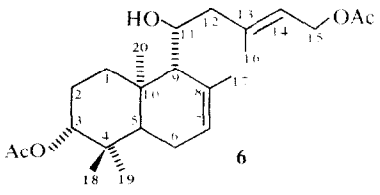

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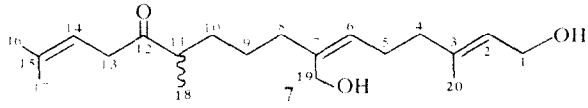

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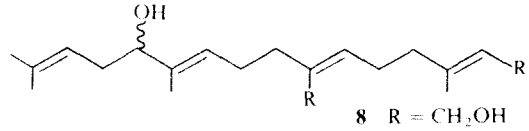

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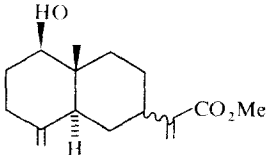
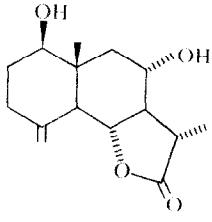
9 R = CHO



10 7α-H
11 7β-H



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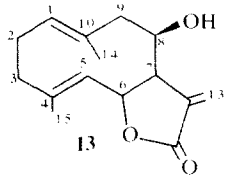

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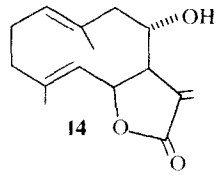

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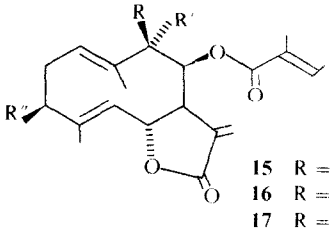
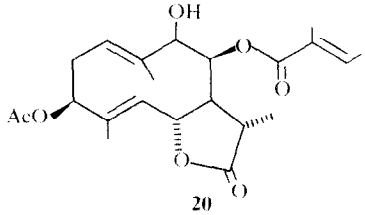


15 R = R′ = H, R″ = OAc
16 R = OH, R′ = R″ = H
17 R = OH, R′ = H, R″ = OAc
18 R, R′ = O, R″ = OAc
19 R = H, R′ = OH, R″ = OAc



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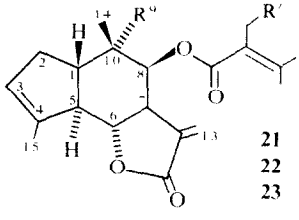
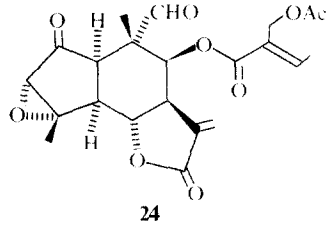


21 R = CHO, R′ = H
22 R = CH_2OH, R′ = H
23 R = CH_2OH, R′ = OAc



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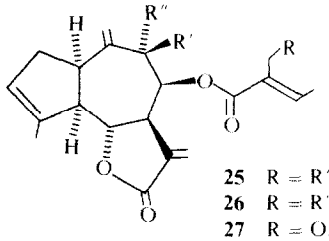
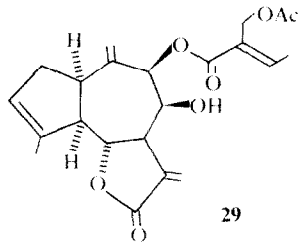


25 R = R′ = OAc, R″ = H
26 R = R″ = H, R′ = OH
27 R = OAc, R′ = OH, R″ = H
28 R = OAc, R′, R″ = O



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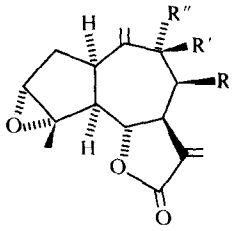
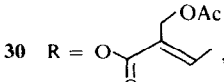
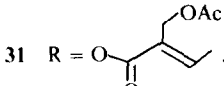
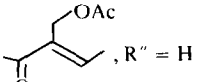
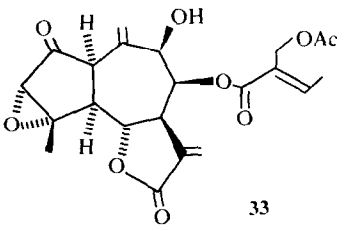


30 R =  , R′, R″ = O

31 R =  , R′ = OH, R″ = H

32 R = OH, R′ = O  , R″ = H



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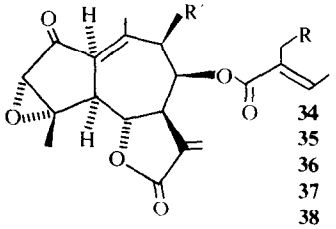
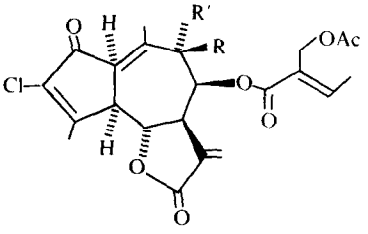
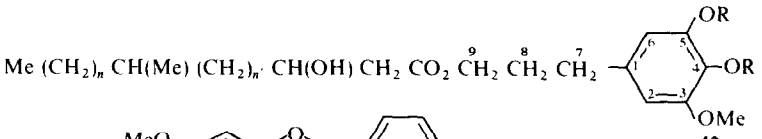


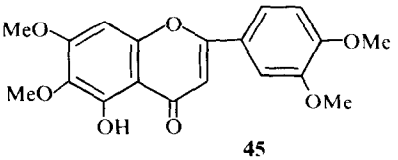
34 R = R′ = H
35 R = R′ = OAc
36 R = OAc, R′ = H
37 R = OAc, R′ = OH
38 R = H, R′ = OH



39 R = OAc, R′ = H
40 R = R′ = H
41 R = OH, R′ = H
42 R, R′ = O



43 $n + n' = 12, 13, 14, 15$
44 R = Ac



45

Table 1. ^{1}H NMR spectral data of compounds **6–9** (270 MHz, $CDCl_3$, TMS as internal standard)

	6*	**6**(+Eu(fod)$_3$)	**7**	**8**	**9**
H-1		2.59 *d* (*br*)	4.09 *dq*	4.07 *d* (*br*)	9.91 *d*
H-1′		2.12 *dd* (*br*)			
H-2		2.71 *ddd*	5.48 *t* (*br*)	5.47 *t* (*br*)	5.97 *d* (*br*)
H-2′		3.36 *d* (*br*)			
H-3	4.52 *dd*	7.73 (*br*)	—	—	—
H-4	—	—	2.2–2.0 *m*	2.3–2.1 *m*	2.79 *m*
H-5		2.02 *dd*			
H-6	1.94 *m*	2.51 *dd* (*br*)	5.19 *t* (*br*)	5.40 *t* (*br*)	6.41 *t* (*br*)
H-6′		2.38 *d* (*br*)			
H-7	5.58 *s* (*br*)	5.96 *d* (*br*)	—	—	—
H-8	—	—	2.2–2.0 *m*	2.3–2.1 *m*	2.27 *t* (*br*)
H-9	2.13 *s* (*br*)	3.61 *s* (*br*)	1.4 *m*		2.14 *dt*
H-10	—	—	1.6 *m*	5.33 *t* (*br*)	5.35 *t* (*br*)
H-11	4.08 *dd* (*br*)	6.08 *m*	2.59 *tq*	—	—
H-12	2.82 *m*	3.76 *dd*	—	3.99 *t* (*br*)	3.97 *t* (*br*)
		3.15 *d* (*br*)			
H-13	—	—	3.15 *d* (*br*)	2.3–2.1 *m*	2.25 *d* (*br*)
H-14	5.48 *t* (*br*)	7.38 (*br*)	5.19 (*br*)	5.10 *m*	5.09 *t* (*br*)
H-15	4.61 *d* (*br*)	7.18 *dd*	—	—	—
		7.11 *dd*			
H-16	1.76 *s* (*br*)	2.56 *s* (*br*)	1.63 *s* (*br*)	1.74 *s* (*br*)	1.73 *s* (*br*)
H-17	1.82 *s* (*br*)	2.32 *s* (*br*)	1.57 *s* (*br*)	1.66 *s* (*br*)	1.65 *s* (*br*)
H-18	0.92 *s*	1.83 *s*	1.09 *d*	1.64 *s* (*br*)	1.61 *s* (*br*)
H-19	0.94 *s*	1.76 *s*	4.08 *s* (*br*)	4.08 *s*	10.09 *s*
H-20	0.87 *s*	1.66 *s*	1.76 *s* (*br*)	1.74 *s* (*br*)	2.02 *d*
OAc	2.05 *s*	4.34 *s*	—	—	—
	2.06 *s*	4.20 *s*	—	—	—

* 400 MHz.

J(Hz): **6**: 1,1′ = 13; 1′,2 = 13; 2,3 = 11; 2′,3 = 5; 5,6 = 12; 5,6′ = 3; 6′,7 = 4; 11,12 = 10; 11,12′ = 2; 12,12′ = 14; 14,15 = 7; **7**: 1,2 = 5,6 = 10,11 = 13,14 ~ 7; **8/9**: 1,2 = 5,6 = 8,9 = 9,10 = 13,14 = 7; 2,20 = 1.5.

with manganese dioxide. Careful spin decoupling allowed the assignment of all signals. As the proton at the hydroxyl-bearing carbon in **9** showed an allylic coupling with the olefinic proton, which itself was coupled with one methyl only, the hydroxyl could only be placed at C-8 or C-12. Spin decoupling showed that the aldehyde group had to be placed at C-1 or C-19. This, however, excluded a C-8 position of the hydroxyl. Its configuration was not determined. The stereochemistry of the double bonds followed from the ^{1}H NMR shifts of the olefinic protons.

The structures of the costic acid derivatives **10** and **11**, which could only be separated by HPLC, followed from the ^{1}H NMR data (Table 2), which were very similar to those of the methyl ester of costic acid. The main differences in the spectra of **10** and **11** were in the signals of H-7, which were only in agreement with an equatorial isopropenyl group in **10** and an axial one in **11**. The position of the hydroxyl group followed from spin decoupling and the chemical shifts of H-15, which excluded a 3-position, while from the couplings of H-1 the β-orientation of the hydroxyl could be deduced in both isomers. The CD curves of **10** and **11** were opposite, as expected (**10** negative and **11** positive Cotton effect). As costic acid showed a negative Cotton effect, the absolute configurations were also established.

The structure and stereochemistry of the eudesmanolide **12** were assigned by careful spin decoupling in deuteriobenzene (Table 2). The 1β-configuration of the hydroxyl group followed from the couplings and by irradiation of the multiplet at δ 1.40, which caused the expected changes of the H-1 and H-3 signals. Similarly, irradiation of the H-8 and H-13 signals allowed the assignments of the signals of H-6 through H-9 and of H-11. The observed larger couplings of H-8 and H-11 required a β-orientation of these hydrogens. **12**, therefore, was 8α-hydroxy-11β,13-dihydroreynosin.

Table 2. ^{1}H NMR spectral data of compounds **10**–**12** (170 MHz, $CDCl_3$)

	10	**11**	**12**	**12**(C_6D_6)
H-1α	3.45 *d* (*br*)	3.40 *dd* (*br*)	3.56 *dd*	2.92 *dd*
H-2	1.56 *m*	1.25–1.9 *m*		1.40 *m*
H-3α	2.13 *ddd* (*br*)	2.09 *ddd* (*br*)		1.60 *ddd*
H-3β	2.32 *ddd*	2.3 *ddd*	2.37 *ddd*	1.95 *ddd*
H-5	1.99–1.3 *m*	1.25–1.9 *m*		1.35 *m*
H-6α			—	—
H-6β			3.99 *dd*	3.36 *dd*
H-7	2.53 *dddd*	3.07 *s* (*br*)		1.40 *m*
H-8α	1.98–1.3 *m*	1.25–1.9 *m*	—	—
H-8β			4.01 *ddd*	3.43 *ddd*
H-9α			1.44 *dd*	1.02 *dd*
H-9β			2.51 *dd*	2.27 *dd*
H-11	—	—	2.58 *dq*	2.08 *dq*
H-13	6.17 *d*	6.19 *s* (*br*)	1.39 *d*	1.53 *d*
H-13′	5.57 *dd*	5.64 *d* (*br*)		
H-14	0.72 *s*	0.75 *s*	0.83 *s*	0.54 *s*
H-15	4.76 *ddd*	4.77 *s* (*br*)	5.08 *s* (*br*)	4.71 *s* (*br*)
H-15′	4.48 *ddd*	4.51 *s* (*br*)	4.73 *s* (*br*)	4.39 *s* (*br*)
OMe	3.76 *s*	3.75 *s*	—	—

J(Hz): **10**: 1α,2β = 12; 2α,3α = 5.5; 2α,3β = 2.5; 2β,3α = 13.5; 2β,3β = 5.5; 3α,3β = 14; 3α,15 = 3α,15′ = 5α,15 = 5α,15′ = 1.5; 6α,7α = 7α,8α = 3.5; 6β,7α = 7α,8β = 12; 7α,13′ = 1; 13,13′ = 1; 15,15′ = 1.5; **11**: 1α,2α = 5; 1α,2β = 12; 2α,3α = 5.5; 2α,3β = 2.5; 2β,3α = 13.5; 2β,3β = 5.5; 3α,3β = 14; 7β,13′ = 2; **12**: 1α,2α = 5; 1α,2β = 12; 2α,3β = 2.5; 2β,3β = 5.5; 3α,3β = 13.5; 5α,6β = 6β,7α = 9.5; 7α,8β = 8β,9α = 11.5; 7α,11β = 12; 8β,9β = 4; 11β,13 = 7.

The structures of the germacradienolides **15**–**17** were deduced from the ^{1}H NMR data (Table 3) of the natural compounds and some of their derivatives. **17** is closely related to similar lactones with an 8β-2-methylbutyryloxy residue [12] and the corresponding angelate [13]. Both obviously had the same stereochemistry at all centres. The critical centre was that at C-9, as from models a clear decision was difficult. We, therefore, oxidized **17** to the corresponding ketone **18**, which on sodium borohydride reduction afforded the 9-epimer **19** as well as the 11,13-dihydro compound **20** with unknown stereochemistry at C-11. Comparison of the ^{1}H NMR spectra of **17** and **19** showed that in **19** the 9-hydroxy group was α-orientated as the H-7 signal was shifted downfield. The ^{1}H NMR data of the ketone **18** showed that a conformation had to be assumed, where the keto group was not in plane with the 1,10-double bond (chemical shift of H-1), and was most probably below the plane. This probably was the reason for the unexpected β-attack of boranate, which normally should be hindered by the 8β-ester residue. The configuration of the angelate [13], therefore, must be corrected also to 9β-hydroxy. As the spectral data and the couplings in the spectra of **15** and **16** were nearly the same as those of **17**, these lactones obviously had the same stereochemistry too.

21–**24** were rearranged guaianolides. The ^{1}H NMR data (Table 4) of **21** showed the typical signals of a tiglate [6.81 *qq*, 1.81 *d* (*br*), 1.82 *s* (*br*)]. A singlet at δ 9.48 indicated an aldehyde group, while typical signals of a *trans*-fused methylene lactone were present too. Spin decouplings allowed the assignment of the signals for H-1 through H-8. The small value of $J_{7,8}$ required an α-proton at C-8, while the orientation of the aldehyde group was deduced from the downfield shift of H-8, especially if compared with that in the spectrum of **22**. The downfield shift of the H-7 signal in the spectrum of **22** supported the proposed stereochemistry, which was further indicated by the downfield shift of the H-1α signal in the spectrum of **21**. The ^{13}C NMR of **22** was in agreement with the proposed structure (see Experimental). The spectrum of **23** clearly showed that the hydroxy group of the ester residue was acetylated. Consequently, the signals of these two lactones were nearly identical. The presence of additional oxygen functions in **24** was deduced from the mass spectrum and from the altered ^{1}H NMR signals compared with those of **21**. The position of the keto group followed from the downfield shift of the H-1 signal, while the α-orientation of a 3,4-epoxide was deduced from the downfield shift of H-5. **21**–**24** most probably were formed by a Wagner–Meerwein rearrangement of a guaianolide of type A, present as tiglate **26** in the plant (see below). We have named **21** without an aldehyde function at C-9 (numbering as in a guaianolide) lasiolaenolide. A compound with the same carbon skeleton has been prepared by rearrangement via a guaianolide 9,10-epoxide [14].

The guaianolides **25**–**27** and **29**–**33** were all derived from the so far unknown Δ 3,4-isomer of dehydrocostus lactone, for which we propose the name lasiolaenin. The

Table 3. ^{1}H NMR spectral data of compounds **15**–**20** (270 MHz, $CDCl_3$)

	15	**16**	**17**	**18**	**19**	**20**
H-1	4.95 *d* (*br*)	5.08 *d* (*br*)	5.13 *d* (*br*)	5.58 *d* (*br*)	5.41 *dd* (*br*)	5.38 *d* (*br*)
H-2α	2.59 *ddd* (*br*)	1.95–1.6 *m*	2.62 *ddd* (*br*)	2.78 *ddd*	2.67 *ddd* (*br*)	2.65 *m*
H-2β	2.36 *ddd*		2.41 *ddd*	2.39 *ddd*	2.44 *ddd*	2.3–2.5 *m*
H-3α	5.26 *dd* (*br*)		5.25 *dd* (*br*)	5.27 *dd*	5.30 *dd* (*br*)	5.28 *dd* (*br*)
H-3β			—	—	—	—
H-5	4.95 *d* (*br*)	4.73 *d* (*br*)	4.87 *d* (*br*)	4.92 *d* (*br*)	4.93 *d* (*br*)	4.83 *d* (*br*)
H-6β	5.18 *dd*	5.14 *dd*	5.15 *dd*	5.26 *dd*	5.13 *dd*	5.04 *dd*
H-7α	2.91 *dddd*	3.02 *dddd*	3.00 *ddd*	3.05 *dddd*	3.33 *ddd*	2.3–2.5 *m*
H-8α	5.78 *ddd* (*br*)	5.97 *s* (*br*)	5.96 *s* (*br*)	5.57 *d*	5.70 *d* (*br*)	5.39 *d*
H-9α	2.32 *dd*	4.33 *dd* (*br*)	4.31 *d* (*br*)	—	—	—
H-9β	2.86 *dd* (*br*)	—	—	—	4.51 *dd* (*br*)	4.47 *s* (*br*)
H-11	—	—	—	—	—	2.3–2.5 *m*
H-13	6.33 *d*	6.33 *d*	6.36 *d*	6.37 *d*	6.32 *d*	1.3 *d*
H-13′	5.64 *d*	5.70 *d*	5.73 *d*	5.63 *d*	5.67 *d*	
H-14	1.52 *s* (*br*)	1.54 *s* (*br*)	1.59 *s* (*br*)	1.71 *s* (*br*)	1.51 *s* (*br*)	1.51 *s* (*br*)
H-15	1.78 *d*	1.79 *d*	1.80 *d*	1.84 *d*	1.78 *d*	1.74 *d*
OH	—	2.77 *d* (*br*)	—	—	1.88 *d*	1.80 *d*
OAc	2.13 *s*	—	2.13 *s*	2.14 *s*	2.13 *s*	2.12 *s*
OTigl	1.83 *s* (*br*)	1.84 *s* (*br*)	1.85 *s* (*br*)	1.87 *s* (*br*)	1.83 *s* (*br*)	1.88 *s* (*br*)
	1.82 *dq*	1.83 *d* (*br*)	1.84 *d* (*br*)	1.87 *d* (*br*)	1.82 *d* (*br*)	1.86 *dq*
	6.82 *qq*	6.88 *m*	6.88 *m*	6.91 *m*	6.84 *m*	6.91 *qq*

J(Hz): **15**: 1,2α = 5; 1,2β = 12; 2α,2β = 12; 2α,3α = 6; 2β,3α = 10.5; 5,6β = 10; 5,15 = 1.5; 6β,7α = 8.5; 7α,13 = 3.6; 7α,13′ = 3; 8α,9α = 2; 8α,9β = 5.5; 9α,9β = 12; **16**: 5,6β = 10; 5,15 = 1.5; 6β,7α = 9; 7α,8α = 0.5; 7α,13 = 3.6; 7α,13′ = 3; 8α,9α = 2; 9α,OH = 2; **17**: 1,2α = 5; 1,2β = 12; 2α,2β = 12; 2α,3α = 6; 2β,3α = 10.5; 5,6β = 10; 5,15 = 1.5; 6β,7α = 8.5; 7α,8α = 0.5; 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 2; **18**: 1,2α = 5.5; 1,2β = 12; 2α,2β = 12; 2α,3α = 5.5; 2β,3α = 10.5; 5,6β = 10; 5,15 = 1.5; 6β,7α = 9; 7α,8α = 1; 7α,13 = 3.5; 7α,13′ = 3; 13,13′ = 0.6; **19**: 1,2α = 4.5; 1,2β = 12.5; 2α,2β = 12; 2α,3α = 6; 2β,3 = 10; 5,6β = 10; 5,15 = 1.5; 6β,7α = 8.5; 7α,13 = 3.5; 7α,13′ = 3; 9α,9β = 5; 9β,OH = 4; **20**: 2α,3α = 6; 2β,3α = 10.5; 5.6β = 10; 5,15 = 1.5; 6β,7α = 9; 8α,9β = 5.3; 9β,OH = 3.5.

hydrogens at C-1 and C-5 were most probably both α-orientated in each lactone, as the couplings were the same as in all known guaianolides of this type [15]. As ligustin, where no configuration at C-1 was reported [16], had been correlated with estafiatin, this lactone also was no exception. Most probably, the configuration at C-1 in the lactones from *Stevia setifera* [17] will have to be corrected. The presence of 6,12-*trans*-methylene lactones in all compounds followed from the observed couplings $J_{5,6}$ and $J_{6,7}$ (Table 5), while the configuration at C-9 caused problems. Inspection of models indicated that the angles between H-8α and both protons at C-9 were nearly identical. Obviously, the configurations at C-8 and C-9 were identical in the lactones **25**–**27** and **29**–**32**. Biogenetical considerations would support the 9α configurations, as in the lactones **15**–**17**. The differences in the ^{1}H NMR spectra of **25** and **26** clearly showed that these lactones differed only in the ester part at C-8, while the data of **27** indicated that the 9-hydroxy group was acetylated. The ^{1}H NMR data of **29** showed by the differences of the chemical shifts of H-8 and H-9 and by spin decoupling that these lactones were isomeric. As the chemical shifts were not very different, we had transformed **27** to the corresponding ketone **28**, its ^{1}H NMR data establishing the proposed assignments of the relative positions at C-8 and C-9 in the lactones **25**–**27**. As expected the 8α-H signal was shifted downfield and was coupled with H-7 only.

The ^{1}H NMR data of **31** and **32** clearly indicated that we were dealing with the epoxides of **25** and **29** respectively, while those of **30** showed that an epoxide of **28** was present. (Table 5). Though the configuration at C-3 and C-4 could not be determined with certainty, α-epoxides seemed to be more likely, as the chemical shift of H-5 should be at higher fields in compounds with a β-epoxide group. **36**, together with **28**, was obtained by oxidation of **27** with pyridine dichromate. This further supported the presence of α-epoxides, as the β-side of **27** was sterically hindered. **33**, was obviously the 2-oxo derivative of **27**; the interpretation of the ^{1}H NMR data, however, caused some difficulties. At room temperature, two conformations in a nearly equal ratio were recognized. At higher temperature, the ratio of these two was changed in favour of the conformer with the H-13 signals more downfield. Inspection of models explained the observed differences in the chemical shifts and couplings of the two conformers in part only. However, **33** on prolonged treatment with Si gel was transformed to **35** (see below). The structures of the lactones **34**–**41** were deduced directly from the ^{1}H NMR data (Table 6) together with spin decoupling in the usual way. In the spectrum of **34** the absence of a function at C-9 was easily deduced from the corresponding H-9 signals, while the changed situations of the double bond followed from the new olefinic methyl signal in all lactones. The chemical shift of the latter agreed with a cisoid arrangement to the

Table 4. ^{1}H NMR spectral data of compounds **21**–**24** (270 MHz, $CDCl_3$)

	21	22	23	24
H-1α	2.90 *ddd*	2.32 *ddd*	2.32 *ddd*	3.42 *d*
H-2α	2.28 *ddq*	2.21 *dd (br)*	2.20 *dd (br)*	—
H-2β	2.48 *dddq*	2.46 *dd (br)*	2.44 *dd (br)*	—
H-3	5.55 *dq*	5.49 *s (br)*	5.49 *s (br)*	3.34 *s*
H-5α	2.49 *dd*	2.62 *dd (br)*	2.63 *dd (br)*	3.09 *dd*
H-6β	4.11 *dd*	4.16 *dd*	4.16 *dd*	3.96 *dd*
H-7α	2.74 *dddd*	3.17 *dddd*	3.19 *dddd*	3.0 *m*
H-8α	6.06 *d (br)*	5.84 *d (br)*	5.89 *d (br)*	5.98 *s (br)*
H-9	9.48 *s*	3.69 *d (br)* 3.52 *d (br)*	3.71 *d (br)* 3.53 *d (br)*	9.51 *s*
H-13	6.15 *d*	6.11 *d*	6.12 *d*	6.26 *d*
H-13′	5.57 *d*	5.52 *d*	5.53 *d*	5.85 *d*
H-14	1.10 *s*	0.99 *s*	1.02 *s*	1.23 *s*
H-15	1.91 *ddd*	1.89 *s (br)*	1.89 *s (br)*	1.80 *s*
OR	1.82 *s (br)*	1.80 *s (br)*	1.98 *s*	1.95 *s*
	1.81 *d (br)*	1.79 *d (br)*	1.95 *d*	1.95 *d*
	6.81 *qq*	6.77 *qq*	4.83 *d*	4.73 *s*
			4.77 *d*	7.09 *q*
			7.08 *q*	

J(Hz): **21**: 1α,2α = 8; 1α,2β = 11.5; 1α,5α = 7.5; 2α,2β = 14.5; 2α,15 = 1; 2β,3 = 1; 2β,15 = 2; 3,15 = 2; 5α,6β = 10.5; 6β,7α = 11.5; 7α,8α = 2.5; 7α,13 = 7α,13′ = 3; **22**: 1α,2α = 8; 1α,2β = 11; 1α,5α = 7.5; 2α,2β = 14; 5α,6β = 11; 6β,7α = 11.5; 7α,8α = 2; 7α,13 = 3.3; 7α,13′ = 3; 14,14′ = 11; **23**: 1α,2α = 8; 1α,2β = 11; 1α,5α = 7.5; 2α,2β = 14; 5α,6β = 11; 6β,7α = 11.5; 7α,8α = 2; 7α,13 = 3.3; 7α,13′ = 3; 14,14′ = 11; **24**: 1α,5α = 7; 5α,6β = 6β,7α = 11.5; 7α,13 = 3.5; 7α,13′ = 3.

keto group at C-2. Furthermore, this situation was supported by the downfield shift of H-5, now being allylic. The configurations at C-3 through C-9 most probably were the same as in the lactones **30**–**33**.

The mass spectra of **39**–**41** indicated the presence of chlorine, which had to be at C-3, as the ^{1}H NMR data of H-5 through H-9 were very similar to those of **34**–**38**. Some of the chemical shifts were altered in the expected way only. The presence of the cross-conjugated ketone caused a considerable downfield shift of H-5, H-14 and H-15 and a slight shift for that of H-9. Oxidation of **41** afforded the diketone **42**, the ^{1}H NMR data of which provided further support for the proposed structure. **34**–**38** were derived from ludartin and **39**–**41** from dehydroleucodin [17]. Inspection of the ^{1}H NMR spectrum of the crude polar fraction showed that at least the major compounds were present. Therefore, **34**–**41** most probably were not artefacts.

The compounds isolated from this *Lasiolaena* species indicated a close relationship to *Agrianthus* by the co-occurrence of highly oxygenated guaianolides. Germacranolides similar to **15**–**17** were isolated from a *Grazielia* species [18], which, however, is placed in the *Disynaphia* group.

EXPERIMENTAL

Air-dried plant material, collected in north-eastern Brazil (voucher RMK 8138), was extracted with Et_2O–petrol. The extracts were separated first by column chromatography (Si gel, act. grade II), then by repeated TLC (Si gel, GF 254) and in part by HPLC (reversed phase, MeOH–H_2O, 7:3). Known compounds were identified by comparison (IR and ^{1}H NMR) with authentic material. The roots (50 g) afforded 1 mg squalene, 2 mg dammadienone, 8 mg dammadienyl acetate and 3 mg dammadienol. The less polar fractions of the aerial parts (150 g) gave 20 mg germacrene D, 15 mg squalene, 2 mg caryophyllene epoxide, 3 mg dammadienone, 10 mg dammadienyl acetate, 5 mg dammadienol, 10 mg lupeyl acetate, 15 mg lupeol, 10 mg **1**, 15 mg **2**, 3 mg **3**, 4 mg **4**, and 10 mg **5**. The more polar fractions were combined in three parts of slightly different polarity (column chromatography, Et_2O and Et_2O–MeOH, 19:1). Each part was further separated first by TLC using $CHCl_3$–acetone, 10:1 and then Et_2O–petrol, 4:1 (developed several times). **10**, **11**, **15**, **25** and **37** could be obtained pure by HPLC only. Finally, 20 mg **6**, 15 mg **7**, 400 mg **8**, 3 mg **10**, 1 mg **11**, 10 mg **12**, 5 mg **13**, 50 mg **14**, 5 mg **15**, 5 mg **16**, 50 mg **17**, 5 mg **21**, 12 mg **22**, 10 mg **23**, 10 mg **24**, 3 mg **25**, 3 mg **26**, 30 mg **27**, 20 mg **29**, 2 mg **30**, 10 mg **31**, 5 mg **32**, 6 mg **33**, 15 mg **34**, 2 mg **35**, 2 mg **36**, 100 mg **37**, 30 mg **38**, 2 mg **39**, 2 mg **40**, 30 mg **41**, 50 mg **43** and 20 mg **45** were obtained.

3α,15-*Diacetoxy*-11-*hydroxy*-ent-*labda*-7,13-*diene* (**6**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1725, 1260 (OAc); MS *m/z* (rel. int.): 406.272 (M$^+$, 1) ($C_{24}H_{38}O_5$), 346 (M − HOAc, 1), 278 (M − Me_2C=$CHCH_2OAc$, 12), 250 (278 − CO, 6), 235 (250 − Me, 3), 190 (250 − HOAc, 79), 175 (190 − Me, 44), 97 (100);

$$[\alpha]_{24}^{\lambda} = \frac{589}{+15}\ \frac{578}{+16}\ \frac{546}{+19}\ \frac{436\ \text{nm}}{+31}\ (c = 0.3, CHCl_3).$$

19-*Hydroxy*-12-*oxo*-10,11-*dihydrogeranylgeraniol* (**7**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1720 (C=O); MS *m/z* (rel. int.): 322.251 (M$^+$, 0.3) ($C_{20}H_{34}O_3$), 304 (M − H_2O, 1), 235 (304 − Me_2C=$CHCH_2^+$, 9), 217 (235 − H_2O, 9), 189 (217 − CO, 10), 161 (189 − CO, 15), 69 (Me_2C=$CHCH_2^+$, 100).

12,19-*Dihydroxygeranylgeraniol* (**8**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3370 (OH); MS *m/z* (rel. int.): 307 (M$^+$ − Me, 0.3), 293 (M − CHO, 0.3), 279 (307 − CO, 0.3), 69 (Me_2C=$CHCH_2^+$, 100). 20 mg **8** in 2 ml Et_2O were stirred for 2 hr with 100 mg MnO_2. TLC (Et_2O–petrol, 1:1) afforded 10 mg **9** as a colourless gum: IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1750, 1685 (C=CCHO); MS *m/z* (rel. int.): 318.220 (M$^+$, 0.5) ($C_{20}H_{30}O_3$), 249 (M − Me_2C=$CHCH_2^+$, 44), 231 (249 − H_2O, 46), 213 (231 − H_2O, 28), 69 (Me_2C=$CHCH_2^+$, 100);

$$[\alpha]_{24}^{\lambda} = \frac{589}{+8}\ \frac{578}{+9}\ \frac{546}{+10}\ \frac{436\,\text{nm}}{+17}\ (c = 1.2, CHCl_3).$$

1β-*Hydroxycostic acid methyl ester* (**10**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 264.173 (M$^+$, 42) ($C_{16}H_{24}O_3$), 246 (M − H_2O, 100), 232 (M − MeOH, 21), 220 (M − CH_2=CHOH, 27), 205 (220 − Me, 31), 187 (205 − H_2O, 29); CD (MeCN) last reading: 198 nm (negative) (costic acid also).

1β-*Hydroxy*-7-epi-*costic acid methyl ester* (**11**). Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 1730 (C=CCO_2R); MS *m/z* (rel. int.): 264.173 (M$^+$, 40) ($C_{16}H_{24}O_3$), 246 (M − H_2O, 100), 232 (M − MeOH, 18), 220 (M − H_2O=CHOH, 77), 215 (220 − Me, 31); CD (MeCN) last reading: 195 nm (positive).

8α-*Hydroxy*-11β,13-*dihydroreynosin* (**12**). Colourless gum, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3605 (OH), 1770 (γ-lactone); MS *m/z* (rel. int.): 266.152 (M$^+$, 0.2) ($C_{15}H_{22}O_4$);

$$[\alpha]_{24}^{\lambda} = \frac{589}{+20}\ \frac{578}{+22}\ \frac{546}{+25}\ \frac{436\,\text{nm}}{+40}\ (c = 0.32, CHCl_3).$$

3β-*Acetoxy*-8β-*tiglinoyloxy*-*costunolide* (**15**). Colourless gum; IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 1765 (γ-lactone), 1740, 1260 (C=CCO_2R); MS

Table 5. ^{1}H NMR spectral data of compounds **25–34** (270 MHz, $CDCl_3$)

	25	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**
H-1α	3.02 *dd* (*br*)	3.0 *m*	3.0 *m*	3.43 *ddd*	3.0 *m*	3.11 *ddd*	3.00 *ddd*	3.02 *ddd*	3.57 *d*	2.98 *d*
H-2α	2.43 *d* (*br*)	2.44 *d* (*br*)	2.44 *d* (*br*)	2.37 *d* (*br*)	2.44 *d* (*br*)	2.13 *dd*	2.19 *dd*	2.29 *dd* (*br*)	—	—
H-2β	2.70 *m*	2.67 *d* (*br*)	2.68 *d* (*br*)		2.66 *d* (*br*)	1.70 *ddd*	2.32 *ddd*	1.98 *ddd*	—	—
H-3	5.63 *s* (*br*)	5.63 *dd* (*br*)	5.64 *s* (*br*)	5.54 *m*	5.59 *m*	3.36 *s*	3.43 *s* (*br*)	3.46 *s* (*br*)	3.37 *s*	3.41 *s*
H-5α	3.09 *d* (*br*)	3.0 *m*	3.0 *m*	2.68 *dd* (*br*)	3.08 *dd* (*br*)	2.46 *dd*	2.44 *dd*	2.42 *dd*	2.93 *dd*	2.55 *dd*
H-6β	4.44 *dd*	4.43 *dd*	4.43 *dd*	4.25 *dd*	4.51 *dd*	4.23 *dd*	4.56 *dd*	4.21 *dd*	5.09 *dd*	4.60 *dd*
H-7α	3.14 *m*	3.10 *dddd*	3.13 *dddd*	3.72 *dddd*	2.96 *m*	3.78 *dddd*	3.13 *dddd*	2.90 *dddd*	3.33 *dddd*	2.65 *dddd*
H-8α	5.95 *dd*	5.87 *dd*	5.94 *dd*	6.02 *d*	4.47 *s* (*br*)	6.02 *d*	5.73 *dd*	4.45 *ddd*	5.40 *dd*	5.45 *dd*
H-9α	5.32 *d*	4.38 *dd* (*br*)	4.39 *dd* (*br*)	—	5.28 *d* (*br*)	—	4.56 *dd*	5.25 *d* (*br*)	4.86 *dd*	5.16 *d* (*br*)
H-13	6.30 *d*	6.30 *d*	6.32 *d*	6.37 *d*	6.39 *d*	6.39 *d*	6.28 *d*	6.40 *d*	6.30 *d*	6.25 *d*
H-13′	5.65 *d*	5.66 *d*	5.72 *d*	5.61 *d*	5.62 *d*	5.62 *d*	5.55 *d*	5.63 *d*	5.48 *d*	5.44 *d*
H-14	5.23 *s* (*br*)	5.34 *s* (*br*)	5.33 *s* (*br*)	5.30 *s*	5.15 *s* (*br*)	5.29 *s*	5.26 *s* (*br*)	5.24 *s* (*br*)	5.40 *s*	5.41 *s*
H-14′	5.19 *s* (*br*)	5.19 *s* (*br*)	5.21 *s* (*br*)	5.12 *d*		5.12 *s*	5.15 *s* (*br*)	5.17 *d*	5.19 *s*	5.34 *s*
H-15	1.86 *s* (*br*)	1.86 *s* (*br*)	1.86 *d* (*br*)	1.92 *d* (*br*)	1.84 *m*	1.64 *s*	1.63 *s*	1.64 *s*	1.75 *s*	1.66 *s*
OH	—	2.32 *d*	2.47 *d*	—	2.70 *d*	—	2.82 *d*	2.59 *d*	2.92 *s*	—
OAc	2.03 *s*	—	—	—	—	—	—	—	—	—
OR	2.03 *s*	1.77 *s* (*br*)	2.0 *s*	2.02 *s*	2.06 *s*	2.02 *s*	2.0 *s*	2.07 *s*	2.01 *s*	2.01 *s*
	1.96 *d*	1.78 *d* (*br*)	1.96 *d*	1.97 *d*	2.00 *d*	1.99 *d*	1.96 *d*	2.00 *d*	1.97 *d*	1.97 *d*
	4.83 *d*	6.80 *m*	4.83 *d*	4.89 *d*	4.98 *s*	4.91 *d*	4.82 *s* (*br*)	4.99 *d*	4.88 *d*	4.88 *d*
	4.73 *d*	—	4.73 *d*	4.79 *d*	7.16 *q*	4.82 *d*	6.15 *q*	4.94 *d*	4.80 *d*	4.81 *d*
	7.10 *q*	—	7.11 *q*	7.16 *q*	—	7.19 *q*	—	7.26 *q*	7.14 *q*	7.17 *q*

J(Hz): **25**: 1,2β = 1,5α = 9; 2α,2β = 16.5; 5α,6β = 6β,7α = 9.5; 7α,8α = 1.5; 7α,13 = 3.7; 7α,13′ = 3; 8α,9α = 3; **26**: 2α,2β = 17; 5α,6β = 6β,7α = 9.5; 7α,8α = 2; 7α,13 = 3.7; 7α,13′ = 3; 7α,8α = 2; 8α,9α = 3.5; 9α,OH = 3; **27**: 2α,2β = 16.5; 5α,6β = 10; 6β,7α = 9; 7α,8α = 2; 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 9α,OH = 4; **28**: 1α,2α = 1α,2β = 1α,5α = 9; 5α,6β = 10.5; 6β,7α = 9; 7α,8α = 4.2; 7α,13 = 3.7; 7α,13′ = 3; **29**: 1α,5α C 8.5; 2α,2β = 16.5; 5α,6β = 9.5; 6β,7α = 9; 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 3; 9α,OH = 2.5; **30**: 1α,2α = 8; 1α,2β = 11; 1α,5α = 8; 2α,2β = 14; 2β,3β = 12; 5α,6β = 11; 6β,7α = 8.5; 7α,8α = 4.2; 7α,13 = 3.5; 7α,13′ = 3; **31**: 1α,2α = 8; 1α,2β = 1α,5α = 8.5; 2α,2β = 14; 5α,6β = 10.5; 6β,7α = 9; 7α,8α = 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 3.5; 9α,OH = 2.5; **32**: 1α,2α = 7.5; 1α,2β = 7; 1α,5α = 3; 2α,3β = 2; 5α,6β = 10.5; 6β,7; = 9; 7α,8α = 2.5; 7α,13 = 3.2; 7α,13′ = 3; 8α,9α = 8α, OH = 4; **33**: 1α,5α = 5α,6β = 6β,7α = 9.5; 7α,9α = 5; 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 5.5; 9α,OH = 3; **34**: 1α,5α = 7; 5α,6β = 7.5; 6β,7α = 10.5; 7α,8α = 4; 7α,13 = 3.5; 7α,13′ = 3; 8α,9α = 5.

Table 6. ^{1}H NMR spectral data of compounds **34**–**42** (270 MHz, $CDCl_3$)

	34	35	36	37	38	39	40	41	42
H-3β	3.41 *s* (*br*)	3.45 *s* (*br*)	3.40 *s* (*br*)	3.42 *s* (*br*)	3.41 *s* (*br*)				
H-5α	3.45 *d* (*br*)	3.49 *d* (*br*)	3.43 *d* (*br*)	3.44 *d* (*br*)	3.45 *d* (*br*)	3.65 *d* (*br*)	3.29 *d* (*br*)	3.56 *d* (*br*)	3.55 *dqq*
H-6β	4.10 *dd*	4.01 *dd*	3.99 *dd*	4.02 *dd*	4.12 *dd*	4.01 *dd*	4.50 *dd*	4.00 *dd*	4.41 *dd*
H-7α	3.09 *dddd*	3.33 *m*	3.27 *dddd*	3.30 *ddd*	3.10 *dddd*	3.40 *dddd*	3.15 *d* (*br*)	3.35 *dddd*	3.30 *dddd*
H-8α	5.70 *d* (*br*)	5.62 *s* (*br*)	5.55 *d*	5.67 *d*	5.70 *d* (*br*)	5.75 *s* (*br*)	5.76 *dd* (*br*)	5.69 *d* (*br*)	5.40 *d*
H-9α	2.82 *dd*	5.94 *s* (*br*)	4.61 *d*	4.65 *d* (*br*)	2.86 *dd*	6.02 *s* (*br*)	2.76 *d* (*br*)	4.77 *d* (*br*)	—
H-9β	2.63 *d* (*br*)	—	—	—	2.66 *d* (*br*)	—	2.95 *dd* (*br*)	—	—
H-13	6.22 *d*	6.22 *d*	6.25 *d*	6.24 *d*	6.21 *d*	6.26 *d*	6.31 *d*	6.29 *d*	6.40 *dd*
H-13′	5.49 *d*	5.53 *d*	5.46 *d*	5.49 *d*	5.46 *d*	5.62 *d*	5.62 *d*	5.55 *d*	5.67 *dd*
H-14	2.23 *d* (*br*)	2.23 *s*	2.22 *s*	2.24 *s*	2.23 *s*	2.40 *s* (*br*)	2.34 *s* (*br*)	2.40 *s* (*br*)	2.41 *d*
H-15	1.82 *s*	1.81 *s*	1.81 *s*	1.81 *s*	1.81 *s*	2.40 *s* (*br*)	2.34 *s* (*br*)	2.38 *s* (*br*)	2.29 *d*
OAc	—	2.16 *s*	—	—	—	2.20 *s*	—	—	—
OH	—	—	4.07 *d*	4.00 *d*	—	—	—	4.12 *d* (*br*)	—
	1.76 *dq*	1.96 *d*	1.76 *dq*	1.97 *d*	1.94 *d*	1.97 *s*	1.96 *d*	1.97 *d*	1.99 *d*
	6.73 *qq*	4.75 *s*	6.79 *qq*	4.74 *s*	4.74 *s*	4.77 *s* (*br*)	4.75 *s* (*br*)	4.76 *d*	4.81 *d*
	—	7.07 *q*	—	7.08 *q*	7.04 *q*	7.04 *q*	7.10 *q*	4.72 *d*	4.75 *d*
	—	—	—	—	—	—	—	7.06 *q*	7.12 *q*

J(Hz): **34**: 5α,6β = 6β,7α = 10.5; 5α,14 = 1; 7α,8α = 2; 7α,13 = 3; 7α,13′ = 3; 7α,8α = 2.5; 8α,9α = 6; 9α,9β = 15; **35**: 5α,6β = 6β,7α = 10.5; 7α,13 = 3.2; 7α,13′ = 2.8; **36**: 5α,6β = 6β,7α = 10.5; 7α,8α = 2; 7α,13 = 3.2; 7α,13 = 3; 9α,OH = 8.5; **37**: 5α,6β = 6β,7α = 10.5; 7α,8α = 2; 7α,13 = 3.2; 7α,13 = 3; 9α,OH = 7; **38**: 5α,6β = 6β,7α = 10.5; 7α,8α = 2; 7α,13 = 7α,13′ = 3; 8α,9α = 6; 9α,9β = 15; 5α,14 = 1; **39**: 5α,6β = 6β,7α = 10.5; 7α,8α = 1.5; 7α,13 = 2.8; 7α,13′ = 2.6; **40**: 5α,6β = 6β,7α = 10.5; 7α,8α = 2.0; 7α,13 = 3.3; 7α,13′ = 2.8; 8α,9α = 4.5; 8α,9β = 0.5; 9α,9β = 17; **41**: 5α,6β = 6β,7α = 10.5; 7α,8α = 1.5; 7α,13 = 3; 7α,13′ = 2.8; 9α,OH = 8.5; **42**: 5α,6β = 6β,7α = 10.5; 5α,14 = 5α,15 = 1; 7α,8α = 1.5; 7α,13 = 3.3; 7α,13′ = 3.0; 13′,13′ = 0.7.

m/z (rel. int.): 388.189 (M^+, 0.3) ($C_{22}H_{28}O_6$), 346 (M − ketene, 1), 246 (346 − TiglOH, 11), 228 (246 − H_2O, 9), 83 ($C_4H_7CO^+$, 100).

9β-Hydroxy-8β-tiglinoyloxy-costunolide (**16**). Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3600 (OH), 1770 (γ-lactone), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 346.178 (M^+, 0.6) ($C_{20}H_{26}O_5$), 328 (M − H_2O, 0.5), 246 (M − TiglOH, 5), 228 (246 − H_2O, 6), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 38).

3β-Acetoxy-9β-hydroxy-8β-tiglinoyloxy-costunolide (**17**). Colourless crystals, mp 207.5° (Et_2O); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1770 (γ-lactone), 1730 (OAc, C=CCO_2R); MS *m/z* (rel. int.): 404.184 (M^+, 0.5) ($C_{22}H_{28}O_7$), 362 (M − ketene, 0.8), 345 (M − OAc, 3), 262 (362 − TiglOH, 7), 244 (262 − H_2O, 12), 83 ($C_4H_7CO^+$, 100);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{+130.4}\ \frac{578}{+136.8}\ \frac{546}{+159.1}\ \frac{436\,nm}{+304.8}\ (c = 1.5).$$

10 mg **17** in 0.2 ml CH_2Cl_2 were stirred for 24 hr with 50 mg pyridine dichromate. TLC afforded 6 mg **18**, colourless gum. For ^{1}H NMR see Table 3. To 6 mg **18** in 1 ml MeOH, 10 mg $NaBH_4$ and, after a min, dil H_2SO_4 were added. TLC (Et_2O–petrol, 4:1) afforded 2 mg **19** and 2 mg **20** (^{1}H NMR see Table 3).

Lasiolaenolide-9-al (**21**). Colourless gum; IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 2740, 1730 (CHO), 1775 (γ-lactone), 1720, 1660 (C=CCO_2R); MS *m/z* (rel. int.): 344.162 (M^+, 8) ($C_{20}H_{24}O_5$), 244 (M − TiglOH, 10), 216 (244 − CO, 6), 83 ($C_4H_7CO^+$, 100).

Lasiolaenolide-9-ol (**22**). Colourless gum: IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3620 (OH), 1770 (γ-lactone), 1715, 1650, (C=CCO_2R); MS *m/z* (rel. int.): 346.178 (M^+, 6) ($C_{20}H_{26}O_5$), 246 (M − TiglOH, 11), 228 (246 − H_2O, 2), 215 (246 − CH_2OH, 8), 83 ($C_4H_7CO^+$, 100); ^{13}C NMR ($CDCl_3$) (C-1–C-15): δ 50.1, 34.1, 124.9, 143.9†, 47.7†, 81.3, 47.5†, 71.0, 70.8, 42.5, 144.0†, 167.4, 120.0, 18.8, 16.8 († may be interchangeable):

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{+18.4}\ \frac{578}{+19.6}\ \frac{546}{+22.5}\ \frac{436\,nm}{+40.5}\ (c = 0.5).$$

5′-Acetoxy-lasiolaenolide-9-al (**23**). Colourless gum; IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3610 (OH), 1765 (γ-lactone), 1720, 1655 (C=CCO_2R); MS *m/z* (rel. int.): 404.184 (M^+, 8) ($C_{22}H_{28}O_7$), 246 (M − RCO_2H, 17), 228 (246 − H_2O, 28), 216 (246 − CH_2O, 78), 99 (MeCH=$C(CH_2OH)CO^+$, 48), 81 (99 − H_2O, 100).

5′-Acetoxy-3α,4α-epoxy-2-oxo-lasiolaenolide-9-al (**24**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2740, 1730 (CHO), 1775 (γ-lactone), 1730 (C=CCO_2R, C=O, OAc); MS *m/z* (rel. int.): 432.142 (M^+, 0.4) ($C_{22}H_{24}O_9$), 404 (M − CO, 0.5), 389 (404 − Me, 2), 246 (M − CO, RCO_2H, 17), 141 (RCO^+, 100), 99 (141 − ketene, 78), 81 (99 − H_2O, 82).

9β-Acetoxy-8β-[5-acetoxy-tiglinoyloxy]-lasiolaenin (**25**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1740 (OAc, C=CCO_2R); MS *m/z* (rel. int.): 444.178 (M^+, 3) ($C_{24}H_{28}O_8$), 402 (M − ketene, 0.5), 384 (M − HOAc, 2), 342 (384 − ketene, 1), 244 (402 − RCO_2H, 5), 226 (244 − H_2O, 38), 141 (RCO^+, 100), 99 (141 − ketene, 29), 81 (99 − H_2O, 95).

9β-Hydroxy-8β-tiglinoyloxy-lasiolaenin (**26**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1720 (C=CCO_2R); MS *m/z* (rel. int.): 344.162 (M^+, 4) ($C_{20}H_{24}O_5$), 244 (M − TiglOH, 5), 226 (244 − H_2O, 6), 83 ($C_4H_7CO^+$, 100).

9β-Hydroxy-8β-[5-acetoxy-tiglinoyloxy]-lasiolaenin (**27**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1728 (C=CCO_2R, OAc); MS *m/z* (rel. int.): 402.168 (M^+, 4) ($C_{22}H_{26}O_7$), 244 (M − RCO_2H, 20), 226 (244 − H_2O, 10), 141 (RCO^+, 100), 99 (141 − ketene, 34) 81 (99 − H_2O, 59);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589}{+15.7}\ \frac{578}{+15.7}\ \frac{546}{+19.1}\ \frac{436\,nm}{+32.7}\ (c = 0.9,\ CHCl_3).$$

10 mg **27** in 0.2 ml CH_2Cl_2 were stirred for 72 hr with 50 mg pyridine dichromate. TLC (Et_2O–petrol, 4:1) afforded 1 mg **30**, identical with the natural compound (IR and ^1H NMR) and 4 mg **28**, colourless gum; MS *m/z* (rel. int.): 400.152 (M^+, 10) ($C_{22}H_{24}O_7$), 340 (M − HOAc, 8) (242 (M − RCO_2, 11), 141 (RCO^+, 100), 99 (141 − ketene, 25).

8β-Hydroxy-9β-[5-acetoxy-tiglinoyloxy]-lasiolaenin (**29**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520 (OH), 1770 (γ-lactone), 1730 (C=CCO_2R, OAc); MS *m/z* (rel. int.): 402.168 (M^+, 0.5) ($C_{22}H_{26}O_7$), 244 (M − RCO_2H, 7), 226 (244 − H_2O, 5), 141 (RCO^+, 100), 99 (141 − ketene, 22), 81 (99 − H_2O, 73).

3α,4α-Epoxy-9-oxo-8β-[5-acetoxy-tiglinoyloxy]-3,4-dihydro-lasiolaenin (**30**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1785 (γ-lactone), 1740 (C=CCO_2R, OAc, C=O); MS *m/z* (rel. int.): 258.189 (M − RCO_2H, 38) ($C_{15}H_{14}O_4$), 243 (258 − Me, 6), 141 (RCO^+, 100), 81 (141 − HOAc, 91);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-20 \quad -21 \quad -25 \quad -51} \quad (c = 0.1, CHCl_3).$$

3α,4α-Epoxy-9β-hydroxy-8β-[5-acetoxy-tiglinoyloxy]-3,4-dihydro-lasiolaenin (**31**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1775 (γ-lactone), 1735 (OAc, C=CCO_2R); MS *m/z* (rel. int.): 260 (M − RCO_2H, 3), 245 (260 − Me, 3), 141 (RCO^+, 72), 81 (141 − HOAc, 100).

3α,4α-Epoxy-8β-hydroxy-9β-[5-acetoxy-tiglinoyloxy]-3,4-dihydro-lasiolaenin (**32**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610 (OH), 1775 (γ-lactone), 1730 (OAc, C=CCO_2R); MS *m/z* (rel. int.): 418.163 (M^+, 0.1) ($C_{22}H_{26}O_8$), 260 (M − RCO_2H, 6), 141 (RCO^+, 100), 99 (141 − ketene, 38), 81 (141 − HOAc, 98).

3α,4α-Epoxy-9β-hydroxy-8β-[5-acetoxy-tiglinoyloxy]-2-oxo-3,4-dihydro-lasiolaenin (**33**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1765 (γ-lactone), 1725 (OAc, C=CCO_2R, C=O); MS *m/z* (rel. int.): 432.142 (M^+, 3) ($C_{22}H_{24}O_9$), 372 (M − HOAc, 0.5), 274 (M − RCO_2H, 12), 256 (274 − H_2O, 12), 141 (RCO^+, 100), 99 (141 − ketene, 27), 81 (141 − HOAc, 75). $[\alpha]_D$ 0 (c = 0.5, $CHCl_3$). 10 mg **33** in 2 ml $CHCl_3$ were stirred with 0.5 g SiO_2 for 24 hr. TLC (Et_2O–petrol, 4:1) afforded 6 mg **37**, identical with the natural compound (^1H NMR).

8β-Tiglinoyloxy-2-oxo-ludartin (**34**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1715, 1650 (C=O, C=CCO_2R); MS *m/z* (rel. int.): 358.142 (M^+, 13) ($C_{20}H_{22}O_6$), 258 (M − TiglOH, 53), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 88);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-83.3 \quad -88.7 \quad -107.6 \quad -297}$$

(c = 0.55, $CHCl_3$).

9β-Acetoxy-9β-[5-acetoxy-tiglinoyloxy]-2-oxo-ludartin (**35**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775 (γ-lactone), 1725 (C=CCO_2R, OAc, C=O); MS *m/z* (rel. int.): 474.153 (M^+, 1) ($C_{24}H_{26}O_{10}$), 316 (M − RCO_2H, 3), 256 (316 − HOAc, 11), 141 (RCO^+, 100), 99 (141 − ketene, 27), 81 (141 − HOAc, 76).

8β-[5-Acetoxy-tiglinoyloxy]-2-oxo-ludartin (**36**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1725 (C=CCO_2R, OAc, C=O); MS *m/z* (rel. int.): 416.147 (M^+, 8) ($C_{22}H_{24}O_8$), 258 (M − RCO_2H, 96), 141 (RCO^+, 66), 99 (141 − ketene, 51), 81 (141 − HOAc, 100).

9β-Hydroxy-8β-[5-acetoxy-tiglinoyloxy]-2-oxo-ludartin (**37**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1735 (OAc, C=CCO_2R, C=O); MS *m/z* (rel. int.): 432.142 (M^+, 1) ($C_{22}H_{24}O_9$), 414 (M − H_2O, 2), 256 (414 − RCO_2H, 12), 141 (RCO^+, 100), 99 (141 − ketene, 25), 81 (141 − HOAc, 71).

9β-Hydroxy-8β-tiglinoyloxy-2-oxo-ludartin (**38**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1720 (C=CCO_2R, C=O); MS *m/z* (rel. int.): 374.137 (M^+, 1) ($C_{20}H_{22}O_7$), 275 (M − OTigl, 12), 83 ($C_4H_7CO^+$, 100), 55 (83 − CO, 82).

9β-Acetoxy-3-chloro-8β-[5-acetoxy-tiglinoyloxy]-dehydroleucodin (**39**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780 (γ-lactone), 1735 (OAc, C=CCO_2R), 1695 (C=CC=O); MS *m/z* (rel. int.): 494 (0.3) and 492.118 (M^+, 1) ($C_{24}H_{25}ClO_9$), 336 (7) and 334 (M − RCO_2H, 23), 294 (21) and 292 (334 − ketene, 75), 141 (RCO^+, 90), 99 (141 − ketene, 38), 81 (141 − HOAc, 100).

3-Chloro-8β-[5-acetoxy-tiglinoyloxy]-dehydroleucodin (**40**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1790 (γ-lactone), 1730 (α-OAc, C=CCO_2R); MS *m/z* (rel. int.): 436 (6) and 434.113 (M^+, 18) ($C_{22}H_{23}ClO_7$), 278 (8) and 276 (M − RCO_2H, 20), 141 (RCO^+, 75), 59 (141 − ketene, 46), 81 (141 − HOAc, 100).

3-Chloro-9β-hydroxy-8β-[5-acetoxy-tiglinoyloxy]-dehydroleucodin (**41**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1735 (OAc, C=CCO_2R); 1700 (C=CCO); MS *m/z* (rel. int.): 452 (3) and 450.108 (M^+, 10) ($C_{22}H_{23}ClO_8$), 414 (M − HCl, 3), 392 (1) and 390 (M − HOAc, 3), 294 (2) and 292 (M − RCO_2H, 5), 141 (RCO^+, 86), 99 (141 − ketene, 36), 81 (141 − HOAc, 100);

$$[\alpha]_{24^\circ}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-60 \quad -62.5 \quad -73 \quad -152.5} \quad (c = 0.4, CHCl_3).$$

10 mg **41** on oxidation with pyridine dichromate afforded after TLC (Et_2O–petrol, 4:1) 5 mg **42**, colourless gum. For ^1H NMR see Table 6.

3-Methoxy-4,5-dihydroxy-phenyl propanol ester (**43**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3560 (OH), 1730 (CO_2R); ^1H NMR ($CDCl_3$): δ 6.43 (*d*, 2-H, *J* = 2 Hz), 6.29 (*d*, 6-H), 2.58 (*t*, 7-H, *J* = 7 Hz), 1.93 (*tt*, 8-H, *J* = 7, 7 Hz), 4.13 (*t*, 9-H, *J* = 7 Hz), 3.87 (*s*, OMe), 5.27 *s* (*br*), 5.24 *s* (*br*) and 2.85 (*s* (*br*) OH), 2.51 (*dd*, *J* = 15, 3.5 Hz), 2.40 (*dd*, *J* = 15, 9 Hz), 4.00 [*m*, $COCH_2CH(OH)$], 1.27 [*s* (*br*), $-(CH_2)_n$], 0.89 (*t* (*br*), Me), 0.87 (*d*, CHMe); MS *m/z* (rel. int.): 536.408 (M^+, 10) ($C_{32}H_{56}O_6$), 522 ($C_{31}H_{52}O_6$, 7), 508 ($C_{30}H_{52}O_6$, 22), 494.361 ($C_{29}H_{50}O_6$, 5), 198 (M − R–CH=C=O, 33), 180 (H_2C=$CHCH_2C_6H_3(OH)_2OMe$, 100), 153 (180 − CH=CH_2, tropylium cation, 30). 5 mg **43** was stirred overnight with Ac_2O. After evapn 3 mg **44** were obtained; ^1H NMR ($CDCl_3$): δ 6.67 (*d*, 2-H, *J* = *J* = 2 Hz), 6.61 (*d*, 6-H), 2.67 (*t*, 7-H, *J* = 7 Hz), 1.98 (*tt*, 8-H, *J* = 7, 7 Hz), 4.16 (*t*, 9-H, *J* = 7 Hz), 3.83 (*s*, OMe), 2.29 *s* and 2.27 *s* (OAc), 2.51 (*dd*, *J* = 15, 3.5 Hz), 2.39 (*dd*, *J* = 15, 9 Hz), 3.99 [*m*, $COCH_2CH(OH)$], 1.27 (*s* (*br*), $CH_2)_n$, 0.88 (*t*, (*br*), Me), 0.86 (*d*, CHMe).

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