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SESQUITERPENE LACTONES FROM *VERNONIA MARGINATA*

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Key Word Index *Vernonia marginata*; Compositae; sesquiterpene lactones; glaucolides; new types of sesquiterpene lactones.

Abstract—A reinvestigation of the polar fraction from *Vernonia marginata* afforded in addition to marginatin 13 new lactones, including six glaucolides, four closely related lactones with a new carbon skeleton, named vernomargolides, two jalcaguaianolides and a pseudoelephantopide, as well as a methyl ester probably derived from a glaucolide. The structures were elucidated by NMR spectroscopy and the stereochemistry was established by NOE difference spectroscopy. Possible biogenetic relationships are discussed briefly.

INTRODUCTION

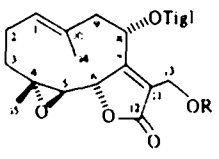
Marginatin is possibly a precursor of a bourbonenolide. In order to isolate this lactone for some reactions [1] we have separated again the polar fraction of *Vernonia marginata* (Torr.) Raf. In addition to marginatin, 13 new lactones were isolated. Their structures are discussed in this paper.

RESULTS AND DISCUSSION

Careful separation of the polar fraction of *V. marginata* afforded in addition to marginatin (**1**) [2] the glaucolides **2**–**6** and **10**, the pseudoelephantopide **7** and the methyl ester **8**, both derived from a corresponding glaucolide, the jalcaguaianolides **9** and **11** as well as four lactones with a new carbon skeleton (**12**–**15**).

The structure of **2** clearly followed from the ^{1}H NMR spectrum in deuteriobenzene at elevated temperature (Table 1) which was close to that of marginatin. The missing acetate group at C-13 led to the expected upfield shift of the H-13 signal. Also the structures of **3** and **4** could be deduced from the ^{1}H NMR spectral data (Table 1) which were close to those of known vernonatalolides which only differed in the nature of the ester groups [1, 3]. The relative position of the ester group in **3** was deduced by comparing the chemical shifts of H-8 and H-13 to those in the corresponding diacetate [1].

The ^{1}H NMR spectra of **5** and **6** (Table 1) showed that these lactones again only differed in the nature of the oxygen group at C-13. The presence of a glaucolide-like lactone was deduced from a pair of broadened doublets (H-13) in the spectrum of **6** and a broadened doublet at δ4.73 which most likely was due to H-6. A lowfield doublet at 6.24 was coupled with a double quartet at 5.20. As the latter was coupled with an olefinic methyl, the two lowfield signals were due to H-8 and H-9. A doublet at δ2.47 was coupled with H-6 and therefore was H-5, indicating that a 4,5-epoxide was present. A double doublet at 5.11 further showed that most likely a hydroxyl group was present at C-1. Inspection of models and NOE



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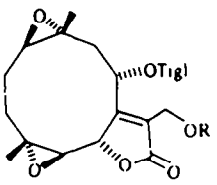

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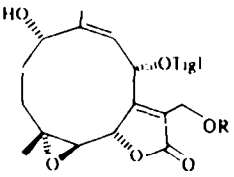
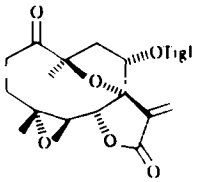


5 R = H **6** R = Ac



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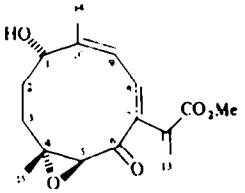

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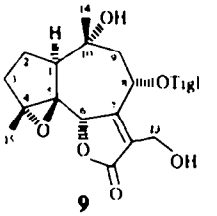

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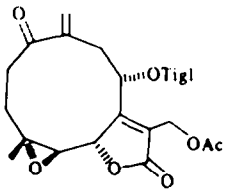

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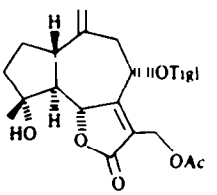

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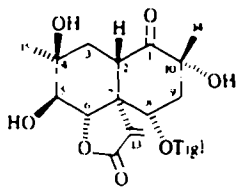

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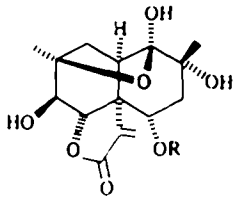
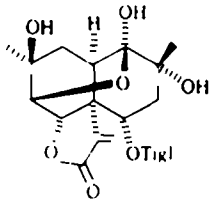


13 R = Tigl
14 R = H



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difference spectroscopy allowed the assignment of the stereochemistry. Thus, clear NOEs were observed between H-3 and H-5, between H-15, H-6 and H-1, between H-14 and H-9, as well as between H-1 and H-8. The ^{13}C NMR spectrum (Table 3) also agreed with the proposed structure. Lactone **6** most likely is formed by reaction of **1** with oxygen in a conformation with the C-4 methyl above and the C-10 methyl below the plane. This would lead to a lactone with an α-hydroxy group and a *Z*-configuration of the 9,10-double bond. The only other reported glaucolide with a 9,10-double bond is fasciculide-B [4]. However, the NMR data clearly show that the proposed structure is not correct. Most likely it is a glaucolide with a 4,5-epoxy group, a 1,10-double bond and ester groups at C-1 and C-8, in accord with the ^1H NMR data.

The structure of **7** was deduced from the ^1H NMR spectrum (Table 1) which was close to that of the corresponding methacrylate [1], while the spectrum of **9** (Table 2) was close to that of the corresponding angelate from *V. jalcana* [1]. The typical signals of a tiglate residue indicated the difference of the two lactones.

The molecular formula of **8** ($C_{16}H_{20}O_5$) and the ^1H NMR spectrum (Table 1) showed that a methyl ester of a sesquiterpene acid was present. In part the ^1H NMR signals were similar to those of **5**. However, several additional olefinic signals were apparent. From the ^{13}C NMR spectrum the presence of a conjugated keto group and six olefinic carbons could be deduced. Spin decoupling of the ^1H NMR spectrum allowed the assignment of all signals, while NOE difference spectroscopy gave further information concerning the stereochemistry and on the mode of connection of the sequences which followed from the decoupling experiments. Thus clear NOEs were observed between H-3α and H-5, between H-15 and H-1, between H-14, H-5 and H-9 and between H-5, H-3α and H-9. These effects required the proposed stereochemistry and further allowed the determination of the conformation with the C-4 methyl above and the C-10

Table 1. ^1H NMR spectral data of compounds **2**–**8** and **10** (400 MHz, $CDCl_3$, TMS as internal standard)

H	2(C_6D_6, 77°)	3	4	5	6	7	8	10
1	4.92 *br d*	2.70 *br d*	2.69 *br d*	5.12 *dd*	5.11 *dd*	–	4.70 *dd*	—
2	1.85 *m*	α 2.12 *br d*	2.12 *br dd*	α 2.10 *dddd*	2.08 *m*	2.58 *m*	2.03 *m*	3.24 *ddd*
2'		β 1.55 *m*	1.54 *m*	β 1.96 *dddd*	1.96 *m*	2.15 *m*		2.63 *ddd*
3	1.74 *m*	β 2.29 *ddd*	2.29 *ddd*	β 2.18 *ddd*	2.17 *m*	1.85 *m*	2.21 *ddd*	1.59 *ddd*
3'	1.06 *m*	α 1.33 *ddd*	1.33 *ddd*	α 0.94 *ddd*	0.95 *ddd*		1.14 *ddd*	2.38 *ddd*
5	2.12 *d*	2.58 *d*	2.59 *d*	2.46 *d*	2.47 *d*	4.07 *d*	4.19 *s*	2.45 *d*
6	4.70 *br d*	4.96 *br d*	4.98 *br d*	4.71 *br d*	4.73 *br d*	4.80 *d*	—	4.82 *d*
8	5.09 *dd*	5.24 *br d*	5.22 *br d*	6.21 *d*	6.24 *d*	5.36 *dd*	6.87 *dq*	5.05 *dd*
9	α 2.54 *dd*	2.74 *br d*	2.75 *br d*	5.19 *dq*	5.20 *dq*	2.98 *dd*	6.05 *dq*	2.89 *dd*
9'	β 2.49 *dd*	1.98 *dd*	2.00 *dd*			1.91 *dd*		3.52 *br ddd*
13	4.54 *br s*	4.49 *br s*	4.88 *dd*	4.68 *br s*	5.10 *br d*	6.45 *s*	6.28 *d*	4.98 *d*
13'			4.79 *dd*		4.96 *br d*	5.73 *s*	5.72 *d*	4.82 *d*
14	1.41 *br s*	1.52 *s*	1.52 *s*	1.79 *d*	1.80 *d*	1.41 *s*	1.92 *dd*	5.96 *d* 5.94 *br s*
15	1.09 *s*	1.47 *s*	1.47 *s*	1.60 *s*	1.60 *s*	1.39 *s*	1.28 *s*	1.43 *s*
OH	2.62 *br s*	2.72 *br s*	—	•	•	••	•	
OAc	–	–·	2.04 *s*	—	2.08 *s*		—	2.07 *s*
OR	6.87 *br q*	6.91 *qq*	6.88 *qq*	6.93 *qq*	6.89 *m*	6.79 *qq*	3.71 *s*	6.90 *qq*
	1.75 *br s*	1.83 *dq*	1.82 *dq*	1.86 *br s*	1.82 *m*	1.77 *dq*		1.82 *dq*
	1.46 *br d*	1.82 *br s*	1.80 *dq*	1.85 *br d*		1.75 *dq*		1.81 *dq*

•Obscured.

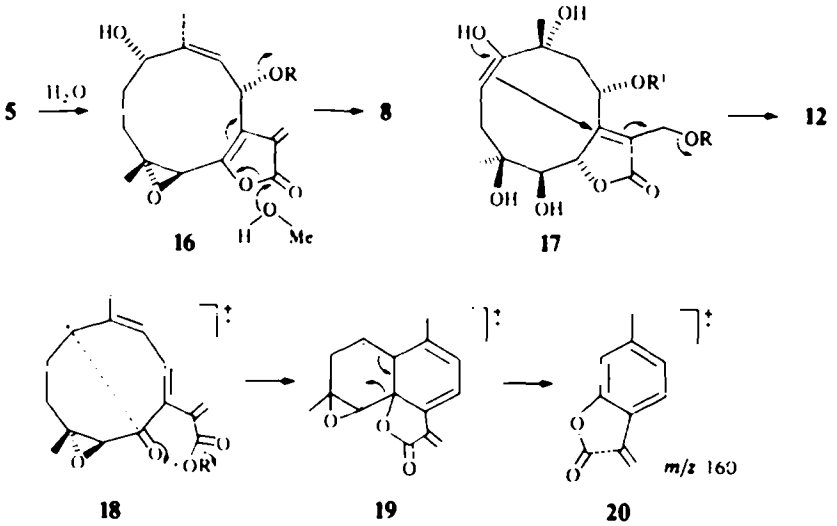
J (Hz): Compound **2**: 1, 2 = 1, 2' = 7; 5, 6 = 9; 8, 9α = 10; 8, 9β = 4; 9α, 9β = 13; compounds **3** and **4**: 1, 2β = 10.5; 2α, 2β = 14; 2α, 3α = 6.5; 2α, 3β = 1.5; 2β, 3α = 3α, 3β = 13.5; 2β, 3β = 5.5; 5, 6 = 9; 8, 9α = 9.5; 9α, 9β = 14; (compound **4**: 6, 13 = 6, 13' = 1; 13, 13' = 13); compounds **5** and **6**: 1, 2α = 11.5; 1, 2β = 5.5; 2α, 2β = 13; 2α, 3α = 7; 2α, 3β = 1.5; 2β, 3α = 13; 2β, 3β = 6.5; 3α, 3β = 13; 5, 6 = 8, 9 = 10; 9, 14 = 1; (compound **6**: 13, 13' = 12); compound **7**: 5, 6 = 10.5; 8, 9α = 8, 9α = 8; 9α, 9β = 13.5; compound **8**: 1, 2α = 11; 1, 2β = 6; 2α, 3α = 7; 2α, 2β = 2.5; 2β, 3α = 13; 2β, 3β = 5.5; 3α, 3β = 13; 8, 9 = 4; 8, 14 = 1.5; 9, 14 = 2.5; 13, 13' = 1; compound **11**: 2, 2' = 15; 2, 3 = 9; 2, 3' = 2; 2', 3 = 12; 2', 3' = 8; 3, 3' = 14; 5, 6 = 10; 8, 9 = 12; 8, 9' = 3; 9, 9' = 13, 13' = 13; 9', 14 = 2. OTigl: 3', 4' = 7; 3', 5' = 4', 5' = 1.

methyl below the plane. Furthermore, it was obvious that the conjugated system was not in the plane, which explains the small coupling $J_{8,9}$. Most likely **8** is formed by degradation of **5** via **16** as shown in Scheme 1. The base peak at m/z 160 in the mass spectrum of **8** is remarkable. Probably the stable ion **20** was formed via **18** and **19**.

The structure of **10** also followed from the ^{1}H NMR spectrum (Table 1). Several signals were close to those of **1**. However, the olefinic methyl singlet was replaced by the signals of exomethylene protons and the presence of a 1-keto group was indicated by a pair of double double doublets at δ3.24 and 2.63. The stereochemistry and the conformation could be deduced from NOE difference spectroscopy. The clear effects were observed between H-15, H-6 and H-8, between H-14 and H-9α, as well as between H-14' and H-2α. Accordingly, C-15 was above and C-14 below the plane. Thus **10** is 10,14-dehydrostilpnotomentolide-8-*O*-tiglate. The structure of **11** followed from the ^{1}H NMR spectral data (Table 1) which were in part close to those of **9**. However, the downfield shift of the H-9 signals and the signals of exomethylene protons indicated a different structural feature at C-10. Furthermore, H-6 now displayed a doublet. Spin decoupling allowed the assignment of all signals and the configurations were established by NOE difference spectroscopy. Especially a clear NOE between H-1 and H-6 and between H-15 and H-6 indicated, together with the couplings, the proposed stereochemistry. Furthermore, the structure was supported by acid-catalysed conversion of **1** to **11**.

The structure elucidation of the lactones **12**–**15** caused some difficulties as they are all derivatives of a so far unknown carbon skeleton. Though the signals in the ^{1}H NMR spectrum (Table 2) could be assigned completely by spin decoupling, the presence of several non-hydrogen bearing carbons did not allow elucidation of larger sequences. However, the ^{13}C NMR spectra of **12** and **13** (Table 3) required a bicyclic carbon skeleton as the singlet at δ40.6 in the spectrum of **12** had to placed at a ring junction. Further information from the NMR data finally led to the structure **12** with a keto group at C-1 (numbering as in **1**–**6**) as the chemical shift of the double doublet at δ3.51 required a neighboring carbonyl group. In agreement with this assumption a lowfield ^{13}C NMR doublet at δ53.8 was observed. As the signals of the exomethylene protons were singlets, no hydrogen was at C-7 indicating that most likely a new carbon bond had to be placed at this carbon. Following the ^{13}C NMR data, an oxygen group at this centre could be excluded. Both the ^{1}H and the ^{13}C NMR data nicely agreed with the proposed structure which was further supported by results of NOE difference spectroscopy. Thus clear NOEs were observed between H-15 and H-5, between H-14 and H-2, between H-3α and H-5 and between H-6 and H-8. The presence of a *trans*-decalin derivative also followed from the couplings of H-2. The possible presence of a corresponding 4,5-epoxide can be excluded from the chemical shifts in the ^{13}C NMR spectrum and the molecular ion of **12**. The unusual chemical shift of H-5 probably was due to the shielding effect of the neighboring lactone ring which appeared very likely when a model was inspected.

The ^{13}C NMR spectrum of **13** (Table 3) showed that the carbonyl group at C-1 was replaced by an acetal carbon (δ105.9 s). The ^{1}H NMR spectral data (Table 2) were in part close to those of **12**. However, nearly all chemical shifts were different, though the splittings of most signals were similar and several showed different couplings. Inspection of models indicated that this was probably due to the presence of a *cis*-decalin derivative which also was required for the proposed acetal formation. The stereochemistry followed from the observed NOEs between H-15 and H-5, between H-14 and H-9, between H-5 and H-3α, between H-8 and H-6, between H-6, H-8 and H-9β and between H-13 and H-2, which established the presence of a *cis*-decalin derivative. The spectral data of **14** indicated that this lactone was the 8-desacyl derivative of **13**. The ^{1}H NMR spectrum of **15** (Table 2) was close to that of **13**. However, the chemical shifts and also some couplings differed slightly. Accordingly, an ether bridge between C-1 and C-5 was proposed for this isomer. The enlarged geminal coupling



Scheme 1.

Table 2. ^{1}H NMR spectral data of compounds **9** and **11**-**15** (400 MHz, $CDCl_3$, TMS as internal standard)

H	9*	11	12	13	14	15
1	2.32 *br d*	2.33 *m*	—	-	—	-
2	2.1–1.9 *m*	1.85 *m*	3.51 *dd*	2.77 *d*	2.74 *d*	2.88 *br d*
3		1.72 *m*	β 1.99 *dd*	β 2.54 *dd*	β 2.48 *dd*	β 2.18 *dd*
3'	0.79 *m*		α 1.65 *dd*	α 1.50 *d*	α 1.51 *d*	α 1.62 *br d*
5	—	1.66 *dd*	3.06 *d*	3.51 *d*	3.55 *d*	4.06 *br d*
6	5.27 *br d*	5.09 *d*	4.62 *d*	4.31 *d*	4.18 *d*	4.49 *d*
8	5.74 *dd*	6.06 *dd*	5.68 *dd*	4.98 *dd*	3.56 *dd*	5.07 *dd*
9α	1.50 *dd*	2.33 *dd*	2.05 *dd*	2.18 *m*	2.03 *dd*	2.13 *dd*
9β	2.62 *dd*	2.93 *dd*	2.27 *dd*		2.19 *dd*	1.99 *dd*
13	4.58 *d*	4.75 *s*	6.48 *br s*	6.41 *br s*	6.52 *s*	6.48 *s*
13'			5.32 *br s*	5.62 *br s*	5.87 *s*	5.80 *s*
14	1.43 *s*	5.01 *br s*	1.55 *s*	1.31 *s*	1.31 *s*	1.29 *s*
14'		4.82 *br s*				
15	1.48 *s*	1.40 *s*	1.19 *s*	1.46 *s*	1.45 *s*	1.26 *s*
OR	6.97 *qq*	6.88 *br q*	6.79 *br q*	6.85 *br q*	—	6.94 *br q*
	1.89 *dq*	1.73 *br d*	1.79 *br d*	1.84 *br s*		1.87 *br s*
	1.86 *dq*	1.72 *br s*	1.78 *br s*	1.82 *br s*		1.84 *br d*
OAc		1.91 *s*				

*OH 3.00 *br s*; 2.47 *br t*.

J (Hz): Compound **9**: 1, 2α = 9; 8, 9α = 12; 8, 9β = 2; 9α, 9β = 13; 13, OH = 7; compound **11**: 1, 5 = 5, 6 = 11; 8, 9α = 7; 8, 9β = 3; 9α, 9β = 15; compound **12**: 2, 3α = 12; 2, 3β = 3; 3α, 3β = 14.5; 5, 6 = 7.5; 8, 9α = 12; 8, 9β = 4; 9α, 9β = 14; compounds **13** and **14**: 2, 3β = 4.5; 3α, 3β = 13; 5, 6 = 3.5; 8, 9α = 8, 9β = 3; 9α, 9β = 16; compound **15**: 2, 3β = 5; 3α, 3β = 16; 5, 6 = 5; 8, 9α = 2; 8, 9β = 3; 9α, 9β = 16; OTigl: 3', 4' = 7; 3', 5' = 4', 5' = 1.

Table 3. ^{13}C NMR data of compounds **5**, **8**, **12** and **13** (100.61 MHz, $CDCl_3$, TMS as internal standard)

C	5	8*	12	13
1	66.8 *d*	67.8 *d*	211.8 *s*	105.9 *s*
2	28.7 *t*	30.0 *t*	53.8 *d*	44.8 *d*
3	32.6 *t*	33.4 *t*	31.1 *t*	35.9 *t*
4	55.4 *s*	62.2 *s*	73.4 *s*	71.6 *s*
5	59.5 *d*	67.1 *d*	78.6 *d*	87.4 *d*
6	80.1 *d*	192.2 *s*	74.9 *d*	80.3 *d*
7	156.4 *s*	140.9 *s*	40.6 *s*	50.6 *s*
8	65.7 *d*	139.2 *d*	70.5 *d*	70.7 *d*
9	122.6 *d*	127.5 *d*	39.9 *t*	35.4 *t*
10	145.3 *s*	143.5 *s*	85.5 *s*	83.9 *s*
11	128.7 *s*	140.8 *s*	133.6 *s*	137.3 *s*
12	172.8 *s*	166.3 *s*	169.3 *s*	168.5 *s*
13	66.4 *t*	125.9 *t*	125.4 *t*	126.1 *t*
14	17.7 *q*	17.1 *q*	27.9 *q*	22.9 *q*
15	16.7 *q*	15.2 *q*	26.3 *q*	22.2 *q*
1'	167.0 *s*	—	166.8 *s*	165.7 *s*
2'	127.7 *s*	—	127.5 *s*	128.1 *s*
3'	139.9 *d*	—	139.9 *d*	139.0 *d*
4'	12.1 *q*	—	11.9 *q*	12.3 *q*
5'	14.8 *q*	—	14.7 *q*	14.8 *q*

*OMe 52.1 *q*.

of H-3 and the fact that now H-5 was not shielded by the lactone oxygens supported the presence of a tetrahydropyrane ring in **15**.

Most likely **12** is formed via **17**, an intermediate which may be formed by hydrolysis of the corresponding glaucolide by attack at C-4, leading to the proposed configurations at C-4 and C-5. The formation of the bond between C-2 and C-7 would be the result of a formal Michael-addition leading to **12** as well as to the corresponding *cis*-decalin which, however, is directly transformed to the isomeric acetals **11** and **15**. The 8-deacyloxy derivative of **12** we have named vernomargolide and therefore **13** is 8α-tigloyloxy-2-epi-vernomargolide-1,4-cyclosemiacetal and **15** is the corresponding 1,5-semiacetal. The carbon skeleton of these lactones has not been reported previously though it has a normal sesquiterpene skeleton. The positive Cotton-effect in the CD spectrum of **14** is in agreement with the Beecham rule [5] which may be an indirect support of the absolute configuration of glaucolides which so far has not been determined, though the proposed one is very likely from biogenetic considerations. The Cotton-effect of **12** most likely is overlapped by that of the carbonyl group leading to a more intense, bathochromically shifted maximum.

The necessary precursor of **7** **15** so far has not been isolated from *V. marginata* or other species. Furthermore several of the required reactions have not been observed. Accordingly, it is unlikely that these lactones are artifacts though the fraction was very old.

EXPERIMENTAL

The polar fraction of the extract [2] of 200 g dried leaves (collected by S. B. Jones in Crosby Co., TX, *ca* 2 miles N of Ralls, voucher Jones 17667, deposited at the University of Georgia Herbarium) was separated first by CC (silica gel) into five crude fractions (1. Et_2O petrol, 1:1; 2. Et_2O petrol, 3:2 and 7:3;

3. Et_2O petrol, 4:1 and 9:1; 4. Et_2O and Et_2O MeOH, 19:1; and 5. Et_2O–MeOH, 9:1 and 5:1). Fraction 1 gave 15 mg **1** while HPLC (MeOH–H_2O, 3:2, RP8, always *ca* 100 bar, flow rate 3 ml/min) of fraction 2 gave 2 mg **4** (R_t 2.2 min) 5 mg **2** (R_t 3.3 min) and 10 mg **1** (R_t 4.8 min) identical with authentic material by ^1H NMR and TLC. TLC (silica gel, PF 254, Et_2O–CH_2Cl_2–C_6H_6, 1:1:1) of fraction 3 gave 10 mg **4** (R_f 0.65), 3 mg **2** (R_f 0.6) and 2 mg **7** (R_f 0.4). HPLC (MeOH–H_2O, 1:1) of fraction **4** gave 5 mg **5** (R_t 3.7 min), 25 mg **6** (R_t 4.0 min), 12 mg **3** (R_t 4.7 min), 3 mg **7** (R_t 4.9 min) and 30 mg **4** (R_t 8.8 min). TLC of fraction 5 ($CHCl_3$–MeOH, 19:1, four developments) gave five bands (5/1 5/5, R_f 0.82, 0.52, 0.40, 0.30, 0.15). HPLC (RP 18, MeOH–H_2O, 3:2) of 5/1 gave 3 mg **8** (R_t 14.0 min). HPLC (RP 18, MeOH–H_2O, 3:2) of 5/2 afforded 10 mg **2** (R_t 10.0 min) and 5 mg **9** (R_t 10.8 min). HPLC (RP 18, MeOH–H_2O, 3:2) of 5/3 gave 10 mg **5** (R_t 7.6 min), 1 mg **10** (R_t 8.2 min), 4 mg **6** (R_t 8.6 min) and 1 mg **11** (R_t 9.2 min). HPLC (RP 8, MeOH–H_2O, 1:1) of 5/4 gave 2 mg **14** (R_t 1.4 min) and 16 mg of a mixture of **12**, **13** and **15** (5/4/2). HPLC of 5/5 (same conditions) gave 6 mg **14** (R_t 1.4 min) and 3 mg **12**, **13** and **15**. TLC of 5/4/2 ($CHCl_3$–MeOH, 9:1, three developments) gave 6 mg **12** (R_f 0.65), 8 mg **13** (R_f 0.6) and 2 mg **15** (R_f 0.58).

13-*Deacetylmarginatin* (**2**). Colourless crystals, mp 151°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540 (OH), 1760 (γ-lactone), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 362.173 [M]$^+$ (1) (calc. for $C_{20}H_{26}O_6$: 362.173), 262 [M − RCO_2H]$^+$ (8), 233 [262 − CHO]$^+$ (3), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (57). CD (MeOH): $\Delta\varepsilon_{284} = -0.13$.

8,13-*Bis-deacylvernonataloide*-8-O-*tiglate* (**3**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 378.168 [M]$^+$ (5) (calc. for $C_{20}H_{26}O_7$: 378.168), 360 [M − H_2O]$^+$ (0.6), 279 [M − OCOR]$^+$ (1.3), 260 [360 − RCO_2H]$^+$ (2.3), 231 [260 − CHO]$^+$ (4), 203 [231 − CO]$^+$ (3), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (59). CD (MeOH): $\Delta\varepsilon_{278} = -0.1$.

8-*Deacylvernonataloide*-8-O-*tiglate* (**4**). Colourless crystals, mp 167°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760 (γ-lactone), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 420.178 [M]$^+$ (1) (calc. for $C_{22}H_{28}O_8$: 420.178), 360 [M − HOAc]$^+$ (1), 321 [M − OCOR]$^+$ (1), 320 [M − RCO_2H]$^+$ (0.5), 260 [320 − HOAc]$^+$ (3), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (88).

1α-*Hydroxy*-13-*deacetyl*-9,10*Z*-*dehydro*-1,10-*dihydromarginatin* (**5**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1710, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 378.168 [M]$^+$ (1.5) (calc. for $C_{20}H_{26}O_7$: 378.168), 361 [M − OH]$^+$ (0.5), 360 [M − H_2O]$^+$ (0.2), 260 [360 − RCO_2H]$^+$ (3), 231 [260 − CHO]$^+$ (3), 203 [231 − CO]$^+$ (5), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (56).

1α-*Hydroxy*-9,10*Z*-*dehydro*-1,10-*dihydromarginatin* (**6**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1765 (γ-lactone, OAc), 1710, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 420.178 [M]$^+$ (1.7) (calc. for $C_{22}H_{28}O_8$: 420.178), 286 [M − 2 × H_2O, RCO_2H]$^+$ (2), 260 [M − HOAc, RCO_2H]$^+$ (5.5), 232 [260 − CO]$^+$ (10), 217 [232 − Me]$^+$ (6), 83 [C_4H_6CO]$^+$ (100), 55 [83 − CO]$^+$ (53). CD (MeOH): $\Delta\varepsilon_{265} = -2.56$.

Pseudoelephantopide-8-O-*tiglate* (**7**). Colourless crystals, mp 146°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (γ-lactone), 1730 (CO), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 376.152 [M]$^+$ (0.7) (calc. for $C_{20}H_{24}O_7$: 376.152), 294 [M − O=C=C(Me)CH=CH_2]$^+$ (4), 276 [M − RCO_2H]$^+$ (2), 252 [294 − CH_2=C=O]$^+$ (7), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (49). CD (MeOH): $\Delta\varepsilon_{292} = -0.2$, $\Delta\varepsilon_{268} = +0.18$, $\Delta\varepsilon_{240} = -1.0$.

1α-*Hydroxy*-9α,5β-*epoxy*-4,10-*dimethyl*-6-*oxo*-7-(1-*carbomethoxy-ethyliden*)-*cyclodeca*-7*Z*,9*Z*-*diene* (**8**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1730 (C=CCO_2R), 1685, 1610 (C=CCO); MS *m/z* (rel. int.): 292.131 [M]$^+$ (3) (calc. for $C_{16}H_{20}O_5$: 292.131), 274 [M − H_2O]$^+$ (6), 260 [M − MeOH]$^+$ (7.5), 160.052 [$C_{10}H_8O_2$]$^{+\bullet}$ (100), 83 [C_5H_7O]$^+$ (78).

8α-*Tigloyloxy*-4α,5α-*epoxyjalcaguaianolide* (**9**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1765 (γ-lactone), 1720, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 360.157 [M − H_2O]$^+$ (2) (calc. for $C_{20}H_{24}O_6$: 360.157), 328 [M − HOAc]$^+$ (2), 260 [360 − RCO_2H]$^+$ (2.5), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (56).

10,14-*Dehydrostilpnotomentolide*-8-O-*tiglate* (**10**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (γ-lactone), 1745 (OAc), 1715 (C=CCO); MS *m/z* (rel. int.): 418.163 [M]$^+$ (7) (calc. for $C_{22}H_{26}O_8$: 418.163), 358 [M − HOAc]$^+$ (3), 319 [M − OCOR]$^+$ (2), 258 [358 − RCO_2H]$^+$ (6), 229 [258 − CHO]$^+$ (5), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (57).

4α-*Hydroxy*-8α-*tigloyloxy*-1β*H*-*jalcaguaianolide*-13-O-*acetate* (**11**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1775 (γ-lactone), 1745 (OAc), 1715 (C=CCO_2R); MS *m/z* (rel. int.): 404.184 [M]$^+$ (1.7) (calc. for $C_{22}H_{28}O_7$: 404.184), 389 [M − Me]$^+$ (0.3), 386 [M − H_2O]$^+$ (0.1), 344 [M − HOAc]$^+$ (0.2), 305 [M − OCOR]$^+$ (1.5), 304 [M − RCO_2H]$^+$ (0.6), 286 [386 − RCO_2H]$^+$ (1.7), 244 [344 − RCO_2H]$^+$ (8), 226 [244 − H_2O]$^+$ (7), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (39).

Compound **1** (5 mg) in 0.5 ml $CDCl_3$ was heated for 3 hr with 1 mg *p*-Ts at 60°. The ^1H NMR of **1** was changed in part (*ca* 35%) to that of **11**. TLC ($CHCl_3$–Et_2O MeOH, 20:5:1) gave 1 mg **11**, identical with the natural compound (^1H NMR, TLC).

8α-*Tigloyloxy*-*vernomargolide* (**12**). Colourless amorphous solid; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1765 (γ-lactone), 1725 (C=O), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 394.163 [M]$^+$ (3) (calc. for $C_{20}H_{26}O_8$: 394.163), 376 [M − H_2O]$^+$ (1), 366 [M − CO]$^+$ (5), 266 [366 − RCO_2H]$^+$ (2), 248 [266 − H_2O]$^+$ (3), 83 [C_4H_7CO]$^+$ (100), 59 [Me_2COH]$^+$ (39), 55 [83 − CO]$^+$ (44); CD (MeCN): $\Delta\varepsilon_{289} = +1.52$, $\Delta\varepsilon_{226} = -3.0$.

8α-*Tigloyloxy*-2-*epi*-*vernomargolide*-1,4-*cyclosemiacetal* (**13**). Colourless amorphous solid; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 394.163 [M]$^+$ (0.5) (calc. for $C_{20}H_{26}O_8$: 394.163), 376 [M − H_2O]$^+$ (1.5), 366 [M − CO]$^+$ (1), 294 [M − RCO_2H]$^+$ (2), 276 [294 − H_2O]$^+$ (3), 248 [276 − CO]$^+$ (2.5), 83 [C_4H_7CO]$^+$ (100), 55 [83 − CO]$^+$ (42).

8α-*Hydroxy*-2-*epi*-*vernomargolide*-1,4-*cyclosemiacetal* (**14**). Colourless amorphous solid; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone); MS *m/z* (rel. int.): 294.110 [M − H_2O]$^+$ (100) (calc. for $C_{15}H_{18}O_6$: 294.110), 276 [294 − H_2O]$^+$ (52), 266 [294 − CO]$^{+\bullet}$ (48), 251 [266 − Me]$^+$ (27), 180 [251 − C_4H_7O]$^+$ (95), 71 [C_4H_7O]$^+$ (57), 59 [C_3H_7O]$^+$ (60), 58 [Me_2CO]$^+$ (84); CD (MeCN): $\Delta\varepsilon_{260} = +0.33$.

8α-*Tigloyloxy*-2-*epi*-*vernomargolide*-1,5-*cyclosemiacetal* (**15**). Colourless amorphous solid; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1760 (γ-lactone), 1715, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 394.163 [M]$^+$ (0.5) (calc. for $C_{20}H_{26}O_8$: 394.163), 294 [M − RCO_2H]$^+$ (3), 276 [294 − H_2O]$^+$ (3), 83 [C_4H_7CO]$^+$ (100).

•This ion is probably formed by splitting the 1,2- and 5,6-bonds, loss of hydroxyl and methoxyl leading to an aromatic methylene lactone (see **20**).

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