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HELIANGOLIDES FROM *VIGUIERA SYLVATICA*

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Key Word Index—*Viguiera sylvatica*; Compositae; sesquiterpene lactones, heliangolides; guaianolides, diterpenes, geranyl nerol derivatives

Abstract—The extract of the aerial parts of *Viguiera sylvatica* gave, in addition to known heliangolides, four new heliangolides related to 1-desoxyniveusin A and one to 11,13-dihydrofurohelianglide as well as three guaianolides, two of them derived from arbiglovin and one from estafiatin. Furthermore, two unreported geranyl nerol derivatives were isolated. The structures were elucidated by high field NMR spectroscopy

INTRODUCTION

Many species from the large New World genus *Viguiera* (tribe Heliantheae) have been studied chemically. Most widespread are heliangolides, especially those with a 3,10-oxygen ring [1]. However, other sesquiterpene lactones as well as kaurane and geranyl nerol derivatives have been reported. We have now studied a species from Costa Rica. The results are discussed in this paper.

RESULTS AND DISCUSSION

The extract of the aerial parts of *Viguiera sylvatica* Klatt. gave *ent*-kaurenic acid and the known heliangolides leptocarpin [2], **5** [3], **6** [4] and **7** [5] as well as **1–4** and **8** Furthermore, the guaianolides **9–11**, the geranyl nerol derivatives **12** and **13** as well as the phenylalanine derivatives **14** and **15** [6] were isolated.

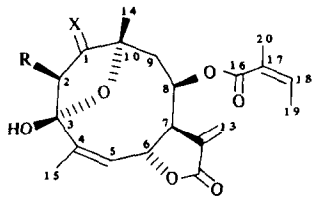
The structure of **1** followed from the ^{1}H NMR spectrum (Table 1) which was similar to that of **5** [3]. The molecular formula ($C_{20}H_{26}O_6$) and the missing low field signal for H-1 indicated that the compound was 1-desoxyniveusin A. The absence of the signals of H-1 and downfield shift of the signals of H-2 showed that lactone **2** was the 1-oxo derivative of **1**.

The ^{1}H NMR data of **3** (Table 1) were close to those of the corresponding isobutyrate [7] where the stereochemistry was established from the results of NOE measurements.

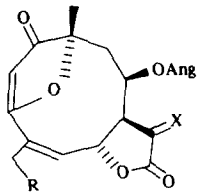
The ^{1}H NMR spectrum of **4** (Table 1) was similar to that of tagitinin **B** which is the corresponding 8-O-isobutyrate [8]. The stereochemistry was confirmed by the observed NOE's between H-14 and H-1α, between H-2 and H-1α as well as between H-8 and H-7 which required *cis*-orientation of H-14 and 2-OH as well as of H-7 and H-8.

The ^{1}H NMR spectrum of **8** (Table 1) was very close to that of **6** [4]. However, the presence of the corresponding 11β,13-dihydro derivative followed from the replacement of the exo-methylene proton signals by a methyl doublet.

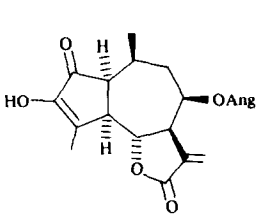
The structure of **9** was deduced from the molecular formula ($C_{20}H_{24}O_7$) and from the ^{1}H NMR spectrum (Table 2). Spin decoupling indicated that a 12,6α-guaianolide must be present with an angeloyloxy group in the 8β-position. The chemical shifts of H-1 and H-5 required neighbouring sp^2 carbons and that of H-14 a hydroxy group at C-10. The absence of a H-3 signal indicated, in agreement with the molecular formula, the presence of a further hydroxy group at C-3. The stereochemistry was confirmed by the observed NOE's [between H-14, H-6



	1	2	3	4	5
R	H	H	H	OH	H
X	H_2	O	βOMe,H	H	αOH,H



	6	7	8
R	H	OH	H
X	CH_2	CH_2	αMe,H



9 10αOH
10 $\Delta^{1(10)}$

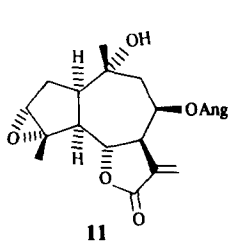


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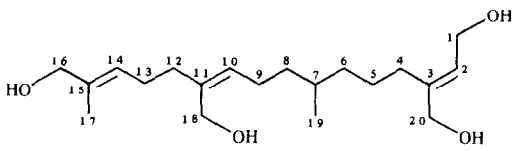
Table 1 ^{1}H NMR spectral data of compounds **1**–**4** and **8** (400 MHz, $CDCl_3$, δ-values)

H	1	2	3†	4	8‡
1	2 30 *m* (2H)	-	4 04 *dd*	2 30 *m* (2H)	-
2	2 14 *m*	3 17 *d*	2 61 *dd*	4 32 *d*	5 56 *s*
2′	1 53 *m*	2 70 *d*	2 00 *d*		
5	5 60 *m*	5 70 *dq*	5 65 *dq*	5 96 *dq*	5 92 *dq*
6	5 43 *ddq*	5 10 *ddq*	5 42 *ddq*	5 70 *ddq*	5 16 *ddq*
7	4 14 *dddd*	3 63 *dddd*	4 14 *dddd*	4 17 *dddd*	2 81 *ddd*
8	5 60 *m*	5 34 *ddd*	5 67 *ddd*	5 63 *ddd*	5 11 *ddd*
9	2 06 *dd*	2 34 *dd*	2 15 *dd*	2 67 *dd*	2 52 *dd*
9′	1 99 *dd*	2 30 *dd*	1 85 *dd*	1 97 *dd*	2 17 *dd*
13	6 26 *d*	6 35 *d*	6 26 *d*	6 25 *d*	1 32 *d*
13′	5 61 *d*	5 76 *d*	5 60 *d*	5 59 *d*	
14	1 52 *s*	1 52 *s*	1 54 *s*	1 50 *s*	1 44 *s*
15	1 85 *dd*	1 94 *dd*	1 82 *dd*	1 85 *dd*	2 07 *dd*
OAng	6 05 *qq*	6 13 *qq*	6 05 *qq*	6 02 *qq*	6 15 *qq*
	1 91 *dq*	1 95 *dq*	1 91 *dq*	1 90 *dq*	1 98 *dq*
	1 75 *dq*	1 81 *dq*	1 74 *dq*	1 73 *dq*	1 82 *dq*

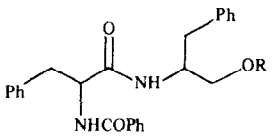
† OMe 3 40 *s*

‡ H-11 2 61 *dq*

J [Hz] 5,15 = 6,15 = 18,20 = 19,20 = 1 5, 18,19 = 7, compound **1** 5,6 = 6,7 = 3 5, 7,8 = 6 5, 8,9 = 11, 8,9′ = 5, 9,9′ = 14 5, compound **2** 2,2′ = 19 5, 5,6 = 6 5, 7,8 = 2, 7,13 = 2 5, 7,13′ = 2 2, 8,9 = 3 5, 8,9′ = 4, 9,9′ = 17, compound **3** 5,6 = 6,7 ~ 4; 7,8 = 8,9′ = 4 5, 7,13 = 2 7, 7,13′ = 2 4, 8,9 = 11, 9,9′ = 14 5, compound **4** 1,2 = 5.5, 5,6 = 2, 6,7 = 4, 7,8 = 8,9 = 4 5, 7,13 = 2 5, 7,13′ = 2 2, 8,9′ = 11, compound **8** 5,6 = 2 5, 6,7 = 2, 7,8 = 6, 7,11 = 8 5, 8,9 = 5, 8 9′ = 3, 9 9′ = 15, 11 13 = 8



12 Δ^6 **13** $\Delta^{7(19)}$, 6-oxo



14 R = Ac **15** R = COPh

12Ac and **13**Ac are the corresponding tetraacetates

(15%) and H-9β (3%); H-15 and H-6 (3%), H-1, H-5 (5%) and H-9α (2%); H-8 and H-7 (6%)]. A corresponding 8β-tigloyloxy derivative with a 14α-methyl group has been isolated from a *Picrademiopsis* species [9]. The ^{1}H NMR data of both compounds were, despite the differences due to different ester groups, almost identical, thus the stereochemistry of tiglate should be revised though the authors stated that no NOE were observed between H-14 and H-6 Perhaps this lactone also has a 14β-methyl group as the ^{1}H NMR data are almost identical The ^{1}H NMR data of

Table 2 ^{1}H NMR spectral data of compounds **9**–**11** (400 MHz, $CDCl_3$, δ-values)

H	9†	10	11‡
1	2 95 *br d*		2 23 *dddd*
5	3 20 *ddq*	3 41 *br d*	2 50 *dd*
6	4 67 *dd*	4 01 *dd*	4 33 *dd*
7	3 14 *dddd*	3 15 *dddd*	4 08 *dddd*
8	5 79 *ddd*	5 76 *ddd*	5 66 *ddd*
9	2 34 *dd*	2 92 *dd*	2 43 *ddd*
9′	2 08 *br dd*	2 76 *br d*	1 64 *dd*
13	6 36 *d*	6 25 *d*	6 27 *d*
13′	5 65 *d*	5 54 *d*	5 45 *d*
14	1 19 *br s*	2 39 *s*	1 29 *s*
15	2 25 *d*	2 23 *d*	1 66 *s*
OAng	6 09 *qq*	6 10 *qq*	6 05 *qq*
	1 95 *dq*	1 89 *dq*	1 92 *dq*
	1 78 *dq*	1 75 *dq*	1 79 *dq*

† 3-OH 5 46 *br s*, 10-OH 4 93 *br s*, ‡ H-2 2 09 and 1 51 *dd*, H-3 3 35 *br s*

J [Hz] Compound **9** 1,5 = 6 5, 5,6 = 11, 5,15 = 1 5, 6,7 = 9 5, 7,8 = 2, 7,13 = 3 3, 7,13′ = 3, 8,9 = 4, 8,9′ = 3 5, 9,9′ = 15 5, 9′,14 ~ 0 5, compound **10** 5,6 = 6,7 = 10; 5,15 = 1 3, 7,8 = 8,9′ = 1 5, 7,13 = 3, 7,13′ = 2 7, 8,9 = 6 5, 9,9′ = 15, compound **11** 1,2 = 6 5 1,2′ = 11, 1,5 = 7 5, 1,9 = 1 3, 2,2′ = 13 5, 5,6 = 11, 6,7 = 9, 7,8 = 4, 7,13 = 3 5, 7,13′ = 3, 8,9 = 8,9′ = 8 5, 9,9′ = 15, OAng 3′,4′ = 7, 3′,5′ = 4′,5′ = 1 5

10 (Table 2) differed from that of **9** by the absence of a H-1 signal. The downfield shift of H-5 and H-14 indicated the presence of a 1(10)-double bond. Accordingly, the data were similar to those of the corresponding isobutyrate [7].

The ^{1}H NMR spectrum of **11** (Table 2) indicated the presence of a guaianolide related to estafiatin [10] where the exomethylene at C-10 was replaced by a hydroxy and a methyl group. Furthermore, again a 8β-angeloyloxy residue had to be proposed. The stereochemistry was deduced from the NOE's [H-14 with H-1 (7%) and H-2α (7%) as well as H-15 (δ1.66) with H-3 (7%). The seven ring conformation followed from the *W*-coupling between H-1 and H-9α requiring a 10β methyl. A related lactone with changed configuration at C-8 was isolated from an *Eremanthus* species [11]

The structures of the diterpenes **12** and **13**, which were isolated as their tetraacetates (**12**Ac and **13**Ac), were established by ^{1}H and ^{13}C NMR spectroscopy (Table 3). In the spectrum of **12**Ac the signals of two olefinic methyls and four acetoxymethylenes were visible. The relative position of these groups could be determined by spin decoupling and the NOE's. Effects were observed between H-1 and H-4, H-18 and H-9; H-16 and H-14; H-17 and H-13; as well as between H-19 and H-5. These effects indicated the presence of a geranyl nerol derivative with oxygen functions at C-16, C-18 and C-20. A related compound with a hydroxy group at C-17 has been isolated from a *Cronquistianthus* species [12]. A further one with an additional oxygen function at C-19 is also known [13] The ^{13}C NMR spectrum of **12**Ac agreed with the proposed structure.

The ^{1}H and ^{13}C NMR spectra of **13**Ac (Table 3) clearly showed that this diterpene was a tetraacetate where one

Table 3 ^{1}H NMR and ^{13}C NMR spectral data of compounds **12**Ac and **13**Ac ($CDCl_3$, δ-values)

H	**12***Ac*	**13***Ac*	C	**12***Ac*†	**13***Ac*‡
1	4 63 *d*	4 67 *d*	1	61 9	61.8
2	5 62 *br t*	5 65 *br t*	2	122 3	123 7
4	2 15 *m*	2 44 *t*	3	135 7	133.9
5		2 82 *t*	4	28 6	23 0
6	5 11 *br t*	-	5	26 3	36 0
8	2 15 *m*	2.32 *br t*	6	123.4	200 0
9		2 21 *m*	7	133 2	147 7
10	5 39 *br t*	5 40 *br t*	8	39 6	31 0
12	2 15 *m*	2 15 *m*	9	26 9	26 6
13			10	130 4	124 7
14	5 44 *br t*	5 43 *br t*	11	139.5	138 4
16	4 44 *br s*	5.45 *br s*	12	34 6	34 6
17	1 65 *d*	1 65 *d*	13	26.5	26 4
18	4 59 *br s*	4 58 *br s*	14	129.0	128 9
19	1 59 *d*	6.01 *br s*	15	130.4	130.5
		5 76 *br s*	16	70 2	70 3
20	4 53 *d*	4 53 *br s*	17	14.0	14 0
OAc	2 09 *s*	2 08 *s*	18	60 5	60.4
	2.07 *s*	2 07 *s*	19	16 0	130 2
	2 06 *s*	2 06 *s* (6H)	20	67 0	66 9
	2 055 *s*				

†OAc 171 1, 171 0, 170 9, 170.7, 2 × 21 0, 2 × 20.9

‡OAc 171 04; 171 00, 170.85, 170 63, 21.01, 20.98; 20 96; 20.93

J [Hz] 1,2 = 5,6 = 9,10 = 13,14 ~ 7, 2,20 = 6,19 = 4,17 ~ 1.

olefinic methyl was replaced by a methylene group. Furthermore, the presence of a keto group followed from the ^{13}C signal at δ200.0 and the triplet at δ2.82 in the ^{1}H NMR spectrum. Spin decoupling indicated that the keto group was at C-6 and the NOE's showed that the double bonds had the same configuration as in **12**Ac and that the acetoxy groups were at C-1, C-16, C-18 and C-20 (effects between H-1 and H-4; H-18 and H-9; H-20 and H-2; H-16, H-14 and H-17; H-4, H-1 and H-20). The roots gave only *ent*-kaurenic acid

The chemistry of this species again showed that the genus can be characterized by the occurrence of heliangolides with a 3,10-oxygen bridge and by diterpenes of the kaurane and geranyl nerol type. The isolated guaianolides are most likely less characteristic as they have been reported only from a few species. The placement of the genus in the subtribe Helianthinae [14, 15] is supported by the chemistry as such compounds are also reported from many other genera of this subtribe.

EXPERIMENTAL

The MeOH–Et_2O–petrol (1:1.1) extract of the aerial parts (886 g, collected in February 1988 in Llano Grande de Cartago, Costa Rica, voucher 103516, deposited in the Herbarium of the University of Costa Rica) was first separated by CC and further by TLC and HPLC as reported previously [16]. The first CC fraction (Et_2O–petrol, 1 9 to 1:1) gave 480 mg *ent*-kaurenic acid The next ones with Et_2O and Et_2O–MeOH (9 1) were separated again by medium pressure chromatography (MPCC) (silica gel, ϕ30–60μ) affording 1 6 g **6** and mixtures Parts of it were separated by TLC and HPLC (always RP 8, flow rate, 3 ml/min). The most polar fraction (MeOH–Et_2O, 1 1) was first acetylated (Ac_2O, DMAP, $CHCl_3$) and then also separated by HPLC (MeOH–H_2O, 17.3) Finally (calculated from the parts which were separated, conditions in parenthesis, HPl MeOH–H_2O 7 3, HP2 3.1, HP3 4 1, HP4 13 7, HP5 3 2, HP6 17 3) 258 mg leptocarpin, 9.3 mg **1** (HPl, R_t 13.5 min), 165 mg **2** (HP3, R_t 4 1 min), 1 7 mg **3** (HP2, R_t 10 4 min), 4 6 mg **4** (HP5, R_t 4 3 min), 86 mg **5** (HP4, R_t 7 4 min), 1 6 g **6**, 7 1 g **7**, 1 9 mg **8** (TLC, Et_2O–petrol, 1 1, 5×, R_f 0 66), 439 mg **9** (HP3, R_t 4.1 min), 2.5 mg **10** (TLC, Et_2O–petrol, 5×, R_f 0.59), 11 6 mg **11** (HP4, R_t 10 0 min), 320 mg **12**Ac (HP6, R_t 7 7 min), 400 mg **13**Ac (HP6, R_t 6.2 min), 22 mg **14** and 2 5 mg **15** were isolated The roots (200 g) gave only *ent*-kaurenic acid (30 mg) Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material

1-*Desoxyniveusin A* (**1**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1}· 3600 (OH), 1775 (γ-lactone), 1710 (C=CCO$_2$R), MS *m/z* (rel. int.). 362 174 [M]$^+$ (5) (calc for $C_{20}H_{26}O_6$: 362 173), 344 [M $-H_2O$]$^+$ (1 5), 262 [M $-RCO_2H$]$^+$ (4), 83 [RCO]$^+$ (100).

1-*Oxo*-1-*desoxyniveusin A* (**2**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1} 3600 (OH), 1770 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel int). 376.152 [M]$^+$ (1.2) (calc. for $C_{20}H_{24}O_7$· 376.152), 358 (0 3), 276 (2), 83 (100), $[\alpha]_D^{24°}$ −67 ($CHCl_3$, c 0.15)

1β-*Methoxy*-1-*desoxyniveusin A* (**3**) Colourless gum; IR $\nu_{max}^{CHCl_3}$, cm^{-1}. 3600 (OH), 1770 (γ-lactone), 1715 (C=CCO$_2$R), MS *m/z* (rel. int). 392.184 [M]$^+$ (5 5) (calc for $C_{21}H_{28}O_7$ 392 183), 374 (1), 292 (2 5), 83 (100).

2β-*Hydroxy*-1-*desoxyniveusin A* (**4**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1} 3600 (OH), 1770 (γ-lactone), 1720 (C=CCO$_2$R); MS *m/z* (rel. int.). 378.168 [M]$^+$ (calc for $C_{20}H_{26}O_7$ 378 168), 360 (0 5), 278 (0.7), 260 (3), 83 (100), $[\alpha]_D^{24°}$ −24 ($CHCl_3$; *c* 0 17)

Desacylciliarin angelate (**8**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1} 1770 (γ-lactone), 1710 (C=CCO$_2$R), 1670 (C=CC=O), MS *m/z* (rel int) 360 157 $[M]^+$ (28) (calc. for $C_{20}H_{24}O_6$, 360.157), 260 (2), 83 (100); $[\alpha]_D^{24^\circ}$ +30 ($CHCl_3$, *c* 0.04)

3,10α-*Dihydroxy*-8β-*angeloyloxyarbiglovin* (**9**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1} 3500 (OH), 1785 (γ-lactone), 1720 (C=CCO$_2$R), 1660 (C=O), MS *m/z* (rel int) 376.153 $[M]^+$ (3) (calc for $C_{20}H_{24}O_7$ 376.152), 358 (3), 276 (6), 258 (11), 83 (100)

3-*Hydroxy*-8β-*angeloyloxy*-1,10-*dehydroarbiglovin* (**10**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1720 (C=CCO$_2$R), MS *m/z* (rel int) 358 142 $[M]^+$ (7), 258 (18), 83 (100), $[\alpha]_D^{24^\circ}$ −36 ($CHCl_3$, *c* 0.31)

10α-*Hydroxy*-8β-*angeloyloxy*-10,14-*dihydroestafiatin* (**11**) Colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1}: 3600 (OH), 1765 (γ-lactone), 1710 (C=CCO$_2$R), MS *m/z* (rel int). 362 173 $[M]^+$ (1) (calc for $C_{20}H_{26}O_6$ 362 174), 262 (3), 244 (5), 83 (100), $[\alpha]_D^{24^\circ}$ −14 ($CHCl_3$, *c* 0.1)

16,18,20-*Trihydroxygeranyl nerol* (**12**) Isolated as its tetraacetate **12**Ac; colourless gum; IR $\nu_{max}^{CHCl_3}$, cm^{-1} 1735 (OAc), MS *m/z* (rel int) 447 $[M-OAc]^+$ (0.7), 386.246 $[M-2\times HOAc]^+$ (4.5) (calc. for $C_{24}H_{34}O_4$ 386.245), 326 (7.5), 266 (11), 133 (86), 105 (100)

16,18,20-*Trihydroxy*-6-*oxo*-7,19-*dehydro*-6,7-*dihydrogeranyl nerol* (**13**) Isolated as its tetraacetate **13**Ac; colourless gum, IR $\nu_{max}^{CHCl_3}$, cm^{-1} 1740 (OAc), 1680 (C=CC=O), MS *m/z* (rel int) 400 226 $[M-2\times HOAc]^+$ (2) (calc for $C_{24}H_{32}O_5$, 400 225), 340 (7), 280 (5), 133 (48), 84 (100)

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