## EXPERIMENTAL

Fresh, wild growing aerial parts (3 kg) collected near Alexandria, Egypt, were extracted with $Et_2O$–petrol (1:2) and the resulting extract was first separated by CC ($SiO_2$) using petrol, $CHCl_3$ and $CHCl_3$–MeOH (20:1). The nonpolar fractions gave 400 mg lupeyl acetate, 600 mg lupeol, 50 mg sitosterol while the polar fractions ($CHCl_3$–MeOH) gave 15 mg sitosterol glucoside, 3 mg lactucin, 5 mg lactupicrin, 75 mg **1** and a mixture which by HPLC (Rp8, MeOH–$H_2O$, 1:1) gave 4 mg 11β,13-dihydrolactucin, $R_t$ 2.4 min) and 16 mg **2** ($R_t$ 3.4 min). Known compounds were identified by comparison with authentic materials (mp, mmp, co-TLC and $^1$H NMR).

*3β-Hydroxy-11β,13-dihydroacanthospermolide* (**1**). Colourless crystals, mp 197°; UV $\lambda_{max}^{MeOH}$ 230 nm; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600 (OH), 2730, 1690, 1630 (C=CCHO), 1770 (γ-lactone); MS *m/z* (rel. int.): 264.136 $[M]^+$ (10) $[C_{15}H_{20}O_4]^+$, 246 $[M-H_2O]^+$ (8), 235 $[M-CHO]^+$ (4.5), 218 $[246-CO]^+$ (20), 109 (100):

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-87 \quad -93 \quad -112 \quad -207} \quad (CHCl_3;\ c\ 0.6).$$

*3β-14-Dihydroxy-11β,13-dihydrocostunolide* (**2**). Colourless crystals, mp 110°; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3600 (OH), 1765 (γ-lactone); MS *m/z* (rel. int.): 266.152 $[M]^+$ (14) (calc. for $C_{15}H_{22}O_4$: 266.150), 248 $[M-H_2O]^+$ (32), 207 $[M-C_7H_5O]^+$ (100), 179 $[207-CO]^+$ (28); $[\alpha]_D^{24°} = +110$ (MeOH; *c* 0.1).

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# HELIANGOLIDES AND ACYCLIC DITERPENE FROM *VIGUIERA GILLIESII*

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**Key Word Index**—*Viguiera gilliesii*; Compositae; aerial parts; heliangolides; acyclic diterpene; structural determination.

**Abstract**—The aerial parts of *Viguiera gilliesii* afforded five heliangolides and one new acyclic diterpene, (*E*,*Z*,*Z*)-3,7,11-trihydroxymethyl-15-methyl-2,6,10,14-hexadecatetraen-1-ol. Structures were elucidated by spectroscopic methods and by comparison of the data with those of closely related compounds.

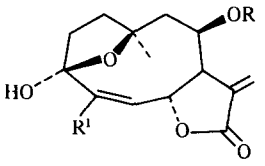
## INTRODUCTION

As part of a general phytochemical investigation of the native vegetation of the Cuyo Region (Argentina), we have studied *Viguiera gilliesii* Hook et Arn collected in Villavicencio (Mendoza). Reports on about 25 *Viguiera* species have appeared so far. Furanoheliangolides and heliangolides as well as diterpenes are characteristic constituents but germacradienolides have also been found.

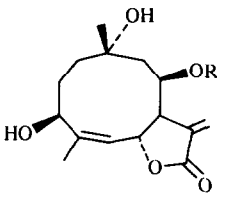
## RESULTS AND DISCUSSION

The aerial parts of *V. gilliesii* afforded a complex mixture of sesquiterpene lactones (**1a, b, 2a, b** and **3**) which could be separated only with difficulty, as well as the acyclic diterpene **4a**.

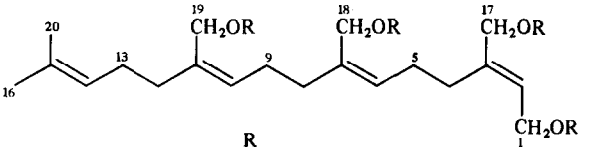
The major lactone, **2a**, colourless oil, $[\alpha]_D$ −77.9 showed a molecular ion at *m/z* 366, which agreed with formula $C_{20}H_{30}O_6$. Its IR spectrum suggested the presence of an α-methylene-γ-lactone, hydroxyl groups and



| | R | $R^1$ |
|---|---|---|
| **1a** | 2-Mebut | Me |
| **1b** | Tigl | Me |
| **1c** | i-Bu | [2] |
| **3a** | 2-Mebut | $CH_2OH$ |
| **3b** | Ang | $CH_2OH$ [3] |



| | R |
|---|---|
| **2a** | 2-Mebut |
| **2b** | Tigl |
| **2c** | Ang [1] |



| | R |
|---|---|
| **4a** | H |
| **4b** | Ac |

an ester group. These functional groups were confirmed by the $^1$H NMR spectrum which was identical with that exhibited by the recently described heliangolide **2c** [1], except for the signals of the esterifying group, which indicated the presence of a 2-methyl butyrate residue. This was confirmed by the mass spectrum, *m/z* 281 $[M-C_5H_9O]^+$, 264 $[M-C_5H_{10}O_2]^+$, 85 $[C_5H_9O]^+$ and 57 $[C_4H_9]^+$ (100%) and by $^{13}$C NMR signals at $\delta$175.2, 40.9, 26.2, 11.3 and 16.4 due to C-16, C-17, C-18, C-19 and C-20 respectively.

Sesquiterpene lactone **2b** which differed from **2a** only in the nature of the acyl residue was separated from **2a** by reverse phase HPLC. The mass spectrum of **2b** exhibited an $[M]^+$ at *m/z* 364 and the typical fragments of tiglic or angelic ester at *m/z* 83 $[C_5H_7O]^+$ and 55 $[C_4H_7]^+$ (100%). That the ester was a tiglate was shown by the $^1$H HMR signal of its vinylic proton which appeared as a quartet at $\delta$6.66.

The less polar fractions of the extract contained what appeared to be a very small amount of an inseparable mixture of **1a** and **1b**. Authentic **1a** was prepared by oxidation of **2a** with Jones' reagent at low temperature. Its $^1$H and $^{13}$C NMR spectra (Table 1) were similar to those of the corresponding isobutyrate **1c** from *Tithonia diversifolia*.

Lactone **3a**, $C_{20}H_{28}O_7$, $[\alpha]_D$ −86.8, exhibited $^1$H and $^{13}$C NMR spectra superimposable on those of **3b** from *Helianthus niveus* [3], except for the signals due to the ester side chain at C-8, which were characteristic of a 2-methylbutyrate residue.

The most polar constituent (**4a**) was an oil whose IR spectrum exhibited hydroxyl absorption and bands

Table 1. $^{13}$C NMR data of compounds **1a**, **2a** and **3a** (20 MHz, $CDCl_3$, TMS as internal standard)

| C | 1a | 2a | 3a |
|---|---|---|---|
| 1 | 37.2 | 35.3 | 37.0 |
| 2 | 40.7 | 29.5 | 40.6 |
| 3 | 106.3 | 77.0 | 105.9 |
| 4 | 136.5 | 138.2 | 136.1 |
| 5 | 127.9 | 127.4 | 131.2 |
| 6 | 75.4 | 73.7 | 74.9 |
| 7 | 49.6 | 47.8 | 49.5 |
| 8 | 71.4 | 74.9 | 71.5 |
| 9 | 37.9 | 38.6 | 39.0 |
| 10 | 83.1 | 71.4 | 82.9 |
| 11 | 141.3 | 136.4 | 143.2 |
| 12 | 169.7 | 170.1 | 169.7 |
| 13 | 122.5 | 123.2 | 122.9 |
| 14 | 28.1 | 31.3 | 28.0 |
| 15 | 22.3 | 23.6 | 65.7 |
| 16 | 175.5 | 175.2 | 175.3 |
| 17 | 41.0 | 40.9 | 40.9 |
| 18 | 26.3 | 26.2 | 26.2 |
| 19 | 11.4 | 11.3 | 11.3 |
| 20 | 16.5 | 16.4 | 16.4 |

characteristic of trisubstituted double bonds. The structure of **4a** was established by conversion to a tetraacetate (**4b**) whose molecular formula $C_{28}H_{42}O_8$ was based on its mass spectrum (22 eV) ($M^+$ at *m/z* 506), number of signals in its $^{13}$C NMR spectrum (Table 2) and integration of its

Table 2. $^{13}$C NMR data of compound **4b**

| C | δ |
|---|---|
| 1 | 60.0 |
| 2 | 122.7 |
| 3 | 138.6 |
| 4 | 28.3 |
| 14 | 123.6 |
| 15 | 131.3 |
| 16 | 25.3 |
| 17 | 66.7 |
| 20 | 17.3 |
| 5, 9, 13 | 26.5, 26.3, 26.1 |
| 8, 12 | 35.0, 34.9 |
| 7, 11 | 134.1, 133.9 |
| 6, 10 | 129.6, 129.4 |
| 18, 19 | 61.3, 61.5 |
| Me–C(=O)– | 20.5 |
| Me–C(=O)– | 170.54, 170.41<br>170.32, 170.10 |

$^1$H NMR spectrum. Compared with the $^1$H NMR spectrum of **4a**, which had two vinyl methyl singlets at $\delta$1.56 and 1.63, a $D_2O$ exchangeable hydroxyl at $\delta$3.56 and a broad eight-proton multiplet at $\delta$3.83–4.23 assignable to four allylic hydroxymethylene groups as well as a three proton vinyl multiplet at $\delta$5.20 and a broadened one-proton vinyl triplet at $\delta$5.56, the $^1$H NMR spectrum of **4b** exhibited an intense acetate frequency at $\delta$2.00 and the expected paramagnetic shift ($\Delta\delta$0.43) of the hydroxymethylene signals. The vinyl resonances of **4b** were resolved into two broadened triplets at $\delta$5.49 (1H), 4.59 (1H) and a two proton multiplet centred at $\delta$5.30. Spin decoupling showed that the broadened triplet at $\delta$4.95 was allylically coupled with two olefinic methyls. The stereochemistry of the 2,3-double bond was presumed from the shift differences of the signal for H-2 in the $^1$H NMR spectrum of **4a** and **4b** [4] and the chemical shifts of C-4 and C-17 in the $^{13}$C NMR spectrum of **4b** [5]. On the basis of these observations, **4a** was identified as (*E*,*Z*,*Z*)-3,7,11-trihydroxymethyl-15-methyl-2,6,10,14-hexadecatetraen-1-ol.

## EXPERIMENTAL

$^1$H NMR: 60 MHz, $CDCl_3$, TMS as internal standard; $^{13}$C NMR: 20 MHz, $CDCl_3$, TMS as standard; MS: 70 eV, direct inlet; CC: silica gel; TLC: silica gel, $C_6H_6$–dioxane–HOAc (45:5:1, 90:25:4 and 90:25:6).

*Plant material. Viguiera gilliesii* was collected in Villavicencio (Mendoza, Argentine) and identified by José A. Ambrosetti (Vouche MERL 32495, IADIZA, Mendoza).

*Extraction and isolation.* The aerial parts (3 kg) were air-dried, finely ground and extracted at room temp. with MeOH (3 times × 24 hr). The crude extract obtained by evapd at red. pres. was dissolved in MeOH containing $H_2O$ (10, 20 and 30%) then partitioned between *n*-hexane, $CCl_4$ and $CHCl_3$, respectively. The $CHCl_3$ extract (67 g) was adsorbed on silica gel packed in $C_6H_6$ and eluted with $C_6H_6$–EtOAc mixtures of increasing polarity.

Fractions 2–6 ($C_6H_6$–EtOAc, 19:1) were combined, to give 0.027 g of a gummy mixture of **1a** and **1b** which was identical in all respects (TLC, IR, $^1$H NMR, MS) with one prepared by oxidation of naturally occuring **2a**–**2b** with Jones' reagent.

Fractions 7–10 ($C_6H_6$–EtOAc, 9:1) provided a gummy residue (8.7 g) which by successive chromatography over deactivated $Al_2O_3$, afforded 5.9 g **2a** as a gum; $[\alpha]_D$ −77.9° ($CHCl_3$; *c* 1.3); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3500–3400, 1735, 1765, 1650; $^1$H NMR ($CDCl_3$): $\delta$0.93 (3H, *t*, *J* = 7 Hz, H-19), 0.98 (3H, *d*, *J* = 7 Hz, H-20), 1.25 (3H, *s*, H-14), 1.66 (3H, *s* (*br*), H-15), 3.33 (1H, *m*, $W_{1/2}$ = 4.5 Hz, H-7), 4.35 (1H, *t*, H-3), 5.00–5.75 (2H, H-5 and H-8), 5.68 (1H, *d*, *J* = 3 Hz, H-13'), 6.23 (1H, *d*, *J* = 2.5 Hz, H-13), 6.05–6.35 (1H, H-6, buried under H-13); MS *m/z* (rel. int.): 366 [M]$^+$ (2), 348 [M − 18]$^+$ (1), 281 [M − 85]$^+$ (3), 264 [M − 120]$^+$ (6), 246 [M − 120 − 18]$^+$ (7), 231 [M − 120 − 18 − 15]$^+$ (6), 228 [M − 120 − 18 − 18]$^+$ (9), 213 [M − 102 − 18 − 18 − 15]$^+$ (13), 85 (43), 57 (100).

*Conversion of* **2a** *to* **1a**. Compound **2a** (105 mg) was dissolved in $Me_2CO$ (5 ml) and Jones' reagent added. The mixture was stirred at 0° for 2 min, then worked up in the usual way. The reaction mixture was chromatographed over silica gel to give 80 mg **1a**, as a colourless oil; $[\alpha]_D$ −98.7 ($CHCl_3$; *c* 1.1); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3500–3400, 1735, 1768, 1648; $^1$H NMR ($CDCl_3$): $\delta$0.93 (3H, *t*, *J* = 7 Hz, H-19), 0.98 (3H, *d*, *J* = 7 Hz, H-20), 1.46 (3H, *s*, H-14), 1.84 (3H, *s* (*br*), H-15), 4.08 (1H, *m*, $W_{1/2}$ = 4.5 Hz, H-7), 5.01–5.85 (3H, H-5 and 8), 5.56 (1H, *d*, *J* = 2.5 Hz, H-13'), 6.28 (1H, *d*, *J* = 3 Hz, H-13), 6.20–6.45 (1H, H-6, buried under H-13); MS *m/z* (rel. int.): 364 [M]$^+$ (1), 346 [M − 18]$^+$ (3), 279 [M − 85]$^+$ (4), 262 [M − 102]$^+$ (25), 244 [M − 120 − 18]$^+$ (14), 229 [M − 102 − 18 − 15]$^+$ (5), 85 (32), 57 (100).

Fractions 11–13 ($C_6H_6$–EtOAc, 17:3) (2.1 g) contained two substances, **2a** and **2b**, which 0.35 g were separated by HPLC (Altex Ultrasphere-ODS, 5 $\mu$m, 250 × 10 mm, $H_2O$–MeOH, 1:1) furnished 0.25 g **2b**, as gum; IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3500–3400, 1712, 1765, 1650; $^1$H NMR ($CDCl_3$): $\delta$1.25 (3H, *s*, H-14), 1.66 (3H, *s*, H-15), 3.33 (1H, *m*, $W_{1/2}$ = 4.5 Hz, H-7), 4.35 (1H, *t*, H-3), 5.00–5.75 (2H, H-5 and 8), 5.68 (1H, *d*, *J* = 3 Hz, H-13'), 6.23 (1H, *d*, *J* = 2.5 Hz, H-13), 6.15–6.35 (1H, H-6, buried under H-13), 6.66 (1H, *q*, H-18); MS *m/z* (rel. int.): 364 [M]$^+$ (4), 346 [M − 18]$^+$ (3), 281 [M − 83]$^+$ (2), 264 [M − 100]$^+$ (7), 246 [M − 100 − 18]$^+$ (10), 231 [M − 100 − 18 − 15]$^+$ (8), 228 [M − 100 − 18 − 18]$^+$ (15), 213 [M − 100 − 18 − 18 − 15]$^+$ (16), 85 (52), 55 (100).

Fractions 15–19 ($C_6H_6$–EtOAc, 3:1) (0.62 g) were rechromatographed over deactivated $Al_2O_3$ to give 0.37 g **3a** as a gum; $[\alpha]_D$ −86.8° ($CHCl_3$; *c* 1.4); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3500–3400, 1732, 1758, 1655; $^1$H NMR ($CDCl_3$): $\delta$0.92 (3H, *t*, *J* = 7 Hz, H-19), 0.98 (3H, *d*, *J* = 7 Hz, H-20), 1.50 (3H, *s*, H-14), 4.15 (2H, *s* (*br*), H-15), 4.05–4.25 (1H, H-7, buried under H-15), 5.30–5.60 (2H, H-6 and H-8), 5.65 (1H, *d*, *J* = 2 Hz, H-13'), 5.85 (1H, *d*, *J* = 4 Hz, H-5), 6.30 (1H, *d*, *J* = 3 Hz, H-13); MS *m/z* (rel. int.): 380 [M]$^+$ (1), 362 [M − 18]$^+$ (2), 278 [M − 102]$^+$ (5), 260 [M − 102 − 18]$^+$ (18), 242 [M − 120 − 18 − 18]$^+$ (15), 85 (48), 57 (100).

Fractions 25–28 ($C_6H_6$–EtOAc, 2:3), provided a gummy residue (3.80 g) of crude **4a**, which was chromatographed over deactivated $Al_2O_3$ to afford a gummy substance (2.15 g); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3400–3300, 1660, 850.

*Acetylation of* **4a**. A soln of 0.32 g **4a** in 1 ml $C_5H_5N$ and 3 ml $Ac_2O$ was left for 18 hr at room temp. Work up in the usual way afforded 0.31 g **4b**, as an oil; IR $\nu_{max}^{KBr}$ cm$^{-1}$: 1740, 1660, 1240, 850; MS (22 eV) *m/z* (rel. int.): 506 [M]$^+$ (< 0.5), 463 [M − 43]$^+$ (< 0.5), 403 [M − 60]$^+$ (< 0.5), 386 (2), 343 (3), 326 (5), 283 (7), 266 (10), 223 (15), 197 (14), 169 (25), 157 (22), 146 (20), 135 (30), 132 (31), 93 (60), 69 (75), 43 (100).

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