

SESQUITERPENE LACTONES OF *HELIANTHUS GRACILENTUS*

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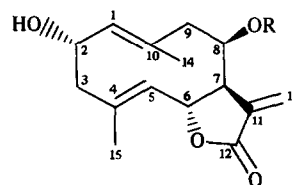
Abstract—A series of four 2 α -hydroxy-8 β -acyloxygermacrolides and the heliangolide niveusin A were isolated from a dichloromethane extract of *Helianthus gracilentus*. The germacrolides include a new compound, 2 α -hydroxy-8 β -isovaleroyloxycostunolide. The terpenoid constituents of *H. gracilentus* are very similar to those of *H. pumilus*, which on morphological grounds is considered to be closely related to *H. gracilentus*.

As part of our continuing biochemical systematic investigation of *Helianthus* (Asteraceae) [1–6], we have studied the terpenoid constituents of *H. gracilentus* A. Gray, a perennial species native to coastal portions of central and southern California. Species of *Helianthus* have proved to be rich sources of sesquiterpene lactones, with germacrolides [*trans,trans*-1(10),4(5)-germacradienolides] and heliangolides [*trans,cis*-1(10),4(5)-germacradienolides] being the principal structural types reported [6]. In this paper, we discuss the isolation and identification of five sesquiterpene lactones from *H. gracilentus*. These consist of a series of four germacrolides differing only in their ester side chains (1–4) [1, 7, 8] and the heliangolide niveusin A (5) [3]. Compound 1 has not been previously reported.

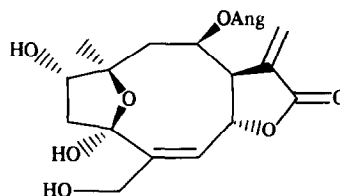
The mass spectrum of 1 gave a molecular ion at m/z 348, consistent with a molecular formula of $C_{20}H_{28}O_5$. The 1H NMR and ^{13}C NMR spectra of 1 showed that this compound differed from compounds 2–4 only in the nature of its five carbon ester side chain (Tables 1 and 2, data for 2 presented for comparison). All spectral data were in accord with an isovalerate side chain. The mass spectrum (m/z 85, base peak, $[C_5H_9O]^+$, side chain acylium ion) showed that, except for the carbonyl group, the side chain was fully saturated. The 1H NMR spectrum exhibited two methyl doublets at δ 0.96 and 0.93 (both $J = 6$ Hz) coupled to a one-proton multiplet at δ 2.1, which was in turn coupled to a two-proton signal at δ 2.17 [cf 9, 10]. Appropriate resonances for an isovaleroyl moiety were also found in the ^{13}C NMR spectrum (171.9s, 43.4t, 25.6d, 22.4q, 22.4q) [cf 10, 11]. Thus compound 1 was the isovalerate analogue of the known germacrolides 2–4. Extensive 1H NMR spin-decoupling experiments confirmed the structure of 1. Sesquiterpene lactones with isovalerate side chains are somewhat unusual in *Helianthus* species [6].

Helianthus gracilentus has been placed in section *Ciliates*, a group of six perennial species of sunflowers native to the western United States and northern Mexico [12, 13]. Sesquiterpene lactones have been isolated from

two other species of this section, *H. ciliaris*, which yielded a furanoheliangolide [14], and *H. pumilus*, which afforded a heliangolide and seven germacrolides including 2–4 [7]. On morphological grounds, *Helianthus pumilus* is believed to be the species most closely related to *H. gracilentus* [12]. The available sesquiterpene lactone data are consistent with this proposal, but also suggest possible affinities between these two species and a number of other sunflowers placed in section *Divaricati* series *Corona-solis* (*H. decapetalus*, *H. divaricatus*, *H. maximiliani*, *H. mollis*, *H. resinosus* and *H. salicifolius*). Like *H. gracilentus* and



- 1 R = *i*-Val*
- 2 R = Ang
- 3 R = 2'S,3'S-Epoxyang
- 4 R = Sar



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**i*Val = isovalerate
 Ang = angelate
 2'S,3'S-Epoxyang = 2'S,3'S-epoxyangelate
 Sar = sarracinate

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Table 1 ^1H NMR data for compounds 1 and 2*

	1	2
H-1	5.05 <i>br d</i>	5.05
H-2	4.76 <i>dt</i>	4.76
H-3a	2.74 <i>dd</i>	2.74
H-3b	2.11 <i>t</i>	2.11
H-5	5.00 <i>br d</i>	5.00
H-6	5.12 <i>dd</i>	5.11
H-7	2.95 <i>m</i>	2.95
H-8	5.78 <i>br dd</i>	5.81
H-9a	2.78 <i>dd</i>	2.87
H-9b	2.32 <i>dd</i>	2.35
H-13a	6.34 <i>d</i>	6.32
H-13b	5.61 <i>d</i>	5.63
H-14	1.54 (3H) <i>br s</i>	1.54 (3H)
H-15	1.78 (3H) <i>br s</i>	1.80 (3H)
H-2'	2.17 (2H) <i>m</i>	—
H-3'	2.1†	6.13 <i>dq</i>
H-4'	0.92 (3H) <i>d</i>	1.99 (3H) <i>br d</i>
H-5'	0.93 (3H) <i>d</i>	1.87 (3H) <i>br s</i>

*Run at 200 MHz in CDCl_3 with TMS as an internal standard. Multiplicities for 2 were the same as those for 1 except, as noted, for the side chain protons. Coupling constants for 1, J (Hz): 1, 2 = 10, 1, 14 = 1.5, 2, 3a = 5.5, 2, 3b = 10; 3a, 3b = 10, 5, 6 = 10.5, 5, 15 = 1.5, 6, 7 = 8.5, 7, 8 = 2, 7, 13a = 3.5, 7, 13b = 3, 8, 9a = 6, 8, 9b = 3, 9a, 9b = 14, 3', 4' = 3', 5' = 6. Coupling constants for 2 are similar, except for the side chain protons 3', 4' = 7.5, 3', 5' = 1.5, 4', 5' = 1.5.

†Partially obscured by overlapping signals.

Table 2 ^{13}C NMR data for compounds 1 and 2*

	1	2
C-1	134.2 <i>d</i>	134.2 <i>d</i>
C-2	69.3 <i>d</i>	69.3 <i>d</i>
C-3	48.8 <i>t</i>	48.9 <i>t</i>
C-4	142.8 <i>s</i>	142.8 <i>s</i>
C-5	129.5 <i>d</i>	129.5 <i>d</i>
C-6	75.4 <i>d</i>	75.7 <i>d</i>
C-7	53.1 <i>d</i>	53.3 <i>d</i>
C-8	71.0 <i>d</i>	71.1 <i>d</i>
C-9	44.2 <i>t</i>	44.1 <i>t</i>
C-10	135.3 <i>s</i>	135.3 <i>s</i>
C-11	136.7 <i>s</i>	136.7 <i>s</i>
C-12	169.6 <i>s</i>	169.6 <i>s</i>
C-13	121.4 <i>t</i>	121.4 <i>t</i>
C-14	20.0 <i>q</i>	19.8 <i>q</i>
C-15	18.7 <i>q</i>	18.7 <i>q</i>
C-1'	171.9 <i>s</i>	166.6 <i>s</i>
C-2'	43.4 <i>t</i>	126.8 <i>s</i>
C-3'	25.6 <i>d</i>	140.3 <i>d</i>
C-4'	22.4 <i>q</i>	20.6 <i>q</i>
C-5'	22.4 <i>q</i>	15.9 <i>q</i>

*Run at 22.6 MHz in CDCl_3 with TMS as an internal standard. Assignments made using off-resonance decoupling experiments and model compounds [1, 7, 11, 18].

H. pumilus, these species also produce 2 α -hydroxy-8 β -acyloxygermacrolides [1, 15, Pearce, J, Gershenzon, J and Mabry, T J, unpublished results, Stewart, E, Gershenzon, J and Mabry, T J, submitted for publication]. Other species of *Helianthus* are currently under investigation.

EXPERIMENTAL

Leaves of *H. gracilentus* were collected at two sites in southern California (Los Angeles Co., 6 miles northeast of Glendora in San Dimas Experimental Station on road to Tanbark Station, October, 1982, Susanne Goode *s n*, and Orange Co., Silverado Canyon, 9 July 1982, Kevin Nixon *s n*, vouchers on deposit at the Herbarium of the University of Texas). Material from both collections had identical TLC patterns and was therefore combined (2.63 kg) and washed with CH_2Cl_2 . The resulting extract was worked up by standard procedures to give 32.7 g of crude syrup [16].

The crude syrup was chromatographed on a silica gel column (1.5 kg) eluted with CH_2Cl_2 . Twenty-seven fractions of 500 ml each were collected. Fractions 17–18 (2.04 g) showed a major spot on TLC and were combined. Repeated prep TLC (silica gel, 1 mm, Et_2O –petrol, 8:1, developed $\times 2$) gave a mixture of 1 and 2. This mixture was purified by passage through a Sephadex LH-20 column, eluted with CH_2Cl_2 –hexane–MeOH (5:4:1), to give 15 mg of 1 still contaminated with a small amount of 2 and 27 mg of 2. Fractions 22 and 23 were allowed to stand in CH_2Cl_2 – Et_2O soln giving 30 mg of crystals of 3 (mollisorin B), mp 163–164° (lit 165–166° [1]). Induced crystallization of fraction 24 (10.5 g) with CH_2Cl_2 – Et_2O mixture yielded 4.65 g crystalline 4 (desacetyl-eupasserin), mp 134–135° (lit 134–135° [1, 17]). Fraction 26 (0.51 g) was separated by prep TLC (CH_2Cl_2 –*iso*-PrOH, 10:1, developed $\times 2$) to give 25 mg of 5 (niveusin A), mp 127–129° (lit 127–128° [3]).

Compounds 2–5 were identified by comparison of their spectral data with those in the literature (2 [7], 3 [1, 7], 4 [8, 17, 18], 5 [3]) and with those of authentic specimens obtained from other species of *Helianthus* [1, 3].

2 α -Hydroxy-8 β -isovaleroyloxycostunolide (1) IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} 3350, 1761, 1735, 1659, 830. MS (probe) 70 eV, m/z (rel int): 348 [M]⁺ (1), 330 [$\text{M} - \text{H}_2\text{O}$]⁺ (1), 246 [$\text{M} - \text{C}_5\text{H}_9\text{O}_2$]⁺ (41). McLafferty rearrangement and cleavage of side chain, 228 [$246 - \text{H}_2\text{O}$]⁺ (17), 218 [$246 - \text{CO}$]⁺ (24), 202 [$246 - \text{CO}_2$]⁺ (39), 163 (74), 135 (69), 107 (49), 85 [$\text{C}_5\text{H}_9\text{O}$]⁺ (100) side chain acylium ion, 57 [$85 - \text{CO}$]⁺ (81).

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