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SESQUITERPENE LACTONES OF *HELIANTHUS GRACILENTUS*

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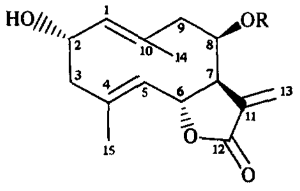
Key Word Index—*Helianthus gracilentus*, Asteraceae, sunflowers, sesquiterpene lactones, germacranolides, germacrolides, heliangolides, desacetyleupasserin, mollisorin B, niveusin A.

Abstract—A series of four 2α-hydroxy-8β-acyloxygermacrolides and the heliangolide niveusin A were isolated from a dichloromethane extract of *Helianthus gracilentus*. The germacrolides include a new compound, 2α-hydroxy-8β-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*.

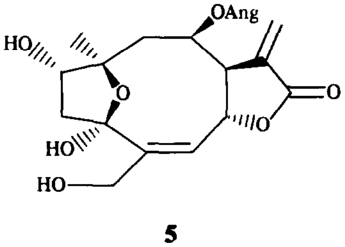
As part of our continuing biochemical systematic investigation of *Helianthus* (Asteraceae) [1–6], we have studied the terpenoid constituents of *H. gracilentus* A. Gray, a perennial species native to coastal portions of central and southern California. Species of *Helianthus* have proved to be rich 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 δ0.96 and 0.93 (both J = 6 Hz) coupled to a one-proton multiplet at *ca* 2.1, which was in turn coupled to a two-proton signal at δ2.17 [cf. 9, 10]. Appropriate resonances for an isovaleroyl moiety were also found in the ^{13}C NMR spectrum (171.9*s*, 43.4*t*, 25.6*d*, 22.4*q*, 22.4*q*) [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 *Ciliares*, 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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*iVal = isovalerate
Ang = angelate
2′*S*,3′*S*-Epoxyang = 2′*S*,3′*S*-epoxyangelate
Sar = sarracinate

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H pumilus, these species also produce 2α-hydroxy-8β-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

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

	1	**2**
H-1	5 05 *br d*	5 05
H-2	4 76 *dt*	4 76
H-3a	2 74 *dd*	2 74
H-3b	2 11 *t*	2 11
H-5	5 00 *br d*	5 00
H-6	5 12 *dd*	5 11
H-7	2 95 *m*	2 95
H-8	5 78 *br dd*	5 81
H-9a	2 78 *dd*	2 87
H-9b	2 32 *dd*	2 35
H-13a	6 34 *d*	6 32
H-13b	5 61 *d*	5 63
H-14	1 54 (3H) *br s*	1 54 (3H)
H-15	1 78 (3H) *br s*	1 80 (3H)
H-2′	2 17 (2H) *m*	—
H-3′	2 1†	6 13 *dq*
H-4′	0 92 (3H) *d*	1 99 (3H) *br d*
H-5′	0 93 (3H) *d*	1 87 (3H) *br s*

*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 *d*	134 2 *d*
C-2	69 3 *d*	69 3 *d*
C-3	48 8 *t*	48 9 *t*
C-4	142 8 *s*	142 8 *s*
C-5	129 5 *d*	129 5 *d*
C-6	75 4 *d*	75 7 *d*
C-7	53 1 *d*	53 3 *d*
C-8	71 0 *d*	71 1 *d*
C-9	44 2 *t*	44 1 t
C-10	135 3 *s*	135 3 *s*
C-11	136 7 *s*	136 7 *s*
C-12	169 6 *s*	169 6 *s*
C-13	121 4 *t*	121 4 *t*
C-14	20 0 *q*	19 8 *q*
C-15	18 7 *q*	18 7 *q*
C-1′	171 9 *s*	166 6 *s*
C-2′	43 4 *t*	126 8 *s*
C-3′	25 6 *d*	140 3 *d*
C-4′	22 4 *q*	20 6 *q*
C-5′	22 4 *q*	15 9 *q*

*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]

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 × 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** (desacetyleupasserin), 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 × 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]

2α-Hydroxy-8β-isovaleroyloxycostunolide (**1**) IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3350, 1761, 1735, 1659, 830 MS (probe) 70 eV, *m/z* (rel int) 348 $[M]^+$ (1), 330 $[M-H_2O]^+$ (1), 246 $[M-C_5H_{10}O_2]^+$ (41) McLafferty rearrangement and cleavage of side chain, 228 $[246-H_2O]^+$ (17), 218 $[246-CO]^+$ (24), 202 $[246-CO_2]^+$ (39), 163 (74), 135 (69), 107 (49), 85 $[C_5H_9O]^+$ (100) side chain acylium ion, 57 $[85-CO]^+$ (81)

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