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FURANOHELIANGOLIDES FROM *VIGUIERA GREGGII*

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Key Word Index—*Viguiera greggii*; Asteraceae; sesquiterpene lactones; heliangolides; zexbrevin; zexbrevin B; 1,2-dehydrozexbrevin B; *Helianthus*.

Abstract—Three furanoheliangolide sesquiterpene lactones were isolated from *Viguiera greggii*, including a novel compound, 1,2-dehydrozexbrevin B, and the previously characterized zexbrevin and zexbrevin B. Structures were determined by spectral methods, chiefly ^{1}H and ^{13}C NMR. Based on present knowledge, there appear to be no major differences between the terpenoid chemistry of *Viguiera* and that of *Helianthus*, a genus believed to be very closely related to *Viguiera* on morphological grounds.

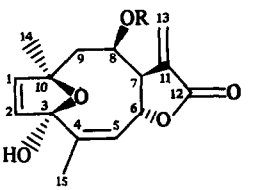
INTRODUCTION

As a part of our ongoing chemosystematic study of *Helianthus* (Asteraceae), we have begun to investigate the terpenoid chemistry of related genera to search for chemical differences which may serve to separate *Helianthus* from closely allied taxa. *Viguiera*, a New World genus of approximately 150 species [1, 2], is believed to be very closely related to *Helianthus* [1, 3]. Previous chemical investigations have reported the presence of sesquiterpene lactones and diterpenes in 18 species of *Viguiera* [4–15]. *Viguiera greggii* (Gray) Blake, a species native to northeastern Mexico, has been placed in series *Brevifoliae* of section *Chloracra*, subgenus *Calanticaria* [1]. No species of this series has been chemically studied yet. Here we report the isolation and structure determination of three furanoheliangolides from *V. greggii*: one new compound, 1,2-dehydrozexbrevin B, (**1**), and two previously identified compounds, zexbrevin (**6**) and zexbrevin B (**5**). In addition, we briefly compare the terpenoid chemistry of *Viguiera*, as it is presently known, with that of *Helianthus*.

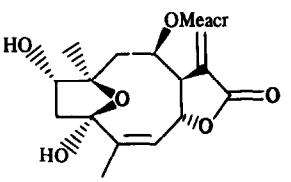
RESULTS AND DISCUSSION

Column chromatography and preparative TLC of the dichloromethane extract of the aerial parts of *V. greggii* led to the isolation of two constituents, **5** and **6**, in about 0.005% yield, and one very minor constituent, **1**, in about 0.0005% yield.

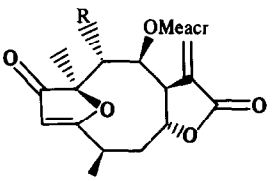
The mass spectrum of compound **1** showed a molecular ion peak at *m/z* 346, corresponding to a formula of $C_{19}H_{22}O_6$. Typical IR (1755 cm^{-1}) and ^{1}H NMR data (two narrowly-split doublets at δ 5.71 and 6.31) indicated the presence of an α-methylene-γ-lactone function. An additional IR absorbance at 1715 cm^{-1} and a strong MS fragment peak at *m/z* 69 (base peak) suggested that **1** had a four carbon, α,β-unsaturated ester side chain. A three-proton spin system in the ^{1}H NMR spectrum involving a methyl group at 1.90 (*d* (*br*), *J* = 1.5 Hz) and two olefinic protons at 5.60 (*dq*, *J* = 1.5, 1.5 Hz) and 6.04 (*d* (*br*), *J* = 1.5 Hz) and ^{13}C NMR signals at 166.1*s*, 135.7*s*, 126.9*t* and 18.1*q* established that this side chain was α-methylacrylate [e.g. 16]. The remainder of the ^{1}H NMR



1 R = Meacr*
2 R = Ac Sarrac
3 R = iBut
4 R = Epoxyang



5



6 R = H
7 R = OAc

* Meacr = α - methylacrylate
Ac Sarrac = acetylsarracinate (5' - OAc - angelate)
iBut = isobutyrate
Epoxyang = 2'R, 3'R - epoxyangelate

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data for 1 were very similar to those for liatrin (2) from *Liatris chapmanii* [17, 18], whose structure was proven by X-ray crystallography, tagitinin F(3) from *Tithonia tagitiflora* [19] and 1,2-dehydroniveusin C-2',3'-epoxide (4) from *Viguiera microphylla* [8] and showed that these compounds differed from 1 only in the nature of their side chain functions. Extensive ^{1}H NMR decoupling experiments and the similarity of the ^{13}C NMR spectrum of 1 to that of 4 helped confirm this structure.

Compound 5 was identified as zexbrevin B by comparison of its ^{1}H NMR, IR, UV, MS, mp and optical rotation with those of an authentic sample and with published data [20]. Since ^{13}C NMR and high field ^{1}H NMR data have not previously been reported for this compound, these are listed in Tables 1 and 2. Zexbrevin B was first isolated from *Zexmenia brevifolia* [20] and described as having a *trans* 4,5-double bond and an 8α-side chain. Later, it became clear that zexbrevin B was a heliangolide, based on the structural elucidation of woodhousin [21], and that its C-8 side chain had a β-orientation [22, 23].

Spectral and physical data for compound 6 showed that it was zexbrevin, first isolated also from *Z. brevifolia* [24]. This compound was also originally described as having an 8α-side chain and later corrected [22, 23]. A recent X-ray analysis of 9α-acetoxyzexbrevin (7) [25] suggested that the C-4 methyl group of zexbrevin should have a β-orientation, rather than α as originally proposed. ^{13}C NMR data are given here (Table 2) since they have only been previously reported from a mixture [16].

The sesquiterpene lactone chemistry of *V. greggii* fits in well with that of the genus as a whole as it is presently known. Heliangolides predominate in *Viguiera* (17 of 20 described sesquiterpene lactones) with at least one heliangolide having been found in each of the 13 species which have been shown to contain sesquiterpene lactones. Ten of the reported heliangolides are furanoheliangolides, possessing a 3,10 oxygen bridge. Although none of the three compounds isolated from *V. greggii* are identical to any previously isolated from *Viguiera* species, the epoxyangeloyl analogues of 1 and 5 have been recently reported from *V. microphylla* [8] which, along with *V. greggii*, is classed in section *Chloracra* [1].

Based on our present knowledge, there are no important differences between the terpenoid chemistries of *Viguiera* and *Helianthus* [26–34 and Gershenzon, J. and Mabry, T. J., unpublished results; see ref. 26 for earlier references]. The sesquiterpene lactones isolated from both genera are principally germacrolides or heliangolides with 12,6-*trans*-fused lactone rings and 8β-isobutyrate- or angelate-derived ester side chains. Identical sesquiterpene lactones are found in both *Helianthus* and *Viguiera*, including budlein A [7, 10, 14, 31], eriofloriin [7, 11, 30] and deacetylvigeustinin [9, 13, 30], and both genera share a number of compounds that differ only in the nature of their ester side chains.

There are small differences between *Viguiera* and *Helianthus* in the abundances of different structural types of sesquiterpene lactones. Most of the compounds isolated from *Viguiera* have been heliangolides, with some germacrolides having also been reported. *Helianthus*, however, has afforded a greater variety of skeletal types; germacrolides and heliangolides predominate, but several eudesmanolides [35] and guaianolides [Gershenzon, J. and Mabry, T. J., unpublished results] are also known.

Similar diterpene skeletons (labdane, kaurane and trachylobane) are also found in both genera [4–6, 26–28, 31, 34] and a few kaurane-type compounds are shared in common.

At this time, then, there are no major terpenoid

Table 1. ^{1}H NMR spectra of the sesquiterpene lactones of *V. greggii* (200 MHz, $CDCl_3$, TMS as int. standard)

H	1	5	6
1	5.81 *d* (5.5)*	4.64 *br dd* (3.5, 7.5)	
2	6.32 *d* (5.5)	(α) 2.37 *d*(*br*) (15) (β) 2.48 *dd* (3.5, 15)	5.56 *s*(*br*)
4			3.06 *dq*(*br*) (7, 7)
5	5.68 *dq* (7, 1.5)	5.63 *dq* (4, 1.5)	(α) 2.61 *ddd* (7, 8.5, 15) (β) 2.06 *d*(*br*) (15)
6	5.98 *dd*(*br*) (3, 7)	5.35 *ddq* (4, 4, 2)	4.48 *dd* (5, 8.5)
7	3.46 *ddd*(*br*) (2, 2.5, 3)	4.20 *dddd* (2, 2.5, 4, 4)	3.30 *ddd*(*br*) (3, 3, 5)
8	5.11 *t*(*br*) (3.5)	5.65†	5.17 *dd*(*br*) (2.5, 5)
9	2.38 (2H) *d* (3.5)	1.79† 2.00 *dd* (5, 14)	2.25 *dd* (2.5, 16) 2.71 *dd* (5, 16)
13a	6.31 *d* (2.5)	6.26 *d* (2.5)	6.36 *d* (3)
13b	5.71 *d* (2)	5.61 *d* (2)	5.70 *d* (3)
14	1.46 (3H) *s*	1.55 (3H) *s*	1.42 (3H) *s*
15	1.94 (3H) *br d* (1.5)	1.86 (3H) *dd* (1.5, 2)	1.39 (3H) *d* (7)
3'a	6.04 *d*(*br*) (1.5)	5.93 *d*(*br*) (1.5)	5.99 *d*(*br*) (1.5)
3'b	5.60 *dq* (1.5, 1.5)	5.52 *dq* (1.5, 1.5)	5.60 *dq* (1.5, 1.5)
4'	1.90 (3H) *d*(*br*) (1.5)	1.83 (3H) *d*(*br*) (1.5)	1.87 (3H) *d*(*br*) (1.5)
1-OH		3.13 *d* (7.5)	
3-OH	2.66 *s*(*br*)	3.64 *s*(*br*)	

*Values in parentheses are coupling constants in Hz.

†Signal obscured.

Table 2. ^{13}C NMR spectra of the sesquiterpene lactones of *V. greggii* (22.6 MHz, $CDCl_3$, TMS as int. standard)

C	1	5	6
1	130.5 *d*	77.8 *d*	205.4 *s*
2	139.2 *d*	44.8 *t*	103.2 *d*
3	108.3 *s*	106.7 *s*	192.4 *s*
4	140.4 *s*	140.1 *s*	31.5 *d*
5	127.7 *d*	128.9 *d*	41.2 *t*
6	74.9 *d*†	75.2 *d*	74.7 *d*
7	47.9 *d*	50.1 *d*	51.9 *d*
8	77.5 *d*†	72.4 *d*	74.7 *d*
9	43.6 *t*	39.5 *t*	43.3 *t*
10	86.9 *s*	86.6 *s*	88.5 *s*
11	139.1 *s*	136.1 *s*	139.6 *s*
12	170.1 *s*	170.0 *s*	168.7 *s*
13	124.5 *t*	123.1 *t*	123.4 *t*
14	31.0 *q*	22.0 *q*‡	22.9 *q*
15	20.7 *q*	22.2 *q*‡	16.1 *q*
1′	166.1 *s*	166.4 *s*	165.8 *s*
2′	135.7 *s*	135.6 *s*	135.3 *s*
3′	126.9 *t*	126.6 *t*	126.9 *t*
4′	18.1 *q*	18.1 *q*	18.1 *q*

*Assignments made using off-resonance decoupling experiments and by analogy with model compounds (1 and 5 [8], 6 [10]).

†,‡Assignments interchangeable.

characters which could be used to distinguish between these two genera. This supports the extremely close relationship between *Viguiera* and *Helianthus* that has been proposed on morphological grounds [1, 3]. More species in both genera, especially *Viguiera*, need to be chemically investigated to substantiate these conclusions.

EXPERIMENTAL

Aerial parts of *V. greggii* (3.68 kg) were collected in Nuevo Leon, Mexico on Highway 57, 2 miles south of the Coahuila border, by John Norris on 26 Aug 1981 (John Norris #73, voucher deposited in the Herbarium of the University of Texas at Austin). The plant material was air-dried and ground and then extracted with CH_2Cl_2 (3 × 7 l.) at room temp. and worked up in the usual manner [36] to give 62.4 g of brown gum. The gum was dissolved in a minimum amount of CH_2Cl_2–MeOH (24:1) and applied to a dry silica gel column (1 kg) developed with this same solvent mixture. After 5 l. of solvent had been passed through, the column was cut into 18 bands of equal thickness from which material was eluted with MeOH and analysed by TLC. The eluants from bands 8–10, numbering from the top of the column, were combined and separated with another silica gel column (460 g) eluted with CH_2Cl_2–MeOH (24:1). Five 500 ml fractions were collected. Fraction 3 gave 228 mg impure **5** which was recrystallized from EtOAc–*iso*-Pr_2O to give 130 mg colourless prisms. The eluant from band 15 was dissolved in warm Et_2O to give crystals of **6**. Recrystallizations from Et_2O–*iso*-PrOH gave 250 mg of pure **6**. The mother liquor was evaporated to give a brown syrup, which was separated on a silica gel column (250 g) eluted with CH_2Cl_2–MeOH (97:3). Twenty-one 50 ml fractions were collected. Fraction 17 was purified over a Sephadex LH-20 column, eluted with MeOH, and by repeated prep. TLC, developed with toluene–EtOAc (3:7) and heptane–*iso*-Pr_2O–MeOH (2:4:1), to give 20 mg of **1**, which on recrystallization from C_6H_6–hexane gave 17 mg colourless prisms.

1,2-Dehydrozexbrevin B (**1**). Mp 192–194°, UV λ_{max}^{EtOH} nm: 205 (4.28). IR ν_{max}^{Nujol} cm^{-1}: 3440 (OH), 1755 (lactone C=O), 1715 (side chain ester C=O), 1660, 1640, 1290, 1180, 1140, 1105, 1040, 1020, 980, 895; EIMS (probe) 70 eV, *m/z* (rel. int.): 346 [M] (1.5), 331 [M − Me]$^+$ (2.5), 329 [M − OH]$^+$ (12), 328 [M − H_2O] (2), 277 [M − C_4H_5O]$^+$ (14) α-cleavage of ester side chain, 261 [M − $C_4H_5O_2$]$^+$ (10) cleavage of side chain at ether oxygen, 260 [M − $C_4H_6O_2$]$^+$ (16) McLafferty rearrangement and cleavage of side chain, 242 [260 − H_2O]$^+$ (19), 217 (27), 69 [C_4H_5O]$^+$ (100) side chain acylium ion, 43 (71), 41 [69 − CO]$^+$ (62).

Zexbrevin B (**5**). Mp, ORD and IR very similar to literature [20]. MS not previously reported, (rel. int.). 364 [M]$^+$ (0.1), 346 [M − H_2O]$^+$ (2.7), 295 [M − C_4H_5O]$^+$ (3), 278 [M − $C_4H_6O_2$]$^+$ (9), 277 [295 − H_2O]$^+$ (16), 217 (20), 205 (52), 69 [C_4H_5O]$^+$ (100), 41 [69 − CO]$^+$ (80).

Zexbrevin (**6**). Mp, ORD and IR very similar to literature [24]. MS not previously reported, *m/z* (rel. int.): 346 [M]$^+$ (4), 318[M − CO]$^+$ (1), 302 [M − CO_2]$^+$ (4), 277 [M − C_4H_5O]$^+$ (2), 261 [M − $C_4H_5O_2$]$^+$ (10), 260 [M − $C_4H_6O_2$]$^+$ (36), 232 [260 − CO]$^+$ (19), 217 [232 − Me]$^+$ (13), 204 [232 − CO]$^+$ (17), 189 [232 − CO − Me]$^+$ (18), 125 (80), 69 [C_4H_5O]$^+$ (100), 41 [69 − CO]$^+$ (63).

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