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FURANOHELIANGOLIDES FROM *HELIANTHUS SCHWEINITZII*

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Abstract—The two furanoheliangolides budlein A and a new compound, $\Delta^{4,15}$-isoatriplicilide tiglate, were isolated from the hexaploid sunflower *Helianthus schweinitzii* Budlein A has been previously isolated from *H angustifolius*, a diploid species suggested as a possible progenitor of *H schweinitzii*

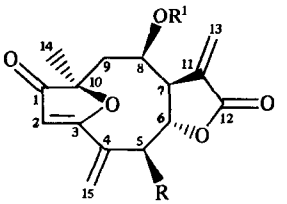
INTRODUCTION

As a part of a chemosystematic survey of *Helianthus* [1–6], we have studied the terpenoid chemistry of *H schweinitzii* T & G, a hexaploid perennial of section *Divaricati*, series *Corona-solis* [7], with a restricted range in the southeastern United States [8] *Helianthus* has proved to be a rich source of sesquiterpene lactones, with germacrolides and heliangolides being the most abundant skeletal types found (see ref [6] for citations to earlier work) In this paper, we report the isolation of two furanoheliangolides from a dichloromethane extract of *H schweinitzii*, budlein A (**4**) [9, 10] and a new $\Delta^{4,15}$ tiglate ester (**1**)

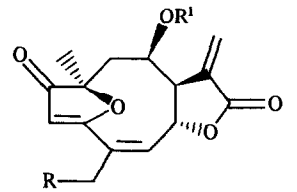
RESULTS AND DISCUSSION

Compound **1**, which had a molecular formula of $C_{20}H_{22}O_6$ from high resolution mass measurements of the molecular ion, possessed an α-methylene-γ-lactone (IR 1760 cm^{-1}, ^{13}C NMR δ168 1 *s*, ^1H NMR δ5 68 *d*, J = 3 Hz, 6 34 *d*, J = 3 5 Hz) The presence of a 2-dihydro-3-furanone ring (**A**), a feature common to other *Helianthus* heliangolides [4, 11–13], was clear from IR (1690, 1585 cm^{-1}), ^{13}C NMR (205 0 *s*, 103 5 *d*, 184 3 *s*) and ^1H NMR spectroscopy (δ5 71 *s*, downfield shift of H-7 to δ3 57) Other structural features included a second *exo*-methylene function (^{13}C NMR δ121 0 *t*, ^1H NMR δ5 62 *d* and 5 76 *d*, both J = 2 Hz), a methyl group adjacent to an oxygen atom (^1H NMR 1 48 (3H) *s*) and a tiglate ester (IR 1720 cm^{-1}, MS *m/z* 83 (100%), typical ^1H and ^{13}C NMR signals [14], see Table 1)

^1H NMR spin decoupling experiments located the signal for H-7 (δ3 57), which was coupled to complex signals at δ4 36 and 5 21, in addition to the two H-13 doublets The signal at 5 21 (*ddd*, J = 2, 3, 5 5 Hz) closely resembled the signal in budlein A assigned to H-8 (5 25 *ddd*, J = 2, 4, 6 Hz), which is that for the proton at the point of attachment of the ester side chain Irradiation at 5 21 in compound **1** simplified two methylene double doublets at 2 28 and 2 66 to an isolated AB pattern The signal at 4 36 was assigned to the proton at the site of lactone ring fusion Irradiation at 4 36 altered methylene signals at 2 93 and 3 11 The proton at 3 11 was spin-coupled to two *exo*-methylene doublets at 5 62 and 5 76 These results are summarized in partial structure **B**.



	R	R^1
1*	H	Tig †
2‡	OH	iVal
3‡	OH	Ang



	R	R^1
4	OH	Ang
5	H	Ang
6	H	iBut
7	H	2—Mebut
8	OH	iVal

*C-10 configuration in **1–8** is *R*

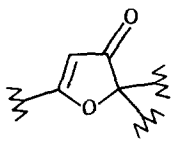
†Ang, angelate, iBut, isobutyrate, iVal, isovalerate, Tig, tiglate, 2-Mebut, 2-methylbutanoate

‡The 5-hydroxyl group of **2**, which was mistakenly depicted as α-oriented in ref [13], should actually be β-oriented because of the magnitude of $J_{5,6}$ (=9 Hz) (Dr W Herz, personal communication, concurs with this revision) Thus, compound **3**, whose structure was correlated with **2** [16], must also have a 5β-hydroxyl group, instead of a 5α-hydroxyl group as originally reported by Bohlmann *et al*

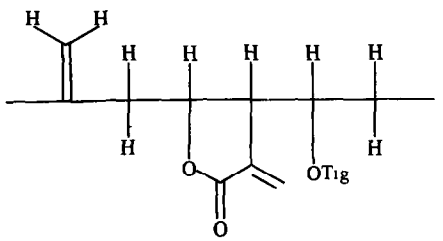
Table 1 ^{1}H NMR spectra of compounds 1–3 ($CDCl_3$, TMS as int standard)*

H	1 (200 MHz)	2 [13] (270 MHz)	3 [16] (400 MHz)
2	5 71 *s*	5 80	5 77
5α	3 11 *dddd* (2, 2, 9 5, 14 5)	4 79 *ddd* (1 5, 1 5, 9)	4 72 *ddd* (1 5, 1 5, 9)
5β	2 93 *br d* (1 5, 14 5)	—	—
6	4 36 *ddd* (1 5, 5 5, 9 5)	4 31 *dd* (5 5, 9)	4 27 *dd* (5 5, 9)
7	3 57 *dddd* (2, 3, 3 5, 5 5)	3 64 (3, 3, 3 5, 5 5)	3 69 (3, 3, 3 5, 5 5)
8	5 21 *ddd* (2, 3, 5 5)	5 18 (2, 3, 5 5)	5 18 (2 5, 3, 5)
9a	2 66 *dd* (5 5, 15 5)	2 62 (5 5, 15)	2 67 (5, 15)
9b	2 28 *dd* (3, 15 5)	2 23 (2, 15)	2 27 (2 5, 15)
13a	6 34 *d* (3 5)	6 35 (3 5)	6 42 (3 5)
13b	5 68 *d* (3)	5 73 (3)	5 74 (3)
14	1 48 (3H) s	1 43 (3H)	1 48 (3H)
15a	5 76 *d* (2)	6 13 (1 5)	6 12 (1 5)
15b	5 62 *d* (2)	5 93 (1 5)	5 92 (1 5)
3′	6 68 *qq* (1 5, 7)	—	—
4′	1 77 (3H) *dq* (7, 1 5)	—	—
5′	1 71 (3H) *br s* (1 5, 1 5)	—	—

*Numbers in parentheses are coupling constants in Hz. Multiplicities for **2** and **3** are similar to those of **1**, except as noted Data for **2** and **3** are from the lit refs indicated, except that, as mentioned in the footnotes to the structures, the configurations at C-5 have been revised Signals of the side chain protons in **2** and **3** have been omitted



A



B

Joining this spin system (**B**) to the dihydrofuranone moiety and attaching the methyl group to the furan ring gave the general formula **1** (without stereochemistry) assuming that the lactone ring was closed to C-6 with the side chain at C-8 as in budlein A (**4**) A UV absorption at 269 nm supported the extended conjugation of the furanone system [15] Compound **1**, therefore, appeared to be the 5-deoxy analogue of **2** [13] and **3** [16] with a C-8 tiglate side chain

The ^{1}H NMR spectrum of **1** closely corresponded to those of **2** and **3** (see Table 1) when allowance was made for the differences in the side chains and for the lack of a 5-hydroxyl group in **1** This correspondence helped confirm that formula **1** was correct and was taken as evidence that the stereochemistry of this compound was the same as that of **2** and **3** at C-6, C-7, C-8 and C-10 The data obtained for **1** were somewhat similar to those for the $\Delta^{4,15}$ sesquiterpene lactones of the goyazensolide series [17–19], which are dihydrofuranone-containing heliangolides with a 6α-side chain and the lactone ring closed to C-8 However, comparison of the ^{1}H NMR and ^{13}C NMR spectral data of **1** with those of compounds of the goyazensolide series revealed clear differences, particularly in the chemical shift of H-8 and the $J_{8,9}$ values, showing that **1** was not a member of this group

Furanoheliangolides, which are common constituents of many genera in the Asteraceae (e g *Calea*, *Eremanthus*, *Lychnophora*, *Viguiera* [20]), have also been reported from five other species of *Helianthus* *H angustifolius* (**4**) [4], *H ciliaris* (**6**) [11], *H grosseserratus* (**2**, **8**) [13], *H lehmannii* (**7**) [12] (now placed in the genus *Helianthopsis* [21]) and *H nuttallii* subsp *nuttallii* (**5**) [Lee, E, Gershenzon, J and Mabry, T J, unpublished results] *Helianthus grosseserratus*, *H nuttallii* and *H schweinitzii* are all members of series *Corona-solis* [7]

Four diploid species of *Helianthus* have been suggested as possible progenitors of the hexaploid *H schweinitzii* [8] Two of these have been previously chemically investigated *H giganteus*, from which no sesquiterpene lactones were reported [22],* and *H angustifolius*, which, like *H schweinitzii*, was shown to contain budlein A [4] Thus, *H schweinitzii* may have originated from a hybridization event involving *H angustifolius* Interestingly, data on the distribution of flavonoids in *Helianthus* provide

*Sesquiterpene lactones have recently been reported from *H giganteus* See Melek, F R, Ahmed, A A, Gershenzon, J and Mabry, T J (1984) *Phytochemistry* **23**, 2573

additional support for this possibility *Helianthus schweinitzii* is the only species of series *Corona-solis* which produces hymenoxin [23] This unusual flavone, which has both 6- and 8-methoxylation, has also been isolated from *H angustifolius* [24]

EXPERIMENTAL

Leaves of *H schweinitzii* were collected at two sites in south-eastern North Carolina (Bladen Co NE of Lake Waccamaw post office- J G #58, #150, and Columbus Co SE of Chadbourn- J G #57, vouchers on deposit at the Herbarium of the University of Texas) and from plants transplanted from these two sites to the U S Dept of Agriculture research facility, Bushland, Texas (C E Rogers and T E Thompson, #849, #850) Material from all locations had identical TLC patterns and was combined (725 g) and washed with CH_2Cl_2 for 5 min Intact rather than ground leaves were extracted since, in many species of *Helianthus*, sesquiterpene lactones appear to be localized in surface glands [Kreitner, G, Gershenzon, J and Mabry, T J, unpublished results] and a rapid surface wash has been shown to give a greater absolute yield of sesquiterpene lactones and reduced amounts of other plant constituents than does an extraction of ground material The wash was worked up in the usual manner [25]

The resulting crude syrup (6 7 g) was separated on a silica gel column (150 g) eluted with a CH_2Cl_2–*iso*-PrOH gradient, initiated with 1% *iso*-PrOH Twenty-four fractions of 500 ml each were collected Fractions 2–3 (1% *iso*-PrOH) were purified by prep TLC (silica gel, 2 mm, CH_2Cl_2–*iso*-PrOH, 15 1) to give 80 mg of crystalline 1 Fractions 8–10 (2% *iso*-PrOH) were subjected to prep TLC (toluene–EtOAc, 1 1) to give 650 mg of **4** as an oil that, when triturated with *iso*-Pr_2O, gave 480 mg of powdery crystals A portion of these was recrystallized from *iso*-Pr_2O–Me_2CO to give 100 mg of colourless needles

$\Delta^{4\ 15}$-*Isoatriplicilide tiglate* (**1**) Mp 150° (dec), UV λ_{max}^{MeOH} nm (log ε) 215 (4 00), 268 (3 52), IR ν_{max}^{Nujol} cm^{-1} 1760 (lactone $\geq$C=O), 1720 (side chain $\geq$C=O), 1690 (unsaturated ketone), 1670, 1645, 1585 (RC=COR), 1250, 1205, 1140, 1110, 1070, 995, 965, 915, 885, 815, MS (probe) 70 eV, *m/z* (rel int) 358 $[M]^+$ (5) $C_{20}H_{22}O_6$ (HRMS 358 1414 found, 358 1416 calc), 314 $[M-CO_2]^+$ (1), 275 $[M-C_5H_7O]^+$ (1) α-cleavage of side chain, 259 $[M-C_5H_7O_2]^+$ (2) cleavage of side chain at ether oxygen, 213 (3), 171 (4), 149 (8), 129 (8) 97 (16), 83 $[C_5H_7O]^+$ (100) side chain acylium ion, 69 (38), 55 $[83-CO]^+$ (73), ^{13}C NMR (22 6 MHz, $CDCl_3$, TMS as int standard) 205 0 (*s*, C-1), 103 5 (*d*, C-2), 184 3 (*s*, C-3), 136 3 (*s*, C-4), 41 9 (*t*, C-5), 77 5 (*d*, C-6), 51 3 (*d*, C-7), 73 9 (*d*, C-8), 43 3 (*t*, C-9), 88 6 (*s*, C-10), 139 4 (*s*, C-11), 168 1 (*s*, C-12), 122 1 (*t*, C-13), 22 2 (*q*, C-14), 121 0 (*t*, C-15), 166 2 (*s*, C-1′), 127 4 (*s*, C-2′), 139 0 (*d*, C-3′), 14 4 (*q*, C-4′), 11 7 (*q*, C-5′) Interchangeable assignments C-4 and C-11, C-13 and C-15 Assignments made using off-resonance decoupling experiments and model compounds [13, 15, 17] Assignments for C-5, C-6, C-8 and C-9 made by single-frequency off-resonance decoupling experiments

Budlein A (**4**) Mp 110–112° (*iso*-Pr_2O–Me_2CO) (lit 106–108° from same solvent [9], see also ref [4]) Spectral data were very similar to those in the literature [4, 9] and identical to those obtained from an authentic specimen

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