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HELIANGOLIDES FROM *HELIANTHUS MAXIMILIANI**

WERNER HERZ and NARENDRA KUMAR

Department of Chemistry, The Florida State University, Tallahassee, FL 32306, U.S.A.

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Key Word Index—*Helianthus maximiliani*; Compositae; Heliantheae; sesquiterpene lactones; heliangolides.

Abstract—The isolation is reported of tifruticin, acetyltifruticin, deoxytifruticin, acetyldeoxytifruticin, an orizabin analog and three heliangolides from *Helianthus maximiliani*.

INTRODUCTION

Several *Helianthus* species have yielded either heliangolides [1–6] or *trans,trans*-germacranolides [7, 8]. We now report the isolation of a group of closely related heliangolides **1a** (tifruticin), **1b**, **2a** (dexoytifruticin), **2b**, **4a**, **7a**, **7c** and **9** from *Helianthus maximiliani* Schrader [9].

RESULTS AND DISCUSSION

Compounds **1a**, **1b**, **2a** and **2b** were identified by comparison with the lactones tifruticin and deoxytifruticin previously isolated from *Tithonia fruticosa* and the acetates prepared from them [10]. The C-8 stereochemistry originally assigned to these substances has been revised to that shown in the formulae on the basis of later work on tirotundin [11], woodhousin [12] and the tagitinins [13]. This was confirmed by oxidation of **2a** to **3a** [10] whose ^{1}H NMR spectrum was indistinguishable from that of tagitinin C (**3b**) [13] except for the signals of the ester side chain.

Lactone **4a**, mp 125–126°, $C_{20}H_{26}O_7$, also was an angelic acid ester (MS and ^{1}H NMR spectrum) and a heliangolide as evidenced by the values of $J_{7,13}$ (Table 1) and the usual coupling between H-15, on the one hand, and H-5 and H-6 on the other. The sequence C-4 through C-9 was established by spin-decoupling in the usual manner (Table 1) and the presence of a hemiacetal linkage involving C-3 and C-10 was suggested by the paramagnetic chemical shifts of H-7 and H-14 as well as the ^{13}C NMR spectrum (Table 2). The remaining oxygen atom required by the empirical formula was shown to be a C-1 hydroxyl group by oxidation *cum* dehydration, in the manner previously observed for similar substances [13,14], to a dienone **5a** analogous to **5b**† and **5c** which occur in other *Helianthus* species [4–6]. An attempt to acetylate **4a** resulted in conversion to **3a**, thus establishing the stereochemistry at all centers except at C-1.

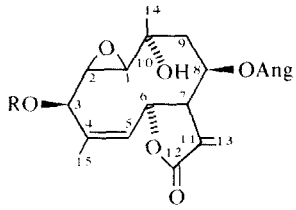
That the C-1 hydroxyl group of **4a** was α-orientated became apparent on comparing its ^{1}H NMR spectrum with the spectra of orizabin (**4b**) and zexbrevin B (**4c**)† on the one hand and zacatechinolide (**6**) [15] on the other. As expected on the basis of model considerations, the H-1 signals of **4a–c** are shifted upfield relative to H-1 of **6** by approximately 0.3 ppm, whereas the H-14 signals of **4a–c** are 0.1 ppm downfield with respect to H-14 of **6**. In addition, the β-oriented C-1 hydroxyl of **6** deshields *syn*-H-9β and *syn*-H-6 by *ca* 0.7 and 0.3 ppm, respectively. In the presence of Eu(FOD)$_3$, (0.05 mol) the H-1 signal of **4a** experienced a downfield shift of 0.14 ppm, in accordance with the proposed stereochemistry.

Lactones **7a**, mp 158–159°, $C_{20}H_{28}O_7$ and **7c**, mp 155–156°, $C_{20}H_{28}O_6$, were both angelate esters of heliangolides (MS and ^{1}H NMR spectrum) whose carbon sequence C-4 through C-9 was established by spin-decoupling in the usual fashion. Lactone **7a** formed a diacetate (**7b**) and **7c** a monoacetate (**7d**), each retaining a tertiary hydroxyl on the carbon atom carrying the remaining methyl group. Lactone **7a** formed an acetonide **7e** involving the tertiary hydroxyl, thus placing one secondary hydroxyl on C-1 and the second on C-3 since the two relevant protons were not spin-coupled to each other. This was confirmed by oxidation of **7e** to the α,β-unsaturated ketone acetonide **7f**; acid treatment of the latter resulted in conversion to **3a** thus establishing the configuration of **7a** at C-7, C-7, C-8 and C-10. Lactone **7c** gave no acetonide; comparison of the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) showed that its lone secondary hydroxyl group was located on C-3 and that its stereochemistry at all centers, as well as that of **7a** at C-3, was identical with that of **1a** and **2a**. The stereochemistry at C-1 shown for **7a** is one which should result in facile formation of an acetonide (models) and is the same as that of **4a**, eurecurvin (**8a**) [16], eupacunin (**8b**) [17] and their congeners.

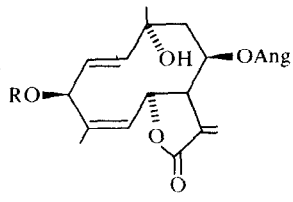
The remaining lactone constituent, mp 152–154°, $C_{20}H_{26}O_6$, appeared to possess formula **9** on the basis of the spectroscopic data, although the paramagnetic shift of the signal tentatively assigned to H-3 seemed unexpectedly large (see Table 3). Acetylation gave a monoacetate

* Work supported in part by a grant (CA-13121) from the U.S. Public Health Service through the National Cancer Institute.

† For comments on the structure and stereochemistry originally [14] assigned to these compounds see Herz, W. and Wahlberg, I. (1973) *J. Org. Chem.* **38**, 2485, and ref. [13]. The assignments for H-6 and H-8 made by the Mexican workers as the result of insufficient resolution at lower field strength seem to require correction.



1a R = H
1b R = Ac



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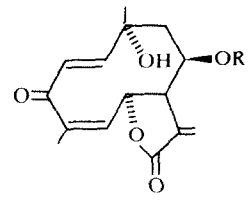
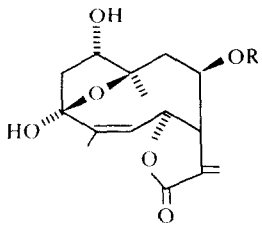
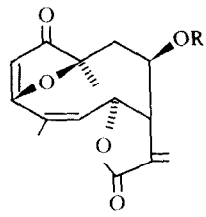


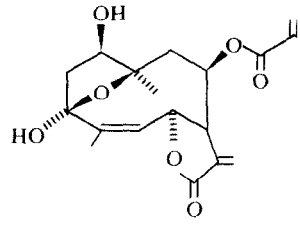
3a R = Ang
3b R = *i*-Bu



4a R = Ang
4b R = *i*-Bu
4c R = MeAcr



5a R = Ang
5b R = *i*-Bu
5c R = *i*-Val



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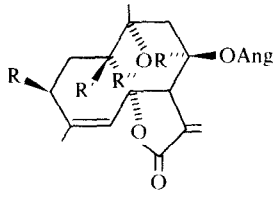
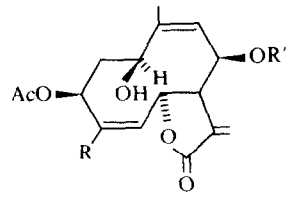
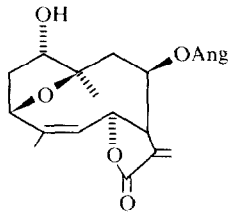


7a R, R′ = OH, R″, R‴ = H
7b R, R′ = OAc, R″, R‴ = H
7c R = OH, R′, R″, R‴ = H
7d R = OAc, R′, R″, R‴ = H
7e R = OH, R″ = H, R′, R‴ = –O(Me)(Me)
7f R = =O, R″ = H, R′, R‴ = –O(Me)(Me)



8a R = CH_2OH, R′ = 2-MeBu
8b R = Me, R′ = Ang



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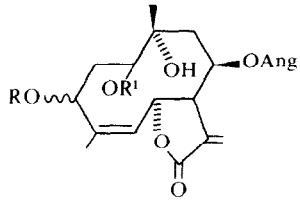
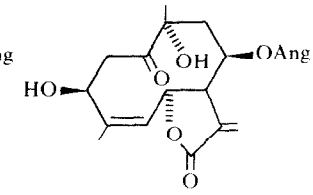


10a R = Ac, R′ = H
10b R = H, R′ = Ac
10c R, R′ = Ac



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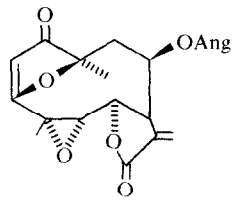

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Table 1. ^{1}H NMR spectra*

	4a	5a	7a	7a†	7b	7c	7c†	7d	7e	7f
H-1	4.02 *d* (4)	—	3.84 *t* (4)	4.33 *dd* (6,3)	5.25 *t* (4)	‡	‡	‡	4.07 *dd* (7,4.5)	4.23 *dd* (12,3)
H-2a	2.48 *dd* (15,4)	5.58	2.02§	2.49§	2.09§	‡	‡	‡	2.05§	3.24 *dd* (12,3)
H-2b	2.38 *d* (15)	—	2.02§	2.49§	2.09§	‡	‡	‡	2.05§	2.57 *dd* (13,12)
H-3	—	—	4.52 *t* (5.5)	4.81 *t* (4.5)	5.33 *t* (5.5)	4.38 *t* (5)	4.62 *t*	5.31 *t*	4.53 *t* (3)	—
H-5	5.62 *dq*§ (3,1.5)	5.93 *dq* (3.5,1)	5.49 *dq* (9,1.5)	5.52 *dq* (9,1)	5.55 *dq*§ (9,1.5)	5.45 *dq*	5.61 *dq*	5.49 *dq*	5.47 *dq*	5.68 *dq*
H-6	5.33 *tq*§ (3,1)	5.33 *tq* (3.5,1)	6.04 *dd* (9,4)	6.96 *dd* (9,3)	5.67 *dd* (9,4)	6.23 *dd* (9.5,4)	7.14 *dd*	5.75 *dd*	6.42 *dd*	5.20 *dd*
H-7	4.21 *m* (4.5,3,2.5,2)	3.68 *m* (3.5,3,2.5,2)	3.25 *dddd* (4,3,2.5,2)	3.62 *ddt* (2,1.8,3)	3.37 *m* (4,3,2.5,2)	3.37 *m*	3.82 *m*	3.39 *m*	3.28 *ddt* (2,1.8,3.5)	3.22§
H-8	5.65 *dt*§ (10.5,5)	5.26 *ddd* (5.5,3,2)	5.43 *ddd* (10.5,4.5,3)	6.22 *ddd*	5.55§	5.41 *ddd* (11,4.5,3)	6.20 *ddd*	5.54§	5.57 *dt* (11,3.5)	5.53 *dt* (10,4)
H-9a	1.99 *dd* (15,10.5)	2.52 *dd* (15,5.5)	2.81 *dd* (15,10.5)	3.47 *dd*	2.23 *dd*	2.82 *dd*	3.57 *dd*	2.35 *dd*	2.88 *dd* (15,11)	2.23 *dd*
H-9b	1.78 *dd*§ (15,3)	2.20 *dd* (15,3)	‡	2.23 *dd* (15,4.5)	‡	1.79§	2.28 *dd*	2.03 *dd*	2.05§	1.78§
H-13a	6.26 *d* (2.5)	6.34 *d* (3)	6.30 *d* (2.5)	6.39 *d* (2)	6.33 *d* (2.5)	6.39 *d*	6.40 *d* (2)	6.31 *d* (2.5)	6.29 *d* (2)	6.32 *d* (2.5)
H-13b	5.62 *d*§ (2)	5.68 *d* (2.5)	5.75 *d* (2)	5.71 *d* (1.8)	5.79 *d* (2)	5.75 *d*	5.71 *d* (1.8)	5.78 *d* (2)	5.68 *d* (1.8)	5.74 *d* (2)
H-14‖	1.57	1.47	1.25	1.56	1.28	1.30	1.53	1.29	1.22	1.29
H-15‖	1.87 *br.* (1.5,1)	2.06 *br.*	1.82 *d* (1.5)	1.77 *br.* (1)	1.85 *d* (1.5)	1.70	1.68 *br.*	1.80 *br.*§	1.74 *d* (1.5)	2.05 *br.*
H-3′	6.04 *dq* (7,1.5)	6.10	6.06 *dq*	5.85 *dq*	6.08 *dq*	6.03 *dq*	5.84 *dq*	6.09 *dq*	6.00 *dq*	6.07 *dq*
H-4′‖	1.92 *dq* (7,1.5)	1.92 *dq*	1.92 *dq*	1.96	1.95	1.90	1.97	1.95	1.94	1.90
H-5′‖	1.74 *q* (1.5)	1.78 *q*	1.77 *q*	1.81	1.78	1.74	1.84	1.80	1.72	1.78
Misc.					2.10‖ 2.08‖ (Ac)			2.11‖ (Ac)	1.42‖ 1.33‖	1.47‖ 1.38‖

* Run at 270 MHz in $CDCl_3$ unless indicated otherwise. Unmarked signals are singlets. Frequencies in ppm downfield from TMS as internal standard. Coupling constants (in parentheses) in hertz. Coupling constants are not given if they correspond to those in preceding column.

† In pyridine-d_5.

‡ Obscured.

§ Overlapping signals.

‖ Intensity of three protons.

10a or **10b** and a diacetate **10c** which were formed as the result of a remarkably facile ether cleavage which presumably involves acetolysis. Comparison of the chemical shifts and coupling constants of **10a** (or **10b**) and **10c** suggests that the preferred conformations of these substances differ.

Structure and stereochemistry of **9** were eventually established by oxidation (Jones reagent, low temperature) which resulted in formation of **4a**, **5a**, **11** and **12**, again as the result of ether cleavage. Isolation of **4a** demonstrates the α-orientation of the C-1 hydroxyl group of **9** which probably accounts for the chemical shift of H-3. In **11**, the ketone group is allocated to C-1 rather than to C-3 because C-3 ketones of this type show a preference for the hemiketal form; absence of the latter is indicated by the chemical shifts of H-7 and H-14 (Table 3). Moreover, 1-hydroxy-3-ketones easily undergo dehydration as indicated by the facile conversion of **7f** to **3a**. β-Orientation

Table 2. ^{13}C NMR spectra*

Carbon	4a	7a†	7b	7c	7e	9	10a	10c
1	77.32 *d*	79.15 *d*	73.80 *d*‡	35.62 *t*	75.81 *d*‖	7601 *d*‡	76.22 *d*‡	75.14 *d*‡
2	44.84 *t*	39.05 *t*	34.85 *t*	29.78 *t*	32.64 *t*	37.29 *t*	35.54 *t*	33.52 *t*
3	106.29	72.20 *d*‡	72.41 *d*‡	74.97 *d*‖	73.52 *d*‖	76.55 *d*	68.59 *d*	69.75 *d*
4	140.48	139.77	135.20	138.38	138.71	143.89	144.07	140.78
5	127.98 *d*	127.33 *d*	128.50 *d*	127.45 *d*	127.97 *d*	123.25 *d*	125.57 *d*	125.80 *d*
6	75.64 *d*	74.22 *d*‡	73.97 *d*‡	74.18 *d*‖	73.72 *d*‖	74.49 *d*‡	74.56 *d*‡	75.14 *d*‡
7	49.81 *d*	48.67 *d*	47.99 *d*	48.09 *d*	49.48 *d*	45.35 *d*	49.34 *d*	47.08 *d*
8	71.67 *d*	73.09 *d*‡	73.16 *d*‡	74.39 *d*‖	77.73 *d*‖	73.13 *d*‡	70.21 *d*‡	70.94 *d*‡
9	39.49 *t*	39.51 *t*	39.11 *t*	38.89 *t*	36.46 *t*	38.04 *t*	38.41 *t*	38.53 *t*
10	86.25	73.09	72.68	71.74	80.88	73.59	72.27	72.58
11	136.24	137.76	135.80	136.72	136.15	137.08	135.83	136.26
12	170.14	169.95	170.61	170.60	170.69	170.32	171.43	169.74
13	123.00 *t*	122.50 *t*	123.98 *t*	123.50 *t*	123.56 *t*	123.54 *t*	123.10 *t*	123.57 *t*
14	22.26 *q*‡	24.17 *q*§	24.78 *q*§	31.48 *q*	24.47 *q*‡	31.07 *q*§	27.73 *q*§	29.30 *q*§
15	21.89 *q*‡	24.04 *q*§	24.48 *q*§	23.87 *q*	23.41 *q*‡	21.52 *q*§	23.53 *q*§	22.52 *q*§
1′	166.48	166.41	166.50	167.14	166.30	166.74	166.79	166.63
2′	126.99	127.92	127.00	127.30	127.24	127.15	127.04	127.14
3′	139.34 *d*	138.06 *d*	139.85 *d*	139.30 *d*	139.06 *d*	139.56 *d*	140.09 *d*	139.64
4′	20.23 *q*	20.42 *q*	20.26 *q*	20.25 *q*	20.23 *q*	20.26 *q*	20.26 *q*	20.23 *q*
5′	15.66 *q*	15.63 *q*	15.74 *q*	15.68 *q*	15.62 *q*	15.71 *q*	15.73 *q*	15.68 *q*
1″			169.50		105.26		169.70	169.68
1‴			169.36					169.43
2″			21.02 *q*		28.32 *q*		21.16 *q*	20.97 *q*
			21.02 *q*		27.92 *q*			20.83 *q*

* Run in $CDCl_3$ at 67.9 MHz unless specified otherwise. Values are in ppm. Unmarked signals are singlets
† Run in pyridine-d_6.
‡, § Assignments may be interchanged.
‖ Assignments by single frequency off-resonance decoupling.

of the C-3 hydroxyl of **11**, i.e. retention during ether cleavage, is suggested by the strong deshielding of H-6. The stereochemistry pictured for the epoxide ring of **12** is predicated on approach of the reagent from the less hindered α-side.

The diacetates **7b** and **10c** differ in configuration at C-1 and/or C-3. To define the difference more precisely, selective oxidation (Jones reagent, low temperature) of **7a** was attempted, but yielded only **3a**, **5a** and **12**.

EXPERIMENTAL

Isolation of lactones. Aerial parts of *Helianthus maximiliani* Schrader, collected by Drs. N. C. Henderson and G. D. Anderson on 20 September 1975 along U.S. Rt. 50 *ca* 2 miles west of Waverley, Coffey County, Kansas (No. 75–106, voucher on deposit in herbarium of University of Missouri–Kansas City), wt 9.5 kg, were extracted with $CHCl_3$ and worked up in the usual fashion [18]. The crude gum, wt 100 g, was adsorbed on 130 g of Si gel (Mallinckrodt 100 mesh) and chromatographed over 1 kg Si gel packed in $CHCl_3$–toluene (1:1). The column was eluted with 500 ml fractions in the following order: fr. 1–4 $CHCl_3$–toluene (1:1), 5–10 $CHCl_3$, 11–18 $CHCl_3$–MeOH (99:1), 19–25 ($CHCl_3$–MeOH (97:3), 26–30 $CHCl_3$–MeOH (19:1), 31–36 $CHCl_3$–MeOH (23:2), 37–45 $CHCl_3$–MeOH (9:1).

Fractions 5–10 showed two spots on TLC which were separated by prep. TLC (EtOAc–hexane, 1:1, three developments). The upper band yielded 3 g of a colorless gum (**2b**), $[\alpha]_D$ − 36.6° (*c* 0.36, $CHCl_3$) which was identified by IR and ^1H NMR comparison with authentic material synthesized earlier [10] from **2a**. The lower band gave 5 g of tifruticin (**1a**), $[\alpha]_D$ − 111° (*c* 0.61, $CHCl_3$) which was identified by direct comparison with an authentic specimen [10].

Fractions 11–15 contained a major component (**7c**) which was recrystallized from $CHCl_3$–hexane, yield 0.45 g, mp 155–156°, $[\alpha]_D$ − 106° (*c* 0.29, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3490, 3440, 1760, 1740, 1650 and 1610; CD curve (MeOH) $[\theta]_{221}$ + 8900 (lactone Cotton effect weak or obscured). The high resolution MS did not show the molecular ion, but had prominent paks at *m/e* (rel. int.): 346 ($M^+ - H_2O$, $C_{20}H_{26}O_5$, 5.3), 265 ($C_{15}H_{21}O_4$, 6.8), 264 ($C_{15}H_{20}O_4$, 20.4), 247 ($C_{15}H_{19}O_3$, 69.7), 246 ($C_{15}H_{18}O_3$, 20.7) 229 ($C_{15}H_{17}O_2$, 100), 228 ($C_{15}H_{16}O_2$, 23.6), 201 ($C_{14}H_{17}O$, 52.3), 153 ($C_9H_{13}O_2$, 48.1), 135 ($C_9H_{11}O_2$, 36.5), 121 (C_8H_9O, 49.4) and 111 (C_9H_{11}, 40.4). The low resolution MS showed a weak peak for the molecular ion at *m/e* 364 ($C_{20}H_{28}O_6$) and strong peaks at *m/e* 99 ($C_5H_7O_2$) and 83 (C_5H_7O). Acetylation of 10 mg of **6c** (Ac_2O–pyridine overnight) gave 8 mg of **6d** which could not be induced to crystallize and had IR bands ($CHCl_3$) at 3460, 1760, 1735, 1720, 1650 and 1240 cm^{-1}.

Fractions 16–18 contained a major constituent (**2a**) which was purified by prep. TLC, yield 2.5 g, and could not be induced to crystallize. It was identified as dexoytifruticin by direct comparison with an authentic specimen [10].

Table 3. ^{1}H NMR spectra*

	9	9†	10a	10c	11	12
H-1	3.74 *dd* (5,3)	4.30 *dd* (6,2.5)	4.68 *dd*¶ (8.5,5)	4.98 *dd*¶ (5,2.5)	—	—
H-2a	2.2§	2.61 *dt* (15.5,5)	2.47 *ddd* (16,6.5,5)	2.43 *ddd*	3.25 *dd* (14,4)	5.62
H-2b	2.2§	2.50 *ddd* (15.5,6.2.5)	2.05 *ddd* (16,8.5.2)	‡	2.79 *dd* (14,7)	—
H-3	5.48 *m*§	5.31 *t* (5.5)	5.16 *dd*¶ (6.5,2)	6.16 *t*¶ (5)	4.56 *dd* (7,4)	—
H-5	5.37 *dd* (4,1.5)	5.54 *dq* (6,1.5)	5.44 *dq* (8,1.5)	5.45 *dq* (6,1.5)	5.20 *dq* (9,1)	3.15 *d* (7)
H-6	5.61 *dd* (4,3)	6.67 *ddbr.* (6,3.5,1)	6.24 *dd* (9,7)	5.62§	6.20 *dd* (9,1.5)	4.34 *dd* (7,4)
H-7	4.00 *ddt* (2,1.8,3.5)	4.54 *ddt*	3.25 *dddd*	3.79 *dddd*	2.55 *dddd* (5,2,1.5,1.5)	3.43 *m*
H-8	5.58 *ddd* (11,4.5,3)	6.26 *ddd*	5.76 *ddd* (8.5,6,3)	5.64 *ddd* (10.5,4.5,3)	5.29 *ddd* (10,5,3)	4.99 *ddbr.* (4.3,2.5)
H-9a	2.28 *dd* (15,11)	3.29 *dd*	2.37 *dd* (15.5)	2.23 *dd* (15,10.5)	2.98 *dd* (15,10)	2.50 *dd* (15.4.5)
H-9b	2.00 *dd* (15,4.5)	2.29 *dd*	2.02 *dd* (15.5,6)	2.11 *dd* (15,4.5)	2.25 *dd* (14,5)	2.20 *dd* (15,2.5)
H-13a	6.29 *d* (2)	6.34 *d*	6.30 *d* (2.6)	6.33 *d* (2.5)	6.21 *d* (2)	6.35 *d* (2.8)
H-13b	5.75 *d* (1.8)	5.60 *d*	5.73 *d* (2.3)	5.78 *d* (2)	5.64 *d* (1.5)	5.68 *d* (2.5)
H-14‖	1.43	1.63	1.31	1.31	1.35	1.40
H-15‖	1.84 *br.*	1.77§	1.80 *br.*	1.79 *br.*	1.67 *br.*	1.62 *br.*
H-3′	6.07 *dq*	5.86 *dq*	6.10 *dq*	6.10 *dq*	5.95 *dq*	6.04 *dq*
H-4′‖	1.96 *dd*	1.99 *dq*	1.95 *dq*	1.96 *dq*	1.84 *dq*	1.84 *dq*
H-5′‖	1.80 *q*	1.77 *q*	1.84 *q*	1.84 *q*	1.75 *q*	1.70 *q*
Misc.			2.10‖ (Ac)	2.11‖ 2.10‖ (Ac)		

* Conditions and symbols same as in Table 1.

¶ Assignments may be interchanged.

Fractions 19–25 contained two substances which were separated by prep. TLC (EtOAc–hexane, 3:2, double development). The upper band (**4a**) was crystallized from $CHCl_3$–hexane, yield 0.50 g, mp 125–126°, $[\alpha]_D$ – 148 (MeOH, *c* 0.28); IR ν_{max}^{KBr} cm^{-1}: 3400, 3200, 1765, 1720, 1650 and 1620. (Calc. for $C_{20}H_{26}O_7$: MW, 378.1678. Found: MW (MS), 378.1684, 27%). Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 360 ($C_{20}H_{24}O_6$, 25.5), 279 ($C_{15}H_{19}O_5$, 28.7), 278 ($C_{15}H_{18}O_5$, 37.8), 244 ($C_{15}H_{16}O_3$, 15.2), 243 ($C_{15}H_{15}O_3$, 44.8) and 242 ($C_{15}H_{14}O_3$, 15.9). The low resolution MS showed the base peak at *m/e* 83 (C_5H_7O). Oxidation of 50 mg of **4a** with Jones reagent at room temp. for 1 hr followed by the usual work-up gave 15 mg of **5a** as a gum which had IR bands at 1770, 1725, 1700, 1650 and 1592 cm^{-1}. Treatment of 50 mg of **4a** with Ac_2O–pyridine overnight followed by the usual work-up gave 15 mg of **3a** [10].

The lower band from fractions 19–25 was recrystallized from $CHCl_3$–hexane to give 0.5 g of **9**, mp 152–154°, $[\alpha]_D$ – 64.2 (MeOH, *c* 0.38); CD (MeOH) $[\theta]_{218}$ + 9900 (lactone Cotton effect weak or obscured); IR ν_{max}^{KBr} cm^{-1}: 3410, 1750, 1730, 1640 and 1620. (Calc. for $C_{20}H_{26}O_6$: C, 52.35; H, 5.64. Found: C, 52.69; H, 6.16%. Calc. for $C_{20}H_{26}O_6$: MW 362.1728. Found: MW (MS) 362.1774, 1%). Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 344 ($C_{20}H_{24}O_5$, 2.1), 281 ($C_{15}H_{20}O_5$, 13.6), 279 ($C_{15}H_{19}O_5$, 8.5), 263 ($C_{15}H_{19}O_4$, 45.2), 262 ($C_{15}H_{18}O_4$, 41), 245 ($C_{15}H_{17}O_3$, 43.19), 244 ($C_{15}H_{16}O_3$, 31.5), 219 ($C_{13}H_{15}O_3$, 47.8), 218 ($C_{13}H_{14}O_3$, 31.2), 216 ($C_{14}H_{16}O_2$, 22.4), 215 ($C_{14}H_{15}O_2$, 17.2), 202 ($C_{13}H_{14}O_2$, 31.3) and 201 ($C_{13}H_{13}O_2$, 45.2). The low resolution MS showed a strong peak at *m/e* 83 (C_5H_7O).

Fractions 26–30 contained a major constituent (**7a**) which was purified by thick-layer chromatography and recrystallized from $CHCl_3$–hexane, yield 5 g, mp 158–159°, $[\alpha]_D$ – 50.7 (MeOH, *c* 0.51), IR ν_{max}^{KBr} cm^{-1}: 3400, 3380, 1755, 1720, 1650 and 1620; CD curve $[\theta]_{224}$ + 8500 (lactone Cotton effect weak or obscured). The high resolution MS did not show the molecular ion but had significant peaks at *m/e* (rel. int.): 362 ($C_{20}H_{26}O_6$, 1.9), 281 ($C_{15}H_{21}O_5$, 28.2), 280 ($C_{15}H_{20}O_5$, 8.8), 263 ($C_{15}H_{19}O_4$, 21.7),

262 ($C_{15}H_{18}O_4$, 10.7), 245 ($C_{15}H_{17}O_3$, 33.5), 244 ($C_{15}H_{16}O_3$, 11.1), 227 ($C_{15}H_{15}O_2$, 14.5) 219 ($C_{13}H_{15}O_3$, 54.5), 218 ($C_{13}H_{14}O_3$, 23.0), 202 ($C_{13}H_{14}O_2$, 26.6), 201 ($C_{13}H_{13}O_2$, 38.9), 193 ($C_{11}H_{13}O_3$, 39.4), 179 ($C_{10}H_{11}O_3$, 28.4), 178 ($C_{10}H_{10}O_3$, 56.4), 175 ($C_{11}H_{11}O_2$, 56.7), 173 ($C_{12}H_{13}O$, 38.0), 167 ($C_9H_{11}O_3$, 37.5), 165 ($C_9H_9O_3$, 41.2), 163 ($C_{10}H_{11}O_2$), 149 ($C_9H_9O_2$, 64.2), 147 ($C_{10}H_{11}O$, 54.4), 137 ($C_8H_9O_2$, 100), 131 ($C_{10}H_{11}$, 54.5) and 121 (C_8H_9O). The low resolution MS showed a weak molecular ion at *m/e* 380 ($C_{20}H_{28}O_7$) and a strong peak at *m/e* 83 (C_5H_7O).

Reactions of **7a**. (a) Acetylation of 0.1 g of **7a** with Ac_2O–pyridine at room temp. overnight and crystallization of the product from $CHCl_3$–hexane gave 80 mg of **7b**, mp 188–189°, $[\alpha]_D$ – 107° ($CHCl_3$, *c* 0.31); IR ν_{max}^{KBr} cm^{-1}: 3470, 1750, 1740, 1725, 1650 and 1238; low resolution MS *m/e*: 464 ($C_{24}H_{32}O_9$, M^+), 446, 422, 404, 364, 344, 322, 304, 244, 226, 99 and 83. (b) A soln of 0.150 g of **7a** in 2 ml of dry Me_2CO was allowed to stand for 1 hr in the presence of dry $CuSO_4$, filtered and evapd at red. pres. Crystallization of the residue from $CHCl_3$–hexane gave 0.155 g of **7e**, mp 197–198°, $[\alpha]_D$ – 79° ($CHCl_3$, *c* 0.38); IR ν_{max}^{KBr} cm^{-1}: 3330, 1760, 1730, 1650, 1620 (sh), 1160, 1100, 1050 and 850; low resolution MS *m/e*: 420 ($C_{23}H_{32}O_7$, M^+), 405, 362, 344, 263, 262, 245, 244 and 83. Oxidation of 80 mg of **7e** with Jones reagent at 0° for 3 hr and crystallization of the product from $CHCl_3$–hexane gave 70 mg of **7f**, mp 132–133°, IR ν_{max}^{KBr} cm^{-1}: 1770, 1730, 1700, 1655, 1150, 1100, 1050 and 850. A soln of 25 mg of **7f** in 2 ml of Me_2CO was stirred with 0.5 ml of conc. HCl for 1 hr, neutralized with $NaHCO_3$, diluted with H_2O and extracted with Et_2O. Purification of the crude product by prep. TLC gave 10 mg of **3a**. (c) Oxidation of 100 mg of **7a** with Jones reagent at 0° for 2 hr in the manner described for **9** below gave a mixture of three products which were separated by prep. TLC. The upper band furnished 10 mg of **3a**. The middle band was identified as **5a** (5 mg) and the lowest band as **12** (see below, 5 mg) by direct comparison.

Reactions of **9**. (a) Acetylation of 0.2 g of **9** with Ac_2O–pyridine at 0° overnight followed by the usual work-up gave a mixture of two products which were separated by prep. TLC ($CHCl_3$–MeOH, 9:1). The upper band (**10c**) was non-crystalline, yield 90 mg; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1755, 1735, 1640 and 1250; low resolution MS *m/e*: 464 ($C_{24}H_{32}O_9$), 446, 422, 404, 362, 344, 322, 305, 304, 262, 244, 226, 99, 83. The lower band (**10a**) was recrystallized from $CHCl_3$–MeOH, yield 50 mg, mp 195–196°, IR ν_{max}^{KBr} cm^{-1}: 3460, 3320, 1755, 422 ($C_{22}H_{30}O_8$), 404, 362, 344, 305, 304, 262, 245, 244, 226, 99 and 83. Further acetylation of **10a** gave **10c**. (b) To a soln of 50 mg of **9** in 5 ml of Me_2CO kept at 0° was added, with stirring over a 15 min period, 0.5 ml of Jones reagent. The mixture was kept at 0° for 1 hr and worked-up in the usual fashion. TLC of the crude product gave three spots which were separated by preparative TLC (EtOAc–hexane, 1:1, three developments). The least polar band gave 3 mg of **5a**. The middle band was again found to be a mixture of two substaces which could be separated by prep. TLC ($CHCl_3$–MeOH, 49:4). The less polar component **11** (13 mg) could not be induced to crystallize; ^1H NMR spectrum in Table 3; MS *m/e*: 378 ($M^+ - H_2O$), 360 ($M^+ - H_2O$), 295 ($M^+ - C_5H_7O$), 279 ($M^+ - C_5H_7O_2$), 261, 244, 235, 217 and 83 (base peak). The more polar substance **12** (15 mg) was also a gum; ^1H NMR spectrum in Table 3; MS *m/e*: 374 (M^+), 331, 330, 99 ($C_5H_7O_2$) and 83 (C_5H_7O). The most polar band from the original chromatogram was recrystallized from $CHCl_3$–hexane, mp 124–126°, yield 3 mg, and was identical with **4a** from the plant.

REFERENCES

1. Iriuchinjima, S., Kuyama, S., Takahashi, N. and Tamura, S. (1966) *Agric. Biol. Chem. (Tokyo)* **30**, 511.
2. Morimoto, H., Sanno, Y. and Oshio, H. (1966) *Tetrahedron* **22**, 3173.
3. Nishikawa, M., Kamiya, K., Takabatake, A. and Oshio, H. (1966) *Tetrahedron* **22**, 3601.
4. Ortega, A., Romo de Vivar, A., Diaz, E. and Romo, J. (1970) *Rev. Latinoam. Quim.* **1**, 81.
5. Bjeldanes, L. F. and Geissman, T. A. (1970) *Phytochemistry* **11**, 327.
6. Bohlmann, F. and Dutta, L. N. (1979) *Phytochemistry* **18**, 676.
7. Herz, W. and De Groote, R. (1977) *Phytochemistry* **16**, 1307.
8. Ohno, N. and Mabry, T. J. (1979) *Phytochemistry*, **18**, 1003.
9. Heiser, C. B., Smith, D. M., Clevenger, S. B. and Martin, W. C. (1969) *Mem. Torrey Bot. Club* **22**, No. 2.
10. Herz, W. and Sharma, R. P. (1975) *J. Org. Chem.* **40**, 3118.
11. Herz, W. and Blount, J. F. (1978) *J. Org. Chem.* **43**, 1268.
12. Herz, W. and Blount, J. F. (1978) *J. Org. Chem.* **43**, 4887.
13. Baruah, N. C., Sharma, R. P., Madhusudanan, K. P., Thyagarajan, G., Herz, W. and Murari, R. (1979) *J. Org. Chem.* **44**, 1831.
14. Ortega, A., Guerrero, C., Romo de Vivar, A., Romo, J. and Palafox, A. (1971) *Rev. Latinoam. Quim.* **2**, 38.
15. Bohlmann, F. and Zdero, C. (1977) *Phytochemistry* **16**, 1065.
16. Herz, W., De Groote, R., Murari, R. and Blount, J. F. (1978) *J. Org. Chem.* **43**, 3559.
17. Kupchan, S. M., Maruyama, M., Hemingway, R. J., Hemingway, J. C., Shibuya, S., Fujita, T., Cradwick, P. T., Hardy, A. D. U. and Sim, G. A. (1971) *J. Am. Chem. Soc.* **93**, 4914.
18. Herz, W. and Högenauer, G. (1962) *J. Org. Chem.* **27**, 905.

NOTE ADDED IN PROOF

After acceptance of our manuscript, Ohno, N. and Mabry, T. J. [(1980) *Phytochemistry* **19**, 609] reported the isolation of a compound of mp 88–89° (niveusin C) from *Helianthus niveus* ssp. (A. Gray) Heiser to which they ascribed the same structure as our **7a**, mp 127–126°. The ^1H and ^{13}C NMR spectra reported for niveusin C were similar to those of **7a** except for the multiplicity of H-1 which was given as a triplet. Direct comparison established the identity of niveusin C and **7a**; in our hands a sample of niveusin C supplied by Professor Mabry melted at 119–120°.