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AN ELEMANOLIDE FROM *ZINNIA GRANDIFLORA*

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Key Word Index—*Zinnia grandiflora*; Compositae; Heliantheae; elemanolide; sesquiterpene lactone.

Abstract—*Zinnia grandiflora* afforded a new elemanolide with a δ-lactone ring.

INTRODUCTION

Elemanolides of type **1** or **2** where R represents a partially oxidized methyl group appear to be characteristic constituents of *Zinnia* species [1–4]. An exception is *Z. haageana* which has yielded a germacradienolide [5]. We now report isolation from *Z. grandiflora* Nutt. of a variant **3** with a δ-lactone ring.

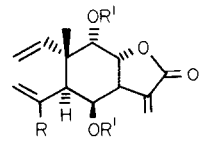
RESULTS AND DISCUSSION

Lactone **3**, $C_{21}H_{26}O_9$ (high-resolution MS), had acetate and α-hydroxyisobutyrate ester functions (loss of C_2H_2O and $C_4H_8O_3$ on electron impact, ^1H NMR methyl singlets at 2.12, 1.56 and 1.56 ppm., ^{13}C NMR signals at 1.69.98*s*, 20.81*q*—acetate, 175.68*s*, 72.21*s*, 27.34*q* and 27.06*q*—α-hydroxyisobutyrate). Signals of the protons on the epoxide ring (ABC system) and the α,β-unsaturated aldehyde function were essentially superimposable on those of zinaflorin III (**2a**) [4] as were the corresponding carbon signals (C–1 54.66*d*, C–2 43.88*t*, C–3 140.00*t*, C–15 193.15*d*). H–5 at 3.39 ppm (carbon doublet at 29.51 ppm) was vicinally coupled to H–6, a triplet at 4.93 ppm, which was in turn coupled to H–7 at 3.33 ppm (carbon doublet at 42.84 ppm); however, H–7 was only minimally coupled to H–13a, b ($J_{7,13} <$ 1 Hz), whereas $J_{7,13}$ of the zinaflorins and their analogs is 3 Hz or larger [1–4], and the frequencies of H–13a, b (6.79 or 6.71 and 5.91 ppm) were also different. Hence **3** differed from the zinaflorins in the type of lactone ring closure.

A priori the differences in the NMR spectra might be attributed to a *cis* rather than *trans* lactone ring closure toward C–8; however, presence of a γ-lactone seemed excluded by the IR spectrum of the new substance which exhibited a very strong carbonyl frequency at 1735 cm^{-1} in addition to the weaker α,β-unsaturated aldehyde band at 1695 cm^{-1}, but had no band in the 1750–1780 cm^{-1} region. Consequently, we postulated the presence of a δ-lactone closed to C–9.

In keeping with this deduction, H–7 was additionally coupled to two mutually coupled protons appearing at 4.61 and 5.45 ppm, the signal at lower field presumably representing the proton under the second ester function (H–8) and that at higher field the proton under the lactone (H–9). The existence of appreciable long-range coupling between H–7 and H–9 (2 Hz) and the magnitude of the other coupling constants ($J_{5,6} = 3.5$, $J_{6,7} = 3.5$, $J_{7,8} = 2.5$, $J_{8,9} = 2$ Hz) indicated the relative stereochemistry shown in formula **3** which puts H–7 and H–9 in a *W* relationship. The stereochemistry at C–1, as in other epoxides of this type, is unknown. The significant structural difference between **1** and **2** on the one hand and **3** on the other was underscored by the chemical shifts of C–5, C–10, C–11, C–12 and C–13 which were at 29.51*d*, 42.90, 130.99, 162.88 and 134.01*t* in **3**, but are found near 31, 40, 139, 169 and 119 ppm in the zinaflorins [4]. Chemical shifts of C–6, C–8 and C–9 (64.06*d*, 77.44*d* and 82.09*d*), the last two being identified by irradiation at the frequencies of the respective protons, also differed significantly from those in the zinaflorin series [4].

Several attempts at selective hydrolysis to ascertain the distribution of the two ester functions over C–6 and C–8 failed. Treatment of **3** with MeOH–MeONa resulted in formation of two very similar γ-lactones **4a, b** (IR frequency at 1778 cm^{-1}) as the



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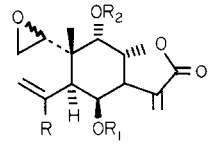
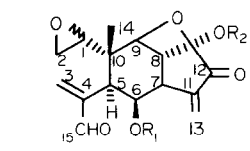


2 R = CHO, R_1 = MeAcr, R_2 = H



3 R_1 = C(=O)–C(OH)(2″ 3″)–Me, R_2 = Ac

or reverse

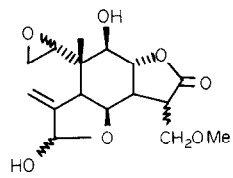


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Table 1. ^{1}H NMR spectra*

	3	4a	4a†
H-1	3.08*dd* (4, 3)	3.36	2.90*dd* (4, 3)
H-2a	2.53*t* (4)	2.9 *m*	2.24*t* (4)
H-2b	2.46*dd* (4, 3)		2.34*dd* (4, 3)
H-3a	6.28*br*	5.39*d* (*br*) (1.5)	5.18*t* (1.5)
H-3b	6.71*br*	5.53*d* (*br*) (1.5)	4.91*t* (1.5)
H-5	3.39*d* (*br*) (3.5)	3.19*d* (*br*) (4)	2.81*d* (*br*) (5)
H-6	4.93*t* (3.5)	4.38*d* (4)	4.33*d* (4.8)
H-7	3.3*m*	3.13*dd* (12, 9)	3.09*m*
H-8	5.45*t* (2.5)	4.67*dd* (9, 3)	4.28*dd* (8.5, 3)
H-9	4.61*t* (2)	3.95*d* (*br*) (4)‡	3.57*t* (3)‡
H-13a	6.79*br*	3.67 *m*	3.53*dd* (10, 5)
H-13b	5.91*br*		3.40*dd* (10, 3.5)
H-14	1.14	0.78	0.33
H-15	9.37*br*	5.60*br*	5.20*br*
H-2′‖	2.12		
H-3″§	1.56		
		2.9*m* (H-11)	2.71*ddd* (12.3, 5, 3.5)
		3.37 (OMe)‖	3.07‖
		3.64 (OH)	

*Run at 270 MHz in $CDCl_3$ unless indicated otherwise. Unmarked signals are singlets. Frequencies in ppm downfield from TMS as int. standard. Coupling constants (in parentheses) in Hz.

†In C_6D_6 with a few drops $CDCl_3$.

‡Sharpens to *d* on addition of D_2O.

§Intensity six protons.

‖Intensity three protons.

result of hydrolysis, rearrangement of the lactone and addition of the elements of MeOH. As the spectral differences were minimal, these substances are probably C-15 rather than C-11 epimers. Formation of a lactol ring involving the aldehyde function and the liberated hydroxyl on C-6 was evidenced by the absence of the IR band at 1695 cm^{-1} and the upfield shift of the H-3a, b signals, as well as the upfield shift of H-15 from 9.37 to 5.60 ppm. Double irradiation in $CDCl_3$ and C_6D_6 solution permitted the assignments given in Table 1. Noteworthy is the change in $J_{7,8}$ from 2.5 to 9 Hz and the vanishing of $J_{7,9}$ as the result of the reorientation of the lactone ring.

EXPERIMENTAL

Extraction of Zinnia grandiflora. Aerial parts of *Zinnia grandiflora* Nutt. collected by Mr. R. J. Barr in the vicinity of Tucson, AZ, in July 1961 (voucher specimen lost in the course of a move), wt 1.05 kg, was extracted with $CHCl_3$ and worked-up as usual [6]. The crude gum (17.7 g) was preadsorbed on 30 g of silicic acid (Mallinckrodt 100 mesh) and was loaded on a column of 270 g of the same adsorbent packed in C_6H_6–$CHCl_3$ (3:1). Fractions were collected as follows: 1, $CHCl_3$–C_6H_6 (1:3, 2 l.), 2, $CHCl_3$–C_6H_6 (1:3, 1.5 l.) and $CHCl_3$ (1 l.), 3–10, $CHCl_3$ (100 ml each), 11–14; $CHCl_3$–MeOH (49:1, 200ml each), 15 and 16, $CHCl_3$–MeOH (19:1, 500 ml each). The material in fraction 16 was purified by TLC (MeOH–$CHCl_3$, 1:24) to yield 0.35 g of **3** as a gum which had IR bands at ($CHCl_3$) at 3520 (weak), 1739 (very strong), 1695 and 1630 cm^{-1}, UV (MeOH) 213 nm (11 600), CD curve (MeOH) $[\theta]_{320}+720$, $[\theta]_{300}+500$, $[\theta]_{280}-98$, $[\theta]_{260}-785$, $[\theta]_{243}-950$, $[\theta]_{235}-1600$ (last reading).

The ^{1}H NMR spectrum is given in Table 1. ^{13}C NMR frequencies are given in the Results and Discussion except for that of C-14 at 13.05*q*; low-resolution MS 422 (M^+, weak) 407, 404, 391, 380, 364, 336, 318, 305, 294, 289, 276, 261, 260, 259, 258, 248, 247, 246, 245, 238, 217, 201. [Calc. for $C_{21}H_{26}O_9$: MW, 422.1577. Found: MW(MS) 422.1574 by peak matching.] A solution of 50 mg of **3** in 5 ml of MeOH and 40 mg of MeONa was stirred at room temp. (N_2 atm.) for 1.5 hr, acidified with dil. HOAc and extracted with EtOAc. Evaporation of the solvent yielded a gummy product (25 mg) which after TLC (6% MeOH–$CHCl_3$) gave two fractions **4a** (12 mg) and **4b** (8 mg), probably epimeric at C-15, IR ($CHCl_3$) of **4a** 3540 (sharp), 3470 (broad), 1778 (γ-lactone), 1690 (very weak, possibly a small amount of aldehyde in equilibrium with lactol), ^{1}H NMR in Table 1, MS 308 (M^+), 290, 276. [Calc. for $C_{16}H_{22}O_7$: MW, 326.1363. Found: MW(MS), 326.1356.] IR and low-resolution MS of **4b** were essentially the same as those of **4a**. The ^{1}H NMR spectrum differed from that of **4a** only in very minor detail.

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