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# ELEMANOLIDES FROM *ZINNIA PERUVIANA**

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**Key Word Index**—*Zinnia peruviana*; Compositae; Heliantheae; elemanolides; sesquiterpene lactones.

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**Abstract**—*Zinnia peruviana* from Honduras afforded two new acetal-type elemanolides as well as a mixture consisting primarily of zinaflorin III.

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## INTRODUCTION

Collections from Mexico, Bolivia and Natal variously referred to *Zinnia pauciflora* L., *Z. multiflora* L. and *Z. peruviana* (L.)L. have furnished rather similar elemanolide mixtures containing lactones of type **1** and **2** [1, 2]. This need occasion no surprise because according to Torres [3] all three collections represent the same taxon, with the last-mentioned epithet taking precedence. We have now studied a collection of *Z. peruviana* from Honduras which has furnished new acetal type elemanolides **3a** and **3b** in addition to the usual lactones mixture of type **2** consisting primarily of zinaflorin III (**2a**) [1].

## RESULTS AND DISCUSSION

The somewhat less polar solid lactone fraction from *Z. peruviana* was a 4:1 mixture of the methacrylate **3a** and the tiglate **3b** which could not be separated by TLC. The composition was established by high-resolution mass spectrometry which provided the molecular ions $C_{19}H_{22}O_7$ for the major and $C_{20}H_{24}O_7$ for the minor component and showed strong peaks at $m/z$ 83 ($C_5H_7O$) and 69 ($C_4H_5O$). The $^1H$ NMR and $^{13}C$ NMR spectra (Tables 1 and 2) exhibited characteristic peaks for the methacrylate and tiglate moieties in the ratio 4:1 but were otherwise free of extraneous signals except for duplication of H-14 and C-11.

The H-7 signal was located by irradiation of the typical narrowly split H-13 frequencies; subsequent double irradiation experiments then permitted determination of the sequence H-5–H-9 in the usual manner, with the methacrylate (or tiglate) attached to C-6 and the lactone closed to C-8 because H-6 appeared at considerably lower field than H-8. As H-5 was also allylically coupled to two vinylic protons (H-15) which were part of another $\rangle C{=}CH_2$ system (carbon triplet at 116.33, carbon singlet at 142.91), expansion to include C-4 and C-15 as in partial structure **A** became feasible. The multiplicity of H-9 indicated that C-9 was attached to a quaternary center.

The remaining seven protons of the molecular formula were accounted for by a methyl singlet and four other signals, all at low field. Three of these were associated with the ABC system of partial structure **B** where $H_A$ was coupled to $H_B$ but not to $H_C$ and next to a quaternary center, like H-9. The corresponding carbon signals were identified as a triplet at 65.52 and a doublet at 81.82 by single frequency resonance spin decoupling (SFRD). The

Table 1. $^1H$ NMR spectral data for compounds **2a** and **3a***

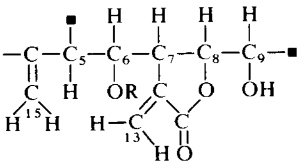
| | **2a**† | **3a**‡ |
|---|---|---|
| H-1 | 3.11 *t* (3) | 4.11 *d* (5) |
| H-2a | 2.61 *m* | 4.88 *d* (8) |
| H-2b | | 3.71 *dd* (8, 5) |
| H-3 | 9.45 *br* | 5.49 |
| H-5 | 3.78 *dbr* (3) | 3.21 *dbr* (2) |
| H-6 | 5.42 *t* (3) | 5.69 *dd* (3, 2) |
| H-7 | 3.38 *dddd* (7, 3.5, 3, 3) | 3.33 *dddd* (8, 3.5, 4, 3) |
| H-8 | 4.90 *dd* (8, 3) | 4.93 *dd* (8, 4) |
| H-9 | 4.03 *t* (3)§ | 3.98 *d* (4) |
| H-13a | 6.26 *d* (3.5) | 6.29 *d* (4) |
| H-13b | 5.70 *d* (3) | 5.75 *d* (3.5) |
| H-14 | 1.02 | 1.31 |
| H-15a | 6.63 *br* (1) | 5.05 *d* (2.5) |
| H-15b | 6.25 *br* (1) | 4.59 *d* (2.5) |
| H-3′a | 6.12 *br* | 6.11 *br* |
| H-3′b | 5.70 *br* | 5.63 *br* |
| H-4′ | 1.98 *br* | 1.94 *br* |

*Run at 270 MHz with TMS as internal standard. Unmarked signals are singlets. Values in parentheses are coupling constants in Hz.

†Minor constituent: H-2a 2.51 *dd*, H-2b 2.44 *dd*, H-3 9.38, H-6 4.59 *dd*, H-7 3.32 *m*, H-9 5.00 *t* (4), H-13a 6.61 *d*, H-13b, 5.88 *d*, H-14 1.07, H-15a 6.71 *br*, H-15b 6.17 *br*, H-3′ 6.85 *m*, H-4′ and H-5′, 1.86 *d* and 1.90 *br*.

‡Frequencies of **3b**, H-14 1.26, H-3′ 6.85 *qq*, H-4′ 1.81 *d*, H-5′ 1.82 *br*.

§Collapses to *d* on addition of $D_2O$.



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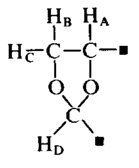


B

Table 2. $^{13}$C NMR spectral data for compounds **2a** and **3a***

| Carbon | **2a**† | **3a(3b)**‡ |
|---|---|---|
| 1 | 55.42 *d* | 81.82 *d* |
| 2 | 44.61 *t* | 65.52 *t*¶ |
| 3 | 194.14 | 103.22 *d* |
| 4 | 146.23 | 142.91 |
| 5 | 31.34 *d* | 31.42 *d*¶ |
| 6 | 71.47 *d*§ | 69.47 *d* |
| 7 | 43.03 *d* | 43.08 *d* |
| 8 | 71.59 *d*§ | 73.99 *d*¶ |
| 9 | 74.52 *d*§ | 68.63 *d* |
| 10 | 40.47 | 42.01¶ |
| 11 | 135.80‖ | 136.04 (136.12) |
| 12 | 170.41 | 169.59 |
| 13 | 119.10 *t* | 119.13 *t* |
| 14 | 12.77 *q* | 17.69 *q* |
| 15 | 139.52 *t* | 116.33 *t* |
| 1′ | 166.28 | 166.19 (166.69) |
| 2′ | 135.20‖ | 135.69 (127.90) |
| 3′ | 18.32 *q* | 18.21 *q* (137.79 *d*) |
| 4′ | 126.62 *t* | 126.16 *t* (14.47 *q*) |
| 5′ | | (12.34 *q*) |

*Run at 67.9 MHz. Unmarked signals are singlets.

†Run in $CDCl_3$. Most signals appear in duplicate due to presence of at least one minor constituent.

‡Run in DMSO-$d_6$.

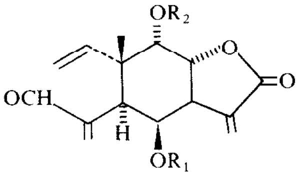
§, ‖Assignments may be interchanged.

¶Assignment made by SFRD.

fourth signal, a singlet at 5.49, was that of a proton ($H_D$ of **B**) on a carbon whose chemical shift (103.22 by SFRD) required attachment to two oxygen atoms. As the $^{13}$C NMR spectrum contained only one carbon singlet and one methyl quartet in addition to the signals required by structures **A** and **B**, formulae **3a** and **3b** (devoid of stereochemistry) followed.

As the lactone ring was *trans*-fused ($J_{7,13} > 3$ Hz), the values for $J_{5,6}$, $J_{6,7}$ and $J_{8,9}$ required the stereochemistry at C-5, C-6 and C-9 shown in the formula (model). The stereochemistry of the C-1, C-3 ether bridge was like that in micordilin (**4**) [4] with H-1 exhibiting zero coupling to the C-2 methylene proton (H-2α) responsible for the signal at lower field (4.88). Its chemical shift is the result of deshielding by the α-oriented hydroxyl group on C-9. The $^{13}$C NMR spectra of **3a** and **3b** compare with that of micordilin (**4**) if allowance is made for the difference in substitution at C-2, C-6 and C-9.

The lactone fraction of higher polarity was a mixture consisting of one main component and other apparently rather similar minor lactones (NMR analysis). TLC permitted identification of the major constituent, still somewhat impure, as **2a**. Frequencies and coupling constants in the $^1$H NMR spectrum (Table 1) were identified by spin decoupling in the usual way and led to the stereochemistry depicted in the formula. The values of $J_{7,13}$ (3 Hz) again required *trans*-fusion of the lactone ring, with C-6 being the locus of the ester function because of the relative frequencies of C-6 and C-8. The stereochemistry of C-5, C-6 and C-8 was dictated by the values of $J_{5,6}$, $J_{6,7}$ and $J_{8,9}$. The stereochemistry at C-1, as in other compounds of type **2**, is unknown. The $^{13}$C NMR spectrum (Table 2) is consonant with the proposed structure. The appearance of weaker NMR



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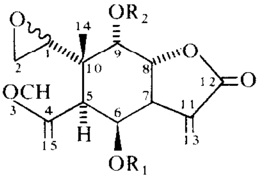
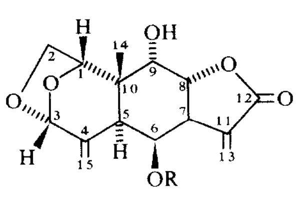
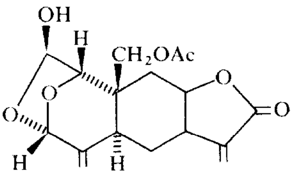


**2a** $R_1$ = MeAcr, $R_2$ = H
**2b** $R_1$ = H, $R_2$ = Tigl
**2c** $R_1$ = H, $R_2$ = Ang
**2d** $R_1$ = H, $R_2$ = MeAcr
**2e** $R_1$ = Tigl, $R_2$ = H



**3a** R = MeAcr
**3b** R = Tigl



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signals at frequencies appropriate for a 6-hydroxy-9-tigloyloxyelemanolide* suggested that **2b** was the main impurity, although the simultaneous presence of **2d** and **2e** could have accounted equally well for the weaker signals in the $^{1}$H NMR and $^{13}$C NMR spectra.

Substance **2a** appears to be identical with zinaflorin III from '*Z. pauciflora*' [1]† and one of several very similar compounds in the elemanolide mixtures from *Z. multiflora*' from Bolivia and *Z. peruviana* from Natal [2]. Identification of the previously unreported elemanolide acetals **3a** and **3b** in the extract of Honduran *Z. peruviana* may reflect minor chemical variability in a species with widespread geographical distribution, a difference in time of collection or small differences in isolation procedures.

## EXPERIMENTAL

*Extraction of* Zinnia peruviana. Aerial parts of *Z. peruviana* (L.)L. (9 kg) collected by Mr. Gustavo Cruz in the Fall of 1974 near Tegucigalpa, Honduras (voucher on deposit in herbarium of U.N.A.H., accession No. PR 43869 of Medicinal Plant Resources Laboratory, U.S.D.A.), was extracted with $CHCl_3$ and worked upas usual [5]. The crude gum (23 g) was adsorbed on 40 g Si gel (Mallinckrodt 100 mesh) and loaded on a column of 360 g Si gel packed in $C_6H_6$–$CHCl_3$ (3:1). Fractions were collected as follows: fraction 1 $C_6H_6$–$CHCl_3$, 3:1 (3.5 l.), 2 $C_6H_6$–$CHCl_3$ 1:1 (2 l.), 3–15 $CHCl_3$ (1 l. each), 16 and 17 $CHCl_3$–MeOH, 97:3 (200 ml each).

Fraction 8 was triturated with EtOAc–hexane whereupon 200 mg of solid material separated which was a 4:1 mixture of **3a** and **3b**. It had mp 280° (dec), and could not be recrystallized satisfactorily; IR $\nu_{max}$ cm$^{-1}$: 3400, 1755 and 1712; UV $\lambda_{max}^{MeOH}$ nm: 211 ($\varepsilon$ 10 000); CD curve (MeOH) $[\theta]_{280}$ 0, $[\theta]_{270}$ −30, $[\theta]_{260}$ −370, $[\theta]_{250}$ −1150, $[\theta]_{245}$ −2180 (last reading). The low resolution MS exhibited the molecular ions of **3a** at $m/z$ 362 and of **3b** at $m/z$ 376, as well as significant peaks at $m/z$ 276 [M − ester side chain]$^+$, 233, 159, 91, 83 and 69. (Calc. for **3a**, $C_{19}H_{22}O_7$: MW, 362.1364. Calc. for **3b**: $C_{20}H_{24}O_7$: MW, 376.1522. Found: MW (MS), 362.1346; 376.1522.)

Fraction 10 on purification by prep. TLC (MeOH–$CHCl_3$, 3:47) yielded 0.24 g of somewhat impure gummy **2a**, IR $\nu_{max}$ cm$^{-1}$: 3600, 2720, 1720, 1700, 1645. The MS did not exhibit the molecular ion but had signifi significnt peaks at $m/z$ 276 [M − ester side chain]$^+$, 261, 258, 247, 83 and 69. The $^{1}$H NMR and $^{13}$C NMR spectra are reported in Tables 1 and 2.

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*Transfer of the ester function from C-6 to C-9 appears to produce the following diagnostic changes in addition to the predictable upfield shift of the H-6 signal by ~1 ppm and the downfield shift of H-9 by the same amount: significant upfield shifts of the H-2 signals, now clearly visible as two distinct *dds*, significant paramagnetic shifts of H-13a, H-13b and paramagnetic shifts of H-14 (~0.07 ppm) and H-15a (~0.15 ppm) (cf. the $^{1}$H NMR spectra of the corresponding angelate and methacrylate **2c** and **2d** [2]).

†The stereochemistry assigned to C-8 and C-9 of the zinaflorins [1] requires revision as the reported values of $J_{7,13}$ indicate *trans*-, not *cis*-, fusion of the $\gamma$-lactone ring and $J_{8,9}$ is not significantly different from that reported here.