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NEW ELEMANOLIDES FROM ZINNIA SPECIES: STRUCTURAL REVISION OF THE ZINNOLIDES [1)]

Alfredo ORTEGA,* Alfonso ROMO DE VIVAR, Rubén A. TOSCANO, and Emma MALDONADO

Instituto de Química de la Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán, 04510 México, D.F.

A study of *Zinnia peruviana* afforded the new elemanolides zinaflorin IV and zinaflorin V. An X-ray crystallographic analysis of zinaflorin IV established its structure and stereochemistry as belonging to the rather unusual group of $C_{14\alpha}$, $H_{5\beta}$ elemanolides.

The generic name zinnolides is proposed for the elemanolides possessing the same relative configuration around the six member ring as that of zinaflorin IV.

In a previous study [2)] of Z. *peruviana* (*syn.* Z. *pauciflora*) we reported the structures 1a, 1b, and 1c for zinaflorins I, II, and III. These structures were revised [3,4)] to 2a, 2b, and 2c respectively, nevertheless some inconsistency of the proposed structures with the reported spectroscopy prompted us to undertake a new study.

Zinnia peruviana collected in Mexico City afforded the new lactone, zinaflorin IV (4a); mp 294-196°C; $[\alpha]_D$ + 137.5 (c 0.145, $CHCl_3$); $C_{20}H_{24}O_7$ [MS: m/z 376 (M^+), 83(100%)]; IR $\nu_{max}^{CHCl_3}$: 3410, 1770, 1705, 1645 cm^{-1}. The above mentioned and the ^1H NMR data (Table 1) are congruent with structure 4a. This structure differs from those reported for 3a and 3b (two acetals previously isolated from the same species [4)]) in stereochemistry and in the ester attached to C_6. Dreiding models of 3a and 3b showed for the trans fused lactone ring a 180° dihedral angle between H_7 and H_8, which is inconsistent with the observed coupling constant ($J_{7,8}$ = 8 Hz), consequently we are proposing for zinaflorin IV a cis fused lactone ring as that found in zinaflorins I-III [2)].

The observed coupling constant (4 Hz) between H_8 and H_9 requires a cis relationship, therefore the C_9-OH must be β-oriented. This stereochemistry is opposite at C_8 and C_9 to that reported for the elemanolides 3a and 3b, whose ^1H NMR

spectra are almost identical to that of zinaflorin IV (except for the signals due to the ester groups).

In order to clarify this point an X-ray crystallographic analysis of this compound was carried out. The crystals belong to an orthorhombic space group $P2_12_12_1$ with unit cell constants: a=13.135 (2), b=8.263 (1), c=17.183 (3) Å, F(000)= 800, ρcalc=1.34 g cm^{-3}, μ=8.04 cm^{-1}, Z=4. Intensity data were measured on a Nicolet R3m four circle diffractometer operated in the θ-2θ scan mode using Cu Kα monochromatic radiation. 1491 reflections collected up to $2\theta < 116°$ yielded 1062 observed independent reflections with $I > 1.73\,\sigma(I)$. The structure was solved by direct methods [5] and refined by a matrix cascade procedure with anisotropic temperature factors for the non-H-atoms and a fixed isotropic temperature factor U=0.06 $Å^2$ for H-atoms to converge until a final R of 0.071. The hydroxilic H-atom was located from a difference F-map. The final difference map had no peaks greater than $\pm$ 0.3e A^{-3}. Absolute configuration was determined after 14 cycles of anomalous dispersion refinement assuming the $H_{7\alpha}$ anantiomorph. The cis fused lactone ring was confirmed showing a dihedral angle H_7-C_7-C_8-H_8 of 34.9 (3)°. The perspective drawing of zinaflorin IV (Fig. 1) obtained by X-ray analysis established its structure as 4a, consequently the closely related lactones 3a and 3b should also pertain to the $H_{5\beta}$, $C_{14\alpha}$ series and their structures must be revised to 4b and 4c, respectively.

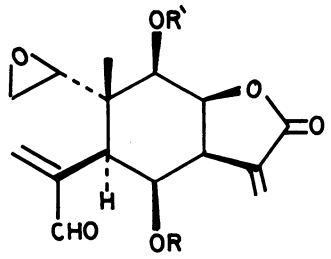
In addition to the new lactone 4a, *Z. peruviana* from Mexico City contains the known elemanolides zinaflorin I, zinaflorin II,[2] and epoxizinnamultifloride 8.[3] The similarity of their published spectroscopic data with those of 4a lead us to postulate the structures 5a, 5b, and 5c for them, respectively.

A collection of *Z. peruviana* from Oaxaca furnished zinaflorin I (5a), zinaflorin II (5b), zinaflorin IV (4a) and the new lactone zinaflorin V (6): mp 169-172°C; $C_{20}H_{24}O_6$ [MS: m/z 360 (M^+), 83 (100%)]; IR $\nu_{max}^{CHCl_3}$: 3470, 1770, 1715, 1695, 1650 cm^{-1}. The above mentioned and the ^1H NMR data (Table 1) are congruent with structure 6.

These findings and the similarity of the reported spectroscopy for all the elemanolides with γ-lactone so far isolated from Zinnia species [2-6] indicate the necessity of a revision. As the stereochemistry around the six member ring of these elemanolides is constant, we propose to name them zinnolides.

TABLE 1. ^{1}H NMR DATA OF COMPOUNDS 4a AND 6 (δ Multiplicity/J in Hz)
(80 MHz, $CDCl_3$, TMS as internal standard)

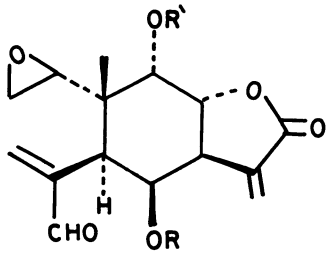
	4a	6
1-H	4.1 *d*/5	5.86 *dd*/18;11
2-H	4.86 *d*/8	5.05 *dbr*/11
2'-H	3.7 *dd*/8;5	4.92 *dbr*/18
3-H	5.04 *d*/2.5	6.43 *s*
3'-H	4.58 *d*/2.5	6.07 *s*
5-H	3.22 *dbr*/3	3.68 *d*/4
6-H	5.7	5.28 *dd*/4;2.5
7-H	3.32 *m*	3.35 *m*
8-H	4.92 *dd*/8;4	4.84 *dd*/8;4
9-H	3.95 *d*/4	3.79 *d*/4
13-H	6.26 *d*/4	6.24 *d*/3.2
13'-H	5.75 *d*/3.5	5.7 *d*/3
14-H	1.28 *s*	1.32 *s*
15-H	5.48 *s*	9.39 *s*
OCOR	6.14 *qbr*	6.8 *qbr*
	2.02 *dbr*	1.81 *br*
	1.82 *br*	



1a R = R'= Ang

1b R = Ang R'= H

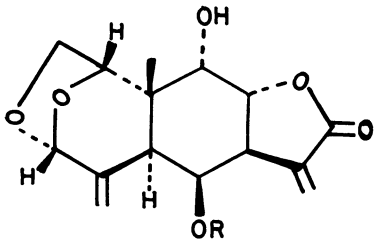
1c R = Meacr R'= H



2a R = R'= Ang

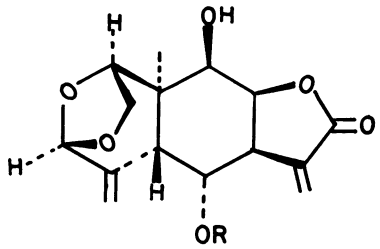
2b R = Ang R'= H

2c R = Meacr R'= H



3a R = Tig

3b R = Meacr



4a R = Ang

4b R = Tig

4c R = Meacr

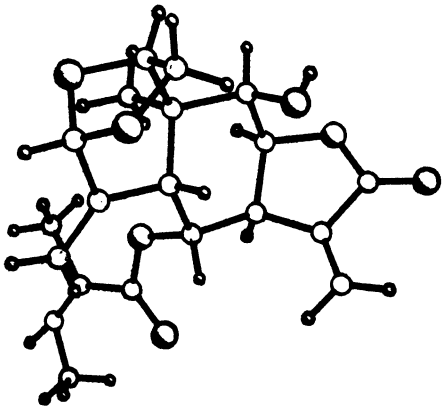
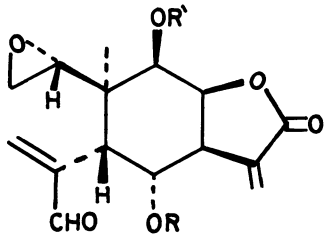


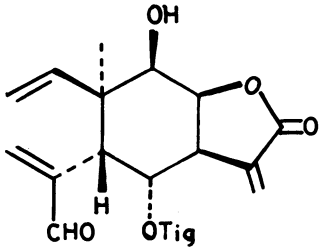
FIG. 1.



5a R = R'= Ang

5b R = Ang R'= H

5c R = Meacr R'= H



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