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ELEMANOLIDES FROM *VERBESINA SEATTONII**

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Key Word Index—*Verbesina seattonii*; compositae, elemanolides; zempoalines C and D; sesquiterpene lactones, X-ray crystallographic analysis.

Abstract—Two novel sesquiterpene lactones were isolated from *Verbesina seattonii*. Their structures were elucidated as elemanolides possessing an intramolecular hemiacetal function on the basis of an extensive spectral analysis and crystal structure determination.

INTRODUCTION

Many papers have been published recently dealing with different types of terpenoids from the genus *Verbesina* [1]; however, in only two species of this genus has the presence of sesquiterpene lactones been reported [2–4]. From the taxonomic point of view, these two species (*V. aff stricta* and *V. aff coahuilensis*) have presented serious problems. We have now restudied the material previously classified as *V. aff stricta* [4]. Detailed morphological examination of the new collection indicated a closer similarity to *V. seattonii* than to *V. stricta*. From this collection the new zempoalines C and D, but not the known zempoalines A and B, were isolated.

RESULTS AND DISCUSSION

In a previous study on *V. seattonii* [4], zempoalines A (**1a**), B (**1b**) and a small amount of a crystalline compound, whose quantity was insufficient for structural elucidation, were isolated. A new collection made in the summer of 1979 gave a large amount of this substance (zempoaline C) and another new compound (zempoaline D).

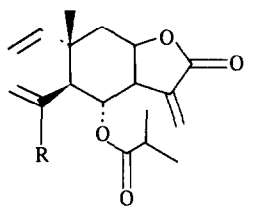
Zempoaline C, mp 119–122°, $[\alpha]_D$ −27.3° seems to be an equilibrium mixture of the hemiacetal **2a** and the aldehyde **3**. The former predominates in 4:1 ratio. The IR spectrum showed signals for hydroxyl (3440 cm^{-1}), α,β-unsaturated-γ-lactone (1770 cm^{-1}) and a saturated ester (1740 cm^{-1}). The mass spectrum exhibited the molecular ion m/z 348 ($C_{19}H_{24}O_6$) and typical peaks corresponding to the fragmentation of the isobutyrate moiety at m/z 260 $[M-C_4H_8O_2]^+$ and 71 $[C_4H_7O]^+$. The material showed a single spot by TLC in different solvent systems; however, its NMR spectrum always indicated the presence of a mixture. For the major component **2a** a singlet (3H) was observed at δ 1.47 corresponding to the methyl at C-10 and a typical ABX system at low field for the vinylic protons (H-1, H-2 and H-2′) in an elemane skeleton. It also showed an AB system at δ 3.5 and 2.67 (*d*, J = 7 Hz) for the 3 and 3′ protons, indicating that C-3 must be bonded to an oxygen function and to a tetrasubstituted carbon. These signals indicated the presence of an epoxide ring between C-3 and C-4. The remaining signals were easily assigned: the characteristic doublets for H-13 and H-13′ appeared at δ 6.5 and 6.34 with J = 4, 3.8 Hz respectively. The complex signal at δ 3.3 corresponded to H-7, since on irradiation at this frequency the doublet of doublets at δ 5.12 (J = 11, 5 Hz) was modified into a doublet (J = 5 Hz). This last signal was assigned to the C-8 proton under the lactone closure. The $J_{7,8}$ (11 Hz) found by irradiation at the frequency of the H-7 and H-9 signals, enabled us to deduce a *cis* γ-lactone closure in spite of the values for $J_{7,13} > 3$ Hz [5]. Hence H-7 and H-8 must be α. Irradiation of the broad doublet at δ 4.21 (H-9, J = 5 Hz), turned the H-8 signal into a doublet ($J_{7,8}$ = 11 Hz) and sharpened the broad singlet at δ 1.67 due to H-5. This experiment confirmed that H-9 was *cis* to H-8 and in a W arrangement with H-5. This requires H-9 and H-5 to be α [6].

The chemical shift of the broad singlet at δ 4.81 and its sharpening when D_2O was added, led us to suspect the presence of a hemiacetal. Oxidation of zempoaline C to the dilactone **4** confirmed the presence of a hemiacetal. The IR spectrum of compound **4** showed absorptions for the γ-lactone (1770 cm^{-1}), ester (1740 cm^{-1}) and δ-lactone (1725 cm^{-1}). In the ^1H NMR spectrum, the signal for H-9 was shifted to lower field (δ 4.79) and the singlet attributable to the proton on C-15 did not appear.

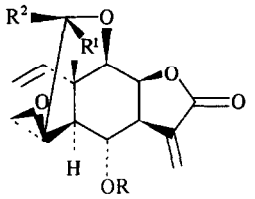
Repeated TLC and crystallization of zempoaline C failed to reduce a set of signals in its ^1H NMR spectrum amongst which the more significant was a singlet (δ 8.9) attributable to an aldehydic proton, indicating a probable equilibrium between **2a** and **3**. When the acetyl derivative **2b** was submitted to acid treatment, zempoaline C was obtained. This fact proved the before mentioned equilibrium between **2a** and **3**. The spectral changes accompanying the formation of **2b** were consistent with the proposed formula. The newly generated –O–CH–OAc signal was identified by its downfield shift to δ 5.78. In this compound, the signal for H-6 was clearly observed as a broad singlet at δ 5.44. The small values of $J_{5,6}$ and $J_{6,7}$ indicated that the isobutyrate group at C-6 is α.

The stereochemistry at C-4 and C-15 was solved by

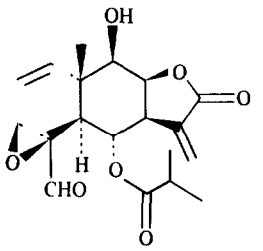
*Contribution No 729 of the Instituto de Química, U.N.A.M.



1a R = CHO
1b R = CH_2OH



	R	R^1	R^2
2a	ibu	H	OH
2b	ibu	H	OAc
2c	ibu	OAc	H
2d	Meacr	H	OH



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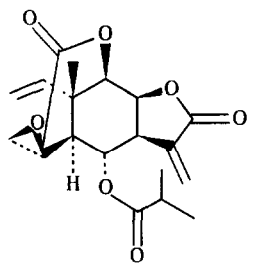

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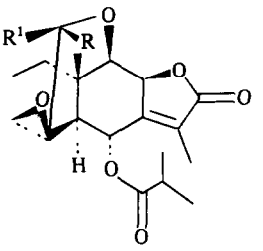
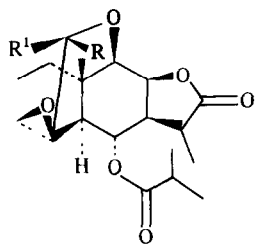


	R	R^1
5a	H	OH
5b	OAc	H



	R	R^1
6a	OAc	H
6b	H	OAc

X-ray crystallographic analysis of zempoaline C acetate (**2b**); the result is shown in Fig. 1. In this perspective view of the molecular structure the C-15-OAc is β oriented; therefore, we propose that the C-15-OH in **2a** must also be β-oriented (*S*).

Catalytic reduction of the acetate **2b** gave the reported hexahydroacetyl verafinine C (**6b**) [3]; therefore zempoaline C (**2a**) is the isobutyrate analogue of verafinine C. This correlation establishes the stereochemistry at C-4 and C-15 for this last compound as it is shown in **2d**.

Hydrogenation of zempoaline C afforded two products, the more polar of which could not be characterized. In the second and less polar compound (**5a**), the C-1 double bond was saturated (δ1.0, *t*, J = 7 Hz) and the one at C-11, C-13 was isomerized to C-7, C-11 (vinylic methyl at δ2.03). The hemiacetal in this compound remains unchanged, since the singlet of H-15 is still observed at δ4.93.

The second new compound, zempoaline D (**2c**), isolated from the less polar fractions, was a crystalline solid, mp 183–184°, $[\alpha]_D$ +98.5°, $C_{21}H_{26}O_8$ (elemental analysis and MS). Its IR spectrum revealed the presence of carbonyl groups at 1775 (α,β-unsaturated-γ-lactone), 1750 and 1744 cm^{-1} (saturated esters). Its ^1H NMR spectrum (Table 1), showed it was a diester of acetic and isobutyric acids. This was confirmed by the *m/z* fragments 43 (100%) and 71 (28%) in the mass spectrum. The spectroscopic features of this compound were very similar to those of zempoaline C-acetate (**2b**). The more conspicuous differences between **2b** and **2c** were the sign of the specific rotation and the $\Delta\nu$ for the H-3 and H-3′ of the AB systems in both compounds (0.23 ppm in **2c** and 0.56 ppm in **2b**). These results suggested that the two compounds differed in the stereochemistry at C-15. Chemical proof for the correctness of this assumption was provided by acid treatment of zempoaline D (**2c**) which gave zempoaline C

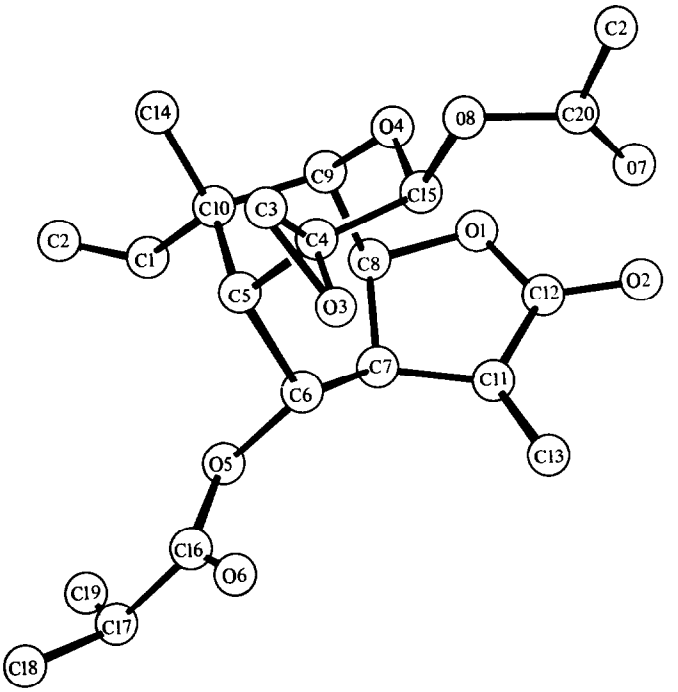


Fig. 1. Molecular structure of zempoaline C acetate.

(**2a** ⇌ **3**). In this compound the absolute configuration of C-15 is *S*, therefore, in zempoaline D, it must be *R*. These conclusions were confirmed by an X-ray structure determination of zempoaline D (Fig. 2).

Upon hydrogenation zempoaline D yielded two products. In the less polar component (**5b**) the C-1 double bond was saturated and the one at 11 (13) was isomerized, as revealed by the ^{1}H NMR spectrum. It showed the C-1-methyl group as a triplet at δ1.1 and the vinyl methyl at δ2.14. The second product (**6**) is the tetrahydro derivative showing a molecular formula $C_{21}H_{30}O_8$ (elemental analysis and MS). Its NMR spectrum showed the C-1-methyl as a triplet at δ0.97 (J = 7 Hz) and the C-11 methyl signal at δ1.42 (*d*, J = 6.5 Hz, 3H).

The refined coordinates for zempoaline C acetate (Fig. 1) and zempoaline D (Fig. 2) are given in Tables 2 and 3, respectively. Bond distances and angles were affected somewhat by large thermal parameters in the C-1 =C-2 regions and particularly in the isobutyrate substituents of both structures. This is probably an indication of some molecular disorder, especially in the isobutyrate group of zempoaline D; nevertheless the main skeleton remains unaffected. The conformation of the four rings in terms of their torsion angles is given in Table 4. The most notable changes caused by epimerization at C-15 are seen in torsion angles about the bonds to C-7.

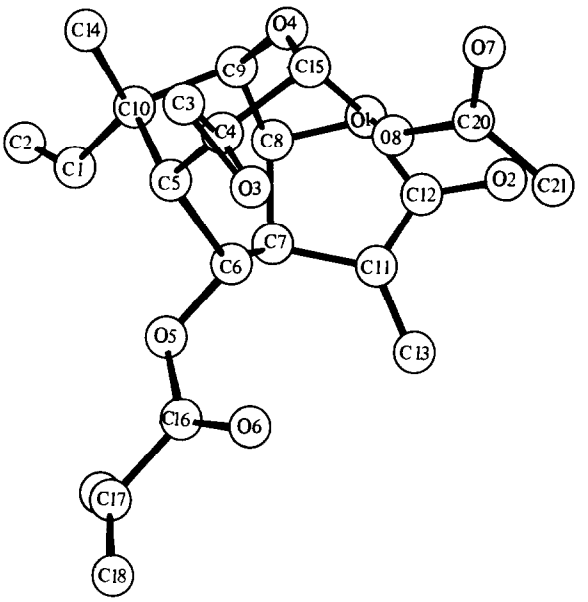


Fig 2. Molecular structure of zempoaline D.

EXPERIMENTAL

Extraction of Verbesina seattonii (*HBK*) *Blake*. Aerial parts of dry plant material (10 kg) collected in 1979, Km 45 of the Highway to Cuernavaca, Morelos, México; MEXU 291035 on deposit in Herbarium of UNAM México, were extracted with $CHCl_3$ and the residue was percolated through a 1 kg bentonite earth (Tonsil) column. Three 3 l fractions were eluted in the following order: hexane, $CHCl_3$ and EtOAc. The last two fractions were chromatographed over 2 kg silica gel (Merck 70–230 mesh). C_6H_6–EtOAc (9:1) eluted 3.475 g zempoaline D (**2c**), mp 183–184° (Me_2CO–*iso*-Pr_2O), $[\alpha]_D$ +98.5° (*c* 0.203,

Table 1. ^{1}H NMR spectral data of compounds **2–6** (80 MHz, $CHCl_3$, TMS as int. standard)

H	**2a⇌3**	**2b**	**2c**	**4**	**5a**	**5b**	**6a**
1	6.15 *dd* 18, 11	6.17 *dd* 18, 11	6.10 *dd* 18, 11	6.21 *dd* 18, 11	1.53 *q** 7	1.74 *q** 7	1.61 *q** 7
2	5 27 *d* 18	5 29 *d* 18	5.38 *d* 18	5 30 *d* 18	1.0 *t*† 7	1.1 *t*† 7	0 97 *t*† 7
2	5.25 *d* 11	5.28 *d* 11	5.32 *d* 11	5.34 *d* 11			
3	3 5 *d* 6	3.3 *d* 5	3.09 *d* 5	3 34 *d* 7	3.95 *d* 6	3.01 *d* 6	3.02 *d* 5
3	2.67 *d* 6	2.74 *d* 5	2.86 *d* 5	2.92 *d* 7	3.11 *d* 6	2.8 *d* 6	2.82 *d* 5
5	1.67 *br s*	1.73 *br s*	1 6 *s*	1 99 *br s*	1.92 *br d* 2	1.83 *dd* 2, 1.5	1.39‡
6	‡	5.44 *br s*	5.65 *d* 4	5 63 *br s*	5.97 *d* 2	5.92 *d* 2	5 72 *d* 5
7	3.3 *m*	3.36 *m*	3 36 *m*	3.4 *m*	—	—	3.1 *m*
8	5.12 *dd* 11, 5	5.09 *dd* 10.5, 5	5.05 *dd* 11, 6	5 21 *dd* 8.5, 3.6	5.2 *br*	5.21 *m*	4.94 *dd* 10, 7
9	4.21 *br d* 5	4.19 *br d* 5	4.31 *br d* 6	4.79 *dd* 3 6, 2	4.19 *dd* 4, 1.5	4.23 *dd* 4, 1.5	4.14 *br d* 7
13	6.5 *d* 4	6.58 *d* 4	6.34 *d* 3 6	6 3 *d* 4	2.03 *d*† 2 5	2 14 *dd*† 2, 0.5	1.42 *d*† 6 5
13	6.34 *d* 3.8	6.3 *d* 3.8	6 04 *d* 3	5.94 *d* 3.8			
14	1.47 *s*	1.48 *s*	1 40 *s*	1.44 *s*	1.27 *s*	1.25 *s*	1 22 *s*
15	4.81 *br s* 8.9 *s*	5 76 *s*	5.87 *s*	—	4.93 *d* 4	5.94 *s*	5.87 *s*
OH	4.54 *br*	—	—	—	4.0 *d* 4		
C_{15}-OAc	—	2.02 *s*†	2.0 *s*†	—	—	1.98 *s*†	2.08 *s*†
C_8-O_{tbu}	2.57 *h* 7	2 57 *h* 7	2.59 *h* 7	2.58 *h* 7	3.0 *h* 7	2.54 *h* 7	2.5 *h* 7
	1 18 *d* 7	1 19 *d* 7	1.22 *d* 7	1.19 *d* 7	1.15 *d* 7	1.17 *d* 7	1.16 *d* 7

*Intensity two protons
†Intensity three protons
‡Superimposed signal.

$CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}. 1775, 1750, 1744, 1645, UV λ_{max}^{EtOH} 220 nm (ε6100); MS *m/z*· 364 $[M-C_2H_2O]^+$, 347 $[M-AcO]^+$, 334 $[M-C_2H_2O-CH_2O]^+$, 318 $[M-C_4H_8O_2]^+$, 259 $[M-AcO-C_4H_8O_2]^+$ [Calc for $C_{21}H_{26}O_8$: C, 62 06; H, 6.45; O, 31 49. Found· C, 61.72; H, 6 43; 0, 31.70%.]

From the following fractions, 11.5 g zempoaline C (**2a ⇌ 3**) were eluted (C_6H_6–EtOAc, 9:1) mp 119–122° (Me_2CO–hexane–*iso*-Pr_2O), $[\alpha]_D$ −27 34° (*c* 0.139, $CHCl_3$), UV λ_{max}^{EtOH} 210 nm (ε5400); IR $\nu_{max}^{CHCl_3}$ cm^{-1}· 3440, 1770, 1740, 1655, 1630; MS *m/z*· 276 $[M-C_4H_8O_2]^+$, 258 $[M-C_4H_8O_2-H_2O]^+$, 294 $[M-C_4H_6O]^+$, 71 (100).

Oxidation of zempoaline C (**2a ⇌ 3**). Pyridinium dichromate (500 mg) [7] was gradually added to a soln of zempoaline C (130 mg) in CH_2Cl_2 (10 ml) The mixture was stirred overnight at room temp., diluted with hexane and filtered through silica gel. The solvent was removed and 106 mg of the dilactone **4** were obtained and crystallized from Me_2CO–*iso*-PrO_2, mp 189–191°, $[\alpha]_D$ +23.11°, (*c* 0.199, $CHCl_3$). UV λ_{max}^{EtOH} 222 nm (ε3600); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770, 1740, 1725, 1655, 1640; MS *m/z*: 362 $[M]^+$, 274 $[M-C_4H_8O_2]^+$, 292 $[M-C_4H_6O]^+$, 71 (9 1), [Calc. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12; O, 30.91. Found: C, 62.75; H, 6.11, O, 31.00%.]

Hydrogenation of zempoaline C acetate (**2b**). A soln of **2b** (95 mg) in EtOAc (10 ml) was hydrogenated overnight with 12 mg PtO_2 at atmospheric pressure. Filtration followed by crystallization of the residue from Me_2CO–hexane yielded 71 mg **6b** (mp 225–227°; lit [3] 228–229°).

Hydrogenation of zempoaline C (**2a ⇌ 3**). 480 mg (**2a ⇌ 3**) were hydrogenated over 51 mg Pd–C (5%) in EtOAc. After 5 hr, the reaction mixture was worked up as usual. Two crystalline products were formed. They were separated by fractional crystallization: from Me_2CO–hexane 305 mg of the more polar compound were obtained, mp 188–189°, $[\alpha]_D$ +24.48° (*c*, 0.196, $CHCl_3$). UV λ_{max}^{EtOH} 221 (ε200); IR $\nu_{max}^{CHCl_3}$ cm^{-1}· 3400, 2820, 1780, 1732, EM *m/z*: 368 $[M]^+$, 297 $[M-C_4H_7O]^+$, 280 $[M-C_4H_8O_2]^+$, 71 (100). [Calc. for $C_{19}H_{28}O_7$: C, 61.91; H, 7.66; O, 30.40 Found: C, 61 74; H, 7.62; O, 30 30%.] Compound **5a**

Table 2. Coordinates and thermal parameters for zempoaline C acetate

Atom	x	y	z	Beqv	Atom	x	y	z	Beqv
O-1	0.6933 (4)	0 8372 (3)	0.5827 (2)	5.98 (8)	C-8	0.6293 (5)	0.8052 (3)	0.6649 (3)	4.5 (1)
O-2	0.7025 (4)	0.7960 (3)	0.4358 (2)	8.1 (1)	C-9	0.7259 (4)	0.7646 (3)	0.7307 (3)	4.3 (1)
O-3	0.6575 (4)	0.4559 (2)	0.7050 (3)	6.34 (9)	C-10	0.6603 (5)	0.7135 (3)	0.8121 (3)	4.4 (1)
O-4	0.8192 (3)	0.6997 (2)	0.6897 (2)	5.03 (7)	C-11	0.5546 (4)	0.7129 (3)	0.5377 (3)	4.5 (1)
O-5	0.3735 (3)	0.6660 (2)	0.7422 (2)	4.89 (7)	C-12	0.6551 (5)	0 7828 (4)	0.5110 (4)	5.6 (1)
O-6	0.3038 (4)	0.5142 (2)	0 7161 (4)	8.4 (1)	C-13	0 5062 (6)	0.6492 (5)	0.4816 (4)	6 9 (1)
O-7	0 8856 (4)	0.5736 (3)	0.4970 (2)	7.9 (1)	C-14	0 7595 (5)	0.6832 (4)	0.8848 (3)	5 8 (1)
O-8	0.8922 (3)	0.5488 (3)	0.6479 (2)	5.07 (7)	C-15	0.7778 (5)	0 6042 (3)	0.6604 (3)	4.5 (1)
C-1	0.5640 (6)	0.7826 (4)	0 8532 (3)	5 5 (1)	C-16	0.2855 (5)	0 5945 (3)	0.7462 (4)	5.0 (1)
C-2	0.5407 (12)	0 8085 (7)	0 9259 (6)	17 0 (3)	C-17	0.1683 (5)	0.6249 (4)	0.7948 (5)	8 1 (2)
C-3	0.7426 (5)	0 4660 (3)	0 7824 (4)	5 9 (1)	C-18	0.1147 (7)	0.5513 (5)	0.8512 (5)	11 0 (2)
C-4	0.6967 (4)	0.5531 (3)	0 7312 (3)	4 4 (1)	C-19	0.1461 (7)	0 7261 (5)	0.8062 (6)	11.0 (2)
C-5	0.5948 (4)	0 6197 (3)	0.7699 (3)	4.0 (1)	C-20	0.9333 (5)	0.5361 (4)	0 5611 (3)	5.4 (1)
C-6	0.4924 (5)	0.6444 (3)	0 6972 (3)	4.1 (1)	C-21	1 0485 (6)	0.4705 (4)	0.5583 (4)	7.2 (1)
C-7	0.5211 (5)	0 7357 (3)	0.6346 (3)	4.0 (1)					

Estimated standard deviations in the least significant digits are shown in parentheses.

Table 3. Coordinates and thermal parameters for zempoaline D

Atom	x	y	z	Beqv	Atom	x	y	z	Beqv
O-1	0.0772 (5)	−0.3255 (7)	−0.7715 (2)	11.5 (2)	C-8	−0.0331 (8)	−0.3764 (10)	−0.7359 (4)	9.8 (3)
O-2	0.2966 (6)	−0.3371 (9)	−0.7677 (3)	14.1 (2)	C-9	−0.1318 (8)	−0.2736 (9)	−0.7200 (3)	9.0 (2)
O-3	−0.0418 (6)	−0.1902 (5)	−0.5126 (2)	9.1 (2)	C-10	−0.2320 (7)	−0.3250 (10)	−0.6639 (4)	9.4 (3)
O-4	−0.0771 (5)	−0.1544 (6)	−0.7007 (2)	9.0 (1)	C-11	0.1654 (8)	−0.4478 (8)	−0.6863 (4)	8.8 (2)
O-5	−0.0689 (5)	−0.5383 (5)	−0.5689 (3)	8.4 (1)	C-12	0.1916 (9)	−0.3652 (11)	−0.7445 (4)	10.8 (3)
O-6	0.0887 (7)	−0.5202 (7)	−0.4921 (3)	15.7 (2)	C-13	0.2597 (9)	−0.5029 (12)	−0.6492 (5)	11.4 (3)
O-7	0.1761 (6)	0.0185 (6)	−0.6161 (4)	12.7 (2)	C-14	−0.3423 (7)	−0.2295 (11)	−0.6557 (5)	11.3 (3)
O-8	0.1081 (5)	−0.1788 (5)	−0.6341 (2)	7.9 (1)	C-15	−0.0273 (7)	−0.1337 (7)	−0.6343 (4)	7.6 (2)
C-1	−0.2854 (8)	−0.4546 (13)	−0.6822 (5)	14.4 (4)	C-16	−0.0018 (9)	−0.5768 (8)	−0.5156 (5)	10.3 (3)
C-2	−0.3649 (14)	−0.4950 (18)	−0.7020 (8)	24.7 (6)	C-17	−0.0556 (10)	−0.6944 (9)	−0.4835 (6)	13.4 (3)
C-3	−0.1668 (9)	−0.1332 (9)	−0.5266 (4)	10.2 (3)	C-18	−0.0123 (17)	−0.7169 (11)	−0.4150 (9)	23.6 (6)
C-4	−0.1012 (7)	−0.2038 (8)	−0.5785 (4)	7.6 (2)	C-19	−0.0535 (25)	−0.7845 (12)	−0.5256 (9)	42.0 (9)
C-5	−0.1479 (7)	−0 3334 (8)	−0.5979 (4)	7.4 (2)	C-20	0.2003 (8)	−0.0864 (9)	−0.6235 (4)	9.0 (2)
C-6	−0.0290 (7)	−0.4212 (7)	−0.6017 (4)	6.6 (2)	C-21	0.3350 (8)	−0.1487 (9)	−0.6244 (4)	9.6 (3)
C-7	0.0187 (7)	−0 4570 (8)	−0.6748 (4)	8.4 (2)					

Estimated standard deviations in the least significant digits are shown in parentheses.

(112 mg) was crystallized from EtOAc–hexane, mp 137–139°, $[\alpha]_D$ −149 1° (*c* 0.175, $CHCl_3$). UV λ_{max}^{EtOH} 228 nm (ε7500); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3430, 1760, 1740, 1625, MS *m/z*: 366 $[M]^+$, 348 $[M-H_2O]^+$, 336 $[M-CH_2O]^+$, 278 $[M-C_4H_8O_2]^+$, 260 $[M-H_2O-C_4H_8O_2]^+$, 71 (100) [Calc. for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15; O, 30.57. Found: C, 62.18; H, 7.15; O, 30.50%.]

Acetylation of zempoaline C (**2a** ⇌ **3**). A soln of zempoaline C (250 mg) in pyridine (1 ml) and Ac_2O (1 ml) was left to stand on a steam bath for 1 hr. It was worked up as usual, yielding 183 mg 15-epizempoaline D (**2b**), mp 184–186° (Me_2CO–hexane), $[\alpha]_D$ −12.18° (*c* 0.197, $CHCl_3$). UV λ_{max}^{EtOH} 221 (ε4300); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1763, 1745, 1655, 1650; MS *m/z*: 364 $[M-C_2H_2O]^+$, 347 $[M-AcO]^+$, 276 $[M-C_2H_2O-C_4H_8O_2]^+$, 258 $[M-AcOH-C_4H_8O_2]^+$, 43 (100), 71 (36.4). [Calc. for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45; O, 31.49. Found: C, 61.80; H, 6.42; O, 31.48%]

Hydrogenation of zempoaline D (**2c**). Compound **2c** (100 mg) was added to a suspension of prehydrogenated Pd–C catalyst (10 mg) in EtOAc (5 ml). After 5 min, the soln was filtered, evaporated and the residue (two products TLC) separated by prep. TLC (C_6H_{14}–EtOAc, 7:3); 55 mg of the more polar component (**6a**) were crystallized from Me_2CO–*iso*-Pr_2O, mp 183–185°, $[\alpha]_D$ +33.3° (*c* 0.192, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1740, 1725; MS *m/z*: 368 $[M-C_2H_2O]^+$, 351 $[M-AcO]^+$, 322 $[M-C_4H_8O_2]^+$, 263 $[M-AcO-C_4H_8O_2]^+$, 43 (100), 71 (85). [Calc. for $C_{21}H_{30}O_8$: C, 61.45; H, 7.37; O, 31.18%.] The less polar compound (**5b**) was a gum. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1753, 1745, 1738; MS *m/z*: 408 $[M]^+$, 366 $[M-C_2H_2O]^+$, 349 $[M-AcO]^+$, 278 $[M-C_2H_2O-C_4H_8O_2]^+$, 260 $[M-C_2H_4O_2-C_4H_8O_2]^+$, 43 (100), 71 (45.8).

Acid hydrolysis of zempoaline C acetate (**2b**). A soln of **2b** (104.8 mg) in Me_2CO (5 ml) was treated with HCl (0.5 ml), the mixture was heated on a steam bath for 0.5 hr and neutralized

Table 4. Selected torsion angles

Atoms	Zempoaline C acetate	Zempoaline D
C-5–C-6–C-7–C-8	−13 8	15.1
C-6–C-7–C-8–C-9	20.3	−3.2
C-7–C-8–C-9–C-10	−48.9	−40.1
C-8–C-9–C-10–C-5	67.4	70.2
C-10–C-5–C-6–C-7	36.2	18 9
O-4–C-9–C-10–C-5	−60 6	−58.9
C-9–C-10–C-5–C-4	62.6	62.5
C-10–C-5–C-4–C-15	−57.8	−55.2
C-5–C-4–C-15–C-4	47.1	37.3
C-4–C-15–O-4–C-9	−46.1	−34.1
C-15–O-4–C-9–C-10	55.2	47.4
C-7–C-8–O-1–C-12	−11.7	2.6
C-8–O-1–C-12–C-11	3.7	−0.5
O-1–C-12–C-11–C-7	6.0	−1 9
C-12–C-11–C-7–C-8	−12.3	3.2
C-11–C-7–C-8–O-1	14.4	−3 4
O-2–C-12–C-11–C-13	4.0	1 3

with satd $NaHCO_3$. The Me_2CO was removed under vacuum. The $CHCl_3$ extract left 61 mg crude zempoaline C (**2a** ⇌ **3**). Recrystallization from Me_2CO–hexane yielded 53 mg pure zempoaline C.

Acid hydrolysis of zempoaline D (**2c**). Conc. HCl (0.5 ml) was added to a soln of **2c** (98.8 mg) in Me_2CO (5 ml). The mixture was treated as above yielding 60 mg of zempoaline C (**2a** ⇌ **3**).

X-ray analysis. X-ray data were collected on an Enraf Nonius CAD4 diffractometer equipped with a graphite monochromator, by ω-2θ scan-mode of variable speed. Data reduction included background, Lorentz and polarization corrections, and in the case of zempoaline D, absorption corrections based on ψ scans of reflections near $\chi = 90°$. The structures were solved by direct methods and refined by full-matrix least squares, treating non-hydrogen atoms anisotropically. Hydrogen atoms were located in a difference Fourier maps and included as fixed contributions. Absolute configurations were determined assuming the H-7α enantiomorph.

Zempoaline C acetate. Crystal data are: $C_{21}H_{26}O_8$, M_r 406.4, orthorhombic space, group $P2_12_12_1$, $a = 10.486$ (2), $b = 13.441$ (2), $c = 14.665$ (4) Å, $Z = 4$, $d_c = 1.306$ g cm^{-3}, MoK_α radiation $\lambda = 0.71073$ Å, $R = 0.045$ for 1170 observed data ($1° < \theta < 22.5°$) having $I > 3\sigma$ (I). *Zempoaline D*, crystal data are: $C_{21}H_{26}O_8$, M_r 406 4, orthorhombic, space group $P2_12_12_1$, $a = 10.213$ (3), $b = 10.721$ (2), $c = 19.438$ (3) Å, $Z = 4$, $d_c = 1.268$ g cm^{-3}, CuK_α radiation, $\lambda = 1.54184$ Å, R = 0.070 for 1310 observations having $2° < \theta < 70°$ and $I > 3\sigma$ (I).

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