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THE PHOTOCHEMISTRY OF TETRAHYDRO ZEXBREVIN†

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Abstract—The photolysis of tetrahydro zexbrevin **2**, gave in high yield the photoisomerization product **3**, its structure was determined by chemical and spectroscopic means. The formation of the photoproduct **3** could involve an intramolecular hydrogen shift. The photoproducts **7** and **9** were also isolated and their structures determined.

The germacranolides constitute an increasingly growing group of sesquiterpenic lactones whose structure is based on 1,5-dimethyl-8-isopropyl cyclodecane (germacrane).[1] They usually contain a 1,5-diene system or the related epoxides, ketones or alcoholic functions.[1,2] Transannular cycloadditions involving the 1,5-diene system, have been found to occur with high degree or regio- and stereospecificity under cationic or radical conditions.[3]

In a study of the photochemical behaviour of isabeline, Mabry *et al.*[4] found that only the conformer in which the 1,5 double bonds are in a parallel alignment underwent a $(2\pi + 2\pi)$ suprafacial cycloaddition. However the irradiation of dihydroisabeline produced a guaianolide by a photo-ene reaction.[4] The photolysis of dihydrocostunolide has been also found to yield a guaianolide by the same mechanism.[5] Isabeline and costunolide are EE germacra-1,5-dienolides or germacrolides.[1] The photo-ene products obtained by photolysis of dihydroisabeline and dihydrocostunolide indicate that both products react in the CC conformation.[3]

Zexbrevin **1** is a germacranolide isolated from *Zexmenia brevifolia.*[6] It belongs to the subgroup of heliangolides[1,2] (E, Z germacradienolides), in which it is common to find an oxygen bridge between C-10 and C-3 forming a furan ring with different degree of insaturation[1,2] Zexbrevin **1** contains a 3(2H)-furanone moiety[6] which confers a high degree of conformational rigidity to the molecule. This fact suggested that it could suffer interesting transformations when subjected to photolytic conditions. In the event zexbrevin **1**, was found to be inert under the photolytic conditions used in this work. The study of the transformations produced on irradiation of tetrahydrozexbrevin (THZ) **2**, is described in this paper.

RESULTS

Photolysis of a methanolic solution of tetrahydrozexbrevin (THZ) **2**, at 253.7 nm resulted in complete disappearance of the starting material in 1 h and formation of several isomeric photoproducts, which were separated by chromatography.

The major photoproduct, phototetrahydro zexbrevin A (photo THZ-A) showed in the IR spectrum, bands at 1730, 1745 and 1765 cm^{-1} which could be ascribed to the isobutyric ester, a cyclopentanone and a γ-lactone functions, respectively. The strong enolic double bond absorption shown by THZ in its IR was no longer present in the IR spectrum of the photo product A. This fact suggested a photoaddition to the C-2, 3 double bond. The ^{1}H NMR spectrum confirmed this assumption, as it did not show the signal attributed to the C-2 vinylic proton present in THZ, the only downfield signal observed was a multiplet at 4.94 ppm (d, d, d, J = 1, 2.5, 4.2 Hz, 1H), which was assigned to the ester attachment or the γ-lactone closure. Upfield there were observed the signals due to the five methyl groups present in the starting material (Table 1). These data can be accommodated by structures 3 or 3′ which could be produced by a photochemically induced 1,5 hydrogen shift from C_8 or C_6 to C_2, followed by a transannular C_3–C_8 or C_3–C_6 bond formation. This type of transannular cyclization has been observed by Nakanishi *et al.*[7] in the photolysis of taxinine.

Sodium borohydride reduction of the major photoproduct gave the dihydroderivative, which showed an hydroxyl IR absorption at 3500 cm^{-1} and the absence of the cyclopentanone band (1745 cm^{-1}). In the ^{1}H NMR spectrum the proton attached to the carbon bearing the hydroxyl group is observed at 4.16 ppm as a doublet of doublets (J = 7 and 9 Hz), which proved that the ketonic group is flanked by a methylene group and a fully substituted carbon atom, as shown in structures **3** and **3′**.

An attempt to saponify the ester group under the conditions used for THZ[6] was unsuccessful even after 72 hr at room temperature.

Treatment of the photoproduct with hydrazine hydrate and potassium hydroxide following Huang–Minlon conditions, gave a crystalline product in which the ketone was reduced and the ester function saponified. The product obtained showed in the IR spectrum a strong hydroxyl absorption at 3400 cm^{-1} and a band at 1750 cm^{-1} which was attributed to a saturated γ-lactone function. In the ^{1}H NMR spectrum the ddd observed at 4.95 ppm (J = 1, 3.5 and 4 Hz) in photo THZ–A has been shifted to 4.88 ppm and appeared as a ddd with larger coupling constants (J = 5, 8 and 12 Hz) indicating a

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substantial conformational change in the product. A singlet at 1.38 ppm could be ascribed to the methyl group attached to a fully substituted carbon atom bearing an etheral function. There were also observed two doublets at 1.36 (J = 7.5 Hz) and 1.04 ppm (J = 6.5 Hz) assigned to the secondary methyl groups of the γ-lactone function and the C_4 methyl group. The hydroxyl group was found to be tertiary, as the product was recovered unchanged after treatment with Jones reagent. Treatment of this product with thionyl chloride in anhydrous pyridine gave the anhydro derivative. Its IR spectrum showed the absence of hydroxyl absorption, the γ-lactone function is responsible for a strong band at 1765 cm^{-1}. In the ^1H NMR spectrum the signal attributed to the proton at the ester attachment or lactone closure, is now shifted to 5.18 ppm (broad doublet), suggesting an allylic nature for this proton and, therefore, a 1,3 relationship with the tertiary hydroxyl group. A quartet observed at 3.06 ppm (J = 7 Hz) was assigned to the C_{11} proton, as it was shown to be coupled to the C_{13} secondary methyl group by irradiation experiments. In the methyl region there were observed a singlet at 1.45 ppm due to the tertiary methyl group and two doublets at 1.34 (J = 7 Hz) and 1.09 ppm (J = 6 Hz) attributed to the secondary methyl groups C_{13} and C_{15}.

The chemical evidence presented would favor structure **3'**, in which the ester group is attached to a tertiary carbon atom. If this was the case, the ^1H NMR spectrum of it would show the presence of two isolated methylene groups. The 300 MHz ^1H NMR spectrum (Table 1) was of great help to solve the problem. The spectra in $CDCl_3$ and benzene allowed us to establish, unambiguously, structure **3** as the correct structure for the major photoproduct A, as it revealed the presence of only one isolated methylene group (C-2) in a cyclopentanone ring[9] (Table 1). An examination of the Dreiding model of the THZ molecule showed that H-6 is almost directly below the 2,3 double bond, thus favoring the 1,5 antarafacial hydrogen migration and 6→3 transannular bond formation.[7,8] If **3** is the correct structure for the photoproduct A, the sodium borohydride reduction product should be represented by structure **4** and the Huang-Minlon product as **5a**. The presence of a tertiary hydroxyl group in **5a** could be explained by saponification of the secondary ester group, opening of the γ-lactone function and relactonization to C-8. This change is evident on an examination of the ^1H NMR spectra of **3** and **5a** already described (*vide supra*). In the ^{13}C NMR spectra of these products the singlet attributed to C_6 is shifted from 83.0 in product **3** to 78.4 ppm in **5a**. When C_8 supports the ester group, it appears as a doublet at 67–69 ppm, as in compounds **2** and **3**. In product **5a** this methine was found at 77.6 ppm, a position appropriate for the lactone closure.[2]

The product obtained on dehydration of **5a** must be therefore represented by **6**.

The methanolysis of **3** was performed in very mild conditions in order to avoid the lactonization to C_8. The product, **5b**, showed in the IR spectrum hydroxyl band at 3445; the cyclopentanone and the γ-lactone are responsible for a strong band at 1755 cm^{-1}. The ^1H NMR spectrum showed only one downfield signal at δ 4.98 as a d,d,d, (J = 4, 7, 12 Hz) as in the spectrum of **5a**, therefore lactonization to C-8 had also occurred in this reaction.

The second photoproduct photo-THZ-B **7** showed in the IR bands at 1785, 1755 and 1730 cm^{-1}, which were assigned to the saturated γ-lactone, a strained cyclopentanone and the ester groups. In the ^1H NMR spectrum (Table 1) a complex absorption at 5.075 ppm (1H) could be assigned to the ester attachment, and it was shown by double resonance experiments, to be coupled to the C_9 methylene (J = 2.5 and 3.5 Hz) and to the C_7 proton (J = 1 Hz). It also showed a singlet at 3.39 ppm which was ascribed to an isolated methine α to a ketone group. An AB system (doublet at 2.61 and 2.52 ppm, J = 11.5 Hz) was attributed to C_5 methylene group, the geminal coupling constant (11.5 Hz) presented by this methylene, suggested that it forms part of a cyclobutane ring.[9] At 0.94 ppm there was observed a triplet, which together with signals at 1.64 and 1.55 (Table 1), could be ascribed to an ethyl group attached to a fully substituted carbon atom. A singlet at 1.32 ppm was assigned to the

Table 1. 300 MHz ^1H NMR spectra of photoproducts THZ A, B, C

	3			7		9	
	$CDCl_3$	bz	m	$CDCl_3$	m	$CDCl_3$	m
H_2	3.03	2,94	d (19)	3.39	s	5,94	s
H_2'	2.35	1.92	d (19)	---	---	---	---
H_4	2.50	2,24	m (2.5,7.5)	1,64	d,q (14.5)	2,60	m
H_4'	---	---	---	1,55	d,q (14.5)	---	---
H_5	2.77	2.45	dd (9,12.5)	2,61	d (11.5)	2,41	ddd (12,13.5,6)
H_5'	1.84	1.35	dd (2.5,12.5)	2.52	d (11.5)	1,99	ddd (6,13.5,10.5)
H_6	---	---	---	---	---	4.70	ddd (10.5,6,10.5)
H_7	2.76	1.86	dd (8,1)	3.27	dd (1,10.5)	2,60	ddd (1.5,9.5,10.5)
H_8	4.94	4.73	ddd (1,2.5,4.2)	5.07	ddd (1,2.5,3.5)	5,24	ddd (1.5,7.5,1.5)
H_9	2.48	2.40	dd (4.2,15.5)	2.04	dd (2,5,15.5)	2.95	dd (7.5,16)
H_9'	1.88	1.30	dd (2.5,15.5)	1,92	dd (3,5,15.5)	1,95	dd (1.5,16)
H_{11}	2.74	1,91	dq (8,6.5)	3.00	dq	2.81	d,q
H_{13}	1.04	0.82	d	1.10	d (7.5)	1.16	d (7.5)
H_{14}	1.29	1.12	s	1.32	s	1.47	s
H_{15}	1.28	0.98	d	0.94	t (7.5)	1.32	d (6.5)
H_2'	2.38	2.47	hept (7)	2.40	hept (7)	2,40	hept (7)
$H_3',_4'$	1.11,1.12	1.19,1.18	d,d (7)	1.38,1.37	d,d (7)	1.12,1.18	d,d (7)

Run in $CDCl_3$, on a Bruker WM-300 instrument. Coupling constants (Hz) in parentheses.

C_{14} angular methyl group, which must be bound to a carbon atom which supports an oxygenated function.

Sodium borohydride reduction of photo-THZ-B gave **8**, whose IR spectrum showed the absence of the 1755 cm^{-1} band and the presence of free and hydrogen bonded hydroxyl group, at 3500 and 3200 cm^{-1}. In the ^{1}H NMR spectrum it presented a new signal (1H) as a doublet of doublets at 4.1 ppm (J = 4 and 10 Hz) which collapsed to a doublet (J = 4 Hz) on addition of D_2O. Therefore, it could be deduced, that the carbon atom bearing the hydroxyl group is flanked by a fully subsuited carbon atom and a methine group. Addition of a shift reagent (Eu(fod)$_3$) produced a strong induced chemical shift on the isopropyl moiety of the ester group and on the C_{13} methyl group, suggesting that the hydroxyl group is oriented to the same face of the molecule as the ester group and the C_{13} methyl group and can be therefore assigned a β configuration.

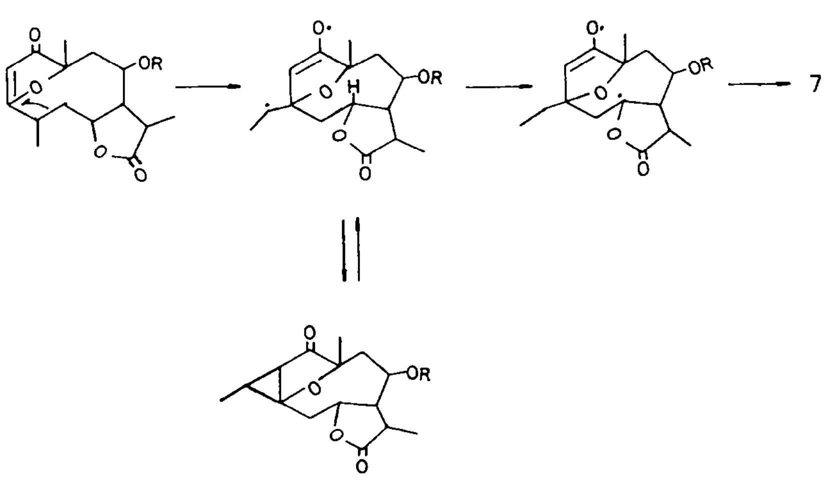
In the ^{13}C NMR spectrum (Table 2), photo THZ-B, 7, showed carbonyl absorption at 202.9, 176.3 and 175.6 ppm, which were assigned to the cyclopentanone, the ester and the lactone carbonyl groups. The chemical shift found for the cyclopentanone carbonyl, could be due to the spatial electronic influence of the *syn* oriented ester group. There are no other sp^2 carbon atoms observed in the ^{13}C NMR spectrum of this compound.

Structure 7 could explain all the data presented for this photo product. Its formation could be explained by a ($\sigma 2a + \pi 2a$) cycloaddition mechanism, which would produce a ring contraction synchronously with a 1,4 hydrogen shift from C_6 to C_4 and bond formation between C_2 and C_6, producing the cyclobutane ring, or by a stepwise mechanism as shown in Scheme 1. If the mechanism proposed is correct, this would be the first example (to our knowledge) in which there is observed a rearrangement of the "lumiketone" type, in an enone in which the C_4 position is not fully substituted.[10a–c]

Table 2. ^{13}C NMR spectra of tetrahydrozexbrevin and its photoproducts[a]

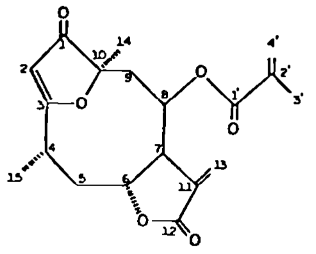
	2[b]	3	7	9	5a
C-1	205.5 s	215.7 s	202.9 s	177.9 s	38.7 t
C-2	103.2 d	37.6 t	62.0 d	116.4 d	23.2 t
C-3	192.3 s	88.5 s	83.5 s	171.2 s	90.6 s
C-4	38.6 d	36.6 d	30.7 t	39.6 d	35.9 d
C-5	41.0 t	42.8 t	46.9 t	41.8 t	41.0 t
C-6	75.8 d	83.0 s	81.9 s	76.6 d	78.4 s
C-7	50.1 d	49.8 d	50.2 d	46.5 d	50.5 d
C-8	67.2 d	69.2 d	67.8 d	66.9 d	77.6 d
C-9	42.9 t	39.2 t	41.2 t	39.3 t	39.9 t
C-10	88.4 s	89.4 s	79.5 s	87.9 s	79.2 s
C-11	31.6 d	35.18 d	35.4 d	21.4 d	29.9 d
C-12	*177.9 s	*177.17 s	*176.4 s	*177.6 s	180.3 s
C-13	11.8 q	8.84 q	9.1 q	12.5 q	*16.1 q
C-14	22.9 q	24.4 q	24.0 q	26.3 q	26.3 q
C-15	16.1 q	15.7 q	8.1 q	22.1 q	*18.7 q
C-1'	*175.0 s	*175.7 s	*175.6 s	*175.9 s	---
C-2'	34.0 d	34.0 d	34.1 d	33.7 d	---
C-3'	*18.9 q	*18.9 q	*18.5 q	*18.9 q	---
C-4'	*18.3 q	*18.1 q	*18.0 q	*18.3 q	---

[a] Run in $CDCl_3$ on a Varian FT-80A instrument. [b] Assignments were made taking into account the data presented in ref. 2. Assignment of multiplets confirmed by single frequency off-resonance decoupling.
* Assignments may be interchanged.

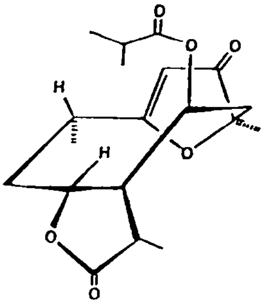


Scheme 1

The third photoproduct isolated (photo THZ-C), was



1



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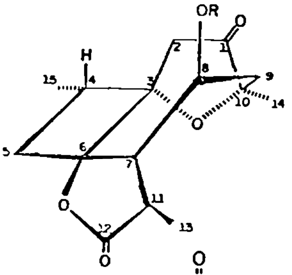
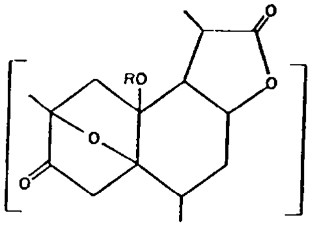
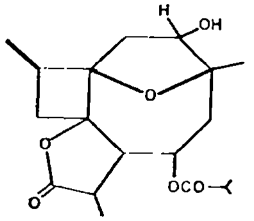


3a R = $\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}$–<
3b R = H



3' R = $\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}$–<



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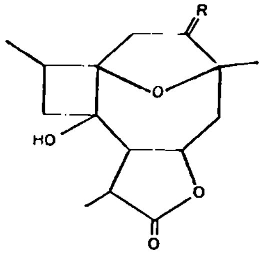
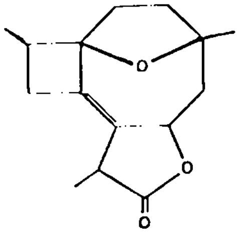


5a R = H_2
5b R = O



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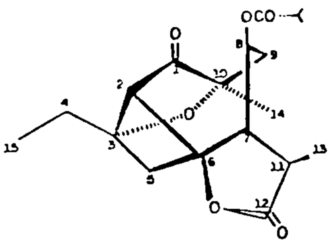

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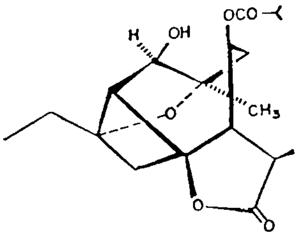

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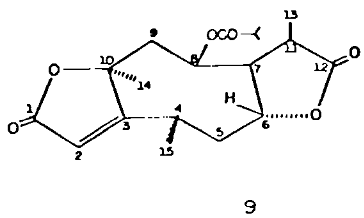

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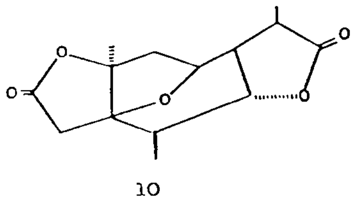

10

also shown to be an isomer of the starting material. It showed in the IR spectrum a strong absorption at 1755 cm^{-1} with shoulders at 1740 and 1765 cm^{-1} and the absence of the strong enolic band present in THZ(2). The ^{1}H NMR spectrum showed a sharp singlet at 5.93 ppm (1H), which was attributed to an isolated vinylic proton. It also showed a broad doublet at 5.24 (1H) and a complex signal at 4.70 ppm (1H), which were assigned to the C_8 and the C_6 protons. The chemical shifts and multiplicity shown by H-8, H-7 and H-6 (Table 1) are very similar to the data found for them in the spectrum of THZ(2), this observation suggested that this part of the molecule had not suffered any change.

Structure **9** proposed for this product, was mainly deduced from the ^{13}C NMR spectrum (Table 2). In this spectrum were observed three carbonyl singlets at 175.9, 177.6 and 177.9 ppm which were assigned to the ester group and the two γ-lactone functions. It also showed a singlet at 171.2 and a doublet at 116.4 ppm, which could be ascribed to the carbon atoms of the trisubstituted double bond of the α,β-unsaturated γ-lactone, by comparison with the data reported in the literature for the γ-lactone moiety of cardenolides.[11] The dilactone structure **9** proposed for this photoproduct, was supported by the 300 MHz ^{1}H NMR spectrum found for it (Table 1).

All attempts to saturate the double bond in 9 under normal catalytic conditions, were unsuccessful.

Methanolysis of **9** followed by treatment with toluenesulphonic acid in methanol, gave the dilactone **10**, in which the free hydroxyl group at C_8 has attacked the C_2–C_3 double bond. It showed a strong absorption at 1770 cm^{-1} in the IR spectrum. In the ^{1}H NMR spectrum two partially superimposed complex signals at 4.42 and 4.35 ppm were ascribed to H-8 and H-6. There was also observed the AB portion of an ABX system at 1.90 and 2.97 ppm, which was attributed to the C-9 methylene group. Two doublets at 2.58 and 2.70 ppm (J = 18 Hz) were assigned to the AB system due to the C-2 methylene.

The formation of photo THZ-C, **9**, could be explained by an initial cleavage α to the carbonyl group, to give a 1,5 biradical *a*, rearrangement of this biradical to the epoxy ketene *b* and subsequent rearrangement to the α,β-unsaturated γ-lactone found in **9**. This sequence of intermediates was proposed by Padwa[12] for the photoinduced rearrangement of 2,5-diphenyl-3(2H)-furanone, therefore the substituted 3(2H) furanone present in THZ, has suffered the rearrangement to the γ-lactone as an isolated moiety.

The isolation of product **3**, as the major photoproduct, indicates that the conformation shown in structure **2** is favored over other possible conformations of THZ.

X-ray crystallographic analysis of the three reaction products of the photolysis of tetrahydro zexbrevin (THZ) has been carried out.

Crystals of these compounds were obtained by slow evaporation of methanolic solutions. Crystal data are given in Table 3.

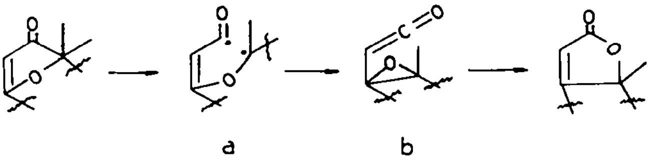

Table 3. Crystal data for phototetrahydro zexbrevin A, B and C

	PHOTO THZ-A	PHOTO THZ-B	11-ISOPHOTO THZ-C*
Mol. Formula	$C_{19}H_{26}O_6$	$C_{19}H_{26}O_6$	$C_{19}H_{26}O_6$
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions	a=16.766(5)	a=11.706(3)	a=11.405(3)
	b=12.185(5)	b=10.035(3)	b=7.189(2)
	c=8.949(2)Å	c=16.177(5)Å	c=23.184(5)Å
	V=1828.2 Å^3	V=1900.2 Å^3	V=1901.1 Å^3
	Z=4	Z=4	Z=4
Calculated density	ρ=1.27 g cm^{-3}	ρ=1.22 g cm^{-3}	ρ=1.22 g cm^{-3}
Observed(total) reflections	1383(1474)	2301(2966)	1432(1544)

* The X-ray crystallographic analysis was performed on a sample of 11-isophoto THZ-C, as we could not obtain an appropriate single crystal of photo THZ-C.

Table 4. Final atomic coordinates ($\times 10^4$) and isotropic thermal parameters ($\times 10^3$) in photo THZ-A. $U_{eq} = (V_{11} \times V_{22} \times V_{33})^{1/3}$

atom	x	y	z	U_{eq} (Å^2)
C(1)	1918(2)	2866(4)	5873(5)	44(1)
C(2)	1135(2)	3490(4)	6070(5)	45(1)
C(3)	537(2)	2583(3)	6332(5)	37(1)
C(4)	-232(3)	2695(4)	7277(5)	50(2)
C(5)	-650(3)	1955(4)	6156(6)	53(2)
C(6)	28(2)	2147(3)	5015(5)	39(1)
C(7)	306(3)	1225(3)	3970(5)	41(1)
C(8)	1189(3)	1226(4)	3574(5)	44(1)
C(9)	1761(3)	954(3)	4834(5)	43(1)
C(10)	1776(2)	1669(4)	6239(5)	44(1)
C(11)	-246(3)	1431(4)	2623(6)	52(2)
C(12)	-333(3)	2663(4)	2614(6)	52(2)
C(13)	4(4)	959(5)	1108(5)	63(2)
C(14)	-574(3)	3854(4)	7402(7)	68(2)
C(15)	2358(3)	1234(4)	7356(6)	59(2)
C(16)	1958(3)	2396(4)	1952(5)	46(1)
C(17)	2095(4)	3557(5)	1441(6)	63(2)
C(18)	1426(5)	3949(6)	491(11)	112(3)
C(19)	2873(4)	3661(6)	627(10)	92(3)
O(1)	2556(2)	3274(3)	5573(5)	70(1)
O(2)	-178(2)	3046(2)	4022(4)	47(1)
O(3)	-508(2)	3265(3)	1621(4)	69(1)
O(4)	1374(2)	2316(2)	2972(4)	43(1)
O(5)	2325(2)	1589(3)	1508(4)	70(1)
O(6)	994(2)	1682(2)	6946(3)	40(1)

Table 5. Final atomic coordinates ($\times 10^4$) and isotropic thermal parameters ($\times 10^3$) in photo THZ-B

$U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$

Atom	x	y	z	U_{eq} (Å^2)
C(1)	9122(3)	8823(3)	23(2	40(1)
C(2)	9380(3)	8366(4)	879(2)	44(1)
C(3)	8653(3)	9266(3)	1426(2)	43(1)
C(4)	9065(3)	10593(4)	1723(2)	55(1)
C(5)	8477(3)	8094(4)	2016(2)	50(1)
C(6)	8744(3)	7167(3)	1281(2)	42(1)
C(7)	7660(3)	6543(3)	911(2)	44(1)
C(8)	7487(3)	6679(3)	-13(2)	40(1)
C(9)	7157(3)	8104(4)	-303(2)	47(1)
C(10)	7880(3)	9236(3)	41(2)	43(1)
C(11)	7774(3)	5071(4)	1183(2)	52(1)
C(12)	9047(3)	4891(4)	1283(3)	58(1)
C(13)	7215(4)	3990(4)	700(3)	71(2)
C(14)	8222(4)	11242(4)	2320(2)	64(1)
C(15)	7666(4)	10536(4)	-427(2)	59(1)
C(16)	8498(3)	5773(4)	-1161(2)	54(1)
C(17)	9647(4)	5254(4)	-1453(2)	64(1)
C(18)	9887(7)	5498(13)	-2278(5)	226(6)
C(19)	9794(7)	3826(8)	-1165(5)	163(4)
O(1)	9756(2)	8921(3)	-562(1)	61(1)
O(2)	9540(2)	6094(2)	1412(1)	53(1)
O(3)	9607(3)	3892(3)	1275(2)	79(1)
O(4)	8542	6241	-392	44 *
O(5)	7629	5658	-1550	78 *
O(6)	7620	9417	912	45 *

Table 6. Final atomic coordinates (× 10^4) and isotropic thermal parameters (× 10^3) in 11-iso-photo THZ-C. $U_{eq} = (U_{11} \times U_{22} \times U_{33})^{1/3}$

Atom				
C(1)	3612(4)	5051(6)	252(2)	65(1)
C(2)	2408(4)	5736(6)	300(2)	63(1)
C(3)	1822(4)	4665(5)	669(2)	48(1)
C(4)	591(4)	4894(6)	903(2)	53(1)
C(5)	453(3)	6763(5)	1194(1)	50(1)
C(6)	1487(3)	7282(5)	1579(1)	43(1)
C(7)	1855(3)	5873(5)	2042(1)	45(1)
C(8)	2918(3)	4654(5)	1907(2)	47(1)
C(9)	2744(3)	2932(5)	1528(2)	51(1)
C(10)	2591(4)	3126(5)	869(2)	53(1)
C(11)	2074(3)	7092(6)	2579(2)	56(1)
C(12)	1463(4)	8866(6)	2443(2)	61(1)
C(13)	1677(5)	6264(9)	3146(2)	83(2)
C(14)	-321(5)	4642(7)	423(2)	78(2)
C(15)	2202(4)	1266(6)	617(2)	70(2)
C(16)	4941(3)	5486(7)	1827(2)	65(1)
C(17)	5807(4)	6867(7)	1582(2)	70(1)
C(18)	5274(4)	8634(9)	1352(3)	90(2)
C(19)	6549(5)	5937(10)	1126(2)	100(2)
O(1)	4414(4)	5565(5)	-35(2)	98(1)
O(2)	3732(3)	3551(4)	611(1)	62(1)
O(3)	1154(2)	8972(4)	1883(1)	58(1)
O(4)	1245(4)	10145(5)	2757(1)	96(2)
O(5)	3821(2)	5872(4)	1683(1)	49(1)
O(6)	5202(3)	4160(6)	2119(2)	100(2)

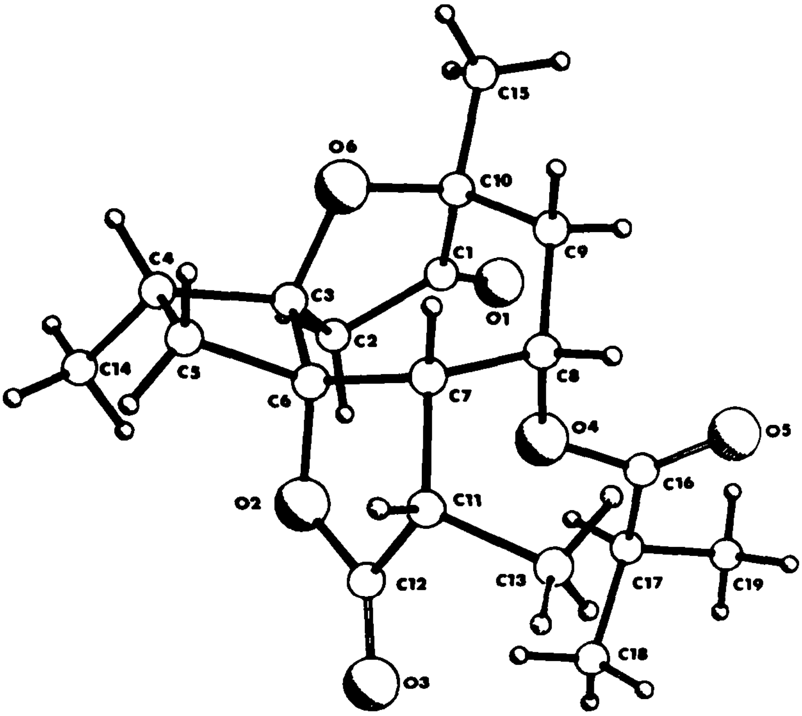

Fig. 1. The molecular structure of phototetrahydro zexbrevin A.

Three dimensional intensity data were collected by the θ-2θ scan method on a Nicolet R3m automated diffractomer using monochromatized Cu-K_α radiation (λ = 1.54178 Å). Lorentz and polarization corrections but not for absorption or extinction were applied to the three sets of data. Anomalous-dispersion corrections were applied to the scattering factors for the oxygen and carbon atoms.

The three non centrosymmetric structures were solved by direct methods. The non-hydrogen atoms were located among the 30 highest peaks of the best E map. The hydrogen atoms were found from a Fourier difference map. The structures were refined by blocked-cascade least-squares, with a fixed isotropic thermal parameters for all other atoms. The final weighted and unweighted R factors are respectively, of 0.059 and 0.072 for photo THZ-A; of 0.052 and 0.055 for photo THZ-B; and 0.052 and 0.066 for 11-iso-photo THZ-C. The quantity minimized in the least squares calculations was $\Sigma\omega(F_o - F_c)^2$ with a statistical weight of the form $\omega = \{\sigma^2(F_o) + K(f_o)^2\}^{-1}$. The final K values for the photo THZ-A, photo THZ-B and 11-iso-photo THZ-C are 0.00594, 0.00124 and 0.00447, respectively.

All computations were performed in the laboratory on a Nova minicomputer with the SHELXTL system of programs.[13]

Tables 4–6 list the final atomic co-ordinates for the three structures and the arrangement of atoms in the molecules is shown in Figs. 1–3.

Detailed results will be published elsewhere.

EXPERIMENTAL

Unless otherwise noted, the following general information applies. M.ps are uncorrected. IR spectra were recorded in $CHCl_3$ and ^{13}C NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported as δ ppm relative to TMS, as internal standard. Analyses were determined by Dr Pascher, Bonn, Germany. Photolysis were carried out with Rayonet Photochemical Reactor (Southern New England Ultraviolet Co.) equipped with RPR-2537 Å lamps.

Isolation of Zexbrevine A

The zexbrevine A **1**, was isolated from *Zexmenia brevifolia* as previously described.[6]

Catalytic hydrogenation of Zexbrevine A

Zexbrevine A, 1 (500 mg), in AcOEt (50 ml) was stirred under H_2 in the presence of 5% Pd/C (50 mg) until the H_2 uptake ceased. The solution was filtered through celite and the solvent removed under vacuum. The product obtained was crystallized from acetone-hexane to give tetrahydrozexbrevine, THZ, 2, m.p. 156–158° (450 mg) (lit.[6] 157–157°); UV λ_{max}^{EtOH} nm 260 (ϵ, 12,000); IR $\nu_{max}^{CHCl_3}$ cm^{-1} 1770, 1735, 1705, 1600. The 300 MHz ^1H NMR and ^{13}C NMR spectra are listed in Table 1 and Table 2.

Photolysis of tetrahydrozexbrevine 2

A solution of **2** (500 mg) in MeOH (300 ml) in quartz vessel was perfused with Argon for 30 min and then irradiated. The reaction was followed by TLC. After 1 hr the starting material had disappeared. The solvent was removed under vacuum to yield a gummy material, which was chromatographed over SiO_2 (10 g). Elution with AcOEt–hexane (1:4) gave photo THZ A **3** (250 mg, 50% yield), m.p. 217–220° (from acetone–hexane), IR ν_{max}, cm^{-1} 1765, 1745, 1730. Found C, 65.07, H, 7.42; O, 27.06; $C_{19}H_{26}O_6$

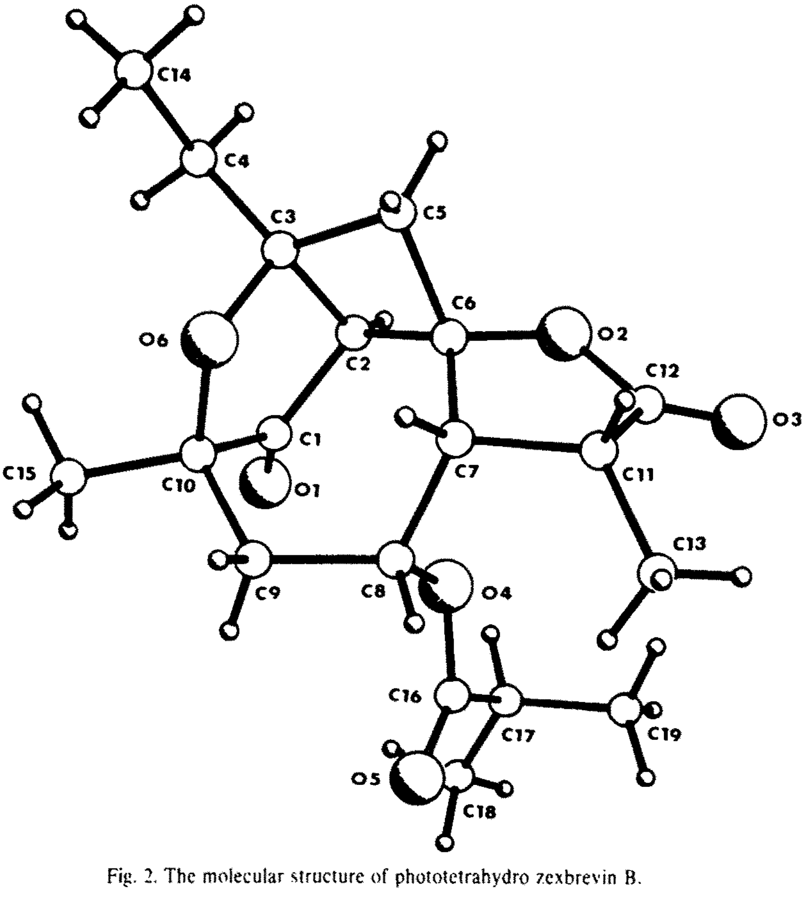

Fig. 2. The molecular structure of phototetrahydro zexbrevin B.

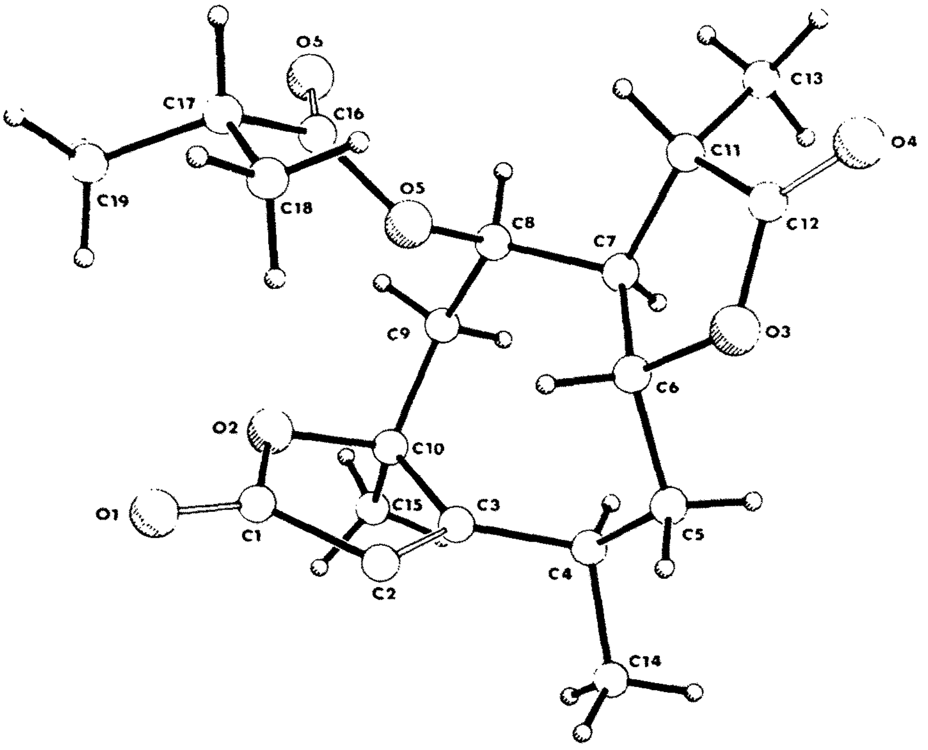

Fig. 3. The molecular structure of 11-iso-phototetrahydro zexbrevin C.

requires C, 65.12; H, 7.48; O, 27.40%. The 300 MHz ^{1}H NMR and ^{13}C NMR spectra are listed in Table 1 and Table 2.

Further elution with the same solvent gave photo THZ B **7** (50 mg 10% yield), m.p. 130–135°; the analytical sample showed m.p. 146–148° (acetone-hexane); ν_{max}, cm^{-1} 1780, 1755, 1735; Found: C, 64.89; H, 7.59; O, 27.88; $C_{19}H_{26}O_6$ requires: C, 65.12; H, 7.48; O, 27.40%. The 300 MHz ^{1}H NMR and ^{13}C NMR spectra are listed in Table 1 and Table 2.

Elution with AcOET–hexane (1:1) gave photo THZ "C" (140 mg 28% yield). The analytical sample showed m.p. 200–202° (acetone-hexane) IR ν_{max} cm^{-1} 1755, 1765 (sh), 1740 (sh), 1640, 860. Found C, 65.35; H, 7.56; O, 27.90. $C_{19}H_{26}O_6$ requires: C, 65.12; H, 7.48; O, 27.40%. The 300 MHz ^{1}H NMR and ^{13}C NMR spectra are listed in Table 1 and Table 2.

Sodium borohydride reduction of photo THZ-A, **3**

Photo THZ-A **3** (100 mg) in methanol (5 ml) was treated with $NaBH_4$ (100 mg) in MeOH at 5° for 15 min. Water was added, the aqueous solution was extracted with AcOEt. The organic solution was washed with water, dried over Na_2SO_4 and the solvent removed. The product obtained was crystallized from methanol to yield **4** m.p. 185–187°; IR ν_{max}cm^{-1} 3500, 1765, 1725. ^{1}H NMR δ: 1.02 (d, J 6.5, H-15), 1.12 (d, J7, H-3′ and H-4′), 1.24, (d, J7, H-13), 1.30 (s, H-14), 4.16 (d, d, J9, 7H-1); 4.96 (d,d,d, J1, 3,5, 4, H-8) MS (low resolution) at *m/z* 352 (M^+); 264 (M^+–$HOCOC_3H_7$); 246, 191, 165 (33.9) (61); 71 (100).

Huang–Minlon reduction of photo THZ-A

The title product **3** (300 mg), in freshly destilled ethylenglycol (5 ml), was treated with hydrazine (64%, 1 ml) and KOH (0.5 g). The reaction mixture was refluxed for 1 hr in argon. The excess of hydrazine was removed until the temperature was rised to the ethylenglycol b.p. 170°. The reflux was maintained for 1 hr more and the reaction mixture was poured onto ice, acidified with dil HCl, and extracted with AcOEt. The organic layer was washed with sat $NaHCO_3$ sol. and water, dried and the solvent removed. The crude product was chromatographed over SiO_2 (15 g). Elution with AcOEt–benzene (1:4) gave a crystalline product **5a**, (200 mg), which was recrystallized from acetone-hexane to constant m.p. 158–160°. IR ν_{max} cm^{-1} 3400, 1750. Found: C 67.55; H, 8.35; O, 23.91. $C_{15}H_{22}O_4$ requires: C, 67.64; H, 8.33; O, 24.03%. ^{1}H NMR δ: 1.04 (d, J 6.5, H-15), 1.36 (d, J7, H-13), 1.38 (s, H-14), 4.88 (d,d,d, J5, 8, 12; H-8) (in Py-d_5: 5.02, H-8). The ^{13}C NMR spectrum is in Table 2.

Dehydration of **5a**

5a(100 mg) in dry pyridine (2.5 ml) was treated with $SOCl_2$ (0.5 ml) in an ice bath for 1 hr; poured onto ice and extracted with AcOEt. The organic solution was washed with dil HCl, water, sat $NaHCO_3$, water, dried and solvent removed under vacuum, to yield a crystalline product, **6** (70 mg). The analytical sample was obtained by crystallization from hexane and showed m.p. 75–78°; IR ν_{max} cm^{-1} 1770; ^{1}H NMR δ: 1.1 (d, J7, H-15), 1.36 (d, J7, H-13), 1.45 (s, H-14), 3.06 (q, H-11); 5.18 (br d; H-8).

Methanolysis of photo THZ-A, **3**

Product **3** (25 mg) in dry MeOH (5 ml) was treated with NaOMe (from 11 mg of Na) for 2 hr at room temp under Ar. After addition of one drop of AcOH, the solvent was removed under vacuum, water was added, and the product extracted to AcOEt, washed with water, dried and the solvent removed. The analytical sample of **5b** showed m.p. 184–185°. IR ν_{max} cm^{-1} 3450, 1760; ^{1}H NMR δ: 1.07 (d, J7, H–15); 1.4 (d, J7, H–13); 1.35 (s), H-14); 4.85 (d,d,d J4, 711, H-8). MS (low resolution *m/z* 280 (M^+); 237 (M^+–C_3H_7); 181 (M^+–C_3H_7–C_2O_2); 166, 153, 139, 137, 125 (100%).

Sodium borohydride reduction of photo THZ-B **7**

The photoproduct **7** (20 mg) in methanol (5 ml), was treated with $NaBH_4$ (20 mg) at −10° for 30′. The reaction was followed by TLC. Water and a drop of AcOH were added. The reaction mixture was extracted with AcOEt and treated, in the usual way, to yield the dihydro derivative **8** (15 mg). The analytical sample showed m.p. 119–121°. IR ν_{max} cm^{-1} 3500, 3200, 1775, 1745; ^{1}H NMR δ $CDCl_3$: 1.16 (d, J7.5, H-3′ and H-4′), 1.07 (d, J7, H-13), 0.93 (t, J7, H-15), 1.35 (s, H-14), 1.62 (m, H-4), 2.05 (m, H-9), 2.25 (s, H-5), 2.36 (h, J7, H-2′), 2.86 (q, d, J11, 7; H-11), 3.25 (d,d, J2, 11, H-7), 3.11 (d, J4, H-2), 3.5 (d, J11, OH), 4.1 (d,d J4, 11; H-1), 5.22 (m, H-8); δ Eu(fod)$_3$: 3.50 and 2.45 (d, J 7.5, H-3′, H-4′); 4.54 (d, J7, H-13), 1.35 (t, J7, H-15), 2.14 (s, H-14), 2.35 (m, H-4), 4.20 and 6.25 (m, H-9, J3.70 and 3.85 (s, H-5), 5.90 (h, J7, H-2′), 6.80 (q, d; H-11); 6.25 (d,d; J2, 11; H-7), 6.15 (d, J4, H-2), 8.51 (m, H-8); 10.00 (d, d; J4, 11.0; H-1); MS at *m/z* 281, 264, 193, 109, 71 (100%).

Oxidation of **8** with Jones reagent in the usual manner gave the photo THZ-B 7.

Preparation of product 10

Photo THZ-C **9** (50 mg) in dry MeOH was treated with NaOMe (prepared from 20 mg of Na). The reaction was left for 2 hr at room temp. The oily residue obtained after the usual work up, was treated with p-TosOH (10 mg) in MeOH (5 ml) at room temp for 48 hr. The oily product obtained was purified by preparative TLC (AcOEt–hexane 1:9) to yield **10** (20 mg), m.p. 200–202°. IR ν_{max} 1770 cm^{-1}; ^{1}H NMR δ: 1.20 (d, J7, H-13 and H-15); 1.55 (s, H-14); 1.90 (d,d J3, 10; H-9); 2.97 (d,d, J10, 15; H-9'); 2.58 (d, J18, H-2a); 2.70 (d, J18, H-2b); 4.35 (d,d,d; J8, 2, 2; H-6); 4.42 (d,d,d; J3, 6, 10; H-18); δ Eu(fod)$_3$: 4.57 and 4.80 (d, J18.6, H-2a and H-2b), 4.07 (d, d, J9, 14.6, H-9 and 9'), 5.27 (d,d,d; J3, 6, 10; H-8), 5.35 (d, d, d, J3, 9, 10; H-6) MS (low resolution) at *m/z* 280 (M^+–H_2O); 165 (M^+–H_2O–$C_5H_5O_2$); 125 (base peak $C_7H_5O_2$): 97 ($C_5H_5O_2$).

Preparation of 11-*iso-photo THZ-C*

The photo THZ-C, **9** (50 mg) in methanol (20 ml) was treated with K_2CO_3 (50 mg) in water (2 ml) for 4 hr at room temp. The product obtained after normal work up, was recrystallized from acetone-iso-propyl ether to constant m.p. 178–180°; ν_{max} cm^{-1}: 1750, 1765, 1640. ^{1}H NMR δ: 5.92 (s, H-2); 5.16 (br. d. J8, H-8); 4.49(d,d,d,J5.5 10; H-6); 3.00 (d,d,J8, 16; H-9a), 1.44 (s, H-14), 1.36 (d, J6; H-13), 1.25 and 1.17 (2d, J7, H-18 and H-19), 1.11 (d, J7, H-15).

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