CHARACTERIZATION AND PHOTOCHEMICAL REACTIVITY OF TRIPHENODIOXAZINE N-OXIDES

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Abstract - N-Oxidation of triphenodioxazine (1) by m-chloroperbenzoic acid in chloroform yields the corresponding 7-oxide (2) and 7,14-dioxide (3). Their coloured solutions in organic solvents are very sensitive to light. Irradiation in the visible in various solvents leads to deoxygenation. The photoreaction of compound 3 in chloroform yields also N(7)-(6'-triphenodioxazinyl)-3,7-dihydrotriphenodioxazin-3-one (4) and the corresponding N-oxides 5 and 6, as well as 1-, 3- and 13-chlorotriphenodioxazine 7-oxides (7-9). The nature of the excited state of these N-oxides is discussed and a mechanism for product formation is proposed.

In previous studies[1,2] we considered the formation of triphenodioxazines from o-aminophenols as well as the redox behaviour of these heterocycles, related to biologically occurring ommochromes, a class of pigments present in the photoreceptors of invertebrates.[3] In pursuance of our effort to explore the chemistry of these little known substances, we presently report the synthesis and photochemistry of triphenodioxazine N-oxides.[4]

RESULTS

Treatment of a triphenodioxazine (1, 1 mM) solution in chloroform with m-chloroperbenzoic acid (3 mM) at 4°C in the dark for 24 h and usual work up yields a mixture of two products. These were separated and purified by chromatography and shown to be the 7-oxide 2 and the 7,14-dioxide 3, obtained as dark red crystals yielding as a pink and respectively a blue solution. In both cases, signals attributable to N→O stretching and to the quinone diimine system were identified in the ir spectrum (Table 1). In the nmr spectrum, a large anisotropic effect on the protons peri to the

N-oxide function(s) was observed, as expected from the analogy with literature data.[5] Mass spectra were also in accordance with the structure and showed the diagnostic[6] M-16 (or respectively M-16 and M-32) peaks. The absorption band in the visible gradually shifts to the red in going from the parent base 1 to the mono oxide 2 and the dioxide 3. (Table II). The spectrum of the protonated form of these N-oxïdes (recorded in 60% H_2SO_4) is practically superimposable to that of protonated 1. This is expected, as protonation of the oxygen atom in the N-oxide function cancels the contribution of charge transfer from oxygen to the heterocyclic ring in the excited state.[5]
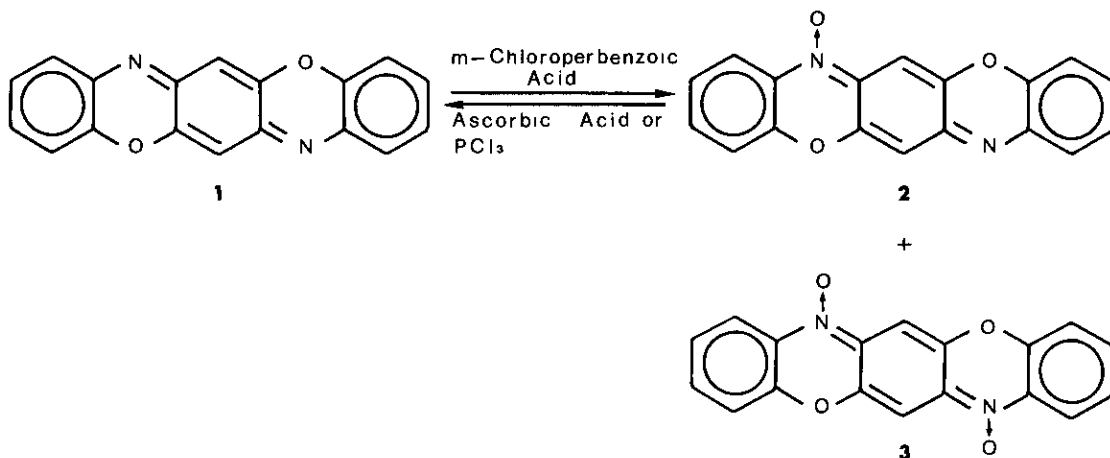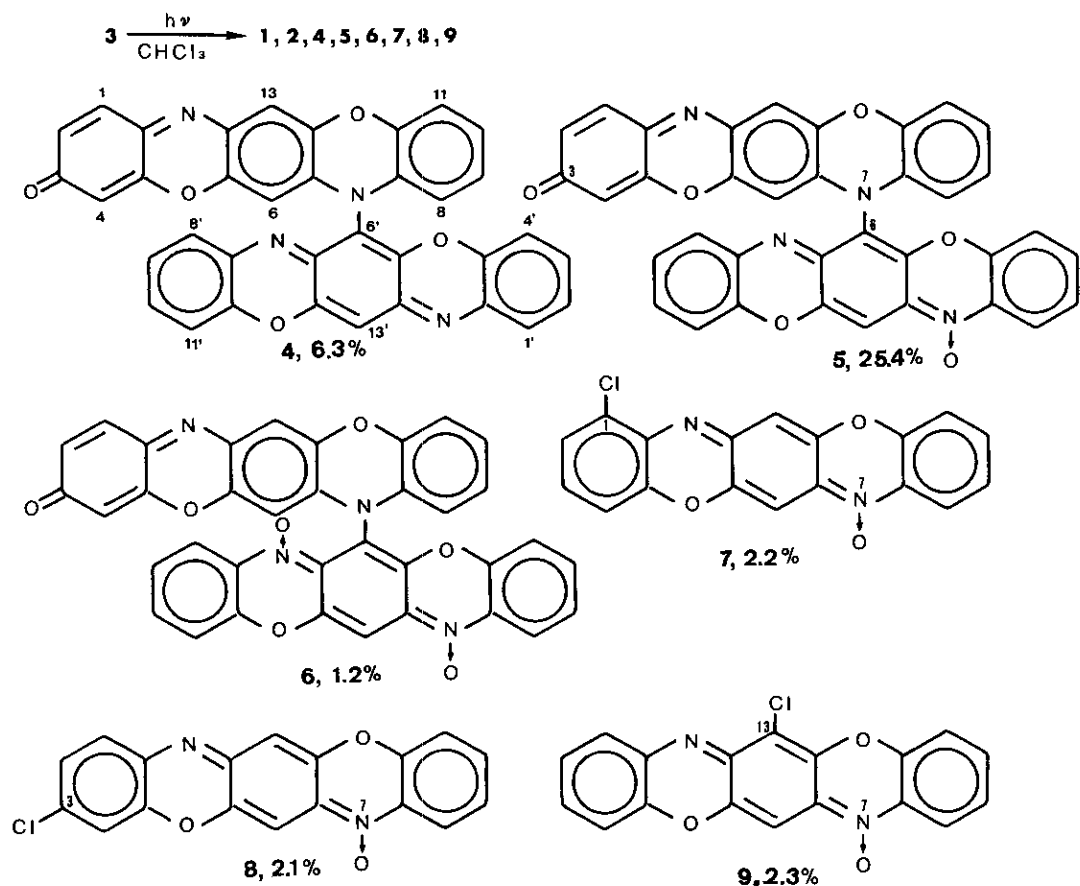

Scheme I

Both N-oxide 2 and N,N'-dioxide 3 are deoxygenated to triphenodioxazine 1 in a dark reaction when treated with ascorbic acid in mixed chloroform-methanol solution (7:3 by volume) or when refluxed with phosphorus trichloride in chloroform (Scheme I).

Both compounds are strongly photoreactive and dilute solutions prepared for spectroscopic characterization must be protected from room light in order to obtain reproducible and meaningful data. The rate of photodecomposition and the products formed depend on substrate concentration, solvent, temperature and wavelength of incident light. As an example, a 10^{-7} M solution of compound 3 in chloroform (1 cm optical path) undergoes complete bleaching in 30 sec when exposed to a 650 W sunlight lamp at a distance of 10 cm, and a 10^{-3} M solution is bleached in 15 min under the same condition.

As for the products formed, the decomposition of N-oxide 2 in a variety of solvents* yields

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* A complete study of the solvent effect in the photoreaction of these N-oxides is hindered by their limited solubility. A good solvent is chloroform. There is a limited solubility in other polar non protic solvent, such as ethers or acetonitrile, but practically none in benzene or alcohols.

$$3 \xrightarrow[\text{CHCl}_3]{h\nu} 1,2,4,5,6,7,8,9$$

Scheme II

quantitatively the parent base 1. Isosbestic points are neatly obeyed during the reaction and TLC analysis shows no other products. The N,N'-dioxide 3 yields only the mono N-oxide 2 and completely deoxygenated 1 in some solvents, e.g. acetonitrile or tetrahydrofuran, whereas the reaction in chloroform is more complicated and yields several highly coloured products along with compounds 1 and 2 (Scheme II where yields are also indicated).

The new products were isolated by preparative tlc and obtained as crystalline materials. Their identification was based on elemental analysis, spectroscopic characterization and chemical properties. The complex ^{1}H nmr spectrum of one of these compounds, a yellow material, contains signals attributable to two different heterocyclic systems, viz. a condensed phenoxazinonic system (labeled A in Table I) and a triphenodioxazine system (B in the Table). Examination of the multiplicity of the nmr signals, comparison with the spectra of model compounds, presence of the molecular ion at 586 m/z in the mass spectrum and other spectroscopic characteristics (Table I), all support the attribution to this compound of formula 4, in which a triphenodioxazin-3-one ring is linked through the nitrogen in position 7 to the carbon in position 6' of a triphenodiaxazine

TABLE 1

Relevant spectroscopic properties for compounds 1, 2, 3, 4, 5, 7, 8, 9.

	^{1}H NMR in CD_2Cl_2, δ										MS	IR
	H-1	2	3	4	6	8	9	10	11	13	M$^+$	cm^{-1}
1	7.45 2H,d^b	7.23 2H,t^b	7.10 2H,t^b	6.5 2H,s							286	1570,1468
2	7.41 d^c	7.20 t^c	7.21 t^c	7.08 d^c	7.12 s	8.02 d^c	7.30 t^c	7.45 t^c	7.18 d^c		302	1575,1270
3	8.38 2H,d^c	7.60 2H,t^c	7.73 2H,t^c	7.47 2H,d^c	7.35 2H,s						318	1580,1270
4 A	8.05 d^d	7.47 d^d		6.40 s	6.30 s		7.03 4H,m			7.02 s	586	1670,1575
4 B^a	7.55 2H,d^e	7.20 2H,t^e	7.30 2H,t^e	7.11 2H,d^e						6.45 s		
5 A	8.01 d^d	7.55 d^d		6.38 s	6.29 s		7.01 4H,m			7.00 s	602	1670,1570,1260
5 B^a	8.03 d^f	7.32 t^f	7.57 t^f	7.30 d^f		7.54 d^g	7.32 t^g	7.40 t^g	7.21 d^g	7.02 s		
7		7.24 d^f	7.12 t^f	6.97 d^f	7.12 s	8.03 d^h	7.31 t^h	7.46 t^h	7.24 d^f	6.57 s	336	1570,1260,1000
8	7.31 d^i	7.11 d^i		7.04 s	7.16 s	8.05 d^h	7.28 t^h	7.41 t^h	7.18 d^h	6.47 s	336	1570,1260,950
9	7.52 d^h	7.21 t^h	7.28 t^h	7.08 d^h	7.11 s	8.05 d^j	7.33 t^j	7.50 t^j	7.35 d^j		336	1570,1260,950

Nmr signals verified by homo-decoupling experiments.

a, protons in primed position. b, J = 9.21 Hz. c, J = 8.04. d, J = 8.46. e, J = 8.01. f, J = 8.10. g, J = 8.14. h, J = 8.07. i, J = 8.41. j, J = 8.70.

TABLE 11

Electronic spectra of compounds 1, 2, 3 in chloroform and H_2SO_4 (60%)

	Absorption, λ max (log ε) nm	Emission,^{a} λ max nm
1	443 (sh), 471 (4.61), 505 (4.74)	525, 558
2	458 (sh), 527 (4.12)	610 (weak)
3	350 (sh), 535 (4.34)	630 (very weak)^b
1$^+$	592 (sh), 640	
3$^+$	590 (sh), 638	

a. By excitation at 500-550 nm of 10^{-5} M solutions.

b. A stronger emission at 603 and 670 nm is observed in glassy 2-methyltetrahydrofuran at 77 K.

ring.

The main product, a dark red solid, shows again a complex nmr spectrum which can be analogously resolved in two separated systems (see Table I). This compound exibits the molecular peak at 602 m/z as well as a conspicuous peak at M^+-16 in the mass spectrum, and is easily transformed into product 4 by treatment with ascorbic acid. Thus, this is a N-oxide of compound 4 and precisely the 14'-oxide (structure 5) as deduced from the shifts observed in part B of the nmr spectrum of this product when compared with deoxygenated 4. A dark violet product, isolated in minute amounts, shows the molecular peak at 618 m/z and M-16 and M-32 peaks in the mass spectrum and in easily reduced to compound 4. Thus, it is recognized as the 7',14'-dioxide 6.

The other products obtained from this photoreaction contain chlorine. Three pink products are recognized as chlorinated triphenodioxazine N-oxides, as shown inter alia by the molecular peak (336 m/z, with a peak at 338 with 33% intensity) and M -16 peak (320, 322) in the mass spectrum. Examination of the nmr spectrum (Table I) allows the assignment to these compounds of the structures of 1-chloro (7), 3-chloro (8) and 13-chlorotriphenodioxazine 7-oxide (9). The three corresponding chlorotriphenodioxazines are also obtained in small amounts as yellow crystalline materials characterized by a strong fluorescence.

Dark experiments under otherwise identical conditions left the dioxide 3 unchanged, showing that the observed reaction is indeed photoinitiated and the results are not an artifact due to reaction or isolation conditions.

DISCUSSION

Summing up, the photodecomposition of triphenodioxazine N-oxides involves deoxygenation in the case of mono N-oxide 2 and deoxygenation, accompanied, at least in chloroform, by further reactions, such as oxygenation at position 3 and chlorination at positions 1,3 and 13 as well as coupling of two rings to yield products 4-6, in the case of N,N'-dioxide 3.

Deoxygenation is usually not the predominating photochemical process in heterocyclic N-oxides and related compounds, isomerization being much more important.[7] The bis nitrone 9, a reasonable model for N,N'-dioxide 3, undergoes photoisomerization to a not isolated oxaziridine derivative and then cleavage to p-benzoquinone and phenylnitrene[8] (Scheme III).

However, it has been previously observed that deoxygenation tends to become the dominant reaction with compounds with low singlet excited state energy,[7] such as the present N-oxides (Singlet energy 48-50 kcal M^{-1}).With N-oxides 2 and 3 decay of the singlet excited state is predominantly non radiative, analogously to what generally observed with N-oxides.

Thus, the parent base is strongly fluorescent, whereas N-oxide 2 shows only a weak emission and the N,N'-dioxide 3 is virtually non emitting at room temperature, although the absorbtion spectra of the three compounds are very similar in shape and extinction coefficients, aside than for the progressive red shift. Furthermore, fluorescence from dioxide 3 is easily observed with the expected shape and position at 77 K in glass* (Table II). Since a significant change of the rate

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* No phosphorescence is detected under this condition.
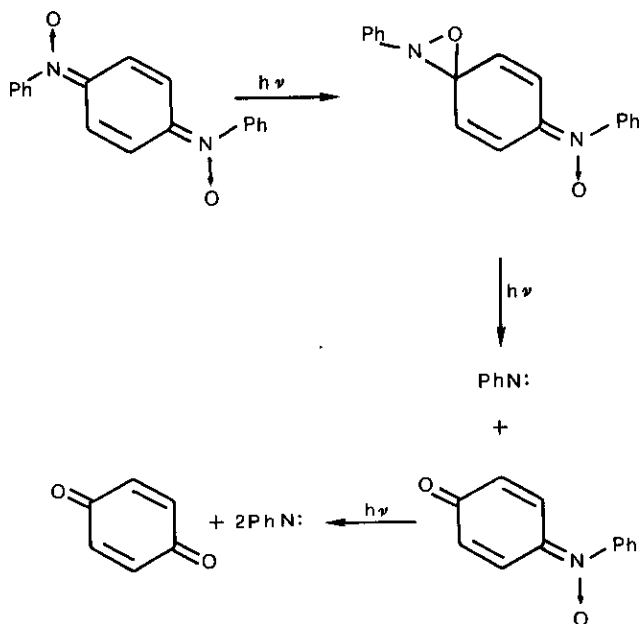
Scheme III

of emission with temperature is unlikely and intersystem crossing is usually negligible in N-oxides, this difference has to be attributed to a change in the rate of internal conversion.

In lower members of the series of heterocyclic N-oxides chemical reaction, initiated by a shift of the oxygen atom is an important part of internal conversion from the excited singlet state. In the present case there is no oxygen shift, but electron density in the N→O function is certainly strongly modified in the excited state. Thus, the oxygen atom acquires a radicalic character, and the observed photochemical reaction can be understood as a hydrogen abstraction. Indeed, the relative quantum yield (measured at 545 nm) for the decomposition of N,N'-dioxide 3 in chloroform, tetrahydrofuran and acetonitrile is respectively 1, 0.3, and 0.01 and thus depends on the strength of the C-H bond in the solvent. Furthermore, no photoreaction takes place in the presence of acetic acid, showing that protonation of the oxygen atom inhibits the charge transfer character of electronic excitation, and thus the acquiring of a radicalic character by the oxygen atom.

A plausible mechanistic pathway for the reaction is illustrated in Scheme IV. Thus, the photochemical excitation of N,N'-dioxide leads to hydrogen abstraction from the solvent, and radical 11 cleaves to N-oxide 2, which undergoes photochemical deoxygenation with a similar mechanism. In chloroform, radical 11 may undergo direct deoxygenation by reaction with the
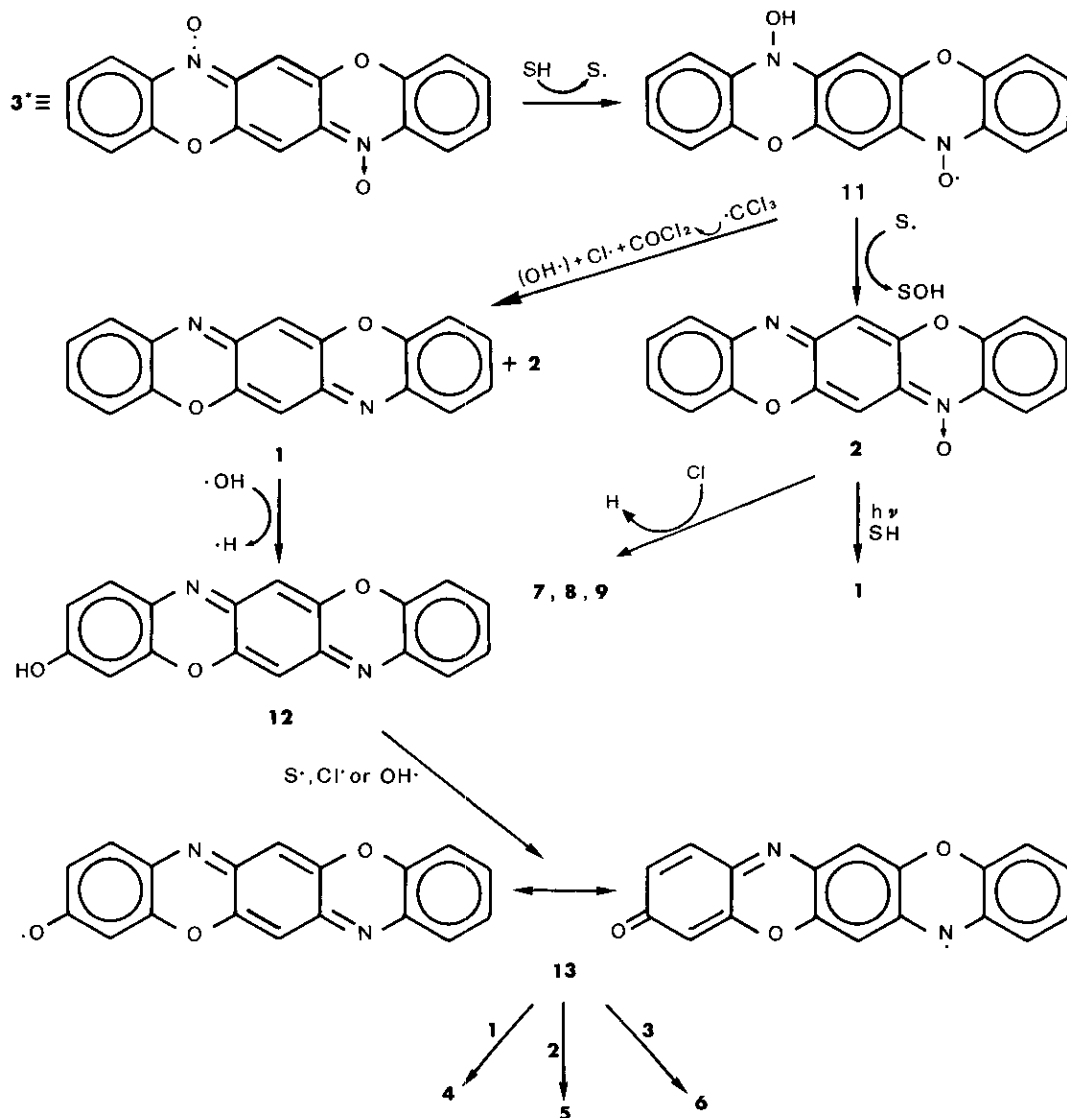
trichloromethyl radical, thus accounting in part for the particular efficiency of the photodecomposition in this solvent, and availability of Cl; and OH' radicals leads to attack onto triphenodioxazine 1 or the corresponding 7-oxide 2. The hydroxyl radical attacks at position 3, the chlorine radical at positions 1,3 and 13. The selectivity is due to stabilization of the intermediate radicalic adducts by mesomeric forms involving the radical site on a nitrogen atom. This reaction yields the chlorinated products 7, 8 and 9 along with 3-hydroxytriphenodioxazine

12. The first three compounds are among the isolated products, while the last one is not found due to the easy hydrogen abstraction from the phenolic position by the free radicals present in solution. Extensively delocalized and stable radical 13 is thus formed and trapped by triphenodioxazine 1 or the N-oxides 2 and 3 always attacking, as expected, onto the quinone position 6 to yield the observed products 4, 5 and 6. Formation of the hydroxy derivative 12 is supported by the occasional finding in the photodecomposition mixture of 3-(3'-chlorobenzoyloxy) triphenodioxazine (14), arising by esterification by traces of m-chlorobenzoic acid present in not sufficiently purified samples of the dioxide.

In conclusion the excited states of these N-oxides react essentially by hydrogen abstraction, and the evolution of the primarily formed radical explains the complex pattern observed in the photoreaction, mainly leading to the oxidative coupling of two triphenodioxazine ring and thus to new bichromophoric pigments.
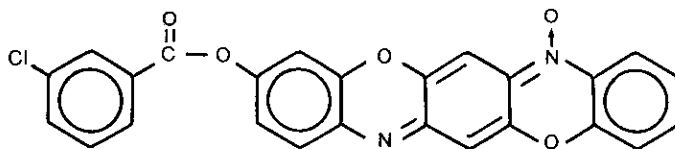
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EXPERIMENTAL

The following spectroscopic apparatus were used: Perkin-Elmer 550S spectrometer for uv, and PE-399-spectrometer for ir. Bruker 270 MHz and 500 MHz spectrometers for nmr using tetramethylsilane as internal reference and Varian/Finnigan CH7a and MAT-312 apparatus for ms. Aminco Bowman MPX spectrofluorometer for emission studies. Melting points are uncorrected. Microanalyses were performed by Divisione di Microanalisi dell'Istituto Farmacologico Italiano di Napoli. Tlc was performed on silica plates F-254, 0.25 mm with fluorescent baking (Merck).

N-Oxidation of Triphenodioxazine with m-Chloroperbenzoic acid in Chloroform. To a solution of 286 mg (1mM) of 1, dissolved in 300 ml of chloroform, 519 mg (3 mM) of m-chloroperbenzoic acid was added slowly under ice-cooling and the mixture was allowed to stand at 4°C, 24 h, in the darkness. The chloroform solution was shaken with 40% sodium carbonate solution, washed with water, dried on anhydrous sodium sulphate, concentrated in vacuo, placed on TLC plates and developed with chloroform-methanol (99:1); with the separation of a pink and a blue band corresponding to products 2 (32 mg) and 3 (240 mg).

Triphenodioxazine-7-oxide (2). From the reaction mixture 2 was isolated as red crystals, mp 130°C (decomp.), Rf 0.6 (chloroform-methanol 98:2). Anal. Calcd. for $C_{18}H_{10}N_2O_3$: C, 71,52; H, 3.33; N, 9.27. Found: C, 71.49; H, 3.37; N, 9.31.

Triphenodioxazine-7, 14-dioxide (3). From the reaction mixture, compound 3 was isolated as red-dark crystals of mp 120°C (decomp) and Rf 0.5 (chloroform-methanol 98:2).

Anal. Calcd. for $C_{18}H_{10}N_2O_4$: C, 67.92; H, 3.17; N, 8.80. Found: C, 67.89; H, 3.20; N, 8.76.

Deoxygenation Reaction of Triphenodioxazine-7-oxide (2) and of Triphenodioxazine-7,14-dioxide (3) with Ascorbic Acid. A solution of 30 mg of 2 and 20 mg of ascorbic acid in 20 ml of a chloroform-methanol mixture (7:3) was stirred for 2h, in the darkness at room temperature. The mixture, diluted with water and extracted many times with chloroform, afforded 26 mg of 1.

A solution of 30 mg of 3 in 40 ml of a chloroform-methanol mixture (7:3) was treated as above with 37 mg of ascorbic acid, for 4 h. Work up in the same manner yielded 25 mg of 1.

Photodecomposition Reaction of Triphenodioxazine-7-oxide (2) and Triphenodioxazine-7,14-dioxide (3) in chloroform. A solution of 100 mg of 2 in 300 ml of chloroform in a quartz tube was exposed to a direct superphot lamp, Osram 650 W, at a distance of 10 cm and at 25°C. The photodecomposition proceeded regularly with an isosbestic point at 483 nm indicating the quantitative 2 — 1 conversion. After completion of the decomposition, the reaction mixture was evaporated in vacuo and yielded 94.7 mg of 1.

A solution of 600 mg of 3 in 1000 ml of chloroform was irradiated as above. After the end of the decomposition, the reaction mixture was evaporated in vacuo, placed on tlc plates and developed with chloroform-methanol (98:2) to yield eight products: 1 (8.6 mg, 1.5%), 2 (12.6 mg, 2.3%), 4 (34.8 mg, 6.3%), 6 (7.2 mg 1.2%), 5 (144 mg, 25.4%), 7 (14.1 mg, 2.2%), 8 (13.2 mg, 2.1%), 9 (14.4 mg, 2.3%).

N(7)-(6'-Triphenodioxazinyl)3,7-dihydrotriphenodioxazin-3-one (4) Yellow crystals, mp 170°C (decomp.) and Rf 0.4 (chloroform-methanol 97:3); uv (chloroform): λ max (log ϵ) 518 (4.6) nm, 483 (4.5), 451$_s$, 420$_s$.Anal. Calcd. for: $C_{36}H_{18}N_4O_5$: C, 73.71; H, 3.09; N, 9.55. Found: C, 73.67; H, 3.11; N, 9.60.

N(7)-(6'-Triphenodioxazin-14'-oxide-yl)3,7-dihydrotriphenodioxazin-3-one (5). Red-blue crystals, mp 140°C (decomp.) and Rf 0.3 (chloroform-methanol 97:3); uv (chloroform): λ max (log ϵ) 513$_s$ nm, 534 (4.28). Anal. Calcd. for: $C_{36}H_{18}N_4O_6$: C, 71.75; H, 3.01; N, 9.29. Found: C, 71.61, H, 3.16; N, 9.45.

1-Chlorotriphenodioxazine-7-oxide (7). Red crystals, mp 140°C (decomp) and Rf 0.6 (chloroform-methanol 98:2); ir (chloroform): 1575 cm^{-1}, 1265, 900; uv (chloroform): λ max (log ϵ) 502s nm, 525 (4.03). Anal. Calcd. for $C_{18}H_9ClN_2O_3$: C, 64.19; H, 269; N, 8.32. Found: C, 64.13; H, 2.62; N, 8.26.

3-Chlorotriphenodioxazine-7-oxide (8). Red crystals, mp 150°C (decomp.) and Rf 0.75 (chloroform-methanol 98:2); uv (chloroform): λ max (log ϵ) 502$_s$ nm, 525 (4.02). Anal. Calcd. for: $C_{18}H_9N_2O_3Cl$: C, 64.19; H, 2.69; N, 8.32. Found: C, 64.13; H, 2.62; N, 8.26.

13-Chlorotriphenodioxazine-7-oxide (9). Red crystals, mp 150°C (decomp.) and Rf 0.8 (chloroform-methanol 97:3); uv (chloroform: λ max (log ϵ) 502$_s$ nm, 525 (4.03). Anal. Calcd. for $C_{18}H_9N_2O_3Cl$: C, 64,19; H, 2.69; N, 8.32. Found: C, 64,14; H, 2.71; N, 8.28.

3-(3'-Chlorobenzoyloxy)triphenodioxazine-7-oxide (14). Occasionally, from the reaction mixture 14 was isolated as dark crystals of mp 140°C (decomp.) and Rf 0.4 (chloroform-methanol 98:2); ir chloroform) 1750 cm^{-1}, 1580, 1270; uv (chloroform):λmax (log ϵ) 506$_s$ nm, 530 (4.1); nmr (deuterio methylene chloride): 8.21 (s, H-2', 1H), 8.11 (d, H-6', 1H, J = 7.5), 8.04 (d, H-8, 1H, J = 8.3),

7.70 (d, H-4', 1H, J = 7.5), 7.55 (d, H-1, 1H, J = 8.3), 7.48 (t, H-10, 1H, J = 8.5), 7.46 (d, H-2, 1H, J = 8.3), 7.45 (t, H-5', 1H, J = 7.5), 7.30 (t, H-9, 1H, J = 8.5), 7.15 (s, H-6, 1H), 7.03 (d, H-11, 1H, J = 8.5), 6.48 (s, H-13, 1H); ms: 456 (20%M), 458 (6%,M+2) 440, (100%, M-16), 442 (32, M-16+2). <u>Anal. Calcd. for</u>: $C_{25}H_{13}N_2O_5Cl$: C, 65.58; H, 2.83; N, 6.11. Found: C, 65.61; H, 2.79; N, 6.13.

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