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Photochemical Studies

XVII. The Photolysis of 1-Phenyl and 1-Cyano Substituted Isoquinoline *N*-Oxides to Benz[f][1,3]oxazepines*

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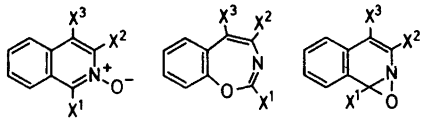
The main product in the photolysis in acetone of 1-cyano-4-bromoisoquinoline *N*-oxide (Ie) is shown to be 2-cyano-5-bromobenz[f][1,3]oxazepine (IIe) by X-ray crystallography. By comparing the infrared and ultraviolet spectra of IIe with those of the photoproducts (IIa–d) previously obtained from isoquinoline *N*-oxides (Ia–d) it is found that IIa–d must also have the benz[f][1,3]oxazepine structure. The hydrolysis of some of these benz[f][1,3]oxazepines is described.

We reported in earlier papers the unambiguous structural proof, by X-ray spectroscopy, for the formation of seven-membered rings in the photolysis of quinoline *N*-oxides [3] and quinoxaline *N*-oxides.[4] In continuation of this work we have examined, by X-ray crystallography, the main photolysis product (IIe) from 1-cyano-4-bromoisoquinoline *N*-oxide (Ie) in acetone.



I II III

	X^1	X^2	X^3
a	C_6H_5	H	H
b	"	CH_3	"
c	CN	H	"
d	"	CH_3	"
e	"	H	Br

* A preliminary report of part of this work has appeared [1] without, however, detailed experimental results, which are reported in the present paper. For paper XVI in this series, see Ref. 2.

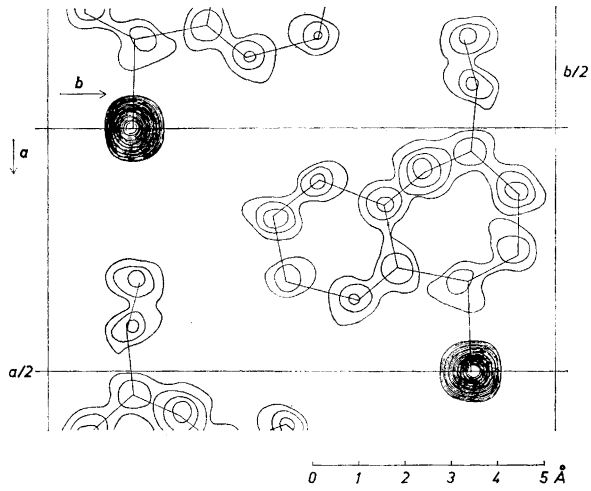
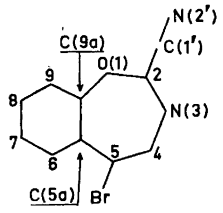


Fig. 1. Electron density projection $\sigma(xy)$ of IIe.

From the atomic distances shown in the electron density projection (Fig. 1) it is obvious that the molecule consists of a six-membered ring fused to a seven-membered ring and that the interatomic bondings are as drawn on the electron density projection. Numbering of IIe:



The highest electron density in the seven-membered ring is at position O(1) and the next highest at position N(3). This is in excellent agreement with the chemical [1,5] and mass spectrometric evidence [1] which show that O(1) should be an oxygen atom and that N(3) should be a nitrogen atom.

A compact model of the molecule was made. The main features of the model are: Atoms C(7), C(6), C(5a), C(9a), C(9), C(8), and O(1) lie in a plane (1) and the atoms C(2), N(3), and C(4) lie in a plane (2). The two planes intersect in a line through O(1)—C(5) with an angle value of approximately 45°. The electron density projection appeared to be in reasonably good agreement with the model when the plane (1) was tilted approximately 30° about a line parallel with C(5a)—C(9).

We thus conclude that the main photolysis product from Ie in acetone is 2-cyano-5-bromobenz[f][1,3]oxazepine (IIe).

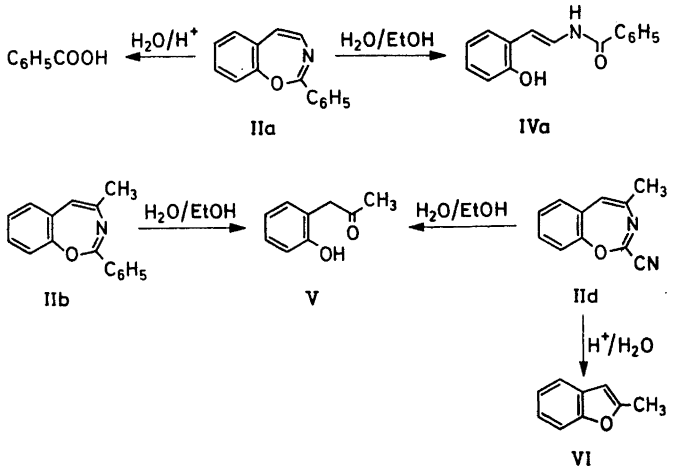
By comparing the infrared absorption bands in the 1600 cm^{-1} region and the long wavelength ultraviolet absorptions of compounds IIa—e (Table 1)

Table 1. Infrared absorption in the 1600 cm^{-1} region and long wavelength ultraviolet absorption of benz[f][1,3]oxazepines.

Compound	IR (in KBr) cm^{-1}	UV (in EtOH) λ_{max}	
		mμ	log ε
IIa	1635	334	3.83
IIb	1640	337	3.80
IIc	1635	337	3.64
IId	1645	343	3.44
IIe	1645	342	4.09

there seems to be no doubt that they all have the benz[f][1,3]oxazepine structures.* As well as acetone also benzene, ethanol and water were used as solvent during irradiations. However, the best yields of benz[f][1,3]oxazepines were obtained in acetone. In ethanol or water the 1-cyano substituted isoquinoline *N*-oxides gave, upon irradiation, very complicated reaction mixtures which were not separated.

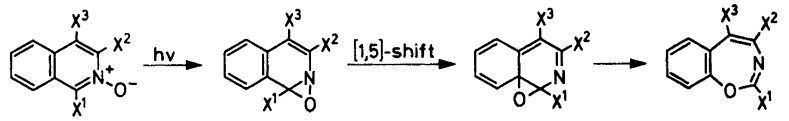
The benz[f][1,3]oxazepines (II) which are imido esters of phenols lead to a variety of compounds by hydrolysis. Thus hydrolysis of 2-phenylbenz-[f][1,3]oxazepine (IIa) in boiling 50 % aqueous ethanol resulted in the formation of 2-(2-hydroxyphenyl)-*N*-benzoylvinylamine (IVa), whereas hydrolysis of IIa under acid conditions permitted the isolation of benzoic acid.[1] Hydrolysis of compounds IIb og IId in aqueous ethanol yielded 1-(2-hydroxyphenyl)-acetone (V), presumably *via* type IV compounds. Acid hydrolysis of 2-cyano-4-methylbenz[f][1,3]oxazepine (IId) resulted in the formation of 2-methyl-coumarone (VI).



* Compounds IIe and IId were first believed to have the oxaziridine structure III.[5–7] (*Cf.* also Ref. 8).

DISCUSSION

It is generally believed [2-9] that the first step in most or all light-induced rearrangements of aromatic amine *N*-oxides is oxaziridine formation; *e.g.* formation of III by irradiation of isoquinoline *N*-oxides (I). Previously, several explanations have been put forward (e.g. Refs. 4, 9) to explain the light-induced ring expansions of aromatic amine *N*-oxides. We have recently modified our previous approach to this and have suggested that the major part of the rearrangement products in the photolysis of quinoline *N*-oxides can be explained by invoking four pathways from the hypothetical oxaziridines.[2] Similarly we wish to point out the rearrangement of the presumed oxaziridine intermediates from isoquinoline *N*-oxides, *i.e.* III, to the benz[f]-[1,3]oxazepines (II) can be formulated as a thermally allowed [1,5]-sigmatropic shift to intermediates VII followed by ring expansion to compounds II. This is analogous to path *c* in Ref. 2.



I III VII II

EXPERIMENTAL

Microanalyses were carried out in the microanalysis department of the University of Copenhagen by Mr. Preben Hansen and his staff.

Melting points (uncorrected) were determined on a Reichert melting point microscope.

Infrared spectra were recorded on a Perkin Elmer Model 337 grating infrared spectrophotometer. Ultraviolet spectra were recorded on a Beckmann DB ultraviolet spectrophotometer.

X-Ray crystallography. 2-Cyano-5-bromobenz[f][1,3]oxazepine crystallizes from pentane as yellow needle-shaped orthorhombic crystals. The cell dimensions, determined from a Guinier-powder diagram, are: $a=10.563\pm0.0023$ Å; $b=21.865\pm0.0047$ Å; $c=3.978\pm0.0006$ Å.

Extinctions: $h00$ absent when h is odd, $0k0$ absent when k is odd, and $00l$ absent when l is odd. The last extinction is uncertain because it is based on very few reflections. However, the threedimensional arrangement of bromine atoms deduced from the Patterson projection $\varrho(u,v)$ and the Patterson projection $\varrho(v,w)$ unequivocally shows that the space group is $P2_12_12_1$. The experimental density is 1.82 g/cm³; the calculated density is 1.77 g/cm³ with $Z=4$. A crystal (needle) of dimensions $0.15\times0.15\times0.40$ mm³ was rotated around the needle axis, and Weissenberg photographs of the $hk0$ reflections were made, using Cu$K\alpha$ radiation. The intensities were estimated visually. Corrections for absorption were not applied.

The Patterson function $\varrho(u,v)$ was calculated from 176 independent $hk0$ reflections and the structure was determined from this by the heavy atom technique. Refinements of the coordinates and the individual isotropic temperature factors were performed using the step method of Bhuiga and Stanley.[10]

The final R-value is 13.42 %. The final parameters are given in Table 2 together with their estimated standard deviations.

Isoquinolines. 1-Phenyl- and 1-phenyl-3-methylisoquinoline were prepared by phenylation of, respectively, isoquinoline and 3-methylisoquinoline, analogously to the method described for 2-phenylquinoline.[11] (Yields varied between 30 and 50 %). 1-Cyano-, 1-

Table 2. Final positional and thermal parameters and their estimated standard deviations.

Atom	x	$\sigma(x)$	y	$\sigma(y)$	B	$\sigma(B)$
C(7)	0.31735	0.0052	0.23468	0.0022	2.03	1.43
C(6)	0.35551	0.0052	0.30304	0.0024	2.33	1.47
C(5a)	0.28464	0.0051	0.34138	0.0022	1.63	1.29
Br	0.00000	—	0.08214	0.0003	2.73	0.13
C(5)	0.31448	0.0056	0.40811	0.0026	2.83	1.59
C(4)	0.25994	0.0058	0.45960	0.0025	2.73	1.51
N(3)	0.13547	0.0039	0.46083	0.0018	1.53	1.03
C(2)	0.04743	0.0045	0.41430	0.0021	1.13	1.09
C(1′)	0.41056	0.0055	0.07537	0.0024	2.53	1.51
N(2′)	0.31704	0.0041	0.08920	0.0019	2.03	1.12
O(1)	0.08913	0.0033	0.36876	0.0015	1.83	0.87
C(9a)	0.15856	0.0046	0.32869	0.0020	0.83	1.07
C(9)	0.10842	0.0053	0.26495	0.0022	1.93	1.32
C(8)	0.17934	0.0048	0.22000	0.0021	1.85	1.18

cyano-3-methyl-, and 1-cyano-4-bromoisoquinoline were prepared by cyanation of the parent *O*-methylated isoquinoline *N*-oxide methylsulfates.[12] (Yields varied between 60 and 80 %). 1-Cyano-4-bromoisoquinoline has a m.p. =124—125°. (Found: C 51.50; H 2.21; N 12.23. Calc. for $C_{10}H_5N_2Br$: C 51.50; H 2.16; N 12.02).

Isoquinoline N-oxides. 1-Phenyl-, 1-phenyl-3-methyl-, and 1-cyano-4-bromoisoquinoline *N*-oxide were prepared by oxidation of the parent isoquinolines with 3-chloroperoxybenzoic acid in a manner described previously.[3] (Yields varied between 70 and 90 %). 1-Cyano-4-bromoisoquinoline *N*-oxide had m.p.=204—205°. (Found: C 48.40; H 2.07; N 11.29. Calc. for $C_{10}H_5N_2OBr$: C 48.19; H 2.01; N 11.24). 1-Cyano- and 1-cyano-3-methylisoquinoline *N*-oxide were prepared by the method described for 1-cyano-3-methylisoquinoline *N*-oxide below:

1-Cyano-3-methylisoquinoline N-oxide. 1-Cyano-3-methylisoquinoline (1.68 g) was treated with acetic acid anhydride (4 ml) and 35 % hydrogen peroxide (4 ml). The mixture was heated on a steam bath for 2 h, after which water (10 ml) was added. Glacial acetic acid was then added until a clear yellow solution appeared (at 100°). The mixture was cooled and 1-cyano-3-methylisoquinoline *N*-oxide (1.80 g) was isolated by filtration. M.p. 195—196°. (Found: C 71.90; H 4.33; N 15.10. Calc. for $C_{10}H_8N_2O$: C 71.74; H 4.35; N 15.22). A similar yield was obtained for 1-cyanoisoquinoline *N*-oxide.

Irradiation of isoquinoline N-oxides. The irradiations were performed as previously described [1] (or using methods *A* or *B*).[2] The best yields of benz[f][1,3]oxazepines were obtained in acetone. Good yields of benzoxazepines could also be obtained using

Table 3. Benz[f][1,3]oxazepines.

Compound		Found			Calc.		
	M.p., °C	% C	% H	% N	% C	% H	% N
IIa	56— 57	81.40	5.02	6.28	81.43	5.01	6.33
IIb	73— 75	81.02	5.49	5.78	81.68	5.57	5.95
IIc	100—101	(70.90	3.38	16.80)[6]	70.58	3.55	16.46
IId	86— 87	71.45	4.55	14.95	71.74	4.35	15.22
IIe	98— 99	48.38	2.19	11.14	48.19	2.01	11.24

benzene as solvent. In ethanol or water the 1-cyano substituted isoquinoline *N*-oxides upon irradiation gave brown multicomponent reaction mixtures, whereas the phenyl substituted quinoline *N*-oxides gave benz[f][1,3]oxazepines as the major products (observed by UV spectroscopy). Thus a saturated aqueous solution of 1-phenyl-3-methylisoquinoline *N*-oxide was irradiated for 5 sec. (method *A*).[2] A UV spectrum recorded immediately after irradiation was superimposable with that of the corresponding benz-[f][1,3]-oxazepine (IIb) in ethanol. The spectrum slowly changed upon leaving the solution to stand.

Hydrolysis of 2-phenylbenz[f][1,3]oxazepine in aqueous ethanol. 2-Phenylbenz[f][1,3]-oxazepine (500 mg) was dissolved in ethanol (50 ml) and water was added (50 ml). The solution was refluxed for five days, the solvents evaporated and the remaining yellow oil purified by preparative layer chromatography (PLC). This resulted in the isolation of one main crystalline fraction (340 mg). Recrystallization from ethanol-water of this fraction raised the m.p. to 151—155°. (Found: C 75.40; H 5.68; N 5.82. Calc. for $C_{15}H_{13}NO_2$: C 75.30; H 5.45; N 5.85). This compound was identified as 2-(2-hydroxyphenyl)-*N*-benzoyl vinylamine.[1] In addition some minor fractions were isolated, but not characterized.

Hydrolysis of 2-phenyl-4-methylbenz[f][1,3]oxazepine in aqueous ethanol. 2-Phenyl-4-methylbenz[f][1,3]oxazepine (100 mg) dissolved in 50 % aqueous ethanol (20 ml) was refluxed for three days and the solvents evaporated. By PLC of the remaining oil seven fractions were obtained. One of these (40 mg, m.p. 63—64°) was identified as 1-(2-hydroxyphenyl)acetone[12] by UV, IR, and NMR spectroscopy. The remainder fractions were not further characterized.

Hydrolysis of 2-cyano-4-methylbenz[f][1,3]oxazepine in aqueous ethanol. This was carried out in a manner analogous to the hydrolyses described above and resulted only in the formation of 1-(2-hydroxyphenyl)acetone.

Hydrolysis of 2-phenylbenz[f][1,3]oxazepine under acid conditions. 2-Phenylbenz[f][1,3]-oxazepine (337 mg) was dissolved in ethanol (15 ml) and 4 N hydrochloric acid (15 ml) was added. The resulting solution was refluxed for 8 h; water (100 ml) was then added, and the solution was extracted three times with ether. The combined ethereal fractions were extracted three times with a saturated sodium hydrogen carbonate solution. After this the ethereal fraction was washed with water and saturated sodium chloride and filtered through anhydrous magnesium sulfate. After evaporation of the ether a colourless oil (244 mg) remained. This oil was shown to consist mainly of two components by gas chromatography. No attempts to identify these were undertaken. The basic extract from above was acidified with hydrochloric acid and extracted three times with ether. After washing three times with water and saturated sodium chloride and filtering through anhydrous magnesium sulfate the ether was evaporated. The remaining crystalline fraction (102 mg) after recrystallization was identified as benzoic acid by IR spectroscopy and a mixed m.p. test.

Hydrolysis of 2-cyano-4-methylbenz[f][1,3]oxazepine under acid conditions. 2-Cyano-4-methylbenz[f][1,3]oxazepine (400 mg) was refluxed with 2 N hydrochloric acid (20 ml) for 1 h. The reaction mixture was extracted three times with chloroform, the chloroform extract dried over anhydrous magnesium sulfate, and the chloroform evaporated. The remaining colorless liquid was shown to be identical with an authentic sample of 2-methylcoumaron (prepared analogously to the method previously described[13]) by IR, UV, and NMR spectroscopy.

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