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ON 1,3-BENZOXAZEPINE AND 3,1-BENZOXAZEPINE

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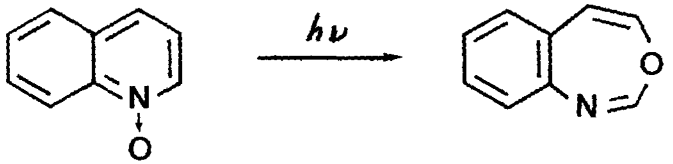
Summary. The photochemistry of quinoline and isoquinoline N-oxides has been reexamined. 3,1-Benzoxazepine, which had not been isolated as yet, was obtained from the former, while the formation of 1,3-benzoxazepine from the latter was demonstrated.

3,1-Benzoxazepines and 1,3-benzoxazepines are believed[1] to be generally formed on irradiation of quinoline and isoquinoline N-oxides, respectively, in aprotic solvents. In fact, these compounds have been obtained only from the irradiation of quinoline N-oxides bearing a cyano or a phenyl group in position 2 and of isoquinoline N-oxides bearing the same substituents in position 1. Despite considerable effort,[2,3] the photochemistry of the parent compounds of the two series is still not fully understood. In fact quinoline N-oxide (1) was shown to give good yields of N-formylindole and N-formyl-2-hydroxyindoline which could be rationalized as products of hydrolysis of 3,1-benzoxazepine (2),[2] while isoquinoline N-oxide (3) gave in acetone lesser yield of N-(o-hydroxystyryl)formamide which was likewise rationalized as derived from 1,3-benzoxazepine (4).[3]

It has recently been shown that some azine N-oxides yield photoisomers which differ from 1,3-oxazepines, although, in some cases, these give on hydrolysis the products expected from 1,3-oxazepines.[4,5] Therefore, it seemed worthwhile to investigate the photochemistry of (1) and (3) further and to ascertain whether the two benzoxazepines (2) and (4) could indeed be prepared from them.

In order to avoid the possibility that the benzoxazepines could react with traces of water as soon as they were formed, the solutions of the N-oxides were dehydrated by azeotropic distillation directly in the irradiation vessel before being photolyzed.[6] Under these conditions, (1) was irradiated in cyclohexane.[7] The solvent was evaporated and the residue was extracted with little cyclohexane. The insoluble part contained some carbostyril (5). Evaporation of the cyclohexane extract and short path distillation of the residue (0.1 mm Hg; 50°C) afforded an oil ($n^{D}_{24°}$ 1.6072). This compound was recognized as (2) on the basis of its spectroscopic properties, which were similar to those of substitued 3,1-benzoxazepines.[1] Com -



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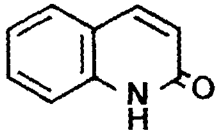

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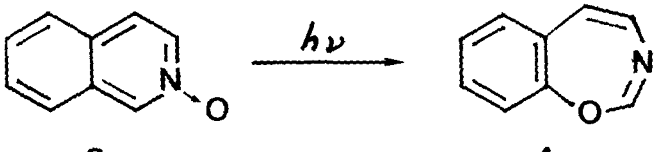

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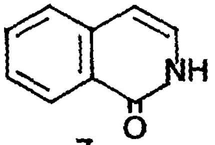

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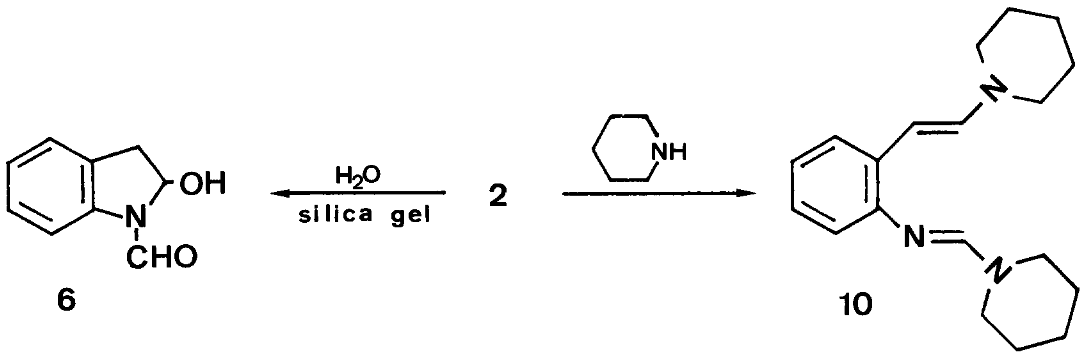
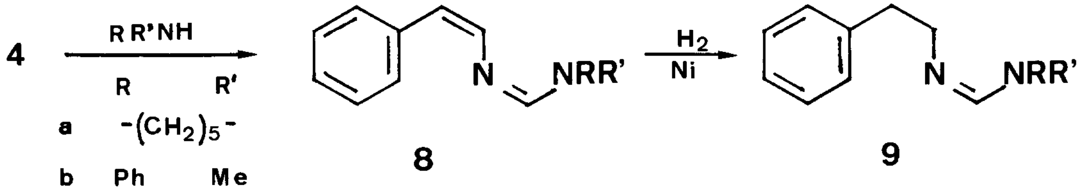
pound (2) proved to be unstable to moisture and chromatography on silica gel yielded the hydration product (6). Direct chromatographic separation of the photolyzate yielded (5) and (6), with no trace of (2). The irradiation of (1) in water yielded (5) almost quantitatively, as has already been reported.[2]

The irradiation of (3) in benzene under similar conditions, followed by solvent evaporation, yielded an oil which we did not succeed in purifying, as it was quickly converted into a solid material, no longer soluble in benzene. Chromatography of this material gave only a little isocarbostyril (7). However, NMR and UV spectra consistent with the formation of (4) as the main product could be obtained from dilute solutions of the photolysate. Apparently, (4) undergoes rapid polymerisation, which is not unexpected in view of its diene structure. Further support for the formation of (4) was sought in its reaction with bases. Thus, the clear solution resulting from the photolysis was concentrated to about one fifth of its volume, some piperidine or *N*-methylaniline was added and the resulting mixtures were refluxed for some minutes. Evaporation and chromatographic separation of the reaction products yielded the stable adducts (8a) and (8b) respectively. These compounds are crystalline materials, soluble in bases. Their structures were suggested by their spectroscopic properties (strongly intramolecularly bonded O-H, two coupled olefinic protons, deshielded singlet corresponding to the amidine proton). Catalytic (Raney-Ni) hydrogenation of (8a) yielded (9a). This reaction also supports the proposed structure.

The formation of (8) from (4) by reaction with amines follows a pathway analogous to the reaction of stable 1,3-benzoxazepines with water[3], thus supporting the attribution of structure (4) to the main product from the photolysis of (3) in benzene. Irradiation of (3) in water yielded (7).





The behaviour of (2) in the presence of amines was also tested. An analogous treatment gave an oil, very soluble in petroleum ether, which was decomposed either by dilute acids or by silica gel. This compound resulted from the addition of two molecules of the amine with elimination of one of water. The structure (10) could be attributed to it on the basis of its spectra (no O-H or N-H, two coupled olefinic protons,[8] deshielded singlet corresponding to the amidine proton). The formation of (10) from (2) may be rationalized as occurring through a reaction with the amine analogous to the reaction with water which yields N-formyl 2-hydroxyindoline (6) (or its open chain tautomer) followed by formation of the enamine and base promoted dehydration.[9]

Thus, it has been shown that 3,1-benzoxazepine, though a moisture-sensitive compound, may be obtained by photolysis of (1), while 1,3-benzoxazepine, which is formed on photolysis of (3) is stable only in dilute solutions and may be trapped with bases. The generalisation previously mentioned[1] is therefore borne out by experiments, as far as the photochemistry of quinoline and isoquinoline N-oxides is concerned.

Table 1. % Yields of photoproducts from the N-oxides (1) and (3).

Substrate	Solvent	Treatment	Yield	Substrate	Solvent	Treatment	Yield
(1)	C_6H_{12}	Extraction	(2) 60%	(3)	C_6H_6	Chromat.	(7) 10%
"	"	Chromat.	(5) 20%, (6) 58%	"	"	Piperidine	(7) 10%, (8a) 46%
"	"	Piperidine	(5) 15%, (10) 75%	"	"	PhNHMe	(7) 10%, (8b) 52%
"	H_2O	Chromat.	(5) 85%	"	H_2O	Chromat.	(7) 80%

Table 2. Selected spectroscopic data on new products.

	NMR (CCl_4)	IR
(2)	6.35s(2-H), 5.78d(J=6 Hz, 4-H), 5.58d(5-H)	1640vs, 1680s
(4)	6.52s(2-H), 6.25d(J=8 Hz, 4-H), 6.57d(5-H)	
(8a)	5.37d(J=9.5 Hz), 6.25d, 7.15s(-N=CH-N-), 13.1s(O-H)	2500br, 1630s, 1600s
(8b)	5.7d(J=9 Hz), 6.55d, 7.87s(-N=CH-N), 13.3s(O-H)	1630s, 1595s
(9a)	3.1-3.4m($-CH_2-CH_2-$), 7.15s(-N=CH-N), 8.45br(O-H)	2600br, 1600s
(10)	5.6d (J=14.5), 6.55d, 7.28s(-N=CH-N)	1630s, 1585m

References and footnotes.

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6. The N-oxides (1) and (3) are hydroscopic and crystallize from benzene with two and one molecule of water, respectively.
7. 2×10^{-3}M solutions of (1) and (3) were irradiated by means of a Hanau high pressure mercury arc through a pyrex filter after nitrogen purging. The experimental details are the same as in ref. 5. All new products have correct analytical data or mass spectrometric molecular weight determination. The mass spectrum of (2) was in accord with the structure (cf. L. Simonotti, S. Facchetti, G.F. Bettinetti, and A. Albini, Gazzetta 106, 49 (1976))
8. The trans configuration of the double bond may be deduced from the coupling constants (cf. J. Sauer, and H. Prahl, Chem.Ber. 102, 1917 (1969))
9. 2-cyano-3,1-benzoxazepine yields a different product with amines. This is formed via a mechanism which is identical with the one proposed here in the initial steps. (see C. Kaneko and I. Yokoe, Tetrahedron Lett. 5355 (1967))

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