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Photolysis of 3-Hydroxy-2,3-dihydro-2,1-benzisoxazole Derivatives Studied by EPR Spectroscopy: Competing N–O and C–O Bond Scission

Sanjay Srivastava and Daniel E. Falvey*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742 U.S.A.

Abstract. Photolysis of 3-hydroxy-2,3-dihydro-2,1-benzisoxazole derivatives gives 2-acetylaniline derivatives as the sole stable products. EPR spectroscopy shows that persistent arylnitroxyl radicals are formed as intermediates and then further photolyzed. A mechanism accounting for these observations is proposed. Copyright © 1996 Elsevier Science Ltd

Photochemical studies of 5-member heterocycles containing N-O or N-S bonds have revealed a variety of fascinating rearrangements and other transformations.[1] Not surprisingly many of these begin by scission of the N-S or N-O bond. For example 1,2-benzisoxazole (indoxazene) rearranges upon photolysis to the 2-cyanophenol and benzoxazole.[2] Irradiation of isoxazoles causes N-O bond cleavage to give a diradical intermediate.[3] Recent work from this laboratory has utilized the photolysis of N-alkyl-anthranilium ions as a source of nitrenium ion intermediates.[4]

$$a: X=Y=H$$
$$b: X=Br; Y=H$$
$$c: X=Cl; Y=H$$
$$d: X=NO_2 ; Y=H$$
$$e: X=H; Y=Cl$$

(1)
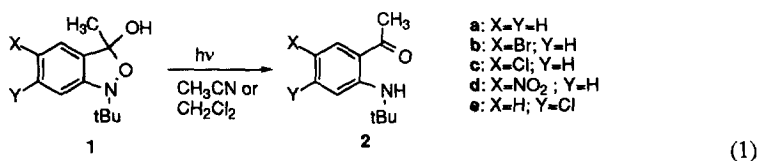
The present report concerns the photochemistry of 3-hydroxybenisoxazolidine derivatives **1**. Earlier we reported that these compounds, which are ground-state nucleophilic adducts of anthranilium ions, are converted to arylamines **2** upon photolysis (eq 1).[4a] Herein are described mechanistic investigations of this reaction. It was of interest to determine whether the initial photochemical step in these photolyses would be the typical N–O bond scission leading to diradical **3**, or an alternative C–O bond scission leading to a resonance stabilized nitroxyl/ketyl diradical **4**. The results discussed herein lead to the conclusion that both pathways are operative. An intermediate resulting from C–O scission (nitroxyl radical **5**) is detected by electron paramagnetic resonance (EPR) spectroscopy and UV-vis spectroscopy. On the other hand, formation of **2** is consistent with N–O bond scission. A general mechanism that is consistent with these observations is presented in Scheme 1 and discussed below.

Ultraviolet (UV) irradiation of **1a-e** give N-tert-butyl-2-acetylanilines (**2**), as the sole photoproducts. The outcome is not noticeably affected by the solvent. Amine **2** is the exclusive photoproduct in both CH3CN

and CH_2Cl_2. Table 1 lists the yields of the products from the photolysis of various benzisoxazoles, **1a-e** in CH_3CN.

In order to determine which if any radical species were intermediates in the photolysis, EPR experiments were carried out. Irradiation of **1a-e** for short periods of time (ca. 2 min.) generated an EPR-active species. The spectrum generated from **1b** in CH_2Cl_2 is typical and shown in Figure 1. The signals are stable in the dark for at least several hours and are unaffected by exposure to air. Prolonged irradiation (>10 min.) leads to the disappearance of the EPR–active species. All of the derivatives showed similar behavior. For a given compound, the same spectrum was observed in both CH_2Cl_2 and CH_3CN. However the former, having a lower dielectric constant, gave better signal-to-noise ratios.

Table 1. Results From Photolysis of **1**

Reactant[a]	Yield of 2 (%)[b]	EPR of Intermediate Radical 5			
		a_N	a_{o}-H	a_{m}-H	a_{p}-H
1a	82	12.9	1.55	0.80 [c]	0.40
1b	73	12.7	1.47	0.83 [c]	-
1c	78	11.8	1.39	0.70 [c]	-
1d	85	7.9	1.40	0.40 [c]	-
1e	86	13.0	1.45	0.60	0.90

[a] See footnote 5.

[b] These compounds have been previously reported (Ref. 4).

[c] Both meta protons were assumed to have the same a_H value to within experimental error (±0.05 G).

The nature of the signal suggests that it is a nitrogen centered radical. In each case there is a large three-line pattern that is further split by smaller hyperfine couplings. The hyperfine coupling constants given in Table 1 were obtained through digital simulation of the observed spectra. We ascribe the observed EPR signal to nitroxyl radical, **5**, on the basis of observations enumerated below.
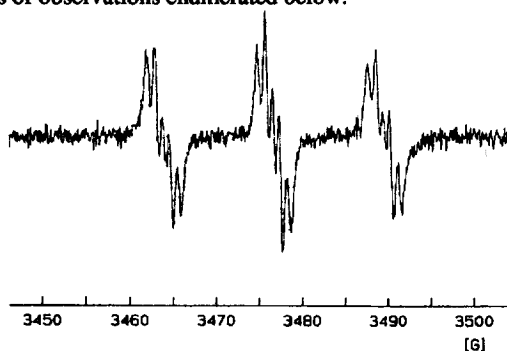

3450	3460	3470	3480	3490	3500

[G]

Figure 1. X-band EPR spectrum generated from the photolysis of **1b** in N_2-purged CH_2Cl_2. The sample was photolyzed for 2 min with a 150 W Hg-Xe lamp and then the spectrum was scanned.

(1) The long lifetime of the EPR signal argues against it being due to either of the diradicals **3** or **4**. Both diradicals are isomeric with the reactant **1** and would thus be expected to spontaneously cyclize. Typical 1,5-diradicals have lifetimes on the order of 100 ns at room temperature.[6]

(2) The nitrogen hyperfine coupling constants (a_N) favor their assignment to the nitroxyl radical 5 rather than the anilino radical 8.[7] The a_N values for mono-substituted N-tert-butylanilino radicals typically range from 9-11 G[7a] whereas those for mono-substituted N-tert-butylarylnitroxyl radicals range from 11-14 G.[7b] The radicals produced from 1a-c and 1e have a_N values of 11.8-13.0 G, falling more nearly in the range expected for a nitroxyl radical than an anilino radical. It has been shown that π–electron withdrawing ring substituents on arylnitroxides act to reduce a_N. This has been attributed to increased delocalization of the nitrogen lone pair into the phenyl ring which in turn results in decreased spin density on nitrogen. All of the radicals have an π–withdrawing ortho-acetyl group and thus fall in the lower part of the expected range. Nitroxyl 5d possesses a strongly electron–withdrawing para-NO_2 group in addition to the acetyl and thus has an unusually low value for a_N (7.9 G).

(3) The proton hyperfine coupling constants a_H are also more consistent with what would be expected for 5.[7] Typical ortho proton hyperfine constants (a_{O-H}) for anilino radicals are 4-5 G and for nitroxides they are 1-2 G.[7b] The observed a_{O-H} values fall between 0.40 and 1.55 G (Table 1), which is again more consistent with those reported values for nitroxides.

Scheme 1
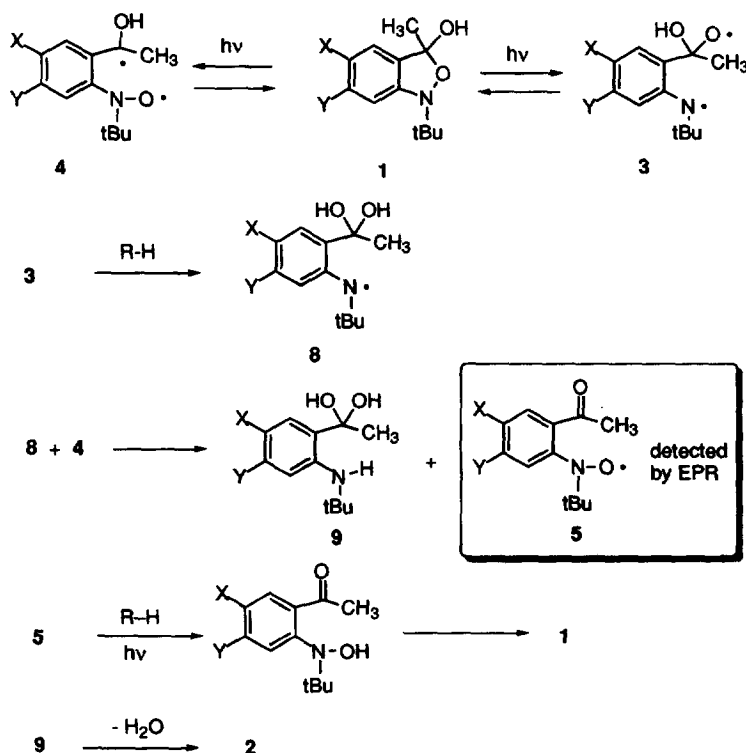
The only isolated photoproduct is arylamine 2 which is the result of a net two-electron reduction of the substrate. The only likely source of electrons or hydrogen atoms is the solvent, CH_3CN or CH_2Cl_2. The mechanism in Scheme 1 accounts for the formation of both 2 and 5. It is proposed that photolysis of 1 causes the reversible formation of two diradicals. Scission of the C–O bond leads to the nitroxyl/ketyl diradical 4.

Scission of the N–O bond provides anilino/alkoxy diradical **3**. It is expected that the latter's unconjugated alkoxy group would be highly reactive and capable of abstracting a H-atom from the solvent, generating anilino radical **8**. Anilino radicals such as **8** are persistent at room temperature.[8] Thus, it is unlikely that **8** would be able to react further with the solvent.[8b] Conversion of **8** to **2** requires a more reactive H-atom donor. A source for this would be the diradical **4**. A disproportionation reaction between **8** and **4** would give the detected nitroxyl radical **5** and the *gem*-diol **9**. The latter loses water to giving **2**, the sole photoproduct.

No products that obviously come from **5** are detected by ^{1}H NMR. In fact the 70-90% yields of **2** suggest that there must be a pathway from this nitroxyl radical to **2**. It is proposed that further photolysis of nitroxyl radical **5** leads to a H-atom transfer from the solvent, either to the nitroxyl oxygen (as shown) or else to the ketone oxygen. In either case this would give a species that is isomeric with the starting material, **1**. Facile isomerization would regenerate the starting material which would be subject to further photolysis. Repetition of this cycle would have the net effect of converting **1** to **2**.

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5. Substrates **1a-e** were prepared from the corresponding substituted N-*tert*-butyl-3-methylanthranilium perchlorate salts (ref. 4) by partitioning the latter between Et_2O and sat'd aqueous $NaHCO_3$. The organic layer was washed with neutral H_2O and the solvent was evaporated to give **1** in quantitative yields. ^{1}H NMR (200 MHz, CD_3CN): **1a:** 7.76 (d, J = 2.6, 1 H), 7.25 (dd, J = 9.2, 2.6, 1 H), 6.97 (d, J = 9.2, 1 H), 2.50 (s, 3 H), 1.39 (s, 9 H); **1b:** mp ºC (78-82). 7.36 (m, 2 H), 6.91 (m, 1 H), 4.57 (s, 1 H), 1.69 (s, 3 H), 1.23 (s, 9 H);**1c:** 7.26 (d, J = 2.2, 1 H), 7.21 (dd, J = 8.6, 2.2, 1 H), 6.99 (d, J = 8.6, 1 H), 4.43 (s, 1 H), 1.70 (s, 3 H), 1.24 (s, 9 H); **1d:** mp ºC (80-84) 8.1(dd, 2H), 7.1 (d, J = 8.9 ,1 H), 4.57 (s, 1H), 1.70 (s, 3H), 1.34 (s, 9H); **1e:** mp ºC (72-76) 7.21 (d, J = 7.6, 1 H), 7.03 (m, 2 H), 4.45 (s, 1 H), 1.69 (s, 3 H), 1.24 (s, 9 H); See also: Anderson, G. B. Ph. D. Thesis, University of Maryland, College Park, MD, 1993.

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