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The Photochemistry of Carbon-Nitrogen Multiple Bonds in Aqueous Solution. 1. Aromatic Oximes, Oxime Ethers, and Nitriles

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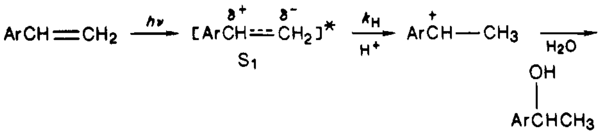
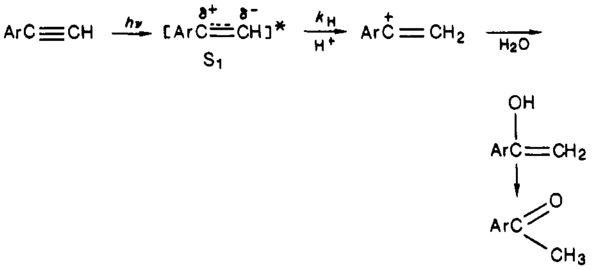
The photochemistry of typical C=N and C≡N compounds was investigated in aqueous solution from pH 2 to 12. It was found that both aromatic aldoximes and ketoximes readily undergo photohydrolysis via their lowest singlet states, with Φ values generally in the 0.01–0.15 range. Both the neutral oxime and oximate anion undergo photohydrolysis, with the former reaction being acid-catalyzed. For both forms of the oxime, evidence was obtained for oxazirane intermediates. For the neutral form, there is also a less efficient hydrolysis mechanism, which is important at pH 8–10 and involves the uncatalyzed addition of water to the C=N bond. A similar uncatalyzed hydrolysis mechanism is found for the oxime ethers at all pH's. The unsubstituted oxime ethers photohydrolyze only by the pH-independent route with a photoefficiency (Φ = 0.01–0.025) that is practically identical with that of the parent oximes in the pH 8–10 range. Attempts were made to photohydrolyze analogously substituted benzonitriles under the same conditions, since fluorescence quenching in acid solution had shown that their lowest singlet states exhibit greatly enhanced basicity. Surprisingly all attempts to photohydrolyze the nitriles were unsuccessful.

Introduction

Recent studies[1] of the photoreactions of carbon–carbon double and triple bonds in conjugation with aromatic systems have shown that they undergo rapid and efficient ($\Phi \sim 0.1$–0.9) photohydration in both neutral and mildly acidic aqueous solution. The reactions (eq 1 and 2) are subject to both specific and general acid catalysis[2] and where the aromatic ring is substituted with an electron-donating group, lead cleanly to Markovnikov addition, via their lowest singlet states. Rates of protonation (k_H) are typically in the 10^6–10^8 M^{-1} s^{-1} range,[1,2] which compared with analogous thermal hydration rate constants ($k_H \sim 10^{-5}$–10^{-6} M^{-1} s^{-1})[3] demonstrates that the rate accelerations achieved by electronic excitation are of the order of 10^{11}–10^{14}. This is believed to arise largely from a high degree of polarization or acquisition of charge-transfer character by their $^1(\pi,\pi^*)$ states, which in turn can give rise to pronounced shifts in excited-state basicity.[4] Reported pK shifts on excitation ($\Delta pK^* = pK_{S_1} - pK_{S_0}$) are commonly in the 5–10 log unit range for aromatic systems.[4,5]

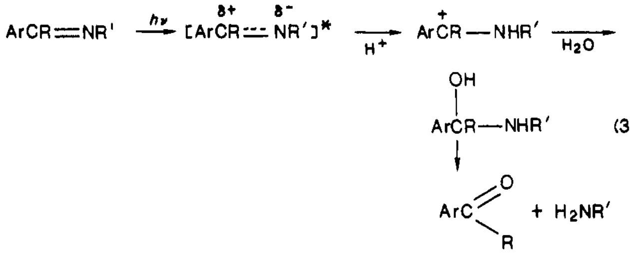


$$\mathrm{ArCH{=}CH_2} \xrightarrow{h\nu} \underset{S_1}{[\mathrm{Ar}\overset{\delta+}{\mathrm{C}}\mathrm{H}{=}\overset{\delta-}{\mathrm{C}}\mathrm{H_2}]^*} \xrightarrow[\mathrm{H^+}]{k_H} \mathrm{Ar}\overset{+}{\mathrm{C}}\mathrm{H{-}CH_3} \xrightarrow{\mathrm{H_2O}} \mathrm{ArCH(OH)CH_3} \qquad (1)$$

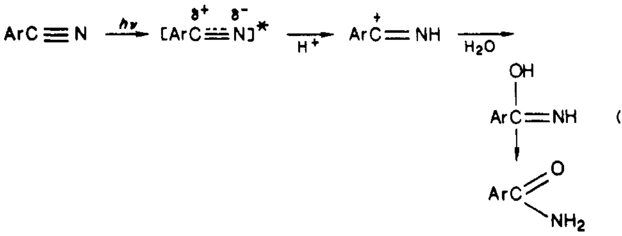


$$\mathrm{ArC{\equiv}CH} \xrightarrow{h\nu} \underset{S_1}{[\mathrm{Ar}\overset{\delta+}{\mathrm{C}}{\equiv}\overset{\delta-}{\mathrm{C}}\mathrm{H}]^*} \xrightarrow[\mathrm{H^+}]{k_H} \mathrm{Ar}\overset{+}{\mathrm{C}}\mathrm{{=}CH_2} \xrightarrow{\mathrm{H_2O}} \mathrm{ArC(OH){=}CH_2} \longrightarrow \mathrm{ArC({=}O)CH_3} \qquad (2)$$

An obvious possible extension of these efficient photohydrations is to the analogous reactions of carbon–nitrogen double and triple bonds. It was hoped that these would exhibit similar changes in ΔpK^* and comparable rate enhancements on electronic excitation. In these cases, however, it was expected that in aqueous solution the net result of addition would be photohydrolysis (eq 3 and 4) rather than photohydration, if singlet states are also involved.



$$\mathrm{ArCR{=}NR'} \xrightarrow{h\nu} [\mathrm{Ar}\overset{\delta+}{\mathrm{C}}\mathrm{R}{=}\overset{\delta-}{\mathrm{N}}\mathrm{R'}]^* \xrightarrow[\mathrm{H^+}]{} \mathrm{Ar}\overset{+}{\mathrm{C}}\mathrm{R{-}NHR'} \xrightarrow{\mathrm{H_2O}} \mathrm{ArCR(OH){-}NHR'} \longrightarrow \mathrm{ArC({=}O)R} + \mathrm{H_2NR'} \qquad (3)$$



$$\mathrm{ArC{\equiv}N} \xrightarrow{h\nu} [\mathrm{Ar}\overset{\delta+}{\mathrm{C}}{\equiv}\overset{\delta-}{\mathrm{N}}]^* \xrightarrow[\mathrm{H^+}]{} \mathrm{Ar}\overset{+}{\mathrm{C}}\mathrm{{=}NH} \xrightarrow{\mathrm{H_2O}} \mathrm{ArC(OH){=}NH} \longrightarrow \mathrm{ArC({=}O)NH_2} \qquad (4)$$

Oximes and oxime ethers were chosen as representative of CN double bonds, for two practical reasons. One is that other types of imino derivatives would already be quite reactive thermally, thus making a study of their purely photochemical hydrolysis very difficult. The second reason is based on their extensive use as carbonyl protecting groups,[6] which makes a study of their removal by hydrolysis both useful and interesting. Normally fairly harsh acidic or basic conditions are required to convert oximes to carbonyl compounds, and it would certainly be an advantage to find a milder method of hydrolyzing oximes and oxime ethers. In the case of CN triple bonds, the choice is obviously restricted to nitriles, but again it would be very useful to develop a method of hydrolysis which involved much milder conditions than those normally used to convert nitriles into amides.[7]

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[1] Wan, P.; Culshaw, S.; Yates, S. *J. Am. Chem. Soc.* **1982**, *104*, 2509.

[2] Wan, P.; Yates, K. *J. Org. Chem.* **1983**, *48*, 869.

[3] Schubert, W. W.; Keefe, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 559. Schubert, W. W.; Lamm, B. *J. Am. Chem. Soc.* **1966**, *88*, 120. Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373. Noyce, D. S.; Schiavelli, M. D. *J. Am. Chem. Soc.* **1986**, *90*, 1020, 1023.

[4] Ireland, J. F.; Wyatt, P. A. H. *Adv. Phys. Org. Chem.* **1976**, *12*, 131.

[5] Klopffer, W. *Adv. Photochem.* **1977**, *10*, 311. Schulman, S. G. *Fluorescence and Phosphorescence Spectroscopy*; Pergamon: Oxford, 1977. Schulman, S. G. In *Modern Fluorescence Spectroscopy*; Wehry, E. L. Ed.; Plenum: New York, 1976; Vol. 2.

[6] Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*; Plenum: New York, 1977; Part B, p 417.

[7] Rappoport, Z. *The Chemistry of the Cyano Group*; Interscience: New York, 1970; 256.

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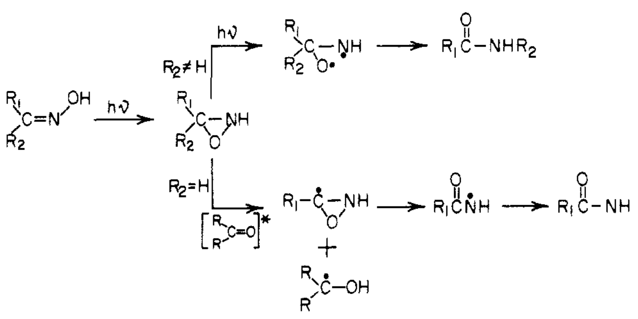
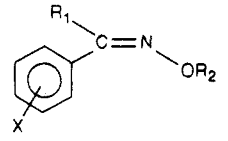
Scheme I



Results

Oximes and Oxime Ethers. Oximes are already known to undergo some photoreactions, the two most common being syn–anti isomerization[8] and the photo-Beckmann reaction.[9] In the latter, oximes are converted to amides, thus resembling the more familiar thermal Beckmann rearrangement.[10] The details of this photolytic conversion are not yet fully understood, but two of the most generally accepted mechanisms[11] are shown in Scheme I. In some studies of this reaction, formation of some carbonyl compound (aldehyde or ketone) was also reported,[11] but apparently no detailed study has been undertaken to determine whether this competing hydrolysis pathway is photochemical or thermal origin.



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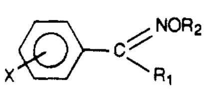
R_1 = H, CH_3
R_2 = H, CH_3
X = H, 2-OCH_3, 4-OCH_3, 3-NH_2, 3-CN, 4-CF_3, 3-NO_2, 4-NO_2

Various oximes of general structure 1 were irradiated in both acidic and basic aqueous solution (pH 2–12) at 254 or 300 nm. Photohydrolysis was found to occur in all cases except where X = NO_2, yielding the corresponding carbonyl compound, as shown in Table I. In addition, as expected, the fastest photoreaction observed was syn–anti isomerization. This was determined by GLC, UV and ^1H NMR analysis of unreacted starting material. No photo-Beckmann products (i.e., amide) were detected in any photolysis experiment. However irradiation times were generally kept short enough (1–2 h; Rayonet RPR reactor, 200-W total lamp output) to ensure less than 50% conversion, in order to avoid possible complications due to a competing or consecutive photo-Beckmann reaction.[12] As shown in Scheme I, this probably involves either absorption of a second photon, by the oxazirane intermediate, or its collision with an excited carbonyl compound. (Both of these possibilities require a high concentration of an oxazirane intermediate, the importance of which will be discussed later.) Thus low photochemical conversions effectively prevent such processes from competing with photohydrolysis. In addition, all hydrolyses were monitored thermally to ensure that none of the observed product had been formed via the known ground-state process. To reduce this possibility, all photolyses were carried out at 4 °C where the thermal hydrolysis was found to be negligible under the reaction conditions used.

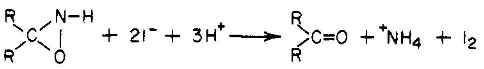
Table I. Formation of Carbonyl Product and Absolute Quantum Yields for Photohydrolysis of Oxime Derivatives



X	R_1	R_2	formation of carbonyl product	Φ^a (pH 8.0)	Φ^b (pH 4.0)
H	H	H	yes	0.01	0.015
2-OMe	H	H	yes	0.02	
3-NO_2	H	H	no^c		
4-NO_2	H	H	no^c		
H	Me	H	yes	0.022	0.053
2-OMe	Me	H	yes	0.041	
3-NH_2	Me	H	yes	0.150	
H	H	Me	yes	0.012	0.012
H	Me	Me	yes	0.025	0.025
3-NO_2	Me	Me	no^c		
4-OMe	Me	Me	yes	0.079	
3-CN	Me	Me	trace	<0.001	
4-CF_3	Me	Me	yes	0.030	

[a] Measured directly by using ferrioxalate actinometry, in solutions buffered at pH 8.0. This corresponds approximately to the minimum in the pH–quantum yield profile for reaction of the neutral oxime. [b] Estimated from plots of Φ/Φ_0 vs. pH in Figures 1 and 2. [c] Only syn–anti isomerization was observed for these compounds.

Scheme II



As shown in Table I, the nitro-substituted oximes and oxime ethers did not photohydrolyze at all, although other substrates with strongly electron-withdrawing groups (CN and CF_3) did give hydrolysis product. Apart from syn–anti isomerization, the nitro compounds are photostable under the conditions employed (i.e., basic, neutral, and acidic aqueous solution). The reason for this unexpected lack of reactivity will be discussed later.

Evidence for Oxazirane Intermediates. Since oxaziranes have been proposed as one of the major primary products in oxime photochemistry,[13] it was important to determine whether such intermediates could be detected in the present photohydrolysis reactions. Direct evidence of oxazirane formation by ^1H NMR or UV spectroscopy could not be obtained, which is not surprising since it is well-known that these derivatives are thermally unstable.[14] This is particularly true where the nitrogen atom of the oxazirane is unsubstituted, as would be inevitable in the present case. However, an indirect method[15] of detection can be used, which involves addition of potassium iodide to the photolyzed solution, followed by detection of any iodine formed using starch indicator. Oxaziranes are known to be good oxidizing agents, as illustrated in Scheme II. In this way, oxazirane formation could be detected for all oximes which hydrolyzed and over the whole pH range used, but only when photolyses were carried out at 4 °C. This illustrates the thermal sensitivity of these intermediates. However it was interesting that no oxazirane could

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[8] Padwa, A.; Albrecht, F. *J. Am. Chem. Soc.* **1974**, *96*, 4849.

[9] Izawa, H.; de Mayo, P.; Tabata, T. *Can. J. Chem.* **1969**, *47*, 51.

[10] March, J. *Advanced Organic Chemistry*; McGraw Hill: New York, 1968; p 821.

[11] Just, G.; Ng, L. S. *Can. J. Chem.* **1968**, *46*, 3381.

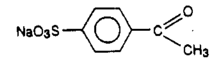
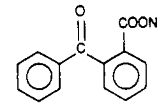
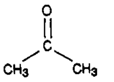
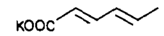
[12] The photo-Beckmann reaction is believed to be a two-photon process, where the second photon is absorbed by an initially formed photoproduct.[9]

[13] See for example: Ogata, Y.; Takagi, K.; Mizuno, K. *J. Org. Chem.* **1982**, *47*, 3684.

[14] Schmitz, E. *Adv. Heterocycl. Chem.* **1978**, *24*, 63.

[15] Oxaziranes are known to be oxidizing agents comparable to hydrogen peroxide. They easily oxidize iodide to iodine, which can be detected in trace amounts by Starch indicator. See: Schnitz, E. *Adv. Heterocycl. Chem.* **1964**, *2*, 92.

Table II. Triplet Energies of Water-Soluble Sensitizers and Quenchers

	E_T,[a] kcal mol^{-1}	λ(irradiation), nm
sensitizers		
	74	300
	69	350
	79	300
quenchers		
O_2	23	254
	~59	254

[a] Values taken from ref 16. The value for potassium sorbate was taken to be approximately equal to that of 1,3-pentadiene.

be detected at any pH for any of the analogous oxime ether photolyses.

From the above results, it is evident that photohydrolysis can occur by at least two different pathways. Any proposed mechanisms must be able to account for the formation of oxazirane (or lack of it) as well as the different pH dependences observed (to be discussed later).

Multiplicity of the Reactive States. To determine the multiplicity of the reactive states involved in photohydrolysis, both triplet-sensitization and triplet-quenching experients were carried out. The reported triplet energies[16] of the water soluble sensitizers and quenchers used are listed in Table II. Triplet energies of aromatic oximes are known to be around 58 kcal mol^{-1}[17] so that all three sensitizers employed should be effective. Enough sensitizer could be added to ensure that it absorbed at least 95% of the incident light at the wavelengths used (see Table II) in the case of the two aromatic sensitizers. In neither case was any photohydrolysis product observed. However, extensive syn–anti isomerization was observed in both cases, demonstrating that the sensitizers had transferred their triplet energy.

With acetone, due to inherent absorption by the oxime (or oxime ether) at 300 nm, the sensitizer only absorbed about 80% of the incident radiation, and in this case photohydrolysis product was observed, as well as syn–anti isomerization. Ketone or aldehyde formation from the acetone-sensitized reaction can be explained in one of three ways. First, the starting material (oxime or oxime ether) may absorb enough light to produce photohydrolysis directly. Although this is the simplest explanation, it is unlikely, since the sensitized reaction appears to be more efficient than that from direct irradiation. Secondly, it is possible that photohydrolysis can occur from a higher triplet level, and acetone might be the only one of the three sensitizers used which has a high enough E_T to populate this level. This also seems very unlikely, since triplets in solution phase are expected to follow Kasha's rule and react only from T_1.[18] The maximum energy gap ($T_2 - T_1$) available for oximes is about 21 kcal mol^{-1}.[19] By analogy with singlet states, it is expected that internal conversion will be the dominant process for energy gaps of less than 50–60 kcal mol^{-1}.[20] The third and most likely explanation is that the excited acetone molecule (^{3}(n,π*)) reacts directly with the ground-state oxime to give a photoaddition product, as outlined in Scheme III, which under the present reaction conditions breaks down to give the observed photohydrolysis product. Since this was peripheral to the main investigation, no further experiments were carried out to clarify this possibility.

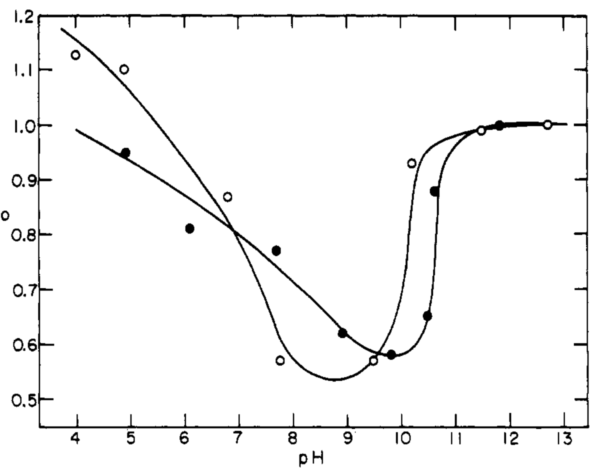
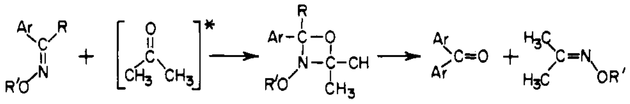


Figure 1. Plot of relative quantum yield (Φ/Φ_0) vs. pH for the photohydrolysis of acetophenone oxime (○) and benzaldoxime (●). Φ_0 is defined as the limiting quantum yield at high pH.

Scheme III



Only two triplet quenchers were used, due to the problem of water solubility. Neither led to any detectable change in either the products of efficiency of photohydrolysis. Parallel irradiation experiments with and without added quencher (either O_2 saturated solutions or 0.033 M potassium sorbate) gave exactly the same yield of carbonyl product within experimental error, from both the oximes and oxime ethers.

It is concluded from the above results that photohydrolysis most probably only occurs from the lowest singlet states of the oxime derivatives and that triplet states, if formed, are unreactive except for syn–anti isomerization. This is supported by the fact that the nitro-substituted derivatives do not show any photohydrolysis. Nitro aromatic compounds of this type are well-known to intersystem cross to T_1 with high efficiency.[21] In the present case, this is also evidenced by their complete absence of fluorescence, whereas some of the other oximes and oxime ethers show weak fluorescence in aqueous solution, and they all fluoresce in organic solvents.

Acid–Base Catalysis. Relative quantum yields for hydrolysis were determined in aqueous solutions of different acidity (in the pH range 3–14) for both oximes and their ethers. Plots of Φ/Φ_0 (where Φ_0 is defined as the limiting quantum yield observed at high pH) vs. pH are shown in Figure 1 for a typical aldoxime and ketoxime. These quantum yield–pH dependences are somewhat un-

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[16] Murov, S. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1973; pp 27–35.

[17] See ref 8 for example.

[18] Turro, N. J. *Modern Molecular Photochemistry*; Benjamin: Menlo Park, CA, 1978; p 103.

[19] This value was estimated by subtracting the approximate triplet energy of typical oximes (58 kcal mol^{-1}) from the triplet energy of acetone (79 kcal mol^{-1}).

[20] See ref 18, p 148.

[21] See for, example: Morrison, H. A. In *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Wiley: New York, 1969. Dopp, D. *Top. Curr. Chem.* **1975**, *55*, 49. Chow, Y. L. In *The Chemistry of Amino, Nitro and Nitroso Compounds and Their Derivatives*; S., Patai, Ed.; Wiley: New York, 1982; Chapter 6.

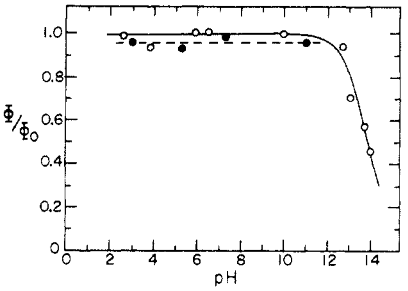

Figure 2. Plot of relative quantum yield (Φ/Φ_0) vs. pH for the photohydrolysis of the methyl ethers of acetophenone oxime (○) and benzaldoxime (●).

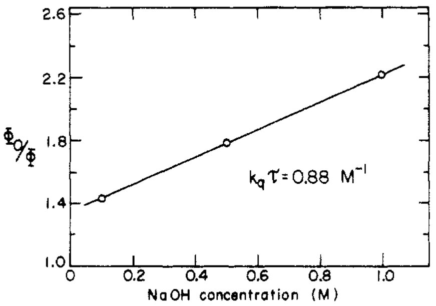

Figure 3. Stern–Volmer plot for the hydroxide ion quenching of photohydrolysis of acetophenone oxime *O*-methyl ether at high pH.

usual, in that they show a minimum efficiency around pH 8–10, with a steady increase toward low pH and a sharp increase toward high pH, and level off at a constant value of Φ above pH 11. It is evident that the curves for benzaldoxime and acetophenone oxime are qualitatively very similar, showing that there is probably no significant difference in the hydrolysis pathways for aldoximes and ketoximes.

In contrast, the hydrolyses of the methyl ethers of these two oximes are essentially pH independent from pH 2 to 12, as shown in Figure 2, although the methyl ether of acetophenone oxime shows a decrease in Φ/Φ_0 above pH 12. This decrease is believed to be due to diffusional quenching of S_1 by hydroxide ion at these high [OH$^-$] concentrations. This is supported by a linear Stern–Volmer plot of Φ_0/Φ vs. [OH$^-$] for the range 0.1–1.0 M NaOH, as shown in Figure 3. Assuming that diffusional quenching of S_1 occurs with a rate constant of 10^9 M^{-1} s^{-1}, the value of $k_q\tau^\circ$ obtained from the Stern–Volmer plot yields an estimate of τ° of 0.9 ns. This short singlet lifetime helps to explain why fluorescence of these oxime derivatives is difficult to observe in aqueous solution (although they fluoresce quite strongly in organic solvents). The photohydrolysis of the methyl ether of benzaldoxime would probably show similar quenching at high enough pH, but this could not be studied conveniently above pH 12 due to significant competition from the thermal hydrolysis pathway in this region. The essential point is that unlike the behavior of the oximes, the photohydrolysis of the methyl ethers is not subject to acid or base catalysis over a very wide pH range (2–12).

Absolute Quantum Yields. Absolute quantum yields were determined by using ferrioxalate actinometry.[22] This was done for all the oximes and oxime ethers which photohydrolyzed at pH 8 (corresponding approximately to the minima in Figure 1) and also at pH 4 for several of the compounds studied (see Table I). It can be seen that for most substrates Φ is in the 0.01–0.15 range, showing the

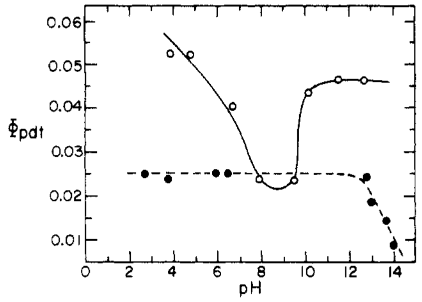

Figure 4. Absolute quantum yields vs. pH for the photohydrolyses of acetophenone oxime (○) and its *O*-methyl ether (●).

photohydrolysis is a moderately efficient process. Values of Φ were also determined as a function of pH for benzaldoxime and acetophenone oxime and their methyl ethers, as illustrated in Figure 4 for the two acetophenone derivatives. It is very interesting to note that the minimum Φ value in the pH-dependent curve of the oxime corresponds very closely to the pH-independent value for its ether. (A similar result was obtained for the two benzaldehyde derivatives) This strongly suggests that the pH-independent pathway is followed by both oximes and methyl ethers, with the former also being able to react via separate acid- and base-catalyzed pathways. Subtraction of the constant Φ values obtained for the methyl ethers from pH 2–12, from the Φ values for the free oximes should therefore give estimates of the efficiency of acid- or base-catalyzed oxazirane formation, since only the oximes show evidence of such intermediates being formed during hydrolysis. (It would in any event be difficult to see how the oxime ethers could form such intermediates.)

Benzonitriles. Photohydrolyses of several substituted benzonitriles (X = H, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, and 4-NO$_2$) were attempted under similar conditions to those used for the oximes and oxime ethers. Irradiations were carried out in both acidic and basic solutions (pH 0–12 range) at 254 and 300 nm, respectively. None of the expected photohydrolysis product (i.e., substituted benzamide) was found with any of the substrates, and only starting material could be recovered from the photolysis solution (in ca. 95% yield). Experiments at higher base concentration (NaOH $\geq$ 0.1 M) with benzonitrile itself showed that small amounts of benzamide could be produced, but under these conditions the photohydrolysis was only slightly more efficient than that of the thermal control reaction.

This lack of photochemical reactivity, in acid solutions particularly, was completely unexpected since the analogous phenylacetylenes all photohydrate cleanly and efficiently,[1] with acid catalysis. (This is true of the 3- and 4-NO$_2$ derivatives as well as those with electron-donating substituents.) One possible explanation for this photostability in acid solution is that the singlet states of benzonitriles are (n,π^*) in character, which would lead to reduced rather than enhanced excited-state basicity. However, it is believed that the lower singlet state of benzonitrile is of (π,π^*) type.[23] In addition, fluorescence quenching experiments were carried out on benzonitrile at different pH values. These showed a very similar type of fluorescence titration curve (as shown in Figure 5) to those previously obtained for phenylacetylenes and styrenes,[1,2] with an inflection point at approximately $H_0 = -1.3$ (24% H$_2$SO$_4$), further indicating that for benzonitrile the lowest singlet state is of $^1(\pi,\pi^*)$ character. Although such inflection points, based on fluorescence titration of the base form alone, do not give accurate estimates[24] of p$K^*{}_1$H$^+$, they do

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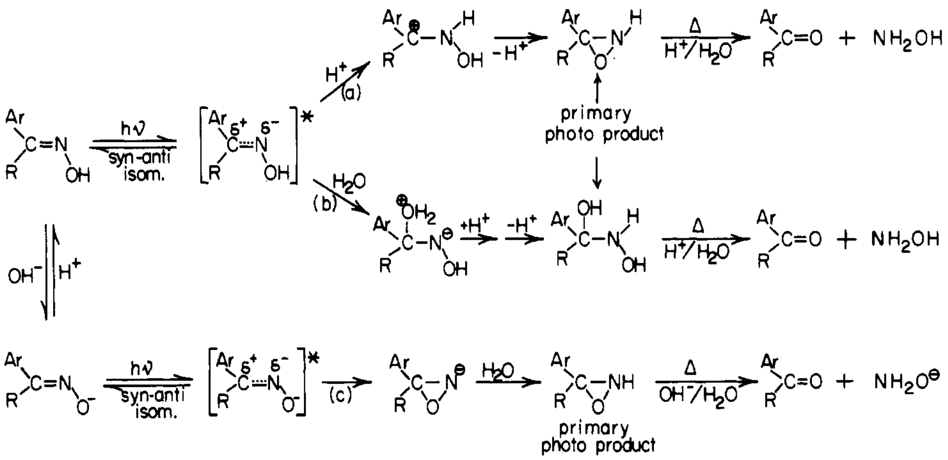
(22) Reference 16, pp 119–123.

(23) Lim, E. C. *Excited States*; Academic: New York, 1974; p 265.

Scheme IV



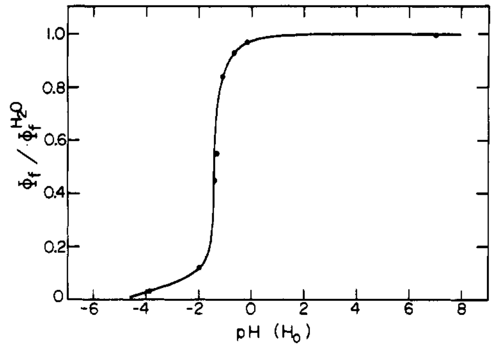


Figure 5. Plot of fluorescence quenching ($\Phi_F^{H_2O}/\Phi_F$) as a function of pH (H_0) for benzonitrile. ($\Phi_F^{H_2O}$ based on observed fluorescence intensity at pH 7).

indicate very strongly that the excited state pK value has been shifted considerably from its known ground state value (p$K_{S_0H^+}$ = −10),[25] and perhaps by as much as 9 logarithmic units. Such a pK shift would be in accord with the expected behavior of aromatic (π,π^*) states of this type, based on many reported examples.[4,5]. In addition, it would be expected that benzonitriles would be at the very least as basic as the corresponding phenylacetylenes, in either their ground or excited states.

Based on the above evidence, it appears that the lack of photohydrolytic reactivity found for the substituted benzonitriles is not due to an insufficiently basic or a too short-lived excited state and that some other explanation must be found for the great difference in photoreactivity between nitriles and either phenylacetylenes or oxime derivatives, as will be discussed later.

Discussion

From the minimum in the quantum yield pH curve for the oximes, which occurs at about pH 8–10 as shown in Figures 1 and 4, it is evident that both forms of the oxime, neutral molecule, and oximate ion, are capable of undergoing photohydrolysis. The ground-state pK values of oximes are approximately 11,[26] so that the sharp rise in efficiency above pH 10 is attributable to increasing ionization of the substrate, before irradiation. Above pH 11, where most of the substrate is present as oximate ion, the quantum yield starts to level off and becomes effectively constant at pH >12. Below pH 9, where substrate is present as the neutral oxime form, the quantum efficiency increases steadily as the pH is lowered and the curves show indications of downward curvature[27] as very low pH values are approached. Based on the attempts to detect oxazirane intermediates and the triplet sensitization and quenching results, it is proposed that oximes photohydrolyze via the mechanistic pathways outlined in Scheme IV. At low pH, oxime is excited to its S_1 state, which is polarized as shown in Scheme IV, followed by rapid proton transfer, on nitrogen (presumably but not certainly with concurrent electronic deactivation)[28] to give a carbocation which rapidly undergoes ring closure via oxygen attack, followed by proton loss to yield an oxazirane. This is believed to be the primary photochemical product, which under the acidic reaction conditions undergoes rapid thermal hydrolysis before or during workup, to yield an aldehyde or ketone plus hydroxylamine. The mechanism for the oximate ion hydrolysis at high pH is believed to be similar, except that catalysis is not involved (except in the sense of converting oxime to oximate). In this case the S_1 state of the oximate ion undergoes ring closure directly to give oxazirane. Again under the reaction conditions involved, thermal hydrolysis of this primary product yields carbonyl compound and hydroxylamine, as its anion.

Since oxaziranes of the type shown in Scheme IV are known to be very unstable thermally,[14] their rapid acid or base hydrolysis in aqueous solution would explain why no photo-Beckmann products are observed (see Scheme I). Increased irradiation times could probably be used to increase isolated yields of photohydrolysis product, providing conditions were adjusted to minimize any possible contamination by photo-Beckmann product, such as by running reactions at ≥25 °C and at pH's above 10 or below 4. The fact that the observed maximum quantum yields are generally only modest ($\Phi \leq 0.15$) can be explained by concomitant and efficient syn–anti isomerization. This could occur directly from S_1 with accompanying deactivation, or via intersystem crossing to T_1 followed isomerization.

The mechanism of photohydrolysis of the corresponding oxime ethers is clearly different from the above, since no oxazirane intermediate could be detected in any case (even at 4 °C), and the reactions are essentially pH independent. It is proposed that the oxime ethers react from their S_1 state by uncatalyzed addition of water across the CN

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[24] Schulman, S. G.; Capomacchia, A. C. *Spectrochim. Acta* **1972**, *28A*, 1.

[25] Arnett, E. M. *Progr. Phys. Org. Chem.* **1963**, *1*, 223.

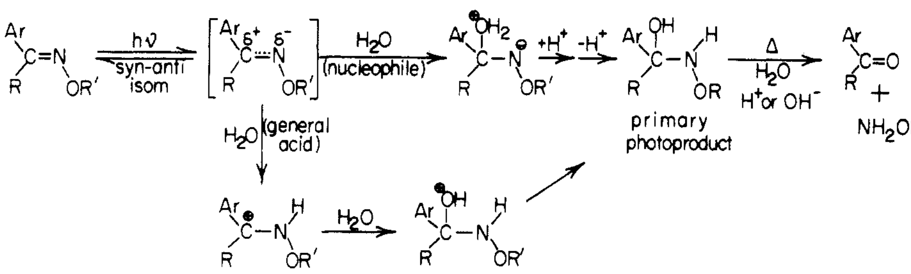
[26] *Handbook of Biochemistry*; CRC: Boca Raton, FL, 1968; p J159.

[27] The curves of Φ vs. pH in this region are similar in appearance to the sigmoidal increases of Φ observed at low pH for photohydration reactions,[1,2] but it would be expected that any inflection point would occur at different acidity in the two cases.

[28] α-Aryl carbocations of this type can be generated adiabatically, as shown recently.[29]

[29] Wan, P.; Yates, K.; Boyd, M. K. *J. Org. Chem.* **1985**, *50*, 2881.

Scheme V



double bond. This is probably initiated by nucleophilic attack of water on carbon (as outlined in Scheme V) to give a zwitterion which then undergoes rapid proton transfers with solvent to give a 1-(*N*-methoxyamino)-1-arylethanol or -methanol as primary photoproduct. Although none of this primary product could be isolated, it again seems highly likely that it would undergo rapid thermal acid- or base-catalyzed hydrolysis before or during workup, to give the observed carbonyl product plus methoxylamine. Another possibility (also shown in Scheme V) is that water addition to S_1 is initiated by water functioning as a general acid (since general acid catalysis has been observed in analogous photohydrations),[2] yielding a similar carbocation to that shown in Scheme IV for neutral oximes. This could not effectively undergo ring closure to give an oxazirane but could undergo fast nucleophilic attack by water to give an oxonium ion, followed by proton loss to give the *1-(N-*methylamino)-1-aryl alcohol. Which of these two possibilities for the uncatalyzed hydrolysis of oxime ethers is correct, would be very difficult to establish firmly since they are kinetically indistinguishable. However, if water were capable of acting as a general acid in this way, it is difficult to see why the reactions would not also be subject to H_3O^+ catalysis, yet the quantum efficiency of oxime ether hydrolysis is clearly not acid dependent from pH 2 to 12. It is concluded that it is most probable that both oxime ethers (at all pH's) and oximes (at pH 8–10) photohydrolyze via nucleophilic attack of water on S_1 as illustrated in Schemes IV and V.

The complete absence of photohydrolysis products for the substituted benzonitriles from pH 0–12 was at first very surprising, since it had been expected that these substrates would react at least as rapidly as the corresponding phenylacetylenes, at least in acid solution.[1] Their lack of reactivity is clearly not due to the inability of H_3O^+ to protonate S_1, as shown by increased fluorescence quenching in aqueous solutions of increasing acidity. This can easily be explained, however, *if* the excited-state surface for hydrolysis qualitatively resembles that for the ground-state reaction. The thermal acid-catalyzed hydrolysis of nitriles is known[9] to occur via preequilibrium protonation on nitrogen to give a carbocation, followed by nucleophilic attack on carbon by water, as shown schematically in Figure 6. (Thus the reactions are subject to specific acid catalysis, and due to the inherent low basicity[25] of nitriles, fairly concentrated acids are required to effect hydrolysis). If the excited-state surface for photohydrolysis is similar in that proton-transfer is not the rate-determining step, then even if the S_1 states did exhibit greatly enhanced basicity and even if k_H for protonation of S_1 were as high as 10^9 M^{-1} s^{-1}[30] (as assumed in estimating the fluorescence lifetime of benzonitrile), then collisional deactivation of the carbocation produced, or direct funneling down to the ground-state surface, would be expected to occur before nucleophilic attack on the carbocation could occur as illustrated in Figure 6. The ground-state carbocation produced in this way (even if a highly vibrationally excited or "hot" cation were involved) would more easily revert to starting material via deprotonation, since it is far from equilibrium, rather than surmount the high thermal barrier to nucleophilic attack. Hence the photohydrolysis would be very inefficient. This is unlike the case of the previously investigated photohydrations of phenylacetylenes and styrenes, since in both ground- and excited-state processes, proton-transfer is the rate-determining step,[1-3] and whether this is followed by rapid deactivation or whether funnelling is involved, the forward reaction has no significant thermal barrier to overcome and efficient photoreactions are observed.

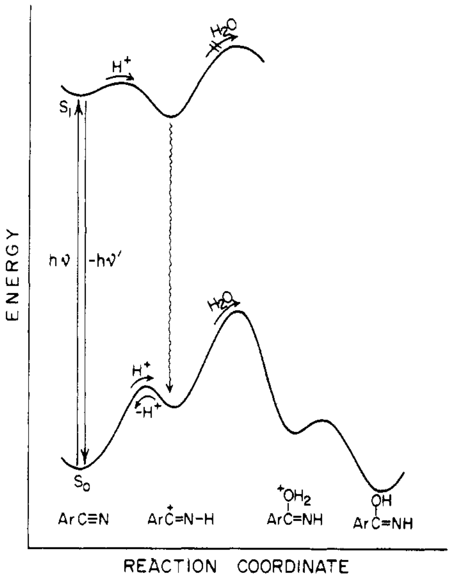


Figure 6. Schematic representation of ground- and excited-state surfaces for acid-catalysed hydrolysis of aromatic nitriles (energy coordinate not drawn to scale).

Conclusions. The photochemistry of carbon–nitrogen multiple bonds in aqueous solution is quite different from that expected on the basis of photohydration studies of carbon–carbon multiple bond systems, in several important respects. Although the photoreactions of oximes in their S_1 states do involve acid catalysis, this does not in general lead to a simple addition of water across the CN double bond but involves rapid ring closure to give oxazirane intermediates. Addition of water across the CN double bond does take place with oxime ethers, due to their inability to form oxaziranes, but this process is not catalyzed by acid or base. A similar uncatalyzed addition can also occur competitively for neutral oximes at pH's either where acid catalysis of neutral oxime is ineffective or where the oximate anion is not involved. At high pH values excited oximate ions can also react via their S_1 states to yield oxaziranes as photohydrolysis intermediates.

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[30] This is probably a lower limit estimate for k_H since analogous photoprotonations on carbon have k_H 10^6–10^8 M^{-1} s^{-1}. Protonation on nitrogen would be expected in general to be considerably faster than protonation on carbon.

Another important difference is that nitro-substituted oximes and oxime ethers do not photohydrolyze at all, indicating that T_1 states of oximes are unreactive, whereas both direct irradiation and triplet sensitization of nitrostyrenes[1] (and nitrophenylacetylenes) leads to efficient anti-Markovnikov addition of water.

Nitriles do not photohydrolyze at all in acid solution, whereas phenylacetylenes photohydrate very efficiently.[1,2] This is believed to be due to one essential difference between the two types of reaction, in that proton-transfer is not the rate-determining step in thermal nitrile hydrolysis, whereas it is in hydration reactions. If the analogous photochemical reactions have potential energy surfaces which mirror the ground-state processes in their general features, this would explain why nitrile photohydrolysis is completely inefficient. It is concluded that attempts to take advantage of enhanced excited-state basicities to produce efficient acid-catalyzed photoreactions under mild conditions are only likely to be successful where proton-transfer is the rate-determining step.

Experimental Section

General. Proton NMR spectra were recorded on a Varian T-60 spectrometer in $CDCl_3$ using Me_4Si as internal standard. UV spectra were recorded on either a Varian 2300 or an SP820 Series 2 spectrophotometer. GLC analyses were carried out with either a Varian Aerograph Series 3400 instrument, equipped with an OV101 fused silica capillary column, 15 m x 0.25 mm i.d., with a film thickness of 0.25 mm, or a Varian Aerograph Series 2700, equipped with a 3% OV101 column on Chromosorb W/HP. Both GLC instruments were equipped with a flame ionization detector. Integrated peak areas were calculated with a Varian CDS 111 processor. Fluorescence spectra were recorded on a Perkin-Elmer MPF-44B fluorescence spectrophotometer at room temperature. All fluorescence spectra recorded were uncorrected. Preparative separations were carried out with 2 mm thick silica gel TLC plates coated with a fluorescent indicator to facilitate detection of the bands or with a Harrison Research Chromatotron, Model 7294, for analytical separations. Irradiations were carried out with a Rayonet RPR-100 reactor with 16 lamps (32 W) unless otherwise specified, at 254, 300, or 350 nm as required. Solutions were bubbled with argon gas for at least 20 min before irradiation to reduce oxygen content. Magnetic stirring was used on preparative runs (i.e., those with over 500 mL of solution). In the analytical photolyses (i.e., those with 20 mL of solvent), the quartz tubes were placed in a merry-go-round apparatus in the photolysis reactor. All photolyses were cooled to ensure no thermal reaction. This was accomplished either by using a cold finger or by carrying out the photolyses in a refrigerated room kept at 4 °C. As added insurance, blanks were also run and analyzed to ensure no significant thermal reaction resulted during the time of irradiation. Although it would have been possible to subtract out any thermal reaction contributions to the photolysis reaction, this procedure was not followed. Instead, the photoreaction was only reported in the cases where >99% of the product resulted from the photochemical pathway.

Aqueous Solutions. Solutions of various pH were prepared either by dilution of concentrated (95%) sulfuric acid or by dissolving Analar grade NaOH, using doubly distilled water. Values of pH were determined with a digital pH meter (Orion Research Company, Model 801) which was calibrated before each usage with two buffers. Buffers ranging in pH from 1.00 to 12.00 were obtained from Fisher Scientific Co.

Syntheses. All oximes were either purchased or prepared by a standard oximation method,[31] a representative example being as follows. Sodium acetate (2 equiv) was added to acetophenone (1 equiv) along with hydroxylamine hydrochloride (2 equiv). All three reactants were dissolved in the minimum amount of 95% ethanol and refluxed for 4 h. After the mixture had been cooled, crystals were collected and recrystallized from $H_2O/EtOH$. The yield of purified product was greater than 80%. All oxime ethers were prepared analogously except that methoxylamine hydrochloride was used instead of hydroxylamine hydrochloride. All three reactants were then used in equimolar amounts.

In certain cases the oxime or oxime ether was contaminated with starting carbonyl compound. The following general procedure was used for purification of the oxime. To a 1:1 mixture of 95% ethanol and glacial acetic acid (20 mL of each) were added Girard's T reagent[32] (ca. 2 g) and the crude oxime (6 g). The mixture was refluxed for an hour and then cooled to room temperature. Addition of H_2O (50 mL) and extraction with CH_2Cl_2 (2 × 50 mL) gave an organic layer, which was washed twice with aqueous $NaHCO_3$, dried with anhydrous $MgSO_4$, filtered, and then rotary evaporated. GLC analysis proved to be the most sensitive detector for the presence of carbonyl substrate. In some cases repeated washings with Girard's T reagent were required to obtain a greater than 99% purity of the oxime.

In general, NMR spectra and GLC retention times were used not only to verify the structure of the oximes and oxime ethers but also to determine their purity. In many cases melting points and infrared spectra were used for additional verification, where literature values were available.[33] In all cases spectral and other information was fully consistent with the expected structure based on the starting aldehyde or ketone. The method of preparation used favors the thermodynamically more stable anti isomer,[34] which was formed in >95% yield compared to the syn isomer. This was shown by the sharpness of the melting points obtained. However, irradiation leads to a steady-state concentration of both isomers, so that no matter which isomer is predominant in the starting material, both are being photolyzed. This could be determined easily for the aldoximes and their ethers, since it is known for these compounds that the aldehydic proton in the anti isomer lies at ~0.7 ppm to higher field than that of the syn isomer.[35] It was only after photolysis that the syn isomer could be detected in the NMR spectrum. However in all cases (whether by GLC retention times or by proton NMR), the presence of the syn isomer could be detected after only 30 s of irradiation.

In the case of the substituted benzonitriles, all substrates were obtained commercially and used without further purification.

Fluorescence Measurements. Solutions for fluorescence studies were prepared by injecting a stock solution of the substrate (in acetonitrile) into the appropriate acid solution via a microliter syringe. Generally this consisted of adding substrate (20 mg) to a 10.0-mL volumetric flask and diluting to the mark with acetonitrile. This solution (10–50 mL) was added to a fluorescence cuvette holding the acid solution (3.0 mL). Fluorescence spectra were then recorded directly.

Triplet Sensitization. All triplet sensitizers were commercially available, and experiments were performed as follows. The oxime or oxime ether (ca. 25 mg) was placed in cosolvent (CH_3CN) (1 mL) and then added to H_2O (20 mL). The ultraviolet spectrum of the solution was then recorded. An aqueous solution (60 mL) containing sensitizer (5 g) was prepared by adding sufficient dilute NaOH to ionize the sensitizer. The pH of the resulting solution was adjusted to neutral. The sensitizer solution (600 mL) was then added to a quartz tube containing the oxime. In the case of acetone a 20% v/v solution was used instead. By utilizing UV spectrophotometry, it was possible to ensure that over 95% of the light is absorbed by the sensitizer. With 2-benzoylbenzoic acid as sensitizer, irradiation was carried out 350 nm whereas with both *p*-acetylbenzenesulfonic acid and acetone the photolysis was run at 300 nm. In the case of acetone, it was found that only 80% of the light was absorbed, due to its low absorptivity at 300 nm. After preparation of the solutions, Ar gas was bubbled through for at least 20 min to displace oxygen. The quartz tubes were then placed in a merry-go-round apparatus and cooled to 4 °C. Irradiation proceeded at the appropriate wavelength for approximately an hour. Workup consisted of NaCl saturation,

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(31) Vogel, A. *Textbook of Practical Organic Chemistry*, 4th ed.; Longman: New York, 1981; p 1113.

(32) Pasto, D. J.; Johnson, C. R. *Organic Structure Determination*; Prentice Shall: Englewood Cliffs, NJ, 1969; p 393.

(33) Rappoport, Z. *Handbook of Tables for Organic Compound Identification*, 3rd ed.; Boca Raton: FL, 1981.

(34) Phillips, W. D. *Ann. N. Y. Acad. Sci.* **1958**, *70*, 817.

(35) Pejkovic, I.; Hranisavljevic, M.; Nesic, S.; Pascual, C.; Simon, W. *Helv. Chim. Acta.* **1965**, *48*, 1157.

extraction with CH_2Cl_2 (2 × 100 mL), drying with anhydrous $MgSO_4$, filtration, and finally rotary evaporation. Analysis by NMR spectroscopy and gas chromatography yielded only the syn and anti isomers of the starting material, except in the acetone-sensitization reaction, where photohydrolysis product was observed as well.

Triplet Quenching. Two quenchers were used, oxygen and potassium sorbate. In the oxygen-quenching runs, each of two quartz tubes contained of oxime (20 mg) dissolved in CH_3CN (1 mL) and H_2O (19 mL). One tube was then saturated with oxygen by passing oxygen gas through the solution for at least 20 min, while the other tube was oxygen depleted by saturation with Ar gas. The solutions were then irradiated at 254 nm for 40 min. Workup of the reaction proceeded in the usual fashion as outlined for the triplet sensitization reactions. GLC analyses showed that there was no observable difference in the yield of carbonyl product between the two tubes.

The procedure for quenching by potassium sorbate was very similar to that used in the triplet sensitization experiments. From UV absorption spectra the concentration of oxime and quencher (0.033 M) was such that the oxime was shown to absorb >95% of the light at 300 nm. After irradiation for approximately 1 h, workup was carried out in the usual manner. GLC analysis of the crude product revealed no difference in the amount of ketone produced relative to the control experiment which had no quencher.

Photolyses. The following experiments were typical of the procedures employed. Preparative and analytical runs for the oxime ethers and nitriles were carried out in a similar manner to those for the oximes.

(a) Acetophenone Oxime (Preparative Run). A solution containing of oxime (300 mg) in acetonitrile (20 mL) was added to water (600 mL). This solution as purged with argon gas for 20 min in a quartz vessel. The quartz tube was then equipped with a stirring bar and cold finger and irradiated at 254 or 300 nm for 1 h. The photolyzed solution was then worked up by extraction with of dichloromethane (2 × 100 mL). After being dried (anhydrous $MgSO_4$) followed by filtration and removal of the solvent by rotary evaporation, the crude product was then analyzed by TLC, proton NMR spectroscopy, and GLC. The product was then purified by preparative TLC, with methylene chloride as the eluent. Acetophenone was the sole product, its structure being confirmed by comparison with an authentic sample. GLC analyses of the crude product revealed that both syn and anti isomers of the oxime were also present.

(b) Acetophenone Oxime (Analytical Run). The oxime (20 mg) was placed in water (17 mL) with acetonitrile (3 mL) as cosolvent. Irradiation of the solution was carried out in a merry-go-round apparatus at 4 °C (refrigerated room) with 254-nm lamps for 1 h. The photolysate was then worked up in the usual manner by extracting with dichloromethane (2 × 100 mL), followed by drying with anhydrous $MgSO_4$. After filtration and removal of solvent, the residue was dissolved in 1–2 mL of acetonitrile and injected into the GLC. Acetophenone was detected as the only hydrolysis product, along with a mixture of syn and anti isomers of the starting oxime. In all cases, photohydrolysis product and recovered oximes (or oxime ethers) corresponded to approximately 95% of starting material.

Product Identification and Analysis. In all cases where photohydrolysis had occurred, identification of the carbonyl compound (purified by TLC) was made by comparison (GLC, UV, and ^1H NMR spectra) with an authentic sample of the substituted benzaldehyde or acetophenone, all of which are available commercially. Quantitative analysis of product mixtures (carbonyl compound and unreacted anti and syn oxime) was carried out on the basis of gas chromatography, using integrated peak areas. The gas chromatograph was calibrated by using known mixtures of benzaldehyde oxime and and benzaldehyde to verify that these closely related oximes and carbonyl compounds do show a 1:1 relationship between amounts of material and peak areas.

Absolute Quantum Yields. Quantum yields were determined using potassium ferrioxalate as the actinometer. Preparation of solutions and use of the actinometer were exactly as described elsewhere.[22] Determinations were carried out by using a Rayonet RPR-100 reactor at 254 nm, with either four or eight lamps in operation, which were allowed to equilibrate for at least 20 min before photolysis of the actinometer solutions. Blanks were run in every case to test the quality of the stock actinometer solutions, which were freshly prepared before each determination. Because the 254-nm lamps emit radiation at >300 nm, none of which is absorbed by any of the oxime derivatives, corrections were made by running parallel ferrioxalate determinations in a plastic cuvette which passed only wavelengths above 300 nm. It was found that 6% of the light emitted by the 254-nm lamps comes from wavelengths above 300 nm. This number is in excellent agreement with tabulated values[36] for the relative spectral energy distribution of these low-pressure Hg lamps. The numerical value of the light intensity per unit time at 254 nm was found to be 3.41×10^{-7} einsteins/min/lamp. All experiments carried out showed that this value is reproducible to within ±5%. Although the majority of light emitted is from the 254-nm line, all wavelengths from 254 to 300 nm are included in the calculation of lamp intensity. However the quantum yield for reaction of ferrioxalate is independent of wavelength in this region. Quantum yield determinations were then based on irradiations of known concentrations of substrate at 254 nm for 1 h in a merry-go-round apparatus using four or eight lamps as appropriate. The extent of product formation was determined by calibrated gas chromatographic analysis of the reaction mixture and the quantum yields determined from the expression

$$\Phi_{\text{pdt}} = \frac{(\text{number of moles of product})}{(I \times t \times \text{number of lamps})}$$

where I is the light intensity per lamp in einsteins/min and t is the irradiation time used. Duplicate determinations showed that the quantum yields were reproducible to within ±10%.

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(36) Reference 16, p 111.