

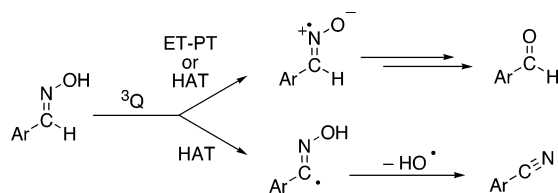
Effect of Structure in Benzaldehyde Oximes on the Formation of Aldehydes and Nitriles under Photoinduced Electron-Transfer Conditions

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The mechanistic aspects of the photosensitized reactions of a series of benzaldehyde oximes (**1a–o**) were studied by steady-state (product studies) and laser flash photolysis methods. Nanosecond laser flash photolysis studies have shown that the reaction of the oxime with triplet chloranil (^3CA) proceeds via an electron-transfer mechanism provided the free energy for electron transfer (ΔG_{ET}) is favorable; typically, the oxidation potential of the oxime should be below 2.0 V. Substituted benzaldehyde oximes with oxidation potentials greater than 2.0 V quench ^3CA at rates that are independent of the substituent and the oxidation potential. The most likely mechanism under these conditions is a hydrogen atom transfer mechanism as this reaction should be dependent on the O–H bond strength only, which is virtually the same for all oximes. Product studies have shown that aldioximes react to give both the corresponding aldehyde and the nitrile. The important intermediate in the aldehyde pathway is the iminoxyl radical, which is formed via an electron transfer–proton transfer (ET–PT) sequence (for oximes with low oxidation potentials) or via a hydrogen atom transfer (HAT) pathway (for oximes with larger oxidation potentials). The nitriles are proposed to result from intermediate iminoyl radicals, which can be formed via direct hydrogen atom abstraction or via an electron-transfer–proton-transfer sequence. The experimental data seems to support the direct hydrogen atom abstraction as evidenced by the break in linearity in the plot of the quenching rates against the oxidation potential, which suggests a change in mechanism. The nitrile product is favored when electron-accepting substituents are present on the benzene ring of the benzaldehyde oximes or when the hydroxyl hydrogen atom is unavailable for abstraction. The latter is the case in pyridine-2-carboxaldoxime (**2**), where a strong intramolecular hydrogen bond is formed. Other molecules that form weaker intramolecular hydrogen bonds such as 2-furaldehyde oxime (**3**) and thiophene-2-carboxaldoxime (**4**) tend to yield increasing amounts of aldehyde.

Introduction

The photooxidation of oximes has been shown to yield the corresponding ketones as the major product.¹ The proposed

mechanism for this transformation involves electron transfer, followed by a proton transfer (ET–PT) and follow-up reactions, including a second oxidation and nucleophilic attack by water, to form the carbonyl compound (Scheme 1).^{1c}

The proposed intermediate in the photooxidation reactions of oximes is the corresponding iminoxyl radical, which is formed via the ET–PT sequence. It must be noted that a hydrogen atom transfer (HAT) pathway would also lead to the formation of this reactive intermediate; however, this pathway was not

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SCHEME 1

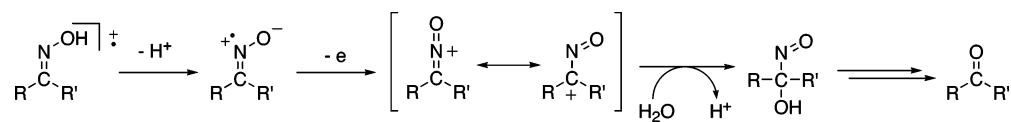


TABLE 1. Summary of Oxidation Potentials, Ionization Potentials, Quenching Rates, and Steady-State Photolysis Data of Meta- and Para-Substituted Benzaldehyde Oximes

oxime	X	E_p^a (V)	ΔG_{ET} (kcal mol ⁻¹) ^b	IP (kcal mol ⁻¹) ^c	k_q^d (M ⁻¹ s ⁻¹)	% C ^e	% N ^f	% A ^f	N/A ^g
1a	<i>p</i> -OCH ₃	1.45	-16.1	184.44	1.02×10^{10}	51	28	23	1.2
1b	<i>m</i> -OCH ₃	1.77	-8.8	189.60	7.24×10^9	74	44	30	1.5
1c	<i>p</i> -CH ₃	1.77	-8.8	191.29	5.98×10^9	32	13	20	0.6
1d	<i>m</i> -CH ₃	1.84	-7.1	193.95	5.86×10^9	28	12	16	0.8
1e	<i>p</i> -F	1.84	-7.1	196.36	3.98×10^9	17	9	8	1.1
1f	<i>p</i> -Cl	1.85	-6.9	196.54	3.46×10^9	26	13	13	0.9
1g	<i>p</i> -H	1.90	-5.8	195.76	6.58×10^8	23	11	12	0.9
1h	<i>m</i> -Cl	1.99	-3.7	199.34	2.96×10^8	21	11	11	1.0
1i	<i>m</i> -F	2.01	-3.2	200.71	3.00×10^8	35	23	12	2.0
1j	<i>m</i> -CN	2.10	-1.2	203.51	1.55×10^8	28	19	8	2.3
1k	<i>m</i> -NO ₂	2.14	-0.2	209.51	4.68×10^7	28	20	9	2.2
1l	<i>m</i> -CF ₃	2.17	+0.5	205.09	1.58×10^8	18	8	10	0.8
1m	<i>p</i> -CN	2.19	+0.9	203.27	6.27×10^7	46	27	19	1.5
1n	<i>p</i> -CF ₃	2.22	+1.6	207.01	1.58×10^8	17	8	8	1.0
1o	<i>p</i> -NO ₂			211.93	1.25×10^8	35	21	15	1.4

^a Oxidation (peak) potentials measured by cyclic voltammetry (0.1 M tetraethylammonium perchlorate in CH₃CN, Ag/AgCl electrode). ^b Calculated using the Weller equation (ref 10): $\Delta G_{ET} = 23.06[E^{ox} - E^{red} - E_T]$ kcal/mol. ^c Ionization potentials calculated by AM1. Listed value is that of the syn isomer.

^d Quenching rate of ³CA determined by laser flash photolysis. ^e Conversion was calculated on the basis of the GC-FID peak area of the oxime before and after photolysis. ^f Product yields (% nitrile and % aldehyde) determined by calibrated GC/FID. ^g Ratio of nitrile and aldehyde products.

believed to be important under those conditions.^{1c} A similar mechanism may be involved in the enzymatic oxidation of oximes; possible pathways for the detoxification of xenobiotics by the cytochrome P450 enzymes include electron transfer initiated processes as well as reactions via hydrogen atom abstraction.² Enzymatic oxidation and photooxidation of oximes yield the same products as shown by a recent study on the use of hydroxyimines as prodrugs for carbonyl-containing drugs such as ketoprofen and nabumetone.³ Oxime radical cations and iminoxyl radicals also are the proposed intermediates in the nitric oxide synthase (NOS) catalyzed metabolism of L-arginine to L-citrulline.^{4,5} The similarities between the P450 and NOS systems have been reported.⁶ Furthermore, iminoxyl radicals have also been proposed as intermediates in the formation of nitric oxide from oximes.^{7,8} Interestingly, very little is known about the structure and reactivity of these reactive intermediates.

In our previous work, we noticed that the photooxidation of aldoximes yielded both the corresponding aldehyde and the nitrile.^{1a} The pathway leading to the aldehyde product is most likely

the same as that leading from the ketoxime to the corresponding ketone (Scheme 1); however, the pathway and intermediates involved in the formation of the nitrile are not yet known. It is interesting to note that the enzymatic oxidation of aldoximes was reported to yield only the corresponding nitriles.⁹ The goal of the work described in this paper is to learn more about the possible pathways and intermediates involved in the photooxidation of aldoximes. We have undertaken an extensive study involving the steady-state (SS) and laser flash photolysis (LFP) of meta- and para-substituted benzaldehyde oximes (**1a–o**) using triplet sensitizers. The photochemical experiments were complemented by electrochemical data as well as semiempirical (AM1) and density functional theory (DFT) calculations on the neutral compounds, the radical cation species, and some of the proposed intermediates.

Results and Discussion

A. Oxidation and Ionization Potentials of Meta- and Para-Substituted Benzaldehyde Oximes. The measured oxidation (peak) potentials (E_p) for the meta- and para-substituted benzaldehyde oximes are listed in Table 1. The oxidative scans are broad and irreversible in every case. No reliable data could be obtained for oxime **1o**. The data shows the expected trend in which electron-accepting substituents increase the observed oxidation potential whereas electron-donating substituents have the opposite effect. Electron transfer is expected to take place with most aldoximes when using chloranil (CA; $E_{red}^* = 2.15$ V) as the sensitizer based on the calculated free energy (ΔG_{ET}) using the Weller equation.¹⁰ The ionization potentials (IP) of the benzaldehyde oximes were determined by theoretical methods (AM1). Both syn and anti isomers were considered. The geometry of the optimized neutral compound was used as

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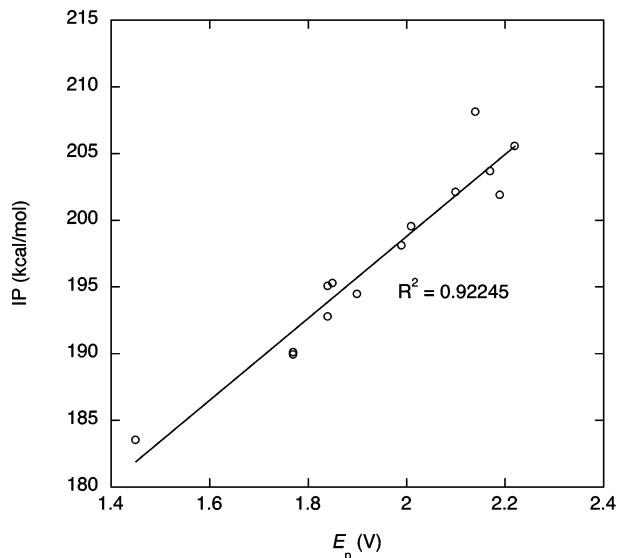


FIGURE 1. Plot of the measured oxidation potentials (E_p) of a series of meta- and para-substituted benzaldehyde oximes against the calculated (AM1) ionization potentials (IP).

a starting point for a geometry optimization of the corresponding radical cation species. The results show that the syn isomers are of lower energy than the corresponding anti isomers but the differences are small (never more than 2 kcal/mol). Previous work has shown that the calculated IP values are very similar when using either DFT or AM1.^{1b,c} A plot of the measured oxidation potentials against the calculated IP (AM1) gives an excellent correlation ($r^2 = 0.92$; Figure 1). The highest IP was calculated for **1o**, which is consistent with the fact that no reliable oxidation potential could be observed for that oxime. These results confirm that the measured oxidation (peak) potentials are an accurate parameter for testing whether the reactions proceed via an initial electron-transfer step.

Further analysis of the electrochemical data revealed that they also correlate well with several polar substituent constants (σ -values) such as σ_{pol}^{11} ($r^2 = 0.82$) and σ_{mb}^{12} ($r^2 = 0.84$), but not with radical substituent constants such as σ_{JJ}^{12} ($r^2 = 0.04$) or σ_{rad}^{13} ($r^2 = 0.02$). Similar results were obtained for a series of substituted acetophenone oximes^{1b,c} and suggest that the electrochemical process results in the formation of cationic species rather than radicals, consistent with a study by Tallec et al.¹⁴

B. Laser Flash Photolysis Studies: Quenching of Triplet Chloranil. All substituted benzaldehyde oximes quenched triplet chloranil (^3CA); the quenching rate constants are listed in Table 1 and varied from a low of $4.68 \times 10^7 \text{ M}^{-1}\text{s}^{-1}$ (**1k**) to a high of $1.02 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$ (**1a**). A plot of the quenching rate against the oxidation potentials shows a linear behavior for those oximes with $E_p < 2 \text{ V}$; however, the quenching rate levels off when using oximes with $E_p > 2 \text{ V}$ (Figure 2A). A similar trend is observed when using the IP data (Figure 2B). The quenching of ^3CA by a series of substituted acetophenone oximes did not show this trend even though some of the measured oxidation potentials were above 2 V.^{1b}

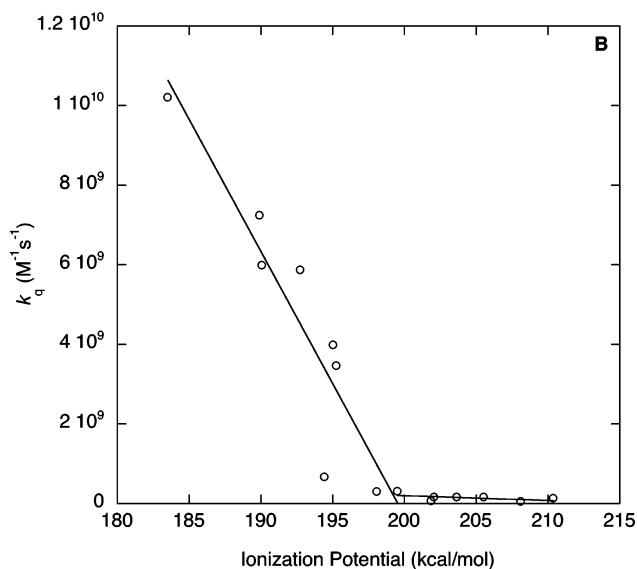
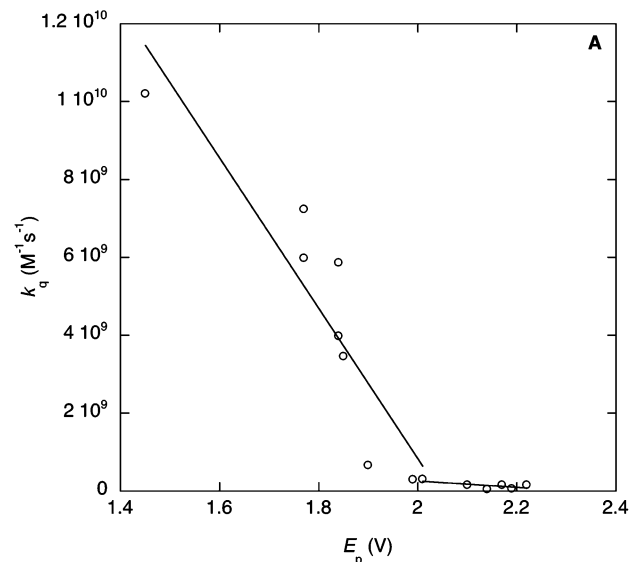


FIGURE 2. Plots of (A) the correlation between the measured oxidation potentials (E_p) of a series of substituted benzaldehyde oximes and the measured quenching rates of triplet chloranil and (B) the correlation between the calculated (AM1) ionization potentials and the measured quenching rates of triplet chloranil. The obvious break in both plots appearing around 2 V or 200 kcal/mol presumably suggests a change in mechanism.

These observations suggest a change of mechanism as a result of the structural differences. Triplet quinones can be quenched by substrates via a number of different pathways (e.g., electron transfer, energy transfer, hydrogen atom transfer, etc.). As proposed before,^{1b} a linear correlation between the measured oxidation potentials and the quenching rates suggests an initial electron-transfer step, which is the case for aldoximes with $E_p < 2 \text{ V}$. However, for aldoximes with $E_p > 2 \text{ V}$ the quenching rate is independent of the substituent, and therefore, electron transfer (ET) is most likely not involved. Other pathways that may become dominant under these conditions are energy transfer or hydrogen atom transfer (HAT). In the case of HAT, the quenching rate would be determined by the O–H bond strength. Bordwell and co-workers have reported that the O–H bond strength in neutral oximes is virtually independent of the

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TABLE 2. Comparison of Hammett Data Obtained from Laser Flash Photolysis (LFP) Experiments on Meta- and Para-Substituted Benzaldehyde and Acetophenone Oximes

	meta		para	
	benz-aldehyde oxime	acetophenone oxime	benz-aldehyde oxime	acetophenone oxime
ρ_{rad}	-45	-30	0.87	0.44
ρ_{pol}	-10.7	-7.1	-2.3	-0.89
$\rho_{\text{rad}}/\rho_{\text{pol}}$	4.2	4.2	-0.38	-0.49
r^2	0.94	0.94	0.84	0.93
ρ_{JJ}	5.75	3.16	0.83	0.56
ρ_{mb}	-1.86	-1.22	-1.51	-0.56
$\rho_{\text{JJ}}/\rho_{\text{mb}}$	-3.1	-2.6	-0.5	-1.0
r^2	0.90	0.95	0.90	0.91

substituent,¹⁵ whereas in oxime radical cations the O–H bond strength is directly related to the substituent.¹⁶ These results suggest that the quenching process changes from an ET process to a HAT process if ET becomes energetically unfavorable. The differences in reactivity between aldoximes and ketoximes may be due to the presence of another abstractable hydrogen in aldoximes. The bond strength of the aldehyde =C–H is approximately 88 kcal/mol,¹⁷ which is almost identical to the O–H bond strength in oximes (assuming that the =C–H bond strength in oximes is similar to that in aldehydes).^{15,18} Such a (competing) pathway is not available in acetophenone oximes.¹⁹

To see if the change in mechanism was directly related to the substituents present on the ring, the quenching data was analyzed in terms of different Hammett parameters. Both polar (σ_{pol} and σ_{mb}) and radical (σ_{rad} and σ_{JJ}) substituent constants were used. In all cases, dual parameter sets (polar + radical) were required to obtain useful data (Table 2). For comparison, the data from the ketoximes studies is also included.

Little difference is seen between the data set obtained from a series of benzaldehyde oximes when compared to the data set from the acetophenone oxime series.^{1b} Despite the clear break that was observed in Figure 2, analysis of the quenching data in terms of polar and radical substituent constants does not lend support for the involvement of different intermediates in the formation of aldehydes and nitriles from aldoximes. However, it must be noted that steady-state experiments (see below) showed that in all cases both the nitrile and the aldehyde were present in the product mixtures, suggesting that possibly more than one pathway can be followed from the proposed intermediate, which would complicate the kinetic analysis of the data. A better mechanistic picture would probably be available if a single aldoxime would react exclusively to give the nitrile product.

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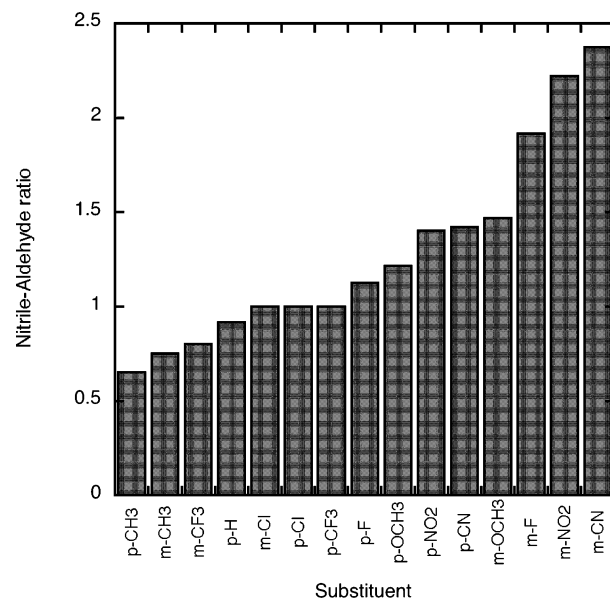
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(18) To the best of our knowledge, the bond strengths of the =C–H bonds in benzaldehyde oximes have not been determined. When comparing the =C–H bond lengths of aldehyde oximes and aldehydes (calculated by DFT methods, B3LYP/6-31G*), it is shown that these are nearly identical (0.001–0.002 Å difference at most). On the basis of these calculated values it is fair to conclude that the =C–H bond strengths in these molecules will be similar.

(19) Hydrogen atom abstraction from the hydroxyl group can be avoided by using *O*-alkyl aldoximes as shown by our studies on a series of aldoxime ethers. The results of this investigation will be published later.

**FIGURE 3.** Plot of the nitrile to aldehyde product ratio as a function of the substituent in the DDQ-sensitized reactions of substituted benzaldehyde oximes.

Furthermore, if the mechanism were to switch from ET to HAT, abstraction of the hydrogen from the OH group would yield an iminoxyl radical, which, according to Scheme 1, would undergo an electron transfer step and follow-up reactions to yield the aldehyde product. This pathway would further cloud the mechanistic aspects of these reactions. Since the quenching data only involves the initial step of the reaction, we have opted to analyze the aldoxime conversion as well as the product distribution in terms of polar and radical Hammett parameters in order to see if any trends would arise.

C. Hammett Studies of Aldehyde and Nitrile Formation in the Steady-State Photolysis of Meta- and Para-Substituted Benzaldehyde Oximes. To learn more about the intermediates involved in the photosensitized reactions of benzaldoximes, a mixture of the substituted benzaldehyde oxime and benzaldehyde oxime in acetonitrile was irradiated in the presence of a triplet sensitizer (2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DDQ). As expected, both the corresponding aldehydes and nitriles were formed in each case. The results from steady-state (SS) photolysis experiments are listed in Table 1. A plot of the nitrile/aldehyde ratio against the substituent shows that in general more of the nitrile is formed when using electron-accepting substituents (e.g., NO₂, CN; Figure 3).

A plot of the nitrile–aldehyde product ratio against the quenching rate (see the Supporting Information) does not show an obvious trend; however, a plot of the ratio against the calculated IP does seem to be in agreement with the data in Figure 3. It is interesting to note that in general the oximes that tend to form more of the nitrile upon irradiation are also those whose rate constants for quenching ³CA are slower. As indicated in the discussion above, it is suspected that these oximes react with the triplet sensitizers via a different mechanism. Note, however, that there are some exceptions. For example, aldoximes **1a** and **1b** quench ³CA very rapidly, yet they produce a significant amount of nitrile. Clearly, more than just a single parameter must be taken into account when analyzing the data. Most importantly, the measured quenching rates only represent the initial step in the overall sequence, and a variety of follow-

SCHEME 2

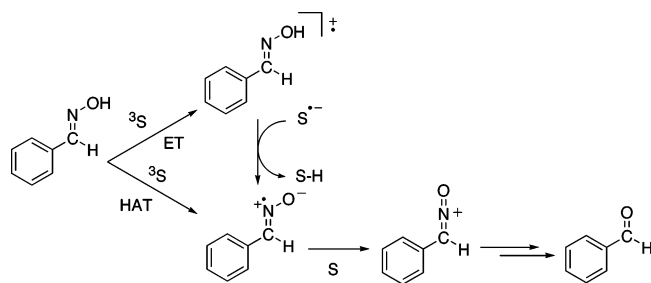
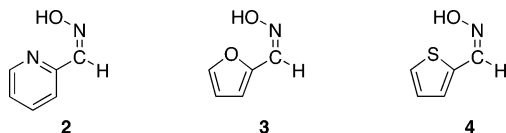


CHART 1. Aldoximes Used for Studies on the Effect of the Presence of an Internal Base on the Formation of an Iminoxyl Radical Intermediate



up reactions can take place. The quenching process is a kinetically controlled reaction, whereas product formation (aldehyde–nitrile ratio) is more likely to be thermodynamically controlled. This may lead to differences between the measured k_q values and the observed nitrile–aldehyde ratios, but at this point is it uncertain why only benzaloximes with certain substituents would show such behavior.

The mechanism for the formation of the aldehydes is assumed to be similar to the pathway involving the formation of acetophenones from acetophenone oximes (Scheme 1). The central intermediate in this pathway is the iminoxyl radical. Oxidation of this radical followed by hydrolysis results in the formation of the corresponding carbonyl compound. We have proposed that oxidation of the iminoxyl radical involves the ground-state sensitizer, which would allow the aldehyde to be formed via two separate pathways; this would explain the formation of the aldehyde in the case of aldoximes with high oxidation potentials (Scheme 2).

What remains uncertain, however, is whether the iminoxyl radical intermediate is also responsible for the formation of the nitrile product or if a different intermediate (and pathway) is involved. It is difficult to obtain any direct evidence for the intermediates involved in these reactions; however, if, as hypothesized above, a HAT process were more important for the formation of the nitrile from benzaldehyde oximes, radical effects would be expected to be more dominant in these reactions.

The data obtained in these studies (Table 1) was analyzed in terms of polar and radical substituent effects. First, the relative conversion was used to see if a pattern would appear. The results are listed in Table 3. For comparison, the data from a similar study on acetophenone oximes is also listed.^{1c} It can be seen from this data set that there are some differences between the aldehyde and ketone oxime series. In all cases, the radical effect is significantly larger than the polar effect; on the basis of these numbers, ionic (polar) effects seem less important in the reactions of benzaldehyde oximes compared to acetophenone oximes.

The data were also analyzed in terms of relative yield of the corresponding aldehydes and nitriles. The results of these analyses are listed in Table 4. Although the data is not always clear (some correlations were poor), a similar trend seems to arise; radical effects are more important than polar effects for

TABLE 3. Comparison of Hammett Data Obtained from Percent Conversion in Steady-State (SS) Photolysis Experiments on Meta- and Para-Substituted Benzaldehyde and Acetophenone Oximes

	meta		para	
	benz-aldehyde oxime	acetophenone oxime	benz-aldehyde oxime	acetophenone oxime
ρ_{rad}	-43	-155	1.10	1.26
ρ_{pol}	-8	-28.7	-0.42	-1.2
$\rho_{\text{rad}}/\rho_{\text{pol}}$	5.4	5.4	-2.60	-1.05
r^2	0.93	0.93	0.90	0.98
ρ_{JJ}	2.72	2.71	1.27	1.29
ρ_{mb}	-0.22	-0.43	-0.17	-0.69
$\rho_{\text{JJ}}/\rho_{\text{mb}}$	-12.4	-6.3	-7.34	-1.87
r^2	0.42	0.39	0.72	0.95

TABLE 4. Hammett Data Obtained from Analysis of Relative Nitrile and Aldehyde Yields in the Steady-State (SS) Photolysis of Meta- and Para-Substituted Benzaldehyde Oximes

		$\rho_{\text{rad}}/\rho_{\text{pol}}$	r^2	$\rho_{\text{JJ}}/\rho_{\text{mb}}$	r^2
nitrile	meta	4.4	0.92	-36.2	0.09
	para	-3.2	0.81	-9.4	0.58
aldehyde	meta	5.5	0.90	-3.7	0.80
	para	-2.1	0.91	-5.6	0.70

the formation of both the aldehyde and the nitrile. However, there are only small differences between the two data sets and the errors do not allow for an accurate evaluation of the type of intermediate involved in the nitrile formation, although the most likely candidate would be a radical species. Due to the differences observed between the results obtained in the acetophenone oxime and benzaldehyde oxime studies, the intermediate is most likely not the iminoxyl radical, but the exact nature of the radical species remains uncertain.

D. Involvement of Iminoxyl Radicals in the Formation of Nitriles from Aldoximes: Effect of an Added Base. To further evaluate the involvement of iminoxyl radicals in the formation of nitriles from aldoximes, we have studied the effect of an added base on the reactions. The proposed mechanism for the regeneration of carbonyl compounds from oximes via photosensitized electron-transfer reactions involves deprotonation of the oxime radical cation.¹ The working hypothesis was that if iminoxyl radicals are not involved in the formation of the nitriles, favoring the iminoxyl radical formation would lead to a decrease in nitrile yield. To confirm this pathway, and to determine whether this reaction can be used more generally to generate iminoxyl radicals selectively, we have studied the influence of an added base on the photosensitized reactions of oximes. For proton-transfer reactions involving radical cation species a variety of bases can be used, but there is some precedent for using amines such as pyridine and collidine.²⁰ We have focused on three aldoximes with a built-in basic site (pyridine-2-carboxaldehyde oxime (2), 2-furaldehyde oxime (3), and thiophene-2-carboxaldehyde oxime (4); Chart 1) which were all expected to participate in the desired intramolecular proton transfer.

All oximes (0.015 M) were studied in the presence of benzaldehyde oxime (**1g**; 0.015 M) itself, which served as an internal reference. The results of these studies are listed in Table 5 and Figure 4.

A few interesting observations can be made. The relative reactivity of the oximes increases from **2** < **3** < **4**. As the

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SCHEME 3

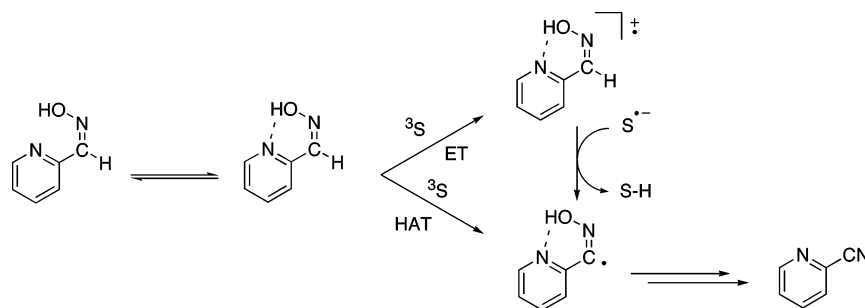


TABLE 5. Summary of Data Obtained from Chloranil-Sensitized Photolysis of Pyridine-2-carboxaldoxime (**2**), 2-Furaldehyde Oxime (**3**), and Thiophene-2-carboxaldoxime (**4**) in the Presence of Benzaldehyde Oxime (**1g**)

	% conversion	% aldehyde	% nitrile
2	34	0	33
1g	59	29	29
relative	0.6	0.0	1.1
3	42	30	10
1g	29	25	4
relative	1.4	1.2	2.5
4	61	47	14
1g	20	16	4
relative	3.1	2.9	3.5

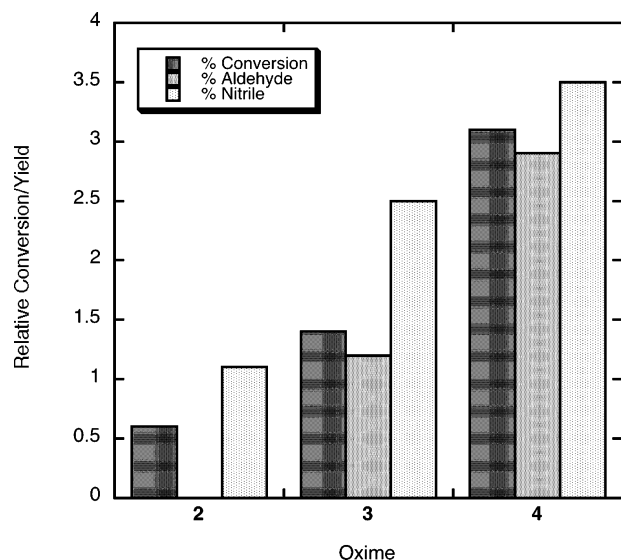


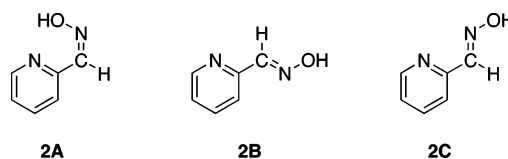
FIGURE 4. Relative oxime conversions, aldehyde yields, and nitrile yields in the photolysis of oximes **2–4** with benzaldehyde (**1g**) as the standard and chloranil as the sensitizer.

relative reactivity increases, the aldehyde and nitrile yields also increase but the nitrile/aldehyde ratio decreases. The most striking observation is the absence of any aldehyde when using oxime **2**. Increasing amounts of aldehyde are observed for the furan (**3**) and thiophene (**4**) oximes. The trend observed in this series ($N < O < S$) is in line with the expected basicity of those atoms. Based on these results, we propose that in these aldoximes the heteroatom acts as a base and forms a hydrogen bond with the proton from the hydroxyl group. The stronger the hydrogen bond, the less likely the hydrogen atom is to be removed and the mechanism changes. Since the hydroxyl hydrogen is “locked up” to some extent, the only other available hydrogen in these substrates is the iminyl hydrogen. Removal

TABLE 6. Results from Theoretical Studies (B3LYP/6-31G*) on the Different Conformations (A–C) of the Neutral and Radical Cations of Pyridine-2-carboxaldoxime (**2**), 2-Furaldehyde Oxime (**3**), and Thiophene-2-carboxaldoxime (**4**)

	absolute energies (Hartrees)		relative energies (kcal/mol)		
	neutral	RC	neutral	RC	IP (kcal/mol)
2A	−416.91125	−416.65160	0.00	0.00	162.92
2B	−416.91033	−416.60738	0.58	27.74	190.09
2C	−416.90498	−416.60349	3.93	30.19	189.18
3A	−398.64152	−398.34480	4.62	12.57	186.18
3B	−398.64889	−398.36098	0.00	2.41	180.65
3C	−398.64625	−398.36483	1.66	0.00	176.58
4A	−721.61572	−721.31785	7.71	17.95	186.90
4B	−721.62539	−721.34475	1.64	1.08	176.10
4C	−721.62801	−721.34646	0.00	0.00	176.66

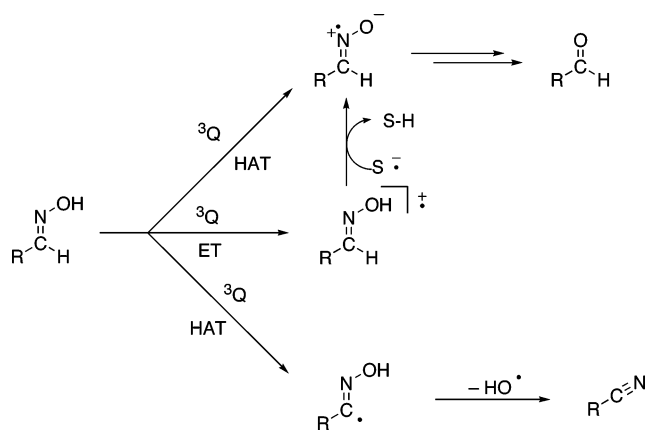
CHART 2. Different Conformations of Pyridine-2-carboxaldoxime (**2**) That Were Studied by Theoretical (B3LYP/6-31G*) Methods. Similar Conformations Were Studied for Oximes **3** and **4**



of this hydrogen would result in the formation of an iminoyl radical, which could react to give the observed nitrile. These observations are in agreement with the results obtained from DFT calculations. Three different conformers (A, B, and C; Chart 2) of the neutral oximes **2**, **3**, and **4** and their radical cations were optimized using the B3LYP/6-31G* basis set. The results listed in Table 6 show that the lowest energy conformer of **2** is the one with the hydroxyl hydrogen directed toward the nitrogen of the pyridine ring (**2A**). The basicity of the nitrogen is clear from the fact that in the optimized structure of the radical cation the hydroxyl proton is actually transferred to the nitrogen. Similar structures for **3** and **4** turn out to be less favorable; the relative energies for **3A** and **4A** are 4.62 and 7.71 kcal/mol higher than the lowest energy conformers, respectively. Similarly, their radical cations are significantly less stable.

These results confirm that the tendency of forming a hydrogen bond decreases in going from **2** > **3** > **4**, which supports the hypothesis that locking up the hydroxyl proton would presumably lead to removal of an alternative hydrogen atom or proton to yield an iminoyl radical (Scheme 3). It is uncertain whether this process involves a hydrogen atom transfer (via reaction with the triplet sensitizer) from the neutral oxime or a proton transfer from the aldoxime radical cation (via reaction with the sensitizer radical anion).

SCHEME 4



Although there is no direct evidence, the results seem to favor the HAT process. First, the quenching data suggests a change in mechanism (from ET to HAT) when using electron-withdrawing groups; this change in mechanism corresponds to larger amounts of nitrile being produced, suggesting that these two observations are connected. Second, the results from theoretical studies are not consistent with a radical cation intermediate. In order for a deprotonation reaction to occur, one would expect significant charge build-up at the iminyl proton. To determine the charge and spin distributions in aldoxime radical cations, *m*-cyanobenzaldehyde oxime (**1j**) was chosen as the species of interest due to the fact that it reacted under steady-state conditions to give the largest amount of nitrile. Optimization of the structure (two conformations each of the syn and anti isomers) by means of DFT (B3LYP/6-31G*) did not show any significant charge buildup at the iminyl proton. The largest charge density is in fact on the hydroxyl proton.

The results from our studies presented here suggest that aldoximes can react to give both aldehydes and nitriles under photoinduced electron transfer conditions. The proposed intermediates in these reactions are iminoxyl radicals (aldehydes) and iminoyl radicals (nitriles) as summarized in Scheme 4. We are currently further investigating the structure and reactivity of the potential reactive intermediates in these reactions.

Conclusions

Benzaldehyde oximes react to give aldehydes and nitriles when irradiated in acetonitrile in the presence of quinone sensitizers. These results are best explained by two different pathways that involve different intermediates. When the energetics for electron transfer are favorable, the preferred pathway involves electron transfer, followed by proton transfer to form an iminoxyl radical. Follow-up reactions eventually lead to the formation of the corresponding aldehyde. This pathway is assumed to be identical to that proposed for ketoximes under similar conditions. When electron transfer becomes energetically unfavorable, a hydrogen atom transfer mechanism becomes dominant. In this case, competition between hydrogen atom abstraction from the hydroxyl group (to form an iminoxyl radical) or from the iminyl carbon (to form an iminoyl radical) is observed. The former process also leads to the formation of the aldehyde, but the latter pathway leads to the production of the nitrile. Electron-accepting substituents present on the benzene ring in benzaldehyde oximes favor the formation of the corresponding nitriles. This is thought to be a result of the

larger oxidation potential observed in those oximes, which would make electron transfer less favorable. Formation of the nitrile was the dominant pathway when the hydroxyl hydrogen was not available for abstraction, such as in the case of pyridine-2-carboxaldoxime (**2**), where a strong intramolecular hydrogen bond is formed. Under these conditions it is proposed that the only hydrogen available for abstraction is the iminyl hydrogen. The strength of the hydrogen bond is determined by the basicity of the heteroatom present in the aldoxime; formation of a stronger hydrogen bond (i.e., presence of a more basic heteroatom) leads to a larger amount of nitrile.

Experimental Section

Materials. All aldoximes used in this study are known compounds. Benzaldehyde oxime, *m*-nitrobenzaldehyde oxime, and *p*-nitrobenzaldehyde oxime were commercially available. All other oximes were prepared from reaction of the corresponding aldehyde with hydroxylamine hydrochloride using standard published procedures.^{21,22} Acetonitrile (spectrophotometric grade) was used as received.

Steady-State Photolysis Experiments. Appropriate amounts of the substituted benzaldehyde oxime (0.015 M), benzaldehyde oxime (0.015 M), and DDQ (0.005 M) were weighed out and dissolved in 5 mL of solvent. For experiments where oxygen was to be excluded, the solution was purged with argon for 15 min prior to photolysis. The solution was placed in a Pyrex tube and irradiated in a Rayonet RPR-100 photochemical reactor, equipped with 16 RPR-3500A (black light phosphor) bulbs ($\lambda = 350$ nm) for 30 min. The progress of the reactions was followed by GC-FID, and the products were identified by GC-MS. Conversion of the starting material and product yields were determined by calibrated GC-FID. The products were confirmed by comparison with authentic (commercially available) samples.

Electrochemistry. The oxidation potentials of the oximes were determined by cyclic voltammetry at a scan rate of 100 mV/s. The reported potentials were referenced to the Fc^+/Fc couple. All measurements were carried out under an argon atmosphere.

Laser Flash Photolysis. The apparatus used for the laser flash photolysis (LFP) experiments was of standard design,²³ and the details have been described elsewhere.²⁴ The quenching rates were obtained as follows. An MeCN (spectrophotometric grade) solution containing chloranil (CA; OD ~ 0.5 – 1) in a glass cuvette was purged with argon for about 5 min. The sample was subjected to the laser pulse (355 nm, 10 Hz, 0.5–2 mJ/pulse; 4 ns pulse width), and the decay of ^3CA at 510 nm was observed. Small amounts (10–25 μL) of the quencher (~ 0.015 M oxime standard solutions in MeCN) were added to the solution after which the decay was measured. The quenching rate was obtained from a plot of the measured decay rates against the quencher concentration.

Computational Methods. Semiempirical (AM1)²⁵ and DFT (B3LYP)²⁶ calculations were performed with Spartan 2004,²⁷

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installed on a PowerMac G4. For the DFT calculations, the 6-31G* basis set²⁸ implemented within the program was used.

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some of these experiments. We are grateful to Professor I. R. Gould (Arizona State University) for the generous use of his laser flash photolysis equipment.

Supporting Information Available: Figures containing certain data analyses, the best fit-data of single-parameter and dual-parameter Hammett analyses described in this work, as well as Cartesian coordinates for isomers A–C of compounds 2–4. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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