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Photosensitized Regeneration of Carbonyl Compounds from Oximes

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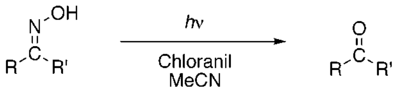
ABSTRACT

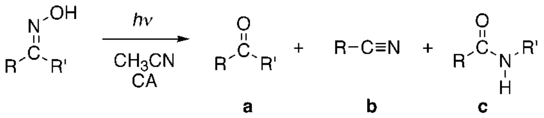


Deprotection of oximes to their corresponding carbonyl compounds through the use of photosensitized electron-transfer reactions proceeds in reasonable to good yields. Better yields are obtained in nonpolar solvents and when triplet sensitizers are used. Preliminary mechanistic studies suggest the involvement of an iminoxyl radical.

There has been a growing interest in the development of methods for the generation of carbonyl compounds from oximes.[1] In addition to the numerous classical methods such as hydrolytic, reductive, and oxidative cleavage reactions, the photochemistry of oximes and its use as a method for the regeneration of carbonyl compounds has also been explored.[2−6] Of particular interest is the work by Haley and Yates, who investigated the photochemical deprotection of oximes to aldehydes and ketones.[6] Both aromatic aldoximes and ketoximes were found to undergo photohydrolysis via their lowest excited singlet state; however, the quantum yields for these processes were generally low ($\Phi = 0.01-0.15$), and certain substituents (e.g., nitro) prevented the photohydrolysis reactions from taking place. Evidence was presented for the formation of an oxaziridine intermediate in these and other photolysis reactions.

Because of the low quantum yields and the poor reactivity of some of the substrates under normal photochemical conditions, we have focused our research efforts on the use of photosensitized electron transfer (PET) as a method for the deprotection of oximes. The main focus of this paper is on the photochemical reactions of a series of aldoximes and aliphatic, cyclic, and aromatic ketoximes in the presence of chloranil (CA). The oximes considered for this research are shown in Figure 1.[7] The general reaction that takes place under these conditions is shown in Scheme 1, and the results of these experiments are listed in Table 1.

Scheme 1



It can be seen that in general the deprotection of oximes to their carbonyl compounds proceeds in reasonable yield, although the material balance sometimes is poor. In several cases, less than 8 h is required to achieve complete

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(7) In a typical experiment, a solution (5 mL) of the oxime (25 mM) and chloranil (CA; 50 mM) in acetonitrile was photolyzed at 350 nm through Pyrex using a Rayonet reactor (16 lamps) for a maximum of 8 h. The progress of the reaction was followed by capillary column gas chromatography with flame ionization detector (GC/FID) or with mass selective detector (GC/MS). The products were identified by means of their mass spectra and by comparison of the retention times with authentic standards on two different columns. The yields were determined by calibrated GC/FID.

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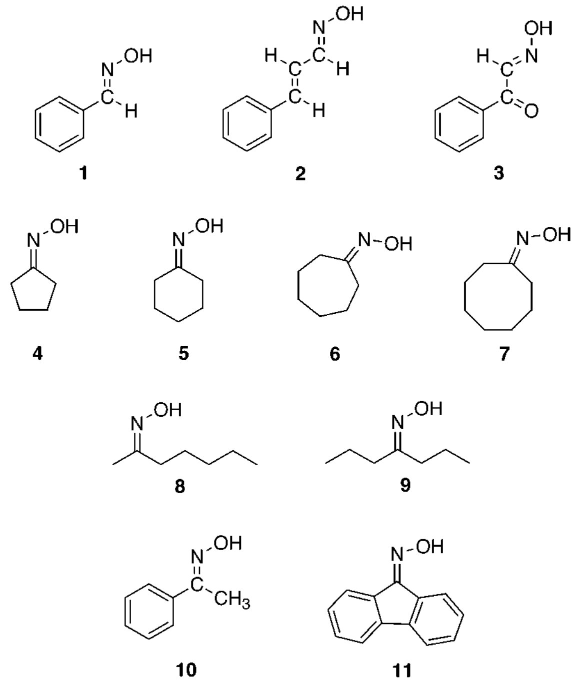


Figure 1. Oximes used in the photoinduced electron-transfer reactions.

conversion of the starting material; however, even during this relatively short period of time, a significant amount of polymerization can occur as noted by the dark color of the solutions after photolysis was completed. The free energy for electron transfer (ΔG_{ET}) was calculated using the Weller equation.[8] From Table 1, it can be seen that the oxidation potentials of the aldoximes are higher than those of the other substrates; however, ΔG_{ET} is exothermic for all oximes and ~0 kcal/mol for **1**. On the basis of these results, we expect ET to be the dominant pathway for all oximes under these conditions.

Photolysis of aldoximes **1**−**3** in the presence of CA results in the formation of aldehydes (**1a**, **2a**, **3a**) and nitriles (**1b**, **2b**, **3b**), except for oxime **1**, which also reacts to give an amide (**1c**). For both **2** and **3**, the nitrile was the major product. This is in stark contrast with the results from the photohydrolysis reactions of aldoximes, where the major pathway was cis−trans isomerization, and only a small amount of the aldehyde was observed.[6] The presence of **1c** in the product mixture is interesting because, to the best of our knowledge, it represents the first example of a PET-induced Beckmann rearrangement of aldoximes. The photochemical Beckmann rearrangement has been proposed to proceed via an oxaziridine intermediate,[2−6] and more recently, Shine and co-workers[9,10] also proposed an oxaziridine radical cation intermediate to explain the formation of oxadiazoles and isoxazoles in the reactions of several aldoximes with thianthrene perchlorate radical cation salt. However, it must be noted that the reduction potential of the thianthrene radical cation is +1.1 V,[11] indicating that the one-electron oxidation of the aldoximes is highly endothermic ($\Delta V \approx +1$ V) and, therefore, unlikely to occur under these conditions. The formation of oxadiazoles in the reactions of aldoximes is most likely due to acid−base reactions of the oxime resulting in the formation of nitrile oxides, which can react with nitriles (such as acetonitrile) to form oxadiazoles.[12]

CA-sensitized photolysis of a series of cyclic ketones (**4**−**7**) results in the formations of the corresponding ketones **4a**−**7a** in low yields (Table 1). Both the yield and the mass balance decrease with increasing ring size. The photolysis of a series of cyclic (C_4−C_8) ketoximes in the absence of a photosensitizer results in the formation of amides, lactams, and ketones.[3d] In those studies, a higher conversion and an increased ketone yield were obtained with an increase in ring size, the opposite of our results. These photochemical reactions proceed via oxaziridine intermediates, which react further (photochemically or thermally) to give lactams and amides. Under our conditions, no lactams or amides were

Table 1. Summary of Results for the Photolyses of Oximes in Acetonitrile in the Presence of Chloranil

					yield (product)[e]		
oxime	$E^{\mathrm{ox}\,a}$ (V)	$\Delta G_{\mathrm{E}}{}^{b}{}_{\mathrm{T}}$ (kcal/mol)	time[c] (h)	conversion[d] (%)	carbonyl	nitrile	amide
benzaldehyde (**1**)	2.15	0	6	99	43 (**1a**)	31 (**1b**)	<5 (**1c**)
cinnamaldehyde (**2**)	1.92	−5.3	4	98	28 (**2a**)	65 (**2b**)	
phenylglyoxal (**3**)	2.04	−2.5	8	71	<5 (**3a**)	59 (**3b**)	
cyclopentanone (**4**)	1.53	−14.3	8	99	40 (**4a**)		
cyclohexanone (**5**)	1.47	−15.7	8	90	43 (**5a**)		
cycloheptanone (**6**)	1.56	−13.6	8	87	33 (**6a**)		
cyclooctanone (**7**)	1.33	−18.9	8	78	27 (**7a**)		
2-heptanone (**8**)	1.68	−10.8	8	99	44 (**8a**)		
4-heptanone (**9**)	1.65	−11.5	8	84	38 (**9a**)		
acetophenone (**10**)	1.65	−11.5	8	99	61 (**10a**)		<10 (**10c**)
9-fluorenone (**11**)	1.79	−8.3	1	94	66 (**11a**)		

[a] Oxidation potentials measured by cyclic voltammetry (0.1 M tetraethylammonium perchlorate in CH_3CN, Ag/AgCl electrode). [b] Calculated using the Weller equation (ref 8): $\Delta G_{\mathrm{ET}} = 23.06[E^{\mathrm{ox}} - E^{\mathrm{red}}\text{-}\ E_{\mathrm{T}}]$ kcal/mol; E_{T} is the triplet energy of CA (2.13 eV) and E^{red} is the reduction potential of CA (0.02V). [c] Irradiation time. [d] Conversion was calculated on the basis of the GC-FID peak area of the oxime before and after photolysis. [e] Absolute yields determined by calibrated GC/FID.

formed, and with the observation that the reactivity is reversed, we believe that the oxaziridine is not an important intermediate in the electron-transfer reactions of cyclic ketoximes.

Photolysis of 2-heptanone oxime (**8**) and 4-heptanone oxime (**9**) under the typical conditions results in the formation of the corresponding ketones (**8a** and **9a**) in 44% and 38% yield, respectively. Comparing the reactivity of the acyclic oximes (**8**, **9**) to that of a similar cyclic oxime (**6**), it can be seen that both have a similar reactivity, suggesting that steric factors may not be very important in the PET reactions of oximes; however, more detailed studies are necessary to confirm this observation.

Photolysis of a solution of acetophenone oxime (**10**) and chloranil in acetonitrile results in the formation of acetophenone (**10a**) and acetamide (**10c**). The presence of **10c** in the product mixture is once again an example of a PET-induced Beckmann rearrangement. Other aromatic oximes did not yield amides upon photolysis in the presence of chloranil. The only product observed for **11** is fluorenone (**11a**), and the reaction was completed within 1 h.

The exact mechanism of the photosensitized regeneration of carbonyl compounds from oximes is unclear. Previous work by Rhodes on benzophenone oxime using ESR has shown that the oxime radical cation undergoes rapid deprotonation to form an iminoxyl radical.[13a] This is consistent with other reports on oximes and iminoxyl radicals.[13] We currently favor this mechanistic pathway rather than the formation of an oxaziridine radical cation. Support for the deprotonation mechanism comes from solvent-dependence studies. The PET reactions of **10** with CA in both polar and nonpolar solvents (Table 2) show that there is a significant solvent effect.

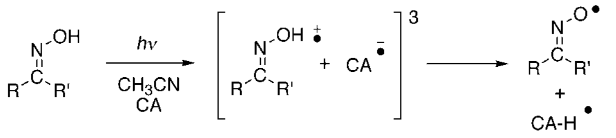
Table 2. Solvent Effects on the Photolysis of CA and Acetophenone Oxime (**10**)[a]

solvent[b]	conversion[c] (%)	yield[c] (%)
benzene	75	45
DCM	79	49
MeOH	13	4
MeCN	71	45
TFE	37	5

[a] [CA] = 0.025 M; [**10**] = 0.025 M; all solutions were irradiated for 2 h. [b] Dichloromethane (DCM), methanol (MeOH), acetonitrile (MeCN), 2,2,2-trifluoroethanol (TFE). [c] Product yields and conversions calculated using calibrated GC/FID.

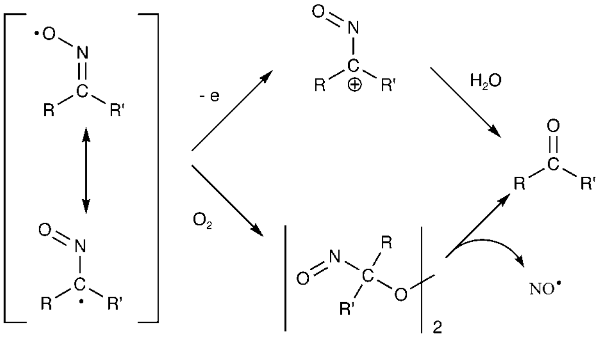
The conversions and the yields are much lower when using the polar protic solvents (MeOH and TFE), but they are approximately the same when using benzene, DCM, or MeCN as the solvents. These results can be explained on the basis of the proposed deprotonation step. Under the conditions of these reactions, the radical anion, a strong base, reacts with the oxime radical cation to yield the iminoxyl radical (Scheme 2). This reaction will be favored in nonpolar solvents where the radical ion pair is close together and the deprotonation can take place rapidly. In contrast, in a more polar solvent the radical ions can diffuse apart and result in lower yields. Furthermore, polar protic solvents such as MeOH and TFE could potentially associate with the oxime or the sensitizer radical anion (e.g., hydrogen bonding) and thus prevent the deprotonation from taking place, which would also result in lower yields.[14]

Scheme 2



At this point, the exact mechanism for the formation of the parent ketones remains uncertain. Two potential pathways starting from the iminoxyl radical are shown in Scheme 3.[15] The first pathway involves oxidation of the iminoxyl radical followed by hydrolysis. Although the oxidation potential of this radical is unknown, it has been shown that certain radicals with heteroatoms in the β-position can have very low oxidation potentials, and as a result, oxidation of this radical could occur via reaction with CA* or possibly even

Scheme 3



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ground-state CA.[16] Clearly, this pathway would show a dependence on the presence of water in the solution. Although it is hard to completely remove water from acetonitrile, reactions with anhydrous acetonitrile gave similar results as those with regular acetonitrile. Due to the long reaction times, it is possible that some water accumulates in the reaction mixture during the photolysis and only small amounts of water would be necessary for this reaction to go to completion. A second pathway is the reaction with oxygen followed by a second iminoxyl radical to form a peroxide. Thermal or photochemical cleavage of the O−O bond and release of NO would result in the formation of the carbonyl compound. This mechanism somewhat resembles that of the iron porphyrin catalyzed oxidation of oximes, which proceeds via a five-coordinate, high-spin oximatoiron(III) porphyrin species.[17] We have found that in the absence of oxygen, the reactions proceed somewhat slower; however, the product distribution did not seem to be affected.[18] At this point, it is not possible to favor either of these mechanisms, nor is it possible to rule out any alternative pathways. Clearly, more experiments are needed to determine the exact nature of the intermediates and the reaction pathways that are being followed.

In conclusion, we have shown that photoinduced electron transfer can be used for the deprotection of oximes to their corresponding carbonyl compounds. Although the reactions have not yet been optimized, this method may offer some potential as a synthetic method for certain types of oximes because of their simplicity. However, in order for this method to become attractive as an alternative for the regeneration of carbonyl compounds from oximes, a number of aspects need to be clarified. The mechanistic details remain obscure; however, the first step in these reactions seems to involve deprotonation of the oxime radical cation to form an iminoxyl radical rather than rearrangement to an oxaziridine. This is supported by both solvent and sensitizer studies. Further studies on the scope and mechanism of these reactions and the reactive intermediates involved are currently underway.

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(14) The proposed first step also implies an important role for the sensitizer as it acts as the base to generate the iminoxyl radical. Preliminary studies on the effect of the photosensitizer on the PET reactions of oximes indicate that photolysis of a solution containing **10** and 1,2,4,5-tetracyanobenzene (TCB) using biphenyl as the co-donor resulted in a low conversion and yield, despite the favorable energetics. This is attributed to the fact that TCB is expected to react via its singlet state and as a result back-electron transfer will be faster than for triplet sensitizers and will lower the yield of the reaction. Furthermore, in the absence of a good base (such as a quinone radical anion), the deprotonation step is slow leading to lower yields.

(15) Several mechanisms can be proposed; however, on the basis of these and other experiments, we believe that the two mechanisms discussed here are among the more viable.

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(18) Further studies on different oximes indicate that there is a more important role for oxygen than is obvious from these earlier experiments. We will report on these and other mechanistic studies in a future publication.