The Photochemistry of Carbon–Nitrogen Multiple Bonds in Aqueous Solution. 2. *o*-Hydroxy-Substituted Aromatic Oximes and Oxime Ethers

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The fluorescence emission and excitation spectra of salicylaldoxime and *o*-hydroxyacetophenone oxime and several of their derivatives have been studied in various solvents. The results support the hypothesis that two major ground-state conformers exist, one having an intramolecular hydrogen bond and the other being hydrogen bonded to solvent. Photolysis in aqueous solution occurs quite readily ($\Phi \simeq 0.1$–0.7) to give substituted benzoxazoles, although hydrolysis to give carbonyl product is competitive, especially in acidified solutions ($\Phi \simeq 0.1$–0.4). The cyclization reaction is believed to occur via two different mechanisms, arising from the inter- and intramolecularly hydrogen-bonded conformers, respectively. One mechanism involves cyclization via the phenolate ion, whereas the other is believed to involve intramolecular proton transfer to give a zwitteronic intermediate.

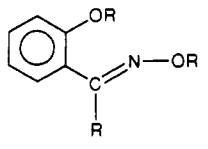
Introduction

Intramolecular proton transfer induced by electronic excitation has been of great interest for many years. Since Weller's classic work on salicylic acid derivatives,[1] many other photochemists have tried to detect the zwitterionic intermediates produced by intramolecular proton transfer, either directly or indirectly.[2] In the majority of cases studied, such intermediates revert back to starting material, resulting in no overall net reaction. Scheme I illustrates such processes. This seemingly trivial reaction, although photochemically nonproductive, is actually quite useful. For example, compounds exhibiting such properties are often used as ultraviolet stabilizers in plastics.[3]

Of more interest to us is the photochemistry of aromatic oximes, as illustrated in the accompanying paper,[4] and in particular the possible reactions of *o*-hydroxy-substituted oximes. Photolyses of these substituted oximes have been shown to lead not to the trival proton-transfer reaction followed by electronic deactivation but to a net photochemical reaction. Although there have been some reports on the photochemistry of *o*-hydroxy-substituted oximes,[5] the actual proton-transfer step has not been extensively studied, and in certain cases these have led to contradictory results.[6] The aim of the present investigation was to throw further light on the intramolecular proton transfer step and to try to explain more fully the mechanism of the cyclization reaction which occurs on irradiation of *o*-hydroxy-substituted aromatic oximes.

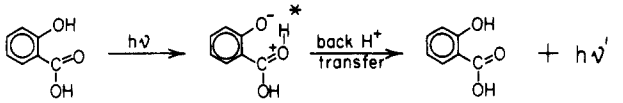
Results and Discussion

Fluorescence Studies. Fluorescence measurements were carried out on several aromatic oxime derivatives of general structure **1** in an attempt to obtain information about possible excited state species and conformations involved in the photochemical reactions of these substrates.

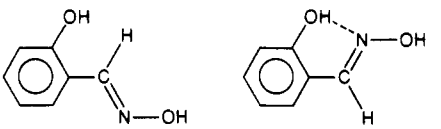


1, R = H, Me

Scheme I. Trivial Photochemical Reaction of Salicylic Acid



The presence or absence of fluorescence and the observed emission maxima in different solvents are given in Table I. It is clear from these results that the fluorescence of *o*-hydroxy-substituted aromatic oximes is very strongly dependent on the type of solvent used. The parent molecule, salicylaldoxime, shows two emission maxima in neutral aqueous solution, at 360 and 450 nm. From the observation of only the latter peak in either basic aqueous or ethanolic solution, it is concluded that the longer wavelength emission is due to the phenolate ion and the 360-nm emission to the neutral oxime. This latter fluorescence is also observed in polar solvents capable of hydrogen bonding, but in solvents incapable of such intermolecular interaction the neutral oxime exhibits no fluorescence at any wavelength. These solvent effects are most easily explained in terms of two different conformations of the oxime moiety relative to the *o*-hydroxy group, as shown by structures **2a** and **2b**.



2a **2b**

In aqueous solution or in solvents capable of strong hydrogen-bonding, conformation **2a** can be stabilized by strong intermolecular interactions of both the hydroxy and oxime groups with solvent, giving rise to the fluorescence at 360 nm. In basic solution (and to some extent in H_2O at pH 7) this conformation can ionize before or after excitation to produce phenolate which gives the fluorescence observed at 450 nm. The idea of two interconverting species is supported by the fluorescence dependence on solvent composition in water–ethanol mixtures as shown in Figure 1, where the 450-nm emission decreases in intensity as the percentage of alcohol is increased.

The fact that no fluorescence is obtained at all in solvents such as pentane, cyclohexane, or acetonitrile can be attributed to conformation **2b** in which only intramolecular hydrogen bonding stabilizes the ground state, which on excitation leads to intramolecular proton transfer to give nonfluorescent zwitterion **3**. Either back proton transfer or photochemical reaction (see later) can lead to radia-

(1) Weller, A. *Z. Elektrochem.* **1956**, *60*, 1144.
(2) Two excellent reviews on the subject are: (a) Kloppfer, W. *Adv. Photochem.* **1977**, *10*, 311. (b) Martynov, I. Yu.; et al. *Russ. Chem Rev. (Engl. Transl.)* **1977**, *46*, 1.
(3) Heller, H. J. *Eur. Polym. J. Suppl.* **1969**, 105.
(4) Haley, M. F.; Yates, K. *J. Org. Chem.*, preceding paper in this issue.
(5) (a) Ferris, J. P.; Antonucci, F. R. *J. Am. Chem. Soc.* **1974**, *96*, 2010. (b) Grellman, K. H.; Tauer, E. *Tetrahedron Lett.* **1974**, *42*, 3707.
(6) It has been reported[5b] that photolysis of salicylaldoxime in hydroxylic solvents results in benzoxazole, whereas in nonpolar solvents, 1,2-benzisoxazole is produced. Photolyses carried out in our conditions resulted in only benzoxazole being produced in all solvents employed.

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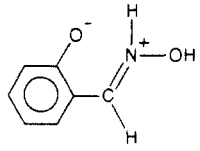


3

tionless electronic deactivation, so that no fluorescence is observed. Many cases are known in which such zwitterionic forms do not fluoresce, and this is one of the three possible results of intramolecular excited-state proton transfer, as defined by Klopffer,[7] the other two being fluorescence and photochromism. It is difficult to explain why none of the *o*-hydroxy-substituted oximes or ethers in Table I show any fluorescence in pentane or cyclohexane, unless internal proton transfer from conformation **2b** provides a mechanism for radiationless deactivation.

Fluorescence excitation spectra were also recorded, as shown in Figure 2, for salicylaldoxime. Two excitation spectra were measured, one for each of the two fluorescence maxima shown in Figure 1 in ethanol–water mixtures. Intensity measurements were made at 360 and 470 nm. Both gave almost identical excitation spectra, as shown in Figure 2, supporting the conclusion that the excited-state phenolate[8] and excited intermolecularly hydrogen-bonded oxime originate from the same ground-state confirmation (presumably **2a**).

Fluorescence measurements on *o*-methoxybenzaldoxime showed that a band at 360 nm was observed in every neutral solvent used (Table I). This is not surprising since there is no possibility of either intramolecular hydrogen bonding (or internal proton transfer) or phenolate formation. This 360-nm band is therefore attributed to normal aromatic aldoxime fluorescence. However, this emission was weak in every solvent and in both basic aqueous and ethanolic solution was absent. The reason for this weak emission, while salicylaldoxime fluoresces quite strongly in this region, is not obvious. One possibility is that excited-state ionization of the *N*-hydroxyl group competes with fluorescence as a means of deactivation, since no fluorescence at all could be detected in basic solution.

Fluorescence studies were also carried out on the *N*-methoxy ether of salicylaldoxime. This showed fluorescence at 375 nm in neutral aqueous solution and emission at 460 nm in basic aqueous or ethanolic solution, as expected for the neutral species and phenolate respectively. However the absence of 375-nm emission in other hydrogeh-bonding solvents, as well as in hydrocarbon solvents, suggests that the intramolecularly hydrogen-bonded conformer (similar to **2b**) is predominant in this case. No satisfactory explanation can be found for this, although it is clear that intermolecular hydrogen bonding favoring conformations like **2a** would be less effective in oxime ethers than in free oximes.[9]

In the case of *o*-hydroxyacetophenone oxime and its methyl ether no significant fluorescence could be detected in any of the solvents studied. The most plausible explanation for this is that the intramolecularly hydrogen-bonded conformer (**4b**) is predominant in all solvents due

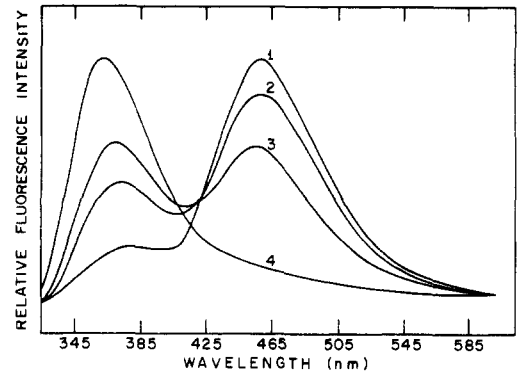


Figure 1. Fluorescence emission spectra of salicylaldehyde in (w/w) ethanol–water mixtures: (1) 25% EtOH; (2) 50% EtOH; (3) 75% EtOH; (4) 95% EtOH. (Only four solvent mixtures are shown, for clarity.)

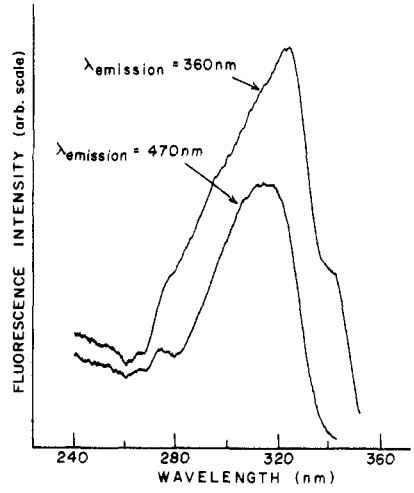
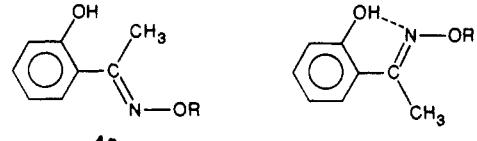


Figure 2. Fluorescence excitation spectra of salicylaldehyde in water.

to very unfavorable steric interactions in the other planar conformer (**4a**). Hence intramolecular hydrogen bonding



4a 4b

and internal proton transfer to give a nonfluorescent zwitterion, is favored over intermolecular hydrogen bonding. It is significant that neither of these *o*-hydroxyacetophenone derivatives shows any long wavelength emission even in basic solution, suggesting that intramolecular proton transfer is quite facile in these systems.

Photolysis Results. Since our principal interest was in photochemical reactions in aqueous solution and to allow a more direct comparison with the photohydrolyses of simple oximes and ethers in the preceding paper,[4] photolyses of *o*-hydroxy oximes and their ethers were carried out in aqueous solution, with few exceptions. Irradiations were performed at 254 or 300 nm. In most cases the major result of photolysis is cyclization to give a benzoxazole as shown in Table II, although photohydrolysis to give the parent aldehyde or ketone (plus hydroxylamine or methoxylamine) is competitive with cyclization, especially in acidified solutions.

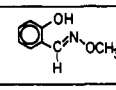
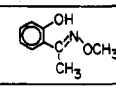
These cyclization products from photolyses of salicylaldoxime and *o*-hydroxyacetophenone oxime have been reported previously,[5] but little evidence was given on how

(7) See ref 2a.

(8) Phenols are known to become much more acidic in their first excited singlet state. Barltrop, J. A.; Coyle, J. D. *Excited States in Organic Chemistry*; Wiley-Interscience: Bristol, 1975; 51.

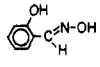
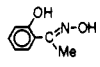
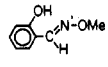
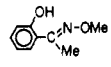
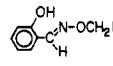
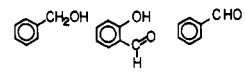
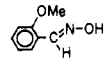
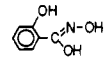
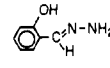
(9) These two conformations, the externally and internally hydrogen-bonded ones, are intuitively the two most important conformations. Both of these preserve the conjugation between the oxime group and the phenyl ring.

Table I. Fluorescence Emission Maxima of Ortho-Substituted Oximes and Ethers in Different Solvents

solvent					
H_2O	360 nm	none	375 nm[c]	none	360 nm[c]
EtOH, MeOH, $HCONH_2$	360 nm	none[a]	none	none	360 nm[a]
pentane, hexane, MeCN	none	none	none[b]	none	360 nm
10^{-3} M NaOH, MeOH/NaOMe	450 nm	none	460 nm	none	none

[a] Very weak emission observed in MeOH at 350 nm. [b] Weak emission observed in MeCN at 350 nm. [c] Weak emission.

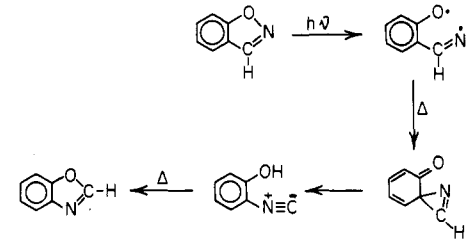
Table II. Products of Photolysis of Ortho-Substituted Oxime Derivatives in Aqueous Solution

substituted oxime	cyclization product	other products
		
		
		
		
		
	none	
	polymer	
	polymer	

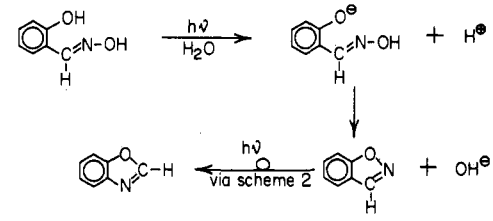
the cyclization actually takes place. In the present investigation the scope of the reaction has been extended to include oxime ethers and the possible existence of oxazirane intermediates[10] on the cyclization pathway, as in the preceding study of oxime photohydrolysis.[4]

Since oximes are known to convert readily into oxaziranes[11] upon photolysis, it seemed probable that this could be an intermediate on the cyclization pathway. However two experiments effectively rule out this possibility. First, the photolysate for the two *o*-hydroxy oximes gave a negative result on addition of potassium iodide followed by starch indicator, even at 0 °C, indicating the absence of oxazirane.[4,12] Second, photolysis of the two methyl ethers both gave the same cyclization product as the corresponding oxime. Since it is not possible for an oxazirane to form from the methyl ether of an oxime, it is concluded that such intermediates are not involved in the cyclization pathway. Interestingly, when acid was added to an aqueous solution of salicylaldoxime, irradiation led to a marked increase in the yield of carbonyl photohydrolysis product and oxazirane could be detected in the photolysate. This indicates that photohydrolysis of *o*-hydroxy oximes can compete with cyclization at higher acid concentrations.[13] As expected the *o*-methoxybenzaldoxime gave only hydrolysis products, even in neutral aqueous solution.

Scheme II. Proposed Mechanism for Photochemical Conversion of 1,2-Benzisoxazole to Benzoxazole



Scheme III. Photochemical Formation of Benzoxazole via Excited-State Phenolate Ion



The next question is how cyclization leads to benzoxazole-type products since it might have been expected that benzisoxazoles would result from simple closure.

The photolytic conversion of 1,2-benzisoxazole to benzoxazole has been described previously[14,15] with a mechanism being proposed by Ferris ane Antonucci.[14] This mechanism (Scheme II), although based on reactions in either Nujol mull or neat reagent, is probably the one responsible for formation of benzoxazole from 1,2-benzisoxazole. This is shown in Scheme II. Although no 1,2-benzisoxazole was detected in any of our experiments, photolysis of it under the present conditions resulted in benzoxazole being produced cleanly. This demonstrates the possible existence of 1,2-benzisoxazole as an intermediate along the pathway of oxime photolysis.

Indeed if Ferris' mechanism is operative, the question remains of how the initial cyclization forms a benzisoxazole. There appear to be two possible mechanisms of cyclization. Each of these mechanisms corresponds to one of the different conformations possible for the *o*-yydroxy-substituted aromatic oximes. For the solvent hydrogen-bonded conformation (**2a**), the one in which ionization occurs in aqueous solution, the phenolate which is produced can simply cyclize by displacing the hydroxyl or alkoxyl group from nitrogen (Scheme III). The main evidence for this lies in experiments carried out in basic solution. When

(10) Besides syn–anti isomerization, oxaziranes are the main primary photochemical product in the photolysis of oximes. See, for example: Oine, T.; Mukai, T. *Tetrahedron Lett.* **1969**, *3*, 157. Ogata, Y.; Takagi, K.; Mizuno, K. *J. Org. Chem.* **1982**, *47*, 3684.

(11) The familiar photo-Beckmann reaction involves oxaziranes as intermediates,[10] as does the photohydrolysis of oximes.[4]

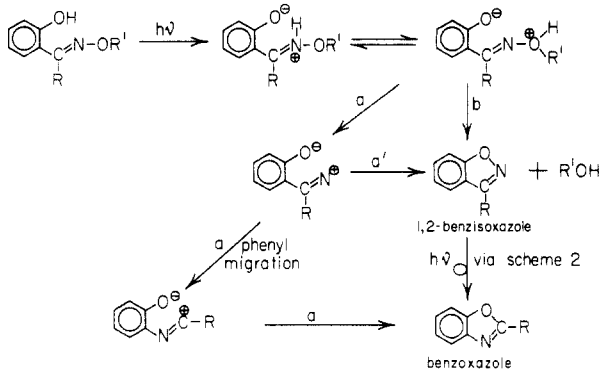
(12) Oxaziranes are known to be very good oxidizing agents, comparable to hydrogen peroxide. If present in solution they easily oxidize iodide ions to iodine, which can be detected in trace amounts by starch indicator. See: Schmitz, E. *Adv. Heterocycl. Chem.* **1964**, *2*, 92.

(13) Work in our laboratory indicates that oxazirane formation is acid catalyzed.[4]

(14) Ferris, J. P.; Antonucci, F. R. *J. Am. Chem. Soc.* **1974**, *96*, 2014.

(15) The following references describe the general photolytic conversion of isoxazoles to oxazoles: (a) Singh, B.; Zweig, A.; Gallivan, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 1199. (b) Kurtz, D. W.; Schechter, H. *Chem. Commun.* **1966**, 689.

Scheme IV. Possible Mechanism of Benzoxazole Formation Not Involving 1,2-Benzisoxazole as an Intermediate (Pathway a)

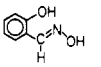
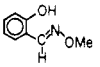
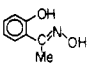
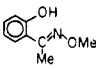
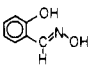


salicylaldoxime is irradiated in aqueous NaOH (pH 11.0), where all the oxime exists as the phenolate ion, only benzoxazole results, and the reaction is very efficient (see later). This strongly suggests that the phenolate anion can itself cyclize to form benzisoxazole. Therefore it follows that when the neutral oxime is photolyzed in water, its production of excited-state phenolate ions can also result in cyclization to form benzisoxazole.

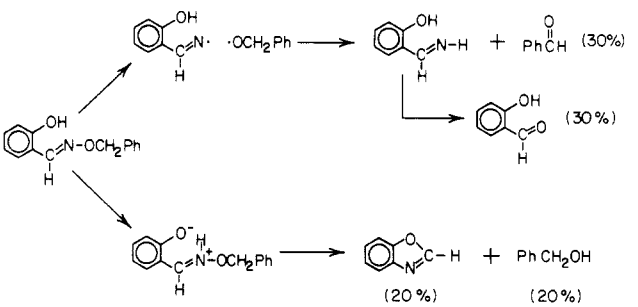
In the intramolecularly hydrogen-bonded conformation (**2b**) photolysis leads to direct transfer of the hydroxyl proton to the nitrogen atom. The zwitterion could then either back transfer the proton and nonradiatively deactivate to form starting material[16] or could react further forming benzoxazole. The actual mechanism of this process is not clear, but two reasonable possibilities are given in Scheme IV. The proton on the nitrogen atom shifts to oxygen, enabling that group to leave, possibly synchronously with nitrogen attack. This creates a positive charge on the nitrogen. From here there are two reasonable possibilites: (1) direct oxygen attack on the nitrogen, forming 1,2-benzisoxazole (pathway b in Scheme IV), which then follows Scheme II to product, or (2) migration of the phenyl ring placing the positive charge on carbon, followed by oxygen attack to form benzoxazole directly (pathway a in Scheme IV). Although pathway b seems more straightforward, there is precedence for ground-state reactions to follow pathway a.[17]

As additional evidence for the mechanism of Scheme IV, quantum yields were determined for salicylaldoxime. The results in Table III show that the reaction forming benzoxazole is much more efficient in water than in either pentane or 95% ethanol. This is consistent with the idea that cyclization occurs by different mechanisms for each of the two conformations available to the oxime. From the fluorescence studies mentioned above, intermolecular hydrogen bonds exist between water and the polar substituents of salicylaldoxime. It is this conformation which ionizes to form phenolate, from which efficient cyclization occurs via Scheme III. In pentane, the inability to detect fluorescence corresponds to all of the oxime being in the conformation which allows intramolecular hydrogen bonding. From this conformation no ionization to solvent is possible as is evidenced by the lack of phenolate fluorescence. It therefore seems reasonable to propose that the reactive intermediate is the zwitterion and that a possible mechanism is that shown in Scheme IV. This process would be less efficient than that in Scheme III due to competition from deactivation back to starting material.

Table III. Absolute Quantum Yields for Photolyses of *o*-Hydroxy-Substituted Aromatic Oximes in Various Solvents

oxime	solvent	absolute quantum yields: cyclization	absolute quantum yields: hydrolysis
	H_2O	0.23	0.03
	H_2O	0.14	0.13
	H_2O	0.26	0.24
	H_2O	0.01	0.38
	pentane	0.04	0.01
	95% ethanol	0.03	0.02
	pH 11.0	0.72	0.05

Scheme V. Available Pathways to the Four Products Observed on Photolysis of Salicylaldoxime Benzyl Ether



When 95% ethanol is used as the solvent, salicylaldoxime exhibits weak fluorescence corresponding to the intermolecularly hydrogen-bonded conformer. It is not unreasonable to expect that the intramolecularly hydrogen-bonded conformer also exists, but because the zwitterion does not fluoresce there is no direct evidence for it. Even though solvent hydrogen bonding occurs, there is no significant ionization occurring to produce phenolate.[18] This means that the mechanism shown in Scheme III cannot be operative. Therefore reaction occurs only from the zwitterionic intermediate as depicted in Scheme IV. It is interesting to note that the quantum yields for benzoxazole formation are very similar in pentane and in 95% ethanol. As expected, the quantum yield is somewhat lower in the latter solvent. This is consistent with the fact that not all of the salicylaldoxime is in the intramolecularly hydrogen-bonded conformation, as it is in pentane.[19]

From the photolysis of the benzyl ether of salicylaldoxime, four products were obtained, as shown in Table II. Both aldehydes, salicylaldehyde and benzaldehyde, were

(16) It is not clear when the deactivation process occurs, that is, whether it is actually coupled with back proton transfer or not.

(17) Numerous reactions are documented in which phenyl groups migrate to an electron-deficient nitrogen atom. See: Carey, F. A.; Sundberg, R. J. Part B "Reactions and Synthesis" *Advanced Organic Chemistry*; Plenum: New York, 1977; Part B, p 328.

(18) In addition, there was no fluorescence peak attributable to the phenolate anion in pentane or 95% ethanol. This suggests that phenolate is not being formed in these solvents.

(19) There could also be some intramolecular hydrogen bonding even in water as solvent, and thus salicylaldoxime may react by a combination of Schemes III and IV.

obtained in equimolar amounts. Benzoxazole and benzyl alcohol are the other two products, both of which are also produced in equimolar amounts. Benzoxazole can be formed by the normal cyclization reaction which these *o*-hydroxy oximes undergo, and in this case the leaving alcohol, benzyl alcohol, can also be detected. It is apparent from their formation in a 1:1 ratio, that both compounds, benzoxazole and benzyl alcohol, arise from the same reaction. The aldehydes on the other hand are produced via a different mechanism but are probably also formed via a common pathway. The two proposed pathways are given in Scheme V.[20]

In addition to the normal cyclization reaction which all the *o*-hydroxy-substituted aromatic oximes undergo, there is also a radical reaction mechanism available only to the benzyl ether derivative as shown in Scheme V. This mechanism involves homolytic cleavage of the nitrogen–oxygen bond followed by hydrogen abstraction by nitrogen. This leads to formation of salicylaldehyde imine and benzaldehyde, with the imine subsequently hydrolyzing thermally to give salicylaldehyde. Since both aldehydes are produced in a 1:1 ratio, this mechanism adequately explains the results. The reason this pathway is not important for the other *o*-hydroxy-substituted aromatic oximes is probably due to the homolytic cleavage step. The oxygen radical may be too high in energy to be produced.[21]

In order to extend the scope of this cyclization reaction even further, other substrates were irradiated but without success. As shown in Table II, for example both salicylhydroxamic acid and salicylaldehyde hydrazone were irradiated, but both gave only polymer. The cyclization reaction seems to proceed efficiently only for simple oximes or oxime ethers. It therefore appears likely that RO^- or ROH (R = H, alkyl, benzyl) must be the leaving group.

Multiplicity of Reactive State. Experiments were performed using potassium sorbate and oxygen as triplet quenchers. No difference in cyclization efficiency was observed in the photolysis of solutions with added quencher relative to those without quencher. The triplet energies of oxygen and potassium sorbate are approximately 23 and 59 kcal/mol, respectively.[22] These should be low enough in energy to quench the triplet state of any of the oximes. No observable quenching by either of these two quenchers is sufficient evidence to presume that the cyclization reaction occurs exclusively from the singlet state.

Absolute Quantum Yields. The absolute quantum yields for a number of the *o*-hydroxy-substituted aromatic oximes are given in Table III. From these data, it can be seen that the cyclization reaction, as well as the hydrolysis photoreaction, is a fairly efficient reaction in most cases. Oxime ethers are not as efficient in photocyclization as are the oximes. In fact there is a marked decrease in quantum yield for the methyl ether of *o*-hydroxyacetophenone oxime. This lower efficiency may be related to the predominance of conformations such as **2b**, which leads to higher zwitterion formation and hence increased possibilities for nonproductive deactivation.

Conclusions

It has been shown indirectly that intramolecular proton transfer occurs during the photolysis of *o*-hydroxy-substituted aromatic oximes and oxime ethers. Fluorescence studies involving solvent effects clearly demonstrate this. Other deactivational processes must occur rapidly after formation of the zwitterion since it can not be directly detected by fluorescence. The dominant process is probably back proton transfer coupled with radiationless deactivation.[16]

The reactions of these *o*-hydroxy-substituted aromatic oximes and their ethers are quite interesting. Their cyclization to form benzoxazoles does not occur via the common oxime photolysis intermediate, the oxazirane. The mechanism of benzoxazole formation is still not completely understood, but two reasonable mechanisms, one for each of the two major conformations that the oxime can adopt, have been proposed. The results in neutral or basic aqueous solution suggest that phenolate photolysis follows the mechanism in Scheme III, in which nucleophilic attack of the oxygen anion on nitrogen forms 1,2-benzisoxazole. The results of photolyses in pentane and 95% ethanol suggest that a different mechanism, such as that outlined in Scheme IV, is operative and that the zwitterion is an intermediate on this cyclization pathway.

Although no 1,2-benzisoxazole could be detected in any case, photolysis of authentic samples under the present reaction conditions gave benzoxazole cleanly. This demonstrates the possible existence of 1,2-benzisoxazole as the initial cyclization product. Irradiation of the benzyl ether of salicylaldoxime also proved interesting. Since its photolysis gives benzoxazole and benzyl alcohol in a 1:1 mole ratio, this is strong evidence that both arise from the same pathway. Another pathway, not available to the other oxime deviatives, apparently[20] involves homolytic cleavage of the N–O bond to produce benzaldehyde and salicylaldehyde, also in equimolar ratio.

Finally it should be noted that up to this point, for the purposes of generalization, *o*-hydroxy aromatic oxime derivatives only cyclize cleanly when the N-substituent is either OH or OR and the C-substituent is H or R.

Experimental Section

All general experimental procedures, preparations, and irradiations were essentially as described in the preceding paper,[4] except for the following additions and modifications.

Product Identification and Analysis. The following experiments were typical of the procedures employed.

(a) Salicylaldoxime. A solution containing 300 mg of oxime in 20 mL of acetonitrile was added to 600 mL of water. This solution was outgassed with argon gas for 20 min in a quartz vessel. The quartz tube was then equipped with a stirring bar and cold finger, and photolyzed at 254 or 300 nm for 1 h. The photolyzed solution was then worked up by extracting twice with 100 mL of dichloromethane. After drying over anhydrous $MgSO_4$ and removal of the solvent by rotary evaporation, the crude product was analyzed by TLC and proton NMR. The product was then separated on a chromatotron instrument[23] equipped with a 2-mm silica gel plate, by using methylene chloride as eluent. Benzoxazole (60% yield) was the sole product that resulted, its structure being confirmed by comparison with an authentic sample obtained from the Aldrich Chemical Company.

(b) *o*-Hydroxyacetophenone Oxime, Methyl Ether. The oxime ether (20 mL) was placed in water (17 mL) along with of

(20) The possibility of a third pathway has been suggested by D. Gravel (personal communication). This involves intramolecular abstraction of a benzylic proton by phenolate, the resulting zwitterion giving aldehyde and imine directly. Although an eight-membered transition state would be involved, its intramolecular nature makes it an attractive possibility. However, more work is needed to establish which mechanism is operative in this case.

(21) If homolytic cleavage does occur for the other oximes, instability of the oxygen radical produced could cause it to recombine quickly to form starting material.

(22) The triplet energy of oxygen is known, However, a value was estimated for potassium sorbate, based on that of 1,3-hexadiene. See: Murov, S. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1973; p 8–22. This reaction is discussed in detail in the accompanying paper.[4]

(23) Harrison Research Model 7294.

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

acetonitrile (3 mL) as cosolvent. Irradiation of the solution proceeded at 4 °C (refrigerated room) at 300 nm for 30 min. The photolysate was worked up by two extractions with 100 mL of dichloromethane, followed by drying with anhydrous $MgSO_4$. The drying agent was filtered off and the solvent removed by rotary evaporation. The remaining residue was dissolved in 1–2 mL of acetonitrile and injected into the GC (column temperature = 90 °C). 2-Methylbenzoxazole was detected, but in very low yield (<1%). The major of product (>95%) was the hydrolysis product, o-hydroxyacetophenone. This was the only substrate exhibiting a low cyclization yield in water.

(c) Salicylaldoxime, Benzyl Ether. The oxime ether (80 mg) was irradiated in 450 mL of H_2O and 150 mL CH_3CN (cosolvent). The solution was deoxygenated by bubbling in Ar gas for 20 min. The quartz tube was then equipped with a cold finger and magnetic stirring bar. Photolysis was carried out at 300 nm,[25] with four products being produced. The reaction was worked up in the usual manner. All four products were analyzed and confirmed by gas chromatography at different temperatures, by comparison with authentic samples, and also by proton NMR. Benzaldehyde and salicylaldehyde were each produced in 30% yield, while benzoxazole and benzyl alcohol were the only other products, each being produced in 20% yield.

(d) 1,2-Benzisoxazole. 1,2-Benzisoxazole (400 mL), dissolved in of acetonitrile (100 mL), was added to 500 mL of water. This solution was outgassed with argon gas for 20 min in a quartz vessel, which was equipped with a magnetic stirring bar and cold finger, and irradiation proceeded at 254 nm for 1 h. Workup of the reaction consisted of two extractions with dichloromethane (2 × 100 mL each), drying with anhydrous $MgSO_4$, and finally rotary evaporation. As verified by TLC (silica gel with dichloromethane as eluent) by proton NMR, and by comparison with authentic material, benzoxazole was produced cleanly in approximately 50% yield.

Absolute Quantum Yields. Quantum yields were determined using potassium ferrioxalate as the actinometer. The preparation and usage of the actinometer has been described elsewhere.[26] The method used for analyzing the product yields was gas chromatography. A sample run is described below. Approximately 20 mg of oxime was dissolved in 18 mL of water and 2 mL of acetonitrile. Ar gas was then bubbled through the solution for a minimum of 20 min. The quartz tube was then placed in a merry-go-round apparatus in a Rayonet photochemical reactor. Either four or eight lamps were used, all at 254 nm, and irradiations usually proceeded for about 45 min. Potassium ferrioxalate was used to calibrate the lamps. This method assumes a certain degree of lamp stability, which our experiments have borne out. The lamps were turned on and allowed to equilibrate for at least 30 min before any measurements were started. The method of calibration is outlined here. A stock solution of potassium ferrioxalate was prepared as described.[26] A 20-mL aliquot of this stock solution was pipetted into a quartz tube which was placed in the merry-go-round apparatus. Because the 254-nm lamps also emit radiation >300 nm, none of which any substrate absorbs, a simultaneous experiment was run to determine how much of this light is produced.[27] Potassium ferrioxalate does absorb above 300 nm, and so this light would certainly affect any measurements of light intensity. To test for this unwanted radiation, 3 mL of actinometer solution was placed in a cuvette which passed only wavelengths greater than 300 nm. Photolysis of both solutions occurred for 20 min, followed by workup of the actinometer solution. The intensity of light from the lamps is simply the number of photons emitted per unit of time. Mathematically, this expression is I(einsteins/min) = (number of protons emitted)/time = (moles of product)/(ϕ × time) = (A × volume)/(ϵ × ϕ × time), where A = optical density of product, ϵ = molar extinction coefficient, ϕ = quantum yield of actinometer reaction, volume = total volume of solution irradiated, and I = intensity of light. The equation then simplifes to I = [(A × volume)/time](7.2072 × 10^{-7} einsteins/mL) by using ϵ = 1.11 × 10^4 L mol^{-1} cm^{-1}, length of cell = 1.00 cm, and ϕ = 1.25 and also incorporating a factor of 10 due to dilution of the photolyte.

The amount of light centered at 254 nm is equal to the total Rayonet light intensity (i.e., quartz tube) minus the intensity of light greater than 300 nm (i.e., the plastic cuvette). It was found that 6% of the light emitted by the 254-nm lamps comes from wavelengths greater than 300 nm. The numerical value for the intensity of light centered at 254 nm is 3.41 × 10^{-7} einsteins/min/lamp. All experiments carried out show that this number can be experimentally reproduced to within ±10%.

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(25) When the photolysis was carried out at 254 nm, no isolable products were produced. Since all four products are relatively photostable, no explanation can be found as to why this occurs.

(26) Murov, S. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1973; p 119.

(27) It is fortunate that the potassium ferrioxalate quantum yield does not change in going from 254 to 300 nm. Thus the light used does not have to be a monochromatic 254-nm line.

Molecular Mechanics Treatment of β-Heteroatom-Substituted Cyclohexanones

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Recent NMR studies[1] indicate an axial preference for β-heteroatom-substituted cyclohexanones. The degree of axial preference essentially follows electronegativity: F > OH ~ OCH_3 > OAc > Cl > Br ~ SEt > CH_3. In fact, third row substituents actually are more stable in the equatorial position. We carried out ab initio calculations which support NMR data in the literature, and the MM2 program has been parameterized to model these systems correctly.

Recent equilibration studies have been carried out on the axial preferences of electron-withdrawing substituents β-substituted on cyclohexanones.[1,2] The axial–equatorial equilibrium for electronegative functional groups has also

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(1) (a) Gorthey, L. A.; Vairamani, M.; Djerassi, C. *J. Org. Chem.* **1985**, 50, 4173. (b) Lu, Y.; Barth, G.; Kieslich, K.; Strong, P. S.; Duax, W. L.; Djerassi, C. *J. Org. Chem.* **1983**, *48*, 4549.

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