(N00014-89J-1301) is gratefully acknowledged. We thank Gandara Amarasinghe and Carolyn Choo for their assistance in obtaining the X-ray powder diffraction spectra, and we are grateful to Dr. Doyle Britton and to Dr. William Gleason for helpful discussions.

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Supplementary Material Available: Calculated X-ray diffraction spectra of polymorphs I, II, and III (see ref 26) (12 pages). Ordering information is given on any current masthead page.

Singlet Oxygen Mediated Fragmentation of Amino Alcohols, 1,2-Diamines, and Amino Ketones[1]

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Abstract: Irradiation of aerated solutions of singlet oxygen sensitizers such as Rose Bengal, Rose Bengal derivative, or palladium tetraphenylporphyrin in the presence of substituted amines (amino alcohols, 1,2-diamines, and amino ketones) results in oxidative fragmentation of the amine in good chemical yield and with low-to-moderate quantum efficiency. For the amino alcohols and 1,2-diamines the reaction course is similar to that initiated by irradiation of electron-transfer "sensitizers" such as thioindigo or cyanoaromatics. In these cases the reaction has been shown to proceed via single electron transfer oxidation of the amine and subsequent cleavage of the amine cation radical. A similar mechanism is proposed for the reaction with singlet oxygen sensitizers in which singlet oxygen initiates reaction by SET oxidation of the amine donors and subsequent reaction from the resulting superoxide–amine cation ion radical pair. For reaction with amino ketones under the same conditions, irradiation results in formation of novel fragmentation products incorporating oxygen. Labeling studies with O-18 enriched oxygen indicate that air is the source of certain of the incorporated oxygen in the products and suggest a mechanism closely related to the other fragmentation processes.

Introduction

Oxidative fragmentation reactions of vicinally substituted amines such as amino alcohols, 1,2-diamines, and amino ketones can be initiated by excited-state single electron-transfer (SET) from ground-state amine to photoexcited acceptors under a variety of conditions.[3-10] These reactions frequently involve relatively clean and moderately efficient reaction in which the substituted amine is converted to two-electron redox products concurrent with cleavage of the carbon–carbon bond between the two functional groups. While the reaction may involve an unassisted fragmentation of the amine cation radical in a number of cases, reaction for certain donor–acceptor combinations may be facilitated by a direct reaction between the acceptor anion radical and amine cation radical generated in the SET quenching process.[7,9] In a number of cases, particularly in those involving amino ketones as donors, reaction can lead to intermediates or products in which a fragment from the donor has been added to the acceptor.[9,10] In a previous communication we reported that similar oxidative fragmentation reactions occur for amino alcohols under conditions (dye sensitization) generally employed to generate singlet oxygen.[1] This study demonstrated that SET quenching of singlet oxygen, especially in nonpolar solvents, can lead to clean cleavage of a variety of amino alcohols under very mild conditions but with moderately low efficiencies. These were attributable, at least in part, to relatively inefficient redox quenching of singlet oxygen. In the present paper we report results which show that the singlet oxygen mediated cleavage of a variety of substituted amines by a similar mechanism is a fairly general process. While the products produced by the SET quenching and subsequent reactions for amino alcohols and 1,2-diamines are similar to those afforded with other photoexcited acceptors, the reaction using singlet oxygen sensitization with amino ketones leads to novel redox chemistry including the formation of a variety of products which result from the attack of superoxide anion on the amino ketone cation radical.

Experimental Section

Materials. The syntheses of amino alcohols, amino ketones, and diamines used in this study, with the exception of **7a**, have been reported.[7,8] Amino alcohols **1** and **2** and amino ketone **7** were further purified by repeated crystallization from ethanol. Amino ketone **7** was synthesized and characterized as follows: 2-Hydroxy-1-(4-methylphenyl)-2-phenyl-1-ethanone was prepared using published procedures.[11,12] Trimethylsilyl cyanide (4.96 g, 50.0 mmol) was added to 4.78 g (45.0 mmol) benzaldehyde with stirring. After the mixture cooled 25 mL of methylene chloride was added, and the solution was allowed to stir overnight. A Grignard reagent was prepared in the usual manner by combining 8.55

(1) A portion of this work has appeared as a communication: Haugen, C. M.; Whitten, D. G. *J. Am. Chem. Soc.* **1989**, *111*, 7281.
(2) Current address: Department of Chemistry, Ithaca College, Ithaca, New York 14850.
(3) For a review of amine SET photochemistry, see: Pienta, N. J. In *Photoinduced Electron Transfer, Part C.*; Fox, M. A., Chanon, M., Eds.; Elsevier: New York, 1988; Part C, p 421.
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(11) Gassman, P. G.; Talley, J. J. *Tetrahedron Lett.* **1978**, 3773.
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g (50.0 mmol) of *p*-bromotoluene and 1.34 g (55.0 mmol) of magnesium and 75 mL of absolute ether and adding to the methylene chloride solution. The mixture was stirred for 2 h and poured onto 500 g of ice and 20 mL of sulfuric acid. The aqueous layer was allowed to stand overnight and then filtered to collect the crystals that deposited during that time. The ether layer was evaporated and taken up with 75 mL methanol with 1 mL of 10% aqueous HCl and also allowed to stand overnight. The solvent was removed, and the resulting solid and the crystals above were recrystallized three times from methanol and water to afford 6.1 g (64%), mp 103–4 (lit. 109[13]). 2-Morpholinyl-2-phenyl-1-(4-methylphenyl)-1-ethanone (7) was prepared by adding 3.0 g of the previously prepared product in 10 mL of DMF and treated with 1.4 mL of thionyl chloride under nitrogen. The mixture was stirred for 3 h and treated with 10 mL of water and 10 mL of methylene chloride. The methylene chloride layer was washed with 3 × 10 mL water and dried ($MgSO_4$). Rotary evaporation afforded a clear oil (the corresponding chloride) which was used without further purification by dissolving in 20 mL of anhydrous ether and 7 mL of morpholine and allowed to stir overnight. Water (20 mL) was added, and the ether layer three times was washed with 20 mL of water, dried (K_2CO_3), evaporated to oil, and subjected to high vacuum. The oil was identified as nearly pure product (3.3 g, 84%) by NMR and GC-MS spectroscopy. Additional purification by thick-layer chromatography of silica gel afforded noncrystalline colorless oil which was pure by NMR, HPLC, and GC-MS analysis. NMR ($CDCl_3$) 1.86 (s, 3 H), 2.30–2.50 (m, 4 H), 3.51–3.66 (m, 4 H), 4.75 (s, 1 H), 6.73–7.04 (m, 5 H), 7.42 (d, J = 6 Hz, 2 H), 7.97 (d, J = 6 Hz, 2 H). Methylephedrine (3) was purchased from Aldrich and used as received. Rose Bengal was purchased from Aldrich and used as received. Rose Bengal derivatives were synthesized and purified according to the method of Neckers et al.[14] $^{18}O_2$ enriched oxygen gas was obtained from Scott Specialty Gases. Eicosane (internal standard) was purchased from Sigma and recrystallized prior to use. Mesodiphenylhelianthrene was obtained from Photon Technologies and used as received. All solvents used in photolysis were spectral grade and were tested for purity by gas chromatographic analysis. Benzene was purchased from Fisher. Deuterated solvents (C_6D_6, CD_3CN, and $CDCl_3$) were used as received.

Methods. General Experimental Conditions. Visible light irradiations of solutions containing Rose Bengal derivatives were carried out using a 200-W Hg lamp or a 100-W tungsten lamp using filters appropriate for isolation of light above 500 nm (cutoff filter 3-70-Corning Glass Works). Where appropriate, samples were degassed by freeze–pump–thaw cycles until the vacuum reached 3 × 10^{-6} Torr or less and sealed under vacuum. Either a Pyrex test tube, NMR tube, or glass cuvette was used for irradiation. Due to the strong visible absorption of Rose Bengal, all samples were prepared and stored in the dark. UV–visible absorption spectra were measured on a Hewlett-Packard 8451 A diode array spectrometer. Routine ^1H NMR spectra were recorded on a General Electric/Nicolet QE-300 spectrometer. Product analyses were performed using a Hewlett-Packard 5890 gas chromatograph coupled with a 5790 HP series mass selective detector, equipped with a 10 m HP-1 capillary column. Products were identified by comparison of retention times and mass spectra with those of authentic samples. Quantitative determinations (starting materials and products) were performed using samples containing an internal standard (eicosane). High-pressure liquid chromatographic analysis was performed using a Waters 990 photodiode array detector HPLC equipped with an octadecyl (C-18) reverse phase column. Products were also measured quantitatively and identified by absorption spectra.

Oxygen Labeling Experiments. Samples containing amino ketone 7 (0.01 M) and Rose Bengal derivative (0.0005 M) in benzene were degassed. After degassing, the samples were reaerated with O-18 enriched oxygen and sealed. The samples were then irradiated (>500 nm) for appropriate lengths of time (8–12 h) after which samples were opened and analyzed immediately by GC/MS for product O-18 enrichment.

Quantum Yield Determination. Irradiation was performed using the lamps described above in conjunction with a monochromator used to isolate light in the region near 546 nm. Samples in glass cuvettes were stirred continuously. Actinometry was performed before and after irradiation to ensure lamp stability. Mesodiphenylhelianthrene in toluene was used as a chemical actinometer following the method of Brauer et al.[15] Concentrations of the sensitizer (0.0005 M, optical density > 2.5) ensured near complete light absorption. Little change in the OD was observed over the course of the irradiation. Product formation was generally monitored up to 10% or less consumption of the starting material. Quantitative determination of the products was performed by GC/MS or HPLC as described above.

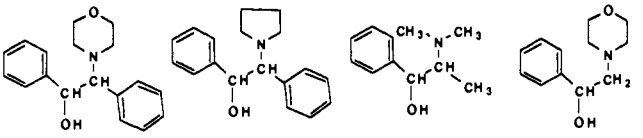
Table I. Quantum Yields for Amine Disappearance under Irradiation of Rose Bengal Derivative Solutions in Air-Saturated Benzene[a]

amine	Φ_{-A}	amine	Φ_{-A}
1	0.012 ± 0.004	5	0.014 ± 0.004
2	0.014 ± 0.004	6	0.018 ± 0.003
3	0.005 ± 0.002	7	0.009 ± 0.003
4	0.016 ± 0.003	7[b]	0.006 ± 0.003

[a] Benzene solutions, concentrations: amine, 0.010 M, Rose Bengal derivative 5 × 10^{-4} M, irradiating wavelength 546 nm, mesodiphenylhelianthrene actinometry. [b] Sensitizer PdTPP.

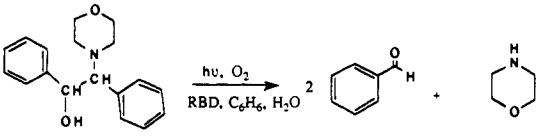
Results

Amino Alcohols. As reported earlier,[1] irradiation of Rose Bengal (RB) or the more organic solvent-soluble Rose Bengal derivative (RBD)[14] in benzene or other organic solvents containing amino alcohols **1–4** in aerated solutions leads to the production of oxidized



1 2 3 4

fragmentation products as shown in eq 1 for **1**. The reaction is quite clean; benzaldehyde and morpholine are the only organic



(1)

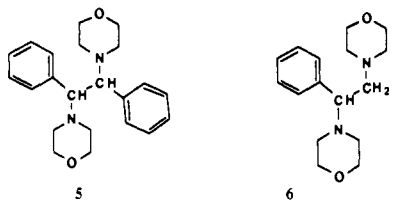
products detectable by NMR or GC-MS and the stoichiometry is two molecules of benzaldehyde per molecule of **1** reacted. Benzaldehyde was found to be relatively stable under the reaction conditions. Hydrogen peroxide was also detected qualitatively as a product of the reaction. No decomposition of **1** occurs when oxygen is excluded from the irradiated solutions. Solutions containing hydrogen peroxide (0.02 M) and either benzaldehyde (0.1 M) or **1** (0.1 M) were not observed to undergo any dark reaction during the time scale of a typical experiment. The reaction is quenched by addition of a singlet oxygen scavenger, diphenylisobenzofuran (DPBF).[16–19] Irradiation of solutions containing varying amounts (0.01–0.1 M) of DPBF (together with RB (0.0005 M) and **1** (0.1 M)) in benzene resulted in a sequential diminishing of benzaldehyde production; 0.1 M DPBF produced effectively complete quenching of reaction according to eq 1.

Quenching of singlet oxygen luminescence by **1** was monitored in methanol-d_4; a quenching constant, k_q = 6.5 × 10^6 M^{-1} s^{-1}, was measured[20] which compares favorably with a range of rates measured for other amines.[21–25] Quantum efficiencies for disappearance of **1**, **2**, and several other amines upon irradiation of RBD/benzene solutions are listed in Table I.[20] The protons of

(13) Arnold, C.; Fuson, R. J. *J. Am. Chem. Soc.* **1936**, *58*, 1295.
(14) Rose Bengal derivative is Rose Bengal benzyl ester, triethylammonium salt: Lamberts, J. J. M.; Neckers, D. C. *Tetrahedron* **1985**, *41*, 2183.
(15) Brauer, J. D.; Schmidt, R.; Gauglitz, G.; Hubig, S. *Photochem. Photobiol.* **1983**, *37*, 595.
(16) Matheson, I. B. C.; Lee, J.; Yamanashi, R. S.; Wolbarsht, M. L. *J. Am. Chem. Soc.* **1974**, *96*, 3343.
(17) An alternate mechanism involving direct formation of superoxide by SET quenching of RB or RBD and "cosensitization" of the amine via capture of RB cation[18,19] is evidently ruled out by the observation of DPBF quenching.
(18) Manring, L. E.; Gu, C.-L.; Foote, C. S. *J. Phys. Chem.* **1983**, *87*, 40.
(19) Rodgers, M. A. J.; Peters, J. *Biochem. Biophys. Res. Commun.* **1980**, *96*, 770.
(20) Quantum yields reported here are somewhat higher than those reported previously;[1] the earlier determinations with partially microparticulate Rose Bengal routinely give lower values than those with the totally soluble Rose Bengal derivative, probably due both to scattering losses and inefficient sensitization of oxygen by aggregated sensitizer. We thank Drs. E. Oliveros, M. T. Maurette, and A. M. Braun for making the determinations of singlet oxygen quenching by **1**.
(21) Smith, W. F., Jr. *J. Am. Chem. Soc.* **1972**, *94*, 186.
(22) Ogryzlo, E. A.; Tang, C. W. *J. Am. Chem. Soc.* **1970**, *92*, 5034.
(23) Ouannes, C.; Wilson, T. *J. Am. Chem. Soc.* **1968**, *90*, 6527.
(24) Saito, I.; Matsuura, T.; Inoue, K. *J. Am. Chem. Soc.* **1981**, *103*, 188.
(25) Manring, L. E.; Foote, C. S. *J. Phys. Chem.* **1982**, *86*, 1257.

1 are readily exchanged by adding D_2O to benzene solutions. Quantum yields for reaction of **1** were compared in benzene with the addition of D_2O and H_2O; the ratio ϕ_H/ϕ_D was found to be 1.3 which compares quite closely to the ratio obtained (1.26) for the thioindigo-mediated reaction investigated earlier.[7]

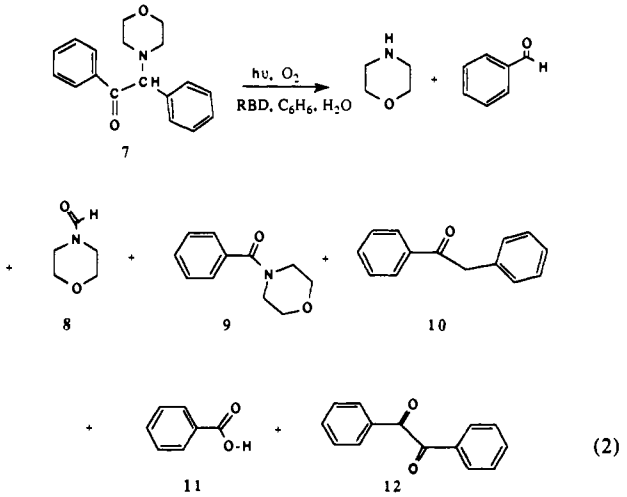
1,2-Diamines. The diamines **5** and **6** were also found to undergo reaction with irradiation of RB or RBD in the presence of oxygen in benzene with a trace of water; the reaction gives carbonyl products and the corresponding secondary amine in a reaction analogous to that shown in eq 1. However, for both **5** and **6**, the



5 6

yield of carbonyl products accounted for only about 70–80% of the diamine reacting and a number of other products were detected. Those that were identified included 1-morpholinyl-2-phenylethane and 1-morpholinyl-1-phenylethane from **6** and the amino ketone **7** from **5**. Since amino ketone **7** also undergoes reaction under conditions where singlet oxygen is generated (vide infra), it is not surprising that its generation is followed by the production of several products obtained on direct irradiation of oxygenated solutions of **7** and RB. Although the reaction is not as clean for the 1,2-diamines as for the corresponding amino alcohols, the quantum yields for amine reaction are about the same for **5** and **6** as for the amino alcohols (Table I).

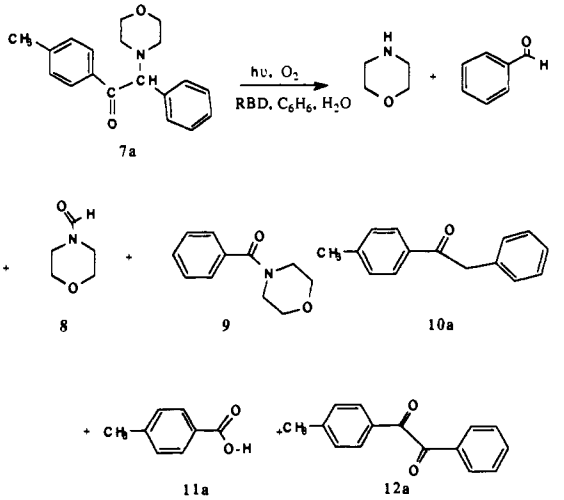
Amino ketones. Recent studies have shown that amino ketones such as 2-morpholinyl-1,2-diphenyl-1-ethanone (**7**) and structurally related aliphatic amino ketones undergo fragmentation reactions upon irradiation of electron-transfer "photosensitizers" such as thioindigo or 9,10-dicyanoanthracene.[9] The oxidative fragmentation reactions occurring for the amino ketones under these conditions are considerably more complex than those of amino alcohols or 1,2-diamines insofar as the number of products formed and the product distributions obtained with variation of the reaction conditions such as solvent, acceptor, and time of reaction. Not surprisingly it was found in this study that irradiation of singlet oxygen sensitizers such as RB or RBD in the presence of **7** leads to a number of different products derived from **7** including both fragmentation products and products derived from other redox modes.[10] All of the products detectable by gas chromatography-mass spectrometry (GC-MS) were identified by their spectra and by comparison with known samples. These accounted for nearly 80% of the reacted **7**; eq 2 summarizes the reaction and the various products identified.



7 8 9 10 11 12 (2)

The major products are benzil (**12**, 56%), benzoic acid (**11**, 12%), benzoylmorpholine (**9**, 9–10%), and formylmorpholine (**8**, 10%) (the accuracy of product production is estimated to be ±2%). The concentrations of these products vary linearly with irradiation time and thus they appear to be primary reaction products. Quantitative analysis of morpholine was not attempted and only trace amounts of benzaldehyde and **10** (compared to the other products accounted for above) were detected as the reaction progressed. As with the reactions described above for the amino alcohols and 1,2-diamines, there is no reaction without light or in the absence of the singlet oxygen sensitizers RB or RBD and there is no reaction when the solution is deaerated. Other visible light absorbing "sensitizers" such as thioindigo and $Ru(bipy)_3^{2+}$ also produce products **8–12** in similar ratios under irradiation with **7** in the presence of oxygen. Palladium(II) tetraphenylporphyrin (PdTPP) was also found to "sensitize" the reaction of **7**; in this case reaction was shown to produce benzaldehyde and morpholine as well as products **9–12** in similar ratios to that for RB, but no production of formylmorpholine (**8**) was detected.

The quantum efficiency for disappearance of **7** (0.1 M) under irradiation with RB in benzene was most conveniently and accurately determined by monitoring the production of the predominant product, benzil; using this method (GC and HPLC analysis of benzil) gives a quantum yield for the disappearance of **7**, $\phi = 0.009 \pm 0.003$. The quantum yield for disappearance of **7** under irradiation of PdTPP was found to be slightly lower, $\phi = 0.006 \pm 0.003$. The rate of quenching of singlet oxygen by amino ketone **7** was determined by measuring the singlet oxygen luminescence at 1270 nm as a function of added amino ketone. Analysis of the Stern–Volmer quenching leads to a rate constant, $k_q = 1.68 \pm 0.03 \times 10^6\ M^{-1}\ s^{-1}$, slightly lower than that observed for amino alcohol **1**.[26] The mono-*p*-methylated derivative of **7**, **7a**, was also studied under the same conditions employed for reaction of **7** and found to give similar products (eq 3).



7a 8 9 10a 11a 12a (3)

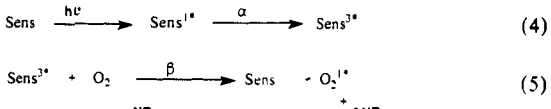
No doubly labeled benzil or unlabeled benzil was detected, and there was no methyl incorporation into the benzaldehyde or benzoylmorpholine product. The reaction of **7** was also investigated using O-18 enriched O_2. In these cases vacuum degassed samples were exposed to the O-18 enriched O_2 and then resealed before irradiation. The samples were analyzed for O-18 incorporation into products by GC-MS analysis. Under these conditions it was found that the benzoic acid and 4-benzoylmorpholine (**9** and **11**) produced incorporate one oxygen label each, while there is no O-18 incorporation into the benzaldehyde or benzil produced in the reaction.

Discussion

The reaction of the three classes of fragmentable amines can be most reasonably described by a mechanism incorporating the generally accepted paths for singlet oxygen generation (eqs 4 and 5).[27,28] It is clear under the concentrations used essentially all

(26) We thank Ms. Lisa Dennis and Professor M. A. J. Rodgers for measuring the rate constant by luminescence quenching at Bowling Green.
(27) Neckers, D. C. *J. Chem. Ed.* **1987**, *64*, 649.
(28) Thomas, M. J.; Foote, C. S. *Photochem. Photobiol.* **1978**, *27*, 683.

of the irradiating light is absorbed by the sensitizer and capture of the sensitizer triplet by oxygen should be an efficient process. Since the products from amines **1–6** are the same as those generated by electron-transfer sensitization, it seems reasonable to ascribe the subsequent steps to quenching of the singlet oxygen via SET (and/or other processes) (eq 6) to yield an ion–radical pair which can either fragment ("product precursors") or decay via return electron transfer (eqs 7 and 8). The quantum yield for the reaction is thus given by eq 9, assuming quenching of singlet



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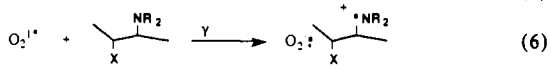
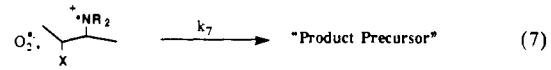


(6)



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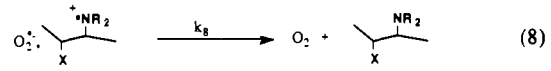
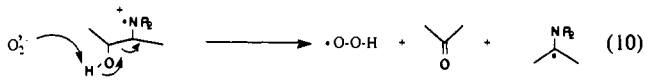


(8)

$$\phi = \alpha\beta\gamma \frac{k_7}{k_7 + k_8} \quad (9)$$

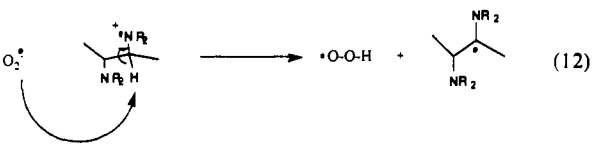
oxygen by amine dominates its unassisted decay and reaction 6 is not reversible. For the sensitizers RB and RBD, α and β are large, and the yield of singlet oxygen should be large.[28] The relatively low quantum yields listed in Table I for all of the reactions examined in this study thus may be attributable either to inefficiency in the SET quenching step or low yields from the ion–radical pair generated in the quenching step. It has been well-established in a number of studies that amines effectively quench singlet oxygen in processes which can either lead to products or simply to net deactivation without the formation of products.[21-25] Both direct and partial charge transfer have been suggested to play roles in this quenching.[21,25] Considering the quenching of singlet oxygen by the substituted amines used in this study, we estimate oxidation potentials of **1**, **2**, **5**, and **7** to be, respectively, 1.1, 0.98, 0.97, and 1.32 V (vs SCE) in acetonitrile. From the reduction potential of oxygen in acetonitrile (−0.892 V vs SCE),[29] a simple "Weller equation"[30] estimate indicates that amine quenching of singlet oxygen via SET to generate a superoxide anion–amine cation radical pair should be uphill by ca. 1 V or more, depending upon the amine. This estimate is for acetonitrile and thus for the less polar solvent benzene in which the current study was made the SET quenching should be even more endoergic. The measured quenching rate constants for direct quenching of singlet oxygen luminescence are much higher than one would predict based on an exclusively electron-transfer quenching and thus it appears reasonable to suggest that the actual quenching involves both a major non-net electron-transfer quenching and a minor ($\gamma \ll 1$) electron-transfer component. Thus we infer that a major limitation on reaction efficiency in the present case is the inefficient quenching of singlet oxygen to give electron-transfer products. A second large source of inefficiency could be in competition between fragmentation and reverse electron transfer in the ion–radical pair. In other studies with amino alcohols and 1,2-diamines we have found limiting quantum yields for electron acceptors reactive from excited singlets in nonpolar solvents are usually quite small (1–30%), while those for acceptors reactive from excited triplets are often near unity.[7-9] This has been attributed to fragmentation rate constants in the range 10^6–10^8 s^{-1} which are somewhat slower than reverse electron transfer from singlet radical ion pairs but faster than those for decay from triplet ion–radical pairs.[7,31] If we assume that return electron transfer from the ion radical pair generated in eq 6 (k_8) is also spin restricted, and hence relatively slow (ca. 10^5), it is reasonable that the quantum yields in the present study are limited mostly by inefficiency in the electron-transfer quenching step discussed above, at least for the diamines and amino alcohols.[32] However, the finding that the quantum efficiency for singlet oxygen-induced fragmentation of **1** shows a similar deuterium isotope retardation as for the thioindigo-induced fragmentation suggests that even here fragmentation and return electron transfer may be competitive. The finding that limiting quantum yields for the diamines and amino alcohols used in this study are similar suggests that rates for the acceptor anion-assisted fragmentation (eq 10) in the case of amino alcohols and unassisted fragmentation (eq 11) for diamine cation radicals may be similar. In other studies we have estimated the rate constant for fragmentation of the cation



(10)

(11)

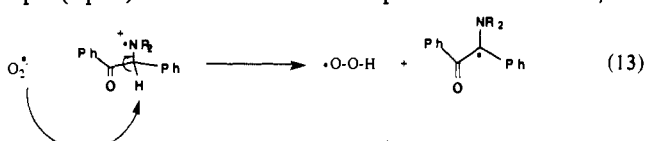
radical generated from **8** to be ca. 1×10^8 s^{-1}.[31] This would imply that return electron transfer may be somewhat faster than suggested by the above discussion. The finding that formation of **7** accompanies the fragmentation of **5** suggests deprotonation of the cation generated from **5** (eq 12) may be competitive with the



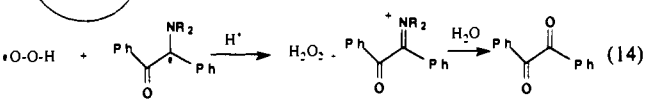
(12)

unassisted fragmentation which appears reasonable in view of the moderate basicity of the superoxide anion[34-36] and acidity of amine cation radicals.[37-39]

While the reactions of the amino alcohols and 1,2-diamines used in this investigation are identical to those observed with other excited acceptors such as thioindigo, the cyanoanthracenes, and anthraquinone, the products observed with amino ketone **7** are quite novel and yet appear reasonably derived via a SET mechanism, despite the fact that the amino ketone is considerably more difficult to oxidize (vide supra). The formation of benzil, the major product, can be reasonably formulated as arising from superoxide mediated deprotonation within the ion–radical pair generated by eq 6 (eq 13) and one or more subsequent redox reactions, for



(13)



(14)

example such as shown in eq 14 leading to the net two-electron-transfer products.[32,33] The question of pathways to the other products shown in eq 2 is perhaps more interesting. The acid (**11**) and benzoyl amide (**9**) always are produced in nearly equal amounts; the finding that each of these products incorporates one atom of labeled oxygen when O-18 enriched oxygen is used in the photooxidation suggests that formation of **9** and **11** can occur in an anion-assisted fragmentation analogous to that proposed with other acceptors and **7**, followed by a recombination and rear-

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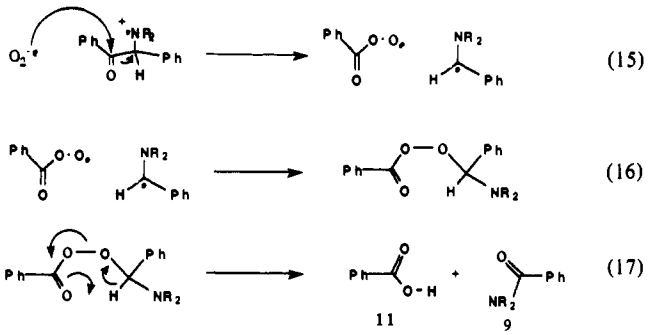
(32) The net reaction in any case is a two-electron redox process for formation of both observed products, benzil and hydrogen peroxide. The energetics for the second step leading to the iminium precursor to benzil are expected to be quite favorable due to the favorable oxidation potential of the α-aminoradical.[33]
(33) Wayner, D. D. M.; McPhee, D. J.; Griller, D. J. *J. Am. Chem. Soc.* **1988**, *110*, 132.

rangement as shown in eqs 15-17. It seems reasonable then that



(15)

(16)

(17)

11 9

the major products produced from the SET quenching in benzene arise from subsequent "cooperative" reactions of the oppositely charged ion-radicals produced within the contact ion pair. The origin of the remaining products is less clear. While benzaldehyde, deoxybenzoin, and benzil are all formed in the direct photolysis of **7**, it seems unlikely that their production in the reaction sensitized via singlet oxygen is possible since no light directly absorbed by **7** was used and we were unable to detect any dehydromorpholine, the expected byproduct of a type II photoelimination reaction.[40,41] We suggest benzaldehyde likely arises from unassisted fragmentation of the amino ketone cation radical; indeed this pathway has been detected in earlier studies of amino ketone reactions through reaction with photoexcited acceptors.[42] The origin of **10** seems most likely to be via reduction of amino ketone **7** by its scavenging of a radical intermediate (such as those generated in eqs 13 and 15) and subsequent reactions of the radical so generated. We have recently observed cases where amino ketones such as **7** give **10** or structurally similar reductive deamination products where the primary excited-state quenching process should be SET oxidation of the amino ketone;[10] activation of amino ketones such as **7** by SET from excited donors leads to **10** as the major product in a relatively clean reaction. The origin of the remaining minor product formylmorpholine is unclear; although it is observed in each case where the reaction is sensitized by RB or RBD, it is not detected when PdTPP is used as a sensitizer, and thus it is possible that it does not arise directly from reaction of **7** but possibly as a product from reaction of morpholine liberated in the photoreaction.

Acknowledgment. We thank the U.S. Department of Energy (Grant Number DE-FG02-86ER13504) for support of this research.

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Generation and Stability of a Simple Thiol Ester Enolate in Aqueous Solution

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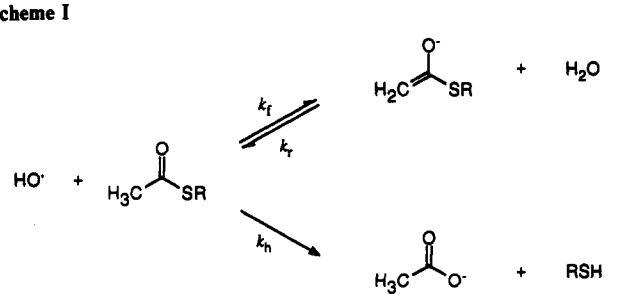
Abstract: The exchange for deuterium of the α-protons of ethyl thioacetate and of acetone in 3-quinuclidinone buffers in D_2O at 25 °C and pD = 7.7-9.3 was followed by ^1H NMR spectroscopy. The exchange reactions lead to the appearance of signals due to the α-CH_2D and α-CHD_2 species that are cleanly resolved from each other and from the signal due to the α-CH_3 species. Observed rate constants for the 3-quinuclidinone-catalyzed exchange were determined during exchange of 30-37% of the first α-proton of each methyl group of ethyl thioacetate or acetone. The rate constants for exchange correspond to those for deprotonation of ethyl thioacetate and acetone by 3-quinuclidinone to give the free enolates, with $k_B = 2.2 \times 10^{-5}$ and 5.2×10^{-4} M^{-1} s^{-1}, respectively. These rate constants were combined with the known pK_a of acetone to estimate $pK_a = 20.4$-21.5 for ethyl thioacetate and $k_{BH} = 1.7 \times 10^8$ to 2×10^9 M^{-1} s^{-1} for the reaction of the free thiol ester enolate with the 3-quinuclidinone cation. The lifetime of the buffer acid-enolate intimate ion pair $BH^+ \cdot {}^-CH_2COSEt$ with respect to proton transfer to give B-CH_3COSEt is estimated to be from 10^{-9} to 10^{-10} s. These results provide evidence against the suggestion that enzyme-catalyzed Claisen condensation and related reactions proceed by concerted mechanisms that are enforced by the insignificant lifetime of the thiol ester enolate in the presence of an acidic amino acid residue at the enzyme.

The enolates of simple[1] thiol esters of coenzyme A are putative intermediates of numerous important enzymatic reactions such as Claisen-type condensation and the dehydration of β-hydroxy thiol esters.[2-5] However, it is not known whether simple thiol ester enolates are long-lived enough to be formed as enzyme-bound intermediates,[6] and there is scant evidence for the formation of

Scheme I



(1) In this paper, a "simple" thiol ester refers to a thiol ester in which the carbonyl group is adjacent to a carbon atom bearing no other electron-withdrawing groups.
(2) (a) Gehring, U.; Lynen, F. In *The Enzymes*, 3rd ed.; Boyer, P. D., Ed.; Academic Press: New York, 1972; Vol. 7, Chapter 13. (b) Higgins, M. J. P.; Kornblatt, J. A.; Rudney, H. Reference 2a, Chapter 14. (c) Spector, L. B. Reference 2a, Chapter 12.
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