Rose Bengal-Induced Photofragmentation: Singlet Oxygen Revisited

Gary A. Epling* and Martha L. Jackson

Department of Chemistry, University of Connecticut, Storrs, CT 06269, USA

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Abstract: The Rose Bengal-induced photofragmentation of β -amino alcohols has been previously reported to proceed through a mechanism involving singlet oxygen sensitization, followed by attack of singlet oxygen and superoxide on the β -amino alcohol. An alternative mechanism involving electron transfer from the amine to the excited state Rose Bengal is supported by new evidence.

Whitten¹⁻⁴ has recently reported several interesting examples illustrating the wide applicability of the photosensitized electron transfer-induced fragmentation of β-amino alcohols discovered by Davidson.⁵ However, Rose Bengal was believed to induce fragmentation by an anomalous type of mechanism⁶—the initial formation of singlet oxygen, which with superoxide subsequently caused fragmentation of the amino alcohol. We were surprised at this report for several reasons. First, the solid Rose Bengal utilized in Whitten's work has been characterized by Neckers as extremely inefficient in its generation of singlet oxygen.⁷ Further, there is considerable evidence that excited state Rose Bengal efficiently accepts an electron from easily oxidizable species such as amines.^{8,9} Consequently, we re-examined the evidence that led to the suggestion of a singlet oxygen mechanism and report new data which suggests that Rose Bengal induces photofragmentation by an electron transfer mechanism.

$$\begin{array}{c} & & hv \\ & & \\ Ph-CH-CH-Ph \end{array} \qquad \begin{array}{c} & & Rose Bengal \\ Benzene / H_2O \end{array} \qquad PhCHO + H-N O$$
1

In Whitten's previous study⁶ evidence was presented to support a singlet oxygen mechanism for the Rose Bengal-induced photofragmentation of morpholino derivative 1. One of the major pieces of evidence presented was the quenching of the photofragmentation in the presence of diphenylisobenzofuran, a singlet oxygen scavenger. The mechanism proposed is summarized in Scheme 1.

Our reservations led us to scrutinize the evidence supporting Scheme 1. We performed Rose Bengalsensitized irradiations of *erythro* 1 using visible light and a variety of conditions; some conditions closely matched Whitten's (powdered Rose Bengal in moist benzene), but other solvents and derivatives of Rose Bengal were also examined. Irradiation of 10^{-2} to 10^{-3} M solutions of *erythro* 1 using 6 x 10^{-4} M of sensitizer led to several significant observations (Table 1). These support electron transfer reaction of Rose Bengal.



(1) The efficiency and products of photoreaction of 1 sensitized by solid Rose Bengal suspended in benzene with 1 were not much different under argon and in aerated solutions (entry #1 and 3). Similarly, the reactions sensitized by other Rose Bengal sensitizers [polymer-bound Rose Bengal (entry #5 and 6), "benzene-soluble" Rose Bengal (Rose Bengal benzyl ester, triethylammonium salt; entry #7 and 8), "ordinary" Rose Bengal solution (disodium salt in water; entry 10 and 11), and Rose Bengal methyl ester methyl ether (entry #12 and 13] all led to the reaction of 1 under both argon and oxygen.

(2) Polymer-bound Rose Bengal ("Sensitox") which is at least 25 times more efficient⁷ in its efficiency of singlet oxygen generation than Rose Bengal powder did not cause a proportionate increase in the efficiency of photofragmentation (entry #3 vs. 6).

 Entry Number	Sensitizer	Atmosphere	Additive	Efficiency of Reaction
1	RB powder [†]	Argon		6.9
2	RB powder [†]	Argon	2,5-dimethylfuran	5.0
3	RB powder [†]	Oxygen	_	10.8
4	RB powder [†]	Oxygen	2,5-dimethylfuran	8.4
5	RB polymer [§]	Argon		14.6
6	RB polymer [§]	Oxygen		14.8
7	RB soluble [‡]	Argon	_	16.
8	RB soluble [‡]	Oxygen	_	71.
9	RB soluble [‡]	Oxygen	2,5-dimethylfuran	66.
10	RB solution [¶]	Argon		53.
11	RB solution [¶]	Oxygen		127.
12	RB soluble ether*	Argon		34.
13	RB soluble ether*	Oxygen		37.

Table 1. Photosensitized Fragmentation of 1 by Rose Bengal.

[†]Rose Bengal disodium salt suspended in benzene.

§Sensitox[™] suspended in benzene.

[§]Rose Bengal ethyl ester triethylammonium salt¹¹ in benzene.

Rose Bengal disodium salt in water.

*Rose Bengal methyl ester methyl ether¹² in benzene.

(3) Soluble Rose Bengal derivatives led to the most efficient photofragmentation of 1, both under oxygen and argon, though their efficiency of singlet oxygen generation is not significantly better than that of Sensitox. Further, they caused photofragmentation under both argon and oxygen. In all cases the reaction even under argon was much more efficient than when using Rose Bengal powder suspended in aerated benzene.

(4) Presence of an equal concentration $(1 \times 10^{-3} \text{ M})$ of the singlet oxygen scavenger 2,5-dimethylfuran had a very small effect on the photofragmentation of **1**. Its rate of reaction with singlet oxygen is only a power of ten lower than diffusion-controlled (4.0 x 10⁸ L M⁻¹ s⁻¹),¹⁰ which is 100-fold faster than the quenching of singlet oxygen by a β -amino alcohol (6.5 x 10⁶ L M⁻¹ s⁻¹).⁶ Thus, a 100-fold reduction in the efficiency of photosensitized fragmentation of **1** should be apparent when the scavenger and **1** are at equimolar concentrations. To see a negligible effect is compelling evidence against the singlet oxygen mechanism.

Consideration of our observations leads us to suggest an alternative mechanism for Rose Bengal-induced photofragmentation of 1, involving electron transfer as the key step (Scheme 2).

Scheme 2.



Whitten's observation of a quenching effect of diphenylisobenzofuran clearly differs from our observation of a minimal effect of 2,5-dimethylfuran. Perhaps the diphenylisobenzofuran stops the reaction by a different mechanism than reaction with singlet oxygen. Quenching of an exciplex (the precursor to the chargeseparated species) or being involved in electron transfer reactions of its own are two possibilities.

Our measured quantum yields for Rose Bengal-sensitized fragmentation of 1 under argon are close to the quantum yields reported by Whitten⁴ for the sensitization of 1 using a variety of other photosensitizers which were effective via electron transfer mechanisms. Whitten reported quantum yields ranging from 6.6 x 10⁻⁵ to 4.4 x 10⁻² with different electron acceptors. Our value using 6 x 10⁻⁴ M aqueous Rose Bengal, under argon, with 1.0 x 10⁻³ M 1 at 30° was $\Phi = 1.7 \times 10^{-2}$. Thus, Rose Bengal more closely resembles the *best* electron transfer sensitizers than the *worst*.

The reaction sensitized by the various Rose Bengal species was generally a little more efficient under oxygen, so it is tempting to suggest that an additional mechanism can occur with oxygen. However, the poor correlation of reactivity and singlet oxygen generation efficiency of the sensitizers and the inability of dimethylfuran to quench the reactions make the involvement of singlet oxygen, as more than a minor pathway of reaction, questionable. Several alternative explanations seem more plausible. The involvement of oxygen in the key electron transfer reaction between the excited sensitizer and the amine (perhaps involving a ternary

D + RB
$$\xrightarrow{hV}$$
 D[†] RB $\xrightarrow{}$ $\xrightarrow{O_2}$ D[†] + O₂ $\xrightarrow{}$ + RB

exciplex) is a possibility. There is considerable precedent for efficient interaction of oxygen with exciplexes. Sharma¹³ found oxygen's "quenching" of the pyrene/perylene exciplex to be much more efficient than the quenching of either excited species. Levin¹⁴ reported that the oxygen-induced quenching of the triplet exciplex between quinone and aromatic amines proceeds *via* oxygen-enhanced charge transfer. Oxygen-enhanced reactivity of photochemically produced exciplexes seems well-documented. Foote,¹⁵ Lewis,¹⁶⁻¹⁸ and Hamity¹⁹ reported oxygen-enhanced exciplex-induced isomerization of *trans-* to *cis*-stilbene and a variety of electron acceptors. The purported reason for this increased reactivity is that oxygen enhances intersystem crossing of the singlet exciplex, or that electron transfer from the acceptor ion to ground state oxygen gives superoxide, a process leading to enhanced reactivity. This latter explanation is directly analogous to our suggestion above.

Though our efforts focused primarily on compound 1, varying the sensitizer and conditions, we investigated briefly other amino alcohols to confirm that our observations were general in nature. With the *threo*-2-morpholino-1,2-diphenylethanol we similarly found Rose Bengal-induced photofragmentation under both argon and oxygen. The efficiencies using aqueous Rose Bengal (Na₂) were: (33, argon; 82, oxygen). Similarly, N-methylephedrine reacted with efficiencies of: 358 (argon), and 456 (oxygen). Thus, both compounds reacted under argon, but showed a small enhancement of reaction efficiency in the presence of oxygen.

In light of the new evidence provided herein, and the attractiveness of alternative roles for oxygen in the oxygen-accelerated processes, it seems doubtful that the singlet oxygen pathway plays more than a minor role in the Rose Bengal-promoted photofragmentation of amino alcohols.

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