

NUCLEOPHILIC AROMATIC PHOTOSUBSTITUTION REACTIONS IN AQUEOUS SOLUTION AND IN ORGANIZED MEDIA

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In alkaline aqueous solution, the lowest excited triplet states of *m*-nitrophenyl ethers undergo clean nucleophilic aromatic photosubstitution with OH^- to give the corresponding alcohol and the *m*-nitrophenoxide ion. Other potentially nucleophilic species such as Br^- , which are readily oxidizable, quench the triplet state by electron transfer without reacting.

In cationic micellar solution, the alkaline photohydrolysis occurs largely at the micellar surface. In anionic micellar solution (sodium dodecyl sulfate, SDS), reaction of the excited *m*-nitrophenyl ether with OH^- occurs predominantly in the intermicellar aqueous phase with an efficiency that depends on the rate of migration of the triplet state from the micelle out into the aqueous phase. These micellar exit rates, measured by laser flash photolysis, are surprisingly fast and lead to the conclusion that the lowest excited triplet state of *m*-nitrophenyl ethers is much more hydrophilic than the ground state. Advantage has been taken of these unique properties of the *m*-nitrophenyl ether chromophore to design novel probes for detecting local concentrations of ions in the electrical double layer around anionic SDS micelles.

Keywords: micelle; photochemistry; laser flash photolysis; nucleophilic substitution; double layer.

INTRODUCTION

The present article provides a brief overview of nucleophilic aromatic photosubstitution reactions of nitroaromatic molecules in homogeneous aqueous solution and in aqueous micellar solutions of cationic and anionic detergents, with emphasis upon recent contributions from our groups.

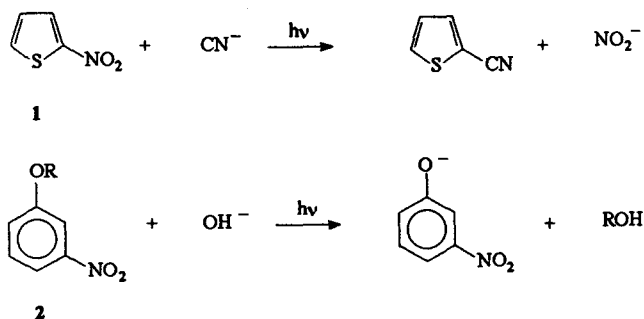
NUCLEOPHILIC AROMATIC PHOTOSUBSTITUTION REACTIONS IN AQUEOUS SOLUTION

Nucleophilic aromatic photosubstitution reactions¹, exemplified in Scheme 1 by the photocyanodenitration of 2-nitrothiophene² (1) and the alkaline photohydrolysis of *m*-nitrophenyl ethers (2), constitute one of the most interesting examples of bimolecular photoreactivity.

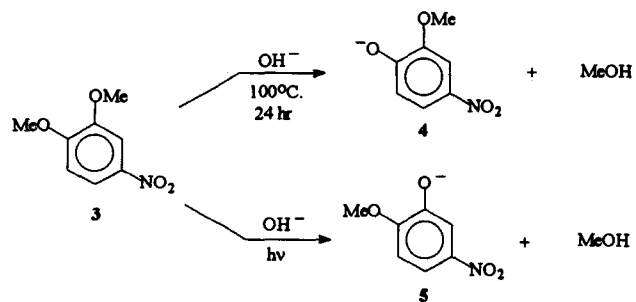
Perhaps the most remarkable feature of these reactions is the enormous difference in both the rate and the orientation of nucleophilic attack upon going from the ground state to the excited triplet state of the nitroaromatic¹⁻³. Thus, at room temperature in the absence of light, neither 1 nor 2 reacts at a measurable rate with the nucleophile (cyanide or hydroxide

ions). In contrast, upon electronic excitation, the lowest excited triplet states of 1 and 2 react with the same nucleophiles at near diffusion-controlled rates ($> 10^9 \text{ M}^{-1}\text{s}^{-1}$), corresponding to an increase in intrinsic reactivity by a factor of at least 10^{10} . In the ground state, nitro groups exert a strong ortho/para-directing effect on nucleophilic aromatic substitution, while in the excited state the nitro group directs the nucleophilic substitution to the meta or the ipso positions. Both of these aspects are nicely exemplified by 4-nitroveratrole (3). Thus, 3 undergoes slow thermal reaction in strongly alkaline medium to give 4 (the product of cleavage of the "para" methoxy group), whereas the excited triplet state of 3 yields exclusively 5 (via photosubstitution of the "meta" methoxy group) in dilute aqueous NaOH solution (Scheme 2). These unique features have led to the use of *m*-nitrophenyl ethers as photoremovable groups for protecting alcohols and oligophosphates during synthesis⁴.

Extensive mechanistic studies^{1-3,5-7} have shown that nucleophilic aromatic photosubstitution reactions of nitroaromatics occur by bimolecular attack of the nucleophile on the lowest excited triplet state, forming an intermediate Meisenheimer or sigma complex which either partitions to products or back to

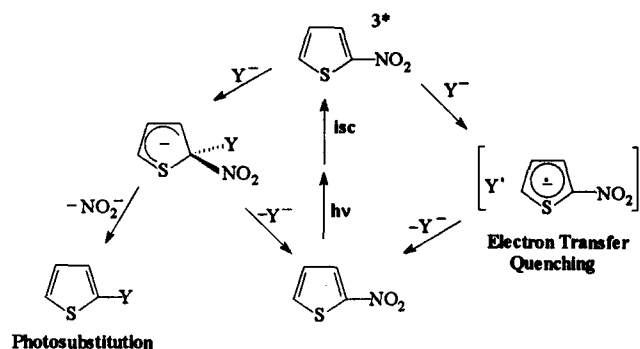


Scheme 1



Scheme 2

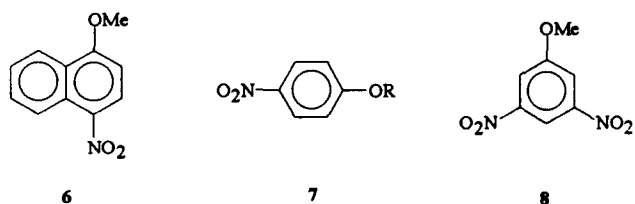
starting materials. For net reaction to occur, the lowest triplet state of the nitroaromatic must be π,π^* in nature (n,π^* triplet states are apparently unreactive with respect to nucleophilic photosubstitution) and the rate constant for nucleophilic attack must exceed that for outer sphere electron transfer from the potential nucleophile to the excited nitroaromatic (Scheme 3)⁶. Good ground state nucleophiles such as I^- , $S_2O_3^{2-}$, SCN^- or Br^- , which are readily oxidizable, transfer an electron to the lowest excited triplet state of 1 and 2 at essentially the diffusion controlled rate, leading to electron-transfer quenching rather than photoreaction⁶. Indeed, efficient nucleophilic photosubstitution is usually observed only with species such as OH^- , CN^- , NCO^- or BH_4^- , which are both relatively good ground-state nucleophiles and rather poor electron donors.



Scheme 3

NUCLEOPHILIC AROMATIC PHOTOSUBSTITUTION IN CATIONIC MICELLAR SOLUTION

Nucleophilic aromatic photosubstitution reactions were among the first bimolecular photoreactions studied in aqueous micellar solution⁸. Thus, Hautala and Letsinger⁹ found that the cationic detergent hexadecyltrimethylammonium chloride (CTACl) markedly increased the quantum yield of photocyanation of 4-methoxy-1-nitronaphthalene (6), but had little or no effect on the photohydrolysis or photocyanation reactions of 4-nitrophenyl ethers (7). Micellar effects on the local concentrations of the reagents and the unique microenvironment of the micellar pseudophase were suggested to contribute to the observed photoreactivity patterns. Subsequent detailed studies by Bonilha *et al.*¹⁰⁻¹¹ of the alkaline photohydrolysis of 3,5-dinitroanisole (8) in the presence of the cationic detergents tetradecyltrimethylammonium chloride (TTACl) and CTACl demonstrated that the observed inhibition is due primarily to a large decrease in the lifetime of the 3,5-dinitroanisole triplet state upon incorporation into the micelle, rather than to an intrinsic change in the photoreactivity of the triplet state.



Studies¹² of the photocyanation of 2-nitrothiophene (1) in micellar hexadecyltrimethylammonium bromide (CTAB) and chloride (CTACl) provided evidence for electron transfer quenching of the 2-nitrothiophene triplet state by Br^- and Cl^- counterions at the micellar surface in competition with the re-

action with CN^- . Competitive electron transfer quenching of the alkaline photohydrolysis of *m*-nitrophenyl ethers (2) by Br^- and $S_2O_3^{2-}$ in micellar CTACl has been analyzed quantitatively by Tedesco¹¹ using a model based on counterion exchange.

NUCLEOPHILIC AROMATIC PHOTOSUBSTITUTION IN ANIONIC MICELLAR SOLUTION

Prior to our studies, the only indication of the effect of anionic detergent micelles on nucleophilic photosubstitution reactions was the report by Hautala and Letsinger⁹ that sodium dodecylsulfate (SDS) decreased the quantum yields for photocyanation and photohydrolysis of 4-nitrophenyl ethers. This is, in fact, the prediction of the pseudophase ion exchange model¹³ for micellar catalysis for a reaction of this type. At higher detergent concentrations, most of the nitrophenyl ether will be incorporated into the SDS micelle. On the other hand, the negative surface charge of the SDS micelle strongly repels or excludes anionic nucleophiles such as CN^- or OH^- . The predicted result is thus a pronounced inhibition of the photosubstitution due to this confinement of the nitroaromatic to the micelle and of the nucleophile to the intermicellar aqueous phase.

Experimental data for the effect of micellar SDS on the alkaline photohydrolysis of a series of homologous *m*-nitrophenyl alkyl ethers (2, R = methyl, *n*-butyl, and *n*-decyl)¹⁴ are shown in Figure 1. Although SDS micelles strongly decrease the quantum yield for photohydrolysis of the hydrophobic, water insoluble *n*-decyl ether, they have very little effect on the photohydrolysis quantum yield of the corresponding *n*-butyl ether and actually increase the quantum yield for the photohydrolysis of *m*-nitroanisole itself!

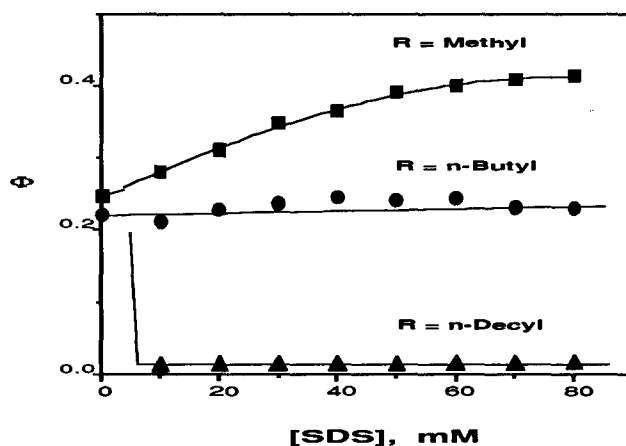
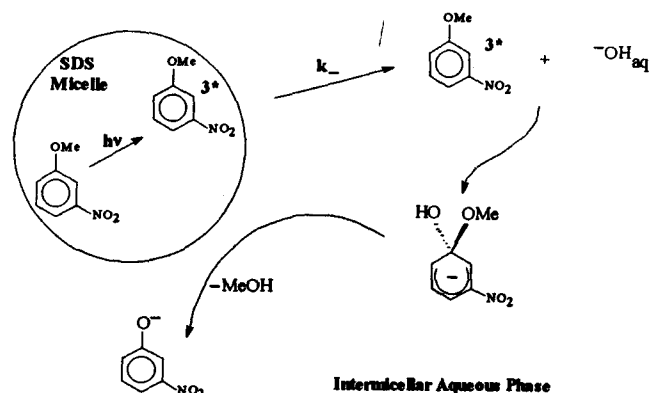


Figure 1. Quantum yields for alkaline photohydrolysis of 1 homologous *m*-nitrophenyl ethers (2) as a function of sodium dodecyl sulfate (SDS) concentration. Quantum yields were determined at 30°C by following the formation of the *m*-nitrophenoxide ion (absorption at 410 nm) in aqueous solutions containing 3×10^{-4} M 2 and 0.010 M NaOH; the solutions were irradiated in a merry-go-round apparatus with 313 nm light from a medium pressure mercury lamp and incident light intensities were determined by ferrioxalate actinometry. For details, see refs. 7, 10 and 14.

This last result, which is in total disagreement with the predictions of the pseudophase ion exchange model¹³, suggests a breakdown of the key assumption of the pseudophase model, i.e., that the distribution of the reactive species between the micelles and the aqueous phase does not change on the time scale of the reaction. This led us to postulate the sequence of events shown in Scheme 4.



Scheme 4

In this Scheme, excitation of *m*-nitroanisole in the micelle produces the long-lived excited triplet state¹⁵, which migrates out of the SDS micelle into the surrounding aqueous phase. Once out in the aqueous phase, the triplet state can be attacked by OH⁻ to give an intermediate sigma (or Meisenheimer) complex. In order to explain an increase in the photohydrolysis quantum yield in the presence of SDS, the sigma complex must migrate back into the micelle and the micelle must cause it to decompose preferentially to product (the *m*-nitrophenoxide ion). In order to confirm this sequence of events, we performed the following laser flash photolysis experiments in order to measure the "solubility" of the excited triplet state of *m*-nitrophenyl ethers in the SDS micelle.

MICELLAR SOLUBILITY OF GROUND AND EXCITED STATES OF *M*-NITROPHENYL ETHERS

The average time ($1/k$) which the unexcited ground state of a solute resides in the SDS micelle can be calculated from the relationship $K_s = k_+/kN$, where K_s is the pseudophase partitioning coefficient for incorporation of solute into the SDS micelle¹⁶, k_+ is the rate constant for micellar entry (typically diffusion controlled, or ca. $3 \times 10^{10} \text{ M}^{-1}\text{s}^{-1}$) and N is the micellar aggregation number (about 65 for SDS). Using the value of $K_s = 55 \text{ M}^{-1}$ for *m*-nitroanisole (determined by micellar liquid chromatography¹⁷), one obtains an estimate of about 120 ns for the residence time of ground state *m*-nitroanisole in the SDS micelle. Similarly, the experimental value of $K_s = 480 \text{ M}^{-1}$ (determined by absorption spectroscopy¹⁸) for the *n*-butyl ether corresponds to a micellar residence time of about 1 μs for the ground state.

The corresponding average residence times of the excited triplet state of the *m*-nitrophenyl ethers can be estimated by laser flash photolysis. The triplet states of *m*-nitrophenyl ethers are readily detected by their triplet-triplet absorption at about 400 nm (Figure 2) and have lifetimes of 1.5-2 μs in aerated aqueous solution. In the absence of SDS, this triplet state is quenched by Br⁻ at essentially the diffusion-controlled rate (bimolecular quenching rate constant, k_q , of $3.8 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$). In an aqueous micellar solution of SDS containing Br⁻, the efficiency of quenching of the triplet state of the *m*-nitrophenyl ether will depend on the rates of entry and exit of the triplet state from the micelles (compare Scheme 4). At high added Br⁻ concentration, micellar exit becomes the rate limiting step for quenching and the triplet lifetime approaches the value of the average residence time ($1/k$) of the triplet state in the micelle.

In 0.10 M SDS, the triplet lifetime of the hydrophobic, water-insoluble *n*-decyl ether is completely unaffected by the addition of Br⁻, confirming that quenching at the micelle sur-

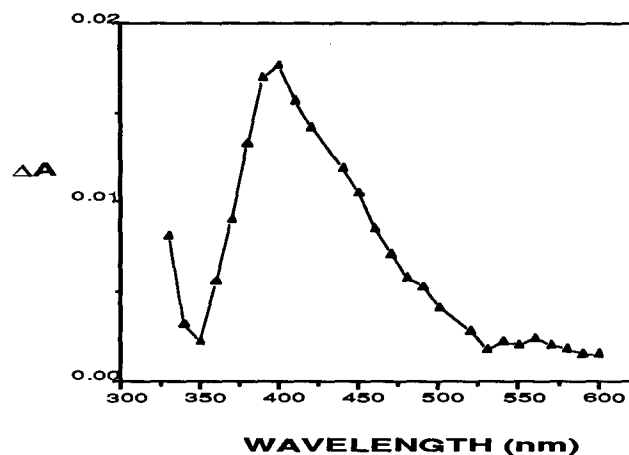


Figure 2. Transient absorption spectrum of the lowest excited triplet of *m*-nitroanisole. An aqueous solution of *m*-nitroanisole ($3 \times 10^{-4} \text{ M}$) was excited by a 308 nm pulse from a XeCl excimer laser.

face is unimportant. In contrast, the triplet states of *m*-nitroanisole and the corresponding *n*-butyl ether are significantly quenched by Br⁻ in aqueous SDS solution. By extrapolating the triplet lifetime to high added quencher concentration (Figure 3), one obtains a micellar residence time of $1/k = 130 \text{ ns}$ for the excited triplet state of the *n*-butyl ether and an estimate of about 50 M^{-1} for its micelle-water partitioning coefficient (K_s^*). Analogous measurements with *m*-nitroanisole indicate that its triplet state exits from the SDS micelle in less than 15 ns ($K_s^* < 10 \text{ M}^{-1}$)! Thus, the excited triplet states of *m*-nitrophenyl ethers are nearly ten times less soluble in the SDS micelle (i.e., more hydrophilic) than their respective ground states.

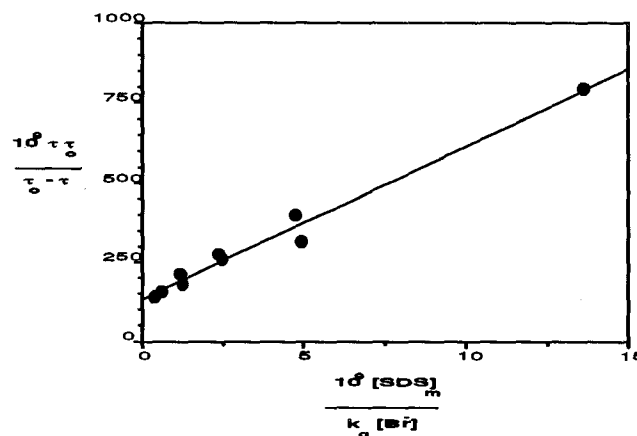
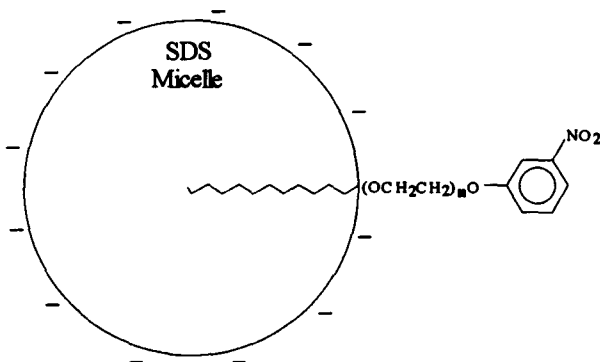


Figure 3. Determination of the mean residence time ($1/k = \text{intercept}$) and the partitioning coefficient ($K_s^* = \text{slope}$) of the lowest excited triplet state of *m*-nitrophenyl butyl ether (2, *R* = *n*-butyl) in the SDS micelle. Triplet lifetimes (τ) were determined by laser flash photolyses (308 nm excitation pulse from an XeCl laser), monitoring the decay of the triplet state at 405 nm (see Figure 1). Lifetimes were determined at 30°C. on aqueous solutions of 2 ($3 \times 10^{-4} \text{ M}$) containing a constant concentration of added salt ($[\text{NaCl}] + [\text{NaBr}] = 0.020 \text{ M}$) and fixed SDS concentrations (0, 0.033, 0.050 or 0.10 M). The triplet lifetime in the absence of added NaBr ($\tau_0 = 1150 \text{ ns}$) is unaffected by SDS (0-0.1 M) and the bimolecular rate constant (k_q) for quenching of the triplet state by Br⁻ in aqueous solution in the absence of SDS is $4 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$.

MICELLAR DOUBLE-LAYER PROBES BASED ON THE M-NITROPHENYL ETHER CHROMOPHORE

Like any other charged colloidal particle, the SDS micelle is surrounded by a diffuse double layer. The local concentration of sodium counterions decreases from a value of about 3-4 M at the micelle surface to a value of the order of 10^{-2} M far from the micelle. Likewise, the local concentration of coions should increase by a factor of about 100 as one moves out from the micellar surface through the double layer. Ideally, one would like to be able to measure these concentrations experimentally as a function of distance out from the micelle surface.

One rather straightforward approach would be to tether an appropriate probe chromophore, whose properties are sensitive to the local concentration of some coionic species added to the system, at various fixed distances out from the micelle surface. Although the approach itself is perhaps intuitively obvious, its practical implementation is not. By taking advantage of the unique properties of the m-nitrophenyl ether triplet state (highly hydrophilic, ca. 2 μ s lifetime, quenchable by anions), however, functional prototypes of "double-layer" probes of this type can in fact be obtained. These first-generation probe molecules consist of a m-nitrophenyl ether chromophore coupled to a hydrophobic anchor (n-dodecyl chain) via hydrophilic spacer segments of varying length (0-4 ethylene oxide subunits):



Confirmation that the probes indeed detect double layer coions was obtained by anchoring them onto anionic SDS micelles and measuring the rate constants for quenching of the m-nitrophenyl ether triplet state by added Br^- by laser flash photolysis (Figure 4). The observed dependence of the Br^- quenching efficiency on the number of ethylene oxide subunits present in the probe confirms that an increase in the spacer length allows the triplet state of the chromophore to explore farther out into the aqueous double-layer region around the micelle. Similarly, addition of salt decreases the electrostatic surface potential of the SDS micelle, increasing the local concentration of Br^- in the double layer near the micelle surface and hence increasing the rate constant for Br^- quenching of the probe triplet state. We are currently using these probes to investigate the distribution of ions in the double layer of more complex systems, including detergent-polymer complexes.

CONCLUDING REMARKS

Electronic excitation of m-nitrophenyl ethers provokes pronounced changes in the reactivity of the molecule. Studies of this reactivity in aqueous micellar solution have also revealed the existence of pronounced differences in the physical properties of the ground and excited states of the molecule. Thus,

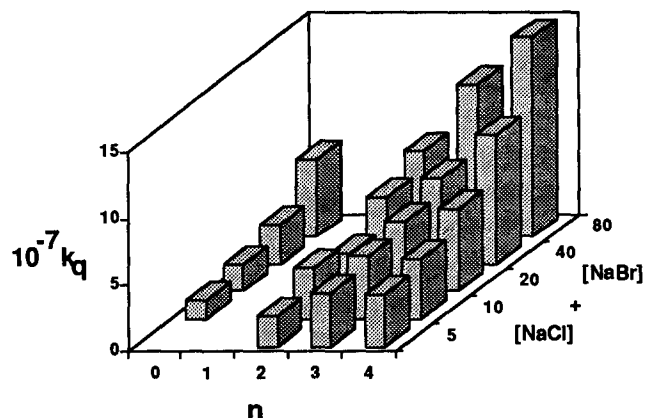


Figure 4. Apparent rate constants (k_q) for quenching of the triplet state of the m-nitrophenyl ether-derived double layer probes by Br^- in aqueous micellar solutions of SDS as a function of the number (n) of ethylene oxide subunits in the spacer segment of the probe and as a function of the total added salt concentration. The values of k_q (in $\text{M}^{-1} \text{s}^{-1}$) were determined from the slope of Stern-Volmer plots of the inverse of the triplet lifetime of the m-nitrophenyl ether chromophore of the probe as a function of total added $[\text{NaBr}]$. For comparison, a value of $k_q = 2.5 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ in the absence of SDS was determined using the 2-methoxyethyl ether of m-nitrophenol as a water-soluble analog of the double layer probes. Triplet lifetimes were measured by laser flash photolysis (355 nm excitation pulse from a Nd-YAG laser, monitoring absorption at 405 nm) at 30° C. on solutions containing $3 \times 10^{-4} \text{ M}$ probe (with $n = 0, 2, 3,$ or 4) dissolved in 0.040 M SDS. For details, see ref. 18.

measurements of the micelle-water partitioning coefficients for these two states show that the lowest excited triplet state is much more hydrophilic (less soluble in the micelle) than the ground state. All of these factors - enhanced reactivity, "meta" rather than "ortho/para" orientation of nucleophilic attack, and large differences in solubility - presumably reflect a massive reorganization of the electron density of the m-nitrophenyl ether chromophore upon electronic excitation.

ACKNOWLEDGMENTS

This work was financed by grants from FAPESP (Projeto temático), CNPq and PADCT and fellowship support from CAPES-PICD and the CNPq. Drs. Juan C. Scaiano (University of Ottawa) and Miguel Neumann (IFQSC, USP-São Carlos) generously provided access to laser flash photolysis facilities in their respective laboratories. Dr. Guiseppe Cilento, to whom this article is dedicated, is thanked for providing the laboratory facilities which have allowed one of us (FHQ) to continue doing science during the last five years.

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This special issue of Química Nova is dedicated to Prof. G. Cilento on the occasion of his 70th birthday and is financed by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).