Tuning Photosensitized Singlet Oxygen Generation Efficiency of Novel aza-BODIPY Dyes

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1. Experimental Section

1.1. General Techniques

The melting points were determined on a Mel-Temp II melting point apparatus. The IR spectra were recorded on a Perkin Elmer Model 882 infrared spectrometer. The electronic absorption spectra were recorded on a Shimadzu UV-3101 or 2401 PC UV-VIS-NIR scanning spectrophotometer. The fluorescence spectra were recorded on a SPEX-Fluorolog F112X spectrofluorimeter. ^1H and ^{13}C NMR were recorded on a 500 MHz Bruker advanced DPX spectrometer. All the solvents used were purified and distilled before use. Quantum yields of fluorescence were measured by the relative methods using optically dilute solutions. Nile blue ($\Phi_{\text{em}} = 0.52$) in methanol was used as the standard. Solvents used were distilled and purified before use.

1.2. Quantification of triplet state properties

Nanosecond laser flash photolysis experiments were carried out by employing an Applied Photophysics model LKS-20 laser kinetic spectrometer using OCR-12 Series Quanta Ray Nd:YAG laser. The analyzing and laser beams were fixed at right angles to each other. The laser energy was 64 mJ at 355 nm. The triplet yields (Φ_{T}) of the aza-BODIPY derivatives were measured employing an earlier described method of energy transfer to β -carotene using $\text{Ru}(\text{bpy})_3^{2+}$, as the reference. For these experiments, $\text{Ru}(\text{bpy})_3^{2+}$ and the aza-BODIPY derivatives, optically matched at 355 nm, were mixed with a known volume of β -carotene solution (end concentration of β -carotene was 2.0×10^{-4} M). The transient absorbance (ΔA) of the β -carotene triplet, formed by the energy transfer from $\text{Ru}(\text{bpy})_3^{2+}$ or the aza-BODIPY triplet, was monitored at 510 nm. Comparison of plateau absorbance following the completion of sensitized triplet formation, properly corrected for the decay of the donor triplets in competition with energy transfer to β -carotene, enabled us to estimate Φ_{T} of BODIPY derivatives based on eq. 1,

$$\Phi_{\text{T}}^{\text{bod}} = \Phi_{\text{T}}^{\text{ref}} \frac{\Delta A_{\text{bod}}}{\Delta A_{\text{ref}}} \frac{k_{\text{obs}}^{\text{bod}}}{k_{\text{obs}}^{\text{bod}} - k_0^{\text{bod}}} \frac{k_{\text{obs}}^{\text{ref}} - k_0^{\text{ref}}}{k_{\text{obs}}^{\text{ref}}} \quad (\text{eq. 1})$$

where superscripts ‘bod’ and ‘ref’ designate the different aza-BODIPY derivatives and $\text{Ru}(\text{bpy})_3^{2+}$, respectively, k_{obs} , is the pseudo-first-order rate constant for the growth of the β -carotene triplet and k_0 is the rate constant for the decay of the donor triplets, in the absence of β -

carotene, observed in solutions containing Ru(bpy)₃²⁺ or aza-BODIPY dye at the same optical density (OD) as those used for sensitization. The direct excitation of β-carotene did not result in any significant triplet formation under these experimental conditions, because of negligible triplet yield. The Φ_T^{ref} in methanol for Ru(bpy)₃²⁺ was taken to be unity. The Φ_T data obtained in this manner are reliable to the extent to which the assumption regarding 100% efficiency of energy transfer to β-carotene is valid.

1.3. Quantification of singlet oxygen generation

Singlet oxygen generation studies were carried out with a light source 200 W xenon lamp (model 3767) on an Oriel optical bench (model 11200) with a grating monochromator (model 77250). The intensity of light was maintained constant throughout the irradiations by measuring the output using an Oriel photodiode detection system (model 7072). Quantum yields for singlet oxygen generation in DMSO were determined by monitoring the photooxidation of DPBF sensitized by the aza-BODIPY derivatives. DPBF is a convenient acceptor because it absorbs in a region of dye transparency and rapidly scavenges singlet oxygen to give colorless products. This reaction occurs with little or no physical quenching. Singlet oxygen quantum yields were measured at low dye concentrations (optical density 0.2-0.3 at the irradiation wavelengths >630 nm) to minimize the possibility of singlet oxygen quenching by the dyes. The photooxidation of DPBF was monitored between 2 s to 2 min, depending on the efficiency of the dye sensitizer. No thermal recovery of DPBF (from a possible decomposition of endoperoxide product) was observed under the conditions of these experiments. The quantum yields of singlet oxygen generation (Φ[¹O₂]) were calculated by a relative method using optically matched solutions and comparing the quantum yield of photooxidation of DPBF sensitized by the dye of interest to the quantum yield of MB (Φ [¹O₂] = 0.52) sensitized DPBF photooxidation as the reference. The following eq. 2 was used,

$$\Phi(^1\text{O}_2)^{\text{bod}} = \Phi(^1\text{O}_2)^{\text{MB}} \frac{m^{\text{bod}} F^{\text{MB}}}{m^{\text{MB}} F^{\text{bod}}} \quad (\text{eq. 2})$$

where superscripts ‘bod’ and ‘MB’ designate aza-BODIPY derivatives and **MB**, respectively, Φ[¹O₂] is the quantum yield of singlet oxygen, m is the slope of a plot of difference in change in absorbance of DPBF (at 418 nm) with the irradiation time and F is the absorption correction factor, which is given by F = 1 – 10^{-OD} (OD at the irradiation wavelength).

2. Materials and Methods

Starting materials. 3,5-dimethoxy benzaldehyde, 4-bromo acetophenone, 4-iodo acetophenone, nitromethane, diethylamine, ammonium acetate, borontrifluoride diethyletherate, triethylamine, N-iodosuccinimide, methylene blue, β -carotene were purchased from Aldrich and S. D. Fine Chemicals, India. 1,3-diphenylisobenzofuran (DPBF) was recrystallized from a mixture (1: 1) of ethanol and chloroform. 4-bromophenyl-3-(3,5-dimethoxyphenyl)prop-2-en-1-one (**1a**), mp 86-88°C, 3-(3,5-dimethoxyphenyl)-1-phenylprop-2-en-1-one (**1b**), mp 80-82°C were synthesized by modifying the reported procedures.¹

2.1. General procedure for the synthesis of 2a-b

To a solution of **1a-b** (2 g, 5.76 mmol) dissolved in 80 mL of methanol was added diethyl amine (4 mL) and nitromethane (2 mL) and refluxed for 24 h. The mixture was neutralized using 1N HCl and extracted with chloroform. The removal of the solvent gave a residue which was separated by column chromatography over silica gel. Elution of the column with a mixture (1:9) of ethyl acetate and hexane gave **2a-b** in good yields.

2a: 75%, IR (KBr) $\nu_{\max}$ 1680, 1562, 1280 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 500 MHz) δ 7.88 (2H, d, $J = 8.5$ Hz), 7.73 (2H, d, $J = 8.5$ Hz), 7.70 (1H, s), 7.41 (1H, s), 6.77 (2H, s), 4.20 (1H, s), 4.11 (1H, s), 4.05 (1H, t), 3.84 (6H, s), 3.05 (2H, s); $^{13}\text{C NMR}$ (CDCl_3 , 125 MHz) δ 161.1, 145.4, 137.9, 137.4, 136.5, 129.9, 122.0, 106.4, 102.9, 100.6, 55.5; FAB-MS m/z Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_5$ 329.352, Found 329.357.

2b: 78%, IR (KBr) $\nu_{\max}$ 1683, 1595, 1298, 1205 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 500 MHz) δ 7.67 (2H, d, $J = 8.5$ Hz), 7.49 (2H, d, $J = 8.5$ Hz), 6.31 (2H, s), 6.25 (1H, s), 4.70 (1H, t), 4.58 (1H, s), 4.05 (1H, t), 3.66 (6H, s), 3.35 (2H, q); $^{13}\text{C NMR}$ (CDCl_3 , 125 MHz) δ 194.8, 160.1, 140.3, 134.0, 130.9, 128.4, 127.7, 104.6, 98.1, 78.3, 54.2, 40.3, 38.3; FAB-MS m/z Calcd for $\text{C}_{18}\text{H}_{18}\text{BrNO}_5$ 408.241, Found 408.239.

2.2. General procedure for the synthesis of 3a-b

The nitromethene derivatives **2a-b** (1g, 2.45 mmol) and ammonium acetate (7.6 g, 95 mmol) were dissolved in ethanol (20 mL) and heated under reflux for 48 h. The precipitated product was filtered, washed with cold ethanol, dried and recrystallized from chloroform to give **3a-b** as a violet compounds.

3a: 40%, mp 220-221 °C; IR (KBr) $\nu_{\max}$ 3062, 1597, 1537, 1348 cm^{-1} ; ^1H -NMR (CDCl_3 , 500 MHz) δ 7.97 (4H, d, J = 8 Hz), 7.62 (2H, d, J = 8 Hz), 7.56 (6H, d, J = 7 Hz), 7.49 (2H, d, J = 7 Hz), 7.11 (2H, s), 6.94 (2H, d, J = 8.5 Hz), 3.95 (6H, s), 3.76 (6H, s); ^{13}C NMR (CDCl_3 , 125 MHz) δ 154.8, 149.5, 149.3, 148.8, 142.7, 132.2, 129.9, 129.1, 127.0, 126.5, 121.9, 114.0, 112.3, 111.0, 56.0, 55.8; FAB-MS m/z Cald for $\text{C}_{36}\text{H}_{31}\text{N}_3\text{O}_4$ 570.231, Found 570.232.

3b: 50%, mp 245-246 °C; IR (KBr) $\nu_{\max}$ 2999, 1589, 1456, 1338, 1278 cm^{-1} ; ^1H -NMR (CDCl_3 , 500 MHz) δ 7.77 (4H, d, J = 8.5 Hz), 7.67 (4H, d, J = 8.5 Hz), 7.10 (2H, s), 7.08 (4H, m), 6.48 (2H, t), 3.69 (12H, s); ^{13}C NMR (CDCl_3 , 125 MHz) δ 161.4, 160.6, 156.4, 154.0, 149.7, 143.3, 140.8, 138.1, 135.2, 132.4, 131.8, 130.9, 128.6, 127.8, 124.5, 123.6, 117.22, 115.5, 106.9, 105.5, 100.9, 100.6, 55.5; FAB-MS m/z Cald for $\text{C}_{36}\text{H}_{29}\text{Br}_2\text{N}_3\text{O}_4$ 727.442, Found 727.453 ($M+1$) $^+$.

2.3. General procedure for the synthesis of 4a-b

Compounds **3a-b** (0.45 mmol) dissolved in dry toluene (80 mL) was treated with triethylamine (0.8 mL, 4.6 mmol) and stirred for 10 min at 30 °C. To this reaction mixture, boron trifluoride diethyl etherate (1 mL, 8.13 mmol) was added and heated at 80 °C for 4 h. The solvent was evaporated, washed with water (2 $\times$ 50 mL) and extracted with chloroform. Removal of the solvent gave a residue, which was separated by column chromatography over silica gel. Elution of the column with a mixture (1:1) dichloromethane and hexane gave the products **4a-b** as a metallic brown solids.

4a: 75%, mp 239-240 °C; IR (KBr) $\nu_{\max}$ 1595, 1500, 1452, 1267, 1122 cm^{-1} ; ^1H -NMR (CDCl_3 , 500 MHz) δ 8.09 (4H, s), 7.85 (2H, q, J = 8.5 Hz), 7.67 (2H, s), 7.57 (6H, s), 7.50 (2H, s), 7.14 (2H, d, J = 8.5 Hz), 3.87 (6H, s), 3.78 (6H, s); ^{13}C NMR (CDCl_3 , 125 MHz) δ 158.1, 150.8, 148.9, 144.7, 143.5, 131.1, 130.9, 129.3, 128.5, 124.7, 122.9, 118.9, 112.5, 55.7, 55.6; FAB-MS m/z Cald for $\text{C}_{36}\text{H}_{30}\text{BF}_2\text{N}_3\text{O}_4$ 617.458, Found 617.456.

4b: 80%, mp 284-285 °C; IR (KBr) $\nu_{\max}$ 1587, 1473, 1398, 1261 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 7.90 (4H, d, J = 8.5 Hz), 7.63 (4H, d, J = 8.5 Hz), 7.12 (4H, s), 6.96 (2H, s), 6.54 (2H, s), 3.76 (12H, s); ^{13}C NMR (CDCl_3 , 125 MHz) δ 160.8, 158.2, 145.7, 144.9, 133.8, 132.0, 131.0, 130.2, 126.0, 119.6, 107.3, 102.3, 99.9, 55.5; FAB-MS m/z Cald for $\text{C}_{36}\text{H}_{28}\text{BBr}_2\text{F}_2\text{N}_3\text{O}_4$ 775.243, Found 775.244.

2.4. Procedure for the synthesis of **5b**

To a solution of **4b** (0.2g, 0.26 mmol) in 40 mL mixture (3:1) of chloroform and acetic acid, *N*-iodo succinimide (260 mg, 1.16 mmol) was added and stirred at 30 °C for 10 h . The reaction mixture was washed with sodium thiosulphate followed by sodium bicarbonate solution and extracted with chloroform. Removal of the solvent gave a residue which was separated by column chromatography over silica gel. Elution of the column with a mixture (1:9) of methanol and chloroform gave 65% of **5b**, mp 308-310 °C; IR (KBr) $\nu_{\max}$ 1587,1506,1477,1336,1278 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 7.93 (3H, d, J = 8.5 Hz), 7.63 (5H, d, J = 11.5 Hz), 6.64 (1H, s), 6.37 (2H, s), 5.30 (1H, s), 3.89 (12H, s); ^{13}C NMR (CDCl_3 , 125MHz) δ 159.0, 157.9, 153.0, 144.3, 142.7, 132.0, 129.5, 125.6, 80.2, 56.9; HRMS (EI^+) m/z Cald for $\text{C}_{36}\text{H}_{24}\text{BBr}_2\text{F}_2\text{I}_4\text{N}_3\text{O}_4$ 1279.642, Found 1279.628 $[\text{M}+1]^+$.

Reference

1. Kumar, C. V.; Ramaiah, D.; Das, P. K.; George, M. V. *J. Org. Chem.* **1985**, *50*, 2818-2825.

Figure S1. ^1H NMR spectrum of the azadipyrromethene derivative **3a** in CDCl_3 .

Figure S2. ^1H NMR spectrum of the azadipyrromethene derivative **3b** in CDCl_3 .

Figure S3. ^1H NMR spectrum of the BODIPY derivative **4a** in $\text{DMSO}-d_6$.

Figure S4. ¹H NMR spectrum of the BODIPY derivative **4b** in CDCl₃.

Figure S5. ¹H NMR spectrum of the BODIPY derivative **5b** in CDCl₃.

Figure S6. Absorption spectra of **3a-b**.

Figure S7. Emission spectrum of **3b**. Excitation wavelength, 630 nm.

Figure S8. (A) Changes in the absorption spectrum of DPBF upon irradiation in the presence of **4a**. a) 0 and f) 600 s (recorded at 120 s interval). (B) Plot of change in absorbance of DPBF at 418 nm vs irradiation time ($\lambda_{\text{irr}} = 630$ nm) in the presence of **4a** against methylene blue (**MB**) as the standard.

Figure S9. (A) Changes in the absorption spectrum of DPBF upon irradiation in the presence of **4b**. a) 0 and f) 360 s (recorded at 60 s interval). (B) Plot of change in absorbance of DPBF at 418 nm vs irradiation time ($\lambda_{\text{irr}} = 630$ nm) in the presence of **4b** against methylene blue (**MB**) as the standard.

Figure S10. Changes in the absorption spectrum of DPBF upon irradiation in the presence of methylene blue (**MB**). a) 0 and e) 10 s (recorded at every 2 s intervals).

Figure S11. Changes in the absorption spectrum of **5b** on continuous irradiation for 2 h.

Figure S12. Changes in the absorption spectrum of DPBF upon irradiation in the presence of compound **5b** in DMSO. a) 0 and g) 60 s (recorded at every 10 s intervals).