Aza-BODIPY Derivatives: Enhanced Quantum Yields of Triplet Excited States and the Generation of Singlet Oxygen and their Role as Facile **Sustainable Photooxygenation Catalysts**

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Abstract: A new series of aza-BODIPY derivatives (4a-4c, 5a,c, and 6b,c) were synthesized and their excited-state properties, such as their triplet excited state and the yield of singletoxygen generation, were tuned by substituting with heavy atoms, such as bromine and iodine. The effect of substitution has been studied in detail by varying the position of halogenation. The core-substituted dyes showed high yields of the triplet excited state and high efficiencies of singlet-oxygen generation when compared to the peripheral-substituted systems. The dye 6c, which was substituted with six iodine atoms on the core and peripheral phenyl ring, showed the highest quantum yields of the triplet excited state $(\Phi_{\rm T}=0.86)$ and of the efficiency of singlet-oxygen generation (Φ_{Λ} =0.80). In-

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terestingly, these dyes were highly efficient as photooxygenation catalysts under artificial light, as well as under normal sunlight conditions. The uniqueness of these aza-BODIPY systems is that they are stable under irradiation conditions, possess strong redlight absorption (620-680 nm), exhibit high yields of singlet-oxygen generation, and act as efficient and sustainable catalysts for photooxygenation reactions.

Introduction

Singlet oxygen, $O_2(^{1}\Delta_g)$, which is the lowest excited electronic state of molecular oxygen, is a reactive species in a wide range of chemical- and biological processes.^[1] It has the ability to interrupt cellular functions in living organisms and exhibits high chemical reactivity toward most organic molecules owing to the spin-allowed nature of its reactions. The quantitative generation of singlet oxygen (Φ_{Δ}) is one of the most-important requirements for an efficient photosensitizer,^[2] because it is thought that biological damage by singlet oxygen and the subsequent oxidation of tissue through direct attack on biological substrates is responsible for the success of photodynamic therapy (PDT).^[3] Most of the photosensitizers that have either been approved for clinical use or are in various phases of clinical trials have a common cyclic tetrapyrrolic structure that is derived from porphyrins.

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Various non-porphyrinic systems have also been investigated, including rose bengal, methylene blue, Nile blue, Nile red, chalcogenopyrylium salts,^[4] squaraine dyes,^[5] etc. However, these classes of photosensitizers possess major drawbacks, such as inherent dark toxicity and low absorption in the NIR region. In addition to applications in PDT, singlet oxygen can mediate a wide range of reactions, such as the photooxygenation of organic substrates.^[6] However, the high energy demand of most common artificial light-sources has limited the use of photochemical methods in industrial applications.^[7] To overcome this disadvantage, sunlight (either direct or focused) has received recent attention as a sustainable light source for such applications.^[7]

Recently, the chemistry of dipyrromethene ligands has attracted much attention owing to their inherent ability to form stable coordination complexes.^[8] The conjugated π system in these ligands endows the complexes with favorable optical properties, such as intense absorption with high molar absorption coefficients ($\epsilon > 10^4 \, \text{m}^{-1} \, \text{cm}^{-1}$) and moderate-to-quantitative fluorescence quantum yields.[9-10] Among these compounds, boron complexes, such as 4,4-difluoro-4bora-3a,4a-diaza-s-indacenes (abbreviated as BODIPYs), hold great promise as ideal sensitizers owing to their favorable properties.^[11] These systems exhibit strong absorption in the range 500-600 nm, as well as significant fluorescence quantum yields and high photostability.^[12] In contrast, azadipyrromethenes and their boron complexes (aza-BODI-PYs) show around 100 nm bathochromically shifted absorption when compared to BODIPYs; these systems have at-

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tracted less attention and have only been studied in the last decade. $^{\left[10,13-16\right] }$

With the objective of developing new and efficient photosensitizers that exhibit near-infrared absorption, we designed a new series of aza-BODIPY derivatives and investigated their photophysical properties under different conditions. Interestingly, the triplet excited state, as well as the efficiencies of singlet-oxygen generation, of these aza-BODIPY derivatives could be successfully tuned from about 1% to 86% through judicial heavy-atom substitution. Moreover, for the first time, we explored the potential use of these aza-BODIPY derivatives as catalysts for photooxygenation reactions. When compared to other commonly used sensitizers, like tetraphenylporphyrin (TPP), rose bengal (RB), and methylene blue (MB),^[18] derivative 6b, which contained four iodine atoms and two bromine atoms, was quite efficient in photooxygenation reactions, thus making it attractive as a catalyst for "sustainable photooxidation".

Results and Discussion

Synthesis and characterization: The strategy that was adopted for the synthesis of various aza-BODIPY derivatives (4a–4c, 5a,c, and 6b,c) is shown in Scheme 1. Compounds 4a–4c were synthesized in a facile three-step route starting



Scheme 1. Synthesis of aza-BODIPY derivatives 4a-4c, 5a,c, and 6b,c.

from chalcones **1a–1c**. The addition of nitromethane to the chalcones in the presence of diethylamine gave the addition products (**2a–2c**) in 75–80% yield. Subsequently, the condensation products (**3a–3c**) were prepared by heating a mixture of compounds **2a–2c** and ammonium acetate at reflux in EtOH for 48 h. The product that precipitated during the reaction was filtered and recrystallized to yield compounds **3a–3c** (40–50%), which had a violet metallic luster. Aza-dipyrromethenes **3a–3c** were subsequently converted into the target aza-BODIPY derivatives (**4a–4c**, 65–70%) by heating compounds **3a–3c** with boron trifluoride diethyl etherate and triethylamine at reflux in toluene for 5 h.

The iodination of aza-BODIPY derivatives 4a-4c was achieved by using *N*-iodosuccinimide (NIS) in a mixture of CHCl₃ and acetic acid (3:1). When 2.5 equivalents of NIS was used, we isolated compounds 5a,c (60–65% yield), which were only iodinated at the core of the pyrrole ring. On the other hand, when the iodination was carried out with 4.5 equivalents of NIS under similar conditions, tetraiodo aza-BODIPY derivatives **6b**,c were obtained in 65–68% yield (after column chromatography on silica gel). All of these products were recrystallized from toluene and characterized by using analytical- and spectroscopic data (see the Supporting Information, Figures S1–S4).

Absorption and fluorescence properties: The starting aza-dipyrromethenes (**3a-3c**) showed absorption in the red region (610-625 nm) with molar extinction coefficients in the range $3-7 \times 10^4 \text{ m}^{-1} \text{ cm}^{-1}$ (see the Supporting Information, Figure S5). Interestingly, in the case of aza-BODIPY derivatives **4a-4c**, we observed a bathochromic shift of about 50– 60 nm in their absorption spectra (Figure 1 A). When com-



Figure 1. A) Absorption and B) fluorescence spectra of representative aza-BODIPY derivatives **4b**, **5c**, and **6c** in DMSO; excitation wavelength: 650 nm.

paring the iodinated systems, core-substituted derivatives **5a** and **5c** showed blue-shifted absorption maximum at 660 and 670 nm, respectively, whilst derivatives **6b,c**, which had substitution both at their periphery and in core, exhibited an absorption maximum at 666 and 676 nm, respectively. All of these derivatives exhibited good solubility in common organic solvents, such as CHCl₃, CH₃CN, THF, DMSO, and DMF.

Figure 1B shows the fluorescence spectra of the corresponding aza-BODIPY derivatives in DMSO. The aza-dipyrromethene derivatives (3b,c) showed an emission maximum between 650 and 665 nm (see the Supporting Information, Figure S5B). In contrast, aza-BODIPYs **4–6** exhibited emission in the range 690–770 nm with a large Stokes shift of about 530–1730 cm⁻¹. These derivatives showed quenched fluorescence because of the presence of heavy atoms, such as bromine and iodine. The absorption- and fluorescence emission properties of these derivatives are summarized in Table 1.

Table 1. Photophysical properties of aza-BODIPY derivatives 4-6.^[a,b]

Compound	λ_{\max} [nm]	λ_{em}	$ au_{\mathrm{T}}$	${oldsymbol{\varPhi}}_{\mathrm{T}}^{\mathrm{[d]}}$	$arPsi_^{[e]}$
	$(\varepsilon \times 10^4)^{[c]}$	[nm]	[µs]		
4a	$680(5.9\pm0.06)$	772	28	$0.01(\pm 0.002)$	0.009(±0.001)
4b	664 (3.8 ± 0.15)	701	44	$0.07(\pm 0.002)$	$0.012(\pm 0.003)$
4c	$675(5.2\pm0.04)$	710	7.8	$0.08(\pm 0.001)$	$0.02(\pm 0.003)$
5a	660 (8.3 ± 0.02)	706	1.9	$0.68(\pm 0.02)$	$0.65(\pm 0.02)$
5c	670 (7.1 ± 0.11)	695	1.8	$0.70(\pm 0.03)$	$0.68(\pm 0.03)$
6b	666 (6.9 ± 0.05)	694	1.5	$0.78(\pm 0.02)$	$0.70(\pm 0.03)$
6c	676 (4.9 $\pm 0.07)$	712	1.6	$0.86(\pm 0.03)$	$0.80(\pm 0.02)$

[a] Average of more than three experiments; [b] in DMSO; [c] in M^{-1} cm⁻¹; [d] yields were calculated by using the triplet–triplet energy-transfer method; [e] quantified through scavenging of ¹O₂ by DPBF.

Characterization and quantification of the triplet excited states: To characterize the transient intermediates, such as triplet excited states, that were involved in these systems, we performed nanosecond-laser flash photolysis studies. Figure 2 shows the transient absorption spectra of compounds 6b and 6c in DMSO after laser excitation (355 nm, 10 ns, 50 mJ per pulse). Excitation of compound 6b afforded transient absorption peaks at 320 and 510 nm with bleach in the region that corresponded to its ground-state absorption. The transient intermediate formed from compound 6b within the laser pulse decayed by a first-order process and led to recovery of the ground-state absorption (Figure 2A, inset), thereby ruling out the formation of any permanent products and/or degradation of the dye under these conditions. This transient absorption was readily quenched by the dissolved oxygen, thus suggesting that the transient species may be due to the triplet excited state.^[5a, 16c] A similar transient absorption spectrum, with bands at 330 and 520 nm, was obtained in the case of compound 6c upon laser excitation at 355 nm (Figure 2B). On the other hand, core-substituted derivatives 5a and 5c showed a transient absorption maximum at 460 nm (see the Supporting Information, Figures S6 and S7), whilst non-iodinated dyes 4a, 4b, and 4c showed transient absorption maxima at 450, 430, and 460 nm, respectively. The triplet quantum yields of these derivatives were determined (Table 1) by using triplet-triplet energytransfer to β -carotene with a tris(bipyridyl)ruthenium(II) complex as a reference.^[19]

Non-halogenated dye **4a** exhibited a low quantum yield of the triplet excited state ($\Phi_T = 0.01$), with a lifetime of 28 µs, whilst bromo- and iodo derivatives **4b** and **4c** showed relatively higher yields of the triplet excited states (about 0.07 and 0.08, respectively). Notably, when the pyrrole ring



Figure 2. A) Transient absorption spectra of compound **6b**, following laser-pulse excitation at 355 nm; time-resolved absorption spectra recorded at (a) 0.1, (b) 0.4, (c) 1, (d) 2, (e) 4, and (f) 10 μ s. Inset: decay of the transient at 510 nm. B) Transient absorption spectra of compound **6c**, following laser-pulse excitation at 355 nm; time-resolved absorption spectra recorded at (a) 0.1, (b) 0.5, (c) 1, (d) 2, (e) 5, and (f) 10 μ s. Inset: decay of the transient at 520 nm.

was iodinated (core-substitution), we observed quantitative yields of the triplet excited states. Thus, we obtained $\Phi_{\rm T}$ = 0.68 and 0.70 for compounds **5a** and **5c**, respectively. Interestingly, when the core of the pyrrole and the peripheral phenyl ring were substituted with iodine atoms, we observed a significant enhancement in the triplet quantum yields ($\Phi_{\rm T}$ =0.78 and 0.86), with lifetimes of 1.5 and 1.6 µs for compounds **6b** and **6c**, respectively. Thus, through changing the substitution pattern, we could tune the triplet excited quantum yields of the aza-BODIPY derivatives from about 1% to as high as 86% for use in potential applications.

Quantification of singlet-oxygen generation: Enhanced triplet quantum yields are favorable for the efficient generation of singlet oxygen and, hence, we examined the efficiency of photosensitized singlet-oxygen generation by these systems. The quantum yields of singlet-oxygen generation were determined by monitoring the photooxidation of 1,3-diphenylisobenzofuran (DPBF) through absorption spectroscopy.^[20] For this purpose, a solution of the aza-BODIPY derivative and DPBF was irradiated by using a 630 nm long pass over a time period of 6–600 s and a decrease in the absorption band (about 10%) of DPBF at 418 nm was observed (Fig-

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Figure 3. A) Absorption spectra of diphenylisobenzofuran (DPBF) upon irradiation in the presence of compound **6c**; (a) 0 and (b) 8 s (recorded at 2 s intervals). B) Plot of the change in absorbance of DPBF at 418 nm versus irradiation time (λ_{irr} = 630 nm) in the presence of compound **6c** and methylene blue (MB) as a standard in DMSO.

ure 3 A). The yields for the generation of singlet oxygen were calculated by using a standard, methylene blue (MB), by plotting the optical-density difference (Δ OD) value of DPBF against the irradiation time (Figure 3B). The aza-dipyrromethene compounds (**3a-3c**) showed negligible efficiency for singlet-oxygen generation; in contrast, non-negligible singlet-oxygen quantum yields of about 0.009 and 0.012 were observed for dyes **4a** and **4b**. The quantum yield for singlet-oxygen generation increased to about 0.02 by the replacement of bromine with iodine, as in the case of compound **4c**.

The aza-BODIPY derivatives **5a,c** and **6b,c**, which had core-iodo substitution, showed expectedly good-to-quantitative yields of singlet-oxygen-generation efficacy. For example, derivative **5a**, which has two iodine atoms at the core of the pyrrole, exhibited a singlet-oxygen quantum yield of about 0.65 (see the Supporting Information, Figure S8), whereas compound **5c**, with two core iodine atoms and two peripheral iodine atoms, showed a quantum yield of about 0.68. On the other hand, dye **6b**, which contained four iodine atoms and two bromine atoms, showed a quantum yield for singlet-oxygen generation of about 0.70, whereas derivative **6c**, which contained six iodine atoms, showed the highest quantum yield of about 0.80 when compared with the standard MB (Φ_{Δ} =0.52).^[21] The resistance of these dyes to photobleaching was investigated by irradiating an oxygen-saturated solution of the dyes for 2 h. We observed negligible changes in their absorption spectra, thus confirming the stability of the aza-BODIPY derivatives under these conditions.

Tuning the singlet-oxygen generation of the aza-BODIPY derivatives: The efficiency of singlet-oxygen generation of the aza-BODIPY derivatives could be tuned by suitably incorporating heavy atoms, such as bromine and iodine, at their core, as well as on the peripheral phenyl rings. We observed negligible singlet-oxygen generation for un-substituted aza-BODIPY 4a, which, upon bromination and iodination, showed improved yields of singlet-oxygen generation. The enhancement of singlet-oxygen generation depended on the halogenation of the parent dye and on the heaviness of the substituent. A comparison between the peripheral phenyl rings of bromo- and iodo-substituted dyes **4b** and **4c**, and that of unsubstituted dye 4a, showed marginal improvements of about 0.3% and 1.1% in the efficiency of singletoxygen generation, respectively (Scheme 2). In contrast, the core-substitution of the aza-BODIPY dyes had a significant influence on the efficiency of singlet-oxygen generation. For example, core-iodinated dyes 5a and 5c showed about 64% and 66% enhancement in the yields of singlet oxygen compared to parent dyes 4a and 4c, respectively.

An interesting observation is the additive effect that was observed for iodination at the core, as well as on the peripheral phenyl rings, of these compounds. For example, compound **6b**, which was substituted at its core and also on its two peripheral phenyl rings, showed about 68% enhancement in singlet-oxygen generation compared to bromo-substituted dye **4b**. Similar observations were made with compound **6c**, which contained two iodine atoms in the core and four iodine atoms on the peripheral phenyl rings. This compound showed the highest additive effect and exhibited an



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Scheme 2. Tuning the quantum yield of the triplet excited state (Φ_T) and singlet-oxygen generation (Φ_Δ) of the aza-BODIPY derivatives.

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enhancement of about 78% singlet-oxygen-generation efficiency compared to compound **4c**. When we compared compounds **6b** and **6c**, which only differed in the nature of the peripheral halogen atoms (bromine versus iodine), we observed an approximate 10% enhancement in the singlet-oxygen yield of compound **6c** compared to compound **6b**. Similarly, a difference of about 10–12% was observed between compounds **5c** and **6c** (Scheme 2). These results demonstrate that the halogenation of the peripheral phenyl rings of the aza-BODIPYs only afford a marginal improvement (about 10–15%) in the quantum yields of singlet-oxygen generation. In contrast, a significant enhancement of about 65–70% was observed in the efficiency of singlet-oxygen generation of the aza-BODIPY systems when the core pyrrole rings were substituted with halogen atoms.

Photooxygenation reactions with aza-BODIPY derivatives: Because the aza-BODIPY derivatives showed high efficiency for singlet-oxygen generation, it was of interest to explore their use as photooxygenation catalysts. Thus, as a representative example, we carried out the photooxidation of a common, well-known substrate, 1-naphthol, to afford 1,4-naphthaquinone, with aza-BODIPY **6b** (Table 2). The

Table 2. Photooxygenation of 1-naphthol into 1,4-naphthaquinone by using various sensitizers and sources of light in MeCN.

Sensitizer	$arPhi_\Delta$	Yield (%) ^[a]				
		200 W Hg lamp ^[b]	Sunlight (di- rect) ^[c]	Sunlight (focu- sed) ^[d]		
6b	0.70	100	100	100		
TPP	0.74	40	40	60		
MB	0.52	26	38	40		
RB	0.79	20	24	20		

[a] Average of more than three experiments. The yields of singlet-oxygen generation with TPP, MB, and RB are taken from reference [7]; energy of the output light was measured by an Oriel photodiode (Model 7072).
[b] 8 h, 6–8 mJ. [c] 1 h, 20-25 mJ. [d] 0.5 h, 200–220 mJ.

reason for choosing compound 6b was due to its high photostability and good solubility in common organic solvents among the aza-BODIPY derivatives, as well as owing to its comparable singlet-oxygen-generation efficiency to that of standard sensitizers, such as TPP, MB, and RB.^[7] The photooxygenation reaction was carried out with various sensitizers and aza-BODIPY 6b under identical conditions with three different irradiation light sources: 1) 200 W Hg lamp (energy of the output light: about 6-8 mJ); 2) direct sunlight (Trivandrum, India, November-December 2011, 8.5°N 76.9°E, 5 m above sea level, energy of output light: about 20-25 mJ); and 3) focused sunlight by using a convex lens (location as above and energy of output light: about 200-220 mJ). The progress of the photooxygenation reaction was analyzed by thin layer chromatography, NMR spectroscopy, and GC.

The preparative photooxygenation reaction was carried out by irradiating a solution of 1-naphthol (0.2 mM) in MeCN (3 mL) in the presence of various sensitizers (2 µM).

The solution was continuously flushed with a stream of oxygen throughout the irradiation. The progress of the reaction was monitored at 15 min intervals by TLC and quantified by NMR spectroscopy and GC by using naphthalene as an internal standard. After a fixed illumination time of 8 h under a 200 W Hg lamp, analysis of the reaction mixture by GC, TLC, and ¹H NMR spectroscopy showed approximately 100% conversion into 1,4-naphthaquinone in the presence of compound 6b as the sensitizer. In contrast, under similar conditions, common sensitizers, such as TPP, MB, and RB, showed very low conversion efficiencies of about 40%, 26%, and 20%, respectively (Table 2). When we carried out the same reaction in direct sunlight, the reaction required about 1 h for 100% conversion of 1-naphthol into 1,4-naphthoquinone to occur in the presence of compound 6b, whereas TPP, MB, and RB showed less than 50% conversion efficiency under these conditions (Scheme 3). Further-



Scheme 3. Photooxygenation of 1-naphthol by using aza-BODIPY 6b.

more, to understand the effect of the intensity of light on the efficiency of the reaction, we carried out the photooxygenation reaction under focused sunlight, as reported previously.^[22] Interestingly, aza-BODIPY derivative **6b** exhibited much-improved efficiency and only required about 30 min irradiation to achieve 100% conversion into 1,4-napthoquinone.

Known sensitizers, such as TPP, MB, and RB, showed lower conversion efficiencies than compound **6b** (Table 2), although they had comparable singlet-oxygen efficiencies. One of the reasons for this observation could be due to their poor photostability under the irradiation conditions. As reported previously, TPP, MB, and RB showed a nonnegligible decrease in absorbance with irradiation time.^[6e] On the other hand, aza-BODIPY derivative 6b showed high efficiency and exceptionally high photostability for more than 8 h (see the Supporting Information, Figure S10), thus demonstrating its superiority over the currently used sensitizers for photooxygenation reactions. Moreover, photooxidation by aza-BODIPY 6b can be carried out effectively by using direct sunlight as the light source. Hence, the energy demand of the entire reaction is extremely low compared to the standard laboratory oxidation reactions and the reactions with photochemical reactors. Therefore, this reaction exemplifies an "efficient, sustainable photochemical reaction" and aza-BODIPY derivative 6b as an attractive "sustainable catalyst" for photooxygenation reactions.

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In conclusion, we have developed a series of new aza-BODIPY dyes by using a high-yielding synthetic route and investigated their efficiencies as catalysts for photooxygenation reactions. All of these derivatives showed strong absorption in the red region with high molar-extinction coefficients. The substitution of these derivatives with heavy atoms at their core, as well as at their periphery, resulted in a significant enhancement in their intersystem-crossing efficiency. The triplet excited state and the efficiency of singletoxygen generation of these systems could be tuned from about 1% to as high as 86%. For the first time, we investigated the potential use of these aza-BODIPY derivatives as catalysts in photooxygenation reactions, in particular, in the conversion of 1-naphthol into 1,4-naphthaquinone by using artificial light, as well as natural sunlight. Our results demonstrate that these new aza-BODIPY derivatives exhibit favorable photophysical properties, including strong NIR absorption and high singlet-oxygen-generation efficiency; thus, these compounds have potential applications as sensitizers in photodynamic therapy and as sustainable photooxygenation catalysts.

Experimental Section

General techniques: Melting points were determined on a Mel-Temp II melting point apparatus.^[23] IR spectra were recorded on a Perkin–Elmer Model 882 IR spectrometer. The electronic absorption spectra were recorded on Shimadzu UV-3101 or -2401 PC UV/Vis/NIR scanning spectro-photometer. The fluorescence spectra were recorded on a SPEX-Fluorolog F112X spectrofluorimeter. ¹H NMR and ¹³C NMR spectroscopy were performed on a 500 MHz Bruker advanced DPX spectrometer. All solvents were measured according to relative methods by using optically dilute solutions.

Quantification of the triplet-state properties: Nanosecond-laser flash photolysis experiments were performed on an Applied Photophysics model LKS-20 laser kinetic spectrometer by using an OCR-12 Series Quanta Ray Nd:YAG laser. The analyzing- and laser beams were fixed at right angles to one another. The laser energy was 64 mJ at 355 nm. The triplet yields $(\Phi_{\rm T})$ of the aza-BODIPY derivatives were measured according to a literature procedure of energy-transfer to β -carotene by using [Ru(bpy)₃]²⁺ as a reference compound.^[19] For these experiments, optically matched (355 nm) solutions of $[Ru(bpy)_3]^{2+}$ or the aza-BODIPY derivatives were mixed with a known volume of β -carotene solution (end concentration of β -carotene: 2.0×10^{-4} M). The transient absorbance (ΔA) of the β -carotene triplet, which was formed by energytransfer from [Ru(bpy)₃]²⁺ or the aza-BODIPY triplet, was monitored at 510 nm. Comparison of the 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 the $\Phi_{\rm T}$ values of the BODIPY derivatives, according to Equation (1), where superscripts "bod" and "ref" designate the different aza-BODIPY derivatives and $[Ru(bpy)_3]^{2+}$, 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) in solutions that contained $[Ru(bpy)_3]^{2+}$ or the aza-BODIPY dye at the same optical density (OD) as those used for sensitization.

$$\phi_{\rm T}^{\rm bod} = \phi_{\rm T}^{\rm ref} \frac{\Delta A^{\rm bod}}{\Delta A^{\rm ref}} \frac{k_{\rm obs}^{\rm bod}}{k_{\rm obs}^{\rm obc} - k_0^{\rm bod}} \frac{k_{\rm obs}^{\rm ref} - k_0^{\rm ref}}{k_{\rm obs}^{\rm bod} - k_{\rm obs}^{\rm ref}} \cdot \cdots$$
(1)

The direct excitation of β -carotene did not result in any significant triplet-formation under these experimental conditions, because of negligible yield of the triplet state. The Φ_T^{ref} value in MeOH for $[\text{Ru}(\text{bpy})_3]^{2+}$ was taken to be unity. The Φ_T data that were obtained in this manner are reliable to the extent to which the assumption regarding 100% efficiency of energy-transfer to β -carotene is valid.

Quantification of singlet-oxygen generation: Singlet-oxygen-generation studies were performed with a 200 W mercury lamp (model 3767) light source on an Oriel optical bench (model 11200) with a grating monochromator (model 77250). The intensity of the light was kept constant throughout the irradiations by measuring the output with an Oriel photodiode detection system (model 7072). Quantum yields for singlet-oxygen generation (in DMSO) were determined by monitoring the photooxidation of DPBF that was 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. The quantum yields of singlet-oxygen generation were measured at low dye concentrations (optical density: 0.2-0.3 at irradiation wavelengths > 630 nm) to minimize the possibility of singlet-oxygen quenching by the dyes. The photooxidation of DPBF was monitored between 2 s and 2 min, depending on the efficiency of the dye sensitizer. No thermal recovery of DPBF (from a possible decomposition of the endoperoxide product) was observed under these experimental conditions. The quantum yields of singletoxygen generation (Φ [¹O₂]) were calculated by a using relative method with optically matched solutions and by comparing the quantum yield of the photooxidation of DPBF that was sensitized by the dye of interest to the quantum yield of MB (Φ [¹O₂]=0.52) as a reference compound^[21] according to Equation (2), where superscripts "bod" and "MB" denote aza-BODIPY derivatives and MB, respectively, Φ_{Λ} is the quantum yield of singlet oxygen, "m" is the slope of a plot with a difference in the change in the 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).

$$\phi \Delta^{\text{bod}} = \phi \Delta^{\text{MB}} \frac{m^{\text{bod}} \mathbf{F}^{\text{MB}}}{m^{\text{MB}} \mathbf{F}^{\text{bod}}} \cdots$$
⁽²⁾

Photooxygenation reactions: Photolysis was performed with a 200 W Mercury lamp (model 3767) light source. The intensity of the output light was kept constant (5–6 mJ) throughout the irradiations by measuring the output with an Oriel photodiode detection system (model 7072). Appropriate filters were used to avoid the photobleaching of the dyes owing to direct exposure to UV light. All of the experiments gave satisfactory results within reasonable periods of time without the formation of any noticeable side-products. The Oriel photodiode detection system (model 7072) was also used to measure the output intensity of the sunlight. All the sensitizers were kept in round-bottomed flasks made of glass, which can absorb UV light and could therefore prevent the photobleaching of the dyes.

Materials and methods: Starting materials 3,5-dimethoxybenzaldehyde, 4-bromoacetophenone, 4-iodoacetophenone, nitromethane, diethylamine, ammonium acetate, boron trifluoride diethyl etherate, triethylamine, *N*-iodosuccinimide (NIS), methylene blue (MB), rose bengal (RB), 1-naphthol, and β-carotene were purchased from Aldrich and S.D. Fine Chemicals, India. 1,3-Diphenylisobenzofuran (DPBF) was recrystallized from a mixture of EtOH/CHCl₃ (1:1). 3-(3,5-Dimehoxyphenyl)-1-phenylprop-2-en-1-one (**1a**; m.p. 81–82 °C, mixture m.p. 80–82 °C),^[24] 4-bromophenyl-3-(3,5-dimethoxyphenyl)prop-2-n-1-one (**1b**; m.p. 86–87 °C, mixture m.p. 86–88 °C),^[24] and 4-iodophenyl-3-(3,5-dimethoxyphenyl)prop-2-n-1-one (**1c**; m.p. 86–87 °C, mixture m.p. 86–88 °C),^[24] and 1-(4-bromophenyl)-4-nitro-1-phenylbutan-1-one (**2a**, viscous liquid),^[16c] and 1-(4-bromophenyl)-3-(3,5-dimethoxyphenyl)-4-nitrobutan-1-one (**2b**, viscous liquid)^[16c] were synthesized according to modified literature procedures.



Synthesis of compound 2c: To a solution of compound 1c (5.76 mmol) in MeOH (80 mL) was added diethyl amine (4 mL) and nitromethane (2 mL) and the mixture was heated at reflux for 24 h. The mixture was neutralized with 1 \bowtie HCl and extracted with CHCl₃. Removal of the solvent gave a residue that was purified by column chromatography on silica gel (EtOH/*n*-hexane, 1:9) to afford compound **2**c.

2c: 75 % yield; ¹H NMR (CDCl₃, 500 MHz): δ = 7.83 (2H, d, *J* = 8.5 Hz), 7.62 (2H, d, *J* = 8.5 Hz), 6.40 (2H, d, *J* = 2 Hz), 6.39 (1H, t, *J* = 2.5 Hz), 4.79 (1H, q), 4.67 (1H, q), 4.15 (1H, m), 3.76 (6H, s), 3.43 ppm (2H, m); ¹³C NMR (CDCl₃, 125 MHz): δ = 196.2, 161.2, 141.3, 138.1, 135.6, 129.4, 101.7, 99.3, 79.3, 53.4, 41.4, 39.3 ppm; IR (KBr): $\bar{\nu}$ = 1685, 1586, 1208 cm⁻¹; MS (FAB): *m*/*z* calcd for C₁₈H₁₈INO₅: 456.032; found: 456.513.

General procedure for the synthesis of compounds 3a-3c: Nitromethane derivatives 2a-2c (2.45 mmol) and ammonium acetate (7.6 g, 95 mmol) were dissolved in EtOH (20 mL) and heated at reflux for 48 h. The precipitated product was filtered, washed with cold EtOH, dried, and recrystallized from CHCl₃ to give compounds 3a-3c as violet crystals with a metallic luster.

3a: 40% yield; m.p. 220–221°C; ¹H NMR (CDCl₃, 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 ppm (6H, s); ¹³C NMR (CDCl₃, 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 ppm; IR (KBr): $\tilde{\nu}$ =3062, 1597, 1537, 1348 cm⁻¹; MS (FAB): *m/z* calcd for C₃₆H₃₁N₃O₄ 570.231; found: 570.232.

3b: 50 % yield; m.p. 245–246 °C; ¹H NMR (CDCl₃, 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 ppm (12 H, s); ¹³C NMR (CDCl₃, 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 ppm; IR (KBr): $\tilde{\nu}$ =2999, 1589, 1456, 1338, 1278 cm⁻¹; MS (FAB): *m*/*z* calcd for C₃₆H₂₉Br₂N₃O₄: 727.442; found: 727.453.

3c: 40% yield; m.p. 236–237°C; ¹H NMR (CDCl₃, 500 MHz): δ =7.87 (4H, d, *J*=8.5 Hz), 7.63 (4H, d, *J*=8.5 Hz), 7.10 (2H, s), 7.08 (4H, d, *J*=2.5), 6.48 (2H, s), 3.69 ppm (12H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =161.4, 156.6, 137.9, 128.8, 117.2, 105.5, 95.6, 55.6, 55.3 ppm; IR (KBr): $\tilde{\nu}$ =2997, 1681, 1591, 1454 cm⁻¹; MS (FAB): *m*/*z* calcd for C₃₆H₂₉I₂N₃O₄: 823.035; found: 823.141.

General procedure for the synthesis of compounds 4a-4c: A solution of compounds 3a-3c (0.45 mmol) in dry toluene (80 mL) was treated with triethylamine (0.8 mL, 4.6 mmol) and the mixture was stirred for 10 min at 30 °C. Next, boron trifluoride diethyl etherate (1 mL, 8.13 mmol) was added and the reaction mixture was heated at 80 °C for 4 h. The solvent was evaporated, washed with water (2×50 mL), and extracted with CHCl₃. Removal of the solvent gave a residue, which was purified by column chromatography on silica gel (CH₂Cl₂/*n*-hexane, 1:1) to afford the products (**4a**-**4c**) as metallic brown solids.

4a: 75 % yield; m.p. 239–240 °C; ¹H NMR (CDCl₃, 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 ppm (6H, s); ¹³C NMR (CDCl₃, 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 ppm; IR (KBr): $\tilde{\nu}$ =1595, 1500, 1452, 1267, 1122 cm⁻¹; MS (FAB): *m*/*z* calcd for C₃₆H₃₀BF₂N₃O₄: 617.458; found: 617.456.

4b: 80 % yield; m.p. 284–285 °C; ¹H NMR (CDCl₃, 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 ppm (12H, s); ¹³C NMR (CDCl₃, 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 ppm; IR (KBr): $\tilde{\nu}$ =1587, 1473, 1398, 1261 cm⁻¹; MS (FAB): *m*/*z* calcd for C₃₆H₂₈BBr₂F₂N₃O₄: 775.243; found: 775.244.

4c: 82% yield; m.p. 259–261 °C; ¹H NMR (CDCl₃, 300 MHz): δ =7.85 (4H, d, *J* = 8.7 Hz), 7.76 (4H, d, *J* = 8.7 Hz), 7.12 (4H, d, *J* = 2.1 Hz), 6.96 (2H, s), 6.54 (2H, s), 3.75 ppm (12H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =160.9, 158.4, 145.8, 144.9, 137.9, 133.9, 131.0, 130.9, 130.8, 119.6, 107.3, 102.3, 98.5, 55.3 ppm; IR (KBr): $\tilde{\nu}$ =1585, 1512, 1489, 1284 cm⁻¹; MS (FAB): *m/z* calcd for C₃₆H₂₈BF₂I₂N₃O₄: 869.024; found: 869.364.

General procedure for the synthesis of compounds 5a,c: *N*-Iodosuccinimide (146 mg, 0.65 mmol) was added to a solution of compounds 4a,c (0.26 mmol) in a mixture of CHCl₃ and acetic acid (40 mL, 3:1) and the mixture was stirred at 30 °C for 4–5 h. The reaction mixture was washed with sodium thiosulfate and sodium bicarbonate solution and extracted with CHCl₃. Removal of the solvent gave a residue that was purified by column chromatography on silica gel (MeOH/CHCl₃, 1:9) to give compounds 5a,c.

5a: 60% yield; m.p. 236–237°C; ¹H NMR (CDCl₃, 500 MHz): δ =7.55 (4H, m), 7.44 (2H, dd, *J*=2 Hz), 7.40 (6H, m), 7.29 (2H, d, *J*=2 Hz), 6.89 (2H, d, *J*=8.5 Hz), 3.89 (6H, s), 3.64 ppm (6H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =160.05, 149.6, 147.4, 146.5, 143.9, 130.2, 129.5, 129.2, 126.9, 123.8, 123.2, 113.1, 109.5, 55.0, 54.7 ppm; IR (KBr): $\tilde{\nu}$ =1598, 1485, 1379, 1263 cm⁻¹; MS (FAB): *m/z* calcd for C₃₆H₂₈BF₂I₂N₃O₄: 870.03 [*M*+H]⁺; found: 871.20.

5c: 65% yield; m.p. 263–264°C; ¹H NMR (CDCl₃, 500 MHz): δ =7.86 (4H, d, *J*=8.5 Hz), 7.79 (4H, d, *J*=9 Hz), 7.13 (2H, s), 6.68 (2H, d, *J*=2.5 Hz), 6.44 (2H, d, *J*=2.5 Hz), 3.88 (6H, s), 3.67 ppm (6H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =159.5, 158.1, 156.7, 146.3, 145.3, 137.4, 137.0, 137.1, 129.7, 123.1, 108.3, 98.9, 98.6, 97.7, 79.3, 55.6, 54.7 ppm; IR (KBr): $\tilde{\nu}$ =1579, 1508, 1423, 1321 cm⁻¹; MS (FAB): *m/z* calcd for C₃₆H₂₆BF₂I₄N₃O₄: 1121.04; found: 1121.38.

General procedure for the synthesis of compounds 6b,c: *N*-iodosuccinimide (260 mg, 1.16 mmol) was added to a solution of compounds 4b,c (0.26 mmol) in a mixture of CHCl₃ and acetic acid (40 mL, 3:1) and the mixture was stirred at 30 °C for 10 h. The reaction mixture was washed with sodium thiosulfate and sodium bicarbonate solution and extracted with CHCl₃. Removal of the solvent gave a residue that was purified by column chromatography on silica gel (MeOH/CHCl₃, 1:9) to give compounds 6b,c.

6b: 65 %; m.p. 308–310 °C; ¹H NMR (CDCl₃, 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 ppm (12H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =159.0, 157.9, 153.0, 144.3, 142.7, 132.0, 129.5, 125.6, 80.2, 56.9 ppm; IR (KBr): $\tilde{\nu}$ =1587, 1506, 1477, 1336, 1278 cm⁻¹; MS (FAB): m/z calcd for C₃₆H₂₄BBr₂F2I₄N₃O₄: 1279.642; found: 1279.628.

6c: 68%; m.p. 305–307°C; ¹H NMR ([D₆]DMSO, 500 MHz): δ =7.97 (4H, t), 7.79 (2H, d, *J*=8.5 Hz), 7.39 (2H, d, *J*=8 Hz), 7.27 (1H, s), 6.70 (2H, d, *J*=9.5 Hz), 5.76 (1H, s), 3.89 ppm (12H, s); ¹³C NMR (CDCl₃, 125 MHz): δ =159.4, 159.3, 154.9, 153.7, 145.6, 143.8, 143.1, 137.6, 137.4, 136.5, 131.8, 130.9, 125.0, 101.5, 94.7, 78.9, 78.5, 55.6, 55.5 ppm; IR (KBr): $\tilde{\nu}$ =1556,1462,1409,1261 cm⁻¹; MS (FAB): *m*/*z* calcd for C₃₆H₂₄BF₂I₆N₃O₄: 1373.61; found: 1373.92.

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Aza-BODIPY derivatives were synthesized and their triplet excited states and yields of singlet-oxygen generation were tuned by halogenation. The dye that was substituted with six iodine atoms showed the highest quantum yields of the triplet excited state $(\Phi_{\rm T}=0.86)$ and singlet oxygen $(\Phi_{\Lambda}=0.80)$. These systems were stable to irradiation, had strong NIR absorption, exhibited high yields of singlet oxygen, and acted as catalysts for photooxygenation reactions (see figure).



Photooxidation -

N. Adarsh, M. Shanmugasundaram, R. R. Avirah, D. Ramaiah*.

Aza-BODIPY Derivatives: Enhanced **Quantum Yields of Triplet Excited** States and the Generation of Singlet Oxygen and their Role as Facile Sustainable Photooxygenation Catalysts



Aza-BODIPY systems..... possess strong red absorption, exhibit high triplet excited states, and singlet-oxygen generation yields. The aza-BODIPY systems synthesized by D. Ramaiah et al. in their Full Paper on page ff., are stable under irradiation conditions, act as green catalysts for photooxygenation reactions, and are efficient sensitizers for photodynamic therapy.

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