

# New Insights into the Exploitation of BODIPY Derivatives as Organic Photocatalysts

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Dedicated to Professor Cesare Gennari on the occasion of his 70th birthday

Boron-dipyrromethene complexes (BODIPYs) are attracting a growing interest for their notable photophysical properties. Specifically, their application in organic photocatalysis is receiving particular attention thanks to their ability to undergo both electron and energy transfer processes, thus acting as promising photoredox catalysts and photosensitizers. Although the number of examples employing these organic dyes is constantly increasing, there are not so many studies that correlate their chemical composition to their photocatalytic

activity. In this work, a rationally designed structure-activity relationship study was performed by selecting a synthetically relevant atom transfer radical addition (ATRA) reaction as a benchmark. We demonstrated how the presence of heavy atoms in the chromophore's core turned out to be essential for achieving high reactivity levels. On the contrary, electron-withdrawing groups in position 8 (meso) undermined the catalytic performances, in agreement with the proposed reaction mechanism.

## Introduction

Boron-dipyrromethene complexes, commonly known as BODIPYs, have become one of the most relevant class of metal-free fluorophores, turning out to be at the forefront of modern science and technology.<sup>[1–3]</sup> Among their distinctive properties, it is worth mentioning the thermal and chemical stability along with the photochemical features of BODIPYs, such as strong visible-light absorption and excellent fluorescence.<sup>[1,4]</sup> These characteristics have generated a broad interdisciplinary research

interest, spanning over chemistry, materials science, biology, and medicine.

More specifically, BODIPYs have found applications as cytotoxic and theragnostic agents, imaging probes, photo-dynamic therapy sensitizers, sensors, laser dyes, and as chromophores for the fabrication of optoelectronic devices.<sup>[5–11]</sup>

In recent years, BODIPYs have also attracted considerable attention within the synthetic community as low-price alternatives to metal-based photocatalysts for the production of valuable organic compounds under mild operative conditions.<sup>[4,12]</sup> Importantly, the photophysical and electrochemical properties of these purely organic photocatalysts can be easily adjusted through *ad hoc* modifications of their molecular structures. As a matter of fact, the BODIPY skeleton may be easily functionalized both at the pyrrolic and *meso* positions (position 8), thus allowing the production of a large number of photo-active derivatives.<sup>[1]</sup>

In 2017, Cozzi and co-workers reported that a BODIPY derivative, namely PC1 (Figure 1b), is capable of triggering atom transfer radical addition (ATRA) reactions of alkenes (1) with bromo malonates (2).<sup>[13]</sup> This is a relevant type of transformation, since it allows to simply prepare densely functionalized alkyl bromides (3) under mild reaction conditions. It is worth noting that also other organic photocatalysts (e.g., Eosin Y) can be used to drive ATRA reactions between olefins and alkyl halides.<sup>[14–16]</sup> From a mechanistic point of view, the BODIPY-based photocatalyst directly reaches an electronically singlet excited state upon light absorption (Figure 1a). The presence of the iodine atoms on the BODIPY skeleton, by means of the heavy atom effect, facilitates the intersystem crossing which drives the conversion of the singlet into the triplet excited state of PC1.<sup>[4,17–20]</sup>


The BODIPY photocatalyst is then reduced to the corresponding radical anion by using sodium ascorbate (NaAsc) as


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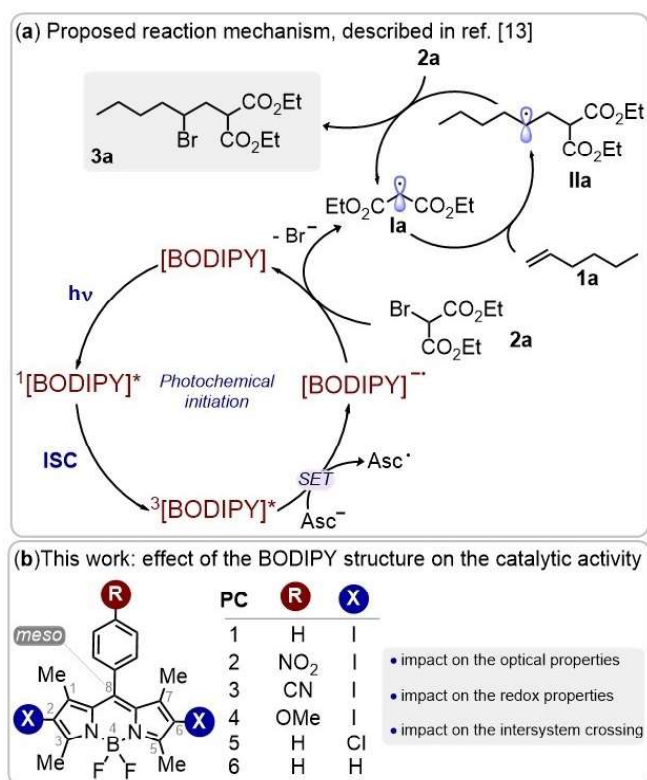
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**Figure 1.** (a) Proposed mechanism for the photocatalytic bromoalkylation of terminal olefins. (b) This work: studying the relationship between the chemical nature of a BODIPY derivative and its photocatalytic activity.

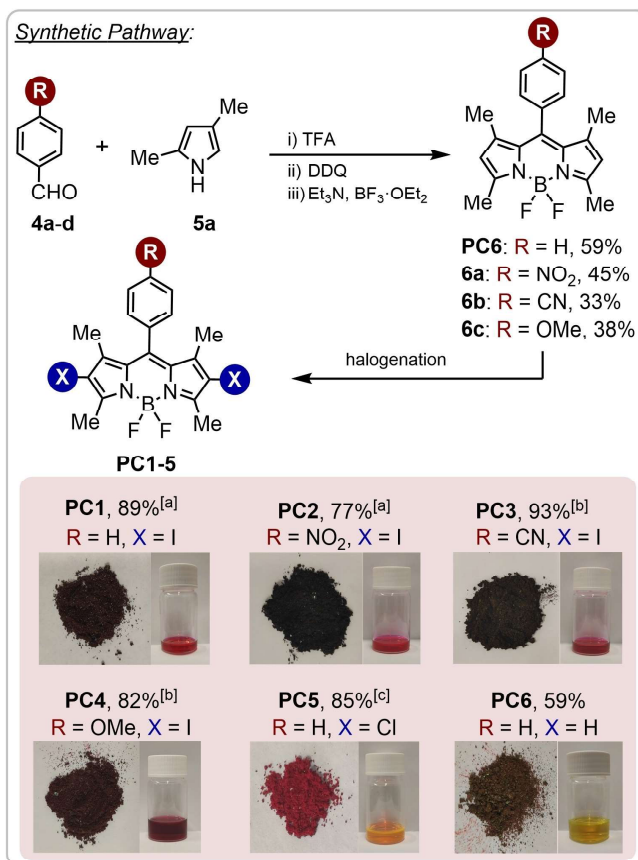
electron donor. This electron-rich intermediate induces the reductive cleavage of the C–Br bond in **2a** by single electron transfer (SET), which affords the electrophilic radical **Ia**. Here, the olefin **1a** intercepts **Ia**, generating **IIa**. This open shell species undergoes halogen-atom transfer (XAT) with **2a**, giving the final product **3a** and regenerating **Ia**.

Despite the importance of this radical transformation, nowadays studies dealing with the understanding of the effect that the chemical structure of the BODIPY-based photocatalyst has on the productivity of the process have not been carried out. Herein, we present an investigation of the structure-activity relationship of different BODIPY derivatives in a model photocatalytic ATRA reaction (Figure 1b). Specifically, six BODIPY derivatives (namely PC1–6) bearing substantial structural differences, either at the pyrrolic (2 and 6) or at the *meso* (8) positions, were synthesized and studied *via* conventional characterization techniques. In particular, the photophysical and redox features of these photocatalytic systems were investigated employing absorption, emission spectroscopies, along with cyclic voltammetry. Afterwards, we performed kinetic studies to gain a better understanding of the factors governing the photocatalytic BODIPY-based bromoalkylation of 1-hexene (**1a**) with ethyl bromomalonate (**2a**). This allowed us to correlate the different structures with the fundamental mechanistic nexus, therefore providing new insights on this photocatalytic transformation.

## Results and Discussion

The BODIPY derivatives (PC1–6) were prepared through a straightforward synthetic pathway, as outline in Figure 2.<sup>[21,22]</sup> At first, an acid catalyzed (TFA: trifluoroacetic acid) condensation of aromatic aldehydes (**4a–d**), containing either *para*-electron-donating or electron-withdrawing groups at the *para*-position, with 2,4-dimethylpyrrole (**5a**) yields the corresponding dipyrromethane intermediates. The subsequent step involves the oxidation of the dipyrromethane frameworks with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), that is followed by treatment with BF<sub>3</sub>·Et<sub>2</sub>O in the presence of Et<sub>3</sub>N. In this way, the desired BODIPY adducts were obtained. Finally, either iodide or chloride atoms were installed both at C2 and C6 positions of the BODIPY's cores by performing halogenation reactions with *N*-iodosuccinimide (NIS) or *N*-chlorosuccinimide (NCS), affording the desired BODIPY derivatives PC1–6 in good yields (see Supporting Information for details).

Afterwards, the photophysical properties of PC1–6 were investigated in air-equilibrated *N,N*-dimethylformamide (DMF) solutions. The main spectroscopic data are depicted in Table 1. All the studied photocatalytic systems show a strong absorption centered in the visible region of the spectrum, which justifies the bright colors observed when they are solubilized in DMF



**Figure 2.** Synthesis of photocatalysts PC1–6. Halogenation conditions employed for the synthesis of PC1–5: [a] *N*-iodosuccinimide (NIS), CH<sub>2</sub>Cl<sub>2</sub>, [b] I<sub>2</sub>/HIO<sub>3</sub>, EtOH, [c] *N*-chlorosuccinimide (NCS), hexafluoro-2-propanol (HFIP). The displayed solutions of PC1–6 are prepared in DMF (1 × 10<sup>-5</sup> M).

**Table 1.** Photophysical properties of BODIPY derivatives employed in this study.

	$\lambda_{\text{abs}}$ [nm] <sup>[a]</sup>	$\lambda_{\text{em}}$ [nm] <sup>[a]</sup>	$\epsilon$ [M <sup>-1</sup> cm <sup>-1</sup> ] <sup>[a,b]</sup>	$\epsilon_{427}$ [M <sup>-1</sup> cm <sup>-1</sup> ] <sup>[a]</sup>	$\Phi_{\text{em}}$ [%] <sup>[a]</sup>	E(PC/PC <sup>•-</sup> ) (V vs SCE) <sup>[c]</sup>
PC1	533	553	82158	3055	1.5	-1.29
PC2	540	563	70794	4301	1.2	-1.18
PC3	539	561	57330	3405	0.9	-1.29
PC4	533	551	74663	3879	4.9	-1.38
PC5	525	540	74342	1721	50	-1.35
PC6	501	511	70832	1267	45	-1.63

[a] The optical measurements were performed in DMF (optical path length = 1 cm). [b] Molar absorption coefficient calculated at the absorption maxima. [c] The electrochemical measurements were performed in deaerated CH<sub>3</sub>CN solutions containing the corresponding PC (1 mM), Bu<sub>4</sub>NPF<sub>6</sub> (0.1 M) as supporting electrode and SCE as reference electrode. Scan rates 0.1 V/s. Ferrocene (Fc) was used as internal reference (E<sub>1/2</sub> = +0.380, Fc<sup>+</sup>/Fc vs SCE).<sup>[26]</sup>

(Figure 2). As expected, the photochemical properties of the BODIPY derivatives are strongly related to their chemical structures.<sup>[4,18,23,24]</sup> In particular, we found that the presence of halogen atoms (I or Cl) at the pyrrolic positions has a major impact on the main photocatalytic features. For instance, comparing the absorption and emission maxima of PC5 and PC1, we observed a red-shift when the halogen's atomic number is higher, whereas the molar absorption coefficients ( $\epsilon$ ) at the absorption maxima are only slightly influenced by the nature of the halogen. On the other hand, PC6, which do not contain any halogen atoms, shows the absorption and emission maxima centered at lower wavelengths. Moreover, the iodine atoms highly affect the main deactivation pathway, followed by the PCs, after excitation with visible light. Specifically, the fluorescence quantum yields ( $\phi_{\text{em}}$ ) of PC1–4 are about 45-times lower than PC6. Indeed, the presence of iodine facilitates the spin-orbit coupling, by the heavy atom effect, thus favoring the intersystem crossing process (ISC) with respect to the fluorescence decay.<sup>[4]</sup> As a matter of fact, a more effective population of the triplet excited state should make the BODIPY derivatives more suitable for application in photocatalysis (Figure 1a).<sup>[13]</sup>

Concerning the *meso*-functionalization, we have observed that the photophysical properties of PC2–4 are quite similar to those of PC1. Indeed, recent computational studies have revealed that the HOMO (highest occupied molecular orbital) and LUMO (lower unoccupied molecular orbital) in *meso*-aryl BODIPYs are mainly located on the chromophore cores and do not involve the aryl substituents.<sup>[23]</sup>

Subsequently, to gain an insight into the redox properties of PC1–6 their ground-state electrochemical potentials were measured by means of cyclic voltammetry (Table 1 and SI). All PCs show electrochemically reversible electron transfer processes in the cathodic region (see SI). In particular, it was found that PC1–5 show less negative potentials compared to PC6. In fact, the presence of halogen atoms directly bonded to the BODIPY core reduces the electron density of the whole molecule, thus making it more prone to be reduced. Besides, the chemical nature of the *meso*-aryl substituent has a low influence on the redox features of the PC, due to its orthogonality with respect to the redox-active moiety. In any case, the E(PC/PC<sup>•-</sup>) of all BODIPY radical anions are adequate

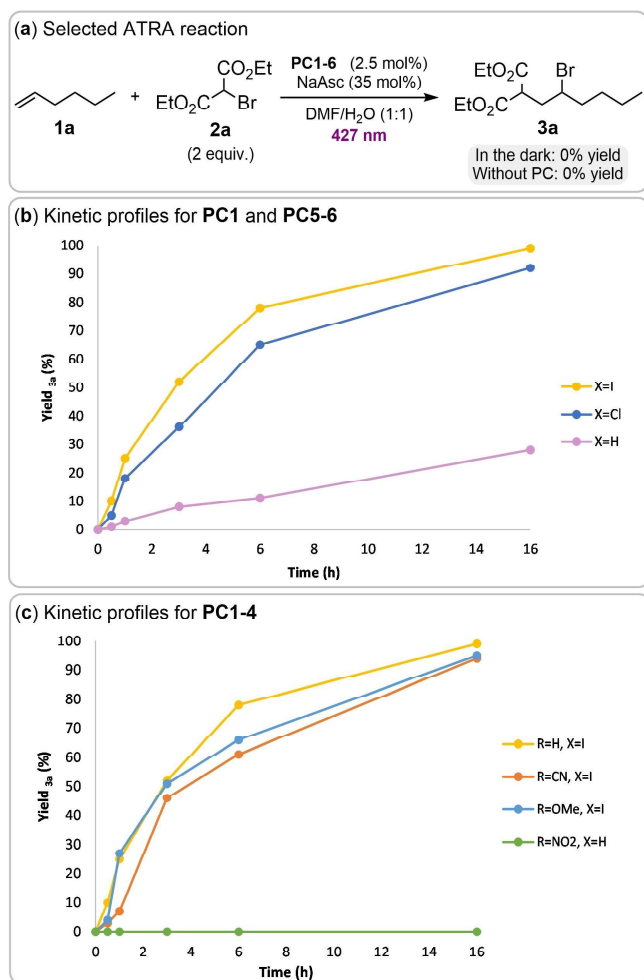
for performing the reduction step on the bromo malonate **2a** (–1.19 V vs saturated calomel electrode, SCE).<sup>[25]</sup>

Based on these findings, we attempted to correlate the structural modifications on the BODIPY scaffolds to the overall catalytic activity by reacting olefin **1a** with bromomalonate **2a** in the presence of PC1–6 as organic chromophores and NaAsc as sacrificial reducing agent under purple light irradiation (427 nm, Figure 3a). As a matter of fact, all BODIPY derivatives present a significant absorption at 427 nm (Table 1). The formation of the corresponding ATRA product **3a** was followed over the time, hence obtaining the kinetic profiles associated to the use of differently functionalized BODIPY photocatalysts (PC1–6, Figure 3b–c). It is worth noting that no reactivity was observed neither in the dark nor in the absence of PC, thus confirming the photochemical nature of the selected transformation and the catalytic role of BODIPYs.

Concerning the resulting kinetic curves, a deterioration of the reaction performances was observed when other functionalities were located at the pyrrolic positions in place of iodine atoms (PC1), namely chlorines (PC5) and hydrogens (PC6, Figure 3b). A moderate decrement of yield of **3a** over the reaction time was noted when using PC5, whereas a drastic drop in performance was found for PC6. As previously mentioned, this behavior is in line with a less favorable ISC process, along with a weaker absorption of the incident photons (Table 1) with respect to PC1 that led to a lower amount of photoactive <sup>3</sup>PC\* under the reaction conditions.

Interestingly, the presence of electron-withdrawing groups (EWGs) at the *meso* position was found to be detrimental for the reactivity (Figure 3c), despite PC1–4 have similar absorptivity at the irradiation wavelength (427 nm) and comparable redox potentials (Table 1). Specifically, the presence of a cyano-substituent on the photocatalyst (PC3) led to a lower initial rate under the standard conditions with respect to the model BODIPY derivative (PC1), although similar final performances over 16 hours. Additionally, strong EWG such as a nitro group (PC2) completely suppressed the reactivity. In light of the redox potentials of bromo malonate **2a** and PC2 (Table 1), the lack of reactivity of PC2 could be explained by a non-spontaneous electron transfer from the radical anion of PC2 to **2a**.

On the other hand, we observed that PC4, which contains a strong electron-donating group (EDG, namely -OMe), shows an initial photocatalytic activity similar to PC1, which are both



**Figure 3.** (a) Selected ATRA reaction between 1-hexene (1a) and ethyl bromomalonate (2a) driven by PC1-6 under purple light irradiation. (b) Kinetic profiles obtained for PC1 and PC5-6. (c) Kinetic profiles obtained for PC1-4.

much higher than those of PC3. This trend might be due to the fact that a more electron rich *meso*-substituent on the BODIPY skeleton could enhance the stability of the corresponding excited state, thus increasing its ability to undergo photo-reduction with sodium ascorbate.<sup>[4,18,27]</sup> Lastly, we investigated the effect of the light source on the reactivity. To this end, we recorded the kinetic profiles of the reaction using PC1 as chromophore and different Kessil lamps (427 nm, 440 nm, 456 nm, 525 nm) as sources of photons (see SI). The green lamp (525 nm) provided the highest productivity levels, due to the high ability of PC1 of absorbing photons of this wavelength ( $\lambda_{\text{abs}}$  maximum = 533 nm, Table 1).

## Conclusion

In summary, six different BODIPY derivatives bearing chemically different substituents in position 2 and 6 or 8 were prepared through a three-step procedure. These organic dyes have been

compared in terms of photocatalytic activity towards a benchmark transformation of synthetic relevance, namely ATRA reaction. The presented structure-activity relationship study allowed to determine the importance of an efficient ISC process – prompted by the presence of heavy atoms on the pyrrolic positions – for the catalytic performances. Parallely, we found out that the presence of electron-withdrawing groups (EWGs) at the *meso* position decreases the activity of the BODIPY-based photocatalyst, while electron donating groups (EDGs) do not significantly affect the reactivity. To conclude, these studies will allow us to design and develop more effective BODIPY-based photocatalytic systems in order to expand the known reactivity towards other synthetically, industrially, or naturally relevant photochemical transformations.

## Experimental Section

General procedure for the photocatalytic ATRA reaction (see SI for details): a Schlenk tube was charged with sodium ascorbate (35 mol%, 0.07 mmol), BODIPY photocatalyst PC1-6 (2.5 mol%, 0.005 mmol), 1-hexene (1a, 0.2 mmol, 1 equiv.), diethyl 2-bromomalonate (2a, 0.4 mmol, 2 equiv.), water and DMF (1:1 v/v, 0.5 M). The reaction mixture was degassed via freeze pump thaw and the vessel refilled with argon. The reaction mixture was located 6 cm away from the light source and stirred for 16 hours. The reaction was quenched by the addition of an aqueous solution of LiCl (5%) and extracted with EtOAc. The organic phase was dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under reduced pressure to give the crude product. Yields were determined by <sup>1</sup>H-NMR spectroscopy using 1,1,2-trichloroethene as the internal standard. The pure product was isolated by flash column chromatography (5% EtOAc/cyclohexane) to afford compound 3a as a colorless oil.

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## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords:** Photocatalysis · Photochemistry · Reaction mechanisms · Redox chemistry · Synthetic methods

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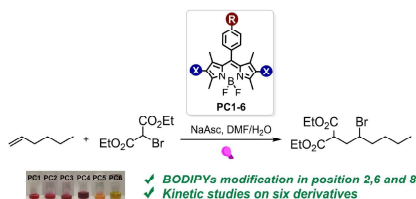
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## RESEARCH ARTICLE

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Special Issue