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ORIGINAL ARTICLE

3, 3,5 and 2,6 Expanded Aza-BODIPYs Via Palladium-Catalyzed Suzuki-Miyaura Cross-Coupling Reactions: Synthesis and Photophysical Properties

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Abstract

Novel symmetrical aza-borondipyrromethene (aza-BODIPY) compounds bearing 4-methoxyphenyl, 4-methoxybiphenyl, 2,4-dimethoxybipheny, 4-bromophenyl and N,N-diphenyl-4-biphenylamine groups on the 3, 3,5 and 2,6 positions of aza-BODIPY core were synthesized via Suzuki-Miyaura coupling reactions while unsymmetrical analogues were obtained from the starting mono Br-substituted aza-BODIPY material which was obtained from nitrosolated pyrrole derivative. The characterizations were performed by means of ^{1}H-NMR, ^{13}C-NMR, FTIR and HRMS-TOF-ESI techniques. The spectral properties of the aza-BODIPY derivatives were investigated using absorption and fluorescence spectroscopy. The novel compounds with extended conjugation have broadband absorption in near infrared region and show significant shifts on their absorption and fluorescence spectra compared to unsubstituted analogues. The highest bathochromic shifts were observed π-extended and strong electron donating groups at 3,5 positions of the aza-BODIPY scaffold. Depend on substitution positions of attached groups to the indacene core, the fluorescence quantum yields of chromophores were determined to be drastic changes. The singlet oxygen generation capability of the compounds were evaluated and 2,6-bromine substituted compounds AA1 and CC1 showed high singlet oxygen quantum yields (71% and 74%, respectively). Enhanced photophysical properties such as intense absorption, extended conjugation and singlet oxygen production make the investigated aza-BODIPYs promising candidates for photodynamic therapy applications and organic photovoltaic cells in NIR region.

Keywords Aza-BODIPY · Unsymmetrical aza-BODIPY · Azadipyrromethenes · Suzuki-Miyaura coupling · NIR region dyes

Introduction

Although, the first reaction of tetraarylazadipyrromethenes with boron (Aza-BODIPY) occurred in the early 1990s [1] these dyes have been recognized by the studies of the O'Shea group since 2002 [2].Aza-BODIPY dyes are aza-analogous of difluorobora-diaza-s-indacenes (BODIPY) and known as attractive fluorophores because of their advantageous features. Sharp absorption and fluorescence bands, large molar extinction coefficients, high fluorescence quantum yields and high photostability [3–5] all contribute to the appeal of these interesting compounds. Aza-BODIPY compounds are well-known NIR dyes because of their large NIR region absorption (700–1100 nm) [6]. This property depends on a large scale 1,3,5,7 aryl substituents. Particularly electron donating groups on 3,5-aryl substituents increase extinction coefficients and absorption maximum, however on 1,7-aryl substituted electron donating groups show minor effects. Furthermore, 2,6-substituted (β-pyrrole) groups may cause hypsochromic shifts on the absorption wavelength and quench fluorescence intensity of aza-BODIPY dyes [7]. Currently, aza-BODIPY dyes are used in diverse applications, such as photodynamic therapy (PDT) [8–10], NIR-emitting chemosensors for heavy metal determination [11], in telecommunication applications with strong two-photon absorption (TPA) properties [12–14], as a chromophore group in pH sensors [15, 16], photosensitized singlet oxygen generation

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[17, 18], organic photovoltaic cells [19, 20] and NIR fluorescent imaging probes [21, 22].

Photodynamic therapy (PDT) is an effective and applicable treatment for various types of cancers and also it has been researched for other diseases. Photosensitizer, light and oxygen are essential components for PDT treatments. Photosensitizers are specific chromophores that produces biological cytotoxic singlet oxygen ($^1O_2$) from the $^3O_2$using the light. This makes the chromophores prominent investigating area for the improvement of PDT applications. So that, there have been many research papers for dye molecules such as porphyrin derivatives [23, 24]. Porphyrins were the first photosensitizers for using clinic treatment [25], which has several disadvantageous. First, absorption and emission wavelength aren't tunable with bonding side groups. Second, photons do not penetrate tissue beyond a few millimeters due to short absorption wavelength and low absorption leading to skin photosensitivity and low excretion rate [26–28]. Because of these disadvantages it has been designed new generation dyes that have intense absorption in near IR region like BODIPY [29–31] and aza-BODIPY [17, 18] derivatives.

Herein, we present new red/NIR absorbing aza-BODIPY series which are decorated with 4-methoxyphenyl, 2,4-dimethoxy phenyl and triphenylamine (TFA) precursors via Palladium-catalyzed Suzuki-Miyaura cross-coupling reactions. Due to mild reaction conditions and commercial availability of starting boronic acid reagents, we preferred the Suzuki-Miyaura coupling. In addition diverse boronic acids in commercial catalogs are safer than the other organometallic reagents [32]. The Suzuki–Miyaura coupling has been successfully employed on 3, 3,5 and 2,6 positions of aza-BODIPY core. 3 and 3,5 substituted aza-BODIPY dyes showed absorption and emission in the NIR region. On the other hand 2,6 substituted aza-BODIPY derivatives showed quenching fluorescence intensity and hypsochromic shifts compared to unsubstituted form. Electron donating groups and extended conjugations dramatically have changed photophysical properties of aza-BODIPY core depending on substitution position. As a consequence, these compounds seem to display enhanced photophysical properties, which will be helpful for developing novel versatile apparatus for organic solar cells, cellular imaging, PDT and two photon absorption applications in longer wavelengths in chemical and biological fields.

Experimental

Materials and Characterization

Compounds 1a, 2a, 3a, 1b, 2b, A, B and B1 were prepared according to a literature procedures [14, 33–35]. All solvents were purchased from common commercial sources. The melting points of the synthesized compounds were determined in open capillares using Barnstead Electrothermal IA9100. Fluorimetric measurements were applied on Perkin Elmer LS55 Spectrometer and electronic excitation spectra were recorded on Shimadzu UV1800 spectrophotometer. Mass spectral analyses were performed on an Agilent 6224 HRMS spectrometer. ^{1}H-NMR spectra were recorded on VARIAN Mercury 400 MHz spectrometer. ^{1}H NMR chemical shifts (δ) are given in ppm down fieldfrom Me_4Si, determined by chloroform (δ = 7.26 ppm. ^{13}C NMR spectra were recorded on VARIAN Mercury 100 MHz spectrometer. ^{13}C NMR chemical shifts (δ) are reported in ppm with the internal $CDCl_3$ δ 77.0 ppm as standard. Perkin–Elmer 100 spectrometer (equippedwith ATR unit) was used for FT-IR spectra of the compounds in the range 650–4000 cm^{-1}.

Determination of Fluorescence Quantum Yields (Φ_F)

In order to determine the fluorescence quantum yields of the dyes, comparative method (Eq. 1) [36] was applied.

$$\Phi_F = \Phi_F(\mathrm{Std})\frac{\mathrm{F}.\mathrm{A}_{\mathrm{Std}}.n^2}{F_{Std}.A.n^2_{Std}} \quad (1)$$

Where Φ_F(Std) is the fluorescence quantum yield of BF_2 Chelate of (3,5-Diphenyl-1H-pyrrol-2-yl)(3,5-diphenylpyrrol-2-ylidene) amine (Φ_F = 0.34 in chloroform) [7]. F and F_{Std} denote the areas under the fluorescence emission curves of samples and the standard, respectively. A and A_{Std} are the respective absorbances of the samples and standard compound at the excitation wavelengths, respectively. The refractive indices, n and n_{Std} of the solvents were applied. The concentration of the dilute solutions at the excitation wavelengths fixed at 5×10^{-6} M in $CHCl_3$. All spectra were recorded at 25 °C on non-deaerated samples.

The Parameters for Singlet Oxygen Quantum Yields (Φ_Δ)

To study the singlet oxygen production properties of compounds, experiments were carried out in CH_2Cl_2 with 1,3-diphenyl isobenzofuran (DPBF) as a chemical singlet oxygen trap [37]. The absorbance of DPBF was tuned around 1.0 at 414 nm and the absorbance of the sensitizers was tuned between from 0.2 to 0.3 in CH_2Cl_2. A solution of the aza-BODIPY derivatives and DPBF was irradiated with a 630 nm Perkin Elmer L5S55 fluorescent light and the decrease in the absorption band of DPBF was monitored at the intervals of 2 s. Singlet oxygen quantum yields (Φ_Δ) were calculated using the standard, methylene blue (MB) (Φ_Δ = 0.57 in CH_2Cl_2), by plotting the ΔOD of DPBF against the irradiation time. The quantum yield Φ_Δ was calculated by the following equation [37]:

$$\Phi_{\Delta sam}=\Phi_{\Delta std}\left(\frac{m_{sam}}{m_{std}}\right)\left(\frac{F_{std}}{F_{sam}}\right) \quad (2)$$

Where sam and std. designate the aza-BODIPY photosensitizer and methylene blue (MB), respectively. m is the slope of difference in change in absorbance of DPBF (414 nm) with the irradiation time, F is the absorption correction factor, which is given by $F = 1–10^{-OD}$. The photosensitizers were irradiated with monochromatic light at the peak absorption wavelength for 2 s. Absorbance was measured for several times after each irradiation. The slope of the graph of absorbance maxima of DPBF at 414 nm versus the photoirradiation time for each photosensitizer was calculated.

Synthesis

Synthesis of 2-(4-Bromophenyl)-4-(4-Methoxyphenyl) -1H-Pyrrole (3b)

1-(4- bromophenyl)-4-nitro-3-(4- methoxyphenyl)butan-1-one (**2b**) (7.02 g, 18.6 mmol) was dissolved in 180 mL MeOH/THF (1:1) mixture at room temperature. A stirred solution was treated with KOH (5.24 g, 93.45 mmol). After 1 h the mixture was added drop wise to a solution of 200 mL %33 H_2SO_4/MeOH (*v*/v) at 0 °C and the solution was stirred for further 1 h at room temperature. Water (250 mL) and ice (250 mL) were added and the mixture was neutralized with aqueous 5 M NaOH and extracted with $CHCl_3$ (100 mL × 3). The solvent was evaporated in vacuo and obtained oil was held in vacuum drying over the night. The oil was treated with acetic acid (174 mL) and NH_4OAc (14.41 g, 0.19 mol) and the solution was heated at 100 °C for 1 h. The reaction mixture was cooled to room temperature, ice (340 mL) was added, and the mixture carefully neutralized with aqueous 5 M NaOH. The resulting solid was collected by filtration, washed with distilled water, dried and crystallized from CH_3Cl, resulting the product as a light blue solid (3.45 g, %56), mp228–231 °C (from chloroform). ^{1}HNMR (400 MHz, DMSO) δ 11.42 (s, 1H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.50 (d, 2H), 7.23 (s, 1H), 6.89 (s, 1H), 6.88 (d, *J* = 8.0 Hz, 2H), 3.73 (s, 3H). ^{13}CNMR (100 MHz, DMSO) δ 157.11, 131.93, 131.39, 130.76, 128.18, 125.49, 125.19, 124.74, 118.02, 116.16, 113.93, 103.62, 54.93. IR (ATR, cm^{-1}) 3437.1, 3014.7, 2835.4, 1242.1. HRMS (TOF-ESI): Calcd ($C_{17}H_{14}BrNO$) $[M + H]^+$: m/z = 328.03371; found, m/z = 328.03328.

Synthesis of 3,5-Bis(4-Methoxyphenyl)-2-Nitroso-1H-Pyrrole (4a)

2,4-bis(4-methoxyphenyl)-1H-pyrrole (3a) (1.95 g, 7.00 mmol) was dissolved in EtOH (70 mL). To a stirred solution was added concentrated HCl(1.40 mL), and followed by a drop wise addition of aqueous $NaNO_2$ (560 mg, 8.05 mmol, in 14 mL of H_2O). The reaction mixture was stirred for 30 min and cooled to 0 °C, and another portion of concentrated HCl (7.00 mL) was added. The solution was allowed to stir for 1 h, and the resulting red solid was collected by filtration and washed with Et_2O. The solid was dissolved in minimal EtOH, an excess of aqueous NaOAc and ice was added, and the solution was stirred for 1 h. The resulting solid was collected by filtration and purified by chromatography on silica (1:1, EtOAc/hex), resulting the product as a green solid (1.68 g, %78), mp. 186–187 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.8 Hz, 2H), 7.07 (s, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H), 3.87 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 162.61, 161.08, 130.83, 129.08, 124.39, 122.17, 114.85, 114.32, 113.79, 55.53, 55.38. IR (ATR, cm^{-1}) 3228.8, 3012.8, 2841.1, 1600.9, 1246.0. HRMS (TOF-ESI): Calcd ($C_{18}H_{16}N_2O_3$) $[M + H]^+$: m/z = 309.12394; found, m/z = 309.12540.

Synthesis of BF_2 Chelate of [3,5-Bis(4-Methoxyphenyl) -1H-Pyrrol-2-Yl]-3,5-Bis(4- Methoxyphenyl)Pyrrol-2-Ylidene] Amine (A1)

A solution of [3,5-bis(4-methoxyphenyl)-1H-pyrrol-2-yl]-3,5-bis(4-methoxyphenyl)pyrrol-2-ylidene]amine (A) (2.00 g, 3.90 mmol) in dry CH_2Cl_2 (300 mL) was treated with *N,N*-diisopropylethylamine (6.08 mL, 39.0 mmol) and the mixture was stirred for 10 min at room temperature. Then, boron trifluoride diethyl etherate (7.22 mL, 58.5 mmol) was added and the reaction mixture was stirred at room temperature for 24 h. The mixture was washed with water, and the organic layer dried over sodium sulfate. Removal of solvent gave a residue, which was purified by column chromatography on silica eluting with hexane/EtOAc (2:1, *V*/V) resulting the product as a dark blue solid (1.84 g, 76%), mp 265–266 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.05 (t, J = 8.2 Hz, 4H), 6.99 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.91 (s, 1H), 3.88 (s, 3H), 3.87 (s, 3H) ^{13}CNMR (100 MHz, $CDCl_3$) δ 161.68, 160.87, 157.78, 145.14, 144.65, 142.74, 131.49, 131.45, 131.40, 130.73, 125.49, 124.38, 117.09, 117.08, 114.13, 114.08, 55.40, 55.38. IR (ATR,m^{-1}) 3005.1, 2837.3, 1597.1, 1384.9, 1251.8. HRMS (TOF-ESI): Calcd ($C_{36}H_{30}BF_2N_3O_4$) $[M]^+$: m/z = 617.22976; found, m/z = 617.23289.

Synthesis of BF_2 Chelate of [4-Bromo-3-(4-Methoxyphenyl) -5-(4- Methoxyphenyl)-1H-Pyrrol-2-Yl] -[4-Bromo-3-(4-Methoxyphenyl)-5-(4-Methoxyphenyl) Pyrrol-2-Ylidene]Amine (AA1)

A solution of BF_2chelate of [3,5-bis(4-methoxyphenyl)-1H-pyrrol-2-yl]-3,5-bis(4-methoxyphenyl)pyrrol-2-

ylidene]amine (**A1**)(1.23 g, 2.00 mmol) in dry CH_2Cl_2 (100 mL) was added to N-bromosuccinimide (NBS) (0.78 g, 4.40 mmol), and the mixture was stirred at room temperature for 24 h. After the reaction was completed, the solvent was evaporated in vacuo. Afterwards, the residue was washed with water, and dried over sodium sulfate. The residual was purified by column chromatography on silica eluting with hexane/EtOAc (2:1) which gave the product as a dark brown solid (1.31 g, 84%), mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 9.2 Hz, 2H), 6.98 (d, J = 9.2 Hz, 2H), 3.88 (s, 3H), 3.85 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 161.55, 160.80, 157.14, 144.01, 141.99, 141.98, 132.40, 132.36, 131.38, 123.51, 121.98, 113.59, 113.52, 55.38, 55.27. IR (ATR, cm^{-1}) 3003.2, 2835.4, 1599.0, 1379.1, 1249.9. HRMS (TOF-ESI): Calcd ($C_{36}H_{28}BBr_2F_2N_3O_4$) $[M + H]^+$: m/z = 776.05657; found, m/z = 776.06088.

Synthesis of BF_2 Chelate of [4-Methoxyphenyl-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)-1H-Pyrrol-2-Yl] -[4-Methoxyphenyl-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)Pyrrol-2-Ylidene]Amine (A2)

A mixture of BF_2 chelate of [4-bromo-3-(4-methoxyphenyl)-5-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[4-bromo-3-(4-methoxyphenyl)-5-(4-methoxyphenyl)pyrrol-2-ylidene]amine (AA1) (0.23 g, 0.30 mmol), 4-methoxyphenylboronic acid (105 mg, 0.69 mmol), $Pd(PPh_3)_4$ (15.6 mg, 0.0014 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) were added to a round bottomed flask, and then degassed argon for 10 min. The mixture of toluene (4 mL), ethanol (2 mL) and water (2 mL) were injected under argon atmosphere. The solution was stirred at 85 °C for 24 h. After cooling to room temperature, the mixture was washed with water and extracted with CH_2Cl_2 (75 mL × 2). The solvent was evaporated under reduced pressure. Afterwards, the residual was purified by column chromatography on silica eluting with toluene, which gave the product as a purple solid (82 mg, 33%) mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 9.2 Hz, 2Hı), 6.74 (d, J = 8.4 Hz, 2H), 3.81 (s, 3H), 3.78 (s, 6H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 160.57, 159.73, 158.61, 157.86, 155.85, 155.81, 145.13, 139.93, 138.46, 132.44, 132.34, 131.78, 125.76, 124.72, 123.38, 113.25, 113.22, 55.20, 55.11. IR (ATR, cm^{-1}) 3034.0, 2835.4, 1599.0, 1373.3, 1247.9. HRMS (TOF-ESI): Calcd ($C_{50}H_{42}BF_2N_3O_6$) $[M + H]^+$: m/z = 830.32133; found, m/z = 830.31900.

Synthesis of BF_2 Chelate of [4-N,N-Diphenylaminophenyl-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)-1H-Pyrrol-2-Yl] -[4-N,N-Diphenylaminophenyl-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)Pyrrol-2-Ylidene]Amine (A4)

Compound A4 was prepared from BF_2 Chelate of [4-Bromo-3-(4-methoxyphenyl)-5-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[4-bromo-3-(4-methoxyphenyl)-5-(4-methoxyphenyl)pyrrol-2-ylidene]amine (AA1) (0.19 g, 0.25 mmol), 4-(diphenylamino)phenylboronic acid (173.5 mg, 0.60 mmol), $Pd(PPh_3)_4$ (13 mg, 0.0012 mmol) and K_2CO_3 (0.23 g, 1.66 mmol) according to the method for A2. The residual was purified by column chromatography on silica eluting with toluene which gave the product as a purple solid (53 mg, 19%) mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H), 7.25 (t, J = 8.0 Hz, 4H), 7.07 (d, J = 7.2 Hz, 2H), 7.01 (t, J = 7.4 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 3.84 (s, 3H), 3.81 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 160.68, 159.78, 157.89, 147.48, 146.66, 145.16, 139.78, 132.44, 129.21, 127.36, 124.76, 124.58, 124.44, 123.26, 123.04, 122.97, 113.23, 113.14, 55.24, 55.14. IR (ATR, cm^{-1}) 3032.1, 2835.4, 1599.0, 1375.2, 1251.8. HRMS (TOF-ESI): Calcd ($C_{72}H_{56}BF_2N_5O_4$) $[M]^+$: m/z = 1103.43936; found, m/z = 1103.44170.

Synthesis of BF_2 Chelate of [5-(4-Methoxyphenyl) -3-(4-Methoxybiphenyl)-1H-Pyrrol-2-Yl] -[5-(4-Methoxyphenyl)-3-(4-Methoxybipheny) Pyrrol-2-Ylidine]Amine (B2)

A mixture of [3-(4-methoxyphenyl)-5-(4-bromophenyl)-1H-pyrrol-2-yl][3-(4-methoxyphenyl)-5-(4-bromophenyl)pyrrol-2-yliden]amine (B) (0.23 g, 0.30 mmol), 4-methoxyphenylboronic acid (105 mg, 0.69 mmol), $Pd(PPh_3)_4$ (15.6 mg, 0.0014 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) were added to a round bottomed flask, and then degassed argon for 10 min. The mixture of toluene (4 mL), ethanol (2 mL) and water (2 mL) were injected under argon atmosphere. The solution was stirred at 85 °C for 24 h. After cooling to room temperature, the mixture was washed with water and extracted with CH_2Cl_2 (75 mL × 2). The solvent was evaporated under reduced pressure. The residual was carried into the next stage without further purification. The resulting solid was dissolved in dry CH_2Cl_2 (100 mL). Then, the reaction mixture was treated with *N,N*-diisopropylethylamine (0.54 mL, 3.00 mmol) and the mixture was stirred for 10 min at room temperature. Afterwards, boron trifluoride diethyl etherate (0.45 mL, 4.50 mmol) was added and the reaction mixture was stirred at room temperature for

24 h. The mixture was washed with water, and the organic layer dried over sodium sulfate.

The solvent is removed in vacuo to obtain a residue, which was purified by column chromatography on silica eluting with toluene, resulting the product as a dark brown solid (61 mg, 26%), mp 279–280 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.8 Hz, 2H), 8.07 (d, J = 8.8 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 7.00 (s, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.90 (s, 3H), 3.86 (s, 6H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 160.84, 159.67, 158.22, 145.57, 143.28, 143.25, 142.85, 137.25, 132.62, 130.85, 130.14, 130.10, 130.05, 129.99, 128.23, 126.64, 125.41, 125.27, 117.50, 114.32, 114.16, 109.99, 55.43, 55.35. IR (ATR, cm^{-1}) 3111.2, 2833.4, 1597.1, 1383.0, 1244.1. HRMS (TOF-ESI): Calcd ($C_{48}H_{38}BF_2N_3O_4$) $[M]^+$: m/z = 769.29236; found, m/z = 769.29487.

Synthesis of BF_2 Chelate of [5-(4-Methoxyphenyl) -3-(2,4-Dimethoxybiphenyl)-1H-Pyrrol-2-Yl] -[5-(4-Methoxyphenyl)-3-(2,4-Dimethoxybipheny) Pyrrol-2-Ylidine]Amine (B3)

B3 was prepared from[3-(4-methoxyphenyl)-5-(4-bromophenyl)-1H-pyrrol-2-yl][3-(4-methoxyphenyl)-5-(4-bromophenyl)pyrrol-2-yliden]amine (B) (0.23 g, 0.30 mmol), 2,4-dimethoxyphenylboronic acid (125.6 mg, 0.69 mmol), $Pd(PPh_3)_4$ (15.6 mg, 0.0014 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) according to the method for B2.The obtained residue was purified by column chromatography on silica eluting with toluene which gave the product as a purple solid (85 mg, 34%), mp 273–274 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.8 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.0 Hz, 1H), 7.01 (s, 1H), 7.01 (d, J = 8.8 Hz, 2H), 6.60–6.58 (m, 2H), 3.91 (s, 3H), 3.86 (s, 6H), 3.83 (s, 6H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 160.78, 160.73, 158.50, 157.71, 145.54, 143.11, 142.36, 140.88, 131.34, 130.82, 129.73, 129.50, 129.31, 129.27, 125.49, 122.65, 117.69, 114.14, 109.99, 104.81, 99.01, 55.53, 55.43. IR (ATR, cm^{-1}) 3117.0, 2831.5, 1600.9, 1379.1, 1259.5. HRMS (TOF-ESI): Calcd ($C_{50}H_{42}BF_2N_3O_6$) $[M + H]^+$: m/z = 830.32133; found, m/z = 830.32234.

Synthesis of BF_2 Chelate of [5-(4-Methoxyphenyl) -3-(4-N,N-Diphenylaminobiphenyl)-1H-Pyrrol-2-Yl] -[5-(4-Methoxyphenyl)-3-(4-N,N-Diphenylaminobiphenyl) Pyrrol-2-Ylidine]Amine (B4)

B4 was prepared from [3-(4-methoxyphenyl)-5-(4-bromophenyl)-1H-pyrrol-2-yl][3-(4-methoxyphenyl)-5-(4-bromophenyl)pyrrol-2-yliden]amine (B) (0.23 g, 0.30 mmol), 4-(diphenylamino)phenylboronic acid (199.5 mg, 0.69 mmol), $Pd(PPh_3)_4$ (15.6 mg, 0.0014 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) according to the method for B2.The residual was purified by column chromatography on silica eluting with toluene which gave the product as a cobalt blue solid (178 mg, 57%), mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 2H), 8.07 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 7.29 (t, J = 7.8 Hz, 4H), 7.15 (d, J = 7.6 Hz, 4H), 7.13 (d, J = 8.8 Hz, 2H), 7.06 (t, J = 7.4 Hz, 2H), 7.01 (s, 2H), 6.99 (s, 1H),3.90 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 160.83, 158.06, 147.83, 147.47, 145.62, 143.13, 142.68, 133.58, 130.85, 130.16, 130.12, 130.08, 130.04, 129.32, 127.78, 126.53, 125.42, 124.72, 123.33, 123.21, 117.53, 114.16, 55.43. IR (ATR, cm^{-1}) 3034.0, 2835.4, 1587.4, 1386.8, 1251.8. HRMS (TOF-ESI): Calcd ($C_{70}H_{52}BF_2N_5O_2$) $[M + H]^+$: m/z 1044.42605; found, m/z = 1044.42421.

Synthesis of [5-(4-Methoxyphenyl)-3-(4-Methoxyphenyl) -1H-Pyrrol-2-Yl]-[5-(4-Methoxyphenyl)-3-(4-Bromophenyl) Pyrrol-2-Ylidene]Amine (C)

3,5-bis(4-methoxyphenyl)-2-nitroso-1H-pyrrole (4a) (1.54 g, 5.0 mmol) and 2-(4-bromophenyl)-4-(4-methoxyphenyl)-1H-pyrrole (3b) (1.64 g, 5.00 mmol) were dissolved in AcOH (25 mL). The reaction mixture was added acetic anhydride (5 mL) and heated to 100 °C for 1 h. Ice (100 mL) and 5 M NaOH (100 mL) was added and the mixture was stirred for 30 min, extracted with CH_2Cl_2 (100 mL × 3). The combined organics were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified on a silica gel column chromatography (1:2, EtOAc/hex), resulting the product as a dark green solid (2.98 g, %96), mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 9.2 Hz, 2H), 7.95 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 9.2 Hz, 2H), 7.14 (s, 1H), 7.05 (d, J = 8.0 Hz, 2H), 6.96 (s, 1H), 6.95 (d, J = 8.0 Hz, 2H), 3.92 (s, 3H), 3.88 (s, 3H), 3.85 (s, 3H). IR (ATR, cm-1) 3074.5, 2831.8, 1589.0, 1246.0. HRMS (TOF-ESI): Calcd ($C_{35}H_{28}BrN_3O_3$) $[M + H]^+$: m/z = 620.13720; found, m/z = 620.13950.

Synthesis of BF_2 Chelate of [5-(4- Methoxyphenyl)-3-(4-Methoxyphenyl)-1H-Pyrrol-2-Yl]-[5-(4-Methoxyphenyl) -3-(4-Bromophenyl)Pyrrol-2-Ylidine]Amine (C1)

C1 was prepared from [5-(4-methoxyphenyl)-3-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[5-(4-methoxyphenyl)-3-(4-bromophenyl)pyrrol-2-ylidene]amine (C) (1.08 g, 1.75 mmol), *N,N*-diisopropylethylamine (3.05 mL, 17.5 mmol),boron trifluoride diethyl etherate (3.24 mL, 26.25 mmol) and dry CH_2Cl_2 (300 mL) according to the method for B1.The residual was purified by column chromatography on silica eluting with hexane/EtOAc (2:1, *v*/v) which gave the product as a dark brown solid (1.02 g, 87%), mp 245–246 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 9.2 Hz,

2H), 8.06 (d, J = 9.2 Hz, 2H), 8.02 (d, J = 9.2 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 6.99 (t, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.84 (s, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H).^{13}CNMR (100 MHz, $CDCl_3$) δ 162.35, 161.10, 160.65, 160.38, 154.90, 131.89, 131.84, 131.79, 131.67, 131.19, 130.96, 130.85, 130.80, 130.76, 130.68, 125.58, 125.02, 124.71, 123.72, 117.96, 117.93, 116.43, 114.32, 114.19, 114.14, 55.45, 55.43, 55.41. IR (ATR, cm^{-1}) 3003.2, 2835.4, 1597.1, 1379.1, 1253.7. HRMS (TOF-ESI): Calcd ($C_{35}H_{27}BBrF_2N_3O_3$) $[M]^+$: m/z = 666.13753; found, m/z = 666.13917.

Synthesis of BF_2 Chelate of [4-Bromo-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)-1H-Pyrrol-2-Yl] -[4-Bromo-3-(4-Methoxyphenyl)-5-(4-Bromophenyl) Pyrrol-2-Ylidene]Amine (CC1)

CC1 was prepared from BF_2 chelate of [5-(4-methoxyphenyl)-3-(4- methoxyphenyl)-1H-pyrrol-2-yl]-[5-(4-methoxyphenyl)-3-(4-bromophenyl)pyrrol-2-ylidine]amine (C1) (0.40 g, 0.60 mmol), N-bromosuccinimide (NBS) (0.22 g, 1.26 mmol) and CH_2Cl_2 (150 mL) according to the method for AA1. The residual was purified by column chromatography on silica eluting with hexane/EtOAc (2:1, *V*/V) which gave the product as a dark brown solid (0.41 g, 83%), mp 292–293 °C. ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.8 Hz, 4H), 7.88 (d, J = 9.2 Hz, 4H), 7.77 (d, J = 9.2 Hz, 2H), 7.59 (s, 4H), 6.99 (d, J = 8.8 Hz, 4H), 6.98 (d, J = 9.2 Hz, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 162.01, 161.11, 160.80, 159.54, 154.22, 144.92, 144.91, 143.37, 143.36, 141.17, 141.16, 132.53, 132.48, 132.33, 131.96, 131.26, 128.81, 125.11, 123.52, 123.19, 121.52, 113.68, 113.64, 55.40, 55.38, 55.33. IR (ATR, cm^{-1}) 3001.2, 2835.4, 1599.0, 1377.2, 1246.0. HRMS (TOF-ESI): Calcd ($C_{35}H_{25}BBr_3F_2N_3O_3$) $[M+H]^+$: m/z = 823.95650; found, m/z = 823.95874.

Synthesis of BF_2 Chelate of [5-(4-Methoxypheny) -3-(4-Methoxypheny)-1H-Pyrrol-2-Yl]-[5-(4-Methoxypheny) -3-(4-Methoxybiphenyl)Pyrrol-2-Ylidine]Amine (C2)

C2 was prepared from[5-(4-methoxyphenyl)-3-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[5-(4-methoxyphenyl)-3-(4-bromophenyl)pyrrol-2-ylidene]amine (C) (0.18 g, 0.30 mmol), 4-methoxyphenylboronic acid (51.47 mg, 0.33 mmol), $Pd(PPh_3)_4$ (7.80 mg, 0.0007 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) according to the method for B2.The obtained residue was purified by column chromatography on silica eluting with toluene, which gave the product as a purple solid (106 mg, 50%), mp 261 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.10 (t, J = 8.4 Hz, 4H), 8.06 (d, J = 9.2 Hz, 2H), 8.05 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.0 Hz, 4H), 6.99 (d, J = 8.4 Hz, 4H), 6.96 (s, 1H), 6.96 (s, 1H), 3.89 (s, 6H), 3.87 (s, 3H), 3.86 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 161.98, 160.85, 160.63, 159.61, 158.99, 156.85, 145.74, 144.97, 143.54, 143.52, 142.49, 142.35, 142.33, 137.86, 132.71, 131.71, 131.66, 131.61, 130.85, 130.73, 130.26, 130.01, 129.96, 129.92, 129.02, 128.20, 126.59, 125.59, 125.28, 124.10, 117.50, 117.15, 117.10, 117.09, 114.31, 114.21, 114.12, 114.10, 55.40, 55.34. IR (ATR, cm^{-1}) 3032.1, 2833.4, 1599.0, 1384.9, 1251.8. HRMS (TOF-ESI): Calcd ($C_{42}H_{34}BF_2N_3O_4$) $[M+H]^+$: m/z =: 694.26888; found, m/z = 694.27082.

Synthesis of BF_2 Chelate of [5-(4-Methoxypheny) -3-(4-Methoxypheny)-1H-Pyrrol-2-Yl]-[5-(4-Methoxypheny) -3-(2,4-Dimethoxybiphenyl)Pyrrol-2-Ylidine]Amine (C3)

C3 was prepared from [5-(4-methoxyphenyl)-3-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[5-(4-methoxyphenyl)-3-(4-bromophenyl)pyrrol-2-ylidene]amine (C) (0.18 g, 0.30 mmol), 2,4-dimethoxyphenylboronic acid (60.05 mg, 0.33 mmol), $Pd(PPh_3)_4$ (7.80 mg, 0.0007 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) according to the method for B2.The obtained residue was purified by column chromatography on silica eluting with toluene which gave the product as a dark brown solid (89 mg, 41%), mp 228–229 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 9.2 Hz, 2H), 8.07 (t, J = 8.6 Hz, 4H), 8.06 (d, J = 9.2 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 4H), 6.61–6.57 (m, 2H), 6.98 (s, 1H), 6.96 (s, 1H), 3.90 (s, 6H), 3.88 (s, 3H), 3.87 (s, 3H), 3.83 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 161.90, 160.81, 160.70, 160.84, 157.69, 157.03, 154.03, 132.51, 131.62, 131.61, 131.55, 131.33, 130.82, 130.74, 129.91, 129.46, 129.23, 129.20, 129.11, 125.36, 124.19, 120.37, 117.41, 117.36, 114.19, 114.13, 114.11, 109.99, 104.79, 99.01, 55.53, 55.48, 55.43, 55.40. IR (ATR, cm^{-1}) 3066.8, 2835.3, 1597.0, 1383.0, 1271.1. HRMS (TOF-ESI): Calcd ($C_{43}H_{36}BF_2N_3O_5$) $[M+Na]^+$: m/z = 746.26140; found, m/z = 746.26448.

Synthesis of BF_2 Chelate of [5-(4-Methoxypheny) -3-(4-Methoxypheny)-1H-Pyrrol-2-Yl]-[5-(4-Methoxypheny) -3-(4-N,N-Diphenylaminobiphenyl)Pyrrol-2-Ylidine]Amine (C4)

C4 was prepared from[5-(4-methoxyphenyl)-3-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[5-(4-methoxyphenyl)-3-(4-bromophenyl)pyrrol-2-ylidene]amine (C) (0.18 g, 0.30 mmol), 4-(diphenylamino)phenylboronic acid (95.41 mg, 0.33 mmol), $Pd(PPh_3)_4$ (7.80 mg,

0.0007 mmol) and K_2CO_3 (0.28 g, 2.00 mmol) according to the method for B2. The obtained residue was purified by column chromatography on silica eluting with toluene which gave the product as a dark brown solid (113 mg, 45%),mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 9.6 Hz, 2H), 8.07 (d, J = 8.8 Hz, 2H), 8.06 (d, J = 9.2 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.29 (t, J = 8.0 Hz, 4H), 7.17–7.14 (m, 4H), 7.13 (s, 1H), 7.06 (t, J = 7.4 Hz, 2H), 7.01 (d, J = 9.2 Hz, 4H), 7.00 (d, J = 8.8 Hz, 4H), 6.97 (s, 1H), 3.90 (s, 6H), 3.88 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 162.76, 161.97, 160.87, 160.85, 147.50, 142.37, 137.61, 136.59, 135.78, 135.69, 131.64, 131.60, 131.34, 130.29, 130.05, 129.99, 129.94, 129.31, 127.76, 126.51, 125.60, 125.32, 124.70, 123.38, 123.18, 114.22, 114.14, 114.12, 55.43, 55.41. IR (ATR, cm^{-1}) 3032.1, 2833.4, 1589.4, 1386.8, 1251.8. HRMS (TOF-ESI): Calcd ($C_{53}H_{41}BF_2N_4O_3$) $[M]^+$: m/z = 830.32400; found, m/z = 830.32609.

Synthesis of BF_2 Chelate of [4-Methoxyphenyl-3-(4-Methoxyphenyl) -5-(4-Methoxyphenyl)-1H-Pyrrol-2-Yl] -[4-Methoxyphenyl-3-(4-Methoxyphenyl)-5-(4-Bromophenyl) Pyrrol-2-Ylidene]Amine (CC2)

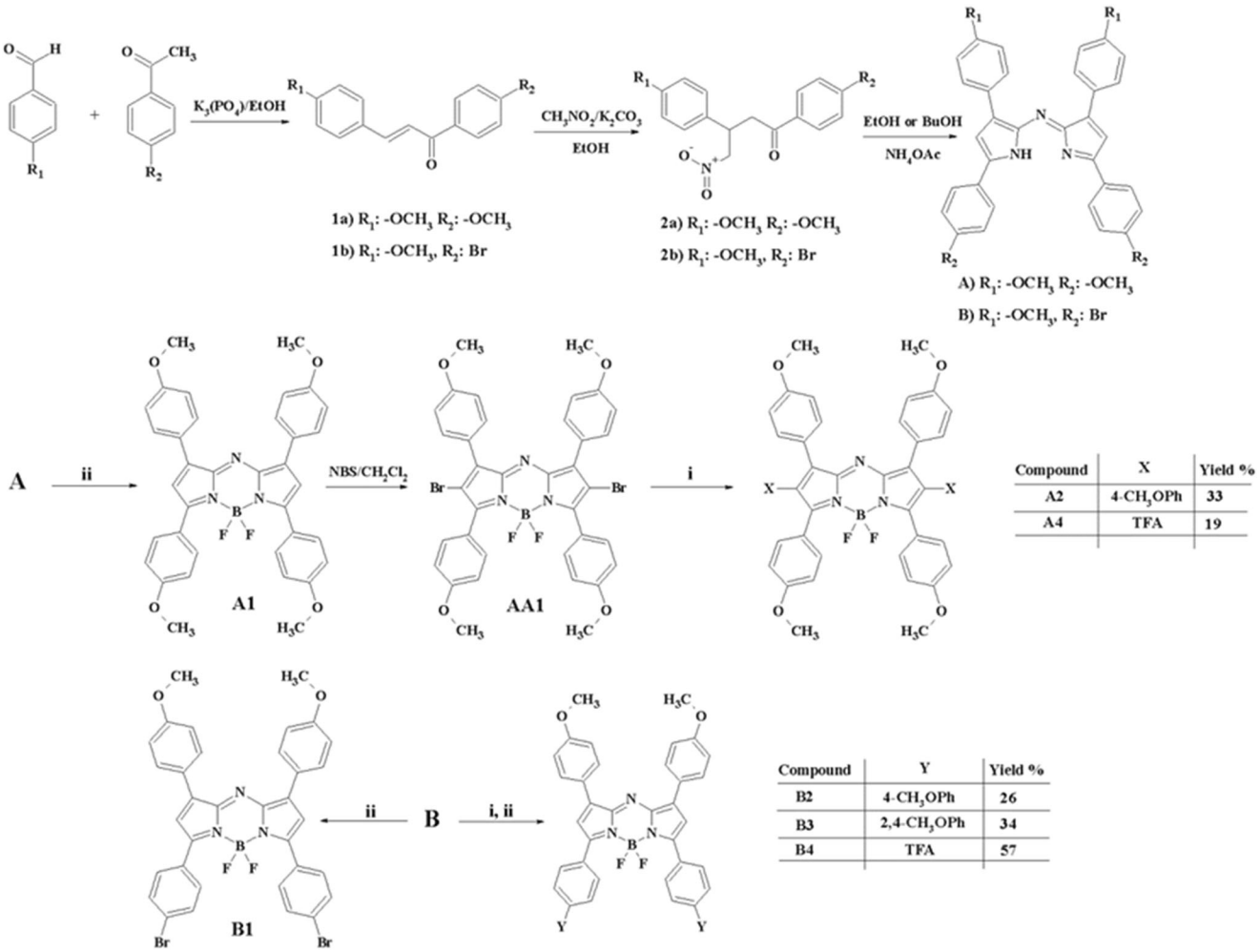
CC2 was prepared from BF_2chelate of [4-Bromo-3-(4-methoxyphenyl)-5-(4-methoxyphenyl)-1H-pyrrol-2-yl]-[4-bromo-3-(4-methoxyphenyl)-5-(4-bromophenyl)pyrrol-2-ylidene]amine (CC1) (0.21 g, 0.25 mmol), 4-methoxyphenylboronic acid (136.8 mg, 0.95 mmol), $Pd(PPh_3)_4$ (19.5 mg, 0.0018 mmol) and K_2CO_3 (0.35 g, 2.50 mmol) according to the method for A2.The obtained residue was purified by column chromatography on silica eluting with toluene which gave the product as a dark brown solid (48 mg, 21%) mp > 350 °C.^{1}HNMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 9.2 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.38, J = 8.4 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 6.90 (d, J = 8.8 Hz, 4H), 6.88 (d, J = 8.8 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 3.81 (s, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.78 (s, 3H). ^{13}CNMR (100 MHz, $CDCl_3$) δ 161.01, 160.39, 160.00, 159.79, 158.79, 158.65, 154.7, 154.65, 146.05, 144.43, 141.14, 139.43, 139.40, 139.39, 132.51, 132.42, 132.11, 131.74, 131.68, 131.12, 131.07, 131.04, 130.92, 130.15, 129.02, 128.20, 125.36, 125.34, 125.28, 124.72, 124.36, 122.75, 113.92, 113.88, 113.32, 55.22, 55.16, 55.12. IR (ATR, cm^{-1}) 3072.6, 2837.3, 1599.0, 1365.6, 1246.0. HRMS (TOF-ESI): Calcd ($C_{49}H_{39}BBrF_2N_3O_5$) $[M+H]^+$: m/z = 880.21922; found, m/z = 880.22060.

Results and Discussion

Synthesis and Coupling Reactions

Symmetrical aza-BODIPY compounds were initially synthesized successfully by condensation of acetophenone and aromatic aldehyde derivatives. Then, unsymmetrical analogues were obtained by pyrrole-nitrosolated pyrrole coupling reactions to compare the photophysical properties of the different substitution patterns as shown in Schemes 1 and 2. Diverse electron donor groups are directly attached at the −2, −3, −5 and − 6 position of aza-BODIPYs. O'Shea's procedures [2, 7] were used in the synthesis of symmetrical aza-BODIPY compounds **A1** and **B1**. Unsymmetrical azadipyrromethene compound **C** was synthesized by condensation of 2-(4-bromophenyl)-4-(4-methoxyphenyl)-1H-pyrrole(3b) and 3,5-(4-methoxyphenyl)-2-nitroso-1H-pyrrole (4a) and afforded in high (96%) yield. The compounds **A1 a**nd **C1** compounds were treated with 2.1 equiv. of N-bromosuccinimide (NBS) in CH_2Cl_2 at room temperature. **AA1** and **CC1** were obtained with 83% and 84% yields, respectively. -3, −3,5, −2,6 aryl bromine substituted azadipyrromethene ligands and aza-BODIPY complexes were designed as starting materials for Suzuki-Miyaura coupling reactions. Reactions were performed with 4-methoxyphenylboronic acid, 2,4-Dimethoxyphenylboronic acid, 4-(diphenylamino)phenylboronic acid as electron donating groups in the presence of tetrakis(triphenylphosphine)palladium(0) $[Pd(PPh_3)_4]$ in H_2O/EtOH/Toluene (1:1:2, by volume) mixture at 85 °C for 24 h. Compounds **B2**-**B4** and **C2**-**C4** were obtained by one pot synthesis using aryl bromine substituted azadipyrromethene ligands. Compounds **A2**, **A4** and **CC2** were synthesized 2,6-dibromine, 2,6-dibromine and 3,4-bromophenyl substituted aza-BODIPY derivatives (Schemes 1 and 2). All reactions have been monitored by TLC analysis and reaction mixture chromatographed by using silica gel.

The yields of the coupling reactions were found to change depending on the reactivity of 3, 3,5 and 2,6 positions of the aza-BODIPY core (Scheme 3). 3 positions of the aza-BODIPY compounds **C2**, **C3** and **C4** have been obtained with 50, 41 and 45% yields, respectively. 3,5 positions of compound **B4** has been obtained higher yield in 57%. On the other hand 3,5 position analogue compounds **B2** and **B3** have been obtained a relatively smaller yield of 26 and 34%. It was observed that the lower yields arise from the poor solubility of the compounds in reaction solvents. Similarly, coupling reactions on the 2,6 substituted aza-BODIPY compounds **A2** and **A4** gave the relatively poor yields **(**33% and 19%, respectively). The poor coupling yields may also be attributed to steric hindrance of the 2,6 positions of the indacene core caused by the existence of 1,7 phenyl groups on the indacene core. Apart from that, when the Suzuki-Miyaura coupling reaction has been performed with 2,3,6 tri-bromine substituted compound **CC1** with excess boronic acid derivative, no all



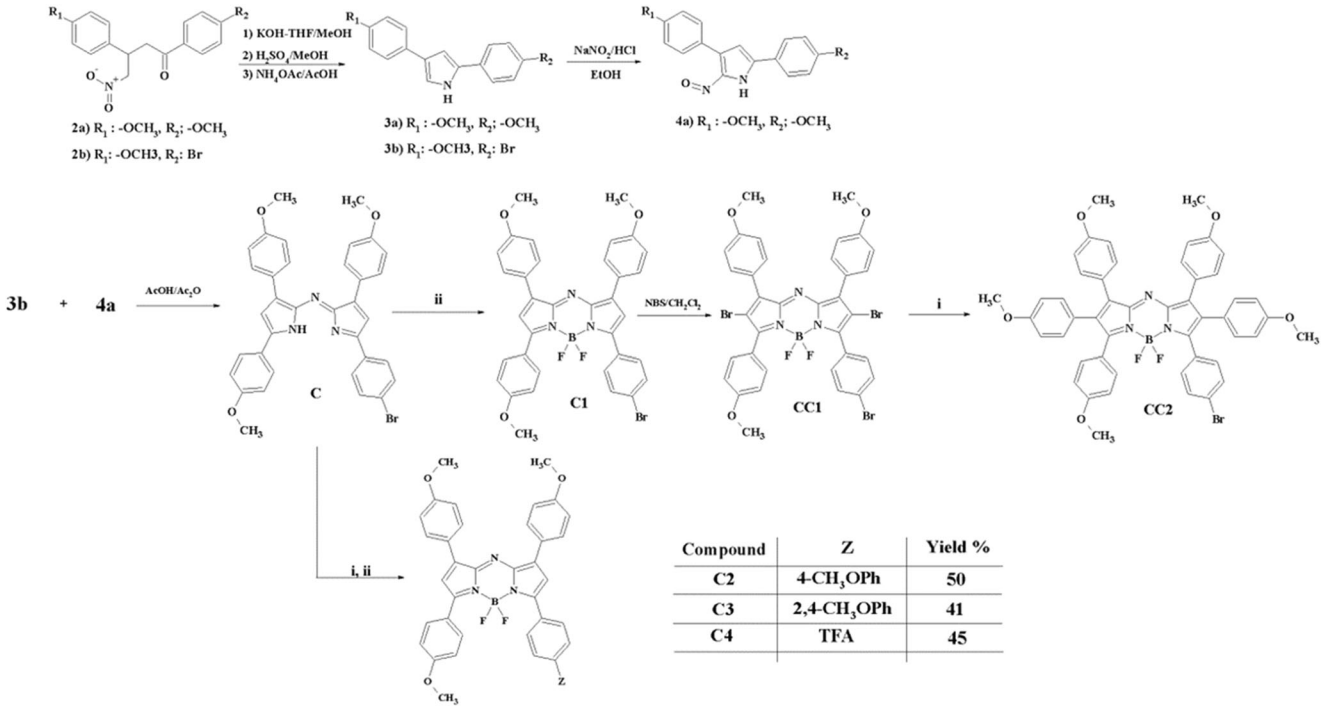
Scheme 1 Synthetic pathway of the symmetrical aza-BODIPY Dyes (i) $Pd(PPh_3)_4$, K_2CO_3, $ArB(OH)_2$, 85 °C, 24 h. (ii) BF_3OEt_2, DIEA, CH_2Cl_2, rt., 24 h

target products have been obtained. Only 2,6 4-methoxyphenyl substituted aza-BODIPY compound has been isolated from this reaction and afforded in 21% yield (Scheme 3). This may indicates the region selectivity in coupling reactions on 2,6 positions compared to 3 or 3,5 positions on the aza-BODIPY scaffold [38, 39].

Spectroscopy and Photophysical Properties

Identification of the compounds was performed through ^{1}H-NMR, ^{13}C-NMR, FTIR and HRMS. In ^{1}HNMR of symmetrical aza-BODIPYs, the 2,6 pyrrole protons appear as a singlet between 6.91 to 7.00 ppm. However, unsymmetrical aza-BODIPY compounds, the pyrrole protons appear as two singlet signals in different ppm and these protons were disappeared in 2,6 phenyl or bromine substituted aza-BODIPY compounds. 1,3,5,7 aryl protons of compounds **A1**, **B1**, **B2**, **B3**, **B4**, **C2**, **C3**, **C4** were observed between 8.05 to 8.15 ppm. On the other hand, 2,6 phenyl substituted **A2**, **A4** and **CC2** compounds were monitored to upfield shift between 7.53 to 7.46, compared to 2,6 unsubstituted aza-BODIPY compounds. These results show that the electronic properties of aza-BODIPY core at 2,6 positions could be changed markedly [40]. Interestingly, ^{1}HNMR of 3 bromine substituted aza-BODIPY compound **CC1** was observed only one sharp singlet peak in 7.59 ppm corresponding to four aryl protons (Fig. 1). Similar singlet peak was observed our previous study at 2,3,5,6 bromine substituted aza-BODIPY compounds [41]. This effect can be observed in para-disubstituted benzene having two identical substituents, because all of the hydrogens are magnetically equivalent stemming from the symmetry in the molecule.

High resolutions mass spectra (HRMS-ESI-TOF) of the compounds **A1**, **A4**, **B2**, **C1** and **A**, **A2**, **B3**, **B4**,**C**, **C2-C4** showed molecular and protonated molecular ion peaks, respectively and compound **C3** gave $[M\text{-}Na]^+$ molecular ion peaks. Isotope peaks were observed depending on the number of bromine atoms to bromine substituted aza-BODIPY compounds consisted with the assigned formulations. For instance, the spectrum for compound **CC1** consisting of three



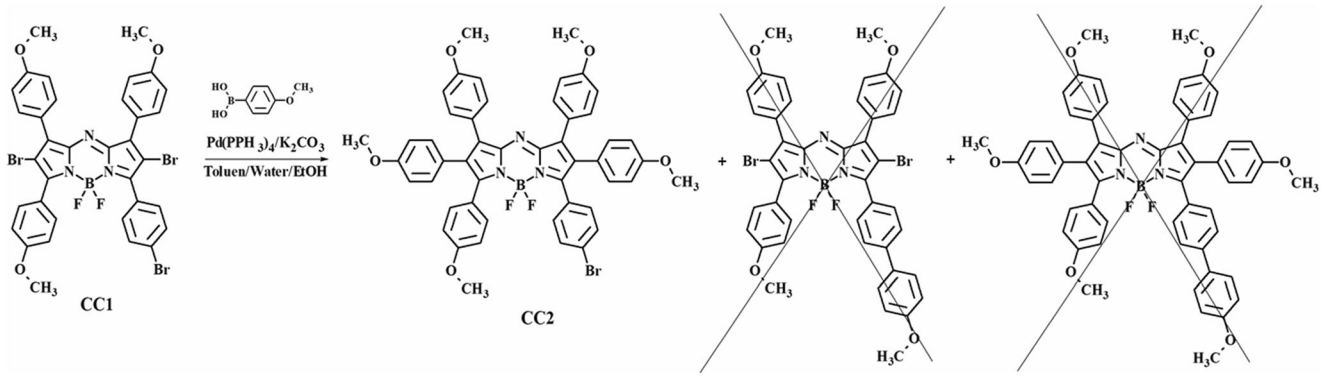
Scheme 2 Synthetic pathway of the unsymmetrical aza-BODIPY dyes (i) $Pd(PPh_3)_4$, K_2CO_3, $ArB(OH)_2$, 85 °C, 24 h. (ii) BF_3OEt_2, DIEA, CH_2Cl_2, rt., 24 h

bromine atoms was revealed M, M + 2, M + 4 and M + 6 peak groups as shown in Fig. 2.

The photophysical parameters, measured in $CHCl_3$ solution (5×10^{-6} M), are reported in Table 1. The absorption spectra of all aza-BODIPY derivatives exhibited two intense peaks, In the UV region (between 311 to 351 nm, corresponding to the $\pi \rightarrow \pi^*$transitions and the major characteristic absorption bands in the NIR region (between 672 to 718 nm, $S_0 \rightarrow S_1$ transitions) (Fig. 3). The extinction coefficients for newly synthesized series are high, in the range of 20,400–51,600 M^{-1} cm^{-1} for high energy region and in the range of 46,600–147,600 M^{-1} cm^{-1} for the low energy region.

The Stokes shifts for these new series are generally narrow (600–1045 cm^{-1}), except for the compound **B4** (1443cm^{-1}). Furthermore, substitution of bromine atoms in the 2,6 positions (**AA1** and **CC1**) involves 12 and 11 nm hypsochromic shift compared to **A1** and **C1.** Owing to the introduction of methoxyphenyl and triphenylamine groups onto the 2 and 6 positions in the aza-BODIPY moiety, compounds **A2** and **A4** shows lower hypsochromic shift compared to **A1**. However, 10 nm bathochromic shift was observed when compared to **AA1** compound. In emission spectra, all 2,6-substituted compounds gave reduced fluorescence quantum yields. Besides, quenched fluorescence was observed for the compound **A4** due to the strong electron donating behavior of directly linked triphenylamine group to the aza-BODIPY core.

The 3 and 3,5 π-extended aza-BODIPYs (**B2**-**B4** and **C2**-**C4**) containing electron donating groups showed significant bathochromic shifts on both absorption and emission spectra



Scheme 3. Synthesis of the compound **CC2**

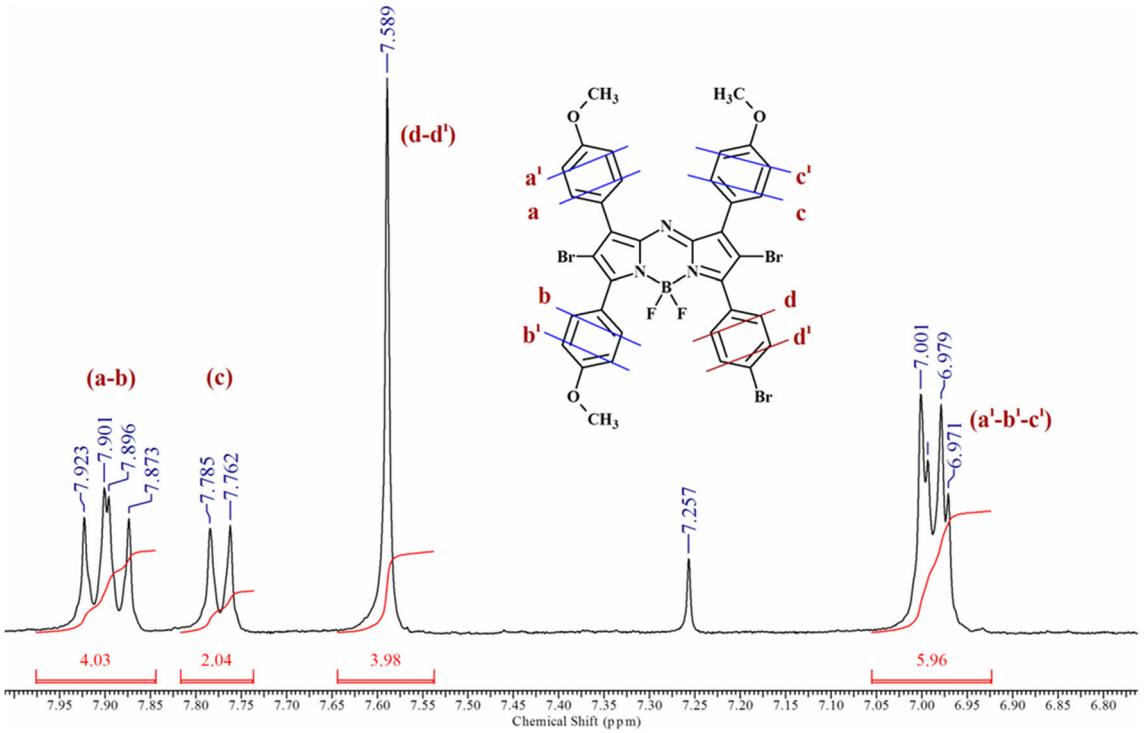


Fig. 1 ^{1}H NMR spectra of the compound **CC1**

depicted in Figs.3 and 4, respectively. 3,5 substituted series **B2**/**B3** (24 and 22 nm) and 3 substituted series compound **C2**/**C3** (12 and 11 nm) showed systematic bathochromic shifts compared to reference compounds **B1** and **C1,** respectively. The largest red-shift in the series was observed for the compound **B4** (λ_{abs} = 718 nm), which has two strong electron-donating and π-extended triphenylamine groups attached to the 3,5positions of the aza-BODIPY moiety. Additionally, the absorption bands of the triphenylamine substituted compounds relatively broader and the Stokes shifts are larger compared to those of methoxy substituted counterparts.

Compounds **C2, C3** and **C4** have electron donating groups on 3 position of the aza-BODIPY core that exhibited red shifted absorption maxima compared to unsubstituted compound **C1.** Note that, the highest molar absorption coefficient was observed 3 π-extended and 2,4-dimethoxyphenyl substituted unsymmetrical aza-BODIPY compound **C3** (ε =147,000 M^{-1} cm^{-1}). And also unsymmetrical compound **C2** showed the highest fluorescence quantum yield (Φ_F = 0.44).

It's clear from the graphs that the triphenylamine group as an electron donor forms a charge transfer state [14].The triphenylamine substituted compounds have lower molar absorption coefficients and quantum yields. Conversely, the aza-BODIPY derivatives with weaker electron donating groups or unsubstituted aza-BODIPYs have higher values (see Table 1). Note that, the fluorescence quantum yields of the compounds **A1**, **B1** and **C1** which have only difference on the 3 position of the core structure as bromine and methoxy group don't differ greatly. This may be explained by the equally capable of donating electrons of relevant ones to the aza-BODIPY core when the appended to 3,5 positions of the core. As a general result, compared to unsubstituted analogues, the bathochromic shifts between 40 and 50 nm both in absorption

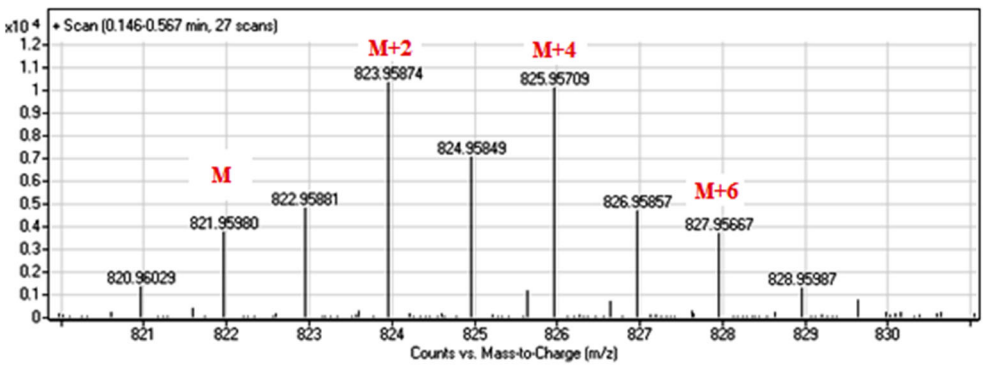


Fig. 2 HRMS-ESI-TOF spectra of the compound **CC1**

Table 1 Summary of the photophysical properties of the aza-BODIPY dyes. All spectra were measured in chloroform

Compound	$\lambda_{abs(nm)}$	$\lambda_{em(nm)}$	$\varepsilon[M^{-1}\ cm^{-1}]$	FWHM (nm)	Stokes Shifts (cm^{-1})	Φ_F
A	324/628	–	46,400/60200	60/90	–	–
A1	336/692	722	20,400/89400	51	600	0.360
AA1	680	718	61,600	57	77	0.015
A2	690	738	46,600	83	943	0.004
A4	311/690	–	42,000/52600	130	–	–
B	315/615	–	54,200/54400	46/90	–	–
B1	330/674	708	20,200/62400	63	712	0.310
B2	344/698	744	22,800/77400	66	886	0.430
B3	315/696	738	27,400/75200	66	819	0.410
B4	351/718	801	51,600/61000	91	1443	0.010
C	318/619	–	33,800/39600	63/97	–	–
C1	331/683	714	24,800/72600	54	636	0.360
CC1	672	711	85,800	58	816	0.004
C2	339/695	729	21,400/68800	59	671	0.440
C3	310/694	733	43,400/147600	58	767	0.230
C4	344/701	735	41,600/83000	73	660	0.036
CC2	680	732	66,200	89	1045	0.001

and emission spectra were provided by coupling reactions for the new dyes.

In order to determine the singlet oxygen production features of the novel compounds, singlet oxygen generation study with 1,3-diphenylisobenzofuran (DPBF) scavenger was carried out in solution (Figs. 5 and 6).

The formation of triplet state by intersystem crossing (ISC) in emissive molecules causes the fluorescence quenching that makes them potential candidates in singlet oxygen production. In this regard, singlet oxygen generation was expected to obtain only non-emissive compounds [42]. Therefore, compounds **A1**, **B1-B3** and **C1-C3** were not expected any singlet oxygen efficiency due to the high fluorescence quantum yields (Table 1). Thus, we have tested non-emissive symmetrical and asymmetrical compounds which substituted 3, 3,5 and 2,6 π-extended and electron donating groups (**A2**, **A4**, **B4**, **C4** and **CC2)**. Our singlet oxygen determination studies shows that compounds **A2**, **A4**, **B4**, **C4** and **CC2** have not changed singlet oxygen efficient of aza-BODIPY dyes, although these compounds have showed weak emission features. This may due to radiationless decay to the ground state instead of energy or electron transfer to the triplet state of designed aza-BODIPY dyes [43]. However, 2,6 dibromine substituted aza-BODIPY compounds **AA1** and **CC1** were showed high singlet oxygen quantum yields because of the heavy atom effect of bromine atoms [7, 41]. So that compounds **AA1** and **CC1** solution with DPBF were observed decrease in absorption spectra at 414 nm (Figs. 5 and 6, respectively). The Singlet oxygen quantum yields of the compounds **AA1** and **CC1** were calculated 71% and 74% in DCM against methylene blue which was used as standard, respectively. Based on the results from literature, halogenated aza-BODIPY compounds generally show higher singlet oxygen production values about %70 ($\Phi\Delta$ =0.70 in DCM) [8, 10, 44]. From this point, it can be concluded that the compounds **AA1** and **CC1** also have to some degree elevated singlet oxygen

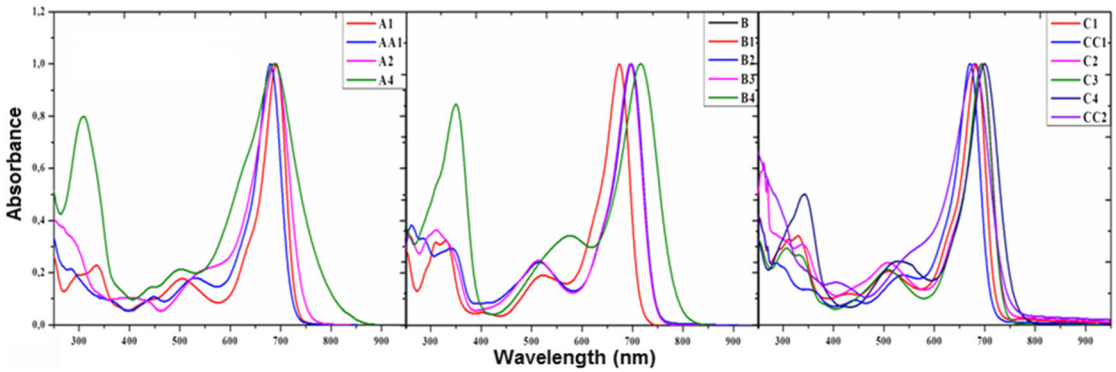


Fig. 3 Normalized absorption spectra of aza-BODIPY dyes (5×10^{-6} M, in $CHCl_3$)

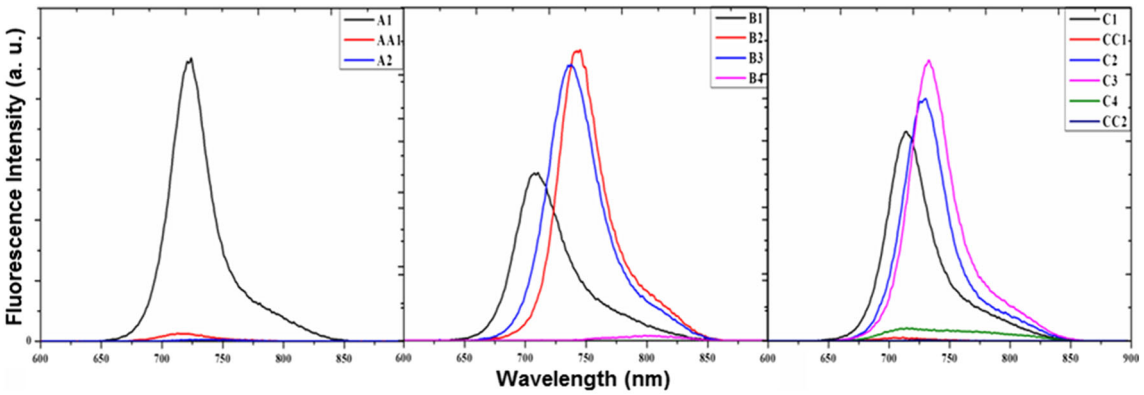


Fig. 4 Emission spectra of the aza-BODIPY dyes (5×10^{-6} M, in $CHCl_3$)

production capabilities. Note that, even the compounds have close features in the production of singlet oxygen, novel compounds could be excited with lower energy. In this respect, extending the π-electron system and asymmetric structure of the aza-BODIPYs via Suzuki-Miyaura coupling do not make them efficient sensitizer in photodynamic therapy applications.

Conclusions

In summary, we prepared 3, 3,5 and 2,6 substituted symmetrical and unsymmetrical aza-BODIPY dyes via Pd-catalyzed Suzuki-Miyaura cross coupling reactions. The Suzuki-Miyaura coupling reactions on aza-BODIPY derivatives in 3,5 [44–46] and 2,6 [40] positions are very limited and also 3 positions reactions of the unsymmetrical aza-BODIPY compounds were the first example in the literature. In this paper, we reported that at 3, 3,5 and 2,6 positions Suzuki-Miyaura reactions effect of photophysical and spectroscopic properties. 2,6 substituted aza-BODIPY compounds showed drastically change in the electronic properties as well as fluorescence, absorption intensities and stokes shifts were altered dramatically. And also these series were synthesized with poor yields compared to 3 and 3,5 positions because of the steric hindrance. The highest bathochromic shifts were observed π-extended and strong electron donating groups at 3,5 positions. Our previous work indicated that extended π-conjugation and strong electron donating groups cause increased two-photon absorption properties of aza-BODIPY dyes at telecommunication wavelengths. Furthermore, 2,6-dibromine substituted aza-BODIPY compounds **AA1** and **CC1** were exhibited significantly high singlet oxygen quantum yields were found to be 71 and 74% respectively. These data may open an effective perspective and these compounds could be good candidates for diverse applications such as photodynamic therapy (PDT) and two photon absorption (2PA). In particular, synthesized compounds may be applicable for n-type semiconductors on

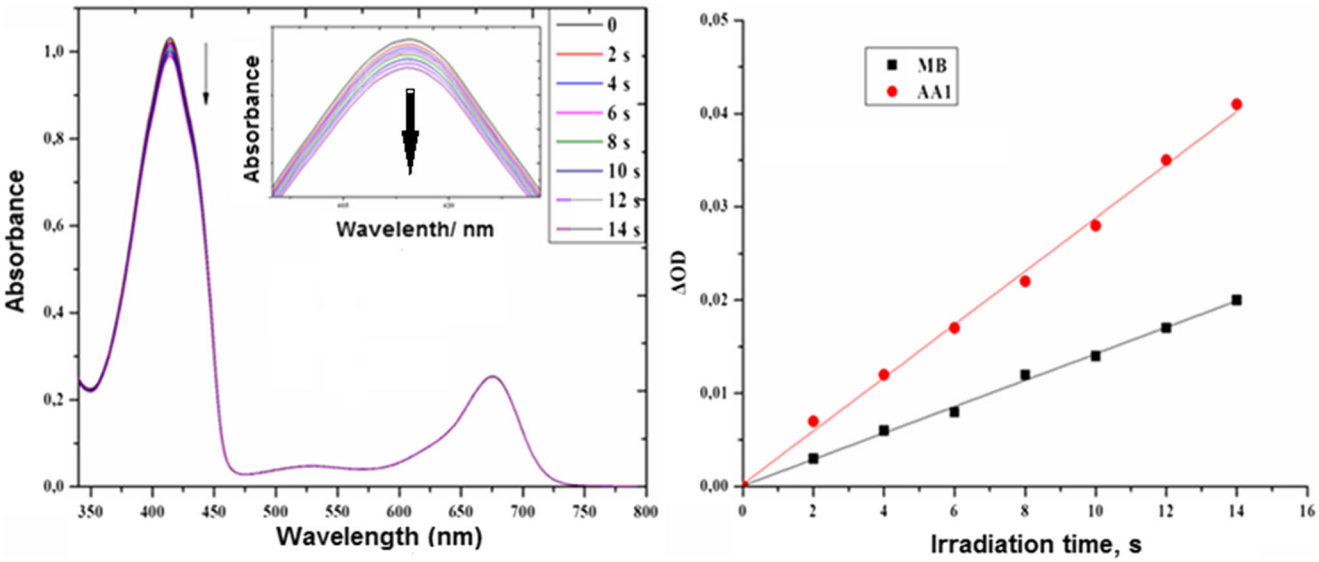


Fig. 5 5Absorption spectra of DPBF upon irradiation in the presence of the compound **AA1** for 14 s (recorded at 2 s interval) and plot of change in absorbance of DPBF at 414 nm vs irradiation time ($\lambda_{ex} = 630$ nm) against methylene blue (MB) as the standard in CH_2Cl_2

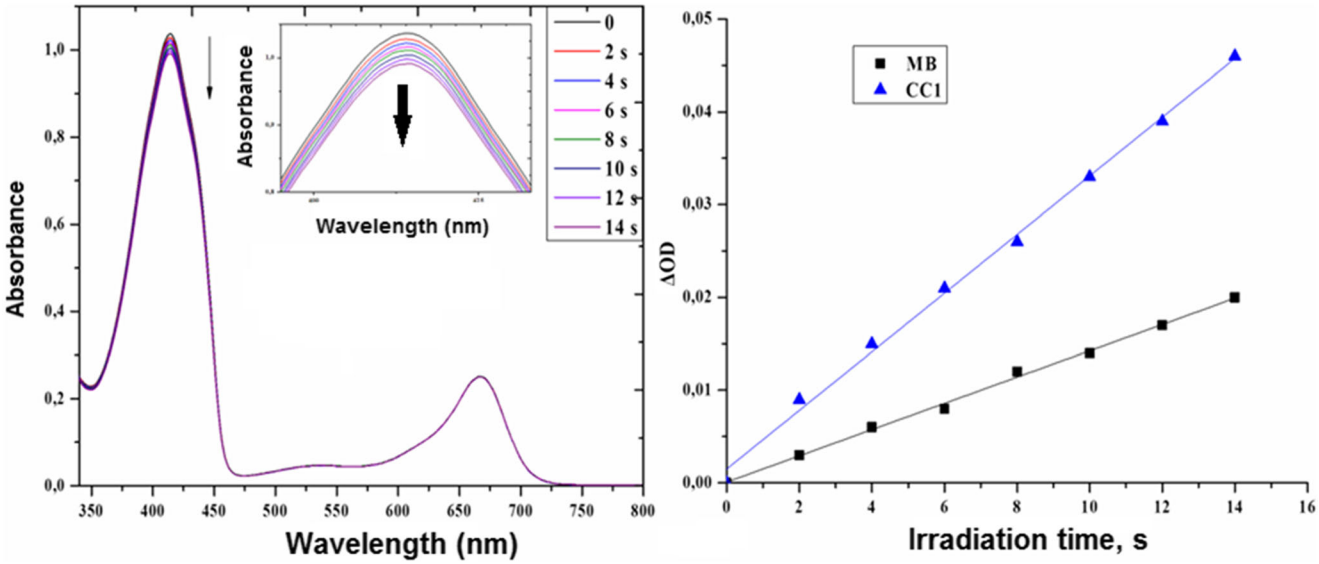


Fig. 6 Absorption spectra of DPBF upon irradiation in the presence of the compound **CC1** for 14 s (recorded at 2 s interval) and plot of change in absorbance of DPBF at 414 nm vs irradiation time ($\lambda_{ex} = 630$ nm) against methylene blue (MB) as the standard in CH_2Cl_2

organic photovoltaic cells (OPVs) due to the several desirable characteristics, for instance, long wavelength absorption, high FWHM and high molar absorption coefficients, as a subject of future study.

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Compliance with Ethical Standards

Conflicts of Interest/Competing Interests The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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