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# Near-Infrared Nitrofluorene Substitued Aza-Boron-dipyrromethenes Dyes

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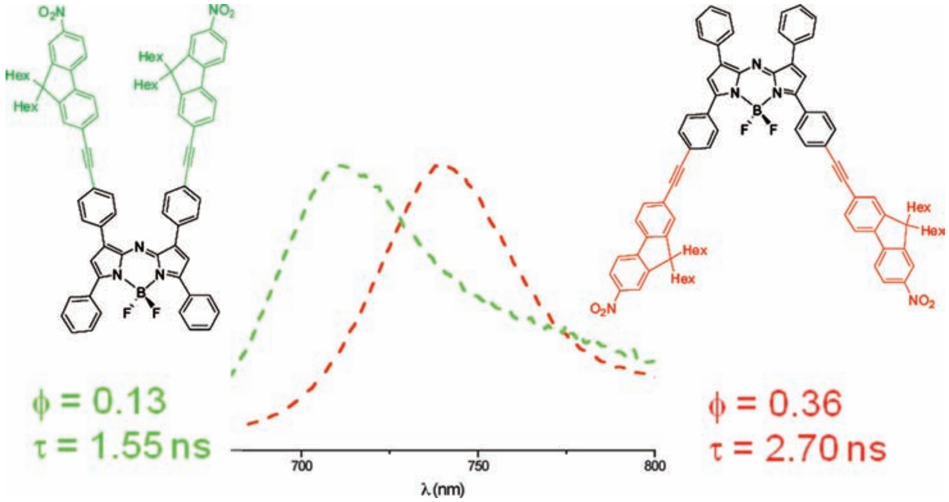
## ABSTRACT



**The synthesis, spectroscopic properties, and TD-DFT calculations of new aza-Boron-dipyromethene dyes featuring pendant nitrofluorenylethynyl substituents are described. This functionalization allows for moving the luminescence in the NIR, conserving a good quantum yield efficiency.**

Previously confined to restricted areas (e.g., optical recording, laser printing and filters),[1] near-infrared (NIR) dyes have found these last years new applications in several important fields such as bioimaging, sensing and photodynamic therapy or photovoltaics, organic light emitting diodes, advanced optoelectronics, and nonlinear optics.[2] The emergence of these technologies triggered the design of new NIR chromophores featuring optimized spectroscopic properties in the 700−1200 nm spectral range. In this context, particular attention has been focused on NIR luminescent dyes for *in vivo* microscopy imaging applications.[2c] Indeed, the NIR region is less absorbed and scattered by biological tissues, allowing deeper penetration and higher contrast. However, the emission red-shift up to the NIR is generally accompanied by a strong decrease of the quantum yield, so a great challenge is to design chromophores featuring high quantum yield (Φ) beyond 700 nm. In this spectral range, cyanine dyes are the most frequently used probes, and some of them are commercially available despite their rather modest quantum yield and photostability.[1,2] Alternatively, Boron-dipyrromethene dyes (**A**, Figure 1) have emerged as a cyanine subclass featuring sharp fluorescence emission band with a high quantum yield and higher photostability in the biological environment.[3] Except in a few cases,[3c] their

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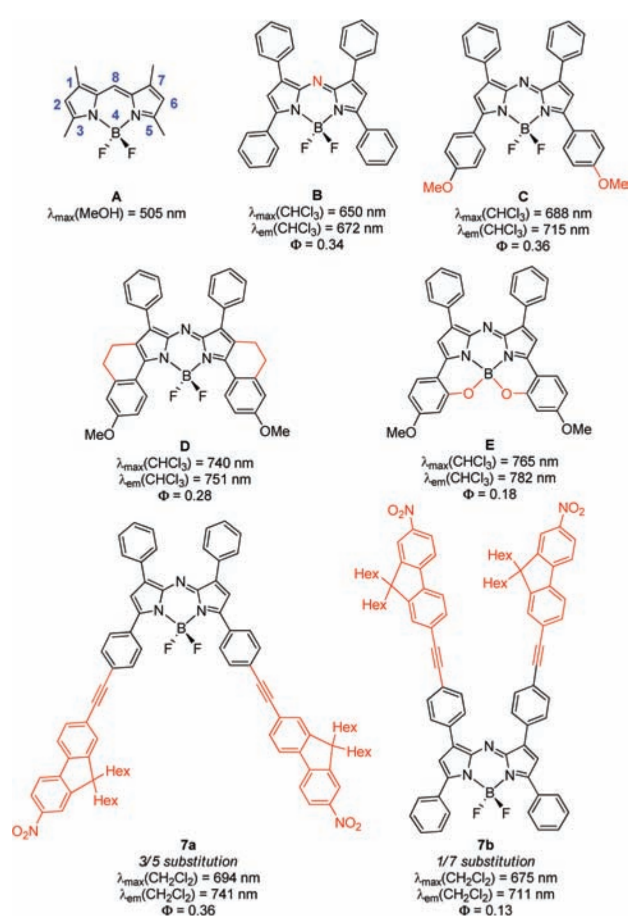
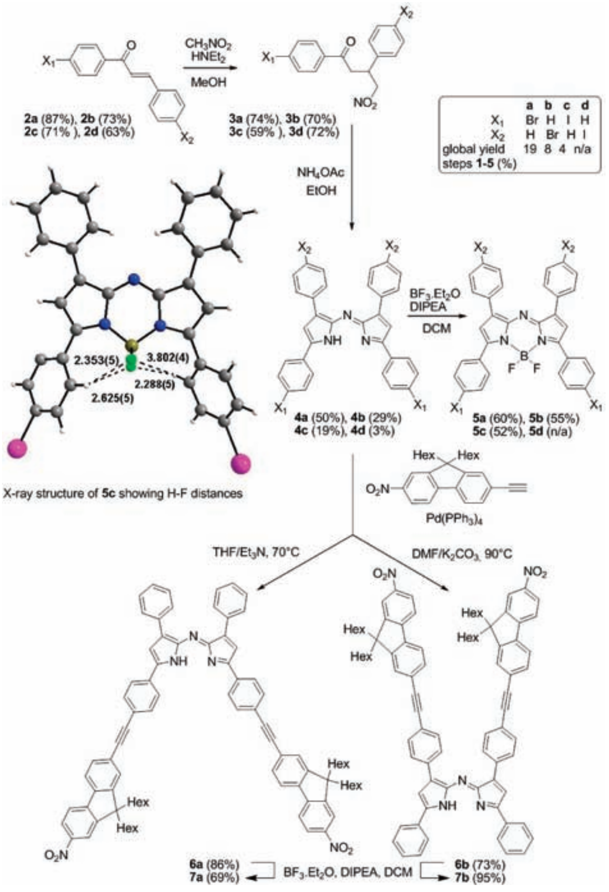


**Figure 1.** Different strategies envisaged to displace the absorption and the emission to the NIR spectral range.

absorption and emission are located in the visible range. Recent studies have shown that it is possible to move the photophysical properties to the red only by substituting the *meso*-carbon by a nitrogen atom (the aza-Boron-dipyromethene dyes **B**, Figure 1).[4b] In this family, the compound **C** functionalized with electro-donating methoxy group exhibited a 715 nm emission with a good 0.36 quantum yield.[4] This chromophore is now the benchmark of the family and was successfully used as bioconjugate or bioprobes for imaging or sensing applications.[5] With **C** as reference, additional NIR bathochromic shifts were achieved upon rigidification of the aza-Boron-dipyromethene skeleton either by annelation (**D,** $\Delta\lambda_{em} = 36$ nm)[6] or by formation of intramolecular B−O six members rings (**E**, $\Delta\lambda_{em} = 67$ nm).[7] Unfortunately, this interesting NIR displacement of the spectroscopic properties was obtained with a significant decrease of the quantum yield efficiency.[6,7]

Here, we show that extension of the conjugated pathway in absence of any electron-donating fragment results in a marked red-shift of the emission conserving the quantum yield efficiency. To that end, we take advantage of the versatile aza-Boron-dipyromethene structure to substitute the 1/7 (**7a**) or 3/5 (**7b**) positions by nitrofluorenylethynyl moieties (Figure 1). The synthesis, characterization, and photophysical properties are described and interpreted on the basis of time-dependent density functional theory (TD-DFT) calculations.

**Scheme 1.** Synthesis of Chromophores



The synthesis of the target compounds **7a**,**b** (Scheme 1) involves as key step a Sonogashira cross-coupling reaction between nitrofluoreneacetylide and an iodo or bromo-functionalized intermediate. In this reaction, starting from aza-Boron-dipyrromethenes **5a**−**c** results in the loss of the $BF_2$ fragment, therefore the aza- dipyrromethenes **4a**−**d** were used as precursors. These latter synthons were prepared using

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(3) (a) Ulrich, G.; Ziessel, R.; Harriman, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 1184–1201. (b) Loudet, A.; Burgess, K. *Chem. Rev.* **2007**, *107*, 4891–4932. (c) Umezawa, K.; Nakamura, Y.; Makino, H.; Citterio, D.; Suzuki, K. *J. Am. Chem. Soc.* **2008**, *130*, 1550–1551. (d) Descalzo, A. B.; Xu, H.-J.; Shen, Z.; Rurack, K. *Ann. N.Y. Acad. Sci.* **2008**, *1130*, 164.

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the classical procedure.[4] Unfortunately, all attempts to optimize the critical cyclization steps—changing the solvent, temperature, ammonium sources - failed and the yield remained rather low, particularly for iodo derivatives **4c**,**d** mostly due to their poor solubility. Crystals suitable for X-ray diffraction analysis were obtained for **4a** and boron containing analogous **5a**−**c** (Supporting Information and Scheme 1). The molecular structures are similar to that of already described aza-Boron-dipyromethene dyes.[8] **5a**−**c** exhibit a strong intramolecular interaction between the two fluorine atoms of the $BF_2$ moiety and the *ortho*-protons from the phenyl in 3/5 positions (Scheme 1), with average distances of 2.737, 2.432, and 2.767 Å, respectively. Considering the global yields, the bromo-functionalized intermediates **4a**,**b** were picked up to achieve the synthesis leading to the formation of **6a**,**b** with 86 and 73% yield, respectively. Finally, the $BF_2$ moiety was introduced classically using boron trifluoride etherate and diisopropylethylamine.

All compounds were fully characterized by $^1H$, $^{13}C$ NMR spectroscopy, high resolution mass spectroscopy or elementary analyses (see Supporting Information). All NMR signals (protons and carbons) of **7a**,**b** were assigned by 2D NMR experiments. Interestingly, the $^{13}C\{^1H\}$ JMOD NMR signal assigned to the two *ortho*-carbon atoms belonging to the phenyl in 3/5 positions appears as a well resolved triplet (Figure 2). Such multiplicity is not observed in the dipyromethene precursors (**6a**,**b**) and is due to a through space (TS) intramolecular coupling with the two fluorine atoms with a $J^{TS}_{C-F}$ coupling constant of about 4.6 and 4.1 Hz for **7a**,**b**, respectively. This peculiar effect has been already reported,[9] and confirms that the H···F interactions observed in the solid already occurs in solution.

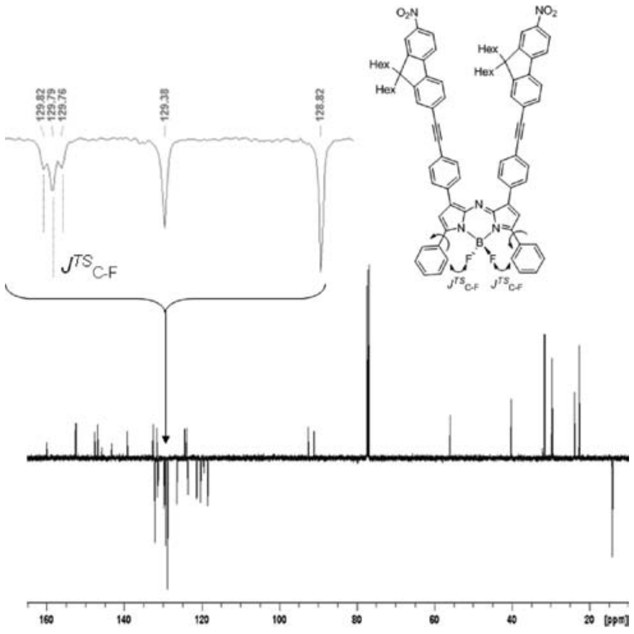

**Figure 2.** JMOD $^{13}C$ NMR (125.75 MHz, $CDCl_3$) of **7b**.

The spectroscopic properties were determined in diluted dichloromethane solutions and are compiled in table 1.

**Table 1.** Spectroscopic Data in Dichloromethane Solution

| dye | $\lambda_{abs}$ nm | $\lambda^{theo}_{abs}$ nm | $\lambda_{em}$ nm | $\varepsilon$ L mol$^{-1}$ cm$^{-1}$ | $\tau$ ns | $\Phi^a$ |
|---|---|---|---|---|---|---|
| **C** | 687 | – | 721 | 87 000 | – | 0.28 |
| **5a** | 658 | – | 687 | 90 000 | – | 0.15 |
| **5b** | 655 | – | 682 | 84 000 | – | 0.12 |
| **5c** | 663 | – | 692 | 76 000 | – | 0.21 |
| **7a** | 694 | 671 | 741 | 100 000 | 2.70 | 0.36 |
| **7b** | 675 | 665 | 711 | 86 000 | 1.55 | 0.13 |

[a] **C** as reference ($CHCl_3$, $\Phi = 0.36$).[4]

Halogen substituted compounds **5a**−**c** show the typical behavior of aza-Boron-dipyromethene dyes with an intense sharp absorption centered around 660 nm and a mirror emission around 685 nm (Figure 3). Lengthening the conjugated skeleton (**7a**,**b**) results in a significant bathochromic shift both in absorption (694 and 675 nm) and emission (741 and 711 nm, respectively). The quantum yields of all compounds were determined using Stern−Volmer plot method using **C** as reference. They are rather modest except for **7a**. Absorption and emission are more red-shifted for a

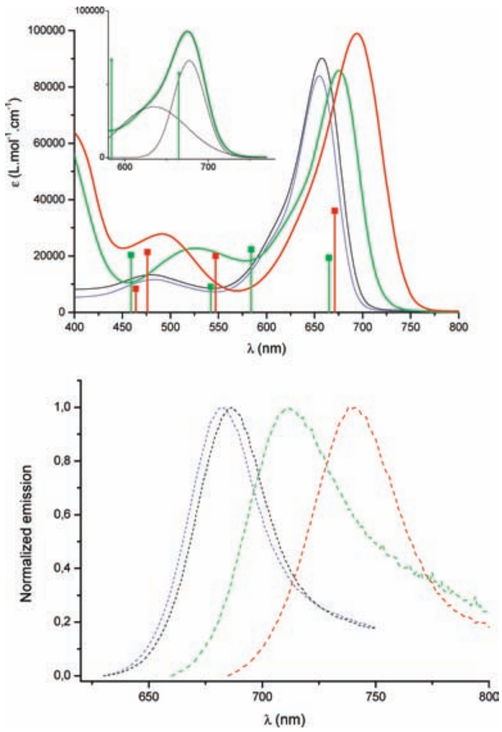

**Figure 3.** Absorption (top) and normalized emission (bottom) for **5a** (black) and **5b** (blue),**7b** (green) and **7a** (red) in DCM. (Inset) Deconvolution of **7b** (green) in two Gaussian curves. Calculated transitions for **7′a,b** are given by vertical lines.

substitution in the 3/5 (**7a**) than in the 1/7 positions (**7b**). This effect is also observed for the dipyromethene precursors (**6a**,**b**) and can be therefore related to the dye structure itself: the *ortho*-pyrollic position inducing a better delocalization. In addition, **7a** exhibits both quantum yield twice higher and lifetime twice longer than **7b**. These phenomena can be rationalized by the rigidification induced by the C−H···F interactions of the extended $\pi$-conjugated substitution in the 3/5 positions occurring for **7a**, restricting free rotation motions hence, nonradiative deactivation processes. When compared to the benchmark **C**, **7a** presents a larger quantum yield efficiency (0.36 against 0.28 in DCM) and its emission is more displaced into the NIR (740 nm against 720 nm). This red-shift observed for **7a** is mainly due to the longer $\pi$-conjugated skeleton whose excited state reorganization induces a larger Stokes shift (914 vs 686 cm$^{-1}$ for **C**).

Finally, the nature of the transitions at the origin of the absorption spectra was investigated by a time-dependent density functional theory (see Supporting Information) in the case of **7′a**,**b** featuring methyl pendant group for simplicity (Table 1). The calculated trends are in good agreement with experimental data; in particular, the more pronounced red-shift for the isomer substituted in the 3/5 positions (**7′a**) is well reproduced.

In both cases, the lower energy transition is composed of a major contribution of the HOMO → LUMO excitation and a minor HOMO-2 → LUMO one (see Supporting Information). The corresponding molecular orbitals are represented in Figure 4 in the case of **7′a**. The HOMO is mainly distributed over the phenyls and alkynes and the central pyrroles whereas the LUMO is centered on the central aza-Boron-dipyromethene core. This monoelectronic excitation presents a marked cyanine character. On the other hand, the HOMO-2 orbital is mainly developed over the periphery of the molecule, delocalized from the phenyl to the fluorenyl moieties suggesting that the second excitation presents a pronounced charge-transfer (CT) character. Consequently, the lowest energy transition can be best described as a mixing of strong cyanine and minor charge transfer type transitions, as already mentioned for Boron-dipyromethene dyes.[10] This admixing contributes to the red-shift of the spectroscopic properties. In addition, the HOMO-1 → LUMO excitation, featuring also a marked CT character (Figure 4) was calculated at 547 and 584 nm for **7′a**,**b**, respectively and cannot be unambiguously attributed to an experimental band. It may correspond either to the second band experimentally observed at 490 and 524 nm for **7a**,**b**, respectively or to the shoulder observed in the lower energy transition (Figure 4, inset), generally assigned to a vibronic contribution.[10]

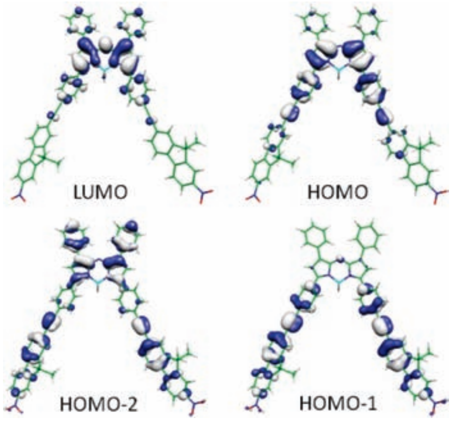

**Figure 4.** Orbitals mainly involved in the calculated excited states of **7′a**.

Importantly, for both CT transitions, the nitro groups do not behave as an acceptor (no contribution to the LUMO), underlining the stronger electro-withdrawing character of the central aza-Boron-dipyromethene moieties.

In conclusion, this paper describes an alternative way to move the photophysical properties of aza-Boron-dipyromethene dyes to the NIR thanks to peripheral substitutions. The extension of conjugation introduces some charge transfer contribution in the lowest energy transitions and results in a larger emission Stokes-shift due to excited state reorganization. Both effects are responsible for the red-shift of the spectroscopic properties. This study also pointed out the more efficient 3/5 substitution in terms of delocalization and higher rigidification due to the presence of intramolecular C−H···F interactions.

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**Supporting Information Available:** Experimental procedures, characterization data, X-ray structures, crystal data, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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