Laterally $\pi$-expanded fluorone dye as an efficient near infrared fluorophore


The synthesis and photophysical properties of new dibenzo[b,i]fluorone dye frameworks (BX and FBX) are described. Both BX and FBX display near infrared sharp absorption and emission upon the addition of base due to the achievement of efficient $\pi$-conjugation based on the small bond alternation strategy.

A considerable attention has been focused on the development of near-infrared (NIR) absorption and emission dyes used for bio-imaging and recordable disks such as CD-R and DVD-R. In general, in order to create the molecules having small HOMO-LUMO gap, expansion of $\pi$-conjugated system is one of the most straightforward strategy. However, large $\pi$-conjugated molecules such as higher acenes are often chemically unstable and difficult to handle because of their intrinsic high reactivity and insolubility. Thus, developing NIR dyes with smaller $\pi$-system (molecular size) is highly desired. Xanthene dyes e.g. rhodamines and fluoresceins display long-wavelength absorption and emission despite their relatively small molecular size. These are achieved by small bond length alternation (BLA) originated from the contributions of resonance structures (Scheme 1). Beside them, rhodamine 110 and fluorescein show high fluorescence quantum yields ($\phi_f$ >70%).

From these advantages, it is expected that $\pi$-expansion of these dyes generates efficient NIR absorption and emission molecules. Representative $\pi$-expanded fluoresceins are shown in Figure 1. Strongin et al. have reported synthesis of seminaphtho[α]fluorone (SNAFR-1), which could display white emission. They also reported the unique naphthofluoroscein (molecule A) displaying the low barrier hydrogen bonding to modulate the HOMO-LUMO gap. Tsukabi et al. reported another type of naphthofluoroscein (molecule B) as a linearly expanded fluorescein displaying broad absorption and emission at pH 11 with $\phi_f$ of 0.17%.

![Scheme 1](image)

Figure 1. Representative $\pi$-expanded fluoresceins and pentacene.

Here, we report the synthesis and photophysical properties of structurally well-defined dibenzo[b,i]fluorones BX and FBX. Importantly, we find that new dibenzofluorones display the sharp and the longest NIR absorption and emission among the naphthofluorones so far reported upon the addition of base. First, as a model compound, fluorone dye X was synthesized from methoxyfluorone 1 according to the literature. Single crystal X-ray diffraction analysis confirms the structures of 1 and its protonated form $\text{XH}^+\cdot\text{Br}^-$ (Figure 2). As we expected, compound 1 has the quinoidal bond length manner at half a part and aromatic one at the other half a part. On the other hand, $\text{XH}^+\cdot\text{Br}^-$ clearly exhibits small BLA because...
of the positively-charged symmetric resonance structure. The total structure is close to an anthracene in terms of the bond length system (all three aromatic rings with slightly short C1-C2, C3-C4, C5-C6, and C7-C8 bonds).

![Scheme 2](image)

Scheme 2. Fluorone (X) structure and its protonated and deprotonated forms.

Figure 2. Single crystal X-ray structures of a) 1 and b) XH+·Br-. The lengths (Å) in red indicate double-bond character and the ones in blue single-bond character.

UV–vis absorption spectra of X, XH+, and X• are shown in Figure 3. The compound X displayed the broad featureless absorption spectrum in the visible region. The addition of TFA largely changed its absorption, exhibiting a relatively sharp absorption at 435 nm which is also related to that of anthracene. On the other hand, the addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base to X exhibits a red-shifted and intensified sharper band at 522 nm. This absorption characteristic originates from the elongated conjugation along the long molecular axis of X.

![Figure 3](image)

Figure 3. UV-vis absorption spectra of X (blue), XH+ (5% TFA, green), and X• (1.2 eq. of DBU, black) in CH2CN.

Synthesis of π-expanded dibenzofluorone dye BX started from the lithiation of 2,7-dimethoxynaphthalene (2) (Scheme 3). A solution of lithiated 2 was treated with methyl benzoate, resulting in the formation of carbinol 3 in 35% yield. Demethylation of 3 with 18 equiv. of BBr3 afforded the cyclized carbinol 4, followed by the addition of H2O (HBr generation) to give the dibenzofluorone dye BX in 83% yield in one-pot 2-step reactions. These compounds have been fully characterized by 1H and 13C NMR and high-resolution MALDI-TOF mass spectroscopy.

![Scheme 3](image)

Scheme 3. Synthesis of dibenzofluorone dye BX. (a) nBuLi, then methyl benzoate, (b) BBr3, (c) H2O with BBr3, and (d) H2O.

It was revealed that π-expanded fluorone BX is easily attacked by nucleophilic molecules such as H2O and methanol to again form the compound 4. Although 2,6-alkoxyphenyl group could be effective to protect the core from the nucleophilic attack, the final BBr3 demethylation should be concerned. Thus, 2,6-difluorophenyl substituent was planned to be introduced to BX for 1) kinetic stabilization as a steric hindrance, 2) solubilization to prevent stacking, and 3) stabilization as an electron withdrawing group to hamper the oxidative transformation. Fluorine atoms are enough tolerant under the current synthetic conditions.

When methyl 2,6-difluorobenzoate was used instead of methyl benzoate, 5 was obtained in 23% yield (Scheme 4). Upon treatment with 18 equiv. of BBr3, the methyl protected expanded fluorone 6 was isolated in 52% yield in one step instead of the corresponding carbinol. Finally FBO was obtained by demethylation with 40 equiv. of BBr3 in 85% yield. All the compounds have been characterized by 1H and 13C NMR and high-resolution MALDI-TOF mass spectroscopy.
Crystals of 6 were grown by the diffusion of cyclohexane vapours into a dichloromethane solution of 6. Single-crystal X-ray structure shows the distinct BLA at half a quinoidal part (Figure 4). In spite of many attempts, the crystals of FBX and its anion form suitable for X-ray measurements could not be obtained so far. Theoretical calculations \(^{12}\) for FBX\(^-\) predict the behaviour as follows; the bond lengths at C1-C2, C5-C5a, C6a-C7, and C10-C11 are shorter than the standard aromatic bond length and those at C2-C3, C3-C4, C4a-C5, C7-C7a, C8-C9, C9-C10, and C11-C11a are longer than that, being a mixed feature between quinoidal and aromatic forms. These are achieved by the basis of the contributions of resonance structures.

**Scheme 4.** Synthesis of dibenzofluorone dye FBX. (a) nBuLi, then methyl 2,6-difluorobenzoate, (b) BBr\(_3\), (c) BBr\(_3\), and (d) DBU or CsF. The carbon designation is described in the scheme.

In summary, \(\pi\)-expanded fluorones BX and FBX were prepared and characterized. Owing to the flat and elongated as a base, the absorption at 817 and 732 nm assigned to the anionic form increases, exhibiting an extensively red-shifted absorption bands reaching into NIR region. Of these bands, the most red-shifted band is remarkably sharp and intensified (optical HOMO–LUMO gap; 1.49 eV, fwhm = 737 cm\(^{-1}\)). These absorption characteristics originate from the elongated conjugation along the long molecular axis of FBX. To further understand the electronic features, the time-dependent density functional theory (TD-DFT) calculations at the B3LYP/6-31G(d) level were carried out (Figure S24). The longest band of FBX mainly comprises the transition from HOMO to LUMO (95%, oscillator strength, \(f = 1.12\)). The transition energies simulated (indicated by vertical bars) tend to be underestimated compared with the observed absorption spectrum of FBX probably because the molecule calculated is in vacuo.

The stability of FBX in DMSO was checked by UV-vis absorption spectral change. The solution was kept in room light under air and the temporal spectral change was measured, as shown in Figure S22. The peak-top of the absorbance of BX is gradually decreased and the half life (\(\tau_{1/2}\)) is calculated to be 2.5 h. In contrast, \(\tau_{1/2}\) of FBX was longer than that of BX and was estimated to be 4.4 h. The stability was remarkably improved by degas and protection from light, achieving practically no degradation during the measurement at all (Figure S23).

Anionic form of FBX exhibits fluorescence bands at 837 and 952 nm in CH\(_3\)CN, and 853 and 967 nm in DMSO. These are well-defined vibronic structure and the apparent mirror image of absorption, suggesting its rigid molecular skeleton. Relative \(\Phi_{\text{f}}\) determined from the fluorescence of indocyanine green (13% in DMSO) \(^{13}\) and fluorescence lifetime (\(\tau_{\text{f}}\)) in DMSO are 6.4% and 0.80 ns, respectively. Most organic NIR fluorophores are limited by their small \(\Phi_{\text{f}}\) which hampers their use in emitting materials. \(^{14}\) FBX demonstrates the longest fluorescence with the highest class of large \(\Phi_{\text{f}}\) in the naphthofluorone series (listed in ref. 9 and Figure S26) in NIR region (around 850 nm) because of its well-delocalized \(\pi\)-conjugation and rigid carbon framework.
conjugated system, FBX in DMSO displays remarkably red-shifted and sharp absorption and fluorescence bands at 817 nm and 853 nm, respectively, higher $\Phi_f$ among organic NIR fluorophores, and a certain chemical stability in the dark. Hence, this work demonstrates the utility of dibenzo[β,l]-fluorone dye as an efficiently π-conjugated material.

This work was partly supported by CREST JST and Grants-in-Aid for Scientific Research (Nos. 25288092, 25620061, 26288038, 26620167, 26600004 and 15H00876 'AnApple'), the Green Photonics Project in NAIST, and the program for promoting the enhancement of research universities in NAIST supported by MEXT. We thank Prof. S. Kato, Mr. Y. Okajima, Ms. Y. Nishikawa, NAIST, for the X-ray diffraction analysis, for fluorescence lifetime measurements, and for the mass spectrometry measurements, respectively. We also thank Prof. A. Osuka and Mr. Y. Okubo, Kyoto Univ. and Prof. K. Tokumaru for fruitful discussion.

Notes and references

Crystallographic data for 1: C$_4$H$_3$O$_2$Br, $M_w$ = 302.31, monoclinic, space group $P2_1/c$ (#14), $a = 10.307(2)$, $b = 6.9664(13)$, $c = 20.194(4)$ Å, $\beta = 108.479(8)^\circ$, $V = 1448.6(5)$ Å$^3$, $T = 90(2)$ K, $Z = 4$, reflections measured 8676, 3148 unique. The final $R_1$ was 0.0483 (> 2$\sigma$I), and the final wR on $I^2$ was 0.1292 (all data), GOF = 1.002. Crystallographic data for X$\beta$Br: C$_4$H$_3$O$_2$Br, $M_w$ = 369.20, orthorhombic, space group $Pna$ (#52), $a = 6.4553(14)$, $b = 15.350(3)$, $c = 15.588(3)$ Å, $V = 1544.6(6)$ Å$^3$, $T = 90(2)$ K, $Z = 4$, reflections measured 8721, 1684 unique. The final $R_1$ was 0.0279 (> 2$\sigma$I), and the final wR on $I^2$ was 0.0791 (all data), GOF = 1.039. Crystallographic data for 6: C$_8$H$_{16}$O$_2$Cl$_2$, $M_w$ = 523.33, monoclinic, space group $C2/c$ (#15), $a = 22.6443(6)$, $b = 6.8474(2)$, $c = 30.7630(8)$ Å, $\beta = 100.073(7)^\circ$, $V = 4696.4(2)$ Å$^3$, $T = 103(2)$ K, $Z = 8$, reflections measured 30130, 4110 unique. The final $R_1$ was 0.0628 (> 2$\sigma$I), and the final wR on $I^2$ was 0.1747 (all data), GOF = 1.046.

8. Although laterally π-expanded fluorone derivatives have been independently synthesized by Tsubaki et al. the details of their photophysical properties were not reported. A. Katori, E. Azuma, K. Kuramochi, and K. Tsubaki, 7th Symposium on Organic π-Electron Systems, Abstract Book, 2013, PA01.

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