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Near-Infrared Sensing Properties of Dimethlyamino-Substituted BF_2–Azadipyrromethenes

Shane O. McDonnell and Donal F. O'Shea*

Centre for Synthesis and Chemical Biology, Conway Institute, School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

donal.f.oshea@ucd.ie

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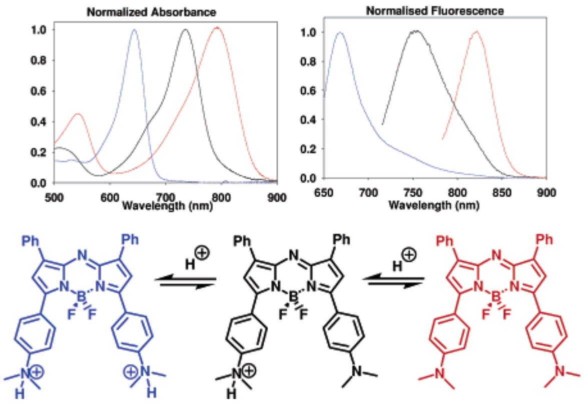
ABSTRACT



The synthesis and sensing characteristics of a new class of organic colorimetric and fluorometric chemosensor which operates in the 850–650 nm spectral region is outlined. Judicious placing of amine substituents on the BF_2-chelated tetraarylazadipyrromethene chromophore generates a triple absorption and emission responsive sensor. Dramatic pH responsive absorption and fluorescence changes can be observed across a broad acidity range, from pH 5 to 6 M HCl, in conjunction with a visible colorimetric change from red to purple to blue.

The development of synthetic routes to organic chromophores with spectral properties in the near-infrared (NIR) and visible red spectral regions continues to attract a sustained research interest due to the lack of suitable classes which could be tailored to specific applications by peripheral substituent variations. New chromophore scaffolds with controllable photophysical properties in the 900−650 nm spectral region offer potential for exploitation in a diverse range of material and biological applications, such as optical data storage,[1] photoconductors,[2] electrochromic devices,[3] chemosensors,[4] immunoassay labels and bioconjugated probes,[5] and in vitro and in vivo imaging agents.[6] We are currently interested in devising new chromophore platforms which can be adapted and optimized as biological chemosensors and imaging agents. Many of the current biological indicators have operational light input/output wavelengths in the 300−600 nm wavelength range, which often limits their applications as these spectral regions suffer from strong interference due to background absorbance and auto-fluorescence from endogenous chromophores in sample media.[7] Despite the optical benefits of utilizing the NIR spectral region for analytical techniques, there is a surprising paupicity of

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organic compounds which have the desired absorption and emission properties.[8] As such, the development of versatile synthetic methods to new NIR chromophores has become an urgent requirement.

The BF_2 chelated-tetraphenylazadipyrromethene **1** and related structural analogues have recently been reported as a class of chromophore with high absorption extinction coefficients (70000−80000 M^{-1} cm^{-1}) and fluorescence quantum yields (0.23−0.36) between 650 and 750 nm (Figure 1).[9] In addition, we have shown that this structural class can be adapted to act as effective fluorosensors based upon a photoinduced electron-transfer mechanism.[10] These photophysical characteristics suggest that this structural class would make an excellent platform from which NIR analogues could be constructed. This we envisaged could be accomplished by substituting the parent chromophore molecule with two basic amine donors, thereby constructing an electron donor−acceptor-donor system in which the amine units are intrinsically connected to the chromophore as shown in **2** (Figure 1). In addition to providing a means of accessing longer wavelength derivatives, the inclusion of amine substituents would offer the potential of providing a more advanced molecular assembly which could generate pronounced photophysical changes as a result of a substrate recognition event by the amine substituents. It was anticipated that this amine receptor−chromophore−amine receptor design would undergo pronounced spectral changes due to variance in the internal charge transfer (ICT) properties of the system in response to acid analyte.[11] In due course, this ICT switching mechanism could potentially be used at physiological pH in conjunction with a more elaborate amine receptor to detect metal ions such as Ca^{2+}, Cu^{2+}, and Mg^{2+}.[12]

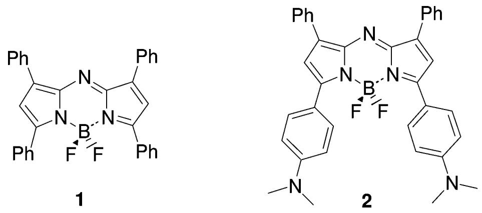
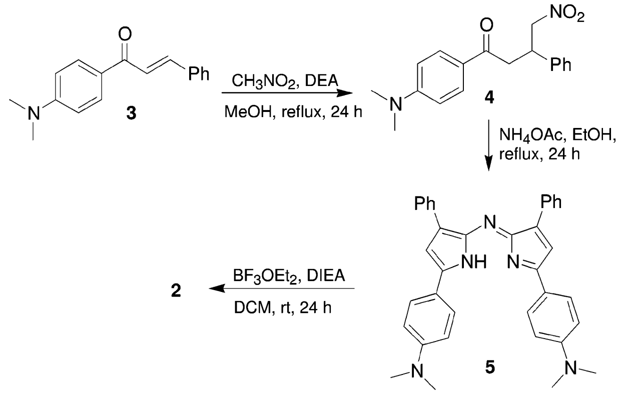


Figure 1. BF_2-chelated tetraarylazadipyrromethenes.

The synthesis of **2** was achieved in a facile three-step route from the α,β-unsaturated ketone **3** (Scheme 1). Addition of nitromethane to **3** gave the 1,3-diaryl-4-nitrobutan-1-one **4** in 71% yield after recrystallization from MeOH. Subsequent generation of the tetraarylazadipyrromethene **5** was achieved by reflux of **4** with ammonium acetate in ethanol for 24 h. Filtration of the precipitate from the crude reaction mixture gave the pure product as a metallic red compound in 47% yield. Compound **5** was converted to our targeted structure **2** by reaction with boron trifluoride diethyl etherate and diisopropylethylamine in dichloromethane for 24 h. An isolated purified yield of 68% was obtained following chromatography on silica gel.

Scheme 1. Synthesis of **2**



Analysis of the crystal structure of **2** confirmed the overall conjugated nature of the chromophore, and as would be expected, both anilino-substituted rings were virtually coplanar with the pyrrole rings, thereby predicting a strong electronic interaction within the chromophore unit (Figure 2, Supporting Information).

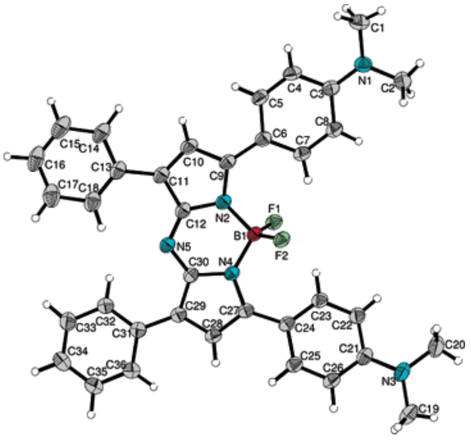


Figure 2. X-ray crystal structure of **2** with thermal ellipsoids drawn at 50% probability level.

To demonstrate the spectroscopic effects of the amine substituents, the absorbance characteristics of **2** were com-

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[8] For representative examples, see; (a) Tarazi, L.; George, A.; Patonay, G.; Strekowski, L. *Talanta* **1998**, *46*, 1413. (b) Meier, H.; Petermann, R. *Helv. Chim. Acta* **2004**, *87*, 1109. (c) Lee, S.; White, A. J. P.; Williams, D. J.; Barrett, A. G. M.; Hoffman, B. M. *J. Org. Chem*. **2001**, *66*, 461.

[9] (a) Killoran, J.; Allen, L.; Gallagher, J. F.; Gallagher, W. M.; O'Shea, D. F. *Chem. Commun.* **2002**, 1862. (b) Gorman, A.; Killoran, J.; O'Shea, C.; Kenna, T.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc*. **2004**, *126*, 10619. (c) McDonnell, S. O.; Hall, M. J.; Allen, L. T.; Byrne, A.; Gallagher, W. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2005**, *127*, 16360. (d) Gallagher, W. M.; Allen, L. T.; O'Shea, C.; Kenna, T.; Hall, M.; Killoran, J.; O'Shea, D. F. *Br. J. Cancer* **2005**, *92*, 1702. (e) Zhao, W.; Carreira, E. M. *Angew. Chem., Int. Ed*. **2005**, *44*, 1677. (f) Sathyamoorthi, G.; Soong, M. L.; Ross, T. W.; Boyer, J. H. *Heteroatom. Chem.* **1993**, *4*, 603.

[10] (a) Killoran, J.; O'Shea, D. F. *Chem. Commun*. **2006**, 1503. (b) Hall, M. J.; Allen, L. T.; O'Shea, D. F. *Org. Biomol. Chem*. **2006**, *4*, 776. (c) Hall, M. J.; McDonnell, S. O.; Killoran, J.; O'Shea, D. F. *J. Org. Chem*. **2005**, *70*, 5571.

[11] For example; Maus, M.; Rurack, K. *New J. Chem.* **2000**, *24*, 677.

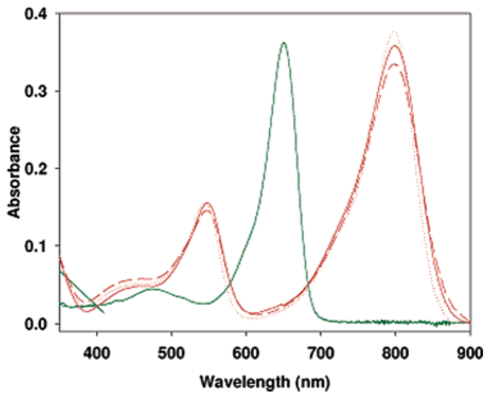

Figure 3. Absorption spectra of **1** in $CHCl_3$ (green $\lambda_{max} = 650$ nm) and **2** in $CHCl_3$ (solid red line $\lambda_{max} = 799$ nm), ethanol (dashed red line $\lambda_{max} = 799$ nm), and toluene (dotted red line $\lambda_{max} = 798$ nm) (4×10^{-6} M conc).

pared to that of the tetraphenyl derivative **1**. We were pleased to record that in organic solvents such as chloroform, **2** had a wavelength of maximum absorbance of 799 nm and an extinction coefficient of 87000 M^{-1} cm^{-1}. Thus, the amine substituents on **2** provided a striking bathochromatic shift of 149 nm in comparison to **1** ($\lambda_{max} = 650$ nm and $\epsilon = 79000$ M^{-1} cm^{-1}) (Figure 3). In addition, the longest wavelength absorbance band of **2** showed very little solvent dependence in polar protic or nonpolar solvents (Figure 3).

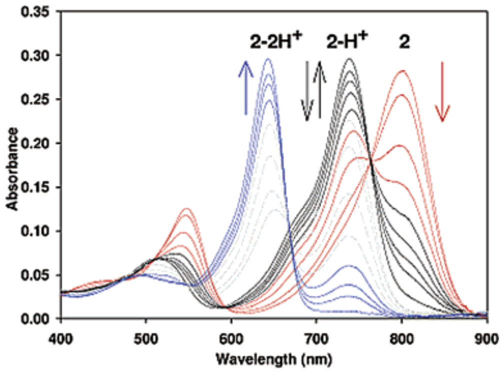

Figure 4. Absorbance TFA titration of **2** in $CHCl_3$ (3.75×10^{-6} M). Isosbestic points at 666 and 760 nm.

To explore the absorption spectral responses of **2** to acid analyte, a chloroform solution of **2** was titrated by the sequential addition of aliquots of trifluoroacetic acid (TFA) which revealed spectacular spectral shifts (Figure 4). Upon addition of TFA, a stepwise disappearance of the 799 nm band and formation of a new band at 738 nm was observed. The sharp isosbestic point at 760 nm indicated the formation of the monoprotonated compound **2-H**$^+$. Continuation of the TFA titration resulted in a stepwise decrease in the 738 nm band of **2-H**$^+$, with the formation of a new absorption band at 643 nm with a second clear isosbestic point at 667 nm. This doubly protonated species **2-2H**$^+$ has a UV−vis spectrum that closely matches unfunctionalized **1**. The ratiometric nature of the distinct and well-separated spectral bands could facilitate in situ monitoring of acid concentration and remain impervious to environmental interference.[13]

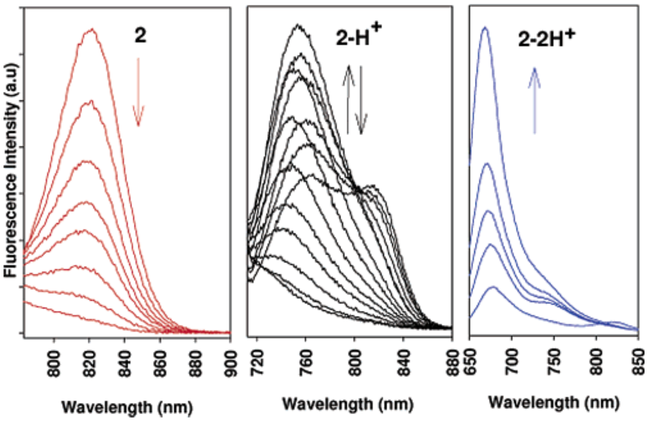

Figure 5. Normalized fluorescence spectra of **2** in chloroform (5×10^{-7} M) titrated with aliquots of TFA. Red trace (excitation at 773 nm, λ_{max} emission = 823 nm), black traces (excitation at 700 nm, λ_{max} emission = 753 nm), blue trace (excitation at 630 nm, λ_{max} emission = 668 nm). Slit widths 10 nm.

Gratifyingly, an examination of the fluorescence properties of **2** revealed a triple emission profile corresponding to the absorbance spectral properties. Excitation of **2** (at 773 nm) in chloroform yielded an emission band with a λ_{max} of 823 nm,[14] which sequentially decreased upon addition of aliquots of TFA (Figure 5, red traces). Excitation at 700 nm during this titration revealed a concommital appearance of an emission band at 753 nm (Figure 5, black traces). Continuation of TFA addition resulted in the disappearance of the 753 nm emission band and the emergence of a new emission band at 668 nm upon excitation at 630 nm (Figure 5, blue traces). The intensity of the emissions at 823 and 753 nm for **2** and **2-H**$^+$ respectively were significantly less than the 668 nm emission potentially due to the charge-transfer properties of these species. This triple emission profile offers the basis for ratiometric fluorosensing applications.[13]

As many sensing applications are conducted in an aqueous environment, **2** was encapsulated with the neutral surfactant Cremophor EL (CrEL) to form stable aqueous solutions. In the aqueous formulated solutions, the starting absorbance

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(13) For examples of ratiometric sensors, see: (a) Mello, J. V.; Finney, N. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1536. (b) Choi, K.; Hamilton, A. D. *Angew. Chem., Int. Ed.* **2001**, *40*, 3912. (c) Xu, Z.; Qian, X.; Cui, J. *Org. Lett.* **2005**, *7*, 3029.

(14) The emission intensity in ethanol was significantly lower when compared to chloroform and toluene (Supporting Information).

maximum of **2** was recorded at 818 nm with emission at 826 nm, a small bathochromic shift when compared to organic solvents (Supporting Information). Evaluation of the spectral features during aqueous hydrochloric acid titration revealed them to be very similar to those observed in chloroform (Supporting Information). A plot of absorbance intensity versus pH and molarity of aqueous HCl is shown in Figure 6. The profiles clearly map out the spectral absorbance changes during the titration from pH = 5 to 6 M HCl and highlight the ratiometric nature of the spectral changes, with two distinct crossover points at pH 1.5 and 3.4 M HCl. In addition to the NIR spectral changes, a sequence of visible color changes also took place during the titration. The starting color of a pH neutral solution of **2** was red, which visibly changed to purple upon the generation of **2-H**$^+$ and then to blue upon formation of **2-2H**$^+$ (Figure 6). The first red to purple color change can be attributed to the spectral changes in the 500−600 nm spectral region occurring in conjunction with the decrease in intensity of the longer wavelength band at 818 nm and the blue color corresponds to the absorption band at 653 nm (Supporting Information). The disappearance and appearance of fluorescence emissions in response to the titration were comparable to those observed in chloroform (Supporting Information).

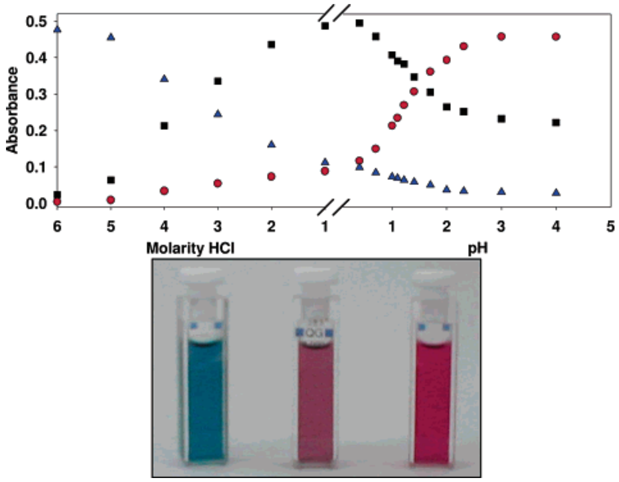

Figure 6. Absorption acidity responses of **2**: red profile (red, ●) (λ_{max} = 818 nm), black profile (black, ■) (λ_{max} = 753 nm), blue profile (blue, ▲) (λ_{max} = 653 nm), and corresponding visible color changes for **2** (red), **2-H**$^+$ (purple), and **2**−**2H**$^+$ (blue). Crossover points at pH 1.5 and 3.4 M HCl.

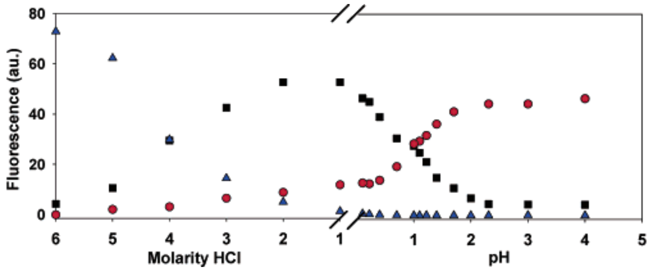

Figure 7. Fluorescence titration responses of **2** at 832 nm (red, ●), 779 nm (black, ■), and 698 nm (blue ▲, shown at one-tenth peak intensity). The wavelengths shown were chosen for maximum signal separation and clarity.

A plot of acidity versus fluorescence response shown in Figure 7 demonstrates the ratiometric nature of the changes.[13] A starting λ_{max} of emission at 826 nm was observed to decrease with addition of aqueous acid, with a corresponding increased emission at 779 nm, which upon continuing the titration decreased, leading to the final emission of the **2-2H**$^+$ at 673 nm.

In summary, a new class of NIR/vis red ratiometric triple channel colorimetric and triple channel fluorometric sensor has been developed with potential to be exploited and adapted to suit a diverse range of analytical, imaging, and material applications. Specifically, **2** could find direct application as a multiresponsive high acidity indicator.[15]

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Supporting Information Available: Synthetic procedures, analytical data, and NMR spectra for **2**, **4**, and **5**. Absorbance spectra in CrEL and emission spectra in ethanol, toluene, and water/CrEL. X-ray crystallographic data of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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