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Design, synthesis and redox properties of a fluorene platform linking two different Bodipy dyes

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ABSTRACT

Several new fluorophores have been prepared by grafting boradiazaindacene (red absorbing) and/or styrylboradiazaindacene (blue absorbing) units as terminal energy acceptors onto a fluorene-derived platform. In one case, an amino-bis(bipyridine) pocket has been attached to enable strong binding of transition metal ions. The stepwise syntheses were largely based on Pd-catalysed cross-coupling reactions. The electrochemistry of the dyes has been analysed by reference to the properties of the various synthetic intermediates, protonation of the tertiary amine site present in the bis(bipyridine) species enabling processes involving this centre to be distinguished from those associated with the boradiazaindacene (*Bodipy*) unit.

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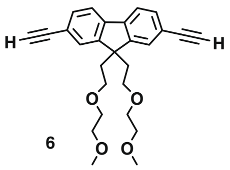
Control of energy and electron transfer processes and high luminescence efficiency are fundamental aspects of natural photosynthesis,[1] and are crucial to the development of light emitting materials for opto-electronic technologies.[2] Concerning the latter, particularly significant observations have been reported concerning molecular photonic wires built around porphyrins using a dipyrromethene dye as the primary light harvester.[3,4] Upon excitation, this dye injects photons into a linear array of metallo-porphyrins along which the photon is transferred rapidly until being trapped by a low-energy acceptor. Careful balancing of the rates of forward and reverse energy transfer allows energy migration to proceed with almost 100% efficiency.[5] This use of a dipyrromethene chromophore pioneered the application of such dyes as energy donors. Since then, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (*F*-Bodipy) dyes, which are dipyrromethene derivatives, have become very popular as a result of their valuable optical properties.[6] Amongst these are pronounced stability, high absorption coefficients ($\sim$80,000–200,000 M^{-1} cm^{-1}) in the visible portion of the electromagnetic spectrum, narrow emission profiles and outstanding emission quantum yields reaching 100% for the best cases.[7]

The numerous applications since found for Bodipy derivatives include use in solar concentrators, in molecular wires,[8] in multichromophoric scaffoldings dedicated to directional energy transfer,[9] in solar cells,[10] in fluorescent sensing materials,[11] in probes for bio-labelling,[12] as well as in laser applications[13] and for grafting to nanoparticles. In some special instances, two-photon absorbing dyes dedicated to cell imaging have been produced.[14] Recently new types of liquid crystals,[15] fluorescent organogelators[16] and controlled polymers were produced by specific decoration at the periphery of the dyes.[17]

In this Letter we describe a modular approach to the rational synthesis of fluorene-substituted Bodipy dyes. Three fundamental considerations underlie their design. First, it is known that fluorene is a fluorescent platform capable of transferring its excitonic energy when properly excited. Second, the fluorene structure is readily functionalised on the meta (2,7-positions) and the central positions (9,9′-positions). Third, *meso*-iodophenyl-substituted Bodipy units, including those with 3-substituents allowing modulation of the extent of π-conjugation and binding of metal cations, can be easily prepared for reaction with acetylenic groups on the 2,7-positions of fluorene.



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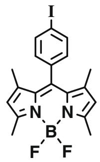

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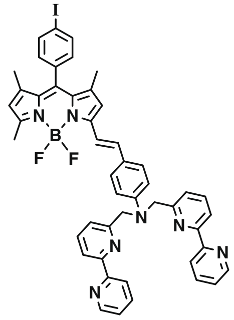

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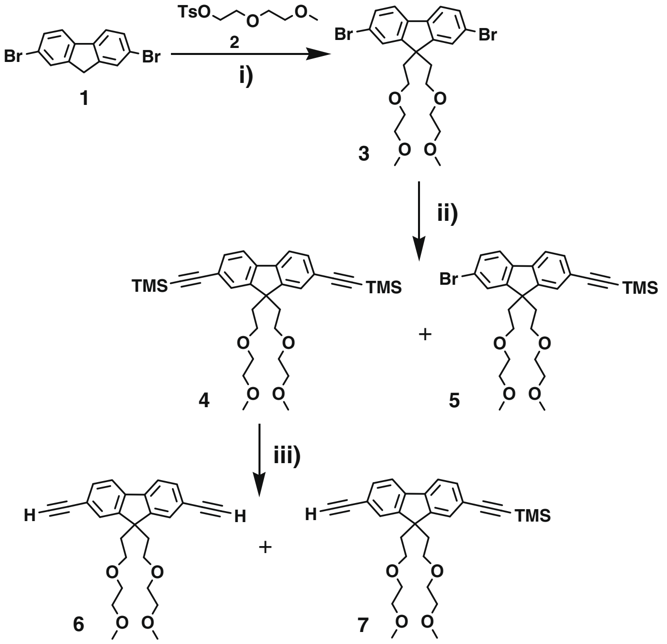
Access to such platforms first required producing the key reactants **6, 10** and **11**. This, indeed, was complicated by the lack of general synthetic procedures for the modification of both fluorene and Bodipy to induce properties such as high solubility and the capacity for tuning the optical and redox properties, as well as for the preparation of multi-chromophoric derivatives.

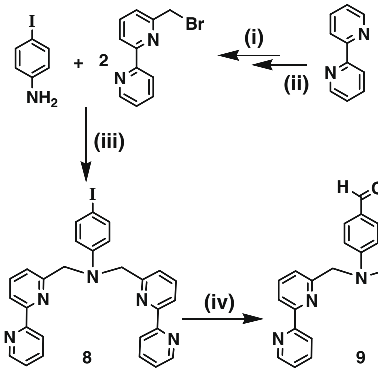
Encouraged by our success in the large scale preparation of dibromofluorene,[11] we attempted to prepare highly soluble unsymmetrical fluorene scaffoldings. To this end, we first explored the synthesis of compounds **6** and **7** by a routine procedure (Scheme 1) which was expected to be unselective with regard to product distribution. Alkylation of 2,7-dibromofluorene with the tosylate derivative **2** was straightforward, leading to compound **3** in 95% yield.[18] Palladium(0) promoted cross-coupling with trimethylsilylacetylene provided a mixture of equimolar quantities of **4** and **5** easily separable by column chromatography due to the presence of the short oligoethylene chains. Stepwise deprotection of the TMS group was feasible by strict control of the reaction time and the separation of **6** and **7** was again easy.

Our next target became the preparation of the carbaldehyde **9**, a key compound for the preparation of the blue-absorbing Bodipy **11**. The design of this complexation pocket was guided by the need to have a tertiary nitrogen atom in the para position of the aldehyde and the presence of 2,2′-bipyridine units for metal ion binding.[19] Alkylation of 4-iodoaniline with 6-bromomethyl-2,2′-bipyridine,[20] itself prepared in two steps from 2,2′-bipyridine, provided compound **8** in fair yield (Scheme 2). Unfortunately, under conventional Villsmeier formylation reactions compound **9** could not be isolated in satisfactory yields (<20%) despite the use of various experimental conditions.[21] As anticipated, metallation with a lithium reagent followed by reaction with anhydrous *N*-formylpiperidine or methylformate failed. After some experimentation, the only reliable protocol we found was the use of a carboformylation reaction[22] catalysed by Pd(0) under a flux of carbon monoxide with sodium formate as the hydrogen source.

As expected from earlier work on Bodipy dyes,[6] aldehyde **9** was conveniently reacted with 8-(4-iodophenyl)-1,3,5,7-tetramethyl-4,4difluoro-4bora-3a,4a-diaza-s-indacene **10**,[23] using Knoevenagel reaction catalysed under basic conditions and leading to the blue dye **11** in good yield (Scheme 3). Interestingly, the tetra-bipyridine derivative **12** could be easily isolated as a side product.



Scheme 1. Reagents and conditions: (i) NaH (3 equiv), DMF, 60 °C, MeO(CH_2)$_2$O(CH_2)$_2$OTs (3 equiv), 12 h, 95%; (ii) trimethylsilylacetylene (3 equiv), [Pd(PPh_3)$_2$$Cl_2$] (10 mol %), CuI (10 mol %), THF/Et_3N, 60 °C, 12 h, 40% of **4**, 40% of **5**; (iii) K_2CO_3 (1 equiv), MeOH, 30 min, rt, 36% of **7**, 58% of **6**.



Scheme 2. Reagents and conditions: (i) CH_3Li, −78 °C; (ii) NBS, dibenzoyl peroxide, CCl_4; (iii) CH_3CN, KI 10 mol %, K_2CO_3 20 equiv, 80 °C, 5 d, 80%; (iv) [Pd(PPh_3)$_2$$Cl_2$] (10 mol %), HCOONa (1.2 equiv), CO 1 atm, DMF, 100 °C, 3 h, 83%.

Cross-coupling of the red Bodipy **10** with 2,7-diethynyl-9,9-bis(2-(2-methoxyethoxy)ethyl)fluorene **6** provided the expected mixture of the mono- and bis-dyes **14** and **13** in 21% and 29% yield, respectively (Scheme 4). No degradation was observed and the unreacted starting material **10** was recycled.

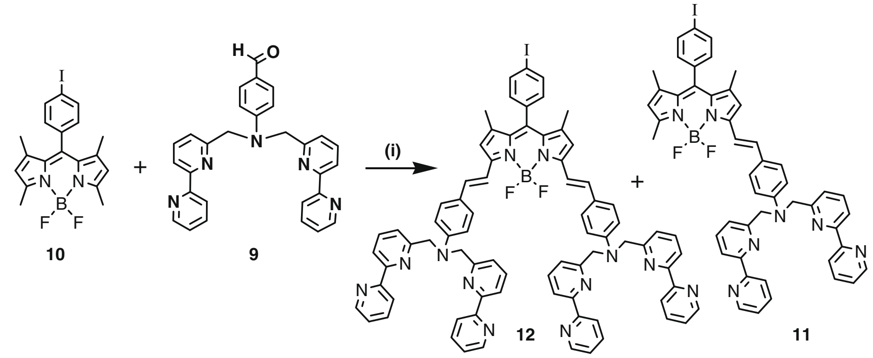
Ultimately, the red-Bodipy **14** was allowed to react with the blue precursor **11** to provide the dual red-blue compound **15**. Purification was extremely tedious and **15** was always contaminated with trace amounts of an unidentified species. This was due to the similar polarities of the target compounds and some side products issued from oxidative homocoupling of the terminal alkyne derivatives. Previously, we overcame this problem through a long purification process.[24]

We next examined a multistep procedure starting from 2-trimethylsilylacetylene-7-bromo-9,9-bis(2-(2-methoxy-ethoxy)ethyl)-fluorene **5** to produce the dual dye **15** by first coupling the red dye using 8-(4-ethynylphenyl)-1,3,5,7-tetramethyl-4,4difluoro-4bora-3a,4a-diaza-s-indacene, a synthetic equivalent of **10**, and then after deprotection of the TMS, cross-coupling the blue dye **11** via the protocol depicted in Scheme 4. Unfortunately, we encountered the same purification problem as previously observed using the routine step-by-step cross-coupling reactions.

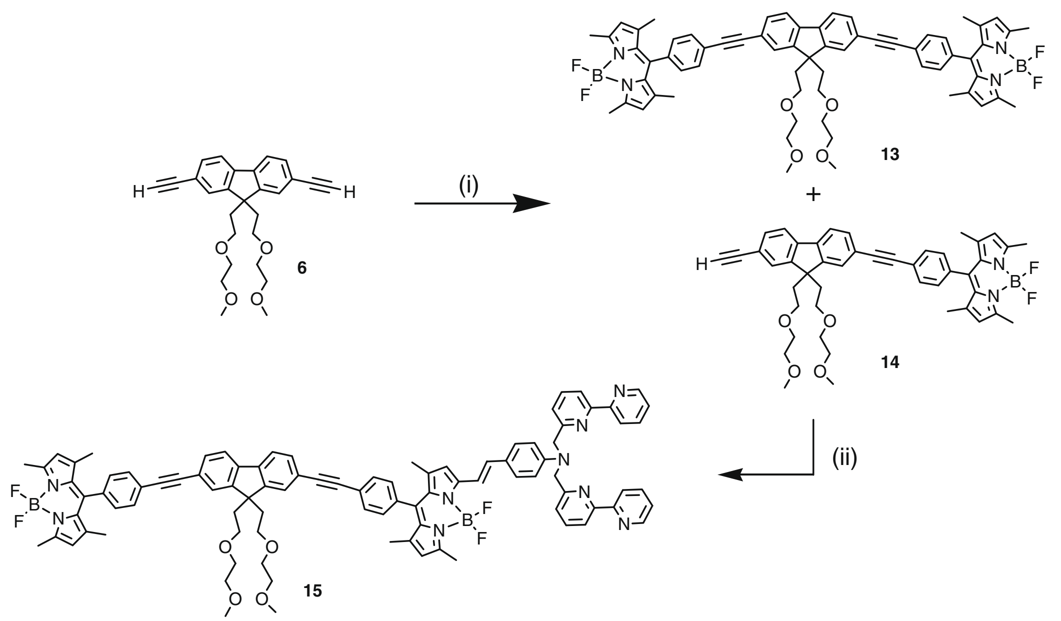
After several additional attempts aimed at diminishing the homocoupling process we succeeded in preparing **15** in an analytically pure form using the protocol shown in Scheme 5. This approach was inspired by the selective mono-functionalization of molecular wires to produce very smart donor–acceptor molecules.[25] Using the bis-Bodipy dye **13** and 4-dimethylaminobenzaldehyde or the aldehyde **9**, selective mono-functionalization was feasible, providing **15** or **16** in a readily purified form (Scheme 5).

Finally, stable model dye **17** was prepared by cross-coupling precursors **7** and **11** under our standard conditions (Scheme 6). It is worth noting that the TMS-deprotected blue dye analogous to **17** is less stable than the protected one, likely due to higher electronic density imported by the styryl fragment compared to its red counterpart **14**. This excluded use of the protocol devised in Scheme 4 for the preparation of compound **17**.

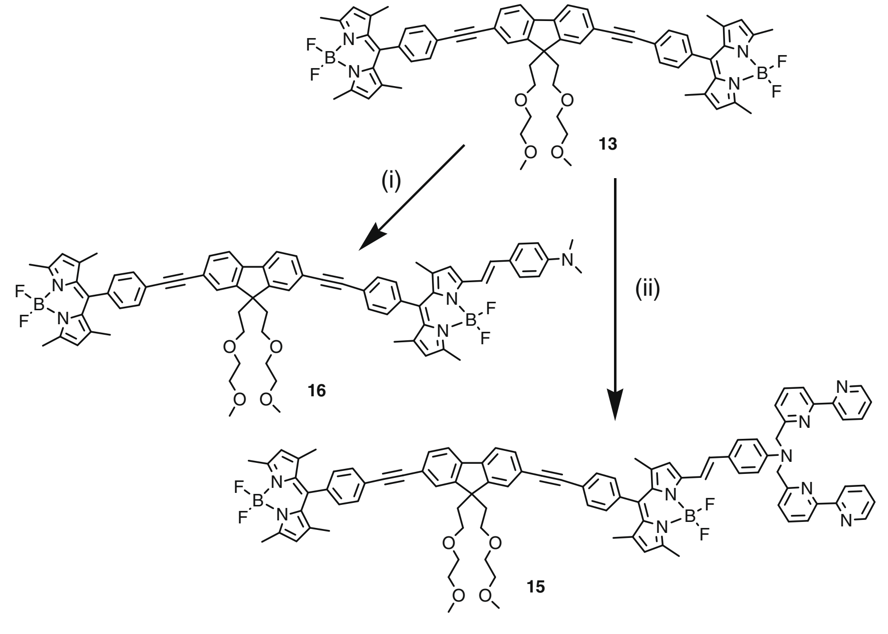
All the Bodipy dyes showed absorption and emissive properties in keeping with their molecular structures. In all dyes the fluorescence of fluorene is quenched, while for the dual dye **15** and **16**, very efficient energy transfer occurs from the high energy donor (tetramethyl Bodipy λ_{em} 510 nm) to the energy acceptor (styryl Bodipy λ_{abs} at 600 nm), which fluoresces at λ_{em} 695 nm. Complete details of these photophysical studies will be disclosed elsewhere.



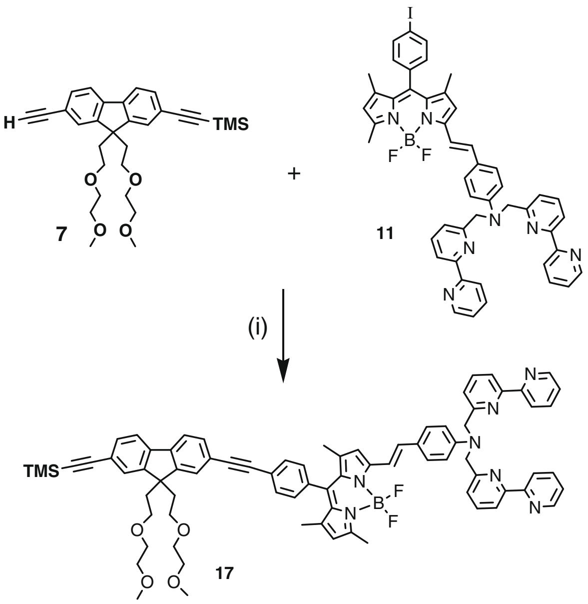
Scheme 3. Reagents and conditions: toluene, piperidine, *p*-TsOH tr., Dean–Stark, 65% for compound **11**.



Scheme 4. Reagents and conditions: (i) Dye **10** (1 equiv), [Pd(PPh$_3$)$_4$] (10 mol %), C_6H_6/Et_3N, 60 °C, 15 h, 25% of **13**, 21% of **14**; (ii) dye **11** (1 equiv), [Pd(PPh$_3$)$_4$] (10 mol %), C_6H_6/Et_3N, 60 °C, 15 h, 42%.



Scheme 5. Keys: (i) 4-dimethylaminobenzaldehyde, toluene, piperidine, *p*-TsOH, concentrated, Dean–Stark, 40%; (ii) aldehyde **9**, toluene, piperidine, *p*-TsOH, concentrated, Dean–Stark, 43%.



Scheme 6. Key: (i) [Pd(PPh$_3$)$_4$] (10 mol %), C$_6$H$_6$/Et$_3$N, 60 °C, 15 h, 40%.

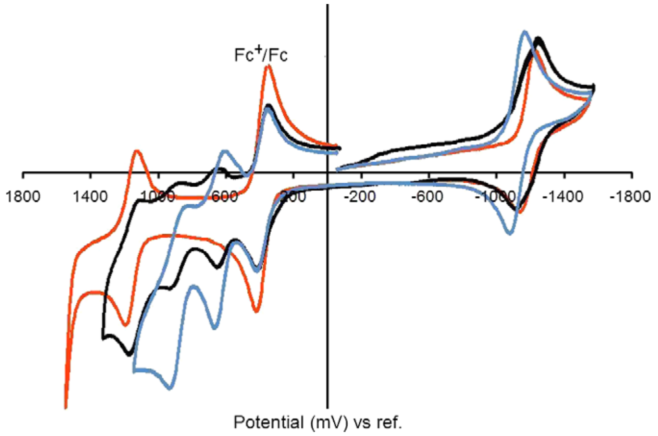


Figure 1. Cyclic voltammograms of dye **14** (red trace), dye **15** (black trace) and dye **17** (blue trace) in dichloromethane at rt. The reversible Fc$^+$/Fc redox couple at +0.38 V correspond to genuine ferrocene.

We have previously shown that Bodipy dyes exhibit a rich electrochemistry associated with the formation of radical cations and radical anions depending on the decoration around the central Bodipy core.[26] For both reference compounds **14** and **17** each bearing a single red and blue chromophore, both redox processes are observed (Table 1). The energy gap between the radical cation and radical anion, 2.35 eV for the red dye and 2.01 eV for the blue dye, is in keeping with the steady state emission of the respective dyes. For the blue dye **17** bearing a tertiary amine an additional irreversible process was observed at 0.63 V. By addition of a weak acid this redox process vanished due to protonation and the Bodipy oxidation potential shifted cathodically by 70 mV due to the decrease of the electron density on the Bodipy core. This observation is in keeping with the concomitant colour change of the dye solution from blue to magenta. For the dual dye the cyclic voltammogram is rich due to the summation of the redox properties of both subunits (Fig. 1). All potentials could be assigned using the data for **14** and **17** and noting the effects of protonation. Only very weak potential shifts resulted from linking both dyes to a common fluorene unit, indicating that both chromophores remain electronically isolated. This conclusion was confirmed by comparison of the absorption and emission spectra of the dual dyes with those of the single dyes.

The dimethylamino fragment in compound **16** is by 70 mV more easily oxidised than the bis-bipyridylmethyl residue in **15**. Nonetheless, in both cases protonation with HCl confirmed the assignment of the amino-N oxidation potentials. Protonation also led to a colour change from blue to magenta associated with an increase of the energy gap from 2.07 eV to 2.20 eV for compound **15H$^+$** and from 2.02 eV to 2.13 eV for compound **16H$^+$** (Fig. 2).

In short, new borondipyrromethene dyes attached to a functionalised fluorene have been developed and dual-Bodipy species have been engineered displaying both a red colour (with emission at 510 nm) and a blue colour (emission at 695 nm). The method established for the synthesis of new dyads in which red and blue dyes are linked via a non-innocent spacer has provided families

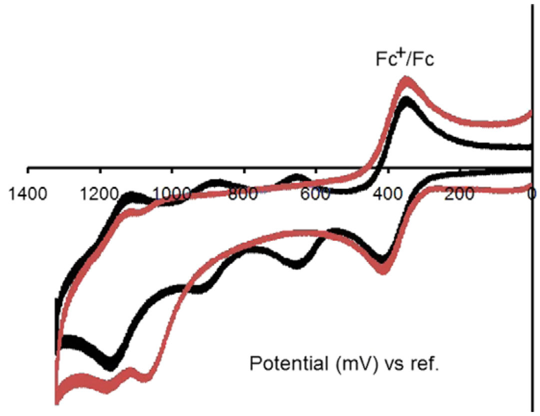


Figure 2. Cyclic voltammograms of dye **15** (black trace) and after addition of excess HCl gas (red trace).

Table 1
Electrochemical data for the hybrid dyes and appropriate reference species[a]

Compd	$E^{0\prime}$ (ox, soln) (V), ΔE (mV)	$E^{0\prime}$ (red, soln) (V), ΔE (mV)
14	+1.16 (70)	−1.19 (80)
17	+0.63 (irrev, $I_a/I_c \approx 4.2$); +0.88 (90)	−1.13 (80)
17 + CF$_3$COOH	+0.95 (80)	—
15	+0.63 (irrev, $I_a/I_c \approx 3.2$); +0.91 (60); +1.15 (60)	−1.16 (70), −1.22 (70)
15 + HCl	+1.04 (60); +1.14 (60)	—
16	+0.56 (irrev, $I_a/I_c \approx 2$); +0.87 (60); +1.15 (70)	−1.15 (60), −1.20 (60)
16 + HCl	+0.98 (80); +1.15 (60)	—

[a] Potentials determined by cyclic voltammetry in deoxygenated CH$_2$Cl$_2$ solution, containing 0.1 M TBAPF$_6$, at a solute concentration of ca. 1.5 mM and at rt. Potentials were standardised versus ferrocene (Fc) as internal reference and converted to the SCE scale assuming that $E_{1/2}$ (Fc/Fc$^+$) = +0.38 V (ΔEp = 60 mV) versus SCE. Error in half-wave potentials is ±15 mV and all potentials are for a single electron transfer unless otherwise noted. For irreversible processes the peak potentials (E_{ap}) are quoted. The text colour denotes the electrochemically active part of the molecule, red for the Knorr-Bodipy, blue for the amino-styryl and magenta for the protonated styryl dye. Black text denotes the amine oxidation potential.

of compounds where all redox processes could be assigned in the light of the electrochemical properties of appropriate reference species and suitable protonation. This work opens up the possibility of engineering sophisticated new dyes based on fluorene linkers. Preliminary fluorescence measurements revealed efficient energy transfer between the red and blue species. Interactions with protons and cations have also been evaluated and more detailed mechanistic studies are currently in progress.

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