

Synthesis of multi-branched dipyrromethene dyes with soluble diethynylphenyl links

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Abstract

Multi-branched dyes were prepared using a convergent step-by-step procedure. The key dibutoxydiethynylphenyl spacing units were first linked to a difluoroboradipyrromethene (yellow fluorophore) dye via the pseudo-meso position and then selectively cross-coupled to a di-(4-phenyliodo)ethynylborodisindolomethene (red emitter via the boron). When ethynylpyrene units were connected at the periphery to the boron of the yellow emitter, efficient cascade singlet energy transfer events occurred from the pyrene to the yellow and to the red emitters.

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Conversion of solar energy into chemical energy, the basis of natural photosynthesis, is a major contemporary challenge for chemists. Photosynthetic organisms have developed efficient antennas that absorb photons throughout the visible spectrum and funnel energy to the reaction center where it is used to bring about the fundamental reactions of photosynthesis.¹ In Nature, various pigments such as chlorophylls, carotenes and bilirubins provide absorptions covering most of the solar spectrum. Appropriate spatial arrangement of the chromophores controls the energy-funneling processes.¹

Artificial systems intended to provide new means for the utilization of solar energy have been based, for example, on transition metal complexes² and semiconductor particles³ but, in most such systems, the efficiency is severely limited by rapid back reactions and the narrow range of strong absorption.⁴ Systems which have provided efficient mimics of photosynthetic energy transfer events have been based

on ethynyl-bridged porphyrin arrays or dendritic polyphenylacetylene chromophores. In the first case, the energy is channeled down from a difluoroborondipyrromethene (F-Bodipy) dye to a low-energy acceptor (metal-free porphyrin) which is the energy trap.⁵ In the second, light is absorbed by peripheral phenylacetylene moieties and this energy supply is trapped by a central perylene residue.⁶ In both cases, the difference in rates of forward and reverse energy transfer allows energy migration to proceed with almost 100% efficiency.^{5,6} Other systems involve unidirectional energy transfer along specific molecular axes,^{7–9} and we have recently described hybrid systems based on boradipyrromethene (Bodipy) dyes with ethynylpyrene and ethynylperylene substituents on boron which involve ultra-fast, quantitative singlet energy transfer from the aromatic fragments to the Bodipy center.¹⁰

From a general point of view Bodipys' are exceptional fluorescent dyes, easily chemically transformable, and amenable to large quantities and high purities.¹¹

Here, we describe the synthesis of molecular devices based on two different Bodipy units linked by an increasing number of dibutoxydiethynylphenyl modules. Thus, a

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boradipyrrromethene unit provided a yellow emitting center and a boraisoindolomethene unit a red emitting dye. The idea was to extend the excitation wavelengths in order to study the efficiency of multi-cascade energy transfer events. The branched arrangement of the final molecules was dictated by the chemistry on the boron of the red emitter and on the pseudo-meso position 8 of the yellow emitter.

The question of present interest was whether trichromophoric molecules could be assembled using the boron-functionalization and alkyne-coupling reactions we have exploited previously. Thus, we first explored the possibility of functionalizing Bodipy **1**¹² with increasing numbers of tetrasubstituted-phenylethynyl units (Scheme 1). Pd(0)-catalyzed cross-coupling of **3**¹³ with 2,5-dibutoxy-4-iodo-1-(trimethylsilylethynyl)benzene (obtained in 43% yield by cross-coupling 1,4-diiodo-2,5-dibutoxybenzene¹⁴ with trimethylsilylacetylene (1 equiv) using Pd(II) catalysts), followed by deprotection and repetition of the coupling, provided the target compounds **4**, **6**, and **8** in an excellent yield. Optimal conditions involved a mixture of benzene/triethylamine at 80 °C. Deprotection with KOH afforded the terminal alkynes **5**, **7**, and **9**.

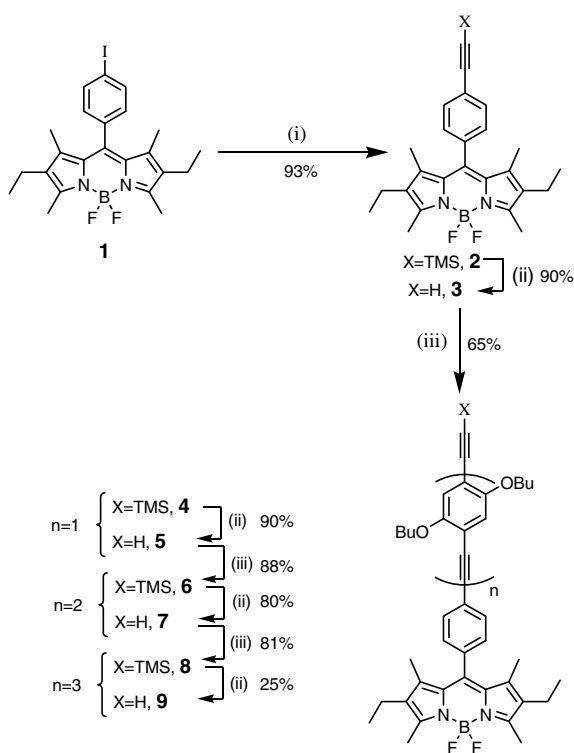
For $n = 3$, the yield for the isolation of compound **9** was poor, perhaps reflecting the instability of the terminal alkyne. Unfortunately, iterative cross-coupling to generate larger scaffoldings ($n > 3$) failed using various experimental conditions. Interestingly, the intense $S_0 \rightarrow S_1$ absorption ($\lambda_{\text{max}} = 526 \text{ nm}$, $\epsilon \sim 68000 \text{ M}^{-1} \text{ cm}^{-1}$) and the fluorescence

($\lambda_{\text{em}} = 542 \text{ nm}$) measured in dichloromethane from the Bodipy subunit are almost the same for **4**, **6** and **8** as for the phenyliodo-substituted derivative **1**.¹³ However, both the absorptivity maximum and its wavelength for the oligo(phenylene-ethynyl) unit change from $33000 \text{ M}^{-1} \text{ cm}^{-1}$, $\lambda = 361 \text{ nm}$ ($n = 1$) to $80000 \text{ M}^{-1} \text{ cm}^{-1}$, $\lambda = 404 \text{ nm}$ ($n = 3$) (Fig. 1).

The pivotal building block **14** was prepared according to Scheme 2. 4-Methoxybenzohydrazide **10** was readily prepared from the ester and converted to hydrazone **11** using 2-acetylphenol in *n*-propanol. The conversion of **11** to diketone **12** with the release of nitrogen¹⁵ was achieved using the stoichiometric amount of $\text{Pb}(\text{CH}_3\text{COO})_4$ under mild conditions. After some experimentation, we found that **13** could be isolated in good yield by the reaction of **12** with ammonium acetate with the release of formaldehyde. Reaction of **13** with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in the presence of the Hünig base readily produced the red emitter **14**. The use of 4-iodo-1-phenylethynylmagnesiumbromide in excess to substitute both fluoro groups led finally to **15** in an overall yield of 17% (Scheme 2). The synthesis of a compound bearing 4-ethylthiophene in place of *p*-methoxyphenyl has recently been reported.¹⁶

The promising characteristics of **5**, **7**, and **9** prompted us to examine the attachment of these yellow, energy transferring dyes to the red emitter **15**. The use of $[\text{Pd}(\text{PPh}_3)_4]$ (5 mol %) enabled the replacement of both iodo substituents of **15** by a double-coupling reaction and provided the triple Bodipy molecules **16–19** in acceptable yields (Scheme 3). Note again that the poor yield for $n = 3$ may reflect the instability of the terminal alkyne **9** under the experimental conditions used.

A single crystal X-ray structure was obtained for **15** as its chloroform solvate (Figs. 2 and 3).¹⁷ The boron center is almost tetrahedral and the bond lengths of the indacene framework remain characteristic of a fully delocalized cyanine unit. The ethyne tethers retain bond lengths typical of triple bonds (ca. 1.20 Å). A slight distortion from planarity is observed for the diisoindolomethene core.¹⁵ A ‘butterfly’ conformation is adopted with ‘wings’ consisting of two planes B–N1–C1–C2–C3–C4–C9 and B–N2–C5–C6–C7–C8–C9 where the dihedral angle is 9.6°. The tilt angles of



Scheme 1. Reagents and conditions: (i) TMS-acetylene, $[\text{PdCl}_2(\text{PPh}_3)_2]$, CuI; (ii) KOH, methanol; (iii) 2,5-dibutoxy-4-iodo-trimethylsilylethynyl-phenyl, $[\text{Pd}(\text{PPh}_3)_4]$, NEt_3 , C_6H_6 , 80 °C.

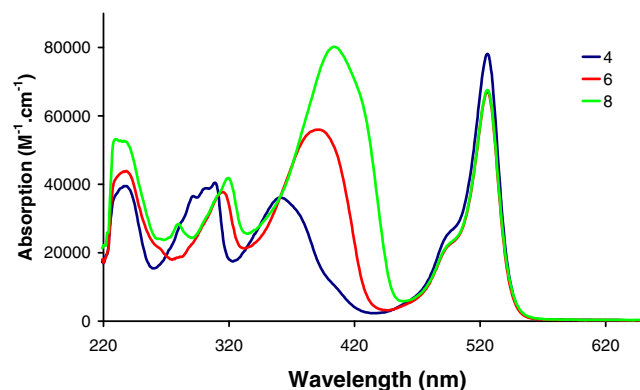
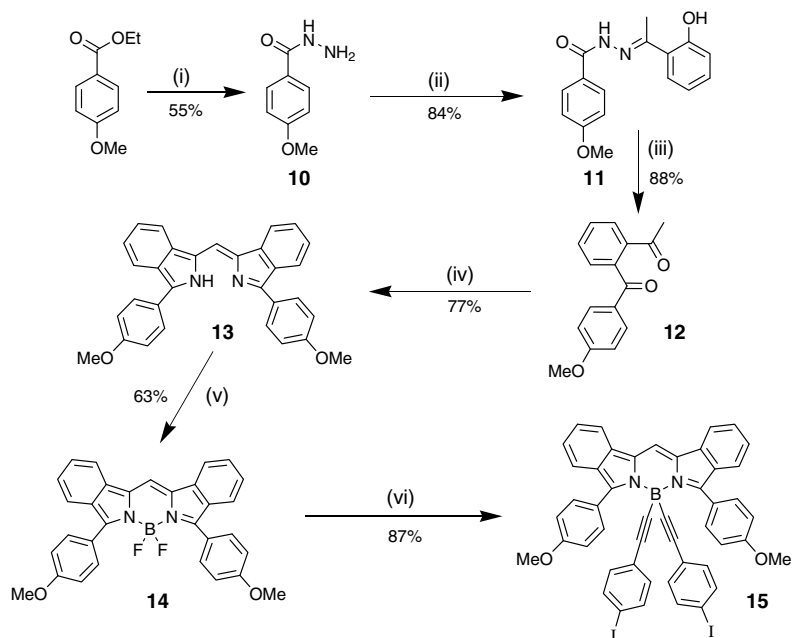
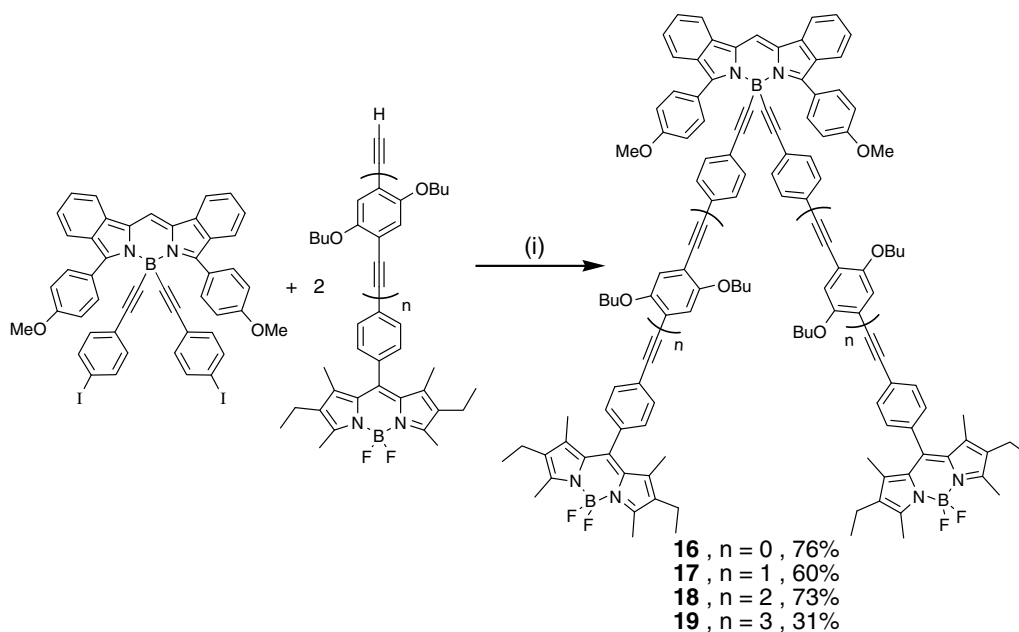


Fig. 1. Absorption spectra of **4**, **6** and **8**, in dichloromethane.



Scheme 2. Reagents and conditions: (i) $\text{NH}_2\text{-NH}_2$; (ii) 2-acetylphenol; (iii) $\text{Pb}(\text{OAc})_4$; (iv) NH_4OAc ; (v) $\text{BF}_3\cdot\text{EtO}_2$, $\text{NEt}(\text{iPr})_2$; (vi) 4-iodo-1-phenylethynylmagnesium bromide.



Scheme 3. Reagents and conditions: (i) $[\text{Pd}(\text{Ph}_3)_4]$, NEt_3 , benzene.

the anisole groups with respect to the indacene mean plane are 67.9° and 73.5° .

The asymmetric unit of the crystal corresponds to one molecule of compound **15** and one deuterated chloroform solvent molecule. The tetrahedral geometry of the solvent molecule is almost aligned to that of the boron center, the deuterium atom pointing toward the boron atom at a distance of 2.93 \AA , and pushing it by 0.25 \AA out of the mean plane of the boradiazaindene core, along the $\text{B} \rightarrow \text{I1}$ axis (viz. the $[441]$ direction). In the crystal structure

of **15**, adjacent molecules are linked around a center of inversion by two reciprocal $\text{C-I} \cdots \text{O}$ interactions with a distance of 3.4 \AA , implicating I2 of the ethyne tether oriented parallel to the $[5-13]$ direction and O1c of the methoxy group at position $(-1-x, -y, -z)$. Those pairs of molecules are piling (alternatively) up and down, parallel to the $[441]$ direction, through iodo $\cdots \pi$ interactions of mean distance of 3.61 \AA , between the other iodo ethyne tether and the centroid of an outermost ring of the indacene core at position $(1+x, 1+y, z)$. Another

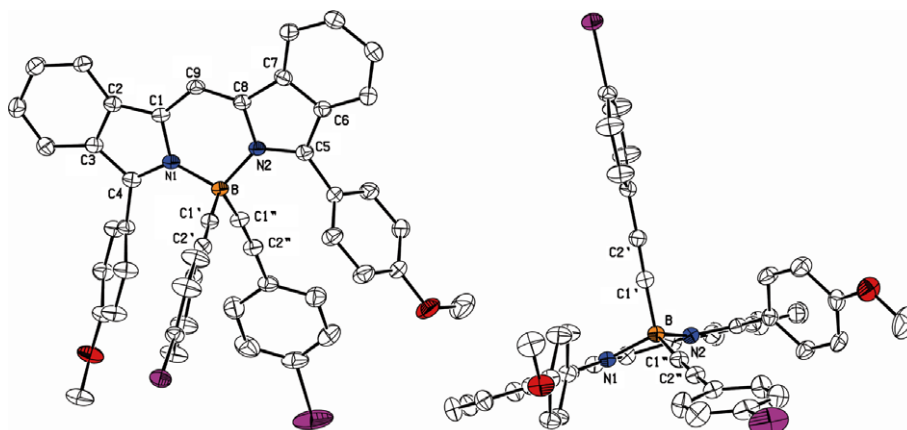


Fig. 2. Two ORTEP views of compound **15** (50% probability), with all hydrogen atoms removed for the sake of clarity. B–N1, B–N2, B–C1', B–C1'' are 1.597(6) Å, 1.591(5) Å, 1.581(6) Å, 1.573(7) Å, respectively, with angles N1BN2, C1'BC1'', N1BC1' and N2BC1'' of 106.7 (3)°, 111.2 (3)°, 108.1 (3)° and 111.8 (4)°, respectively.

3.78 Å contact between the methyl group C7c and the innermost ring (N1, C1–C4) of the indacene core at position $(-1 + x, y, z)$ stabilizes the molecular packing in the same direction (Fig. 3).

The orthogonality of the phenyl and the indacene planes in the yellow fluorophore and the tetrahedral geometry at boron means that orbital overlap between the different chromophores is negligible. Consequently, the absorption

spectra are linear combinations of the absorption features of the separate modules. Worthwhile noting is the fact that by increasing the size of the scaffolding, a bathochromic shift of its absorption is found (Fig. 4). In contrast to this red-shift of the spacer absorptions, the $S_0 \rightarrow S_1$ transitions of the yellow fluorophore at 520 nm and of the red emitter at 630 nm remain insensitive to the size of the branched system.

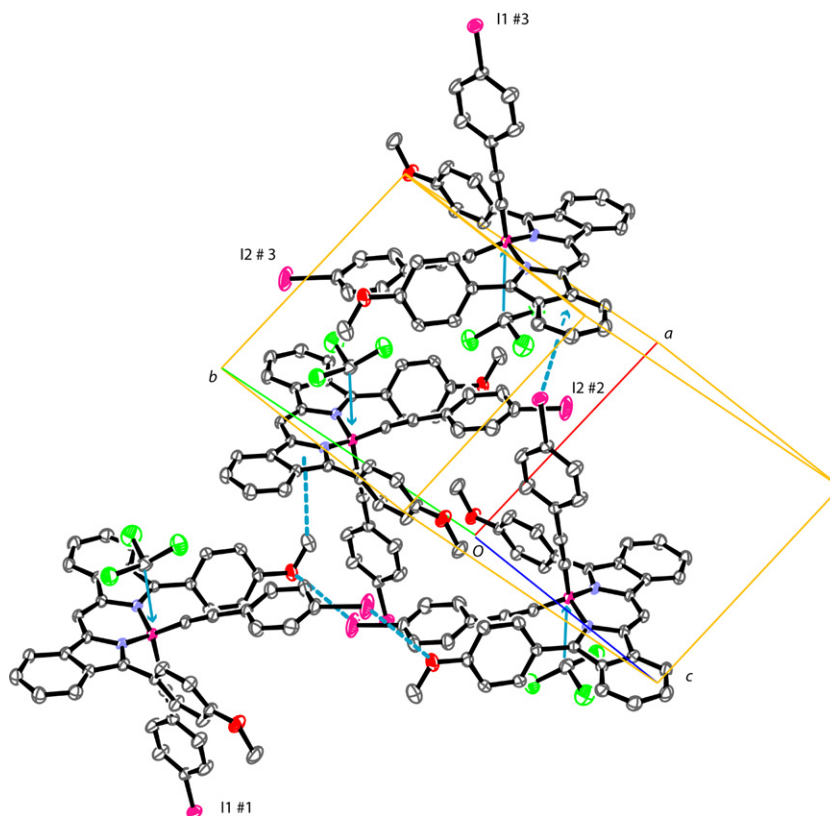
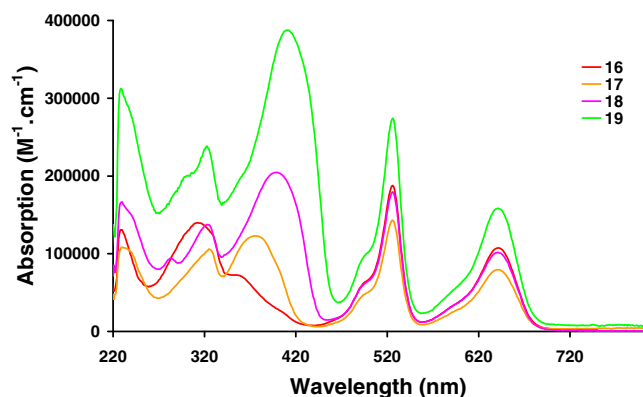
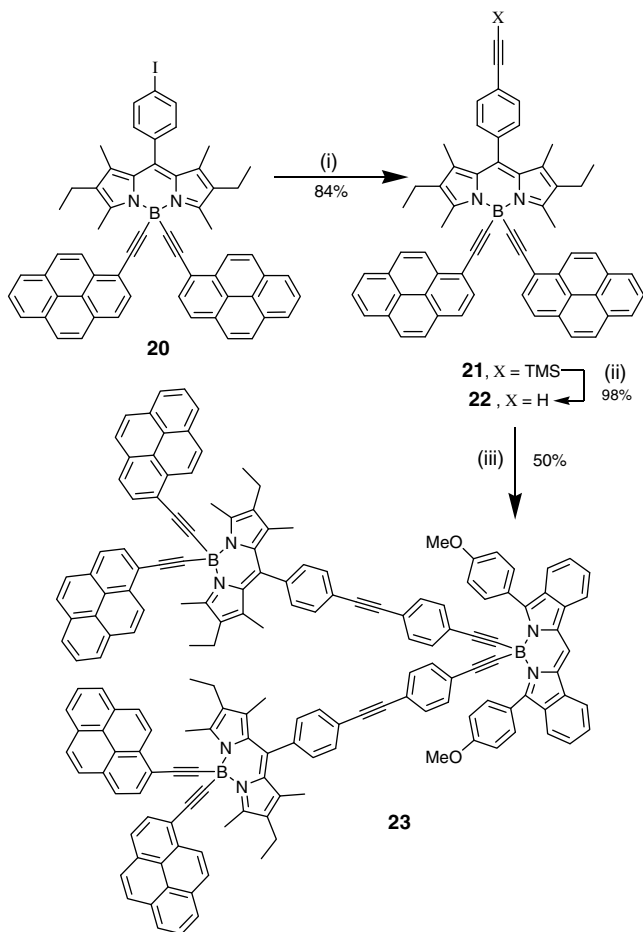


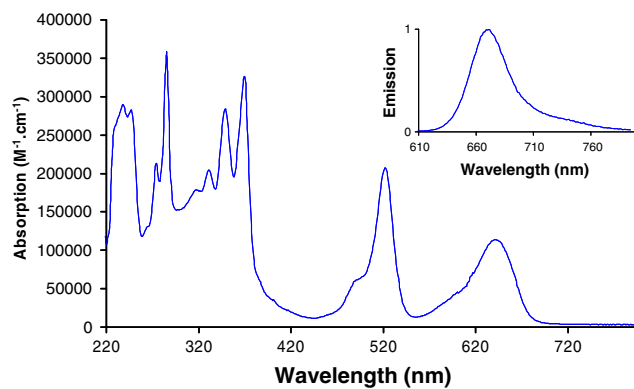
Fig. 3. View of the structure of compound **15** surrounded by three neighboring molecules in the crystal at respective positions #1: $-1 - x, -y, -z$, #2: $1 + x, 1 + y, z$, #3: $-1 + x, y, z$. Intermolecular contacts are indicated by dashed lines in blue. Black arrows highlight the direction of the deuterium atom of CDCl_3 .

Fig. 4. Absorption spectra of **16**–**19**, in dichloromethane.

As expected from previous work, replacement of fluorene by pyrenylethynyl units on the yellow Bodipy centers leads to very fast ($k > 10^{10} \text{ s}^{-1}$) and very efficient fluorescence energy transfer (FRET) from the pyrene to the Bodipy fragment.¹⁰ This markedly enhances the possible gap between the excitation and emission wavelengths.



Scheme 4. Reagents and conditions: (i) TMS-acetylene, $[\text{Pd}(\text{PPh}_3)_2\text{Cl}_2]$ 3 mol %, CuI 10 mol %; (ii) KOH, methanol; (iii) 0.5 equiv compound **15**, $[\text{Pd}(\text{PPh}_3)_4]$, NEt_3 , C_6H_6 , 60 °C.

Fig. 5. Absorption and emission spectra of **23**, in dichloromethane.

In order to embed ethynylpyrene subunits in the framework, it was found preferable to substitute the fluorene ligands of the yellow fluorophore early in the syntheses rather than after obtaining molecules **16**–**19**. We ultimately succeeded in preparing the trisubstituted derivatives **21** and **22**, carrying two types of different acetylenic derivatives, through substitution at boron by means of the ethynylpyrene-Grignard reagents,¹⁸ followed by cross-coupling with TMS-acetylene (Scheme 4). The soluble compound **21** was easily purified and was stable over days in solution. Finally, the tethering of two modules **22** to the red emitter **15** was feasible under mild standard conditions using Pd(0) as catalyst. The hyperbranched multi-dye **23** was isolated pure in 50 % yield and characterized by EI-MS (found: m/z 2297.1, calcd: 2297.0).

Once more, the absorption spectrum of **23**, in dichloromethane is a linear combination of those of the precursors (Fig. 5). The presence of the pyrene does not shift the $S_0 \rightarrow S_1$ absorption of either Bodipy subunit ($\lambda = 522 \text{ nm}$, $\epsilon = 207000 \text{ M}^{-1} \text{ cm}^{-1}$ and $\lambda = 641 \text{ nm}$, $\epsilon = 114000 \text{ M}^{-1} \text{ cm}^{-1}$). The pyrene residue imports its characteristic absorption between 230 and 370 nm. Excitation of either Bodipy chromophore produced very strong fluorescence at 670 nm ($\Phi_{\text{em}} = 87\%$, $\lambda_{\text{ex}} = 641 \text{ nm}$ and $\Phi_{\text{em}} = 44\%$, $\lambda_{\text{ex}} = 522 \text{ nm}$). This result is in keeping with a 50% efficiency of energy transfer from the yellow to the red emitter with a 4% residual emission of the yellow Bodipy at 541 nm. For pyrene excitation at 370 nm, the quantum yield for the emission of the blue Bodipy was still high ($\Phi_{\text{em}} = 51\%$), with a 3% residual emission of the yellow Bodipy. For excitation at 271 nm, a quantum yield of 65% of the red emitter was found, consistent with direct excitonic energy transfer from the bridge to the red emitter without funneling through the yellow fluorophore.

Our design opens up the possibility of engineering new sophisticated dyes bearing photon absorbers at the periphery and energy transducers in the heart. All photons would be funneled to a low-energy acceptor before the final emission. Substitution at boron imports a new dimensionality for grafting additional chromophores, opening up the possibility of constructing dendritic scaffoldings in a convergent manner. Work in progress is focused on increasing

the dimensionality of these multi-branched systems and introducing additional energy relays.

Acknowledgments

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- The crystal data of 15*: C₄₇H₃BI₂N₂O₂, CDCl₃, *M* = 1040.72, triclinic, space group *P* $\bar{1}$, *a* = 11.401(1), *b* = 13.646(1), *c* = 16.046(2) Å, α = 95.72(1)°, β = 105.60(2)°, γ = 111.69(2)°, *V* = 2178.8(6) Å³, *Z* = 2, *D*_c = 1.586 g cm⁻³, μ (Mo K α) = 1.669 mm⁻¹, *F*(0 0 0) = 1024, prismatic crystal, dark blue, size = 0.42 × 0.34 × 0.28 mm, 36360 reflections measured [*R*_{int} = 0.024], 9713 unique, *wR*₂ = 0.143 for all data, conventional *R* = 0.049 [(*I*/ σ)_{max} = 0.001] on *F*-values of 7608 reflections with *I* > 2 σ (*I*), *S* = 1.064 for all data and 525 parameters. Unit cell determination and intensity data collection ($2\theta = 54.7^\circ$) were performed on a Enraf-Nonius KAPPA CCD diffractometer at 293(2) K. Structure solution by direct methods and refinement by full-matrix least-squares on *F*². Programs: COLLECT [Nonius, B. V. (1999)], HKL2000 [Otwinowski, Z. and Minor, W. (1997)], SHELX97 [Sheldrick, G. M. (1997)]. CCDC [Deposit No: 669879] contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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