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Highly Substituted Bodipy Dyes with Spectroscopic Features Sensitive to the Environment

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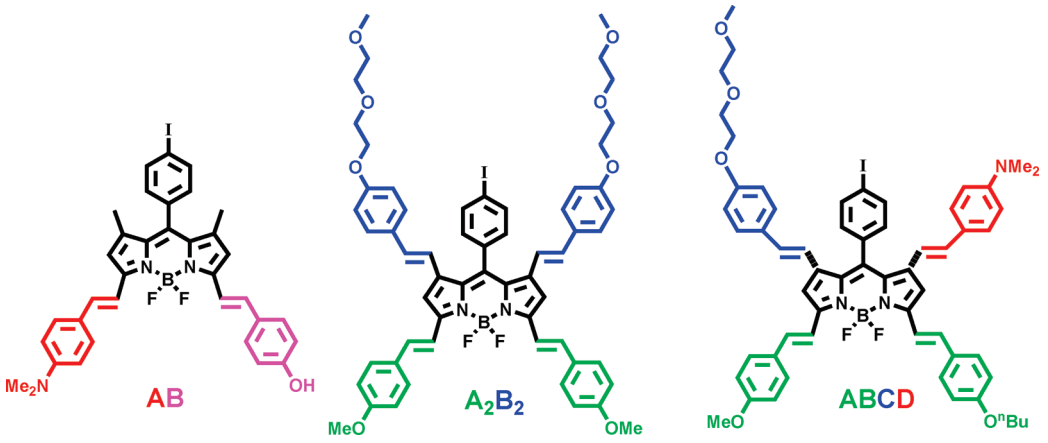

A general method for the synthesis of butterfly-shaped difluoroboradiaza-*s*-indacenes with different substituents has been developed. The mixed AB dye was produced in two successive Knoevenagel reactions involving first 4-dimethylaminobenzaldehyde and second 4-hydroxybenzaldehyde. Two pathways to A_2B_2 and ABCD derivatives were investigated starting from a tetramethyl-substituted Bodipy. The pivotal compound is a bis-styryl phenol derivative also produced by a Knoevenagel reaction without the need to protect the phenol functions. Methylation of the phenol functions provides mono- and bis-derivatives which have been used to construct tetrastyryl A_2B_2 and ABCD derivatives, respectively. Stepwise alkylation of the monomethoxyphenol dye provided a mixed dye that was converted to a tris-substituted compound, isolated as a mixture of regioisomers. The fourth styryl function was introduced by using 4-dimethylaminobenzaldehyde and forcing conditions. These highly colored dyes display outstanding optical properties with absorption wavelengths spanning from 573 to 718 nm and emission wavelengths from 585 to 800 nm. The high quantum yields, nanosecond excited state lifetimes, and weak Stokes shifts are typical of singlet emitters. The presence of both dimethylamino and phenol residues in some of these dyes makes them sensitive to acids and bases, allowing the tuning of the optical properties over a large wavelength range as a function of pH. A unique three-color ratiometric pH sensor based on both absorption and fluorescence has been characterized and studied in detail. The tris- and tetra-substitution of the methyl groups by vinyl residues induces a weaker bathochromic shift than that due to mono- and disubstitution. Consequently, replacing an alkoxy function by a dimethylamino moiety in the tetra-substituted derivatives has little effect on the spectroscopic features.

Introduction

There is a growing interest in the use of fluorescent dyes as markers in biomedical analysis, for multiplexing purposes, and as energy acceptors in FRET conjugates (FRET = Förster resonance energy transfer).[1] To engender water solubility and other requirements imposed for use in bioassays,

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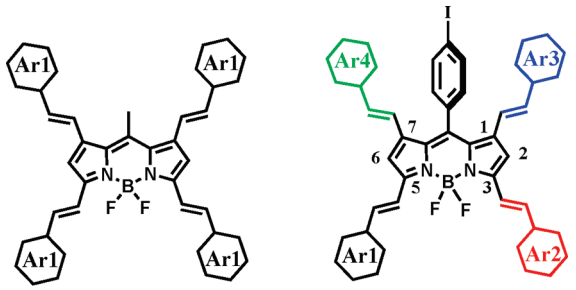
sophisticated functionalization of the known basic dye skeletons is necessary.[2]

Currently, propelled by scientific reviews highlighting their exceptional chemical stability and promising spectroscopic features,[3,4] there is a major interest in the engineering of difluoroboradiaza-*s*-indacene dyes (Bodipy). Advantages of the basic Bodipy core are its absorptive properties in the visible and the absence of deactivation complications due to triplet state population. However, the synthetic methodologies for its construction are limited, and the provision of larger quantities may represent a bottleneck for further studies and development in biomedical analysis. Postfunctionalization of the Bodipy core allows the preparation of sophisticated Bodipy dyes resolving specific problems linked to (i) sensing of protons[5] or various cations[6,7] by opto-electronic switching, (ii) light-harvesting in porphyrin based arrays[8] or other sophisticated architectures,[9,10] (iii) Stokes shift discrimination in energy transfer based on molecular cassettes,[11,12] (iv) water solubility of dyes for use as bioconjugate or bioprobes for imaging applications,[13,14] (v) multicascade energy transfer processes,[15] and (vi) photon concentration.[4,16]

The recent description of tetrastyryl-substituted Bodipys made from a single aldehyde and providing molecules of the type I (Chart I)[17] has prompted us to disclose our specific substitution procedure giving rise to tetrastyryl Bodipy dyes bearing four different side arms and giving molecules of type II, some of these dyes being sensitive to their environment. As well, the present methodology offers a wide range of possibilities for the synthesis of molecules with a precise molecular architecture, the geometry and environment of which are well programmed to generate upgraded functionality providing desired physicochemical and sensing properties.

CHART I. Representation of Two Types of 1,3,5,7-Tetrastyryl Bodipy Derivatives



The proper combination of different side arms provides a gamut of opportunities to fine-tune the optical properties of such innovative dyes, in part by rendering them sensitive to their environment (e.g., pH, polarity, viscosity, local temperature, ...). The most attractive aspect of this design is that it provides the capacity to tune the absorption and emission properties over a large spectral range, each arm being sensitive to a particular pH range (e.g., a phenol on one side and a dimethylamino function opposite). In general, the great advantage of ratiometric fluorescent probes derives from the recording of fluorescence intensities at two different wavelengths. This provides an increase in the accuracy and reproducibility of analyte detection compared to measurements performed at a single wavelength,[18,19] with no need to take into account the dye concentration and environmental effects. Strong ratiometric fluorescence responses have been achieved in solid films and fluorescent monolayers as well as in solution.[20,21]

Results and Discussion

The objective of the present work was therefore to develop a general procedure for the introduction of four different vinyl functions onto a single Bodipy core. To this end, we first explored the synthesis of the mixed derivative **4** (Scheme 1), potentially a species suitable for ratiometric pH determination (vide infra).

Condensation of **1** with 4-hydroxybenzaldehyde under previously described conditions[22] provided mixtures of the monosubstituted **2a** and disubstituted **2b** derivatives which were easily separated by column chromatography due to the presence of the polar phenol function. Unfortunately,

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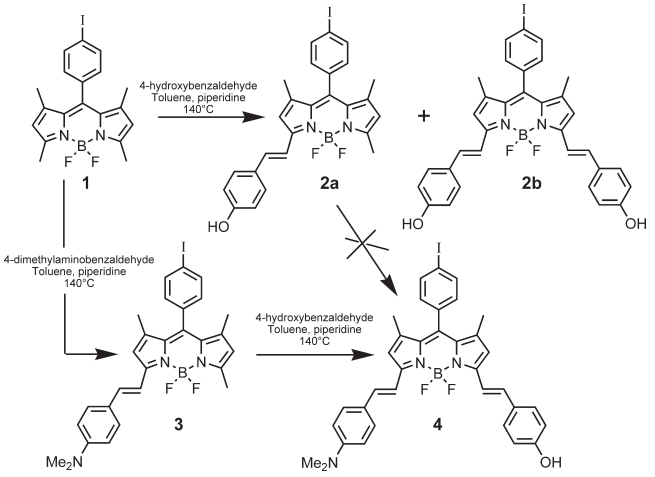
SCHEME 1. Approaches to Mixed Vinyl-Bodipys



synthesis of the mixed derivative **4** from **2a** failed due to purification difficulties. More successful was the reaction of **3**[23] with 4-hydroxybenzaldehyde, providing **4** in 68% isolated yield. This compound was interesting in its own right because of its orthogonal functionality, the dimethylamino residue being sensitive to protons and the phenol to base. Previous results[24] justified the expectation that the extended delocalization engendered by the 3,5-substitution should result in dramatic color changes being associated with protonation/deprotonation reactions. Note that a bisstyryl derivative with two different side arms has been applied as a molecular logic gate.[25] In any case, the experimental protocol developed for the synthesis of the dual dye **4** was encouraging in that it provided an expeditious route to tetrasubstituted derivatives (Scheme 2). Reaction of **2b** with iodomethane provided a mixture of mono- and dialkylated derivatives **5**[26] and **7** easily separated by column chromatography due to the marked difference in polarity between them. A similar protocol was used for the preparation of the unsymmetrical dye **8** but using bromobutane as the reagent. The first mixed A_2B_2 tetrasubstituted Bodipy **6** was prepared in 45% yield from the polar 4-[2-(2-methoxyethoxy)ethoxy]-benzaldehyde using forcing conditions (140 °C, highly concentrated reagent mixtures, excess of the aldehyde).[17,22] Overall, the substrate readily tolerates vinyl group functionalization in both the 3,5- substitution positions.

Our next target became the preparation of a heterotetrasubstituted dye using our optimized conditions. The major product obtained during the condensation of dye **8** with 4-[2-(2-methoxyethoxy)ethoxy]benzaldehyde was compound **9**, isolated as a 50/50 mixture of two regioisomers having similar physical properties and which could not be separated properly, despite the presence of the polar polyoxoethylene chain (Figure S1, Supporting Information). The remaining methyl group could be easily substituted with the reactive 4-dimethylaminobenzaldehyde reagent, providing the first multifunctionalized derivative **10** isolated as a mixture of equal amounts of both regioisomers (Chart II).

The ^{1}H NMR spectra of the series of derivatized dyes showed some interesting features. In particular, in the NMR spectrum of **8**, the vinylic protons in the 3,5-positions appear as two doublets, the most shielded at 7.22 ppm, whereas a singlet is found at 6.62 ppm for the β-pyrrolic protons. The 16.5 Hz coupling constant of the doublets confirms the *trans* geometry of the double bonds, a situation expected in light of the reaction conditions. In the case of the symmetrically tetrasubstituted derivative **6**, the vinylic protons in the 1 and 7 positions are in the shielding cone of the iodophenyl ring and are shifted from 7.22 to 5.70 ppm (^3J = 16.0 Hz), whereas the β-pyrrolic protons are deshielded from 6.62 to 7.09 ppm. This diagnostic effect is confirmed for compound **10**, where two shielded doublets are found at 5.76 and 5.70 ppm (^3J = 16.2 Hz) for the vinylic protons and the β-pyrrolic protons are deshielded at 7.33 ppm. However, for the unsymmetrical dye **9**, a single shielded doublet is found at 5.57 ppm (^3J = 16.2 Hz), whereas two β-pyrrolic proton peaks are found at 7.34 and 6.95 ppm. These observations are in keeping with previous results obtained with homotetrasubstituted Bodipy dyes.[17]

The molecular structure of **6** confirms the presence of four vinyl arms in a *trans* conformation, giving the molecule a butterfly shape (Figure 1). The iodophenyl unit is constrained to be orthogonal (dihedral angle of 88.5(2)°) to the F-Bodipy core by the two side chains at the 1 and 7 positions. The dihedral angle between the iodophenyl unit and the B−F2 plane is 1.8(4)° and that between the latter and the indacene core is 89.8(4)°. The boron center is essentially tetrahedral, with an N−B−N angle of 107.5(3)° and an F−B−F angle of 108.6 (4)°. The average B−N and B−F bond lengths are 1.535(6) and 1.391(6) Å, respectively. More surprising is the less pronounced double bond character than is usually observed for the N1−C4, N2−C5 bonds, with an average bond length value of 1.374(6) Å compared to the mean N1−C1, N2−C8 value of 1.388(6) Å. The central core of the molecule appears *quasi*-planar with slight tilts between 10° and 18° from the central nucleus mean plane involving three out of the four phenyl rings.

For steric reasons associated with the molecular packing involving smoothly undulating layers parallel to the [1 4 −1] plane, with an interplanar distance of ca. 3.5 Å (Figure 2), one ethyleneglycol side chain is folded above the mean plane like a "scorpion tail" whereas terminal atoms of the second side chain are lifted up out of the mean plane, attracted by the nearby iodo atoms at a distance of 3.6 Å. Successive molecules along the [100] direction are linked by a double aromatic $\pi-\pi$ stacking interaction involving pyrrole and phenyl rings with a ring-centroid separation of 3.7 Å (Figure 3).

Optical Properties

Spectroscopic data relevant to the present discussion are collected in Table 1 and typical examples are given in Figure 4.

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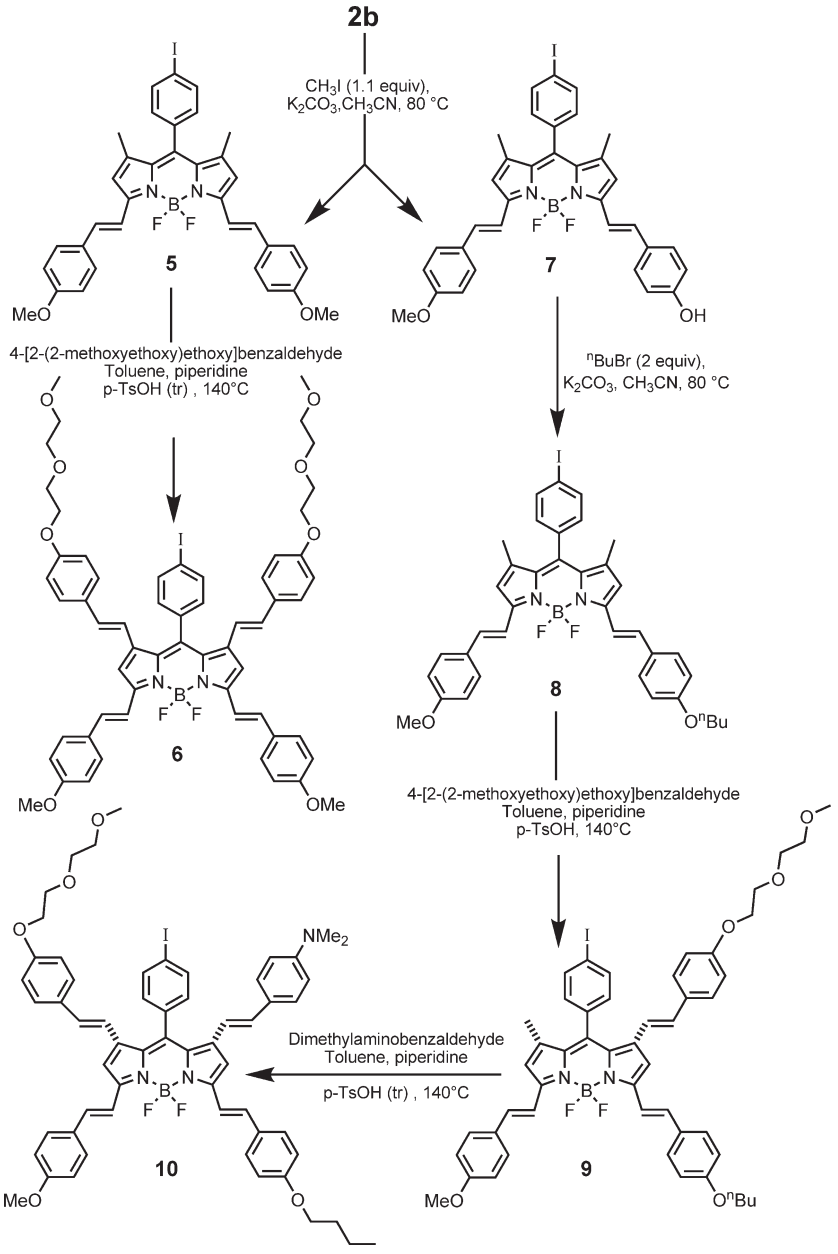
SCHEME 2. Synthesis of Tetravinyl-Substituted Bodipys



All dyes exhibit absorption and emission patterns typical for Bodipy fluorophores,[29] with profiles and excited state lifetimes characteristic of singlet emitters. In solution, the absorption spectrum shows that the strong $S_0 \rightarrow S_1$ ($\pi-\pi^*$) transition located at 660 nm for dye **8** is progressively shifted to 679 and 708 nm, respectively, for dyes **9** and **6**, highlighting the increase of conjugation. Notice that the bathochromic shift is less pronounced on grafting vinyl moieties in the 1,7 positions than in the 3,5 positions, a shift of 156 nm being found for dye **8** with respect to dye **1**. Increasing the substitution pattern from two to three (compare **8** and **9**) further shifts the absorption by 19 nm, whereas tetrasubstitution with four vinyl residues only increases this shift by 29 nm (compare **9** and **6**). Note that, by switching an alkoxy moiety for a dimethylamino group in dye **10**, the bathochromic shift is further increased by 16 nm with respect to **6**.

Another point of interest is the intramolecular charge transfer band (ICT) located at 372 nm ($\varepsilon = 71\,300\ M^{-1}\,cm^{-1}$) in dye **8**, which progressively and smoothly shifts to lower energies for the tris- and tetrasubstituted derivatives (at 377 nm, $\varepsilon = 61\,500\ M^{-1}\,cm^{-1}$ in **9** and at 384 nm, $\varepsilon = 70\,000\ M^{-1}\,cm^{-1}$ in **6**). In the latter case, the band around 380 nm is clearly a composite of several transitions, as would be expected from the presence of different donor groups on the phenyl rings. Note that a new absorption band near 500 nm appears on increasing the level of styryl substitution (Figure 4a–c). This is probably due to the $S_0 \rightarrow S_2$ ($\pi-\pi^*$) transition that is located

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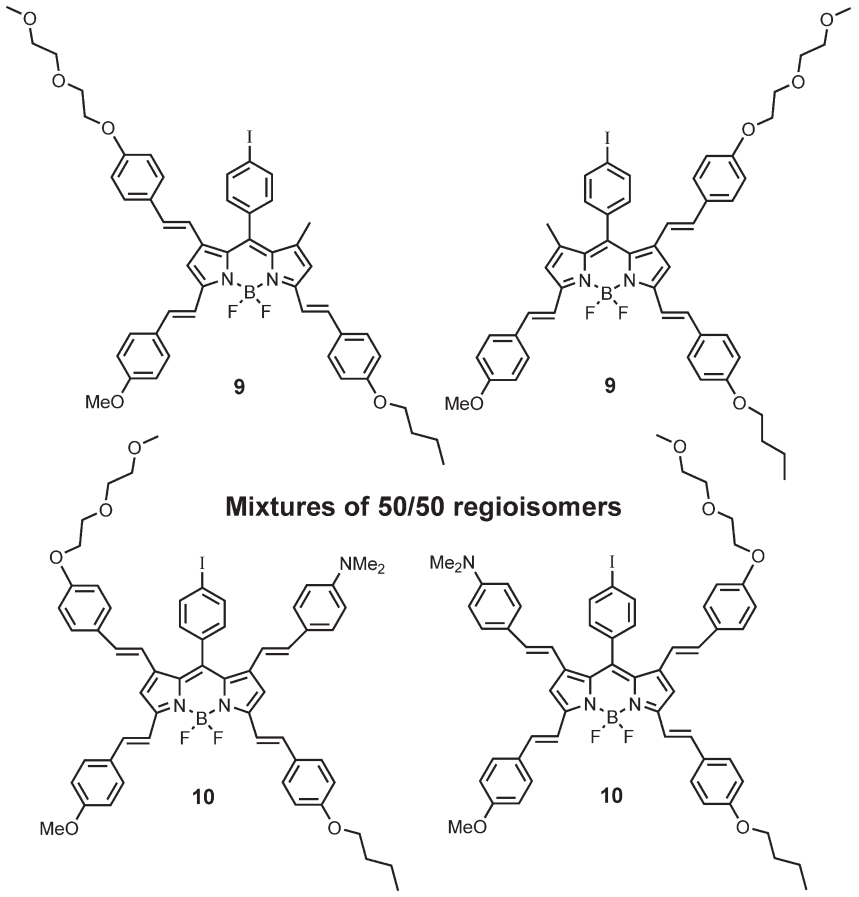
CHART II. Representation of the Two Regioisomers of the 1,3,5-Trisvinyl Bodipy and 1,3,5,7-Tetravinyl Bodipy Derivatives



beneath the ICT band in compounds **7** and **8**, and progressively shifted to lower energies.[30]

In all cases the fluorescence spectrum shows good mirror symmetry with the lowest energy absorption transition (Figure 4), confirming that these transitions are due to the same state and from a weakly polarized excited state. The weak Stokes shifts are in the 330 to 750 cm^{-1} range for the series of dyes with the exception of dye **4**, and the nanosecond regime of the excited state lifetimes are in keeping with a singlet excited state. This is further confirmed by the absence of any significant dynamic quenching of the luminescence by molecular oxygen, excluding the presence of an emissive triplet excited state. In addition, for most of these dyes no significant solvatochromic effect was observed in the absorption and fluorescence spectra, confirming weak polarization of the ground and the excited states. These photophysical data are in accord with those of related functionalized boron-dipyrromethene dyes.[31] In fact, the radiative rate constants depend critically on the nature of the styryl substitent and relatively weakly on the degree of substitution *bis* versus *tris* and *tetra* (Table 1). Notice that ethanol and dioxane have been chosen as solvent because no aggregation or decomposition of the dyes under irradiation have been observed. These solvents also made possible the used of HCl gas and NMe_4OH as source of acid and base, respectively.

In the case of dyes **4** and **10**, the higher nonradiative rate constants are due to the lower emission quantum yields and may be attributed either to the higher conformational flexibility induced by the dimethylaminophenyl residue or to the interaction with an energetically low-lying localized state. Finally, for all the new dyes the excitation spectrum fairly matches the absorption spectrum, confirming that all transitions participitate in the emission process (Figure 4).

The optical behavior of the mixed distyryl derivative **4** is of particular interest owing to the major changes in color resulting from orthogonal deprotonation of the phenol or protonation of the dimethylamino functions. In the neutral species, the lone pair of the dimethylamino residue induces a bathochromic shift, and the absorption peak appears at 676 nm in ethanol. This lies between those observed for di(methoxystyryl)-[34] and bis(dimethylaminostyryl)-Bodipy.[23] The protonation of the dimethylamino group induces a hypsochomic shift as well as a hyperchromic shift of the S_0-S_1 band, due to the loss of the lone pair delocalization (Figure 5).[10,35] There is

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(31) (a) Rurack, K.; Kollmannsberger, M.; Resch-Genger, U.; Daub, J. *J. Am. Chem. Soc.* **2000**, *122*, 968–969. (b) Rurack, K.; Kollmannsberger, M.; Daub, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 385–387.

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a simultaneous modification in the UV region, with the disappearance of three bands at 470, 408, and 391 nm, replaced by a single strong absorption at 362 nm. In contrast, the deprotonation of the phenol group causes a strong bathochromic shift, with an S_0-S_1 absorption band at 718 nm due to the delocalization of the phenolate charge over the entire conjugated pathway (Figure 5). The absorption spectrum of the deprotonated species is red-shifted with respect to the bis-(dimethylaminostyryl-Bodipy), and does not significantly change with the polarity of the solvent.[35]

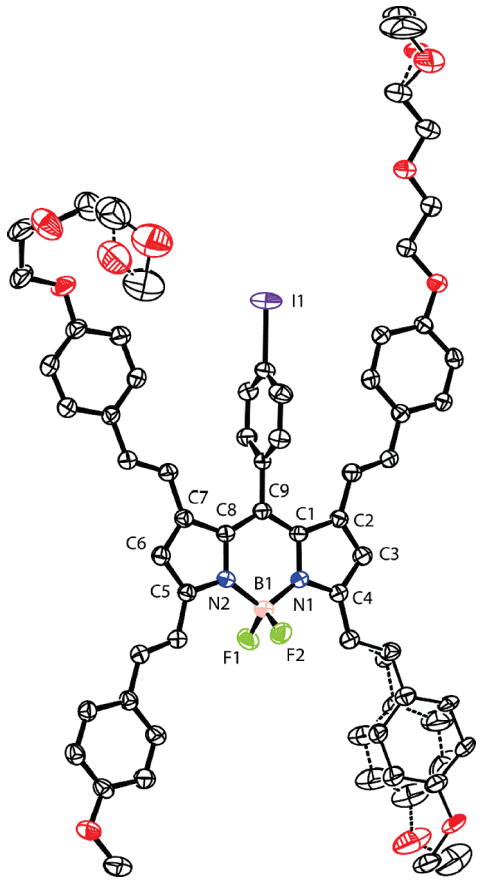

FIGURE 1. Ortep[27] view of X-ray crystal structure of **6** at the 30% probability level. Dashed lines represent a minor conformation of disordered atoms.

Interestingly, the emission properties of the neutral dye **4** are sensitive to the solvent polarity with an emission at 714 nm in dioxane and 743 nm in ethanol and an associated drop of quantum yields from 23% to 8%, respectively. The charge transfer character is almost inhibited after protonation of the dimethylamino group, with a strong blue shift of the emission at 656 nm in dioxane and 662 nm in ethanol and quantum yields reaching 40% and 23%, respectively. Conversely, when the phenol group is deprotonated in ethanol, an enhanced charge transfer take place and a strong red-shift of the emission at 799 nm with a 6% quantum yield results (Figure 6).

This molecular system can be seen as a model three-color ratiometric system for pH measurement. The titration of compound **4** in ethanol with HCl (Figure 7a) shows the disappearance of the low energy band at 676 nm and a simultaneous growth of a band at 637 nm with three well-defined isosbestic points at 649, 524, and 377 nm. The addition of NMe_4OH to **4** induces weakening of the 676 nm band and the rise of a new band at 721 nm, with four well-defined isosbestic points at 693, 563, 410, and 351 nm (Figure 4b). The analysis of these two titrations using SPECFIT[36] gave association constants of $\log K_{H^+} = 2.8 \pm 0.1$ and $\log K_{OH^-} = 3.8 \pm 0.1$.

A spectrofluorometric titration was performed in a similar manner, with excitation at the respective isosbestic points. During the protonation, a strong emission takes place at 660 nm at the expense of the emission at 744 nm (Figure 8a). The addition of the base induces a reduction of the broad peak at 744 nm and the appearance of near-IR emission around 800 nm (Figure 8b).

Concluding Remarks

Our design opens up the possibility of engineering sophisticated dyes in which the polyaromatic moieties are coupled electronically with the central dipyrromethene core via vinyl tethers. The use of different aldehydes and alkylation of the phenol residues in a specific sequence of reactions enables the preparation of mono-, di-, tri-, and tetrasubstituted derivatives. The last two forms were isolated here as mixtures of regioisomers. These novel dyes display spectroscopic properties in keeping with the family of Bodipy dyes, with intense absorption in the visible part of the spectrum due to strong oscillator strengths, nanosecond excited state lifetimes, weak Stokes shifts and elevated emission quantum yields. The dyes carrying dimethylamino or phenol residues are sensitive to their environment (solvent, acid, base) and in one case a

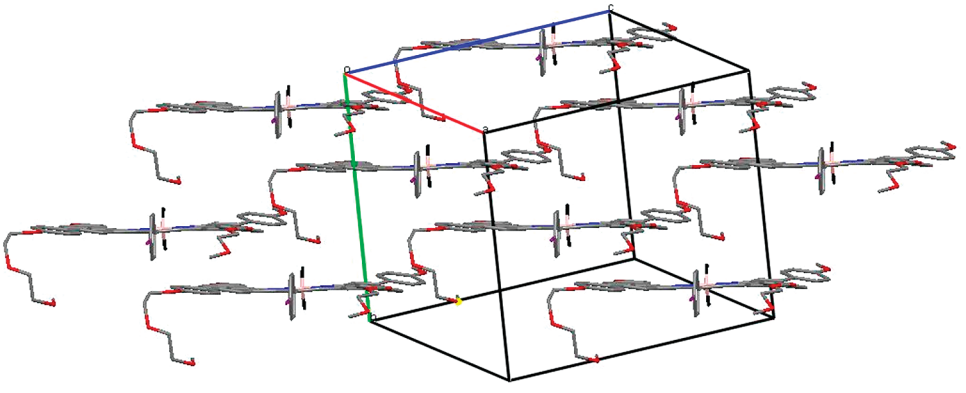

FIGURE 2. Packing view[28] of the crystal structure of **6**.

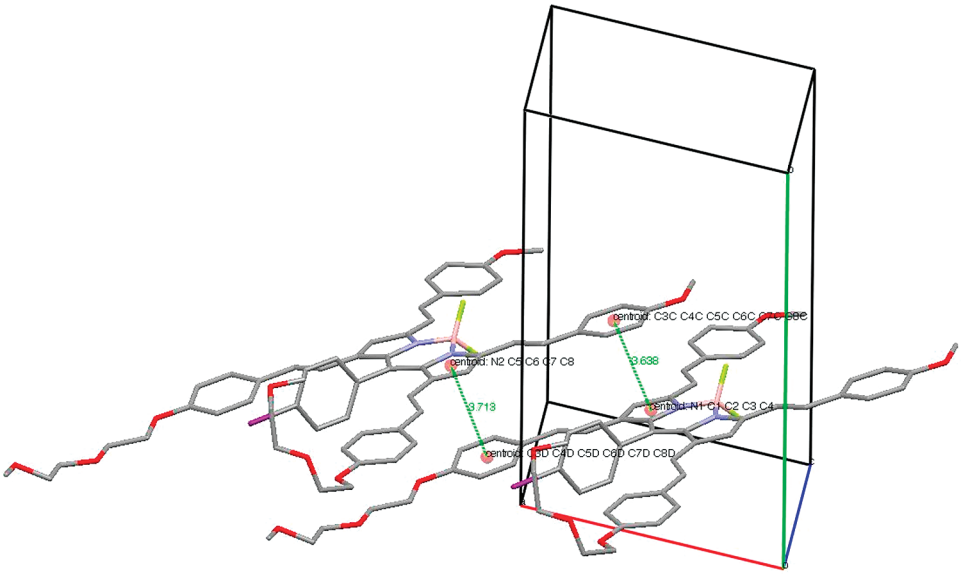

FIGURE 3. Close-up of the $\pi-\pi$ stacking interaction developed along the *b* axis between a molecule in general position and its neighbor in position $x + 1$, y, z.

TABLE 1. Selected Spectroscopic Data

dye	λ_{abs}(nm)	ε ($M^{-1}\cdot cm^{-1}$)	λ_{em} (nm)	Φ_f @ λ_{exc} (nm)[a]	τ (ns)	k_r[b] (10^7 s^{-1})	k_{nr}[b] (10^7 s^{-1})	solvent
2a	573	100 000	585	57% @ 570	6.3	9.0	6.8	dioxane
2b	647	114 000	662	50% @ 570	1.8	27.8	27.8	dioxane
4	676	91 000	744	8% @ 650	1.7	4.7	54.1	EtOH
4/H$^+$	637	115 000	660	23% @ 610	1.9	12.1	40.5	EtOH/HClg
4/OH$^-$	718	95 500	799	6% @ 685	1.3	4.6	72.3	EtOH/NMe_4OH
6	689	162 000	708	34% @ 665	5.8	5.8	11.4	dioxane[c]
7	646	125 000	663	60% @ 570	2.1	28.6	19.0	dioxane
8	646	120 000	660	57% @ 570	4.5	12.7	9.5	dioxane
9	666	132 000	679	61% @ 590	2.0	30.5	19.5	dioxane
10	700	142 000	714	13% @ 610	4.7	18.6	124	dioxane
10/H$^+$	695		713	15% @ 610	4.6	3.2	18.5	dioxane/HCl(g)

[a]Solution concentration ca. 5×10^{-7} M. Using Cresyl Violet, as reference ($\phi_F = 0.50$ in ethanol)[32] and tetramethoxydiisoindomethene-difluoroborate ($\phi_F = 0.51$ in methanol).[33] All Φ_F values are corrected for changes in refractive index. [b]Calculated by using the following equations: $k_r = \Phi_F/\tau_F$, $k_{nr} = (1 - \Phi_F)/\tau_F$, assuming that the emitting state is produced with unit quantum efficiency. [c]Very similar results obtained in EtOH.

ratiometric pH sensor operating in absorption and emission over a large spectral range has been characterized. While the spectra of the other dyes are less sensitive to solvent, their absorption and emission wavelengths are shifted to the near-infrared by a progressive increase of the number of substituents. Our subsequent work will be focused on efforts to prepare water-soluble dyes suitable for action as pH sensors under biological conditions.

Experimental Section

General Procedure 1 for Knoevenagel Condensations. In a round-bottomed flask equipped with a Dean−Stark apparatus, the benzaldehyde derivative (1.5 equiv), piperidine (2 mL), and a crystal of *p*-TsOH were added to a stirred solution of the Bodipy dye (about 0.5 g scale) dissolved in 20 mL of toluene. The solution was heated at its boiling point until it had evaporated to dryness. The resulting solid was washed with water three times and extracted with dichloromethane. The organic phase was dried over $MgSO_4$ and absorbent cellulose, and the solvent was evaporated under reduced pressure. The resulting crude residue was purified by column chromatography on SiO_2, elution with CH_2Cl_2/ethyl acetate (90/10) affording the desired compound, then recrystallization from appropriate solvents.

(36) Astron., K. G. *Astron. Soc. Pac. Conf. Ser.* **1994**, *61*, 437–446.

General Procedure 2 for Alkylation. In a round-bottomed flask containing K_2CO_3 (1.2 equiv) and 30 mL of CH_3CN was added the phenol-substituted Bodipy (about 0.5 g scale) and the mixture was stirred at 80 °C for 1 h. After cooling to room temperature, CH_3I (1 equiv) was added and the mixture was stirred at 80 °C overnight. The mixture was washed with water three times and extracted with dichloromethane. The organic phase was dried over absorbent cellulose and the solvent was evaporated under reduced pressure. The resulting crude residue was purified by column chromatography on SiO_2 and elution with CH_2Cl_2/ethyl acetate (90/10) affording the target derivatives in acceptable yields.

Compounds 2a and 2b. Prepared using the general procedure 1 from compound **1** (560 mg, 1.24 mmol), 4-hydroxybenzaldehyde (230 mg, 1.88 mmol), piperidine (2 mL), and a crystal of *p*-TsOH in toluene (20 mL), affording 175 mg of **2a** (25%) and 400 mg of **2b** (48%).

2a: ^{1}H NMR (CD_2Cl_2 300 MHz) δ 1.43 (s, 3H), 1.47 (s, 3H), 6.03 (s, 1H), 6.61 (s,1H), 6.82 (d, 2H, ^3J = 8.6 Hz), 7.07 (d, 2H, ^3J = 8.3 Hz), 7.34 (d, 1H vinylic proton, ^3J = 17 Hz), 7.41−7.47 (m, 3H), 7.84 (d, 2H, ^3J = 8.3 Hz). ^{13}C NMR (CD_2Cl_2, 75 MHz) 14.2, 14.8, 15.1, 22.7, 34.5, 95.1, 116.2, 116.9, 117.9, 121.7, 129.5, 129.7, 130.7, 131.8, 132.9, 135, 136.7, 138.8, 139.1, 143.4, 153.8, 155.5, 157.3. ESI-MS 554.0 ([M], 100). Anal. Calcd for $C_{26}H_{22}BF_2IN_2O$ (M_r = 554.17): C, 56.35; H, 4.00; N, 5.05. Found: C, 56.04; H, 3.69; N, 4.74.

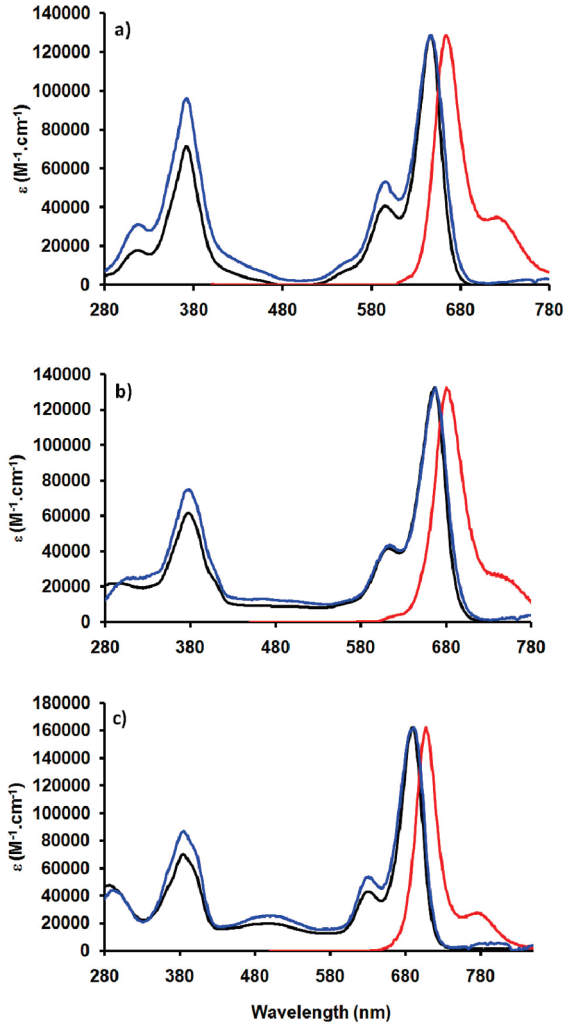

FIGURE 4. Absorption (black), emission (red), and excitation (blue) spectra in dioxane, at rt for (a) the bisstyryl derivative **8**, (b) the trisstyryl derivative **9**, and (c) the tetrastyryl derivative **6**.

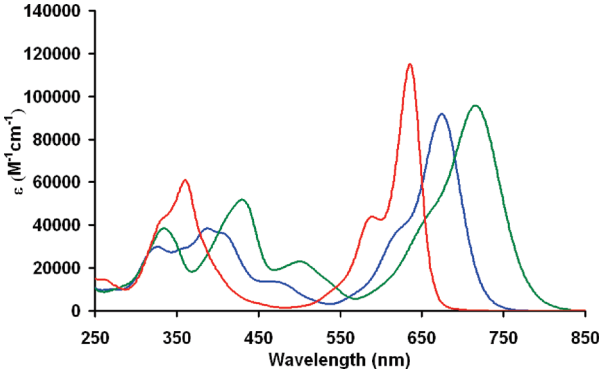

FIGURE 5. Absorption spectra of **4** in EtOH, at neutral pH (blue), in the presence of excess HCl (red) and excess Me_4NOH (green).

2b: ^{1}H NMR ($(CD_3)_2CO$ 300 MHz) δ 1.51 (s, 6H), 6.84 (s, 2H), 6.95 (d, 2H, ^3J = 8.6 Hz), 7.32 (d, 2H, ^3J = 8.6 Hz), 7.42−7.60 (m, 8H), 8.01 (d, 2H, ^3J = 8.6 Hz), 8.82 (s, 2H). ^{13}C NMR ($(CD_3)_2CO$, 50 MHz) δ 95.3, 116.9, 118.7, 129.3, 129.9, 131.8, 139.2, 142.3, 159.7. ESI-MS 659.1 ([M + H$^+$], 100). Anal. Calcd for $C_{33}H_{26}BF_2IN_2O_2$ (M_r = 658.28): C, 60.21; H, 3.98; N, 4.26. Found: C, 59.96; H, 3.65; N, 3.99.

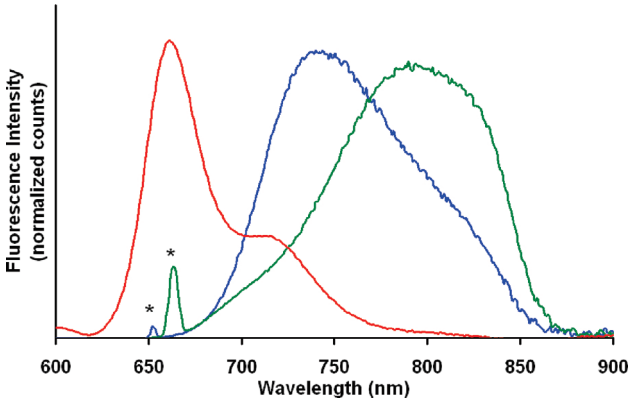

FIGURE 6. Emission spectra of **4** in ethanol, at rt, neutral (blue), in the presence of excess HCl (red), and excess Me_4NOH (green). An asterisk (*) shows residual excitation peaks.

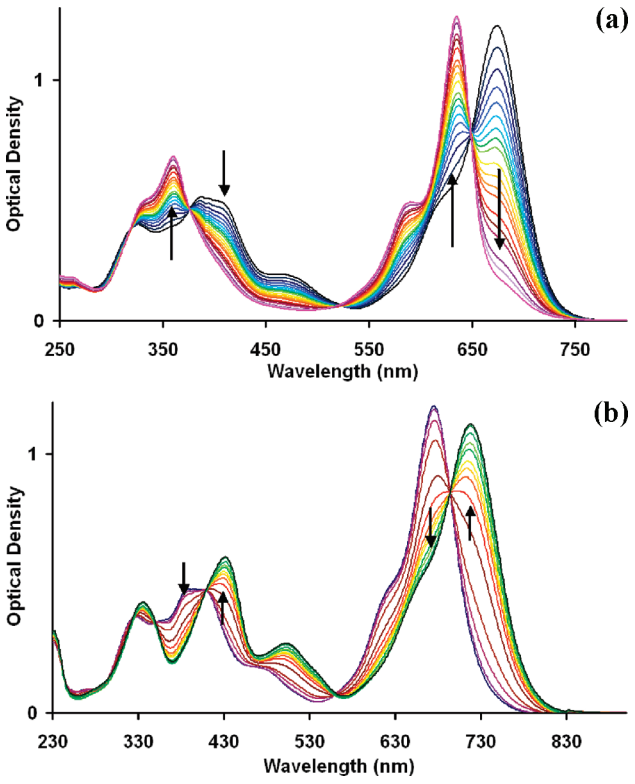

FIGURE 7. (a) Absorption spectral changes during the titration of **4** (10^{-5} mol) in ethanol (0.01 M nBu_4PF_6), by successive addition of aliquots of HCl from a 10^{-2} M mother solution of HCl(g) in EtOH. All spectra are corrected for dilution. (b) Titration of **4** (10^{-5} mol) in ethanol (0.01 M nBu_4PF_6), by addition of aliquots of NMe_4OH (0.1, 0.2, 0.5, 1 equiv from a 10^{-4} M solution in EtOH). Corrected for dilution.

Compound 4. Prepared using the general procedure 1 from compound **3** (56 mg, 96 μmol) and 4-hydroxybenzaldehyde (17 mg, 0.14 mmol), piperidine (2 mL), a crystal of *p*-TsOH, and toluene (20 mL), affording compound **4** (45 mg, 68% isolated yield). ^{1}H NMR (DMSO 300 MHz) δ 1.42 (s, 3H), 1.43 (s, 3H), 3.00 (s, 6H), 6.77−6.93 (m, 6H), 7.22−7.51 (m, 10H), 7.93 (d, 2H, ^3J = 8.3 Hz), 9.93 (ls, 1H). ^{13}C NMR (DMSO, 50 MHz) δ 14.4, 14.5, 54.9, 95.6, 112.2, 112.9, 115.2, 116.1, 117.6, 118.30, 118.36, 118.42, 123.7, 127.5, 128.9, 129.0, 130.9, 131.7, 132.4, 134.0, 135.2, 136.2, 138.0, 138.5, 139.9, 140.7, 141.4, 151.1,

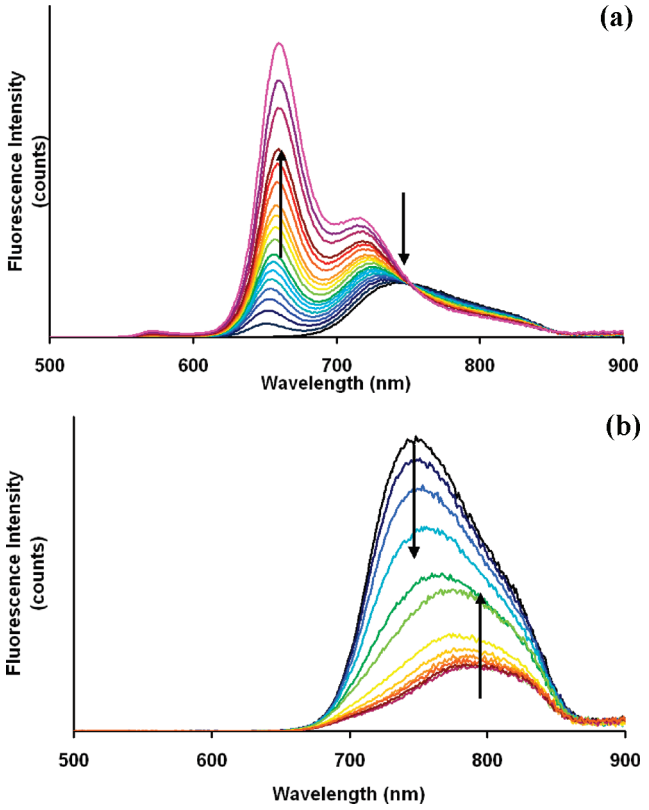

FIGURE 8. (a) Evolution of the emission spectra of **4** (10^{-5} mol) in ethanol (0.01 M nBu$_4$PF$_6$), during the addition of aliquots of HCl (10^{-2} M in EtOH) and excitation at 380 nm. Corrected for dilution. Evolution of the emission spectra during the titration of **4** (10^{-5} mol) in ethanol (0.01 M nBu$_4$PF$_6$), by addition of aliquots of NMe$_4$OH (10^{-4} M in EtOH) and excitation at 410 nm. Corrected for dilution.

121.3, 153.6, 158.9. ESI-MS 685.1 ([M], 100). Anal. Calcd for $C_{35}H_{31}BF_2IN_3O$ (M_r = 685.35): C, 61.34; H, 4.56; N, 6.13. Found: C, 61.04; H, 4.19; N, 5.87.

Compound 6. Prepared using the general procedure 1 from compound **5** (55 mg, 80 μmol), 4-(2-(2-methoxyethoxy)ethoxy)-benzaldehyde (90 mg, 0.4 mmol), piperidine (2 mL), and a crystal of p-TsOH in toluene (20 mL), affording compound **6** (40 mg, 45% isolated yield). ^{1}H NMR (CD_2Cl_2 400 MHz) δ 3.36 (s, 6H), 3.53−3.56 (m, 4H), 3.66−3.68 (m, 4H), 3.82 (t, 4H, ^3J = 4.7 Hz), 3.86 (s, 6H), 4.13 (t, 4H, ^3J = 4.7 Hz), 5.71 (d, 2H vinylic protons, ^3J = 16 Hz), 6.85−6.98 (m, 14H), 7.09 (s, 2H), 7.28 (d, 2H, ^3J = 8.2 Hz), 7.38 (d, 2H vinylic protons, ^3J = 16.4 Hz), 7.59−7.64 (m, 6H), 8.04 (d, 2H, ^3J = 8.2 Hz). ^{13}C NMR (CD_2Cl_2, 50 MHz) δ 59.1, 67.9, 71.1, 72.3, 95.8, 111.4, 114.8, 115.3, 117.2, 119.4, 128.4, 129.5, 129.7, 130.2, 131.9, 132.8, 135.6, 136.9, 139.1, 142.7, 153.9, 159.4, 161.3. ESI-MS 1098.3 ([M], 100). Anal. Calcd for $C_{59}H_{58}BF_2IN_2O_8$ (M_r = 1098.81): C, 64.49; H, 5.32; N, 2.55. Found: C, 64.22; H, 5.02; N, 2.41.

Compounds 5 and 7. Prepared using the general procedure 2 from compound **2b** (370 mg, 0.56 mmol), K_2CO_3 (85.6 mg, 0.62 mmol), and CH_3I (91.7 mg, 0.56 mmol) in CH_3CN (30 mL), affording 188 mg of **7** (50%) and 60 mg of **5** (16%).

7: ^{1}H NMR ((CD$_3$)$_2$CO 200 MHz) δ 1.50 (s, 6H), 3.86 (s, 3H), 6.85 (s, 2H), 6.95 (d, 2H, ^3J = 8.4 Hz), 7.04 (d, 2H, ^3J = 8.7 Hz), 7.31 (d, 2H, ^3J = 8.4 Hz), 7.50−7.64 (m, 8H), 8.01 (d, 2H, ^3J = 8.4 Hz), 8.91 (s, 1H). ^{13}C NMR ((CD$_3$)$_2$CO, 50 MHz)) δ 15.3, 15.4, 56.1, 95.7, 115.7, 117.3, 119.1, 129.6, 130.5, 130.3, 130.7, 132.2, 136.0, 137.3, 138.1, 139.6, 160.2, 162.1. ESI-MS 672.2 ([M], 100). Anal. Calcd for $C_{34}H_{28}BF_2IN_2O_2$ (M_r = 672.31): C, 60.74; H, 4.20; N, 4.17. Found: C, 60.52; H, 4.35; N, 4.02.

Compound 8. Prepared using the general procedure 2 from compound **7** (132 mg, 0.19 mmol), bromobutane (55 mg, 0.39 mmol), K_2CO_3 (55 mg, 0.39 mmol), in CH_3CN (30 mL), affording 167 mg of **8** (85%). ^{1}H NMR (CD_2Cl_2, 200 MHz) δ 0.96 (t, 3H, ^3J = 7.3 Hz), 1.45−1.54 (m, 8H),1.75 (q, 2H, ^3J = 7.0 Hz), 3.81 (s, 3H), 3.98 (t, 2H, ^3J = 6.4 Hz), 6.62 (s, 2H), 6.89−6.93 (m, 4H), 7.06 (d, ^3J = 8.3 Hz), 7.22 (d, 2H vinylic protons, ^3J = 16.5 Hz), 7.51−7.57 (m, 6H), 7.83 (d, 2H, ^3J = 8.3 Hz). ^{13}C NMR (CD_2Cl_2, 50 MHz) δ 13.7, 14.8, 19.3, 31.3, 55.4, 68.4, 94.8, 114.4, 114.9, 116.6, 116.8, 117.6, 129.1, 129.2, 129.4, 130.7, 132.9, 134.8, 136.1, 136.3, 136.7, 138.4, 141.9, 142.0, 152.7, 152.9, 160.4, 160.7. ESI-MS 728.2 ([M], 100). Anal. Calcd for $C_{38}H_{36}BF_2IN_2O_2$ (M_r = 728.41): C, 62.66; H, 4.98; N, 3.85. Found: C, 62.52; H, 4.75; N, 4.05.

Compound 9. Prepared using the general procedure 2 from compound **8** (100 mg, 0.13 mmol), 4-(2-(2-methoxyethoxy)-ethoxy)benzaldehyde (154 mg, 0.68 mmol), piperidine (2 mL), and a crystal of p-TsOH in toluene (20 mL), affording 45 mg of **9** (35%). ^{1}H NMR ((CD$_3$)$_2$CO 300 MHz) δ 0.99 (t, 3H ^3J = 7.4 Hz), 1.49−1.56 (m, 2H), 1.63 (s, 3H), 1.75−1.83 (m, 2H), 3.30 (s, 3H), 3.49−3.53 (m, 2H), 3.64−3.67 (m, 2H), 3.82 (t, 2H, ^3J = 4.6 Hz), 3.88 (s, 3H), 4.08 (t, 2H, ^3J = 6.4 Hz), 4.16 (t, 2H, ^3J = 4.6 Hz), 5.57 (d, 1H vinylic proton, ^3J = 16.1 Hz), 6.94−7.07 (m, 10H), 7.34−7.41 (m, 3H), 7.57−7.66 (m, 8H), 8.11 (d, 2H, ^3J = 8.3 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 15.6, 19.4, 31.4, 55.5, 59.3, 67.6, 68.3, 69.9, 70.9, 72.1, 95.3, 110.7, 114.4, 114.5, 114.97, 115.0, 115.3, 117.3, 117.2, 118.5, 118.5, 119.1, 128.5, 129.2, 129.3, 129.5, 129.6, 129.8, 130.1, 131.21, 131.25, 131.6, 135.2, 137.1, 137.4, 138.5, 158.9, 160.2, 160.5, 160.8. ESI-MS 934.1 ([M], 100). Anal. Calcd for $C_{50}H_{50}BF_2IN_2O_5$ (M_r = 934.65): C, 64.25; H, 5.39; N, 3.00. Found: C, 64.50; H, 5.60; N, 3.15.

Compound 10. Prepared using the general procedure 1 from compound **9** (10 g, 11 μmol), 4-(dimethylamino)benzaldehyde (3 mg, 21 μmol), piperidine (2 mL), and a crystal of p-TsOH in toluene (20 mL), affording compound **10** (13 mg, 56% isolated yield). ^{1}H NMR ((CD$_3$)$_2$CO 300 MHz) δ 0.99 (t, 3H, ^3J = 7.4 Hz), 1.48−1.56 (m, 2H), 1.74−1.84 (m, 2H), 2.99 (s, 6H), 3.31 (s, 3H), 3.49−3.53 (m, 2H), 3.64−3.67 (m, 2H), 3.80−3.83 (m, 2H), 3.87 (s, 3H), 4.07 (t, 2H, ^3J = 6.4 Hz), 4.15 (t, 2H, ^3J = 4.8 Hz), 5.70 (d, 1H vinylic proton, ^3J = 16.2 Hz), 5.76 (d, 1H vinylic proton, ^3J = 16.2 Hz), 6.71 (d, 2H, ^3J = 8.9 Hz), 6.90−7.05 (m, 12H), 7.33−7.41 (m, 4H), 7.57−7.68 (m, 8H), 8.16 (d, 2H, ^3J = 8.3 Hz). ^{13}C NMR ((CD$_3$)$_2$CO, 50 MHz) δ 14.1, 19.9, 32.3, 40.2, 55.7, 58.8, 68.40, 68.46, 70.2, 71.2, 72.7, 96.2, 111.3, 113.1, 115.4, 115.8, 115.9, 117.2, 117.2, 119.8, 125.9, 126.2, 128.8, 128.9, 129.7, 129.8, 130.1, 130.2, 130.3, 130.8, 132.2, 133.3, 133.9, 136.3, 136.8, 137.7, 137.5, 137.7, 139.7, 151.6, 160.1, 161.2, 161.3, 161.7. ESI-MS 1065.7 ([M], 100). Anal. Calcd for $C_{59}H_{59}BF_2IN_3O_5$ (M_r = 1065.82): C, 66.49; H, 5.58; N, 3.94. Found: C, 66.24; H, 5.37; N, 3.76.

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Supporting Information Available: General methods, preparative experimental procedures, details of the X-ray crystal structure determination of compound **6**, absorption and emission spectra for all compounds, analytical data, and NMR plots for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.