4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) Dyes Modified for Extended Conjugation and Restricted Bond Rotations

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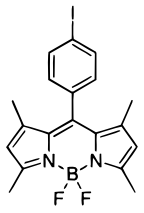
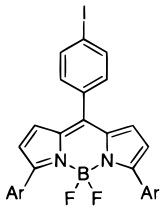
Five new, constrained, aryl-substituted 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY) dyes (**3f**,**g** and **4h**−**j**) were prepared and investigated to see if they have more favorable fluorescence characteristics than the unconstrained systems **2** that were prepared in previous studies. Dye types **3** and **4** have relatively rigid conformations caused by the heteroatom (**3f** and **3g**) or ethylene bridge (**4h**−**j**) linkers that preclude free rotation of the substituted-benzene molecular fragments. In the event, the new dye types **3** and **4** have longer $\lambda_{max\ abs}$ (620−660 nm) and $\lambda_{max\ fluor}$ (630−680 nm) values than compounds **2**. They also exhibit higher extinction coefficients (>100 000 M^{-1} cm^{-1}, except for **3g**). Their fluorescent quantum yields are high (up to 0.72 for **4j**), with the exception of compound **3g**, which has a quantum yield of only 0.05. The redox properties of dyes **3** and **4** have also been examined.

Introduction

A project to develop new fluorescent labels for DNA sequencing and other biotechnological applications has led us to modify the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene[1] (BODIPY) framework to obtain dyes that fluoresce strongly over a broad range of different wavelengths. Alkyl-substituted BODIPY dyes such as **1** are well-known.[1] These emit strongly in the 510 nm region; hence, alternative labels that complement these with higher wavelength fluorescence maxima were sought. In previous studies, we had reasoned that aryl substituents would shift the fluorescence to longer wavelengths and increase the molar extinction coefficients of these molecules. Consequently, systems **2** were prepared and examined via a variety of spectroscopic methods.[2,3] These experiments were successful insofar as the fluorescence emission maxima of these molecules were shifted to longer wavelengths (588−626 nm). However, the aryl substituents did not markedly increase the extinction coefficients of these molecules and the fluorescence quantum yields of **2** were significantly lower than that of the alkyl-substituted dye **1**.

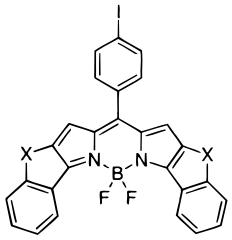


1
$\lambda_{max.\ fluor.}$ = 510 nm
Φ = 0.64 ($CHCl_3$)

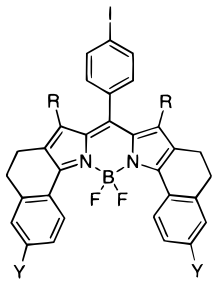


2
Ar = **a**, Ph; **b**, 1-Naph; **c**, 4-$MeOC_6H_4$
d, 4-FC_6H_4; **e**, 2-$MeOC_6H_4$
$\lambda_{max.\ fluor.}$ = 588 - 626 nm
Φ = 0.08 - 0.42 ($CHCl_3$)

A possible rationale for the reduced quantum yields of the aryl-substituted dyes **2** relative to the alkyl-substituted systems **1** is that energy is lost from the excited state via thermal pathways involving rotation of the aromatic substituents. In general, molecular constraints are well-known to enhance fluorescence, hence one of the objectives of this work was to prepare dyes that are related to systems **2** but are more rigid. This paper reports syntheses, spectral properties, and electrochemical data for the "planar aromatic" dyes **3** and **4**.



3
X = **f**, O; **g**, S



4
h, R = Y = H; **i**, R = H, Y = OMe
j, R = Me, Y = H

Results and Discussion

Syntheses of the Pyrrole-Derived Starting Materials. The first steps necessary for synthesis of compounds **3** and **4** were preparation of the requisite pyrrole derivatives. These syntheses are summarized in Scheme 1. The benzofuro[3,2-*b*]pyrrole **5f** is a known compound; it was prepared according to the literature procedure[4] but with a significant modification in the final step. The literature decarboxylation was previously performed using copper(II) chromite in quinoline (43% yield). In the current work, NaOH in ethylene glycol[5] was shown to give a better yield (80%) via an easier purification

(1) Treibs, A.; Kreuzer, F.-H. *Liebigs Ann. Chem.* **1968**, *718*, 208−23.
(2) Thoresen, L. H.; Kim, H.; Welch, M. B.; Burghart, A.; Burgess, K. *Synlett* **1998**, 1276−8.
(3) Burghart, A.; Kim, H.; Welch, M. B.; Thoresen, L. H.; Reibenspies, J.; Burgess, K.; Bergström, F.; Johansson, L. B.-A. *J. Org. Chem.* **1999**, *64*, 7813−9.
(4) Krutosikova, A.; Kovac, J.; Dandarova, M.; Bobalova, M. *Collect. Czech. Chem. Commun.* **1982**, *47*, 3288−96.
(5) Lash, T. D. *Tetrahedron* **1998**, *54*, 359−74.

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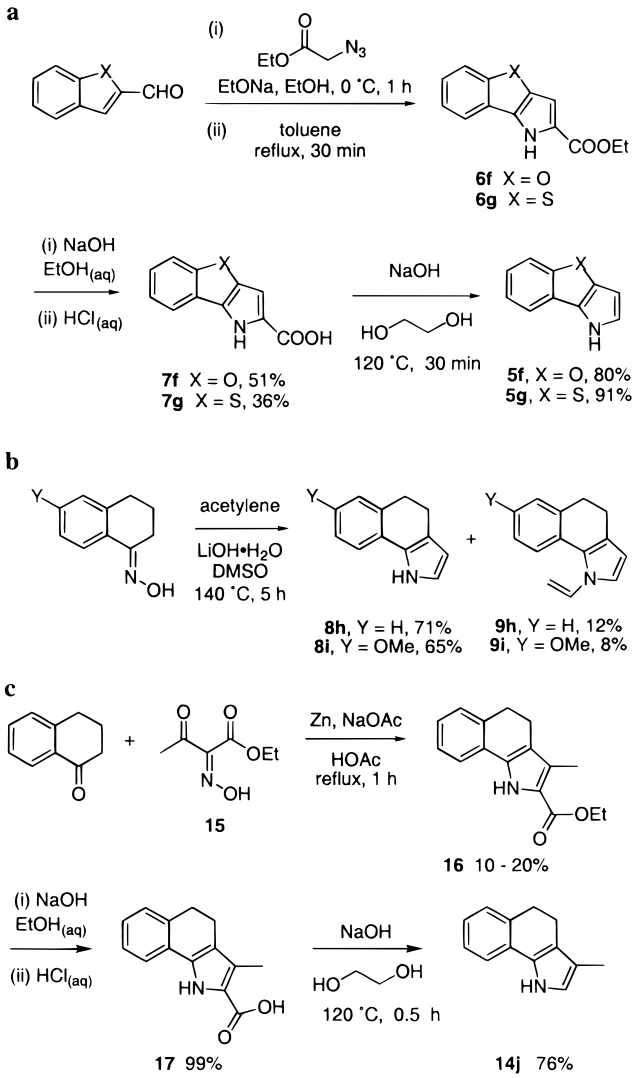
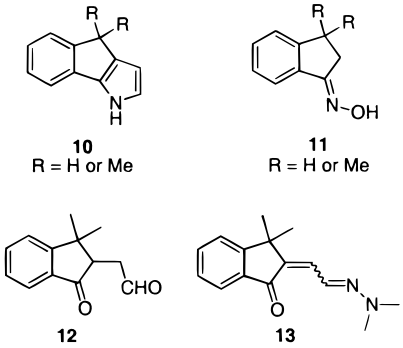
Scheme 1. Syntheses of the Pyrrole-Based Starting Materials



procedure. Thianaphtheno[3,2-*b*]pyrrole **5g** is also a known compound, but it was previously made via a relatively long and tedious route.[6] In the current work, the approach used for compound **5f** was successfully adopted for compound **5g**, as indicated in Scheme 1a.

Scheme 1b shows the route used to obtain the 4,5-dihydro-1*H*-benz[*g*]indoles **8h** and **8i**. These compounds were obtained by procedures of Trofimov that involve reaction of the appropriate ketoxime with ethyne in KOH/DMSO.[7] Those conditions afforded the product contaminated with between 30 and 40% of the corresponding *N*-vinyl derivative **9h** that presumably results from over-reaction of **8h** with ethyne. Other contributions by Trofimov and co-workers reported that use of LiOH/DMSO suppressed formation of *N*-vinyl byproducts.[8] Our studies demonstrated a similar effect in the synthesis of compound **8h**, as shown in Scheme 1b. Compound **8i** had, to the best of our knowledge, not been made previously, but was produced in this study using the method illustrated in Scheme 1b.

Interestingly, and for reasons that are unclear, the Trofimov methodology did not give the desired products **10** when the oximes **11** were reacted under the conditions described in Scheme 1b. Moreover, our attempts to form the desired product **10** (R = Me) via condensation of the keto-aldehyde **12** and NH_3 (or its equivalents) were also unsuccessful (compound **13** was made as an intermediate in the synthesis of **12**). No further attempts were made to prepare compound **10**.



The literature procedure for preparation of the 3-methyl-4,5-dihydro-1*H*-benz[*g*]indole **14j** calls for Na/NH_3 reduction in an autoclave.[9] In this work, we attempted to find a more convenient procedure that could be easily scaled up. The route that was developed involved a Knorr pyrrole synthesis[10] of the carboxypyrrole derivative **16** followed by hydrolysis and decarboxylation as indicated in Scheme 1c. Unfortunately, the yield of **16** obtained from the Knorr synthesis was low, but the procedure could be carried out on a 20 g scale to give a crystalline product without chromatographic separation.

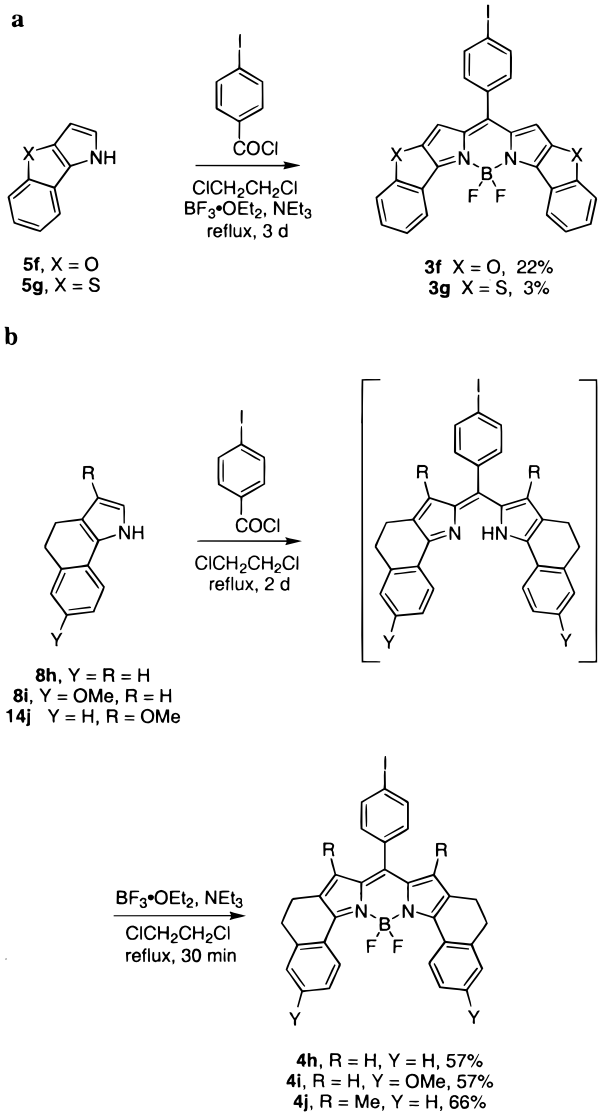
Syntheses of Dyes 3 and 4. The pyrrole-based starting materials **5f**,**g**, **8h**,**i**, and **14j** can be divided into two classes with respect to their reactivity toward electrophiles. Compounds **5f** and **5g** are relatively stable; they will not react with 4-iodobenzoyl chloride unless a suitable Lewis acid is added. Conversely, **8h**,**i** and **14j** degrade on silica gel and darken after several hours on contact with the air. They react with 4-iodobenzoyl chloride in the absence of Lewis acids. In view of these reactivity differences, two synthetic methods were devised for the preparation of the BODIPY systems **3** and **4** (Scheme 2).

As mentioned above, the heterocycles **5f** and **5g** did not react with 4-iodobenzoyl chloride, even in refluxing toluene. A reaction did occur when boron trifluoride etherate was added, but a complex mixture of products resulted. However, addition of triethylamine, presumably to attenuate the Lewis acidity of the BF_3, gave the desired material more selectively (Scheme 2a). The yields obtained in this transformation were low, especially for the sulfur-containing compound **3g**. However, the products were easy to track by TLC and during flash chromatography, since they display red fluorescence.

The more reactive nucleophiles **8h**,**i** and **14j** reacted smoothly in refluxing 1,2-dichloroethane to form the dipyrromethene intermediates. These dipyrromethenes are isolable, but it was more convenient in this work to add boron trifluoride/triethylamine and resume the reflux

(6) Shkurko, O. P.; Mamaev, V. P. *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk* **1967**, *2*, 112−7.
(7) Trofimov, B. A. *Adv. Heterocycl. Chem* **1990**, *51*, 177−301.
(8) Korostova, S. E.; Trofimov, B. A.; Sobenina, L. N.; Mikhaleva, A. I.; Sigalov, M. V. *Chem. Heterocycl. Comput.* **1982**, *14*, 1043−5.
(9) Enders, D.; Maassen, R.; Han, S.-H. *Liebigs Ann.* **1996**, 1565−74.
(10) Quizon-Colquitt, D. M.; Lash, T. D. *J. Het. Chem.* **1993**, *30*, 477−82.

Scheme 2. Syntheses of Dyes 3 and 4



to give the desired BODIPY products **4**. Overall yields of the products in this approach were satisfactory (Scheme 2b).

Fundamental UV and Fluorescence Properties of Dyes 3 and 4. Dyes **3** and **4** are strongly colored solids that have a metallic luster (**3f**, green; **3g**, dark blue; **4h**, gray-blue; **4i**, copper; **4j**, copper). They form intensely colored solutions (**3f**, green; **3g**, dark blue; **4h**, bright blue; **4i**, greenish blue; **4j**, bright blue) that appear to glow with a beautiful red fluorescence when irradiated. These dyes have absorption maxima between 620 and 660 nm and their emission maxima between 630 and 680 nm. All five except **3g** have very high extinction coefficients (>100 000 M^{-1} cm^{-1}). Their fluorescence quantum yields were found to vary considerably (0.05 for **3g**; 0.72 for **4j**). Table 1 lists the salient spectral properties of these compounds.

Structure and Conformations of Dyes 3 and 4. Compounds **3g** and **4h**−**i** all give long-range, through-space, $^{13}C-^{19}F$ coupling involving the carbon closest to the boron in the crowded bay region. These data have been communicated.[11] A crystal structure of compound

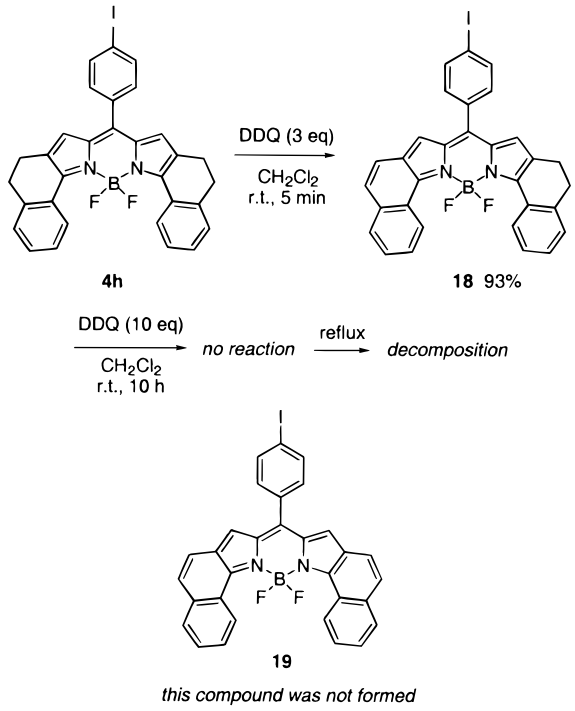
(11) Chen, J.; Reibenspies, J.; Derecskei-Kovacs, A.; Burgess, K. *Chem. Commun.* **1999**, 2501−2.

Table 1. Selected Optical Properties of Compounds 3f,g and 4h−j

dye	$\lambda_{max\ (abs)}$ (nm)	ϵ (M^{-1} cm^{-1})	$\lambda_{max\ (em)}$ (nm)	Stokes shift (nm)	Φ^a
3f	637	151 000	647	10	0.34
3g	658	54 250	673	15	0.05
4h	634	126 250	647	13	0.38
4i	658	139 500	673	15	0.13
4j	619	145 750	629	10	0.72
18	634	41 000	668	34	0.17

[a] Measured in $CHCl_3$ using cresyl violet perchlorate[19] in MeOH as reference ($\Phi = 0.54$).

Scheme 3. Oxidation of Compound 4h



4i was reported as part of that study along with semiempirical calculations to simulate the conformations of other compounds in this series. Calculations were also performed for compound **4i** and then compared with the crystallographic data to test the simulation approach. In the event, the correspondence was good, therefore validating the method used for the calculations. No further discussion of those particular data will be presented here, but the scope of the study was expanded as described below.

BODIPY **4h** was oxidized using excess DDQ at room temperature in CH_2Cl_2. This oxidation reaction rapidly and cleanly gave the half-oxidized compound **18**, not the doubly oxidized compound **19**. Further treatment of compound **18** with DDQ (>10 equiv) at room temperature for overnight gave no reaction. If this solution was heated to reflux, then a complicated mixture resulted (Scheme 3).

Steric effects could account for the fact that only one ring of compound **4h** was oxidized easily. To test this hypothesis, semiempirical calculations were performed on the series **4h**, **18**, and **19** (Cl for I analogues) using the protocol described previously.[11] The results are shown in Figure 1.

The average interatomic distance between the fluorine atoms and their closest hydrogen neighbors in compound **4h** was calculated to be 2.35 Å. Oxidation to compound

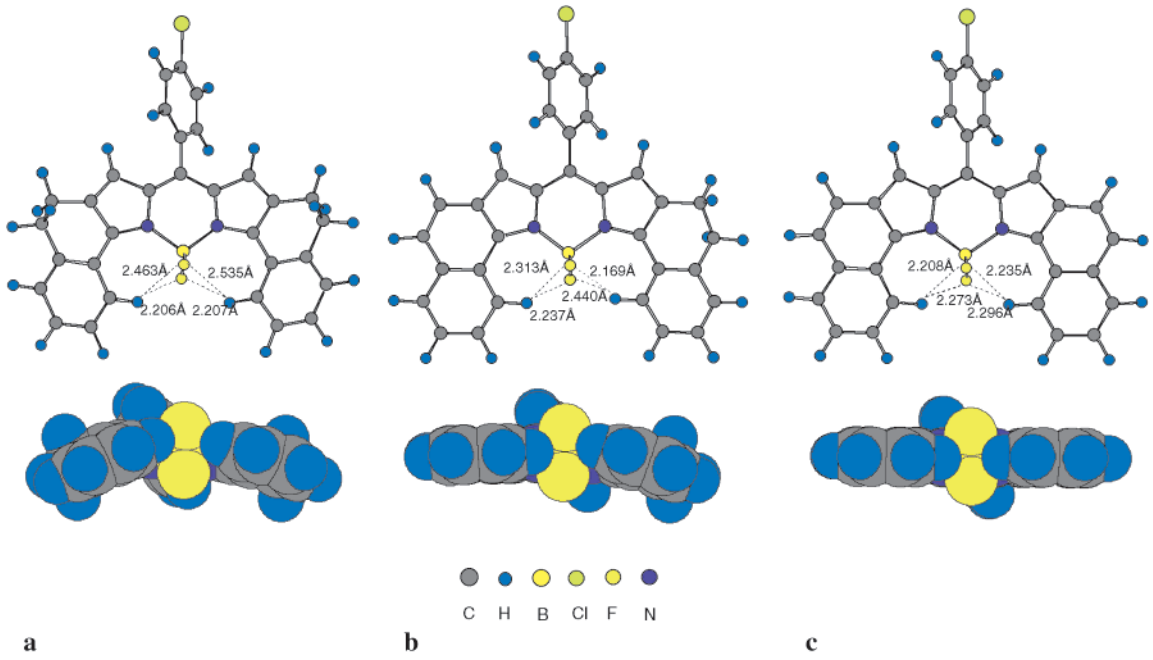


Figure 1. Simulated structures of chlorine-for-iodine analogues of **a**, compound **4h**; **b**, compound **18**; and, **c**, the hypothetical compound **19**.

18 caused a slight compression of this interatomic distance to an average of 2.29 Å. Compounds **4h** and **18** had similar F···C couplings (11.0 and 11.5/11.3 Hz, respectively). Simulations for compound **19** implied that, if it were formed, it would have a flat structure as indicated in Figure 1c. The corresponding interatomic distances for this hypothetical structure were predicted to be 2.25 Å. This is considerably shorter than the sum of the van der Waals radii for hydrogen and fluorine.[12] Consequently, it seems probable that the activation energy required to form compound **19** is excessive compared with the half oxidized form **18** due to steric reasons.

The optical properties of compound **18** were not as we had expected (Table 1). First, the maximum absorbance of **18** was not red shifted relative to **4h**; in fact the two values were coincident, though the fluorescence emission was red-shifted by 21 nm relative to **4h**. Second, despite the more conjugated characteristics of **18**, it has an extinction coefficient that is approximately three times *smaller* than compound **4h**. Finally, the quantum yield for **18** was less than half that of **4h**. The consequence of these characteristics is that compound **18** is not a particularly fluorescent compound and has limited potential as a molecular label.

Electrochemical Studies of Dyes 3f and 4. The BODIPY derivatives **3f** and **4** were examined via cyclic voltammetry (**3g**, the least soluble dye in the series, was excluded). This technique gives a measure of the accessibility and distribution of redox states; extent of π-conjugation and conformational parameters can be deduced from these data. Throughout, CH_2Cl_2 solutions and a scan rate of 100 mVs^{-1} were used. All systems displayed reversible waves for one-electron oxidation and for one-electron reduction (Table 2). Some of the dyes exhibited a second redox step for either oxidation and/or reduction. Notably, the methoxy-substituted BODIPY **4i** gave four distinct redox steps: two oxidations and two reductions

(12) Bondi, A. *Phys. Chem* **1964**, *68*, 441.

Table 2. Electrochemical Data for Compounds 3f and 4h−j[a]

	$E_{1/2}$ (V)			E_{pc} (V)
	first ox. wave	second ox. wave	first red. wave	second red. wave
3f	+0.81	*b*	−1.05	−1.92
4h	+0.57	*b*	−1.29	−2.07
4i	+0.33	+0.91	−1.39	−2.11
4j	+0.51	*b*	−1.44	*b*

[a] All data are referenced versus ferrocene. [b] Electrochemical wave could not be detected under the conditions chosen.

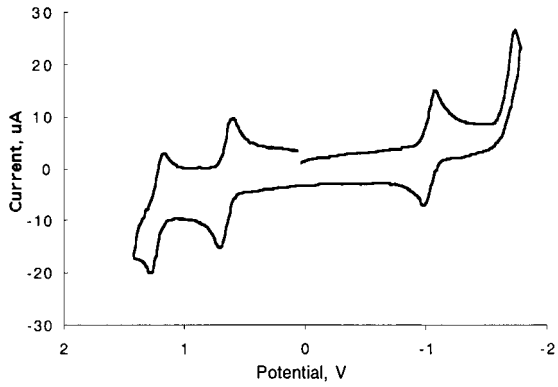


Figure 2. Cyclic voltammogram of dye **4i** in CH_2Cl_2 (referenced versus Ag wire).

(Figure 2). Both oxidation waves for this compound were shown to be reversible; this implies that even the dication is sufficiently long-lived to be reduced in the back sweep under these conditions.

Within the series of compounds **3f** and **4**, the methoxy-BODIPY **4i** was shown to have the lowest oxidation potential ($E_{1/2}$ = 0.33 V vs ferrocene), as expected. Overall, the rigid BODIPYs **3f** and **4** exhibit much lower oxidation potentials than systems **2** whose conjugation is effectively less extended.[3] Comparison of compounds **4h** and **4j** (R = H, and Me, respectively) affords insights

into the effect of the two methyl groups flanking the central 4-iodobenzene ring in **4j**. Curiously, compound **4j** is easier to oxidize but harder to reduce. The electronic effect imparted by the methyl R-groups seems to lower the oxidation potential of **4j**. The fact that **4j** is more difficult to reduce may be indicative of less effective conjugation of the indacene system with the 4-iodophenyl group. This would be caused by steric interactions involving the methyl groups that prevent the aryl substituent from becoming coplanar with the rest of the dye system.[13] Compound **3f** exhibits unique redox properties within the series. It is very easily reduced having the least negative reduction potential in the series, but on the other hand, it has the highest oxidation potential.

Separations between the first and the second oxidation or reduction steps provide information regarding charge distribution. Small separation implies that the charge of the corresponding radical ion is confined to a particular region of the molecule, and the second redox step occurs predominantly at a remote site. The expected outcome in such a situation is a dication or dianion with relatively localized and distinct charges. Large separations, however, are indicative of a widely delocalized charge in the radical ion. Compound types **3f** and **4** display relatively large separations both for oxidation and reduction, indicative of delocalization. The smallest separation observed was 580 mV (oxidation of **4i**; $E_{1/2} = 0.33$ and 0.91 V). This is in striking contrast to, for example, tetraanisylethylene for which the first and second oxidation potentials are separated by only 120 mV.[14]

Conclusions

Relative to the unconstrained aromatic dyes **2**, compound types **3** and **4** have several desirable attributes with respect to applications as fluorescent labels. They absorb and fluoresce more intensely at longer wavelengths, and the quantum yields for this process are generally higher, with the exception of compound **3g**. These observations confirm the hypothesis that restricted rotation of the aryl fragments in these molecules is advantageous.

The sulfur compound **3g** has a lower extinction coefficient and quantum yield than the other compounds in this series; the spectroscopic disparities between **3g** and the rest of the series cannot be explained with confidence. It is also less soluble than the others in common organic solvents. However, the other BODIPYs reported here may find a range of applications including our own objective of developing new fluorescent labels for biotechnological applications.

Experimental Section

General Experimental Procedures. All chemicals were obtained from commercial suppliers and used without further purification. Toluene and THF were distilled from Na/benzophenone prior to use. Dichloromethane used for the electrochemical studies was distilled from CaH_2, and 1,2-dichloroethane was distilled from CaH_2. All NMR spectra were recorded on a Varian instrument at 300 MHz (^{1}H), 75 MHz (^{13}C), 64 MHz (^{11}B), or 282 MHz (^{19}F). NMR chemical shifts are expressed in ppm relative to internal solvent peaks, and coupling constants were measured in Hz. For ^{11}B NMR, $BF_3 \cdot Et_2O$ has been used as an external reference; similarly, $CFCl_3$ was used as an external standard for the ^{19}F spectra.

Geometry optimizations at the AM1 level using the MOPAC module within the MSI Cerius2 program package were performed as described previously.[11]

Benzofuro[3,2-*b*]pyrrole 5f. Acid **7f**[4] (0.25 g, 1.24 mmol) and NaOH (0.20 g, 5 mmol) were mixed in ethylene glycol (10 mL) and heated at 140 °C for 10 min under nitrogen. The reaction mixture was cooled to room temperature, diluted with water (100 mL), and extracted with Et_2O (3 × 50 mL). The combined ether solution was washed with water and brine and dried over Na_2SO_4. Evaporation gave a gray solid that was then dissolved in approximately 10 mL of CH_2Cl_2 and passed through a short column of silica gel. This gave **5f** as white solid after removal of solvent (0.17 g, 79%). The ^{1}H NMR data obtained for this compound match that in the literature for preparation of the same material via a different route.[4]

BODIPY 3f. Pyrrole **5f** (0.15 g, 0.96 mmol) and 4-iodobenzoyl chloride (0.15 g, 0.56 mmol) were dissolved in toluene (20 mL) and heated to reflux under nitrogen, and then Et_3N (1.0 mL, 7.2 mmol) and BF_3 etherate (1.2 mL, 9.8 mmol) were added. The heating was continued, and two more batches (0.05 g, 0.19 mmol each) of 4-iodobenzoyl chloride were added, one at 40 h and one at 60 h. The solvent was removed after 3 d, and the resulting dark brown residue was purified via a simple chromatography on silica gel column, eluting with 3:1 hexanes/CH_2Cl_2, to remove the polar residues, then a more careful flash chromatography, using the same solvent combination. This gave compound **3f** as a dark green solid after the removal of solvent (60 mg, 22%): mp >300 °C; R_f value 0.42 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.21 (d, $J = 7.5$ Hz, 2H), 7.91 (d, $J = 8.4$ Hz, 2H), 7.51−7.35 (m, 6H), 7.36 (d, $J = 8.4$ Hz, 2H), 6.36 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 164.8, 154.6, 146.1, 143.8, 138.7, 137.8, 133.4, 132.1, 130.5, 124.2, 123.9, 117.0, 112.8, 104.3, 96.8; ^{19}F NMR ($CDCl_3$) δ −150.6 (q, $J = 28$ Hz); ^{11}B NMR ($CDCl_3$) δ 0.41 (t, $J = 28$ Hz); FABHRMS calcd for $C_{27}H_{14}BF_2IN_2O_2$ 574.0163, found 574.0167.

Ethyl Thianaphtheno[3,2-*b*]pyrrole-2-carboxylate 6g. Benzothiophene-2-carbaldehyde (0.21 g, 1.3 mmol) and ethyl azidoacetate (0.33 g. 2.6 mmol) were dissolved in EtOH (10 mL). A solution of EtONa in EtOH (21 wt %, 0.95 mL, 2 equiv) was added dropwise at 0 °C. The mixture was then stirred for another 1 h. A yellow precipitate formed. Excess saturated $NH_4Cl_{(aq)}$ was added, and the mixture was filtered to give a yellow solid that was washed with water and dried under vacuum. It was then dissolved in 20 mL of toluene and refluxed for 30 min. Evaporation of the solvent gave a yellow residue, which was recrystallized from EtOH giving **6g** as pale yellow solid: mp 188−189 °C; R_f value 0.29 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 10.15 (bs, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 7.84 (d, $J = 8.4$ Hz, 1H), 7.29−7.42 (m, 2H), 7.22 (d, $J = 1.5$ Hz, 1H), 4.49 (q, $J = 7.2$ Hz, 2H), 1.47 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (acetone-d_6) δ 161.6, 144.5, 137.3, 128.4, 127.6, 125.7, 125.4, 124.9, 123.7, 121.3, 108.5, 61.0, 14.9.

Thianaphtheno[3,2-b]pyrrole-2-carboxylic Acid 7g. Ester **6g** (0.31 g, 1.17 mmol) and NaOH (1 g, 25 mmol) were mixed in 20 mL of EtOH and 10 mL of H_2O. The mixture was refluxed for 1 h, acidified to approximately pH 3 using 6 N HCl, and filtered. Acid **7g** was obtained after washing and drying as pale yellow solid (0.24 g, 36% from the benzothiophene-2-carbaldehyde starting material): mp 235 °C dec; R_f value 0.70 (1:1 acetone/MeOH); ^{1}H NMR (DMSO-d_6) δ 12.75 (s, 1H), 12.73 (s, 1H), 8.13 (d, $J = 7.2$ Hz, 1H), 7.91 (d, $J = 7.8$ Hz, 1H), 7.34−7.42 (m, 2H), 7.12 (d, $J = 2.1$ Hz, 1H).

Thianaphtheno[3,2-*b*]pyrrole 5g. Acid **7g** (0.24 g, 1.1 mmol) and NaOH (0.4 g, 10 mmol) were mixed in 10 mL of ethylene glycol and heated to 140 °C under nitrogen. After 30 min, 100 mL of ice/water was added, and the mixture was filtered. The yellow solid was washed thoroughly with water and dried. It was then dissolved in approximately 10 mL of CH_2Cl_2 and passed through a short column of silica gel to give **5g** as white solid after removal of solvent (0.175 g, 91%): mp 113−114 °C; R_f value 0.26 (4:1 hexanes/EtOAc); ^{1}H NMR

(13) Li, F.; Yang, S. I.; Ciringh, Y.; Seth, J.; Martin, C. H.; Singh, D. L.; Kim, D.; Birge, R. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Am. Chem. Soc.* **1998**, *120*, 10001−17.

(14) Rathore, R.; Lindeman, S. V.; Kumar, A. S.; Kochi, J. K. *J. Am. Chem. Soc.* **1998**, *120*, 6931−9.

(acetone-d_6) δ 11.05 (bs, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.24−7.29 (m, 2H), 6.56 (d of d, J = 2.5 Hz, 2.0 Hz, 1H); ^{13}C NMR (acetone-d_6) δ 142.5, 133.5, 128.2, 124.7, 124.6, 124.3, 123.2, 122.8, 119.2, 102.3.

BODIPY 3g. Pyrrole **5g** (0.18 g, 1.04 mmol), 4-iodobenzoyl chloride (0.14 g, 0.52 mmol), BF_3 etherate (1.2 mL, 9.8 mmol), and Et_3N (1.0 mL, 7.2 mmol) were mixed in toluene (100 mL) and refluxed for 5 d. Evaporation gave a dark brown residue, which was passed through a silica gel column, eluting with 3:1 hexanes/CH_2Cl_2, to give a crude product. This was purified via flash chromatography, eluting with 4:1 hexanes/CH_2Cl_2, to give **3g** as dark blue solid (10 mg, 3%): mp >300 °C; R_f value 0.38 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.75 (d, J = 6.9 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 7.66 (d of d, J = 6.9 Hz, 2.0 Hz, 2H), 7.45−7.52 (m, 4H), 7.35 (d, J = 8.4 Hz, 2H), 6.84 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 148.3, 140.4, 137.7, 137.5, 133.4, 132.3, 129.6, 126.7 (t, J = 5.2 Hz), 125.7, 125.6, 124.1, 119.8, 96.9; ^{19}F NMR ($CDCl_3$) δ −147.0 (q, J = 30 Hz).

BODIPY 4h. Pyrrole **8h**[8] (0.26 g, 1.54 mmol) and 4-iodobenzoyl chloride (0.19 g, 0.71 mmol) were dissolved in 1,2-dichloroethane (50 mL), and the solution was refluxed for 2 d under nitrogen. A deep blue solution was formed. The solution was cooled to 25 °C, triethylamine (0.5 mL, 3.6 mmol) was added, and the mixture was stirred for 5 min. Then BF_3 etherate (0.75 mL, 6.1 mmol) was added, and the mixture was refluxed for 30 min under nitrogen. The solvent was then removed, and the residue was passed through a silica gel column using 3:1 hexanes/CH_2Cl_2. The crude compound was then further purified via flash chromatography, slowly eluting with 5% EtOAc in hexanes to give **4h** as blue solid (0.26 g, 57%): mp >300 °C; R_f value 0.41 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.80 (d, J = 7.8 Hz, 2H), 7.85 (d, J = 8.7 Hz, 2H), 7.45 (d of t, J = 7.8 Hz, 1.7 Hz, 2H), 7.35−7.25 (m, 6H), 6.53 (s, 2H), 2.90 (t, J = 6 Hz, 4H), 2.68 (t, J = 6 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 152.6, 140.5, 137.9, 137.3, 135.8, 134.5, 133.2, 132.1, 129.8, 128.4 (t, J = 11 Hz), 128.3, 128.2, 127.5, 125.0, 95.8, 30.5, 22.3; ^{19}F NMR ($CDCl_3$) δ −137.3 (q, J = 34 Hz); ^{11}B ($CDCl_3$) δ 3.98 (t, J = 34 Hz); FABHRMS calcd for $C_{31}H_{22}BF_2IN_2$ 598.0891, found 598.0889. Anal. Calcd for $C_{31}H_{22}BF_2IN_2$: C, 62.24; H, 3.71; N, 4.88. Found: C, 62.35; H, 3.89; N, 4.73.

7-Methoxy-4,5-dihydro-1*H*-benz[*g*]indole 8i. Lithium hydroxide monohydrate (1.0 g, 23.8 mmol) and 6-methoxytetralone oxime[15] (1.0 g, 5.2 mmol) were mixed in 25 mL of DMSO. Acetylene was bubbled into the mixture. This was then heated to 140 °C with stirring under nitrogen for 5 h. Ice/water (250 mL) was added, and the product was extracted into Et_2O (3 × 100 mL). The combined ether solution was washed with water and brine and dried over Na_2SO_4. Evaporation gave a light brown residue. This was flash chromatographed 2:1 hexanes/CH_2Cl_2 to give the vinyl pyrrole side product **9i** (0.10 g, 8%). Further eluting with 1:1 hexanes/CH_2Cl_2 gave the desired pyrrole **8i** as a sticky white solid (0.67 g, 65%): ^{1}H NMR ($CDCl_3$) δ 8.23 (bs, 1H), 7.05 (d, J = 8.1 Hz, 1H), 6.90 (d, J = 2.7 Hz, 1H), 6.75 (d of d, J = 8.1 Hz, 2.7 Hz, 1H), 6.72 (t, J = 2.4 Hz, 1H), 6.20 (t, J = 2.4 Hz, 1H), 3.88 (s, 3H), 3.00 (t, J = 7 Hz, 2H), 2.82 (t, J = 7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 157.2, 136.7, 127.5, 122.7, 119.2, 118.2, 117.3, 114.6, 111.1, 107.7, 55.2, 30.4, 21.7. This compound was not particularly stable with respect to long-term storage at room temperature.

BODIPY 4i. Pyrrole **8i** (0.65 g, 3.27 mmol) and 4-iodobenzoyl chloride (0.44 g, 1.72 mmol) were dissolved in 1,2-dichloroethane (50 mL), and the solution was refluxed for 2 d under nitrogen. A deep greenish blue solution resulted. The solution was cooled to room temperature, triethylamine (1.0 mL, 7.2 mmol) was added, the solution was stirred for 5 min at room temperature, BF_3 etherate (1.2 mL, 9.8 mmol) was added, and the mixture was refluxed for 30 min under nitrogen. The solvent was then removed, and the residue was passed down a silica gel column (1:1 hexanes/CH_2Cl_2) to remove polar impurities. The residue was then flash chromatographed using 5% EtOAc in hexanes eluant. This gave **4i** as a copper colored solid after removal of solvents (0.61 g, 57%): mp >300 °C; R_f value 0.22 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.75 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 6.98 (d of d, J = 8.7 Hz, 2.7 Hz, 2H), 6.81 (d, J = 2.7 Hz, 2H), 6.47, (s, 2H), 3.88 (s, 6H), 2.88 (bs, 4H), 2.67 (bs, 4H); ^{13}C NMR ($CDCl_3$) δ 160.7, 151.9, 142.8, 137.3, 136.0, 135.4, 134.9, 132.2, 132.1, 130.1 (t, J = 11 Hz), 124.4, 121.5, 114.7, 112.4, 95.5, 55.3, 30.9, 22.3; ^{19}F NMR ($CDCl_3$) δ −137.5 (q, J = 34 Hz); ^{11}B NMR ($CDCl_3$) δ 9.29 (t, J = 34 Hz); FABHRMS calcd for $C_{33}H_{26}BF_2IN_2O_2$ 658.1093, found 658.1142. Anal. Calcd for $C_{33}H_{26}BF_2IN_2O_2$: C, 60.21; H, 3.98; N, 4.26. Found: C, 60.49; H, 4.01; N, 4.35.

Keto-aldehyde 12. 3,3-Dimethyl-1-indanone[16] (0.31 g, 1.94 mmol) was dissolved in 50 mL of dry THF and cooled to 0 °C. LDA (2 M in THF/*n*-heptane, 1.2 mL, 2.4 mmol) was added dropwise, and the resulting yellow solution was stirred at 0 °C for 30 min. Glyoxal mono(dimethylhydrazone)[17] (0.3 g, 3 mmol) was then added, and the resulting yellow solution was stirred at room temperature for 3 h. Excess $NH_4Cl_{(aq)}$ was added, and the mixture was extracted with Et_2O (3 × 150 mL). The combined ether solution was washed with water and brine and dried over Na_2SO_4. Removal of solvent gave a yellow viscous oil, which was purified on silica gel column, eluting with 3% Et_2O in CH_2Cl_2. This gave **13** as a yellow solid (mixture of two isomers, 0.40 g, 85%).

Compound **13** (0.40 g, 1.65 mmol) was dissolved in 10 mL of THF and was added dropwise to a solution of 2.0 g $SnCl_2 \cdot 2H_2O$[18] in 5 mL of concentrated HCl and 5 mL of H_2O with vigorous stirring at 0 °C. After the addition, the yellow solution was further stirred for 10 min at room temperature. Water (100 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with water and brine and dried over Na_2SO_4. Evaporation gave a brown oil. This was then dissolved in small amount of CH_2Cl_2 and passed through a short column of silica gel. Removal of solvent gave **12** as light yellow oil (0.26 g, 78%): ^{1}H NMR ($CDCl_3$) δ (d, J = 1.2 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 2.97−3.09 (m, 2H), 2.52−2.65 (m, 1H), 1.50 (s, 3H), 1.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 205.3, 200.6, 162.4, 135.0, 133.6, 127.4, 123.3, 123.2, 53.9, 41.3, 40.3.

Ethyl 3-Methyl-4,5-dihydro-1*H*-benz[*g*]indole-2-carboxylate 16. A solution of 1-tetralone (17.5 g, 0.12 mole) and NaOAc (75 g, 0.9 mole) in propionic acid (300 mL) was heated to reflux. Oxime **15**[10] (16 g, 0.1 mole), dissolved in 200 mL of propionic acid, was added dropwise, while simultaneously adding small portions of activated Zn dust (40 g, 0.6 mol). After the additions, the mixture was refluxed for 1 h and cooled to about 70 °C. It was then poured to 4 L of ice/water and was allowed to stand overnight. A yellow solid precipitated and was isolated by filtration. The solid was thoroughly washed with water until the filtrates were neutral. The dried solid was then washed several times with hexanes to remove unreacted 1-tetralone and other nonpolar impurities. The solid was then recrystallized from EtOH several times to give **16** as white solid (2.3 g, 11.5% based on recovered 1-tetralone): mp 136−138 °C; R_f value 0.40 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 9.28 (bs, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.15−7.30 (m, 3H), 4.40 (q, J = 7.2 Hz, 2H), 2.98 (t, J = 7.5 Hz, 2H), 2.69 (t, J = 7.5 Hz, 2H), 2.34 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 161.5, 136.3, 131.2, 128.5, 128.0, 126.8, 126.6, 125.5, 121.6, 120.0, 119.4, 60.0, 29.6, 19.5, 14.6, 10.5.

3-Methyl-4,5-dihydro-1*H*-benz[*g*]indole-2-carboxylic Acid 17. Ester **16** (500 mg, 1.96 mmol) and NaOH (0.5 g, 12.5 mmol) were mixed in 100 mL of EtOH and 50 mL of H_2O and refluxed for 2 h. The solution was cooled and acidified by 6 N

(15) Sawa, Y.; Kato, T.; Masuda, T.; Hori, M.; Fujimura, H. *Chem. Pharm. Bull.* **1975**, *23*, 1917−27.

(16) Pearson, B. D.; Ayer, R. P.; Cromwell, N. H. *J. Org. Chem.* **1962**, *27*, 3038−44.

(17) Severin, T.; Supp, W.; Manninger, G. *Chem. Ber.* **1979**, *112*, 3013−22.

(18) Severin, T.; Adam, R.; Lerche, H. *Chem. Ber.* **1975**, *108*, 1756−67.

(19) Magde, D.; Brannon, J. H. *J. Phys. Chem.* **1979**, *83*, 696−9.

HCl. The resulting precipitate was filtered and dried to give **17** as gray solid (440 mg, 99%): mp 129−134 °C; ^{1}H NMR (acetone-d_6) δ 11.0 (bs, 1H), 9.75 (bs, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.15−7.30 (m, 3H), 2.93 (t, J = 7.5 Hz, 2H), 2.66 (t, J = 7.5 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (acetone-d_6) δ 165.0, 137.1, 133.0, 129.1, 129.0, 127.6, 126.9, 122.2, 122.1, 119.8, 30.1, 20.1, 10.6.

3-Methyl-4,5-dihydro-1*H*-benz[*g*]indole 14j. Acid **17** (440 mg, 1.94 mmol) and NaOH (0.5 g, 12.5 mmol) were mixed in 20 mL of ethylene glycol and heated to 140 °C under nitrogen. After 20 min, ice/water (100 mL) was added, and the precipitate was filtered and washed with H_2O. This solid was then dissolved in small amount of CH_2Cl_2 and passed through a short column of silica gel, eluting with 1:1 CH_2Cl_2/hexanes to give **14j** as white solid (270 mg, 76%). The ^{1}H NMR for this material correlates well with that published for the same material prepared via a different route.[9]

BODIPY 4j. Pyrrole **14j** (260 mg, 1.42 mmol) and 4-iodobenzoyl chloride (190 mg, 0.71 mmol) were dissolved in 250 mL of 1,2-dichloroethane and refluxed under nitrogen for 3 d. The mixture was cooled to room temperature, triethylamine (0.5 mL, 3.6 mmol) was added, the mixture was stirred at room temperature for 5 min, BF_3 etherate (1 mL, 8.1 mmol) was added, and the mixture was refluxed for 30 min. Evaporation gave a dark brown residue that was passed though a short silica gel column (30% CH_2Cl_2 in hexanes, eluant) and then flash chromatographed eluting with 3% EtOAc in hexanes. This gave **4j** as copper-colored solid (210 mg, 47%): mp >300 °C; R_f value 0.39 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 8.83 (d, J = 8.1 Hz, 2H), 7.92 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 8.1 Hz, 2H), 7.33 (t, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 2.91 (t, J = 7.1 Hz, 4H), 2.56 (t, J = 7.1 Hz, 4H), 1.42 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 151.0, 140.7, 138.3, 138.1, 135.8, 135.7, 133.6, 132.2, 130.7, 129.5, 128.6 (t, J = 12 Hz), 128.3, 128.1, 127.3, 94.7, 30.5, 20.4, 12.4; ^{19}F NMR ($CDCl_3$) δ −135.0 (q, J = 34 Hz); ^{11}B NMR ($CDCl_3$) δ 1.42 (t, J = 35 Hz); FABHRMS calcd for $C_{31}H_{26}BF_2N_2I$ 626.1202, found 626.1314. Anal. Calcd for $C_{31}H_{26}BF_2N_2I$: C, 63.29; H, 4.18; N, 4.47. Found: C, 63.53; H, 4.25; N, 4.51.

Compound 18. BODIPY **4h** (20 mg, 0.033 mmol) was dissolved in 10 mL of CH_2Cl_2. DDQ (23 mg, 0.1 mmol) was added, and the solution was stirred at room temperature and monitored by TLC. After 5 min, TLC showed that the reaction was completed. Solvent was removed, and the residue was purified by passing a short column of silica gel using 2:1 hexanes/CH_2Cl_2 as eluent. This gave **18** as a dark blue solid (18.5 mg, 93%): mp >300 °C; R_f value 0.35 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) δ 9.41 (d, J = 8.1 Hz, 1H), 9.13 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 8.1 Hz, 2H), 7.83 (s, J = 7.8 Hz, 1H), 7.70 (t, J = 7.8 Hz, 1H), 7.39−7.61 (m, 6H), 7.38 (d, J = 8.1 Hz, 2H), 6.99 (s, 1H), 6.76 (s, 1H), 3.00 (t, J = 6.7 Hz, 2H), 2.79 (t, J = 6.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 158.4, 145.9, 142.0, 140.5, 138.7, 137.5, 137.0, 136.5, 135.1, 134.3, 132.3, 131.7, 130.2 (t, J = 11.5 Hz), 129.7, 129.0, 128.6, 128.0, 127.5, 127.4, 127.3, 127.1(t, J = 11.3 Hz), 126.7, 124.7, 123.9, 121.5, 120.6, 96.4, 30.4, 22.6; ^{19}F NMR ($CDCl_3$) δ −138.8 (q, J = 33.5 Hz); HRFABMASS: calcd for $C_{31}H_{20}BF_2IN_2$ 596.0742, found 596.0732.

Optical Spectroscopy. All experiments were conducted in chloroform solutions (4 μM for absorption spectra, 1 μM for emission spectra). Quantum yields were determined as described earlier.[3]

Cyclic Voltammetry. These experiments were conducted in anhydrous CH_2Cl_2 at room temperature. The potentials are reported vs ferrocene as internal standard using a scan rate of 100 mV s^{-1}, glassy carbon working electrode, $Ag/AgNO_3$ reference electrode, platinum counter-electrode, and a supporting electrolyte 0.1 M tetrabutylammonium hexafluorophosphate.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for new compounds; ^{19}F and ^{11}B NMR spectra for new dyes. This material is available free of charge via the Internet at http://pubs.acs.org.

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