

6-15-2018

Tetrafluorobenzo-Fused BODIPY: A Platform for Regioselective Synthesis of BODIPY Dye Derivatives

Andrea Savoldelli
Università degli Studi di Roma Tor Vergata

Qianli Meng
Louisiana State University

Roberto Paolesse
Università degli Studi di Roma Tor Vergata

Frank R. Fronczek
Louisiana State University

Kevin M. Smith
Louisiana State University

See next page for additional authors

Follow this and additional works at: https://digitalcommons.lsu.edu/chemistry_pubs

Recommended Citation

Savoldelli, A., Meng, Q., Paolesse, R., Fronczek, F., Smith, K., & Vicente, M. (2018). Tetrafluorobenzo-Fused BODIPY: A Platform for Regioselective Synthesis of BODIPY Dye Derivatives. *Journal of Organic Chemistry*, 83 (12), 6498-6507. <https://doi.org/10.1021/acs.joc.8b00789>

This Article is brought to you for free and open access by the Department of Chemistry at LSU Digital Commons. It has been accepted for inclusion in Faculty Publications by an authorized administrator of LSU Digital Commons. For more information, please contact ir@lsu.edu.

Authors

Andrea Savoldelli, Qianli Meng, Roberto Paolesse, Frank R. Fronczek, Kevin M. Smith, and M. Graça H. Vicente



Published in final edited form as:

J Org Chem. 2018 June 15; 83(12): 6498–6507. doi:10.1021/acs.joc.8b00789.

Tetrafluorobenzo-Fused BODIPY: A Platform for Regioselective Synthesis of BODIPY Dye Derivatives

Andrea Savoldelli[†], Qianli Meng[‡], Roberto Paolesse[†], Frank R. Fronczek[‡], Kevin M. Smith[‡], M. Graça H. Vicente^{*,‡}

[†]Dipartimento di Scienze e Tecnologie Chimiche, University of Rome Tor Vergata, Via della Ricerca Scientifica 1, 00133 Rome, Italy

[‡]Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803, United States

Abstract

A novel route for the synthesis of unsymmetrical benzo-fused BODIPYs is reported using 4,5,6,7-tetrafluoroisindole as a precursor. The reactivity of the 3,5-dibromo tetrafluorobenzo-fused BODIPY was investigated under nucleophilic substitution and Pd(0)-catalyzed cross-coupling reaction conditions. In addition to the 3,5-bromines, one α -fluoro group on the benzo-fused ring can also be functionalized, and an unusual homocoupling with formation of a bisBODIPY was observed. This new class of fluorinated BODIPYs could find various applications in medicine and materials.

Graphical Abstract



INTRODUCTION

4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene dyes, usually abbreviated as BODIPYs, have been extensively studied in recent years. These small molecules offer unique properties, including high photostability, high molar absorption coefficients, and high fluorescence quantum yields,¹ which have supported their exploitation as imaging probes,² fluorescent organic devices,³ chemical sensors,⁴ and as photosensitizers.⁵ The properties of this class of molecule can be easily and finely tuned with the insertion of various substituents. One of the

*Corresponding Author: vicente@lsu.edu.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b00789.

X-ray data for BODIPYs 1, 4d, 4e, 6, and 7 (CIF) Additional UV-vis and emission spectra; ¹H, ¹³C, ¹⁹F, and ¹¹B NMR and 2D NMR spectra (PDF)

The authors declare no competing financial interest.

most exploited routes in BODIPY functionalization relies on the synthesis of a core-halogenated precursor (chlorinated,⁶ brominated,⁷ or iodinated⁸ BODIPY), which can be readily synthesized with high regioselectivity and represents a versatile precursor in nucleophilic substitution reactions using N-, S-, O-, and C-centered nucleophiles⁹ and in Pd(0)-catalyzed cross-coupling reactions.¹⁰ Many BODIPY applications require the synthesis of long-wavelength absorbing and emitting species (ca. 600–800 nm), although most BODIPYs reported to date emit at wavelengths lower than 600 nm. Among the possible solutions to this issue, BODIPYs with an aromatic ring fused at the β, β' -pyrrolic positions are particularly interesting, since they generally provide highly planar BODIPY platforms featuring largely red-shifted absorptions and emissions, as well as enhanced hydrophobicity and cell permeability.^{11,12} Recently, much research has been directed at the discovery of new synthetic pathways to introduce benzo-fused rings in the BODIPY scaffold, mainly using 4,5,6,7-tetrahydroisindole,^{8d,12} norbornane-derived pyrroles,¹³ or 3-halogeno-1-formyliso-indoles¹⁴ as reagents (Scheme 1), where only the last example represents a route not requiring harsh conditions.

Exploitation of 1,2,3-unsubstituted isoindoles is usually prevented by their high instability, both in solution and in the solid state. A special case is represented by 4,5,6,7-tetrafluoroisindole, which has already been demonstrated to be stable in the solid state because of its crystal packing.¹⁵ For this reason, we decided to explore the preparation of asymmetrical benzo-fused BODIPYs using 4,5,6,7-tetrafluoroisindole as the starting material. We report here a synthetic route to unsymmetrically substituted BODIPY 1 and the investigation of the reactivity of this novel dye toward functionalization by Pd(0)-catalyzed cross-coupling and nucleophilic substitution reactions, leading to a variety of regioselectively functionalized products. This methodology could be applied in the preparation of fluorinated BODIPYs with various applications, including in ¹⁹F NMR and near-IR imaging.¹⁶

RESULTS AND DISCUSSION

Synthesis.

4,5,6,7-Tetrafluoroisindole has already been reported in the literature¹⁵ as a stable intermediate in the synthesis of fluorinated benzoporphyrins. We decided to investigate the reactivity of this tetrafluoroisindole in the presence of 2-formyl-3,4-dimethylpyrrole under typical reaction conditions for BODIPY syntheses,¹⁷ using POCl₃ as the acid catalyst and BF₃·Et₂O as the boron source, obtaining 1 in 60% yield (Scheme 2). Slow diffusion of hexane into a dichloromethane solution afforded crystals suitable for X-ray analysis, thus allowing the unambiguous characterization of this compound (Figure 1). The C₉N₂B BODIPY core of 1 is slightly nonplanar, with a mean deviation 0.043 Å, and it is bowed, with the two five-membered rings tipped on the same side of the best plane. Its central six-membered C₃N₂B ring has a slight envelope conformation, with the B atom lying 0.087 Å out of the plane of the other five atoms. One F coordinated to B is thus farther out of the plane than the other, by 1.278 and 0.969 Å. The C–C(Me) distances are 1.4946(14) and 1.4915(13) Å, and the C–F distances are in the range 1.3390(11)–1.3408(11) Å.

Isoindole BODIPY 1 was then brominated at the 3,5-positions, using liquid bromine in dichloromethane,⁷ to give 2 in nearly quantitative yield (Scheme 2). The low solubility of 2 in all of the common organic solvents prevented both its chromatographic separation and NMR characterization; however, recrystallization of the crude reaction product afforded 2 in high purity, as evidenced by TLC analysis, UV-vis spectroscopy, and confirmed by ESI-HRMS. The reactivity of BODIPY 2 was investigated under nucleophilic substitution and Pd(0)-catalyzed cross-coupling Suzuki and Stille reactions, to generate various functionalized fluorinated BODIPYs, as described below.

Nucleophilic Substitution Reactions.

We investigated the reactivity of 2 toward nucleophilic substitution processes with C-, N-, O-, or S-centered nucleophiles, as shown in Scheme 3. Nucleophilic substitutions on 3,5-halogenated BODIPYs have been previously reported in the literature,⁹ and these reactions generally produce the target 3,5-functionalized products in high yields. In our case, we selected THF or toluene as solvents because of the complete insolubility of isoindole BODIPY 2 in acetonitrile, which is usually used in nucleophilic substitution reactions. Although 2 is only slightly soluble in THF and toluene, all of the generated products were soluble in these solvents, which facilitated their isolation and characterization.

Sulfur-centered nucleophiles were demonstrated to be highly reactive, affording the corresponding 3,5-disubstituted products at room temperature in short reaction times. For example, when benzylmercaptan (3 equiv) was used in a short reaction time (15 min), BODIPY 4e was isolated in 40% yield (Scheme 3). In the case of an aromatic thiol, such as 4-methylbenzenethiol, the reactivity is even higher. The disubstituted BODIPY 4d was obtained in 3 min using 2 equiv of thiol reagent in THF at room temperature. For both of the disubstituted compounds 4d and 4e, crystals suitable for X-ray analysis were obtained from slow diffusion of hexane into a dichloromethane solution (Figure 1), allowing the unambiguous characterization of these compounds. The C₉N₂B BODIPY core of 4d is nearly planar, with a mean deviation 0.023 Å. The phenyl rings of the 4-methylbenzenethiol substituents form dihedral angles of 87.4° and 68.1° with the core plane. There are two independent molecules in the asymmetric unit of 4e, and each has the S-CH₂-Ph nearest the fluorinated phenyl ring disordered into two conformations. In one of the two molecules, the C₉N₂B BODIPY core is very nearly planar, with a mean deviation 0.014 Å. In the other, the C₉N₂B core has a slightly bowed conformation, with a mean deviation of 0.068 Å, the B atom having the largest out-of-plane deviation of 0.160 Å.

The use of 3 equiv of 4-methylbenzenethiol at room temperature in THF led to the isolation of the unexpected trisubstituted compound 5d in 75% yield, as confirmed by ¹⁹F NMR spectroscopy (see the Supporting Information) and ¹H-¹⁹F HOESY (see Figure 5), where one of the fluorine atoms on the benzo-fused ring was also substituted (Scheme 3). Interestingly, only one trisubstituted regioisomer was obtained, indicating a higher reactivity for the α rather than the β fluoro group, as observed in fluorinated phthalocyanines.¹⁸ Increasing the number of equivalents of 4-methylbenzenethiol did not result in additional substitution reactions of the remaining fluorine atoms.

High regioselectivity was also observed in the case of carbon-, oxygen-, and nitrogen-centered nucleophiles, where the 3-bromo adjacent to the benzo-fused ring showed the highest reactivity. Using 5 or 10 equiv of 3-ethyl-2,4-dimethylpyrrole as the nucleophile, at 80 °C in toluene, produced monosubstituted 3a or disubstituted 4a BODIPYs respectively, in 60–77% yields (Scheme 3). The ^{19}F NMR spectra of these compounds (see the Supporting Information) showed two different multiplet signals for the two fluorines linked to the boron atom, confirming a hydrogen bonding interaction between the fluorine atoms linked to the boron and the N-hydrogen of the peripheral pyrrole, as previously observed.^{9d,14d} Moreover, in the ^1H NMR spectra of both 3a and 4a (see the Supporting Information and Figure 2), one of the methyl groups corresponding to the pyrrolic substituent shows a signal that is clearly split into two singlets, and a similar split is also observed in the case of one of the two pyrrolic N-hydrogens. Therefore, we hypothesize that the first pyrrole unit introduced at the 3-position can also have a hydrogen bonding interaction with the α fluorine group of the adjacent benzo-fused ring, in both cases forming a seven-membered ring structure; the two structures coexist in solution in the time scale of the ^1H NMR experiment, causing the splitting of the signals as shown in Figure 2.

Even higher regioselectivity was observed in the case of oxygen- and nitrogen-centered nucleophiles. Using an excess of 4-methoxyphenol as the oxygen nucleophile, in the presence of K_2CO_3 at room temperature, only the monosubstituted BODIPY 3c was produced (Scheme 3). A similar result was observed when piperidine was used as the nucleophile, producing BODIPY 3b in 93% yield. Unlike previous reports,^{9a} attempts to push the reaction to the formation of the disubstituted products failed, suggesting a peculiar deactivation in the reactivity of the second bromine atom. Even though the formation of 3b was readily accomplished after 15 min at room temperature, formation of the disubstituted product was not detected, even upon increasing the reaction time, the amount of nucleophile, and the reaction temperature.

Furthermore, an unexpected result occurred when aniline was used as the nitrogen nucleophile, in THF at room temperature. After 1 h, complete consumption of the starting material was observed, along with formation of bisBODIPY 6 in 65% yield (Scheme 3). No monomeric products were obtained under these conditions. We hypothesize that, upon formation of the monosubstituted product at the 3-position, the remaining bromine group, which is deactivated toward nucleophilic substitution, undergoes an unusual homocoupling reaction to produce 6. Previous literature reports¹⁹ have used aniline as a reducing agent in the synthesis of metal nanoparticles in water solutions. This peculiar reactivity of aniline in our homocoupling reaction is still under investigation. Crystals of BODIPY 6 suitable for X-ray analysis were obtained from slow diffusion of hexane into a dichloromethane solution, allowing the unambiguous characterization of this compound, as shown in Figure 3. The dimeric molecule lies on a crystallographic two-fold axis, so the two BODIPYs are identical by symmetry. The torsion angle about the central C–C bond is $-94.9(2)^\circ$; thus the two BODIPY cores are approximately orthogonal, forming a dihedral angle of 86.8° . Each $\text{C}_9\text{N}_2\text{B}$ BODIPY core has the same slightly bowed conformation seen in 1, with a mean deviation of 0.057 \AA . The envelope distortion of the central $\text{C}_3\text{N}_2\text{B}$ ring is more pronounced than in 1, with the B atom lying 0.190 \AA out of the plane of the other five atoms and the F atoms 0.730 and 1.457 \AA out of plane. This greater distortion may be explained by an

intramolecular hydrogen bond from the aniline substituent to one of the F atoms on B, with N...F distance 2.8514(19) Å and angle about H 136.3(18)°.

2D NMR Identification of Products.

For all of the monosubstituted BODIPYs 3a, 3b, and 3c, multiple 2D NMR experiments were performed in order to verify the position of the substituent. Figure 4 shows the HMBC and NOESY spectra obtained for 3b (corresponding spectra for 3a and 3c can be found in the Supporting Information). HMQC and HMBC experiments were performed; the first procedure is selective for directly bonded ^1H - ^{13}C atoms, while the latter detects long-range ^1H - ^{13}C coupling (up to 4 bond distance coupling). In the HMBC spectrum of 3b, the ^1H signal at 3.82 ppm, corresponding to the 2,6- CH_2 group of piperidine, correlates to four different carbon atoms (Figure 4). The peaks at 23.27, 26.18, and 53.76 ppm proved to be the piperidine carbon atom signals from the HMQC experiment; therefore, the signal at 157.44 ppm belongs to the carbon atom at either the 3- or the 5-position of the BODIPY. Since neither of the two methyl groups of 3b is coupled to that specific carbon atom, it has to be the one at the C-3 position, and similarly for the pyridine substituent. Moreover, from the NOESY experiment (Figure 4), while the hydrogen atoms for one of the methyl groups (2.17 ppm) show a through-space interaction with the hydrogen atom at the 8-position, no correlation is detected between the methyl groups and the hydrogen atoms of piperidine.

A different approach was used for the structural characterization of trisubstituted compound **5d**. In order to establish the position of the thiol substituent on the benzo-fused ring, ^1H - ^{19}F HOESY experiments were performed. These showed a cross-peak between the BODIPY hydrogen at the 8-position and the fluorine atom labeled as F4 in Figure 5. On the other hand, in the monodimensional ^{19}F NMR spectrum of BODIPY **5d**, fluorines F2, F3, and F4 produced three distinctive signals, two doublets and one triplet, all with the same J value. This indicates that the remaining fluorine atom is in the vicinal position, and therefore, the thiol substituent regioselectively displaced the F1 atom.

Pd(0)-Catalyzed Cross-Coupling Reactions.

The reactivity of BODIPY **2** was also investigated under Pd(0)-catalyzed cross-coupling reactions. Good yields of the targeted bifunctionalized products were obtained using Suzuki and Stille cross-couplings (Scheme 4), while significant decomposition was observed in the case of Sonogashira and Heck coupling reactions, probably due to the harsher reaction conditions and the larger amount of base required in the latter reactions. $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ was used as the catalyst for both Stille and Suzuki coupling reactions, since $\text{Pd}(\text{PPh}_3)_4$ was observed to be less effective, and K_2CO_3 was used as the base in the Suzuki coupling reactions. The 3,5-dicoupled products **7**, **8**, and **9** were obtained in moderate yields upon refluxing in toluene, or in 1:1 toluene/THF for up to 4 h. BODIPY **7** was obtained from a Suzuki coupling reaction, and crystals suitable for X-ray analysis were obtained from slow diffusion of hexane into a dichloromethane solution, allowing for the unambiguous characterization of this compound (Figure 6). The BODIPY cores of three independent molecules in the asymmetric unit all have similar slightly bowed conformations. Mean 12-atom deviations for the three are 0.054, 0.080, and 0.088 Å, and in all three cases, the B atom has the largest deviation, by 0.153, 0.192, and 0.182 Å, respectively. Dihedral angles

between the 12-atom BODIPY core and the phenyl groups at the 3,5-positions in 7 range from 60.7° to 68.3° over the three independent molecules, with an average value of 65.2°.

BODIPYs **8** and **9** were obtained from both Suzuki and Stille coupling reactions in moderate yields, with better results in the case of the Stille cross-coupling reactions due to the shorter reaction times (typically 1 h) and no base requirement,^{6d} which minimized BODIPY decomposition.

Spectroscopic Characterization.

The spectroscopic properties of the fluorinated BODIPYs in THF are summarized in Table 1. Figure 7 shows the normalized UV-vis absorption and emission spectra of selected BODIPYs (additional spectra can be found in the Supporting Information). For all of the BODIPYs, the absorption spectra showed typical BODIPY features, with a strong band between 560 nm for **1** and 690 nm for **4a**, corresponding to the $S_0 \rightarrow S_1$ transition, and a blue-shifted vibrational transition as a shoulder. Only dimer **6** showed different behavior, similar to that previously reported for bisBODIPYs,²⁰ with two distinctive absorption bands with similar molar extinction coefficients (see the Supporting Information). The two main differences observed between **6** and the previously reported bisBODIPYs are (1) lower molar absorption coefficient and (2) low fluorescence quantum yield observed for **6**. Both of these differences are due to the presence of the aniline substituents at the pyrrolic α -positions in **6**. Aniline monosubstituted monomeric BODIPYs^{9a,21} are known to display lower molar absorption coefficients and lower fluorescence quantum yields compared with their 3-halogenated precursors. Moreover, the fluorescence quantum yields of bisBODIPY dimers are usually lower than the corresponding monomeric species, due to the enhancement of the intersystem crossing efficiency as a result of an exciton-split excited state.²⁰

Both monosubstituted compounds **3b** and **3c** showed very high fluorescence quantum yields despite the presence of bromine, almost similar to the precursor BODIPY **1**, with a larger Stokes shift for **3b**. In these cases, the remaining bromine group at the pyrrolic α -position does not significantly affect the emission properties, as is normally observed when bromine occupies a pyrrolic β -position due to the heavy halogen atom effect, which facilitates intersystem crossing²². This result is consistent with previous literature, which reports low fluorescence quantum yields in the case of poly-brominated compounds.^{7d,23} BODIPY **3b** also displayed a lower molar absorption coefficient compared with the other monomeric BODIPYs, due to the N-substitution at the α -pyrrolic position, in agreement with previous observations.^{9a,21} Furthermore, no fluorescence emission was detected for **3a** and **4a** in THF, as previously reported for 3-pyrrole substituted isoindole BODIPYs, due to the solvent polarity.¹⁴ However, in nonpolar solvents such as hexane and toluene, these types of compounds typically show high fluorescence quantum yields. In addition, **4a** showed the most red-shifted absorption spectrum, 130 nm shift compared with starting BODIPY **1**, due to the significant enhancement of the π -electron delocalization system, in part as a result of the pyrrolic NH \cdots F hydrogen bond. BODIPY **9** bearing 3,5-furyl groups also showed a large red-shifted absorption spectrum, by 109 nm relative to **1**, as previously observed.^{9e} On the other hand, BODIPYs **7** and **8** showed only moderately red-shifted absorption and emission spectra relative to **1**, in the order of 35 nm, due to the larger dihedral angles (ca. 65°)

between the 3,5-phenyl rings and the BODIPY core, as seen in Figure 6. Both BODIPYs **7** and **8** show very high fluorescence quantum yields of nearly 1, while **9** showed a drastic decrease in the quantum yield, due to the greater freedom of rotation of the furyl group compared with phenyl, leading to increased energy lost to nonradiative decay to the ground state.

The fluorinated BODIPYs substituted with oxygen or nitrogen atoms at the 3-position, such as **3b** and **3c**, showed slight red-shifted absorptions and emissions relative to **1** (2–13m), increased Stokes shifts, particularly in the case of **3b**, and slightly decreased quantum yields. Among the 3,5-disubstituted BODIPYs with sulfur atoms, **4d** bearing the aromatic thiol substituent displayed a larger red-shifted absorption and emission spectra relative to **4e** substituted with benzylthiol, along with decreased fluorescence quantum yield. In addition, replacement of one α -fluoro atom on the benzo-fused ring with another 4-methylphenylthio group further red-shifted the absorption and emission of **5d** compared with the disubstituted **4d**, by 17 and 19 nm, respectively.

CONCLUSION

A novel fluorinated and 3,5-brominated benzo-fused BODIPY **2** was synthesized from a 4,5,6,7-tetrafluoroisindole precursor, followed by bromination in high yields. The functionalization of **2** under nucleophilic substitution reactions using C-, N-, O-, or S-centered nucleophiles led to the preparation of mono-, di-, or trisubstituted products, and a bisBODIPY. The most reactive position was the bromo group on the isindole unit, followed by the bromo group on the pyrrole ring, followed by an α -fluoro group on the isindole. All the products were obtained under mild conditions, and their structures were confirmed by 1D and 2D NMR spectroscopy, and in the case of **4d** and **4e**, by X-ray crystallography. Isoindole BODIPY **2** was also reactive under Suzuki and Stille cross-coupling reactions, the latter producing the targeted 3,5-functionalized products in higher yields. The spectroscopic properties of the fluorinated BODIPYs were investigated in THF solution. The starting tetrafluoroisindole BODIPY **1** showed typical BODIPY spectra with absorption and emission at 560 and 568 nm, respectively, and very high fluorescence quantum yield ($\Phi = 0.98$). Functionalization at the 3- and or 5-positions with phenyl, phenol, or piperidine resulted in red-shifted spectra, retaining of high fluorescence quantum yields, and, in the case of piperidine, lower molar absorptivity. On the other hand, disubstitution (and in the case of **5d**, trisubstitution) with furyl, benzothio, and methylphenylthio groups significantly decreased the fluorescence quantum yields. Isoindole BODIPYs **3a** and **4a** with trialkylpyrrole substituents showed the largest red-shifted absorptions but were nonfluorescent in THF. The unusual product bisBODIPY **6** showed unique spectroscopic properties, significantly different from those of the monomeric BODIPYs, displaying two major absorption bands at 517 and 602 nm and very low fluorescence quantum yield.

EXPERIMENTAL SECTION

Silica gel 60 (70–230 mesh, Sigma-Aldrich) was used for column chromatography. Reagents and solvents were of the highest grade commercially available and were used without further purification. Dry solvents were collected from a PS-400 Solvent Purification System

(Innovative Technology, Inc.). ^1H , ^{13}C , ^{11}B , and ^{19}F NMR spectra were recorded with a Bruker DPX-400 (400 MHz) or a Bruker DPX-500 (500 MHz) spectrometer. Experiments were performed in CDCl_3 at 300 K. Chemical shifts are expressed in ppm relative to TMS. High resolution mass spectra were obtained using ESI-TOF. UV-vis spectra were recorded in THF on a Varian Cary 50 spectrophotometer. Melting points were determined in an open capillary and are uncorrected. Fluorescence spectra were recorded in THF on a Fluorolog-3 Modular spectrofluorometer. The relative fluorescence quantum yields were obtained by comparing the area under the corrected emission spectrum of a test sample with that of rhodamine 6G (0.80 in methanol) or methylene blue (0.03 in methanol) as external standards.²⁴ All spectra were recorded at room temperature using nondegassed samples, spectroscopic grade solvents, and a 10 mm quartz cuvette. Dilute solutions ($0.01 < A < 0.05$) were used to minimize the reabsorption effects, and in all cases, correction for the refractive index was applied. 4,5,6,7-Tetrafluoroisindole¹⁵ and 3,4-dimethyl-1*H*-pyrrole-2-carbaldehyde²⁵ were prepared following literature methods, and in each case, the characterization data were in agreement with reported data.

X-ray Crystallographic Data.

Diffraction data were collected at low temperature (100 K for **1**, 105 K for **7** and **4e**, 110 K for **6** and **4d**) on a Bruker Kappa Apex-II DUO diffractometer with MoK α (for **1** and **6**) radiation ($\lambda = 0.71073 \text{ \AA}$) or CuK α (for **7**, **4d**, and **4e**) radiation ($\lambda = 1.54184 \text{ \AA}$). Refinement was by full-matrix least-squares using SHELXL, with hydrogen atoms in idealized positions. Disordered solvent contribution was removed using the SQUEEZE procedure for **6**, **4d**, and **4e**. The structure of **7** has three independent molecules, and the crystal was a twin. The structure of **4d** has two independent molecules, both of which have disorder of one of the benzyl groups, and the crystal was also a twin. CCDC 1589624–1589628.

BODIPY 1.—150 μL of POCl_3 (1.59 mmol) was added to a stirring solution of 4,5,6,7-tetrafluoroisindole (100 mg, 0.53 mmol) and 3,4-dimethyl-1*H*-pyrrole-2-carbaldehyde (65.1 mg, 0.53 mmol) in 12 mL of CH_2Cl_2 at 0°C under N_2 . After 2 h stirring, another 35 mL CH_2Cl_2 was added and 1.12 mL of TEA (7.95 mmol) was slowly added to the solution always at 0°C . Finally 1.96 mL of $\text{BF}_3\cdot\text{Et}_2\text{O}$ (15.90 mmol) was slowly added. The solution was stirred at 0°C for 15 min, warmed up to r.t., and left stirring for another 6 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 as eluent, obtaining 108.8 mg of pure product. Yield = 60%. m.p.: $275\text{--}277^\circ\text{C}$. UV-vis (THF): λ_{max} , nm (log ϵ) 522 (sh, 4.34), 540 (sh, 4.54), 560 (4.76). ^1H NMR (400 MHz, CDCl_3): δ , ppm 8.36 (s, 1H), 7.64 (s, 1H), 7.61 (s, 1H), 2.27 (s, 3H, CH_3), 2.06 (s, 3H, CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 167.4, 145.3, 134.7, 132.5, 128.8, 123.9, 68.2, 38.8, 30.4, 28.9, 23.8, 22.9, 14.0, 10.9, 9.8. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm -142.46 (dt, 1F, $J' = 3.96 \text{ Hz}$, $J'' = 18.69 \text{ Hz}$), -143.58 (q, 2F, $J' = 28.73 \text{ Hz}$), -147.06 (t, 1F, $J' = 18.84 \text{ Hz}$), -151.48 (dt, 1F, $J' = 3.38 \text{ Hz}$, $J'' = 18.50 \text{ Hz}$), -159.28 (t, 1F, $J' = 18.42 \text{ Hz}$). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 0.28 (t, 1B, $J = 28.6 \text{ Hz}$). HRMS (ESI-TOF) m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{15}\text{H}_9\text{BF}_6\text{N}_2$ 342.0872; found 342.0873.

BODIPY 2.—22.4 μL of Br_2 (0.438 mmol) was slowly added to a stirring solution of 50 mg of BODIPY (0.146 mmol) in 8 mL of CH_2Cl_2 at 0 °C. After 20 min stirring, no starting material was detected by UV-vis spectroscopy and TLC. 40 mL of $\text{Na}_2\text{S}_2\text{O}_3$ sat. aq. was added to the solution, and the mixture was extracted with CH_2Cl_2 . The organic phase was dried over anhydrous sodium sulfate. The product was not soluble in common organic solvents to allow further purification, so it was recrystallized from CH_2Cl_2 /hexane, obtaining 67.9 mg of pure product, and considered pure based on TLC analysis. Yield = 93%. m.p.: 267–269 °C. UV-vis (THF): λ_{max} , nm 588. HRMS (ESI-TOF) m/z [M^*] $^-$ calcd for $\text{C}_{15}\text{H}_7\text{BBBr}_2\text{F}_6\text{N}_2$ 497.8979; found 497.8969.

BODIPY 3a.—A solution of BODIPY 2 (15 mg, 0.03 mmol) and 20.3 μL of 3-ethyl-2,4-dimethylpyrrole (0.15 mmol) in 3 mL of toluene was stirred at 80 °C for 10 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1/1 as eluent, obtaining 9.8 mg of pure product. Yield = 60%. m.p.: 193–194 °C. UV-vis (THF): λ_{max} , nm (log ϵ) 464 (4.14), 615 (sh, 4.47), 654 (4.76). ^1H NMR (400 MHz, CDCl_3): δ , ppm 9.51 (2s, 1H, NH), 7.32 (s, 1H, CH_{meso}), 2.45 (q, 2H, J = 7.64 Hz, CH_2CH_3), 2.35 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.12 (t, 3H, J = 7.64 Hz, CH_2CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 133.7, 133.4, 132.1, 132.0, 129.1, 129.1, 126.0, 125.7, 124.6, 116.8, 116.7, 116.6, 116.5, 110.3, 31.7, 30.9, 17.7, 14.9, 12.0, 11.4, 11.3, 10.1, 9.9. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –123.98 (dq, 1F, J' = 34.55 Hz, J'' = 94.94 Hz), –137.31 (dt, 1F, J' = 6.39 Hz, J'' = 18.54 Hz), –147.27 (t, 1F, J = 19.55 Hz), –150.83 (dt, 1F, J' = 6.00 Hz, J'' = 19.51 Hz), –151.84 (dq, 1F, J' = 27.79 Hz, J'' = 94.86 Hz), –158.41 (t, 1F, J = 19.06 Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.01 (t, 1B, J = 31.9 Hz). HRMS (ESI-TOF) m/z [$\text{M} - \text{HF}$] $^+$ calcd for $\text{C}_{23}\text{H}_{18}\text{BBBrF}_5\text{N}_3$ 521.0806; found 521.0805.

BODIPY 3b.—17.8 μL of piperidine (0.18 mmol) was added to a stirring solution of BODIPY 2 (15 mg, 0.03 mmol) in 3 mL of THF. The solution was left stirring at r.t. for 15 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 7:3 as eluent, obtaining 14.1 mg of pure product. Yield = 93%. m.p.: 207–209 °C. UV-vis (THF): λ_{max} , nm (log ϵ) 488 (sh, 4.02), 528 (sh, 4.23), 562 (4.36). ^1H NMR (400 MHz, CDCl_3): δ , ppm 7.06 (s, 1H, CH_{meso}), 3.82 (m, 4H, piperidine), 2.17 (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 1.85 (m, 4H, piperidine), 1.74 (m, 2H, piperidine). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 157.4, 140.8, 128.7, 124.5, 123.9, 120.8, 117.3, 113.5, 113.4, 111.6, 53.8, 53.8, 53.7, 53.7, 29.7, 25.9, 25.9, 23.6, 9.9, 9.8. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –133.09 (dt, 1F, J' = 7.76 Hz, J'' = 19.14 Hz), –133.76 (q, 2F, J' = 32.90 Hz), –146.06 (t, 1F, J' = 20.04 Hz), –149.70 (dt, 1F, J' = 7.88 Hz, J'' = 20.15 Hz), –158.42 (t, 1F, J' = 19.82 Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.07 (t, 1B, J = 32.1 Hz). HRMS (ESI-TOF) m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{20}\text{H}_{17}\text{BBBrF}_6\text{N}_3$ 503.0712; found 503.0700.

BODIPY 3c.—24 mg of K_2CO_3 (0.18 mmol) was added to a stirring solution of BODIPY 2 (15 mg, 0.03 mmol) and 4-methoxyphenol (10.8 mg, 0.09 mmol) in 3 mL of THF/ CH_3CN 1:1. The solution was left stirring at r.t. for 40 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane

1/1 as eluent, obtaining 5.7 mg of pure product. Yield = 35%. m.p.: 190–192 °C. UV–vis (THF): λ_{max} , nm (log ϵ) 536 (sh, 4.33), 570 (4.80). ^1H NMR (500 MHz, CDCl_3): δ , ppm 7.38 (s, 1H, CH_{meso}), 7.07 (d, 1H, $J = 9.07$ Hz, Ph), 6.87 (d, 1H, $J = 9.07$ Hz, Ph), 3.80 (s, 3H, OCH₃), 2.26 (s, 3H, CH₃), 2.01 (s, 3H, CH₃). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 157.2, 150.2, 135.9, 132.3, 126.6, 119.8, 118.9, 117.9, 116.0, 114.9, 114.8, 114.6, 103.2, 98.5, 67.9, 55.8, 55.7, 32.7, 23.5, 14.1, 10.2, 9.9. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –133.75 (dt, 1F, $J' = 6.16$ Hz, $J'' = 20.27$ Hz), –145.20 (q, 2F, $J' = 29.18$ Hz), –145.63 (t, 1F, $J' = 20.16$ Hz), –148.49 (dt, 1F, $J' = 5.68$ Hz, $J'' = 19.18$ Hz), –157.69 (t, 1F, $J' = 19.74$ Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 0.62 (t, 1B, $J = 27.1$ Hz). HRMS (ESI-TOF) m/z [$m + \text{H}$] $^+$ calcd for $\text{C}_{22}\text{H}_{14}\text{BBrF}_6\text{N}_2\text{O}_2$ 542.0345; found 542.0317.

BODIPY 4a.—A solution of BODIPY **2** (15 mg, 0.03 mmol) and 20.3 μL of 3-ethyl-2,4-dimethylpyrrole (0.30 mmol) in 3 mL of toluene was stirred at 80 °C for 60 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1/1 as eluent, obtaining 13.5 mg of pure product. Yield = 77%. m.p.: 153–155 °C. UV–vis (THF): λ_{max} , nm (log ϵ) 475 (3.73), 645 (sh, 4.36), 690 (4.67). ^1H NMR (500 MHz, CDCl_3): δ , ppm 9.58 (2s, 1H, NH), 8.20 (s, 1H, NH), 7.33 (s, 1H, CH_{meso}), 2.48 (q, 2H, $J = 7.56$ Hz, CH_2CH_3), 2.36 (s, 3H, CH₃), 2.34 (q, 2H, $J = 7.52$ Hz, CH_2CH_3), 2.17 (s, 3H, CH₃), 2.14 (s, 3H, CH₃), 2.12 (2s, 3H, CH₃), 2.09 (s, 3H, CH₃), 1.88 (s, 3H, CH₃), 1.14 (t, 3H, $J = 7.56$ Hz, CH_2CH_3), 1.02 (t, 3H, $J = 7.52$ Hz, CH_2CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 147.5, 144.8, 137.3, 134.5, 132.9, 132.5, 129.7, 128.4, 126.7, 125.4, 123.9, 121.8, 108.9, 67.9, 17.9, 17.7, 17.7, 15.4, 14.9, 14.9, 14.8, 12.1, 12.0, 11.9, 11.4, 11.4, 11.3, 10.9, 9.9, 9.6, 9.5. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –118.58 (m, 1F), –137.88 (dt, 1F, $J' = 5.84$ Hz, $J'' = 19.80$ Hz), –146.41 (m, 1F), –147.57 (t, 1F, $J = 19.51$ Hz), –151.60 (dt, 1F, $J' = 5.40$ Hz, $J'' = 19.40$ Hz), –158.94 (t, 1F, $J = 20.16$ Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.32 (t, 1B, $J = 32.4$ Hz). HRMS (ESI-TOF) m/z [M^*] $^+$ calcd for $\text{C}_{31}\text{H}_{31}\text{BF}_6\text{N}_4$ 583.2577; found 583.2573.

BODIPY 4d.—8.4 μL of TEA (0.06 mmol) was added to a solution of BODIPY **2** (15 mg, 0.03 mmol) and 4-methylbenzenethiol (7.5 mg, 0.06 mmol) in 3 mL of THF. The solution was left stirring at r.t. for 3 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1/1 as eluent, obtaining 4.4 mg of pure product. Yield = 25%. m.p.: 222–224 °C. UV–vis (THF): λ_{max} , nm (log ϵ) 592 (sh, 4.50), 629 (4.86). ^1H NMR (400 MHz, CDCl_3): δ , ppm 7.43 (s, 1H, CH_{meso}), 7.37 (d, 2H, $J = 8.00$ Hz, Ph), 7.35 (d, 2H, $J = 8.08$ Hz, Ph), 7.14 (d, 2H, $J = 7.96$ Hz, Ph), 7.10 (d, 2H, $J = 8.00$ Hz, Ph), 2.35 (s, 3H, CH₃), 2.33 (s, 3H, CH₃), 2.22 (s, 3H, CH₃), 1.67 (s, 3H, CH₃). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 194.1, 187.1, 160.2, 154.9, 153.0, 139.1, 138.3, 137.9, 135.0, 134.7, 131.5, 131.4, 131.3, 130.4, 130.1, 130.1, 129.4, 118.9, 88.1, 53.4, 29.7, 21.2, 10.1, 9.9. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –137.16 (q, 2F, $J = 30.34$ Hz), –140.06 (dt, 1F, $J' = 4.56$ Hz, $J'' = 20.36$ Hz), –147.79 (t, 1F, $J = 19.21$ Hz), –152.46 (dt, 1F, $J' = 4.48$ Hz, $J'' = 19.44$ Hz), –158.98 (t, 1F, $J = 20.20$ Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.09 (t, 1B, $J = 29.2$ Hz). HRMS (ESI-TOF) m/z [M^*] $^+$ calcd for $\text{C}_{29}\text{H}_{21}\text{BF}_6\text{N}_2\text{S}_2$ 586.1152; found 586.1162.

BODIPY 4e.—12.5 μL of TEA (0.09 mmol) was added to a solution of BODIPY 2 (15 mg, 0.03 mmol) and 10.6 μL of benzylmercaptan (0.09 mmol) in 3 mL of THF. The solution was left stirring at r.t. for 15 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1/1 as eluent, obtaining 7.0 mg of pure product. Yield = 40%. m.p.: 167–168 °C. UV-vis (THF): λ_{max} , nm (log ϵ) 582 (sh, 4.53), 610 (4.81). ^1H NMR (400 MHz, CDCl_3): δ , ppm 7.35 (s, 1H, CH_{meso}), 7.33–7.15 (m, 10H, Ph), 4.48 (s, 2H, CH_2), 4.33 (s, 2H, CH_2), 2.17 (s, 3H, CH_3), 1.75 (s, 3H, CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 206.9, 157.3, 152.2, 137.8, 137.2, 135.8, 135.5, 133.3, 129.4, 129.3, 128.5, 128.5, 127.7, 127.5, 126.9, 118.9, 53.4, 42.3, 41.2, 41.1, 41.1, 31.9, 31.6, 30.9, 29.7, 22.7, 14.1, 10.0, 9.7. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –136.59 (q, 2F, J = 30.16 Hz), –142.88 (dt, 1F, J' = 4.84 Hz, J'' = 20.04 Hz), –147.56 (t, 1F, J = 19.21 Hz), –152.05 (dt, 1F, J' = 4.96 Hz, J'' = 20.00 Hz), –158.90 (t, 1F, J = 19.80 Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.09 (t, 1B, J = 29.0 Hz). HRMS (ESI-TOF) m/z $[\text{M} - \text{F}]^+$ calcd for $\text{C}_{29}\text{H}_{21}\text{BF}_6\text{N}_2\text{S}_2$ 567.1159; found 567.1154.

BODIPY 5d.—23 μL of TEA (0.17 mmol) was added to a solution of BODIPY 2 (30 mg, 0.06 mmol) and 4-methylbenzenethiol (20.7 mg, 0.18 mmol) in 3 mL of THF. The solution was left stirring at r.t. for 3 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1:1 as eluent, obtaining 36.2 mg of pure product. Yield = 75%. m.p.: 210–212 °C. UV-vis (THF): λ_{max} , nm (log ϵ) 606 (sh, 4.47), 646 (4.87). ^1H NMR (125 MHz, CDCl_3): δ , ppm 7.43 (s, 1H, CH_{meso}), 7.37 (d, 2H, J = 8.10 Hz, Ph), 7.34 (d, 2H, J = 8.10 Hz, Ph), 7.29 (d, 2H, J = 8.15 Hz, Ph), 7.11 (d, 2H, J = 8.65 Hz, Ph), 7.09 (d, 2H, J = 8.65 Hz, Ph), 7.07 (d, 2H, J = 8.25 Hz, Ph), 2.33 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 1.64 (s, 3H, CH_3). ^{13}C NMR (500 MHz, CDCl_3): δ , ppm 173.9, 153.1, 151.2, 144.1, 139.0, 138.2, 137.9, 137.9, 135.4, 131.5, 131.4, 130.9, 130.5, 130.0, 129.9, 129.4, 125.9, 118.7, 118.6, 113.9, 65.1, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.1, 24.9, 22.7, 21.2, 21.1, 14.1, 10.1, 9.9. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –115.14 (d, 1F, J = 20.91 Hz), –134.08 (d, 1F, J = 21.13 Hz), –137.24 (q, 2F, J = 30.83 Hz), –142.58 (t, 1F, J = 21.10 Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.10 (t, 1B, J = 28.6 Hz). HRMS (ESI-TOF) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{36}\text{H}_{28}\text{BF}_5\text{N}_2\text{S}_3$ 691.1506; found 691.1522.

bisBODIPY 6.—828 μL of aniline (0.09 mmol) was added to a stirring solution of BODIPY 2 (15 mg, 0.03 mmol) in 3 mL of THF. The solution was left stirring at r.t. for 1 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH_2Cl_2 /hexane 1/1 as eluent, obtaining 8.4 mg of pure product. Yield = 65%. m.p.: 177–179 °C. UV-vis (THF): λ_{max} , nm (log ϵ) 517 (4.31), 602 (4.32). ^1H NMR (500 MHz, CDCl_3): δ , ppm 8.29 (m, 2H, NH), 7.34 (t, 4H, J = 7.90 Hz, Ph), 7.30–7.27 (m, 4H, Ph + CH_{meso}), 7.10 (d, 4H, J = 7.65 Hz, Ph), 2.27 (s, 6H, CH_3), 1.91 (s, 6H, CH_3). ^{13}C NMR (125 MHz, CDCl_3): δ , ppm 167.8, 151.8, 138.3, 137.1, 132.5, 130.9, 130.7, 130.2, 129.5, 128.8, 127.3, 126.6, 124.2, 124.1, 123.3, 115.5, 115.4, 10.9, 9.9, 9.5, 9.5. ^{19}F NMR (376 MHz, CDCl_3): δ , ppm –127.32 (dt, 1F, J' = 7.52 Hz, J'' = 23.16 Hz), –141.67 (m, 1F), –145.68 (t, 1F, J' = 20.40 Hz), –146.70 (m, 1F), –149.00 (dt, 1F, J' = 7.12 Hz, J'' = 19.78 Hz), –157.79 (t, 1F, J = 20.60 Hz). ^{11}B NMR (128 MHz, CDCl_3): δ , ppm 1.26 (br t, 1B). HRMS (ESI-TOF) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{42}\text{H}_{27}\text{B}_2\text{F}_{12}\text{N}_6$ 863.2359; found: 863.2341.

BODIPY 7.—30 mg of BODIPY 2 (0.06 mmol) was dissolved in 6 mL of THF/toluene 1:1 and purged with nitrogen. To the resulting solution, 4-(trifluoromethyl)phenylboronic acid (114 mg, 0.60 mmol) and Pd(PPh₃)₂Cl₂ (8.4 mg, 0.012 mmol) were added. Then, 1.2 mL of K₂CO₃ 1 M aq. was added, and the mixture was heated at 75 °C for 4 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH₂Cl₂/hexane 4:6 as eluent, obtaining 8.3 mg of pure product. Yield = 22%. m.p.: 268–270 °C. UV–vis (THF): λ_{\max} , nm (log ϵ) 556 (sh, 4.46), 590 (4.83). ¹H NMR (400 MHz, CDCl₃): δ , ppm 7.82–7.76 (m, 2H, Ph), 7.74 (s, 1H, CH_{meso}), 7.73–7.67 (m, 4H, Ph), 7.63 (d, 2H, J = 8.2 Hz, Ph), 2.36 (s, 3H, CH₃), 1.94 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ , ppm 156.4, 140.2, 134.9, 134.3, 133.3, 132.1, 131.8, 131.2, 130.9, 130.5, 130.0, 129.9, 129.9, 127.8, 126.0, 125.3, 125.2, 125.1, 125.1, 125.0, 125.0, 124.8, 124.8, 124.7, 122.7, 122.7, 122.6, 122.5, 10.1, 9.8. ¹⁹F NMR (376 MHz, CDCl₃): δ , ppm δ –62.77 (s, 3F, CF₃), –62.86 (s, 3F, CF₃), –130.55 (q, 2F, J = 27.92 Hz), –140.86 (td, 1F, J' = 18.84, J'' = 4.60 Hz), –147.37 (t, 1F, J = 19.26 Hz), –151.24 (td, 1F, J' = 19.00, J'' = 4.60 Hz), –158.45 (t, 1F, J = 18.65 Hz). ¹¹B NMR (128 MHz, CDCl₃): δ , ppm 0.99 (t, 1B, J = 30.3 Hz).

BODIPY 8.—Stille coupling: BODIPY 2 (30 mg, 0.06 mmol) was dissolved in 4 mL of dry toluene and the solution was purged with nitrogen. To this solution, 196 μ L of tributylphenylstannane (0.60 mmol) and 8.4 mg of Pd(PPh₃)₂Cl₂ (0.012 mmol) were added. The mixture was heated at 100 °C for 90 min. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH₂Cl₂/hexane 8:2 as eluent, obtaining 15.4 mg of pure product. Yield = 52%. Suzuki coupling: BODIPY 2 (30 mg, 0.06 mmol) was dissolved in 6 mL of THF/toluene 1:1 and the solution was purged with nitrogen. To this solution, 7.2 mg of phenylboronic acid (0.60 mmol) and 8.4 mg of Pd(PPh₃)₂Cl₂ (0.012 mmol) were added. Then, 1.2 mL of K₂CO₃ 1 M aq. was added, and the mixture was heated at 75 °C for 3 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH₂Cl₂/hexane 6:4 as eluent, obtaining 13.3 mg of pure product. Yield = 45%. m.p.: 254–256 °C. UV–vis (THF): λ_{\max} , nm (log ϵ) 554 (sh, 4.49), 589 (4.88). ¹H NMR (500 MHz, CD₂Cl₂): δ , ppm 7.73 (s, 1H, CH_{meso}), 7.62 (m, 2H, Ph), 7.52–7.41 (m, 8H, Ph), 2.33 (s, 3H, CH₃), 1.91 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ , ppm 158.1, 149.9, 139.9, 134.1, 131.8, 130.4, 130.1, 130.0, 129.9, 129.6, 129.6, 129.6, 129.2, 128.0, 127.9, 127.6, 125.5, 125.5, 125.4, 122.1, 122.1, 118.9, 118.8, 115.6, 9.9, 9.6. ¹⁹F NMR (376 MHz, CDCl₃): δ , ppm δ –130.91 (q, 2F, J = 38.92 Hz), –142.67 (td, 1F, J' = 24.80, J'' = 6.0 Hz), –148.43 (t, 1F, J = 23.31 Hz), –153.65 (td, 1F, J' = 23.31, J'' = 6.00 Hz), –160.94 (t, 1F, J = 23.31 Hz). ¹¹B NMR (128 MHz, CDCl₃): δ , ppm 0.99 (t, 1B, J = 38.4 Hz). HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₇H₁₇BF₆N₂ 494.1389; found 494.1383.

BODIPY 9.—Stille coupling: BODIPY 2 (30 mg, 0.06 mmol) was dissolved in 4 mL of toluene dry and the solution was purged with nitrogen. To this solution, 189 μ L of 2-(tributylstannyl)furane (0.60 mmol) and 8.4 mg of Pd(PPh₃)₂Cl₂ (0.012 mmol) were added. The mixture was heated at 100 °C for 1 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH₂Cl₂/hexane 8:2 as eluent, obtaining 9.1 mg of pure product. Yield = 32%. Suzuki coupling: BODIPY (30 mg,

0.06 mmol) was dissolved in 6 mL of THF/toluene 1:1 and the solution was purged with nitrogen. To this solution, 67.2 mg of 2-furanylboronic acid (0.60 mmol) and 8.4 mg of Pd(PPh₃)₂Cl₂ (0.012 mmol) were added. Then, 1.2 mL of K₂CO₃ 1 M aq. was added, and the mixture was heated at 75 °C for 2 h. The solvent was removed under reduced pressure, and the residue was chromatographed on a silica gel column using CH₂Cl₂/hexane 6:4 as eluent, obtaining 6.3 mg of pure product. Yield = 22%. m.p.: 275–276 °C. UV–vis (THF): λ_{max} , nm (log ϵ) 625 (sh, 4.52), 669 (4.85). ¹H NMR (500 MHz, CDCl₃): δ , ppm 7.75 (d, 1H, J = 1.8 Hz), 7.67 (d, 1H, J = 1.7 Hz), 7.63 (dd, 2H, J = 7.0, J' = 3.7 Hz), 7.46 (s, 1H, CH_{meso}), 6.70 (dd, 1H, J = 3.6, J' = 1.7 Hz), 6.65 (dd, 1H, J = 3.7, J' = 1.7 Hz, 1H), 2.29 (s, 3H, CH₃), 2.24 (s, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃): δ , ppm 146.9, 145.6, 145.1, 144.9, 143.9, 139.3, 139.2, 137.1, 135.5, 128.5, 126.2, 118.6, 118.0, 117.9, 117.9, 117.2, 117.1, 117.1, 112.9, 112.9, 29.7, 11.4, 9.7. ¹⁹F NMR (376 MHz, CDCl₃): δ , ppm δ –135.72 (td, 1F, J = 18.60, J' = 4.96 Hz), –139.96 (q, 2F, J = 31.42 Hz), –148.61 (t, 1F, J = 19.35 Hz), –153.30 (td, 1F, J = 19.28, J' = 4.88 Hz), –159.13 (t, 1F, J = 18.62 Hz). ¹¹B NMR (128 MHz, CDCl₃): δ , ppm 1.53 (t, 1B, J = 31.7 Hz). HRMS (ESI-TOF) m/z [M + H]⁺ calcd for C₂₃H₁₃BF₆N₂O₂ 474.1053; found 474.1083.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

This work was supported by the U.S. National Institutes of Health (R01 CA179902) and the National Science Foundation (CHE 1362641). The authors thankfully acknowledge the Tor Vergata Scuola di Dottorato support for study abroad.

REFERENCES

- (1). (a)Loudet A; Burgess K BODIPY Dyes and Their Derivatives: Syntheses and Spectroscopic Properties. *Chem. Rev* 2007, 107, 4891–4932. [PubMed: 17924696] (b)Ulrich G; Ziessele R; Harriman A The Chemistry of Fluorescent Bodipy Dyes: Versatility Unsurpassed. *Angew. Chem., Int. Ed* 2008, 47, 1184–1201.(c)Lu H; Mack J; Yang Y; Shen Z Structural Modification Strategies for the Rational Design of Red/NIR Region BODIPYs. *Chem. Soc. Rev* 2014, 43, 4778–4823. [PubMed: 24733589] (d)Ge Y; O'Shea DF Azadipyrromethenes: From Traditional Dye Chemistry to Leading Edge Applications. *Chem. Soc. Rev* 2016, 45, 3846–3864. [PubMed: 27181703]
- (2). (a)Hendricks JA; Keliher EJ; Wan D; Hilderbrand SA; Weissleder R; Mazitschek R Synthesis of [18F]BODIPY: Bifunctional Reporter for Hybrid Optical/Positron Emission Tomography Imaging. *Angew. Chem., Int. Ed* 2012, 51, 4603–4606.(b)Zeng L; Miller EW; Pralle A; Isacoff EY; Chang CJ A Selective Turn-On Fluorescent Sensor for Imaging Copper in Living Cells. *J. Am. Chem. Soc* 2006, 128, 10–11. [PubMed: 16390096] (c)Devaraj NK; Hilderbrand S; Upadhyay R; Mazitschek R; Weissleder R Bioorthogonal Turn-On Probes for Imaging Small Molecules inside Living Cells. *Angew. Chem., Int. Ed* 2010, 49, 2869–2872.(d)Martin A; Byrne A; Dolan C; Forster RJ; Keyes TE Solvent Switchable Dual Emission from a Bichromophoric Ruthenium-BODIPY Complex. *Chem. Commun* 2015, 51, 15839–15841.(e)Li Z; Bittman R Synthesis and Spectral Properties of Cholesterol- and FTY720-containing Boron Dipyrromethene Dyes. *J. Org. Chem* 2007, 72, 8376–8382. [PubMed: 17914846]
- (3). (a)Rousseau T; Cravino A; Bura T; Ulrich G; Ziessele R; Roncali J BODIPY Derivatives as Donor Materials for Bulk Heterojunction Solar Cells. *Chem. Commun* 2009, 1673–1675.(b)Loudet A; Bandichhor R; Wu L; Burgess K Functionalized BF₂ Chelated Azadipyrromethene Dyes. *Tetrahedron* 2008, 64, 3642–3654. [PubMed: 19458781] (c)Coskun A; Deniz E; Akkaya EU

Effective PET and ICT Switching of Boradiazaindacene Emission: A Unimolecular, Emission-Mode, Molecular Half-Subtractor with Reconfigurable Logic Gates. *Org. Lett* 2005, 7, 5187–5189. [PubMed: 16268534] (d)Boens N; Leen V; Dehaen W Fluorescent Indicators Based on BODIPY. *Chem. Soc. Rev* 2012, 41, 1130–1172. [PubMed: 21796324] (e)Kowada T; Maeda H; Kikuchi K BODIPY-based Probes for the Fluorescence Imaging of Biomolecules in Living Cells. *Chem. Soc. Rev* 2015, 44, 4953–4972. [PubMed: 25801415]

- (4). (a)Wang F; Zhou L; Zhao C; Wang R; Fei Q; Luo S; Guo Z; Tian H; Zhu W-H A Dual-response BODIPY-based Fluorescent Probe for the Discrimination of Glutathione from Cystein and Homocystein. *Chem. Sci* 2015, 6, 2584–2589. [PubMed: 29560246] (b)Keum D; Kim S; Kim Y A Fluorescence Turn-on Sensor for the Detection of Palladium Ions that Operates Through in situ Generation of Palladium Nanoparticles. *Chem. Commun* 2014, 50, 1268–1270.(c)Yuan M; Zhou W; Liu X; Zhu M; Li J; Yin X; Zheng H; Zuo Z; Ouyang C; Liu H; Li Y; Zhu D A Multianalyte Chemosensor on a Single Molecule: Promising Structure for an Integrated Logic Gate. *J. Org. Chem* 2008, 73, 5008–5014. [PubMed: 18522421] (d)Hudnall TW; Gabbai FP A BODIPY Boronium Cation for the Sensing of Fluoride Ions. *Chem. Commun* 2008, 4596–4597.
- (5). (a)Yogo T; Urano Y; Ishitsuka Y; Maniwa F; Nagano T Highly Efficient and Photostable Photosensitizer Based on BODIPY Chromophore. *J. Am. Chem. Soc* 2005, 127, 12162–12163. [PubMed: 16131160] (b)Kamkaew A; Burgess K Double-Targeting Using a TrkC Ligand Conjugated to Dipyrrrometheneboron Difluoride (BODIPY) Based Photodynamic Therapy (PDT) Agent. *J. Med. Chem* 2013, 56, 7608–7614. [PubMed: 24063347] (c)Kamkaew A; Lim SH; Lee HB; Kiew LV; Chung LY; Burgess K BODIPY Dyes in Photodynamic Therapy. *Chem. Soc. Rev* 2013, 42, 77–88. [PubMed: 23014776] (d)Gibbs JH; Zhou Z; Kessel D; Fronczek FR; Pakhomova S; Vicente MGH Synthesis, Spectroscopic, and *in vitro* Investigations of 2,6-Diiodo-BODIPYs with PDT and Multi-mode Imaging Applications. *J. Photochem. Photobiol. B* 2015, 145, 35–47. [PubMed: 25771382] (e)Neelakandan PP; Jimenez A; Thoburn JD; Nitschke J R An Autocatalytic System of Photooxidation-driven Substitution Reactions on a FeII4L6 Cage Framework. *Angew. Chem., Int. Ed* 2015, 54, 14378–14382.
- (6). (a)Baruah M; Qin W; Basaric N; De Borggraeve WM; Boens N BODIPY-Based Hydroxyaryl Derivatives as Fluorescent pH Probes. *J. Org. Chem* 2005, 70, 4152–4157. [PubMed: 15876108] (b)Rohand T; Qin W; Boens N; Dehaen W Palladium-catalyzed Coupling Reactions for the Functionalization of BODIPY Dyes with Fluorescence Spanning the Visible Spectrum. *Eur. J. Org. Chem* 2006, 2006, 4658–4663.(c)Duran-Sampedro G; Agarrabeitia AR; Garcia-Moreno I; Costela A; Banuelos J; Arbeloa T; Lopez Arbeloa I; Chiara JL; Ortiz MJ Chlorinated BODIPYs: Surprisingly Efficient and Highly Photostable Laser Dyes. *Eur. J. Org. Chem* 2012, 2012, 6335–6350.(d)Zhao N; Xuan S; Fronczek FR; Smith KM; Vicente MG Stepwise Polychlorination of 8-chloro-BODIPY and Regioselective Functionalization of 2,3,5,6,8-pentachloro-BODIPY. *J. Org. Chem* 2015, 80, 8377–8383. [PubMed: 26186141] (e)Xuan S; Zhao N; Ke X; Zhou Z; Fronczek FR; Kadish KM; Smith KM; Vicente MGH Synthesis and Spectroscopic Investigation of a Series of Push-Pull Boron Dipyrrromethenes (BODIPYs). *J. Org. Chem* 2017, 82, 2545–2557. [PubMed: 28150499]
- (7). (a)Hayashi Y; Yamaguchi S; Cha WY; Kim D; Shinokubo, Synthesis of Directly Connected BODIPY Oligomers Through Suzuki-Miyaura Coupling. *Org. Lett* 2011, 13, 2992–2995. [PubMed: 21591621] (b)Lakshmi V; Ravikanth M Synthesis of Sterically Crowded Polyarylated Boron-Dipyrrromethenes. *J. Org. Chem* 2011, 76, 8466–8471. [PubMed: 21910483] (c)Lai Y-C; Su S-Y; Chang CC Special Reactive Oxygen Species Generation by a Highly Photostable BODIPY-Based Photosensitizer for Selective Photodynamic Therapy. *ACS Appl. Mater. Interfaces* 2013, 5, 12935–12943.(d)Jiao L; Pang W; Zhou J; Wei Y; Mu X; Bai G; Hao E Regioselective Stepwise Bromination of Boron Dipyrrromethene (BODIPY) Dyes. *J. Org. Chem* 2011, 76, 9988–9996. [PubMed: 22077955] (e)Lakhe D; Jairaj KK; Pradhan M; Ladiwala U; Agarwal N Synthesis and Photophysical Studies of Heteroaryl Substituted BODIPY Derivatives for Biological Applications. *Tetrahedron Lett* 2014, 55, 7124–7129.
- (8). (a)Jiao L; Yu C; Uppal T; Liu M; Li Y; Zhou Y; Hao E; Hu X; Vicente MGH Long Wavelength Red Fluorescent Dyes from 3,5-Diiodo-BODIPYs. *Org. Biomol Chem* 2010, 8, 2517–2519. [PubMed: 20390194] (b)Ye JH; Hu Z; Wang Y; Zhang W; Zhang Y A New Practical and Highly Efficient Iodination of BODIPY Derivatives with Hypervalent Iodine Reagent. *Tetrahedron Lett* 2012, 53, 6858–6860.(c)Ortiz MJ; Agarrabeitia AR; Duran-Sampedro G; Prieto JB; Lopez TA;

Massad WA; Montejano HA; García NA; Arbeloa IL Synthesis and Functionalization of New Polyhalogenated BODIPY Dyes. Study of Their Photophysical Properties and Singlet Oxygen Generation. *Tetrahedron* 2012, 68, 1153–1162.(d)Meng Q; Fronczek FR; Vicente MGH Synthesis and Spectroscopic Properties of β, β' -Dibenzo-3,5,8-triaryl-BODIPYs. *New J. Chem* 2016, 40, 5740–5751.

- (9). (a)Rohand T; Baruah M; Qin W; Boens N; Dehaen W Functionalisation of Fluorescent BODIPY Dyes by Nucleophilic Substitution. *Chem. Commun* 2006, 266–268.(b)Leen V; Leemans T; Boens N; Dehaen W 2- and 3-Monohalogenated BODIPY Dyes and Their Functionalized Analogues: Synthesis and Spectroscopy. *Eur. J. Org. Chem* 2011, 2011, 4386–4396.(c)Li L; Nguyen B; Burgess K Functionalization of the 4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) core. *Bioorg. Med. Chem. Lett* 2008, 18, 3112–3116. [PubMed: 18037291] (d)Jiang T; Zhang P; Yu C; Yin J; Jiao L; Dai E; Wang J; Wei Y; Mu X; Hao E Straightforward Synthesis of Oligopyrroles through a Regioselective SNAr Reaction of Pyrroles and Halogenated Boron Dipyrins. *Org. Lett* 2014, 16, 1952–1955. [PubMed: 24670106] (e)Zhao N; Vicente MGH; Fronczek FR; Smith KM Synthesis of 3,8-Dichloro-6-ethyl-1,2,5,7-tetramethyl-BODIPY from an Asymmetric Dipyrroketone and Reactivity Studies at the 3,8,5-positions. *Chem. - Eur. J* 2015, 21, 6181–6192. [PubMed: 25761150]
- (10). (a)Leen V; Braeken E; Luckermans K; Jackers C; Van der Auweraer M; Boens N; Dehaen W A Versatile, Modular Synthesis of Monofunctionalized BODIPY Dyes. *Chem. Commun* 2009, 4515–4517.(b)Han J; Gonzalez O; Aguilar-Aguilar A; Pena-Cabrera E; Burgess K 3- and 5-Functionalized BODIPYs via the Liebeskind-Srogl Reaction. *Org. Biomol. Chem* 2009, 7, 34–36. [PubMed: 19081940] (c)Wang H; Fronczek FR; Vicente MGH; Smith KM Synthesis and Functionalization of 3,5,8-Trichlorinated BODIPY Dyes. *J. Org. Chem* 2014, 79, 10342–10352. [PubMed: 25268574]
- (11). Zhao N; Xuan S; Zhou Z; Fronczek FR; Smith KM; Vicente MGH Synthesis, Spectroscopic and Cellular Properties of Near-IR [a]-Phenanthrene-fused BODIPYs. *J. Org. Chem* 2017, 82, 9744–9750. [PubMed: 28845980]
- (12). Uppal T; Hu X; Fronczek FR; Maschek S; Bobadova-Parvanova P; Vicente MGH Synthesis, Computational Modelling and Properties of Benzo-appended BODIPYs. *Chem. - Eur. J* 2012, 18, 3893–3905. [PubMed: 22367756]
- (13). (a)Shen Z; Rohr H; Rurack K; Uno H; Spieles M; Schulz B; Reck G; Ono N Boron-diindomethene (BDI) Dyes and Their Tetrahydrobicyclo Precursors - en route to a New Class of Highly Emissive Fluorophores for the Red Spectral Range. *Chem. - Eur. J* 2004, 10, 4853–4871. [PubMed: 15372665] (b)Wada M; Ito S; Uno H; Murashima T; Ono N; Urano T; Urano Y Synthesis and Optical Properties of a New Class of Pyrromethene-BF₂ Complexes Fused with Rigid Bicyclo Rings and Benzo Derivatives. *Tetrahedron Lett* 2001, 42, 6711–6713.(c)Tomimori Y; Okujima T; Yano T; Mori S; Ono N; Yamada H; Uno H Synthesis of π -expanded O-chelated Boron-dipyrromethene as an NIR Dye. *Tetrahedron* 2011, 67, 3187–3193.
- (14). (a)Yu C; Jiao L; Tan X; Wang J; Xu Y; Wu Y; Yang G; Wang Z; Hao E Straightforward Acid-Catalyzed Synthesis of Pyrrolyldipyrromethenes. *Angew. Chem., Int. Ed* 2012, 51, 7688–7691. (b)Yu C; Xu Y; Jiao L; Zhou J; Wang Z; Hao E Isoindole-BODIPY Dyes as Red to Near-Infrared Fluorophores. *Chem. Eur. J* 2012, 18, 6437–6442. [PubMed: 22517763] (c)Yu C; Wu Q; Wang J; Wei Y; Hao E; Jiao L Red to Near-Infrared Isoindole BODIPY Fluorophores: Synthesis, Crystal Structures, and Spectroscopic and Electrochemical Properties. *J. Org. Chem* 2016, 81, 3761–3770. [PubMed: 27031115]
- (15). Uno H; Masuda G; Tukiji M; Nishioka Y; Iida T Novel Preparation of Fluorinated Isoindoles and their Conversion to Fluorinated Benzoporphyrins. *Tetrahedron Lett* 2007, 48, 7512–7515.
- (16). Bhupathiraju NVSDK; Rizvi W; Batteas JD; Drain CM Fluorinated Porphyrinoids as Efficient Platforms for New Photonic Materials, Sensors, and Therapeutics. *Org. Biomol. Chem* 2016, 14, 389–408. [PubMed: 26514229]
- (17). Wu L; Burgess K A New Synthesis of Symmetric Boraindacene (BODIPY) dyes. *Chem. Commun* 2008, 4933–4935.
- (18). (a)Aggarwal A; Singh S; Zhang Y; Anthes M; Samaroo D; Gao R; Drain CM Synthesis and Photophysics of an Octathioglycosylated Zinc(II) Phthalocyanine. *Tetrahedron Lett* 2011, 52, 5456–5459. [PubMed: 21966031] (b)Pereira JB; Carvalho EFA; Faustino MAF; Fernandes R; Neves MGPM; Cavaleiro JAS; Gomes NCM; Cunha A; Almeida A; Tome JPC Phthalocyanine

Thio-pyridinium Derivatives as Antibacterial Photo-sensitizers. *Photochem. Photobiol* 2012, 88, 537–547. [PubMed: 22332603] (c) Lourenco LMO; Pereira PMR; Maciel E; Valega M; Domingues FMJ; Domingues MRM; Neves MGPMS; Cavaleiro JAS; Fernandes R; Tome JPC Amphiphilic Phthalocyanine-cyclo-dextrin Conjugates for Cancer Photodynamic Therapy. *Chem. Commun* 2014, 50, 8363–8366.

- (19). (a) Yang J-P; Yin H-J; Jia J-J; Wei Y Facile Synthesis of High-Concentration, Stable Aqueous Dispersions of Uniform Silver Nanoparticles using Aniline as a Reductant. *Langmuir* 2011, 27, 5047–5053. [PubMed: 21434661] (b) Guo Z; Zhang Y; Huang L; Wang M; Wang J; Sun J; Xu L; Gu N One-step Controlled Synthesis of Anisotropic Gold Nanostructures with Aniline as the Reductant in Aqueous Solution. *J. Colloid Interface Sci* 2007, 309, 518–523. [PubMed: 17300797] (c) Song J; Chu Y; Liu Y; Li L; Sun W Room-temperature Controllable Fabrication of Silver Nanoplates Reduced by Aniline. *Chem. Commun* 2008, 1223–1225.
- (20). Broring M; Kruger R; Link S; Kleeberg C; Kohler S; Xie X; Ventura B; Flamigni L Bis(BF₂)-2,2'-bidipyrins (BisBODIPYs): Highly Fluorescent BODIPY Dimers with Large Stokes Shifts. *Chem. - Eur. J* 2008, 14, 2976–2983. [PubMed: 18306269]
- (21). Qin W; Leen V; Rohand T; Dehaen W; Dedeker P; Van der Auweraer M; Robeyns K; Van Meervelt L; Beljonne D; Van Averbek B; Clifford JN; Driesen K; Binnemans K; Boens N Synthesis, Spectroscopy, Crystal Structure, Electrochemistry, and Quantum Chemical and Molecular Dynamics Calculations of a 3-Anilino Difluoroboron Dipyrromethene dye. *J. Phys. Chem. A* 2009, 113, 439–447. [PubMed: 19099456]
- (22). (a) Ortiz MJ; Agarrabeitia AR; Duran-Sampedro G; Prieto JB; Lopez TA; Massad WA; Montejano HA; Garcia NA; Arbeloa IL Synthesis and Functionalization of New Polyhalogenated BODIPY Dyes. Study of Their Photophysical Properties and Singlet Oxygen Generation. *Tetrahedron* 2012, 68, 1153–1162. (b) Lim SH; Thivierge C; Nowak-Sliwinska P; Han JY; van den Bergh H; Wagnieres G; Burgess K; Lee HB In Vitro and In Vivo Photocytotoxicity of Boron Dipyrromethene Derivatives for Photodynamic Therapy. *J. Med. Chem* 2010, 53, 2865–2874. [PubMed: 20199028]
- (23). (a) Lakshmi V; Ravikanth M Brominated Boron Dipyrins: Synthesis, Structure, Spectral and Electrochemical Properties. *Dalton Trans* 2012, 41, 5903–5911. [PubMed: 22460271] (b) Wang J; Hou Y; Lei W; Zhou Q; Li C; Zhang B; Wang X DNA Photocleavage by a Cationic BODIPY Dye Through Both Singlet Oxygen and Hydroxyl Radical: New Insight Into the Photodynamic Mechanism of BODIPYs. *ChemPhysChem* 2012, 13, 2739–2747. [PubMed: 22619214]
- (24). Olmsted J Calorimetric Determinations of Absolute Fluorescence Quantum Yields. *J. Phys. Chem* 1979, 83, 2581–2584.
- (25). Kancharla P; Reynolds KA Synthesis of 2,2'-Bipyrrole-5-carboxaldehydes and Their Application in the Synthesis of B-ring Functionalized Prodiginines and Tambjamins. *Tetrahedron* 2013, 69, 8375–8385.

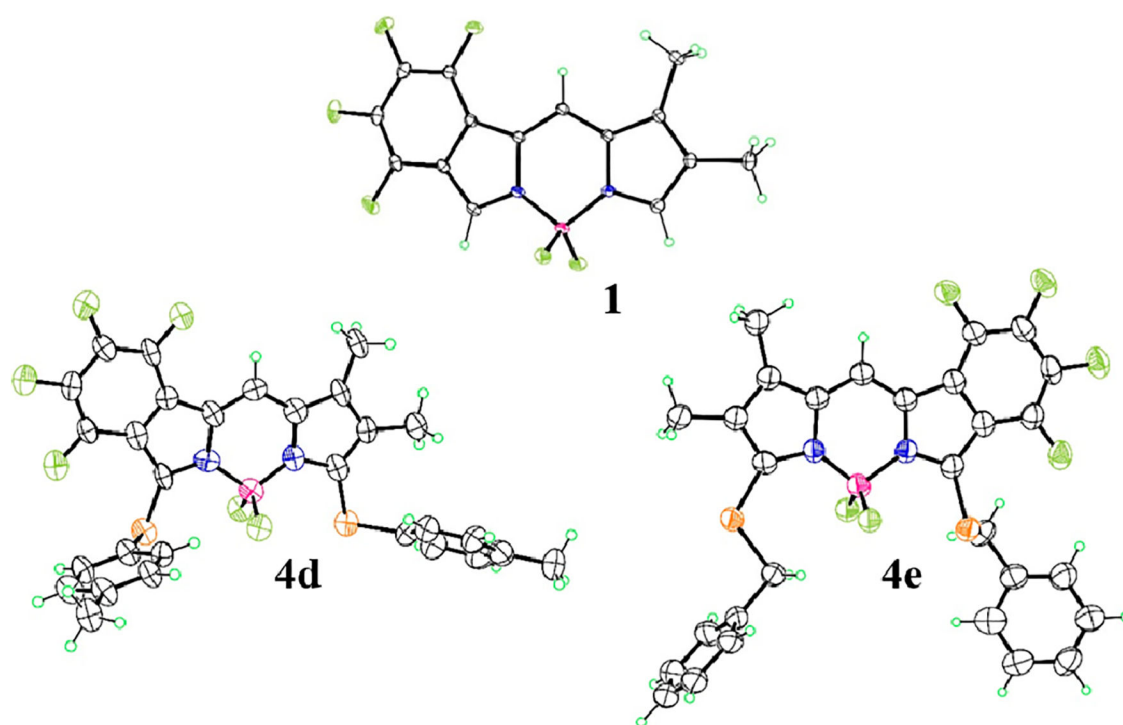


Figure 1.
Molecular structures of BODIPYs **1**, **4d**, and **4e** with 50% ellipsoids.

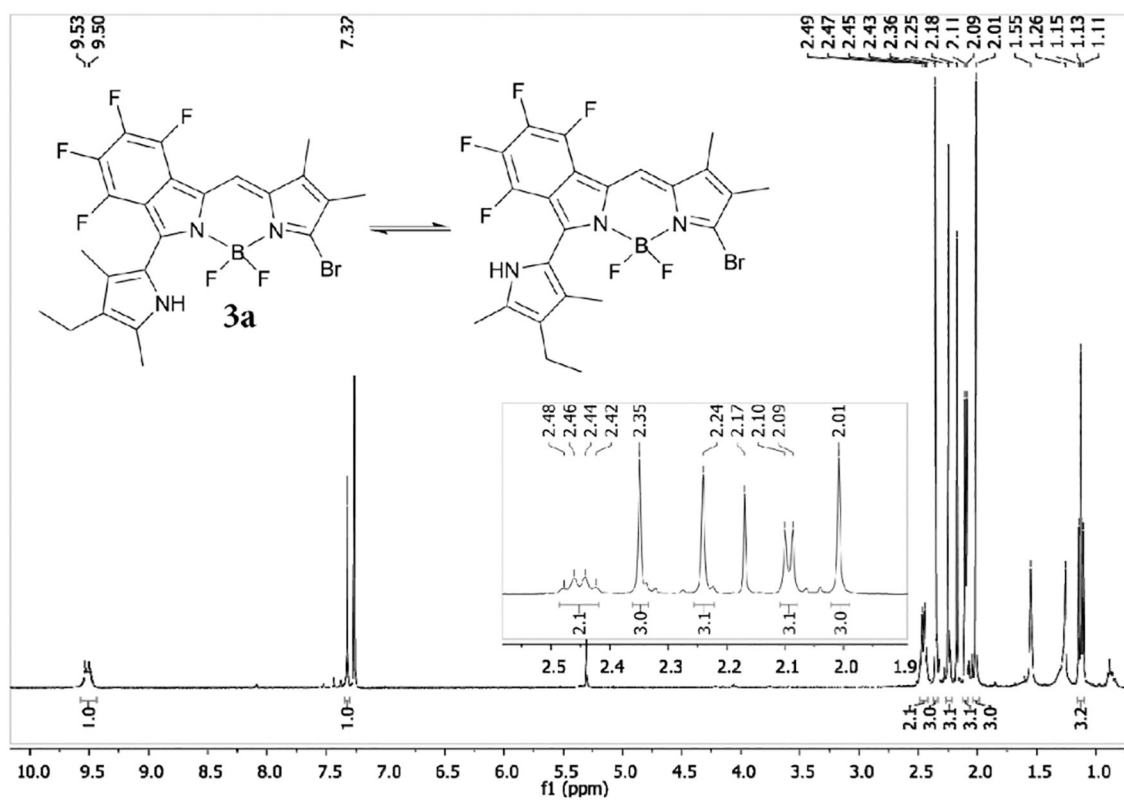


Figure 2.
 ^1H NMR spectrum of compound **3a** in CDCl_3 .

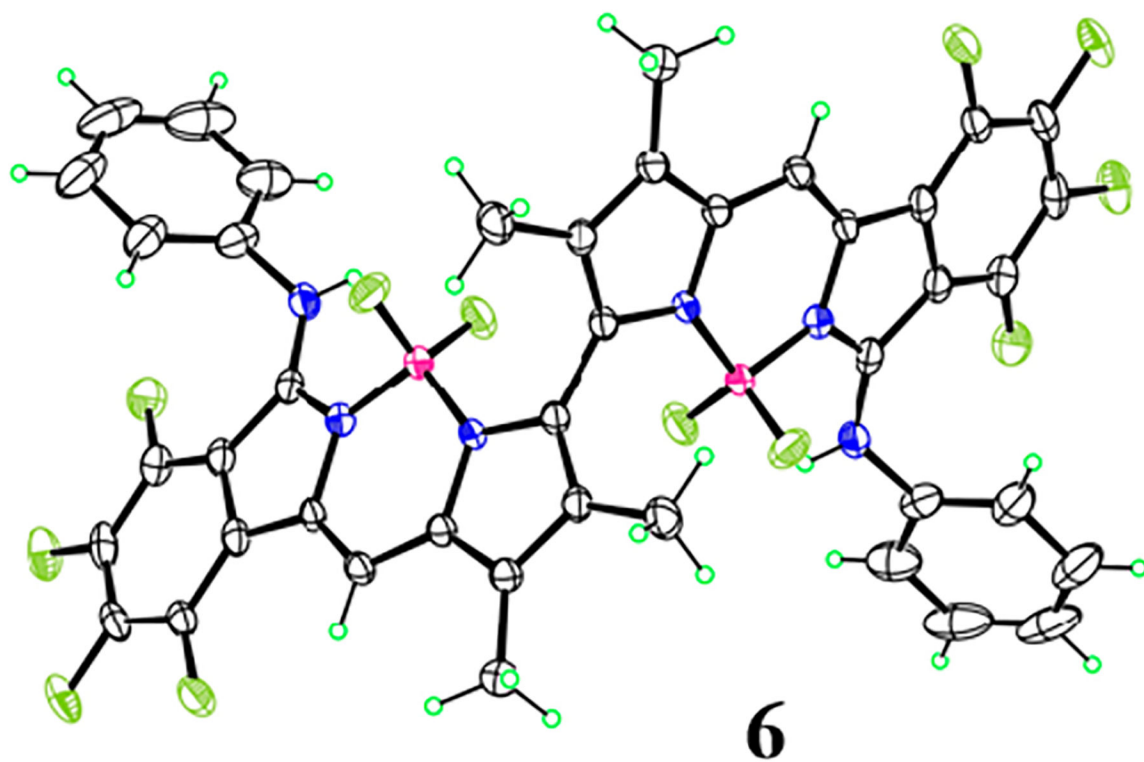


Figure 3.
Molecular structure of dimer **6** with 50% ellipsoids.

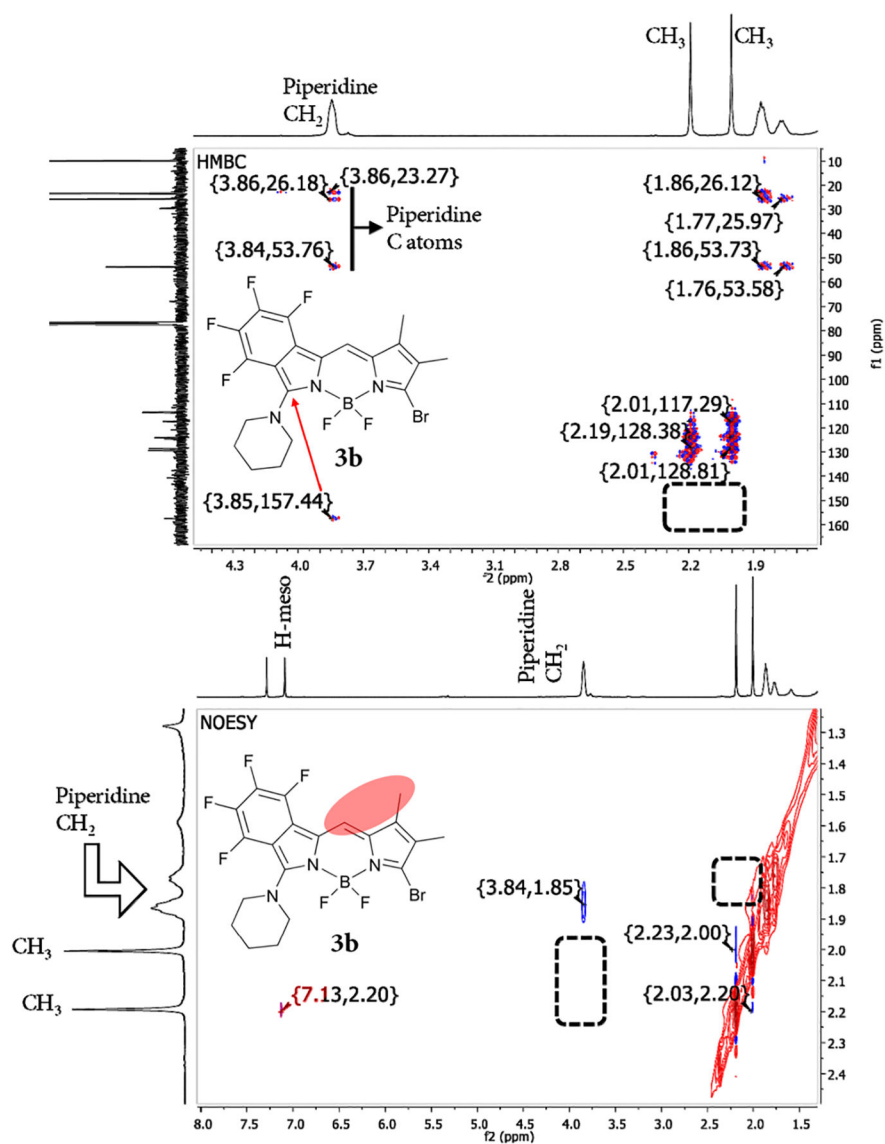


Figure 4.
HMBC and NOESY spectra for BODIPY **3b** in CDCl₃.

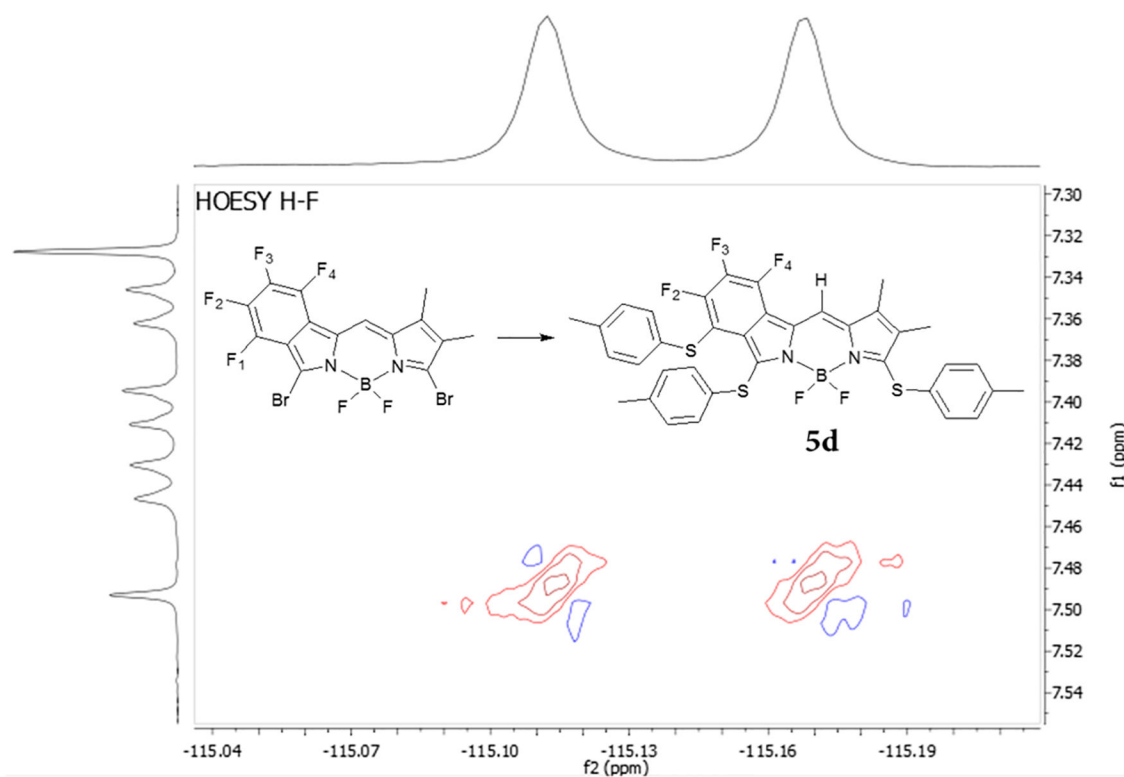


Figure 5.
 ^1H - ^{19}F HOESY spectrum for compound **5d** in CDCl_3 .

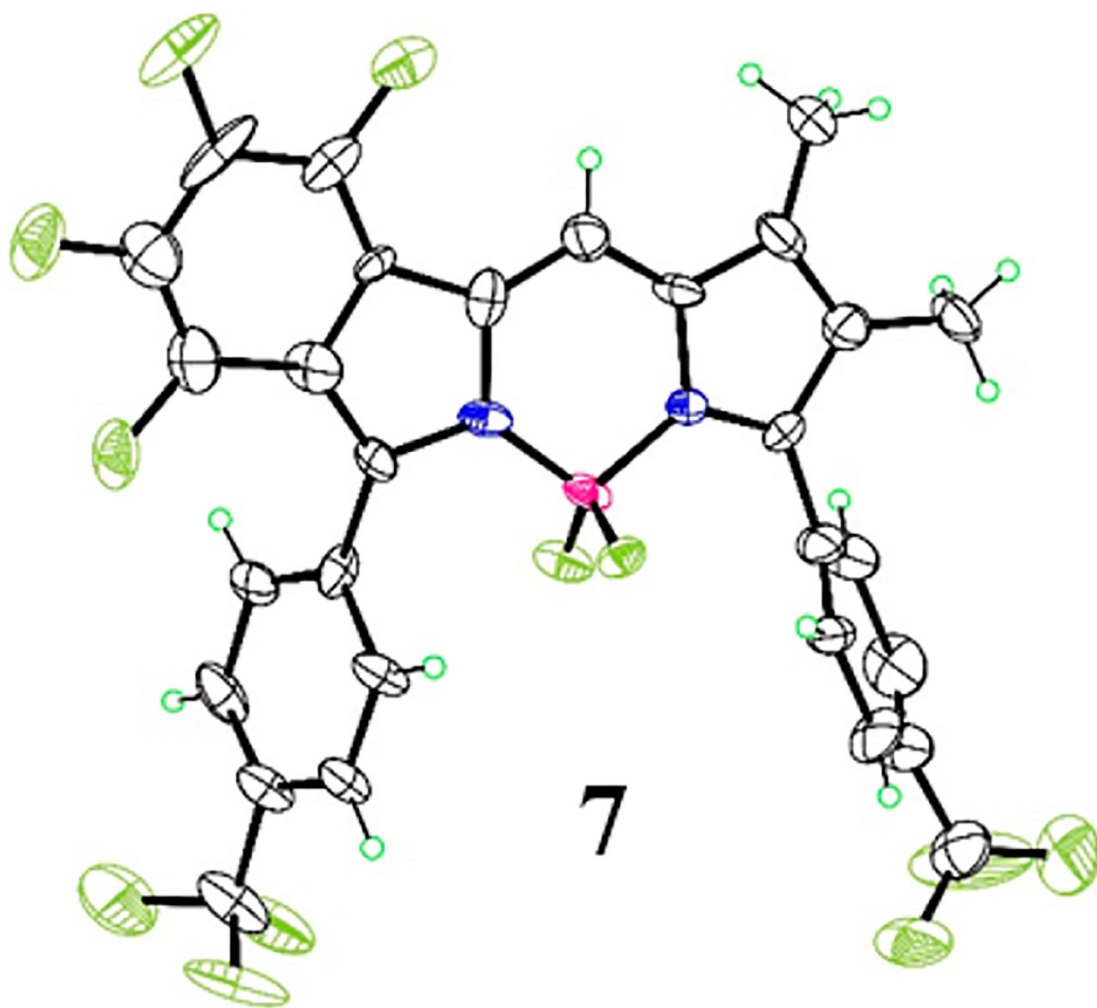


Figure 6.
Molecular structure of BODIPY **7** with 50% ellipsoids. Only one of the three independent molecules is shown.

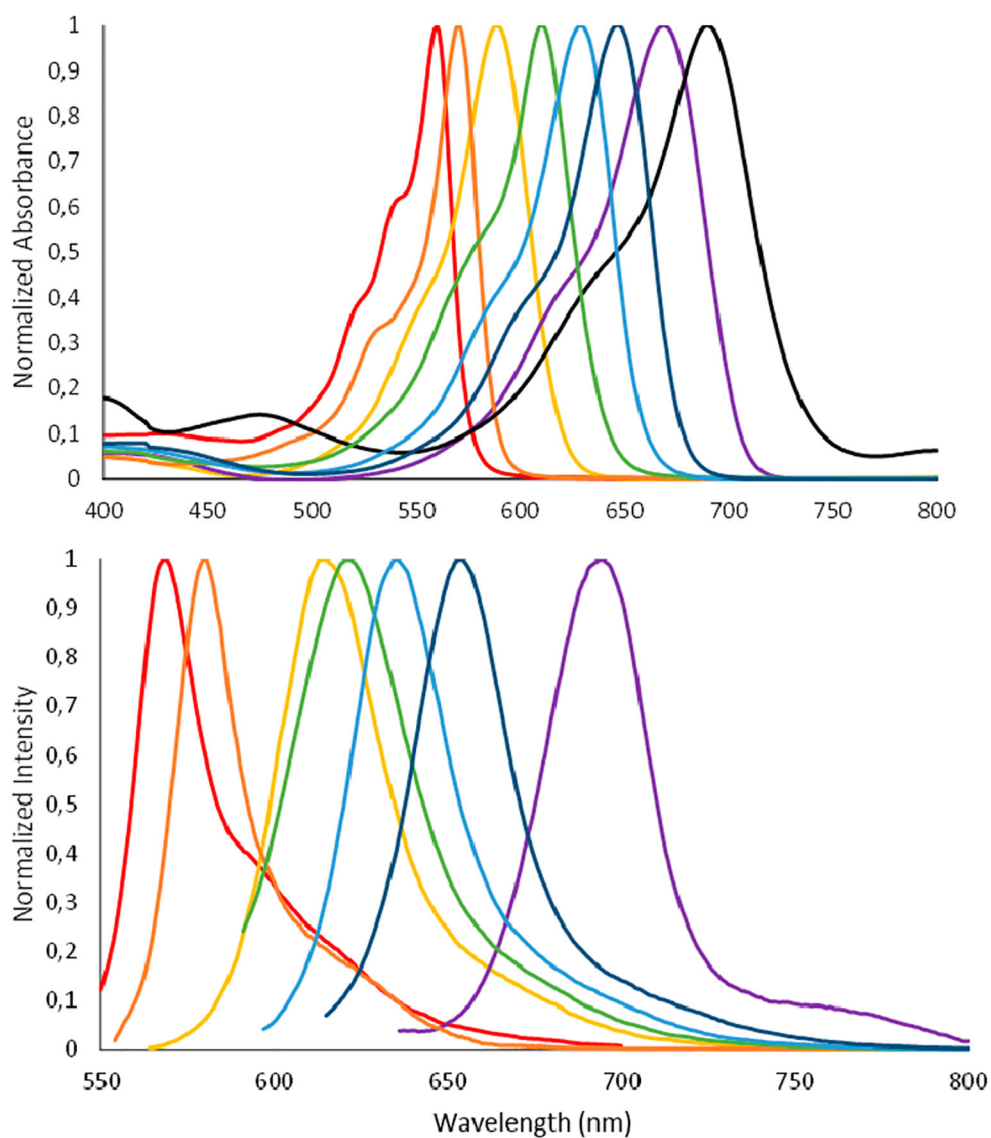
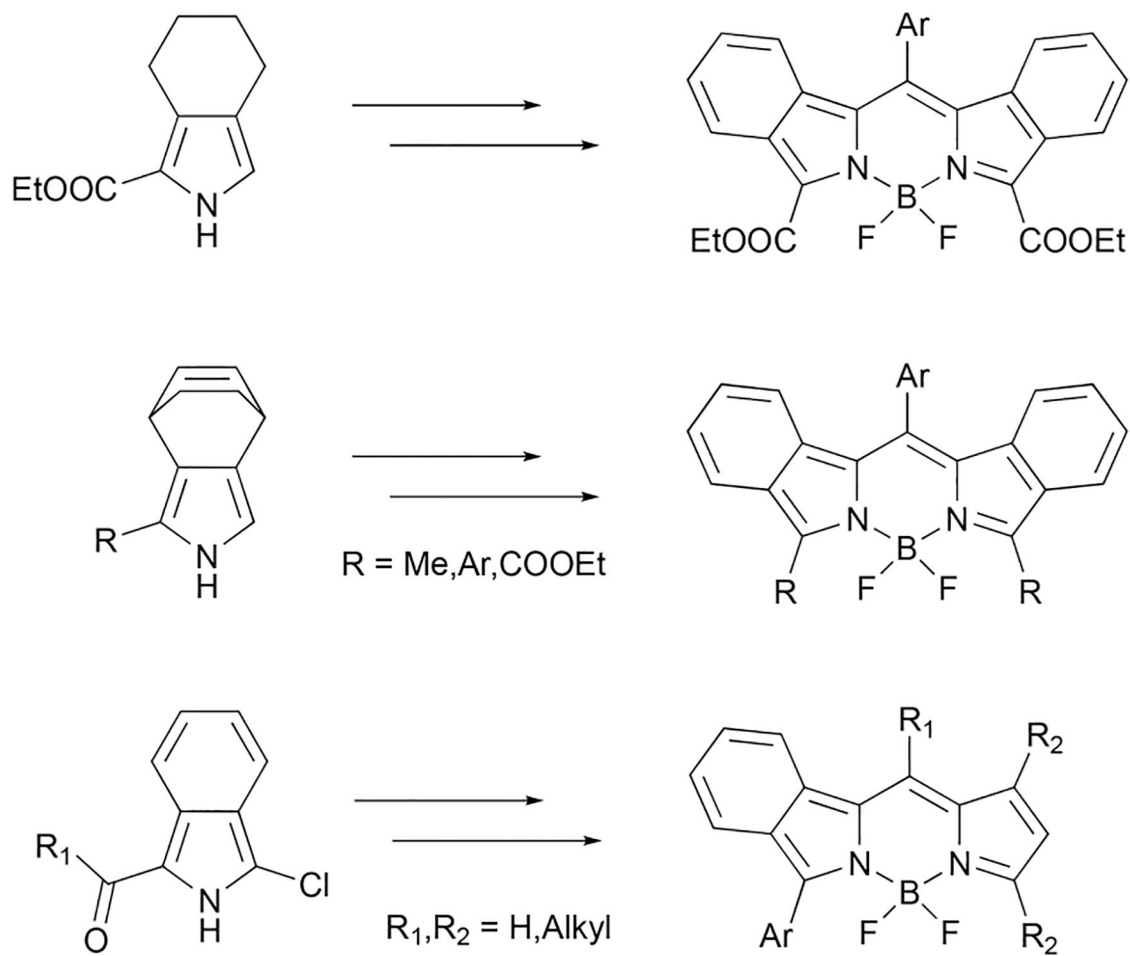
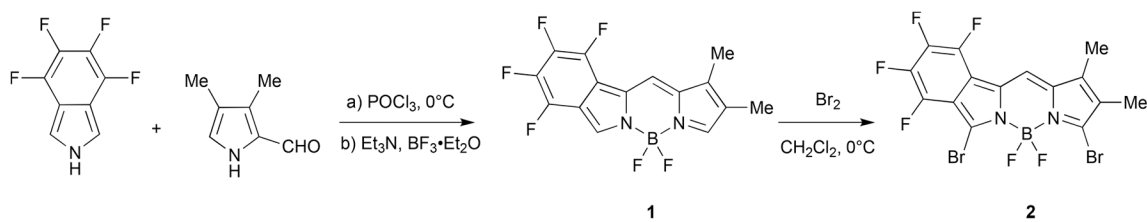


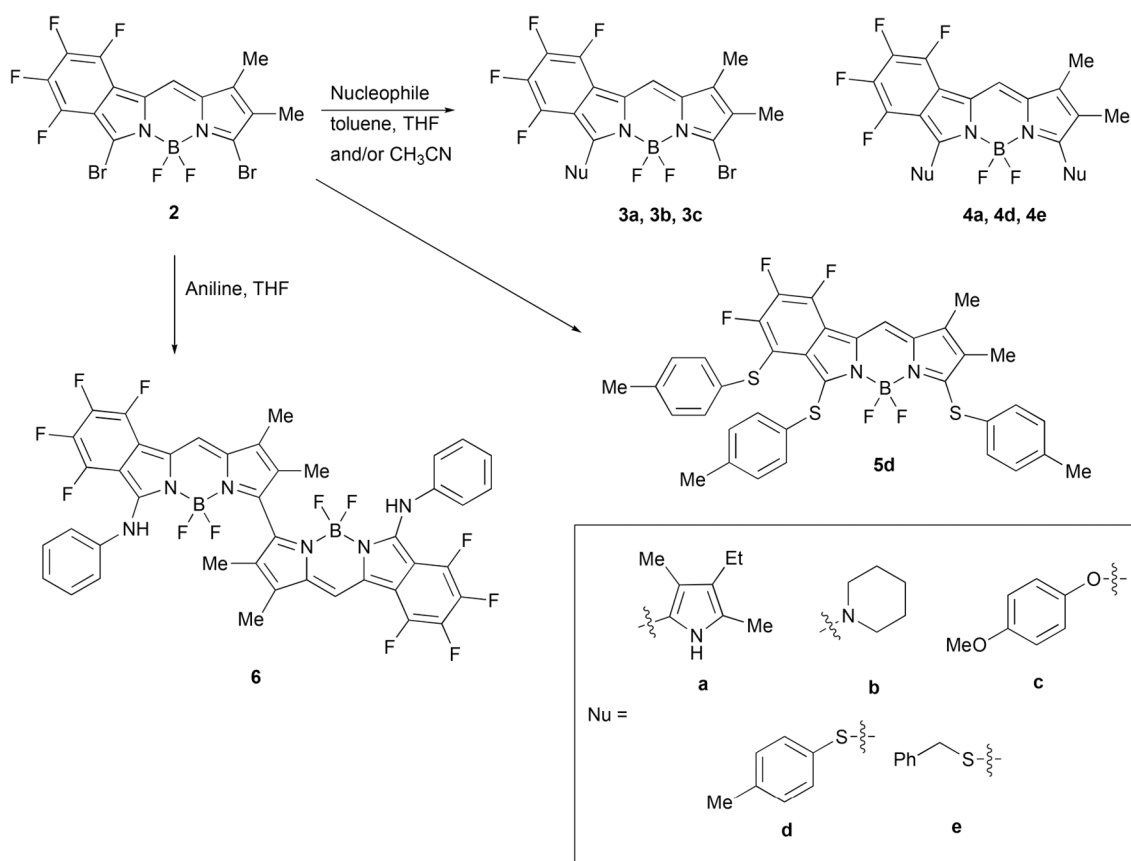
Figure 7. Normalized UV-vis absorption (top) and emission (bottom) spectra in THF for BODIPYs **1** (red), **3c** (orange), **4a** (black), **4d** (light blue), **4e** (green), **5d** (blue), **8** (yellow), and **9** (purple).

**Scheme 1.**

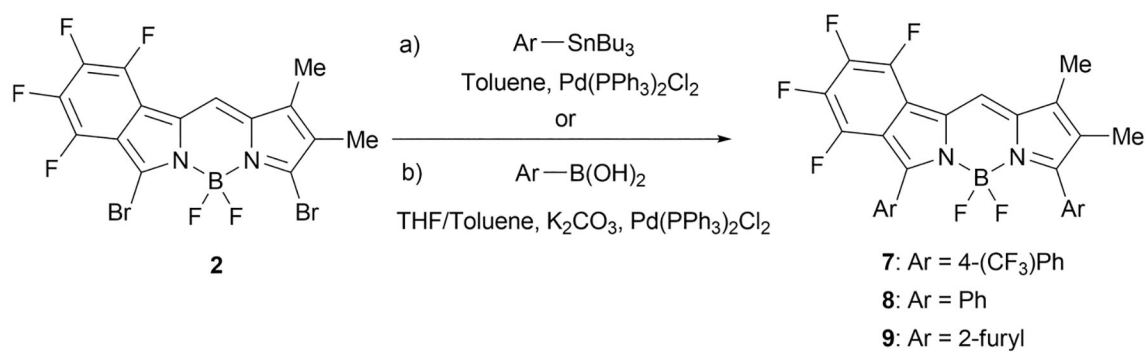
Pathways Reported in the Literature for the Synthesis of Benzo-Fused BODIPYs



Scheme 2.
Synthesis of BODIPYs 1 and 2



Scheme 3.
Nucleophilic Substitution Reactions of BODIPY 2

**Scheme 4.**

Stille (a) and Suzuki (b) Cross-Coupling Reactions of BODIPY 2

Table 1.

Spectral Properties of the BODIPY Dyes in THF at r.t.

compd	Abs λ_{max} (nm)	ϵ (M ⁻¹ cm ⁻¹)	Em λ_{max} (nm)	Stokes shift (nm)	Φ^a
1	560	56 900	568	8	0.98
3a	654	57 700			
3b	562	22 800	581	19	0.92
3c	570	62 800	580	10	0.93
4a	690	47 000			
4d	629	72 600	635	6	0.21
4e	610	64 200	621	11	0.37
5d	646	73 800	654	8	0.27
6	517, 602	20 300, 20 800	606	4	<0.01
7	590	68 200	602	12	0.98
8	589	75 700	615	26	0.99
9	669	71 300	694	25	0.10

^aFluorescence quantum yields were calculated using rhodamine 6G or methylene blue (0.80 and 0.03 in methanol, respectively) as references with a Fluorolog-3 Modular spectrofluorometer.