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

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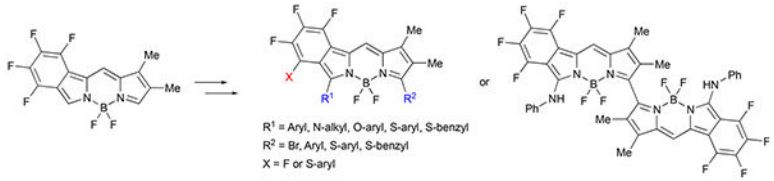
Abstract

A novel route for the synthesis of unsymmetrical benzo-fused BODIPYs is reported using 4,5,6,7-tetrafluoroisoindole 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

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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; ^{1}H, ^{13}C, ^{19}F, and ^{11}B NMR and 2D NMR spectra (PDF)

The authors declare no competing financial interest.

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most exploited routes in BODIPY functionalization relies on the synthesis of a core-halogenated precursor (chlorinated,[6] brominated,[7] or iodinated[8] 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 nucleophiles[9] 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-tetrahydroisoindole,[8d,12] norbornane-derived pyrroles,[13] or 3-halogeno-1-formyliso-indoles[14] 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-tetrafluoroisoindole, 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-tetrafluoroisoindole 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 ^{19}F NMR and near-IR imaging.[16]

RESULTS AND DISCUSSION

Synthesis.

4,5,6,7-Tetrafluoroisoindole has already been reported in the literature[15] as a stable intermediate in the synthesis of fluorinated benzoporphyrins. We decided to investigate the reactivity of this tetrafluoroisoindole in the presence of 2-formyl-3,4-dimethylpyrrole under typical reaction conditions for BODIPY syntheses,[17] using $POCl_3$ as the acid catalyst and $BF_3{\cdot}Et_2O$ 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 C_9N_2B 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 C_3N_2B 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.

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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; how-ever, 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-methylbenze-nethiol, 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 C_9N_2B 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-CH_2-Ph nearest the fluorinated phenyl ring disordered into two conformations. In one of the two molecules, the C_9N_2B BODIPY core is very nearly planar, with a mean deviation 0.014 Å. In the other, the C_9N_2B 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 ^{19}F NMR spectroscopy (see the Supporting Information) and ^{1}H–^{19}F 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.

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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 monosub-stituted 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 ^{1}H 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 ^{1}H 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 reports[19] 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)°; thus the two BODIPY cores are approximately orthogonal, forming a dihedral angle of 86.8°. Each C_9N_2B BODIPY core has the same slightly bowed conformation seen in 1, with a mean deviation of 0.057 Å. The envelope distortion of the central C_3N_2B ring is more pronounced than in 1, with the B atom lying 0.190 Å out of the plane of the other five atoms and the F atoms 0.730 and 1.457 Å out of plane. This greater distortion may be explained by an

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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 $^{1}H–^{13}C$ atoms, while the latter detects long-range $^{1}H–^{13}C$ coupling (up to 4 bond distance coupling). In the HMBC spectrum of 3b, the ^{1}H 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, $^{1}H–^{19}F$ 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. $Pd(PPh_3)_2Cl_2$ was used as the catalyst for both Stille and Suzuki coupling reactions, since $Pd(PPh_3)_4$ 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

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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 S0 → S1 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 crossing[22]. 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···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°)

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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-tetrafluoroisoindole 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 isoindole unit, followed by the bromo group on the pyrrole ring, followed by an α- fluoro group on the isoindole. 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 tetrafluoroisoindole BODIPY **1** showed typical BODIPY spectra with absorption and emission at 560 and 568 nm, respectively, and very high fluorescence quantum yield (Φ = 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

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(Innovative Technology, Inc.). ^{1}H, ^{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-Tetrafluoroisoindole[15] and 3,4-dimethyl-1*H*-pyrrole-2-carbaldehyde[25] 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 MoKα (for **1** and **6**) radiation (λ = 0.71073 Å) or CuKα (for **7**, **4d**, and **4e**) radiation (λ = 1.54184 Å). 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-tetrafluoroisoindole (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 $BF_3{\cdot}Et_2O$ (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.: 275–277 °C. UV-vis (THF): λ_{max}, nm (log ε) 522 (sh, 4.34), 540 (sh, 4.54), 560 (4.76). ^{1}H 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 Hz, J'' = 18.69 Hz), −143.58 (q, 2F, J' = 28.73 Hz), −147.06 (t, 1F, J' = 18.84 Hz), −151.48 (dt, 1F, J' = 3.38 Hz, J'' =18.50 Hz), −159.28 (t, 1F, J' = 18.42 Hz). ^{11}B NMR (128 MHz, $CDCl_3$): δ, ppm 0.28 (t, 1B, J = 28.6 Hz). HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{15}H_9BF_6N_2$ 342.0872; found 342.0873.

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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 $Na_2S_2O_3$ 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 $C_{15}H_7BBr_2F_6N_2$ 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). ^{1}H 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* $[M - HF]^+$ calcd for $C_{23}H_{18}BBrF_5N_3$ 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). ^{1}H 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* $[M + H]^+$ calcd for $C_{20}H_{17}BBrF_6N_3$ 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

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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). ^{1}H 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* $[m + H]^+$ calcd for $C_{22}H_{14}BBrF_6N_2O_2$ 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). ^{1}H 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, CH_3), 2.34 (q, 2H, J = 7.52 Hz, CH_2CH_3), 2.17 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.12 (2s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.88 (s, 3H, CH_3), 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 $C_{31}H_{31}BF_6N_4$ 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). ^{1}H NMR (400 MHz, $CDCl_3$): δ, ppm 7.43 (s, 1H, CH*meso*), 7.37 (d, 2H, J = 8.00 Hz, Ph), 7.3(5 (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, CH_3), 2.33 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 1.67 (s, 3H, CH_3). ^{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 $C_{29}H_{21}BF_6N_2S_2$ 586.1152; found 586.1162.

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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). ^{1}H 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* $[M - F]^+$ calcd for $C_{29}H_{21}BF_6N_2S_2$ 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). ^{1}H 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* $[M + H]^+$ calcd for $C_{36}H_{28}BF_5N_2S_3$ 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). ^{1}H 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* $[M + H]^+$ calcd for $C_{42}H_{27}B_2F_{12}N_6$ 863.2359; found: 863.2341.

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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 $Pd(PPh_3)_2Cl_2$ (8.4 mg, 0.012 mmol) were added. Then, 1.2 mL of K_2CO_3 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 CH_2Cl_2/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). ^{1}H NMR (400 MHz, $CDCl_3$): 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, CH_3), 1.94 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): 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. ^{19}F NMR (376 MHz, $CDCl_3$): δ, ppm δ −62.77 (s, 3F, CF_3), −62.86 (s, 3F, CF_3), −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). ^{11}B NMR (128 MHz, $CDCl_3$): 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 μL of tributylphenylstannane (0.60 mmol) and 8.4 mg of $Pd(PPh_3)_2Cl_2$ (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 CH_2Cl_2/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 $Pd(PPh_3)_2Cl_2$ (0.012 mmol) were added. Then, 1.2 mL of K_2CO_3 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 CH_2Cl_2/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). ^{1}H NMR (500 MHz, CD_2Cl_2): δ, ppm 7.73 (s, 1H, CH*meso*), 7.62 (m, 2H, Ph), 7.52–7.41 (m, 8H, Ph), 2.33 (s, 3H, CH_3), 1.91 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): 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. ^{19}F NMR (376 MHz, $CDCl_3$): 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). ^{11}B NMR (128 MHz, $CDCl_3$): δ, ppm 0.99 (t, 1B, J = 38.4 Hz). HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{27}H_{17}BF_6N_2$ 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 μL of 2-(tributylstannyl)furane (0.60 mmol) and 8.4 mg of $Pd(PPh_3)_2Cl_2$ (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 CH_2Cl_2/hexane 8:2 as eluent, obtaining 9.1 mg of pure product. Yield = 32%. Suzuki coupling: BODIPY (30 mg,

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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 $Pd(PPh_3)_2Cl_2$ (0.012 mmol) were added. Then, 1.2 mL of K_2CO_3 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 CH_2Cl_2/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). ^{1}H NMR (500 MHz, $CDCl_3$): 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, CH_3), 2.24 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): 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. ^{19}F NMR (376 MHz, $CDCl_3$): 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, IF, J' = 19.28, J'' = 4.88 Hz), −159.13 (t, 1F, J = 18.62 Hz). ^{11}B NMR (128 MHz, $CDCl_3$): δ, ppm 1.53 (t, 1B, J = 31.7 Hz). HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{23}H_{13}BF_6N_2O_2$ 474.1053; found 474.1083.

Supplementary Material

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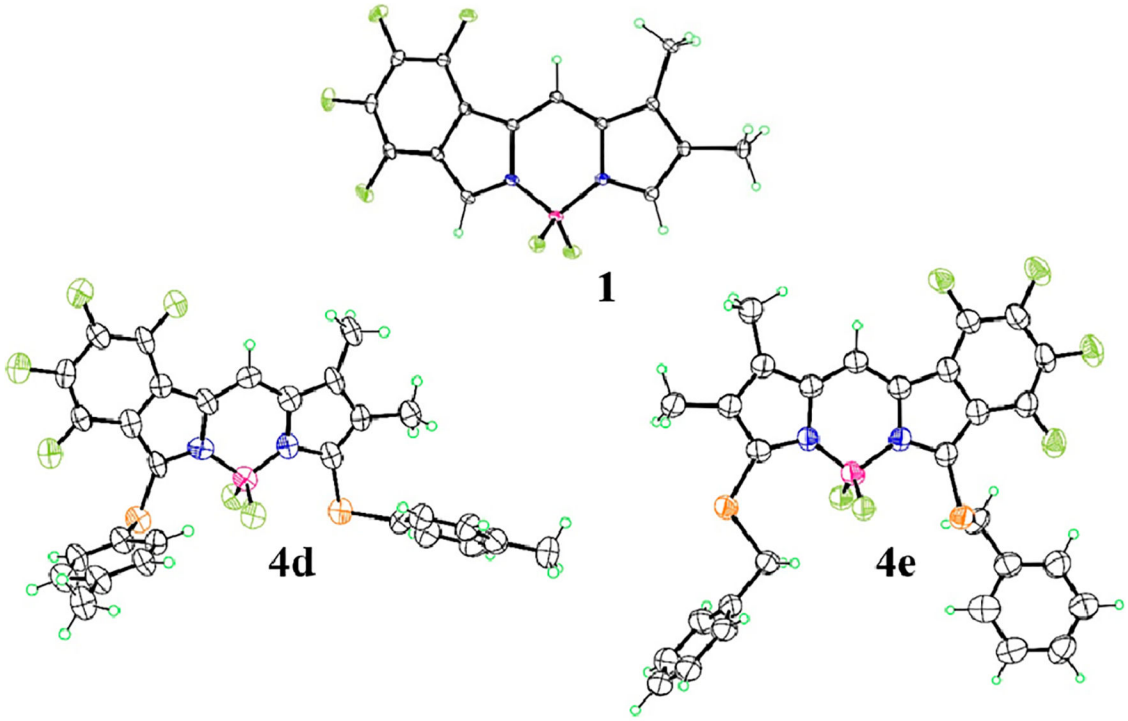

Figure 1.
Molecular structures of BODIPYs **1**, **4d**, and **4e** with 50% ellipsoids.

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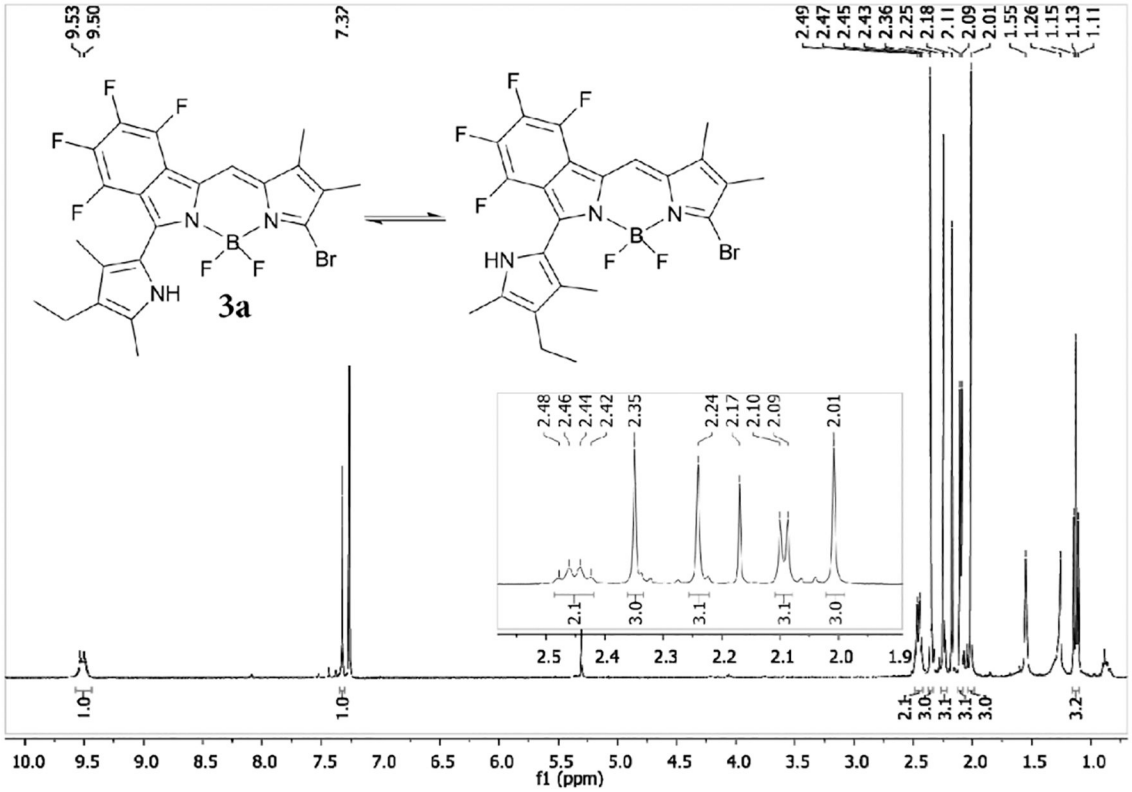

Figure 2.
^{1}H NMR spectrum of compound **3a** in $CDCl_3$.

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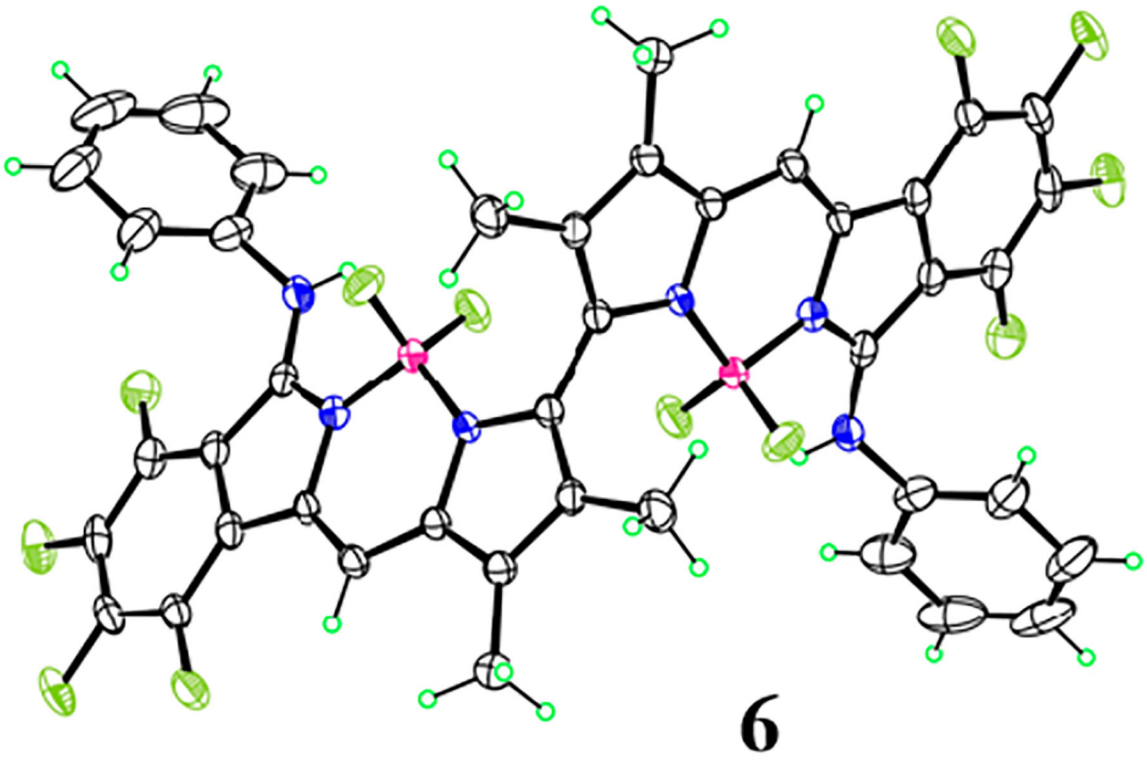

Figure 3.
Molecular structure of dimer **6** with 50% ellipsoids.

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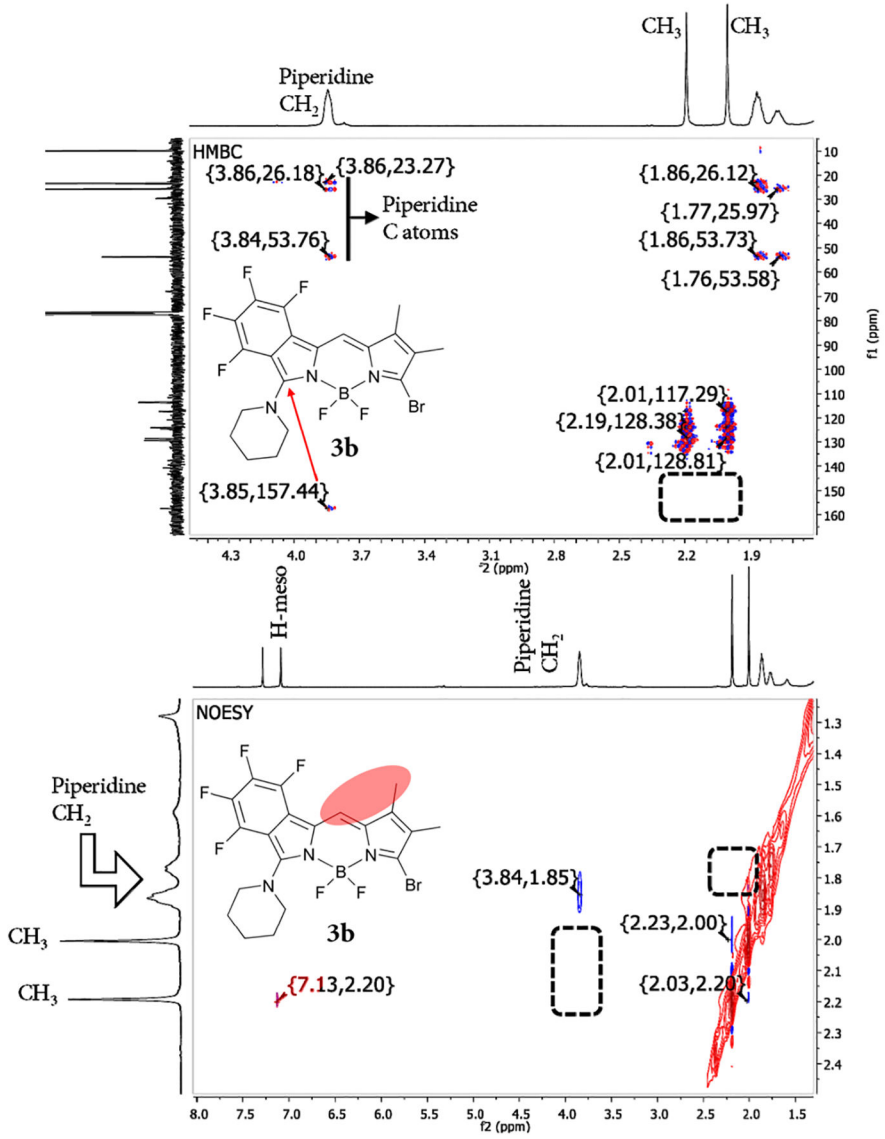

Figure 4.

HMBC and NOESY spectra for BODIPY **3b** in $CDCl_3$.

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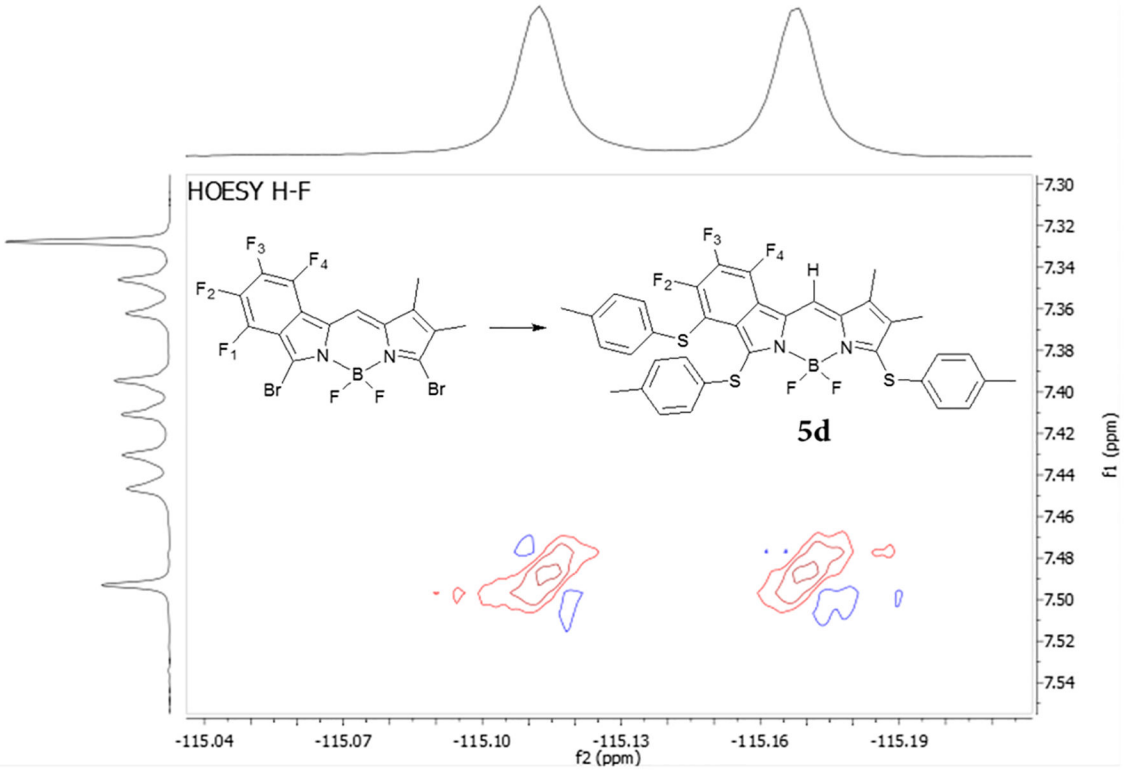

Figure 5.
^{1}H–^{19}F HOESY spectrum for compound **5d** in $CDCl_3$.

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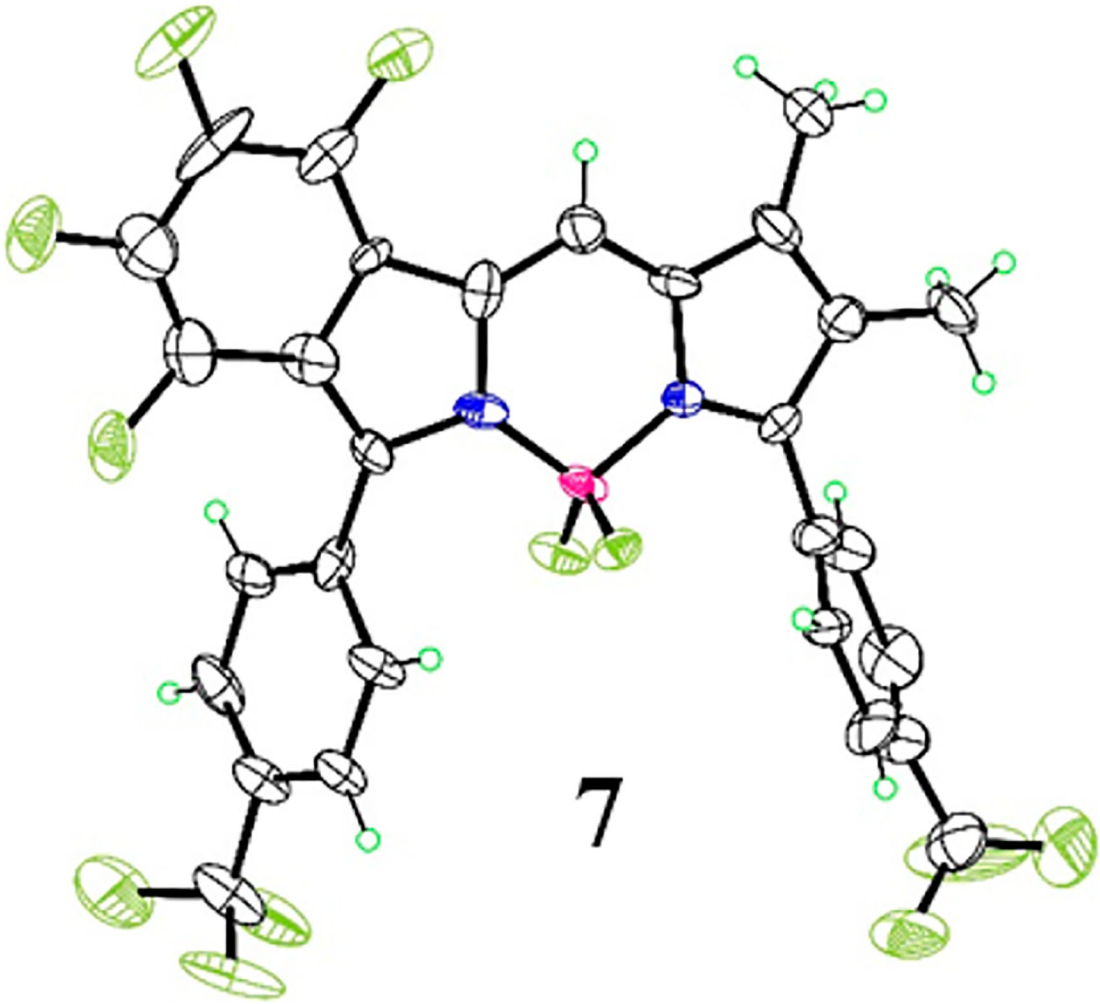

Figure 6.
Molecular structure of BODIPY **7** with 50% ellipsoids. Only one of the three independent molecules is shown.

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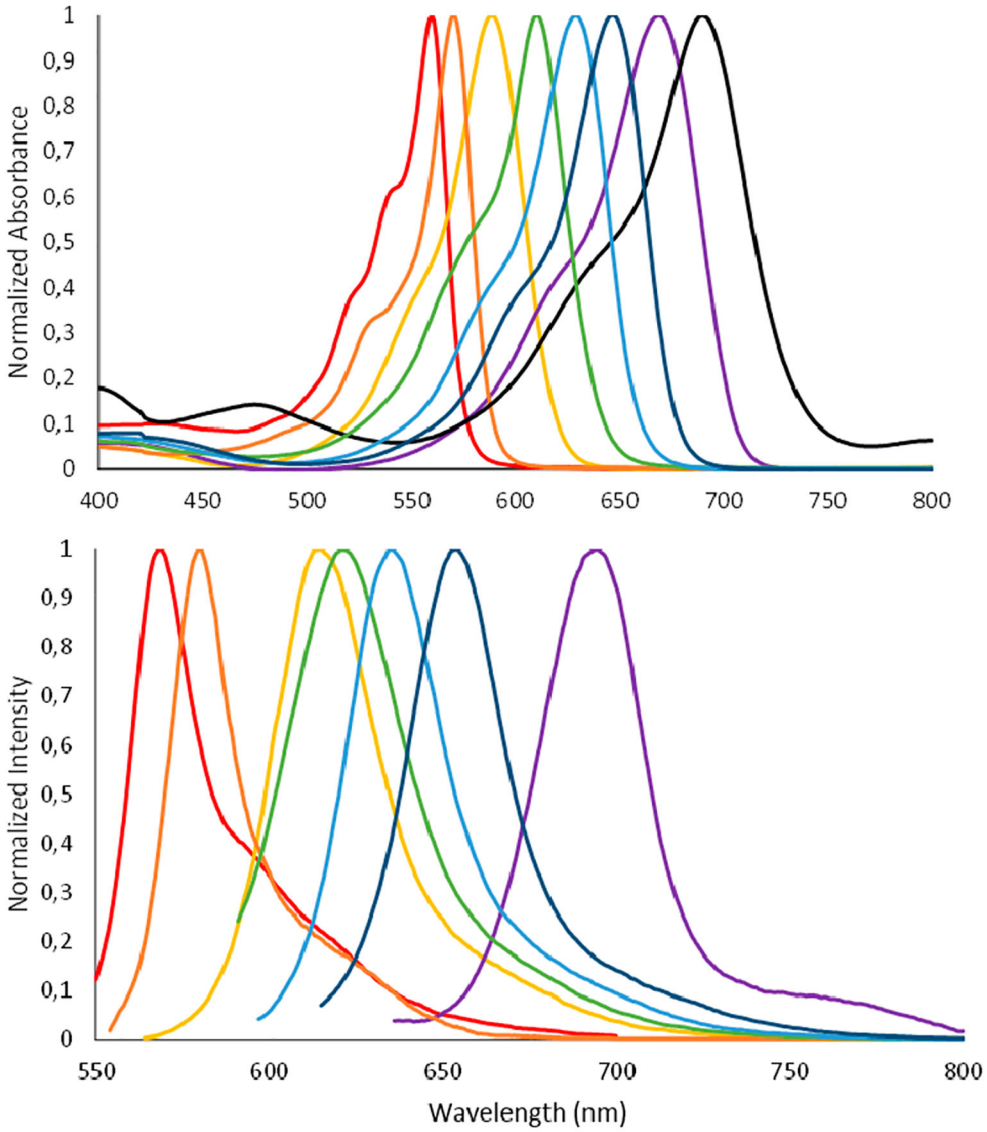

Figure 7.

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).

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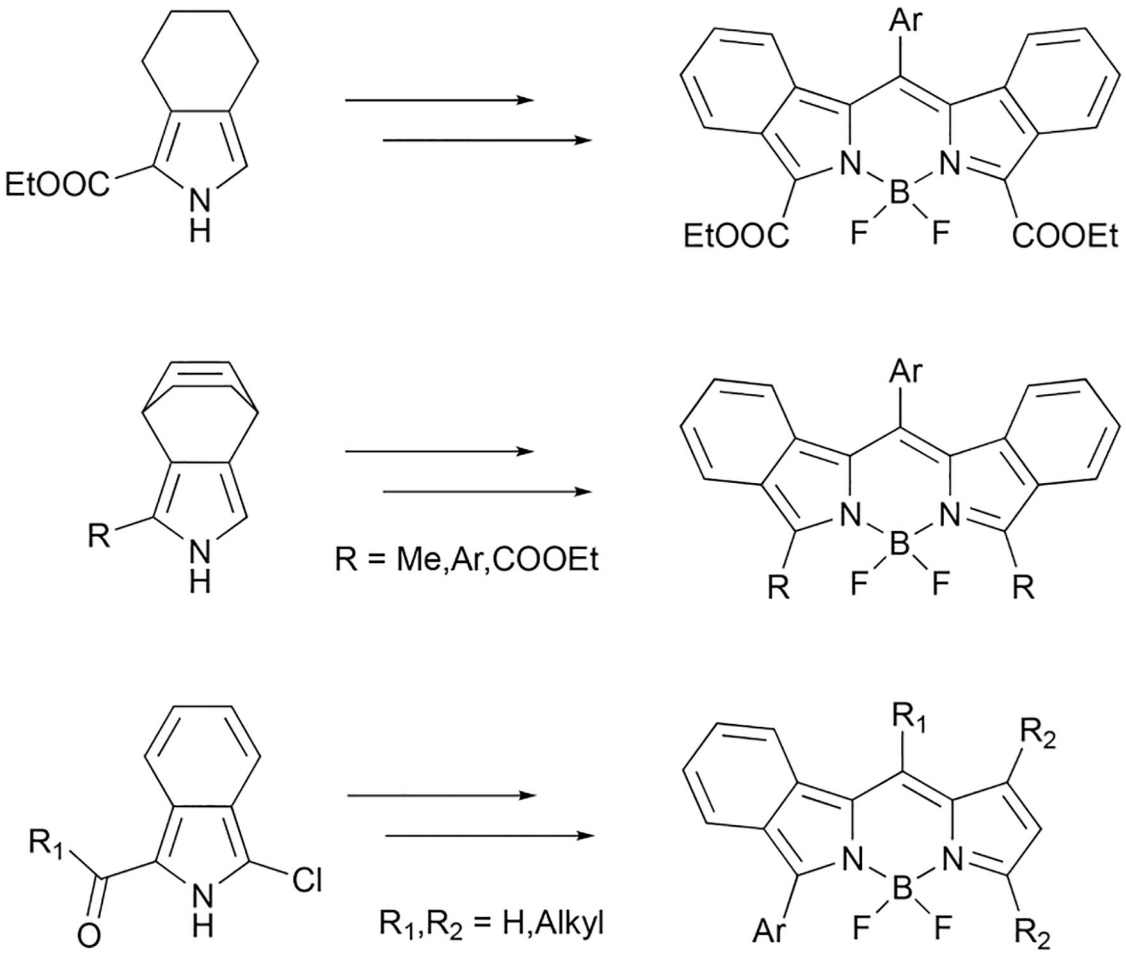
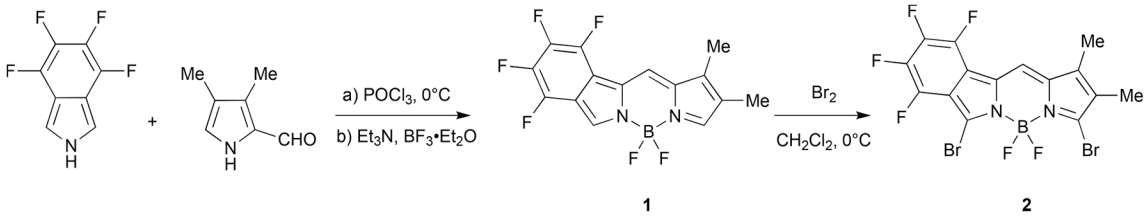


Scheme 1.
Pathways Reported in the Literature for the Synthesis of Benzo-Fused BODIPYs



Scheme 2.
Synthesis of BODIPYs 1 and 2

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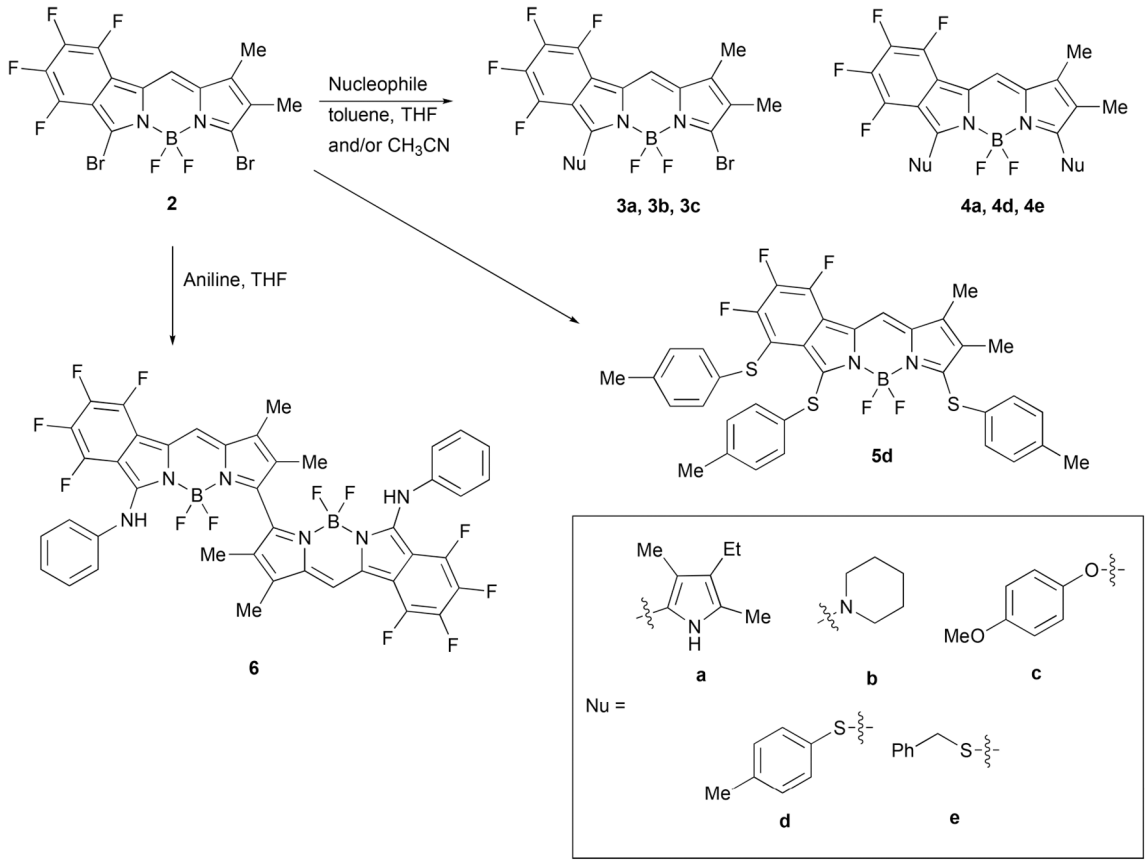

Scheme 3.
Nucleophilic Substitution Reactions of BODIPY 2

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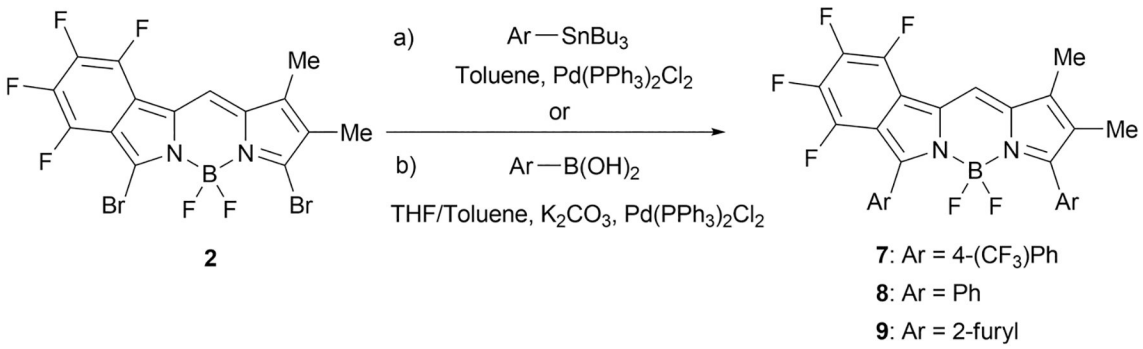

Scheme 4.
Stille (a) and Suzuki (b) Cross-Coupling Reactions of BODIPY 2

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Table 1.

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

cmpd	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

[a]Fluorescence 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.