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Functionalization of 3,5,8-Trichlorinated BODIPY Dyes

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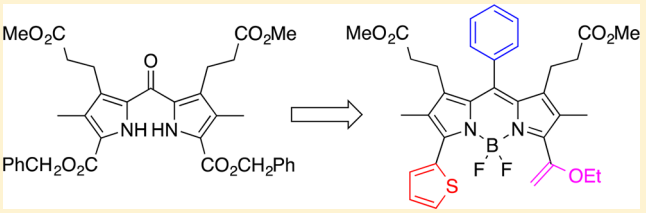
Supporting Information

ABSTRACT: Catalytic hydrogenation of dibenzyl 5-dipyrroketone-2,9-dicarboxylates followed by decarboxylative iodination affords a 2,9-diiododipyrroketone which gives a 2,5,9-trichlorodipyrromethene hydrochloride after nucleophilic addition/elimination, with adventitious chloride to replace the two iodide groups. Treatment with $BF_3{\cdot}Et_2O$ gives a 3,5,8-trichloro-BODIPY that readily undergoes regioselective Stille coupling at the 8-position, or homo/mixed couplings at the 3,8- or 3,5- and 8-positions. Stepwise and controlled replacement of the 3,5- and 8-chlorine atoms using Stille reagents results in formation of a completely unsymmetrical trisubstituted BODIPY. Several examples of unsymmetrical BODIPYs were synthesized and characterized using this methodology. Structure features of new BODIPYs are discussed within the context of 14 new X-ray structures, and photophysical parameters of all new BODIPY compounds are reported and discussed.



INTRODUCTION

4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (known as BODIPY) is a class of very versatile fluorophores that has been widely recognized and exploited in the last several decades. These dyes have found various applications as labeling agents, chemical sensors, photosensitizers, and energy-related cassettes and in luminescent devices.[1−4] BODIPY dyes have advantages compared with other fluorophores, including large molar absorption coefficients and high fluorescence quantum yields, redox active, relatively high thermal and photochemical stability, and easy functionalization that enables the tuning of their properties, such as absorption/emission wavelengths, charge-transfer, and amphiphilicity.[5−7] Due in part to their relatively low molecular weight, BODIPYs and their conjugates usually show good permeability across the membranes of living cells, making them suitable for biological and medical applications.[4−10]

Various methods have been developed for the functionalization of BODIPYs to change their photophysical, hydrophobic, and charge-transfer properties. These methods include, but are not limited to, electrophilic and nucleophilic substitutions, palladium-catalyzed cross-couplings, aromatic ring fusion, and Knoevenagel condensations.[5−7] Among these, aromatic ring fusion[7,11,12] and cross-coupling reactions[13−16] are particularly useful for inducing bathochromic shifts of the BODIPY optical transitions via extension of π-conjugation, while substitution reactions[17−21] are often used to modify the molecular amphiphilicity upon introduction of heteroatom-based groups, and for bioconjugations. Halogenated BODIPYs are particularly versatile substrates for functionalization purposes via both cross-coupling and nucleophilic substitution reactions, and all halogens (fluoride, chloride, bromide, and iodide) have been introduced into the pyrrolic positions of BODIPY (or a dipyrromethane or pyrrole precursor), mainly using electrophilic substitution.[5,6,22−26] In particular, functionalization of the BODIPY core at the 3,5-positions significantly affects the spectroscopic and photophysical properties, and this strategy has been exploited for the synthesis of a variety of functionalized BODIPYs, from 3,5-dichloro- or 3,5-diiodo-BODIPY precursors.[13,14,17−21] On the other hand, a very useful method for facile transformation of dipyrroketones into 5-chlorodipyrromethene salts using phosgene was developed by Fischer and Orth[27] and has since been exploited by others[28,29] and ourselves.[30] The resulting 8-chloro-BODIPYs are reactive toward palladium-catalyzed cross-coupling reactions and to nucleophilic aromatic substitutions using N-, O-, and S-based nucleophiles. Palladium-catalyzed Suzuki, Stille, Sonogashira, and Heck cross-coupling reactions have all been performed on 3,5-chloro-BODIPY, while Suzuki, Stille, and Sonogashira reactions have been achieved at the 8-position. Among these, the milder Stille reaction conditions, using $Pd(PPh_3)_4$ and a organotin reagent in toluene, in the absence of a base, gave 8-aryl, -alkyl, and -ethynyl-BODIPYs in yields >93%,[30] making it a highly efficient methodology for the functionalization of chloro-BODIPYs. Herein we report the synthesis of a symmetrical 3,5,8-trichloro-BODIPY (**5**) and describe both its global and regioselective functionalization using Stille coupling reactions to afford both symmetric and unsymmetric BODIPY dyes with extended π-conjugated systems. The spectroscopic properties of the 19 new BODIPY derivatives synthesized and structurally characterized, including 14 X-ray structures, are compared and discussed.

RESULTS AND DISCUSSION

Syntheses. 3,5,8-Trichloro-BODIPY **5**, bearing two methyl propanoate groups that could subsequently be used for bioconjugation, was prepared as shown in Scheme 1.

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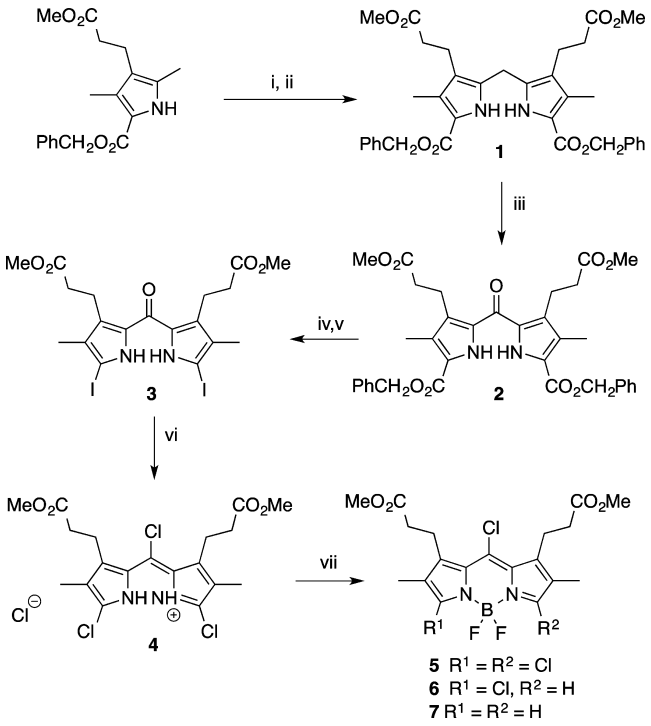
Scheme 1. Synthesis of Halogenated BODIPYs by Phosgenation of Dipyrroketone 2[a]



[a]Reaction conditions: (i) Br_2, Et_2O; (ii) MeOH, Δ (70% yield, two steps); (iii) $Pb(OAc)_4/PbO_2$, (60%); (iv) Pd/C, H_2, THF, (92%); (v) I_2, $NaHCO_3$, $MeOH/H_2O$, (75%); (vi) $COCl_2$ (toluene soln); (vii) $BF_3{\cdot}Et_2O$, DIEA, (**5**, 55%), (**6**, 11%), (**7**, 5%).

Symmetrical dipyrromethane **1** was obtained by treatment of benzyl 4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate on a 10−20 g scale with 1 equiv of bromine in diethyl ether, followed by heating in methanol. It was then oxidized with $Pb(OAc)_4/PbO_2$ in acetic acid[31] to give the corresponding dipyrrylketone **2** in 60% yield. Unlike our previously reported tetra- and hexaalkyldipyrrylketones,[30] the electron-deficient dipyrrylketone **2** could not be converted into the corresponding 5-chlorodipyrromethene hydrochloride by reaction with phosgene. Therefore, dipyrrylketone **2** was subjected instead to palladium-catalyzed debenzylation in a hydrogen atmosphere, followed by decarboxylative iodination to provide the 3,5-diiododipyrrylketone **3** in 69% overall yield.[32] Upon treatment with excess phosgene, the 3,5-diiododipyrrylketone **3** was converted into the fully conjugated *meso*-chlorodipyrromethene hydrochloride **4** which was not isolated but immediately complexed with $BF_3{\cdot}Et_2O$ in situ under basic conditions, to afford BODIPY **5** as the major product in 55% yield from **3**. BODIPYs **6** and **7** were also isolated as minor byproducts, obtained in 11% and 5% yields from **3**, respectively, after chromatographic separation. The trans-halogenation of 3,5-diiododipyrrylketone **3** to give **4** is probably a result of nucleophilic addition/elimination by chloride during the process, as nucleophilic substitutions at the 3,5- and 8-positions of the BODIPY have been shown to occur in the presence of a variety of nucleophiles.[17,28,30] On the other hand, byproducts **6** and **7** likely resulted from dehalogenation of the 3- and 3,5-positions, respectively, under the reaction conditions. The structures of BODIPYs **5** and **7** were unequivocally identified by their X-ray structures, shown in Figure 1.

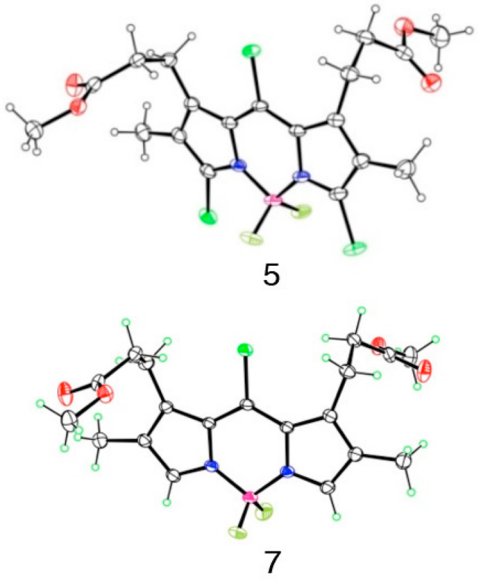


Figure 1. X-ray structures of BODIPYs **5** and **7**, with 50% ellipsoids.

Both molecules have essentially C_2 symmetry, with **7** lying on a crystallographic 2-fold axis, and **5** having nearly the same conformation. The torsion angle about the CH_2-CH_2 bonds of the methyl propanoate substituents is −66.1° in **7**, while in **5**, the two torsion angles differ by 21.2°, but their mean value, −66.2°, closely matches that in **7**. The central C_3N_2B ring is slightly more twisted in **5**, with N atoms lying ±0.11 Å out of the C_3B plane, compared to ±0.05 Å in **7**. The N_2B and BF_2 planes form a dihedral angle of 89.2° in **5** and 89.9° in **7**.

Because, as mentioned above, the milder palladium-catalyzed Stille cross-coupling reaction[33,34] gave the highest yields of functionalized BODIPYs,[30] in this study we investigated Stille couplings, using four different stannane reagents, in increasing order of reactivity: tributylphenyltin, trimethyl-[(tributylstannyl)ethynyl]silane, tributyl(1-ethoxyvinyl)tin, and 2-(tributylstannyl)thiophene, to produce 8-mono-, 3,8-di-, and 3,5,8-trisubstituted BODIPYs, as shown in Schemes 2−5.

Anticipating regioselectivity in the reactions of the 3,5,8-trichloro-BODIPY **5**, we first addressed the global Stille coupling to demonstrate that functionalization at the 3,5,8-positions of BODIPY **5** can be performed in one step. A typical procedure involved refluxing a toluene mixture of 3,5,8-trichloro-BODIPY **5** and excess organotin reagent (4.5 equiv), in the presence of $Pd(PPh_3)_4$, for 5−24 h. The global Stille reactions proceeded in moderate to good yields, producing the corresponding 3,5,8-trisubstituted BODIPYs **8**−**10** in 42−83% yields (Scheme 2). The least reactive tin reagent used, the tributylphenyltin, required the longest time refluxing in toluene for 24 h, and gave the lowest yield of product. Products **8**−**10** showed red-shifted absorptions compared with the starting material 3,5,8-trichloro-BODIPY **5**, which absorbs at λ_{max} 538 nm; BODIPY **10** showed the most red-shifted absorption (λ_{max} 648 nm), followed by BODIPY **8** (λ_{max} 594 nm) and **9** (λ_{max} 546 nm) (see Table 1). This is a result of a nearly perpendicular orientation of the phenyl groups on the trisubstituted BODIPYs **9**, particularly the 8-phenyl, which prevents orbital interactions, whereas the linear trimethylsilylethynyl group lies in the plane of the BODIPY core, efficiently extending its π-conjugation (see Figure 2). In addition, in the case of the electron-rich thienyl group, the

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Scheme 2. Global Stille Coupling Reactions of 3,5,8-Trichloro-BODIPY 5 To Give BODIPYs 8−10

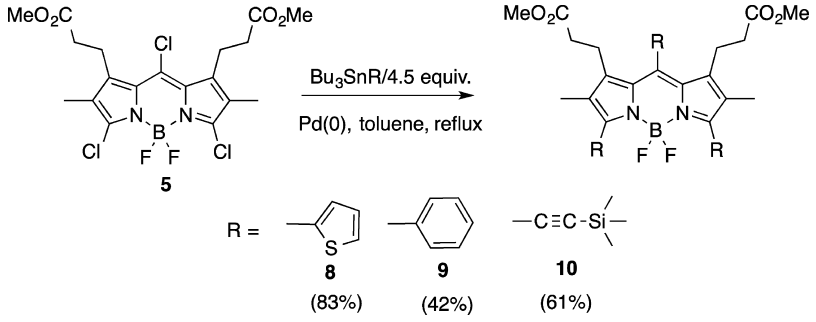

Table 1. Spectroscopic Properties of BODIPYs in Dichloromethane Solution at Room Temperature[a]

BODIPY	abs λ_{max} (nm)	emission λ_{max} (nm)	Stokes shift (cm^{-1})	Φ_f	ε
5	538	550	406	0.58	112200
6	534	549	512	0.45	60300
7	528	547	658	0.30	38000
8	594	649	1427	0.10	43700
9	546	576	954	0.43	29500
10	648	660	280	0.01	88000
11	548	559	359	0.24	77600
12	534	544	344	0.86	69200
13	584	597	372	0.03	67600
14	560	591	936	0.27	17800
15	609	616	186	0.22	89100
16	574	629	1524	0.45	38900
17	594	600	168	0.34	47900
18	636	702	1478	0.08	29500
19	601	634	866	0.05	38900
20	616	625	234	0.21	46800
21	645	679	776	0.05	29500
22	555	587	982	0.53	33300
23	559	597	1138	0.67	13000

[a]Fluorescence quantum yields (Φ_f) were calculated as follows: rhodamine 6G was used as the standard for compounds **5**−**9** and for compounds **11** and **12**; rhodamine B was used as the standard for compounds **13**, **14**, **16**, **17**, **22**, and **23**; methylene blue was used as the standard for compounds **10**, **15**, **18**−**21**.

thiophene tends to decrease the HOMO−LUMO gap, therefore increasing the absorbance wavelength relative to the phenyl analogue (vide infra).[35] Figure 2 shows the X-ray structures of BODIPYs **8** and **10**.

Unlike the structures of **5** and **7** (Figure 1), both **8** and **10** have their propanoate substituents extended, with torsion angles about their CH_2−CH_2 bonds 170.4° and 179.7° for **8**, 157.7° and 179.7° for **10**. All three of the thiophenes in **8** exhibit disorder by 2-fold rotation about the C−C bonds joining them to the rest of the molecule, with only the major conformers shown in Figure 2. The central C_3N_2B ring in both molecules has a slight boat distortion, with B and the C opposite it lying, respectively, 0.18 and 0.04 Å on the same side of the plane formed by the other four atoms for **8**, 0.19 and 0.04 Å for **10**. The N_2B and BF_2 planes form a dihedral angle of 89.8° in both **8** and **10**. The 12-atom BODIPY core of **8** makes a dihedral angle of 89.6° with the 8-thiophene plane and 68.1° and 39.9° with the other two.

Regioselective coupling reactions were performed on the 3,5,8-trichloro-BODIPY **5** using the same organotin reagents as

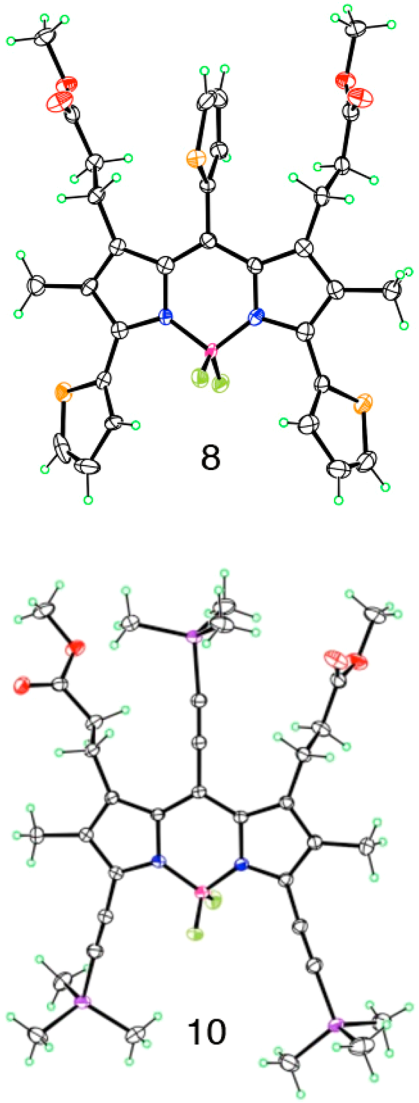

Figure 2. X-ray structures of BODIPYs **8** and **10**, with 50% ellipsoids.

described above for the synthesis of **8**−**10**, but in a 1:1 ratio to the BODIPY rather than in excess. We anticipated mono-substitution at the most electrophilic 8-position of the BODIPY.[23] The coupling reaction with 2-(tributylstannyl)-thiophene in refluxing toluene for 5 h gave the monothienyl-BODIPY **11** as the sole product, in 72% yield (Scheme 3). Under similar conditions, BODIPY **13** was also obtained in a reasonable yield (65%) along with trace amount of the corresponding 3,8-disubstituted product. Using the least

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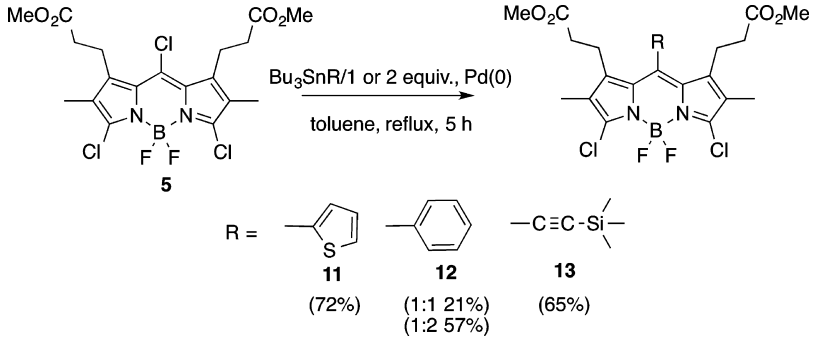
Scheme 3. Regioselective Stille Coupling Reactions of BODIPY 5 at the 8-Position To Give BODIPYs 11−13



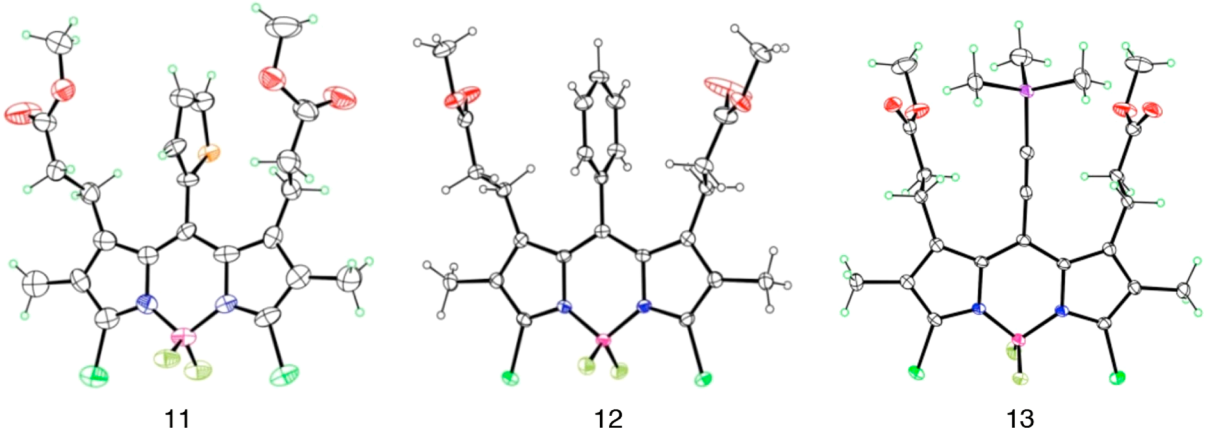


Figure 3. X-ray structures of BODIPYs **11**−**13**, with 50% ellipsoids.

reactive tin reagent, BODIPY **12** was obtained in only 21% yield; however, the yield of **12** was increased to 57% when 2 equiv (rather than 1) of organotin were used, and no disubstitution product was detected. The 1,7-propanoate groups likely lead to an increased dihedral angle between the BODIPY core and the phenyl group, resulting in blue-shifted absorption and emission bands. The X-ray structures of BODIPYS **11**−**13** are shown in Figure 3.

Both **11** and **12** have two independent molecules in the crystal (only one shown in Figure 3), and the thiophene in both molecules of **11** is disordered. The propanoate substituents of all three molecules are extended, with torsion angle magnitudes in the range 175.9−179.8° for **11**, 170.0−176.6° for **12**, and 178.5° and 179.8° for **13**. In the central C_3N_2B ring of all three molecules, only the B atom is distinctly out of plane, by a mean distance of 0.10 Å for **11**, 0.14 Å for **12**, and 0.12 Å for **13**. In all three molecules, the BN_2 and BF_2 planes form dihedral angles of 89.7° to 89.8°. The 12-atom BODIPY core of **11** forms dihedral angles of 89.3° and 90.0° with the thiophene planes in the two independent molecules. The BODIPY core of **12** forms dihedral angles with the phenyl rings of 86.5° and 87.8° for the two independent molecules.

For the three new 8-substituted BODIPYs **11**−**13**, different functional groups were introduced at the 3,5-positions by Stille coupling reactions using 2.4 equiv of selected organotin reagents, as shown in Scheme 4. Specifically, the 8-thienyl-BODIPY **11** was functionalized at the 3,5-positions with phenyl and trimethylsilylethynyl groups to provide BODIPYs **14** and **15**, the 8-phenyl-BODIPY **12** was functionalized with thienyl and trimethylsilylethynyl groups to give BODIPYs **16** and **17**, and BODIPY **13** was functionalized with phenyl and thienyl groups to produce BODIPYs **18** and **19**. These double Stille reactions proceeded in good yields (51−78%), the highest obtained using the most reactive 2-(tributylstannyl)thiophene reagent and the lowest using the least nucleophilic tributylphenyltin. Five of these differentially substituted BODIPY compounds (specifically **15**−**19**) were also characterized by single crystal X-ray crystallography, shown in Figure 4.

Of the thiophene-containing molecules, **15** has its thiophene ordered, **18** has one ordered and the other disordered, and **16** has both disordered. BODIPY **19** has disorder both in the phenyl and COOMe conformations. Only the major conformers are shown in Figure 4. All five molecules have their methyl propanoate substituents extended, with torsion angle magnitudes about the CH_2−CH_2 bonds in the range 168.9−179.3°. There is some variation in the conformations of the central C_3N_2B rings. BODIPY **16** has the B atom 0.19 Å out of the best plane of the other five atoms, while in the two independent molecules of **19**, the deviations are 0.19 and 0.35 Å. BODIPYs **15** and **17** have the slight boat distortion, with deviations 0.12 (for B) and 0.05 Å (for C) in **15**, and 0.22 and 0.04 Å, respectively, for **17**. The central C_3N_2B ring of **18** differs from the others, having a twist conformation with the B atom 0.07 Å and a N atom 0.13 Å on opposite sides of the plane of the other four atoms. The BN_2/BF_2 dihedral angles in **15**, **16**, **17**, and **19** are all 89.6−90.0°, while that of **18** is slightly smaller, 88.9°. In **15**, the BODIPY core forms a dihedral angle of 77.0° with the thiophene plane. In **16** and **17**, respectively, the BODIPY core forms a dihedral angle of 87.6° and 80.0° with the phenyl plane. In **18**, the BODIPY core forms dihedral angles of 58.1° and 44.9° with the two thiophene planes. In **19**,

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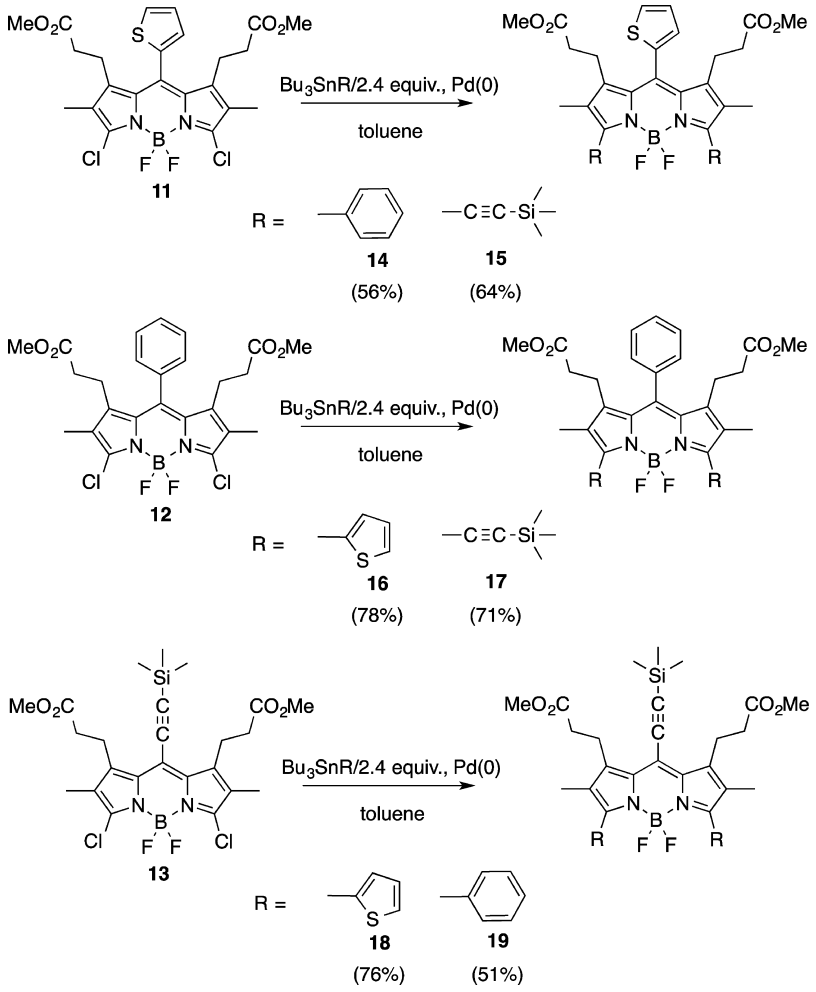
Scheme 4. Double Stille Coupling Reactions of BODIPYs 11−13 To Give Differentially Functionalized BODIPYs 14−19



the BODIPY core forms dihedral angles in the range 60.5−74.9° (mean value 70.5°) with the phenyl planes in the two independent molecules.

The synthesis of asymmetric BODIPYs was also accomplished using first 2 equiv of organotin reagent, followed by a second organotin; this strategy produces asymmetrical BODIPYs on account of the higher reactivity at the 8-position and the molecular symmetry about the 3,5-positions. The reaction of BODIPY **5** with 2 equiv of trimethyl-[(tributylstannyl)ethynyl]silane produced the 3,8-disubstituted BODIPY **20** as the major product in 53% yield, along with a trace amount of the trisubstituted-BODIPY **10** (Scheme 5). BODIPY **20** was then treated with 2-(tributylstannyl)thiophene to yield BODIPY **21** in 63% yield. The structure of BODIPYs **20** and **21** were confirmed by their X-ray crystallography, shown in Figure 5.

As with all previous structures, except for **5** and **7**, the methyl propanoate substituents of **20** and **21** are extended, with torsion angle magnitudes about the CH_2−CH_2 bonds in the range 175.0° to 179.0°. The conformation of the central rings are fairly planar, similar to those of **11**−**13**, with the B atom 0.11 Å out of the C_3N_2 plane for **20** and 0.15 Å for **21**. The BN_2/BF_2 dihedral angle is typical of these compounds, 89.6° for **20** and 89.5° for **21**. In **21**, the BODIPY core forms a dihedral angle of 43.1° with the thiophene plane.

Attempts to introduce three different groups at the 3-, 5-, and 8-positions of the BODIPY core were also investigated by consecutive Stille reactions using different organotin reagents, to produce a completely asymmetric BODIPY. The phenyl group was first regioselectively introduced at the most reactive 8-position to give the 8-phenyl BODIPY **12**. Next, thiophene was introduced at the 3-position of BODIPY **12** using 1 equiv of 2-(tributylstannyl)thiophene, resulting in the isolation of asymmetric BODIPY **22** in 43% yield along with a trace amount of BODIPY **16** (Scheme 6). Finally, an ethoxyvinyl group was introduced into the 5-position of BODIPY **22** by reaction with tributyl(1-ethoxyvinyl)tin to provide the fully asymmetric BODIPY **23** in 51% yield.

Spectroscopic Properties. The spectroscopic properties of all BODIPYs synthesized, including UV/visible absorption and steady-state fluorescence emission, were studied in dichloromethane solution, and the results are summarized in Table 1. Furthermore, as an example, Figure 6 shows the normalized absorption and fluorescence spectra for BODIPYs **5**, **9**, **13**, and **15** (others are presented in Supporting Information). All BODIPYs show typical absorption and emission spectra for this type of compound, with strong absorption bands corresponding to the S_0−S_1 transition (log ε = 4.1−5.1), a shoulder at shorter wavelength due to the 0−1 vibrational band of the same transition, and Stokes-shifted emission bands. The Stokes shifts vary considerably for this group of BODIPYs, from 186 to 1524 cm^{-1}; BODIPYs **8**, **16**, and **18**, bearing 3,5-thienyl groups, have the largest Stokes shifts (1427−1524 cm^{-1}) followed by BODIPYs **21**−**23**, bearing only

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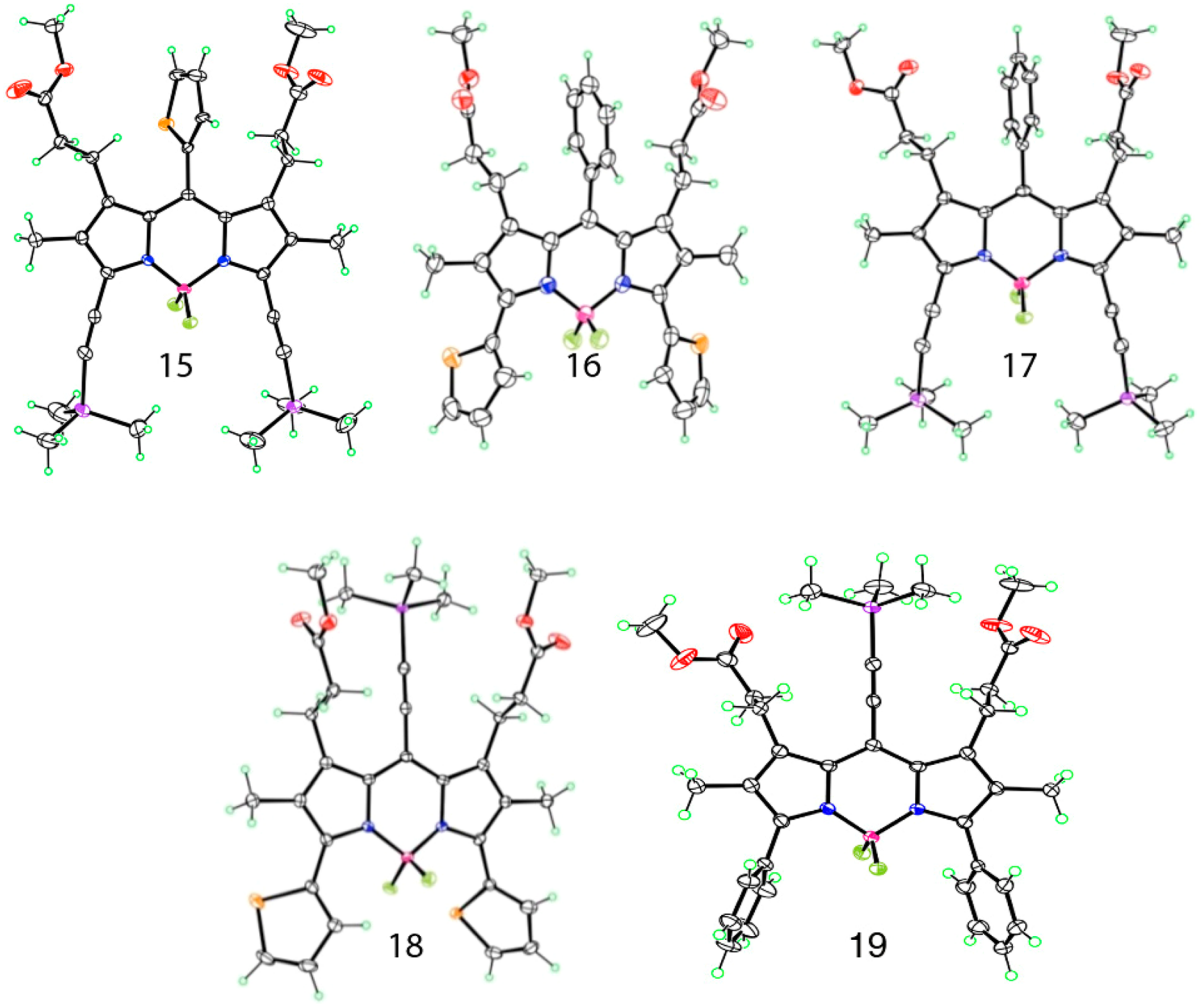
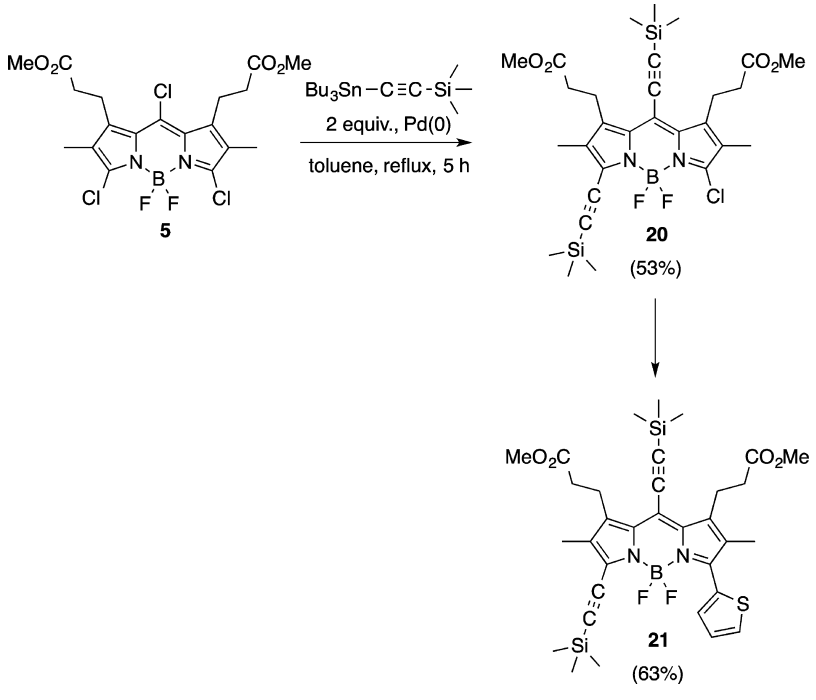


Figure 4. X-ray structures of BODIPYs **15**–**19**, with 50% ellipsoids.

Scheme 5. Consecutive Stille Coupling Reactions of BODIPY 5 To Give Differentially Functionalized BODIPYs 20 and 21



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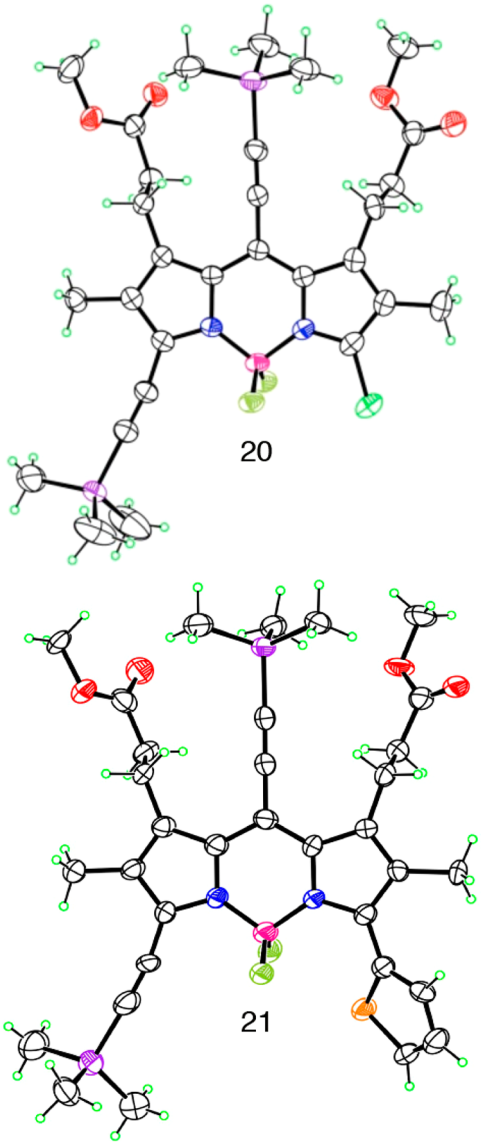


Figure 5. X-ray structures of BODIPYs **20** and **21**, with 50% ellipsoids.

one thienyl group at the 5-position. In agreement with these values, Stokes shifts of ca. 1500 cm^{-1} have been reported for 3,5-thienyl-substituted BODIPYs, and larger values were achieved upon boron substitution with alkynylaryl groups via intramolecular energy transfer.[11,36] It has also been shown that 8-thienyl-substituted BODIPYs normally show small Stokes shifts (ca. 350 cm^{-1}) typical of BODIPY derivatives,[2] and that 2,6-dithienyl-BODIPYs can show even larger Stokes shifts, presumably due to increased geometry relaxation, i.e., the geometry difference between the S_0 and the S_1 states, upon photoexcitation.[37,38]

The introduction of chlorines at the 3,5-positions slightly red-shifts the absorption and emission bands and increases the molar extinction coefficients and fluorescence quantum yields, as previously observed, due to the decrease in nonradiative deactivation processes.[24,39,40] As expected, the global Stille coupling on BODIPY **5** caused pronounced red-shifts in the absorption and emission bands, particularly for the 3,5,8-trimethylsilylethynyl-BODIPY **10** which showed a 110 nm bathochromic shift compared with **5** due to larger electronic coupling with the BODIPY chromophore, therefore extending the π-conjugation system and decreasing the HOMO−LUMO gap.[41] On the other hand, the aromatic substituents on **8** and **9**, particularly the 8-aryl groups, orient themselves nearly perpendicular to the BODIPY core to minimize steric interactions, inducing smaller red-shifts. In addition, the electron-releasing effect of the thiophene group tends to decrease the HOMO−LUMO gap,[35] inducing larger red-shifts compared with the phenyl-substituted analogues (see below). Similarly, the 3,5,8-trisubstituted BODIPYs **14**−**19**, **21**, and **23** obtained by mixed Stille coupling reactions all show bathochromic shifts (21−107 nm) compared with BODIPY **5**; the greatest red-shifts were observed for the trimethylsilylethynyl-containing BODIPYs **15**, **17**−**19**, and **21**, and the smallest for the phenyl-containing BODIPYs **14** and **16**.

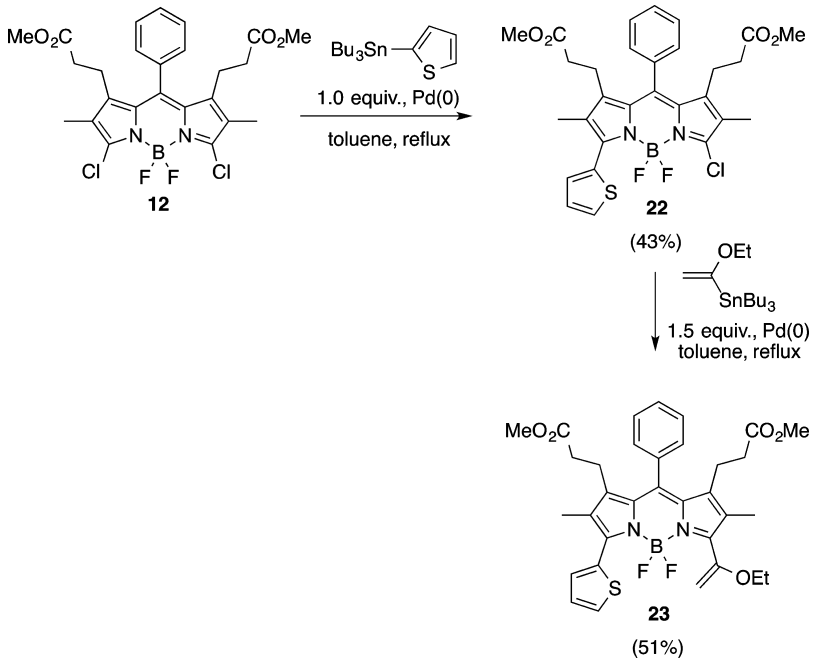
Regioselective coupling at only the 8-position caused a slight blue-shift in the case of 8-phenyl-BODIPY **12**, and a slight red-shift in the case of 8-thienyl-BODIPY **11**, as previously observed,[30] indicating that the most pronounced effect on the absorption and emission wavelengths of the BODIPYs arise from 3,5-aryl (rather than 8-) substitution. The large dihedral angle (ca. 87° from crystal structure) between the 8-phenyl group and the BODIPY core in **12** as a result of 1,7-disubstitution induces blue-shifted absorption and emission spectra. On the other hand, an 8-trimethylsilylethynyl group, as found in BODIPY **10**, effectively extends the π-conjugation, inducing a 46 nm bathochromic shift. In agreement with these results, it has been previously observed that an 8-(2-phenylethynyl) group induces ca. 40 nm red-shifts although small Stokes shifts.[41,42] Although the 8-thienyl group forms an even larger dihedral angle with the BODIPY core in **11** (ca. 89° from crystal structure), the electron-releasing effect of the thienyl group decreases the HOMO−LUMO gap, therefore increasing the absorbance and emission wavelengths relative to BODIPY **12**.[35]

The fluorescence quantum yields determined in dichloromethane were significantly higher for the phenyl-substituted BODIPYs compared with the thienyl- and trimethylsilylethynyl-substituted BODIPY analogues. For example, the 8-phenyl-BODIPY **12** showed the highest quantum yield (Φ_f = 0.86) of all BODIPYs in this series, whereas the 3,5,8-trimethylsilylethynyl-BODIPYs **10** showed the lowest (Φ_f = 0.01). These results are in agreement with our previous studies[30,35] and reflect the greater freedom of rotation of the smaller thienyl group in comparison with phenyl, even in the presence of the 1,7-propanoate substituents, increasing the amount of energy lost to nonradiative decay to the ground state. The aryl-ring rotation has been demonstrated to be critical in determining the excited-state dynamics of BODIPYs, and in particular their fluorescence quantum yields.[43,44] On the other hand, the trimethylsilylethynyl groups increase the nonradiative molecular relaxation which decreases the fluorescence quantum yields. We have previously shown that upon deprotection of the trimethylsilyl group, the resulting 8-ethynyl-BODIPY shows increased fluorescence quantum yield.[30]

CONCLUSIONS

A very useful method for transformation of dipyrroketones into 5-chlorodipyrromethene hydrochlorides by using phosgene is inhibited by the presence of conjugated 2,9-ester substituents. However, catalytic debenzylation followed by decarboxylative iodination affords a 2,9-diiodopyrroketone which does undergo the phosgene reaction to provide 2,5,9-trichlordipyrromethene hydrochlorides after nucleophilic addition/elimination with

Scheme 6. Stille Coupling Reactions of BODIPY 12 To Give 23 Featuring Three Different Groups on the 3,5,8-Positions



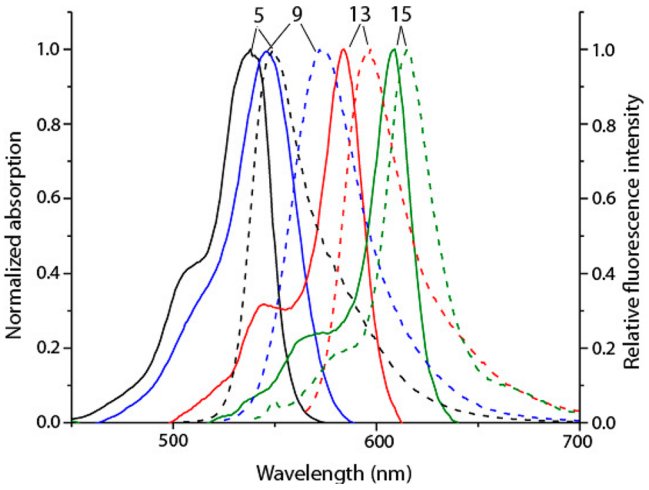


Figure 6. Normalized UV/visible absorption (solid line) and fluorescence emission (dashed line) spectra of selected BODIPYs **5**, **9**, **13**, and **15** (left to right) in dichloromethane solution.

chloride to replace the two iodo groups. Treatment of these 3,5,8-trichlorodipyrromethene salts with $BF_3{\cdot}Et_2O$ gives a 3,5,8-trichloroBODIPY that readily undergoes regioselective Stille coupling at the 8-position, or a combination of differential 3,8-disubstitution or 3,5- and 8-trisubstitution. X-ray structures of 14 new BODIPYs are reported and analyzed. Global Stille coupling at the 3,5,8-positions of BODIPY **5** caused up to 110 nm bathochromic shifts (in the case of the 3,5,8-trimethylsilylethynyl-BODIPY **10**) in the absorption and emission bands of the BODIPYs. Regioselective and consecutive Stille coupling reactions produced a variety of asymmetric BODIPYs; the 3,5-aryl and 3(5)- and/or 8-ethynyl substitution induced the largest bathochromic shifts whereas the presence of a 3(5)-thienyl substituent caused the largest Stokes shifts (up to 1524 cm^{-1}). The 8-phenyl-BODIPYs showed the highest fluorescence quantum yields (Φ_f = 0.34−0.86), followed by the 8-thienyl-BODIPYs (Φ_f = 0.10−0.27), whereas the 8-ethynyl-BODIPYs showed the lowest quantum yields (Φ_f = 0.01−0.21).

EXPERIMENTAL SECTION

General. ^1H and ^{13}C NMR spectra were measured on a 400 MHz NMR spectrometer at room temperature. Chemical shifts (δ) are given in ppm relative to TMS. High-resolution mass spectra were obtained using the ESI-TOF mode. UV−visible absorption spectra and fluorescence emission spectra were recorded on a commercial spectrophotometer (190−900 nm scan range). The slit width was set at 3.0 nm. Relative fluorescence quantum yields (Φ_f) were calculated as follows: rhodamine 6G was used as the standard for compounds **5**−**9** and for compounds **11** and **12**; rhodamine B was used as the standard for compounds **13**, **14**, **16**, **17**, **22**, and **23**; methylene blue was used as the standard for compounds **10**, **15**, **18**−**21**. All commercial reagents were used without further purification. Water- and air-sensitive reactions were performed under argon protection and in dry solvents.

Dibenzyl 3,7-Bis(2-methoxycarbonylethyl)-2,8-dimethyldipyrromethane-1,9-dicarboxylate ***1***. Benzyl 4-(2-methoxycarbonylethyl)-3,5-dimethylpyrrole-2-carboxylate (15.7 g, 0.05 mol) was dissolved in anhydrous diethyl ether (500 mL), and bromine (2.56 mL, 0.05 mol) was added dropwise. The solution turned brown during addition, and the mixture was further stirred at room temperature overnight, whereupon a thick precipitate was apparent. Then the diethyl ether was removed under vacuum to give a pink solid that was dissolved in methanol (100 mL) and refluxed overnight. When the solution was cooled to room temperature, a precipitate appeared, which was filtered and washed with cold methanol to give a white solid (10.70 g, 70%) of dipyrromethane **1**. Mp 102−104 °C, (lit.[45] mp 102−103 °C). ^1H NMR (400 MHz; $CDCl_3$): δ 9.00 (s, 2H), 7.38−7.31 (m, 10H), 5.25 (s, 4H), 3.97 (s, 2H), 3,56 (s, 6H), 2.75 (t, 4H), 2.51 (t, 4H), 2.28 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): 173.9, 161.4, 136.5, 130.9, 128.5, 128.0, 127.9, 127.2, 120.2, 118.0, 65.5, 51.8, 34.5, 22.4, 19.2, 10.4; HRMS (ESI-TOF) calcd for $C_{35}H_{39}N_2O_8$ $[M + H]^+$ 615.6928, found 615.6908.

Dibenzyl 3,7-Bis(2-methoxycarbonylethyl)-2,8-dimethyldipyrroketone-1,9-dicarboxylate ***2***. A solution of dipyrromethane **1** (2.0 g, 3.25 mmol) in acetic acid (80 mL) was treated with $Pb(OAc)_4$ (3.12 g, 7.0 mmol) and stirred at room temperature for 4 d under argon. Then PbO_2 (2.4 g, 9.3 mmol) was added, and the solution was stirred for another 2 d. The solution was centrifuged, and the supernatant was

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poured into ice−water. The precipitate was collected and dissolved in diethyl ether before being washed with water, 5% aqueous $NaHCO_3$, and brine and then dried over anhydrous Na_2SO_4. Then the solution was concentrated to a minimum volume and crystallized in a refrigerator to give product as a yellowish white solid (1.2 g, 60%), mp 170−171 °C (lit.[46] mp 173−174 °C). ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.38−7.31 (m, 10H), 5.00 (s, 4H), 3,67 (s, 6H), 3.01 (broad, 4H), 2.71 (broad, 4H), 2.27 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 176.7, 173.6, 161.7, 135.0, 132.2, 130.2, 128.7, 128.4, 127.7, 127.0, 121.7, 66.8, 51.6, 35.2, 20.3, 10.4; HRMS (ESI-TOF) calcd for $C_{35}H_{36}N_2O_9$ $[M + H]^+$: 629.2499, found 629.2497.

1,9-Diiodo-3,7-bis(2-methoxycarbonylethyl)-2,8-dimethyldipyrroketone ***3***. Dipyrroketone **2** (6.14 g, 0.01 mol) was dissolved in 300 mL of THF, and then 5% Pd/C (350 mg) catalyst was added. The suspension was stirred under a H_2 atmosphere overnight. After TLC showed that reaction was complete, it was stopped and the reaction solution was passed through a Celite cake to remove the catalyst. The sticky solid on the top of the Celite cake was redissolved and neutralized in water with aqueous ammonia, and the solution was passed through the Celite cake once again. The filtrate was acidified with acetic acid which caused a precipitate to appear from the aqueous solution. The solid was collected by filtration. The THF filtrate was evaporated and combined with the solid to give a total of 4.0 g (92%) of the 1,9-dicarboxylic acid product. This dicarboxylic acid was suspended in a solution of H_2O (250 mL)/MeOH (100 mL), and $NaHCO_3$ (4.48 g, 51.2 mmol) was added to the solution, which was sonicated to form a slurry and then a clear solution. Then a solution of I_2 (3.84 g, 14.72 mmol) in methanol (60 mL) was added to the mixture dropwise at room temperature with vigorous stirring, and some brown solid was formed during the addition. When the addition of iodine was complete, the stirring was continued for another 2 h and the precipitate was filtered and washed with water, saturated aqueous $NaHCO_3$, and water again, followed by hexane to remove any excess I_2, to yield a yellowish solid. The product was left to air-dry or dissolved in CH_2Cl_2 and dried over anhydrous Na_2SO_4 before removal of the solvent to give diiodopyrroketone **3** (4.2 g, 75%), mp 162 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 9.47 (s, 2H), 3.65 (s, 6H), 2.70 (t, J = 7.6 Hz, 4H), 2.61 (t, J = 7.6 Hz, 4H), 2.04 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 173.8, 173.5, 132.7, 128.5, 126.4, 51.8, 33.9, 20.9, 12.2; HRMS (ESI-TOF) calcd for $C_{19}H_{23}I_2N_2O_5$ $[M + H]^+$: 612.9691, found: 612.9697.

BODIPYs ***5−7***. Diiodopyrroketone **3** (1.0 g, 1.63 mmol) was dissolved in $CHCl_3$ (150 mL), and excess phosgene in toluene solution was added to the solution, which turned deep red with time; the reaction was monitored by UV/vis spectrophotometry, and the reaction was stopped when a sharp absorption peak appeared at about 480 nm. Then N_2 gas was passed through the solution to purge it of excess phosgene into an aqueous $NaHCO_3$ solution trap. Solvent was removed in vacuo to give a reddish solid, which was dissolved in 150 mL of $CHCl_3$, followed by addition of DIEA (2 mL, 7.0 equiv). The solution was stirred for 30 min, $BF_3{\cdot}OEt_2$ (2.1 mL, 10 equiv) was added, and the solution turned bright red with a yellow fluorescence under long wavelength UV light. The reaction was monitored by UV/vis spectroscopy, which showed a sharp peak at 538 nm. The mixture was stirred for 24 h before being washed with water, saturated aqueous $NaHCO_3$, and brine and then dried over anhydrous Na_2SO_4 to give a red solid. The product was purified by silica gel column chromatography, eluting with ethyl acetate/hexane (1:4) to give the product **5** (430 mg, 55%) as the major fraction and **6** (88.5 mg, 11%) and **7** (40.2 mg, 5%) as minor products. BODIPY **5**: mp 156−157 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 3.72 (s, 6H), 3.20 (t, J = 8.0 Hz, 4H), 2.57 (t, J = 8.0 Hz, 4H), 2.05 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.5, 144.0, 142.3, 134.9, 128.5, 127.3 52.0, 33.8, 22.8, 8.9; HRMS (ESI-TOF) calcd for $C_{19}H_{20}$ $BCl_3FN_2O_4$ $[M - F]^+$: 475.0566, found: 475.0562; UV/vis (CH_2Cl_2): λ_{max} (ε) = 538 nm (112 200). BODIPY **6**: mp 116−118 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.57 (s, 1H), 3.71 (s, 3H), 3.71 (s, 3H), 3.20 (m, 4H), 2.58 (m, 4H), 2.07 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.5, 172.5, 143.5, 142.6, 142.4, 136.8, 130.1, 129.1, 128.7, 127.3, 126.8, 52.0, 51.9, 33.9, 33.9, 22.8, 22.2, 9.9, 8.9; HRMS (ESI-TOF) calcd for $C_{19}H_{21}BCl_2FN_2O_4$ $[M - F]^+$ 441.0955, found 441.0935, UV/vis (CH_2Cl_2): λ_{max} (ε) = 534 nm (60 300). BODIPY **7**: mp 148−149 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.58 (s, 2H), 3.73 (s, 3H), 3.21 (t, J = 8.1 Hz, 4H), 2.59 (t, J = 8.1 Hz, 4H), 2.08 (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.8, 143.1, 142.5, 138.7, 130.4, 128.8, 51.9, 34.0, 22.2, 9.8; HRMS (ESI-TOF) calcd for $C_{19}H_{22}BClFN_2O_4$ $[M - F]^+$ 407.1345, found 407.1342. UV/vis (CH_2Cl_2): λ_{max} (ε) = 528 nm (38 000).

General Procedure for Stille Coupling Reactions. Global Coupling Reactions. BODIPY **5** (15 mg, 0.03 mmol) and $Pd(PPh_3)_4$ (2.0 mg, 5%) were added to a round-bottomed flask. The flask was flushed with argon, and then anhydrous toluene (15 mL) was injected, followed by injection of the organotin reagent (0.14 mmol, 4.5 equiv). The solution was refluxed for 12 h until the starting material disappeared from TLC and the UV/vis spectrum showed a sharp peak around 600 nm. Then the toluene was removed, and the residue was taken up in CH_2Cl_2, washed with water and brine, and then dried over anhydrous Na_2SO_4. The crude product was purified by chromatography to give the fully (tri-) substituted products.

BODIPY ***8***. (16.0 mg, 83%), mp 198 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.56−7.49 (m, 5H), 7.20−7.09 (m, 4H), 3.63 (s, 6H), 2.33−2.22 (m, 6H), 2.00 (s, 6H), 1.94−1.86 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.5, 149.7, 142.4, 134.4, 133.2, 133.0, 131.7, 129.7, 128.8, 128.0, 127.4, 127.2, 51.6, 35.1, 21.4, 10.6; HRMS (ESI-TOF) calcd for $C_{31}H_{30}BF_2N_2O_4S_3$ $[M + H]^+$ 639.1429, found 639.1429. UV/vis (CH_2Cl_2): λ_{max} (ε) = 594 nm (43 700).

BODIPY ***9***. (8.2 mg, 42%), mp 165−166 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.53−7.38 (m, 15H), 3.60 (s, 6H), 2.12 (m, 4H), 2.00 (m, 4H), 1.80 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.4, 156.6, 142.23, 134.6, 132.0, 131.3, 129.7, 129.4, 128.8, 128.7, 128.4, 128.3, 127.8, 51.5, 34.5, 21.7, 9.7; HRMS (ESI-TOF) calcd for $C_{37}H_{35}BFN_2O_4$ $[MW - F]^+$ 601.2674, found 601.2656. UV/vis (CH_2Cl_2): λ_{max} (ε) = 546 nm (29 500).

BODIPY ***10***. (12.6 mg, 61%), mp 171 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 3.69 (s, 6H), 3.25 (t, J = 8.0 Hz, 4H), 2.25 (t, J = 8.0 Hz, 4H), 2.08 (s, 6H). 0.32 (s, 9H), 0.28 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.8, 140.5, 136.0, 134.7, 132.8, 118.3, 114.0, 113.3, 99.2, 96.4, 51.7, 34.2, 21.4, 14.1, 9.5; HRMS (ESI-TOF) calcd for $C_{34}H_{48}BF_2N_2O_4Si_3$ $[M + H]^+$ 680.3014, found 680.3001. UV/vis (CH_2Cl_2): λ_{max} (ε) = 648 nm (88 000).

Regioselective Stille Coupling Reactions. The selective coupling reactions followed the procedure used for the global coupling reactions. The only difference was that 1 equiv of organotin reagent was used instead of excess organotin reagents.

BODIPY ***11***. Starting with BODIPY **5** (29.2 mg, 0.059 mmol), 23.07 mg (72%) of the monosubstituted BODIPY was obtained, mp 212 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.56 (dd, J = 5.0, 1.3 Hz, 1H), 7.15 (d, J = 1.8 Hz, 1H), 7.09 (d, J = 1.6, 1H), 3.62 (s, 6H), 2.28−2.02 (m, 6H), 1.96 (s, 6H), 1.89−1.83 (m, 2H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.1, 145.0, 143.3, 133.5, 132.8, 131.0, 129.1, 128.5, 127.4, 126.9, 51.7, 34.8, 21.5, 8.8; HRMS (ESI-TOF) calcd for $C_{23}H_{23}BCl_2FN_2O_4S$ $[MW - F]^+$ 523.0833, found 523.0836. UV/vis (CH_2Cl_2): λ_{max} (ε) = 548 nm (77 600).

BODIPY ***12***. A 1:1 ratio of BODIPY **5** (30.4 mg, 0.061 mmol) and tributylphenyltin (20.0 μL, 0.061 mmol) was used to give the product **12** (7.0 mg, 21%); a 1:2 ratio of BODIPY **5** (32.6 mg, 0.066 mmol) and tributylphenyltin (40.0 μL, 0.122 mmol) was used to give the product **12** (19.45 mg, 57%), mp 172 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.56−7.38 (m, 5H), 3.58 (s, 6H), 2.04 (m, 4H), 1.95 (m, 10H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 171.9, 144.4, 143.2, 141.1, 133.3, 130.1, 129.9, 129.0, 128.1, 126.5, 51.6, 34.3, 21.4, 8.7; HRMS (ESI-TOF) calcd for $C_{25}H_{25}BCl_2FN_2O_4$ $[M - F]^+$: 517.1268, found: 517.1278. UV/vis (CH_2Cl_2): λ_{max} (ε) = 534 nm (69 200).

BODIPY ***13***. Starting with BODIPY **5** (20.0 mg, 0.04 mmol), 15.2 mg (65%) of **13** was isolated, mp 121 °C; ^{1}H NMR (400 MHz; $CDCl_3$) δ 3.71 (s, 6H), 3.30 (t, J = 8.8 Hz, 4H), 2.59 (t, J = 8.8 Hz, 4H), 2.04 (s, 6H), 0.30 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.6, 143.0, 142.1, 131.7, 126.4, 119.3, 114.8, 98.4, 51.8, 34.2, 21.7, 8.8; HRMS (ESI-TOF) calcd for $C_{24}H_{29}BCl_2FN_2O_4Si$ $[M - F]^+$ 537.1321, found 537.1340. UV/vis (CH_2Cl_2): λ_{max} (ε) = 584 nm (67 600).

Consecutive Stille Coupling Reactions. BODIPY **11** (16.5 mg, 0.030 mmol) and $Pd(PPh_3)_4$ (3.4 mg, 5%) were added to a round-bottomed flask and flushed with argon several times. Anhydrous toluene (10 mL) was added, followed by injection of tributylphenyltin (28.0 μL, 3.0 equiv); the solution was refluxed for 12 h until a sharp peak appeared in the UV/vis spectrum at 562 nm in CH_2Cl_2. The reaction was stopped, and the toluene was removed; the residue was taken up in CH_2Cl_2, which was washed with water and brine and then dried over anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography, eluting with ethyl acetate/hexane (1:4) to give the product as a purple-red solid. All the other Stille cross-coupling reactions followed this procedure.

BODIPY ***14***. (10.6 mg, 56%), mp >260 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.59−7.14 (m, 13H), 3.65 (s, 6H), 2.29−2.27 (m, 6H), 2.07−1.96 (m, 2H), 1.86 (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.6, 157.2, 142.5, 134.5, 132.3, 131.9, 129.6, 128.9, 128.7, 128.3, 127.9, 127.8, 127.2, 51.6, 35.1, 21.5, 9.8; HRMS (ESI-TOF) calcd for $C_{35}H_{33}BFN_2O_4S$ $[M - F]^+$ 607.2238, found 607.2234. UV/vis (CH_2Cl_2): λ_{max} (ε) = 560 nm (17 800).

BODIPY ***15***. Starting with BODIPY **11** (14.3 mg, 0.026 mmol) afforded the product **15** (11.1 mg, 64%), mp 187 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.54 (m, 1H), 7.14 (m, 1H), 7.08 (m, 1H), 3.63 (s, 6H), 2.19 (m, 6H), 2.02 (s, 6H), 1.90 (m, 2H), 0.33 (s, 18H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.4, 141.7, 137.8, 134.0, 133.6, 133.2, 129.0, 128.1, 127.2, 113.7, 96.2, 51.6, 34.9, 21.2, 9.5, 0.3; HRMS (ESI-TOF) calcd for $C_{33}H_{42}BF_2N_2O_4SSi_2$ 667.2465, found 667.2473. UV/vis (CH_2Cl_2): λ_{max} (ε) = 609 nm (89 100).

BODIPY ***16***. Starting with BODIPY **12** (15.1 mg, 0.029 mmol) afforded the product **16** (14.4 mg, 78%), mp 166 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.59−7.47 (m, 9H), 7.14 (dd, J = 5.1, 3.6 Hz, 2H), 3.60 (s, 6H), 2.14−2.09 (m, 4H), 1.99−1.96 (m, 10H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.3, 149.3, 142.2, 141.2, 134.5, 132.0, 131.8, 131.5, 129.5, 129.3, 128.9, 128.5, 128.4, 127.3, 51.5, 34.5, 21.3, 10.5; HRMS (ESI-TOF) calcd for $C_{33}H_{31}BFN_2O_4S_2$ $[M - F]^+$ 613.1802, found 613.1803. UV/vis (CH_2Cl_2): λ_{max} (ε) = 574 nm (38 900).

BODIPY ***17***. Starting with BODIPY **12** (17.3 mg, 0.033 mmol) gave **17** (15.7 mg, 71%), mp 182 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.52−7.45 (m, 3H), 7.37−7.28 (m, 2H), 3,57 (s, 6H), 2.06−2.00 (m, 10H), 1.94−1.89 (m, 4H), 0.33 (s, 18H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.2, 149.3, 141.5, 140.5, 137.3, 133.8, 132.9, 129.6, 128.8, 128.3, 112.8, 96.2, 51.5, 34.3, 21.1, 9.5, 1.0; HRMS (ESI-TOF) calcd for $C_{35}H_{43}BF_2N_2NaO_4Si_2$ $[M + Na]^+$ 683.2720, found 683.2723. UV/vis (CH_2Cl_2): λ_{max} (ε) = 594 nm (47 900).

BODIPY ***18***. Starting with BODIPY **13** (12.6 mg, 0.023 mmol) gave **18** (11.3 mg, 76%), mp 179 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.54−7.49 (m, 4H), 7.11 (ddd, J = 5.2, 3.8, 1.6 Hz, 2H), 3.72 (s, 6H), 3.39 (t, J = 8.2 Hz, 4H), 2.64 (t, J = 8.2 Hz, 4H), 2.09 (s, 6H), 0.32 (s, 18H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 173.0, 147.9, 141.2, 133.8, 131.9, 131.7, 129.1, 128.7, 127.3, 119.2, 113.6, 99.4, 51.7, 34.4, 31.6, 21.6, 10.6, 1.1; HRMS (ESI-TOF) calcd for $C_{32}H_{35}BFN_2O_4S_2Si$ [MW − F]$^+$ 633.1885, found 633.1883. UV/vis (CH_2Cl_2): λ_{max} (ε) = 636 nm (29 500).

BODIPY ***19***. Starting with BODIPY **13** (11.0 mg, 0.02 mmol) gave product **19** (6.5 mg, 51%), mp 195 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.45−7.36 (m, 10H), 3.72 (s, 6H), 3.39 (t, J = 7.8 Hz, 4H), 2.67 (t, J = 7.8 Hz, 4H), 1.89 (s, 6H), 0.33 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 173.0, 155.5, 141.3, 133.1, 131.9, 129.7, 128.8, 128.1, 127.7, 113.3, 99.3, 51.6, 34.4, 21.0, 9.7, 1.1; HRMS (ESI-TOF) calcd for $C_{36}H_{39}BFN_2O_4Si$ $[M - F]^+$ 621.2756, found 621.2757. UV/vis (CH_2Cl_2): λ_{max} (ε) = 601 nm (38 900).

BODIPY ***20***. BODIPY **5** (15.0 mg, 0.03 mmol) and $Pd(PPh_3)_4$ (3.4 mg, 5%) were added to a round-bottomed flask. The flask was flushed with argon and then anhydrous toluene (15 mL) was injected, followed by injection of the organotin reagent trimethyl-[(tributylstannyl)ethynyl]silane (22.3 μL, 0.06 mmol). The mixture was refluxed until the starting material disappeared as observed by TLC and the UV/vis spectrum showed a sharp peak around 615 nm. Then the toluene was removed and the residue was taken up in CH_2Cl_2 and washed with water, brine and then dried over anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography to give the disubstituted product **20** (10.0 mg, 53%), mp 122 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 3.68 (s, 3H), 3.68 (s, 3H), 3.25 (m, 4H), 2.56 (m, 4H), 2.07 (s, 3H), 2.02 (s, 3H), 0.30 (s, 9H), 0.27 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.8, 172.7, 144.0, 142.1, 140.5, 135.2, 133.3, 132.9, 126.6, 118.9, 114.4, 113.1, 98.7, 96.0, 51.8, 51.7, 34.2, 34.1, 21.7, 21.4, 9.5, 8.2, 0.3, 1.2; HRMS (ESI-TOF) calcd for $C_{29}H_{39}BClF_2N_2O_4Si_2$ $[M + H]^+$ 619.2198, found 619.2185. UV/vis (CH_2Cl_2): λ_{max} (ε) = 616 nm (46,800).

BODIPY ***21***. BODIPY **20** (10 mg, 0.016 mmol) and $Pd(PPh_3)_4$ (2.0 mg, 5%) were added to a round-bottomed flask. The flask was flushed with argon, and then anhydrous toluene (15 mL) was injected, followed by injection of the organotin reagent 2-(tributylstannyl)-thiophene (8.0 μL, 1.5 equiv); the mixture was then refluxed for 5 h. The toluene was removed, and the residue was taken up in CH_2Cl_2, washed with water and brine, and then dried over anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography to give the fully substituted product **21** (6.8 mg, 63%), mp 151 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.75 (d, J = 3.44 Hz, 1H), 7.58 (d, J = 4.92 Hz, 1H), 7.20 (t, J = 4.24 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.37 (t, J = 7.88 Hz, 2H), 3.28 (t, J = 7.36 Hz, 3H), 2.64 (t, J = 7.88 Hz, 3H), 2.57 (t, J = 7.36 Hz, 3H), 2.15 (s, 3H), 2.09 (s, 3H). 0.30 (s, 9H), 0.28 (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.9, 151.9, 150.2, 142.5, 139.2, 133.6, 132.9, 132.6, 131.7, 129.7, 129.5, 127.5, 118.5, 113.6, 112.0, 99.3, 96.6, 51.7, 51.6, 34.4, 34.2, 21.6, 21.4, 10.9, 9.6. 1.0; HRMS (ESI-TOF) calcd for $C_{33}H_{42}BF_2N_2O_4SSi_2$ $[M + H]^+$ 667.2465, found 667.2478. UV/vis (CH_2Cl_2): λ_{max} (ε) = 645 nm (29 500).

BODIPY ***22***. BODIPY **12** (21.6 mg, 0.042 mmol) and $Pd(PPh_3)_4$ (5.3 mg, 5%) were added to a round-bottomed flask. The flask was flushed with argon, and then anhydrous toluene (15 mL) was injected, followed by injection of the organotin reagent 2-(tributylstannyl)-thiophene (14.0 μL, 1.0 equiv); the mixture was then refluxed for 5 h. The toluene was removed, and the residue was taken up in CH_2Cl_2, washed with water and brine, and then dried over anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography hexane/ethyl acetate (4:1) to give product **22** (10.5 mg, 43%), mp 164 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.58−7.18 (m, 8H), 3.58 (s, 6H), 2.11−1.91 (m, 14H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.2, 172.1, 150.4, 143.2, 143.1, 142.2, 141.1, 133.9, 132.0, 131.6, 130.4, 130.1, 129.7, 129.0, 129.0, 128.9, 128.2, 127.4, 126.1, 51.6, 34.4, 26.9, 21.9, 10.5, 7.5; HRMS (ESI-TOF) calcd for $C_{29}H_{28}BClF_2N_2NaO_4S$ $[M + Na]^+$ 607.1417, found 607.1391. UV/vis (CH_2Cl_2): λ_{max} (ε) = 555 nm (33 300).

BODIPY ***23***. BODIPY **22** (9.4 mg, 0.016 mmol) and $Pd(PPh_3)_4$ (2.1 mg, 5%) were added to a round-bottomed flask. The flask was flushed with argon, and then anhydrous toluene (15 mL) was injected, followed by injection of the organotin reagent tributyl(1-ethoxyvinyl) (11.0 μL, 1.5 equiv); the mixture was refluxed for 5 h. The toluene was removed, and the residue was taken up in CH_2Cl_2, washed with water and brine, and then dried over anhydrous Na_2SO_4. The crude product was purified by silica gel column chromatography hexane/ethyl acetate (4:1) to give the fully substituted BODIPY **23** (5.6 mg, 51%), mp, >260 °C. ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.59−7.15 (m, 8H), 4.62 (s, 2H), 3.90 (q, J = 7.1, 2H), 3.57 (s, 6H), 2.11−1.91(m, 14H), 1.35(t, J = 7.1, 3H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 172.4, 172.3, 152.3, 151.5, 142.6, 142.30 142.0, 141.9, 135.4, 134.4, 133.4, 131.5, 129.5, 129.3, 129.3, 128.8, 128.6, 128.4, 128.4, 128.2, 127.2,91.1, 63.7, 53.4, 51.5, 34.5, 21.4, 21.1, 14.3, 10.5, 9.3; HRMS (ESI-TOF) calcd for $C_{33}H_{36}BF_2N_2O_5S$ $[M + H]^+$ 621.2406, found 621.2406. UV/vis (CH_2Cl_2): λ_{max} (ε) = 559 nm (13 000).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra and of the normalized absorption and fluorescence spectra of all new BODIPYs, thermal ellipsoid plots and tables of fractional atomic coordinates and displacement parameters for all X-ray structures, and all 14 X-ray CIFs. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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