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Synthesis and Transformations of 5-Chloro-2,2′-Dipyrrins and Their Boron Complexes, 8-Chloro-BODIPYs**

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Abstract

Symmetric dipyrrylketones **1a**,**b** were synthesized in two steps from the corresponding α-free pyrroles, by reaction with thiophosgene followed by oxidative hydrolysis under basic conditions. The dipyrrylketones produced the corresponding 5-chloro-dipyrrinium salts or 5-ethoxy-dipyrrins on reaction with phosgene or Meerwein's salt, respectively. Boron complexation of the dipyrrins afforded the corresponding 8-functionalized BODIPYs (borondipyrromethenes) in high yields. The 5-chloro-dipyrrinium salts reacted with methoxide or ethoxide ions to produce monopyrrole esters, presumably via a 5,5-dialkoxy-dipyrromethane intermediate. In contrast, 8-chloro-BODIPYs underwent a variety of nucleophilic substitutions of the chloro group in the presence of alkoxide ions, Grignard reagents, and thiols. In the presence of excess alkoxide or Grignard reagent, at room temperature or above, substitution at the boron center also occurred. The 8-chloro-BODIPY was a particularly useful reagent for the preparation of 8-aryl-, 8-alkyl-, and 8-vinyl-substituted BODIPYs in very high yields, using Pd^0-catalyzed Stille cross-coupling reactions. The X-ray structures of eleven BODIPYs and two pyrroles are presented, and the spectroscopic properties of the synthesized BODIPYs are discussed.

Keywords

bodipy; dipyrrin; dipyrrylketone; fluorescence

Introduction

Dipyrrylketones (see Figure 1, *A*) have received little attention in polypyrrole chemistry. Dipyrrylketones are actually bis-vinylogous amides [ν_{max} (C=O) ca. 1575 cm^{-1}] that do not readily react as normal ketones. For instance, dipyrrylketones are not usually reduced by borohydride.[1] However, upon protonation they experience a significant and completely

**BODIPY=difluoroborondipyrromethene.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201304310 and contains ^{1}H-, ^{11}B-, and ^{13}CNMR spectra, pyrrole X-ray structures and absorption/emission profiles for all BODIPYs.

reversible redshift in their optical spectra [$\lambda_{max}(CH_2Cl_2)$ from 340 to 428 nm], clearly demonstrating the presence of the 5-hydroxy-dipyrrylmethene salt (Figure 1, *B*).

Various syntheses of dipyrrylketones are well documented. The most efficient synthesis of unsymmetrical dipyrrylketones involves a modified Vilsmeier–Haack reaction that uses a 2-dimethylamidopyrrole with phosphoryl chloride, and a 2-unsubstituted pyrrole as a nucleophile.[2] Unsymmetrical dipyrrylketones can also be obtained by treatment of a pyrrole-2-acyl chloride with a pyrrole-Grignard derivative. Symmetrical dipyrroketones can be accessed by phosgenation of a pyrrole-Grignard reagent or by oxidative hydrolysis of the corresponding thioketones.[3] Another approach to symmetrical dipyrrylketones involves direct oxidation of the 5-*meso*-carbon of a dipyrrylmethane by using $PbO_2/Pb(OAc)_4$ or $Br_2/SOCl_2$.[4] 1,9-Diformyldipyrrylketones have been used in a MacDonald-type porphyrin synthesis to give oxyporphyrins (oxophlorins).[5] The dipyrrylketone system is also present in b-oxobilanes,[6] which are open-chain tetrapyrroles that can be cyclized with trimethyl orthoformate to afford oxophlorins, and subsequently, porphyrins.[1]

4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacenes,[7, 8] known as BODIPY dyes, have been recognized as one of the most versatile fluorophores in the last three decades because of their sharp fluorescence emissions, high quantum yields, and relatively high chemical and thermal stabilities.[9, 10] BODIPY dyes are, therefore, intensively employed as biological labeling reagents[11, 12] in protein and DNA research. BODIPYs are normally synthesized from the corresponding 2,2′-dipyrrins, also known as dipyrromethenes, upon complexation with boron, normally accomplished by the use of $BF_3{\cdot}OEt_2$ in the presence of a tertiary amine, such as NEt_3, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), or *N*,*N*-diisopropylethylamine (DIEA). The synthesis of the dipyrrin precursors usually follows a route involving acid-catalyzed condensation of two pyrroles with a carbon-linking unit; symmetric systems are normally obtained by condensation of pyrrole with an aldehyde,[13] acyl chloride,[14] or anhydride,[15] whereas unsymmetrical systems are normally obtained by the condensation of a 2-formyl- or 2-acyl-pyrrole with an α-free pyrrole.[16] Using these approaches, a variety of 8-substituted BODIPYs have been reported. An alternative synthetic route[17] to symmetric BODIPYs is from dipyrrylketones, such as **1**, which can be obtained by reaction of a pyrrole with thiophosgene, followed by oxidative hydrolysis. Dipyrrylketones are shown to be valuable intermediates in the synthesis of 5-chloro-2,2′-dipyrrins and their boron complexes, which can undergo further reactions with nucleophiles. Herein, we report our results in the synthesis of 5-chloro-2,2′-dipyrrins and 8-chloro-BODIPYs from dipyrrylketones, their reactions with nucleophiles, and their use in Pd^0-catalyzed cross-coupling reactions. This work advances previous knowledge[17] by reporting new chemistry of 5-chloro-dipyrrins (including a novel fragmentation reaction), describing reactions of 8-chloro-BODIPYs with carbon nucleophiles, and reporting highly efficient organotin reactions.

Results and Discussion

Symmetric dipyrrylketones **1a**,**b** were obtained in two steps (Scheme 1) by treatment of the corresponding α-free pyrrole **2a**,**b** with thiophosgene, followed by oxidative hydrolysis of the resulting dipyrrylthioketone.[3, 18, 19] Alternatively, the dipyrrylketones could be

obtained in similar overall yields by reaction of a 2-*N*,*N*-dimethylamidopyrrole with excess phosphoryl chloride, followed by treatment with pyrroles unsubstituted at the 2-position, such as **2a**,**b**, and then 10% aqueous Na_2CO_3. The dipyrrylketones were characterized by FTIR because they show a characteristic band for the amide-like 5-carbonyl group at approximately ν=1575 cm^{-1} in chloroform, and by HRMS (ESI), and ^{1}H- and ^{13}C NMR spectroscopies. Dipyrrylketones **1a**,**b** were 5-chlorinated[20] in 91–93% yields by reaction with phosgene in dichloromethane or chloroform, to give the corresponding 5-chloro-dipyrrin salts **3a**,**b**. Other chlorinating agents, including $POCl_3$ and $(COCl)_2$, also gave the desired products, although in lower yields. The 5-chloro-dipyrrins **3a** and **3b** showed characteristic UV/Vis absorptions at λ_{max}=485 and 505 nm in dichloromethane, respectively, and were also characterized by their HRMS (ESI) and ^{1}H and ^{13}C NMR spectra. Complexation of the 5-chloro-dipyrrins **3a**,**b** with boron, by using $BF_3{\cdot}OEt_2$ under basic conditions, gave the corresponding BODIPYs **4a**,**b** in 94–96% yield. Compounds **4a** and **4b** were characterized by strong UV/Vis absorptions at 503 and 527 nm and brighter fluorescence emissions at 512 and 542 nm, respectively. Single crystals suitable for X-ray structure analysis were obtained for both 8-chloro-BODIPYs **4a**,**b** (Figure 2). The non-hydrogen atoms, except for fluorine in **4a**, are fairly coplanar, with a mean deviation of 0.052 Å, and the BF_2 plane is almost orthogonal, with a dihedral angle of 89.88(2)°. Compound **4b** has three molecules in the asymmetric unit, two of which have the ethyl groups relatively *syn*, and one has an *anti* ethyl group. Analogous dihedral angles in the three molecules are in the range 88.45(2)–89.37(2)°. BODIPYs **5a**,**b** were also obtained from dipyrrylketones **1a**,**b** upon reaction with Meerwein's salt (triethyloxonium tetrafluoroborate).[21] Treatment of **1a** and **1b** with Meerwein's salt in chloroform, at room temperature, gave orange-red colored solutions, indicating the formation of the fully conjugated 5-ethoxy-dipyrrins. After aqueous workup, the crude residues were complexed with boron by using similar conditions to those reported above, to produce BODIPYs **5a**,**b** in 71–82% overall yields (Scheme 1). BODIPYs **5a**,**b** could also be obtained from **4a**,**b**, but in lower yield (46–52 %), by nucleophilic addition/elimination of the 8-chloro group, by using sodium ethoxide in ethanol (see below). BODIPYs **5a**,**b** showed intense UV/Vis absorptions at 487 and 508 nm, respectively, and characteristic resonances for the ethoxy group in their ^{1}H NMR spectra at approximately δ=4.12 (q) and 1.53 (t) ppm. The molecular X-ray structures for both BODIPYs **5a**,**b** were also obtained (Figure 2). Molecule **5a** almost has C_s symmetry, with the BF_2 plane and dipyrryl plane forming a dihedral angle of 89.37(4)°, and the atoms of the OEt group lying at mean of 0.012 Å from the BF_2 plane; **5b** has a similar structure, with a dihedral angle of 88.68(1)°, but the dipyrryl ethyl groups are *anti* to each other.

The reactions of 5-chloro-dipyrrinium **3a** and BODIPY **4a** in the presence of nucleophiles were further investigated. In the presence of sodium methoxide in methanol, THF, or chloroform, compound **3a**, surprisingly, produced the monopyrrole methyl ester **6** in 81% yield (Scheme 1). If sodium ethoxide was used, the corresponding ethyl ester **7** was obtained (66% yield). The reaction was followed by UV/Vis spectroscopy until complete disappearance of the absorption band of the 5-chloro-dipyrrin occurred. Pyrroles **6** and **7** were fully characterized, including by X-ray crystallography (see the Supporting Information). Two oxygen atoms are added in this unprecedented dipyrrole cleavage

reaction to form **6** or **7**, therefore, it is suggested that intermediate 5,5-dimethoxydipyrromethane **8** is involved (Scheme 2), and this intermediate undergoes a base-catalyzed version of the known pyrrole deacylation reaction to give **6** or **7** and the corresponding 2-unsubstituted pyrrole.[22] Weaker nucleophiles, including KCN and nBu$_4$NF, did not produce any substitution product. However, the 5-chlorodipyrrin **3a** reacted with ethyl magnesium bromide in THF, at room temperature or under reflux, to give a mixture of the desired 5-ethyl-dipyrrin **9** and the reduced *meso*-free compound **10** (Scheme 3), which could not be separated by chromatography. Complexation of the mixture with boron by using $BF_3{\cdot}OEt_2$ in DIEA produced the corresponding BODIPYs in 20 and 53% yields, respectively, after separation. BODIPY **11** was obtained in higher yield (75%) by reaction of **4a** with ethyl magnesium bromide in THF at −78°C; in this case only 10% of the 8-unsubstituted BODIPY was isolated. When the reaction was performed at 0 °C and the mixture was warmed up to room temperature,[23–25] the triethyl substituted BODIPY, **12**, was the only product obtained, in 83% yield. Both BODIPYs **11** and **12** had characteristic UV/Vis absorptions, both at 499 nm, and *m/z* at 276.1713 and 296.2507, respectively. The ^{1}H NMR spectra of BODIPYs **11** and **12** showed the characteristic 8-ethyl protons centered at δ=3.01 (q) and 1.31 (t) ppm, respectively; the B–ethyl protons of BODIPY **12** appeared as broad signals at δ=0.79 and 0.30 ppm.

Because the 8-chloro-BODIPY **4a** gave higher yields for the substitution products compared with dipyrrin **3a**, owing to the higher stability of the BODIPY core and easier product purification, additional substitution reactions were investigated for **4a**, as shown in Scheme 4 and Table 1. Reaction of BODIPY **4a** with sodium methoxide in methanol at room temperature produced the corresponding substitution product **13** in 67% yield, along with dimethoxy (21%) and trimethoxy (very minor) side products, in which one or both the fluorine atoms were also replaced.[26] When the reaction was performed at 80°C trimethoxy-BODIPY **15** was the major product, isolated in 65% yield along with the dimethoxy side product in 16% yield. BODIPY **14** was prepared in 81% yield by reaction of **4a** with sodium phenoxide at room temperature in THF. Both BODIPYs **5a** and **13** showed significantly blueshifted UV/Vis absorptions, both centered at 487 nm, and for **14** at 491 nm, compared with the starting BODIPY **4a**. However, substitution of the fluorine atoms, as in BODIPY **15**, had no significant effect on the λ_{max} value, as previously observed. The ^{1}H NMR spectra of BODIPYs **13** and **15** showed the 8-OMe protons at δ=3.98 and 3.97 ppm, respectively, whereas the B-OMe protons of **15** appeared at δ=2.89 ppm. Two sulfur nucleophiles were also reacted with BODIPY **4a**, in THF and in the presence of K_2CO_3 as the base (Scheme 4). 2-Mercaptobenzothiazole gave BODIPY **16** in 56% yield, whereas 1-mercaptomethyl-*p*-carborane[27] gave **17** in 92% yield. BODIPYs **16** and **17** showed redshifted UV/Vis absorptions at 539 and 529 nm, respectively. The ^{1}H NMR spectra of these BODIPYs showed the aromatic protons of **16** at δ=7.28–7.98 ppm and the SCH_2 protons of **17** at δ=2.95 ppm. Both BODIPYs **16** and **17** were characterized by X-ray crystallography (Figure 2). In BODIPY **16**, the dipyrryl and BF_2 planes form a dihedral angle of 88.03(7)°, whereas the mercaptobenzothiazole plane forms a dihedral angle of 77.03(2)° with the dipyrryl unit. In BODIPY **17**, the dipyrryl and BF_2 planes form a dihedral angle of 88.8 (1)°, the linkage between dipyrryl and *para*-carborane is extended, with a C-S-

CH_2-C torsion angle of 175.3(6)°. The best plane of the CSCC linkage forms a dihedral angle of 83.8(2)° with the dipyrryl plane.

Though 8-chloro-BODIPYs react efficiently in nucleophilic addition–elimination reactions with strong nucleophiles (Scheme 4 and [17]), the 8-chloro-BODIPY **4a** was unreactive in the presence of weaker nucleophiles, such as KCN and nBu$_4$NF.

Pd^0-catalyzed cross-coupling procedures on BODIPYs have been explored, including the Suzuki,[28] Stille,[29] Heck,[30] and Sonogoshira[31] reactions. These transformations have been performed either directly on the BODIPY core[32–35] or on a substituent,[36] and have facilitated the functionalization of BODIPYs, especially coupling reactions of 3,5- and 2,6-dihalogenated-BODIPYs. In comparison with the pyrrolic positions, the *meso*-carbon is more electrophilic, as suggested by Mulliken charge distribution and reactivity studies.[37] Recently, various Pd^0-catalyzed cross-coupling reactions were performed on 8-halo-BODIPYs[17] with arylboronic acids or aryltin reagents under Suzuki or Stille conditions, and with phenylacetylene under Sonogashira conditions. The products from these reactions were obtained in 36–76% yields, with the lowest yield obtained for the 8-chloro-BODIPY under Suzuki conditions. Concurrently, we were also investigating the Pd^0-catalyzed coupling reactions of 8-chloro-BODIPY **4a** and the effect of the 1,7-methyl groups on the cross-coupling reactions. A Suzuki reaction[38] between 8-chloro-BODIPY **4a** and phenylboronic acid using [Pd(PPh$_3$)$_4$] as the catalyst and K_2CO_3 as the base in 1,2-dimethoxyethane (DME), at reflux for 24 h, produced the 8-phenyl-BODIPY **18** in 47% yield. A side product from this reaction was the corresponding *meso*-unsubstituted BODIPY, along with other pyrrolic byproducts from loss of the BF_2 moiety under the relatively harsh conditions. BODIPY **18** was synthesized in higher yield (see Table 1) under milder Stille cross-coupling conditions[39] by using tributylphenylstannane and [Pd(PPh$_3$)$_4$], without any base. The reaction mixture was heated at reflux in toluene and TLC analysis indicated that the reaction was complete within five hours, having proceeded in almost quantitative yield. Therefore, we investigated additional Pd^0-catalyzed Stille cross-coupling reactions of 8-chloro-BODIPY **4a** (Table 1). Various organotin reagents bearing alkyl, alkenyl, alkynyl, and heterocyclic aromatic groups were used in the cross-coupling reactions. All of the coupling reactions produced the corresponding 8-functionalized BODIPYs in almost quantitative yields, except for the reaction with tributylethynyltin, which produced BODIPY **22** in only 31% yield.[40] However, use of the trimethylsilyl-protected organotin reagent afforded a 71% yield of the trimethylsilylalkyne substituted BODIPY **23**. The yields for the alkynyl derivatives **22** and **23** are lower than for all other coupling products (Table 1), particularly for **22**, probably because of the higher reactivity of the unprotected *meso*-alkynyl group.

The structures of BODIPYs **18**–**25** were confirmed by ^{1}H and ^{13}C NMR spectroscopy, HRMS (ESI-TOF) mass spectrometry, UV/Vis spectroscopy, and X-ray crystallography (Figure 2); BODIPYs **12**, **15** and the mono MeO–B–F compound were also investigated by using ^{11}B NMR spectroscopy. The ^{1}H NMR spectrum of 8-phenyl-BODIPY **18** showed aromatic protons between δ= 7.27–7.49 ppm, consistent with literature reports,[41] and a *m/z* peak at 324.1717 in the mass spectrum. The *meso*-methyl group of BODIPY **19** appeared at δ=2.40 ppm in its ^{1}H NMR spectrum and the product showed a *m/z* peck at 262.1556 in the

mass spectrum. For BODIPYs **20** and **21**, the ^{1}H NMR spectrum showed the alkene protons at δ=5.56 (d), 5.69 (d), and 6.74 (dd) ppm or as two doublets at δ=4.38(d) and 4.50(d) ppm, respectively. The ethoxy group of **21** produced signals at δ=3.89 (q) and 1.39 (t) ppm in the ^{1}H NMR spectrum and the mass spectra for BODIPYs **20** and **21** showed *m/z* at 274.1557 and 318.1817, respectively. BODIPY **22** showed a typical peak at δ=3.92 ppm for the terminal alkynyl proton (absent in **23**) in its ^{1}H NMR spectrum, and *m/z* at 272.1380. The *meso*-rings of BODIPYs **24** and **25** showed peaks between δ=6.06–6.77 and 6.98–7.51 ppm, respectively, and the *N*-CH_3 of **24** showed a peak at δ=3.40 ppm in the ^{1}H NMR spectra. These two BODIPYs were also characterized by *m/z* at 327.1799 and 352.1094, respectively. The X-ray crystal structures of BODIPYs **18**, **19**, **20**, **24**, and **25** were obtained by slow diffusion of hexane into a dichloromethane solution, and are shown in Figure 2. BODIPY **18** deviates from its potential C_s symmetry because the BF_2 and phenyl planes are twisted in opposite directions, away from orthogonality with the dipyrryl plane. The BF_2 moiety forms a dihedral angle of 88.13(5)° and the phenyl moiety a dihedral angle of 82.40(3)°. BODIPY **19** is unusual in that its dipyrryl group lies in a crystallographic mirror and its BF_2 group lies across it; thus, they are exactly orthogonal. The X-ray structure for BODIPY **20** was also obtained (Figure 2). Its dipyrryl and BF_2 planes form a dihedral angle of 88.82(2)°. The ethene substituent is not quite orthogonal to the dipyrryl nor coplanar with the BF_2 moiety, a C–C–C=C torsion angle about the bond being 72.65(10)°. BODIPY **24** deviates only slightly from C_s symmetry, with the BF_2 plane forming a dihedral angle of 89.51(9)° with the dipyrryl plane and the methylpyrrole plane forming an angle of 85.77(4)° with it. In Figure 2, only one of the major orientations of the disordered thiophene is shown for BODIPY **25**; it forms a dihedral angle of 84.31(8)° with dipyrryl, and the BF_2 plane forms a dihedral angle of 88.56(4)° with the dipyrryl plane.

The spectroscopic properties of the BODIPYs were investigated and their UV/Vis absorption and steady-state fluorescence emission spectra in dichloromethane were recorded. As an example, Figure 3 shows the normalized absorption and fluorescence spectra of BODIPYs **4a**, **5a**, and **22** (see the Supporting Information for all other BODIPY spectra). Table 2 summarizes the spectroscopic data obtained for the BODIPYs, including their maximum absorption and fluorescence wavelengths, molar extinction coefficients, and fluorescence quantum yields in dichloromethane. As expected, literature compounds **18** and **19** showed absorption and emission profiles similar to those previously reported.[42] The new BODIPYs, **4a** and **4b**, show spectra of comparable shape and characteristics to other BODIPYs described in the literature, with a strong absorption band corresponding to the S_0–S_1 (π–π^*) transitions centered at 503 and 527 nm, respectively. The approximate 25 nm redshift observed in the absorption and emission maxima is due to the increased alkyl substitution of the BODIPY core (i.e., the 2,6-diethyl substituents in **4b** and **5b**).[41] The replacement of the 8-chloro group on BODIPY **4a** with an alkyl (**11** and **19**), alkoxy (**5a** and **13**), or phenoxy (**14**) moiety caused blueshifts of the absorption and emission maxima in the order of 16–19 nm for the alkoxy-BODIPYs, 12–13 nm for the aryloxy-BODIPY and 4–7 nm for the alkyl-BODIPYs. On the other hand, substitution with a phenyl (**18**) or vinyl (**20**) group had no noticeable effect on the absorption and emission wavelengths, whereas ≈10 nm redshifts were observed for BODIPYs **21**, **24**, and **25**, and the largest redshifts were obtained for the *meso*-thio (**16**) and *meso*-alkynyl (**22**) BODIPYs (≈40 nm). The

fluorescence quantum yields for BODIPYs **4a** and **4b** were found to be 0.51 and 0.33, respectively, owing to the heavy-atom effect of the chlorine and introduction of the two ethyl groups in **4b**. In accordance with the literature,[17] replacement of the *meso*-chloro with an alkoxy or phenoxy group caused a significant increase in quantum yield, particularly for BODIPYs **5a** and **14** ($\Phi_f \approx 1.0$), whereas substitution with a *meso*-thiol had the opposite effect, Φ_f of 0.04 and 0.09 were found for BODIPYs **16** and **17**, respectively. Substitution of the 8-chloro group with an alkyl (methyl and ethyl) or phenyl group also increased the quantum yields to $\Phi_f \approx 0.8$ (for **11** and **19**) and 0.62 for **18**. However, the quantum yields for the *meso*-alkenyl, alkynyl, pyrrolyl, and thienyl-BODIPYs **20**–**25** were appreciably lower, particularly for **20**, the fluorescence of which was essentially quenched, due to the greater freedom of rotation for these smaller groups increasing the energy lost to non-radiative decay.[43] Boron substitution had no significant effect on the absorption and emission wavelengths, but did influence the fluorescence quantum yield. Although boron substitution with two methoxy groups significantly increased the quantum yield of BODIPY **15** (Φ_f=1.0) relative to **13** (Φ_f= 0.57), substitution with two ethyl groups reduced the quantum yield of BODIPY **12** (Φ_f=0.32) relative to **11** (Φ_f=0.83).

Conclusion

The synthesis of BODIPY dyes from dipyrrylketone precursors has been explored. New BODIPY compounds were obtained that are usually very difficult to synthesize by conventional methods. The transformation of dipyrrylketones into 5-chlorodipyrrins was studied, and further reactions involving electrophilic, nucleophilic addition/elimination, and coupling reactions were reported. In this context an unexpected cleavage reaction of 5-chloro-dipyrrins to give monopyrrole-2-carboxylates was discovered. The use 5-chloro-dipyrrins represents an alternative method with broad applicability for the modification of BODIPYs, especially at their 8-*meso*-carbon. Variations in the photophysical properties of the various new BODIPYs are discussed and interpreted, emphasizing the significant effect caused by *meso*-substitution. Finally, the X-ray structures of eleven BODIPYs are reported and analyzed within the context of BODIPY solid-state structural characteristics.

Experimental Section

General

Commercially available reagents were purchased from Sigma–Aldrich Co., and were used without further purification. All air and moisture sensitive reactions were performed under an argon atmosphere Melting points were measured on an Electrothermal MEL-TEMP instrument. Analytical thin-layer chromatography (TLC) was performed on polyester backed TLC plates 254 (precoated, 200 μm, Sorbent Technologies). Column chromatography was performed on silica gel (Sorbent Technologies, 60 Å, 40–63 μm) ^{1}H-, ^{13}C- and ^{11}B NMR spectra were recorded, by using a Bruker AV-400 spectrometer, in $CDCl_3$ (7.26 ppm, ^{1}H and 77.0 ppm, ^{13}C, and $BF_3.Et_2O$ at 0.0 ppm, ^{11}B). Chemical shifts are given in parts per millions (ppm) relative to tetramethylsilane (TMS, 0 ppm); multiplicities are indicated as br (broad), s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). All spectra were

recorded at room temperature. Mass spectra were obtained at the LSU Department of Chemistry Mass Spectrometry Facility using an Applied Biosystems QSTAR XL ESI-TOF.

1,3,7,9-Tetramethyldipyrryl-5-ketone 1a—A solution of thiophosgene (1.15 g, 10.0 mmol) in toluene (10 mL) was added dropwise to a solution of 2,4-dimethylpyrrole (2.0 g, 21.0 mmol) in dry ether (30 mL) at 0 °C. The mixture was stirred for about 1 h (until TLC analysis showed the starting material had disappeared). Then, methanol (30 mL) was added and the reaction mixture was stirred for another 30 min. The solvents were removed in vacuo and the residue was purified on a silica-gel column eluted with toluene/chloroform (4:1). The thioketone product was obtained as an orange solid. (980 mg, 40%); m.p. 180–181 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=8.96 (s, 2H), 5.91 (s, 2H), 2.27 (s, 6H), 2.07 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=175.30, 133.30, 127.98, 127.56, 111.74, 13.09, 12.65 ppm; HRMS (ESI): *m/z* calcd for $C_{13}H_{16}N_2S$: 233.1107 [M+H^+]; found: 233.1106. To the thioketone (232 mg, 1.0 mmol) in EtOH (95 %, 100 mL) was added KOH (1.0 g), and to this mixture was added aqueous H_2O_2 (5 %, 10 mL) dropwise in an ice bath. Then, the solution was heated in a steam bath for about 5 min. The solution was cooled to room temperature and water (300 mL) was added and the solution was extracted with chloroform three times. The organic layers were collected and washed with water, brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was purified by sublimation to give the product dipyrrylketone as a pale yellow solid. (170 mg, 78%); m.p. 232–233°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=8.63 (s, 2H), 5.85 (s, 2H), 2.28 (s, 6H), 2.19 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=175.30, 133.30, 127.98, 127.56, 111.74, 13.09, 12.65 ppm; IR $\tilde{\nu}_{max}$ (C=O) (Nujol)=1573 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} (ε)=295 (8600), 341 nm (14 600); HRMS (ESI): *m/z* calcd for $C_{13}H_{16}N_2O$: 217.1335 [M+H^+]; found: 217.1334.

2,8-Diethyl-1,3,7,9-tetramethyl-5-dipyrrylketone 1b

Method A: 4-Ethyl-3,5-dimethylpyrrole-2-dimethylamide (8.0 g. 41.2 mmol) was dissolved in excess $POCl_3$ and warmed at 50°C for 15 min before being evaporated to dryness. The resulting complex (λ_{max}=380 nm) was taken up in CH_2Cl_2 (20 mL). 3-Ethyl-2,4-dimethylpyrrole (5.6 g, 45.5 mmol) was then added and the mixture was heated under reflux for 90 min. The brown solution (λ_{max}=408 nm) was stirred vigorously with 10% aq Na_2CO_3 (100 mL) and heated under reflux for 2 h. The dipyrrylketone product, precipitated from solution as a yellow solid, was filtered off and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL) and the combined organic extracts were washed with water and dried over anhydrous $MgSO_4$ before evaporation to small volume. The yellow solid that precipitated was combined with the earlier solid and was recrystallized from CH_2Cl_2 to give **1b** (10.1 g, 89%) as pale yellow needles.

Method B: The synthesis of **1b** followed the procedure reported above for **1a**. Thioketone yield: (1.30 g, 43%); m.p. 172–174°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=8.95 (s, 2H), 2.37 (q, J=7.5 Hz, 4H), 2.23 (s, 6H), 2.00 (s, 6H), 1.05 ppm (t, J=7.5 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=189.39, 136.19, 134.67, 126.67, 125.56, 17.47, 14.99, 11.73, 10.88 ppm; HRMS (ESI): *m/z* calcd for $C_{17}H_{25}N_2S$: 289.1733 [M+H^+]; found: 289.1739. Dipyrrylketone **1b** yield: (224 mg, 82%); m.p. 205–207 °C (literature[41] 207°C); ^{1}H NMR

(400 MHz; $CDCl_3$): δ=8.61 (s, 2H), 2.40 (q, J=7.5 Hz, 4H), 2.23 (s, 6H), 2.14 (s, 6H), 1.07 ppm (t, J=7.5 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=175.23, 129.65, 127.24, 125.27, 124.25, 17.37, 15.20, 11.41, 10.70 ppm; IR $\tilde{\nu}_{max}$ (C=O) ($CHCl_3$ or Nujol)=1575 cm^{-1}; UV/Vis ($CHCl_3$): λ_{max} (ε)=288 (11700), 357 nm (25 000); HRMS (ESI): *m/z* calcd for $C_{17}H_{25}N_2O$: 273.1967 [M+H^+]; found: 273.2013.

5-Chloro-1,3,7,9-tetramethyldipyrromethene hydrochloride 3a—Dipyrrylketone **1a** (314 mg, 1.45 mmol) was dissolved in $CHCl_3$ and phosgene in toluene solution was added before stirring at room temperature for 1 h. When the reaction was complete according to UV/Vis spectroscopy and TLC analysis, nitrogen gas was passed through solution to purge it of excess phosgene, which was directed to a $NaHCO_3$ solution trap. Solvent was then removed in vacuo and the red solid was recrystallized from $CHCl_3$/petroleum ether to give **3a** as a red solid (356 mg, 91%); m.p.> 260°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=12.93 (s, 2H), 6.23 (s, 2H), 2.59 (s, 6H), 2.34 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=153.70, 144.35, 139.63, 128.18, 120.71, 16.27, 14.38 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)= 485 nm (23 500); HRMS (ESI): *m/z* calcd for $C_{13}H_{16}ClN_2$: 235.0997; found: 235.0992.

5-Chloro-2,8-diethyl-1,3,7,9-tetramethyldipyrromethene hydrochloride 3b— Yield: (439 mg, 93%); m.p.>300°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=12.50 (s, 2H), 2.35 (s, 6H), 2.15 (s, 6H), 2.40 (q, J=7.6 Hz, 4H), 1.05 ppm (t, J=7.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=152.41, 138.81, 137.68, 133.13, 128.08, 17.44, 14.28, 12.72, 12.63 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=509 nm (57 500); HRMS (ESI): *m/z* calcd for $C_{17}H_{24}ClN_2$: 291.1623; found: 291.1635; elemental analysis calcd (%) for $C_{17}H_{24}Cl_2N_2$: C 62.4, H 7.3, N 8.6; found: C 62.7, H 7.5, N 8.8.

BODIPY 4a: Chloro-dipyrrin hydrochloride **3a** (235 mg, 0.87 mmol) was dissolved in $CHCl_3$ and DIEA (8 mmol, 9.0 equiv) was added before the mixture was stirred for 30 min. Then, $BF_3{\cdot}OEt_2$ (14 mmol, 16 equiv) was added. The resulting mixture was stirred overnight at room temperature. The solution was washed with saturated aq $NaHCO_3$, brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was purified by chromatography on silica gel (eluted with CH_2Cl_2/hexane) to give the BODIPY **4a** (230 mg, 94%); m.p. 235–237°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ= 6.09 (s, 2H), 2.52 (s, 6H), 2.45 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=155.26, 142.84, 136.54, 129.72, 121.36, 16.68, 14.54 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=503 nm (61 700); HRMS (ESI): *m/z* calcd for $C_{13}H_{15}ClF_2N_2$: 282.1016; found: 282.1010.

BODIPY 4b: BODIPY **4b** was prepared, using the same procedure as described above, from 5-chloro-dipyrrin hydrochloride **3b** (325 mg, 96%); m.p. 173–175 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=2.50 (s, 6H), 2.41 (m, 10H), 1.05 ppm (t, J=7.6 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=153.36, 138.10, 135.16, 133.20, 129.16, 17.11, 14.75, 13.82, 12.49 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=527 nm (31 600); HRMS (ESI): *m/z* calcd for $C_{17}H_{22}BClFN_2$: 319.1549 [M^+−F]; found: 319.1550.

BODIPY 5a

Method A: Dipyrrylketone **1a** (60 mg, 0.27 mmol) was dissolved in dry $CHCl_3$ (20 mL) and triethyloxonium tetrafluoroborate (105.1 mg, 0.54 mmol) was added. The solution turned red with time and UV/Vis spectroscopy showed a sharp peak at 438 nm. The mixture was stirred overnight and then washed with water, brine and finally dried over anhydrous Na_2SO_4. After evaporation, the residue was dissolved in $CHCl_3$ (30 mL) and DIEA (1.62 mmol, 6 equiv) was added and the solution was stirred for about 30 min before addition of $BF_3{\cdot}OEt_2$ (2.7 mmol, 10 equiv); the solution was then stirred overnight. UV/Vis spectroscopy showed a sharp peak at 487 nm. Then, the mixture was washed with aq $NaHCO_3$, brine and then dried over anhydrous Na_2SO_4. The residue was purified by silica-gel column chromatography (eluted with CH_2Cl_2/hexane) to give BODIPY **5a** as an orange red solid (64 mg, 82%).

Method B: BODIPY **4a** (56.4 mg, 0.20 mmol) was dissolved in MeOH in an ice bath and NaOEt (20.4 mg, 0.3 mmol) was added. The mixture was stirred for 45 min and was monitored by TLC analysis and UV/Vis spectroscopy. The solvent was removed in vacuo and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was purified by chromatography (eluted with CH_2Cl_2/hexane) to give an orange solid (26.8 mg, 46%); m.p. 126–128 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.02 (s, 2H), 4.12 (q, J=7.1 Hz, 2H), 2.51 (s, 6H), 2.38 (s, 6H), 1.53 ppm (t, J=7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ= 159.12, 154.13, 139.13, 127.94, 119.57, 74.14, 15.31, 14.45, 13.75 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=487 nm (58 900); HRMS (ESI): *m/z* calcd for $C_{15}H_{19}BF_2N_2O$: 292.1668; found: 292.1654.

BODIPY 5b: Method A: Yield: (66 mg, 71%); **Method B**: Yield: (36.2 mg, 52%); m.p. 135–137 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=4.09 (q, J=7.1 Hz, 2H), 2.48 (s, 6H), 2.48 (q, J=7.5 Hz, 4H), 2.32 (s, 6H), 1.55 (t, J= 7.1 Hz, 3H), 1.06 ppm (t, J=7.5 Hz, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=158.04, 152.19, 134.73, 131.53, 73.88, 17.04, 15.29, 14.68, 12.41, 11.22 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=508 nm (27 500); HRMS (ESI): *m/z* calcd for $C_{19}H_{27}BFN_2O$ (M^+-F): 329.2200; found: 329.2167.

Methyl 3,5-dimethylpyrrole-2-carboxylate 6—Dipyrromethene **3a** (47.0 mg, 0.17 mmol) was dissolved in $CHCl_3$ and 0.5 M NaOMe in MeOH (1.0 mL, 0.5 mmol) was added at room temperature; the mixture was stirred overnight and the reaction was monitored by TLC analysis and spectrophotometry. The solution was washed with water, brine and then dried over anhydrous Na_2SO_4. The solvent was removed and the product was purified by silica-gel column chromatography (eluted with MeOH/CH_2Cl_2); Yield: 21 mg, 80.8%; m.p. 93–95°C (literature[44] 98–99°C); ^{1}H NMR (400 MHz; $CDCl_3$): δ=9.27 (s, 1H), 5.79 (s, 1H), 3.83 (s, 3H), 2.30 (s, 3H), 2.25 ppm (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=163.43, 132.97, 129.14, 117.53, 111.34, 50.92, 12.96, 12.82 ppm; HRMS (ESI): *m/z* calcd for $C_8H_{12}NO_2$: 154.0868 [M+H^+]; found: 154.0870 (see the Supporting Information for X-ray structure).

Ethyl 3,5-dimethylpyrrole-2-carboxylate 7—This compound was prepared as described for pyrrole **6**, except that sodium ethoxide was used as the base in ethanol. Yield:

19.0 mg, 66.2%; m.p. 118–119°C (literature[45] 125°C); ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.68 (s, 1H), 5.79 (s, 1H), 4.31 (q, *J*=7.1 Hz, 2H), 2.30 (s, 3H), 2.24 (s, 3H), 1.34 ppm (t, *J*=7.1 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=161.69, 132.28, 129.02, 117.78, 111.35, 59.68, 14.57, 13.07, 12.77 ppm; HRMS (ESI): *m/z* calcd for $C_9H_{14}NO_2$: 168.1019 [M+H^+]; found: 168.1016 (see the Supporting Information for X-ray structure).

BODIPY 11

Method A: 5-Chloro-dipyrrin **3a** (100 mg, 0.37 mmol) was dissolved in $CHCl_3$ (40 mL) and 1.0 M EtMgBr in THF (1.30 mL, 1.30 mmol) was added dropwise at 0 °C; the reaction was left stirring for 1 h at 0 °C and then for another 2 h at room temperature. Then, the solution was poured into ice water to destroy excess EtMgBr, and extracted with $CHCl_3$. The organic layers were combined and washed with water, brine and then dried over anhydrous Na_2SO_4. After evaporation, the residue (a mixture of compounds **9** and **10**) in $CHCl_3$ (30 mL) and DIEA (0.45 mL, 7 equiv, 2.58 mmol) in an ice bath was treated with $BF_3{\cdot}OEt_2$ (0.53 mL, 12.0 equiv, 4.3 mmol) and the mixture was stirred overnight. The solvent was removed and the residue was purified on a silica-gel column (eluted with CH_2Cl_2/hexane) to give BODIPY **11**. Yield: 20.1 mg, 19.6%.

Method B: ChloroBODIPY **4a** (56.4 mg, 0.2 mmol) was dissolved in anhydrous THF and 1.0 M EtMgBr in THF (0.5 mL, 0.5 mmol) was added dropwise to the solution at −70°C with vigorous stirring. When the reaction was complete, according to TLC analysis and spectrophotometry, the solution was poured into ice water to destroy the excess Grignard reagent. Then the mixture was extracted three times with $CHCl_3$, the organic phases were combined and washed with water, brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated and the residue was purified by silicagel column chromatography (eluted with CH_2Cl_2/hexane) to give the product as an orange-red solid (40 mg, 75%); m.p. 214–216°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.05 (s, 2H), 3.01 (q, *J*=7.5 Hz, 2H), 2.52 (s, 6H), 2.44 (s, 6H), 1.32 ppm (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=153.87, 147.87, 140.30, 131.20, 121.55, 21.29, 16.30, 15.45, 14.45 ppm; HRMS (ESI): *m/z* calcd for $C_{15}H_{19}BF_2N_2$: 276.1718; found: 276.1713; UV/Vis (CH_2Cl_2): λ_{max} (ε) 499 nm (56 200). The *meso*-unsubstituted BODIPY was also eluted from the column (6.0 mg, 10%); m.p. 185–187°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=7.04 (s, 1H), 6.05 (s, 2H), 2.53 (s, 6H), 2.25 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=156.75, 141.20, 133.41, 120.07, 119.02, 14.67, 11.28 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=507 nm (19 600); HRMS (ESI): *m/z* calcd for $C_{13}H_{15}BF_2N_2$: 248.1405; found: 248.1404.

BODIPY 12: 1.0 M Ethyl magnesium bromide (1.0 mL, 1.0 mmol) in THF was added to chloroBODIPY **4a** (56.4 mg, 0.2 mmol) in THF (20 mL) at room temperature and stirred for 1 h; the reaction was quenched by addition of aq NH_4Cl and then extracted with $CHCl_3$. The organic extract was washed with water, brine and then dried over anhydrous Na_2SO_4. BODIPY **12** was isolated as the sole product by using silica-gel column chromatography (eluted with CH_2Cl_2/hexane). Yield: 49 mg, 83 %; m.p. 135–137 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.08 (s, 2H), 3.07 (q, *J*=7.5 Hz, 2H), 2.46 (s, 6H), 2.44 (s, 6H), 1.31 (t, *J*=7.5 Hz, 3H), 0.79 ppm (m, 4H), 0.30 (m, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=150.08, 135.52, 131.77, 122.06, 21.34 16.97, 16.39, 15.93, 9.00, 1.02 ppm; ^{11}B NMR (128 MHz; $CDCl_3$):

δ= 1.37 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=499 nm (15 800); HRMS (ESI): *m/z* calcd for $C_{19}H_{30}BN_2$: 296.2533; found: 296.2507.

BODIPY 13: 8-Chloro-BODIPY **4a** (56.4 mg, 0.2 mmol) was dissolved in MeOH (30 mL) in an ice bath and NaOMe (16.5 mg, 0.3 mmol) was added; the mixture was stirred for 45 min and the reaction was monitored by TLC analysis and spectrophotometry. The solvent was removed in vacuo and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was purified by silica-gel column chromatography (eluted with CH_2Cl_2/hexane). The major fraction was the desired BODIPY product **13**. Yield: 37.1 mg, 67%; m.p. 160–161°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.03 (s, 2H), 3.98 (s, 3H), 2.51 (s, 6H), 2.40 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=159.95, 154.76, 138.33, 128.30, 119.56, 64.32, 49.12, 14.47, 13.76 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)= 487 nm (89 100); HRMS (ESI): *m/z* calcd for $C_{14}H_{18}BF_2N_2O$: 278.1511; found: 278.1504. The monomethoxyboron-substituted BODIPY was also separated as a minor fraction from the column (Yield: 12.0 mg, 21%); ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.02 (s, 2H), 3.97 (s, 3H), 2.89 (s, 3H), 2.51 (s, 6H), 2.37 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=159.95, 154.76, 138.33, 128.30, 119.56, 64.24, 49.12, 14.47, 13.76 ppm; ^{11}B NMR (128 MHz; $CDCl_3$): δ=1.58 ppm; HRMS (ESI): *m/z* calcd for $C_{14}H_{17}BFN_2O$: 259.1418 [M^+−OMe]; found: 259.1392. A small amount of the dimethoxyboron BODIPY **15** was also isolated from the column, but in insufficient quantity to fully characterize.

BODIPY 14: 8-Chloro-BODIPY **4a** (56.4 mg, 0.2 mmol) was dissolved in THF (30 mL) in an ice bath and sodium phenoxide (34.8 mg, 0.3 mmol) was added; the mixture was stirred for 2 h at room temperature and monitored by TLC analysis and spectrophotometry. The solvent was removed in vacuo and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was purified by silica-gel column chromatography (eluted with CH_2Cl_2/hexane) to give an orange solid (55 mg, 81%); m.p. 188–190 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=7.36–7.25 (m, 2H), 7.08–7.06 (m, 1H), 7.01–6.99 (m, 2H), 5.99 (s, 2H), 2.55 (s, 6H), 2.04 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=157.52, 155.78, 151.59, 140.42, 130.08, 127.62, 122.84, 119.99, 114.70, 14.60, 14.14 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=491 nm (51 300); HRMS (ESI): *m/z* calcd for $C_{19}H_{20}BF_2N_2O$: 340.1668; found: 340.1662.

BODIPY 15: 8-Chloro-BODIPY **4a** (56.4 mg, 0.2 mmol) was dissolved in MeOH (30 mL) and NaOMe (54.0 mg, 0.75 mmol) was added before the solution was heated at reflux temperature, under argon for 12 h. The solvent was removed and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was separated by silica-gel chromatography (eluted with MeOH/CH_2Cl_2). Yield: 38 mg, 65%; m.p. 93–95°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.01 (s, 2H), 3.97 (s, 3H), 2.86 (s, 6H), 2.48 (s, 6H), 2.41 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ= 159.92, 154.87, 137.38, 129.02, 119.33, 64.13, 49.04, 14.41, 13.81 ppm; ^{11}B NMR (128 MHz; $CDCl_3$): δ=2.39 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=487 nm (46 800); HRMS (ESI): *m/z* calcd for $C_{16}H_{23}BN_2NaO_3$: 324.173 [M^++Na]; found: 324.1719. The monomethoxyboron-substituted BODIPY (see above) was also separated as a minor fraction from the column (Yield: 9.3 mg, 16 %).

BODIPY 16: A solution of 8-chloro-BODIPY **4a** (56.4 mg, 0.2 mmol), 2-mercaptobenzothiozole (40.0 mg, 0.24 mmol), and K_2CO_3 (41.5 mg, 0.3 mmol) in THF (30 mL) was stirred at room temperature for 12 h or until the starting material was almost completely consumed. The solvent was removed in vacuo and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was purified by silica-gel column chromatography (eluted with CH_2Cl_2/hexane). Yield: 46.1 mg, 56%; m.p. 208–210°C. ^{1}H NMR (400 MHz; $CDCl_3$): δ=7.90 (dt, J=8.4, 0.9 Hz, 1H), 7.68 (m, 1H), 7.44 (ddd, J=8.4, 7.3, 1.3 Hz, 1H), 7.31 (ddd, J= 8.3, 7.3, 1.2 Hz, 1H), 6.10 (s, 2H), 2.58 (s, 6H), 2.46 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=166.56, 158.25, 153.59, 144.75, 135.37, 134.42, 128.70, 126.46, 124.76, 123.07, 122.00, 121.08, 17.26, 14.97 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=539 nm (49 000); HRMS (ESI): *m/z* calcd for $C_{20}H_{18}BFN_3S$: 394.1019 [M−F]; found: 394.1010.

BODIPY 17: A solution of 8-chloro-BODIPY **4a** (56.4 mg, 0.2 mmol), *p*-carborane thiol (45.6 mg, 0.24 mmol), and K_2CO_3 (41.5 mg, 3.0 mmol) in THF (30 mL) was stirred at room temperature for 12 h or until the starting material was consumed, The solvent was removed in vacuo and the residue was taken up in $CHCl_3$ and washed with water, brine and then dried over anhydrous Na_2SO_4. The product was purified by column chromatography (eluted with CH_2Cl_2/hexane) to give a red solid (80 mg, 92%); m.p. 150–152°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.06 (s, 2H), 2.95 (s, 2H), 2.51 (s, 3H), 2.49 (s, 3H), 2.17–1.68 ppm (m, 11H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=156.14, 143.51, 136.84, 134.23, 122.50, 59.04, 46.04, 31.91, 16.91, 14.68 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=529 nm (17 000); HRMS (ESI): *m/z* calcd for $C_{16}H_{26}B_{11}F_2N_2S$: 437.2808; found: 437.3033.

General procedure for Stille coupling reactions

8-Chloro-BODIPY **4a** (56.4 mg, 0.2 mmol), [$Pd(PPh_3)_4$] (10.0 mg, 5% mmol) and organotin reagent (0.24–0.30 mmol) were added to a round-bottomed flask. The flask was flushed with argon and then anhydrous toluene was added, followed by injection of the Stille reagents. The mixture was refluxed for 5 h, after which time the reaction was complete; the toluene was then removed and the residue was taken up in dichloromethane and washed with water, brine and then dried over anhydrous Na_2SO_4. The crude product was purified by silica-gel column chromatography (eluting with CH_2Cl_2/hexane).

BODIPY 18—Yield: 60.1 mg, 93%; m.p. 165–166°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=7.49–7.47 (m, 3H), 7.29–7.27(m, 2H), 5.98 (s, 2H), 2.56 (s, 6H), 1.37 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ= 154.90, 142.19, 140.52, 131.14, 123.79, 121.11, 17.24, 14.55 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=501 nm (57 500); HRMS (ESI): *m/z* calcd for $C_{19}H_{20}BF_2N_2$: 324.1718; found: 324.1717.

BODIPY 19—Yield: 50.7 mg, 97%; m.p. 245–247°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.05 (s, 2H), 2.56 (s, 6H), 2.51 (s, 6H), 2.40 ppm (s, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=153.59, 141.43, 141.01, 132.06, 121.25, 17.31, 16.37, 14.43 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=487 nm (66 000); HRMS (ESI): *m/z* calcd for $C_{14}H_{18}BF_2N_2$: 262.1562; found: 262.1556.

BODIPY 20—Yield: 53.1 mg, 97%; m.p. 228–230°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.74 (dd, *J*=14.3, 9.1 Hz, 1H), 6.03 (s, 2H), 5.69 (dd, *J*=12.0, 2.2 Hz, 1H), 5.56 (d, *J*=17.5, 1.8 Hz, 1H), 2.53 (s, 6H), 2.23 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=154.90, 142.19, 140.52, 131.14, 123.79, 121.11, 17.24, 14.55 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=505 nm (46 000); HRMS (ESI): *m/z* calcd for $C_{15}H_{18}BF_2N_2$: 274.1562; found: 274.1557.

BODIPY 21—Yield: 59.1 mg, 93%; m.p. 105–107 °C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.03 (s, 2H), 4.46 (d, *J*=2.9 Hz, 1H), 4.37 (d, *J*=2.8 Hz, 1H), 3.89 (q, *J*=7.0 Hz, 2H), 2.52 (s, 6H), 2.23 (s, 6H), 1.39 ppm (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=155.97, 153.56, 142.50, 134.98, 131.29, 88.11, 63.67, 14.65, 14.34 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=513 nm (40 700); HRMS (ESI): *m/z* calcd for $C_{17}H_{22}BF_2N_2O$: 318.1824; found: 318.1817.

BODIPY 22—Yield: 16.8 mg, 31 %; m.p.>260°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.07 (s, 2H), 3.92 (s, 1H), 2.53 (s, 6H), 2.45 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=155.07, 142.61, 133.28, 121.06, 118.92, 94.42, 79.19, 15.47, 14.63 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)= 544 nm (37 200); HRMS (ESI): *m/z* calcd for $C_{15}H_{16}BF_2N_2$: 272.1405; found: 272.1380.

BODIPY 23—Yield: 21.7 mg, 71.1% (starting with 25 mg, 0.088 mmol of **4a**); m.p.≈250°C "(decomposed)"; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.06 (s, 2H), 2.52 (s, 6H), 2.46 (s, 6H), 0.29 ppm (s, 9H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=154.40, 142.23, 133.05, 120.78, 120.05, 115.01, 110.44, 15.54, 14.61, 0.68 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=545 nm (42 500); HRMS (ESI): *m/z* calcd for $C_{18}H_{23}BFN_2Si$: 325.1708 [M^+−F]; found: 325.1699.

BODIPY 24—Yield: 62.1 mg, 95%; m.p. 179–181°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=6.77 (dd, *J*=2.7, 1.7 Hz, 1H), 6.21 (dd, *J*=3.6, 2.7 Hz, 1H), 6.07 (dd, *J*=3.6, 1.7 Hz, 1H), 6.01 (s, 2H), 3.40 (s, 3H), 2.55 (s, 6H), 1.50 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ= 156.14, 143.34, 133.13, 131.73, 124.64, 122.47, 121.01, 109.34, 108.84, 33.84, 14.67, 12.68 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=513 nm (53 700); HRMS (ESI): *m/z* calcd for $C_{18}H_{21}BF_2N_2$: 327.1827.

BODIPY 25—Yield: 69.8 mg, 99%; m.p. 197–199°C; ^{1}H NMR (400 MHz; $CDCl_3$): δ=7.50 (dd, *J*=5.0, 1.3 Hz, 1H), 7.13 (dd, *J*=5.1, 3.5 Hz, 1H), 6.99 (dd, *J*=3.5, 1.3 Hz, 1H), 6.00 (s, 2H), 2.55 (s, 6H), 1.58 ppm (s, 6H); ^{13}C NMR (100 MHz; $CDCl_3$): δ=156.07, 143.50, 134.64, 133.99, 132.41, 127.81, 127.61, 127.41, 121.50, 14.64, 13.55 ppm; UV/Vis (CH_2Cl_2): λ_{max} (ε)=514 nm (74 100); HRMS (ESI): *m/z* calcd for $C_{17}H_{17}BF_2N_2NaS$: 352.1102 [M^++Na]; found: 352.1094.

Crystal data and refinement

Diffraction data were collected at low temperature (90 or 100 K) on either a Nonius KappaCCD diffractometer equipped with MoKα radiation (λ=0.71073 Å) or a Bruker Kappa Apex-II DUO diffractometer equipped with Mo or $Cu_{K\alpha}$ radiation (λ=1.54184 Å).

Refinement was by full-matrix least squares using SHELXL, with H atoms in idealized positions. Compound **4b** has three independent molecules. Compound **19** lies on a mirror plane in the crystal, and its central Me group is disordered into two conformations. Disorder of the thiophene was present in **25**, and the crystal of **17** was a non-merohedral twin.

Crystal data—For **4a**: $C_{13}H_{14}BClF_2N_2$; monoclinic; $P2_1/c$; a= 8.6711(17), b=12.274(3), c=11.850(2) Å; β=97.570(8)°; Z=4; T= 100 K; R=0.040. **4b**: $C_{17}H_{22}BClF_2N_2$; triclinic; $P1$; a=8.6228(5), b= 12.4360(7), c=12.4491(6) Å; α=93.806(3), β=107.076(3), γ= 100.514(3)°; Z=3; T=100 K; R=0.052. **5a**: $C_{15}H_{19}BF_2N_2O$; monoclinic; $P2_1/n$; a=10.5564(9), b=11.8910(10), c=12.4508(14) Å; β= 112.982(4)°; Z=4; T=90 K; R=0.036. **5b**: $C_{19}H_{27}BF_2N_2O$; monoclinic; Cc; a=13.9165(9), b=17.1597(10), c=8.4065(5) Å; β= 114.970(5)°; Z=4; T=100 K; R=0.034. **16**: $C_{20}H_{18}BF_2N_3S_2$; monoclinic; $P2_1/c$; a=11.7044(17), b=14.871(2), c=10.9035(17) Å; β= 93.116(10)°; Z=4; T=100 K; R=0.038. **17**: $C_{16}H_{27}B_{11}F_2N_2S$; monoclinic; $P2_1/c$; a=13.8364(9), b=13.3718(11), c=12.0936(12) Å; β= 93.295(6)°; Z=4; T=100 K; R=0.136. **18**: $C_{19}H_{19}BF_2N_2$; monoclinic; $P2_1/n$, a=11.812(3), b=7.0804(17), c=19.362(5) Å; β=99.545(14)°; Z=4; T=100 K, R=0.049. **19**: $C_{14}H_{17}BF_2N_2$; orthorhombic; $Pnma$; a=11.3154(16), b=7.0396(10), c=16.013(2) Å; Z=4; T=100 K; R= 0.039. **20**: $C_{15}H_{17}BF_2N_2$; monoclinic; $P2_1/n$; a=10.0991(5), b= 11.7547(6), c=11.9808(7) Å; β=107.886(3)°; Z=4; T=100 K; R= 0.046. **24**: $C_{18}H_{20}BF_2N_3$; monoclinic; $P2_1$; a=7.2814(11), b= 12.4570(19), c=9.2579(15) Å; β=100.858(8)°; Z=2; T=100 K; R= 0.042. **25**: $C_{17}H_{17}BF_2N_2S$; monoclinic; $P2_1/c$; a=6.6072(10), b= 18.543(2), c=12.7436(15) Å; β=92.804(6)°; Z=4; T=90 K; R= 0.034. CCDC-959961–959970, 959972 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Steady-state absorption and fluorescence spectroscopy

The absorption measurements were carried out on an Agilent 8453 spectrophotometer and the steady-state fluorescence spectroscopic studies were performed in dichloromethane on a PTI Quanta-Master4/2006SE spectrofluorimeter. The slit width was 3 nm for both the excitation and emission. For the fluorescence quantum yield measurements, dilute solutions with absorbance between 0.04–0.06 at the excitation wavelength were used. The fluorescence quantum yields of BODIPYs were obtained by comparing the area under the corrected emission spectrum of the test sample with that of rhodamine 6G in ethanol. All spectra were recorded at room temperature by using non-degassed samples, spectroscopic grade solvents and a 10 mm quartz cuvette.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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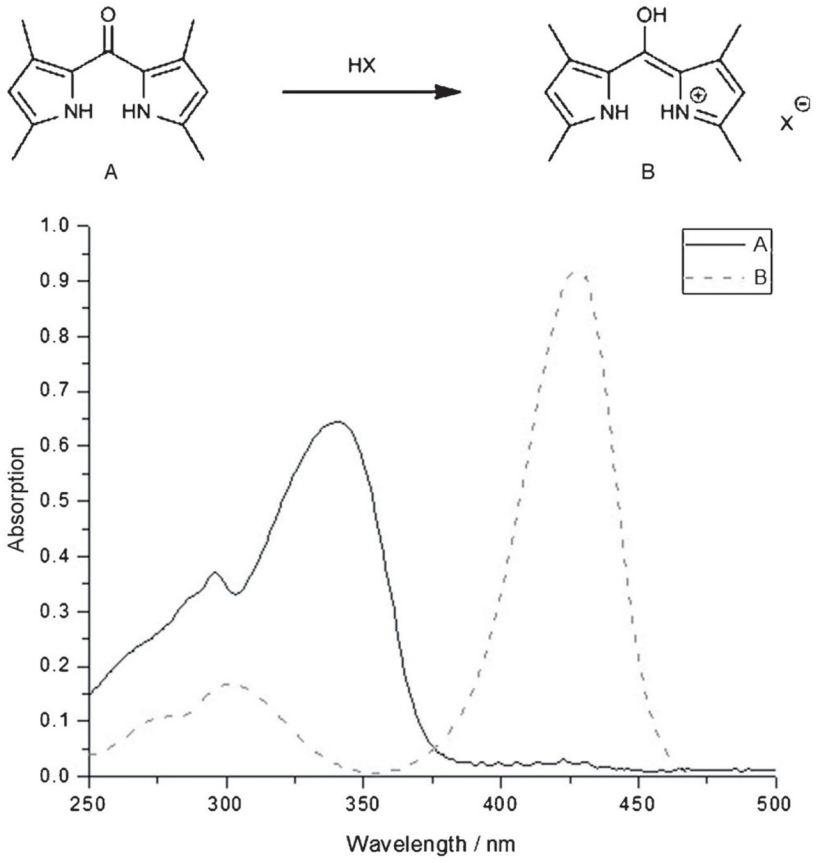


Figure 1.

Optical spectra, in dichloromethane, of dipyrrylketone (**A**) and dipyrrinium salt (**B**) after treatment with HCl (g).

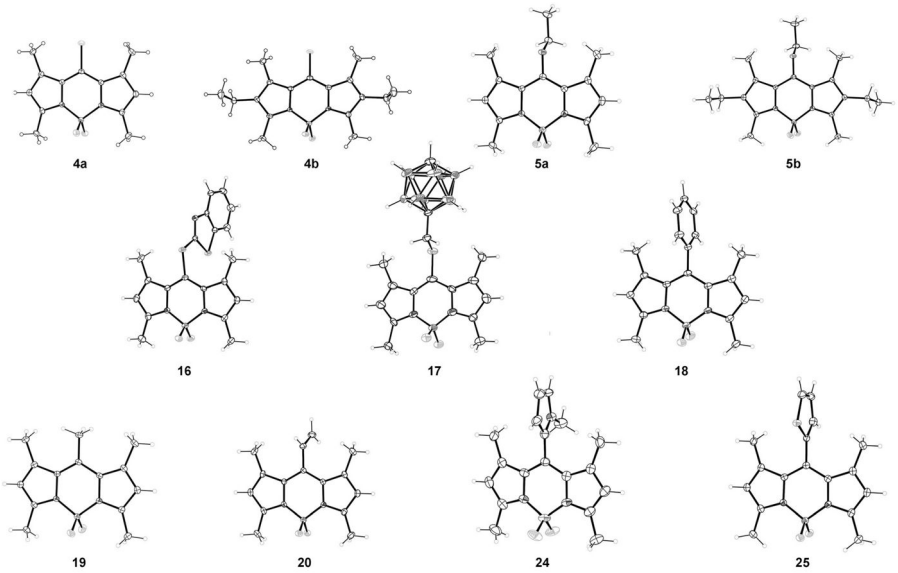


Figure 2.
Molecular structures of some BODIPY products.

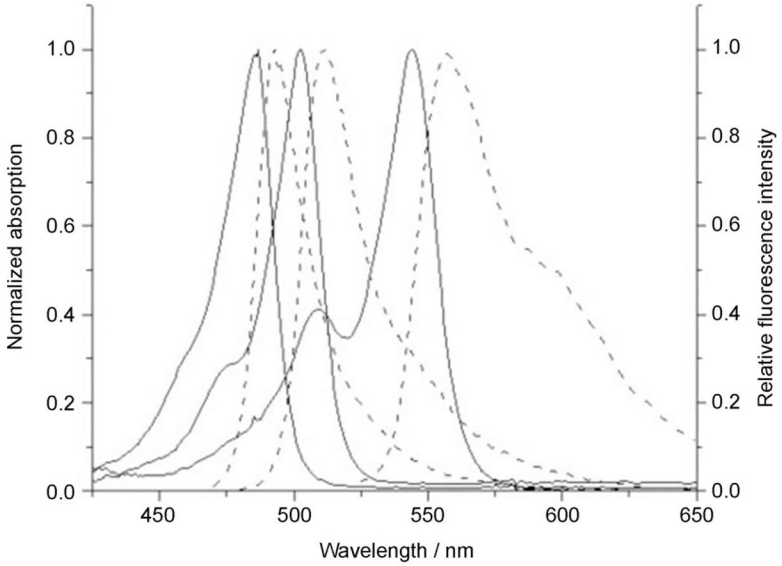
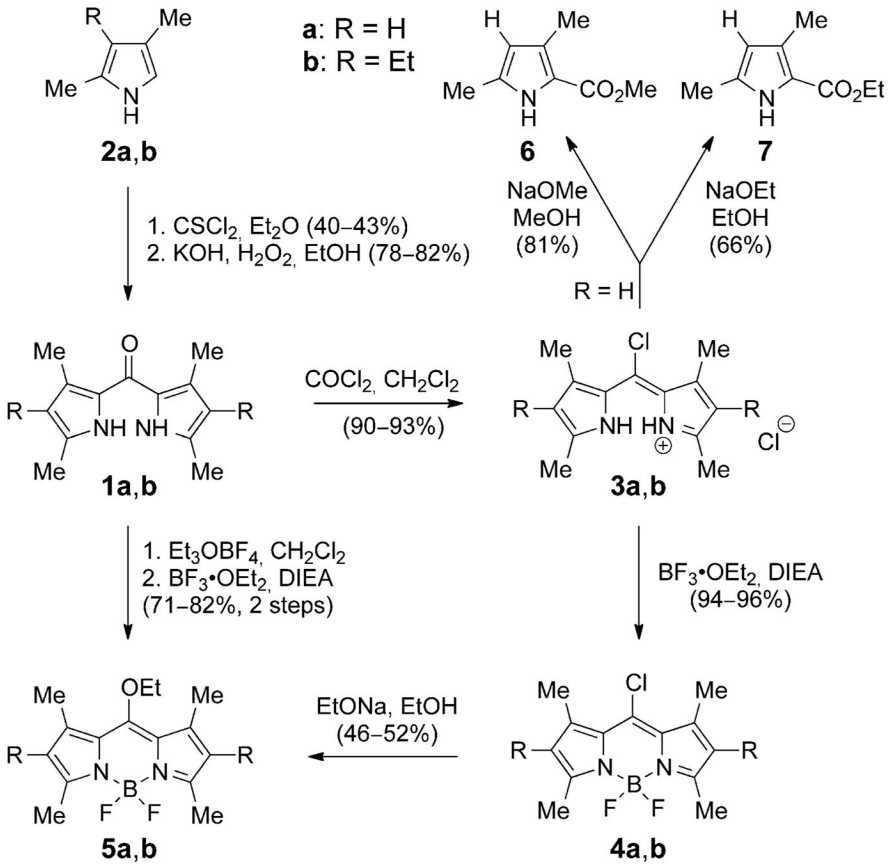


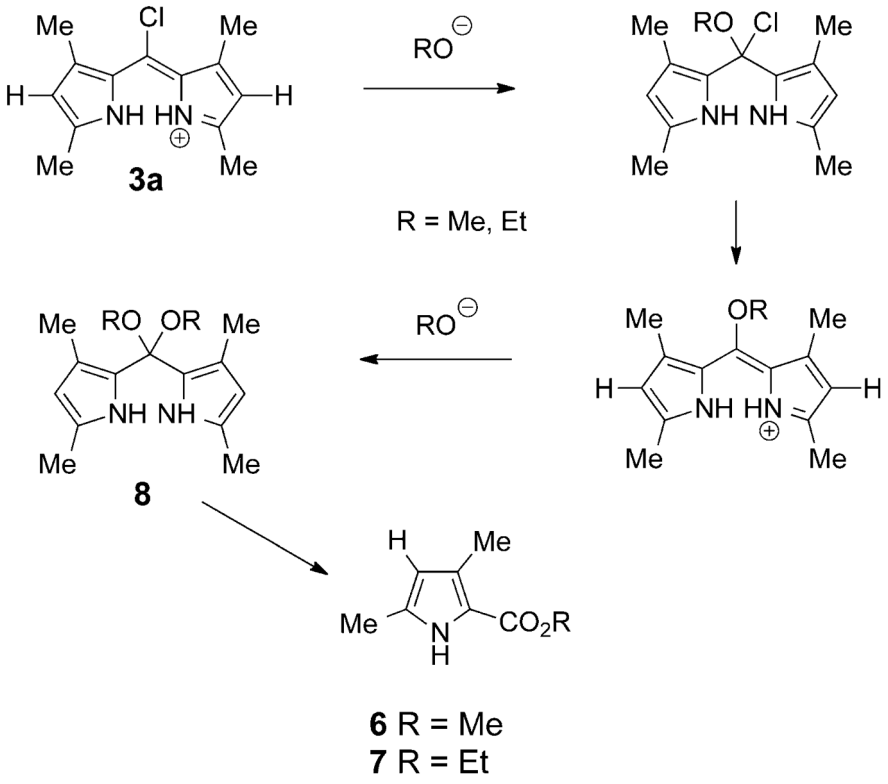
Figure 3.

Normalized UV/Vis absorption (solid line) and fluorescence emission spectra (dashed line) of selected BODIPYs **5a**, **4a**, and **22** (left to right), in dichloromethane.



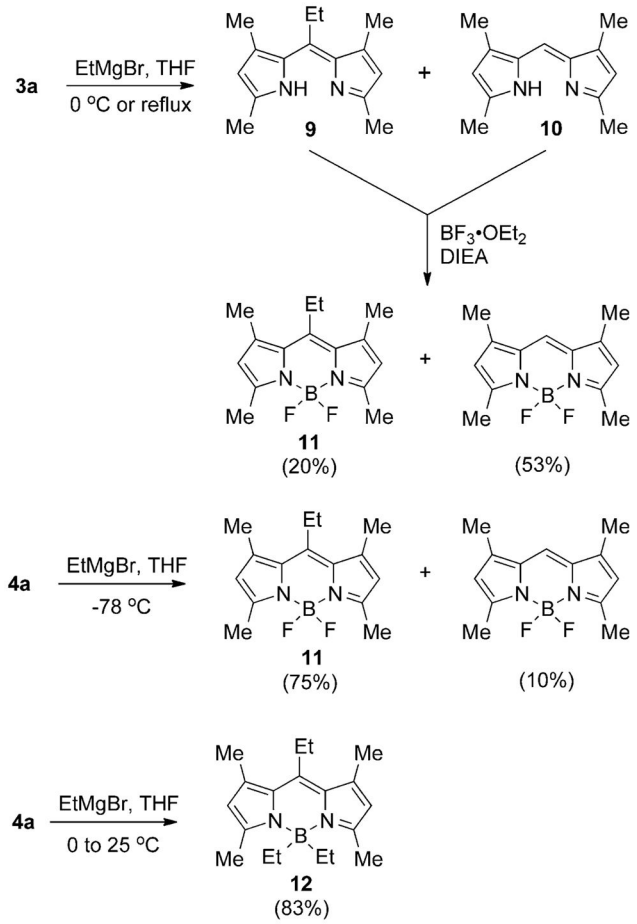
Scheme 1.

Synthesis of 5-chloro-dipyrrins **3** and BODIPYs **4** and **5**.



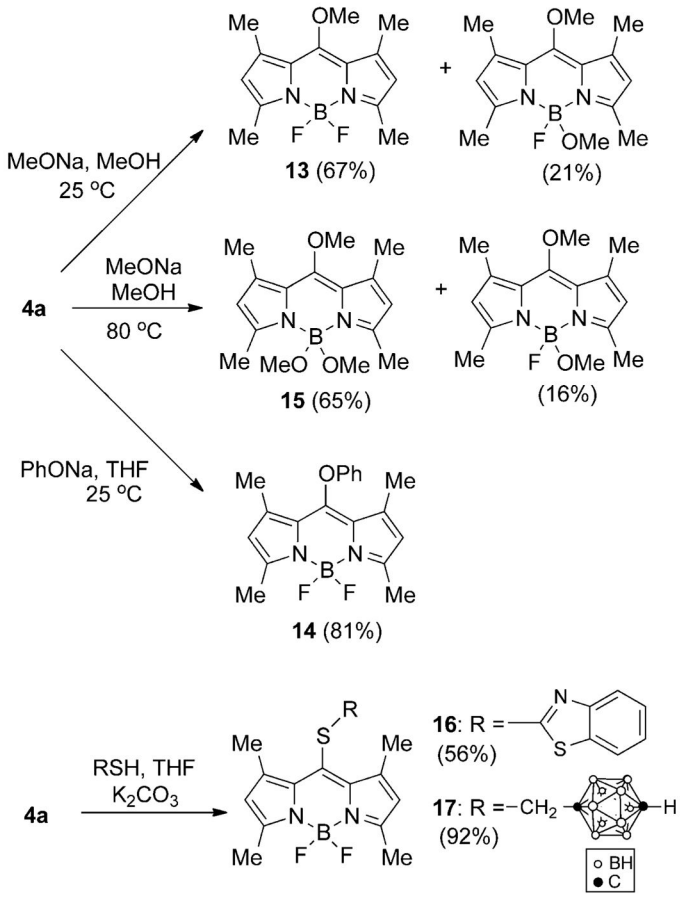
Scheme 2.

Proposed mechanism for the conversion of **3a** into **6** and **7**.



Scheme 3.

Reactions of chlorinated **3a** and **4a** with Grignard reagents.

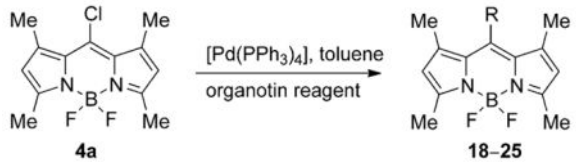


Scheme 4.

Nucleophilic substitutions/eliminations of BODIPY **4a**.

Table 1

Stille coupling reactions of 8-chloro-BODIPY **4a**.



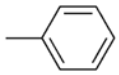
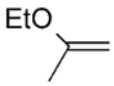
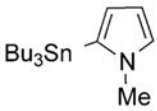
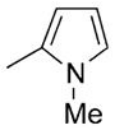
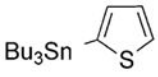
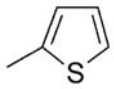
BODIPY	Organotin	R	Yield [%]
18	Bu_3SnPh		93
19	Me_4Sn	—CH_3	97
20	$Bu_3Sn(CH{=}CH_2)$		97
21	$Bu_3Sn(EtOC{=}CH_2)$		93
22	$Bu_3Sn(C{\equiv}CH)$	—C≡CH	31
23	Bu_3Sn-C≡C–$Si(Me)_3$	—C≡C–$Si(Me)_3$	71
24			95
25			99

Table 2

Spectral properties of BODIPYs in dichloromethane solution at room temperature. The fluorescence quantum yields (λ_{exc}=490 nm) were calculated by using, rhodamine 6G (0.80 in ethanol) as the reference.

BODIPY	Absorbance λ_{max} [nm]	Emission λ_{max} [nm]	Φ_f	Log ε [$M^{-1}cm^{-1}$]
4a	503	512	0.51	4.79
4b	527	542	0.33	4.50
5a	487	493	0.99	4.77
5b	508	518	0.67	4.44
11	499	505	0.83	4.75
12	499	507	0.32	4.20
13	487	493	0.57	4.95
14	491	499	0.99	4.71
15	487	496	1.00	4.67
16	539	553	0.04	4.69
17	529	542	0.09	4.23
18	501	511	0.62	4.76
19	497	508	0.77	4.82
20	505	511	0.00	4.67
21	513	522	0.14	4.61
22	544	556	0.29	4.57
23	545	556	0.13	4.63
24	513	521	0.10	4.73
25	514	521	0.05	4.87