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8-Alkenylborondipyrromethene dyes. General synthesis, optical properties, and preliminary study of their reactivity

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ABSTRACT

A new series of 8-alkenylBODIPY dyes were prepared via the Liebeskind–Srogl cross-coupling starting from 8-thiomethyl-substituted BODIPY. Ten derivatives were prepared using alkenylboronic acids in good to excellent yields (79–97%), and one additional example was prepared from an alkenylstannane in 74% yield. The products display Michael acceptor-like reactivity. The alkenyl fragment quenches the fluorescence of the BODIPY core, which is turned back on by reducing the double bond.

1. Introduction

Among the known compounds that exhibit fluorescence, borondipyrromethene (BODIPY[1]) dyes occupy a privileged position. Regarded as little more than a curiosity for over two decades,[2] these compounds have evolved to become some of the most widely used dyes in the scientific literature.[3] Among their most useful properties are: highly colored, display narrow absorption bands, they can be tailor-made to vary both the quantum yield (Φ_F) and emission wavelength (λ_{em}).[4]

The success of new BODIPY-based applications depends to a great extent on the ability to modify its core structure either to change the absorption/emission properties or increase Φ_F. Of similar relevance is the possibility to incorporate to the dye core functional groups that would permit the tagging of targets, such as biomolecules, polymers, etc., under mild conditions. To that end, we have described a new methodology to prepare a variety of BODIPY dyes starting from 8-thiomethylbodipy **1** (Fig. 1).[5]

Herein we report an extension of the methodology illustrated in Fig. 1 to prepare a series of 8-alkenyl-BODIPY dyes **2** in high yields. Why would these derivatives be important? When one realizes that the BODIPY nucleus is a strong electron-withdrawing moiety, one may next conclude that the double bond at the *meso*-position is highly activated in analogy to those of α,β-unsaturated carbonyl compounds (Fig. 2). In theory, then, it could be envisioned to

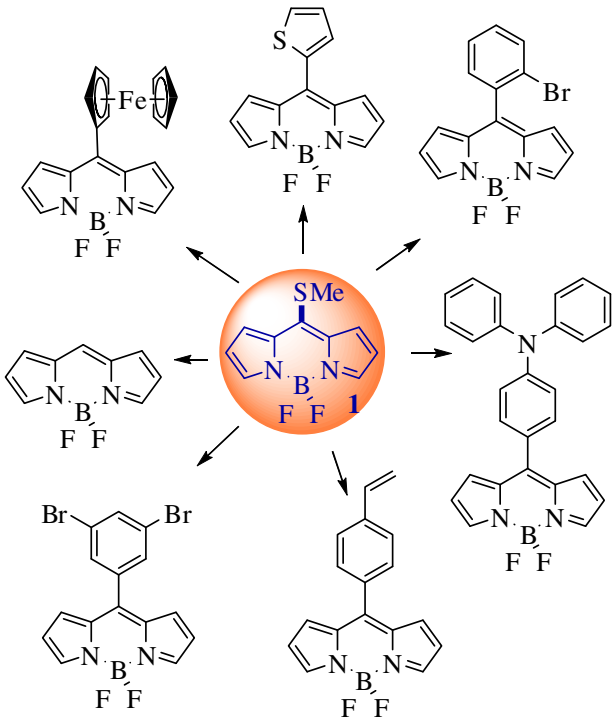

Fig. 1. Selected BODIPY derivatives prepared from **1**.

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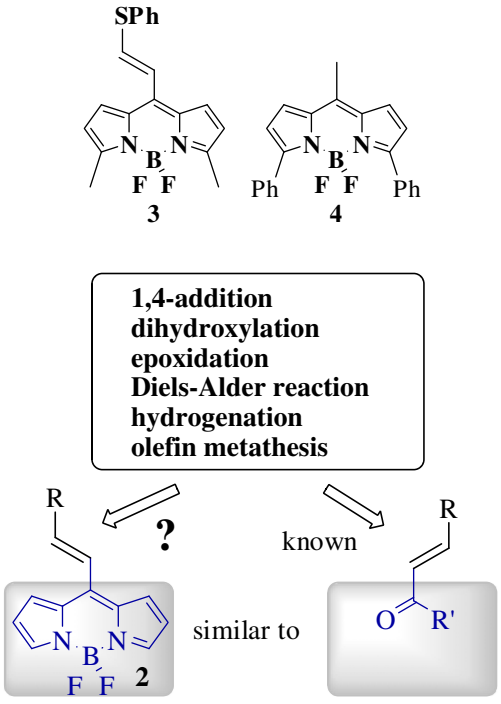


Fig. 2. Analogy between the electronic properties of **2** and those of an α,β-unsaturated carbonyl compound.

subject the double-bond of **2** to the well-known chemistry of the activated double-bonds to generate a potentially very useful novel family of highly functionalized fluorescent dyes.

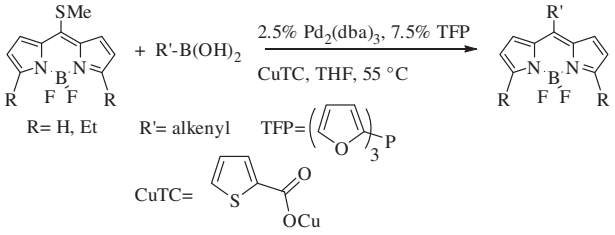
To the best of our knowledge, there are only three reports that describe the preparation of 8-alkenyl-BODIPYs in addition to the two examples we described earlier.[5a] In one report, Biellmannet al. describe the synthesis and optical properties of **3**.[6] In the others, Kovtun et al. describe a method to prepare 8-alkenyl-substituted BODIPYs via a Knoevenagel-type condensation starting from **4**.[7]

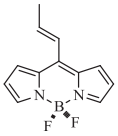
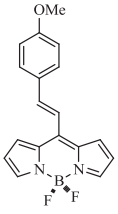
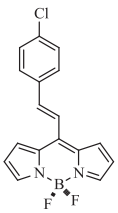
2. Results and discussion

The Liebeskind–Srogl[8] cross-coupling (LSCC, the Pd-catalyzed, Cu(I)-mediated cross-coupling reaction of either a sulfonium salt or a thioether with organostannanes or boronic acids) conditions used to obtain 8-aryl-BODIPYs[5a] were applied to synthesize the target compounds (Table 1).

It was demonstrated that the LSCC is a powerful methodology not only to functionalize the *meso*-position with aryl and heteroaryl groups, but also with alkenyl fragments. All of the alkenylboronic acid tested coupled very efficiently (63–97%) in remarkably short reaction times. The electronic properties of the phenyl-containing alkenylboronic acid did not have a detrimental effect on the yield (entries 2, 3, 4, and 6) since both electron-rich and electron-deficient phenyl groups reacted as efficiently. Steric factors did not seem to negatively affect the yields either (entries 5, 8, and 10), except for the somewhat longer reaction time in entry 8. Alkyl-substitution on the 3- and 5-BODIPY positions did not appear to have a significant effect on the overall process. No *cis–trans*

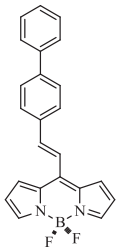
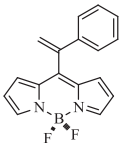
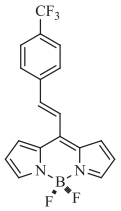
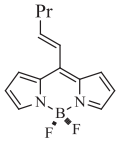
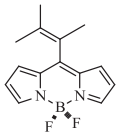
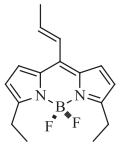
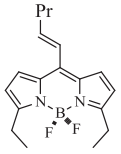
Table 1
Synthesis of 8-alkenylBODIPY dyes using the Liebeskind–Srogl cross-coupling reaction



Entry	Product	Cmpd (yield)[a]
1		5 (97)
2		6 (95)
3		7 (96)

(*continued on next page*)

Table 1 (*continued*)

Entry	Product	Cmpd (yield)[a]
4		8 (84)
5		9 (88)
6		10 (90)
7		11 (80)
8		12 (88)
9		13 (84)
10		14 (79)

[a] Isolated yield.

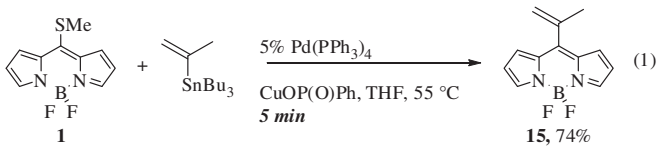
isomerization was observed in any case in the ^{1}H NMR spectrum of the crude material.

In addition to the examples shown in Table 1, one more reaction was carried out to evaluate the reactivity of **1** with one alkenylstannane (Eq. 1).

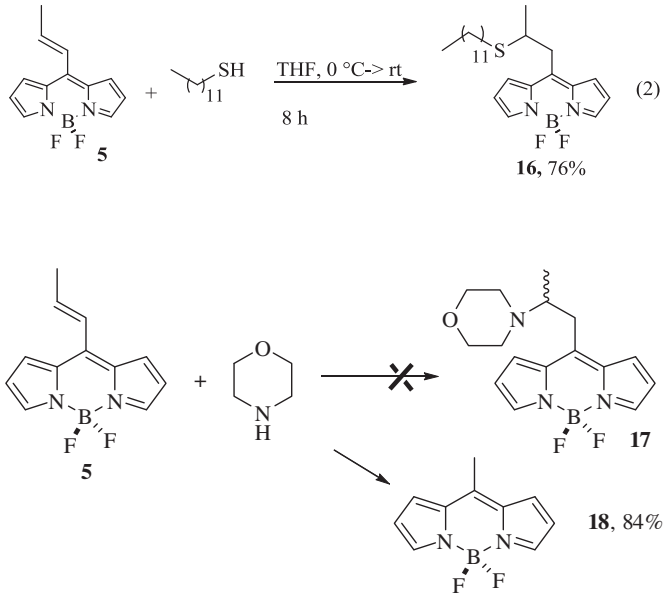
Thus, 8-(1-methylethenyl)BODIPY **15** was obtained in good yield after only 5 min.[9]

Next, it was decided to evaluate the reactivity of the double-bond of **5** toward Michael-type nucleophilic addition. In this context, dodecane-1-thiol was added to **5** under mild conditions to give the expected adduct **16** in 76% (Eq. 2) confirming the foreseen reactivity.

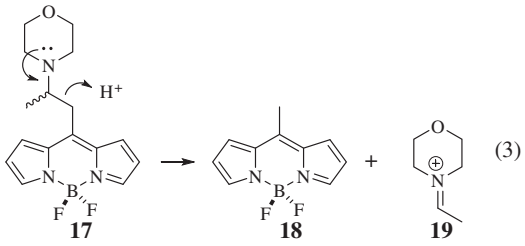
An interesting observation was made when trying to add secondary amines to **5** (Scheme 1).



Instead of forming morpholine adduct **17**, highly fluorescent 8-methylBODIPY[10] **18** was isolated in 84% yield, presumably, via a retro-aza–aldol type process (Eq. 3).[11] No attempt to trap iminium salt **19** was made.



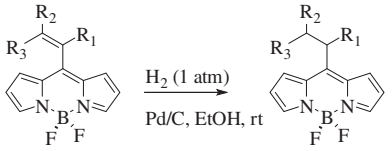
Scheme 1. Attempted addition of morpholine to **5**.



Additional insight of the reactivity of this BODIPY family was gained after a selected number of alkenyl derivatives was subjected to Pd-catalyzed hydrogenation conditions (Table 2).

Pd-catalyzed reduction took place smoothly at 1 atm to furnished 8-alkylBODIPYs **20**–**23** in good yields and reaction times (20 min → 1.5 h). BODIPY 12 (entry 4) failed to react under these conditions, presumably due to the higher steric demand of the double bond.

Table 2
Pd-catalyzed reduction of some alkenylBODIPYs



Entry	BODIPY starting material	Yield[a] %	Product
1	5	80	**20**
2	9	62[b]	**21**
3	11	75	**22**
4	12	n.r.	—
5	15	70[c]	**23**

[a] Isolated yields.
[b] Run at 35 °C.
[c] This reaction was run at 0 °C, otherwise the yield decreased.

3. Optical properties

The optical properties of selected derivatives prepared in this work were determined (Table 3).

The BODIPY derivatives containing alkenyl functionalities at the *meso*-position, i.e., **5**, **11**, and **9**, show 'redder' absorption (~7 nm) and emission (17–41 nm) than their parent molecule **24**, suggestive of their high conjugation. Their emission efficiencies (Φ_F's), however, decreased dramatically from 15- to 110-fold. Compound **13** is the analogue of **5** with two ethyl groups at the 3,5-positions and its absorption maximum is 21 nm red-shifted from that of **5**. Surprisingly, it is completely nonluminescent in THF. Similar phenomenon was observed in **10** with electron-withdrawing trifluoromethyl groups. On the other hand, the absorption and emission behaviors of molecules with sp^3-hybridized carbons at the *meso*-position display remarkable high Φ_F. Compounds **20**, **21**, **23**, and **16** have similar properties to those of **24**. They all absorb at around 500 nm and emit at 511–519 nm with small Stoke's shift (14–21 nm). Except for **20**, with the highest Φ_F, they display similar Φ_F values to that of the parent system **24**.

Table 3
Optical properties of selected products[a]

Compd	λ_{ab}	λ_{em}[b]	$\%\Phi_F$
24	500	516	77[c]
5	507	554	5
11	507	557	4
9	506	533	1
13	521	Nil[d]	—
10	519	Nil[d]	—
20	494	515	91
21	501	515	78
23	496	511	78
16	499	519	75

[a] Measured in THF solutions, concentration=10 μM. Abbreviations: λ_{ab}=absorption maximum, λ_{em}=emission maximum, Φ_F=fluorescence quantum yield estimated using fluorescein as standard (Φ_F=79% in 0.1 M NaOH aqueous solution).
[b] Excited at their absorption maxima.
[c] Taken from Ref. 5b as comparison.
[d] Not determined because of the non-emissive nature of the dye molecules.

Fig. 3 shows the visual observations of THF solutions of **5** and **20** taken under day light and UV light. The THF solution of **5** is orange-red and emit faintly under UV light. On the contrary, its saturated structural counterpart **20** gives intense green light under UV irradiation. In going from **5** to **20**, the Φ_F value is boosted 18-fold, which is even higher than that of **24**.

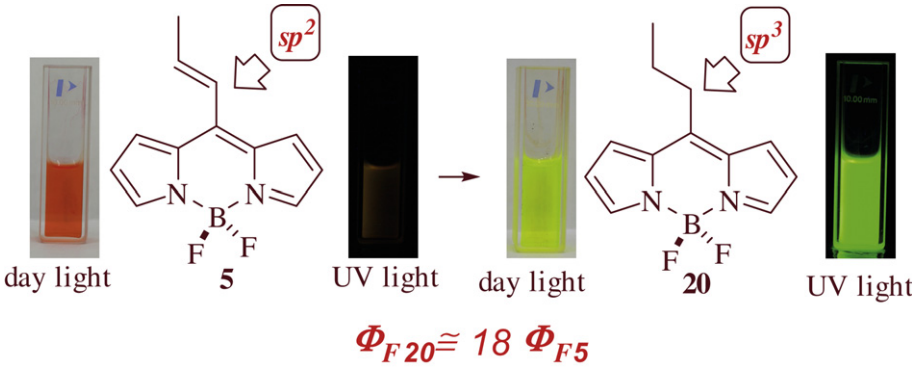


Fig. 3. Change in optical properties in going from an 8-akenylBODIPY to an 8-alkylBODIPY.

4. Conclusions

In summary, we have extended the applications of the LiebeskindeSrogl cross-coupling to the preparation of a series of 8-alkenylBODIPY dyes. The reactivity of the components is excellent since the reaction times varied from 5 min to less than 1 h. Selected products were smoothly reduced to the corresponding 8-alkylBODIPY analogues. The new alkenylBODIPY derivatives display Michael acceptor-like reactivity. Although the double-bond quenches the fluorescence of the BODIPY core, it is turned back on by reducing the alkenyl moiety. This property hints at the potential applications of these derivatives as chemodosimeters in relevant bioreductive processes. In the course of this work, an indirect and efficient synthesis of highly fluorescent 8-methylBODIPY was discovered.

5. Experimental section

5.1. Measurements

^{1}H and ^{13}C NMR spectra were recorded on a 200 MHz spectrometer in deuteriochloroform ($CDCl_3$) with either tetramethylsilane (TMS) (0.00 ppm ^{1}H, 0.00 ppm ^{13}C) or chloroform (7.26 ppm ^{1}H, 77.00 ppm ^{13}C) as internal reference unless otherwise stated. Data are reported in the following order: chemical shift in ppm, multiplicities (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), sex (sextet), hex (hextet), m (multiplet), exch (exchangeable), app (apparent)), coupling constants, *J* (Hz), and integration. IR peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67–100%), m (medium 40–67%), and w (weak 20–40%). Melting points are not corrected. High-resolution mass spectra of chromatographically homogeneous samples were obtained at 70 eV. Analytical thin-layer chromatography was performed on silica gel plates with F-254 indicator. THF was dried over activated 4 Å molecular sieves. All reactions were performed under a dry N_2 atmosphere in oven- and or flame-dried glassware.

5.2. Starting materials

8-Thiomethylbodipy **1**, its 3,5-diethyl analogue[6] and CuTC,[12] were prepared according to the literature procedures. All of the other reactants, ligands, and catalysts were commercially available.

5.3. Typical procedure (TP) for the cross-coupling of 8-thiomethylBODIPY with boronic acids

All of the reactions started with 0.084 mmol (20.0 mg) of thiomethylbodipy **1** or, 0.068 mmol (20.0 mg) of diethyl thiomethylbodipy, as limiting reagent and the other components of the reaction were added in the amounts stated in the TP. An oven-dry Schlenk tube, equipped with a stir bar, was charged with the boronic acid (3 equiv), thiomethylbodipy **1** (1 equiv) and dry THF (2 mL) under N_2. The stirred solution was sparged with N_2 for 10 min, whereupon CuTC (3 equiv), $Pd_2(dba)_3$ (2.5 mol %), and TFP (7.5 mol %) were added under N_2. The reaction mixture was immersed into a pre-heated oil bath at 55 °C. After TLC showed that the reaction went to completion, the reaction mixture was allowed to reach room temperature and was adsorbed on SiO_2-gel.

After flash-chromatography (SiO_2-gel, EtOAc/hexanes gradient) purification, *meso* substituted BODIPYs were obtained as highly-colored crystalline solids or oils. For purposes of characterization, the solid products were crystallized from CH_2Cl_2/petroleum ether.

*5.3.1. BODIPY **5**[5a].* According to TP. Reaction time: 20 min. TLC (20% EtOAc/hexanes) R_f=0.3; dark cherry crystals; mp 137–138 °C; yield=97%; IR (KBr, cm^{-1}): 1636 (m), 1546 (s), 1473 (w), 1411 (s), 1392 (s), 1351 (w), 1260 (m), 1205 (m), 1120 (s), 1072 (s), 961 (m), 774 (w); ^{1}H NMR: δ 7.86 (s, 2H), 7.27–7.25 (m, 2H), 6.85–6.61 (m, 2H), 6.60–6.40 (m, 2H), 2.09 (d, *J*=5.4 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.3, 144.1, 143.2, 133.9, 128.8, 124.8, 117.9, 20.2; HRMS FABS ($M+H^+$) calcd for $C_{12}H_{12}BF_2N_2$: 233.1061. Found 233.1066.

*5.3.2. BODIPY **6**[5a].* According to TP. Reaction time 15 min. TLC (20% EtOAc/hexanes) R_f=0.8; dark red needles; mp 166–167 °C; yield=95%; ^{1}H NMR: d 7.87 (s, 2H), 7.56 (d, *J*=8.8 Hz, 2H), 7.53 (d, *J*=14.2 Hz, 1H), 7.37 (s, 2H), 7.32 (d, *J*=12.0 Hz, 1H), 7.00 (d, *J*=9.0 Hz, 2H), 6.56 (m, 2H); δ ^{13}C (50 MHz, $CDCl_3$): δ 162.0, 145.2, 144.5, 142.5, 133.9, 130.1, 128.7, 128.0, 119.1, 117.7, 114.9, 55.7; HRMS FABS ($M+H^+$) calcd for $C_{18}H_{16}BF_2N_2O$: calcd 325.1323. Found 325.1319.

*5.3.3. BODIPY **7**.* According to TP. Reaction time 15 min. TLC (20% EtOAc/hexanes) R_f=0.6; cherry crystals; mp 174–175 °C; yield=96%; IR (KBr, cm^{-1}): 1621(w), 1547 (m), 1529 (w), 1489 (w), 1470 (w), 1411 (m), 1392 (m), 1268 (w), 1195 (w), 1121 (m), 1078 (s), 962 (m), 951(m), 785(w), 755(w); ^{1}H NMR: δ 7.90 (s, 2H), 7.56 (d, *J*=8 Hz, 2H), 7.47–7.42 (m, 4H), 7.34 (d, *J*=4.0 Hz, 2H), 6.58 (d, *J*=4.2 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 143.5, 143.2, 136.7, 134.2, 134.0, 129.7, 129.3, 128.5, 121.8, 118.3; HRMS FABS ($M+H^+$) calcd for $C_{17}H_{13}BClF_2N_2$: 329.0828. Found 329.0821.

*5.3.4. BODIPY **8**.* According to TP. Reaction time 20 min. TLC (20% EtOAc/hexanes) R_f=0.6; bright red crystals; mp 168–169 °C; yield=84%; IR (KBr, cm^{-1}): 3106 (w), 1616 (m), 1547 (s), 1473 (w), 1410 (s), 1393 (m), 1353 (w), 1262 (m), 1195 (w), 1116 (s), 1080 (s), 1044 (m), 965 (m), 948 (m), 768 (m); ^{1}H NMR: δ 7.90 (s, 2H), 7.71–7.62 (m, 6H), 7.55–7.43 (m, 5H), 7.40 (d, *J*=4.2 Hz, 2H), 6.58 (d, *J*=4.0 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.6, 144.0, 143.6, 143.1, 140.2, 134.7, 134.1, 129.2, 128.7, 128.3, 128.0, 127.3, 121.3, 118.0;

HRMS FABS ($M+H^+$) calcd for $C_{23}H_{18}BF_2N_2$: 371.1531. Found 371.1534.

*5.3.5. BODIPY **9**.* According to TP. Reaction time 30 min. TLC (20% EtOAc/hexanes) R_f=0.6; orange solid; mp 133–135 °C; yield=88%; IR (KBr, cm^{-1}): 2923 (w), 1548 (s), 1477 (w), 1412 (m), 1386 (s), 1353 (w), 1258 (m), 1179 (w), 1112 (s), 1077 (s), 946 (m), 779 (m), 762 (m), 745(m); ^1H NMR: δ 7.91 (s, 2H), 7.43–7.33 (m, 5H), 6.98 (d, J=4.2, Hz, 2H), 6.47 (d, J=3.6 Hz, 2H), 6.07 (s, 1H), 5.60 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.7, 142.4, 140.3, 135.5, 131.1, 129.2, 129.1, 129.0, 127.1, 121.0, 118.6; HRMS FABS ($M+H^+$) calcd for $C_{17}H_{14}BF_2N_2$: 295.1218. Found 295.1212.

*5.3.6. BODIPY **10**.* According to TP. Reaction time 20 min. TLC (20% EtOAc/hexanes) R_f=0.7; bright cherry crystals; mp 164–166 °C; yield=80%; IR (KBr, cm^{-1}): 1625 (m), 1577 (w), 1551 (s), 1473 (w), 1412 (s), 1395 (s), 1322 (s), 1266 (w), 1198 (m), 1154 (m), 1120 (s), 1080 (s), 1066 (s), 963 (m), 953 (m), 826 (w), 784 (w), 743 (w); ^1H NMR: δ 7.92 (s, 2H), 7.72 (s, 4H), 7.49 (s, 2H), 7.35 (d, J=4.2 Hz, 2H), 6.59 (d, J=3.2 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.0, 142.9, 142.4, 138.9, 134.0, 132.3, 131.9, 128.7, 128.2, 126.3, 123.6, 118.5; LRMS ($C_{18}H_{12}BF_5N_2$) calcd 362.101 found 362.104. Anal. Calcd: C, 59.70; H, 3.34; N, 7.74. Found: C, 59.66; H, 3.31; N, 7.76.

*5.3.7. BODIPY **11**.* According to TP. Reaction time 10 min. TLC (20% EtOAc/hexanes) R_f=0.7; bright red needles; mp 78–79 °C; yield=89%; IR (KBr, cm^{-1}): 2962 (w), 2926 (w), 2873 (w), 1634 (m), 1555 (s), 1411 (s), 1397 (s), 1269 (m), 1208 (m), 1120 (s), 1084 (s), 1034 (m), 961 (m), 759 (m), 721 (w); ^1H NMR: δ 7.86 (s, 2H), 7.25 (m, 2H), 6.84–6.72 (m, 2H), 6.53 (d, J=3.2 Hz, 2H), 2.4–2.2 (m, 2H), 1.65–1.40 (m, 2H), 1.03 (t, J=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 149.3, 144.6, 143.2134.0, 128.7, 123.6, 118.0, 36.4, 22.1, 14.0; HRMS FABS ($M+H^+$) calcd for $C_{14}H_{16}BF_2N_2$: 261.1375. Found 261.1379.

*5.3.8. BODIPY **12**.* According to TP. Reaction time 53 min. TLC (20% EtOAc/hexanes) R_f=0.5; orange oil; yield=88%; IR (KBr, cm^{-1}): 3112 (w), 2980 (w), 2920 (w), 2852 (w), 1555 (s), 1477 (w), 1411 (m), 1387 (s), 1356 (m), 1259 (s), 1203 (m), 1149 (m), 1111 (s), 1072 (s), 980 (m), 936 (m), 780 (m), 744 (m), 652 (w), 586 (w), 537 (w), 417 (w); ^1H NMR: δ 7.84 (s, 2H), 7.02 (d, J=4.0 Hz, 2H), 6.49 (d, J=3.2 Hz, 2H), 2.05 (s, 3H), 1.91 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 152.4, 143.7, 134.6, 133.9, 129.7, 122.7, 118.3, 23.0, 21.9, 20.4; HRMS FABS ($M+H^+$) calcd for $C_{14}H_{16}BF_2N_2$: 261.1375. Found 261.1277.

*5.3.9. BODIPY **13**.* According to TP. Reaction time 10 min. TLC (20% EtOAc/hexanes) R_f=0.6; dark bright crystals; mp 104–106 °C; yield=84%; IR (KBr, cm^{-1}): 2969 (w), 1575 (m), 1485 (m), 1431 (w), 1327 (w), 1199 (w), 1128 (s), 1056 (m), 1010 (w), 970 (s), 801 (s), 714 (w); ^1H NMR: δ 7.12 (d, J=4.0 Hz, 2H) 6.71–6.43 (m, 2H), 6.34 (d, J=4.2 Hz, 2H), 3.05 (q, J=7.4 Hz, 4H), 2.03 (d, J=1.2 Hz, 3H), 1.33 (t, J=7.6 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 162.7, 140.8, 140.1, 133.3, 128.0, 124.5, 116.7, 22.2, 19.8, 13.0; HRMS FABS ($M+H^+$) calcd for $C_{16}H_{20}BF_2N_2$: 289.1687. Found 289.1681.

*5.3.10. BODIPY **14**.* According to TP. Reaction time 35 min. TLC (20% EtOAc/hexanes) R_f=0.8; dark bright crystals; mp 52–53 °C; yield=79%; IR (KBr, cm^{-1}): 2968 (m), 2932 (m), 2874 (m), 1641 (m), 1553 (s), 1487 (s), 1461 (m), 1437 (s), 1400 (m), 1378 (m), 1341 (m), 1319 (s), 1256 (s), 1226 (s), 1197 (m), 1129 (s), 1083 (s), 1051 (s), 1011 (s), 967 (s), 939 (s), 881 (m), 799 (m), 753 (m), 716 (m), 513 (m); ^1H NMR: δ 7.10 (d, J=4.0 Hz, 2H), 6.68–6.41 (m, 2H), 6.33 (d, J=4.4 Hz, 2H), 3.04 (q, J=7.6 Hz, 4H), 2.31 (q, J=7.2 Hz, 2H), 1.57 (sext, J=7.2 Hz, 2H), 1.32 (t, J=7.6 Hz, 6H), 0.99 (t, J=7.4 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 162.7, 146.0, 140.2, 133.3, 127.9, 123.3, 116.6, 36.2, 22.2, 13.9, 13.0; HRMS FABS ($M+H^+$) calcd for $C_{18}H_{24}BF_2N_2$: 317.2001. Found 317.2008.

5.4. Synthesis of BODIPY 15

An oven-dry Schlenk tube, equipped with a stir bar, was charged with the 2-(tributylstannyl) propene (83.8 μL, 0.2520 mmol), thiomethylbodipy **1** (20 mg, 0.0840 mmol), and dry THF (2 mL) under N_2. The stirred solution was sparged with N_2 for 10 min, whereupon copper (I) diphenylphosphinate (70.8 mg, 0.2520 mmol), and tetrakis(triphenylphosphine)palladium (0) (5.4 mg, 0.0042 mmol) were added under N_2. The reaction mixture was immersed into a pre-heated oil bath at 55 °C for 5 min, after which it was cooled down to room temperature and the solvent was removed in vacuo. The product was purified by Flash chromatography (silica-gel, AcOEt/hexanes gradient) to give **15** as a cherry crystalline solid (14.4 mg, 74%). TLC (20% EtOAc/hexanes) R_f=0.4; mp 99–101 °C; IR (KBr, cm^{-1}): 1636 (s), 1551 (w), 1478 (s), 1388 (m), 1353 (s), 1255 (m), 1170 (s), 1115 (s), 1081 (m), 780 (w), 764 (w), 747 (w), 955 (s); ^1H NMR: δ 7.90 (s, 2H), 7.18 (d, J=3.8 Hz, 2H), 6.55 (s, 2H), 5.54 (s, 1H), 5.28 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 150.1, 144.4, 138.6, 134.2, 130.2, 120.7, 118.4, 25.9; HRMS FABS ($M+H^+$) calcd for $C_{12}H_{12}BF_2N_2$: 233.1062. Found 233.1059.

5.5. Conjugated addition of dodecane-1-thiol to BODIPY 5

A reaction tube, equipped with a stir bar, was charged with **5** (20.0 mg, 0.0862 mmol) and dry THF (2 mL) then, the dodecanothiol (34.9 mg, 0.1723 mmol) was added. The reaction mixture was immersed into a pre-cooled ice-water bath at 0 °C. After TLC showed that the reaction went to completion, the reaction mixture was adsorbed on SiO_2-gel. The product was purified by gravity column chromatography (silica-gel, AcOEt/hexanes gradient) to give **16** as a orange crystalline solid. TLC (20% EtOAc/hexanes) R_f=0.4; mp 50–51 °C; yield=76%; IR (KBr, cm^{-1}): 2924 (m), 2851 (w), 1572 (s), 1414 (m), 1396 (m), 1262 (m), 1192 (w), 1121 (m), 1073 (m), 1034 (w), 956 (w), 782 (w), 750 (w), 711 (w); ^1H NMR: δ 7.88 (s, 2H), 7.28 (d, J=2.2 Hz, 2H), 6.56 (d, J=2.0 Hz, 2H), 2.57 (app. t, J=7.4 Hz, 2H), 1.56 (m, 2H), 1.32–1.26 (m, 25H) 0.89 (t, J=6.6 Hz, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 147.2, 144.1, 135.8, 128.5, 118.4, 43.1, 39.1, 32.1, 31.6, 29.9, 29.8, 29.7, 29.5, 29.4, 29.1, 22.9, 21.9, 14.3; HRMS FABS ($M+H^+$) calcd for $C_{24}H_{38}BF_2N_2S$: 435.2817. Found 435.2821.

5.6. Synthesis of 8-methylBODIPY 18[10]

A reaction tube, equipped with a stir bar, was charged with **5** (20.0 mg, 0.0862 mmol) and dry THF (2 mL) then, the morpholine (15 μL, 0.1723 mmol) was added. The reaction mixture was stirred for 30 min at room temperature. After TLC showed that the reaction went to completion, the solvent was removed in vacuo and the reaction mixture was adsorbed on SiO_2-gel. The product was purified by gravity column chromatography (silica-gel, AcOEt/hexanes gradient) to give **18** as an orange crystalline solid. TLC (20% EtOAc/hexanes) R_f=0.3; mp 118–120 °C; yield=84%; IR (KBr, cm^{-1}): 1576 (s), 1541 (m), 1413 (m), 1393 (s), 1376 (m), 1357 (m), 1264 (s), 1224 (w), 1207 (m), 1122 (s), 1064 (s), 1030 (m), 951 (m), 767 (m), 713 (m), 599 (w), 431 (w); ^1H NMR: δ 7.85 (s, 2H), 7.30 (d, J=3.6 Hz, 2H), 6.55 (s, 2H), 2.63 (s, 3H).

5.7. General procedure (GP) for the catalytic reduction of alkenylBODIPYs

All the reactions started with 20.0 mg of the respective alkenylBODIPY. A reaction tube, equipped with a stir bar, was charged with the corresponding alkenylBODIPY (1 equiv) and ethanol

(2 mL) under H_2 (balloon). Pd/C (5 mol %) s was added. After TLC showed that the reaction went to completion, the solvent was removed under reduced pressure and the reaction mixture was adsorbed on SiO_2-gel. After flash-chromatography (silica-gel, EtOAc/hexanes gradient) purification, the products were obtained as highly-colored crystalline solids or oils.

*5.7.1. BODIPY **20**.* According to GP. Reaction time: 1 h. TLC (20% EtOAc/hexanes) R_f=0.4; orange crystals; mp 65–66 °C; yield=80%; IR (KBr, cm^{-1}): 3111 (w), 2962 (w), 2927 (w), 2875 (w), 1730 (w), 1571 (s), 1414 (m), 1396 (m), 1357 (w), 1262 (m), 1238 (w), 1197 (m), 1115 (s), 1072 (s), 955 (m), 779 (w), 739 (w), 706 (w); ^{1}H NMR: δ 7.86 (s, 2H), 7.30 (m, 2H), 6.54 (d, J=3.6 Hz, 2H), 2.92 (t, J=7.8 Hz, 2H), 1.90–1.70 (m, 2H), 1.06 (t, J=7.2 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 151.1, 143.6, 135.5, 128.1, 118.1, 33.2, 27.3, 14.7; HRMS FABS ($M+H^+$) calcd for $C_{12}H_{14}BF_2N_2$: 235.1218. Found 235.1213.

*5.7.2. BODIPY **21**.* According to GP at 35 °C. Reaction time: 1.5 h. TLC (20% EtOAc/hexanes) R_f=0.7; dark green crystals; mp 70–72 °C; yield=62%; IR (KBr, cm^{-1}): 3112 (w), 2922 (w), 1556 (s), 1416 (w), 1394 (m), 1354 (w), 1253 (s), 1095 (s), 1083 (s), 1070 (m), 1055 (m), 1030 (w), 983 (w), 941 (w), 771 (w), 734 (w), 701 (w); ^{1}H NMR: δ 7.84 (s, 2H), 7.37–7.29 (m, 5H), 7.16 (d, J=3.5 Hz, 2H), 6.47 (d, J=3.0 Hz, 2H), 4.75 (q, J=7.2 Hz, 1H), 1.93 (d, J=7.4 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 155.0, 143.7, 143.0, 135.0, 129.5, 129.0, 127.3, 118.4, 40.8, 22.1; HRMS FABS ($M+H^+$) calcd for $C_{17}H_{16}BF_2N_2$: 297.1375. Found 297.1372.

*5.7.3. BODIPY **22**.* According to GP. Reaction time: 20 min. TLC (20% EtOAc/hexanes) R_f=0.8; orange crystals; mp 51–52 °C; yield=75%; IR (KBr, cm^{-1}): 2956 (w), 2929 (m), 2861 (w), 1565 (s), 1482 (m), 1463 (w), 1410 (m), 1392 (s), 1355 (m), 1257 (s), 1228 (m), 1257 (s), 1195 (m), 1112 (s), 1062 (s), 1034 (s), 952 (m), 767 (m), 732 (m), 704 (m); ^{1}H NMR: δ 7.85 (s, 2H), 7.29 (m, 2H), 6.54 (d, J=3.4 Hz, 2H), 2.93 (t, J=7.8 Hz, 2H), 1.90–1.70 (m, 2H), 1.50–1.20 (m, J=3.8 Hz, 4H), 0.91 (t, J=6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 151.5, 143.4, 135.4, 128.0, 118.1, 33.8, 32.3, 31.3, 22.5, 14.0; HRMS FABS ($M+H^+$) calcd for $C_{14}H_{18}BF_2N_2$: 263.1531. Found 263.1536.

*5.7.4. BODIPY **23**.* According to GP at 0 °C. Reaction time: 1 h. TLC (20% EtOAc/hexanes) R_f=0.3; orange crystals; mp 99–101 °C; yield=77%; IR (KBr, cm^{-1}): 3112 (w), 2968 (w), 2933 (w), 2879 (w), 1558 (s), 1477 (m) 1465 (m), 1413 (s), 1397 (s), 1345 (m), 1258 (s), 1207 (m), 1166 (m), 1117 (s), 1073 (s), 946 (s), 785 (m), 760 (w), 747 (m), 457 (w), 411 (w); ^{1}H NMR: δ 7.85 (s, 2H), 7.41 (d, J=4.0 Hz, 2H), 6.53 (d, J=3.0 Hz, 2H), 3.60–3.40 (m, J=6.8 Hz, 1H), 1.56 (d, J=7.4 Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 157.8, 143.4, 134.3, 128.8, 118.0, 32.6, 25.0; HRMS FABS ($M+H^+$) calcd for $C_{12}H_{14}BF_2N_2$: 235.1218. Found 235.1222.

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Supplementary data

Copies of the ^{1}H and ^{13}C NMR spectra of all the compounds described. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.07.067.

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