Thiocyanation of BODIPY Dyes and their Conversion to Thioalkylated Derivatives

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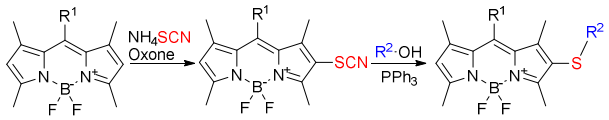


New photophysical features

Thiocyanation and formation of thioalkylated BODIPYs is a simple and reliable way for their chemical modification and photophysical tuning.

ABSTRACT

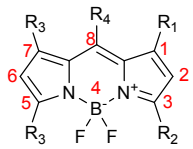
A high-yielding method for the direct thiocyanation of BODIPY dyes is described. In 1,3-dimethyl BODIPYs, the thiocyanato group adds at position 2, whereas the insertion occurs at position 5 in 3-amino BODIPYs. The transformation of the thiocyanato group enables the synthesis of thioalkylated BODIPYs. 2-Thioalkylated BODIPYs and 3-thiocyanato-5-piperidino BODIPYs exhibit interesting spectroscopical features. Hence, the described synthetic methodology can be used for the photophysical tuning of BODIPY dyes.

INTRODUCTION

Thiocyanato-functionalized organic compounds are very important in organic synthesis because of their synthetic versatility, which is usually applied in the preparation of other sulfur-containing functionalities. The thiocyanato group is known to undergo nucleophilic attack both at the sulfur atom (by softer nucleophiles) and at the carbon atom (by harder nucleophiles), which both result in the formation of sulfur-containing products.[1,2] Therefore, the direct thiocyanation of aromatic compounds is a very important reaction in organic synthesis, and several reports on the thiocyanation of organic compounds can be found in the literature[3].

Here, we investigate a method for direct thiocyanation applied to BODIPY dyes, a group of fluorescent organic dyes characterized by a cyanin-type structure that is a complex of a dipyrrin and a difluoroboryl unit.[4] This class of dyes is interesting because of their easy tunability and intense fluorescence, which led to the recent development of several methods of chemical modification.[5] To the best of our knowledge, thiocyanato-substituted boron dipyrrins have not been previously reported, although they can be considered starting materials for BODIPY sulfides.[6-10] For this study, ten BODIPYs (Table 1) were synthesized using established procedures[11-18] and were used as starting materials for further reactions.

Table 1. BODIPYs used as starting material in this study and structure numbering of the BODIPY core.



Nº	R_1	R_2	R_3	R_4	Ref
1	Me	Me	H	H	11
2	Me	Me	Me	H	12
3	Me	Me	Me	Me	13
4	Me	Me	Me	4-aminophenyl	14
5	Me	Me	Me	2-thienyl	15
6	Me	Me	Me	4-nitrophenyl	15
7	Me	Me	Me	4-pyridyl	15
8	H	H	H	Me	16
9	H	H	H	2,6-Cl_2Ph[a]	17
10	H	NC_5H_{11}[b]	H	2,6-Cl_2Ph[a]	[c]

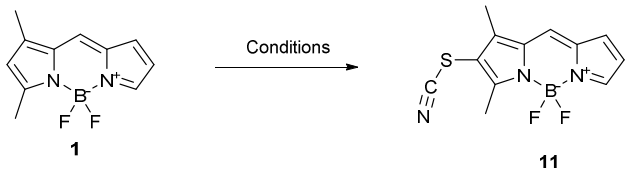
[a]2,6-dichlorophenyl [b]N-piperidinyl
[c]Prepared here in 64% yield from **9**[18]

RESULTS AND DISCUSSION

1,3-Dimethyl BODIPY **1** was initially studied as a substrate for direct thiocyanation. Preliminary tests showed that the addition of the thiocyanate anion did not suffice for reagent conversion, even in harsher conditions (Table 2 - entries 1 and 2), so we tested the application of oxone as an additive, which resulted in the partial conversion of compound **1**. From two-dimensional NMR, we could conclude that the monothiocyanated BODIPY **11**, which is substituted at the most electron-rich position (position 2) between the methyl groups, was obtained. The optimal conditions to carry out the reaction were determined in the methodological experiments described in table

2. Using 3 equivalents of ammonium thiocyanate and 3 equivalents of oxone, we were able to obtain compound **11** in a mild, fast, simple and high-yielding method.

Table 2. Optimization of the thiocyanation of compound 1

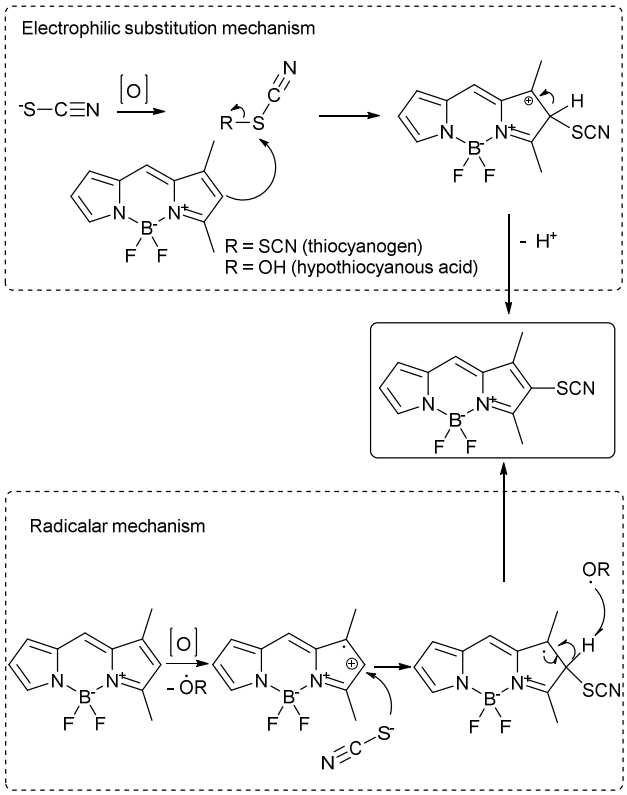


1 **11**

Entry	Oxone	NH_4SCN	Condition[a]	Yield[b]
1	0 eq	1 eq	rt, 16 h	-[c]
2	0 eq	2 eq	Reflux, 16 h	-[c]
3	1.2 eq	1.2 eq	rt, 4 h	17%[d]
4	1.5 eq	1.5 eq	rt, 4 h	37%[d]
5	5 eq	5 eq	rt, 24 h	75%[e]
6	3 eq	3 eq	rt, 1 h	82%

[a]Solvent: Methanol [b]Isolated yields of compound **11.**
[c]TLC - No conversion. [d]TLC - Partial conversion
[e]TLC - Full conversion with some other products formed

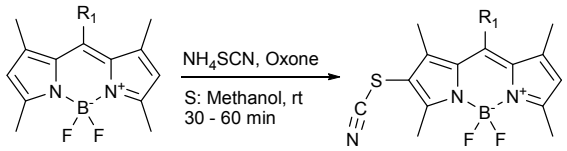
In our view, a mechanism based on electrophilic substitution likely accounts for the observed results[19,20]. The addition of the oxidant leads to the formation of a thiocyanogen, an electrophilic dimeric species, which is attacked by the nucleophilic position of the BODIPY dye. Additionally, oxone is known to lead to the formation of the hypothiocyanate anion $(OSCN)^{-1}$ and hypothiocyanous acid (HOSCN), which might also be electrophilic intermediates in this reaction (Scheme 1). Alternatively, a radical mechanism has been proposed and considered for similar reactions[20,22]. In this case, the BODIPY itself would be oxidized to a radical cation intermediate and stabilized by the tertiary carbons. This intermediate could be reactive towards the thiocyanato anion, leading to the thiocyanation reaction (Scheme 1).



Scheme 1. Proposed mechanisms for the thiocyanation reaction.

With an established method for the direct thiocyanation of fluorophore **1**, we applied this procedure to other BODIPYs (**2**-**10**, Table 1) with different substituents. Our results indicate that tetramethyl-BODIPYs **2**-**7** are quite prone to this substitution, regardless of the type of *meso*-substitution. In general, moderate to excellent yields were obtained for said conversion, with the exception of anilino-substituted compound **4,** from which **14** was obtained with 44% yield (Table 3 – entry 3). This lower yield can be hypothesized to result from side reactions of the oxidizing agent with the free amine, which is known to be sensitive to oxidation[23].

Table 3. Direct thiocyanation of a library of 1,3,5,7-tetramethyl BODIPYs

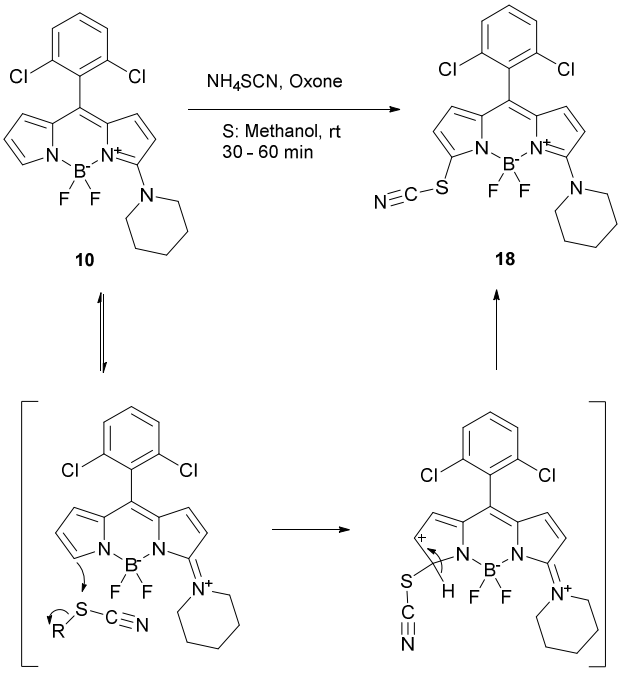


2-7 **12-17**

Entry	Starting compound	Product	R_1	Yield[a]
1	2	12	H	80%
2	3	13	Me	85%
3	4	14	4-aminophenyl	44%
4	5	15	2-thienyl	81%
5	6	16	4-nitrophenyl	73%
6	7	17	4-pyridil	98%

[a] Isolated yields

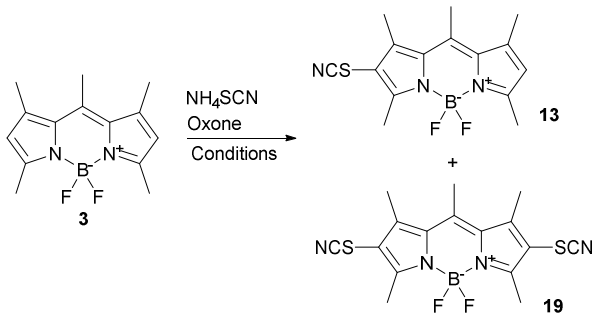
It is interesting to note that the direct thiocyanation seemed to be dependent on the presence of the methyl group in the BODIPY core, given that only the starting material was recovered for non-methylated BODIPYs **8** and **9**. This result might reflect the need for electron-donating groups to enhance the nucleophilicity at the reacting position and supports a reaction mechanism based on electrophilic substitution. To test this hypothesis, we performed the thiocyanation of compound **10**, in which the piperidine group acts as a strong electron-donating group. To our delight, full conversion and a high yield were observed, further supporting our hypothesis; however, the thiocyanation occurred with a different regiochemistry, and the 3,5-disubstituted BODIPY **18** was obtained (Scheme 2). We believe that the insertion of the piperidino group breaks the cyanine-type conjugation of the BODIPY due to cross-conjugation. This would isolate the other pyrrolic ring and enhance its pyrrolic character, which accounts for the electrophilic attack at position 5 of BODIPY **10** to yield compound **18** (Scheme 2).



Scheme 2. Successful thiocyanation of non-methylated BODIPY 10

We also studied the possibility of dithiocyanation by using a large excess of oxone and ammonium thiocyanate. The planned reaction occurred when the amounts of oxone and ammonium thiocyanate were increased (Table 4), but the insertion of a second thiocyanate group seemed to be more difficult. Even when a large excess of oxone and ammonium thiocyanate was used, we could not observe full conversion, and a mixture of monothiocyanato (**13**) and dithiocyanato (**19**) BODIPYs were obtained. Additionally, although heating seems to accelerate the reaction, it also lowers the overall yields. The best condition was 15 equivalents of ammonium thiocyanate and oxone in a 24-hour reaction, after which near-full conversion was observed, yielding 78% dithiocyanated BODIPY **19**.

Table 4. Optimization studies on the dithiocyanation of BODIPY 3



Reagents		Condition[a]	Isolated yields	
Oxone	NH_4SCN		**13**	**19**
5 eq	5 eq	rt, 2 h	82%	trace
5 eq	5 eq	reflux 4 h	71%	21%
5 eq	5 eq	rt, 24 h	83%	9%
15 eq	15 eq	rt, 6 h	56%	38%
15 eq	15 eq	reflux, 4 h	34%[c]	23%
15 eq	15 eq	rt, 24 h	39%	46%
15 eq[b]	15 eq[b]	rt, 24[b] h	11%	78%

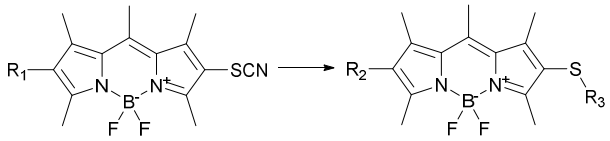
[a] BODIPY 0.1 - 0.2 mmol in 10-20 mL of methanol
[b] Initially 5 eq. After 16 hours, portionwise addition of an extra 10 eq.
[c] TLC - Degradation is observed.

To convert the thiocyanate in compound **13** into a free thiol group, we tried several reducing reactants, but disappointingly, none of the hydride reagents ($LiAlBH_4$, $NaBH_4$ and $NaBH_3CN$), zinc/HCl or dithioeritrol were viable procedures for said conversion. To obtain a thioaryl derivative, compound **13** was submitted to Liebeskind[24,25] conditions with phenylboronic acid, but the procedure was unsuccessful.

Regardless of our initial unsatisfactory attempts, compound **13** could be converted to thioalkyl derivatives using a previously published[26] direct alkylation method, in which an alcohol is used as an alkyl donating group and triphenylphosphine is used as an additive. Table 5 shows that this reaction was successfully performed by using ethyl

alcohol, allyl alcohol, and benzyl alcohol, yielding BODIPYs **20**, **21** and **22,** respectively, in moderate yields. It is interesting to note that by using BODIPY **19** as a starting material, alkylation in both positions was accomplished in a similar manner, yielding BODIPY **23** (Table 5, entry 4).

Table 5. Formation of thioalkylated derivatives from thiocyanated BODIPYs



R^1	Conditions	Outcome		
		R^2	R^3	product
H	R^3OH[a], PPh_3[b]	H	Et	**20** (35%)
H	R^3OH[a], PPh_3[b]	H	allyl	**21** (63%)
H	R^3OH[c], PPh_3[b]	H	Bn	**22** (52%)
SCN	R^3OH[a], PPh_3[d]	SEt	Et	**23** (31%)

[a] Alcohol used as solvent in the reaction.
[b] 1.2 eq of PPh_3.
[c] 6 eq of BzOH, 1,4 dioxane used as solvent
[d] 2.3 eq of PPh_3

In general, the addition of a thiocyanato group does not greatly influence the spectroscopical features of the BODIPYs studied, except for the piperidinyl-substituted BODIPY **18** (Table 6)[27]. Conversely, the emission spectra of thioalkylated BODIPYs (**20** - **23**) were red-shifted and very broadened compared with the starting materials, whereas no striking effects were observed in the absorption spectra (Figure 1 - top). Consequently, 2-thioalkylated BODIPYs had significantly higher Stokes shifts. Unfortunately, a significant reduction in the fluorescence quantum yields was also observed for those compounds, particularly in more polar solvents (Table 6).

Table 6 Photophysical properties of selected compounds in two different solvents.

Comp.	Solvent	λ (nm)		Stokes Shift[a]	QY[b]
		abs	em		
2[c]					
	MeOH	502	509	274	0.95
	Toluene	506	512	272	0.98
10					
	MeOH	476	551	2860	0.02
	Toluene	507	561	1899	0.27
12					
	MeOH	493	507	560	0.96
	Toluene	505	518	497	0.91
18					
	MeOH	459	562	3993	0.004
	Toluene	483	561	1899	0.09
19					
	MeOH	490	507	684	0.62
	Toluene	501	518	655	0.97
20					
	MeOH	499	570	2496	0.05
	Toluene	507	561	1899	0.23
22					
	MeOH	500	538	1413	0.10
	Toluene	508	542	1235	0.37
23					
	MeOH	509	583	2494	0.04
	Toluene	517	576	1981	0.22

[a] Results given in cm^{-1}

[b] Relative quantum yields (Fluorescein standard)

[c] Data from a previous paper published by our group[15]

Remarkable spectral shifts were observed for the piperidinyl-substituted BODIPYs (**10** and **18**). Amination of BODIPYs is known to result in spectral changes that vary according to the nitrogen position.[28-31] Moreover, in general, 3-amino BODIPYs show

solvatochromic behavior with a broad red-shifted emission and a blue-shifted absorption.[28, 32-36] Similarly, we observed that the addition of the piperidinyl group by itself (compound **10**) diminished the quantum yields and drastically changed the shapes of the absorption and emission bands, significantly broadening them. These effects were also observed for **18** and were highly influenced by solvent polarity (Figure 1, Bottom). Compound **10** showed a very large Stokes shift, resulting from the blue-shifted absorption peak and a red-shifted emission peak. These effects were even more evident after the addition of a thiocyanato group at position 5 (compound **18**), in which the large Stokes shift was close to the previously reported "mega-Stokes" BODIPYs,[37,38] which can lead to important applications.

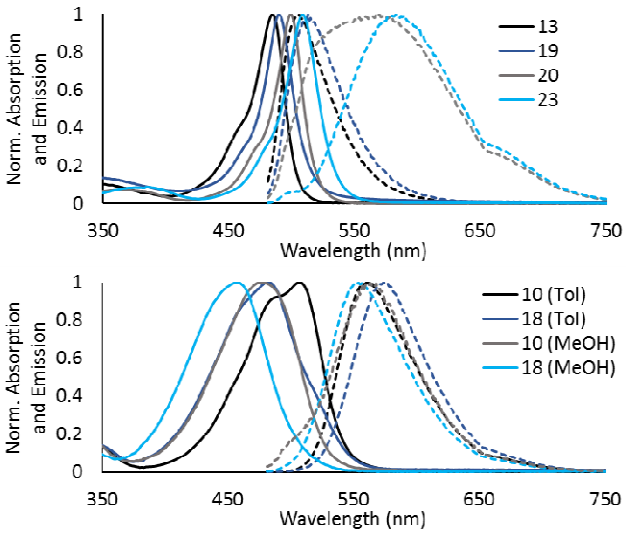


Figure 1. Top: Absorption and emission spectra in methanol of thiocyanated BODIPY **13** and dithiocyanated BODIPY **19** compared with the respective thioethylated derivatives **20** and **23**. Bottom: Absorption and emission spectra of compounds **10** and **18** in toluene and methanol, showing the large Stokes shifts.

CONCLUSION

We demonstrated herein a straightforward method for the direct thiocyanation of BODIPY dyes using ammonium thiocyanate and oxone. This reaction occurs at the available nucleophilic positions of the BODIPY core, and it is clear that electron-donating groups are needed for this reaction. Thus, 1,3,5,7 tetramethylated BODIPYs are good starting materials for this transformation. Though direct thiocyanation was not achieved in non-methylated BODIPYs, the addition of an electron-donating amine group at position 3 enabled the addition of a thiocyanato group with a different regiochemistry, yielding 3-piperidinyl-5-thiocyanato BODIPY, an interesting compound with a significant Stokes shift. Thiocyanato-substituted BODIPYs can be used in the formation of thioalkylated BODPYs in a reaction with an alcohol and triphenyl phosphine. Hence, the described synthetic methodology can be explored for the photophysical tuning of BODIPY dyes.

EXPERIMENTAL

General. Reactions were performed in round-bottom flasks with magnetic stirring and monitored by thin layer chromatography plates visualized by exposure to ultraviolet light. Organic solvents were evaporated on a rotary evaporator at 40−50 ℃. Prior to the spectroscopic analyses, the BODIPYs were crystallized from a 1:1 mixture of *n*-pentane and DCM and residual solvent peaks might appear. Chemical structures were determined by ^{13}C-NMR (75 or 101 MHz), ^{1}H-NMR (300, 400 or 600 MHz), low-

resolution mass spectrometry (electrospray ionization and/or electron impact ionization) and high-resolution mass spectrometry (electrospray ionization with time-of-flight or electron impact ionization with a double focusing magnetic sector). For some specific compounds, infrared spectroscopy (IR), COSY, HSBC and HMQC were also used. Melting points were taken on a typical apparatus and are uncorrected.

Absorption spectra were obtained on a UV/vis spectrophotometer, and fluorescence emission spectra were obtained on a fluorimeter using an excitation wavelength (λ_{exc}) of 470 nm. Quantum yields were calculated using a comparative method with a fluorescein standard (fluorescein in 0.1 M NaOH(aq) – φ = 0.91, λ_{exc} = 470 nm). From the emission spectra of five diluted BODIPY samples, the integrated fluorescence was calculated. The results were plotted against the absorbance, the slope of each curve was calculated and the quantum yield of the tested compound (ϕ_x) was calculated using the following formula:

$$\phi_x = \phi_{st}\left[\frac{m_x}{m_{st}}\right]\left[\frac{n_x}{n_{st}}\right]^2$$

where ϕ_{st} is the quantum yield of the standard, m_x and m_{st} are the slopes for the test compound and standard compound, respectively, and n_x and n_{st} are the refractive indexes of the solvents.

10-(2,6-dichlorophenyl)-5,5-difluoro-3-(piperidin-1-yl)-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 10. To a stirring solution of BODIPY **9** (336 mg, 1 mmol) in DMF (10 mL) at room temperature, piperidine (0.22 mL, 2.17 mmol) was added. The solution was then purged with oxygen and left stirring at room temperature in an oxygen

atmosphere for 24 hours. The mixture was poured into ethyl ether (250 mL) and washed with aqueous $NaHCO_3$ (2 x 200 mL) and then water (2 x 200 mL). Compound **10** (268 mg, 0.638 mmol, 64% yield) was obtained as a reddish powder after column purification (PE/DCM, 1:1). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 7.44 – 7.39 (m, 3H), 7.36 – 7.29 (m, 1H), 6.62 (d, *J* = 5.2 Hz, 1H), 6.33 – 6.25 (m, 2H), 6.06 (d, *J* = 3.3 Hz, 1H), 3.97 – 3.92 (m, 4H), 1.87 – 1.73 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$, δ) 162.2, 136.5, 135.9, 134.0, 133.0, 130.6, 130.4, 130.3, 128.2, 124.8, 115.9, 115.1, 113.4, 52.1, 26.4, 24.2. HRMS (EI): calculated for $C_{20}H_{18}BCl_2F_2N_3$: 419.0939, found 419.0946. LRMS (EI): 419, 421. mp 253 ℃

5,5-difluoro-1,3-dimethyl-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 11. To a stirring solution of BODIPY **1** (20 mg, 0.091 mmol) in methanol (10 mL) at room temperature, ammonium thiocyanate (17 mg, 0.22 mmol) and oxone (83 mg, 0.26 mmol) were added. The solution was stirred at room temperature for 1 hour followed by solvent evaporation under reduced pressure. Compound **11** (20.6 mg, 0.074 mmol, 82% yield) was obtained as a reddish powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.87 (s, 1H), 7.41 (s, 1H), 7.16 (d, *J* = 4.1 Hz, 1H), 6.59 (d, *J* = 4.1 Hz, 1H), 2.71 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 160.4, 147.6, 145.3, 134.6, 133.5, 131.4, 127.7, 119.5, 109.7, 109.0, 13.4, 10.96. IR (cm^{-1}): 2154 (S-C≡N). HRMS (ESI): calculated for $C_{12}H_{10}BF_2N_3S$ $[M + H]^+$: 278.0729; Found: 278.0719, $[M - F]^+$: 258.0667; found: 258.0641. LRMS (EI): 277, 257 (M^+ − HF). mp 175 ℃ dec

5,5-difluoro-1,3,7,9-tetramethyl-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 12. To a stirring solution of BODIPY **2** (25.0 mg, 0.101 mmol) in

methanol (10 mL) at room temperature, ammonium thiocyanate (25 mg, 0.320 mmol) and oxone (85 mg, 0.280 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation under reduced pressure. Compound **12** (24.7 mg, 0.0809 mmol, 80% yield) was obtained as a reddish powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.15 (s, 1H), 6.21 (s, 1H), 2.65 (s, 3H), 2.59 (s, 3H), 2.39 (s, 3H), 2.30 (s, 3H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$, δ) 163.5, 155.1, 145.8, 141.6, 136.1, 130.9, 121.9, 121.3, 110.5, 105.8, 15.3, 12.8, 11.6, 10.56. IR (cm^{-1}): 2158 (S-C≡N). HRMS (ESI): calculated for ($C_{14}H_{14}BF_2N_3S$) $[M + H]^+$: 306.1042; found: 306.1062, $[M - F]^+$: 286.0980; found: 286.0999. mp 217 ℃

5,5-difluoro-1,3,7,9,10-pentamethyl-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 13. To a stirring solution of BODIPY **3** (28.0 mg, 0.107 mmol) in methanol (10 mL) at room temperature, ammonium thiocyanate (24 mg, 0.323 mmol) and oxone (95 mg, 0.324 mmol) were added. The solution was stirred at room temperature for 1 hour followed by solvent evaporation under reduced pressure. Compound **13** (29.2 mg, 0.091 mmol, 85% yield) was obtained as a reddish powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 6.22 (s, 1H), 2.67 (s, 3H), 2.65 (s, 3H), 2.59 (s, 3H), 2.57 (s, 3H), 2.46 (s, 3H). ^{13}CNMR (101 MHz, $CDCl_3$, δ) 160.0, 152.7, 145.7, 142.8, 140.5, 138.9, 134.4, 130.8, 124.2, 110.9, 17.9, 17.2, 15.5, 15.0, 12.9 ppm. IR (cm^{-1}): 2154 (S-C≡N). HRMS (ESI): calculated for ($C_{15}H_{16}BF_2N_3S$) $[M + Na]^+$: 342.1024; found: 342.1026, $[M + K]^+$: 358.0763; found: 358.0763. LRMS (ESI): 300 ($M^+ - F$). mp 187 ℃.

4-(5,5-difluoro-1,3,7,9-tetramethyl-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinin-10-yl)aniline 14. To a stirring solution of BODIPY **4** (17 mg, 0.050 mmol) in methanol (7 mL) at room temperature, ammonium thiocyanate (12 mg, 0.158 mmol) and oxone (46 mg, 0.150 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation under reduced pressure. Compound **14** (8.7 mg, 0.022 mmol, 44% yield) was obtained as an orange powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:3). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.10 (d, J = 8.3 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 6.13 (s, 1H), 2.69 (s, 3H), 2.59 (s, 3H), 1.62 (s, 3H), 1.52 (s, 3H). ^{13}C NMR (126 MHz, DMSO, δ) 160.5, 152.2, 150.1, 147.3, 145.0, 141.9, 133.6, 129.9, 128.4, 123.7, 119.6, 114.2, 111.4, 107.9, 14.8, 14.6, 12.6, 12.5. IR (cm^{-1}): 2152 (S-C≡N). HRMS (ESI): calculated for $C_{20}H_{19}BF_2N_4S$, $[M + H]^+$: 397.1470; found: 397.1470, $[M - F]^+$: 377.1402; found: 377.1410, $[M + Na]^+$: 419.1289; found: 419.1288, $[M + K]^+$: 435.1029; found: 435.1027. LRMS (ESI): 397 $[M + H]^+$, 377 $[M – F]^+$. mp 132 ℃.

5,5-difluoro-1,3,7,9-tetramethyl-2-thiocyanato-10-(thiophen-2-yl)-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 15. To a stirring solution of BODIPY **5** (44.8 mg, 0.136 mmol) in methanol (12 mL) at room temperature, ammonium thiocyanate (31 mg, 0.408 mmol) and oxone (123 mg, 0.401 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation under reduced pressure. Compound **15** (42.3 mg, 0.109 mmol, 81% yield) was obtained as a red powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.57 (dd, J_1 = 5.1 Hz, J_2 = 1.2 Hz, 1H), 7.18 (dd, J_1 = 5.1 Hz, J_2 = 3.5 Hz, 1H), 7.01 (dd, J_1 = 3.5 Hz, J_2 = 1.2 Hz, 1H), 6.17 (s, 1H), 2.70 (s, 3H), 2.61 (s, 3H), 1.72 (s, 3H), 1.64

(s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 162.7, 154.6, 148.0, 143.5, 135.5, 135.0, 133.7, 130.6, 128.3, 128.3, 128.1, 124.3, 110.7, 107.9, 15.3, 14.2, 13.0, 12.1. IR (cm^{-1}): 2146 (S-C≡N). HRMS (ESI): calculated for $C_{18}H_{16}BF_2N_3S_2$, $[M + H]^+$: 388.0920; found: 388.0926, $[M - F]^+$: 368.0857; found: 368.0870, $[M + Na]^+$: 410.0744; found: 410.0739, $[M + K]^+$: 426.0484; found: 426.0478. LRMS (ESI): 368 $[M – F]^+$. mp 207 ℃

5,5-difluoro-1,3,7,9-tetramethyl-10-(4-nitrophenyl)-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 16. To a stirring solution of BODIPY **6** (82.7 mg, 0.22 4 mmol) in methanol (10 mL) at room temperature, ammonium thiocyanate (52 mg, 0.683 mmol) and oxone (208 mg, 0.676 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation under reduced pressure. Compound **16** (69.7 mg, 0.1092 mmol, 73% yield) was obtained as a red powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 8.44 (d, J = 8.7 Hz, 2H), 7.55 (d, J = 8.7 Hz, 2H), 6.19 (s, 1H), 2.71 (s, 3H), 2.63 (s, 3H), 1.52 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 163.1, 155.2, 148.7, 146.7, 142.6, 140.9, 139.4, 133.0, 129.5, 128.9, 124.7, 124.6, 110.3, 108.3, 15.2, 15.2, 13.2, 13.0. IR (cm^{-1}): 2152 (S-C≡N). HRMS (ESI): calculated for $C_{20}H_{17}BF_2N_4O_2S$, $[M + Na]^+$: 449.1031; found: 449.1016, $[M + K]^+$: 465.0770; found: 465.0773. $[M - F]^+$: 407.1144; found: 407.1143, LRMS (EI): 426. Mp 247 ℃.

5,5-difluoro-1,3,7,9-tetramethyl-10-(pyridin-4-yl)-2-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 17. To a stirring solution of BODIPY **7** (30.7 mg, 0.094 mmol) in methanol (10 mL) at room temperature, ammonium thiocyanate (22 mg, 0.289 mmol) and oxone (88 mg, 0.286 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation

under reduced pressure. Compound **17** (35.3 mg, 0.092 mmol, 98% yield) was obtained as a red powder after column purification (C_6H_{14}/EtOAc, 3:1 – 1:2). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 8.78 (d, *J* = 4.8 Hz, 1H), 7.91 (t, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 6.09 (s, 1H), 2.64 (s, 3H), 2.55 (s, 3H), 1.39 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 163.4, 155.1, 152.4, 149.9, 147.0, 142.6, 138.4, 133.9, 129.6, 125.0, 124.9, 124.3, 110.6, 107.8, 15.38, 14.32, 13.09, 12.3. IR (cm^{-1}): 2144 (S-C≡N). HRMS (ESI): calculated for $C_{19}H_{17}BF_2N_4S$, $[M + H]^+$: 383.1313; Found: 383.1307, $[M - F]^+$: 363.1246; found: 363.1265, $[M + K]^+$: 421.0872; found: 421.0860. LRMS (ESI): 383 $[M + H]^+$. mp 196 ℃

10-(2,6-dichlorophenyl)-5,5-difluoro-3-(piperidin-1-yl)-7-thiocyanato-5*H*-5λ^4,6λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 18. To a stirring solution of BODIPY **10** (105.mg, 0.250 mmol) in methanol (20 mL) at room temperature, ammonium thiocyanate (57 mg, 0.750 mmol) and oxone (230 mg, 0.750 mmol) were added. The solution was stirred at room temperature for 1 hour, followed by solvent evaporation under reduced pressure. Compound **18** (101 mg, 0.218 mmol, 85% yield) was obtained as a yellow powder after column purification (PE/DCM, 1:1 – 1:4). ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.48 – 7.41 (m, 2H), 7.39 – 7.32 (m, 1H), 6.66 (d, *J* = 5.4 Hz, 1H), 6.62 (d, *J* = 3.8 Hz, 1H), 6.45 (d, *J* = 5.4 Hz, 1H), 5.99 (d, *J* = 3.8 Hz, 1H), 4.11 – 3.93 (m, 4H), 1.93 – 1.72 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, δ) δ 162.6, 137.9, 136.4, 134.7, 134.2, 131.9, 130.7, 128.2, 122.1, 121.7, 117.6, 116.0, 114.8, 110.9, 52.5, 26.4, 23.9. HRMS (EI) calculated for $C_{21}H_{17}BCl_2F_2N_4S$ 476.0612, found 476.0627. LRMS (EI): 476, 478. mp 222 ℃

5,5-difluoro-1,3,7,9,10-pentamethyl-2,8-dithiocyanato-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 19. To a stirring solution of BODIPY **3** (40.0 mg, 0.153 mmol) in methanol (10 mL) at room temperature, ammonium thiocyanate (45 mg, 0.76 mmol) and oxone (235 mg, 0.76 mmol) were added. The solution was stirred at room temperature for 6 hours, and TLC control showed full reagent consumption and only partial conversion to BODIPY **19**. Five portions of ammonium thiocyanate (18 mg, 0.304 mmol) and oxone (94 mg, 0.304 mmol) were added to the stirring mixture at intervals of 20 minutes. The solution was stirred at room temperature for 16 more hours (total reaction time: 24 hours), after which almost full conversion to compound **19** was observed. The solid residue was filtered off, and the solvent was evaporated under reduced pressure. Compound **19** (29.2 mg, 0.091 mmol, 85% yield) was obtained as a reddish powder after column purification (PE/DCM, 1:1 – 1:4). Compound **13** was obtained (5.0 mg, 0.015 mmol, 11% yield) as a secondary product. Characterization of compound **19**: ^{1}H NMR (400 MHz, $CDCl_3$, δ) 2.77 (s, 3H), 2.73 (s, 6H), 2.68 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 157.6, 146.3, 146.2, 132.5, 111.2, 109.7, 17.9, 16.3, 13.3 ppm. IR (cm^{-1}): 2260 (S-C≡N). HRMS (EI): calculated for $C_{16}H_{15}BF_2N_4S_2$ 376.0799, found 376.0836. LRMS (EI): 376, 318 (M^+ − SCN). mp 224 ℃ dec.

2-(ethylthio)-5,5-difluoro-1,3,7,9,10-pentamethyl-5*H*-4λ^4,5λ^4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 20. To a stirring solution of BODIPY **11** (112.4 mg, 0.352 mmol) in ethanol (10 mL) at 70℃, triphenylphosphine (109 .0 mg, 0.414 mmol) was added. The solution was stirred at reflux for 1 hour, followed by solvent evaporation under reduced pressure. Compound **20** (39.9 mg, 0.124 mmol, 35% yield) was obtained as a reddish powder after column purification (PE/DCM, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, δ) 6.10 (s,

1H), 2.65 (s, 3H), 2.63 (s, 3H), 2.57 – 2.49 (m, 8H), 2.43 (s, 3H), 1.16 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$, δ) 156.4, 155.3, 143.9, 142.4, 141.8, 132.8, 131.6, 128.7, 122.1, 30.6, 17.6, 17.0, 15.9, 15.0, 14.7, 13.2. HRMS (EI): calculated for $C_{16}H_{21}BF_2N_2S$ 322.14866, found 322.15114. LRMS (EI): 322, 293 (M^+ − Et). mp 172 ℃

2-(allylthio)-5,5-difluoro-1,3,7,9,10-pentamethyl-5*H*-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 21. To a stirring solution of BODIPY **11** (36.0 mg, 0.113 mmol) in allyl alcohol (30 mL) at 70℃, triphenylphosphine (35.0 mg, 0.133 mmol) was added. The solution was stirred at reflux for 0.5 hour, followed by solvent evaporation under reduced pressure. Compound **21** (19.4 mg 0.058 mmol, 52% yield) was obtained as a dark reddish powder after column purification (PE/DCM, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$, δ) δ 6.10 (s, 1H), 5.79 (ddt, J_1 = 17.2, J_2 = 9.9, J_3 = 7.4 Hz, 1H), 4.94 (dd, *J* = 9.9, 1.4 Hz, 1H), 4.87 (dd, *J* = 17.2, 1.4 Hz, 1H), 3.13 (d, *J* = 7.4 Hz, 2H), 2.63 (s, 6H), 2.53 (s, 6H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, δ) 156.5, 155.2, 143.9, 142.4, 141.7, 133.9, 132.3, 131.3, 122.0, 121.2, 117.3, 39.6, 17.5, 16.9, 15.8, 14.5, 13.2. HRMS (EI): calculated for $C_{17}H_{21}BF_2N_2S$ 334.1487, found 334.1452. LRMS (EI): 334, 293 (M^+ − allyl). mp 137 ℃

2-(benzylthio)-5,5-difluoro-1,3,7,9,10-pentamethyl-5*H*-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 22. To a stirring solution of BODIPY **11** (40.2 mg, 0.126 mmol) in 1,4-dioxane (5 mL) at 100℃, benzyl alcohol (80 µL, 0.773 mmol) and triphenylphosphine (35.0 mg, 0.133 mmol) were added. The solution was stirred at reflux for 1 hour, followed by solvent evaporation under reduced pressure. Compound **22** (30.7 mg 0.080 mmol, 63.4% yield) was obtained as a red powder after column purification (PE/DCM, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$, δ) 7.25 – 7.17 (m, 3H), 7.06 –

6.98 (m, 2H), 6.10 (s, 1H), 3.63 (s, 2H), 2.58 (s, 3H), 2.53 (s, 3H), 2.43 (s, 3H), 2.35 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, δ) 156.9, 155.3, 144.4, 142.4, 141.8, 138.2, 132.7, 131.3, 129.0, 128.4, 127.0, 122.1, 121.0, 41.0, 17.5, 16.9, 15.2, 14.6, 12.6. HRMS (EI): calculated for $C_{21}H_{23}BF_2N_2S$ 384.1643, found 384.1660. LRMS (EI): 384, 293 (M^+ − benzyl). mp 183 ℃.

2,8-bis(ethylthio)-5,5-difluoro-1,3,7,9,10-pentamethyl-5*H*-4λ4,5λ4-dipyrrolo[1,2-c:2',1'-*f*][1,3,2]diazaborinine 23. To a stirring solution of BODIPY **19** (40.0 mg, 0.106 mmol) in ethanol (10 mL) at 70℃, triphenylphosphin e (63.0 mg, 0.240 mmol) was added. The solution was stirred at reflux for 1 hour, followed by solvent evaporation under reduced pressure. Compound **20** (12.4 mg, 0.032 mmol, 30.5% yield) was obtained as a reddish powder after column purification (PE/DCM, 2:1). ^{1}H NMR (600 MHz, $CDCl_3$, δ) 2.69 (s, 3H), 2.66 (s, 6H), 2.57 (s, 6H), 2.55 (q, *J* = 7.3 Hz, 4H), 1.16 (t, *J* = 7.3 Hz, 6H).^{13}C NMR (75 MHz, $CDCl_3$, δ) 157.7, 145.1, 142.1, 132.0, 122.9, 30.4, 17.5, 16.0, 14.9, 13.2. HRMS (EI): calculated for $C_{18}H_{25}BF_2N_2S_2$, $[M - Et]^+$: 353.1129; found 353.1217. LRMS (EI): 382, 353 (M^+ − Et). mp 229 ℃.

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27. Complete table containing the photophysical properties of previously unpublished compounds in four solvents is shown in supplemental material (Table S1).

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