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Managing nucleophilic addition reactions to tune the physical properties of 2-substituted pentamethylBODIPY derivatives

By

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Experimental

General Considerations

All reagents were purchased from Aldrich. Purification by column chromatography was carried out using silica (Silicycle: ultrapure flash silica). Analytical thin-layer chromatography was performed on aluminum-backed sheets precoated with silica 60 F254 adsorbent (0.25 mm thick; Silicycle) and visualized under UV light. Routine ¹H, ¹³C{1H}, ¹¹B{1H} and ¹⁹F NMR spectra were recorded at 400, 100, 128 and 376 MHz, respectively, on a Bruker AV 400 instrument at ambient temperature. Chemical shifts (δ) are reported in parts per million (ppm) from low to high field and referenced to a residual nondeuterated solvent (CHCl₃) for ¹H and ¹³C nuclei and BF₃•OEt₂ (¹¹B nucleus; δ = 0 ppm) C₆F₆ (¹⁹F nucleus; $\delta = 0$ ppm). Standard abbreviations indicating multiplicity are used as follows: s = singlet; d = doublet; q = quartet and br = broad. High resolution mass spectroscopy (HRMS) results were obtained from Queen University, Kingston Ontario. Electron impact (EI) mass spectrometry and Electrospray ionization (ESI) techniques were used for the ionization; time of flight (TOF) was used for analysis. UV-Vis data was taken using Cary Series UV-Vis-NIR Spectrophotometer from Agilent Technologies and dichloromethane (having the onset peak at 230 nm) was used as a solvent. Fluorescence emission data was taken using LS50B Luminescence from Perkin Elmer. The GAUSSIAN 09 computational package¹ was used to perform ground-state geometry optimization calculations employing Becke's three-parameter hybrid exchange functional and the Lee-Yang-Parr non-local correlation functional B3LYP²⁻⁴ and 6-311G* basis set was used for all the atoms. Time-dependent density functional theory calculations were also performed using this methodology, and the first 200 singlet excited states were calculated. Calculations by the first-principles method were used to obtain accurate excitation energies and oscillator strengths.

5,5-dimethoxy-1,3,7,9,10-pentamethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinine-2-carbaldehyde, (2): BODIPY (100 mg, 0.34 mmol) was dissolved in 10 mL of dry DCM, in



the presence of AlCl₃ (92 mg, 69 mmol). The resulting mixture was refluxed for 5 min prior to the addition of MeOH (5 mL) the reaction stirred 10 mins at room temperature. Solvents were removed *in vacuo* and products were isolated through column chromatography 19:1 DCM:MeOH to yield the desired product as a waxy brown solid (67%, 72 mg). ¹H NMR (400 MHz, CDCl₃): $\delta = 10.11$ (s, 1H, Hg), 6.23 (s, 1H, Ha), 2.82 (s, 6H, Hb), 2.77 (s, 3H, Hf), 2.76 (s, 3H, He), 2.70 (s, 3H, Hd),

2.57 (s, 3H, H_c), 2.49 (s, 3H, H_b). ¹³C NMR (100 MHz, CDCl₃): δ = 186.44, 160.90, 160.28, 155.56, 143.79, 143.08, 138.78, 136.59, 124.40, 49.02, 31.58, 22.64, 18.07, 17.35, 14.92, 14.24, 14.10, 12.16. ¹¹B{¹H} NMR (CDCl₃, 128 MHz): δ = 2.54. ¹⁹F NMR (CDCl₃, 376 MHz): δ = no signal. HRMS (HREI): *m/z* 314.180 ([M]⁺), calculated for [¹²C₁₇¹H₂₃¹¹B¹⁶O₃N₂]⁺: *m/z* 314.1802.

(E)-10-(2-(dimethylamino)vinyl)-5,5-difluoro-1,3,7,9-tetramethyl-5H-4l4,5l4-dipyrrolo[1,2c:2',1'-f][1,3,2]diazaborinine-2,8-dicarbaldehyde, (3): A solution of 10 mL of dry DMF in dry



1,2-dichloroethane (30 mL) was cooled in an ice bath and POCl₃ (12 mL) was added dropwise. The mixture was warmed to room temperature and stirred 30 min. A solution of formyl BODIPY (270 mg, 0.93 mmol) in dry 1,2-dichloroethane (30 mL) was added in one portion and the mixture was stirred for 2 hr at 40°C while being monitored by TLC. The mixture was neutralized in 300 mL of saturated NaHCO₃ at 0°C and allowed to warm to room temperature overnight. The organic layer was extracted with CH₂Cl₂ (3 x 25 mL).

mg, 0.34 mmol) and (carboxymethylene)triphenylphosphorane

The combined organic layers were dried over MgSO₄, filtered and volatiles were removed in *vacuo*. The crude material was purified via column chromatography using 9:1 CH₂Cl₂: MeOH as the eluent, affording the desired product as a red solid (170 mg, 57%). ¹H NMR (CDCl₃): $\delta = 10.10$ (s, 2H, H_{a,g}), 7.33 (d, ³J_{HH} = 12 Hz, 1H, H_h), 6.16 (d, ³J_{HH} = 12 Hz, 1H, H_d), 3.34 (m, 6H, H_i), 2.78 (s, 6H, H_{b,e}), 2.55 (s, 6H, H_{c,f}). ¹³C{¹H} NMR (CDCl₃, 100 MHz): $\delta = 186.3$, 160.8, 152.2, 150.5, 133.6, 129.5, 125.6, 99.8, 29.7, 14.6, 12.2, 12.1. ¹¹B {¹H} NMR (CDCl₃, 128 MHz): $\delta = 0.96$ (t, ¹*J*_{BF} = 32 Hz). ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -144.4$ (q). HRMS (EI): *m/z* 373.1781 ([M]⁺), calculated for [¹²C₁₉¹H₂₂¹¹B¹⁹F₂N₃¹⁶O₂]⁺: *m/z* 373.1773.

ethyl (E)-3-((Z)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5dimethyl-2H-pyrrol-4-yl)acrylate, (4): In a 250 mL round bottom flask, formyl BODIPY (100



(259 mg, 0.776 mmol) were dissolved in a mixture of 20 mL dry DCM and was stirred overnight at room temperature in an inert atmosphere (N₂). Volatiles were removed *in vacuo* and the crude material was purified *via* column chromatography using 3:1 hexanes:EtOAc as the eluent affording the desired product as a orange solid (60 mg, 50%). ¹H NMR (CDCl₃): $\delta = 7.70$ (d, J_{HH} = 16.22 Hz, 1H, H_g), 6.09 (d, J_{HH} = 16.23 Hz, 1H, H_h), 6.13 (s, 1H, H_a), 4.26 (m, 1H, H_i), 2.66 (s, 3H, H_f), 2.63 (s, 3H, H_e), 2.54 (s, 3H, H_d), 2.48 (s, 3H, H_b), 2.43 (s, 3H, H_c), 1.34 (t, 3H, H_j) ¹³C{¹H} NMR (CDCl₃, 100 MHz): $\delta = 167.77$, 156.82, 156.77, 152.69, 143.36, 143.30, 142.35, 138.22, 136.06, 133.58, 131.72, 124.88, 124.85, 122.92, 118.04, 60.53, 17.78, 17.26, 15.11, 14.79, 14.53, 14.45. ¹¹B {¹H} NMR (CDCl₃, 128 MHz): $\delta = 0.60$ (t). ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -145.27$ (q). HRMS (EI): *m/z* 360.1829 ([M]⁺), calculated for [¹²C₁₉¹H₂₃¹¹B¹⁹F₂N₂¹⁶O₂]⁺: *m/z* 360.1821.

(E) - 1 - ((Z) - 2 - (1 - (difluoroboranyl) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl - 3, 5 - dimethyl - 1H - pyrrol - 2 - yl) ethylidene) - 3, 5 - dimethyl -

2H-pyrrol-4-yl)-5-methylhex-1-en-3-one, (5): Into a 250 mL round bottom flask charged



with EtOH (40 mL), formyl BODIPY (100 mg, 0.34 mmol), p - TsOH (10 mole %), acetone and MgSO₄ were added. The reaction was brought to reflux at 80°C for 24 h. The solution was dried under *vacuo* and further extracted with DCM. The organic layer was dried with MgSO₄ and the solvent was removed in *vacuo*. The product was purified

through an aluminium oxide column with a 7:3 (DCM/hexanes) solvent mixture ($R_f = 0.53$), and the fluorescent orange band was collected. After removing the volatiles, a dark red powder of product was obtained (20.1 mg, 16%). ¹H NMR (CDCl₃): $\delta = 7.58-7.62$ (d, $J_{HH} = 16$ Hz, 1H, H_g), 6.42-6.46 (d, $J_{HH} = 16$ Hz, 1H, H_h), 6.15 (s, 1H, H_a), 2.66 (s, 6H, H_{e,f}), 2.55 (s, 3H, H_d), 2.51 (s, 3H, H_c), 2.49 (s, 3H, H_b), 2.45 (s, 2H, H_i), 2.21-2.26 (q, 3H, H_j), 0.98-1.00 (dd, $J_{HH} = 8$ Hz, 3H, H_k). ¹³C {¹H} NMR (CDCl₃, 100 MHz): $\delta = 200.3$, 157.1, 142.3, 133.9, 126.4, 123.1, 53.6, 34.8, 31.7, 29.2, 25.6, 25.4, 22.8, 18.9, 18.6, 17.8, 17.3, 15.2, 14.3, 11.6. ¹¹B {H} NMR (CDCl₃, 128 MHz): $\delta = 0.58$ (t, ¹ $J_{BF} = 30.9$ Hz). ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -145.35$ (q). HRMS (EI): m/z 373.2259 [(M)⁺], calculated for [¹²C₂₁¹H₂₇¹¹B¹⁹F₂N₂¹⁶O]⁺: m/z 372.2668.

2-((5,5-difluoro-1,3,7,9,10-pentamethyl-5H-4l4,5l4-dipyrrolo[1,2-c:2',1'-

f][1,3,2]diazaborinin-2-yl)methylene)malononitrile, (6): Formyl BODIPY (100 mg, 0.34



mmol) and malonitrile (57 mg, 0.86 mmol) were dissolved in $CHCl_3$ (15 mL). Four drops of Et_3N was added and the reaction was refluxed overnight. Solvent was removed *in vacuo* and the resulting residue

was triturated in hot MeOH and washed with cold MeOH to yield the desired product as an orange-red solid (100 mg, 86%). ¹H NMR (CDCl₃): δ = 7.79 (s, 1H, H_g), 6.27 (s, 1H, H_a), 2.69 (s, 3H, H_f), 2.59 (s, 6H, H_{d,e}), 2.49 (s, 6H, H_{b,c}). ¹³C{¹H} NMR (CDCl₃, 100 MHz): δ = 161.3, 153.6, 151.3, 146.3, 142.6, 136.5, 142.9, 122.8, 114.4, 113.3, 82.3, 46.2, 29.69, 17.9, 17.3, 15.0, 13.9, 8.6. ¹¹B {H} NMR (CDCl₃, 128 MHz): δ = 0.46 (t, ¹*J*_{BF} = 32 Hz). ¹⁹F NMR (CDCl₃, 376 MHz): δ = -144.4 (q). HRMS (HREI): *m/z* 340.0570 ([M]⁺), calculated for [¹²C₁₈¹H₁₇¹¹B¹⁹F₂N₄]⁺: *m/z* 338.1514.

(*E*)-2-cyano-3-((*Z*)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5dimethyl-2H-pyrrol-4-yl)acrylic acid, (7): Formyl BODIPY (100 mg, 0.35 mmol) was dissolved



in minimal amount of CHCl₃ and cyanoacetic acid (56 mg, 0.66 mmol) and a drop of piperidine were added. The mixture was refluxed overnight and after being cooled to room temperature, the organic layer was washed with 1 M HCl. Volatiles were removed in vacuo. The crude was recrystallized using DCM/Hexanes (3:2) to obtain a red solid (56 mg, 45%). ¹H NMR

(CDCl₃): $\delta = 8.30$ (s, 1H, H_g) 6.22 (s, 1H, H_a) 2.68 (s, 1H, H_f) 2.62 (s, 1H, H_e) 2.58 (s, 1H, H_d), 2.51 (s, 1H, H_c), 2.47 (s, 1H, H_b). ¹³C{¹H} NMR (CDCl₃, 100 MHz): $\delta = 192.4$, 158.9, 151.9, 148.8, 144.9, 142.8, 137.9, 134.4, 132.2, 123.8, 123.6, 116.4, 45.1, 17.1, 14.8, 14.0. ¹¹B {H} NMR (CDCl₃, 128 MHz): $\delta = 0.855$. ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -145.9$ (q). HRMS (HREI): *m/z* 380.13523 ([M+Na]⁺), calculated for [¹²C₁₈¹H₁₈¹¹B¹⁹F₂N₃¹⁶O₂]⁺: *m/z* 357.1460.

(E)-1-((Z)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)-N-phenylmethanimine, (8): Formyl BODIPY (100 mg, 0.34 mmol), aniline (64



mg, 0.68 mmol), p - TsOH (cat.) and MgSO₄ in anhydrous EtOH was stirred under reflux for 4 h. The residue was purified by column chromatography using basic alumina and a starting eluent of 1:1 DCM:hexanes to a gradient of 9:1 DCM:EtOAc (R_f , 1:1 DCM:hexanes = 0.44), yielding **8** as a red solid (18 mg, 15%). ¹H NMR (400 MHz, CDCl3): δ = 8.54 (s, 1H, H_g), 7.41 (t, 2H, H_i), 7.16-7.22 (m, 5H, H_h, H_i, H_j) 6.16 (s, 1H, H_a), 2.85 (s, 3H, H_f), 2.78 (s, 3H, H_e), 2.72 (s, 3H, H_d), 2.50 (s, 3H, H_c), 2.49 (s, 3H, H_b). ¹³C NMR (100 MHz, CDCl₃): δ = 157.00, 154.62, 154.38, 153.50, 142.83, 139.61, 133.77, 131.66, 125.45, 123.06, 32.07, 31.07, 29.85, 29.81, 29.51, 22.84, 17.85, 17.23, 14.85, 14.27, 13.63. ¹¹B {¹H} NMR (CDCl₃, 128 MHz) δ = 0.63 (t, ¹J_{BF} = 32.3 Hz). ¹⁹F NMR (CDCl₃, 376 MHz) δ = -145.51 (q). HRMS (EI): *m/z* 365.1871 ([M]⁺), calculated for [¹²C₂₁¹H₂₂¹¹B¹⁹F₂N₃]⁺: *m/z* 365.1875.

4-(((E)-((Z)-2-(1-(1-difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5dimethyl-2H-pyrrol-4-yl)methylene)amino)aniline, (9): Formyl BODIPY (290 mg, 1



mmol), dianiline (1 mmol), p - TsOH (cat.) and MgSO₄ were added to a round bottom flask with EtOH. The mixture was stirred and refluxed for 6 h and then diluted with EtOAc and washed with water and saturated aqueous NaHCO₃. The organic layer was extracted and dried with Na₂SO₄ and filtered. The residue was precipitated with DCM and MeOH.

The resultant product was washed with MeOH. ¹H NMR (400 MHz, CDCl₃): $\delta = 8.54$ (s, 1H, H_g), 7.09 (s, 1H, H_i), 7.07 (s, 1H, H_k), 6.73 (s, 1H, H_h), 6.71 (s, 1H, H_j), 6.14 (s, 1H, H_a), 3.67 (s, 2H, H_l), 2.81 (s, 3H, H_f), 2.74 (s, 3H, H_e), 2.68 (s, 3H, H_d), 2.56 (s, 3H, H_c), 2.46 (s, 3H, H_b). Carbon NMR was not obtained due to limited solubility. ¹¹B {¹H} NMR (CDCl₃, 128MHz) $\delta = 0.56$ (t, ¹*J*_{BF} = 31.55 Hz). ¹⁹F NMR (CDCl₃, 376 MHz) $\delta = -145.53$ (q). HRMS (EI): *m/z* 380.1981 ([M]⁺), calculated for [¹²C₂₁¹H₂₃¹¹B¹⁹F₂N₄]⁺: *m/z* 380.1984.

E)-1-((*Z*)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5-dimethyl-2Hpyrrol-4-yl)-N-(4-methoxyphenyl)methanimine, (10): Formyl BODIPY (100 mg, 0.34 mmol), p



- anisidine (85 mg, 0.69 mmol), p – TsOH (cat.) and anhydrous Na₂SO₄ in EtOH was stirred under reflux for 1 h. The residue was purified by column chromatography using basic alumina and 4:1 hexane:EtOAc, yielding

compound 4 as a dark red-brown solid (0.03 g, 22%). ¹H NMR (400 MHz, CDCl₃): $\delta = 8.53$ (s, 1H, H_g), 7.26 (d, $J_{HH} = 8.0 \text{ Hz} 2\text{H}$, H_h), 6.94 (d, $J_{HH} = 8.0 \text{ Hz}$, 2H, H_i), 6.15 (s, 1H, H_a), 3.83 (s, 3H, H_i), 2.82 (s, 3H, H_f), 2.75 (s, 3H, H_e), 2.69 (s, 3H, H_d), 2.58 (s, 3H, H_c), 2.46 (s, 3H, H_b). ¹³C NMR (CDCl₃): $\delta = 157.96$, 156.51, 154.58, 152.56, 146.43, 143.18, 142.73, 125.55, 122.83, 121.97, 114.50, 55.66, 29.84, 17.78, 17.14, 14.79, 13.68. ¹¹B {¹H} NMR (CDCl₃, 128 MHz) $\delta =$ 0.63 (t, ¹ J_{BF} = 32.2 Hz). ¹⁹F NMR (CDCl₃, 376 MHz): -145.46 (q). HRMS (EI): *m/z* 395.1979 ([M]⁺), calculated for $[{}^{12}C_{22}{}^{1}H_{24}{}^{11}B^{19}F_2N_3{}^{16}O]^+$: *m/z* 395.1980.

4-(((E)-((Z)-2-(1-(1-difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)methylene)amino)benzonitrile, (11): 20 mL microwave vial with a handful of



molecular sieves was sparged with N₂ for 10 minutes, and then flame dried. Formyl BODIPY (100 mg, 0.34 mmol) was added to 5 mL of toluene and sparged for 5 minutes with N₂. 4-aminobenzonitrile (63 mg, 0. 53 mmol) was added to the solution and sparged again with N_2 for 5 minutes. After capping the microwave vial, the mixture was

stirred for 4 ¹/₂ hours in an oil bath set to 108°C. After cooling to room temperature, the residue was purified by column chromatography using basic alumina and a starting eluent of 5:1 DCM:hexane (R_f , 1:1 DCM:hexanes = 0.53), yielding 11 as a red solid (93 mg, 73%). ¹H NMR (400 MHz, CDCl₃) δ 8.46 (s, 1H, H_g), 7.66 (d, J_{HH} = 8.5 Hz, 2H, H_i), 7.17 (d, J_{HH} = 8.5 Hz, 2H, H_{h}), 6.08 – 6.31 (m, 1H, H_{a}), 2.81 (s, 3H, H_{f}), 2.75 (s, 3H, H_{e}), 2.70 (s, 3H, H_{d}), 2.58 (s, 3H, H_{c}), 2.48 (s, 3H, H_b). ¹³C NMR (CDCl₃): δ = 167.66, 156.82, 156.77, 152.69, 143.36, 143.30, 142.35, 138.22, 136.06, .133.58, 131.72, 124.88, 122.92, 118.04, 60.53, 17.78, 17.26, 15.11, 14.79, 14.53, 14.45. ¹¹B {¹H} NMR (CDCl₃, 128 MHz) $\delta = 0.60$ (t). ¹⁹F NMR (CDCl₃, 376 MHz): -145.27 (q). HRMS (EI): m/z 390.183 ([M]⁺), calculated for $[{}^{12}C_{22}{}^{1}H_{21}{}^{11}B{}^{19}F_{2}N_{4}]^{+}$: m/z 390.1827.

(E)-N-(4-bromophenyl)-1-((Z)-2-(1-(1-(diflurorboranyl)-3,5-dimethyl-1H-pyrrol-2-



yl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)methanimine, (12): A microwave vial was flame dried under nitrogen environment. After being cooled to room temperature, formyl BODIPY (100 mg, 0.34 mmol) and 5 mL of dry toluene were added to the vial. The solution was stirred and 4-bromoaniline (237 mg, 1.38 mmol) was added. The reaction mixture was then left to stir for 4 h in an

oil bath at 110°C, and monitored by TLC for consumption of starting material. The solvent was removed in vacuo, and the residue was purified by column chromatography using basic alumina and a starting eluent of 6:4 hexanes: DCM (R_f , 1:1 DCM:hexanes = 0.22), yielding 12 as a pinkred solid (46 mg, 26%). ¹H NMR (400 MHz, CDCl₃): $\delta = 8.51$ (s, 1H, Hg), 7.50 (d, J_{HH} = 8.7 Hz, 2H, H_i). 7.06 (d, $J_{HH} = 8.7$ Hz, 2H, H_b), 6.20 (s, 1H, H_a), 2.83 (s, 3H, H_f), 2.77 (s, 3H, H_e), 2.72 (s, 3H, H_d), 2.59 (s, 3H, H_c), 2.49 (s, 3H, H_b). Carbon NMR was not obtained due to limited quantity of sample. ¹¹B {¹H} NMR (CDCl₃, 128 MHz) $\delta = 0.62$ (t). ¹⁹F NMR (CDCl₃, 376 MHz): -145.52 (q). HRMS (EI): m/z 443.0981 ([M]⁺), calculated for $[{}^{12}C_{21}{}^{1}H_{21}{}^{11}B{}^{19}F_2N_3Br]^+$: *m/z* 443.0980.

(E)-1-((Z)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)-N-(4-methylphenethyl)methanimine, (13): Formyl BODIPY (100 mg, 0.34



mmol), 2-(p-Tolyl)ethylamine (70 mg, 0.52 mmol), p -TsOH (cat.) and anhydrous Na₂SO₄ in EtOH was stirred under reflux for 1 h. The solution was then dried under vacuo and triturated in EtOH, yielding 16 (80 mg, 54%). NMR (400 MHz, CDCl₃): $\delta = 8.20$ (s, 1H, H_g), 7.11 (m, 4H, $H_{i,k}$), 6.11 (s, 1H, H_a), 3.79 (t, $J_{HH} = 7.2$ Hz, 2H, H_i),

2.97 (t, $J_{HH} = 7.1$ Hz, 2H, H_h), 2.66 (s, 3H, H_f), 2.64 (s, 3H, H_e), 2.60 (s, 3H, H_d), 2.54 (s, 3H, H_c), 2.43 (s, 3H, H_b), 2.32 (s, 3H, H_l). ¹³C{¹H} NMR (CDCl₃, 100 MHz): δ = 155.15, 142.45, 139.17, 137.03, 135.48, 128.95, 64.59, 53.41, 37.42, 21.01, 14.59, 13.24. ¹¹B{¹H} NMR (CDCl₃, 128 MHz): $\delta = 0.81$ (t). ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -145.8$ (q). HRMS (EI): m/z 407.2341 ([M]⁺), calculated for $[{}^{12}C_{24}{}^{1}H_{28}{}^{11}B{}^{19}F_2N_3]^+$: *m/z* 407.2344.

$(E)-N^{1}-(ferrocenylmethyl)-1-((Z)-2-(1-(1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-$

vl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)methanimine,



(14): Formyl BODIPY (450 mg, 1.55 mmol), methylamine ferrocene (500 mg, 2.33 mmol), p-TsOH (cat.) and anhydrous NaSO₄ in EtOH were stirred under reflux for 60 h. The solution was dried under *vacuo* and triturated in EtOH, yielding **14** (360 mg, 49%) ¹H NMR (CDCl₃, 400 MHz): δ = 8.41 (s, 1H, H_g), 6.13 (s, 1H, H_a), 4.47 (s, 2H, H_h), 4.19 (d, 2H, H_i), 4.15 (s, 5H, H_k), 4.13 (d, 2H, H_j), 2.76 (s, 3H, H_f), 2.70 (s, 3H, H_e), 2.66 (s, 3H, H_d), 2.55 (s, 3H, H_c), 2.45 (s, 3H, H_b). Compound decomposed during ¹³C-NMR acquisition. ¹¹B{¹H} NMR (CDCl₃, 160 MHz): δ = 0.62 (t). ¹⁹F NMR (CDCl₃, 470 MHz): δ = -145.71 (q). HRMS (ESI): 488.1768 *m/z* [(M+H)⁺], calcd for ¹²C₂₆¹H₂₉¹¹B¹⁹F₂Fe¹⁴N₃: 488.17665*m/z*.

(E)-1-((Z)-2-(1(-1-(difluoroboranyl)-3,5-dimethyl-1H-pyrrol-2-yl)ethylidene)-3,5-dimethyl-2H-pyrrol-4-yl)-N-(4-((E)-phenyldiazenyl)phenyl)methanimine, (15): Formyl BODIPY (100



mg, 0.34 mmol), 4-diazoaniline (70 mg, 0.34 mmol), p-Toluenesulfonic acid (10 mole %), and MgSO₄ were added into a 250 mL round bottom flask charged with EtOH (~40 mL). The reaction was brought to reflux at 80°C for 24 h. The solution was then dried under *vacuo* and further extracted with DCM. The organic layer

was kept and dried with MgSO₄ and brought to *vacuo*. The product was purified through an aluminium oxide column 4:1 (hexanes/EtOAc) ($R_f = 0.81$), and a pink band was collected. After removing the volatiles, the resulting residue was dissolved in hexanes and stored in a -36°C fridge to crystalize the pure derivative **14** and to remove trace amounts of formyl BODIPY. The crystals were filtered through a Buchner funnel, and dark red crystals (19%, 30.1 mg) were obtained. ¹H NMR (CDCl₃): $\delta = 8.58$ (s, 1H, H_g), 7.97-7.99 (dd, ¹J_{HH} = 8 Hz, 2H, H_j), 7.91-7.93 (dd, J_{HH} = 8 Hz, 2H, H_i), 7.54-7.50 (m, 2H, H_k), 7.48-7.46 (m, 1H, H_l), 7.28-7.26 (dd, J_{HH} = 8 Hz, 2H, H_h), 6.18 (s, 1H, H_a), 2.85 (s, 3H, H_f), 2.79 (s, 3H, H_e), 2.71 (s, 3H, H_d), 2.58 (s, 3H, H_c), 2.48 (s, 3H, H_b). ¹³C{¹H} NMR (CDCl₃, 100 MHz): $\delta = 186.3$, 155.9, 154.8, 153.0, 143.9, 130.8, 129.2, 128.2, 127.7, 124.3, 122.9, 122.6, 121.6, 121.5, 121.2, 120.4, 18.0, 17.9, 17.3, 14.9, 14.2. ¹¹B {H} NMR (CDCl₃, 128 MHz): $\delta = 0.63$ (t, ¹J_{BF} = 30.9 Hz). ¹⁹F NMR (CDCl₃, 376 MHz): $\delta = -145.53$ (q). HRMS (EI): *m/z* 469.2248 [(M)⁺], calculated for [¹²C₂₇¹H₂₆¹¹B¹⁹F₂¹⁴N₅]⁺: *m/z* 469.2249.

1-(difloroboranyl)-2-((Z)-1-(4-((E)-(2-(2,4-dinitrophenyl))hydrazono)methyl)-3,5-dimethyl-2Hpyrrol-2-ylidene)ethyl)-3,5-dimethyl-1H-pyrrole, (16): A 50 mL round bottom flask was



charged with formyl BODIPY (50 mg, 0.18 mmol) in DCM (10 mL). Brady's Reagent (10 mL) was added in one portion and the reaction was stirred at room temperature for 15 min. The solution was filtered leaving the product as dark purple

crystals (50 mg, 61%). ¹H NMR (400 MHz, DMSO): $\delta = 11.12$ (s, 1H, H_h), 8.97 (s, 1H, H_k), 858 (d, $J^3=9.4$ Hz, 1H, H_j), 8.15 (d, ${}^{3}J = 9.4$ Hz, 1H, H_i), 8.04 (s, 1H, H_g), 6.54 (s, 1H, H_a), 2.71 (s, 3H, H_f), 2.50 (s, 6H, H_{e,d}), 2.41 (s, 3H, H_c), 2.36 (s, 3H, H_b). Carbon NMR was not obtained due to limited solubility. ¹¹B {¹H} NMR (CDCl₃, 128 MHz) $\delta = 0.56$ (t, ${}^{1}J_{BF} = 31.9$ Hz,) ¹⁹F NMR (DMSO, 376 MHz) $\delta = -146.41$ (q). HRMS (EI): m/z 470.1697 ([M]⁺), calculated for [${}^{12}C_{21}{}^{11}H_{21}{}^{11}B{}^{19}F_{2}{}^{14}N_{6}{}^{16}O_{4}]^{+}$: m/z 470.1685.

1-(difluoroboranyl)-2-((Z)-1-(3,5-dimethyl-4-((E)-(2-phenylhydrazono)methyl)-2H-pyrrol-2ylidene)ethyl-3,5-dimethyl-1H-pyrrole, (17): A 50 mL round bottom flask was charged with



formyl BODIPY (100 mg, 0.34 mmol) in DCM (20 mL). Phenyl hydrazine (0.5 mL) was added in one portion and the reaction was stirred at room temperature for 2 h while being monitored by TLC for consumption of starting material. The solution was purified by column chromatography using DCM ($R_f = 0.4$), yielding **15** as a black solid (0.071 g, 55%). ¹H NMR

 $((CD3)_2CO): \delta = 9.27 \text{ (s, 1H, H_h), 8.01 (s, 1H, H_g), 7.22 (t, 2H, H_j), 7.07 (d, J_{HH} = 8.0 \text{ Hz, 2H,} \\ H_i), 6.75 (t, 1H, H_k), 6.21 (s, 1H, H_f), 2.74 (s, 3H, H_e), 2.71 (s, 3H, H_d), 2.63 (s, 3H, H_c), 2.46 \\ 2.48 (s, 3H, H_b). \text{ Carbon NMR was not obtained due to limited solubility. } {}^{11}B{}^{1}H} \text{ NMR (CDCl_3, 128 \text{ MHz}): } \delta = 0.60 (t). {}^{19}\text{F NMR (CDCl_3, 376 \text{ MHz}): } \delta = -145.2 (q). \text{ HRMS (EI): } m/z \text{ 380.1981} \\ ([M]^+), \text{ calculated for } [{}^{12}C_{21}{}^{11}H_{23}{}^{11}B{}^{19}F_2N_4]^+: m/z \text{ 380.1984}.$



Scheme 1. Synthesis of formylBODIPY (1).



Figure 1: The frontier molecular orbitals for methylated BODIPY and unsubstituted BODIPY displaying their susceptibility to nucleophilic attack. The methylated BODIPY is more susceptible to oxidation, whereas the unsubstituted BODIPY displays susceptible to reduction.

List of Abbreviations

- AlCl₃ Aluminum chloride
- AcOH Acetic acid
- BODIPY 4,4-Difluoro-4-bora-3a, 4a diaza-s-indacene
- DCM Dichloromethane
- DFT Density function theory
- DMF Dimethylformamide
- Et₂O diethyl ether
- EtOAc Ethyl acetate
- EtOH Ethanol
- FMO Frontier Molecular Orbitals
- HOMO Highest occupied molecular orbital
- LUMO Lowest unoccupied molecular orbital
- MeOH Methanol
- NBS *N*-Bromosuccinimide
- n-BuLi n-Butyllithium
- NEt₃ Triethylamine
- NIS N-Iodosuccinimide
- PCC Pyridinium chlorochromate
- 1, 10 Phen 1, 10-Phenanthroline
- TD-DFT Time dependent density functional theory
- TFA Trifluoroacetic acid
- THF Tetrahydrofuran
- TLC Thin Layer Chromatography
- TPA Triphenylamine
- *p*-TsOH *p*-Toluenesulfonic acid

Proposed mechanism for the formation of molecule **3**





Figure 3. UV-Vis spectra (in DCM) for target molecules **8**, **16** and **17**; comparing the effect of Schiff-base formation on a family of BODIPY dyes.

гö 50--5.53 -5.67 -2.73 -2.75 -2.75 0 21.01 1 Z ້ພ∵"ແ Figure A1: HNMR spectrum of compound formylBODIPY 1 in CDCl₃.

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Figure A2: HNMR spectrum of compound 2 in CDCl₃.



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Figure A3: HNMR spectrum of compound 3 in CDCl₃.





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Figure A9: HNMR spectrum of compound 9 in CDCl₃.



Figure A10: HNMR spectrum of compound 10 in CDCl₃.

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Figure A11: HNMR spectrum of compound 11 in CDCl₃.



Figure A12: HNMR spectrum of compound 12 in CDCl₃.

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Figure A14: HNMR spectrum of compound 14 in CDCl₃.

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Figure A16: HNMR spectrum of compound 16 in DMSO.



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Figure A17: HNMR spectrum of compound 17 in (CD₃)₂CO.

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