Supporting Information For

3-Cyanoallyl Boronates Are Versatile Building Blocks in the Synthesis of Polysubstituted Thiophenes

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General experimental information

General: Solvents used in the cross-coupling reaction were degassed with nitrogen gas prior to use. All other solvents were of reagent grade quality, and used as received. Unless otherwise noted, all reagents were purchased from commercial sources and used as received. Chromatography: Flash column chromatography was carried out using Silicycle 230-400 mesh silica gel. Thin-layer chromatography (TLC) was performed on Macherey Nagel precoated glassbacked TLC plates (SIL G/UV254, 0.25 mm) and visualized using a UV lamp (254 nm) or KMnO₄ stain in case of no UV activity. Nuclear Magnetic Resonance Spectroscopy: NMR spectra were recorded at 25°C on Bruker Advance III 400 MHz spectrometer, Varian Mercury 400, Agilent DD2 500, or Agilent DD2 600 instrument. Recorded shifts for protons are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvents (DMSO- d_6 : 2.50 or Acetonitrile- d_3 : δ 1.94, centre line). Chemical shifts for carbon resonances are reported in parts per million (δ scale) downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent (DMSO- d_6 : 39.52 or Acetonitrile- d_3 : δ 1.32, centre line). Carbons exhibiting significant line broadening brought about by boron substituents were not reported (quadrupolar relaxation). ¹¹B NMR was recorded at 25°C on a Bruker Advance III 400 MHz spectrometer or on an Agilent DD2 600 MHz spectrometer with an Agilent OneNMR probe and referenced to an external standard of BF_3 . Et₂O. Data are represented as follows: chemical shift δ in ppm, multiplicity (s singlet, d doublet, t triplet, q quartet, m multiplet, br broad), coupling constant J in Hz and integration. Mass Spectrometry: High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities or on JEOL AccuTOF-DART instrument.

Synthesis of electron-poor allylboronates

2-[2-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)ethylidene]propanedinitrile (3a)



To a stirred solution of α -boryl aldehyde¹ (111 mg, 0.56 mmol) in CH₃CN (10 mL) was added malononitrile (41 mg, 0.62 mmol) and Et₂NH (0.06 mL, 0.58 mmol) successively at room

mg, 0.55 mmol) and Et₂NH (0.05 mL, 0.50 mmol)

temperature. The reaction mixture was stirred at 45 °C for 1 h before it was cooled to room temperature. Solvent was evaporated and the residue was purified by using silica gel flash column chromatography (EtOAc with 0.1% Et₃N) gave **3a** as brown solid (125 mg, 91%). TLC (EtOAc, $R_f = 0.08$); m.p 120-121 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.03 – 7.90 (t, *J* = 9.0 Hz, 1H), 4.28 (d, *J* = 17.1 Hz, 2H), 4.08 (d, *J* = 17.1 Hz, 2H), 2.95 (s, 3H), 2.22 (d, *J* = 9.0 Hz, 2H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 173.8, 168.2, 113.2, 111.8, 85.2, 62.0, 46.1; ¹¹B NMR (128 MHz, DMSO-*d*₆) δ 11.1; HRMS (DART-TOF) calculated for [C₁₀H₁₀BN₃O₄+NH₄]⁺ 265.1108, found 265.1108.

(2E)-2-cyano-4-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)but-2-enoate (3b) CN To a stirred solution of α -boryl aldehyde (100 mg, 0.50 mmol) in CH₃CN (20 mL) was added ethyl cyanoacetate (62

successively at room temperature. The reaction mixture was stirred at 45 $\,^{\circ}$ C for 2 h before it was cooled to room temperature. Solvent was evaporated and the residue was purified by using silica gel flash column chromatography (EtOAc with 0.1% Et₃N) gave **3b** as white solid (137 mg, 93%). TLC (EtOAc, $R_f = 0.14$); m.p 178-180 °C; ¹H NMR $(400 \text{ MHz}, \text{DMSO-}d_6) \delta 7.83 - 7.51 \text{ (m, 1H)}, 4.33 - 4.17 \text{ (m, 4H)}, 4.07 \text{ (d, } J = 17.1 \text{ Hz},$ 2H), 2.94 (s, 3H), 2.14 (d, J = 9.0 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.3, 165.4, 161.1, 114.3, 106.9, 61.9, 61.7, 46.0, 13.9; ¹¹B NMR (128)MHz, DMSO- d_6) 10.9; HRMS (DART-TOF) δ calculated for $[C_{12}H_{15}BN_2O_6+NH_4]^+$ 312.1367, found 312.1375.

(2E)-N-benzyl-2-cyano-4-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)but-2-

enamide (3c)



To a stirred solution of α -boryl aldehyde (100 mg, 0.25 mmol) in CH₃CN (10 mL) was added *N*-benzyl-2-cyanoacetamide (181 mg, 1 mmol) and Et₂NH (0.052

mL, 0.50 mmol) successively at room temperature. The reaction mixture was stirred at 45 °C for 2 h before the it was cooled to room temperature. Solvent was evaporated and the residue was purified by silica gel flash column chromatography (35% acetonitrile in toluene with 1% Et₃N) gave **3c** as a beige solid (149 mg, 84%). TLC (3:2 Toluene/Acetonitrile, $R_f = 0.3$); m.p. = 100-101 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 8.81 (t, *J* = 5.9 Hz, 1H), 7.59 (t, *J* = 8.7 Hz, 1H), 7.34 – 7.23 (m, 5H), 4.36 (d, *J* = 5.9 Hz, 2H), 4.28 (d, *J* = 17.1 Hz, 2H), 4.09 (d, *J* = 17.0 Hz, 2H), 2.95 (s, 3H), 2.07 (d, *J* = 8.7 Hz, 2H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 168.5, 160.7, 158.6, 139.1, 128.3, 127.3, 126.9, 115.3, 110.6, 61.89, 46.1, 42.8; ¹¹B NMR (DMSO-*d*₆, 128 MHz) δ 11.7; HRMS (DART-TOF) calculated for [C₁₇H₁₈BN₃O₅+H]⁺ 356.1412, found 356.1417.

(2E)-2-cyano-4-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)but-2-enamide (3d)



To a stirred solution of α -boryl aldehyde (100 mg, 0.50 mmol) in CH₃CN (10 mL) was added cyanoacetamide (42

mg, 0.50 mmol) and Et₂NH (0.05 mL, 0.50 mmol)

successively at room temperature. The reaction mixture was stirred at 45 °C for 2 h before it was cooled to room temperature. Solvent was evaporated and the residue was purified by using silica gel flash column chromatography (50% Et₂O/CH₃CN to CH₃CN with 0.1% Et₃N) gave **3c** as white solid (117 mg, 88%). TLC (CH₃CN, R_f = 0.8); m.p 238-240 °C; ¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.61 (t, *J* = 8.8 Hz, 1H), 4.04 (d, *J* = 17.0 Hz, 2H), 3.90 (d, *J* = 17.0 Hz, 2H), 2.96 (s, 3H), 2.15 – 2.10 (m, 4H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.4, 162.4, 158.2, 115.4, 111.2, 61.8, 45.9; ¹¹B NMR (128 MHz, Acetonitrile-*d*₃) δ 11.3; HRMS (DART-TOF) calculated for [C₁₀H₁₂BN₃O₅+H]⁺ 266.0948, found 266.0954.

Synthesis of 5-(MIDA)boryl-2-aminothiophenes

Unless otherwise noted, 5-(MIDA)boryl-2-aminothiophenes were synthesized by the following procedure: To a solution of α -boryl aldehyde (1.0 equiv) in DMF (0.05 M) was added nitrile (1.1 equiv), sulfur (2.0 equiv) and diethylamine (1.0 equiv) successively. The reaction mixture was stirred at 45 °C and monitored by TLC until the complete consumption of α -boryl aldehyde (usually 3 h for all examples except 16 h for compound **4j**). Then the reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography using EtOAc to CH₃CN/EtOAc as eluent.

2-amino-5-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)thiophene-3carbonitrile (4a)

The title compound was obtained as a light brown solid 73% O_{CN}^{NMe} (102 mg) following the standard procedure using α borylaldehyde (100 mg, 0.50 mmol), malononitrile (37 mg, 0.55 mmol), Et₂NH, (0.052 mL, 0.50 mmol), sulfur (24 mg, 0.075 mmol) and DMF (17 mL). Reaction time: 3 h. TLC (EtOAc, R_f= 0.38); m.p 271-272 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 6.88 (s, 1H), 5.68 (s, 2H), 4.02 (d, J = 17.1 Hz, 2H), 3.87 (d, J = 17.1Hz, 2H), 2.68 (s, 3H); ¹³C NMR (DMSO- d_6 , 126 MHz) δ 168.8, 167.8, 131.8, 116.4, 85.1, 61.3, 47.2; ¹¹B NMR (DMSO- d_6 , 128 MHz) δ 10.8; HRMS (ESI+) calculated for [C₁₀H₁₀BN₃O₄S+H]⁺ 279.0575, found 279.0594.

ethyl 2-amino-5-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)thiophene-3carboxylate (4b)



The title compound was obtained as brown solid in 81% (61 $-NH_2$ mg) following the standard procedure using α -boryl aldehyde CO₂Et (49 mg, 0.25 mmol), ethyl cyanoacetate (31 mg, 0.27 mmol),

Et₂NH (0.025 mL, 0.25 mmol), sulfur (16 mg, 0.50 mmol) and DMF (6 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.43$); m.p 172-173 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.30 (s, 2H), 6.92 (s, 1H), 4.26 (d, *J* = 17.2 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.07 (d, *J* = 17.2 Hz, 2H), 2.65 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 169.4, 167.4, 164.8, 132.1, 106.2, 61.7, 59.3, 47.7, 14.9; ¹¹B NMR (128 MHz, DMSO-

 d_6) δ 11.1; HRMS (DART-TOF) calculated for $[C_{12}H_{15}BN_2O_6S+H]^+$ 327.0822, found 327.0820.

2-(5-amino-4-benzoylthiophen-2-yl)-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (4c)



The title compound was obtained as brown solid in 86% (773 mg) following the standard procedure using α -boryl aldehyde (500 mg, 2.51 mmol), nitrile **2c** (400 mg, 2.76 mmol), Et₂NH (0.26 mL, 2.51 mmol), sulfur (161 mg,

5.02 mmol) and DMF (50 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.47$); m.p 223-225 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.37 (s, 2H), 7.58 (dd, *J* = 7.7, 1.9 Hz, 2H), 7.52 – 7.44 (m, 3H), 6.82 (s, 1H), 4.25 (d, *J* = 17.3 Hz, 2H), 4.04 (d, *J* = 17.2 Hz, 2H), 2.67 (s, 3H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 189.7, 170.5, 169.4, 141.4, 133.6, 130.9, 128.6, 128.2, 115.3, 61.8, 47.8; ¹¹B NMR (96 MHz, Acetonitrile-*d*₃) δ 10.4; HRMS (DART-TOF) calculated for [C₁₆H₁₅BN₂O₅S+H]⁺ 359.0873, found 359.0878.

2-amino-5-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)thiophene-3carboxamide (4d)



The title compound was obtained as red solid in 85% (127 mg) following the standard procedure using α-boryl aldehyde
² (100 mg, 0.50 mmol), nitrile 2d (46 mg, 0.55 mmol), Et₂NH (0.05 mL, 0.50 mmol), sulfur (32 mg, 1.0 mmol) and DMF

(10 mL). Reaction time: 3 h. TLC (acetone, $R_f = 0.30$); m. p. 180-181 °C; ¹H NMR (500 MHz, Acetonitrile- d_3) δ 7.10 (s, 1H), 6.66 (s, 2H), 4.04 (d, J = 17.0 Hz, 2H), 3.92 – 3.80 (m, 2H), 2.70 (s, 3H); ¹³C NMR (126 MHz, Acetonitrile- d_3) δ 168.1, 167.7, 165.4, 131.2, 109.4, 61.1, 47.1; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.4; HRMS (DART-TOF) calculated for [C₁₀H₁₂BN₃O₅S+H]⁺ 298.0669, found 298.0672.

2-[5-amino-4-(4-fluorobenzoyl)thiophen-2-yl]-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (4e)



The title compound was obtained as pale yellow solid in 91% (172 mg) following the standard procedure using α -boryl aldehyde (100 mg, 0.50 mmol), nitrile **2e** (90 mg, 0.55 mmol), Et₂NH (0.05 mL, 0.50 mmol),

sulfur (32 mg, 1.0 mmol) and DMF (12 mL). Reaction time: 3 h. TLC (CH₃CN/Et₂O = 1:2, $R_f = 0.70$); m.p 248-249 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.36 (s, 2H), 7.66 (dd, *J* = 8.8, 5.6 Hz, 2H), 7.30 (t, *J* = 8.9 Hz, 2H), 6.82 (s, 1H), 4.26 (d, *J* = 16.8 Hz, 2H), 4.05 (d, *J* = 17.2 Hz, 2H), 2.67 (s, 3H); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 187.8, 170.1, 168.9, 137.4, 132.9, 130.4, 115.2, 115.0, 114.7, 61.3, 47.3; ¹¹B NMR (192 MHz, CD₃CN) δ 10.3; HRMS (DART-TOF) calculated for [C₁₆H₁₄BFN₂O₅S+H]⁺ 377.0778, found 327.0770.

2-[5-amino-4-(4-nitrobenzoyl)thiophen-2-yl]-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (4f)



The title compound was obtained as orange solid in 84% 2 (151 mg) following the standard procedure using α-boryl aldehyde (89 mg, 0.45 mmol), nitrile **2f** (94 mg, 0.49

mmol), Et₂NH (0.05 mL, 0.45 mmol), sulfur (29 mg, 0.90 mmol) and DMF (9 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.33$); m.p 270-271 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.53 (s, 2H), 8.30 (d, *J* = 8.7 Hz, 2H), 7.82 (d, *J* = 8.7 Hz, 2H), 6.74 (s, 1H), 4.26 (d, *J* = 17.2 Hz, 2H), 4.04 (d, *J* = 17.2 Hz, 2H), 2.68 (s, 3H); ¹³C NMR (126 MHz, DMSO-*d*₆) δ 187.4, 171.2, 169.3, 148.7, 146.9, 132.8, 129.4, 124.0, 115.1, 61.8, 47.8; ¹¹B NMR (128 MHz, DMSO-*d*₆) δ 11.0; HRMS (DART-TOF) calculated for [C₁₆H₁₄BN₃O₇S+H]⁺ 404.0723, found 404.0723.

2-[5-amino-4-(thiophene-2-carbonyl)thiophen-2-yl]-6-methyl-1,3,6,2dioxazaborocane-4,8- dione (4g)



The title compound was obtained in 86% (215 mg) following the standard procedure using α -boryl aldehyde (137 mg, 0.69 mmol), nitrile **2g** (100 mg, 0.69 mmol), Et₂NH (0.07 mL, 0.69 mmol), sulfur (44 mg, 1.38 mmol)

and DMF (14 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.29$); m. p 250-252 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 7.76 (dd, J = 3.7, 1.1 Hz, 1H), 7.71 (dd, J = 5.0, 1.1 Hz, 1H), 7.46 (s, 2H), 7.42 (s, 1H), 7.20 (dd, J = 5.0, 3.8 Hz, 1H), 4.06 (d, J = 17.0 Hz, 2H), 3.92 (d, J = 17.1 Hz, 2H), 2.76 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 179.6, 170.1, 168.9, 145.2, 131.9, 131.7, 130.5, 128.0, 114.2, 61.4, 47.3; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.1; HRMS (DART-TOF) calculated for [C₁₄H₁₃BN₂O₆S₂+H]⁺ 365.0437, found 365.0436.

2-amino-5-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)thiophene-3-carbothioamide (4h)



The title compound was obtained as brown thick oil in 79% (124 mg) following the standard procedure using α -boryl aldehyde (100 mg, 0.50 mmol), nitrile **2h** (55 mg, 0.55 mmol), Et₂NH (0.05 mL, 0.50 mmol), sulfur (32 mg, 1.0

mmol) and DMF (10 mL). Reaction time: 5 h. TLC (EtOAc, $R_f = 0.05$); m.p 166-168 °C; ¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.94 (s, 1H), 7.15 (s, 1H), 6.91 (s, 1H), 5.72 (br s, 2H), 4.05 (d, *J* = 17.2 Hz, 2H), 3.89 (m, 2H), 2.71 (s, 3H); ¹³C NMR (126 MHz, Acetonitrile-*d*₃) δ 190.9, 168.07, 168.0, 167.8, 166.9, 132.3, 129.5, 115.4, 113.6, 88.0, 61.9, 61.4, 61.3, 61.2, 47.3, 47.2; ¹¹B NMR (128 MHz, Acetonitrile-*d*₃) δ 9.8; HRMS (DART-TOF) calculated for [C₁₀H₁₂BN₃O₄S₂+H]⁺ 313.0471, found 313.0458.

2-[5-amino-4-(1-benzofuran-2-carbonyl)thiophen-2-yl]-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione(4i)



The title compound was obtained as brown solid in 82% (164 mg) following the standard procedure using α -boryl aldehyde (100 mg, 0.50 mmol), nitrile **2i** (184 mg, 1.0 mmol), Et₂NH (0.05 mL, 0.50 mmol), sulfur

(32 mg, 1.0 mmol) and DMF (12 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.34$); m.p 260-261 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 7.80 (d, J = 0.6 Hz, 1H), 7.78 (dd, J = 1.3, 0.7 Hz, 1H), 7.73 (br s, 1H), 7.64 (dd, J = 8.4, 0.9 Hz, 1H), 7.59 (d, J = 1.0 Hz, 1H), 7.51 (ddd, J = 8.4, 7.2, 1.3 Hz, 1H), 7.36 (ddd, J = 8.0, 7.2, 1.0 Hz, 1H), 4.09 (d, J = 17.0 Hz, 2H), 3.94 (d, J = 17.1 Hz, 2H), 2.78 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 175.5, 171.3, 168.9, 154.4, 153.6, 131.7, 127.1, 126.9, 123.7, 122.9, 114.4, 111.8, 111.5, 61.3, 47.3; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.1; HRMS (DART-TOF) calculated for [C₁₈H₁₅BN₂O₆S+H]⁺ 399.0822, found 399.0821.

2-[5-amino-4-(benzenesulfonyl)thiophen-2-yl]-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (4j)



The title compound was obtained as a red powder in 33% (33 \sim NH₂ mg) following the standard procedure using α -borylaldehyde \sim SO₂Ph (50 mg, 0.253 mmol), nitrile **2j** (100 mg, 0.56 mmol), Et₂NH

(0.026 mL, 0.25 mmol), sulfur (21 mg, 0.63 mmol) and DMF (7 mL). Reaction time : 16 h. TLC (EtOAc, $R_f = 0.4$); m.p. = 234-236 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 7.92 – 7.89 (m, 2H), 7.65 – 7.61 (m, 1H), 7.59 – 7.54 (m, 2H), 6.96 (s, 1H), 6.15 (br s, 2H), 4.01 (d, J = 17.0 Hz, 2H), 3.87 (d, J = 17.1 Hz, 2H), 2.67 (s, 3H); ¹³C NMR (DMSO- d_6) δ 168.84, 162.87, 143.25, 132.78, 130.56, 129.33, 125.84, 111.91, 61.51, 47.43; ¹¹B NMR (DMSO- d_6 , 128 MHz) 9.97; HRMS (DART-TOF) calculated for [C₁₅H₁₅BN₂O₆S₂+H]⁺ 395.0537, found 395.0542.

2-[5-amino-4-(1H-pyrrole-2-carbonyl)-1H-pyrrol-2-yl]-6-methyl-1,3,6,2dioxazaborocane-4,8-dione (4k)



The title compound was obtained as pale brown solid in 88% (153 mg) following the standard procedure using α -boryl aldehyde (100 mg, 0.50 mmol), nitrile **2k** (74 mg, 0.55 mmol), Et₂NH (0.05 mL, 0.50 mmol), sulfur (32 mg,

1.0 mmol) and DMF (12 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0.23$); m.p 258-260 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 10.06 (br s, 1H), 7.47 (s, 1H), 7.29 (s, 1H), 7.05 (td, J = 2.7, 1.3 Hz, 1H), 6.93 (ddd, J = 3.8, 2.5, 1.3 Hz, 1H), 6.43 – 6.21 (m, 1H), 4.06 (d, J = 17.1 Hz, 2H), 3.92 (d, J = 17.1 Hz, 2H), 2.76 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 177.9, 168.9, 168.6, 132.2, 131.6, 123.2, 114.5, 114.3, 109.3, 61.4, 47.3; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.3; HRMS (DART-TOF) calculated for [C₁₄H₁₄BN₃O₅S+H]⁺ 348.0825, found 348.0825.

2-[5-amino-4-(3-methoxybenzoyl)thiophen-2-yl]-6-methyl-1,3,6,2dioxazaborocane-4,8-dione (4l)



The title compound was obtained as pale brown solid in 90% (194 mg) following the standard procedure using α -boryl aldehyde (111 mg, 0.56 mmol), nitrile **21** (108 mg, 0.62 mmol), Et₂NH (0.06 mL, 0.62 mmol),

sulfur (39 mg, 1.22 mmol) and DMF (20 mL). Reaction time: 3 h. TLC (EtOAc, $R_f = 0..31$); m.p. 230-232 °C; ¹H NMR (500 MHz, Acetonitrile- d_3) δ 7.51 (s, 2H), 7.41 (ddd, J = 8.2, 7.5, 0.4 Hz, 1H), 7.23 (ddd, J = 7.5, 1.5, 1.0 Hz, 1H), 7.19 (dd, J = 2.6, 1.5 Hz, 1H), 7.10 (ddd, J = 8.2, 2.7, 1.0 Hz, 1H), 7.00 (s, 1H), 4.03 (d, J = 17.0 Hz, 2H), 3.87 (d, J = 17.1 Hz, 2H), 3.85 (s, 3H), 2.73 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 188.8, 170.1, 168.9, 158.9, 142.3, 133.2, 129.3, 120.0, 116.3, 114.8, 112.8, 61.3, 55.1, 47.3; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.1; HRMS (DART-TOF) calculated for [C₁₇H₁₇BN₂O₆S+H]⁺ 389.0978, found 389.0974.

Synthesis of borylated bromothiophene

2-bromo-5-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)thiophene-3carboxamide (5a)



To a stirred solution of aminothiophene (**4d**, 37 mg, 0.124 mmol) in CH₃CN (3 mL) was added CuBr₂ (42 mg, 0.187 mmol) and *t*-BuONO (16 mg, 0.155 mmol) successively at 0 $^{\circ}$ C. The cold bath was left in place but not recharged, and the

reaction mixture was stirred overnight. The mixture was filtered through a short pad of celite and the filtrate was concentrated under reduced pressure. The residue was purified by using silica gel flash chromatography (50% acetone/hexanes to 75% acetone/hexanes) to afford the title compound as brown solid (28 mg, 63%). TLC (EtOAc, $R_f = 0.43$); m.p 173-174 °C. ¹H NMR (400 MHz, Acetonitrile- d_3) δ 7.41 (s, 1H), 6.66 (br s, 1H), 6.18 (br s, 1H), 4.12 (d, J = 17.1 Hz, 2H), 3.97 (d, J = 17.2 Hz, 2H), 2.72 (s, 3H); ¹³C NMR (126 MHz, Acetonitrile- d_3) δ 167.8, 163.8, 136.8, 134.1, 117.5, 61.6, 47.6; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 9.7; HRMS (DART-TOF) calculated for [C₁₀H₁₀BBrN₂O₅S+H]⁺ 359.9698, found 359.9698.

Suzuki-Miyaura cross-coupling of borylated thiophene

3-benzoyl-5-phenylthiophen-2-amine² (6a)



To screw cap vial affixed with a rubber septum was added RuPhos Pd G3 (17 mg, 0.02 mmol), followed by aminothiopene 4c (85 mg, 0.24 mmol) and sodium carbonate (64 mg, 0.6 mmol). The vial was then evacuated and

backfilled with nitrogen three times. A degassed solution of DMF/H₂O (10/1, 2.0 mL) was then added through the septum, followed by degassed bromobenzene (0.021 mL, 0.2 mmol). The reaction mixture was then heated to 60 °C in a sand-bath. The reaction was stirred for 24 hours at which time TLC analysis indicated that the starting material had been consumed. The crude reaction mixture was then filtered through a small plug of silica before being concentrated *in vacuo*. The resulting residue was purified by column chromatography using 5-20% EtOAc/Hexanes as the eluent. The desired product was isolated in 78% yield (43.4 mg). TLC (1:4 EtOAc/Hexanes, $R_f = 0.40$); ¹H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 8.1 Hz, 8H), 7.49 (d, *J* = 27.7 Hz, 4H), 7.39 (d, *J* = 9.3 Hz, 7H), 7.31 (d, *J* = 15.4 Hz, 2H), 7.26 (d, *J* = 1.5 Hz, 2H), 7.23 – 7.19 (m, 1H), 7.12 (s, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 191.4, 165..9, 140.8, 133.9, 130.9, 128.9, 128.4, 128.2, 126.9, 124.9, 124.1, 122.9, 116.1.

5-phenyl-3-(thiophene-2-carbonyl)thiophen-2-amine (6b)



To screw cap vial affixed with a rubber septum was added RuPhos Pd G3 (9 mg, 0.011 mmol), followed by aminothiopene **4g** (43 mg, 0.12 mmol) and sodium carbonate

(25 mg, 0.30 mmol). The vial was then evacuated and backfilled with nitrogen three times. A degassed solution of DMF/H₂O (10/1, 1.0 mL) was then added through the septum, followed by degassed bromobenzene (0.01 mL, 0.10 mmol). The reaction mixture was then heated to 60 °C in a sand-bath. The reaction was stirred for 24 hours at which time TLC analysis indicated that the starting material had been consumed. The crude reaction mixture was then filtered through a small plug of silica before being

concentrated *in vacuo*. The resulting residue was purified by column chromatography using 5-20% EtOAc/Hexanes as the eluent. The desired product was isolated in 71% yield (20 mg). TLC (1:4 EtOAc/Hexanes, $R_f = 0.30$); m.p = 160-162 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ 7.75 (dd, J = 3.7, 1.1 Hz, 1H), 7.61 (dd, J = 5.0, 1.1 Hz, 1H), 7.50 (s, 1H), 7.49 – 7.44 (m, 2H), 7.35 (dd, J = 8.5, 6.9 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.16 (dd, J = 5.0, 3.7 Hz, 1H), 7.00 (br s, 2H); ¹³C NMR (101 MHz, Chloroform-*d*) δ 181.4, 165.8, 145.0, 133.8, 131.3, 130.9, 128.9, 127.5, 126.9, 124.9, 124.6, 121.6, 115.5; HRMS (DART-TOF) calculated for $[C_{15}H_{11}NOS_2+H]^+$ 286.0360, found 286.0360.

3-benzoyl-5-(pyrimidin-5-yl)thiophen-2-amine (6c)



To screw cap vial affixed with a rubber septum was added RuPhos Pd G3 (7 mg, 0.008 mmol), followed by aminothiopene **4c** (35 mg, 0.098 mmol), sodium carbonate (28 mg, 0.26 mmol) and 5-bromopyrimidine (14 mg, 0.088

mmol). The vial was then evacuated and backfilled with nitrogen three times. A degassed solution of DMF/H₂O (10/1, 1.5 mL) was then added through the septum. The reaction mixture was then heated to 60 °C in a sand-bath. The reaction was stirred for 24 hours at which time TLC analysis indicated that the starting material had been consumed. The crude reaction mixture was concentrated *in vacuo*. The resulting residue was purified by column chromatography using 50% EtOAc/Hexanes as the eluent. The desired product was isolated in 65% yield (16 mg). TLC (2:1 EtOAc/Hexanes, $R_f = 0.30$); m.p = 165-167 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ 9.03 (s, 1H), 8.74 (s, 2H), 7.81 – 7.63 (m, 2H), 7.60 – 7.40 (m, 3H), 7.26 (s, 1 H), 7.26 – 7.21 (br s, 2H); ¹³C NMR (101 MHz, Chloroform-*d*) δ 191.3, 166.5, 156.2, 152.2, 140.3, 131.2, 128.4, 128.4, 128.0, 126.0, 116.2, 115.6; HRMS (DART-TOF) calculated for [C₁₅H₁₁N₃OS+H]⁺ 282.0701, found 282.0702.

3-[5-amino-4-(3-methoxybenzoyl)thiophen-2yl]benzonitrile (6d) 13 To screw cap vial affixed with a rubber septum was added RuPhos Pd G3 (8 mg, 0.009 mmol), followed by aminothiopene 4I (37 mg, 0.095 mmol), sodium carbonate (30 mg, 0.28 mmol) and 3-bromobenzonitrile (17 mg, 0.093 mmol). The vial was then evacuated and backfilled with nitrogen three times. A degassed solution of DMF/H₂O (10/1, 2.0 mL) was then added through the septum. The reaction mixture was then heated to 60 °C in a sand-bath. The reaction was stirred for 24 hours at which time TLC analysis indicated that the starting material had been consumed. The crude reaction mixture was concentrated in vacuo and dry-loaded onto Celite. The resulting residue was purified by reverse-phase flash column chromatography. The desired product was isolated in 54% yield (17 mg) as light yellow solid. TLC (1:4 EtOAc/Hexanes, $R_f =$ 0.6 Hz, 1H, 7.75 - 7.66 (m, 3H), 7.55 (dt, J = 7.7, 1.4 Hz, 1H), 7.52 - 7.40 (m, 2H), 7.33 (s, 1H), 7.28 (ddd, J = 7.5, 1.5, 1.0 Hz, 1H), 7.22 (dd, J = 2.7, 1.5 Hz, 1H), 7.14 (ddd, J = 8.3, 2.7, 1.0 Hz, 1H), 3.87 (s, 3H); ¹³C NMR (151 MHz, Acetonitrile- d_3) δ 190.3, 167.0, 159.5, 135.1, 129.8, 129.6, 129.4, 128.6, 127.7, 124.7, 120.3, 118.4, 116.7, 115.2, 112.9, 112.7, 55.1; HRMS (DART-TOF) calculated for $[C_{19}H_{14}N_2O_2S+H]^+$ 335.0849, found 335.0841.

5-(4-aminophenyl)-3-benzoylthiophen-2-amine (6e)



To screw cap vial affixed with a rubber septum was added RuPhos Pd G3 (8 mg, 0.009 mmol), followed by aminothiopene **4c** (40 mg, 0.112 mmol), sodium carbonate (30 mg, 0.28 mmol) and 4-bromoaniline (16

mg, 0.093 mmol). The vial was then evacuated and backfilled with nitrogen three times. A degassed solution of DMF/H₂O (10/1, 1.5 mL) was then added through the septum. The reaction mixture was then heated to 60 °C in a sand-bath. The reaction was stirred for 24 hours at which time TLC analysis indicated that the starting material had been consumed. The crude reaction mixture was concentrated *in vacuo* and dry-loaded onto Celite. The resulting residue was purified by reverse-phase flash column chromatography. The desired product was isolated in 37% yield (10 mg) as

light yellow solid. The product is not stable and color changed from light yellow dark brown. Dark brown precipitate was observed during the measurement of NMR. TLC (1:3 EtOAc/Hexanes, $R_f = 0.2$); ¹H NMR (500 MHz, Acetonitrile-*d*₃) δ 7.75 – 7.64 (m, 3H), 7.59 – 7.44 (m, 6H), 7.26 – 7.12 (m, 2H), 6.92 (s, 1H), 6.69 – 6.61 (m, 2H); ¹³C NMR (126 MHz, Acetonitrile-*d*₃) δ 190.1, 165.6, 146.5, 141.1, 130.5, 129.3, 128.2, 127.9, 125.7, 124.2, 123.3, 119.5, 114.9; HRMS (DART-TOF) calculated for [C₁₇H₁₄N₂OS+H]⁺ 295.0905, found 295.0900.

Synthesis of 2-(MIDA)boryl thieno[2,3-b]pyridines

Unless otherwise noted, 2-(MIDA)boryl thieno[2,3-b]pyridines were synthesized by the following procedure: To a solution of 5-(MIDA)boryl-2-aminothiophene (30 mg, 0.084 mmol) in DMF (3 mL) was added ketone (0.09 mmol, 1.1 equiv) and trimethylchlorosilane (0.42 mmol, 5 equiv) successively. The reaction mixture was stirred at 100 °C and monitored by LCMS until the complete consumption of the aminothiophene. Then the reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography using EtOAc to CH_3CN/Et_2O as eluent.

6-methyl-2-{4-phenyl-5H,6H,7H,8H-thieno[2,3-b]quinolin-2-yl}-1,3,6,2dioxazaborocane-4,8-dione (8a)

The title compound was obtained as pale yellow solid in 95% (33 mg) following the standard procedure. Reaction time: 1 h. TLC (EtOAc, R_f = 0.41); m.p 322-325 °C; ¹H

NMR (500 MHz, Acetonitrile- d_3) δ 7.65 – 7.46 (m, 3H), 7.44 – 7.33 (m, 2H), 6.96 (s, 1H), 4.09 (d, J = 17.1 Hz, 2H), 3.93 (d, J = 17.0 Hz, 2H), 3.08 (t, J = 6.6 Hz, 2H), 2.69 (s, 3H), 2.63 (t, J = 6.4 Hz, 2H), 1.94 – 1.90 (m, 2H), 1.80 – 1.75 (m, 2H); ¹³C NMR (126 MHz, Acetonitrile- d_3) δ 167.9, 161.2, 156.2, 144.3, 137.2, 131.6, 128.8, 128.5, 128.0, 127.3, 125.9, 61.7, 47.6, 33.2, 27.0, 22.7, 22.5; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.9; HRMS (DART-TOF) calculated for [C₂₂H₂₁BN₂O₄S+H]⁺ 421.1393, found 421.1398.

6-methyl-2-{8-phenyl-4-thia-2-azatricyclo[7.3.0.0³,⁷]dodeca-1(9),2,5,7-tetraen-5-yl}-1,3,6,2-dioxazaborocane-4,8-dione (8b)



The title compound was obtained as pale yellow solid in 91% (31 mg) following the standard procedure. Reaction time: 1 h. TLC (EtOAc, $R_f = 0.38$); m.p. 305-306 °C; ¹H

NMR (400 MHz, Acetonitrile- d_3) δ 7.66 – 7.43 (m, 5H), 7.29 (s, 1H), 4.11 (d, J = 17.1 Hz, 2H), 3.95 (d, J = 17.1 Hz, 2H), 3.12 (t, J = 7.6 Hz, 2H), 2.96 (t, J = 7.3 Hz, 2H), 2.70 (s, 3H), 2.21-2.13 (m, 2 H); ¹³C NMR (126 MHz, Acetonitrile- d_3) δ 167.9, 165.0, 163.3, 140.5, 137.0, 131.5, 130.7, 128.9, 128.6, 128.3, 127.0, 61.7, 47.6, 34.1, 29.5, 23.6; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.5; HRMS (DART-TOF) calculated for [C₂₁H₁₉BN₂O₄S+H]⁺ 407.1237, found 407.1240.

2-{4,6-diphenylthieno[2,3-b]pyridin-2-yl}-6-methyl-1,3,6,2-dioxazaborocane-4,8-dione (8c)

The title compound was obtained as pale yellow solid in 79% (29 mg) following the standard procedure. Reaction time: 12 h. TLC (EtOAc, Rf = 0.49); m.p > 350 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 8.23 – 8.04 (m, 2H), 7.80 (s, 1H), 7.74 – 7.62 (m, 2H), 7.55 – 7.30 (m, 6H), 4.01 (d, *J* = 17.1 Hz, 2H), 3.86 (d, *J* = 17.2 Hz, 2H), 2.62 (s, 3H); ¹³C NMR (126 MHz, Acetonitrile- d_3) δ 167.9, 165.3, 154.4, 145.7, 138.8, 138.4, 130.7, 129.2, 128.9, 128.9, 128.9, 128.8, 116.4, 61.8, 47.7; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 11.2; HRMS (DART-TOF) calculated for [C₂₄H₁₉BN₂O₄S+H]⁺ 443.1237, found 443.1250.

6-methyl-2-(6-methyl-4,8-dioxo-1,3,6,2-dioxazaborocan-2-yl)-4-phenylthieno[2,3-b]pyridine-5-carboxylate (8d)

The title compound was obtained as pale yellow solid in 88% (33 mg) following the standard procedure. Reaction time: 12 h. TLC (EtOAc, $R_f = 0.33$); m.p > 350 °C; ¹H NMR (400 MHz, Acetonitrile- d_3) δ 7.58 – 7.50 (m, 3H), 7.49 – 7.44 (m, 2H), 7.24 (s, 1H), 4.26 – 4.07 (m, 4H), 3.95 (d, J = 17.1 Hz, 2H), 2.71 (s, 3H), 2.68 (s, 3H), 1.01 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, Acetonitrile- d_3) δ 168.2, 167.5, 163.9, 152.2, 142.7, 136.1, 130.2, 128.4, 128.2, 127.0, 124.9, 61.4, 61.0, 47.3, 22.0, 12.6; ¹¹B NMR (128 MHz, Acetonitrile- d_3) δ 10.1; HRMS (DART-TOF) calculated for [C₂₂H₂₁BN₂O₆S+H]⁺ 453.1292, found 453.1295.

6-methyl-2-{17-phenyl-13-thia-11-azatetracyclo[8.7.0.0²,⁷.0¹²,¹⁶]heptadeca-1(10),2,4,6,11,14,16-heptaen-14-yl}-1,3,6,2-dioxazaborocane-4,8-dione (8e)

The title compound was obtained as pale yellow solid in 81% (32 mg) following the standard procedure. Reaction time: 16 h. TLC (EtOAc, $R_f = 0.44$); m.p > 350 °C; ¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 8.45 – 8.37 (m, 1H), 7.65 – 7.50 (m, 3H), 7.48 – 7.25 (m, 5H), 7.10 (s, 1H), 4.12 (d, *J* = 17.2 Hz, 2H), 3.96 (d, *J* = 17.2 Hz, 2H), 2.88 (s, 4H), 2.73 (s, 3H); ¹³C NMR (126 MHz, Acetonitrile-*d*₃) δ 167.9, 162.2, 150.6, 143.5, 139.0, 136.8, 134.8, 132.4, 129.3, 129.2, 128.5, 128.2, 127.7, 127.6, 127.0, 125.9, 125.3, 61.7, 47.6, 27.7, 25.3; ¹¹B NMR (128 MHz, Acetonitrile-*d*₃) δ 10.1; HRMS (DART-TOF) calculated for [C₂₆H₂₁BN₂O₄S+H]⁺ 469.1393, found 469.1394.

Copies of ¹H NMR, ¹³C NMR and ¹¹B NMR













































-11.01

















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-80

30

100 90

80

70

60

50















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