A Highly Efficient Monophosphine-Based Catalyst for the Palladium-Catalyzed Suzuki-Miyaura Reaction of Heteroaryl Halides and Heteroaryl Boronic Acids and Esters

Kelvin Billingsley and Stephen L. Buchwald*

*Department of Chemistry, Massachusetts Institute of Technology,
Cambridge, MA 02139*

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General. All reactions were carried out under an argon atmosphere. *n*-Butanol (HPLC grade) was purchased from Alfa Aesar. *Sec*-Butanol (anhydrous) and *tert*-amyl alcohol (reagent grade) were purchased from Aldrich. Commercially available materials were used without further purification unless otherwise noted. SPhos (**1**) and XPhos (**2**) were synthesized in our laboratories but are commercially available from Aldrich Chemical Co. or Strem Chemicals, Inc. Aryl halides were purchased from Aldrich Chemical Co. Liquid aryl bromides were purified by passing through a pad of basic alumina prior to use. Boron reagents were purchased from Aldrich or Frontier Scientific. Anhydrous granular potassium phosphate was purchased from Mallinckrodt Chemicals and ground with a mortar and pestle and stored in a bench-top dessicator.

All new compounds were characterized by ^1H NMR, ^{13}C NMR, IR spectroscopy and elemental analysis. Known compounds were characterized by ^1H NMR and melting points (for solids) and compared to their literature values. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300. Infrared spectra were recorded on an ASI Applied Systems ReactIR 1000 (neat samples were placed directly on the DiComp probe). Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. All ^1H NMR experiments are reported in δ units, parts per million (ppm) downfield of TMS and were measured relative to the signals for the residual benzene (7.16 ppm), chloroform (7.26 ppm), dimethylsulfoxide (2.50 ppm) or methanol (3.31 ppm). All ^{13}C NMR spectra were reported in ppm relative to residual chloroform (77 ppm), dimethylsulfoxide (39.5 ppm) or methanol (49 ppm) and were obtained with ^1H decoupling. Melting points were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on Hewlett-Packard 6890 gas chromatography instrument with a FID detector using 25m x 0.20 mm capillary column with cross-linked methyl siloxane as a stationary phase.

The yields in tables 1-2 and 4-9 refer to isolated yields (average of two runs) of compounds estimated to be $\geq 95\%$ pure as determined by ^1H NMR and GC analysis and/or combustion analysis.

I. Experimental for Reactions of Thiophene Boronic Acids

General Procedure A: Pd-Catalyzed Suzuki-Miyaura Couplings of Thiophene Boronic Acids.

An oven-dried Schlenk tube was charged with $\text{Pd}_2(\text{dba})_3$ (2.3 mg, 0.0025 mmol), ligand (0.01 mmol), thiophene boronic acid (48 mg, 0.375 mmol) and powdered, anhydrous K_3PO_4 (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.50 mL) was added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 $^\circ\text{C}$ until aryl halide had been completely consumed as determined by gas chromatography.

At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

General Procedure B: Pd-Catalyzed Suzuki-Miyaura Couplings of Thiophene Boronic Acids at Low Catalyst Loading.

Procedure A was followed with the following changes: A separate vial was initially charged with Pd(OAc)₂ (1.0 mol%) and SPhos (2.0 mol%). The vial was sealed with a Teflon-coated screwcap, a needle was inserted through the cap and the vial was then evacuated and backfilled with argon. Butanol (1 mL) was added and the mixture was briefly heated. 250 μ L of this solution (0.25% Pd, 0.50% SPhos) was then added to the Schlenk flask containing the base, boronic acid and aryl halide. Butanol (250 μ L) was added in the final solvent addition.

2,3'-Bithiophene-5-carbaldehyde (Table 1, entry 1). Following general procedure B, a mixture of 5-chlorothiophene-2-carbaldehyde (26.6 μ L, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in tert-amyl alcohol with stirring for 4 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 78% yield (38 mg) as a yellow solid, mp 122-123 °C. ¹H NMR (300 MHz, CDCl₃) δ : 9.84 (s, 1H), 7.67 (d, J = 3 Hz, 1H), 7.56 (dd, J = 3,1 Hz, 1H), 7.37 (dd, J = 5,3 Hz, 1H), 7.33 (dd, J = 5,1 Hz, 1H), 7.26 (d, J = 5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 182.7, 148.7, 141.5, 137.5, 134.4, 127.2, 125.9, 124.0, 122.7. IR (neat, cm⁻¹): 3087, 1653, 1456, 1232. Anal. Calcd. for C₈H₆OS₂: C, 55.64; H, 3.11. Found C, 55.59; H, 3.02.

2,5-Dimethyl-3-(thiophen-3-yl)pyrazine (Table 1, entry 2). Following general procedure B, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μ L, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in tert-amyl alcohol with stirring for 4 h. The crude product was purified via flash column chromatography on silica gel (15% EtOAc/Hexanes) to provide the title compound in a 97% yield (42 mg) as

a yellow oil. ^1H NMR (300 MHz, CDCl_3) δ : 8.26 (s, 1H), 7.64 (ddd, $J = 3, 2, 1$ Hz, 1H), 7.49 (ddd, $J = 5, 2, 1$ Hz, 1H), 7.40 (ddd, $J = 5, 3, 1$ Hz, 1H), 2.67 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ : 150.3, 147.9, 147.7, 139.9, 128.4, 125.7, 125.6, 23.1, 21.1. IR (neat, cm^{-1}): 2921, 1564, 1530, 1435, 1372, 1329, 1166. ^1H NMR spectrum included.

3-(2,6-Dimethylphenyl)thiophene (Table 1, entry 3). Following general procedure A, a mixture of 2-chloro-*m*-xylene (33.1 μL , 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in butanol with stirring for 10 h. The crude product was purified via flash column chromatography on silica gel (Hexanes) to provide the title compound in a 77% yield (36 mg) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ : 7.41 (dd, $J = 5, 3$ Hz, 1H), 7.18 (dd, $J = 8, 7$ Hz, 1H), 7.11 (t, $J = 1$ Hz, 2H), 7.05 (dd, $J = 3, 1$ Hz, 1H), 6.96 (dd, $J = 5, 1$ Hz, 1H), 2.11 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ : 140.7, 137.1, 128.7, 127.2, 125.2, 122.2, 20.8. IR (neat, cm^{-1}): 2924, 2851, 1678, 1527, 1435, 1372, 1166. ^1H NMR spectrum included.

5-(Thiophen-3-yl)-1*H*-indole (Table 1, entry 4). An oven-dried Schlenk tube was charged with a mixture of 5-chloroindole (37.9 mg, 0.25 mmol), $\text{Pd}_2(\text{dba})_3$ (2.3 mg, 0.0025), XPhos (4.8 mg, 0.01 mmol), and powdered, anhydrous K_3PO_4 (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.50 mL) was added via syringe, and the reaction mixture was heated to 100 $^\circ\text{C}$. 3-thiophene boronic acid (48 mg, 0.375 mmol) in *n*-butanol (1.00 mL) was added via syringe pump through the septum over 1 h. The septum was then replaced with a Teflon screwcap under argon and the Schlenk tube was sealed. The reaction mixture was heated at 100 $^\circ\text{C}$ for 15 h. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel eluting with ethyl acetate and the eluent was concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 90% yield (45 mg) as a yellow solid, mp 80-82 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 8.12 (bs, 1H), 7.90 (t, $J = 1$ Hz, 1H), 7.48 (dd, $J = 8, 2$ Hz, 1H), 7.46 (dd, $J = 5, 1$ Hz, 1H), 7.40-7.44 (m, 2H), 7.22 (t, $J = 3$ Hz, 1H), 6.60 (t, $J = 3$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ : 143.6, 135.1, 128.2, 128.1, 126.8, 125.8, 124.8, 121.3, 118.8, 118.5,

111.2, 102.9. IR (neat, cm^{-1}): 2951, 2920, 1463, 854, 785. Anal. Calcd. for $\text{C}_{12}\text{H}_9\text{NS}$: C, 72.33; H, 4.55. Found C, 72.10; H, 4.72.

3,3'-Bithiophene (Table 1, entry 5).¹ Following general procedure A, a mixture of 3-chlorothiophene (23.2 μL , 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in butanol with stirring for 10 h. The crude product was purified via flash column chromatography on silica gel (Hexanes) to provide the title compound in a 96% yield (36 mg) as a white solid, mp 119-121 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 7.39 (dd, $J = 3, 2$ Hz, 1H), 7.35-7.36 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ : 137.2, 126.3, 126.1, 119.7. IR (neat, cm^{-1}): 3414, 1652, 1465, 1418, 1089. Anal. Calcd. for $\text{C}_8\text{H}_6\text{S}_2$: C, 57.79; H, 3.64. Found C, 57.98; H, 3.60.

2-Methyl-5-(thiophen-3-yl)benzo[d]oxazole (Table 1, entry 6). Following general procedure A, a mixture of 5-chloro-2-methylbenzoxazole (41.9 mg, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in butanol with stirring for 10 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 91% yield (49 mg) as a white solid, mp 85-87 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 7.84 (d, $J = 2$ Hz, 1H), 7.52-7.54 (dd, $J = 8, 2$ Hz, 1H), 7.47 (d, $J = 8$ Hz, 1H), 7.44 (t, $J = 3$ Hz, 1H), 7.41 (d, $J = 1$ Hz, 1H), 7.40 (d, $J = 1$ Hz, 1H), 2.65 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ : 164.5, 150.3, 142.1, 132.6, 126.6, 126.3, 123.3, 120.2, 117.1, 110.2, 14.6. IR (neat, cm^{-1}): 3075, 1621, 1578, 1268, 920. Anal. Calcd. for $\text{C}_{12}\text{H}_9\text{NOS}$: C, 66.95; H, 4.21. Found C, 66.81; H, 4.37.

2-(Thiophen-3-yl)pyrimidine (Table 1, entry 7).² Following general procedure A, a mixture of 2-chloropyrimidine (28.6 mg, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), 4 $\text{\AA}$ molecular sieves (62.5 mg), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in tert-amyl alcohol with stirring for 4 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a

¹ Wang, L.; Zhang, Y.; Liu, L.; Wang, Y. *J. Org. Chem.* **2006**, *71*, 1284.

² Dawood, K. M.; Kirschning, A. *Tetrahedron* **2005**, *61*, 12121.

84% yield (38 mg) as a white solid, mp 92-94 °C. ^1H NMR (300 MHz, CDCl_3) δ : 8.72 (dd, $J = 5,1$ Hz, 2H), 8.28 (dd, $J = 5,2$ Hz, 1H), 7.88 (dd, $J = 5,1$ Hz, 1H), 7.37 (dt, $J = 4,1$ Hz, 1H), 7.10 (dt, $J = 4,1$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ : 161.8, 157.2, 141.5, 127.9, 127.3, 126.1, 118.6. IR (neat, cm^{-1}): 3120, 1636, 1556, 1526, 1433, 1377, 1089. ^1H NMR spectrum included.

STANDARD PROTON PARAMETERS

3-(2,6-Dimethyl-phenyl)-thiophene (CDCl₃).

expt 02pu1

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4kb/4kb_111247_071- dof 0
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ifrq 500.235 dnt 10000
tn M1 dseq 1.0
at 3.200 dres 1.0
np 64000 hmoa n
sw 10000.0 PROCESSING
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bs 8 proc 131072
ss 1 fn
lprw 50 math f
pw 9.6 verr
dl 8 verr
tof 1400.2 vexp
nt 16 vbs
ct 16 wnt
clock n
gain not used
flags n
in n
dp v
hs nn
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ls 100.00
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rfp 3621.7
th 7
ins 1.000
na ph

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STANDARD PROTON PARAMETERS

2-Thiophen-3-yl-pyrimidine (CDCl₃).

expt 02pu1

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ACQUISITION 505 dm nmh c
ifrq 500.235 dseq 1.0
tn M1 dres 1.0
at 3.200 hmoa n
np 64000 PROCESSING
sw 10000.0 vfile ft
fb not used proc 131072
bs 8 fn
ss 1 math f
lprw 50
pw 9.6 verr
dl 8 verr
tof 1400.2 vexp
nt 16 wnt
ct 16
clock n
gain not used
flags n
in n
dp v
hs nn
DISPLAY
sp -501.4
vp 5505.6
vs 151
sc 0
vc 250
hnm 22.02
ls 100.00
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rfp 3621.7
th 7
ins 1.000
na ph

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5-Chloro-2,3'-bithiophene (Table 2, entry 1). Following general procedure B, a mixture of 2-bromo-5-chlorothiophene (27.4 μ L, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $Pd(OAc)_2$ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in butanol with stirring for 4 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in a 82% yield (41 mg) as a white solid, mp 74-76 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 7.35 (dd, J = 5,3 Hz, 1H), 7.31 (dd, J = 3,2 Hz, 1H), 7.23 (dd, J = 5,2 Hz, 1H), 6.95 (d, J = 4 Hz, 1H), 6.85 (d, J = 4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 137.8, 134.8, 128.1, 126.7, 126.4, 125.6, 122.2, 119.7. IR (neat, cm^{-1}): 3089, 1446, 769. 1H NMR spectrum included.

2-(5-Chloro-thiophen-2-yl)quinoxaline (Table 2, entry 2). Following general procedure A, a mixture of 2-chloroquinoxaline (41.2 mg, 0.25 mmol), 5-chloro-2-thiophene boronic acid (60.9 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 4 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in a 96% yield (59 mg) as a yellow solid, mp 71-73 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 9.13 (s, 1H), 8.05 (dd, J = 8,1 Hz, 1H), 8.01 (dd, J = 8,1 Hz, 1H), 7.59 (d, J = 4 Hz, 1H), 6.99 (d, J = 4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 146.4, 141.9, 141.3, 141.1, 141.0, 134.9, 130.6, 129.4, 129.1, 129.0, 127.6, 126.0. IR (neat, cm^{-1}): 3075, 2924, 2851, 1611, 1549, 1432, 1227. Anal. Calcd. for $C_{12}H_8N_2SCl$: C, 58.42; H, 2.86. Found C, 58.39; H, 2.82.

3-(3,4-Dimethylphenyl)thiophene (Table 3, entry 1). Following general procedure A, a mixture of 3,4-dimethylchlorobenzene (0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 24 h. The crude product was analyzed via gas chromatography with dodecane as an internal standard. A 93% conversion of the aryl chloride was detected.

3-(3,4-Dimethylphenyl)thiophene (Table 3, entry 2). Following general procedure A, a mixture of 3,4-dimethylchlorobenzene (0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), 3,3'-bithiophene (41 mg, 0.0625 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 24 h. The crude product was analyzed via gas chromatography with dodecane as an internal standard. A 7% conversion of the aryl chloride was detected.

3-(3,4-Dimethylphenyl)thiophene (Table 3, entry 3). Following general procedure A, a mixture of 3,4-dimethylchlorobenzene (0.25 mmol), 3-thiophene boronic acid (48 mg,

0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 24 h. The crude product was analyzed via gas chromatography with dodecane as an internal standard. A 100% conversion of the aryl chloride was detected.

3-(3,4-Dimethylphenyl)thiophene (Table 3, entry 4). Following general procedure A, a mixture of 3,4-dimethylchlorobenzene (0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), 3,3'-bithiophene (41 mg, 0.0625 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 24 h. The crude product was analyzed via gas chromatography with dodecane as an internal standard. A 100% conversion of the aryl chloride was detected.

5-(Thiophen-3-yl)pyridin-2-amine (Table 4, entry 1). Following general procedure A, a mixture of 2-amino-5-chloropyridine (32.1 mg, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 15 h. The crude product was purified via flash column chromatography on silica gel (40% EtOAc/Hexanes) to provide the title compound in a 95% yield (42 mg) as a white solid, mp 141-143 °C. ¹H NMR (300 MHz, CD₃OD) δ : 8.18 (d, J = 2 Hz, 1H), 7.77 (dd, J = 8,2 Hz, 1H), 7.44-7.48 (m, 2H), 7.35 (dd, J = 5,2 Hz, 1H), 6.64 (d, J = 8 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 157.3, 145.8, 139.3, 136.0, 126.4, 125.7, 122.6, 118.7, 108.5. IR (neat, cm⁻¹): 3439, 2924, 2851, 1653, 1500, 1201, 1089. ¹H NMR spectrum included.

4-Methyl-6-(thiophen-3-yl)pyrimidin-2-ylamine (Table 4, entry 2). Following general procedure A, a mixture of 2-amino-4-chloro-6-methylpyrimidine (35.9 mg, 0.25 mmol), 3-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), 4Å molecular sieves (62.5 mg), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 4 h. The crude product was purified via flash column chromatography on silica gel (40% EtOAc/Hexanes) to provide the title compound in a 80% yield (37 mg) as a yellow solid, mp 182-184 °C. ¹H NMR (300 MHz, CD₃OD) δ : 8.15 (dd, J = 3,1 Hz, 1H), 7.68 (dd, J = 5,1 Hz, 1H), 7.49 (dd, J = 5,3 Hz, 1H), 6.96 (s, 1H), 2.35 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ : 203.5,

170.0, 162.7, 127.8, 127.7, 127.4, 122.1, 107.5, 23.8. IR (neat, cm^{-1}): 3350, 3187, 1645, 1580, 1552, 1466, 1418, 1238, 1089. ^1H NMR spectrum included.

1-(Thiophen-2-yl)isoquinoline (Table 5, entry 1).³ Following general procedure B, a mixture of 1-chloroisoquinoline (40.9 mg, 0.25 mmol), 2-thiophene boronic acid (48 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in sec-butanol with stirring for 10 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 96% yield (51 mg) as a yellow solid, mp 67-69 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.56 (d, J = 7 Hz, 1H), 8.51 (d, J = 8 Hz, 1H), 7.86 (dd, J = 8, 1 Hz, 1H), 7.68-7.71 (dt, J = 7, 1 Hz, 1H), 7.62 (m, 2H), 7.58 (d, J = 6 Hz, 1H), 7.53-7.54 (dt, J = 6, 1 Hz, 1H), 7.20-7.22 (ddd, J = 6, 3, 1, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 153.5, 142.7, 142.1, 130.1, 128.7, 127.9, 127.6, 127.4, 127.1, 126.8, 126.1, 119.9. IR (neat, cm⁻¹): 3053, 2918, 2851, 1617, 1550, 1434, 1340. Anal. Calcd. for C₁₃H₉NS: C, 73.90; H, 4.29. Found C, 73.69; H, 4.17.

2,5-Dimethyl-3-(thiophen-2-yl)pyrazine (Table 5, entry 2). Following general procedure A, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μ L, 0.25 mmol), 2-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 $^{\circ}C$ in sec-butanol with stirring for 4 h. The crude product was purified via flash column chromatography on silica gel (15% EtOAc/Hexanes) to provide the title compound in a 96% yield (45 mg) as a colorless oil. 1H NMR (300 MHz, $CDCl_3$) δ : 8.21 (s, 1H), 7.53 (dd, J = 4,1 Hz, 1H), 7.46 (dd, J = 5,1 Hz, 1H), 7.14 (dd, J = 5,4 Hz, 1H), 2.77 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 150.2, 146.2, 146.1, 143.0, 141.0, 128.4, 127.8, 127.5, 23.9, 21.0. IR (neat, cm^{-1}): 2921, 1564, 1530, 1435, 1372, 1329, 1166. Anal. Calcd. for $C_8H_6N_2S$: C, 59.23; 3.73. Found C, 59.35; H, 3.72.

2-(Thiophen-2-yl)pyrimidine (Table 5, entry 3). Following general procedure A, a mixture of 2-chloropyrimidine (28.6 mg, 0.25 mmol), 2-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), 4 $\text{\AA}$ molecular sieves (62.5 mg), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^{\circ}C$ in tert-amyl alcohol with stirring for 6 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 85% yield (34 mg) as a white solid, mp 79-80 $^{\circ}C$. 1H NMR (300 MHz, $CDCl_3$) δ : 8.67 (dd, J = 5,1 Hz, 2H), 8.00 (dd, J = 5,2 Hz, 1H), 7.47 (dd, J = 5,1 Hz, 1H), 7.14 (dt, J = 4,1 Hz, 1H), 7.06 (dt, J = 4,1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 161.4, 157.1, 143.1, 129.9, 128.9, 128.3, 118.4. IR (neat, cm^{-1}): 3120, 1636, 1556, 1526, 1433, 1377. 1H NMR spectrum included.

2,4-Dimethoxy-6-(thiophen-2-yl)-1,3,5-triazine (Table 5, entry 4). Following general procedure A, a mixture of 2-chloro-4,6-dimethoxy-1,3,5-triazine (43.9 mg, 0.25 mmol), 2-thiophene boronic acid (48 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), 4 $\text{\AA}$ molecular sieves (62.5 mg),), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^{\circ}C$ in tert-amyl alcohol with stirring for 6 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 84% yield (48 mg) as a white solid, mp 81-83 $^{\circ}C$. 1H NMR (300 MHz, $CDCl_3$) δ : 8.11 (dd, J = 4,1 Hz, 1H), 7.56 (dd, J = 5,1 Hz, 1H), 7.12 (dd, J = 5,4 Hz, 1H), 4.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 172.4, 170.5, 140.5, 132.4,

131.8, 128.2, 55.1. IR (neat, cm^{-1}): 2998, 2951, 2873, 1555, 1497, 1378, 1359, 1335, 1105, 1045, 817. ^1H NMR spectrum included.

1-[5-(3,6-Dimethyl-pyrazin-2-yl)thiophen-2-yl]ethanone (Table 5, entry 5). Following general procedure A, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μL , 0.25 mmol), 5-Acetyl-2-thiophene boronic acid (63.8 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in tert-amyl alcohol with stirring for 6 h. The crude product was purified via flash column chromatography on silica gel (25% EtOAc/Hexanes) to provide the title compound in a 98% yield (57 mg) as a white solid, mp 85-87 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ : 8.27 (s, 1H), 7.69 (d, $J = 5$ Hz, 1H), 7.53 (d, $J = 5$ Hz, 1H), 2.76 (s, 3H), 2.57 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ : 190.8, 150.7, 150.4, 146.9, 145.2, 145.0, 142.5, 132.5, 128.0, 26.9, 23.8, 21.0. IR (neat, cm^{-1}): 2922, 2851, 1658, 1526, 1445, 1362, 1271, 1166. ^1H NMR spectrum included.

STANDARD PROTON PARAMETERS

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 date Dec 8 2005 dfreq 125.795
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 pw 9.0
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 ct 16 wnt
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 op y
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2-Thiophen-2-yl-pyrimidine (CDCl3)

STANDARD PROTON PARAMETERS

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 sw 10000.4 PROCESSING
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 pw 9.0
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 vs 120
 sc 0
 uc 250
 hzmm 22.00
 is 100.00
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 rfp 2621.7
 th
 ins
 ne ph 0.000

2,4-Dimethoxy-6-thiophen-2-yl-[1,3,5]triazine (CDCl3).

II. Experimental for Reactions of Pyridine Boronic Acids

General Procedure C: Pd-Catalyzed Suzuki-Miyaura Couplings of Pyridine Boronic Acids.

An oven dried Schlenk tube was charged with Pd₂(dba)₃ (2.3 mg, 0.0025 mmol), ligand (0.01 mmol), pyridine boronic acid (46.1 mg, 0.375 mmol) and powdered, anhydrous K₃PO₄ (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.50 mL) was added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 °C until aryl halide had been completely consumed as determined by gas chromatography. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and

the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

3-(2,6-Dimethylphenyl)pyridine (Table 6, entry 1).⁴ Following general procedure C, a mixture of 2-chloro-*m*-xylene (33.1 μ L, 0.25 mmol), 3-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (15% EtOAc/Hexanes) to provide the title compound in an 81% yield (37 mg) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ : 8.60 (dd, *J* = 5,1 Hz, 1H), 8.44 (d, *J* = 2Hz, 1H), 7.51 (dt, *J* = 8,2 Hz, 1H) 7.37 (dd, *J* = 8,5 Hz, 1H) 7.21 (dd, *J* = 8,7 Hz, 1H), 7.13 (d, *J* = 7Hz, 2H), 2.03 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ : 150.0, 148.1, 137.8, 136.7, 136.3, 127.8, 127.5, 123.3, 20.9. IR (neat, cm⁻¹): 3023, 2921, 1653, 1565, 1463, 1406. ¹H NMR spectrum included.

3-(Thiophen-3-yl)pyridine (Table 6, entry 2).² Following general procedure C, a mixture of 3-chlorothiophene (23.2 μ L, 0.25 mmol), 3-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 90% yield (36 mg) as a white solid, mp 70-72 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.87 (d, *J* = 2Hz, 1H), 8.53 (dd, *J* = 5,2 Hz, 1H), 7.84-7.86 (ddd, *J* = 8,3,2 Hz, 1H), 7.52 (dd, *J* = 3,1 Hz, 1H), 7.44 (dd, *J* = 5,3 Hz, 1H), 7.39 (dd, *J* = 5,2 Hz, 1H), 7.30-7.33 (ddd, *J* = 8,5,1 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 148.2, 147.6, 138.7, 133.4, 131.5, 126.9, 125.8, 123.6, 121.4. IR (neat, cm⁻¹): 3100, 3077, 2925, 1574, 1431, 1322, 1222. Anal. Calcd. for C₉H₇NS: C, 67.05; H, 4.38. Found C, 66.93; H, 4.55.

3,3'-Bipyridinyl (Table 6, entry 3).⁵ Following general procedure C, a mixture of 3-chloropyridine (23.8 μ L, 0.25 mmol), 3-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01

⁴ Billingsley, K. L.; Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 3484-3488.

⁵ Zhang, J.; Zhao, L.; Song, M.; Mak, T. C. W.; Wu, Y. *Tetrahedron* **2006**, *691*, 1301.

mmol) was heated to 120 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (EtOAc) to provide the title compound in a 97% yield (38 mg) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ : 8.83 (d, J = 2 Hz, 1H), 8.64 (dd, J = 5, 1 Hz, 1H), 7.87 (dt, J = 8, 2 Hz, 1H), 7.40 (dd, J = 8, 5 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 149.2, 148.1, 134.4, 133.4, 123.7. IR (neat, cm⁻¹): 3031, 2962, 1585, 1465, 1425, 1396, 1260, 1024. ¹H NMR spectrum included.

3,3'-Bipyridin-6-amine (Table 6, entry 4).⁴ Following general procedure C, a mixture of 2-amino-5-chloropyridine (32.1 mg, 0.25 mmol), 3-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 24 h. The crude product was purified via flash column chromatography on silica gel (10% Methanol/EtOAc) to provide the title compound in a 95% yield (40 mg) as a yellow solid, mp 134-136 °C. ¹H NMR (300 MHz, DMSO) δ : 8.63 (t, J = 1 Hz, 1H), 8.60 (dt, J = 5, 1 Hz, 1H), 8.31 (t, J = 1 Hz, 1H), 7.88 (dt, J = 8, 1 Hz, 1H), 7.61 (s, 1H), 7.48 (dd, J = 8, 5 Hz, 1H), 6.62 (bs, 2H). ¹³C NMR (75 MHz, DMSO) δ : 159.5, 149.3, 148.9, 145.4, 136.4, 134.6, 132.5, 123.9, 116.7. IR (neat, cm⁻¹): 3328, 3198, 1624, 1511, 1474, 1425, 1384. ¹H NMR spectrum included.

5-(Trifluoromethyl)-3,3'-bipyridin-2-amine (Table 6, entry 5).⁴ Following general procedure C, a mixture of 2-amino-3-chloro-5-trifluoromethylpyridine (49.1 mg, 0.25 mmol), 3-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 24 h. The crude product was purified via flash column chromatography on silica gel (10% Methanol/EtOAc) to provide the title compound in a 95% yield (57 mg) as a white solid, mp 167-169 °C. ¹H NMR (300 MHz, DMSO) δ : 8.63 (t, J = 1 Hz, 1H), 8.60 (dt, J = 5, 2 Hz, 1H), 8.31 (t, J = 1 Hz, 1H), 7.88 (dt, J = 8, 2 Hz, 1H), 7.60 (d, J = 2 Hz, 1H), 7.48 (dd, J = 8, 5 Hz, 1H), 6.62 (bs, 1H). ¹³C NMR (75 MHz, CD₃OD) δ : 160.9, 150.2, 150.0, 146.7, 146.6, 138.8, 136.6, 136.5, 134.9, 125.8, 119.0. IR (neat, cm⁻¹): 3407, 2254, 2128, 1649, 1269, 1049, 1025, 1003. ¹H NMR spectrum included.

4-(Thiophen-3-yl)pyridine (Table 6, entry 6). Following general procedure C, a mixture of 3-chlorothiophene (23.2 μ L, 0.25 mmol), 4-pyridine boronic acid (46.1 mg,

0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 90% yield (36 mg) as a white solid, mp 124-126 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.60 (d, J = 5 Hz, 2H), 7.65 (t, J = 3 Hz, 1H), 7.45-7.47 (m, 2H), 7.43 (d, J = 5 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ : 150.3, 142.5, 139.4, 127.1, 125.6, 123.0, 120.7. IR (neat, cm⁻¹): 3092, 3036, 2924, 1594, 1553, 1425. Anal. Calcd. for C₉H₇NS: C, 67.05; H, 4.38. Found C, 67.03; H, 4.53.

2,5-Dimethyl-3-(pyridin-4-yl)pyrazine (Table 6, entry 7).⁴ Following general procedure C, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μ L, 0.25 mmol), 4-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (20% EtOAc/Hexanes) to provide the title compound in a 83% yield (39 mg) as a yellow solid, mp 56-58 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.73 (d, J = 4 Hz, 2H), 8.39 (s, 1H), 7.49 (d, J = 4 Hz, 2H), 2.58 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ : 150.8, 149.9, 148.1, 146.4, 143.1, 130.5, 123.5, 22.3, 21.1. IR (neat, cm⁻¹): 2925, 2857, 1724, 1598, 1449, 1404, 1370. Anal. Calcd. for C₁₁H₁₁N₃: C, 71.33; H, 5.99. Found C, 71.22; H, 6.16.

3,4'-Bipyridin-6-amine (Table 6, entry 8).⁴ Following general procedure C, a mixture of 2-amino-5-chloropyridine (32.1 mg, 0.25 mmol), 4-pyridine boronic acid (46.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 24 h. The crude product was purified via flash column chromatography on silica gel (10% Methanol/EtOAc) to provide the title compound in a 95% yield (40 mg) as a yellow solid, mp 171-173 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.43 (d, J = 6 Hz, 2H), 8.29 (d, J = 2 Hz, 1H), 7.80 (dd, J = 8, 3 Hz, 1H), 7.55 (d, J = 6 Hz, 2H), 6.63 (d, J = 8 Hz, 1H), 4.90 (bs, 2H). ¹³C NMR (75 MHz, CD₃OD) δ : 161.8, 151.3, 150.6, 148.1, 147.0, 137.6, 123.3, 123.1, 121.6, 110.5. IR (neat, cm⁻¹): 3428, 2925, 2856, 1633, 1519, 1488, 1394, 1221. Anal. Calcd. for C₁₀H₉N₃: C, 70.16; H, 5.30. Found C, 70.00; H, 5.49.

5-(6-Ethoxypyridin-3-yl)thiophene-2-carbaldehyde (Table 6, entry 9).⁴ Following general procedure C, a mixture of 5-chloro-2-thiophenecarbaldehyde (26.6 μ L, 0.25 mmol), 2-ethoxy-5-pyridine boronic acid (62.6 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (15% EtOAc/Hexanes) to provide the title compound in a 91% yield (53 mg) as a orange solid, mp 62-64 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 9.83 (s, 1H), 8.43 (d, J = 3 Hz, 1H), 7.76 (dd, J = 8,2 Hz, 1H), 7.68 (t, J = 2 Hz, 1H), 7.26 (d, J = 4 Hz, 1H), 6.73 (d, J = 8 Hz, 1H), 4.35 (q, J = 7 Hz, 2H), 1.37 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 182.5, 164.4, 150.8, 144.7, 142.1, 137.5, 136.4, 123.5, 122.4, 111.4, 62.2, 14.5. IR (neat, cm^{-1}): 2977, 2900, 1598, 1564, 1446, 1381, 1287, 1236, 1064. Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.78; H, 4.75. Found C, 61.78; H, 4.91.

3-(2,6-Dimethoxypyridin-3-yl)-2,5-dimethylpyrazine (Table 6, entry 10). Following general procedure C, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μ L, 0.25 mmol), 2,6-dimethoxy-5-pyridine boronic acid (68.6 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol) Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (20% EtOAc/Hexanes) to provide the title compound in a 85% yield (52 mg) as a white solid, mp 86-88 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 8.28 (s, 1H), 7.55 (d, J = 8 Hz, 1H), 6.42 (d, J = 8 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 2.53 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 163.4, 159.3, 150.1, 150.0, 149.5, 142.1, 141.8, 113.3, 101.4, 53.6, 53.2, 21.5, 21.0. IR (neat, cm^{-1}): 2997, 2946, 1602, 1582, 1485, 1441, 1378, 1318, 1235, 1103, 1021. Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16. Found C, 63.82; H, 6.17.

2-(2,6-Dimethoxypyridin-3-yl)quinoxaline (Table 6, entry 11).⁴ Following general procedure C, a mixture of 2-chloroquinoxaline (41.2 mg, 0.25 mmol), 2,6-dimethoxy-5-pyridine boronic acid (68.6 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 12 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in a 91% yield (61 mg) as a yellow solid, mp 95-

96 °C.. ¹H NMR (300 MHz, CDCl₃) δ : 9.48 (s, 1H), 8.37 (d, J = 8 Hz, 1H), 8.07 (d, J = 8 Hz, 2H), 7.67-7.73 (m, 2H), 6.51 (d, J = 8 Hz, 1H), 4.07 (s, 3H), 3.99 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ : 164.1, 160.4, 150.3, 146.4, 142.7, 142.4, 140.7, 129.7, 129.1, 129.0, 128.9, 111.6, 102.8, 53.8, 53.6. IR (neat, cm⁻¹): 2947, 1600, 1578, 1483, 1383, 1305, 1267, 1226, 1030, 1014. ¹H NMR spectrum included.

STANDARD PROTON PARAMETERS

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[3,3']Bipyridinyl (CDCl3).

STANDARD PROTON PARAMETERS

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 at 3.200 dnf 1.0
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 na ph

[3,3']Bipyridinyl-6-ylamine (CD3OD).

STANDARD PROTON PARAMETERS

exp1 s2pul **IV272**
 SAMPLE DEC. & VT
 date Jan 12 2006 dfrq 125.795
 solvent CD3OD dn C13
 file exp dpuw 37
 ACQUISITION dot 8
 sfrq 500.237 dn mm
 tn H1 dnm C
 at 2.200 dnf 10000
 mp 64000 dscq 1.0
 pw 10000.0 dres n
 fb not used homo n
 bs 2 PROCESSING
 ts 1 wfile ft
 spwr 53 drc C13
 pw 9.6 fn 131072
 d1 0 nath f
 tof 1490.2
 nt 16 werr
 ct 16 wexp
 alock n wbs
 gain not used wnt
 FLAGD a
 tn a
 dp y
 hs n
 DISPLAY
 sp -501.4
 wp 5500.9
 vs 82
 sc 8
 wc 256
 hzmm 22.02
 ts 100.00
 rff 2652.4
 rfp 1656.8
 th 7
 tns 1.000
 nm ph

5-Trifluoromethyl-[3,3']bipyridinyl-2-ylamine (CD3OD).

STANDARD PROTON PARAMETERS

exp1 s2pul **IV287**
 SAMPLE DEC. & VT
 date Jan 17 2006 dfrq 125.795
 solvent CDCl3 dn C13
 file exp dpuw 37
 ACQUISITION dot 8
 sfrq 500.235 dn mm
 tn H1 dnm C
 at 2.200 dnf 10000
 mp 64000 dscq 1.0
 pw 10000.0 dres n
 fb not used homo n
 bs 2 PROCESSING
 ts 1 wfile ft
 spwr 53 drc C13
 pw 9.6 fn 131072
 d1 0 nath f
 tof 1490.2
 nt 16 werr
 ct 16 wexp
 alock n wbs
 gain not used wnt
 FLAGD n
 tn n
 dp y
 hs n
 DISPLAY
 sp -501.4
 wp 6500.5
 vs 121
 sc 8
 wc 256
 hzmm 26.02
 ts 100.00
 rff 4622.3
 rfp 3021.7
 th 6
 tns 1.000
 nm ph

2-(2,6-Dimethoxy-pyridin-3-yl)-quinoxaline (CDCl3).

III. Experimental for the Synthesis of Pyrrole Boronate Esters.

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(triisopropyl-silanyl)-1*H*-pyrrole, E1.⁴ An oven-dried Schlenk tube was charged with PdCl₂(CH₃CN)₂ (59 mg, 3.0 mol%) and SPhos (278 mg, 9.0 mol%). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). Toluene (10 mL) was added via syringe, through the septum, followed by the addition of 3-bromo-1-(triisopropyl-silanyl)-1*H*-pyrrole⁶ (2.27 g, 7.52 mmol), pinacol borane (1.15 g, 1.31 mL, 9.02 mmol) and triethylamine (2.64 mL, 18.8 mmol). Additional toluene (4 mL) was then added and the vessel was sealed with a Teflon screwcap. The reaction mixture was heated to 90 °C and stirred for 18 h. At this point the reaction mixture was allowed to cool to room temperature. The solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 85% yield (2.25 g) as a light yellow solid, m.p. 59 °C. ¹H NMR (300 MHz, CDCl₃) δ : 7.24 (dd, *J* = 2,1 Hz, 1H), 6.81 (dd, *J* = 3,2 Hz, 1H), 6.63 (dd, *J* = 3,1 Hz, 1H), 7.00 (dd, *J* = 7,1 Hz, 1H), 1.46 (sept, *J* = 7 Hz, 3H), 1.33 (s, 12H), 1.09 (d, *J* = 7 Hz, 18H). ¹³C NMR (75 MHz, CDCl₃) δ : 133.6, 124.9, 115.6, 110.0, 82.6, 24.8, 17.7, 11.6. IR (neat, cm⁻¹): 2949, 2873, 1540, 1466, 1381, 1296, 1142. Anal. Calcd. for C₁₉H₃₆BNO₂Si: C, 65.31; H, 10.39. Found C, 65.32; H, 10.30.

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1*H*-pyrrole, E2. An oven dried 10-mL round bottom flask was charged with **E** (174.5 mg, 0.500 mmol). The flask was capped with a rubber septum and then evacuated and backfilled with argon. Anhydrous THF (2 mL) was added via syringe, through the septum, followed by the slow addition of 1.0 M TBAF in THF (0.525 mL, 0.525 mmol) over five minutes at room temperature. After 2 h, 10 mL of water was added to the reaction and the extracted with 10 mL portions of diethyl ether (this process was repeated three times). The organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in 91% yield (88 mg) as a white solid, mp

⁶ Alzare, A.; Guzman, A.; Ruiz, A.; Velards, E.; Muchowski, J. *J. Org. Chem.* **1992**, 57, 1653-1656.

77-79 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.71 (bs, 1H), 7.25 (dd, J = 3,2 Hz, 1H), 6.84 (dd, J = 4,2 Hz, 1H), 6.56 (dd, J = 4,3 Hz, 1H), 1.32 (s, 12H). ¹³C NMR (75 MHz, CDCl₃) δ : 130.5, 127.0, 118.7, 113.7, 82.9, 24.8. IR (neat, cm⁻¹): 3149, 2979, 2933, 1747, 1561, 1490, 1371, 1329, 1292, 1181, 1066. ¹H NMR spectrum included.

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(carboxylic acid *tert*-butyl ester)-1*H*-pyrrole, E3. An oven-dried Schlenk tube was charged with PdCl₂(CH₃CN)₂ (15.6 mg, 0.06 mmol) and SPhos (74 mg, 0.18 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). Toluene (4 mL) was added via syringe, through the septum, followed by the addition of 3-bromo-1-(carboxylic acid *tert*-butyl ester)-1*H*-pyrrole⁷ (488 mg, 1.99 mmol), pinacol borane (306 mg, 0.347 mL, 2.39 mmol) and triethylamine (0.694 mL, 4.98 mmol). Additional toluene (1 mL) was then added and the vessel was sealed with a Teflon screwcap. The reaction mixture was heated to 80 °C and stirred for 24 h. At this point the reaction mixture was allowed to cool to room temperature. The solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 50% yield (265 mg) as a light yellow solid, m.p. 76-77 °C. ¹H NMR (300 MHz, CDCl₃) δ : 7.63 (d, J = 1 Hz, 1H), 7.25 (d, J = 3 Hz, 1H), 6.46 (dd, J = 3,1 Hz, 1H), 1.57 (s, 9H), 1.31 (s, 12H). ¹³C NMR (75 MHz, CDCl₃) δ : 148.5, 128.7, 120.7, 116.1, 83.8, 83.2, 27.9, 24.7. IR (neat, cm⁻¹): 2979, 2933, 1747, 1561, 1459, 1371, 1329, 1143. ¹H NMR spectrum included.

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(benzyl)-1*H*-pyrrole, E4. An oven dried 25-mL round bottom flask was charged with 3-bromo-1-(triisopropyl-silanyl)-1*H*-pyrrole¹ (795 mg, 2.62 mmol). The flask was capped with a rubber septum and then evacuated and backfilled with argon. Anhydrous THF (8 mL) was added via syringe, through the septum, followed by the slow addition of 1.0 M TBAF in THF (2.75 mL, 0.525 mmol) over 5 min at room temperature. After 2 h, 10 mL of water was added to the reaction and then extracted with 10 mL portions of diethyl ether (this process was repeated three times). The organic layers were dried over magnesium sulfate and

⁷ Leroy, J; Porhiel, E; Bondon, A. *Tetrahedron* **2002**, 58, 6713-6722.

concentrated under reduced pressure. The crude product is unstable and was immediately transferred to an oven dried 25-mL round bottom flask. The flask was capped with a rubber septum and then evacuated and backfilled with argon. Anhydrous DMSO (6 mL) was added via syringe, through the septum, followed by the addition of KOH (294 mg, 5.24 mmol) and benzyl bromide (0.467 mL, 3.93 mmol). After 1 h, 10 mL of water was added to the reaction and the extracted with 10 mL portions of diethyl ether (this process was repeated three times). The organic layers were dried over magnesium sulfate and concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (Hexanes) to provide 3-bromo-1-(benzyl)-pyrrole as a white solid. 3-bromo-1-(benzyl)-pyrrole, $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (9.9 mg, 0.09 mmol) and SPhos (47 mg, 0.11 mmol) were charged into an oven dried Schlenk tube. The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). Toluene (2 mL) was added via syringe, through the septum, followed by the addition of pinacol borane (195 mg, 0.221 mL, 1.52 mmol) and triethylamine (0.443 mL, 3.18 mmol). Additional toluene (1 mL) was then added and the vessel was sealed with a Teflon screwcap. The reaction mixture was heated to 90 °C and stirred for 24 h. At this point the reaction mixture was allowed to cool to room temperature. The solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ : 7.26-7.34 (m, 3H), 7.14-7.17 (m, 3H), 6.72 (dd, $J = 2, 1$ Hz, 1H), 6.54 (dd, $J = 2, 1$ Hz, 1H), 5.06 (s, 2H), 1.33 (s, 12H). ^{13}C NMR (75 MHz, CDCl_3) δ : 137.4, 130.2, 128.6, 127.7, 127.2, 122.2, 114.4, 82.7, 53.2, 24.7. IR (neat, cm^{-1}): 2977, 2929, 2865, 1587, 1543, 1497, 1454, 1294, 1214, 1150, 1108. ^1H NMR spectrum included.

STANDARD PROTON PARAMETERS

expt 52pul

SAMPLE

date Aug 9 2005 dfrq DEC. & VT 125.795

solvent CDCl3 dn C13

file /data/stouch/- dprw 37

4kb/arb_IVIS_08090- dof 0

ACQUISITION

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tn M1 dseq

at 3.280 dres 1.0

np 64000 homo n

sw 10000.0 dnt PROCESSING

td not used

bs 8 proc

ss 1 utfile

tpwr 50 math

pw 9.8

sl 0

tof 1498.2 warr

nt 16 wexp

ct 16 vds

clock n vnt

gain not used

FLAGS

tl n

in n

dp y

hs nm

DISPLAY

sp -501.4

vp 5505.0

vs 190

sc 0

uc 250

hmm 22.02

ls 100.00

rft 4622.3

rfg 3631.7

th 7

ins 1.000

na ph

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1H-pyrrole, E2.

STANDARD PROTON PARAMETERS

expt 52pul

SAMPLE

date Jun 10 2006 dfrq DEC. & VT 125.795

solvent CDCl3 dn C13

file /data/stouch/- dprw 37

4kb/arb_IVIS_08090- dof 0

ACQUISITION

sfrq 500.235 dnt 10000

tn M1 dseq

at 3.280 dres 1.0

np 64000 homo n

sw 10000.0 dnt PROCESSING

td not used

bs 8 proc

ss 1 utfile

tpwr 50 math

pw 9.8

sl 0

tof 1498.2 warr

nt 16 wexp

ct 16 vds

clock n vnt

gain not used

FLAGS

tl n

in n

dp y

hs nm

DISPLAY

sp -500.7

vp 5505.0

vs 191

sc 0

uc 250

hmm 22.02

ls 100.00

rft 4631.7

rfg 3631.7

th 7

ins 1.000

na ph

3-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-1-(carboxylic acid tert-butyl ester)-1H-pyrrole, E3.

IV. Experimental for Reactions of Pyrrole Boronate Esters.

General Procedure D: Pd-Catalyzed Suzuki-Miyaura Couplings of Heteroaryl Halides with E1.

An oven-dried Schlenk tube was charged with Pd(OAc)₂ (1.1 mg, 0.005 mmol), SPhos (4.1 mg, 0.01 mmol), **E1** (131 mg, 0.375 mmol) and powdered, anhydrous K₃PO₄ (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.45 mL) and water (0.05 mL) were added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 °C until aryl halide had been completely consumed as determined by gas chromatography. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel

(eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

General Procedure E: Pd-Catalyzed Suzuki-Miyaura Couplings Heteroaryl Halides with E1 at Low Catalyst Loadings.

Procedure E was followed with the following changes: A separate vial was initially charged with Pd(OAc)₂ (1.0 mol%) and SPhos (2.0 mol%). The vial was sealed with Teflon coated screwcap, a needle was inserted through the cap and the vial was then evacuated and backfilled with argon. *n*-Butanol (1 mL) was added and the mixture as briefly heated. 250 μ L of this solution (0.25% Pd, 0.50% SPhos) was then added to the Schlenk flask containing the base and boronic acid. 200 μ L of butanol and 50 μ L of water were added in the final solvent addition. The temperature was raised to 100 °C.

5-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]-1*H*-indole (Table 8, entry 1).⁴ Following general procedure E, a mixture of 5-bromoindole (49 mg, 0.25 mmol), **E1** (131 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 97% yield (82 mg) as a red oil. ¹H NMR (300 MHz, CDCl₃) δ : 8.01 (bs, 1H), 7.82 (d, *J* = 1 Hz, 1H) 7.46 (dd, *J* = 8,1 Hz, 1H), 7.36 (d, *J* = 8 Hz, 1H), 7.16 (t, *J* = 3 Hz, 1H), 7.10 (t, *J* = 1 Hz, 1H), 6.86 (t, *J* = 2 Hz, 1H), 6.71 (dd, *J* = 2,1 Hz, 1H), 6.56 (m, 1H), 1.55 (sept, *J* = 7 Hz), 1.20 (d, *J* = 7 Hz, 18H). ¹³C NMR (75 MHz, CDCl₃) δ : 134.4, 128.3, 128.1, 127.8, 125.0, 124.3, 120.3, 120.0, 116.8, 111.0, 108.8, 102.5, 17.8, 11.7. IR (neat, cm⁻¹): 3481, 3400, 2949, 2867, 1709, 1467, 1327, 1119. ¹H NMR spectrum included.

4-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]isoquinoline (Table 8, entry 2). Following general procedure E, a mixture of 4-bromoisoquinoline (52 mg, 0.25 mmol), **E1** (131 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 93% yield (82 mg) as a yellow solid,

mp 74-75 °C. ¹H NMR (300 MHz, CDCl₃) ≥: 9.12 (s, 1H), 8.66 (s, 1H) 8.31 (d, J = 8 Hz, 1H), 7.97 (d, J = 8 Hz, 1H), 7.67 (ddd, J = 8,7,1 Hz, 1H), 7.56 (ddd, J = 8,7,1 Hz, 1H), 7.02 (t, J = 1 Hz, 1H), 6.92 (t, J = 2 Hz, 1H), 6.62 (dd, J = 2,1 Hz, 1H), 1.55 (sept, J= 7 Hz, 3H), 1.19 (d, J= 7 Hz, 18H). ¹³C NMR (75 MHz, CDCl₃) ≥: 150.3, 142.3, 134.4, 130.0, 128.8, 128.6, 127.7, 126.7, 125.1, 124.8, 123.6, 121.5, 112.1, 17.8, 11.5. IR (neat, cm⁻¹): 3149, 1709, 1362, 1224. Anal. Calcd. for C₂₂H₃₀N₂Si: C, 75.4; H, 8.6. Found C, 75.62; H, 8.83.

3-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]quinoline (Table 8, entry 3). Following general procedure E, a mixture of 3-bromoquinoline (34 μL, 0.25 mmol), **E1** (131 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in 83% yield (73 mg) as a white solid, mp 103-104 °C. ¹H NMR (300 MHz, CDCl₃) ≥: 9.17 (d, J = 2 Hz, 1H), 8.17 (d, J= 2 Hz, 1H), 8.06 (d, J = 8 Hz, 1H), 7.78 (dd, J = 8,1 Hz, 1H), 7.56-7.62 (ddd, J = 8,7,2 Hz, 1H), 7.45-7.51 (ddd, J = 7,7,1 Hz, 1H), 7.23 (t, J = 1 Hz, 1H), 6.87 (dd, J = 2,1 Hz, 1H), 6.75 (dd, J = 2,1 Hz, 1H), 1.55 (sept, J = 7 Hz, 3H), 1.20 (d, J= 7 Hz, 18H). ¹³C NMR (75 MHz, CDCl₃) ≥: 149.4, 146.3, 129.4, 129.0, 128.4, 127.9, 127.4, 126.5, 125.8, 123.4, 121.3, 108.6, 99.6, 17.7, 11.5. IR (neat, cm⁻¹): 2953, 2871, 2366, 1713, 1497, 1123. ¹H NMR spectrum included.

3-(Thiophen-2-yl)-1-(triisopropylsilyl)-1*H*-pyrrole (Table 8, entry 4).^{4,8} Following general procedure E, a mixture of 2-bromothiophene (0.25 mmol, 24.2 μL), **E1** (131 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in 99% yield (75 mg) as a red oil. ¹H NMR (300 MHz, CDCl₃) ≥: 7.04-7.08 (ddd, J = 5,5,1 Hz, 1H), 6.96-7.00 (m, 1H) 6.81 (t, J = 2 Hz, 1H), 6.76 (dd, J = 3,2 Hz, 1H), 6.51 (dd, J = 3,2 Hz, 1H), 6.32 (t, J = 2 Hz, 1H),

⁸ The data presented in Figure 2 was generated via this procedure. The amount of *n*-butanol and water added during the solvent charge is the only variation. The experiment where no water was added was considered anhydrous. However, Karl-Fischer titration was not performed. GC yields were calculated based upon a dodecane internal standard.

1.49 (sept, $J = 7$ Hz, 3H), 1.15 (d, $J = 7$ Hz, 18H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 139.7, 127.4, 125.1, 121.4, 120.8, 120.7, 120.5, 109.2, 17.8, 11.6. IR (neat, cm^{-1}): 2949, 2867, 1706, 1462, 1112. Anal. Calcd. for $\text{C}_{17}\text{H}_{27}\text{NSSi}$: C, 65.45; H, 8.24. Found C, 65.43; H, 8.77.

2-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]pyridine (Table 8, entry 5).⁴ Following general procedure E, a mixture of 2-bromopyridine (23.8 μL , 0.25 mmol), **E1** (131 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 $^\circ\text{C}$ in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexane) to provide the title compound in a 91% yield (68 mg) as a white solid, mp 74-75 $^\circ\text{C}$. ^1H NMR (300 MHz, CDCl_3) $\geq$: 8.52-8.55 (ddd, $J = 7, 2, 1$ Hz, 1H), 7.56-7.61 (m, 1H), 7.48 (dt, $J = 7, 1$ Hz, 1H), 7.43 (t, $J = 1$ Hz, 1H), 7.00 (ddd, $J = 7, 5, 1$ Hz, 1H), 6.80 (ddd, $J = 8, 3, 1$ Hz, 1H), 1.55 (sept, $J = 7$ Hz, 3H), 1.10 (d, $J = 7$ Hz, 18H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 154.7, 149.2, 136.2, 127.0, 125.4, 123.3, 120.0, 119.2, 108.9, 17.8, 11.6. IR (neat, cm^{-1}): 2946, 2867, 1635, 1591, 1541, 1488, 1464, 1429, 1145, 1082. Anal. Calcd. for $\text{C}_{18}\text{H}_{28}\text{N}_2\text{Si}$: C, 71.94; H, 9.39. Found C, 72.07; H, 9.35.

5-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]thiophene-2-carbaldehyde (Table 8, entry 6). Following general procedure E, a mixture of 5-chlorothiophene-2-carbaldehyde (26.6 μL , 0.25 mmol), **E1** (131 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 $^\circ\text{C}$ in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in an 82% yield (68 mg) as a yellow oil. ^1H NMR (300 MHz, CDCl_3) $\geq$: 9.80 (s, 1H), 7.64 (d, $J = 3$ Hz, 1H), 7.13 (s, 1H), 7.12 (d, $J = 1$ Hz, 2H), 6.79 (t, $J = 2$ Hz, 1H), 6.56 (dd, $J = 3, 1$ Hz, 1H), 1.46 (sept, $J = 7$ Hz, 3H), 1.12 (d, $J = 7$ Hz, 18H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 182.3, 150.8, 139.1, 138.0, 125.9, 122.6, 121.8, 120.1, 109.3, 17.6, 11.5. IR (neat, cm^{-1}): 3001, 2365, 1709, 1362, 1223. ^1H NMR spectrum included.

2-[1-(Triisopropylsilyl)-1*H*-pyrrol-3-yl]quinoxaline (Table 8, entry 7). Following general procedure E, a mixture of 2-chloroquinoxaline (41.2 mg, 0.25 mmol), **E1** (131 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 $^\circ\text{C}$ in 2.5:1 *n*-butanol/water with stirring for 2 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in a

83% yield (73 mg) as a yellow oil. ^1H NMR (300 MHz, CDCl_3) δ : 9.10 (s, 1H), 8.03 (dt, $J = 7, 1$ Hz, 2H), 7.68 (dt, $J = 7, 1$ Hz, 1H), 7.59-7.62 (m, 2H), 7.03 (dd, $J = 3, 2$ Hz, 1H), 6.89 (dd, $J = 3, 2$ Hz, 1H), 1.52 (sept, $J = 7$ Hz, 3H), 1.14 (d, $J = 7$ Hz, 18 H). ^{13}C NMR (75 MHz, CDCl_3) δ : 149.6, 143.7, 142.6, 140.6, 129.7, 128.9, 128.8, 127.8, 126.2, 125.1, 124.8, 109.5, 17.7, 11.6. IR (neat, cm^{-1}): 3061, 2947, 2867, 1713, 1577, 1552, 1498, 1463, 1385, 1257, 1100. ^1H NMR spectrum included.

STANDARD PROTON PARAMETERS

exp5 52pu1 **II139**

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np	64000	dsq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	wtfile	ft
sgpr	53	proc	
pw	9.5	fn	131072
si	1	math	f
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ct	16	wexp	
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hzmm	7.75		
ls	100.00		
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rfd	3631.7		
th	7		
ins	1.000		
me	ph		

3-[1-(Trisopropyl-silanyl)-1H-pyrrol-3-yl]-quinoline (CDCl3).

STANDARD PROTON PARAMETERS

exp1 52pu1 **II163**

date	Jan 17 2006	dfreq	125.795
solvent	CDCl3	dn	C13
file	exp1	dpr	32
ACQUISITION			
sfreq	500.235	dn	mm
in	1	dm	C
at	3.200	def	10000
np	64000	dsq	
sw	10000.0	dres	1.0
fb	not used	homo	n
bs	8	PROCESSING	
ss	1	wtfile	ft
sgpr	53	proc	
pw	9.5	fn	131072
si	1	math	f
tof	1490.2		
nt	16	werr	
ct	16	wexp	
elock	n	vbs	
gain	not used	wnt	
FLAGS			
ti	n		
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-501.4		
vp	6500.5		
vs	95		
vc	1		
vc	250		
hzmm	26.02		
ls	100.00		
rfl	4622.3		
rfd	3621.7		
th	6		
ins	1.000		
me	ph		

5-[1-(Trisopropyl-silanyl)-1H-pyrrol-3-yl]-thiophene-2-carbaldehyde (CDCl3).

General Procedure F: Pd-Catalyzed Suzuki-Miyaura Couplings of Aryl and Heteroaryl Bromides with F.

An oven-dried Schlenk tube was charged with Pd(OAc)₂ (1.1 mg, 2.0 mol%), SPhos (4.1 mg, 4.0 mol%), **F** (79.1 mg, 0.375 mmol) and powdered, anhydrous K₃PO₄ (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.5 mL) were added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 °C until aryl halide had been completely consumed as determined by gas chromatography. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

***Tert*-Butyl 2-mesityl-1*H*-pyrrole-1-carboxylate (Table 8, entry 8).**⁴ Following general procedure F, a mixture of 2-bromomesitylene (38.3 μ L, 0.25 mmol), **F** (79.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in *n*-butanol with stirring for 5 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 89% yield (63 mg) as a yellow oil. ¹H NMR (300 MHz, CDCl₃) δ : 7.39 (dd, *J* = 3, 1H), 6.87 (s, 2H), 6.27 (t, *J* = 3 Hz, 1H), 5.99 (dd, *J* = 3 Hz, 1H), 2.30 (s, 3H), 2.02 (s, 6H), 1.21 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ : 149.4, 137.8, 137.1, 131.9, 131.8, 127.5, 130.8, 113.1, 110.6, 82.7, 27.3, 21.1, 20.2. IR (neat, cm⁻¹): 2979, 1733, 1339. Anal. Calcd. for C₁₈H₂₃NO₂: C, 75.8; H, 8.1. Found C, 75.82; H, 8.25.

***Tert*-Butyl 2-(5-formyl-thiophen-2-yl)-1*H*-pyrrole-1-carboxylate (Table 8, entry 9).**⁴ Following general procedure E, a mixture of 5-chlorothiophene-2-carbaldehyde (26.6 μ L, 0.25 mmol), **F** (79.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in *n*-butanol with stirring for 3 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 77% yield (53 mg) as a yellow oil. ¹H NMR (300 MHz, CDCl₃) δ : 9.87 (s, 1H), 7.67 (d, *J* = 4 Hz, 1H), 7.40 (dd, *J* = 4, 2 Hz, 1H), 7.19 (d, *J* = 4 Hz, 1H), 6.44 (dd, *J* = 3, 2 Hz, 1H), 6.24 (t, *J* = 3 Hz, 1H), 1.48 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ : 183.6, 149.3, 145.8, 143.3, 136.7, 129.1, 126.8, 125.3, 118.7, 111.8, 85.4, 28.4. IR (neat, cm⁻¹): 2979, 1745, 1664, 1475, 1431, 1337, 1317, 1139. ¹H NMR spectrum included.

***Tert*-Butyl 2-(1*H*-indol-5-yl)-1*H*-pyrrole-1-carboxylate (Table 8, entry 10).** Following general procedure F, a mixture of 5-bromoindole (49 mg, 0.25 mmol), **F** (79.1 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in *n*-butanol with stirring for 5 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 79% yield (55 mg) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ : 8.18 (bs, 1H), 7.62 (dd, *J* = 4, 2 Hz, 1H), 7.36 (dd, *J* = 4, 2 Hz, 1H), 7.33 (s, 1H), 7.20 (t, *J* = 3 Hz, 1H), 7.17 (d, *J* = 2 Hz, 1H), 6.55 (m, 1H), 6.25 (t,

$J = 3$ Hz, 1H), 6.20 (dd, $J = 3,2$ Hz, 1H), 1.30 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 149.6, 136.4, 135.0, 127.3, 125.9, 124.5, 123.9, 121.8, 121.1, 113.9, 110.4, 110.0, 102.5, 83.1, 27.5. IR (neat, cm^{-1}): 3180, 2979, 1731, 1323. Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{NO}_3\text{S}$: C, 60.63; H, 5.45. Found C, 60.87; H, 5.49.

***Tert*-Butyl 2-(thiophen-2-yl)-1*H*-pyrrole-1-carboxylate (Table 8, entry 11).⁹**

Following general procedure F, a mixture of 2-bromothiophene (24.2 μL , 0.25 mmol), **F** (79.1 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in *n*-butanol with stirring for 5 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in an 84% yield (52 mg) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) $\geq$: 7.39 (dd, $J = 3,2$ Hz, 1H), 7.31 (dd, $J = 6,2$ Hz, 1H) 7.07 (dd, $J = 4,2$ Hz, 1H), 7.01 (dd, $J = 5,3$ Hz, 2H), 6.33 (dd, $J = 4,2$ Hz, 1H), 6.23 (t, $J = 3$ Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 149.0, 134.9, 127.7, 126.8, 126.3, 125.5, 123.1, 116.5, 110.5, 83.7, 27.6. IR (neat, cm^{-1}): 3452, 2980, 1738, 1636, 1475, 1396, 1370, 1327, 1308, 1143. ^1H NMR spectrum included.

***Tert*-Butyl 2-(isoquinolin-4-yl)-1*H*-pyrrole-1-carboxylate (Table 8, entry 12).⁴**

Following general procedure F, a mixture of 4-bromoisoquinoline (52 mg, 0.25 mmol), **F** (79.1 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $\text{Pd}(\text{OAc})_2$ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 $^\circ\text{C}$ in *n*-butanol with stirring for 5 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 95% yield (70 mg) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) $\geq$: 9.23 (s, 1H), 8.47 (s, 1H) 8.00 (dd, $J = 7,2$ Hz, 1H), 7.54-7.67 (m, 4H), 6.37 (t, $J = 3$ Hz, 1H), 6.33 (dd, $J = 3,2$ Hz, 1H), 0.90 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) $\geq$: 148.4, 147.9, 137.0, 134.4, 132.4, 131.2, 126.8, 123.5, 123.4, 119.4, 115.7, 107.3, 83.9, 28.2. IR (neat, cm^{-1}): 2979, 1733, 1462, 1370. Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$: C, 73.45; H, 6.16. Found C, 73.19; H, 6.21.

⁹ Johnson, C.; Stemp, G.; Anand, N.; Stephen, S.; Gallagher, T. *Synlett* **1998**, 1025-1027.

STANDARD PROTON PARAMETERS

exp1 szpu1

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 date Jun 29 2005 dfrq 125.795
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 akb/shh_111214_062~ dof 0
 985 dn nan
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 in H1 dseq
 at 3.200 dres 1.0
 np 64000 homo n
 Tb 10000.0 PROCESSING
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 tpwr 50 math f
 pw 9.6
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 tot 1490.2 wexp
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 ct 16 wdt
 clock n
 gain not used
 FLAGS
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 in n
 dp y
 ns nn
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 sc 0
 wc 250
 hznm 22.92
 is 100.00
 rfi 4633.0
 rfp 3631.7
 th 7
 ms 1.000
 ns ph

2-(5-Formyl-thiophen-2-yl)-pyrrole-1-carboxylic acid tert-butyl ester (CDCl3).

STANDARD PROTON PARAMETERS

exp1 szpu1

SAMPLE DEC. & VT
 date Jan 10 2006 dfrq 125.795
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 file exp dpur 37
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 at 3.200 dseq
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 Tb 10000.0 homo n
 not used wtf file ft
 bs 1 fn 131072
 tpwr 50 math f
 pw 9.6
 d1 0 warr
 tot 1490.2 wexp
 nt 16 wdt
 ct 16 wdt
 clock n
 gain not used
 FLAGS
 i1 n
 in n
 dp y
 ns nn
 DISPLAY
 sp -502.0
 vp 5505.2
 vs 126
 sc 0
 wc 250
 hznm 22.92
 is 100.00
 rfi 4633.0
 rfp 3631.7
 th 7
 ms 1.000
 ns ph

2-Thiophen-2-yl-pyrrole-1-carboxylic acid tert-butyl ester (CDCl3).

V. Experimental for Reactions of Indole Boronic Acids.

General Procedure G: Pd-Catalyzed Suzuki-Miyaura Couplings of Indole Boronic Acids.

An oven-dried Schlenk tube was charged with Pd₂(dba)₃ (2.3 mg, 0.0025 mmol), ligand (0.01 mmol), indole boronic acid (0.375 mmol) and powdered, anhydrous K₃PO₄ (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *n*-Butanol (0.50 mL) was added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 °C until aryl halide had been completely consumed as determined by gas chromatography. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

5-(3,6-Dimethyl-pyrazin-2-yl)-1-methyl-1*H*-indole (Table 9, entry 1).⁴ Following general procedure G, a mixture of 3-chloro-2,5-dimethylpyrazine (30.2 μL, 0.25 mmol), 1-methyl-5-indole boronic acid (65.3 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (25% EtOAc/Hexanes) to provide the title compound in a 90% yield (53 mg) as a yellow oil. ¹H NMR (300 MHz, CDCl₃) δ : 8.29 (s, 1H), 7.82 (s, 1H), 7.43 (t, *J* = 8 Hz, 1H), 7.40 (t, *J* = 8 Hz, 1H), 7.10 (d, *J* = 3 Hz, 1H), 6.54 (d, *J* = 3 Hz, 1H), 3.83 (s, 3H), 2.59 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ : 154.1, 150.0, 148.3, 136.6, 130.1, 129.6, 128.3, 122.6, 121.7, 109.1, 101.5, 32.9, 22.9, 21.2. IR (neat, cm⁻¹): 3099, 2959, 1923, 2824, 1617, 1514, 1449, 1426, 1331, 1245, 1150, 1105. ¹H NMR spectrum included.

1-Methyl-5-(pyridin-3-yl)-1H-indole (Table 9, entry 2). Following general procedure G, a mixture of 3-chloropyridine (23.8 μ L, 0.25 mmol), 1-methyl-5-indole boronic acid (65.3 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in butanol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (25% EtOAc/Hexanes) to provide the title compound in a 77% yield (40 mg) as a brown solid, mp 81-83 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 8.92 (d, J = 2 Hz, 1H), 8.55 (dd, J = 5,1 Hz, 1H), 7.93 (dt, J = 7,1 Hz, 1H), 7.84 (s, 1H), 7.45 (t, J = 7 Hz, 1H), 7.43 (t, J = 7 Hz, 1H), 7.35 (dd, J = 8,5 Hz, 1H), 7.11 (d, J = 3 Hz, 1H), 6.56 (d, J = 3 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 148.5, 147.4, 137.9, 136.5, 134.4, 129.8, 129.2, 129.2, 129.0, 123.4, 121.0, 119.5, 109.8, 101.4, 32.9. IR (neat, cm^{-1}): 3094, 3026, 2926, 1615, 1512, 1472, 1410, 1341, 1247. 1H NMR spectrum included.

5-(1-Methyl-1H-indol-5-yl)thiophene-2-carbaldehyde (Table 9, entry 3).⁴ Following general procedure G, a mixture of 5-chloro-2-thiophenecarbaldehyde (26.6 μ L, 0.25 mmol), 1-methyl-5-indole boronic acid (65.3 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), $Pd(OAc)_2$ (0.25 mol%) and SPhos (0.50 mol%) was heated to 100 °C in butanol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 96% yield (57 mg) as a yellow solid, mp 138-140 °C. 1H NMR (300 MHz, $CDCl_3$) δ : 9.87 (s, 1H), 7.96 (d, J = 2 Hz, 1H), 7.74 (d, J = 4 Hz, 1H), 7.56 (dd, J = 8,2 Hz, 1H), 7.39 (d, J = 4 Hz, 1H), 7.35 (d, J = 8 Hz, 1H), 7.10 (d, J = 3 Hz, 1H), 6.55 (d, J = 3 Hz, 1H), 2.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 182.7, 156.9, 141.1, 137.9, 137.3, 130.3, 128.8, 124.6, 122.8, 120.5, 119.3, 109.9, 101.8, 33.0. IR (neat, cm^{-1}): 3020, 2854, 1741, 1659, 1607, 1512, 1446, 1377, 1231, 1056. 1H NMR spectrum included.

5-(1H-Indol-5-yl)-2-methylbenzoxazole (Table 9, entry 4).⁴ Following general procedure G, a mixture of 5-chloro-2-methylbenzoxazole (41.8 mg, 0.25 mmol), 5-indole boronic acid (60.4 mg, 0.375 mmol), K_3PO_4 (106 mg, 0.50 mmol), Pd_2dba_3 (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on deactivated silica gel (10% Triethylamine/Hexanes) and eluent (40% EtOAc/Hexanes) to provide the title compound in a 91% yield (56 mg) as a brown oil. 1H NMR (300 MHz,

CDCl₃) $\geq$: 8.35 (bs, 1H), 7.90 (d, J = 1 Hz, 1H), 7.87 (d, J = 1 Hz, 1H), 7.60 (dd, J = 8,2 Hz, 1H), 7.53 (dd, J = 8,1 Hz, 1H), 7.47 (d, J = 1 Hz, 1H), 7.46 (d, J = 1 Hz, 1H), 7.26 (t, J = 3 Hz, 1H), 6.63 (t, J = 3 Hz, 1H), 2.68 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) $\geq$: 164.3, 150.0, 142.0, 139.4, 135.2, 133.2, 128.4, 124.9, 124.3, 122.1, 119.5, 118.0, 111.3, 110.0, 102.9, 14.6. IR (neat, cm⁻¹): 3411, 3238, 2963, 2929, 1577, 1458, 1275. ¹H NMR spectrum included.

5-(Thiophen-3-yl)-1H-indole (Table 9, entry 5). Following general procedure G, a mixture of 3-chlorothiophene (23.2 μ L, 0.25 mmol), 5-indole boronic acid (60.4 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (5% EtOAc/Hexanes) to provide the title compound in a 90% yield (45 mg) as a yellow solid, mp 80-82 °C. ¹H NMR (300 MHz, CDCl₃) $\geq$: 8.12 (bs, 1H), 7.90 (t, J = 1 Hz, 1H), 7.48 (dd, J = 8,2 Hz, 1H), 7.46 (dd, J = 5,1 Hz, 1H), 7.40-7.44 (m, 2H), 7.22 (t, J = 3 Hz, 1H), 6.60 (t, J = 3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) $\geq$: 143.6, 135.1, 128.2, 128.1, 126.8, 125.8, 124.8, 121.3, 118.8, 118.5, 111.2, 102.9. IR (neat, cm⁻¹): 2951, 2920, 1463, 854, 785. Anal. Calcd. for C₁₂H₉NS: C, 72.33; H, 4.55. Found C, 72.10; H, 4.72.

1H,1'H-5,5'-Biindolyl (Table 9, entry 6). Following general procedure G, a mixture of 5-chloroindole (37.9 mg, 0.25 mmol), 5-indole boronic acid (60.4 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on deactivated silica gel (10% Triethylamine/Hexanes) and eluent (40% EtOAc/Hexanes) to provide the title compound in a 71% yield (41 mg) as a red oil. ¹H NMR (300 MHz, CDCl₃) $\geq$: 8.14 (bs, 1H), 7.90 (d, J = 1 Hz, 1H), 7.53 (dd, J = 8,2 Hz, 1H), 7.46 (dd, J = 8,1 Hz, 1H), 7.26 (d, J = 1 Hz, 1H), 7.24 (d, J = 3 Hz, 1H), 6.62 (d, J = 3 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) $\geq$: 134.8, 134.7, 128.4, 124.6, 122.4, 119.3, 111.0, 102.9. IR (neat, cm⁻¹): 3411, 1637, 1456, 1415, 1293, 1092. ¹H NMR spectrum included.

5-(1H-Indol-5-yl)pyridin-2-amine (Table 9, entry 7).⁴ Following general procedure G, a mixture of 2-amino-5-chloropyridine (32.1 mg, 0.25 mmol), 5-indole boronic acid (60.4 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and

XPhos (4.8 mg, 0.01 mmol) was heated to 120 °C in butanol with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (EtOAc) to provide the title compound in a 77% yield (40 mg) as a red oil. ¹H NMR (300 MHz, CD₃OD) δ : 8.14 (dd, J = 2,1 Hz, 1H), 7.77 (dd, J = 8,3 Hz, 1H), 7.67 (dd, J = 2,1 Hz, 1H), 7.41 (dt, J = 8,1 Hz, 1H), 7.26 (dd, J = 8,1 Hz, 1H), 7.24 (d, J = 3 Hz, 1H), 6.67 (dd, J = 8,1 Hz, 1H), 6.46 (dd, J = 3,1 Hz, 1H). ¹³C NMR (75 MHz, CD₃CN) δ : 159.0, 147.0, 137.2, 136.2, 130.9, 129.6, 128.6, 126.5, 121.3, 118.5, 112.6, 109.0, 102.7. IR (neat, cm⁻¹): 3394, 3025, 2924, 2532, 1620, 1499, 1468, 1389, 1316. ¹H NMR spectrum included.

STANDARD PROTON PARAMETERS
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 at 3.200 dat 10000
 np 84000 dseq
 sw 10000.0 dres 1.0
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 ss 1 wfile
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 pw 9.8 tn 131072
 d1 0 math f
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 ct 16 wexp
 alock n wbs
 gain not used wnt
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 nm ph

5-(1H-Indol-5-yl)-2-methyl-benzoxazole (CD3OD)

STANDARD PROTON PARAMETERS
 exp1 s2pu1 **1V89**
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 solvent CD300 dn C13 125.796
 file exp dpwr 37
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 at 3.200 dat 10000
 np 84000 dseq
 sw 10000.0 dres 1.0
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 bs 0 PROCESSING
 ss 1 wfile
 tpwr 59 proc ft
 pw 9.8 tn 131072
 d1 0 math f
 tof 1490.2
 nt 16 verr
 ct 16 wexp
 alock n wbs
 gain not used wnt
 FLAGS
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 in n
 dp y
 hs nn
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 vs 71
 sc 0
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 hzmm 22.02
 is 100.00
 rfi 2651.4
 rfp 1650.0
 th 7
 ins 1.000
 nm ph

1H,1'H-[5,5']Biindolyl (CD3OD)

VI. Experimental for Reactions of Furan Boronic Acids.

General Procedure H: Pd-Catalyzed Suzuki-Miyaura Couplings of Furan Boronic Acids.

An oven-dried Schlenk tube was charged with $\text{Pd}_2(\text{dba})_3$ (2.3 mg, 0.0025), ligand (0.01 mmol), furan boronic acid (42 mg, 0.375 mmol) and powdered, anhydrous K_3PO_4 (106 mg, 0.50 mmol). The Schlenk tube was capped with a rubber septum and then evacuated and backfilled with argon (this sequence was carried out two times). *tert*-Amyl alcohol (0.50 mL) was added via syringe, through the septum, followed by the addition of the aryl halide (0.25 mmol) in a like manner (aryl halides that were solids were added with other reagents before evacuation). The septum was then replaced with a Teflon screwcap and the Schlenk tube was sealed. The reaction mixture was heated to 100 °C until aryl halide had been completely consumed as determined by gas chromatography. At this point the reaction mixture was allowed to cool to room temperature. The reaction solution was then filtered through a thin pad of silica gel (eluting with ethyl acetate) and

the eluent was concentrated under reduced pressure. The crude material so obtained was purified via flash chromatography on silica gel.

2-(Furan-3-yl)pyrazine (Table 9, entry 8). Following general procedure H, a mixture of 2-chloropyrazine (28.6 mg, 0.25 mmol), 3-furan boronic acid (42 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd(OAc)₂ (2.3 mg, 0.005 mmol) and SPhos (4.1 mg, 0.01 mmol) was heated to 100 °C in sec-butanol with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (15% EtOAc/Hexanes) to provide the title compound in a 96% yield (35 mg) as a brown solid, mp 64-66 °C. ¹H NMR (300 MHz, CDCl₃) δ : 8.76 (s, 1H), 8.52 (dd, J = 3.1 Hz, 1H), 8.08 (dd, J = 2.1 Hz, 1H), 7.53 (dd, J = 3.1 Hz, 1H), 6.93 (dd, J = 3.1 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 147.7, 144.3, 144.2, 142.4, 141.8, 141.7, 124.1, 108.2. IR (neat, cm⁻¹): 3135, 3111, 3080, 2924, 1863, 1588, 1577, 1510, 1417, 1299, 1071. Anal. Calcd. for C₈H₆N₂O: C, 65.75; H, 4.23. Found C, 65.61; H, 4.23.

5-(Quinoxalin-2-yl)furan-2-carbaldehyde (Table 9, entry 9). Following general procedure H, a mixture of 2-chloroquinoxaline (41.2 mg, 0.25 mmol), 5-formyl-2-furan boronic acid (52.5 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 10 h. The crude product was purified via recrystallization (Hexanes) to provide the title compound in a 82% yield (46 mg) as a brown solid, mp 140-142 °C. ¹H NMR (300 MHz, CDCl₃) δ : 9.82 (s, 1H), 9.42 (s, 1H), 8.09-8.12 (m, 2H), 7.76-7.82 (m, 2H), 7.49 (d, J = 4 Hz, 1H), 7.42 (d, J = 4 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ : 177.9, 156.1, 153.4, 142.5, 142.1, 142.0, 141.9, 130.9, 130.6, 129.4, 129.3, 122.1, 113.1. IR (neat, cm⁻¹): 2834, 1667, 1635, 1483, 1256, 1073. ¹H NMR spectrum included.

2-(Quinolin-2-yl)furan-3-carbaldehyde (Table 9, entry 10). Following general procedure H, a mixture of 2-chloroquinoline (40.9 mg, 0.25 mmol), 3-formyl-2-furan boronic acid (52.5 mg, 0.375 mmol), K₃PO₄ (106 mg, 0.50 mmol), Pd₂dba₃ (2.3 mg, 0.0025 mmol) and XPhos (4.8 mg, 0.01 mmol) was heated to 100 °C in tert-amyl alcohol with stirring for 10 h. The crude product was purified via flash column chromatography on silica gel (10% EtOAc/Hexanes) to provide the title compound in a 70% yield (39 mg) as a yellow solid, mp 104-105 °C. ¹H NMR (300 MHz, CDCl₃) δ : 11.21 (s, 1H), 8.25 (d,

$J = 8$ Hz, 1H), 8.08 (d, $J = 8$ Hz, 1H), 7.97 (d, $J = 8$ Hz, 1H), 7.83 (d, $J = 8$ Hz, 1H), 7.75 (dt, $J = 8, 1$ Hz, 1H), 7.58 (dt, $J = 8, 1$ Hz, 1H), 7.52 (d, $J = 2$ Hz, 1H), 7.00 (d, $J = 2$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ : 189.5, 157.6, 148.3, 147.1, 136.9, 130.2, 129.7, 128.3, 127.6, 127.3, 126.2, 118.3, 110.0. IR (neat, cm^{-1}): 3120, 2885, 1674, 1594, 509, 1411, 1274, 1165. ^1H NMR spectrum included.

STANDARD PROTON PARAMETERS

exp1 52pu1

SAMPLE DEC. A VT
 date Dec 19 2005 dfrq 125.795
 solvent CDCl3 dn C13
 file /data/study/~/dpwr 37
 nb/ivb_iv271_1213- daf 4
 nn
 ACQUISITION den c
 sfrq 500.235 daf 10000
 tn HJ dseq
 nt 3.200 dres 1.0
 np 61000 homo n
 sw 10000.0
 PROCESSING
 fb not used wfile ft
 bs 0 proc 131072
 ss 1 fn f
 ipwr 50 math
 pw 9.8
 d1 0 verr
 tof 1498.2 wexp
 at 16 wnt
 ct 16 wnt
 clock n
 gain not used
 FLAOS
 fl n
 fa n
 dp y
 bs nn
 DISPLAY
 sp -501.4
 vp 6504.5
 vs 50
 sc 0
 vc 250
 hzmm 26.02
 is 100.00
 rfl 1622.3
 rfp 3621.7
 ts 7
 ins 1.000
 nm ph

2-Quinolin-2-yl-furan-3-carbaldehyde (CDCl3).