An Efficient Catalyst for Suzuki-Miyaura Coupling of Potassium Aryl Trifluoroborates with Aryl Chlorides

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Experimental Section

General. All reactions were carried out under an argon atmosphere. Methanol (laboratory grade) was purchased from Mallinckrodt Chemicals, degassed by sparging with argon (~5 min.) and stored in a Schlenk tube. Absolute ethanol was purchased from Pharmco Products Inc., degassed as above and stored in a Schlenk tube. Commercially obtained materials were used without further purification unless noted otherwise. S-Phos was synthesized in our laboratories, but is commercially available from Aldrich Chemical Co. or Strem Chemicals, Inc. Aryl chlorides were purchased from Aldrich Chemical Co., except 4-*n*-butylchlorobenzene, which was obtained from Alfa Aesar. Liquid aryl chlorides were purified by filtration through a thin pad of basic alumina prior to use. Boronic acids were purchased from Aldrich Chemical Co. Potassium *o*-tolyltrifluoroborate,¹ potassium naphthyltrifluoroborate¹ and potassium 3-pyridyl-trifluoroborate² were prepared as

(1) Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867.

(2) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

previously described. Anhydrous granular potassium carbonate 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, and IR spectroscopy and by elemental analysis. For the compounds that did not return satisfactory elemental analyses (3-(4-*n*-butylphenyl)pyridine and 2,5-dimethyl-3-(1-naphthyl)pyrazine), a copy of the ^1H and ^{13}C NMR spectra are included at the end of the supporting information. Known compounds were characterized by ^1H NMR spectroscopy and melting point (for solids) and compared to their literature values. ^1H , ^{13}C and ^{19}F NMR spectra were recorded on a Varian Mercury 300 or a Varian Inova 500. 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, part per million (ppm) downfield from TMS and were measured relative to the signals for residual chloroform (7.26 ppm). All ^{13}C NMR spectra are reported in ppm relative to residual chloroform (77 ppm) and were obtained with ^1H decoupling. All ^{19}F NMR spectra are reported in ppm relative to CFCl_3 (0 ppm). Melting points (uncorrected) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on a 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 2 and 3 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.

Potassium 4-*tert*-Butylphenyl trifluoroborate. To a stirred solution of 4-*tert*-butylphenyl boronic acid (3.6 g, 20 mmol) in 15 mL laboratory grade methanol was added a solution of potassium

hydrogen fluoride (5.2 g, 66 mmol) in 16 mL H₂O. Upon addition of the potassium hydrogen fluoride solution, a white precipitate formed. This mixture was stirred for an additional 30 min. and filtered and washed twice with 5 mL ice-cold methanol. The resulting white solid was dissolved in ~30 mL CH₃CN and stirred for 5 min. Filtration of this mixture followed by concentration under reduced pressure afforded the title compound as a white solid (4.0 g, 83%), mp > 260 °C. ¹H NMR (300 MHz, *d*₆-DMSO) δ: 7.25 (d, *J* = 8 Hz, 2H), 7.11 (d, *J* = 8 Hz, 2H), 1.25 (s, 9H). ¹³C NMR (125 MHz, *d*₆-DMSO) δ: 146.9, 131.2 (d, *J* = 2 Hz), 122.9, 33.9, 31.5. ¹⁹F NMR (282 MHz, *d*₆-DMSO) δ: -138.4.

General Procedure: Pd-catalyzed Suzuki-Miyaura couplings of potassium aryl trifluoroborates with aryl chlorides.

A threaded-top test tube containing a magnetic stir bar was charged with Pd(OAc)₂, S-Phos, the potassium aryl trifluoroborate and powdered, anhydrous K₂CO₃. The test tube was capped with a screwtop cap lined with a disposable teflon septum and evacuated and backfilled with argon (this process was repeated three times) through a 18 gauge needle. The aryl chloride was added via syringe through the septum followed by addition of the solvent through the septum. The test tube was placed back under argon through the needle and the screw top cap was quickly removed and replaced with a new cap with an unpunctured septum. The reaction mixture was heated to the specified temperature with vigorous stirring for the specified time. The reaction mixture was allowed to cool, diluted with ethyl acetate (10 mL), filtered through a thin pad of silica gel (eluting with ethyl acetate or 25% methanol in ethyl acetate for pyridyl derivatives) and concentrated under reduced pressure. The crude material obtained was purified by flash column chromatography on silica gel.

4'-tert-Butyl-3,5-dimethoxybiphenyl (Table 2, entry 1). Following the general procedure, a mixture of 5-chloro-1,3-dimethoxybenzene (173 mg, 1.0 mmol), potassium 4-tert-butylphenyltrifluoroborate (252 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 50 °C with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (5% ethyl acetate/hexanes) to provide the title compound as a white solid (252 mg, 93%), mp 55-57 °C. ¹H NMR (300 MHz, CDCl₃) δ: 7.47-7.57 (m, 4H), 6.76 (d, *J* = 2 Hz, 2H), 6.48 (d, *J* = 2 Hz, 1H), 3.86 (s, 6H), 1.39 (s, 9H). ¹³C NMR (75 MHz, CDCl₃) δ: 160.9, 150.6, 143.3, 138.3, 126.8, 125.7, 105.3, 98.9, 55.3, 34.5, 31.3. IR (neat, cm⁻¹): 3064, 2966, 1596, 1459, 1266. Anal. Calcd. for C₁₈H₂₂: C, 79.96; H, 8.20. Found C, 79.90; H, 8.36.

4'-tert-Butyl-biphenyl-3-methylcarboxylate (Table 2, entry 2).³ Following the general procedure, a mixture of methyl 3-chlorobenzoate (171 mg, 1.0 mmol), potassium 4-tert-butylphenyltrifluoroborate (252 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 50 °C with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (5% ethyl acetate/hexanes) to provide the title compound as a white solid (256 mg, 96%), mp 81-82 °C (lit. 65-67 °C).⁴ ¹H NMR (300 MHz, CDCl₃) δ: 8.29 (s, 1H), 8.01 (d, *J* = 7 Hz, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.59 (d, *J* = 8 Hz, 2H), 7.46-7.53 (m, 3H), 3.95 (s, 3H), 1.38 (s, 9H).

(3) Wang, X.; Parlow, J. J.; Porco, J. A. *Org. Lett.* **2000**, 2, 3509

4'-tert-Butyl-2,6-dimethylbiphenyl (Table 2, entry 3).⁴ Following the general procedure, a mixture of 2-chloro-*m*-xylene (141 mg, 1.0 mmol), potassium 4-*tert*-butylphenyltrifluoroborate (252 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 50 °C with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (1% ethyl acetate/hexanes) to provide the title compound as a white solid (219 mg, 92%), mp 75-76 °C (lit. 71-73 °C).⁵ ¹H NMR (300 MHz, CDCl₃) δ: 7.43 (d, *J* = 8 Hz, 2H), 7.08-7.19 (m, 3H), 7.08 (d, *J* = 8 Hz, 2H), 2.05 (s, 6H), 1.38 (s, 9H).

4'-tert-Butyl-4-*n*-butylbiphenyl (Table 2, entry 4). Following the general procedure, a mixture of 4-*n*-butylchlorobenzene (168 mg, 1.0 mmol), potassium 4-*tert*-butylphenyltrifluoroborate (252 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), a solution of Pd(OAc)₂ in THF (100 μL, 0.11 mg, 0.0005 mmol), and a solution of S-Phos in THF (200 μL, 0.41 mg, 0.001 mmol) in methanol (1.7 mL) was heated to 67 °C with stirring for 16 h. The crude product was purified via flash column chromatography on silica gel (1% ethyl acetate/hexanes) to provide the title compound as a white solid (241 mg, 91%), mp 42-43 °C. ¹H NMR (500 MHz, CDCl₃) δ: 7.52 (d, *J* = 8 Hz, 2H), 7.50 (d, *J* = 8 Hz, 2H), 7.45 (d, *J* = 8 Hz, 2H), 7.24 (d, *J* = 8 Hz, 2H), 2.64 (t, *J* = 8 Hz, 2H), 1.61-1.66 (m, 2H), 1.36-1.42 (m, 2H), 1.36 (s, 9H), 0.95 (t, *J* = 8 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ: 149.9, 141.7, 138.4, 138.3, 128.7, 126.8, 126.6, 125.6, 35.3, 34.5, 33.7, 31.4, 22.4, 14.0. IR (neat, cm⁻¹): 3064, 2987, 1422, 1264. Anal. Calcd. for C₂₀H₂₆: C, 90.16; H, 9.84. Found C, 89.82; H, 10.00.

(4) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550

2'-Methyl-4-methoxybiphenyl (Table 2, entry 5).⁵ Following the general procedure, a mixture of 4-chloroanisole (143 mg, 1.0 mmol), potassium *o*-tolyltrifluoroborate (218 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 67 °C with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (3% ethyl acetate/hexanes) to provide the title compound as a colorless oil (176 mg, 89%). ¹H NMR (300 MHz, CDCl₃) δ: 7.20-7.26 (m, 4H), 6.94 (d, *J* = 8 Hz, 4H), 3.84 (s, 3H), 2.27 (s, 3H).

1-(2'-Methyl-4-biphenyl)-pyrrole (Table 2, entry 6). Following the general procedure, a mixture of 1-(4-chlorophenyl)-pyrrole (178 mg, 1.0 mmol), potassium *o*-tolyltrifluoroborate (218 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 67 °C for 12 h. The crude product was purified via flash column chromatography on silica gel (3% ethyl acetate/hexanes) to provide the title compound as a white solid (224 mg, 96%), mp 84-85 °C. ¹H NMR (300 MHz, CDCl₃) δ: 7.39-7.48 (m, 4H), 7.27-7.32 (m, 4H), 7.17 (t, *J* = 2 Hz, 2H), 6.41 (t, *J* = 2 Hz, 2H), 2.34 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ: 140.9, 139.4, 139.3, 135.3, 130.4, 130.3, 129.7, 127.4, 125.9, 120.1, 119.3, 110.4, 20.5. IR (neat, cm⁻¹): 3136, 3103, 3043, 2970, 1611, 1526, 1488. Anal. Calcd. for C₁₇H₁₅: C, 87.52; H, 6.48. Found C, 87.42; H, 6.54.

2,2'-Dimethyl-(1,1';3',1'')terphenyl (Table 2, entry 7). Following the general procedure, a mixture of 3-chloro-2-methylbiphenyl (203 mg, 1.0 mmol), potassium *o*-tolyltrifluoroborate (218 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 67 °C for 12 h. The crude product was purified via

(5) Lipshutz, B. H.; Siegmann, K.; Garcia, E.; Kayser, F. *J. Am. Chem. Soc.* **1993**, *115*, 9276

flash column chromatography on silica gel (1% ethyl acetate/hexanes) to provide the title compound as a white solid (216 mg, 84%), mp 70-71 °C. ¹H NMR (300 MHz, CDCl₃) δ: 7.31-7.43 (m, 5H), 7.20-7.30 (m, 5H), 7.14-7.28 (m, 1H), 7.11 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ: 142.5, 142.4, 142.3, 142.0, 135.8, 133.3, 129.8, 129.3, 129.3, 128.8, 128.4, 128.0, 127.1, 126.7, 125.6, 125.2, 19.9, 17.8. IR (neat, cm⁻¹): 3064, 2987, 1463, 1426, 1266. Anal. Calcd. for C₂₀H₁₈: C, 92.98; H, 7.02. Found C, 92.17; H, 7.00.

2,2',6-Trimethylbiphenyl (Table 2, entry 8).⁶ Following the general procedure, a mixture of 2-chloro-*m*-xylene (141 mg, 1.0 mmol), potassium *o*-tolyltrifluoroborate (297 mg, 1.5 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (4.4 mg, 0.02 mmol), and S-Phos (16.4 mg, 0.04 mmol) in methanol (2 mL) was heated to 50 °C for 20 h. The crude product was purified via flash column chromatography on silica gel (1% ethyl acetate/hexanes) to provide the title compound as a colorless oil (183 mg, 93%). ¹H NMR (300 MHz, CDCl₃) δ: 7.30-7.10 (m, 6H), 7.03-6.98 (m, 1H), 1.97 (s, 3H), 1.93 (s, 6H).

3-(1-Naphthyl)pyridine (Table 3, entry 1).⁷ Following the general procedure, a mixture of 3-chloropyridine (114 mg, 1.0 mmol), potassium naphthyltrifluoroborate (257 mg, 1.1 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 67 °C with stirring for 12 h. The crude product was purified via flash column chromatography on silica gel (ethyl acetate: hexanes, 1:1) to provide the title compound as a colorless oil (201 mg, 98%). ¹H NMR (300 MHz, CDCl₃) δ: 8.77 (d, *J* = 2 Hz, 1H), 8.70 (dd, *J* = 2, 5 Hz, 1H), 7.90-7.96 (m, 2H), 7.79-7.85 (m, 2H), 7.41-7.59 (m, 5H).

(6) Kamikawa, T.; Hayashi, T. *Synlett* **1997**, 163.

(7) Katoh, T.; Ogawa, K.; Inagaki, Y. *Tetrahedron* **1997**, 53, 3557.

5-(1-Naphthyl)-2-thiophenecarboxaldehyde (Table 3, entry 2). Following the general procedure, a mixture of 5-chloro-2-thiophenecarboxaldehyde (174 mg, 1.0 mmol), potassium naphthyltrifluoroborate (257 mg, 1.1 mmol), K_2CO_3 (415 mg, 3.0 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), and S-Phos (8.2 mg, 0.02 mmol) in methanol (2 mL) was heated to 67 °C with stirring for 18 h. The crude product was purified via flash column chromatography on silica gel (hexanes to 5% ethyl acetate:hexanes) to provide the title compound as a orange solid (213 mg, 89%), mp 56-57 °C. 1H NMR (500 MHz, $CDCl_3$) δ : 9.97 (s, 1H), 8.14-8.18 (m, 1H), 7.92-7.94 (m, 2H), 7.85 (d, J = 4 Hz, 1H), 7.60 (dd, J = 2, 8 Hz, 1H), 7.51-7.57 (m, 3H), 7.36 (d, J = 4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ : 182.9, 152.3, 143.5, 136.6, 133.8, 131.1, 131.0, 129.7, 128.6, 128.5, 128.3, 127.0, 126.4, 125.2, 125.0. IR (neat, cm^{-1}): 3063, 2809, 2744, 1663, 1449. Anal. Calcd. for $C_{15}H_{10}OS$: C, 75.60; H, 4.23. Found C, 75.31; H, 4.18.

2,5-Dimethyl-3-(1-naphthyl)pyrazine (Table 3, entry 3). Following the general procedure, a mixture of 3-chloro-2,5-dimethylpyrazine (143 mg, 1.0 mmol), potassium naphthyltrifluoroborate (257 mg, 1.1 mmol), K_2CO_3 (276 mg, 2.0 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol), and S-Phos (4.1 mg, 0.01 mmol) in methanol (2 mL) was heated to 40 °C with stirring for 11 h. The crude product was purified via flash column chromatography on silica gel (1:4 ethyl acetate:hexanes) to provide the title compound as a colorless oil (203 mg, 87%). 1H NMR (300 MHz, $CDCl_3$) δ : 8.45 (s, 1H), 7.93 (dd, J = 4, 8 Hz, 2H), 7.57 (t, J = 8 Hz, 1H), 7.51 (dt, J = 2, 8 Hz, 1H), 7.44 (d, J = 7 Hz, 2H), 7.39 (t, J = 7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ : 152.6, 150.4, 149.7, 142.5, 136.2, 133.6, 131.1, 128.9, 128.4, 126.7, 126.5, 126.0, 125.3, 125.0, 21.7, 21.2. IR (neat, cm^{-1}): 3047, 2923, 1698, 1439, 1368, 1113.

3-(4-*n*-Butylphenyl)pyridine (Table 3, entry 4). Following the general procedure, a mixture of 4-*n*-butylchlorobenzene (169 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (1:2 ethyl acetate:hexanes) to provide the title compound as a yellow oil (170 mg, 80%). ¹H NMR (300 MHz, CDCl₃) δ: 8.85 (d, *J* = 2 Hz, 1H), 8.57 (dd, *J* = 2, 5 Hz, 1H), 7.86 (td, *J* = 2, 8 Hz, 1H), 7.50 (td, *J* = 2, 8 Hz, 2H), 7.34 (ddd, *J* = 1, 5, 8 Hz, 1H), 7.30 (d, *J* = 8 Hz, 2H), 2.67 (t, *J* = 8 Hz, 2H), 1.64 (m, 2H), 1.39 (sextet, *J* = 8 Hz, 2H), 0.95 (t, *J* = 8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ: 148.2, 148.1, 143.0, 136.5, 135.1, 134.1, 129.1, 126.9, 123.5, 35.3, 33.6, 22.3, 13.9. IR (neat, cm⁻¹): 3027, 2929, 2868, 1474, 1428, 1397.

3,3'-Bipyridine (Table 3, entry 5).⁸ Following the general procedure, a mixture of 3-chloropyridine (114 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (1:6 methanol:ethyl acetate) to provide the title compound as a yellow oil (119 mg, 76%). Although melting point data exists,⁹ we were unable to crystallize this compound. The ¹H and ¹³C NMR spectra are included at the end of the supporting information. ¹H NMR (300 MHz, CDCl₃) δ: 8.84 (d, *J* = 2 Hz, 1H), 8.65 (dd, *J* = 2, 5 Hz, 1H), 7.88 (td, *J* = 2, 8 Hz, 1H), 7.41 (dd, *J* = 5, 8 Hz, 1H).

(8) Fort, Y.; Becker, S.; Caubère, P. *Tetrahedron*, **1994**, *50*, 11893.

3-Pyridylpyrazine (Table 3, entry 6).⁹ Following the general procedure, a mixture of chloropyrazine (115 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (1:6 methanol:ethyl acetate) to provide the title compound as a light yellow oil (120 mg, 77%). ¹H NMR (500 MHz, CDCl₃) δ: 9.24 (d, *J* = 3 Hz, 1H), 9.06 (d, *J* = 3 Hz, 1H), 8.72 (dd, *J* = 2, 5 Hz, 1H), 8.68 (t, *J* = 3 Hz, 1H), 8.58 (d, *J* = 3 Hz, 1H), 8.33 (td, *J* = 2, 7 Hz, 1H).

2-(3-Pyridyl)quinoline (Table 3, entry 7).^{9a,10} Following the general procedure, a mixture of 2-chloroquinoline (164 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K₂CO₃ (415 mg, 3.0 mmol), Pd(OAc)₂ (9.0 mg, 0.04 mmol), and S-Phos (32.8 mg, 0.08 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (1:1 ethyl acetate:hexanes) to provide the title compound as a yellow solid (171 mg, 83%), mp 69-70 °C (lit. 72 °C).^{9a} ¹H NMR (500 MHz, CDCl₃) δ: 9.35 (d, *J* = 3 Hz, 1H), 8.70 (dd, *J* = 2, 5 Hz, 1H), 8.50 (td, *J* = 2, 8 Hz, 1H), 8.26 (d, *J* = 8 Hz, 1H), 8.17 (d, *J* = 8 Hz, 1H), 7.87 (d, *J* = 8 Hz, 1H), 7.84 (d, *J* = 8 Hz, 1H), 7.75 (dt, *J* = 2, 8 Hz, 1H), 7.56 (dt, *J* = 2, 8 Hz, 1H), 7.45 (ddd, *J* = 2, 5, 8 Hz, 1H).

5-(3-Pyridyl)-2-thiophenecarboxaldehyde (Table 3, entry 8). Following the general procedure, a mixture of 5-chloro-2-thiophenecarboxaldehyde (147 mg, 1.0 mmol), potassium 3-

(9) (a) Bonnet, V.; Mongin, F.; Trécourt, F.; Breton, G.; Marsais, F.; Knochel, P.; Quéguiner, G. *Synlett*, **2002**, 6, 1008. (b) Hasebe, M.; Kogawa, K.; Tsuchiya, T. *Tet. Lett.*, **1984**, 25, 3887.

(10) Sakamoto, T.; Kondo, Y.; Murata, Y.; Yamanata, H. *Tetrahedron*, **1993**, 43, 9713.

pyridyltrifluoroborate (278 mg, 1.5 mmol), K_2CO_3 (415 mg, 3.0 mmol), $\text{Pd}(\text{OAc})_2$ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (3:1 ethyl acetate:hexanes) to provide the title compound as a red solid (142 mg, 75%). mp 79-81 °C. ^1H NMR (500 MHz, CDCl_3) δ : 9.91 (s, 1H), 8.93 (d, $J = 3$ Hz, 1H), 8.61 (dd, $J = 2, 5$ Hz, 1H), 7.92 (td, $J = 2, 8$ Hz, 1H), 7.77 (d, $J = 4$ Hz, 1H), 7.45 (d, $J = 4$ Hz, 1H), 7.37 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ : 182.7, 150.2, 149.9, 147.2, 143.5, 137.2, 133.5, 129.1, 125.1, 123.8. IR (neat, cm^{-1}): 3086, 3043, 2811, 1659, 1445, 1414. Anal. Calcd. for $\text{C}_{10}\text{H}_7\text{NOS}$: C, 63.47; H, 3.73. Found C, 63.42; H, 3.75.

3-(3-Pyridyl)ethylbenzoate (Table 3, entry 9). Following the general procedure, a mixture of 3-chloromethylbenzoate (171 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K_2CO_3 (415 mg, 3.0 mmol), $\text{Pd}(\text{OAc})_2$ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (2:1 ethyl acetate:hexanes) to provide the title compound as a light yellow oil (181 mg, 81%). ^1H NMR (500 MHz, CDCl_3) δ : 8.87 (d, $J = 2$ Hz, 1H), 8.62 (dd, $J = 2, 5$ Hz, 1H), 8.26 (t, $J = 2$ Hz, 1H), 8.08 (td, $J = 2, 8$ Hz, 1H), 7.91 (td, $J = 2, 8$ Hz, 1H), 7.77 (td, $J = 2, 8$ Hz, 1H), 7.55 (t, $J = 8$ Hz, 1H), 7.39 (dd, $J = 5, 8$ Hz, 1H), 4.41 (q, $J = 7$ Hz, 2H), 1.41 (t, $J = 7$ Hz, 3H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ : 166.6, 149.4, 148.7, 138.7, 136.1, 134.8, 132.0, 131.8, 129.7, 129.4, 128.6, 124.1, 61.7, 14.6. IR (neat, cm^{-1}): 3062, 2981, 2937, 1716, 1586. Anal. Calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2$: C, 73.99; H, 5.77. Found C, 73.37; H, 5.93.

5-(3-Pyridyl)-1,3-dimethoxybenzene (Table 3, entry 10). Following the general procedure, a mixture of 5-chloro-1,3-dimethoxybenzene (173 mg, 1.0 mmol), potassium 3-pyridyltrifluoroborate (278 mg, 1.5 mmol), K_2CO_3 (415 mg, 3.0 mmol), $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), and S-Phos (24.6 mg, 0.06 mmol) in methanol (2 mL) was heated to 72 °C with stirring for 22 h. The crude product was purified via flash column chromatography on silica gel (1:1 ethyl acetate:hexanes) to provide the title compound as a light yellow oil (177 mg, 82%). 1H NMR (500 MHz, $CDCl_3$) δ : 8.83 (d, J = 3 Hz, 1H), 8.58 (dd, J = 3, 5 Hz, 1H), 7.84 (td, J = 2, 8 Hz, 1H), 7.34 (dd, J = 5, 8 Hz, 1H), 6.70 (d, J = 2 Hz, 2H), 6.50 (t, J = 2 Hz, 1H). ^{13}C NMR (125MHz, $CDCl_3$) δ : 161.2, 148.7, 148.3, 139.9, 136.6, 134.4, 123.4, 105.4, 99.8, 55.4. IR (neat, cm^{-1}): 3002, 2939, 2838, 1594, 1457. Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found C, 72.18; H, 6.18.

TE84145

Pulse Sequence: s2pul
Solvent: CDCl3
Acquire temperature:
INOVA-500 "BoltWinkie"
PULSE SEQUENCE
Pulse 19.0 degrees
Acq time 3.27 sec
Waltz 1898.8 Hz
8 repetitions
OBSERVE H1 499.753775 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 26 sec

TEB4145

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
User: I-14-87
INOVA-500 "b11wink1e"
PULSE SEQUENCE
Relax. delay 3.000 sec
Pulse 45.0 degrees
Acq. time 0.869 sec
Width 37718.1 Hz
604 repetitions
OBSERVE C13, 125.6831966 MHz
DECOUPLE H1, 499.7562709 MHz
Power Scaled on
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 1 hr, 11 min, 51 sec

TEB4165

Pulse Sequence: s2pul
Solvent: CDCl3
Acquisition Temperature: 25.00
INVOA-500 "Bullwinkle"
PULSE SEQUENCE
Pulse 190.0 degrees
Acq time 3.297 sec
Width 3998.8 Hz
8 repetitions
OBSERVE H1, 499.753772 MHz
DATA PROCESSING
FT size 65536
Total time 0 min, 26 sec

TEB4165

Pulse Sequence: s2pul

Solvent: CDCl₃

Ambient temperature

INNOVA-500 "bullwinkle"

PULSE SEQUENCE

Relax 3.000 sec

Relax 4.000 sec

Acq time 0.869 sec

Width 37718.1 Hz

252 repetitions

OBSERVE C13, 125.6631983 MHz

DECOUPLE H1, 499.7562709 MHz

Power 34 dB

continuously on

WALTZ-16 modulated

DATA PROCESSING

Time domain 1.0 Hz

FI size 131072

Total time 11 hr, 58 min, 8 sec

3,3'-bipy
Solvent: CDCl₃
Ambient temperature
INNOVA-500 "Rocky"
PULSE SEQUENCE
Pulse 90.0 degrees
Acq. time 3.200 sec
Width 10000.0 Hz
Repetitions 500
Observed frequency 500.2312763 MHz
Spectrum name
DATA PROCESSING
FT size 131072
Total time 1 minute

3,3'-bipy
 Solvent: CDCl3
 Ambient temperature
 INOVA-500 "rocky"
 PULSE SEQUENCE 2.000 sec
 Relax delay 2.000 sec
 Pulse delay 0.050 sec
 Acq time 1.736 sec
 Width 37735.8 Hz
 60 repetitions
 OBSERVE C13, 125.7832609 MHz
 DECOUPLE H1, 500.2332753 MHz
 Power 37 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 3 minutes

STANDARD 1H OBSERVE

Pulse Sequence: s2pu1

Solvent: DMSO

Ambient temperature

Mercury-300 "mrhat"

Relax. delay 1.000 sec

Pulse 34.1 degrees

Acq. time 1.995 sec

Width 4506.5 Hz

16 repetitions

OBSERVE H1, 300.1000564 MHz

DATA PROCESSING

FT size 32768

Total time 0 min, 0 sec

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pu1
 Solvent: DMSO
 Ambient temperature
 User: 1-14-87
 INOVA-500 "bullwinkle"
 PULSE SEQUENCE
 Relax. delay 3.000 sec
 Pulse 54.0 degrees
 Acq. time 0.869 sec
 Width 3718.1 Hz
 436 repetitions
 OBSERVE C13, 125.6638354 MHz
 DECOUPLE H1, 499.7586447 MHz
 Power 34 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 131072
 Total time 11 hr, 58 min, 8 sec

19F OBSERVE
STANDARD PARAMETERS

Pulse Sequence: s2pul
Solvent: DMSO
Ambient temperature
Mercury-300 "mhat"

Relax. delay 4.000 sec
Pulse 20.5 degrees
Acq. time 0.300 sec
Width 100.0 kHz
8 repetitions
OBSERVE F19, 282.3749492 MHz
DATA PROCESSING
Line broadening 0.3 Hz
FT size 65536
Total time 0 min, 02sec