Supporting Information
for
Pd-Catalyzed *N*-Arylation of Heteroarylamines

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General procedures for Pd-catalyzed C-N bond forming reactions between aryl halides and heteroaryl amines (Tables 2 and 3): A re-sealable Schlenk tube was charged with Pd₂(dba)₃, Xantphos, heteroaryl amine (Ar'NH₂, 1.05-1.4 equiv), aryl halide (ArX, 1.0 mmol, 1.0 equiv), inorganic base, and degassed solvent as indicated in the tables. For those cases where water was use, it was added in dropwise while stirring the mixture. The Schlenk tube was capped and carefully subjected to three cycles of evacuation-backfilling with N₂. It was then sealed and immersed into a 100 °C oil bath. After 15-23 h, the mixture was cooled, diluted with THF, filtered, concentrated, and chromatographed on SiO₂ flash column to give the product.

Work Up Method B (for compounds with poor solubility in THF): The reaction mixture was cooled, filtered, and washed with toluene and water (and 1 N HCl for Table 3, entry 5). After drying the crude solid, it was recrystallized from acidic DMAc (with aq HCl) and water to give the product.

2-(3',5'-Dimethylphenylamino)pyridine (Table 2, entry 1): Following the general procedure using 1.05 equiv of 2-aminopyridine gave the title compound as an off-white solid (189 mg, 95%). M.p. 81-82 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.22-8.21 (m, 1 H), 7.51-7.47 (m, 1 H), 6.99-6.90 (m, 4 H), 6.73-6.71 (m, 2 H), 2.33 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 156.5, 148.5, 140.5, 139.0, 137.7, 124.8, 118.4, 114.8, 108.2, 21.5; IR (thin film, cm⁻¹) 3230 (br),

1606, 1589, 1585, 1472, 1464, 1446, 1342, 768. Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13; Found: C, 78.50; H, 7.04; N, 14.13.

2,2'-Dipyridylamine (Table 2, entry 2): Following the general procedure using 1.05 equiv of 2-amino-pyridine gave the commercially available title compound as a white solid (160 mg, 94%).

3-Methyl-2-(2'-tolylamino)pyridine (Table 2, entry 3): Following the general procedure using 1.2 equiv of 2-amino-3-methyl-pyridine gave the title compound as a white solid (189 mg, 95%).

M.p. 69.5-70.5 °C; 1H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, $J = 5.0, 1.4$ Hz, 1 H), 7.89 (d, $J = 8.0$ Hz, 1 H), 7.38 (dt, $J = 7.2, 0.8$ Hz, 1 H), 7.25 (d, $J = 7.5$ Hz, 2 H), 7.02 (td, $J = 4.8$ Hz, 1.0 Hz, 1H), 6.72 (dd, $J = 7.2, 5.0$ Hz, 1 H), 5.94 (br s, 1 H), 2.32 (s, 3 H), 2.26 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 145.7, 139.2, 137.9, 130.5, 128.4, 126.8, 122.9, 121.4, 118.3, 115.1, 18.1, 17.4; IR (thin film, cm^{-1}) 3230 (br), 1599, 1578, 1507, 1490, 1463, 1411, 743. Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13; Found: C, 78.50; H, 7.03; N, 14.00.

2-(3'-Formylphenylamino)pyrimidine (Table 2, entry 4): Following the general procedure using 1.1 equiv of 2-aminopyrimidine gave the title compound as a white solid (180 mg, 90%).

M.p. 159-160 °C; 1H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1 H), 8.48 (d, $J = 4.8$ Hz, 2 H), 8.25 (s, 1 H), 7.88 (dt, $J = 7.0, 1.0$ Hz, 1 H), 7.77 (br s, 1 H), 7.56 (t, $J = 6.8$ Hz, 1 H), 7.50 (t, $J = 7.8$ Hz, 1 H), 6.80 (t, $J = 4.8$ Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.3, 159.9, 158.1, 140.4, 137.2, 129.5, 125.0, 124.0, 119.7, 113.2; IR (thin film, cm^{-1}) 3256 (br), 1709, 1687, 1584, 1545, 1279, 1254, 790. Anal. Calcd. for $C_{11}H_9N_3O$: C, 66.32; H, 4.55; N, 21.09; Found: C, 66.04; H, 4.35; N, 20.92.

2-(2'-Methoxyphenylamino)pyrimidine (Table 2, entry 5): Following the general procedure using 1.1 equiv of 2-aminopyrimidine gave the previously reported title compound as a white

solid (183 mg, 91%).¹ M.p. 56.0-56.7 °C (lit. mp¹ 58.5-59.0 °C); ¹H NMR (400 MHz, CDCl₃) δ 8.52 (dd, *J* = 7.4, 2.2 Hz, 1 H),² 8.44 (d, *J* = 4.8 Hz, 2 H), 7.80 (br s, 1 H), 7.04-6.97 (m, 2 H), 6.91 (dd, *J* = 7.5, 2.0 Hz, 1 H), 6.70 (t, *J* = 4.8 Hz, 1 H), 3.90 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 160.2, 158.0, 148.0, 129.3, 121.9, 121.0, 118.6, 112.4, 110.1, 55.8.

***o*-Tolylaminopyrazine** (Table 2, entry 6): Following the general procedure using 1.1 equiv of aminopyrazine gave the title compound as a white solid (181 mg, 98%). M.p. 93-94 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 1.4 Hz, 2 H), 7.95 (d, *J* = 2.2 Hz, 1 H), 7.49 (d, *J* = 7.8 Hz, 1 H), 7.27 (d, *J* = 7.9 Hz, 1 H), 7.23 (d, *J* = 7.7 Hz, 1 H), 7.13 (td, *J* = 7.4, 1.1 Hz, 1 H), 6.56 (br s, 1 H), 2.30 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 153.1, 142.2, 137.2, 134.7, 132.2, 131.8, 131.3, 127.1, 125.4, 123.5, 18.0; IR (thin film, cm⁻¹) 3238 (br), 1598, 1514, 1493, 1001. Anal. Calcd. for C₁₁H₁₁N₃: C, 71.33; H, 5.99; N, 22.69; Found: C, 71.20; H, 5.84; N, 22.52.

3-(3'-Carbomethoxyphenylamino)-5,6-dimethyl-1,2,4-triazine (Table 2, entry 7): Following the general procedure using 1.1 equiv of 3-amino-5,6-dimethyl-1,2,4-triazine gave the title compound as a light yellow solid (223 mg, 86%). M.p. 184.1-184.6 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (s, 1 H), 8.24 (br s, 1 H), 8.09 (dd, *J* = 8.0, 1.4 Hz, 1 H), 7.72 (d, *J* = 7.7 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 1 H), 3.94 (s, 3 H), 2.60 (s, 3 H), 2.47 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 167.1, 159.5, 159.4, 150.0, 139.5, 131.0, 129.1, 123.6, 123.5, 120.2, 52.2, 21.9, 18.8; IR (thin film, cm⁻¹) 1720, 1619, 1551, 1518, 1275, 1117. Anal. Calcd. for C₁₃H₁₄N₄O₂: C, 60.45; H, 5.46; N, 21.69; Found: C, 60.10; H, 5.19; N, 21.55.

5-(2'-Pyridylamino)-1-ethylpyrazole (Table 2, entry 8): Following the general procedure using 1.4 equiv of 5-amino-1-ethylpyrazole gave the title compound as an off-white solid (172 mg, 91%). M.p. 80.7-82.2 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.08 (dd, *J* = 4.9, 0.9 Hz, 1 H), 7.52-

¹ Takeuchi, H.; Watanabe, K. *J. Phys. Org. Chem.* **1998**, *11*, 478.

7.44 (m, 3 H), 6.74-6.71 (m, 1 H), 6.45 (d, $J = 8.4$ Hz, 1 H), 6.12 (d, $J = 0.9$ Hz, 1 H), 4.07 (q, $J = 7.3$ Hz, 2 H), 1.38 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 157.5, 148.1, 138.9, 138.4, 137.9, 115.4, 107.1, 100.8, 42.8, 15.3; IR (thin film, cm^{-1}) 3218 (br), 1600, 1554, 1483, 1442, 1310, 771. Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_4$: C, 63.81; H, 6.43; N, 29.77; Found: C, 63.64; H, 6.22; N, 29.70.

Ethyl 2-(4'-*t*-butylphenylamino)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (Table 2, entry 9): Following the general procedure using 1.05 equiv of ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate gave the title compound as a viscous light yellow oil (303 mg, 85%). ^1H NMR (400 MHz, CDCl_3) δ 10.12 (br s, 1 H), 7.39-7.35 (m, 2 H), 7.27-7.22 (m, 2 H), 4.32 (q, $J = 7.2$ Hz, 2 H), 2.80-2.77 (m, 2 H), 2.59-2.57 (m, 2 H), 1.85-1.76 (m, 4 H), 1.39 (t, $J = 7.2$ Hz, 3 H), 1.34 (s, 9 H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.9, 158.3, 145.8, 138.7, 132.2, 126.2, 118.5, 117.6, 106.0, 59.7, 34.4, 31.5, 26.9, 24.6, 23.3, 23.0, 14.5; IR (thin film, cm^{-1}) 1655, 1586, 1548, 1258, 1239, 1206, 1037, 822, 781. Anal. Calcd. for $\text{C}_{21}\text{H}_{27}\text{NO}_2\text{S}$: C, 70.55; H, 7.61; N, 3.92; Found: C, 70.39; H, 7.53; N, 3.93.

2-(*N*-Methyl-*N*-3'-pyridylamino)pyridine (Table 2, entry 10): Following the general procedure using 1.05 equiv of 2-methylaminopyridine gave the title compound as a light yellow oil (169 mg, 91%). ^1H NMR (400 MHz, CDCl_3) δ 8.57 (d, $J = 2.6$ Hz, 1 H), 8.40 (dd, $J = 4.7$, 1.4 Hz, 1 H), 8.24-8.22 (m, 1 H), 7.58 (ddd, $J = 8.2$, 2.6, 1.5 Hz, 1 H), 7.38 (ddd, $J = 8.5$, 7.2, 2.0 Hz), 7.30 (dd, $J = 8.2$, 4.7 Hz, 1 H), 6.70-6.67 (m, 1 H), 6.59 (d, $J = 8.5$ Hz, 1 H), 3.48 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 158.3, 148.1, 147.6, 145.8, 143.3, 137.2, 132.7, 124.0, 114.5, 109.2, 38.4; IR (thin film, cm^{-1}) 1597, 1580, 1561, 1483, 1474, 1440, 1416, 1357,

² The chemical shift of this proton is different from reported in reference 1.

1136, 982, 772, 713. Anal. Calcd. for C₁₁H₁₁N₃: C, 71.3; H, 6.0; N, 22.7; Found: C, 70.9; H, 6.1; N, 22.4.

2-(N-Methyl-N-4'-pyridylamino)pyridine (Table 2, entry 11): Following the general procedure using 1.05 equiv of 2-methylaminopyridine gave a crude product after column. It was then partitioned between 10 mL 1 N HCl and 10 mL CH₂Cl₂. The aqueous layer was washed with 2 mL CH₂Cl₂, basified with 2 mL 10 N NaOH, extracted with CH₂Cl₂ (15 + 10 mL). The last two CH₂Cl₂ extracts were dried with MgSO₄ and concentrated to give the pure title compound as a yellow oil (153 mg, 83%). ¹H NMR (400 MHz, CDCl₃) δ 8.38 (ddd, *J* = 4.8, 2.0, 0.7 Hz, 1 H), 8.35 (dd, *J* = 4.8, 1.6 Hz, 2 H), 7.57 (ddd, *J* = 9.2, 7.3, 2.0 Hz, 1 H), 7.12 (dt, *J* = 8.4, 0.9 Hz, 1 H), 6.97 (dd, *J* = 4.8, 1.6 Hz, 2 H), 6.93 (ddd, *J* = 7.2, 5.0, 0.9 Hz, 1 H), 3.49 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 157.4, 152.8, 150.4, 148.9, 137.6, 118.2, 115.3, 113.1, 37.1; IR (thin film, cm⁻¹) 1602, 1582, 1568, 1473, 1359, 990, 781.

2-(2'-Pyridylamino)thiazole (Table 3, entry 1): Following the general procedure using 1.2 equiv of 2-aminothiazole gave a crude solid contaminated with a Xantphos-related impurity. It was triturated in 6 mL toluene-hexanes(1:1) at 60 °C for 1 h, cooled, filtered, washed with 0.5 mL toluene-hexanes (1:1), and dried to give the previously reported pure title compound as a white solid (133 mg, 75%).³

2-(2'-Pyrimidylamino)thiazole (Table 3, entry 2): Following the general procedure using 1.05 equiv of 2-aminothiadiazole gave the previously reported pure title compound as a white solid (171 mg, 96%).³

³ Kaplan, G. M.; Frolov, A. N.; El'tsov, A. V. *J. Org. Chem. USSR (Engl. Transl.)* **1991**, 27, 177.

2-(4'-Nitrophenylamino)thiazole (Table 3, entry 3): Following the general procedure⁴ using 1.05 equiv of 2-aminothiadiazole gave the previously reported title compound as a yellow solid (201 mg, 91%).⁵

2-Pyrazinylamino-4-methylthiazole (Table 3, entry 4): Following the general procedure using 1.2 equiv of 2-amino-4-methylthiazole gave a crude solid contaminated with a Xantphos-related impurity. It was sonicated in 3 mL toluene-hexanes (1:1), filtered, washed with 1 mL toluene-hexanes (1:1), and dried to give the pure title compound as a white solid (167 mg, 87%). M.p. 193.5-194.2 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 11.56 (s, 1 H), 8.40 (s, 1 H), 8.23 (d, *J* = 2.8 Hz, 1 H), 8.04 (d, *J* = 2.8 Hz, 1 H), 6.59 (s, 1 H), 2.22 (s, 3 H); ¹³C NMR (100 MHz, DMSO-d₆) δ 158.8, 149.2, 147.1, 141.0, 135.6, 135.4, 106.5; IR (thin film, cm⁻¹) 3217, 3057, 1601, 1523, 1392, 1318, 1008, 825. Anal. Calcd. for C₈H₈N₄S: C, 49.98; H, 4.19; N, 29.14; Found: C, 49.85; H, 3.86; N, 29.02.

Ethyl 2-(2'-quinolinylamino)-4-phenylthiazole-5-carboxylate (Table 3, entry 5): Following the general procedure using 1.1 equiv of ethyl 2-amino-4-phenylthiazole-5-carboxylate on a 0.5 mmol scale gave the title compound as a light yellow solid (184 mg, 98%). M.p. 200.8-201.4 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.29 (br s, 1 H), 8.08 (d, *J* = 8.3 Hz, 1 H), 7.88 (d, *J* = 1.4 Hz, 1 H), 7.86 (s, 1 H), 7.70-7.65 (m, 2 H), 7.62 (d, *J* = 8.8 Hz, 1 H), 7.42-7.32 (m, 4 H), 6.05 (d, *J* = 8.8 Hz, 1 H), 4.36 (q, *J* = 7.1 Hz, 2 H), 1.37 (t, *J* = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, DMSO-d₆) δ 162.4, 161.1, 156.6, 150.3, 146.1, 138.9, 135.1, 130.7, 130.2, 129.2, 128.4, 128.0, 126.5, 124.9, 113.9, 113.3, 60.9, 14.6; IR (thin film, cm⁻¹) 3196, 1710, 1685, 1590, 1545, 1412, 1331,

⁴ However, instead of diluted with THF, the cooled reaction mixture was filtered and washed with toluene and water before it was subjected to the flash column.

⁵ Nayak, A.; Misra, S. B. *J. Ind. Chem. Soc.* **1986**, 63, 986.

1286, 1141, 1077, 820, 755, 697. Anal. Calcd. for C₂₁H₁₇N₃O₂S: C, 67.18; H, 4.56; N, 11.19; Found: C, 67.19; H, 4.68; N, 11.06.

2-(2'-Pyridylamino)-1,3,4-thiadiazole (Table 3, entry 6): Following the general procedure using 1.4 equiv of 2-amino-1,3,4-thiadiazole gave a crude solid contaminated with a Xantphos-related impurity. It was triturated in 6 mL toluene at 60 °C for 1 h, cooled, filtered, washed with 1.5 mL toluene, and dried to give the pure title compound as a white solid (114 mg, 64%). M.p. 256-257 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 11.61 (br s, 1 H), 8.94 (s, 1 H), 8.28-8.27 (m, 1 H), 7.74-7.69 (m, 1 H), 7.07 (d, *J* = 8.4 Hz, 1 H), 6.94 (dd, *J* = 7.2, 5.5 Hz, 1 H); ¹³C NMR (100 MHz, DMSO-d₆) δ 160.4, 151.4, 147.1, 147.0, 138.9, 117.2, 111.7; IR (thin film, cm⁻¹) 1635, 1554, 765. Anal. Calcd. for C₇H₆N₄S: C, 47.18; H, 3.39; N, 31.44; Found: C, 47.00; H, 3.25; N, 31.36.

2-(2'-Pyridylamino)-benzothiazole (Table 3, entry 7): Following the general procedure using 1.2 equiv of 2-aminobenzothiazole gave a reaction mixture that was purified as following. The mixture was diluted with THF (44 mL), filtered, and concentrated to give a crude solid. It was then stirred in 6 mL toluene, filtered, stirred in 2.5 mL toluene for overnight, filtered, stirred in 4.5 mL toluene at 50 °C for 6 h and then room temperature for overnight, filtered, washed with 1.5 mL toluene, and dried to give the previously reported pure title compound as a white solid (201 mg, 89%).⁶

2-(3',5'-Dimethylphenylamino)benzothiazole (Table 3, entry 8): Following the general procedure⁷ using 1.2 equiv of 2-aminobenzothiazole gave the title compound as a white solid (214 mg, 84%). M.p. 107.4-109.0 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.49 (td, *J* = 7.9, 1.2 Hz, 1 H), 7.35 (d, *J* = 7.7 Hz, 1 H), 7.13 (td, *J* = 7.6, 1.0 Hz, 1 H), 6.95

⁶ Harris, R. L. N. *Aust. J. Chem.* **1972**, 25, 993.

(br s, 1 H), 6.83 (s, 1 H), 6.68 (s, 2 H), 2.24 (s, 6 H); ^{13}C NMR (100 MHz, CDCl_3) δ 139.7, 139.3, 137.4, 134.3, 131.6, 128.7, 125.0, 124.1, 118.0, 115.3, 110.2, 21.3; IR (thin film, cm^{-1}) 3185, 2234, 1601, 1577, 1578, 1448, 1396, 1290, 846, 757, 684. Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{S}$: C, 70.83; H, 5.55; N, 11.01; Found: C, 70.69; H, 5.44; N, 10.99.

2-(3',5'-Dimethylphenylamino)-1-methylbenzimidazole (Table 3, entry 9): Following the general procedure using 1.2 equiv of 2-amino-1-methylbenzimidazole gave the title compound as a white solid (185 mg, 74%). M.p. 213-214 $^{\circ}\text{C}$; ^1H NMR (400 MHz, DMSO-d_6) δ 7.8.67 (s, 1H), 7.44 (s, 2 H), 7.34 (d, $J = 4.6$ Hz, 1 H), 7.25-7.23 (m, 1 H), 7.01 (t, $J = 3.8$ Hz, 2 H), 6.56 (s, 1 H), 3.64 (s, 3 H), 2.23 (s, 6 H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.0, 142.3, 141.4, 138.0, 134.8, 123.2, 121.2, 120.1, 116.6, 116.1, 108.5, 29.4, 21.8; IR (thin film, cm^{-1}) 3213, 1620, 1573, 1525, 1370, 1237, 845, 740. Anal. Calcd. for $\text{C}_{16}\text{H}_{17}\text{N}_3$: C, 76.46; H, 6.82; N, 16.72; Found: C, 76.36; H, 6.62; N, 16.68.

⁷ After diluting the cooled reaction mixture, 0.1 mL conc. HCl was added before filtration.