

Supporting Information

A Mild and Efficient Copper-catalyzed Amination of Aryl Bromides with Primary Alkyl Amines

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General considerations:

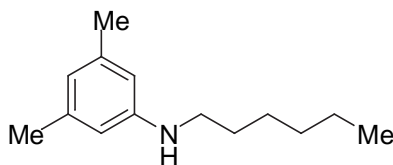
Copper(I) iodide (98%, fine powder) was purchased from Strem Chemical. Anhydrous potassium phosphate free flowing was purchased from Fluka. Anhydrous DMF was purchased from Aldrich (Sure-seal® bottle). All aryl halides and amines were used as received. *N,N*-Diethylsalicylamide was purchased from Aldrich and used as received (it has been discontinued in the 2002 Aldrich Catalog). *N,N*-Dialkylsalicylamides were prepared according to the literature procedures.¹ Silica gel (230-400 mesh) and ethyl acetate were purchased from Merck. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA 30091. ¹H NMR and ¹³C NMR were recorded on a Varian 300 MHz instrument with chemical shifts reported relative to residual deuterated solvent peaks. Gas chromatographic analyses were performed on a Hewlett Packard 6890 instrument with FID detector and a Hewlett Packard 10 m × 0.2 mm i.d. HP-1 capillary column. Mass spectra (GC-MS) were recorded on a Hewlett Packard model GCD. HPLC were conducted on a Hewlett Packard Series 1100 system using Daicel OD column (0.46 cm × 25 cm). All yields reported in the publication represent an average of at least two independent runs. Characterization data for previously unknown compounds were determined from a single run with isolated yields. Compounds described in the literature were characterized by comparing their ¹H, ¹³C NMR or MS to the previously reported data.

General Procedure A: Cu-Catalyzed Amination of Functionalized Aryl Bromides

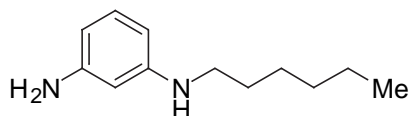
CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (39 mg, 0.20 mmol), aryl bromide (if solid; 1.0 mmol), and K₃PO₄ (425 mg, 2.0 mmol) were added to a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (if liquid; 1.0 mmol), amine (1.5 mmol), and DMF (0.5 mL) were added by syringe at room temperature. The reaction mixture was stirred at 90 °C for 18-22 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL, GC standard) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted with ethyl acetate (4 × 10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the residue was purified by flash column chromatography on silica gel to afford the desired product.

General Procedure B: Solvent-free Cu-Catalyzed Amination of Aryl Bromides

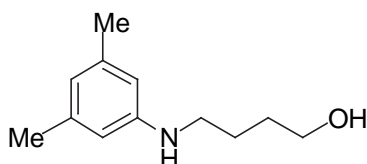
CuI (10 mg, 0.05 mmol), *N,N*-diethylsalicylamide (10 mg, 0.05 mmol), aryl bromide (if solid; 1.0 mmol), and K₃PO₄ (425 mg, 2.0 mmol) were added to a screw-capped test tube with a Teflon-lined septum. The tube was then evacuated and backfilled with argon (3 cycles). Aryl bromide (if liquid; 1.0 mmol) and amine (1.5 mmol) were added by syringe at room temperature. The reaction mixture was stirred at 100 °C for 22 h. The reaction mixture was allowed to reach room temperature. Ethyl acetate (~2 mL), water (~10 mL), ammonium hydroxide (~0.5 mL) and dodecane (227 µL, GC standard) were added. The organic phase was analyzed by GC or GC-MS. The reaction mixture was further extracted with ethyl acetate (4 × 10 mL). The combined organic phases were washed with brine and dried over Na₂SO₄. Solvent was removed in *vacuo* and the residue was purified by flash column chromatography on silica gel to afford the desired product.

Table 1. Copper-Catalyzed Amination of Functionalized Aryl Bromides**3-5-Dimethyl-N-hexylaniline² (Table 1, entry 1).**

Using general procedure A, 5-bromo-*m*-xylene (136 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 90 °C, 18 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as the eluent to afford the title product as a colorless liquid (186 mg, 91% yield). R_f = 0.4 (hexane/ethyl acetate = 20:1). ^1H NMR (300 MHz, CDCl_3) δ 6.35 (s, 1 H), 6.24 (s, 2 H), 3.52 (brs, 3 H), 3.05 (t, 2 H, J = 6.9 Hz), 1.51-1.64 (m, 2 H), 1.27-1.42 (m, 6 H), 0.89 (t, 3 H, J = 6.6 Hz). MS (EI) m/z (relative intensity) 205 (M^+ , 100).

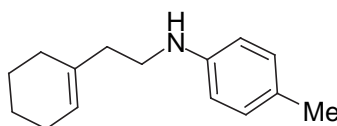
**3-Amino-N-hexylaniline (Table 1, entry 2).**

Using general procedure A, 3-bromoaniline (172 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 90 °C, 18 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (2:1) as eluent to afford the title product as a colorless oil (154 mg, 80% yield). R_f = 0.4 (hexane/ethyl acetate = 2:1). ^1H NMR (300 MHz, CDCl_3) δ 6.92 (t, 1 H, J = 8.1 Hz), 6.04 (d, 1 H, J = 2.4 Hz), 6.02 (d, 1 H, J = 1.8 Hz), 5.93 (t, 1 H, J = 2.1 Hz), 3.52 (brs, 3 H), 3.05 (t, 2 H, J = 6.9 Hz), 1.51-1.64 (m, 2 H), 1.27-1.42 (m, 6 H), 0.89 (t, 3 H, J = 6.6 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 149.9, 147.6, 130.2, 104.8, 104.2, 99.5, 44.3, 32.1, 30.0, 27.3, 14.5. IR (neat, cm^{-1}) 3357 (broad), 3213, 2954, 2927, 2856. MS (EI) m/z (relative intensity) 192 (M^+ , 30), 121 (100). Anal. Calcd. for $\text{C}_{12}\text{H}_{20}\text{N}_2$; C: 74.95, H: 10.48; Found C: 74.65, H: 10.53.



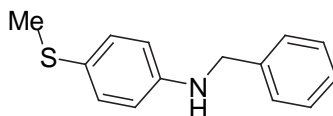
4-(N-(3,5-Dimethylphenyl))aminobutanol (Table 1, entry 3).

Using general procedure A, 5-bromo-*m*-xylene (136 μ L, 1.0 mmol), 4-aminobutanol (138 μ L, 1.5 mmol), 90 °C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (2:1) as the eluent to afford the title product as a colorless oil (174 mg, 90% yield). R_f = 0.4 (hexane/ethyl acetate = 1:1). ^1H NMR (300 MHz, CDCl_3) δ 6.35 (s, 1 H), 6.24 (s, 2 H), 3.67 (t, 2 H, J = 6.3 Hz), 3.12 (t, 2 H, J = 6.3 Hz), 2.23 (s, 6 H), 1.65-1.70 (m, 4 H). ^{13}C NMR (75 MHz, CDCl_3) δ 148.5, 139.1, 119.7, 111.2, 63.0, 44.3, 30.8, 26.6, 21.9. IR (neat, cm^{-1}) 3369 (broad), 3022, 2937, 2919, 2863. MS (EI) m/z (relative intensity) 193 (M^+ , 20), 174 (100), 134 (80). Anal. Cald. for $\text{C}_{12}\text{H}_{19}\text{NO}$; Cald. C: 74.57, H: 9.91; Found C: 74.21, H: 9.87.



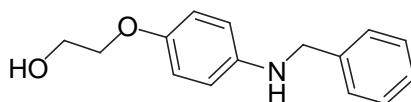
N-[2-(1-Cyclohexenyl)ethyl]-4-methylaniline³ (Table 1, entry 4).

Using general procedure A, 4-bromotoluene (171 mg, 1.0 mmol), 2-(1-cyclohexenyl)ethylamine (209 μ L, 1.5 mmol), 90 °C, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as the eluent to afford the titled product as a colorless liquid (205 mg, 95% yield). R_f = 0.6 (hexane/ethyl acetate = 10:1). ^1H NMR (300 MHz, CDCl_3) δ 6.99 (d, 2 H, J = 8.1 Hz), 6.56 (d, 2 H, J = 8.3 Hz), 5.52 (m, 1 H), 3.59 (brs, 1 H), 3.14 (t, 2 H, J = 6.9 Hz), 2.25 (t, 2 H, J = 6.8 Hz), 2.24 (s, 3 H), 2.02 (m, 2 H), 1.95 (m, 2 H), 1.62 (m, 2 H), 1.58 (m, 2 H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.1, 143.9, 129.7, 126.4, 123.5, 113.1, 41.8, 37.6, 27.8, 25.2, 22.8, 22.4, 20.4.



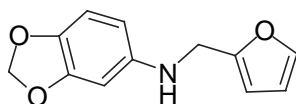
4-(*N*-Benzyl)aminothioanisole (Table 1, entry 5).

Using general procedure A, 4-bromothioanisole (203 mg, 1.0 mmol), benzylamine (164 μ L, 1.5 mmol), 90 $^{\circ}$ C, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (15:1) as the eluent to afford the title product as a white solid (201 mg, 88% yield). R_f = 0.4 (hexane/ethyl acetate = 10:1). Melting point: 63-65 $^{\circ}$ C. ^1H NMR (300 MHz, CDCl_3) δ 7.26-7.37 (m, 5 H), 7.22 (d, 2 H, J = 8.4 Hz), 6.59 (d, 2 H, J = 8.7 Hz), 4.33 (d, 2 H, J = 5.4 Hz), 4.09 (brs, 1 H), 2.42 (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 147.1, 139.3, 131.6, 128.9, 127.6, 127.5, 124.6, 113.7, 48.6, 19.6. IR (neat, cm^{-1}) 3213, 2954, 2927, 2856. MS (EI) m/z (relative intensity) 229 (M^+ , 100), 138 (85), 91 (80). Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{NS}$; C: 73.32, H: 6.59; Found C: 73.09, H: 6.67.



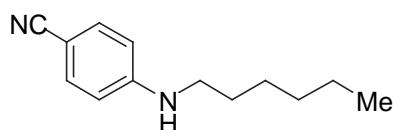
2-(4-(*N*-Benzyl)amino)phenoxy)ethanol (Table 1, entry 6).

Using general procedure A, 2-(4-bromophenoxy)ethanol (217 mg, 1.0 mmol), benzylamine (164 μ L, 1.5 mmol), 90 $^{\circ}$ C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (2:1) as the eluent to afford the title product as a white solid (201 mg, 84% yield). R_f = 0.5 (hexane/ethyl acetate = 1:1). Melting point: 71-72 $^{\circ}$ C. ^1H NMR (300 MHz, CDCl_3) δ 7.21-7.33 (m, 5 H), 6.76 (d, 2 H, J = 8.7 Hz), 6.56 (2 H, J = 9.0 Hz), 4.26 (s, 2 H), 3.87-3.99 (m/brs, 5 H), 2.23 (brs, 1 H). ^{13}C NMR (75 MHz, CDCl_3) δ 151.2, 143.0, 139.7, 128.8, 127.7, 127.4, 116.1, 114.3, 70.3, 62.0, 49.5. IR (neat, cm^{-1}) 3050, 3006, 2989. MS (EI) m/z (relative intensity) 243 (M^+ , 40), 91 (100). HRMS (EI) Calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_2$, 243.1254; Found 243.1262.

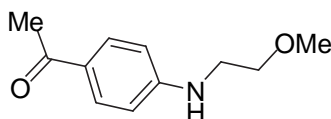


3,4-(Methylenedioxy)-*N*-furfurylaniline (Table 1, entry 7).

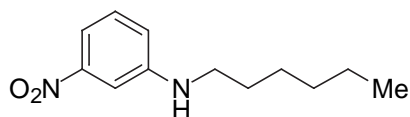
Using general procedure A, 4-bromo-1,2-(methylenedioxy)benzene (120 μ L, 1.0 mmol), furfurylamine (132 μ L, 1.5 mmol), 90 $^{\circ}$ C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (8:1) as the eluent to afford the title product as a colorless oil (187 mg, 87% yield). R_f = 0.5 (hexane/ethyl acetate = 5:1). ^1H NMR (300 MHz, CDCl_3) δ 7.36-7.37 (m, 1 H), 6.66 (d, 1 H, J = 8.4 Hz), 6.30-6.33 (m, 2 H), 6.21-6.23 (m, 1 H), 6.11 (dd, 2 H, J = 2.4 Hz, 8.4 Hz), 5.85 (s, 2 H), 4.25 (s, 2 H), 3.83 (brs, 1 H). ^{13}C NMR (75 MHz, CDCl_3) δ 152.8, 148.4, 143.4, 142.1, 140.2, 110.5, 108.8, 107.3, 105.1, 100.9, 96.7, 42.8. IR (neat, cm^{-1}) 3233, 2984, 2947, 2866. MS (EI) m/z (relative intensity) 217 (M^+ , 55), 136 (50), 81 (100). Anal. Cald. for $\text{C}_{12}\text{H}_{11}\text{NO}_3$; C: 66.35, H: 5.10; Found C: 66.50, H: 5.12.

**4-(*N*-Hexyl)aminobenzonitrile (Table 1, entry 8).**

Using general procedure A, 4-bromobenzonitrile (182 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 90 $^{\circ}$ C, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (6:1) as the eluent to afford the title product as a light yellow solid (145 mg, 72% yield). R_f = 0.6 (hexane/ethyl acetate = 3:1). Melting point: 32-34 $^{\circ}$ C. ^1H NMR (300 MHz, CDCl_3) δ 7.38 (d, 2 H, J = 8.7 Hz), 6.52 (d, 2 H, J = 9.0 Hz), 4.20 (brs, 1 H), 3.12 (q, 2 H, J = 5.4 Hz), 1.62 (quint, 2 H, J = 7.2 Hz), 1.31-1.41 (m, 6 H), 0.90 (t, 3 H, J = 6.3 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 151.6, 133.8, 120.8, 112.2, 98.4, 43.6, 31.9, 29.5, 27.1, 23.0, 14.5. IR (neat, cm^{-1}) 3213, 2954, 2927, 2856. MS (EI) m/z (relative intensity) 202 (M^+ , 15), 131 (100). Anal. Cald. for $\text{C}_{13}\text{H}_{18}\text{N}_2$; C: 77.18, H: 8.97; Found C: 77.24, H: 9.11.

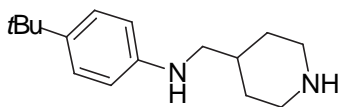
***N*-(2-Methoxyethyl)-4-acetylaniline (Table 1, entry 9).**

Using general procedure A, 4-bromoacetophenone (199 mg, 1.0 mmol), 2-methoxyethylamine (130 μ L, 1.5 mmol), 90 °C, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) as the eluent to afford the title product as a light yellow solid (148 mg, 77% yield). R_f = 0.6 (hexane/ethyl acetate = 2:3). Melting point: 30-32 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.82 (d, 2 H, J = 8.7 Hz), 6.58 (d, 2 H, J = 8.7 Hz), 4.63 (brs, 1 H), 3.61 (t, 2 H, J = 5.1 Hz), 3.39 (s, 3 H), 3.34 (t, 2 H, J = 5.1 Hz), 2.49 (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 160.3, 151.6, 133.8, 120.8, 112.2, 43.6, 31.9, 29.5, 27.1. IR (neat, cm^{-1}) 3213, 2954, 2927, 2856, 1703. MS (EI) m/z (relative intensity) 193 (M^+ , 15), 178 (100). Anal. Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}_2$; C: 68.37, H: 7.82, Found C: 68.08, H: 7.83.



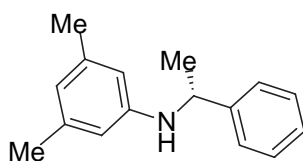
3-Nitro-N-hexylaniline (Table 1, entry 10).

Using general procedure A, 3-bromonitrobenzene (202 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 90 °C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (6:1) as the eluent to afford the title product as light yellow solid (174 mg, 78% yield). R_f = 0.5 (hexane/ethyl acetate = 5:1). Melting point: 43-45 °C. ^1H NMR (300 MHz, CDCl_3) δ 7.47 (ddd, 1 H, J = 1.2 Hz, 2.4 Hz, 8.4 Hz), 7.34 (t, 1 H, J = 2.1 Hz), 7.23 (t, 1 H, J = 8.1 Hz), 6.82 (ddd, 1 H, J = 0.6 Hz, 2.4 Hz, 8.1 Hz), 3.97 (brt, 1 H, J = 2.0 Hz), 3.14 (dt, 2 H, J = 1.5 Hz, 5.7 Hz), 1.58-1.66 (m, 2 H), 1.29-1.43 (m, 6 H), 0.91 (t, 3 H, J = 7.2 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 149.4, 149.3, 129.8, 118.8, 111.8, 106.2, 44.1, 31.9, 29.6, 27.1, 23.0, 14.5. IR (neat, cm^{-1}) 3413, 2956, 2929, 2858. MS (EI) m/z (relative intensity) 222 (M^+ , 10), 151 (100). Anal. Calcd. for $\text{C}_{12}\text{H}_{19}\text{N}_2\text{O}_2$; C: 64.84, H: 8.16; Found C: 64.89, H: 8.14.



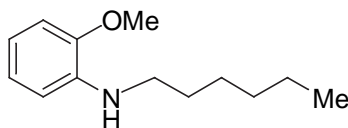
4-[N-(4-*tert*-Butylphenyl)aminomethyl]piperidine (Table 1, entry 11).

Using general procedure A, 4-*tert*-butylbromobenzene (173 μ L, 1.0 mmol), 4-(aminomethyl)piperidine (173 mg, 1.5 mmol), 90 $^{\circ}$ C, 22 h. The crude product was purified by column chromatography on silica gel using CH_2Cl_2 (saturated with NH_3)/MeOH = 10:1 as eluent afforded the title product as a white solid (196 mg, 80% yield). R_f = 0.3 (CH_2Cl_2 (saturated with NH_3)/MeOH = 10:1). Melting point; 112-114 $^{\circ}$ C. ^1H NMR (300 MHz, CDCl_3) δ 7.20 (d, 2 H, J = 8.7 Hz), 6.55 (d, 2 H, J = 8.7 Hz), 3.66 (brs, 1 H), 2.98-3.12 (m, 4 H), 2.60 (t, 2 H, J = 12.0 Hz), 1.91 (brs, 1 H), 1.68-1.81 (m, 2 H), 1.29 (s, 9 H), 1.05-1.15 (m, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.2, 139.9, 126.2, 112.5, 50.9, 46.8, 36.5, 34.2, 31.9, 21.5. IR (neat, cm^{-1}) 3357 (broad), 3203, 2959, 2937, 2854. MS (EI) m/z (relative intensity) 246 (M^+ , 100). Anal. Calcd. for $\text{C}_{16}\text{H}_{26}\text{N}_2$; C: 77.99, H: 10.64; Found C: 77.59, H: 10.60.

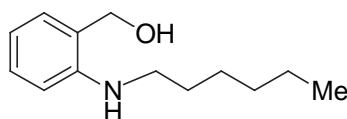


(*R*)-Methyl-*N*-(3,5-dimethylphenyl)benzylamine (Table 1, entry 12).

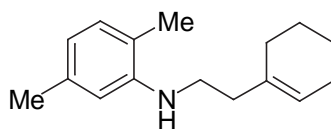
Using general procedure A, 5-bromo-*m*-xylene (136 μ L, 1.0 mmol), (*R*)- α -methylbenzylamine (193 μ L, 1.5 mmol, 98% ee), 100 $^{\circ}$ C, 30 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as the eluent to afford the title product as a colorless liquid (160 mg, 71% yield, 98% ee). R_f = 0.4 (hexane/ethyl acetate = 20:1). HPLC conditions: Daicel OD column (0.46 cm \times 25 cm), 0.7 mL/min, UV lamp (254 nm), hexane/2-propanol (9:1), T_s = 6.41 min; T_R = 7.80 min. ^1H NMR (300 MHz, CDCl_3) δ 7.17-7.36 (m, 5 H), 6.29 (s, 1 H), 6.14 (s, 2 H), 4.46 (q, 1 H, J = 6.9 Hz), 3.89 (brs, 1 H), 2.15 (s, 6 H), 1.48 (d, 3 H, J = 6.6 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 147.5, 145.6, 138.9, 128.8, 126.9, 126.0, 119.5, 111.4, 53.6, 25.4, 21.9. IR (neat, cm^{-1}) 3406, 3060, 3025, 2966, 2919, 2865. MS (EI) m/z (relative intensity) 225 (M^+ , 50), 210 (100), 121 (90). Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{N}$; C: 85.28, H: 8.50; Found C: 85.41, H: 8.63.

Table 2. Copper-catalyzed Amination of *o*-Substituted and Heterocyclic Aryl Bromides.**2-Methoxy-N-hexylaniline⁴ (Table 2, entry 1).**

Using general procedure A, 2-bromoanisole (125 μ L, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 100 $^{\circ}$ C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as the eluent to afford the title product as a colorless liquid (184 mg, 89% yield). R_f = 0.5 (hexane/ethyl acetate = 15:1). ^1H NMR (300 MHz, CDCl_3) δ 7.16-7.22 (m, 1 H), 7.01 (dd, 1 H, J = 1.8, 7.2 Hz), 6.59-6.65 (m, 2 H), 4.78 (brs, 1 H), 3.11 (t, 2 H, J = 7.2 Hz), 1.65 (quint, 2 H, J = 7.5 Hz), 1.28-1.44 (m, 6 H), 0.90 (t, 3 H, J = 6.9 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 148.0, 129.9, 129.3, 124.3, 116.3, 110.8, 53.2, 43.9, 32.1, 29.8, 27.3, 23.1, 14.5.

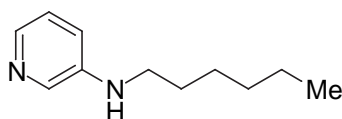
**2-(N-Hexylamino)benzylalcohol (Table 2, entry 2).**

Using general procedure A, 2-bromobenzylalcohol (187 mg, 1.0 mmol), *n*-hexylamine (198 μ L, 1.5 mmol), 90 $^{\circ}$ C, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (6:1) as eluent to afford the title product as a colorless liquid (168 mg, 81% yield). R_f = 0.7 (hexane/ethyl acetate = 2:1). ^1H NMR (300 MHz, CDCl_3) δ 7.16-7.22 (m, 1 H), 7.01 (dd, 1 H, J = 1.8, 7.2 Hz), 6.59-6.65 (m, 2 H), 4.79 (brs, 1 H), 4.69 (s, 2 H), 3.11 (t, 2 H, J = 7.2 Hz), 1.65 (quint, 2 H, J = 7.5 Hz), 1.28-1.44 (m, 6 H), 0.90 (t, 3 H, J = 6.9 Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 148.0, 129.9, 129.3, 124.3, 116.3, 110.8, 65.2, 43.9, 32.1, 29.8, 27.3, 23.1, 14.5. IR (neat, cm^{-1}) 3390 (broad), 2954, 2927, 2858. MS (EI) m/z (relative intensity) 207 (M^+ , 20), 136 (25), 118 (100). Anal. Cald. for $\text{C}_{13}\text{H}_{21}\text{NO}$; C: 75.32, H: 10.21; Found C: 75.60, H: 10.25.



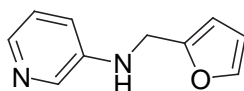
2-(N-2-(1-Cyclohexenyl)ethyl)amino-*para*-xylene (Table 2, entry 3)

Using general procedure A, 2-bromo-*p*-xylene (138 μL , 1.0 mmol), 2-(1-cyclohexenyl)ethylamine (209 μL , 1.5 mmol), 100 $^{\circ}\text{C}$, 24 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (30:1) as the eluent to afford the title product as a colorless oil (180 mg, 79% yield). R_f = 0.5 (hexane/ethyl acetate = 20:1). ^1H NMR (300 MHz, CDCl_3) δ 6.90 (d, 1 H, J = 7.2 Hz), 6.44 (d, 1 H, J = 7.5 Hz), 6.42 (s, 1 H), 5.54-5.55 (m, 1 H), 3.50 (brs, 1 H), 3.16 (t, 2 H, J = 6.6 Hz), 2.31 (t, 2 H, J = 7.8 Hz), 2.29 (s, 3 H), 2.04 (s, 3 H), 2.01-2.02 (m, 2 H), 1.91-1.98 (m, 2 H), 1.54-1.62 (m, 4 H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.4, 136.9, 135.3, 129.9, 124.1, 119.1, 117.4, 110.9, 99.9, 41.4, 38.0, 28.0, 25.8, 23.3, 22.8, 22.0, 17.3. IR (neat, cm^{-1}) 3413, 3016, 2923, 2856, 2836. MS (EI) m/z (relative intensity) 229 (M^+ , 20), 134 (100). Anal. Calcd. for $\text{C}_{16}\text{H}_{23}\text{N}$; C: 83.79, H: 10.11, Found C: 83.82, H: 10.29.



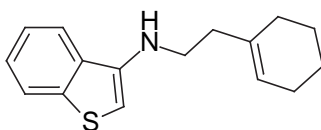
N-Hexyl-3-aminopyridine⁵ (Table 2, entry 4).

Using general procedure A, 3-bromopyridine (96 μL , 1.0 mmol), *n*-hexylamine (198 μL , 1.5 mmol), 90 $^{\circ}\text{C}$, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) as the eluent to afford the title product as a light brown solid (162 mg, 91% yield). R_f = 0.2 (hexane/ethyl acetate = 1:1). Melting Point: 72-74 $^{\circ}\text{C}$. ^1H NMR (300 MHz, CDCl_3) δ 8.19 (d, 1 H, J = 2.7 Hz), 8.01 (dd, 1 H, J = 1.5 Hz, 4.8 Hz), 7.09 (dd, 1 H, J = 4.8 Hz, 8.4 Hz), 6.92-6.96 (m, 1 H), 4.13 (brs, 1 H), 3.11 (t, 2 H, J = 7.2 Hz), 1.65-1.69 (m, 2 H), 1.28-1.44 (m, 6 H), 0.90 (t, 3 H, J = 6.9 Hz). MS (EI) m/z (relative intensity) 178 (M^+ , 100).



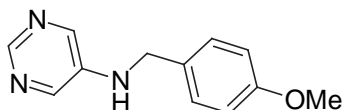
3-N-(furfuryl)aminopyridine (Table 2, entry 5).

Using general procedure A, 3-bromopyridine (96 μL , 1.0 mmol), furfurylamine (133 μL , 1.5 mmol), 90 $^{\circ}\text{C}$, 20 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (1:1) as the eluent to afford the title product as a yellow liquid (158 mg, 91% yield). R_f = 0.2 (hexane/ethyl acetate = 1:1). ^1H NMR (300 MHz, CDCl_3) δ 8.09 (d, 1 H, J = 2.7 Hz), 8.00 (dd, 1 H, J = 1.5 Hz, 4.8 Hz), 7.37 (dd, 1 H, J = 0.6 Hz, 1.8 Hz), 7.09 (dd, 1 H, J = 4.8 Hz, 8.4 Hz), 6.92-6.96 (m, 1 H), 6.32-6.34 (m, 1 H), 6.24 (d, 1 H, J = 3.3 Hz), 4.34 (d, 2 H, J = 5.7 Hz), 4.13 (brs, 1 H). ^{13}C NMR (75 MHz, CDCl_3) δ 147.5, 145.6, 138.9, 128.8, 126.9, 126.0, 122.4, 119.5, 111.4, 53.6, 25.4, 21.9. IR (neat, cm^{-1}) 3403, 3080, 3020, 2960, 2909, 2865. MS (EI) m/z (relative intensity) 174 (M^+ , 30), 96 (100). Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}$; C: 68.95, H: 5.79; Found C: 68.70, H: 5.88.



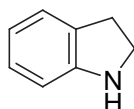
3-(*N*-(1-Cyclohexenyl)ethyl)aminothianaphthlene (Table 2, entry 6).

Using general procedure A, 3-bromothianaphthlene (131 μL , 1.0 mmol), 2-(1-cyclohexenyl)ethylamine (209 μL , 1.5 mmol), 90 $^{\circ}\text{C}$, 22 h. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (20:1) as the eluent to afford the title product as a colorless liquid (211 mg, 82% yield). R_f = 0.4 (hexane/ethyl acetate = 20:1). ^1H NMR (300 MHz, CDCl_3) δ 7.74-7.77 (m, 1 H), 7.48-7.51 (m, 1 H), 7.30-7.33 (m, 2 H), 6.02 (s, 1 H), 5.58 (s, 1 H), 3.88 (brs, 1 H), 3.26 (t, 2 H, J = 6.6 Hz), 2.37 (t, 2 H, J = 6.6 Hz), 1.97-2.05 (m, 4 H), 1.55-1.66 (m, 4 H). ^{13}C NMR (75 MHz, CDCl_3) δ 141.7, 139.3, 135.1, 124.8, 123.9, 123.6, 123.4, 119.5, 114.5, 94.8, 43.4, 37.9, 28.3, 25.7, 23.3, 22.8. IR (neat, cm^{-1}) 3413, 3016, 2923, 2856, 2836. MS (EI) m/z (relative intensity) 257 (M^+ , 20), 162 (100). Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NS}$; C: 74.66, H: 7.44, Found C: 74.57, H: 7.38.



5-(*N*-(4-Methoxybenzyl))aminopyrimidine (Table 2, entry 7).

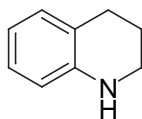
Using general procedure A, 5-bromopyrimidine (159 mg, 1.0 mmol), 4-methoxybenzylamine (196 μ L, 1.5 mmol), 90 °C, 22 h. The crude product was purified by column chromatography on silica gel using dichloromethane (saturated with ammonia)/ethyl acetate (1:1) as the eluent to afford the title product as a white solid (183 mg, 85% yield). R_f = 0.2 (dichloromethane(saturated with ammonia)/ethyl acetate = 1:1). Melting point: 155-157 °C. ^1H NMR (300 MHz, CDCl_3) δ 8.55 (s, 1 H), 8.09 (s, 2 H), 7.25 (d, 2 H, J = 8.1 Hz), 6.87 (d, 2 H, J = 8.7 Hz), 4.26 (s, 3 H), 3.79 (s, 3 H). ^{13}C NMR (75 MHz, CDCl_3) δ 159.3, 148.7, 141.6, 141.0, 129.6, 129.0, 114.8, 55.7, 47.3. IR (neat, cm^{-1}) 3113, 2924, 2920, 2806. MS (EI) m/z (relative intensity) 215 (M^+ , 30). Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{N}_3\text{O}$; C: 66.96, H: 6.09; Found C: 66.78, H: 6.06.

Table 3. Intramolecular Copper-catalyzed Amination of Aryl Halides.**Indoline⁶ (Table 3, entry 1).**

Using general procedure A, 2-bromophenylethylamine (200 mg, 1.0 mmol). Reaction time and temperature were according to Table 3. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (10:1) as the eluent to afford the title product as a colorless liquid. $R_f = 0.2$ (hexane/ethyl acetate = 10:1). ^1H NMR (300 MHz, CDCl_3) δ 7.08 (d, 1 H, $J = 7.8$ Hz), 6.96-7.01 (m, 1 H), 6.67 (dt, 1 H, $J = 1.2$ Hz, 7.8 Hz), 6.61 (d, 1 H, $J = 7.5$ Hz), 3.73 (brs, 1 H), 3.52 (t, 2 H, $J = 8.1$ Hz), 3.01 (t, 2 H, $J = 8.1$ Hz). ^{13}C NMR (75 MHz, CDCl_3) δ 151.7, 129.5, 127.4, 124.8, 118.8, 109.7, 47.7, 30.3. MS (EI) m/z (relative intensity) 118 ($\text{M}^+ - 1$, 100).

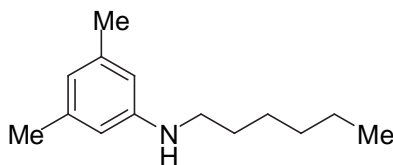
Indoline⁷ (Table 3, entries 3 and 4).

Using general procedure A, 2-chlorophenylethylamine (141 μL , 1.0 mmol) was used. Reaction time and temperature were according to Table 3. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (10:1) as the eluent to afford the title product as a colorless liquid. The characterization data matched that of the compound in Table 3, entry 1.

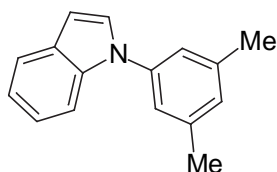
**1,2,3,4-Tetrahydroquinoline⁶ (Table 3, entry 2).**

Using general procedure A, 2-(bromophenyl)propylamine (214 mg, 1.0 mmol) was used. The crude product was purified by column chromatography on silica gel using hexane/ethyl acetate (10:1) as the eluent to afford the title product as a colorless liquid (106 mg, 80% yield). $R_f = 0.4$ (hexane/ethyl acetate = 10:1). ^1H NMR (300 MHz, CDCl_3) δ 6.93 (t, 2 H, $J = 7.5$ Hz), 6.58 (dt, 1 H, $J = 6.9$ Hz, 0.9 Hz), 6.45 (d, 1 H, $J = 7.2$

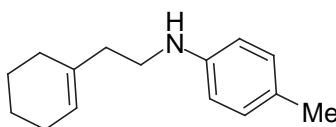
Hz), 3.78 (brs, 1 H), 3.29 (t, 2 H, $J = 5.4$ Hz), 2.75 (t, 2 H, $J = 6.3$ Hz), 1.89-1.97 (m, 2 H). MS (EI) m/z (relative intensity) 133 ($M^+ - 1$, 100).

Table 4. Solvent-free Cu-catalyzed Amination of Aryl Bromides.**3-5-Dimethyl-N-hexylaniline² (Table 4, entry 1).**

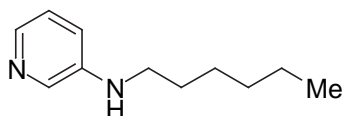
Using general procedure B. All characterization data matched that of the compound in Table 1, entry 1.

**N-(3,5-Dimethylphenyl)indole⁸ (Table 4, entry 2).**

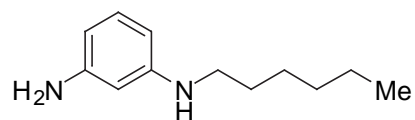
Using general procedure B. All characterization data matched that of the literature data.

**N-[2-(1-Cyclohexenyl)ethyl]-4-methylaniline³ (Table 4, entry 3).**

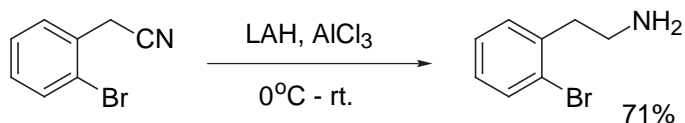
Using general procedure B. All characterization data matched that of the compound in Table 1, entry 4.

**N-Hexyl-3-aminopyridine⁵ (Table 4, entry 4).**

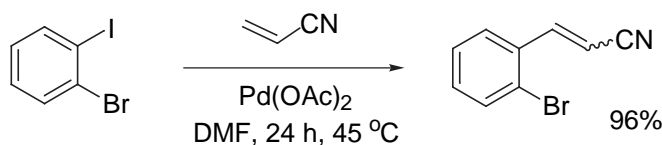
Using general procedure B. All characterization data matched that of the compound in Table 2, entry 4.

**3-Amino-N-hexylaniline (Table 4, entry 5).**

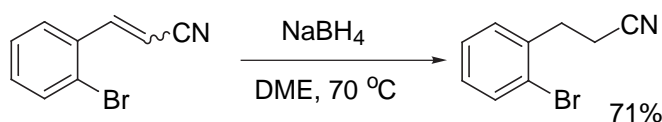
Using general procedure B. All characterization data matched that of the compound in Table 1, entry 2.

Preparation of the substrates for intramolecular amination of aryl halides.**2-(2-Bromophenyl)ethan-1-amine.⁹**

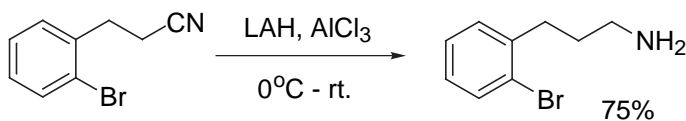
The literature procedure was followed without modification.

**2-Bromocinnamionitrile.^{10,11}**

The literature procedure was followed without modification.

**3-(2-Bromophenyl)propanedinitrile.^{12,13}**

The literature procedure was followed without modification.

**3-(2-Bromophenyl)propan-1-amine.⁶**

The literature procedure was followed without modification.

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