Palladium-Catalyzed Synthesis of Arylamines from Aryl Halides and Lithium Bis(trimethylsilyl)amide as an Ammonia Equivalent

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Supporting information

General Methods. Reactions were conducted using standard drybox techniques. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer with residual protiated solvent used as a reference and coupling constants reported in Hertz (Hz). All ^{13}C NMR spectra were proton decoupled. GC analyses were performed on an HP-6890 instrument using a DB-1301 narrow bore column for high temperature ramp applications (max. 120 ˚C/min). GCMS spectra were recorded on an HP5890 instrument equipped with a HP5971A Mass Spectral Analyzer using an HP-1 methyl silicone column. Elemental analyses were performed by Robertson Microlabs, Inc., Madison, NJ. Chromatographic purifications were performed by flash chromatography using silica gel (200-400 mesh) from Natland International Corporation. Yields for final products in Tables 2 and 3 refer to isolated yields and are the average of at least two runs. Spectroscopic data and combustion analyses are reported for all new compounds. Previously reported products were isolated in greater than 95% purity as determined by ^{1}H NMR spectroscopy and capillary gas chromatography (GC).

General Procedure.

In a screw-capped vial containing aryl halide (1.0 mmol) were placed $P^{t}Bu_3$ (0.05-0.002 mmol), $Pd(dba)_2$ (0.05-0.002 mmol), and LiHMDS (1.1 mmol), followed by toluene (2.5 mL). The vial was sealed with a cap fitted with a PTFE septum and removed from the dry

box. The reaction mixture was stirred at room temperature, and the reaction progress was monitored by GC.

Work-up Procedure 1.

Upon consumption of aryl halide, the crude reaction mixture was diluted with Et_2O (20 mL), and the silylamide was deprotected by adding one drop of aqueous 1 N HCl. The mixture was transferred to a separatory funel and washed with aqueous 1 N NaOH (20mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated at reduced pressure. The residue was purified by chromatography on silica gel using EtOAc as eluent.

Work-up Procedure 2.

Upon consumption of the aryl halide, the crude mixture was diluted with Et_2O. The silylamide was deprotected, and the corresponding aniline was precipitated as the hydrochloride salt by addition of 2 N HCl in Et_2O (3 mL). The precipitate was isolated by filtration and washed with Et_2O. After air-drying, the precipitate was dissolved in CH_2Cl_2 (20 mL). The resulting was solution transferred to a separatory funel and extracted with 2 N NaOH (20 mL). The aqueous phase was diluted with saturated aqueous NH_4Cl (20 mL) and extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to afford the pure anilines.

Work-up procedures 1 and 2 gave similar yields in all cases, except for reactions of the acid-sensitive products (3-(1,3-dioxolan-2-yl)aniline and 1,3-benozodioxol-5-amine (Tables 2 and 3, entries 14 and 18)). These products were isolated by method 1.

***N*-4-(*tert*-Butylphenyl)-*N*,*N*-bis(trimethylsilyl)amine.**

^{1}H NMR: δ 7.18(d, *J* = 8.4 Hz, 2H), 6.79(d, *J* = 8.4 Hz, 2H), 1.30(s, 9H), 0.05(s, 18H). ^{13}C NMR: δ 146.82, 145.40, 130.18, 125.74, 34.85, 32.22, 2.77. Anal. Calc'd for $C_{16}H_{31}NSi_2$: C, 65.45; H, 10.64; N, 4.77. Found: C, 65.25; H, 10.58; N, 4.95.

4-*tert*-Butylaniline (Table 2 and 3, entry 1).

^{1}H NMR: δ 7.19(d, *J* = 8.6 Hz, 2H), 6.63(d, *J* = 8.6 Hz, 2H), 3.54(s, 2H), 1.33(s, 9H). ^{13}C NMR: δ 144.21, 141.87, 126.5, 115.3, 77.67, 31.98.

Aniline (Tables 2 and 3, entry 2).

^{1}H NMR: δ 7.17(ddd, *J* = 7.4, 6.6, 0.8 Hz, 2H), 6.77(dt, *J* = 7.4, 1.0 Hz, 1H), 6.69(ddd, *J* = 6.6, 1.0, 0.8 Hz, 2H), 3.65(s, 2H). ^{13}C NMR: δ 147.01, 129.96, 119.22, 115.77.

Methyl 4-aminobenzoate (Tables 2 and 3, entry 3).

^{1}H NMR: δ 7.86(dd, *J* = 8.7, 0.9 Hz, 2H), 6.63(dd, *J* = 8.7, 0.9 Hz, 2H), 4.06(s, 2H), 3.86(s, 3H). ^{13}C NMR: δ 167.13, 150.74, 131.51, 119.67, 113.73, 51.51.

(4-Aminophenyl)(phenyl)methanone (Tables 2 and 3, entry 4).

^{1}H NMR: δ 7.66(m, 2H), 7.65(d, *J* = 8.8 Hz, 2H), 7.47(dt, *J* = 7.3, 1.5 Hz, 1H), 7.37(ddd, *J* = 8.3, 7.3, 1.3 Hz, 2H), 6.61(d, *J* = 8.8 Hz, 2H), 4.07(s, 2H). ^{13}C NMR: δ 195.1, 150.83, 183.68, 132.81, 131.28, 129.44, 127.92, 127.31, 113.54.

***p*-Toluidine (Tables 2 and 3, entry 5).**

^{1}H NMR: δ 7.02(d, *J* = 8.3 Hz, 2H), 6.65(d, *J* = 8.3 Hz, 2H), 3.57(s, 2H), 2.31(s, 3H). ^{13}C NMR: δ 144.33, 130.22, 128.17, 115.73, 20.93.

4-Butylaniline (Tables 2 and 3, entry 6).

^{1}H NMR: δ 6.98(d, *J* = 8.2 Hz, 2H), 6.63(d, *J* = 8.2 Hz, 2H), 3.53 (s, 2H), 2.50(t, *J* = 7.6 Hz, 2H), 1.51(dt, *J* = 7.6, 7.4 Hz, 2H), 1.35(tq, *J* = 7.4, 7.2 Hz, 2H), 0.92(t, *J* = 7.2 Hz, 3H). ^{13}C NMR: δ 143.83, 132.95, 129.01, 115.06, 34.63, 33.87, 22.19, 13.87.

***N*,*N*-Dimethylbenzene-1,4-diamine (Tables 2 and 3, entry 7).**

^{1}H NMR: δ 6.73-6.66(m, 4H), 3.35(s, 2H), 2.84(s, 6H). ^{13}C NMR: δ 144.79, 137.85, 116.53, 115.54, 42.09.

4-(Trifluoromethyl)aniline (Tables 2 and 3, entry 8).

^{1}H NMR: δ 7.30(d, *J* = 8.5 Hz, 2H), 6.60(d, *J* = 8.5 Hz, 2H), 3.86(s, 2H). ^{13}C NMR: δ 150.04, 127.36(q, *J* = 3.6 Hz), 125.50(q, *J* = 270.5 Hz), 120.84(q, *J* = 32.4 Hz), 114.85.

4-Methoxyaniline (Tables 2 and 3, entry 9).

^{1}H NMR: δ 6.74(d, *J* = 8.7 Hz, 2H), 6.64(d, *J* = 8.7 Hz, 2H), 3.73(s, 3H), 3.41(s, 2H). ^{13}C NMR: δ 152.74, 139.56, 116.39, 114.65, 55.71.

4-Fluoroaniline (Tables 2 and 3, entry 10).

^{1}H NMR: δ 8.86(m, 2H), 6.63(m, 2H), 3.50(s, 2H). ^{13}C NMR: δ 157.10(d, *J* = 235.5 Hz), 143.00, 116.75(d, *J* = 7.5 Hz), 116.33(d, *J* = 22.3 Hz).

1,1'-Biphenyl-4-amine (Tables 2 and 3, entry 11).

^{1}H NMR: δ 7.54(dd, *J* = 6.6, 1.2 Hz, 2H), 7.47-7.36(m, 4H), 7.27(dt, *J* = 7.4, 1.2 Hz, 1H), 6.77(d, *J* = 8.9 Hz, 2H). ^{13}C NMR: δ 145.69, 141.02, 131.45, 128.53, 127.89, 126.27, 126.13, 115.26.

4-Phenoxyaniline (Tables 2 and 3, entry 12).

^{1}H NMR: δ 7.27(dd, *J* = 8.6, 7.5 Hz, 2H), 7.02(dt, *J* = 7.5, 1.0 Hz, 1H), 6.93(dd, *J* = 8.6, 1.0 Hz, 2H), 6.88(d, *J* = 8.4 Hz, 2H), 6.68(d, *J* = 8.5 Hz, 2H), 3.58 (s, 2H). ^{13}C NMR: δ 158.70, 153.40, 141.85, 129.42, 122.00, 120.98, 117.15, 116.44.

3-Methoxyaniline (Tables 2 and 3, entry 13).

^{1}H NMR: δ 7.06(dd, *J* = 8.1, 8.1 Hz, 1H), 6.33(ddd, *J* = 8.1, 2.4, 0.7 Hz, 1H), 6.30(ddd, *J* = 8.1, 2.3, 0.7 Hz, 1H), 6.25(dd, *J* = 2.4, 2.3 Hz, 1H), 3.78(s, 3H), 3.65(s, 2H). ^{13}C NMR: δ 160.89, 147.92, 130.31, 108.12, 104.08. 101.18, 55.34.

3-(1,3-Dioxolan-2-yl)aniline (Tables 2 and 3, entry 14).

^{1}H NMR: δ 7.17(t, *J* = 7.8 Hz, 1H), 6.87(d, *J* = 7.6 Hz, 1H), 6.81(t, *J* = 1.9 Hz, 1H), 6.68(m, 1H), 5.74(s, 1H), 4.11-4.02(m, 4H), 3.71(s, 2H). ^{13}C NMR: δ 147.14, 139.63, 129.96, 117.25, 116.54, 113.42, 104.29, 65.84.

3-(Trifluoromethyl)aniline (Tables 2 and 3, entry 15).

^{1}H NMR: δ 7.24(dd, *J* = 8.0, 7.6 Hz, 1H), 6.98(dd, *J* = 7.6, 0.4 Hz, 1H), 6.89(broad s, 1H), 6.81(dd, *J* = 8.0, 0.4 Hz, 1H), 3.84(s, 2H). ^{13}C NMR: 146.58, 131.35 (q,

J=22.2Hz), 129.60, 124.07(q, *J*=272.2Hz), 117.82, 114.87(q, *J*=3.9Hz), 111.17(q, *J*=3.5Hz).

m-Toluidine (Tables 2 and 3, entry 16).

^{1}H NMR: δ 7.08(t, *J* = 7.6 Hz, 1H), 6.61(d, *J* = 7.5 Hz, 1H), 6.54-6.52(m, 2H), 3.58(s, 2H), 2.30(s, 3H). ^{13}C NMR: δ 146.96, 139.76, 129.80, 120.08, 116.55, 112.88, 22.08.

2-Fluoro-1,1'-biphenyl-4-amine (Tables 2 and 3, entry 17).

^{1}H NMR: δ 7.36(m, 1H), 7.34(s, 1H), 7.25(m, 2H), 7.15(m, 1H), 7.07(t, *J* = 8.5 Hz, 1H), 6.36(dd, *J* = 8.2, 2.3 Hz, 1H), 6.30(dd, *J* = 10.2, 2.2 Hz, 1H), 3.65(s, 2H). ^{13}C NMR: δ 160.96(d, *J* = 246.0 Hz), 147(d, *J* = 11.0 Hz), 136.60, 131.71(d, *J* = 3.4 Hz), 129.07(d, *J* = 2.9 Hz), 128.79, 127.16, 119.39(d, *J* = 13.9 Hz), 111.58, 102.91(d, *J* = 105.2 Hz). Anal. Calc'd for $C_{12}H_{10}FN$: C, 76.99; H, 5.38; N, 7.48. Found: C, 77.19; H, 5.55; N, 7.36.

1,3-Benozodioxol-5-amine (Tables 2 and 3, entry 18).

^{1}H NMR: δ 6.64(d, *J* = 8.1 Hz, 1H), 6.29(d, *J* = 2.2 Hz, 1H), 6.13(dd, *J* = 8.1, 2.2 Hz, 1H), 5.86(s, 2H), 3.44(s, 2H). ^{13}C NMR: δ 148.82, 142.02, 140.97, 109.21, 107.50, 101.30, 98.70.

2-Naphthylamine (Tables 2 and 3, entry 19).

^{1}H NMR: δ 7.69(d, *J* = 8.0 Hz, 1H), 7.66(d, *J* = 8.4 Hz, 1H), 7.59(d, *J* = 8.4 Hz, 1H), 7.36(dd, *J* = 6.8, 1.2 Hz, 1H), 7.22(dd, *J* = 8.0, 1.6 Hz, 1H), 6.95(d, *J* = 2.1 Hz, 1H), 6.55(dd, *J* = 8.4, 2.1 Hz, 1H), 3.83(s, 2H). ^{13}C NMR: δ 143.96, 134.78, 129.09, 128.49, 127.58, 126.22, 125.67, 122.35, 118.20, 108.47.

6-Methoxy-2-naphthylamine (Tables 2 and 3, entry 20).

^{1}H NMR: δ 7.57(d, *J* = 8.4 Hz, 1H), 7.52(d, *J* = 8.7 Hz, 1H), 7.09(dd, *J* = 8.9, 2.6 Hz, 1H), 7.04(d, *J* = 2.6 Hz, 1H), 6.98(d, *J* = 2.1 Hz, 1H), 6.94(dd, *J* = 8.3, 2.1 Hz, 1H), 3.89 (s, 3H), 3.72 (s, 2H). ^{13}C NMR: δ 155.22, 142.15, 130.03, 128.51, 127.77, 127.18, 118.83, 118.59, 109.10, 105.91, 55.14.

Pyridin-2-amine (Tables 2 and 3, entry 21).

^{1}H NMR: δ 8.03(m, 1H), 7.38(m, 1H), 6.60(m, 1H), 6.46(d, *J* = 8.3 Hz, 1H), 4.60(s, 2H). ^{13}C NMR: δ 159.12, 148.63, 138.29, 114.45, 109.2.

Benzene-1,4-diamine (Tables 2 and 3, entry 22).

^{1}H NMR: δ 6.60(s, 4H), 3.35(s, 4H). ^{13}C NMR: δ 139.25, 117.40.

Benzene-1,3-diamine (Tables 2 and 3, entry 23).

^{1}H NMR: δ 6.94(t, *J* = 7.8 Hz, 1H), 6.12(dd, *J* = 7.8, 2.3 Hz, 2H), 6.04(t, *J* = 2.3 Hz, 1H), 3.57(s, 4H). ^{13}C NMR: δ 147.37, 130.09, 105.87, 101.79.