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SUPPORTING INFORMATION

Title: Optimization of the Conditions for Copper-Mediated *N*-Arylation of Heteroarylamines
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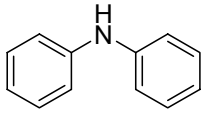
General: All reactions were processed under a nitrogen atmosphere in oven-dried Schlenk-type glassware. Elemental analyses were performed by Elementar Vario EL III. IR spectra were recorded on a Bruker Equinox-55. ^{1}H NMR spectra were recorded on a Varian Inova 400 MHz instrument with chemical shifts reported relative to tetramethylsilane (TMS). GC-MS spectra were determined on a Varian 3800 spectrometer. Gas chromatography analyses were performed on a Hewlett Packard 5890 instrument. All materials were weighed in the air. Flash column chromatography was performed with silia gel (100–200 mesh). All reagents were used as purchased from commercial suppliers without further purification.

General procedure of copper-mediated *N*-arylation of heteroarylamines: The heteroarylamine (1.1 mmol), CuI (0.019–0.19 g, 0.1–1.0 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), aryl halide (1 mmol) and DMEDA (0.1–1.0 mmol) were added by syringe at room temperature. The reaction mixture was stirred at 100 ^{o}C for 20 h, and cooled to room temperature. Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the residue was purified by column chromatography on silica gel.

Experimental procedures and characterization data for several compounds contained in table 2(2c, 2d, 2e, 2f, 2g)

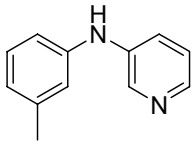
Diphenylamine (table 2, 2c): Aniline (0.102 g, 1.1 mmol) , CuI (0.019 g, 0.1 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), iodobenzene (0.204 g, 1.0 mmol) and DMEDA (0.009 g, 0.1 mmol) were added by syringe at room temperature. The reaction mixture was Stirred at 100 ^{o}C for 21 h, and cooled to room temperature. Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (1.75×20 cm, petroleum ether : ethyl acetate, 7:1) to provide 0.14 g (83% yield) product.



2c

m.p.: 52–54 ^{o}C; ^{1}H NMR(400 MHz,$CDCl_3$): δ 6.93–7.26(br m, 10H), 5.63(s, 1H); IR (cm^{-1}): 3435, 3095, 3070, 3050, 1598, 1506, 1490, 1382, 1315, 878, 862, 694; MS m/z 169 (M^+), 141, 115, 83, 77, 66, 51; Anal. $C_{12}H_{11}N$(169.23): Calcd.C 85.17, H 6.55, N 8.28, Found C 85.11, H 6.42, N 8.37.

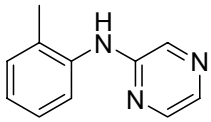
***N*-m-tolylpyridin-3-amine (table 2, 2d):** 3-Aminopyridine (0.104 g, 1.1 mmol) , CuI (0.048 g, 0.25 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), 3-bromotoluene (0.171 g, 1.0 mmol) and DMEDA (0.022 g, 0.25 mmol) were added by syringe at room temperature. The reaction mixture was Stirred at 100 ^{o}C for 22 h, and cooled to room temperature. Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (1.75×20 cm, petroleum ether : ethyl acetate, 7:1) to provide 0.149 g (81% yield) product.



2d

m.p.: 113–115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 2.8 Hz, 1H), 8.16 (dd, *J* = 4.4Hz, *J* = 1 Hz, 1H), 7.36–7.44 (m, 1H), 7.10–7.15 (m, 2H), 6.91 (s, 1H), 6.86–6.90 (m, 2H), 5.92 (bs, 1H), 2.30 (s, 3H); IR (cm^{-1}) 3280, 3015, 1620, 1560, 769, 690; MS m/z 184 (M^{+}); Anal. for $C_{12}H_{12}N_2$(184.24): Calcd. C 78.23, H 6.57, N 15.21. Found C 78.02, H 6.69, N 14.96.

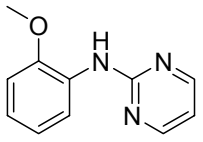
***N*-o-tolylpyrazin-2-amine (table 2, 2e):** Aminopyrazine (0.105 g, 1.1 mmol) , CuI (0.067 g, 0.35 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), 2-bromotoluene (0.171 g, 1.0 mmol) and DMEDA (0.031 g, 0.35 mmol) were added by syringe at room temperature. The reaction mixture was Stirred at 100 ^{o}C for 24 h, and cooled to room temperature. Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (1.75×20 cm, petroleum ether : ethyl acetate, 7:1) to provide 0.137 g (74% yield) product.



2e

m.p.: 92–94 ^{o}C; ^{1}H NMR(400 MHz, $CDCl_3$): δ 8.09 (d, J = 1.4 Hz, 2 H), 7.96 (d, J = 2.2 Hz, 1 H), 7.49 (d, J = 7.8 Hz, 1H), 7.26 (d, J = 7.9 Hz, 1 H), 7.23 (d, J = 7.7 Hz, 1 H), 7.12 (td, J = 7.4, 1.1 Hz, 1 H), 6.55 (br s,1 H), 2.31 (s, 3 H); IR (cm^{-1}) 3241, 1600, 1520, 1496, 750; MS m/z 185 (M^{+}); Anal. $C_{11}H_{11}N_3$(185.23): Calcd. C 71.33, H 5.99, N 22.69; Found C 71.09, H 5.89, N 22.48.

***N*-(2-methoxyphenyl)pyrimidin-2-amine (table 2, 2f):** Aminopyrimidine (0.105 g, 1.1 mmol) , CuI (0.095 g, 0.5 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), 2-bromoanisole (0.187 g, 1.0 mmol) and DMEDA (0.044 g, 0.5 mmol) were added by syringe at room temperature. The reaction mixture was Stirred at 100 ^{o}C for 24 h, and cooled to room temperature. Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (1.75×20 cm, petroleum ether : ethyl acetate, 7:1) to provide 0.141 g (70% yield) product.

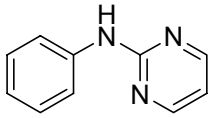


2f

m.p.: 56–57 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (dd, J = 7.4, 2.2 Hz, 1 H), 8.42 (d, J = 4.8 Hz, 2 H), 7.78 (br s, 1 H), 7.02–6.95 (m, 2 H), 6.89 (dd, J = 7.5, 2.0 Hz, 1 H), 6.68 (t, J = 4.8 Hz, 1 H), 3.88 (s, 3 H); IR (m^{-1}): 3345, 2960, 2830, 1650, 1526, 1260, 759; MS m/z 201(M^{+}); Anal. $C_{11}H_{11}N_3O$(201.22): Calcd. C 65.66, H 5.51, N 20.88; Found C 65.74, H 5.40, N 20.69.

***N*-phenylpyrimidin-2-amine (table 2, 2g):** Aminopyrimidine (0.105 g, 1.1 mmol) , CuI (0.095 g, 0.5 mmol) and anhydrous K_2CO_3 (0.276 g, 2 mmol) were added to a Schlenk type three neck flask fitted with thermometer, magnetic stirbar and septum. The flask was evacuated and back filled with N_2 three times. Dioxane (5 mL), bromobenzene (0.157 g, 1.0 mmol) and DMEDA (0.044 g, 0.5 mmol) were added by syringe at room temperature. The reaction mixture was Stirred at 100 ^{o}C for 22 h, and cooled to room temperature.

Concentrated ammonia (4 mL) and saturated solution of NaCl (20 mL) were added, and the mixture was extracted with ethyl acetate (3×15 mL). The organic layers were concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (1.75×20 cm, petroleum ether : ethyl acetate, 7:1) to provide 0.134 g (78% yield) product.



2g

m.p.: 112–113^{o}C; ^{1}H NMR (400 MHz,$CDCl_3$): δ 8.37 (d, J = 4.8, 2H), 7.00–7.69 (m, 6H), 6.67 (t, J = 4.81, H); IR (m^{-1}): 3236, 3086, 1606, 1582, 1502, 1451, 1250, 794; MS m/z 171 (M^{+}); Anal. $C_{10}H_9N_3$(171.20): Calcd. C 70.16, H 5.30, N 24.55; Found C 70.01, H 5.10, N 24.38.