# Orthogonal Cu- and Pd-Based Catalyst Systems for the O- and N-Arylation of Aminophenols

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*Supporting Information*

## General Reagent Information

All reactions were carried out under an argon atmosphere. Dimethylsulfoxide (DMSO), 1,4-dioxane (dioxane), *tert*-butanol (*t*-BuOH) were purchased from Aldrich Chemical Co. in Sure-Seal bottles and were used as recieved. Butyronitrile was purchased from Aldrich Chemical Co., and was dried over molecular sieves (3 A). Copper(I) iodide (98%) was purchased from Strem. BrettPhos precatalyst[1] was prepared as described in ref. 1. Powdered $K_3PO_4$ was purchased from Riedel-de Haën. *Anhydrous finely powdered* $Cs_2CO_3$ was a generous gift from Chemetall. Both potassium carbonate and sodium *tert*-butoxide (NaO*t*-Bu) were purchased from Aldrich Chemical Co. The bulk of the bases were stored under nitrogen in a Vacuum Atmospheres glovebox. Small portions (~3 g) were removed from the glovebox in glass vials, stored in the air in a desiccator filled with anhydrous calcium sulfate, and weighed in the air. Aminophenols were purchased from commercial sources and used without further purification. Aryl halides were purchased from commercial sources and, when necessary, filtered through neutral alumina or distilled prior to use. Flash column chromatography was performed using a Biotage SP4 Flash Purification System using KP-Sil silica cartridges. In all cases, ethyl acetate was used to transfer the crude reaction material onto the silica gel samplet. A gradient elution using hexane and ethyl acetate was performed, based on the recommendation from the Biotage TLC Wizard.

**General Analytical Information.** All compounds were characterized by $^1$H NMR, $^{13}$C NMR spectroscopy. Copies of the $^1$H NMR, $^{13}$C NMR can be found at the end of the Supporting Information. Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 MHz instrument. All $^1$H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All $^{13}$C NMR spectra are reported in ppm relative to deuterochloroform (77.23 ppm), unless otherwise stated, and all were obtained with $^1$H decoupling. All IR spectra was taken on a Perkin – Elmer 2000 FTIR. All GC analyses were performed on a Agilent 6890 gas chromatograph with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.). Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA 30091.

**Experimental Procedure.**

**General procedure for the Cu-catalyzed O-arylation of 3-aminophenol with aryl halide**

**Table 2. General procedure A (ArI).** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (9.5 mg, 0.05 mmol, 5 mol%), 2-picolinic acid, **1** (12.3 mg, 0.10 mmol, 10 mol%), aryl iodide (if solid; 1.0 mmol ), 3-aminophenol (or substituted 3-aminophenol, 1.2 mmol) and $K_3PO_4$ (424 mg, 2.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, remaining liquid reagents were added, followed by dimethylsulfoxide (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 80 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through a pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**Table 2. General procedure B (ArBr).** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (19 mg, 0.10 mmol, 10 mol%), 2-picolinic acid, **1** (24.6 mg, 0.20 mmol, 20 mol%), aryl bromide (if solid; 1.0 mmol ), 3-aminophenol (or substituted 3-aminophenol, 1.2 mmol) and $K_3PO_4$ (424 mg, 2.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, remaining liquid reagents were added, followed by dimethylsulfoxide (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 90 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**General procedure for the Pd-catalyzed N-arylation of 3-aminophenol with aryl halide.**

**Table 2. General procedure C.** An oven-dried screw cap test tube was charged with a magnetic stir bar, BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), aryl bromide (if solid; 1.0 mmol), 3-aminophenol (or substituted 3-aminophenol, 1.2 mmol) and NaO*t*-Bu (240 mg, 2.5 mmol). The tube was evacuated and refilled with argon (three times). Under a counterflow of argon, remaining liquid reagents were added, followed by 1,4-dioxane (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 90 ºC (or, at indicated temperature) and the reaction mixture was stirred vigorously for 1hr (or, for indicated period of time). The reaction mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, dried over $Na_2SO_4$, concentrated in vacuo, and purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**Table 2. General procedure D.** An oven-dried screw cap test tube was charged with a magnetic stir bar, BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), aryl chloride (if solid; 1.0 mmol), 3-aminophenol (or substituted 3-aminophenol, 1.2 mmol) and NaO*t*-Bu (240 mg, 2.5 mmol). The tube was evacuated and refilled with argon (three times). Under a counterflow of argon, remaining liquid reagents were added, followed by 1,4-dioxane (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 90 ºC (or, at indicated temperature) and the reaction mixture was stirred vigorously for 70 min (or, for indicated period of time). The reaction mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, dried over $Na_2SO_4$, concentrated in vacuo, and purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**General procedure for the Cu-catalyzed O-arylation of 4-aminophenol with aryl halide**

**Table 3. General procedure A (ArI).** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (19 mg, 0.10 mmol, 10 mol%), aryl iodide (if solid; 1.0 mmol ), 4-aminophenol (or substituted 4-aminophenol, 2.0 mmol) and $K_2CO_3$ (828 mg, 6.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, ligand CyDMEDA, **2** (32 μL, 0.20 mmol, 20 mol%) and remaining liquid reagents were added, followed by butyronitrile (3.0 mL) by syringe. The tube was placed in a preheated oil bath at 70 ºC and the reaction mixture was stirred vigorously for 24 h (unless otherwise mentioned). The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**General procedure for the Pd-catalyzed N-arylation of 4-aminophenol with aryl halide.**

**Table 3. General procedure B.** An oven-dried screw cap test tube was charged with a magnetic stir bar, BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), aryl bromide (if solid; 1.0 mmol or aryl chloride, as indicated), 4-aminophenol (or substituted 4-aminophenol, 1.2 mmol) and NaO*t*-Bu (240 mg, 2.5 mmol). The tube was evacuated and refilled with argon (three times). Under a counterflow of argon, remaining liquid reagents were added, followed by 1,4-dioxane (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 110 ºC (or, at indicated temperature) and the reaction mixture was stirred vigorously for 1hr (or, for indicated period of time). The reaction mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, dried over $Na_2SO_4$, concentrated in vacuo, and purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**General procedure for the Cu-catalyzed N-arylation of 2-aminophenol with aryl iodide**

**Table 4.** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (19 mg, 0.10 mmol, 10 mol%), aryl iodide (if solid; 1.0 mmol ), 2-aminophenol (227 mg, 3.0 mmol) and $K_3PO_4$ (424 mg, 2.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, remaining liquid reagents were added, followed by 1,4-dioxane (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 110 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1).

**General procedure for the copper catalyzed competition experiments with 1:1 aniline : p-substituted phenol.**

An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (9.5 mg, 0.05 mmol, 5 mol%), 2-picolinic acid, **1** (12.3 mg, 0.10 mmol, 10 mol%), 4-iodotoluene (218 mg, 1.0 mmol ), aniline (273 µL, 3.0 mmol), p-substituted phenol (3.0 mmol) and $K_3PO_4$ (212 mg, 1.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, remaining liquid reagents were added, followed by DMSO (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 70 ºC and the reaction mixture was stirred vigorously for 1 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and analyzed by GC and GC-MS spectroscopy.

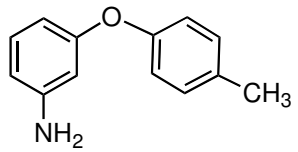
**General procedure for the copper catalyzed competition experiments with 1:1 phenol : p-substituted aniline.**

An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (9.5 mg, 0.05 mmol, 5 mol%), 2-picolinic acid, **1** (12.3 mg, 0.10 mmol, 10 mol%), 4-iodotoluene (218 mg, 1.0 mmol ), phenol (282 mg, 3.0 mmol), p-substituted aniline (3.0 mmol, if solid) and $K_3PO_4$ (212 mg, 1.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, remaining liquid reagents were added, followed by DMSO (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 70 ºC and the reaction mixture was stirred vigorously for 1 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more

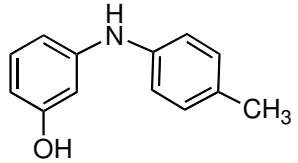
with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and analyzed by GC and GC-MS spectroscopy.

**General procedure for the competition experiments with 1:1 phenol : aniline and BrettPhos precatalyst.**

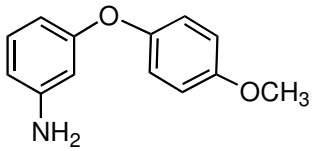
An oven-dried screw cap test tube was charged with a magnetic stirbar, BrettPhos precatalyst, **8** (8.0 mg, 0.01 mmol, 1.0 mol%), BrettPhos, **I** (5.4 mg, 0.01 mmol, 1.0 mol%), phenol (282 mg, 3.0 mmol) and NaO*t*-Bu (115 mg, 1.2 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, aniline (273 µL, 3.0 mmol) and chlorobenzene (102 µL, 1.0 mmol) followed by 1,4-dioxane (2.0 mL) by syringe. The tube was placed in a preheated oil bath at 80 ºC and the reaction mixture was stirred vigorously for 30 min. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and analyzed by GC and GC-MS spectroscopy.



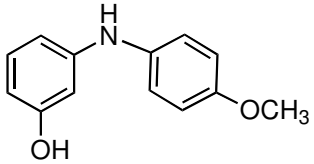

**3-(*p*-tolyloxy)aniline (Table 2, entry 1a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (160 mg, 80%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.10 (d, 2H, J = 8.0), 7.04 (t, 1H, J = 8.0), 6.90 (d, 2H, J = 5.0), 6.35 (dt, 2H, J = 8.0), 6.27 (s, 1H), 3.64 (s, 2H), 2.31 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.2, 154.7, 148.1, 133.1, 130.5, 130.3, 119.6, 109.9, 108.6, 105.2, 20.9. IR (KBr disc, $cm^{-1}$): 3379, 2921, 1617, 1506, 1220, 1145, 961. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.35; H, 6.66.



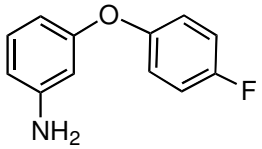

**3-(*p*-tolylamino)phenol (Table 2, entry 1b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 1b) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a dark grey solid (183 mg, 92%, entry 1b). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.10-7.07 (m, 3H), 6.99 (d, 2H, J = 6.1), 6.57-6.54 (m, 1H), 6.46 (s, 1H), 6.35-6.32 (m, 1H), 5.48 (s, 2H), 2.31 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 146.0, 140.0, 131.7, 130.6, 130.1, 120.0, 109.5, 107.4, 103.5, 21.0. IR (KBr disc, $cm^{-1}$): 3392, 3025, 2920, 2863, 2360, 2341, 1607, 1516, 1493, 1457, 1400, 1333, 1271, 1243, 1156, 1082, 997, 970, 816, 769, 688, 668, 630, 535, 499. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.36; H, 6.54. m.p. 82 ºC.



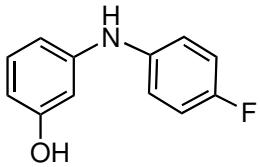

**3-(4-methoxyphenoxy)aniline (Table 2, entry 2a and 2b)**. The general procedure A (entry 2a) and procedure B (entry 2b) for the Cu-catalyzed O- arylation of 3-aminophenol with aryl halide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow solid (166 mg, 77%, entry 2a; 134 mg, 62%, entry 2b). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.03 (t, 1H, J = 8.0), 6.96 (d, 2H, J = 8.0), 6.84 (d, 2H, J = 8.0), 6.35-6.29 (m, 2H), 6.23 (s, 1H), 3.77 (s, 3H), 3.63 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.9, 156.0, 150.2, 148.1, 130.4, 121.2, 114.9, 109.5, 107.8, 104.4, 55.8. IR (KBr disc, $cm^{-1}$): 3373, 2923, 2851, 1653, 1617, 1506, 1457, 1210, 1143. Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.79; H, 6.14. m. p. 66 ºC.



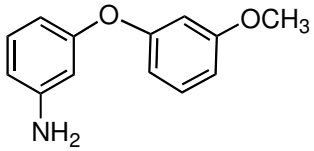

**3-(4-methoxyphenylamino)phenol (Table 2, entry 2c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 2c) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (198 mg, 92%, entry 2c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.05-7.01 (m, 3H), 6.83 (d, 2H, J = 4), 6.43 (d, 1H, J = 8.0), 6.35 (s, 1H), 6.27 (d, 1H, J = 8.0), 5.48 (s, 2H), 3.77 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.8, 155.5, 147.1, 135.5, 130.6, 123.1, 114.9, 108.4, 106.7, 102.4, 55.9. IR (KBr disc, $cm^{-1}$): 3411, 3365, 2835, 2360, 1602, 1527, 1507, 1444, 1337, 1244, 1185, 1109, 1032, 839, 829, 775, 689, 668, 622, 519, 451. Anal. Calcd for $C_{13}H_{13}NO_2$ : C, 72.54; H, 6.09. Found: C, 72.50; H, 5.94. m.p. 67-68 ºC.



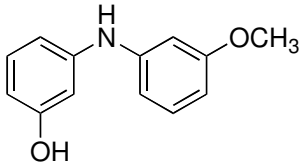

**3-(4-fluorophenoxy)aniline (Table 2, entry 3a and 3b)**. The general procedure A (entry 3a) and procedure B (entry 3b) for the Cu-catalyzed O- arylation of 3-aminophenol with aryl halide were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (181 mg, 89%, entry 3a; 114 mg, 56%, entry 3b). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: δ: 7.06 (t, 1H, J = 8.0), 7.02-6.95 (m, 4H), 6.39-6.37 (m, 1H), 6.34-6.31 (m, 1H), 6.26 (t, 1H, J = 4), 3.67 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 160.2, 159.1, 157.8, 152.9, 148.2, 130.6, 121.0, 120.9, 116.5, 110.2, 108.4, 105.1. IR (KBr disc, $cm^{-1}$): 3468, 3380, 3220, 3073, 2341, 1874, 1623, 1501, 1464, 1291, 1199, 1144, 1090, 1011, 997, 961, 836, 776, 688. Anal. Calcd for $C_{12}H_{10}FNO$: C, 70.93; H, 4.96. Found: C, 70.91; H, 4.87.



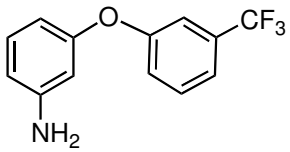

**3-(4-fluorophenylamino)phenol (Table 2, entry 3c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 3c) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a white solid (183 mg, 90%, entry 3c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.08-6.92 (m, 5H), 6.49 (d, 1H, J = 8.0), 6.41 (s, 1H), 6.32 (d, 1H, J = 8.0), 5.55 (s, 1H), 5.08 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.7, 157.3, 156.7, 146.0, 138.5, 130.7, 121.8, 116.3, 116.1, 109.3, 107.5, 103.2. IR (KBr disc, cm$^{-1}$): 3378, 1608, 1508, 1497, 1447, 1338, 1233, 1165, 1095, 969, 829, 780, 764, 686, 534, 507.Anal. Calcd for $C_{12}H_{10}FNO$: C,70.93 ; H, 4.96. Found: C, 70.77; H, 4.92. m.p. 93 ºC.



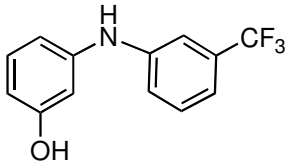

**3-(3-methoxyphenoxy)aniline (Table 2, entry 4a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (170 mg, 79%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.33 (t, 1H, J = 8.0), 7.07 (t, 1H, J = 8.0), 6.64-6.57 (m, 3H), 6.40 (d, 2H, J = 8.0), 6.31 (s, 1H), 3.75 (s, 3H), 3.59 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 161.1, 158.6, 158.3, 148.2, 130.6, 130.2, 111.4, 110.4, 109.2, 109.1, 105.8, 105.2, 55.5. IR (KBr disc, cm$^{-1}$): 3466, 3377, 3219, 3004, 2941, 2836, 2595, 2414, 1918, 1576, 1489, 1283, 1152, 1039, 997, 971, 922, 845, 768, 685. Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.26; H, 6.10.



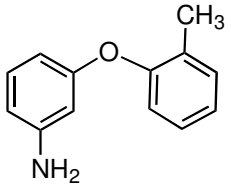

**3-(3-methoxyphenylamino)phenol (Table 2, entry 4b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a purple oil (191 mg, 89%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.19 (t, 1H, J = 10.1), 7.08 (t, 1H, J = 8.0), 6.66-6.59 (m, 3H), 6.54 (t, 1H, J = 2.1), 6.50-6.47 (m, 1H), 6.39-6.36 (m, 1H), 5.71 (s, 1H), 4.83 (s, 1H), 3.78 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 160.7, 156.8, 144.7, 144.2, 130.6, 130.4, 111.2, 110.6, 108.2, 106.8, 104.7, 104.3, 55.5. IR (KBr disc, cm$^{-1}$): 3388, 2836, 2360, 2341, 1595, 1492, 1412, 1339, 1276, 1205, 1157, 1083, 1045, 998, 981, 837, 765, 685, 668. Anal. Calcd for $C_{13}H_{13}NO_2$ : C, 72.54; H, 6.09. Found: C, 72.30; H, 6.10.



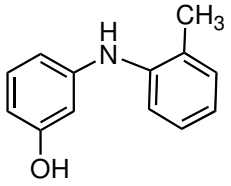
**3-(3-(trifluoromethyl)phenoxy)aniline (Table 2, entry 5a and 5b)**. The general procedure A (entry 5a) and procedure B (entry 5b) for the Cu-catalyzed O- arylation of 3-aminophenol with aryl halide were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (215 mg, 85%, entry 5a; 172 mg, 68%, entry 5b). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.39 (t, 1H, J = 8.0), 7.32 (d, 1H, J = 8.0), 7.26 (s, 1H), 7.18-7.17 (m, 1H), 7.12 (t, 1H, J = 8.0), 6.48-6.45 (m, 1H), 6.41-6.39 (m, 1H), 6.34 (t, 1H, J = 4), 3.71 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.0, 157.5, 148.5, 130.9, 130.4, 121.9, 119.8, 119.7, 115.6, 115.5, 111.2, 109.4, 106.2. IR (KBr disc, $cm^{-1}$): 3472, 3384, 3219, 3071, 1625, 1606, 1585, 1490, 1464, 1449, 1328, 1279, 1220, 1170, 1146, 1093, 1064, 998, 966, 890, 850, 795, 698, 656, 526, 452. Anal. Calcd for $C_{13}H_{10}F_3NO$: C, 61.66; H, 3.98. Found: C, 61.50; H, 3.93.



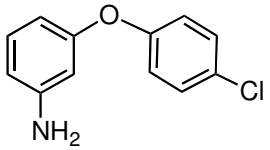

**3-(3-(trifluoromethyl)phenylamino)phenol (Table 2, entry 5c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (205 mg, 81%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.33 (t, 1H, J = 8.0), 7.24 (s, 1H), 7.18 (d, 1H, J = 8.0), 7.15-7.11 (m, 2H), 6.64 (dd, 1H, J = 8.0, J = 4), 6.56 (s, 1H), 6.44 (dd, 1H, J = 8.0, J = 4), 5.80 (s, 1H), 4.81 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 143.8, 143.6, 130.8, 130.1, 120.7, 117.7, 117.6, 114.3, 114.2, 111.2, 109.2, 105.4. IR (KBr disc, $cm^{-1}$): 3396, 2360, 1595, 1526,, 1496, 1467, 1420, 1339, 1242, 1158, 1124, 1069, 999, 976, 846,776, 691, 658. Anal. Calcd for $C_{13}H_{10}F_3NO$: C, 61.66; H, 3.98. Found: C, 61.40; H, 4.03.



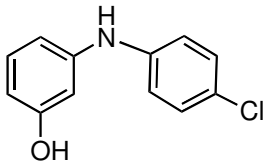

**3-(*o*-tolyloxy)aniline (Table 2, entry 6a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (162 mg, 81%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, 1H, J = 8.0), 7.16 (t, 1H, J = 8.0), 7.08-7.03 (m, 2H), 6.94 (d, 1H, J = 8.0), 6.35 (d, 1H, J = 8.0), 6.30 (d, 1H, J = 4), 6.21 (s, 1H), 3.63 (s, 2H), 2.24 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.3, 154.5, 148.2, 131.6, 130.5, 130.4, 127.3, 124.2, 120.4, 109.5, 107.6, 104.1, 16.4. IR (KBr disc, $cm^{-1}$): 3467, 3380, 3218, 3025, 2925, 2457, 2294, 1914, 1803, 1623, 1489, 1383, 1286, 1230, 1188, 1148, 1112, 1068, 1042, 996, 962, 841, 765, 687. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.23; H, 6.51.



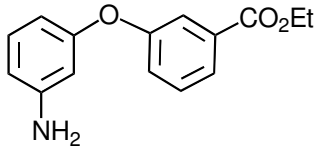
**3-(*o*-tolylamino)phenol (Table 2, entry 6b and 6c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 6b) and general procedure D for aryl chloride (entry 6c, 90 min) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (171 mg, 86%, entry 6b; 165 mg, 83%, entry 6c; 137 mg). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, 1H, J = 8.0), 7.19 (d, 1H, J = 8.0), 7.11 (t, 1H, J = 8.0), 7.07 (t, 1H, J = 8.0), 6.97 (t, 1H, J = 8.0), 6.48 (d, 1H, J = 10.0), 6.37 (s, 1H), 6.32 (d, 1H, J = 8.0), 5.34 (s, 1H), 4.95 (s, 1H), 2.22 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 146.2, 140.8, 131.2, 130.6, 129.6, 127.0, 122.9, 120.5, 109.8, 107.3, 103.8, 18.1. IR (KBr disc, $cm^{-1}$): 3384, 2361, 2338, 1599, 1491, 1250, 1155, 968, 840, 748, 688, 668. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.11; H, 6.65.




**3-(4-chlorophenoxy)aniline (Table 2, entry 7a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (199 mg, 91%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.27-7.24 (m, 2H), 7.09 (t, 1H, J = 8.0), 6.95-6.91 (m, 2H), 6.42-6.40 (m, 1H), 6.38-6.35 (m, 1H), 6.29 (t, 1H, J = 2.1), 3.69 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.2, 156.1, 148.4, 130.7, 129.9, 128.3, 120.5, 110.7, 109.0, 105.7. IR (KBr disc, $cm^{-1}$): 3467, 3383, 3220, 3057, 2452, 1890, 1623, 1576, 1485, 1287, 1227, 1161, 1145, 1089, 1011, 997, 960, 830, 773, 688, 494.

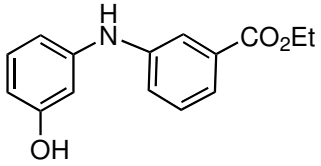



**3-(4-chlorophenylamino)phenol (Table 2, entry 7b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (204 mg, 93%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.22 (d, 2H, J = 8.0), 7.10 (t, 1H, J = 8.0), 7.01 (d, 2H, J = 8.0), 6.59 (d, 1H, J = 8.0), 6.50 (s, 1H), 6.40 (d, 1H, J = 8.0), 5.67 (s, 1H), 4.74 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 144.7, 141.4, 130.7, 129.5, 126.2, 119.9, 110.4, 108.3, 104.4. IR (KBr disc, $cm^{-1}$): 3503, 3410, 1588, 1489, 1330, 1130, 1273, 1152, 964, 822, 767, 689, 668, 529, 498. Anal. Calcd for $C_{12}H_{10}ClNO$: C, 73.34; H, 6.59. Found: C, 73.59; H, 6.69. m.p. 111-112 ºC.

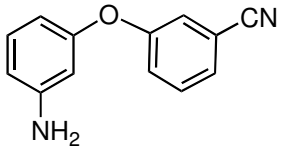



**Ethyl 3-(3-aminophenoxy)benzoate (Table 2, entry 8a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (226 mg, 88%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.74 (d, 1H, J = 8.0), 7.66 (s, 1H),

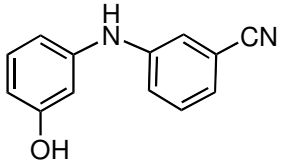
7.35 (t, 1H, J = 8.0), 7.18-7.16 (m, 1H), 7.07 (t, 1H, J = 8.0), 6.42-6.39 (m, 1H), 6.36-6.34 (m, 1H, ), 6.29 (t, 1H, J = 2.1), 4.33 (q, 2H, J = 8.0), 3.71 (s, 2H), 1.34 (t, 3H, J = 8.0). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 166.3, 158.2, 157.5, 148.4, 132.4, 130.7, 129.8, 124.5, 123.6, 120.1, 110.7, 109.0, 105.8, 61.4, 14.5. IR (KBr disc, $cm^{-1}$): 3468, 3377, 2982, 1713, 1627, 1603, 1582, 1489, 1465, 1442, 1392, 1368, 1283, 1215, 1168, 1147, 1100, 1076, 1022, 999, 970, 924, 851, 815, 759, 696, 684. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88. Found: C, 70.30; H, 5.87.




**Ethyl 3-(3-hydroxyphenylamino)benzoate (Table 2, entry 8b and 8c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL), aryl bromide (1.0 mmol) at 110 ºC for 80 min (entry 8b) and general procedure D for aryl chloride (1.0 mmol) at 110 ºC for 90 min (entry 8c) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (221 mg, 86%, entry 8b; 222 mg, 86%, entry 8c). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.74 (s, 1H), 7.58 (d, 1H, J = 8.0), 7.32- 7.26 (m, 2H), 7.13 (t, 1H, J = 8.0), 6.63-6.57 (m, 2H), 6.44 (d, 1H, J = 8.0), 5.80 (s, 1H), 5.21 (s, 1H), 4.35 (q, 2H, J = 8.0), 1.38 (t, 3H, J = 8.0). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 167.5, 157.2, 144.2, 143.3, 131.5, 130.6, 129.5, 122.3, 122.0, 119.0, 110.4, 108.8, 105.0, 61.6, 14.5. IR (KBr disc, $cm^{-1}$): 3372, 2982, 1695, 1599, 1529, 1492, 1420, 1369, 1293, 1236, 1157, 1108, 1083, 1022, 1000, 979, 851, 752, 700, 684, 532. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88. Found: C, 70.16; H, 5.93.

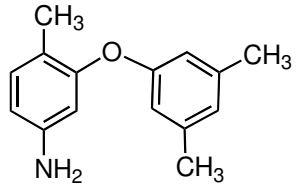



**3-(3-aminophenoxy)benzonitrile (Table 2, entry 9a)**. The general procedure B for the Cu-catalyzed O- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (152 mg, 70%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.36 (t, 1H, J = 8.0), 7.30 (d, 1H, J = 8.0), 7.21-7.18 (m, 2H), 7.10 (t, 1H, J = 8.0), 6.48-6.46 (m, 1H), 6.36-6.33 (m, 1H), 6.31 (s, 1H), 3.77 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.3, 156.8, 148.7, 131.0, 130.8, 126.5, 123.1, 121.3, 118.6, 113.5, 111.6, 109.6, 106.5. IR (KBr disc, $cm^{-1}$): 3376, 3465, 3224, 3068, 2232, 1576, 1489, 1428, 1323, 1251, 1173, 1154, 997, 971, 929, 852, 780, 681, 526, 452. Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79. Found: C, 74.28; H, 4.68.

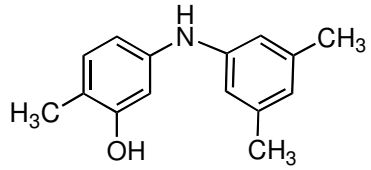



**3-(3-hydroxyphenylamino)benzonitrile (Table 2, entry 9b, entry 9c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5

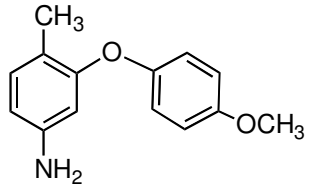
mmol), *t*-BuOH (2.0 mL), aryl bromide (1.0 mmol) at 110 ºC for 80 min (entry 9b) and general procedure D with aryl chloride (1.0 mmol) at 110 ºC for 90 min (entry 9c) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as off-white solid (197 mg, 94%, entry 9b; 183 mg, 87%, entry 9c). $^{1}$H NMR (400 MHz, $CD_3CN$) δ: 7.31-7.14 (m, 3H), 7.14-7.07 (m, 2H), 6.89 (s, 2H), 6.55-6.40 (m, 2H), 6.35 (d, 1H, J = 8.0), 2.13 ($H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 157.9, 144.6, 143.2, 130.4, 123.2, 120.9, 118.9, 112.7, 110.1, 108.9, 105.1. $^{1}$H NMR (400 MHz, $d_6$-DMSO) δ: 9.36 (s, 1H), 8.47 (s, 1H), 7.38-7.31 (m, 3H), 7.15 (d, 1H, J = 4), 7.05 (t, 1H, J = 8.0), 6.55 (s, 2H), 6.35 (d, 1H, J = 8.0), 3.34 ($H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 158.3, 144.7, 142.9, 130.5, 130.1, 122.2, 120.6, 119.2, 117.9, 111.9, 109.1, 108.7, 104.9. IR (KBr disc, cm$^{-1}$): 3359, 2232, 1595, 1490, 1337, 1157, 777, 680. Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.27; H, 4.79. Found: C, 73.98; H, 4.82. m.p. 122 ºC.



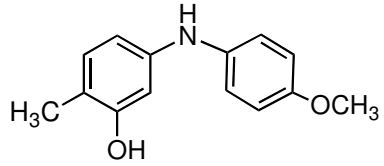

**3-(3,5-dimethylphenoxy)-4-methylaniline (Table 2, entry 10a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (198 mg, 87%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.03 (d, 1H, J = 8.0), 6.73 (s, 1H), 6.60 (s, 2H), 6.42 (dd, 1H, J = 8.0), 6.27 (s, 1H), 3.53 (s, 2H), 2.30 (s, 6H), 2.16 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.1, 155.5, 145.9, 139.7, 132.0, 124.4, 119.7, 115.5, 111.1, 107.1, 21.6, 15.6. IR (KBr disc, cm$^{-1}$): 3460, 3375, 3216, 3022, 2919, 2861, 2734, 1615, 1595, 1508, 1464, 1380, 1295, 1276, 1206, 1167, 1140, 1115, 1027, 996, 954, 930, 838, 808, 687, 659, 616. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.09; H, 7.52.



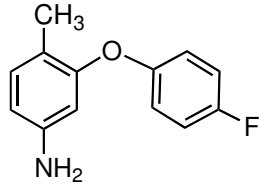

**5-(3,5-dimethylphenylamino)-2-methylphenol (Table 2, entry 10b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol (entry 10b) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (213 mg, 94%, entry 10b). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.99 (d, 1H, J = 8.0), 6.66 (s, 2H), 6.58 (s, 2H), 6.50 (d, 1H, J = 4), 5.41 (s, 1H), 4.94 (s, 1H), 2.27 (s, 6H), 2.19 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 154.5, 143.6, 142.8, 139.3, 131.7, 122.9, 116.5, 115.7, 111.2, 105.4, 21.7, 15.3. IR (KBr disc, cm$^{-1}$): 3387, 2919, 1599, 1522, 1473, 1399, 1338, 1233, 1186, 1114, 998, 833. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.07; H, 7.61. m. p. 118 ºC.



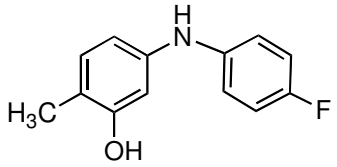
**3-(4-methoxyphenoxy)-4-methylphenylamine (Table 2, entry 11a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown oil (195 mg, 85%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.98 (d, 1H, J = 8.0), 6.91-6.83 (m, 4H), 6.34 (dd, 1H, J = 8.0, J = 4), 6.14 (s, 1H), 3.78 (s, 3H), 3.57 (s, 2H), 2.16 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 155.5, 151.2, 145.8, 132.0, 119.7, 118.8, 115.0, 110.3, 105.6, 55.9, 15.6. IR (KBr disc, $cm^{-1}$): 3455, 3372, 3220, 3002, 2948, 2835, 1869, 1628, 1584, 1505, 1463, 1441, 1381, 1303, 1278, 1246, 1211, 1181, 1164, 1116, 1034, 998, 958, 833, 770, 700. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.10; H, 6.64.



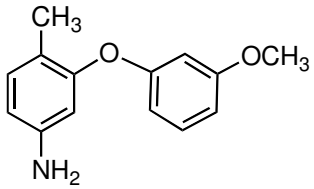
**3-[(4-methoxyphenyl)amino]-6-methylphenol (Table 2, entry 11b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (176 mg, 77%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.99 (d, 2H, J = 6.1), 6.94 (d, 1H, J = 8.0), 6.82 (d, 2H, J = 8.0), 6.42 (d, 1H, J = 6.1), 6.34 (s, 1H), 5.38 (s, 2H), 3.77 (s, 3H), 2.16 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 155.1, 154.8, 144.6, 136.4, 131.7, 122.1, 115.4, 114.9, 109.0, 103.3, 55.9, 15.3. IR (KBr disc, $cm^{-1}$): 3389, 2935, 2835, 2360, 2341, 1624, 1511, 1464, 1399, 1324, 1299, 1240, 1168, 1115, 1033, 998, 828, 773, 668, 627, 515. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.46; H, 6.58. m. p. 97-100 ºC.



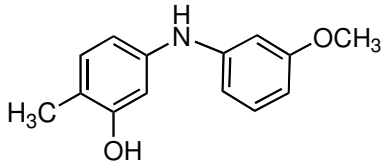
**3-(4-fluorophenoxy)-4-methyl-phenylamine (Table 2, entry 12a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (182 mg, 84%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.01-6.96 (m, 3H), 6.90-6.84 (m, 2H), 6.39 (dd, 1H, J = 8.0, J = 4), 6.19 (d, 1H), 3.61 (s, 2H), 2.17 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.6, 157.3, 155.7, 153.9, 146.0, 132.2, 119.3, 119.1, 116.4, 116.2, 111.2, 106.5, 15.2. IR (KBr disc, $cm^{-1}$): 3455, 3376, 3216, 3052, 2927, 2428, 1869, 1628, 1583, 1500, 1462, 1432, 1383, 1306, 1275, 1196, 1160, 1117, 1093, 998, 956, 833, 811, 780, 702, 648, 619, 507. Anal. Calcd for $C_{13}H_{12}FNO$: C, 71.87; H, 5.57. Found: C, 71.96; H, 5.51.



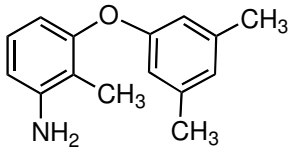
**3-[(4-fluorophenyl)amino]-6-methylphenol (Table 2, entry 12b and 12c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 12b) and general procedure D with aryl chloride (entry 12c, 70 min) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (183 mg, 84%, entry 12b; 187 mg, 86%, entry 12c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.99-6.91 (m, 5H), 6.47 (dd, 1H, J = 8.0, J = 4), 6.42 (s, 1H), 5.44 (s, 1H), 4.85 (s, 1H), 2.16 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.3, 156.9, 154.6, 143.5, 139.4, 131.8, 120.6, 116.2, 116.0, 110.1, 104.2, 15.2. IR (KBr disc, $cm^{-1}$): 3488, 3399, 1624, 1586, 1522, 1328, 1227, 1154, 1110, 1091, 999, 841, 829, 820, 806, 785, 710, 598, 505. Anal. Calcd for $C_{13}H_{12}FNO$: C, 71.87; H, 5.57. Found: C, 71.87; H, 5.56. m. p. 106-107 ºC.



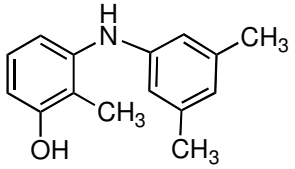
**3-(3-methoxyphenoxy)-4-methyl-phenylamine (Table 2, entry 13a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a white solid (186 mg, 81%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.17 (t, 1H, J = 8.0), 6.99 (d, 1H, J = 8.0), 6.60-6.57 (m, 1H), 6.51-6.47 (m, 2H), 6.41 (dd, 1H, J = 8.0, J = 4), 6.27 (d, 1H), 3.75 (s, 3H), 3.54 (s, 2H), 2.10 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 161.1, 159.4, 155.0, 146.0, 132.1, 130.2, 119.7, 111.4, 109.8, 108.0, 107.3, 103.7, 55.5, 15.5. IR (KBr disc, $cm^{-1}$): 3455, 3373, 3218, 3004, 2941, 2836, 1603, 1508, 1489, 1452, 1382, 1306, 1282, 1194, 1168, 1141, 1115, 1041, 999, 965, 922, 848, 810, 768, 688, 598. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34.; H, 6.59. Found: C, 73.31; H, 6.56. m. p. 51 ºC.



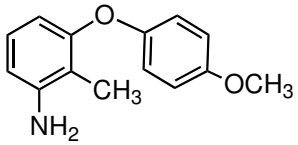
**3-[(3-methoxyphenyl)amino]-6-methylphenol (Table 2, entry 13b, entry 13c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 13b) and general procedure D with aryl chloride (entry 13c, 70 min) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (208 mg, 91%, entry 13b; 211 mg, 92%, entry 13c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.15 (t, 1H, J = 8.0), 7.0 (d, 1H, J = 8.0), 6.63-6.57 (m, 4H), 6.45 (d, 1H, J = 8.0), 5.61 (s, 1H), 4.66 (s, 1H), 3.78 (s, 3H), 2.19 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 106.1, 103.9, 100.6, 99.6, 96.0, 95.5, 90.9, 89.0, 88.6, 87.1,87.0, 86.2, 69.7, 55.8. IR (KBr disc, $cm^{-1}$): 3388, 2938, 1599, 1523, 1493, 1464, 1399, 1274, 1234, 1207, 1155, 1115, 1046, 1000, 837, 807, 769, 689.



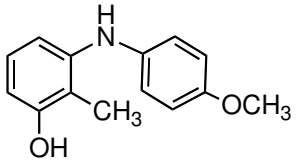
**3-(3,5-dimethylyphenoxy)-2-methylphenylamine (Table 2, entry 14a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a white solid (195 mg, 86%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.00 (t, 1H, J = 8.0), 6.70 (s, 1H), 6.57 (s, 2H), 6.52 (d, 1H, J = 8.0), 6.41 (d, 1H, J = 8.0), 3.71 (s, 2H), 2.28 (s, 6H), 2.07 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.5, 155.2, 146.5, 139.6, 127.1, 124.2, 115.1, 114.8, 111.0, 110.7, 21.6, 10.0. IR (KBr disc, $cm^{-1}$): 3472, 3384, 2918, 2859, 2360, 2341, 1616, 1580, 1472, 1379, 1297, 1246, 1204, 1165, 1146, 1120, 1075, 1041, 952, 905, 792, 838, 792, 724, 686, 668. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.16; H, 7.58. m. p. 79-80 ºC.



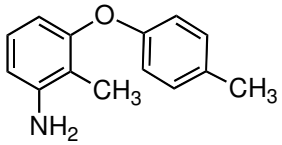
**3-[(3,5-dimethylphenyl)amino]-2-methylphenol (Table 2, entry 14b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (213 mg, 94%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.03 (t, 1H, J = 8.0), 6.89 (d, 1H, J = 8.0), 6.63 (s, 3H), 6.49 (d, 1H, J = 8.0), 5.39 (s, 1H), 5.29 (s, 1H), 2.33 (s, 6H), 2.18 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 154.7, 144.3, 143.0, 139.3, 126.8, 122.7, 115.6, 115.3, 112.6, 109.2, 21.7, 10.2. IR (KBr disc, $cm^{-1}$): 3391, 3025, 2918, 2859, 1705, 1591, 1524, 1471, 1402, 1378, 1333, 1278, 1202, 1171, 1075, 1036, 994, 955, 910, 832, 775, 732, 707, 690. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.05; H, 7.61. m. p. 74-75 ºC.



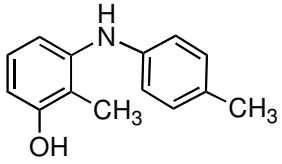
**3-(4-methoxyphenoxy)-2-methyl-phenylamine (Table 2, entry 15a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (183 mg, 80%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.94 (t, 1H, J = 8.0), 6.91-6.83 (m,4H), 6.46 (d, 1H, J = 8.0), 6.28 (d, 1H, J = 10.1), 3.78 (s, 3H), 3.69 (s, 2H), 2.09 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.4, 155.3, 151.7, 146.5, 127.0, 119.4, 114.9, 113.8, 110.5, 109.1, 55.9, 9.8. IR (KBr disc, $cm^{-1}$): 3472, 3382, 3223, 3000, 2933, 2835, 2053, 1623, 1584, 1504, 1471, 1441, 1380, 1297, 1240, 1215, 1166, 1123, 1103, 1073, 1035, 1007, 924, 832, 791, 743, 708, 551, 512. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.59; H, 6.69.



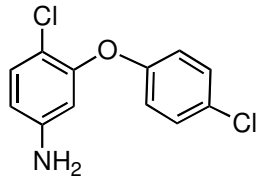
**3-[(4-methoxyphenyl)amino]-2-methylphenol (Table 2, entry 15b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a white solid (197 mg, 86%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.99-6.96 (m, 2H), 6.90 (t, 1H, J = 8.0), 6.85-6.83 (m, 2H), 6.59 (d, 1H, J = 8.0), 6.33 (d, 1H, J = 6.1), 5.24 (s, 1H), 4.84 (s, 1H), 3.78 (s, 3H), 2.12 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 155.2, 154.5, 144.9, 136.7, 126.8, 122.4, 114.9, 112.0, 108.8, 107.4, 55.8, 9.7. IR (KBr disc, $cm^{-1}$): 3415, 1653, 1616, 1559, 1521, 1472, 1326, 1292, 1245, 1178, 1109, 1074, 1030, 835, 826, 768, 709, 668, 517. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59. Found: C, 73.36; H, 6.45. m. p. 123-124 ºC.



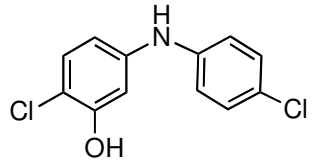
**3-(4-methoxyphenoxy)-2-methylphenylamine (Table 2, entry 16a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a white solid (166 mg, 78%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.12 (d, 2H, J = 10.1), 7.01 (t, 1H, J = 8.0), 6.87 (d, 2H, J = 8.0), 6.51 (d, 1H, J = 8.0), 6.40 (d, 1H, J = 8.0), 3.71 (s, 2H), 2.35 (s, 3H), 2.10 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.2, 155.6, 146.6, 131.9, 130.3, 127.2, 117.6, 114.5, 110.9, 110.1, 20.9, 10.0. IR (KBr disc, $cm^{-1}$): 3473, 3385, 3220, 3029, 2921, 2859, 1886, 1623, 1584, 1505, 1471, 1380, 1307, 1247, 1223, 1169, 1122, 1073, 1043, 1015, 924, 816, 790, 747, 723. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.73; H, 7.12. m. p. 51 ºC.



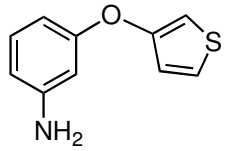
**3-[(4-methylphenyl)amino]-2-methylphenol (Table 2, entry 16b and 16c)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 16b) and general procedure D with aryl chloride (entry 16c, 70 min) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (196 mg, 92%, entry 16b; 194 mg, 91%, entry 16c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.11 (d, 2H, J = 8.0), 6.98 (t, 1H, J = 8.0), 6.93 (d, 2H, J = 8.0), 6.81 (d, 1H, J = 8.0), 6.43 (d, 1H, J = 8.0), 5.13 (s, 2H), 2.33 (S, 3H), 2.17 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 154.6, 143.7, 141.5, 130.8, 126.8, 119.0, 114.0, 111.0, 108.6, 20.9, 10.0. IR (KBr disc, $cm^{-1}$): 3409, 1613, 1525, 1473, 1326, 1294, 1121, 1086, 1074, 1029, 818, 770, 712, 505. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.60; H, 7.00. m. p. 105 ºC.



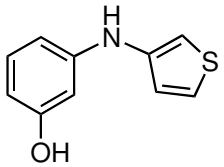

**3-(4-chlorophenoxy)-4-chloro-phenylamine (Table 2, entry 17a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (164 mg, 65%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, 2H, J = 8.0), 7.15 (d, 1H, J = 8.0), 6.86 (d, 2H, J = 8.0), 6.39 (dd, 1H, J = 8.0, J = 4), 6.25 (d, 1H), 3.68 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 155.8, 152.6, 146.9, 131.3, 129.9, 128.3, 119.3, 114.6, 112.2, 107.7. IR (KBr disc, $cm^{-1}$): 3475, 3388, 3219, 3062, 1878, 1622, 1485, 1440, 1320, 1222, 1175, 1146, 1090, 1055, 1010, 967, 827, 718, 671, 665, 645, 496, 460. Anal. Calcd for $C_{12}H_9Cl_2NO$: C, 56.72; H, 3.57. Found: C, 57.00; H, 3.50.



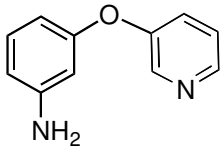

**3-[(4-chlorophenyl)amino]-6-chlorophenol (Table 2, entry 17b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (8 mg, 1.0 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL), aryl bromide (1.0 mmol) at 110 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (230 mg, 91%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, 2H, J = 8.0), 7.15 (d, 1H, J = 8.0), 7.00 (d, 2H, J = 8.0), 6.71 (s, 1H), 6.53 (d, 1H, J = 8.0), 5.68 (s, 1H), 5.54 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.2, 143.6, 141.1, 129.6, 129.5, 126.6, 120.0, 119.8, 111.7, 110.9, 104.9. IR (KBr disc, $cm^{-1}$): 3492, 3413, 1611, 1588, 1485, 1328, 1291, 1209, 1164, 1089, 1049, 1006, 973, 859, 824, 816, 790, 692, 672, 608. Anal. Calcd for $C_{12}H_9Cl_2NO$: C, 56.72; H, 3.57. Found: C, 56.88; H, 3.62. m. p. 109 ºC.



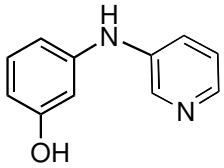

**Benzenamine, 3-(3-thienyloxy)- (Table 2, entry 18a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (103 mg, 54%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.21 (dd, 1H, J = 4, J = 4), 7.06 (t, 1H, J = 8.0), 6.83 (dd, 1H, J = 6.1, J = 2.1), 6.61 (dd, 1H, J = 4), 6.42-6.37 (m, 2H), 6.34 (t, 1H, J = 2.1), 3.67 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.3, 154.3, 148.1, 130.5, 125.2, 121.2, 110.2, 108.0, 107.3, 104.7. IR (KBr disc, $cm^{-1}$) 3376, 3109, 2360, 1617, 1534, 1490, 1387, 1285, 1223, 1179, 1157, 1134, 971, 846, 765, 668. Anal. Calcd for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.77; H, 4.71.



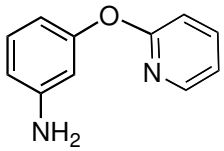
**Phenol, 3-[(3-thienyl)amino]- (Table 2, entry 18b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%) at 110 ºC for 24 h (entry 18b) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a wax of red solid (147 mg, 77%, entry 11b; 128 mg, 67%, entry 11c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.25 (m, 1H), 7.04 (t, 1H, J = 8.0), 6.91 (d, 1H, J = 4.0), 6.76 (s, 1H), 6.52 (d, 1H, J = 4.0), 6.45 (s, 1H), 6.31 (d, 1H, J = 8.0), 5.69 (s, 1H), 4.72 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 146.5, 141.1, 130.7, 125.5, 123.4, 108.4, 107.8, 107.1, 102.5. IR (KBr disc, $cm^{-1}$): 3388, 1611, 1558, 1494, 1448, 1411, 1374, 1279, 1185, 1156, 1080, 997, 980, 835, 756, 685. Anal. Calcd for $C_{10}H_9NOS$: C, 62.80; H, 4.74. Found: C, 62.55; H, 4.83.



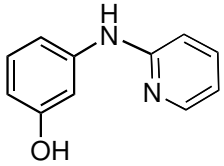
**3-(pyridin-3-yloxy)aniline (Table 2, entry 19a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (122 mg, 66%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 8.38-8.31 (m, 2H), 7.26-7.23 (m, 2H), 7.08 (t, 1H, J = 8.0), 6.44-6.30 (m, 3H), 3.62 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 157.7, 154.1, 148.5, 144.5, 141.7, 130.8, 125.8, 124.2, 111.0, 108.9, 105.7. IR(KBr disc, $cm^{-1}$) 3343, 3215, 1607, 1572, 1490, 1476, 1424, 1325, 1286, 1229, 1188, 1167, 1147, 1102, 1022, 997, 960, 851, 806, 775, 707, 690.



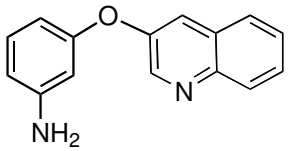
**3-(pyridin-3-ylamino)phenol (Table 2, entry 19b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (8.0 mg, 1.0 mol%), BrettPhos **I** (5.4 mg, 1.0 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) and aryl bromide (1.0 mmol) at 110 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (165 mg, 89%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ: 8.32 (s, 1H), 8.05 (s, 1H), 7.44 (d, 1H, J = 8.0), 7.19-7.16 (m, 2H), 7.06 (t, 1H, J = 8.0), 6.72 (s, 1H), 6.56-6.54 (m, 1H), 6.34 (d, 2H, J = 8.0), 2.13 (s, $H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 158.2, 144.2, 141.5, 140.2, 130.5, 123.9, 123.5, 109.2, 108.4, 104.2. $^{1}$H NMR (400 MHz, $d_6$-DMSO) δ: 9.34 (s, 1H), 8.36 (s, 1H), 8.30 (s, 1H), 8.05 (s, 1H), 7.49 (d, 1H, J = 8.0), 7.27-7.25 (m, 1H), 7.07 (t, 1H, J = 8.0), 6.56 (s, 2H), 6.33 (d, 1H, J = 8.0), 3.34 (s, $H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 158.9, 144.3, 141.0, 140.7, 140.0, 130.7, 124.4, 123.2, 108.6, 108.5, 104.4. IR (KBr disc, $cm^{-1}$): 3333, 3054, 2600, 1704, 1579, 1487, 1456, 1414, 1334, 1277, 1250, 1189, 1175, 1157, 1131, 1110, 1050, 1024, 997, 973, 848, 799, 772, 706, 691, 668, 638, 531. m.p. 152-153 ºC.



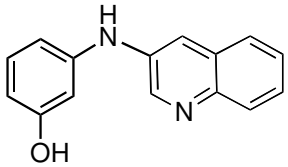
**3-(pyridin-2-yloxy)aniline (Table 2, entry 20a)**. The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (154 mg, 83%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 8.22 (s, 1H), 7.66 (dt, 1H, J = 6.0, J = 2.7), 7.15 (t, 1H, J = 8.0), 6.99-6.97 (m, 1H), 6.87 (d, 1H, J = 8.0), 6.52-6.45 (m, 3H), 3.72 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 164.1, 155.6, 148.3, 148.2, 139.7, 130.6, 118.7, 111.9, 111.8, 111.3, 108.2. IR (KBr disc, $cm^{-1}$): 3348, 1587, 1571, 1490, 1467, 1429, 1285, 1246, 1169, 1148, 996, 961, 855, 774, 691. m.p. 74 ºC.



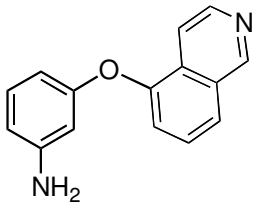
**3-(pyridin-2-ylamino)phenol (Table 2, entry 20b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (8.0 mg, 1.0 mol%), BrettPhos **I** (5.4 mg, 1.0 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) and aryl bromide (1.0 mmol) at 110 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (179 mg, 96%). $^{1}$H NMR (400 MHz, $CD_3CN$) δ: 8.23 (d, 1H, J = 8.0), 7.50 (t, 1H, J = 8.0), 7.33 (s, 1H), 7.19 (s, 1H), 7.06 (t, 1H, J = 8.0), 6.95 (d, 1H, J = 8.0), 6.86 (s, 1H), 6.70-6.81 (m, 2H), 6.41 (d, 1H, J =8.0), 2.13 (s, $H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 157.4, 147.6, 143.5, 137.4, 129.6, 114.7, 110.2, 110.1, 108.1, 105.4. $^{1}$H NMR (400 MHz, $d_6$-DMSO) δ: 9.24 (s, 1H), 8.93 (s, 1H), 8.18-8.17 (m, 1H), 7.59-7.55 (m, 1H), 7.32 (s, 1H), 7.05 (d, 2H, J = 4.0), 6.85 (d, 1H, J=8.0), 6.75 (t, 1H, J = 6.0), 6.35-6.32 (m, 1H), 3.38 (s, $H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 161.8, 160.1, 151.4, 147.0, 141.3, 133.4, 118.3, 115.0, 113.3, 111.8, 109.3. IR (KBr disc, $cm^{-1}$): 3352, 3055, 2349, 2286, 1702, 1597, 1572, 1525, 1482, 1467, 1447, 1326, 1274, 1178, 1154, 1103, 1052, 997, 975, 851, 767, 736, 692, 663, 632, 596, 532, 513. m.p. 136-138 ºC.



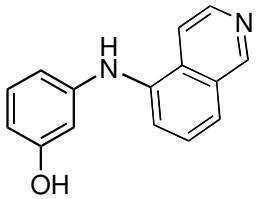
**3-(quinolin-3-yloxy)aniline (Table 2, entry 21a)**. The general procedure B for the Cu-catalyzed O- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as an off-white solid (145 mg, 62%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 8.79 (s, 1H), 8.08 (d, 1H, J = 8.0), 7.67-7.50 (m, 4H), 7.14 (t, 1H, J = 8.0), 6.50-6.39 (m, 3H), 3.79 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 157.7, 151.4, 148.7, 145.7, 145.0, 131.1, 129.5, 128.9, 128.1, 127.5, 127.4, 120.7, 111.4, 109.3, 106.1. IR (KBr disc, $cm^{-1}$): 3459, 3326, 3210, 1630, 1603, 1584, 1490, 1224, 1344, 1277, 1213, 1178, 1139, 985, 958, 887, 865, 835, 785, 756, 685. m.p. 118-119 ºC.



**3-(quinolin-3-ylamino)phenol (Table 2, entry 21b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (8.0 mg, 1.0 mol%), BrettPhos **I** (5.4 mg, 1.0 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) and aryl bromide (1.0 mmol) at 110 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow solid (222 mg, 93%). $^1$H NMR (400 MHz, $d_6$-DMSO) δ: 9.44 (s, 1H), 8.75 (s, 1H), 8.67 (s, 1H), 7.92-7.80 (m, 3H), 7.52-7.49 (m, 2H), 7.15 (t, 1H, J=8.0), 6.73-6.72 (m, 2H), 6.43-6.40 (m, 1H), 3.38 (s, $H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 159.0, 145.9, 144.0, 143.0, 138.1, 130.8, 129.4, 129.1, 127.5, 127.2, 126.3, 114.9, 109.0, 105.0. IR (KBr disc, cm$^{-1}$): 3337, 3057, 1701, 1597, 1540, 1491, 1456, 1419, 1385, 1357, 1282, 1216, 1192, 1157, 961, 845, 780, 749, 689, 668, 613, 532. m.p. 207-208 ºC.

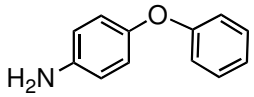


**3-(isoquinolin-5-yloxy)aniline (Table 2, entry 22a)**. The general procedure B for the Cu-catalyzed O- arylation of 3-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (149 mg, 63%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 9.26 (s, 1H), 8.53 (d, 1H, J = 4.0), 7.97 (d, 1H, J = 8.0), 7.70 (d, 1H, J = 12.0), 7.48 (t, 1H, J=8.0), 7.15-7.10 (m, 2H), 6.48-6.36 (m, 3H), 3.75 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.3, 152.6, 152.4, 148.4, 143.3, 130.8, 130.0, 129.6, 127.5, 122.5, 117.0, 115.2, 110.9, 109.0, 105.7. IR (KBr disc, cm$^{-1}$): 3338, 1607, 1584, 1489, 1457, 1430, 1375, 1319, 1271, 1239, 1179, 1146, 1090, 1032, 996, 955, 830, 754, 690. Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12. Found: C, 76.05; H, 5.11. m.p. 102 ºC.

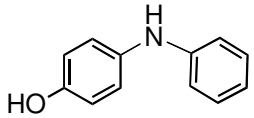


**3-(isoquinolin-5-ylamino)phenol (Table 2, entry 22b)**. The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with BrettPhos precatalyst, **8** (8.0 mg, 1.0 mol%), BrettPhos **I** (5.4 mg, 1.0 mol%), 3-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) and aryl bromide (1.0 mmol) at 110 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (219 mg, 93%). $^1$H NMR (400 MHz, $CD_3CN$) δ: 9.19 (s, 1H), 8.52 (d, 1H, J = 4.0), 7.83 (d, 1H, J = 4.0), 7.63 (d, 1H, J = 4.0), 7.51 (m, 2H), 7.07 (t, 1H, J = 8.0), 6.88 (s, 1H), 6.84 (s, 1H), 6.58 (d, 1H, J =4.0), 6.49 (s, 1H), 6.34 (d, 1H, J = 4.0), 2.13 (s, $H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 158.1, 152.9, 142.6, 130.4, 127.8, 121.1, 115.4,

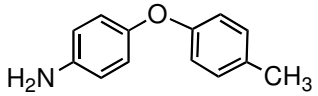
109.8, 108.1, 104.7. $^1$H NMR (400 MHz, $d_6$-DMSO) δ: 9.30 (d, 1H, J = 8.0), 8.52 (d, 1H, J = 4.0), 8.31 (s, ,1H), 8.06 (d, 1H, J = 8.0), 7.68 (d, 1H, J = 8.0), 7.60-7.54 (m, 2H), 7.08 (t, 1H, J = 8.0), 6.61-6.59 (m, 2H), 6.36 (d, 1H, J = 8.0), 3.38 (s, $H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 158.9, 153.1, 145.7, 142.7, 139.6, 130.5, 130.1, 129.4, 128.4, 120.4, 117.1, 116.3, 109.5, 108.5, 105.4. IR (KBr disc, cm$^{-1}$): 3357, 1705, 1590, 1490, 1448, 1385, 1330, 1281, 1256, 1185, 1155, 1044, 965, 827, 750, 692, 533. m.p. 178 ºC.



**4-Phenoxyaniline (Table 3, entry 1a)**.[2] The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (124 mg, 67%; note that the corresponding N-arylated product was isolated in 2% yield). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.26 (t, 2H, J = 8.0), 6.99 (t, 1H, J = 8.0), 6.91 (d, 2H, J = 6.1), 6.86 (d, 2H, J = 8.0), 6.66 (d, 2H, J = 8.0), 3.57 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.1, 148.8, 142.9, 129.7, 122.3, 121.4, 117.4, 116.4. IR (KBr disc, cm$^{-1}$): 3392, 1624, 1589, 1506, 1486, 1384, 1227, 1159, 1070, 1021, 914, 869, 828, 785, 694, 507. Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99. Found: C, 77.79; H, 5.94. m. p. 83-84 ºC.



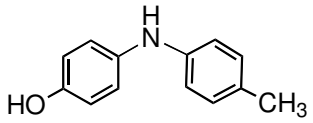
**4-Hydroxy diphenylamine (Table 3, entry 1b)**.[3] The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (entry 1b) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (170 mg, 92%, entry 1b). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.23 (t, 2H, J = 8.0), 7.17 (d, 2H, J = 8.0), 6.90 (d, 2H, J = 8.0), 6.86 (t, 1H, J = 6.1), 6.77 (d, 2H, J = 8.0), 5.45 (s, 1H), 4.64 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 151.1, 145.3, 136.1, 129.6, 122.7, 120.0, 116.4, 116.1. IR (KBr disc, cm$^{-1}$): 3378, 1599, 1507, 1457, 1412, 1318, 1238, 1102, 822, 744, 693, 511. Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99. Found: C, 78.00; H, 5.94. m. p. 70 ºC.



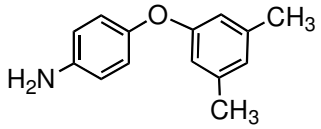
**4-(4-Methylphenoxy)aniline (Table 3, entry 2a and entry 2b)**.[4] The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (127 mg, 64%, entry 2a; note that the corresponding N-arylated product was isolated in 2% yield).

**Table 3, entry 2b.** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (19 mg, 0.10 mmol, 10 mol%), aryl bromide (1.0 mmol ), 4-aminophenol (2.0 mmol) and $K_2CO_3$ (828 mg, 6.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, ligand CyDMEDA, **2** (32 μL, 0.20 mmol, 20 mol%) and remaining liquid reagents were added, followed by butyronitrile (3.0 mL) by syringe. The tube was placed in a preheated oil bath at 80 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to

room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1) generating the title compound as a grey solid (80 mg, 40%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.08 (d, 2H, J = 8.0), 6.86-6.83 (m, 4H), 6.67 (d, 2H, J = 8.0), 3.57 (s, 2H), 2.30 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.7, 149.4, 142.6, 131.8, 130.2, 120.9, 117.6, 116.4, 20.8. IR (KBr disc, cm$^{-1}$) 3397, 1635, 1499, 1384, 1224, 869, 817, 509. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.15; H, 6.45. m. p. 123 ºC.



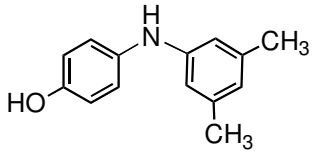

**Phenol, 4-[(4-methylphenyl)amino]- (Table 3, entry 2c)**.[5] The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (entry 2c) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as an off white solid (179 mg, 90%, entry 2c). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.02 (d, 2H, J = 5.0), 6.97-6.93 (m, 2H), 6.83 (d, 2H, J = 8.0), 6.76-6.72 (m, 2H), 5.36 (s, 1H), 4.70 (s, 1H), 2.26 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 150.7, 142.5, 136.9, 130.0, 129.7, 121.5, 116.8, 116.3, 20.8. IR (KBr disc, cm$^{-1}$): 3409, 2360, 1614, 1516, 1224, 1099, 814, 668, 506. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.21; H, 6.61. m. p. 122 ºC.



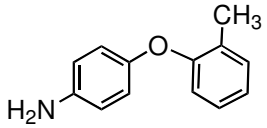

**4-(3,5-dimethylphenoxy)aniline (Table 3, entry 3a and 3b)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a dark brown solid (162 mg, 76%, entry 3a).

**Table 3, entry 3b.** An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (19 mg, 0.10 mmol, 10 mol%), aryl bromide (1.0 mmol ), 4-aminophenol (2.0 mmol) and $K_2CO_3$ (828 mg, 6.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, ligand CyDMEDA, **2** (32 μL, 0.20 mmol, 20 mol%) and remaining liquid reagents were added, followed by butyronitrile (3.0 mL) by syringe. The tube was placed in a preheated oil bath at 80 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1) generating the title compound as a dark brown solid (89 mg, 42%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 6.98 (d, 2H, J = 8.0), 6.68-6.57 (m, 3H), 6.55

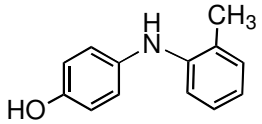
(s, 2H), 3.58 (s, 1H), 2.23 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.1, 148.9, 142.7, 139.6, 124.1, 121.4, 116.5, 115.1, 21.7. IR (KBr disc, $cm^{-1}$): 3372, 2918, 2360, 1615, 1594, 1508, 1299, 1215, 1164, 1135, 1026, 950, 834, 688, 668, 506. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.56; H, 7.08. m. p. 87 ºC.



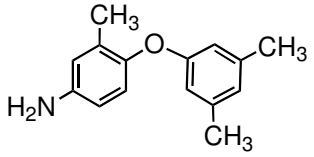
**Phenol, 4-[(3,5-dimethylphenyl)amino]- (Table 3, entry 3c)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (177 mg, 83%, entry 3c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.99 (d, 2H, J = 8.0), 6.76 (d, 2H, J = 8.0), 6.49 (m, 3H), 5.36 (s, 1H), 4.57 (s, 1H), 2.21 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 151.2, 145.4, 139.4, 136.2, 122.8, 122.0, 116.4, 114.0, 21.7. IR (KBr disc, $cm^{-1}$): 3383, 3027, 2360, 1603, 1507, 1335, 1235, 1103, 1035, 827, 692. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.57; H, 6.99. m. p. 84-85 ºC.



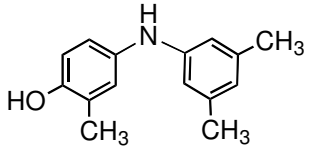
**4-(2-Methylphenoxy)aniline (Table 3, entry 4a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (93 mg, 47%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.22 (d, 1H, J = 8.0), 7.11 (t, 1H, J = 8.0), 7.04 (t, 1H, J = 4.0), 6.80-6.54 (m, 5H), 3.53 (s, 2H), 2.27 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.5, 149.8, 142.1, 131.4, 128.9, 127.1, 122.8, 120.0, 117.6, 116.5, 16.5. IR (KBr disc, $cm^{-1}$): 3366, 1617, 1507, 1384, 1233, 1112, 1044, 875, 837, 750. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58. Found: C, 78.36; H, 6.65. m. p. 61-62 ºC.



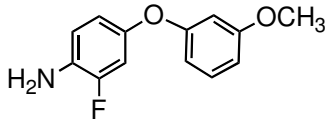
**Phenol, 4-[(2-methylphenyl)amino]- (Table 3, entry 4b and entry 4c)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with BrettPhos precatalyst, **8** (8 mg, 1.0 mol%), 4-aminophenol (1.2 mmol), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) at 110 ºC for 24 h with aryl bromide (1.0 mmol) (entry 4b) and aryl chloride (1.0 mmol) (entry 4c) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (179 mg, 90%, entry 5b; 183 mg, 92%, entry 5c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.18 (d, 1H, J = 8.0), 7.11 (t, 1H, J = 8.0), 7.02 (d, 1H, J = 8.0), 6.97 (d, 2H, J = 8.0), 6.86 (t, 1H, J = 6.1), 6.81-6.79 (m, 2H), 5.71 (s, 1H), 5.29 (s, 1H), 2.26 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 151.1, 143.6, 136.6, 131.1, 127.1, 125.7, 122.7, 120.4, 116.5, 115.5, 18.1. IR (KBr disc, $cm^{-1}$): 3394, 1603, 1584, 1506, 1312, 1231, 1111, 1049, 825, 749, 713, 525. m. p. 86-87 ºC.



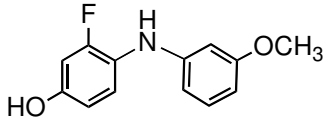
**4-(3, 5-Dimethylphenoxy)-5-methylaniline (Table 3, entry 5a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as grey solid (86 mg, 38%; note that the corresponding N-arylated product was isolated in 16% yield). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.78 (d, 1H, J = 8.0), 6.62 (s, 1H), 6.58 (d, 1H, J = 4.0), 6.52-6.49 (m, 1H), 6.46 (s, 2H), 3.58 (s, 2H), 2.23 (s, 6H), 2.10 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.3, 146.4, 143.1, 139.5, 131.8, 123.5, 122.3, , 118.1, 114.0, 113.8, 113.6, 21.6, 16.5. IR (KBr disc, $cm^{-1}$): 3376, 2919, 1615, 1596, 1498, 1294, 1212, 1158, 1138, 1025, 952, 836, 785. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.13; H, 7.44. m. p. 99-101 ºC.




**4-[(3,5-Dimethylphenyl)amino]-2-methylphenol (Table 3, entry 5b and entry 5c)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (entry 5b) and aryl chloride (entry 5c, 80 min reaction time) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (216 mg, 95%, entry 6b; 213 mg, 94%, entry 6c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.90 -6.51 (m, 6H), 5.36 (s, 1H), 4.64 (s, 1H), 2.25 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 149.5, 145.5, 139.2, 135.9, 124.9, 124.3, 121.6, 120.1, 115.8, 113.7, 21.6, 16.1. IR (KBr disc, $cm^{-1}$): 3388, 2919, 1599, 1503, 1336, 1208, 1110, 1036, 829. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.29; H, 7.69.

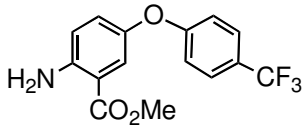



**2-Fluoro-4-(3-methoxyphenoxy)aniline (Table 3, entry 6a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (114 mg, 49%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.16 (t, 1H, J = 8.0), 6.75-6.70 (m, 2H), 6.67-6.64 (m, 1H), 6.59-6.56 (m, 1H), 6.50-6.47 (m, 2H), 3.58 (s, 3H), 3.56 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 161.1, 159.7, 152.9, 150.5, 148.4, 130.9, 130.3, 117.4, 116.2, 109.9, 108.4, 103.9, 55.5. IR (KBr disc, $cm^{-1}$): 3347, 3214, 3059, 1572, 1490, 1424, 1326, 1286, 1230, 1188, 1147, 1102, 1043, 1022, 997, 960, 851, 806, 774, 707, 689. Anal. Calcd for $C_{13}H_{12}FNO_2$: C, 66.94; H, 5.19. Found: C, 6685; H, 5.15.

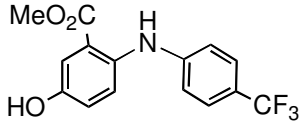



**4-[(3-Methoxyphenyl)amino]-3-fluorophenol (Table 3, entry 6b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (reaction time, 3 h) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (196 mg, 84%, entry 7b). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.18 (t, 1H, J = 10.1), 7.12 (t, 1H, J = 8.0), 6.63 (dd, 1H, J = 12, J = 4.0), 6.55-6.52 (m, 1H), 6.49-6.46 (m, 1H), 6.44-6.39 (m, 2H), 5.40 (s, 1H), 4.74 (s, 1H), 3.73 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 160.8, 152.0, 151.9, 146.1, 130.4,

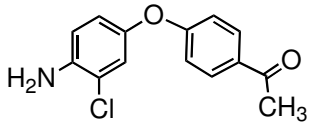
123.7, 111.3, 108.9, 105.4, 104.4, 104.1, 102.0, 55.5. IR (KBr disc, $cm^{-1}$): 3386, 1603, 1506, 1291, 1209, 1156, 1101, 1047, 964, 840, 765, 688. Anal. Calcd for $C_{13}H_{12}FNO_2$: C, 66.94; H, 5.19. Found: C, 67.13; H, 5.25. m. p. 110-111 ºC.



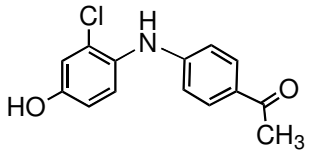

**Methyl-2-amino-5-(4-trifluoromethylphenoxy)benzoate (Table 3, entry 7a)**. An oven-dried screw cap test tube was charged with a magnetic stirbar, copper(I) iodide (9.5 mg, 0.05 mmol, 5 mol%), aryl iodide (0.5 mmol ), methyl-2-amino-5-hydroxybenzoate (1.0 mmol) and $K_2CO_3$ (414 mg, 3.0 mmol). The tube was then evacuated and back-filled with argon. The evacuation/backfill sequence was repeated two additional times. Under a counterflow of argon, ligand CyDMEDA, **2** (16 μL, 0.10 mmol, 10 mol%) and butyronitrile (2.0 mL) were added by syringe. The tube was placed in a preheated oil bath at 70 ºC and the reaction mixture was stirred vigorously for 24 h. The reaction mixture was cooled to room temperature. Ethyl acetate (10 mL) and $H_2O$ (1 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted twice more with ethyl acetate (10 mL). Combined organic layer was dried over $Na_2SO_4$ and filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified via the Biotage SP4 (silica- packed SNAP cartridge, KP-Sil, 10 g) using hexane: ethyl acetate (3:1) affording the title compound as a brown solid (104 mg, 67%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, 1H), 7.53 (d, 2H, J = 8.0), 7.05 (dd, 1H, J = 8.0), 6.96 (d, 2H, J = 8.0), 6.71 (d, 1H, J = 8.0), 5.72 (s, 2H), 3.85 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 168.0, 161.8, 148,.1, 144.8, 127.9, 127.2, 124.4, 124.1, 122.9, 118.4, 116.6, 111.3, 52.0. IR (KBr disc, $cm^{-1}$): 3482, 3377, 1696, 1614, 1590, 1499, 1338, 1292, 1190, 1159, 1123, 1106, 1068, 1011, 840, 581, 523. Anal. Calcd for $C_{15}H_{12}F_3NO_3$: C, 57.88; H, 3.89. Found: C, 58.09; H, 3.91. m. p. 89-90 ºC.



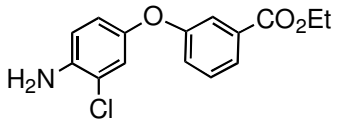

**Methyl-5-hydroxy-2-(4-trifluoromethylbenzenamine)benzoate (Table 3, entry 7b)**. The general procedure B for the Pd-catalyzed N- arylation of methyl-2-amino-5-hydroxybenzoate (0.6 mmol) with BrettPhos precatalyst, **8** (1.6 mg, 0.002 mmol, 0.2 mol%), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL), aryl chloride (0.5 mmol) at 110 ºC for 3 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow solid (135 mg, 87%, entry 7b). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.48-7.43 (m, 3H), 7.31 (d, 1H, J = 8.0), 7.15 (d, 2H, J = 8.0), 6.95 (d, 2H, J =8.0), 4.63 (s, 1H), 3.87 (s, 3H). $^1$H NMR (400 MHz, $d_6$-DMSO) δ: 9.58 (s, 1H), 8.65 (s, 1H), 7.50 (d, 2H, J = 8.0), 7.17-6.15 (m, 2H), 6.97-6.94 (m, 3H), 3.77 (s, 3H), 3.36 (s, $H_2O$). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 167.6, 152.8, 148.5, 134.9, 127.1, 123.8, 122.0, 121.2, 117.1, 115.7, 52.7. IR (KBr disc, $cm^{-1}$): 3452, 2360, 1675, 1653, 1617, 1576, 1559, 1507, 1457, 1433, 1279, 1155, 1101, 888, 818, 784, 688, 668, 537. Anal. Calcd for $C_{15}H_{12}F_3NO_3$: C, 57.88; H, 3.89. Found: C, 58.16; H, 3.96. m. p. 138 ºC.



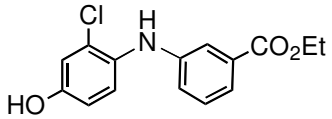
**1-[4-(4-amino-3-chlorophenoxy)phenyl]ethanone (Table 3, entry 8a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. 4-amino-3-chlorophenol hydrochloride was purchased from Aldrich Chemical Co. and 8.0 mmol $K_2CO_3$ was used for the reaction. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (195 mg, 75%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.91 (d, 2H, J = 8.0), 7.00 (s, 1H), 6.92-6.89 (d, 2H, J = 8.0), 6.81-6.78 (m, 2H), 4.03 (s, 2H), 2.55 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 197.0, 162.9, 146.9, 140.6, 131.7, 130.8, 122.1, 120.6, 119.8, 116.7, 116.5, 26.7. IR (KBr disc, $cm^{-1}$): 3464, 3363, 1675, 1594, 1493, 1419, 1359, 1302, 1259, 1234, 1192, 1165, 1112, 1041, 959, 916, 876, 837, 698, 591, 569, 444. Anal. Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62. Found: C, 64.36; H, 4.64. m. p. 65 ºC.



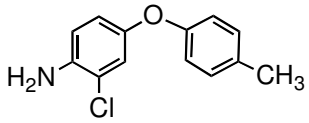

**1-[4-(2-4-hydroxyphenylamino)phenyl]ethanone (Table 3, entry 8b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide was followed with BrettPhos precatalyst, **8** (8 mg, 1.0 mol%), $K_2CO_3$ (4.0 mmol), *t*-BuOH (2.0 mL) at 110 ºC for 24 h. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (227 mg, 87%). $^1$H NMR (400 MHz, $CD_3CN$) δ: 7.75 (d, 2H, J = 8.0), 7.22-7.19 (m, 2H), 6.95 (s, 1H), 6.79-6.76 (m, 1H), 6.71-6.67 (m, 3H), 2.51 (s, 3H), 3.36 (s, 3H), 2.13 (s, $H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 196.0, 155.2, 150.1, 130.5, 129.8, 128.2, 127.9, 116.8, 115.2, 113.1, 25.6. $^1$H NMR (400 MHz, $d_6$-DMSO) δ: 8.27 (s, 1H), 7.74 (d, 2H, J = 8.0), 7.18 (d, 1H, J = 8.0), 6.93 (d, 1H, J = 4.0), 6.79 (d, 1H, J = 8.0), 6.62 (d, 2H, J = 8.0), 3.36 (s, $H_2O$), 2.41 (s, 3H). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 195.9, 156.4, 150, 131, 128, 127, 115, 116, 112.9, 26.7. IR (KBr disc, $cm^{-1}$): 1590, 1499, 1384, 1359, 1327, 1280, 1202, 1178, 1043, 959, 918, 843, 799, 591, 574, 478. Anal. Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62. Found: C, 63.97; H, 4.69. m. p. 143-144 ºC.



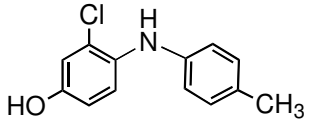

**Ethyl 3-(4-amino-3-chlorophenoxy)benzoate (Table 3, entry 9a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. 4-amino-3-chlorophenol hydrochloride was purchased from Aldrich Chemical Co., 8.0 mmol $K_2CO_3$ was used for the reaction (48 h). Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (125 mg, 43%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.71-7.69 (m, 1H), 7.55 (s, 1H), 7.32 (t, 1H, J = 8.0), 7.10-7.08 (m, 1H,), 6.96 (d, 1H, J = 4.0), 6.79-6.72 (q, 2H, J = 8.0), 4.33 (q, 2H, J = 8.0), 3.94 (s, 2H), 1.34 (t, 3H, J = 8.0). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 166.3, 158.6, 148.2, 139.9, 132.4, 129.8, 123.9, 122.1, 121.4, 119.9, 118.5, 116.7, 61.4, 14.5. IR (KBr disc, $cm^{-1}$): 3373, 2982, 1717, 1624, 1585, 1498, 1484, 1443, 1414, 1368, 1273, 1217, 1188, 1100, 1076, 1022, 948, 906, 815, 755, 682. Anal. Calcd for $C_{15}H_{14}ClNO_3$: C, 61.76; H, 4.84. Found: C, 61.70; H, 4.78.



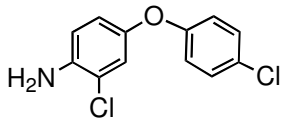

**Ethyl 3-(2-chloro-4-hydroxyphenylamino)benzoate (Table 3, entry 9b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide was followed with BrettPhos precatalyst, **8** (8 mg, 1.0 mol%), $K_2CO_3$ (4.0 mmol), *t*-BuOH (2.0 mL) at 110 ºC for 24 h. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a yellow oil (224 mg, 77%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.58 (s, 1H), 7.53 (d, 1H, J = 8.0), 7.26 (t, 1H, J = 8.0), 7.16 (d, 1H, J = 8.0), 7.08 (d, 1H, J = 8.0), 6.95 (s, 1H), 6.72 (dd, 2H, J = 8.0, J = 4.0), 5.76 (s, 1H), 4.35 (q, 2H, J = 8.0), 1.36 (t, 3H, J = 8.0). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 167.8, 152.0, 144.6, 132.0, 131.4, 129.6, 126.5, 122.2, 121.7, 121.2, 117.4, 117.2, 115.1, 61.7, 14.5. IR (KBr disc, $cm^{-1}$): 3375, 2983, 1689, 1607, 1589, 1520, 1444, 1414, 1370, 1283, 1228, 1108, 1082, 1043, 1022, 997, 950, 908, 856, 753, 682, 636. Anal. Calcd for $C_{15}H_{14}ClNO_3$: C, 61.76; H, 4.84. Found: C, 61.60; H, 5.01.



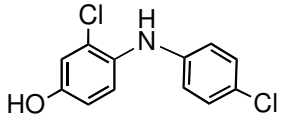

**2-Chloro-4-(4-methylphenoxy)-aniline (Table 3, entry 10a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide (1.0 mmol), CuI (7.5 mol%), 4-amino-3-chlorophenol hydrochloride (1.5 mmol) and butyronitrile (3 mL)at 80 ºC was followed. 4-amino-3-chlorophenol hydrochloride was purchased from Aldrich Chemical Co. and 6.0 mmol $K_2CO_3$ was used for the reaction. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (135 mg, 58%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.09 (d, 2H, J = 8.0), 6.96 (d, 1H), 6.84 (d, 2H, J = 6.1), 6.79 (dd, 1H, J = 8.0, J = 4.0), 6.71 (d, 1H, J = 8.0), 3.89 (s, 2H), 2.30 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.1, 149.4, 139.2, 132.5, 130.4, 120.8, 119.8, 119.4, 118.0, 116.7, 20.9. IR (KBr disc, $cm^{-1}$): 3468, 3379, 3031, 2922, 1884, 1596, 1493, 1413, 1259, 1222, 1192, 1166, 1105, 1039, 1016, 916, 875, 812, 711, 498. Anal. Calcd for $C_{13}H_{12}ClNO$: C, 66.81; H, 5.18. Found: C, 66.85; H, 5.20. m. p. 44 ºC.



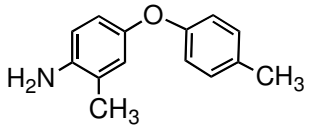

**3-Chloro-4-(p-tolylamino)phenol (Table 3, entry 10b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (24 h reaction time and 4.0 mmol base) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown oil (182 mg, 78%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.14-7.07 (m, 3H), 6.94-6.90 (m, 3H), 6.64 (dd, 1H, J = 10.1, J = 2.1), 5.66 (s, 1H), 4.63 (s, 1H), 2.30 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 149.8, 140.8, 134.5, 131.4, 130.2, 123.9, 119.3, 119.0, 117.1, 115.0, 20.9. IR (KBr disc, $cm^{-1}$): 3404, 2360, 1612, 1517, 1318, 1262, 1042, 912, 808, 668, 508. Anal. Calcd for $C_{13}H_{12}ClNO$: C, 66.81; H, 5.18. Found: C, 66.63; H, 5.28.



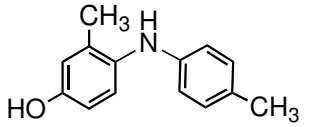
**2-Chloro-4-(4-chlorophenoxy)aniline (Table 3, entry 11a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. 4-amino-3-chlorophenol hydrochloride was purchased from Aldrich Chemical Co. and 8.0 mmol $K_2CO_3$ was used for the reaction (48 h). Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (102 mg, 40%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.21 (d, 2H, J = 8.0), 6.95 (d, 1H, J = 4.0), 6.83 (d, 2H, J = 8.0), 6.78-6.71 (m, 2H), 3.93 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 157.2, 148.3, 139.8, 129.8, 127.7, 121.3, 119.8, 118.9, 116.7. IR (KBr disc, $cm^{-1}$): 3383, 1623, 1585, 1499, 1483, 1258, 1225, 1163, 1095, 1009, 916, 877, 827, 497. Anal. Calcd for $C_{12}H_9Cl_2NO$: C, 56.72; H, 3.57. Found: C, 56.74; H, 3.53.




**3-Chloro-4-(4-chlorophenylamino)phenol (Table 3, entry 11b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with $K_2CO_3$ (4.0 mmol), *t*-BuOH (2.0 mL) and aryl bromide (1.0 mmol) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a purple solid (196 mg, 77%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.22-7.07 (m, 2H), 6.90-6.85 (m, 3H), 6.68 (m, 2H), 5.65 (s, 1H), 5.13 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 150.8, 142.4, 133.1, 129.5, 125.8, 125.5, 121.0, 118.7, 117.2, 115.1. IR (KBr disc, $cm^{-1}$): 1596, 1518, 1469, 1326, 1241, 1196, 1088, 1040, 909, 855, 831, 814, 798, 711, 689, 674, 576, 566, 498. Anal. Calcd for $C_{12}H_9Cl_2NO$: C, 56.72; H, 3.57. Found: C, 56.97; H, 3.60. m. p. 102 ºC.

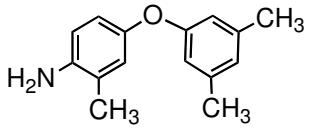



**2-Methyl-4-(4-methylphenoxy)-aniline (Table 3, entry 12a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red solid (126 mg, 55%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.07 (d, 2H, J = 8.0), 6.82 (d, 2H, J = 6.1), 6.76 (s, 1H), 6.72 (dd, 1H, J = 8.0), 6.62 (d, 1H, J = 8.0), 3.48 (s, 2H), 2.29 (s, 3H), 2.13 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.8, 149.2, 140.8, 131.7, 130.2, 124.2, 122.1, 118.4, 117.6, 116.1, 20.8, 17.8. IR (KBr disc, $cm^{-1}$): 3375, 3027, 2923, 1607, 1497, 1457, 1420, 1272, 1232, 1168, 1150, 1105, 1000, 955, 880, 816, 668, 498. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.79; H, 7.03. m. p. 54 ºC.

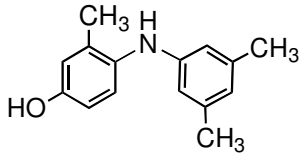



**3-methyl-4-(*p*-tolylamino)phenol (Table 3, entry 12b and entry 12c)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (entry 12b, 24 h reaction time) and aryl chloride (entry 12c, 24 h reaction time) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a dark red wax (185 mg, 87%, entry 12b; 200 mg, 94%, entry 12c). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.10-7.01 (m, 3H), 6.74-6.62 (m, 4H), 5.09 (s, 1H), 4.63 (s, 1H), 2.28 (s, 3H), 2.20 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 151.9, 143.8, 134.6, 133.6, 130.1, 128.8, 124.4, 117.9, 115.9, 113.7, 20.8, 18.3. IR (KBr disc, $cm^{-1}$): 3384, 3024, 2919, 2862,

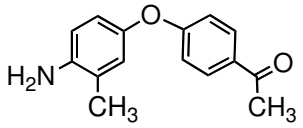
1614, 1586, 1516, 1395, 1289, 1231, 1157, 1109, 1035, 1002, 953, 862, 811, 731, 605, 503.



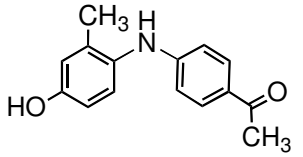
**2-Methyl-4-(3,5-dimethylphenoxy)-aniline (Table 3, entry 13a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a black solid (120 mg, 53%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.78 (d, 1H, J = 4.0), 6.75 (dd, 1H, J = 8.0, J = 4.0), 6.65 (s, 1H), 6.63 (s, 1H), 6.55 (s, 2H), 3.50 (s, 2H), 2.25 (s, 6H), 2.14 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.2, 148.8, 140.9, 139.5, 124.1, 124.0, 122.6, 118.9, 116.0, 115.1, 21.6, 17.8. IR (KBr disc, $cm^{-1}$): 3375, 3024, 2918, 1595, 1501, 1471, 1417, 1380, 1314, 1297, 1230, 1162, 1029, 998, 965, 876, 838, 818, 688, 567. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.16; H, 7.59. m. p. 78-79 ºC.



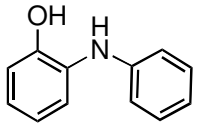
**4-(3,5-dimethylphenylamino)-3-methyl-phenol (Table 3, entry 13b and entry 13c)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide (entry 13b, 3 h reaction time) and aryl chloride (entry 13c, 3 h reaction time) were followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red wax (220 mg, 97%, entry 13b; 220 mg, 97%, entry 13c). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.08 (d, 1H, J = 12.0), 6.73 (s, 1H), 6.65 (d, 1H, J = 8.0), 6.45 (s, 1H), 6.36 (s, 2H), 5.09 (s, 1H), 4.65 (s, 1H), 2.22 (s, 6H), 2.06 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.3, 146.4, 139.2, 134.5, 133.9, 125.6, 121.0, 117.8, 113.7, 112.9, 21.7, 18.3. IR (KBr disc, $cm^{-1}$): 3380, 3026, 2918, 1603, 1500, 1399, 1378, 1334, 1291, 1215, 1155, 1033, 1002, 946, 861, 826, 730, 692.



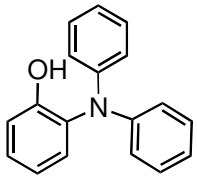
**1-[4-(4-amino-3-methylphenoxy)phenyl]ethanone (Table 3, entry 14a)**. The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a red oil (121 mg, 50%; note that the corresponding N-arylated product was isolated in 3% yield). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, 2H, J = 8.0), 6.89 (d, 2H, J = 8.0), 6.81-6.71 (m, 2H), 6.69 (d, 1H, J = 8.0), 3.61 (s, 2H), 2.51 (s, 3H), 2.12 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 197.2, 163.7, 146.9, 142.1, 131.2, 130.8, 124.3, 123.0, 119.5, 116.3, 26.6, 17.8. IR (KBr disc, $cm^{-1}$): 3367, 1673, 1597, 1497, 1458, 1418, 1359, 1271, 1238, 1166, 1112, 1001, 955, 881, 838, 632, 591, 573.



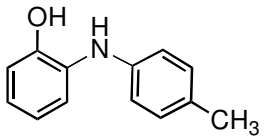
**1-(4-(4-hydroxy-2-methylphenylamino)phenyl)ethanone (Table 3, entry 14b)**. The general procedure B for the Pd-catalyzed N- arylation of 4-aminophenol with aryl bromide was followed with BrettPhos precatalyst, **8** (8 mg, 1.0 mol%), $K_2CO_3$ (2.5 mmol), *t*-BuOH (2.0 mL) at 110 ºC for 24 h. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as off-white solid (234 mg, 97%). $^1$H NMR (400 MHz, $CD_3CN$) δ: 7.75 (d, 2H, J = 8.0), 7.05 (d, 1H), 6.95 (s, 1H), 6.79 (s, 1H), 6.72-6.60 (m, 1H), 6.50-6.59 (m, 3H), 2.42 (s, 3H), 2.21 (s, 3H), 2.13 (s, $H_2O$). $^{13}$C NMR (100 MHz, $CD_3CN$) δ: 195.8, 144.1, 152.1, 136.6, 130.9, 127.9, 127.1, 113.6, 112.2, 25.5, 17.3. $^1$H NMR (400 MHz, $d_6$-DMSO) δ: 9.32 (s, 1H), 8.06 (s, 1H), 7.72 (d, 2H, J = 8.0), 6.97 (d, 1H, J = 8.0), 6.71 (d, 1H, J = 4.0), 6.64 (dd, 1H, J = 8.0, J = 4.0), 6.55 (d, 2H, J = 8.0), 2.39 (s, 3H), 2.07 (s, 3H). $^{13}$C NMR (100 MHz, $d_6$-DMSO) δ: 195.1, 155.2, 152.2, 135.6 , 130.6, 129.9, 127.6, 125.8, 117.4, 113.6, 111.7, 26.0, 17.9. IR (KBr disc, cm$^{-1}$): 3420, 3270, 2253, 2126, 1659, 1595, 1525, 1502, 1462, 1361, 1278, 1219, 1177, 1052, 1026, 1007, 957, 865, 824, 761, 596, 565. Anal. Calcd for $C_{15}H_{15}NO_2$ : C, 74.67; H, 6.27. Found: C, 74.46; H, 6.36. m. p. 164-165 ºC.




**2-(phenylamino)phenol (Table 4, entry 1).**[6] The general procedure for the Cu-catalyzed N- arylation of 2-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (170 mg, 92%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.27-7.20 (m, 3H), 7.09 (s, 1H), 7.01 (s, 1H), 6.92 (d, 2H, J = 5.0), 6.82 (d, 2H, J = 2.5), 6.06 (s, 1H), 5.27 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 150.9, 145.6, 129.9, 129.7, 126.1, 124.5, 121.8, 121.3, 120.6, 116.2, 115.7. IR (KBr disc, cm$^{-1}$): 3402, 3048, 1599, 1496, 1463, 1427, 1308, 1226, 1176, 1099, 1028, 886, 748, 694. Anal. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99. Found: C, 77.63; H, 5.85. m. p. 57 ºC.

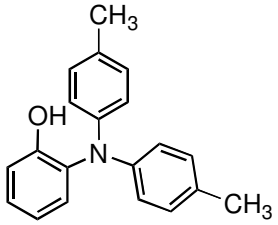



**2-(diphenylamino)phenol (Table 4, entry 1)**[7] was isolated as a brown solid (8 mg, 3%) from the above reaction. $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.28-7.20 (m, 4H), 7.18-7.14 (m, 1H), 7.07-6.96 (m, 8H), 6.91-6.87 (m, 1H), 5.47 (s, 1H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.6, 146.9, 133.3, 129.6, 127.9, 122.9, 121.9, 121.7, 116.7. IR (KBr disc, cm$^{-1}$) 3521, 1588, 1490, 1285, 1203, 1030, 816, 751, 693, 626.

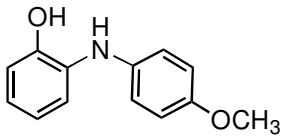



**2-(*p*-tolylamino)phenol (Table 4, entry 2).** The general procedure for the Cu-catalyzed N- arylation of 2-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a black solid (179 mg, 90%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.13 (d, 1H, J = 5.0), 7.03-6.92 (m, 4H), 6.87 (d, 1H, J = 2.5), 6.69 (d, 2H, J = 5.0), 5.77 (s, 1H), 5.16 (s, 1H), 2.25 (s, 3H). $^{13}$C NMR (100

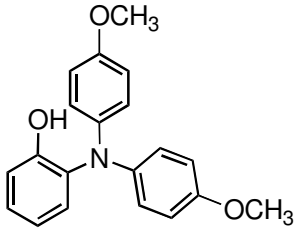
MHz, $CDCl_3$) δ: 150.0, 142.8, 130.7, 130.6, 130.3, 125.1, 123.1, 121.4, 117.2, 115.8, 20.9. IR (KBr disc, $cm^{-1}$): 3403, 3024, 2920, 1607, 1521, 1457, 1308, 1230, 1180, 1098, 1040, 887, 815, 748, 499. m. p. 52 ºC.



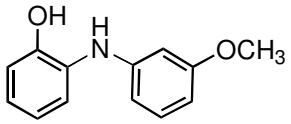

**2-(bis(4-methylphenyl)amino)phenol (Table 4, entry 2)** was isolated as a yellow solid (14 mg, 5%) from the above reaction. $^1H$ NMR (400 MHz, $CDCl_3$) δ: 7.13 (t, 1H, J = 3.8), 7.05-6.97 (m, 5H), 6.90-6.87 (m, 6H), 5.61 (s, 1H), 2.23 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 152.4, 144.8, 133.8, 132.3, 130.2, 129.2, 127.4, 122.0, 121.5, 116.6, 20.9. IR (KBr disc, $cm^{-1}$): 3528, 2920, 1607, 1590, 1505, 1315, 1283, 1229, 1148, 1031, 814, 752, 713, 593, 578, 508. m. p. 66 ºC.




**2-(4-Methoxyphenylamino)phenol (Table 4, entry 3).** The general procedure for the Cu-catalyzed N- arylation of 2-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (176 mg, 82%). $^1H$ NMR (400 MHz, $CDCl_3$) δ: 7.06 (d, 1H, J = 5.0), 6.97-6.79 (m, 7H), 5.66 (s, 1H), 5.15 (s, 1H), 3.74 (s, 3H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 154.6, 148.5, 138.2, 132.1, 123.6, 121.3, 120.7, 119.8, 115.6, 115.1, 56.0. IR (KBr disc, $cm^{-1}$): 3401, 2835, 1607, 1506, 1456, 1242, 1180, 1098, 1033, 887, 823, 751. Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.26; H, 6.04. m. p. 90-92 ºC.

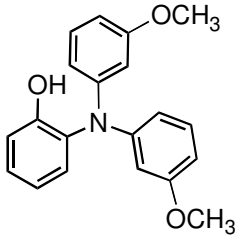



**2-(bis(4-methoxyphenyl)amino)phenol (Table 4, entry 3)** was isolated as a black oil (22 mg, 7%) from the above reaction. $^1H$ NMR (400 MHz, $CDCl_3$) δ: 7.12 (dt, 1H, J = 8.0, J = 2.5), 7.01-6.95 (m, 2H), 6.89 (d, 4H, J = 3.8), 6.85 (dt, 1H, J = 5.0), 6.78-6.75 (m, 4H), 5.58 (s, 1H), 3.74 (s, 6H). $^{13}C$ NMR (100 MHz, $CDCl_3$) δ: 155.5, 152.1, 141.0, 134.3, 128.6, 127.0, 123.4, 121.4, 116.5, 114.9, 55.7. IR (KBr disc, $cm^{-1}$): 3519, 2952, 2835, 1701, 1653, 1589, 1505, 1464, 1241, 1180, 1108, 1036, 828, 783, 753, 583, 526.

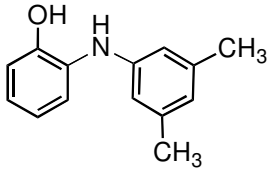



**2-(3-Methoxyphenylamino)phenol (Table 4, entry 4).** The general procedure for the Cu-catalyzed N- arylation of 2-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown oil

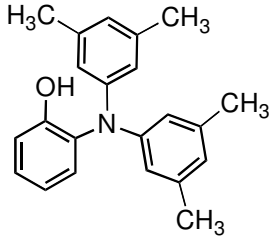
(193 mg, 90%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.17 (d, 1H, J = 5.0), 7.13-7.05 (m, 2H), 6.96 (d, 1H, J = 5.0), 6.87 (t, 1H, J = 5.0), 6.42 (dd, 1H, J = 5.0, J = 2.5), 6.37 (dd, 1H, J = 3.8, J = 1.3), 6.30 (s, 1H), 5.83 (s, 1H), 5.25 (s, 1H), 3.77 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 161.0, 151.0, 147.0, 130.4, 129.1, 126.2, 124.8, 121.2, 115.6, 108.8, 105.7, 102.1, 55.4. IR (KBr disc, $cm^{-1}$): 3375, 3047, 2958, 2836, 2360, 1595, 1506, 1263, 1204, 1156, 1101, 1040, 994, 958, 841, 750, 689, 668, 567, 452. Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09. Found: C, 72.37; H, 6.07.




**2-(bis(3-methoxyphenyl)amino)phenol (Table 4, entry 4)** was isolated as a black oil (10 mg, 3%) from the above reaction. $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.26-7.07 (m, 4H), 7.07 (d, 1H, J = 5.0), 6.97 (d, 1H, J = 5.0), 6.88 (t, 1H, J = 5.0), 6.65-6.56 (m, 6H), 5.49 (s, 1H), 3.72 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 160.7, 152.5, 148.0, 133.1, 130.3, 129.5, 128.0, 121.7, 116.8, 114.7, 108.3, 108.2, 55.4. IR (KBr disc, $cm^{-1}$): 3518, 2938, 2835, 1595, 1489, 1318, 1281, 1255, 1209, 1163, 1140, 1048, 848, 755, 691.

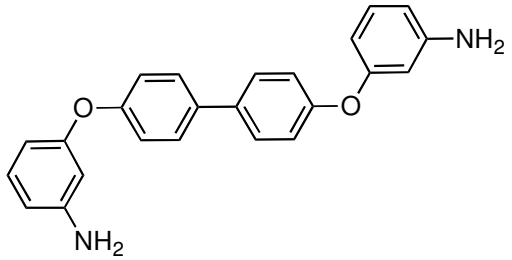



**2-(3,5-Dimethylphenylamino)phenol (Table 4, entry 5).** The general procedure for the Cu-catalyzed N- arylation of 2-aminophenol with aryl iodide was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (202 mg, 95%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.14 (d, 1H, J = 5.0), 7.09 (t, 1H, J = 5.0), 6.96 (d, 1H, J = 5.0), 6.87 (t, 1H, J = 5.0), 6.51 (s, 1H), 6.37 (s, 2H), 5.79 (s, 1H), 5.10 (s, 1H), 2.32 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 151.0, 145.6, 139.5, 129.8, 125.9, 124.6, 122.5, 121.2, 115.8, 114.1, 21.7. IR (KBr disc, $cm^{-1}$): 3403, 2918, 2360, 1653, 1599, 1507, 1327, 1268, 1100, 1035, 832, 747. Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.56; H, 6.95. m. p. 74 ºC.

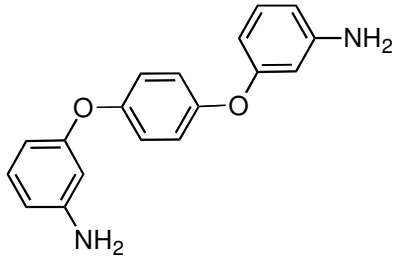



**2-(bis(3,5-dimethylphenyl)amino)phenol (Table 4, entry 5)** was isolated as a yellow solid (9 mg, 3%) from the above reaction. $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.16 (td, 1H, J = 5.0), 7.07 (dd, 1H, J = 5.0), 7.00 (dd, 1H, J = 6.3, J = 1.3), 6.89 (dt, 1H, J = 5.0), 6.64 (d, 6H, J = 2.5), 5.53 (s, 1H), 2.27 (s, 12H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 152.5, 147.1, 139.3, 133.7, 129.5, 127.5, 124.8, 121.5, 120.0, 116.6, 21.6. IR (KBr disc, $cm^{-1}$):

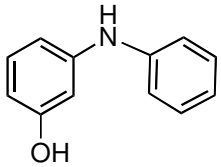
3528, 2918, 1591, 1492, 1377, 1327, 1288, 1225, 1189, 1034, 842, 793, 749, 698, 676. m. p. 129-130 ºC.




**3,3'-(biphenyl-4,4'-diylbis(oxy))dianiline (Figure 4, compound 9).**[8] The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with copper(I) iodide (19 mg, 10 mol%), 2-picolinic acid, **1** (24.6 mg, 0.20 mmol, 20 mol%), aryl iodide (1.0 mmol ), 3-aminophenol (3.0 mmol) and $K_3PO_4$ (1060 mg, 5.0 mmol) at 90 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (331 mg, 90%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, 4H, J = 8.0), 7.14-7.03 (m, 6H), 6.41 (d, 4H, J = 8.0), 6.34 (s, 2H), 3.68 (s, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.4, 156.5, 148.0, 135.6, 130.4, 128.1, 119.3, 110.2, 109.0, 107.8, 105.6. IR (KBr disc, $cm^{-1}$): 3406, 3311, 1600, 1589, 1497, 1467, 1497, 1466, 1400, 1328, 1290, 1246, 1165, 1152, 1133, 1120, 1073, 995, 966, 856, 832, 774, 686, 650. m. p. 144 ºC.

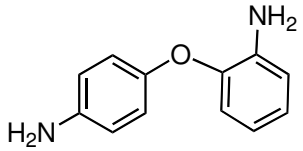



**3,3'-(1,4-phenylenebis(oxy))dianiline (Figure 4, compound 10).** The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with copper(I) iodide (19 mg, 10 mol%), 2-picolinic acid, **1** (24.6 mg, 0.20 mmol, 20 mol%), aryl iodide (1.0 mmol ), 3-aminophenol (3.0 mmol) and $K_3PO_4$ (1060 mg, 5.0 mmol) at 90 ºC for 24 h was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (234 mg, 80%). $^1$H NMR (400 MHz, $CDCl_3$) δ: 7.06 (t, 2H, J = 5.0), 6.97 (s, 4H), 6.38-6.35 (m, 4H), 6.29-6.28 (m, 2H), 3.67 (s, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 159.1, 152.7, 148.2, 130.6, 120.8, 120.0, 110.1, 108.5, 105.1. IR (KBr disc, $cm^{-1}$): 3457, 3367, 1623, 1489, 1463, 1286, 1204, 1168, 1148, 1097, 997, 962, 844, 777, 688, 502. Anal. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.95; H, 5.52. Found: C, 73.66; H, 5.59. m. p. 97 ºC.

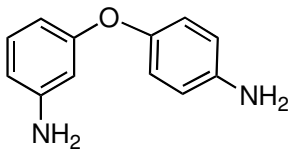



**3-(phenylamino)phenol (Figure 4, compound 12)**.[9] The general procedure C for the Pd-catalyzed N- arylation of 3-aminophenol with aryl bromide (entry 2c) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a

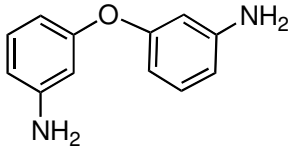
grey solid (174 mg, 94%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.26 (t, 2H, J = 8.0), 7.07 (t, 3H, J = 8.0), 6.96 (t, 1H, J = 8.0), 6.62 (d, 1H, J = 8.0), 6.52 (s, 1H), 6.38 (d, 1H), 5.64 (br, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 156.6, 145.2, 142.8, 130.7, 129.6, 121.8, 118.9, 110.3, 108.0, 104.4. IR (KBr disc, $cm^{-1}$): 3378, 1597, 1498, 1458, 1419, 1336, 1244, 1158, 1086, 969, 833, 769, 741, 685, 699. m. p. 81 ºC.




**2-(4-aminophenoxy)aniline (Figure 4, compound 14).** The general procedure A for the Cu-catalyzed O- arylation of 4-aminophenol with aryl iodide (2-iodoaniline) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a grey solid (66 mg, 33%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.88 (t, 1H, J = 5.0), 6.83-6.79 (m, 2H), 6.78-6.71 (m, 2H), 6.66-6.61 (m, 3H), 3.68 (s, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 149.3, 145.2, 142.2, 137.9, 123.6, 119.5, 118.6, 118.0, 116.3, 116.2. IR (KBr disc, $cm^{-1}$): 3354, 3038, 1619, 1500, 1458, 1268, 1215, 1155, 1031, 880, 835, 746. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04. Found: C, 71.69; H, 6.01. m. p. 76-77 ºC.




**3-(4-aminophenoxy)aniline (Figure 4, compound 15).**[10] The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide (4-iodoaniline) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (156 mg, 54%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 6.88 (t, 1H, J = 8.0), 6.83 (d, 2H, J = 8.0), 6.63 (d, 2H, J = 8.0), 6.32-6.22 (m, 2H), 6.21 (s, 1H), 3.69 (s, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 160.3, 148.5, 148.1, 142.9, 130.4, 121.5, 116.5, 109.3, 107.6, 104.1. IR (KBr disc, $cm^{-1}$): 3429, 3354, 3217, 3040, 2920, 2425, 1873, 1623, 1586, 1508, 1490, 1463, 1384, 1317, 1281, 1215, 1171, 1162, 1145, 1072, 1010, 995, 962, 836, 771, 688, 535, 505. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04. Found: C, 71.68; H, 5.97. m. p. 73 ºC.




**3,3'-oxydianiline (Figure 4, compound 16).**[11] The general procedure A for the Cu-catalyzed O- arylation of 3-aminophenol with aryl iodide (3-iodoaniline) was followed. Isolation and biotage purification (hexane/ethyl acetate) afforded the title compound as a brown solid (156 mg, 78%). $^{1}$H NMR (400 MHz, $CDCl_3$) δ: 7.05 (t, 2H, J = 8.0), 6.38 (d, 4H, J = 12.0), 6.30 (s, 2H), 3.64 (s, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ: 158.5, 148.1, 130.4, 110.2, 109.3, 105.9. IR (KBr disc, $cm^{-1}$): 3440, 3346, 3219, 3051, 1603, 1489, 1462, 1310, 1284, 1193, 1156, 1139, 1070, 995, 979, 930, 847, 769, 688. Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04. Found: C, 71.90; H, 5.95. m. p. 76-77 ºC.

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