The Copper-Catalyzed Coupling of Alkyl Amines and Aryl Iodides: An Efficient System Even in an Air Atmosphere

Fuk Yee Kwong, Artis Klapars and Stephen L. Buchwald*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Supporting Information

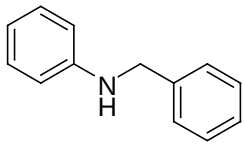
General Considerations: Unless otherwise noted, all chemicals were used as received. Iodobenzene, 4-iodoacetophenone, 4-iodobenzonitrile, 4-iodoanisole, 4-iodotoluene, 3-iodobenzonitrile, 3-iodoanisole, 3-iodonitrobenzene, 2-iodotoluene, 2-iodoanisole and benzylamine were purchased from Alfa Aesar. 4-Chloroiodobenzene, 5-iodo-*m*-xylene, 3-bromoiodobenzene, 3-iodobenzotrifluoride, 3-iodotoluene, 1-iodonaphthalene, hexylamine, 2-methylbenzylamine, *N*-methylbenzylamine, pyrrolidine, piperidine, morpholine, *N*-methylpiperazine, proline and aniline were purchased from Aldrich. Copper(I) iodide was purchased from Strem Chemical. Anhydrous potassium phosphate was purchased from Fluka. 2-Propanol, ethylene glycol and hexane were purchased from Mallinckrodt. Silica gel (230-400 mesh) and ethyl acetate were purchased from Merck. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. ^{1}H NMR and ^{13}C NMR were recorded on a Br ker 300 and 400 MHz instrument with chemical shifts reported relative to residual deuterated solvent peaks. Gas chromatographic analyses were performed on a Hewlett Packard 6890 instrument with FID detector and a Hewlett Packard 10 m × 0.2 mm i.d. HP-1 capillary column. Mass spectra (GC-MS) were recorded on a Hewlett Packard model GCD. All yields reported in the publication represent an average of at least two independent runs. Characterization data for previously unknown compounds were determined from a single run with isolated yields.

Compounds described in the literature were characterized by comparing their ^{1}H NMR and GC-MS to the previously reported data.

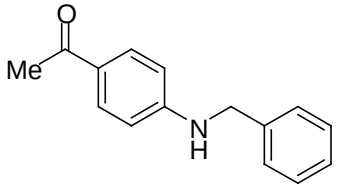
General Procedure for Cu-catalyzed amination under argon atmosphere: Copper (I) iodide (10 mg, 0.05 mmol) and potassium phosphate (425 mg, 2.00 mmol) were put into a Teflon septum screw-capped test tube. The tube was evacuated and back filled with argon. 2-Propanol (1.0 ml), ethylene glycol (111 μl, 2.00 mmol), benzylamine (131 μl, 1.20 mmol) and iodobenzene (112 μl, 1.00 mmol) were added successively by micro-syringe at room temperature. The reaction mixture was heated at 80 °C to give a pale yellow suspension. The reaction was heated for the specified time and then allowed to cool to room temperature. Diethyl ether (2 ml) and water (2 ml) were then added to the reaction mixture. The organic layer was analyzed by GC. The reaction mixture was further extracted by diethyl ether (4 × 10 ml). The combined organic phases were washed with brine and dried over sodium sulfate. The solvent was removed by rotary evaporation to give a brown residue which was purified by column chromatography on silica gel.

General Procedure for Cu-catalyzed amination under air conditions: Copper (I) iodide (10 mg, 0.05 mmol) and potassium phosphate (425 mg, 2.00 mmol) were put into a Telfon septum screw-capped test tube followed by the addition of 2-propanol (1.0 ml), ethylene glycol (111 μl, 2.00 mmol), benzylamine (131 μl, 1.20 mmol) and iodobenzene (112 μl, 1.00 mmol) by micro-syringe at room temperature. The tube was capped and the reaction mixture was heated at 80 °C to give a yellow suspension. The reaction was heated for the specified time and then allowed to cool to room temperature. Diethyl ether (2 ml) and water (2 ml) were then added to the reaction mixture. The organic layer was analyzed by GC. The reaction mixture was further extracted

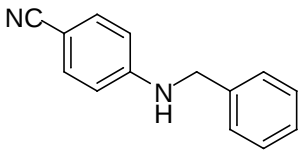
with diethyl ether (4 × 10 ml). The combined organic phases were washed with water, brine and dried over sodium sulfate. The solvent was removed by rotary evaporation to give the brown residue which was purified by column chromatography on silica gel.



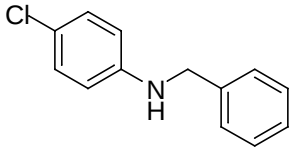
***N*-(Phenyl)benzylamine (Table 2, entry 1)**[1] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.6) afforded *N*-(phenyl)benzylamine[1] (166 mg, 91% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.1, 6.8 Hz, 2H), 7.04-7.07 (m, 5H), 6.58 (t, *J* = 7.0 Hz, 1H), 6.43 (d, *J* = 6.9 Hz, 2H), 4.32 (s, 2H), 4.00 (br s, 1H).



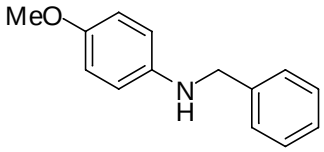
4-(*N*-benzyl)aminoacetophenone (Table 2, entry 3).[2] The general procedure under argon was followed using copper(I) iodide (2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 4-iodoacetophenone (246 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/1, R_f = 0.2) afforded 4-(*N*-benzyl)aminoacetophenone[2] (203 mg, 90% yield) as yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.8 Hz, 2H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.54 (d, *J* = 7.8 Hz, 2H), 4.32 (s, 2H), 4.03 (br s, 1H), 2.55 (s, 3H).



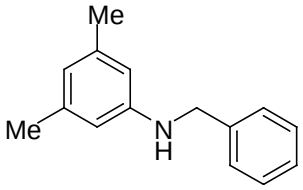
4-(*N*-Benzyl)aminobenzonitrile (Table 2, entry 5).[3] The general procedure under argon was followed using copper (I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 4-iodobenzonitrile (229 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/1, R_f = 0.4) afforded 4-(*N*-benzyl)aminobenzonitrile[3] (164 mg, 79% yield) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 (d, *J* = 7.5 Hz, 2H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.61 (d, *J* = 7.8 Hz, 2H), 4.32 (s, 2H), 4.01 (br s, 1H).



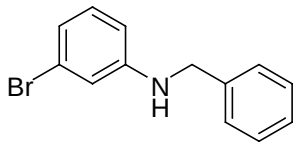
***N*-(4-Chlorophenyl)benzylamine (Table 2, entry 6).**[4] The general procedure under argon was followed using copper (I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 4-chloroiodobenzene (239 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/1, R_f = 0.4) afforded *N*-(4-chlorophenyl)benzylamine[4] (182 mg, 84% yield) as light yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.04-7.07 (m, 5H), 6.37 (d, *J* = 7.5 Hz, 2H), 4.32 (s, 2H), 4.04 (br s, 1H).



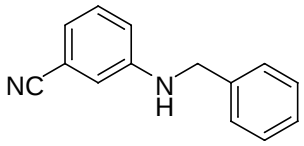
***N*-Benzyl-4-methoxyaniline (Table 2, entry 7).**[4] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 4-iodoanisole (234 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded *N*-benzyl-4-methoxyaniline[4] (192 mg, 90% yield) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.55 (d, *J* = 8.0 Hz, 2H), 6.32 (d, *J* = 7.9 Hz, 2H), 4.32 (s, 2H), 4.09 (br s, 1H), 3.73 (s, 3H).



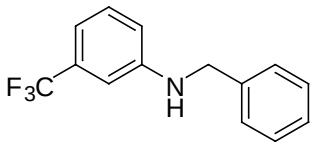
5-(*N*-Benzyl)amino-*m*-xylene (Table 1, entry 8).[5] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 5-iodo-*m*-xylene (144 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded 5-(*N*-benzyl)amino-*m*-xylene[5] (177 mg, 84% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.18 (s, 1H), 6.04 (s, 2H), 4.32 (s, 2H), 4.03 (br s, 1H), 2.35 (s, 6H).



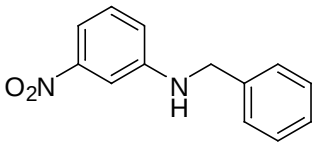
***N*-(3-Bromophenyl)benzylamine (Table 2, entry 10).**[6] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 3-bromoiodobenzene (128 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(3-bromophenyl)benzylamine[6] (217 mg, 83% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.93 (dd, *J* = 7.8, 8.0 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.60 (s, 1H), 6.37 (d, *J* = 7.8 Hz, 1H), 4.32 (s, 2H), 4.03 (br s, 1H).



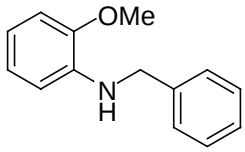
***N*-(3-Cyanophenyl)benzylamine (Table 2, entry 13).**[3] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 3-iodobenzonitrile (229 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.5) afforded *N*-(3-cyanophenyl)benzylamine[3] (165 mg, 80% yield) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 7.8, 8.0 Hz, 1H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.08 (m, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.68 (s, 1H), 4.32 (s, 2H), 4.13 (br s, 1H).



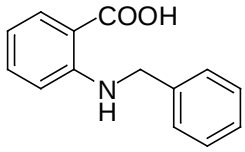
***N*-(3-Trifluoromethylphenyl)benzylamine (Table 2, entry 14).**[7] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 3-iodobenzonitrile (144 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 20/1, R_f = 0.4) afforded *N*-(3-trifluoromethyl-phenyl)benzylamine[7] (229 mg, 91% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.08 (m, 3H), 6.97 (dd, *J* = 7.8, 7.5 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 6.43 (d, *J* = 7.5 Hz, 1H), 4.33 (s, 2H), 3.99 (br s, 1H).



***N*-(3-Nitrophenyl)benzylamine (Table 2, entry 16).**[8] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (109 μl, 1.00 mmol), 3-iodonitrobenzene (349 mg, 1.40 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) afforded *N*-(3-nitrophenyl)benzylamine[8] (164 mg, 72% yield) as orange solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.5 Hz, 1H), 7.36 (s, 1H), 7.30 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.08 (m, 3H), 6.82 (d, *J* = 7.5 Hz, 1H), 4.33 (s, 2H), 3.97 (br s, 1H).

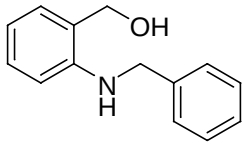


***N*-(2-Methoxyphenyl)benzylamine (Table 2, entry 17).**[3] The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 2-iodoanisole (130 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 1-butanol (1.0 mL) at 100 °C. Column chromatography using a solvent mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.4) afforded *N*-(2-methoxyphenyl)benzylamine[3] (149 mg, 70% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.60 (dd, *J* = 7.8, 7.4 Hz, 1H), 6.55 (d, *J* = 7.6 Hz, 1H), 6.47 (dd, *J* = 7.5, 7.8 Hz, 1H), 6.32 (d, *J* = 7.5 Hz, 1H), 4.30 (s, 2H), 4.09 (br s, 1H).

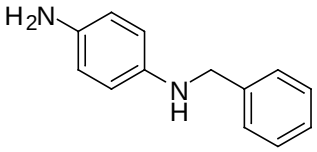


2-(*N*-Benzyl)aminobenzoic acid (Table 2, entry 18-20).[9] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (636 mg, 3.00 mmol), benzylamine (131 μl, 1.20 mmol), 2-iodobenzoic acid (248 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). After heated for a specified duration, the reaction was allowed to reach room temperature. Water and diluted HCl (10%) was added until ~pH 3. Diethyl ether (2 mL) was added and the organic layer was analyzed by tlc. The reaction mixture was further extracted by diethyl ether (4 x 10 mL) and the combined organic phase was washed with brine and dried over Na_2SO_4. The solvent was rotary evaporated and the yellowish-brown residue was purified by column chromatography using a solvent mixture (diethyl ether/ ethyl acetate = 1/ 1, R_f = 0.3) to afford 2-(*N*-benzyl)aminobenzoic acid[9] (161 mg, 71% yield) as light

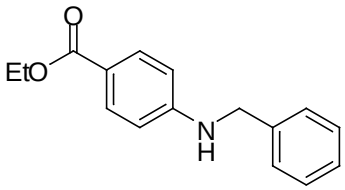
yellow solid. For aryl bromide substrate: copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (636 mg, 3.00 mmol), benzylamine (131 μl, 1.20 mmol), 2-bromobenzoic acid (201 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 1-butanol (1.0 mL) was used and heated to 100 °C. The above workup procedures was followed and obtained 2-(*N*-benzyl)aminobenzoic acid[9] (120 mg, 53% isolated yield) as light yellow solid. For aryl chloride substrate: copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (636 mg, 3.00 mmol), benzylamine (131 μl, 1.20 mmol), 2-chlorobenzoic acid (157 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 1-butanol (1.0 mL) was used and heated to 100 °C. The above workup procedures was followed and obtained 2-(*N*-benzyl)aminobenzoic acid[9] (109 mg, 48% yield) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.01 (s, 1H), 7.91 (d, *J* = 6.9 Hz, 1H), 7.38 (dd, *J* = 7.0, 7.5 Hz, 1H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.79 (dd, *J* = 7.5, 6.9 Hz), 6.64 (d, *J* = 7.0 Hz, 1H), 4.31 (s, 2H), 4.10 (br s, 1H).



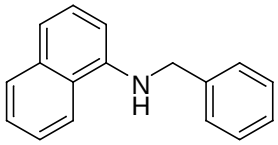
2-(*N*-Benzyl)aminobenzylalcohol (Table 2, entry 21).[10] The general procedure under argon was followed using copper (I) iodide (10 mg, 0.5 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 2-iodobenzylalcohol (234 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 4/ 1, R_f = 0.3) afforded 2-(*N*-benzyl)aminobenzylalcohol[10] (203 mg, 95% yield) as off-white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.0 Hz, 2H), 7.05-7.07 (m, 3H), 6.97 (dd, *J* = 7.8, 7.6 Hz, 2H), 6.51 (t, *J* = 7.5 Hz, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 4.79 (s, 2H), 4.32 (s, 2H), 4.10 (br s, 1H), 2.08 (s, 1H).



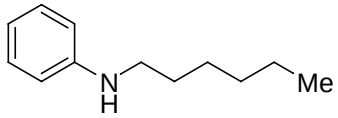
4-(*N*-Benzyl)aminoaniline (Table 2, entry 22).[11] The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (218 μl, 2.0 mmol), 4-iodoaniline (219 mg, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL) at 90 °C. Column chromatography using a solvent gradient (hexane/ ethyl acetate = 2/ 1 to 1/ 1, R_f = 0.2) afforded 4-(*N*-benzyl)aminoaniline[11] (101 mg, 51% yield) as beige solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.24 (d, *J* = 6.9 Hz, 2H), 6.18 (d, *J* = 7.0 Hz, 2H), 4.33 (s, 2H), 4.03 (br s, 1H), 3.99 (br s, 2H).



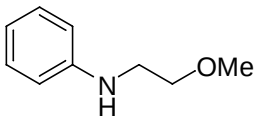
Ethyl 4-(*N*-benzyl)aminobenzoate (Table 2, entry 23).[12] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), ethyl 4-iodobenzoate (167 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and ethanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 5/ 1, R_f = 0.4) afforded ethyl 4-(*N*-benzyl)aminobenzoate[12] (113 mg, 50% yield) as light yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.0 Hz, 2H), 7.14 (dd, *J* = 7.2, 7.1 Hz, 2H), 7.06-7.07 (m, 3H), 6.54 (d, *J* = 7.0 Hz, 2H), 4.29-4.32 (m, 4H), 3.97 (br s, 1H), 1.30 (t, *J* = 11.3 Hz, 3H).



***N*-(1-Naphthyl)benzylamine (Table 2, entry 24).**[13] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), benzylamine (131 μl, 1.20 mmol), 1-iodonaphthlene (146 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(1-naphthyl)benzylamine[13] (163 mg, 70% yield) as light yellow solid. M.p. 69-70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.86 (m, 2H), 7.25-7.48 (m, 10H), 6.67 (dd, *J* = 1.6, 8 Hz), 4.91 (br s, 1H), 4.51 (s, 2H).

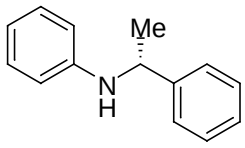


***N*-(Phenyl)hexylamine (Table 3, entry 1).**[14] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00 mmol), hexylamine (159 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded *N*-(phenyl)hexylamine[14] (152 mg, 86% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.04 (dd, *J* = 7.0, 6.9 Hz, 2H), 6.59 (t, *J* = 7.0 Hz, 1H), 6.43 (d, *J* = 7.1 Hz, 2H), 4.30 (br s, 1H), 3.06 (t, *J* = 10.9 Hz, 2H), 1.52 (m, 2H), 1.29-1.33 (m, 6H), 0.96 (t, *J* = 12.1 Hz, 3H).

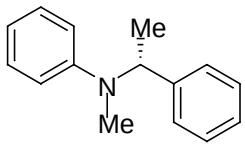


***N*-(2-Methoxyethyl)aniline (Table 3, entry 4).**[15] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00 mmol), 2-methoxyethylamine (104 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent

mixture (hexane/ ethyl acetate = 10/ 1, R_f = 0.2) afforded *N*-(2-methoxyethyl)aniline[15] (138 mg, 91% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.04 (dd, *J* = 7.0, 6.8 Hz, 2H), 6.59 (t, *J* = 7.0 Hz, 1H), 6.43 (d, *J* = 7.0 Hz, 2H), 4.66 (br s, 1H), 3.60 (t, *J* = 11.6 Hz, 2H), 3.29 (t, *J* = 11.9 Hz, 2H), 3.23 (s, 3H).

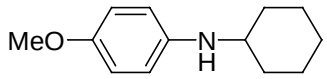


(*R*)-*N*-(Phenyl)-α-methylbenzylamine (Table 2, entry 9).[16] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), (*R*)-α-methylbenzylamine (155 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded (*R*)-*N*-(phenyl)-α-methylbenzylamine[16] (150 mg, 76% yield, 99% *ee*) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.28 (m, 4 H), 7.24-7.19 (m, 1 H), 7.11-7.06 (m, 2 H), 6.66-6.61 (m, 1 H), 6.53-6.48 (m, 2 H), 4.48 (q, 1 H, *J* = 6.6 Hz), 4.03 (brs, 1 H), 1.51 (d, 3 H, *J* = 6.6 Hz); HPLC conditions: (column: Daicel OD-H; solvent: 10% ^{i}PrOH in hexane; flow rate: 0.7 mL/ min; UV lamp: 254 nm; retention time: 6.74 min). The racemic form of the product was prepared in the same manner.

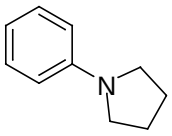


***N*-Methyl-*N*-phenylbenzylamine (Table 3, entry 8).**[17] The general procedure under argon was followed using copper(I) iodide (19 mg, 0.10 mmol), K_3PO_4 (425 mg, 2.00 mmol), *N*-methylbenzylamine (155 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 1-butanol (1.0 mL) at 90 °C. Column chromatography using a solvent

mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.5) afforded *N*-methyl-*N*-phenylbenzylamine[17] (146 mg, 74% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.28 (m, 4 H), 7.24-7.18 (m, 1 H), 7.11-7.06 (m, 2 H), 6.66-6.61 (m, 1 H), 6.53-6.48 (m, 2 H), 4.48 (s, 2H), 4.03 (brs, 1 H), 2.85 (s, 3H).

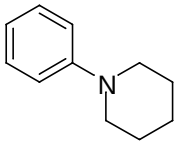


***N*-(4-Methoxyphenyl)cyclohexylamine (Table 3, entry 9).** An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.5 mg, 0.0499 mmol, 5.0 mol%), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. Cyclohexylamine (144 μL, 1.26 mmol), ethylene glycol (0.11 mL, 1.97 mmol), and a solution of 4-iodoanisole (235 mg, 1.00 mmol) in 1-butanol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 100 ¡C for 14 h. The resulting thick, green-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2. The colorless organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 5:1; 15 mL fractions). Fractions 9-17 provided 143 mg (70% yield) of the product as white crystals. Mp: 41-42 ¡C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.79-6.72 (m, 2H), 6.60-6.53 (m, 2H), 3.74 (s, 3H), 3.22 (br s, 1H), 3.16 (tt, *J* = 10.2, 3.6 Hz, 1H), 2.10-1.98 (m, 2H), 1.80-1.69 (m, 2H), 1.68-1.58 (m, 1H), 1.40-1.04 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 141.6, 114.8, 114.7, 55.8, 52.7, 33.6, 25.9, 25.0. IR (neat, cm^{-1}): 3388, 1509, 1239, 1038, 818. Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.06; H, 9.33. Found: C, 76.00; H, 9.32.

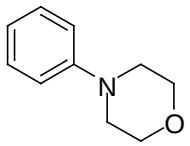


***N*-(Phenyl)pyrrolidine (Table 3, entry 10).**[18] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00

mmol), pyrrolidine (100 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(phenyl)pyrrolidine[18] (133 mg, 90% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.19 (m, 2 H), 6.65 (dt, 1 H, *J* = 7.2, 0.9 Hz), 6.56 (dd, 2 H, *J* = 8.7, 0.9 Hz), 3.30-3.26 (m, 4 H), 2.02-1.97 (m, 4 H).

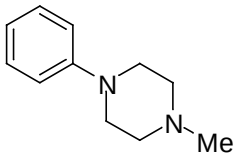


***N*-(Phenyl)piperidine (Table 3, entry 13).**[19] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), piperidine (119 μl, 1.20 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.4) afforded *N*-(phenyl)piperidine[19] (129 mg, 80% yield) as colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19-7.25 (m, 2 H), 6.65 (dt, *J* = 7.2, 1.1 Hz, 1H), 6.56 (dd, 2 H, *J* = 8.7, 1.0 Hz), 2.99-3.10 (m, 4 H), 1.89-2.01 (m, 6 H).

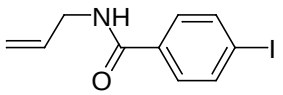


***N*-(Phenyl)morpholine (Table 3, entry 14).**[20] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), morpholine (130 μl, 1.50 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 20/ 1, R_f = 0.2) afforded *N*-(phenyl)morpholine[20] (124 mg, 76% yield) as colorless liquid. ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.23-7.19 (m, 2 H), 6.66 (m, 1 H), 6.54 (dd, 2 H, *J* = 8.7, 0.9 Hz), 3.68-3.70 (m, 4 H), 2.91-3.01 (m, 4 H).

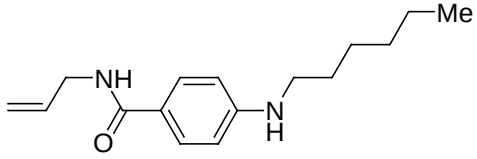


***N*-phenyl-*N* -(methyl)piperazine (Table 3, entry 15).**[17] The general procedure under argon was followed using copper(I) iodide (10 mg, 0.05 mmol), K_3PO_4 (425 mg, 2.00 mmol), *N*-(methyl)piperazine (166 μl, 1.50 mmol), iodobenzene (112 μl, 1.00 mmol), ethylene glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ethyl acetate = 20/1, R_f = 0.1) afforded *N*-phenyl-*N* -(methyl)piperazine[17] (125 mg, 71% yield) as colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (dd, J = 7.1, 7.0 Hz, 2 H), 6.65 (d, *J* = 7.2 Hz, 2H), 6.56 (t, *J* = 8.0 Hz, 1H), 3.38-3.45 (m, 4 H), 2.59-2.64 (m, 4 H), 2.27 (s, 3H).

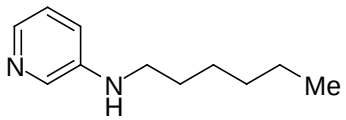


***N*-Allyl-4-iodobenzamide.** A solution of 4-iodobenzoyl chloride (2.07 g, 7.77 mmol) in dichloromethane (10 mL) was added to a stirred solution of allylamine (2.0 mL, 26.7 mmol) in dichloromethane (10 mL) at 0 ¡C. After 1 h at room temperature, the clear solution was poured into ethyl acetate (100 mL) and washed with 2×100 mL of diluted aq HCl followed by 2×100 mL of saturated aq $NaHCO_3$. The colorless organic phase was dried ($MgSO_4$) and concentrated. The residue was recrystallized from 50 mL of hexane-ethyl acetate to provide 2.14 g (96% yield) of the product as fine, white needles. Mp: 122-123 ¡C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81-7.75 (m, 2H), 7.53-7.48 (m, 2H), 6.22 (br s, 1H), 5.93 (ddt, *J* = 17.2, 11.7, 5.8 Hz, 1H), 5.26 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.19 (dq, *J* = 11.7, 1.5 Hz, 1H), 4.07 (tt, *J* = 5.8, 1.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 137.8, 133.9, 133.8, 128.5, 117.0, 98.4, 42.5. IR (neat, cm^{-1}):

3307, 1623, 1584, 1540, 1297, 930, 845, 668. Anal. Calcd. for $C_{10}H_{10}NOI$: C, 41.84; H, 3.51. Found: C, 42.01; H, 3.51.

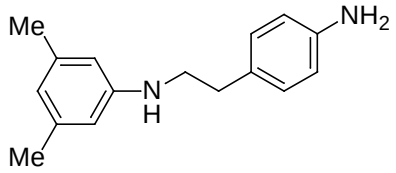


***N*-Allyl-4-(1-hexylamino)benzamide (Table 3, entry 16).** An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), *N*-allyl-4-iodobenzamide (288 mg, 1.00 mmol), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. *n*-Hexylamine (160 μL, 1.21 mmol), ethylene glycol (115 μL, 2.06 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 ¡C for 24 h. The resulting thick, light brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2. The organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; hexane-ethyl acetate 3:2; 15 mL fractions). Fractions 12-23 provided 226 mg (87% yield) of the product as a white solid. Mp: 91-92 ¡C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.61 (m, 2H), 6.58-6.53 (m, 2H), 6.07 (br s, 1H), 5.94 (ddt, *J* = 17.1, 10.2, 5.7 Hz, 1H), 5.24 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.15 (dq, *J* = 10.2, 1.5 Hz, 1H), 4.06 (tt, *J* = 5.7, 1.5 Hz, 2H), 4.01 (br s, 1H), 3.17-3.10 (m, 2H), 1.66-1.58 (m, 2H), 1.44-1.27 (m, 6H), 0.93-0.86 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 151.1, 134.7, 128.6, 122.2, 116.2, 111.6, 43.5, 42.2, 31.5, 29.3, 26.7, 22.6, 14.0. IR (neat, cm^{-1}): 3346, 1621, 1598, 1571, 1538, 1515, 1337, 1287, 1264, 1189, 918, 832, 766. Anal. Calcd. for $C_{16}H_{24}N_2O$: C, 73.81; H, 9.29. Found: C, 73.77; H, 9.34.

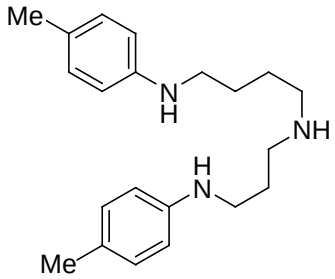


***N*-(Hexyl)-3-aminopyridine (Table 3, entry 17).**[21] The general procedure under argon or air was followed using copper(I) iodide (10 mg, 0.05 mmol or 2.0 mg, 0.01 mmol), K_3PO_4 (425 mg, 2.00 mmol), *n*-hexylamine (158 μl, 1.20 mmol), 3-iodopyridine (205 mg, 1.00 mmol), ethylene

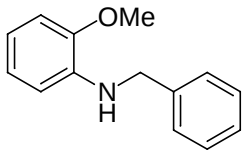
glycol (111 μl, 2.00 mmol) and 2-propanol (1.0 mL). Column chromatography using a solvent mixture (hexane/ ethyl acetate = 2/ 1, R_f = 0.2) afforded *N*-(hexyl)-3-aminopyridine[21] (151 mg, 85% yield) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 (d, *J* = 2.9 Hz, 1H), 7.94 (dd, *J* = 1.2, 4.3 Hz, 1H), 7.08 (dd, *J* = 4.6, 16.6 Hz, 2H), 3.64 (br s, 1H), 3.08-3.15 (m, 2H), 1.58-1.68 (m, 2H), 1.29-1.43 (m, 2H), 0.82-0.93 (m, 3H).



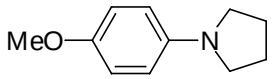
2-(4-Aminophenyl)-*N*-(3,5-dimethylphenyl)ethylamine (Table 3, entry 18). An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol, 5.0 mol%), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. 5-Iodo-*m*-xylene (145 μL, 1.00 mmol), 2-(4-aminophenyl)ethylamine (160 μL, 1.21 mmol), ethylene glycol (115 μL, 2.06 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred magnetically at 80 ¡C for 22 h. The resulting thick, gray-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2. The yellow-brown organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×20 cm; hexane-ethyl acetate 3:2; 15 mL fractions). Fractions 11-19 were concentrated and the residue was recrystallized from hexanes to give 167 mg (69% yield) of the product as white needles. Mp: 91-92 ¡C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04-6.97 (m, 2H), 6.67-6.61 (m, 2H), 6.36 (s, 1H), 6.24 (s, 2H), 3.65-3.50 (br m, 3H), 3.30 (t, *J* = 6.8 Hz, 2H), 2.79 (t, *J* = 7.0 Hz, 2H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 144.7, 138.8, 129.5, 129.2, 119.3, 115.3, 110.9, 45.3, 34.6, 21.5. IR (neat, cm^{-1}): 3361, 3215, 1600, 1515, 1472, 1337, 1273, 1181, 820. Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39. Found: C, 80.05; H, 8.31.



***N*-(4-Methylphenyl)-*N'*-[3-(4-methylphenylamino)propyl]-1,4-butanediamine (Table 3, entry 19).** An oven-dried resealable 15 mL Schlenk tube was charged with CuI (9.6 mg, 0.0504 mmol), 4-iodotoluene (260 mg, 1.19 mmol), K_3PO_4 (440 mg, 2.07 mmol), evacuated and backfilled with argon. *N*-(3-Aminopropyl)-1,4-butanediamine (79 μL, 0.503 mmol), ethylene glycol (115 μL, 2.06 mmol), and isopropyl alcohol (1.0 mL) were added under argon. The Schlenk tube was sealed with a Teflon valve and the reaction mixture was stirred at 80 ¡C for 23 h. The resulting thick, gray-brown suspension was allowed to reach room temperature, poured into a solution of 30% aq ammonia (1 mL) in water (20 mL), and extracted with 3×15 mL of CH_2Cl_2. The organic phase was dried (Na_2SO_4), concentrated, and the residue was purified by flash chromatography on silica gel (2×15 cm; dichloromethane - dichloromethane saturated with 30% aq ammonia - methanol 30:20:2; 15 mL fractions). Fractions 12-24 were concentrated and the residue was recrystallized from hexanes (2 mL) to give 119 mg (73% yield) of the desired product as fine white crystals. Mp: 83-84 ¡C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (d, J = 8.4 Hz, 4H), 6.56-6.50 (m, 4H), 4.04 (br s, 1H), 3.56 (br s, 1H), 3.17 (t, J = 6.6 Hz, 2H), 3.11 (t, J = 6.6 Hz, 2H), 2.74 (t, J = 6.6 Hz, 2H), 2.64 (t, J = 6.9 Hz, 2H), 2.23 (s, 6H), 1.79 (quintet, J = 6.6 Hz, 2H), 1.70-1.54 (m, 4H), 0.95 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.3, 146.1, 129.7, 126.3, 112.89, 112.85, 49.8, 48.5, 44.2, 43.3, 29.6, 27.8, 27.3, 20.4. IR (neat, cm^{-1}): 3396, 3301, 1617, 1520, 1318, 1302, 1256, 1125, 807. Anal. Calcd. for $C_{21}H_{31}N_3$: C, 77.49; H, 9.60. Found: C, 77.44; H, 9.65.



***N*-Benzyl-2-methoxyaniline[22] (Table 4, entry 5).** Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), potassium phosphate (425 mg, 2.0 mmol) and 2-phenylphenol (34 mg, 0.2 mmol) was charged to a screw-capped test tube with Teflon lined septum. The tube was evacuated and back-filled with argon three cycles. Benzylamine (1 mL) and 2-bromoanisole (125 μL, 1.0 mmol) was added by microsyringe at room temperature. The reaction mixture was heated at 100 °C for 22 hours. The reaction mixture was allowed to reach room temperature. Water (5 mL) was added and the suspension was extracted by ethyl acetate (4 × 10 mL). The combined organic phases were washed with water, brine and dried over Na_2SO_4. Solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel with an eluent (CH_2Cl_2/Hexane = 1/1) to afford the product[22] as a colorless liquid (181 mg, 85% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.39 (m, 5H), 6.78-6.87 (m, 2H), 6.68 (dt, *J* = 7.5, 1.5 Hz, 1H), 6.60 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.62 (br s, 1H), 4.36 (d, *J* = 5.4 Hz, 2H), 3.86 (s, 3H). MS: *m/z* (relative intensity), 213 (M^+, 40), 198 (20), 91 (100).



***N*-(4-Methoxyphenyl)pyrrolidine[22] (Table 4, entry 6).** Copper (I) iodide (10 mg, 0.05 mmol, 5 mol%), potassium phosphate (425 mg, 2.0 mmol) and 2-phenylphenol (34 mg, 0.2 mmol) was charged to a screw-capped test tube with Teflon lined septum. The tube was evacuated and back-filled with argon three cycles. Pyrrolidine (1 mL) and 4-bromoanisole (125 μL, 1.0 mmol) was added by microsyringe at room temperature. The reaction mixture was heated at 110 °C for 22 hours. The reaction mixture was allowed to reach room temperature. Water (5 mL) was added and the suspension was extracted by ethyl acetate (4 × 10 mL). The combined organic phases were washed with water, brine, and dried over Na_2SO_4. Solvent was removed *in vacuo*

and the residue was purified by column chromatography on silica gel with a solvent gradient (CH_2Cl_2/Hexane = 1/2 to 2/1) to afford the product[1] as a light yellow solid (129 mg, 73% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.84 (dt, *J* = 9.0, 3.9 Hz, 2H), 6.54 (dt, *J* = 9.0, 3.6 Hz, 2H), 3.76 (s, 3H), 3.21-3.25 (m, 4H), 1.96-2.01 (m, 4H). MS: *m/z* (relative intensity), 177 (M^+, 70), 162 (100), 120 (20).

References and Notes:

(1) Apodaca, R.; Xiao, W. *Org. Lett*. **2001**, *3*, 1745-1748.

(2) Nose, A.; Kudo, T. *Chem. Pharm. Bull*. **1986**, *34*, 4817-4820.

(3) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem*. **2000**, *65*, 1158-1174.

(4) Burton, R. D.; Bartberger, M. D.; Zhang, Y.; Eyler, J. R.; Schanze, K. S. *J. Am. Chem. Soc*. **1996**, *118*, 5655-5664.

(5) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144-1157.

(6) Beletskaya, I. P.; Bessmertnykh, A. G.; Guilard, R. *Synlett* **1999**, 1459-1461.

(7) Desmurs, J. R.; Lecouve, J. P.; Kempf, H.; Betremieux, I.; Ratton, S. *New J. Chem.* **1992**, *16*, 99-106.

(8) Leardini, R.; Nanni, D.; Tundo, A.; Zanardi, G.; Ruggieri, F. *J. Org. Chem.* **1992**, *57*, 1842-1848.

(9) Chang, M. R.; Takeuchi, Y.; Hashigaki, K.; Yamato, M. *Heterocycles* **1992**, *33*, 147-152. Moore, J. A.; Sutherland, G. J.; Sowerby, R.; Kelly, E. G.; Palermo, S.; Webster, W. *J. Org. Chem.* **1969**, *34*, 887-892.

(10) Coppola, G. A. *J. Herterocyl. Chem*. **1986**, *23*, 223-224.

(11) Araki, T.; Tsukube, H. *J. Polym. Sci., Polym. Lett. Ed.* **1979**, *17*, 501-505.

(12) (a) Albright, J. D.; DeVries, V. G.; Largis, E. E.; Miner, T. G. Reich, M. F.; Schaffer, S.; Shepherd, R. G.; Upeslacis, J. *J. Med. Chem*. **1983**, *26*, 1378-1393. (b) Onaka, M.; Umezono, A.; Kawai, M.; Izumi, Y. *J. Chem. Soc., Chem. Commun*. **1985**, 1202-1203.

(13) (a) Janin, Y. L.; Bisagni, E. *Synthesis* **1993**, 57-59. (b) Crossley, M. L.; Dreisback, P. F.; Hofmann, C. M.; Parker, R P. *J. Am. Chem. Soc*. **1952**, *74*, 573-578.

(14) Bomann, M. D.; Guch, I. C.; DiMare, M. *J. Org. Chem*. **1995**, *60*, 5995-5996.

(15) Fancher, L. W.; Gless, R. D., Jr.; Wong, R. Y. *Tetrahedron Lett*. **1988**, *29*, 5095-5098.

(16) Kainz, S.; Brinkmann, A.; Leitner, W.; Pfaltz, A. *J. Am. Chem. Soc.* **1999**, *121*, 6421-6429.

(17) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* **1999**, *55*, 12829-12842.

(18) Ishikawa, T.; Uedo, E.; Tani, R.; Saito, S. *J. Org. Chem*. **2001**, *66*, 186-191.

(19) (a) Beller, M.; Breindl, C.; Riermeier, T. H.; Tillack, A. *J. Org. Chem*. **2001**, *66*, 1403-1412. (b) Li, G. Y. *Angew. Chem., Int. Ed*. **2001**, *40*, 1513-1516.

(20) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett*. **2000**, *41*, 2875-2879.

(21) Wagaw, S.; Buchwald, S. L. *J. Org. Chem*. **1996**, *61*, 7240-7241.

[22] Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem*. **2000**, *65*, 1158-1174.