Supporting Information for

Cu(I) Mediated Reductive Amination of Boronic Acids with Nitrosoaromatics

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General Methods

All reactions were performed under an atmosphere of dry N_2 or Ar in oven-dried glassware unless otherwise noted. Solvents (THF, DMA, DMF, toluene and NMP) for reaction media were ACS reagent grade and purchased from Aldrich. They were dried over 4Å molecular sieves and titrated for water level with a Fisher Coulomatic K-F titrator before using. All solvents were purged with dry N_2 or Ar before using unless otherwise noted. Hexanes, ethyl acetate (EtOAc), and ethyl ether (Et_2O) used for extraction and chromatography were obtained from EM Science and used as purchased. Solutions of $NH_3 \cdot H_2O$ refers to aqueous solution. Purification by preparative plate chromatography was performed on EM Science Kieselgel 0.5 mm/1 mm 60 F_{254} plates. Analytical thin-layer chromatography (TLC) was carried out using Merck Kieselgel 0.25 mm 60 F_{254} plates with visualization by UV or phosphomolybdic acid.

^{1}H NMR spectra were recorded on a Varian Inova 400 MHz NMR spectrometer at room temperature in $CDCl_3$ and were internally referenced to $CDCl_3$ (7.26 ppm); ^{13}C NMR spectra were recorded on a Varian Inova 100 MHz NMR spectrometer at room temperature in $CDCl_3$ and were internally referenced to $CDCl_3$ (77.23 ppm). Data are reported in the following order: chemical shifts are given (δ); multiplicities are indicated (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), pent (pentuplet), hex (hextet), hept (heptet), m (multiplet), exch (exchangeable), app (apparent)); coupling constants, *J*, are reported (Hz); integration is provided. Infrared (IR) spectroscopy was performed on a Nicolet 510 FT-IR. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak 20-40%), and br (broad). Uncalibrated melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. High resolution mass spectra were obtained on a JEOL JMS-SX102/SX102A/E instrument.

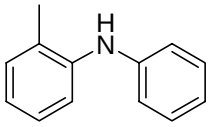
Starting Materials

All boronic acids were obtained from Frontier Scientific, Inc. Nitrosobenzene, 2-nitrosotoluene, copper(I) chloride, copper(I) iodide, copper(I) acetate, copper(I) trifluoromethanesulfonate benzene complex, copper(I) trifluoromethanesulfonate toluene complex and 1,4-hydroquinone were purchased from Aldrich. Ascorbic acid (food grade) was obtained from J. T. Baker Inc. Cu(I)-thiophene-2-carboxylate (CuTC)[1], Cu(I) 3-methylsalicylate (CuMeSal)[2] and 4-chloro-2-methyl-1-nitrosobenzene[3] were prepared following literature procedures.

[1] Allred, G.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 2748.

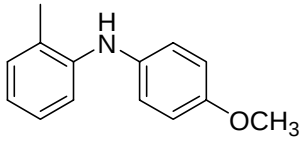
General Experimental Procedure for Amination using a Stoichiometric Amount of CuCl: A Schlenk tube containing the nitrosoarene (0.3 mmol) and CuCl (30 mg, 0.3 mmol) was flushed with argon. Dry DMF (8 mL) was added and the dark brown mixture was stirred at 55 °C for 40 min. The boronic acid (0.33 mmol) dissolved in DMF (3 mL) was then added to the reaction vessel via syringe. The mixture was heated at 55 °C for 16 h, cooled, and partitioned between Et_2O (20 mL) and 1 M NH_4OH (20 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL) and the combined organic layers were dried with $MgSO_4$. The residue after evaporation was subjected to preparative plate silica chromatography using a mixture of hexanes and EtOAc as the eluent.

2-Methyldiphenylamine (Table 1, entry 1).[4]



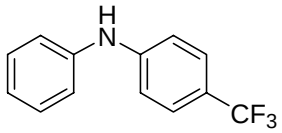
2-Nitrosotoluene (37 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and phenylboronic acid (40 mg, 0.33 mmol) in DMF (8 mL) gave product (46 mg, 83%) as a light brown solid: TLC (silica gel, 7:1 hexanes : Et_2O, R_f = 0.68). Mp 38-39 °C (Et_2O; lit. 37 °C[4]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.28 (m, 5 H), 6.89-6.98 (m, 4 H), 5.39 (s, br, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 141.4, 131.1, 129.5, 128.5, 126.9, 122.1, 120.6, 118.9, 117.6, 18.1. IR (KBr, cm^{-1}): 3400 (s).

N-(2-Methylphenyl)-*p*-anisidine (Table 1, entry 2).[5]



2-Nitrosotoluene (37 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 4-methoxy phenylboronic acid (50 mg, 0.33 mmol) in DMF (8 mL) gave product (52 mg, 81%) as a light brown solid: TLC (silica gel, 6:1 hexanes : Et_2O, R_f = 0.41). Mp 81.5-82 °C (Et_2O; lit. 78-81 °C[5]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79-7.16 (m, 8 H), 5.21 (s, br, 1H), 3.80 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 143.3, 136.2, 130.7, 126.7, 125.2, 122.1, 119.9, 115.1, 114.6, 55.5, 17.7. IR (KBr, cm^{-1}): 3392 (s).

Phenyl-(4-trifluoromethylphenyl)-amine (Table 1, entry 3).[6]



Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 4-trifluoromethyl phenylboronic acid (63 mg, 0.33 mmol) in DMF (8 mL) gave product (50 mg, 70%) as a brown solid: TLC (silica gel, 4:1 hexanes : Et_2O, R_f = 0.22). Mp 61-62 °C (Et_2O; lit. 63-64 °C[6]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 11.2, 2H), 7.31-7.37 (m,

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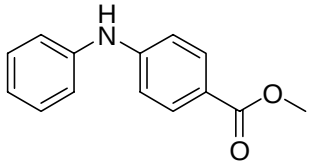
[2] Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2002**, *4*, 4309.
[3] Wratten, S. J.; Fujiwara, H.; Solsten, R. T. *J. Agric. Food Chem.* **1987,** *35,* 484.
[4] Anderson, K. W.; Mendez-Perez, M.; Priego, J.; Buchwald, S. L. *J. Org. Chem.* **2003**, *68*, 9563.
[5] Ali, M. H.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 2560.
[6] Kozachuk, D. N.; Serguchev, Yu. A.; Kremlev, M. M.; Fialkov, Yu. A.; Yagupol'skii, L. M. *Zh. Obshch. Khim.* **1974**, 1230.

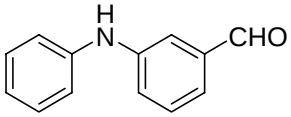
2H), 7.14-7.17 (m, 2H), 7.06 (t, *J* = 10.4, 3H), 5.93 (s, br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 141.3, 129.8, 126.9 (q), 124.8 (d), 123.1, 121.8 (q), 120.2, 115.5. IR (KBr, cm^{-1}): 3399 (s). HRMS(FAB) Calcd for $C_{13}H_{10}NF_3$: 237.0756. Found: 237.0765.

4-Phenylamino-benzoic acid methyl ester (Table 1, entry 4).[4]



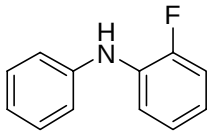
Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 4-methoxycarbonyl phenylboronic acid (59 mg, 0.33 mmol) in DMF (8 mL) gave product (49 mg, 72%) as an off-white solid: TLC (silica gel, 1:1 hexanes : Et_2O, R_f = 0.42). Mp 109-110 °C (Et_2O; lit. 108-110 °C[4]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.93 (m, 2H), 7.32-7.36 (m, 2H), 6.97-7.18 (m, 5H), 6.07 (s, br, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 148.3, 141.0, 131.7, 129.7, 123.3, 121.3, 120.6, 114.7, 51.9. IR (KBr, cm^{-1}): 3342 (s), 1695 (s), 1590 (s).

3-Phenylamino-benzaldehyde (Table 1, entry 5).



Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 3-formyl phenylboronic acid (50 mg, 0.33 mmol) in DMF (8 mL) gave product (47 mg, 80%) as a yellow solid: TLC (silica gel, 1:1 hexanes : Et_2O, R_f = 0.39). Mp 64-65 °C (hexanes/Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.27-7.54 (m, 6H), 7.0-7.14 (m, 3H), 5.90 (s, br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 144.6, 142.0, 137.8, 130.2, 129.8, 122.9, 122.7, 122.5, 119.2, 116.5. IR (KBr, cm^{-1}): 3334 (s), 1685 (s), 1592 (s). Anal. Calcd for $C_{13}H_{11}NO$ (MW 197.23): C, 79.16; H, 5.62; N, 7.10; O, 8.11. Found: C, 79.11; H, 5.63; N, 7.11; O, 8.18.

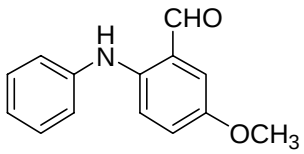
2-Fluorodiphenylamine (Table 1, entry 6).[7]



Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 2-fluoro phenylboronic acid (46 mg, 0.33 mmol) in DMF (8 mL) gave product (34 mg, 61%) as a brown oil: TLC (silica gel, 4:1 hexanes : Et_2O, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.35 (m, 3H), 6.98-7.14 (m, 5H), 6.82-6.88 (m, 1H). 5.81 (s, br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2 (d), 142.2, 129.6, 124.5, 124.4, 122.0, 120.6 (d), 118.9, 117.3, 115.6 (d). IR (neat, cm^{-1}): 3414 (s).

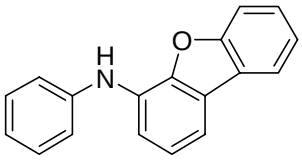
5-Methoxy-2-phenylamino-benzaldehyde (Table 1, entry 7) .

[7] Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029.



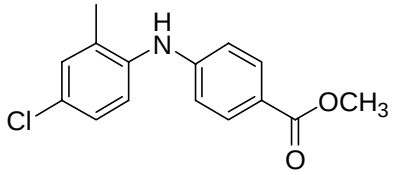
Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 2-formyl 4-methoxy phenylboronic acid (59 mg, 0.33 mmol) in DMF (8 mL) gave product (53 mg, 78%) as a yellow oil: TLC (silica gel, 1:1 hexanes : Et_2O, R_f = 0.50). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (s, 1H), 9.91 (s, br, 1H), 7.44-7.57 (m, 5H), 7.23-7.32 (m, 3H), 4.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 151.5, 142.4, 140.6, 129.6, 124.5, 123.8, 122.3, 119.7, 118.0, 115.3, 56.1. IR (neat, cm^{-1}): 3298 (s), 1663 (s), 1595 (s), 1576 (s). Anal. Calcd for $C_{14}H_{13}NO_2$ (MW 227.26): C, 73.99; H, 5.77; N, 6.16. Found: C, 73.63; H, 5.86; N, 5.94.

N-Phenyl-2-dibenzofuranamine (Table 1, entry 8).



Nitrosobenzene (33 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 4-dibenzofuranboronic acid (70 mg, 0.33 mmol) in DMF (8 mL) gave product (50 mg, 64%) as an off-white solid: TLC (silica gel, 4:1 hexanes : Et_2O, R_f = 0.41). Mp 102-102.5 °C (Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.97 (m, 1H), 7.21-7.59 (m, 10H), 6.99-7.03 (m, 1H), 6.20 (s, br, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 146.5, 142.5, 129.6, 129.2, 127.2, 125.0, 123.5, 123.1, 121.8, 121.1, 118.6, 113.6, 112.6, 111.9. IR (KBr, cm^{-1}): 3405 (m), 1635 (s), 1608 (s). HRMS(FAB+) Calcd for $C_{18}H_{13}ON$: 259.0993. Found: 259.0997.

4-[(2-Methyl-4-chlorophenyl)amino]-benzoic acid methyl ester (Table 1, entry 9).



4-Chloro-2-methyl-1-nitrosobenzene (47 mg, 0.3 mmol), CuCl (30 mg, 0.3 mmol) and 4-methylcarbonyl phenylboronic acid (59 mg, 0.33 mmol) in DMF (8 mL) gave product (58 mg, 70%) as a white solid: TLC (silica gel, 4:1 hexanes : Et_2O, R_f = 0.20); Mp 104.0-105.0 °C (hexane/Et_2O).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.91 (m, 2H), 7.14-7.24 (m, 3H), 6.75-6.79 (m, 2H), 5.68 (s, br, 1H), 3.86 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 148.9, 137.7, 133.6, 131.7, 131.2, 129.6, 127.1, 124.2, 121.1, 114.4, 51.9, 18.1. IR (KBr, cm^{-1}): 3345 (s), 1696 (s), 1608 (s). HRMS(FAB+) Calcd for $C_{15}H_{14}O_2NClLi$ ($M+Li^+$): 282.0873. Found. 282.0873.

General Experimental Procedure for Amination Using a Catalytic Amount of CuMeSal and Ascorbic Acid: A Schlenk tube containing the nitroso compound (0.3 mmol), the boronic acid (0.33 mmol), and CuMeSal (6 mg, 0.03 mmol) was flushed with argon. Dry DMF (8 mL) was added and the mixture was stirred at 55 °C for 1 h. One-half equiv of ascorbic acid (30 mg, 0.15 mmol) dissolved in DMF (1 mL) was added to the reaction vessel. One hour later another ½ equiv of ascorbic acid (30 mg, 0.15 mmol) dissolved in DMF (1 mL) was added. The mixture was heated at 55 °C

for another 4 h, cooled, and partitioned between Et_2O (20 mL) and 1 M NH_4OH (20 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL) and the combined organic layers were dried with $MgSO_4$. The residue after evaporation was subjected to preparative plate silica chromatography (gradient of hexanes and EtOAc) giving the desired product.

General Experimental Procedure for Amination Using a Catalytic Amount of CuMeSal and 1,4-Hydroquinone: A Schlenk tube containing the nitroso compound (0.3 mmol), the boronic acid (0.33 mmol), 1,4-hydroquinone (33 mg, 0.3 mmol) and CuMeSal (6 mg, 0.03 mmol) was flushed with argon. Dry DMA (8 mL) was added and the dark brown mixture was stirred at 60 °C for 16 h. The mixture was cooled and partitioned between Et_2O (20 mL) and 1 M NH_4OH (20 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL) and the combined organic layers were dried with $MgSO_4$. The residue after evaporation was subjected to preparative plate silica chromatography using a mixture of hexanes and EtOAc as the eluent. Compound characterization data are given above.