Reductive Monoalkylation of Aromatic and Aliphatic Nitro Compounds and the Corresponding Amines with Nitriles

Ruel Nacario, Shailaja Kotakonda, David M. Fouchard, L. M. Viranga Tillekeratne, and Richard A. Hudson

General Methods:

Reagents were purchased from Aldrich and Fischer and used without further purification. Reactions were carried out in oven-dried glassware. Unless stated otherwise, all reactions were carried out at room temperature and pressure and were monitored initially by TLC on pre-coated silica gel IB-F (4463-02 Baker-Flex, J.T. Baker), by NMR and by GC-MS. TLC separations were detected under UV light or by charring after spraying with ninhydrin solution. Column chromatography was performed on 100-200 mesh silica gel (Fisher Scientific). NMR spectra were recorded on 400 or 600 MHz Varian NMR spectrometers. ^1H NMR chemical shifts were referenced to tetramethylsilane (TMS) (0.0, CDCl_3) while ^{13}C NMR chemical shifts were referenced to CDCl_3 (77.0, CDCl_3). Coupling constants (J) were expressed in Hertz (Hz). GCMS-EI was performed on a Hewlett Packard G1800B GCD Plus Gas Chromatograph equipped with Electron Ionization Detector and a $12\text{m} \times 0.2\text{ mm}$ column. Helium was used as the carrier gas with a constant flow of 0.5 mL/min. The oven temperature was held at 45 °C for 4 min then increased at 20 °C/min to 280 °C with a final holding time of 5.0 min. Yields reported in Tables 1-4 are based on weight of isolated products; product ratios are based on GC-MS analysis of the isolated products.

General Procedure A: A mixture of starting material (100 mg) and 5 % palladium on carbon (0.039 g, 1.81×10^{-5} mol) in 80 % acetonitrile-water (5 mL) was stirred at room temperature. Ammonium formate (0.60 g, 6.4×10^{-3} mol) was added in small portions. The reaction was monitored by TLC for the disappearance of the spot (lowest R_f) corresponding to the primary amine. The reaction mixture was then filtered, washed successively with acetonitrile and dichloromethane and the filtrate evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and filtered. The filtrate was then evaporated *in vacuo* to give a product.

N-Ethyl-4-methoxyaniline: Starting from 4-nitroanisole (0.10 g, 6.5×10^{-4} mol) using general procedure A gave a dark-brown liquid (0.09 g, 93 %). R_f 0.43 (10:1 hexanes:ethyl acetate) ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 1.23 (t, $J = 7.2$ Hz, 3H), 3.10 (q, $J = 7.2$ Hz, 2H), 3.74 (s, 3H), 6.58 (d, $J = 9$ Hz, 2H), 6.78 (d, $J = 9$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.2, 39.7, 56.1, 114.3, 115.1, 143.0, 152.3; GCMS (EI) m/z 151.

N-Ethyl aniline: Starting from nitrobenzene (0.10 g, 8.1×10^{-4} mol) using general procedure A gave a light orange liquid (0.08 g, 85 %). R_f 0.42 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 1.27 (t, $J = 7.2$ Hz, 3H), 3.17 (q, $J = 7.2$ Hz, 2H), 3.63 (br. s, 1H), 6.63 (m, 2H), 6.72 (m, 1H), 7.20 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.2, 38.7, 113.1, 117.5, 129.5, 148.7; GCMS (EI) m/z 121.

N-Ethyl-4-methylaniline: Starting from 4-nitrotoluene (0.1 g, 7.3×10^{-4} mol), and ammonium formate (NH_4HCO_2 , 0.80 g, 1.3×10^{-3} mol) but otherwise using general procedure A gave an orange-brown liquid (0.0747 g, 75.8 %). R_f 0.43 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 1.23 (t, $J = 7.2$ Hz, 3H), 2.23 (s, 3H), 3.13 (q, $J = 7.2$ Hz, 2H), 6.54 (d, $J = 8.4$ Hz, 2H), 6.78 (d, $J = 9$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.3, 20.7, 39.1, 113.3, 126.7; 130.1, 146.6; GCMS (EI) m/z 135.

General Procedure B: Starting material (100 mg) was dissolved in acetonitrile (4 mL) and stirred at room temperature. 5 % Pd/C (0.039 g, 1.8×10^{-5} mol) and NH_4HCO_2 (0.60 g, 9.5×10^{-3} mol) dissolved in H_2O (1.0 mL) was then added to the reaction mixture while stirring. The reaction was monitored by TLC for the disappearance of the spot (lowest R_f) corresponding to the primary amine intermediate. The reaction mixture was then filtered, washed successively with methanol and CH_2Cl_2 and the filtrate evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and the organic layer was separated, dried in Na_2SO_4 and filtered. The filtrate was then evaporated *in vacuo* to give the product.

N-Ethyl aniline: Starting from aniline (0.10 g, 1.07×10^{-3} mol) using general procedure B gave a light yellow liquid (0.116 g, 89.5 %). R_f 0.46 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 1.19 (t, $J = 7.2$ Hz, 3H), 3.17 (q, $J = 7.2$ Hz, 2H), 6.64 (m, 2H), 6.73 (m, 1H), 7.21 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.1, 38.7, 113.0, 117.4, 129.5, 148.7; GCMS (EI) m/z 121.

N-Ethyl-methylaniline: Starting from *p*-toluidine (0.106 g, 9.9×10^{-4} mol) using general procedure B gave a yellow-orange liquid (0.119g, 95 %). R_f 0.43 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.33 (t, $J = 7.2$ Hz, 3H), 2.36 (s, 3H), 3.22 (q, $J = 7.2$ Hz, 2H), 6.64 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.3, 20.7, 39.1, 113.3, 126.7; 130.1, 146.6; GCMS (EI) m/z 135.

N-Ethyl-4-methoxyaniline: Starting from *p*-anisidine (0.103 g, 8.43×10^{-4} mol), acetonitrile (4.0 mL, 7.3×10^{-2} mol) using general procedure D gave an orange-brown liquid product (0.126 g, 100 %). R_f 0.41 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.26 (t, $J = 7.2$ Hz, 3H), 3.13 (q, $J = 7.2$ Hz, 2H), 3.77 (s, 3H), 6.62 (d, $J = 8.8$ Hz, 2H), 6.82 (d, $J = 9.2$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.2, 39.7, 56.0, 114.4, 115.1, 143.0, 152.3; GCMS (EI) m/z 151.

N-Ethyl-2-methoxyaniline: Starting from 2-nitroanisole (0.11 g, 7.18×10^{-4} mol) and using general procedure B gave a yellow-orange liquid (0.104 g, 96 %). R_f 0.71 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.33 (t, $J = 7.2$ Hz, 3H), 3.20 (q, $J = 7.2$ Hz, 2H), 3.88 (s, 3H), 6.64-6.73 (m, 2H), 6.79-6.82 (m, 1H), 6.90-6.94 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.1, 38.4, 55.6, 109.6, 110.1, 116.5, 121.6, 138.7, 147.0; GCMS (EI) m/z 151.

N-Ethyl-2-methoxyaniline: Starting from *o*-anisidine (0.1 g, 8.1×10^{-4} mol) and using general procedure B gave a yellow-orange liquid (0.12 g, 98 %). R_f 0.68 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.35 (t, $J = 7.2$ Hz, 3H), 3.23 (m,

2H), 3.90 (s, 3H), 4.18 (br. s, 1H), 6.67-6.75 (m, 2H), 6.82-6.84 (m, 1H), 6.93-6.97 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.2, 38.4, 55.61, 109.6, 110.1, 116.5, 121.6, 138.7, 147.0; GCMS (EI) m/z 151.

N-Ethyl-2-methylaniline: Starting from 2-nitrotoluene (0.10 g, 7.3×10^{-4} mol) and using general procedure B gave a clear, colorless liquid (0.081 g, 82.4 %). R_f 0.71 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.37 (t, $J = 7.2$ Hz, 3H), 2.20 (s, 3H), 3.25 (q, $J = 7.2$ Hz, 2H), 6.67-6.74 (m, 2H), 7.12 (d, 1H), 7.18-7.22 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.3, 17.8, 38.7, 109.9, 117.0; 122.0, 127.4, 130.29, 146.7; GCMS (EI) m/z 135.

N-Ethyl-methylaniline: Starting from *o*-toluidine (0.10 g, 9.3×10^{-4} mol) and using general procedure B gave a clear, colorless liquid product (0.118g, 94 %): R_f 0.32 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.40 (t, $J = 7.2$ Hz, 3H), 2.24 (s, 3H), 3.29 (q, $J = 7.2$ Hz, 2H), 6.71-6.78 (m, 2H), 7.16 (d, 1H), 7.22-7.26 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.3, 17.8, 38.7, 110.0, 117.1; 122.0, 127.5, 130.3, 146.7; GCMS (EI) m/z 135.

N-Ethyl-3-methylaniline: Starting from 3-nitrotoluene (0.10 g, 7.3×10^{-4} mol) and using general procedure B gave a light-yellow liquid (0.13 g, 100 %): R_f 0.71 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.30 (t, $J = 7.2$ Hz, 3H), 2.34 (s, 3H), 3.19 (q, $J = 7.2$ Hz, 2H), 3.53 (br. s, 1H), 6.47-6.49 (br. complex m, 2H), 6.59 (d,

1H), 7.11-7.15 (m, 1H); ¹³C NMR (400 MHz, CDCl₃, δ_C) 15.2, 21.9, 38.8, 110.2, 117.02; 122.0, 127.4, 139.2, 148.8; GCMS (EI) *m/z* 135.

N-Ethyl-3-methylaniline: Starting from *m*-toluidine (0.10 g, 9.3 x 10⁻⁴ mol) and using general procedure B gave a yellow-orange liquid (0.126 g, 100 %): *R_f* 0.70 (10:1 hexanes:ethyl acetate); ¹H NMR (400 MHz, CDCl₃, δ_H) 1.33 (t, *J* = 7.2 Hz, 3H), 2.38 (s, 3H), 3.22 (q, *J* = 7.2 Hz, 2H), 6.51-6.52 (br. complex m, 2H), 6.63 (d, 1H), 7.15-7.19 (m, 1H); ¹³C NMR (400 MHz, CDCl₃, δ_C) 15.2, 22.0, 38.78, 110.3, 113.9; 118.5, 129.4, 139.2, 148.9; GCMS (EI) *m/z* 135.

N-Ethyl-3-methoxyaniline: Starting from *m*-anisidine (0.10 g, 8.1 x 10⁻⁴ mol) and using general procedure B gave an orange-brown liquid (0.125 g, 86 %): *R_f* 0.47 (10:1 hexanes:ethyl acetate); ¹H NMR (400 MHz, CDCl₃, δ_H) 1.27 (t, *J* = 7.2 Hz, 3H), 3.16 (q, 2H), 3.80 (s, 3H), 3.64 (br. s, 1H), 6.20-6.21 (m, 1H), 6.25-6.32 (m, 2H), 7.10-7.14 (m, 1H); ¹³C NMR (400 MHz, CDCl₃, δ_C) 15.1, 38.7, 55.3, 109.6, 102.5, 106.2, 130.2, 150.2, 161.12; GCMS (EI) *m/z* 151.

N-Ethyl hexylamine: Starting from 1-nitrohexane (0.10 g, 7.6 x 10⁻⁴ mol) and using general procedure B gave a volatile product. GCMS (EI) *m/z* 129.

N-Ethyl cyclohexylamine: Starting from cyclohexylamine (0.10 g, 1.0 x 10⁻³ mol) and using general procedure B gave a light yellow liquid (0.05 g, 39 %). ¹H NMR (400 MHz, CDCl₃, δ_H) 1.23-1.27 (br. complex m, 3H), 1.48 (t, *J* = 7.2 Hz, 3H), 1.56-1.66 (br.

complex m, 3H), 1.80-1.90 (br. complex m, 2H), 2.21-2.24 (br. complex m, 2H), 2.89-2.97 (br. complex m, 1H), 3.03 (q, $J = 7.2$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.6, 24.8, 25.0, 29.3, 39.7, 56.9; GCMS (EI) m/z 127.

General Procedure C: Starting material (100 mg, nitroaryl or nitroalkyl) was dissolved in MeOH and stirred at room temperature. 5 % Pd/C (0.039 g, 1.8×10^{-5} mol) and NH_4HCO_2 (0.60 g, 9.5×10^{-3} mol) dissolved in H_2O (1.0 mL) was then added to the reaction mixture while stirring. The reaction was monitored by TLC or GCMS (for nitroalkyl) for the *in situ* reduction of nitro compound to the corresponding primary amine. Nitrile (8 eq) was then added to the reaction mixture and stirring was continued until the primary amine intermediate (lowest R_f) was no longer detected by TLC. The reaction mixture was filtered, washed successively with methanol and CH_2Cl_2 and the filtrate evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and the organic layer was separated, dried in Na_2SO_4 and filtered. The filtrate was then evaporated *in vacuo* to give the product.

N-Propyl-4-methoxyaniline: Starting from 4-nitroanisole (0.05 g, 3.3×10^{-4} mol), MeOH (2 mL), 5 % Pd/C (0.0193 g, 9.1×10^{-6} mol), NH_4HCO_2 (0.30 g, 3.2×10^{-3} mol), H_2O (1.0 mL), propionitrile (0.186 mL, 2.66×10^{-3} mol) using general procedure C gave a wine-red liquid (0.054 g, 99 %): R_f 0.27 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.01 (t, $J = 7.2$ Hz, 3H), 1.60-1.68 (m, 2H), 3.05 (t, $J = 7.2$ Hz, 2H), 3.76 (s, 3H), 6.60 (d, $J = 9.2$ Hz, 2H), 6.80 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 23.1, 47.1, 56.1, 114.3, 115.13, 143.1, 152.2; GCMS (EI) m/z 165.

N-Butyl-4-methoxyaniline: Starting from 4-nitroanisole (0.099 g, 6.5×10^{-4} mol), MeOH (2 mL), 5 % Pd/C (0.039 g, 1.86×10^{-4} mol), NH_4HCO_2 (0.499 g, 7.93×10^{-3} mol), H_2O (1 mL), butyronitrile (4 mL, 4.57×10^{-2} mol) using general procedure C gave an orange liquid (0.116 g, 100 %): R_f 0.34 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 0.95 (t, $J = 7.8$ Hz, 3H), 1.39-1.45 (m, 2H), 1.55-1.62 (m, 2H), 3.06 (t, $J = 7.2$ Hz, 2H), 3.74 (s, 3H), 6.57 (d, $J = 9.0$ Hz, 2H), 6.80 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.1, 32.0, 44.9, 56.1, 114.2, 115.1, 143.1, 152.18; GCMS (EI) m/z 179.

N-Heptyl-4-methoxyaniline: Starting from 4-nitroanisole (0.050 g, 3.25×10^{-4} mol), MeOH (1.85 mL), 5 % Pd/C (0.019 g, 8.9×10^{-6} mol), NH_4HCO_2 (0.299 g, 3.19×10^{-3} mol), H_2O (0.5 mL), n-hexanoylnitrile (0.16 mL, 1.0×10^{-3} mol) using general procedure C gave a dark-brown oily liquid (0.050 g, 74 %): R_f 0.41 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 0.90 (t, 3H), 1.29-1.44 (br. complex m, 6H), 1.56-1.64 (m, 2H), 3.06 (t, 2H), 3.74 (s, 3H), 6.57 (d, 2H), 6.78 (d, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.3, 22.9, 27.1, 29.9, 31.9, 45.3, 56.1, 114.3, 115.1, 143.1, 152.2; GCMS (EI) m/z 207.

N-Propyl aniline: Starting from nitrobenzene (0.1 g, 8.1×10^{-4} mol), MeOH (3.5 mL), propionitrile (0.59 mL, 6.74×10^{-3} mol) using general procedure C gave a light brown liquid (0.095 g, 86 %). R_f 0.60 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.04 (t, $J = 7.6$ Hz, 3H), 1.63-1.72 (m, 2H), 3.11 (q, $J = 6.8$ Hz, 2H), 6.64 (m, 2H),

6.73 (m, 1H), 7.21 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 23.0, 45.0, 113.0, 117.0, 129.5, 148.0; GCMS (EI) m/z 135.

N-Butyl aniline: Starting from nitrobenzene (0.10 g, 8.1×10^{-4} mol), MeOH (3.4 mL), butyronitrile (0.57 mL, 6.6×10^{-3} mol) using general procedure C gave a light brown liquid (0.085 g, 71 %). R_f 0.58 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.99 (t, $J = 7.2$ Hz, 3H), 1.41-1.50 (m, 2H), 1.59-1.67 (m, 2H), 3.13 (q, $J = 7.2$ Hz, 2H), 6.63 (m, 2H), 6.71 (m, 1H), 7.20 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.1, 20.6, 32.0, 43.9, 113.0, 117.3, 129.5, 148.8; GCMS (EI) m/z 149.

N-Propyl-4-methylaniline: Starting from 4-nitrotoluene (0.05 g, 3.72×10^{-4} mol), MeOH (1.8 mL), 5 % Pd/C (0.019 g, 9.10×10^{-6} mol), NH_4HCO_2 (0.30 g, 3.2×10^{-3} mol), propionitrile (0.46 mL, 6.5×10^{-3} mol) using general procedure C gave a light brown liquid (0.055 g, 100 %). R_f 0.48 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.02 (t, $J = 7.2$ Hz, 3H), 1.62-1.71 (m, 2H), 2.27 (s, 3H), 3.09 (t, $J = 7.2$ Hz, 2H), 6.57 (d, $J = 8.4$ Hz, 2H), 7.02 (d, $J = 8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 20.6, 23.0, 46.5, 113.2, 126.5; 129.9, 146.6; GCMS (EI) m/z 149.

N-Butyl-4-methylaniline: Starting from 4-nitrotoluene (0.101 g, 7.36×10^{-4} mol), MeOH (3.5 mL), butyronitrile (0.510 mL, 2.92×10^{-3} mol) using general procedure C gave a light brown liquid (0.120 g, 100 %). R_f 0.52 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.98 (t, $J = 7.2$ Hz, 3H), 1.41-1.50 (m, 2H), 1.58-1.66 (m, 2H), 2.27 (s, 3H), 3.11 (t, $J = 7.2$ Hz, 2H), 6.56 (d, $J = 8.4$ Hz, 2H), 7.01 (d, $J = 8$ Hz, Ar,

2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.1, 20.6, 20.6, 32.0, 44.3, 113.2, 126.5, 129.9, 146.6; GCMS (EI) m/z 163.

N-Propyl-2-methoxyaniline: Starting from 2-nitroanisole (0.11 g, 7.2×10^{-4} mol), MeOH (3.6 mL), propionitrile (0.41 mL, 5.75×10^{-3} mol) using general procedure C gave a light yellow liquid (0.119 g, 100 %). R_f 0.69 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.06 (t, $J = 7.2$ Hz, 3H), 1.68-1.78 (m, 2H), 3.14 (m, 2H), 3.88 (s, 3H), 4.25 (br. s, 1H), 6.65-6.73 (m, 2H), 6.80-6.82 (m, 1H), 6.90-6.95 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 23.0, 45.8, 55.6, 109.6, 110.0, 116.3, 121.6, 138.8, 147.0; GCMS (EI) m/z 165.

N-Butyl-2-methoxyaniline: Starting from 2-nitroanisole (0.11 g, 7.2×10^{-4} mol), MeOH (3.5 mL), butyronitrile (0.5 mL, 5.75×10^{-3} mol) using general procedure C gave a yellow orange liquid product (0.129 g, 100 %). R_f 0.80 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.98 (t, $J = 7.2$ Hz, 3H), 1.28-1.38 (m, 2H), 1.68-1.78 (m, 2H), 3.14 (t, $J = 7.2$ Hz, 2H), 3.88 (s, 3H), 4.20 (br. s, 1H), 6.61-6.69 (m, 2H), 6.76-6.79 (m, 1H), 6.87-6.91 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.3, 21.0, 31.9, 43.6, 55.6, 109.5, 109.9, 116.3, 121.5, 138.8, 147.0; GCMS (EI) m/z 179.

N-Propyl-2-methylaniline: Starting from 2-nitrotoluene (0.10 g, 7.3×10^{-4} mol), MeOH (3.6 mL), propionitrile (0.42 mL, 5.83×10^{-3} mol) using general procedure C gave a light yellow liquid (0.12 g, 100 %). R_f 0.76 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.06 (t, $J = 7.2$ Hz, 3H), 1.68-1.77 (m, 2H), 2.17 (s, 3H), 3.16 (t, $J = 7.2$ Hz,

2H), 6.64-6.70 (m, 2H), 7.08 (d, 1H), 7.14-7.18 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 17.7, 23.0, 46.0, 109.8, 116.9; 121.9, 127.4, 130.3, 146.6; GCMS (EI) m/z 149.

N-Butyl-2-methylaniline: Starting from 2-nitrotoluene (0.10 g, 7.3×10^{-4} mol), MeOH (3.5 mL), butyronitrile (0.51 mL, 5.83×10^{-3} mol) using general procedure C gave a light yellow liquid product (0.127 g, 100 %): R_f 0.78 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.00 (t, $J = 7.6$ Hz, 3H), 1.43-1.53 (m, 2H), 1.64-1.71 (m, 2H), 2.15 (s, 3H), 3.17 (t, $J = 7.2$ Hz, 2H), 6.62-6.68 (m, 2H), 7.07 (d, 1H), 7.13-7.17 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 17.7, 20.6, 32.0, 43.9, 109.8, 116.8; 121.9, 127.4, 130.2, 146.7; GCMS (EI) m/z 163.

N-Propyl-3-methylaniline: Starting from 3-nitrotoluene (0.1 g, 7.29×10^{-4} mol), MeOH (3.6 mL), propionitrile (0.42 mL, 5.83×10^{-3} mol) using general procedure C gave a reddish-brown liquid (0.097 g, 89 %): R_f 0.59 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.08 (t, $J = 7.2$ Hz, 3H), 1.68-1.73 (m, 2H), 2.36 (s, 3H), 3.14 (t, $J = 7.2$ Hz, 2H), 6.51 (br. m, 2H), 6.59-6.61 (d, 1H), 7.12-7.16 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 21.9, 23.1, 46.1, 110.2, 113.8; 118.3, 129.4, 139.2, 148.9; GCMS (EI) m/z 149.

N-Butyl-3-methylaniline: Starting from 3-nitrotoluene (0.10 g, 7.29×10^{-4} mol), MeOH (3.5 mL), butyronitrile (0.51 mL, 5.83×10^{-3} mol) using general procedure C gave a light yellow liquid (0.119 g, 100 %): R_f 0.70 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.97 (t, $J = 7.2$ Hz, 3H), 1.39-1.49 (m, 2H), 1.57-1.64 (m, 2H), 2.29 (s, 3H),

3.10 (t, $J = 7.2$ Hz, 2H), 6.42-6.44 (br. complex m, 2H), 6.53 (d, 1H), 7.05-7.09 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.6, 21.9, 32.0, 43.9, 110.1, 113.69; 118.2, 129.3, 139.1, 148.9; GCMS (EI) m/z 163.

N-Propyl hexylamine: Starting from 1-nitrohexane (0.10 g, 7.6×10^{-4} mol), MeOH (3.6 mL), propionitrile (0.4 mL, 6.10×10^{-3} mol) using general procedure C gave a light yellow liquid (0.044 g, 50 %): ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.84-0.98 (complex m, 6H), 1.15-1.83 (br. complex m, 10H), 2.36 (m, 3H), 2.56 (m, 3H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.8, 14.4, 22.9, 23.2, 28.1, 30.7, 32.6, 49.9, 52.2; GCMS (EI) m/z 143.

General Procedure D: Starting material (100 mg, primary amine) was dissolved in MeOH and stirred at room temperature. 5 % Pd/C (0.039 g, 1.8×10^{-5} mol) and NH_4HCO_2 (0.60 g, 9.5×10^{-3} mol) dissolved in H_2O (1.0 mL) was then added to the reaction mixture while stirring. Nitrile (8 eq) was then added to the reaction mixture and stirring was continued until the primary amine intermediate (lowest R_f) was no longer detected by TLC. The reaction mixture was filtered, washed successively with methanol and CH_2Cl_2 and the filtrate evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2 and the organic layer was separated, dried in Na_2SO_4 and filtered. The filtrate was then evaporated *in vacuo* to give the product.

N-Ethyl aniline: Starting from aniline (0.10 g, 1.1×10^{-3} mol), MeOH (3.3 mL), acetonitrile (0.45 mL, 8.56×10^{-3} mol) using general procedure D gave a light yellow liquid (0.108, 83.0 %). R_f 0.45 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 ,

δ_{H}) 1.20 (t, $J = 7.2$ Hz, 3H), 3.19 (q, $J = 7.2$ Hz, 2H), 6.65 (m, 2H), 6.75 (m, 1H), 7.22 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.3, 38.8, 113.1, 117.6, 129.6, 148.8; GCMS (EI) m/z 121.

N-Propyl-4-methoxyaniline: Starting from *p*-anisidine (0.103 g, 8.42×10^{-4} mol), MeOH (3.6 mL), propionitrile (0.5 mL, 6.69×10^{-3} mol) using general procedure D gave a yellow-orange liquid (0.137 g, 99 %). R_{f} 0.33 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.01 (t, $J = 7.2$ Hz, 3H), 1.62-1.67 (m, 2H), 3.05 (t, $J = 7.2$ Hz, 2H), 3.76 (s, 3H), 6.61 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 23.1, 47.1, 56.1, 114.3, 115.1, 143.1, 152.1; GCMS (EI) m/z 165.

N-Butyl-4-methoxyaniline: Starting from *p*-anisidine (0.104 g, 8.42×10^{-4} mol), MeOH (4.0 mL), butyronitrile (0.6 mL, 6.69×10^{-3} mol) using general procedure D gave a yellow-orange liquid (0.151 g, 100 %). R_{f} 0.37 (10:1 hexanes:ethyl acetate); 0.99 (t, $J = 7.2$ Hz, 3H), 1.43-1.48 (m, 2H), 1.58-1.63 (m, 2H), 3.09 (t, $J = 7.2$ Hz, 2H), 3.77 (s, 3H), 6.61 (d, $J = 8.8$ Hz, 2H), 6.82 (d, $J = 8.8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.6, 32.0, 45.0, 56.0, 114.3, 115.1, 143.1, 152.2; GCMS (EI) m/z 179.

N-Ethyl-aniline: Starting from aniline (0.10 g, 1.07×10^{-3} mol), MeOH (3.6 mL), acetonitrile (0.45 mL, 8.56×10^{-3} mol) using general procedure D gave a dark orange-brown liquid (0.08 g, 83 %). R_{f} 0.59 (10:1 hexanes:ethyl acetate); ^1H NMR (600 MHz, CDCl_3 , δ_{H}) 1.29 (t, $J = 7.2$ Hz, 3H), 3.19 (q, $J = 7.2$ Hz, 2H), 3.64 (br. s, 1H), 6.65 (m,

2H), 6.72 (m, 1H), 7.21 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 15.2, 38.7, 113.0, 117.5, 129.5, 148.7; GCMS (EI) m/z 121.

N-Propyl aniline: Starting from aniline (0.1 g, 1.07×10^{-3} mol), MeOH (3.3 mL), propionitrile (0.61 mL, 8.56×10^{-3} mol) using general procedure D gave a light brown liquid product (0.09 g, 99.6 %). R_f 0.60 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.03 (t, $J = 7.6$ Hz, 3H), 1.63-1.72 (m, 2H), 3.11 (q, $J = 7.2$ Hz, 2H), 3.66 (br. s, 1H), 6.64 (m, 2H), 6.73 (m, 1H), 7.21 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 23.0, 46.1, 113.0, 117.3, 129.5, 148.8; GCMS (EI) m/z 135.

N-Butyl aniline: Starting from aniline (0.10 g, 1.07×10^{-3} mol), MeOH (2.6 mL), butyronitrile (0.75 mL, 8.56×10^{-3} mol) using general procedure D gave a brown liquid (0.160 g, 100 %). R_f 0.66 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.01 (t, $J = 7.2$ Hz, 3H), 1.43-1.52 (m, 2H), 1.60-1.68 (m, 2H), 3.14 (q, $J = 7.2$ Hz, 2H), 6.65 (m, 2H), 6.74 (m, 1H), 7.22 (m, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.6, 32.0, 44.0, 113.0, 117.3, 129.5, 148.9; GCMS (EI) m/z 149.

N-Propyl-4-methylaniline: Starting from *p*-toluidine (0.103 g, 9.6×10^{-4} mol), MeOH (3.5 mL), propionitrile (0.46 mL, 6.5×10^{-3} mol) using general procedure D gave a red-orange liquid (0.143 g, 100 %). R_f 0.49 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.01 (t, $J = 7.2$ Hz, 3H), 1.62-1.70 (m, 2H), 2.27 (s, 3H), 3.07 (t, $J = 7.2$ Hz, 2H), 6.56 (d, $J = 8.4$ Hz, 2H), 7.01 (d, $J = 8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 20.6, 23.0, 46.5, 113.2, 126.5, 129.9, 146.5; GCMS (EI) m/z 149.

N-Butyl-4-methylaniline: Starting from *p*-toluidine (0.107 g, 9.96×10^{-4} mol), MeOH (3.3 mL), butyronitrile (0.65 mL, 7.5×10^{-3} mol) using general procedure D gave a red-orange liquid (0.163 g, 100 %). R_f 0.50 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.02 (t, $J = 7.6$ Hz, 3H), 1.43-1.53 (m, 2H), 1.60-1.68 (m, 2H), 2.30 (s, 3H), 3.11 (t, $J = 7.2$ Hz, 2H), 6.59 (d, $J = 8.4$ Hz, 2H), 7.04 (d, $J = 8$ Hz, 2H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.6, 20.7, 32.0, 44.3, 113.2, 126.4, 130.0, 146.6; GCMS (EI) m/z 163.

N-Propyl-2-methoxyaniline: Starting from *o*-anisidine (0.10 g, 8.12×10^{-4} mol), MeOH (3.5 mL), propionitrile (0.46 mL, 6.5×10^{-3} mol) using general procedure D gave a light yellow liquid (0.134 g, 100 %). R_f 0.62 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.07 (t, $J = 7.6$ Hz, 3H), 1.70-1.78 (m, 2H), 3.15 (m, 2H), 3.89 (s, 3H), 6.66-6.74 (m, 2H), 6.81-6.83 (m, 1H), 6.92-6.96 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 23.0, 45.8, 55.6, 109.7, 110.0, 116.3, 121.6, 138.8, 147.0; GCMS (EI) m/z 165.

N-Butyl-2-methoxyaniline: Starting from *o*-anisidine (0.10 g, 8.1×10^{-4} mol), MeOH (3.4 mL), butyronitrile (0.57 mL, 6.50×10^{-3} mol) using general procedure D gave a yellow orange liquid (0.150 g, 100 %). R_f 0.78 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.02 (t, $J = 7.6$ Hz, 3H), 1.44-1.54 (m, 2H), 1.66-1.73 (m, 2H), 3.17 (m, 2H), 3.88 (s, 3H), 4.22 (br. s, 1H), 6.65-6.72 (m, 2H), 6.80-6.82 (m, 1H), 6.90-6.95 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.7, 31.9, 43.7, 55.6, 109.6, 110.0, 116.3, 121.6, 138.8, 147.0; GCMS (EI) m/z 179.

N-Propyl-2-methylaniline: Starting from *o*-toluidine (0.100 g, 9.3×10^{-4} mol), MeOH (3.5 mL), propionitrile (0.53 mL, 7.4×10^{-3} mol) using general procedure D gave a light yellow liquid (0.139 g, 99.9 %): R_f 0.77 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.14 (t, $J = 7.2$ Hz, 3H), 1.75-1.85 (m, 2H), 2.24 (s, 3H), 3.23 (t, $J = 7.2$ Hz, 2H), 3.54 (br. s, 1H), 6.72-6.78 (m, 2H), 7.16 (d, 1H), 7.22-7.27 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 17.8, 23.1, 46.1, 109.9, 116.9; 122.0, 127.5, 130.4, 146.7; GCMS (EI) m/z 149.

N-Butyl-2-methylaniline: Starting from *o*-toluidine (0.100 g, 9.3×10^{-4} mol) MeOH (3.3 mL), butyronitrile (0.65 mL, 7.5×10^{-3} mol) using general procedure D gave a light yellow liquid (0.152 g, 100 %): R_f 0.76 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.01 (t, $J = 7.6$ Hz, 3H), 1.44-1.54 (m, 2H), 1.64-1.71 (m, 2H), 2.16 (s, 3H), 3.18 (t, $J = 7.2$ Hz, 2H), 6.63-6.69 (m, 2H), 7.08 (d, 1H), 7.14-7.18 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 17.7, 20.7, 32.0, 43.9, 109.8, 116.8, 121.9, 127.4, 130.2, 146.7; GCMS (EI) m/z 163.

N-Propyl-3-methylaniline: Starting from *m*-toluidine (0.10 g, 9.3×10^{-4} mol), MeOH (3.5 mL,) propionitrile (0.52 mL, 7.46×10^{-3} mol), reddish-brown liquid (0.132 g, 100 %): R_f 0.59 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.12 (t, $J = 7.2$ Hz, 3H), 1.70-1.79 (m, 2H), 2.41 (s, 3H), 3.17 (t, $J = 7.2$ Hz, 2H), 6.55 (br. m, 2H), 6.64-6.66 (d, 1H), 7.17-7.21 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 22.0, 23.1, 46.2, 110.2, 113.8; 118.3, 129.4, 139.2, 149.0; GCMS (EI) m/z 149.

N-Butyl-3-methylaniline: Starting from *m*-toluidine (0.10 g, 9.3×10^{-4} mol), MeOH (3.3 mL), butyronitrile (0.65 mL, 7.5×10^{-3} mol) using general procedure D gave a light yellow liquid product (0.127 g, 100 %). R_f 0.70 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.00 (t, $J = 7.2$ Hz, 3H), 1.42-1.49 (m, 2H), 1.59-1.65 (m, 2H), 2.32 (s, 3H), 3.13 (t, $J = 7.2$ Hz, 2H), 3.57 (br. s, 1H), 6.45-6.46 (br. complex m, 2H), 6.55 (d, 1H), 7.08-7.12 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.2, 20.6, 21.9, 32.0, 44.0, 110.1, 113.7, 118.3, 129.3, 139.2, 148.9; GCMS (EI) m/z 163.

N-Propyl-3-methoxyaniline: Starting from *m*-anisidine (0.10 g, 8.12×10^{-4} mol), MeOH (3.5 mL), propionitrile (0.46 mL, 6.50×10^{-3} mol) using general procedure D gave a brown liquid (0.134 g, 100 %): R_f 0.44 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 1.02 (t, $J = 7.2$ Hz, 3H), 1.61-1.70 (m, 2H), 3.009 (t, $J = 7.2$ Hz, 2H), 3.80 (s, 3H), 6.19-6.20 (m, 1H), 6.24-6.30 (m, 2H), 7.08-7.13 (m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 11.9, 23.0, 46.0, 55.3, 98.9, 102.4, 106.2, 130.2, 150.2, 161.2; GCMS (EI) m/z 165.

N-Butyl-3-methoxyaniline: Starting from *m*-anisidine (0.10 g, 8.1×10^{-4} mol), MeOH (3.43 mL), butyronitrile (0.57 mL, 6.50×10^{-3} mol) using general procedure D gave an orange brown liquid product (0.146 g, 100 %): R_f 0.72 (10:1 hexanes:ethyl acetate); ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.93 (t, $J = 7.2$ Hz, 3H), 1.39-1.47 (m, 2H), 1.55-1.63 (m, 2H), 3.06-3.11 (m, 2H), 3.76 (s, 3H), 6.16-6.17 (m, 1H), 6.21-6.27 (m, 2H), 7.05-7.09

(m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.4, 31.9, 43.9, 54.2, 55.2, 98.8, 102.3, 106.1, 130.1, 150.2, 161.1; GCMS (EI) m/z 179.

N-Propyl cyclohexylamine: Starting from cyclohexylamine (0.10 g, 1.0×10^{-3} mol), propionitrile (0.58 mL, 8.08×10^{-3} mol) using general procedure D gave a light yellow liquid product (0.102 g, 77 %). ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.76-0.80 (complex m, 1H), 0.84 (t, $J = 7.2$ Hz, 3H), , 0.94-1.04 (brm, 2H), 1.05-1.22 (brm, 3H), 1.37-1.46 (m, 2H), 1.60-1.70 (brm, 2H), 1.77-1.82 (brm, 2H), 2.27-2.37 (brm, 1H), 2.51 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 12.0, 23.8, 25.3, 26.4, 33.9, 49.1, 57.0; GCMS (EI) m/z 141.

N-butyl cyclohexylamine: Starting from cyclohexylamine (0.25 g, 2.5×10^{-3} mol), butyronitrile (1.77 mL, 2.02×10^{-2} mol) using general procedure D gave an oily crystalline solid (0.334 g, 85 %). ^1H NMR (400 MHz, CDCl_3 , δ_{H}) 0.82 (t, $J = 7.2$ Hz, 3H), 1.00-1.94 (brm, 14H), 2.64 (complex m, 1H); ^{13}C NMR (400 MHz, CDCl_3 , δ_{C}) 14.3, 21.0, 25.3, 29.3, 33.3, 46.6, 54.0, 57.1; GCMS (EI) m/z 155.