

# A Multi-Ligand Based Pd Catalyst for C–N Cross-Coupling Reactions

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## *Supporting Information*

### ***General Reagent Information***

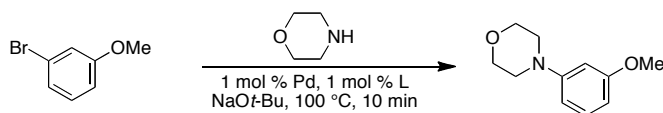
All reactions were carried out under an argon atmosphere. The 1,4-dioxane and *tert*-butanol were purchased from Aldrich Chemical Company in Sure-Seal bottles and were used as received. Toluene was purchased from J.T. Baker in CYCLE-TAINER<sup>®</sup> solvent-delivery kegs and vigorously purged with argon for 2 h. The solvent was further purified by passing it under argon pressure through two packed columns of neutral alumina and copper (II) oxide. Aryl halides, amines, and aryl triflates were purchased from Aldrich Chemical Co., Alfa Aesar, Acros Organics or TCI America and were used as received without further purification. Aryl mesylates that were not commercially available were synthesized using literature procedures.<sup>1</sup> A solution of methylamine in THF was purchased from Alfa Aesar. Anhydrous cesium carbonate was a gift from Chemetall. Sodium *tert*-butoxide was purchased from Aldrich Chemical Company and anhydrous tribasic potassium phosphate was purchased from Fluka Chemical Company. The bases were stored in a nitrogen-filled glovebox and were taken out in small quantities and stored on the bench for up to two weeks. Ligands **1**<sup>2</sup> and **2**,<sup>3</sup> precatalysts **3**<sup>2</sup> and **4**,<sup>4</sup> and Pd complexes **5** and **7**<sup>2</sup> were synthesized using literature procedures. Flash chromatography was performed using a Biotage SP4 instrument with prepacked silica cartridges.

### ***General Analytical Information***

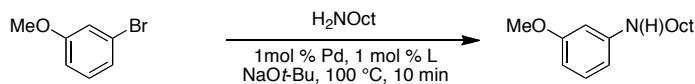
All compounds were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR spectroscopy, as well as, in most instances, elemental analysis. Copies of the <sup>1</sup>H and <sup>13</sup>C spectra can be found at the end of the Supporting Information. Nuclear Magnetic Resonance spectra were recorded

on a Varian 300 MHz instrument and a Varian 500 MHz instrument. All  $^1\text{H}$  NMR experiments are reported in  $\delta$  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  $^{13}\text{C}$  NMR spectra are reported in ppm relative to deuteriochloroform (77.23 ppm), unless otherwise stated, and all were obtained with  $^1\text{H}$  decoupling. All IR spectra were 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 Microlabs Inc., Norcross, GA.

***Experimental Procedures for Examples Described in Table 1***

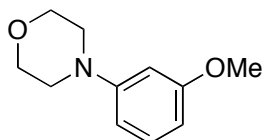


**General Procedure for Table 1a:** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with the ligand (1.0 mol %), the precatalyst (1 mol %), and NaOt-Bu (134 mg, 1.4 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the 3-bromoanisole (127  $\mu\text{L}$ , 1.0 mmol), morpholine (122  $\mu\text{L}$ , 1.4 mmol), and 1,4-dioxane (1 mL) were added via syringe. The solution was heated to 100 °C for 10 min and then was cooled to room temperature, diluted with ethyl acetate and washed with water. A known amount of dodecane was added to the solution as an internal standard and then the reaction mixture was analyzed via GC.

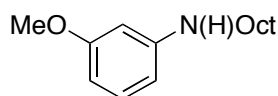


**General Procedure for Table 1b:** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with the ligand (1.0 mol %), the precatalyst (1 mol %), and NaOt-Bu (134 mg, 1.4 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the 3-bromoanisole (127  $\mu\text{L}$ , 1.0 mmol), octylamine (231  $\mu\text{L}$ , 1.4 mmol), and 1,4-

dioxane (1 mL) were added via syringe. The solution was heated to 100 °C for 10 min and then was cooled to room temperature, diluted with ethyl acetate and washed with water. A known amount of dodecane was added to the solution as an internal standard and then the reaction mixture was analyzed via GC.



**4-(3-Methoxyphenyl)morpholine.**<sup>5</sup> An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with **2** (4.7 mg, 1.0 mol %), **3** (8 mg, 1 mol %), and NaOt-Bu (134 mg, 1.4 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the 3-bromoanisole (127  $\mu$ L, 1.0 mmol), morpholine (122  $\mu$ L, 1.4 mmol), and 1,4-dioxane (1 mL) were added via syringe. The solution was heated to 100 °C for 10 min and then was cooled to room temperature, diluted with ethyl acetate, washed with water and concentrated in vacuo. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-25% EtOAc/hexanes) to provide the title compound as a clear oil (173 mg, 90%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.20 (t,  $J$  = 8.1 Hz, 1H), 6.54 (d,  $J$  = 8.1 Hz, 1H), 6.46 (m, 2H), 3.86 (t,  $J$  = 5.1 Hz, 4H), 3.80 (s, 3H), 3.15 (t,  $J$  = 5.1 Hz, 4H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 160.9, 153.0, 130.1, 108.7, 104.9, 102.4, 67.1, 55.4, 49.5 ppm. IR (neat, cm<sup>-1</sup>): 2834, 1602, 1497, 1449, 1267, 1205, 1170, 1122, 957, 836. Anal. Calcd. for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>: C, 68.37; H, 7.82. Found: C, 68.64; H, 7.93.



**3-Methoxy-N-octylaniline.** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with **2** (4.7 mg, 1.0 mol %), **3** (8 mg, 1 mol %), and NaOt-Bu (134 mg, 1.4 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the 3-bromoanisole (127  $\mu$ L, 1.0 mmol), octylamine (231  $\mu$ L, 1.4 mmol), and 1,4-dioxane (1 mL) were added via syringe. The solution was heated to 100 °C for 10 min and then was

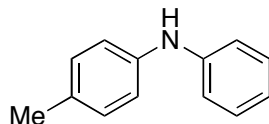
cooled to room temperature, diluted with ethyl acetate, washed with water and concentrated in vacuo. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-25% EtOAc/hexanes) to provide the title compound as a clear oil (mg, %).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.11 (t,  $J = 8.1$  Hz, 1H), 6.25 (m, 3H), 3.81 (s, 3H), 3.67 (bs, 1H), 3.12 (t,  $J = 6.9$  Hz, 2H), 1.64 (m, 2H), 1.34 (m, 10H), 0.94 (m, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 161.1, 150.2, 130.2, 106.2, 102.4, 98.8, 55.3, 44.2, 32.1, 29.8, 29.7, 29.6, 27.5, 23.0, 14.4 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3406, 2927, 2855, 1615, 1497, 1212, 1162, 1051, 755, 687. Anal. Calcd. for  $\text{C}_{15}\text{H}_{25}\text{NO}$ : C, 76.55; H, 10.71. Found: C, 76.98; H, 10.80.

### *Experimental Procedures for Examples Described in Table 2*

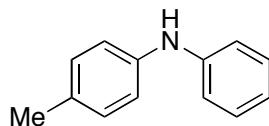
**General Procedure A:** An oven-dried test tube, which was equipped with a magnetic stir bar, was charged with the base (1.4 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the aryl halide (1.0 equiv), amine (1.4 equiv), and solvent (0.5 mL/mmol) were added via syringe (aryl chlorides and amines that were solids were added with the base). A solution of **2** and **3** (0.002M, 0.005 – 0.1 mol % **2**, 0.005 – 0.1 mol % **3**) was added and then the reaction mixture was heated to 110 °C until the starting material was completely consumed as monitored by GC. The reaction mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, concentrated in vacuo, and purified via the Biotage SP4.

**General Procedure B:** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with **2** (0.1 – 1 mol %), **3** (0.1 – 1 mol %) and the base (1.4 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the aryl halide (1.0 equiv), amine (1.4 equiv), and solvent (2 mL/mmol) were added via syringe (aryl chlorides and amines that were solids were added with the catalyst and base). The solution was heated to 110 °C until the starting material was completely consumed as monitored by GC. The reaction

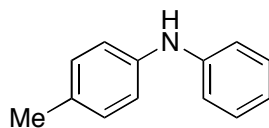
mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, concentrated in vacuo, and purified via the Biotage SP4.



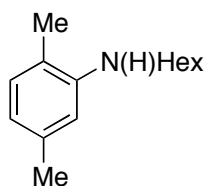
**4-Methyl-N-phenylaniline.**<sup>6</sup> Following general procedure A, a mixture of chlorobenzene (204  $\mu$ L, 2.0 mmol), *p*-toluidine (299 mg, 2.8 mmol), BrettPhos Precat (0.01 mol %), RuPhos (0.01 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-25% EtOAc/hexanes) to provide the title compound as a white solid (364 mg, 99%), mp = 88 – 90  $^{\circ}$ C (lit. 86 – 87  $^{\circ}$ C).  $^1$ H NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.32 (t,  $J$  = 7.5 Hz, 2H), 7.17 (d,  $J$  = 8.1 Hz, 2H), 7.08 (m, 4H), 6.97 (t,  $J$  = 7.5 Hz, 1H), 5.64 (bs, 1H), 2.39 (s, 3H) ppm.  $^{13}$ C NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 144.3, 140.7, 131.3, 130.3, 129.8, 120.7, 119.3, 117.3, 21.2 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3394, 2917, 1595, 1514, 1309, 1078, 809, 747, 694, 505. Anal. Calcd. for  $\text{C}_{13}\text{H}_{13}\text{N}$ : C, 85.21; H, 7.15. Found: C, 85.16; H, 7.28.



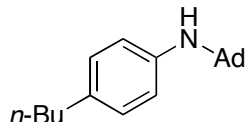
**4-Methyl-N-phenylaniline.**<sup>6</sup> Following general procedure A, a mixture of bromobenzene (211  $\mu$ L, 2.0 mmol), *p*-toluidine (299 mg, 2.8 mmol), BrettPhos Precat (0.005 mol %), RuPhos (0.005 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-25% EtOAc/hexanes) to provide the title compound as a white solid (364 mg, 99%), mp = 89 – 90  $^{\circ}$ C (lit. 86 – 87  $^{\circ}$ C).  $^1$ H NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.34 (t,  $J$  = 7.2 Hz, 2H), 7.19 (d,  $J$  = 8.4 Hz, 2H), 7.10 (m, 4H), 6.99 (t,  $J$  = 7.2 Hz, 1H), 5.65 (bs, 1H), 2.41 (s, 3H) ppm.  $^{13}$ C NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 144.3, 140.6, 131.2, 130.2, 129.7, 120.6, 119.2, 117.2, 21.1 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3395, 2916, 1595, 1514, 1309, 809, 771, 747, 694, 505. Anal. Calcd. for  $\text{C}_{13}\text{H}_{13}\text{N}$ : C, 85.21; H, 7.15. Found: C, 85.17; H, 7.27.



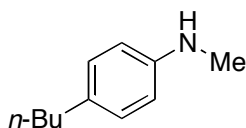
**4-Methyl-N-phenylaniline.**<sup>6</sup> Following general procedure A, a mixture of iodobenzene (224  $\mu$ L, 2.0 mmol), *p*-toluidine (299 mg, 2.8 mmol), BrettPhos Precat (0.005 mol %), RuPhos (0.005 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-25% EtOAc/hexanes) to provide the title compound as a white solid (286 mg, 78%), mp = 87 – 89  $^{\circ}$ C (lit. 86 – 87  $^{\circ}$ C).  $^1$ H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.32 (t,  $J$  = 7.5 Hz, 2H), 7.17 (d,  $J$  = 8.1 Hz, 2H), 7.08 (m, 4H), 6.97 (t,  $J$  = 7.2 Hz, 1H), 5.64 (bs, 1H), 2.39 (s, 3H) ppm.  $^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 144.2, 140.6, 131.2, 130.2, 129.6, 120.6, 119.2, 117.2, 21.0 ppm. IR (neat, cm<sup>-1</sup>): 3395, 2916, 1596, 1514, 1501, 1309, 810, 747, 694, 506. Anal. Calcd. for C<sub>13</sub>H<sub>13</sub>N: C, 85.21; H, 7.15. Found: C, 85.24; H, 7.34.



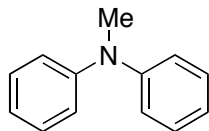
**N-Hexyl-2,5-dimethylaniline.**<sup>7</sup> Following general procedure A, a mixture of 2-chloro-*p*-xylene (269  $\mu$ L, 2.0 mmol), hexylamine (370  $\mu$ L, 2.8 mmol), BrettPhos Precat (0.05 mol %), RuPhos (0.05 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a clear oil (385 mg, 94%).  $^1$ H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.17 (d,  $J$  = 7.0 Hz, 1H), 6.71 (d,  $J$  = 7.5 Hz, 1H), 6.69 (s, 1H), 3.60 (bs, 1H), 3.37 (t,  $J$  = 7.5 Hz, 2H), 2.55 (s, 3H), 2.33 (s, 3H), 1.89 (pentet,  $J$  = 7.5 Hz, 2H), 1.67 (pentet,  $J$  = 7.0 Hz, 2H), 1.59 (m, 4H), 1.18 (t,  $J$  = 7.0 Hz, 3H) ppm.  $^{13}$ C NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$ : 146.8, 137.1, 130.3, 119.1, 117.7, 111.0, 44.4, 32.2, 30.1, 27.5, 23.2, 22.0, 17.4, 14.6 ppm. IR (neat, cm<sup>-1</sup>): 3430, 2956, 1616, 1584, 1523, 1467, 1376, 1298, 999, 793.



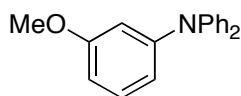
***N*-(4-Butylphenyl)adamantan-1-amine.** Following general procedure B, a mixture of 4-*n*-butylchlorobenzene (169  $\mu$ L, 1.0 mmol), adamantan-1-amine (181 mg, 1.2 mmol), BrettPhos Precat (8 mg, 1.0 mol %), RuPhos (5 mg, 1 mol %), NaO*t*-Bu (134 mg, 1.4 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a clear oil (228 mg, 81%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.01 (d,  $J$  = 8.4 Hz, 2H), 6.79 (d,  $J$  = 8.7 Hz, 2H), 3.38 (bs, 1H), 2.55 (t,  $J$  = 7.8 Hz, 2H), 2.12 (s, 3H), 1.86, (s, 5H), 1.66 (m, 7H), 1.38 (sextet,  $J$  = 7.8 Hz, 2H), 0.96 (t,  $J$  = 7.5 Hz, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 143.5, 134.7, 128.8, 120.9, 52.6, 43.9, 36.8, 35.1, 34.1, 30.2, 22.7, 14.3 ppm. IR (neat,  $\text{cm}^{-1}$ ): 2907, 2850, 1614, 1513, 1453, 1356, 1309, 1242, 1092, 823. Anal. Calcd. for  $\text{C}_{20}\text{H}_{29}\text{N}$ : C, 84.75; H, 10.31. Found: C, 84.61; H, 10.44.



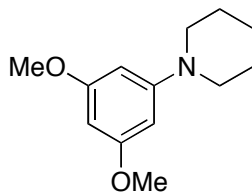
**4-Butyl-*N*-methylaniline.**<sup>2</sup> Following general procedure B, a mixture of 4-*n*-butylchlorobenzene (169  $\mu$ L, 1.0 mmol), methylamine (2 M in THF, 1 mL, 2.0 mmol), BrettPhos Precat (8 mg, 1.0 mol %), RuPhos (5 mg, 1 mol %), NaO*t*-Bu (134 mg, 1.4 mmol), and *t*-BuOH (1 mL) was heated to 80  $^{\circ}$ C for 16 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a clear oil (145 mg, 89%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.10 (d,  $J$  = 8.4 Hz, 2H), 6.63 (d,  $J$  = 8.7 Hz, 2H), 3.56 (bs, 1H), 2.88 (s, 3H), 2.60 (t,  $J$  = 7.8 Hz, 2H), 1.65 (pentet,  $J$  = 7.8 Hz, 2H), 1.43 (sextet,  $J$  = 7.8 Hz, 2H), 1.01 (t,  $J$  = 7.2 Hz, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 147.6, 132.0, 129.4, 112.8, 35.1, 34.4, 31.3, 22.7, 14.3 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3412, 2927, 2872, 1618, 1522, 1466, 1316, 1263, 1183, 816. Anal. Calcd. for  $\text{C}_{11}\text{H}_{17}\text{N}$ : C, 80.93; H, 10.50. Found: C, 81.02; H, 10.60.



***N*-Methyl-*N*-phenylaniline.**<sup>8</sup> Following general procedure A, a mixture of chlorobenzene (204  $\mu$ L, 2.0 mmol), *N*-methylaniline (303  $\mu$ L, 2.8 mmol), BrettPhos Precat (0.01 mol %), RuPhos (0.01 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a yellow oil (359 mg, 98%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.49 (t,  $J = 7.2$  Hz, 4H), 7.25 (d,  $J = 7.8$  Hz, 4H), 7.18 (t,  $J = 7.2$  Hz, 2H), 3.51 (s, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 149.5, 129.7, 121.8, 120.9, 40.7 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3036, 1591, 1497, 1343, 1253, 1131, 1029, 864, 750, 694. Anal. Calcd. for  $\text{C}_{13}\text{H}_{13}\text{N}$ : C, 85.21; H, 7.15. Found: C, 85.20; H, 7.23.

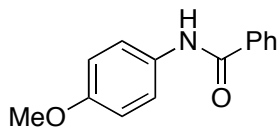


**3-Methoxy-*N,N*-diphenylaniline.**<sup>9</sup> Following general procedure A, a mixture of 3-chloroanisole (246  $\mu$ L, 2.0 mmol), diphenylamine (473 mg, 2.8 mmol), BrettPhos Precat (0.05 mol %), RuPhos (0.05 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (NH-packed 55 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a clear oil (540 mg, 99%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.39 (t,  $J = 8.4$  Hz, 4H), 7.28 (m, 5H), 7.16 (t,  $J = 7.2$  Hz, 2H), 6.86 (m, 2H), 6.73 (m, 1H), 3.83 (s, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 160.9, 149.6, 148.2, 130.3, 129.7, 124.9, 123.3, 116.9, 110.2, 108.5, 55.6 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3035, 2834, 1587, 1485, 1312, 1222, 1173, 1049, 754, 696. Anal. Calcd. for  $\text{C}_{19}\text{H}_{17}\text{NO}$ : C, 82.88; H, 6.22. Found: C, 83.00; H, 6.22.





**1-(3,5-Dimethoxyphenyl)piperidine.** Following general procedure A, a mixture of 3,5-dimethoxychlorobenzene (346 mg, 2.0 mmol), piperidine (276  $\mu$ L, 2.8 mmol), BrettPhos Precat (0.05 mol %), RuPhos (0.05 mol %), NaOt-Bu (268 mg, 2.8 mmol), and 1,4-dioxane (1 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-40% EtOAc/hexanes) to provide the title compound as a yellow oil (350 mg, 78%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.14 (d,  $J$  = 2.1 Hz, 2H), 6.02 (t,  $J$  = 2.1 Hz, 1H), 3.78 (s, 6H), 3.16 (m, 4H), 1.71 (m, 4H), 1.59 (m, 2H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 161.7, 154.4, 95.6, 91.4, 55.3, 50.8, 26.1, 24.7 ppm. IR (neat,  $\text{cm}^{-1}$ ): 2934, 2851, 1594, 1461, 1203, 1152, 1127, 1072, 995, 817. Anal. Calcd. for  $\text{C}_{13}\text{H}_{19}\text{NO}_2$ : C, 70.56; H, 8.65. Found: C, 70.75; H, 8.68.

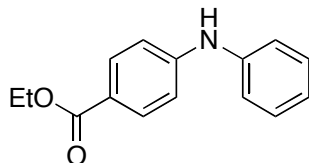


**N-(4-Methoxyphenyl)benzamide.**<sup>10</sup> Following general procedure B, a mixture of 4-chloroanisole (123  $\mu$ L, 1.0 mmol), benzamide (169 mg, 1.4 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{K}_3\text{PO}_4$  (297 mg, 1.4 mmol), and *t*-BuOH (2 mL) was heated to 110  $^{\circ}$ C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0-50% EtOAc/hexanes) to provide the title compound as a white solid (187 mg, 82%), mp = 153 – 154  $^{\circ}$ C (lit. 154 – 155  $^{\circ}$ C).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.89 (bs, 1H), 7.86 (d,  $J$  = 7.0 Hz, 2H), 7.54 (m, 3H), 7.47 (m, 2H), 6.90 (d,  $J$  = 9.0 Hz, 2H), 3.82 (s, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 156.8, 135.2, 131.9, 131.2, 129.0, 127.3, 122.4, 114.4, 55.8 ppm. IR (neat,  $\text{cm}^{-1}$ ): 1645, 1515, 1384, 1251, 1107, 1031, 824, 716, 692, 652. Anal. Calcd. for  $\text{C}_{14}\text{H}_{13}\text{NO}_2$ : C, 73.99; H, 5.77. Found: C, 74.18; H, 5.71.

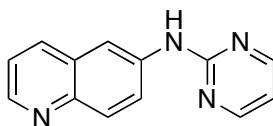
### *Experimental Procedures for Examples Described in Table 2*

**General Procedure C:** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with **2** (0.1 – 1 mol %), **3** (0.1 – 1 mol %) and the base (1.4 equiv). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then the aryl halide (1.0 equiv), amine (1.4

equiv), and solvent (2 mL/mmol) were added via syringe (aryl chlorides and amines that were solids were added with the catalyst and base). The solution was heated to 110 °C until the starting material was completely consumed as monitored by GC. The reaction mixture was then cooled to room temperature, concentrated in vacuo, and purified via the Biotage SP4.

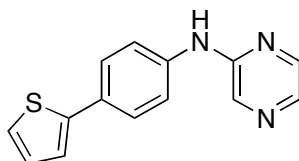


**Ethyl 4-(phenylamino)benzoate.**<sup>11</sup> Following general procedure C, a mixture of chlorobenzene (202  $\mu$ L, 0.5 mmol), ethyl 4-aminobenzoate (462 mg, 2.8 mmol), BrettPhos Precat (0.1 mol %), RuPhos (0.1 mol %), Cs<sub>2</sub>CO<sub>3</sub> (913 mg, 2.8 mmol), and *t*-BuOH (2 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0 – 40% EtOAc/hexanes) to provide the title compound as a white solid (414 mg, 86%), mp = 109 – 111 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.95 (d,  $J$  = 8.7 Hz, 2H), 7.34 (t,  $J$  = 8.4 Hz, 2H), 7.18 (d,  $J$  = 7.8 Hz, 2H), 7.06 (t,  $J$  = 7.5 Hz, 1H), 7.01 (d,  $J$  = 9.0 Hz, 2H), 6.30 (bs, 1H), 4.35 (q,  $J$  = 7.2 Hz, 2H), 1.39 (t,  $J$  = 7.2 Hz, 3H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 166.9, 148.4, 141.2, 131.7, 129.7, 123.2, 121.5, 120.5, 114.8, 60.8, 14.7 ppm. IR (neat, cm<sup>-1</sup>): 3337, 1690, 1678, 1590, 1529, 1339, 1279, 1174, 753, 695.

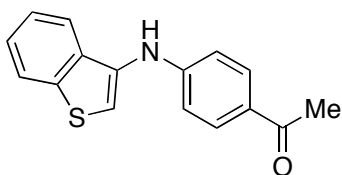


***N*-(Pyrimidin-2-yl)quinolin-6-amine.** Following general procedure C, a mixture of 6-chloroquinoline (82 mg, 0.5 mmol), 2-aminopyrimidine (67 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %), Cs<sub>2</sub>CO<sub>3</sub> (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 50-100% EtOAc/hexanes) to provide the title compound as a yellow solid (111 mg, 99%), mp = 150 – 152 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 8.77 (d,  $J$  = 2.4 Hz, 1H), 8.48 (d,  $J$  = 4.8 Hz, 2H), 8.37 (s, 2H), 8.05 (m, 2H),

7.71 (d,  $J = 9.3$  Hz, 1H), 7.32 (m, 1H), 6.77 (t,  $J = 4.5$  Hz, 1H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 160.3, 158.3, 148.8, 145.2, 137.8, 135.7, 130.2, 129.3, 124.1, 121.7, 114.5, 113.3 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3270, 3038, 1581, 1539, 1501, 1448, 1412, 1224, 795, 730. Anal. Calcd. for  $\text{C}_{13}\text{H}_{10}\text{N}_4$ : C, 70.26; H, 4.54. Found: C, 70.37; H, 4.44.

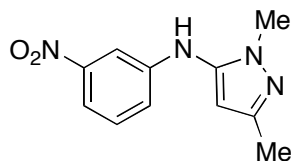


***N*-(4-(Thiophen-2-yl)phenyl)pyrazin-2-amine.** Following general procedure C, a mixture of 2-(4-bromophenyl)thiophene (120 mg, 0.5 mmol), aminopyrazine (67 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{Cs}_2\text{CO}_3$  (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 50-100% EtOAc/hexanes) to provide the title compound as a yellow solid (118 mg, 94%), mp = 167 – 170 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.25 (d,  $J = 1.2$  Hz, 1H), 8.14 (s, 1H), 8.01 (d,  $J = 2.7$  Hz, 1H), 7.61 (d,  $J = 8.7$  Hz, 2H), 7.47 (d,  $J = 8.7$  Hz, 2H), 7.26 (m, 2H), 7.07 (m, 1H), 6.62 (bs, 1H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 142.2, 138.8, 135.4, 133.5, 129.9, 128.3, 127.1, 124.6, 122.8, 120.4 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3226, 3022, 1601, 1558, 1458, 1436, 1200, 1008, 821, 711. Anal. Calcd. for  $\text{C}_{14}\text{H}_{11}\text{N}_3\text{S}$ : C, 66.38; H, 4.38. Found: C, 66.65; H, 4.27.

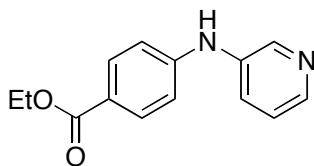


**1-(4-(Benzo[*b*]thiophen-3-ylamino)phenyl)ethanone.** Following general procedure C, a mixture of 2-(4-bromophenyl)thiophene (120 mg, 0.5 mmol), aminopyrazine (67 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{Cs}_2\text{CO}_3$  (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 50-100% EtOAc/hexanes) to provide the title compound as a yellow solid (118 mg, 94%), mp = 149 – 150 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.85 (d,  $J = 8.7$  Hz, 3H), 7.62 (d,  $J = 7.2$  Hz, 1H), 7.38 (m, 2H), 7.21 (s,

1H), 6.87 (d,  $J = 8.7$  Hz, 2H), 6.21 (bs, 1H), 2.52 (s, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 149.9, 139.1, 135.0, 133.0, 130.9, 128.9, 125.4, 124.5, 123.5, 121.2, 115.2, 114.0, 26.4 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3334, 1647, 1597, 1533, 1357, 1280, 1177, 827, 759, 727. Anal. Calcd. for  $\text{C}_{16}\text{H}_{13}\text{NOS}$ : C, 71.88; H, 4.90. Found: C, 71.43; H, 4.95.

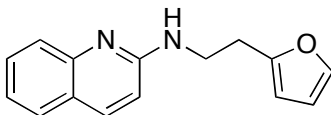


**1,3-Dimethyl-N-(3-nitrophenyl)-1H-pyrazol-5-amine.** Following general procedure C, a mixture of 3-nitrochlorobenzene (79 mg, 0.5 mmol), 1,3-dimethyl-1H-pyrazol-5-amine (78 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{Cs}_2\text{CO}_3$  (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 20-100% EtOAc/hexanes) to provide the title compound as a yellow solid (112 mg, 97%), mp = 123 – 124 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.65 (d,  $J = 8.4$  Hz, 1H), 7.54 (s, 1H), 7.34 (t,  $J = 8.4$  Hz, 1H), 7.01 (d,  $J = 8.1$  Hz, 1H), 6.20 (bs, 1H), 5.89 (s, 1H), 3.64 (s, 3H), 2.24 (s, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 149.5, 148.1, 146.4, 139.5, 130.4, 120.1, 114.8, 108.9, 99.7, 34.9, 14.3 ppm. IR (neat,  $\text{cm}^{-1}$ ): 2940, 1622, 1595, 1560, 1531, 1484, 1342, 1317, 735, 672. Anal. Calcd. for  $\text{C}_{11}\text{H}_{12}\text{N}_4\text{O}_2$ : C, 56.89; H, 5.21. Found: C, 56.73; H, 5.34.

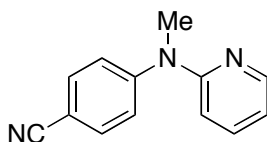


**Ethyl 4-(pyridin-3-ylamino)benzoate.** Following general procedure C, a mixture of ethyl 4-bromobenzoate (82  $\mu\text{L}$ , 0.5 mmol), 3-aminopyridine (66 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{Cs}_2\text{CO}_3$  (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 20-100% EtOAc/hexanes) to provide the title compound as a white solid (116 mg, 96%), mp = 142 – 145 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.45 (s, 1H), 8.25 (d,  $J = 4.5$  Hz, 1H), 7.92 (d,  $J = 8.4$  Hz, 2H), 7.53 (d,  $J = 8.1$  Hz, 1H), 7.23 (m, 1H), 7.01 (d,  $J = 8.4$  Hz, 2H), 6.88 (bs, 1H), 4.32 (q,  $J = 7.2$  Hz, 2H), 1.35 (t,  $J = 7.2$  Hz, 3H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 166.7, 147.3, 143.6, 142.2,

138.4, 131.7, 126.4, 124.2, 122.5, 115.3, 60.9, 14.6 ppm. IR (neat,  $\text{cm}^{-1}$ ): 2993, 1700, 1609, 1577, 1485, 1332, 1273, 1174, 1106, 719. Anal. Calcd. for  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2$ : C, 69.41; H, 5.82. Found: C, 69.19; H, 5.93.

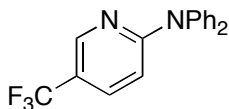


***N*-(2-(Furan-2-yl)ethyl)quinolin-2-amine.** An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum, was charged with **2** (1 mol %), **3** (01 mol %), and 2-chloroquinoline (82 mg, 0.7 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then 2-(furan-2-yl)ethanamine (82 mg, 0.7 mmol) and a solution of LHMDS in THF (1 M, 0.7 mL, 0.7 mmol) were added via syringe. The solution was heated to 110 °C for 24 h and then the reaction mixture was then cooled to room temperature, diluted with ethyl acetate, washed with water, and concentrated in vacuo. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 20-100% EtOAc/hexanes) to provide the title compound as a brown oil (116 mg, 97%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.50 (m, 2H), 7.56 (m, 2H), 7.36 (s, 1H), 7.23 (t,  $J = 7.2$  Hz, 1H), 6.58 (d,  $J = 9.0$  Hz, 1H), 6.32 (s, 1H), 6.11 (s, 1H), 4.95 (bs, 1H), 3.82 (q,  $J = 6.6$  Hz, 2H), 3.02 (t,  $J = 6.6$  Hz, 2H) ppm.  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$ : 156.9, 153.8, 148.3, 141.7, 137.5, 129.8, 127.7, 126.5, 123.7, 122.3, 111.9, 110.6, 106.6, 40.4, 28.5 ppm. IR (neat,  $\text{cm}^{-1}$ ): 3425, 2926, 1619, 1526, 1401, 1246, 1145, 818, 756, 732.



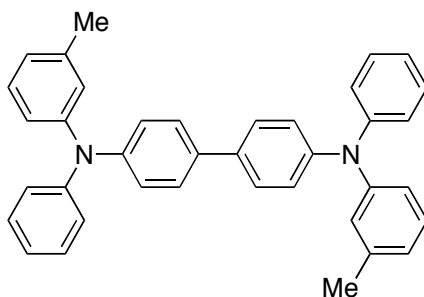
**4-(Methyl(pyridin-2-yl)amino)benzonitrile.** Following general procedure C, a mixture of 4-iodobenzonitrile (115 mg, 0.5 mmol), *N*-methylpyridin-2-amine (72  $\mu\text{L}$ , 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %),  $\text{Cs}_2\text{CO}_3$  (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 20-100% EtOAc/hexanes) to provide the title compound as a clear oil (102 mg, 97%).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 8.30 (d,  $J = 4.2$  Hz, 1H), 7.52 (m, 3H), 7.20, (d,  $J = 8.4$  Hz, 2H), 6.94 (d,  $J = 8.4$  Hz, 1H), 6.84 (m,

1H), 3.49 (s, 3H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 157.8, 150.8, 148.7, 137.9, 133.5, 121.5, 119.6, 117.3, 113.5, 104.9, 38.1 ppm. IR (neat, cm<sup>-1</sup>): 2221, 1607, 1587, 1509, 1473, 1439, 1352, 1178, 1116, 776. Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>N<sub>3</sub>: C, 74.62; H, 5.30. Found: C, 74.18; H, 5.41.



***N,N*-Diphenyl-5-(trifluoromethyl)pyridin-2-amine.** Following general procedure C, a mixture of 2-chloro-5-trifluoromethylpyridine (64 μL, 0.5 mmol), diphenylamine (118 mg, 0.7 mmol), BrettPhos Precat (1 mol %), RuPhos (1 mol %), Cs<sub>2</sub>CO<sub>3</sub> (228 mg, 0.7 mmol), and *t*-BuOH (1 mL) was heated to 110 °C for 24 h. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 100% toluene) to provide the title compound as a clear oil (141 mg, 90%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ: 8.44 (s, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.39 (m, 4H), 7.23 (m, 6H), 6.72 (d, *J* = 8.7 Hz, 1H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: 161.0, 146.1, 146.0, 145.1, 134.6, 134.5, 130.2, 129.9, 127.3, 126.1, 122.7, 118.2, 117.8, 111.4 ppm (observed complexity due to C-F splitting). <sup>19</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ: -61.8 ppm. IR (neat, cm<sup>-1</sup>): 3042, 1593, 1493, 1400, 1325, 1165, 1120, 1079, 748, 692. Anal. Calcd. for C<sub>18</sub>H<sub>13</sub>N<sub>2</sub>F<sub>3</sub>: C, 68.78; H, 4.17. Found: C, 69.08; H, 4.32.

### ***Experimental Procedures for Examples Described in Figure 2***



***N*-(4-(1*H*-Pyrrol-1-yl)phenyl)-*N*-phenyl-3-(trifluoromethyl)aniline.**<sup>12</sup> An oven-dried test tube, which was equipped with a magnetic stir bar and fitted with a teflon septum,

was charged with **2** (0.2 mol %), **3** (0.2 mol %), NaOt-Bu (230 mg, 2.4 mmol), and benzidine (92 mg, 0.5 mmol). The vessel was evacuated and backfilled with argon (this process was repeated a total of 3 times) and then 3-bromotoluene (121  $\mu$ L, 1.0 mmol), chlorobenzene (102  $\mu$ L, 1.0 mmol), and 1,4-dioxane (1 mL) were added via syringe. The solution was heated to 110 °C for 24 h and then the reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with water, and concentrated in vacuo. The crude product was purified via the Biotage SP4 (silica-packed 50 g snap column; 0 – 40% EtOAc/hexanes) to provide the title compound as a white foam (253 mg, 98%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.54 (d, *J* = 8.7 Hz, 4H), 7.34 (t, *J* = 8.1 Hz, 4H), 7.23 (m, 10H), 7.80 (m, 6H), 6.95 (d, *J* = 7.5 Hz, 2H) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ : 148.2, 148.0, 147.2, 139.5, 134.9, 129.6, 127.6, 125.5, 124.6, 124.4, 124.2, 123.0, 122.0, 21.8 ppm. IR (neat, cm<sup>-1</sup>): 3032, 1594, 1489, 1315, 1276, 1178, 909, 808, 734, 696.

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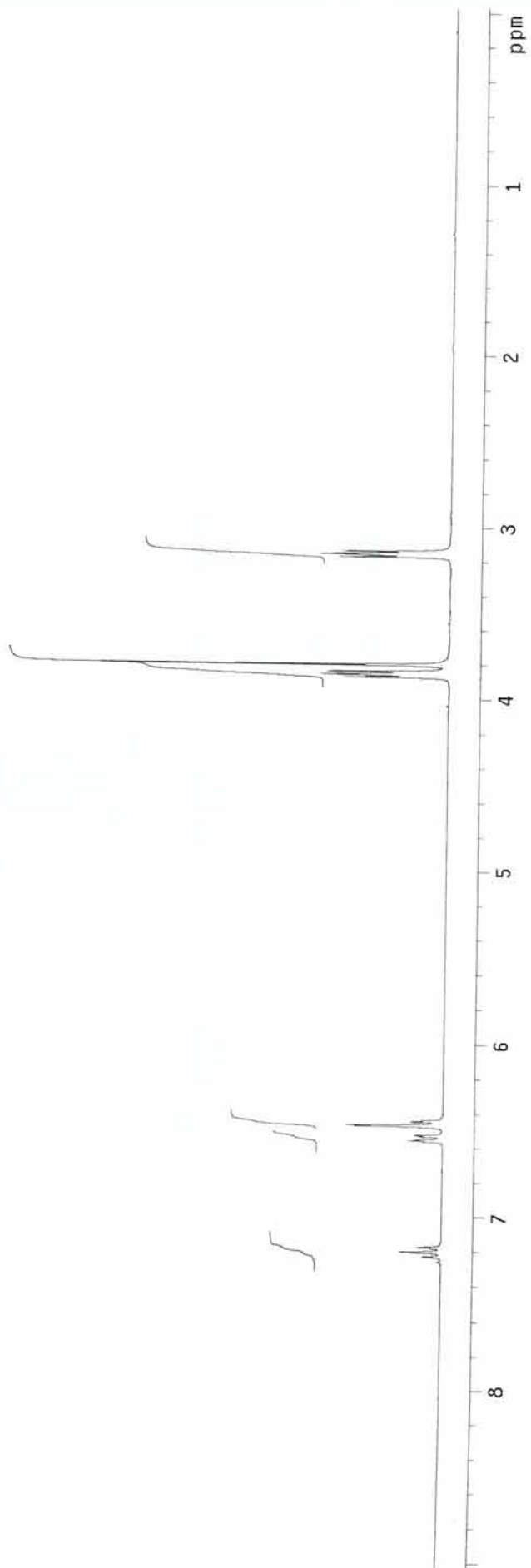
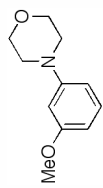
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<sup>9</sup> Urgaonkar, S.; Verkade, J. G. *J. Org. Chem.*, **2004**, *69*, 9135.

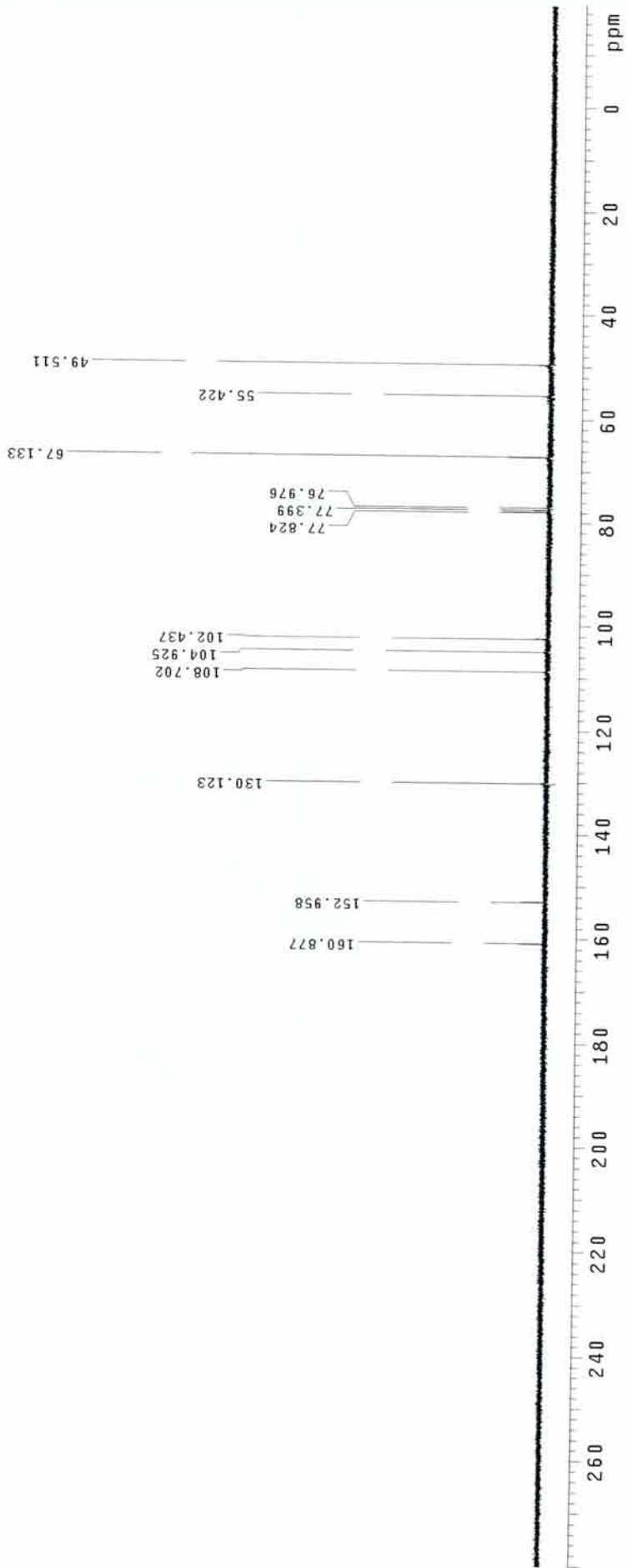
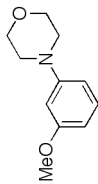
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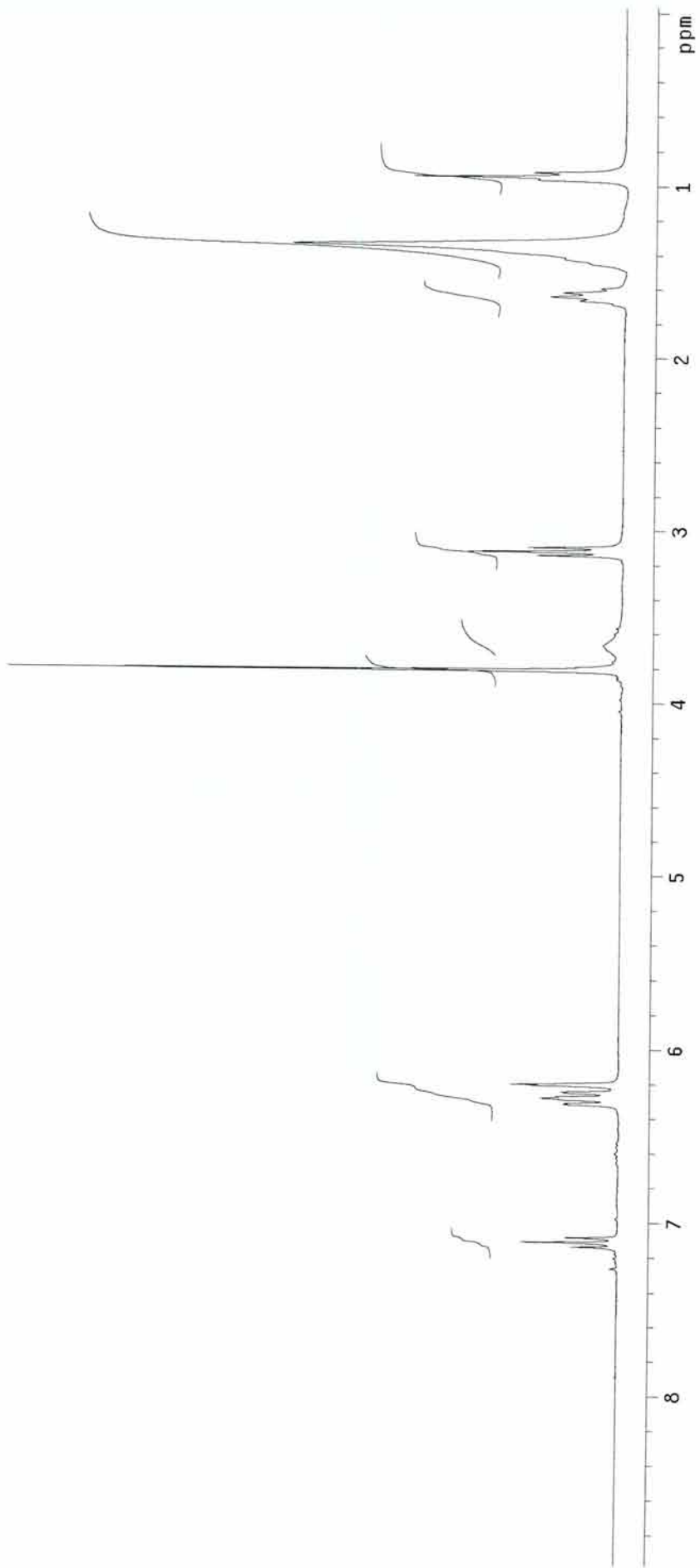
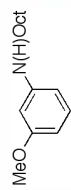
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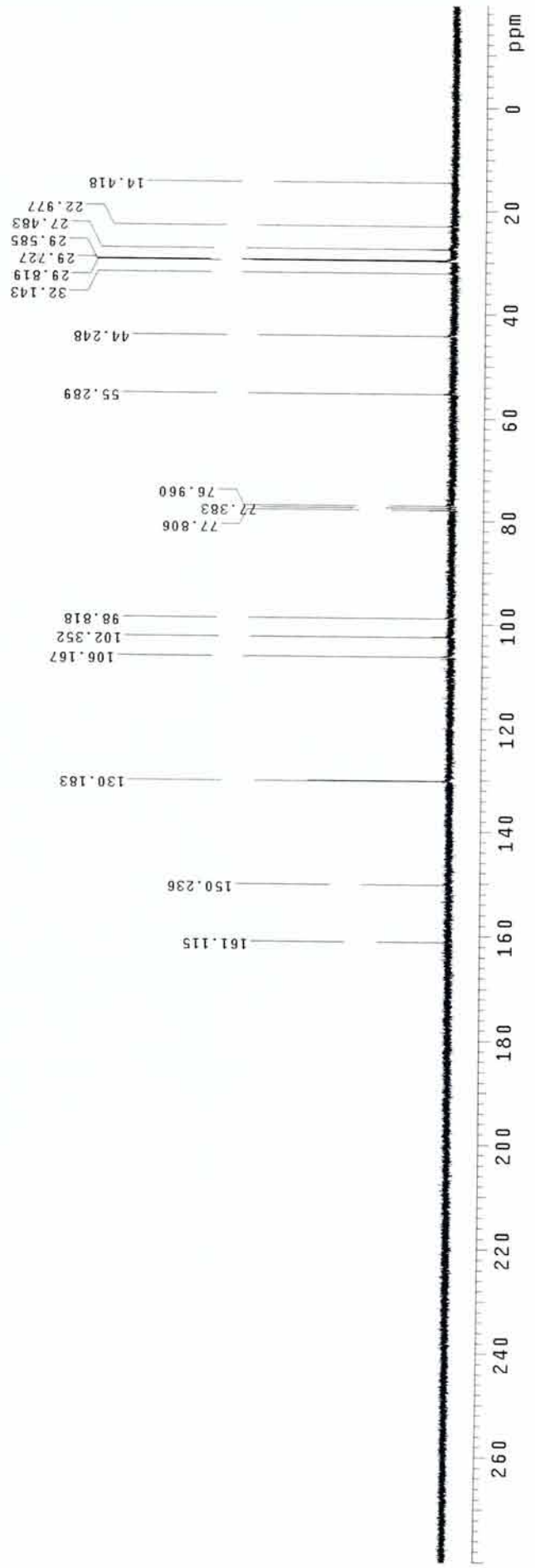
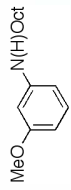
<sup>12</sup> Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354.

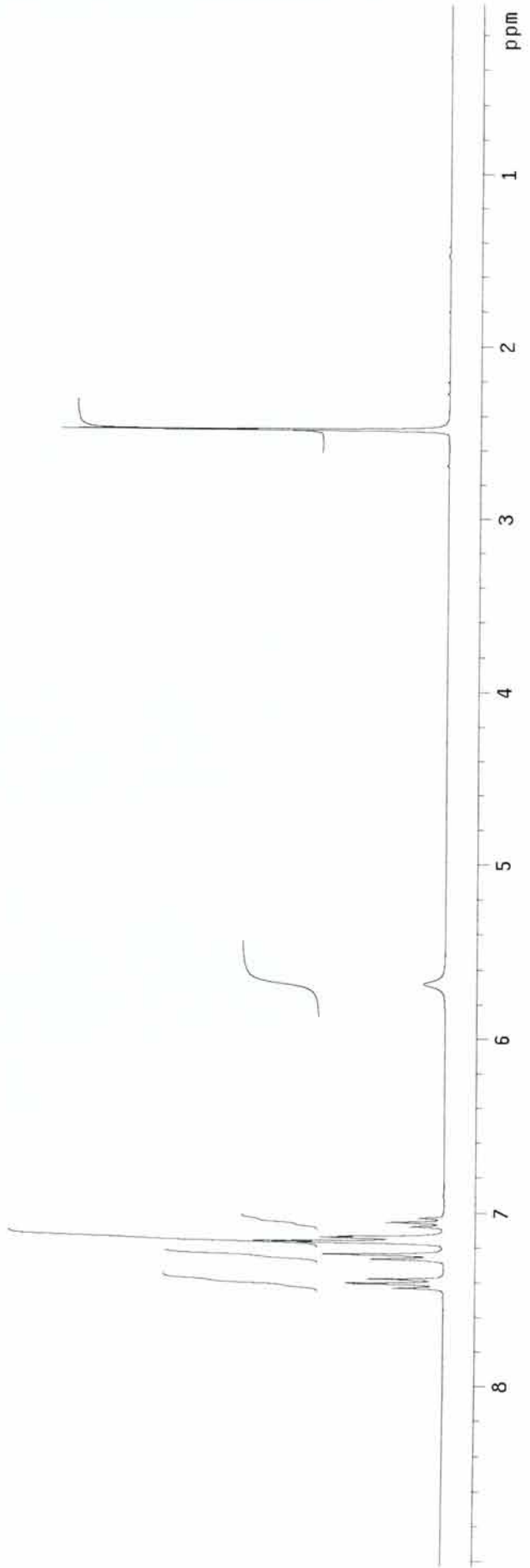
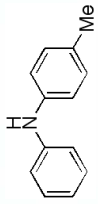


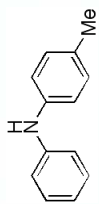
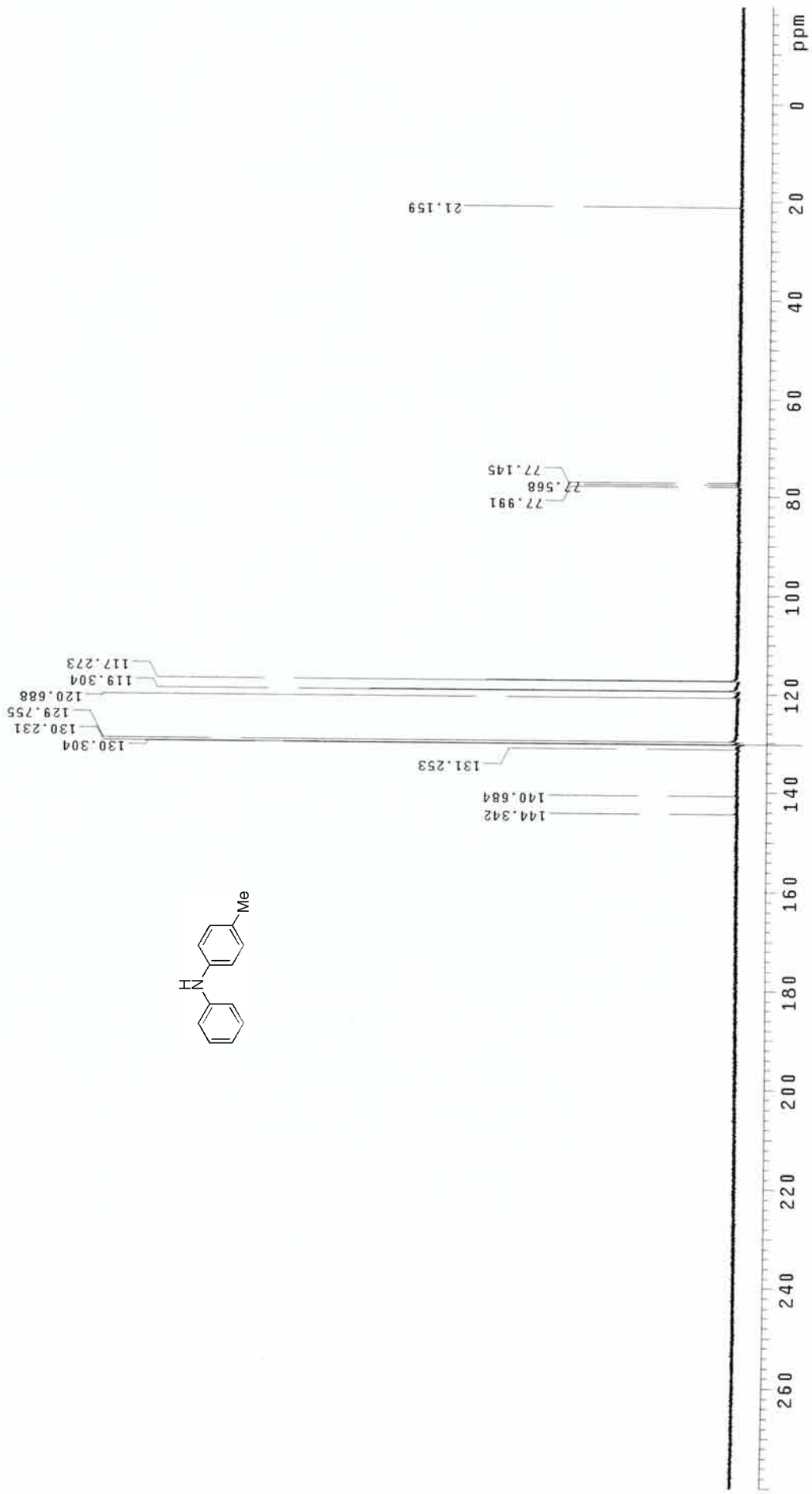


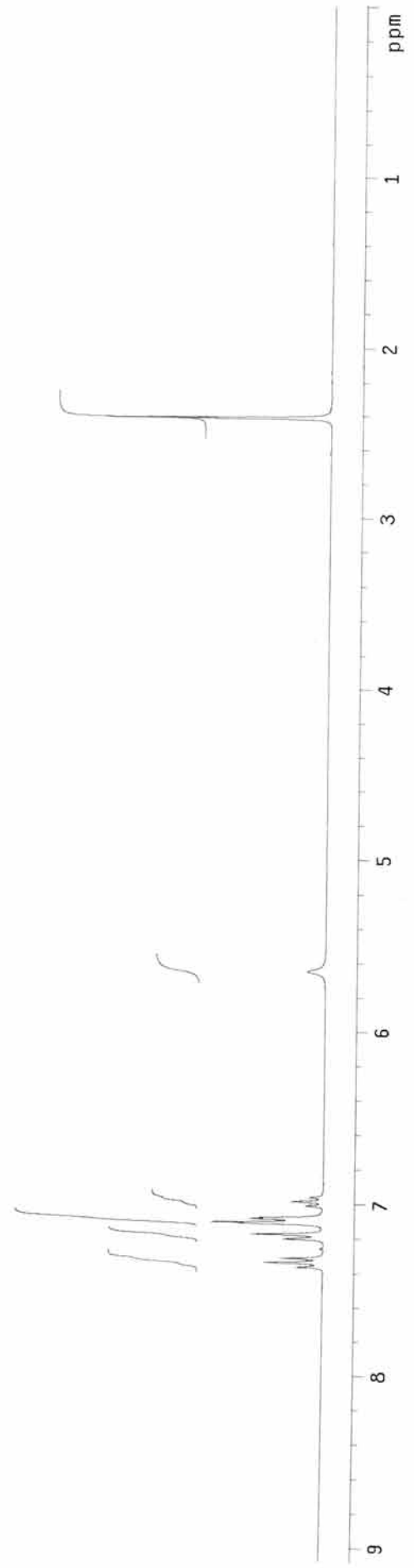
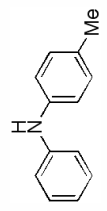


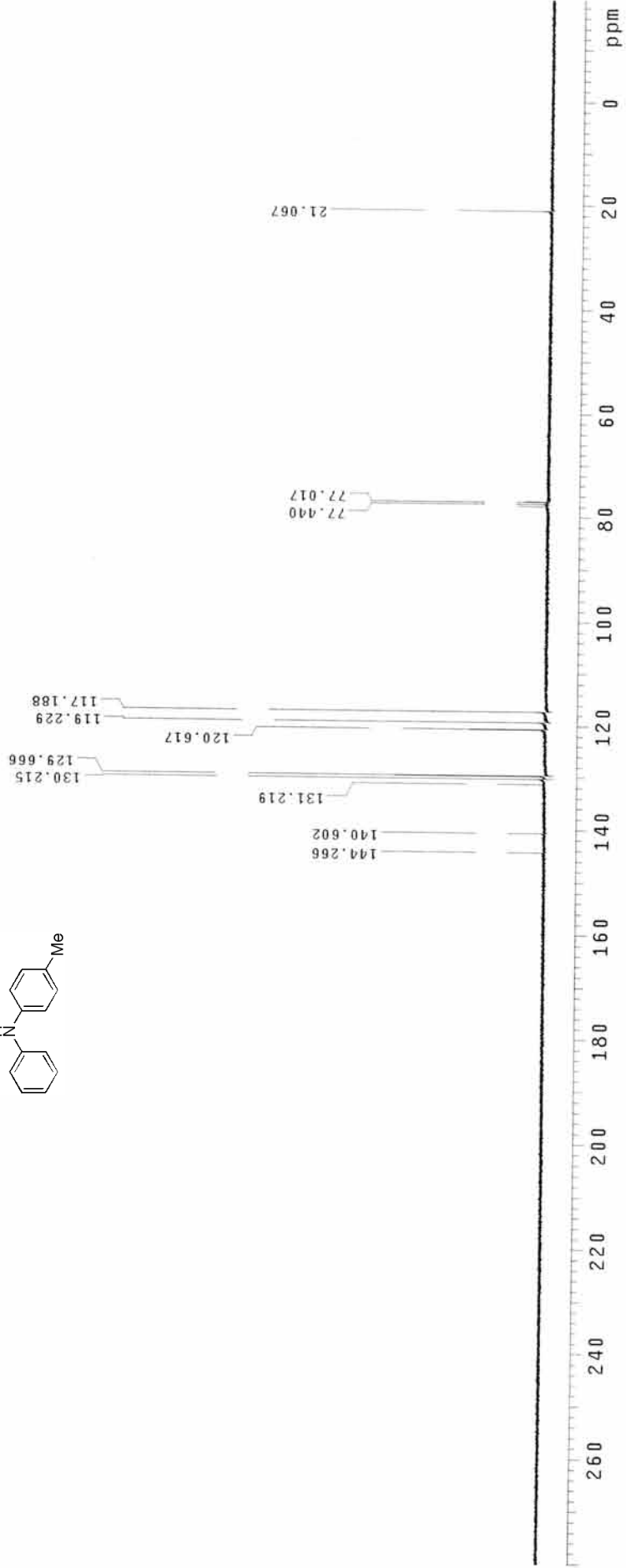
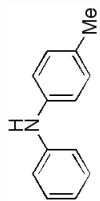


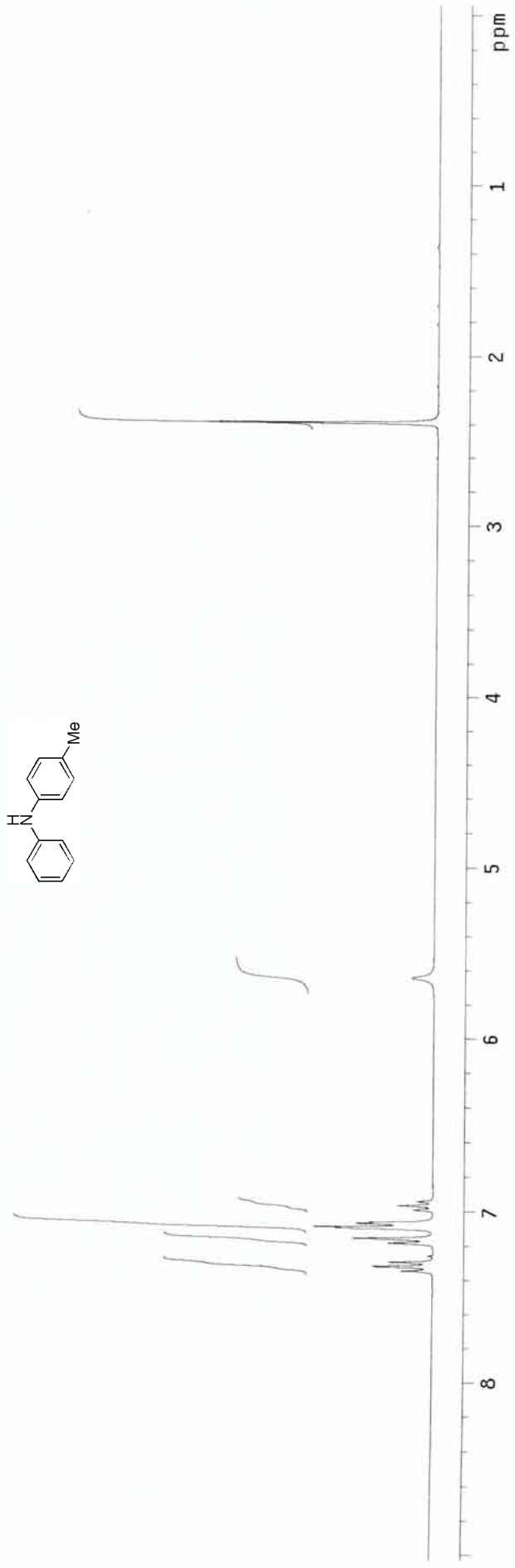
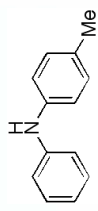




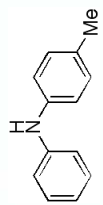
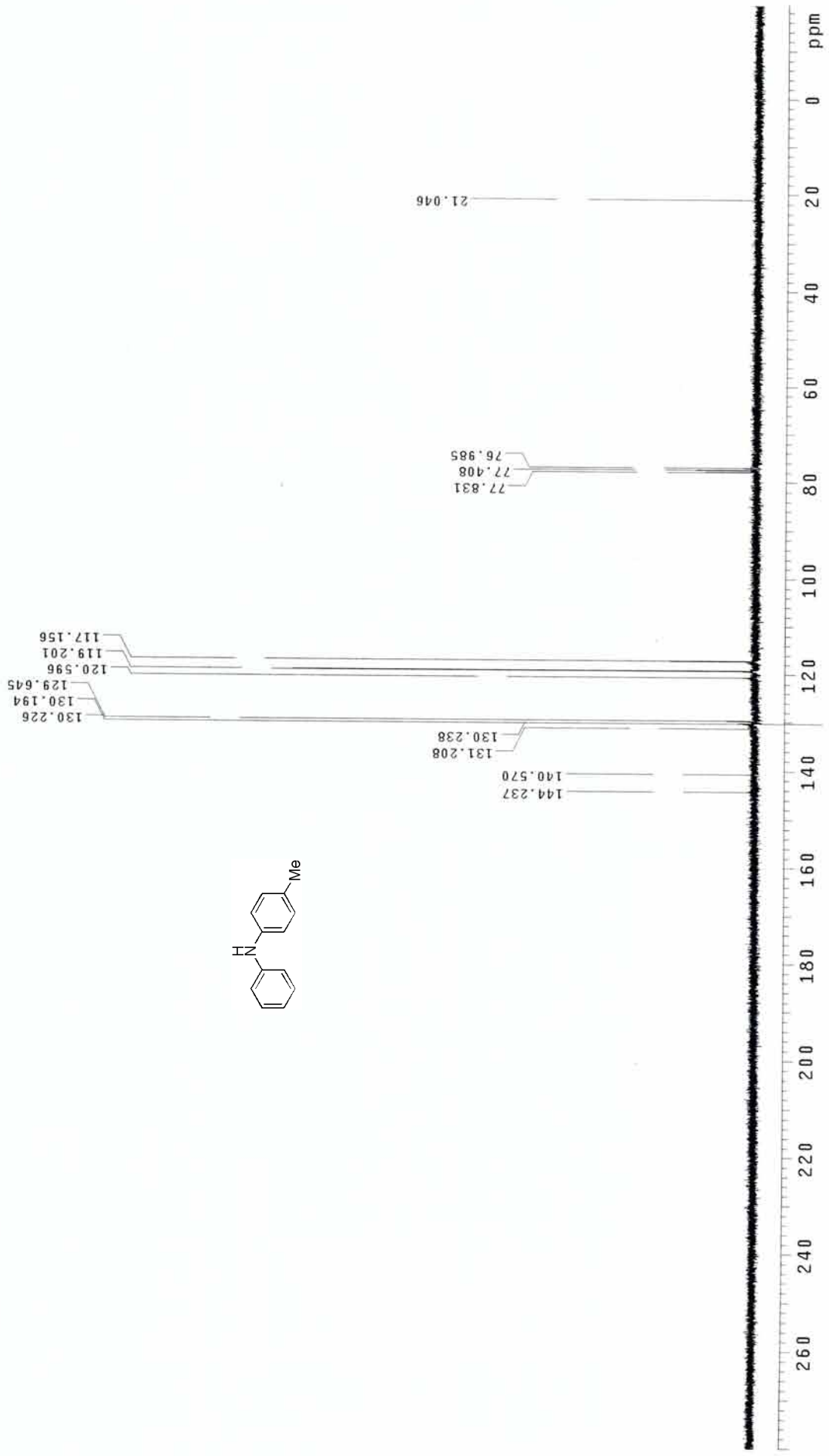


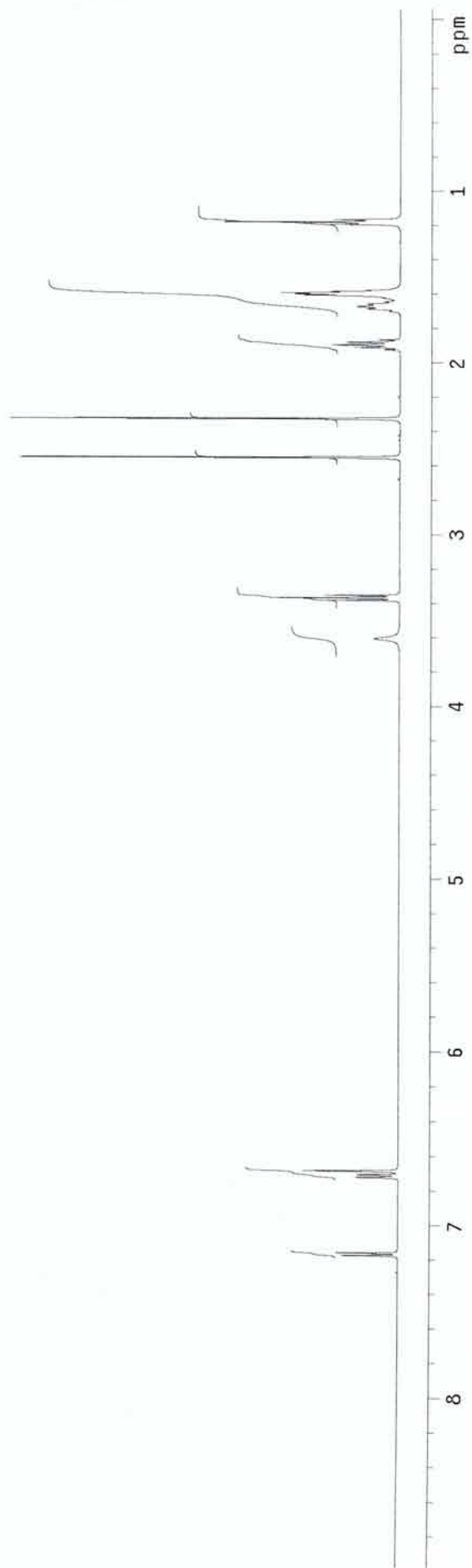
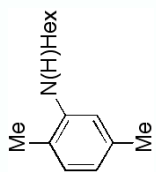


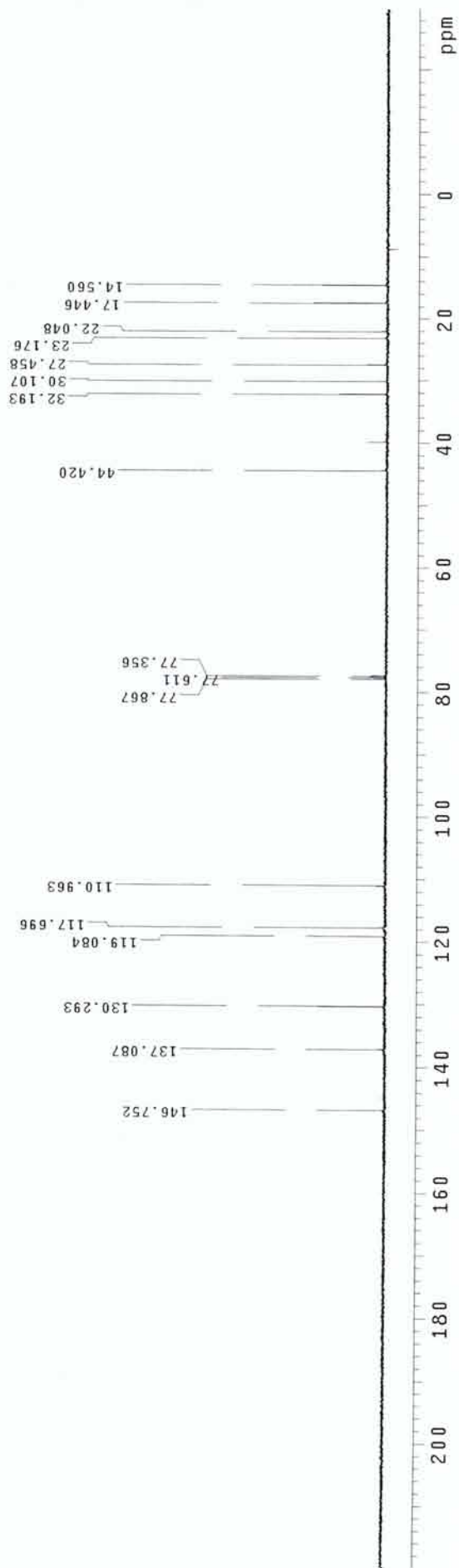
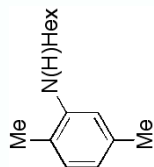


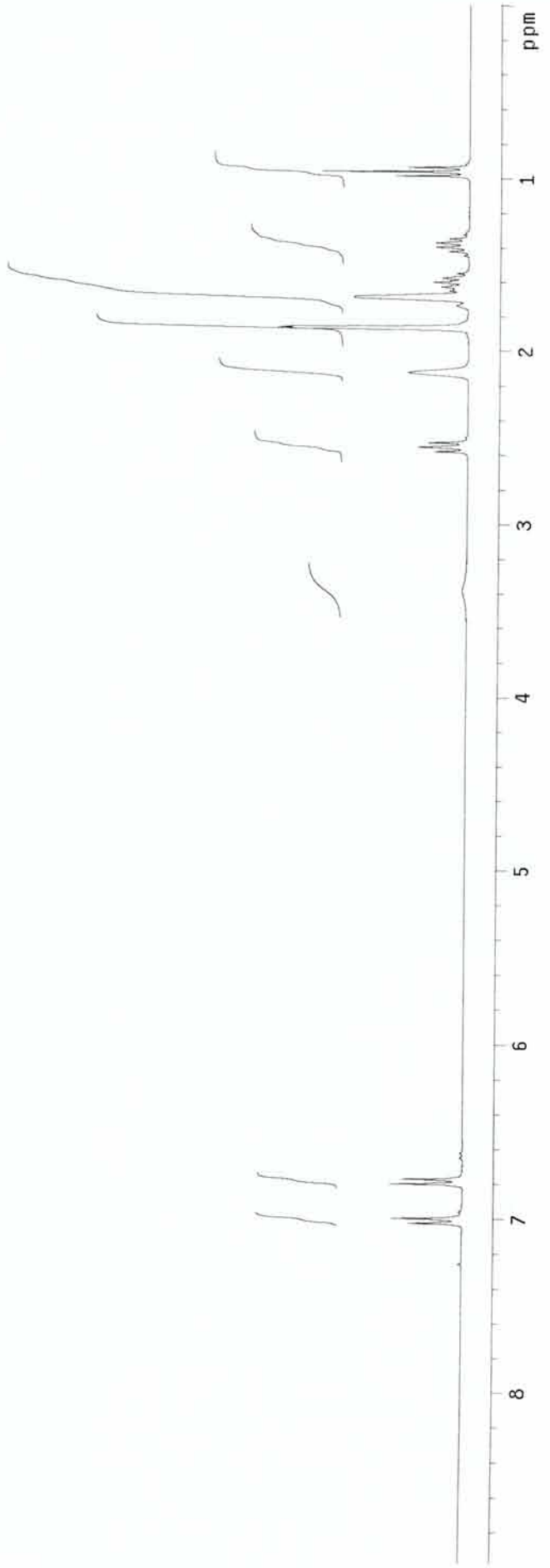
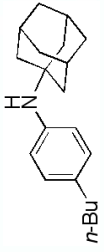


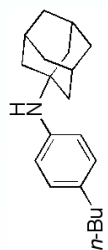
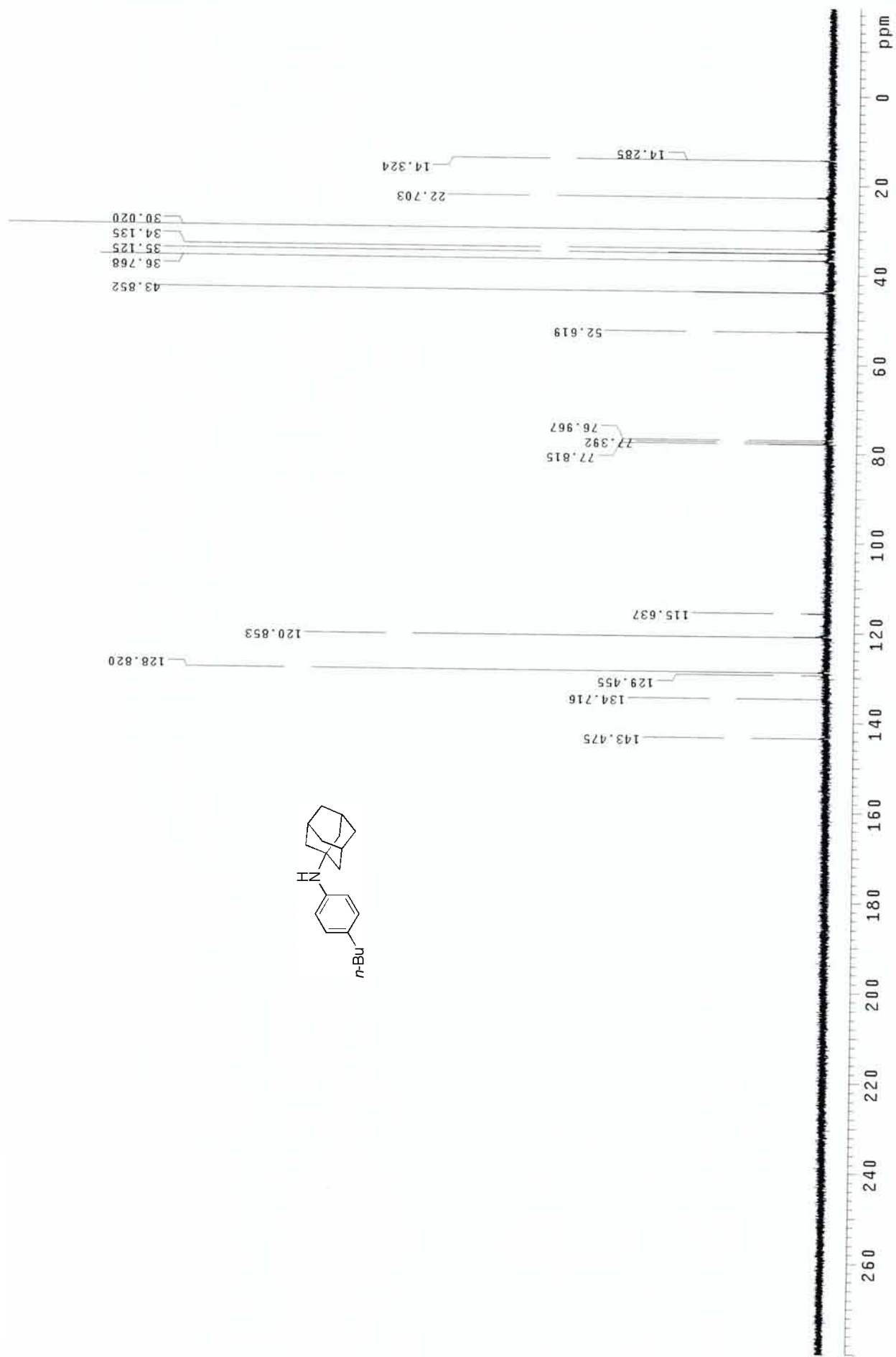


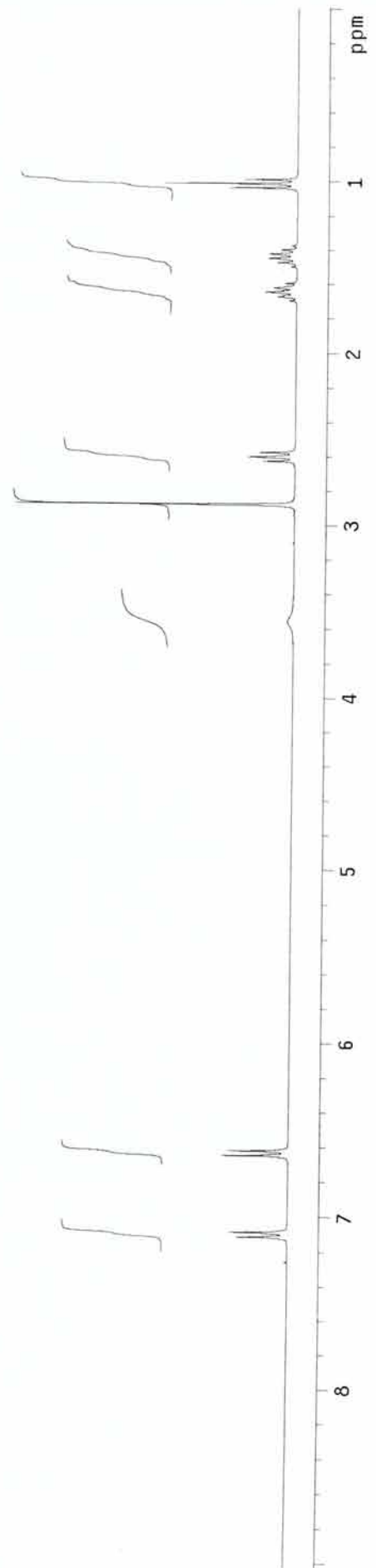
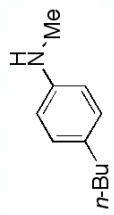


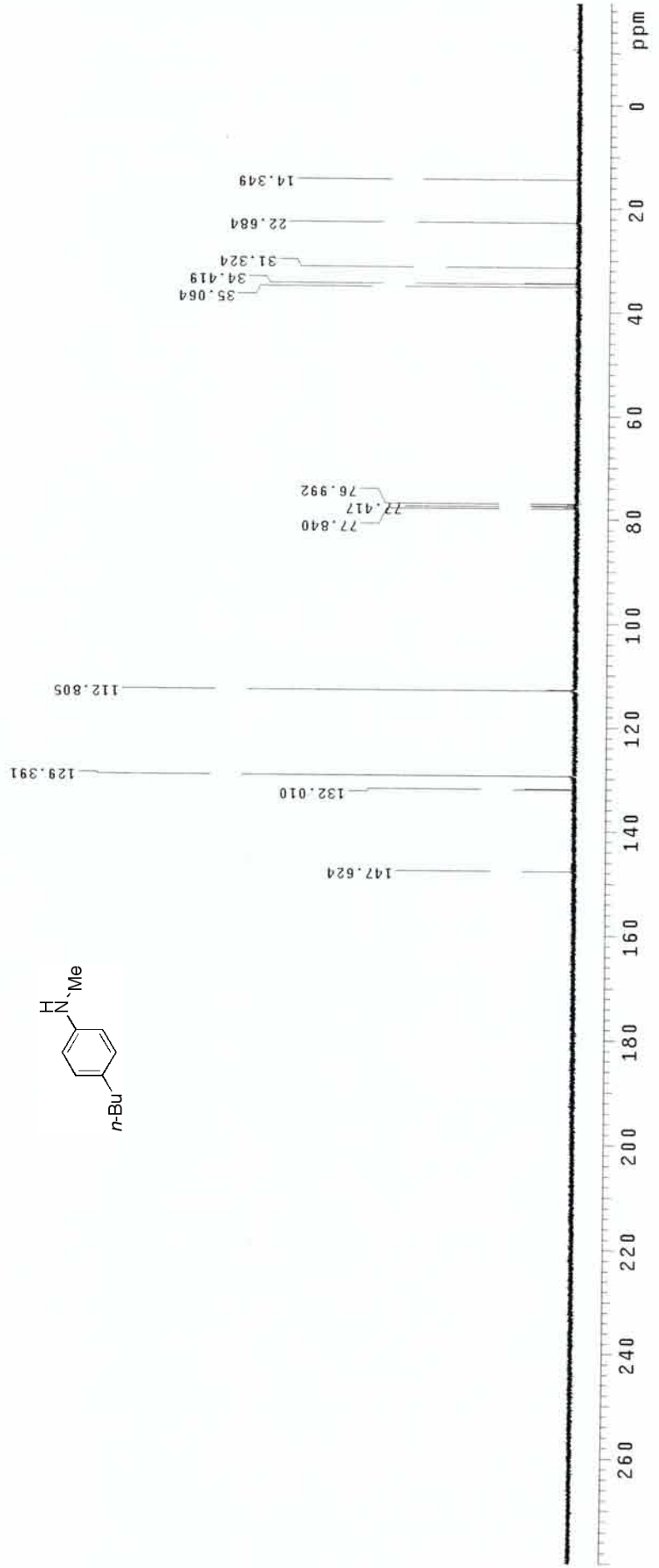
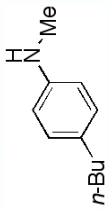


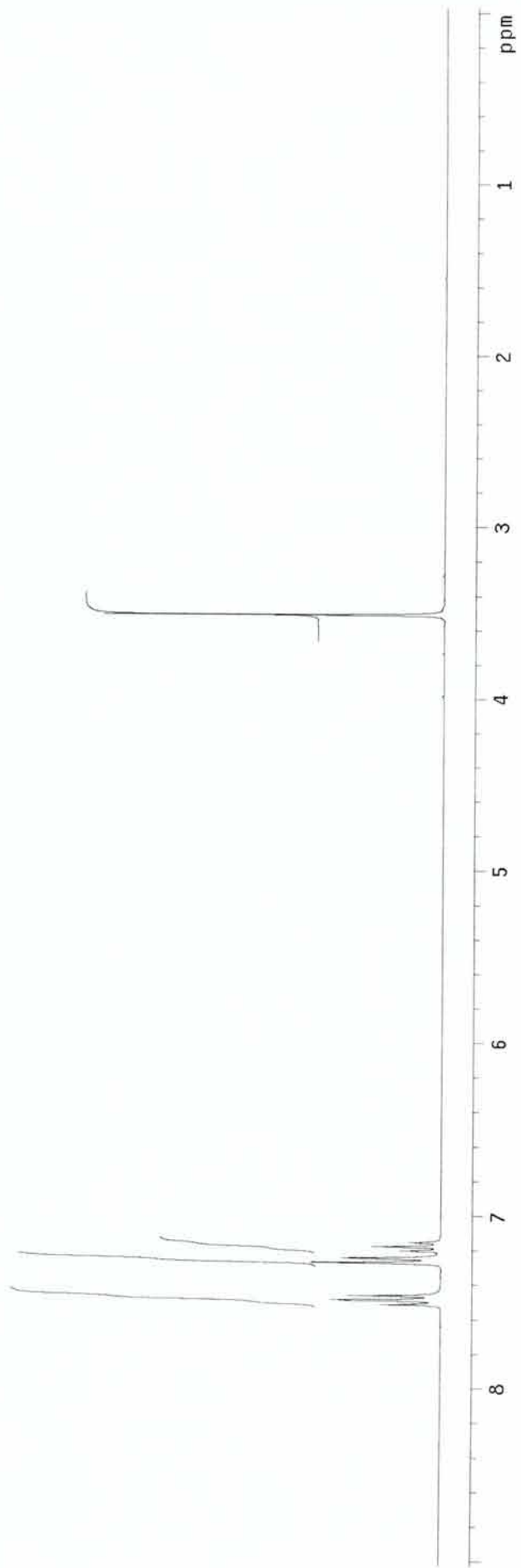
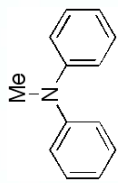




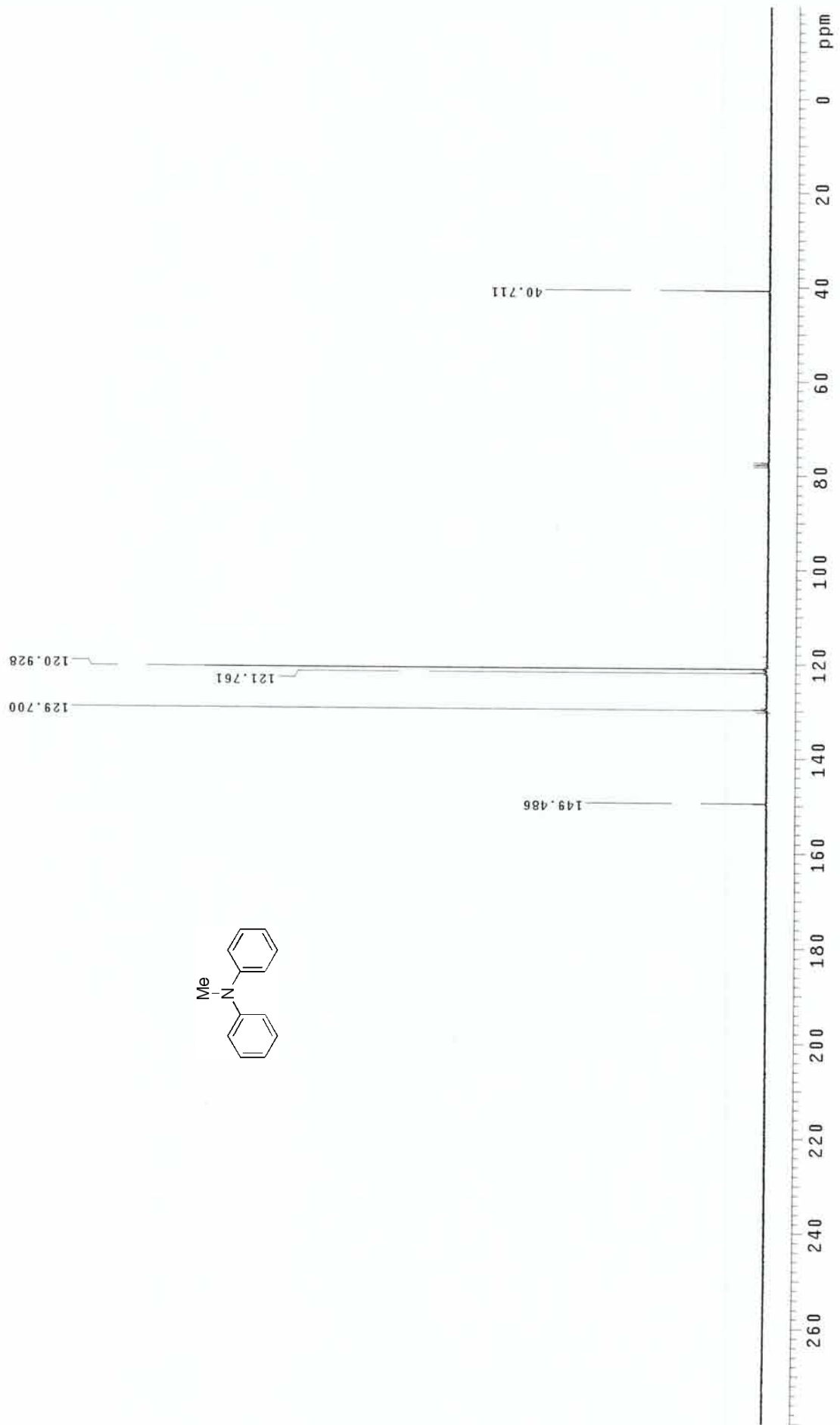
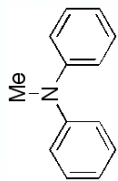


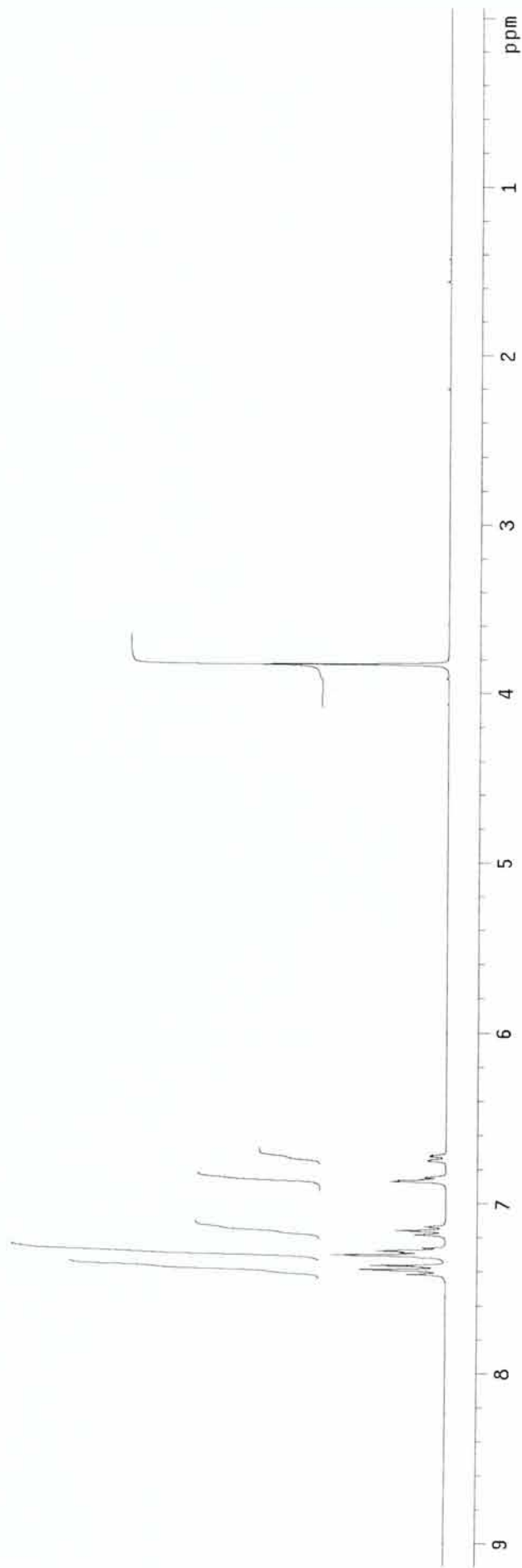
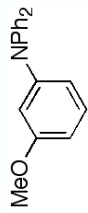


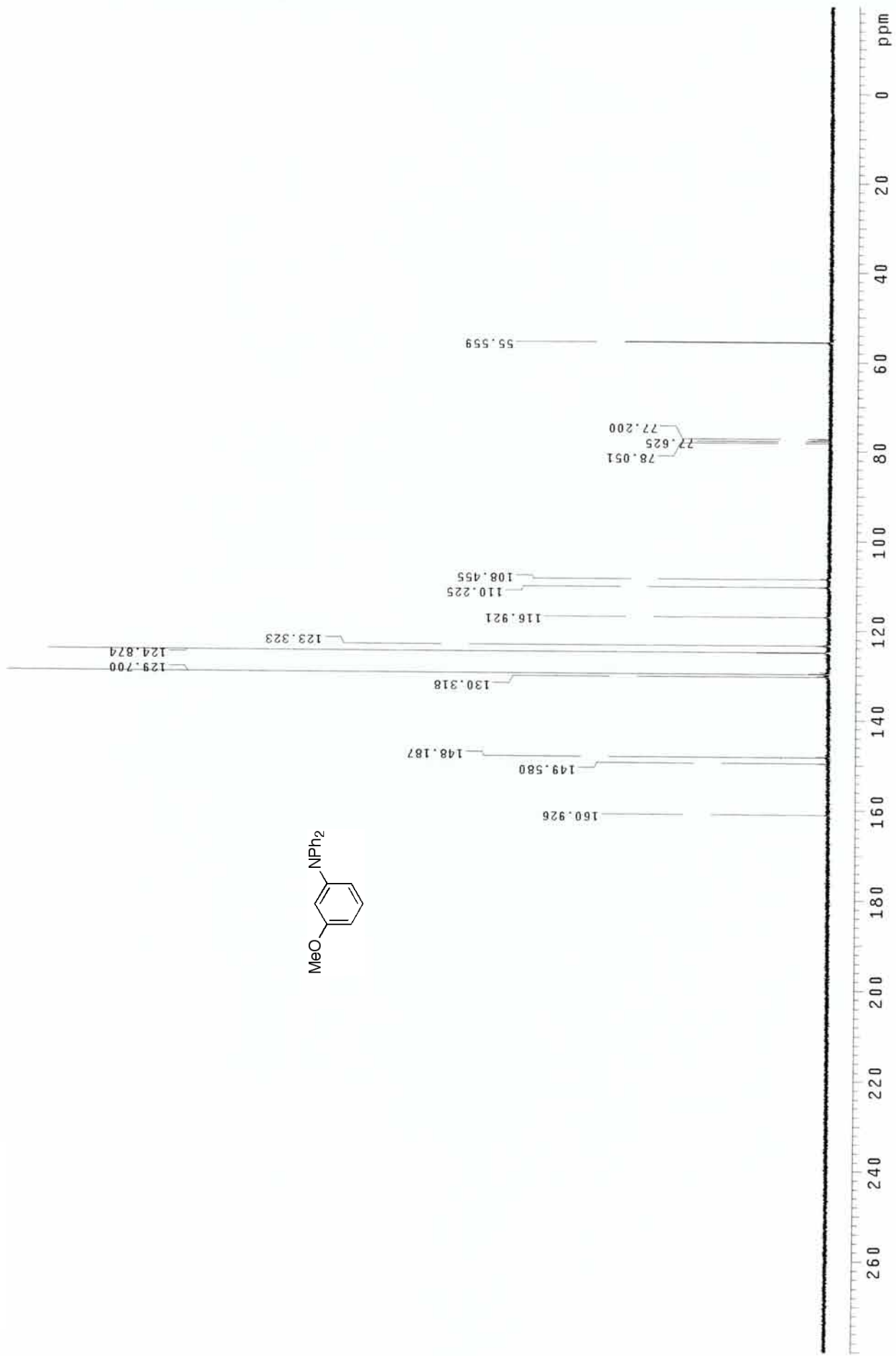


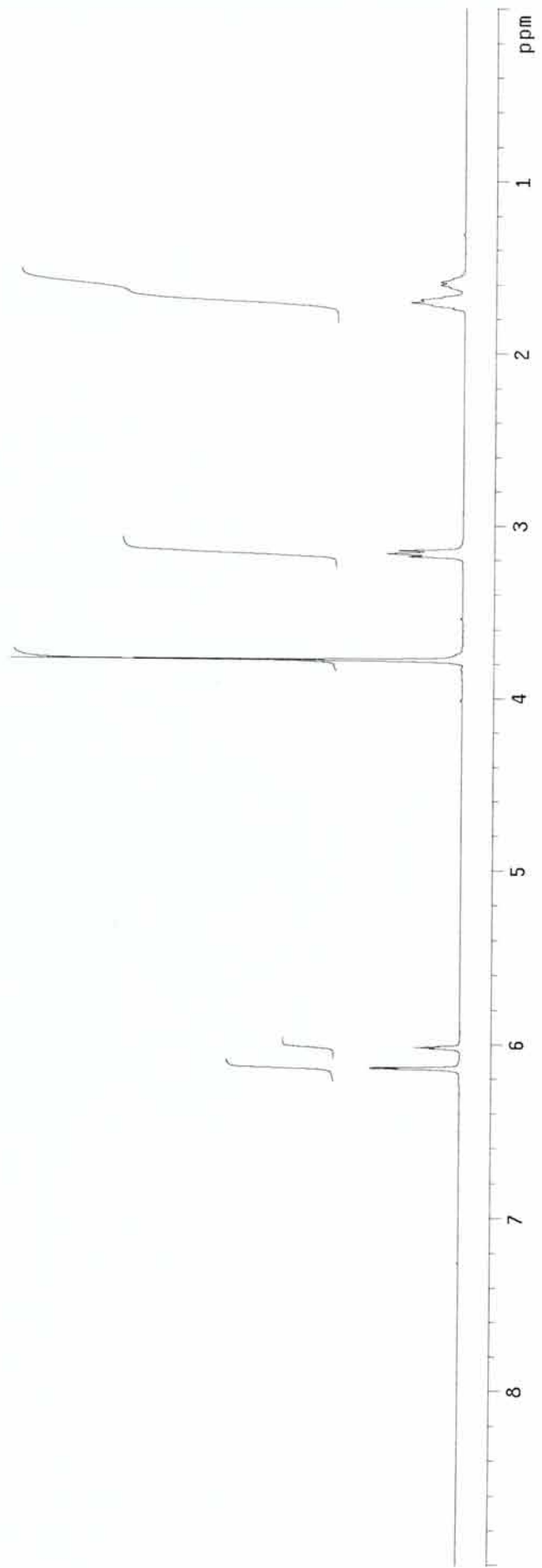
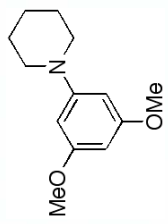


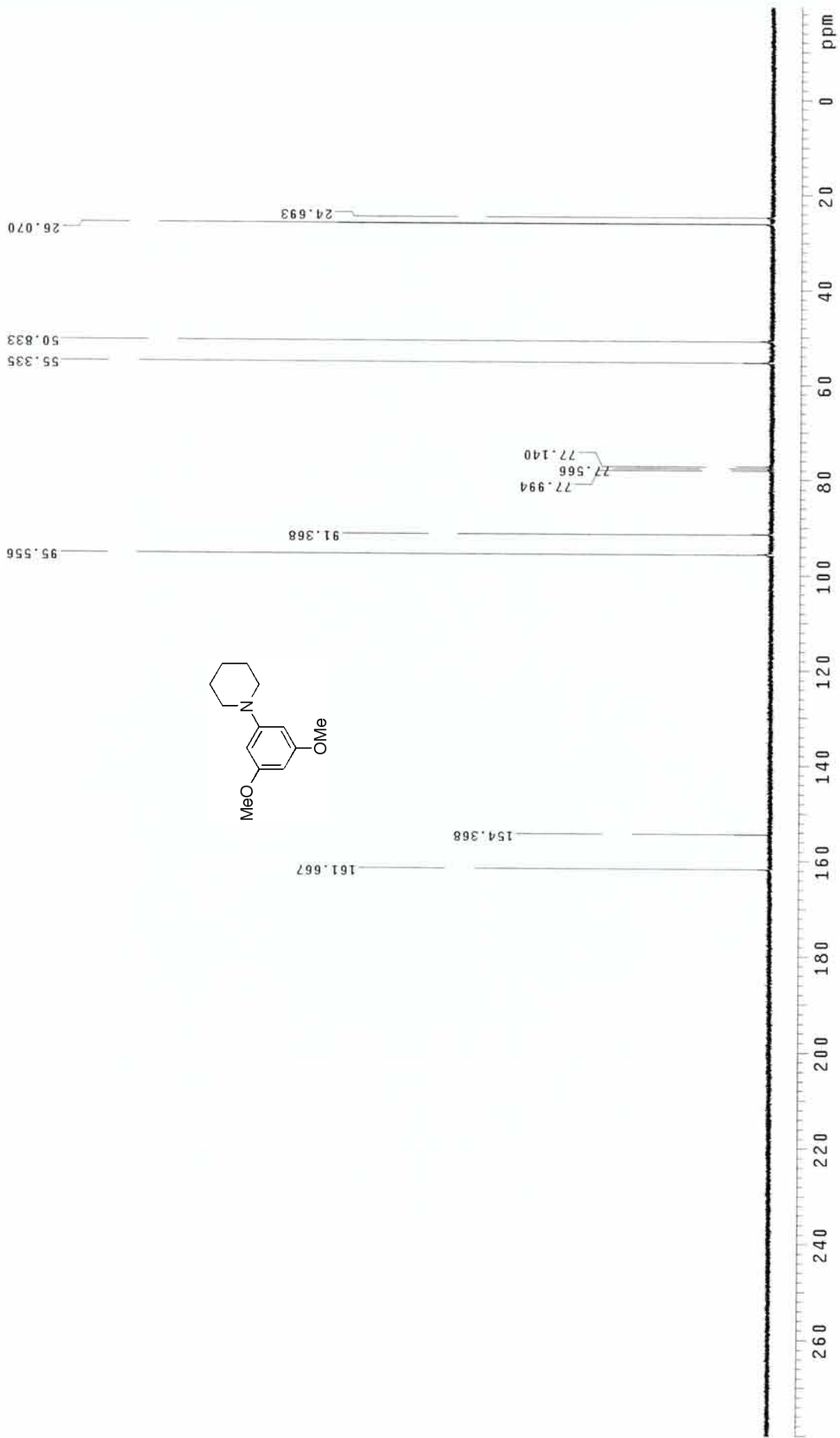


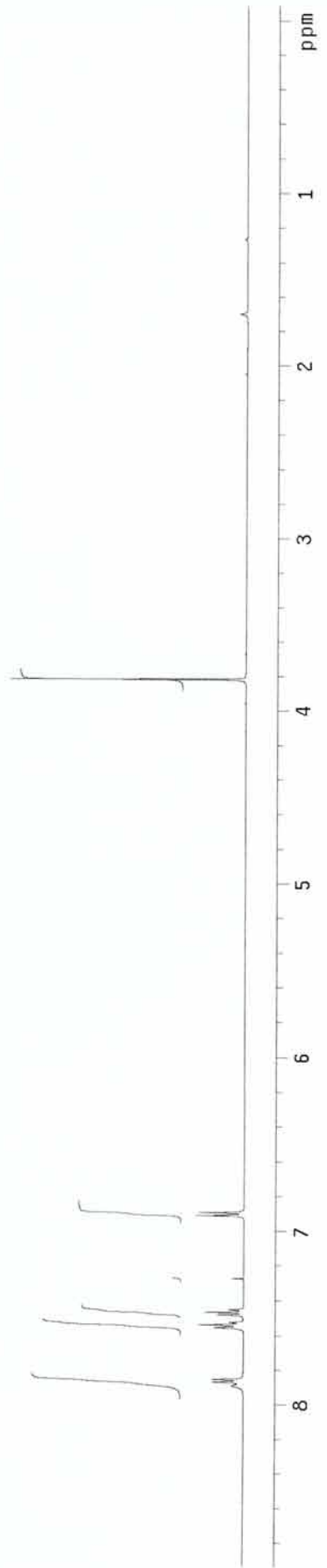
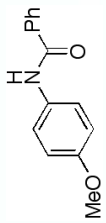


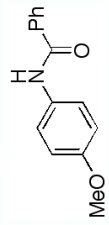












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127.251  
122.405  
114.448

55.750  
39.829

ppm  
0  
20  
40  
60  
80  
100  
120  
140  
160  
180  
200

