

Pyrrole-2-Carboxylic Acid as a Ligand for the Cu-Catalyzed Reactions of Primary Anilines with Aryl Halides

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Supporting Information

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General Considerations

All reactions were carried out in resealable test tubes with teflon septa under an argon or nitrogen atmosphere. Copper(I) iodide (98%) was purchased from Strem. Pyrrole-2-carboxylic acid was purchased from Aldrich. Finely milled K_3PO_4 was purchased from Fluka. The base was flame-dried under vacuum and cooled under nitrogen immediately prior to usage. The base is hygroscopic and excessive amounts of water lead to the formation of phenol and diaryl ether byproducts. Anilines were purchased from commercial sources and, when necessary, purified by distillation or sublimation. Aryl halides were purchased from commercial sources and, when necessary, were distilled or filtered through a plug of alumina before use. Anhydrous dimethylsulfoxide (DMSO) and *N,N'*-dimethylformamide (DMF) were purchased from Aldrich in SureSeal® bottles and used as received. Flash column chromatography was performed using a Biotage SP4 Flash Purification System using SNAP 10g silica cartridges. In all cases, dichloromethane was used to transfer the crude reaction material onto the silica gel samplet. The samplet was then air-dried before usage. A gradient elution using hexanes and ethyl acetate was performed, based on the recommendation from the Biotage TLC Wizard.

Yields reported in the publication are of isolated material and represent an average of at least two independent runs. Yields reported in the supporting information refer to a single experiment. Compounds described in the literature were characterized by comparing their 1H NMR and ^{13}C NMR spectra, and melting points (m.p.) to the previously reported data; their purity was confirmed by gas chromatography (GC) or elemental analysis. GC analyses were performed on a Hewlett Packard 6890 instrument with an FID detector and a Hewlett Packard 10 m x 0.2 mm i.d. HP-1 capillary column using dodecane as an internal standard. Elemental analyses were performed by Atlantic Microlabs, Inc., Norcross, GA. Previously unknown

compounds were synthesized, purified and analyzed from a single run and the reactions used to form them were then repeated to determine an average yield. They were characterized by ^1H NMR, ^{13}C NMR, m.p., IR and elemental analysis. ^1H NMR and ^{13}C NMR spectra were recorded on Varian 500 MHz instruments with chemical shifts reported relative to the deuterated solvent or TMS. IR spectra were recorded on a Perkin-Elmer System 2000 FT-IR instrument for all previously unknown compounds (KBr disc). Melting points (uncorrected) were obtained on a Mel-Temp II capillary melting point apparatus.

General procedure for the Cu-catalyzed cross-coupling of anilines with aryl halides

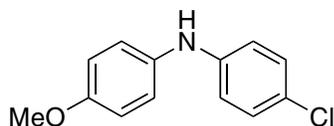
An oven-dried screw-cap test tube was charged with K_3PO_4 (424 mg, 2.0 mmol). The tube was sealed and the base was flame-dried under vacuum, and cooled under a purge of N_2 . CuI (19 mg, 0.10 mmol), Pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), aryl halide (1.0 mmol, if solid), amine (2.0 mmol, if solid) and a magnetic stir bar were added to the cooled vessel. The tube was then evacuated and back-filled with nitrogen. The evacuation/backfill sequence was repeated two additional times. Aryl halide (1.0 mmol, if liquid), amine (2.0 mmol, if liquid) and DMSO (0.50 mL) were then added by syringe. The vessel was immersed in a preheated oil bath and the reaction mixture was stirred vigorously until TLC and/or GC analysis of the crude reaction mixture indicated that the aryl halide had been completely consumed. The reaction mixture was cooled to room temperature. Ethyl acetate (15 mL), $\text{NH}_4\text{Cl}_{(\text{aq})}$ (2 mL), and H_2O (1 mL) were added and the mixture was stirred. The organic layer was separated, and filtered through a plug of silica. The aqueous layer was extracted twice more with ethyl acetate (10 mL), and each extract was sequentially filtered through the pad of silica gel. The filtrate was concentrated and the resulting residue was purified by flash chromatography (hexanes/ethyl

acetate, gradient elution) to provide the desired product.

Experimental procedure for the reactions described in Table 1

An oven-dried screw-cap test tube was charged with CuI (9.5 mg, 0.050 mmol), ligand (0.20 mmol, if solid), and a magnetic stir bar. The tubes were transferred into a nitrogen-filled glove box where flame-dried anhydrous K₃PO₄ (212 mg, 1.0 mmol) was added. The tubes were sealed with a Teflon septum and removed from the glovebox, where iodobenzene (56 μ L, 0.5 mmol), aniline (92 μ L, 1.0 mmol) and DMSO (0.25 mL) were successfully added by syringe. The vessel was immersed in a preheated oil bath and the reaction mixture was stirred vigorously for 12 h at 80 °C. The reaction mixture was cooled to room temperature. Dodecane (112 μ L), ethyl acetate (15 mL), NH₄Cl_(aq) (2 mL), and H₂O (1mL) were added, and the mixture was stirred. The organic layer was sampled and analyzed by GC.

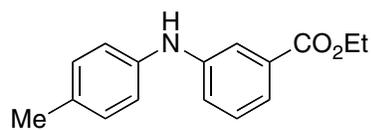
Experimental procedures for compounds in Table 2



4-chloro-*N*-(4-methoxyphenyl)aniline (Entry 1)

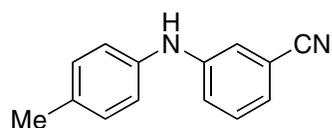
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 4-chloriodobenzene (238 mg, 1.00 mmol), and *p*-anisidine (182 mg, 1.5 mmol) with DMSO (0.50 mL) as solvent for 20 h at 80 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as an off-white solid (188 mg, 81 %). m.p. 49-50.5 °C (lit. 50-51°C).ⁱ ¹H NMR (500 MHz, CDCl₃) δ 7.18-7.13 (2H, m), 7.09-7.03 (2H, m), 6.90-6.80 (m, 4H), 5.48 (1H, bs), 3.81 (3H, s).

^{13}C NMR (125 MHz, CDCl_3) δ 155.8, 144.1, 135.4, 129.4, 124.5, 122.7, 116.8, 114.9, 55.8.



ethyl 3-(*p*-tolylamino)benzoate (Entry 2)

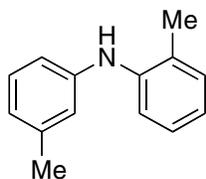
The general procedure was followed using CuI (9.5 mg, 0.05 mmol), pyrrole-2-carboxylic acid (11 mg, 0.10 mmol), K_3PO_4 (424 mg, 2.0 mmol), ethyl-3-iodobenzoate (167 μL , 1.00 mmol), and *p*-toluidine (214 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 80 $^\circ\text{C}$. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as a tan solid (199 mg, 78 %). m.p. 95-96 $^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 7.66 (1H, dd, J = 1.8, 2.0 Hz), 7.54 (1H, ddd, J = 1.1, 1.5, 7.6 Hz), 7.29 (1H, t, J = 7.8 Hz), 7.20 (1H, ddd, J = 0.9, 2.5, 8.1 Hz), 7.13-7.11 (2H, m), 7.04-7.01 (2H, m), 5.73 (1H, bs), 4.37 (2H, q, J = 7.1 Hz), 2.33 (3H, s), 1.39 (3H, t, J = 7.1 Hz). ^{13}C NMR (125 MHz, CDCl_3) δ 166.9, 144.4, 139.8, 131.8, 130.2, 120.4, 121.2, 120.6, 119.5, 117.5, 61.1, 20.9, 14.5. IR (KBr disc, cm^{-1}) 3356, 1701, 1604, 1589, 1526, 1487, 1367, 1280, 1219, 1106, 1025, 829, 801, 752. Anal. Calc. for $\text{C}_{16}\text{H}_{17}\text{NO}_2$: C 75.27, H 6.71. Found: C 75.51, H 6.74.



3-(*p*-tolylamino)benzonitrile (Entry 3)ⁱⁱ

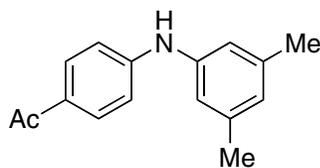
The general procedure was followed using CuI (9.5 mg, 0.05 mmol), pyrrole-2-carboxylic acid (11 mg, 0.10 mmol), K_3PO_4 (424 mg, 2.0 mmol), 3-iodobenzonitrile (229 mg, 1.00 mmol), and *p*-toluidine (214 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 90 $^\circ\text{C}$. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as a tan solid (150mg, 72 %). m.p. 71-73 $^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3) δ 7.30-7.28 (1H, m),

7.20-7.15 (2H, m), 7.13 (1H, ddd, $J = 0.9, 2.4, 7.4$ Hz), 7.09 (1H, ddd, $J = 1.1, 1.4, 7.5$ Hz), 7.05-7.02 (2H, m), 5.78 (1H, bs), 2.35 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 145.5, 138.4, 133.3, 130.4, 130.3, 123.1, 120.1, 119.3, 118.1, 113.2, 21.0. IR (KBr disc, cm^{-1}) 3398, 2226, 1598, 1523, 1489, 1312, 996, 867, 818, 780, 681. Anal. Calc. for $\text{C}_{14}\text{H}_{12}\text{N}_2$: C 80.74, H 5.81. Found: C 80.49, H 5.74.



2-methyl-*N-m*-tolylaniline (Entry 4)ⁱⁱⁱ

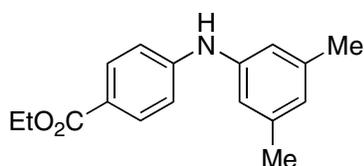
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 2-iodotoluene (127 μL , 1.00 mmol), and *m*-toluidine (216 μL , 2.0 mmol) with DMSO (0.50 mL) as solvent for 30 h at 80 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as a tan oil (144 mg, 75 %). ^1H NMR (500 MHz, CDCl_3) δ 7.26 (1H, d, $J = 6.9$ Hz), 7.22 (1H, d, $J = 7.5$ Hz), 7.17 (2H, m), 6.97-6.94 (1H, m), 6.81-6.75 (m, 3H), 5.36 (1H, bs), 2.33 (3H, s), 2.28 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 144.0, 141.5, 139.3, 131.1, 129.3, 128.3, 126.9, 122.0, 122.5, 118.9, 118.3, 114.7, 21.7, 18.1.



1-(4-(3,5-dimethylphenylamino)phenyl)ethanone (Entry 5)

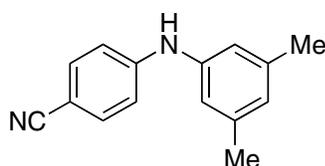
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 5-iodo-*m*-xylene (144 μL , 1.00 mmol), and 1-

(4-aminophenyl)ethanone (270 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 90 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a yellow solid (136 mg, 57 %). m.p. 131-134 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.90-7.86 (2H, m), 7.01-6.97 (2H, m), 6.81 (2H, s), 6.74 (1H, s), 6.02 (1H, bs), 2.54 (3H, s), 2.32 (6H, s). ¹³C NMR (125 MHz, CDCl₃) δ 196.6, 148.8, 140.6, 139.5, 130.8, 129.0, 125.4, 118.7, 114.6, 26.4, 21.6. IR (KBr disc, cm⁻¹) 3331, 1653, 1570, 1342, 1274, 1181, 1168, 827. Anal. Calc. for C₁₆H₁₇NO: C 80.30, H 7.16. Found: C 80.22, H 7.18.



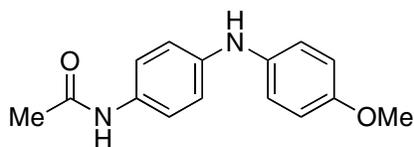
ethyl 4-(3,5-dimethylphenylamino)benzoate (Entry 6)

The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 5-iodo-*m*-xylene (144 μL, 1.00 mmol), and ethyl-4-aminobenzoate (330 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 90 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a white solid (138 mg, 51%). m.p. 119-120 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.94-7.91 (2H, m), 7.00-6.96 (2H, m), 6.81 (2H, m), 6.72 (1H, m), 5.96 (1H, s), 4.35 (2H, q, *J* = 7.1 Hz), 2.31 (3H, s), 1.38 (3H, t, *J* = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃) δ 166.7, 148.3, 141.0, 139.4, 131.6, 125.1, 121.4, 118.3, 114.8, 60.6, 21.6, 14.6. IR (KBr disc, cm⁻¹) 2241, 1697, 1595, 1509, 1352, 1285, 1170, 830, 769. Anal. Calc. for C₁₇H₁₉NO₂: C 75.81, H 7.11. Found: C 76.13, H 6.94.

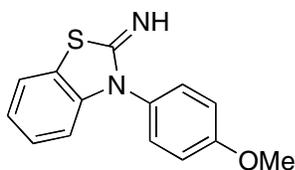


4-(3,5-dimethylphenylamino)benzonitrile (Entry 7)^{iv}

The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 5-iodo-*m*-xylene (144 μL, 1.00 mmol), and 4-aminobenzonitrile (236 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 90 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a yellow solid (113 mg, 51%). m.p. 154-155 °C. ¹H NMR (500 MHz, CDCl₃) δ 2.32 (3H, s), 7.49-7.46 (2H, m), 6.97-6.94 (2H, m), 6.80 (2H, s), 6.77 (1H, s), 6.00 (1H, bs). ¹³C NMR (125 MHz, CDCl₃) δ 148.1, 139.7, 139.4, 133.7, 125.7, 120.0, 118.9, 114.8, 101.1, 21.3. IR (KBr disc, cm⁻¹) 3335, 2214, 1591, 1532, 1350, 1170, 826. Anal. Calc. for C₁₅H₁₄N₂: C 81.05, H 6.35. Found: C 80.76, H 6.33.

*N*-(4-(4-methoxyphenylamino)phenyl)acetamide (Entry 8)

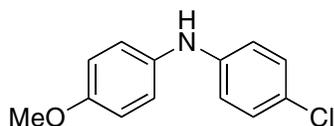
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 4-iodoanisole (234 mg, 1.00 mmol), and *N*-(4-aminophenyl)acetamide (300 mg, 2.0 mmol) with DMSO (0.70 mL) as solvent for 24 h at 80 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a white solid (212 mg, 83 %). m.p. 138-139 °C (lit. 138 °C).^v ¹H NMR (500 MHz, CDCl₃) δ 7.33-7.30 (2H, m), 7.16 (1H, bs), 7.10-7.02 (2H, m), 6.90-.84 (m, 4H), 5.47 (1H, bs), 3.80 (3H, s), 2.15 (3H, s). ¹³C NMR (125 MHz, CDCl₃) δ 168.4, 155.2, 142.1, 136.3, 130.4, 122.2, 121.7, 116.7, 114.9, 55.8, 24.6. IR (KBr disc, cm⁻¹) 3270, 1653, 1512, 1297, 1248, 1035, 819. Anal. Calc. for C₁₅H₁₆N₂O₂: C 70.29, H 6.29. Found: C 70.55, H 6.32.



3-(4-methoxyphenyl)benzo[*d*]thiazol-2(3*H*)-imine (Entry 9)

The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₂CO₃ (280 mg, 2.0 mmol), 4-iodoanisole (234 mg, 1.00 mmol), and 2-aminobenzothiazole (298 mg, 2.0 mmol) with DMSO (0.80 mL) as solvent for 24 h at 90 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a white solid (169 mg, 66 %). m.p. 91.5-92 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.53 (1H, td, *J* = 0.6, 7.8 Hz), 7.-7.41 (1H, m), 7.31 (1H, dd, *J* = 0.6, 8.2 Hz), 7.13-7.07 (3H, m), 6.07 (1H, bs), 6.84-6.82 (2H, bs), 3.78 (3H, s). ¹³C NMR (125 MHz, CDCl₃) δ 159.3, 139.0, 136.6, 131.2, 130.7, 125.0, 124.2, 119.9, 115.4, 115.3, 110.4, 55.6. IR (KBr disc, cm⁻¹) 3220, 2235, 1591, 1580, 1493, 1404, 1289, 1246, 1175, 1021, 824, 753. Anal. Calc. for C₁₄H₁₂N₂OS: C 65.60, H 4.72. Found: C 65.64, H 4.75.

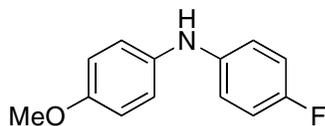
Experimental procedures for compounds in Table 3



4-chloro-*N*-(4-methoxyphenyl)aniline (Entry 1)

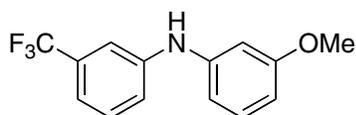
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 1-bromo-4-chlorobenzene (191 mg, 1.00 mmol), and *p*-anisidine (248 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 100 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title

compound as a tan solid (180 mg, 77 %). m.p. 50-51 °C (lit. 50-51°C).^{vi} ¹H NMR (500 MHz, CDCl₃) δ 7.18-7.13 (2H, m), 7.09-7.03 (2H, m), 6.90-6.80 (m, 4H), 5.48 (1H, bs), 3.81 (3H, s).



4-fluoro-*N*-(4-methoxyphenyl)aniline (Entry 2)

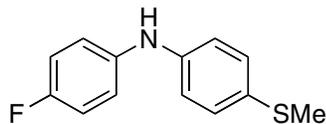
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 1-bromo-4-fluorobenzene (109 μL, 1.00 mmol), and *p*-anisidine (248 mg, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 80 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a tan solid (155 mg, 71 %). m.p. 57-59 °C (lit. 59 °C).^{vii} ¹H NMR (500 MHz, CDCl₃) δ 7.03-7.00 (2H, m), 6.96-6.85 (6H, m), 5.40 (1H, bs), 3.81 (3H, s). ¹³C NMR (125 MHz, CDCl₃) δ 158.3, 155.2, 141.3 (d), 136.7, 121.4, 117.9 (d), 116.1, 115.9, 114.9, 55.8.



3-methoxy-*N*-(3-(trifluoromethyl)phenyl)aniline (Entry 3)^{viii}

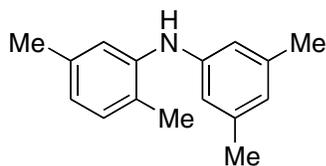
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 3-bromoanisole (127 μL, 1.00 mmol), and 3-aminobenzotrifluoride (250 μL, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 100 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as an orange oil (153 mg, 57%). ¹H NMR (500 MHz, CDCl₃) δ 7.36 (1H, t, *J* = 7.9 Hz), 7.30 (1H, s), 7.26-7.20 (2H, m), 7.16 (1H, d, *J* = 7.8 Hz), 6.70 (1H, dd, *J* = 1.2, 8.1 Hz), 6.67 (1H, s), 6.59 (1H, d, *J* = 8.2 Hz), 5.85 (1H, bs), 3.81 (3H, s). ¹³C NMR (125 MHz, CDCl₃) δ 160.9, 143.9, 143.4, 132.1, 130.5, 130.0, 129.9, 120.4, 117.3 (q), 113.0 (t), 111.4 (d), 107.6 (d),

104.7, 55.4.



4-fluoro-*N*-(4-(methylthio)phenyl)aniline (Entry 4)

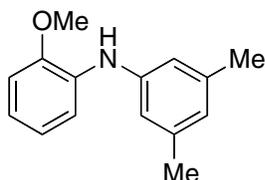
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 4-bromothioanisole (203 mg, 1.00 mmol), and 4-fluoroaniline (189 μ L, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 100 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as a brown oil (170 mg, 73 %). ¹H NMR (500 MHz, CDCl₃) δ 7.21-7.17 (2H, m), 7.02-6.92 (4H, m), 6.89-6.86 (2H, m), 5.56 (1H, bs), 2.41 (3H, s). ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 142.4, 139.0 (d), 130.3, 129.7, 120.6 (d), 117.7, 116.1 (d), 18.2. IR (KBr disc, cm⁻¹) 3396, 1595, 1508, 1314, 1223, 817, 506. Anal. Calc. for C₁₃H₁₂FNS: C 66.93, H 5.18. Found: C 67.16, H 5.20.



N-(3,5-dimethylphenyl)-2,5-dimethylaniline (Entry 5)

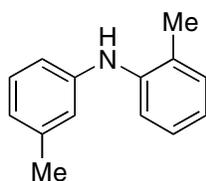
The general procedure was followed using CuI (19 mg, 0.10 mmol), 2-isobutyrylcyclohexanone (33 μ L, 0.20 mmol), K₃PO₄ (424 mg, 2.0 mmol), 5-bromo-*m*-xylene (136 μ L, 1.00 mmol), and 2,5-dimethylaniline (249 μ L, 2.0 mmol) with DMF (0.50 mL) as solvent for 24 h at 110 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 \rightarrow 4:1) afforded the title compound as a yellow oil (166 mg, 74 %). ¹H NMR (500 MHz, CDCl₃) δ 7.05-7.02 (2H, s), 6.72 (1H, td, *J* = 0.4, 7.6 Hz), 6.56 (2H, d, *J* = 0.6 Hz), 6.53 (1H, t, *J* = 0.6 Hz), 5.22 (1H, bs), 2.26

(3H, s), 2.23 (6H, s), 2.17 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 144.2, 141.3, 139.2, 136.6, 130.9, 125.4, 122.8, 122.4, 119.9, 116.8, 115.4, 21.6, 21.4, 17.7. IR (KBr disc, cm^{-1}) 3383, 3020, 2919, 1601, 1578, 1522, 1466, 1221, 1177, 829, 802. Anal. Calc. for $\text{C}_{14}\text{H}_{12}\text{F}_3\text{NO}$: C 62.92, H 4.53. Found: C 63.13, H 4.46.



N-(2-methoxyphenyl)-3,5-dimethylaniline (Entry 6)^{ix}

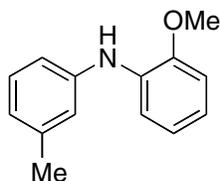
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 5-bromo-*m*-xylene (136 μL , 1.00 mmol), and *o*-anisidine (225 μL , 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 100 $^\circ\text{C}$. Workup and chromatographic purification (hexanes / ethyl acetate 4:1 \rightarrow 1:0) afforded the title compound as an orange oil (155 mg, 68%). ^1H NMR (500 MHz, CDCl_3) δ 7.33-7.31 (1H, m), 6.91-6.84 (3H, m), 6.81 (2H, d, $J = 0.6$ Hz), 6.62 (1H, t, $J = 0.6$ Hz), 6.10 (1H, s), 3.89 (3H, s), 2.30 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 148.4, 142.8, 139.1, 123.2, 121.0, 119.8, 118.7, 116.5, 115.0, 110.6, 55.8, 21.6.



2-methyl-*N*-*m*-tolylaniline (Entry 7)³

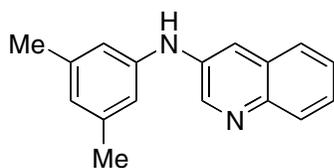
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 2-bromotoluene (120 μL , 1.00 mmol), and *m*-toluidine (216 μL , 2.0 mmol) with DMSO (0.50 mL) as solvent for 30 h at 100 $^\circ\text{C}$. Workup and

chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as a tan oil (129 mg, 66 %). ^1H NMR (500 MHz, CDCl_3) δ 7.26 (1H, d, $J = 6.9$ Hz), 7.22 (1H, d, $J = 7.5$ Hz), 7.17 (2H, m), 6.97-6.94 (1H, m), 6.81-6.75 (3H, m), 5.36 (1H, bs), 2.33 (3H, s), 2.28 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 144.0, 141.5, 139.3, 131.1, 139.3, 128.3, 126.9, 122.0, 122.5, 118.9, 118.3, 114.7, 21.7, 18.1.



2-methoxy-*N-m*-tolylaniline (Entry 8)^x

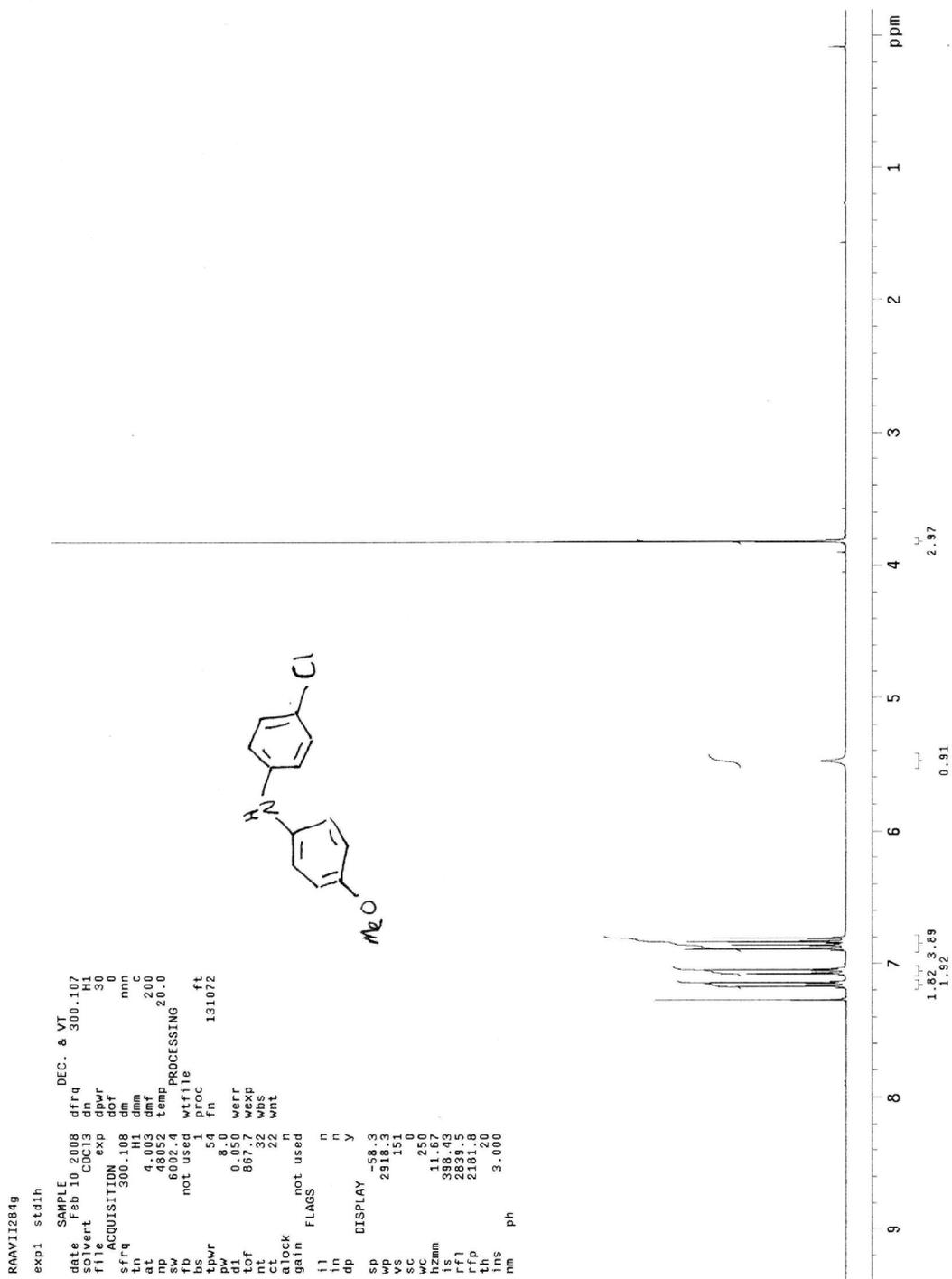
The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 2-bromoanisole (125 μL , 1.00 mmol), and *m*-toluidine (216 μL , 2.0 mmol) with DMSO (0.50 mL) as solvent for 30 h at 100 °C. Workup and chromatographic purification (hexanes / ethyl acetate 1:0 → 4:1) afforded the title compound as an orange oil (142 mg, 66%). ^1H NMR (500 MHz, CDCl_3) δ 7.36-7.33 (1H, m), 7.23-7.18 (1H, m), 7.02-6.87 (5H, m), 6.81 (1H, d, $J = 7.5$ Hz), 6.16 (1H, bs), 3.29 (3H, s), 2.36 (3H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 148.4, 142.8, 139.3, 133.2, 129.3, 122.2, 121.0, 119.9, 119.4, 115.8, 114.9, 110.6, 55.8, 21.7.

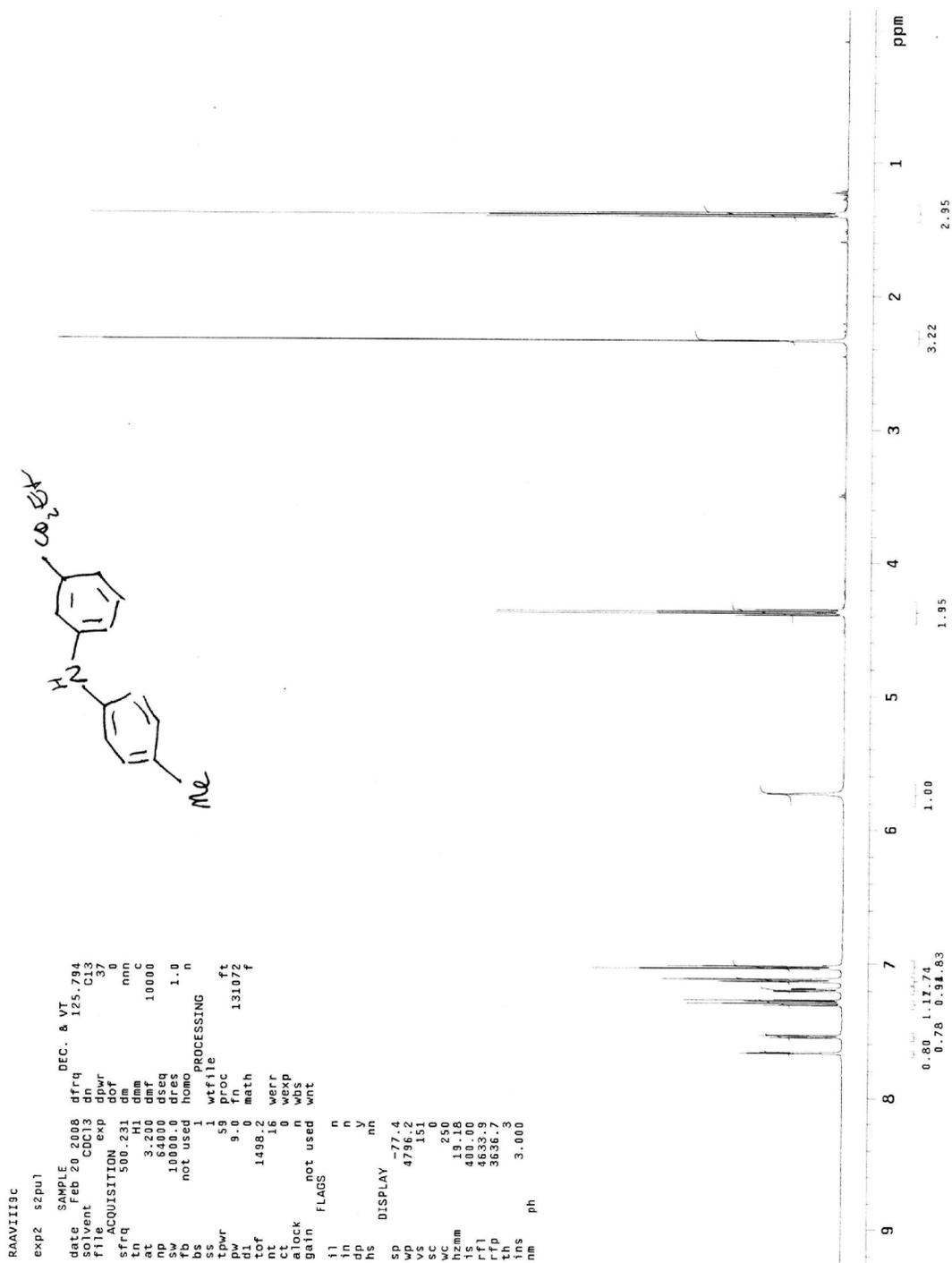


N-(3,5-dimethylphenyl)quinolin-3-amine (Entry 9)

The general procedure was followed using CuI (19 mg, 0.10 mmol), pyrrole-2-carboxylic acid (22 mg, 0.20 mmol), K_3PO_4 (424 mg, 2.0 mmol), 3-bromoquinoline (136 μL , 1.00 mmol), and

3,5-dimethylaniline (248 μ L, 2.0 mmol) with DMSO (0.50 mL) as solvent for 24 h at 100 $^{\circ}$ C. Workup and chromatographic purification (hexanes / ethyl acetate 4:1 \rightarrow 1:0) afforded the title compound as a green oil (135 mg, 54 %). ^1H NMR (500 MHz, CDCl_3) δ 8.72 (1H, d, J = 2.8 Hz), 8.02 (1H, dd, J = 0.6, 8.2 Hz), 7.70 (1H, d, J = 2.8 Hz), 7.65 (1H, dd, J = 1.2, 8.1 Hz), 7.54-7.46 (2H, m), 6.82 (2H, s), 6.71 (1H, d, J = 0.6 Hz), 6.12 (1H, s), 2.32 (6H, s). ^{13}C NMR (125 MHz, CDCl_3) δ 145.3, 143.7, 141.9, 139.6, 137.4, 120.2, 129.1, 127.2, 126.6, 126.5, 124.4, 117.2, 116.5, 21.6. IR (KBr disc, cm^{-1}) 3265, 3038, 1596, 1491, 1470, 1361, 1215, 1140, 908, 834, 781, 749, 732.



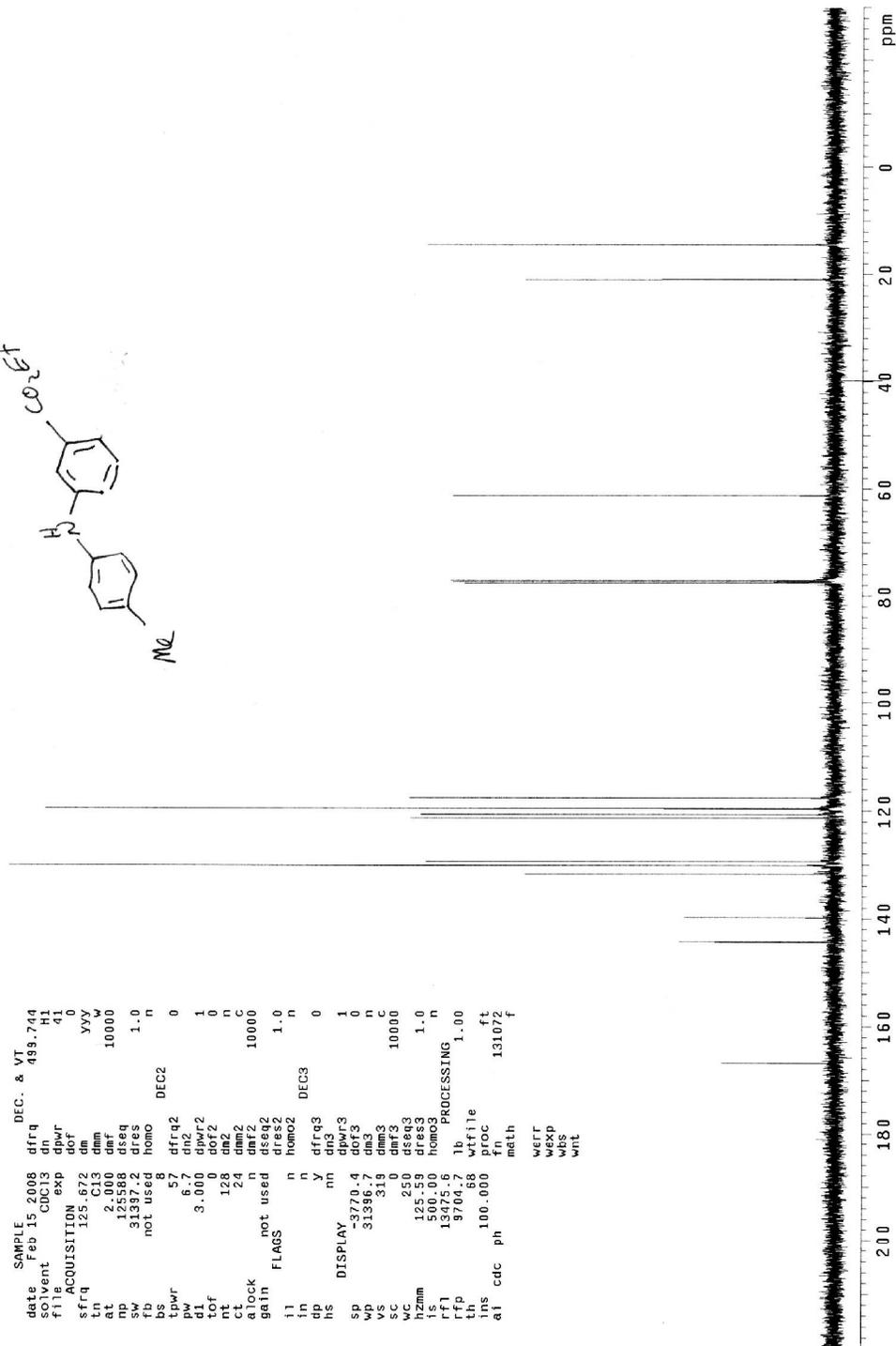
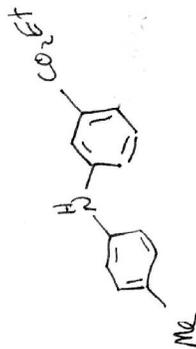


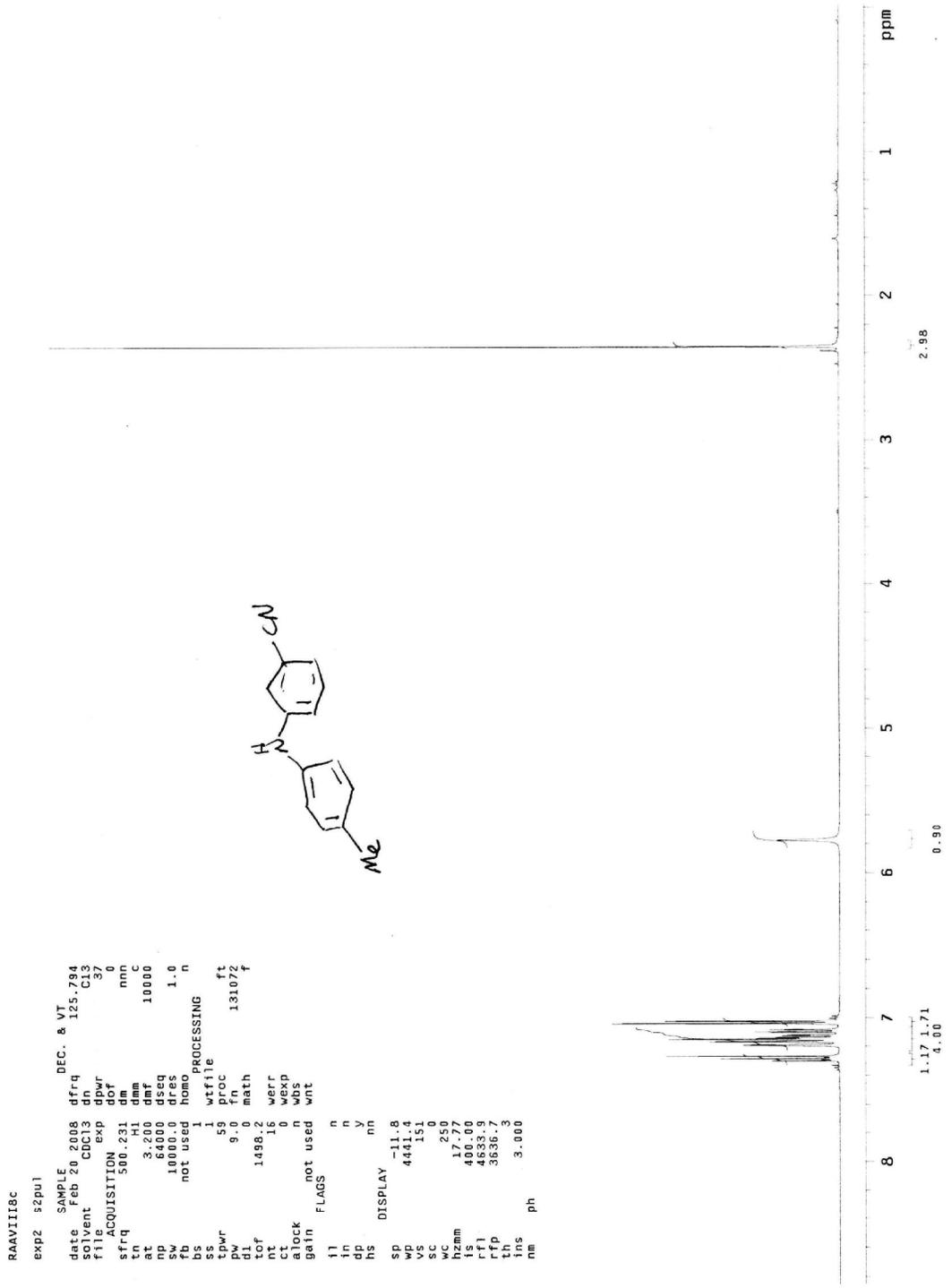
STANDARD CARBON PARAMETERS

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in 2.003 dnm 10000
np 125588 dseq 1-0
sw 31937.2 dres 1-0
fb not used homo DEC2
bs 8
tpwr 57 dfrq2 0
pw 6.7 dn2 1
tpr 3.00 dn3 1
tof 0 dfr2 0
nt 128 dn2 n
ct 24 dnm2 C
alock n dmf2 10000
gain not used dseq2
FLAGS n dres2 1-0
in n homo2 DEC3
dd n
hs Y dfrq3 0
nm dn3
DISPLAY nm dpwr3 1
sp -3770.4 dof3 0
wp 31396.7 dm3 n
vs 319 dnm3 C
wc 0 dseq 10000
h2mm 250 dres3
is 125.59 dres3 1-0
rfl 500.00 homo3
rff 13475.6 lb PROCESSING
th 68 wfile 1.00
ms 100.000 proc ft
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werr
wexp
wbs
wnt

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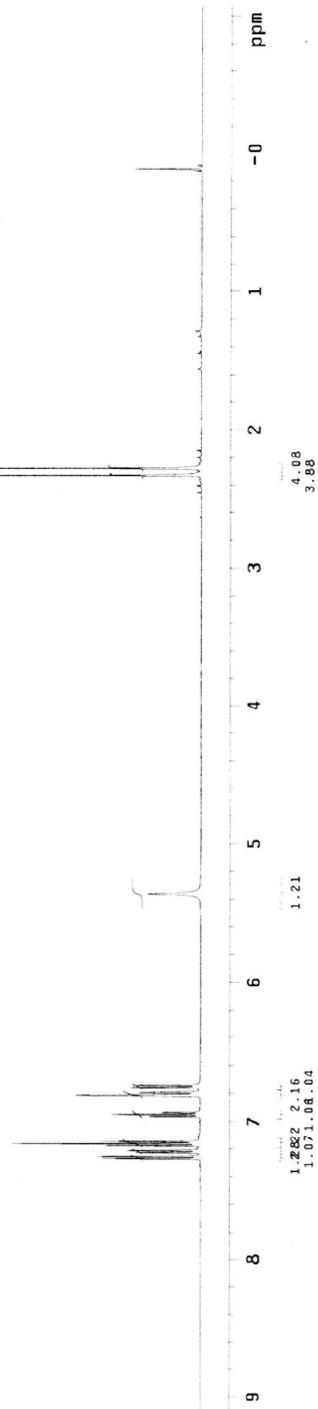
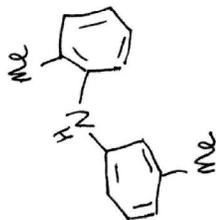




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RAAVIIB8
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solvent  CDCl3      dn    C13
file     ACQ13      exp    37
          ACQUISITION exp dof  0
sfrq    500.231    dm    nnn
tn       H1      dmm
at       3.200    dmf
pp       100000   dsq
pb       not used homo  1.0
bs       not used
ss       1       wfile
tpwr     59      proc   ft
pw       9.0     fn     131072
dl       1498    2     math
dt       15     werr
ct       10     wexp
alock    not used
gain     not used
          FLAGS
ll       n
nn       n
dd       v
hs       mn
          DISPLAY
SP      -11.8
WD      4441.4
VS      151
SC      250
PC      17.27
Hzmm    400.00
rf1     4633.9
rfp     3636.7
th      3
ins     3.000
nm      ph
  
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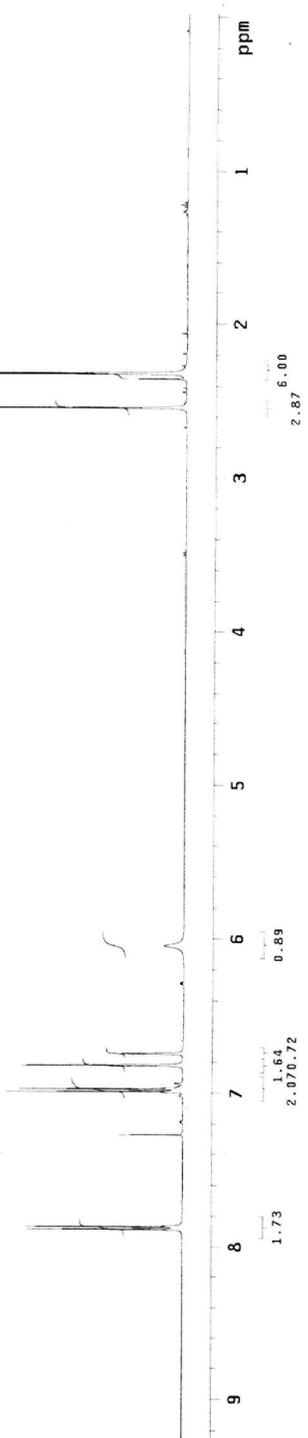
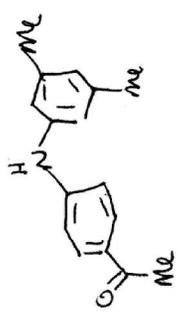
RAAVIII46b
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 date Mar 6 2008 dfrq 125.794
 solvent CDCl3 chn C3
 file ACQUISITION exp 37
 sfrq 500.231 dm nnn
 tn H1 dmm C
 at 3.200 dmf 10000
 np 64000 dseq
 pw 100000 pps 1.0
 fs not used
 ps 2
 NOMO PROCESSING
 ss 1 wfile ft
 tpwr 59 proc
 pw 9.0 fn 131072
 djf 1498.0 math
 ct ic werr
 ct 16 wexp
 alock n wbs
 gain not used
 wnt
 FLAGS
 ll n
 ln n
 op n
 ps n
 DISPLAY
 sp -536.8
 wp 5177.4
 vs 151
 sc 0
 sz 20
 szmm 21
 rfl 100.00
 rfp 4633.4
 th 3636.7
 ins 3.000
 nm ph



```

RAAVIII17A
exp2 s2pu1
SAMPLE
date Feb 20 2008 dfrq DEC. & VT 125.784
solvent CDCl3 dn 37
file 00C13 exp dpwr 0
ACQUISITION exp dof 0
sfrq 500.231 dm nnn
tn H1 dmm
at 2.00 dmf 10000
sv 1000.0 drc 1.0
tb not used homo 1.0 n
bs 1
ss 1 wtf file
tpwr 59 proc ft
pw 9.0 fn 131072
tof 1498.2 math
nt 16 werr
ct 0 wexp
alock not used n wbs
gain not used wnt
flags n
il n
ip y
dp y
hs nn
DISPLAY
sp -11.8
wp 4651.7
vs 151
vc 250
hzm 187.61
is 400.00
rfl 4633.9
rfp 3636.7
th 3
ns 6.000
na ph

```

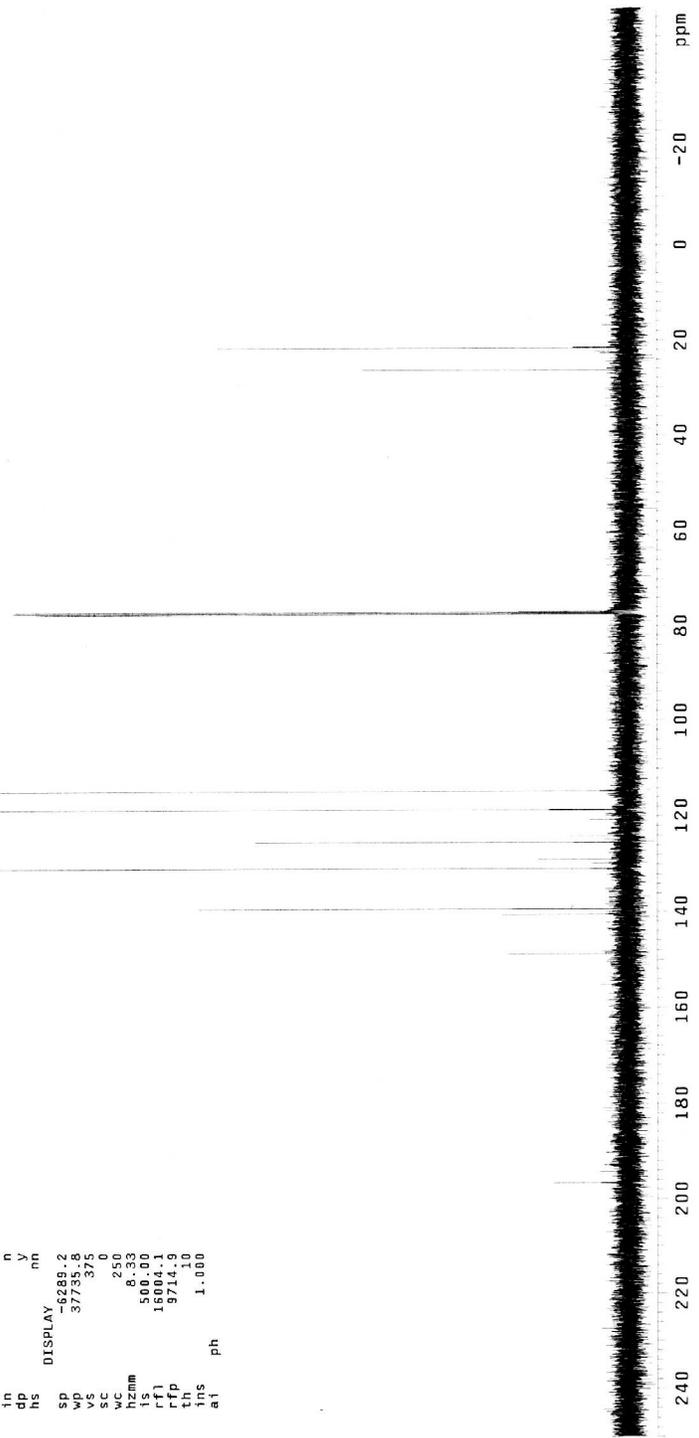
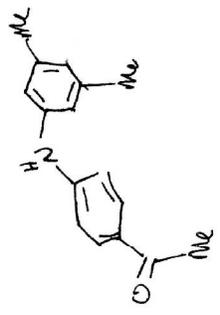


STANDARD CARBON PARAMETERS

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exp1 s2pu1
SAMPLE DEC. & VT.
date Feb 20 2008 dfrq 500.239
file CDE3 dnm 37
ent exp dnmr -500.0
ACQUISITION Exp dnr
sfrq 125.795 dm y
tn C13 dm w
at 1.736 dar
np 151010 dseq
fw 37735.8 fies 1.0
not used homa
bs not used B PROCESSING n
ss 1 lb PROCESSING 0.30
tpwr 53 wfile
pw 6.9 proc ft
dl 0.763 fn 131072
tof 53.4 math
ct 250 werr
alock n wexp
gain not used was
flags not used wnt
il n
in n
ip y
is nm
DISPLAY
sp -6289.2
wp 37735.8
vs 375
sc 0
vc 230
wvmm 8.30
is 500.00
rfj 16004.1
rfp 19714.9
th 1.0
ins 1.000
at ph

```

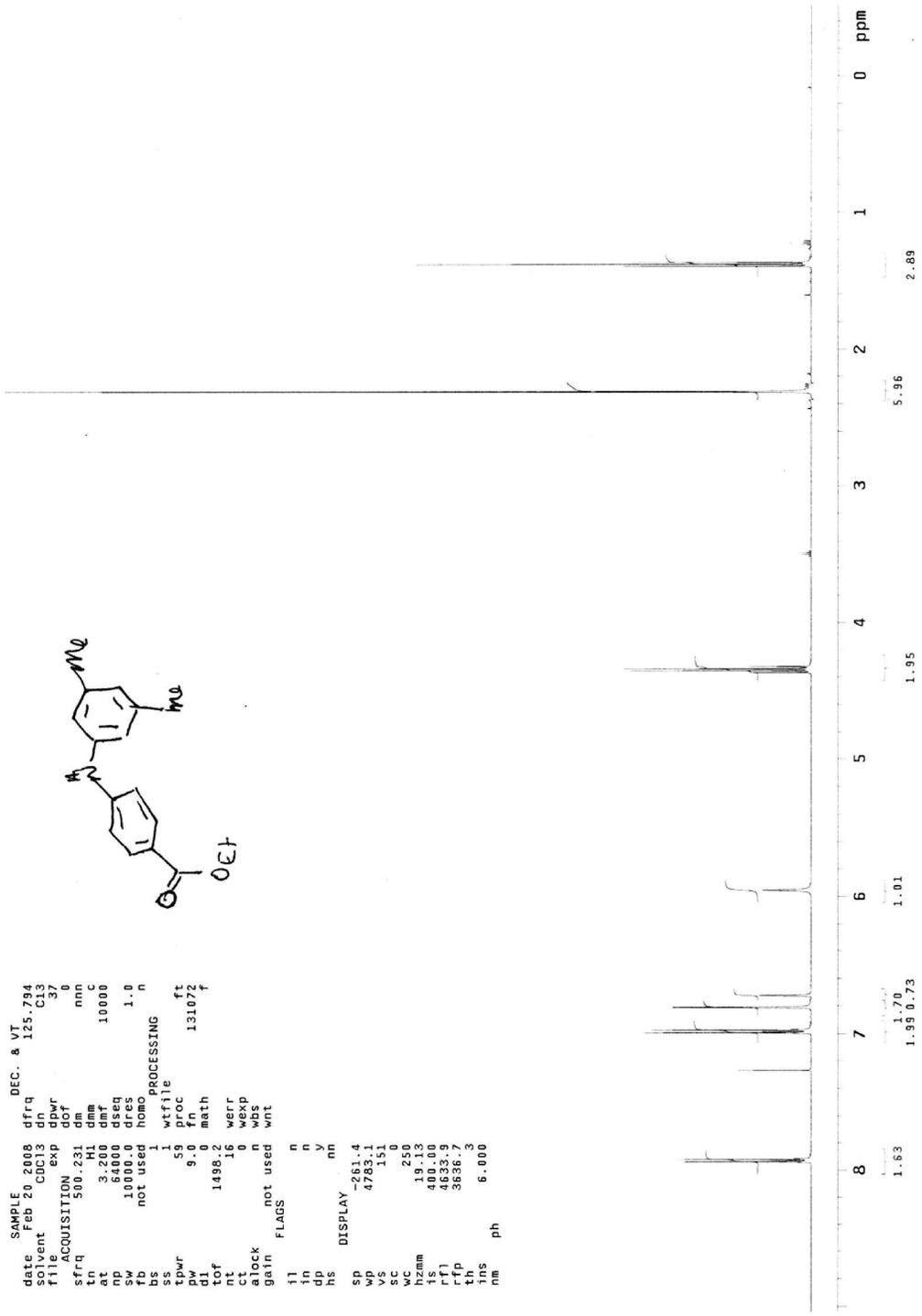
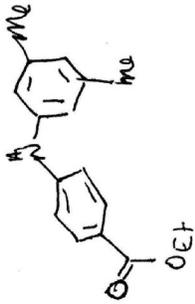


RAAVIII17b

```

exp2 s2pu1
SAMPLE
date Feb 20 2008 DEC. & VT
solvent CDC13 dn 125.794
file CDC13 exp 37
ACQUISITION
sfrq 500.231 dm nnn
in 3.200 mg
ns 6400 dseq 10000
sw 10000.0 dres 1.0
fb not used homo n
bs 1 wtfile
ss 1 proc ft
tpwr 99 math 131072
dv 1.0
tof 1498.2 werr
nt 16 wexp
ct 0 wbs
alock n
gain not used wnt
flags
il n
in n
dp n
hs nn
DISPLAY
sp -261.4
wp 4783.11
sc 1.0
wc 250
hzmm 19.13
is 400.00
rfi 4633.9
rfp 3636.7
tms 2
nm 6.000
ph

```

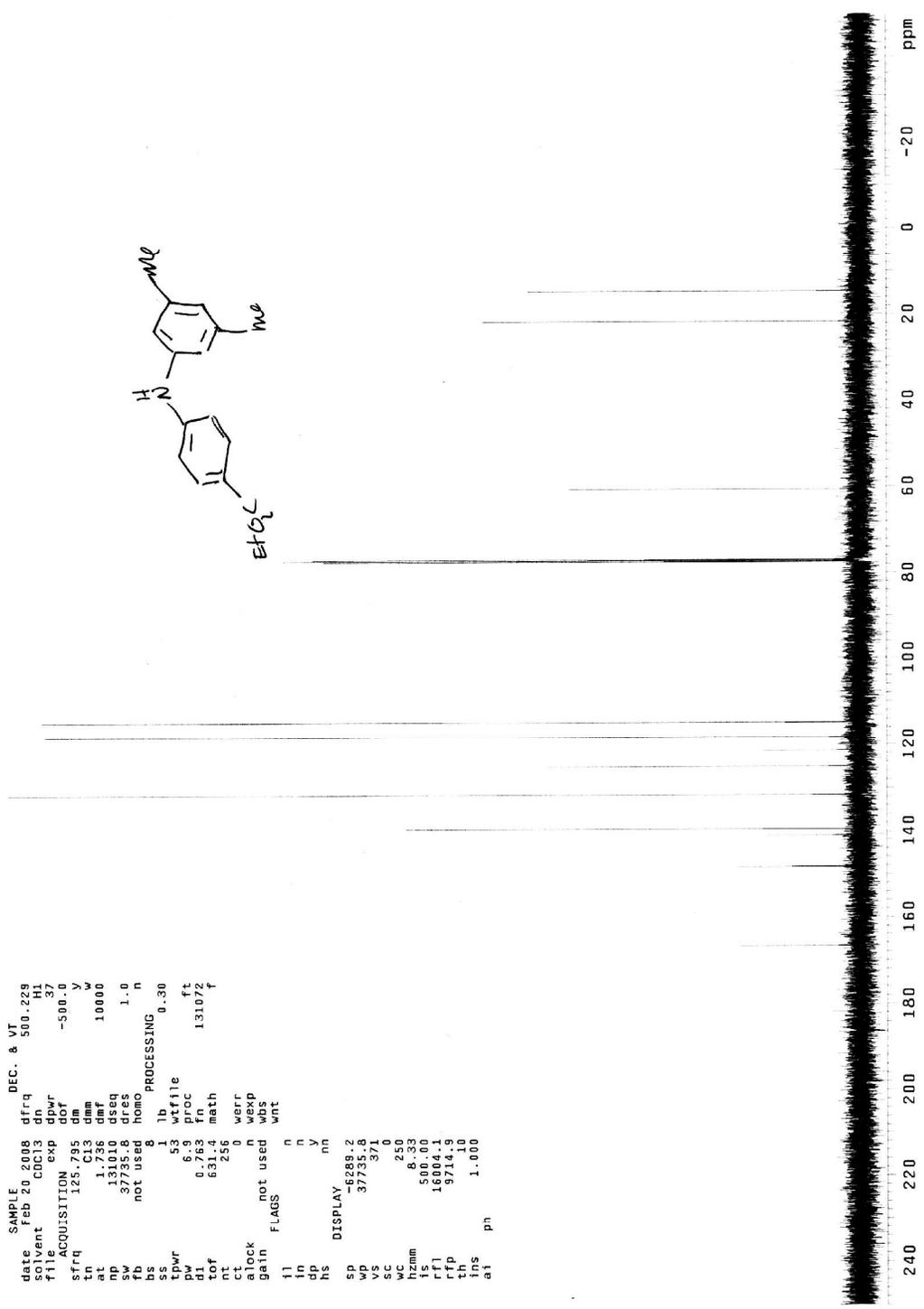
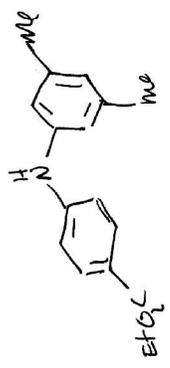


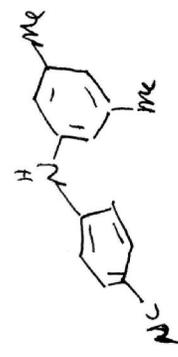
STANDARD CARBON PARAMETERS

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date Feb 20 2008 dfrq 500.229
solvent CUC13 dm 37
fl ACQUISITION exp dof -500.0
sfrq 125.795 dm
tn C13 dnm
at 1.736 dmf 10000
np 131010 dseq
sw 37735.8 dres 1.0
bs not used homo n
ss 8 lb PROCESSING 0.30
tpwr 53 wifile
pw 6.9 proc ft
di 0.763 fn 131072
tof 631.4 math f
ct 250
slck n wexp
gain not used wbs
FLAG wnt
ll n
ln n
dp y
hs nm
DISPLAY
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ph

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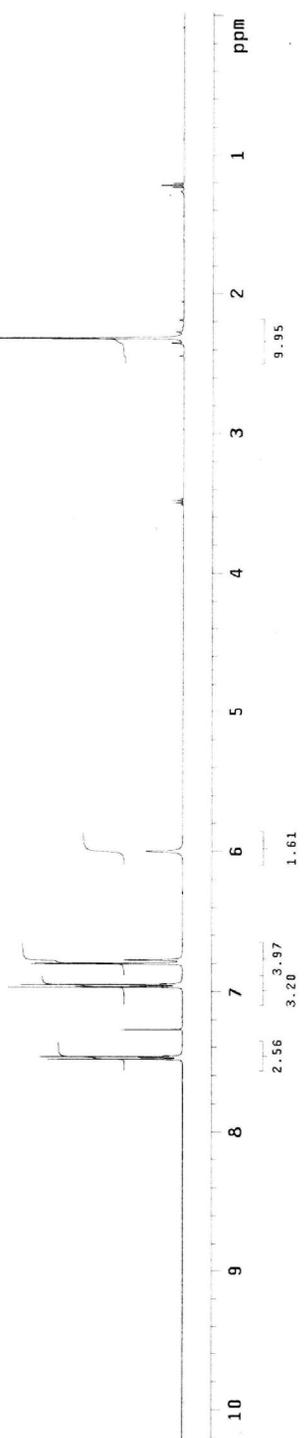




```

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file CDC13 exp dpwr 37
ACQUISITION exp dof 0
sfrq 500.231 dm nnn
tn H1 dmm
at 3.200 dmf
pw 10000.0 dms 10000
sw 10000.0 dres 1.0
fb not used homo 1.0
bs 1
ss 1 wtfile
tpwr 59 proc ft
pw 9.0 fn 131.072
tOf 1498.2 math
nt 16 werr
ct 0 wexp
alock n wbs
gain not used wnt
flags not used
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f1000 n

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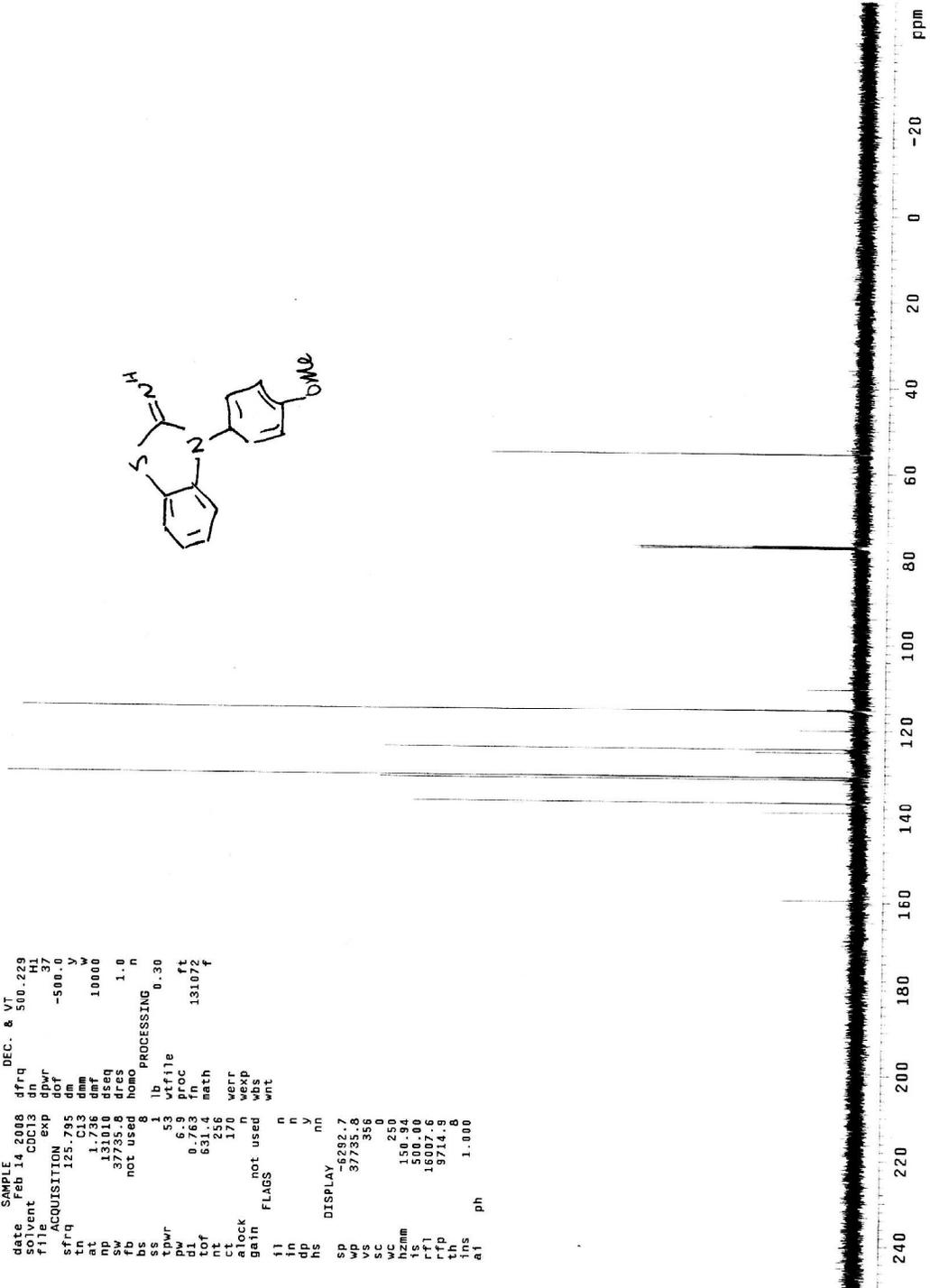
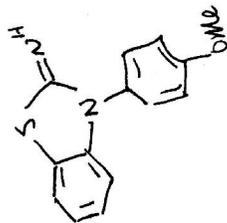


STANDARD CARBON PARAMETERS

```

exp2 s2pu1
SAMPLE DEC. & VT
date Feb 14 2008 ifrq 500.229
solvent CDCl3 dn H1
file exp 37
ACQUISITION exp dof -500.0
sfrq 125.795 dm
at 1.75 dmf 10000
np 131010 dseg
sw 37735.8 dres 1.0
fb not used homo 1.0
bs not used homo 1.0
PROCESSING 0.30
sswr 1 lb #file
dw 53 wrfile
di 63 proc ft
tof 0.763 proc 131072
nt 631.4 math
ct 256 verr
alock 170 werr
gain not used n wexp
flags not used wbs
il n wnt
in n
dp n
hs y
DISPLAY nn
sp -6292.7
wv 37735.8
vc 350
wc 250
hzmh 150.94
ls 500.00
rfi 16007.6
thp 9714.9
tms 1.000
at ph

```

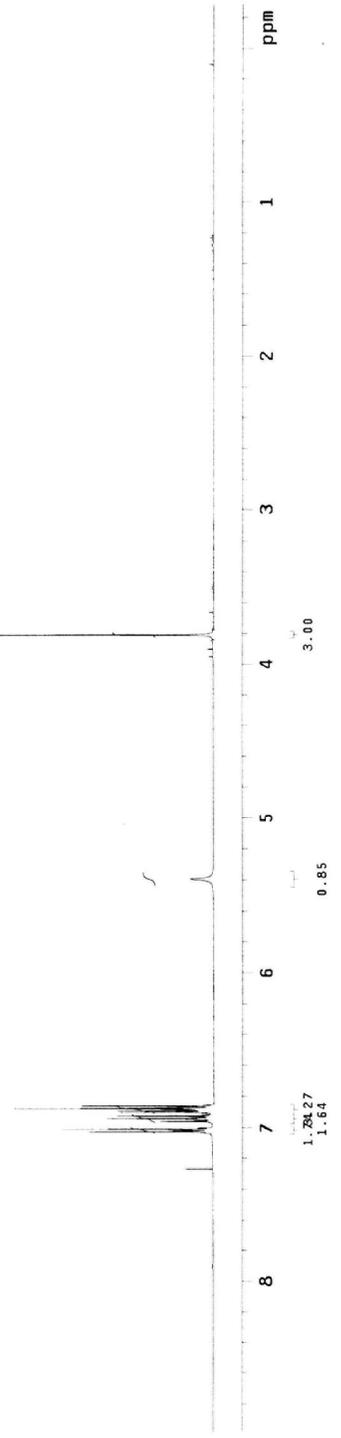
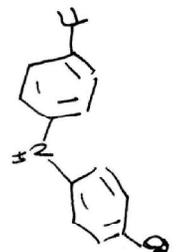


RAAVII246

```

exp1 s2pul
SAMPLE
date Feb 2 2008 DEC. & VT
solvent CDCl3 dn C13
file exp 37 dpwr 0
ACQUISITION
sfrq 500.231 dm nnn
in 3.20 dm
at 2.00 dm
sw 6400 hz
sb 10000.0 dres
fb not used homo 1.0
bs 8
ss 1 wfile
tpwr 58 proc ft
pv 9.0 fn 131072
tof 1498.2 meth
nt 16 werr
ct 16 wexp
alock n
gain not used wnt
il n
in n
dp v
hs nn
DISPLAY
sp -143.7
wp 4638.6
vs 151
vc 250
hzmm 18.55
is 100.00
rfl 4634.5
rfp 3636.7
th
ms 3.000
nm ph

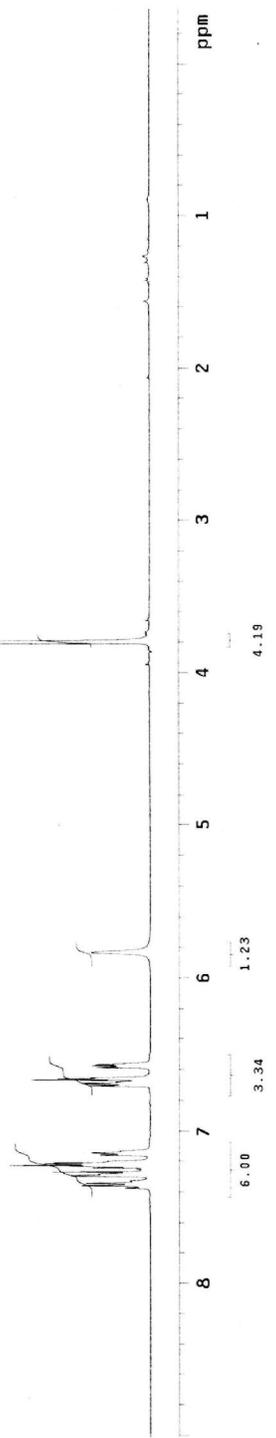
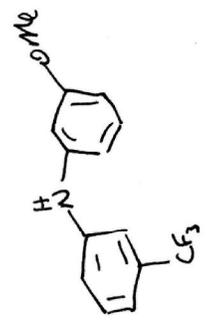
```



RAAVIII57

```

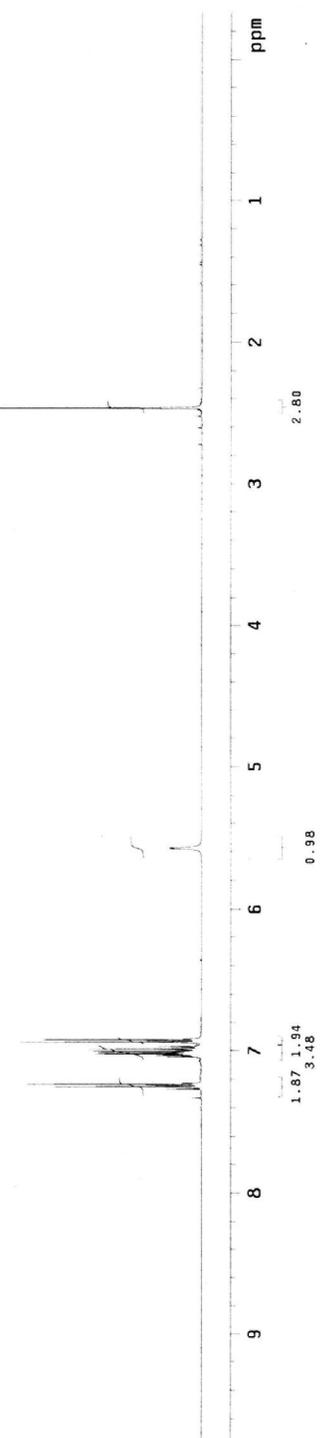
exp2 $2pu1
SAMPLE Mar 20 2008 DEC. & VT
date Mar 20 2008 dfrq 125.784
file CDC13 C13
ACQUISITION exp 37
sfrq 500.231 dm nnn
tn 3.200 dm C
at 6400 dmf 10000
cp 10000 dseq
Tb not used homo 1.0
bs not used homo 1.0
ss 1 wtf file ft
tpwr 59 proc 131072
pw 9.0 fn
DI 1498.0 math
CF 16 wexp
CT 16 wexp
alock n wbs
gain not used wnt
FLAGS n
I1 n
I2 n
I3 n
I4 n
I5 n
I6 n
I7 n
I8 n
I9 n
I10 n
I11 n
I12 n
I13 n
I14 n
I15 n
I16 n
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I89 n
I90 n
I91 n
I92 n
I93 n
I94 n
I95 n
I96 n
I97 n
I98 n
I99 n
I100 n
nm ph
  
```

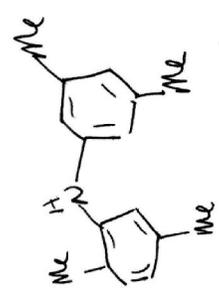




```

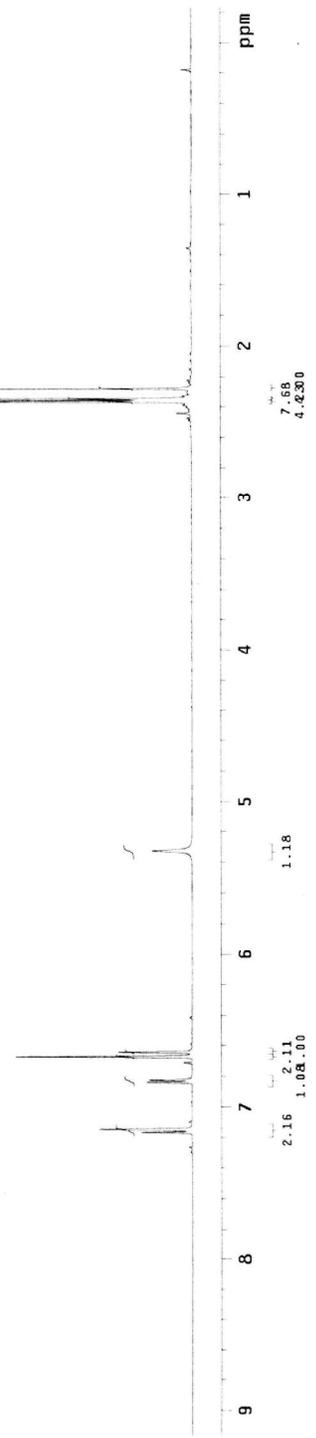
RAAVIII56
exp2  szpul
SAMPLE
date   Mar 20 2008   dfrq   DEC. & VT
solvent CDC13        dn     125.794
file    37          d1     37
ACQUISITION Exp    dof    0
          500.231   dm     nnn
          H1       dmm    10000
          C
          3.200   dmf
          64000  dseq
          10000.0 dres   1.0
          not used homo PROCESSING n
          1       wfile
          59      proc   ft
          9.0     fn     131072
          1498.2 math
          16      wexp
          16      wbp
          n       wbs
          not used gain
          FLAGS
          ll      n
          ln      n
          dp      y
          hs      mn
          DISPLAY
          sp      -169.4
          wp      5045.9
          vs      151
          sc      0
          wcmm    20.250
          fmm     100.00
          rfm     4833.9
          rfp     3636.7
          th      2.000
          ins     ph
  
```





```

RAAVII254a
exp2 s2pu1
SAMPLE
date Feb 2 2008 dfrq DEC. & VT 125.794
p1 cent CDC13 dnu 37
File ACQUISITION exp dof 0
sfrq 500.231 dm nnn
tn H1 dmm 10000
at 3.200 dmf
np 64000 dseq
pw 1000000 dres 1.0
bs not used homoPROCESSING n
ss 1 wtf file
tpwr 59 proc ft
pw 9.0 fn 131072
dl 0 math
tof 1498.12 wexp
ct 16 wexp
alock n wbs
gain not used wnt
FLAGS
ll n
ln n
gp n
hs nn
SP DISPLAY -118.3
wp 4704.2
vs 151
sc 0
vcmm 18.20
ls 100.00
rf1 4635.2
rff 3636.7
th
ins 1.000
nm ph
    
```

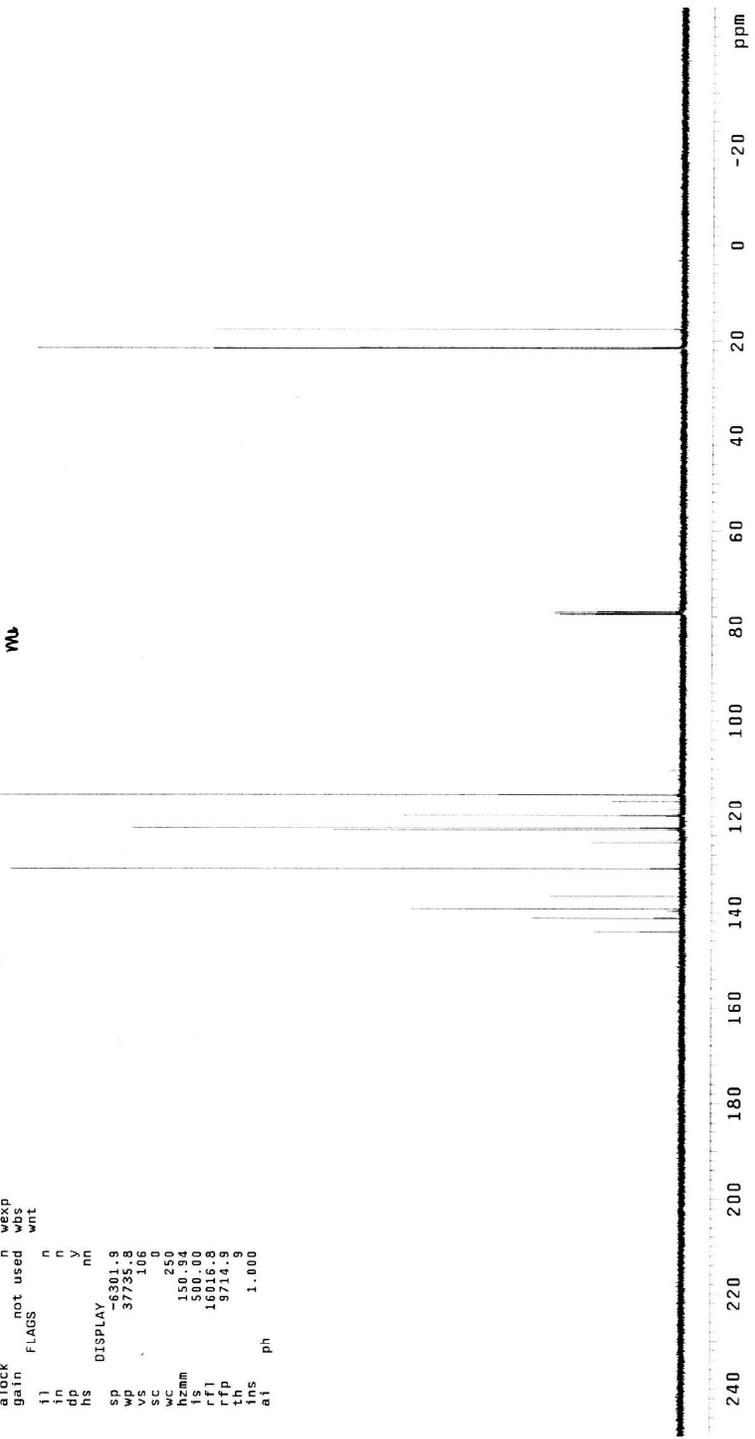
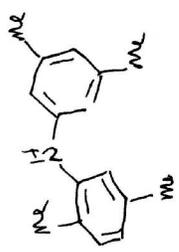


STANDARD CARBON PARAMETERS

```

exp1 s2pu1
SAMPLE 2, 2008 DEC. & VT
date Feb 2008 dfrq 500.229
solvent CDC13 dn HI
file CDC13 exp 37
ACQUISITION exp dof -500.0
sfrq 125.795 dm y
tn 1 C13 dmm w
at 131076 dmq
sw 37735.8 dres 1.0
fb not used homo n
bs 8 PROCESSING n
ss 1 lb 0.30
tpwr 53 wtfile
pw 0.79 proc
tof 6314 math 131072
nt 255
ct 104 werr
alock n wexp
gain not used wbs
FLAG not used wnt
il n
in n
ip v
hs nn
DISPLAY
sp -6301.9
wp 37735.8
xs 106
xc 0
wc 250
hzmm 150.94
fs 500.00
rfl 16016.8
rfp 9714.9
tn 9
tms at
at ph

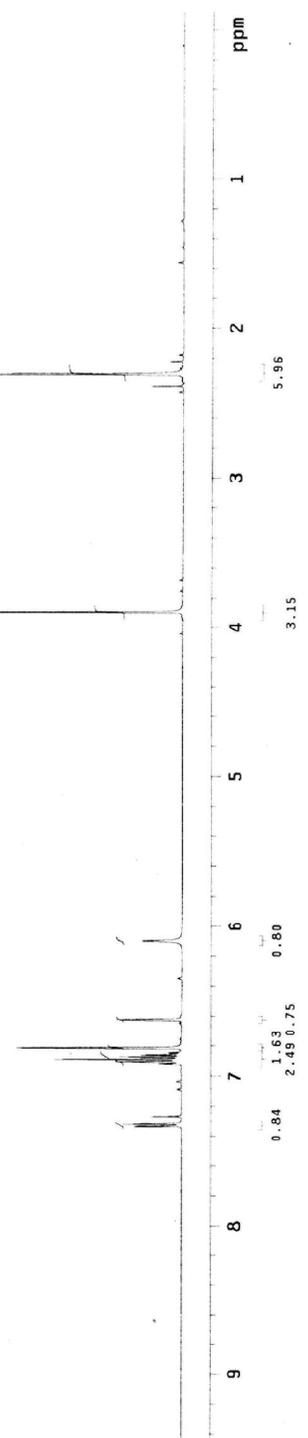
```





```

RAAVIII63
exp2 $2pu]
SAMPLE Mar 20 2008 dfrc DEC. & VT
solvent CDC13 d1n 125.784
file ACQUISITION exp dof 37
sfrq 500.231 dm nnn
tn H1 dmm
at 3.200 dmf 10000 C
sp 1000.0 dseq
pb not used homo 1.0
bs not used homo PROCESSING
ss 1 wtfile
tpwr 59 proc ft
pw 9.0 fn 131072
ti 1498.2 math
tf 64 werr
ct 26 wexp
alock n wbs
gain not used wnt
flags n
il n
ih y
ip y
is nn
DISPLAY
sp -64.4
wp 4783.1
vs 151
vc 250
hzmm 19.13
ts 100.00
rfl 4834.0
rfp 3836.7
th 4
ins 6.000
nm ph
    
```

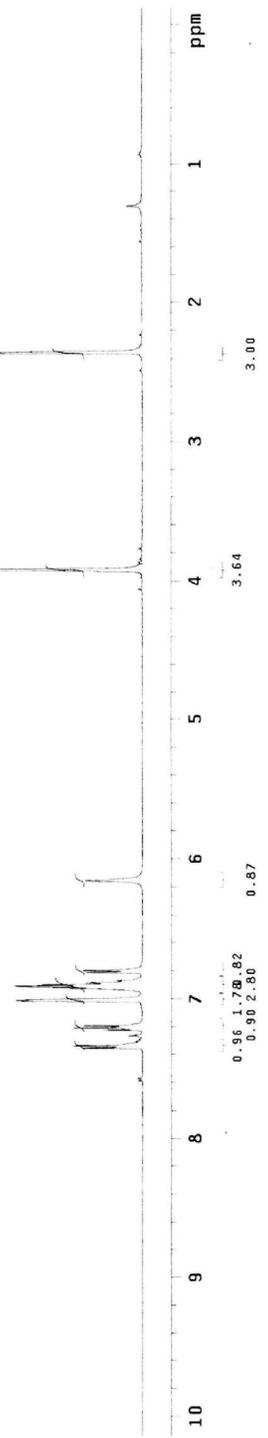
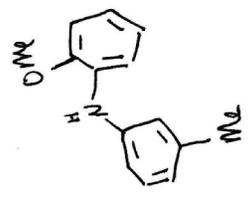


RAAVIII46A

```

expl szpu1
date Mar 8 2008 dfrq DEC. & VT
solvent CDCl3 c13 125.784
file ACQUISITION exp dof 37
sfrq 500.231 dm nnn
tn 3.200 dmf 10000 C
dp 100000 dseq 1.0
bs not used homo 2
ss 1 wtfile
tpwr 59 proc ft
pw 9.0 fn 131072
dlf 1498.2 math
dt 16 werr
ct 16 wexp
alock n wbs
gain not used wnt
ll n
ln n
dp U
hs nn
SP -63.9
WP 5137.9
VS 151
SC 250
hzmm 20.55
lsmm 100.00
rfl 4633.6
rff 3636.7
th ns
nm ph

```

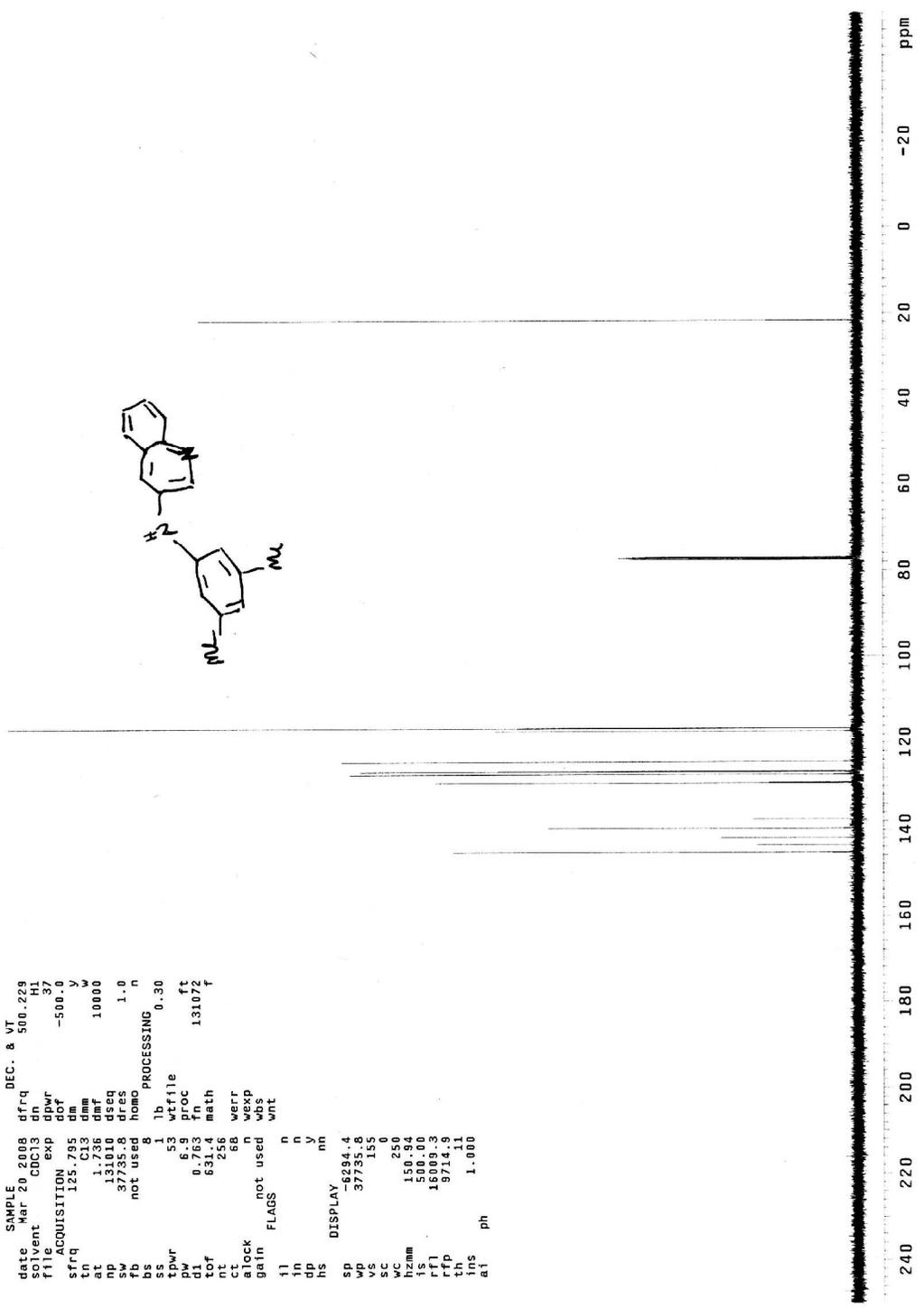
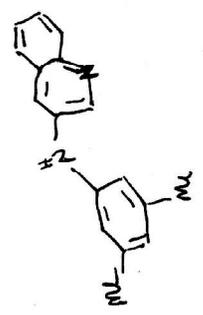


STANDARD CARBON PARAMETERS

```

exp1 s2pu1
SAMPLE Mar 20 2008 dfrq DEC. & VT
solvent CDC13 dn H1
file ACQUISITION exp dpwr 37
sfrq 128.795 dpr -500.0
tn C13 dm y
at 1.736 dmf 10000
np 131010 dseq
sw 37735.8 dres 1.0
fb not used homo n
bs g lb PROCESSING 0.30
tpwr 53 wtf file
pw 6.9 proc ft
dl 0.763 fn 131072
tof 631.4 math
nt 256
ct 58 werr
atlock n resp
gain not used wts
flags not used wnt
fl n
in n
dp y
hs nh
DISPLAY 6284.4
sp 37735.8
vs 155
sc 0
wc 250
hzmm 150.94
ls 500.00
rfi 1909.9
rfp 37735.8
th 11
ins 1.000
ai ph

```



References

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