

Ligand-free Iron/Copper Cocatalyzed N-Arylations of Aryl Halides with Amines under Microwave Irradiation

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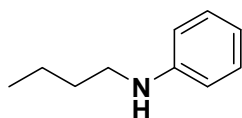
General Information

The reagents (chemicals) were purchased from commercial chemical reagent company, and used without further purification unless otherwise stated. All of the microwave-assistant reactions were performed in an Initiator™ EXP microwave system (Biotage, Inc.) at the specified temperature using the standard mode of operation. Analytical thin-layer chromatography (TLC) was HSGF 254. All products were characterized by their NMR and LRMS and HRMS spectra. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multipet (m) and broad (br).

General procedure for the Coupling reaction: A mixture of Fe_2O_3 (32 mg, 0.2 mmol), $\text{Cu}(\text{acac})_2$ (26 mg, 0.1 mmol), and Cs_2CO_3 (650 mg, 2.0 mmol) was dissolved in DMSO (3 mL). Subsequently, iodobenzene (160 μL , 1.5 mmol), morpholine (88 μL , 1.0 mmol) and H_2O (3 mL) were added to this mixture. The vial was sealed and the mixture was then irradiated for 30 min at 150 °C. The mixture was then cooled to room temperature, and diluted with dichloromethane, washed with brine, dried over using anhydrous Na_2SO_4 , and concentrated in vacuum. The residue was purified by flash column chromatography (petroleum ether/ethyl acetate = 10 : 1) to yield the expected product **1g** (135 mg, 83%yield). The identity and purity of the product was confirmed by ^1H and ^{13}C NMR spectroscopic analysis.

Spectroscopic and Analytical Data

N-butylbenzenamine (1a)

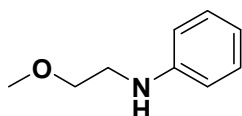


^1H NMR (300 MHz, CDCl_3): δ 7.19-7.14 (m, 2H), 6.70-6.66 (m, 1H), 6.61-6.58 (m, 2H), 3.12-3.07 (m, 2H), 1.61-1.54 (m, 2H), 1.46-1.38 (m, 2H), 0.98-0.93 (m, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 148.4, 129.1, 117.0, 112.6, 43.6, 31.6, 20.2, 13.8.

MS (EI, m/z): 149 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{10}\text{H}_{15}\text{N}$ $[\text{M}]^+$: 149.1204; Found: 149.1208.

N-(2-methoxyethyl)benzenamine (1b)

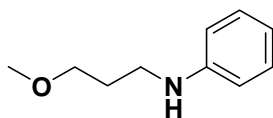


^1H NMR (300 MHz, CDCl_3): δ 7.20-7.15 (m, 2H), 6.74-6.69 (m, 1H), 6.64-6.61 (m, 2H), 3.58 (t, $J=5.1$ Hz, 2H), 3.37 (s, 3H), 3.27 (t, $J=5.1$ Hz, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 148.1, 129.1, 117.5, 113.0, 70.9, 58.6, 43.3.

MS (EI, m/z): 151 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_9\text{H}_{13}\text{NO}$ $[\text{M}]^+$: 151.0997; Found: 151.0990.

N-(3-methoxypropyl)benzenamine (1c)

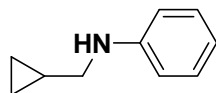


^1H NMR (300 MHz, CDCl_3): δ 7.19-7.14 (m, 2H), 6.71-6.66 (m, 1H), 6.62-6.59 (m, 2H), 3.50 (t, $J=6.0$ Hz, 2H), 3.35 (s, 3H), 3.21 (t, $J=6.0$ Hz, 2H), 1.91-1.83 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 148.4, 129.1, 117.0, 112.6, 71.1, 58.6, 41.6, 29.2.

MS (EI, m/z): 165 [M]⁺; HRMS (EI): Calcd. for C₁₀H₁₅NO [M]⁺: 165.1154; Found:
165.1149.

N-(cyclopropylmethyl)benzenamine (1d)

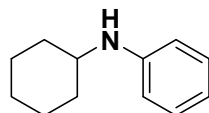


¹H NMR (300 MHz, CDCl₃): δ 7.19-7.14 (m, 2H), 6.71-6.66 (m, 1H), 6.61-6.58 (m, 2H), 2.94 (d, *J*=6.3Hz, 2H), 1.11-1.06 (m, 1H), 0.57-0.51 (m, 2H), 0.25-0.20 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 148.4, 129.2, 117.2, 112.7, 49.0, 10.8, 3.4.

MS (EI, m/z): 147 [M]⁺; HRMS (EI): Calcd. for C₁₀H₁₃N [M]⁺: 147.1048; Found:
147.1044.

N-cyclohexylbenzenamine (1e)

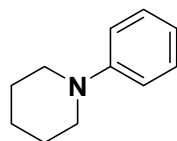


¹H NMR (300 MHz, CDCl₃): δ 7.18-7.12 (m, 2H), 6.68-6.63 (m, 1H), 6.59-6.56 (m, 2H), 3.29-3.21 (m, 1H), 2.08-2.03 (m, 2H), 1.79-1.72 (m, 2H), 1.68-1.62 (m, 1H), 1.44-1.08 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): δ 147.3, 129.2, 116.8, 113.1, 51.6, 33.4, 25.9, 25.0.

MS (EI, m/z): 175 [M]⁺; HRMS (EI): Calcd. for C₁₂H₁₇N [M]⁺: 175.1361; Found:
175.1362.

N-phenylpiperidine (1f)

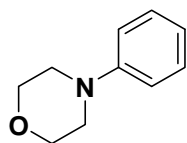


^1H NMR (300 MHz, CDCl_3): δ 7.26-7.21 (m, 2H), 6.94-6.92 (m, 2H), 6.83-6.78 (m, 1H), 3.14 (t, $J=5.7$ Hz, 4H), 1.74-1.66 (m, 4H), 1.59-1.54 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 152.2, 128.9, 119.2, 116.5, 50.6, 25.8, 24.2.

MS (EI, m/z): 161 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{N}$ $[\text{M}]^+$: 161.1204; Found: 161.1201.

4-phenylmorpholine (1g)

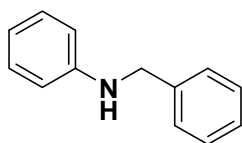


^1H NMR (300 MHz, CDCl_3): δ 7.30-7.25 (m, 2H), 6.92-6.85 (m, 3H), 3.85 (t, $J=4.8$ Hz, 4H), 3.14 (t, $J=4.8$ Hz, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 151.2, 129.1, 120.0, 115.6, 66.9, 49.3.

MS (EI, m/z): 163 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{10}\text{H}_{13}\text{NO}$ $[\text{M}]^+$: 163.0997; Found: 163.0995.

N-benzylbenzenamine (1h)

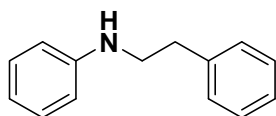


^1H NMR (300 MHz, CDCl_3): δ 7.34-7.24 (m, 5H), 7.18-7.12 (m, 2H), 6.73-6.68 (m, 1H), 6.61-6.58 (m, 2H), 4.27 (s, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 148.0, 139.3, 129.2, 128.6, 127.4, 127.1, 117.5, 112.8, 48.2.

MS (EI, m/z): 183 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{13}\text{H}_{13}\text{N}$ $[\text{M}]^+$: 183.1048; Found: 183.1090.

N-phenethylbenzenamine (1i)

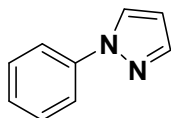


^1H NMR (300 MHz, CDCl_3): δ 7.35-7.30 (m, 2H), 7.26-7.15 (m, 5H), 6.75-6.69 (m, 1H), 6.61-6.59 (m, 2H), 3.40 (t, $J=6.9$ Hz, 2H), 2.91 (t, $J=6.9$ Hz, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 147.9, 139.2, 129.2, 128.7, 128.5, 126.4, 117.4, 112.9, 45.0, 35.4.

MS (EI, m/z): 197 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{14}\text{H}_{15}\text{N}$ $[\text{M}]^+$: 197.1204; Found: 197.1218.

1-phenyl-1H-pyrazole (1j)

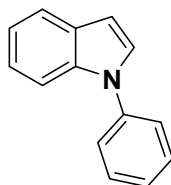


^1H NMR (300 MHz, CDCl_3): δ 7.92-7.91 (m, 1H), 7.74-7.69 (m, 3H), 7.48-7.42 (m, 2H), 7.31-7.26 (m, 1H), 6.47-6.45 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.0, 140.0, 129.3, 126.6, 126.3, 119.0, 107.4.

MS (EI, m/z): 144 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_9\text{H}_8\text{N}_2$ $[\text{M}]^+$: 144.0687; Found: 144.0691.

1-phenyl-1H-indole (1k)



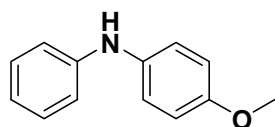
^1H NMR (300 MHz, CDCl_3): δ 7.70-7.67 (m, 1H), 7.57-7.54 (m, 1H), 7.49-7.46 (m, 4H), 7.34-7.30 (m, 2H), 7.24-7.14 (m, 2H), 6.67-6.66 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 139.8, 135.8, 129.5, 129.3, 127.9, 126.4, 124.3, 122.3,

121.1, 120.3, 110.4, 103.5.

MS (EI, m/z): 193 [M]⁺; HRMS (EI): Calcd. for C₁₄H₁₁N [M]⁺: 193.0891; Found:
193.0886.

4-methoxy-N-phenylaniline (1l)

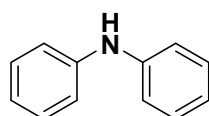


¹H NMR (300 MHz, CDCl₃): δ 7.23-7.19 (m, 2H), 7.08-7.06 (m, 2H), 6.91-6.81 (m, 5H), 5.49 (s, br, 1H), 3.70 (s, 3H).

¹³C NMR (100 MHz, CDCl₃): δ 155.2, 145.1, 135.7, 129.3, 122.1, 119.5, 115.6, 114.6, 55.5.

MS (EI, m/z): 199 [M]⁺; HRMS (EI): Calcd. for C₁₃H₁₃NO [M]⁺: 199.0997; Found:
199.0999.

Diphenylamine (1m)

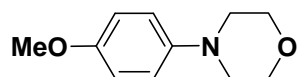


¹H NMR (300 MHz, CDCl₃): δ 7.29-7.25 (m, 4H), 7.08-7.06 (m, 4H), 6.96-6.91 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 143.0, 129.3, 121.0, 117.8.

MS (EI, m/z): 169 [M]⁺; HRMS (EI): Calcd. for C₁₂H₁₁N [M]⁺: 169.0891; Found:
169.0886.

4-(4-methoxyphenyl)morpholine (2a)



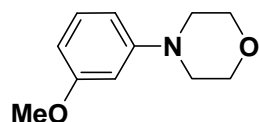
¹H NMR (300 MHz, CDCl₃): δ 6.91-6.83 (m, 4H), 3.87-3.84 (m, 4H), 3.77 (s, 3H),

3.07-3.04 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 153.9, 145.5, 117.8, 114.5, 67.0, 55.5, 50.8.

MS (EI, m/z): 193 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}_2$ $[\text{M}]^+$: 193.1103; Found: 193.1108.

4-(3-methoxyphenyl)morpholine (2b)

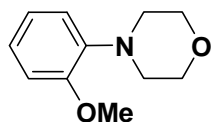


^1H NMR (300 MHz, CDCl_3): δ 7.23-7.17 (m, 1H), 6.56-6.52 (m, 1H), 6.47-6.44 (m, 2H), 3.85 (t, $J=4.8$ Hz, 4H), 3.80 (s, 3H), 3.15 (t, $J=4.8$ Hz, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 160.5, 152.6, 129.8, 108.3, 104.6, 102.1, 66.7, 55.0, 49.1.

MS (EI, m/z): 193 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}_2$ $[\text{M}]^+$: 193.1103; Found: 193.1105.

4-(2-methoxyphenyl)morpholine (2c)

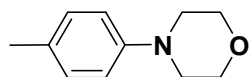


^1H NMR (300 MHz, CDCl_3): δ 7.03-6.99 (m, 1H), 6.94-6.92 (m, 2H), 6.89-6.86 (m, 1H), 3.89 (t, $J=4.8$ Hz, 4H), 3.86 (s, 3H), 3.07 (t, $J=4.8$ Hz, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 152.1, 141.0, 123.1, 120.9, 117.9, 111.1, 67.1, 55.2, 51.1.

MS (EI, m/z): 193 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}_2$ $[\text{M}]^+$: 193.1103; Found: 193.1110.

4-p-tolylmorpholine (2d)

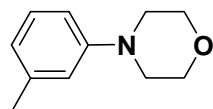


^1H NMR (300 MHz, CDCl_3): δ 7.21-7.19 (m, 2H), 7.05-7.02 (m, 2H), 3.87 (t, $J=4.5$ Hz, 4H), 2.93 (t, $J=4.5$ Hz, 4H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 153.4, 148.8, 130.0, 129.6, 116.3, 115.1, 66.8, 50.1, 20.4.

MS (EI, m/z): 177 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}$ $[\text{M}]^+$: 177.1154; Found: 177.1158.

4-m-tolylmorpholine (2e)

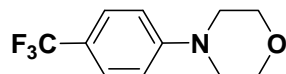


^1H NMR (300 MHz, CDCl_3): δ 7.20-7.17 (m, 1H), 6.77-6.73 (m, 3H), 3.89-3.86 (m, 4H), 3.19-3.16 (m, 4H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 151.2, 138.8, 128.9, 120.9, 116.5, 112.8, 66.8, 49.4, 21.7.

MS (EI, m/z): 177 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{15}\text{NO}$ $[\text{M}]^+$: 177.1154; Found: 177.1151.

4-(4-(trifluoromethyl)phenyl)morpholine (2g)

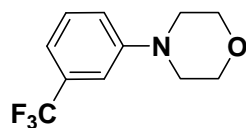


^1H NMR (300 MHz, CDCl_3): δ 7.50 (d, $J=6.6$ Hz, 2H), 6.92 (d, $J=6.6$ Hz, 2H), 3.87 (t, $J=3.6$ Hz, 4H), 3.24 (t, $J=3.6$ Hz, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 153.3, 126.5, 126.4, 114.3, 66.6, 48.1.

MS (EI, m/z): 231 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{12}\text{F}_3\text{NO}$ $[\text{M}]^+$: 231.0871; Found: 231.0871.

4-(3-(trifluoromethyl)phenyl)morpholine (2h)

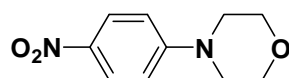


^1H NMR (300 MHz, CDCl_3): δ 7.39-7.33 (m, 1H), 7.17-7.11 (m, 2H), 7.08-7.05 (m, 1H), 3.91-3.88 (m, 4H), 3.22-3.20 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 151.4, 129.6, 118.4, 116.3, 116.2, 111.9, 111.8, 66.7, 48.8.

MS (EI, m/z): 231 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{11}\text{H}_{12}\text{F}_3\text{NO}$ $[\text{M}]^+$: 231.0871; Found: 231.0873.

4-(4-nitrophenyl)morpholine (2j)

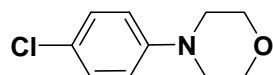


^1H NMR (300 MHz, CDCl_3): δ 8.16-8.12 (m, 2H), 6.93-6.90 (m, 1H), 6.84-6.81 (m, 1H), 3.87 (t, $J=5.1$ Hz, 4H), 2.93 (t, $J=5.1$ Hz, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 155.0, 138.9, 126.2, 125.9, 115.6, 112.6, 66.3, 47.1.

MS (EI, m/z): 208 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_3$ $[\text{M}]^+$: 208.0848; Found: 208.0855.

4-(4-chlorophenyl)morpholine (2k)

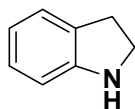


^1H NMR (300 MHz, CDCl_3): δ 7.23-7.20 (m, 2H), 6.84-6.81 (m, 2H), 3.86-3.83 (m, 4H), 3.13-3.09 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 149.8, 129.0, 124.8, 116.8, 66.7, 49.3.

MS (EI, m/z): 197 [M]⁺; HRMS (EI): Calcd. for C₁₀H₁₂CINO [M]⁺: 197.0607; Found:
197.0610.

Indoline (3a)

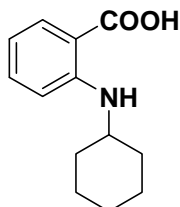


¹H NMR (300 MHz, CDCl₃): δ 7.13-7.10 (m, 1H), 7.04-6.98 (m, 1H), 6.73-6.70 (m, 1H), 6.68-6.62 (m, 1H), 3.64 (s, br, 1H), 3.52 (t, *J*=8.1 Hz, 2H), 3.01 (t, *J*=8.1 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 151.4, 129.3, 127.1, 124.5, 118.6, 109.4, 47.2, 29.7.

MS (EI, m/z): 119 [M]⁺; HRMS (EI): Calcd. for C₈H₉N [M]⁺: 119.0735; Found:
119.0730.

2-(cyclohexylamino)benzoic acid (3b)

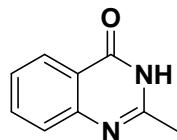


¹H NMR (300 MHz, CDCl₃): δ 7.99-7.96 (m, 1H), 7.38-7.33 (m, 1H), 6.73-6.70 (m, 1H), 6.58-6.53 (m, 1H), 3.43-3.42 (d, br, 1H), 2.07-2.02 (m, 3H), 1.80-1.77 (m, 2H), 1.43 (s, 1H), 1.40-1.28 (m, 5H).

¹³C NMR (100 MHz, CDCl₃): δ 174.8, 151.0, 135.4, 132.8, 114.0, 111.8, 108.3, 50.6, 32.8, 25.8, 24.7.

MS (EI, m/z): 219 [M]⁺; HRMS (EI): Calcd. for C₁₃H₁₇NO₂ [M]⁺: 219.1259; Found:
219.1264.

2-methylquinazolin-4(3H)-one (3c)



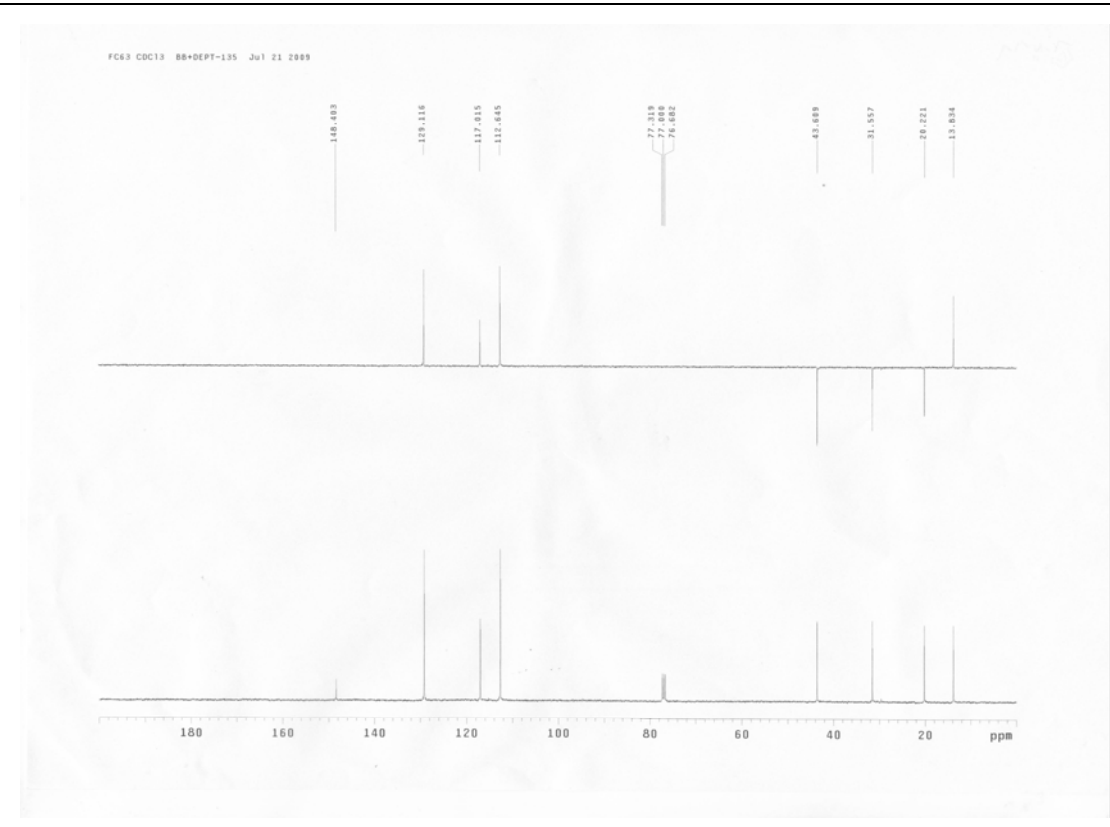
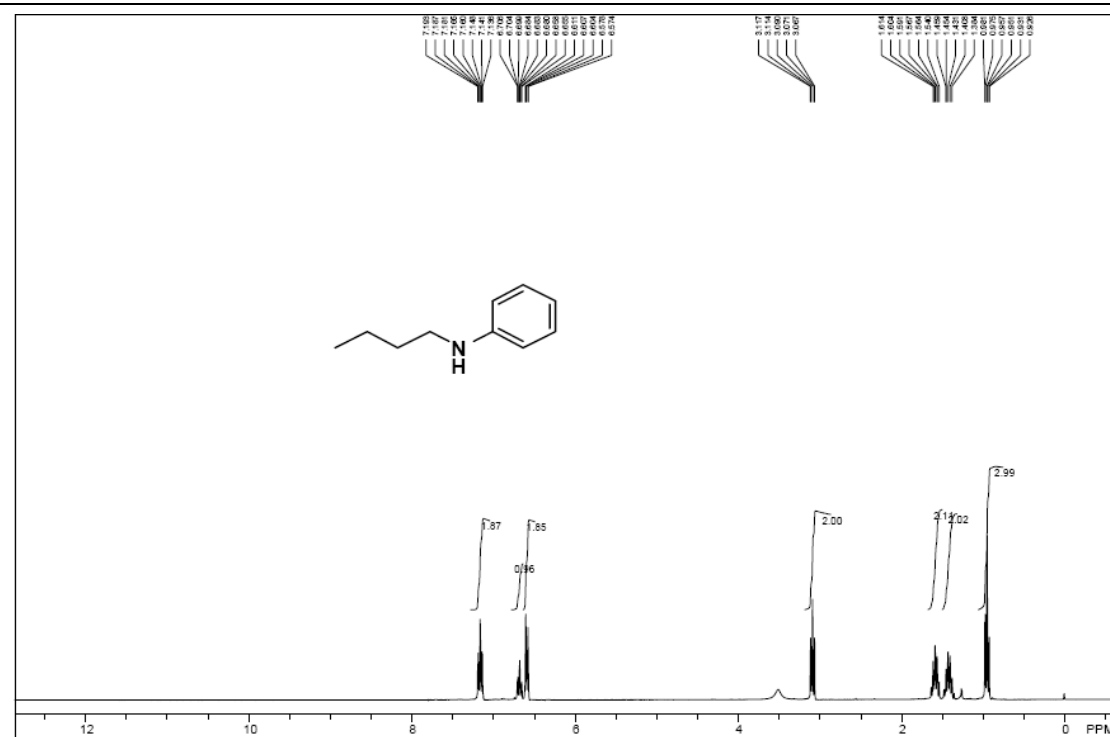
^1H NMR (300 MHz, DMSO- d_6): δ 12.2 (s, br, 1H), 8.07(d, 1H, $J = 7.8$ Hz), 7.76 (t, 1H, $J = 7.2$ Hz), 7.56 (d, 1H, $J = 7.8$ Hz), 7.44 (t, 1H, $J = 7.2$ Hz), 2.35 (s, 3H).

^{13}C NMR (100 MHz, DMSO- d_6): δ 161.7, 154.3, 149.0, 134.2, 126.6, 125.8, 125.7, 120.6, 21.4.

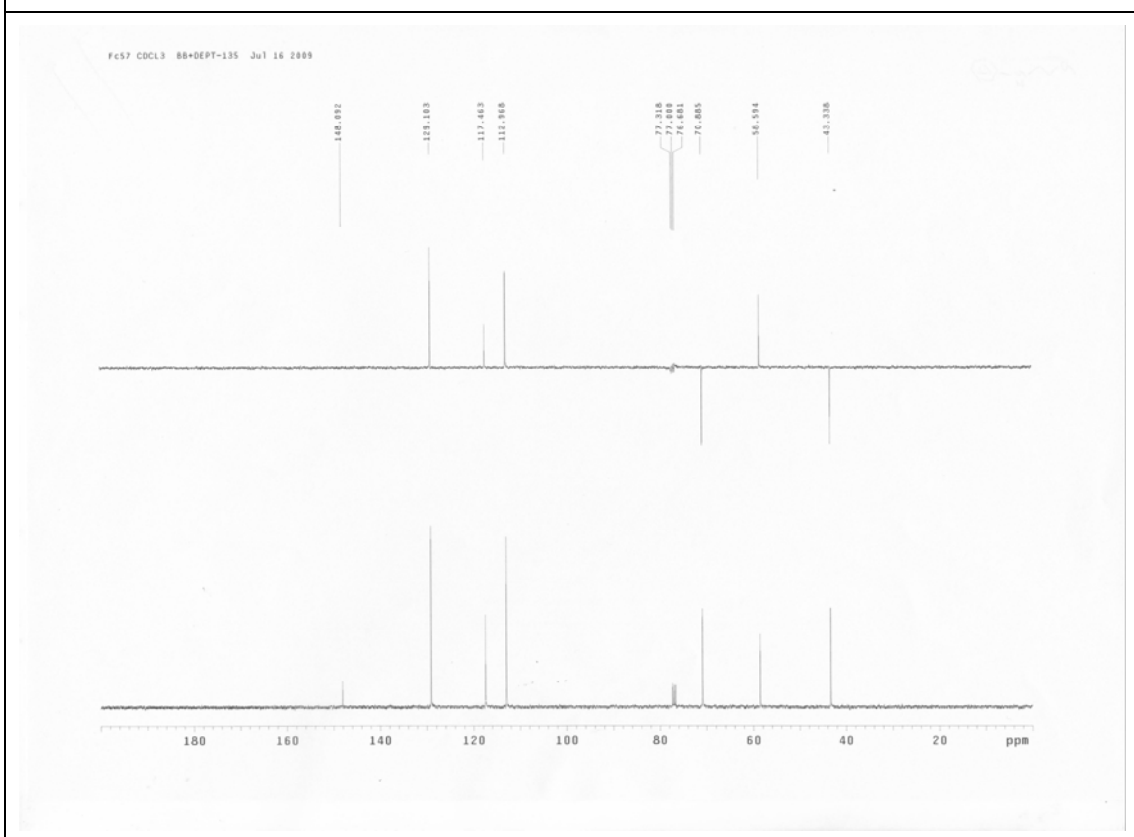
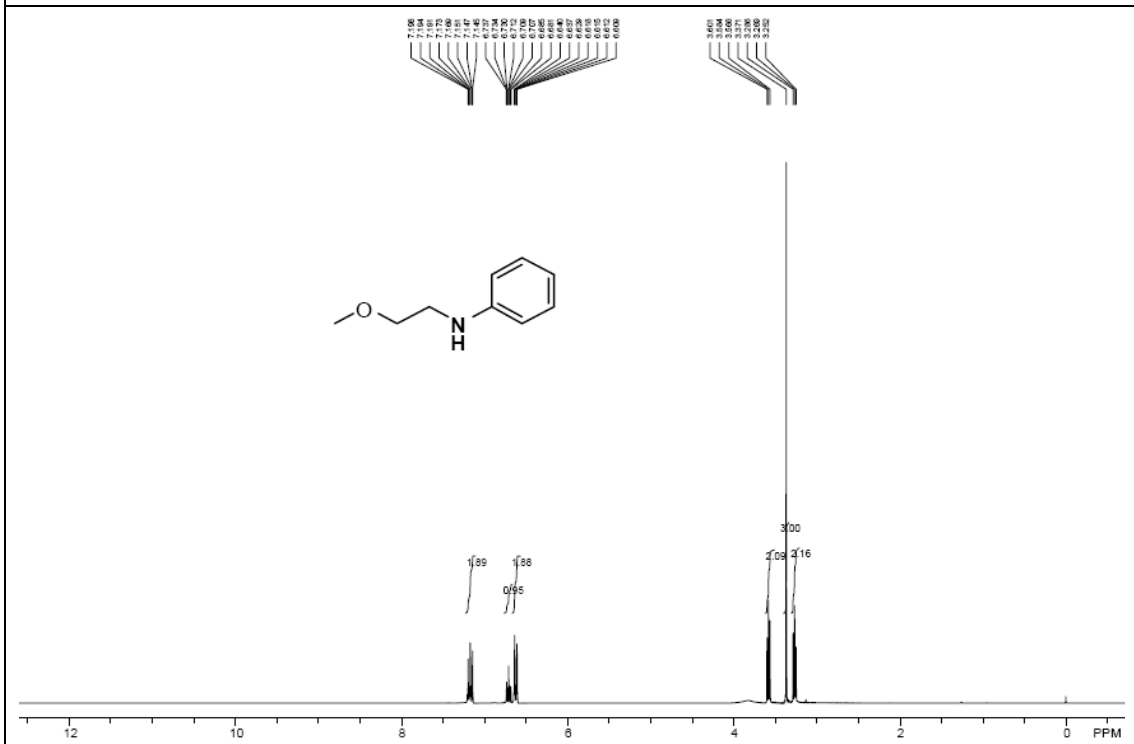
MS (EI, m/z): 160 $[\text{M}]^+$; HRMS (EI): Calcd. for $\text{C}_9\text{H}_8\text{N}_2\text{O}$ $[\text{M}]^+$: 160.0637; Found: 160.0641.

Copies of ^1H NMR and ^{13}C NMR of Compounds

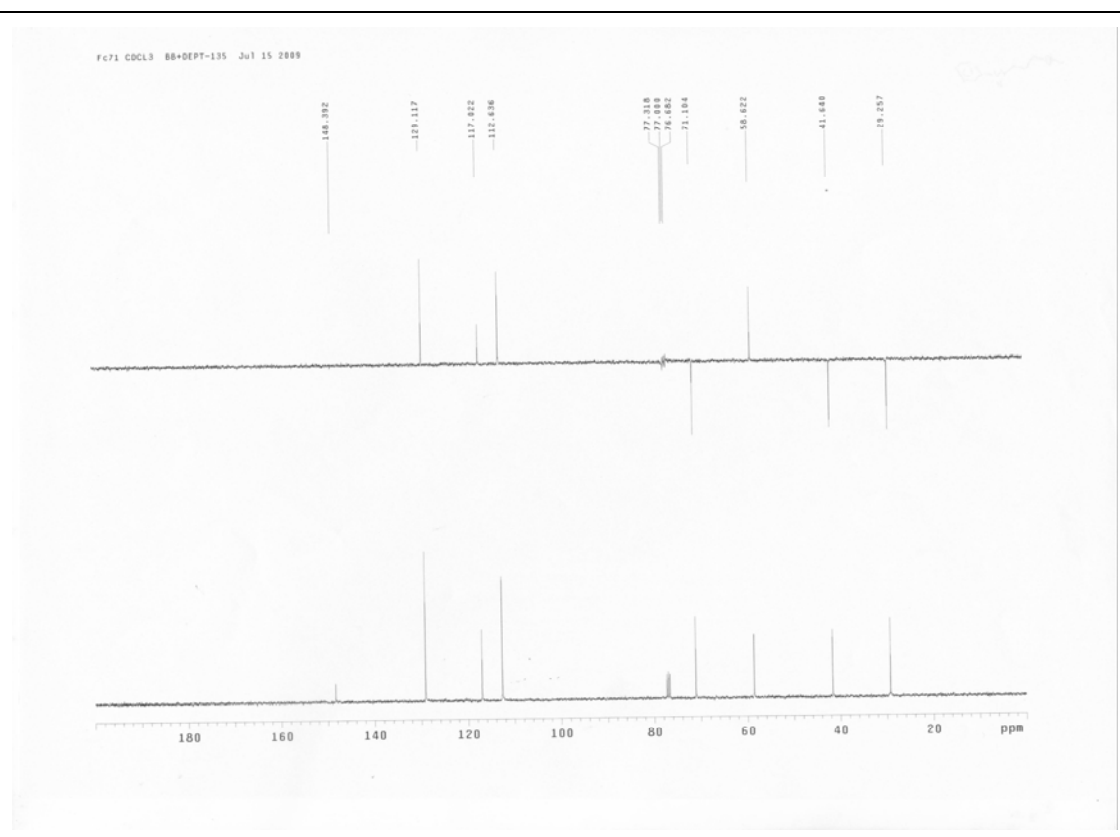
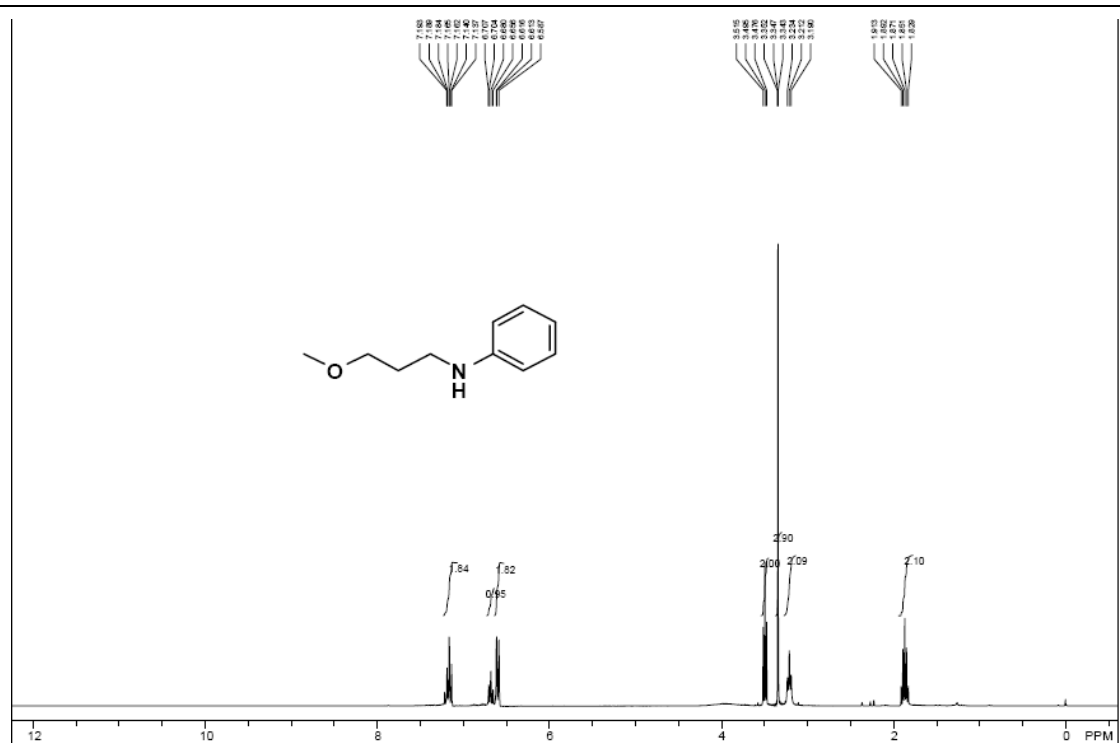
N-butylbenzenamine (1a)



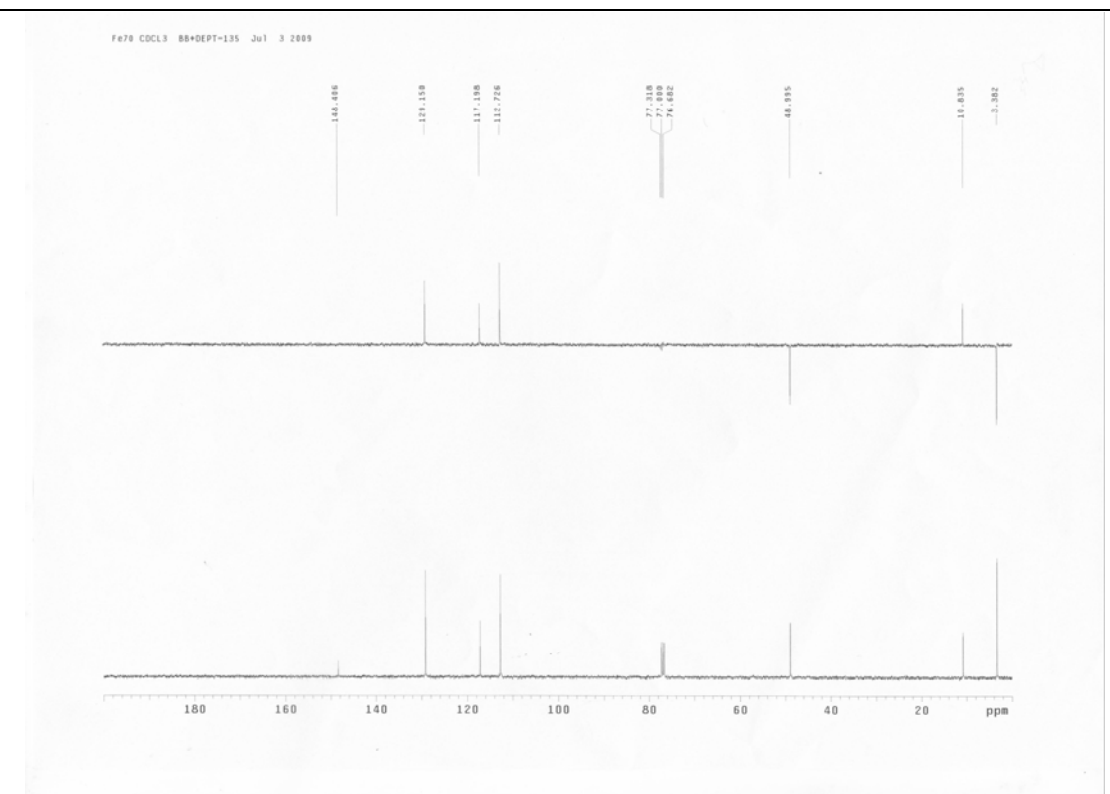
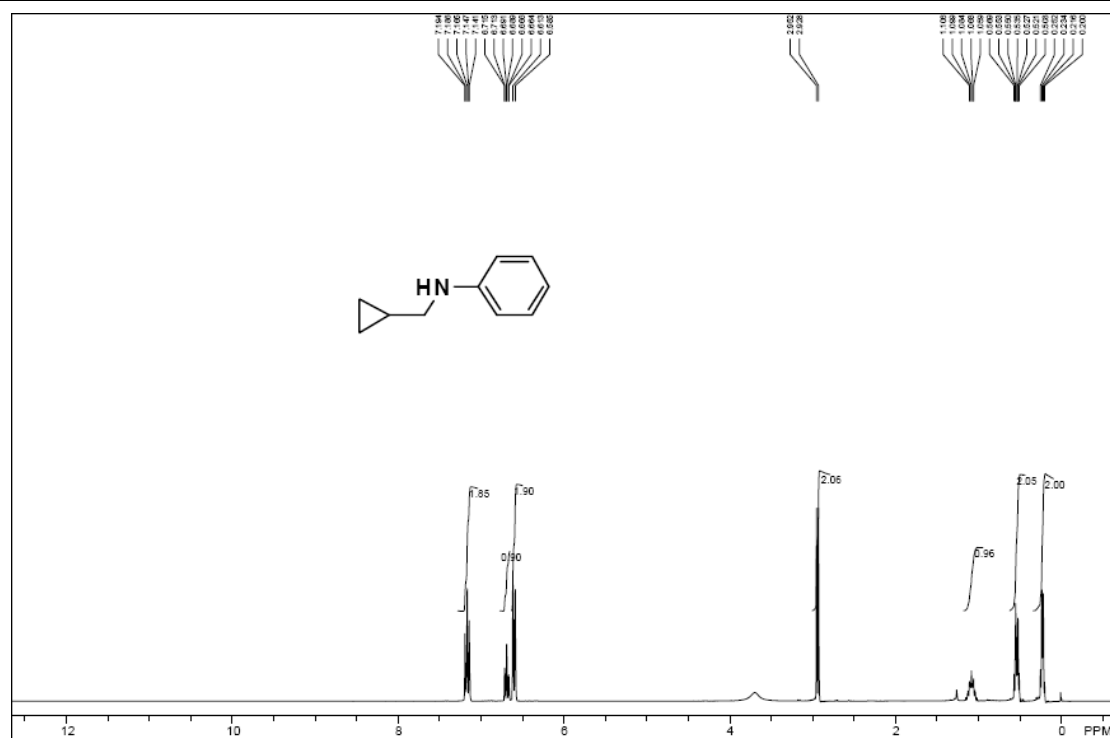
N-(2-methoxyethyl)benzenamine (1b)



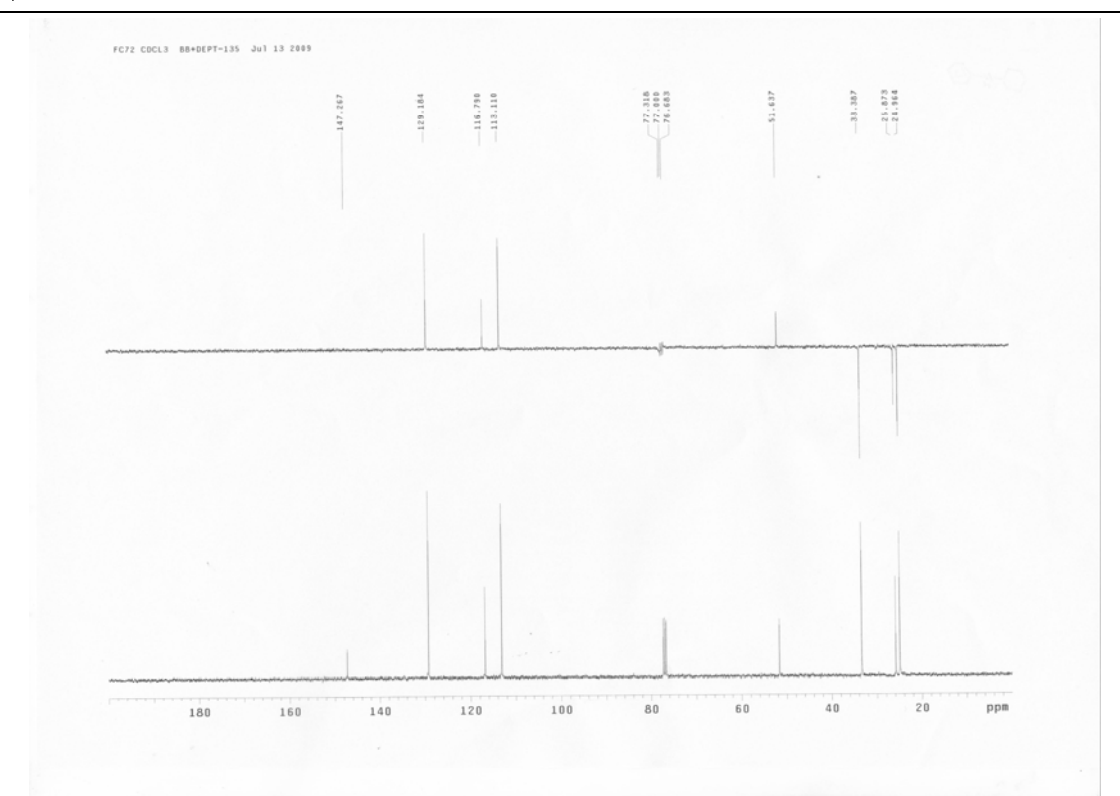
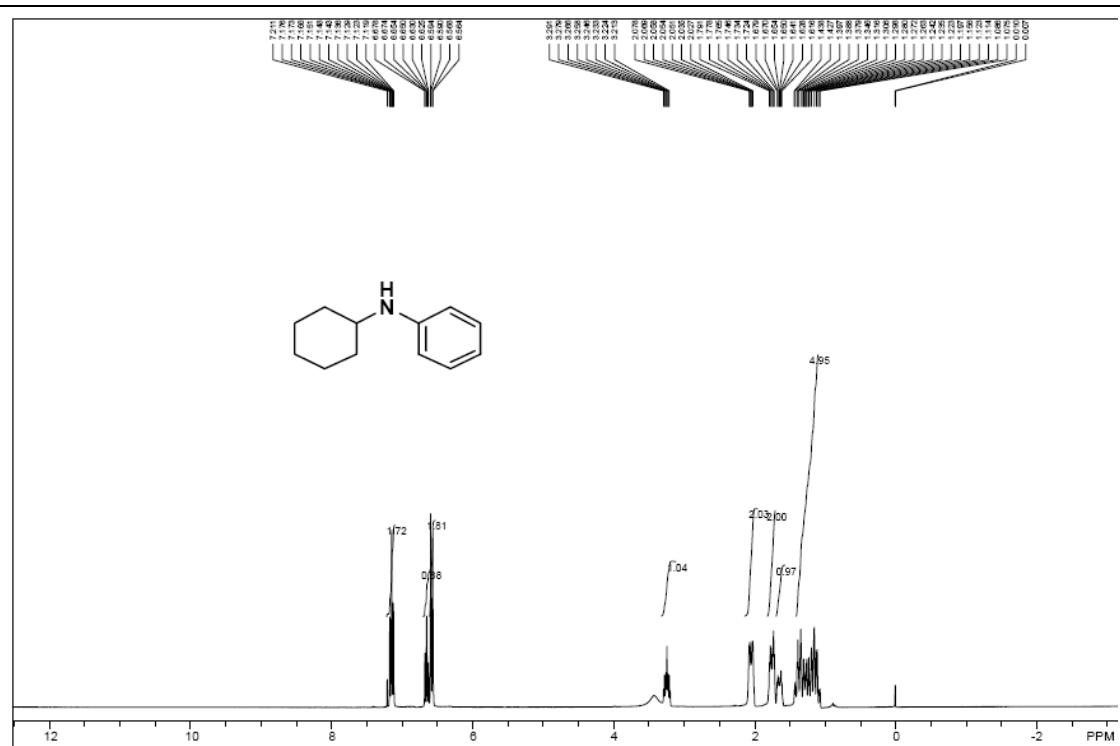
N-(3-methoxypropyl)benzenamine (1c)



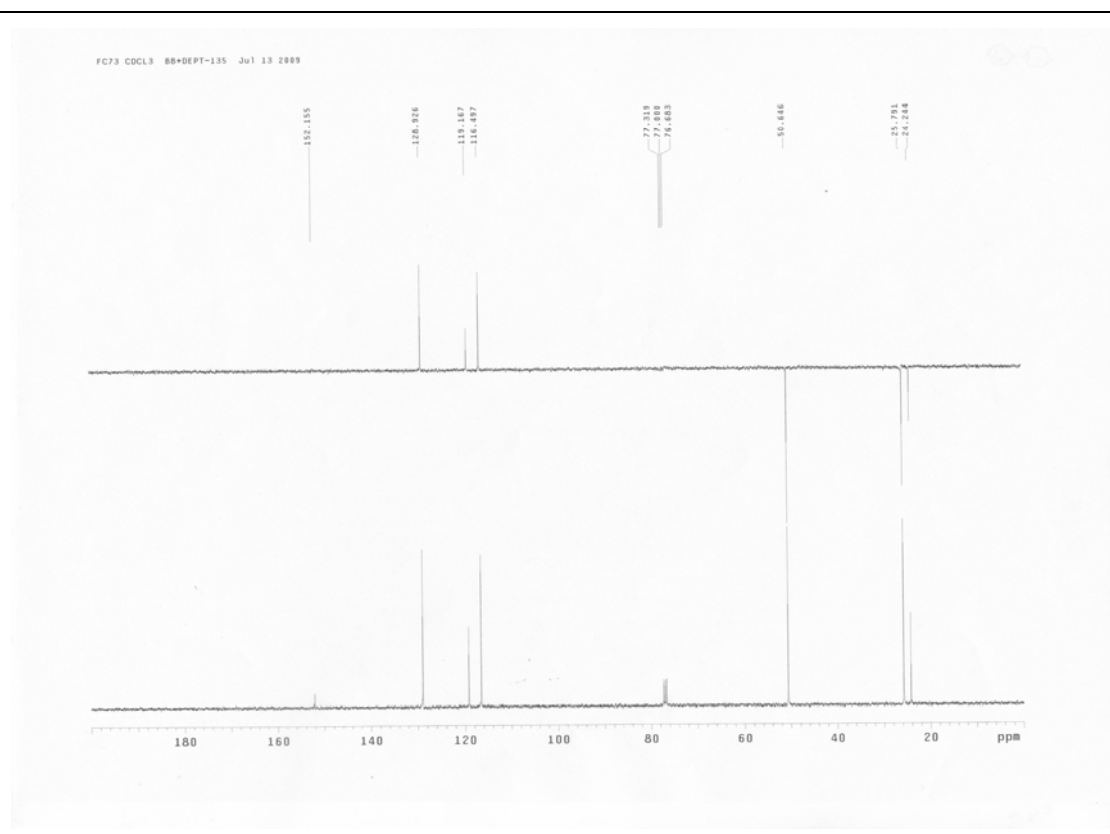
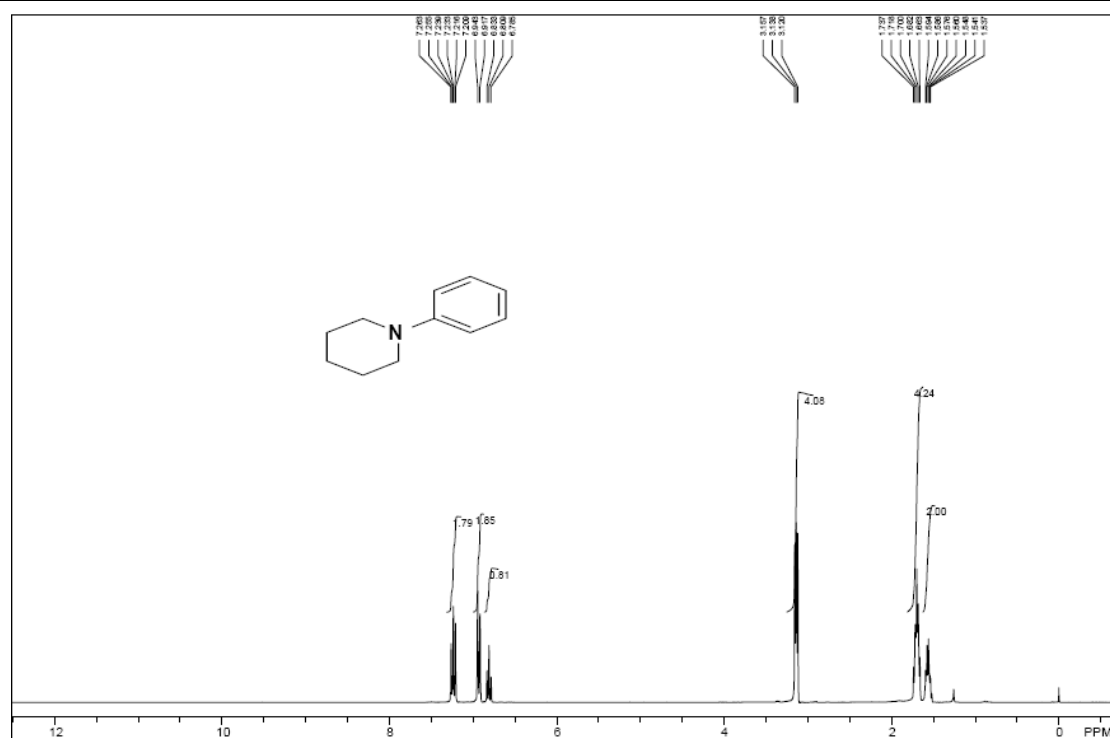
N-(cyclopropylmethyl)benzenamine (1d)



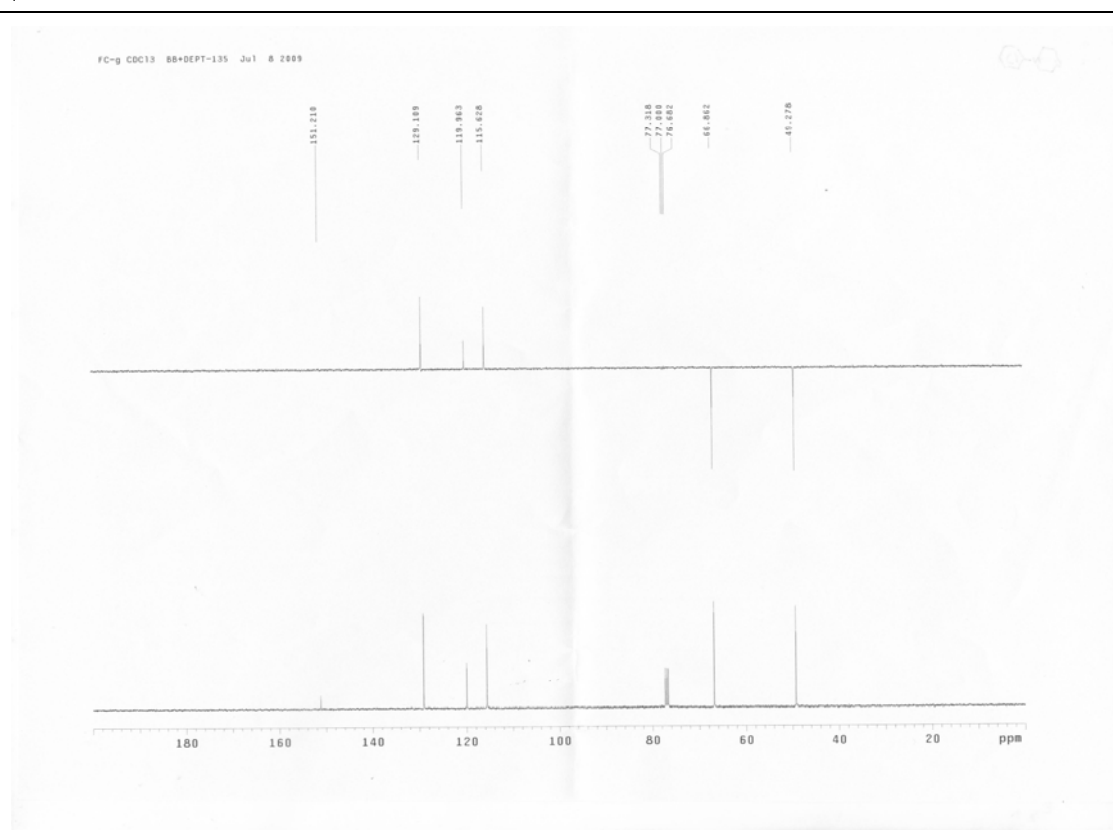
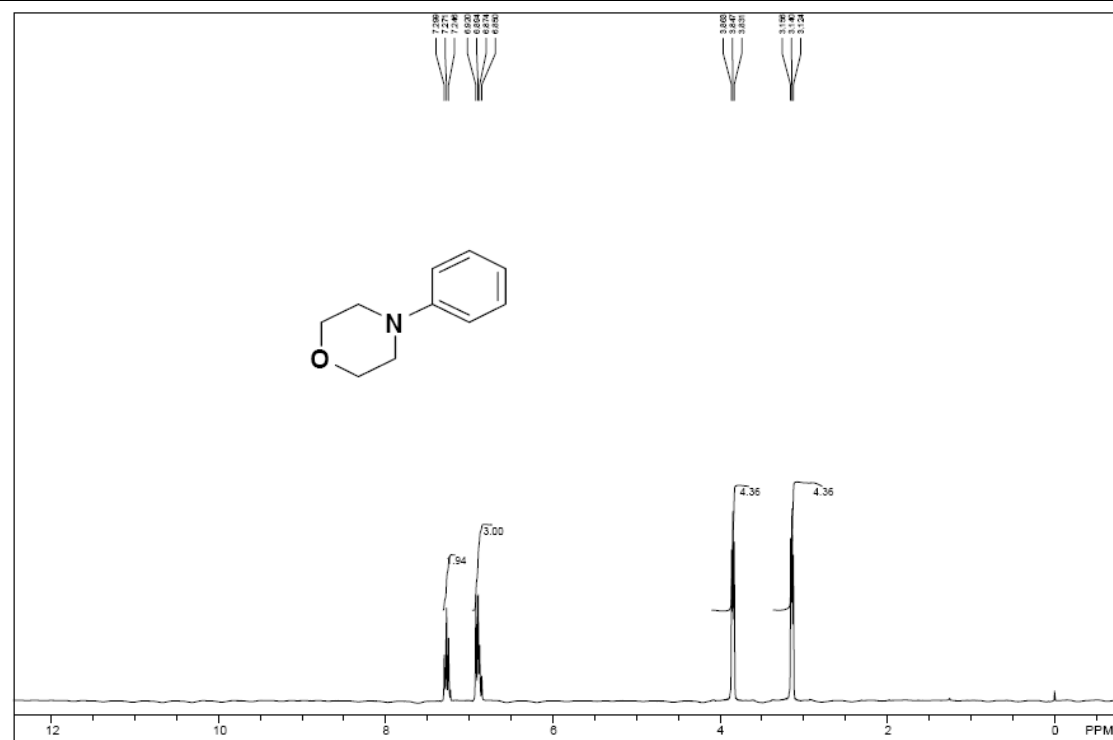
N-cyclohexylbenzenamine (1e)



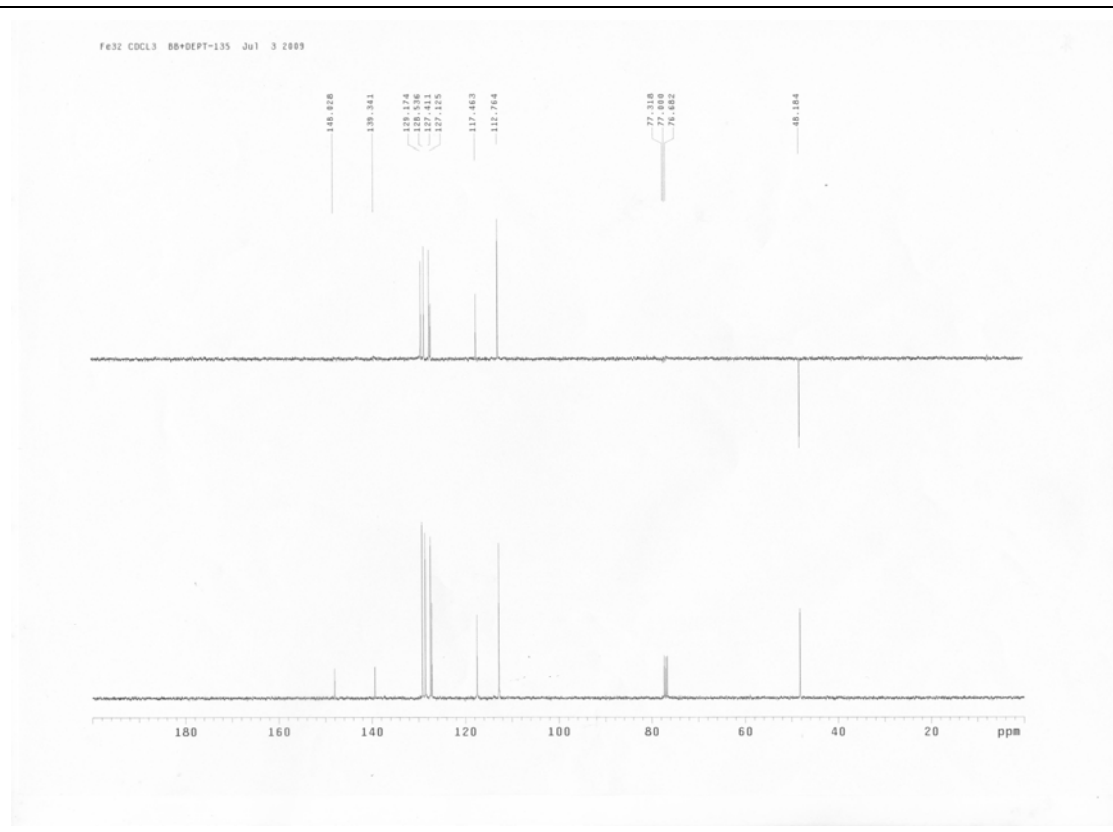
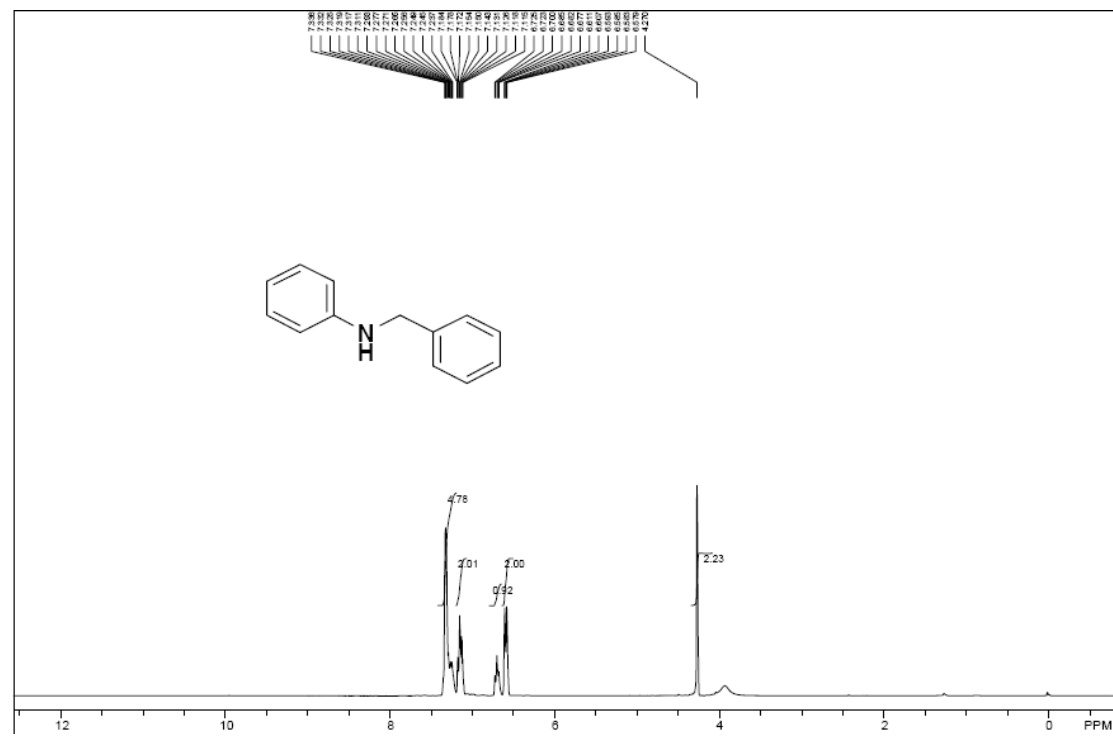
N-phenylpiperidine (1f)



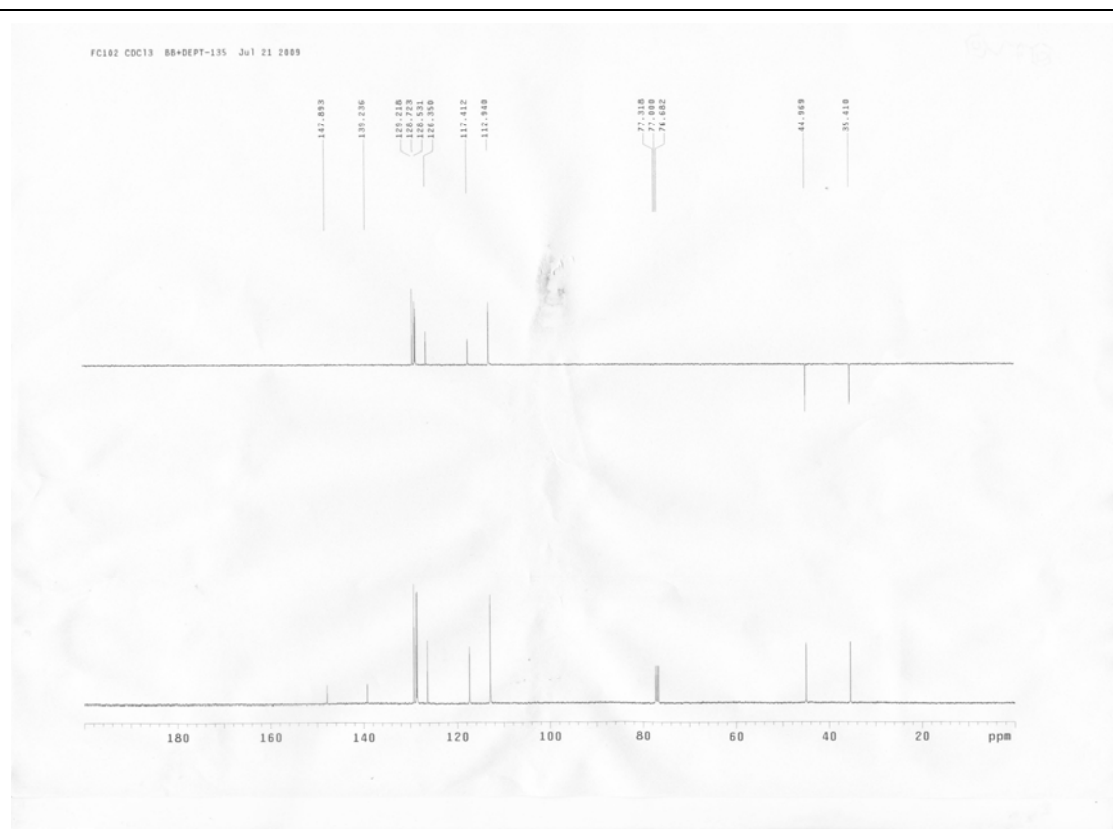
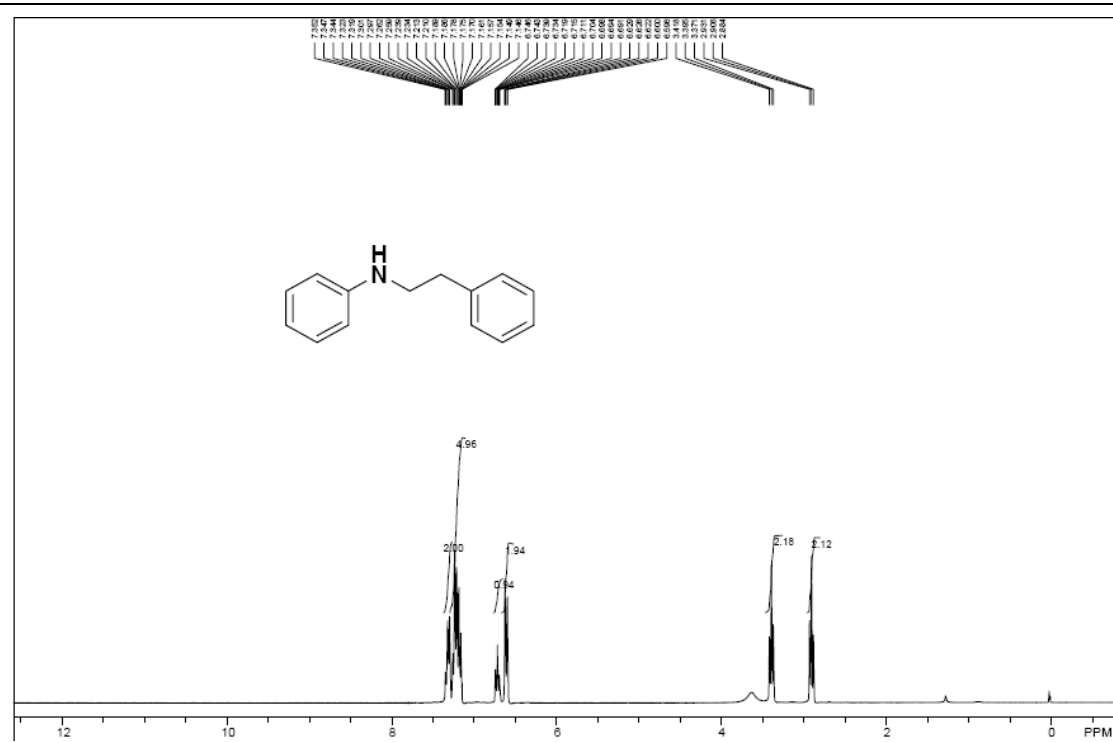
4-phenylmorpholine (1g)



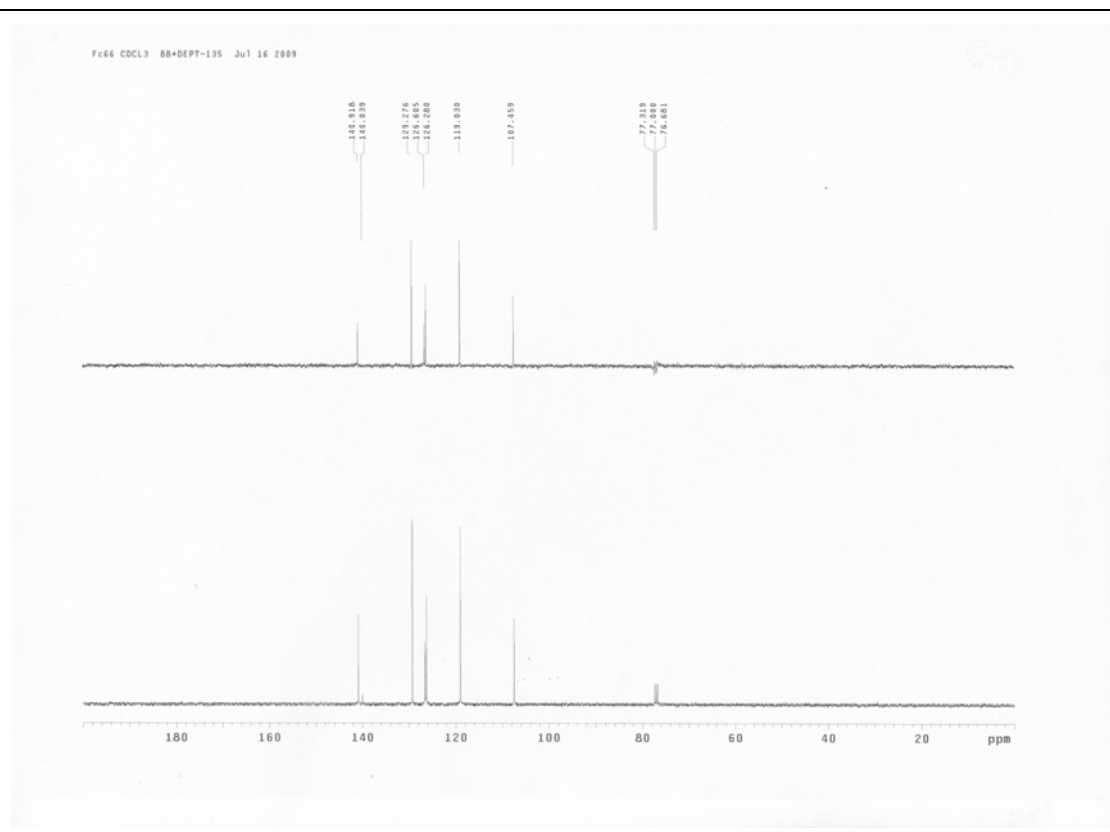
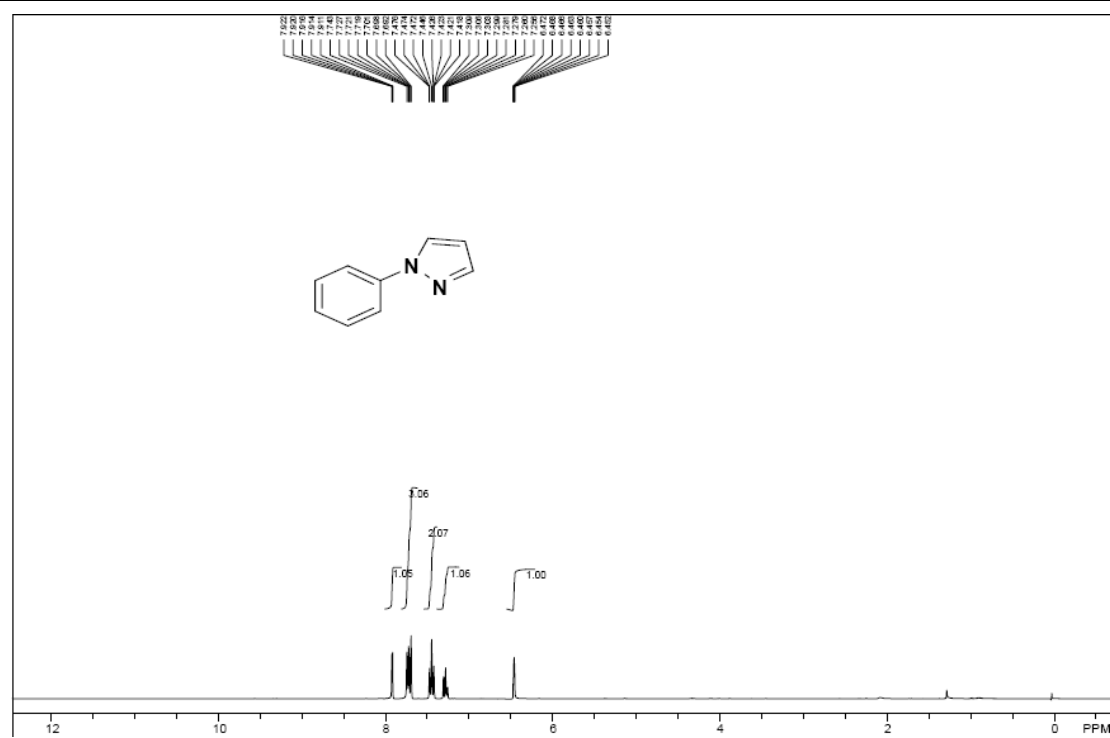
N-benzylbenzenamine (1h)



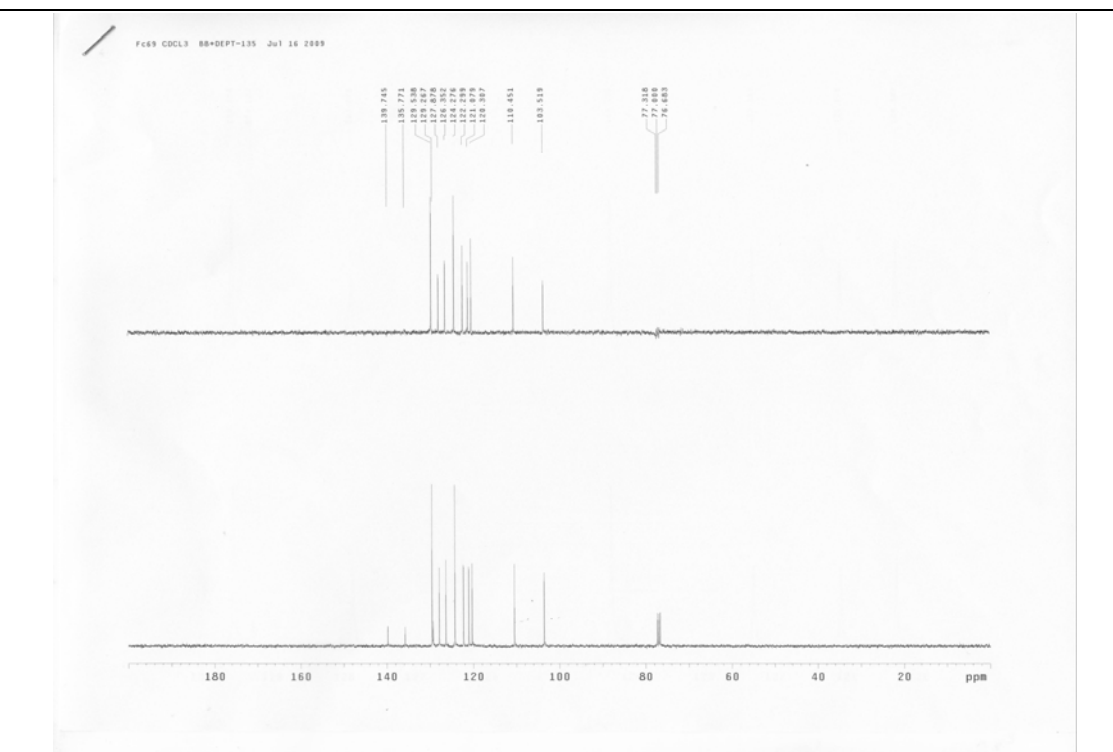
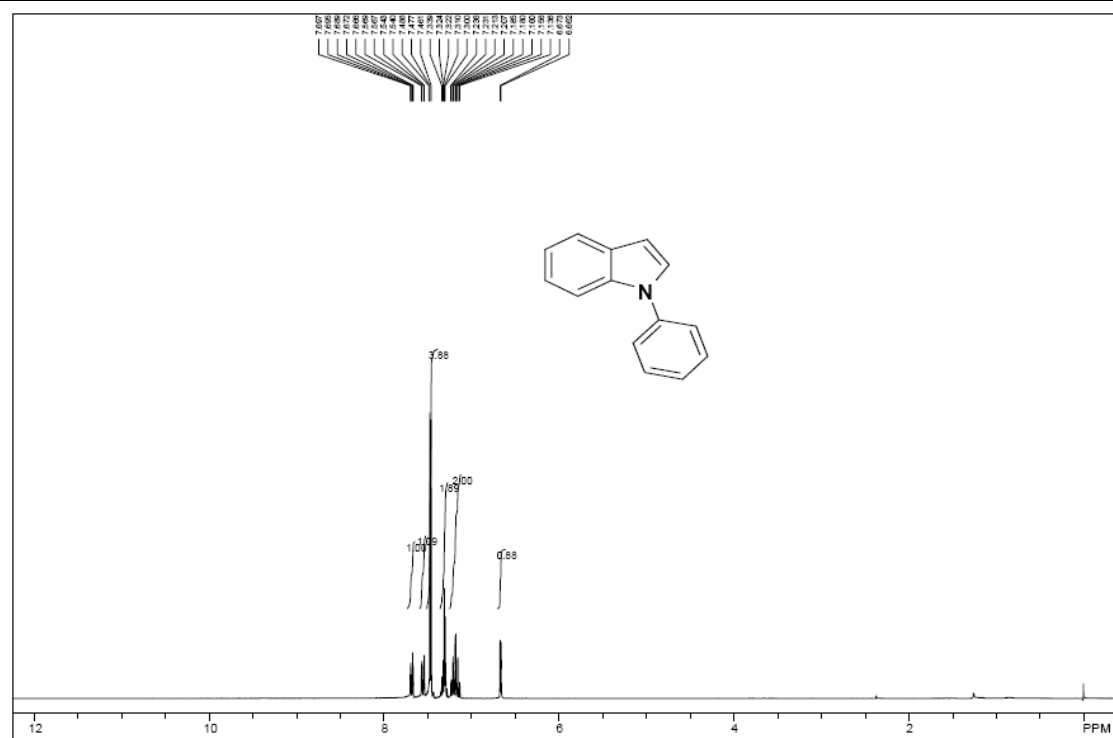
N-phenethylbenzenamine (1i)



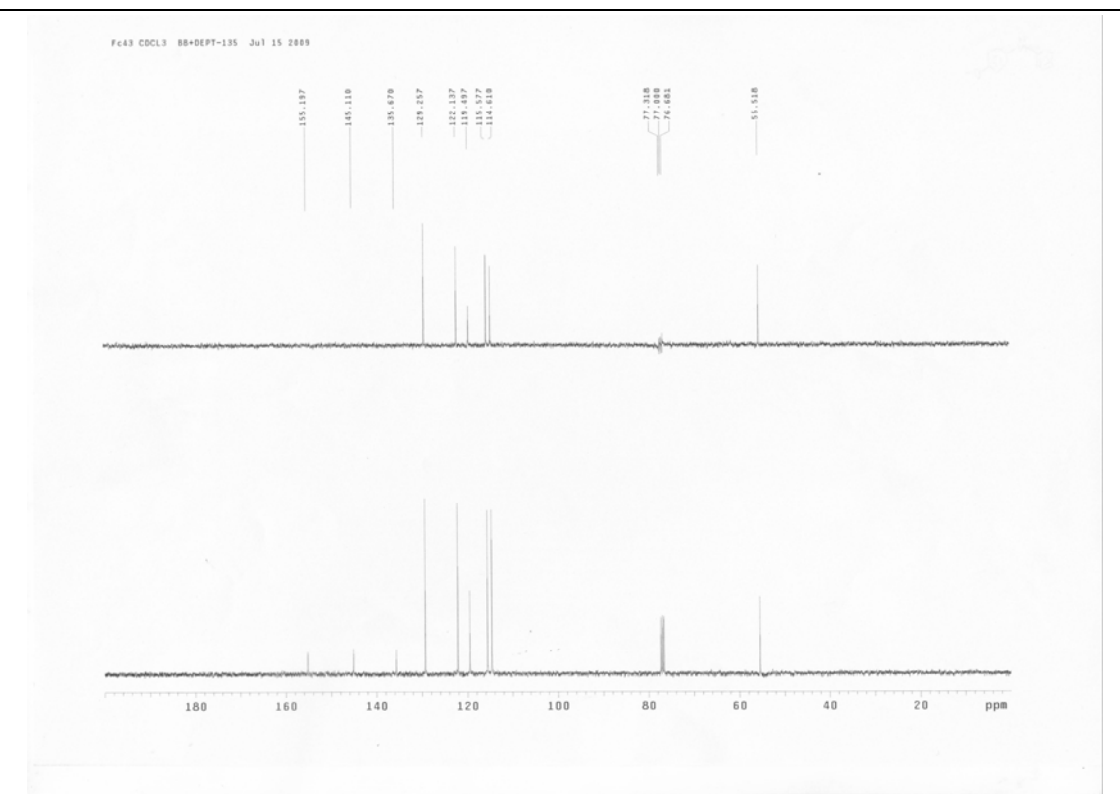
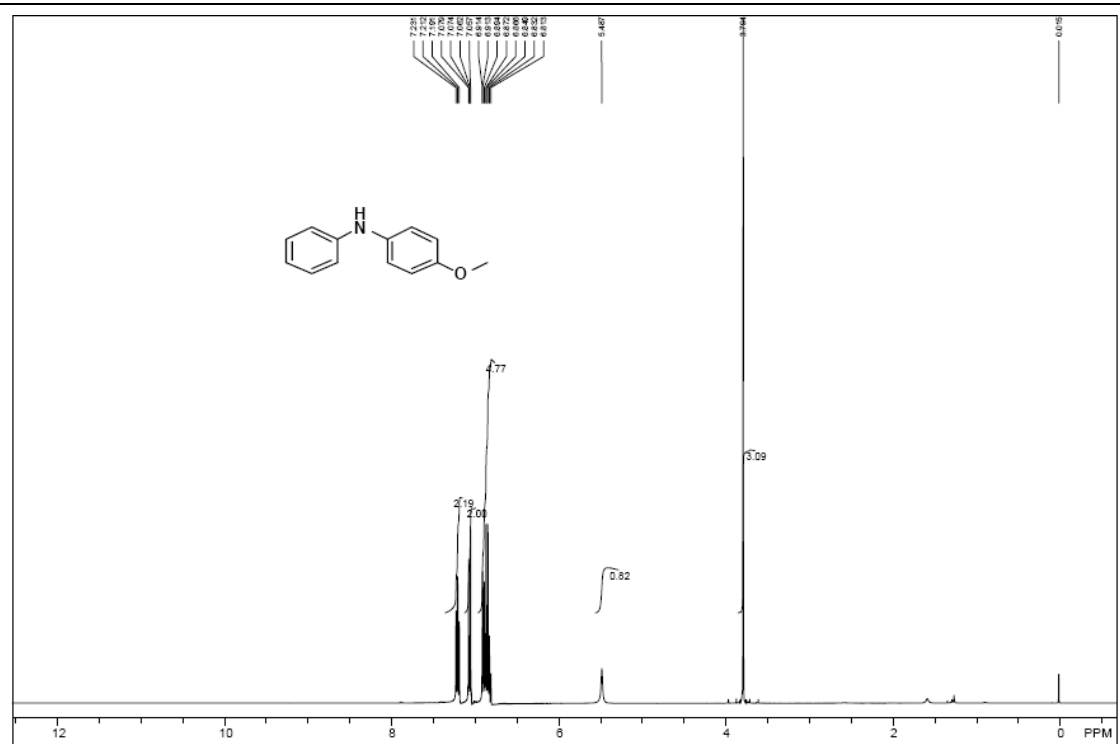
1-phenyl-1H-pyrazole (1j)



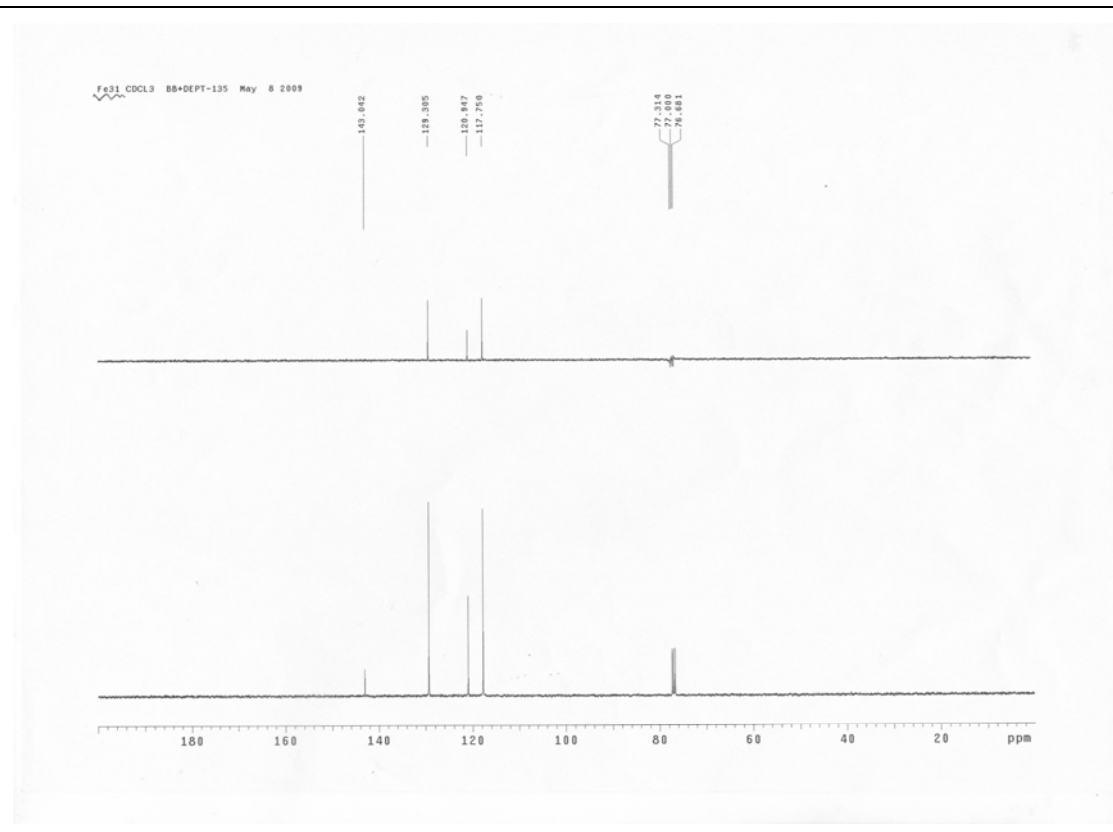
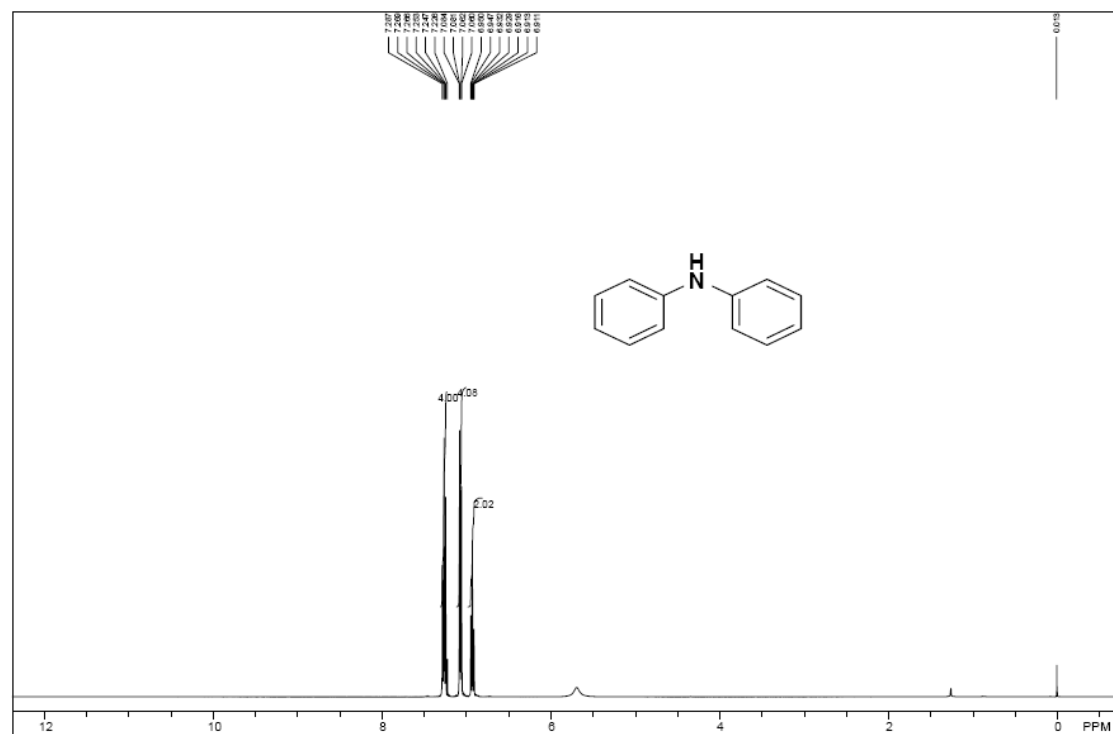
1-phenyl-1H-indole (1k)



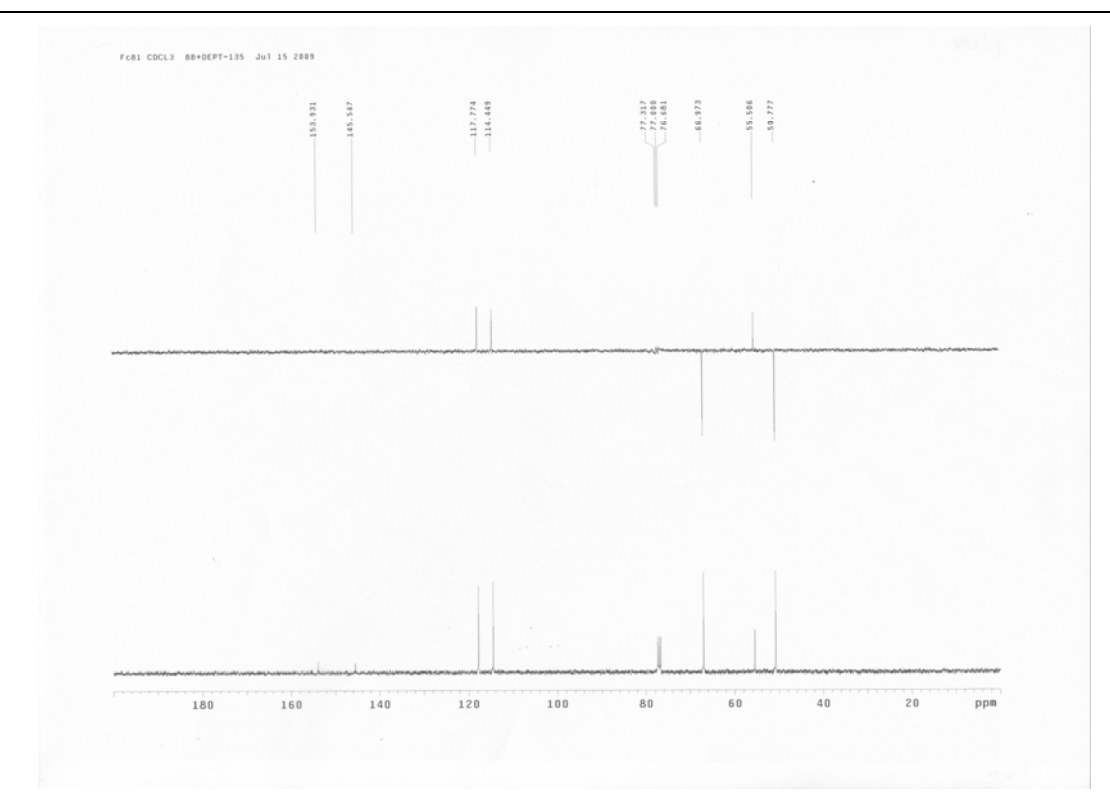
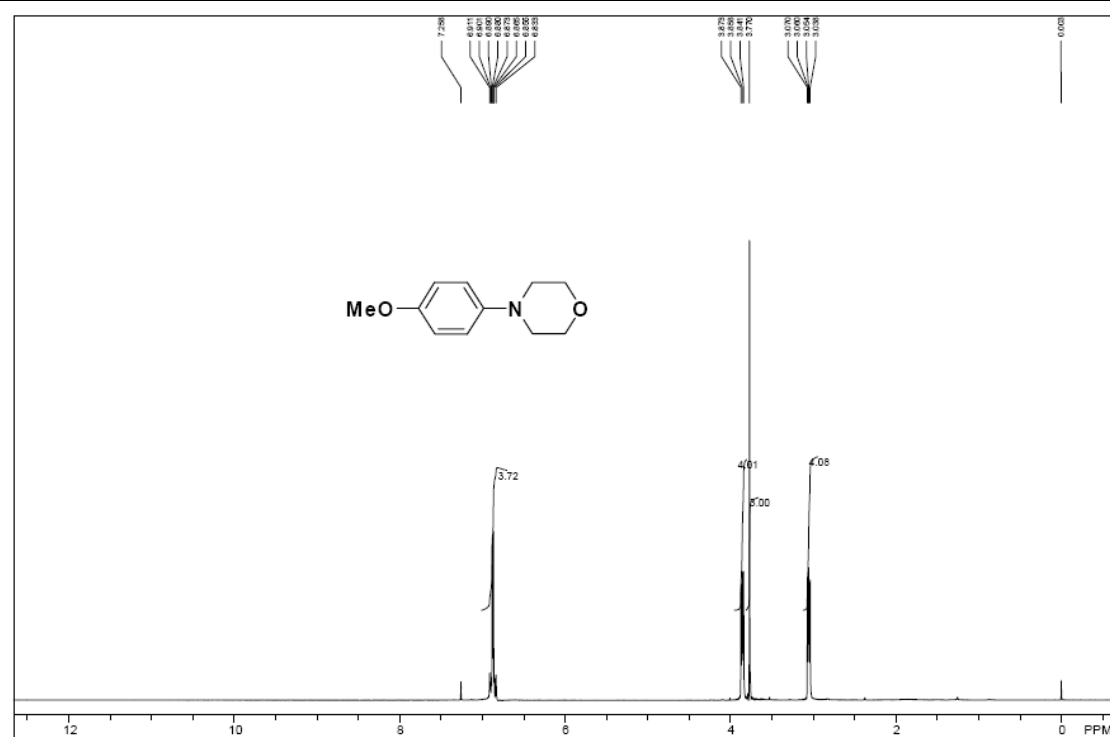
4-methoxy-N-phenylaniline (11)



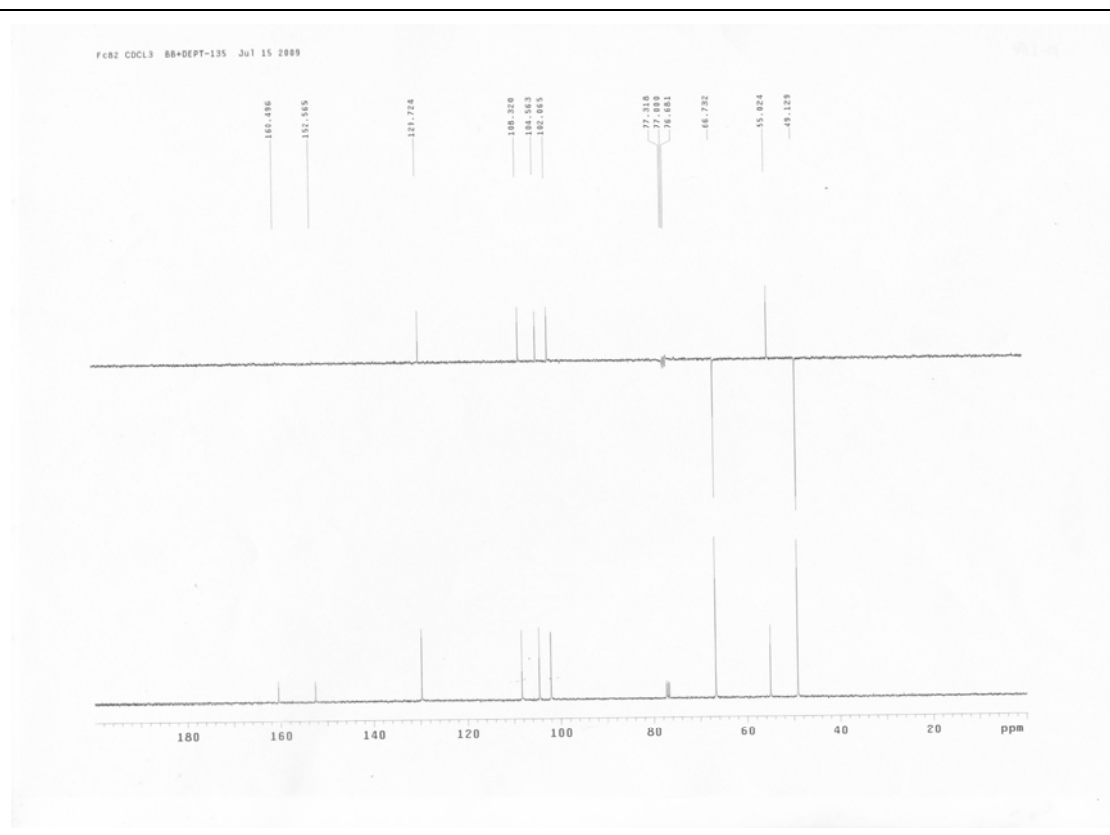
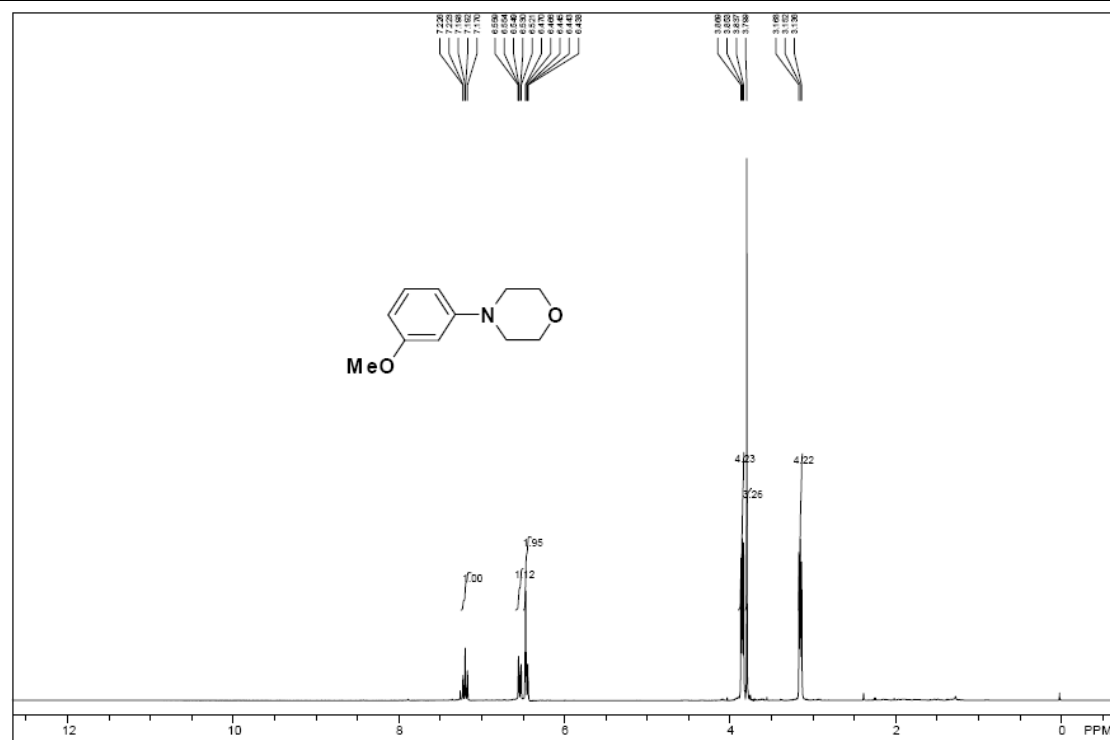
Diphenylamine (1m)



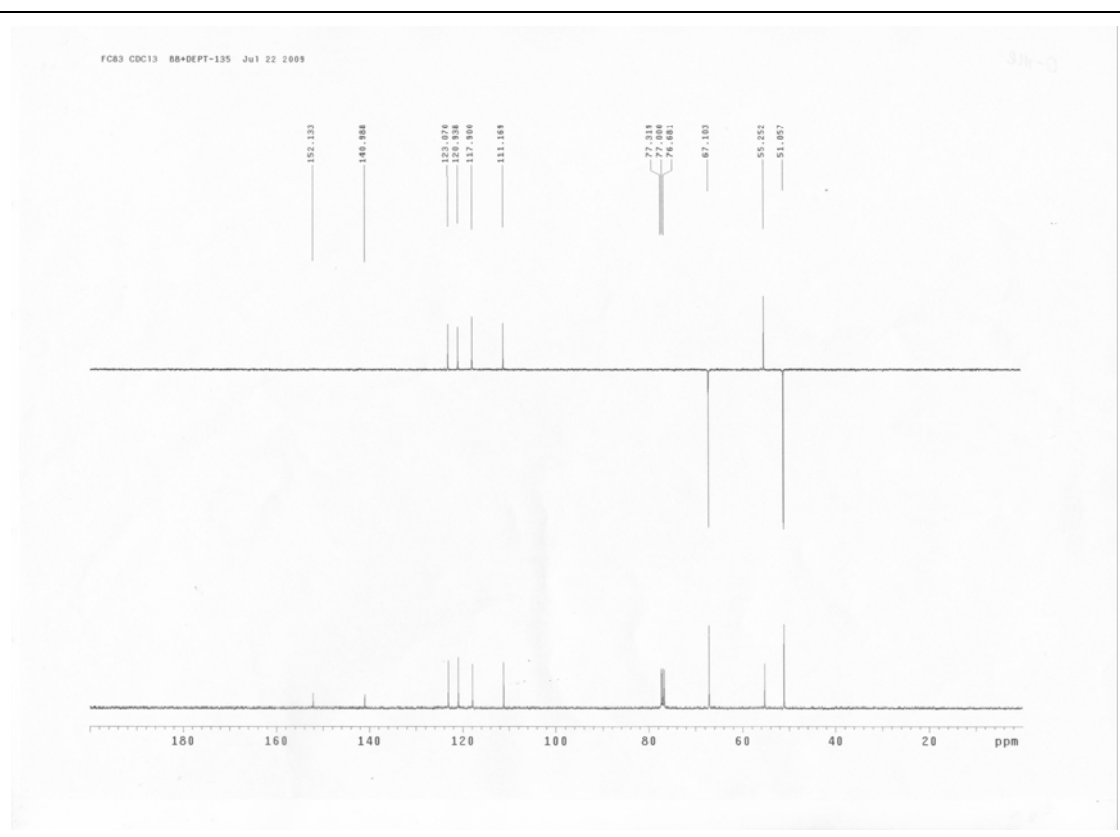
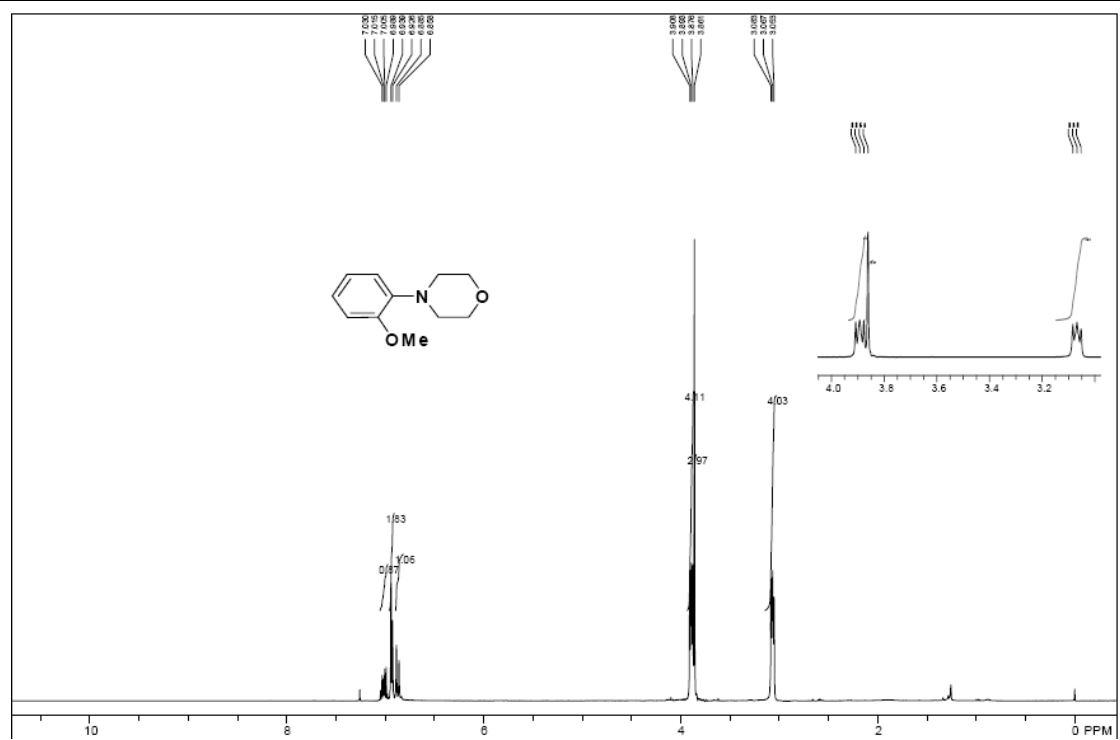
4-(4-methoxyphenyl)morpholine (2a)



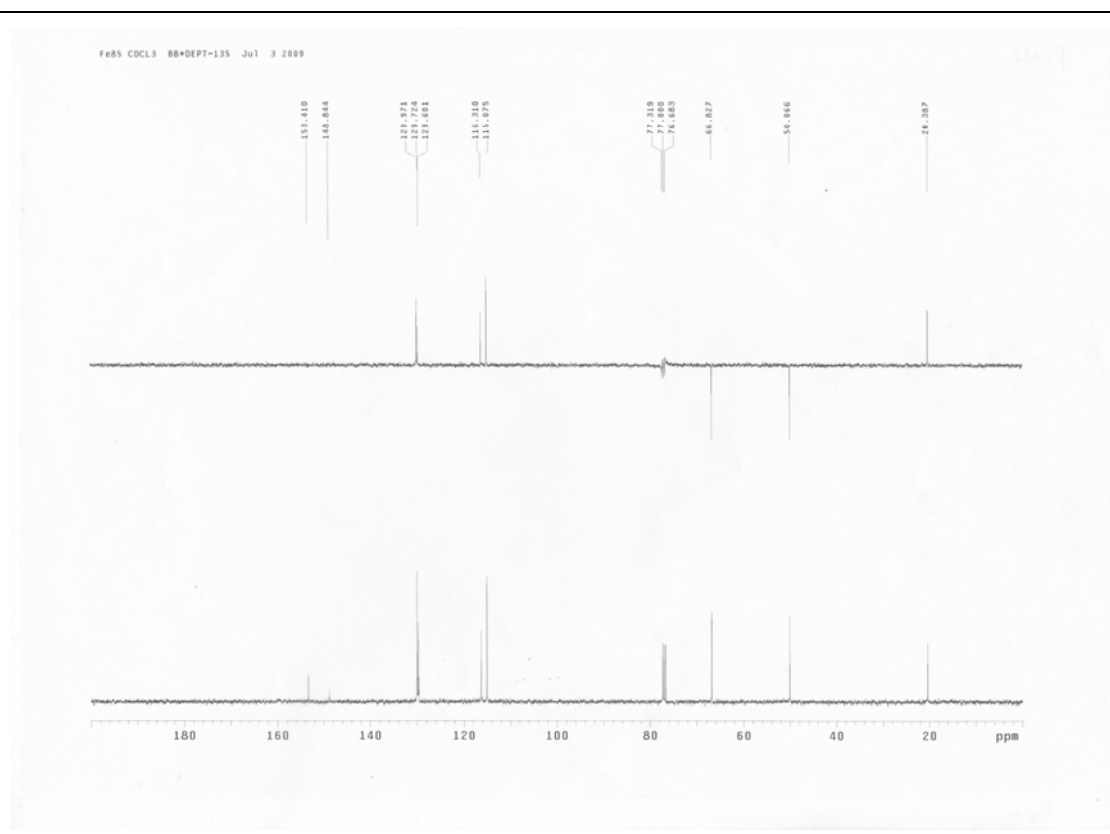
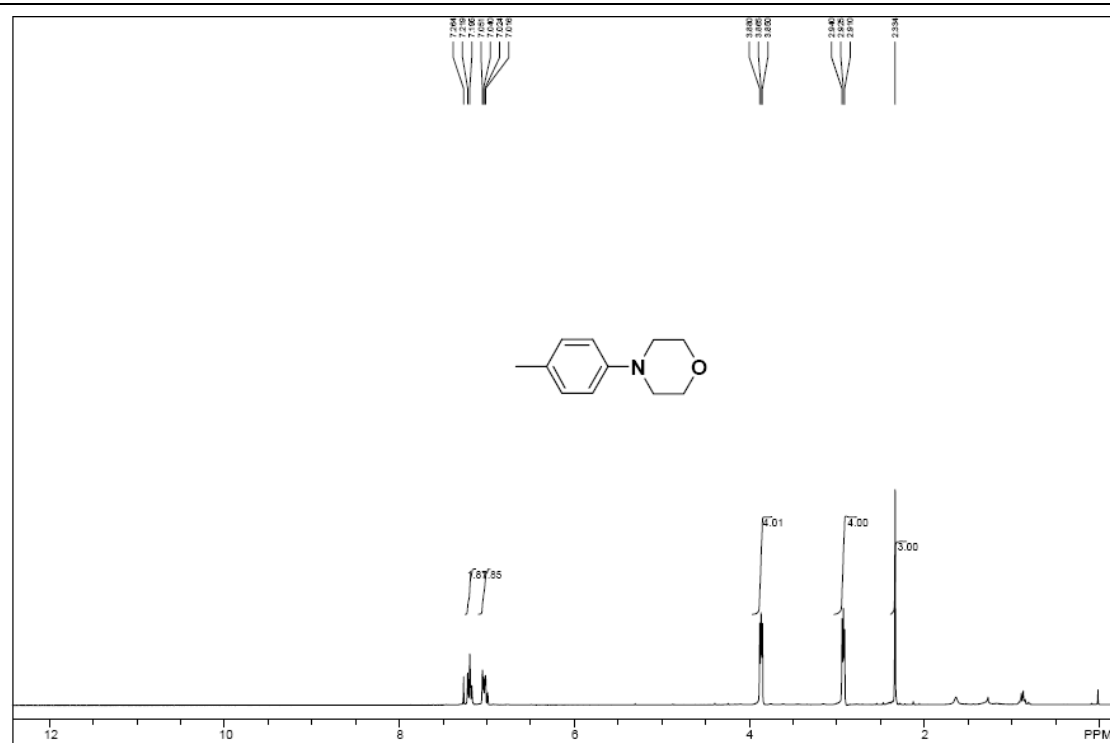
4-(3-methoxyphenyl)morpholine (2b)



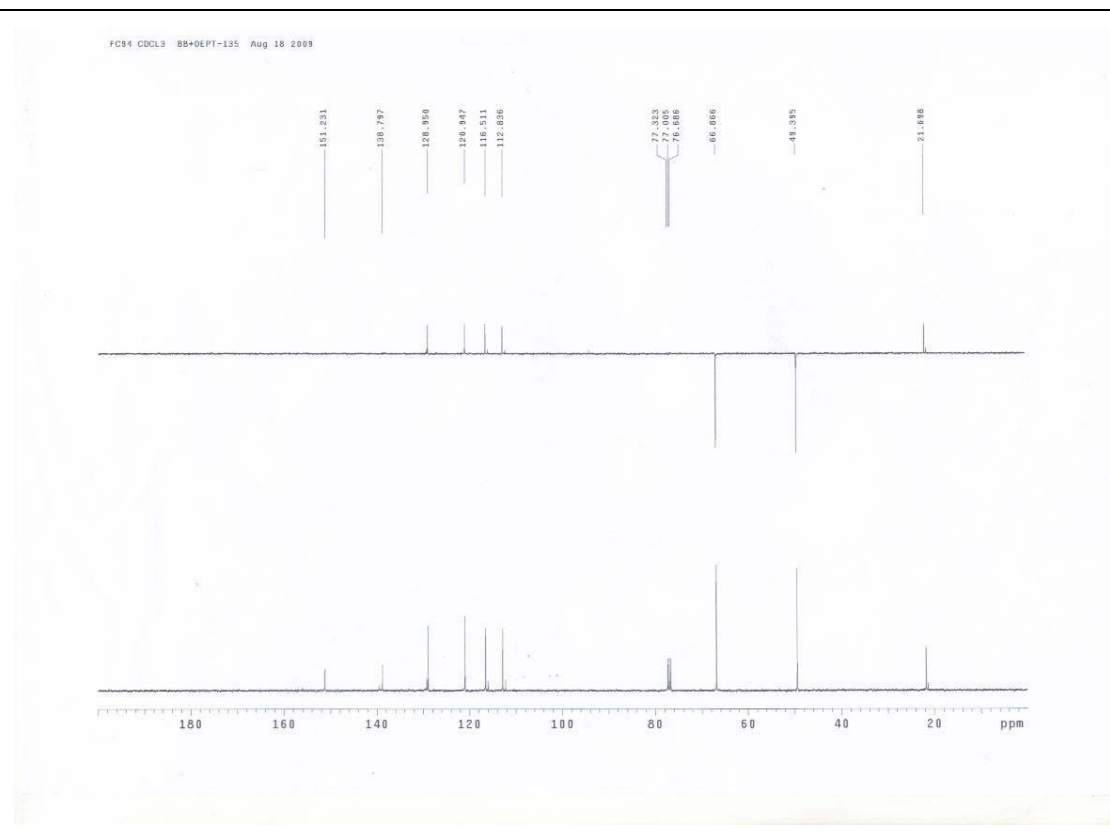
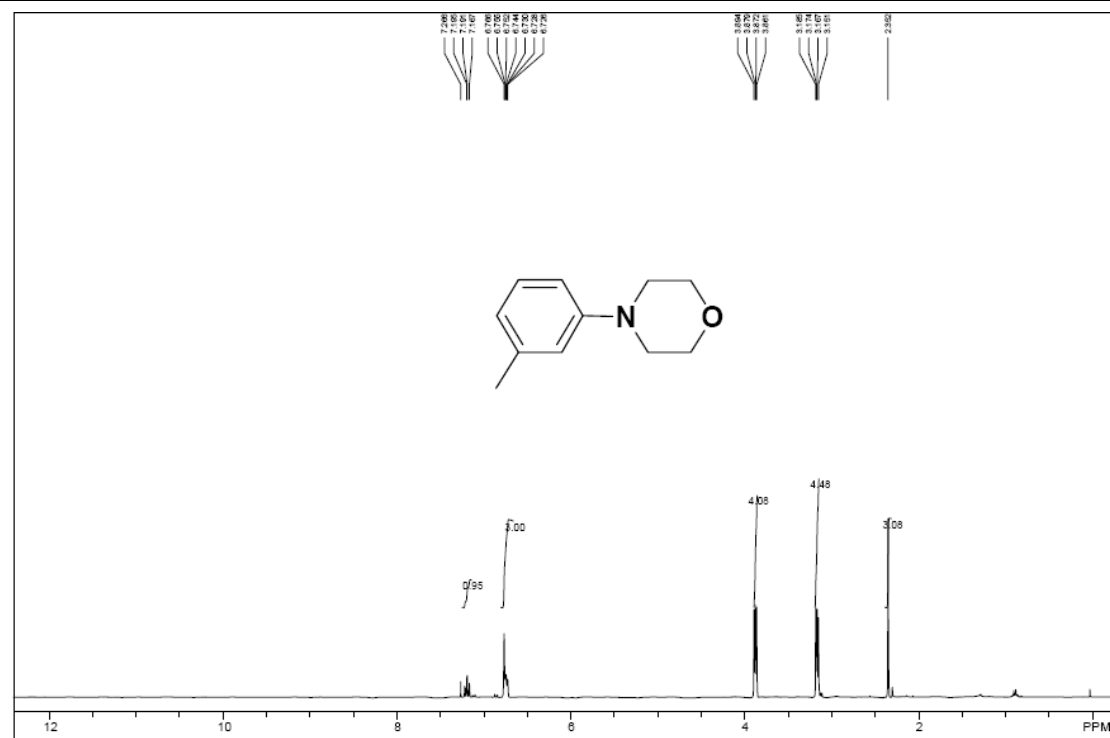
4-(2-methoxyphenyl)morpholine (2c)



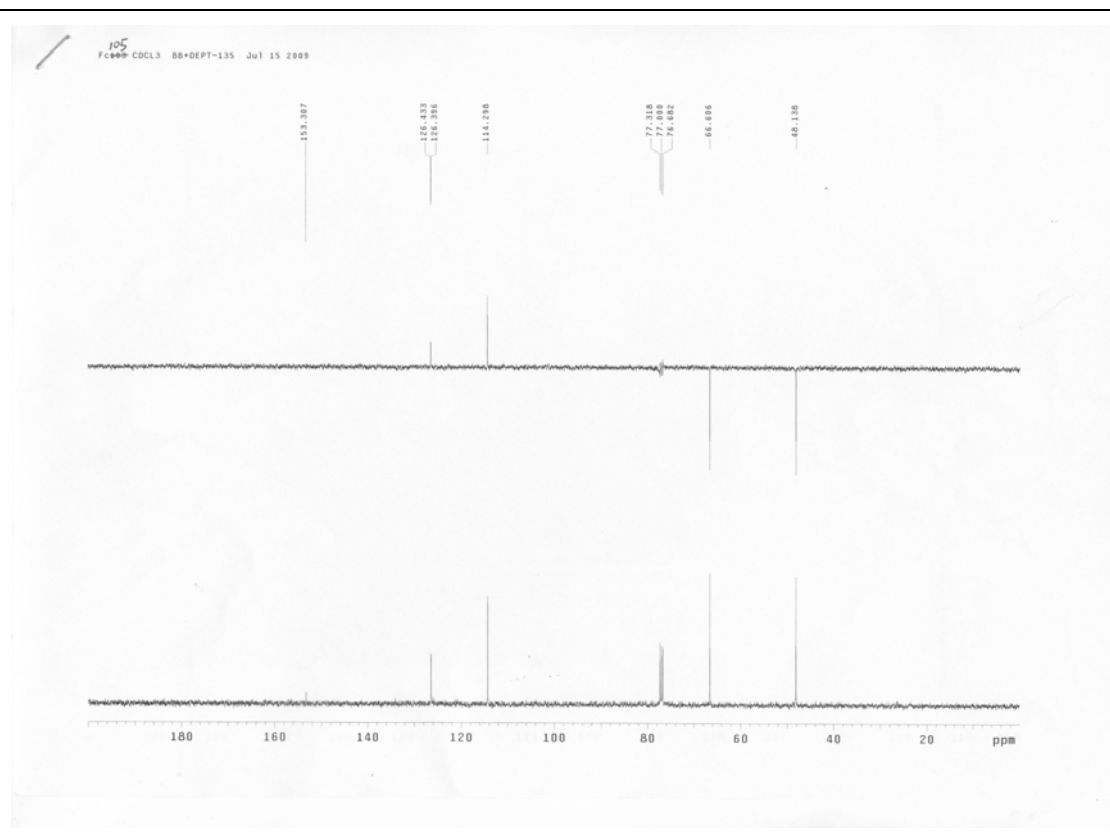
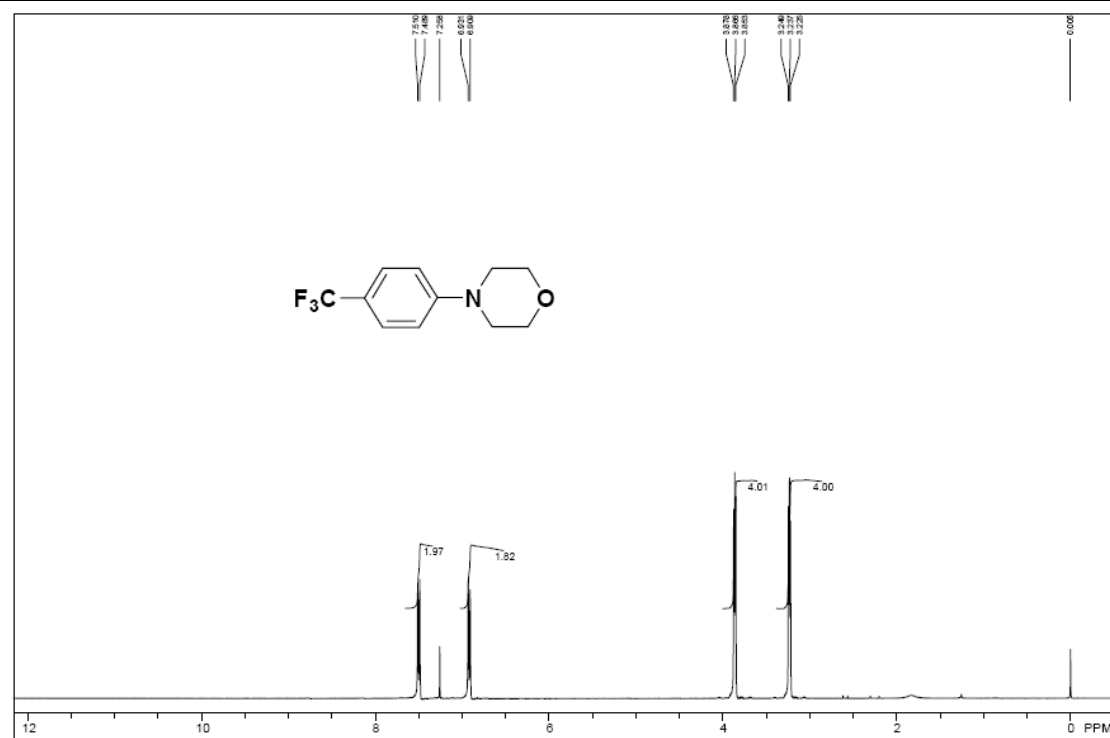
4-p-tolymorpholine (2d)



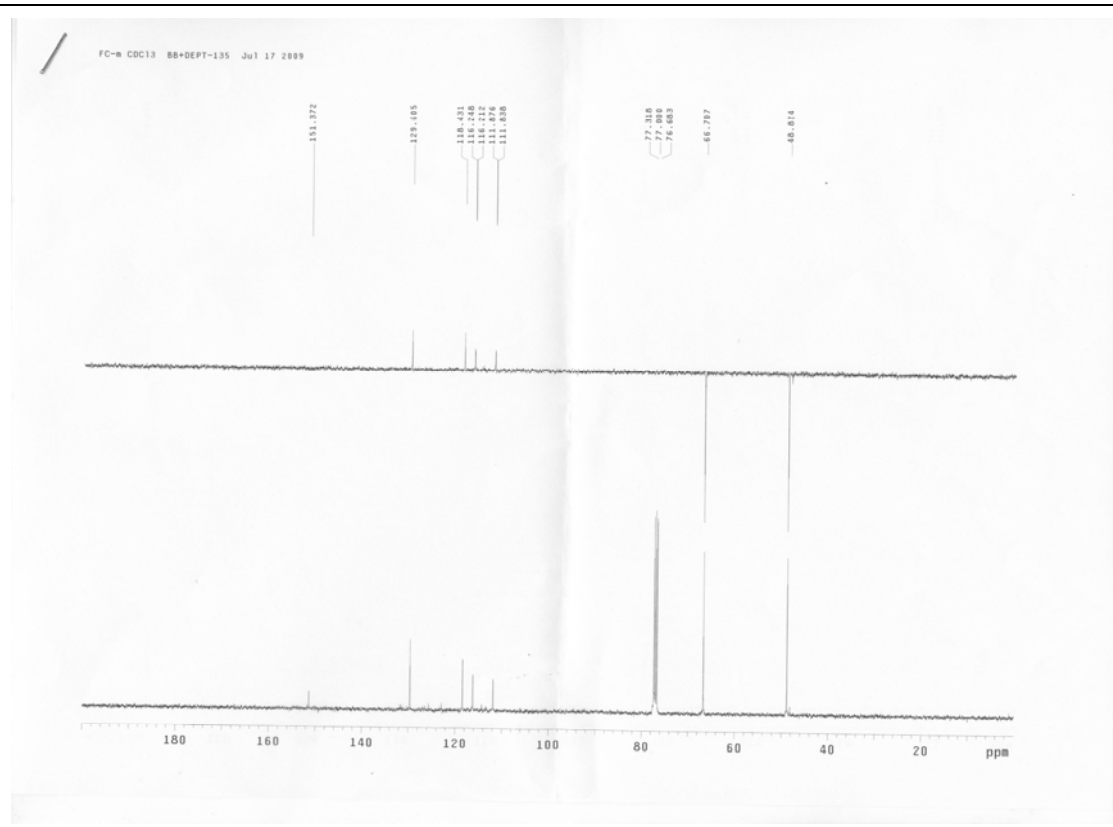
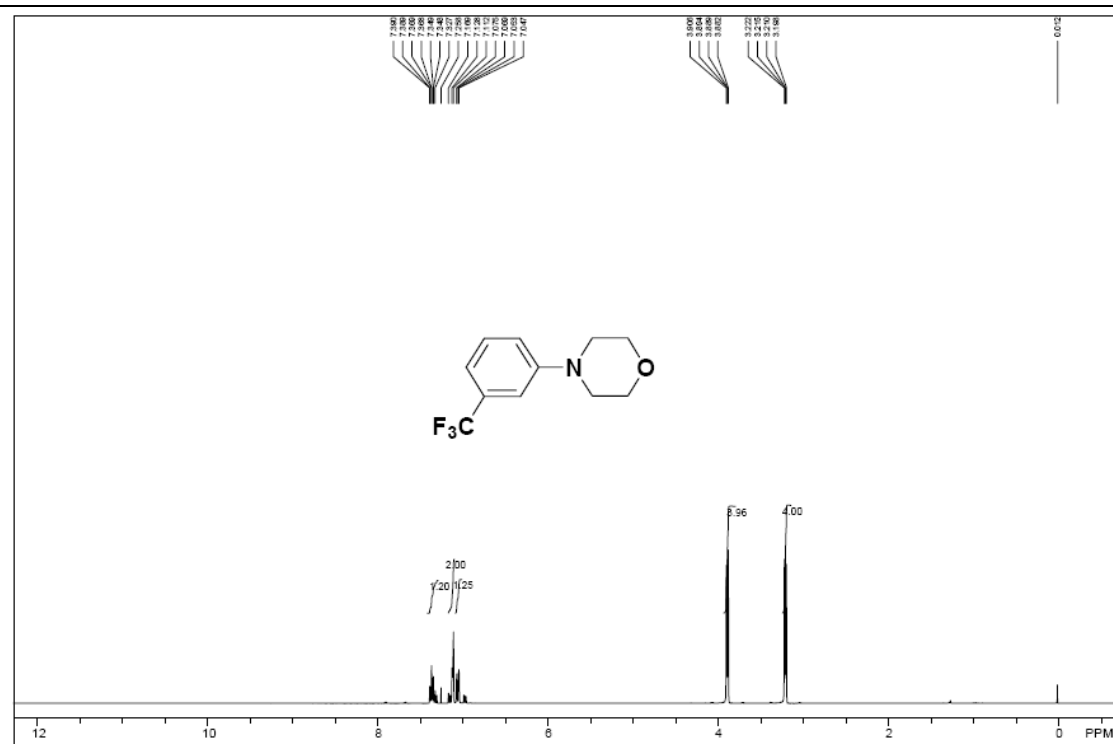
4-m-tolylmorpholine (2e)



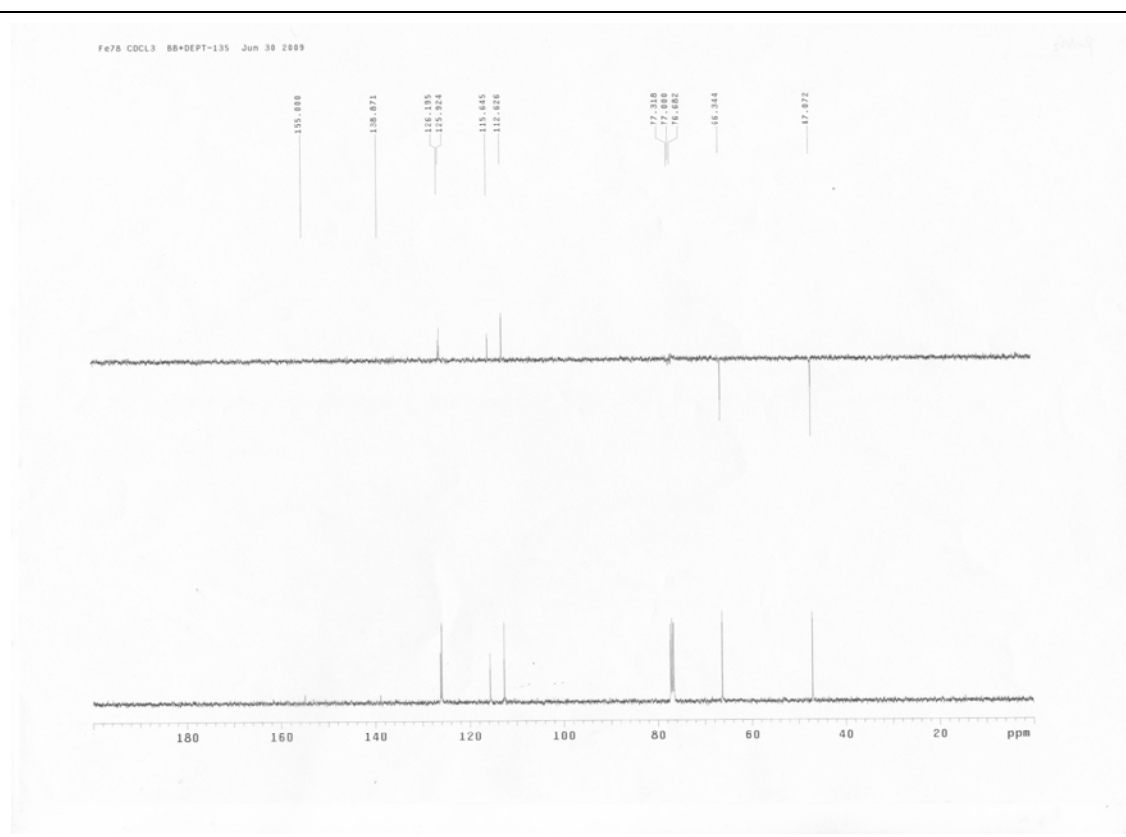
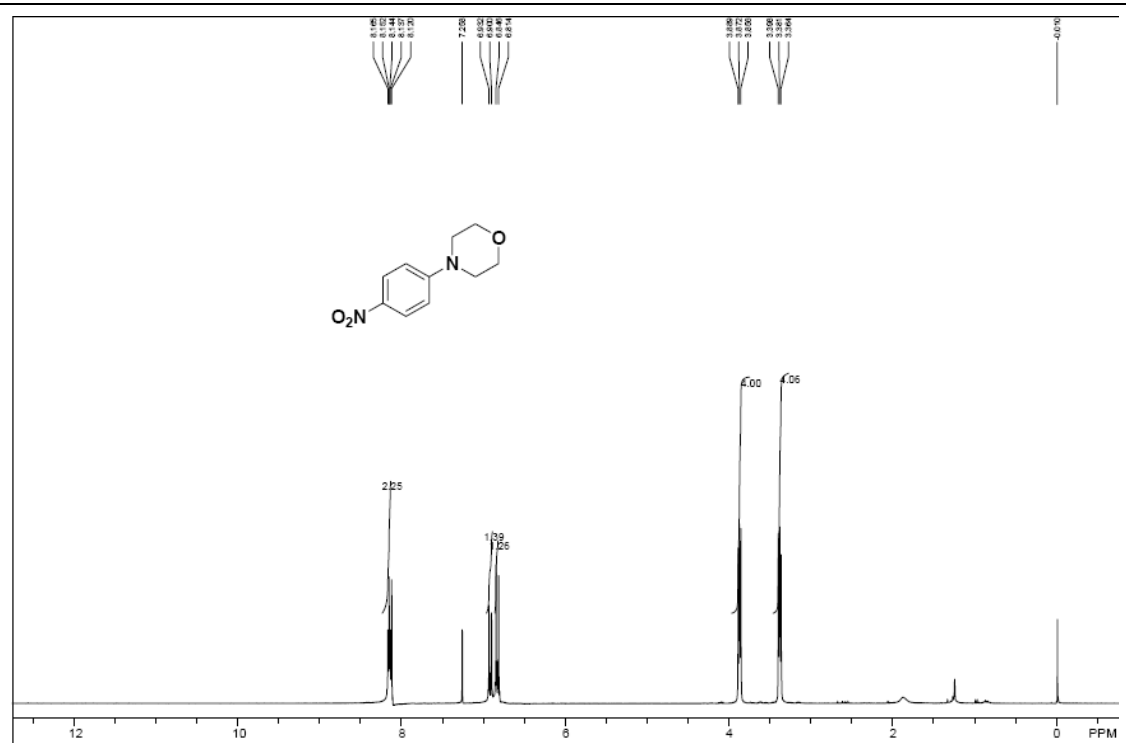
4-(4-(trifluoromethyl)phenyl)morpholine (2g)



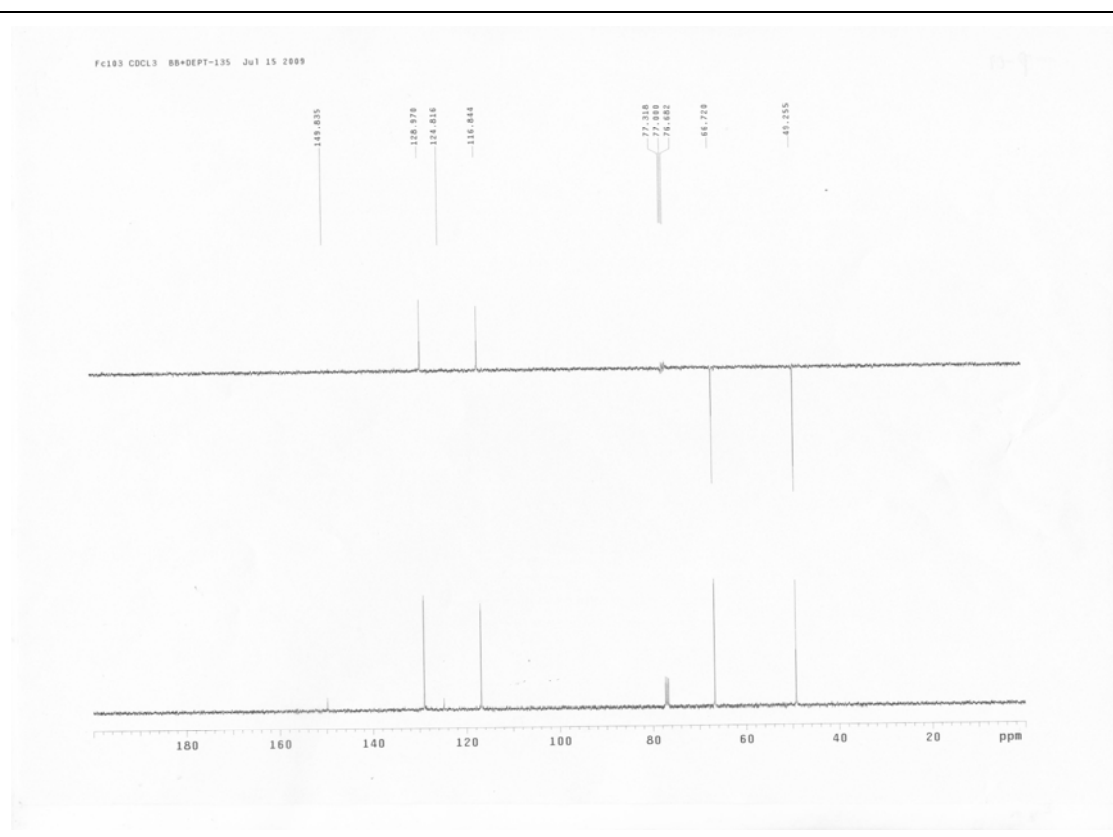
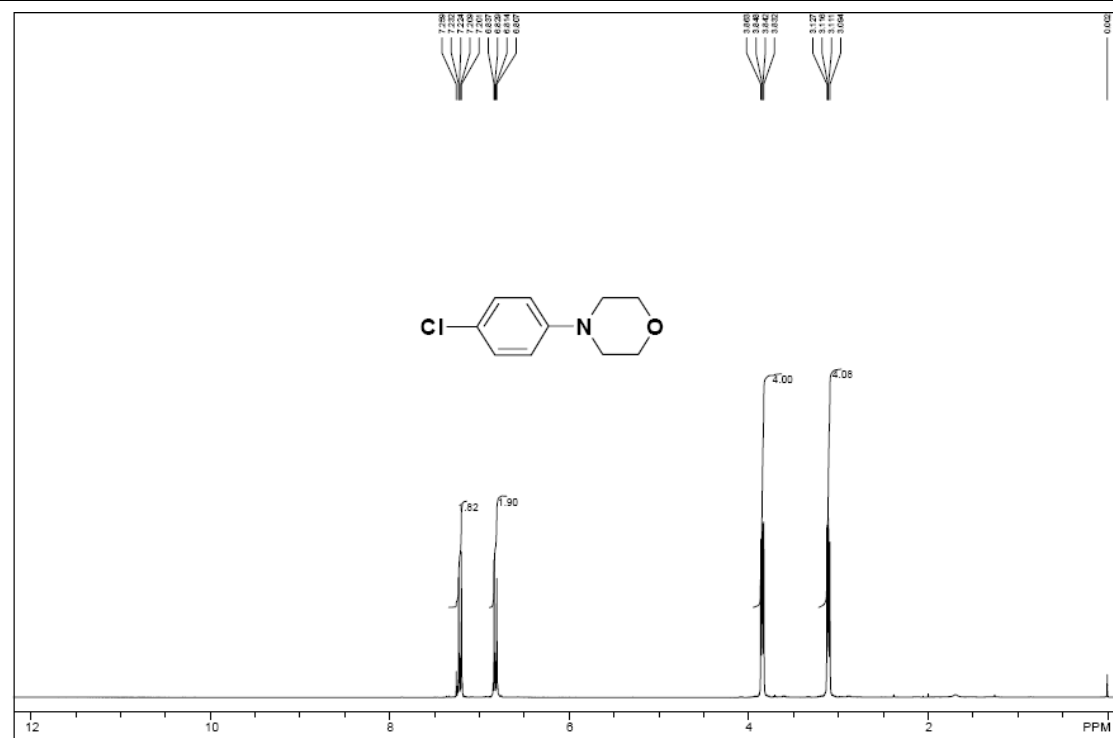
4-(3-(trifluoromethyl)phenyl)morpholine (2h)



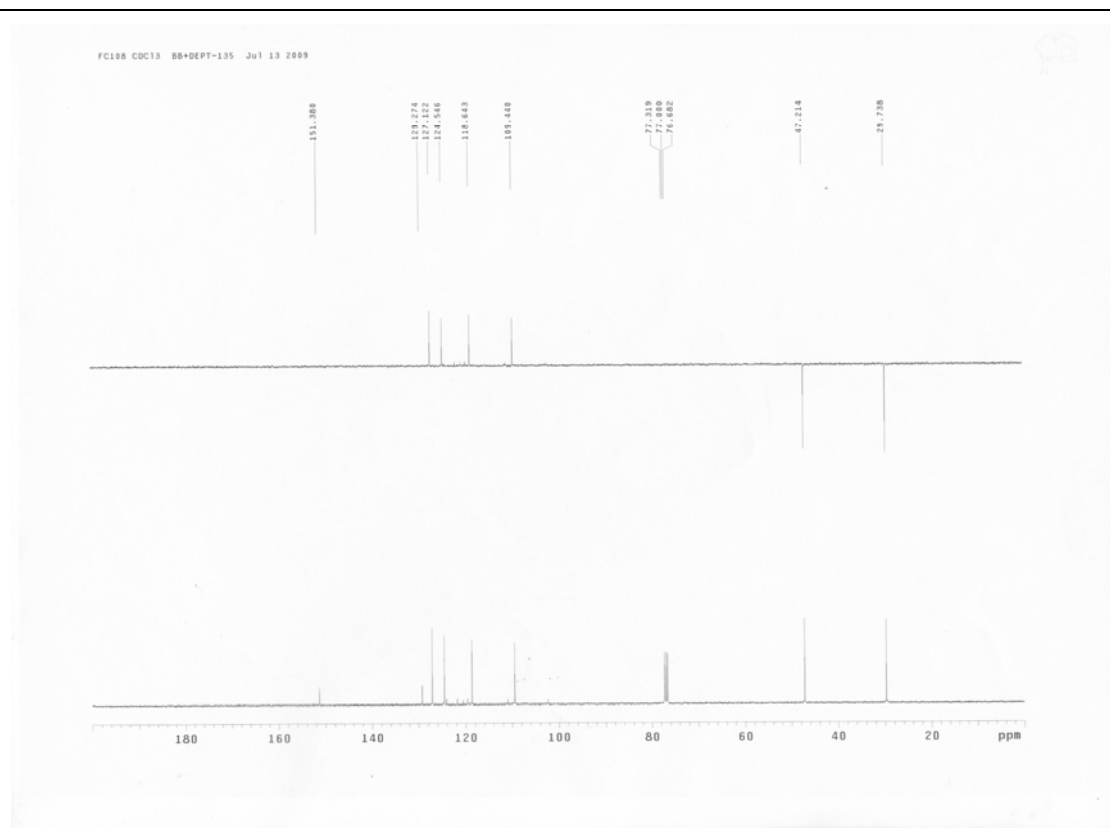
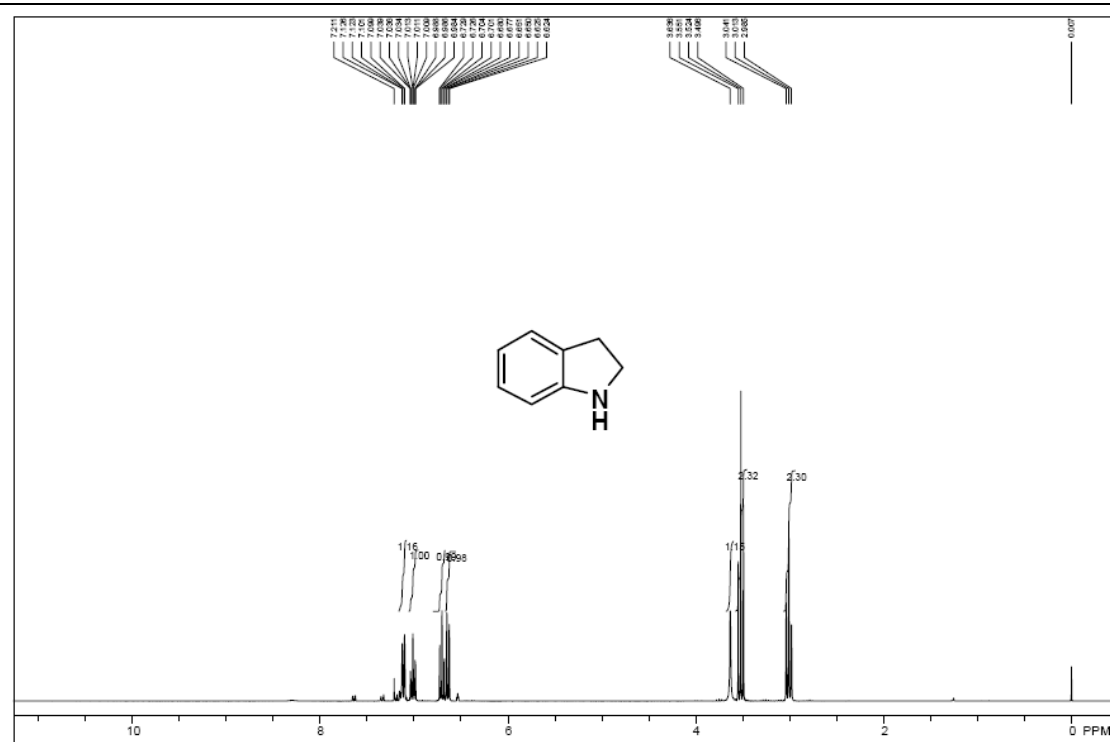
4-(4-nitrophenyl)morpholine (2j)



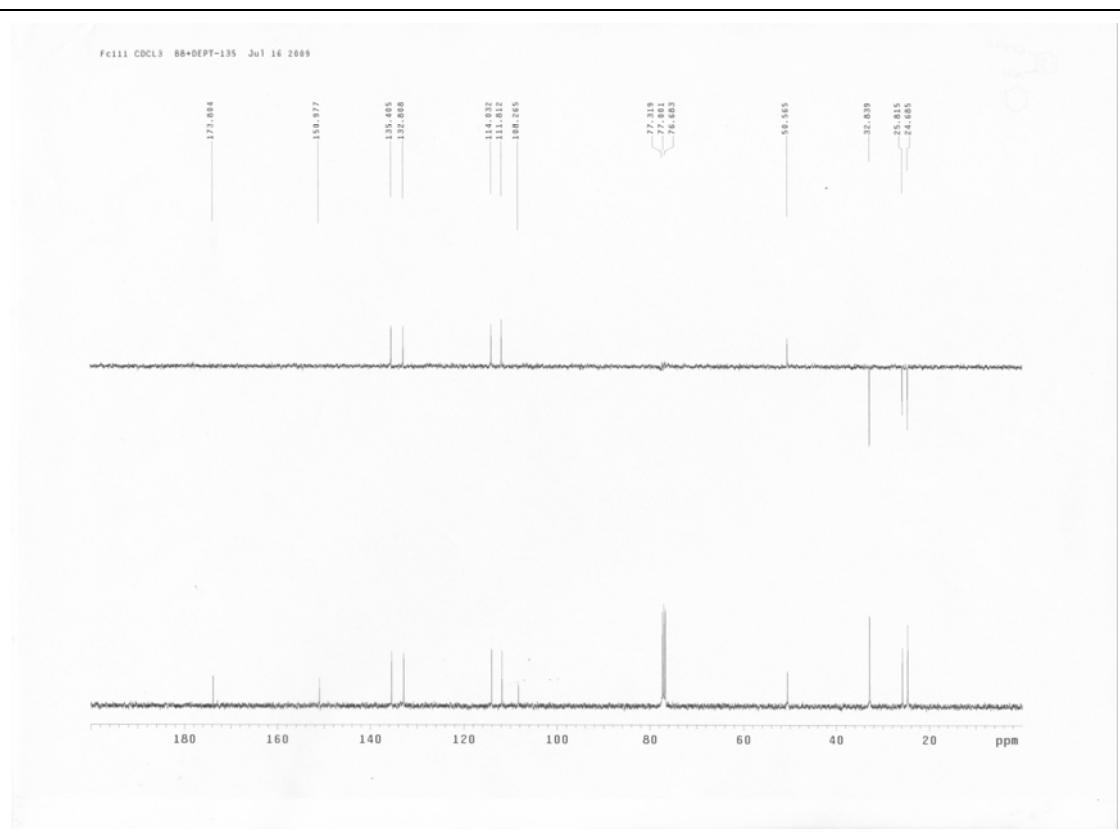
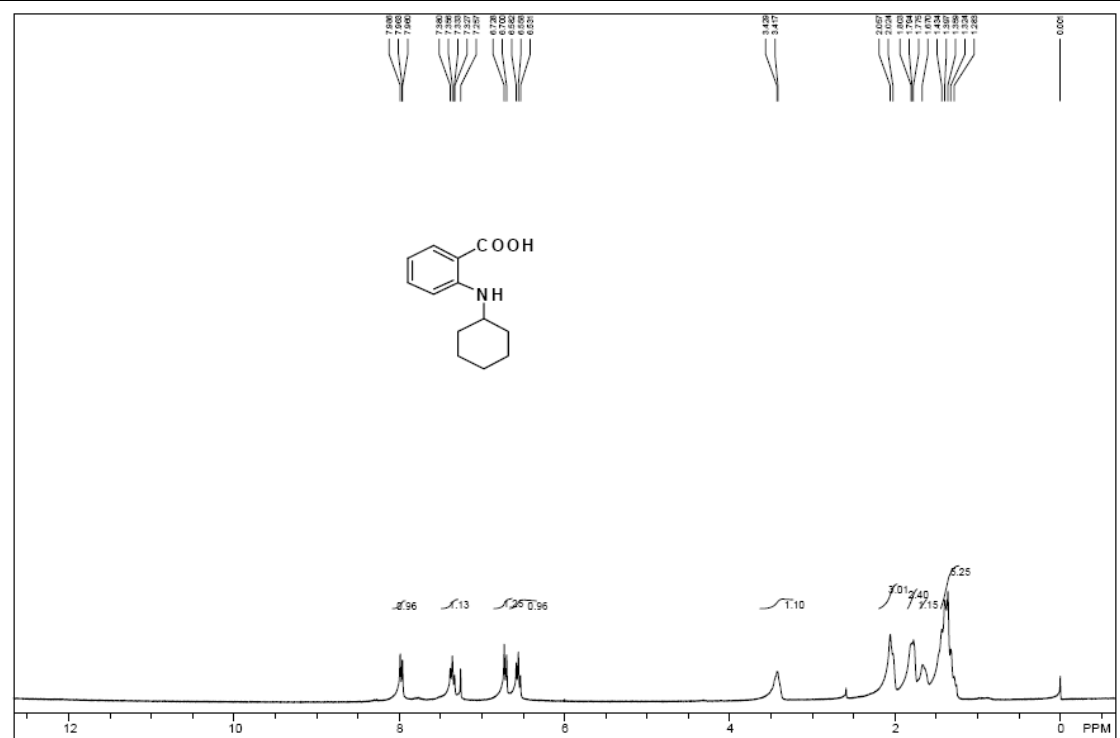
4-(4-chlorophenyl)morpholine (2k)



Indoline (3a)



2-(cyclohexylamino)benzoic acid (3b)



2-methylquinazolin-4(3H)-one (3c)

