Electronic Supplementary Material (ESI) for RSC Advances

PhIO promoted synthesis of nitrile imines and nitrile oxides within micellar core in aqueous media: A regiocontrolled approach to synthesize densely functionalized pyrazole and isoxazoline derivatives

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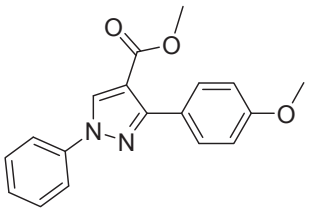
1. Materials and Methods

^{1}H-NMR and ^{13}C-NMR spectral analysis were carried out on Bruker-Advance Digital 300 MHz and 75 MHz instruments where tetramethylsilane (TMS) was used as internal standard. Infrared spectra were recorded in KBr pallets in reflection mode on a Perkin Elmer RX-1 FTIR spectrophotometer. High Resolution Mass Spectra was obtained using a QTOFMICRO YA263 mass spectrometer. Suitable single crystals of compound **5a** and **6f** were mounted on a Bruker-AXS SMART APEX II diffractometer equipped with a graphite monochromator. Optical images were obtained using a CARL-ZEISS Axi-Observer optical microscope. DLS study was performed in a MALVERN Zetasizer DLS.All the reactions were monitored by thin layer chromatography carried out on Merck aluminum-blocked silica gel plates coated with silica gel G under UV light and also by exposure to iodine vapor for detection. Melting points were determined on a Köfler Block apparatus and are uncorrected. Synthetic grade chemicals from Sigma-Aldrich, Spectrochem and E-Merck were used for carrying out the organic reactions. For column chromatography Spectrochem 100-200 mesh silica gel was used.

General Procedure for the synthesis of pyrazoles:

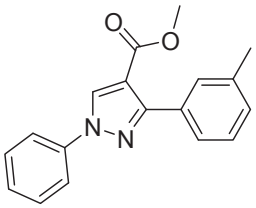
A mixture of aldehyde (1mmol), phenyl hydrazine (1 mmol) and olefin derivatives (1mmol) were added to a well stirred solution of SDS (10 mol %) in 5 ml H_2O at room temperature. Then PhIO (2.5 mmol) was added portion wise to the resulting mixture carefully maintaining the temperature at 0 ^oC. When the addition was complete, the reaction was allowed to attain room temperature and stirring was continued for the required period of time (monitored by TLC). After completion of the reaction, the mixture was extracted with ethyl acetate (3x10ml). Removal of ethyl acetate under reduced pressure and purification of the crude product by column chromatography (silica gel 100-200 mesh, ethyl acetate-hexane as eluent) provided pure products. All compounds were well characterized by ^1H, ^{13}C NMR, FT-IR and HRMS analysis.

3-(4-Methoxy-phenyl)-1-phenyl-1*H*-pyrazole-4-carboxylic acid methyl ester (4a)



Yield: 85%, (0.261 g); M.p. 91-92 ^0C (Lit: 94-95 ^0C); Characteristics: White crystalline solid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.68 (d, 3H, *J*=8.7 Hz), 7.59-7.54(m, 2H), 7.43 (d, 2H, *J*=8.1 Hz), 7.01-6.98 (m, 2H), 3.89 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.3, 160.3, 144.2, 136.4, 129.3, 127.2, 127.1, 121.0, 114.4, 113.3, 55.3, 51.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{17}N_2O_3$: 309.1239, found: 309.1236 ; IR (KBr) cm^{-1}: 1133.2, 1240.2, 1500.1, 1598.9, 1730.6, 2967.3, 3024.5; Anal. Calcd for $C_{18}H_{16}N_2O_3$: C: 70.12; H: 5.23; N: 9.09%, found: C: 70.10; H: 5.21; N: 9.07%.

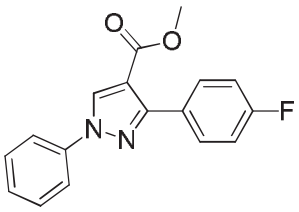
1-Phenyl-3-*m*-tolyl-1*H*-pyrazole-4-carboxylic acid methyl ester (4b)



Yield: 88%, (0.257 g); M.p. 99-100 ^{0}C; Characteristics: White amorphous solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.58 (d, 1H, *J*=7.5 Hz), 7.47-7.05 (m, 8H), 3.74(s, 3H), 3.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ159.8, 151.7, 140.0, 138.5, 134.0, 132.1, 129.2, 128.6, 126.4, 126.1, 123.1, 118.0, 109.6, 52.1, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{17}N_2O_2$: 293.1290, found: 293.1288; IR (KBr) cm^{-1}: 1177.0, 1236.2, 1516.3, 1601.3, 1732.3, 2933.2; Anal. Calcd for $C_{18}H_{17}N_2O_2$: C: 73.95; H: 5.52; N: 9.58%, found: C: 73.91; H: 5.49; N: 9.54%.

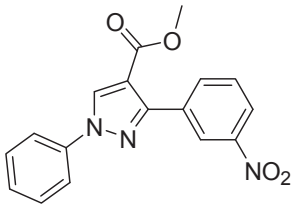
Methyl 3-(4-fluorophenyl)-1-phenyl-1*H*-pyrazole-4-carboxylate (4c)



Yield: 91%, (0.269 g); M.p. 128-129 ^{0}C (Lit: 130-131 ^{0}C); Characteristics: White crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80-7.75 (m, 2H), 7.41 (s, 5H), 7.22 (s, 1H), 7.07-7.02 (m, 2H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.6, 161.3 (C-F), 159.5, 150.7, 140.2, 134.4, 128.8, 128.4, 127.7, 127.3, 126.1, 115.9, 115.5, 109.3, 52.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}FN_2O_2$: 297.1039, found: 297.1036; IR (KBr) cm^{-1}: 1158.9, 1232.4, 1439.7, 1500.4, 1738.6, 2957.5, 3064.5 ; Anal. Calcd for $C_{17}H_{13}FN_2O_2$: C: 68.91; H: 4.42; N: 9.45%, found: C: 68.90; H: 4.43; N: 9.44%

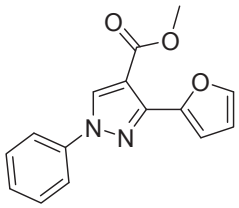
3-(3-Nitro-phenyl)-1-phenyl-1*H*-pyrazole-4-carboxylic acid methyl ester (4d)



Yield: 89%, (0.287 g); M.p. 120-121 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62(s, 1H), 8.15-8.05(m, 2H), 7.78 (d, 1H, *J*=8.4 Hz), 7.55-7.41(m, 4H), 7.33 (s, 1H), 7.24 (t, 1H, *J*=8Hz), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.1, 149.2, 142.8, 139.1, 135.1, 131.1, 129.8, 129.5, 128.6, 128.2, 126.1, 123.7, 123.1, 120.7, 113.5, 109.7, 52.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}N_3O_4$: 324.0984, found: 324.0980; IR (KBr) cm^{-1}: 1089.7, 1248.8, 1347.1, 1525.1, 1601.8, 1736.9, 2955.3, 3285.9 ; Anal. Calcd for $C_{17}H_{13}N_3O_4$: C: 63.16; H: 4.05; N: 13.00%, found: C: 63.11; H: 4.01; N: 13.01%

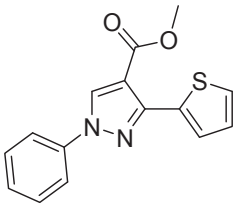
3-Furan-2-yl-1-phenyl-1*H*-pyrazole-4-carboxylic acid methyl ester (4e)



Yield: 87%, (0.233 g); M.p. 88-89 ^{0}C; Characteristics: Yellow amorphous solid;

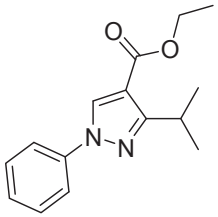
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.37(m, 6H), 7.22 (s, 1H), 6.71(s, 1H), 6.42(s, 1H), 3.74(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ159.3, 152.4, 143.6, 142.4, 129.3, 128.6, 126.1, 121.5, 113.6, 111.8, 111.5, 110.1, 109.2, 106.8, 52.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{13}N_2O_3$: 269.0926, found:269.0923; IR (KBr) cm^{-1}: 1108.7, 1242.1, 1504.4, 1733.1, 2904.2, 3010.2; Anal. Calcd for $C_{15}H_{12}N_2O_3$: C: 67.16; H: 4.51; N: 10.44%, found: C: 67.15; H: 4.50; N: 10.46%

1-Phenyl-3-thiophen-2-yl-*1H*-pyrazole-4-carboxylic acid methyl ester (4f)



Yield: 86%, (0.244 g); M.p. 101-102 ^{0}C (Lit: 102-103 ^{0}C); Characteristics: Yellow amorphous solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.60 (m, 2H), 7.41-7.33(m, 3H), 7.27-7.11 (m, 2H), 7.04 -6.98 (m, 2H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.4, 147.1, 140.0, 137.5, 135.2, 134.2, 130.2, 128.6, 127.6, 127.5, 126.1, 125.4, 124.7, 109.4, 52.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{13}N_2O_2S$: 285.0698, found: 285.0696; IR (KBr) cm^{-1}: 1015.4, 1241.8, 1500.6, 1732.8, 2911.3, 3001.6 ; Anal. Calcd for $C_{15}H_{12}N_2O_2S$: C: 63.36; H: 4.25; N: 9.85%, found: C: 63.39; H: 4.28; N: 9.86%

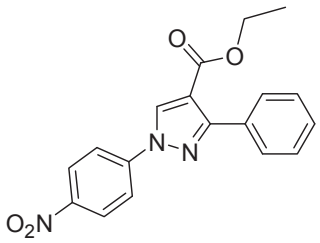
3-Isopropyl-1-phenyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (4g)



Yield: 91%, (0.235 g); Characteristics: Yellow oil;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.36-7.34 (m, 5H), 4.15 (q, 2H, *J*=7.2 Hz), 3.02-2.97(m, 1H), 1.26 (d, 6H, *J*=5.4 Hz), 1.21(t, 3H, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ163.3, 159.4, 136.5, 130.9, 130.0, 128.8, 126.1, 115.4, 109.3, 61.0, 26.6, 23.1, 14.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{19}N_2O_2$: 259.1447, found: 259.1444; IR (KBr) cm^{-1}: 1242.1, 1357.3, 1502.1, 1578.1, 1601.1, 1736.1, 2922..9 ; Anal. Calcd for $C_{15}H_{18}N_2O_2$: C: 69.74; H: 7.02; N: 10.84%, found: C: 69.71; H: 7.01; N: 10.83%

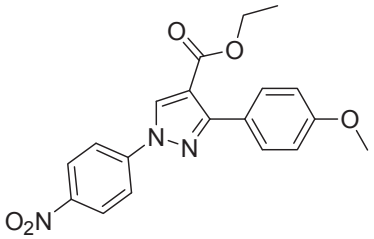
1-(4-Nitro-phenyl)-3-phenyl-1*H*-pyrazole-4-carboxylic acid ethyl ester (4h)



Yield: 92%, (0.310 g); M.p. 115-116 ^{0}C (Lit118 ^{0}C); Characteristics: Yellow crystalline solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.28 (d, 2H, *J*=8.7 Hz), 7.80 (d, 2H, *J*=8.7 Hz), 7.66 (d, 2H, *J*=8.7 Hz), 7.40-7.29 (m, 4H), 4.26 (q, 2H, *J*=7.1), 1.27 (t, 3H, *J*=7.2); ^{13}C NMR (75 MHz, $CDCl_3$): δ

158.9, 152.8, 147.2, 145.0, 134.9, 131.5, 128.9, 126.5, 125.9, 124.0, 123.9, 111.0, 67.7, 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}N_3O_4$: 338.1141, found: 338.1140 ; IR (KBr) cm^{-1}: 1110, 1241.7, 1306.8, 1526.4, 1597.9, 1721.7, 2937.8, 3132.8; Anal. Calcd for $C_{18}H_{15}N_3O_4$: C: 64.09; H: 4.48; N: 12.46%, found: C: 64.09; H: 4.46; N: 12.42%

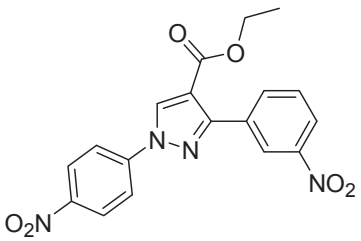
3-(4-Methoxy-phenyl)-1-(4-nitro-phenyl)-1*H*-pyrazole-4-carboxylic acid ethyl ester (4i)



Yield: 81%, (0.297 g); M.p. 89-90 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (d, 2H, *J*=9Hz), 7.75 (d, 1H, *J*=8.7 Hz), 7.67 (d, 2H, *J*=9 Hz), 7.27 (s, 1H), 6.98-6.91 (m, 3H), 4.27 (q, 2H, *J*=7.1), 3.81 (s, 3H), 1.29 (t, 3H, *J*=7.1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3, 160.1, 153.6, 152.2, 140.8, 132.4, 132.1, 129.6, 128.0, 123.9, 122.0, 116.5, 115.6, 113.1, 105.9, 61.7, 56.3, 14.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}N_3O_5$: 368.1246, found:368.1243; IR (KBr) cm^{-1}: 1033.9, 1240.1, 1528.9, 1601.9, 1722.1, 2940.3, 3140.3 ; Anal. Calcd for $C_{19}H_{17}N_3O_5$: C: 62.12; H: 4.66; N: 11.44%, found: C: 62.11; H: 4.62; N: 11.49%

3-(3-Nitro-phenyl)-1-(4-nitro-phenyl)-1*H*-pyrazole-4-carboxylic acid ethyl ester (4j)

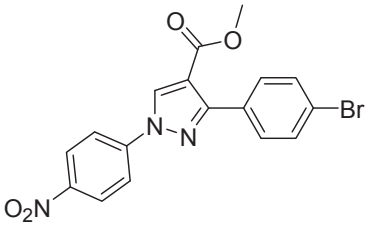


Yield: 86%, (0.328 g); M.p. 93-95 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.37-8.35 (m, 2H), 8.24-8.19 (m, 2H), 7.72 (d, 2H, *J*=9 Hz), 7.62 (t, 1H, J=8.1 Hz), 7.46 (s, 1H), 4.33 (q, 2H, *J*=7.2), 1.34 (t, 3H, *J*=7.1Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 158.3, 150.3, 148.6, 147.5, 144.6, 141.8, 139.1, 135.4, 134.6, 133.5, 132.2, 129.4, 127.9, 126.3, 124.2, 61.9, 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{15}N_4O_6$:

383.0992, found:383.0990; IR (KBr) cm^{-1}: 1078.2, 1238.7, 1310.2, 1530.1, 1607.9, 1730.8, 2960.6, 3149.8; Anal. Calcd for $C_{18}H_{14}N_4O_6$: C: 56.55; H: 3.69; N: 14.65% found: C: 56.51; H: 3.68; N: 14.61%

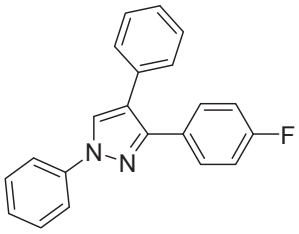
3-(4-Bromo-phenyl)-1-(4-nitro-phenyl)-1*H*-pyrazole-4-carboxylic acid methyl ester (4k)



Yield: 87%, (0.349 g); M.p. 121-122 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89 (d, 2H, *J*=8.7 Hz), 7.55 (d, 2H, *J*=9 Hz),7.45-7.14(m, 5H), 3.79(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 147.7, 145.2, 133.6, 132.9, 130.2, 128.8, 128.5, 127.5, 126.1, 124.6, 124.3, 116.2, 52.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{17}H_{13}BrN_3O_4$: 402.0089, found:402.0085; IR (KBr) cm^{-1}: 1006.7, 1239.1, 1530.0, 1599.1, 1713.12933.9, 3135.6; Anal. Calcd for $C_{17}H_{12}BrN_3O_4$: C: 50.77; H: 3.01; N: 10.45%, found: C: 50.74; H: 3.00; N: 10.44%

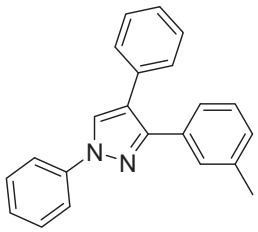
3-(4-Fluoro-phenyl)-1,4-diphenyl-1*H*-pyrazole (4l)



Yield: 85%, (0.267 g); M.p. 93-95 ^{0}C; Characteristics: White crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H), 7.55 (d, 2H, *J*=8.1Hz), 7.31(t, 2H, *J*=7.8 Hz), 7.12-7.04 (m, 8H), 6.8 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.3 (C-F), 137.8, 132.9, 132.8, 130.2, 129.4, 129.1, 128.9, 128.5, 125.6, 124.8, 120.4, 116.0, 115.9, 115.8, 115.7, 115.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{16}FN_2$: 315.1298, found: 315.1296; IR (KBr) cm^{-1}: 1159.4, 1294.6, 1431.7, 1604.4, 1655.5, 2850.5 ; Anal. Calcd for $C_{21}H_{15}FN_2$: C: 80.24; H: 4.81; N: 8.91%, found: C: 80.22; H: 4.80; N: 8.99%

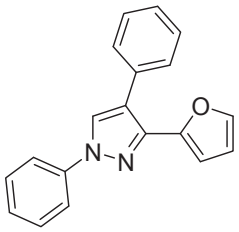
1,4-Diphenyl-3-*m*-tolyl-1*H*-pyrazole (4m)



Yield: 81%, (0.251 g); M.p. 81-82 ^{0}C; Characteristics: Yellow amorphous solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46-7.41 (m, 3H), 7.33-7.27 (m, 4H), 7.23-7.20 (m, 3H), 7.10 (t, 2H, *J*=7.5 Hz), 6.95 (d, 2H, *J*=7.5 Hz), 6.84 (s, 1H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.0, 139.9, 139.1, 137.6, 137.1, 131.0, 130.4, 129.5, 129.1, 127.9, 126.6, 126.9, 124.4, 123.5, 120.9, 21.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{22}H_{19}N_2$: 311.1548, found:311.1545; IR (KBr) cm^{-1}: 1129.9, 1291.6, 1430.5, 1600.5, 1651.3, 2890.6; Anal. Calcd for $C_{22}H_{18}N_2$: C: 85.13; H: 5.85; N: 9.03, found: C: 85.15; H: 5.88; N: 9.07%

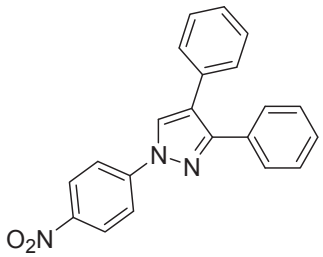
3-Furan-2-yl-1,4-diphenyl-1*H*-pyrazole (4n)



Yield: 84%, (0.240 g); M.p. 73-74 ^{0}C; Characteristics: Yellow amorphous solid;

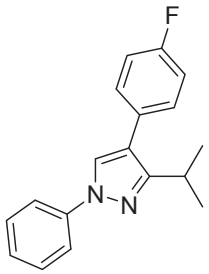
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, 2H, *J*=7.5 Hz), 7.48-7.26 (m, 6H), 7.14-7.07 (m, 4H), 6.46-6.40(m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.0, 147.2, 141.9, 139.3, 130.4, 130.3, 129.1, 126.4, 121.4, 118.8, 115.2, 114.9, 110.7, 108.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{19}H_{15}N_2O$: 287.1184, found: 287.1181; IR (KBr) cm^{-1}: 1094.5, 1240.6,1430.6, 1500.9, 1699.1, 2698.7 ; Anal. Calcd for $C_{19}H_{14}N_2O$: C: 79.70; H: 4.93; N: 9.78%, found: C: 79.71; H: 4.91; N: 9.74%

1-(4-Nitro-phenyl)-3,4-diphenyl-1*H*-pyrazole (4o)



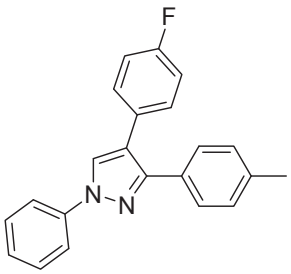
Yield: 83%, (0.283 g); M.p. 99-101 ^{0}C (Lit: 102-103 ^{0}C); Characteristics: Yellow amorphous solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.16-8.07 (m, 2H), 7.68 (d, 1H, *J*=7.5 Hz), 7.60-7.31 (m, 11H), 7.23 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.9, 152.0, 139.1, 133.5, 132.2, 132.1, 129.4, 127.9, 126.3, 124.2, 122.4, 116.2, 113.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{16}N_3O_2$, found:342.1239; IR (KBr) cm^{-1}: 1136.5, 1255.0, 1550.4, 1607.4, 1728.5, 2960.2, 3148.3; Anal. Calcd for $C_{21}H_{15}N_3O_2$: C: 73.89; H: 4.43; N: 12.31%, found: C: 73.87; H: 4.45; N: 12.30%

4-(4-Fluoro-phenyl)-3-isopropyl-1-phenyl-1*H*-pyrazole (5a)



Yield: 94%, (0.263 g); M.p. 80-81 ^{0}C; Characteristics: Yellow crystalline solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.62 (d, 2H, *J*=7.8 Hz), 7.40-7.14 (m, 5H), 7.06-6.97 (m, 2H), 3.13(m, 1H), 1.25 (d, 6H, *J*=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ157.2 (C-F), 140.2, 137.5, 130.1, 129.9, 129.4, 127.5, 126.5, 126.1, 125.4, 121.6, 118.8, 115.6, 115.3, 114.9, 26.5, 22.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{18}FN_2$: 281.1454, found: 281.1450; IR (KBr) cm^{-1}: 1174.8, 1241.2, 1504.3, 1575.5, 1608.9, 2850.8; Anal. Calcd for $C_{18}H_{17}FN_2$: C: 77.12; H: 6.11; N: 9.99%, found: C: 77.10; H: 6.10; N: 9.98 %

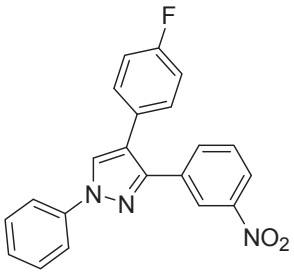
4-(4-fluorophenyl)-1-phenyl-3-(*p*-tolyl)-1*H*-pyrazole (5b)



Yield: 87%, (0.285 g); M.p. 83-84 ^{0}C; Characteristics: Yellow amorphous solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63(d, 3H, *J*=8.1 Hz), 7.54-7.34 (m, 3H), 7.28-6.94 (m, 8H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.0 (C-F), 154.8, 150.5, 137.8, 137.5, 132.6, 131.4, 130.2, 129.3, 129.2, 129.1, 128.9, 125.4, 116.9, 116.6, 116.1, 115.8, 21.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{22}H_{18}FN_2$: 329.1454, found: 329.1450; IR (KBr) cm^{-1}: 1098.6, 1244.2, 1446.5, 1520.1, 1605.5, 2866.3; Anal. Calcd for $C_{22}H_{17}FN_2$: C: 80.47; H: 5.22; N: 8.53%, found: C: 80.47; H: 5.23; N: 8.52%

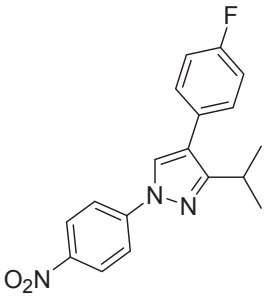
4-(4-Fluoro-phenyl)-3-(3-nitro-phenyl)-1-phenyl-1*H*-pyrazole (5c)



Yield: 89%, (0.319 g); M.p. 101-103 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (s, 1H), 8.10-8.07 (m, 1H), 7.94-7.88 (m, 2H), 7.78-7.71 (m, 3H), 7.46-7.20(m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$): δ158.8 (C-F), 155.5, 143.3, 142.6, 134.4, 129.6, 128.8, 125.3, 125.2, 124.8, 124.4, 124.0, 122.9, 122.1, 117.8, 117.4, 117.1, 113.8, 110.8, 110.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{21}H_{15}FN_3O_2$: 360.1148, found:360.1144; IR (KBr) cm^{-1}: 1130.8, 1249.3, 1327.6, 1529.5, 1611.0, 2950.1, 3026.5; Anal. Calcd for $C_{21}H_{14}FN_3O_2$: C: 70.19; H: 3.93; 11.69%, found: C: 70.20; H: 3.92; N: 11.68%

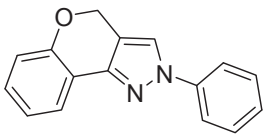
4-(4-Fluoro-phenyl)-3-isopropyl-1-(4-nitro-phenyl)-1*H*-pyrazole (5d)



Yield: 86%, (0.279 g); M.p. 85-86 ^{0}C; Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.19 (d, 2H, *J*= 9 Hz), 8.04 (d, 2H, *J*= 8.6 Hz), 7.64-7.61(m, 2H), 7.37-7.24(m, 2H), 3.13 (m, 1H), 1.23 (d, 6H *J*=6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.2 (C-F), 147.2, 137.5, 130.5, 130.2, 127.5, 125.9, 124.9, 123.8, 123.6, 123.4, 116.1, 115.6, 114.3, 26.6, 22.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{18}H_{17}FN_3O_2$: 326.1305, found: 326.1301; IR (KBr) cm^{-1}: 1025.6, 1246.6, 1509.4, 1598.5, 1631.2, 2896.3, 3010.2; Anal. Calcd for $C_{18}H_{16}FN_3O_2$: C: 66.45; H: 4.96; N: 12.92%, found: C: 66.44; H: 4.94; N: 12.95%

2-Phenyl-2,4-dihydro-chromeno[4,3-c]pyrazole (7a)



Yield: 91%, (0.226 g); M.p. 79-80 ^{0}C (Lit: 81-82 ^{0}C); Characteristics: Yellow crystalline solid;

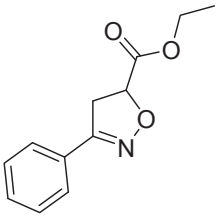
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (dd, 1H, J=7.5 Hz, 1.8 Hz), 7.65-7.60 (m, 2H), 7.41-7.34 (m, 3H), 7.24-7.12 (m, 1H), 6.98-6.87 (m, 3H), 5.27 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4, 154.1, 135.8, 133.1, 130.0, 129.6, 129.1, 126.3, 122.7, 122.3, 122.1, 122.1, 119.2, 117.4, 63.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{16}H_{13}N_2O$: 249.1028, found:249.1025; IR (KBr) cm^{-1}: 1089.6, 1229.8, 1471.3, 1502.8, 1599.3, 1689.9, 2800.3; Anal. Calcd for $C_{16}H_{12}N_2O$: C: 77.40; H: 4.87; N: 11.28%, found: C: 77.45; H: 4.84; N: 11.25%

General Procedure for the synthesis of isoxazolines

The reaction was performed via the same method for pyrazoles. A mixture of aldehyde (1mmol), hydroxyl amine hydrochloride (1 mmol), sodium acetate (1 mmol), and olefin derivatives (1mmol)

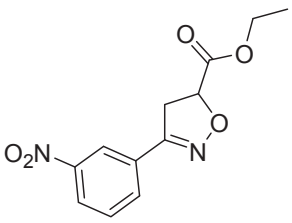
were added to a well stirred solution of SDS (10 mol %) in 5 ml H_2O at room temperature. Then PhIO (1.5 mmol) was added portion wise to the resulting mixture carefully maintaining the temperature at 0 ^oC. When the addition was complete the reaction was allowed to attain room temperature and stirring was continued for the required period of time (monitored by TLC). After completion of the reaction, the mixture was extracted with ethyl acetate (3x10ml). Removal of ethyl acetate under reduced pressure and purification of the crude product by column chromatography (silica gel 100-200 mesh, ethyl acetate-hexane as eluent) provided pure products. All compounds were well characterized by ^1H, ^{13}C NMR, FT-IR and HRMS analysis.

3-Phenyl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6a)



Yield: 92%, (0.201 g); M.p. 28-29 ^0C (Lit: 31-33 ^0C); Characteristics: Yellow amorphous solid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.68-7.63 (m, 2H), 7.45-7.41 (m, 3H), 5.16 (dd, 1H, *J*=10.4, 7.8 Hz), 4.26 (q, 2H, *J*=7.1Hz), 3.65-3.62 (m, 2H), 1.32 (t, 3H, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 156.1, 133.7, 130.5, 128.8, 128.5, 126.9, 126.8, 78.1, 62.0, 38.9, 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{14}NO_3$: 220.0974, found: 220.0971; IR (KBr) cm^{-1}: 1032.6, 1210.1, 1449.1, 1736.1, 2963.7, 3471.2 ; Anal. Calcd for $C_{12}H_{13}NO_3$: C: 65.74; H: 5.98; N: 6.39%, found: C: 65.71; H: 5.96; N: 6.36%

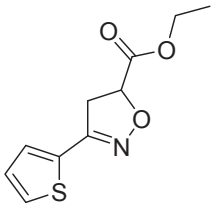
3-(3-Nitro-phenyl)-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6b)



Yield: 89%, (0.235 g); M.p. 66-67 ^0C (Lit: 65-67 ^0C); Characteristics: White crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.17 (d, 1H, *J*=8.4 Hz), 7.98 (d, 1H *J*=7.8 Hz), 7.56-7.51(m, 1H), 5.22 (dd, 1H, *J*=10.2, 7.8 Hz), 4.20 (q, 2H, *J*=7.1 Hz), 3.70-3.63 (m, 2H,), 1.25(t, 3H, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 154.6, 148.3, 132.4, 130.1, 129.8, 124.9, 121.9, 78.8, 62.4, 38.4, 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{13}N_2O_5$: 265.0824, found: 265.0820; IR (KBr) cm^{-1}: 1145.7, 1210.9, 1463.7,1548.1, 1720.6, 2863.3, 2933.4, 3012.3, 3548.5 ; Anal. Calcd for $C_{12}H_{13}N_2O_5$: C: 54.55; H: 4.58; N: 10.60%, found: C: 54.54; H: 4.56; N: 10.62%

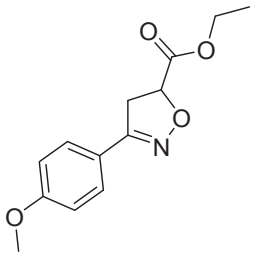
3-Thiophen-2-yl-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6c)



Yield: 84%, (0.189 g); Characteristics: Yellow oil;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.57(m, 1H), 7.37-7.34 (m, 1H), 7.19-7.17(m, 1H), 5.09 (dd, 1H, *J*=10.2, 7.8 Hz), 4.18 (q, 2H, *J*=6.9 Hz), 3.60-3.57 (m, 2H,), 1.24(t, 3H, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 163.1, 134.8, 129.0, 129.1, 127.4, 78.2, 62.1, 38.9, 14.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{10}H_{12}NO_3S$: 226.0538, found: 226.0536; IR (KBr) cm^{-1}: 1156.3, 1216.2, 1440.4, 1608.2, 1730.1, 2866.3, 2998.3, 3263.6 ; Anal. Calcd for $C_{10}H_{11}NO_3S$: C: 53.32; H: 4.92; N: 6.22%, found: C: 53.35; H: 4.90; N: 6.21%

3-(4-Methoxy-phenyl)-4,5-dihydro-isoxazole-5-carboxylic acid ethyl ester (6d)

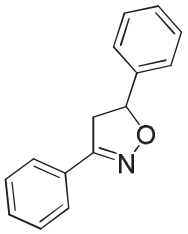


Yield: 85%, (0.209 g); Characteristics: Yellow oil;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55-7.51(m, 2H), 6.88-6.82(m, 2H), 5.05 (dd, 1H, *J*=10.2, 7.8 Hz), 4.18 (q, 2H, *J*=7.2 Hz), 3.76 (s, 3H), 3.55-3.51 (m, 2H,), 1.24(t, 3H, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 161.3, 155.6, 128.6, 121.8, 114.4,113.7, 78.1, 62.1 ,55.6, 39.2, 14.2; HRMS (ESI-

TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{16}NO_4$: 250.1079, found: 250.1075; IR (KBr) cm^{-1}: 1201.6, 1446.1, 1601.5, 1710.6, 2933.6, 3022.1, 3456.9; Anal. Calcd for $C_{13}H_{15}NO_4$: C: 62.64; H: 6.07; N: 5.62%, found: C: 62.65; H: 6.05; N: 5.61%

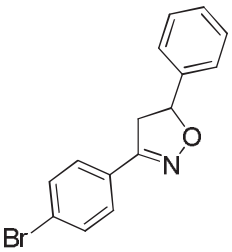
3,5-Diphenyl-4,5-dihydro-isoxazole (6e)



Yield: 90%, (0.200 g); M.p. 70-72 ^{0}C (Lit: 75-76 ^{0}C); Characteristics: Yellow crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.51 (m, 2H), 7.31-7.21 (m, 8H), 5.61 (dd, 1H, *J*=10.2, 8.1Hz), 3.65 (dd, 1H, *J*=16.6,10.8 Hz), 3.21 (dd, 1H, *J*=16.8, 8.4Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ156.0, 140.8, 137.4, 130.2, 129.1, 129.0, 128.1, 128.0, 126.1, 125.9, 82.5, 43.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{14}NO$: 224.1075, found: 224.1072; IR (KBr) cm^{-1}: 1059.3, 1212.7, 1453.0, 1599.6, 2830, 3030.2, 3532.2 ; Anal. Calcd for $C_{15}H_{13}NO$: C: 80.69; H: 5.87; N: 6.27%, found: C: 80.66; H: 5.89; N: 6.29%

3-(4-bromophenyl)-5-phenyl-4,5-dihydroisoxazole (6f)

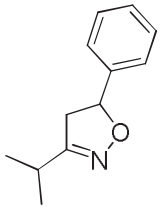


Yield: 90%, (0.272 g); M.p. 140-141 ^{0}C (Lit: 141-142 ^{0}C); Characteristics: White crystalline solid;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53-7.46 (m, 5H), 7.37-7.29 (m, 4H), 5.73 (dd, 1H, *J*=10.8, 8.4Hz), 3.73 (dd, 1H, *J*=16.7,10.8 Hz), 3.33 (dd, 1H, *J*=16.5, 8.4Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.3, 140.7, 132.7, 132.1, 131.2, 129.0, 128.4, 128.3, 126.1, 82.9, 42.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{13}BrNO$: 302.0181, found: 302.0179; IR (KBr) cm^{-1}: 1101.4, 1439.6, 1598.2,

2892.3, 3021.2, 3466.5 ; Anal. Calcd for $C_{15}H_{12}BrNO$: C: 59.62; H: 4.00; N: 4.64% , found: C: 59.60; H: 4.02; N: 4.62%

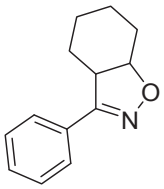
3-isopropyl-5-phenyl-4,5-dihydroisoxazole (6g)



Yield: 91%, (0.172 g); Characteristics: Yellow oil;

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27-7.17 (m, 5H), 5.44 (dd, 1H, *J*=10.5, 8.1 Hz), 3.28 (dd, 1H, *J*=17.1,10.8 Hz), 2.81(dd, 1H, *J*=16.8, 8.1 Hz), 2.65 (m, 1H), 1.11 (d, 6H, J=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ157.1, 135.4, 131.5, 126.0, 123.1, 122.1, 121.9, 120.0, 75.4, 37.3, 21.9, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{12}H_{16}NO$: 190.1232, found: 190.1230; IR (KBr) cm^{-1}: 1010.6, 1310.9, 1567.1, 2900.6, 3028.9, 3412.9; Anal. Calcd for $C_{12}H_{16}NO$: C: 76.16; H: 7.99; N: 7.40%, found: C: 76.18; H: 7.97; N: 7.42%

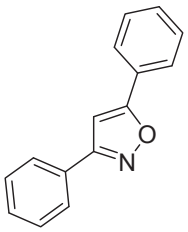
3-Phenyl-3a,4,5,6,7,7a-hexahydro-benzo[*d*]isoxazole (6h)



Yield: 92%, (0.185 g); M.p. 80-81 ^{0}C (Lit: 79-81 ^{0}C); Characteristics: White crystalline solid;

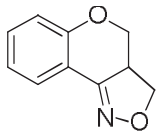
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59-7.56 (m, 2H), 7.35-7.30 (m, 3H), 4.83-4.75 (m, 1H), 3.68-3.63(m, 1H), 2.01-1018 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2, 129.5, 128.7, 127.0, 84.9, 51.4, 31.1, 30.1, 27.0, 23.7 ; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{13}H_{16}NO$: 202.1232, found: 202.1230 ; IR (KBr) cm^{-1}: 1310.4, 1400.6, 1558.3, 1701.8, 2904.5, 3010.5, 3396.3; Anal. Calcd for $C_{13}H_{16}NO$: C: 77.58; H: 7.51; N: 6.96%, found: C: 77.55; H: 7.50; N: 6.92%

3,5-Diphenyl-isoxazole (6i)



Yield: 86%, (0.190 g); M.p. 139-140 ^{0}C (Lit: 140-142 ^{0}C); Characteristics: white crystalline solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98-7.94(m, 2H), 7.54-7.48(m, 8H), 6.98 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 161.8, 137.4, 133.7, 130.0, 129.9, 129.2, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1, 127.6, 97.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calculated for $C_{15}H_{12}NO$: 222.0919, found: 222.0914; IR (KBr) cm^{-1}: 1201.4, 1455.4, 1540.2, 1604.4, 21910.5, 3042.5, 3112.2, 3564.8 ; Anal. Calcd for $C_{15}H_{11}NO$: C: 81.43; H: 5.01; N: 6.33%, found: C: 81.41; H: 5.05; N: 6.35%

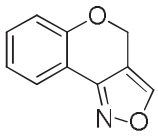
3a,4-Dihydro-3*H*-chromeno[4,3-*c*]isoxazole (7b)



Yield: 92%, (0.161 g); M.p. 60-62 ^{0}C (Lit: 62-64 ^{0}C); Characteristics: White crystalline solid;

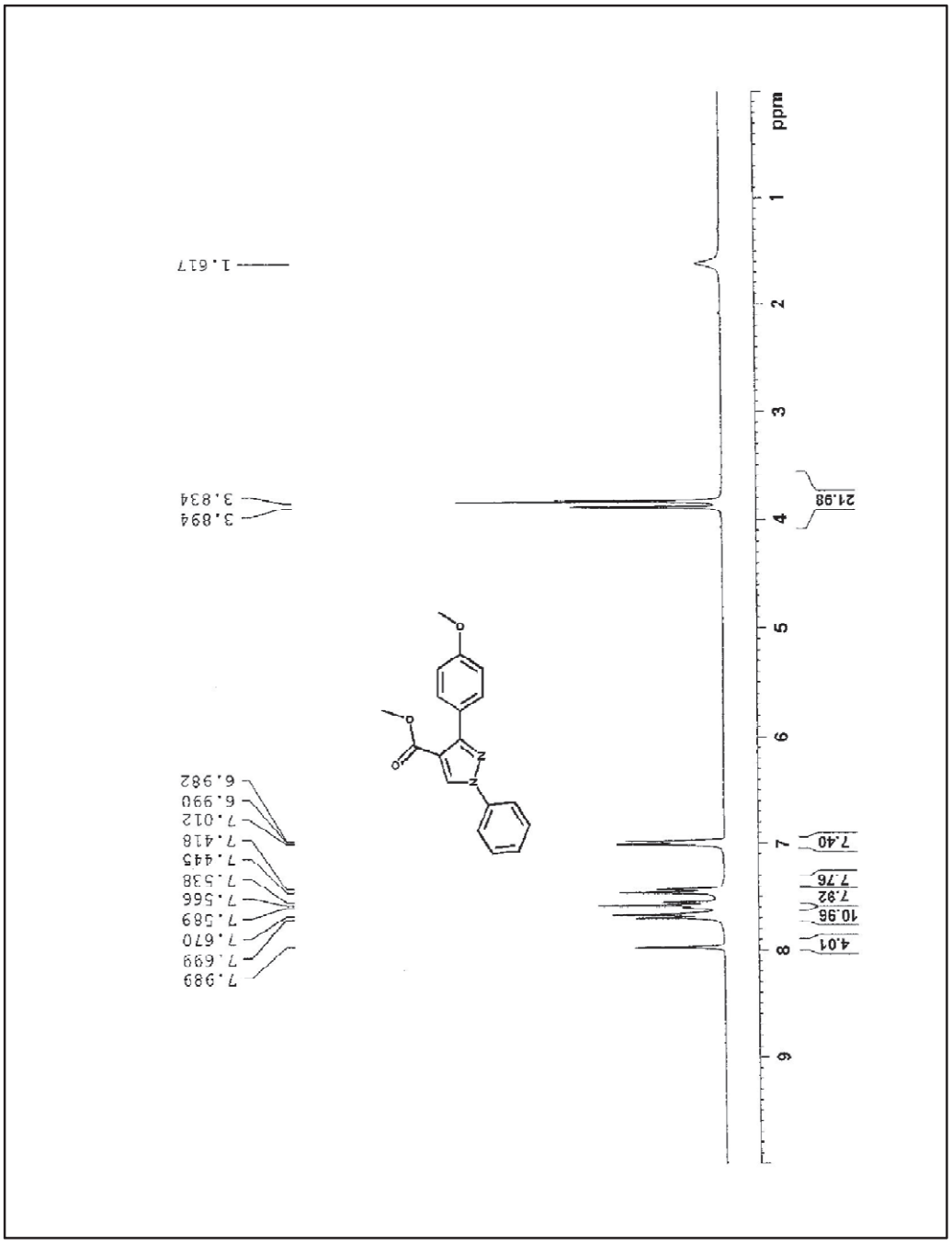
^{1}H NMR (300 MHz, CDCl3): δ 7.68 (d, 1H, *J*=7.5 Hz), 7.26-7.18 (m, 1H), 6.92-6.83(m, 2H,), 4.60-4.53(m, 2H), 4.01-3.94 (m, 1H), 3.89-3.75 (m, 2H); 13C NMR (75 MHz, CDCl3): δ 155.6, 152.8, 132.5, 125.6, 121.8, 117.4, 113.0, 70.6, 69.2, 45.9; HRMS (ESI-TOF) m/z: [M+H]+ Calculated for $C_{10}H_{10}NO_2$:176.0712, found:176.0710; IR (KBr) cm^{-1}: 1026.3, 1209.2, 1410.4, 1560.3, 1710.1, 2896.3, 3010.5, 3566.9; Anal. Calcd for $C_{10}H_9NO_2$: C: 68.56; H: 5.18; N: 8.00%, found: C: 68.58; H: 5.16; N: 8.01%

4*H*-Chromeno[4,3-*c*]isoxazole (7c)

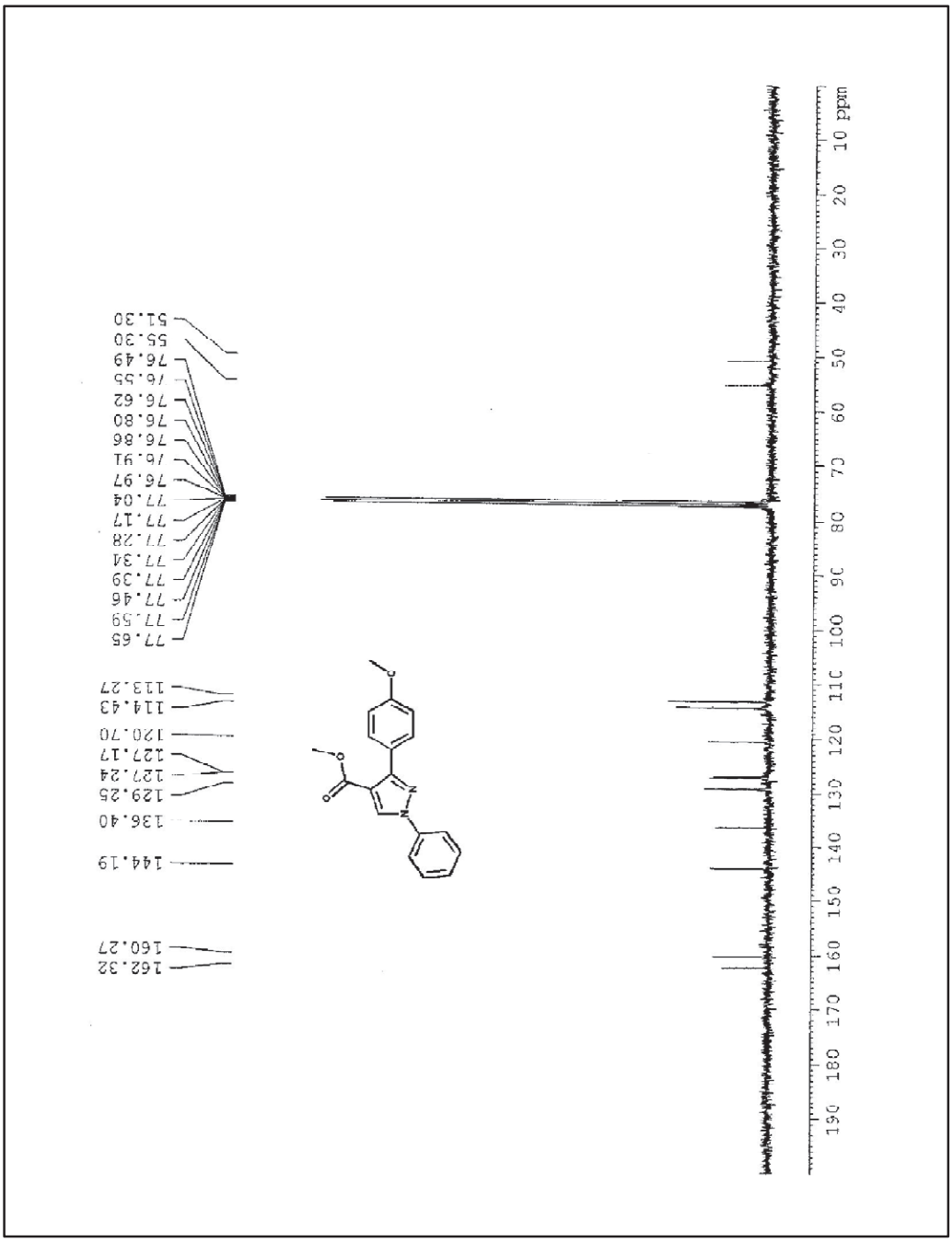


Yield: 90%, (0.155 g); M.p. 42- 43 ^{0}C (Lit: 42 ^{0}C); Characteristics: White crystalline solid; ^{1}H NMR (300 MHz, CDCl3): δ 8.24(s, 1H), 7.91 (dd, 1H, J=7.6, 1.5 Hz), 7.42-7.36(m, 1H,), 7.16-7.04(m, 2H), 5.27 (s, 2H); 13C NMR (75 MHz, CDCl3): δ 154.8, 153.6, 150.6, 132.1, 124.5, 122.4, 117.9, 113.9, 111.1, 61.3; HRMS (ESI-TOF) m/z: [M+H]+ Calculated for $C_{10}H_8NO_2$:174.0555, found:174.0553; IR (KBr) cm^{-1}: 1045.6, 1211.8,1496.8, 1501.1, 1705.1, 2988.9, 3112.5, 3496.9; Anal. Calcd for $C_{10}H_7NO_2$: C: 69.36; H: 4.07; N: 8.09%, found: C: 69.38; H: 4.09; N: 8.07%

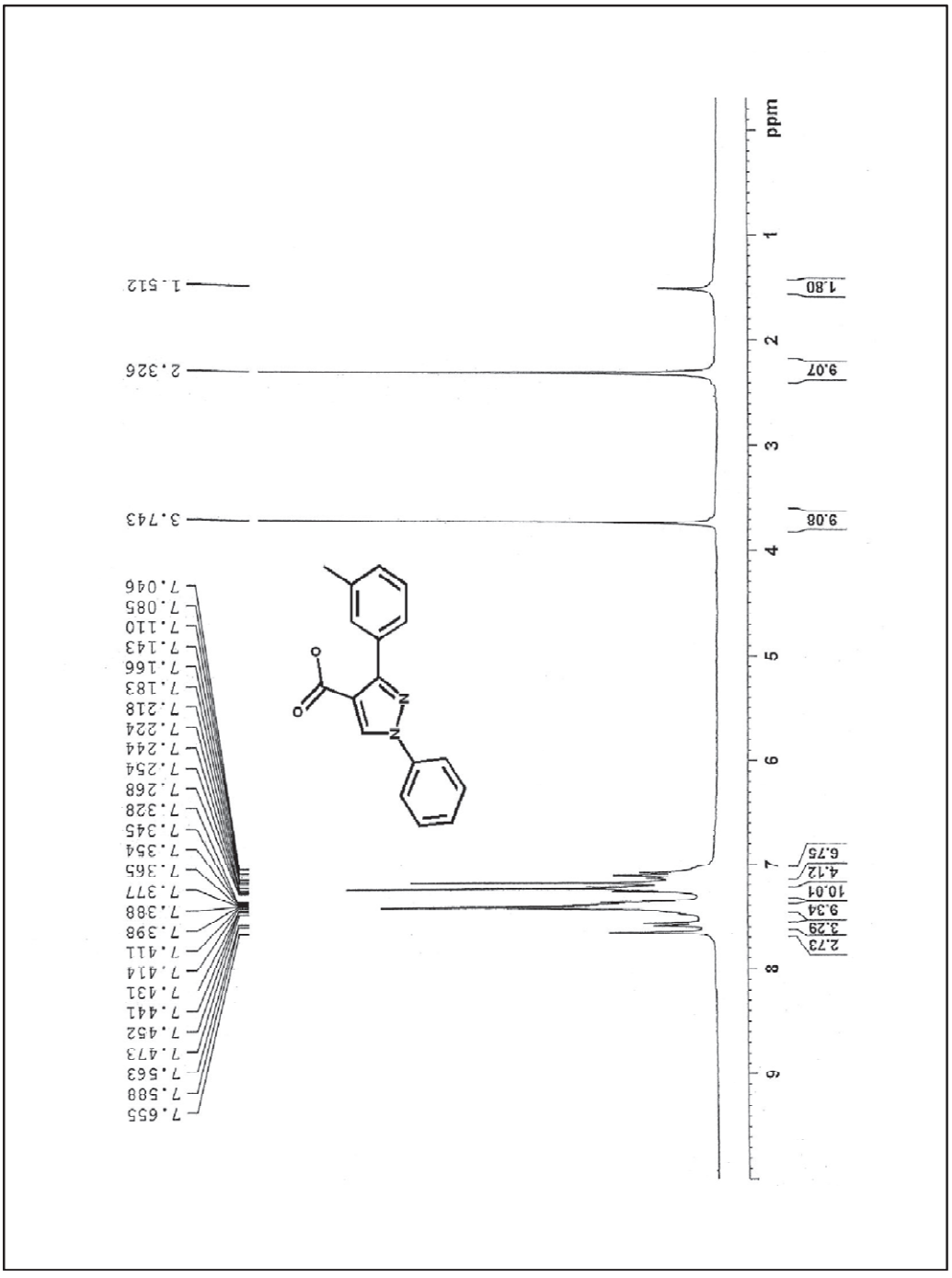
2. [1]HNMR and [13]CNMR Spectra of the Compounds (4a-4o, 5a-5d, 6a-6i, 7a-7c):



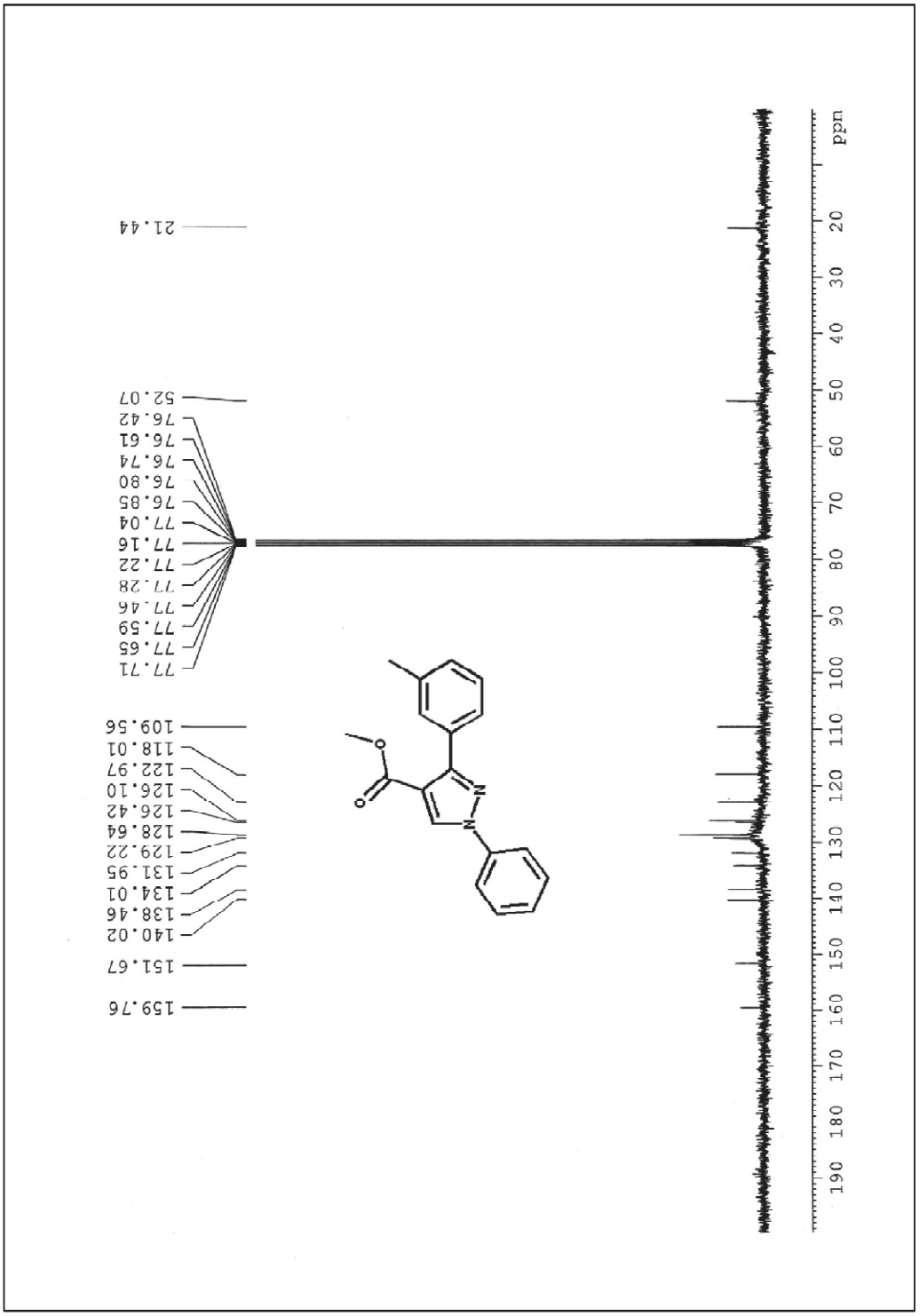
[1]H NMR of Compound 4a



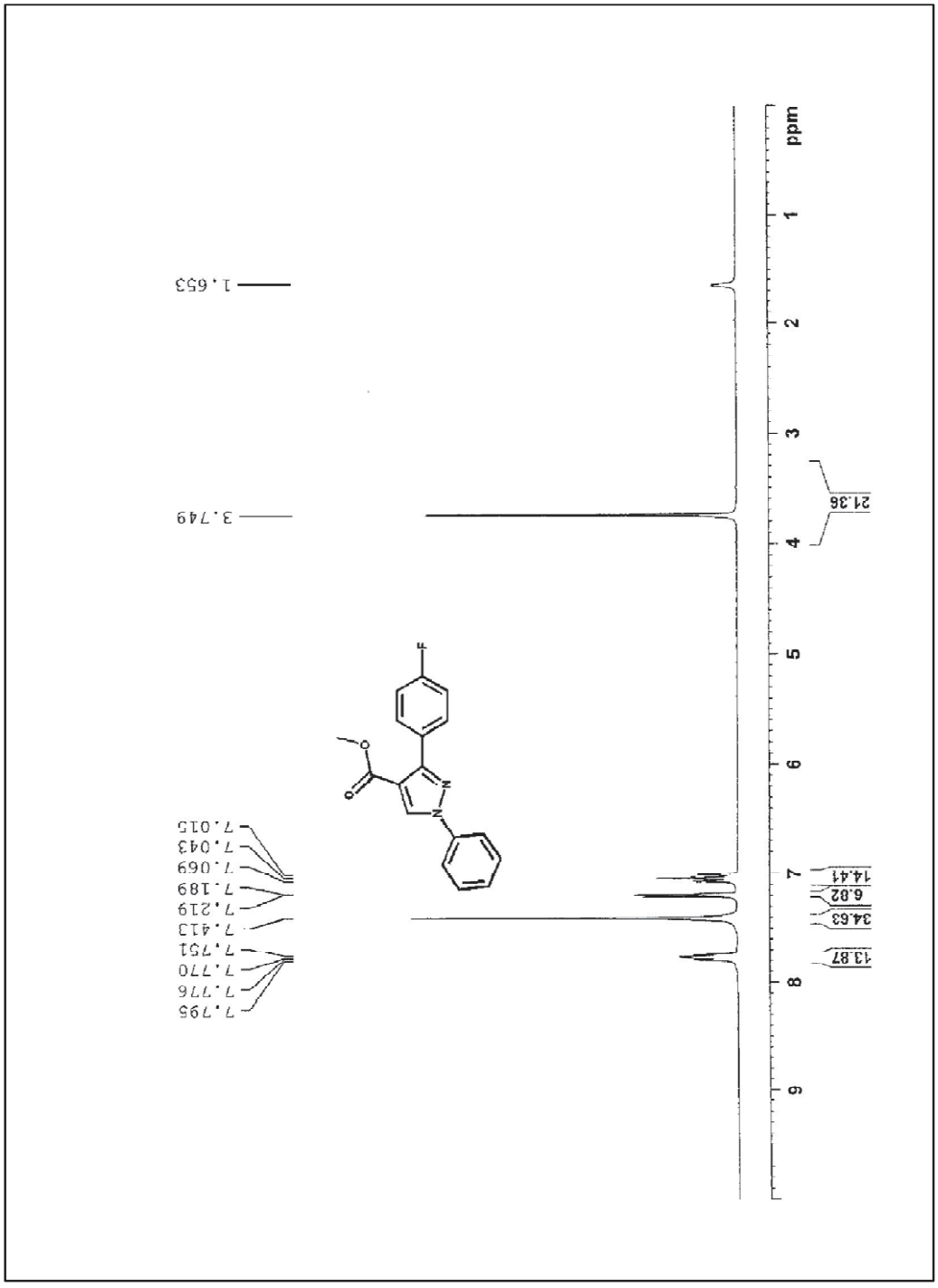
^{13}C NMR of Compound 4a



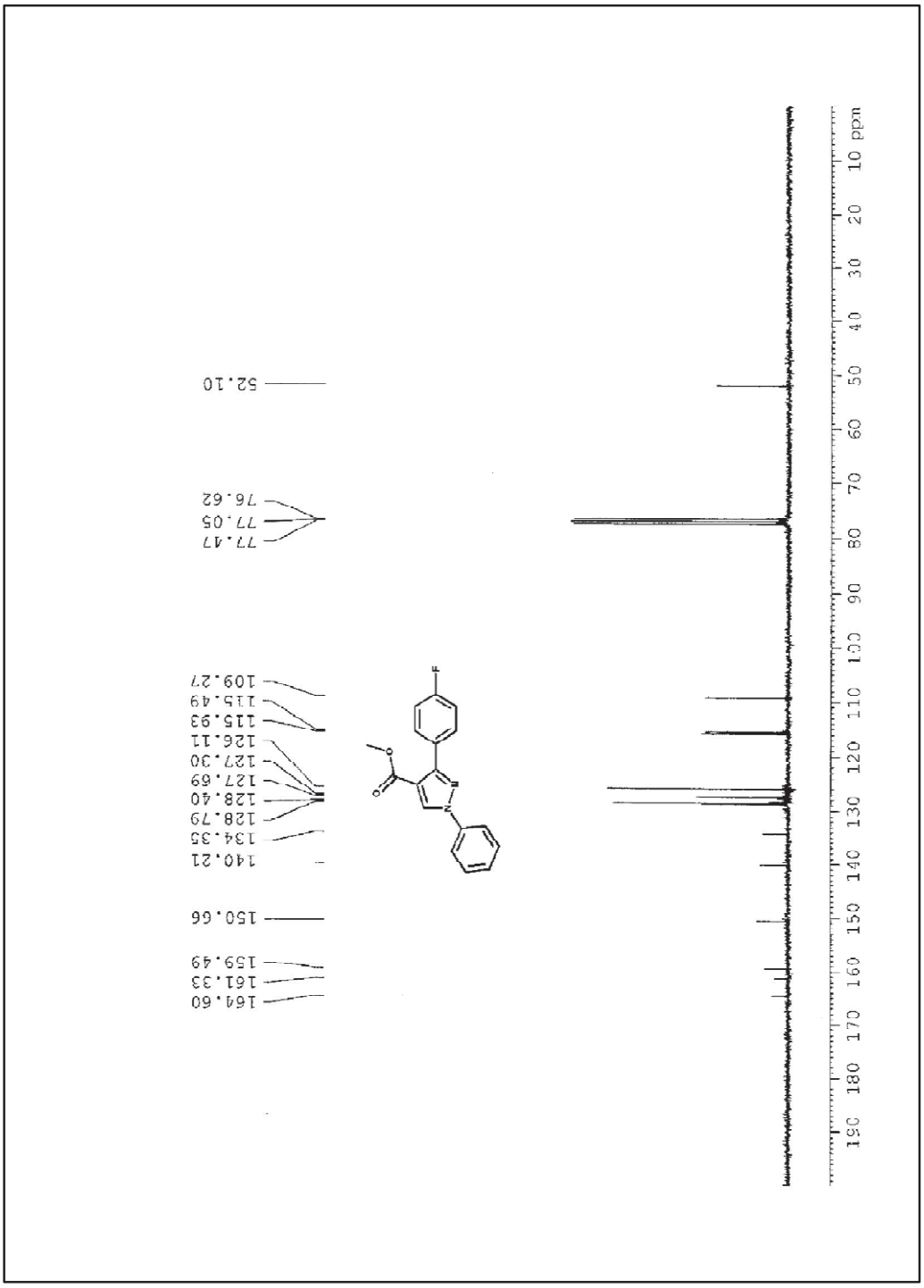
[1]H NMR of Compound 4b



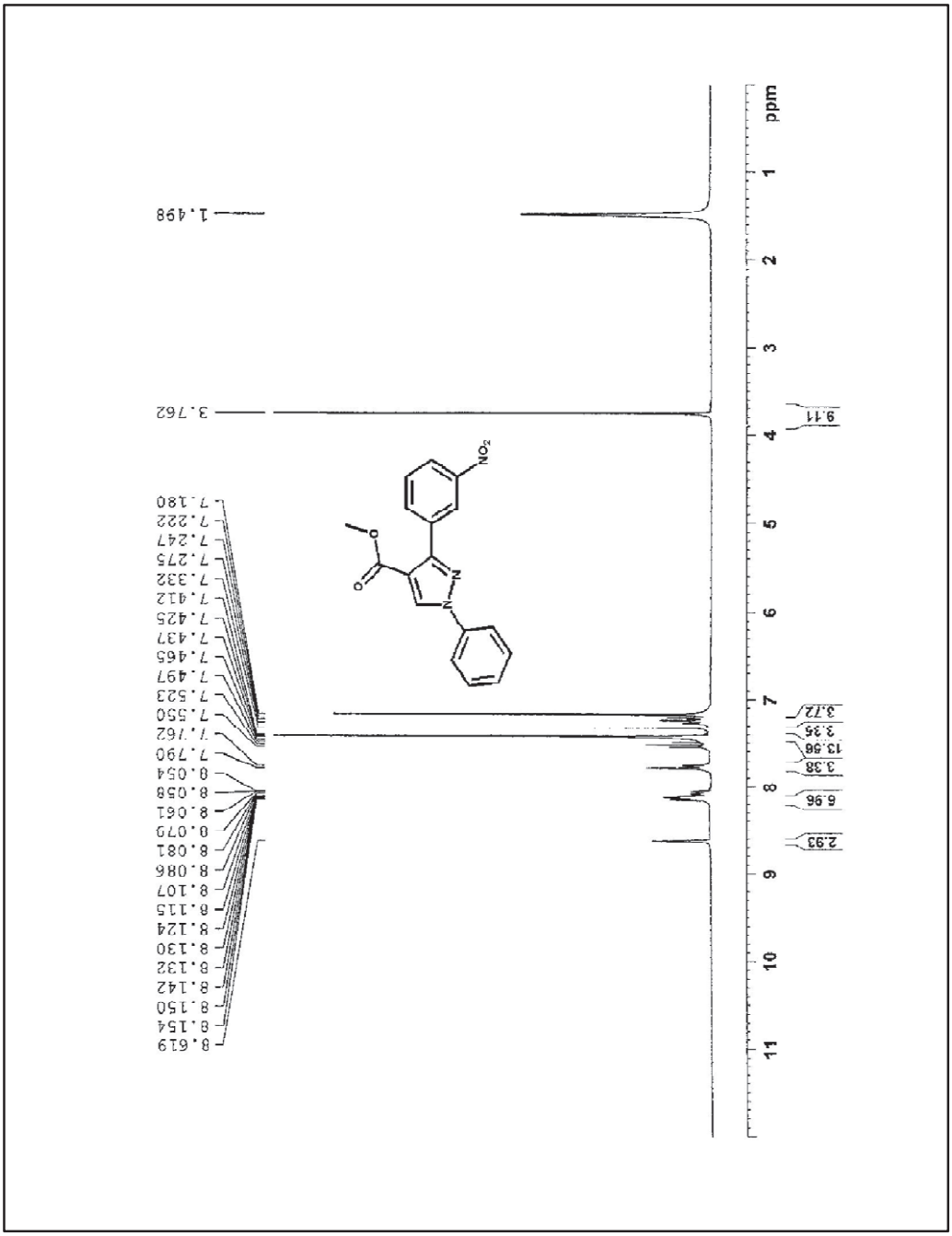
^{13}C NMR of Compound 4b



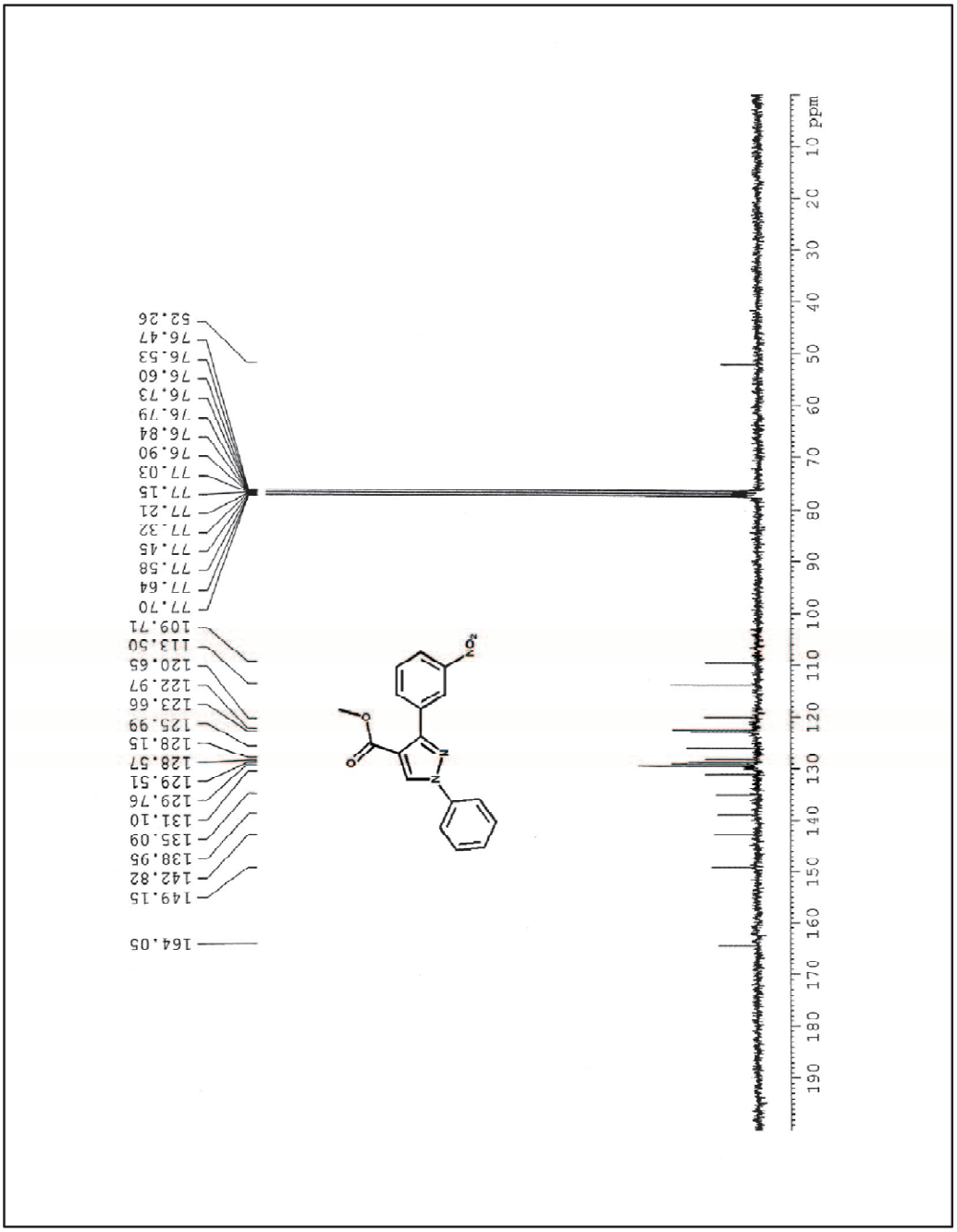
[1]H NMR of Compound 4c



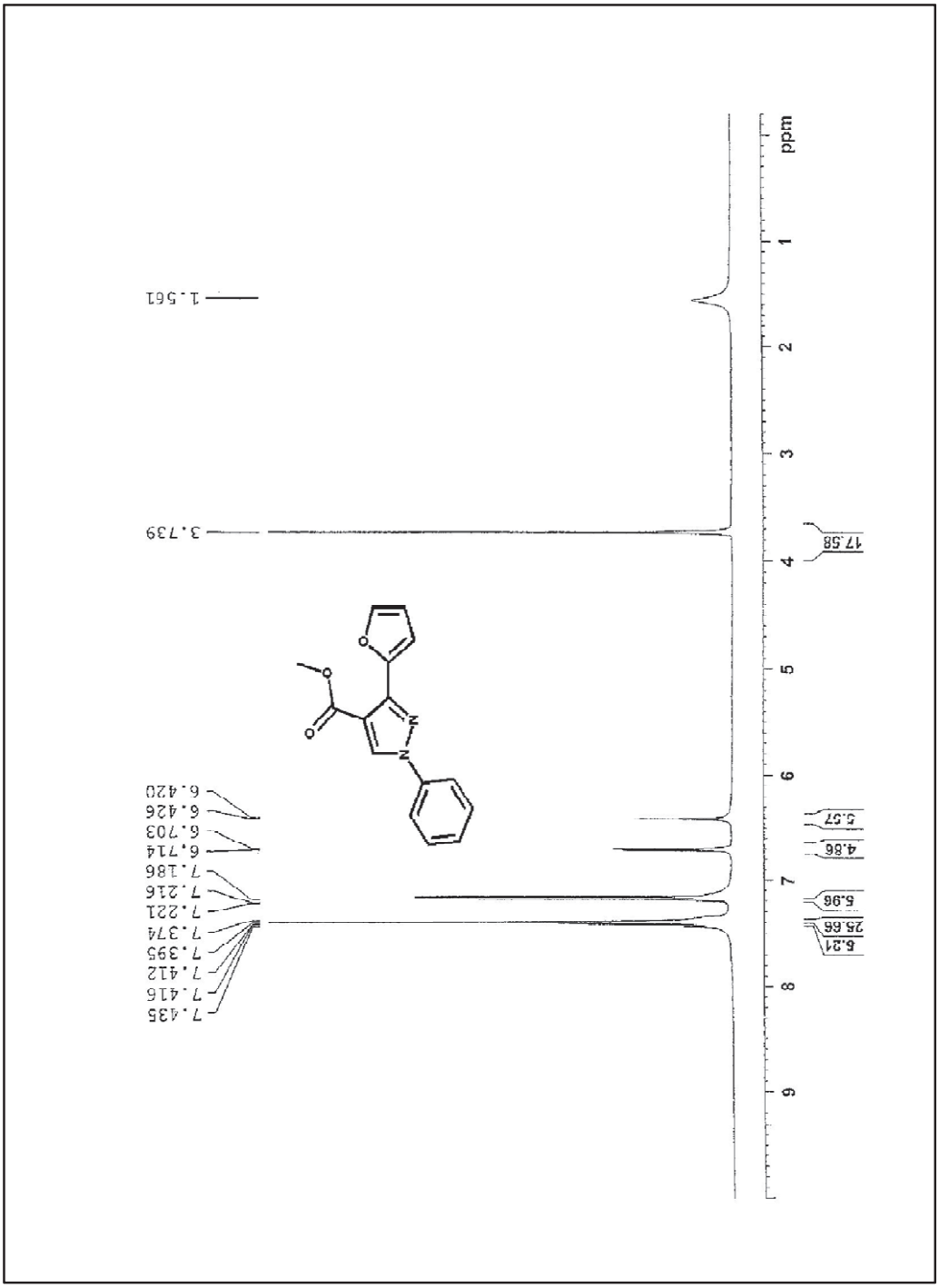
^{13}C NMR of Compound 4c



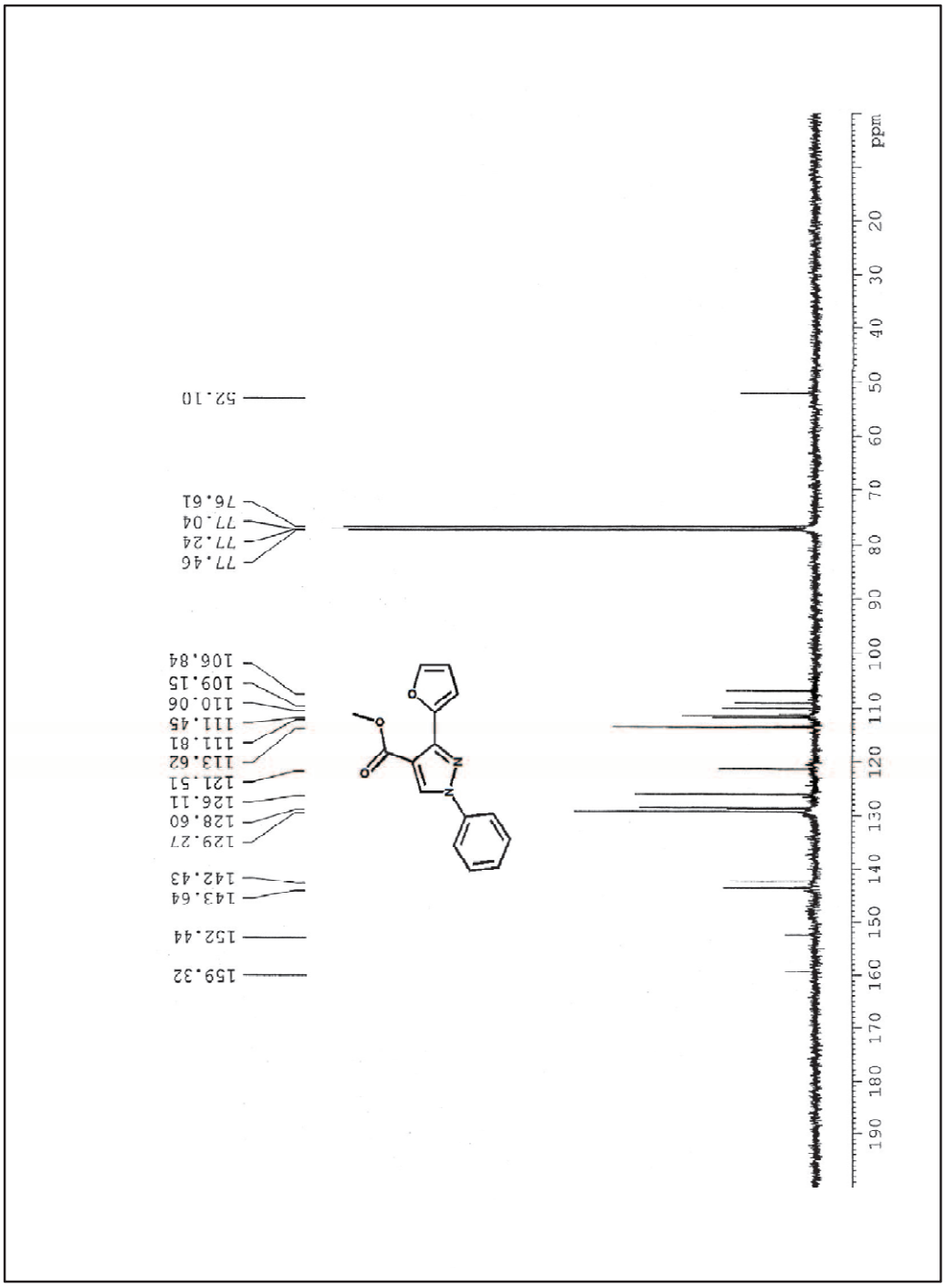
^{1}H NMR of Compound 4d



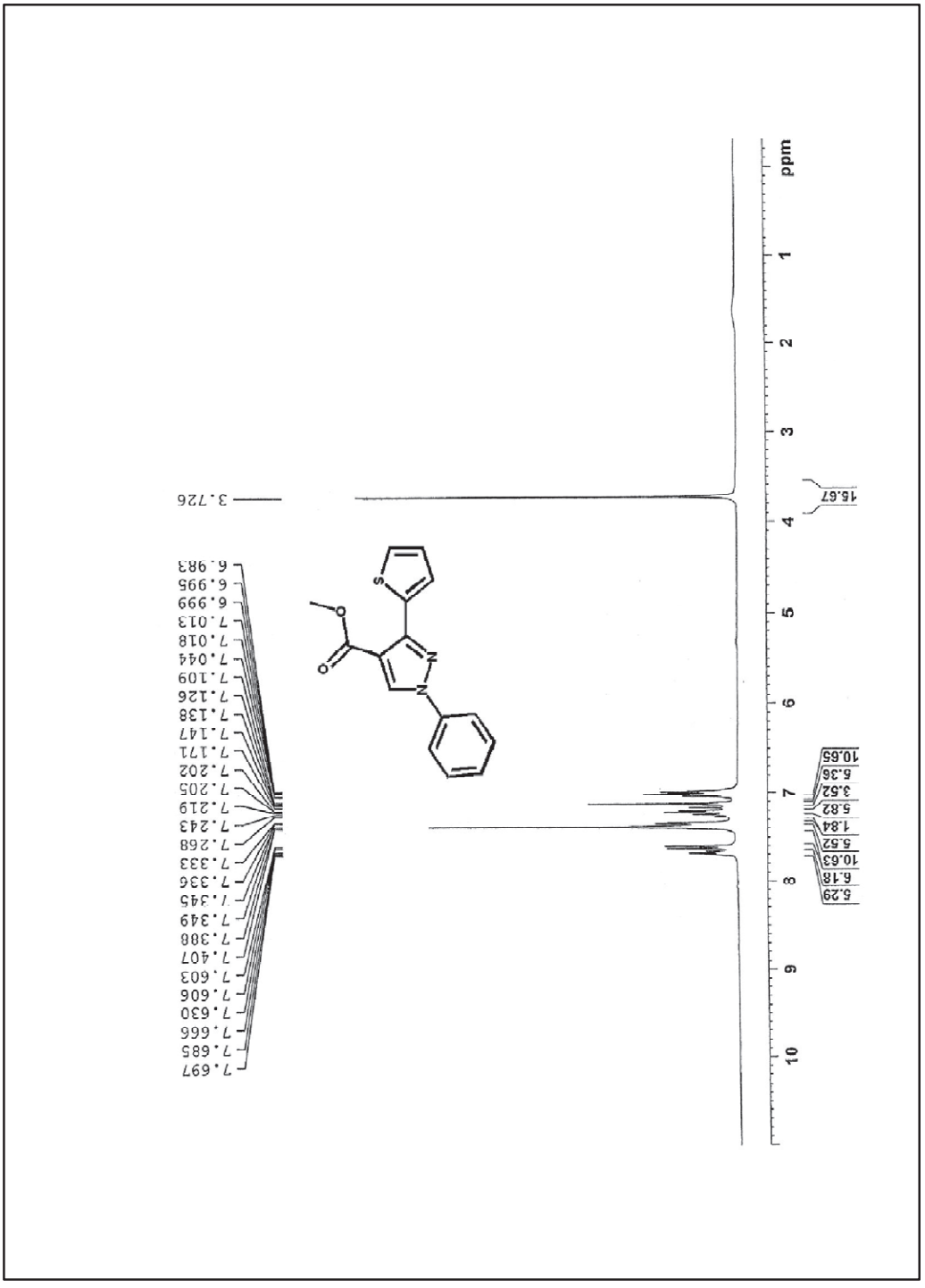
^{13}C NMR of Compound 4d



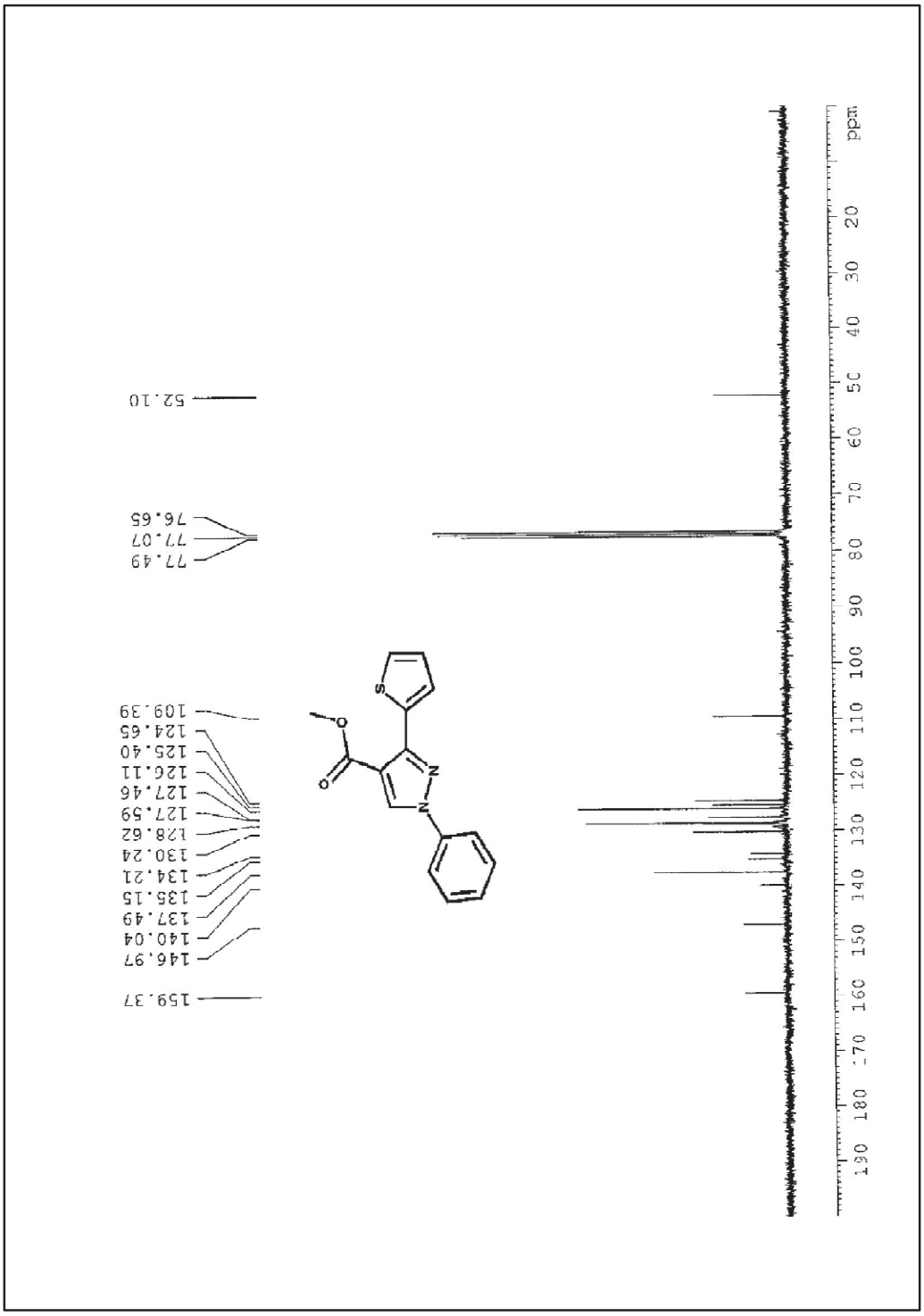
^{1}H NMR of Compound 4e



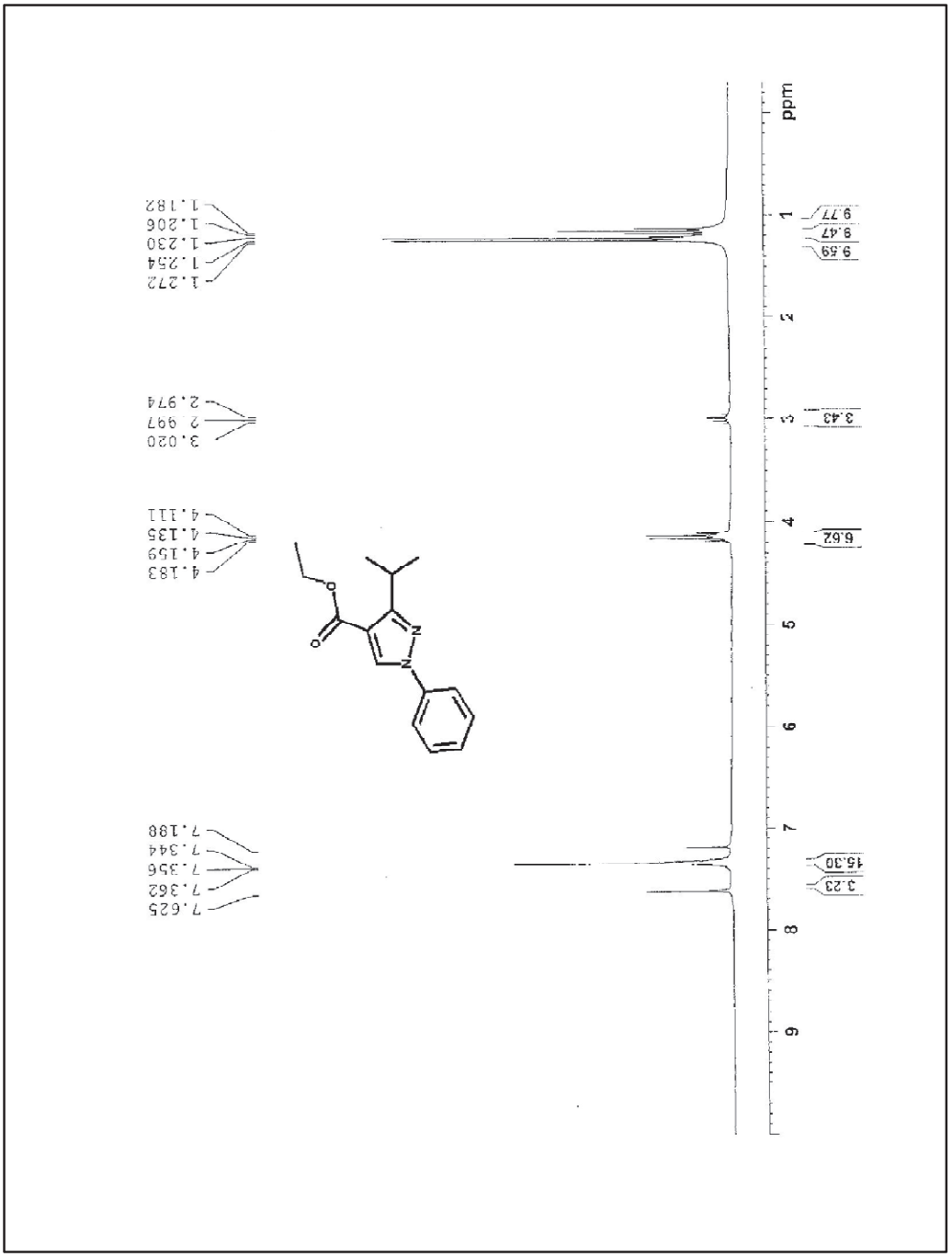
^{13}C NMR of Compound 4e



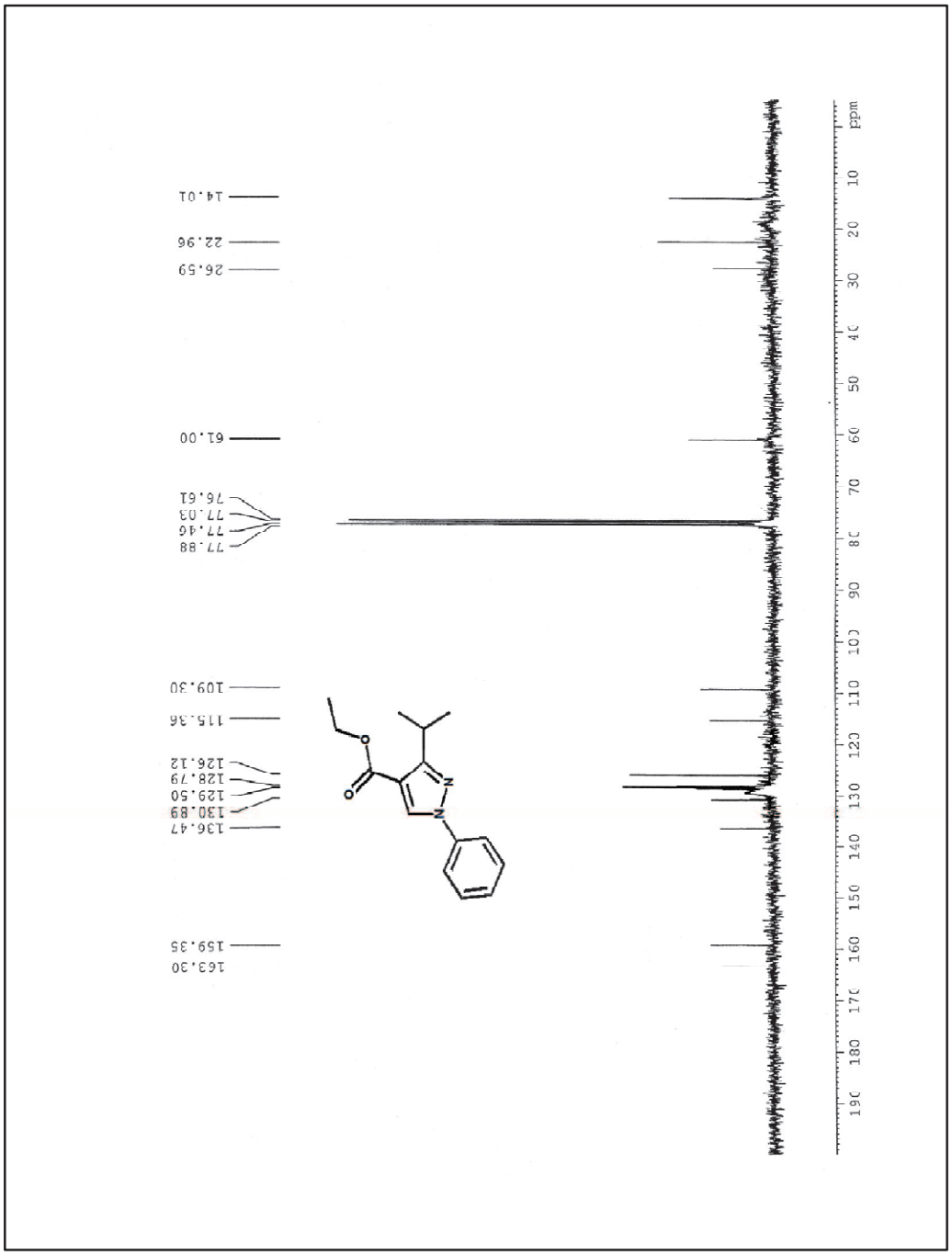
^{1}H NMR of Compound 4f



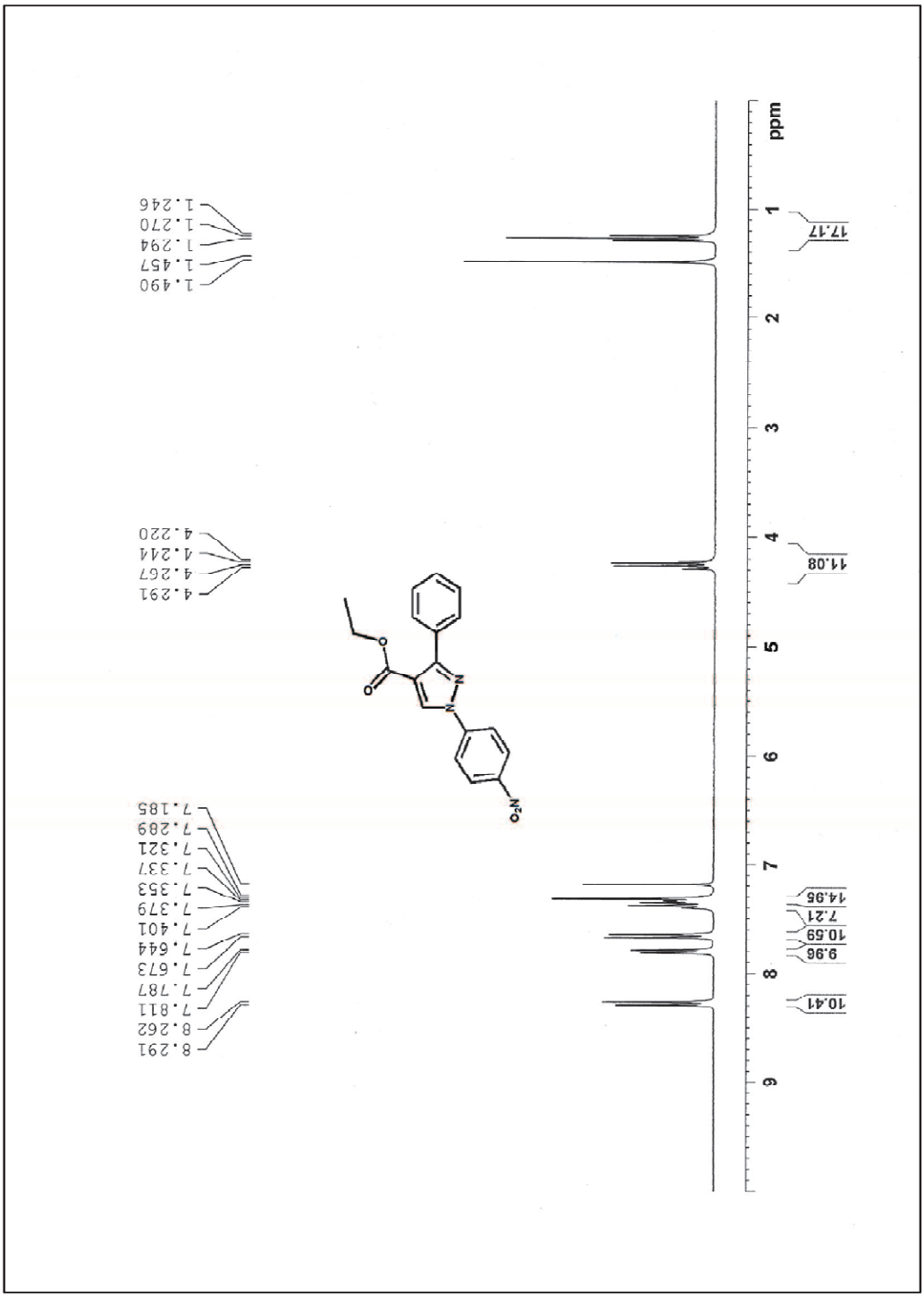
^{13}C NMR of Compound 4f



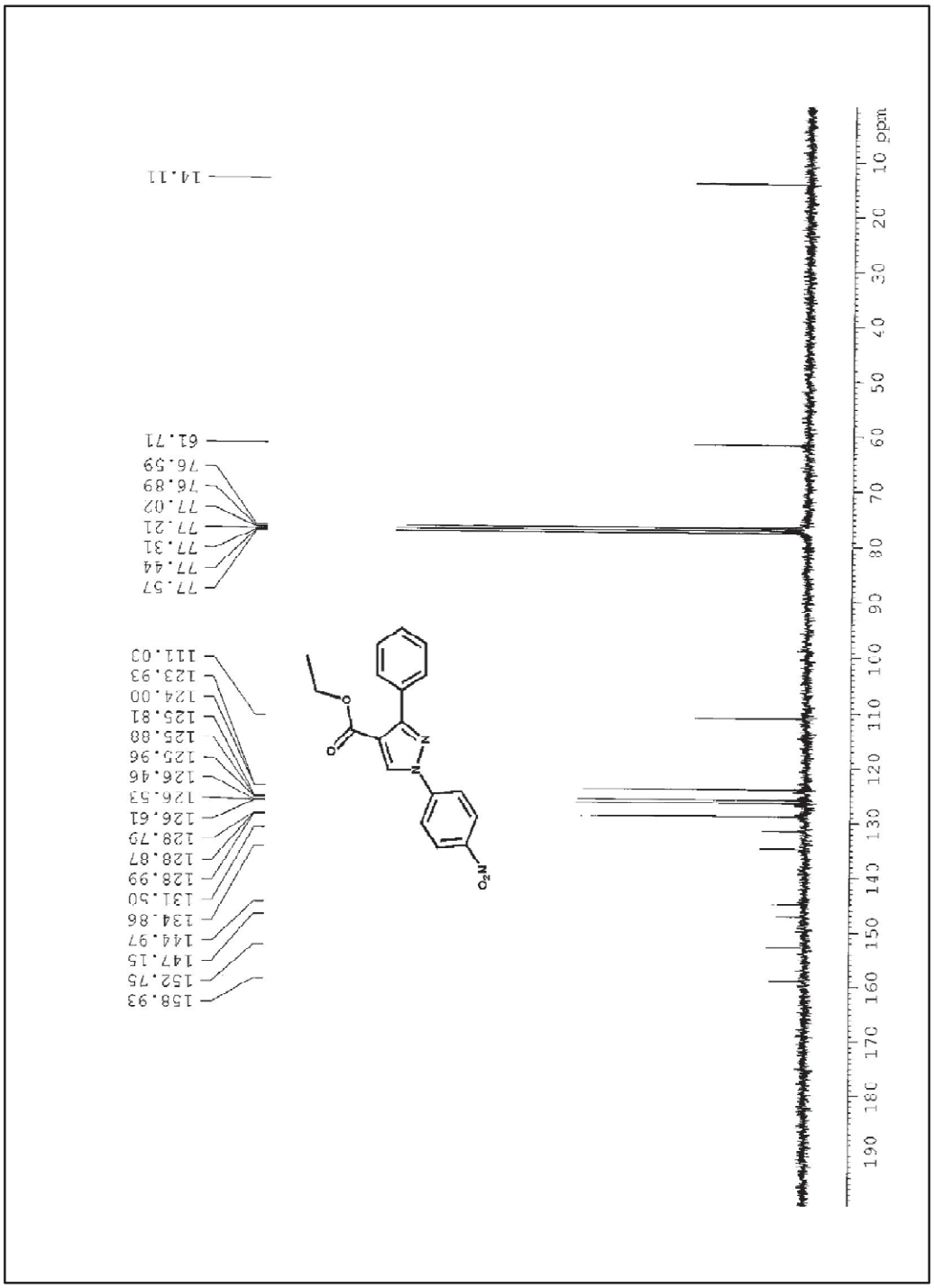
^{1}H NMR of Compound 4g



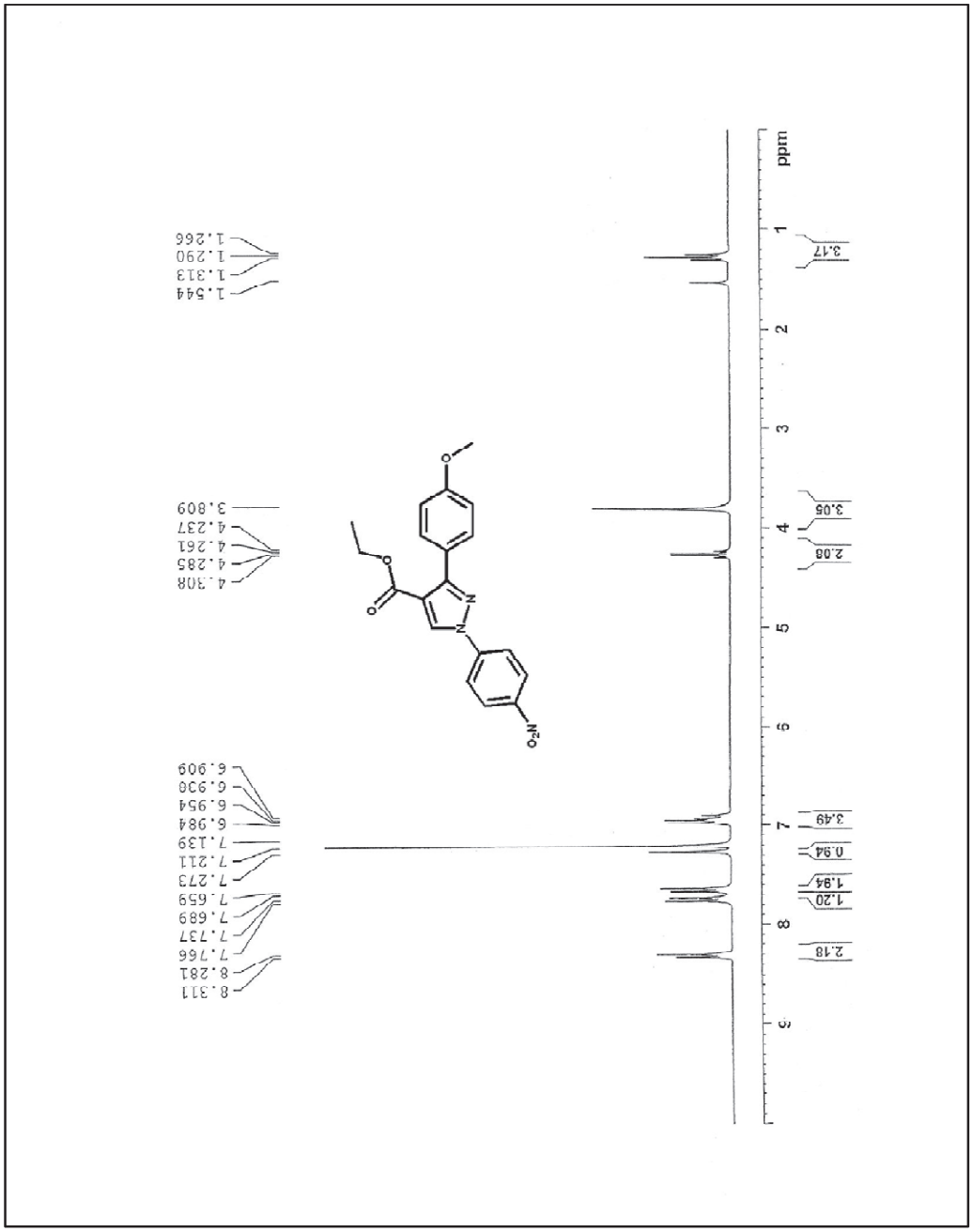
^{13}C NMR of Compound 4g



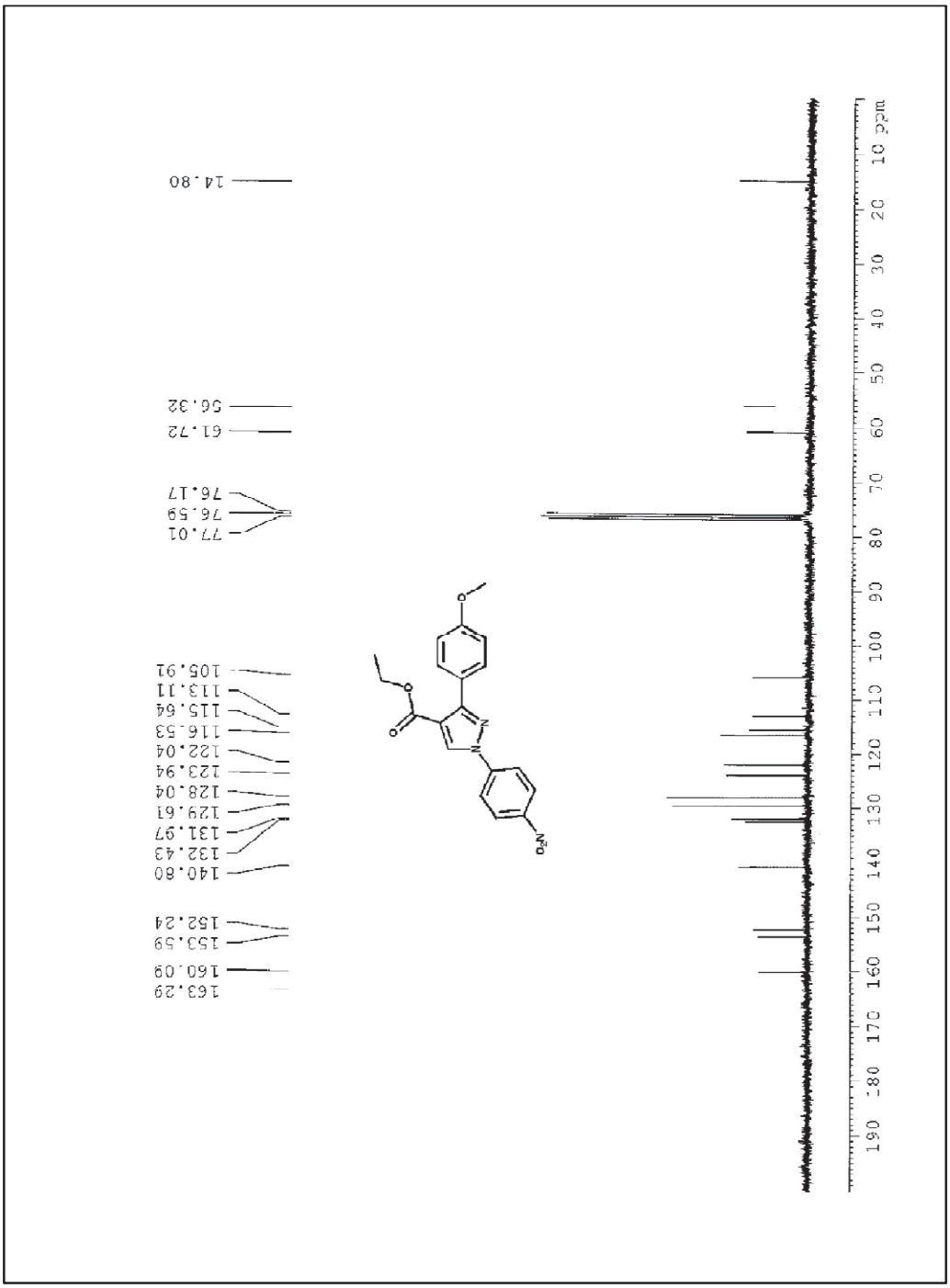
[1]H NMR of Compound 4h



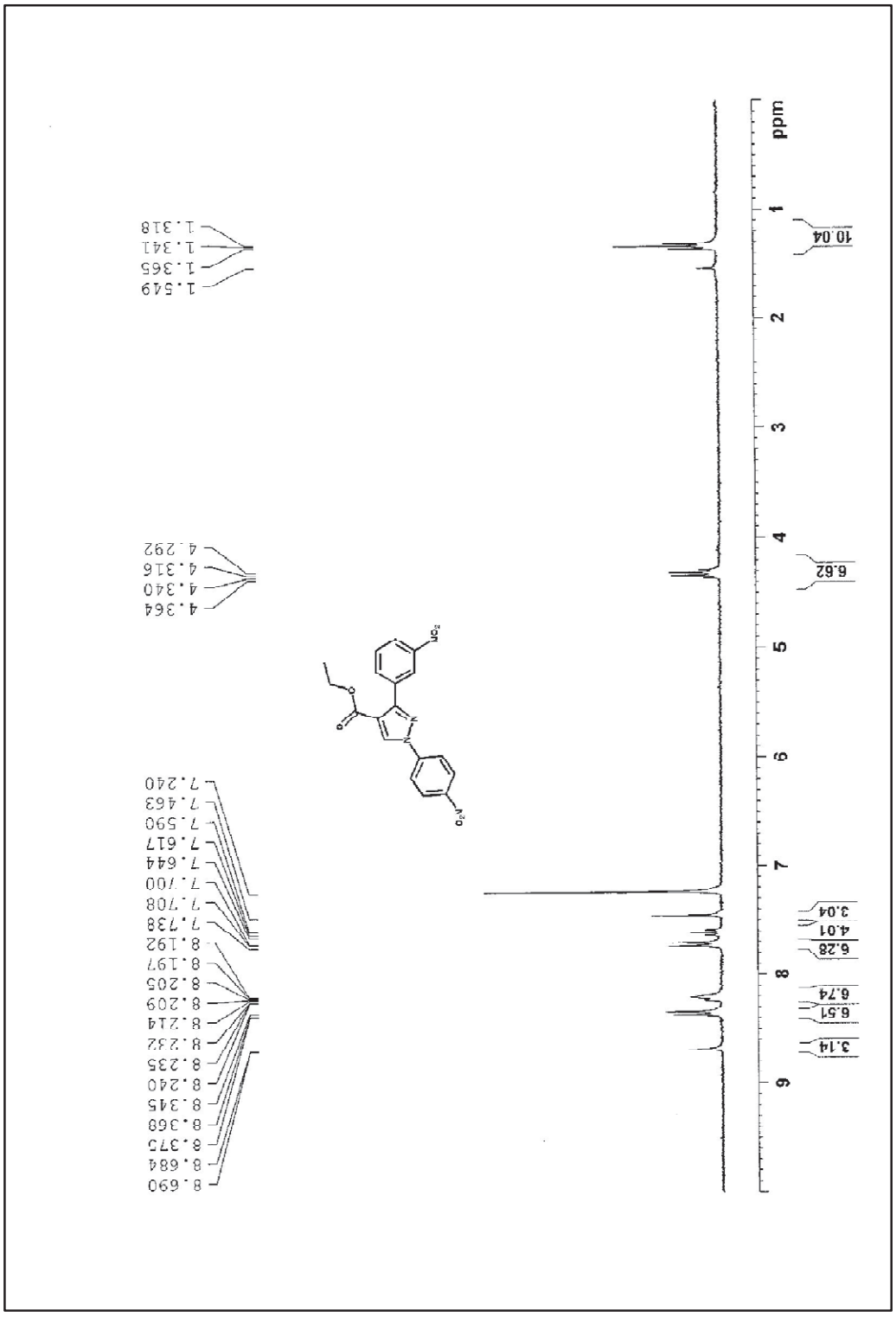
^{13}C NMR of Compound 4h



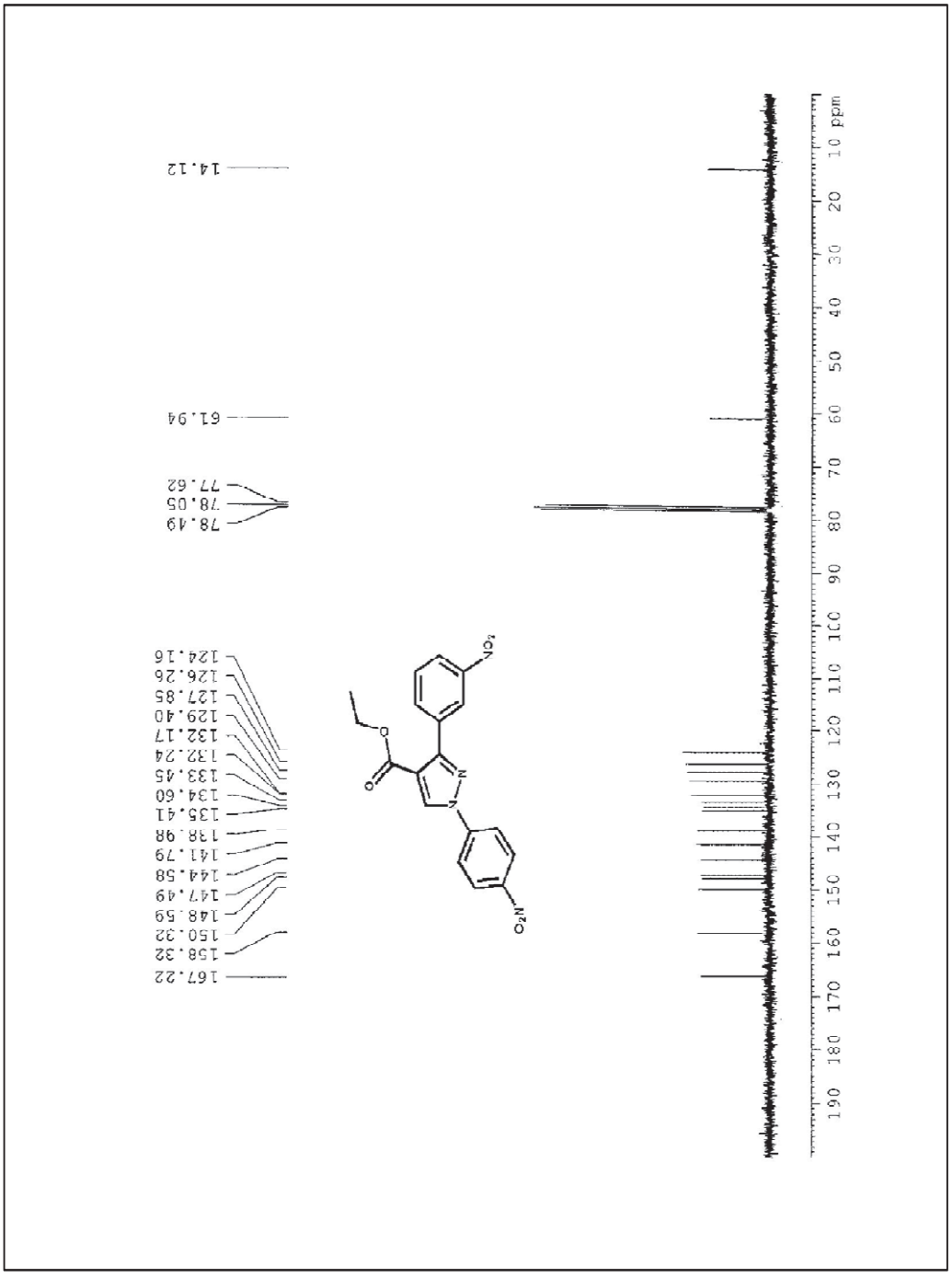
^{1}H NMR of Compound 4i



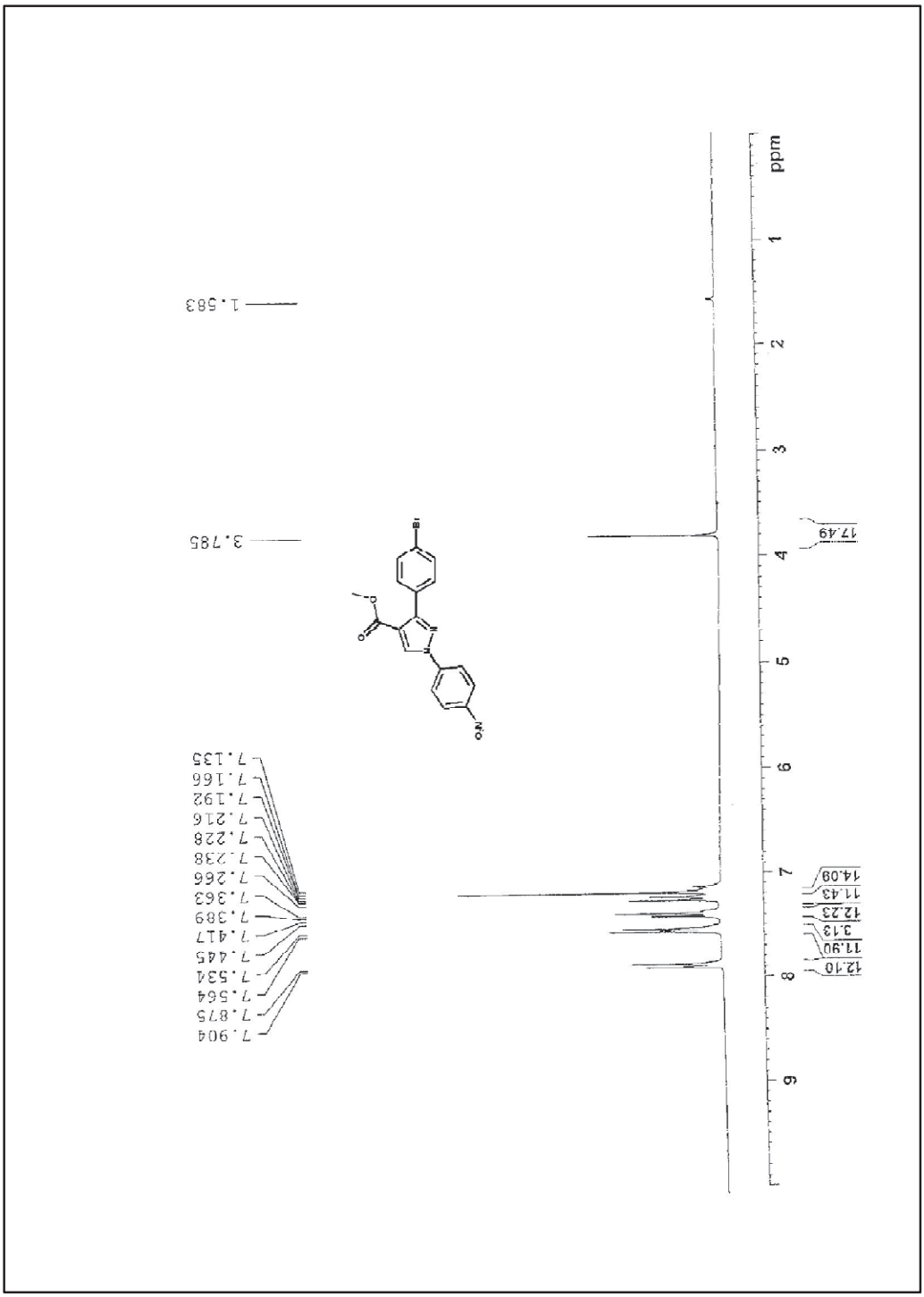
^{13}C NMR of Compound 4i



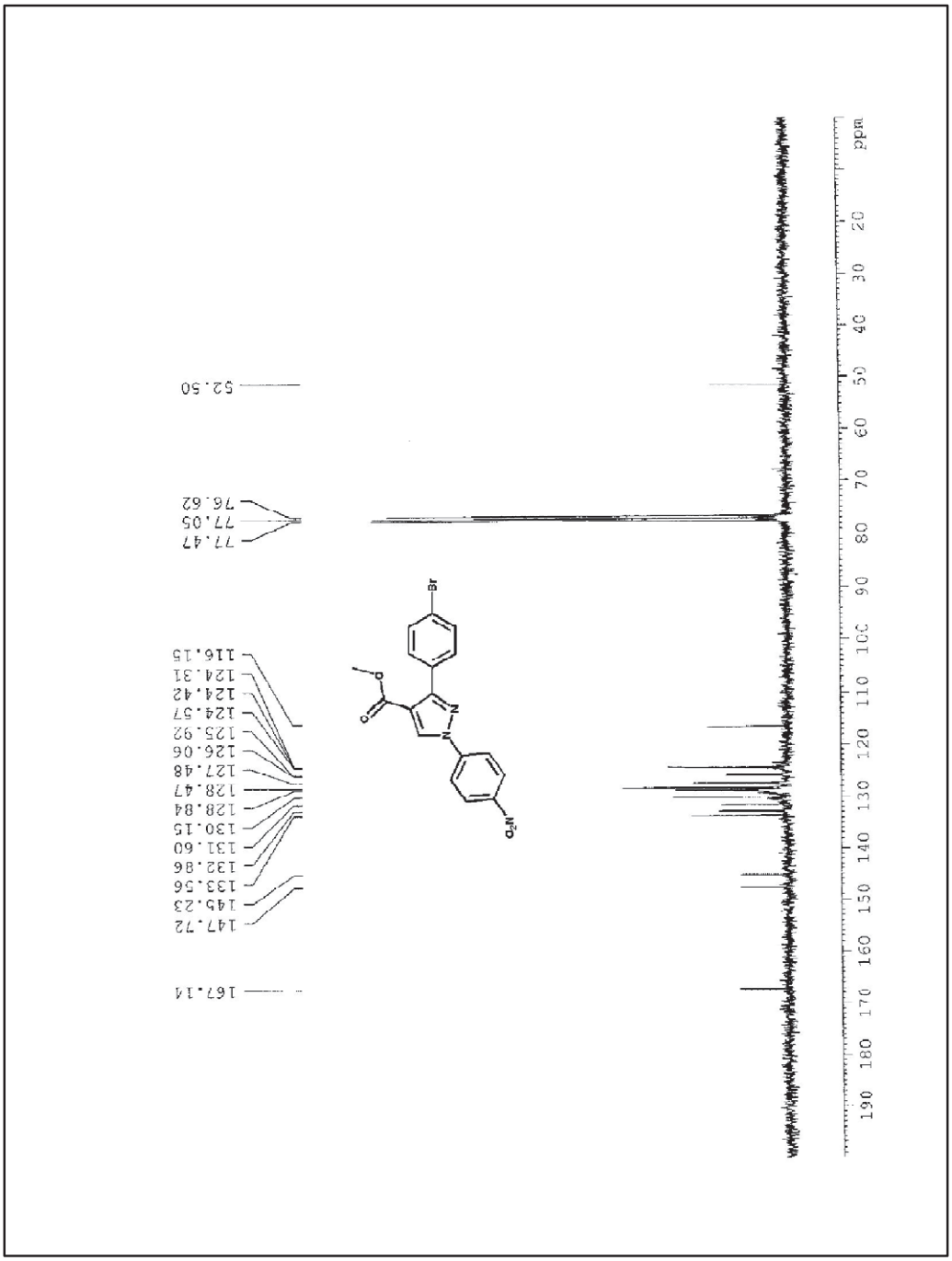
[1]H NMR of Compound 4j



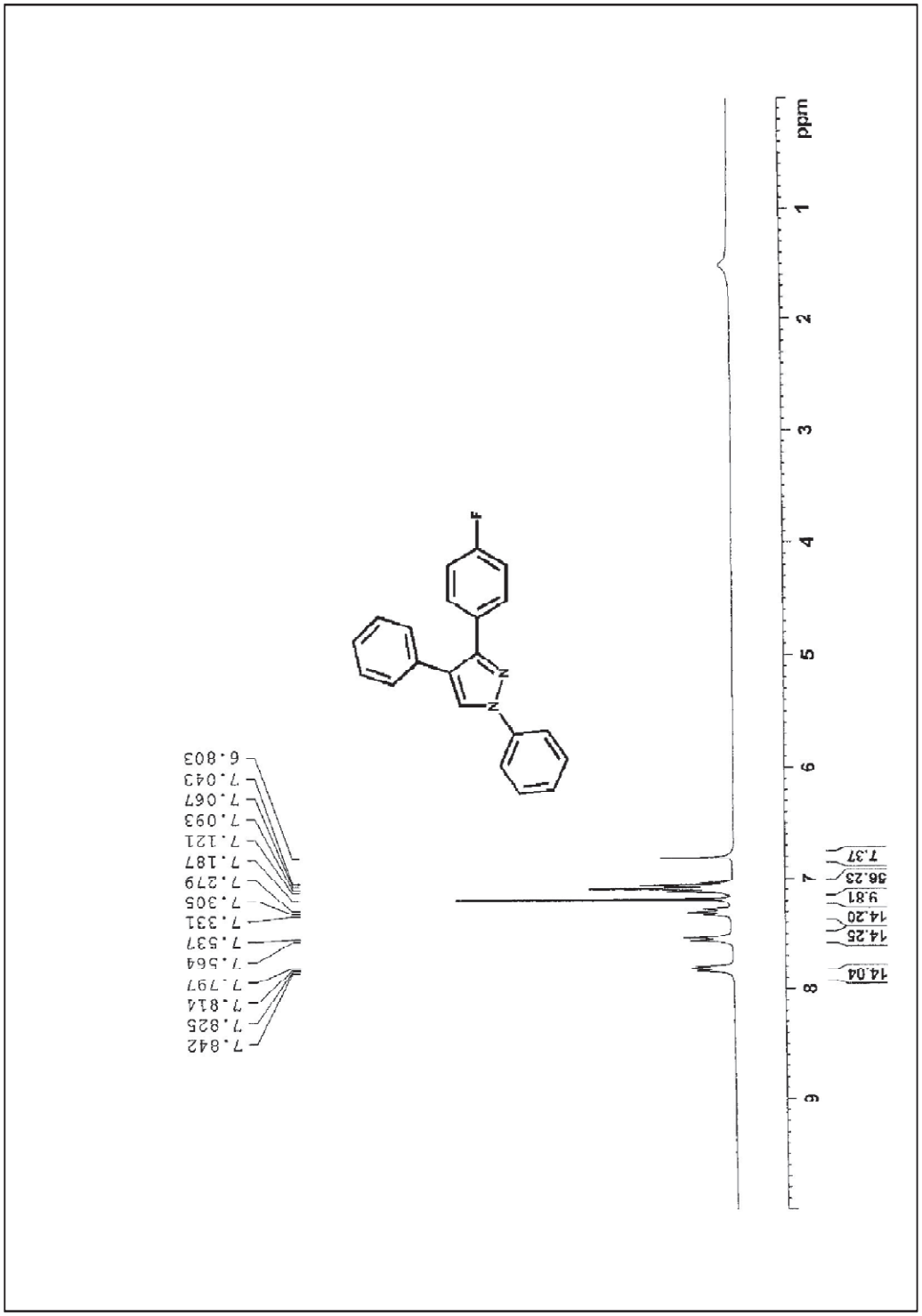
^{13}C NMR of Compound 4j



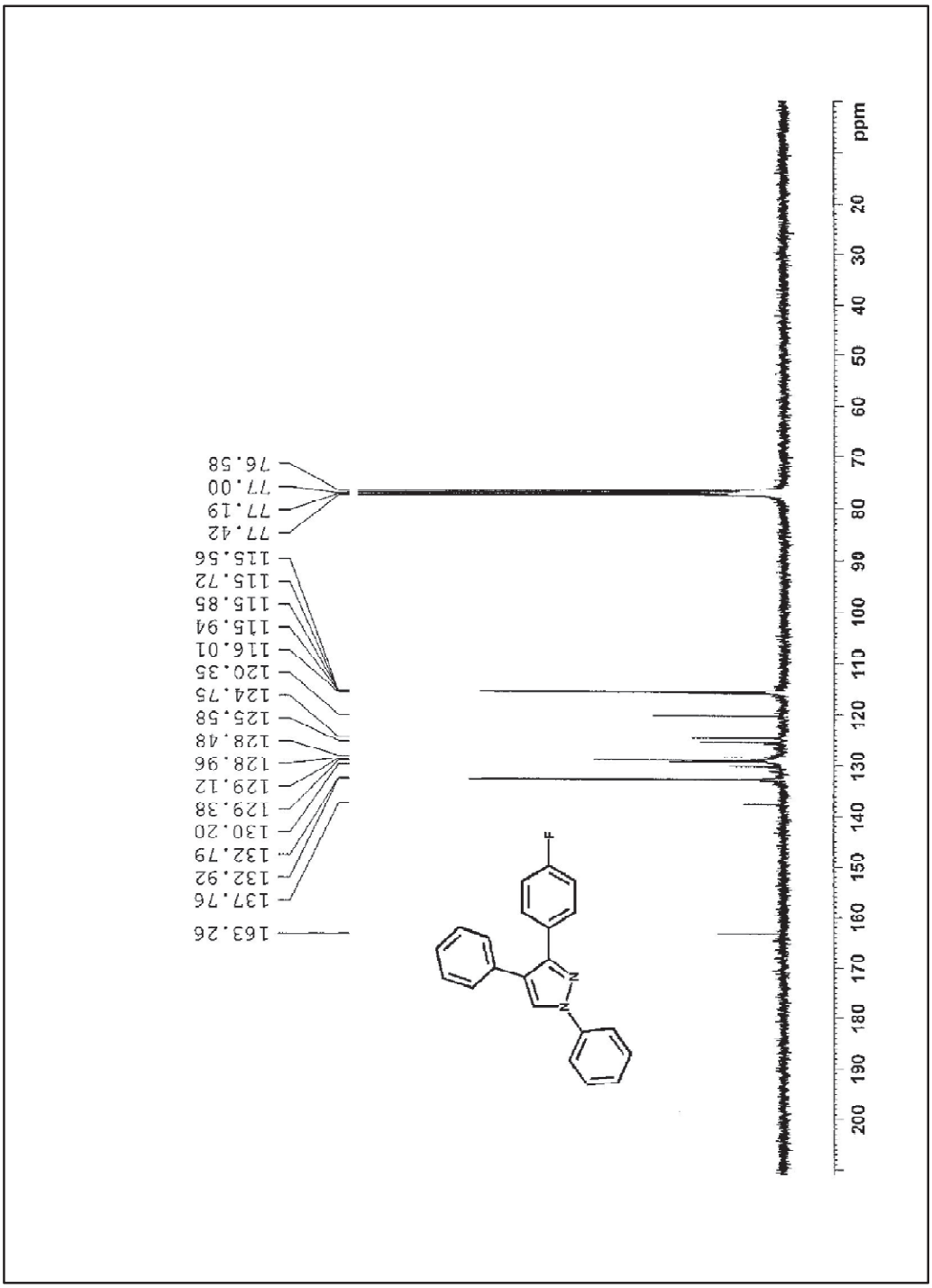
^{13}C NMR of Compound 4k



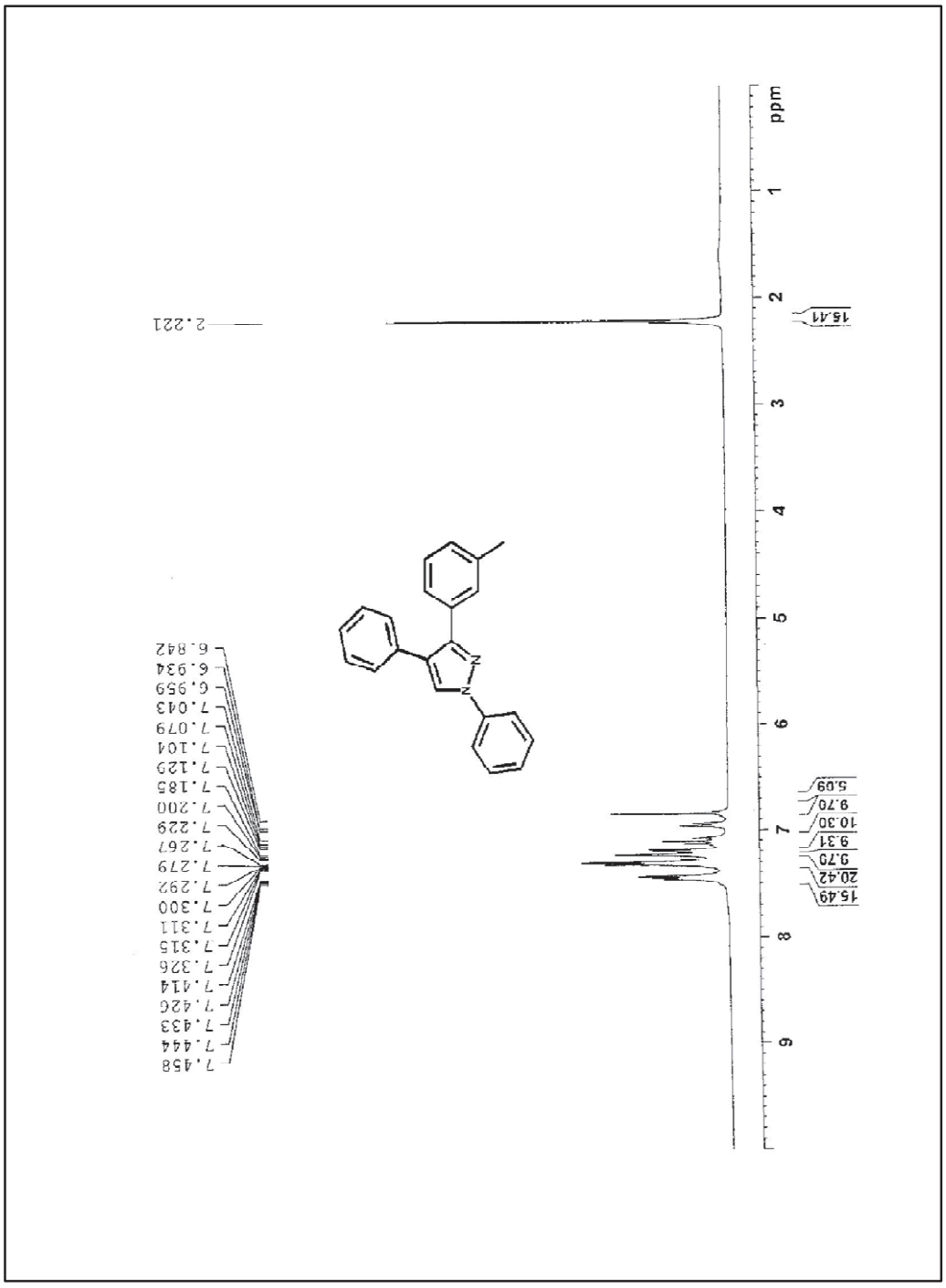
^{13}C NMR of Compound 4k



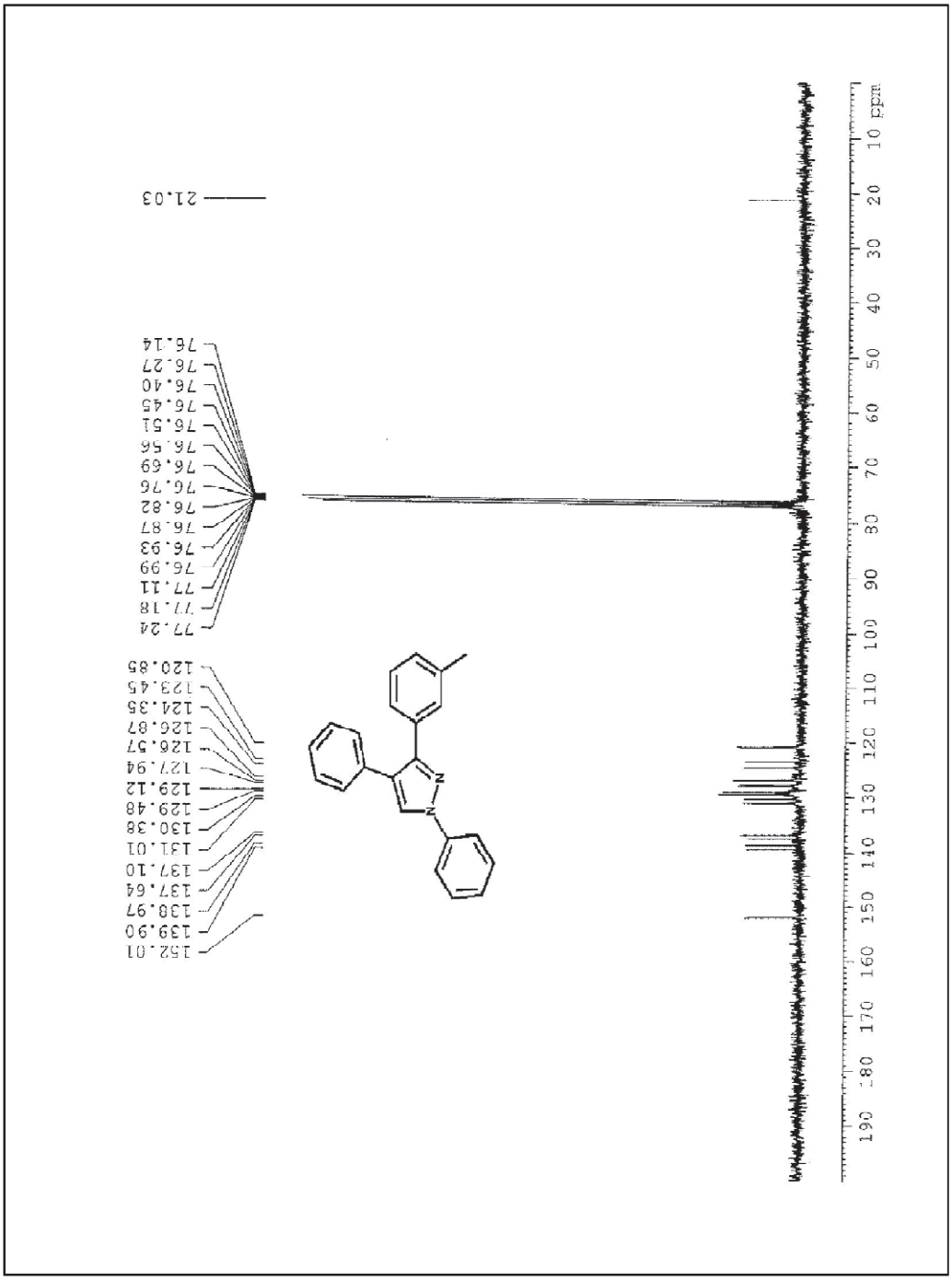
^{1}H NMR of Compound 4l



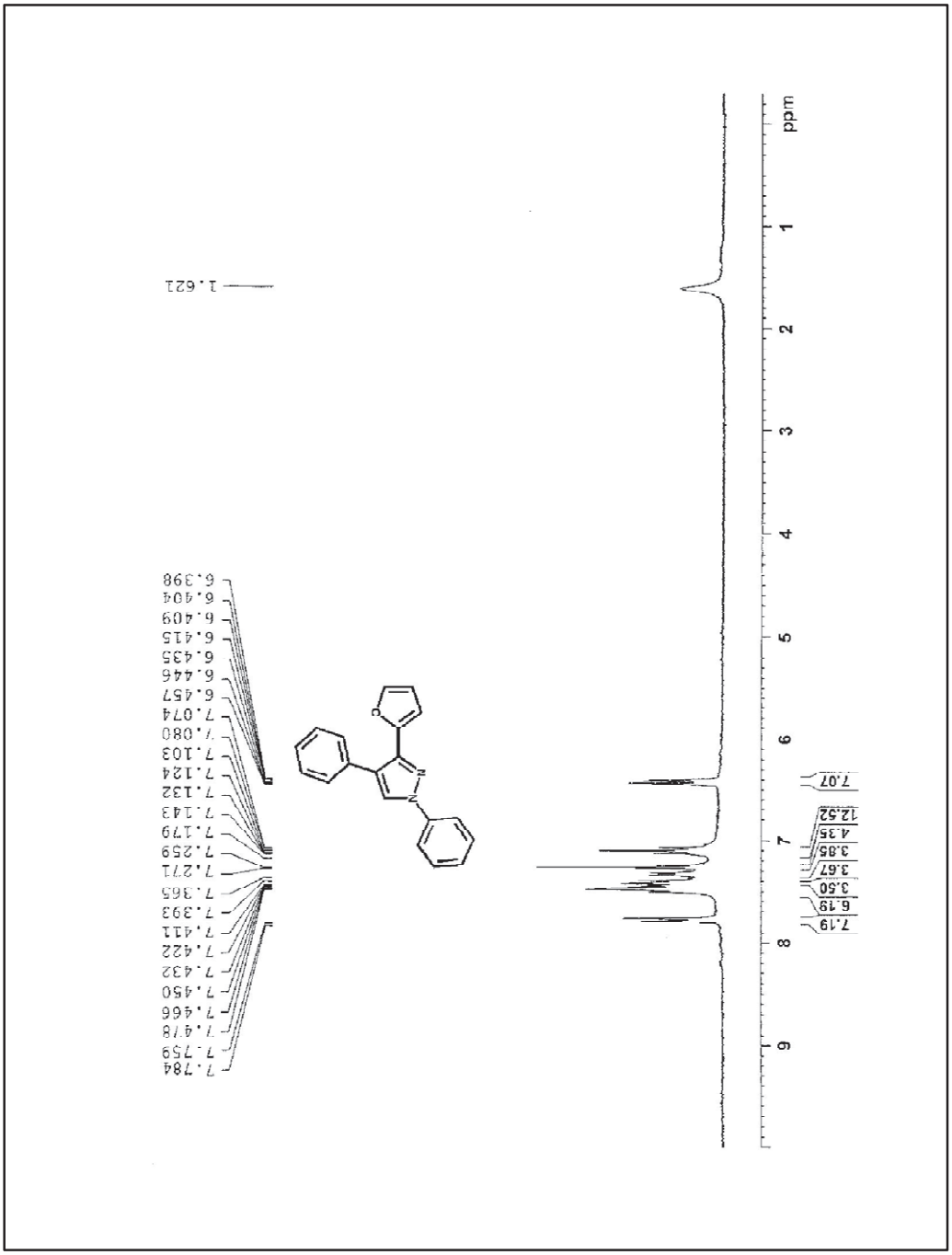
^{13}C NMR of Compound 4l



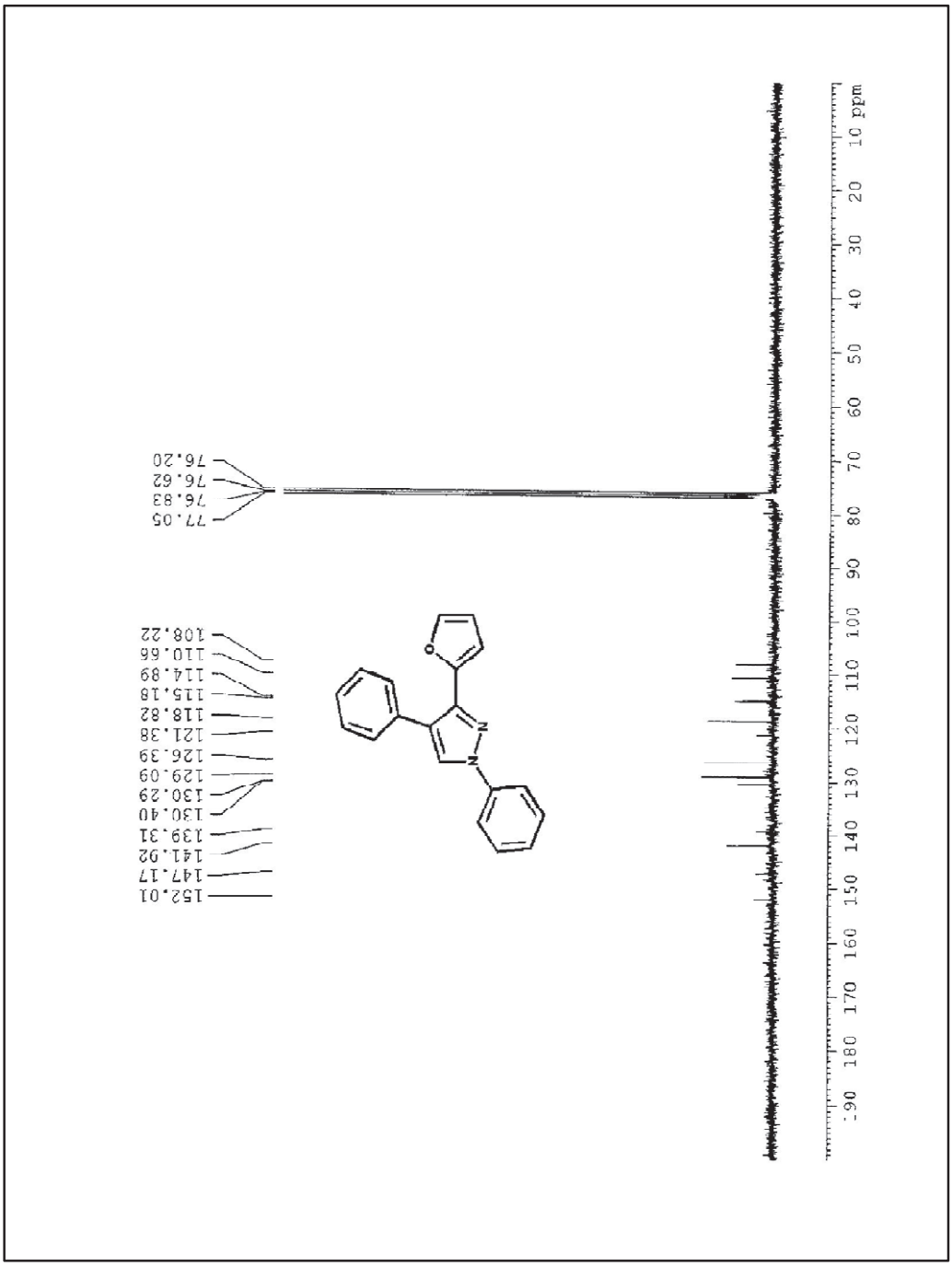
^{1}H NMR of Compound 4m



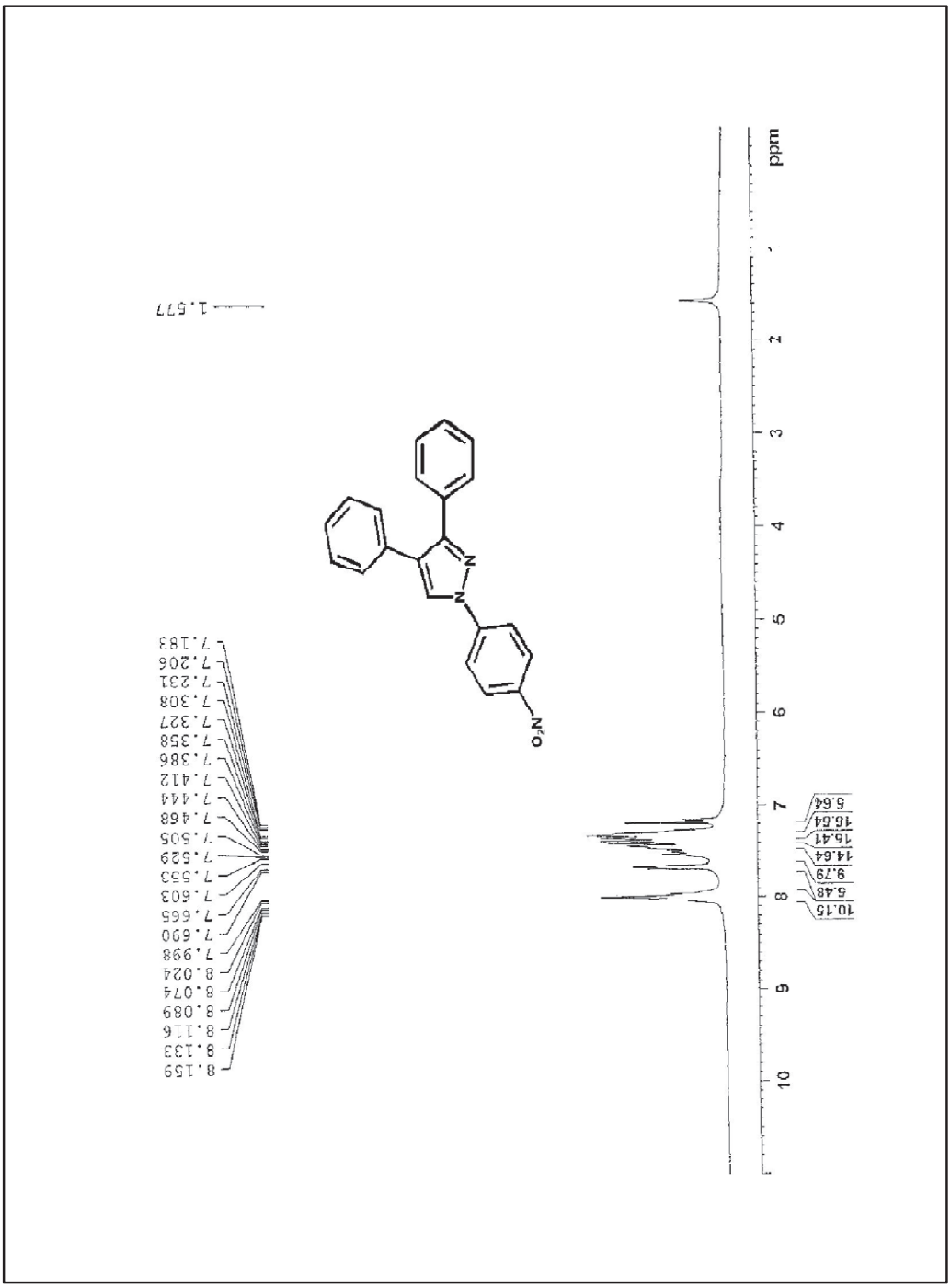
^{13}C NMR of Compound 4m



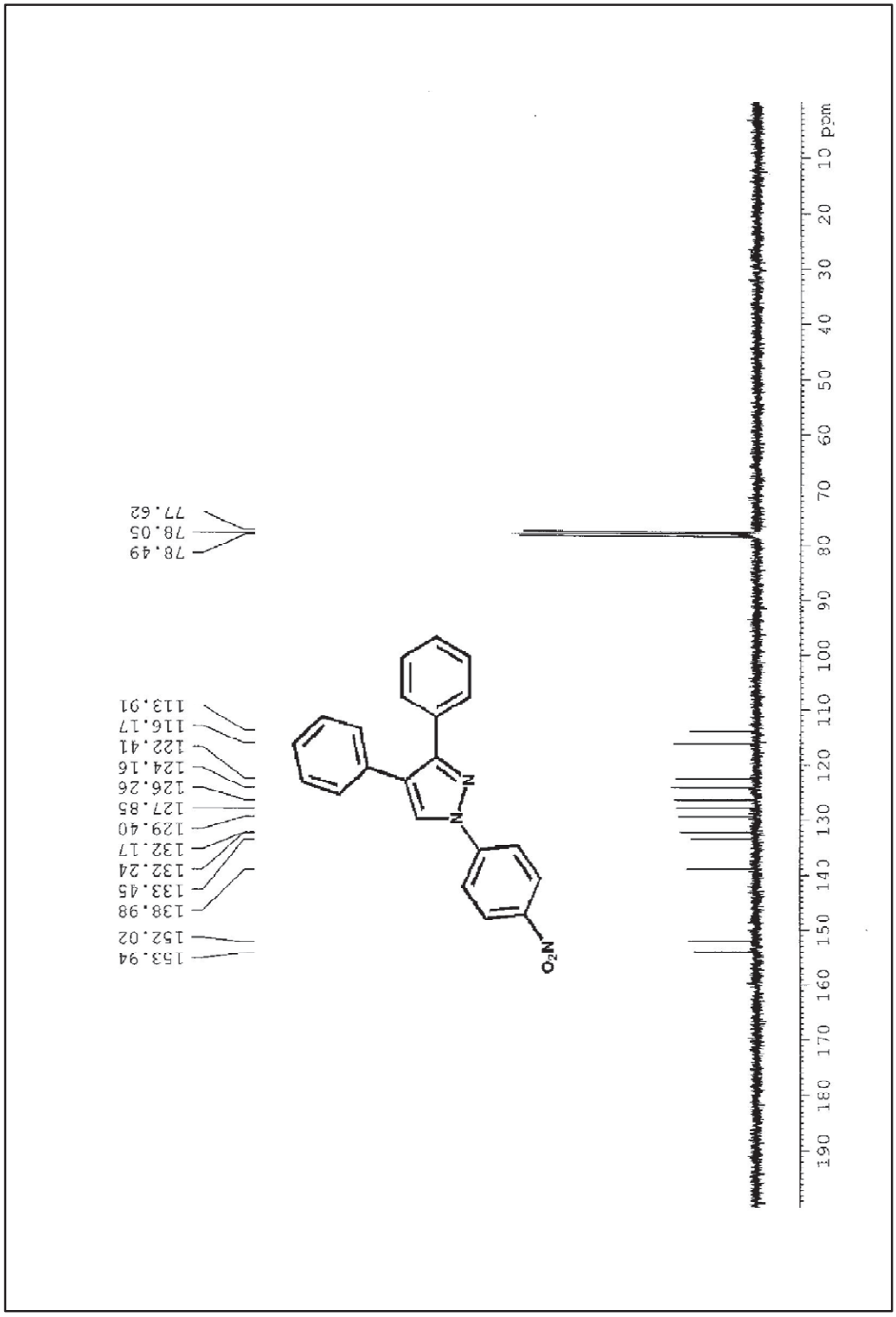
^{1}H NMR of Compound 4n



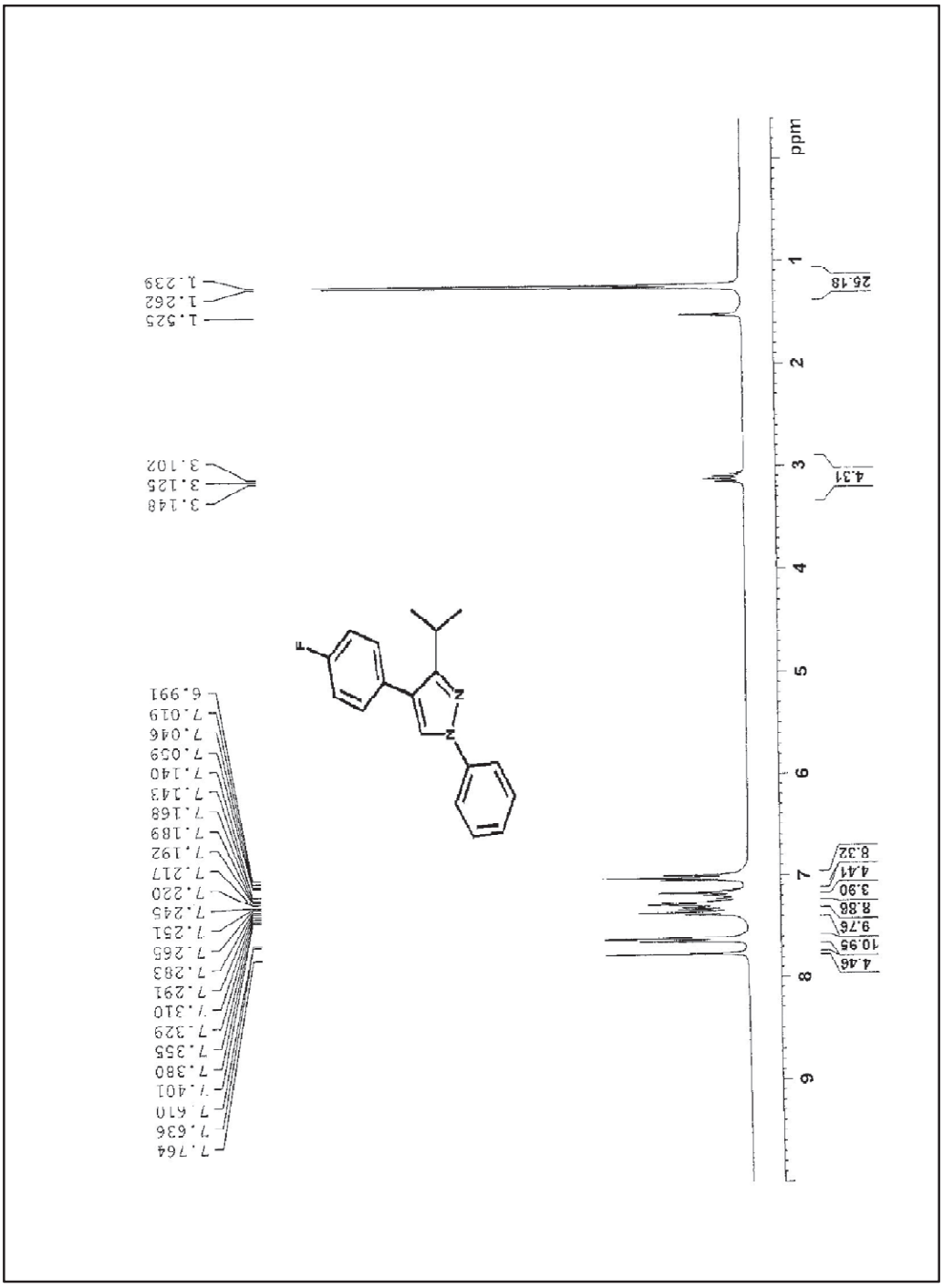
^{13}C NMR of Compound 4n



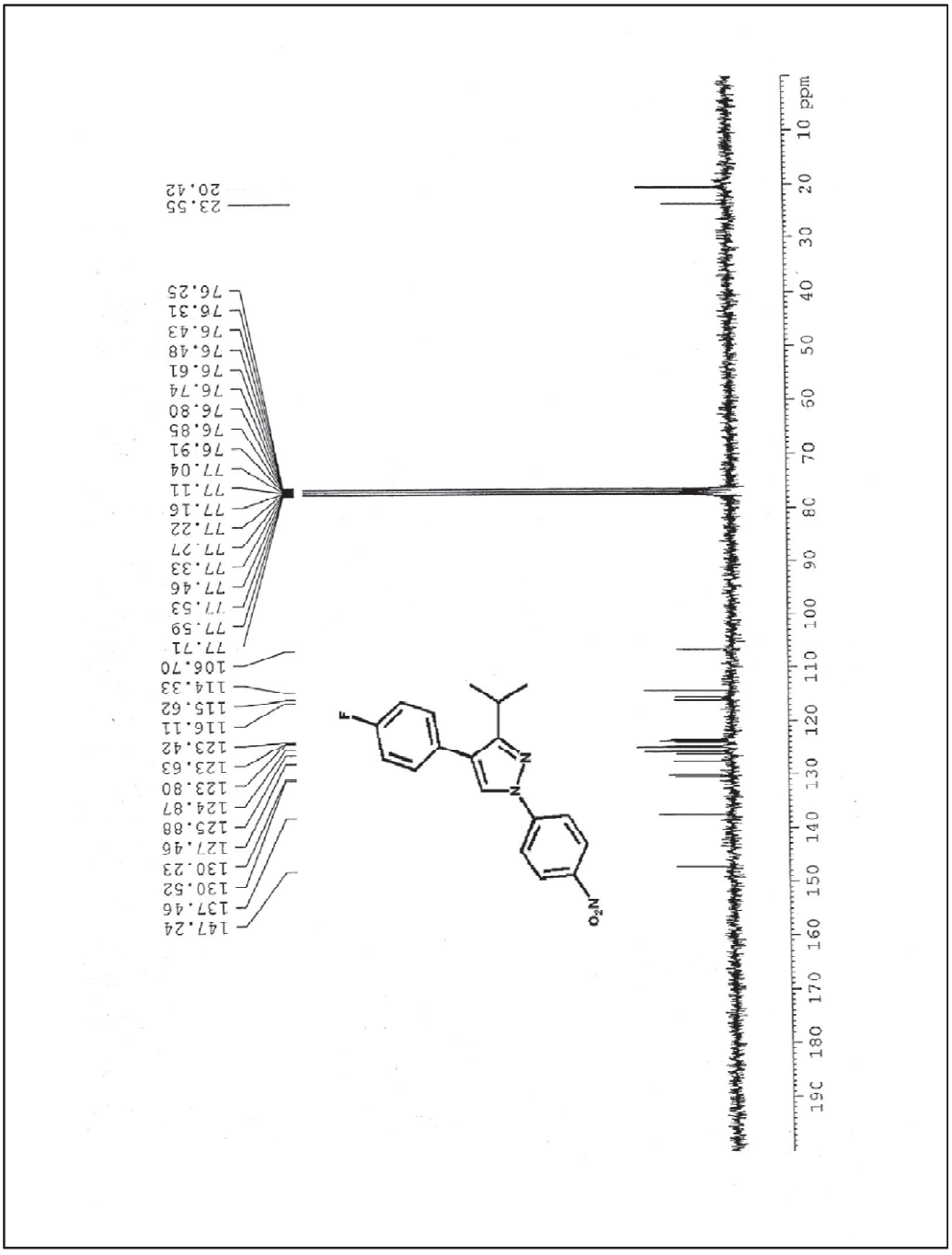
^{1}H NMR of Compound 4o



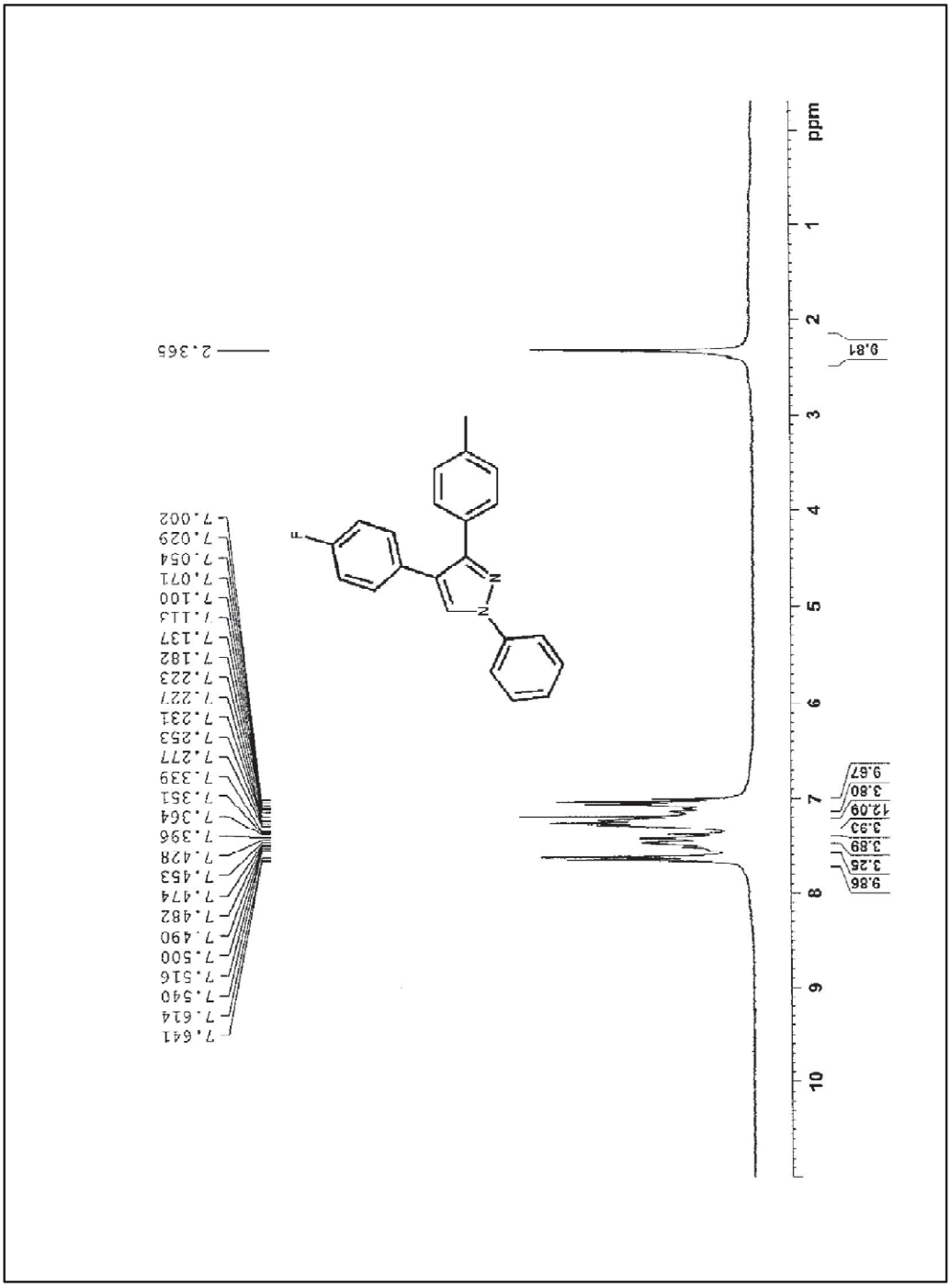
^{13}C NMR of Compound 4o



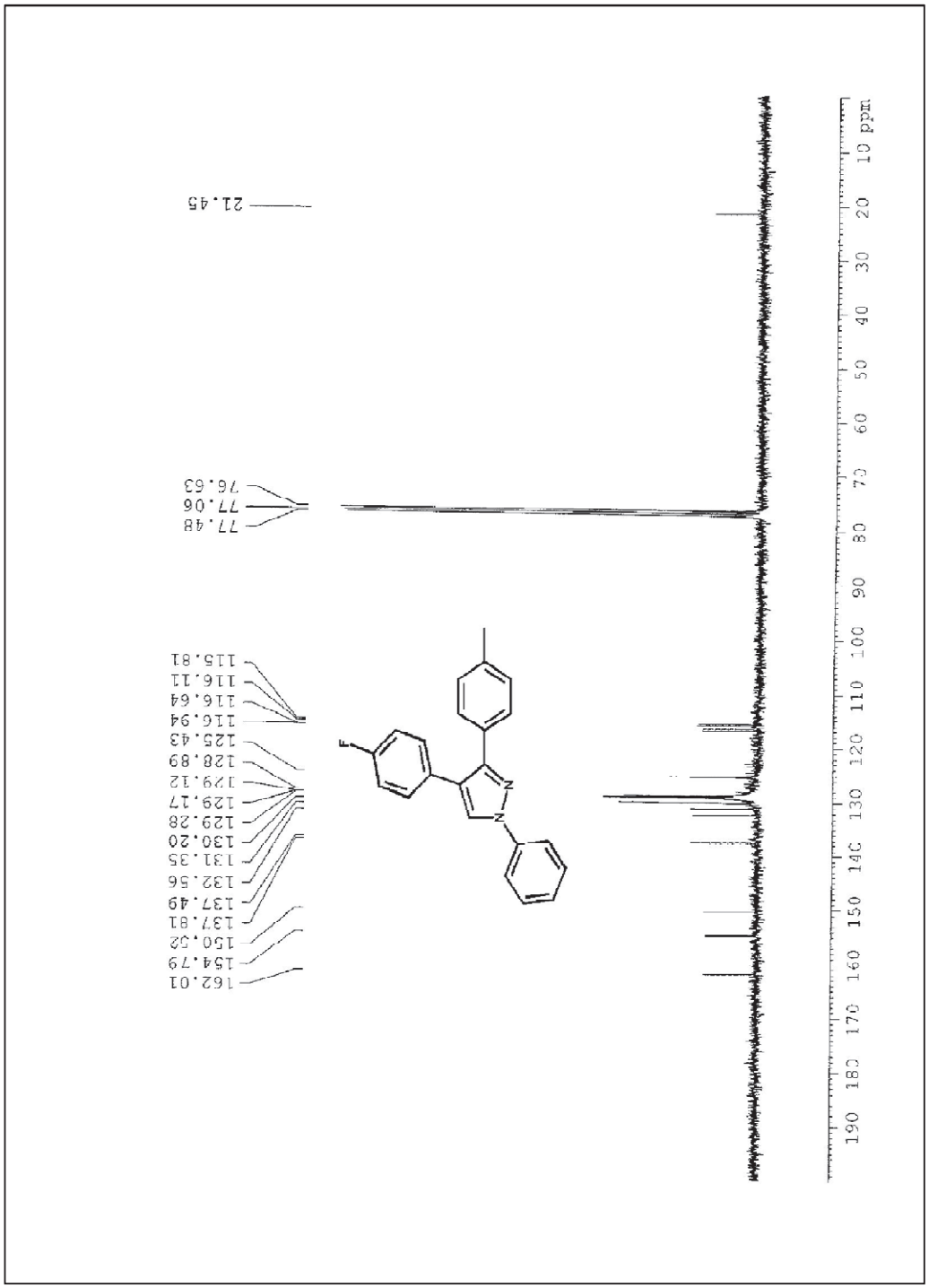
^{1}H NMR of Compound 5a



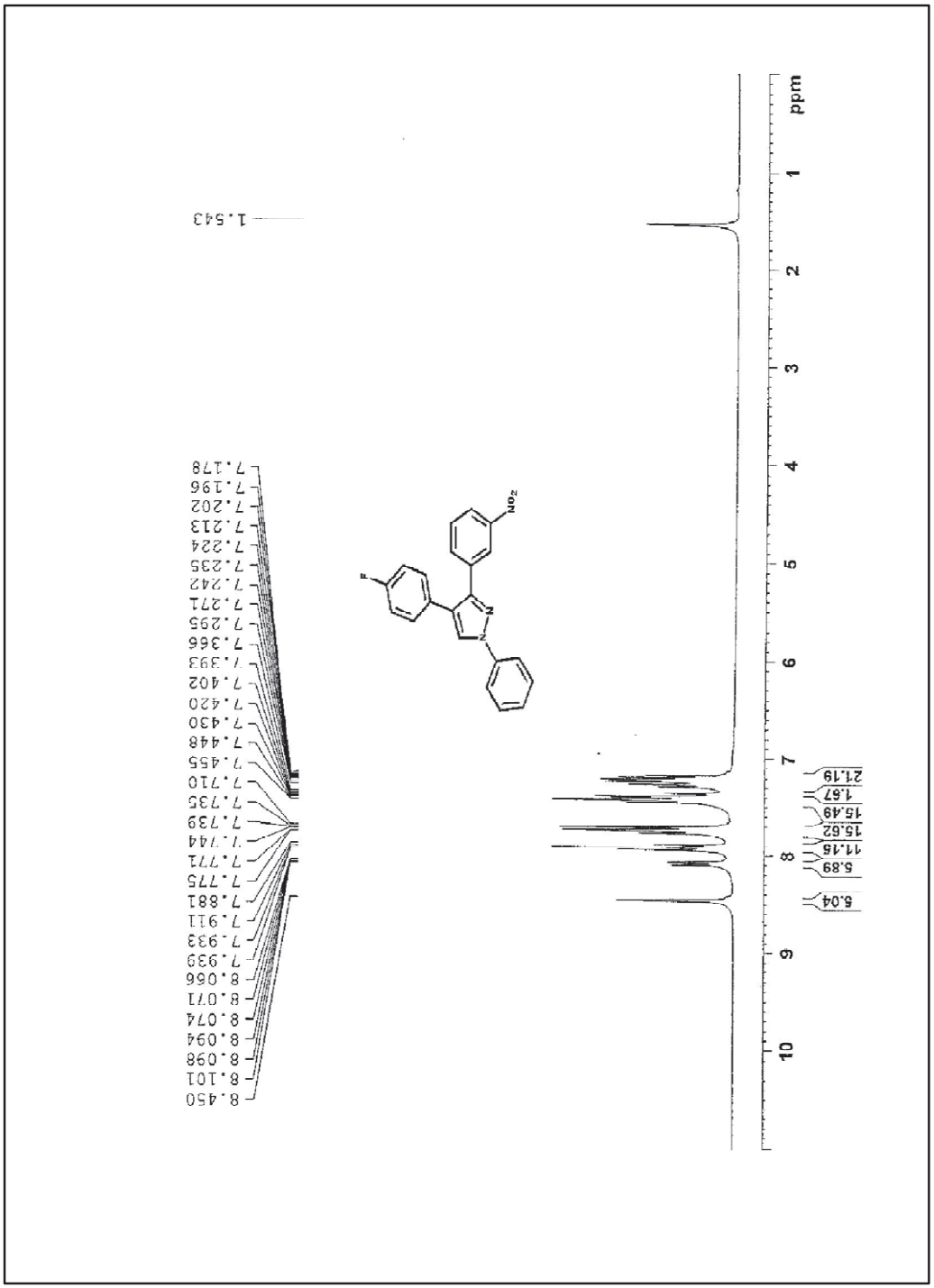
^{13}C NMR of Compound 5a



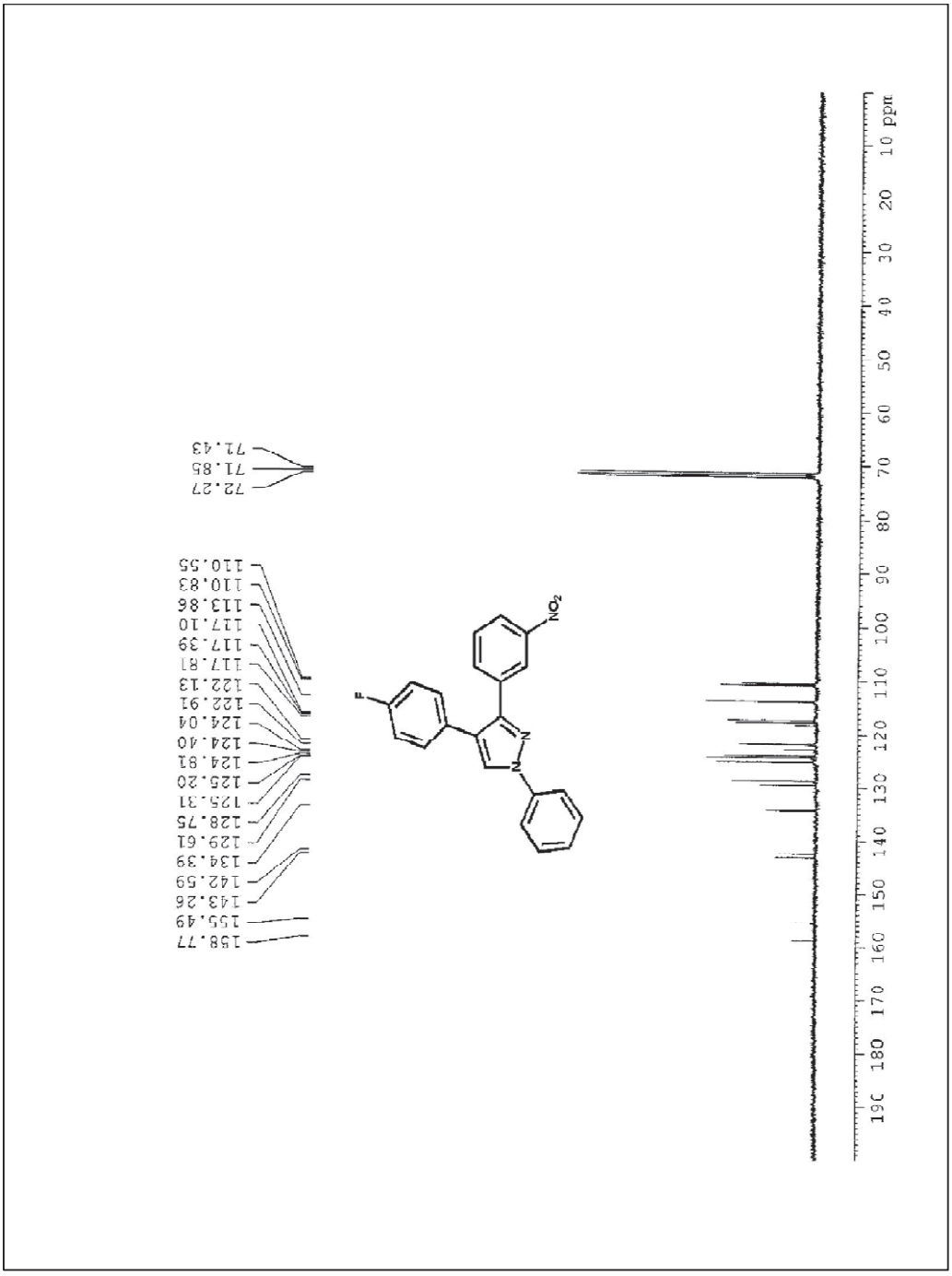
^{1}H NMR of Compound 5b



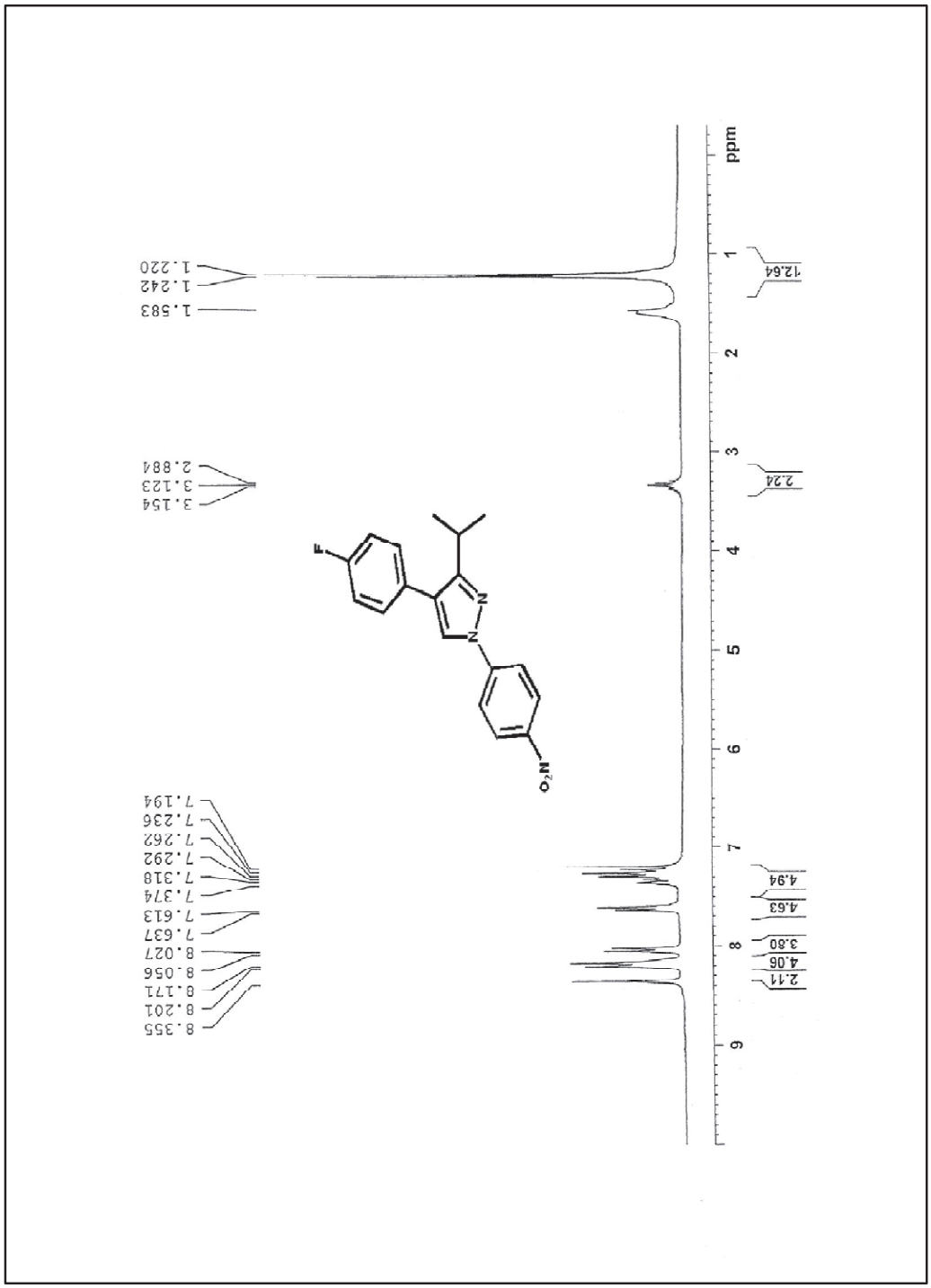
^{13}C NMR of Compound 5b



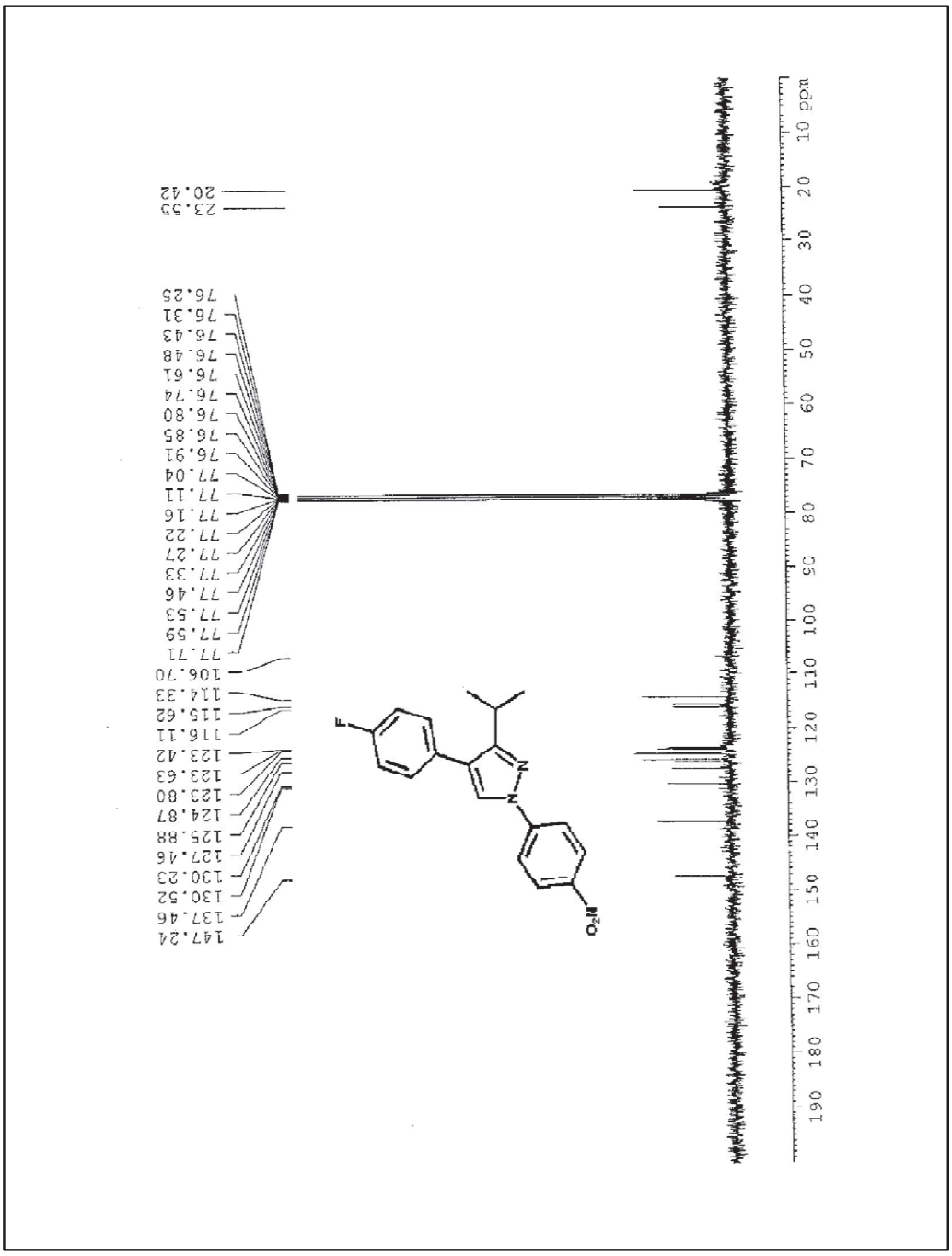
[1]H NMR of Compound 5c



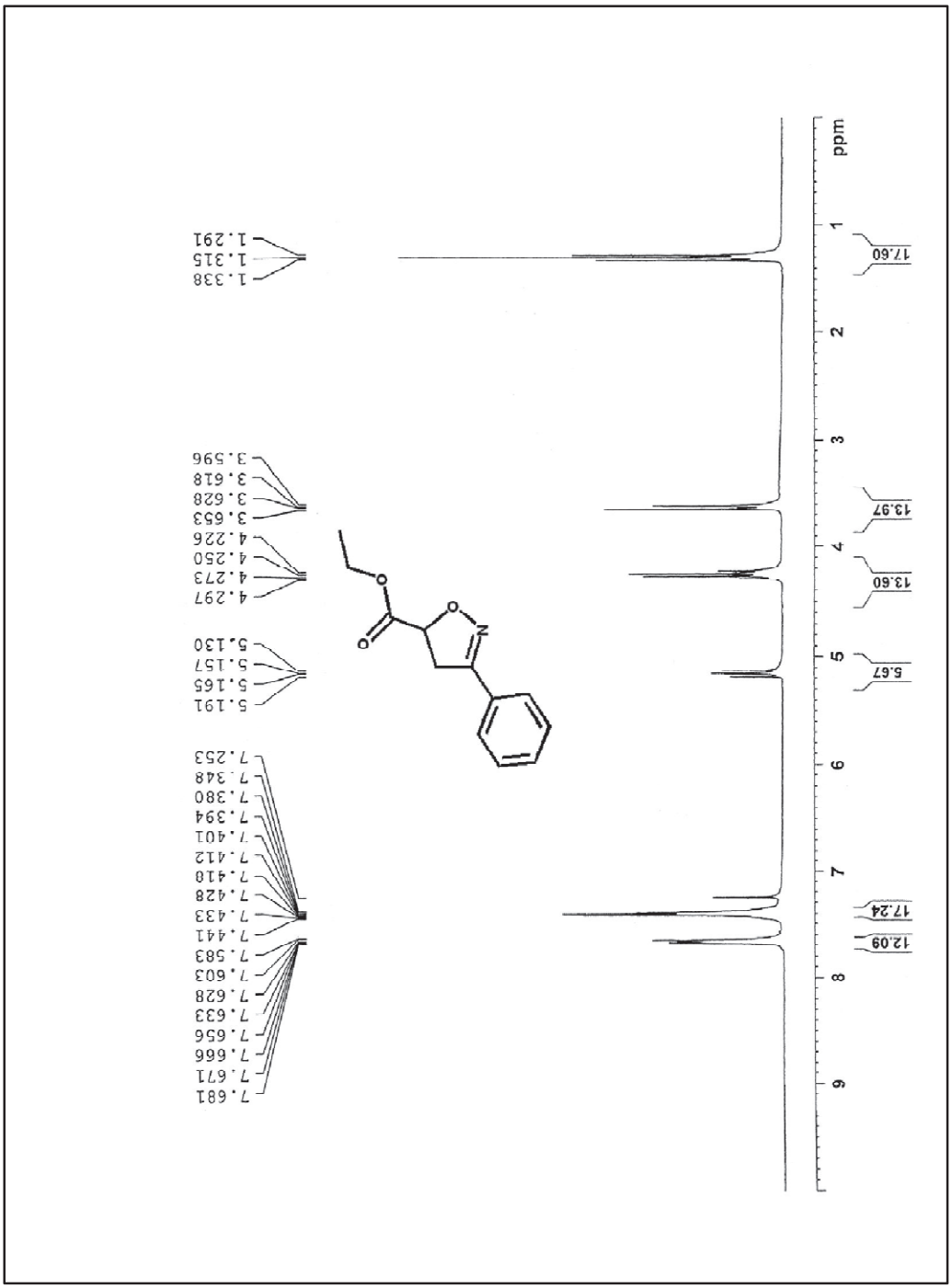
^{13}C NMR of Compound 5c



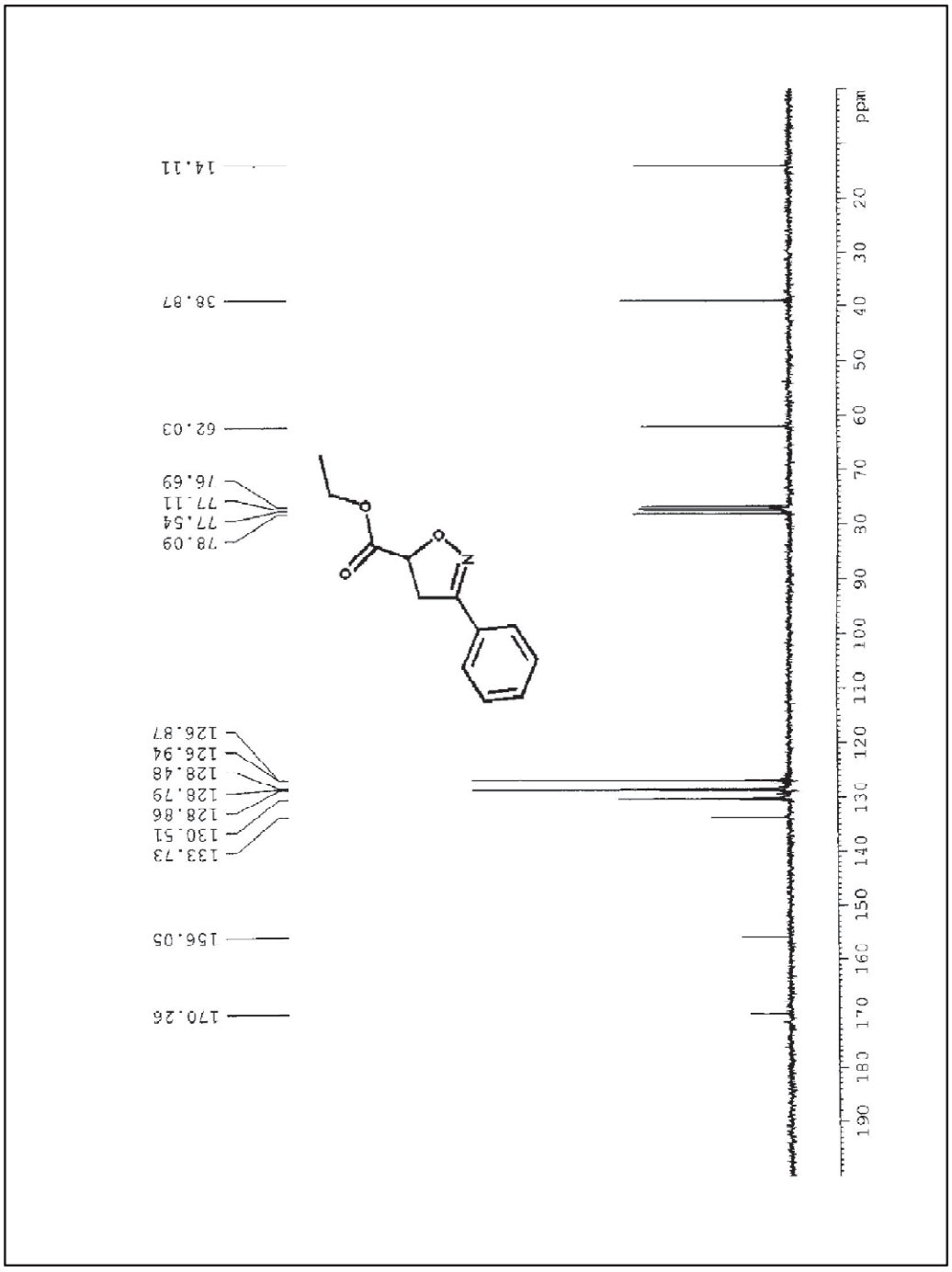
[1]H NMR of Compound 5d



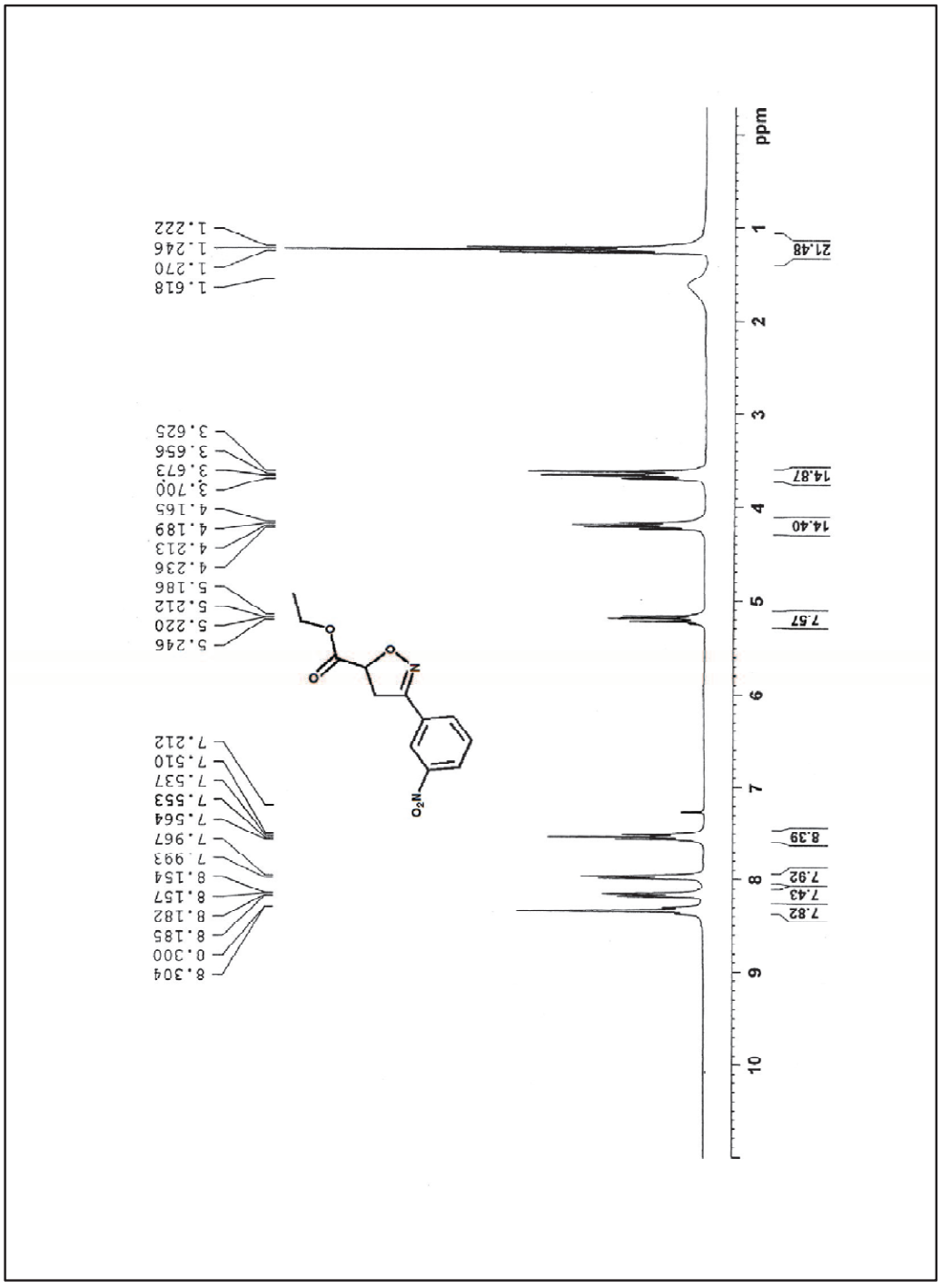
^{13}C NMR of Compound 5d



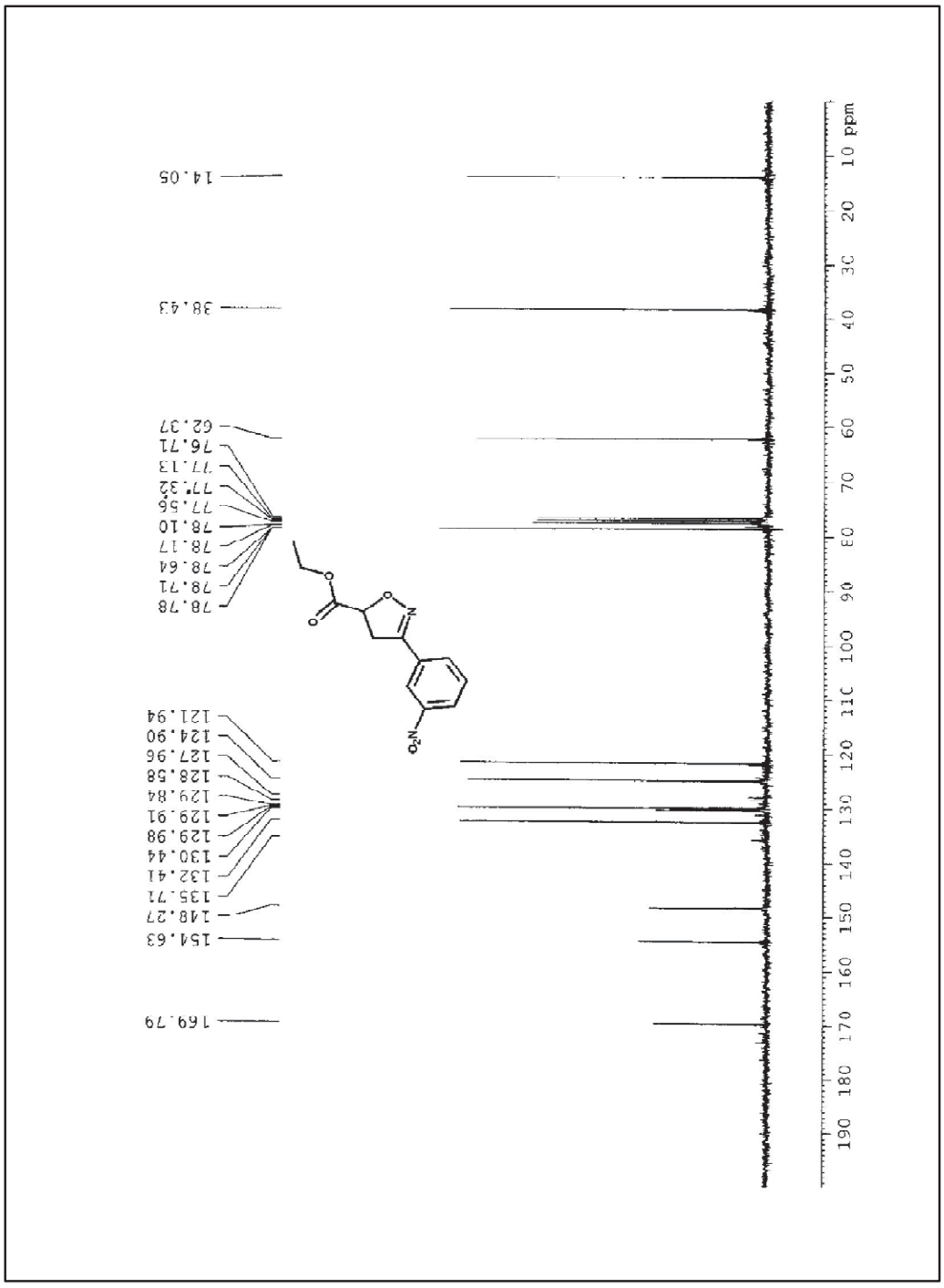
^{1}H NMR of Compound 6a



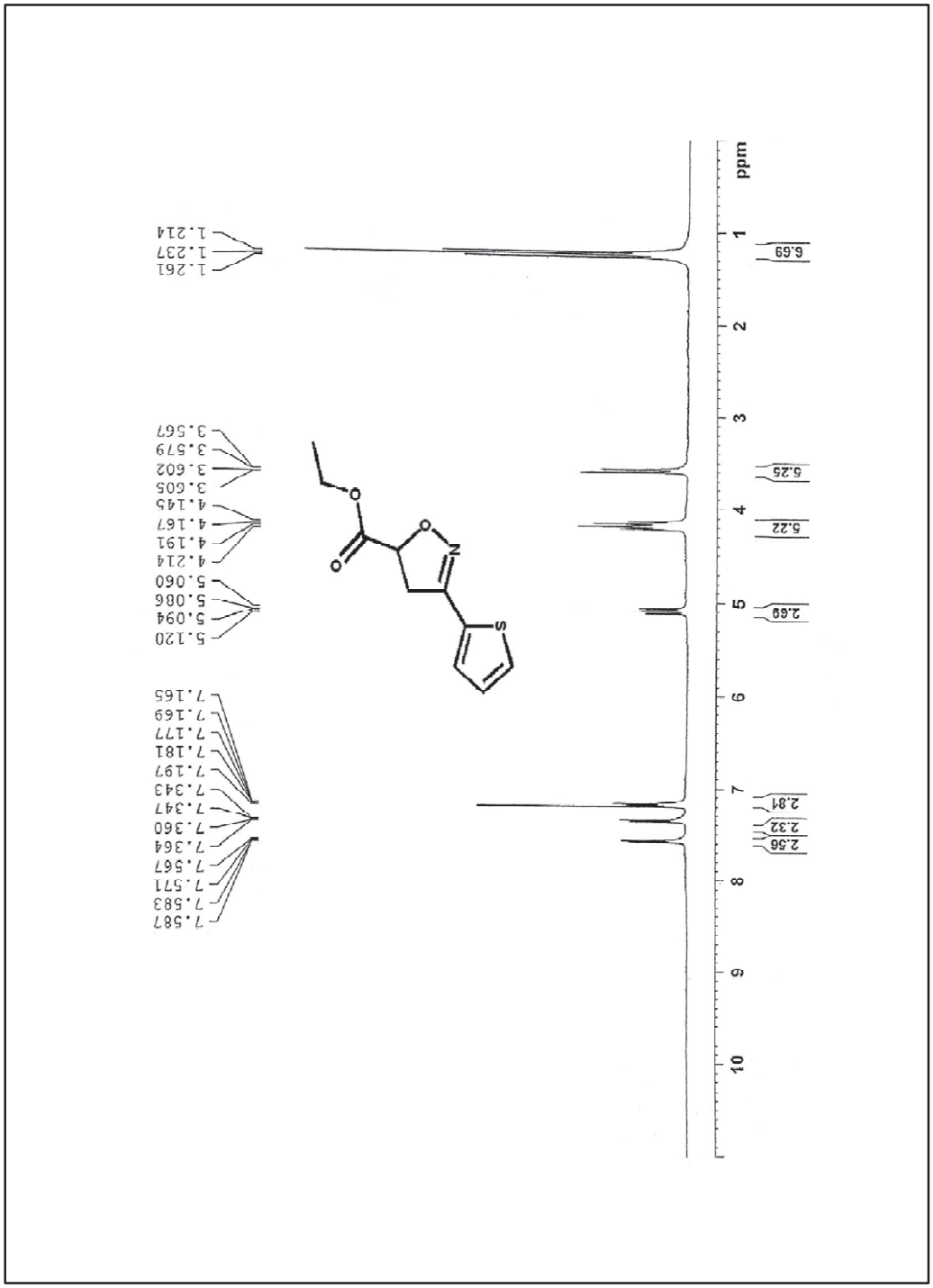
^{13}C NMR of Compound 6a



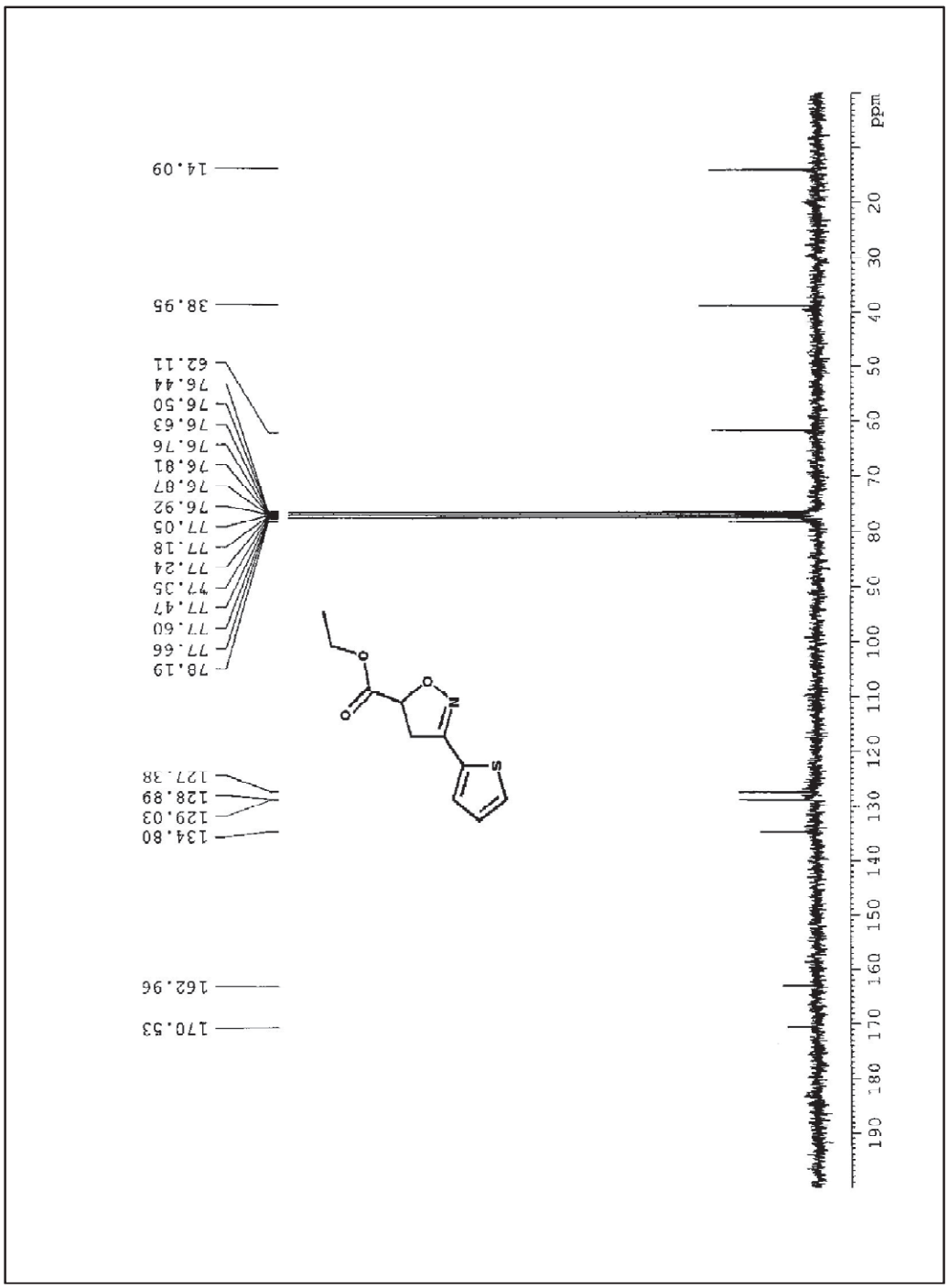
^{1}H NMR of Compound 6b



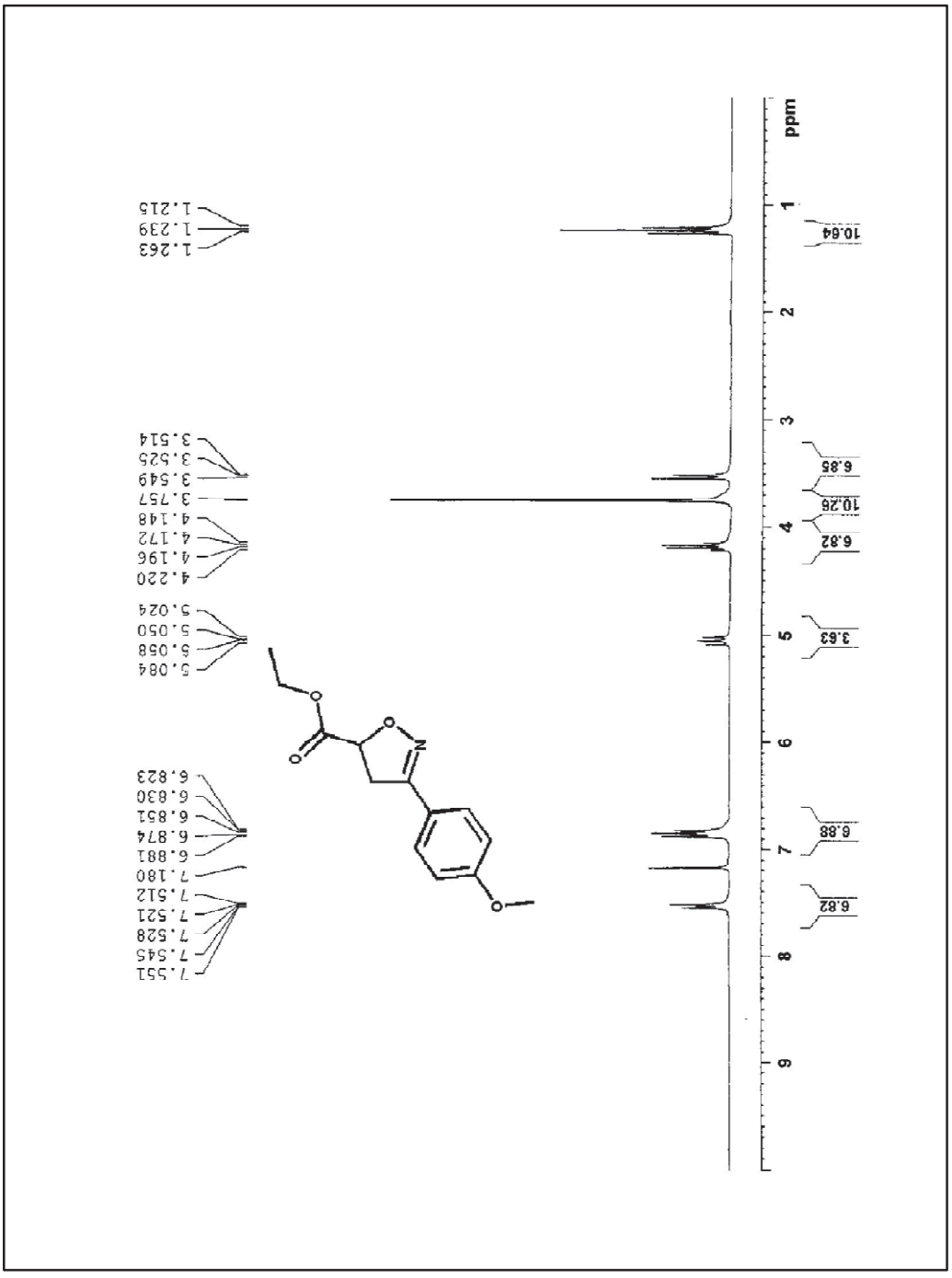
^{13}C NMR of Compound 6b



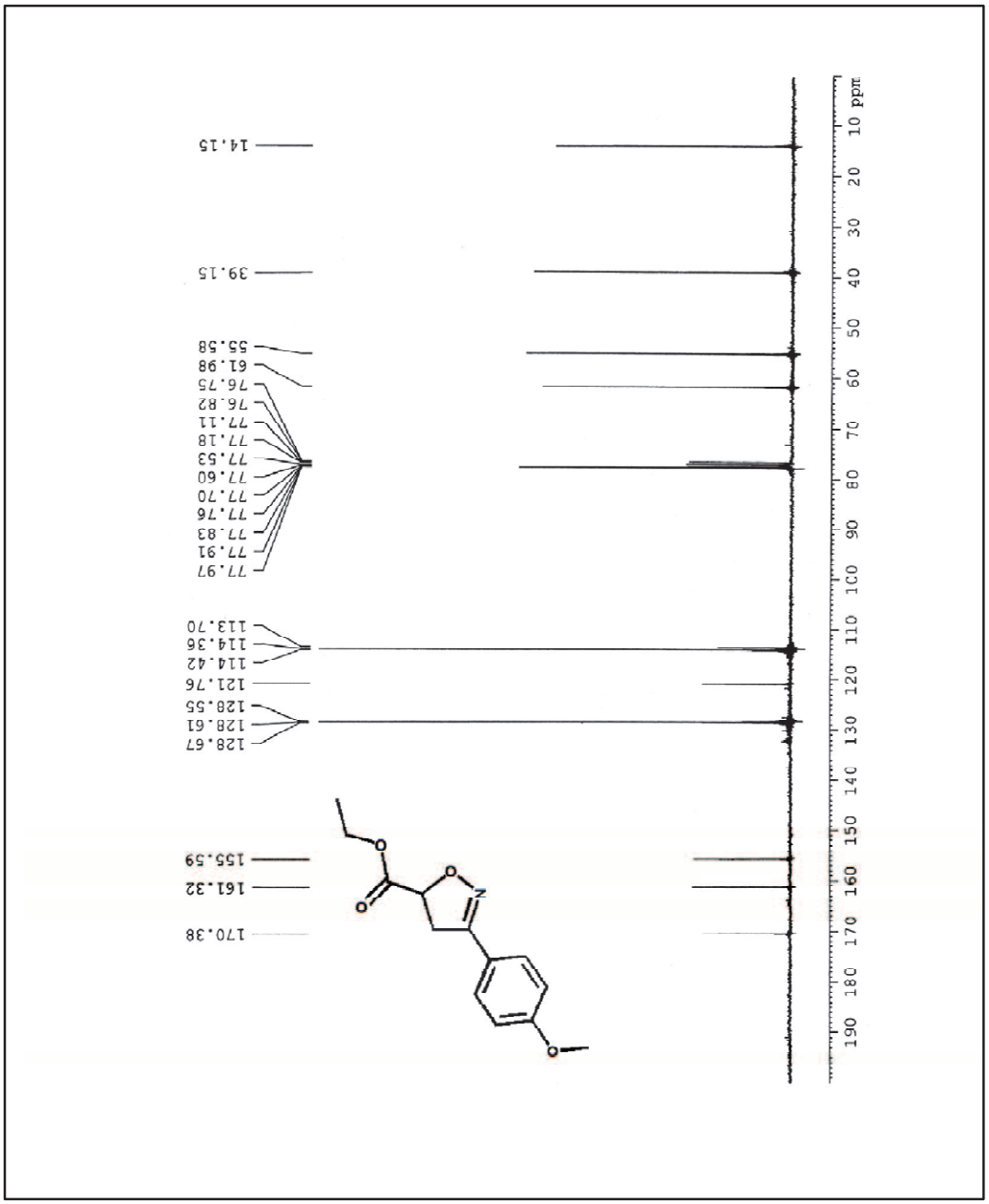
^{1}H NMR of Compound 6c



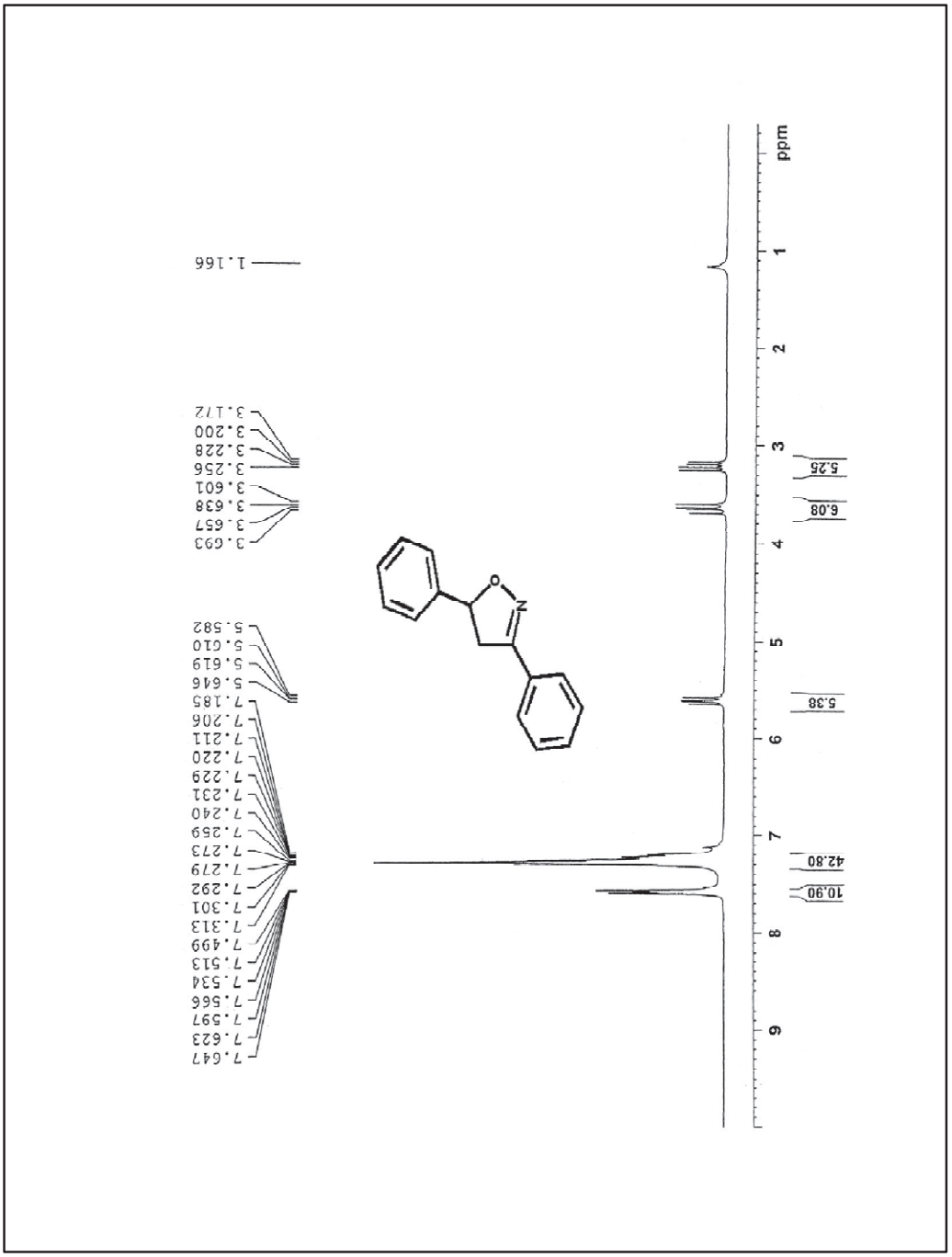
^{13}C NMR of Compound 6c



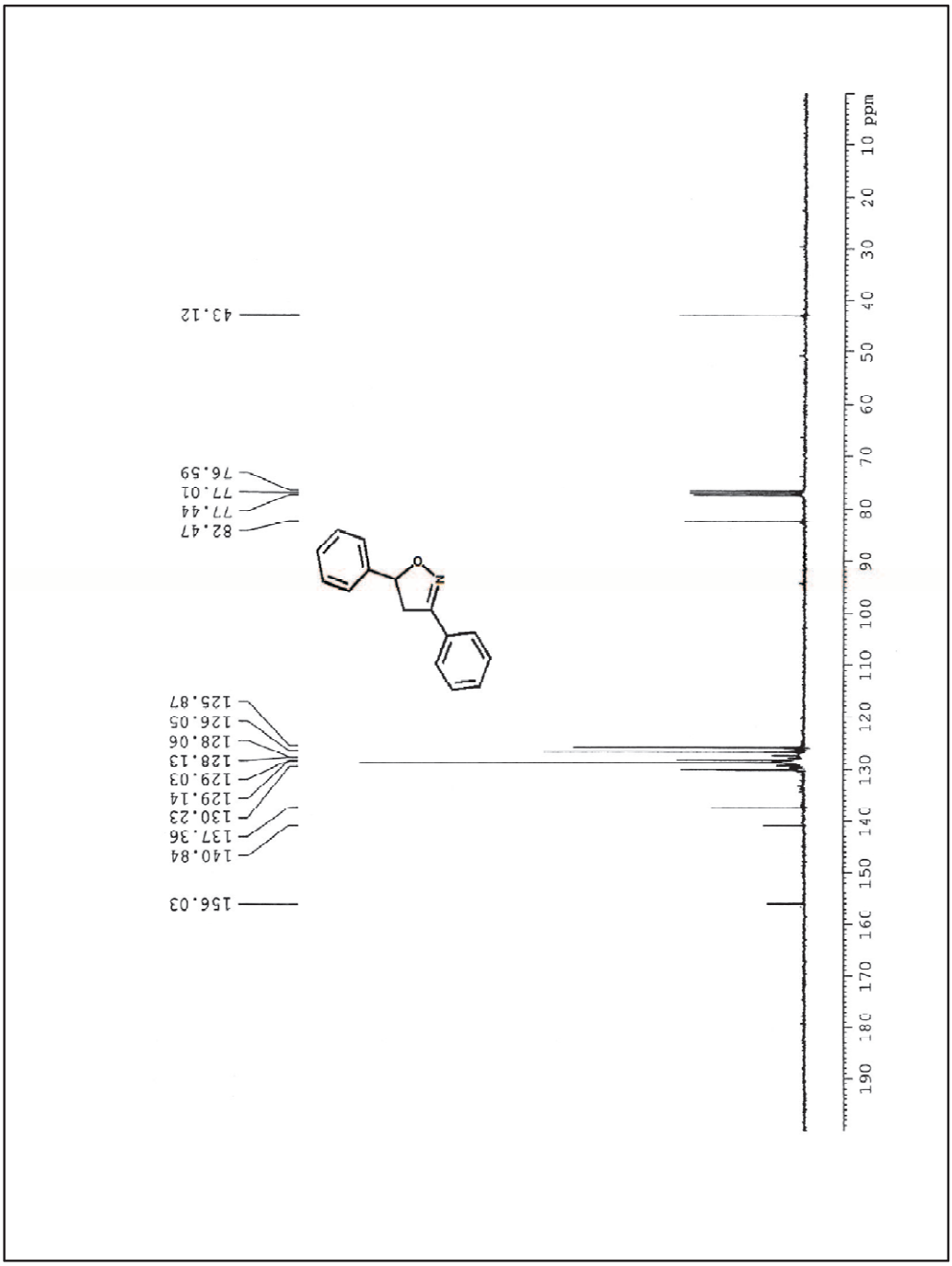
^{1}H NMR of Compound 6d



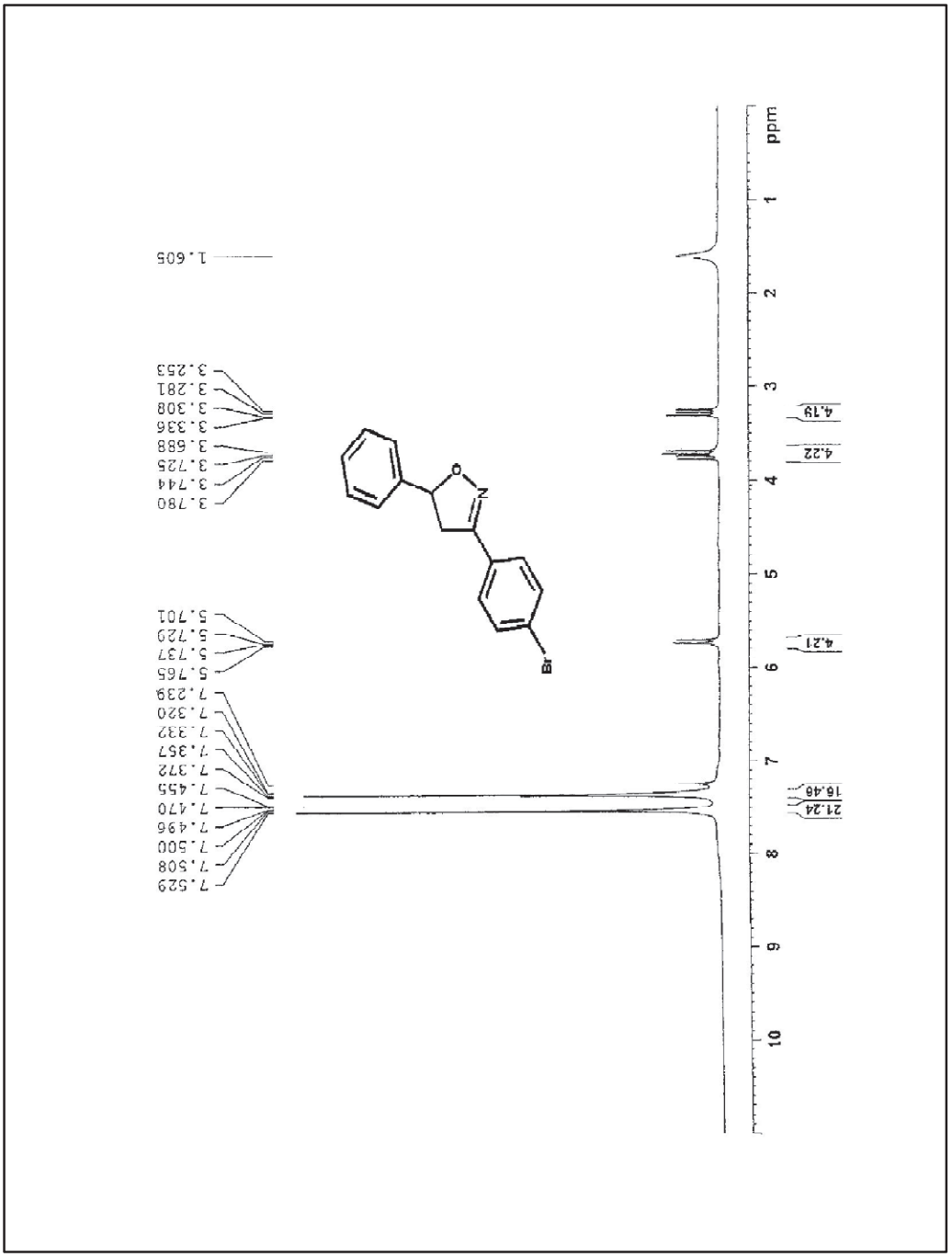
^{13}C NMR of Compound 6d



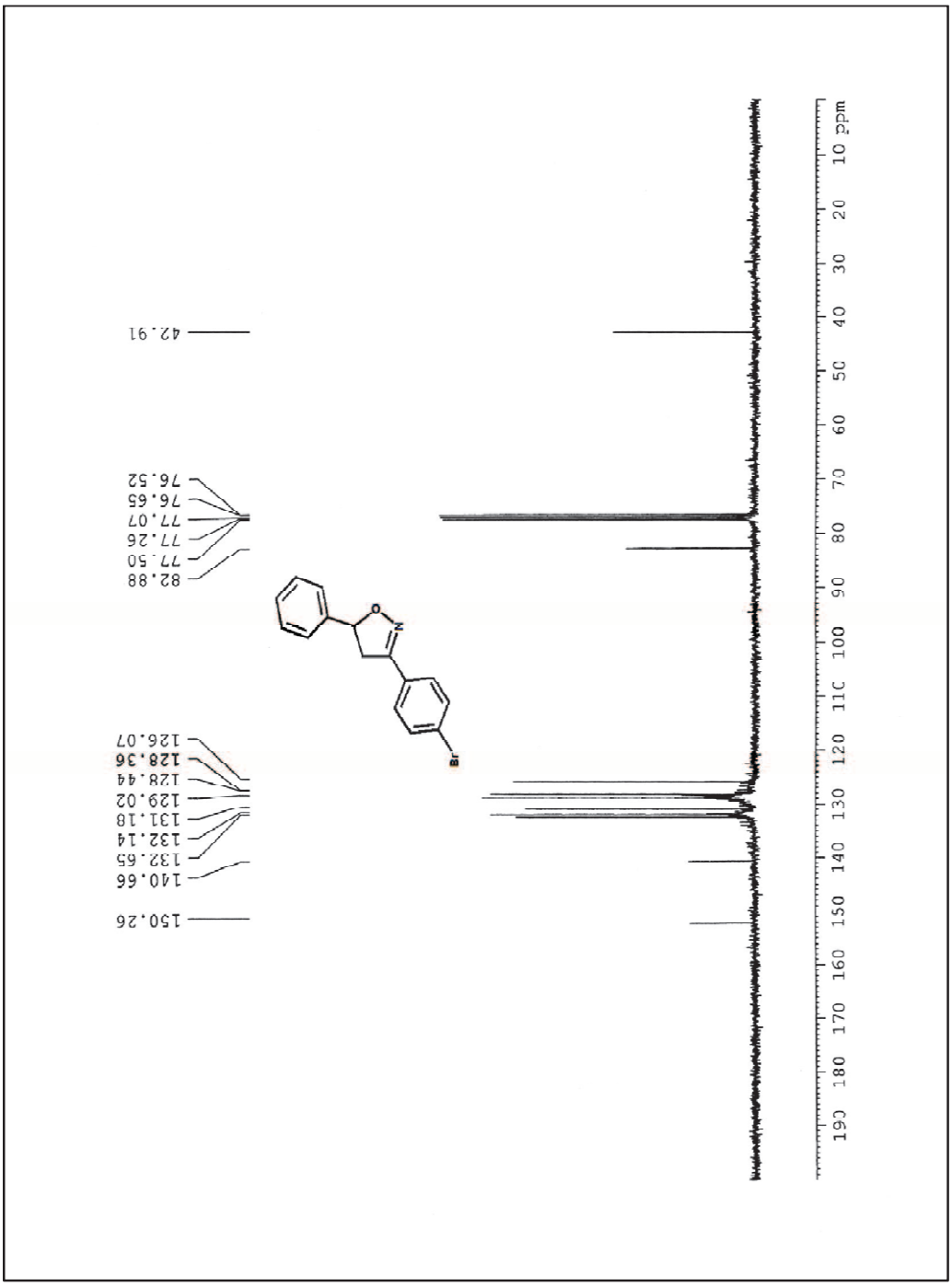
^{1}H NMR of Compound 6e



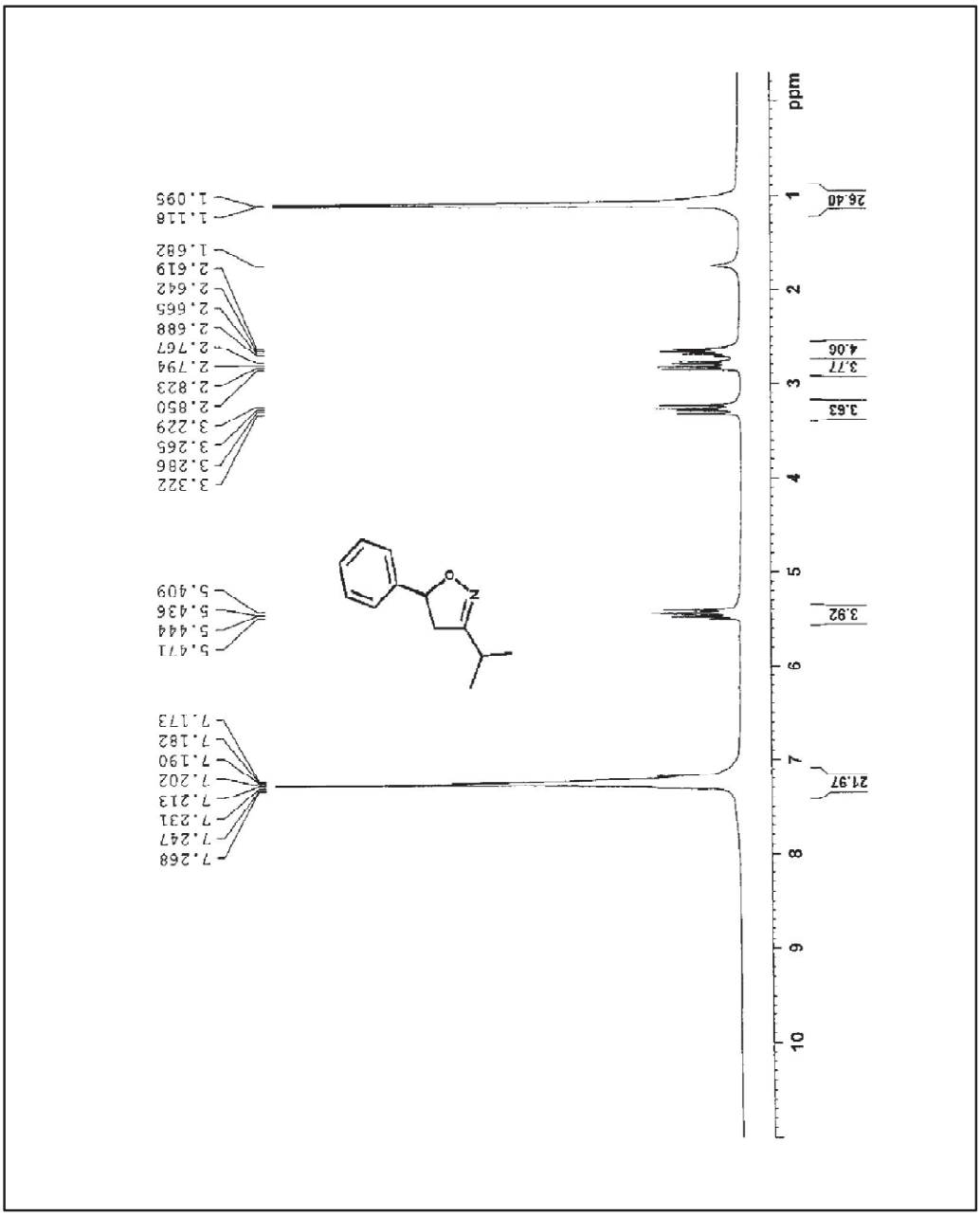
^{13}C NMR of Compound 6e



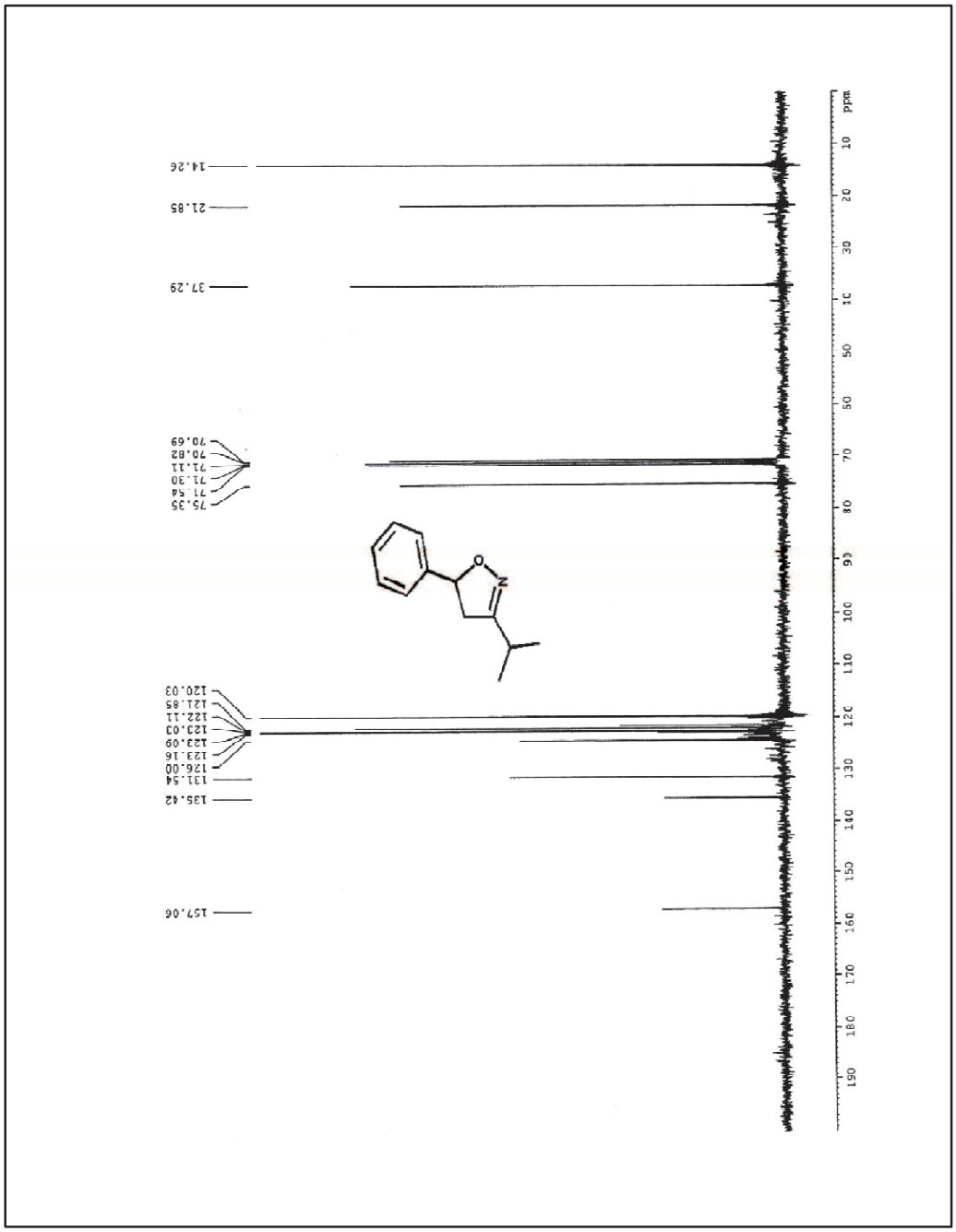
^{1}H NMR of Compound 6f



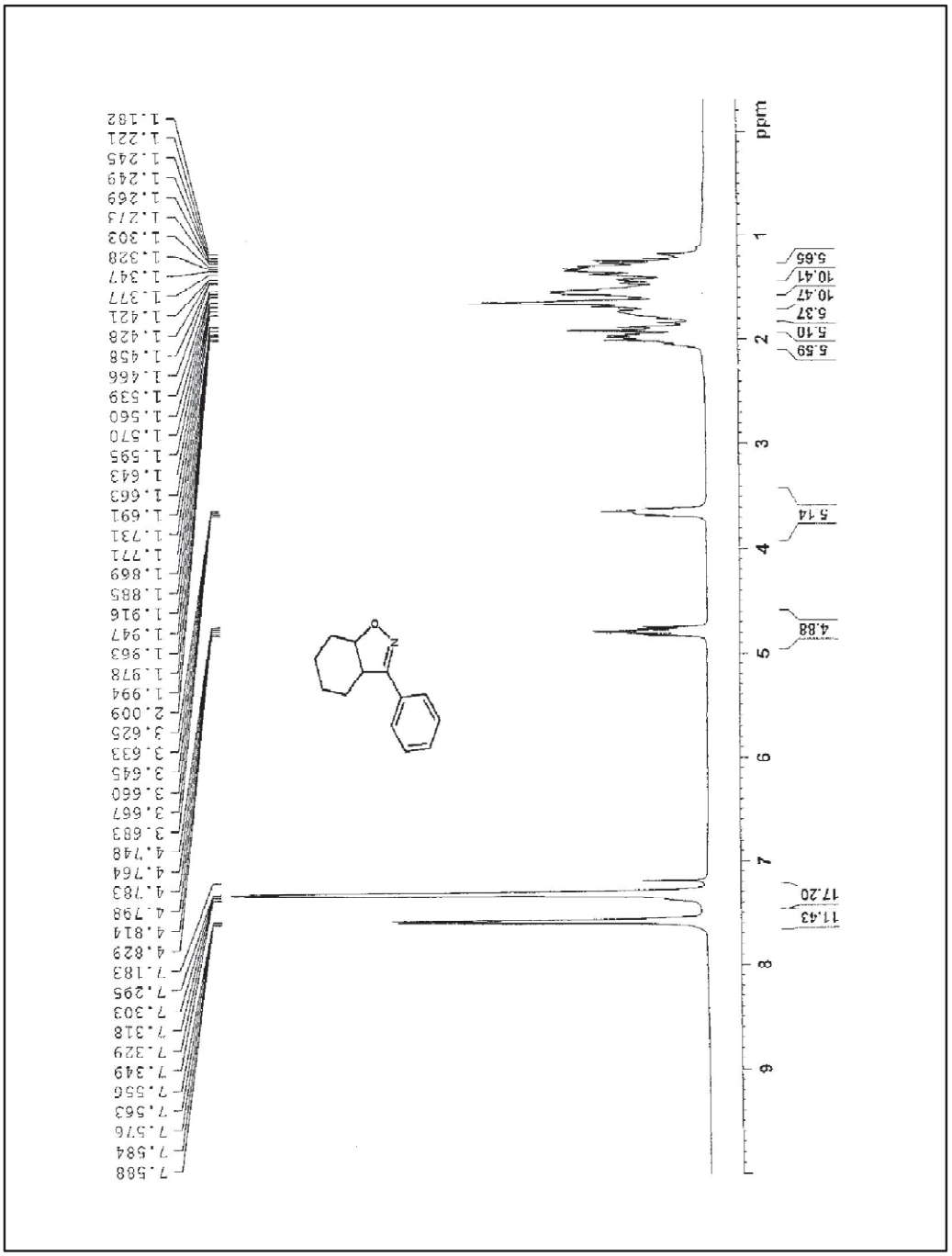
^{13}C NMR of Compound 6f



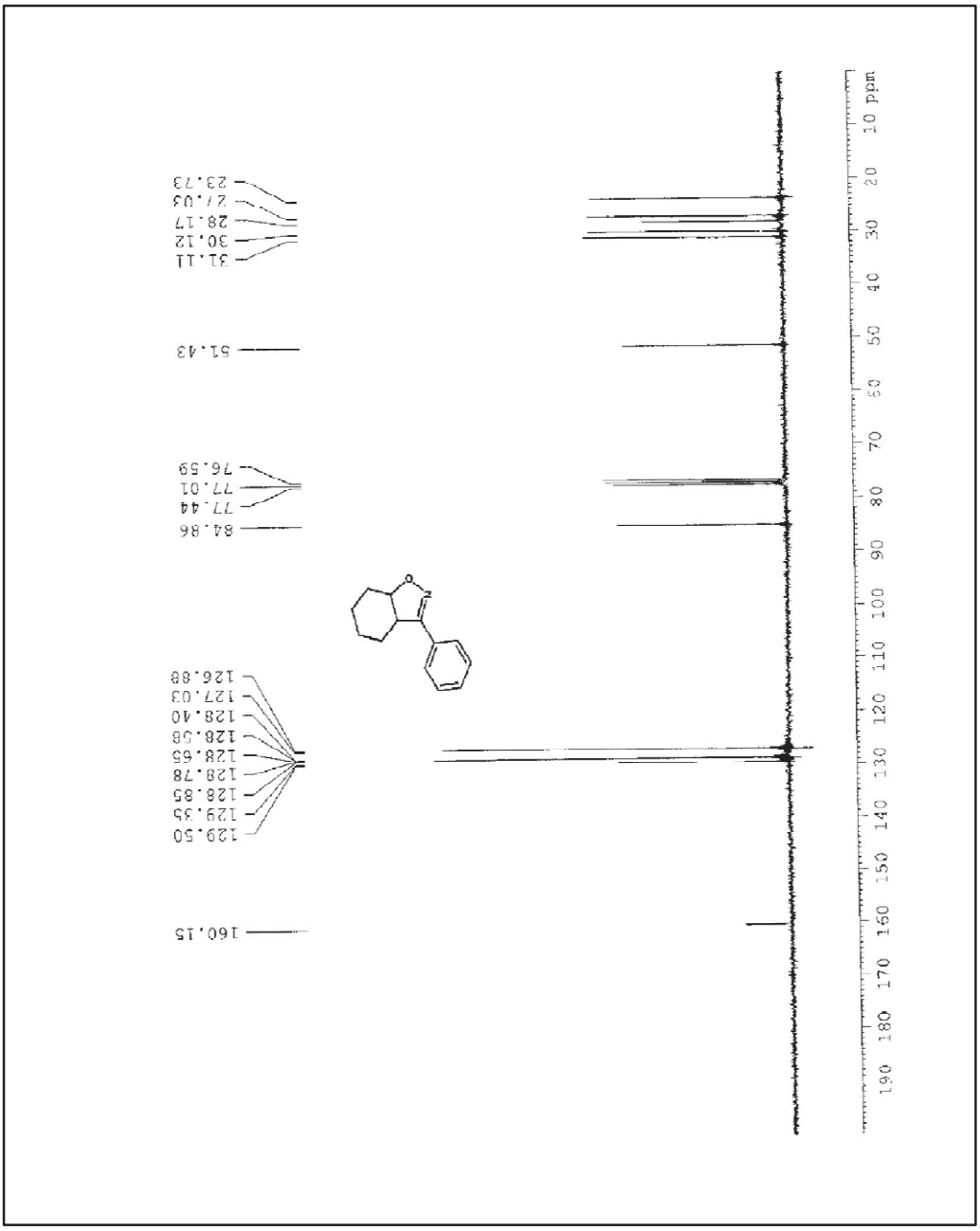
^{1}H NMR of Compound 6g



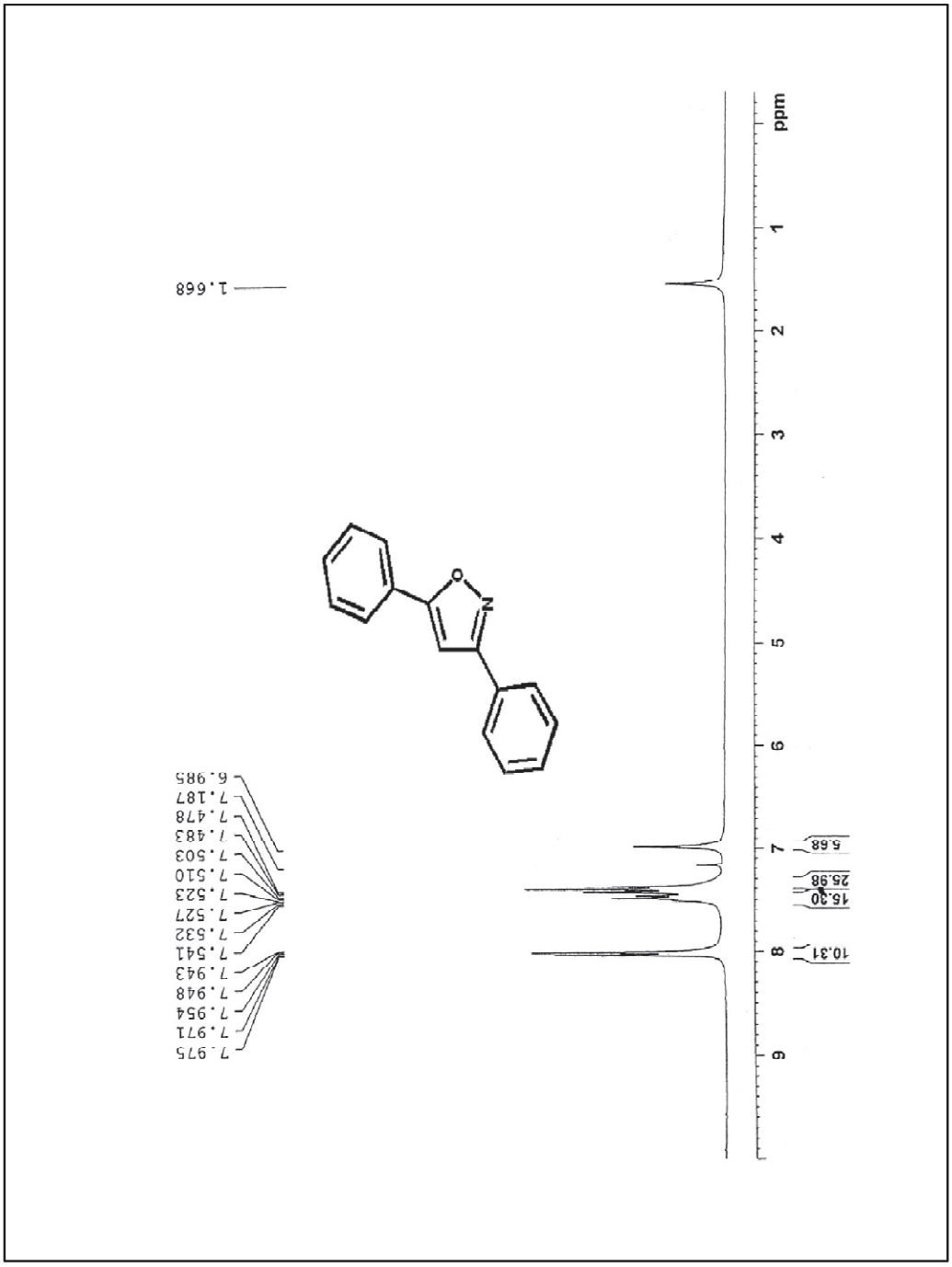
^{13}C NMR of Compound 6g



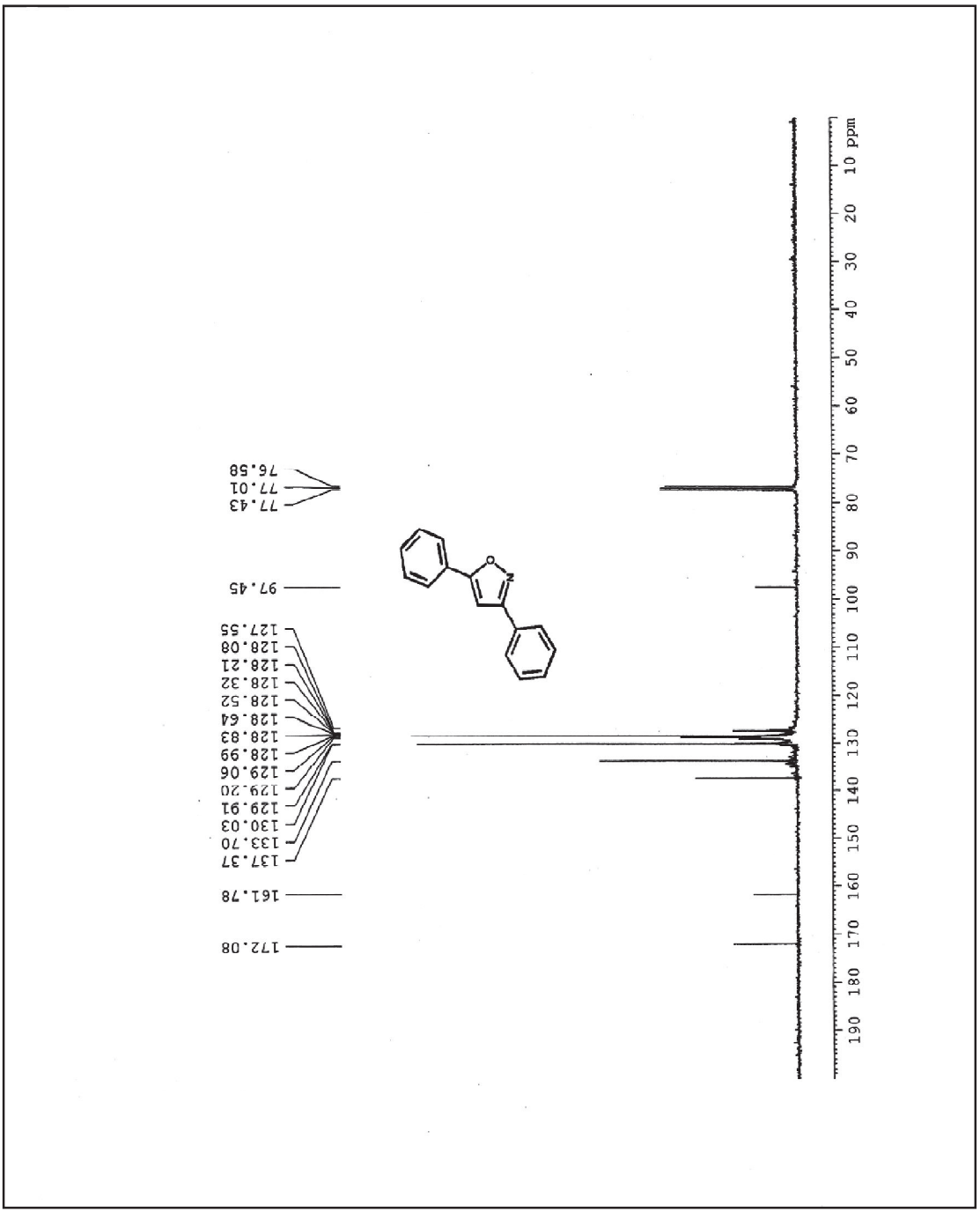
^{1}H NMR of Compound 6h



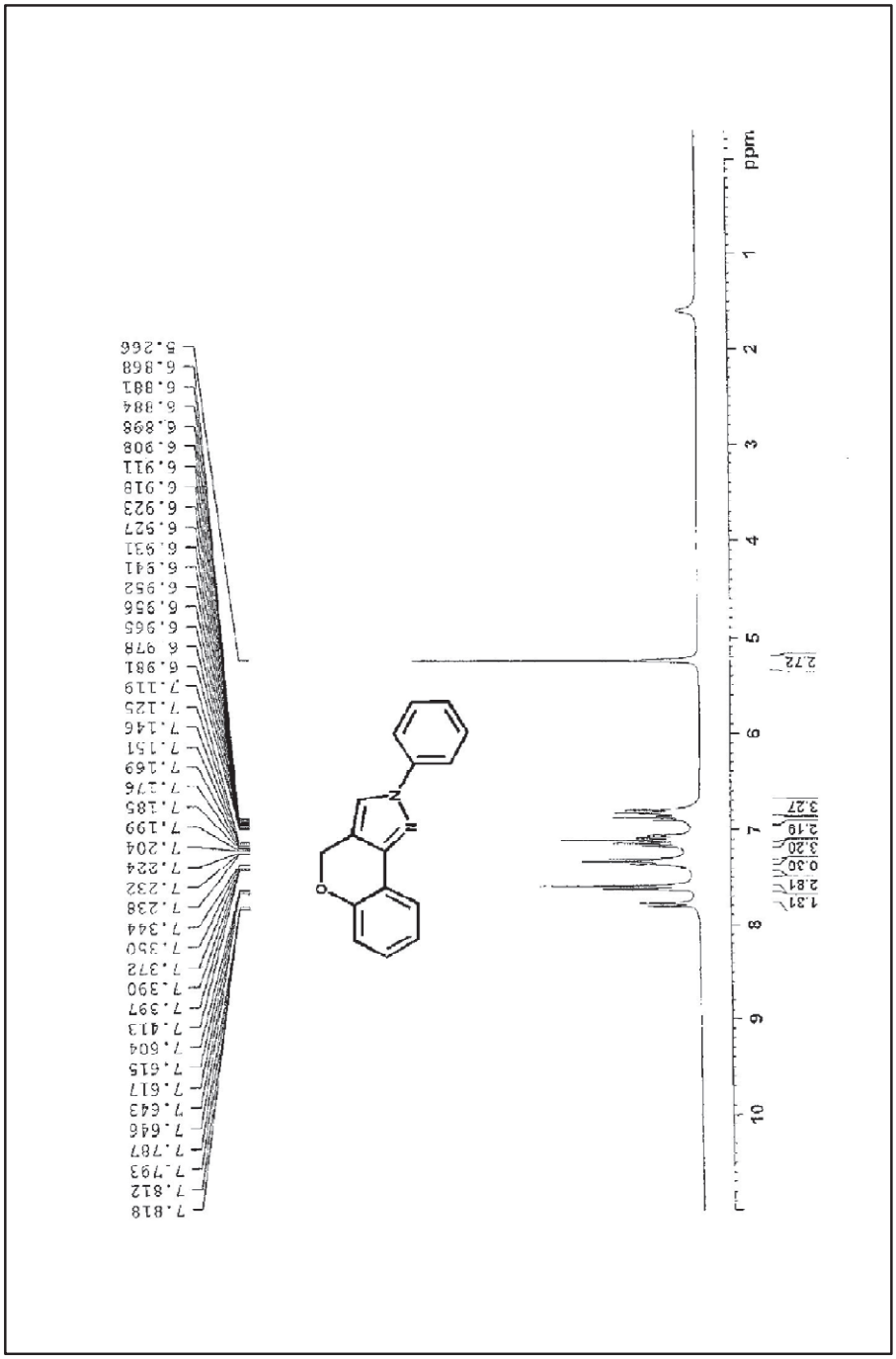
^{13}C NMR of Compound 6h



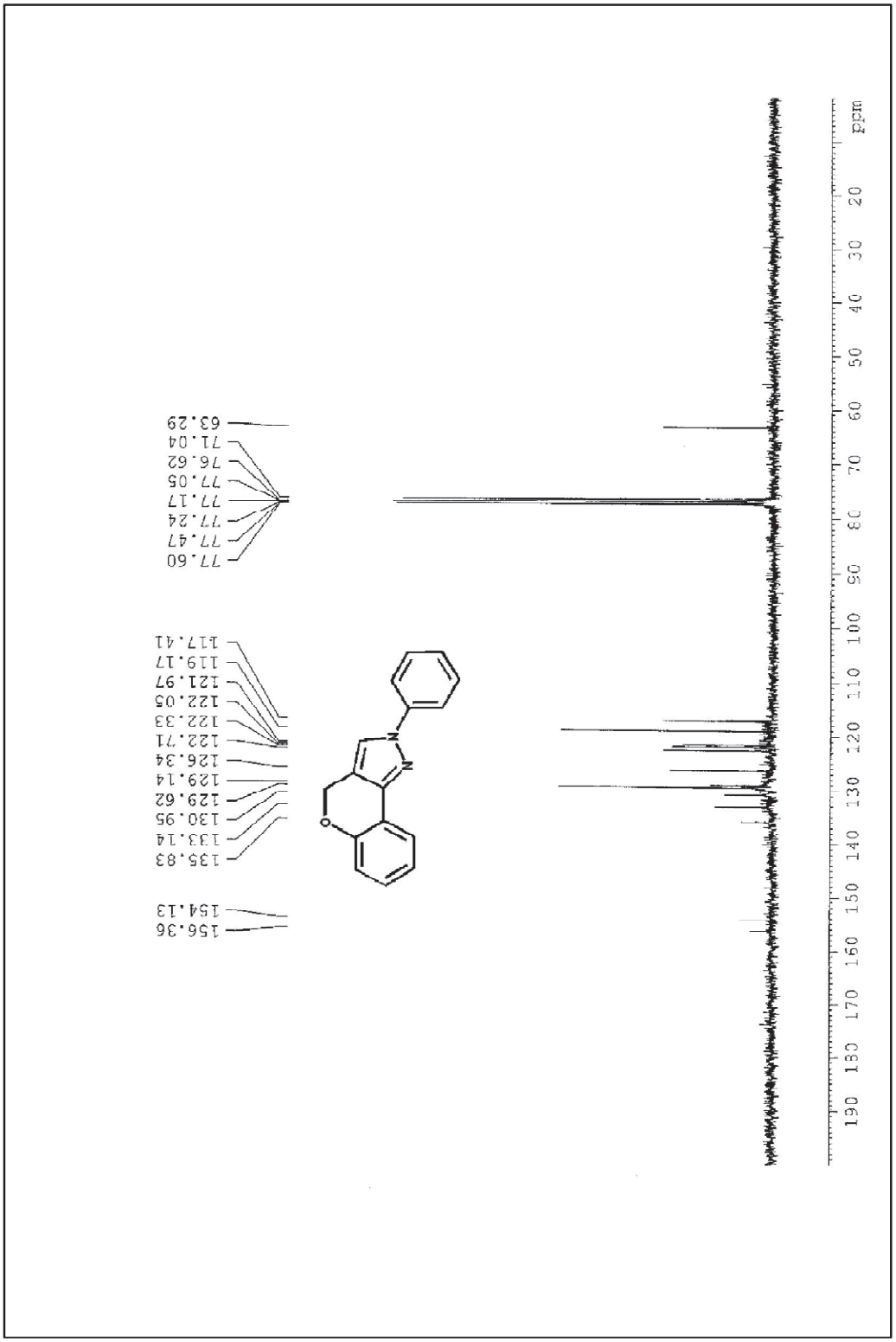
^{1}H NMR of Compound 6i



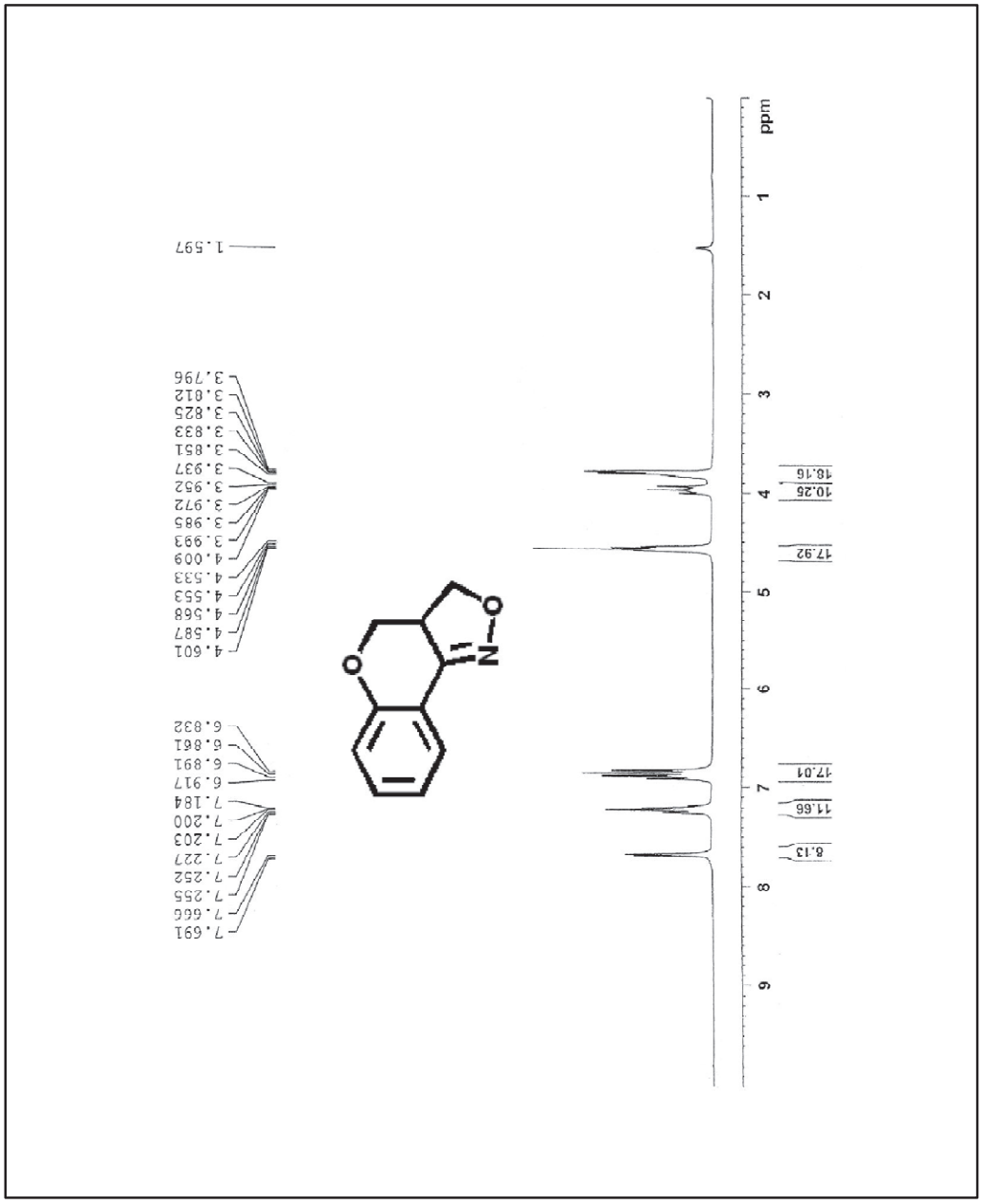
^{13}C NMR of Compound 6i



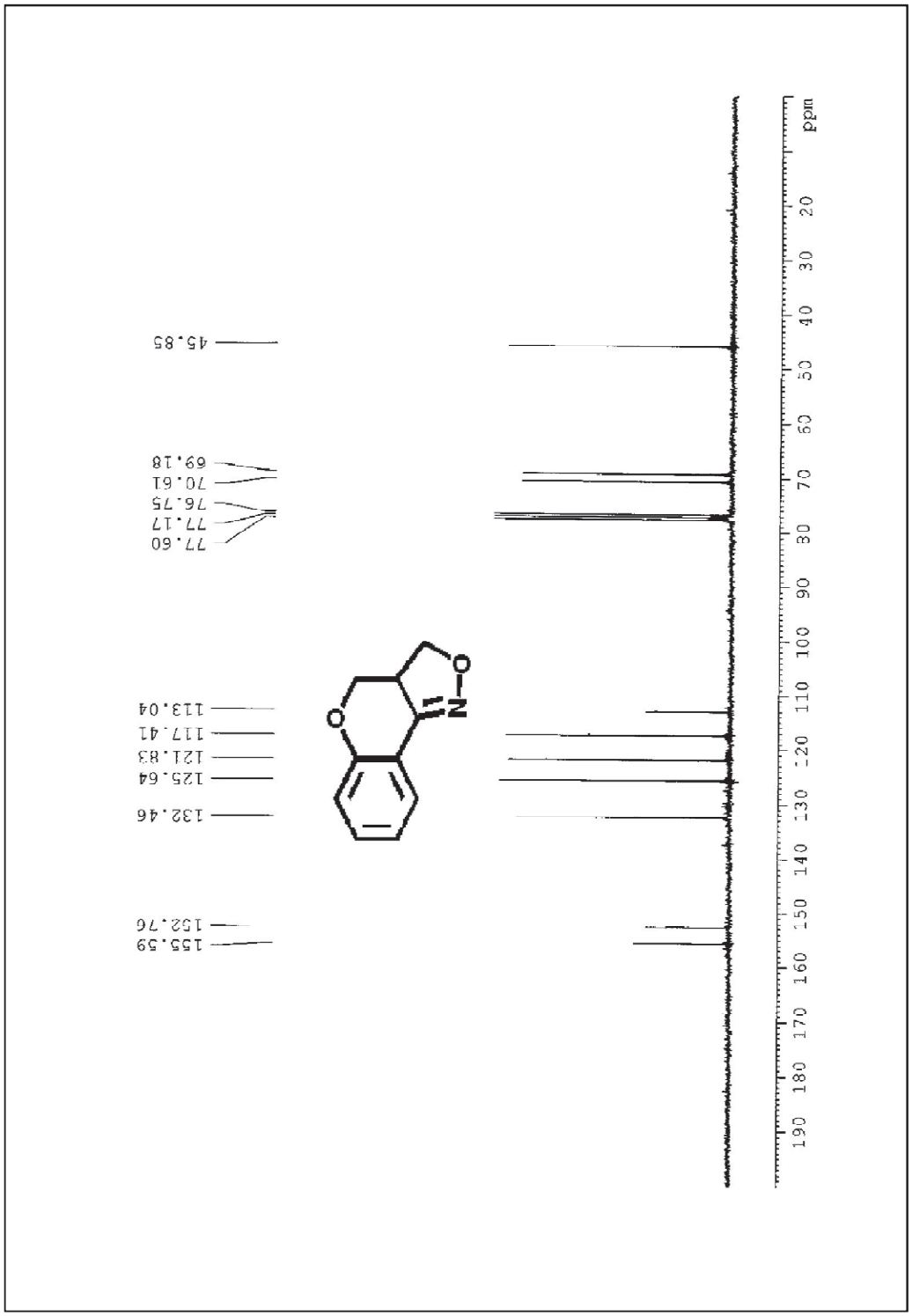
^{1}H NMR of Compound 7a



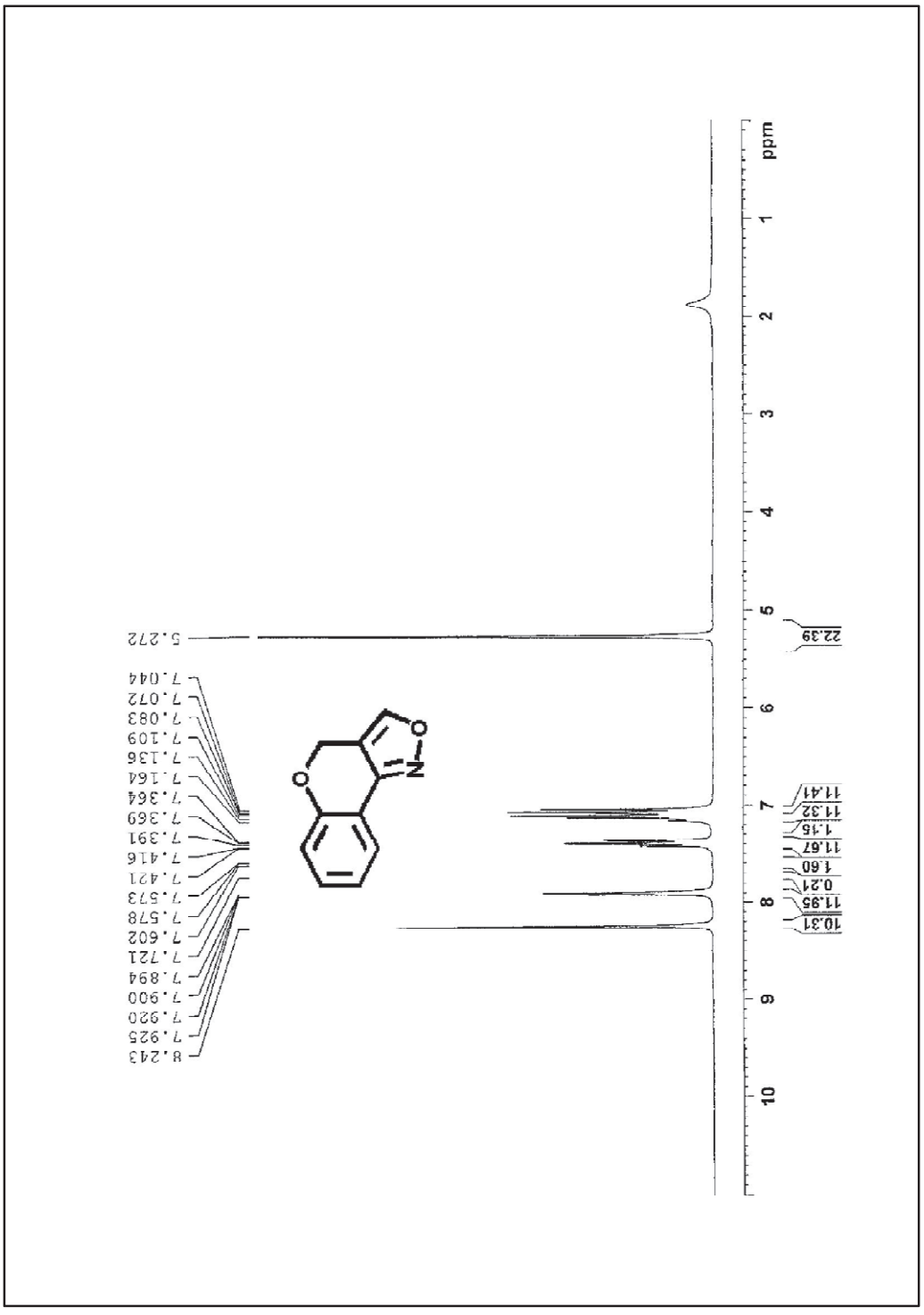
^{13}C NMR of Compound 7a



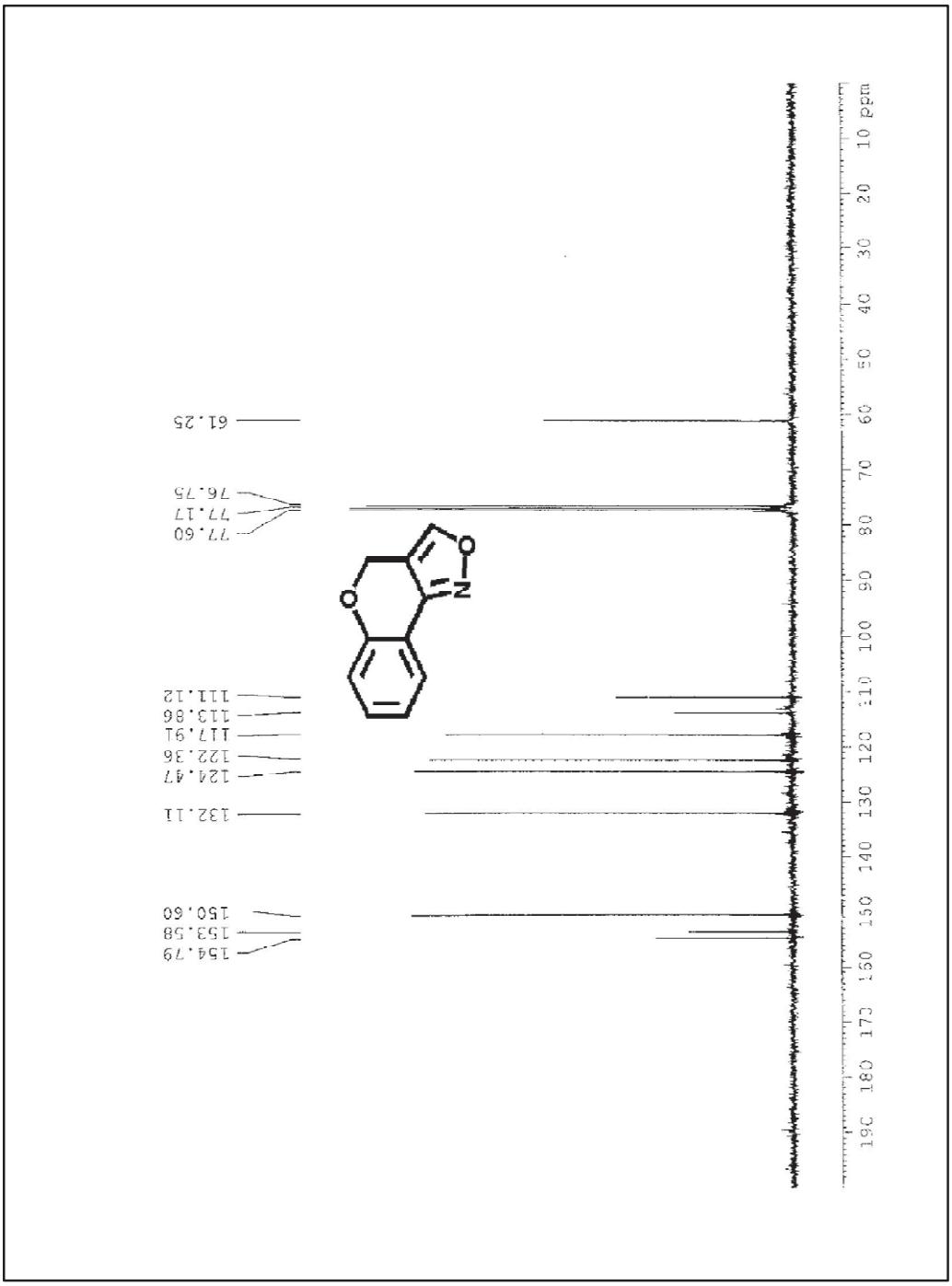
^{1}H NMR of Compound 7b



^{13}C NMR of Compound 7b



^{1}H NMR of Compound 7c



^{13}C NMR of Compound 7c