One Pot Synthesis of N-Arylpyrazoles from Arylhalides

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Supporting Information

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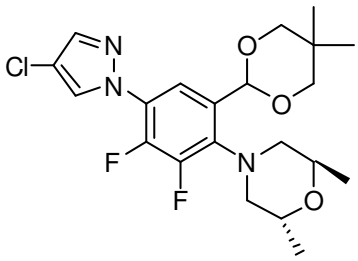
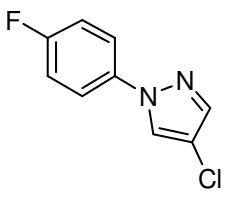
General Methods:

Proton (^{1}H NMR) and carbon (^{13}C NMR) magnetic resonance spectra where obtained in $CDCl_3$ at 400 MHz and 100 MHz, respectively unless otherwise noted. The following abbreviations were utilized to describe peak patterns when appropriate: br = broad, s = singlet, d = doublet, and m = multiplet. High-resolution mass measurements were obtained on an Agilent ToF mass spectrometer. All air and moisture sensitive reactions were carried out under an atmosphere of dry nitrogen using heat-dried glassware and standard syringe techniques. Tetrahydrofuran (THF) and acetonitrile were purchased from EMD anhydrous and were used without further drying. Flash chromatography was performed using an Analogix Intelliflash 280 with Sepra Si 50 silica gel using ethyl acetate/heptane mixtures as solvent unless otherwise indicated.

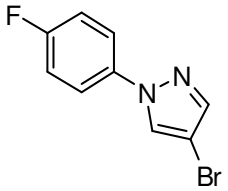


(2R,6R)-4-(4-(4-chloro-1H-pyrazol-1-yl)-6-(5,5-dimethyl-1,3-dioxan-2-yl)-2,3-difluorophenyl)-2,6-dimethylmorpholine (4): To a solution of aryl bromide (0.20 g, 0.476 mmol, 1.0 equiv) in THF (3 mL) at -78 °C was added *n*-buLi (2.5 M in hexanes, 0.190 mL, 1.05 equiv) and stirred for 5 mins. To the reaction was then added di-tert-butylazodicarboxylate (0.115 g, 1.05 equiv) and the reaction was stirred at -78 °C for 5 mins then allow to warm to room temperature (removed ice-bath). After 30 mins, 2-chloromalonaldehyde (186 mg, 1.75 mmol, 5.0 equiv) and 4 N HCl (~2 mL) was added and the reaction was heated to 100 °C for 5 mins. The reaction was cooled to room temperature and neutralized with sodium bicarbonate to pH ~7, extracted with ethyl acetate. The organic layer was dried with sodium sulfate, filtered and concentrated. The compound was purified used column chromatography to give a white solid (157 mg, 60 %). ^{1}H-NMR (DMSO-d6): δ = 0.74 (s, 3 H), 1.17 (s, 3 H), 1.21 (d, *J* = 1.4 Hz, 6 H), 2.74 (dd, *J* = 11.1, 5.9 Hz, 2 H), 3.09-3.17 (m, 2 H), 3.61-3.69 (m, 4 H), 3.95-4.13 (m, 2 H), 5.80 (s, 1 H), 7.70 (dd, *J* = 8.1, 2.2 Hz, 1 H), 7.94 (s, 1 H), 8.48 (d, *J* = 2.3 Hz, 1 H); ^{19}F-NMR (DMSO-d6): δ = -143.7. -147.3; HRMS [M+H] for $C_{21}H_{27}N_3O_3F_2Cl$, calcd., 442.1703, found, 442.1706.

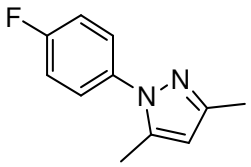


4-chloro-1-(4-fluorophenyl)-1H-pyrazole (7): To a solution 4-fluoroiodobenzene (222 mg, 1.0 mmol, 1.0 equiv) in THF (4 mL) at -78 °C was added n-BuLi (2.5 M in hexanes, 0.420 mL, 1.05 equiv).

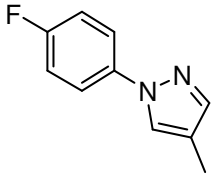
The reaction was stirred for 5 mins than di-tert-butylazodicarboxylate (242 mg, 1.05 equiv) in THF (1 mL) was added in one portion. The reaction changed from slightly yellow to amber color. The reaction was removed from the ice-bath and allowed to warm to room temperature over 30 mins. To the reaction mixture was added 2-chloromaldehyde (118 mg, 1.05 equiv) followed by 4 N HCl in Dioxane (~5 mL). The reaction changed from an amber color to light yellow with the addition of the acid. The reaction was then heated to 80 °C for 10 mins (the reaction turned dark amber color) then cooled to room temperature. The reaction was neutralized with sodium bicarbonate to pH ~7 and extracted with ethyl acetate (5 mL x 3). The organic layer was dried with sodium sulfate, filtered, and concentrated to give an amber oil, which by TLC showed only one major spot above baseline (8:2 heptane/ethyl acetate). The reaction was purified via silica gel chromatography to give an off-white solid (125 mg, 64 %), ^{1}H-NMR ($CDCl_3$): δ = 7.11-7.18 (m, 2 H), 7.55-7.61 (m, 2 H), 7.62 (s, 1 H), 7.83 (d, *J* = 0.78 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 112.7, 116.5, 116.7, 121.0 ,121.1, 125.2, 139.8, 160.4, 162.8; ^{19}F-NMR ($CDCl_3$): δ = −115.4 ; HRMS [M+H] for $C_9H_7N_2FCl$, calcd., 197.0276, found, 197.0281.



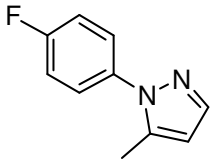
4-bromo-1-(4-fluorophenyl)-1H-pyrazole (8): To a solution 4-fluoroiodobenzene (222 mg, 1.0 mmol, 1.0 equiv) in THF (4 mL) at -78 °C was added n-BuLi (2.5 M, 0.42 mL, 1.05 equiv). The reaction was stirred for 5 mins than di-tert-butylazodicarboxylate (242 mg, 1.05 equiv) in THF (1 mL) was added in one portion. The reaction changed from slightly yellow to amber color. The reaction was removed from the ice-bath and allowed to warm to room temperature over 30 mins. To the reaction mixture was added 2-bromomaldehyde (158 mg, 1.05 equiv) followed by 10% H_2SO_4 in Dioxane (~5 mL). The reaction changed from an amber color to light yellow with the addition of the acid. The reaction was then heated to 80 °C for 10 mins (the reaction turned dark amber color) then cooled to room temperature. The reaction was neutralized with sodium bicarbonate to pH ~7 and extracted with ethyl acetate (5 mL x 3). The organic layer was dried with sodium sulfate, filtered, and concentrated to give an amber oil, which by TLC showed only one major spot above basiline (8:2 heptane/ethyl acetate). The reaction was purified via silica gel chromatography to give a yellow solid (165 mg, 68 %), ^{1}H-NMR ($CDCl_3$): δ = 7.11-7.18 (m, 2 H), 7.56-7.61 (m, 2 H), 7.65 (s, 1 H), 7.86 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 95.9, 116.5, 116.7, 121.1, 121.1, 127.4, 141.8, 160.4, 162.9; ^{19}F-NMR ($CDCl_3$): δ = -115.3; HRMS [M+H] for $C_9H_7N_2FBr$ calcd., 240.9771, found, 240.9771.



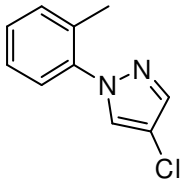
1-(4-fluorophenyl)-3,5-dimethyl-1H-pyrazole (9): Title compound prepared in a similar manor to that of **7** to give **9** an off-white solid (129 mg, 68 %). ^{1}H-NMR ($CDCl_3$): δ = 2.24 (s, 3 H), 2.26 (s, 3 H), 5.99 (s, 1 H), 7.14 (t, *J* = 8.6 Hz, 2 H), 7.39 (dd, *J* = 8.6, 4.9 Hz, 2 H); ^{13}C-NMR ($CDCl_3$): δ = 7.7, 8.9, 102.3, 111.2, 111.4, 122.1, 131.5, 134.9, 144.5, 155.8, 158.3; ^{19}F-NMR ($CDCl_3$): δ = -114.9; MS(API) calc: 191.1; found: 191.1 (M+H).



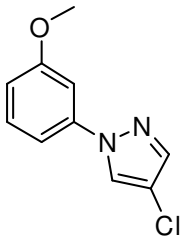
1-(4-fluorophenyl)-4-methyl-1H-pyrazole (10): Title compound prepared in a similar manor to that of **7** to give **10** an off-white solid (130 mg, 74 %), ^{1}H-NMR ($CDCl_3$): δ = 2.14 (s, 3 H), 7.06-7.15 (m, 2 H), 7.50 (s, 1 H), 7.55-7.61 (m, 2 H), 7.62 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 9.1, 116.2, 120.6, 120.7, 125.7, 142.0, 159.8, 162.3; ^{19}F-NMR ($CDCl_3$): δ = -117.2; HRMS [M+H] for $C_{10}H_{10}N_2F$, calcd., 177.0822, found, 177.0827.



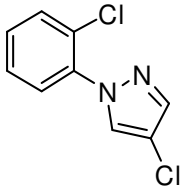
1-(4-fluorophenyl)-5-methyl-1H-pyrazole (11): Title compound prepared in a similar manor to that of **7** to give **11** (88 mg, 50 %) ; ^{1}H-NMR ($CDCl_3$): δ = 2.29 (s, 3 H), 6.16 (dd, *J* = 1.8, 0.8 Hz, 1 H), 7.04-7.18 (m, 2 H), 7.32-7.44 (m, 2 H), 7.53 (d, *J* = 1.8 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 12.5, 107.1, 116.0, 116.3, 126.9, 127.0, 136.2, 138.9, 140.1, 160.8, 163.3; ^{19}F-NMR ($CDCl_3$): δ = -114.3; MS(API) calc: 177.1; found: 177.1 (M+H).



4-chloro-1-o-tolyl-1H-pyrazole (12): Title compound prepared in a similar manor to that of **7** to give **12** a clear oil (140 mg, 73 %), ^{1}H-NMR ($CDCl_3$): δ = 2.24 (s, 3 H), 7.20-7.36 (m, 4 H), 7.58 (s, 1 H), 7.63 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 18.2, 111.2, 126.2, 126.9, 128.7, 129.1, 131.6, 133.9, 138.9, 139.7; HRMS [M+H] for $C_{10}H_{10}N_2Cl$, calcd., 193.0527, found, 193.0528.

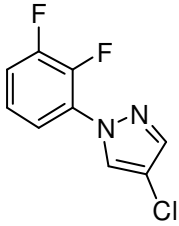


4-chloro-1-(3-methoxyphenyl)-1H-pyrazole (13): Title compound prepared in a similar manor to that of **7** to give **13** a clear oil (125 mg, 60 %) ^{1}H-NMR ($CDCl_3$): δ = 3.84 (s, 3 H), 6.81-6.87 (m, 1 H), 7.12-7.16 (m, 1 H), 7.23 (t, *J* = 8.3 Hz, 1 H), 7.61 (s, 1 H), 7.87 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 55.7, 105.1, 111.1, 112.6, 113.1, 119.9, 125.2, 130.5, 139.6, 160.8; HRMS [M+H] for $C_{10}H_{10}N_2OCl$, calcd., 209.0476, found, 209.0482.

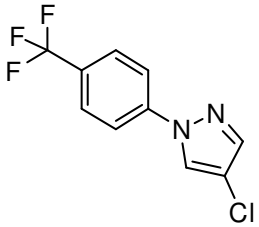


4-chloro-1-(2-chlorophenyl)-1H-pyrazole (14). To a solution of chloroiodobenzene (0.250g, 1.05 mmol) and di-tert-butylazodicarboxylate (0.274g, 1.15 mmol) in 5 mL dry THF at -78 ºC under N_2 was added dropwise *n*-butyllithium (2.5 M in hexanes, 0.45 mL, 1.12 mmol) over 3 minutes. The reaction gradually changed from bright yellow to orange during the addition. After five minutes MS indicated complete conversion to the intermediate hydrazide product. The cooling bath was removed and the reaction was quenched with 4 mL 4M HCl/dioxane while still cold then 2-chloromalonaldehyde (0.141g, 1.32 mmol) was added and the reaction was allowed to warm to ambient temperature. Then the reaction was kept in a closed vial while heating at 80 ºC for 20 minutes. MS then indicated complete conversion to the pyrazole product (213.0, 215.1 M+H, M+2+H). The reaction was cooled to ambient temperature and poured onto saturated sodium bicarbonate then extracted with ethyl acetate. The combined organic layers were washed with brine and dried over sodium

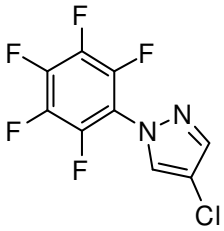
sulfate. Evaporation *in vacuo* gave a brown oil that was purified by silica gel chromatography (2-15% MTBE/Heptane) to give 0.121g (54%) of **14** as a colorless oil. ^{1}H-NMR ($CDCl_3$): δ = 7.86 (s, 26 H), 7.65 (s, 26 H), 7.53 (dd, J=7.61, 1.95 Hz, 1 H), 7.50 (dd, J=7.42, 1.95 Hz, 1 H), 7.35 (m, 2 H). ^{13}C-NMR ($CDCl_3$): δ = 111.67, 127.76, 128.02, 128.37, 129.37, 129.67, 130.95, 137.95, 139.67; MS(API) calc: 211.99; found: 213.0 (M+H).



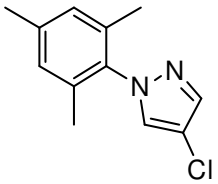
4-chloro-1-(2,3-difluorophenyl)-1H-pyrazole (15): Title compound prepared in a similar manor to that of 7 to give **15** (115 mg, 55 %), ^{1}H-NMR ($CDCl_3$): δ = 7.07-7.22 (m, 2 H), 7.61-7.65 (m, 1 H), 7.66-7.67 (m, 1 H), 7.99 (dd, *J* = 2.7, 0.6 Hz, 1 H); ^{19}F-NMR ($CDCl_3$): δ = -136.2, -150.3 MS(API) calc: 215.0; found: 215.1 (M+H).



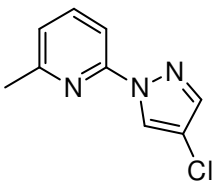
4-chloro-1-(4-(trifluoromethyl)phenyl)-1H-pyrazole (16): Title compound prepared in a similar manor to that of **7** to give **16** an off-white solid (184 mg, 75 %), ^{1}H-NMR ($CDCl_3$): δ = 7.67 (s, 1 H), 7.70-7.80 (m, 4 H), 7.96 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 113.7, 118.8, 122.6, 124.9, 125.4, 127.0-127.2 (m), 128.1, 128.6, 128.8, 129.2, 129.5, 140.6, 142.1; ^{19}F-NMR ($CDCl_3$): δ = -62.8; HRMS [M+H] for $C_{10}H_7N_2F_3Cl$, calcd., 247.0244, found, 247.0247.



4-chloro-1-(perfluorophenyl)-1H-pyrazole (17): Title compound prepared in a similar manor to that of **7** to give **17** an off-white solid (201 mg, 75 %), ^{1}H-NMR ($CDCl_3$): δ = 7.65 (q, *J* = 1.2 Hz, 1 H), 7.75 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 133.3, 130.0, 136.8-137.0, 139.3-139.7, 141.5-141.8, 141.5, 142.8-143.0, 144.1-144.3; ^{19}F-NMR ($CDCl_3$): δ = -147.6, -152.7, -160.7; HRMS [M+H] for $C_9H_3N_2F_5Cl$, calcd., 268.9899, found, 268.9908.

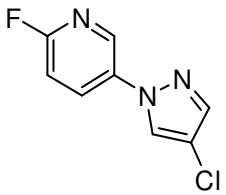


4-chloro-1-mesityl-1H-pyrazole (18): Title compound prepared in a similar manor to that of **7** to give **18** a yellow oil (94 mg, 43 %),^{1}H-NMR ($CDCl_3$): δ = 1.97 (s, 6 H), 2.32 (s, 3 H), 6.93 (d, *J* = 0.6 Hz, 2 H), 7.41 (d, *J* = 0.8 Hz, 1 H), 7.63 (d, *J*= 0.6 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 11.4, 21.3, 129.0, 129.1, 135.9, 138.7, 139.5; HRMS [M+H] for$C_{12}H_{14}N_2Cl$, calcd., 221.0840, found, 221.0843.

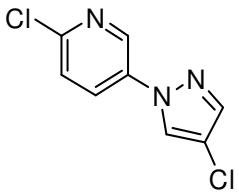


2-(4-chloro-1H-pyrazol-1-yl)-6-methylpyridine (19): Title compound prepared in a similar manor to that of **7** to give **19** a white solid (123 mg, 64 %), ^{1}H-NMR ($CDCl_3$): δ = 2.35 (s, 3 H), 7.59-7.63 (m, 1 H), 7.61 (d, *J* = 8.4 Hz, 1 H), 8.16-8.22 (m, 1 H), 8.48 (d, *J* = 0.8 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 18.1, 111.6, 112.8, 125.0, 131.7,

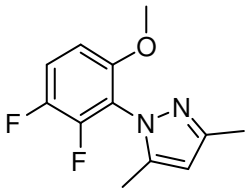
139.6, 140.2, 147.2, 149.3; HRMS [M+H] for $C_9H_9N_3Cl$, calcd., 194.0479, found, 194.0482.



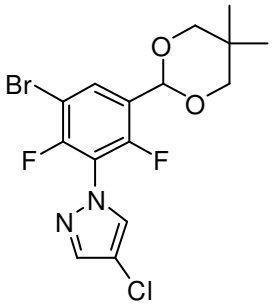
5-(4-chloro-1H-pyrazol-1-yl)-2-fluoropyridine (20): Title compound prepared in a similar manor to that of **7** to give **20** an off-white solid (115 mg, 58 %), ^{1}H-NMR ($CDCl_3$): δ = 7.05 (dd, *J* = 8.8, 3.3 Hz, 1 H), 7.67 (s, 1 H), 8.03-8.18 (m, 1 H), 8.46-8.50 (m, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 110.4, 110.7, 125.2, 132.5, 132.96, 138.0, 138.1, 140.7, 160.8, 163.2; ^{19}F-NMR ($CDCl_3$): δ = -69.8; HRMS [M+H] for $C_8H_6N_3FCl$ calcd., 198.0228, found, 198.0237.



2-chloro-5-(4-chloro-1H-pyrazol-1-yl)pyridine (21): Title compound prepared in a similar manor to that of **7** to give **21** a white solid (143 mg, 67%), ^{1}H-NMR ($CDCl_3$): δ = 7.43 (dd, *J* = 8.7, 0.7 Hz 1 H), 7.68 (s, 1 H), 7.98 (dd, *J* = 8.6, 2.8 Hz, 1 H), 8.68 (dd, *J* = 2.8, 0.7 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 114.0, 124.9, 125.0, 129.4, 139.9, 140.9, 149.4; HRMS [M+H] for $C_8H_6N_3Cl_2$, calcd., 213.9933, found, 213.9937.

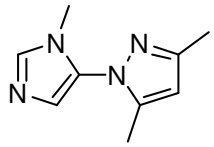


1-(2,3-difluoro-6-methoxyphenyl)-3,5-dimethyl-1H-pyrazole (22): Title compound prepared in a similar manor to that of **7** to give **22** a white solid (63 mg, 25 %), ^{1}H-NMR ($CDCl_3$): δ = 1.97 (s, 3 H), 2.12 (s, 3 H), 3.74 (s, 3 H), 6.00 (s, 1 H), 6.97 - 7.09 (m, 1 H), 7.56 (dd, *J* = 9.5, 9.5 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 10.9, 13.9, 57.2, 106.1, 108.1, 118.3, 142.1, 143.5, 143.6, 145-146 (m), 148.4, 148.5, 149.4, 153.0; ^{19}F-NMR ($CDCl_3$): δ = -144.5, -147.6; HRMS [M+H] for $C_{12}H_{13}N_2OF_2$, calcd., 239.0990, found, 239.0999

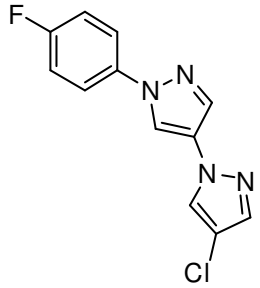


1-(3-bromo-5-(5,5-dimethyl-1,3-dioxan-2-yl)-2,6-difluorophenyl)-4-chloro-1H-pyrazole (23): To a starting aryl (327 mg, 1.06 mmol, 1.0 equiv) in THF (4 mL) at -78 °C was added lithium hexamethyldisilazane (1.0 M in THF, 1.06 mL, 1.06 mmol, 1.0 equiv). The reaction was stirred for 30 mins than DBAD (119 mg, 1.12 mmol, 1.05 equiv) in THF (1 mL) was added in one portion. The reaction went from slightly yellow to brown color. The reaction was removed from the ice-bath and allowed to warm to room temperature over 30 mins. To the reaction mixture was added 2-chloromaldehyde (118 mg, 1.12 mmol, 1.05 equiv) followed by 4 N HCl in Dioxane (~5 mL). The reaction went from amber to light yellow with the addition of the acid. The reaction was then heated to reflux ~100 °C for 5 mins (the reaction turned dark amber color) then cooled to room temperature. The reaction was carefully neutralized with sodium bicarbonate to pH ~7 and extracted with ethyl acetate (5 mL x 3). The organic layer was dried with sodium sulfate, filtered, and concentrated to give an amber oil, which by TLC showed only one major spot above baseline (8:2 heptane/ethyl acetate). The reaction was purified via column

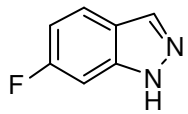
chromatography to give a white solid (265 mg, 61 %). ^{1}H-NMR ($CDCl_3$): δ = 0.80 (s, 3 H), 1.29 (s, 3 H), 3.65 (d, *J* = 10.4 Hz, 2 H), 3.75 (d, *J* = 10.4 Hz, 2 H), 5.62 (s, 1 H), 7.62 (s, 1 H), 7.71 (s, 1 H), 7.95 (t, *J* 7.2 Hz, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 21.9, 23.2, 30.5, 78.0, 95.3, 130.1, 131.8, 140.8; ^{19}F-NMR ($CDCl_3$): δ = -110.5, -126.5; MS(API) calc: 407.0/409.0; found: 407.0/408.0 (M+H).



3,5-dimethyl-1-(1-methyl-1H-imidazol-5-yl)-1H-pyrazole (24): Ethyl magnesium chloride (2.0 M in THF, 0.550 mL, 1.1 mmol, 1.1 equiv) was taken up in THF (5.0 mL) and charged with 5-bromo-1-methyl-1*H*-imidazole (159 mg, 1.0 mmol, 1.0 equiv) in THF (1.0 mL). Upon slow addition the solution became cloudy white. After complete addition the reaction became yellow/brown and stayed cloudy. After 20 min, the reaction was charged with DBAD (0.250 g, 1.1 mmol, 1.1 equiv) following which the reaction was allowed to warm to ambient temperature. To the reaction was added 4N HCl/dioxane (10.0 mL) and charged with the acetylacetone (0.112 mL, 1.1 mmol, 1.1 equiv) then heated to reflux. After 30 min at reflux MS showed the desired product formation. The reaction mixture was cooled to room temperature and concentrated. The crude brown oil was purified via column chromatography using methanol/DCM (1:9) to give **24** has an oil (86 mg, 45 %), ^{1}H-NMR ($CDCl_3$): δ = 2.05 (s, 3 H), 2.14 (s, 3 H), 3.32 (s, 3 H), 6.05 (s, 1 H), 6.99 (s, 1 H), 7.68 (s, 1 H); ^{13}C-NMR ($CDCl_3$): δ = 149.9, 143.1, 138.0, 124.7, 106.6, 31.1, 14.0, 11.5; HRMS [M+H] for $C_9H_{12}N_4$, calcd., 177.1138, found, 177.1134.

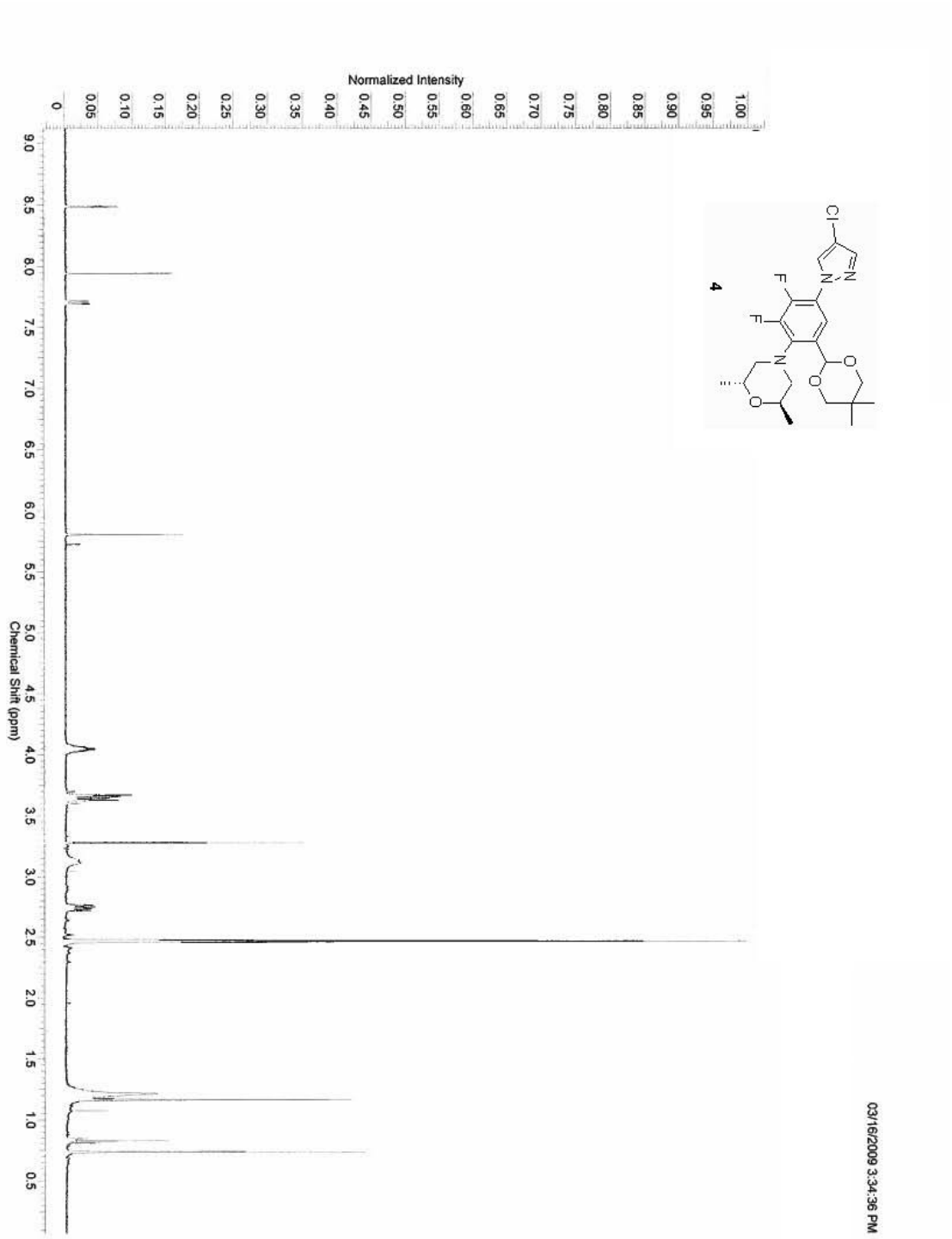


4-(4-bromo-1H-pyrazol-1-yl)-1-(4-fluorophenyl)-1H-pyrazole (23): Title compound prepared in a similar manor to that of **7** to give **23** (32 mg, 50 %). ^{1}H-NMR ($CDCl_3$): δ = 7.11 - 7.21 (m, 2 H) 7.59 (s, 1 H) 7.62 - 7.69 (m, 2 H) 7.72 (s, 1 H) 7.88 (s, 1 H) 8.12 - 8.17 (m, 1 H); ^{19}F-NMR ($CDCl_3$): δ = -115.1; MS(API) calc: 263.1; found: 263.1 (M+H).



6-fluoro-1H-indazole (27): To a solution aryl halide (100 mg, 0.35 mmol, 1.0 equiv) in THF (2 mL) at -78 °C was added n-BuLi (2.5 M in hexanes, 0.145 mL, 0.363 mmol, 1.05 equiv) The reaction was stirred for 5 mins than DBAD (84 mg, 0.363 mmol, 1.05 equiv) in THF (1 mL) was added in one portion. The reaction was removed from the ice-bath and allowed to warm to room temperature over 30 mins. To the reaction mixture was added 4 N HCl in Dioxane (~5 mL). The reaction went from amber to light yellow with the addition of the acid. The reaction was then heated to reflux ~100 °C for 5 mins then cooled to room temperature. The reaction was carefully neutralized with sodium bicarbonate to pH ~7 and extracted with ethyl acetate (5 mL x 3). The organic layer was dried with sodium sulfate, filtered, and concentrated to give an amber oil, which by TLC showed only one major spot above baseline (8:2 heptane/ethyl acetate). The reaction was purified via column chromatography to give a white solid (36 mg, 76 %), ^{1}H-NMR ($CDCl_3$): δ = 6.94-7.01 (m, 1 H), 7.13-7.20 (m, 1 H), 7.67-7.75 (m, 1 H), 8.07 (s, 1 H); ^{13}C-NMR

($CDCl_3$): δ = 95.5. 95.7. 111.2. 111.4. 122.4, 122.6, 135.4, 161.5, 163.9; ^{19}F-NMR ($CDCl_3$): δ = -114.5; HRMS [M+H] for $C_7H_6N_2F$, calcd., 137.0509, found, 137.0512.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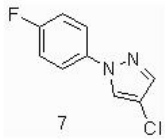

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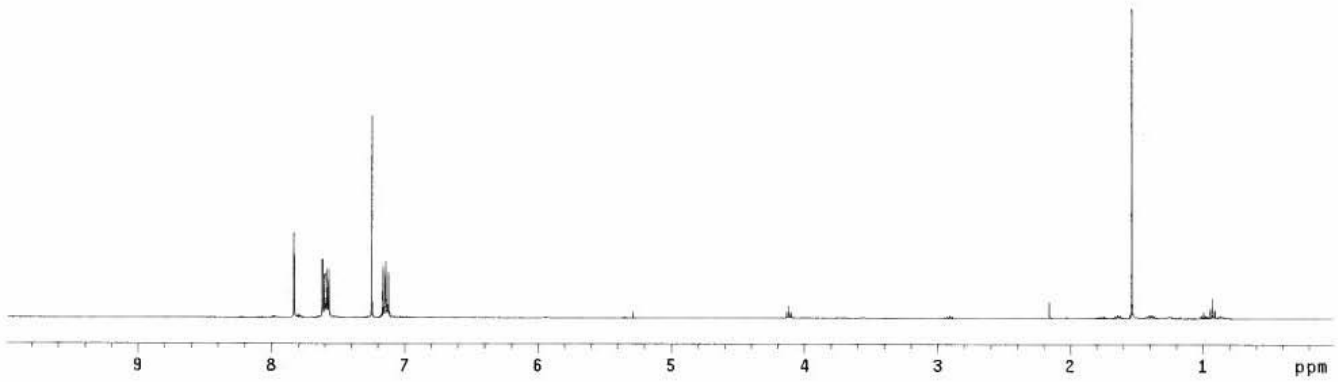

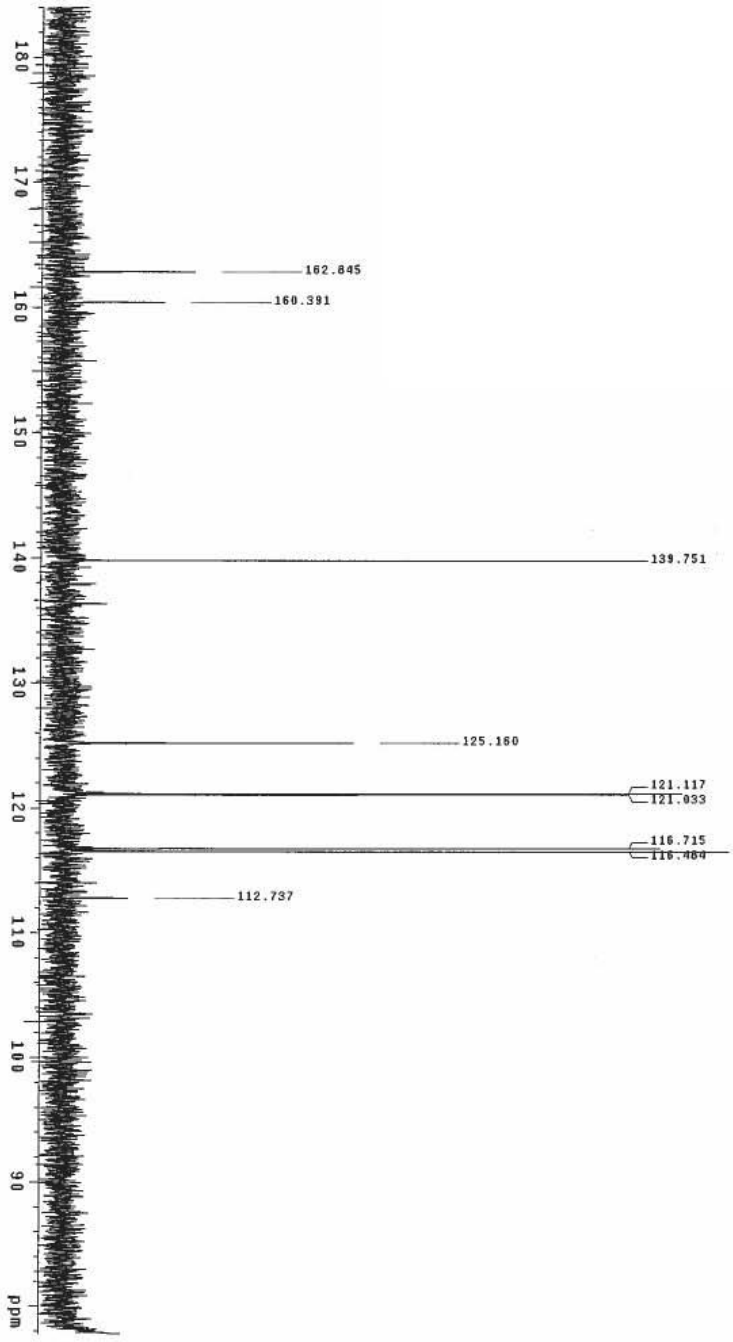
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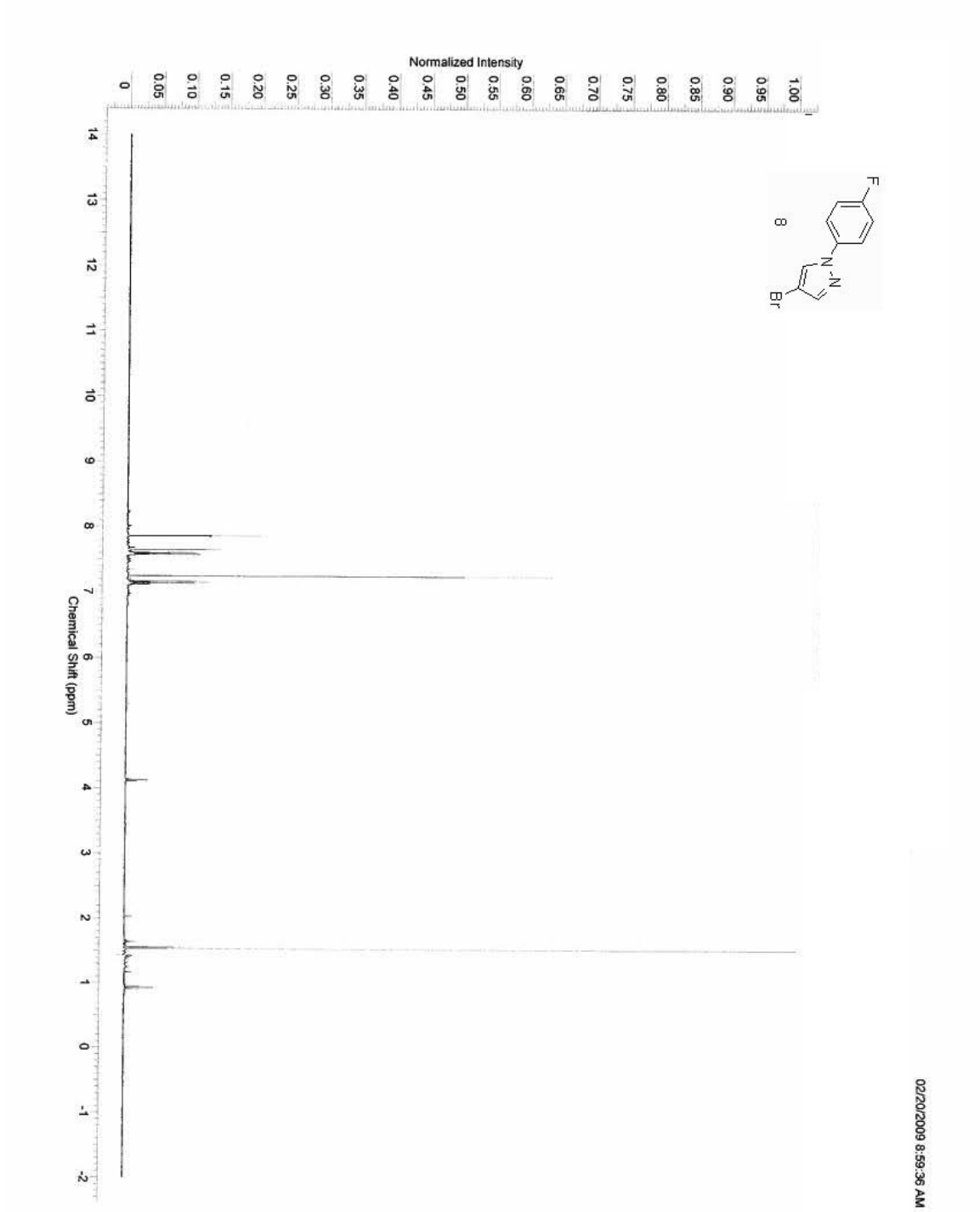
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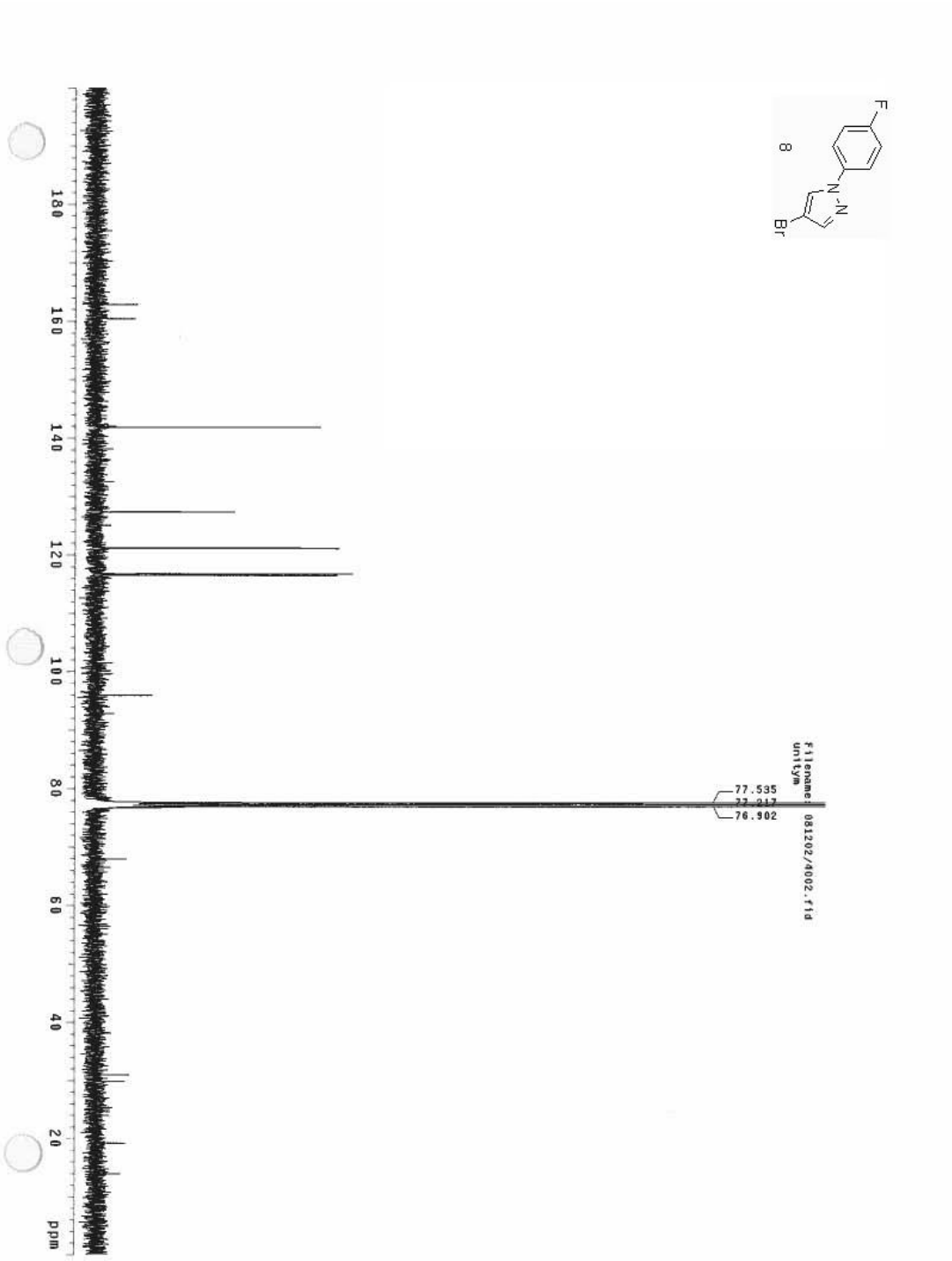
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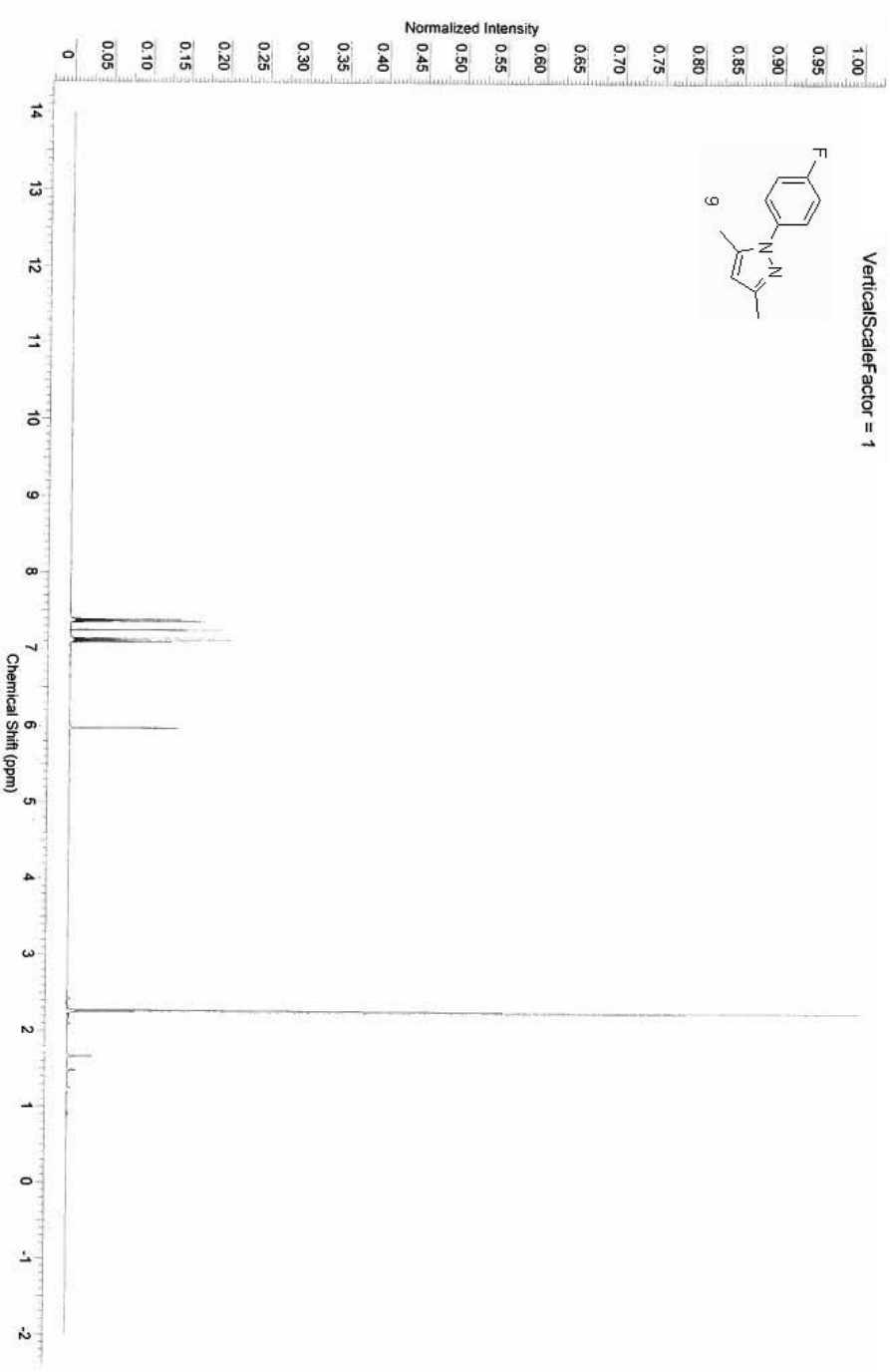
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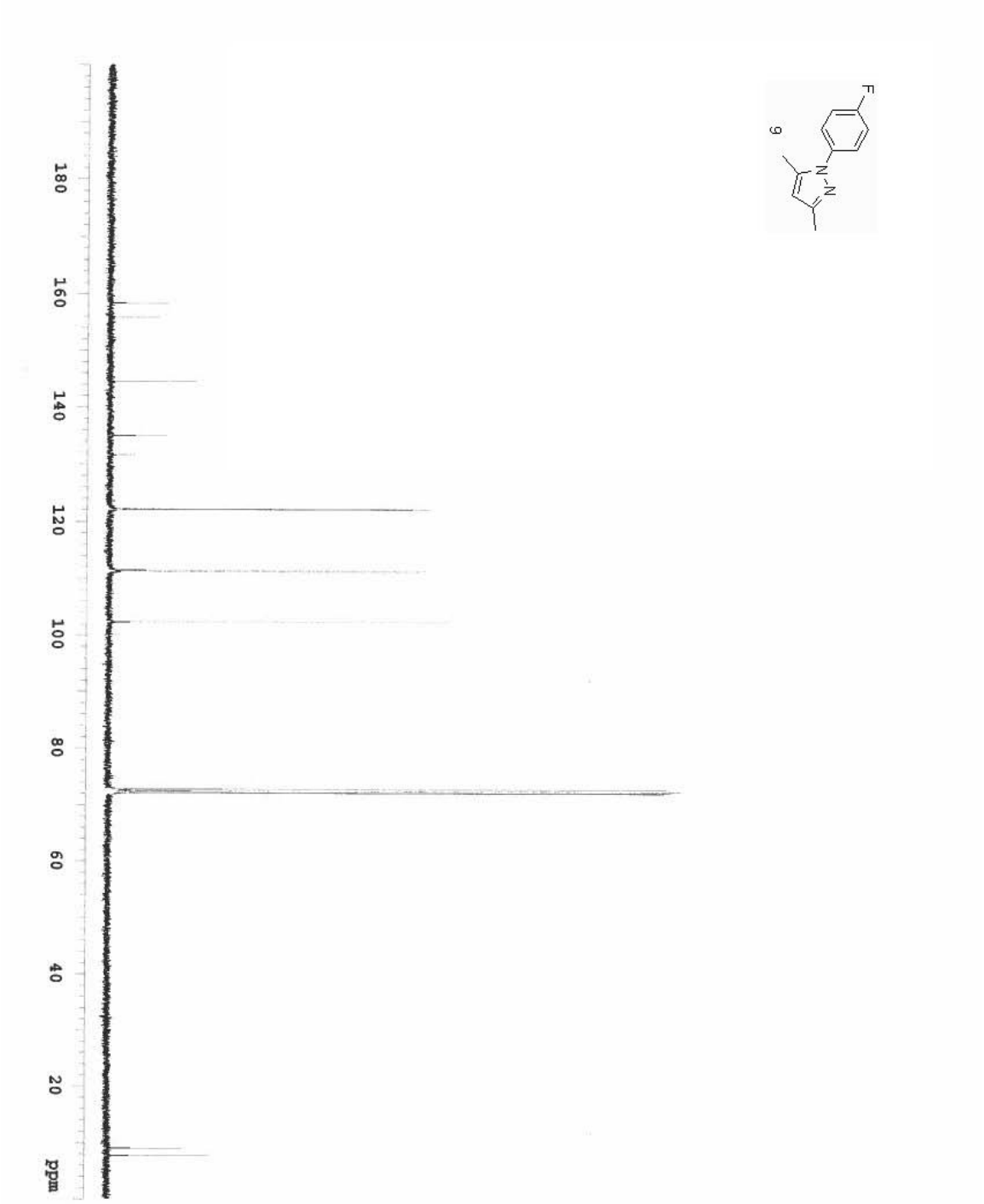
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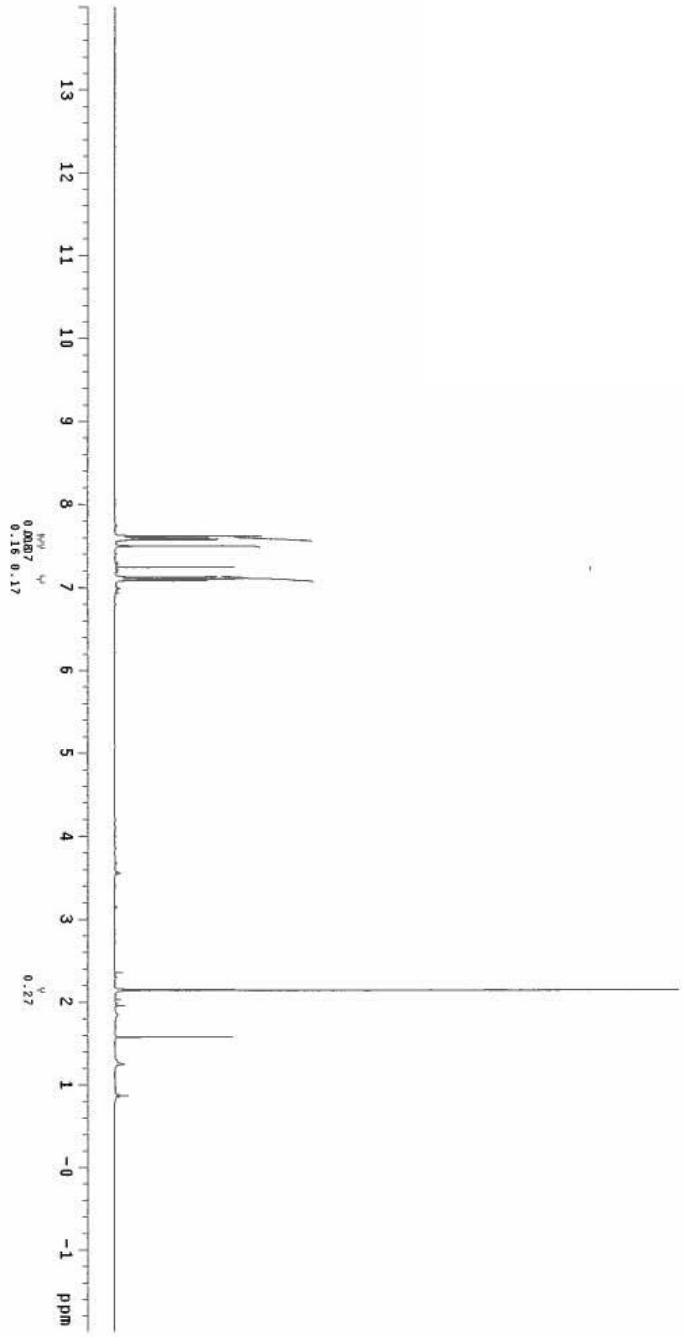
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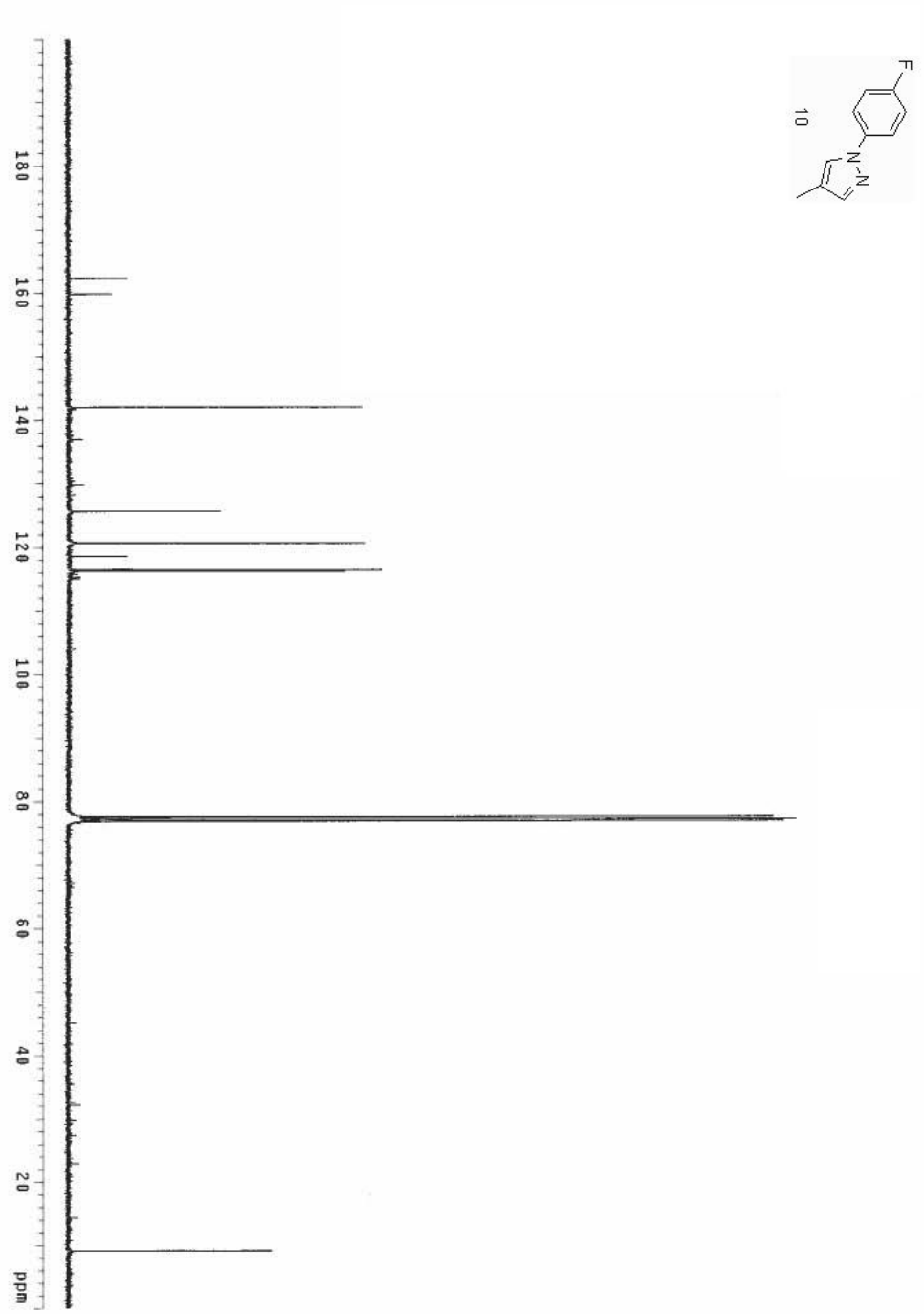
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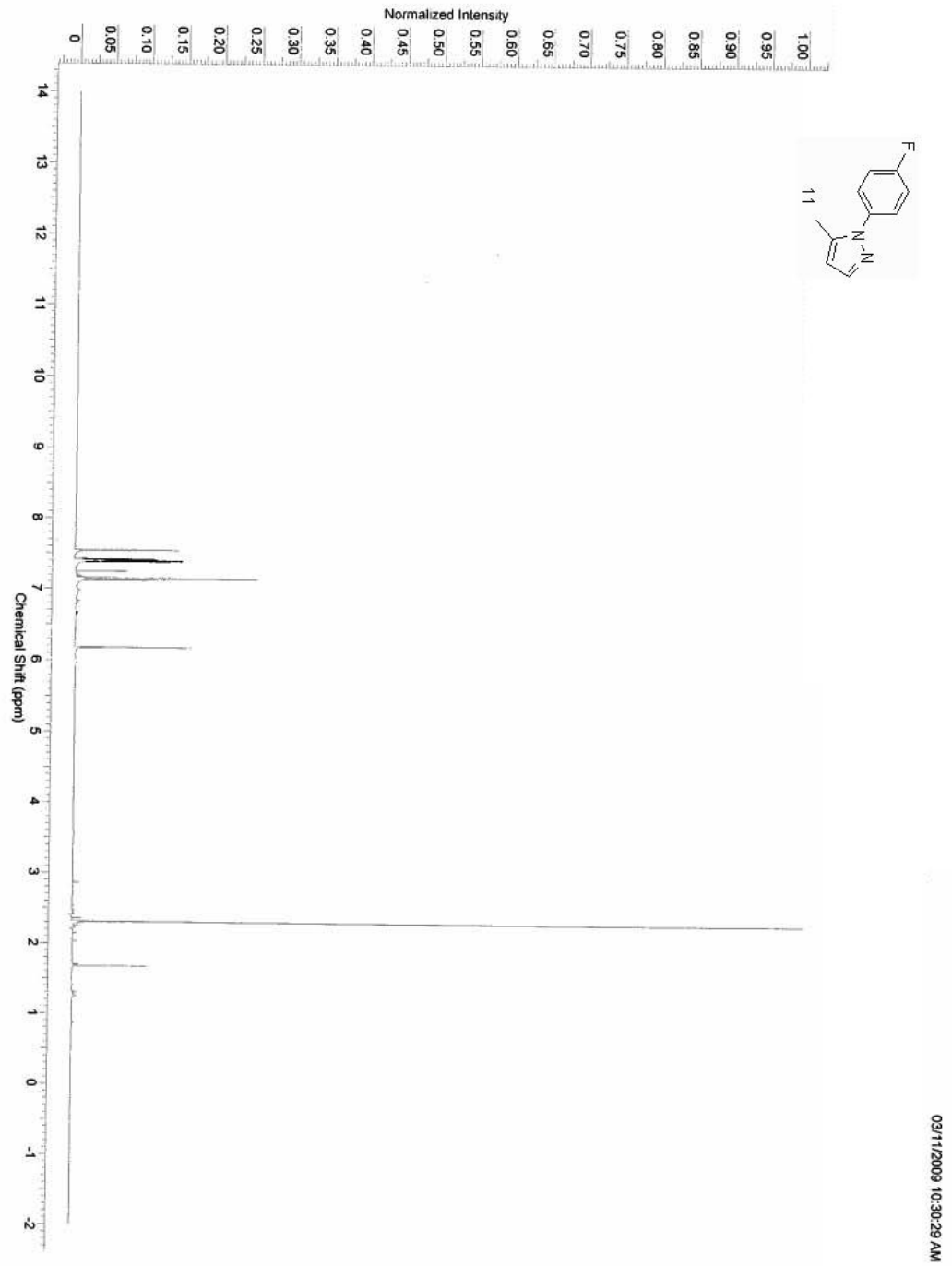
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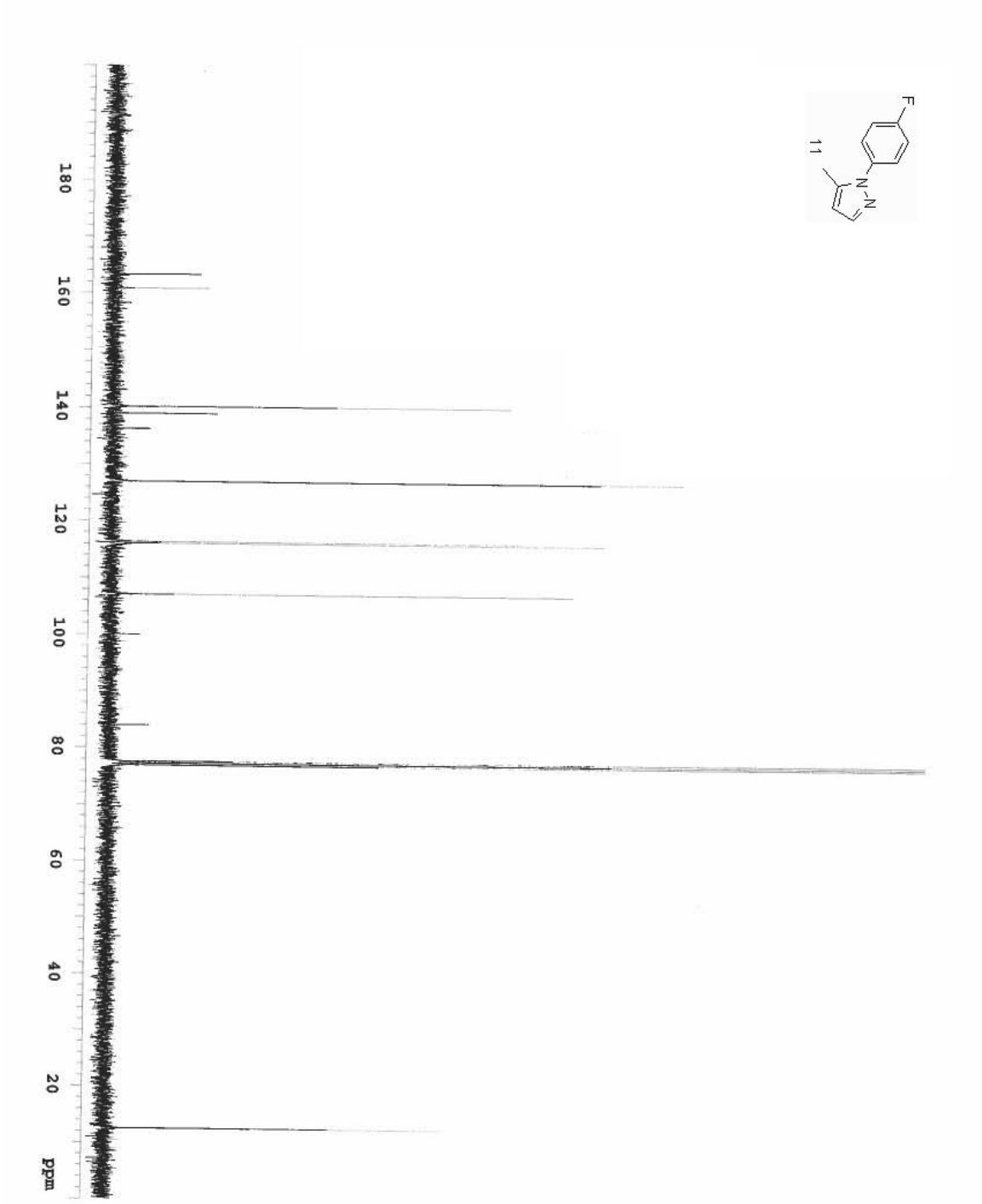
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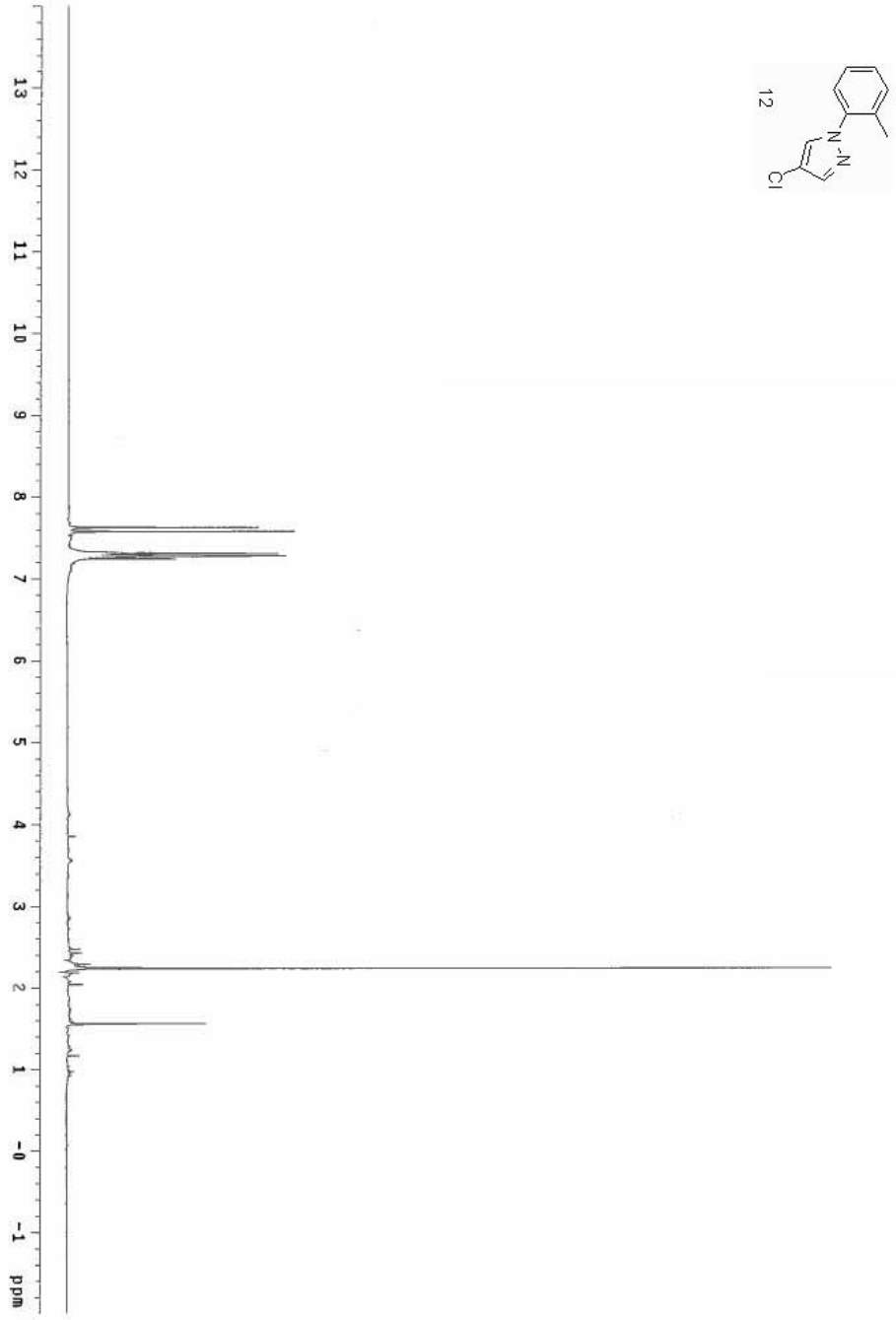
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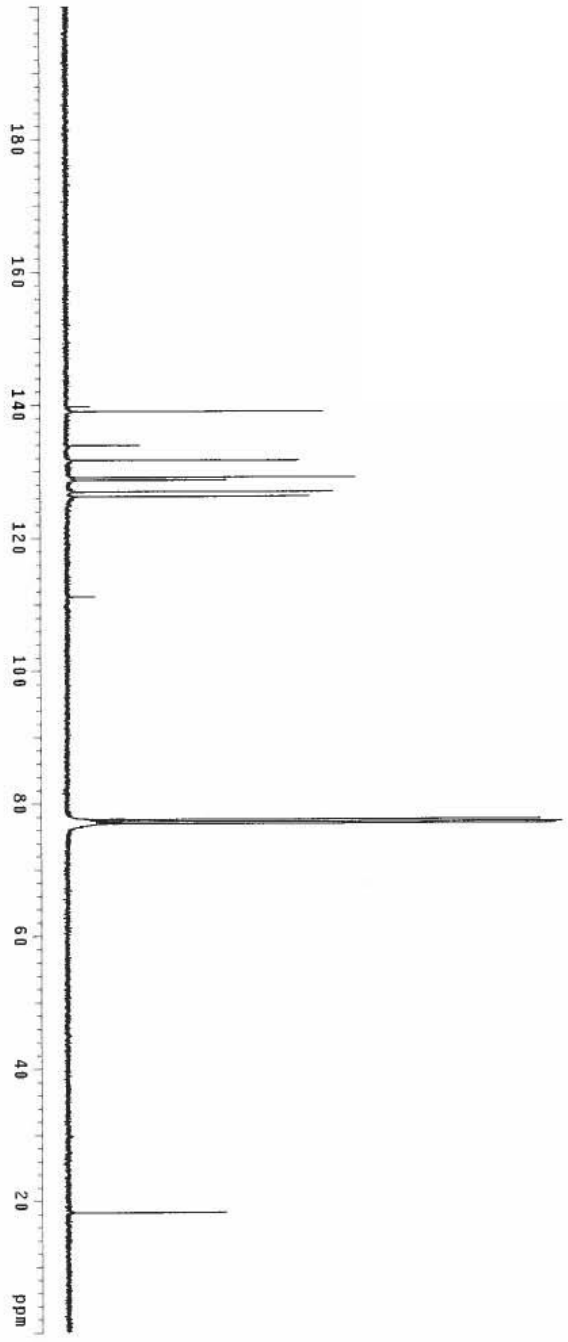
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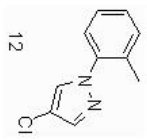
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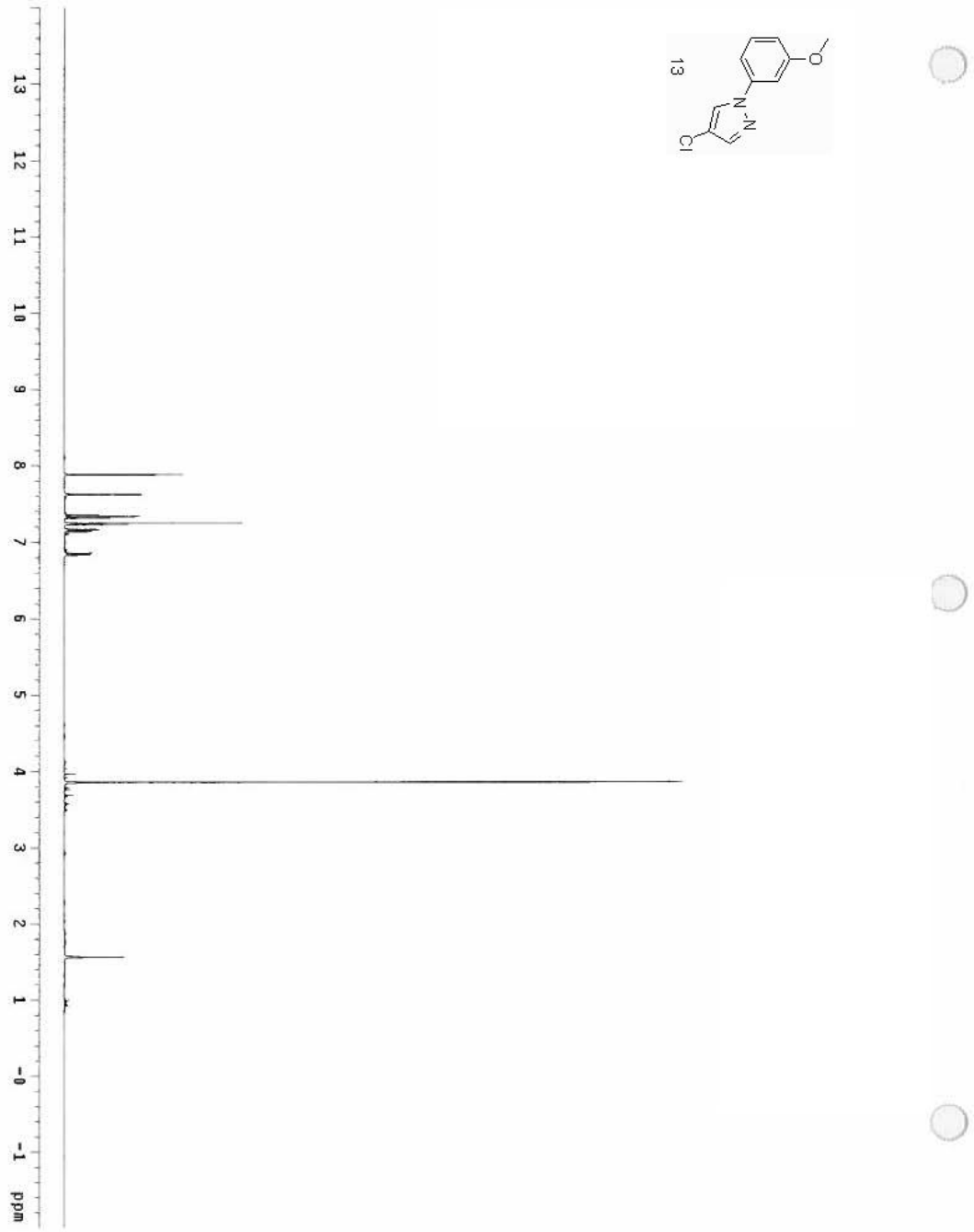
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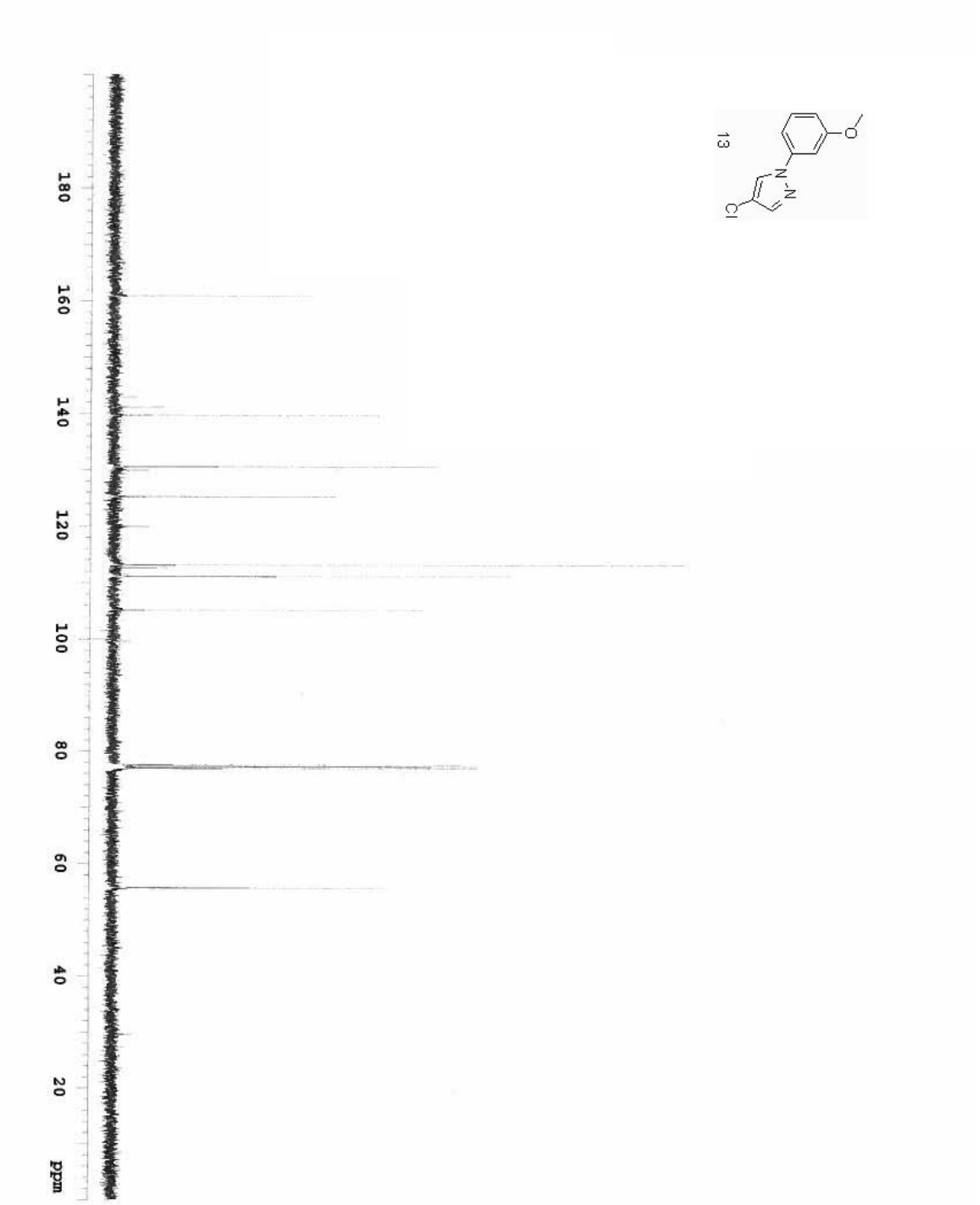
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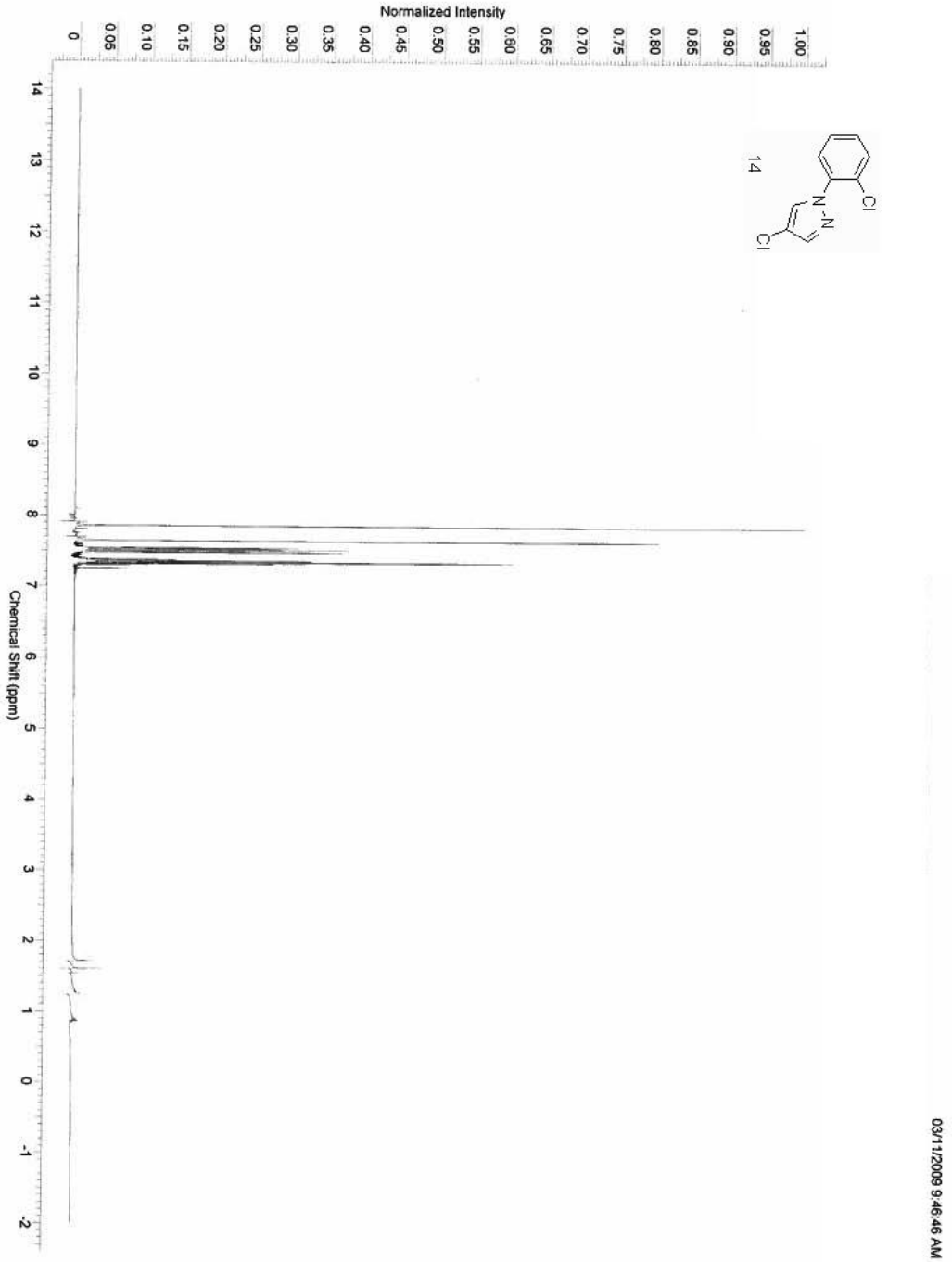
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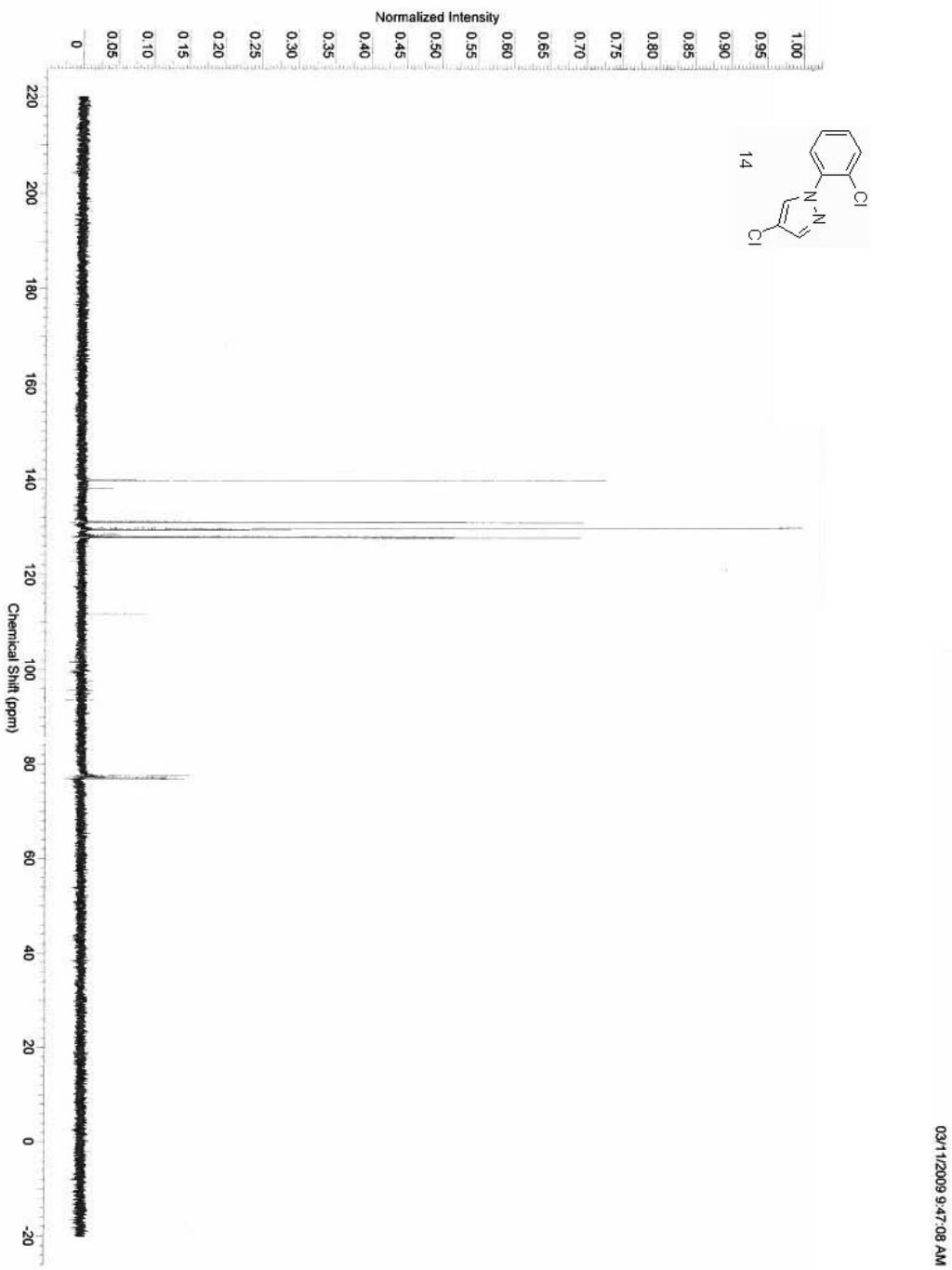
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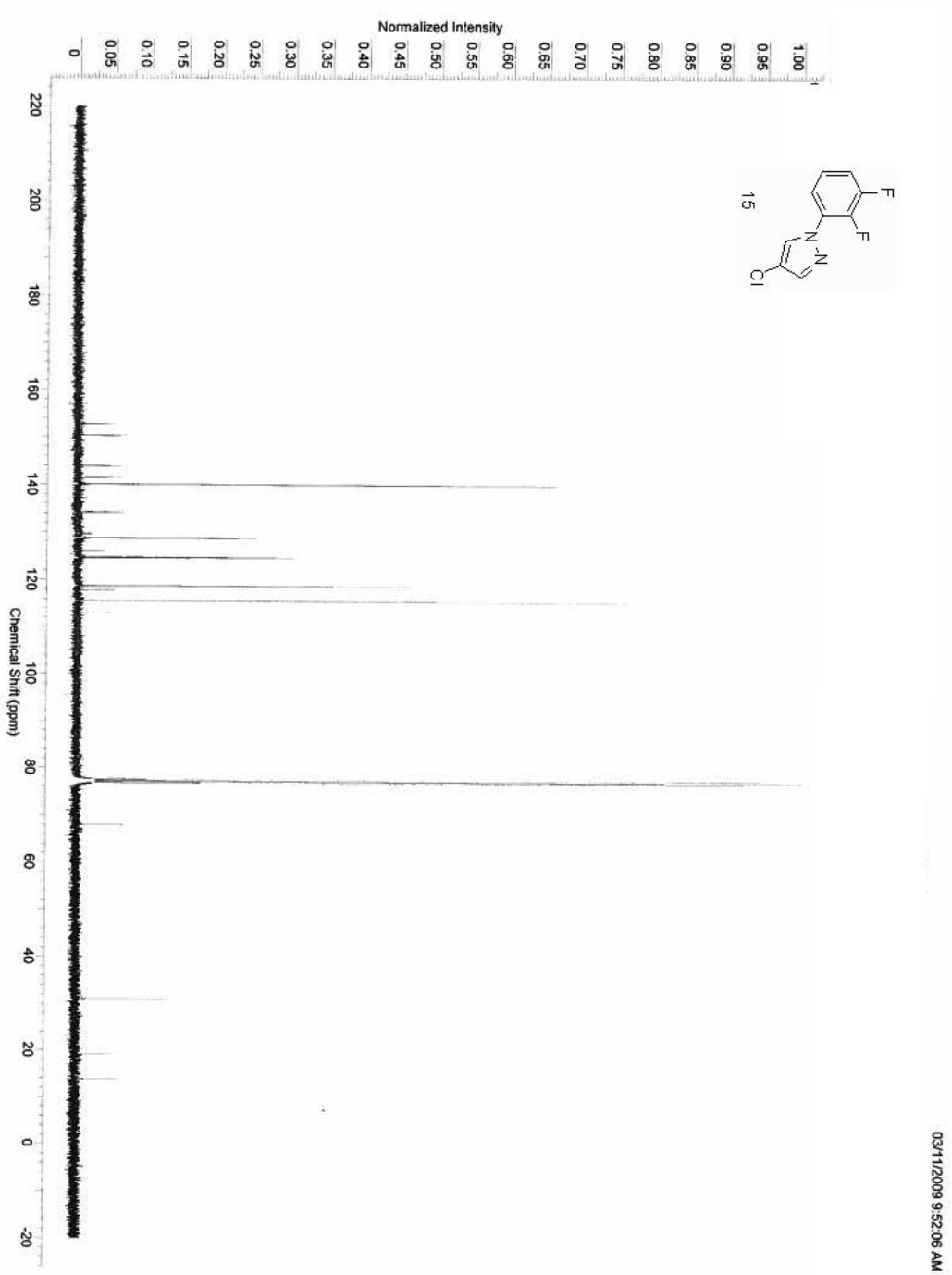
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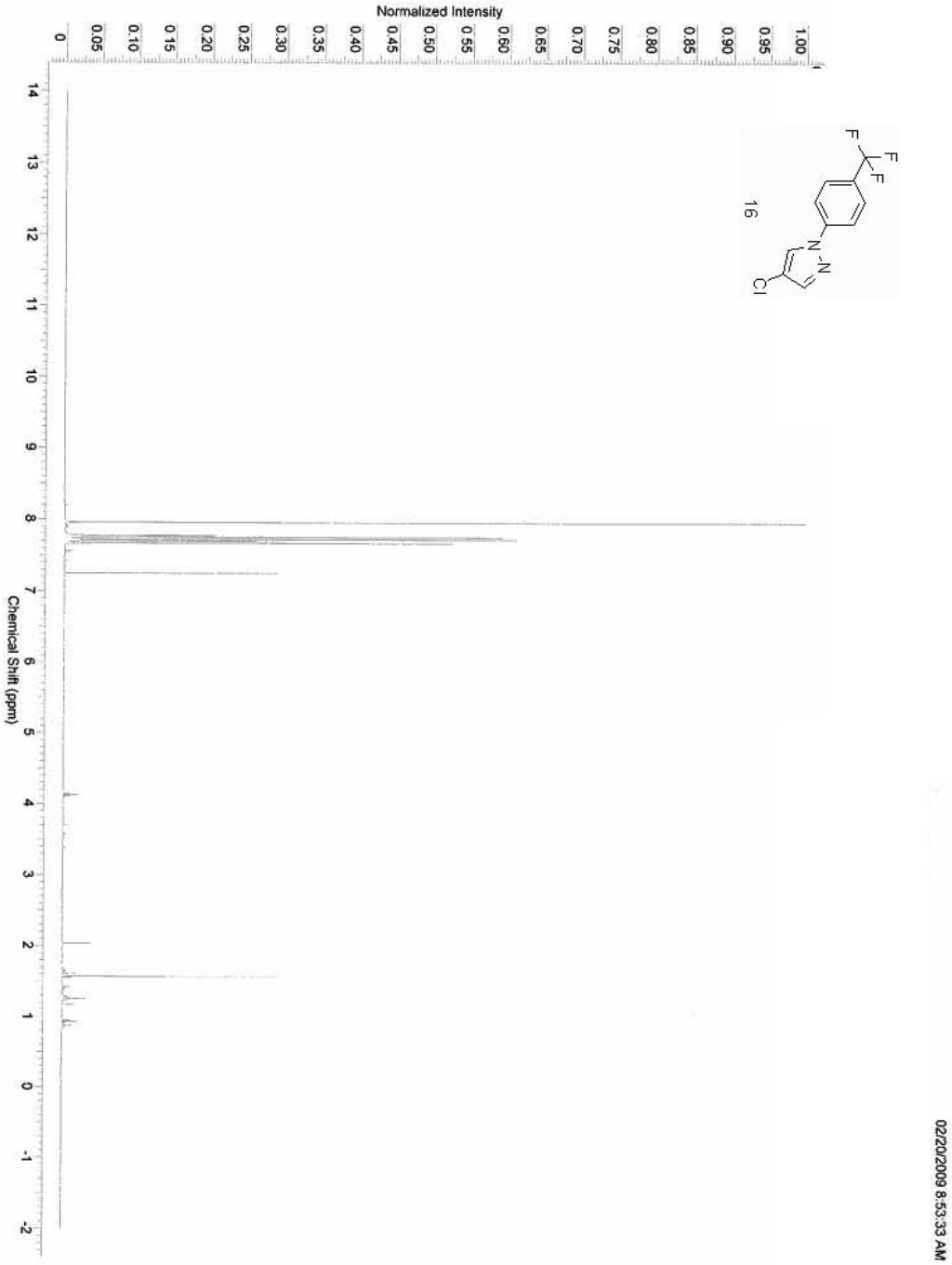
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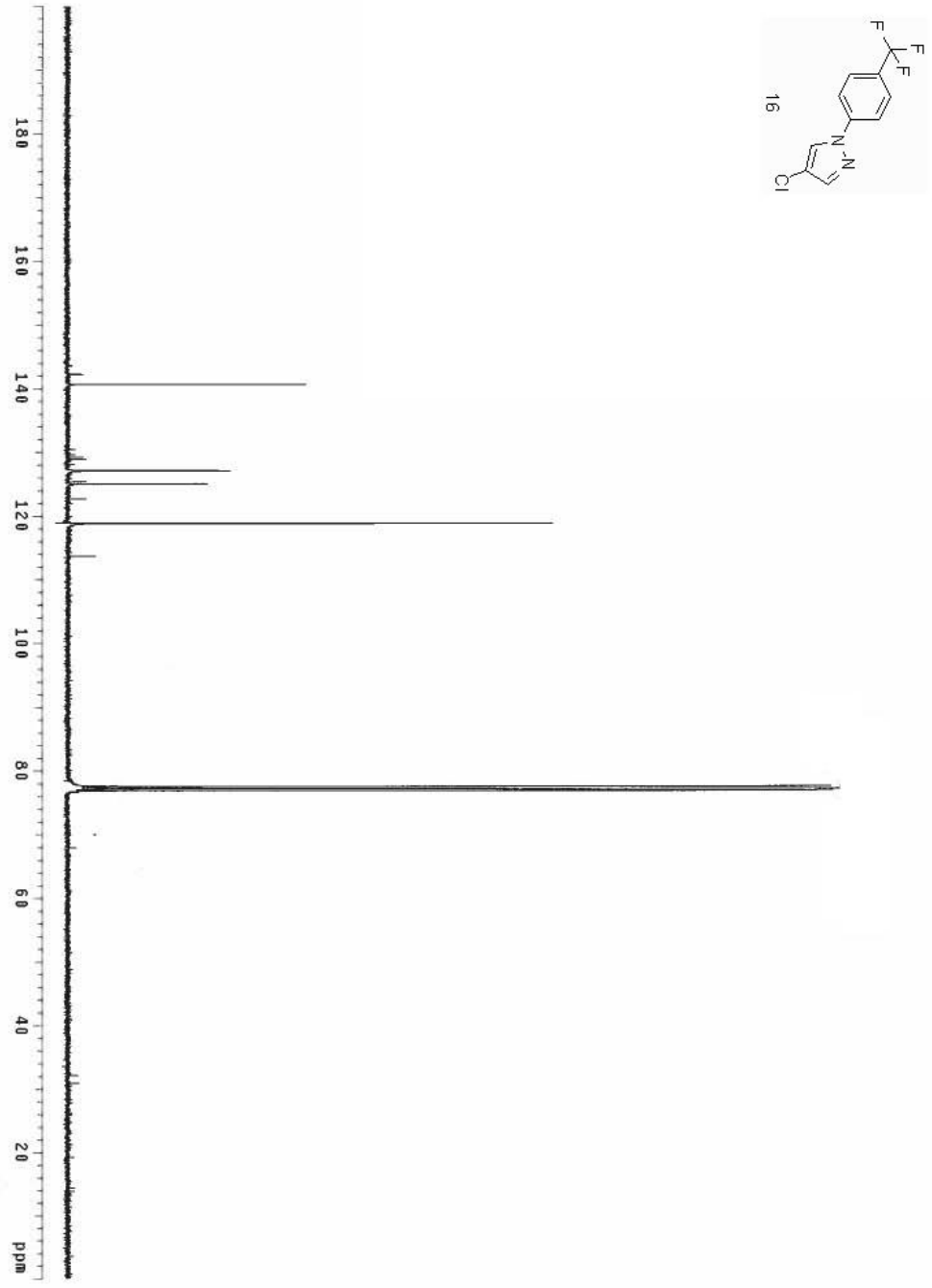
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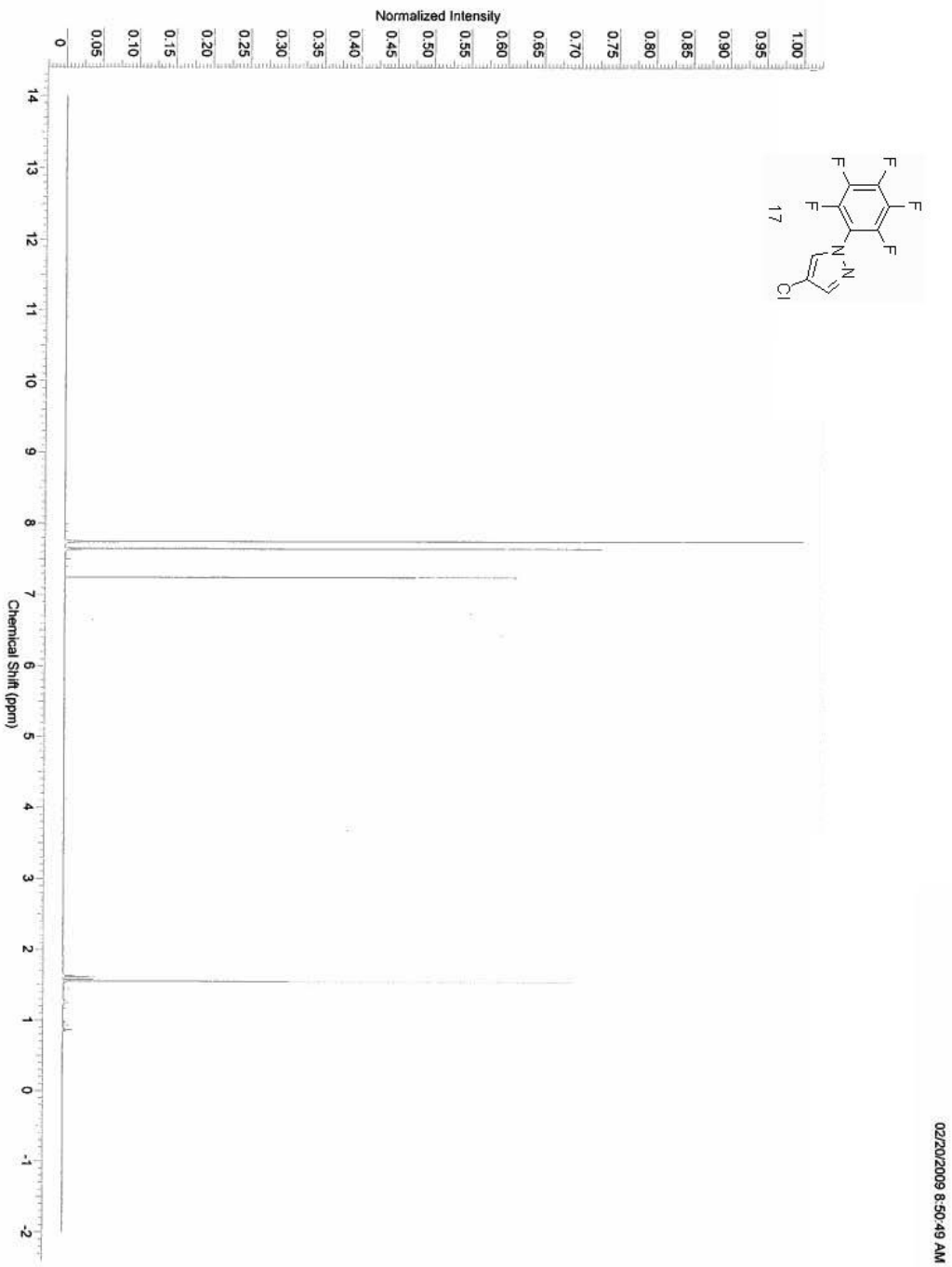
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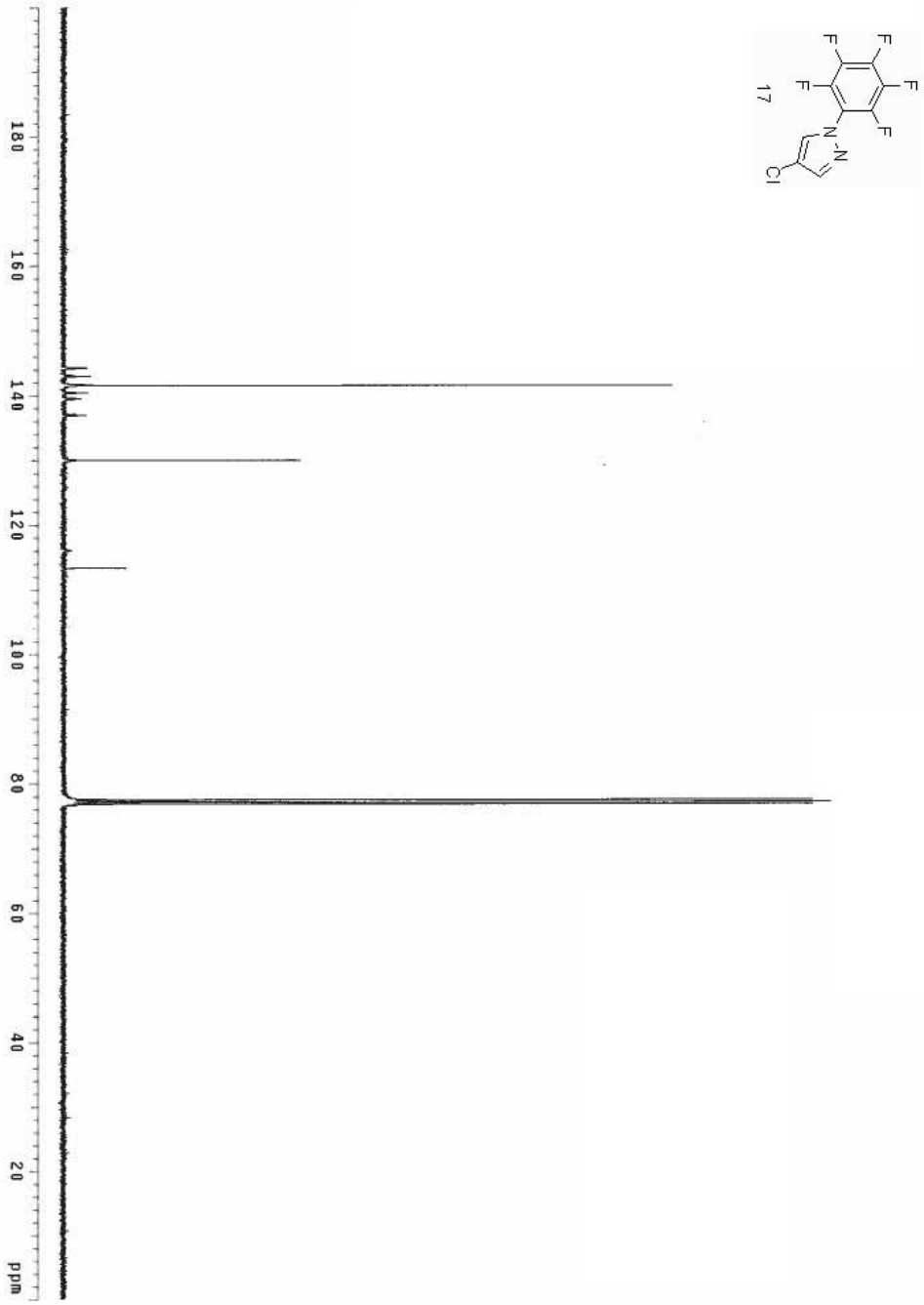
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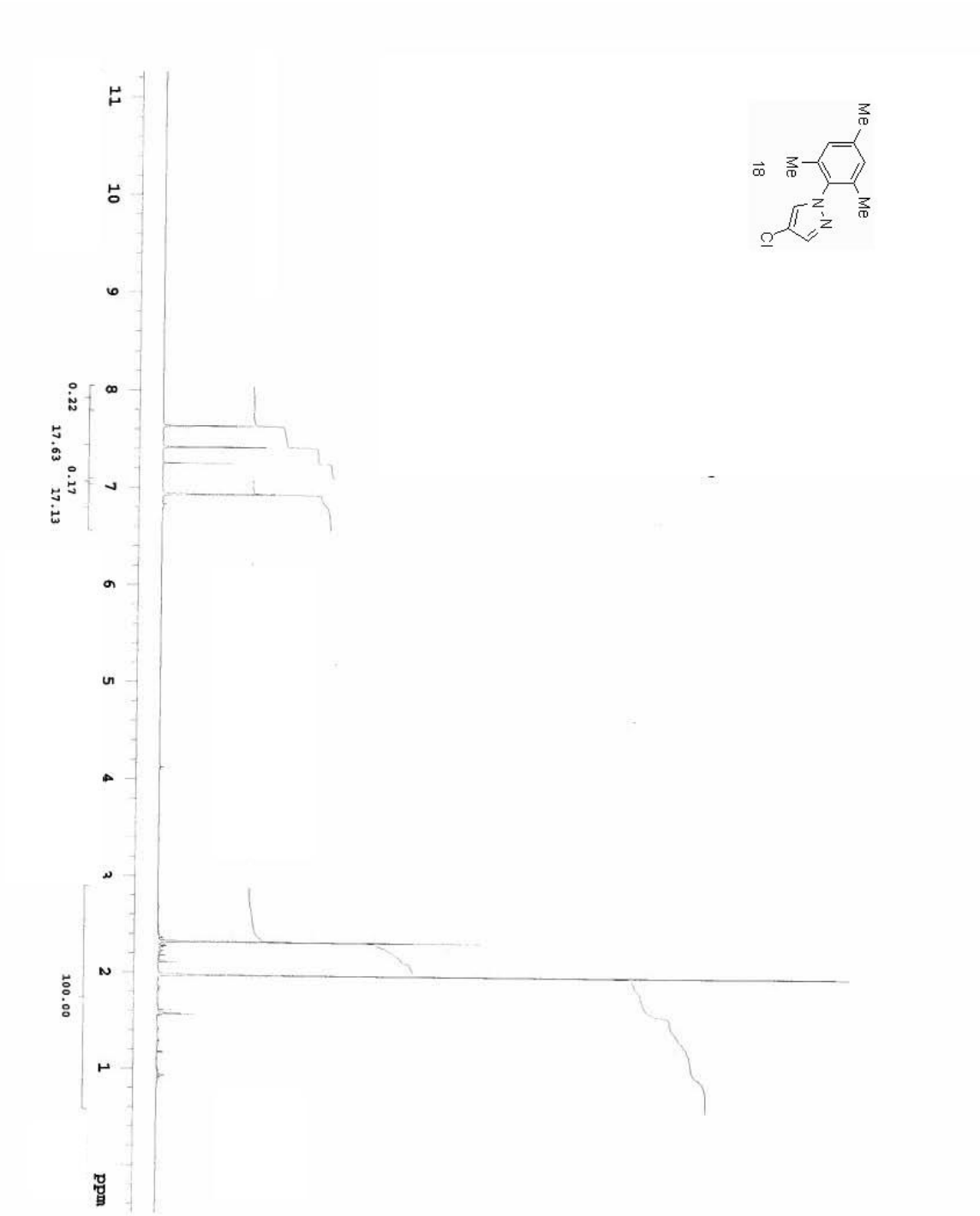
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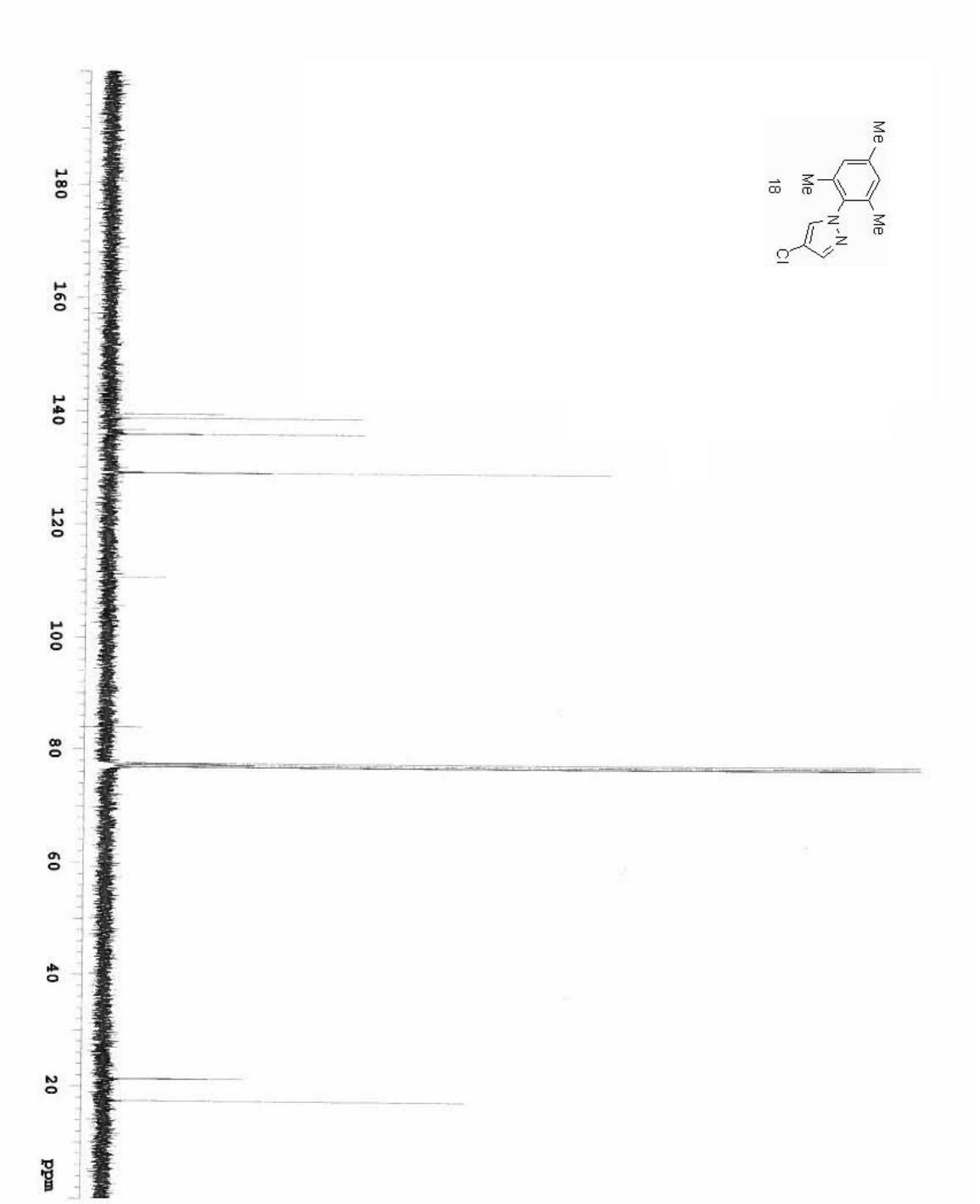
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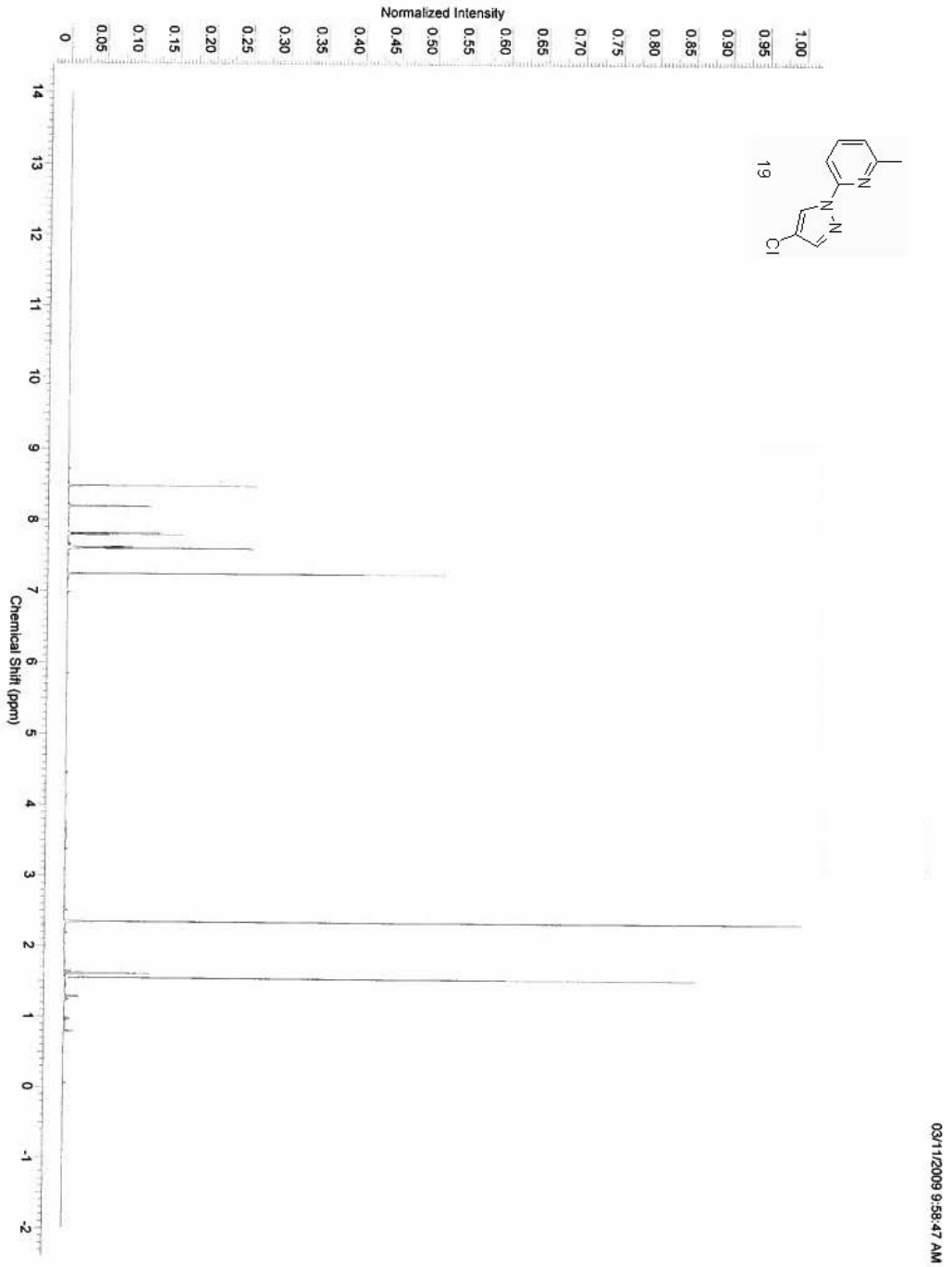
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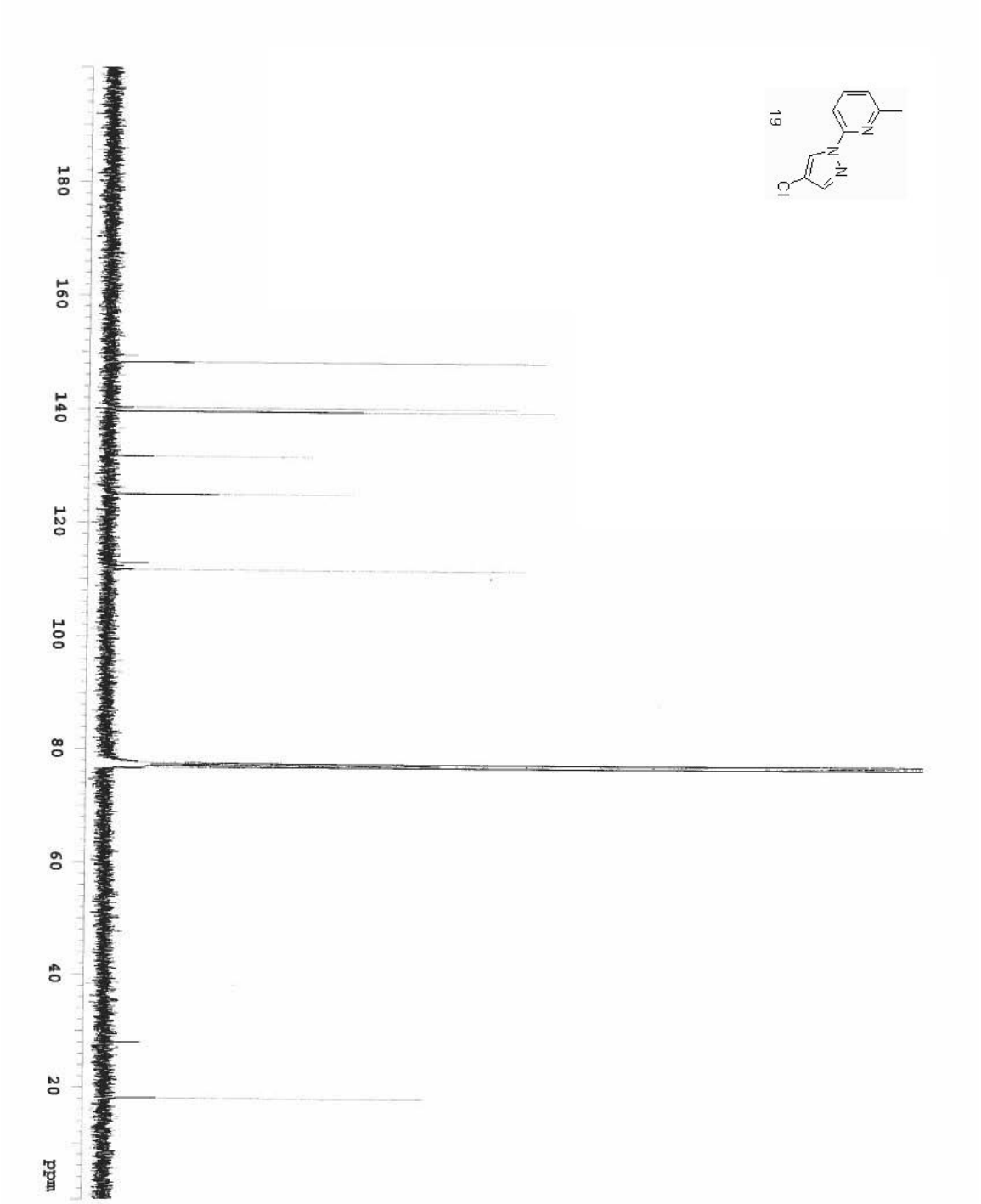
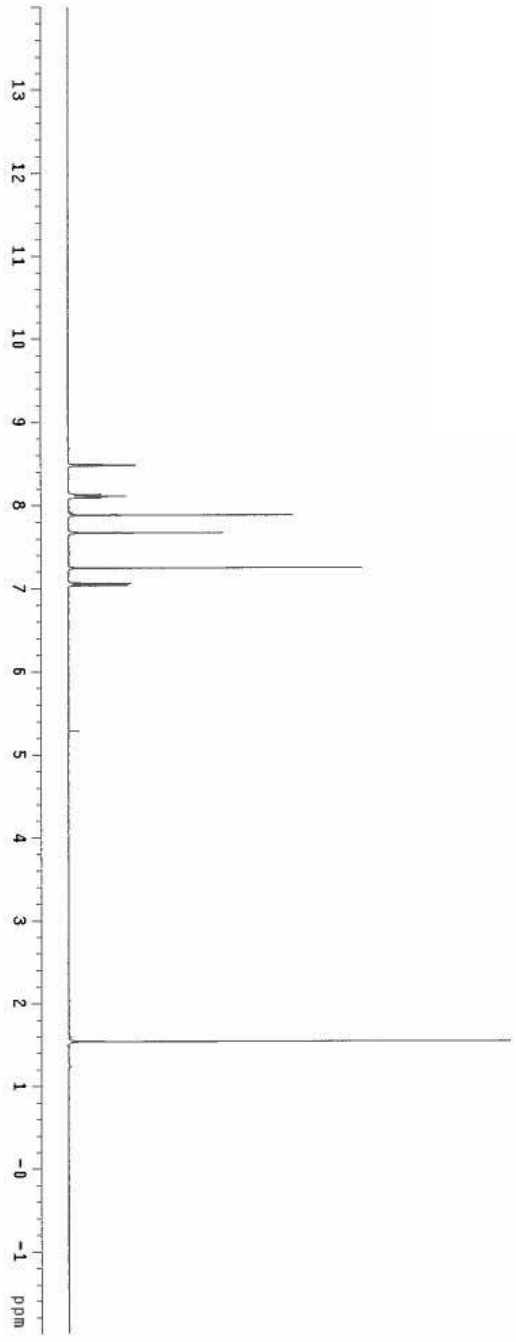
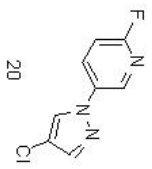
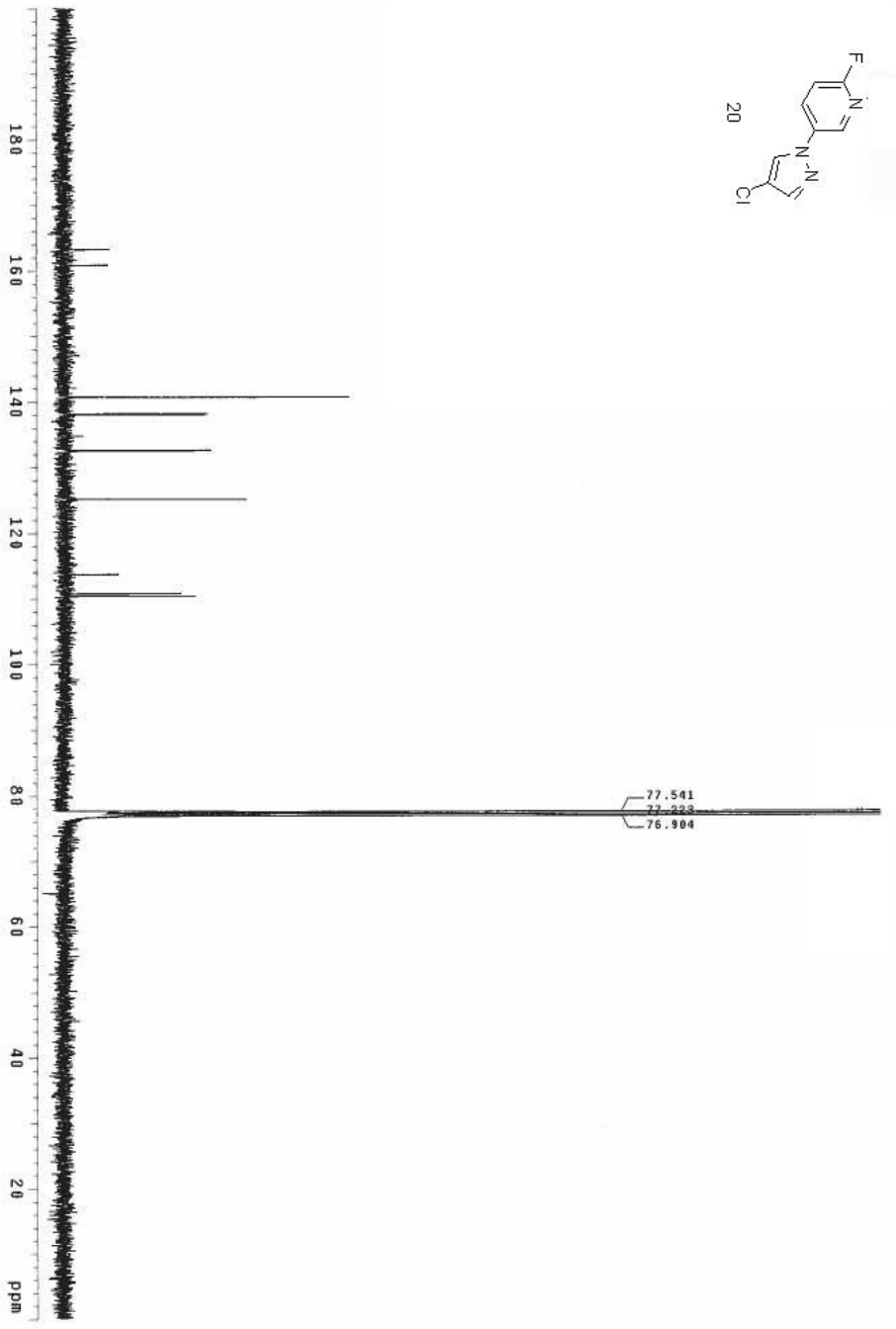
Cl
03/11/2009 9:58:47 AM

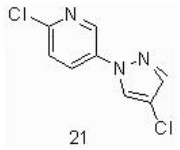

19
Cl
N
N
N
180
160
140
120
100
80
60
40
20
ppm



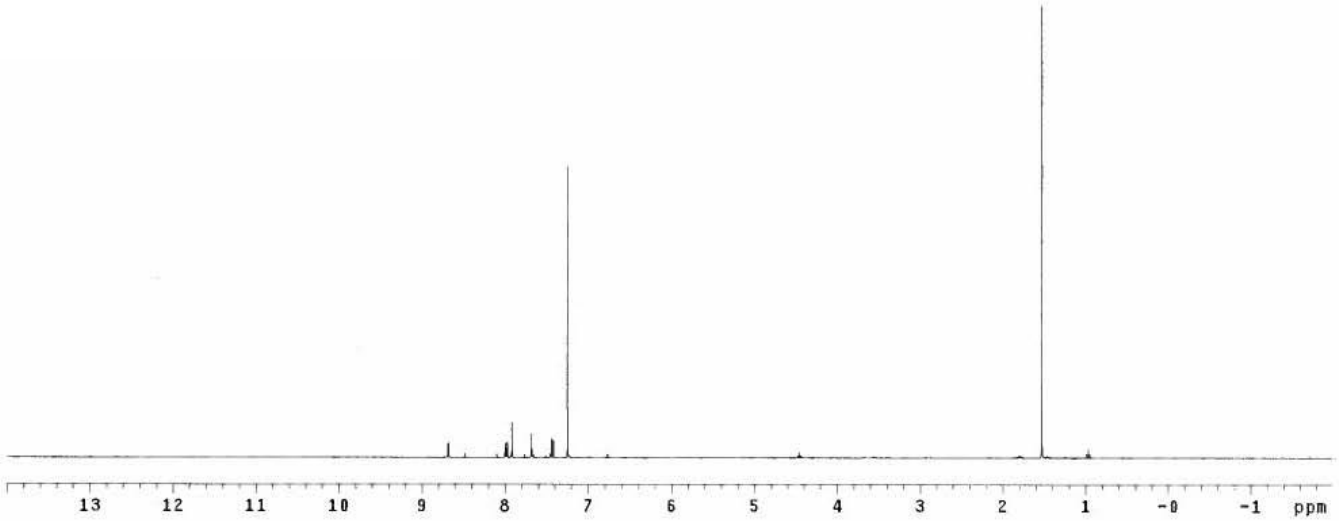


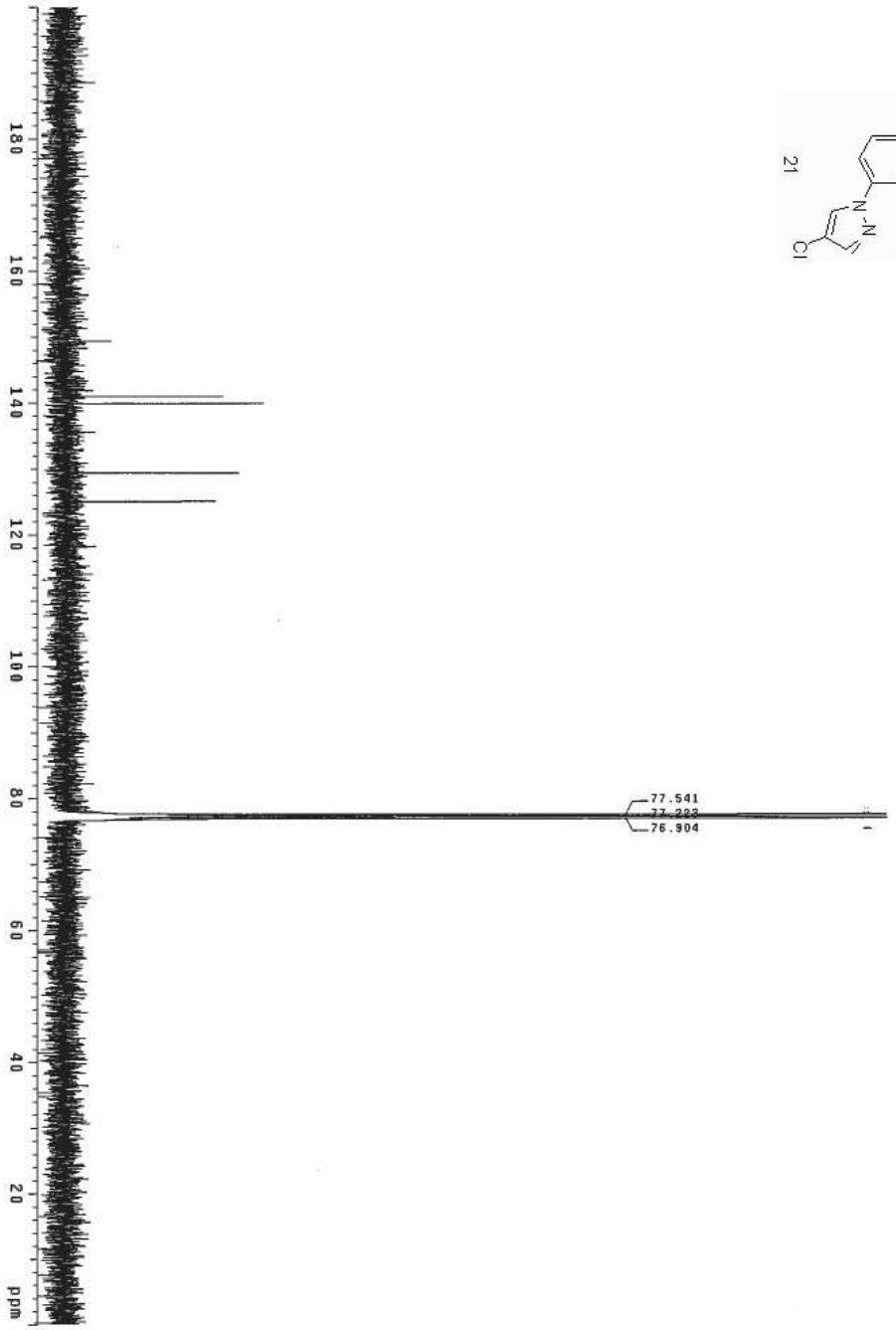
20

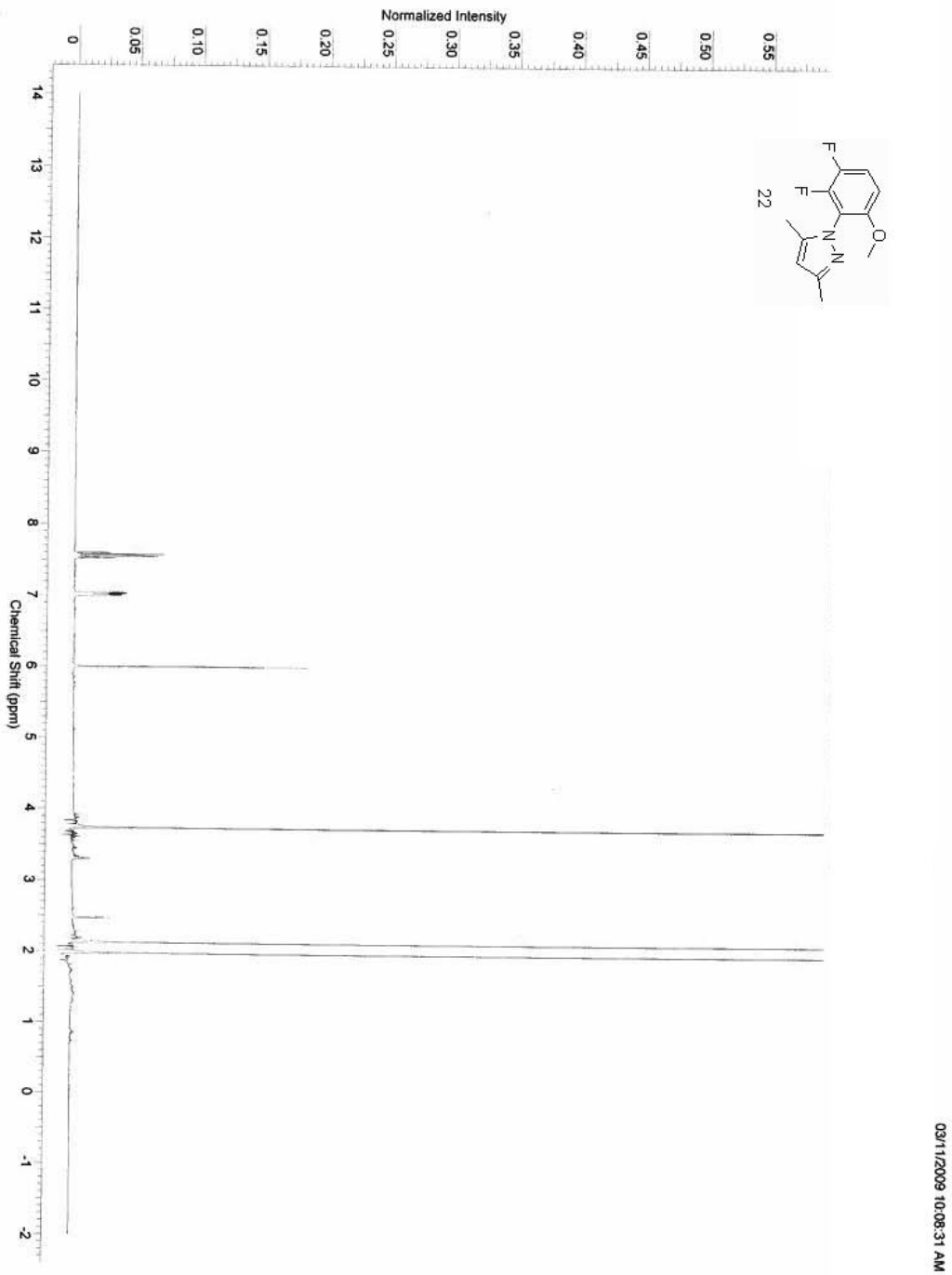

20
F
N
N
N
Cl
77.541
77.223
76.904
180
160
140
120
100
80
60
40
20
ppm

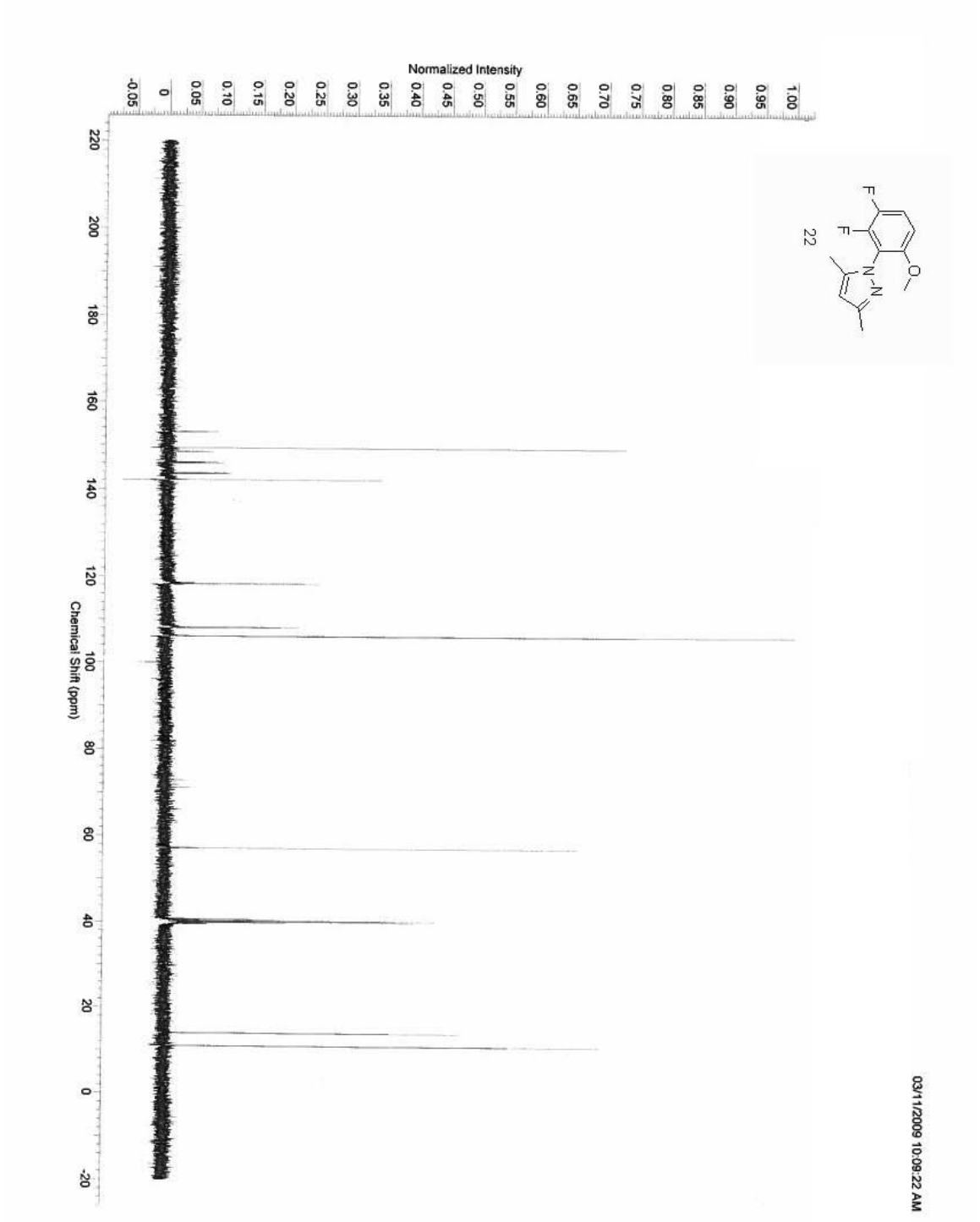


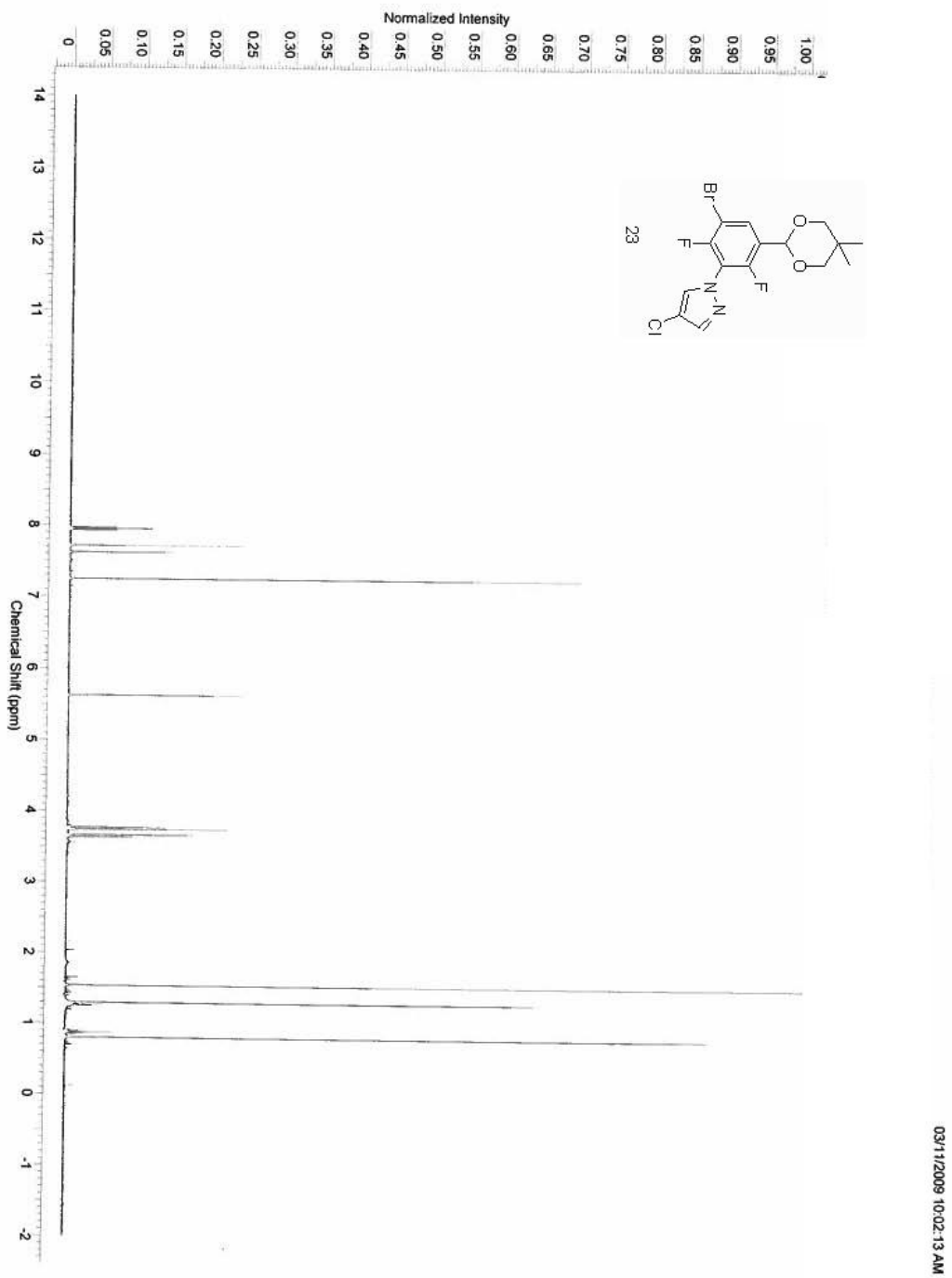
21

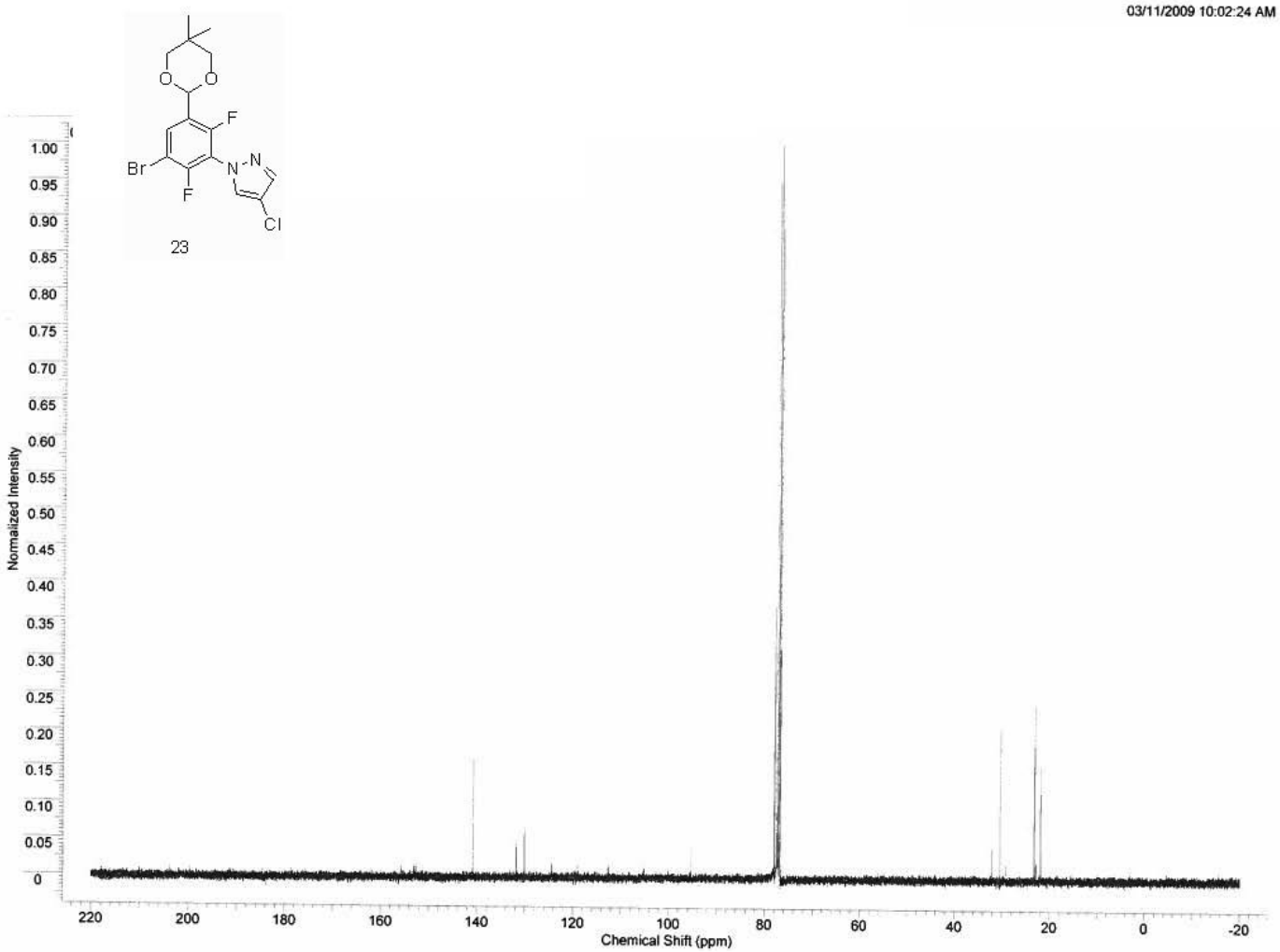


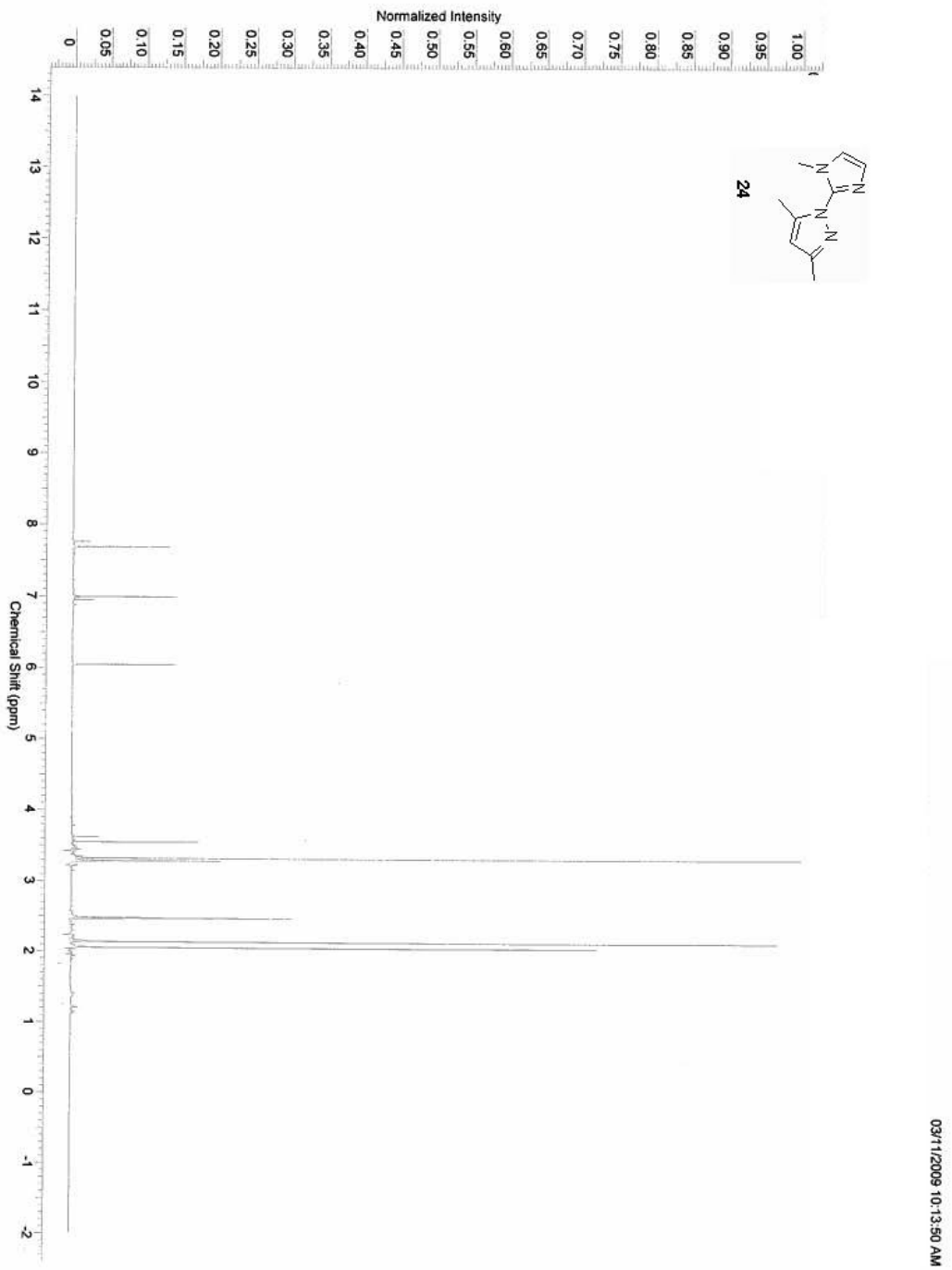

180
160
140
120
100
80
60
40
20
ppm
77.541
77.223
76.904
21
Cl
N
N
N
Cl

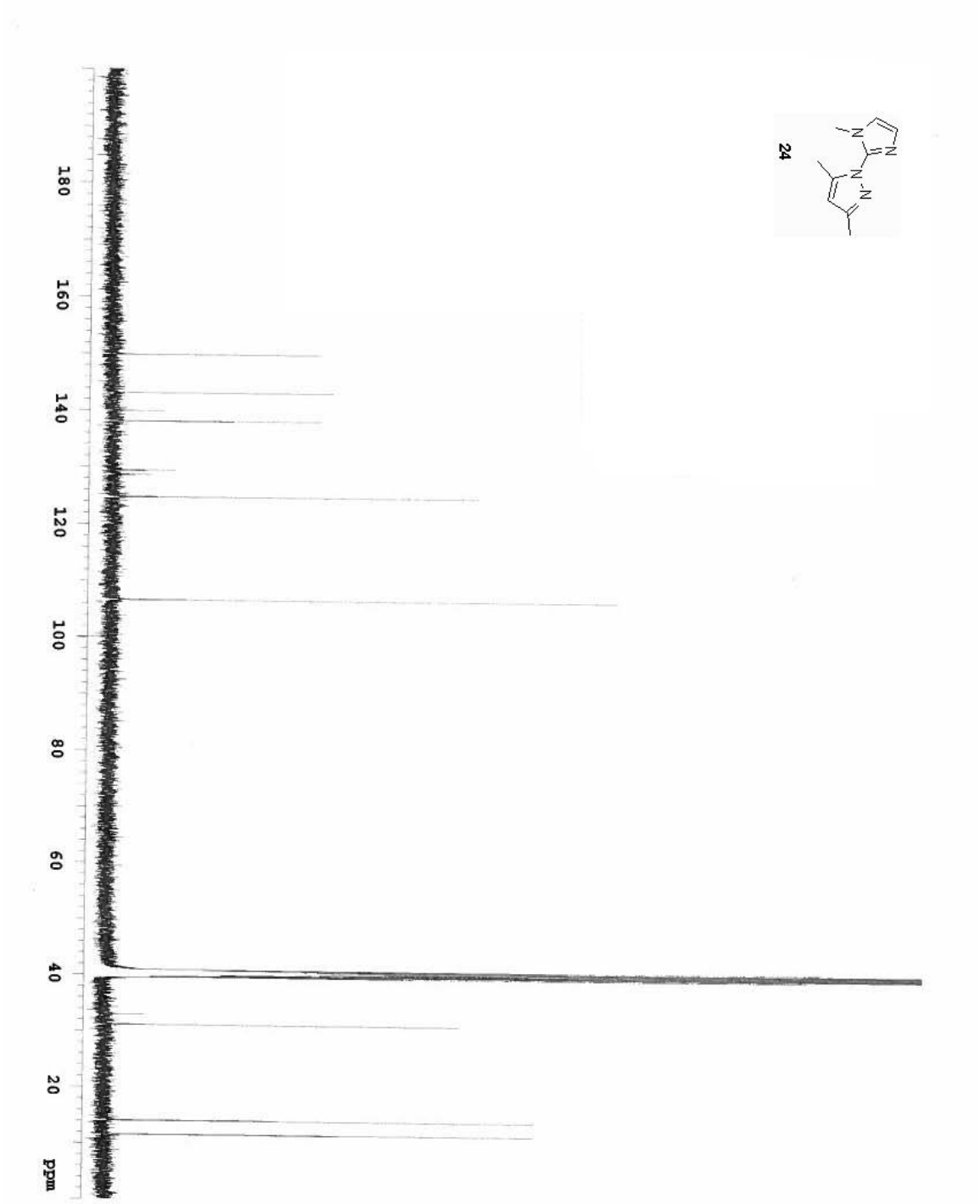

Normalized Intensity
0
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
Chemical Shift (ppm)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
F
F
N
N
O
22
03/11/2009 10:08:31 AM

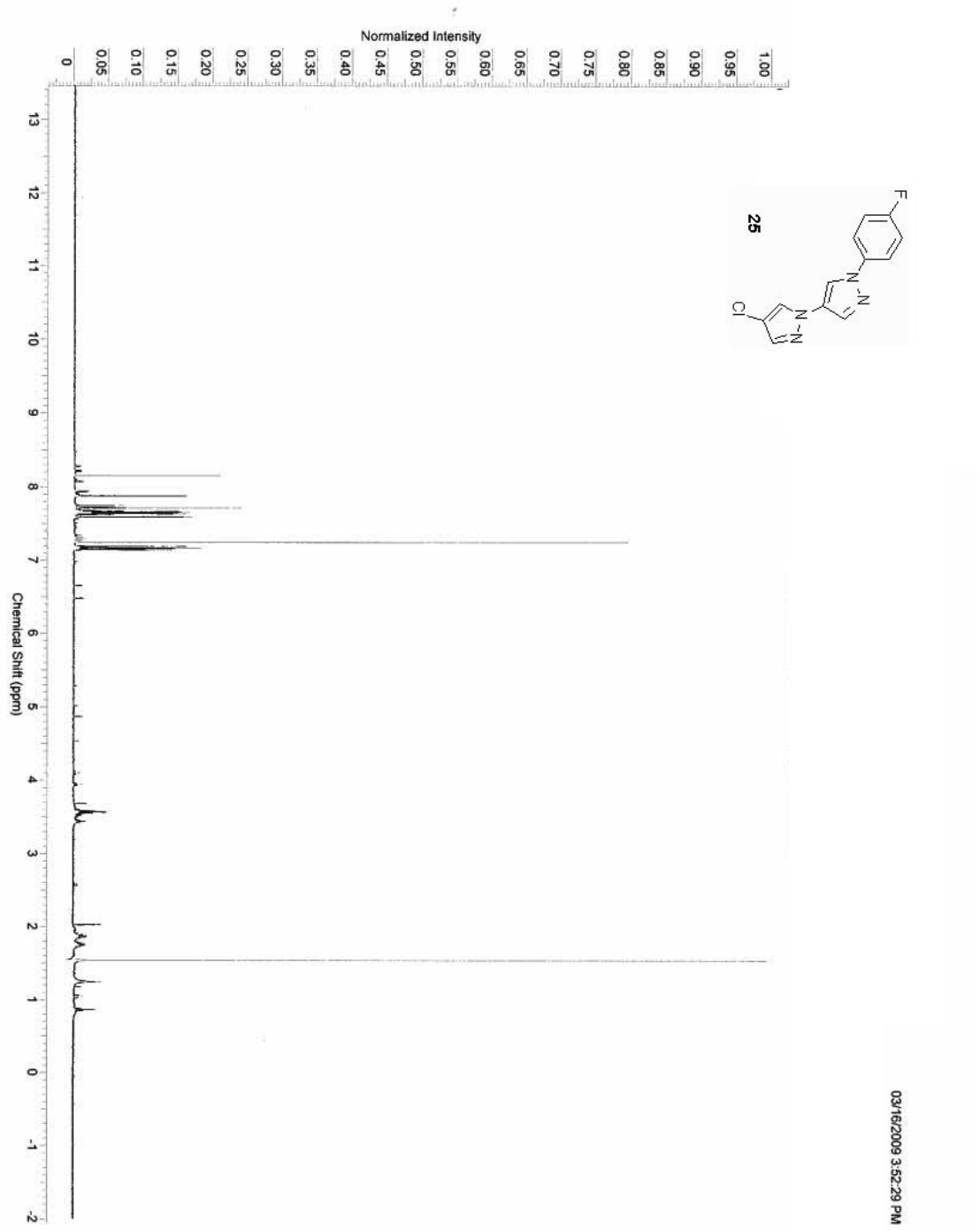

Normalized Intensity
-0.05
0
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60
0.65
0.70
0.75
0.80
0.85
0.90
0.95
1.00
Chemical Shift (ppm)
220
200
180
160
140
120
100
80
60
40
20
0
-20
F
F
O
N
N
22
03/11/2009 10:09:22 AM


Normalized Intensity
Chemical Shift (ppm)
23
Br
F
F
Cl
03/11/2009 10:02:13 AM


03/11/2009 10:02:24 AM
23
Br
F
F
N
N
Cl
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)


Normalized Intensity
Chemical Shift (ppm)
24
03/11/2009 10:13:50 AM


24
180
160
140
120
100
80
60
40
20
ppm


Normalized Intensity
0
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60
0.65
0.70
0.75
0.80
0.85
0.90
0.95
1.00
Chemical Shift (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
25
F
Cl
N
N
N
N
03/16/2009 3:52:29 PM