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Supporting Information

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A Novel and Efficient Iron-Copper Co-Catalyzed Arylation of Nitrogen Nucleophiles

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General Experimental Procedures

All reactions were carried out in 35 mL Schlenk tubes or in Carousel "reaction stations RR98030" Radley tubes, under a pure and dry nitrogen atmosphere. DMF was distilled from CaH_2 and was stored on 4 Å activated molecular sieves under a nitrogen atmosphere. Cesium carbonate (Acros), CuO (Acros) and $Fe(acac)_3$ (Acros) and all other solid materials were stored in the presence of P_4O_{10} in a bench-top desiccator under vacuum at room temperature and weighed in the air. Aryl iodide and aryl bromides were purchased from commercial sources (Aldrich, Acros, Avocado, Fluka, Lancaster). If solids, they were recrystallized in an appropriate solvent.[1] If liquids, they were distilled under vacuum and stored under an atmosphere of nitrogen. Special care was taken with liquid iodobenzene which was regularly distilled and stored protected from light. Column chromatography was performed with SDS 60 A C.C silica gel (35-70 μm). Thin layer chromatography was carried out using Merck silica gel 60 F_{254} plates. All products were characterized by their NMR, GC/MS and IR spectra. NMR spectra were recorded at 20°C on a Bruker AC 400 MHz or on a DRX-250 spectrometer working respectively at 400 MHz for ^1H, at 100 MHz for ^{13}C. Chemical shifts are reported in ppm/TMS for ^1H and $\{^1H\}^{13}C$ (δ 77.00 for $\underline{C}DCl_3$ signal). The first-order peak patterns are indicated as s (singulet), d (doublet), t (triplet), q (quadruplet). Complex non-first-order signals are indicated as m (multiplet). Gas chromatography - mass spectra (GC/MS) were recorded on an Agilent Technologies 6890 N instrument with an Agilent 5973 N mass detector (EI) and a HP5-MS 30 m x 0.25 mm capillary apolar column (Stationary phase: 5 % diphenyldimethylpolysiloxane film, 0.25 μm). GC/MS method: Initial temperature: 45°C; Initial time: 2 min; Ramp: 2°C/min until 50°C then 10 °C/min; Final temperature: 250°C; Final time: 10 min. IR spectra were recorded on a Nicolet 210 FT-IR instrument (neat, thin film for liquid products and KBr pellet or in carbon tetrachloride solution for solid products). FAB+ mass spectra and HRMS were recorded on a JEOL JMS-DX300 spectrometer (3 keV, xenon) in a *m*-nitrobenzylalcohol matrix. Melting points were determined using a Büchi B-540 apparatus and are uncorrected.

General Procedure for Copper-Iron Co-catalyzed Coupling Reaction (1 mmol and 2 mmol scale)

After standard cycles of evacuation and back-filling with dry and pure nitrogen, an oven-dried Radley tube (Carousel "reaction stations RR98030") equipped with a magnetic stirring bar was charged with CuO (0.1 eq.), $Fe(acac)_3$ (0.3 eq.), the nucleophile (1.5 eq.), Cs_2CO_3 (2 eq.) and the aryl halide (1 eq.), if a solid. The tube was evacuated, back-filled with nitrogen. If a liquid, aryl bromide was added under a stream of nitrogen by syringe at room temperature, followed by anhydrous and degassed DMF (1.0 mL). The tube was sealed under a positive pressure of nitrogen, stirred and heated to 90 or 125 °C or 140°C for the required time period. After cooling to room temperature, the mixture was diluted with dichloromethane (~ 20 mL) and filtered through a plug of celite®, the filter cake being further washed with dichloromethane (~ 5 mL). The filtrate was washed twice with water (~ 10 mL x 2). Gathered aqueous phases were twice extracted with dichloromethane (~ 10 mL). Organic layers were gathered, dried over Na_2SO_4, filtered and concentrated in vacuum to yield the crude product obtained was purified by silica gel chromatography with an eluent of hexanes and dichloromethane. The products were characterized by NMR, IR and mass spectra with those of authentic samples.

General Procedure for Reactivity Comparison of Different Catalyst System (0.5 mmol scale)

After standard cycles of evacuation and back-filling with dry and pure nitrogen, an oven-dried Radley tube (Carousel "reaction stations RR98030") equipped with a magnetic stirring bar was charged with indicated catalysts, the pyrazole (51 mg, 1.5 eq.), Cs_2CO_3 (325 mg, 2 eq.). The tube was evacuated, back-filled with nitrogen. Iodobenzene (56 µL, 0.5 mmol, 1 eq.) or bromobenzene (53 µL, 0.5 mmol, 1 eq.) was added under a stream of nitrogen by syringe at room temperature, followed by anhydrous and degassed DMF (0.5 mL). The tube was sealed under a positive pressure of nitrogen, stirred and heated to 100 °C for 15 hours. After cooling to room temperature, the mixture was diluted with dichloromethane (~ 20 mL) and filtered through a plug of celite®, the filter cake being further washed with dichloromethane (~ 5 mL). 65 µL of 1,3-dimethoxybenzene (internal standard) were added. A small sample of the reaction mixture was taken and filtered through a plug of celite®, the filter cake being further washed with dichloromethane. The filtrate was washed three times with water and analyzed by gas chromatography. The GC yields were determined by obtaining the correction factors using authentic samples of the expected products.

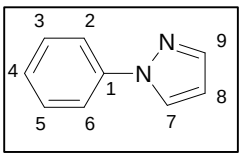
Experimental procedures and characterization data

1-Phenyl-1H-pyrazole[2]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with bromobenzene (212 µL, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 270 mg (94 % yield) of the desired product as a light yellow oil.

Identification



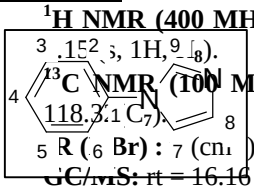
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.96 (dd, 1H, H_7), 7.71-7.75 (m, 3H, $H_{2,6,9}$), 7.47-7.50 (m, 2H, $H_{3,5}$), 7.28-7.34 (m, 1H, H_4), 6.49-6.50 (dd, 1H, H_8).
^{13}C NMR (100 MHz, $CDCl_3$): δ 141.09 (C_9), 140.22 (C_1), 129.45 ($C_{3,5}$), 126.75 (C_7), 126.46 (C_4), 119.23($C_{2,6}$), 107.61(C_8).
IR (KBr) : ν (cm^{-1}) = 3142, 3050, 2924, 1600, 1520, 1500, 1393, 1332, 1198, 1120, 1046, 936, 914, 755, 689, 654, 610, 515.
GC/MS: rt = 14.53 min, M/Z = 144.
HRMS: 145.0766 (M+H). Theoretical:145.0766

1-Phenyl-1H-imidazole[3]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-imidazole (102 mg, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : hexane/ethylacetate=20/80) to provide 130 mg (90 % yield) of the desired product as a light yellow oil.

Identification



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H, H_9), 7.40-7.43 (m, 2H, $H_{3,5}$), 7.28-7.34 (m, 3H, $H_{2,4,6}$), 7.22 (s, 1H, H_7), 1.15 (s, 1H, H_8).
^{13}C NMR (100 MHz, $CDCl_3$): δ 137.35 (C_1), 135.59 (C_9), 130.32 (C_8), 129.92 ($C_{3,5}$), 127.56 (C_4), 121.53($C_{2,6}$), 118.31 (C_7).
IR (KBr) : ν (cm^{-1}) = 3115, 3067, 1600, 1509, 1304, 1247, 1112, 1057, 962, 905, 815, 759, 692, 658, 520.
GC/MS: rt = 16.16 min, M/Z = 144.
HRMS: 145.0768 (M+H). Theoretical:145.0766

4-Pyrazol-1-yl-benzoic acid ethylester[4]

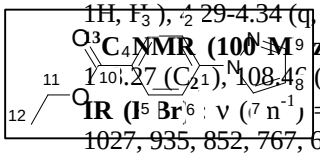
Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with ethyl 4-bromobenzoate (336 µL, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=80/20) to provide 400 mg (93 % yield) of the desired product as a white solid.

Identification

Mp: 66°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-8.07 (d, 2H, $H_{3,5}$), 7.92-7.93 (d, 1H, H_7), 7.68-7.72 (m, 3H, $H_{2,6,9}$), 6.42-6.43 (t, 1H, H_3), 4.29-4.34 (q, 2H, H_{11}), 1.32-1.35 (t, 3H, H_{12}).



^{13}C NMR (100 MHz, $CDCl_3$): δ 165.90 (C_{10}), 143.20 (C_1), 141.89 (C_9), 131.12 ($C_{3,5}$), 128.17 (C_4), 126.90 (C_7), 117.27 ($C_{2,6}$), 108.48 (C_8), 61.13 (C_{11}), 14.35 (C_{12}).

IR (KBr) : ν (cm^{-1}) = 3128, 2993, 2962, 2904, 1702, 1608, 1526, 1481, 1392, 1341, 1280, 1201, 1178, 1111, 1048, 1027, 935, 852, 767, 692, 652, 610, 525, 505, 478.

GC/MS: rt = 20.94 min, M/Z = 216.

HRMS: 217.0983 (M+H). Theoretical:217.0977

1-(4-Methoxy-phenyl)-1H-pyrazole[2]

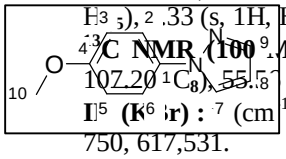
Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with 1-iodo-4-methoxybenzene (468 mg, 2.0mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 340 mg (98 % yield) of the desired product as a white solid.

Identification

Mp: 42°C (Litt.[2]:45.5°C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.73 (d, 1H, H_7), 7.60-7.61 (d, 1H, H_9), 7.47-7.51 (m, 2H, $H_{2,6}$), 6.85-6.89 (m, 2H, $H_{3,5}$), 2.33 (s, 1H, H_8), 3.73 (s, 3H, H_{10}).



^{13}C NMR (100 MHz, $CDCl_3$): δ 158.21 (C_4), 140.60 (C_9), 133.99 (C_1), 126.84 (C_7), 120.88 ($C_{2,6}$), 114.50 ($C_{3,5}$), 107.20 (C_8), 55.51 (C_{10}).

IR (KBr) : ν (cm^{-1}) = 3124, 3003, 2936, 2913, 2836(C-O), 1594, 1522, 1464, 1444, 1396, 1246, 1171, 1039, 938, 831, 750, 617,531.

GC/MS: rt = 17.99 min, M/Z = 174.

HRMS: 175.0872 (M+H). Theoretical:175.0871

1-Biphenyl-4-yl-1H-pyrazole[5]

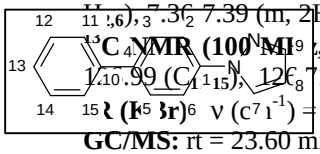
Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with 4-bromo-1,1'-biphenyl (446 mg, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 410 mg (93 % yield) of the desired product as a white crystal.

Identification

Mp: 134°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H, H_7), 7.67-7.70 (m, 3H, $H_{3,5,9}$), 7.59-7.61 (m, 2H, $H_{11,15}$), 7.52-7.55 (m, 2H, $H_{2,6}$), 7.36-7.39 (m, 2H, $H_{12,14}$), 7.26-7.30 (m, 1H, H_{13}), 6.40-6.41 (t, 1H, H_8).



^{13}C NMR (100 MHz, $CDCl_3$): δ 141.20 (C_9), 140.11 (C_1), 139.33 ($C_{4,10}$), 128.91 ($C_{12,14}$), 128.08 ($C_{3,5}$), 127.52 (C_7), 126.99 ($C_{11,15}$), 126.71 (C_{13}), 119.45 ($C_{2,6}$), 107.73 (C_8).

IR (KBr) ν (cm^{-1}) = 3129, 3106, 3026, 1607, 1529, 1484, 1393, 1331, 1050, 938, 835, 763, 699, 553, 516.

GC/MS: rt = 23.60 min, M/Z = 220.

HRMS: 221,1068 (M+H). Theoretical:221.1079

4-Pyrazol-1-yl-benzonitrile[2]

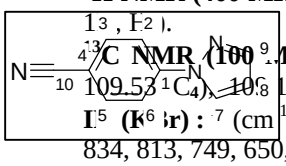
Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with 4-bromobenzonitrile (364 mg, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 330 mg (98 % yield) of the desired product as a white solid.

Identification

Mp: 89°C (Litt.[2]:87.5°C).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.93 (d, 1H, H_7), 7.75-7.78 (m, 2H, $H_{3,5}$), 7.65-7.70 (m, 3H, $H_{2,6,9}$), 6.46-6.47 (dd, 1H, H_3).



^{13}C NMR (100 MHz, $CDCl_3$): δ 142.95 (C_1), 142.50 (C_9), 133.68 ($C_{3,5}$), 126.94 (C_7), 118.93 ($C_{2,6}$), 118.44 (C_{10}), 109.53 (C_4), 108.15 (C_8).

IR (KBr) : ν (cm^{-1}) = 3153, 3136, 3066, 2226(CN), 1610, 1528, 1513, 1392, 1342, 1252, 1199, 1176, 1127, 1030, 934, 834, 813, 749, 650, 572, 545.

GC/MS: rt = 18.92 min, M/Z = 169.

HRMS: 170.0700 (M+H). Theoretical:170.0718

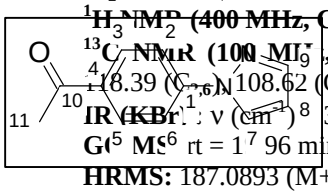
1-(4-Pyrazol-1-yl-phenyl)-ethanone[2]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with 1-(4-bromophenyl)ethanone (398 mg, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 300 mg (81 % yield) of the desired product as a white solid.

Identification

Mp: 108°C (Litt.[2]: 110°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-8.00 (m, 3H, $H_{3,5,7}$), 7.70-7.76 (m, 3H, $H_{2,6,9}$), 6.46 (s, 1H, H_8), 2.56 (s, 3H, H_{11}).

^{13}C NMR (100 MHz, $CDCl_3$): δ 196.84 (C_{10}), 143.33 (C_1), 142.09 (C_9), 134.80 (C_4), 130.01 ($C_{3,5}$), 126.91 (C_7), 118.39 ($C_{2,6}$), 108.62 (C_8), 26.60 (C_{11}).

IR (KBr) : ν (cm^{-1}) = 3135, 3114, 3101, 1673(C=O), 1605, 1528, 1395, 1264, 1210, 935, 838, 762, 611, 589, 518.

GC/MS: rt = 17.96 min, M/Z = 186.

HRMS: 187.0893 (M+H). Theoretical:187.0871

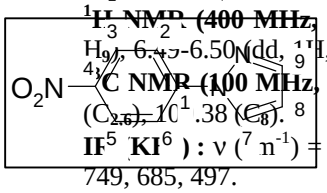
1-(4-Nitro-phenyl)-1H-pyrazole[2]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (205 mg, 3.0 mmol) was coupled with 1-bromo-4-nitrobenzene (404 mg, 2.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 340 mg (90 % yield) of the desired product as a yellow solid.

Identification

Mp: 170°C (Litt.[2]:169-170°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26-8.29 (m, 2H, $H_{3,5}$), 7.97 (d, 1H, H_7), 7.81-7.84 (m, 2H, $H_{2,6}$), 7.73-7.74 (d, 1H, H_9), 6.45-6.50 (dd, 1H, H_8).

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.42 (C_4), 142.81 (C_9), 133.52 (C_1), 134.80 (C_4), 127.08 (C_7), 125.42 ($C_{3,5}$), 118.62 ($C_{2,6}$), 107.38 (C_8).

IR (KBr) : ν (cm^{-1}) = 3152, 3119, 3085, 1596, 1532, 1517, 1392, 1334(NO_2), 1206, 1112, 1050, 1030, 929, 852, 764, 749, 685, 497.

GC/MS: rt = 20.30 min, M/Z = 189.

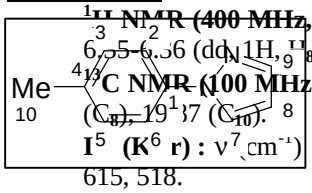
HRMS: 190.0615 (M+H). Theoretical:190.0617

1-(4-Tolyl)-1H-pyrazole[2]

Experimental procedure

Following the general procedure (125°C, 24 hours), 1H-pyrazole (102 mg, 1.5 mmol) was coupled with 1-bromo-4-methylbenzene (122 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=70/30) to provide 90 mg (57 % yield) of the desired product as a uncolored oil.

Identification



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78-7.79 (m, 1H, H_7), 7.62 (d, 1H, H_9), 7.47-7.49 (d, 2H, $H_{2,6}$), 7.14-7.17 (t, 2H, $H_{3,5}$), 6.55-6.56 (dd, 1H, H_8), 2.29 (s, 3H, H_{10}).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.72 (C_9), 136.95 (C_1), 135.18 (C_4), 128.88 ($C_{3,5}$), 125.63 (C_7), 118.13 ($C_{2,6}$), 106.27 (C_8), 19.37 (C_{10}).

IR (KBr) : ν (cm^{-1}) = 3123, 3040, 2922, 2863, 1610, 1525, 1394, 1331, 1196, 1123, 1046, 1031, 937, 915, 815, 749, 615, 518.

GC/MS: rt = 16.08 min, M/Z = 158.

HRMS: 159.0913 (M+H). Theoretical:159.0922

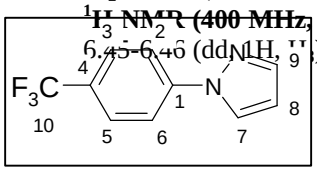
1-(4-Trifluoromethyl-phenyl)-1H-pyrazole[2]

Experimental procedure

Following the general procedure (140°C, 24 hours), 1H-pyrazole (102 mg, 1.5 mmol) was coupled with 1-chloro-4-(trifluoromethyl)benzene (134 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 80 mg (38 % yield) of the desired product as a white solid.

Identification

Mp: 93°C (Litt.[2]:94-95°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.93 (d, 1H, H_7), 7.76-7.78 (d, 2H, $H_{3,5}$), 7.70 (d, 1H, H_9), 7.64-7.66 (d, 2H, $H_{2,6}$), 6.45-6.46 (dd, 1H, H_8).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.53 (C_1), 141.96 (C_9), 126.81 (C_7), 126.74 (m, $C_{3,5}$), 125.29 (C_4), 122.59 (C_{10}), 118.81 ($C_{2,6}$), 108.53 (C_8).
IR (KBr) : ν (cm^{-1}) = 3152, 3136, 2964, 2925, 1619, 1532, 1414, 1394, 1334, 1123, 1106, 1071, 935, 852, 824, 756, 605, 591.
GC/MS: rt = 14.54 min, M/Z = 212.
HRMS: 213.0659 (M+H). Theoretical:213.0640

4-(1H-pyrazol-1-yl)aniline[2]

Experimental procedure

Following the general procedure (125°C, 24 hours), 1H-pyrazole (102 mg, 1.5 mmol) was coupled with 4-iodoaniline (220 mg, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 90 mg (57 % yield) of the desired product as a orange solid.

Identification

Mp: 42°C (Litt.[2]: 42-43°C).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, 1H, H_7), 7.59 (d, 1H, H_9), 7.34-7.38 (m, 2H, $H_{2,6}$), 6.63-6.67 (m, 2H, $H_{3,5}$), 6.33-6.34 (m, 1H, H_8), 3.67 (s, 2H, H_{10}).
^{13}C NMR (100 MHz, $CDCl_3$): δ 145.33 (C_4), 140.24 (C_9), 132.39 (C_1), 126.76 (C_7), 121.11 ($C_{2,6}$), 115.46 ($C_{3,5}$), 106.83 (C_8).
IR (KBr) : ν (cm^{-1}) = 3381, 3298, 3192, 1632, 1525, 1398, 1280, 1176, 1126, 1051, 1033, 943, 823, 751, 612, 521.
GC/MS: rt = 19.16 min, M/Z = 159.
HRMS: 160.0873 (M+H). Theoretical:160.0875

1-(3-Methoxy-phenyl)-1H-pyrazole[6]

Experimental procedure

Following the general procedure (125°C, 24 hours), 1H-pyrazole (102 mg, 1.5 mmol) was coupled with 1-bromo-3-methoxybenzene (126 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=40/60) to provide 150 mg (86 % yield) of the desired product as a uncolored oil.

Identification

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, 1H, H_7), 7.61 (d, 1H, H_9), 7.19-7.23 (m, 2H, $H_{4,6}$), 7.11-7.12 (m, 1H, H_3), 6.69-6.72 (dd, 1H, H_2), 6.32-6.33 (dd, 1H, H_8), 3.73 (s, 3H, H_{10}).
^{13}C NMR (100 MHz, $CDCl_3$): δ 160.54 (C_5), 141.33 (C_1), 141.03 (C_9), 130.18 (C_3), 126.92 (C_7), 112.35 (C_4), 111.10 (C_2), 107.63 (C_8), 105.05 (C_6), 55.47 (C_{10}).
IR (KBr) : ν (cm^{-1}) = 3143, 3003, 2960, 2938, 2836(C-O), 1608, 1519, 1502, 1439, 1393, 1338, 1313, 1296, 1270, 1227, 1116, 1046, 947, 844, 751, 686, 656, 623, 569.
GC/MS: rt = 17.77 min, M/Z = 174.
HRMS: 175.0870 (M+H). Theoretical:175.0871

1-Phenyl-pyrrolidin-2-one[3]

Experimental procedure

Following the general procedure (90°C, 30 hours), pyrrolidin-2-one (116 µL, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/ethylacetate=80/20) to provide 130 mg (81 % yield) of the desired product as a yellow solid.

Identification

Mp: 68°C (Litt.[3]: 69-70°C).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.55 (m, 2H, $H_{3,5}$), 7.28-7.32 (dd, 2H, $H_{2,6}$), 7.08 (s, 1H, H_4), 3.78-3.82 (t, 2H, H_7), 2.53-2.55 (t, 2H, H_9), 2.08-2.12 (m, 2H, H_8).
^{13}C NMR (100 MHz, $CDCl_3$): δ 174.22 (C_{10}), 139.42 (C_1), 128.84 ($C_{3,5}$), 124.51 (C_4), 119.97 ($C_{2,6}$), 48.80 (C_7), 32.79 (C_9), 18.06 (C_8).
IR (KBr) : ν (cm^{-1}) = 3001, 2968, 2898, 1681, 1596, 1499, 1463, 1401, 1307, 1229, 1117, 905, 842, 765, 695, 660, 637, 596, 504.
GC/MS: rt = 18.72 min, M/Z = 161.
HRMS: 162.0911 (M+H). Theoretical:162.0919

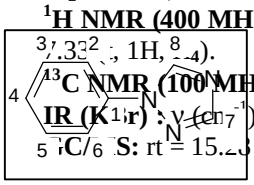
1-Phenyl-1H-[1,2,4]triazole[3]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-[1,2,4]triazole (104 mg, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50) to provide 120 mg (83 % yield) of the desired product as a light yellow solid.

Identification

Mp: 46°C (Litt.[3]: 46°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H, H_8), 8.03 (s, 1H, H_7), 7.58-7.61 (m, 2H, $H_{2,6}$), 7.40-7.44 (t, 2H, $H_{3,5}$), 7.31-7.35 (t, 1H, H_4).

^{13}C NMR (100 MHz, $CDCl_3$): δ 152.62 (C_7), 140.91 (C_8), 136.99 (C_1), 129.77 ($C_{3,5}$), 128.21 (C_4), 120.04 ($C_{2,6}$).

IR (KBr) : ν (cm^{-1}) = 3105, 2924, 2852, 1600, 1514, 1416, 1359, 1278, 1223, 1152, 1055, 981, 876, 754, 681, 671, 503.

GC/MS: rt = 15.23 min, M/Z = 145.

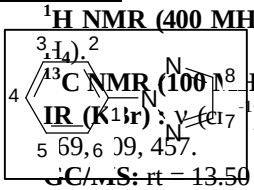
HRMS: 146.0721 (M+H). Theoretical: 146.0718

2-Phenyl-2H-[1,2,3]triazole[7] and 1-Phenyl-1H-[1,2,3]triazole[8]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-[1,2,3]triazole (87µL, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : dichloromethane/hexanes=50/50 then pure dichloromethane) to provide 60 mg of 2-Phenyl-2H-[1,2,3]triazole (41 % yield) as a uncolored oil and 70 mg of 1-Phenyl-1H-[1,2,3]triazole (48 % yield) as a light yellow solid.

Identification



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-8.02 (m, 2H, $H_{7,8}$), 7.72 (s, 2H, $H_{2,6}$), 7.38-7.42 (m, 2H, $H_{3,5}$), 7.24-7.28 (m, 1H, H_4).

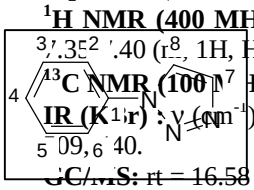
^{13}C NMR (100 MHz, $CDCl_3$): δ 139.90 (C_1), 135.51 ($C_{7,8}$), 129.30 ($C_{3,5}$), 127.56 (C_4), 118.97 ($C_{2,6}$).

IR (KBr) : ν (cm^{-1}) = 3125, 3060, 2926, 2854, 1598, 1500, 1410, 1376, 1260, 1215, 1149, 1069, 950, 821, 756, 695, 669, 609, 457.

GC/MS: rt = 13.50 min, M/Z = 145.

HRMS: 145.0653 (M). Theoretical: 145.0640

Mp: 56°C (Litt.[8]: 53-55°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, 1H, H_8), 7.78 (d, 1H, H_7), 7.66-7.69 (m, 2H, $H_{2,6}$), 7.44-7.48 (m, 2H, $H_{3,5}$), 7.35-7.40 (m, 1H, H_4).

^{13}C NMR (100 MHz, $CDCl_3$): δ 137.06 (C_1), 134.54 (C_7), 129.79 (C_8), 128.80 ($C_{3,5}$), 121.78 (C_4), 120.70 ($C_{2,6}$).

IR (KBr) : ν (cm^{-1}) = 3147, 3130, 3065, 1596, 1503, 1463, 1319, 1229, 1176, 1092, 1038, 982, 910, 793, 762, 684, 640, 609, 440.

GC/MS: rt = 16.58 min, M/Z = 145.

HRMS: 146.0719 (M+H). Theoretical: 146.0718

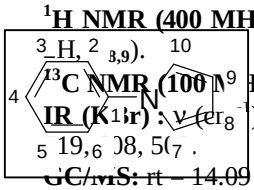
1-Phenyl-1H-pyrrole[3]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-pyrazole (104 µL, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : hexanes) to provide 130 mg (91 % yield) of the desired product as a white solid.

Identification

Mp: 60°C (Litt.[3]: 62°C).



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.34 (m, 4H, $H_{2,3,5,6}$), 7.14-7.15 (t, 1H, H_4), 6.99-7.00 (t, 2H, $H_{7,10}$), 6.26-6.27 (t, 2H, $H_{8,9}$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.82 (C_1), 129.60 ($C_{3,5}$), 125.66 (C_4), 120.57 ($C_{2,6}$), 119.37 ($C_{7,10}$), 110.46 ($C_{8,9}$).

IR (KBr) : ν (cm^{-1}) = 3142, 3102, 2924, 1603, 1556, 1511, 1459, 1400, 1326, 1255, 1189, 1083, 1014, 919, 895, 758, 719, 608, 507.

GC/MS: rt = 14.09 min, M/Z = 143.

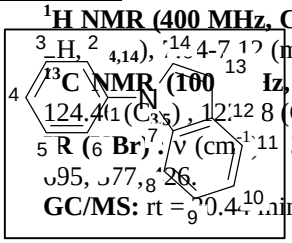
HRMS: 143.0740 (M). Theoretical: 143.0735

1-Phenyl-1H-indole[3]

Experimental procedure

Following the general procedure (90°C, 30 hours), 1H-indole (176 mg, 1.5 mmol) was coupled with iodo-benzene (112 µL, 1.0 mmol). The crude brown oil was purified by flash chromatography on silica gel (eluent : hexanes) to provide 180 mg (93 % yield) of the desired product as a light green oil.

Identification



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57-7.59 (m, 1H, H_{11}), 7.44-7.47 (m, 1H, H_8), 7.36-7.37 (d, 4H, $H_{2,3,5,6}$), 7.20-7.23 (m, 3H, $H_{4,14}$), 7.04-7.12 (m, 2H, $H_{9,10}$), 6.56-6.57 (m, 1H, H_{13}).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.93 (C_1), 135.95 (C_7), 129.72 ($C_{2,6}$), 129.45 (C_{12}), 128.06 (C_{14}), 126.54 (C_4) , 124.41 (C_5) , 122.18 (C_9) , 121.26 (C_{11}) , 120.49 (C_{10}) , 110.64 (C_8) , 103.70 (C_{13}).

IR (KBr): ν (cm^{-1}) 3104, 3055, 3032, 2924, 1597, 1515, 1497, 1456, 1331, 1233, 1213, 1135, 1014, 908, 773, 741, 695, 677, 626.

GC/MS: rt = 10.41 min, M/Z = 193.

HRMS: 193.0924 (M+H). Theoretical: 193.0891

References

[1] D. D.Perrin,, W. L. F.Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New-York, **1985**.

[2] H.-J.Cristau, P. P. Cellier, J.-F. Spindler, M. Taillefer, *Org. Lett.* **2004**, *6*, 695-709.

[3] H.-J. Cristau, P. P. Cellier, J.-F. Spindler, M. Taillefer, *Chem.Eur. J.* **2004**, *10*, 5607-5622.

[4] M. Artico, R. Silvestri, G. Stefancich, L. Avigliano, A. Di Giulio, M. Maccarrone, E. Agostinelli, B. Mondove, L. Morpurgo, *Eur. J. Med. Chem.* **1992**, 219-228.

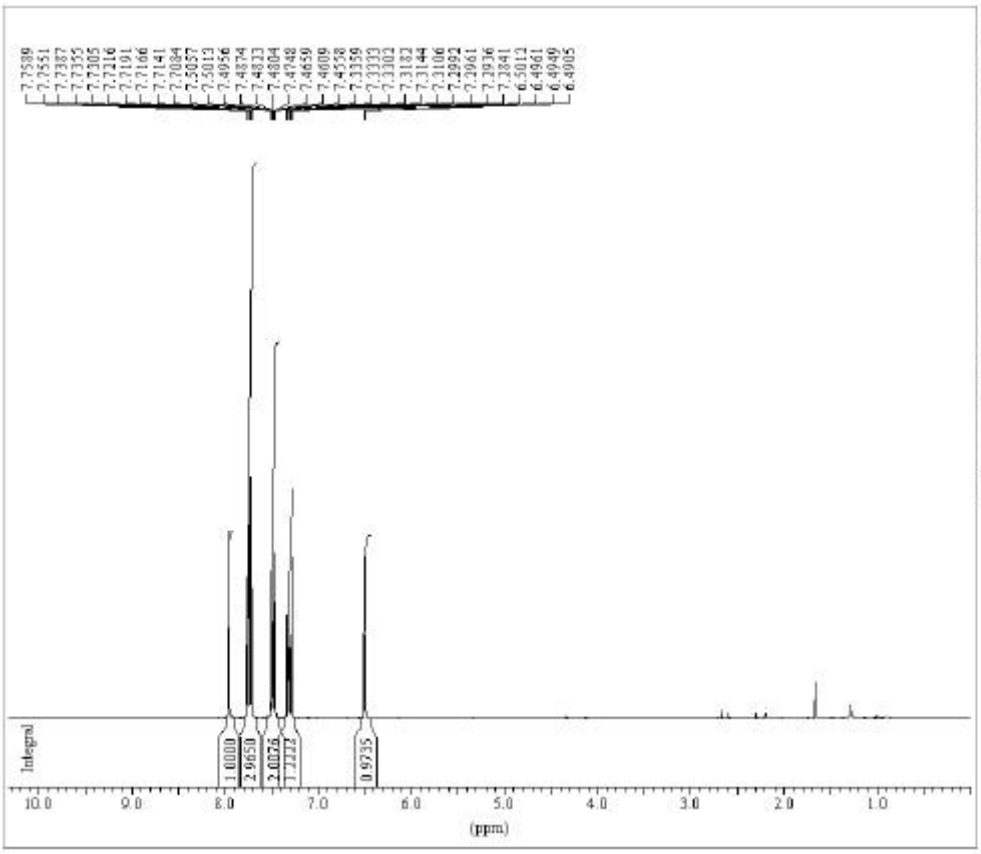
[5] M. A. Khan, B. M. Lynch, Y.-Y. Hung, *Can. J. Chem.* **1963**, 1540-1547.

[6] Taku Asaumi, Naoto Chatani, Takuya Matsuo, Fumitoshi Kakiuchi, and Shinji Murai, *J. Org. Chem.* **2003**, *68(19)* , 7538-7540.

[7] T. Kaihoh, T. Itoh, K. Yamaguchi, A. Ohsawa,. *Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry*, **1991**, 2045-8.

[8] Pankaja K. Kadaba, *J. Org. Chem.* **1992**, *57*, 3078-3085.

1-Phenyl-1H-pyrazole

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TE              295.2 K
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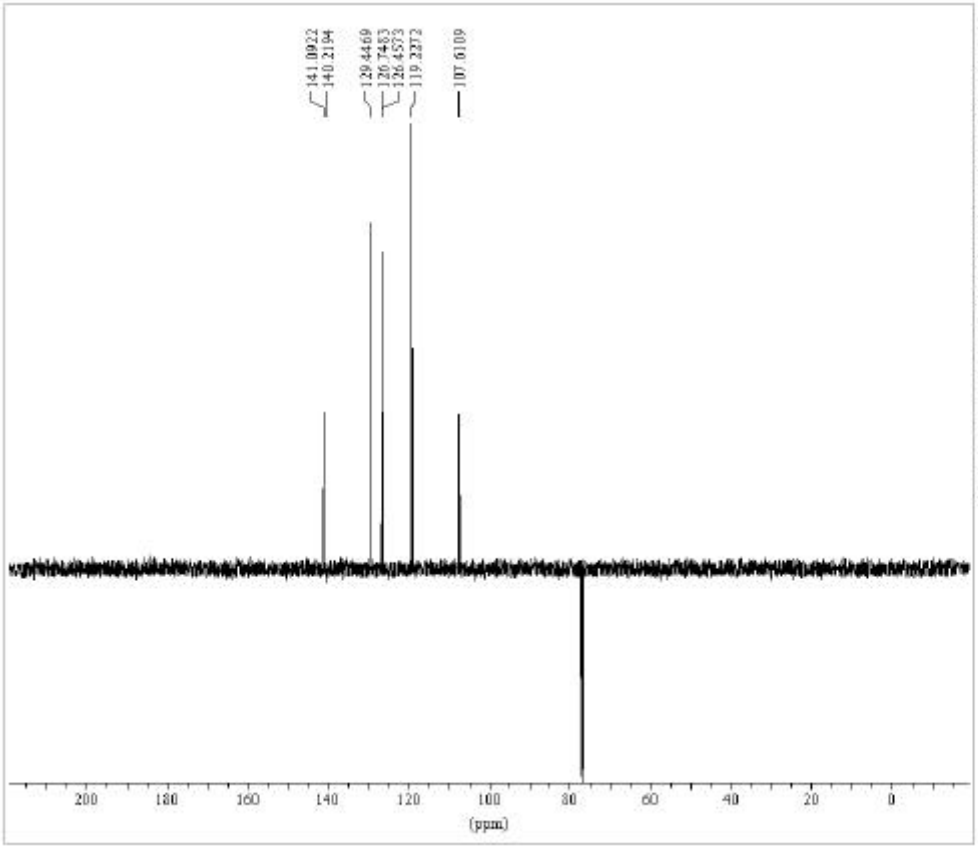


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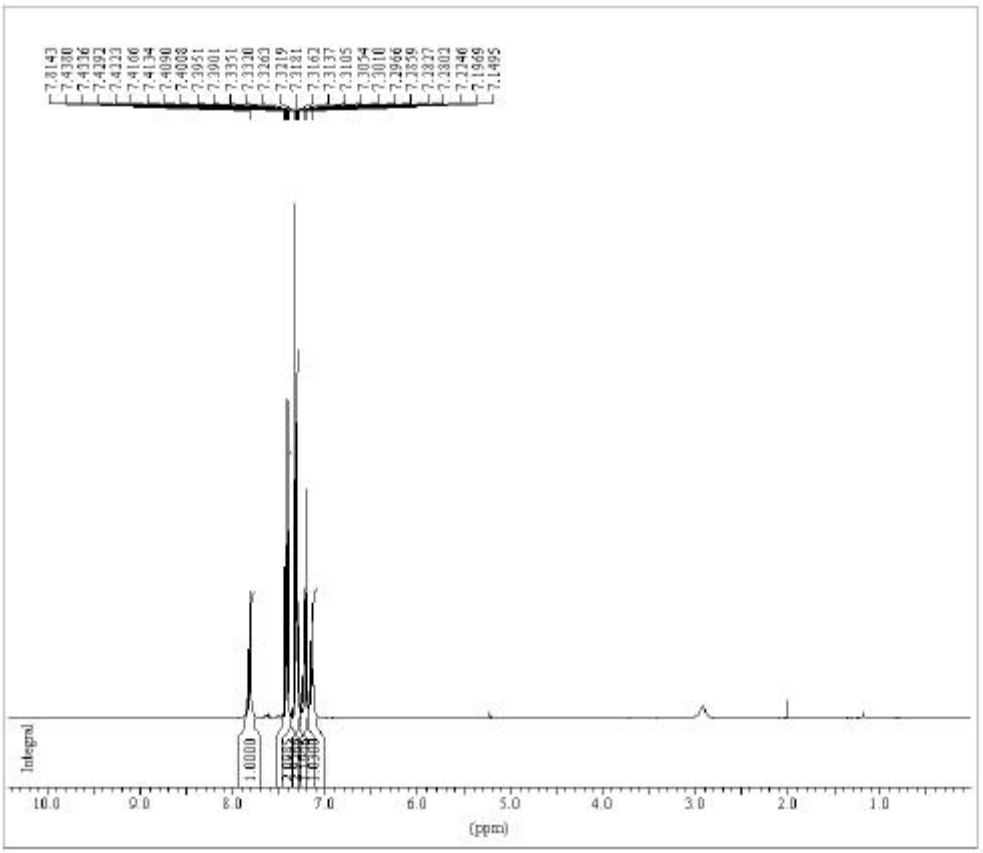
1-Phenyl-1H-imidazole

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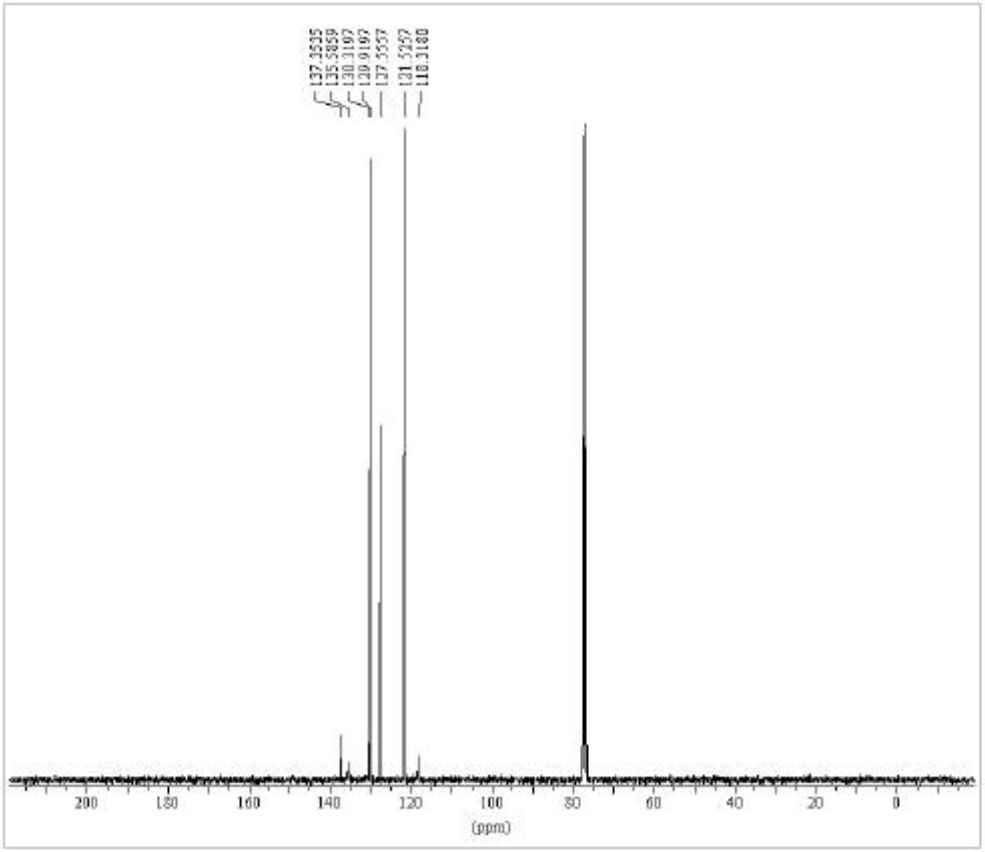


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*** 1D NMR Plot Parameters ***
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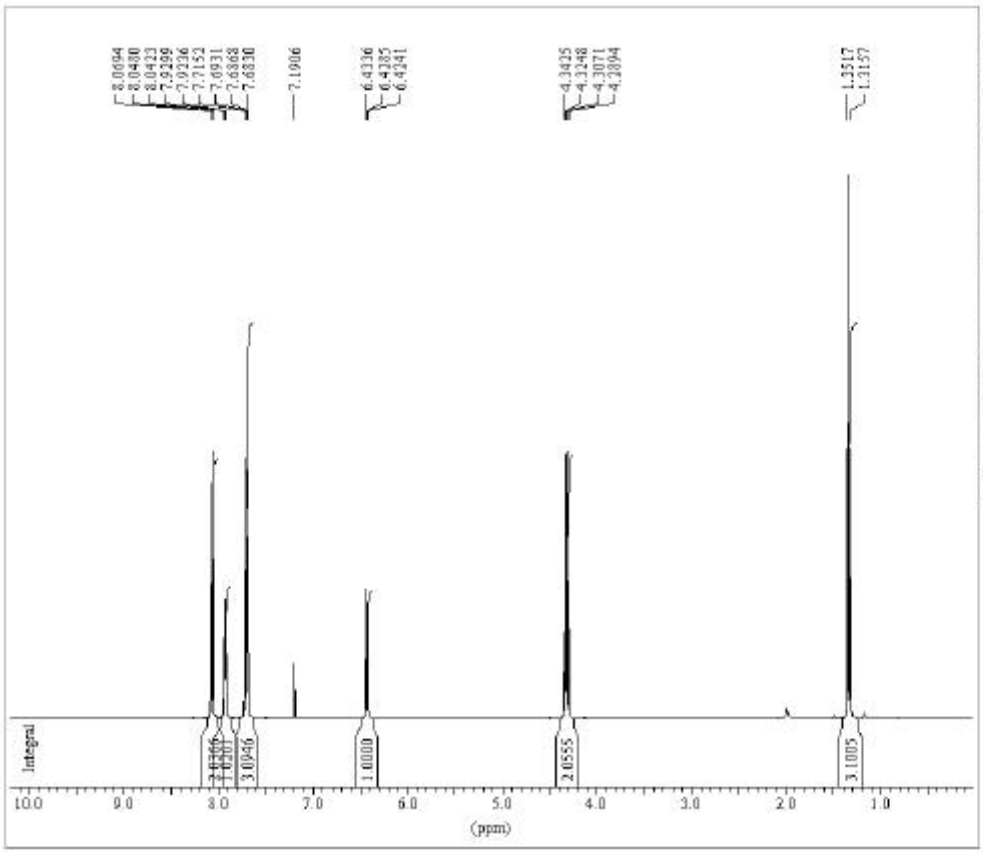
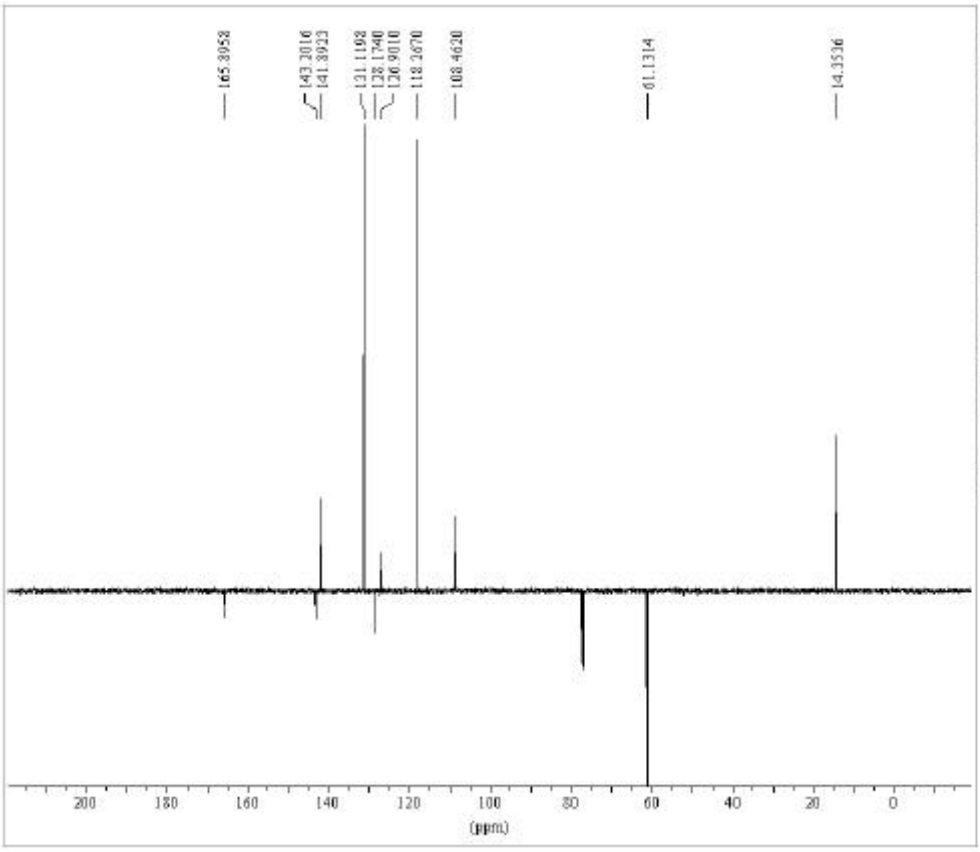
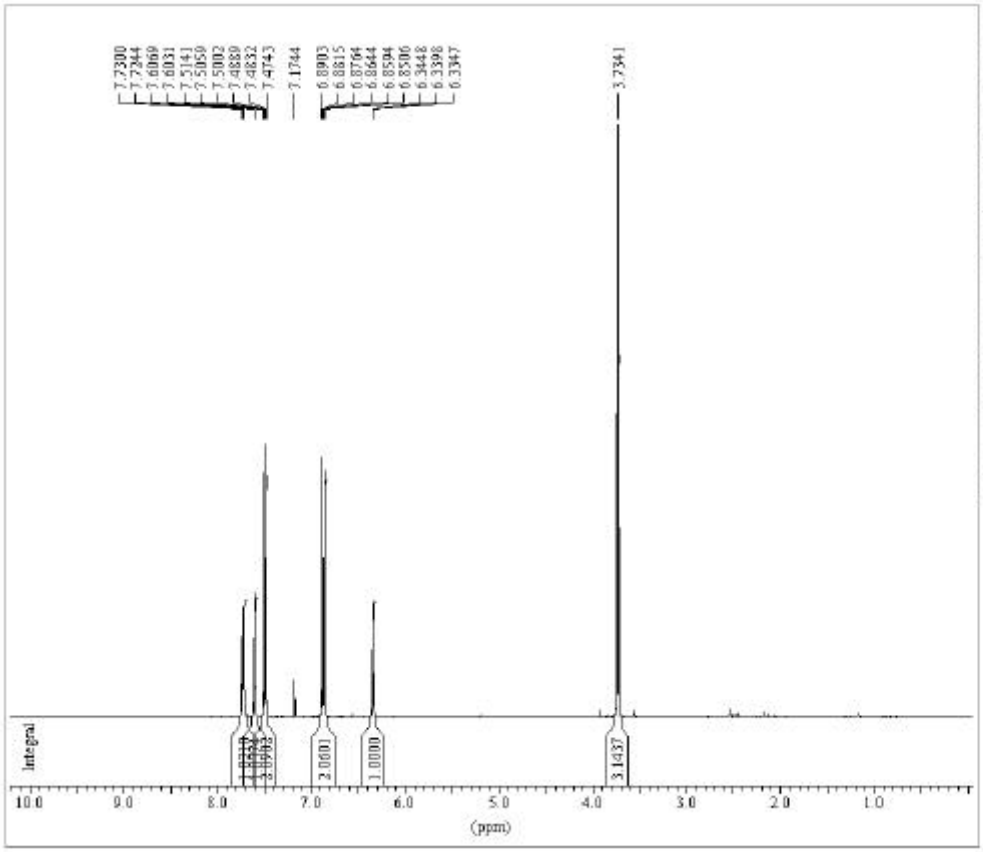
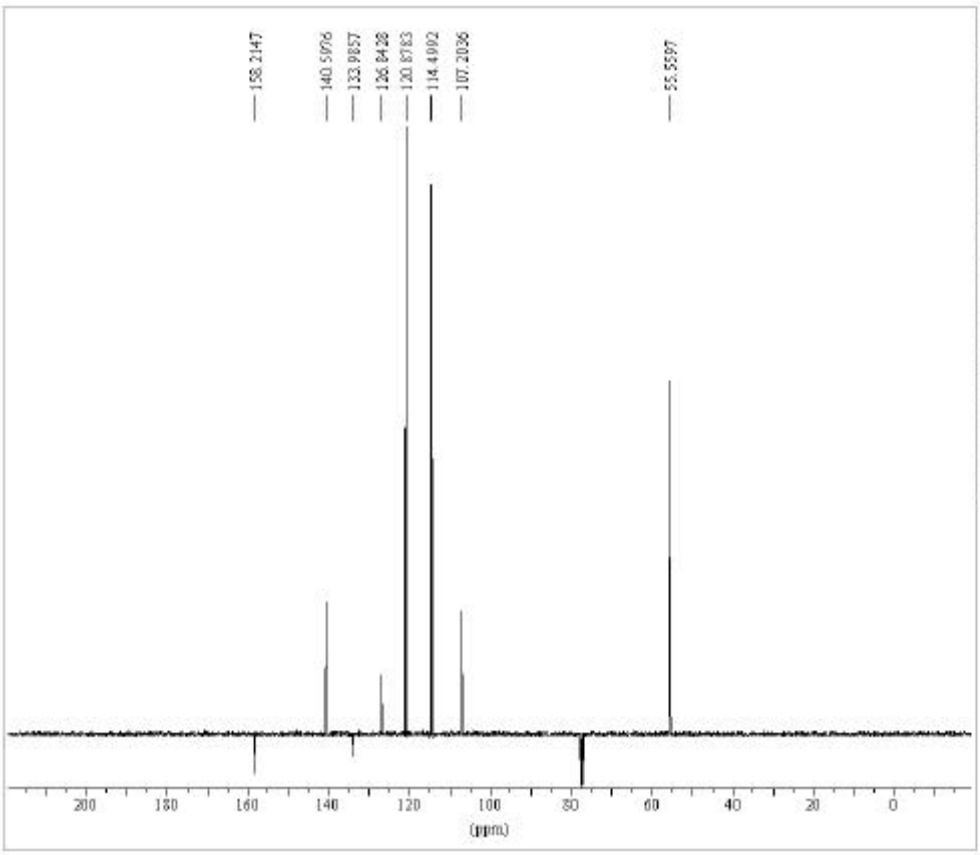
4-Pyrazol-1-yl-benzoic acid ethylester



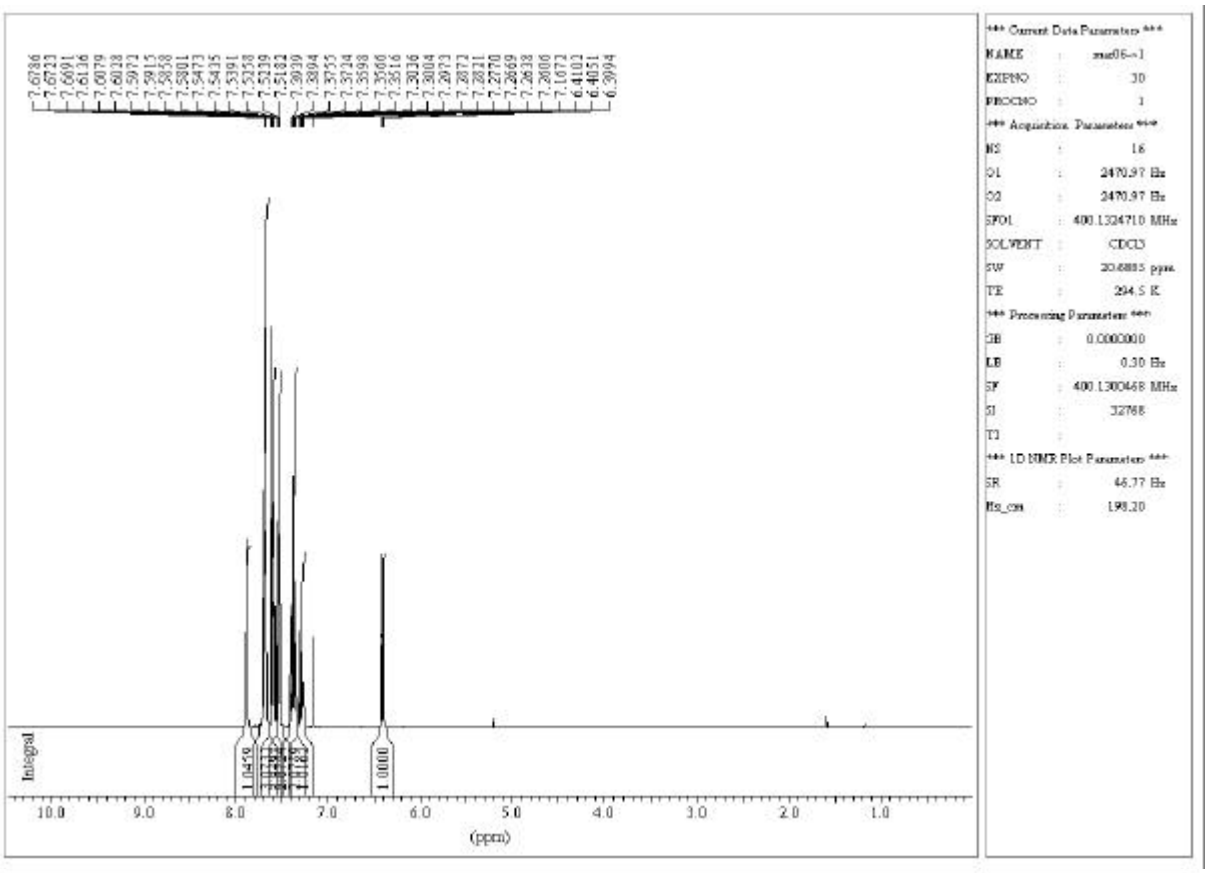


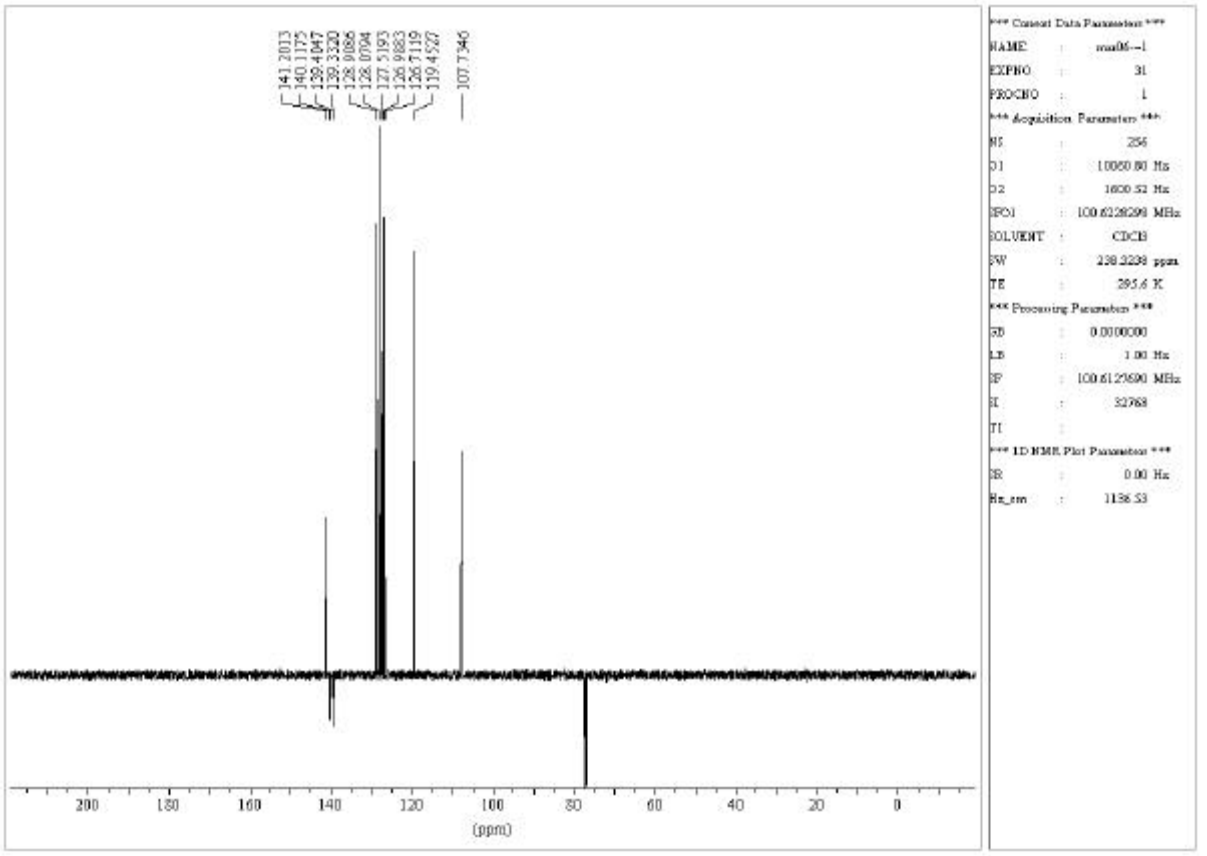
1-(4-Methoxy-phenyl)-1H-pyrazole



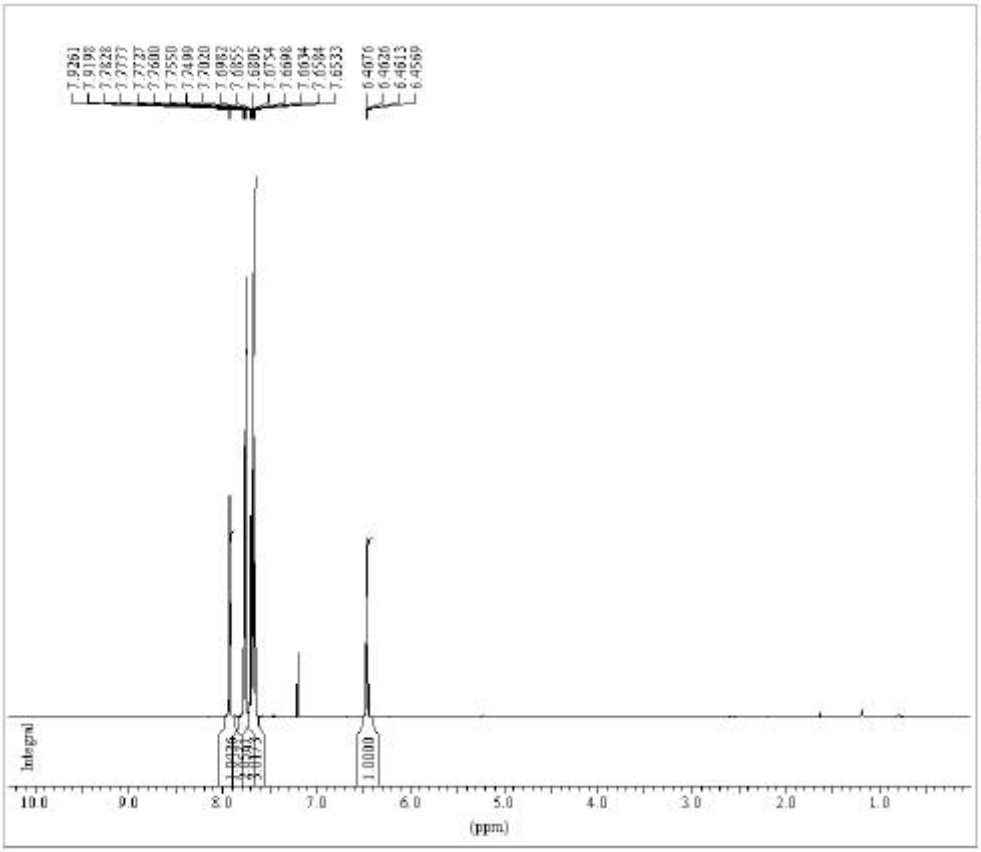


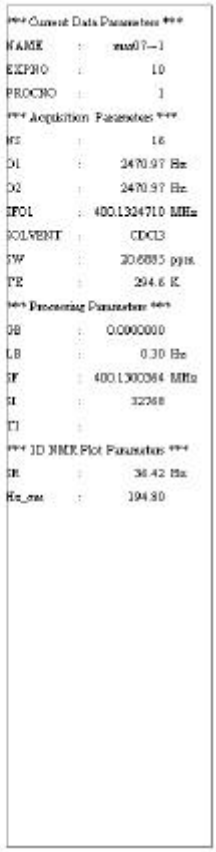
1-Biphenyl-4-yl-1H-pyrazole

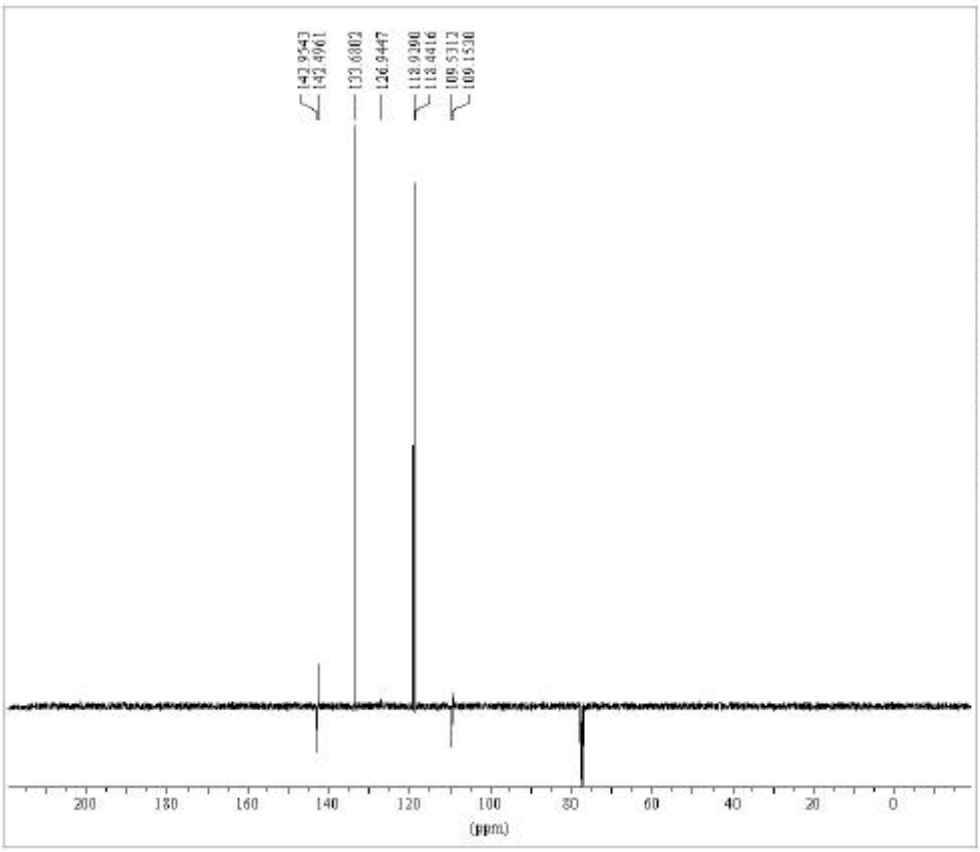




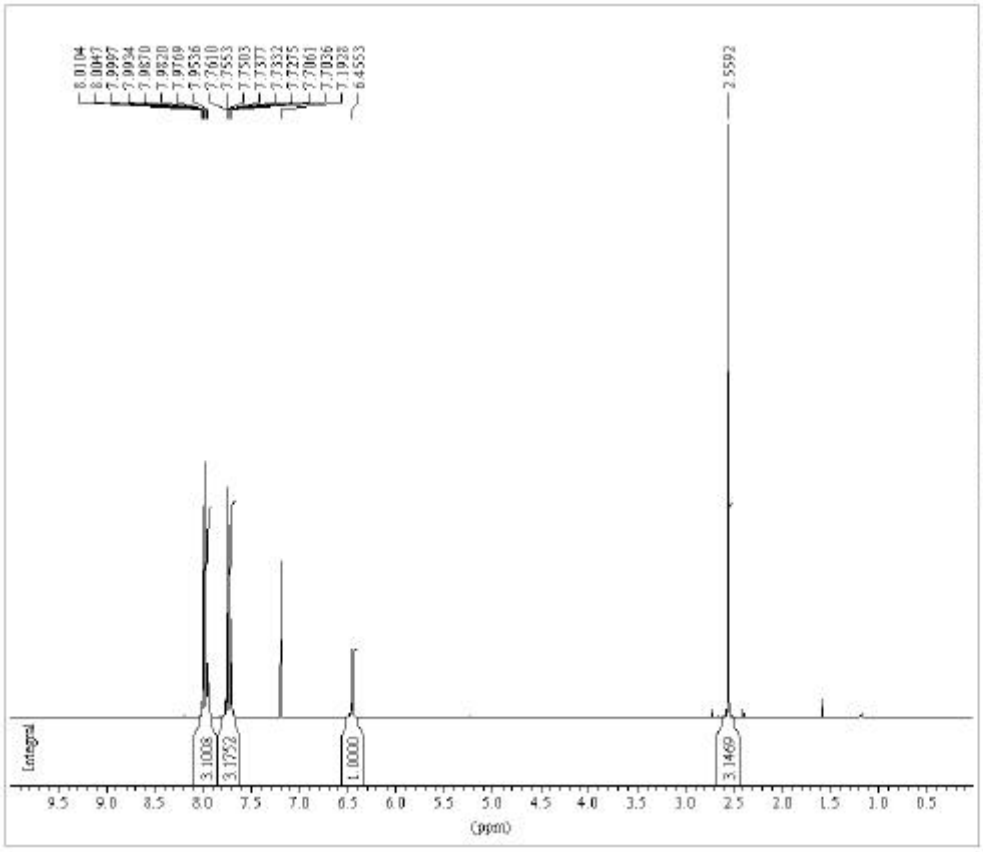
4-Pyrazol-1-yl-benzonitrile







1-(4-Pyrazol-1-yl-phenyl)-ethanone



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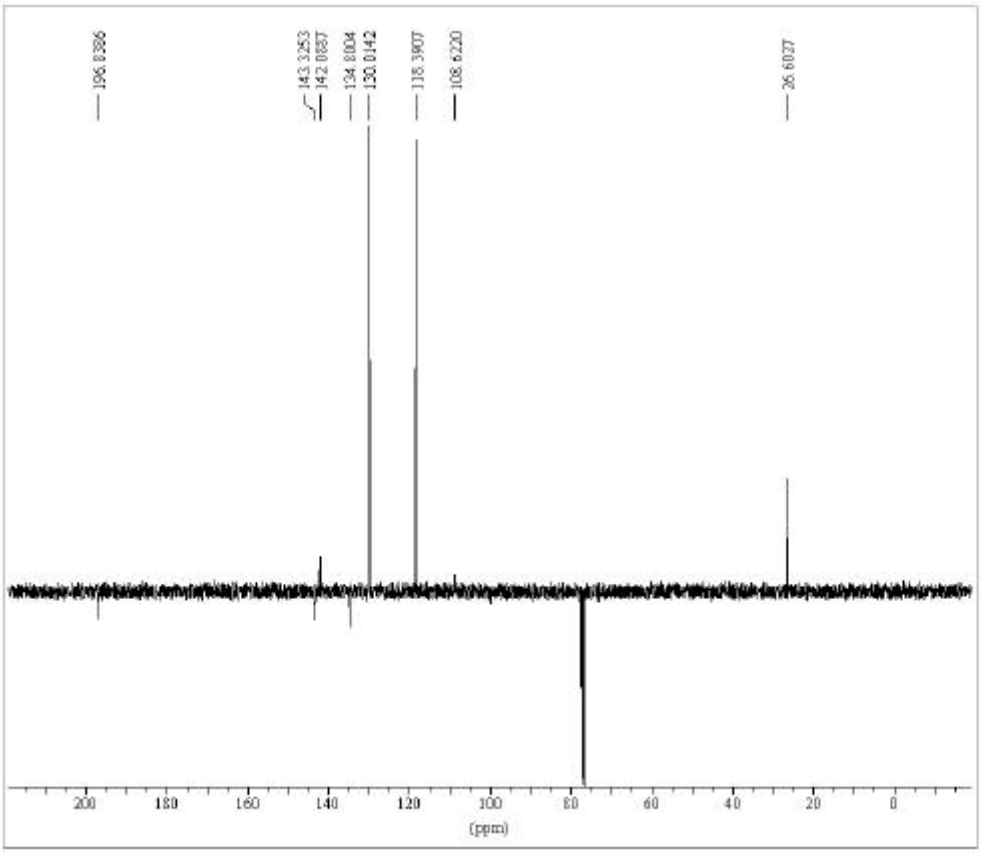

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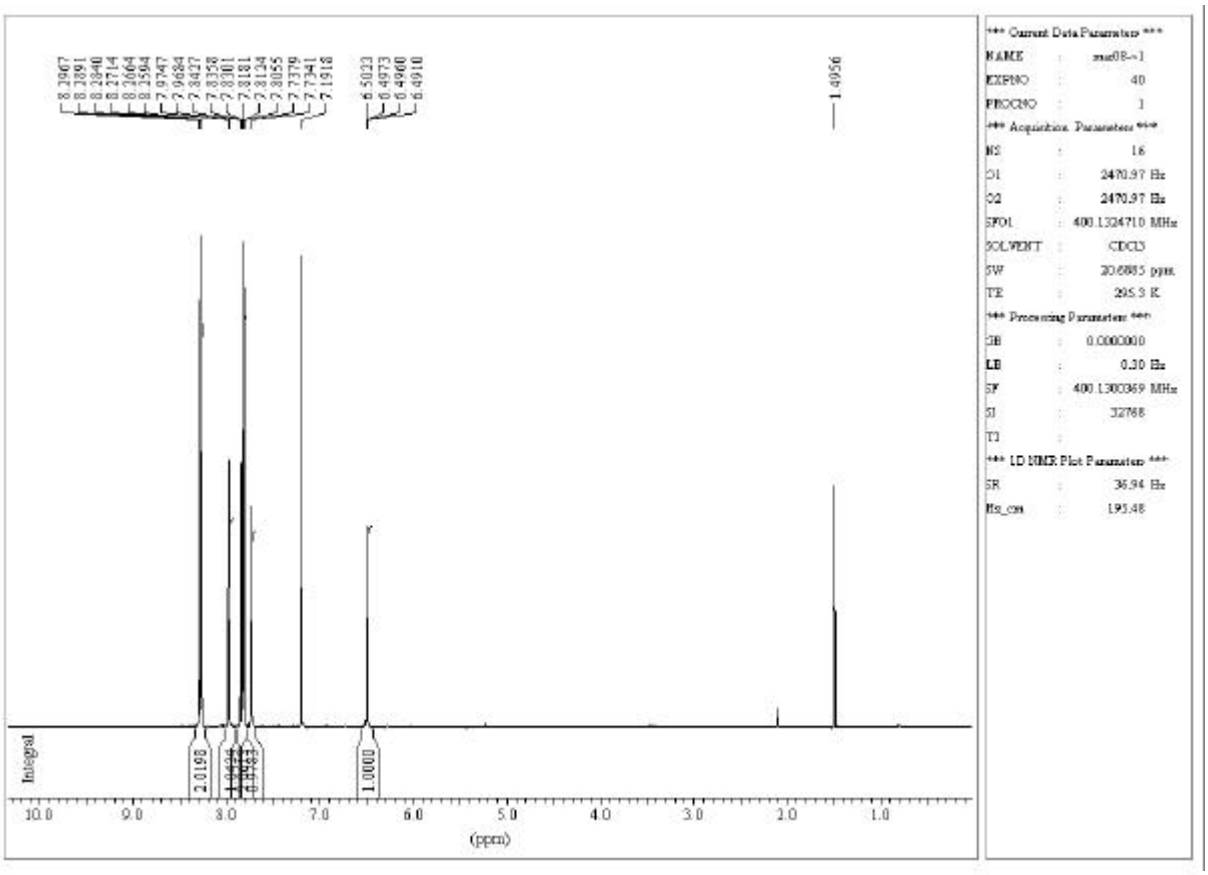
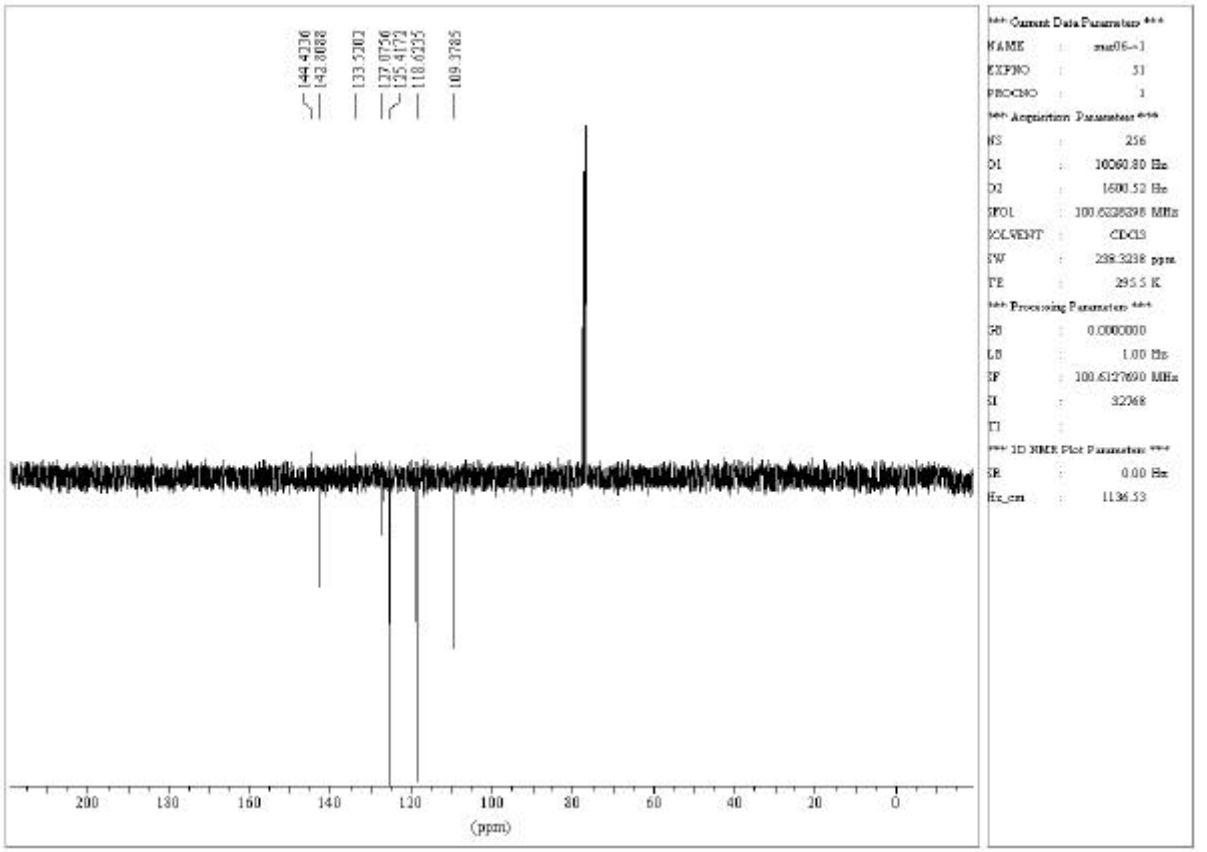
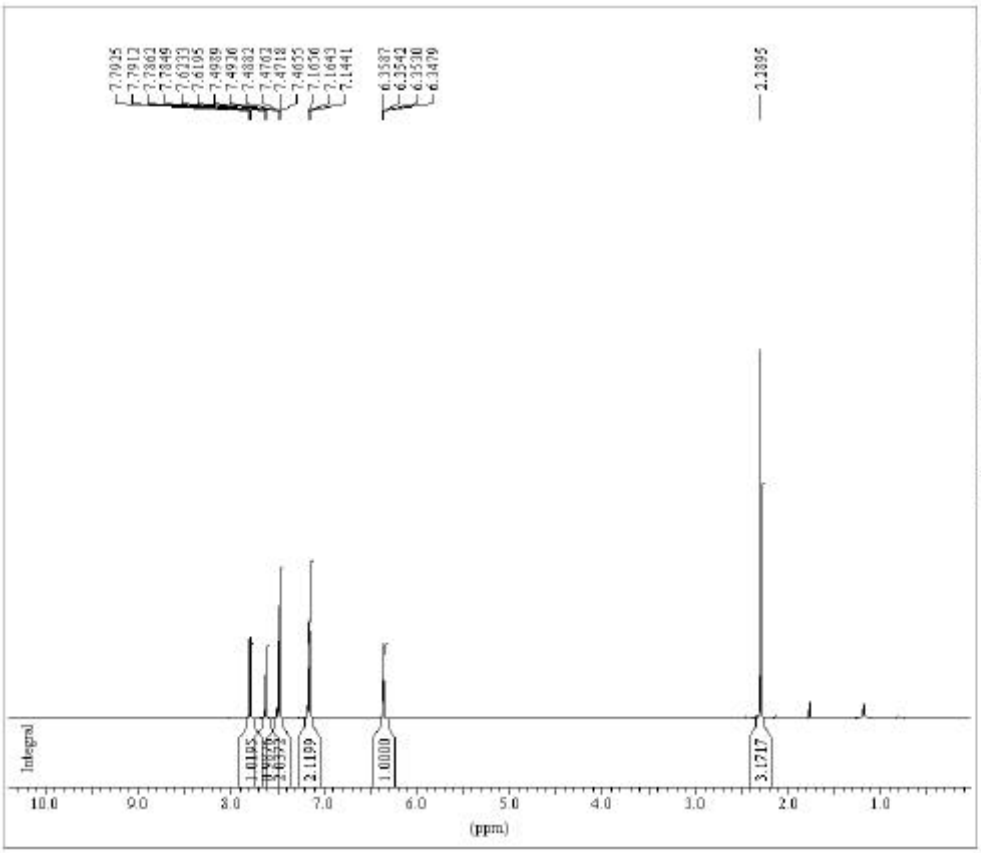
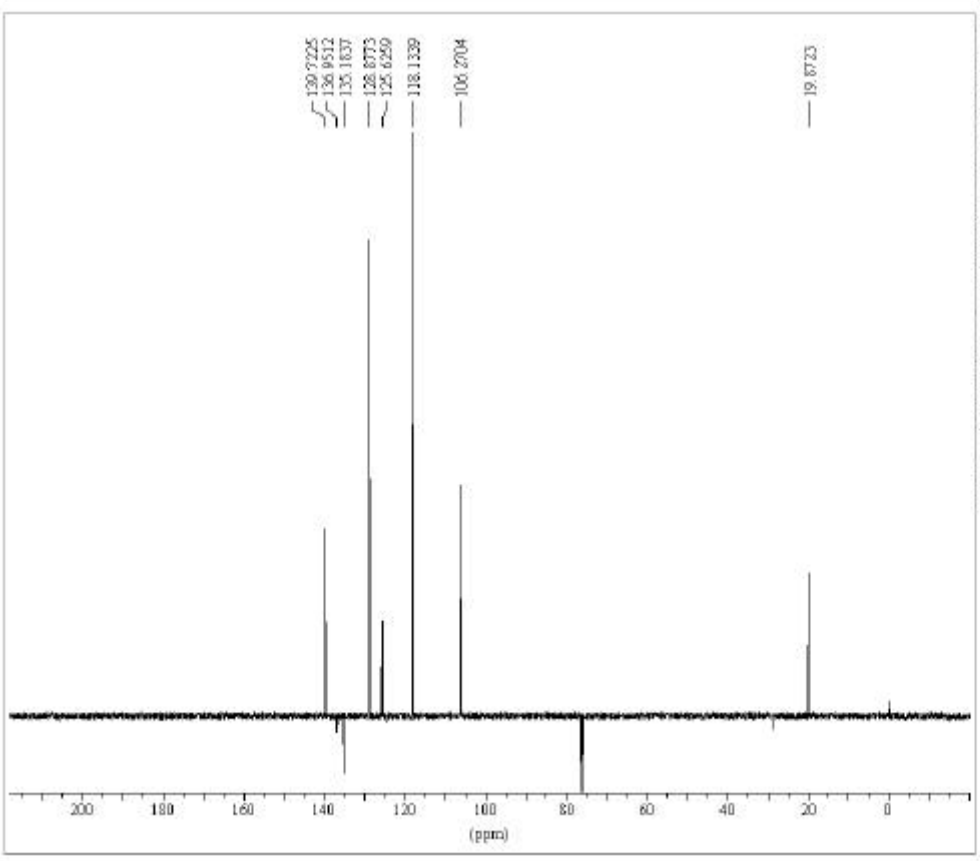
1-(4-Nitro-phenyl)-1H-pyrazole

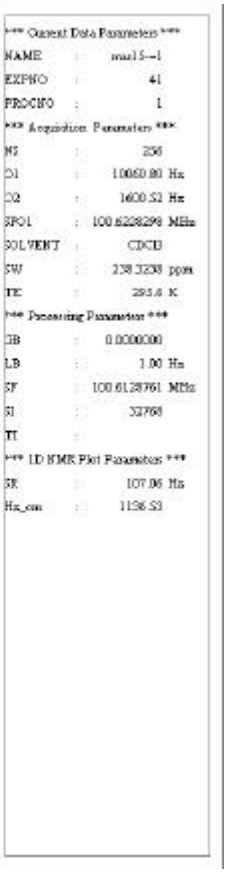




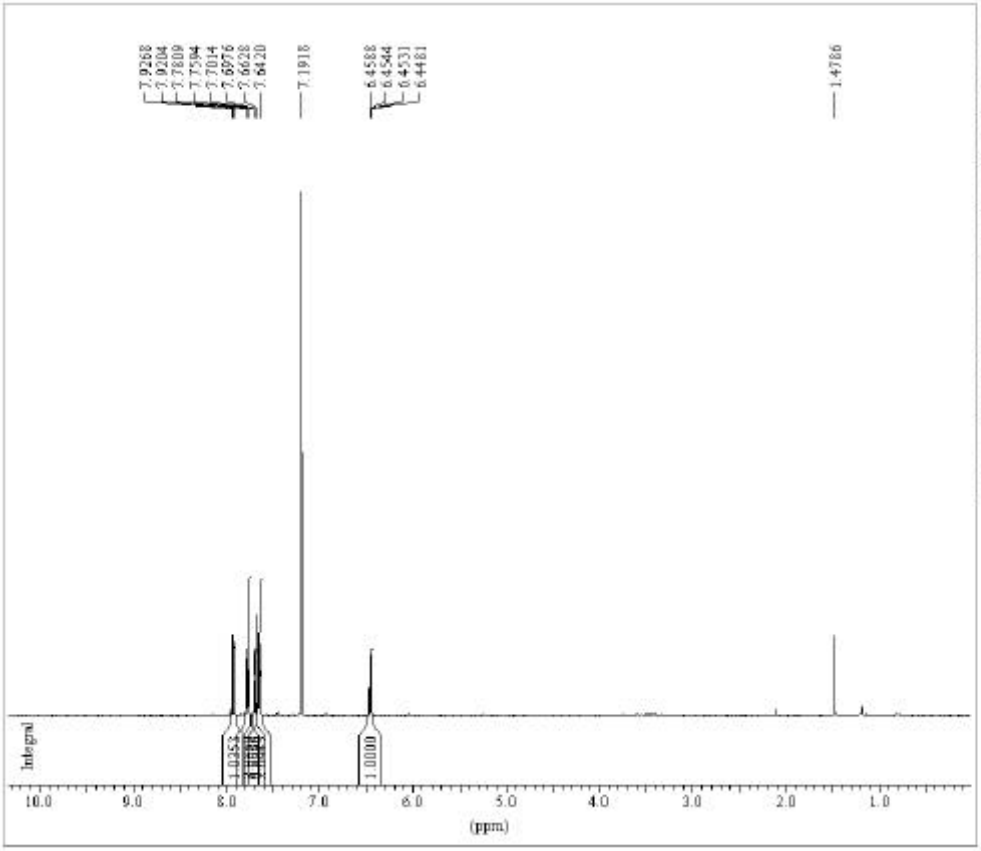
1-(4-Tolyl)-1H-pyrazole







1-(4-Trifluoromethyl-phenyl)-1H-pyrazole



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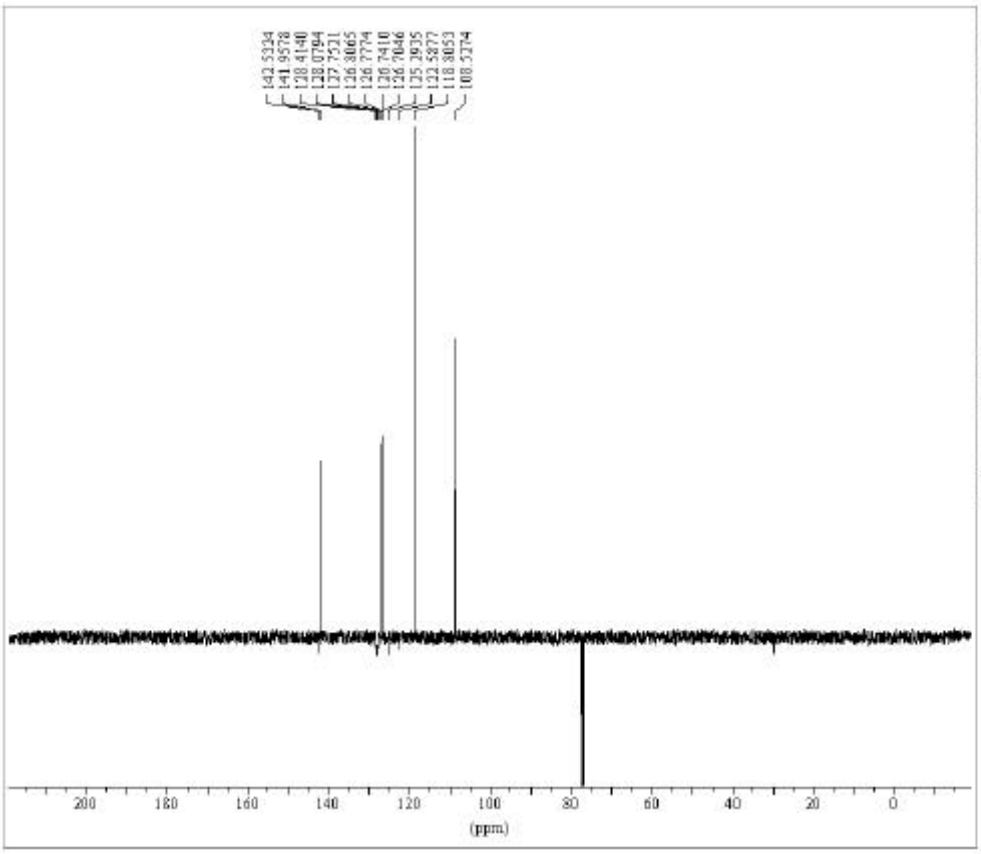

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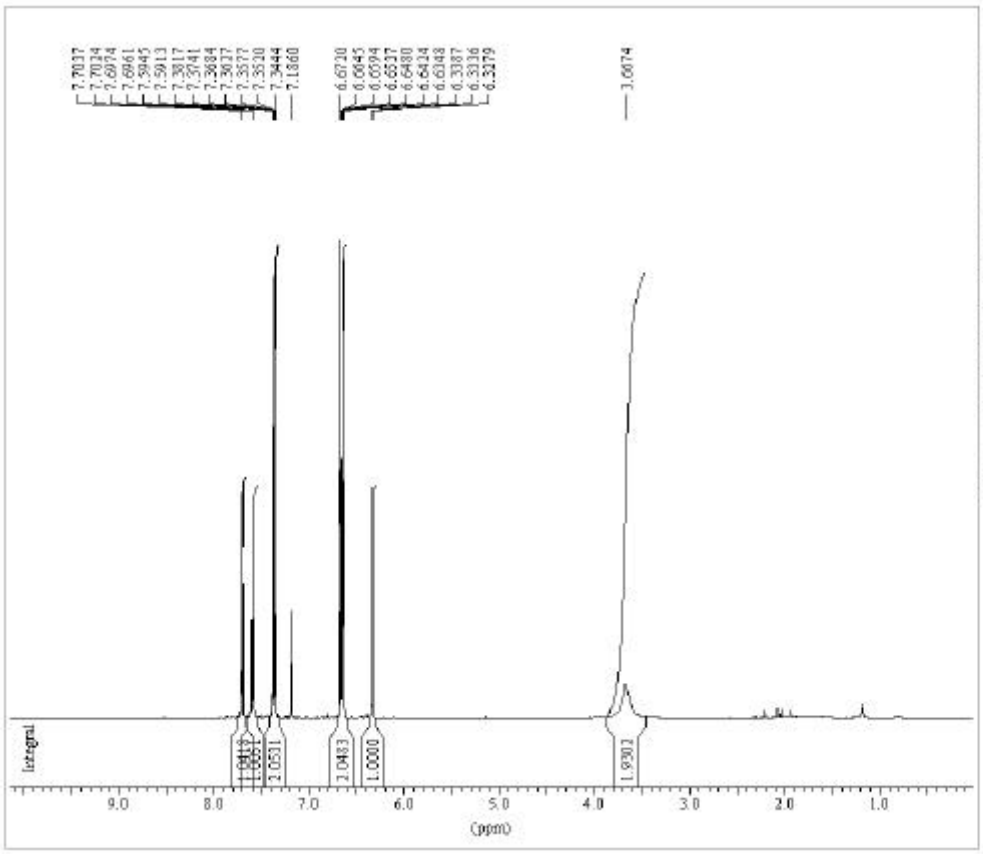
Hz_cm	:	1136.53

4-(1H-pyrazol-1-yl)aniline




```
***Current Data Parameters***
NAME            mz27-1
EXPNO           20
PROCNO          1
***Acquisition Parameters***
NS              16
D1              2470.97 Hz
D2              2470.97 Hz
SFO1            400.1324710 MHz
SOLVENT         CDCl3
SW              20.6885 ppm
TE              296.3 K
***Processing Parameters***
GB              0.0000000
LB              0.30 Hz
SF              400.1300393 MHz
SI              32768
TI
***1D NMR Plot Parameters***
SR              39.26 Hz
Hz_cm           192.08
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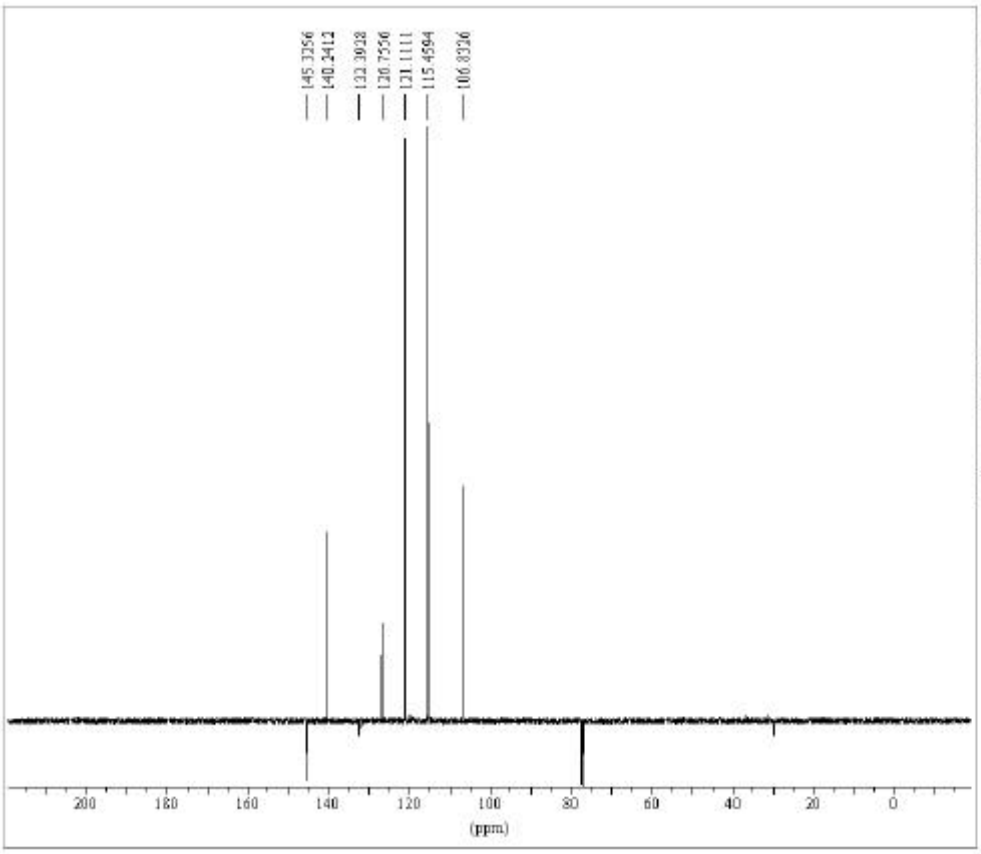
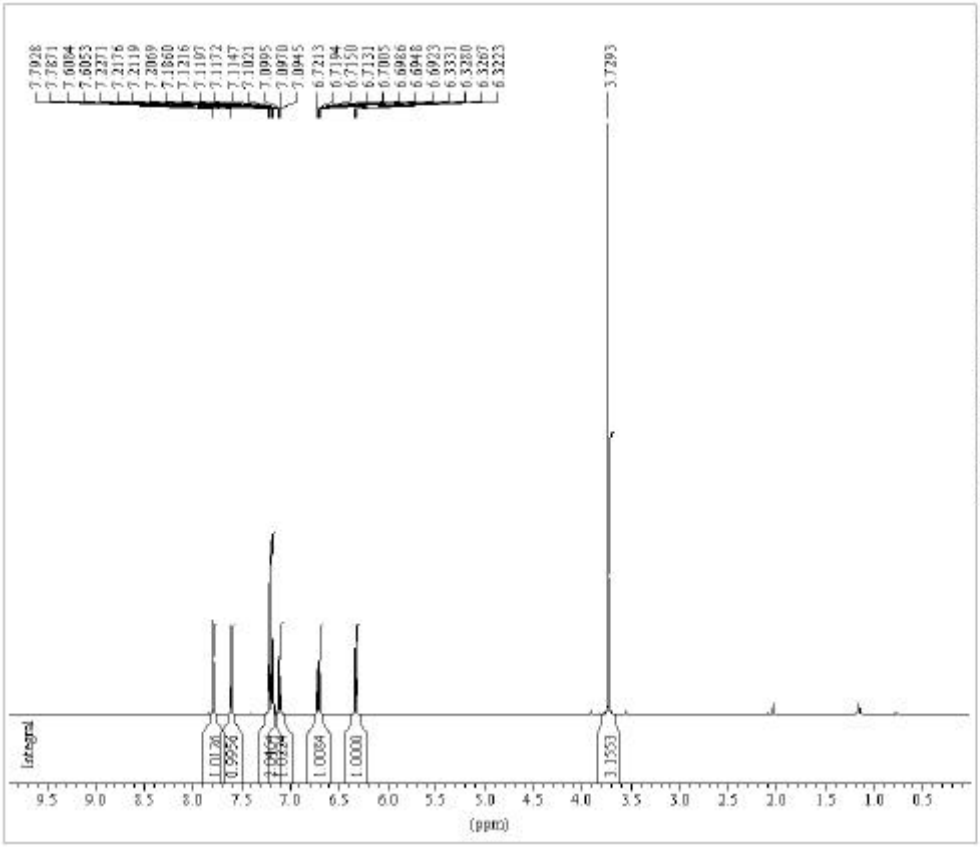
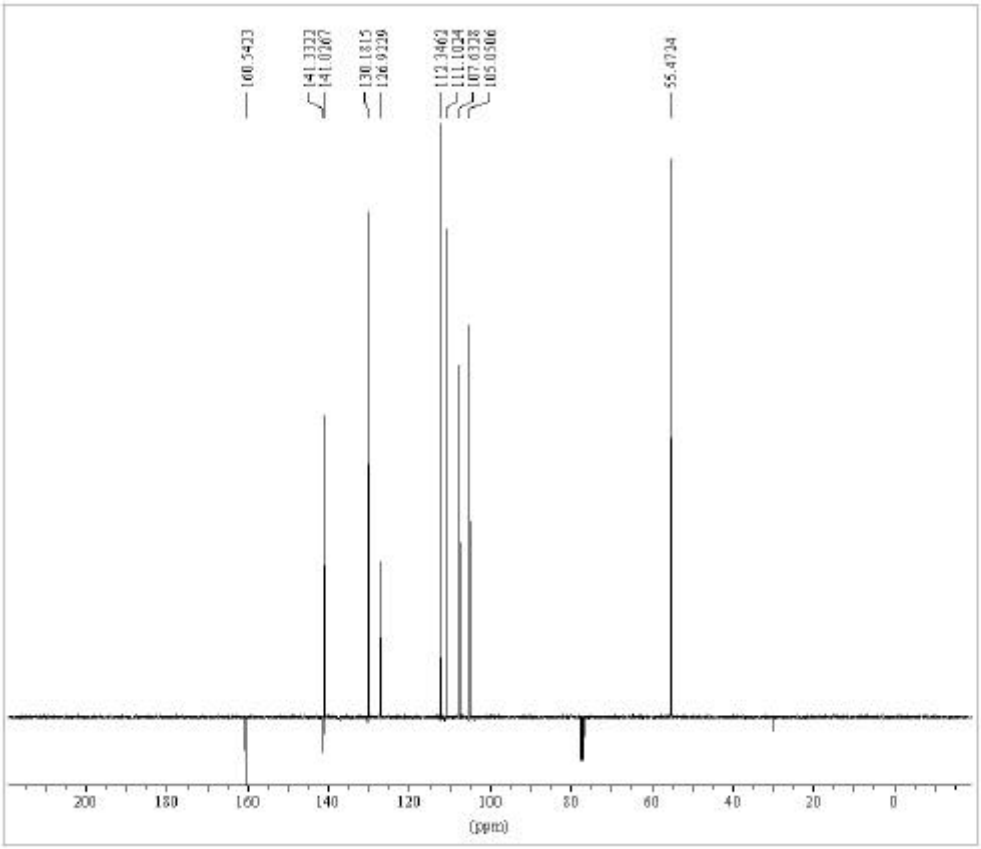



```
***Current Data Parameters***
NAME            mz22-1
EXPNO           40
PROCNO          1
***Acquisition Parameters***
NS              256
D1              10060.80 Hz
D2              1600.52 Hz
SFO1            100.6338398 MHz
SOLVENT         CDCl3
SW              238.3238 ppm
TE              295.8 K
***Processing Parameters***
GB              0.0000000
LB              1.00 Hz
SF              100.6127690 MHz
SI              32768
TI
***1D NMR Plot Parameters***
SR              0.00 Hz
Hz_cm           1136.53
```

1-(3-Methoxy-phenyl)-1H-pyrazole

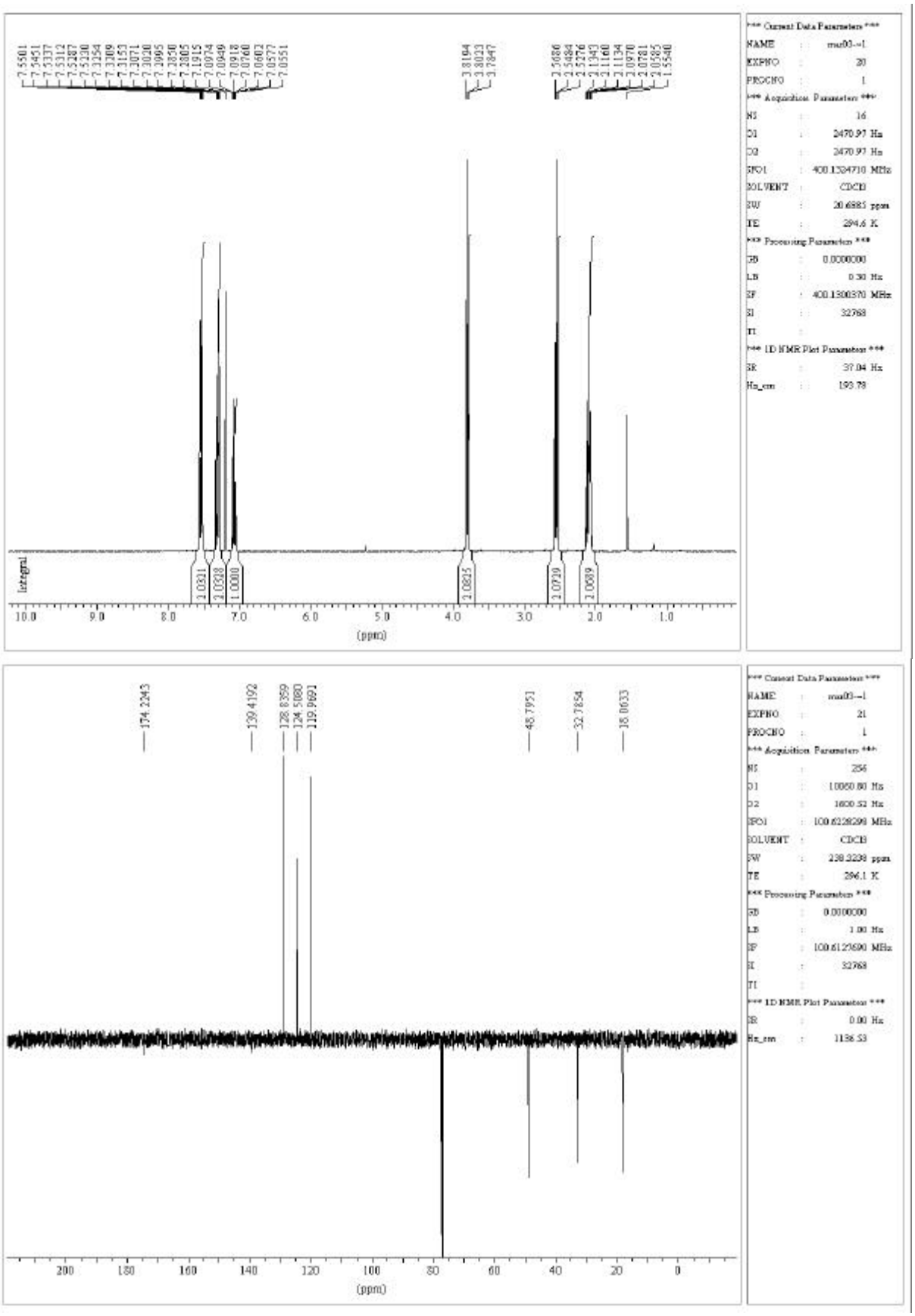


*** Current Data Parameters ***
NAME : mar08--1
EXPNO : 20
PROCNO : 1
*** Acquisition Parameters ***
NS : 16
D1 : 2470.97 Hz
D2 : 2470.97 Hz
SFO1 : 400.1304710 MHz
SOLVENT : CDCl3
SW : 20.6885 ppm
TE : 295.1 K
*** Processing Parameters ***
GB : 0.0000000
LB : 0.30 Hz
SF : 400.1300514 MHz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
SR : 51.82 Hz
Hz_cm : 187.30

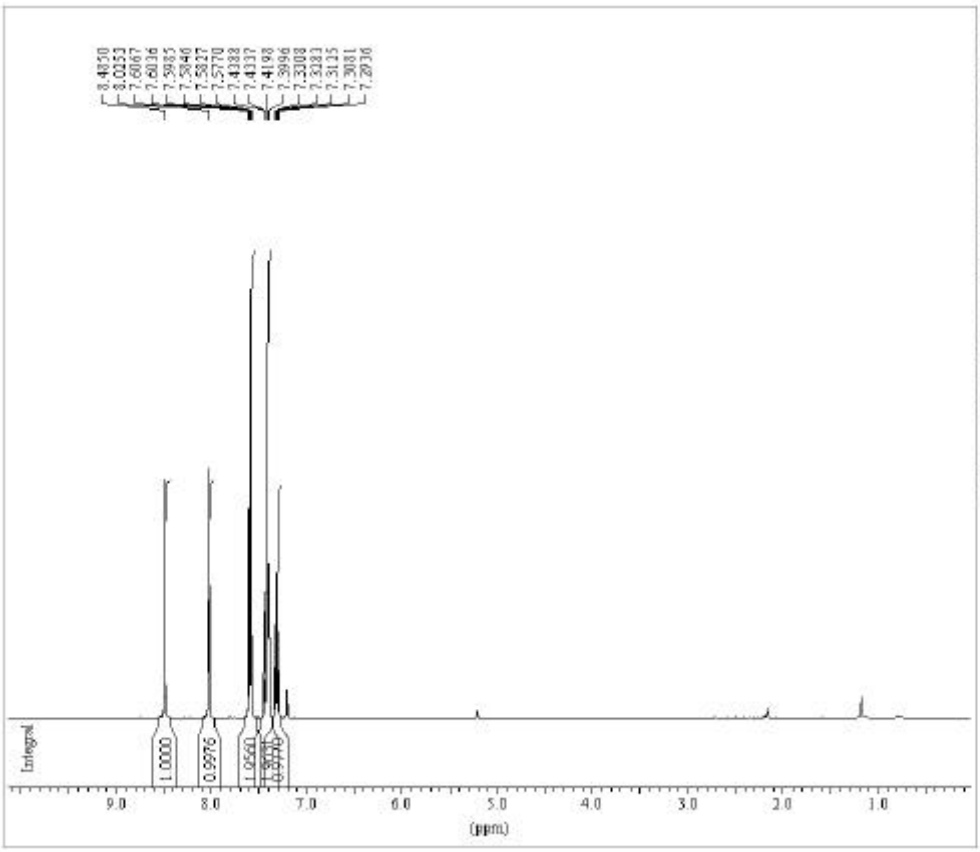


*** Current Data Parameters ***
NAME : mar09--1
EXPNO : 40
PROCNO : 1
*** Acquisition Parameters ***
NS : 256
D1 : 10060.80 Hz
D2 : 1609.52 Hz
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
TE : 295.5 K
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SF : 100.6127690 MHz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
SR : 0.00 Hz
Hz_cm : 1136.53

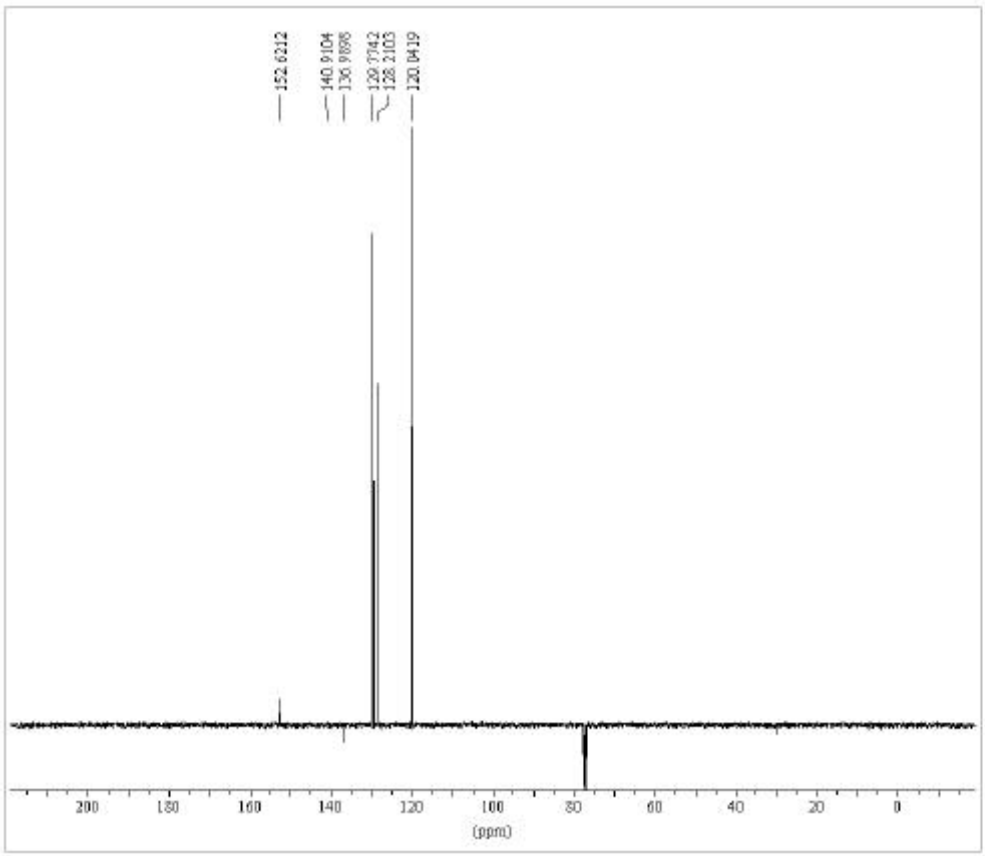
1-Phenyl-pyrrolidin-2-one



1-Phenyl-1H-[1,2,4]triazole

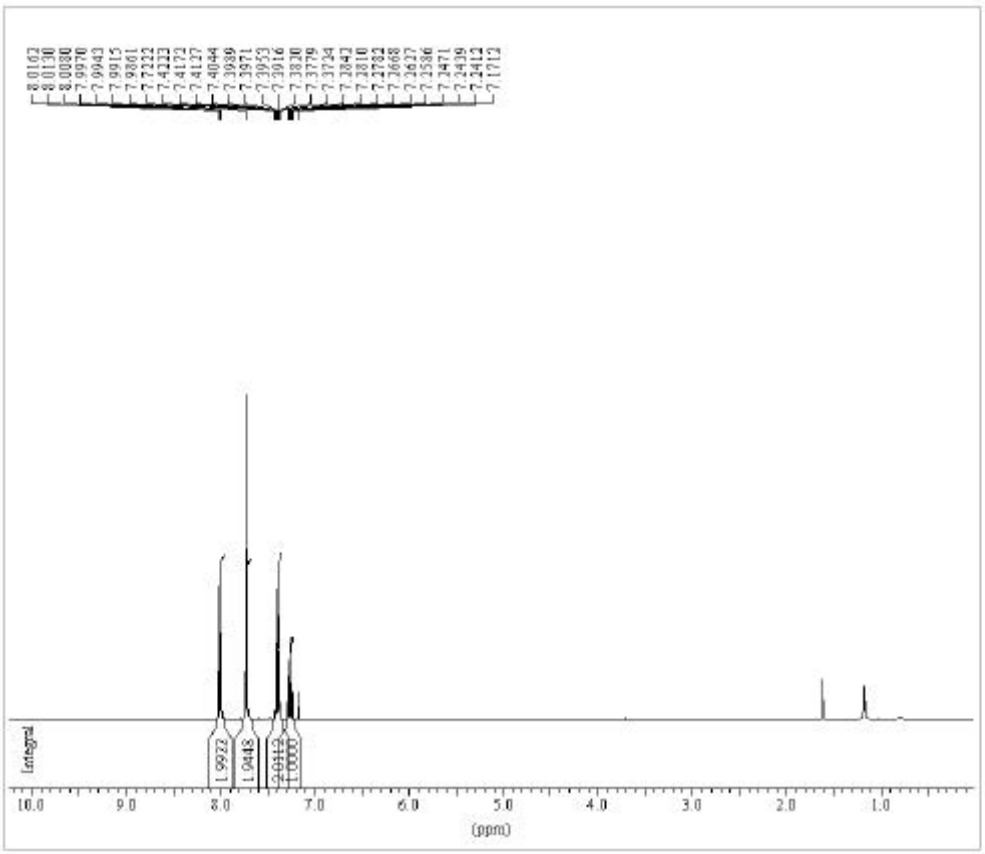


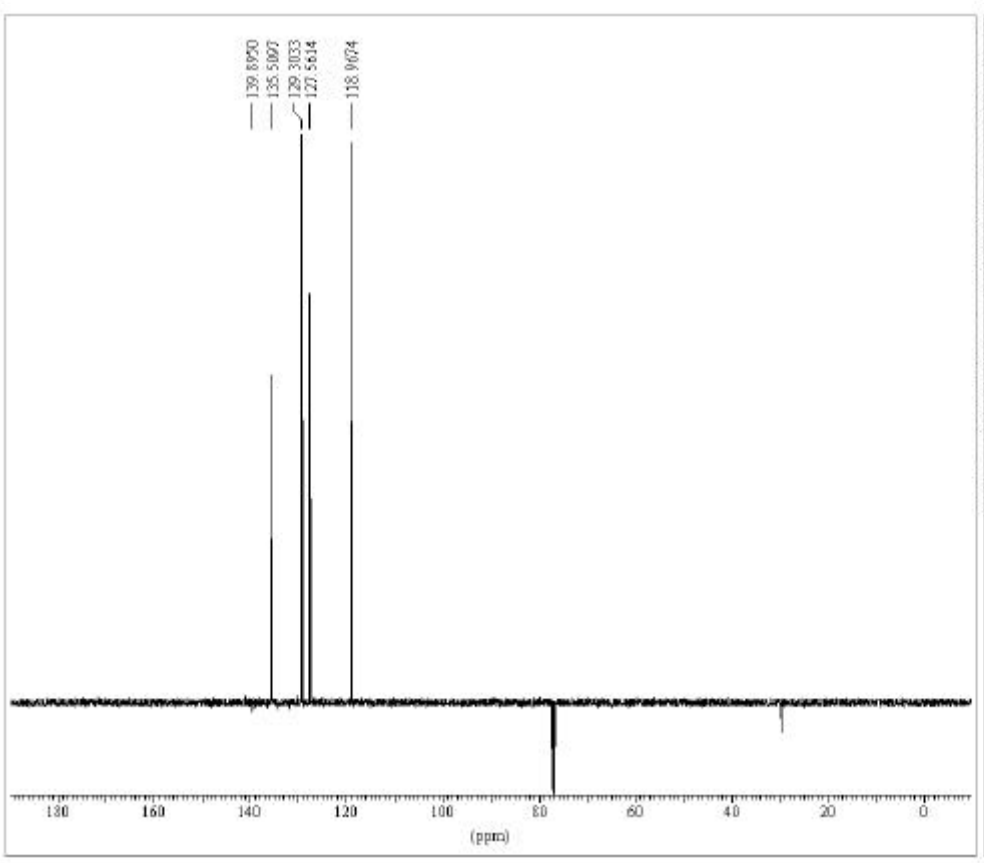
*** Current Data Parameters ***
NAME : mai16--1
EXPNO : 10
PROCNO : 1
*** Acquisition Parameters ***
NS : 16
D1 : 2470.97 Hz
D2 : 2470.97 Hz
SFO1 : 400.1324710 MHz
SOLVENT : CDCl3
SW : 20.6885 ppm
TE : 295.0 K
*** Processing Parameters ***
GB : 0.0000000
LB : 0.30 Hz
SF : 400.1300313 MHz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
SR : 31.23 Hz
Hz_cm : 191.75



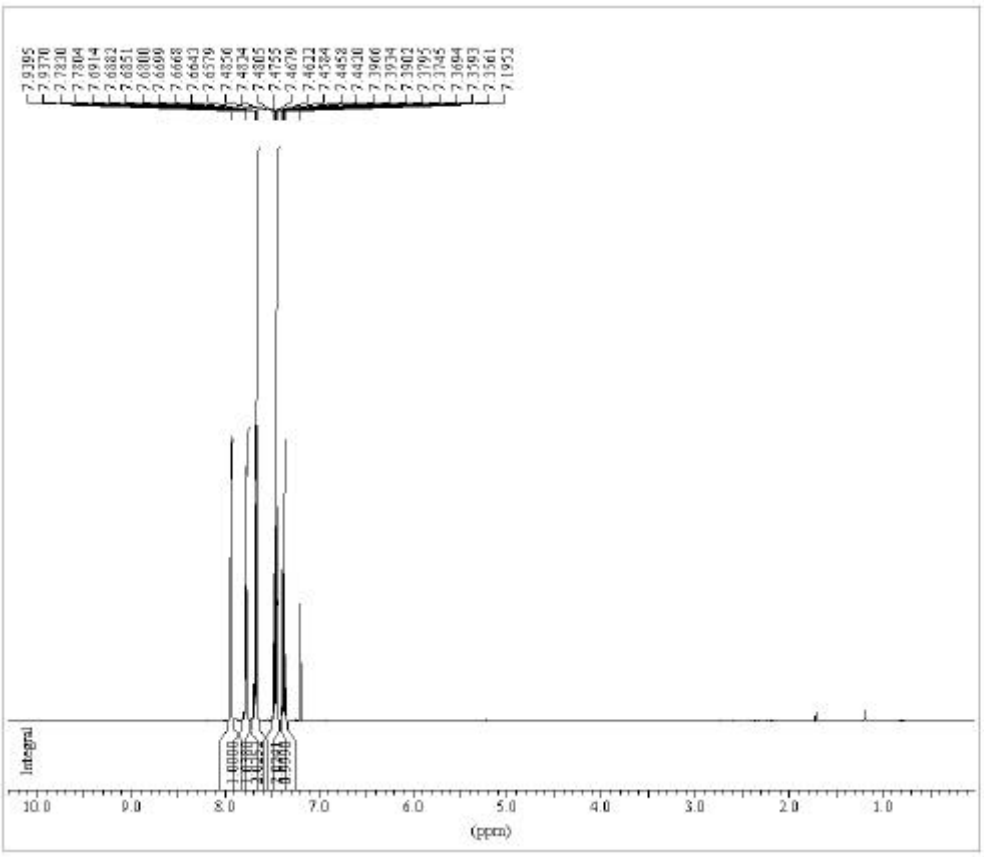
*** Current Data Parameters ***
NAME : mai16--1
EXPNO : 11
PROCNO : 1
*** Acquisition Parameters ***
NS : 256
D1 : 10060.80 Hz
D2 : 1600.52 Hz
SFO1 : 100.6228298 MHz
SOLVENT : CDCl3
SW : 238.3238 ppm
TE : 295.3 K
*** Processing Parameters ***
GB : 0.0000000
LB : 1.00 Hz
SF : 100.6123690 MHz
SI : 32768
TI :
*** 1D NMR Plot Parameters ***
SR : 0.00 Hz
Hz_cm : 1138.53

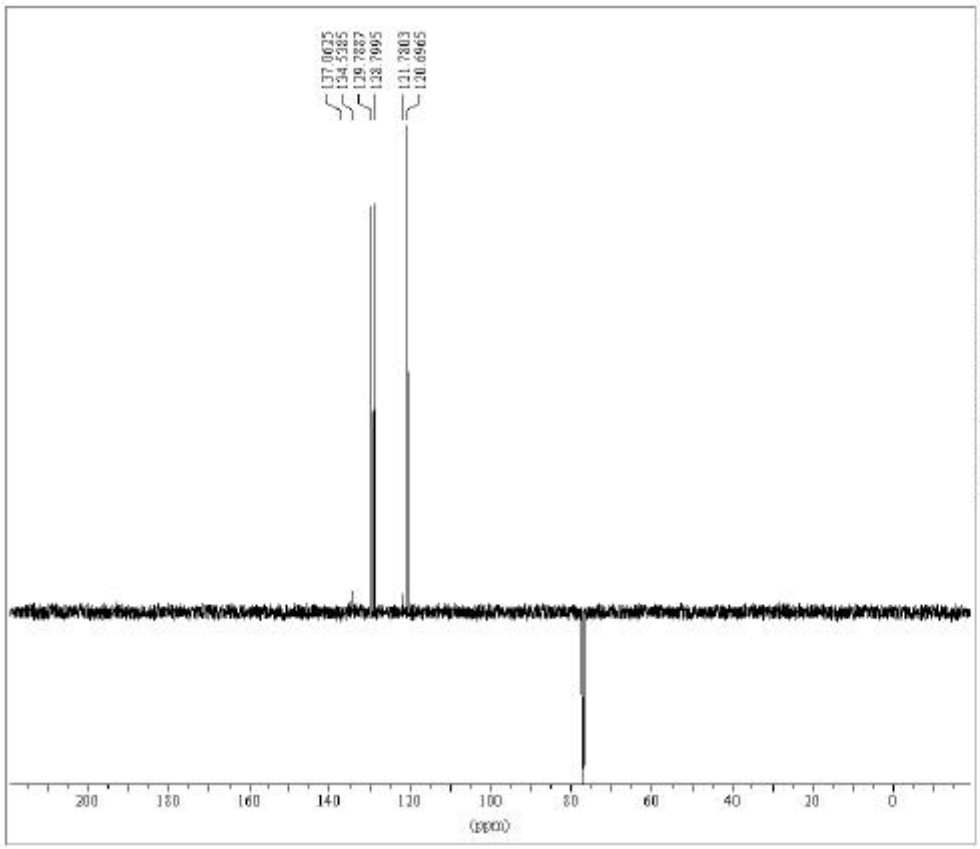
2-Phenyl-2H-[1,2,3]triazole



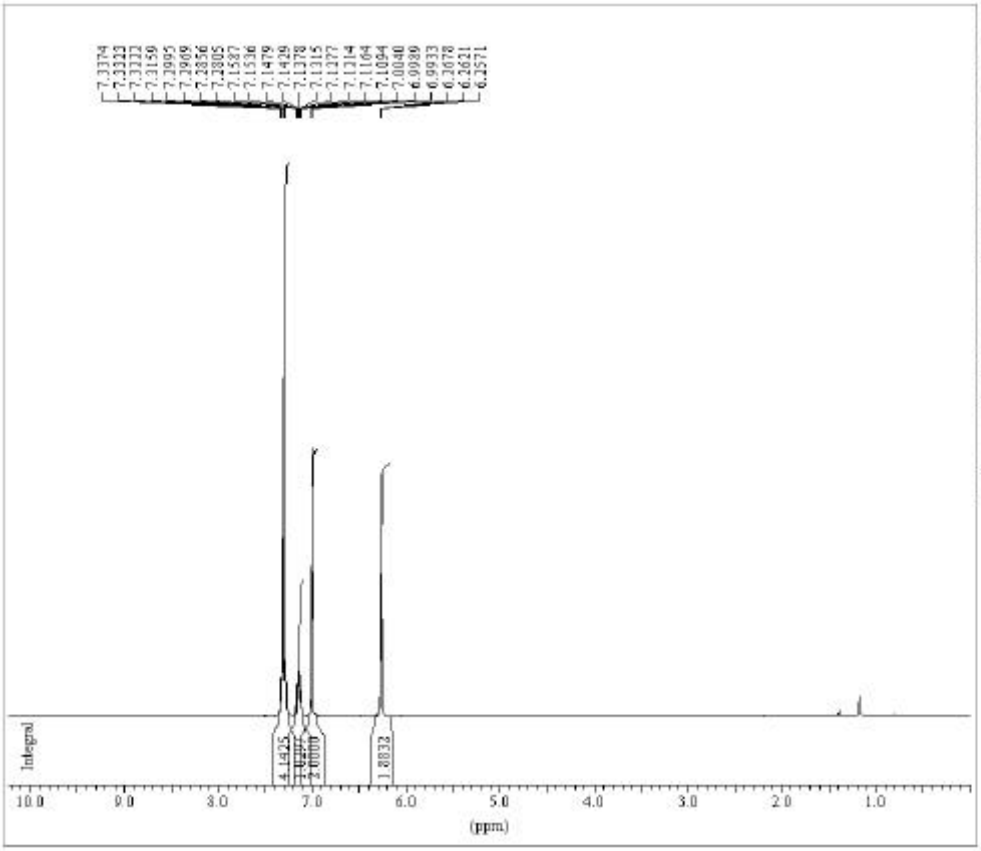


1-Phenyl-1H-[1,2,3]triazole

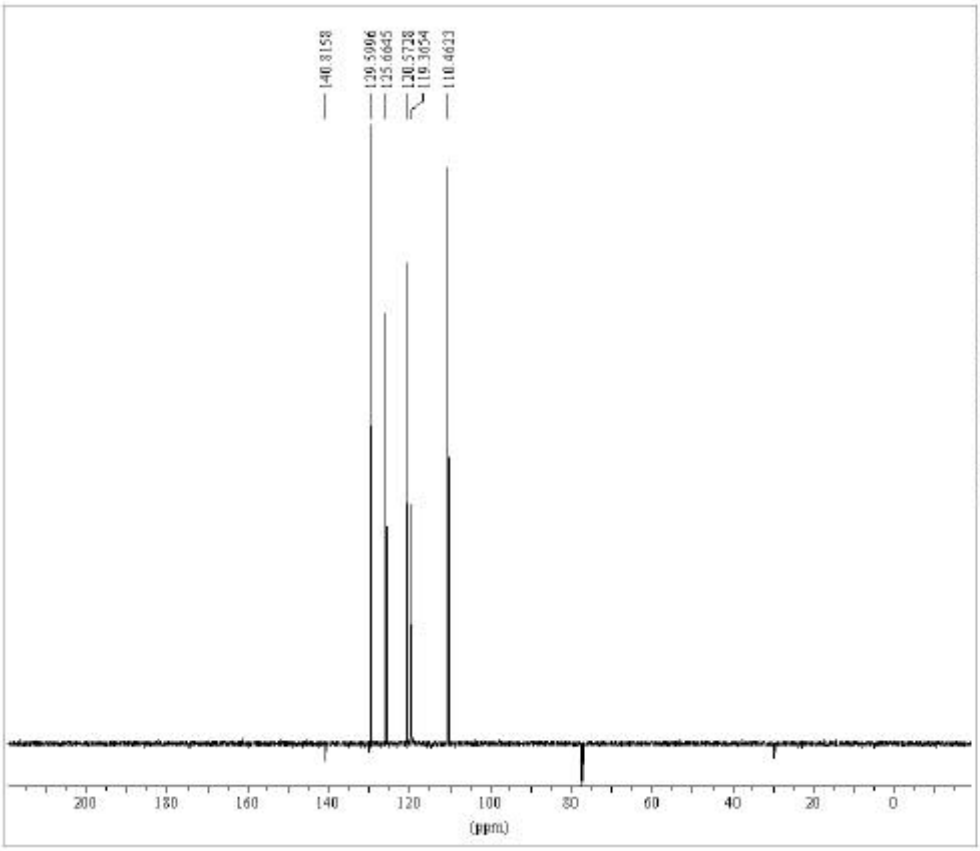




1-Phenyl-1H-pyrrole

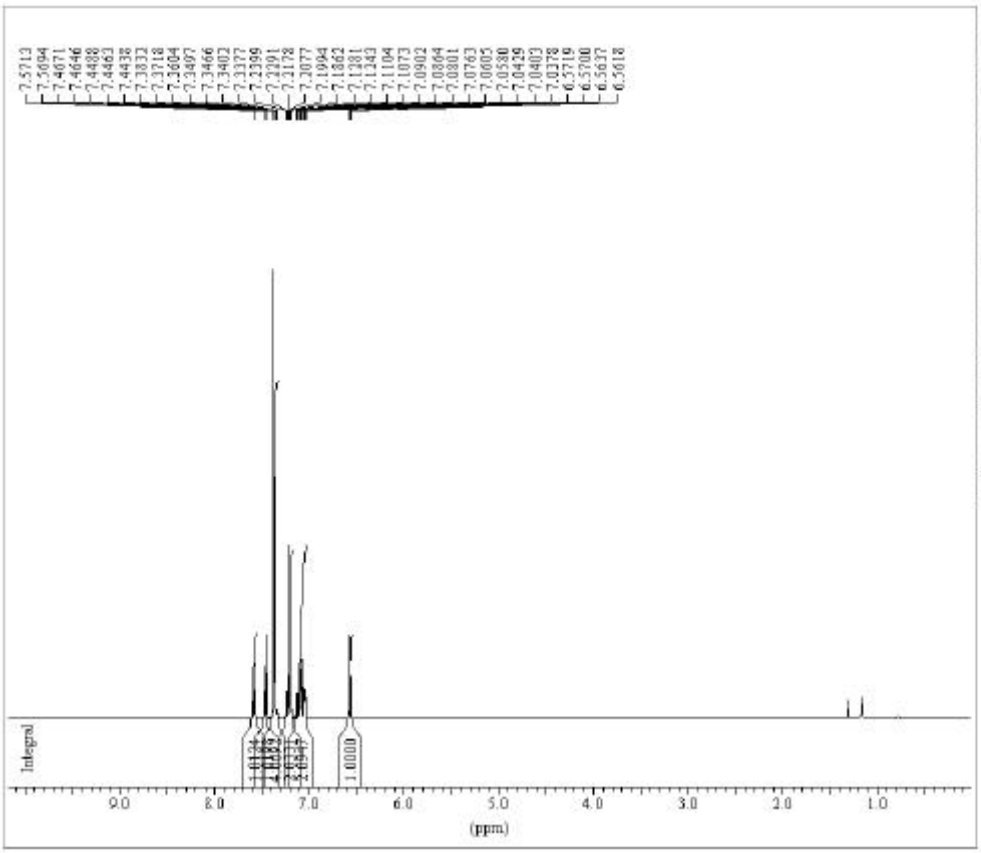



```
*** Current Data Parameters ***
NAME            mol 7--1
EXPNO                 10
PROCNO                 1
*** Acquisition Parameters ***
NS                    16
D1              2470.97 Hz
D2              2470.97 Hz
SFO1          400.1324710 MHz
SOLVENT             CDCl3
SW              20.6885 ppm
TE              294.9 K
*** Processing Parameters ***
GB              0.0000000
LB                 0.30 Hz
SF          400.1300699 MHz
SI                 32768
TI
*** 1D NMR Plot Parameters ***
SR                 69.89 Hz
Hz_cm             194.46
```



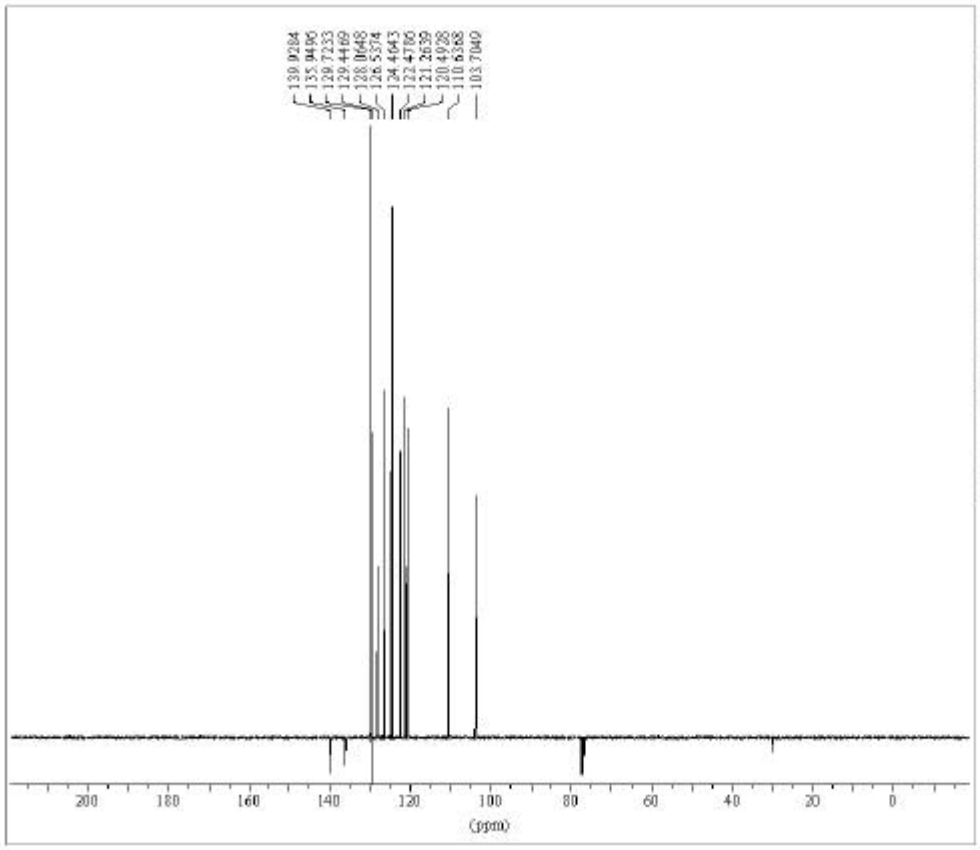

```
*** Current Data Parameters ***
NAME            mol 7--1
EXPNO                 11
PROCNO                 1
*** Acquisition Parameters ***
NS                   256
D1             10060.80 Hz
D2              1600.32 Hz
SFO1          100.6238298 MHz
SOLVENT             CDCl3
SW              238.3238 ppm
TE              295.4 K
*** Processing Parameters ***
GB              0.0000000
LB                 1.00 Hz
SF          100.6127690 MHz
SI                 32768
TI
*** 1D NMR Plot Parameters ***
SR                 0.00 Hz
Hz_cm            1136.53
```

1-Phenyl-1H-indole



*** Current Data Parameters ***

NAME	:	mar21--1
EXPNO	:	20
PROCNO	:	1
*** Acquisition Parameters ***		
NS	:	16
D1	:	2470.97 Hz
D2	:	2470.97 Hz
SFO1	:	400.1324710 MHz
SOLVENT	:	CDCl3
SW	:	20.6885 ppm
TE	:	295.2 K
*** Processing Parameters ***		
SB	:	0.0000000
LB	:	0.30 Hz
SF	:	400.1300085 MHz
SI	:	32768
TI	:	
*** 1D NMR Plot Parameters ***		
SR	:	98.54 Hz
Hz_cm	:	192.76



*** Current Data Parameters ***

NAME	:	mar22--1
EXPNO	:	20
PROCNO	:	1
*** Acquisition Parameters ***		
NS	:	256
D1	:	10060.80 Hz
D2	:	1600.52 Hz
SFO1	:	100.6228298 MHz
SOLVENT	:	CDCl3
SW	:	238.3238 ppm
TE	:	295.6 K
*** Processing Parameters ***		
SB	:	0.0000000
LB	:	1.00 Hz
SF	:	100.6127690 MHz
SI	:	32768
TI	:	
*** 1D NMR Plot Parameters ***		
SR	:	0.00 Hz
Hz_cm	:	1136.53