A Novel One-pot Method for the Preparation of Pyrazoles by 1,3-Dipolar Cycloadditions of Diazo Compounds Generated *In Situ*

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CONTENTS

1. General Methods

2. Synthesis of 3,5-Disubstituted Pyrazoles

3. Preparation of 3-Substituted Pyrazoles

4. NMR Spectras

5. References

1. General Methods

Flash chromatography was performed on silica gel (Merck Kiesegel 60 F_{254} 230-400 mesh). TLC was carried out on aluminium backed silica plates (0.2 mm, 60 F_{254}) which were developed using standard visualising agents: UV fluorescence (254 and 366 nm), ninhidrin/Δ, phosphomolybdic acid/Δ, anisaldehyde/Δ, permanganate/Δ. Melting points (m.p.) were determined on a Khöfler hot stage. Infrared spectras were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer using an ATR sample accessory unless otherwise specified. Only selected absorbencies ($\bullet_{max}$/cm^{-1}) are reported. Optical rotations were measured using a Perkin-Elmer 241MC polarimeter. $[\alpha]_D^{20}$ values are given in 10^{-1} deg mL mg^{-1}. ^{1}H NMR spectras were recorded at 270, 300 or 400 MHz on Delta GX/270, Eclipse-300 or Delta GX/400 instruments at rt unless otherwise specified. Chemical shifts (δ_H) are quoted in parts per million (ppm) and referenced to TMS. ^{13}C NMR spectras were recorded at 68, 75 or 100 MHz on Delta GX/270, Eclipse-300 or Delta GX/400 instruments at rt unless otherwise specified. Chemical shifts (δ_C) are quoted in parts per million (ppm), referenced to the appropriate residual solvent peak and are assigned as s, d, t, q for C, CH, CH_2 and CH_3. Degenerate peaks were prefixed by the number of carbons. DEPT ^{13}C NMR spectras are reported instead of simple ^{13}C NMR spectras in those cases when quaternary carbons were not recorded in ^{13}C NMR spectras, most probably due to longer relaxation times which is a consequence of the neighboring nitrogen atoms present in highly conjugated systems.[1] Low resolution mass spectras (m/z) were recorded on a Micromass Analytical Autospec spectrometer with only molecular ions (M^+ or $[M+H]^+$), and major peaks being reported with intensities quoted as percentages of the base peak. High-resolution mass spectras were recorded on a Micromass Analytical Autospec spectrometer. Microanalyses were performed using a Carlo Erba EA1108. GC-MS analysis were performed using an Agilent 6890 apparatus equipped with a capillary column HP-5MS (HP190915-433, 5% Phenyl Methyl Siloxane, 30 m × 250 μm × 0.25 μm nominal) under the following conditions: helium 1 mL/min (constant flow mode), injector 250ºC (splitless

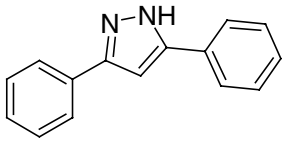
mode), detector EI (agilent MSD 5973), oven 70ºC (3 min), 15ºC/min (15.3 min), 300ºC (8 min). All chemicals were purchased from common chemical suppliers and used as delivered.

2. Synthesis of 3,5-Disubstituted Pyrazoles

Representative Procedure for the Preparation of 3-Phenyl-5-substituted Pyrazoles (table 1)

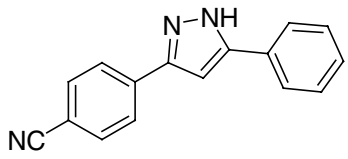
Benzaldehyde was added to a solution of *p*-toluenesulphonylhydrazide (279 mg, 1.5 mmol). After stirring for 3 h at RT, a solution of 5N NaOH (300 •L, 1.5 mmol) was added and the mixture was stirred for a further 20 min. Phenylacetylene (823 •L, 7.5 mmol) was added and the mixture was stirred at 50ºC for 48 h. The volatiles were evaporated under reduced pressure and the residue was dissolved in a 1:1 mixture of water-ethyl acetate (70 mL). The organic layer was separated and dried over $MgSO_4$. After filtration and removal of the solvent under reduced pressure, the crude material was purified by flash chromatography (eluent petroleum ether/ethyl acetate 3:1) to afford 292 (202 mg, 61%) as an off white solid.

3,5-Diphenyl-1H-pyrazole (table 1, entry 1)[2]



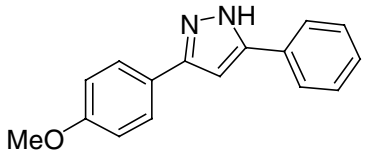
White solid (61% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.35; m.p. 201-203•C (petroleum ether/ethyl acetate) (lit.,[2] 201•C); ^{1}H NMR (270 MHz, $CDCl_3$) • 6.85 (1H, s, Pz H-4), 7.28-7.42 (6H, m, Ph), 7.74 (4H, dd, *J* = 6.6 and 1.6 Hz, Ph); ^{13}C NMR (68 MHz, $CDCl_3$) • 100.1 (d), 125.7 (4d), 128.2 (2d), 128.9 (4d), 134.4 (2s), 148.7; IR •$_{max}$/cm^{-1} 2829, 1460, 1272, 1180, 1074, 974, 974, 750, 685; MS m/z (EI) 220 (M^+, 100), 191 (28), 165 (8), 104 (8), 77 (13).

4-(5-Phenyl-1*H*-3-pyrazolyl)benzonitrile (table 1, entry 2)



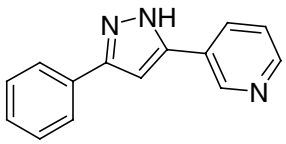
Yellow needles (61% yield); eluent DCM/MeOH 9:1, R_f = 0.45; m.p. 250-252•C (methanol); ^{1}H NMR (300 MHz, 105•C, d_6-DMSO) • 7.18 (1H, s, Pz H-4), 7.34 (1H, t, *J* = 7.3 Hz, H_p-Ph), 7.45 (2H, t, *J* = 7.3 Hz, H_m-Ph), 7.80 (4H, m), 8.01 (2H, d, *J* = 8.3 Hz, H_o-ArCN), 11.98 (1H, br .s, N*H*); ^{13}C NMR (DEPT, 75 MHz, 105•C, d_6-DMSO) • 101.4 (d), 125.9 (2d), 126.4 (2d), 128.6 (d), 129.3 (2d), 133.1 (2d); IR •$_{max}$/cm^{-1} 2862, 2223, 1608, 1456, 1268, 1179, 1058, 974, 838, 755, 678; MS m/z (EI) 245 (M^+, 100), 218 (38), 190 (12), 123 (12), 89 (10), 77 (16), 63 (6); HRMS: found 245.0955, $C_{16}H_{11}N_3$ requires 245.0953. Anal. Calc'd for $C_{16}H_{11}N_3$: C, 78.35; H, 4.52; N, 17.13. Found: C, 78.20; H, 4.18; N, 17.10.

3-(4-Methoxyphenyl)-5-phenyl-1*H*-pyrazole (table 1, entry 3)[3]



Colourless cubic solid (51% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.20; m.p. 160-162•C (methanol) (lit.,[3] 166-168•C); ^{1}H NMR (400 MHz, $CDCl_3$) • 3.84 (3H, s, CH_3), 6.76 (1H, s, Pz H-4), 6.94 (2H, d, *J* = 8.8 Hz, $ArOCH_3$), 7.34 (1H, tt, *J* = 7.1 and 2.9 Hz, *p*-Ph), 7.42 (1H, tt, *J* = 7.5 and 2.8 Hz, *m*-Ph), 7.66 (2H, d, *J* = 8.8 Hz, $ArOCH_3$), 7.73 (2H, dt, *J* = 7.5 and 2.8 Hz, *o*-Ph); ^{13}C NMR (100 MHz, $CDCl_3$) • 55.4 (q), 99.5 (d), 114.3 (2d), 123.8 (s), 125.6 (2d), 126.9 (2d), 128.0 (d), 128.7 (2d), 131.4 (s), 148.3 (s), 148.9 (s), 159.7 (s); IR •$_{max}$/cm^{-1} 2833, 1613, 1508, 1458, 1251, 1174, 1028, 974, 831, 760, 688; GC-MS retention time 18.14 min., m/z (EI) 250 (M^+, 100), 235 (43), 207 (32), 178 (50), 152 (21), 77 (21).

3-(5-Phenyl-1*H*-3-pyrazolyl)pyridine (table 1, entry 4)[4]



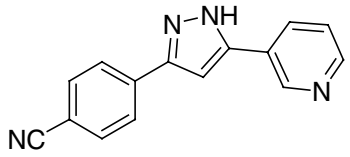
White solid (33% yield); eluent petroleum ether/ethyl acetate 1:3, R_f = 0.25; m.p. 187-189•C (methanol) (lit.,[4] 187-188•C ethanol); ^{1}H NMR (270 MHz, $CDCl_3$) • 6.76 (1H, s, Pz H-4), 7.18-7.34 (4H, m), 7.57 (2H, dt, *J* = 7.0 and 1.6 Hz, H_o-Ph), 8.01 (1H, dt, *J* = 8.0 and 1.9 Hz, H-4 Py), 8.34 (1H,

d, J = 3.9 Hz, H-6 Py), 8.82 (1H, d, J = 1.9 Hz, H-1 Py); ^{13}C NMR (DEPT, 68 MHz, $CDCl_3$) • 100.2 (d), 124.0 (d), 125.5 (2d), 128.4 (d), 128.8 (2d), 133.5 (d), 146.3 (d), 148.0 (d); IR •$_{max}$/cm^{-1} 3114, 2827, 1572, 1435, 960, 799, 759, 681, 662; GC-MS retention time 17.09 min., m/z (EI) 221 (M^+, 100), 192 (23), 207 (32), 178 (50), 152 (21), 77 (21).

Representative Procedure for the Preparation of 3-(3-Pyridinyl)-5-substituted-Pyrazoles (table 1)

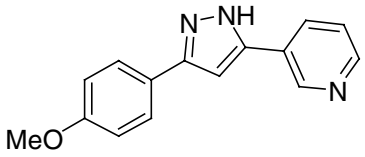
Benzaldehyde was added to a solution of *p*-toluenesulphonylhydrazide (279 mg, 1.5 mmol). After stirring for 3 h at RT, a solution of 5N NaOH (300 •L, 1.5 mmol) was added and the mixture was stirred for a further 20 min. 3-Ethynylpyridine (773 mg, 7.5 mmol) was added and the mixture was stirred at 50ºC for 48 h. The solvent was evaporated under reduced pressure and the residue was dissolved in a 1:1 mixture of water-ethyl acetate (70 mL). The organic layer was separated and dried over $MgSO_4$. After filtration and removal of the solvent under reduced pressure, the crude material was purified by flash chromatography (eluent petroleum ether/ethyl acetate 1:3) to afford 295 (120 mg, 36%) as an off white solid.

4-[5-(3-Pyridyl)-1*H*-3-pyrazolyl]benzonitrile (table 1, entry 6)



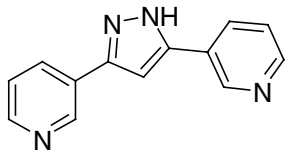
White solid (19% yield); eluent DCM/MeOH 9:1, R_f = 0.5; m.p. 250-252•C (DCM/MeOH); ^{1}H NMR (300 MHz, 60•C, d_6-DMSO) • 7.36 (1H, s, Pz H-4), 7.46 (1H, dd, J = 7.9 and 4.8 Hz, H-5 Py), 7.86 (2H, d, J = 8.2, H_m-ArCN), 8.00 (2H, d, J = 8.2 Hz, H_o-ArCN), 8.15 (1H, d, J = 7.9 Hz, H-4 Py), 8.54 (1H, dd, J = 4.8 and 1.3 Hz, H-6 Py), 9.05 (1H, d, J = 1.3 Hz, H-1 Py), 12.29 (1H, br .s, N*H*); ^{13}C NMR (DEPT, 75 MHz, 60•C, d_6-DMSO) • 102.1 (d), 124.3 (d), 126.5 (2d), 133.0 (2d), 133.2 (d), 147.2 (d), 149.5 (d); IR •$_{max}$/cm^{-1} 2853, 2223, 1739, 1612, 1570, 1504, 1458, 1411, 1380, 963, 840, 799, 705; MS m/z (EI) 246 (M^+, 100), 217 (16), 190 (12), 164 (10); HRMS: found 246.0904, $C_{15}H_{10}N_4$ requires 246.0905. Anal. Calc'd for $C_{15}H_{10}N_4$: C, 73.16; H, 4.09; N, 22.75. Found: C, 73.01; H, 3.70; N, 22.51.

3-[3-(4-Methoxyphenyl)-1*H*-5-pyrazolyl]pyridine (table 1, entry 7)



White solid (54% yield); eluent DCM/MeOH 9:1, R_f = 0.28; m.p. 203-205•C (methanol); ^{1}H NMR (300 MHz, 110•C, d_6-DMSO) • 3.77 (3H, s, OC*H*$_3$), 6.99 (2H, d, *J* = 8.6 Hz, H$_o$-ArOCH$_3$), 7.01 (1H, s, Pz H-4), 7.37 (1H, dd, *J* = 7.7 and 4.8 Hz, H-5 Py), 7.72 (2H, d, *J* = 8.2, H$_m$-ArOCH$_3$), 8.12 (1H, dt, *J* = 7.9 and 1.9 Hz, H-4 Py), 8.50 (1H, dd, *J* = 4.8 and 1.3 Hz, H-6 Py), 9.03 (1H, d, *J* = 1.3 Hz, H-1 Py), 11.74 (1H, br .s, N*H*); ^{13}C NMR (DEPT, 75 MHz, 105•C, d_6-DMSO) • 55.8 (q), 99.9 (d), 115.0 (d), 124.1 (d), 127.3 (2d), 132.9 (2d), 147.1 (d), 149.0 (d); IR •$_{max}$/cm^{-1} 3129, 3029, 2835, 1619, 1514, 1504, 1432, 1303, 1256, 1184, 1169, 1074, 1025, 973, 839, 795, 697; GC-MS retention time 18.26 min., m/z (EI) 251 (M$^+$, 100), 236 (35), 208 (22), 152 (20); HRMS: found 251.1059, $C_{15}H_{13}N_3O_2$ requires 251.1059. Anal. Calc'd for $C_{15}H_{13}N_3O_2$: C, 71.70; H, 5.21; N, 16.72. Found: C, 71.30; H, 5.19; N, 16.76.

3-[5-(3-Pyridyl)-1*H*-3-pyrazolyl]pyridine (table 1, entry 8)[5]



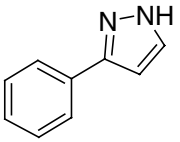
White solid (24% yield); eluent DCM/MeOH 19:1, R_f = 0.30; m.p. 223-225•C (DCM/MeOH) (lit.,[5] 230.5-232•C isopropanol); ^{1}H NMR (400 MHz, $CDCl_3$) • 6.95 (1H, s, Pz H-4), 7.38 (2H, dd, *J* = 7.7 and 4.8 Hz, H-5 Py), 8.12 (2H, d, *J* = 7.7 Hz, H-4 Py), 8.46 (2H, m, H-6 Py), 8.90 (2H, m, H-1 Py); ^{13}C NMR (DEPT, 100 MHz, $CDCl_3$) • 100.8 (d), 124.1 (2d), 133.6 (2d), 146.2 (2d), 148.4 (2d); IR •$_{max}$/cm^{-1} 3113, 2820, 1414, 1025, 960, 798, 704, 693; GC-MS retention time 17.80 min., m/z (EI) 222 (M$^+$, 100), 193 (13), 166 (11), 140 (15), 118 (15), 78 (20), 63 (26), 51 (28).

3. Preparation of 3-Substituted Pyrazoles

Representative Procedure for the Preparation of 3-Substituted Pyrazoles (table 2)

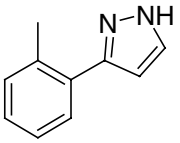
Benzaldehyde was added to a solution of *p*-toluenesulphonylhydrazide (279 mg, 1.5 mmol). After stirring for 3 h at RT, a solution 5N NaOH (300 •L, 1.5 mmol) was added and the mixture was stirred for a further 20 min. 1-Vinylimidazole (679 •L, 7.5 mmol) was added and the mixture was stirred at 50ºC for 48 h. The volatiles were evaporated under reduced pressure and the residue was dissolved in a 1:1 mixture of water-ethyl acetate (70 mL). The organic layer was separated and dried over $MgSO_4$. After filtration and removal of the solvent under reduced pressure, the crude material was purified by flash chromatography (eluent petroleum ether/ethyl acetate 3:1) to afford 3-(Phenyl)-1*H*-pyrazole (121 mg, 56%) as a white solid.

3-(Phenyl)-1*H*-pyrazole (table 2, entry 1)[6]



White solid (56% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.40; m.p. 102-104•C (petroleum ether/ethyl acetate) (lit.,[6] 99•C); ^{1}H NMR (400 MHz, $CDCl_3$) • 6.63 (1H, d, *J* = 2.2 Hz, Pz H-4), 7.34 (1H, tt, *J* = 7.4 and 2.6 Hz, *p*-Ph), 7.42 (1H, tt, *J* = 8.8 and 2.0 Hz, *m*-Ph), 7.63 (1H, d, *J* = 2.2 Hz, Pz H-5), 7.75 (1H, d, *J* = 8.8 Hz, *o*-Ph), 10.24 (1H, br. s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 102.7 (d), 125.9 (2d), 128.1 (d), 128.8 (2d), 132.2 (s), 133.4 (d), 149.8 (s); IR •$_{max}$/cm^{-1} 3160, 2917, 1455, 1353, 1071, 1047, 952, 917, 825, 749, 693; GC-MS retention time 11.35 min., m/z (EI) 144 (M^+, 100), 115 (42), 89 (22), 77 (22), 63 (14), 51 (14).

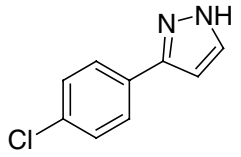
3-(2-Methylphenyl)-1*H*-pyrazole (table 2, entry 2)



Off white solid (47% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.2; m.p. 46-48•C (petroleum ether/ethyl acetate); ^{1}H NMR (270 MHz, $CDCl_3$) • 2.41 (3H, s, CH_3), 6.39 (1H, d, *J* = 2.3 Hz, Pz H-4), 7.16-7.29 (3H, m, Ar), 7.46 (1H, d, *J* = 7.2 Hz, *o*-Ar), 7.49 (1H, d, *J* = 2.3 Hz, Pz H-5), 11.23 (1H, br. s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 20.9 (q), 105.5 (d), 126.0 (d), 128.3 (d), 129.3 (d),

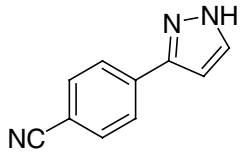
130.9 (d), 131.6 (s), 134.2 (d), 136.2 (s), 147.2 (s); IR •$_{max}$/cm^{-1} 3163, 2921, 1449, 1038, 953, 932, 752, 722; GC-MS retention time 11.72 min., m/z (EI) 158 (M$^+$, 100), 130 (88), 103 (15), 77 (15), 63 (13), 51 (12); HRMS: found 158.0841, $C_{10}H_{10}N_2$ requires 158.0844. Anal. Calc'd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.99; H, 6.25; N, 18.08.

3-(4-Chlorophenyl)-1*H*-pyrazole (table 2, entry 5)[6]



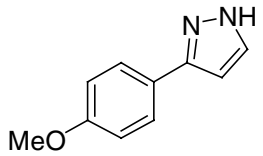
White solid (71% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.2; m.p. 184-186•C (petroleum ether/ethyl acetate) (lit.,[7] 195-197•C); ^{1}H NMR (270 MHz, $CDCl_3$) • 6.55 (1H, d, *J* = 2.0 Hz, Pz H-4), 7.31 (2H, d, *J* = 8.8 Hz, *o*-Ar), 7.55 (1H, d, *J* = 2.0 Hz, Pz H-5), 7.64 (2H, d, *J* = 8.8 Hz, *m*-Ar), 11.81 (1H, br. s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 102.8 (d), 127.2 (2d), 129.0 (2d), 130.9 (d), 132.7 (s), 133.9 (s), 148.8 (s); IR •$_{max}$/cm^{-1} 3162, 2919, 1510, 1447, 1090, 1047, 1012, 953, 832, 757, 734; GC-MS retention time 13.05 min., m/z (EI) 178 (M$^+$, 100), 151 (13), 115 (34), 89 (17), 75 (15), 63 (13).

4-(1*H*-3-Pyrazolyl)benzonitrile (table 2, entry 4)



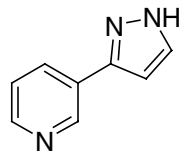
White solid (79% yield); eluent petroleum ether/ethyl acetate 2:1, R_f = 0.25; m.p. 141-143•C (methanol); ^{1}H NMR (400 MHz, $CDCl_3$) • 6.71 (1H, d, *J* = 2.3 Hz, Pz H-4), 7.65 (1H, d, *J* = 2.3 Hz, Pz H-5), 7.68 (2H, d, *J* = 8.6 Hz, *o*-Ar), 7.90 (2H, d, *J* = 8.6 Hz, *m*-Ar), 8.90 (1H, br .s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 103.6 (d), 111.3 (s), 119.0 (s), 126.2 (2d), 131.3 (d), 132.7 (2d), 137.3 (s), 149.2 (s); IR •$_{max}$/cm^{-1} 3281, 2222, 1608, 1174, 1044, 947, 843, 774; GC-MS retention time 14.26 min., m/z (EI) 169 (M$^+$, 100), 140 (19), 115 (14), 89 (10), 75 (11), 63 (10), 51 (8); HRMS: found 169.0644, $C_{10}H_7N_3$ requires 169.0639.

3-(4-Methoxyphenyl)-1*H*-pyrazole (table 2, entry 3)[8]



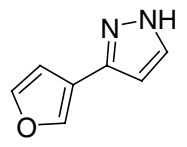
White solid (62% yield); eluent petroleum ether/ethyl acetate 2:1, R_f = 0.40; m.p. 128-130•C (methanol) (lit.,[8] 129-131•C); ^{1}H NMR (270 MHz, $CDCl_3$) • 3.82 (3H, s, OCH_3), 6.52 (1H, d, *J* = 1.9 Hz, Pz H-4), 6.92 (2H, d, *J* = 8.8 Hz, *o*-Ph), 7.58 (1H, d, *J* = 1.9 Hz, Pz H-5), 7.66 (2H, d, *J* = 8.8 Hz, *m*-Ph), 9.40 (1H, br .s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 55.4 (q), 102.1 (d), 114.3 (2d), 124.8 (s), 127.2 (2d), 133.7 (d), 148.5 (s), 159.6 (s); IR •$_{max}$/cm^{-1} 3113, 2838, 1610, 1508, 1453, 1438, 1248, 1180, 1096, 1026, 831, 772; GC-MS retention time 13.41 min., m/z (EI) 174 (M^+, 100), 159 (64), 131 (61), 102 (12), 77 (26), 63 (10), 51 (11).

3-(1*H*-3-Pyrazolyl)pyridine (table 2, entry 8)[9]



White gum (32% yield); eluent ethyl acetate, R_f = 0.28; ^{1}H NMR (270 MHz, $CDCl_3$) • 6.68 (1H, d, *J* = 1.2 Hz, Pz H-4), 7.33 (1H, dd, *J* = 7.6 and 5.3 Hz, Py H-5), 7.64 (1H, d, *J* = 1.2 Hz, Pz H-5), 8.09 (1H, d, *J* = 7.6 Hz, Py H-4), 8.56 (1H, d, *J* = 5.3 Hz, Py H-6), 9.06 (1H, s, Py H-2); ^{13}C NMR (68 MHz, $CDCl_3$) • 102.9 (d), 123.8 (d), 129.0 (s), 131.8 (d), 133.3 (d), 147.1 (d), 147.5 (s), 148.7 (d); IR •$_{max}$/cm^{-1} 3138, 2907, 1418, 1028, 924, 758, 703; GC-MS retention time 12.38 min., m/z (EI) 145 (M^+, 100), 118 (10), 91 (8), 63 (15).

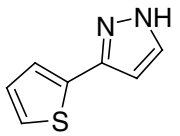
3-(3-Furyl)-1*H*-pyrazole (table 2, entry 6)



Orange solid (33% yield); eluent petroleum ether/ethyl acetate 2:1, R_f = 0.25; m.p. 93-95•C (petroleum ether/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) • 6.40 (1H, d, *J* = 2.2 Hz, Pz H-4), 6.70

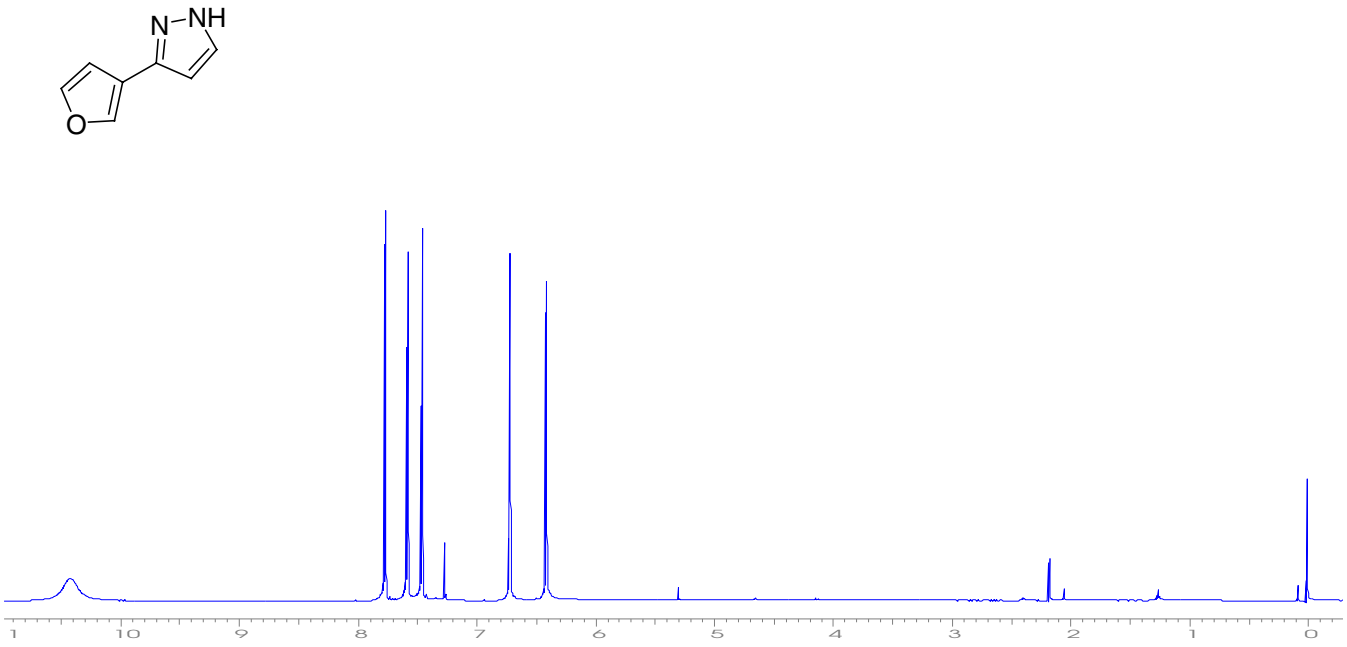
(1H, m, Fur H-4), 7.45 (1H, t, *J* = 1.6 Hz, Fur H-5), 7.57 (1H, d, *J* = 2.2 Hz, Pz H-5), 7.76 (1H, m, Fur H-2), 10.41 (1H, br .s, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$) • 102.9 (d), 109.2 (d), 118.6 (s), 132.7 (d), 139.3 (d), 142.2 (s), 143.6 (d); IR •$_{max}$/cm^{-1} 3139, 1614, 1520, 1348, 1192, 1153, 1047, 985, 895, 872, 796, 757; GC-MS retention time 9.80 min., m/z (EI) 134 (M^+, 100), 105 (34), 79 (17), 51 (31); HRMS: found 134.0482, $C_7H_6N_2O$ requires 134.0480.

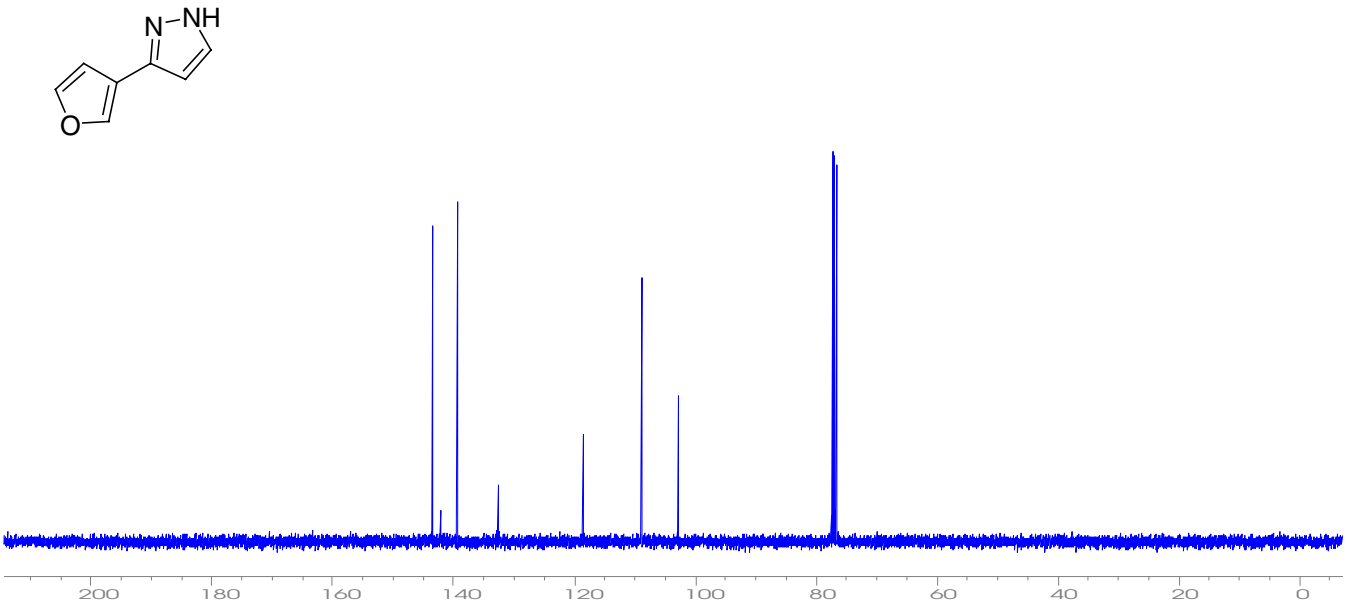
3-(2-Thienyl)-1*H*-pyrazole (table 2, entry 7)[10]

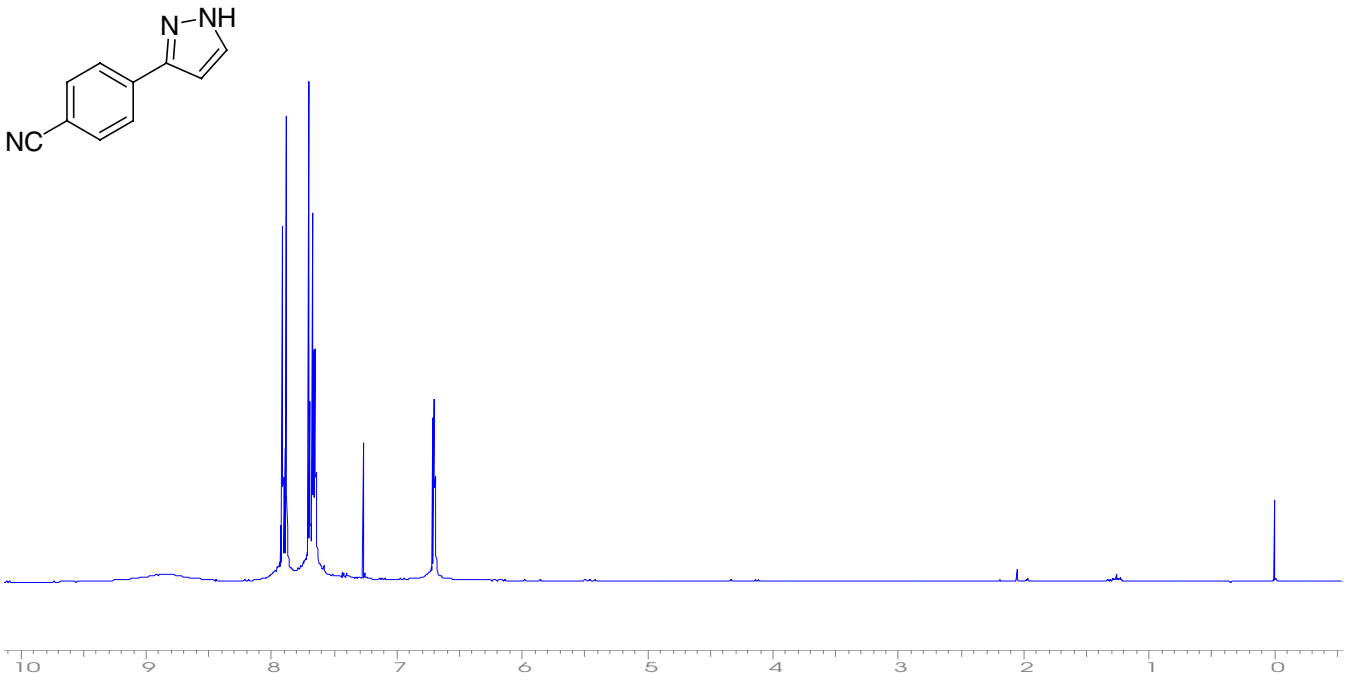


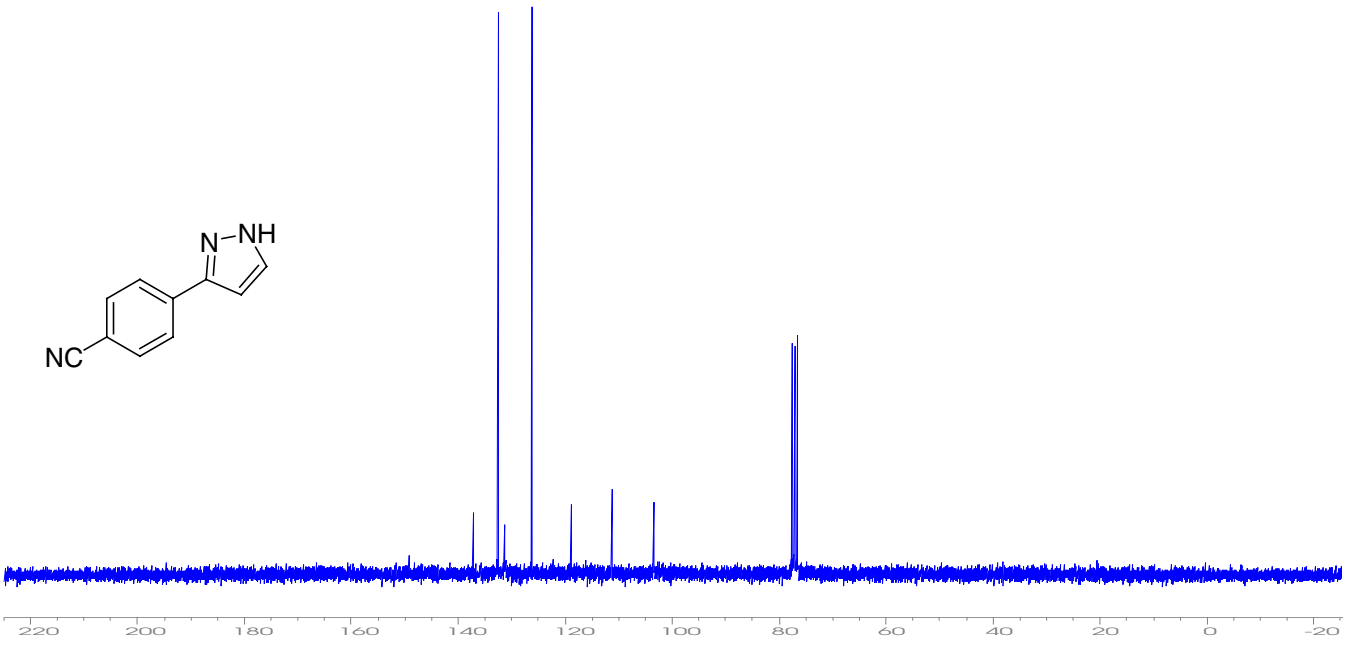
Off white solid (32% yield); eluent petroleum ether/ethyl acetate 3:1, R_f = 0.17; m.p. 90-92•C (petroleum ether/ethyl acetate) (lit.,[10] 96.5-98 •C); ^{1}H NMR (270 MHz, $CDCl_3$) • 6.52 (1H, d, *J* = 2.3 Hz, Pz H-4), 7.05 (1H, dd, *J* = 5.0 and 3.7 Hz, Th H-4), 7.25 (1H, dd, *J* = 5.0 and 1.0 Hz, Th H-5), 7.33 (1H, dd, *J* = 3.7 and 1.0 Hz, Th H-3), 10.76 (1H, br .s, N*H*); ^{13}C NMR (68 MHz, $CDCl_3$) • 102.7 (d), 124.2 (d), 124.7 (d), 127.7 (d), 131.5 (d), 135.9 (s), 145.7 (s); IR •$_{max}$/cm^{-1} 3161, 2918, 1563, 1473, 1408, 1048, 909, 845, 690; GC-MS retention time 11.59 min., m/z (EI) 150 (M^+, 100), 121 (28), 96 (16), 78 (12).

4. NMR Spectras


N–NH
O
1
10
9
8
7
6
5
4
3
2
1
0


N–NH
O
200
180
160
140
120
100
80
60
40
20
0





5. References

(1) Silverstein, R. M. *Spectrometric Identification of Organic Compounds*; 6th ed.; Wiley: New York, 1998.

(2) Simon, D.; Lafont, O.; Farnoux, C. C.; Miocque, M. *J. Heterocycl. Chem.* **1985**, *22*, 1551-1557.

(3) Beam, C. F.; Foote, R. S.; Hauser, C. R. *J. Chem. Soc.* **1971**, 1658-1660.

(4) Musante, B. *Gazz. chim. ital.* **1949**, *79*, 683-688.

(5) Ferles, M.; Liboska, R.; Trška, P. *Collect. Czech. Chem. Commun.* **1990**, *55*, 1228-1233.

(6) Singh, G.; IIa, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1945-1950.

(7) Reddy, D. B.; Sarma, M. R.; Reddy, A. S.; Reddy, N. S. *Indian J. Chem., Sect. B* **2000**, *39*, 901-903.

(8) Grimmett, M. R.; Lim, K. H. R.; Weavers, R. T. *Aust. J. Chem.* **1979**, *32*, 2203-2213.

(9) Plate, R.; Plaum, M. J. M.; Boer, T. B.; Andrews, J. S.; Rae, D. R.; Gibson, S. *Bioorg. Med. Chem. Lett.* **1996**, *4*, 227-237.

(10) Tsuchiya, T.; Enkaku, M.; Sawanishi, H. *Chem. Pharm. Bull.* **1979**, *27*, 2188-2193.