$Zn(OAc)_2•2H_2O$-Catalyzed Efficient Synthesis of 5-Substituted 1*H*-Tetrazoles

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Experimental

1. Materials & Methods

All of the compounds were obtained from commercial sources and utilized without undergoing any further purification processes. Before being used, the solvents for chromatography go through the distillation process. In DMSO-*d6*, ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded using Bruker UXNMR FT-400 MHz (Avance) devices. The tetramethylsilane (δ 0.0) internal standard serves as the reference point against which chemical shifts are compared and represented as parts per million. At a temperature of 200 ^0C and an energy of 70 eV, EI-MS were obtained using a VG 7070H Micromass mass spectrometer. For the purpose of recording melting points, an electrothermal melting point equipment has been utilized. The IR spectra were obtained by employing KBr pellets and a Perkin Elmer 240-C instrument in the collection process. The analytical TLC for all reactions was performed on plates that had been pre-coated by Merck (silica gel 60F-254 on glass). In order to perform column chromatography, acme silica gel was utilized (100-200 mesh)

2. Typical protocol for the preparation of 5-substituted 1H-tetrazoles

The following ingredients were added to toluene in a 25 ml round-bottomed flask: aldehyde (1 mmol), hydroxylamine hydrochloride (1.2 mmol), sodium azide (1 mmol), and $Zn(OAc)_2•2H_2O$ (10 mol%). The mixture was allowed to reflux while being vigorously stirred (Table 3). After the reaction was complete, the reaction mixture was cooled to room temperature, as demonstrated by TLC. The reaction mixture was diluted with 5 mL of water. Using 2x5 mL of ethyl acetate, the product was extracted. Drying the organic layer with

anhydrous $MgSO_4$ was accomplished. After the organic layer was concentrated under vacuum, the product was refined either by recrystallizing in hot ethanol or by column chromatography on silica gel (60-120 Mesh, 20% EtOAc/petroleum ether mixture). The spectral data of the corresponding tetrazoles was in agreement with the literature data.[28-35]

3. Spectral data

5-Phenyl-1*H*-tetrazole (Table 3, entry 1): White solid; mp 215-217 ^{0}C; IR (KBr): 3449 (NH), 3061 (=C-H), 1642, 1562 (C=N), 1474, 1164 (C-N) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-*d6*): δ= 8.06-8.03 (m, 2 H), 7.62-7.58 (m, 3 H); ^{13}C NMR (75 MHz, DMSO-*d6*): δ 124.0 (C6), 126.8 (C1,C5), 129.3 (C2,C4), 131.1 (C3), 155.3 (C7) ppm; MS (EI): *m/z* (%) = 146 (12.78) [M$^+$].

5-*p*-Tolyl-1*H*-tetrazole (Table 3, entry 2) White solid; mp 250-251 ^{0}C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ=2.39 (s, 3H), 7.41 (d, *J*=8.0 Hz, 2H), 7.93 (d, *J*=8.0 Hz, 2H), 16.64 (brs, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-*d6*): δ=21.50, 121.98, 127.31, 130.40, 141.54, 155.74 ppm

5-(4-Methoxyphenyl)-1*H*-Tetrazole (Table 3, Entry 3) White solid; m.p. 231-233 ºC; 1H NMR (400 MHz; DMSO-*d6*) δ: 3.74 (s, 3H), 7.10 (d, *J*= 8.4 Hz, 2H), 7.93 (d, *J*= 8.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 55.3 (C12), 114.7 (C2,C4), 116.1 (C6), 128.5 (C1,C5), 155.1 (C7), 161.3 (C3) ppm

5-(4-Bromophenyl)-1*H*-Tetrazole (Table 3, Entry 4) White solid; m.p. 263-265 ºC; FT-IR (KBr, Cm^{-1}): 503, 746, 831, 1019, 1055, 1077, 1156, 1407, 1432, 1482, 1563, 1606, 1653, 2633, 2732, 2761, 2845, 2903, 2998, 3063, 3091; ^{1}H NMR (400 MHz; DMSO-*d6*) δ: 4.15 (brs, 1H), 7.70 (d, *J*= 8.5 Hz, 2H), 7.89 (d, *J*= 8.5 Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 123.3 (C3), 124.6 (C6), 128.7 (C1,C5), 132.2 (C2,C4), 154.9 (C7) ppm

5-(2-Nitrophenyl)-1*H*-tetrazole (Table 3, Entry 5): White solid; M.p. 162-164 °C; ^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.08 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.95 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.87 (td, *J* = 7.6, 1.1 Hz, 1H), 7.79 (td, *J* = 8.0, 1.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 154.87, 148.79, 133.58, 131.80, 131.53, 124.84, 121.11 ppm

5-(4-Nitrophenyl)-*1H*-tetrazole (Table 3, Entry 6): Yellow solid; m.p. 218-220 ºC; FT-IR (KBr, cm^{-1}): 710, 730, 854, 867, 996, 1105, 1143, 1316, 1340, 1358, 1489, 1534, 1563, 2659, 2820, 2901, 2976, 3081, 3109, 3236, 3441; ^{1}H NMR (400 MHz, DMSO-*d6*) δ: 8.31 (d, *J*= 5.2 Hz, 2H), 8.46 (d, *J*= 5.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 125.1, 128.6, 131.0, 149.2, 155.9 ppm

5-(4-Chlorophenyl)-*1H*-Tetrazole (Table 3, Entry 7): White solid; m.p. 259-260 ºC; FT-IR (KBr, cm^{-1}): 507, 743, 831, 988, 1019, 1051, 1095, 1158, 1436, 1485, 1562, 1611, 1670, 2536, 2621, 2723, 2855, 2908, 2981, 3009, 3062, 3084; ^{1}H NMR (400 MHz, DMSO-*d6*) δ: 7.53 (d, *J*= 8.5 Hz, 2H), 7.74 (d, *J*= 8.5 Hz, 2H) ppm; ^{13}C NMR (100 MHz, DMSO-*d6*) δ: 123.7 (C6), 124.3 (C1,C5), 131.4 (C2,C4), 145.7 (C3), 147.8 (C7) ppm

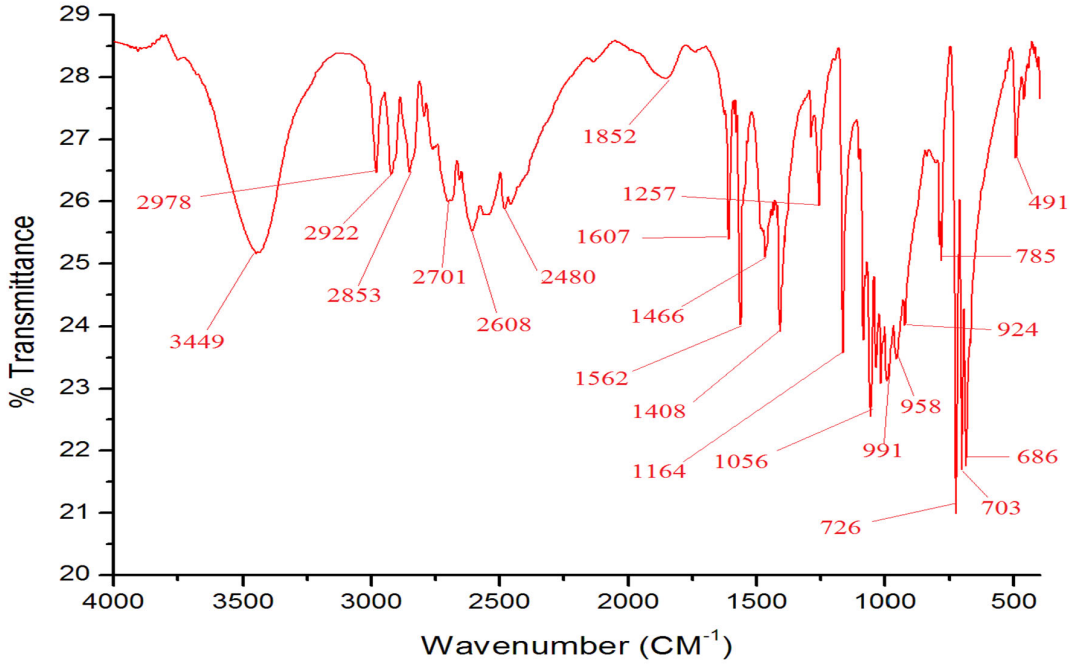
5-(4-Hydroxyphenyl)-*1H*-tetrazole (Table 3, Entry 8): White solid; mp: 234-235 °C; FT-IR (KBr, cm^{-1}): 514, 753, 832, 1281, 1412, 1467, 1512, 1598, 1615, 3019, 3067, 3102, 3253, 3438; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 6.96 (2H, d, *J* = 8.5 Hz), 7.85 (2H, d, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 114.3, 116.1, 128.5, 154.1, 159.9 ppm

5-(Naphthalen-1-yl)-*1H*-tetrazole (Table 3, Entry 9): White solid; mp: 262-263 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.63-7.70 (3H, m), 7.99 (1H, dd, *J* = 7.2 Hz, *J* = 1.0 Hz), 8.08-8.11 (1H, m), 8.19 (1H, bd, *J* = 8.2 Hz), 8.56 (1H, dd, *J* = 7.3 Hz, *J* = 1.8 Hz); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 121.4, 125.0, 125.3, 126.7, 127.7, 128.4, 128.6, 129.9, 131.4, 133.4, 155.1.

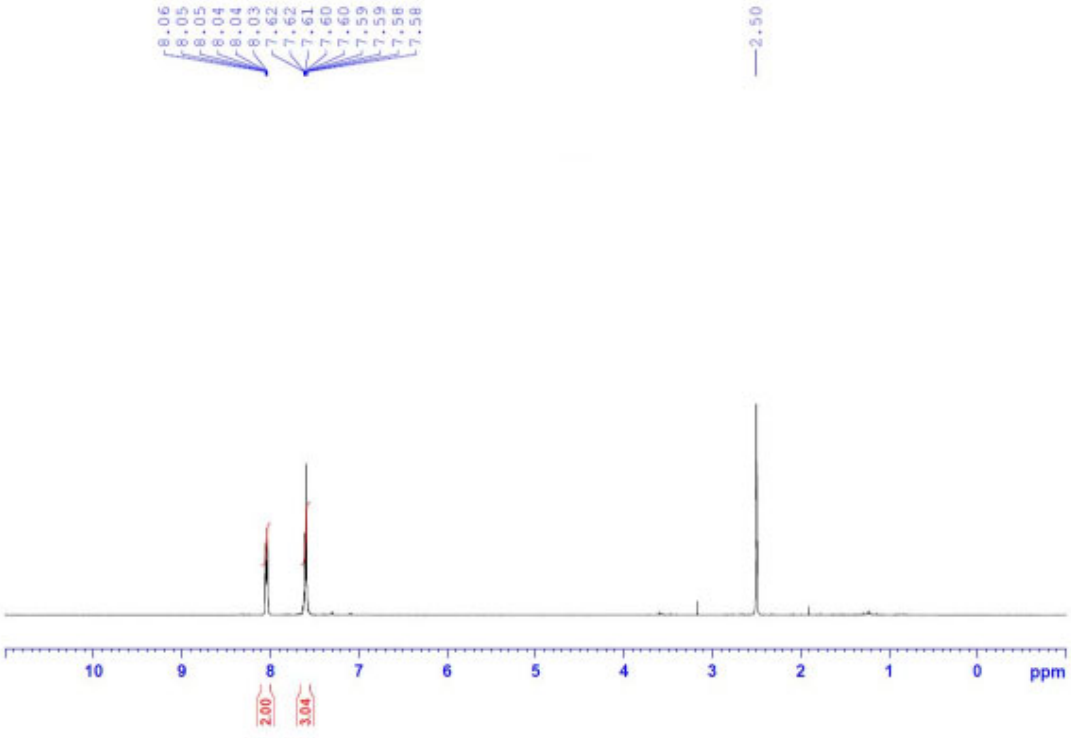
5-(2-Pyridyl)-*1H*-tetrazole (Table 3, Entry 10): White solid; mp: 210-211 °C; ^{1}H NMR (400 MHz, DMSO-*d6*): δ 7.41 (1H, m), 7.78 (1H, m), 8.02 (1H, d, *J* = 8.0 Hz), 8.50 (1H, d, *J* = 3.2 Hz); ^{13}C NMR (100 MHz, DMSO-*d6)* δ 123.0, 126.5,138.6, 144.1, 150.5, 155.2.

5-(Furan-2-yl)-1H-tetrazole (Table 3, Entry 11): White solid; mp 208–209 °; IR (KBr): 3430, 3083, 1649, 1545, 1453 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-*d6*): δ = 8.10 (d, *J* = 5.3 Hz, 1 H), 7.31 (d, *J* = 5.3 Hz, 1 H), 6.62 (t, *J* = 5.3 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-*d6*): δ = 150.16, 147.35, 142.64, 114.70, 113.85; MS (EI): m/z (%) = 136 (15.8) [M^{+}]

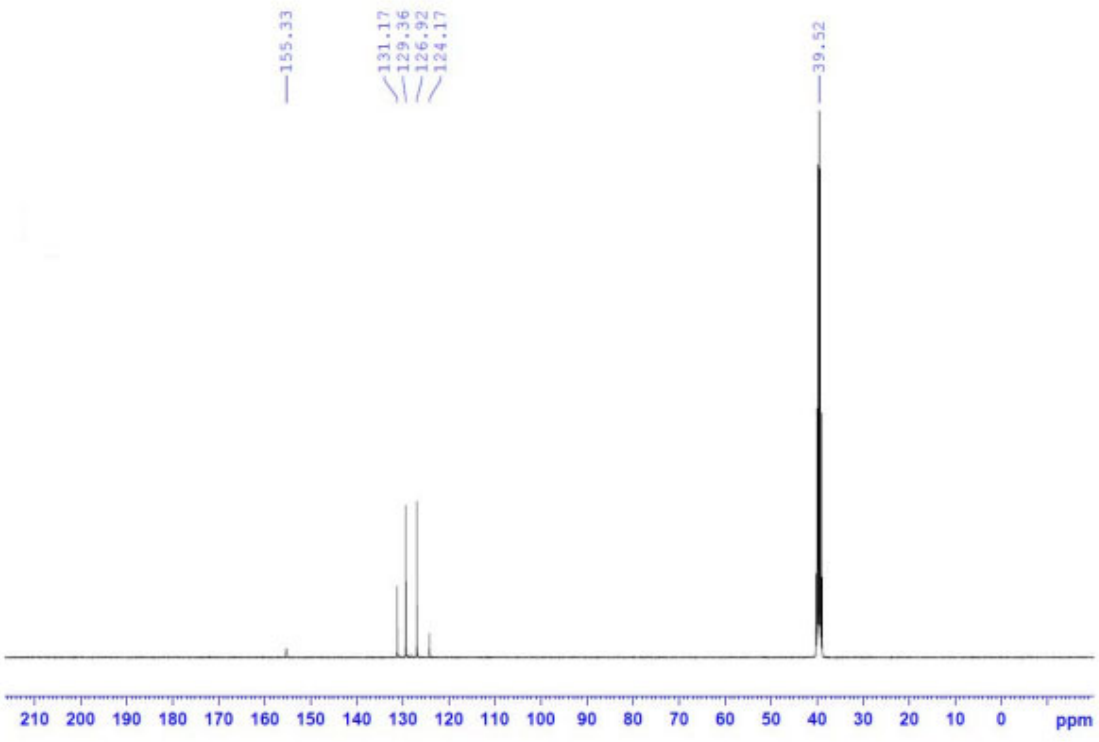
(*E*)-5-Styryl-1*H*-tetrazole (Table 3, Entry 12): White solid; mp 154–155 °C; IR (KBr): 3429, 3045, 1631, 1568, 1468 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.78 (d, *J* = 16.4 Hz, 1H), 7.60-7.55 (m, 2 H), 7.42-7.38 (m, 3 H), 7.20 (d, *J* = 16.4 Hz, 1 H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.24, 136.21, 133.17, 127.62, 127.18, 125.48, 110.05; MS (EI): *m*/*z* (%) = 172 (9.7) [M^{+}]



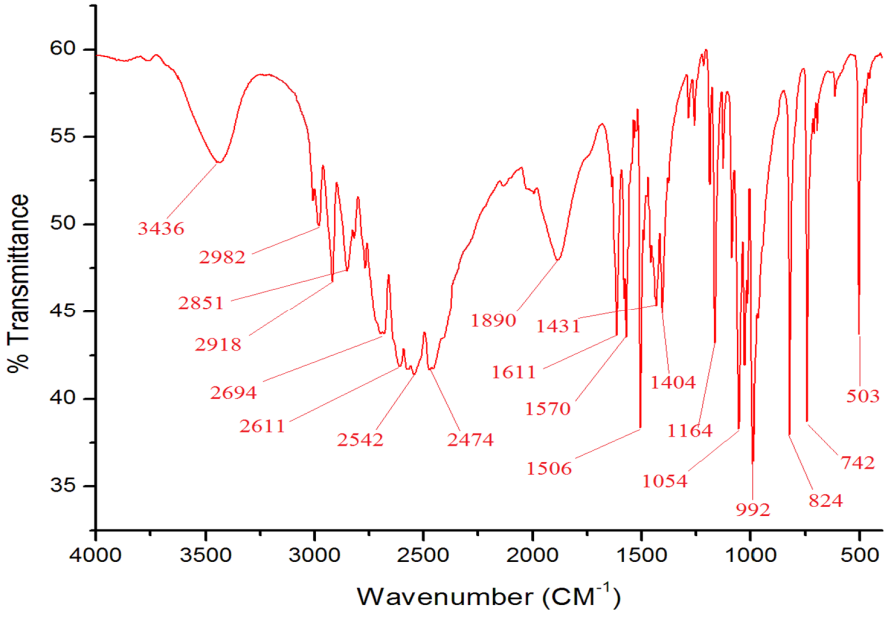
5-Phenyl-1*H*-tetrazole (IR)



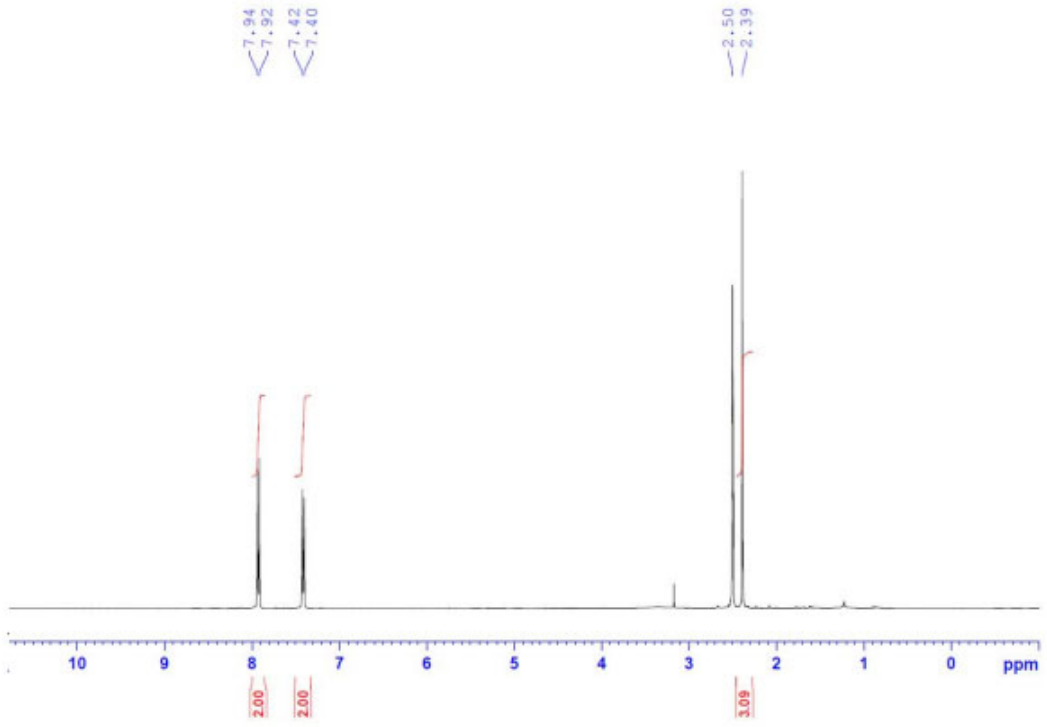
5-Phenyl-1*H*-tetrazole (^{1}H NMR)



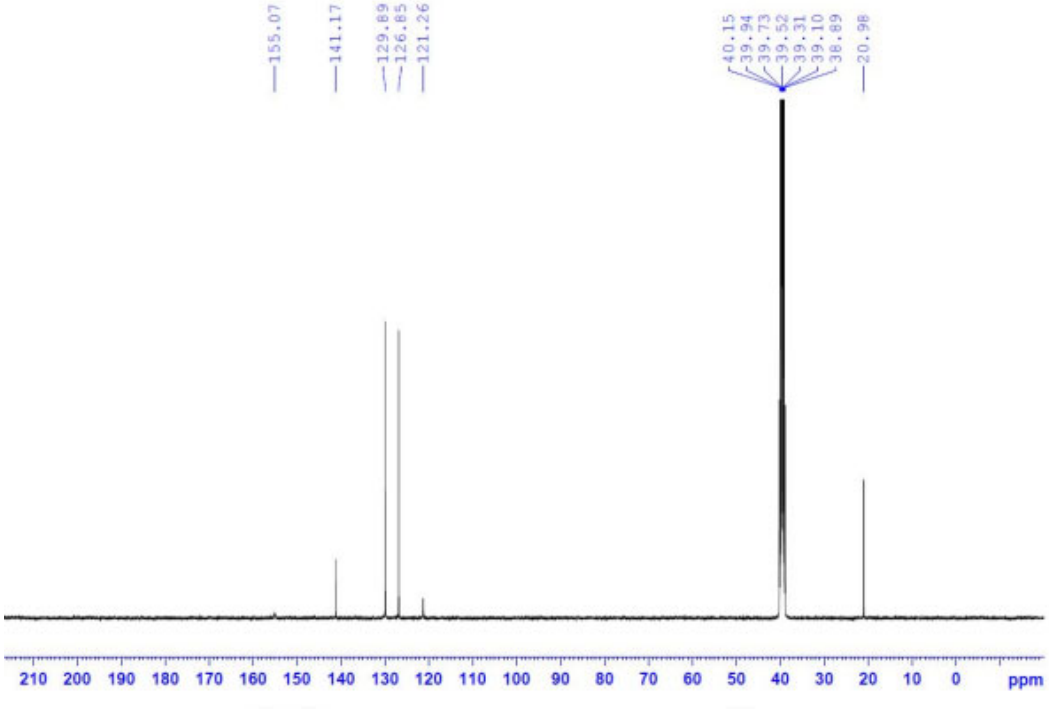
5-Phenyl-1*H*-tetrazole (**^{13}C NMR**)



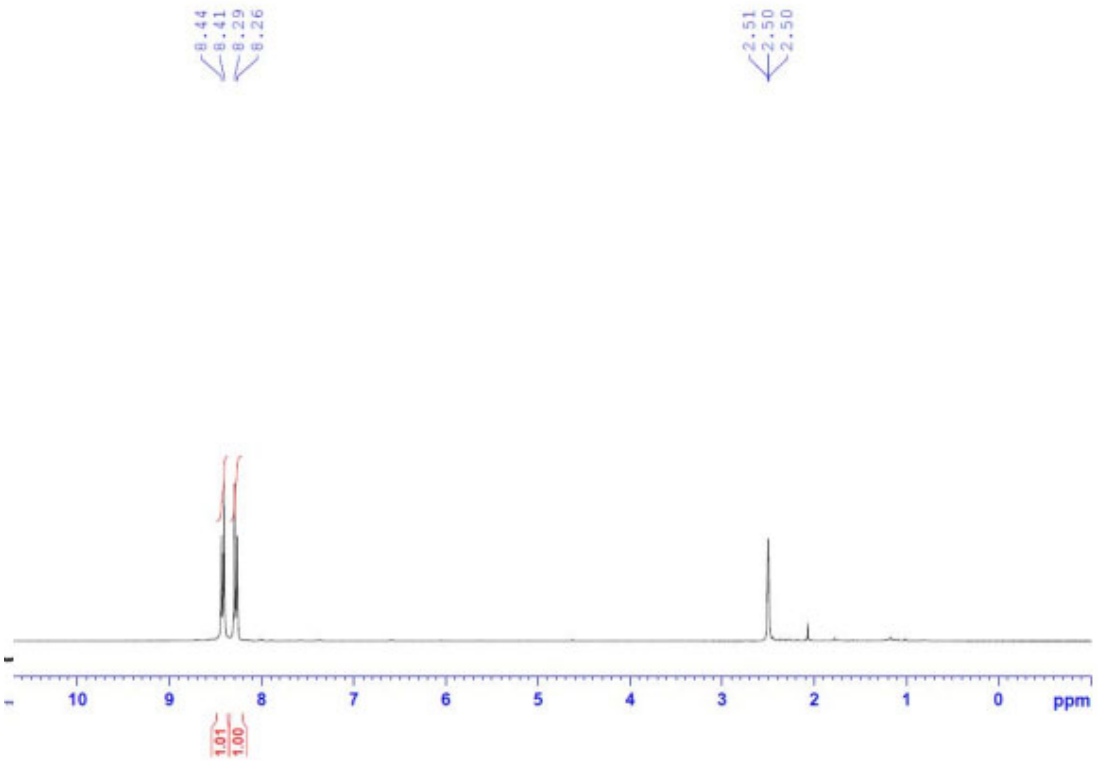
5-(4-Methylphenyl)-1*H*-tetrazole (**IR**)



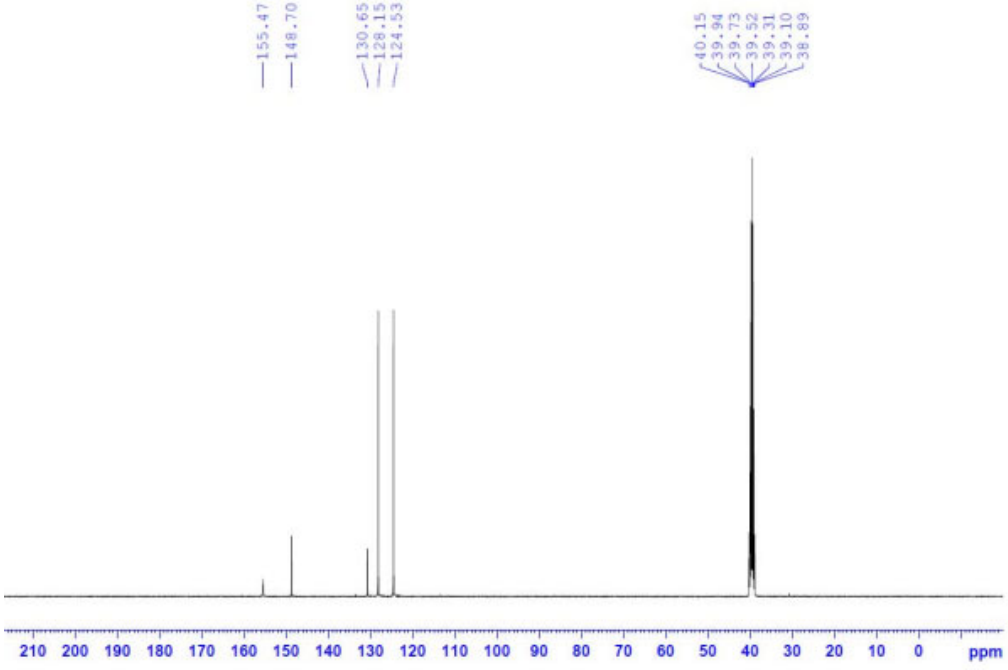
5-(4-Methylphenyl)-1*H*-tetrazole (**^{1}H NMR**)



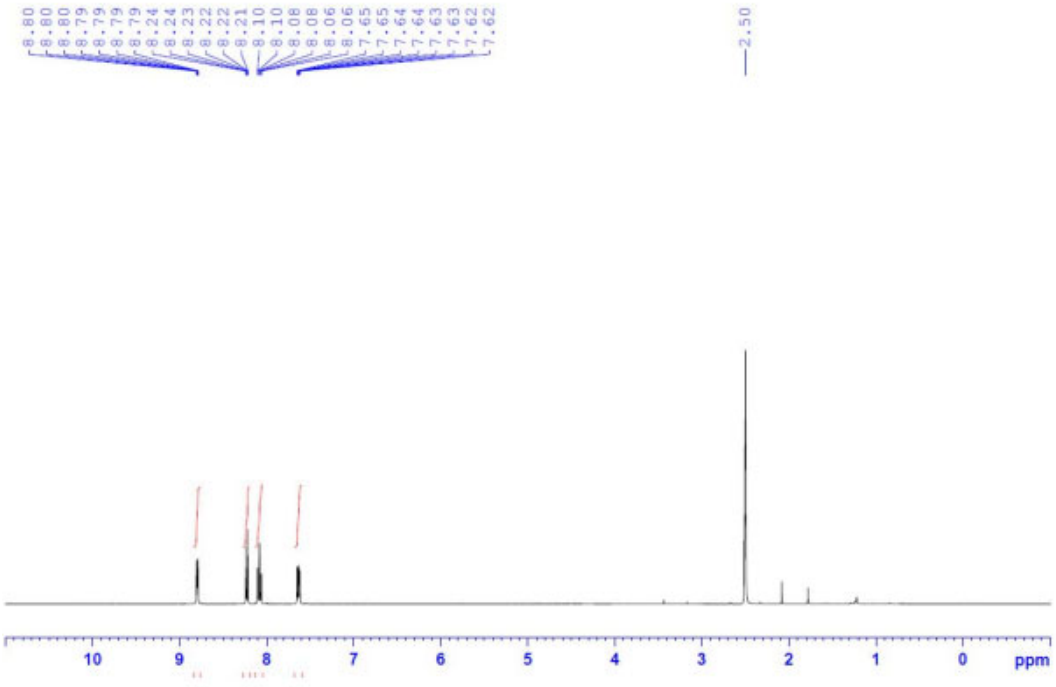
5-(4-Methylphenyl)-1*H*-tetrazole (**^{13}C NMR**)



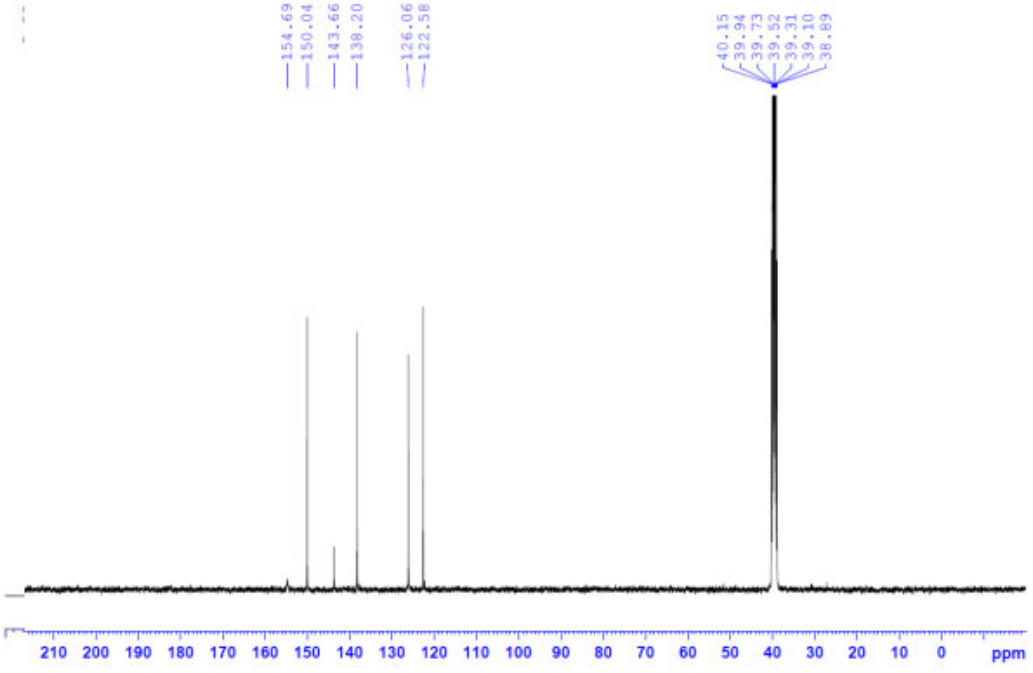
5-(4-Nitrophenyl)-1*H*-tetrazole (**^{1}H NMR**)



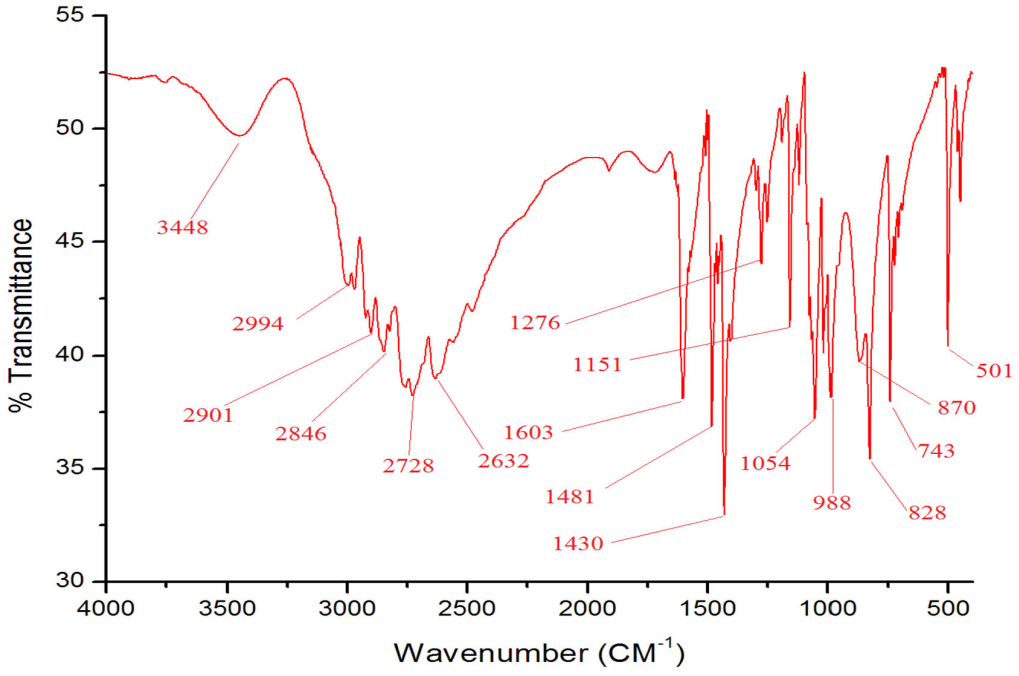
5-(4-Nitrophenyl)-1*H*-tetrazole (**^{13}C NMR**)



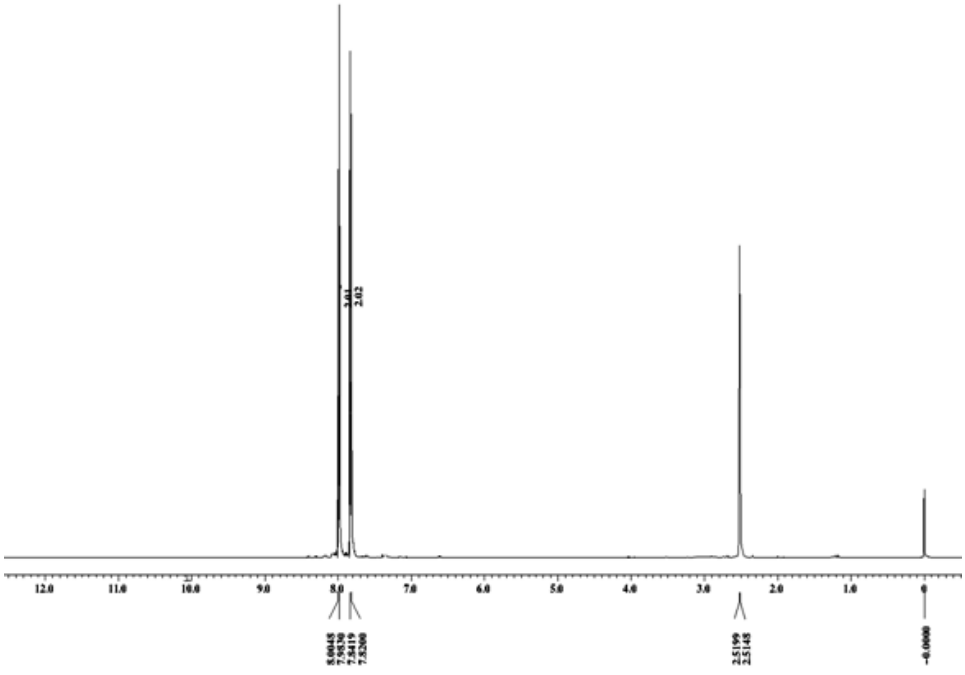
2-(1*H*-Tetrazol-5-yl)pyridine (**^{1}H NMR**)



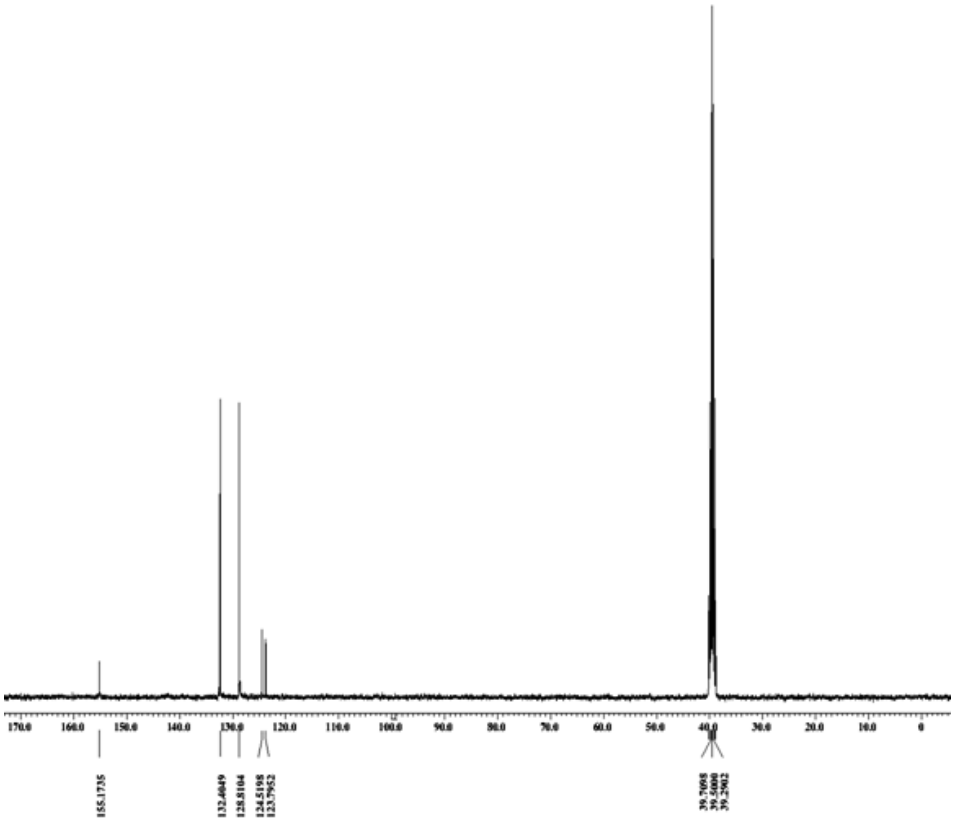
2-(1*H*-Tetrazol-5-yl)pyridine (**^{13}C NMR**)



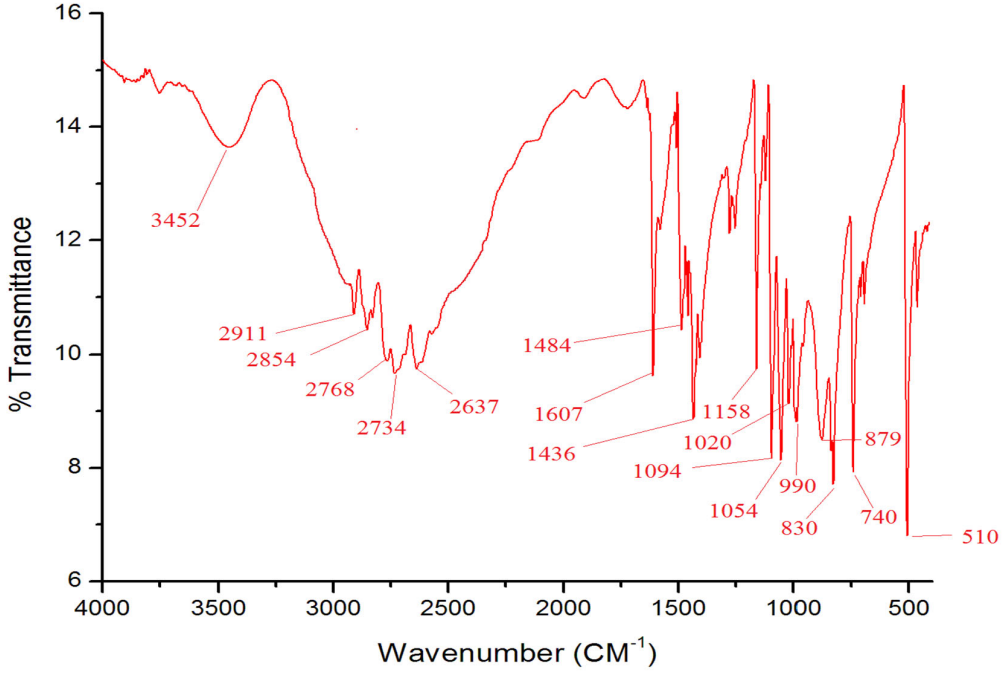
5-(4-Bromophenyl)-1*H*-tetrazole (IR)



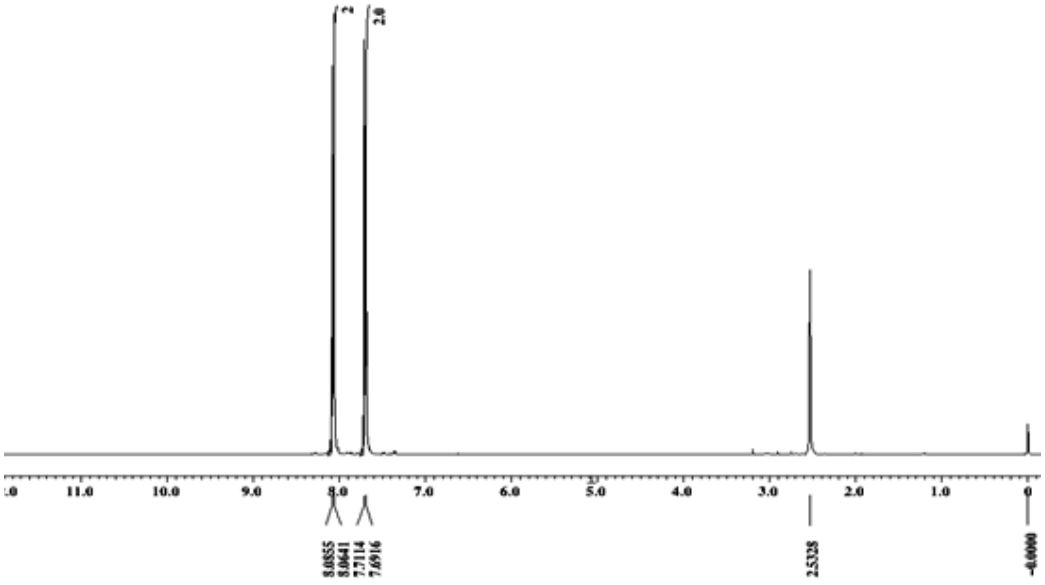
5-(4-Bromophenyl)-1*H*-tetrazole (^{1}H NMR)



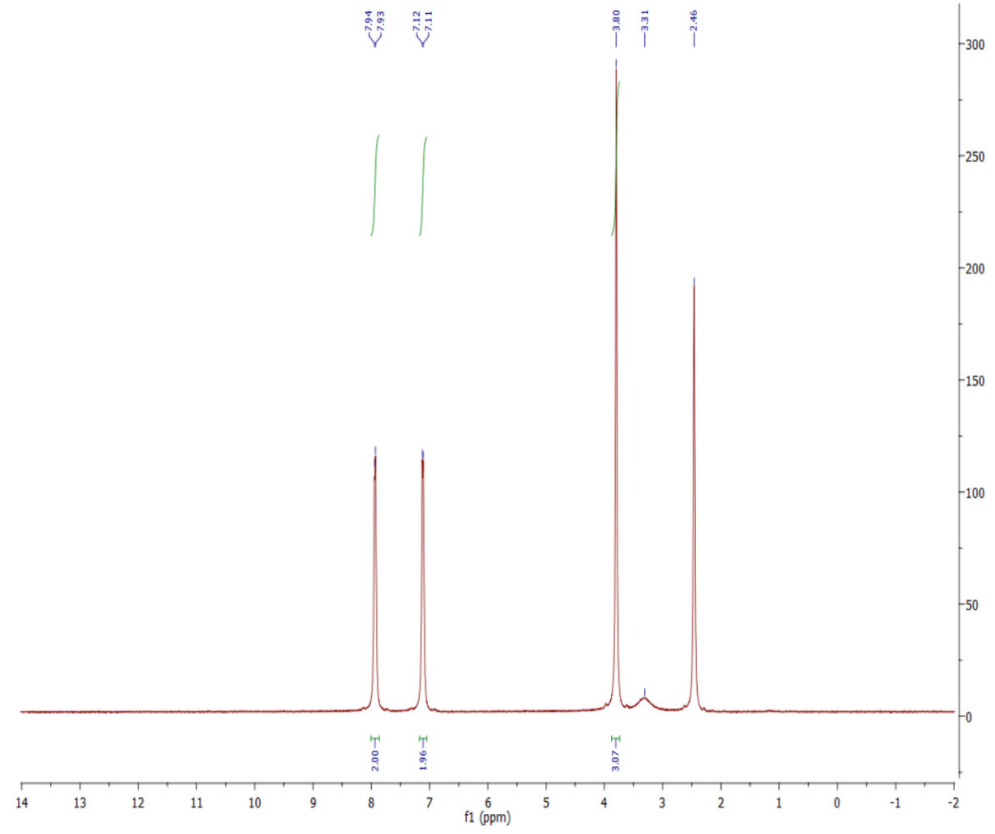
5-(4-Bromophenyl)-1*H*-tetrazole (**^{13}C NMR**)



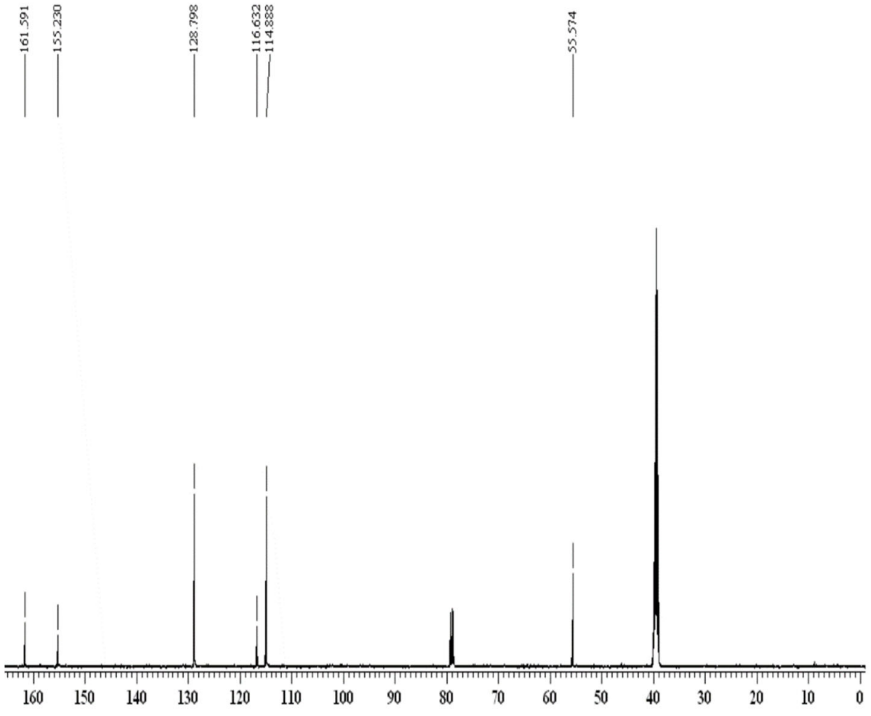
5-(4-Chlorophenyl)-1*H*-tetrazole (IR)



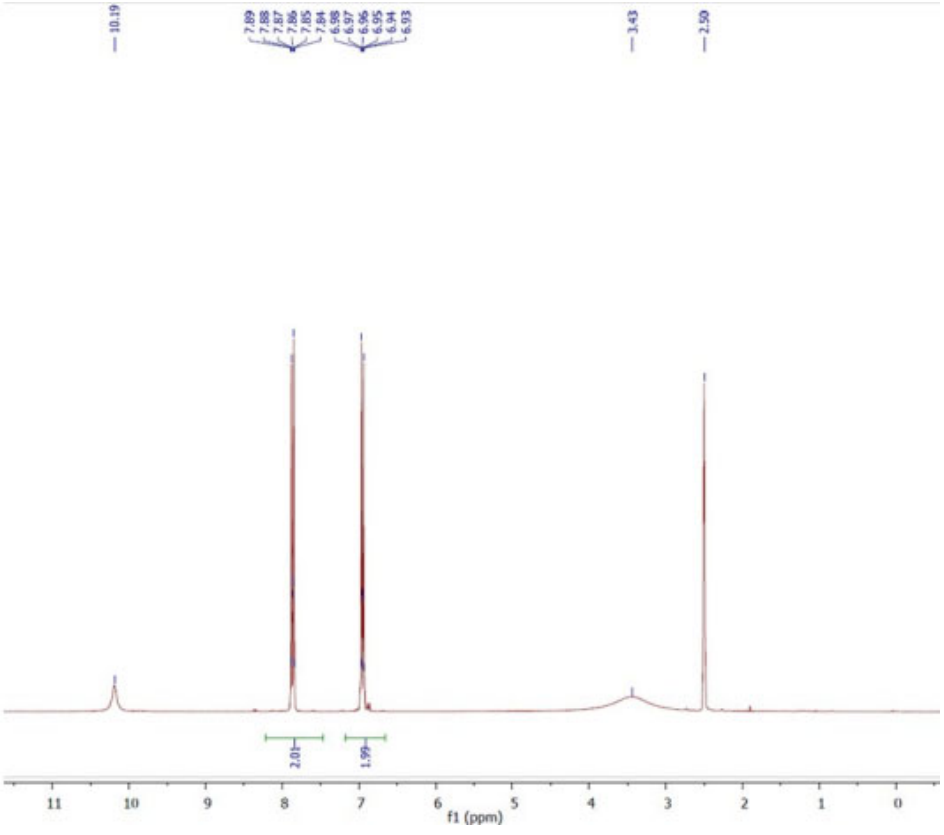
5-(4-Chlorophenyl)-1*H*-tetrazole (**^{1}H NMR**)



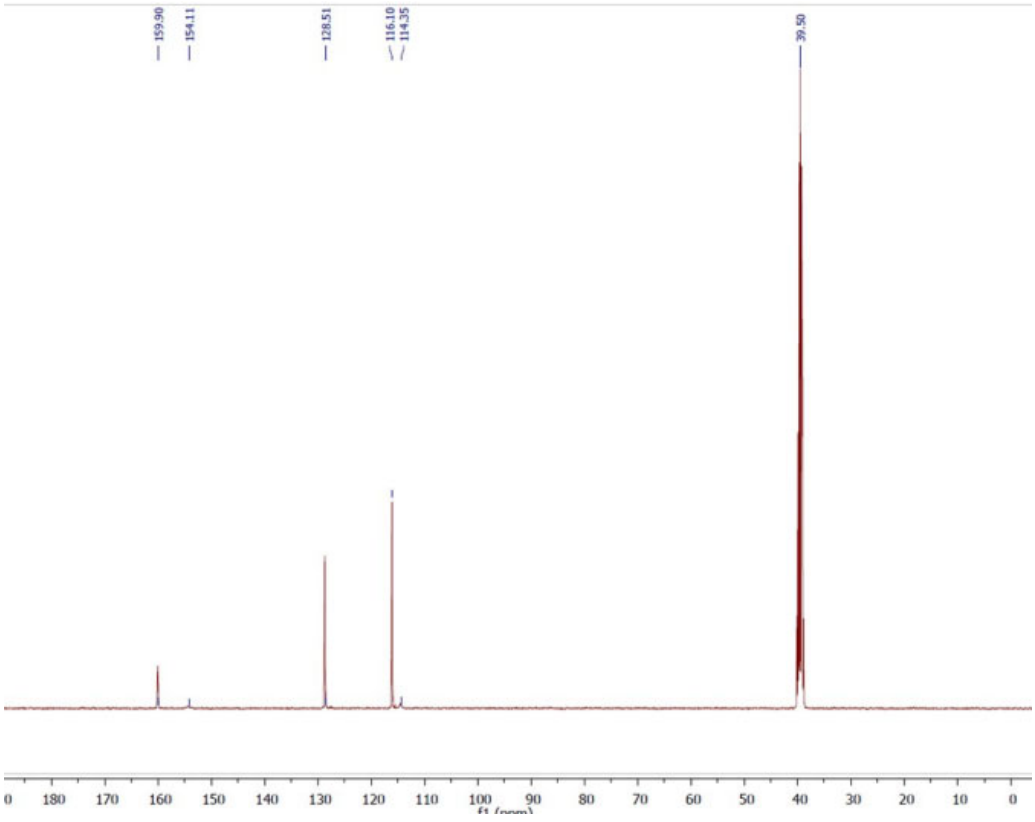
5-(4-Methoxyphenyl) 1*H*-tetrazole (**^{13}C NMR**)



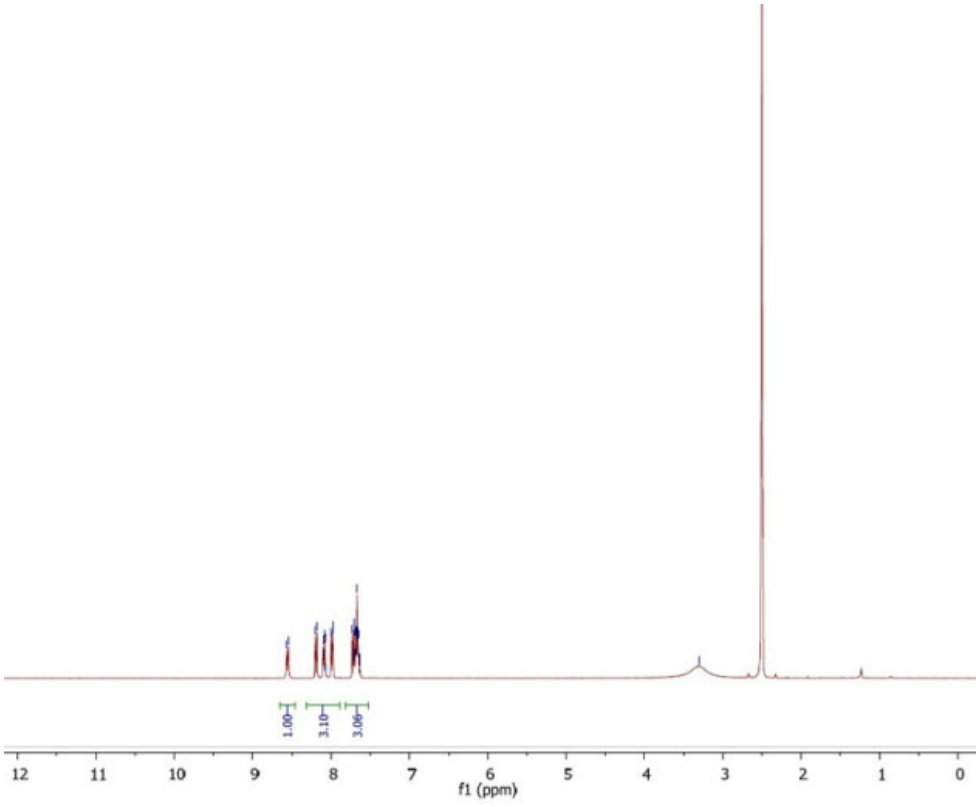
5-(4-Methoxyphenyl) 1*H*-tetrazole (^{13}C NMR)



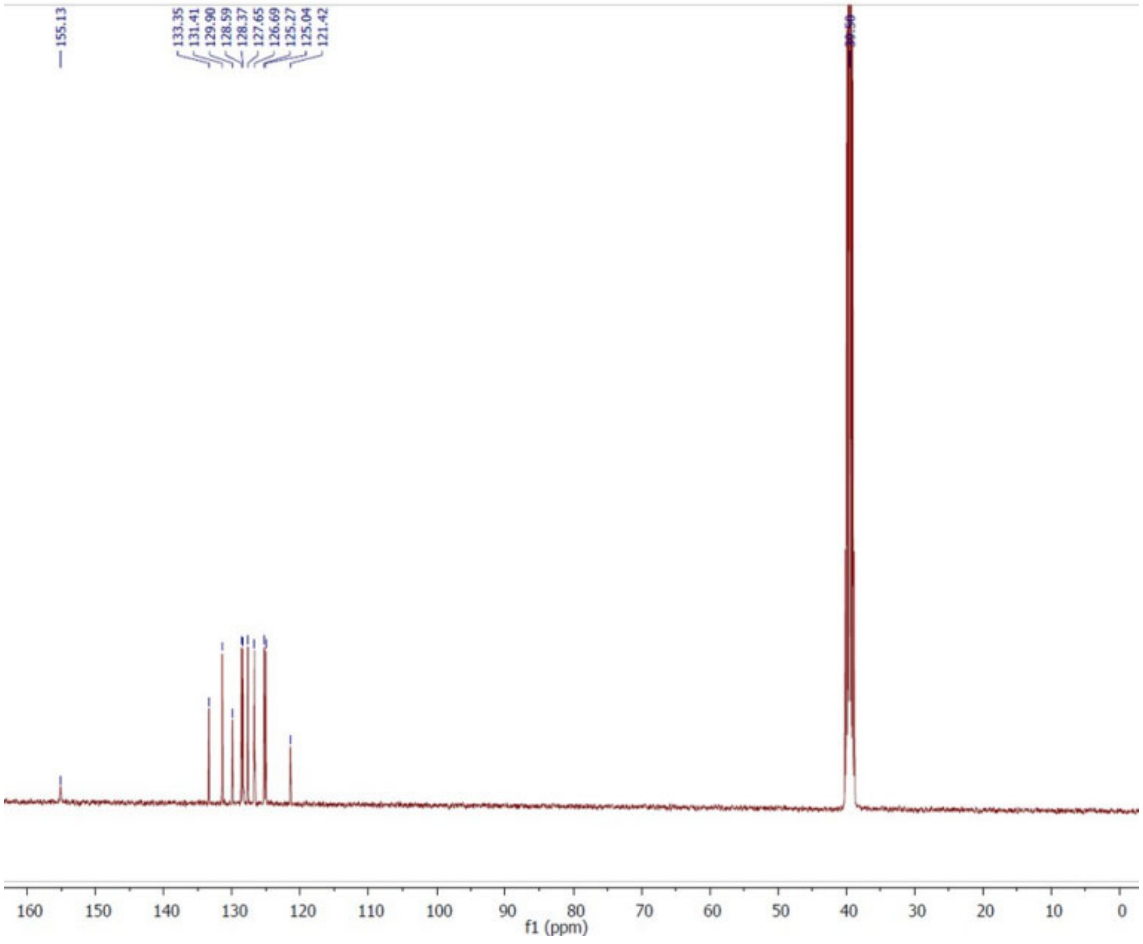
5-(4-Hydroxyphenyl)-*1H*-tetrazole (^{1}H NMR)



5-(4-Hydroxyphenyl)-*1H*-tetrazole (**^{13}C NMR**)



5-(Naphthalen-1-yl)-*1H*-tetrazole (**^{1}H NMR**)



5-(Naphthalen-1-yl)-*1H*-tetrazole (**^{13}C NMR**)