Electronic Supplementary Information (ESI)

"I_2-Mediated Regioselective C-3 Azidation of indoles"

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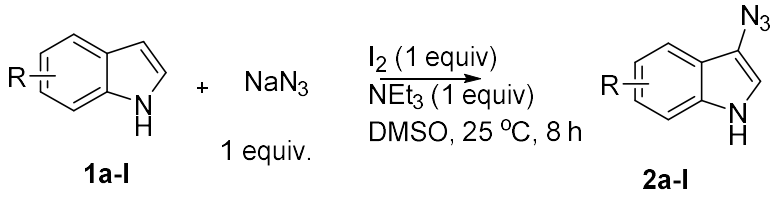
1. General Information

Solvents were purified and dried by standard procedures before use. IR spectra were recorded on a Perkin-Elmer model 683 B and absorption is expressed in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. Deuterated solvent DMSO-D_6, MeOH-D_4, Acetone-D_6 and $CDCl_3$+ CCl_4 (70:30) were used as internal standard and singlet at 96.1 ppm in ^{13}C NMR corresponds to carbon of CCl_4. Purification was done using column chromatography (100-200 mesh). ESI-MS were recorded on a Thermo Finnigan LCQ Advantage spectrometer in ESI mode with a spray voltage of 4.8 kV. All chemicals are purchased from Sigma-Aldrich and used without further purification.

2. Experimental section

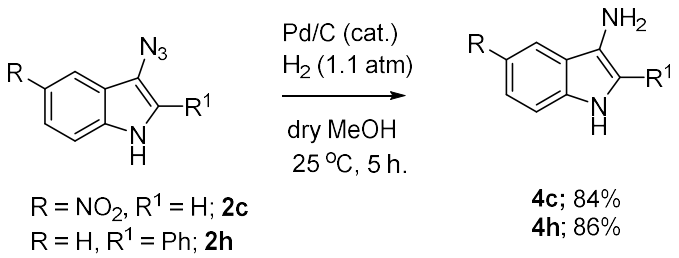
2.1. General experimental procedure for the azidation of indoles:



1a-l **2a-l**

To a stirred solution of indole **1a-l** (1 mmol) in dry DMSO (8 mL), was added iodine (1 mmol, 254 mg), triethyl amine (1 mmol, 0.14 mL) and sodium azide (1 mmol, 65 mg) at 0 °C and the reaction mixture was then stirred at 25 °C under open air. After completion of the reaction as monitored by TLC, it was quenched with H_2O (5 mL) at 0 °C. It was then extracted with EtOAc (3 x 20 mL) followed by washing with brine (3 x 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. Concentration of organic solvent under reduced pressure gave the crude product, which was purified by column chromatography over silica gel using pet. ether /EtOAc (9:1) as eluent to afford 3-azido indole compounds **2a-l** in high purity.

2.2 General experimental procedure for the reduction of azido indoles:

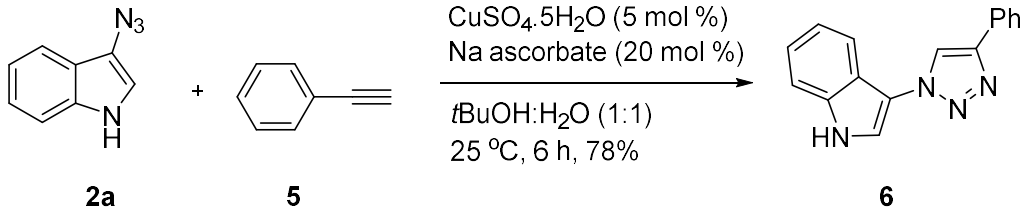


R = NO_2, R^1 = H; **2c**
R = H, R^1 = Ph; **2h**

4c; 84%
4h; 86%

To a stirred solution of azido indoles (**2c** and **2h**) (1 mmol) in degassed MeOH (6 mL), was added Pd/C (10 wt %) at 25 °C and the reaction mixture was then stirred at 25 °C under H_2 (1 atm) atmosphere for 5 h. After completion of the reaction (as monitored by TLC), the reaction mixture was filtered over celite bed, washed with methanol (25 mL). Concentration of organic solvent under reduced pressure gave the crude product, which was purified by column chromatography over silica gel using pet. ether /EtOAc (7:3) as eluent to afford 3-amino indoles **4c** and **4h** in high purity.

2.4 Experimental procedure for synthesis of trizole from azido indole:



2a **5** **6**

To a stirred solution of $CuSO_4.5H_2O$ (5 mol %), Na ascorbate (20 mol %) in ^{t}BuOH: H_2O (1:1), was added phenylacetylene (1 mmol) followed by the addition of azido indole (1 mmol) at 25 °C. The reaction mixture was then stirred at room temperature in open air for 6 h. After completion of the reaction (6 h), the reaction mixture was concentrated under reduced pressure to remove ^{t}BuOH. The aqueous layer was then extracted with EtOAc (3 x 20 mL) followed by

washing with brine (3 x 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. Concentration of EtOAc under reduced pressure gave the crude product which was purified by column chromatography with pet. ether: ethyl acetate (7:3) as eluent to give pure triazole **6** in 78% yield.

3-Azido-1*H*-indole (2a):

Yield: 92% (150 mg), colorless solid, **mp**: 60 ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 2255, 2128, 1739, 1658, 1468, 1201, 1026**;** **^{1}H NMR** (400 MHz, DMSO-d_6): δ 7.09-7.14 (m, 1H), 7.15-7.21 (m, 1H), 7.42 (t, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 2.7 Hz, 1H),11.45 (br. s., 1H); **^{13}C NMR** (100 MHz, DMSO-d_6): δ 88.7, 112.1, 117.9, 119.9, 122.2, 124.7, 126.1, 135.4; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_6N_4+H]^+$: 159.0671; found: 159.0665.

3-Azido-5-methoxy-1*H*-indole (2b):

Yield: 90% (170 mg), colorless solid, **mp**: 60ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 2252, 2126,1738, 1659, 1490, 1206, 1027 ; **^{1}H NMR** (200 MHz, DMSO-d_6) δ 11.31 (br. s., 1H), 7.48 (d, *J* = 2.7 Hz, 1H), 7.26-7.38 (m, 1H), 6.76-6.89 (m, 2H), 3.43 (s, 3H); **^{13}C NMR** (50 MHz, DMSO-d_6) δ 154.1, 130.4, 126.4, 125.1, 112.8, 99.1, 88.3, 55.3; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_9H_8N_4O+H]^+$: 189.0776; found: 189.0772.

3-Azido-5-nitro-1*H*-indole (2c):

Yield: 86% (170 mg), yellow solid; **mp**: 60ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 2255, 2128, 1658, 1338, 1025; **^{1}H NMR** (200 MHz, DMSO-d_6) δ 12.21 (br. s., 1H), 8.31 (d, *J* = 2.3 Hz, 1H), 8.06 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.87 (d, *J* = 2.7 Hz, 1H), 7.63 (d, *J* = 9.0 Hz, 1H); **^{13}C NMR** (50

MHz, DMSO-d_6) δ 140.9, 138.2, 128.6, 125.3, 117.1, 114.6, 112.6, 90.7; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_5N_5O_2+H]^+$: 204.0521; found: 204.0526.

3-Azido-5-bromo-1*H*-indole (2d):

Yield: 82% (200 mg), brown solid, **mp**: 60ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 2250, 2124, 1659, 1028; **^{1}H NMR** (200 MHz, DMSO-d_6): δ 11.68 (br. s., 1H), 7.54 (d, J = 1.8 Hz, 1H), 7.62 (d, J = 2.5 Hz, 1H), 7.41 (d, J = 8.6 Hz, 1H), 7.29 (dd, J = 8.6, 1.9 Hz, 1H); **^{13}C NMR** (50 MHz, DMSO-d_6): δ 134.1, 127.9, 126.51, 124.8, 120.1, 114.2, 112.4, 87.8; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_5BrN_4+H]^+$: 236.9776; found: 236.9769.

3-Azido-5-chloro-1*H*-indole (2e):

Yield: 87% (190 mg), colorless solid; **mp**: 60 ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 2250, 2124, 1659, 1028; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.69 (br. s., 1H), 7.59 - 7.71 (m, 1H), 7.46 (d, J = 8.2 Hz, 1H), 7.40 (s, 1H), 7.16 - 7.21 (m, 1H); **^{13}C NMR** (50 MHz, DMSO-d_6) δ 133.9, 127.2, 126.7, 124.6, 122.3, 117.0, 113.8, 88.0; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_5ClN_4+H]^+$: 193.0281; found: 193.0285.

3-Azido-4-bromo-1*H*-indole (2f):

Yield: 81% (195 mg), colorless solid, **mp**: 60 ºC decomposed; **IR** (KBr, cm^{-1}): ν_{max} 625, 762, 823, 1024, 1658, 2122, 2253, 3436**^{1}H NMR** (200 MHz, DMSO-d_6) δ 11.85 (br. s., 1H), 7.66 (d, J = 2.7 Hz, 1H), 7.48 (d, J = 8.1 Hz, 1H), 7.27 (d, J = 6.8 Hz, 1H), 6.99 - 7.11 (m, 1H); **^{13}C NMR** (50 MHz, DMSO-d_6) δ 136.7, 127.6, 124.4, 123.2, 122.3, 112.3, 112.1, 87.7; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_5BrN_4+H]^+$: 236.9776; found: 236.9771.

3-Azido-2-methyl-1*H*-indole (2g):

Yield: 85% (155 mg), brown oil; **IR** (KBr, cm^{-1}): ν 700, 747, 798, 949, 1057, 1311, 1429, 1662, 2096, 2220, 2913, 2995, 3442; **^{1}H NMR** (200 MHz, DMSO-d_6) δ 11.41 (br. s., 1H), 7.28-7.37 (m, 2H), 7.03-7.16 (m, 2H), **^{13}C NMR** (50 MHz, DMSO-d_6) δ 135.0, 133.5, 127.1, 121.7, 119.9, 117.4, 111.5, 88.0, 12.1; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_9H_8N_4+H]^+$: 173.0827; found: 173.0821

3-Azido-2-phenyl-1*H*-indole (2h):

Yield: 87% (210 mg), brown solid, **mp**: 60ºC decomposed; IR (KBr, cm-1): ν 700, 798, 949, 1060, 1312, 1429, 1661, 2096, 2221, 2912, 2995, 3440; **^{1}H NMR** (200 MHz, DMSO-d_6) δ 11.87 (s, 1H), 7.85-7.93 (m, 2H), 7.51-7.60 (m, 2H), 7.41-7.48 (m, 3H), 7.09-7.27 (m, 2H); **^{13}C NMR** (50 MHz, DMSO-d_6) δ 134.7, 133.4, 130.3, 127.9, 127.5, 126.9, 122.2, 119.5, 117.6, 111.1, 86.8, 38.7; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_{14}H_{10}N_4+H]^+$: 235.0984; found: 235.0986.

Ethyl 3-azido-1*H*-indole-2-carboxylate (2i):

Yield: 89% (216 mg), colorless solid, **mp**: 60ºC decomposed; IR (KBr, cm-1): ν 685, 745, 1020, 1197, 1261, 1377, 1458, 1685, 2111, 2856, 2922, 3294; **^{1}H NMR** (400 MHz, MeOH-d_4) δ 7.93 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 8.7 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.46-7.61 (m, 1H), 4.77 (q, J = 7.0 Hz, 2H), 1.78 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, MeOH-d_4) δ 161.9, 137.5, 128.8, 127.4, 125.6, 122.5, 121.7, 114.1, 97.8, 62.3, 40.0, 15.1; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_{11}H_{10}N_4O_2+H]^+$: 231.0882; found: 231.0885.

3-Azido-1-methyl-1*H*-indole (2j):

Yield: 54% (93 mg), colorless oil; IR (KBr, cm-1): ν 701, 747, 1055, 1244, 1314, 1428, 2094, 2913, 2995; **^{1}H NMR** (200 MHz, DMSO-d_6) δ 7.34-7.62 (m, 3H), 7.06-7.30 (m, 2H), 3.77 (s, 3H); **^{13}C NMR** (50 MHz, DMSO-d_6) δ 135.54, 128.2, 126.0, 121.8, 119.5, 117.8, 109.9, 87.0,

39.9, 39.1, 38.7, 38.3, 32.8; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_9H_8N_4+H]^+$: 173.0827; found: 173.0831.

1-Benzylindoline-2,3-dione (2k):

Yield: 60% (142 mg), orange solid, **mp.** 135-136 °C; IR (KBr, cm-1): ν 626, 753, 1003, 1077, 1175, 1470, 1614, 1732, 3029, 3084, 3454; **^{1}H NMR** (200 MHz,$CDCl_3$) δ 7.60-7.66 (m, 1H), 7.44-7.55 (m, 1H), 7.31-7.38 (m, 5H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.95 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 183.2, 158.3, 150.7, 138.3, 134.5, 129.1, 128.2, 127.4, 125.4, 123.9, 117.7, 110.9, 44.1; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_{15}H_{11}NO_2+H]^+$: 238.0868; found: 238.0872.

3-azido-5-nitro-1*H*-indazole (2l):

Yield: 60% (135 mg), colorless solid, **mp**: 60 ºC decomposed; IR (KBr, cm-1): ν 745, 1084, 1341, 1457, 1528, 1619, 2105, 2856, 2923, 3400; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.46 (d, *J* = 1.8 Hz, 1H), 8.25 (dd, *J* = 9.2, 1.8 Hz, 1H), 7.77 (d, *J* = 9.2 Hz, 1H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 142.9, 142.3, 123.7, 122.3, 121.5, 117.1, 112.2; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_7H_4N_6O_2H+]^+$: 205.0474; found: 205.0469.

5-nitro-1*H*-indol-3-amine (4c):

Yield: 92% (200 mg), brown sticky gum; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 10.83-11.03 (m, 1H), 7.56 (br. s., 1H), 7.40-7.50 (m, 1H), 7.28 (br. s., 1H), 7.09 (br. s., 1H), 6.35-6.45 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$) δ 133.6, 126.7, 125.5, 122.9, 114.2, 112.3, 111.2, 100.1, 38.6; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_8H_8N_3O_2H+]^+$: 178.0617; found: 178.0620.

2-phenyl-1*H*-indol-3-amine (4h):

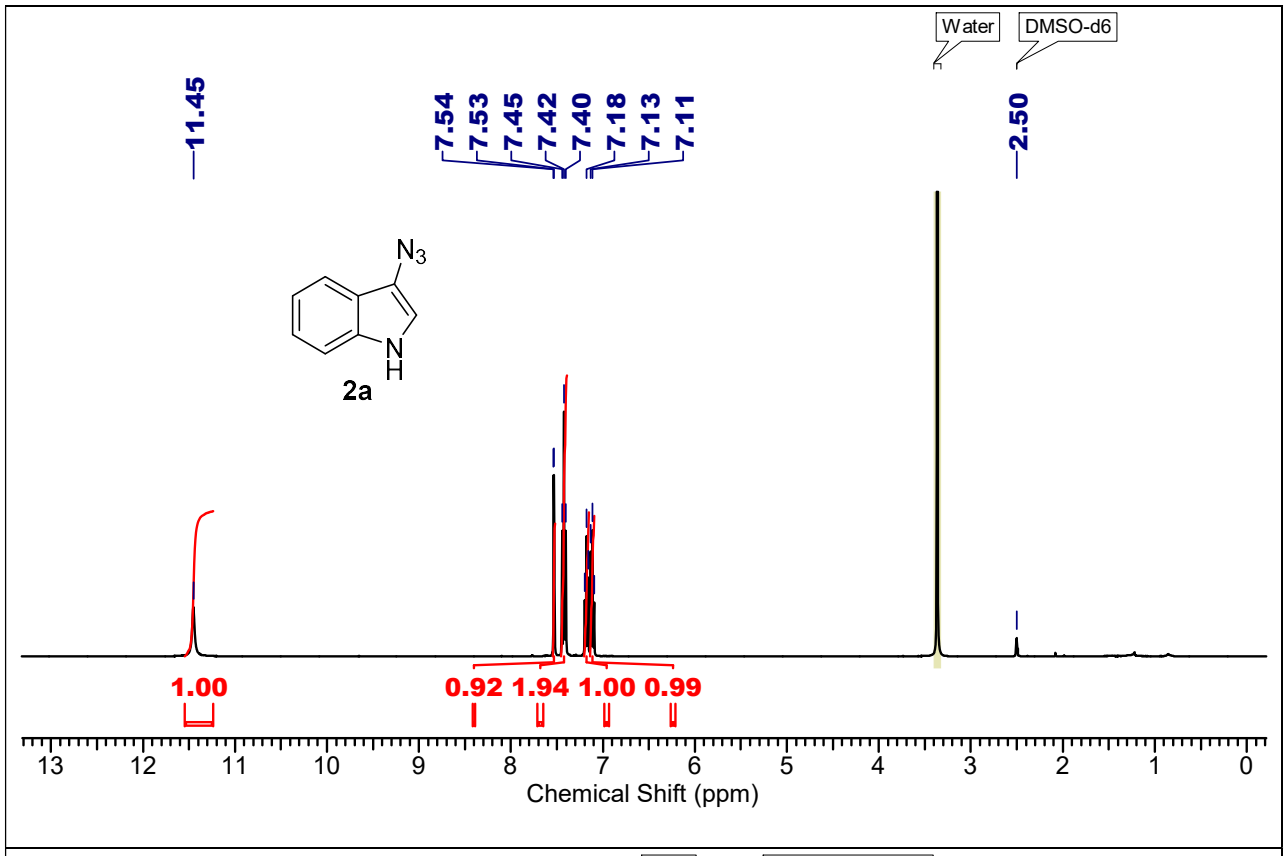
Yield: 92% (198 mg), gum; **^{1}H NMR** (400 MHz, DMSO-d_6) δ 6.69 (t, *J* = 7.6 Hz, 1H), 6.93-7.03 (m, 2H), 7.27-7.39 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 3H), 7.64-7.70 (m, 2H), 11.18 (s, 1H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ 136.1, 134.4, 133.1, 128.8, 128.7, 128.2, 127.3, 121.2, 119.2, 118.5, 111.1, 110.8; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_{14}H_{12}N_2+H]^+$: 209.1079 ; found: 209.1084.

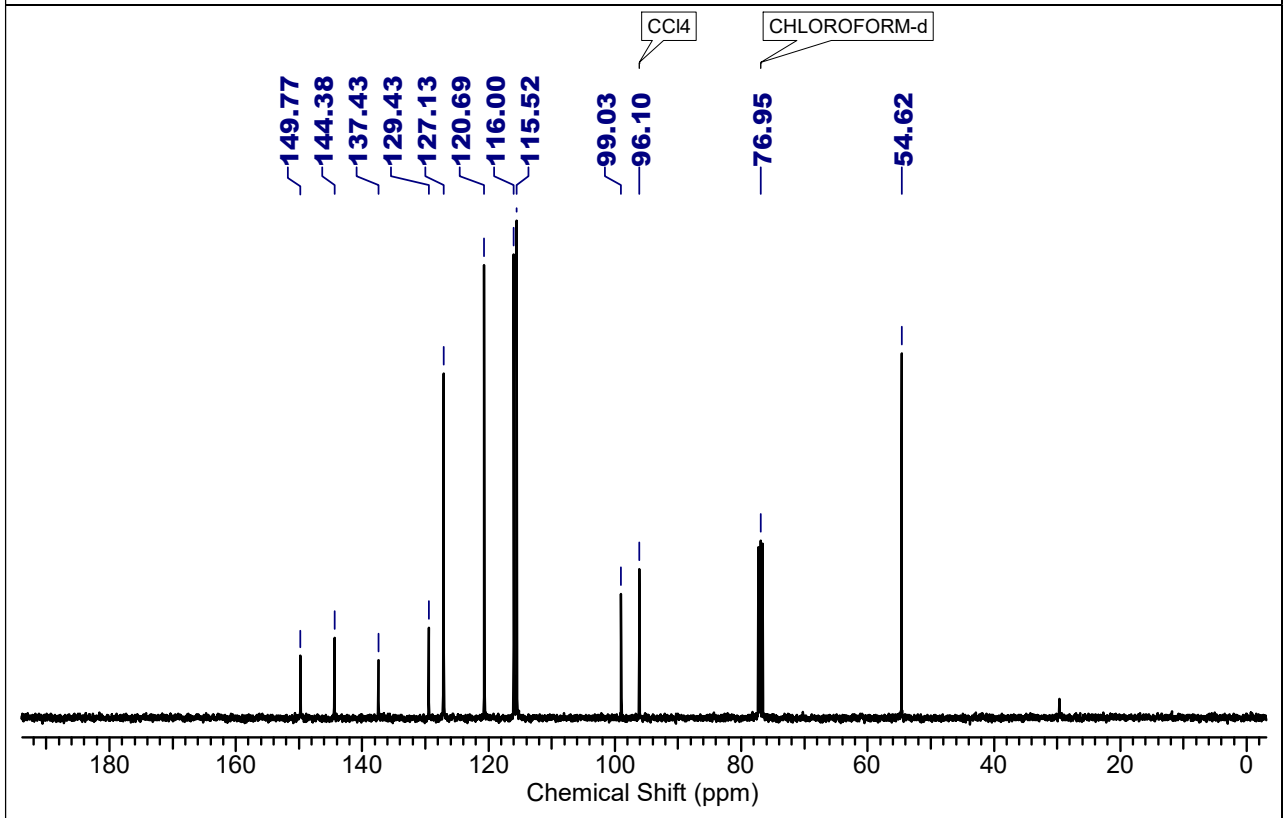
3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-indole (5):

Yield: 92% (245 mg), amber colored gum; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (br. s., 2H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.37-7.48 (m, 4H), 7.24-7.34 (m, 4H), 7.10-7.21 (m, 3H), 6.80 (d, *J* = 1.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.5, 136.1, 133.2, 129.5, 125.4, 122.9, 121.4, 121.4, 120.8, 119.9, 119.9, 111.5, 110.5, 99.4; **HRMS (ESI)**: $[M+H]^+$ calcd for $[C_{16}H_{12}N_4H+]^+$: 261.1140; found: 261.1146.

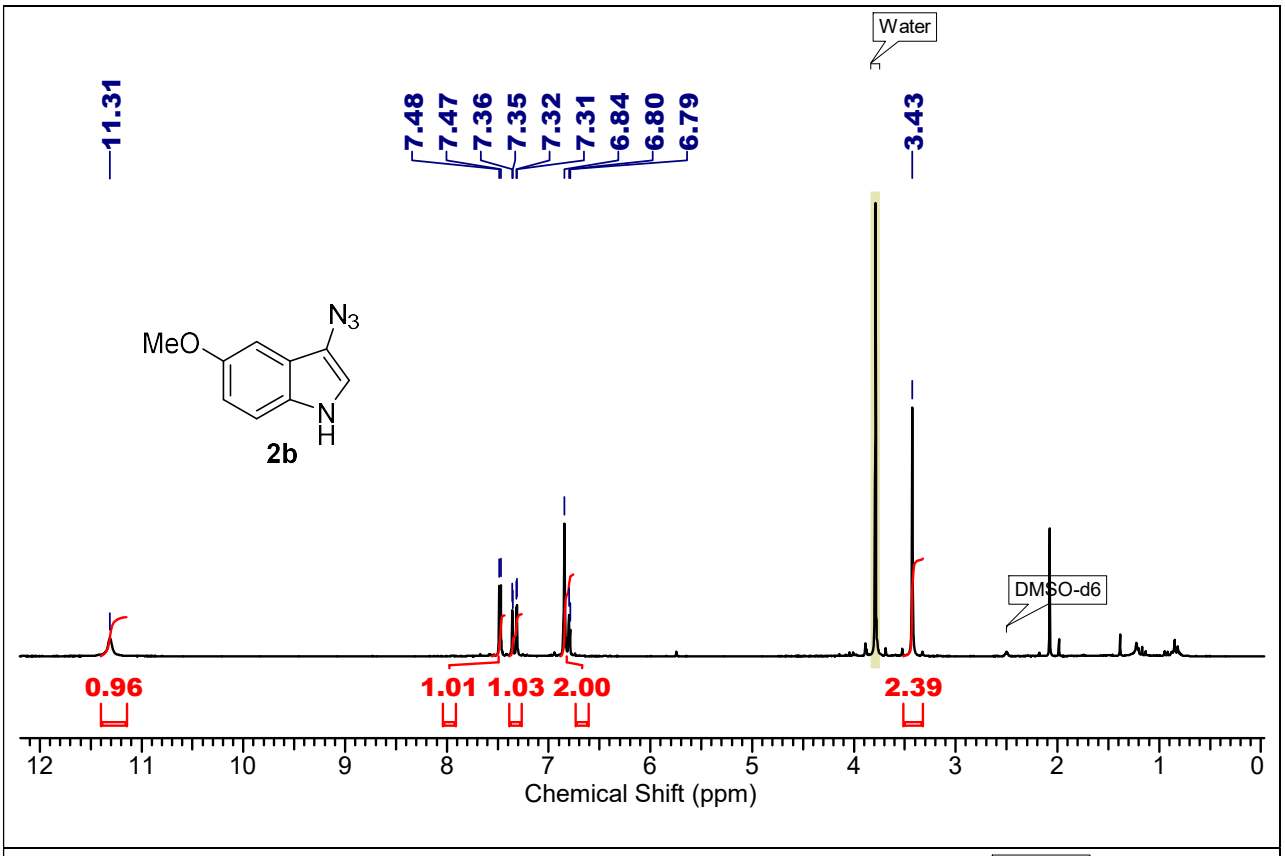
3-iodo-1H-indole (7):

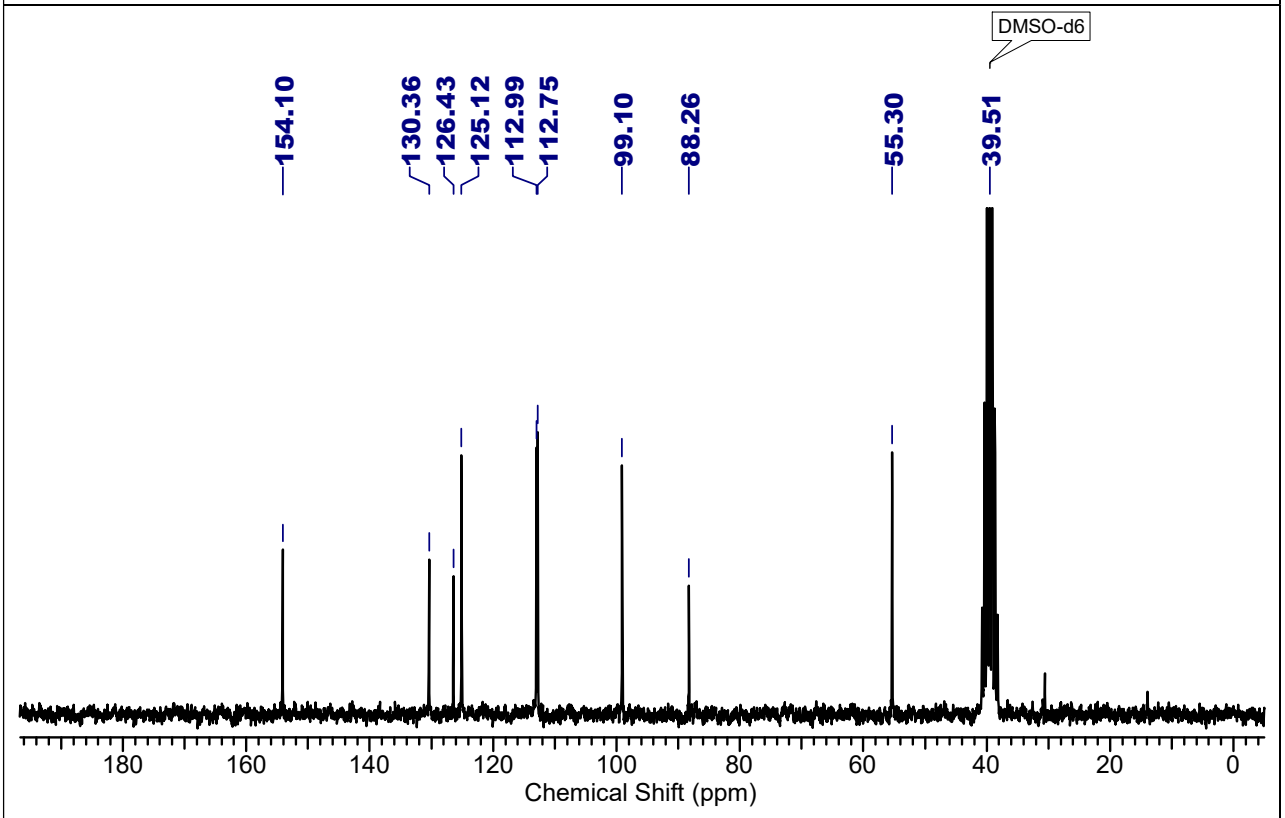
Yield: 75% (183 mg), brown oil: ^{1}H NMR (500 MHz, DMSO-d6) δ 7.10 (t, J = 7.4 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 7.27 (d, J = 7.6 Hz, 1H), 7.40 (d, J = 8.2 Hz, 1 H), 7.54 (d, J=2.7 Hz, 1H), 11.5 (br. s., 1 H): δ ^{13}C NMR (126 MHz, DMSO-d6) 56.0, 112.0, 119.8, 120.0, 122.2, 129.4 , 129.7, 136.0: HRMS (ESI): [M+H]+ calcd for [C8H6NIH+]+: 243.9623; found: 243.9619.



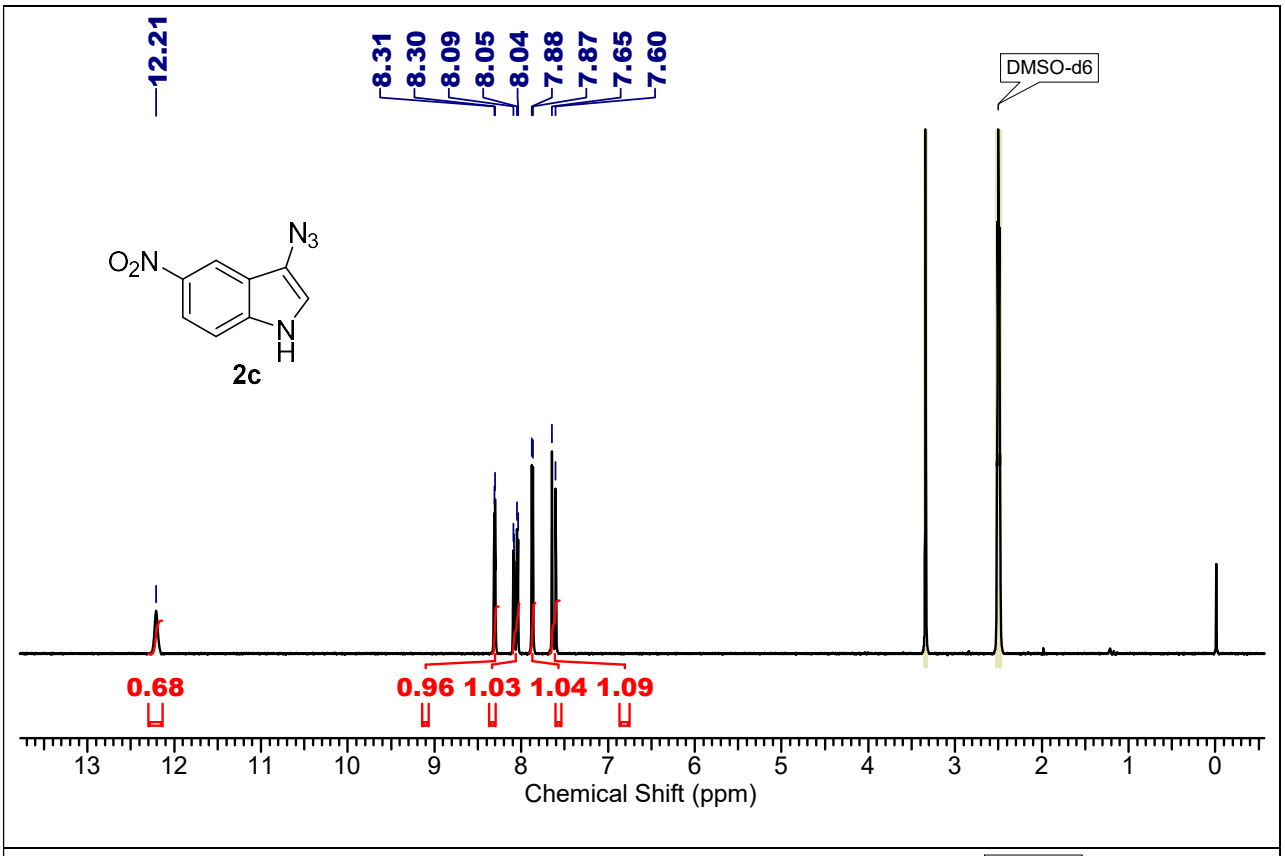


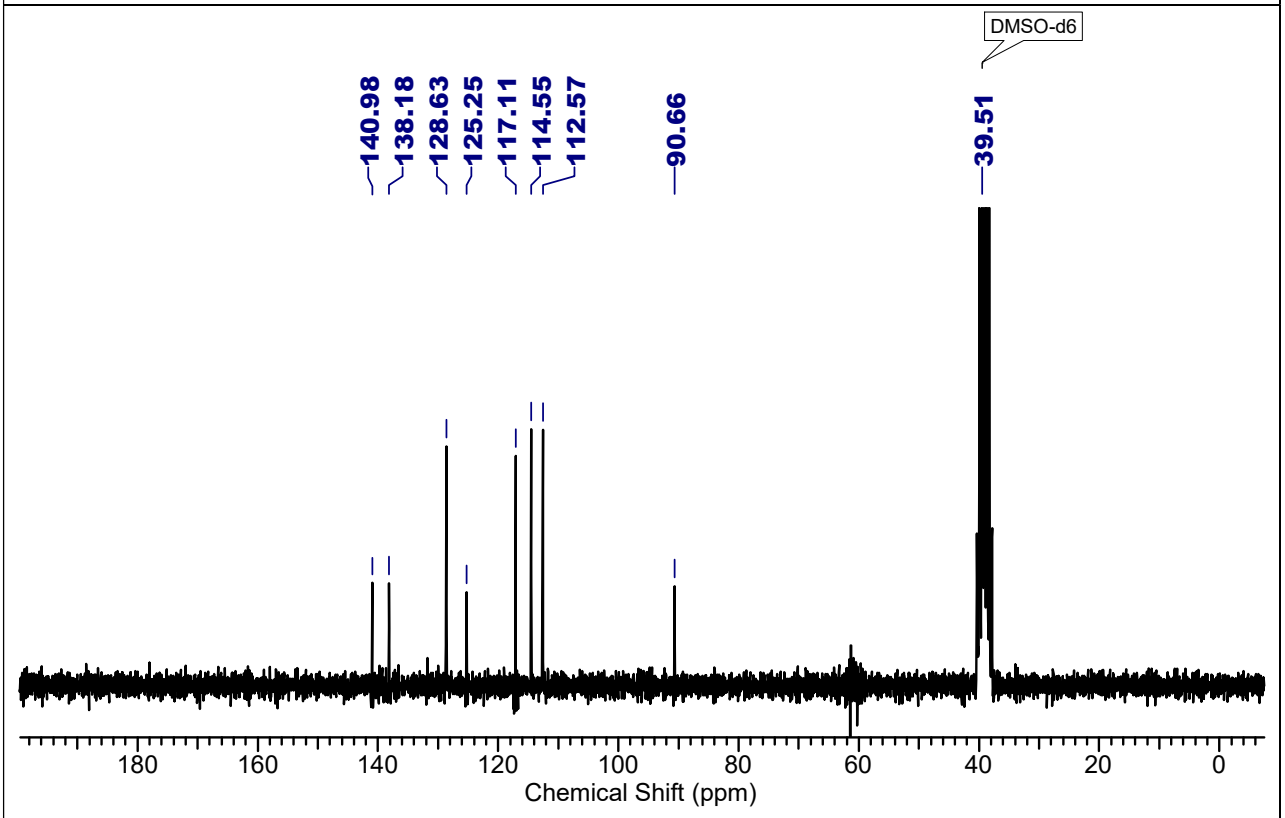
^{1}H and ^{13}C Spectra of 3-azido-1*H*-indole **(2a)**



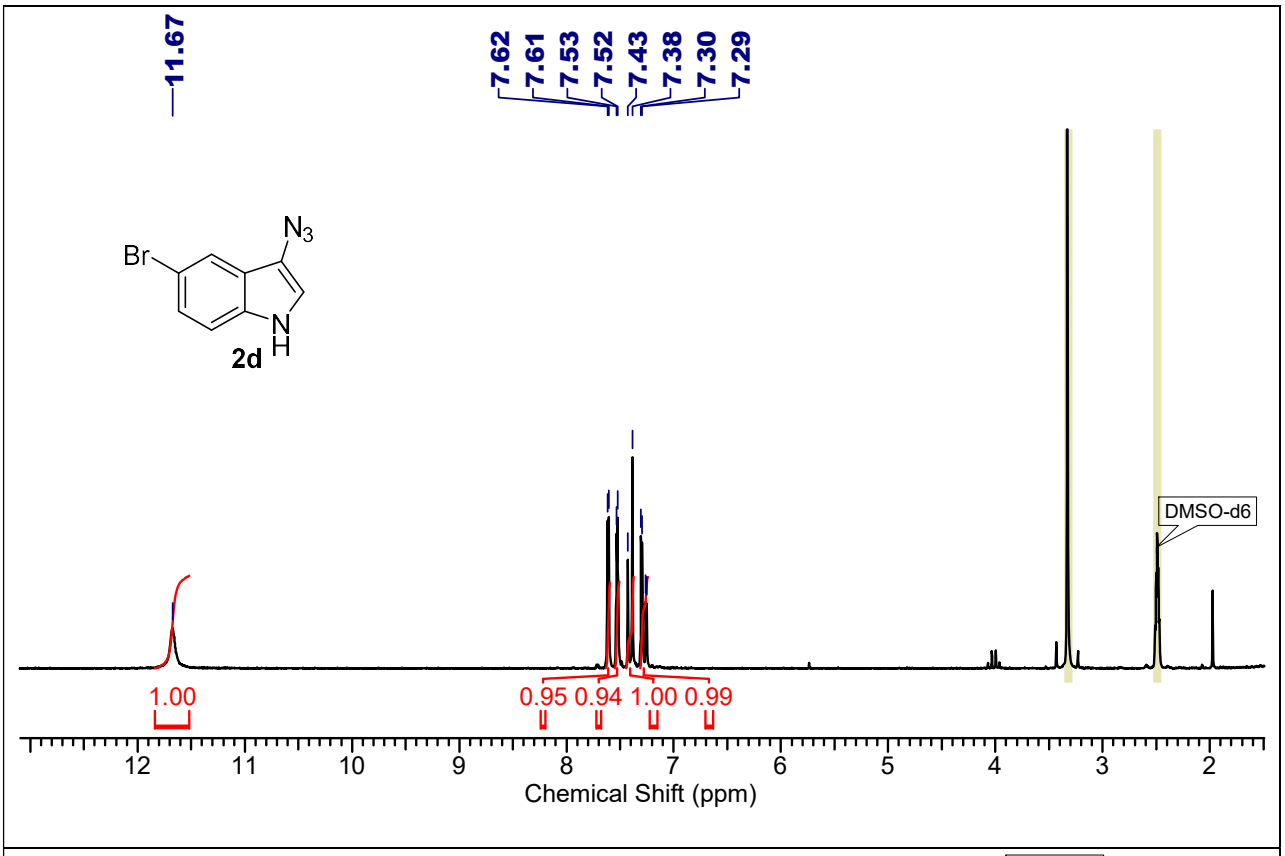


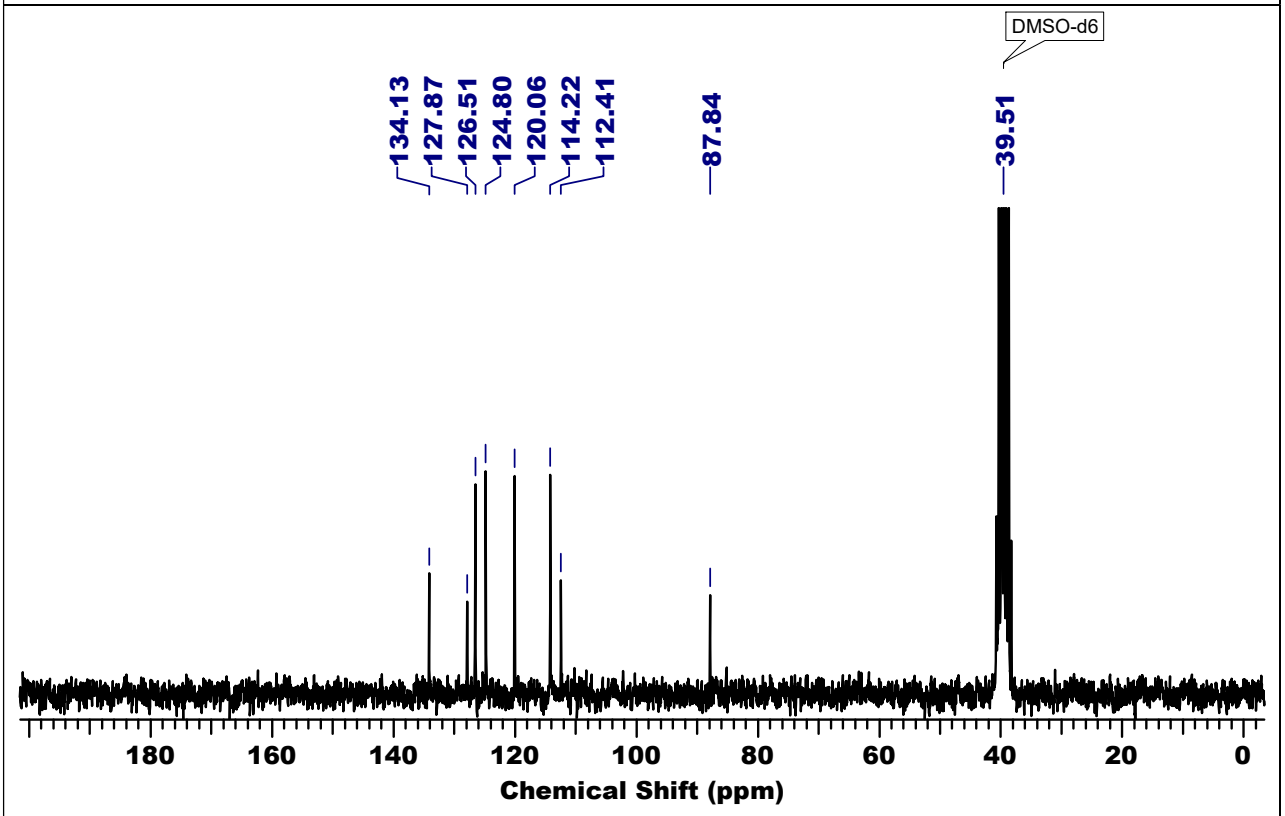
^{1}H and ^{13}C Spectra of 3-azido-5-methoxy-1*H*-indole **(2b)**



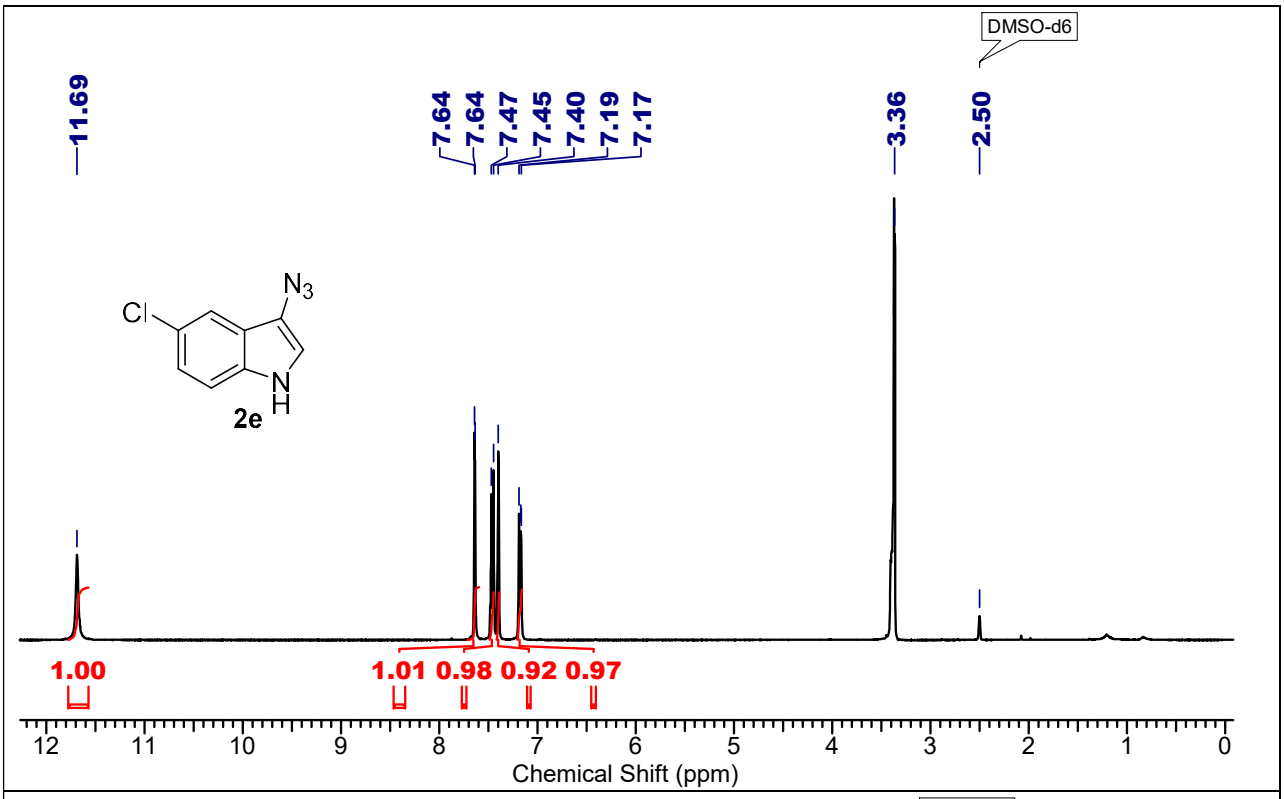


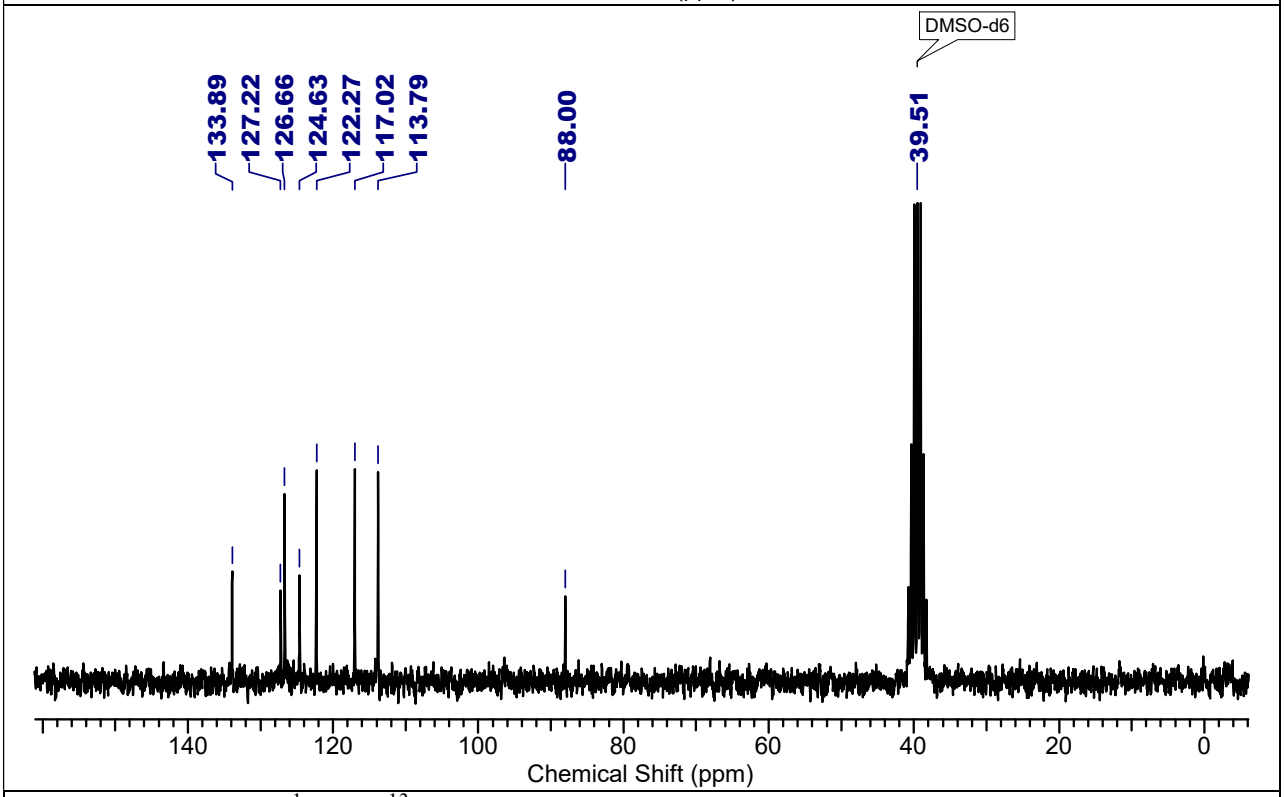
^{1}H and ^{13}C Spectra of 3-azido-5-nitro-1*H*-indole **(2c)**



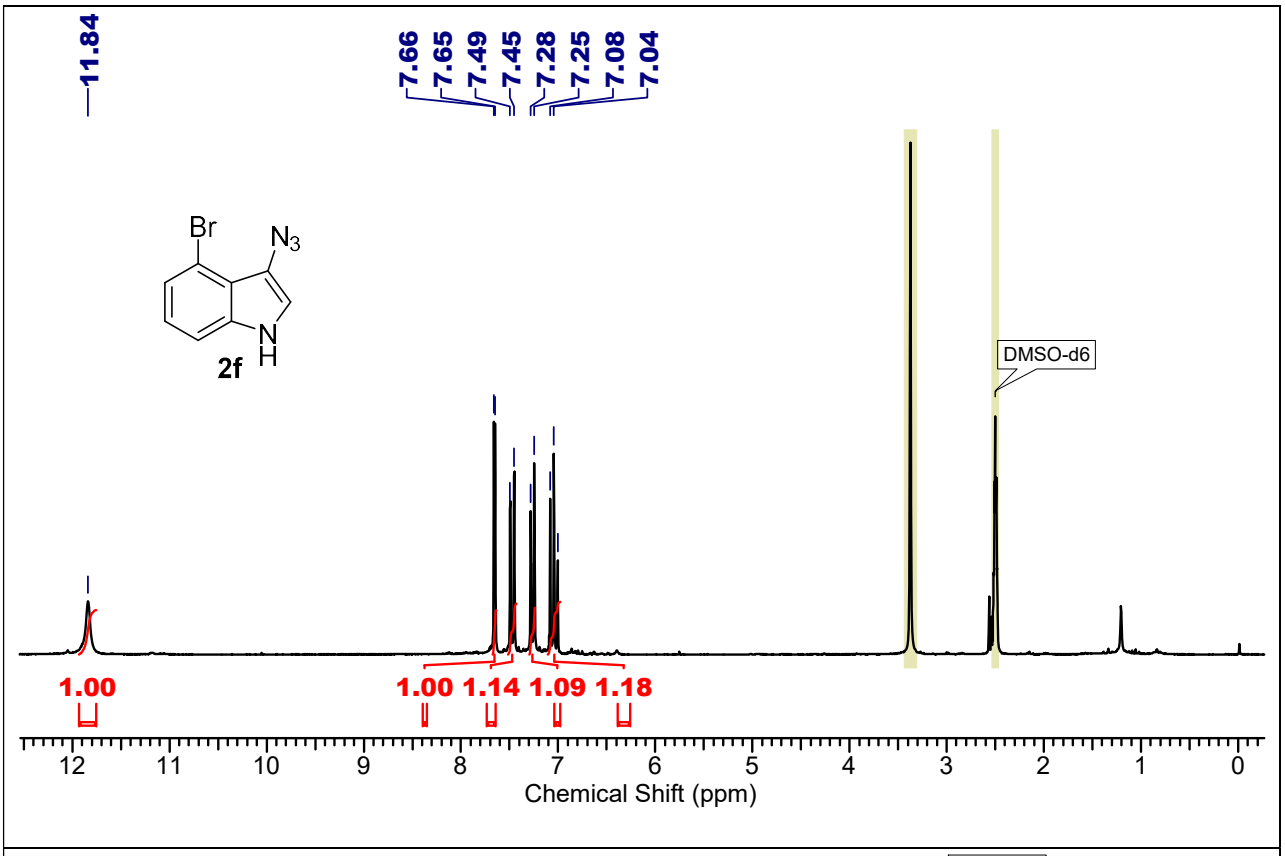


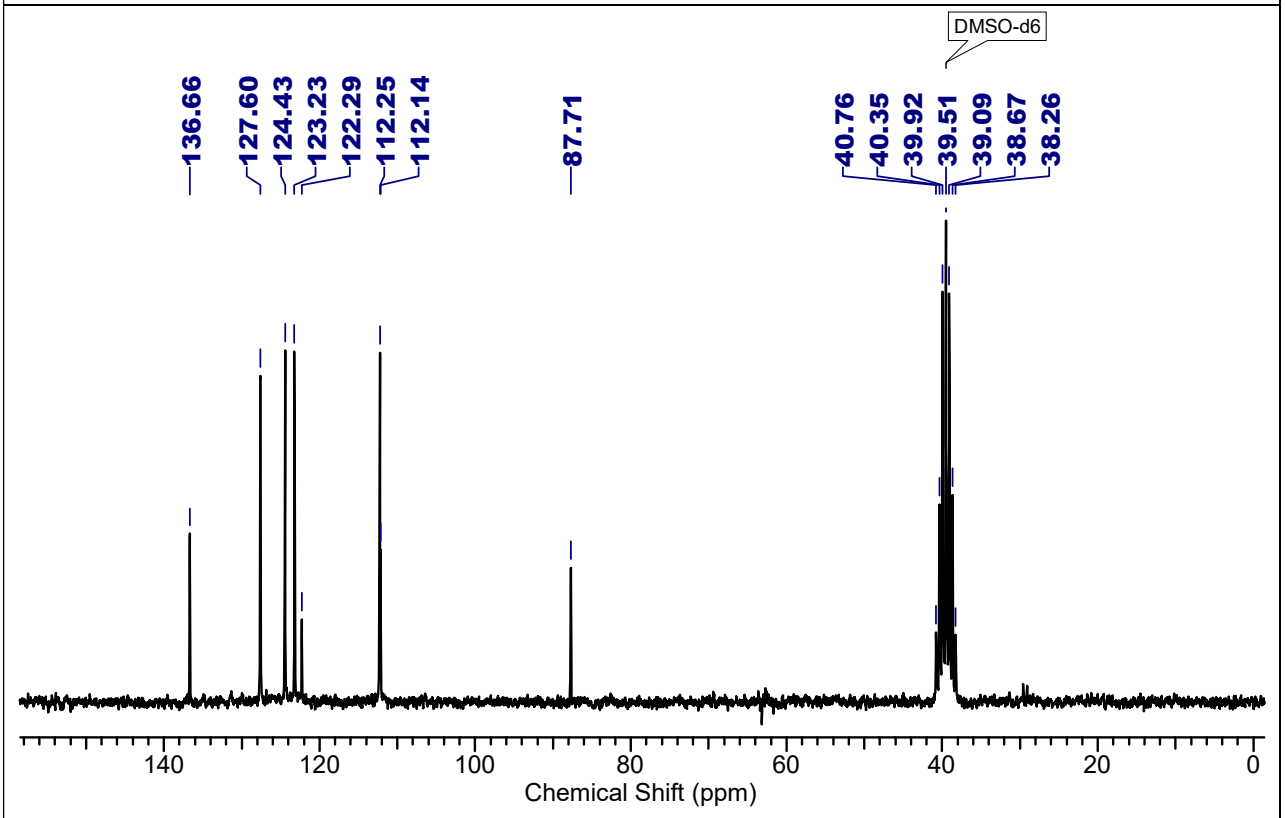
^{1}H and ^{13}C Spectra of 3-azido-5-bromo-1*H*-indole **(2d)**



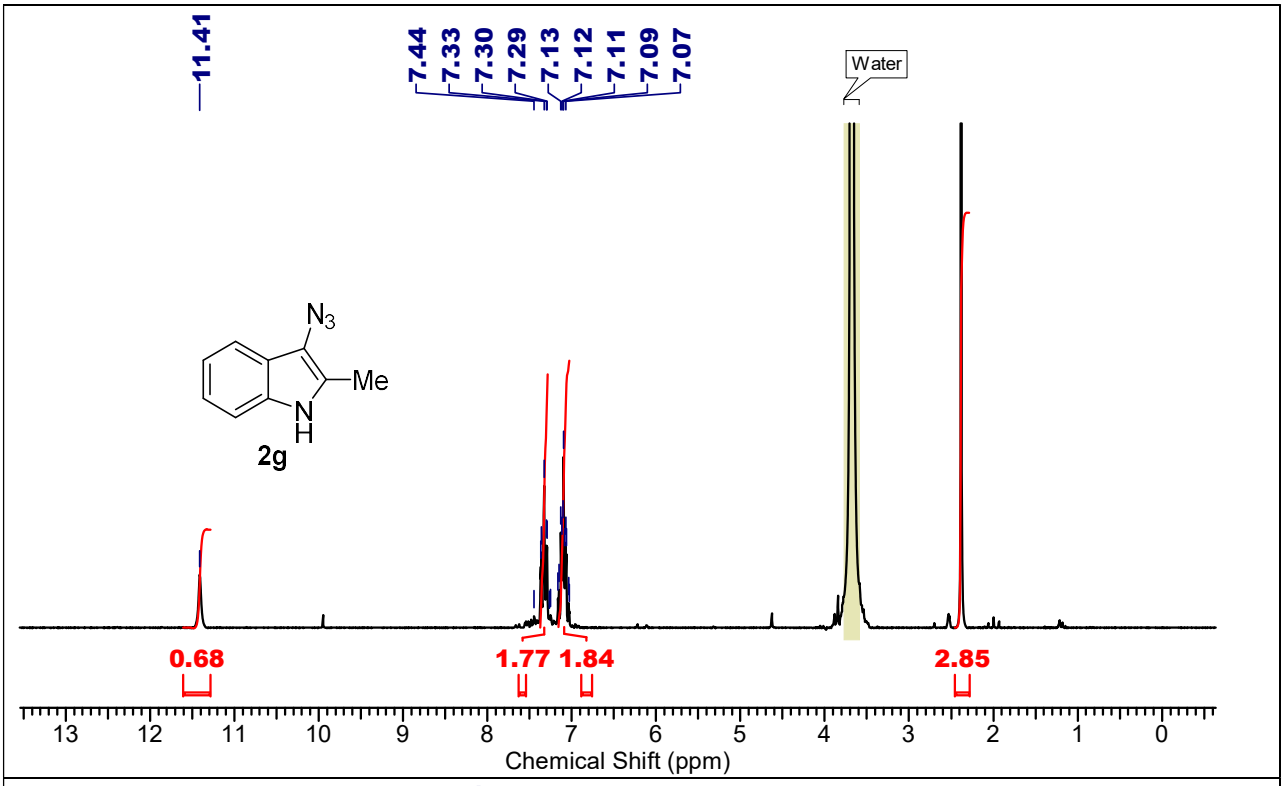


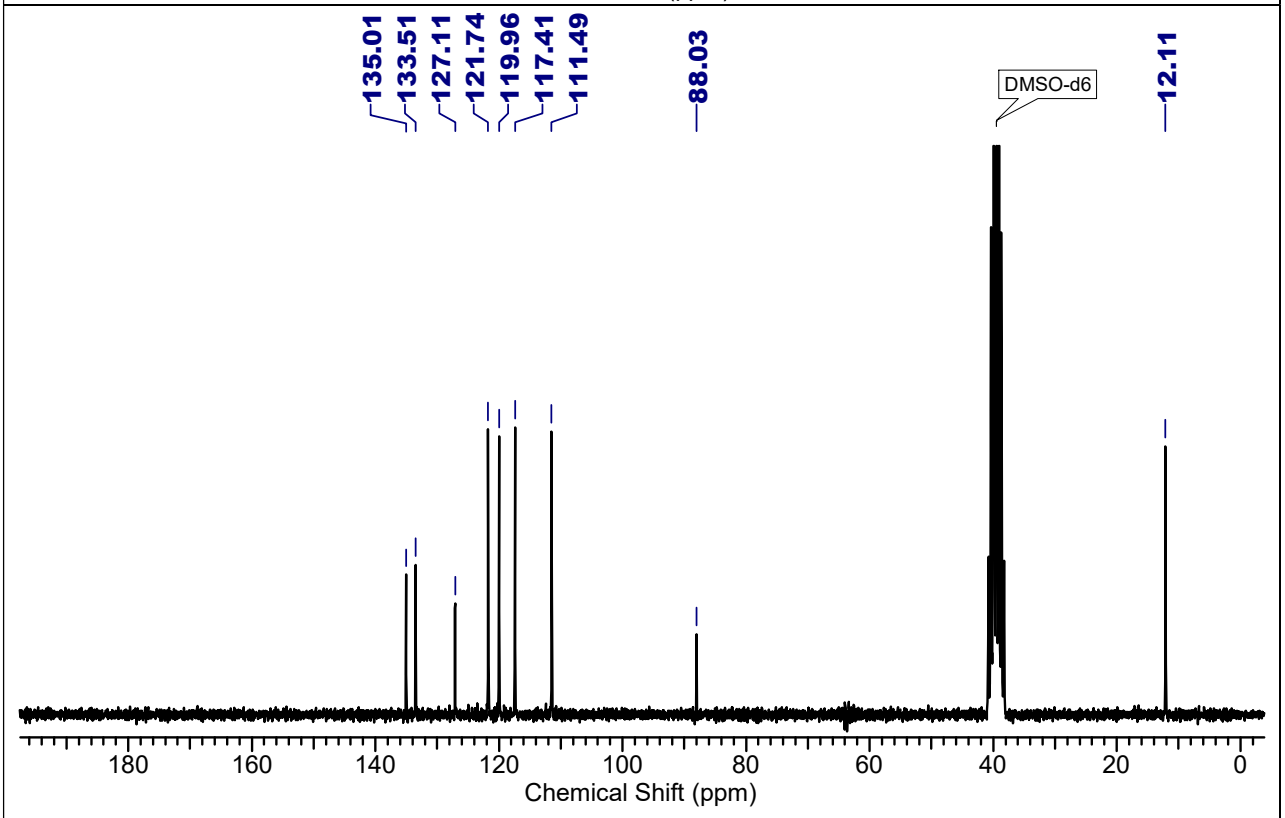
^{1}H and ^{13}C Spectra of 3-azido-5-chloro-1*H*-indole **(2e)**



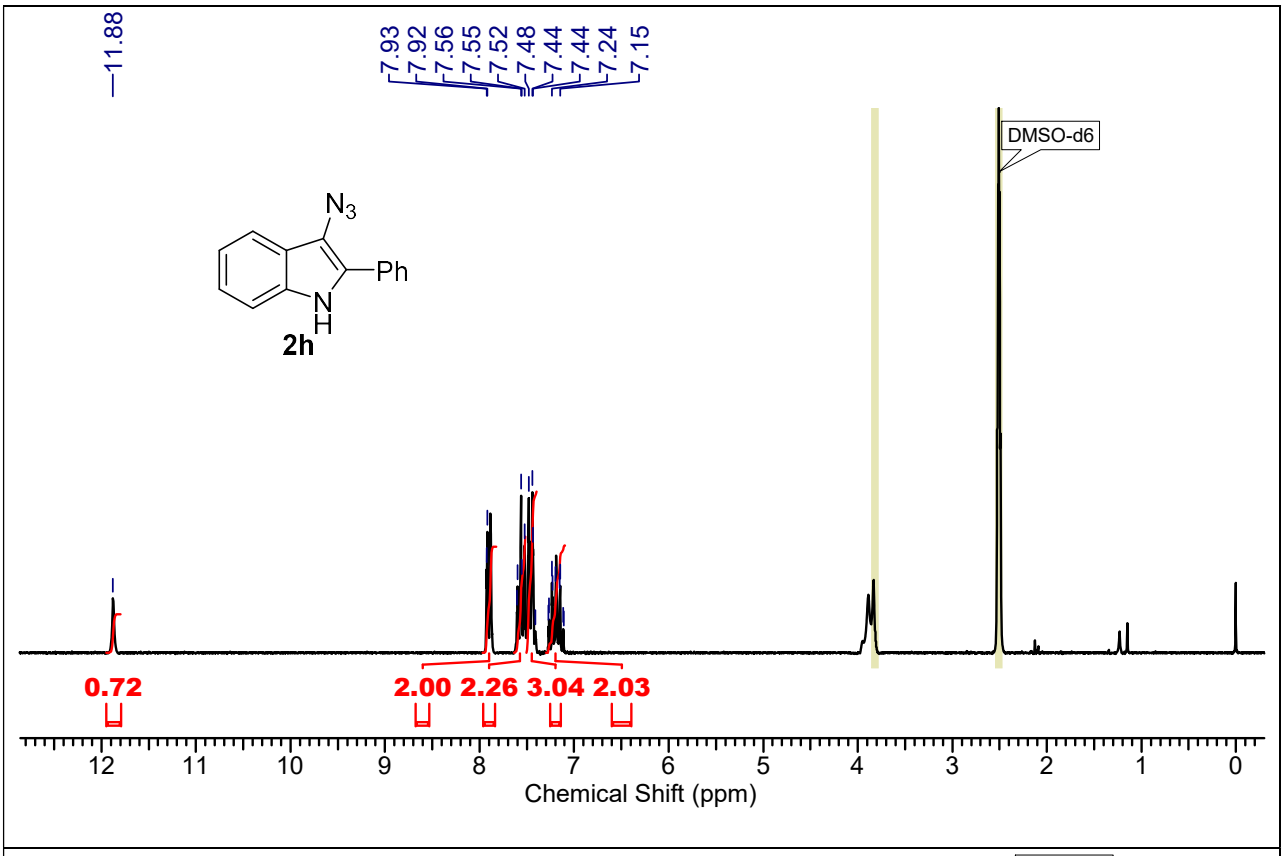


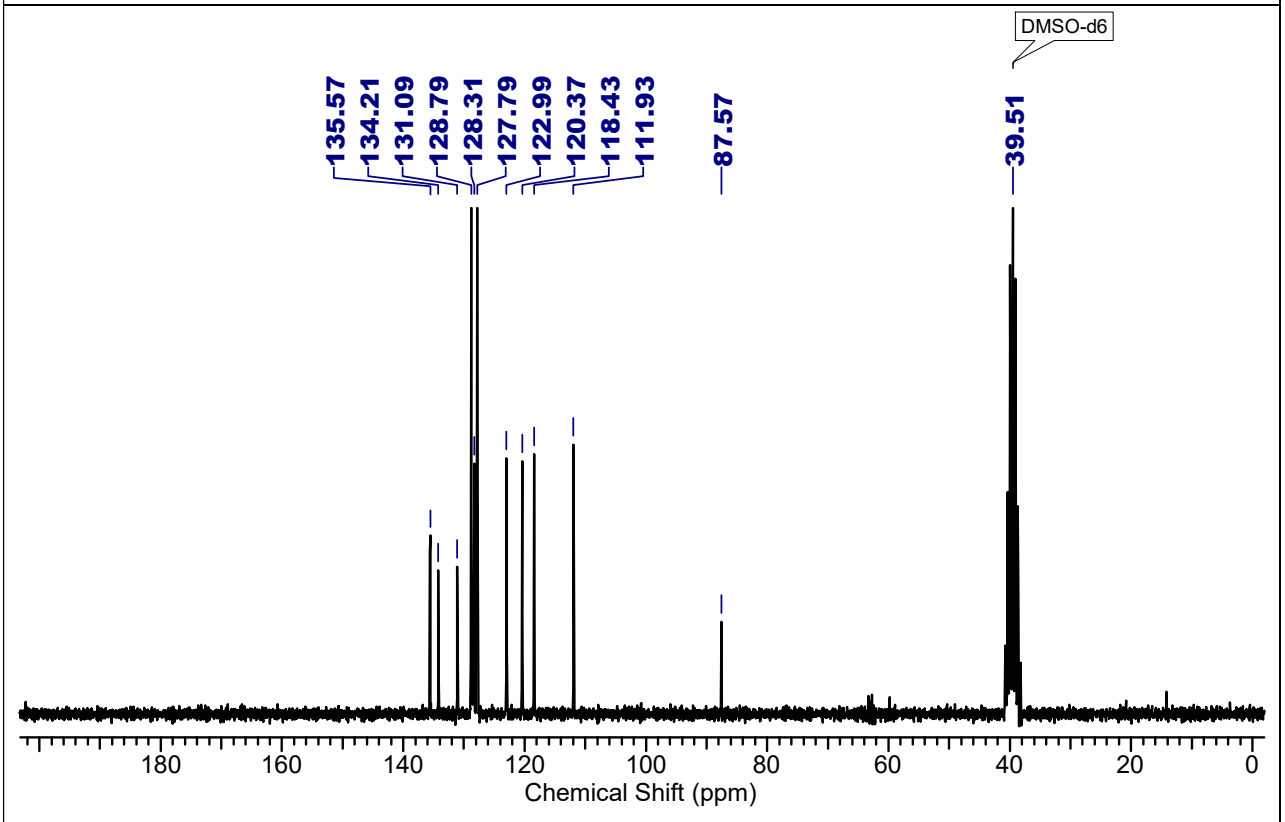
^{1}H and ^{13}C Spectra of 3-azido-4-bromo-1*H*-indole **(2f)**



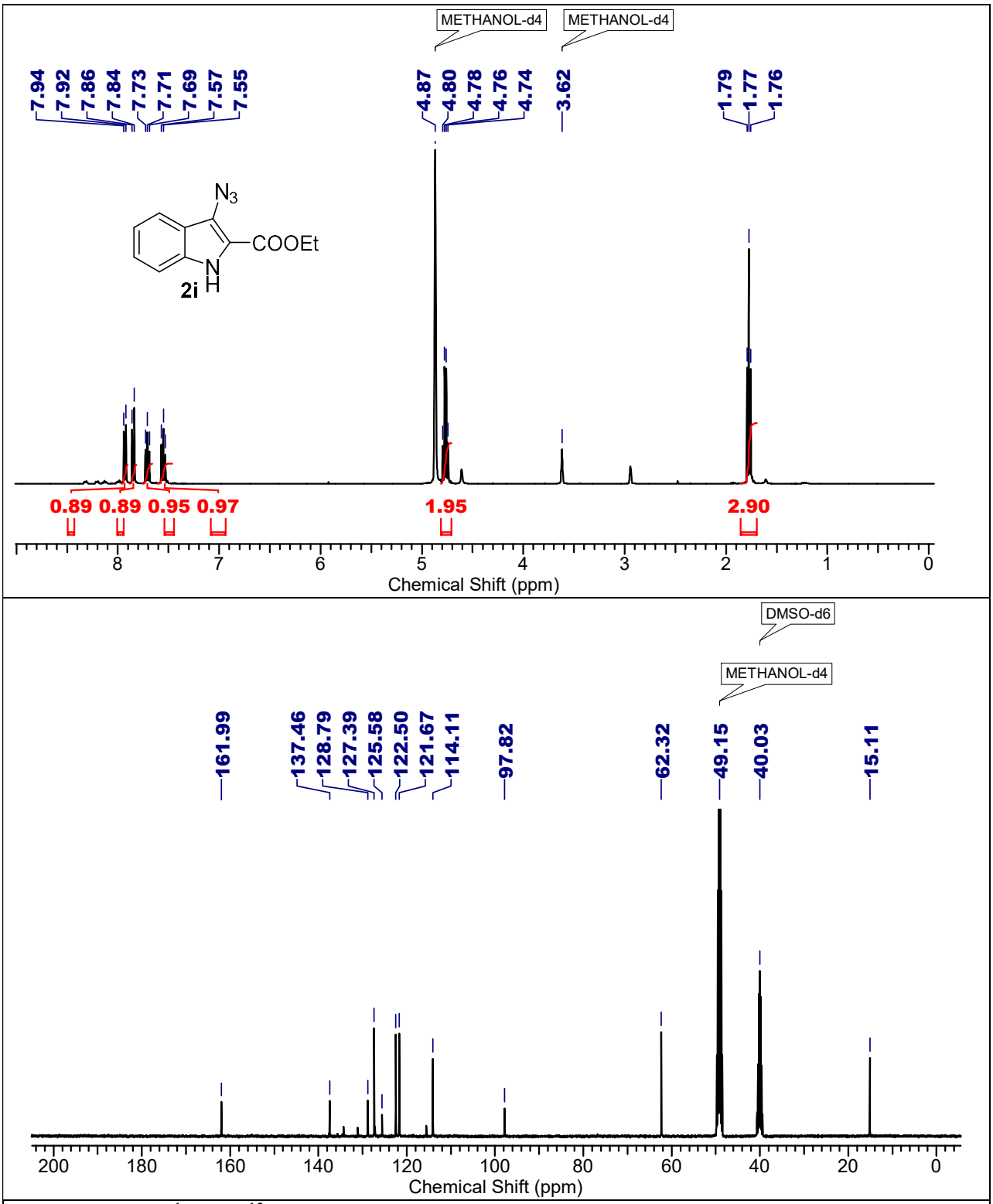


^{1}H and ^{13}C Spectra of 3-azido-2-methyl-1*H*-indole **(2g)**

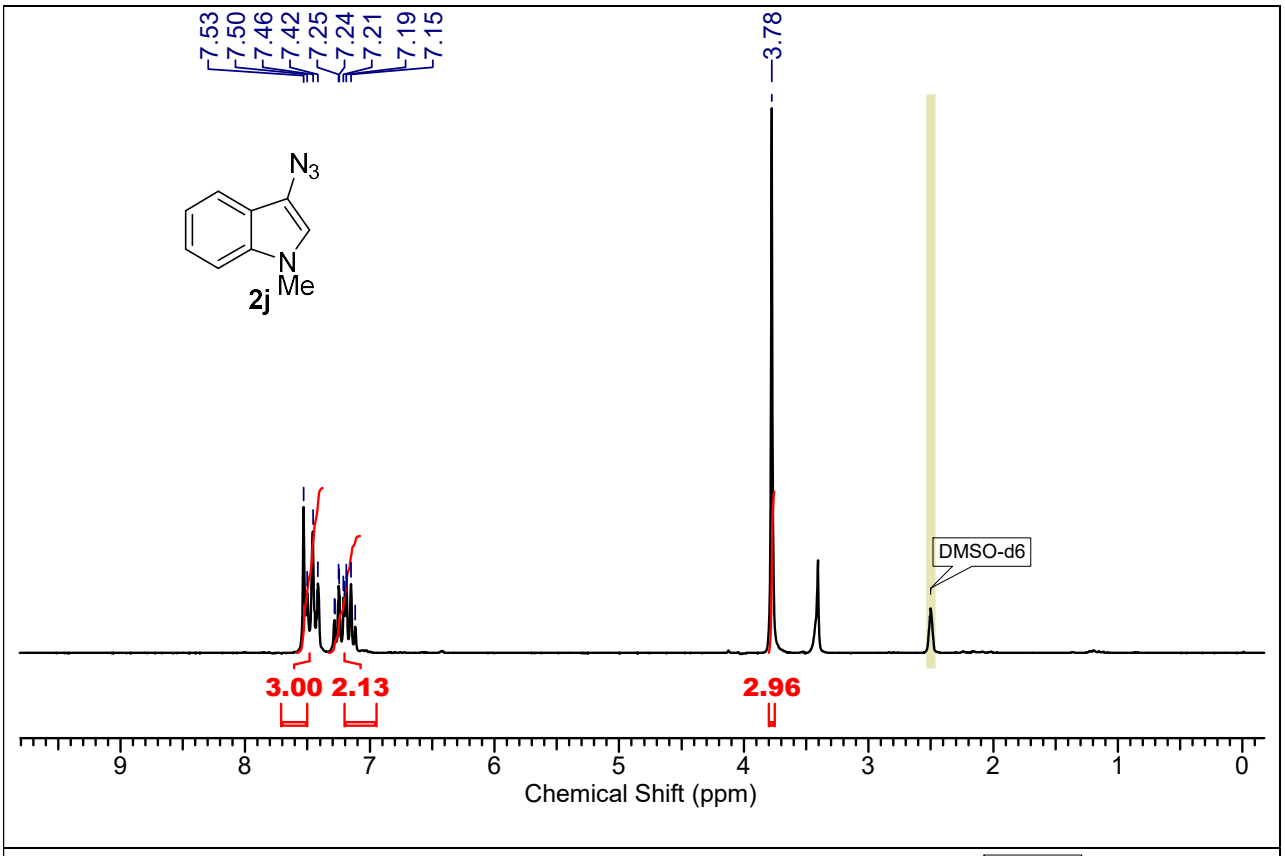


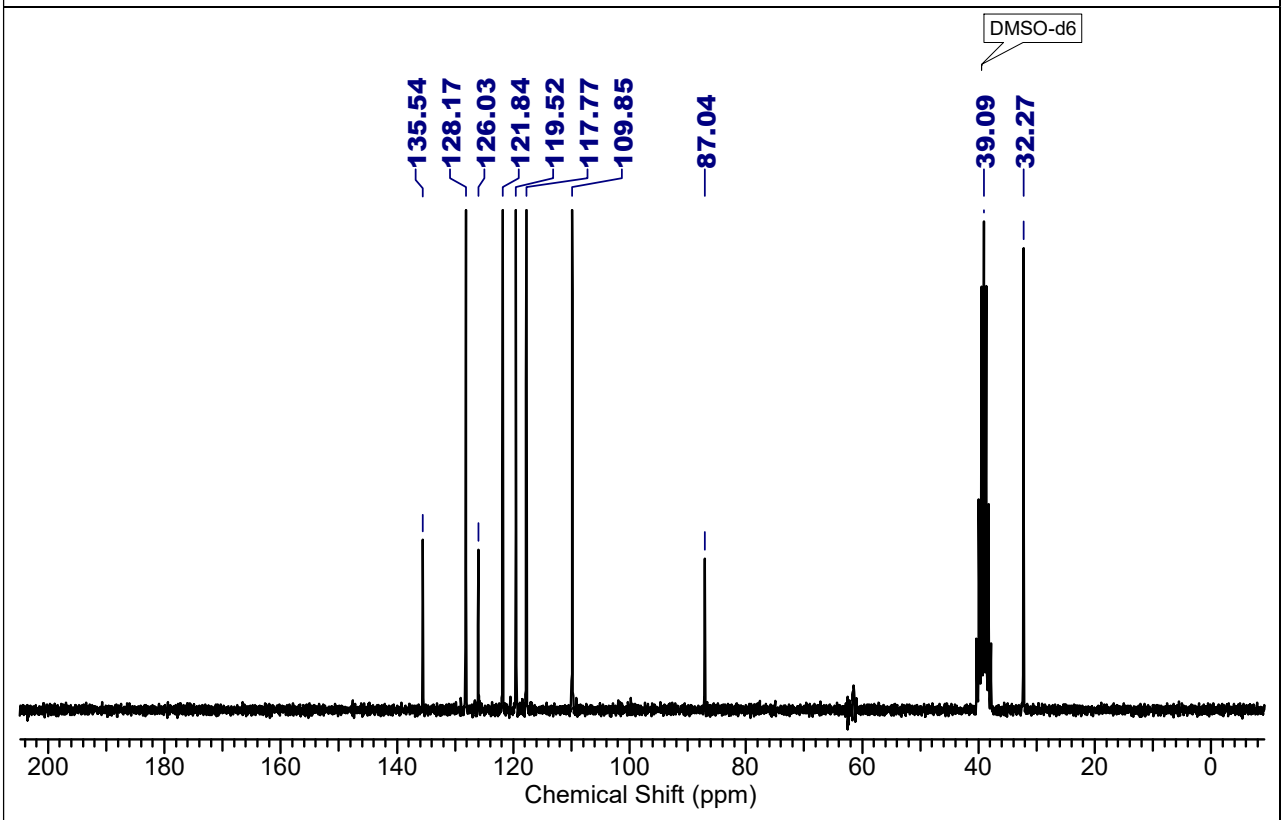


^{1}H and ^{13}C Spectra of 3-azido-2-phenyl-1*H*-indole **(2h)**

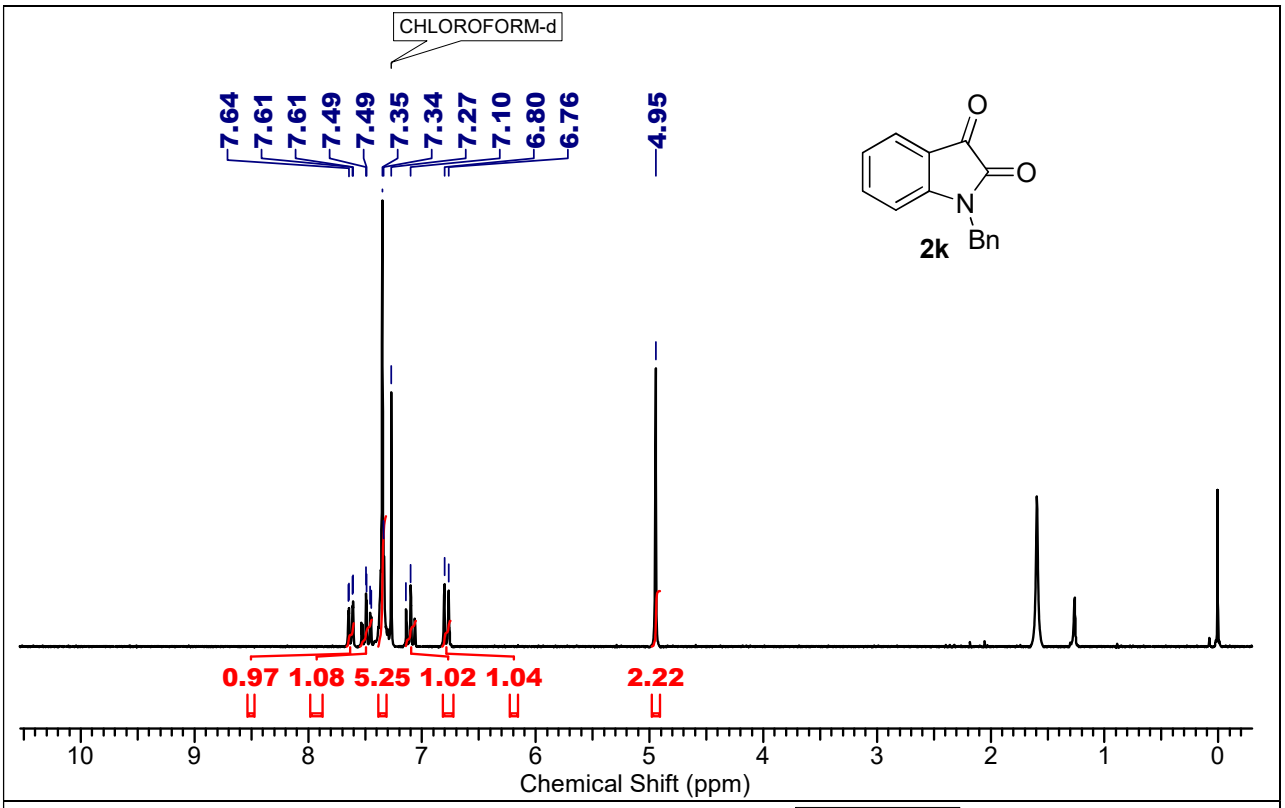


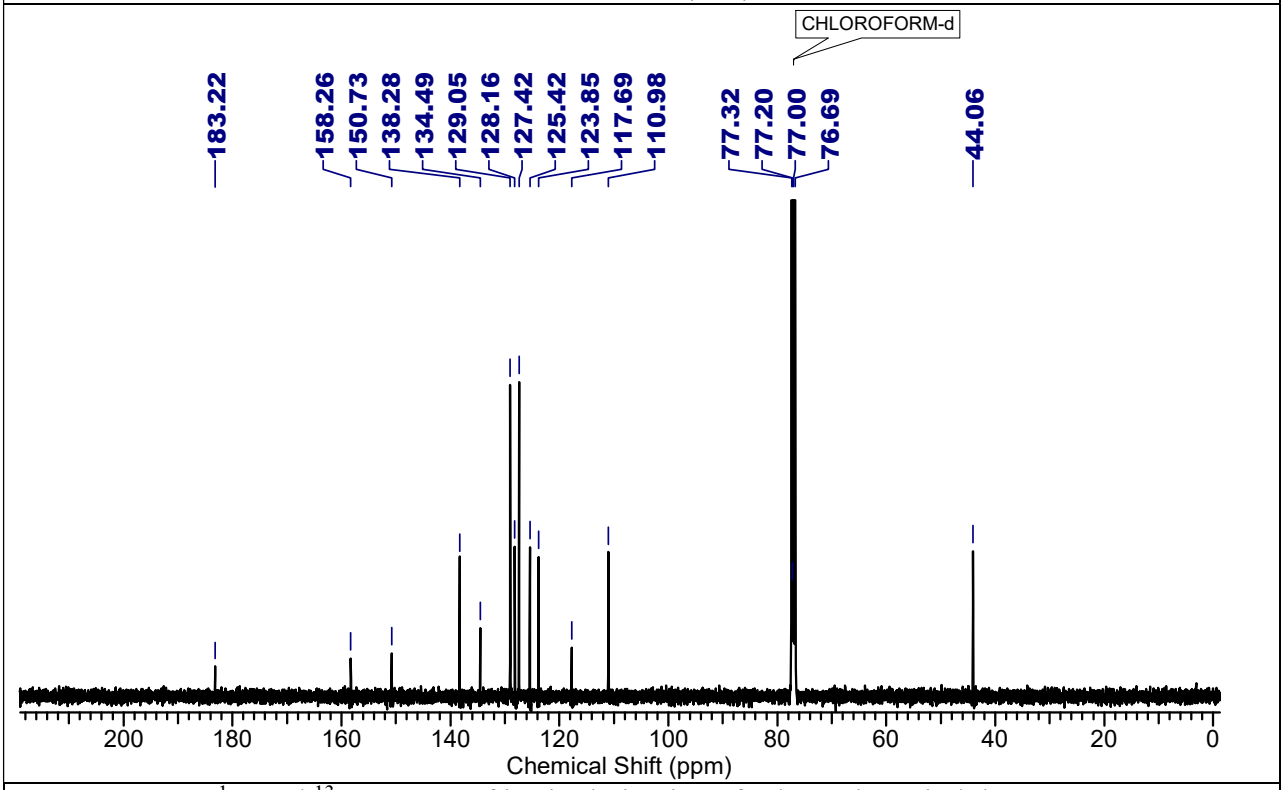
^{1}H and ^{13}C Spectra of ethyl 3-azido-1*H*-indole-2-carboxylate **(2i)**



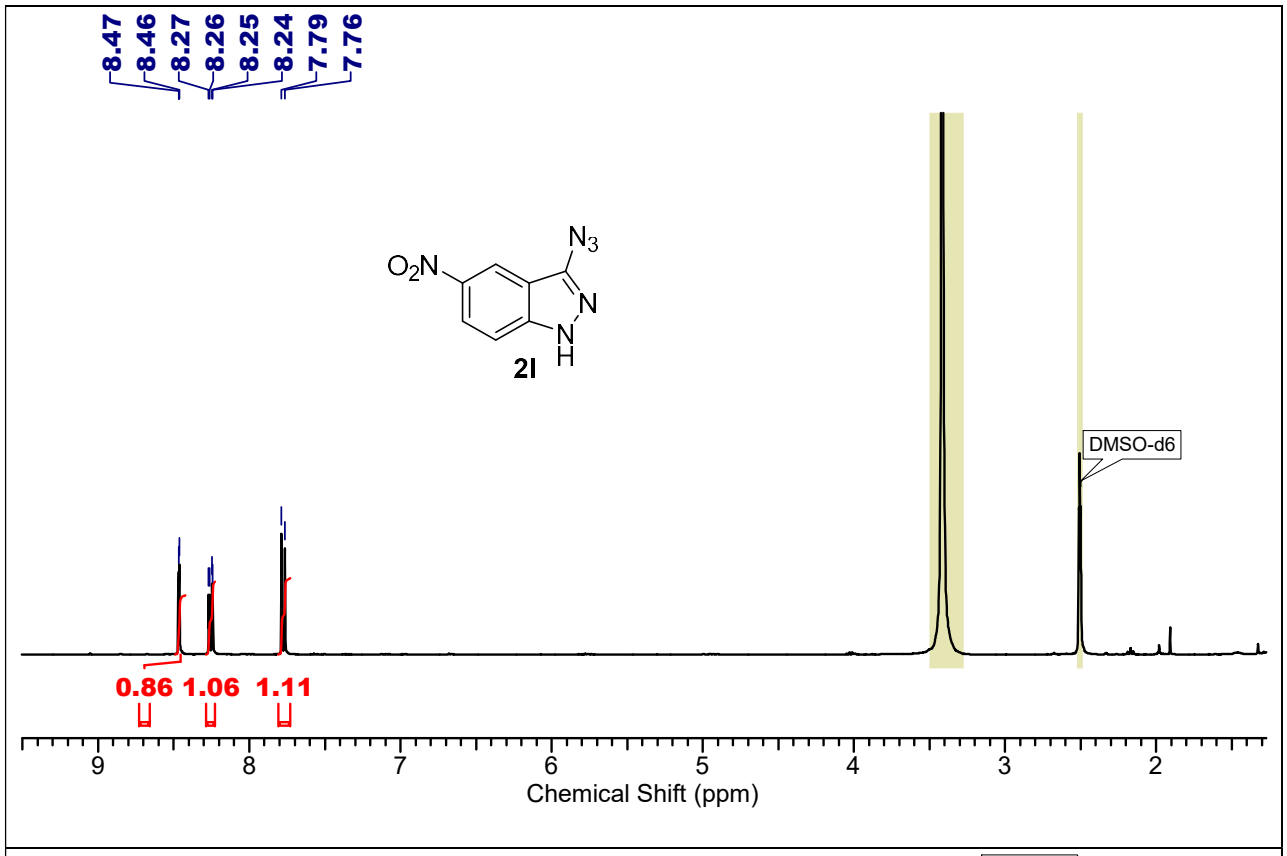


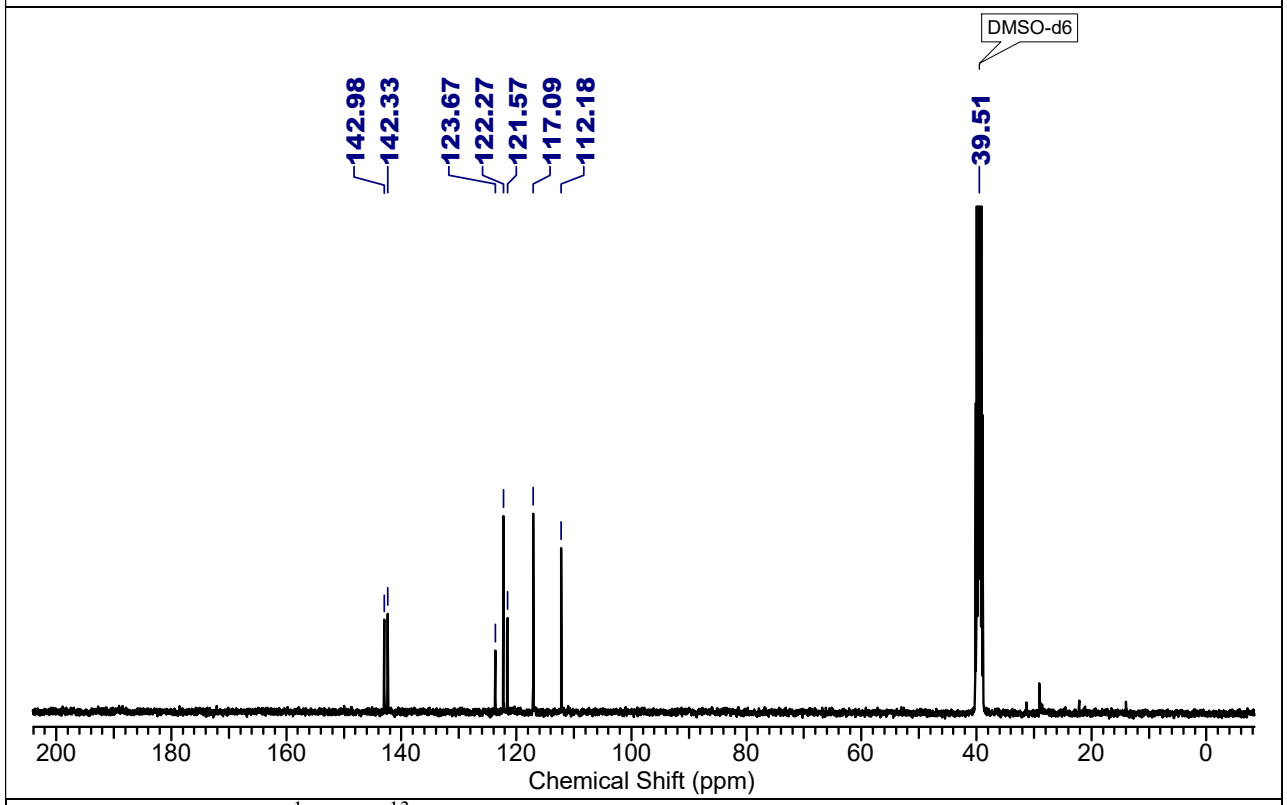
^{1}H and ^{13}C Spectra of 3-azido-1-methyl-1*H*-indole **(2j)**



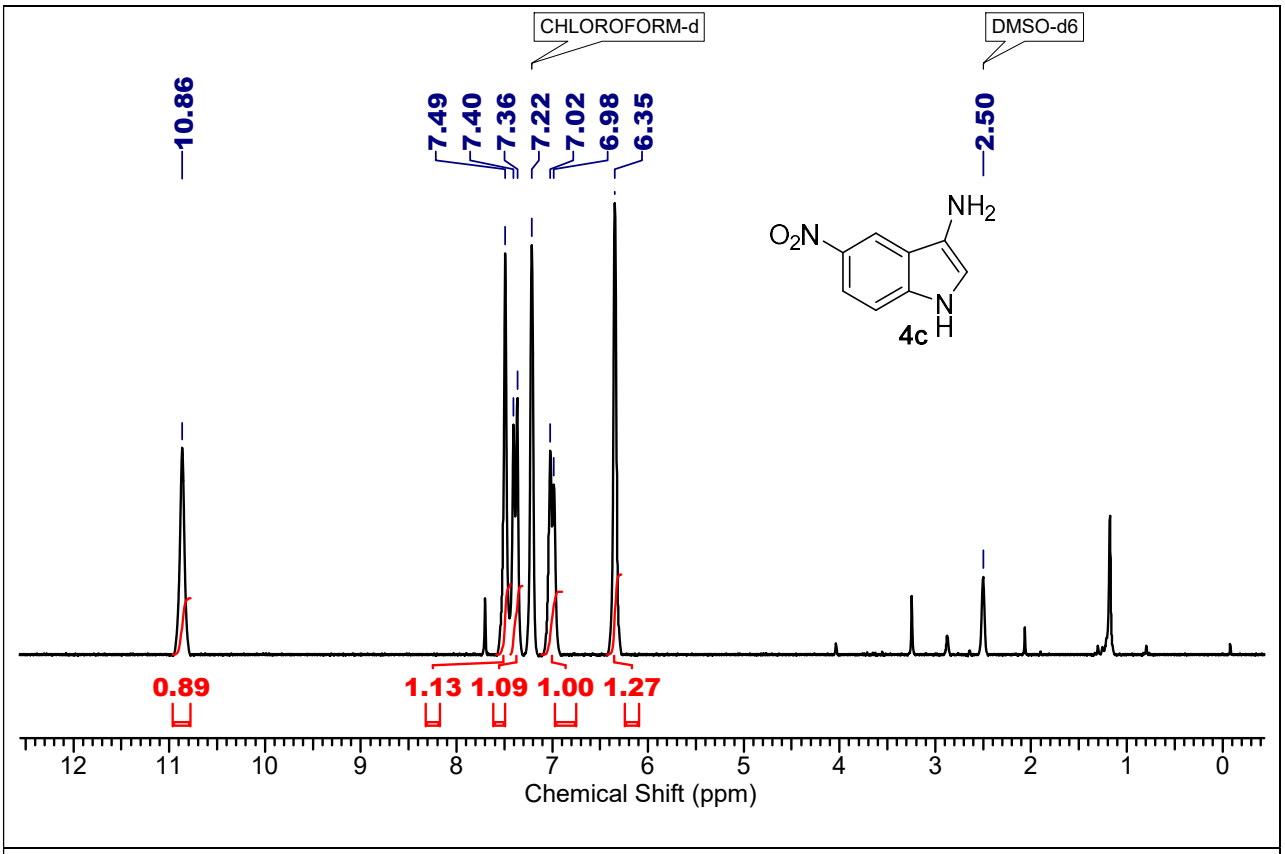


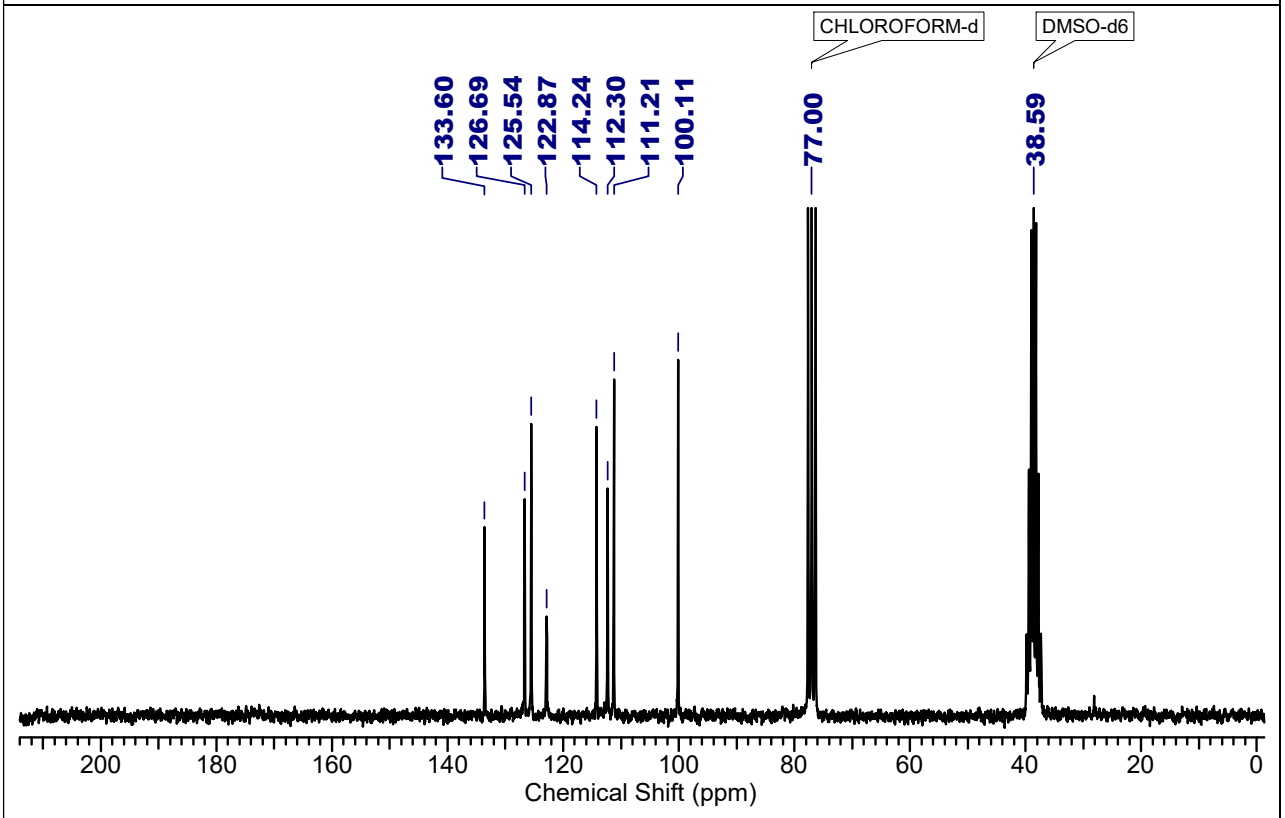
^{1}H and ^{13}C Spectra of isatin derivative of 1-benzyl-1*H*-indole **(2k)**



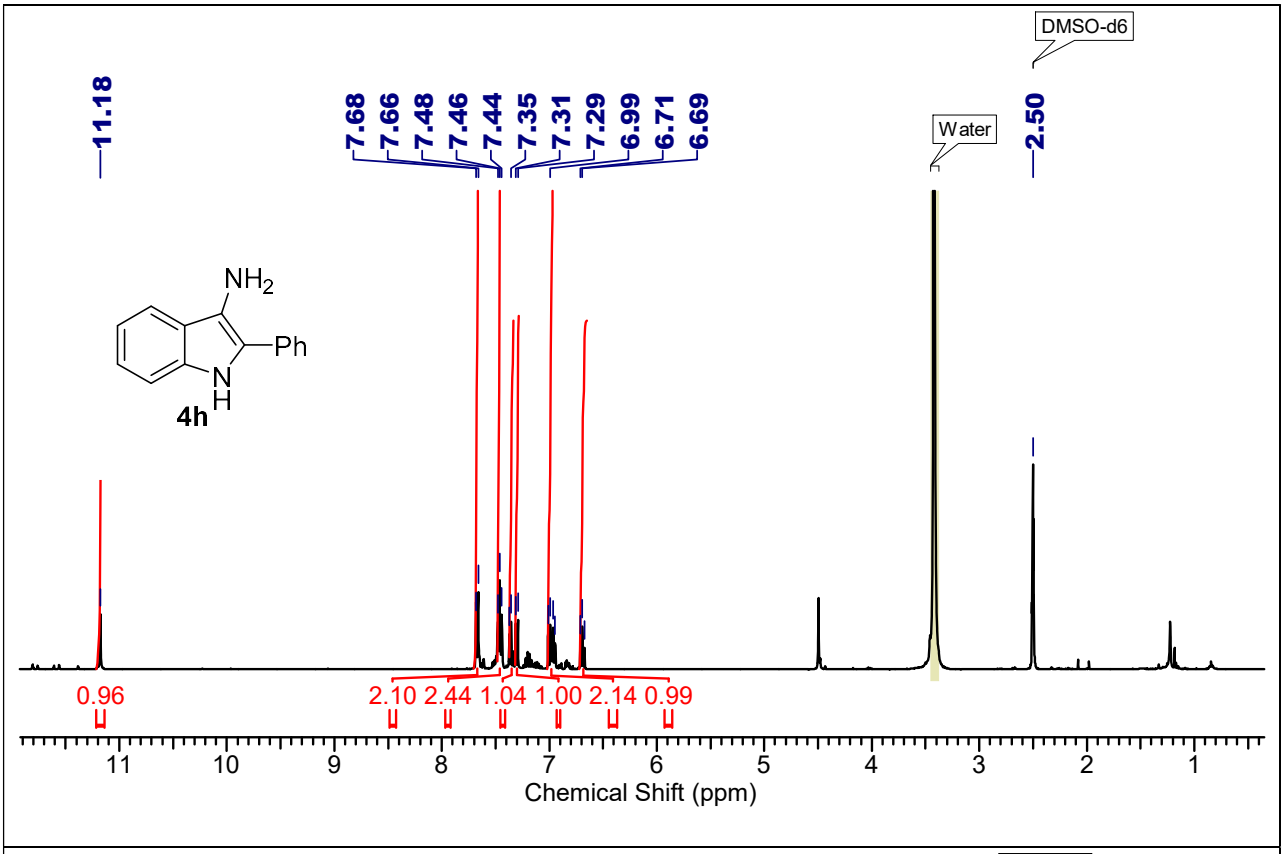


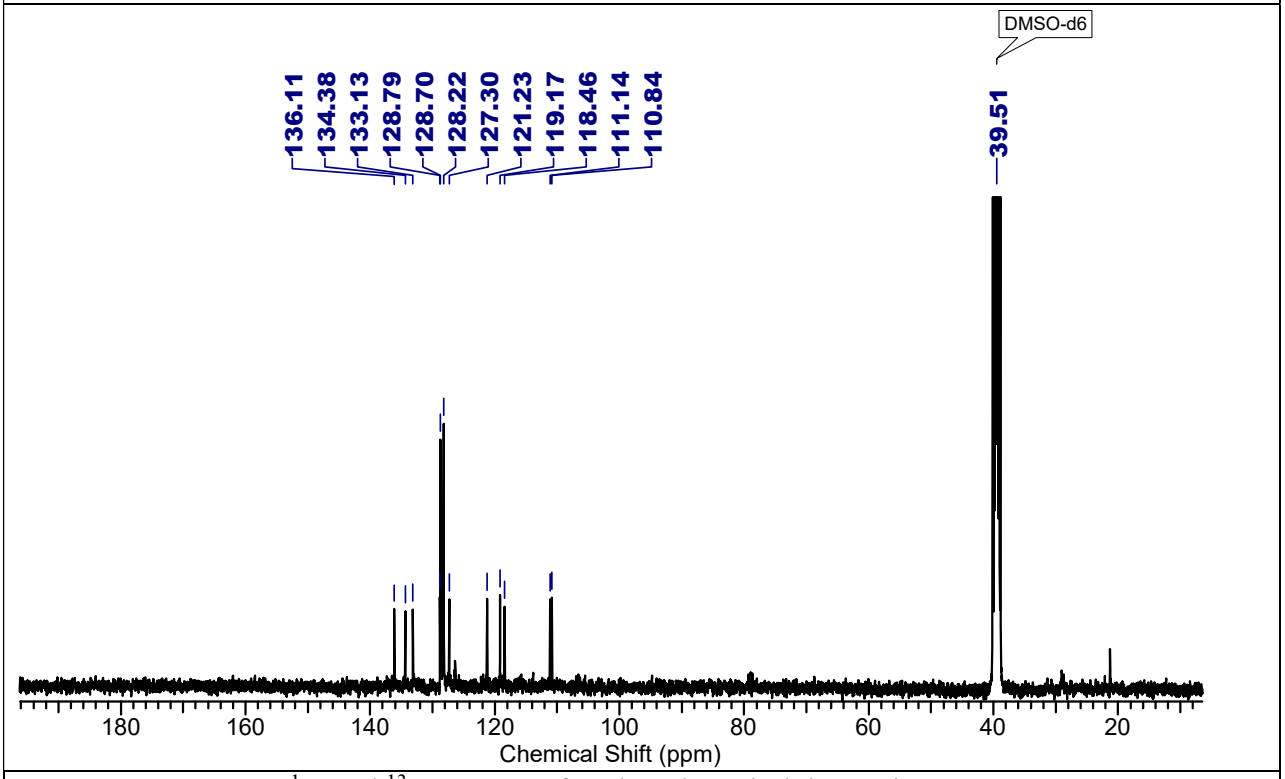
^{1}H and ^{13}C Spectra of 3-azido-5-nitro-1*H*-indazole **(2l)**



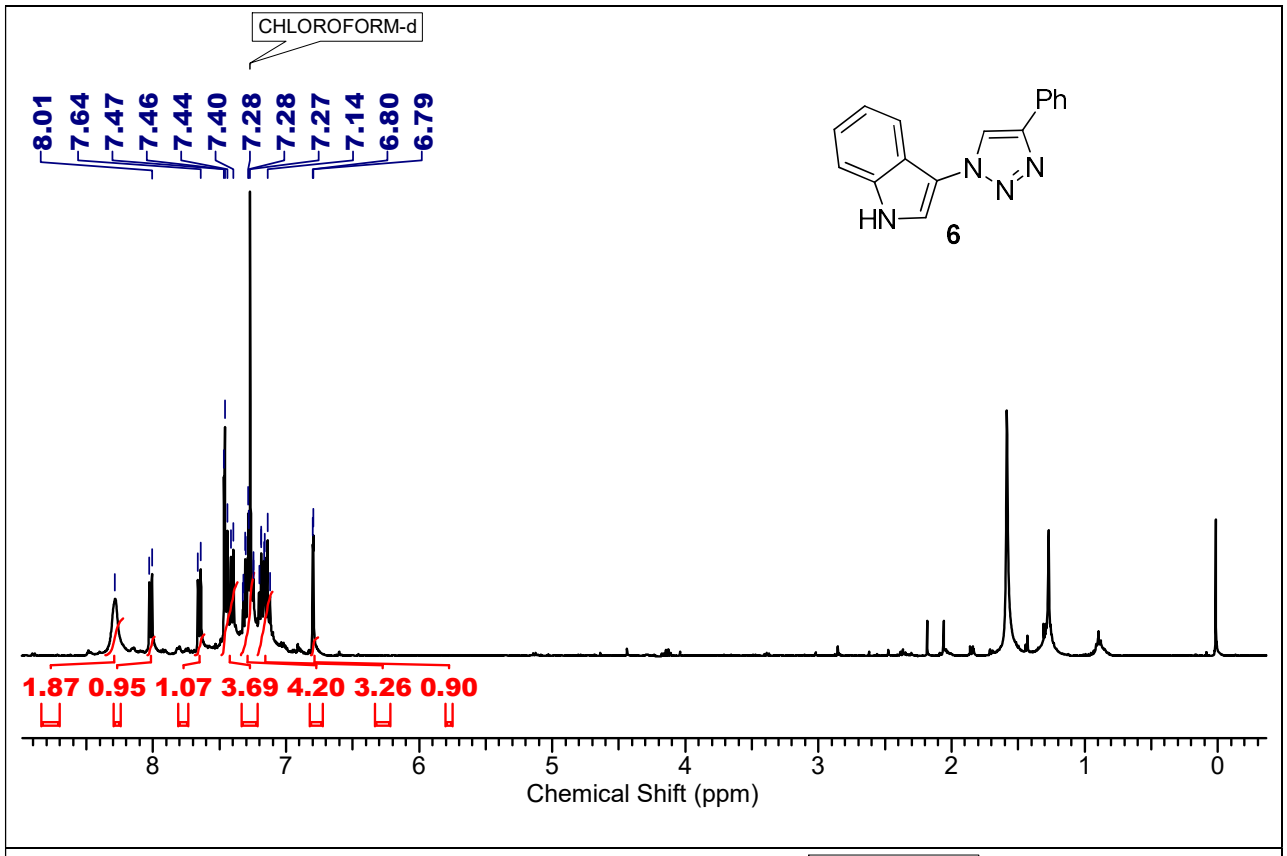


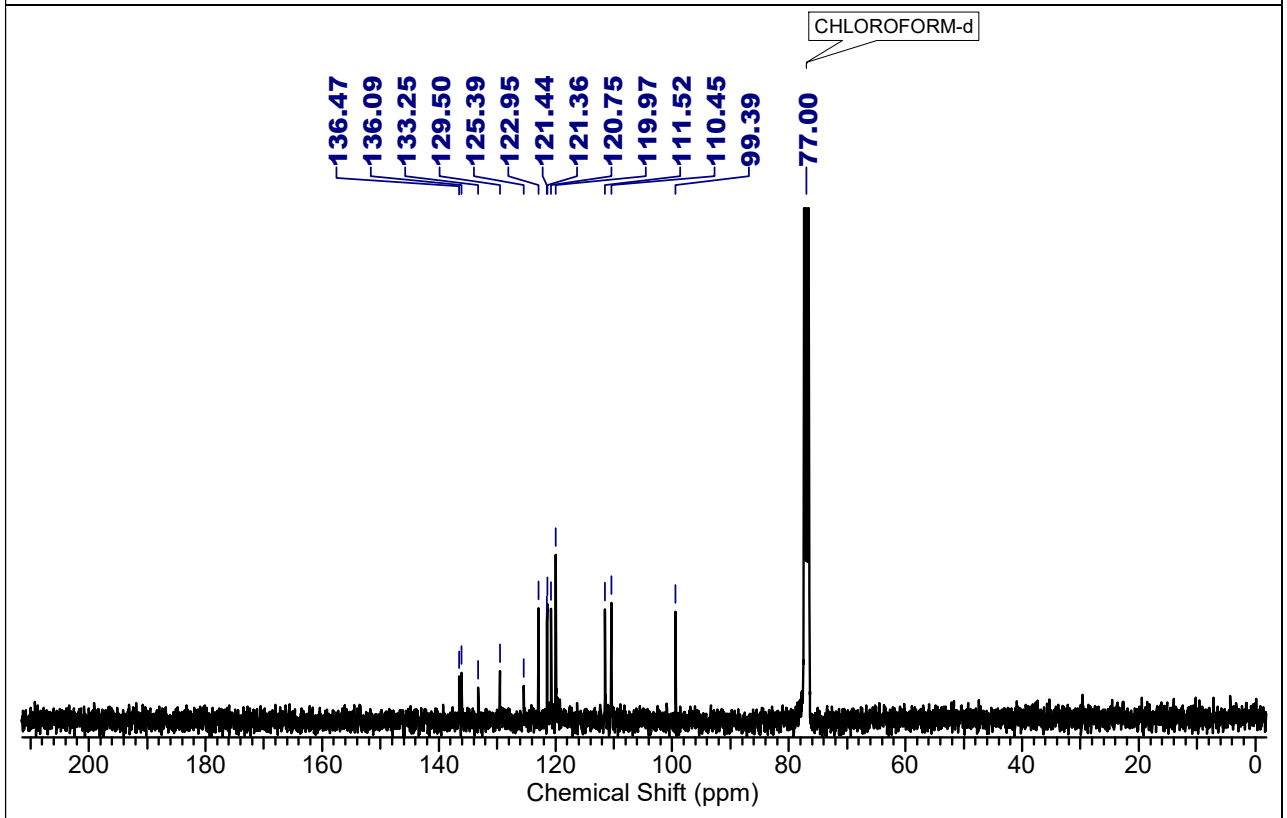
^{1}H and ^{13}C Spectra of 5-nitro-1*H*-indol-3-amine **(4c)**



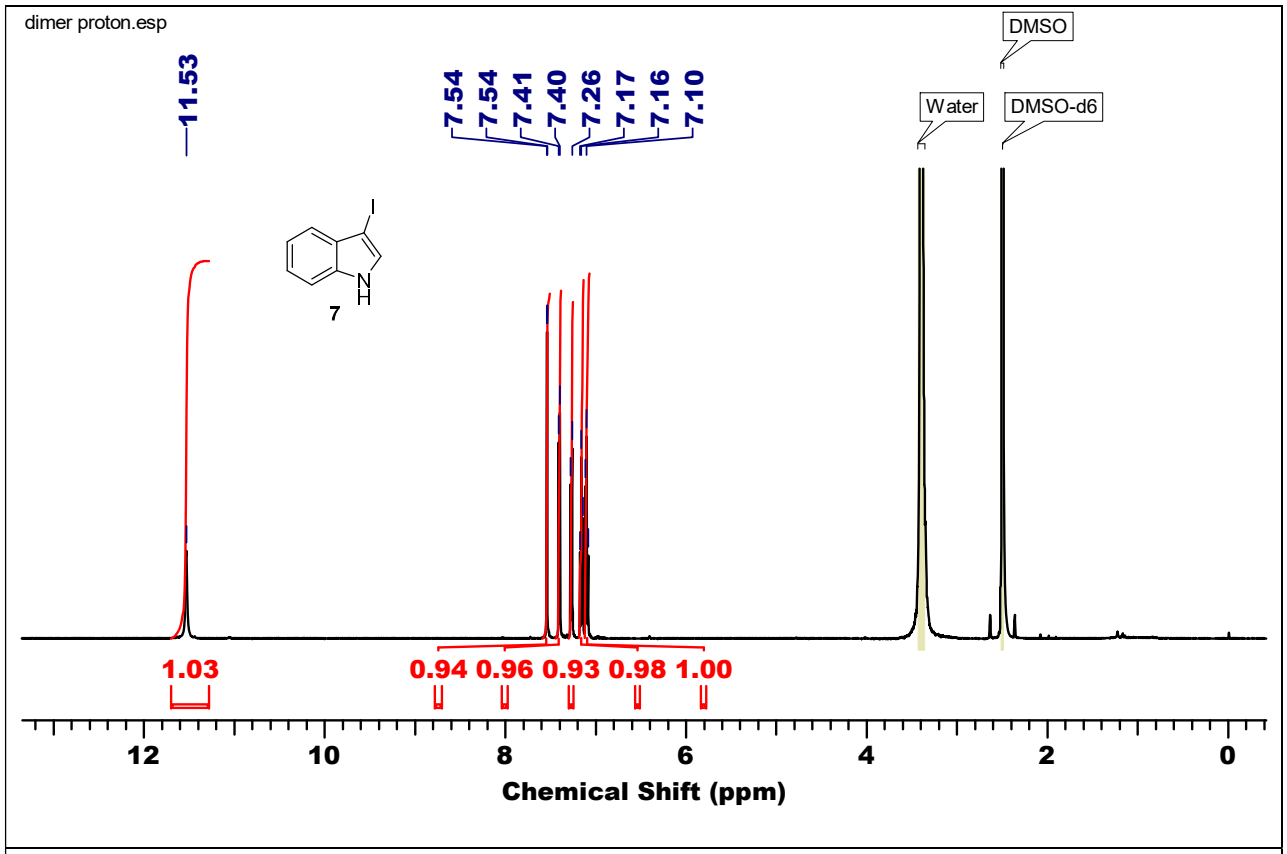


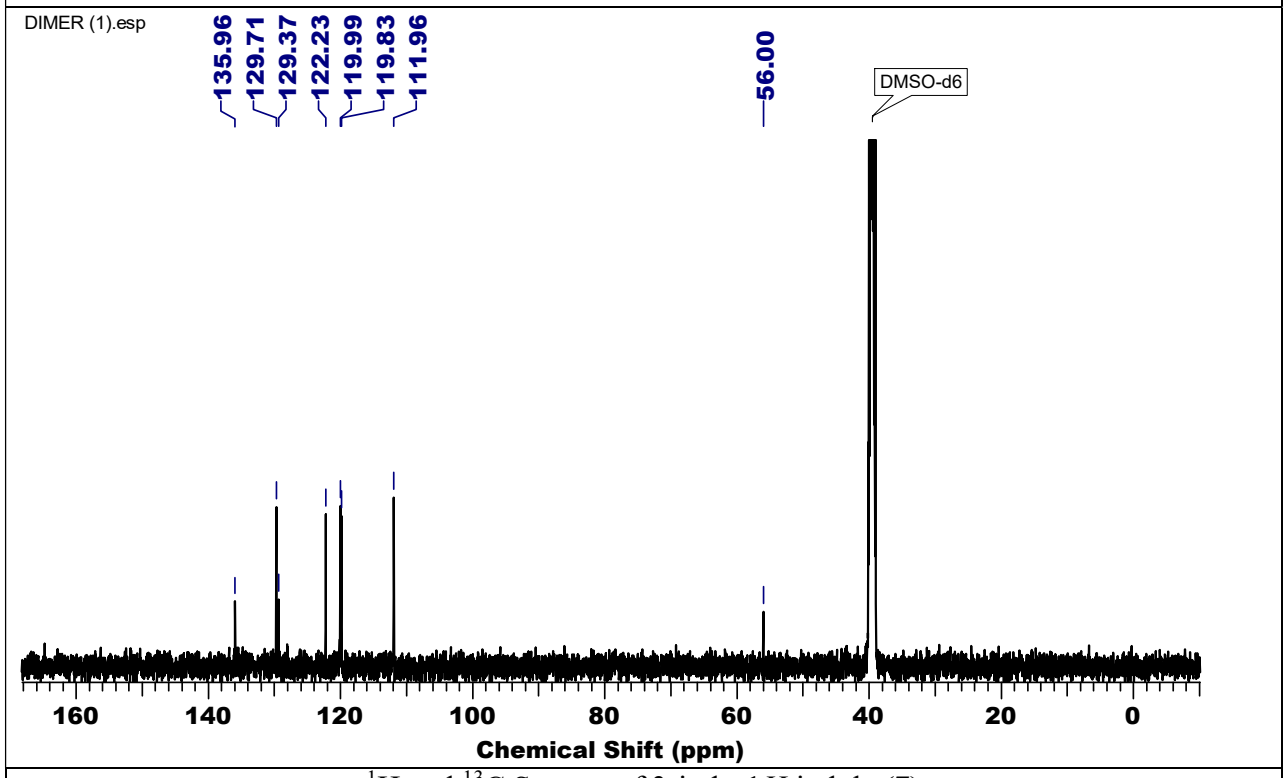
^{1}H and ^{13}C Spectra of 2-phenyl-1*H*-indol-3-amine **(4h)**





^{1}H and ^{13}C Spectra of 3-(4-phenyl-1H-1,2,3-triazol-1-yl)-1H-indole **(7)**





^{1}H and ^{13}C Spectra of 3-iodo-1*H*-indole **(7)**