# Palladium-Catalyzed Synthesis of 2-Cyanoindoles from 2-*gem*-Dihalovinylanilines

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**Supporting Information**

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# 1 General Considerations

Unless otherwise stated all reactions were run under an atmosphere of argon in oven or flame dried glassware. Catalytic reactions were run in 3-dram vials with open-top caps fitted with a Teflon septum. Reactions were monitored by thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 plates and visualized under UV light or by immersion in potassium permanganate ($KMnO_4$) stain. Flash column chromatography was performed on Silicycle 40-60 μm silica gel and in the case of 2-cyanoindoles, the silica was suspended in 5% $NEt_3$ in hexanes before loading the column. PhMe was distilled over CaH. DMA was purchased from Sigma-Aldrich in a Sure/Seal bottle and used without further purification. $Pd(t\text{-}Bu_3P)_2$ was purchased from Johnson Matthey. All reagents and organic building blocks were purchased from commercial supplier (Sigma Aldrich, Strem, Alfa Aesar, TCI, Combi-blocks) and used without further purification.

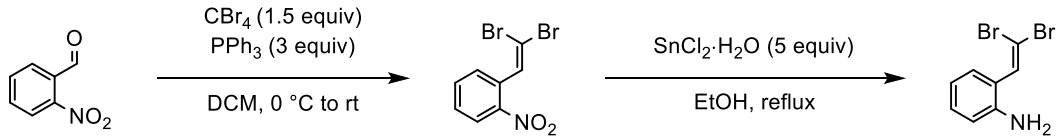
$^1H$ and $^{13}C$ NMR spectra were obtained on the Agilent DD2 500 equipped with a 5mm Xsens Cold Probe. The spectra were internally referenced to the solvent peak. $^{19}F$ NMR spectra were obtained on the Varian Mercury 400 or 500 operating at 470 or 564 MHz. Measurements were taken at 296 K and chemical shifts are reported in parts per million (ppm). Data is reported in the following format: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), integration. Melting points were measured on a Fisher-Johns Melting Point Apparatus and are uncorrected. High resolution mass spectra (HRMS) were obtained on a Micromass 70S-250 spectrometer (EI) or an ABI/Sciex QStar Mass Spectrometer (ESI) or a JEOL AccuTOF model JMS-T1000LC mass spectrometer equipped with an IONICS® Direct Analysis in real Time (DART) ion source.

# 2 Synthesis of 2-*gem*-Dihalovinylanilines

## 2.1 Synthetic Remarks

Compounds **1a-d**, **1f**, **1g**, **1i**, **1j**, **1m**, and **1n** were synthesized according to literature procedure.[1] Compound **1e** was synthesized according to literature procedure.[2] Compound **1k** and **1p** were synthesized according to literature procedure.[3] Compound **1o** was synthesized according to literature procedure.[4] Compound **1q** was synthesized according to literature procedure.[5] In all cases, spectral data matched literature reports.

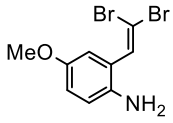
## 2.2 General Procedure for 2-*gem*-Dihalovinylanilines



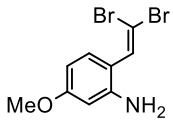

To a solution of nitrobenzaldehyde (9.07 g, 60 mmol, 1 equiv) and $CBr_4$ (29.85 g, 90 mmol, 1.5 equiv) in DCM (300 ml, 0.2 M with respect to the aldehyde) at 0 °C was added a solution of $PPh_3$ (47.21 g, 180 mmol, 3 equiv) in

DCM (200 ml, 0.9 M) dropwise over a 30-minute period, maintaining the temperature under 5 °C. The reaction was stirred for 30 min before warming to rt, and stirred for an additional 30 min. Consumption of the starting material was monitored by TLC. The reaction was filtered through a short pad of silica gel, eluting with 10% EtOAc in hexanes until all product was collected as monitored by TLC to reduce the amount of triphenylphosphine oxide present. The crude was concentrated to an oil, taken up into EtOH (200 ml, 0.3 M) and was added $SnCl_2 \cdot H_2O$ (67.7 g, 300 mmol, 5 equiv). The reaction was refluxed at 90 °C for 45 min, cooled, and was basified using $K_2CO_3$ to pH 10. The aqueous layer was extracted 5 times with EtOAc, and the organic layer was washed with $H_2O$, brine and dried over $Na_2SO_4$. The product was purified by silica gel flash chromatography.

### 2.3 Experimental and Characterization Data



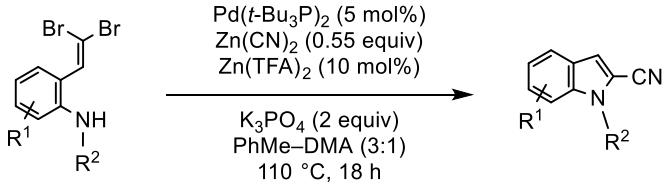

**2-(2,2-dibromovinyl)-4-methoxyaniline (1h) –** The compound was synthesized according to General Procedure A using 5.4 mmol of the aldehyde. The product was purified by flash chromatography using hexanes–EtOAc (5:1, v:v) as the mobile phase and was isolated as an off-white solid (901.1 mg, 2.935 mmol, 76%, mp = 66-67 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.35 (s, 1H), 6.91 (d, *J* = 2.9 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.67 (d, *J* = 8.6 Hz, 1H), 3.76 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 152.4, 137.1, 133.9, 122.8, 117.4, 116.2, 113.8, 92.7, 55.8. **IR** (thin film, $cm^{-1}$) 3439, 3360, 2996, 2947, 2907, 2830, 1609, 1497, 1464, 1427. **HRMS** (DART, M+1) Calculated for $C_9H_{10}Br_2NO$ 305.9129, found 305.9126.




**2-(2,2-dibromovinyl)-5-methoxyaniline (1l) –** The compound was synthesized according to General Procedure A using 3.84 mmol of the aldehyde. The product was purified by flash chromatography using hexanes–EtOAc (9:1, v:v) as the mobile phase and was isolated as an off-white solid (949 mg, 3.09 mmol, 58%, mp = 59-60 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.44 – 6.99 (m, 2H), 6.37 (d, *J* = 8.7 Hz, 1H), 6.21 (s, 1H), 3.97 – 3.55 (m, 5H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 160.6, 145.1, 133.3, 130.1, 114.4, 104.1, 100.6, 91.0, 54.9. **IR** (thin film, $cm^{-1}$) 3464, 3377, 3207, 2997, 2959, 2936, 2835, 1612, 1566, 1462. **HRMS** (DART, M+1) Calculated for $C_9H_{10}Br_2NO$ 305.9129, found 305.9127.

## 3 Palladium-Catalyzed Synthesis of 2-Cyanoindoles

### 3.1 General Procedure for Substrate Scope



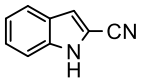

To an oven dried 3-dram vial, substrate (0.5 mmol, 1 equiv), $Zn(CN)_2$ (32.3 mg, 0.275 mmol, 0.55 equiv), $Zn(TFA)_2$ (14.6 mg, 0.05 mmol, 10 mol %), and $K_3PO_4$ (212.3 mg, 1 mmol, 2 equiv) were added. After the vial was purged with Ar for 5 min, 1 ml of PhMe and 1 ml of DMA was added. To a second oven dried vial, Pd(*t*-$Bu_3P)_2$

(12.8 mg, 0.025 mmol, 5 mol %) was added and purged with Ar for 5 min. The catalyst was dissolved in 2 ml of PhMe and the solution was transferred to the substrate mixture. The reaction was stirred at 1000 rpm and 110 °C for 18 h. The reaction contents were transferred into a separatory funnel, diluted in EtOAc, and the organic phase was washed multiple times with water and brine. The organic layer was concentrated, and the product was purified by silica gel flash chromatography. It was necessary to let the silica stand in 5% $NEt_3$ in hexanes before loading the column to achieve better separation and prevent minor decomposition.

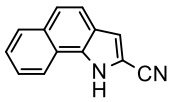
### 3.2 Procedure for 1 mmol Scale Reaction:

To an oven dried vial, substrate (1 mmol, 1 equiv), $Zn(CN)_2$ (64.6 mg, 0.55 mmol, 0.55 equiv), $Zn(TFA)_2$ (29.1 mg, 0.1 mmol, 10 mol %), and $K_3PO_4$ (424.5 mg, 2 mmol, 2 equiv) were added. After the vial was purged with Ar for 5 min, 2 ml of PhMe and 2 ml of DMA was added. To a second oven dried vial, Pd(*t*-$Bu_3P)_2$ (25.6 mg, 0.05 mmol, 5 mol %) was added and purged with Ar for 5 min. The catalyst was dissolved in 4 ml of PhMe and the solution was transferred to the substrate mixture. The reaction was stirred at 1000 rpm and 110 °C for 18 h. The reaction contents were transferred into a separatory funnel, diluted in EtOAc, and the organic phase was washed multiple times with water and brine. The organic layer was concentrated, and the product was purified by silica gel flash chromatography. It was necessary to let the silica stand in 5% $NEt_3$ in hexanes before loading the column to achieve better separation and prevent minor decomposition.

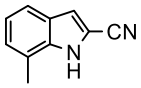
### 3.3 Experimental and Characterization Data



**1*H*-indole-2-carbonitrile (2a) –** The compound was synthesized according to General Procedure B. The product was purified by flash chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as a white solid (**0.5 mmol scale:** 52.6 mg, 0.37 mmol, 74%, **1 mmol scale**: 202.2 mg, 0.73 mmol 73%, mp = 94-95 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 7.68 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.50 – 7.34 (m, 2H), 7.25 – 7.16 (m, 2H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 137.1, 126.4, 126.3, 122.2, 121.8, 114.6, 114.5, 111.9, 106.2. **IR** (thin film, $cm^{-1}$) 3131, 3078, 3051, 2974, 2926, 2236, 1653, 1558, 1522, 1410, 1348. **HRMS** (DART, M+1) Calculated for $C_9H_7N_2$ 143.0609, found 143.0607.

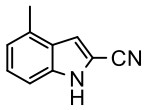


**1*H*-benzo[*g*]indole-2-carbonitrile (2b) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as an off-white solid (71.0 mg, 0.37 mmol, 74%, 237-240 °C). **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 13.28 (s, 1H), 8.39 (ddt, *J* = 8.2, 1.4, 0.8 Hz, 1H), 7.98 (ddt, *J* = 8.0, 1.3, 0.5 Hz, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.64 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.48 (s, 1H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 133.0, 131.4, 128.6, 126.3, 125.9, 122.3, 122.2, 121.5, 121.2, 120.5, 114.9, 114.4, 103.8. 3316, 3080, 3051, 3001, 2214, 1535, 1450. **IR** (thin film, $cm^{-1}$) 3316, 3080, 3051, 3001, 2214, 1535, 1450. **HRMS** (Dart, M+1) Calculated for C13H9N2 193.0766, found 193.0770.

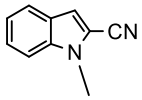


**7-methyl-1*H*-indole-2-carbonitrile (2c) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (18:1:1, v:v:v) as the mobile phase and was isolated as an off-white solid (55.3 mg, 0.354 mmol, 71%, 151-152 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.65 (s, 1H), 7.53 (ddt, *J* = 8.0, 1.5, 0.7 Hz, 1H), 7.22 (d, *J* = 2.1 Hz, 1H), 7.19 (dt, *J* = 7.1, 1.0 Hz, 1H), 7.14 (dd, *J* = 7.9, 7.1 Hz, 1H), 2.52 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 136.9, 126.6, 126.0, 122.2, 121.2, 119.9, 115.0, 114.6, 106.0, 16.7. **IR** (thin film, $cm^{-1}$) 3288,

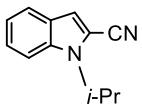
3063, 2964, 2915, 2857, 2227, 1617, 1526, 1432, 1363. **HRMS** (Dart, M+18) Calculated for $C_{10}H_{12}N_3$ 174.1031, found 174.1031.



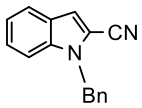
**4-methyl-1*H*-indole-2-carbonitrile (2d) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (18:1:1, v:v:v) as the mobile phase and was isolated as an off-white solid (54.0 mg, 0.346 mmol, 69%, 83-84 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.92 (s, 1H), 7.35 – 7.20 (m, 3H), 7.01 (dt, *J* = 6.8, 1.1 Hz, 1H), 2.56 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 136.8, 131.8, 126.4, 126.4, 121.5, 114.5, 113.0, 109.3, 105.4, 18.6. **IR** (thin film, cm$^{-1}$) 3480, 3326, 3131, 3063, 2918, 2854, 2226, 1615, 1518, 1473. **HRMS** (Dart, M+1) Calculated for $C_{10}H_9N_2$ 157.0766, found 157.0771.



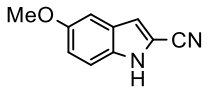
**1-methyl-1*H*-indole-2-carbonitrile (2e) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (40:1:1, v:v:v) as the mobile phase and was isolated as an off-white solid (55.8 mg, 0.36 mmol, 72%). Spectral data match literature reports.[6] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.67 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.41 (ddd, *J* = 8.5, 6.8, 1.1 Hz, 1H), 7.36 (dq, *J* = 8.5, 1.0 Hz, 1H), 7.21 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 7.16 (d, *J* = 0.9 Hz, 1H), 3.91 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 138.0, 126.1, 125.8, 122.3, 121.3, 113.6, 112.6, 110.2, 110.1, 31.5.



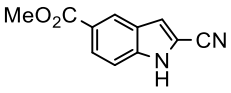
**1-isopropyl-1*H*-indole-2-carbonitrile (2f) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (40:1:1, v:v:v) as the mobile phase and was isolated as a colorless oil (66.3 mg, 0.36 mmol, 72 %). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.66 (ddd, *J* = 8.1, 0.9 Hz, 1H), 7.52 – 7.45 (m, 1H), 7.37 (ddd, *J* = 8.6, 7.0, 1.2 Hz, 1H), 7.22 – 7.15 (m, 2H), 4.92 (m, *J* = 7.0 Hz, 1H), 1.71 (d, *J* = 7.0 Hz, 6H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 136.5, 126.5, 125.4, 122.4, 121.1, 114.5, 114.2, 111.0, 107.8, 49.4, 22.0. **IR** (thin film, cm$^{-1}$) 3117, 3053, 2980, 2936, 2882, 2222, 1612, 1514, 1447. **HRMS** (DART, M+1) Calculated for $C_{12}H_{13}N_2$ 185.1079, found 185.1076.



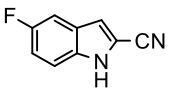
**1-benzyl-1*H*-indole-2-carbonitrile (2g) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–MTBE (40:1, v:v:v to 20:1, v:v:v) as the mobile phase and was isolated as a colorless oil (89.7 mg, 0.386 mmol, 77 %). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.70 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.39 – 7.27 (m, 5H), 7.25 – 7.16 (m, 4H), 5.48 (s, 2H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 137.6, 136.1, 129.0, 128.2, 126.9, 126.5, 126.1, 122.5, 121.7, 113.8, 113.6, 110.8, 110.1, 49.1. **IR** (thin film, cm$^{-1}$) 3119, 3063, 3032, 2926, 2220, 1616, 1603, 1518, 1452. **HRMS** (DART, M+1) Calculated for $C_{16}H_{13}N_2$ 233.1079, found 233.1078.



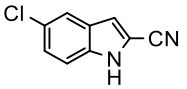
**5-methoxy-1*H*-indole-2-carbonitrile (2h) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–$NEt_3$ (17:2:1, v:v:v) as the mobile phase and was isolated as a white solid (65.9 mg, 0.38 mmol, 77%, 146-147 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.53 (s, 1H), 7.34 – 7.28 (m, 1H), 7.11 (d, *J* = 1.0 Hz, 1H), 7.08 – 7.03 (m, 2H), 3.85 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 155.4, 132.1, 126.7, 118.0, 114.2, 113.9, 112.6, 106.4, 101.9, 55.7. **IR** (thin film, cm$^{-1}$) 3287, 3121, 2955, 2940, 2835, 2241, 1450, 1362, 1173. **HRMS** (DART, M+1) Calculated for $C_{10}H_9N_2O$ 173.0715, found 173.0717.



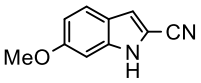
**methyl 2-cyano-1*H*-indole-5-carboxylate (2i) –** The compound was synthesized with the following modification to General Procedure B: Pd(*t*-$Bu_3P)_2$ (19.2 mg, 0.0376 mmol, 7.5 mol %), $Zn(TFA)_2$ (21.9 mg, 0.075, 15 mol %), at 120 °C. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as a white solid (48 mg, 0.240 mmol, 48%, decomp at 230 °C). **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 12.74 (s, 1H), 8.38 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.91 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.55 (dt, *J* = 8.8, 0.9 Hz, 1H), 7.53 (d, *J* = 0.9 Hz, 1H), 3.86 (s, 3H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 166.5, 139.2, 125.7, 125.5, 124.6, 122.5, 114.7, 114.0, 112.5, 107.7, 52.0. **IR** (thin film, $cm^{-1}$) 3234, 3161, 2958, 2926, 2854, 2228, 1683, 1614, 1428. **HRMS** (DART, M+1) Calculated for $C_{11}H_9N_2O_2$ 201.0664, found 201.0666.



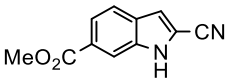
**5-fluoro-1*H*-indole-2-carbonitrile (2j) –** The compound was synthesized with the following modification to General Procedure B: Pd(*t*-$Bu_3P)_2$ (19.2 mg, 0.0376 mmol, 7.5 mol %), $Zn(TFA)_2$ (21.9 mg, 0.075, 15 mol %), at 120 °C. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (18:1:1, v:v:v) as the mobile phase and was isolated as an off-white solid (53.6 mg, 0.335 mmol, 67%, 111-112 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 9.02 (s, 1H), 7.37 (ddt, *J* = 9.0, 4.3, 0.8 Hz, 1H), 7.31 (ddd, *J* = 9.0, 2.5, 0.6 Hz, 1H), 7.19 – 7.11 (m, 2H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 158.72 (d, *J* = 238.2 Hz), 133.62, 126.56 (d, *J* = 10.8 Hz), 115.64 (d, *J* = 27.1 Hz), 114.31 (d, *J* = 5.4 Hz), 114.11, 112.98 (d, *J* = 9.5 Hz), 107.70, 106.52 (d, *J* = 23.9 Hz). **$^{19}$F NMR** (564 MHz, Chloroform-*d*) δ -121.44 (m). **IR** (thin film, $cm^{-1}$)3295, 3090, 2991, 2917, 2227, 1635, 1578, 1520, 1492. **HRMS** (DART, M+1) Calculated for $C_9H_6FN_2$ 161.0515, found 161.0518.



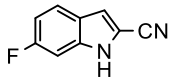
**5-chloro-1*H*-indole-2-carbonitrile (2k) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (18:1:1, v:v:v) as the mobile phase and was isolated as an off-white solid (61.5 mg, 0.35 mmol, 70%, decomp at 144 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.68 (s, 1H), 7.66 (dt, *J* = 1.7, 0.9 Hz, 1H), 7.36 – 7.34 (m, 2H), 7.14 (dd, *J* = 2.1, 0.7 Hz, 1H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 135.1, 127.7, 127.1, 126.9, 121.3, 113.8, 113.5, 112.8, 107.6. **IR** (thin film, cm-1) 3310, 3115, 3069, 2963, 2924, 2232, 1518, 1483, 1414, 1346. **HRMS** (DART, M+1) Calculated for $C_9H_6ClN_2$ 177.0220, found 177.0219.



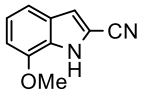
**6-methoxy-1*H*-indole-2-carbonitrile (2l) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as a white solid (58.7 mg, 0.34 mmol, 68%, 98-99 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.14 (s, 1H), 6.88 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.82 (s, 1H), 3.86 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 159.5, 138.0, 122.8, 120.4, 114.7, 114.7, 113.3, 104.6, 93.6, 55.5. **IR** (thin film, cm-1) 3358, 3011, 2965, 2932, 2218, 1628, 1582, 1510, 1448, 1400. **HRMS** (DART, M+1) Calculated for $C_{10}H_9N_2O$ 173.0715, found 173.0713.



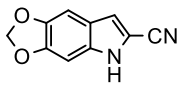
**methyl 2-cyano-1*H*-indole-6-carboxylate (2m) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as an off-white solid (75.2 mg, 0.376 mmol, 75%, decomp at 216 °C). **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 8.07 (dt, *J* = 1.6, 0.9 Hz, 1H), 7.78 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.71 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.44 (d, *J* = 0.9 Hz, 1H), 3.87 (s, 3H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 166.5, 136.2, 129.1, 126.4, 121.9, 121.0, 114.2, 114.0, 113.0, 109.1, 52.2. **IR** (thin film, $cm^{-1}$) 3279, 2361, 2330, 2226, 1692, 1559, 1534, 1560, 1441. **HRMS** (DART, M+1) Calculated for $C_{11}H_9N_2O_2$ 201.0664, found 201.0666.



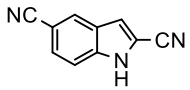
**6-fluoro-1*H*-indole-2-carbonitrile (2n) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–PhMe (3:1, v:v) as the mobile phase and was isolated as a white solid (48.6 mg, 0.303 mmol, 61%, 139-140 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 7.62 (ddt, *J* = 8.8, 5.3, 0.7 Hz, 1H), 7.19 (dd, *J* = 2.2, 1.0 Hz, 1H), 7.10 (dddd, *J* = 9.1, 2.3, 1.0, 0.6 Hz, 1H), 7.00 (ddd, *J* = 9.4, 8.8, 2.2 Hz, 1H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 162.9 (d, *J* = 244.3 Hz), 137.0 (d, *J* = 13.0 Hz), 123.4 (d, *J* = 10.4 Hz), 122.8, 114.6, 113.9, 111.5 (d, *J* = 25.3 Hz), 106.7, 97.9 (d, *J* = 26.6 Hz). **$^{19}$F NMR** (470 MHz, Chloroform-*d*) δ -114.31 (m). **IR** (thin film, cm$^{-1}$) 3277, 3140, 3072, 2928, 2857, 2229, 1627, 1590, 1522, 1450. **HRMS** (DART, M+1) Calculated for $C_9H_6FN_2$ 161.0515, found 161.0516.



**7-methoxy-1*H*-indole-2-carbonitrile (2o) –** The compound was synthesized according to General Procedure B. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v) as the mobile phase and was isolated as a white solid (66.6 mg, 0.39 mmol, 77%, 125-126 °C). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.85 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.16 (d, *J* = 2.2 Hz, 1H), 7.13 (dd, *J* = 8.1, 7.7 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 3.98 (s, 3H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 146.1, 128.2, 127.3, 122.2, 114.4, 114.1, 114.1, 105.9, 104.8, 55.5. **IR** (thin film, cm-1) 3343, 3080, 3007, 2963, 2938, 2911, 2839, 2228 1628, 1584, 1530, 1447. **HRMS** (DART, M+1) Calculated for $C_{10}H_9N_2O$ 173.0715, found 173.0716.

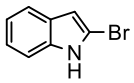


**5*H*-[1,3]dioxolo[4,5-*f*]indole-6-carbonitrile (2p) –** The compound was synthesized with the following modification to General Procedure B: Pd(*t*-$Bu_3P)_2$ (19.2 mg, 0.0376 mmol, 7.5 mol %), $Zn(TFA)_2$ (21.9 mg, 0.075, 15 mol %), at 120 °C. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (40:5:2, v:v:v) as the mobile phase and was isolated as a white solid (48.9 mg, 0.26 mmol, 53%, 210-211 °C). **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 12.20 (s, 1H), 7.16 (s, 1H), 7.06 (s, 1H), 6.94 (s, 1H), 6.02 (s, 2H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 147.9, 144.1, 132.9, 120.1, 114.9, 113.3, 103.7, 101.1, 98.8, 92.0. **IR** (thin film, cm$^{-1}$) 3311, 3125, 3009, 2917, 2209, 1528, 1499, 1475. **HRMS** (DART, M+18) Calculated for $C_{10}H_{10}N_3O_2$ 204.0773, found 204.0772.



**1*H*-indole-2,5-dicarbonitrile (2q) –** The compound was synthesized with the following modification to General Procedure B: $Zn(CN)_2$ (129.2 mg, 1.1 mmol, 2.2 equiv), Pd(*t*-$Bu_3P)_2$ (19.2 mg, 0.0376 mmol, 7.5 mol %), $Zn(TFA)_2$ (21.9 mg, 0.075, 15 mol %), at 120 °C. The product was purified by flash column chromatography using hexanes–EtOAc–DCM (8:1:1, v:v:v) as the mobile phase and was isolated as a white solid (51.0 mg, 0.305 mmol, 61%, 227-228 °C). **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 8.26 (dd, *J* = 1.5, 0.9 Hz, 1H), 7.71 – 7.57 (m, 2H), 7.50 (d, *J* = 0.8 Hz, 1H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 138.4, 128.1, 127.5, 125.5, 119.7, 113.9, 113.8, 113.7, 113.7, 108.6, 103.4. **IR** (thin film, cm$^{-1}$) 3250, 3130, 3054, 2991, 2928, 2857, 2227, 1618, 1476. **HRMS** (DART, M+H) Calculated for $C_{10}H_6N_3$ 168.0562, found 168.0564.

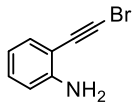
## 4 Mechanistic Studies



**2-bromo-1*H*-indole (2a') –** was synthesized according to literature procedure and the spectral data matched reported value.[5] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.03 (s, 1H), 7.56 (ddt, *J* = 7.8, 1.5, 0.8 Hz, 1H), 7.29 (dq, *J* = 8.1, 0.9 Hz, 1H), 7.20 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 7.15 (ddd, *J* = 7.8,

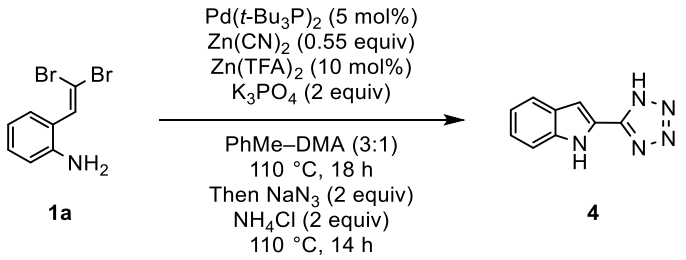
7.1, 1.1 Hz, 1H), 6.56 (dd, *J* = 2.1, 0.9 Hz, 1H). **$^{13}$C NMR** (125 MHz, Chloroform-*d*) δ 136.4, 128.7, 122.2, 120.5, 119.6, 110.3, 108.7, 104.8.

Upon treatment of **2a'** to General Procedure B, **2a** was isolated (66.1 mg, 0.465 mmol, 93%) by flash column chromatography using hexanes–EtOAc–DCM (17:2:1, v:v:v). as the mobile phase.




2-**(bromoethynyl)aniline (3)** – was synthesized according to literature procedure and the spectral data matched reported value.[7] **$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ 7.15 (ddd, *J* = 7.7, 1.6, 0.5 Hz, 1H), 7.06 (ddd, *J* = 8.2, 7.2, 1.6 Hz, 1H), 6.69 (ddd, *J* = 8.2, 1.2, 0.5 Hz, 1H), 6.48 (ddd, *J* = 7.7, 7.2, 1.2 Hz, 1H), 5.42 (s, 2H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 150.3, 132.2, 129.9, 115.7, 114.0, 105.1, 77.4, 55.8.
Upon treatment of **3** to General Procedure B, 60% of **3** was recovered.

## 5 Derivatization




**2-(1*H*-tetrazol-5-yl)-1*H*-indole (4)** – To an oven dried 3-dram vial, **4** (138.5 mg, 0.5 mmol, 1 equiv), $Zn(CN)_2$ (32.3 mg, 0.275 mmol, 0.55 equiv), $Zn(TFA)_2$ (14.6 mg, 0.05 mmol, 10 mol %), and $K_3PO_4$ (212.3 mg, 1 mmol, 2 equiv) were added. After the vial was purged with Ar for 5 min, 1 ml of PhMe and 1 ml of DMA was added. To a second oven dried vial, Pd(*t*-$Bu_3P)_2$ (12.8 mg, 0.025 mmol, 5 mol %) was added and purged with Ar for 5 min. The catalyst was dissolved in 2 ml of PhMe and the solution was transferred to the substrate mixture. The reaction was stirred at 1000 rpm and 110 °C for 18 h. Once the vial had cooled to rt, $NaN_3$ (65 mg, 1 mmol, 2 equiv) and $NH_4Cl$ (53.5 mg, 1 mmol, 2 equiv) were added and the reaction was reheated to 110 ºC and stirred at 1000 rpm for 14 h. The reaction contents were transferred into a separatory funnel, diluted in EtOAc, and the organic phase was washed multiple times with water and brine. The organic layer was concentrated, and the product was purified by silica gel flash chromatography using DCM–MeOH–AcOH (100:1:1, v:v:v) as the mobile phase and was isolated as a white solid (60.2 mg, 0.325 mmol, 65%). Spectral data was in accordance to reported data.[8] **$^1$H NMR** (500 MHz, DMSO-$d_6$) δ 12.16 (s, 1H), 7.67 (d, *J* = 7.9 Hz, 1H), 7.51 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.19 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.08 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H). **$^{13}$C NMR** (125 MHz, DMSO-$d_6$) δ 150.3, 137.5, 127.5, 123.6, 122.1, 121.2, 120.2, 112.3, 103.7.

## 6 References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(2) Nagamochi, M.; Fang, Y. -Q.; Lautens, M. *Org. Lett*. **2007**, *9*, 2955.

(3) Gupta, S.; Koley, D.; Ravikumar, K.; Kundu, B. *J. Org. Chem.* **2013**, *78*, 8624.

(4) Yuen, J.; Fang, Y. -Q.; Lautens, M. *Org. Lett.* **2006**, *8*, 653.

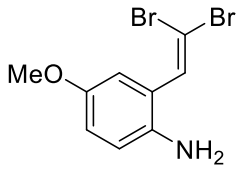
(5) Newman, S. G.; Lautens, M. *J. Am. Chem. Soc.* **2010**, *132*, 11416.

(6) Ushijima, S.; Moriyama, K. *Tetrahedron,* **2011**, *67*, 958.

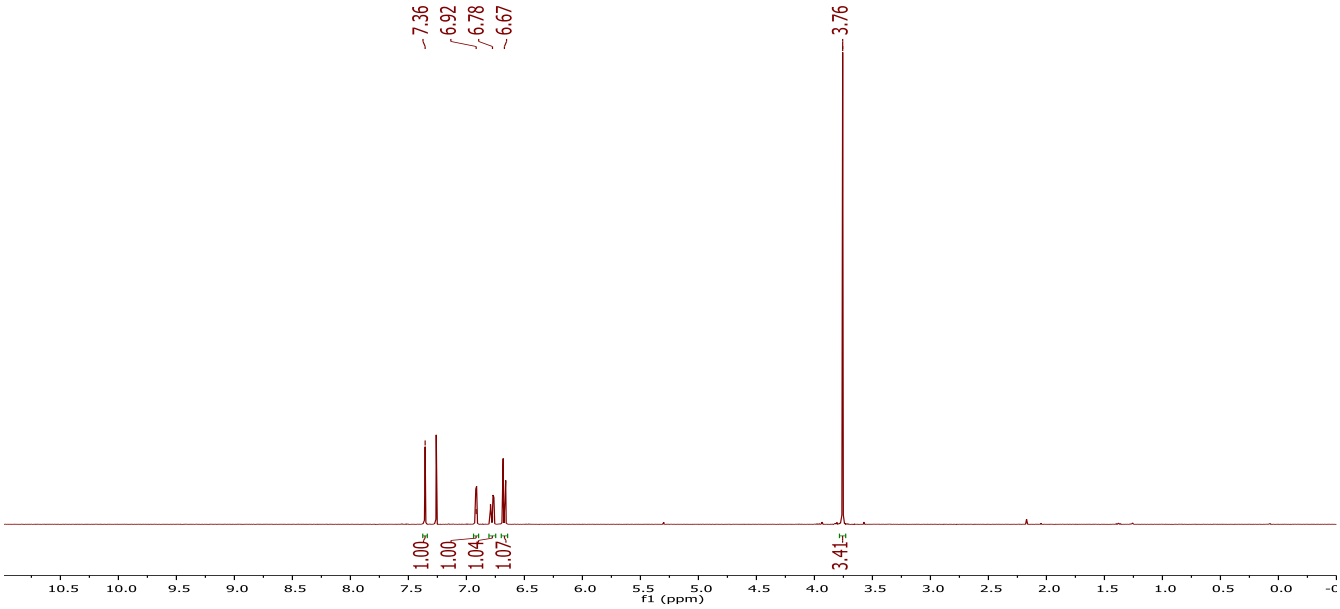
(7) Kunzer, A. R.; Wendt, M. D. *Tetrahedron Lett*. **2011**, *52*, 1815.

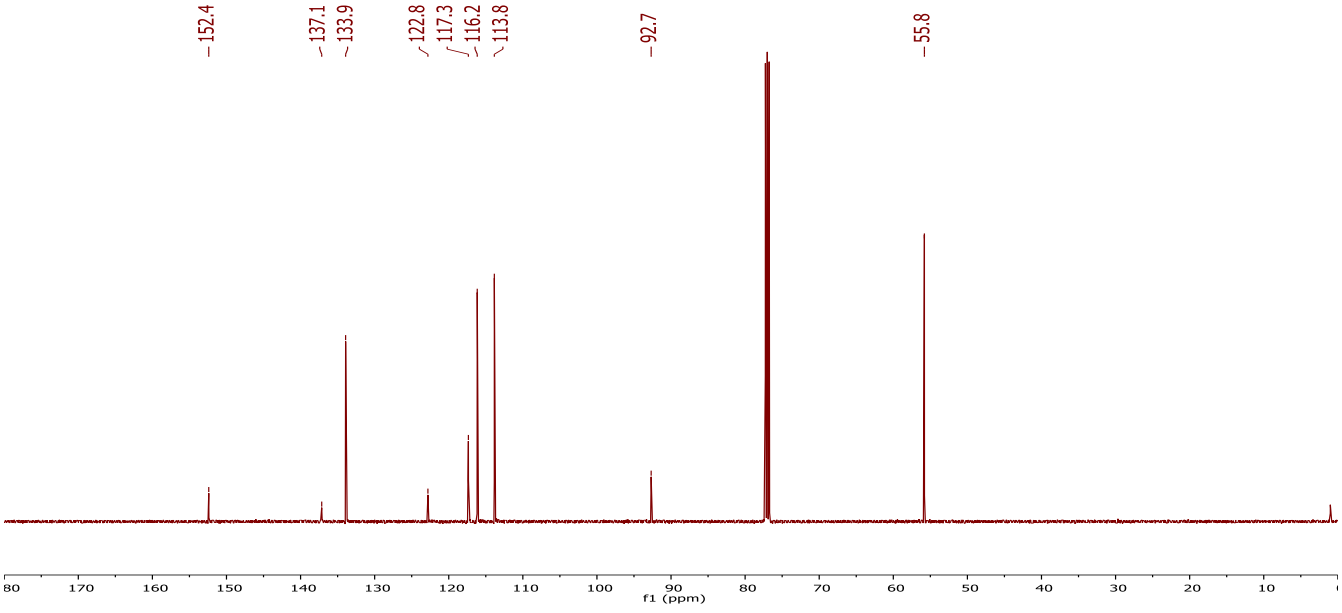
(8) Kou, X.; Zhao, M.; Qiao, X.; Zhu, Y.; Tong, X.; Shen, Z. *Chem. - Eur. J.* **2013**, *19*, 16880.

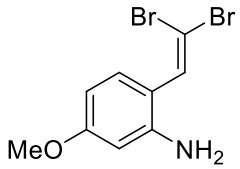
## 7 $^{1}H$, $^{13}C$, and $^{19}F$ NMR Spectra



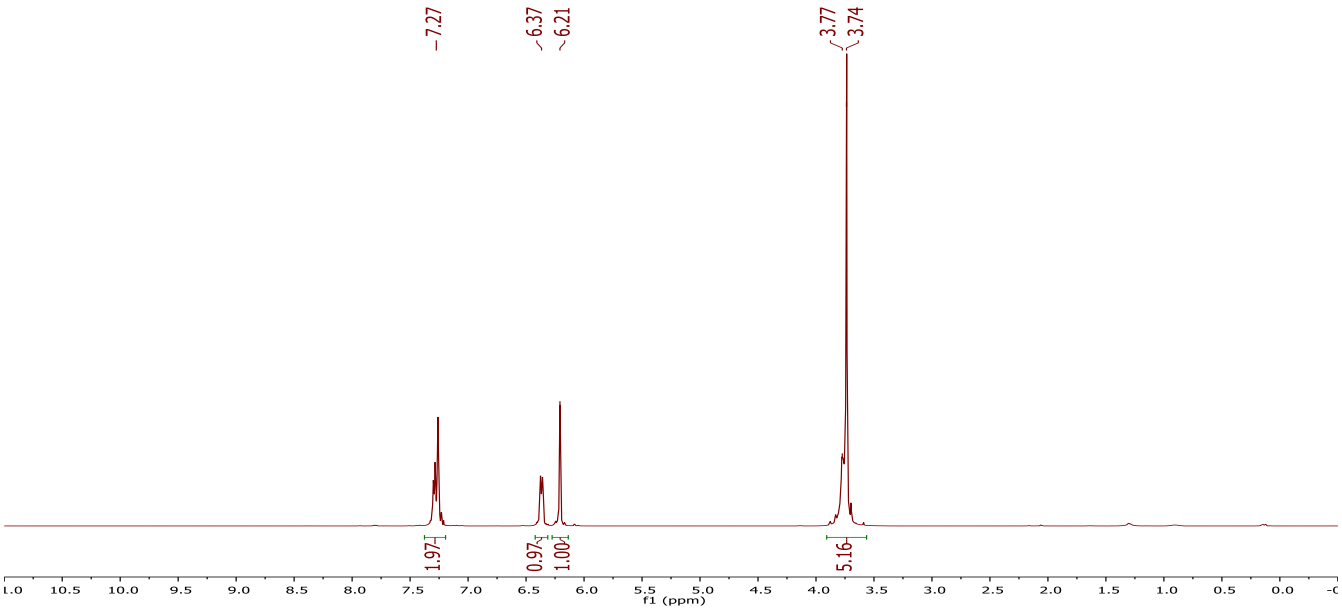

**1h**




Br
Br
MeO
NH2

**1l**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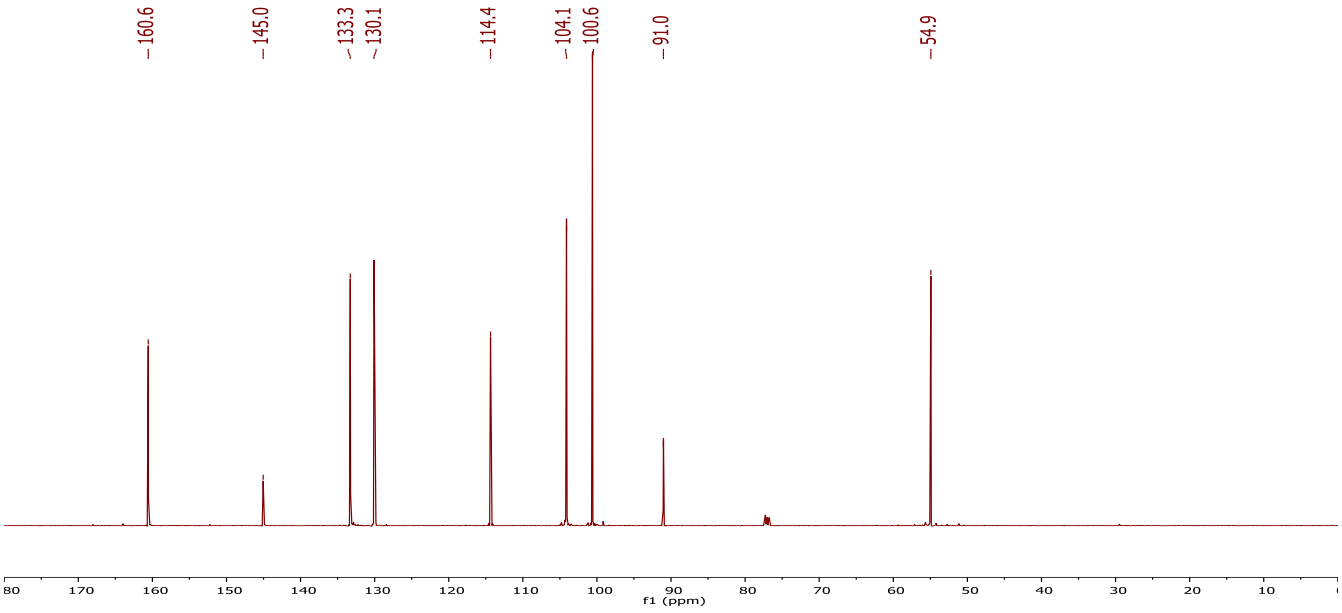
6.21
3.77
3.74
1.97
0.97
1.00
5.16
f1 (ppm)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130.1
114.4
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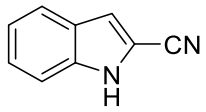
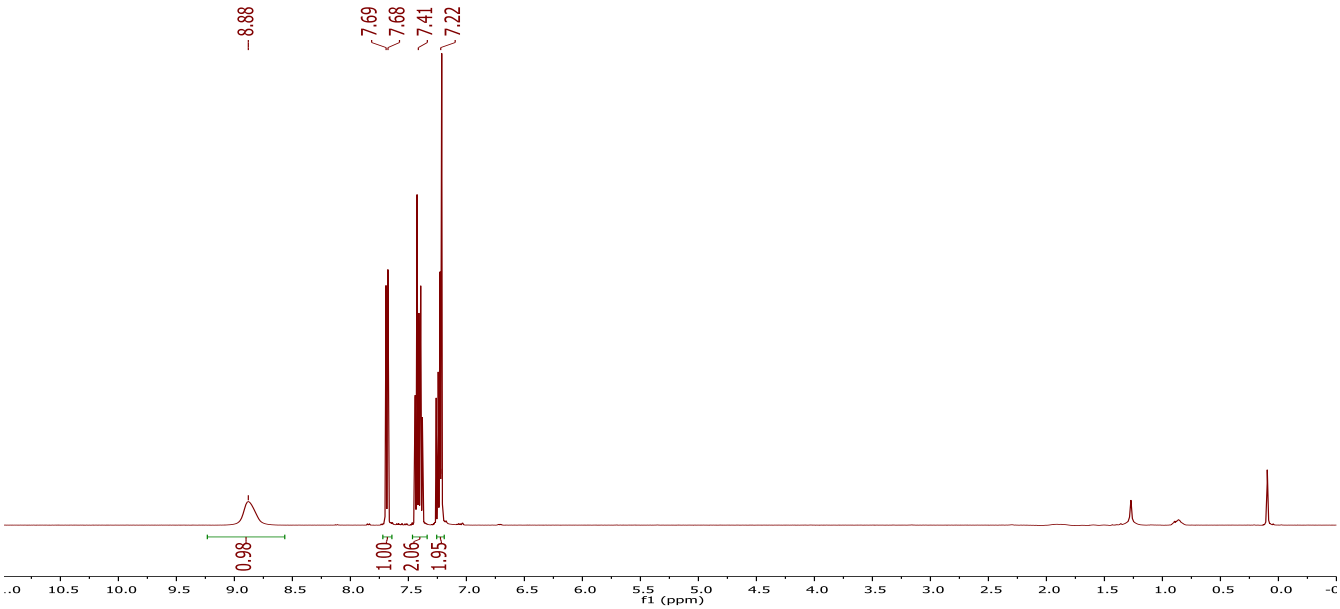
54.9
f1 (ppm)


CN
N
H

**2a**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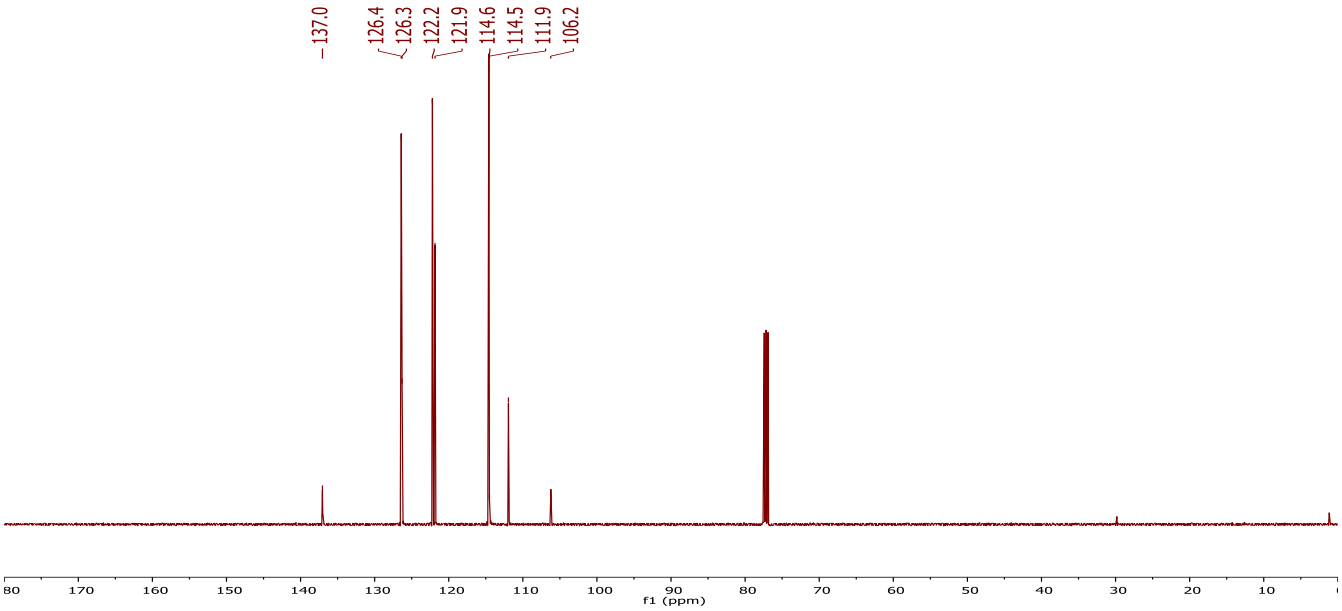
1.00
2.06
1.95
f1 (ppm)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121.9
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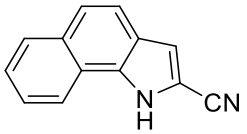
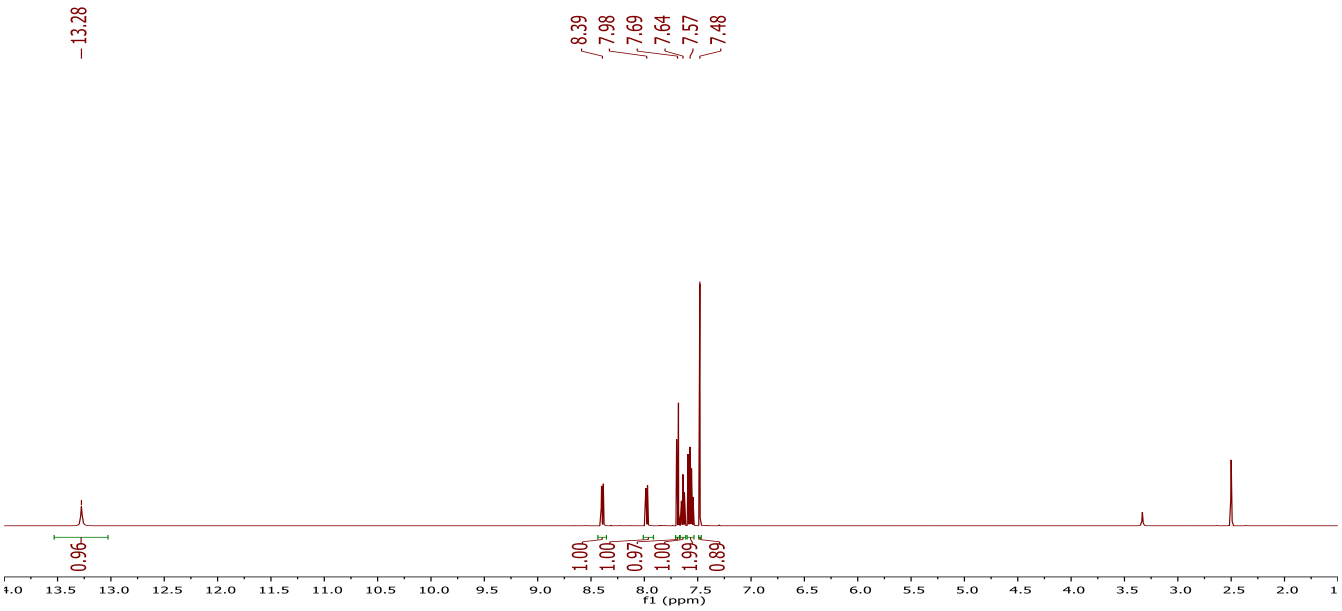
106.2
f1 (ppm)


N
H
CN

**2b**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0.96
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1.00
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1.00
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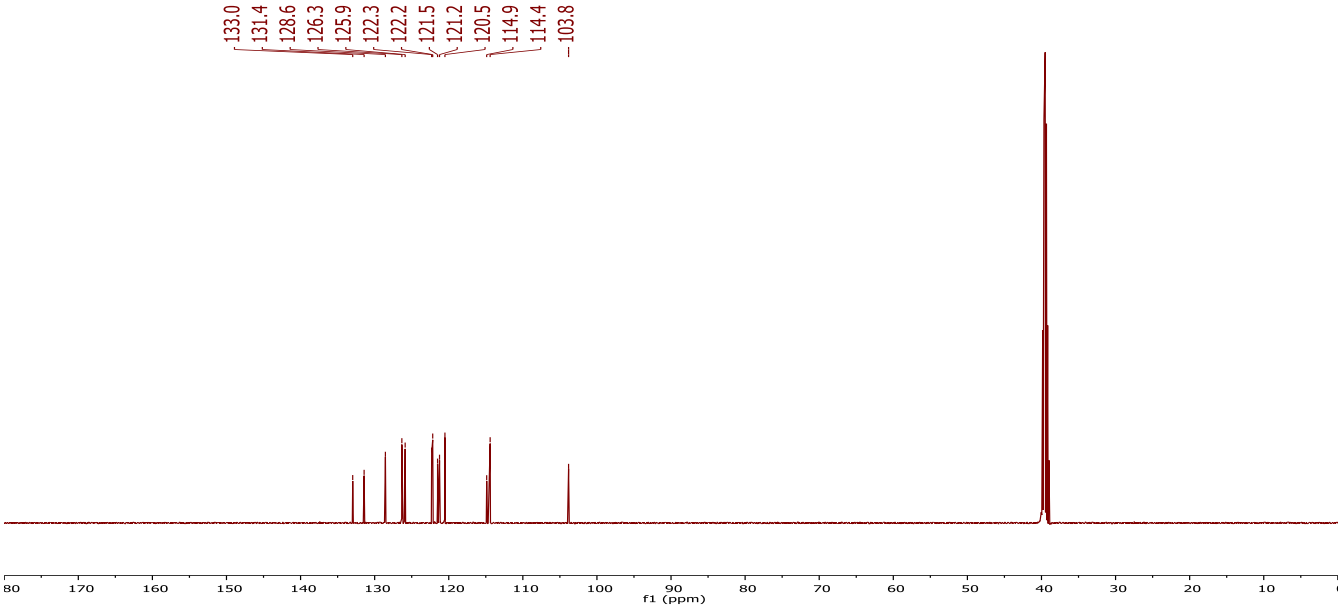
f1 (ppm)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121.5
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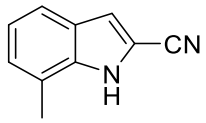
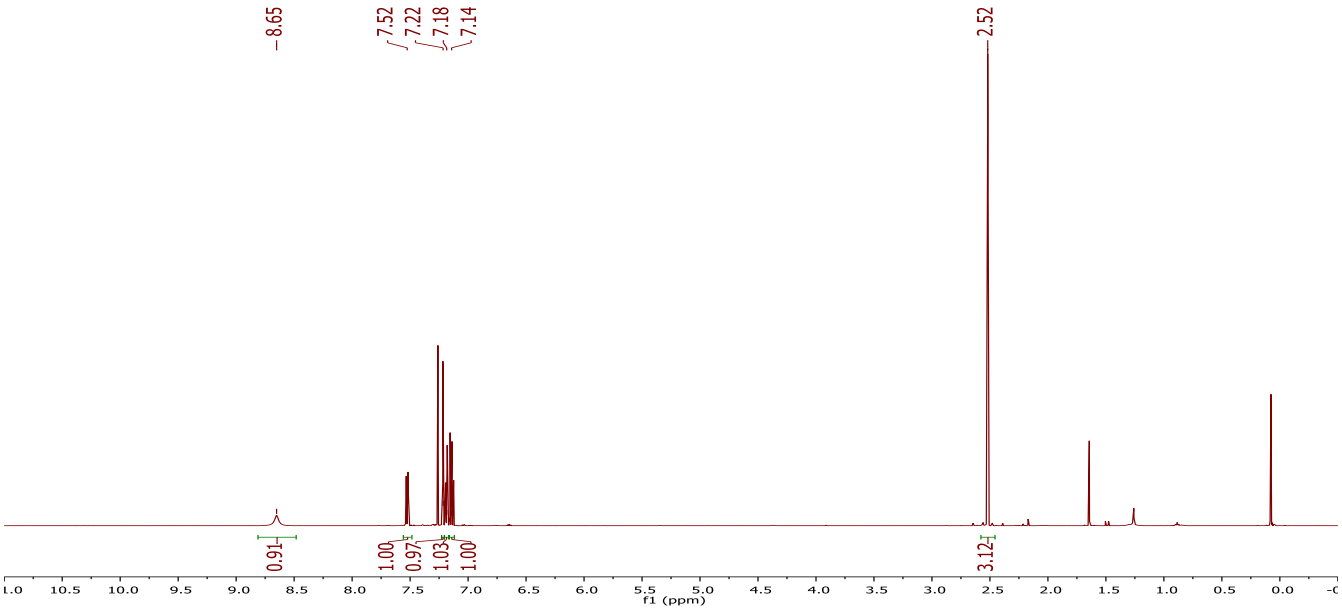
103.8
f1 (ppm)


CN
N
H

**2c**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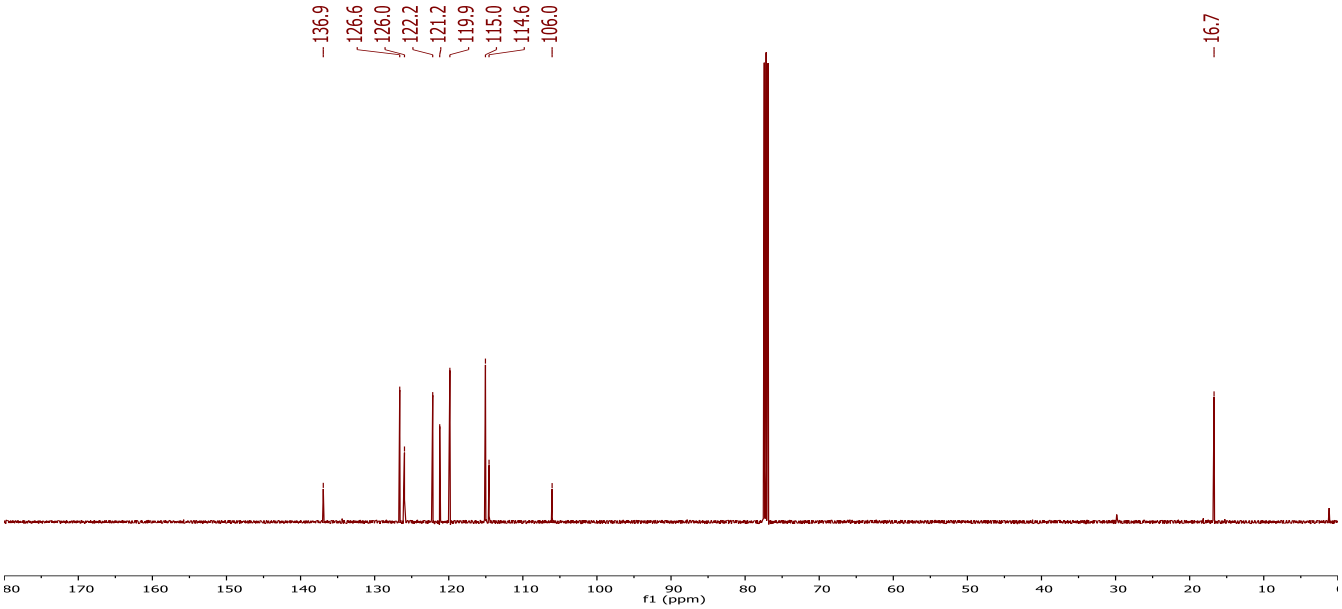
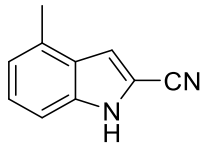
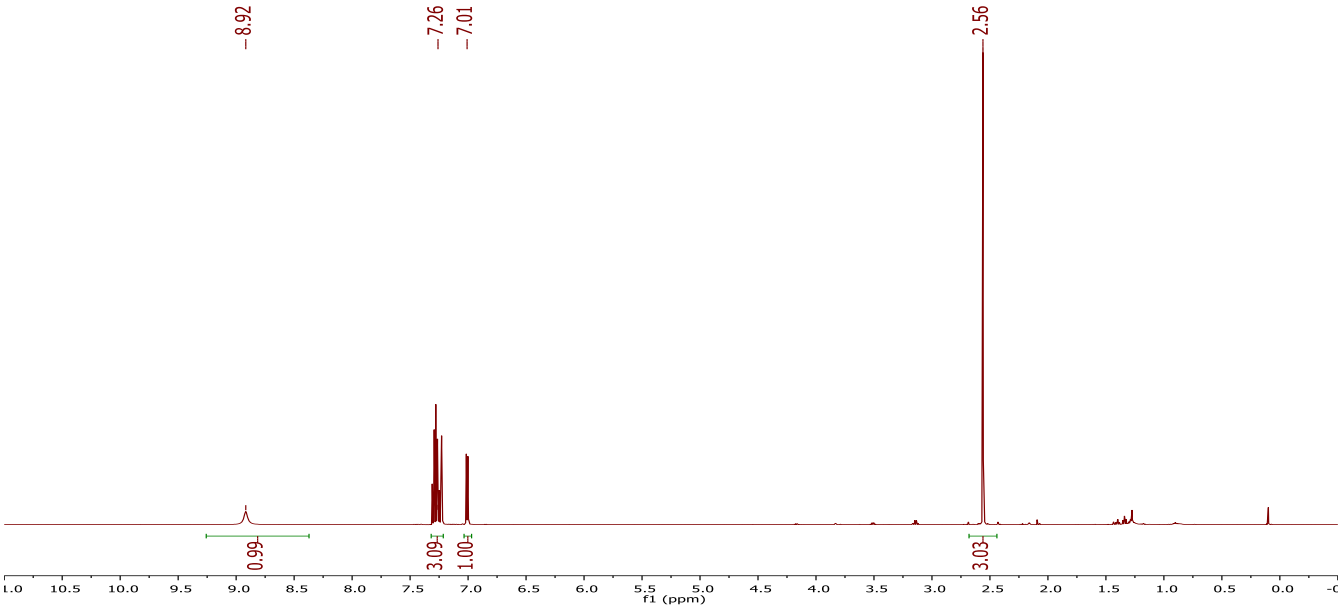
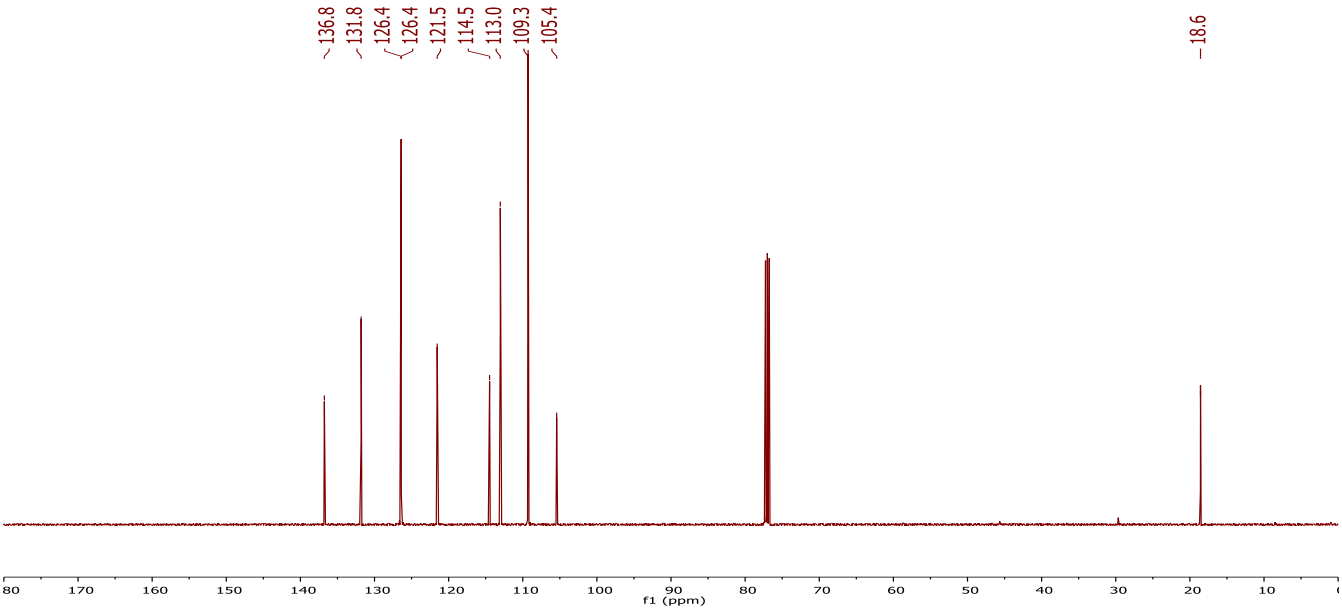
7.18
7.14
2.52
0.91
1.00
0.97
1.03
1.00
3.12
f1 (ppm)

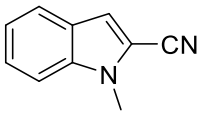

136.9
126.6
126.0
122.2
121.2
119.9
115.0
114.6
106.0
16.7
f1 (ppm)


CN
N
H

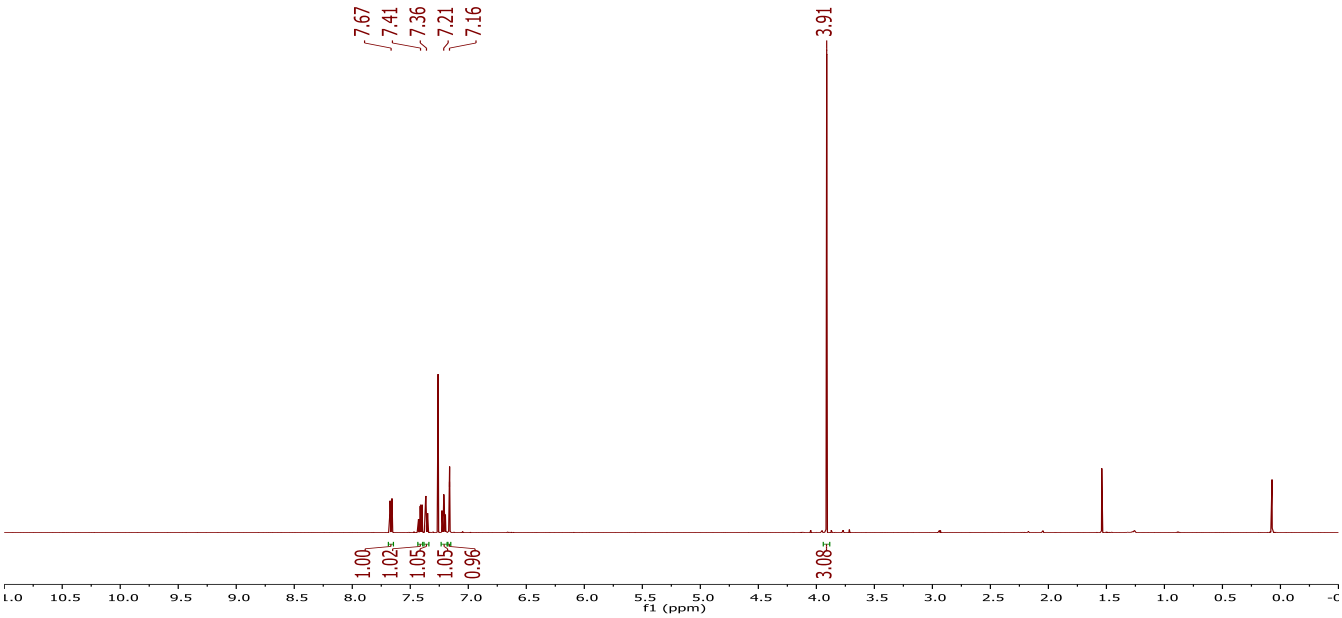
**2d**

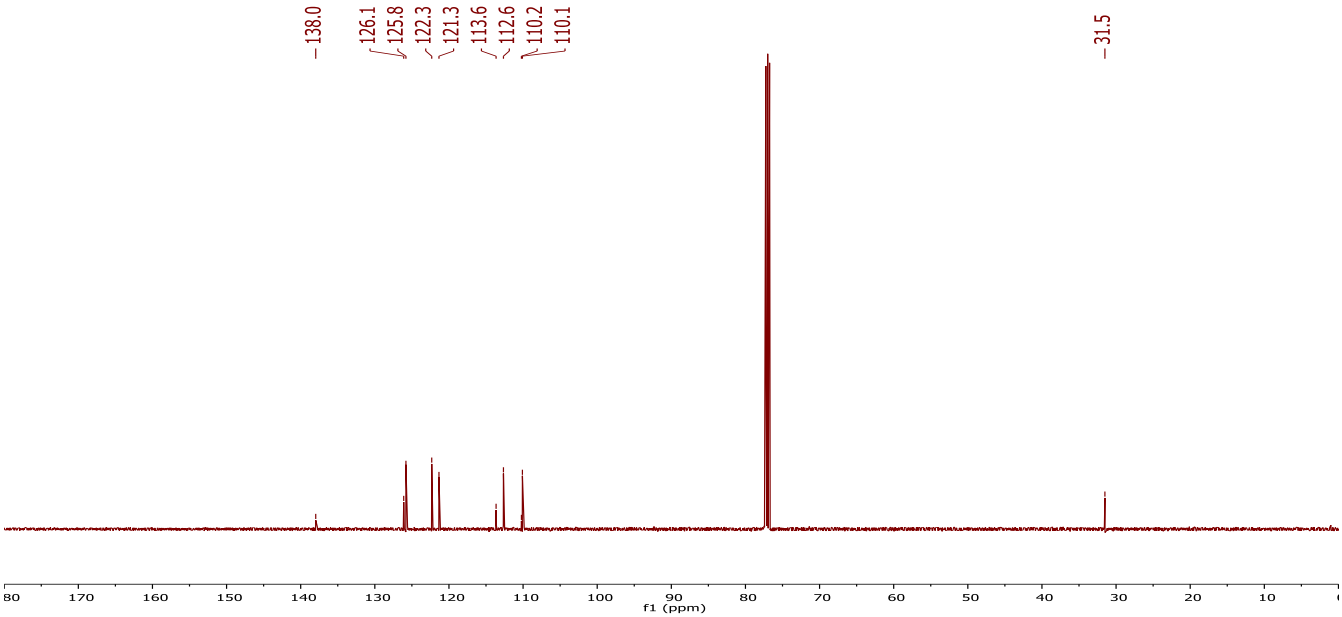

8.92
7.26
7.01
2.56
0.99
3.09
1.00
3.03
f1 (ppm)

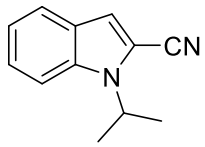

136.8
131.8
126.4
126.4
121.5
114.5
113.0
109.3
105.4
18.6
f1 (ppm)


CN
N

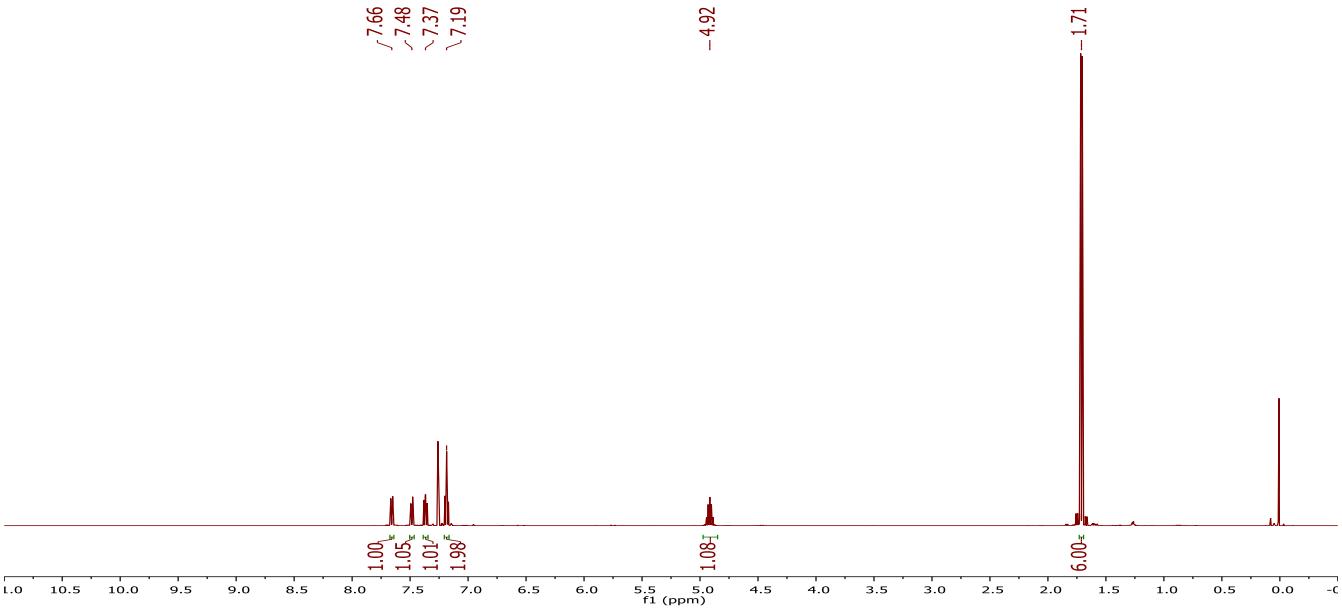
**2e**

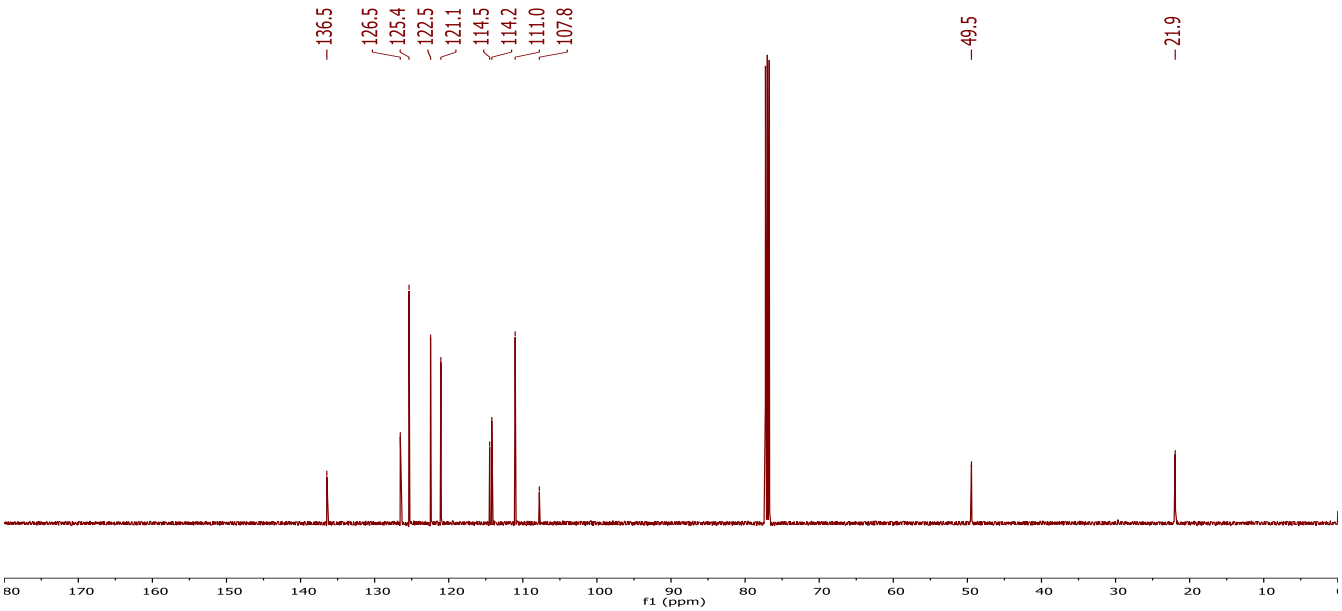

7.67
7.41
7.36
7.21
7.16
3.91
1.00
1.02
1.05
1.05
0.96
3.08
f1 (ppm)

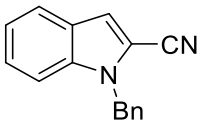

138.0
126.1
125.8
122.3
121.3
113.6
112.6
110.2
110.1
31.5
f1 (ppm)


CN
N

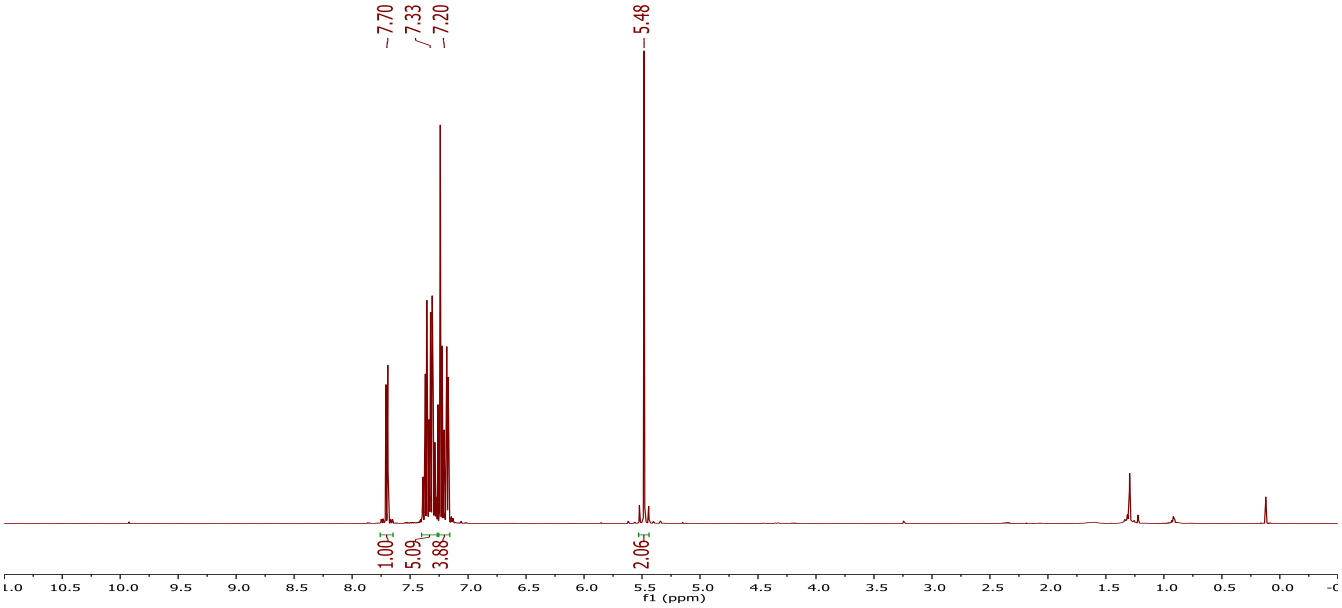
**2f**

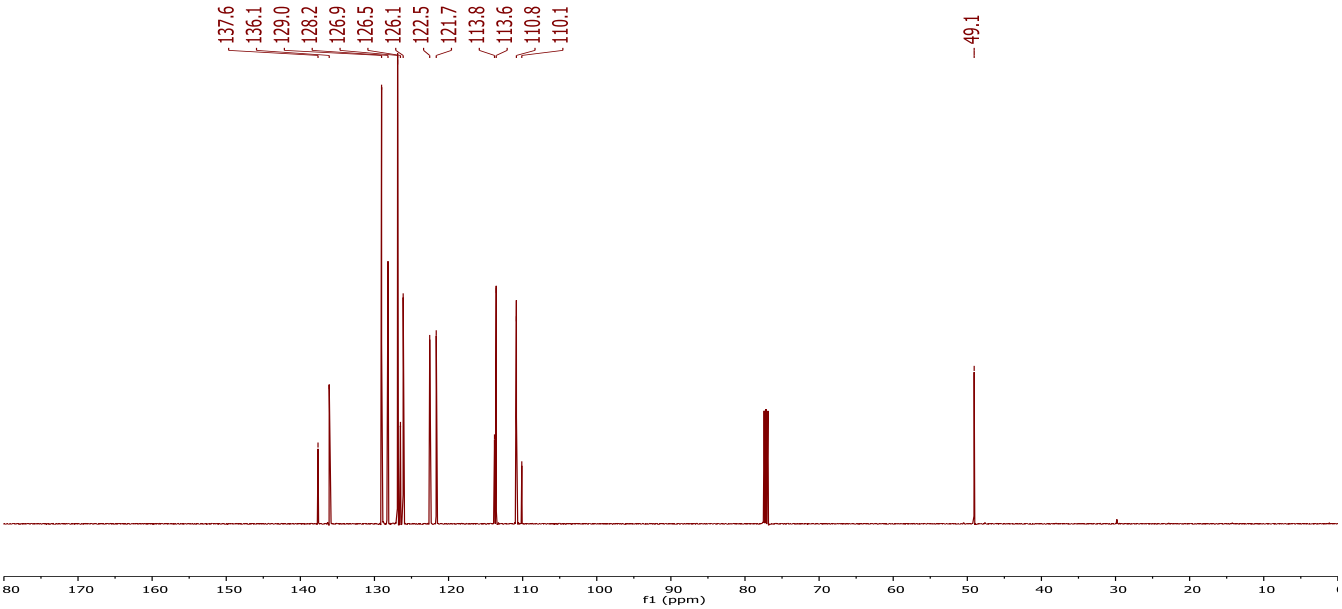

7.66
7.48
7.37
7.19
4.92
1.71
1.00
1.05
1.01
1.98
1.08
6.00
f1 (ppm)

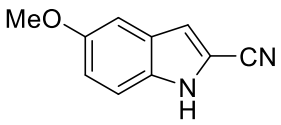

136.5
126.5
125.4
122.5
121.1
114.5
114.2
111.0
107.8
49.5
21.9
f1 (ppm)


CN
N
Bn

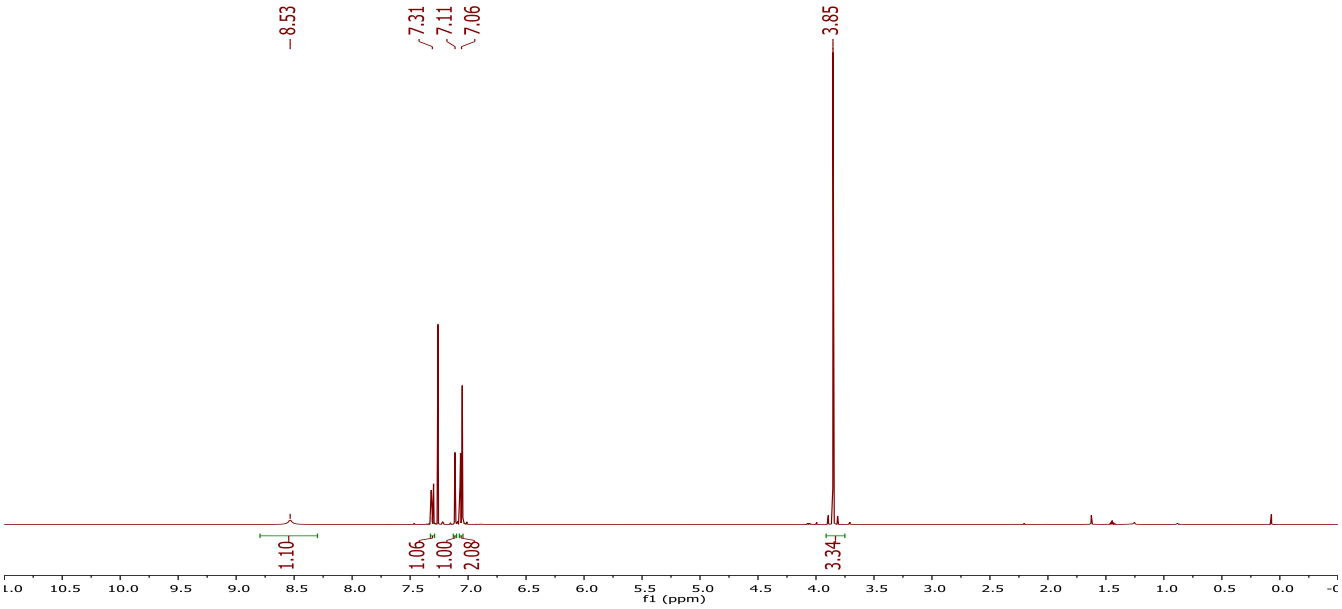
**2g**

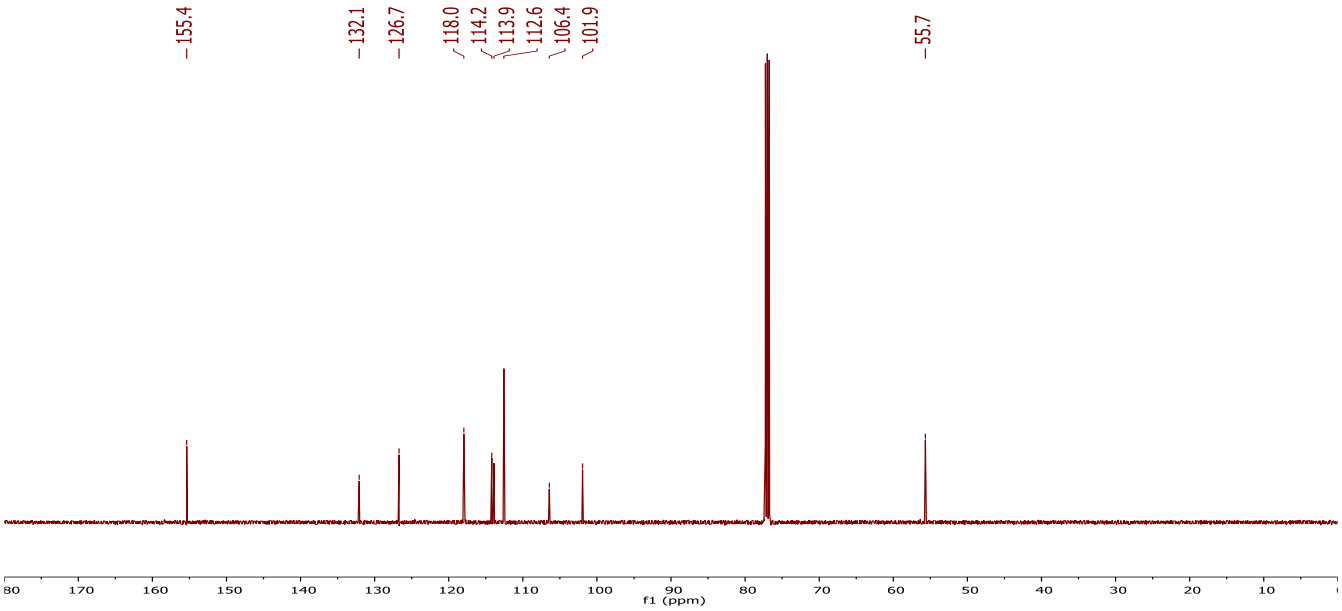

7.70
7.33
7.20
5.48
1.00
5.09
3.88
2.06
f1 (ppm)

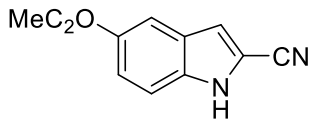

137.6
136.1
129.0
128.2
126.9
126.5
126.1
122.5
121.7
113.8
113.6
110.8
110.1
49.1
f1 (ppm)


MeO
CN
N
H

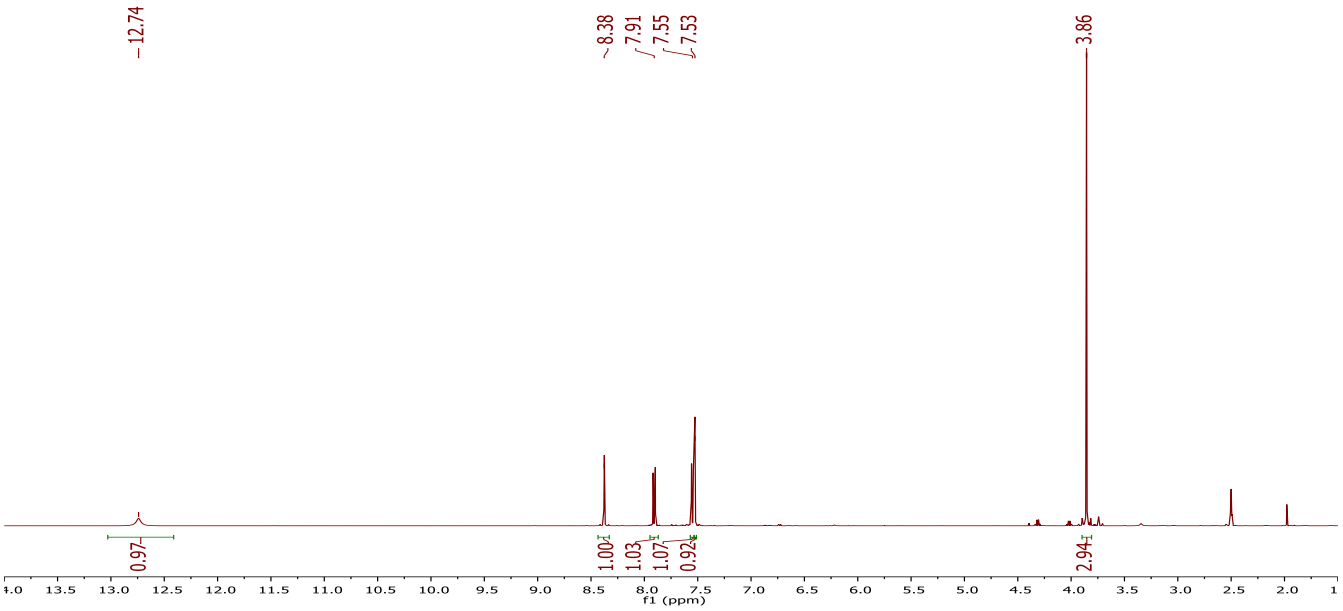
**2h**

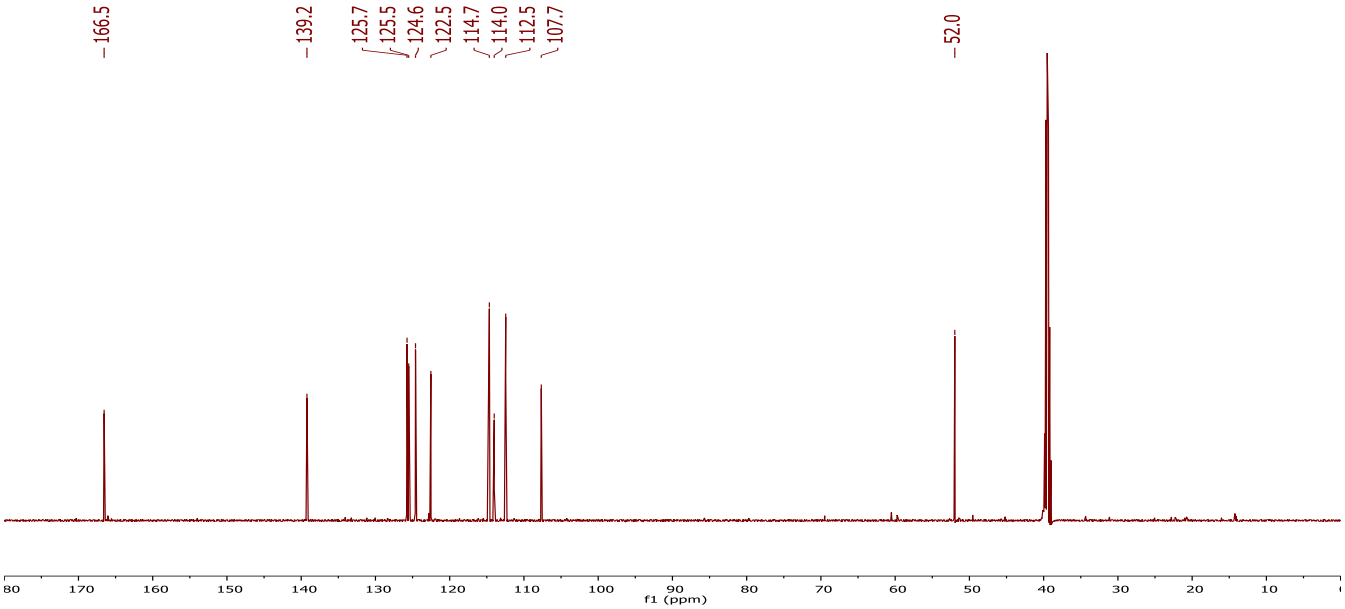

8.53
7.31
7.11
7.06
3.85
1.10
1.06
1.00
2.08
3.34
f1 (ppm)

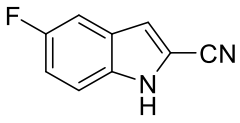

155.4
132.1
126.7
118.0
114.2
113.9
112.6
106.4
101.9
55.7
f1 (ppm)


MeC2O
CN
N
H

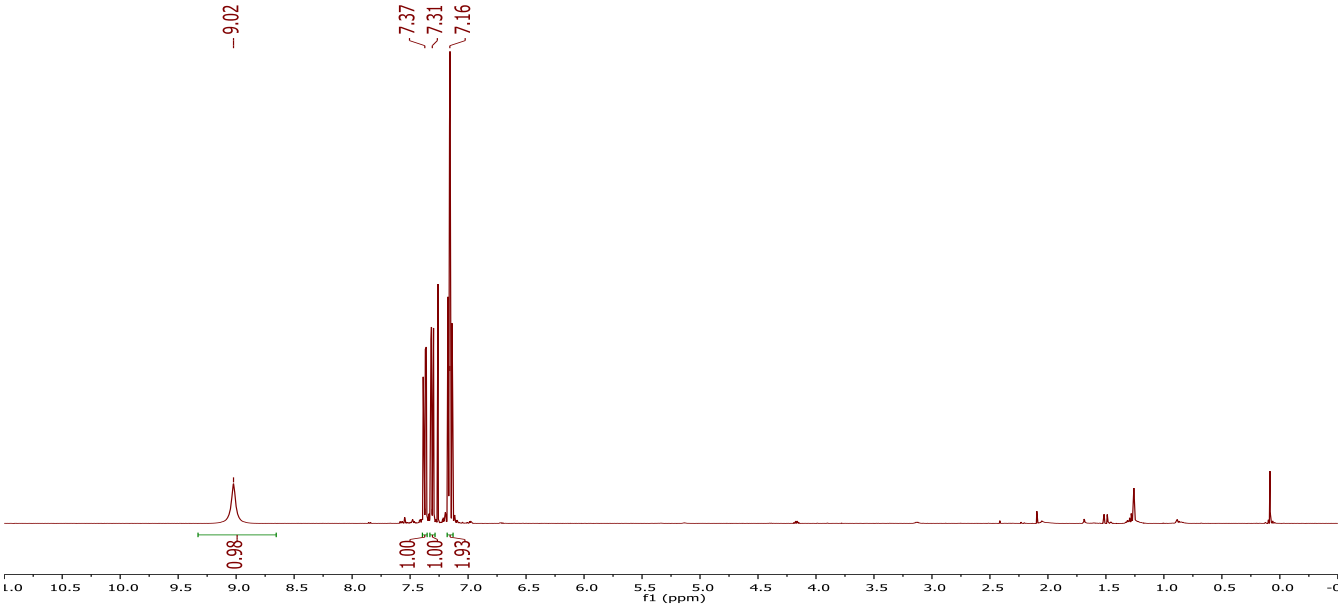
**2i**

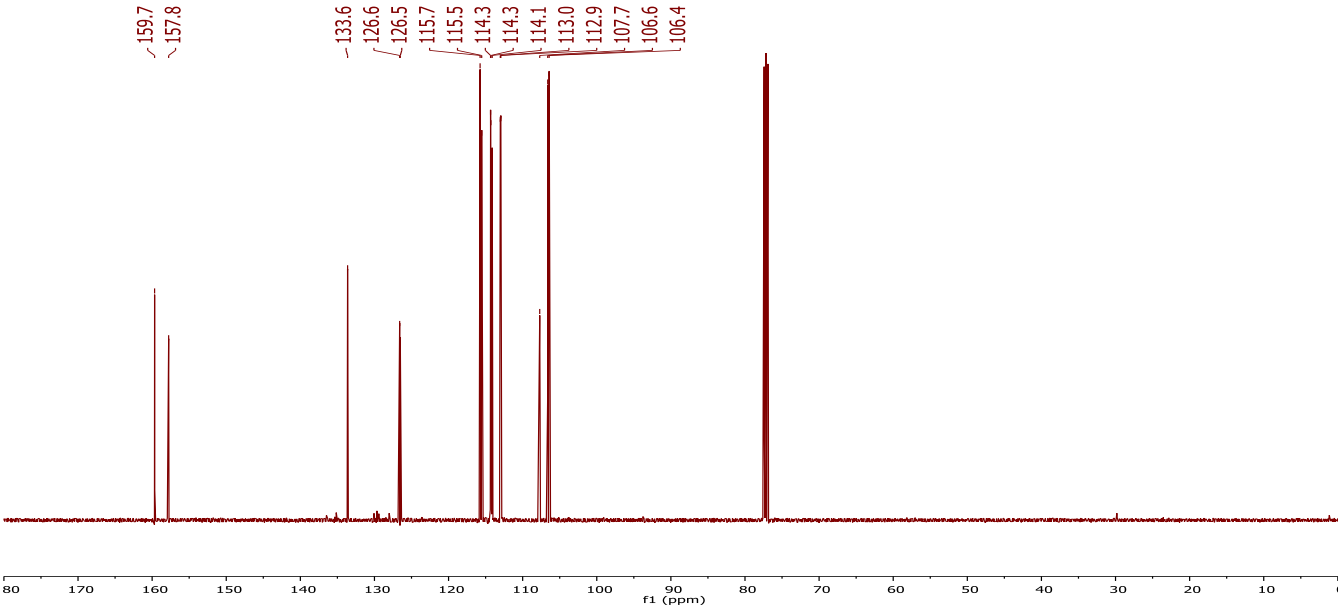

12.74
8.38
7.91
7.55
7.53
3.86
0.97
1.00
1.03
1.07
0.92
2.94
f1 (ppm)

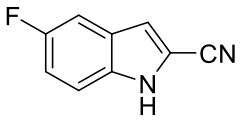

166.5
139.2
125.7
125.5
124.6
122.5
114.7
114.0
112.5
107.7
52.0
f1 (ppm)


F
CN
N
H

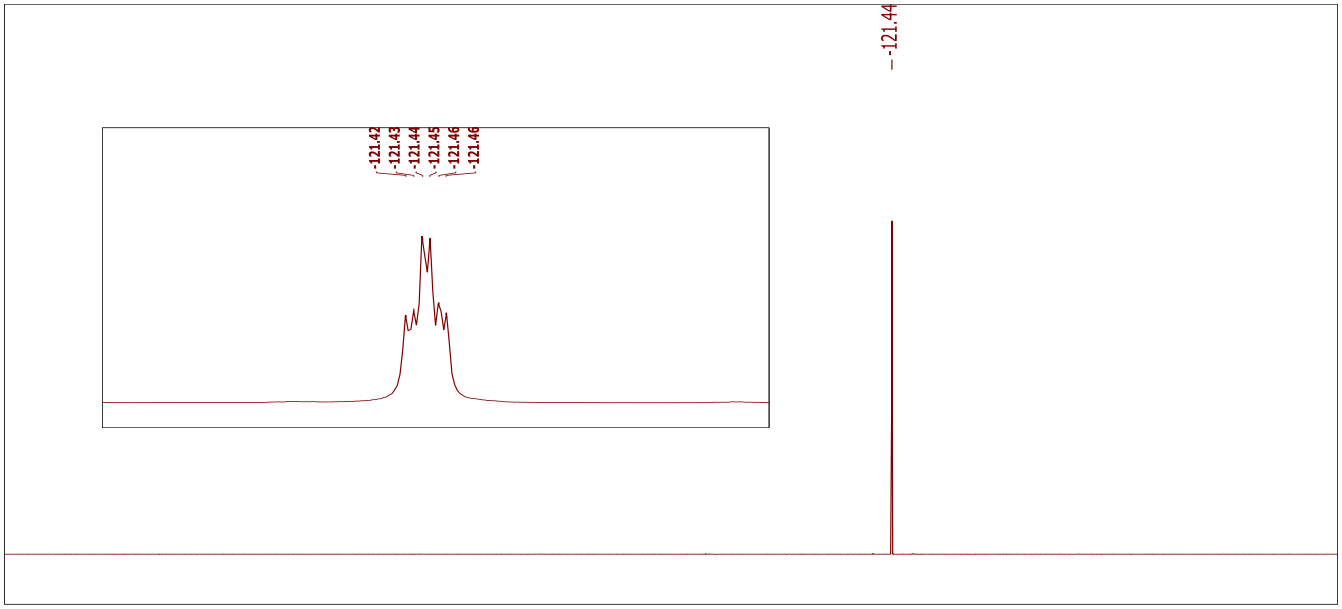
**2j**

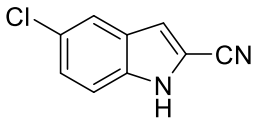

9.02
7.37
7.31
7.16
0.98
1.00
1.00
1.93
f1 (ppm)


159.7
157.8
133.6
126.6
126.5
115.7
115.5
114.3
114.3
114.1
113.0
112.9
107.7
106.6
106.4
f1 (ppm)

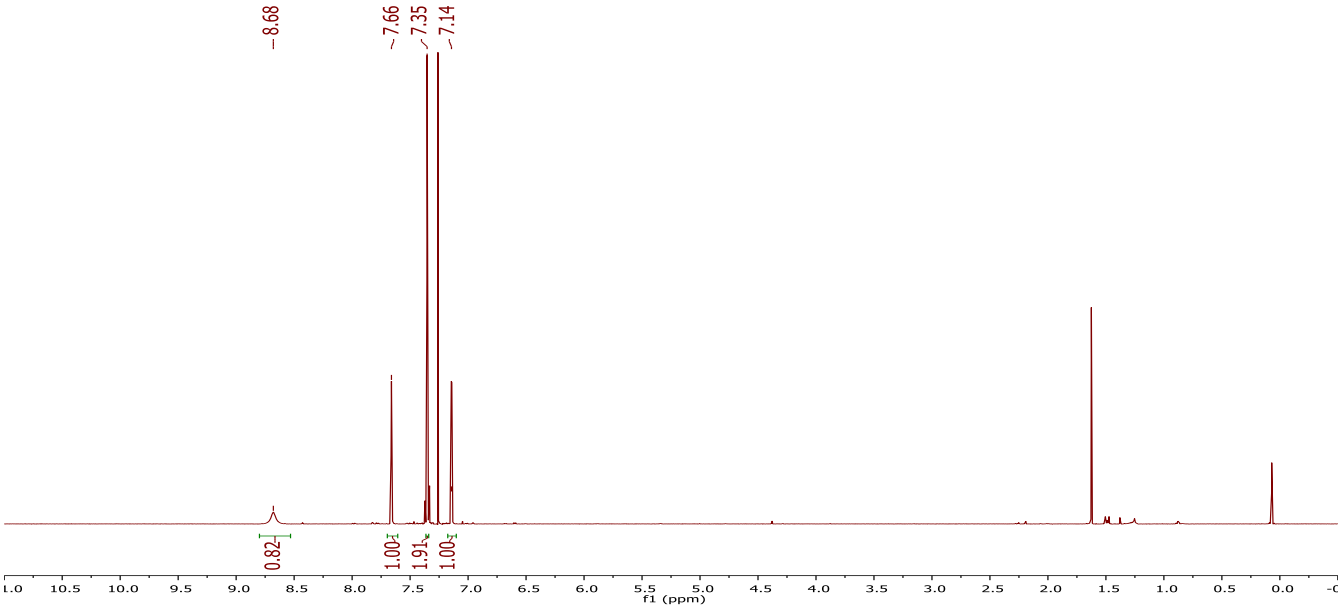


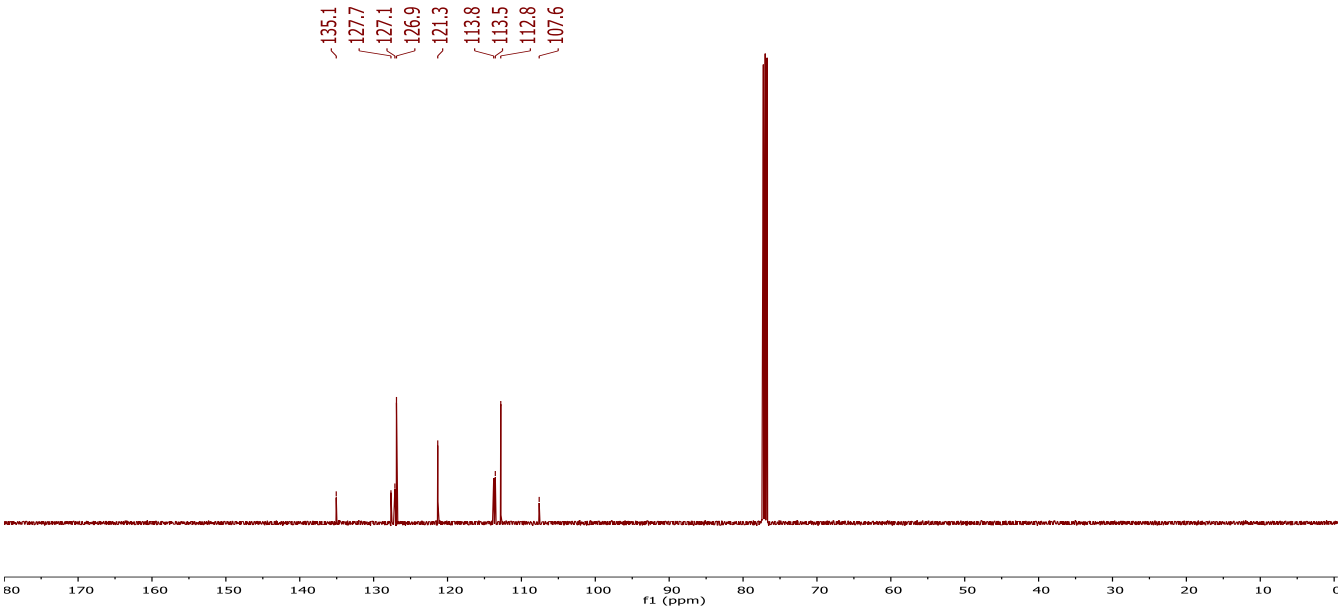

**2j**

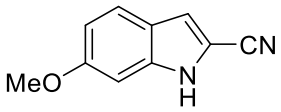



Cl
CN
N
H

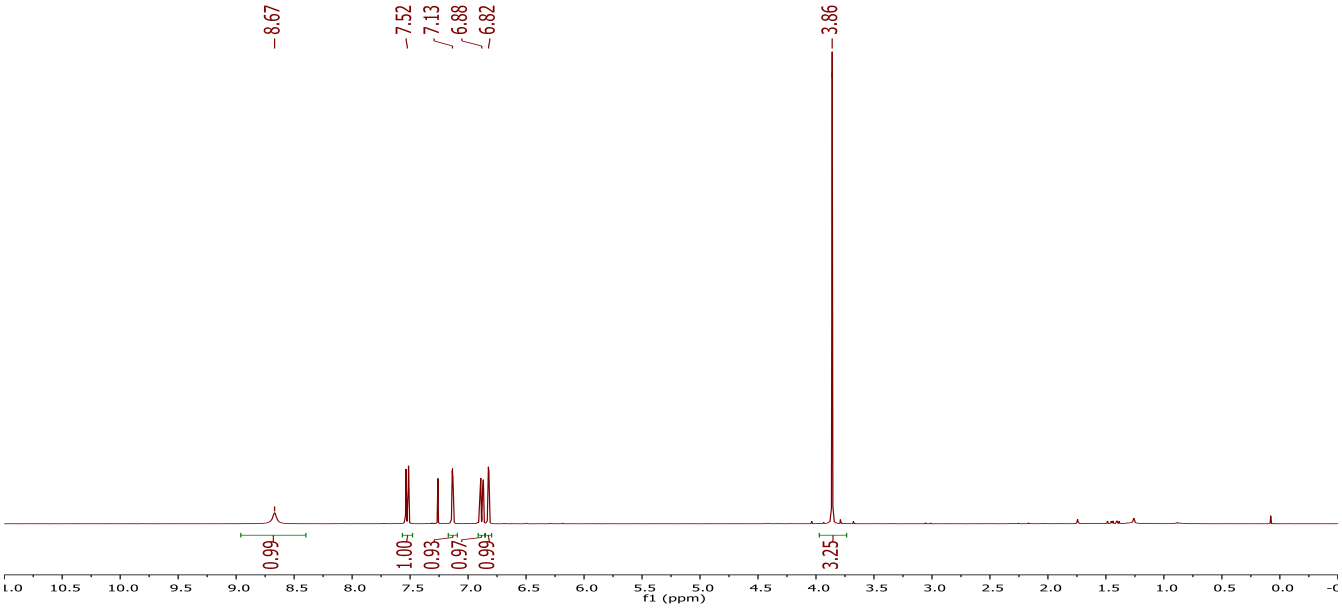
**2k**

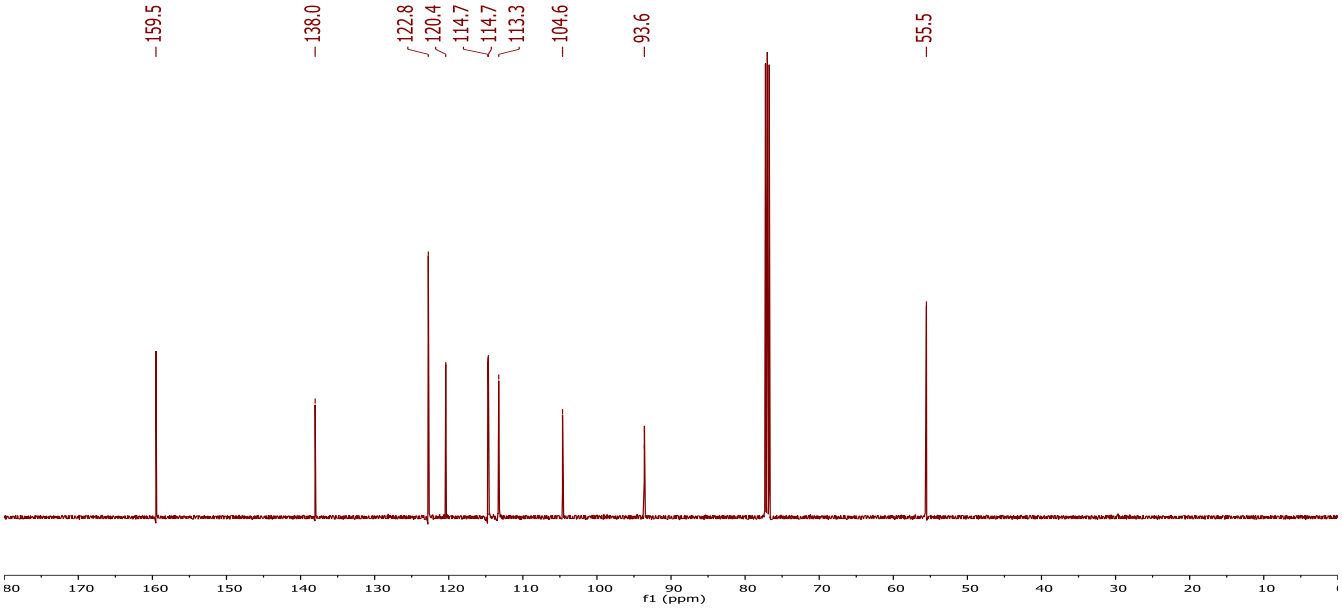

8.68
7.66
7.35
7.14
0.82
1.00
1.91
1.00
f1 (ppm)

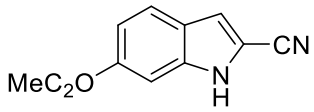

135.1
127.7
127.1
126.9
121.3
113.8
113.5
112.8
107.6
f1 (ppm)


MeO
CN
N
H

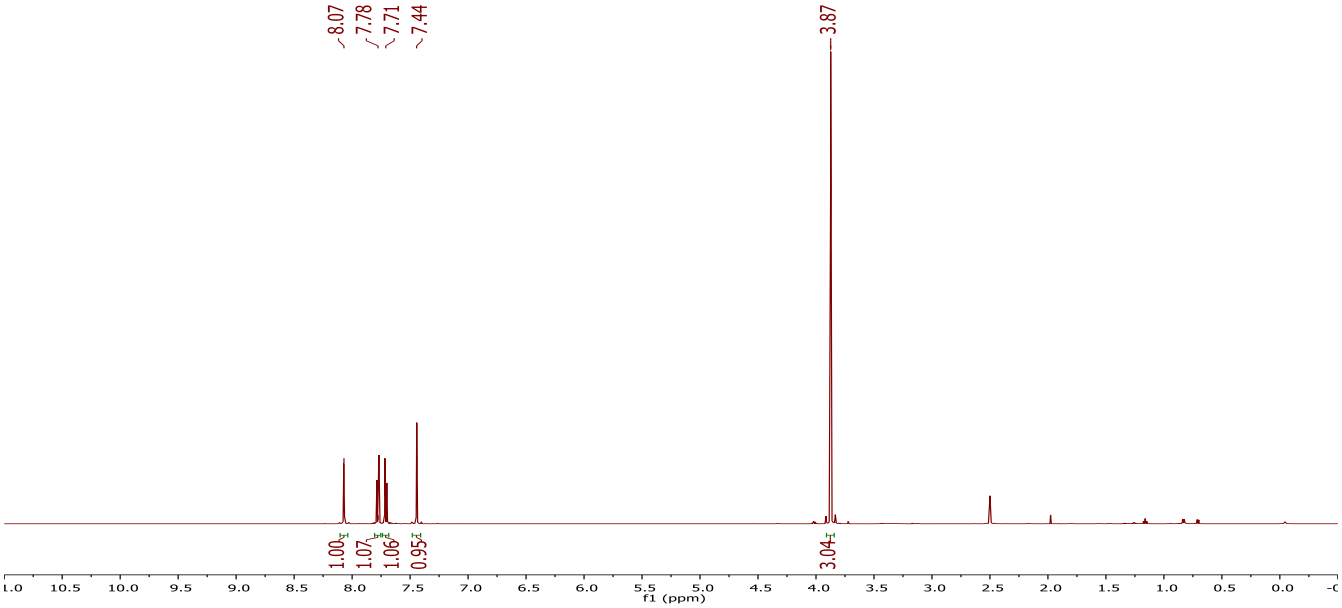
**2l**

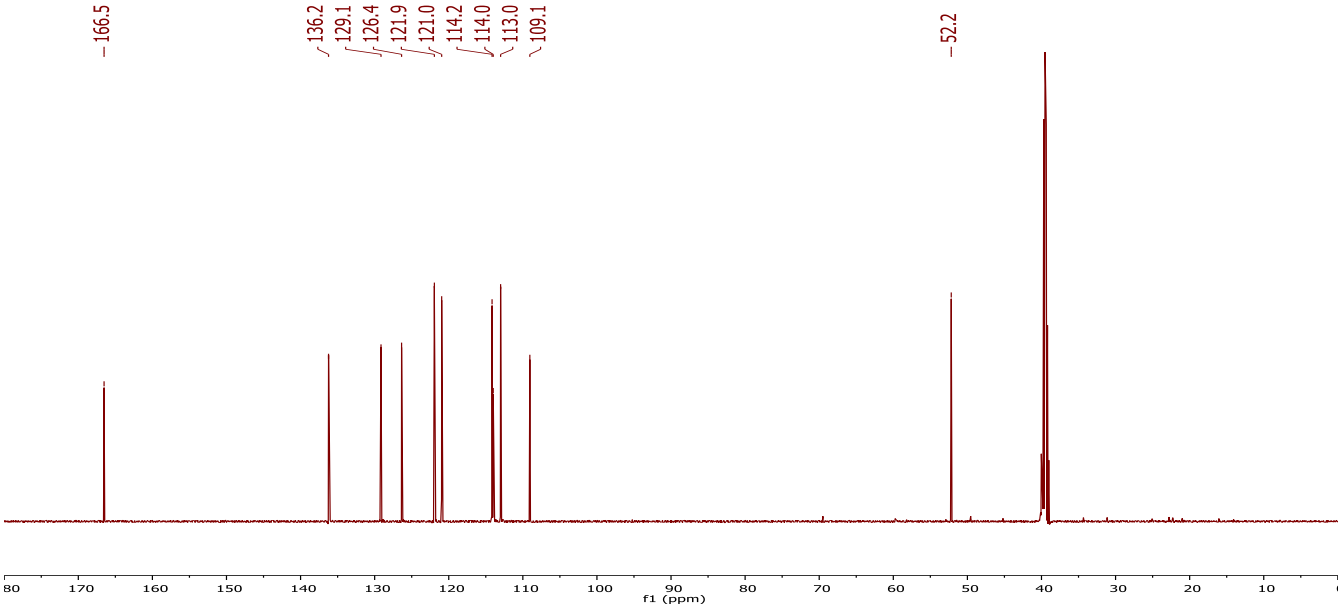

8.67
7.52
7.13
6.88
6.82
3.86
0.99
1.00
0.93
0.97
0.99
3.25
f1 (ppm)

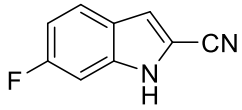

159.5
138.0
122.8
120.4
114.7
114.7
113.3
104.6
93.6
55.5
f1 (ppm)


CN
MeC2O
N
H

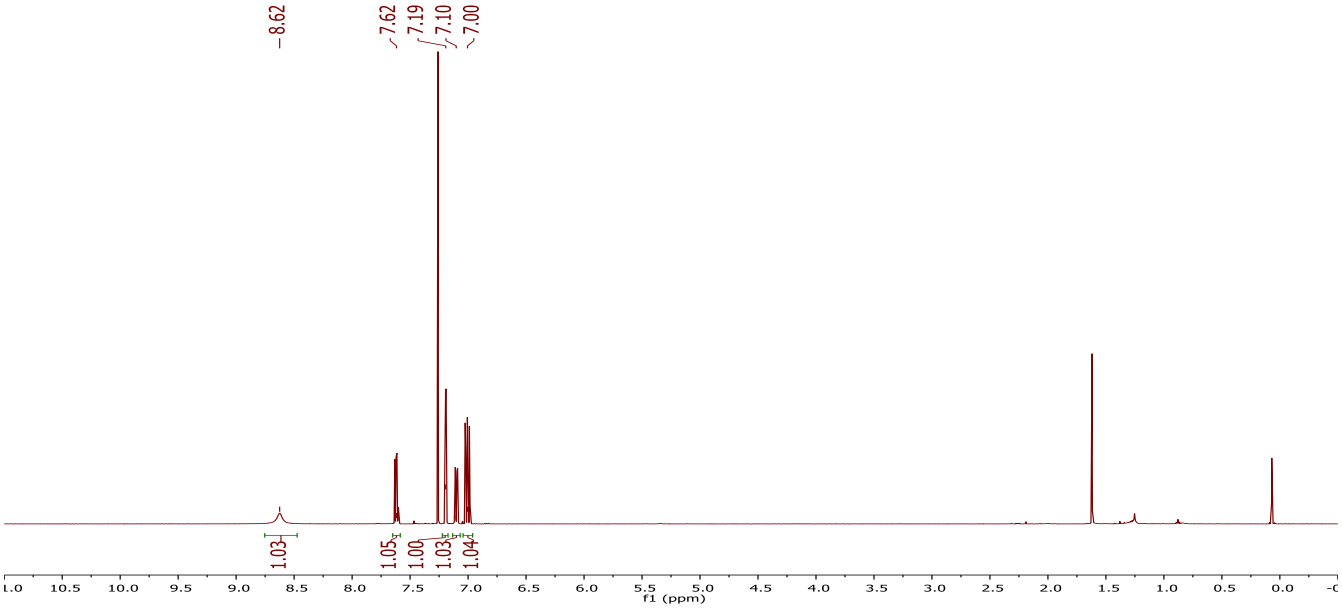
**2m**

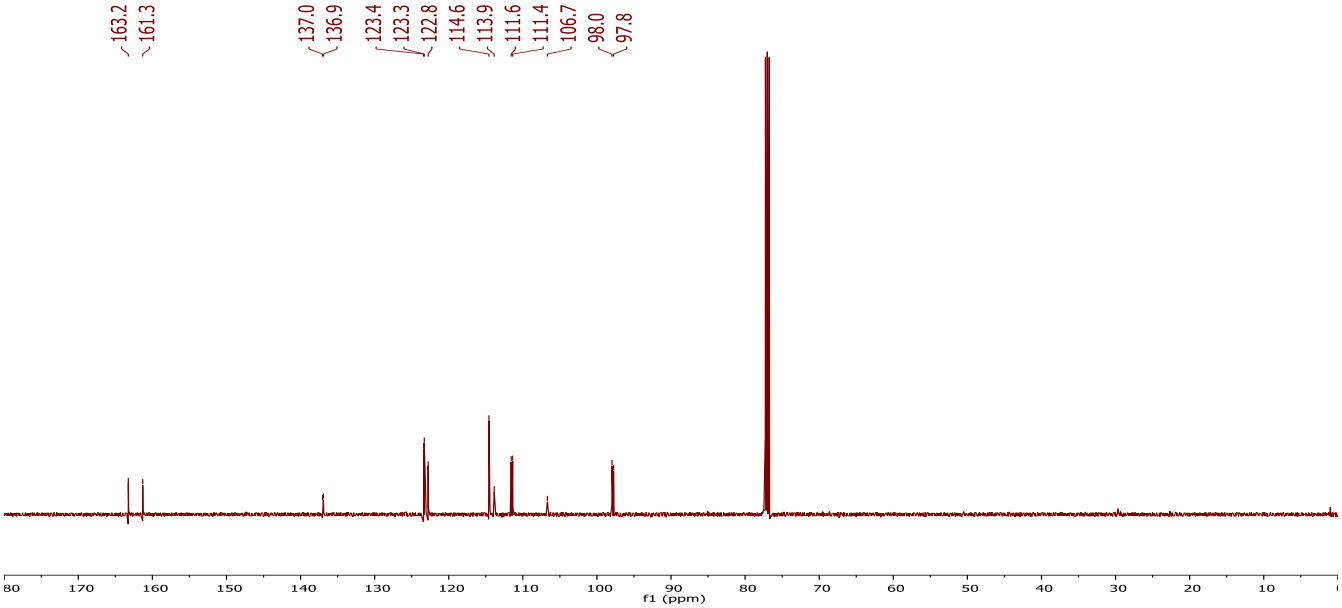

8.07
7.78
7.71
7.44
3.87
1.00
1.07
1.06
0.95
3.04
f1 (ppm)

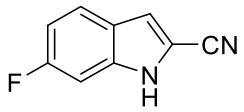

166.5
136.2
129.1
126.4
121.9
121.0
114.2
114.0
113.0
109.1
52.2
f1 (ppm)


F
N
H
CN

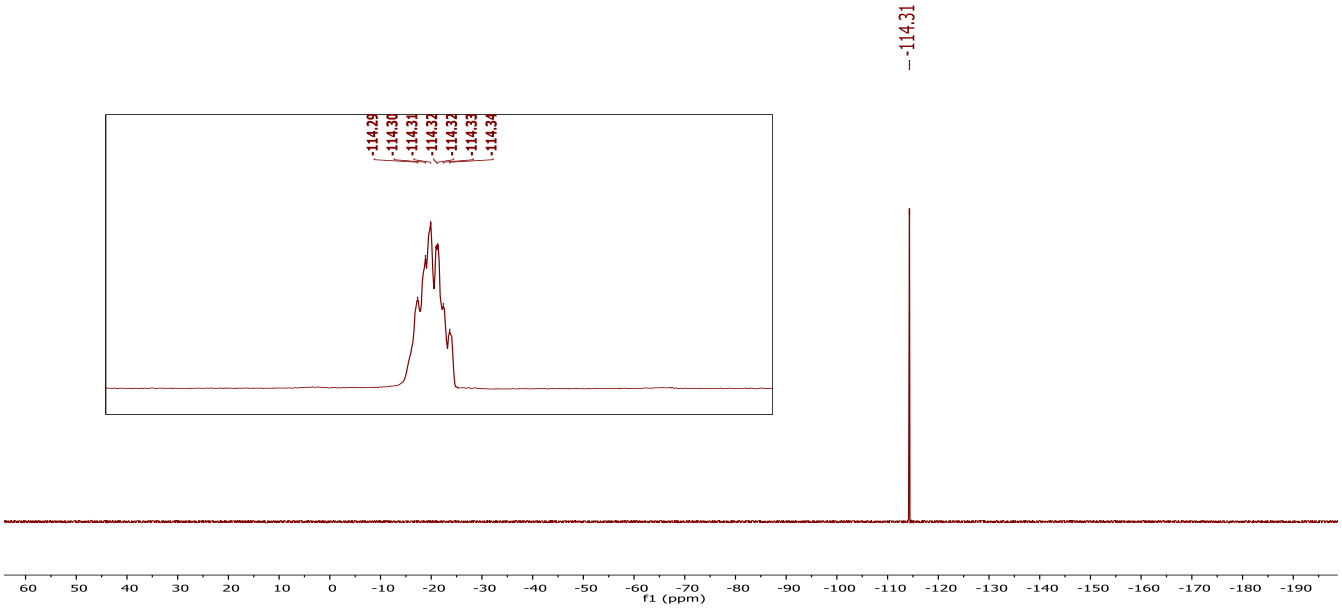
**2n**

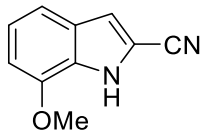

8.62
7.62
7.19
7.10
7.00
1.03
1.05
1.00
1.03
1.04
f1 (ppm)


163.2
161.3
137.0
136.9
123.4
123.3
122.8
114.6
113.9
111.6
111.4
106.7
98.0
97.8
f1 (ppm)

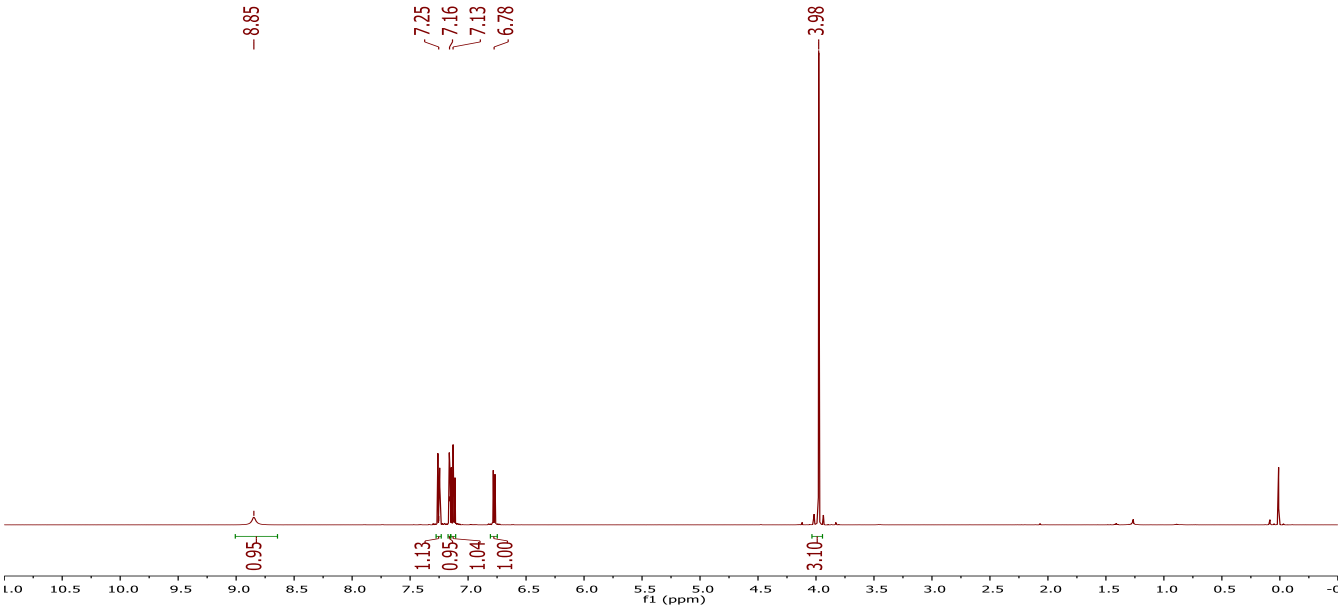

CN
F
N
H

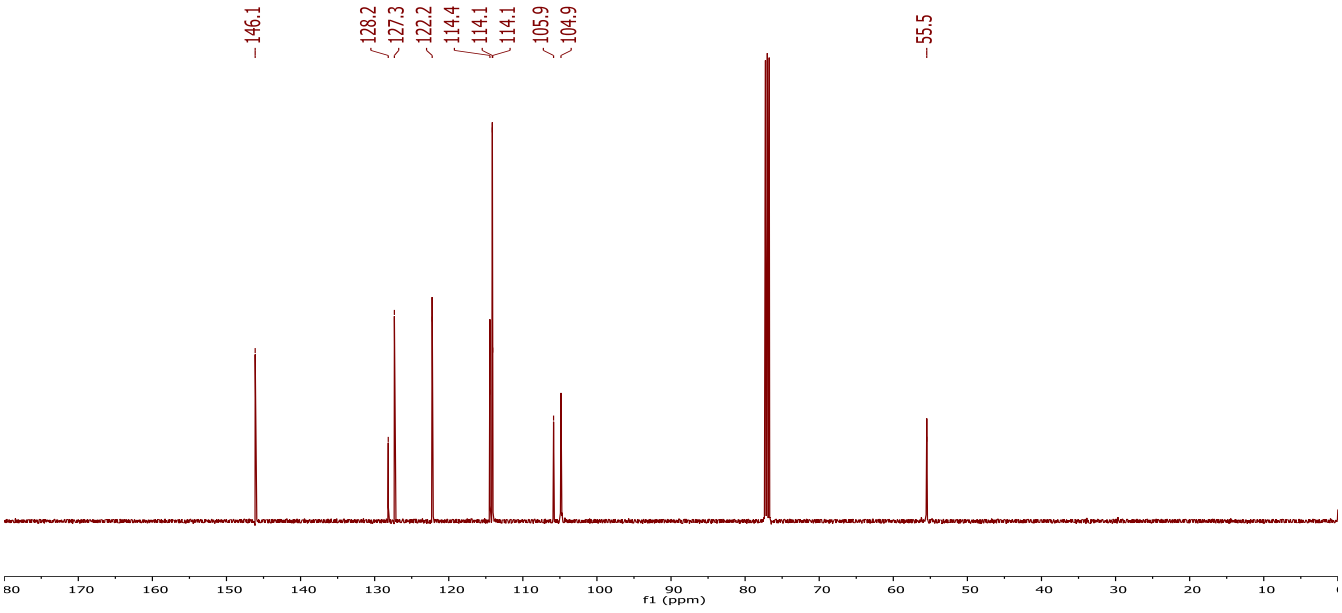
**2n**

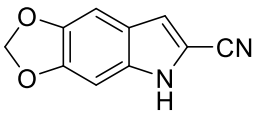

-114.31
-114.29
-114.30
-114.31
-114.32
-114.32
-114.33
-114.34
60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)


CN
N
H
OMe

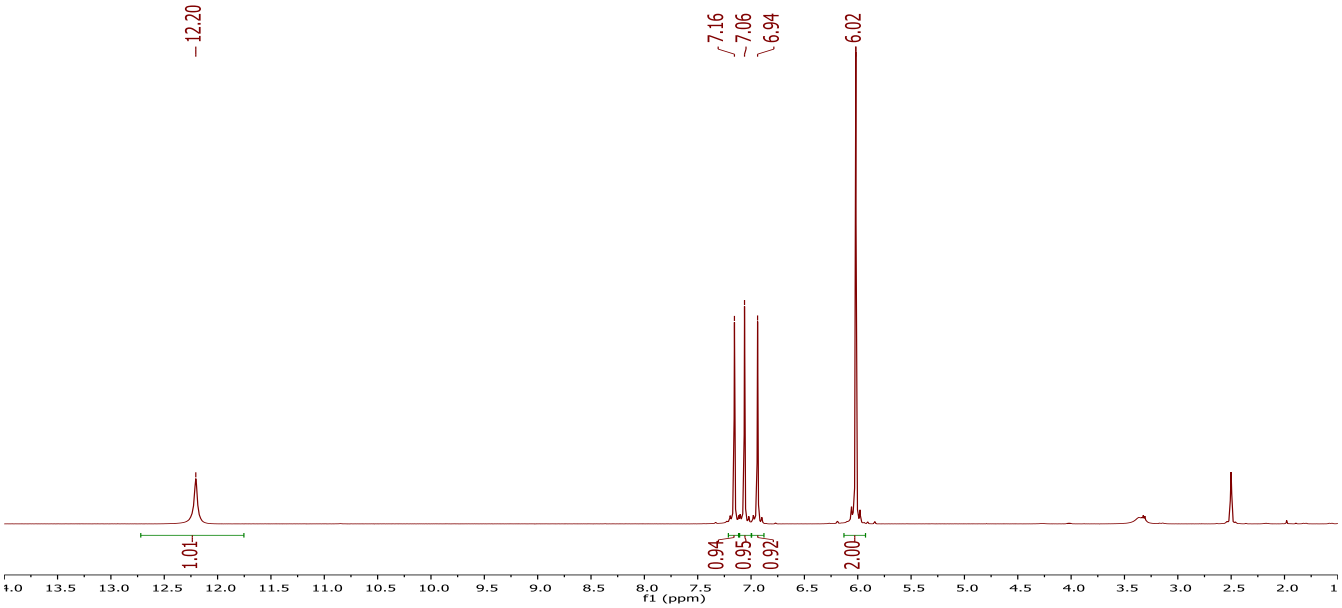
**2o**

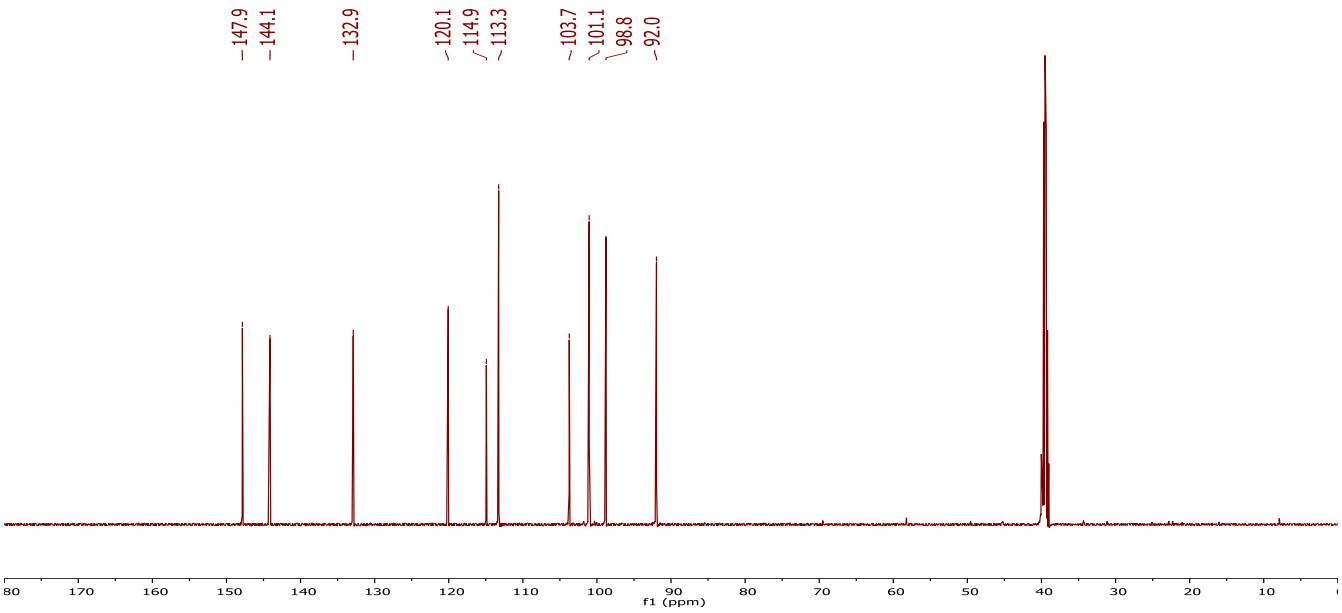

8.85
7.25
7.16
7.13
6.78
3.98
0.95
1.13
0.95
1.04
1.00
3.10
f1 (ppm)

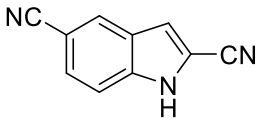

146.1
128.2
127.3
122.2
114.4
114.1
114.1
105.9
104.9
55.5
f1 (ppm)


O
O
CN
N
H

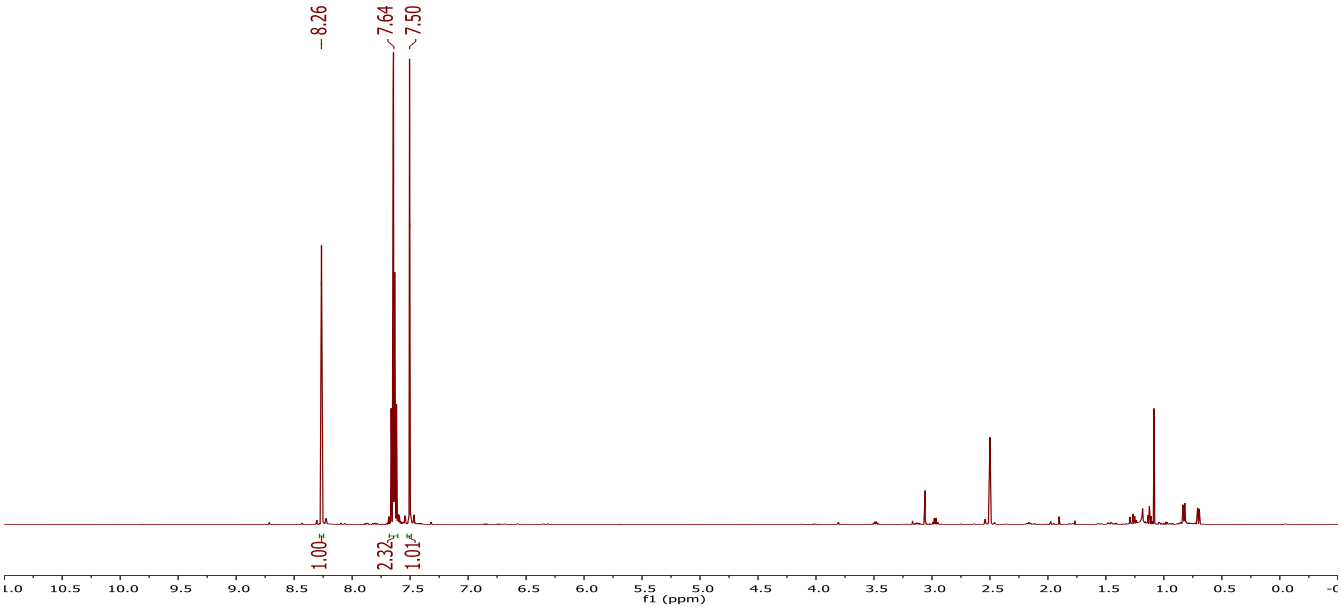
**2p**

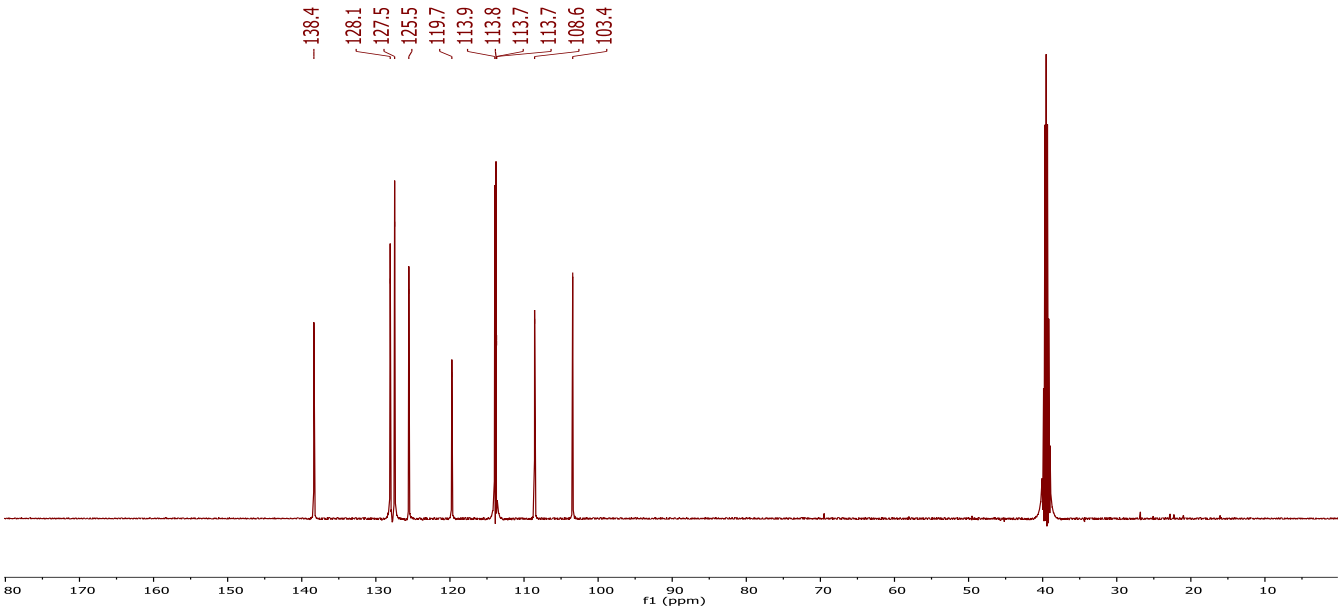

12.20
7.16
7.06
6.94
6.02
1.01
0.94
0.95
0.92
2.00
f1 (ppm)


147.9
144.1
132.9
120.1
114.9
113.3
103.7
101.1
98.8
92.0
f1 (ppm)


NC
CN
N
H

**2q**


8.26
7.64
7.50
1.00
2.32
1.01
f1 (ppm)


138.4
128.1
127.5
125.5
119.7
113.9
113.8
113.7
113.7
108.6
103.4
f1 (ppm)