Electronic Supplementary Material (ESI) for Green Chemistry.

Isocyanide 2.0

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General information

Materials and methods

All formamides were prepared in house by either performing the formylation reaction of primary amines or anilines either with ethyl formats[1, 2], or formic acid[3, 4] or formic acetic anhydride[5, 6] or our recently described Leukart-Wallach reductive amination procedure[7] (Fig. S1).

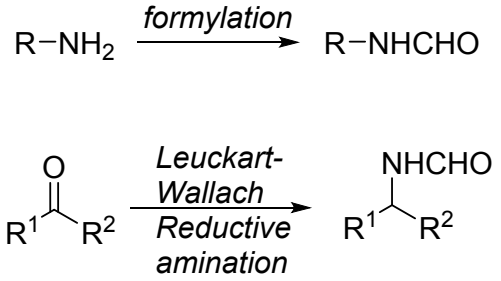


Fig. S1. Formamide syntheses.

Other reagents and solvents were purchased from Sigma Aldrich, Abcr GmbH, Acros, Fluorochem and AK Scientific and were used without further purification. Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker Avance 500 spectrometer (^{1}H NMR (500 MHz), ^{13}C NMR (126 MHz)). Chemical shifts for ^{1}H NMR were reported relative to TMS (δ 0 ppm) or internal solvent peak ($CDCl_3$ δ 7.26 ppm, DMSO-d_6 δ 2.50 ppm or CD_3OD δ 3.31 ppm) and coupling constants were in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, d = doublet, t = triplet, dd = double doublet, m = multiplet, brs = broad singlet. Chemical shifts for ^{13}C NMR reported in ppm relative to the solvent peak ($CDCl_3$ δ 77.00 ppm, DMSO-d_6 δ 39.50 ppm, CD_3OD δ 49.00 ppm). Thin layer chromatography was performed on precoated silica gel 60 F_{254} plates (Merck, Darmstadt). Silica Gel used for purification was purchase from Screening devices b.v. Reagents were available from commercial suppliers and used without any purification unless otherwise noted. Yields given refer to isolated and spectroscopically pure compounds unless otherwise stated. Melting points were determined using an OEM Electrothermal melting point apparatus 1A 8103. Electrospray ionization mass spectra (ESI-MS) were recorded on a Waters Investigator Semi-prep 15 SFC-MS instrument. High-resolution mass spectra were recorded using a QTOF Bruker Maxis Plus, mass range 100-1500 m/z, spectra rate 2.00 Hz. The literature known % yields of each isocyanide were reported and mention there with corresponding literature reference.

Details about the parallel synthesis of isocyanides on 1mmol scale:

After successfully demonstrating the synthesis of 96 isocyanides each of 0.2 mmol scale in 96 well plate, we decided to test the isocyanides synthesis in parallel fashion. For this purpose, we run the reactions on the 1-mmol scale of formamides randomly selected from the library which we used for the 96-well plate, along with few new formamides. (Table. 3). The reactions were carried out in 3-ml vials. The experimental procedure was very much similar to that outlined with the 96-member library. The reactions were performed in 3-ml vials. To the solutions/suspensions of the formamides (1.0mmol) in dichloromethane (2 M, 0.5 ml) was added triethylamine (5 equiv) at room temperature. The reaction mixtures were cooled in an ice bath, followed by the dropwise addition of phosphorous oxychloride (1 mmol) under vigorous stirring. The reaction mixtures were stirred at 0 ^{o}C for 5-10 min (Fig. S2a). After completion of the reactions as indicated by TLC, the reaction mixtures were transferred into columns (2 g silica, 6 cm X 0.75 cm) pre-packed with 100-200 mesh size silica (Fig. S2b). The isocyanides were eluted through the columns using a gradient solvent system from 0 to 100% dichloromethane in diethyl ether (2-ml solutions of 0, 25, 50, 75 and 100 %, dichloromethane in diethyl ether) (Fig. S2c). Fractions of 2-3 ml were collected, with the first two or three fractions usually being the most concentrated ones (Fig. S2d). Evaporation of the solvents under reduced pressure afforded the pure isocyanides (Fig. S2e).

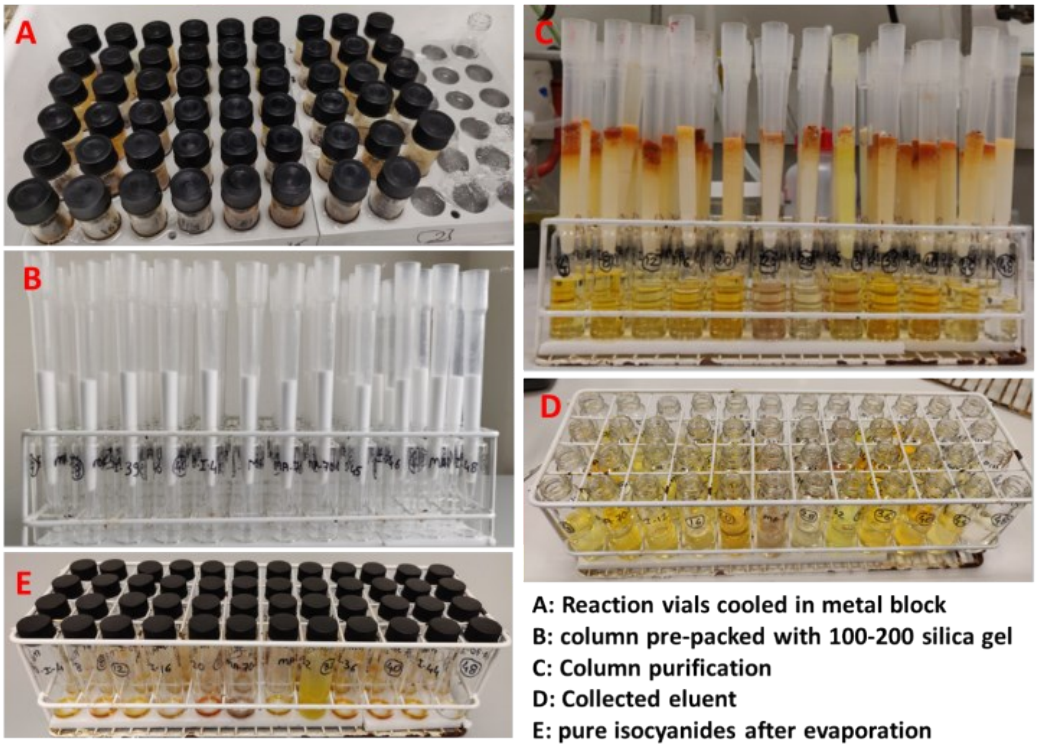


Fig. S2: Parallel synthesis of 56 isocyanides on a 1-mmol scale.

General synthetic procedures

General synthetic procedure (A): synthesis of isocyanides on a 0.2-mmol scale: To the pre-weighed formamides (0.2mmol) in a 1.5-ml glass deep well plate was added 0.1 ml dichloromethane (2M), followed by the addition of triethylamine (5 equiv) at room temperature. The well plate was cooled in an ice bath and phosphorous oxychloride (1 equiv, 1M solution in CH_2Cl_2) was added to the reaction mixture inside the wells using an 8-channel pipette. After 4 minutes, the reaction mixtures were diluted with 0.5 ml diethyl ether and transferred to a 96-well filtration plate packed with 400 mg silica 100-200 mesh size. The isocyanide-containing solution in each well was allowed to flow down through the wells -which served as columns- by gravity and collected in 1.5-ml deep 96-well collection plates. The remaining isocyanides in the columns were washed first with diethyl ether and afterwards with 0.5-ml solutions of 25%, 50%, 75%, and 100% dichloromethane in diethyl ether and collected. Evaporation of the solvents under reduced pressure afforded the pure isocyanides.

General synthetic procedure (B): **synthesis of isocyanides on a 1-mmol scale:** The reactions were carried out in 3-ml vials. To the suspensions of the formamides (1 mmol) in dichloromethane (2 M, 0.5 ml) was added triethylamine (5 equiv) at room temperature. The reaction mixtures were cooled in an ice bath, followed by the dropwise addition of phosphorous oxychloride (1 mmol) under vigorous stirring. The reaction mixtures were stirred at 0^{o}C for 3-6 min. After completion of the reactions as indicated by TLC, the reaction mixtures were transferred into columns (2 g silica, 6 cm X 0.75 cm) pre-packed with 100-200 mesh size silica. The isocyanides were eluted through the columns using a gradient solvent system from 0 to 100% dichloromethane in diethyl ether (1-ml solutions of 0, 25, 50, 75 and 100 %, dichloromethane in diethyl ether). Fractions of 2-3 ml were collected, with the first two fractions usually being the most concentrated ones. Evaporation of the solvents under reduced pressure afforded the pure isocyanides.

General synthetic procedure (C) for 100 mmol scaleup batches: To the stirred solution of the formamide in dichloromethane (2M) was added triethylamine (5 equiv) at room temperature. Subsequently, phosphorus oxychloride (1.0 equiv) was added dropwise at 0 ^{o}C and the reaction mixture was stirred for 5 minutes. After completion of the reaction (indicated by TLC), the crude reaction mixture was loaded directly on a column (15 x 5 cm) packed with silica 100-200 mesh size (140 gm), and a layer of sand (1cm) was put on top of silica gel. Diethyl ether (100ml) was used as the mobile phase and fractions of 25ml were collected. The compound eluted within the first four fractions. Then, the polarity of eluent (25ml) was

increased by adding 25, 50, 75 % dichloromethane in diethyl ether. The solvents were evaporated under reduced pressure to afford the pure product.

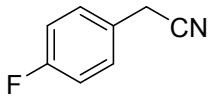
Synthetic procedure (D) for 500 mmol scaleup batch of 1-Adamantyl isocyanide (H-2): To the solution of 1-adamantyl formamide (0.5 mol) in dichloromethane (2M) was added triethylamine (5.0 equiv) at room temperature. Phosphorus oxychloride (1.0 equiv) was added at 0 ^{o}C at vigorously stirring and keeping internal temperature of reaction below 4 ^{o}C. After addition, the reaction mixture was stirred for 10 min. After completion of the reaction as indicated by TLC, the compound was purified using column chromatography. The crude reaction mixture was loaded directly on a column (20 x 9 cm) dry-packed with 600 g silica 100-200 mesh size. Diethyl ether (500ml) was used as the mobile phase and fractions of 250 ml were collected. Then, the polarity of eluent (250ml) was increased by adding 25, 50, 75 % dichloromethane in diethyl ether. The compound eluted within the first four fractions. The solvent was evaporated under reduced pressure to afford the pure product as a yellow solid, 78 gm, 97% yield.

General synthetic procedure (E) for the Ugi-tetrazole reaction (UT-4CR): To the stirred solution of the oxo component (1.0 mmol) and the amine (1.0 mmol) in methanol (1 mL) were added the freshly prepared isocyanide (1.0 mmol) and trimethylsilyl azide (1.0 mmol) at 0^{o}C. After addition, the reaction was stirred at room temperature for 18 h. The reaction was concentrated *in vacuo* and purified by flash column chromatography to give the pure product.

General synthetic procedure (F) for the Ugi four component reaction (U-4CR): To the stirred solution of the oxo component (1.0 mmol) and the amine (1.0 mmol) in methanol (1 mL) were added acid (1.0 mmol) and the freshly prepared isocyanide (1.0 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction was concentrated *in vacuo* and purified by flash column chromatography to give the pure product.

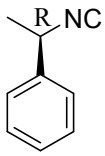
In the following references are given for previously described isocyanides for comparison of analytical data (NMR), yields and synthesis methods.

A-1: 1-Fluoro-4-(isocyanomethyl)benzene[8]



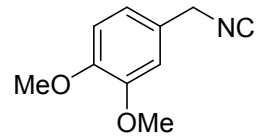
The product was obtained with procedure **A**, 0.2 mmol scale, 26.5 mg, 98% yield, liquid; (lit. yield = 79%)[8]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, *J*= 8.5, 5.2 Hz, 2H) , 7.10 – 7.04 (m, 2H), 4.60 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (d, *J* = 247.3 Hz), 157.7 (t, *J* = 5.1 Hz), 128.4 (d, *J* = 8.3 Hz), 128.1 (d, *J* = 3.1 Hz), 115.8 (d, *J* = 21.8 Hz), 44.7 (t, *J* = 7.1 Hz); HRMS (ESI) m/z calculated for C_7H_6F $[M+H-HCN]^+$: 109.0448; found $[M+H-HCN]^+$: 109.0449.

A-2 / I-7: (*R*)-(1-Isocyanoethyl)benzene[9]



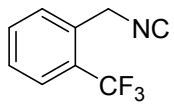
The product was obtained with procedure **A**, 0.2 mmol scale, 24.9mg, 95% yield, liquid; and with procedure **B**, 1.0 mmol, 113 mg, 86% yield; (lit. yield = 55%, by Hoffman method)[9]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.34 (m, 5H), 4.86 (qt, *J* = 6.9, 2.0 Hz, 1H), 1.72 (dt, *J* = 6.9, 2.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3 (t, *J* = 5.3 Hz), 129.0, 128.3, 125.4, 53.8 (t, *J* = 6.4 Hz), 25.2; HRMS (ESI) m/z calculated for C_8H_9 $[M+H-HCN]^+$: 105.0699; found $[M+H-HCN]^+$: 105.0698.

A-3: 4-(Isocyanomethyl)-1,2-dimethoxybenzene[10]



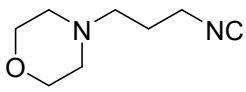
The product was obtained with procedure **A**, 0.2 mmol scale, 34.0 mg, 96% yield, pale yellow solid; (lit. yield = 96%)[10]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 – 6.82 (m, 3H), 4.57 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1 (t, *J* = 5.4 Hz), 149.2, 149.0, 124.7, 119.1, 111.1, 109.7, 55.9, 55.8, 45.2 (t, *J* = 7.0 Hz); HRMS (ESI) m/z calculated for $C_9H_{11}O_2$ $[M+H-HCN]^+$: 151.0754; found $[M+H-HCN]^+$: 151.0754.

A-4 / I-14: 1-(Isocyanomethyl)-2-(trifluoromethyl)benzene[11]



The product was obtained with procedure **A**, 0.2 mmol scale, 34.8 mg, 94% yield, liquid; and with procedure **B**, 1.0 mmol, 131 mg, 71% yield; (lit. yield = 41%)[11]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 4.87 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.3 (t, *J* = 5.6 Hz), 132.7, 130.2, 128.6, 128.4, 126.2 (q, *J* = 5.7 Hz), 123.8 (q, *J* = 273.0 Hz), 42.8 – 42.5 (m); HRMS (ESI) m/z calculated for $C_8H_6F_3$ $[M+H-HCN]^+$: 159.0416; found $[M+H-HCN]^+$: 159.0419.

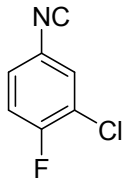
A-5 / I-58: 4-(3-Isocyanopropyl)morpholine[12]



The product was obtained with procedure **A**, 0.2 mmol scale, 4.6 mg, 15% yield, liquid; and with procedure **B**, 1.0 mmol, 138 mg, 90%

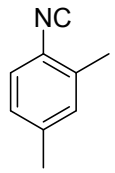
yield; (lit. yield = 90%)[12]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (d, *J* = 4.7 Hz, 4H), 3.52 – 3.43 (m, 2H), 2.52 – 2.35 (m, 6H), 1.88 – 1.80 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9 (t, *J*= 5.7 Hz), 66.8, 54.7, 53.5, 39.4 (t, *J*= 6.4 Hz), 26.0; HRMS (ESI) m/z calculated for $C_8H_{15}N_2O$ $[M+H]^+$: 155.1179; found $[M+H]^+$: 155.1181.

A-6: 2-Chloro-1-fluoro-4-isocyanobenzene[13]



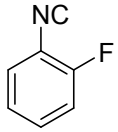
The product was obtained with procedure **A**, 0.2 mmol scale, 29.2 mg, 94% yield, solid; (lit. yield = 88%)[13]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 6.3, 2.4 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.18 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 158.3 (d, *J* = 254.3 Hz), 128.9, 126.5 (d, *J* = 8.0 Hz), 123.2 (t, *J* = 13.2 Hz), 122.3 (d, *J* = 19.2 Hz); 117.5 (d, *J* = 23.2 Hz); HRMS (ESI) m/z calculated for C_7H_6ClFNO $[M+H+H_2O]^+$: 174.0116; found $[M+H+H_2O]^+$: 174.0119.

A-7: 1-Isocyano-2,4-dimethylbenzene[14]



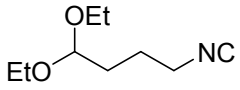
The product was obtained with procedure **A**, 0.2 mmol scale, 24.1 mg, 92% yield, solid; (lit. yield = 61%)[14]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.1 Hz, 1H), 7.07 (s, 1H), 6.99 (d, *J* = 8.1 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8 (t, *J* = 6.0 Hz), 139.4, 134.5, 131.0, 127.2, 126.2, 124.0 (t, *J* = 13.5 Hz), 21.2, 18.4; HRMS (ESI) m/z calculated for $C_9H_{10}N$ $[M+H]^+$: 132.0808; found $[M+H]^+$: 132.0810.

A-8: 1-Fluoro-2-isocyanobenzene[15]



The product was obtained with procedure **A**, 0.2 mmol scale, 20.6 mg, 85% yield, liquid; (lit. yield = 80%)[15]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H), 7.23 – 7.15 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 157.4 (d, *J* = 256.9 Hz), 130.9 (d, *J* = 7.4 Hz), 128.0, 126.3, 124.6 (d, *J* = 4.0 Hz), 116.6 (d, *J* = 18.4 Hz); HRMS (ESI) m/z calculated for C_7H_7FNO $[M+H+H_2O]^+$: 140.0506; found $[M+H+H_2O]^+$:140.0508.

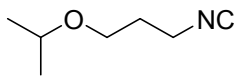
A-9 / I-35: 1,1-Diethoxy-4-isocyanobutane



The product was obtained with procedure **A**, 0.2 mmol scale, 27.4 mg, 80% yield, liquid; and with procedure **B**, 1.0 mmol, 138 mg, 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.49 (d, *J* = 5.0 Hz, 1H), 3.68 – 3.60 (m, 2H), 3.53 – 3.38 (m, 4H), 1.81 – 1.71 (m, 4H), 1.20 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (126 MHz,

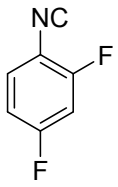
$CDCl_3$) δ 155.8 (t, *J* = 5.8 Hz), 102.0, 61.5, 41.4 (t, *J* = 6.6 Hz), 30.3, 24.4, 15.2; HRMS (ESI) m/z calculated for $C_9H_{18}NO_2$ $[M+H]^+$: 172.1332; found $[M+H]^+$: 172.1334.

A-10 / I-43: 1-Isocyano-3-isopropoxypropane[16]



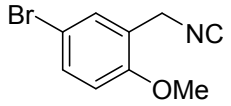
The product was obtained with procedure **A**, 0.2 mmol scale, 22.9 mg, 90% yield, liquid; and with procedure **B**, 1.0 mmol, 118 mg, 93% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 3.59 – 3.44 (m, 5H), 1.91 – 1.82 (m, 2H), 1.12 (d, *J* = 6.2 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.7 (t, *J* = 5.7 Hz), 71.7, 63.3, 38.6 (t, *J* = 6.5 Hz), 29.6, 21.9; HRMS (ESI) m/z calculated for $C_7H_{14}NO$ $[M+H]^+$: 128.1070; found $[M+H]^+$: 128.1071.

A-12: 2,4-Difluoro-1-isocyanobenzene



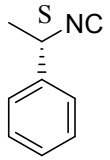
The product was obtained with procedure **A**, 0.2 mmol scale, 25.3 mg, 91% yield, solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 1H), 7.00 – 6.89 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 162.5 (dd, *J* = 254.8, 10.6 Hz), 157.9 (dd, *J* = 259.7, 12.5 Hz), 128.9 (d, *J* = 10.2 Hz), 128.5, 112.2 (dd, *J* = 23.2, 4.0 Hz), 105.4 (dd, *J* = 26.9, 22.1 Hz); SFC-MS (ESI) m/z calculated for $C_7H_4F_2N$ $[M+H]^+$: 140.03; found $[M+H]^+$: 140.07

B-1 / I-1: 4-Bromo-2-(isocyanomethyl)-1-methoxybenzene



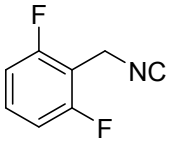
The product was obtained with procedure **A**, 0.2 mmol scale, 39.3 mg, 87% yield, semisolid; and with procedure **B**, 1.0 mmol, 213 mg, 95% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.5 Hz, 1H), 7.41 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 1H), 4.58 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9 (t, *J* = 5.0 Hz), 155.1, 132.2, 130.2, 122.7, 112.7, 111.8, 55.6, 40.6 (t, *J* = 7.5 Hz); HRMS (ESI) m/z calculated for C_8H_8BrO $[M+H\text{-}HCN]^+$: 198.9759; found $[M+H\text{-}HCN]^+$: 198.9757

B-2: (S)-(1-Isocyanoethyl)benzene[17]



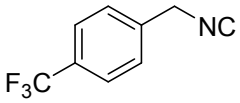
The product was obtained with procedure **A**, 0.2 mmol scale, 22.3 mg, 85% yield, liquid; (lit. yield = 50%)[17]. ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 5H), 4.86 – 4.80 (m, 1H), 1.71 – 1.67 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3 (t, *J* = 4.9 Hz), 138.5, 128.9, 128.3, 125.4, 53.8 (t, *J* = 6.5 Hz), 25.1; HRMS (ESI) m/z calculated for C_8H_9 $[M+H\text{-}HCN]^+$: 105.0699; found $[M+H\text{-}HCN]^+$: 105.0698.

B-3: 1,3-Difluoro-2-(isocyanomethyl)benzene[18]



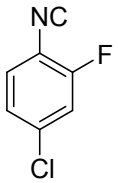
The product was obtained with procedure **A**, 0.2 mmol scale, 27.2 mg, 89% yield, liquid; (lit. yield = 50%)[18]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 1H), 7.03 – 6.95 (m, 2H), 4.68 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.9 (dd, J = 251.8, 6.7 Hz), 157.2, 131.3 (t, J = 10.3 Hz), 111.7 (dd, J = 20.0, 5.0 Hz), 109.3 (t, J = 18.7 Hz), 33.0; HRMS (ESI) m/z calculated for $C_7H_5F_2$ $[M+H-HCN]^+$: 127.0354; found $[M+H-HCN]^+$: 127.0356.

B-4 / I-15: 1-(Isocyanomethyl)-4-(trifluoromethyl)benzene[19]



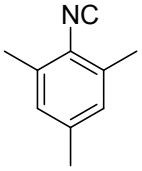
The product was obtained with procedure **A**, 0.2 mmol scale, 36.3 mg, 98% yield, liquid; and with procedure **B**, 1.0 mmol, 137 mg, 74% yield; (lit. yield = 87%)[19]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 4.75 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0 (t, J = 5.0 Hz), 136.1 (d, J = 1.0 Hz), 130.8 (q, J = 33.0 Hz), 126.9, 126.0 (q, J = 3.8 Hz), 123.7 (q, J = 273.0 Hz), 45.1 (t, J = 7.6 Hz); HRMS (ESI) m/z calculated for $C_8H_6F_3$ $[M+H-HCN]^+$: 159.0422; found $[M+H-HCN]^+$: 159.0419.

B-5: 4-Chloro-2-fluoro-1-isocyanobenzene



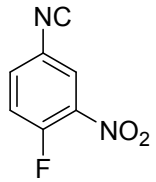
The product was obtained with procedure **A**, 0.2 mmol scale, 26.7 mg, 86% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, J = 8.0 Hz, 1H), 7.24 (dd, J = 9.0, 2.2 Hz, 1H), 7.20 – 7.16 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.7, 157.3 (d, J = 260.7 Hz), 136.3 (d, J = 8.8 Hz), 128.5, 125.2 (d, J = 4.1 Hz), 117.6 (d, J = 21.9 Hz); HRMS (ESI) m/z calculated for C_7H_6ClFNO $[M+H+H_2O]^+$: 174.0116; found: $[M+H+H_2O]^+$: 174.0120.

B-6 / I-24: 2-Isocyano-1,3,5-trimethylbenzene[20]



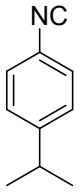
The product was obtained with procedure **A**, 0.2 mmol scale, 25.6 mg, 88% yield, solid; and with procedure **B**, 1.0 mmol, 135 mg, 93% yield; (lit. yield = 45%)[20]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (s, 2H), 2.37 (s, 6H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7 (t, J = 5.6 Hz), 138.7, 134.5, 128.4, 124.1, 21.1, 18.7; HRMS (ESI) m/z calculated for $C_{10}H_{12}N$ $[M+H]^+$: 146.0964; found $[M+H]^+$: 146.0966.

B-7 / I-33: 1-Fluoro-4-isocyano-2-nitrobenzene[21]



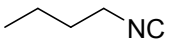
The product was obtained with procedure **A**, 0.2 mmol scale, 26.7 mg, 80% yield, solid; and with procedure **B**, 1.0 mmol, 143 mg, 86% yield; (lit. yield = 82%)[21]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 6.4, 2.6 Hz, 1H), 7.71 – 7.65 (m, 1H), 7.40 (t, *J* = 9.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 155.1 (d, *J* = 270.3 Hz), 137.3, 133.2 (d, *J* = 9.2 Hz), 124.4 (d, *J* = 2.2 Hz), 122.7, 120.0 (d, *J* = 22.9 Hz); SFC-MS (ESI) m/z calculated for $C_7H_4FN_2O_2$ $[M+H]^+$: 167.12; found $[M+H]^+$: 167.13.

B-8 / I-30: 1-Isocyano-4-isopropylbenzene[13]



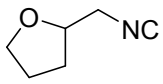
The product was obtained with procedure **A**, 0.2 mmol scale, 24.9 mg, 86% yield, liquid; and with procedure **B**, 1.0 mmol, 131 mg, 90% yield; (lit. yield = 77%)[13]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H), 2.94 (h, *J*= 6.9, 1H), 1.26 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1 (t, *J* = 5.6 Hz), 150.3, 127.2, 126.1, 124.1 (t, *J* = 13.5 Hz), 33.8, 23.5; HRMS (ESI) m/z calculated for $C_{10}H_{12}N$ $[M+H]^+$: 146.0964; found $[M+H]^+$: 146.0967.

B-9 / I-36: 1-Isocyanobutane[22]



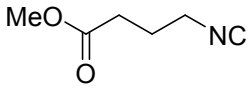
The product was obtained with procedure **A**, 0.2 mmol scale, 13.5 mg, 81% yield; and with procedure **B**, 1.0 mmol, 71 mg, 85% yield, liquid; (lit. yield = 96% reaction run at -78°C)[22]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.41 – 3.36 (m, 2H), 1.71 – 1.62 (m, 2H), 1.52 – 1.43 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5, 41.2 (t, *J* = 6.4 Hz), 31.0, 19.5, 13.1; HRMS (ESI) m/z calculated for $C_5H_{12}NO$ $[M+H+H_2O]^+$: 102.0913; found $[M+H+H_2O]^+$: 102.0914.

B-10 / I-44: 2-(Isocyanomethyl)tetrahydrofuran[23]



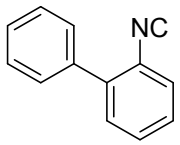
The product was obtained with procedure **A**, 0.2 mmol scale, 21.7 mg, 98% yield; and with procedure **B**, 1.0 mmol, 102 mg, 92% yield, liquid; (lit. yield = 72%)[23]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.14 – 4.04 (m, 1H), 3.98 – 3.89 (m, 1H), 3.84 – 3.76 (m, 1H), 3.53 – 3.46 (m, 2H), 2.15 – 2.04 (m, 1H), 2.03 – 1.88 (m, 2H), 1.82 – 1.71 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2 (t, *J* = 5.7 Hz), 75.8, 68.9, 45.7 (t, *J* = 6.9 Hz), 28.7, 25.6; HRMS (ESI) m/z calculated for $C_6H_{10}NO$ $[M+H]^+$: 112.0757; found $[M+H]^+$: : 112.0758.

B-11: Methyl 4-isocyanobutanoate[24]



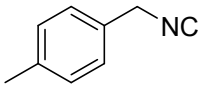
The product was obtained with procedure **A**, 0.2 mmol scale, 23.6 mg, 93% yield, liquid; (lit. yield = 93%)[24]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 3H), 3.49 – 3.42 (m, 2H), 2.52 – 2.42 (m, 2H), 2.02 – 1.90 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 156.6 (t, J = 5.7 Hz), 51.7, 40.6 (t, J = 6.6 Hz), 30.0, 24.1; HRMS (ESI) m/z calculated for $C_6H_{12}NO_3$ $[M+H+H_2O]^+$: 146.0812; found $[M+H+H_2O]^+$: 146.0814.

B-12: 2-Isocyano-1,1'-biphenyl[25]



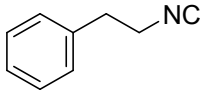
The product was obtained with procedure **A**, 0.2 mmol scale, 33.6 mg, 94% yield, liquid; (lit. yield = 84%)[25]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.41 (m, 8H), 7.41 – 7.36 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 138.8, 136.9, 130.5, 129.5, 128.9, 128.5, 128.3, 128.1, 127.8, 124.5; HRMS (ESI) m/z calculated for $C_{13}H_{10}N$ $[M+H]^+$: 180.0808; found $[M+H]^+$: 180.0809.

C-1 / I-2: 1-(Isocyanomethyl)-4-methylbenzene[26]



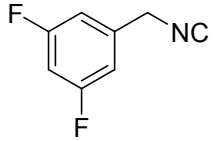
The product was obtained with procedure **A**, 0.2 mmol scale, 25.7 mg, 98% yield, liquid; and with procedure **B**, 1.0 mmol, 113 mg, 86% yield; (lit. yield = 80%)[26]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.3 Hz, 2H), 7.21 (d, J = 8.3 Hz, 2H), 4.59 (s, 2H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.1 (t, J = 5.2 Hz), 138.1, 129.5, 126.5, 45.2 (t, J = 7.1 Hz), 21.0; HRMS (ESI) m/z calculated for C_8H_9 $[M+H-HCN]^+$: 105.0699; found $[M+H-HCN]^+$: 105.0698.

C-2: (2-Isocyanoethyl)benzene[27]



The product was obtained with procedure **A**, 0.2 mmol scale, 24.4 mg, 97% yield, liquid; (lit. yield = 45%)[27]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.32 – 7.27 (m, 1H), 7.27 – 7.22 (m, 2H), 3.61 (tt, J = 7.1, 1.9 Hz, 2H), 2.99 (tt, J = 7.1, 2.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4 (t, J = 5.6 Hz), 136.6, 128.7, 128.6, 127.2, 42.9 (t, J = 6.7 Hz), 35.6; HRMS (ESI) m/z calculated for C_8H_9 $[M+H-HCN]^+$: 105.0699; found $[M+H-HCN]^+$: 105.0698.

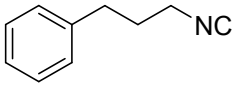
C-3: 1,3-Difluoro-5-(isocyanomethyl)benzene



The product was obtained with procedure **A**, 0.2 mmol scale, 27.5 mg, 90% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 – 6.87 (m, 2H), 6.81 (tt, J = 8.8, 2.3 Hz, 1H), 4.65 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3 (dd,

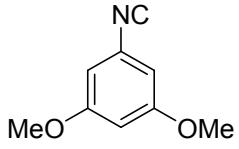
J = 250.6, 12.8 Hz), 159.4 (t, *J* = 5.0 Hz), 135.8 (t, *J* = 9.7 Hz), 109.7 (dd, *J* = 20.2, 6.8 Hz), 104.0 (t, *J* = 25.1 Hz), 44.8 (t, *J* = 7.7 Hz); HRMS (ESI) m/z calculated for $C_7H_5F_2$ [M+H-HCN]$^+$: 127.0354; found [M+H-HCN]$^+$: 127.0356.

C-4 / I-16: (3-Isocyanopropyl)benzene[28]



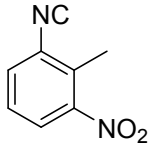
The product was obtained with procedure **A**, 0.2 mmol scale, 21.2 mg, 73% yield, liquid; (lit. yield = 95%, reaction temp. 110^{o}C)[28]. and with procedure **B**, 1.0 mmol, 138 mg, 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 8.2 Hz, 2H), 7.25 – 7.18 (m, 3H), 3.37 (ddt, *J* = 8.5, 3.9, 2.0 Hz, 2H), 2.79 (t, *J* = 7.4 Hz, 2H), 2.04 – 1.96 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2 (t, *J* = 5.6 Hz), 139.8, 128.6, 128.5, 126.4, 40.7 (t, *J* = 6.5Hz), 32.1, 30.5; HRMS (ESI) m/z calculated for $C_{10}H_{14}NO$ [M+H+H_2O]$^+$: 164.1070; found [M+H+H_2O]$^+$: 164.1073.

C-5 / I-21: 1-Isocyano-3,5-dimethoxybenzene[10]



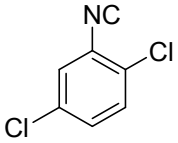
The product was obtained with procedure **A**, 0.2 mmol scale, 23.5 mg, 72% yield, solid; and with procedure **B**, 1.0 mmol, 116.6 mg, 71% yield; (lit. yield = 91%, reaction temp -60 ^{o}C)[10]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.51 (d, *J* = 2.3 Hz, 2H), 6.47 (t, *J* = 2.3 Hz, 1H), 3.79 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.4, 161.0, 127.6, 104.7, 102.1, 55.6; HRMS (ESI) m/z calculated for $C_9H_{10}NO_2$ [M+H]$^+$: 164.0706; found [M+H-HCN]$^+$: 164.0709.

C-6 / I-25: 1-Isocyano-2-methyl-3-nitrobenzene



The product was obtained with procedure **A**, 0.2 mmol scale, 27.2 mg, 84% yield, solid; and with procedure **B**, 1.0 mmol, 159 mg, 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.62 (d, 8.1 Hz, 1H), 7.41 (t, *J* = 8.1 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 150.4, 130.8, 130.2, 128.3 (t, *J* = 12.5 Hz), 127.3, 124.9, 15.2; SFC-MS (ESI) m/z calculated for $C_8H_7N_2O_2$ [M+H]$^+$: 163.05; found [M+H]$^+$: 163.10.

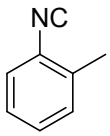
C-7: 1,4-Dichloro-2-isocyanobenzene[29]



The product was obtained with procedure **A**, 0.2 mmol scale, 28.9 mg, 84% yield, solid; (lit. yield = 90% from gem-dihalide)[29]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 2.2 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 135.8, 131.8, 130.1, 129.2,

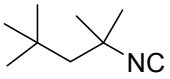
128.6, 128.0; HRMS (ESI) m/z calculated for $C_7H_6Cl_2NO$ $[M+H+H_2O]^+$: 189.9821; found $[M+H+H_2O]^+$: 189.9824.

C-8: 1-Isocyano-2-methylbenzene[30]



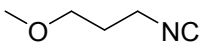
The product was obtained with procedure **A**, 0.2 mmol scale, 17.1 mg, 73% yield, liquid; (lit. yield = 93%)[30]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.27 (m, 2H), 7.23 – 7.18 (m, 1H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5 (t, *J* = 5.8 Hz), 134.9, 130.5, 129.2, 126.6, 126.5, 18.5; HRMS (ESI) m/z calculated for C_8H_8N $[M+H]^+$: 118.0651; found $[M+H]^+$: 118.0653.

C-9: 2-Isocyano-2,4,4-trimethylpentane[31, 32]



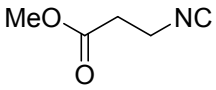
The product was obtained with procedure **A**, 0.2 mmol scale, 24.2 mg, 87% yield, liquid; (lit. yield = 63%)[32]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.59 (d, *J* = 2.3 Hz, 2H), 1.48 (d, *J* = 2.0 Hz, 6H), 1.07 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.4 (t, *J* = 4.7 Hz), 56.8 (t, *J* = 4.9 Hz), 53.8, 31.8, 31.6, 31.0; HRMS (ESI) m/z calculated for C_8H_{17} $[M+H-HCN]^+$: 113.1325; found $[M+H-HCN]^+$: 113.1326.

C-10 / I-45: 1-Isocyano-3-methoxypropane[16]



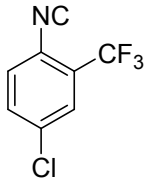
The product was obtained with procedure **A**, 0.2 mmol scale, 16.0 mg, 81% yield, liquid; and with procedure **B**, 1.0 mmol, 94 mg, 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.50 – 3.42 (m, 4H), 3.30 (s, 3H), 1.94 – 1.78 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (t, *J* = 5.7 Hz), 67.9, 58.6, 38.4 (t, *J* = 6.6 Hz), 29.2; HRMS (ESI) m/z calculated for $C_5H_{12}NO_2$ $[M+H+H_2O]^+$: 118.0862; found $[M+H+H_2O]^+$: 118.0862.

C-11 / I-48: Methyl 3-isocyanopropanoate[33]



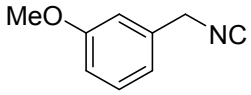
The product was obtained with procedure **A**, 0.2 mmol scale, 17.2 mg, 76% yield, liquid; and with procedure **B**, 1.0 mmol, 92 mg, 81% yield; (lit. yield = 22%)[33]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 3H), 3.67 (t, *J* = 6.7 Hz, 2H), 2.71 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.7, 157.2 (t, *J* = 4.2 Hz), 52.1, 37.0 (t, *J* = 7.3 Hz), 33.8; HRMS (ESI) m/z calculated for $C_5H_8NO_2$ $[M+H]^+$: 114.0550; found $[M+H]^+$: 114.0550.

C-12: 4-Chloro-1-isocyano-2-(trifluoromethyl)benzene[34]



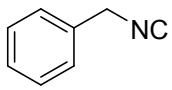
The product was obtained with procedure **A**, 0.2 mmol scale, 34.1 mg, 83% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 2.3 Hz, 1H), 7.59 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 135.7, 133.1, 130.1, 128.5(d, *J* = 2.8 Hz), 127.3 (q, *J* = 5.0 Hz), 121.40 (q, *J* = 274.0 Hz); SFC-MS (ESI) m/z calculated for $C_8H_4ClF_3N$ $[M+H]^+$: 204.99; found $[M+H]^+$: 205.25.

D-1 / I-3: 1-(Isocyanomethyl)-3-methoxybenzene[19]



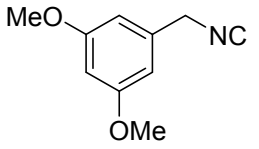
The product was obtained with procedure **A**, 0.2 mmol scale, 25.0 mg, 85% yield, liquid; (lit. yield = 94%)[19]. ^{1}H NMR (500 MHz, $CDCl_3$) 7.33 – 7.28 (m, 1H), 6.93 – 6.90 (m, 1H), 6.90 – 6.86 (m, 2H), 4.60 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.9, 157.5 (t, *J* = 5.2 Hz), 133.6, 129.9, 118.6, 113.7, 112.1, 55.2, 45.3 (t, *J* = 7.2 Hz); HRMS (ESI) m/z calculated for C_8H_9O $[M+H-HCN]^+$: 121.0648; found $[M+H-HCN]^+$: 121.0649.

D-2: (Isocyanomethyl)benzene[35]



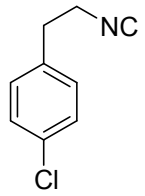
The product was obtained with procedure **A**, 0.2 mmol scale, 22.3 mg, 95% yield; with procedure **C**, 100 mmol scale, 11.35 gm, 97% yield, liquid; (lit. yield = 64%)[35]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H), 7.38 – 7.33 (m, 3H), 4.65 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6 (t, *J* = 5.3 Hz), 132.3, 129.0, 128.4, 126.6, 45.5 (t, *J* = 7.3 Hz); HRMS (ESI) m/z calculated for C_7H_7 $[M+H-HCN]^+$: 91.0542; found $[M+H-HCN]^+$: 91.0542.

D-3 / I-11: 1-(Isocyanomethyl)-3,5-dimethoxybenzene[36]



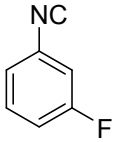
The product was obtained with procedure **A**, 0.2 mmol scale, 32.9 mg, 93% yield, semisolid; and with procedure **B**, 1.0 mmol, 142 mg, 80% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (d, *J* = 2.2 Hz, 2H), 6.40 (d, *J* = 2.2 Hz, 1H), 4.55 (s, 2H), 3.78 (s, 6H)l; ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.1, 157.6 (t, *J* = 5.5 Hz), 134.4, 104.4, 99.9, 55.3, 45.4 (t, *J* = 7.2 Hz); HRMS (ESI) m/z calculated for $C_9H_{11}O_2$ $[M+H-HCN]^+$: 151.0754; found $[M+H-HCN]^+$: 151.0756.

D-4 / I-17: 1-Chloro-4-(2-isocyanoethyl)benzene[11]



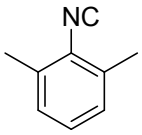
The product was obtained with procedure **A**, 0.2 mmol scale, 31.8 mg, 96% yield, liquid; and with procedure **B**, 1.0 mmol, 144 mg, 87% yield; (lit. yield = 83%)[11]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 3.59 (t, *J* = 7.0 Hz, 2H), 2.94 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.8 (t, *J* = 5.5 Hz), 135.0, 133.0, 130.0, 128.8, 42.7 (t, *J* = 6.7 Hz), 34.7; HRMS (ESI) m/z calculated for $C_9H_{11}ClNO$ $[M+H+H_2O]^+$: 184.0524; found $[M+H+H_2O]^+$: 184.0527.

D-5: 1-Fluoro-3-isocyanobenzene[37]



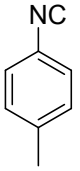
The product was obtained with procedure **A**, 0.2 mmol scale, 21.1 mg, 87% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (td, *J* = 8.2, 5.9 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.16 – 7.08 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5 (t, *J* = 4.6 Hz), 162.4 (d, *J* = 249.8 Hz), 130.9 (d, *J* = 9.0 Hz), 122.4 (d, *J* = 3.6 Hz), 117.0 (d, *J* = 21.1 Hz), 114.1 (d, *J* = 25.4 Hz); HRMS (ESI) m/z calculated for C_7H_7FNO $[M+H-+H_2O]^+$: 140.0506; found $[M+H+H_2O]^+$: 140.0509.

D-6: 2-Isocyano-1,3-dimethylbenzene[38]



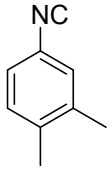
The product was obtained with procedure **A**, 0.2 mmol scale, 24.4 mg, 93% yield, solid; (lit. yield = 74%)[38]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.15 (m, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 2.42 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5 (t, *J* = 5.7 Hz), 134.8, 128.6, 127.7, 126.6 (t, *J* = 6.2 Hz), 18.9; HRMS (ESI) m/z calculated for $C_9H_{10}N$ $[M+H]^+$: 132.0808; found $[M+H]^+$: 132.0810.

D-7: 1-Isocyano-4-methylbenzene[30]



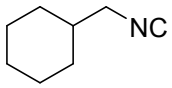
The product was obtained with procedure **A**, 0.2 mmol scale, 20.2 mg, 86% yield, liquid; (lit. yield = 91%)[30]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1 (t, *J* = 5.6 Hz), 139.7, 129.9, 126.1, 124.0 (t, *J* = 13.8 Hz), 21.3; HRMS (ESI) m/z calculated for C_8H_8N $[M+H]^+$: 118.0651; found $[M+H]^+$: 118.0652.

D-8: 4-Isocyano-1,2-dimethylbenzene[39]



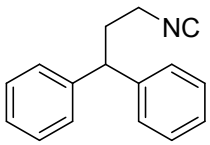
The product was obtained with procedure **A**, 0.2 mmol scale, 23.4 mg, 89% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 1H), 7.12 – 7.08 (m, 2H), 2.27 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6, 138.4, 138.0, 130.3, 127.2, 123.6, 19.6, 19.5; HRMS (ESI) m/z calculated for $C_9H_{10}N$ $[M+H]^+$: 132.0808; found $[M+H]^+$: 132.081.

D-9 / I-38: (Isocyanomethyl)cyclohexane



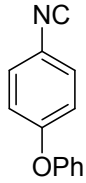
The product was obtained with procedure **A**, 0.2 mmol scale, 20.7 mg, 84% yield, liquid; and with procedure **B**, 1.0 mmol, 121 mg, 98% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.24 – 3.15 (m, 2H), 1.84 – 1.73 (m, 4H), 1.71 – 1.57 (m, 2H), 1.32 – 1.21 (m, 2H), 1.19 – 1.11 (m, 1H), 1.09 – 0.98 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (t, J = 5.6 Hz), 47.9 (t, J = 6.7 Hz), 37.3, 30.1, 25.9, 25.5; HRMS (ESI) m/z calculated for $C_8H_{16}NO$ $[M+H+H_2O]^+$: 142.1226; found $[M+H+H_2O]^+$: 142.1229.

D-10 / I-46: (3-Isocyanopropane-1,1-diyl)dibenzene



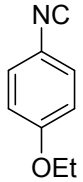
The product was obtained with procedure **A**, 0.2 mmol scale, 38.1 mg, 86% yield, solid; and with procedure **B**, 1.0 mmol, 164 mg, 74% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, J = 7.9 Hz, 4H), 7.35 – 7.26 (m, 6H), 4.22 (t, J = 8.0 Hz, 1H), 3.34 (t, J = 6.7 Hz, 2H), 2.51 – 2.42 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5 (t, J = 5.2 Hz), 142.7, 128.6, 127.5, 126.6, 47.4, 39.8 (t, J = 6.4 Hz), 34.4; HRMS (ESI) m/z calculated for $C_{16}H_{16}N$ $[M+H]^+$: 222.1277; found $[M+H]^+$: 222.1280.

D-11: 1-Isocyano-4-phenoxybenzene



The product was obtained with procedure **A**, 0.2 mmol scale, 31.2 mg, 80% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.36 (m, 2H), 7.33 (d, J = 8.9 Hz, 2H), 7.21-7.19 (m, 1H), 7.06 – 7.01 (m, 2H), 6.98-6.93 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3, 158.2, 155.6, 130.0, 128.7, 127.9, 127.7, 124.5, 119.8, 118.5; HRMS (ESI) m/z calculated for $C_{13}H_{10}NO$ $[M+H]^+$: 196.0757; found $[M+H]^+$: 196.0759.

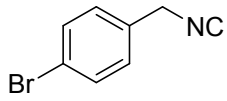
D-12 / I-34: 1-Ethoxy-4-isocyanobenzene[40]



The product was obtained with procedure **A**, 0.2 mmol scale, 24.4 mg, 83% yield, liquid; and with procedure **B**, 1.0 mmol, 128 mg, 87% yield; (lit. yield = 64%)[40]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.9 Hz, 2H), 6.89-6.85 (m, 2H), 4.03 (q, J = 7.0 Hz, 2H), 1.42 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (t,

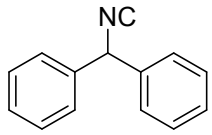
J = 5.9 Hz), 159.2, 130.0, 127.7, 114.9, 63.8, 14.6; HRMS (ESI) m/z calculated for $C_9H_{10}NO$ $[M+H]^+$:148.0757; found $[M+H]^+$: 148.0759.

E-1: 1-Bromo-4-(isocyanomethyl)benzene[41]



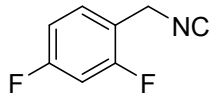
The product was obtained with procedure **A**, 0.2 mmol scale, 31.8 mg, 81% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 4.63 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (t, J = 5.0 Hz), 132.1, 131.2, 128.3, 122.5, 45.0 (t, J = 7.2 Hz); HRMS (ESI) m/z calculated for C_7H_6Br $[M+H-HCN]^+$: 168.9647; found $[M+H-HCN]^+$: 168.9651.

E-2 / I-8: (Isocyanomethylene)dibenzene[42]



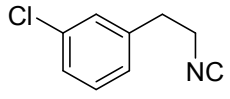
The product was obtained with procedure **A**, 0.2 mmol scale, 35.6 mg, 92% yield, solid; and with procedure **B**, 1.0 mmol, 162 mg, 84% yield; (lit. yield = 93%)[42]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 10H), 5.91 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2 (t, J = 4.3 Hz), 137.4, 128.9, 128.3, 126.4, 61.8 (t, J = 6.7 Hz); HRMS (ESI) m/z calculated for $C_{13}H_{11}$ $[M+H-HCN]^+$: 167.0855; found $[M+H-HCN]^+$: 167.0857.

E-3: 2,4-Difluoro-1-(isocyanomethyl)benzene[41]



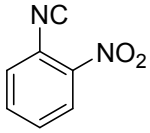
The product was obtained with procedure **A**, 0.2 mmol scale, 26.9 mg, 88% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 1H), 6.99 – 6.93 (m, 1H), 6.91 – 6.84 (m, 1H), 4.65 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.1 (dd, J = 250.7, 11.8 Hz), 159.9 (dd, J = 251.0, 12.4 Hz), 158.6 (t, J = 5.1 Hz), 129.7 (dd, J = 9.9, 4.7 Hz), 116.0, 111.9 (dd, J = 21.7, 3.8 Hz), 104.2 (t, J = 25.3 Hz), 39.3 (t, J = 7.2 Hz); HRMS (ESI) m/z calculated for $C_7H_5F_2$ $[M+H-HCN]^+$: 127.0354; found $[M+H-HCN]^+$: 127.0356.

E-4: 1-Chloro-3-(2-isocyanoethyl)benzene[19]



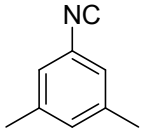
The product was obtained with procedure **A**, 0.2 mmol scale, 32.3 mg, 98% yield, liquid; (lit. yield = 82%)[19]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 2H), 7.22 (s, 1H), 7.12 (d, J = 6.2 Hz, 1H), 3.61 (t, J = 7.1 Hz, 2H), 2.96 (t, J = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9 (t, J = 5.3 Hz), 138.5, 134.5, 130.0, 128.7, 127.5, 126.9, 42.6 (t, J = 7.2 Hz), 35.1; HRMS (ESI) m/z calculated for $C_9H_{11}NOCl$ $[M+ H + H_2O]^+$: 184.0524; found $[M+H+H_2O]^+$: 184.0527.

E-5 / I-32: 1-Isocyano-2-nitrobenzene[43]



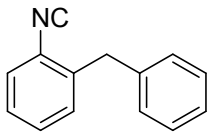
The product was obtained with procedure **A**, 0.2 mmol scale, 26.6 mg, 90% yield, solid; and with procedure **B**, 1.0 mmol, 117 mg, 79% yield; (lit. yield = 86%)[43]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 8.5 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.62 (t, J = 7.7 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 144.1, 134.3, 130.2, 129.8, 125.5; HRMS (ESI) m/z calculated for $C_7H_5N_2O_2$ $[M+H]^+$: 149.0346; found $[M+H]^+$: 149.0347.

E-6: 1-Isocyano-3,5-dimethylbenzene[44]



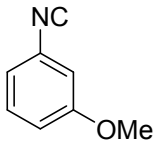
The product was obtained with procedure **A**, 0.2 mmol scale, 21.2 mg, 81% yield, liquid; (lit. yield = 76%)[44]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (s, 1H), 6.99 (s, 2H), 2.31 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8 (t, J = 5.4 Hz), 139.2, 130.9, 126.2 (t, J = 13.2 Hz), 123.8, 20.8; HRMS (ESI) m/z calculated for $C_9H_{12}NO$ $[M+H+H_2O]^+$: 150.0913; found $[M+H+H_2O]^+$: 150.0916.

E-7 / I-28: 1-Benzyl-2-isocyanobenzene



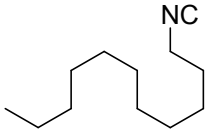
The product was obtained with procedure **A**, 0.2 mmol scale, 30.9 mg, 80% yield, liquid; and with procedure **B**, 1.0 mmol, 147 mg, 76% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.33 (m, 4H), 7.33 – 7.23 (m, 5H), 4.18 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 138.3, 137.5, 130.1, 129.3, 128.8, 128.4, 127.0, 126.7, 126.4, 125.9 (t, J = 12.5 Hz), 37.8; HRMS (ESI) m/z calculated for $C_{14}H_{12}N$ $[M+H]^+$: 194.09643; found $[M+H]^+$: 194.0967.

E-8 / I-31: 1-Isocyano-3-methoxybenzene[45, 46]



The product was obtained with procedure **A**, 0.2 mmol scale, 19.5 mg, 75% yield, liquid; and with procedure **B**, 1.0 mmol, 106 mg, 80% yield; (lit. yield = 42%)[45]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (t, J = 8.1 Hz, 1H), 6.95 – 6.89 (m, 2H), 6.85 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) 163.6 (t, J = 5.5 Hz), 159.8, 130.0, 127.1 (t, J = 13.5 Hz), 118.4, 115.4, 111.6, 55.3; HRMS (ESI) m/z calculated for C_8H_8NO $[M+H]^+$: 134.0600; found $[M+H]^+$: 134.0603.

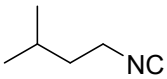
E-9 / I-39: 1-Isocyanoundecane



The product was obtained with procedure **A**, 0.2 mmol scale, 30.8 mg, 85% yield, liquid; and with procedure **B**, 1.0 mmol, 156 mg, 86% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.34 (t, J = 6.8 Hz, 2H), 1.71 – 1.58 (m, 2H), 1.46 – 1.35 (m, 2H), 1.34 – 1.19 (m, 14H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR (126

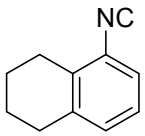
MHz, $CDCl_3$) δ 155.5, 41.4 (t, *J* = 6.3 Hz), 31.7, 29.4, 29.3, 29.2, 29.1, 28.9, 28.5, 26.1, 22.5, 13.9; HRMS (ESI) m/z calculated for $C_{12}H_{26}NO$ $[M+H+H_2O]^+$: 200.2009; found $[M+H+H_2O]^+$: 200.2013.

E-10/ I-47: 1-Isocyano-3-methylbutane[23]



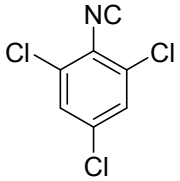
The product was obtained with procedure **A**, 0.2 mmol scale, 16.7 mg, 86% yield, liquid; and with procedure **B**, 1.0 mmol, 93 mg, 96% yield; (lit. yield = 72%). ^1H NMR (500 MHz, $CDCl_3$) δ 3.40 – 3.33 (m, 2H), 1.75 (h, *J*= 6.7, 1 H), 1.58 – 1.50 (m, 2H), 0.89 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5 (t, *J* = 5.8 Hz), 39.6 (t, *J* = 6.4 Hz), 37.6, 25.0, 21.7; HRMS (ESI) m/z calculated for $C_6H_{14}NO$ $[M+H+H_2O]^+$: 116.107; found $[M+H+H_2O]^+$: 116.1071.

E-11: 5-Isocyano-1,2,3,4-tetrahydronaphthalene[34]



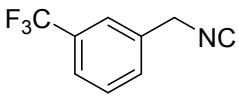
The product was obtained with procedure **A**, 0.2 mmol scale, 28.6 mg, 91% yield, solid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 6.7, 2.4 Hz, 1H), 7.16 – 7.10 (m, 2H), 2.84 (t, *J* = 6.5 Hz, 2H), 2.80 (t, *J* = 6.3 Hz, 2H), 1.88 (tdd, *J* = 8.1, 4.9, 2.4 Hz, 2H), 1.85 – 1.78 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 139.1, 133.8, 130.0, 126.4 (t, *J*= 12.6 Hz), 125.7, 123.8, 29.3, 25.8, 22.4, 22.3; HRMS (ESI) m/z calculated for $C_{11}H_{12}N$ $[M+H]^+$: 158.0964; found $[M+H]^+$: 158.0967.

E-12: 1,3,5-Trichloro-2-isocyanobenzene[47]



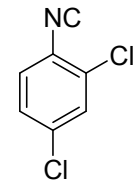
The product was obtained with procedure **A**, 0.2 mmol scale, 28.9 mg, 70% yield, solid;^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3, 135.6, 132.9, 128.4, 127.6; HRMS (ESI) m/z calculated for $C_7H_5Cl_3NO$ $[M+H+H_2O]^+$: 223.9431; found $[M+H+H_2O]^+$: 223.9433.

F-1 / I-4: 1-(Isocyanomethyl)-3-(trifluoromethyl)benzene



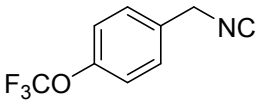
The product was obtained with procedure **A**, 0.2 mmol scale, 31.8 mg, 86% yield, liquid; and with procedure **B**, 1.0 mmol, 163 mg, 88% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.58 – 7.52 (m, 2H), 4.71 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8 (t, *J* = 5.1 Hz), 133.2, 131.3 (q, *J*=32.6), 129.9, 129.5, 125.3 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 273.4 Hz), 123.4 (q, *J* = 3.7 Hz), 45.0 (t, *J* = 7.4 Hz); HRMS (ESI) m/z calculated for $C_8H_6F_3$ $[M+H-HCN]^+$: 159.0416; found $[M+H-HCN]^+$: 159.0419.

F-2 / I-9: 2,4-Dichloro-1-isocyanobenzene[47, 48]



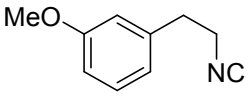
The product was obtained with procedure **A**, 0.2 mmol scale, 24.8 mg, 72% yield, solid; and with procedure **B**, 1.0 mmol, 138 mg, 81% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 2.1 Hz, 1H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.28 (dd, *J* = 8.6, 2.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 135.7, 131.7, 130.0, 128.5, 127.9, 124.0 (t, *J* = 4.3 Hz); HRMS (ESI) m/z calculated for $C_7H_6Cl_2NO$ $[M+H+H_2O]^+$: 189.9821; found $[M+H+H_2O]^+$: 189.9824.

F-3 / I-12: 1-(Isocyanomethyl)-4-(trifluoromethoxy)benzene[49]



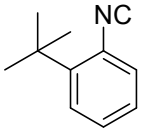
The product was obtained with procedure **A**, 0.2 mmol scale, 34.2 mg, 85% yield, liquid; and with procedure **B**, 1.0 mmol, 195 mg, 97% yield; (lit. yield = 80%)[49]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 4.64 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3 (t, *J* = 5.1 Hz), 149.1, 130.9, 128.1, 121.4, 120.4 (q, *J* = 257.7 Hz), 44.7 (t, *J* = 7.4 Hz); HRMS (ESI) m/z calculated for $C_8H_6F_3O$ $[M+H-HCN]^+$: 175.0365; found $[M+H-HCN]^+$: 175.0368.

F-4 / I-18: 1-(2-Isocyanoethyl)-3-methoxybenzene[19]



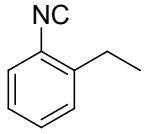
The product was obtained with procedure **A**, 0.2 mmol scale, 29.3 mg, 91% yield, liquid; and with procedure **B**, 1.0 mmol, 156 mg, 97% yield; (lit. yield = 94%)[19]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 1H), 7.20 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.94 (td, *J* = 7.4, 1.1 Hz, 1H), 6.89 (dd, *J* = 8.2, 1.1 Hz, 1H), 3.84 (s, 3H), 3.64 – 3.58 (m, 2H), 3.04-2.99 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.2, 155.5 (t, *J* = 5.3 Hz), 130.6, 128.4, 124.6, 120.3, 110.1, 55.0, 41.1 (t, *J* = 6.5 Hz), 30.9; HRMS (ESI) m/z calculated for $C_{10}H_{12}NO$ $[M+H]^+$: 162.0913; found $[M+H]^+$: 162.0917.

F-5 / I-22: 1-(*Tert*-butyl)-2-isocyanobenzene[50]



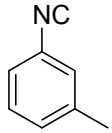
The product was obtained with procedure **A**, 0.2 mmol scale, 28.3 mg, 89% yield, liquid; and with procedure **B**, 1.0 mmol, 145 mg, 91% yield; (lit. yield = 50%)[50]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.32 (td, *J* = 7.7, 1.5 Hz, 1H), 7.21 (td, *J* = 7.5, 1.4 Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1 (t, *J* = 5.5 Hz), 145.4, 129.9, 129.2, 126.7, 125.1, 125.0 (t, *J* = 12.0 Hz), 34.8, 29.0; HRMS (ESI) m/z calculated for $C_{11}H_{14}N$ $[M+H]^+$: 160.1121; found $[M+H]^+$: 160.1123.

F-6 / I-26: 1-Ethyl-2-isocyanobenzene[51]



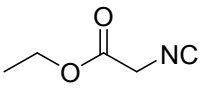
The product was obtained with procedure **A**, 0.2 mmol scale, 24.1 mg, 92% yield, liquid; and with procedure **B**, 1.0 mmol, 124 mg, 95% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.28 (d, J = 8.1 Hz, 1H), 7.23 – 7.18 (m, 1H), 2.78 (q, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7 (t, J = 5.8 Hz), 140.3, 129.3, 128.7, 126.5, 125.6 (t, J = 12.7 Hz), 25.2, 13.6; HRMS (ESI) m/z calculated for $C_9H_{10}N$ $[M+H]^+$: 132.0808; found $[M+H]^+$: 132.0810.

F-7: 1-Isocyano-3-methylbenzene[30]



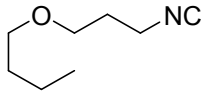
The product was obtained with procedure **A**, 0.2 mmol scale, 19.2 mg, 82% yield, liquid; (lit. yield = 93%)[30]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.24 (m, 1H), 7.22 – 7.15 (m, 3H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.3 (t, J = 5.6 Hz), 139.6, 130.1, 129.1, 126.8, 123.4, 21.1; HRMS (ESI) m/z calculated for C_8H_8N $[M+H]^+$: 118.0651; found $[M+H]^+$: 118.0653.

F-8: Ethyl 2-isocyanoacetate[52]



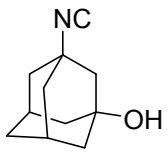
The product was obtained using procedure **A**, 0.2 mmol scale 21.2 mg, 94% yield, liquid; (lit. yield = 100%)[52]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.28 (q, J = 7.1 Hz, 2H), 4.21 (s, 2H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.9, 161.1, 62.7, 43.5 (t, J = 8.6 Hz), 13.9; SFC-MS (ESI) m/z calculated for $C_5H_8NO_2$ $[M+H]^+$: 114.05; found $[M+H]^+$: 114.08

F-9 / I-40: 1-(3-Isocyanopropoxy)butane



The product was obtained with procedure **A**, 0.2 mmol scale, 24.6 mg, 87% yield, liquid; and with procedure **B**, 1.0 mmol, 120 mg, 85% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 – 3.43(m, 4H), 3.38 (t, J = 6.6 Hz, 2H), 1.90 – 1.82 (m, 2H), 1.53 – 1.46 (m, 2H), 1.36 – 1.27 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.8 (t, J = 5.7 Hz), 70.7, 65.9, 38.5 (t, J = 6.5 Hz), 31.5, 29.3, 19.1, 13.7; HRMS (ESI) m/z calculated for $C_8H_{16}NO$ $[M+H]^+$: 142.1226; found $[M+H]^+$: 142.1228.

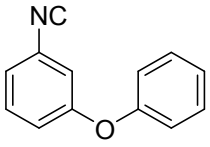
F-10 / I-50: (1s,3r,5*R*,7*S*)-3-Isocyanoadamantan-1-ol[32]



The product was obtained with procedure **A**, 0.2 mmol scale, 17.7 mg, 50% yield, solid; and with procedure **B**, 1.0 mmol, 106 mg, 60% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 – 2.25 (m, 2H), 1.98 (s, 2H), 1.95 – 1.91 (m, 4H), 1.77 (brs, 1H), 1.69 – 1.65 (m, 4H), 1.58 – 1.49 (m, 2H); ^{13}C NMR (126 MHz,

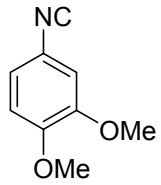
$CDCl_3$) δ 152.0 (t, *J* = 4.8 Hz), 68.1, 55.9 (t, *J* = 6.0 Hz), 50.4, 43.2, 42.1, 33.9, 29.9; HRMS (ESI) m/z calculated for $C_{11}H_{16}NO$ $[M+H]^+$: 178.1226; found $[M+H]^+$: 178.1229.

F-11: 1-Isocyano-3-phenoxybenzene[13]



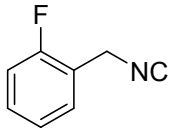
The product was obtained with procedure **A**, 0.2 mmol scale, 28.9 mg, 74% yield liquid; (lit. yield = 85%)[13]. ^1H NMR (500 MHz, $CDCl_3$) δ 7.39 (t, *J* = 8.1 Hz, 2H), 7.33 (t, *J* = 8.1 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.06 – 7.02 (m, 3H), 6.96 (s,1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 158.4, 155.6, 130.5, 130.1, 124.5, 120.7, 119.7, 119.2, 115.9; HRMS (ESI) m/z calculated for $C_{13}H_{10}NO$ $[M+H]^+$: 196.0757; found $[M+H]^+$: 196.0761.

F-12: 4-Isocyano-1,2-dimethoxybenzene[53, 54]



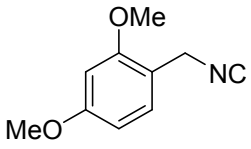
The product was obtained with procedure **A**, 0.2 mmol scale, 27.7 mg, 85% yield, solid; ^1H NMR (500 MHz, $CDCl_3$) δ 6.98 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.86 (d, *J* = 2.3 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4, 149.8, 149.1, 130.1, 119.2, 110.8, 109.5, 56.1, 56.0; HRMS (ESI) m/z calculated for $C_9H_{10}NO_2$ $[M+H]^+$: 164.0706; found $[M+H]^+$: 164.0709.

G-1 / I-5: 1-Fluoro-2-(isocyanomethyl)benzene[41]



The product was obtained with procedure **A**, 0.2 mmol scale, 19.2 mg, 71% yield, liquid; and with procedure **B**, 1.0 mmol, 127 mg, 94% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (t, *J* = 7.6 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.22 (td, *J* = 7.5, 1.2 Hz, 1H), 7.12 – 7.05 (m, 1H), 4.68 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6 (d, *J* = 248.0 Hz), 158.2 (t, *J* = 5.6 Hz), 130.3 (d, *J* = 8.0 Hz), 128.5 (d, *J* = 3.2 Hz), 124.6 (d, *J* = 3.8 Hz), 119.7 (d, *J* = 14.5 Hz), 115.4 (d, *J* = 20.6 Hz), 39.7 (q, *J* = 7.0 Hz); HRMS (ESI) m/z calculated for C_8H_9NOF $[M+H+H_2O]^+$: 154.0663; found $[M+H+H_2O]^+$: 154.0665.

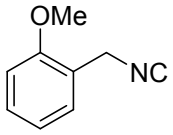
G-2 / I-10: 1-(Isocyanomethyl)-2,4-dimethoxybenzene[55]



The product was obtained with procedure **A**, 0.2 mmol scale, 30.5 mg, 86% yield, solid; and with procedure **B**, 1.0 mmol, 150 mg, 85% yield; (lit. yield = 80%)[55]. ^1H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.4 Hz, 1H), 6.51 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.46 (d, *J* = 2.4 Hz, 1H), 4.54 (s, 2H), 3.83 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.1, 157.3, 156.1 (t, *J* = 5.3

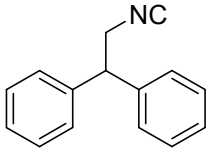
Hz), 128.6, 113.3, 104.1, 98.3, 55.3, 40.7 (t, J = 7.0 Hz); HRMS (ESI) m/z calculated for $C_9H_{11}O_2$ $[M+H-HCN]^+$: 151.0754; found $[M+H-HCN]^+$: 151.0755**.**

G-3: 1-(Isocyanomethyl)-2-methoxybenzene[8]



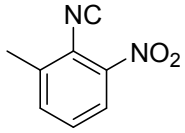
The product was obtained with procedure **A**, 0.2 mmol scale, 26.2 mg, 89% yield, liquid; (lit. yield = 79%)[8]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 7.5 Hz, 1H), 7.34 (td, J = 7.9, 1.7 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 4.64 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9 (t, J = 5.5 Hz), 156.2, 129.6, 128.8, 127.6, 120.7, 110.2, 55.3, 41.1 (t, J = 7.3 Hz); HRMS (ESI) m/z calculated for C_8H_9O $[M+H-HCN]^+$: 121.0648; found $[M+H-HCN]^+$: 121.0648.

G-4 / I-19: (2-Isocyanoethane-1,1-diyl)dibenzene[27]



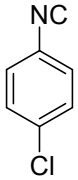
The product was obtained with procedure **A**, 0.2 mmol scale, 39.8 mg, 96% yield, liquid; and with procedure **B**, 1.0 mmol, 174 mg, 84% yield; (lit. yield = 93%)[27]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 4H), 7.36 – 7.28 (m, 6H), 4.40 (t, J = 7.6 Hz, 1H), 4.02 (d, J = 7.6 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.3, 139.9, 128.7, 127.7, 127.2, 50.3, 46.0 (t, J = 6.5 Hz); HRMS (ESI) m/z calculated for $C_{15}H_{14}N$ $[M+H]^+$: 208.1121; found $[M+H]^+$: 208.1124.

G-5: 2-Isocyano-1-methyl-3-nitrobenzene[56]



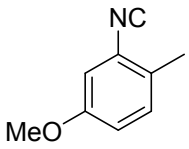
The product was obtained with procedure **A**, 0.2 mmol scale, 23.0 mg, 71% yield, solid; (lit. yield = 89% with phosgene)[56]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 2.3 Hz, 1H), 8.17 (dd, J = 8.5, 2.3 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.2, 146.2, 142.4, 131.4, 126.9 (t, J = 12.5 Hz), 123.9, 121.6, 18.9; HRMS (ESI) m/z calculated for $C_8H_7N_2O_2$ $[M+H]^+$: 163.0502; found $[M+H]^+$: 163.0507.

G-6 / I-27: 1-Chloro-4-isocyanobenzene[57]



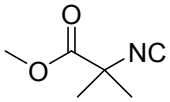
The product was obtained with procedure **A**, 0.2 mmol scale, 22.3 mg, 81% yield, solid; and with procedure **B**, 1.0 mmol, 111 mg, 81% yield; (lit. yield = 39%)[57]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, J = 8.7 Hz, 2H), 7.30 (d, J = 8.7 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.5, 135.2, 129.6, 127.5, 124.9 (t, J = 14.0 Hz); HRMS (ESI) m/z calculated for C_7H_5ClN $[M+H]^+$: 138.0105; found $[M+H]^+$: 138.0107.

G-7 / I-29: 2-Isocyano-4-methoxy-1-methylbenzene[58]



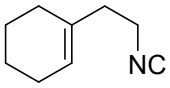
The product was obtained with procedure **A**, 0.2 mmol scale, 24.1 mg, 82% yield, liquid; and with procedure **B**, 1.0 mmol, 137 mg, 93% yield; (lit. yield = 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, J = 8.3 Hz, 1H), 6.85 – 6.78 (m, 2H), 3.75 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.2, 157.7, 130.9, 126.6 (t, J = 12.8 Hz), 126.5, 115.5, 111.2, 55.3, 17.4; HRMS (ESI) m/z calculated for $C_9H_{10}NO$ $[M+H]^+$: 148.0757; found $[M+H]^+$: 148.0759.

G-8: Ethyl 2-isocyano-2-methylpropanoate[59]



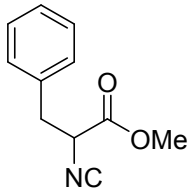
The product was obtained with procedure **A**, 0.2 mmol scale, 20.8 mg, 82% yield, liquid; (lit. yield = 62%)[59]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H), 1.65 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.0, 157.8 (t, J = 4.1 Hz), 59.4 (t, J = 1.1 Hz), 53.4, 27.4; HRMS (ESI) m/z calculated for $C_6H_{10}NO_2$ $[M+H]^+$: 128.0706; found $[M+H]^+$: 128.0708.

G-9 / I-41: 1-(2-Isocyanoethyl)cyclohex-1-ene[60]



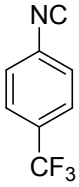
The product was obtained with procedure **A**, 0.2 mmol scale, 22.7 mg, 84% yield, liquid; and with procedure **B**, 1.0 mmol, 123 mg, 91% yield; (lit. yield = 82%)[60]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55 – 5.44 (m, 1H), 3.47 – 3.32 (m, 2H), 2.35 – 2.18 (m, 2H), 2.03 – 1.92 (m, 2H), 1.92 – 1.80 (m, 2H), 1.68 – 1.55 (m, 2H), 1.55 – 1.45 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5 (t, J = 5.6 Hz), 132.2, 124.5, 40.0 (t, J = 6.5 Hz), 37.3, 27.6, 24.9, 22.4, 21.9; HRMS (ESI) m/z calculated for $C_9H_{14}N$ $[M+H]^+$: 136.1121; found $[M+H]^+$: 136.1122.

G-10: Methyl 2-isocyano-3-phenylpropanoate[61]



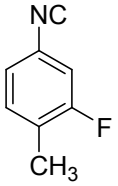
The product was obtained with procedure **A**, 0.2 mmol scale, 41.5 mg, 91% yield, liquid; with procedure **C**, 100 mmol scale, 16.40 gm, 87% yield; (lit. yield = 93%)[61]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 3H), 7.28 – 7.22 (m, 2H), 4.46 (dd, J = 8.4, 4.8 Hz, 1H), 3.80 (s, 3H), 3.26 (dd, J = 13.9, 4.8 Hz, 1H), 3.14 (dd, J = 13.9, 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 160.9, 134.3, 129.2, 128.8, 127.8, 58.0, 53.4, 38.9; SFCMS (ESI) m/z calculated for $C_{11}H_{12}NO_2$ $[M+H]^+$: 190.08; found $[M+H]^+$: 190.10

G-11: 1-Isocyano-4-(trifluoromethyl)benzene[13]



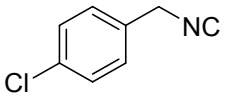
The product was obtained with procedure **A**, 0.2 mmol scale, 29.4 mg, 86% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.6 Hz, 2H), 7.25 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 149.2 (d, *J* = 1.9 Hz), 128.1, 125.0 (t, *J* = 14.0 Hz), 121.9, 120.2 (q, *J* = 258.9 Hz); SFC-MS (ESI) m/z calculated for $C_8H_5F_3N$ $[M+H]^+$: 172.12; found $[M+H]^+$: 172.23

G-12: 2-Fluoro-4-isocyano-1-methylbenzene[62]



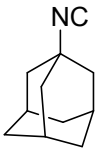
The product was obtained with procedure **A**, 0.2 mmol scale, 32.1 mg, 85% yield, solid; (lit. yield = 81%)[62]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (t, *J*= 8.0, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4 (t, *J* = 5.5 Hz), 160.6 (d, *J* = 247.3 Hz), 132.0 (d, *J* = 6.1 Hz), 128.1, 127.2 (d, *J* = 17.1 Hz), 122.0 (d, *J* = 4.0 Hz), 113.5 (d, *J* = 26.3 Hz), 14.5 (d, *J*=3.3); HRMS (ESI) m/z calculated for C_8H_7FN $[M+H]^+$: 136.0557; found $[M+H]^+$: 136.0559.

H-1 / I-6: 1-Chloro-4-(isocyanomethyl)benzene[63]



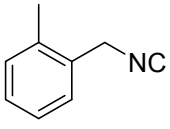
The product was obtained with procedure **A**, 0.2 mmol scale, 29.4 mg, 97% yield, liquid; and with procedure **B**, 1.0 mmol, 148 mg, 98% yield; (lit. yield = 75%)[63]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J*= 8.5, 2H), 7.21 (d, *J* = 8.5, 2.3 Hz, 2H), 4.59 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2 (t, *J* = 5.0 Hz), 132.0, 131.2, 128.2, 122.3, 44.9 (t, *J* = 7.3 Hz); HRMS (ESI) m/z calculated for C_7H_6Cl [M+H-HCN]$^+$: 125.0153; found [M+H-HCN]$^+$: 125.0154.

H-2 / I-49: (3s,5s,7s)-1-Isocyanoadamantane[64]



The product was obtained with procedure **A**, 0.2 mmol scale, 28.6 mg, 89% yield, solid, M.P. :189-190 ^{o}C; and with procedure **B**, 1.0 mmol, 150 mg, 93% yield; and with procedure **D**, 500.0 mmol, 78.10 gm, 97% yield; (lit. yield = 93%)[64]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.11 – 2.04 (m, 3H), 2.04 – 1.98 (m, 6H), 1.71 – 1.61 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.5 (t, *J* = 5.1 Hz), 54.1 (t, *J* = 5.7 Hz), 43.5, 35.4, 28.5; HRMS (ESI) m/z calculated for $C_{10}H_{15}$ $[M+H-HCN]^+$: 135.1168; found $[M+H-HCN]^+$: 135.1169.

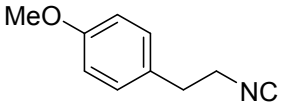
H-3 / I-13: 1-(Isocyanomethyl)-2-methylbenzene[26]



The product was obtained with procedure **A**, 0.2 mmol scale, 22.8 mg, 87% yield, liquid; and with procedure **B**, 1.0 mmol, 96 mg, 73% yield; (lit. yield = 66%)[26]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 7.0, 2.0 Hz, 1H), 7.32 –

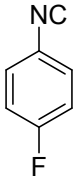
7.26 (m, 2H), 7.23 (dd, J = 7.0, 2.0 Hz, 1H), 4.58 (s, 2H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5 (t, J = 5.1 Hz), 135.4, 130.5, 130.4, 128.6, 127.3, 126.4, 43.9 (t, J = 7.0 Hz), 18.6; HRMS (ESI) m/z calculated for C_8H_9 $[M+H-HCN]^+$: 105.0699 ; found $[M+H-HCN]^+$: 105.0698.

H-4 / I-20: 1-(2-Isocyanoethyl)-4-methoxybenzene[65]



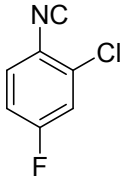
The product was obtained with procedure **A**, 0.2 mmol scale, 27.1 mg, 84% yield, liquid; and with procedure **B**, 1.0 mmol, 129 mg, 80% yield; (lit. yield = 93%)[65]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 3.82 (s, 3H), 3.58 (t, J = 7.1 Hz, 2H), 2.93 (t, J = 7.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.6, 156.2 (t, J = 5.7 Hz), 129.5, 128.5, 113.9, 55.1, 43.1 (t, J = 6.4 Hz), 34.6; HRMS (ESI) m/z calculated for $C_{10}H_{12}NO$ $[M+H]^+$: 162.0913; found $[M+H]^+$: 162.0915.

H-5 / I-23: 1-Fluoro-4-isocyanobenzene[44]



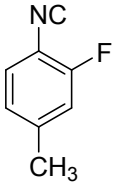
The product was obtained with procedure **A**, 0.2 mmol scale, 17.7 mg, 73% yield, liquid; and with procedure **B**, 1.0 mmol, 104 mg, 86% yield; (lit. yield = 49%)[44]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.10 – 7.03 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3 (t, J = 6.4 Hz), 162.2(d, J = 251.7 Hz), 128.2 (d, J = 9.0 Hz), 122.7 (t, J = 13.7 Hz), 116.5 (d, J = 23.5 Hz); HRMS (ESI) m/z calculated for C_7H_5FN $[M+H]^+$: 122.0401; found $[M+H]^+$: 122.0402.

H-6: 2-Chloro-4-fluoro-1-isocyanobenzene



The product was obtained with procedure **A**, 0.2 mmol scale, 22.2 mg, 71% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, J = 8.9, 5.3 Hz, 1H), 7.24 (dd, J = 8.0, 2.7 Hz, 1H), 7.06 – 7.01 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 161.9 (d, J = 255.3 Hz), 158.7, 132.3 (d, J = 11.1 Hz), 129.2 (d, J = 9.6 Hz), 117.8 (d, J = 26.3 Hz), 115.1 (d, J = 23.0 Hz); HRMS (ESI) m/z calculated for C_7H_6ClFNO $[M+H+H_2O]^+$: 174.0116; found $[M+H+H_2O]^+$: 174.0119.

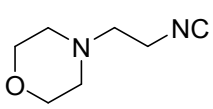
H-7: 2-Fluoro-1-isocyano-4-methylbenzene



The product was obtained with procedure **A**, 0.2 mmol scale, 19.7 mg, 73% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, J = 8.0 Hz, 1H), 7.06 (d, J = 8.2 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 160.4 (d, J = 247.8 Hz), 131.9 (d, J = 6.0 Hz), 127.1 (d, J = 17.2 Hz), 124.9 (t, J = 12.4 Hz),

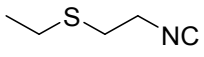
121.9 (d, J = 3.9 Hz), 113.3 (d, J = 26.4 Hz), 14.3 (d, J = 3.2 Hz); HRMS (ESI) m/z calculated for C_8H_7FN $[M+H]^+$: 136.0557; found $[M+H]^+$: 136.0560.

H-8 / I-59: 4-(2-Isocyanoethyl)morpholine[66]



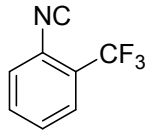
The product was obtained with procedure **B**, 1 mmol scale, 79.8 mg, 57% yield, liquid; (lit. yield = 74%)[66]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (dt, J = 5.3, 2.0 Hz, 4H), 3.48 (td, J = 6.5, 2.0 Hz, 2H), 2.68 – 2.62 (m, 2H), 2.51 – 2.45 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.7(t, J = 5.6 Hz), 66.5, 56.8, 53.1, 39.1 (d, J = 6.9 Hz); HRMS (ESI) m/z calculated for $C_7H_{13}N_2O$ $[M+H]^+$: 141.1022; found $[M+H]^+$: 141.1023

H-9 / I-42: Ethyl(2-isocyanoethyl)sulfane



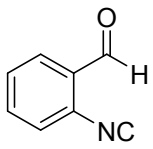
The product was obtained with procedure A, 0.2 mmol scale, 21.2 mg, 92% yield, liquid; and with procedure **B**, 1.0 mmol, 90 mg, 78% yield; ^{1}H NMR (500 MHz, $CDCl_3$) δ3.59 – 3.48 (m, 2H), 2.83 – 2.72 (m, 2H), 2.61 (q, J = 7.4 Hz, 2H), 1.23 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.9 (t, J = 5.3 Hz), 41.7 (t, J = 6.7 Hz), 30.5, 25.9, 14.5; HRMS (ESI) m/z calculated for C_4H_9S $[M+H\text{-}HCN]^+$: 89.0419; found $[M+H\text{-}HCN]^+$: 89.0418.

H-12: 1-Isocyano-2-(trifluoromethyl)benzene[67]



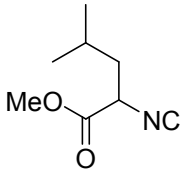
The product was obtained with procedure A, 0.2 mmol scale, 23.9 mg, 70% yield, liquid; (lit. yield = 89%)[67]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.57 – 7.51 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 132.9, 129.4, 128.8, 128.1, 126.8 (q, J = 4.7 Hz), 122.2 (q, J = 273.2 Hz); HRMS (ESI) m/z calculated for $C_8H_7F_3NO$ $[M+H+H_2O]^+$: 190.0474; found $[M+H+H_2O]^+$: 190.0477.

I-51: 2-Isocyanobenzaldehyde[68]



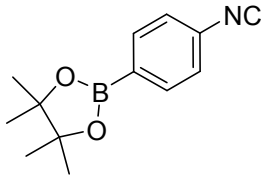
The product was obtained a procedure **B**, 1.0 mmol scale 111.4 mg, 85% yield, liquid; (lit. yield = 55%)[68] ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.42 (s, 1H), 7.95 (dd, J = 7.8, 1.6 Hz, 1H), 7.68 (dd, J = 7.8, 1.6 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.7, 170.7, 134.9, 129.9, 129.9, 128.7, 127.9; HRMS (ESI) m/z calculated for C_8H_6NO $[M+H]^+$: 132.0444; found $[M+H]^+$: 132.0445.

I-52: Methyl 2-isocyano-4-methylpentanoate[61]



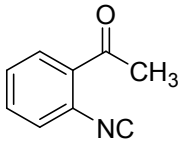
The product was obtained a procedure **B**, 1.0 mmol scale 151.9 mg, 98% yield, liquid; (lit. yield = 93%)[61]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.27 (dd, *J* = 9.9, 4.6 Hz, 1H), 3.80 (d, *J* = 1.3 Hz, 3H), 1.94 – 1.79 (m, 2H), 1.73 – 1.62 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 160.0, 55.0 (t, *J* = 7.7Hz), 53.2, 41.2, 24.7, 22.5, 20.8; SFC-MS (ESI) m/z calculated for $C_8H_{14}NO_2$ $[M+H]^+$: 156.10; found $[M+H\text{-}HCN]^+$: 156.12.

I-53: 2-(4-Isocyanophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane[69]



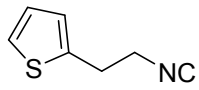
The product was obtained a procedure **B**, 1.0 mmol scale 219.8 mg, 96% yield, semisolid; (lit. yield = 93%)[69]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 2H), 7.44 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 1.34 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 135.2, 132.1, 128.6, 128.5, 126.1 (t, *J* = 11.0 Hz), 84.2, 24.6; HRMS (ESI) m/z calculated for $C_{13}H_{17}BNO_2$ $[M+H]^+$: 230.1347; found $[M+H]^+$: 230.1348.

I-54: 1-(2-Isocyanophenyl)ethan-1-one[70]



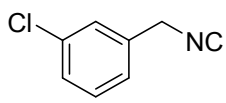
The product was obtained a procedure **B**, 1.0 mmol scale 127.6mg, 88% yield, semisolid; (lit. yield = 88%)[70]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.55 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51 – 7.45 (m, 2H), 2.70 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.0, 170.1, 132.6, 129.5, 129.5, 128.9, 29.7; HRMS (ESI) m/z calculated for C_9H_7NO $[M+H]^+$: 146.0600; found $[M+H]^+$: 146.0602.

I-55: 2-(2-Isocyanoethyl)thiophene[62]



The product was obtained a procedure **B**, 1.0 mmol scale 128.8 mg, 94% yield, liquid; (lit. yield = 71%)[62]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.95 – 6.92 (m, 1H), 3.64 (tt, *J* = 7.0, 1.9 Hz, 2H), 3.21 (td, *J* = 7.0, 2.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.0 (t, *J* = 5.5Hz), 138.3, 127.1, 126.1, 124.5, 43.0 (t, *J* = 6.7Hz), 29.9; HRMS (ESI) m/z calculated for C_7H_8NS $[M+H]^+$: 138.0372; found $[M+H]^+$: 138.0373.

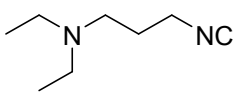
I-56: **1-Chloro-3-(isocyanomethyl)benzene[12]**



The product was obtained using procedure **B**, 1.0 mmol scale 137.4 mg, 91% yield, liquid; (lit. yield = 92%)[12]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 3H), 7.25 – 7.22 (m, 1H), 4.63 (s, 2H); ^{13}C NMR (126

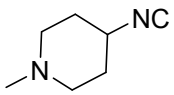
MHz, $CDCl_3$) δ 158.6 (t, *J* = 5.0 Hz), 134.9, 134.1, 130.3, 128.7, 126.8, 124.7, 44.9 0 (t, *J* = 7.4 Hz); SFC-MS (ESI) m/z calculated for C_8H_7ClN $[M+H]^+$: 152.02; found $[M+H]^+$: 152.03.

I-57: *N,N*-Diethyl-3-isocyanopropan-1-amine[23]



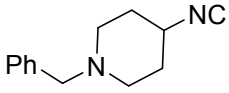
The product was obtained a procedure **B**, 1.0 mmol scale 64.4 mg, 46% yield, liquid; (lit. yield = 72%)[23]. ^1H NMR (500 MHz, $CDCl_3$) δ 3.47 – 3.39 (m, 2H), 2.54 – 2.43 (m, 6H), 1.82 – 1.71 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.6 (t, *J* = 5.8 Hz), 49.0, 46.9, 39.5 (t, *J* = 6.4 Hz), 27.1, 11.7; HRMS (ESI) m/z calculated for $C_8H_{17}N_2$ $[M+H]^+$: 141.1386; found $[M+H]^+$: 141.1385.

I-60: 4-Isocyano-1-methylpiperidine



The product was obtained a procedure **B**, 1.0 mmol scale 34.7 mg, 28% yield, liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 3.81 – 3.54 (m, 1H), 2.69 – 2.50 (m, 2H), 2.44 – 2.26 (m, 5H), 2.04 – 1.92 (m, 2H), 1.92 – 1.81 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 51.6, 48.9, 46.1, 31.6; HRMS (ESI) m/z calculated for $C_7H_{13}N_2$ $[M+H]^+$: 125.1073; found $[M+H]^+$: 125.1072.

I-61: 1-Benzyl-4-isocyanopiperidine

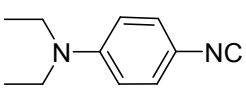


The product was obtained a procedure **B**, 0. 1.0 mmol scale 192.0 mg, 96% yield, liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 5H), 3.79 – 3.59 (m, 1H), 3.51 (s, 2H), 2.74 – 2.56 (m, 2H), 2.50 – 2.18 (m, 2H), 2.05 – 1.91 (m, 2H), 1.91 – 1.80 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.1, 137.9, 129.0, 128.3, 127.2, 62.9, 49.6, 31.8; HRMS (ESI) m/z calculated for $C_{13}H_{17}N_2$ $[M+H]^+$: 201.1386; found $[M+H]^+$: 201.1384.

I-62: 3-Isocyano-N,N,2,2-tetramethylpropan-1-amine

The product was obtained a procedure **B**, 1.0 mmol scale 79.8 mg, 57% yield, liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 3.26 (t, *J* = 1.6 Hz, 2H), 2.28 (s, 6H), 2.17 (s, 2H), 0.93 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0 (t, *J* = 5.9 Hz), 66.4, 50.2 (t, *J* = 6.2 Hz), 48.5, 36.3, 23.3; HRMS (ESI) m/z calculated for $C_8H_{17}N_2$ $[M+H]^+$: 141.1386; found $[M+H]^+$: 141.1386.

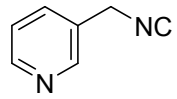
I-63: *N,N*-Diethyl-4-isocyanoaniline[67]



The product was obtained a procedure **B**, 1.0 mmol scale 132.3 mg, 76% yield, liquid; (lit. yield = 90%)[67]. ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 9.0 Hz, 2H), 6.53 (d, *J* = 9.0 Hz, 2H), 3.35 (q, *J* = 7.1 Hz,

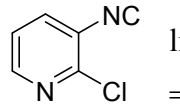
4H), 1.16 (t, J = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.7 (t, J = 5.8 Hz), 147.7, 127.4, 113.8 (t, J = 13.8 Hz), 110.9, 44.3, 12.2; HRMS (ESI) m/z calculated for $C_{11}H_{15}N_2$ $[M+H]^+$: 175.1230; found $[M+H]^+$: 175.1231.

I-64: 3-(Isocyanomethyl)pyridine[23]



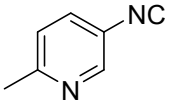
The product was obtained a procedure **B**, 1.0 mmol scale 70.8 mg, 60% yield, liquid; (lit. yield = 72%)[23]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (dd, J = 4.9, 1.6 Hz, 1H), 8.59 (d, J = 2.4 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.36 (dd, J = 7.9, 4.9 Hz, 1H), 4.67 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2 (t, J = 5.2), 150.0, 148.1, 134.3, 123.8, 43.2 (t, J = 7.5 Hz); HRMS (ESI) m/z calculated for $C_7H_7N_2$ $[M+H]^+$: 119.0604; found $[M+H]^+$: 119.0603.

I-66: 2-Chloro-3-isocyanopyridine



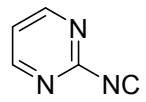
The product was obtained a procedure **B**, 1.0 mmol scale 126.0 mg, 92% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (dd, J = 4.8, 1.8 Hz, 1H), 7.78 (dd, J = 7.9, 1.8 Hz, 1H), 7.34 (dd, J = 7.9, 4.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 159.1, 149.4, 147.6, 136.0, 122.7; HRMS (ESI) m/z calculated for $C_6H_4ClN_2$ $[M+H]^+$: 139.0058; found $[M+H]^+$: 139.0060.

I-67: 5-Isocyano-2-methylpyridine



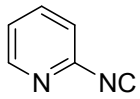
The product was obtained a procedure **B**, 1.0 mmol scale 55.5 mg, 47% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 8.3, 2.4 Hz, 1H), 7.21 (d, J = 8.3 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 159.5, 146.7, 133.5, 123.4, 24.4; SFC-MS (ESI) m/z calculated for $C_7H_9N_2O$ $[M+H+H_2O]^+$: 137.07; found $[M+H+H_2O]^+$: 137.08.

I-68: 2-Isocyanopyrimidine



The product was obtained a procedure **B**, 1.0 mmol scale 42.0 mg, 40% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 4.9 Hz, 2H), 7.48 (t, J = 4.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9, 159.2, 158.3, 121.8; SFC-MS (ESI) m/z calculated for $C_5H_6N_3O$ $[M+H+H_2O]^+$: 124.05; found $[M+H+H_2O]^+$: 124.07.

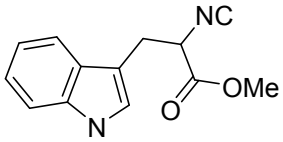
I-69: 2-Isocyanopyridine[71]



The product was obtained a procedure **B**, 1.0 mmol scale 31.2 mg, 30% yield, liquid; (lit. yield = 50%)[71]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.5 (dd, J = 4.9, 1.1 Hz, 1H), 7.8 (td, J = 7.8, 1.9 Hz, 1H), 7.4 (ddd, J = 7.8, 4.9, 1.1 Hz, 1H), 7.4 (dt, J = 7.8, 1.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 149.8, 140.4 (t, J = 17.2 Hz),

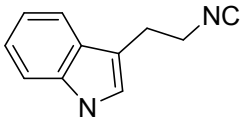
138.7, 124.7, 121.4; HRMS (ESI) m/z calculated for $C_6H_7N_2O$ $[M+H+H_2O]^+$: 123.06; found $[M+H+H_2O]^+$: 123.12.

I-72: Methyl 3-(1*H*-indol-3-yl)-2-isocyanopropanoate[72]



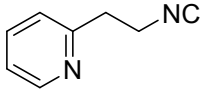
The product was obtained a procedure **B**, 1.0 mmol scale 214.3mg, 94% yield, solid; (lit. yield = 69%)[72]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.16 (d, *J* = 7.6 Hz, 1H), 4.55 (dd, *J* = 7.9, 4.7 Hz, 1H), 3.76 (s, 3H), 3.48 (dd, *J* = 14.7, 4.7 Hz, 1H), 3.36 (dd, *J* = 14.7, 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 160.0, 136.0, 126.6, 123.7, 122.3, 119.7, 118.0, 111.4, 108.4, 57.4, 53.3, 29.4; HRMS (ESI) m/z calculated for $C_{13}H_{13}N_2O_2$ $[M+H]^+$: 229.0972; found $[M+H]^+$: 229.0971.

I-73: 3-(2-Isocyanoethyl)-1*H*-indole[73]



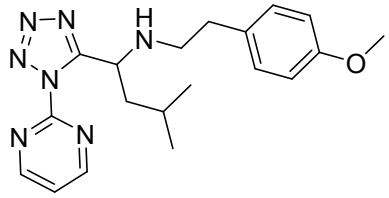
The product was obtained a procedure **B**, 1.0 mmol scale 142.8 mg, 84% yield, solid; (lit. yield = 92%)[73]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.24 – 7.19 (m, 1H), 7.17 – 7.12 (m, 1H), 7.10 (d, *J* = 2.4 Hz, 1H), 3.63 (td, *J* = 7.1, 2.0 Hz, 2H), 3.14 (td, *J* = 7.1, 2.0 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.6 (d, *J* = 4.5 Hz), 136.1, 126.6, 122.6, 122.2, 119.5, 118.1, 111.4, 110.8, 42.3 (d, *J* = 6.4 Hz), 25.7; HRMS (ESI) m/z calculated for $C_{11}H_{11}N_2$ $[M+H]^+$: 171.0917; found $[M+H]^+$: 171.0916.

I-74: 2-(2-Isocyanoethyl)pyridine



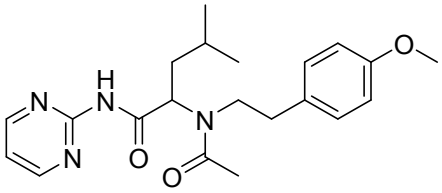
The product was obtained a procedure **B**, 1.0 mmol scale 89.8 mg, 68% yield, liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.2 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.22 – 7.11 (m, 2H), 3.79 (td, *J* = 6.8, 1.9 Hz, 2H), 3.13 – 3.03 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1 (t, *J* = 5.6 Hz), 149.4, 136.6, 123.5, 122.1, 40.8 (td, *J* = 6.7 Hz), 37.3; HRMS (ESI) m/z calculated for $C_8H_9N_2$ $[M+H]^+$: 133.0760; found $[M+H]^+$: 133.0761.

UT-1: *N*-(4-Methoxyphenethyl)-3-methyl-1-(1-(pyrimidin-2-yl)-1*H*-tetrazol-5-yl)butan-1-amine.



The product was obtained with procedure **E**, 1.0 mmol scale, 146.7 mg, 40% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (d, *J* = 4.8 Hz, 2H), 7.46 (t, *J* = 4.9 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 2H), 4.81 (t, *J* = 6.9 Hz, 1H),

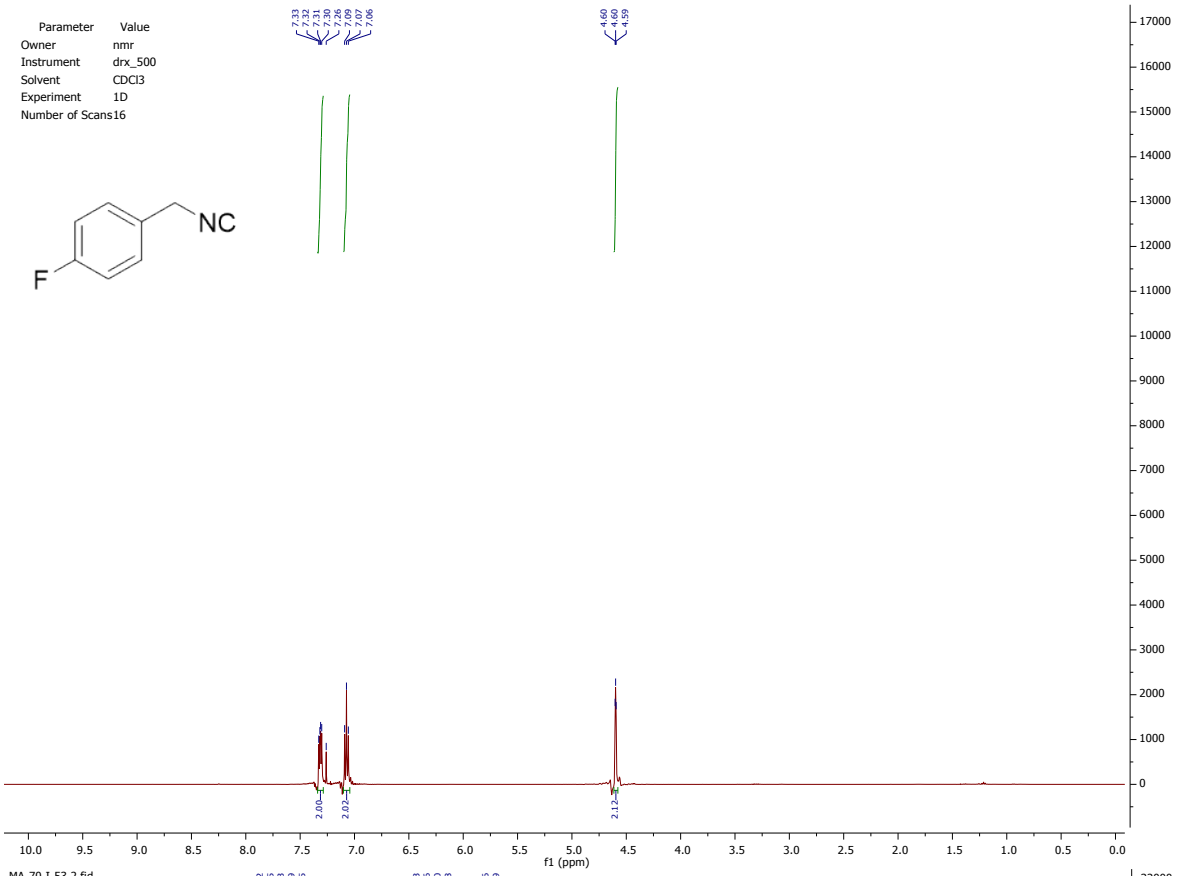
3.73 (s, 3H), 2.79 – 2.72 (m, 1H), 2.68 – 2.58 (m, 3H), 2.24 – 1.97 (m, 1H), 1.80 – 1.72 (m, 3H), 0.92 – 0.86 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 158.7, 157.8, 154.0, 131.7, 129.4, 121.1, 113.7, 55.2, 52.3, 47.8, 43.2, 35.3, 24.8, 22.8, 22.2; SFC-MS (ESI) m/z calculated for $C_{19}H_{26}N_7O$ $[M+H]^+$: 368.46; found $[M+H]^+$: 368.45.

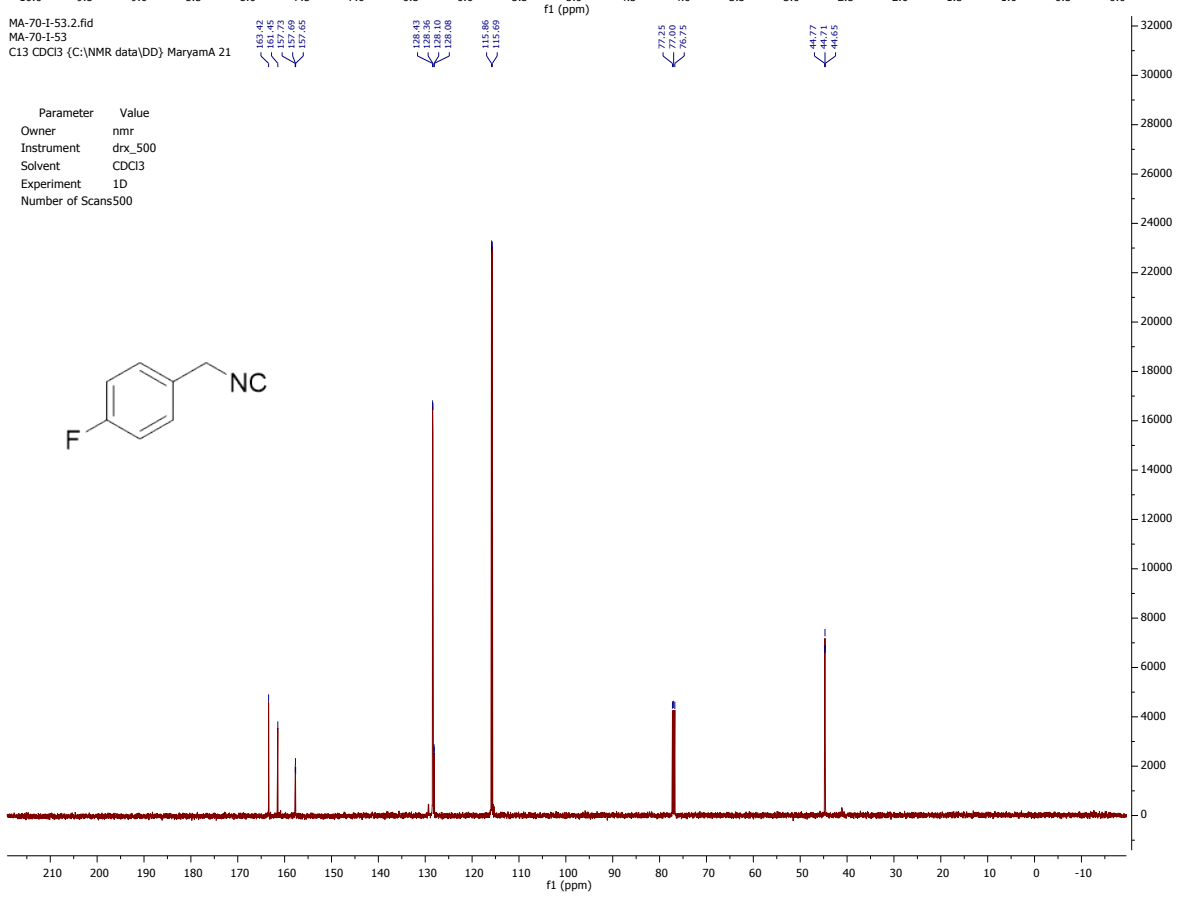


U-1: 2-(*N*-(4-Methoxyphenethyl)acetamido)-4-methyl-*N*-(pyrimidin-2-yl)pentanamide.

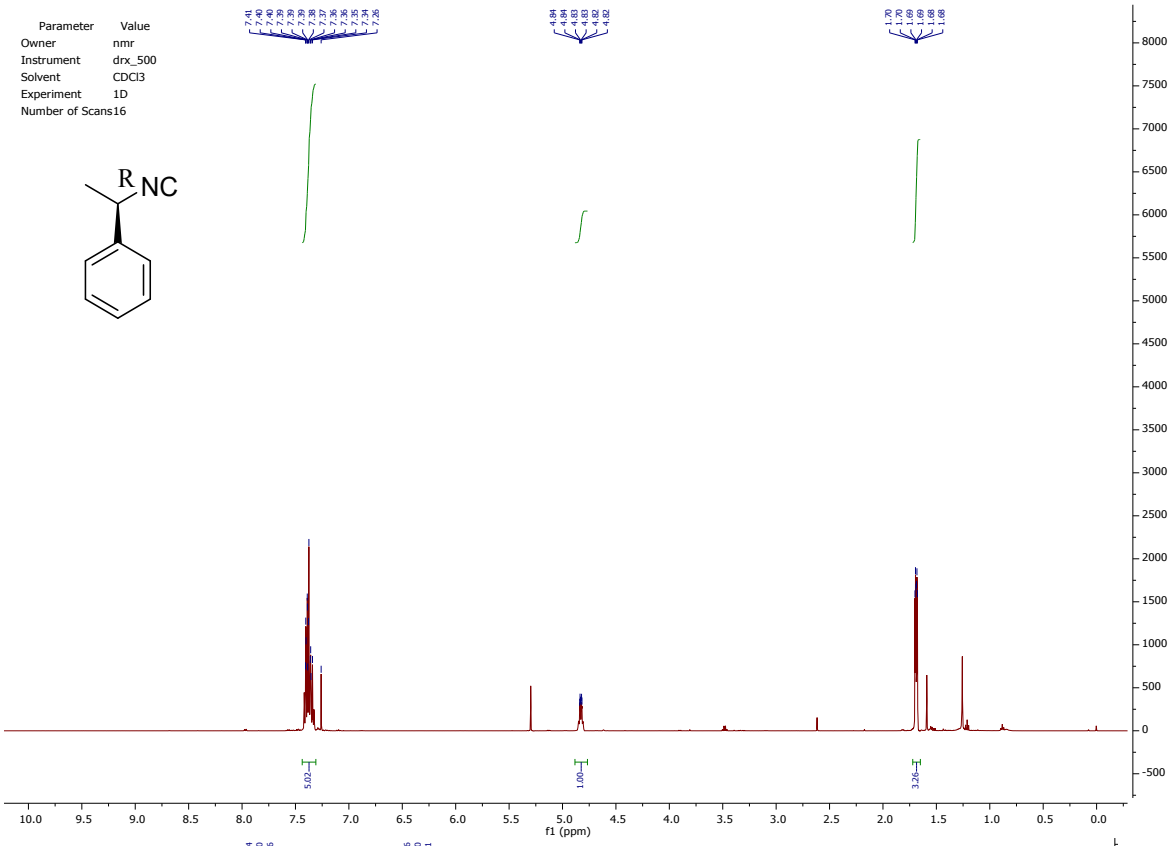
The product was obtained with procedure **F**, 1.0 mmol scale, 115.0 mg, 30% yield, solid; ^{1}H NMR (500 MHz, $CDCl_3$+1drop Of CH_3OD) δ 9.69 (s, 1H), 8.60 (d, *J* = 4.9 Hz, 2H), 7.06 (d, *J* = 8.7 Hz, 2H), 6.99 (t, *J* = 4.9 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 2H), 5.07 (t, *J* = 7.7 Hz, 1H), 3.74 (s, 3H), 3.54 – 3.47 (m, 2H), 2.90 – 2.82 (m, 1H), 2.78 – 2.69 (m, 1H), 2.13 (s, 3H), 2.05 – 1.97 (m, 1H), 1.76 – 1.68 (m, 1H), 1.62 – 1.54 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 169.4, 158.3, 157.5, 129.8, 129.6, 116.7, 114.0, 114.0, 55.2, 50.7, 48.4, 36.6, 35.0, 24.9, 22.6, 22.5, 21.9; HRMS (ESI) m/z calculated for $C_{21}H_{29}N_4O_3$ $[M+H]^+$: 385.2234; found $[M+H]^+$: 385.2238.

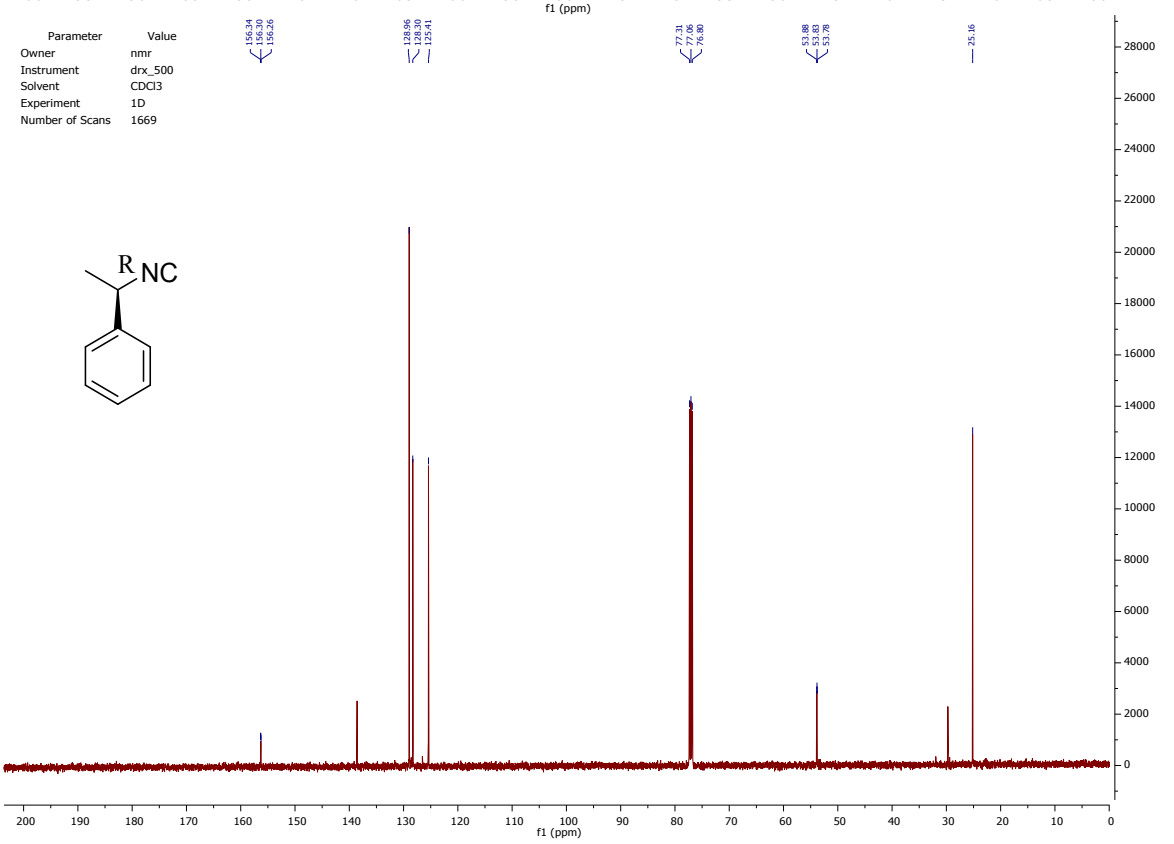
A-1: 1-Fluoro-4-(isocyanomethyl)benzene



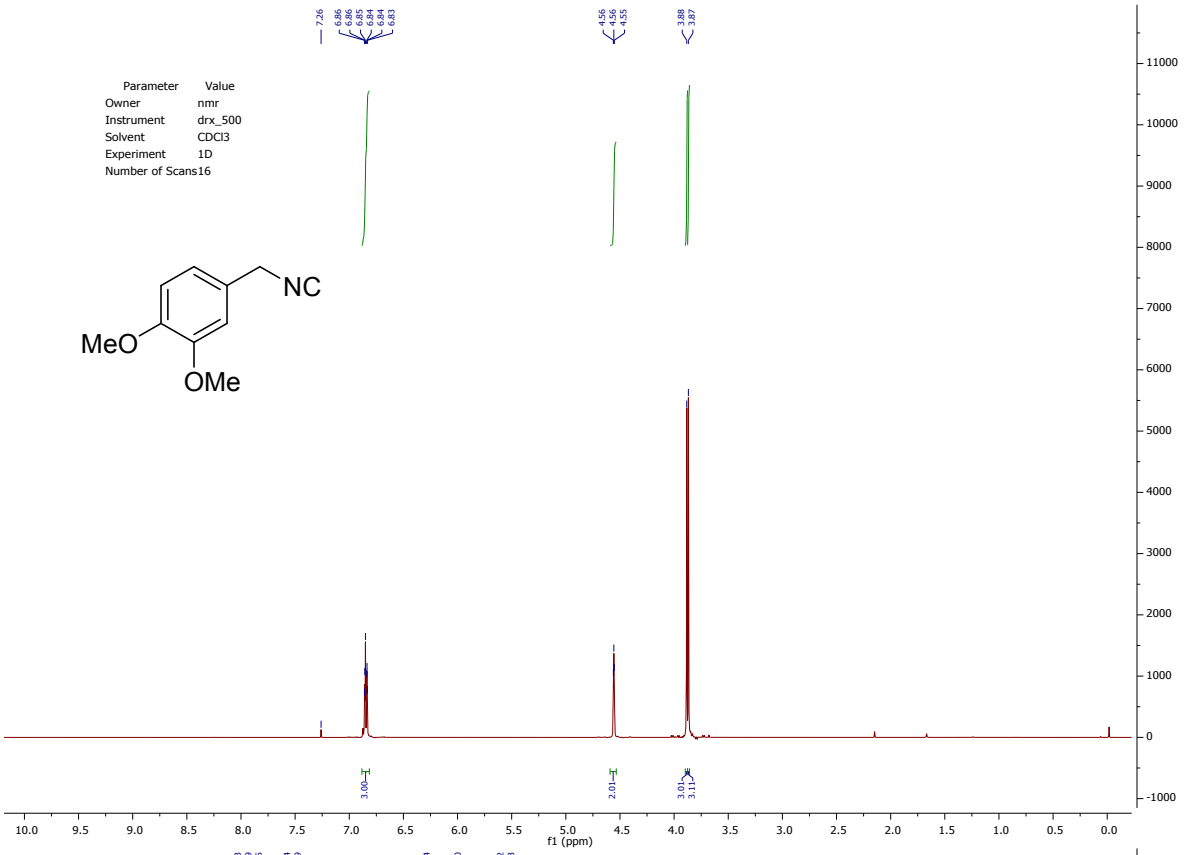


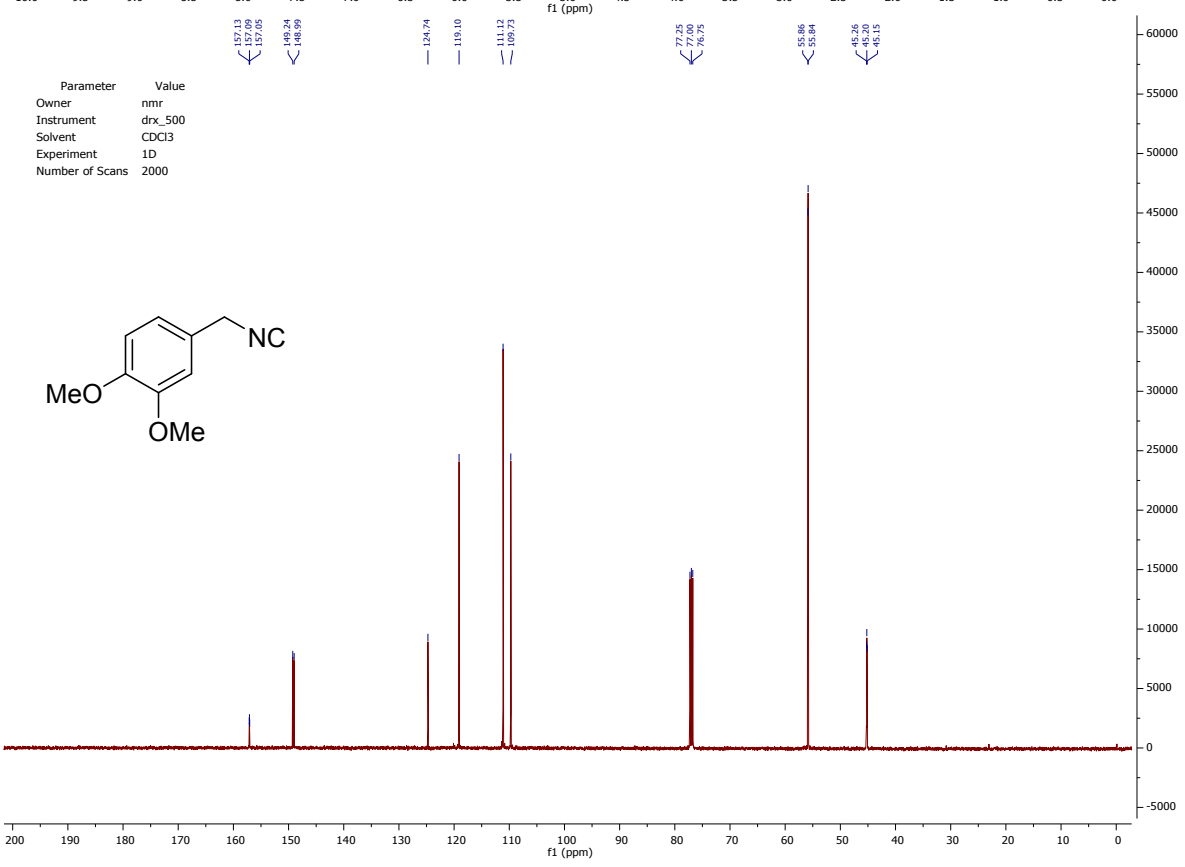
A-2 / I-7: (*R*)-(1-Isocyanoethyl)benzene



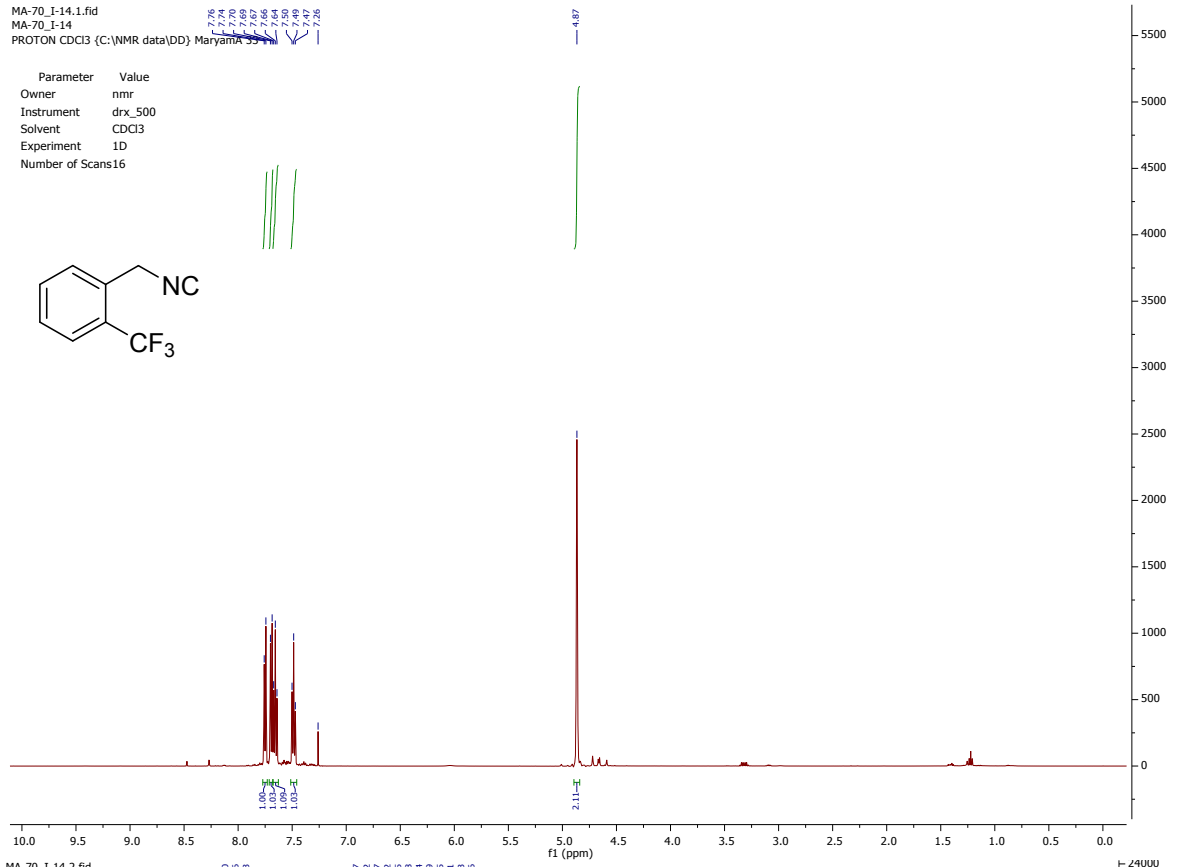


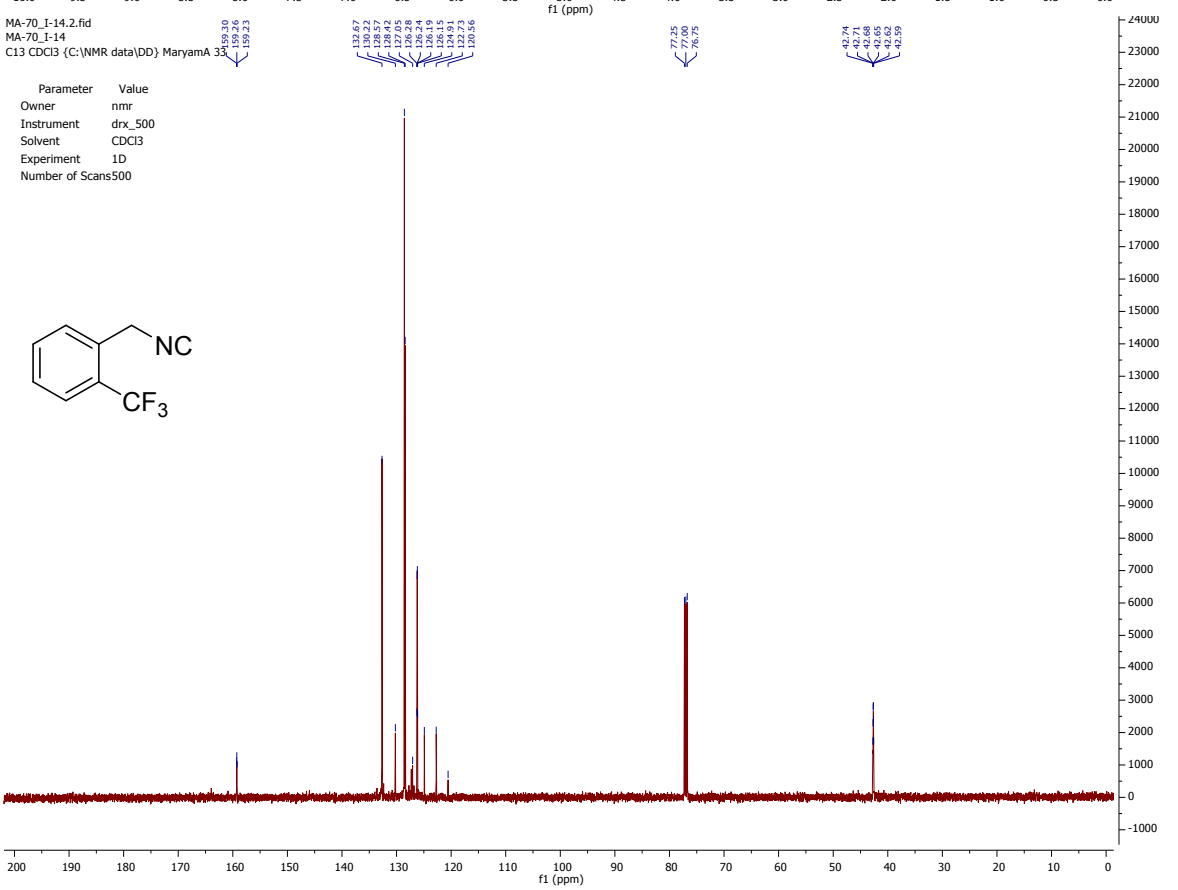
A-3: 4-(Isocyanomethyl)-1,2-dimethoxybenzene



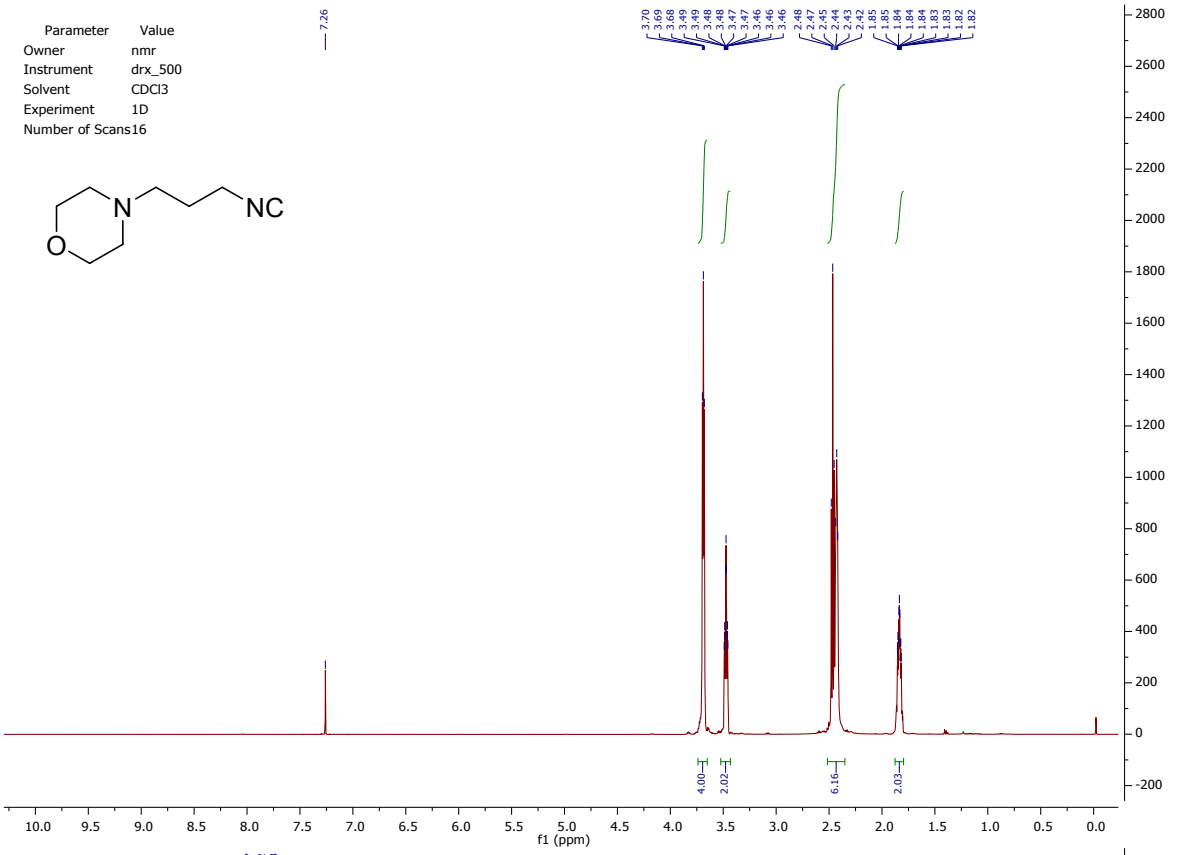


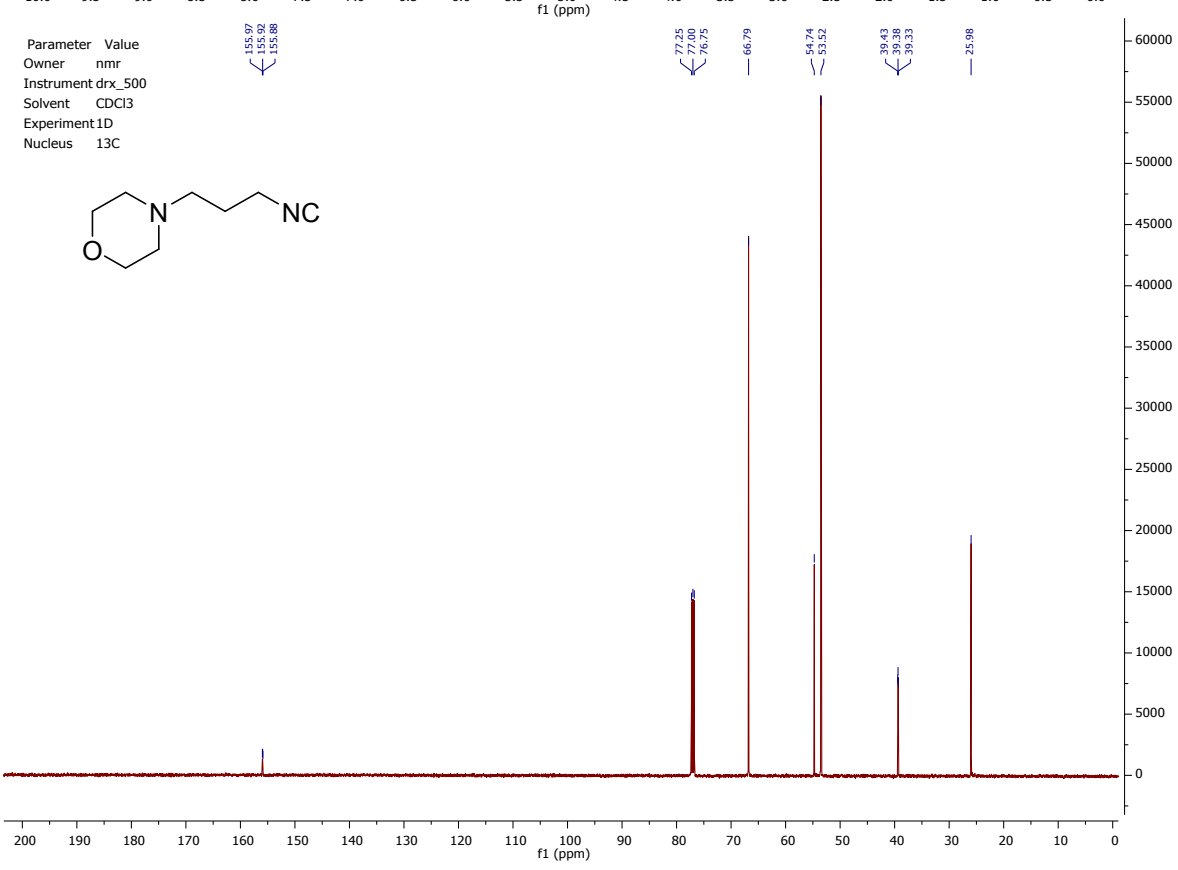
A-4 / I-14: 1-(Isocyanomethyl)-2-(trifluoromethyl)benzene



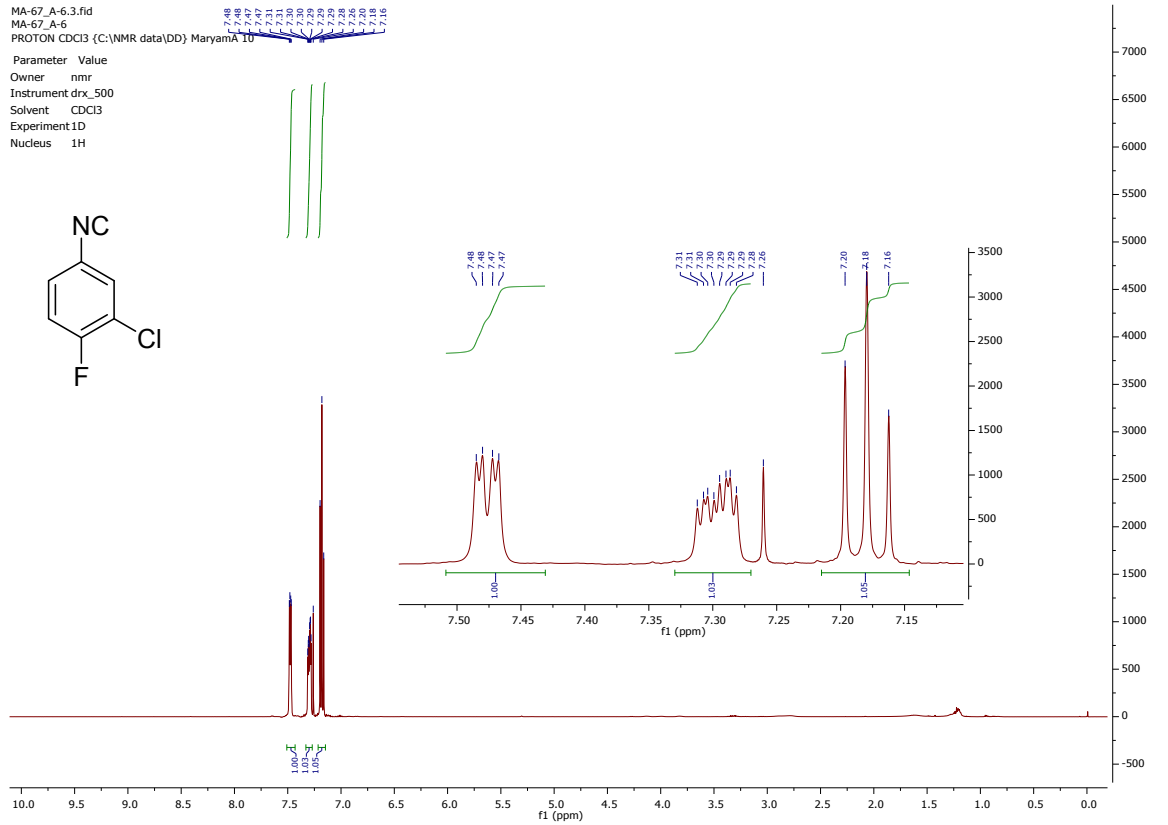


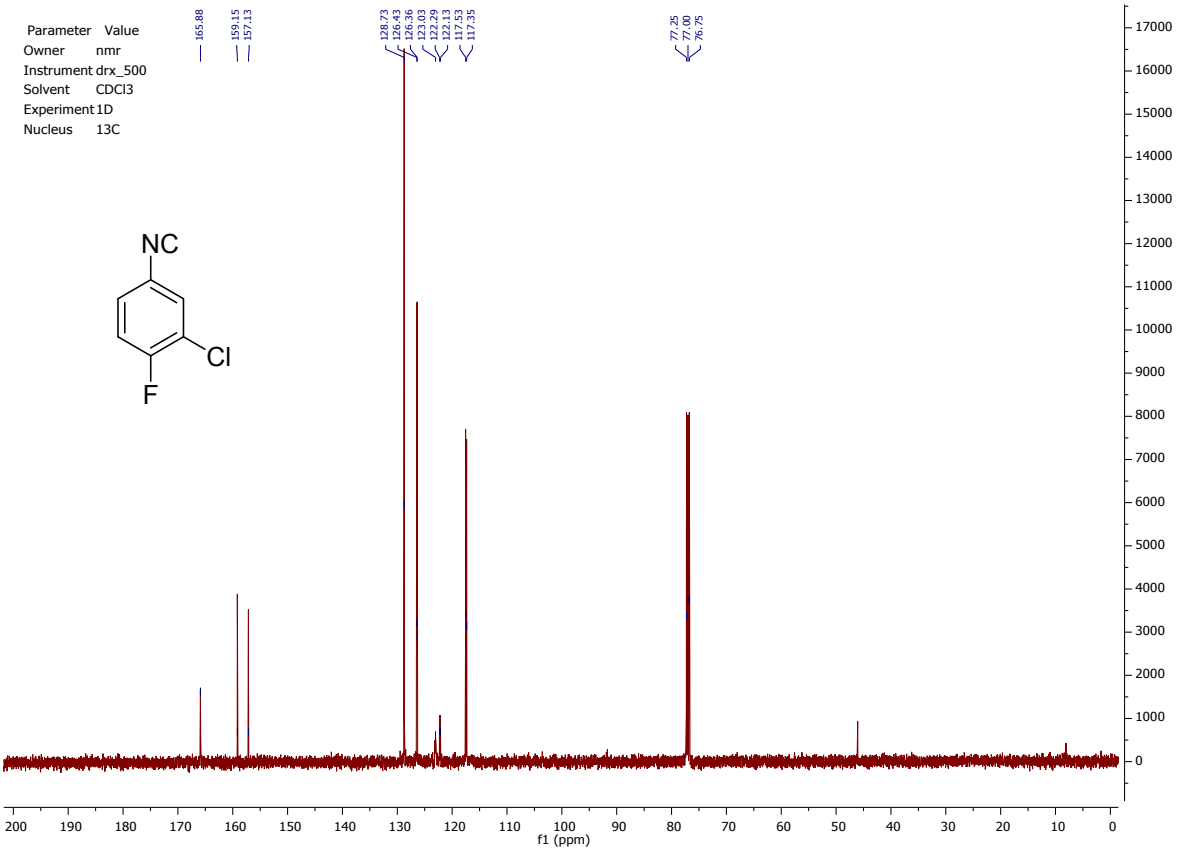
A-5 / I-58: 4-(3-Isocyanopropyl)morpholine



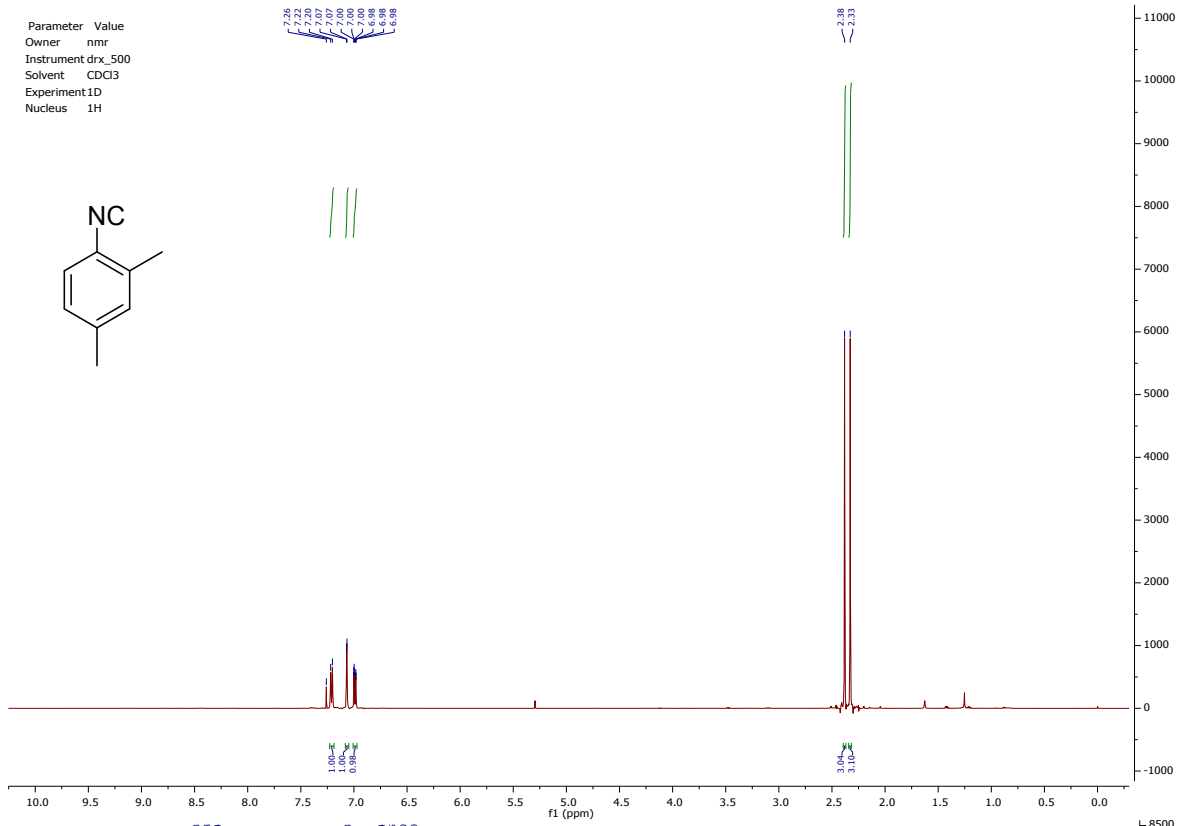


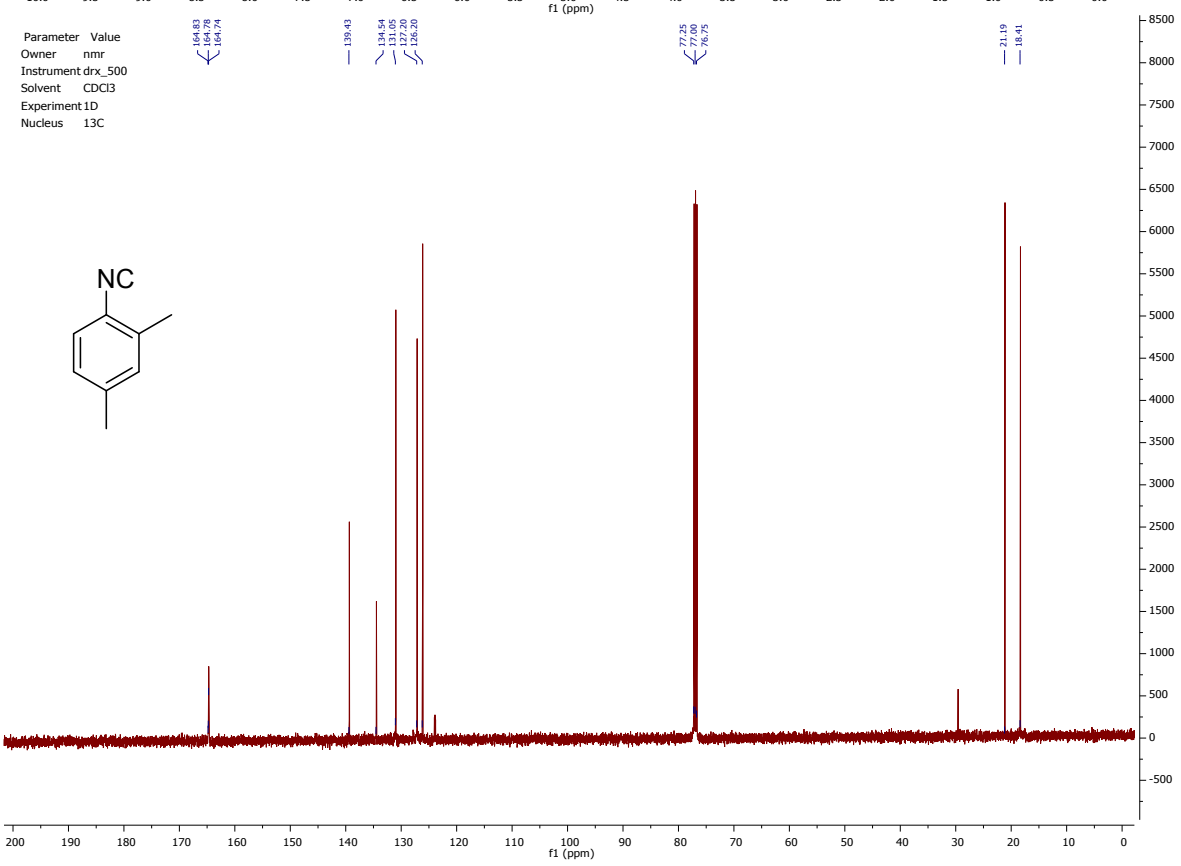
A-6: 2-Chloro-1-fluoro-4-isocyanobenzene



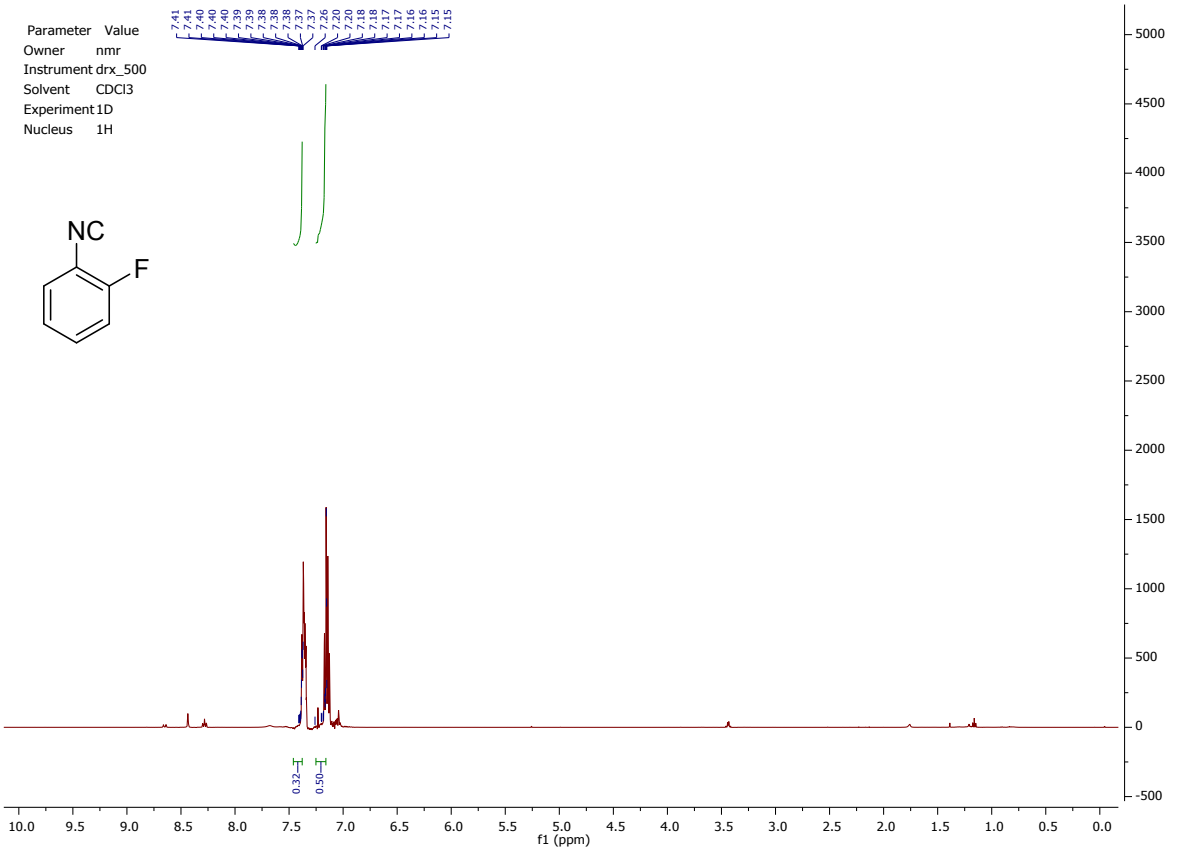


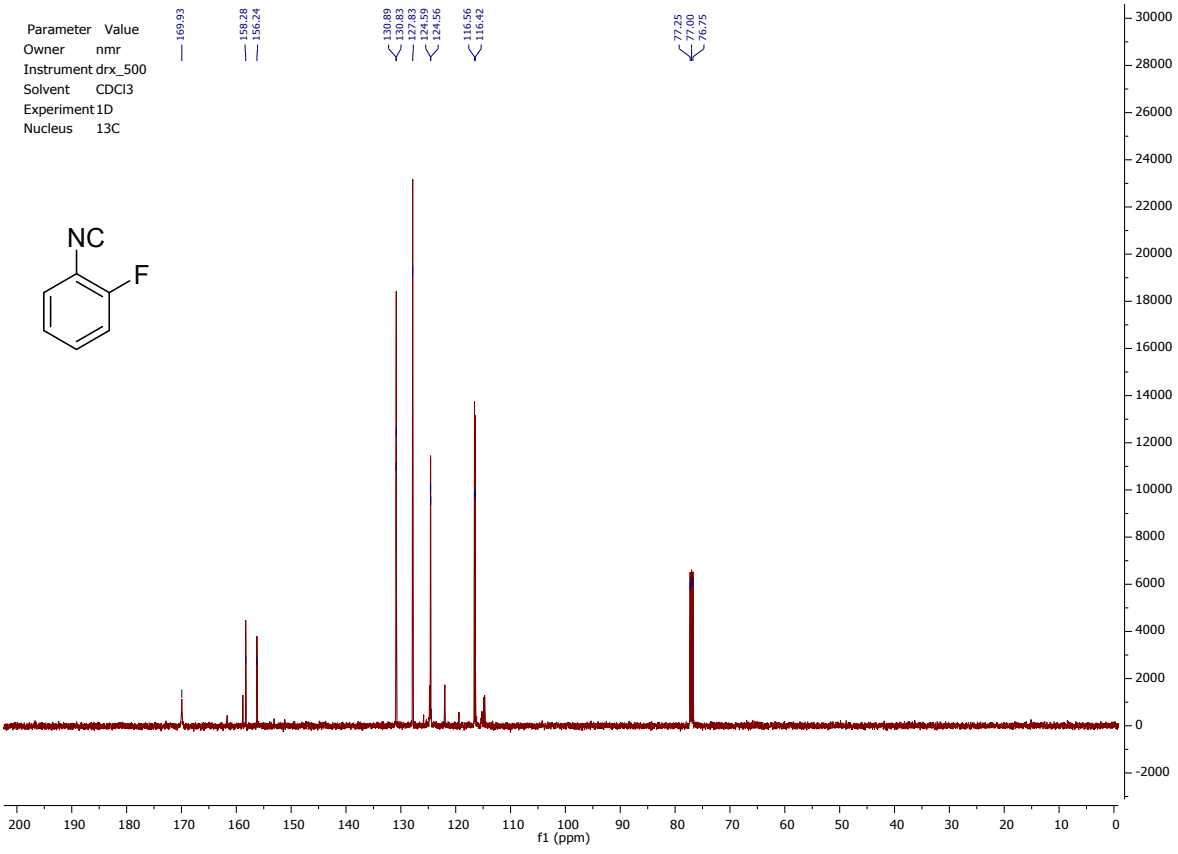
A-7: 1-Isocyano-2,4-dimethylbenzene



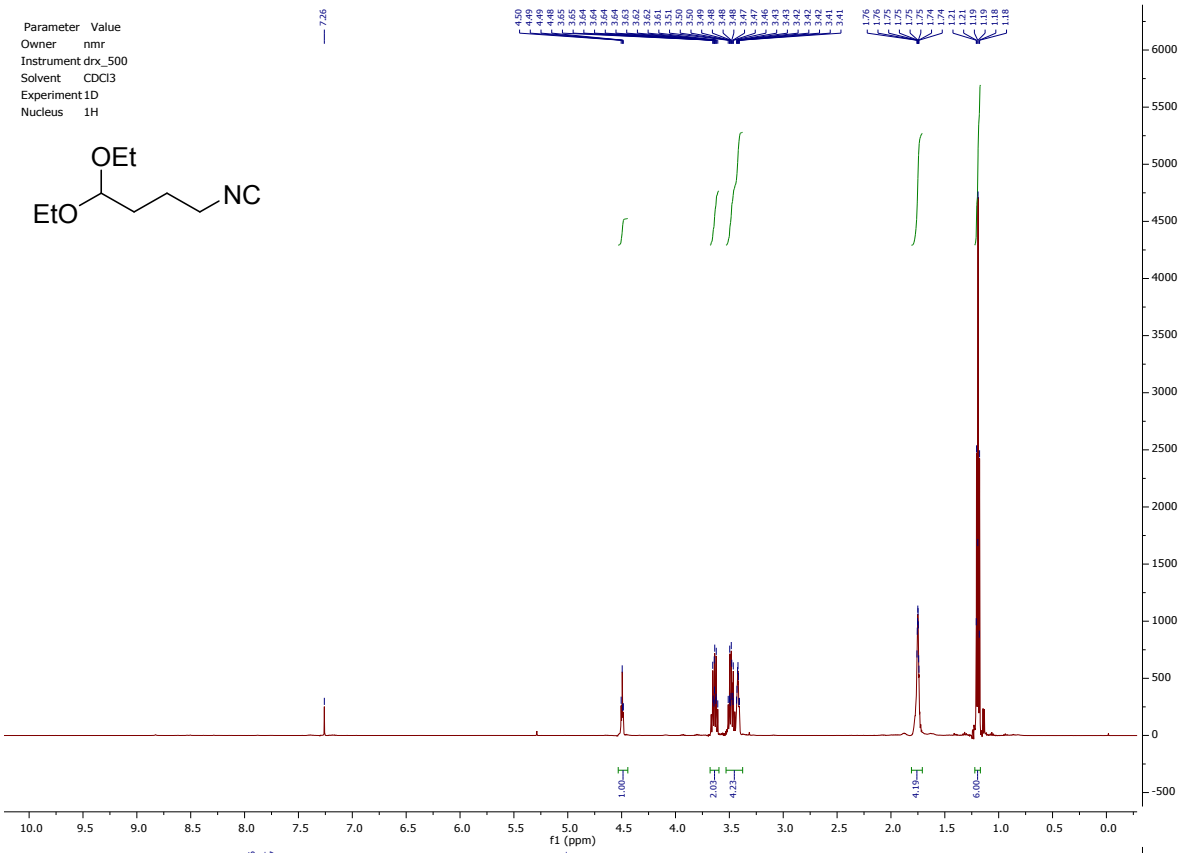


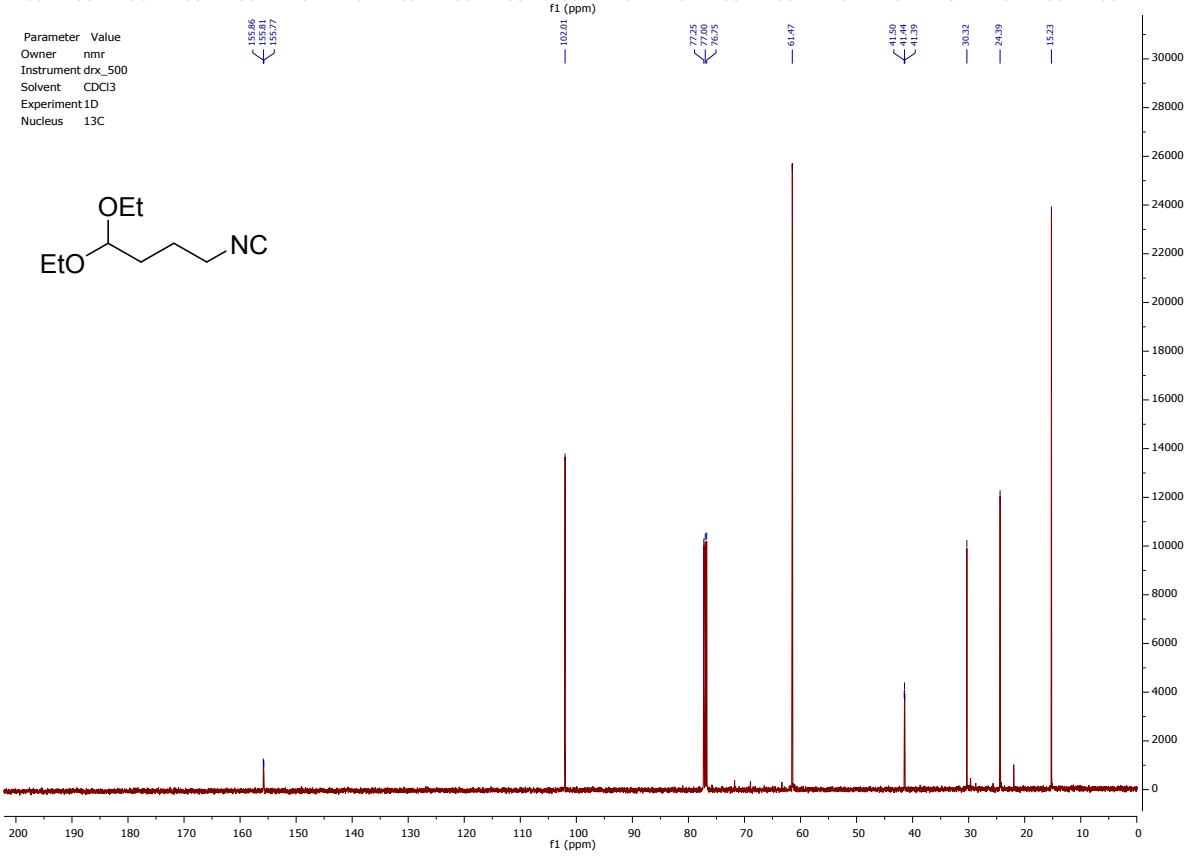
A-8: 1-Fluoro-2-isocyanobenzene



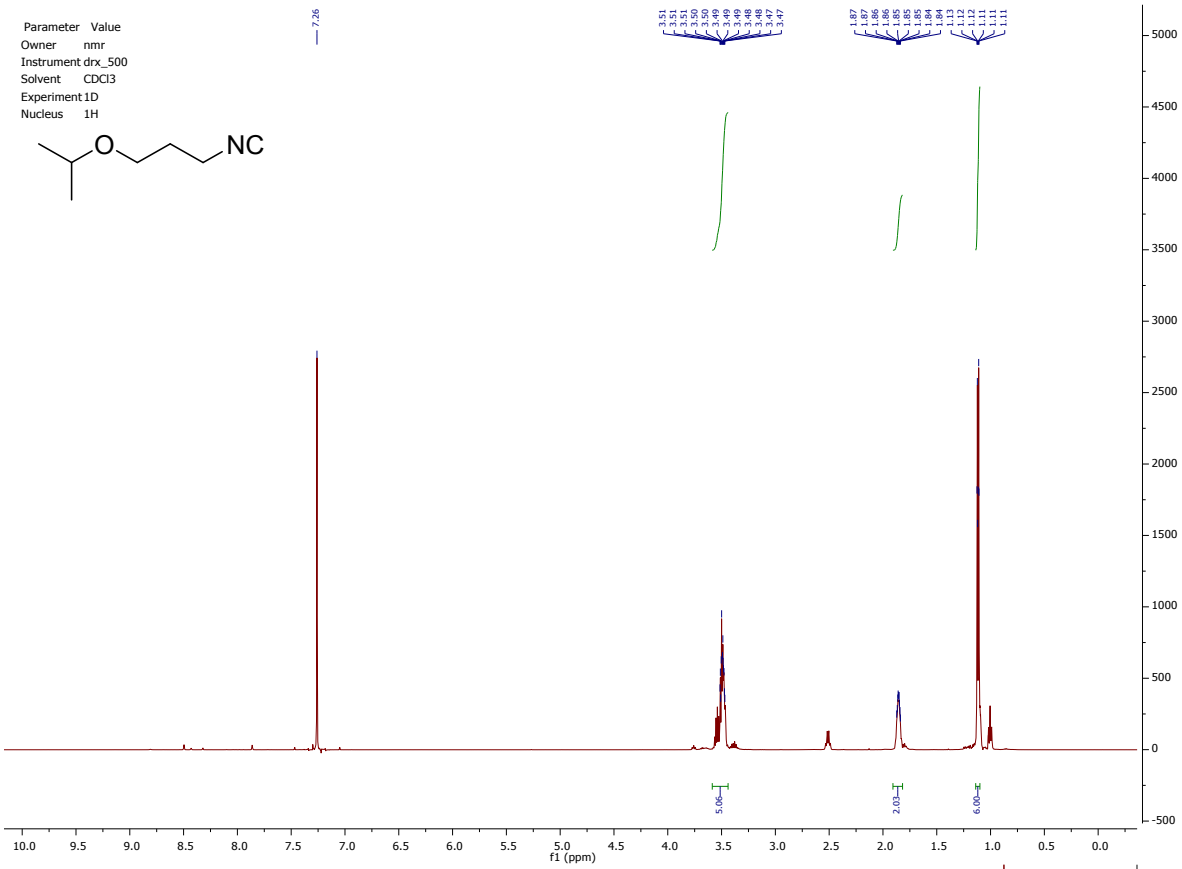


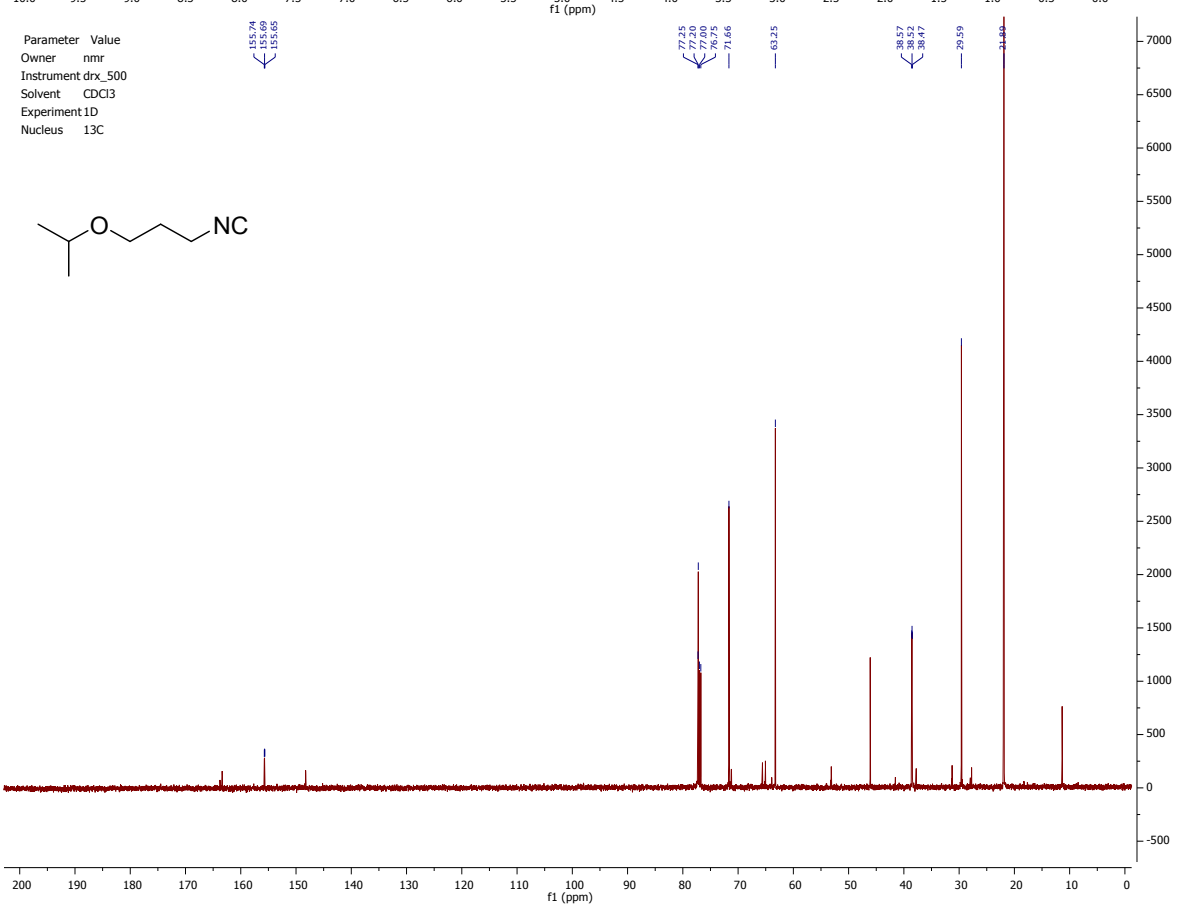
A-9 / I-35: 1,1-Diethoxy-4-isocyanobutane



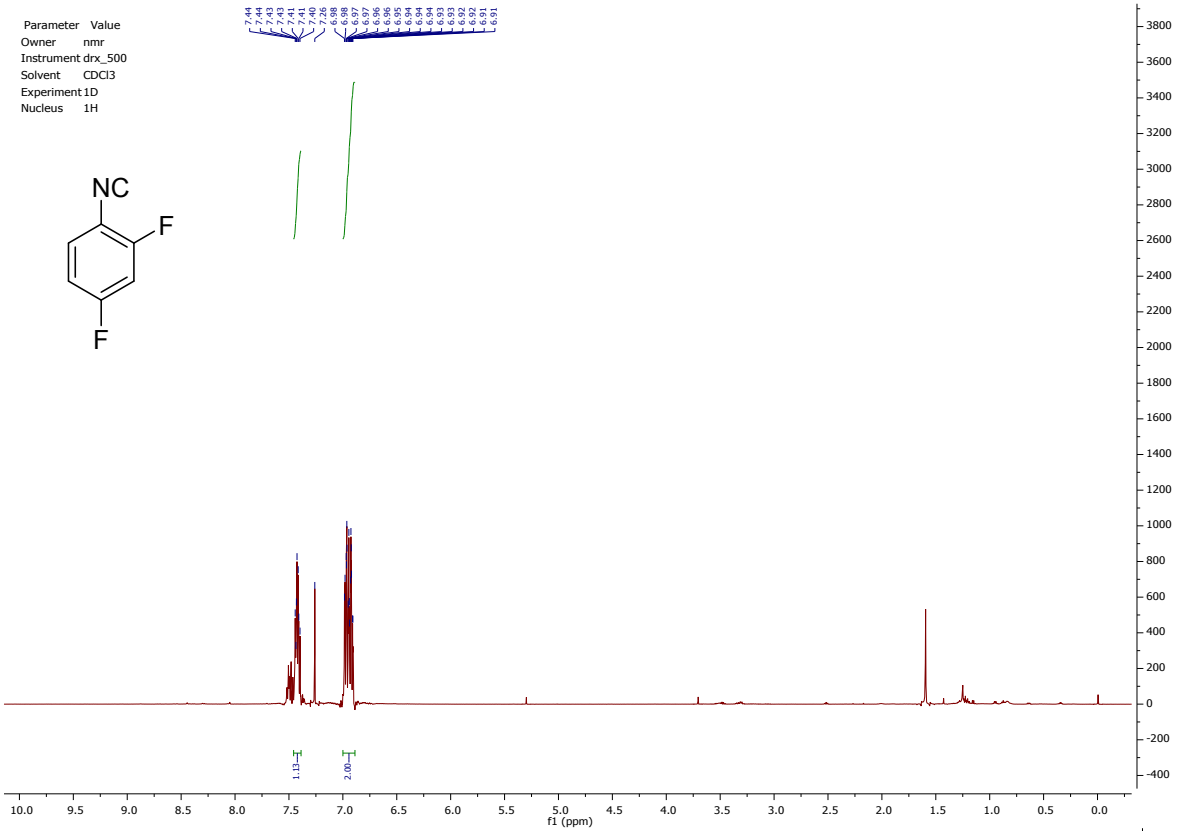


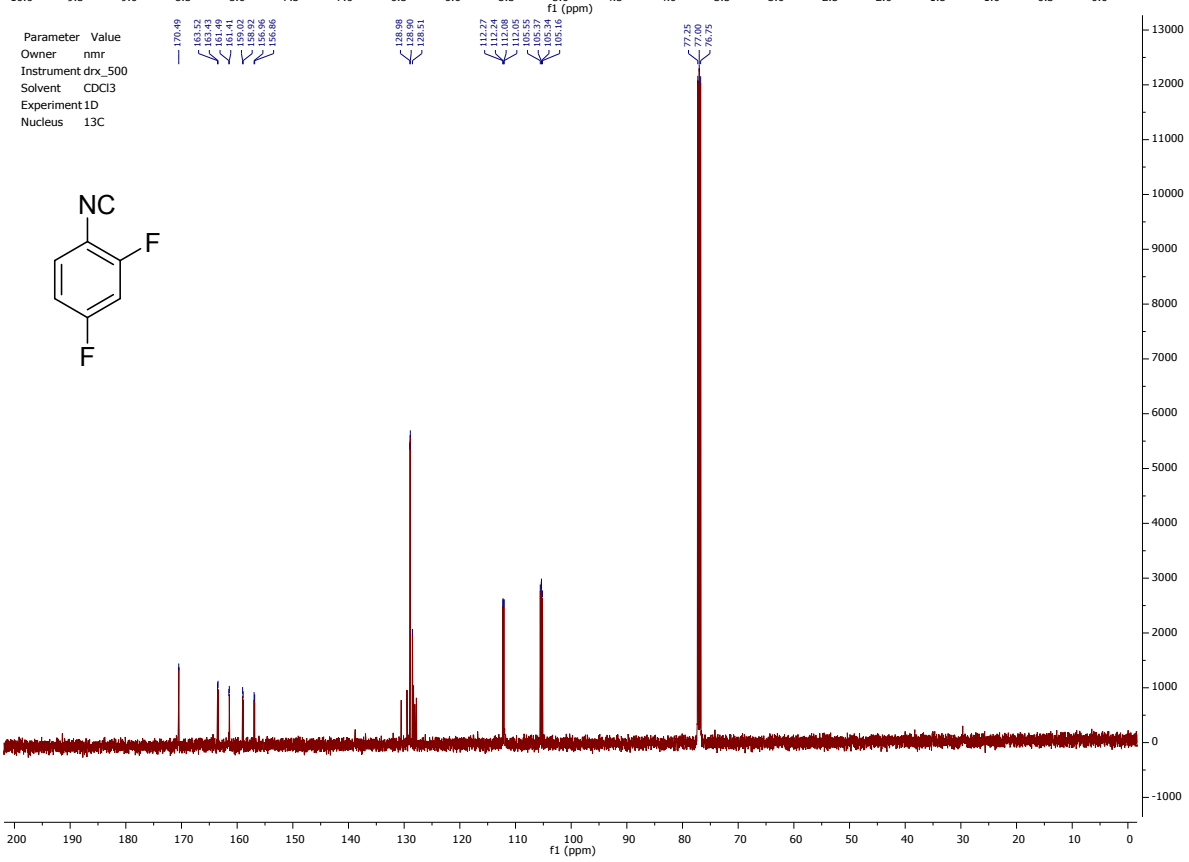
A-10 / I-43: 1-Isocyano-3-isopropoxypropane



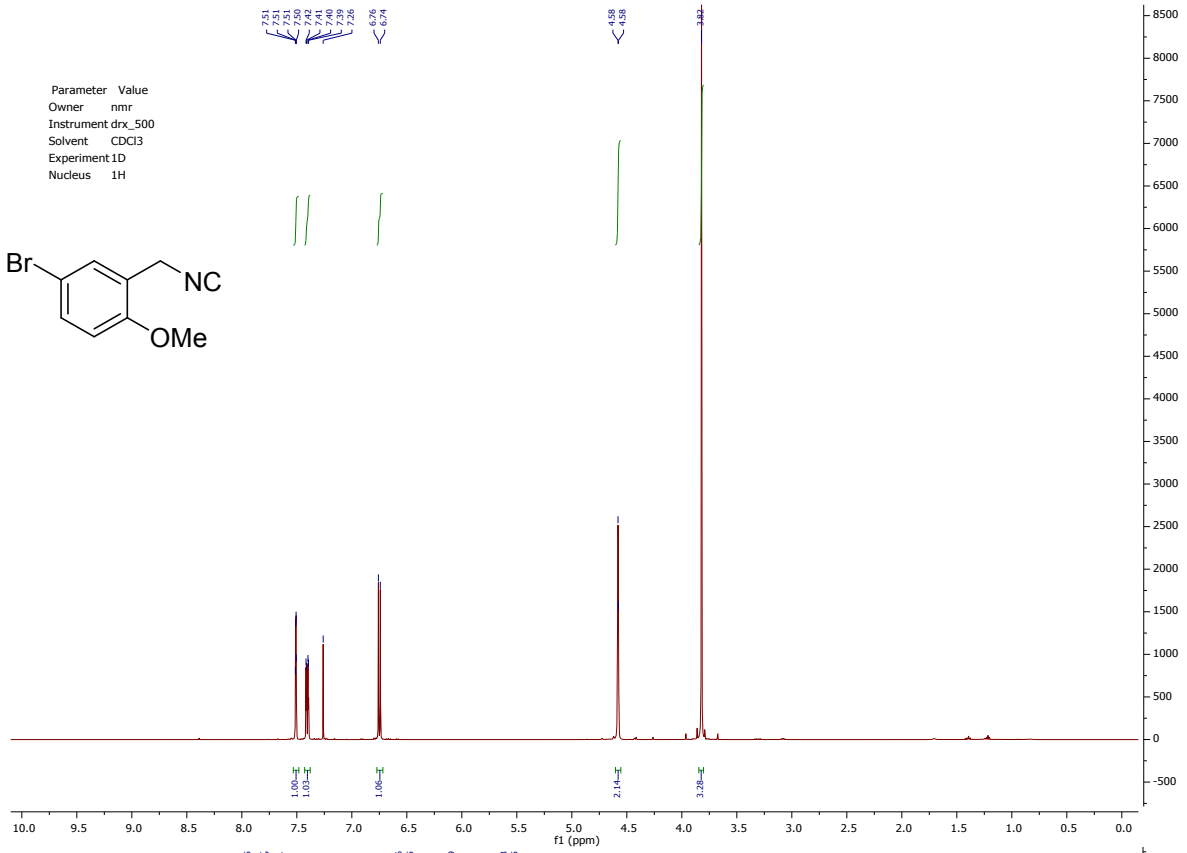


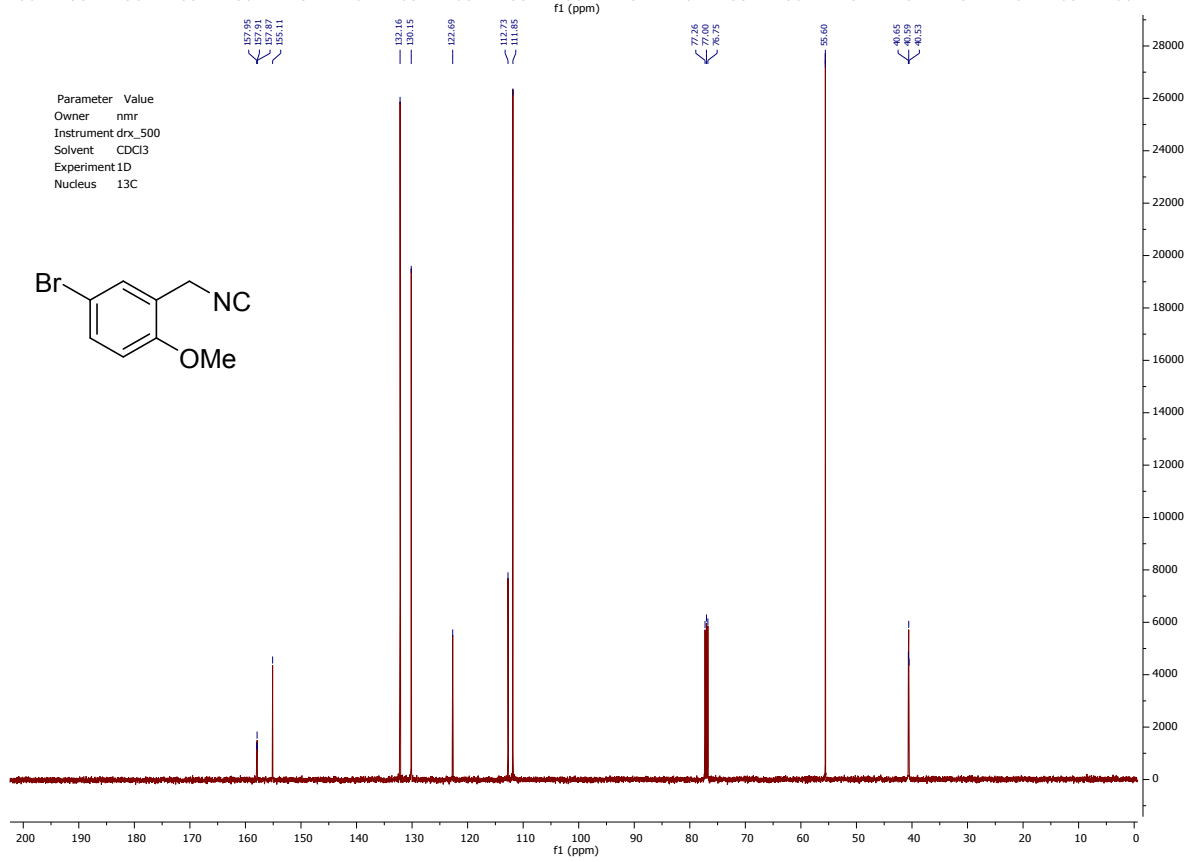
A-12: 2,4-Difluoro-1-isocyanobenzene



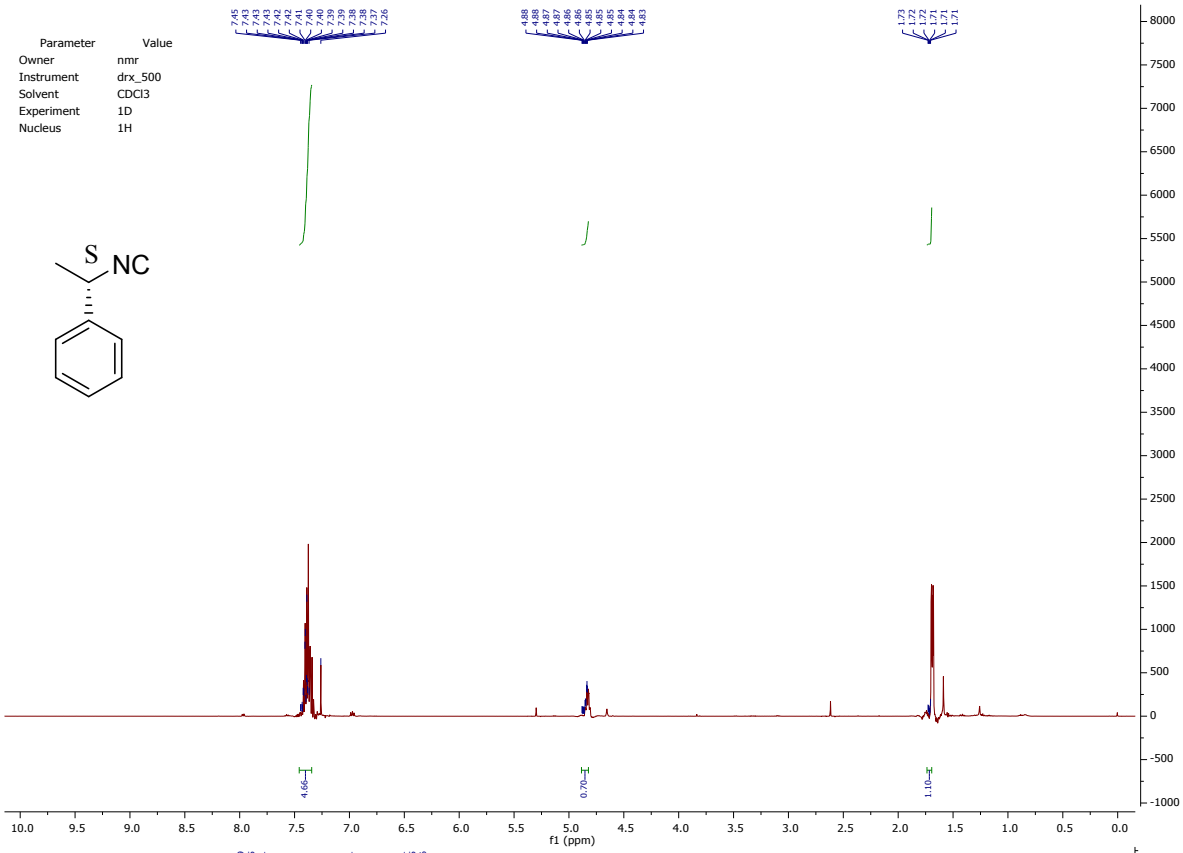


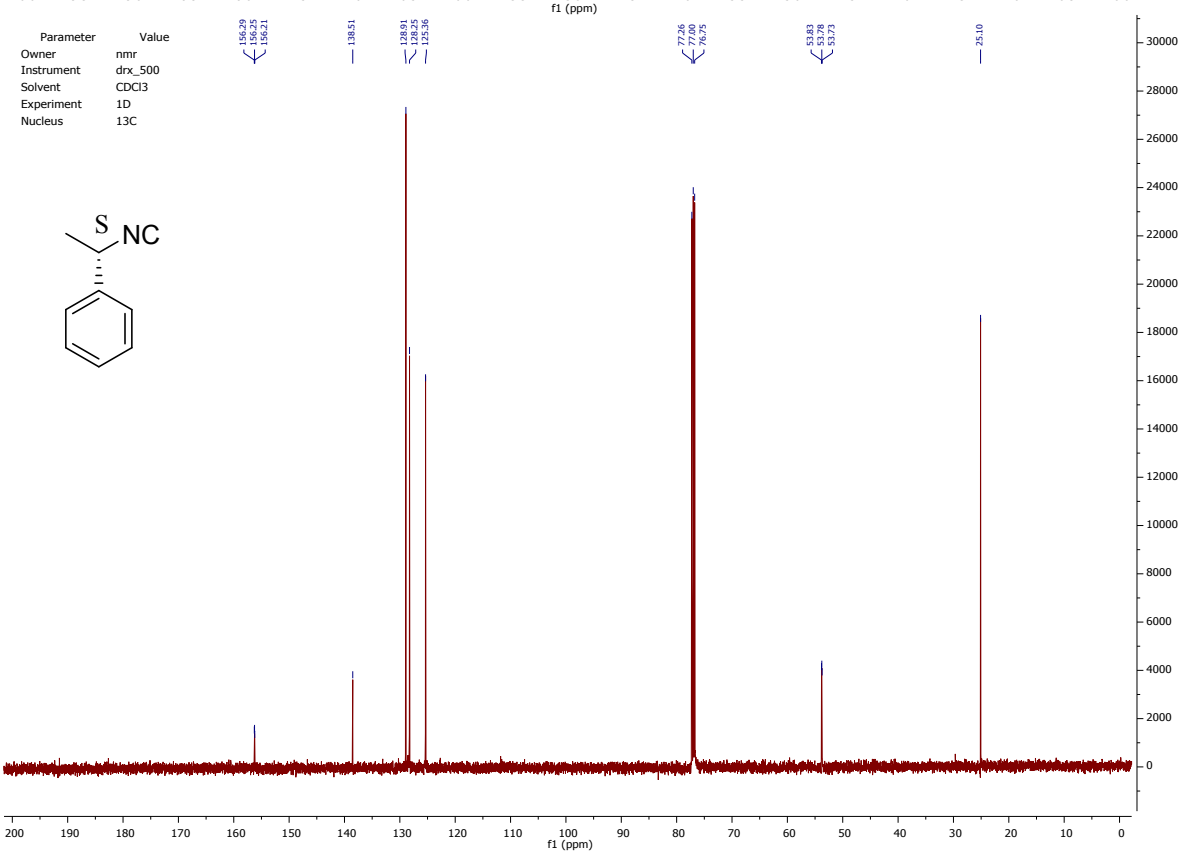
B-1 / I-1: 4-Bromo-2-(isocyanomethyl)-1-methoxybenzene



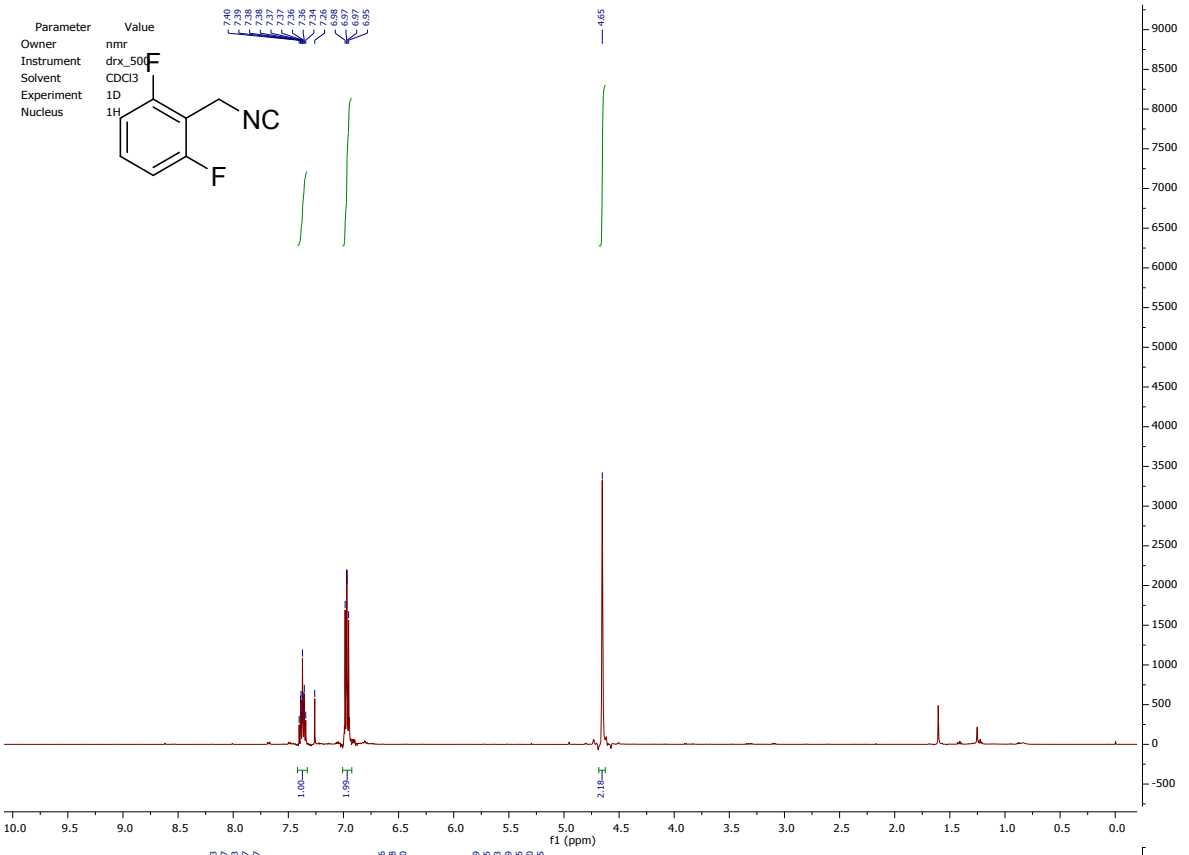


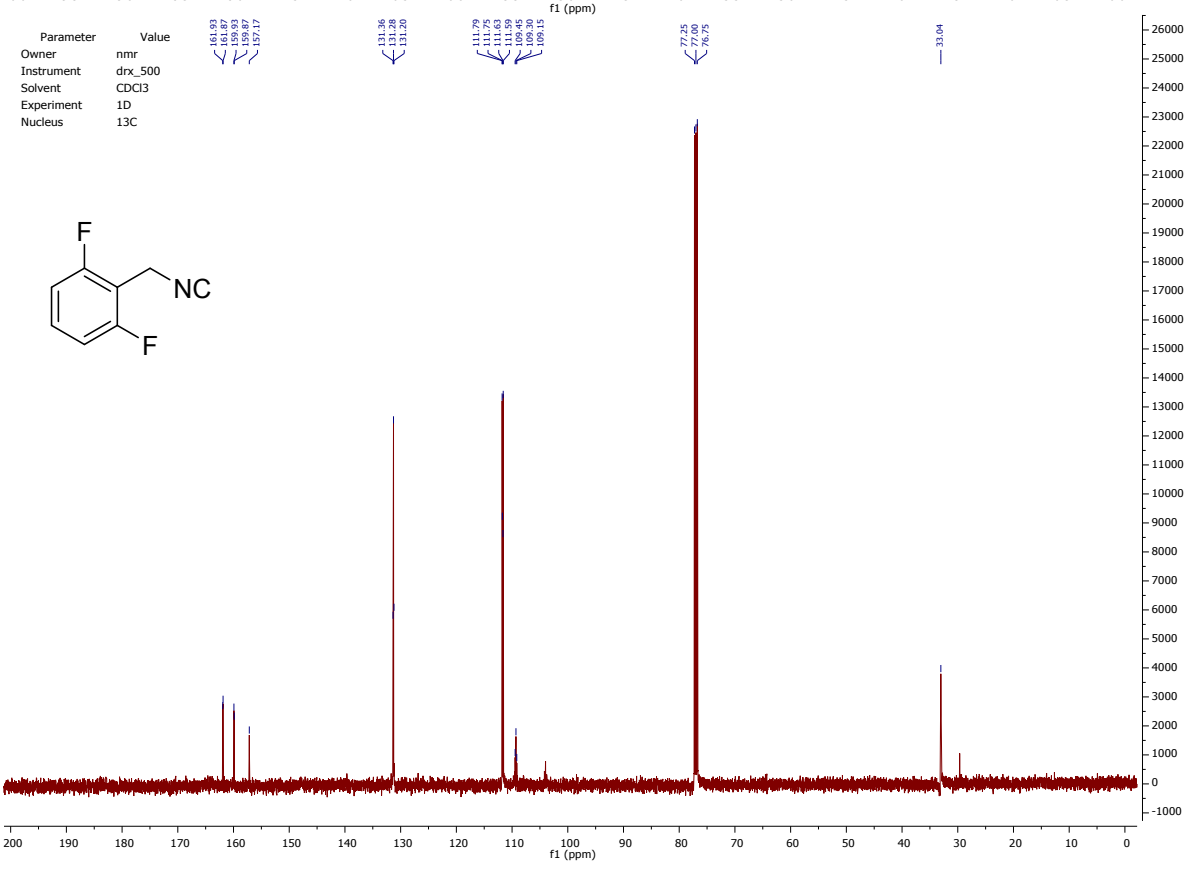
B-2: (*S*)-(1-Isocyanoethyl)benzene



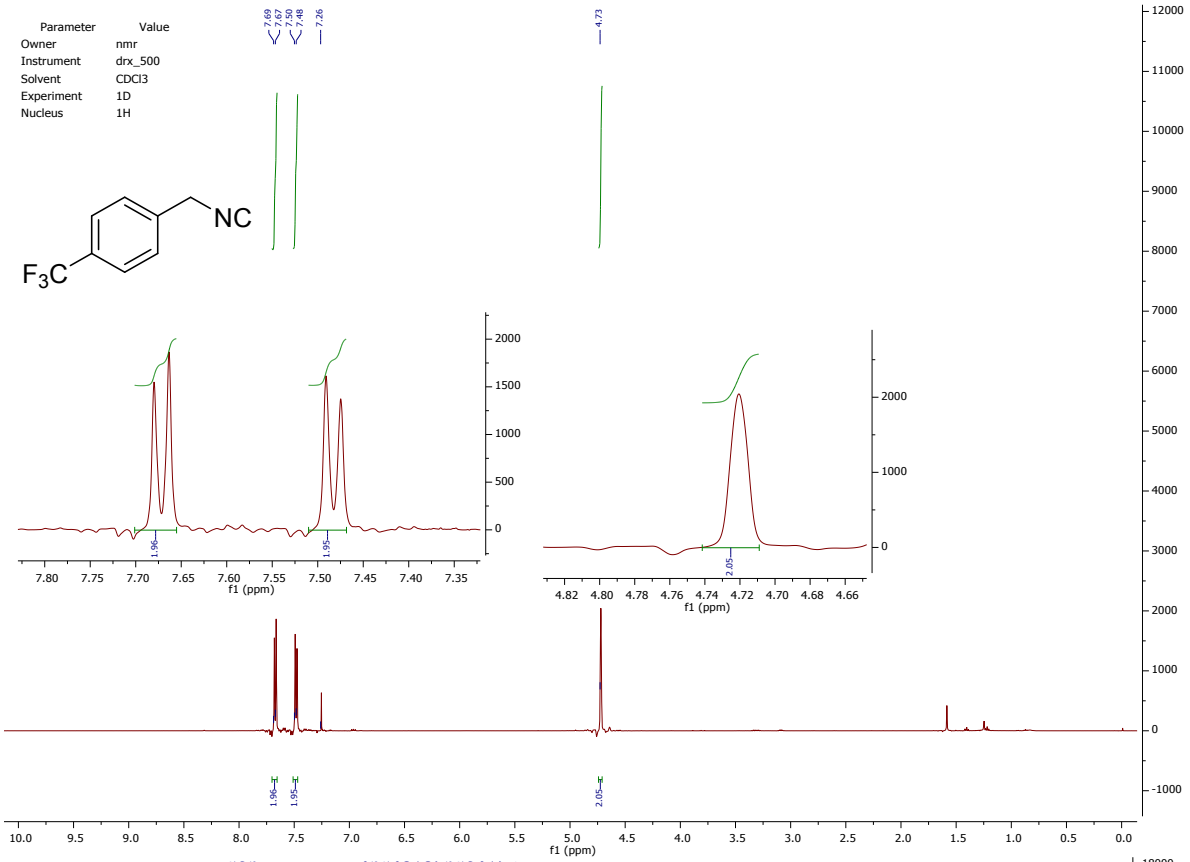


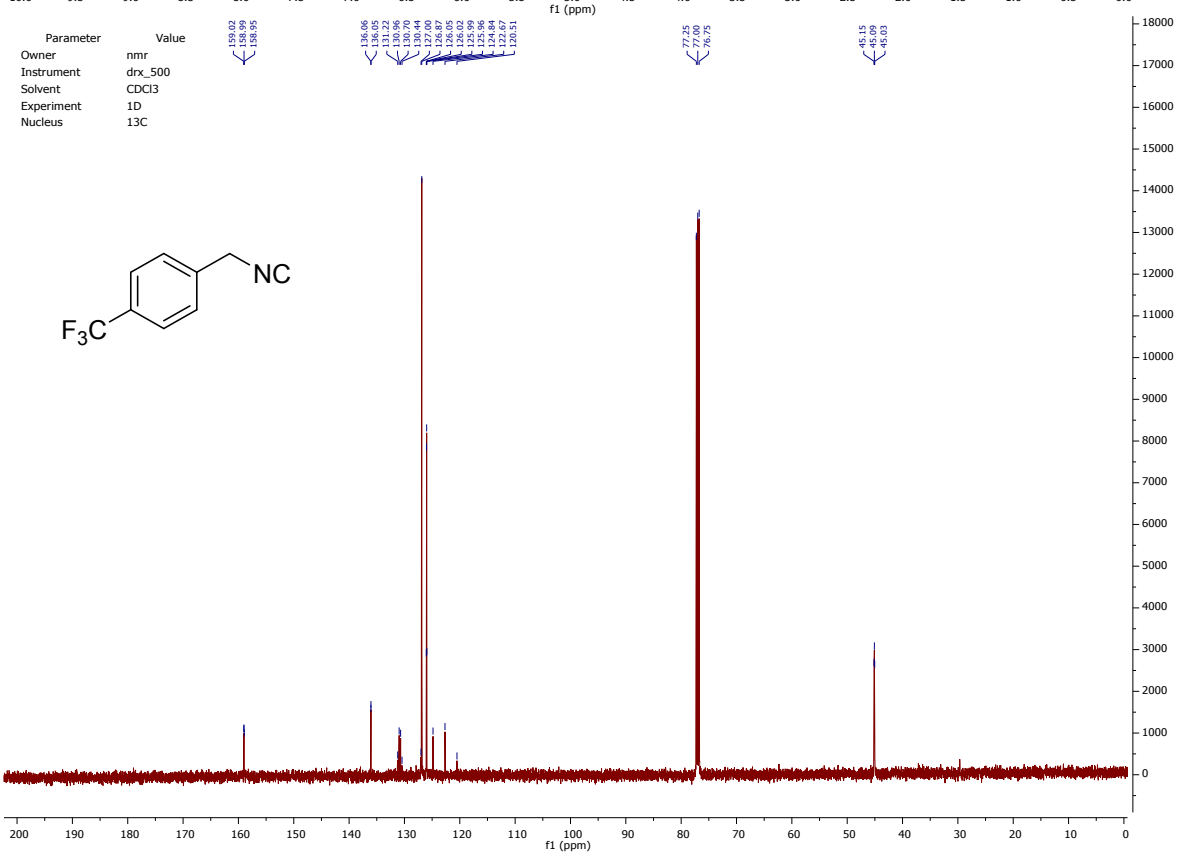
B-3: 1,3-Difluoro-2-(isocyanomethyl)benzene



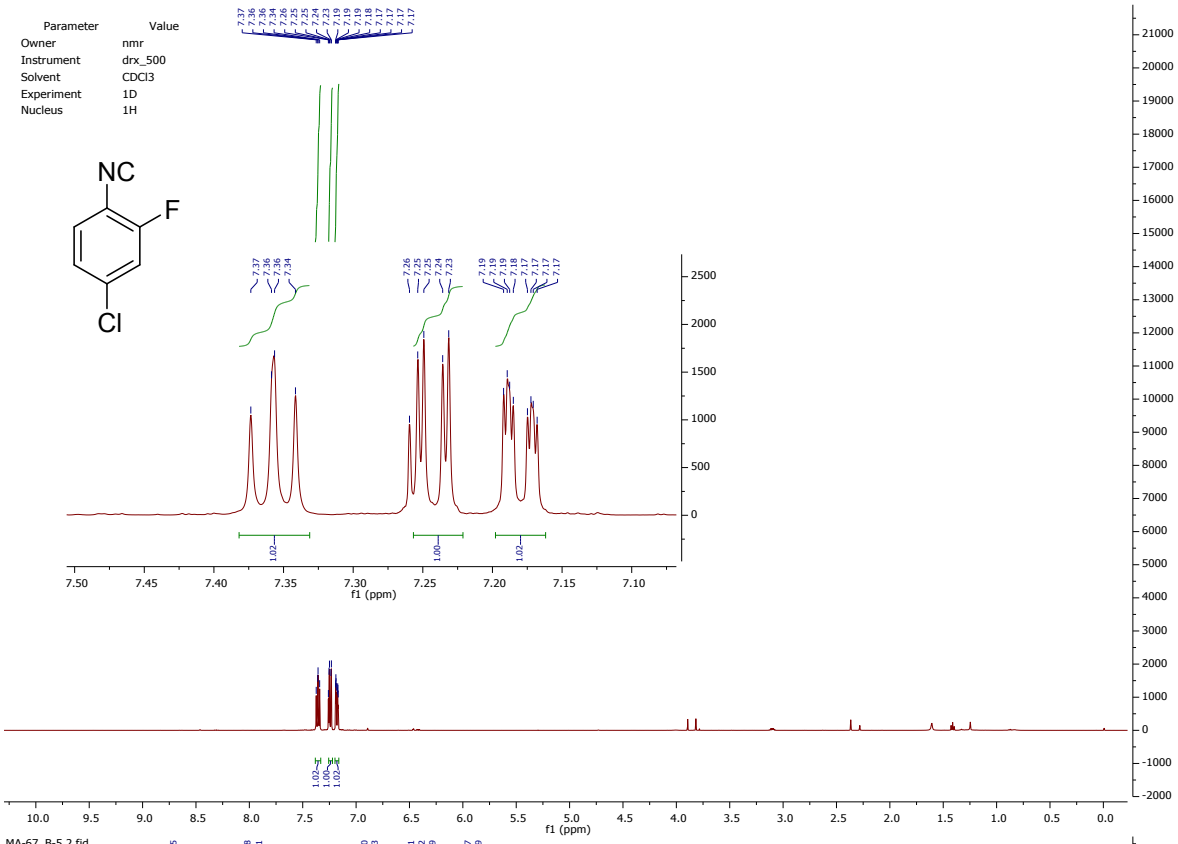


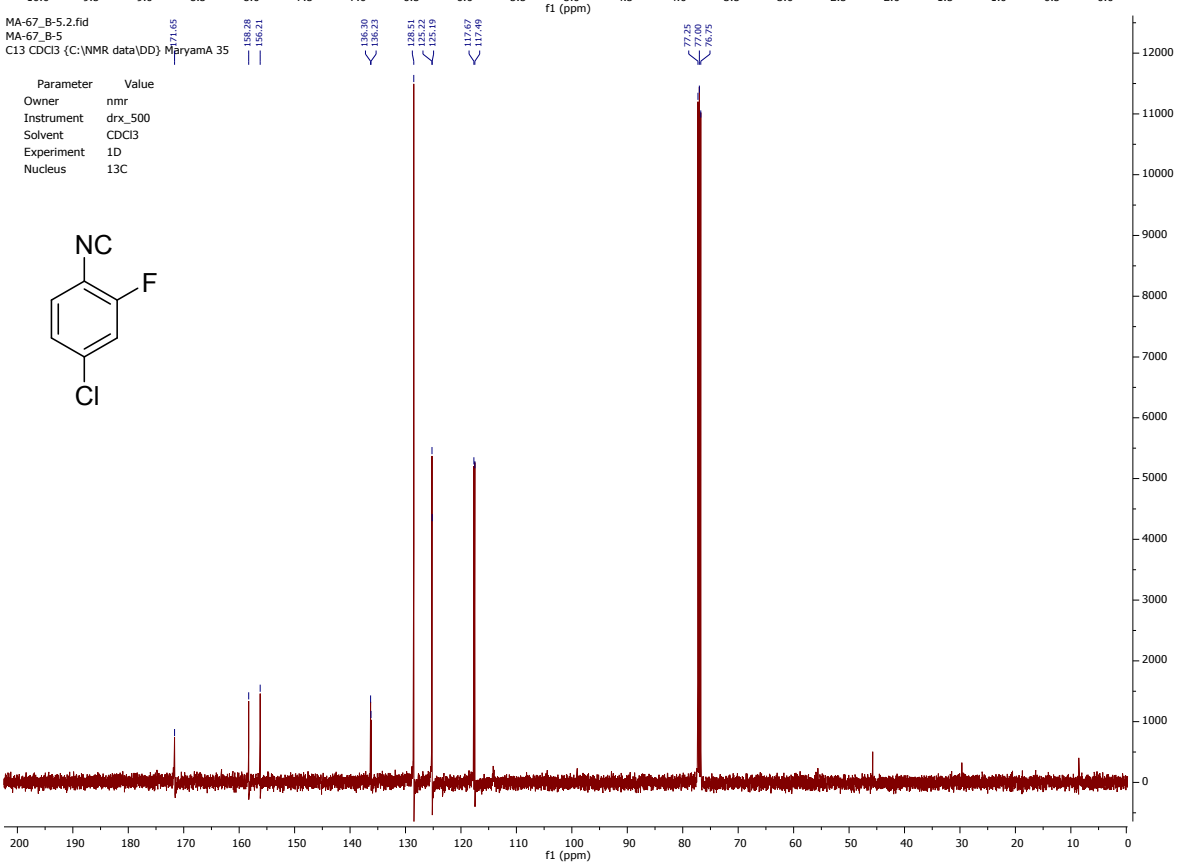
B-4 / I-15: 1-(Isocyanomethyl)-4-(trifluoromethyl)benzene



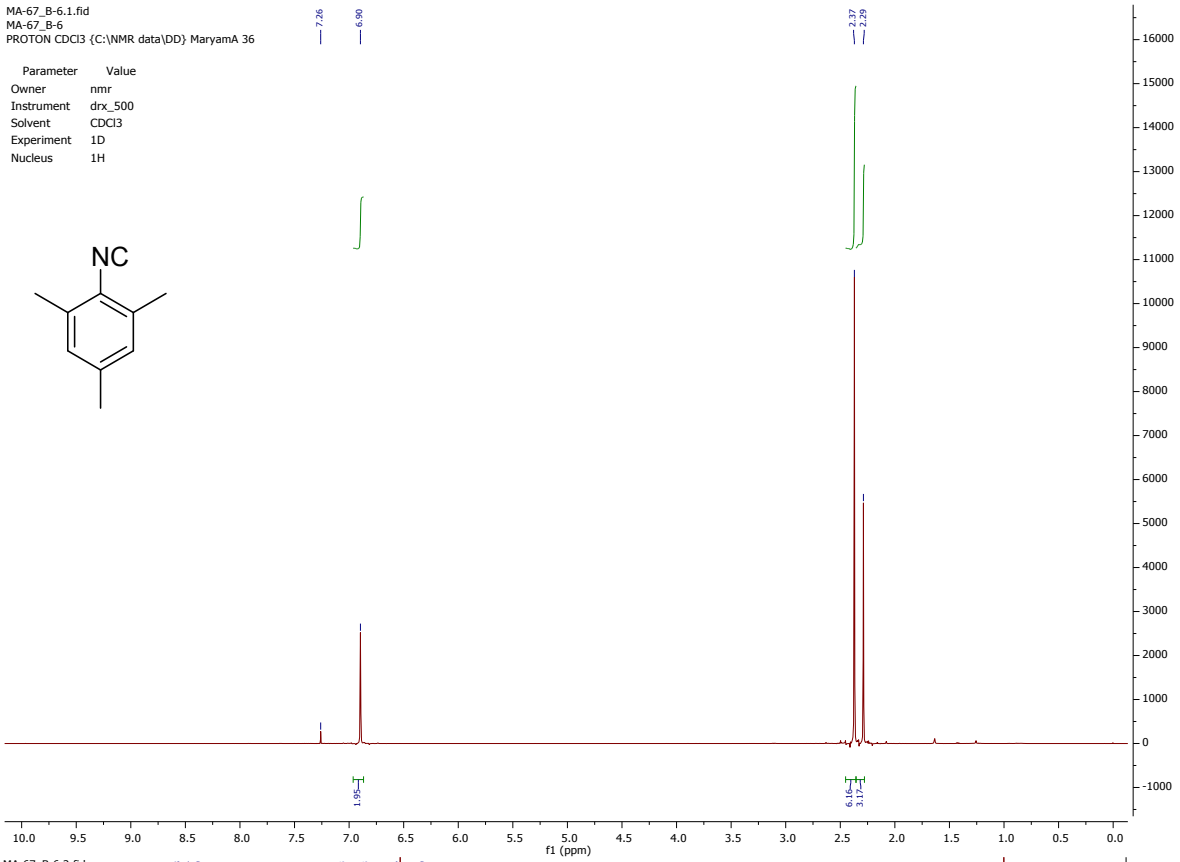


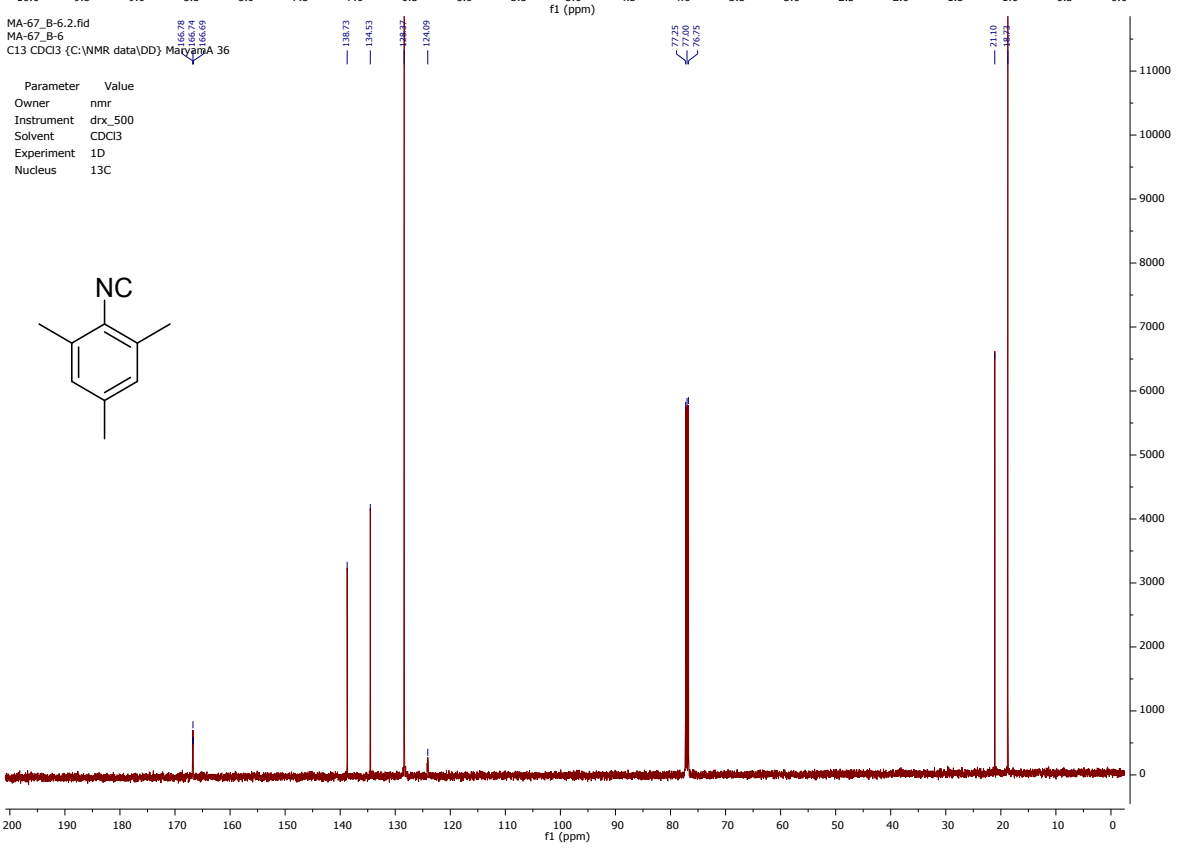
B-5: 4-Chloro-2-fluoro-1-isocyanobenzene



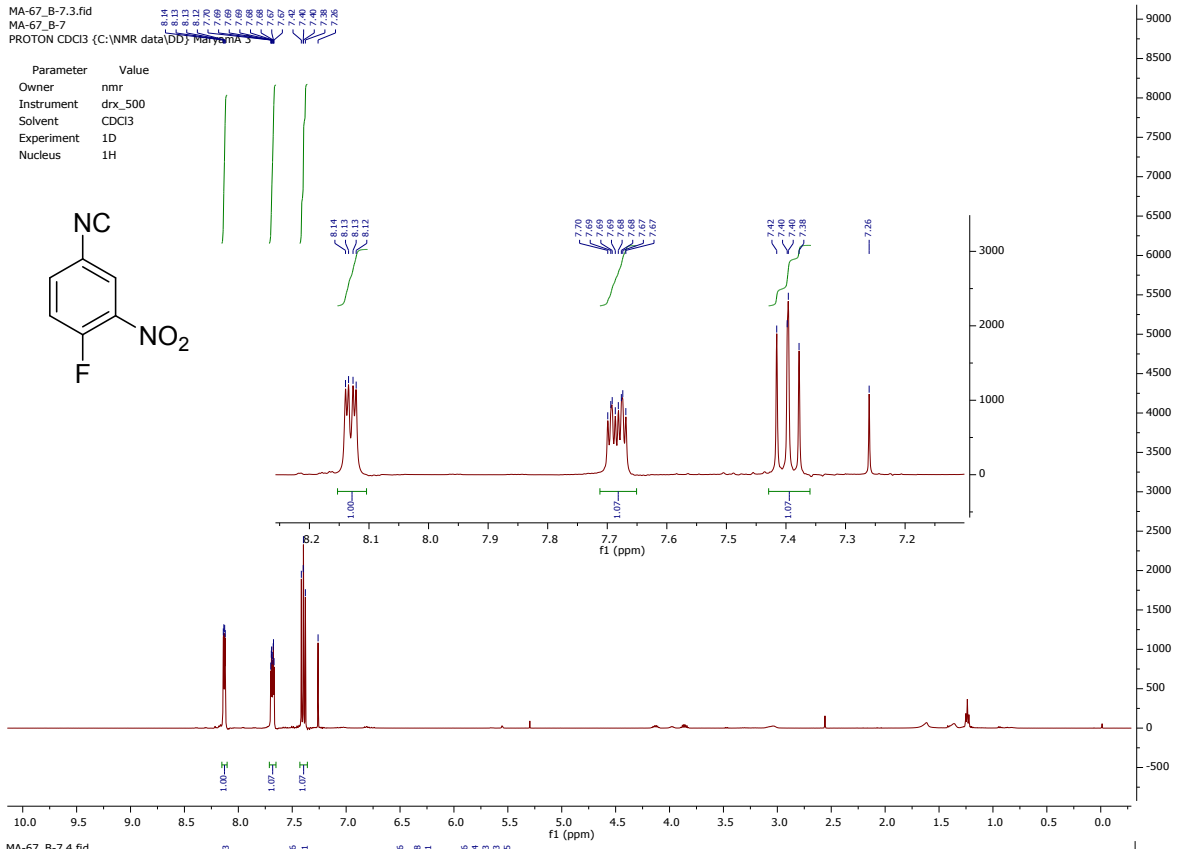


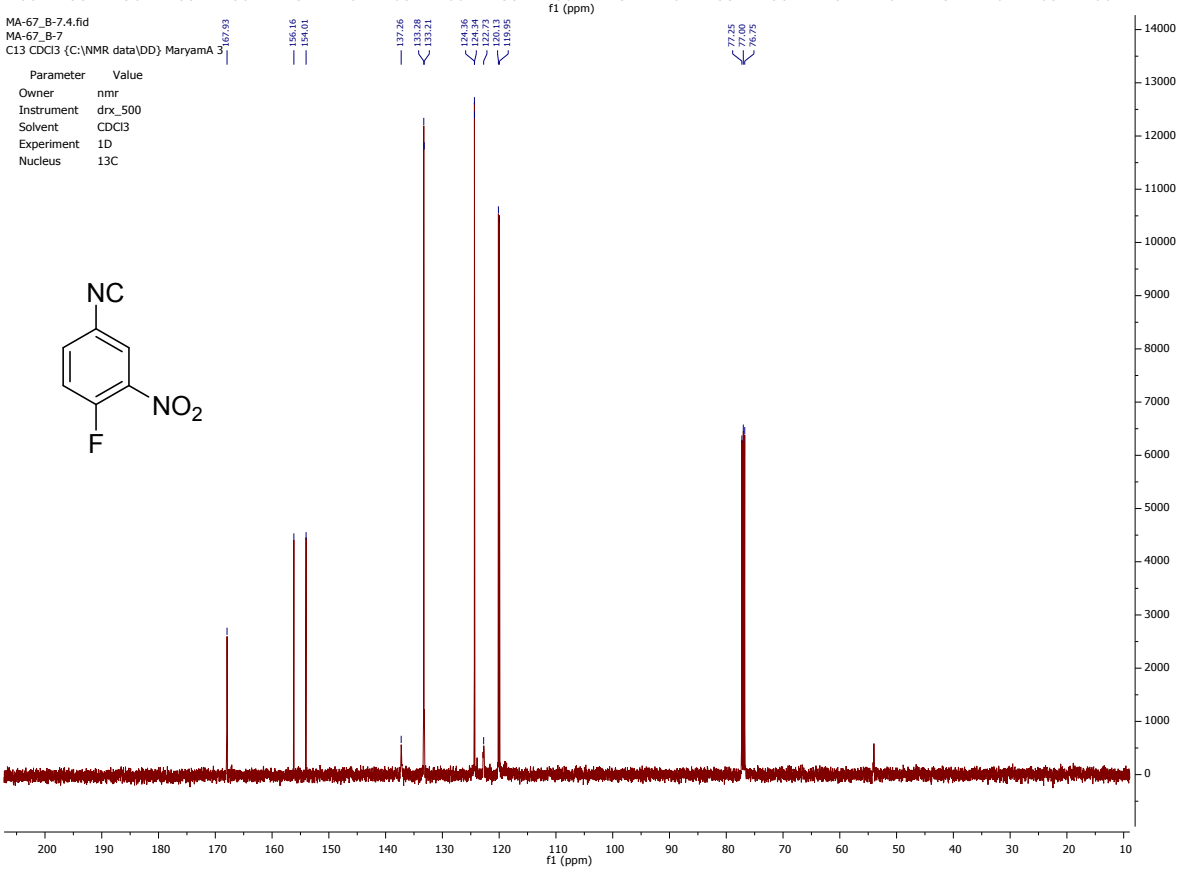
B-6 / I-24: 2-Isocyano-1,3,5-trimethylbenzene



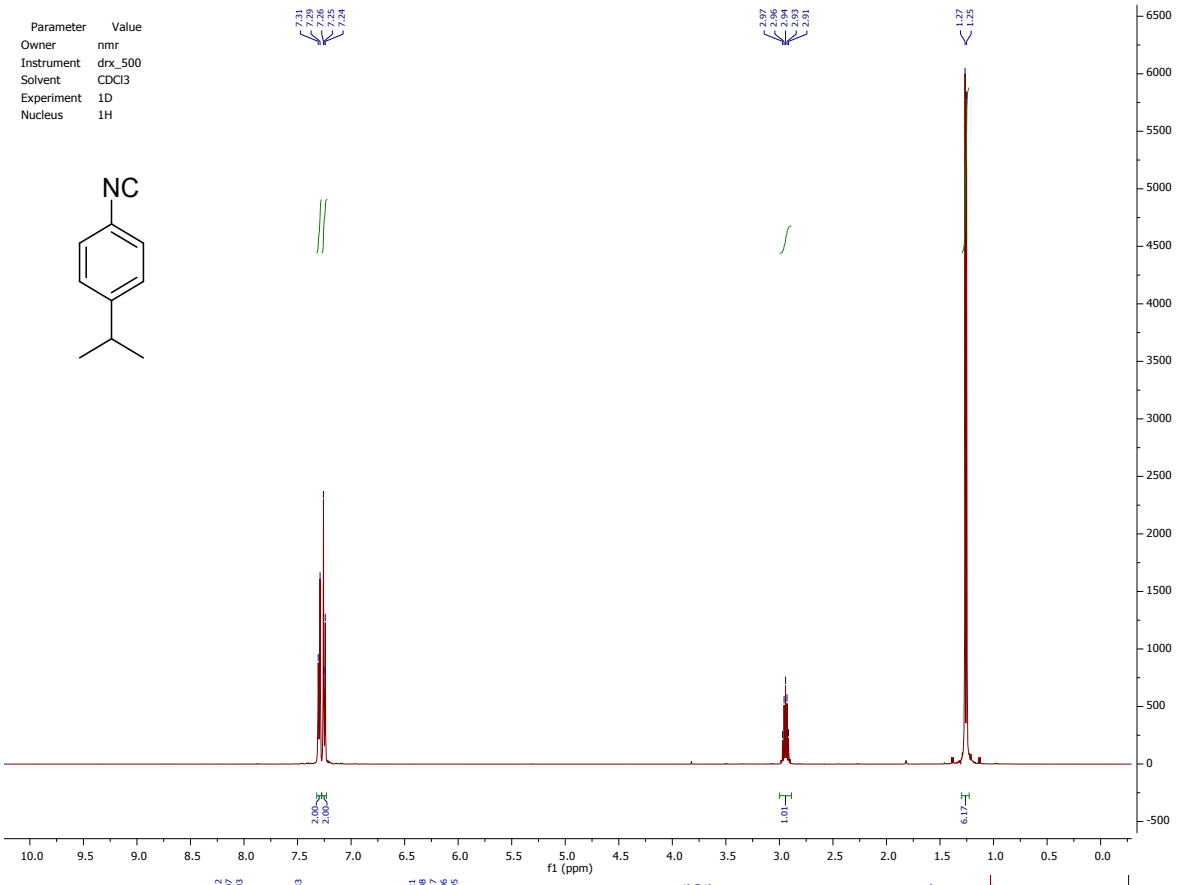


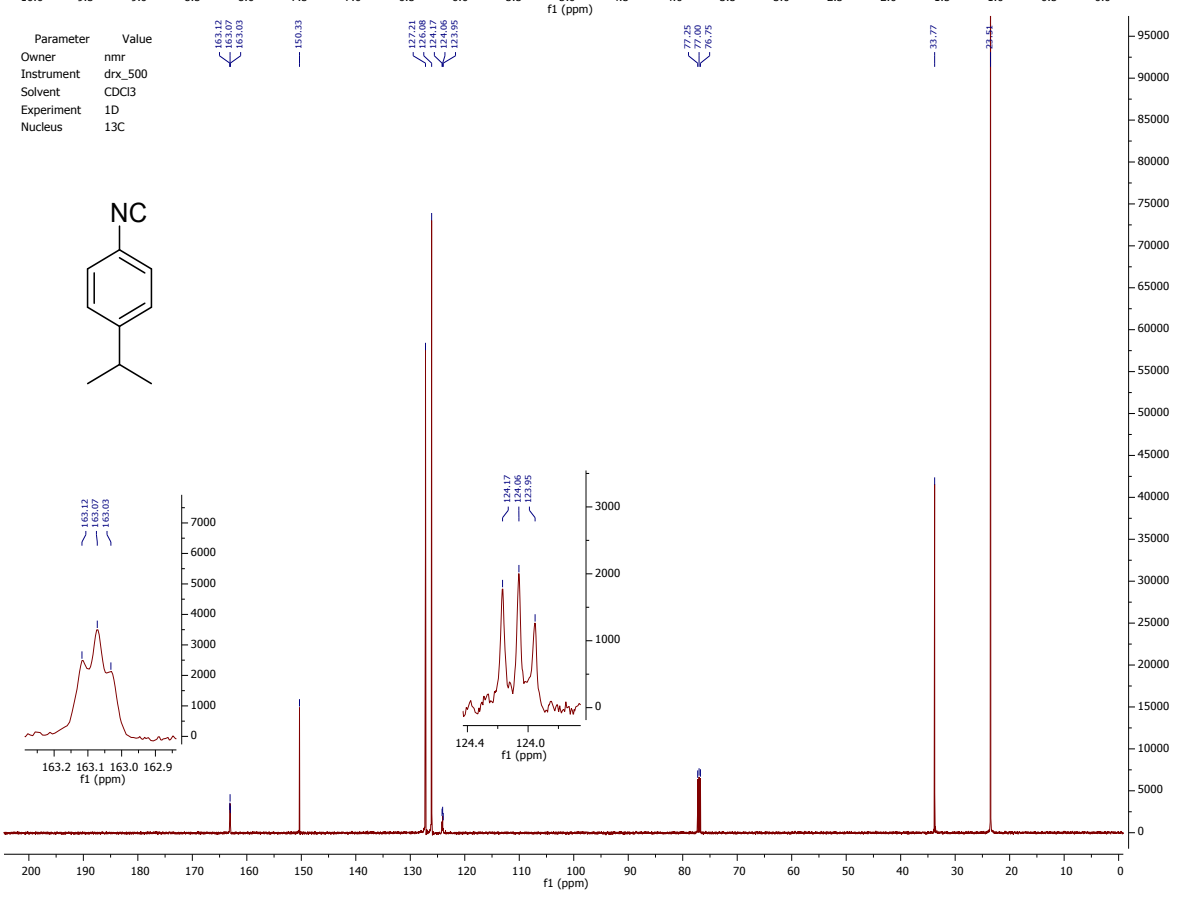
B-7 / I-33: 1-Fluoro-4-isocyano-2-nitrobenzene



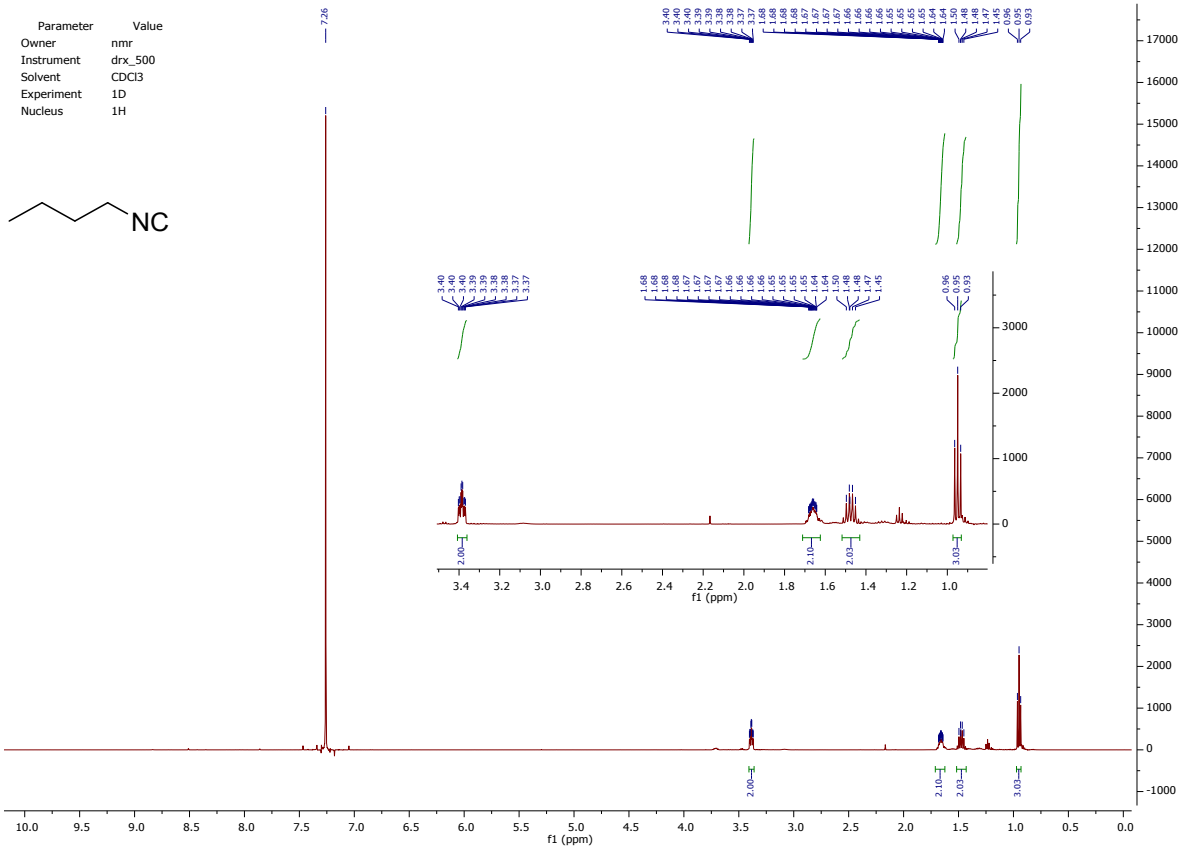


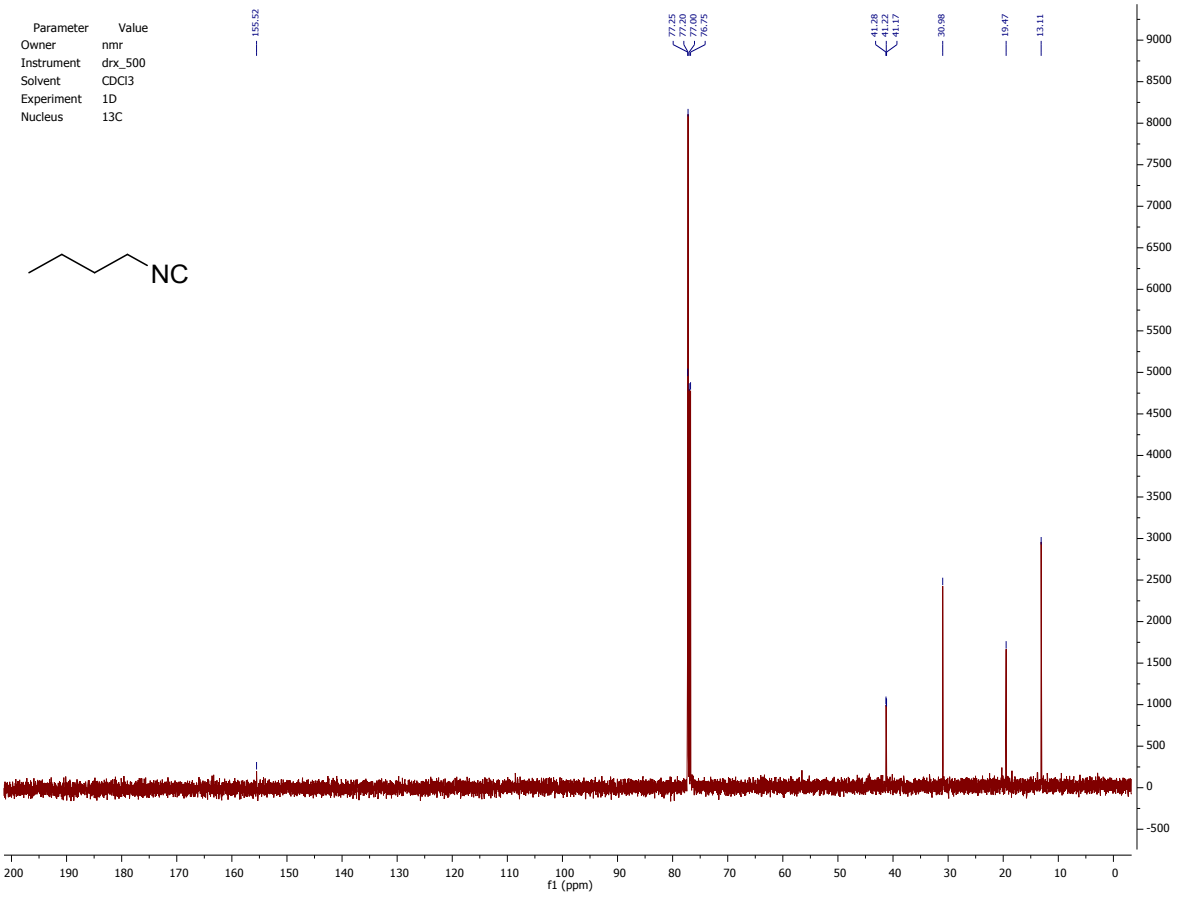
B-8 / I-30: 1-Isocyano-4-isopropylbenzene



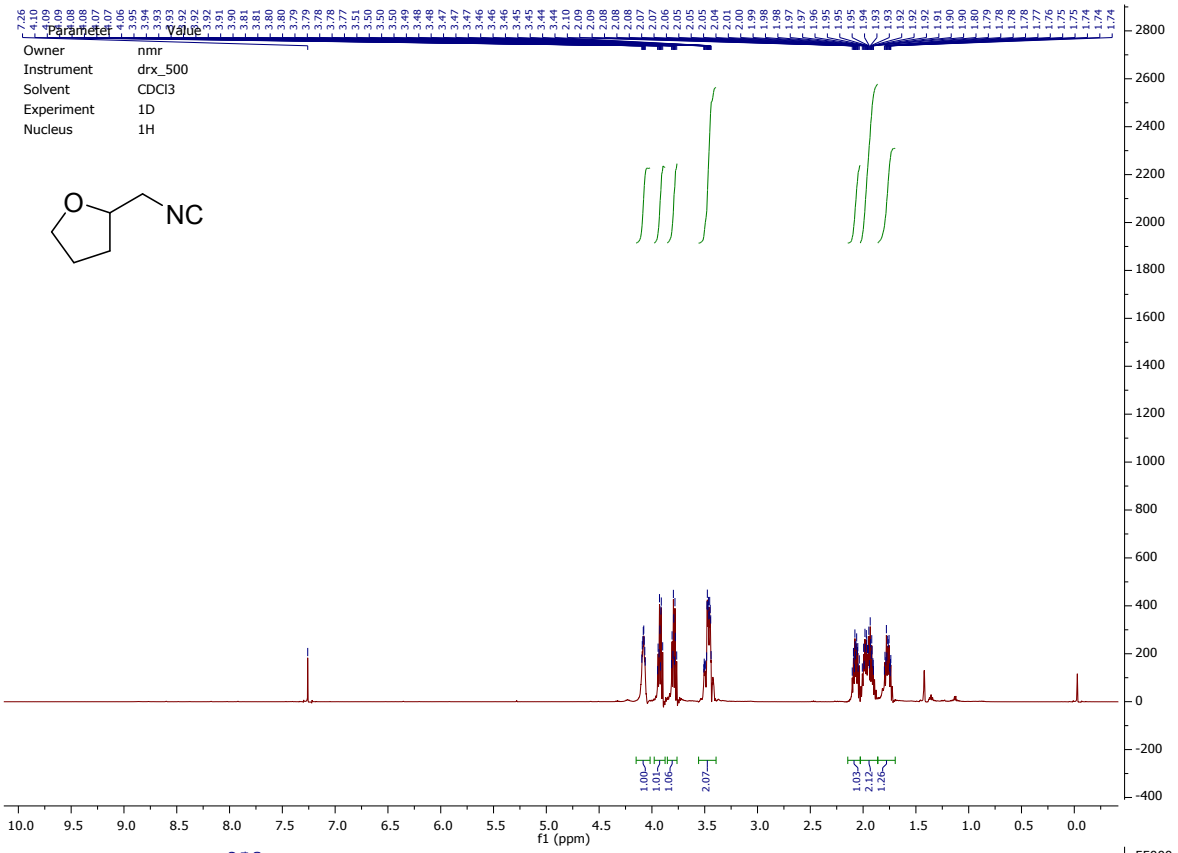


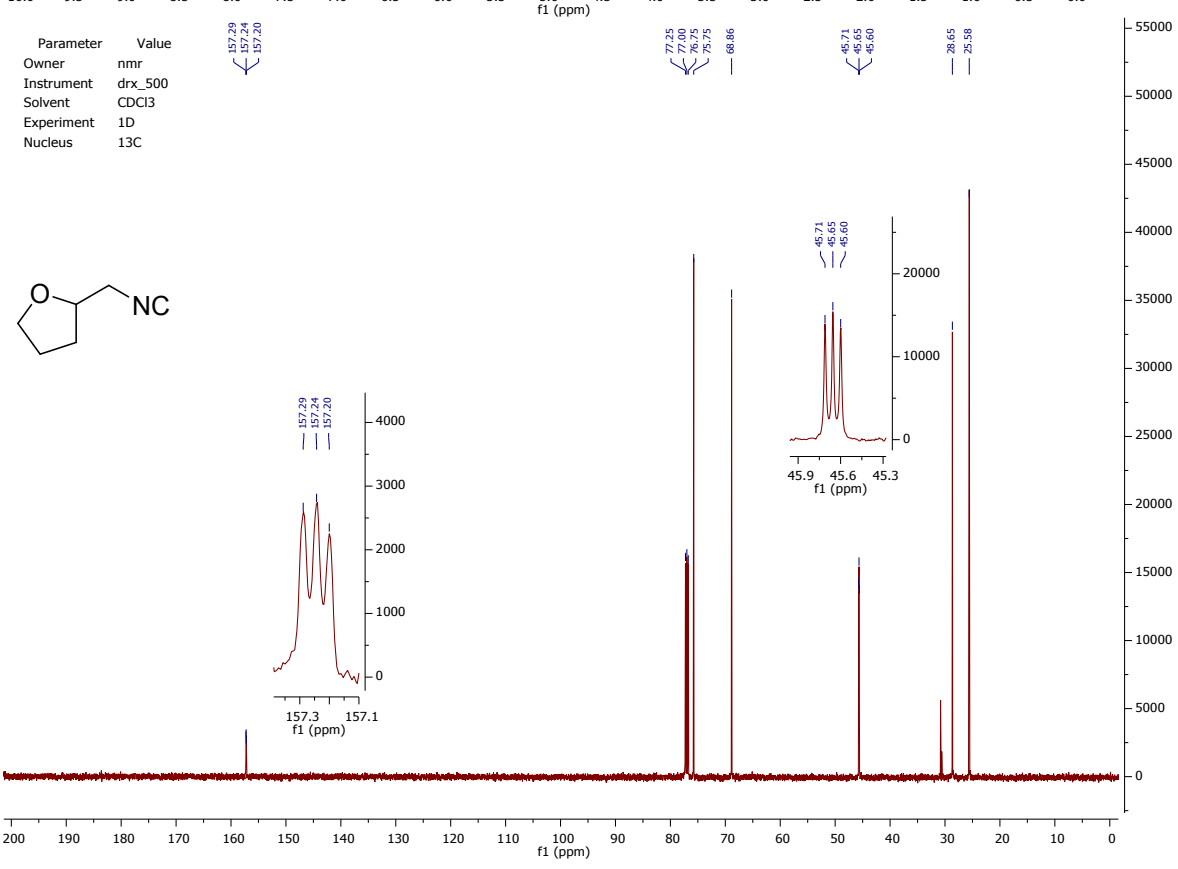
B-9 / I-36: 1-Isocyanobutane



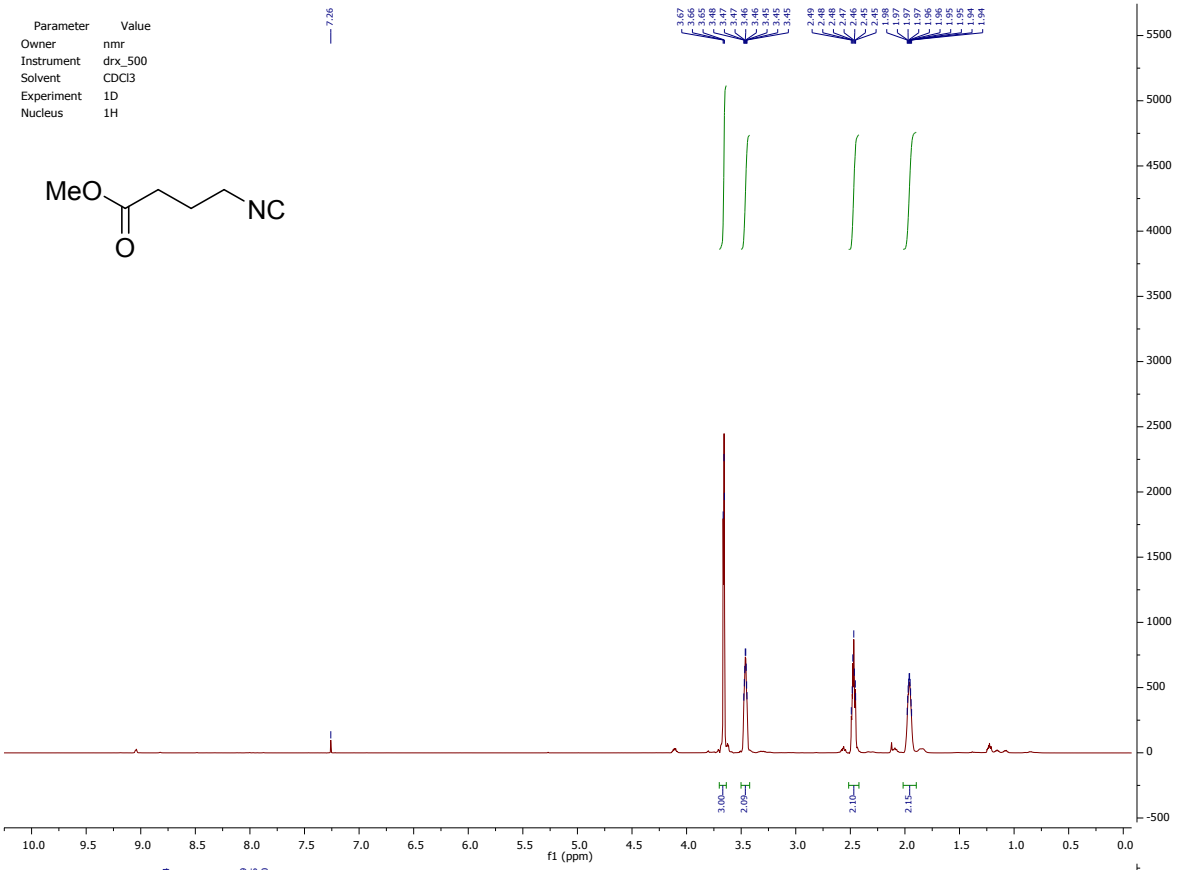


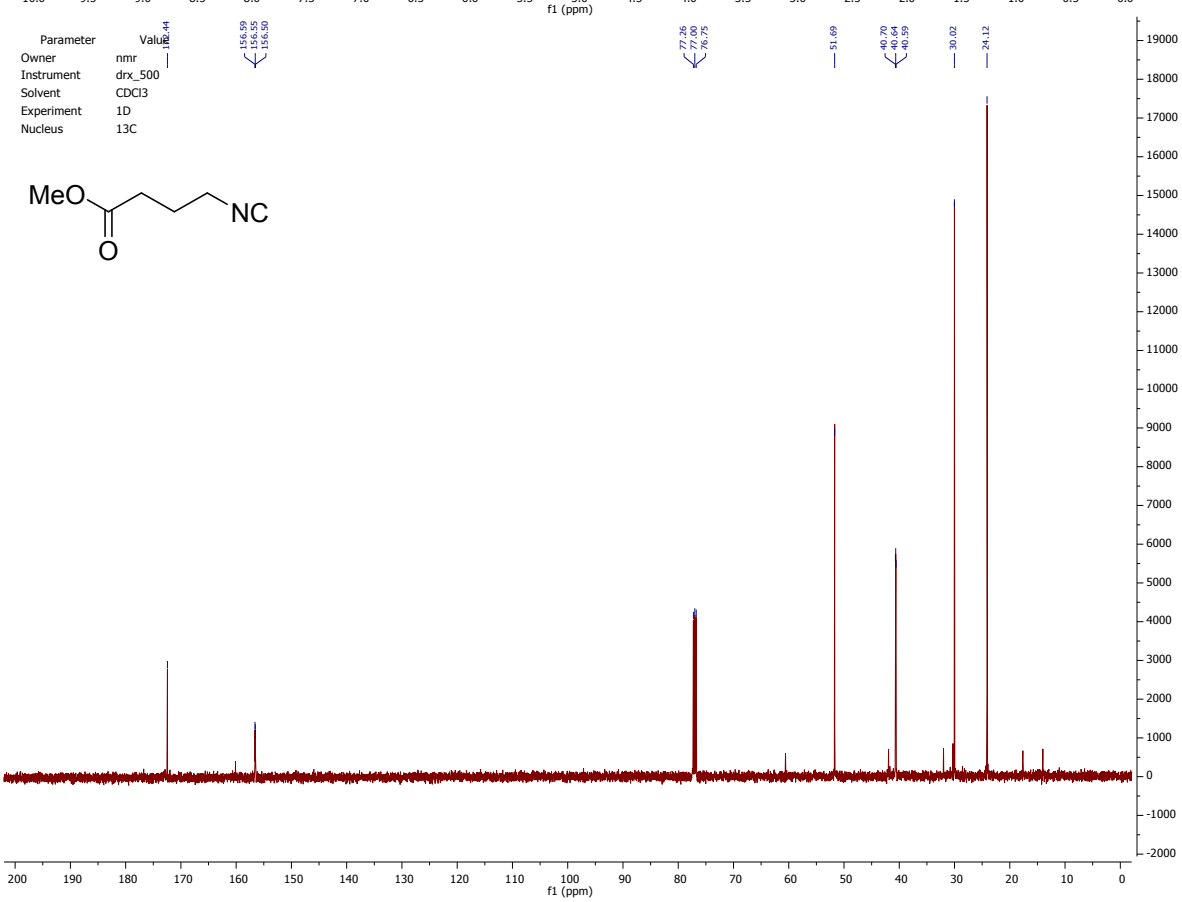
B-10 / I-44: 2-(Isocyanomethyl)tetrahydrofuran



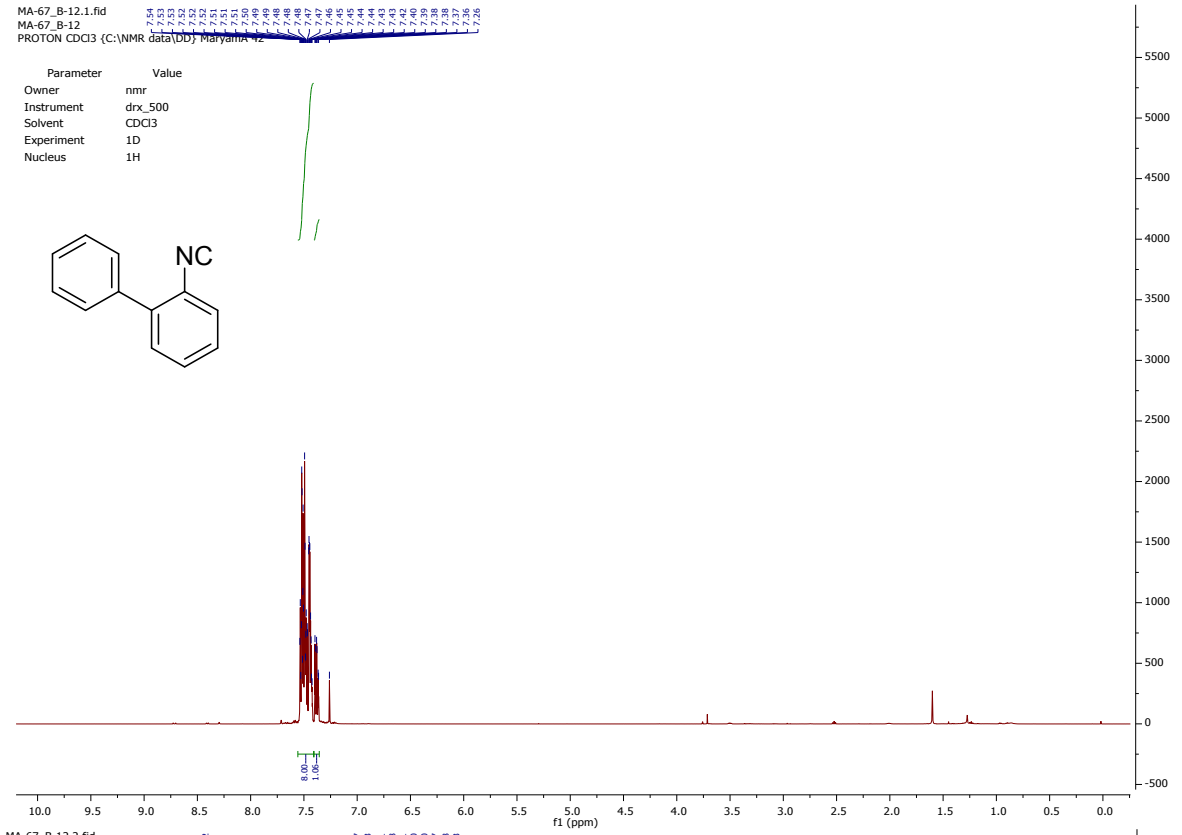


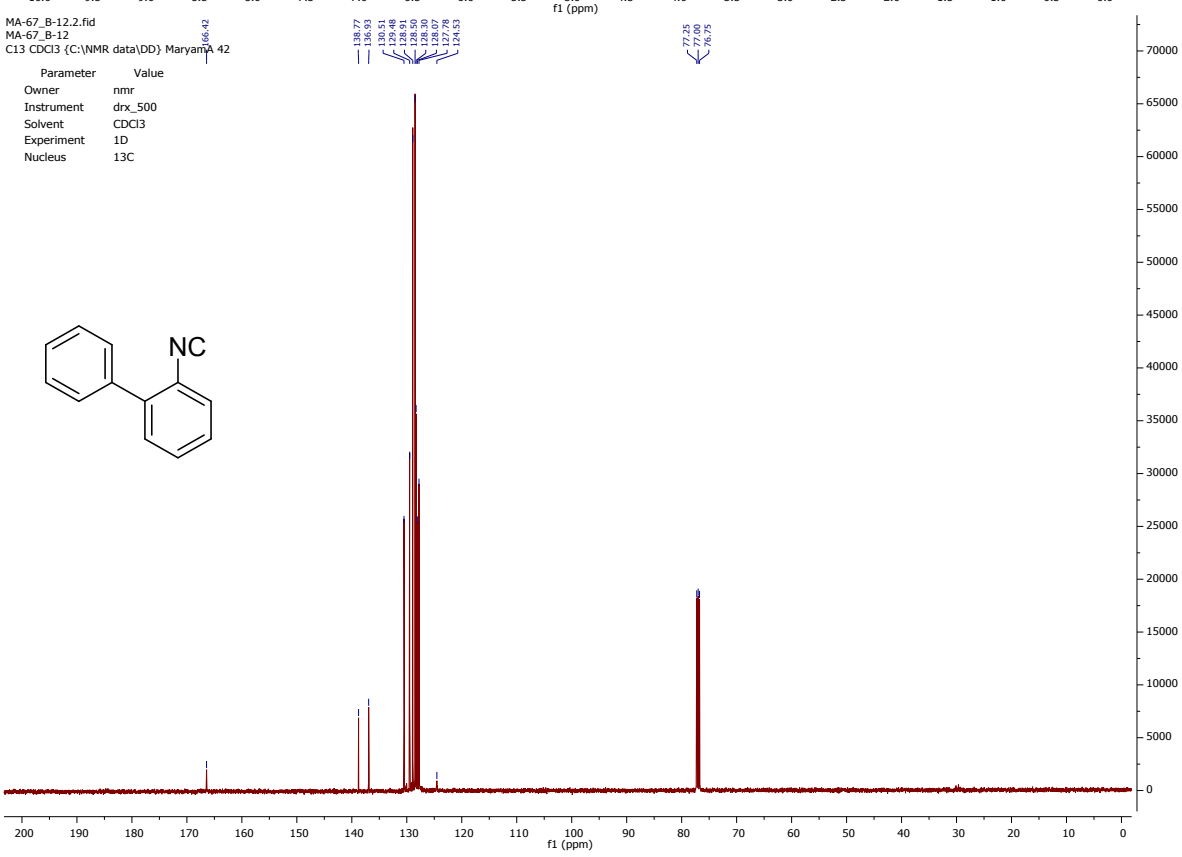
B-11: Methyl 4-isocyanobutanoate



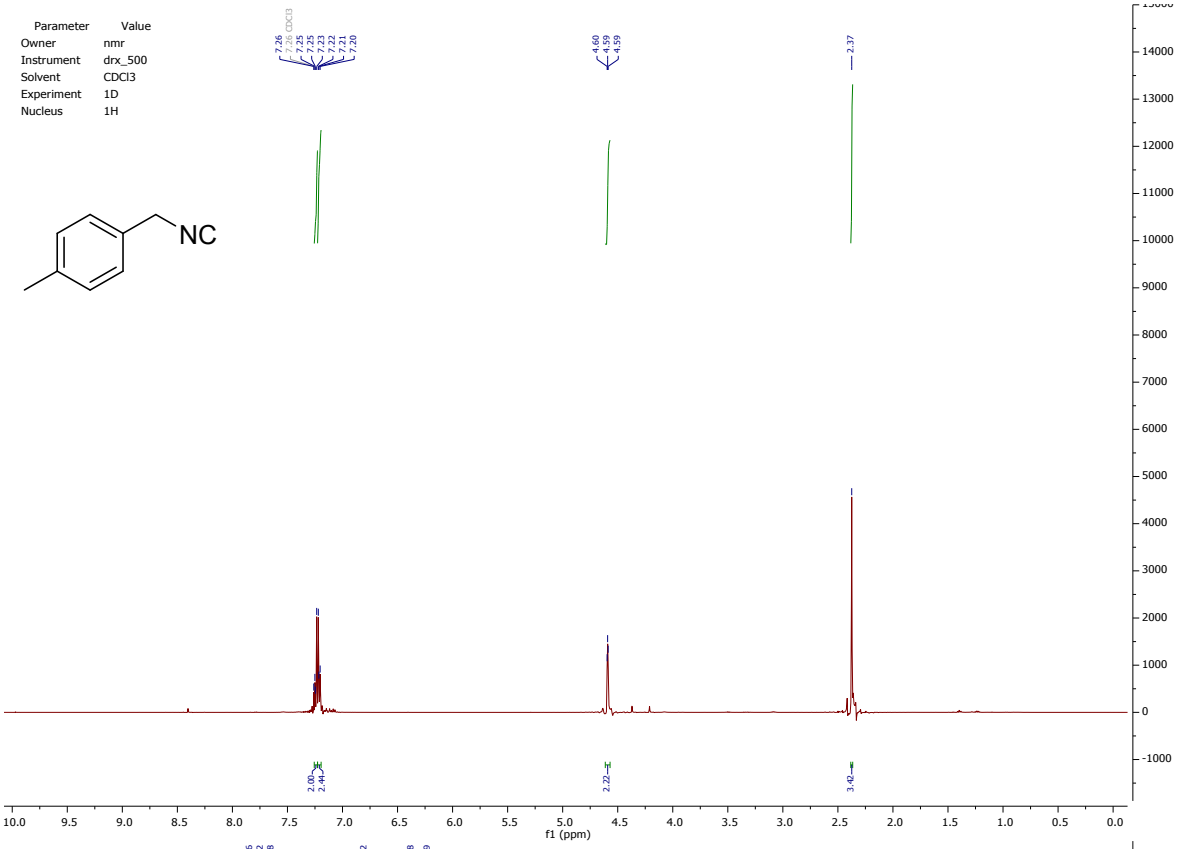


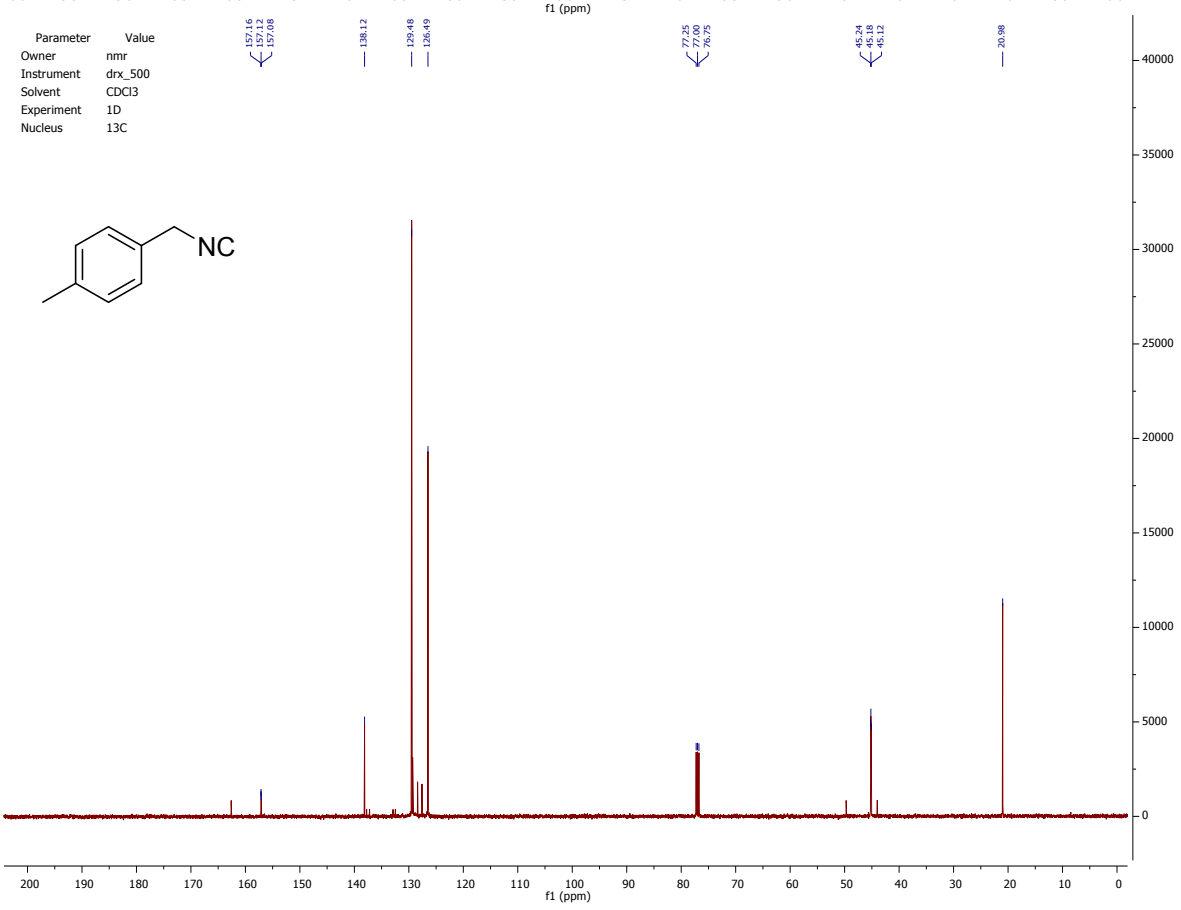
B-12: 2-Isocyano-1,1'-biphenyl



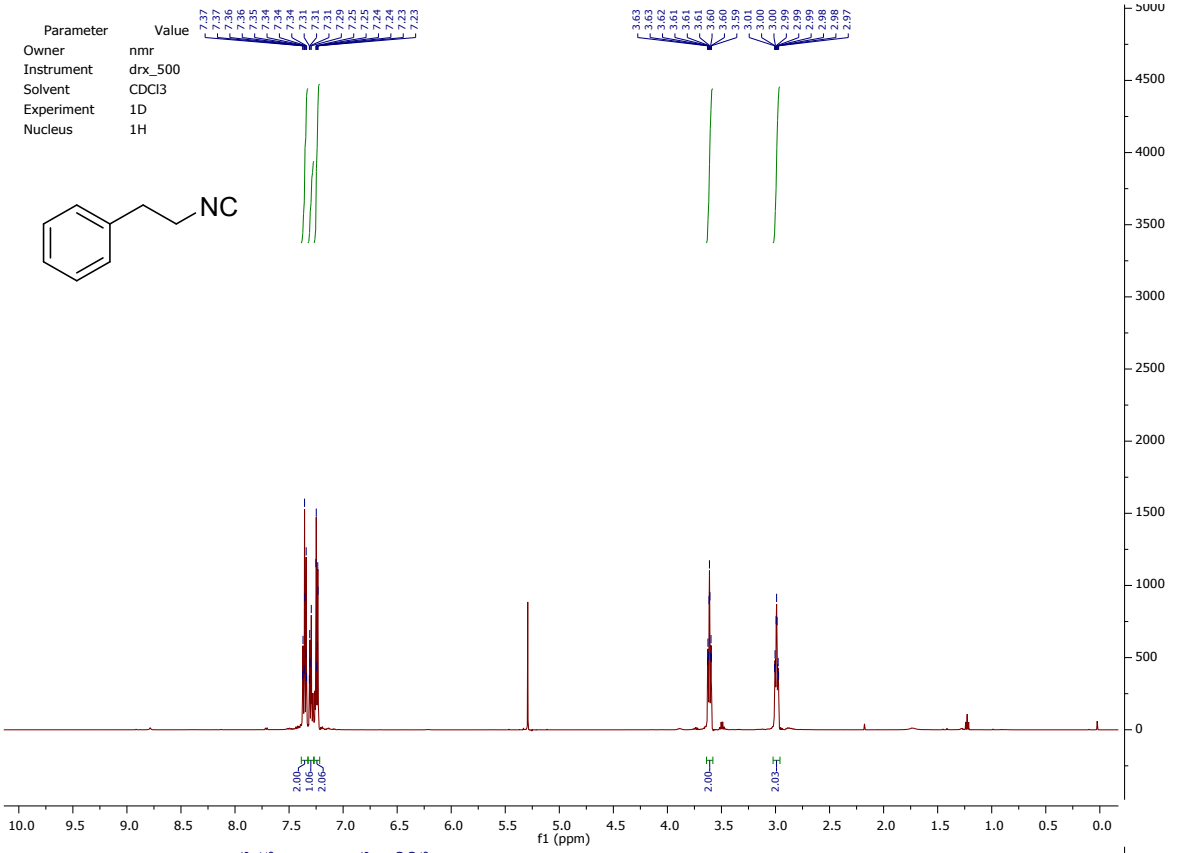


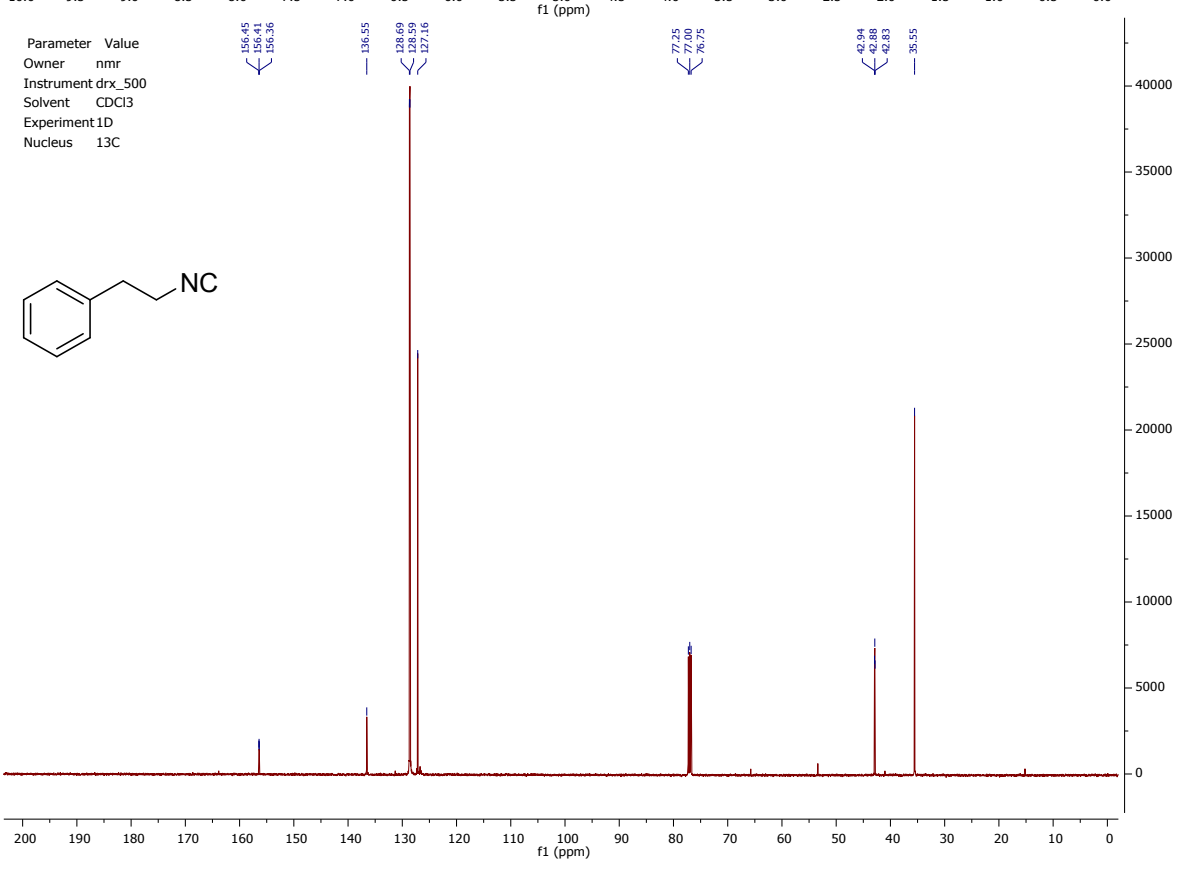
C-1 / I-2: 1-(Isocyanomethyl)-4-methylbenzene



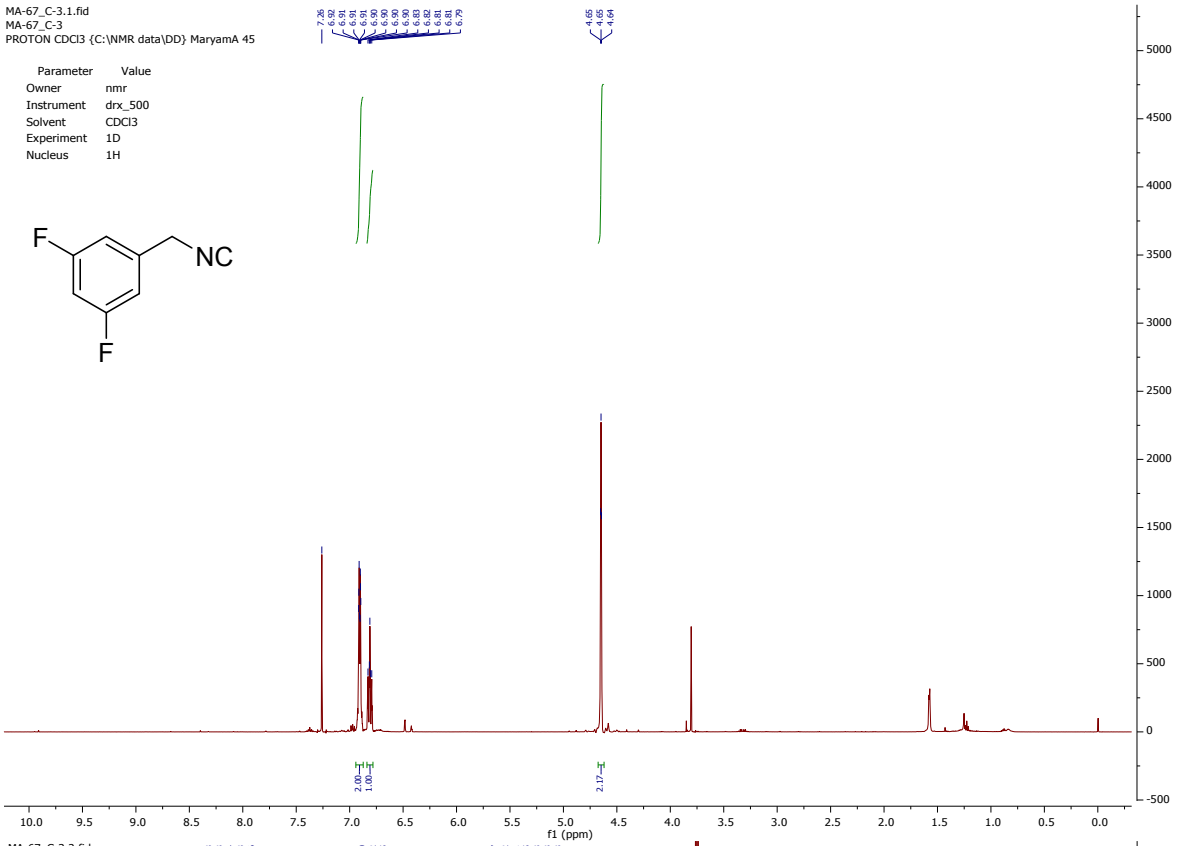


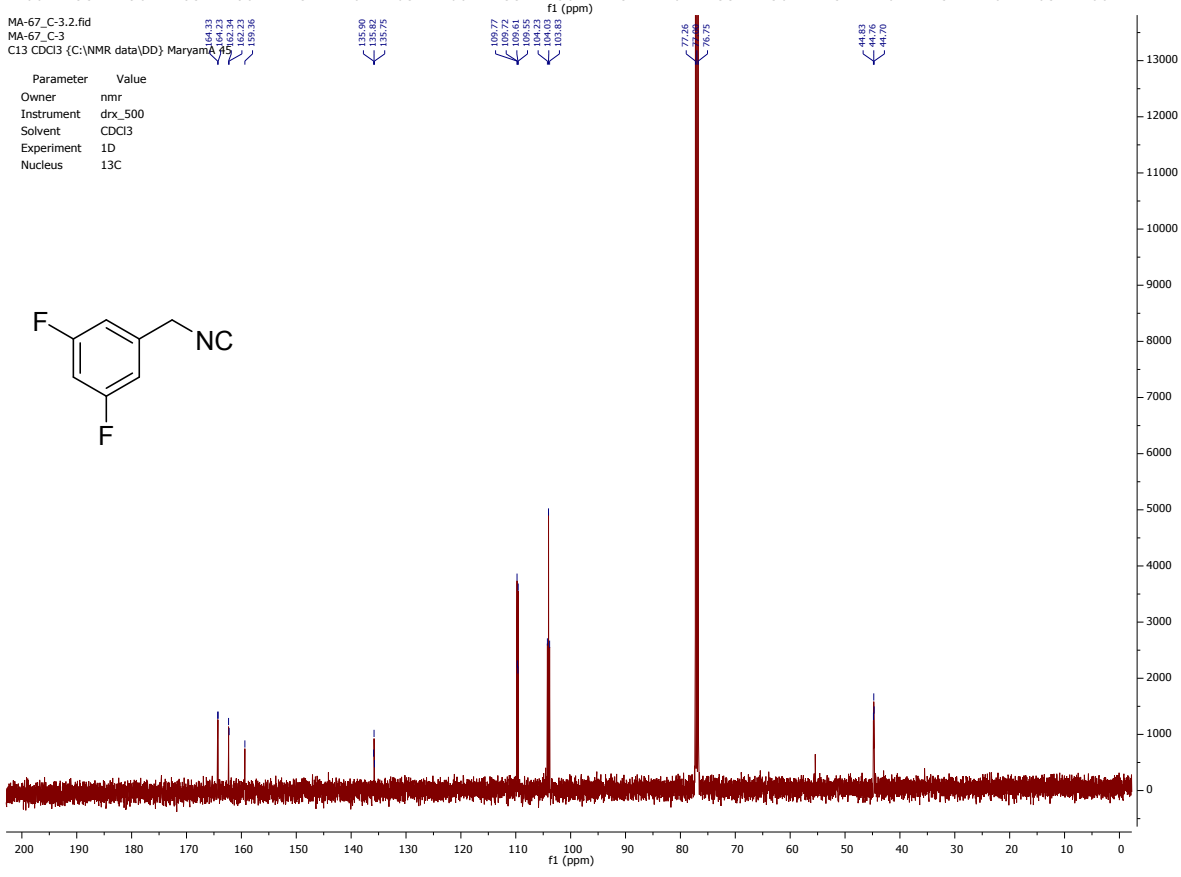
C-2: (2-Isocyanoethyl)benzene



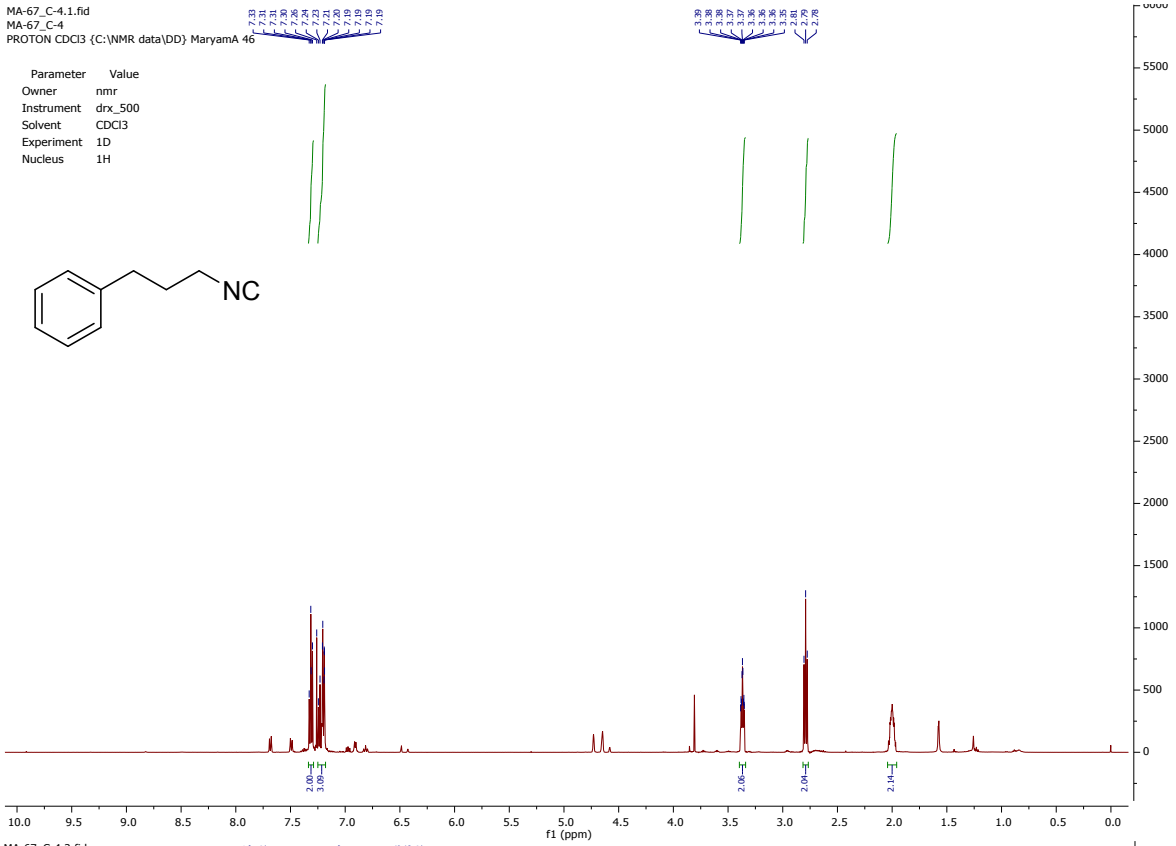


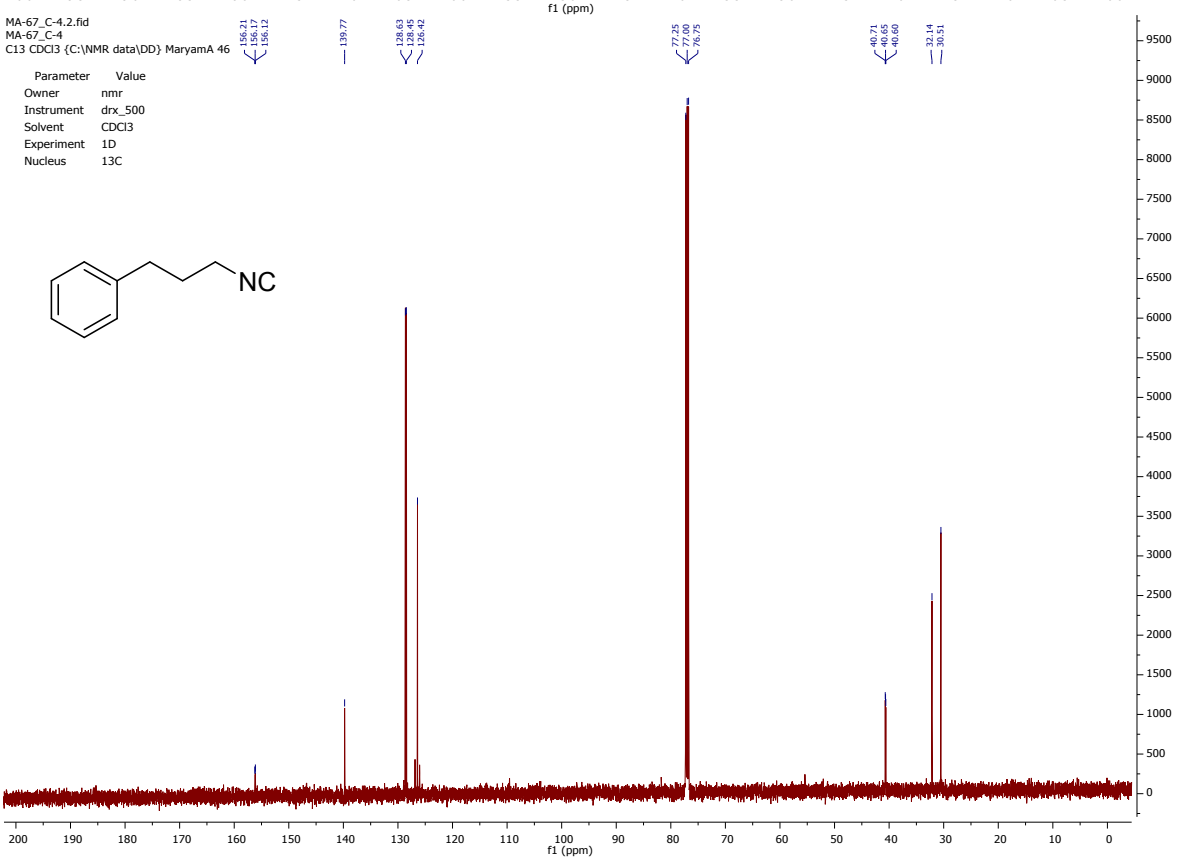
C-3: 1,3-Difluoro-5-(isocyanomethyl)benzene



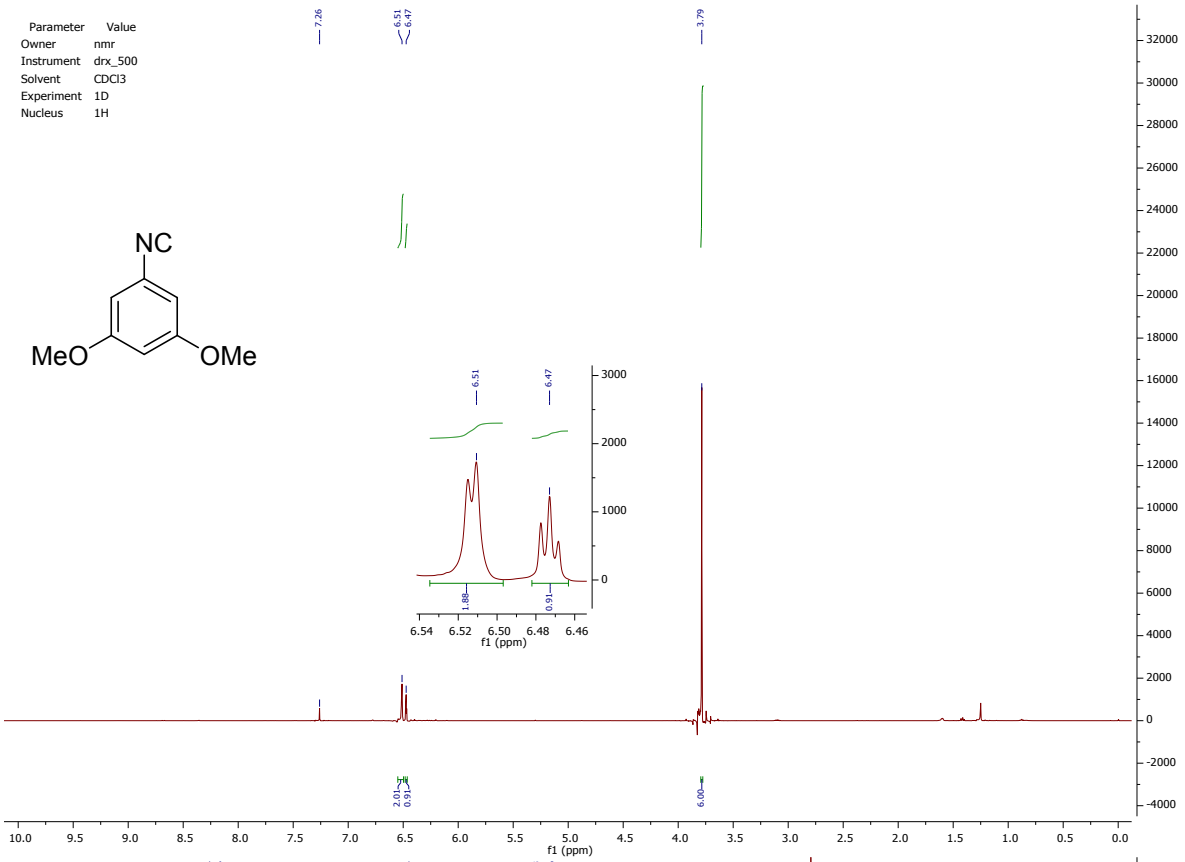


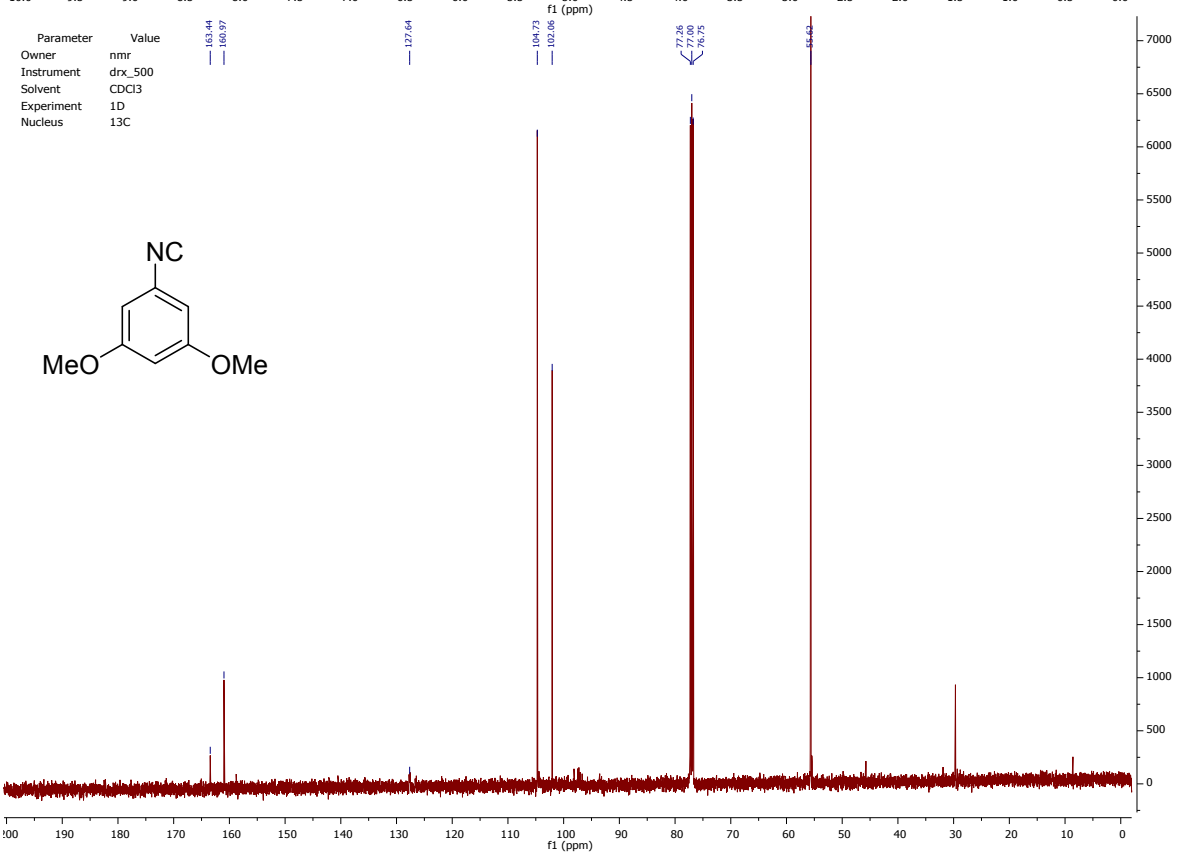
C-4 / I-16: (3-Isocyanopropyl)benzene



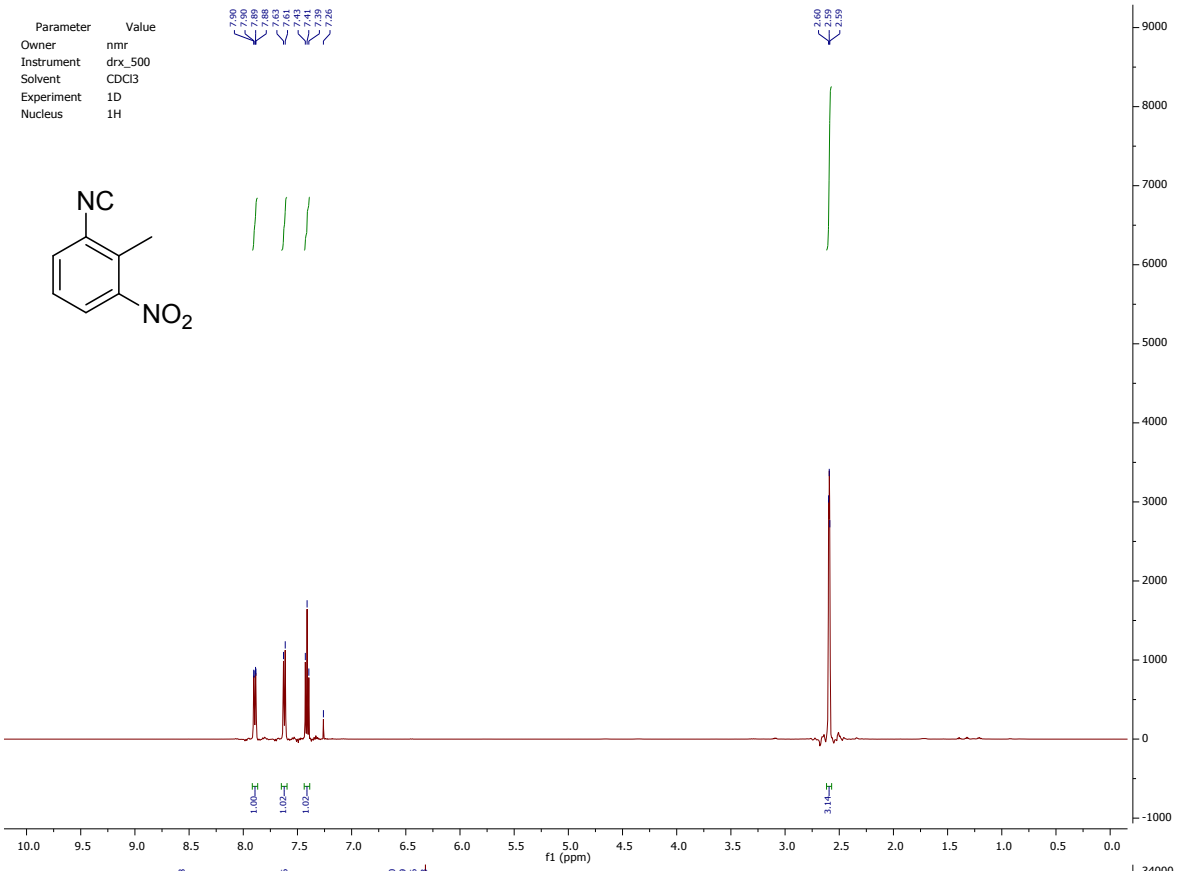


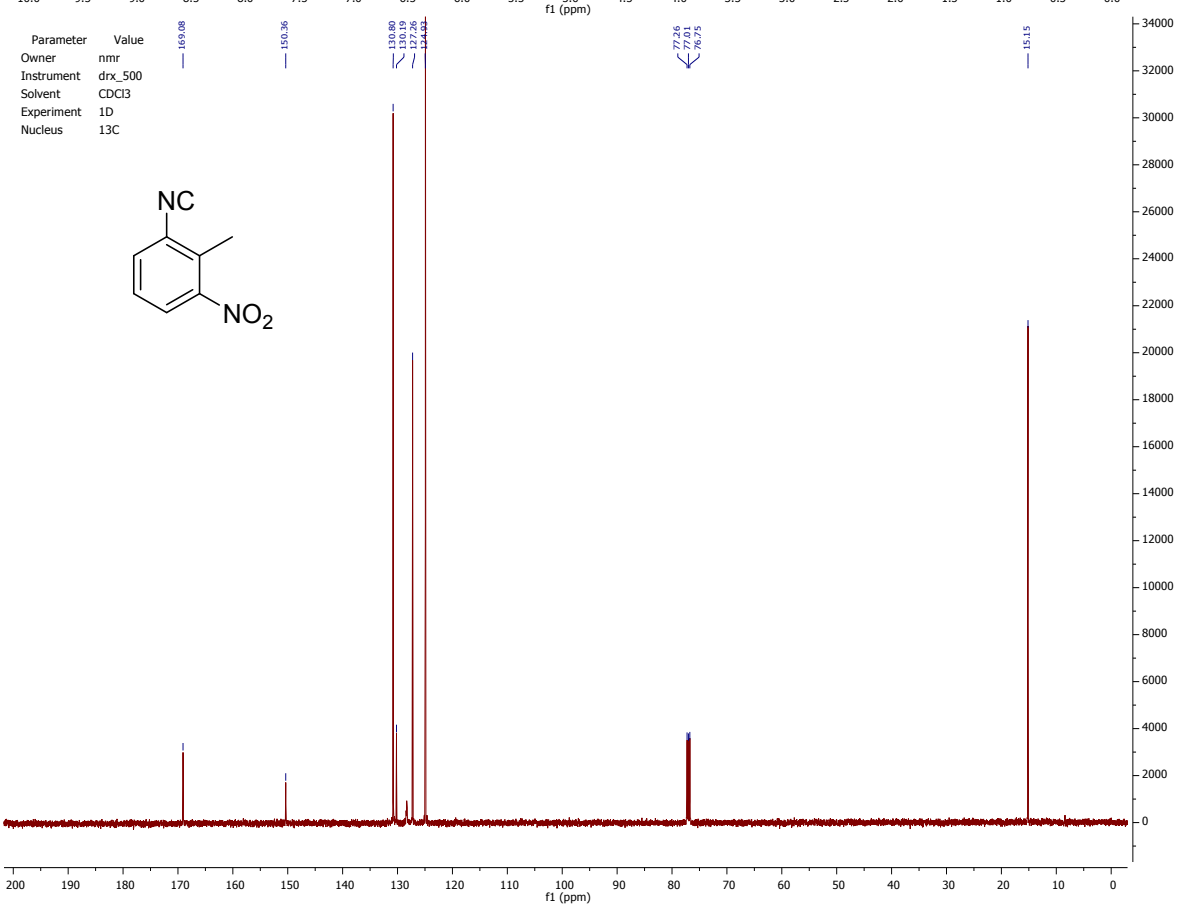
C-5 / I-21: 1-Isocyano-3,5-dimethoxybenzene



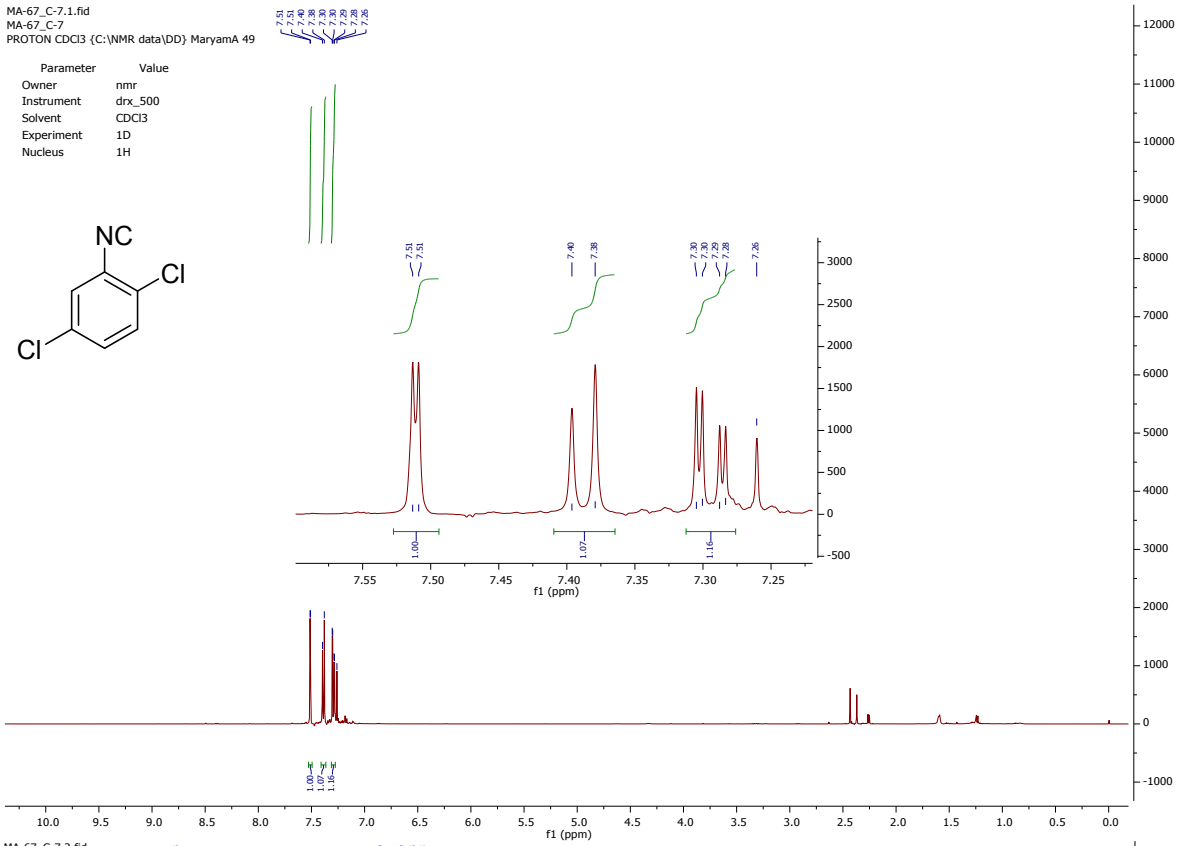


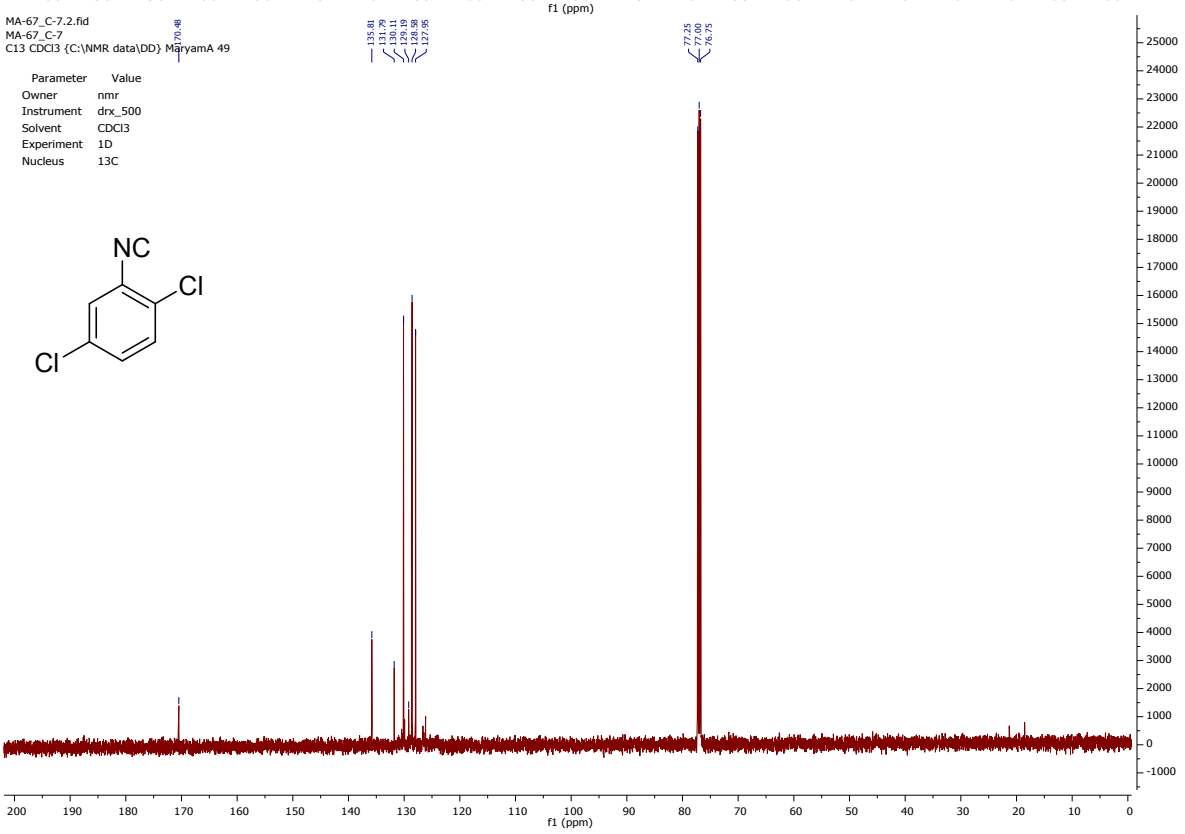
C-6 / I-25: 1-Isocyano-2-methyl-3-nitrobenzene



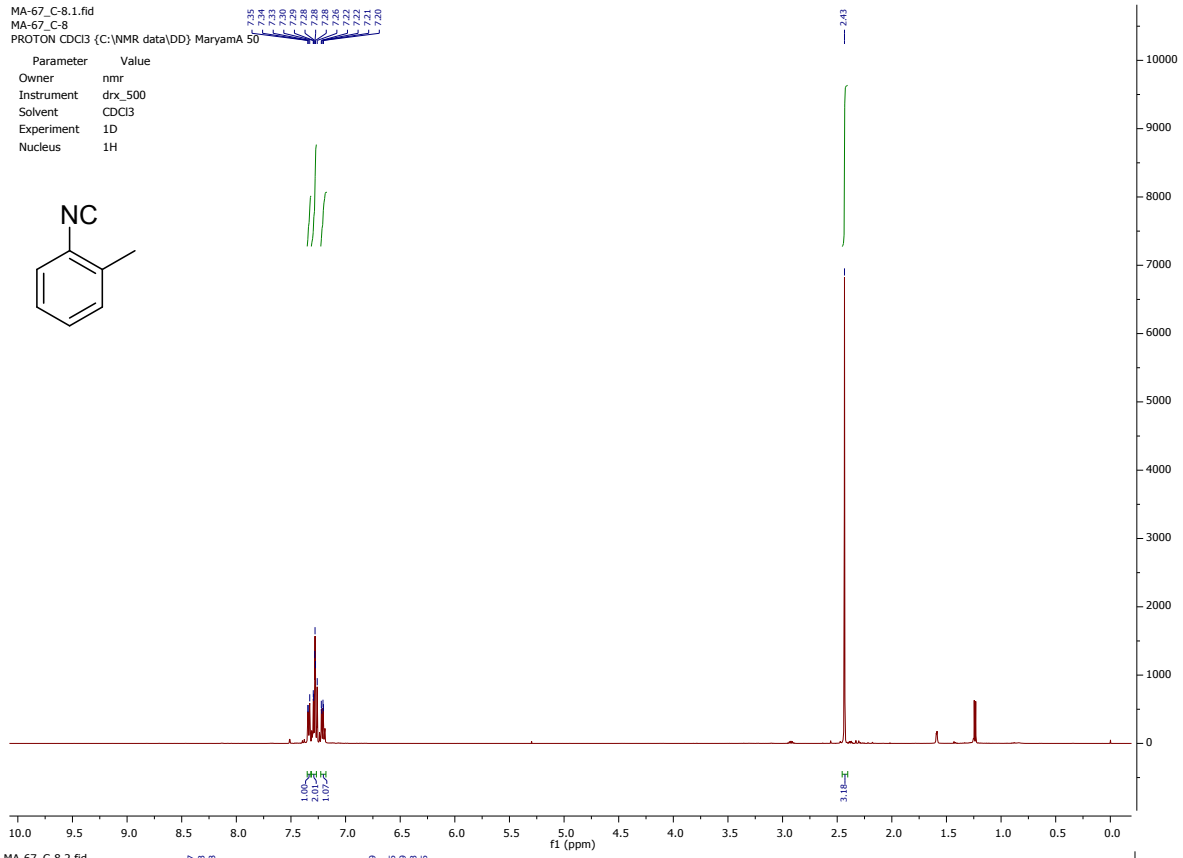


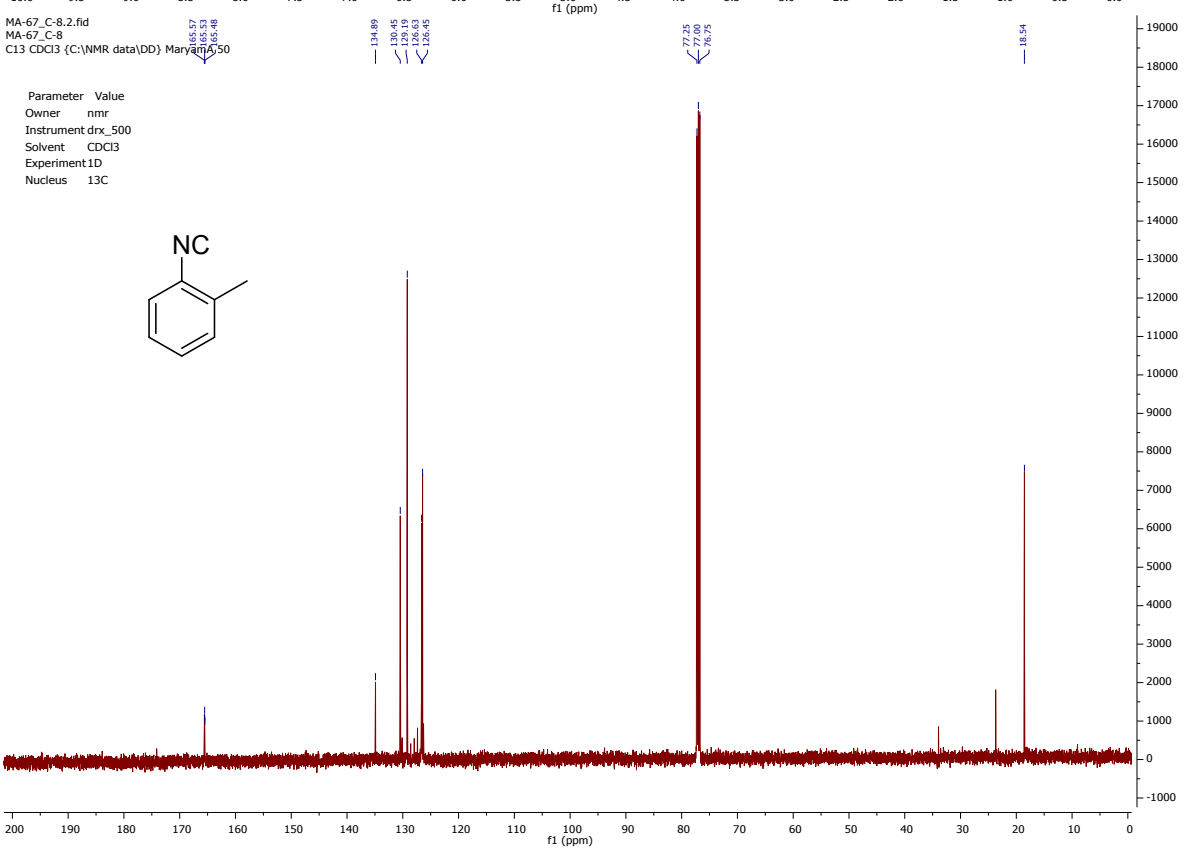
C-7: 1,4-Dichloro-2-isocyanobenzene



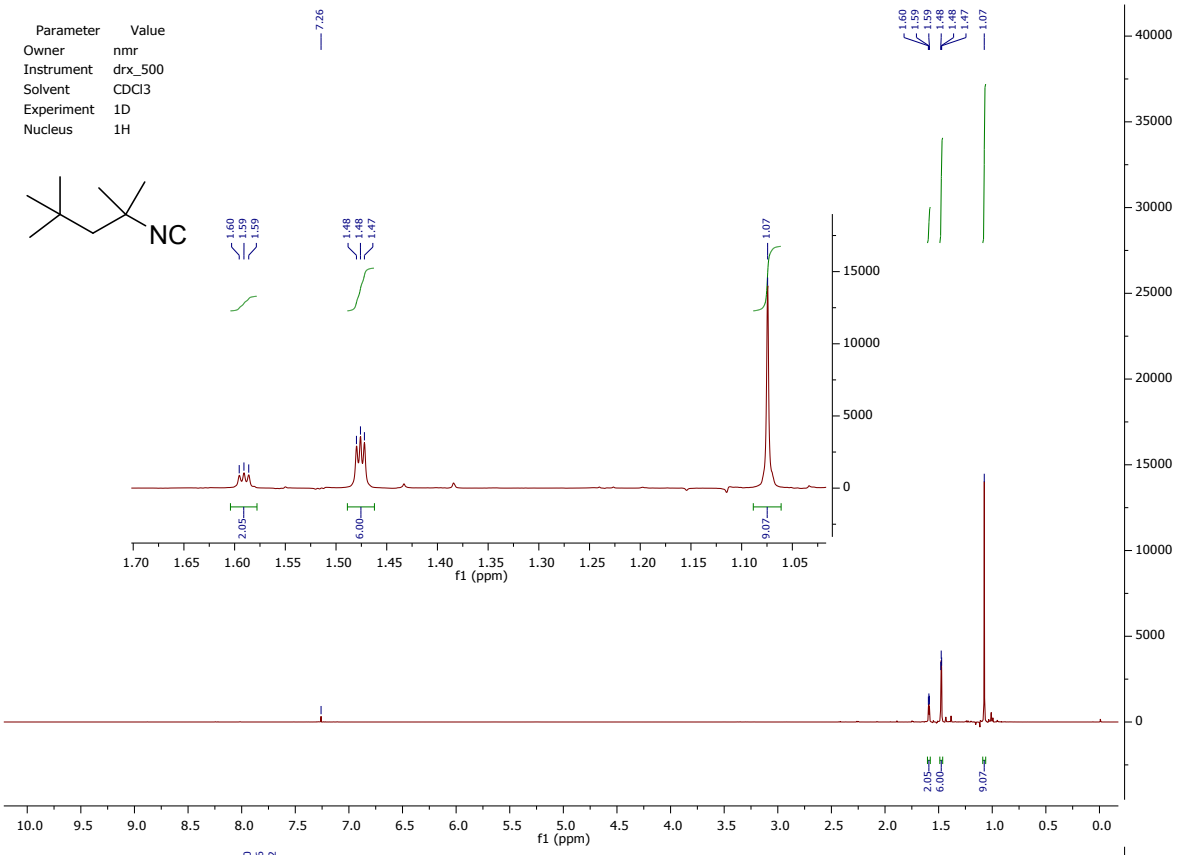


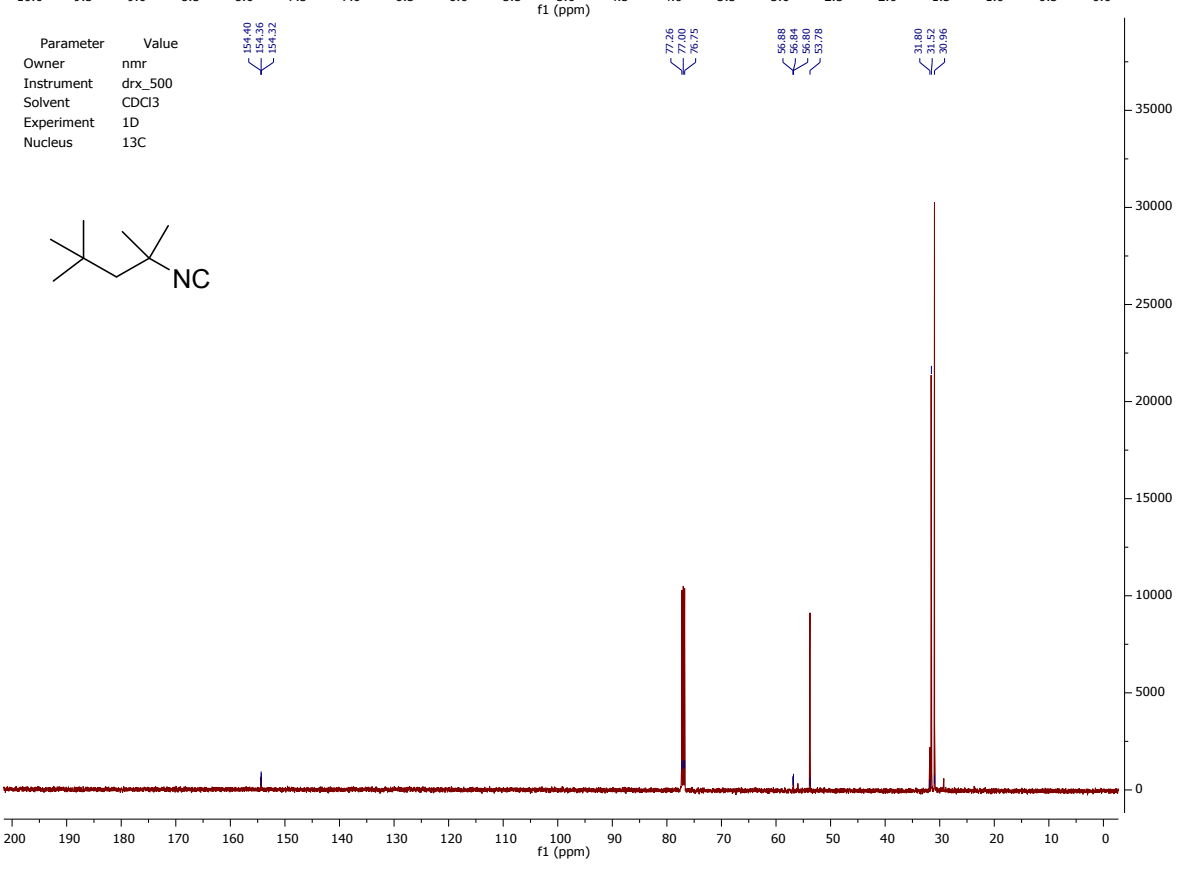
C-8: 1-Isocyano-2-methylbenzene



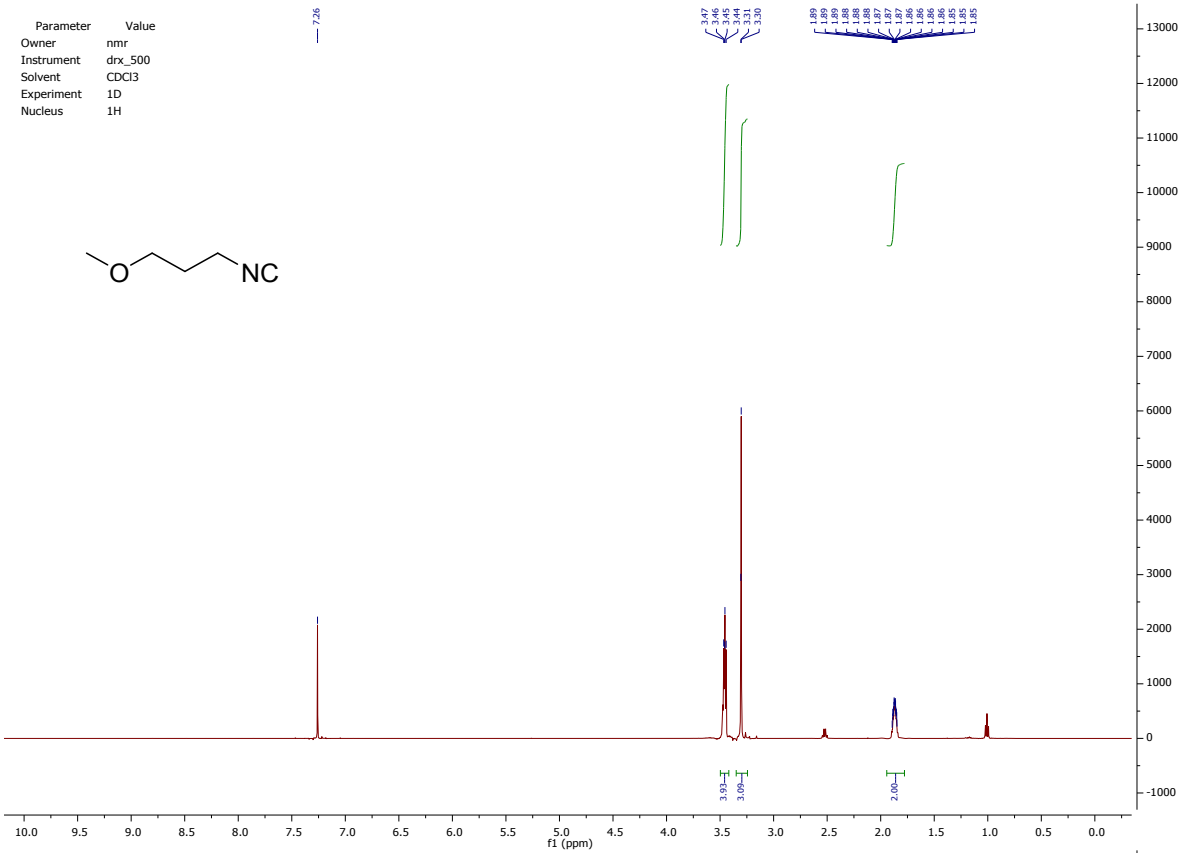


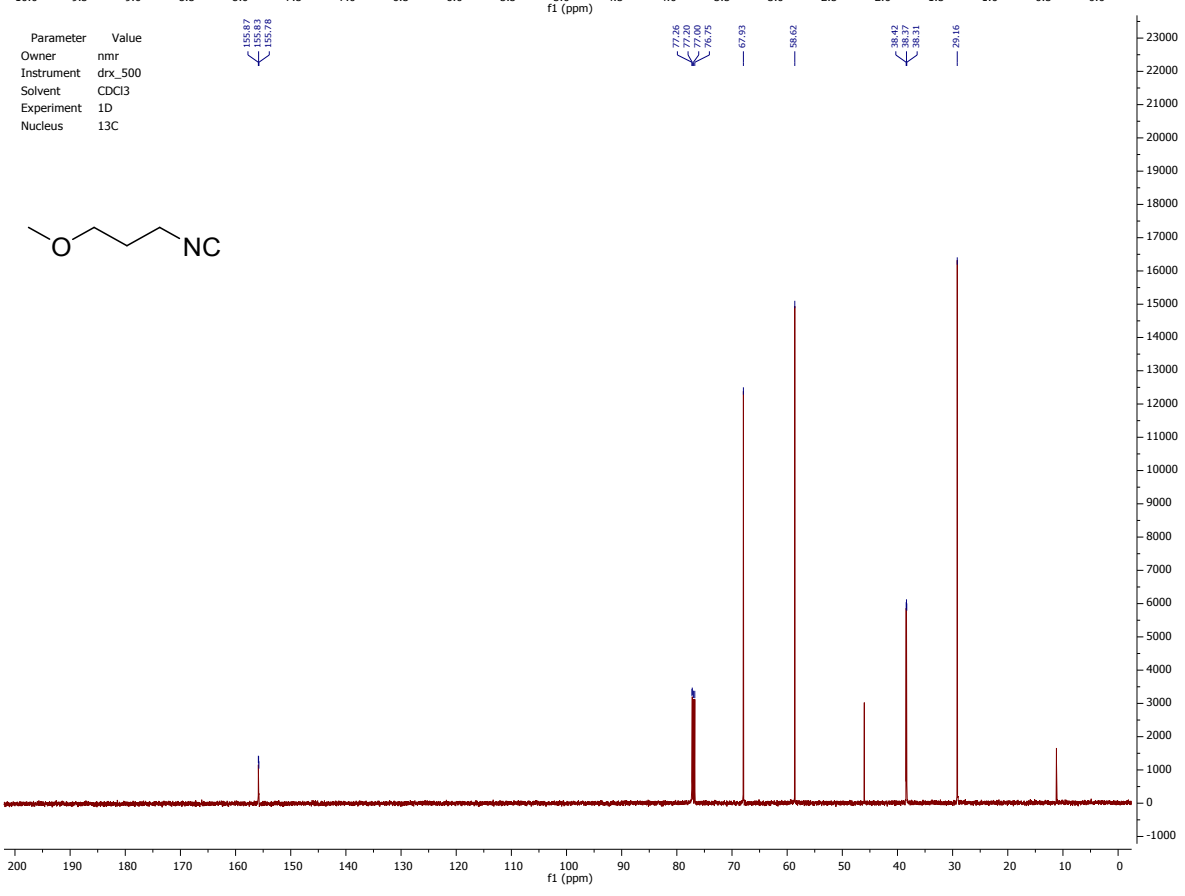
C-9: 2-Isocyano-2,4,4-trimethylpentane



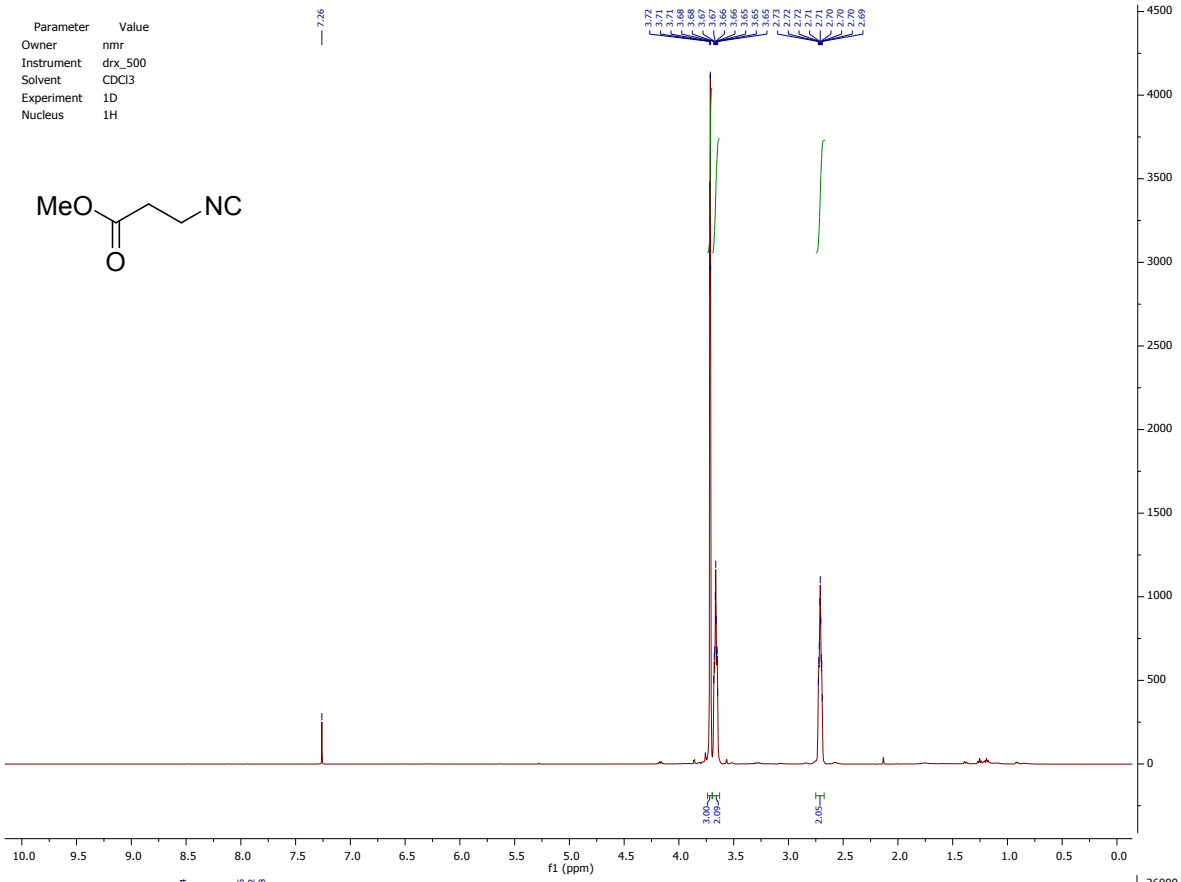


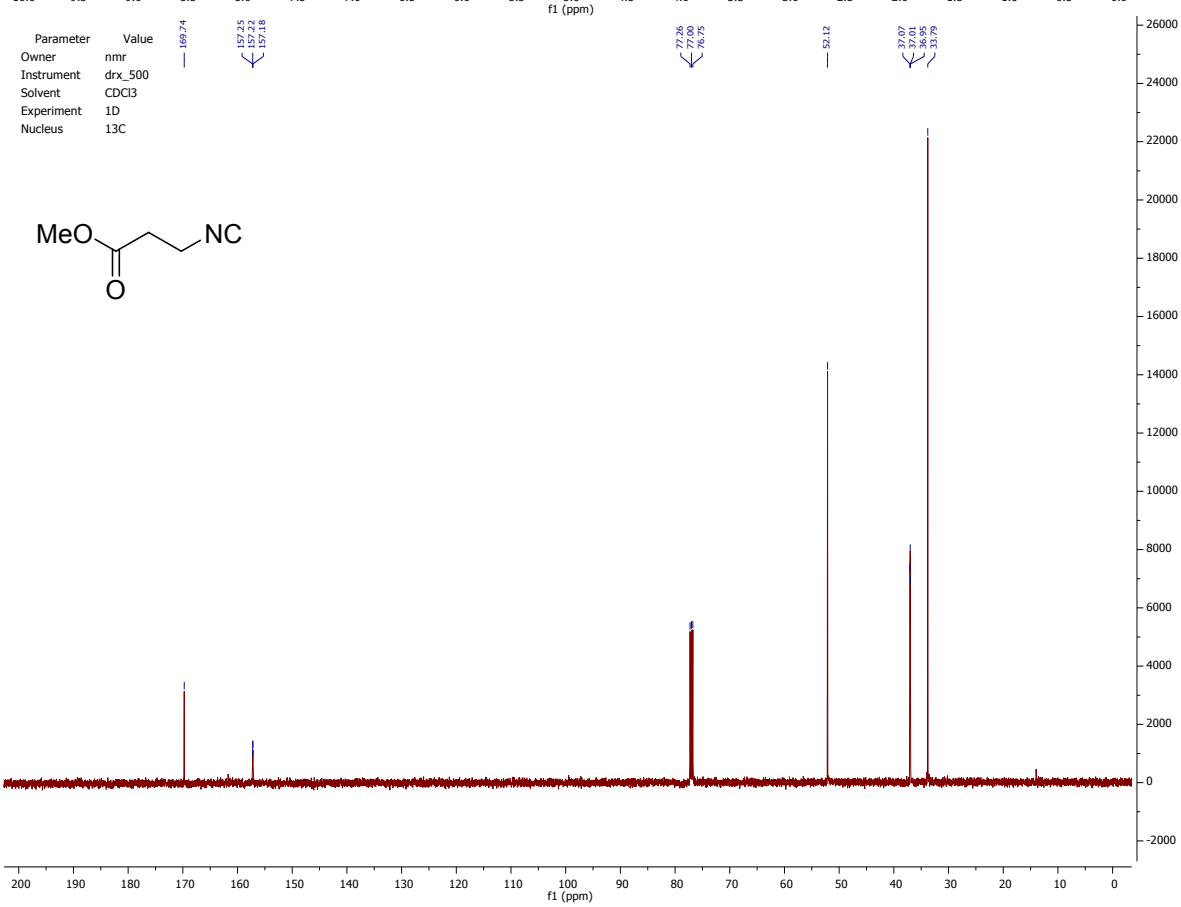
C-10 / I-45: 1-Isocyano-3-methoxypropane



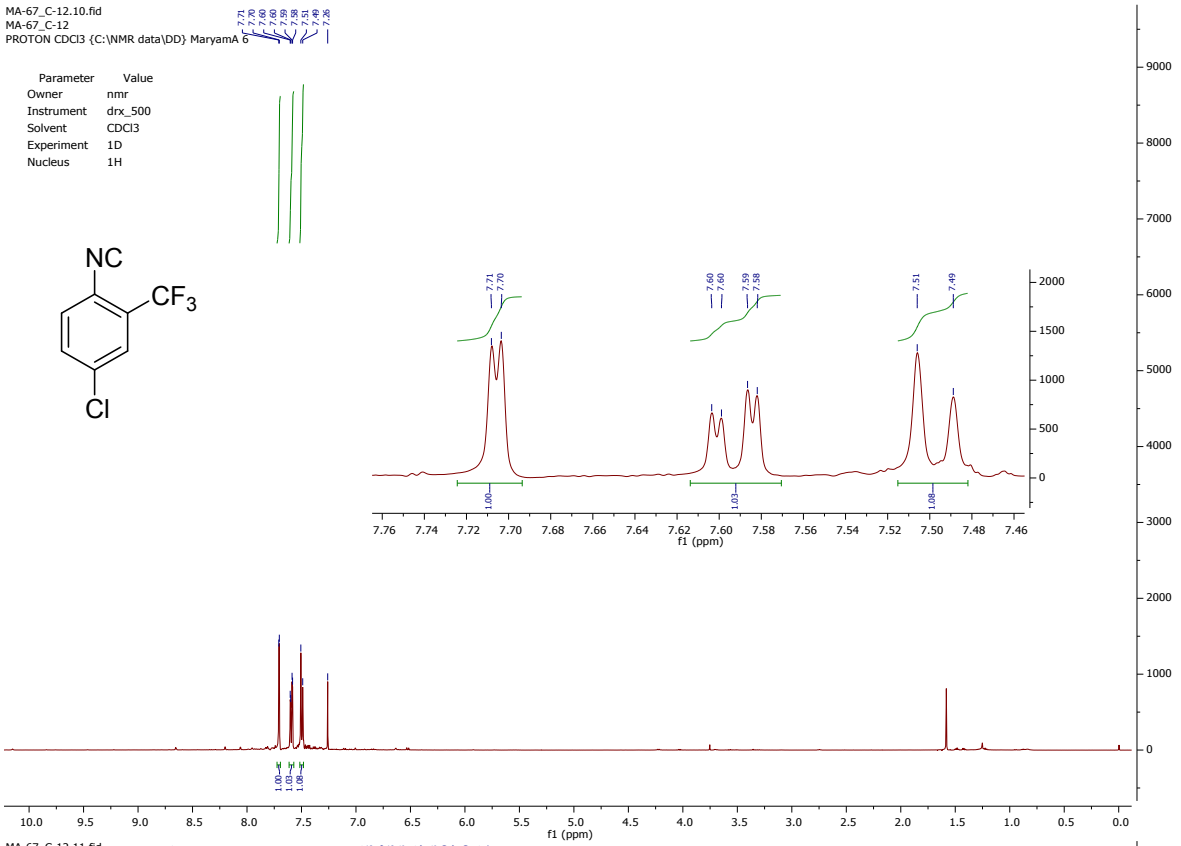


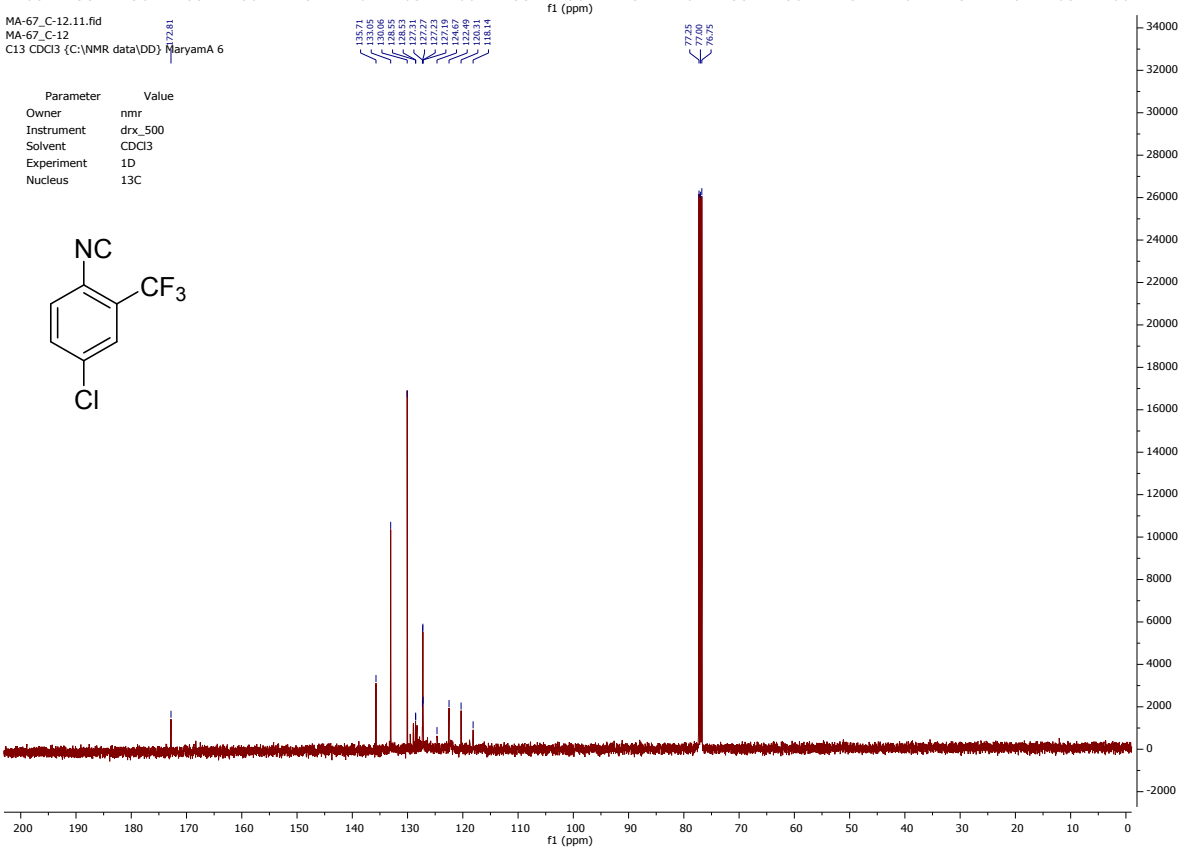
C-11 / I-48: Methyl 3-isocyanopropanoate



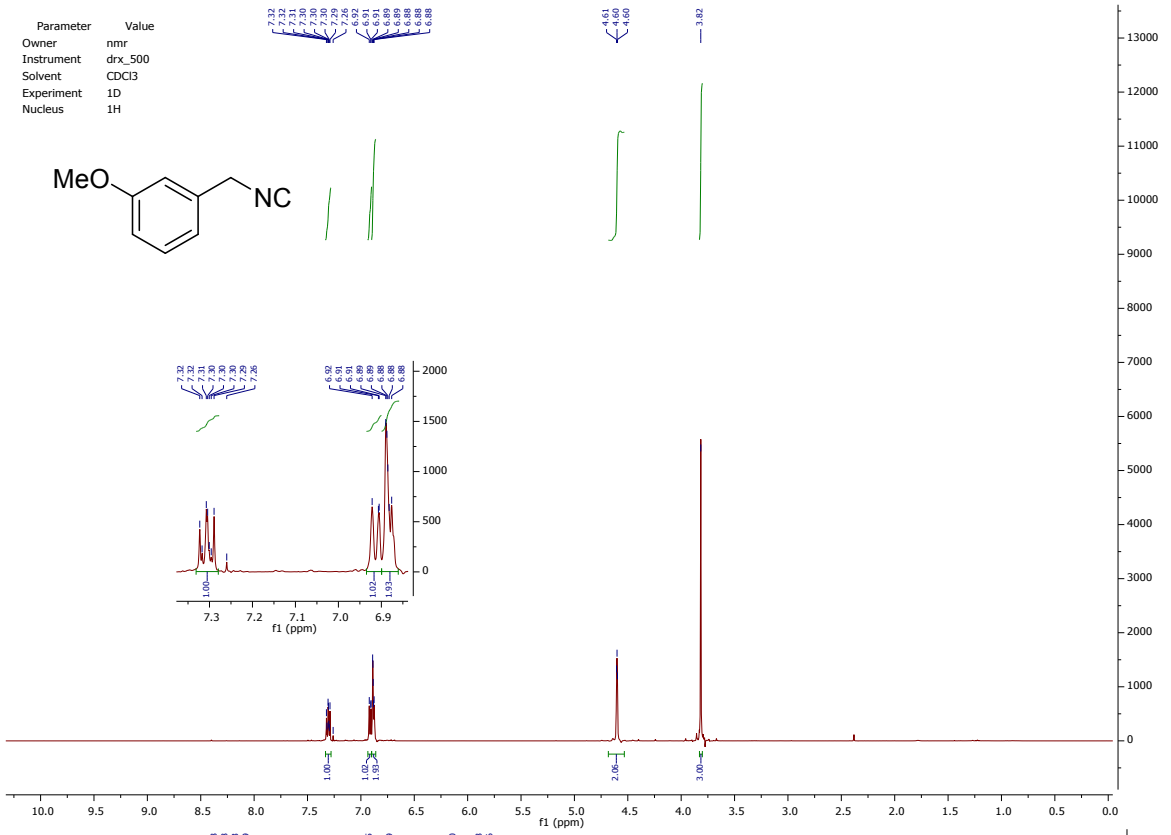


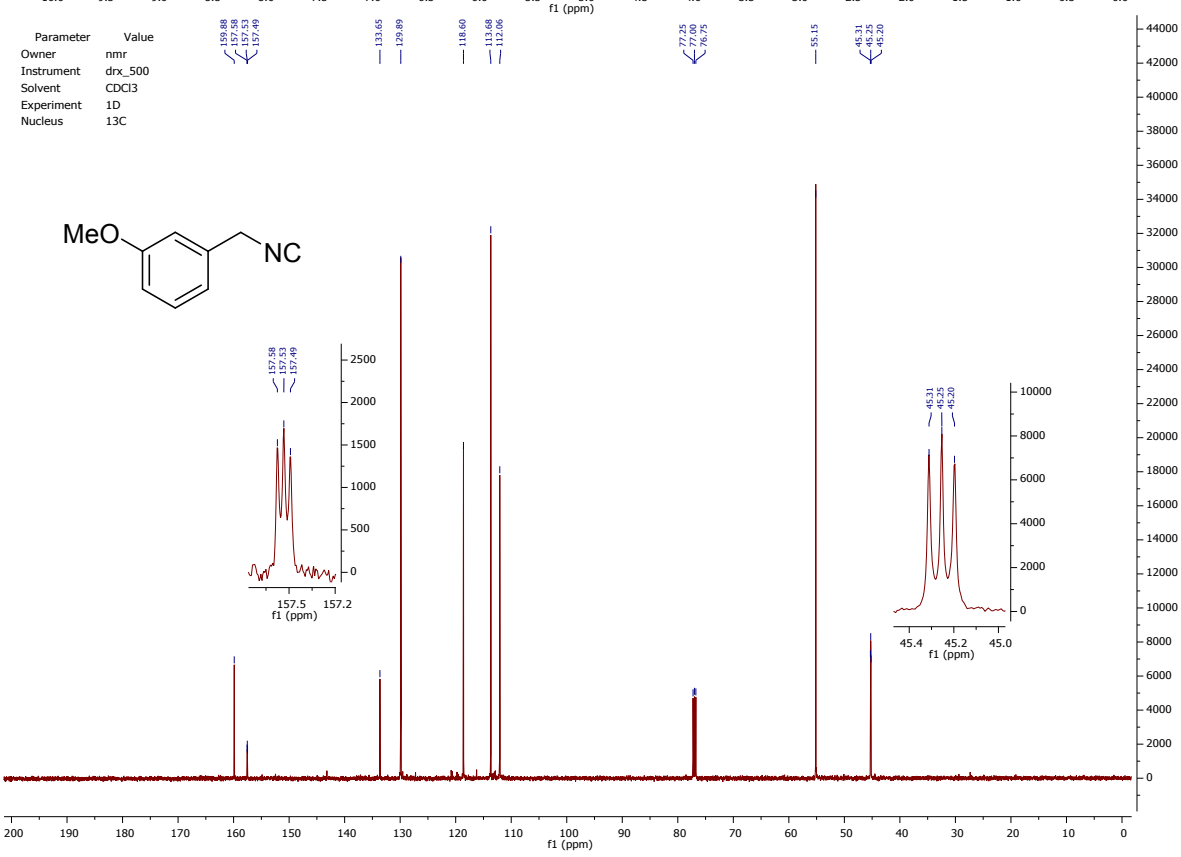
C-12: 4-Chloro-1-isocyano-2-(trifluoromethyl)benzene



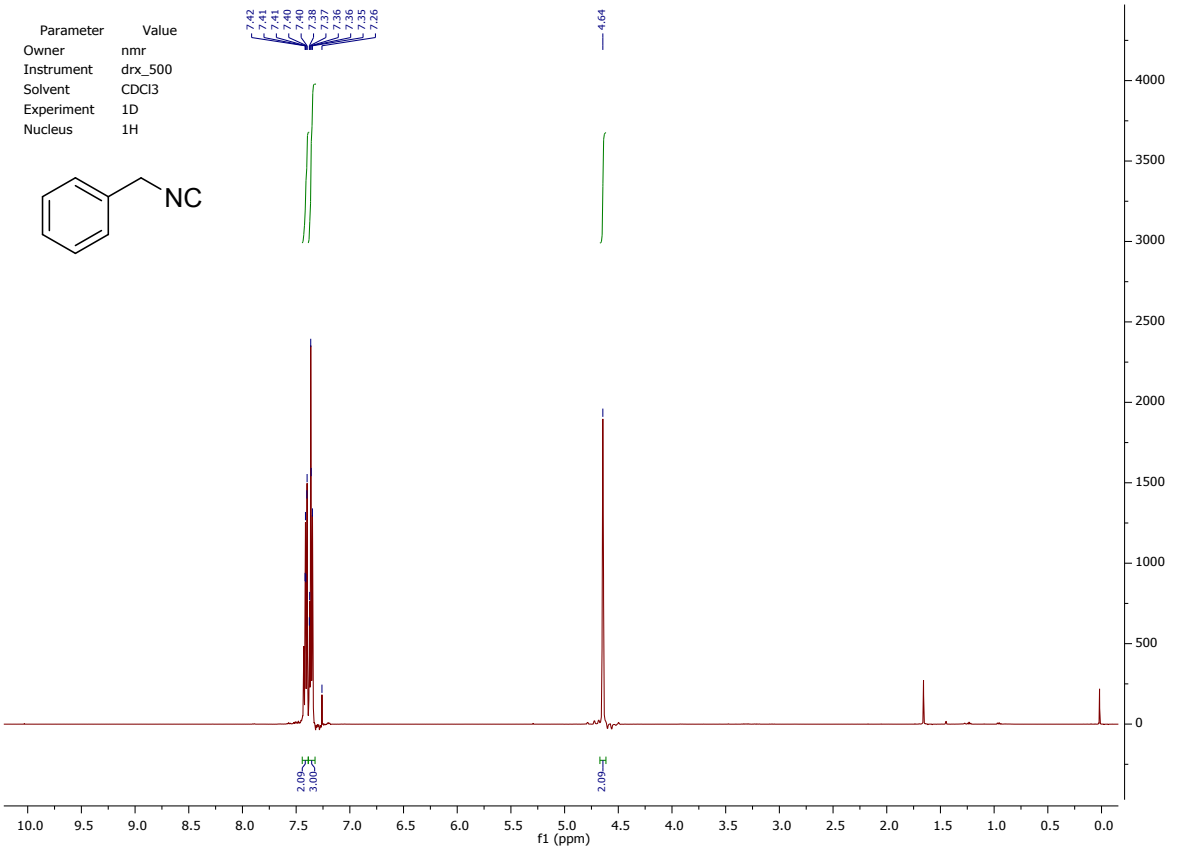


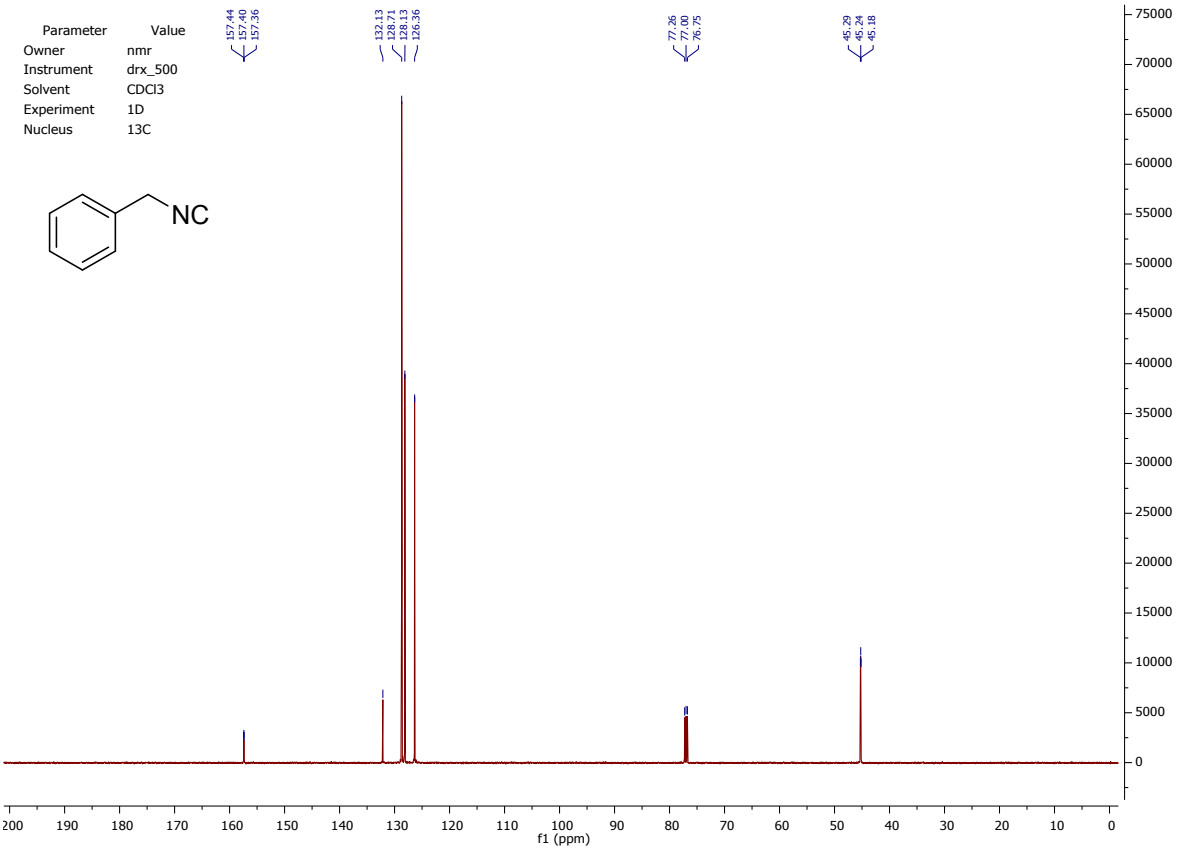
D-1 / I-3: 1-(Isocyanomethyl)-3-methoxybenzene



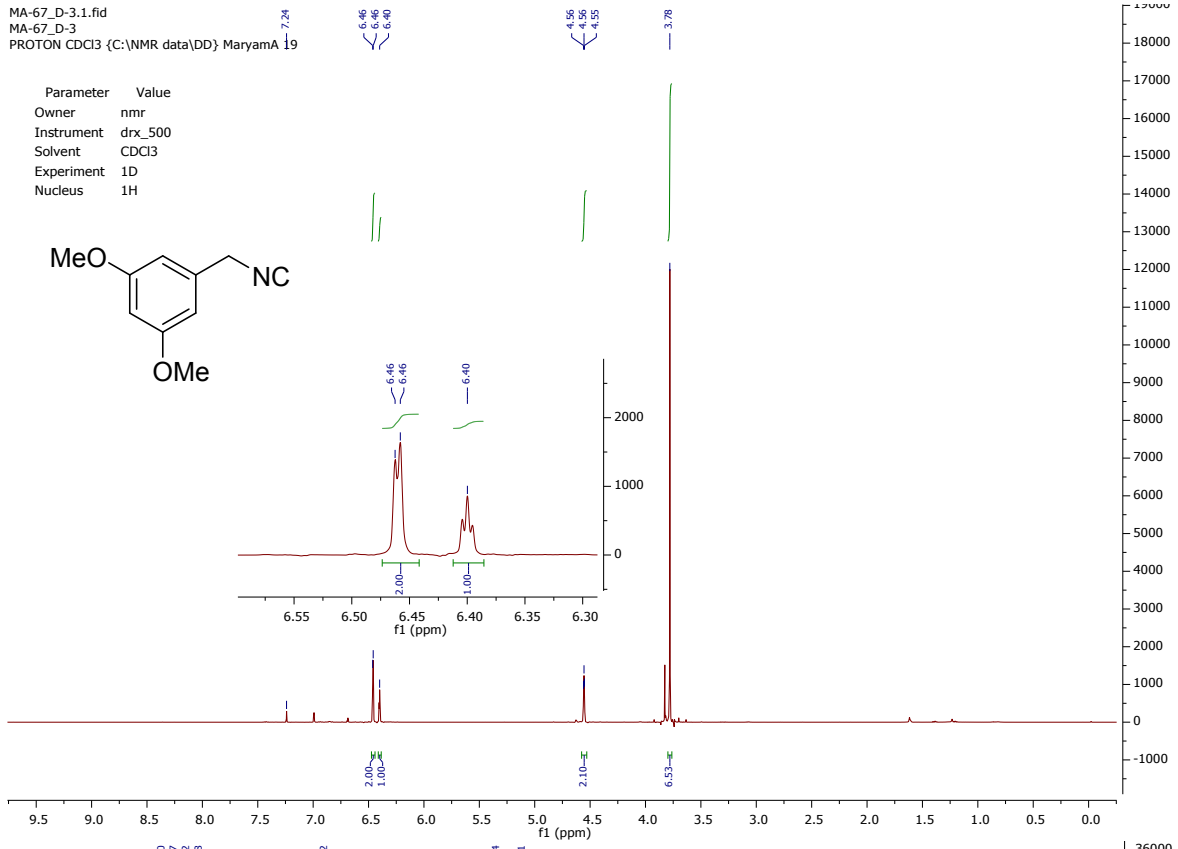


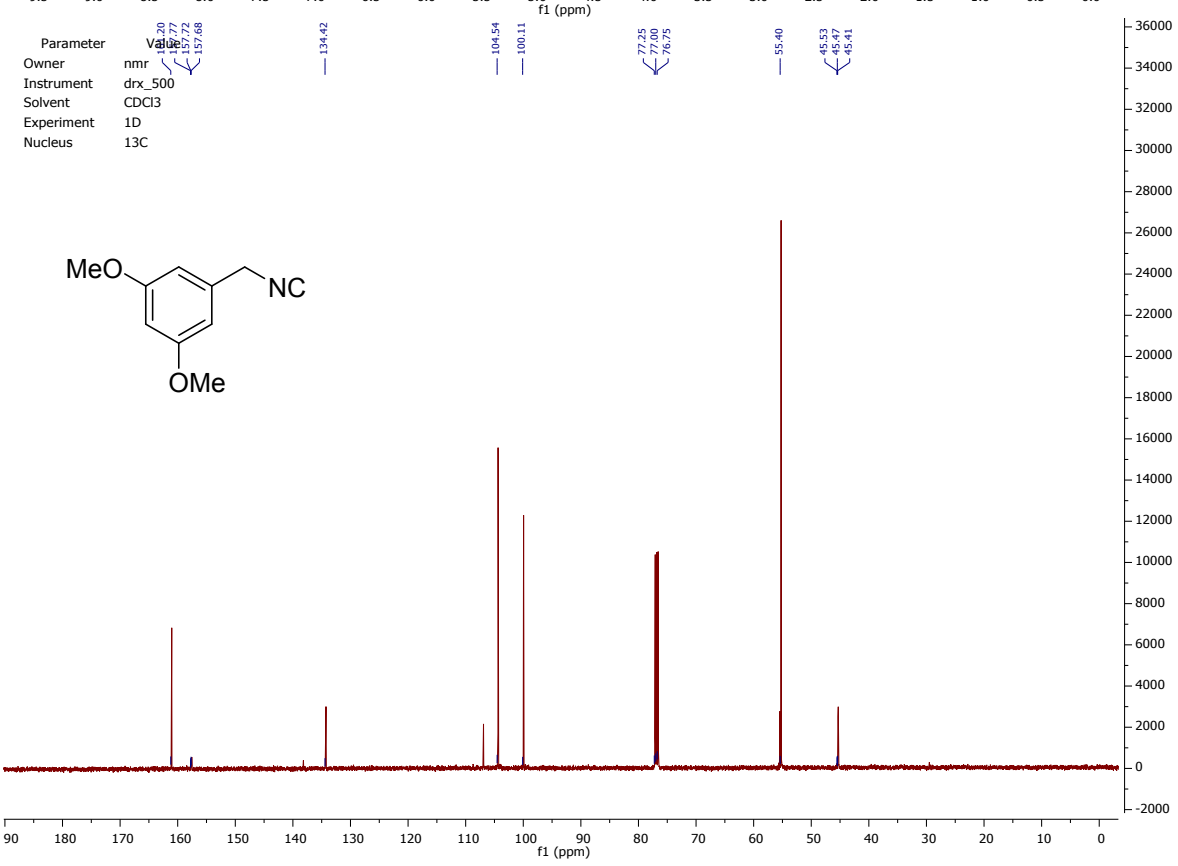
D-2: (Isocyanomethyl)benzene.



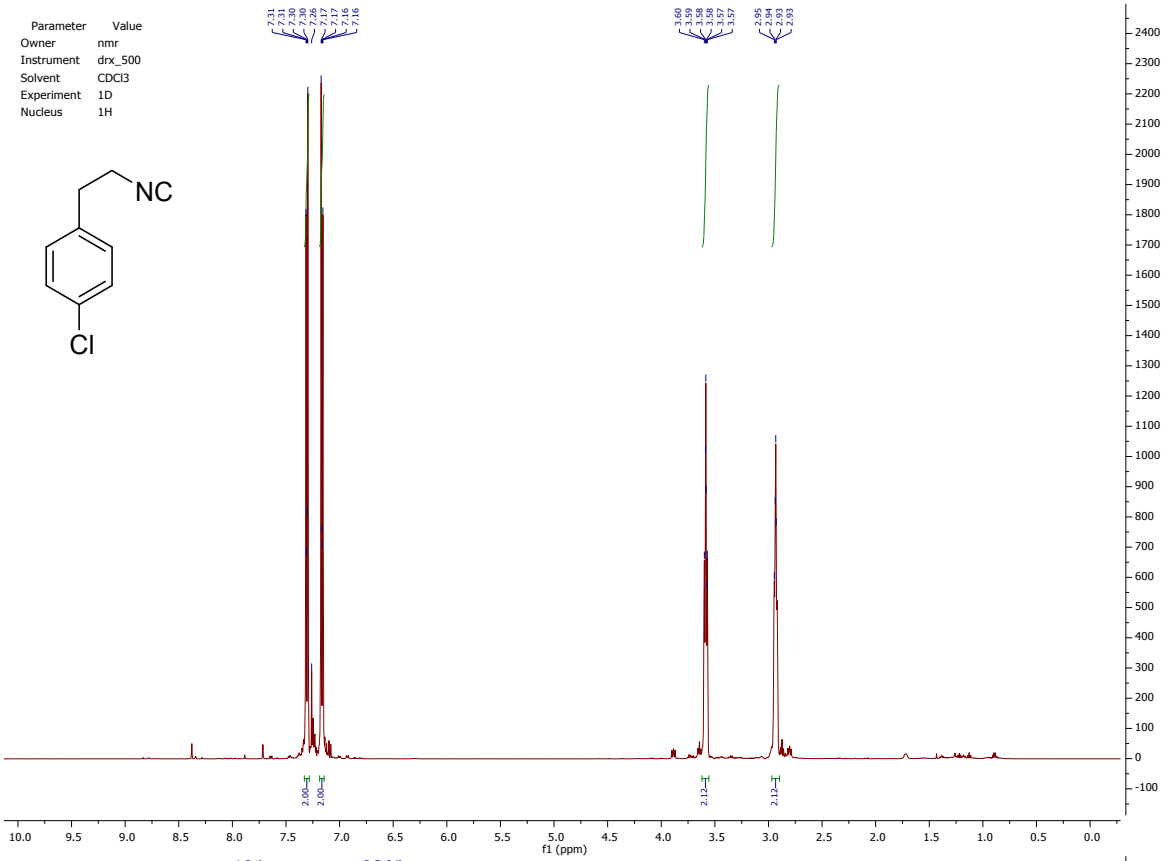


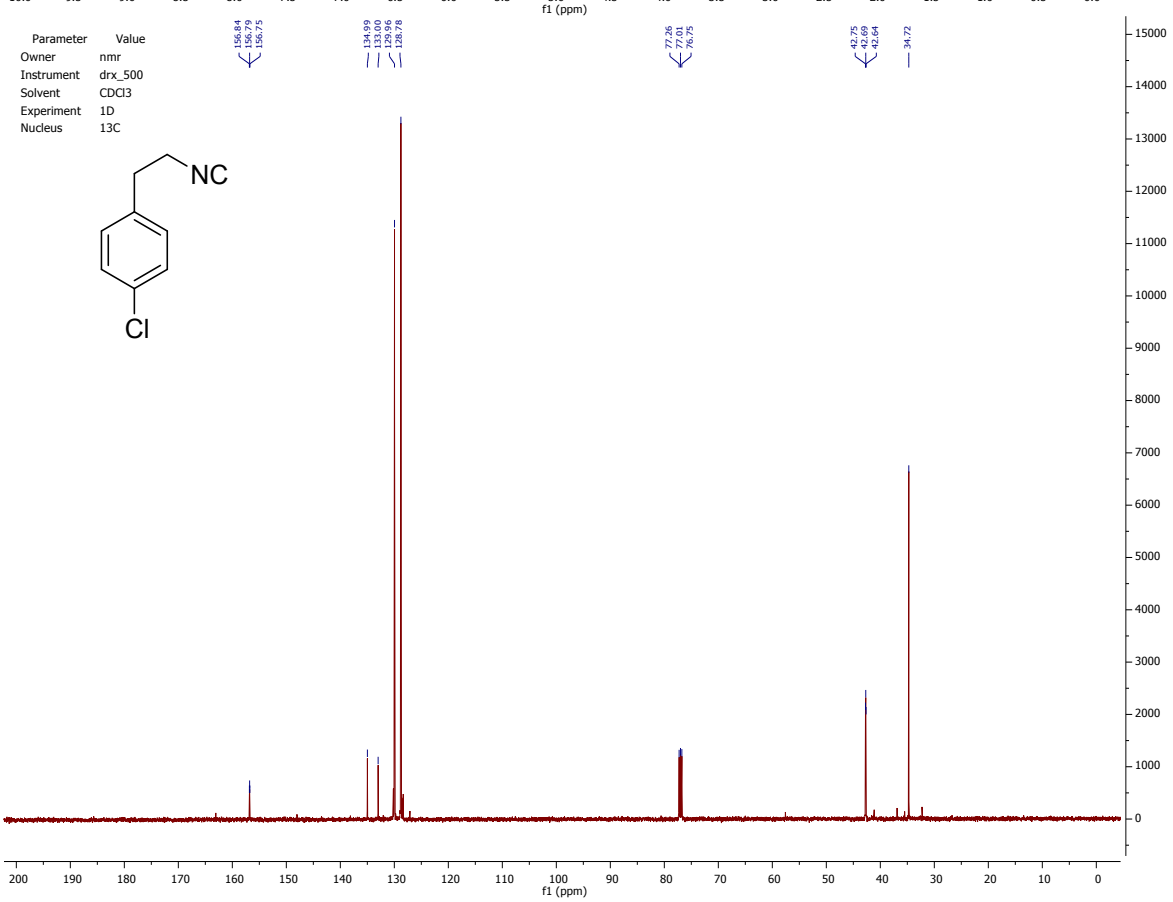
D-3 / I-11: 1-(Isocyanomethyl)-3,5-dimethoxybenzene



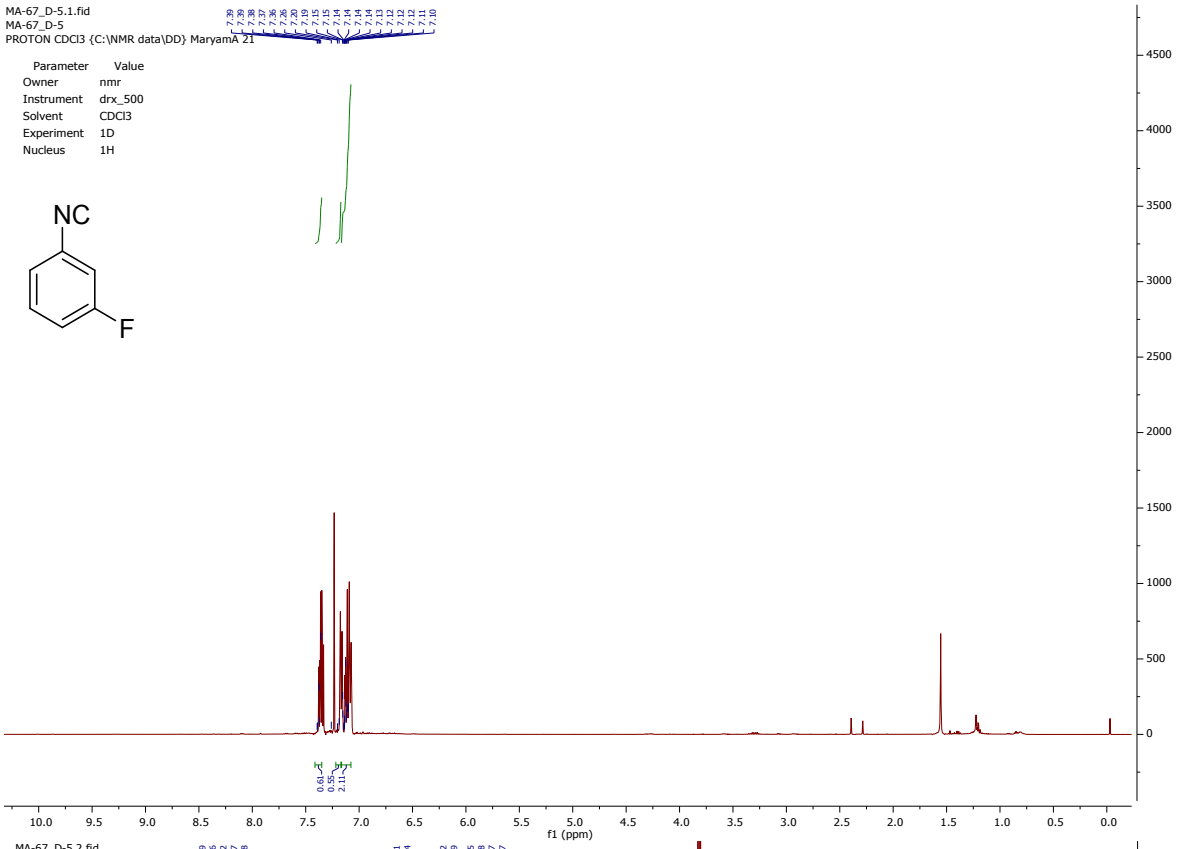


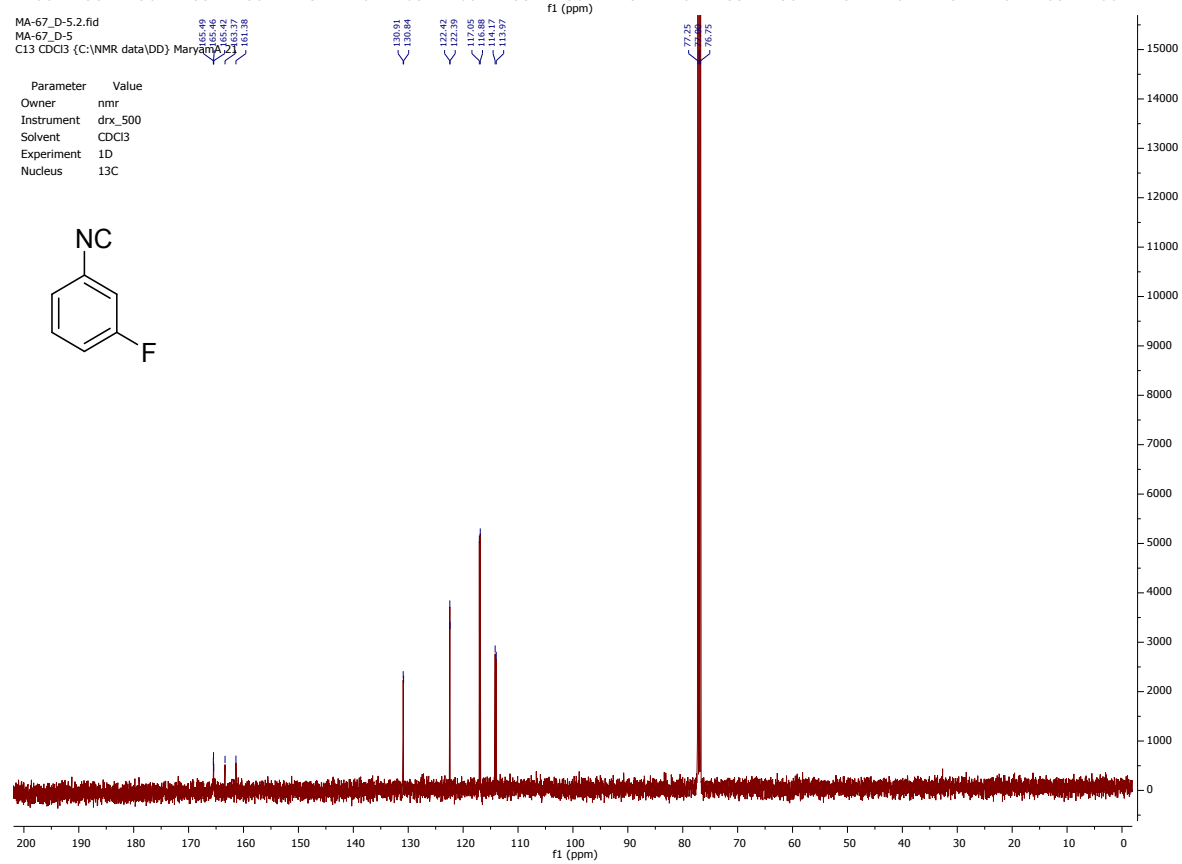
D-4 / I-17: 1-Chloro-4-(2-isocyanoethyl)benzene



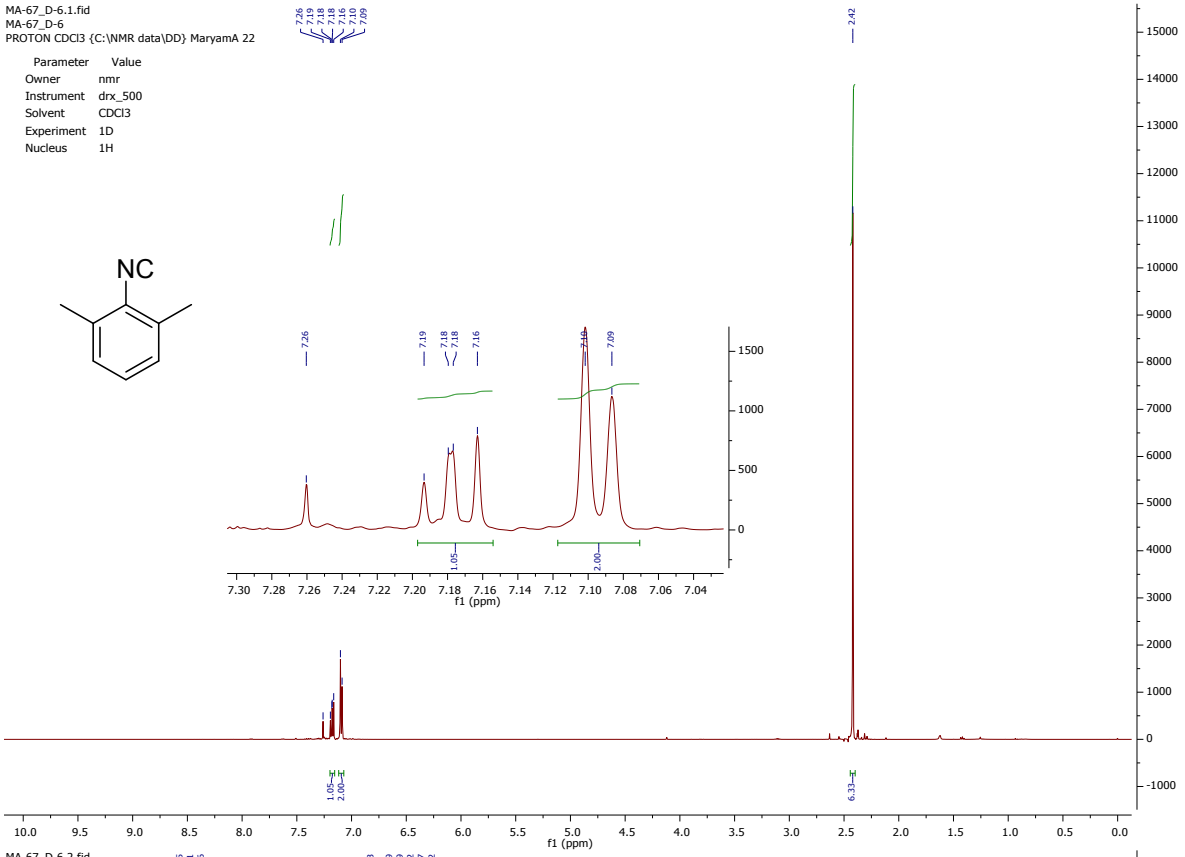


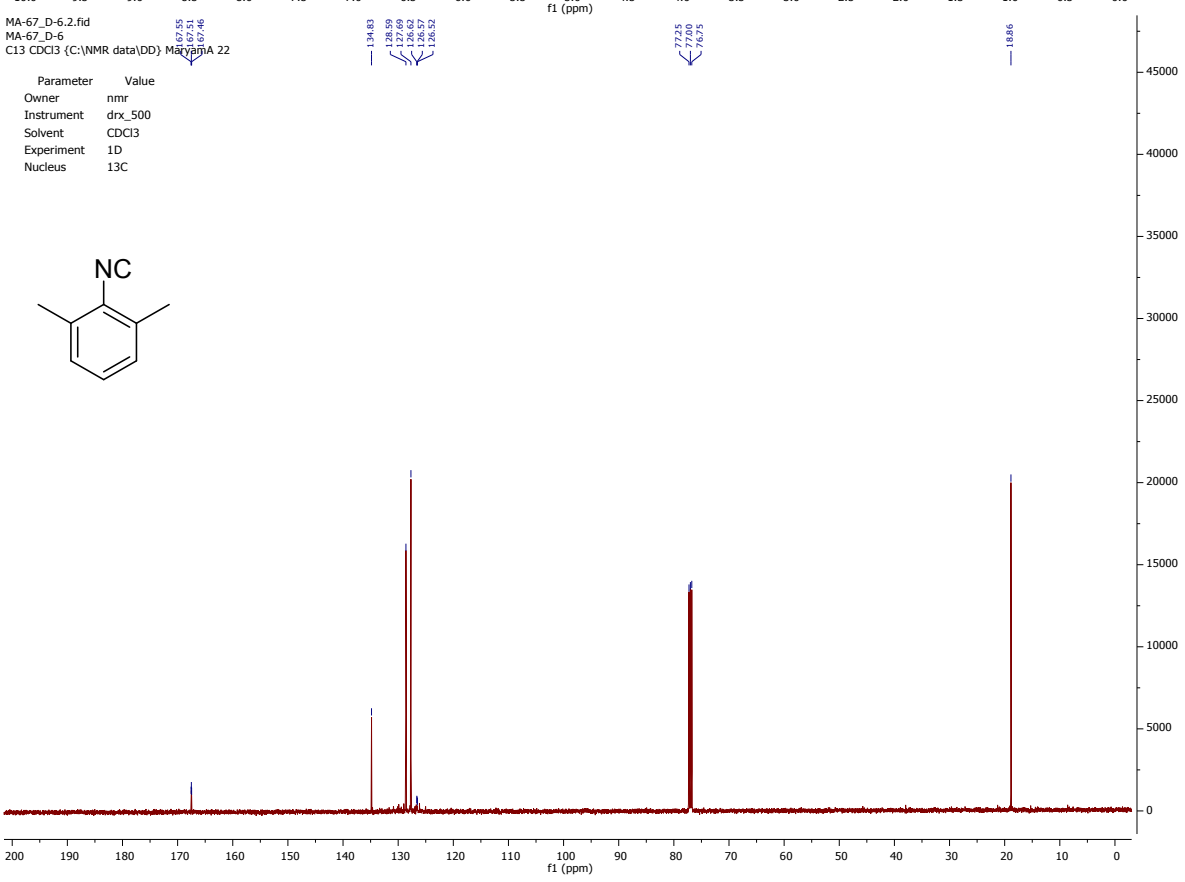
D-5: 1-Fluoro-3-isocyanobenzene



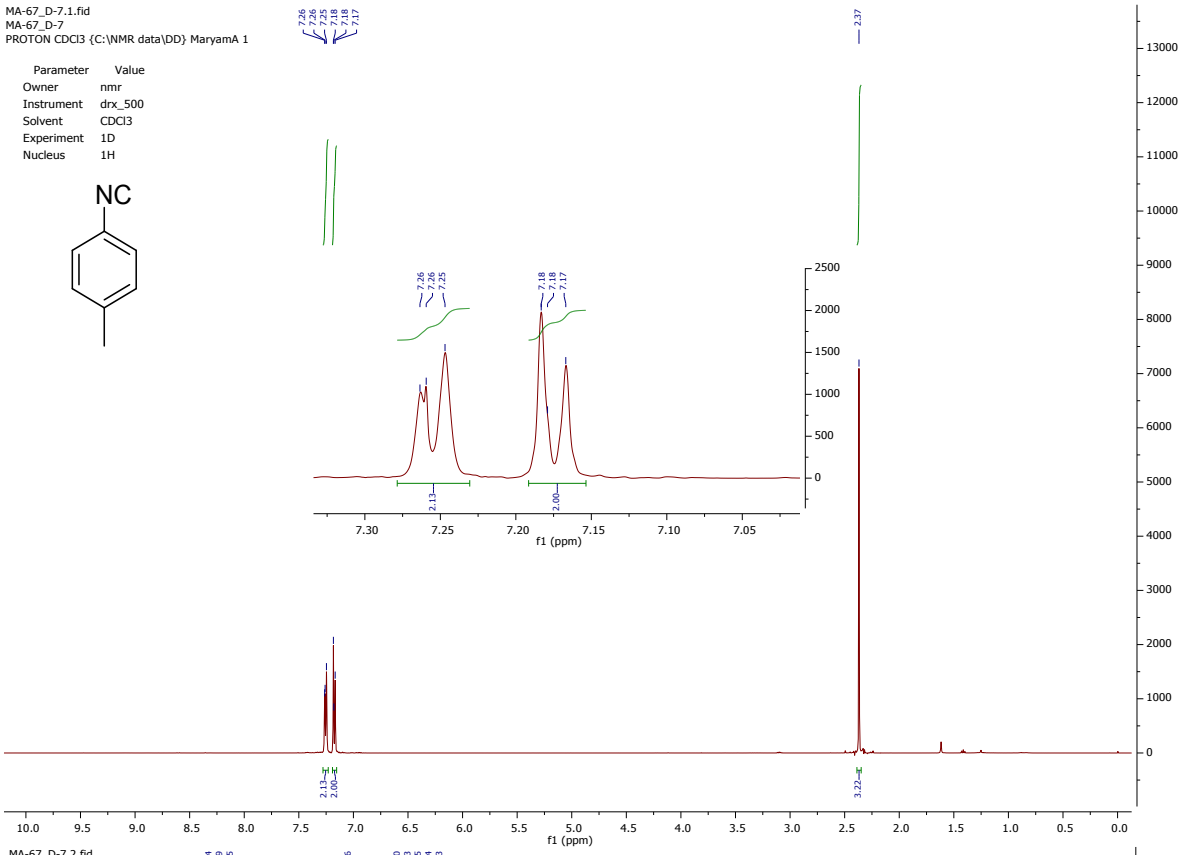


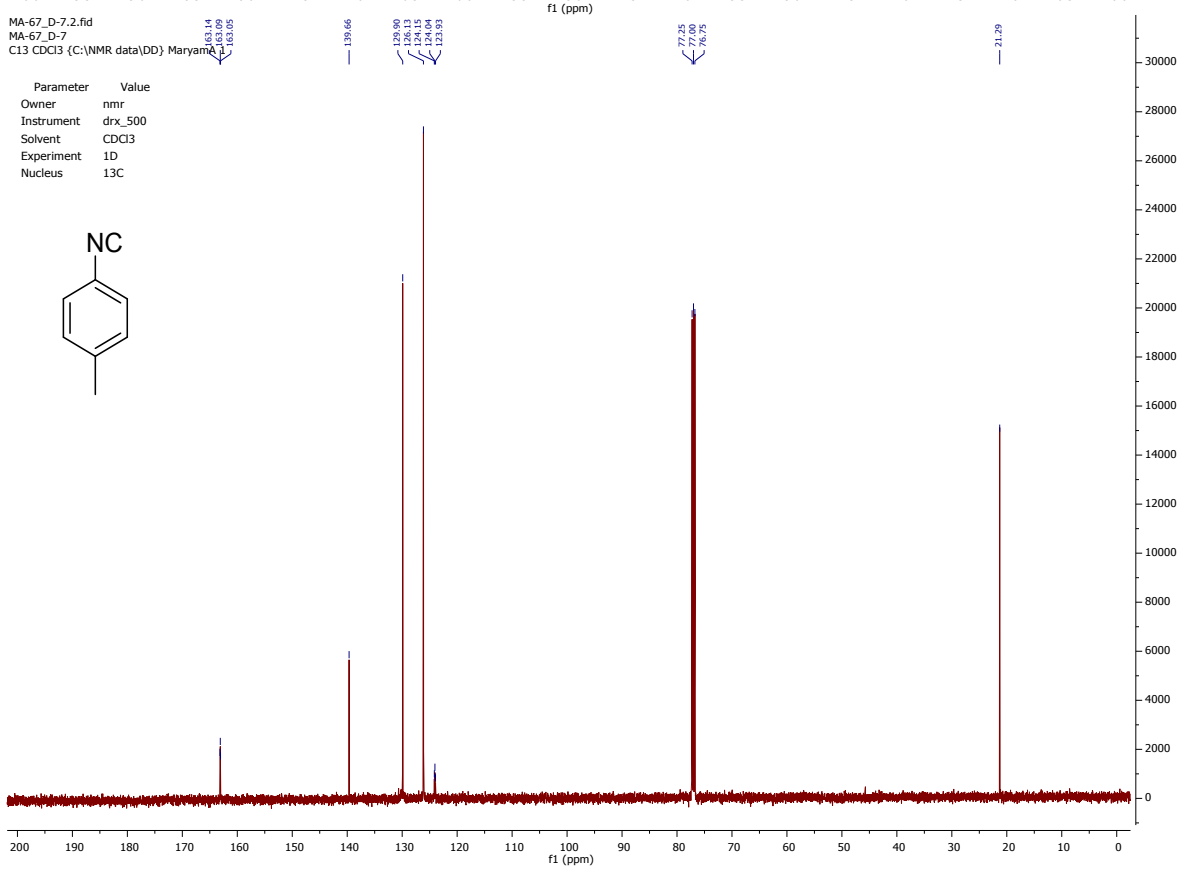
D-6: 2-Isocyano-1,3-dimethylbenzene



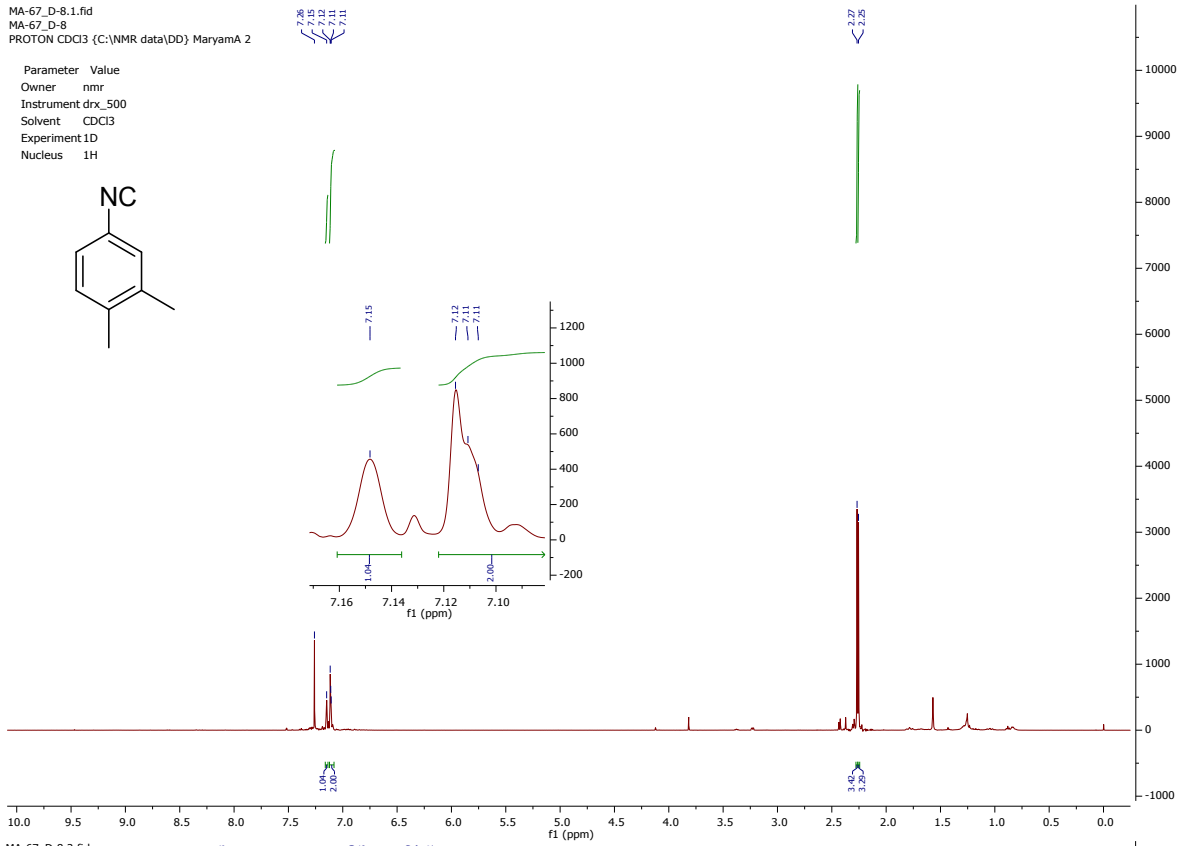


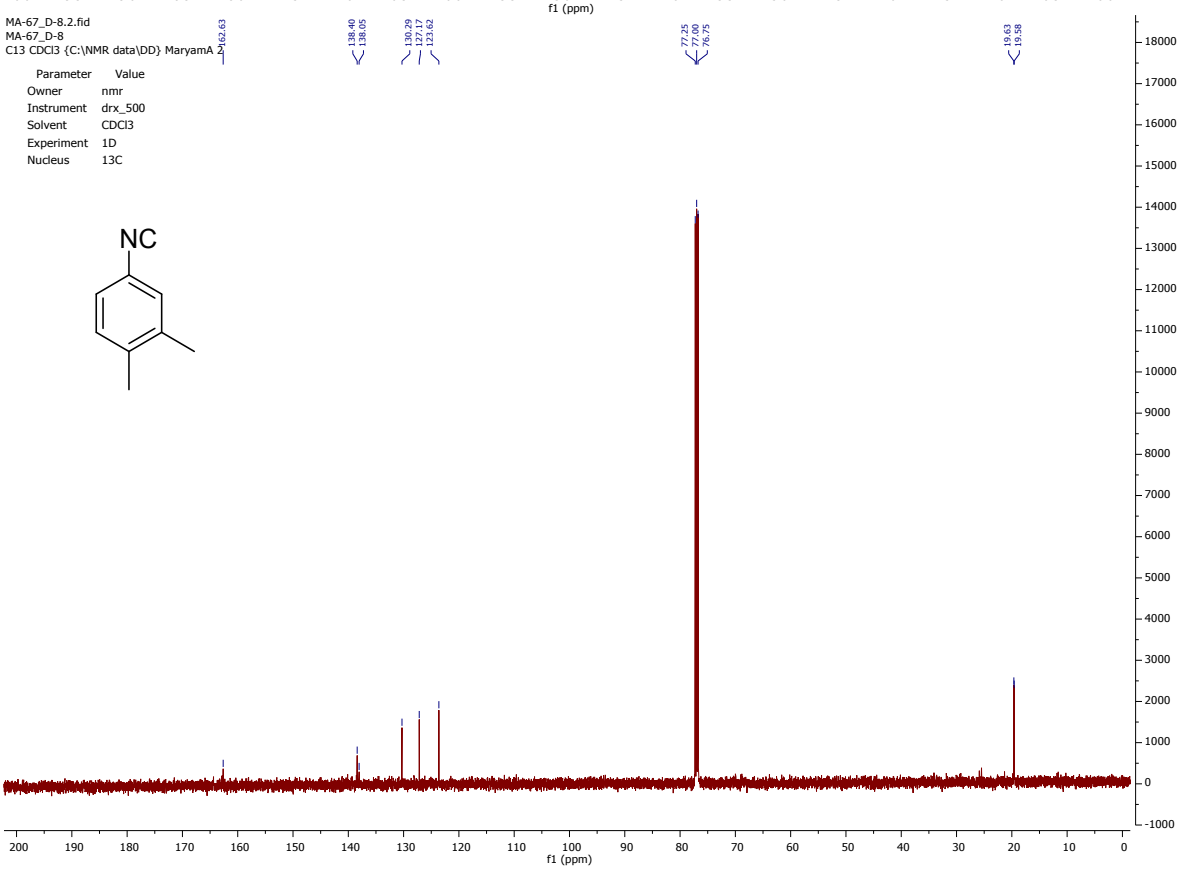
D-7: 1-Isocyano-4-methylbenzene



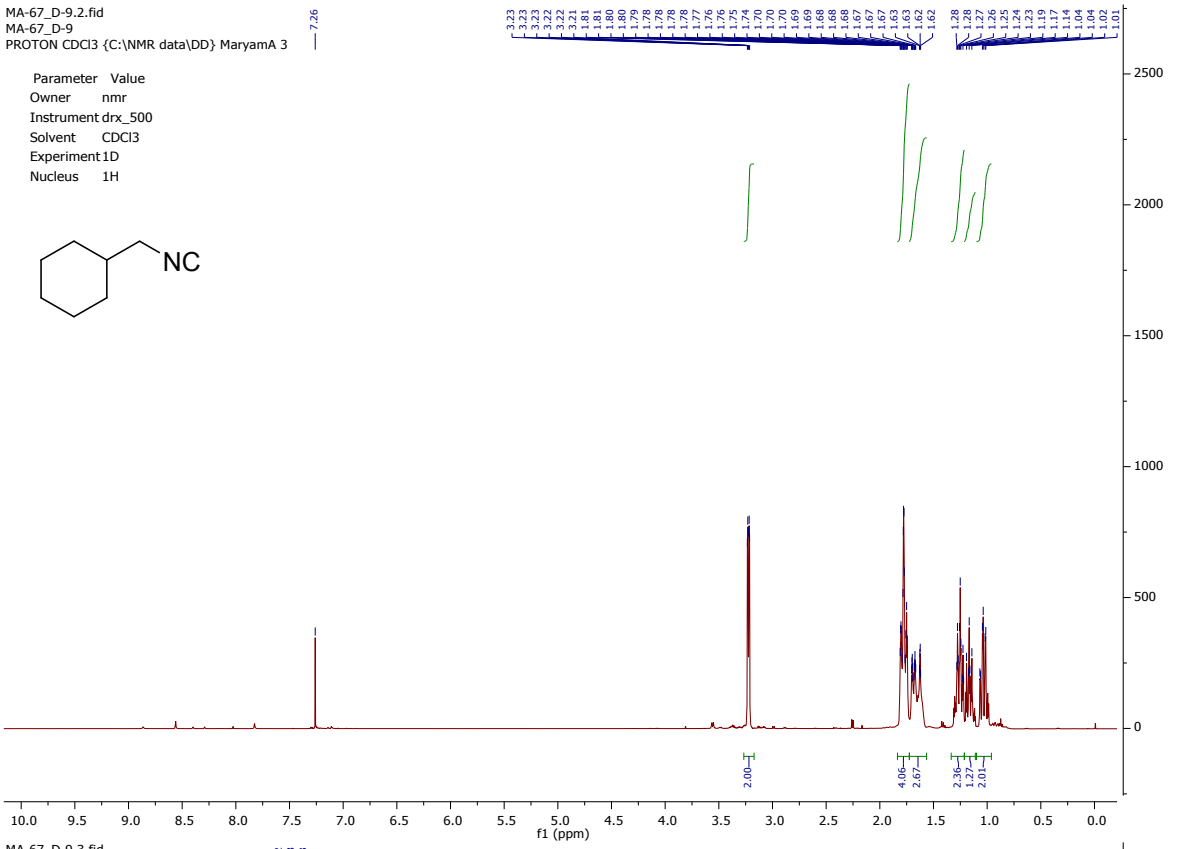


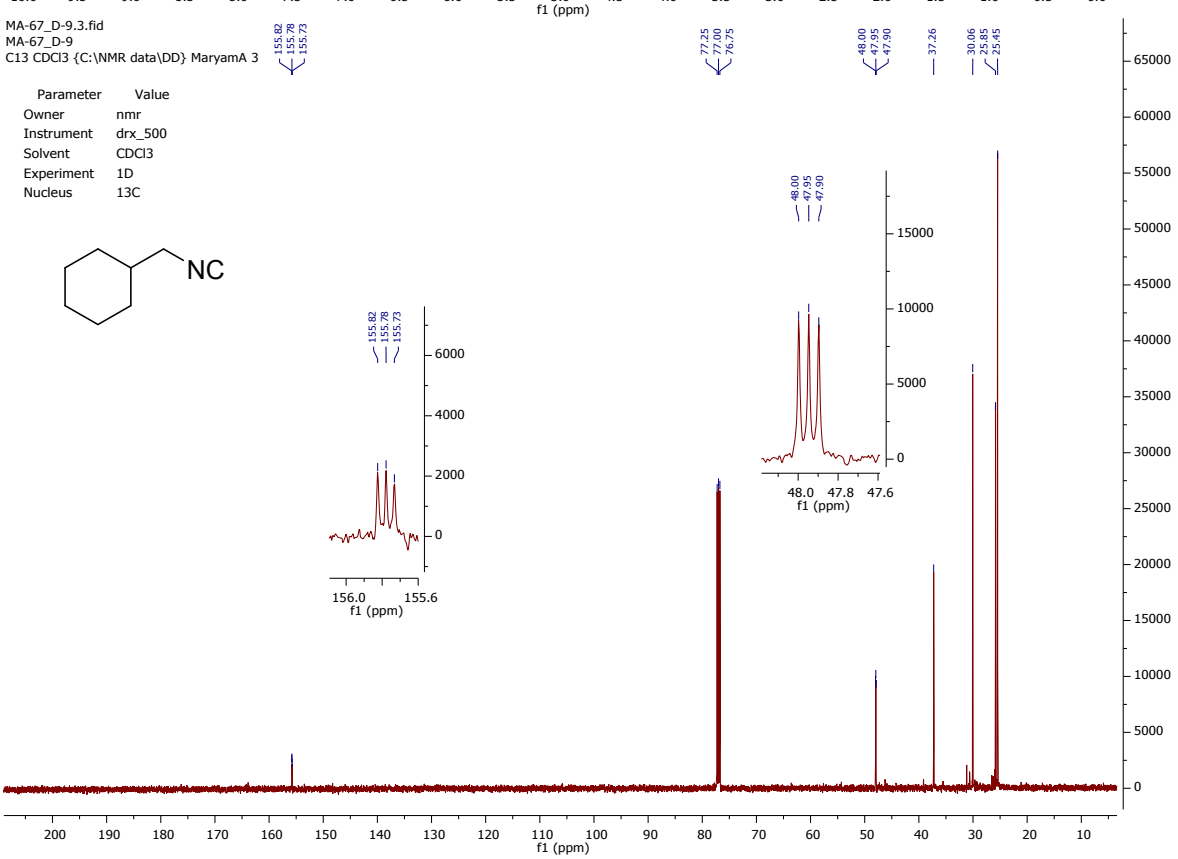
D-8: 4-Isocyano-1,2-dimethylbenzene



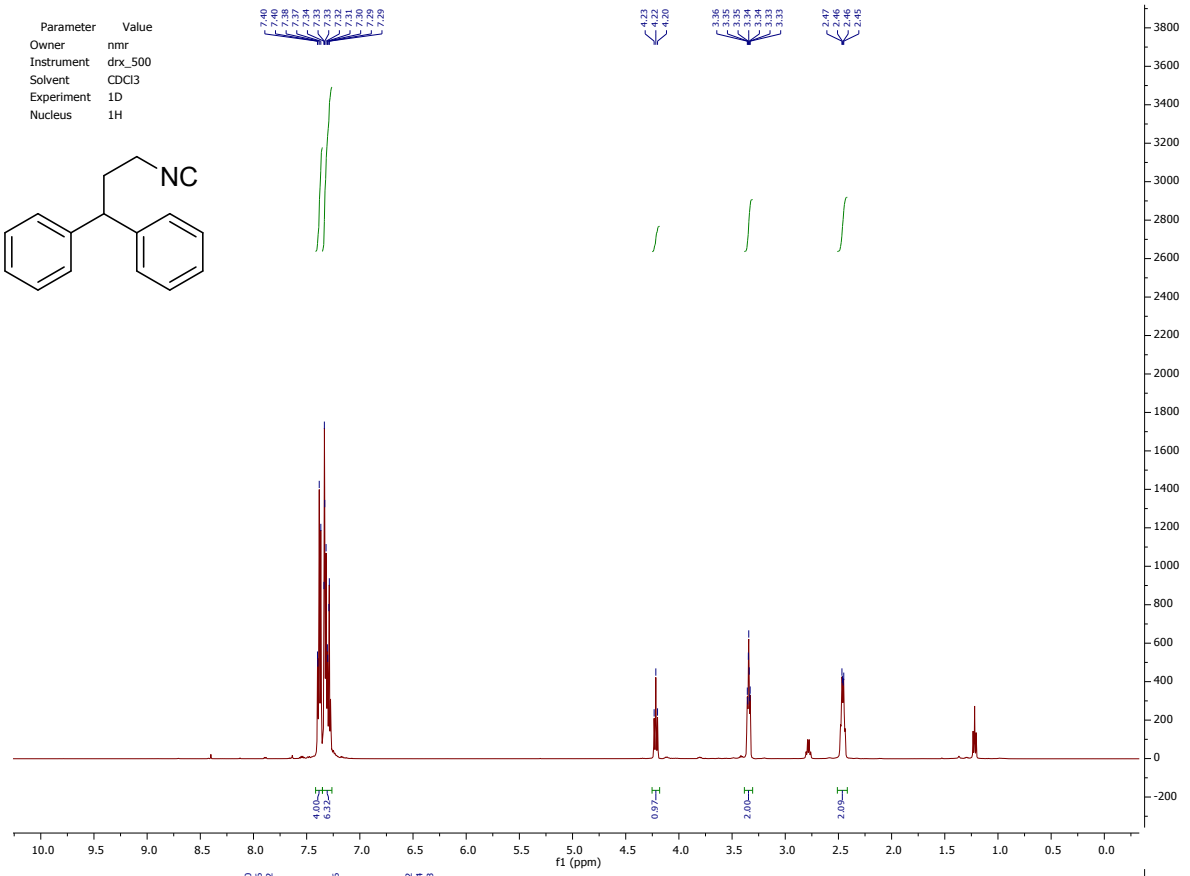


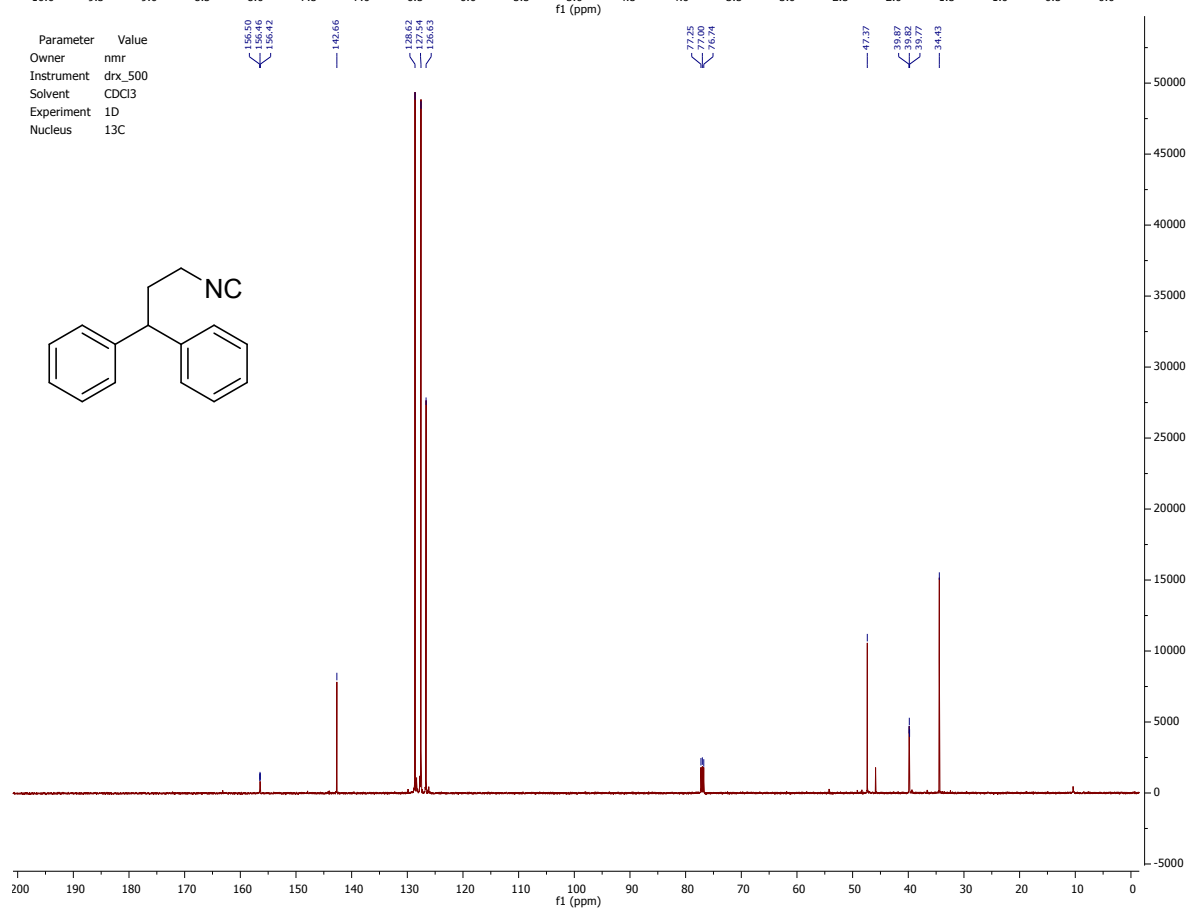
D-9 / I-38: (Isocyanomethyl)cyclohexane



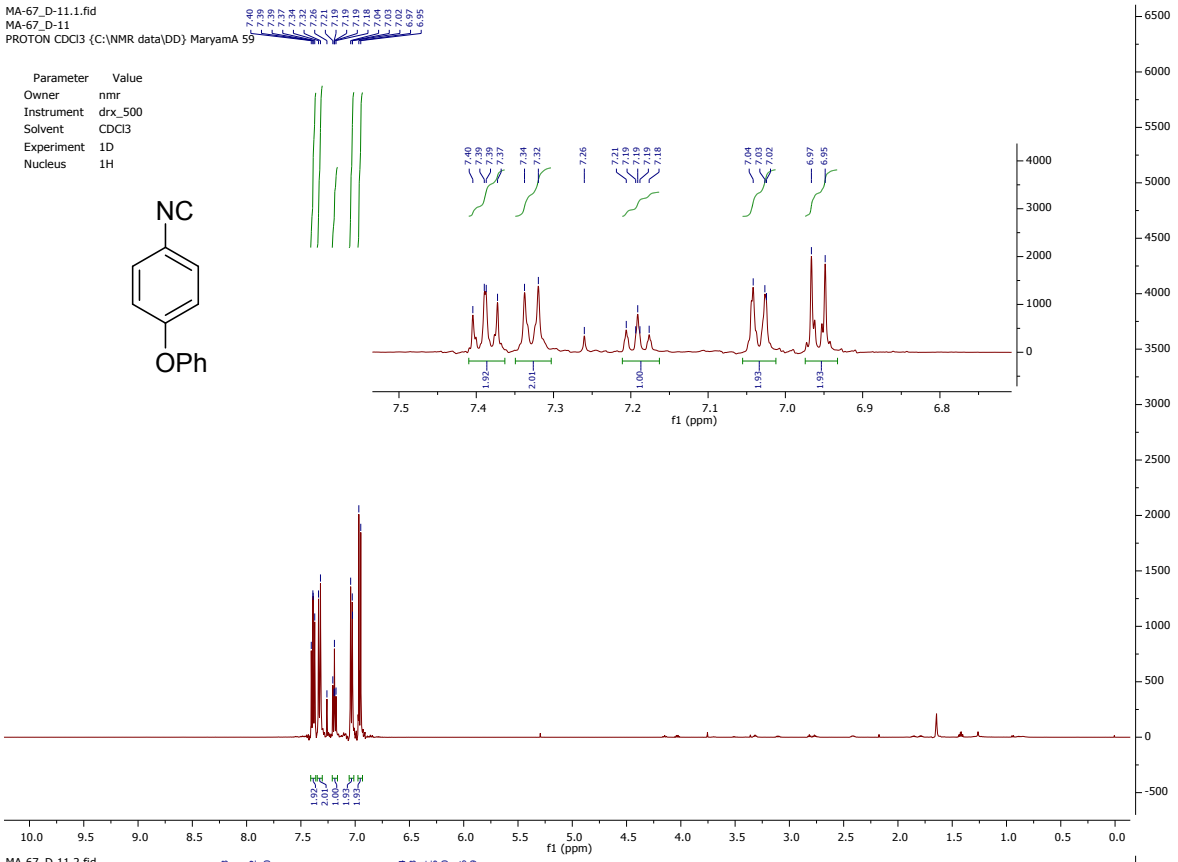


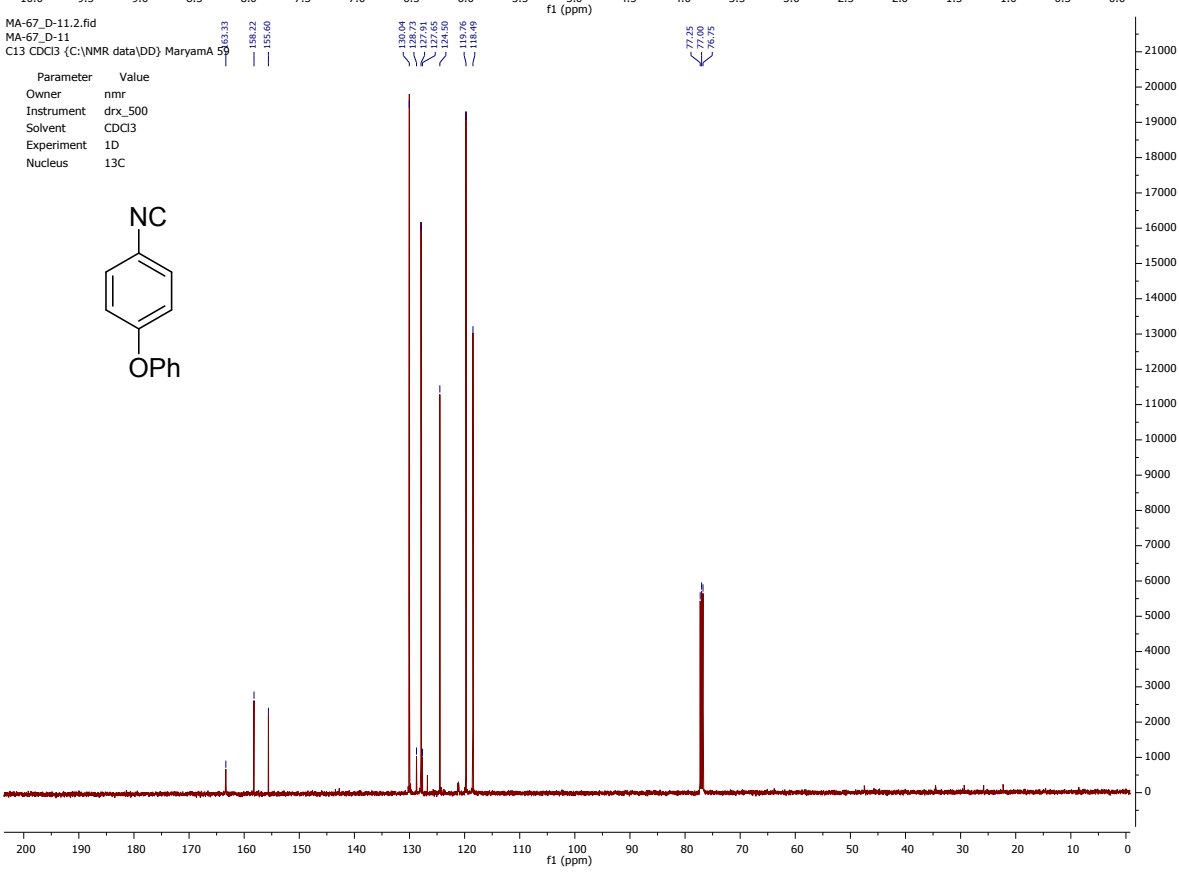
D-10 / I-46: (3-Isocyanopropane-1,1-diyl)dibenzene



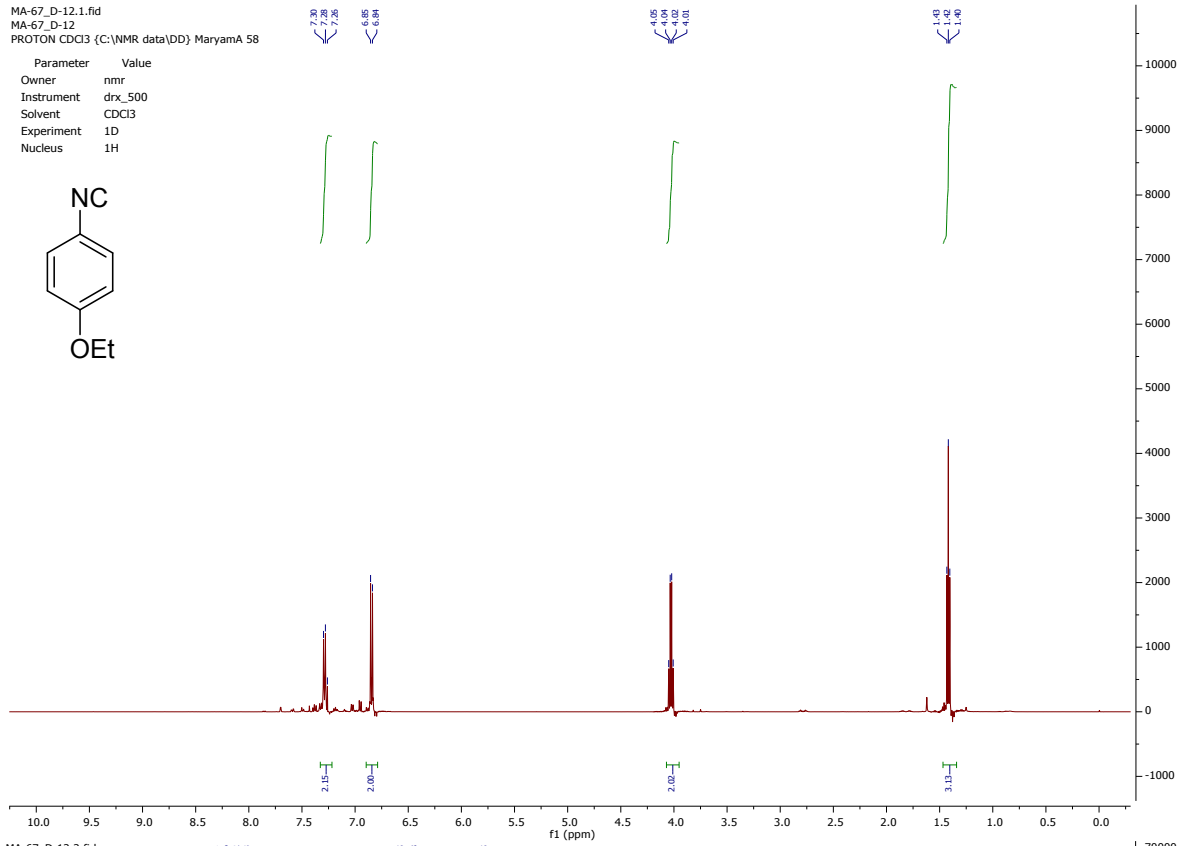


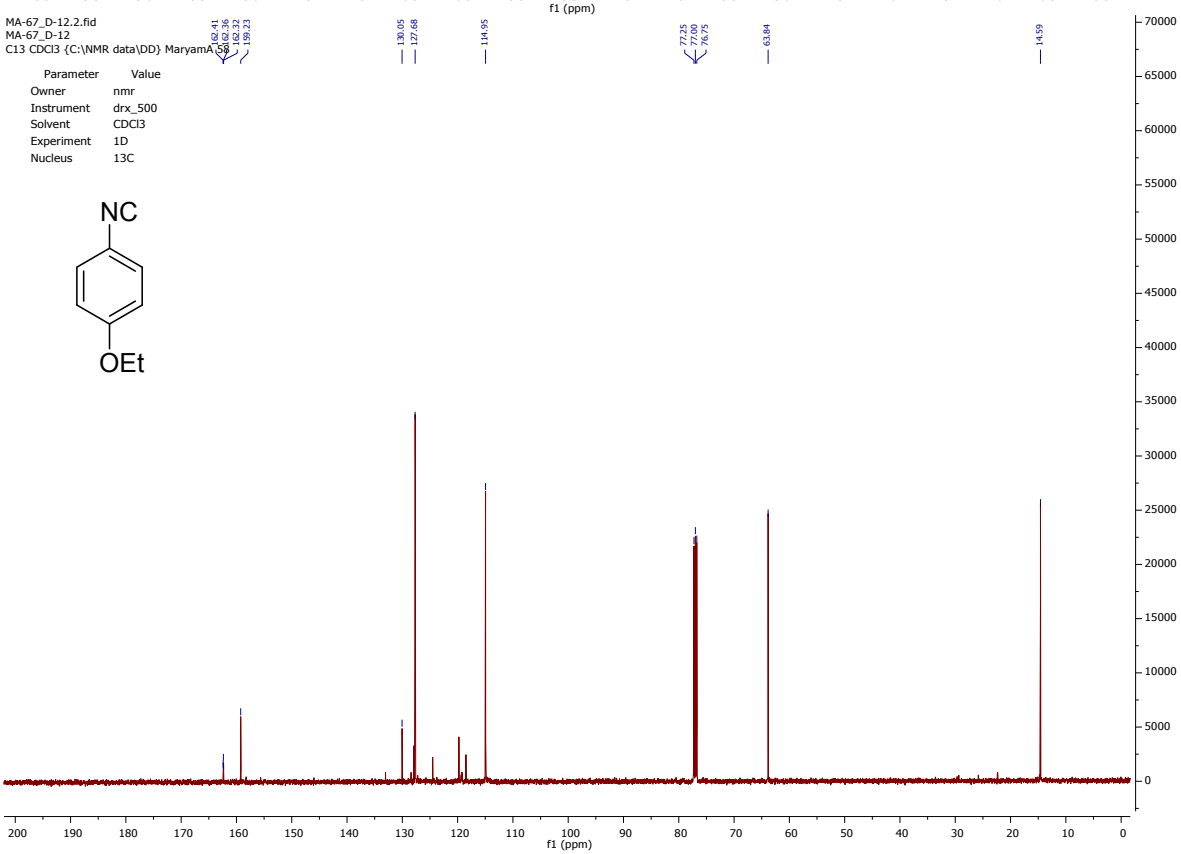
D-11: 1-Isocyano-4-phenoxybenzene



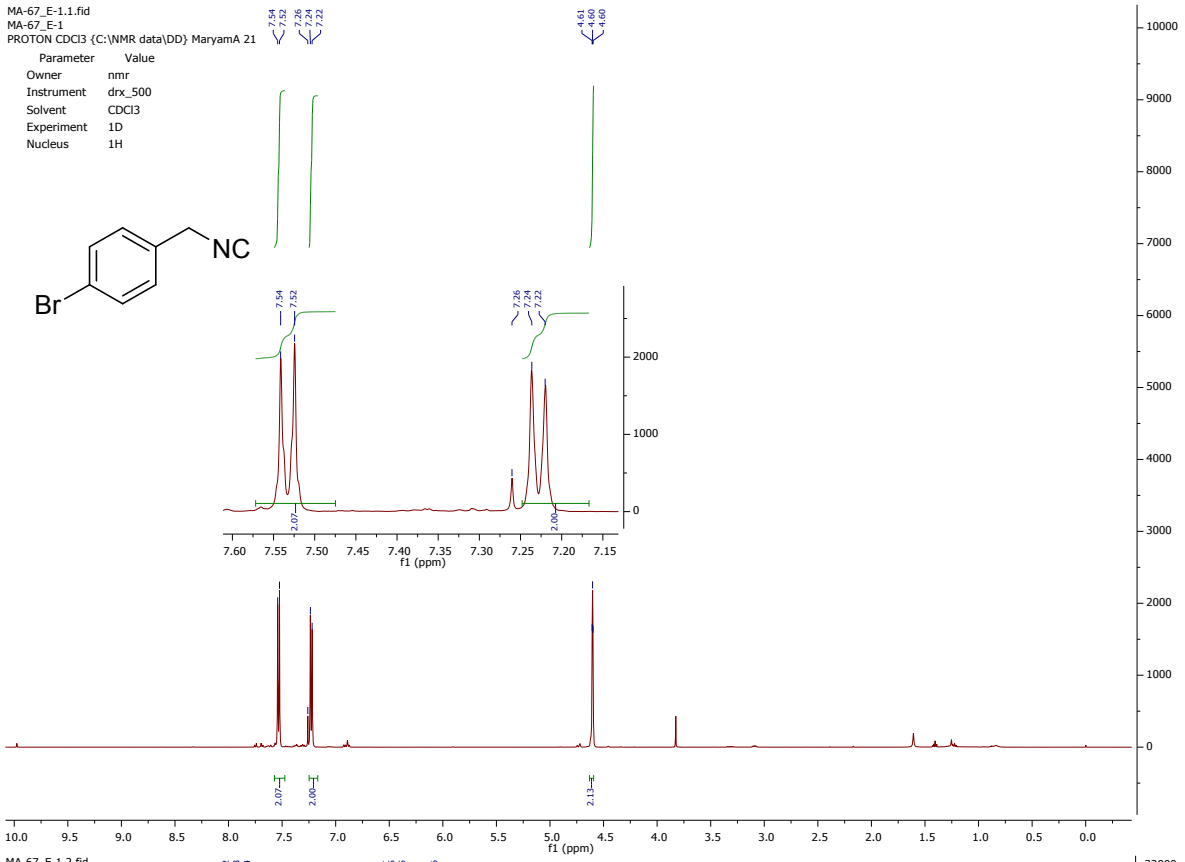


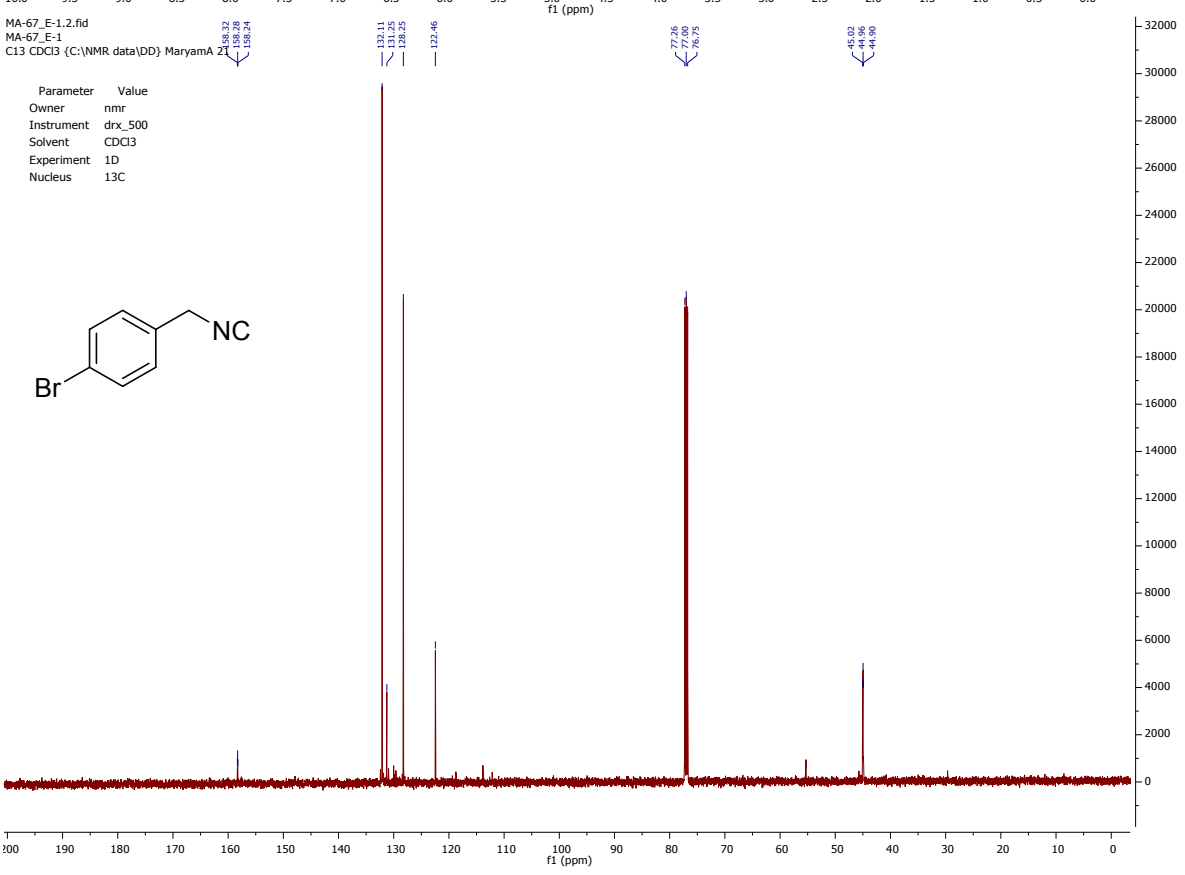
D-12 / I-34: 1-Ethoxy-4-isocyanobenzene



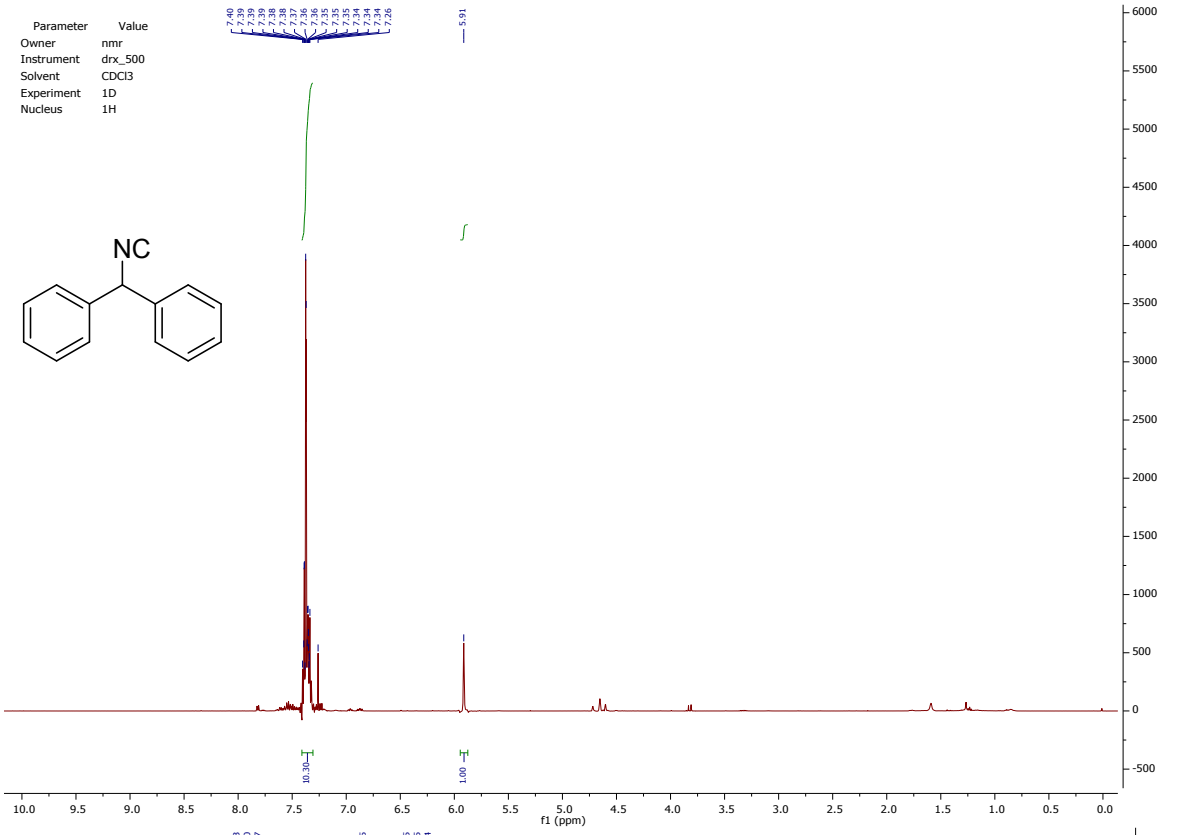


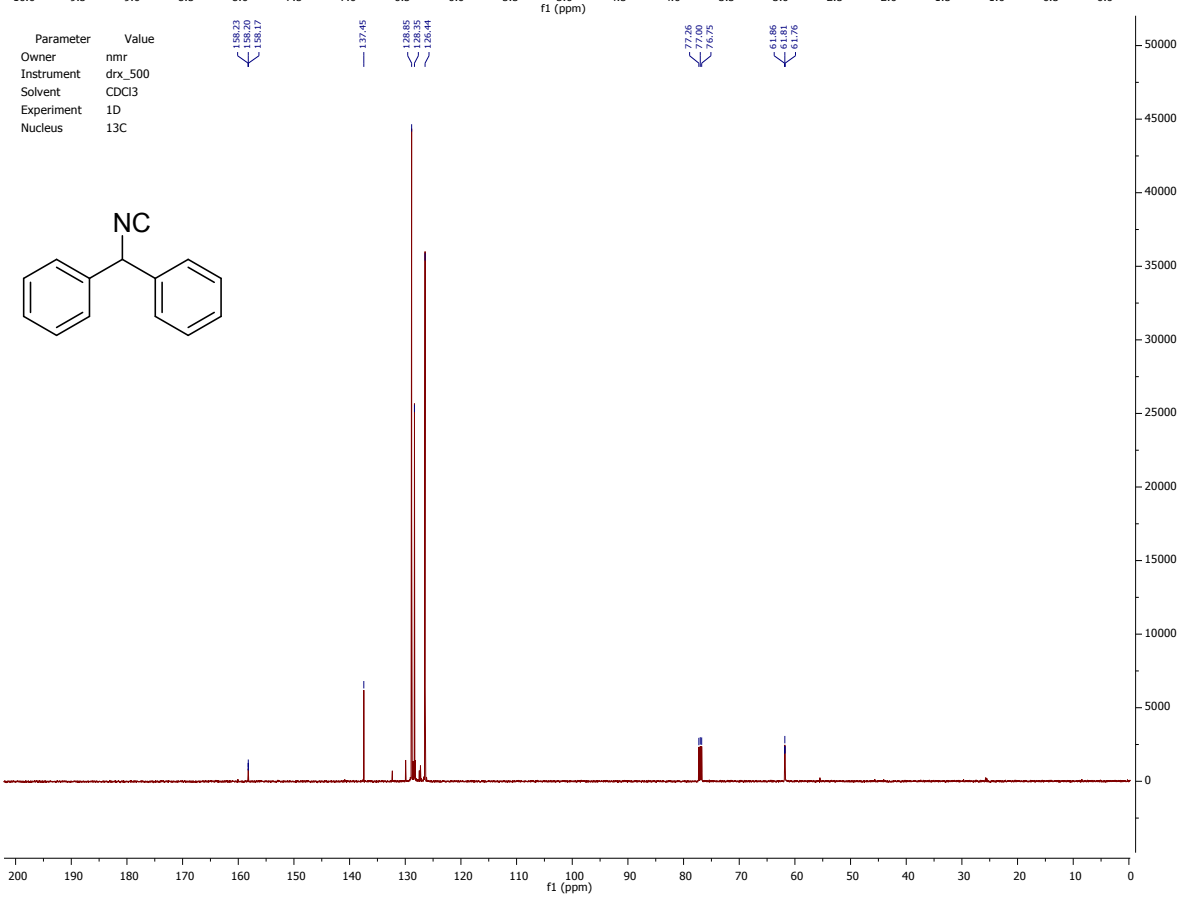
E-1: 1-Bromo-4-(isocyanomethyl)benzene



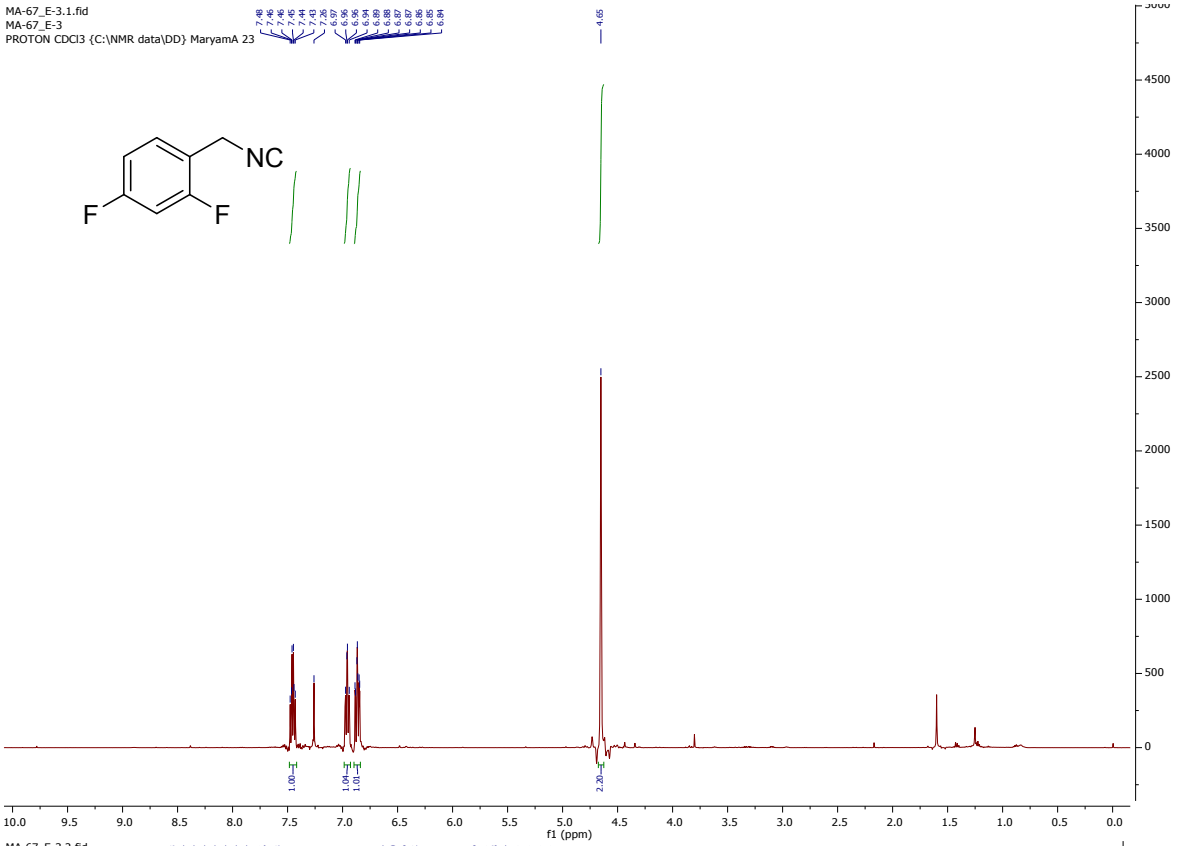


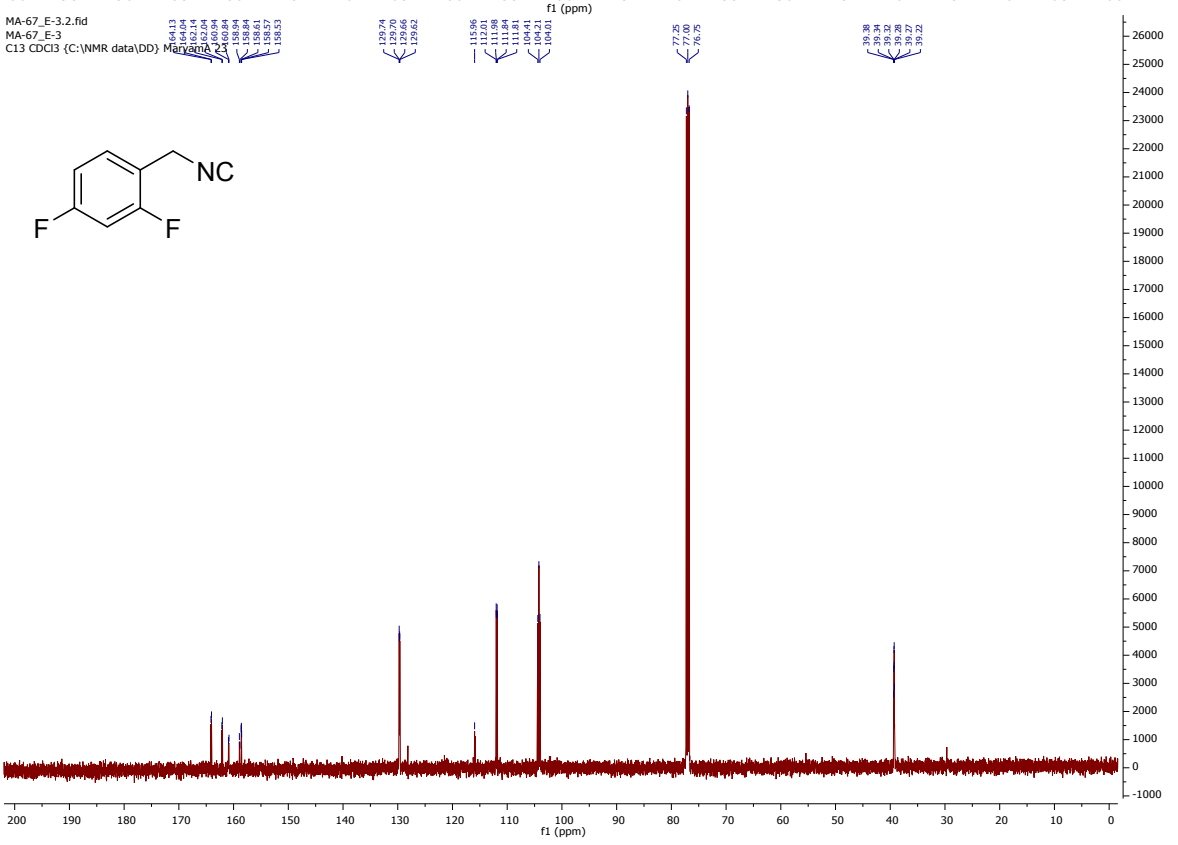
E-2 / I-8: (Isocyanomethylene)dibenzene



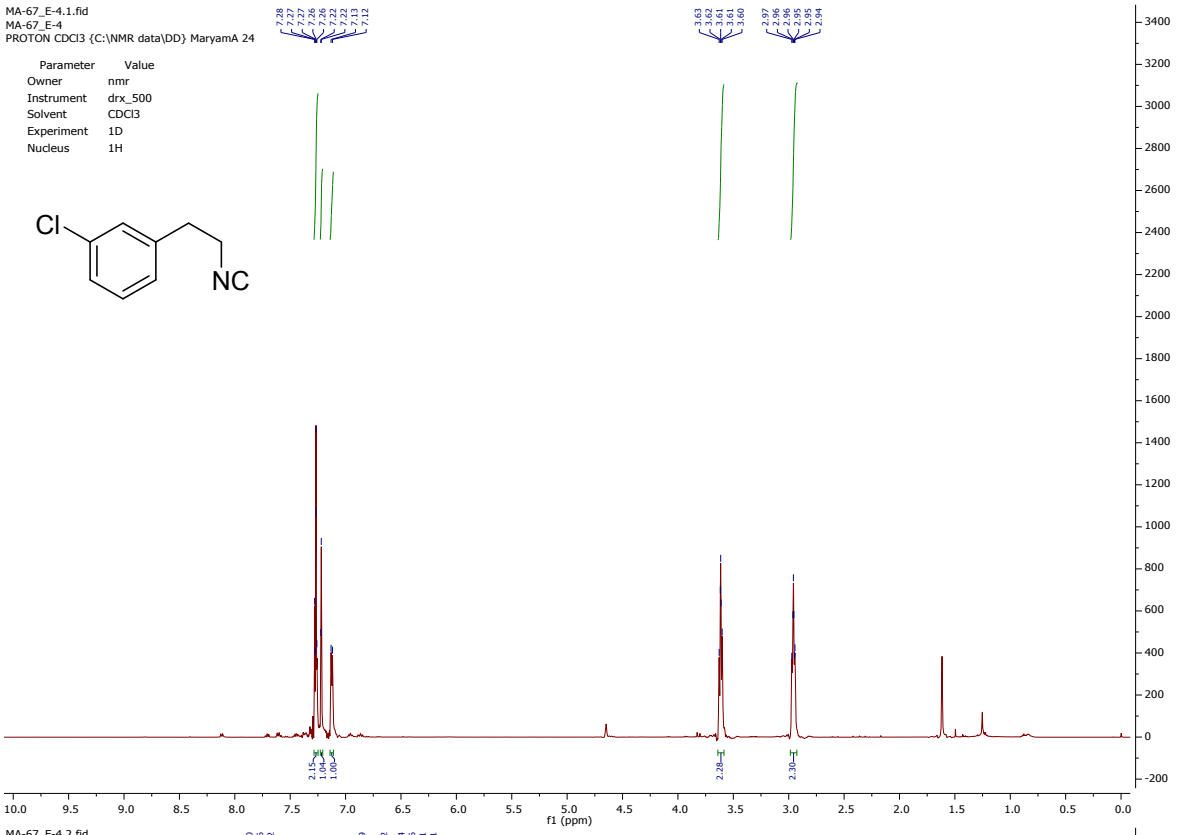


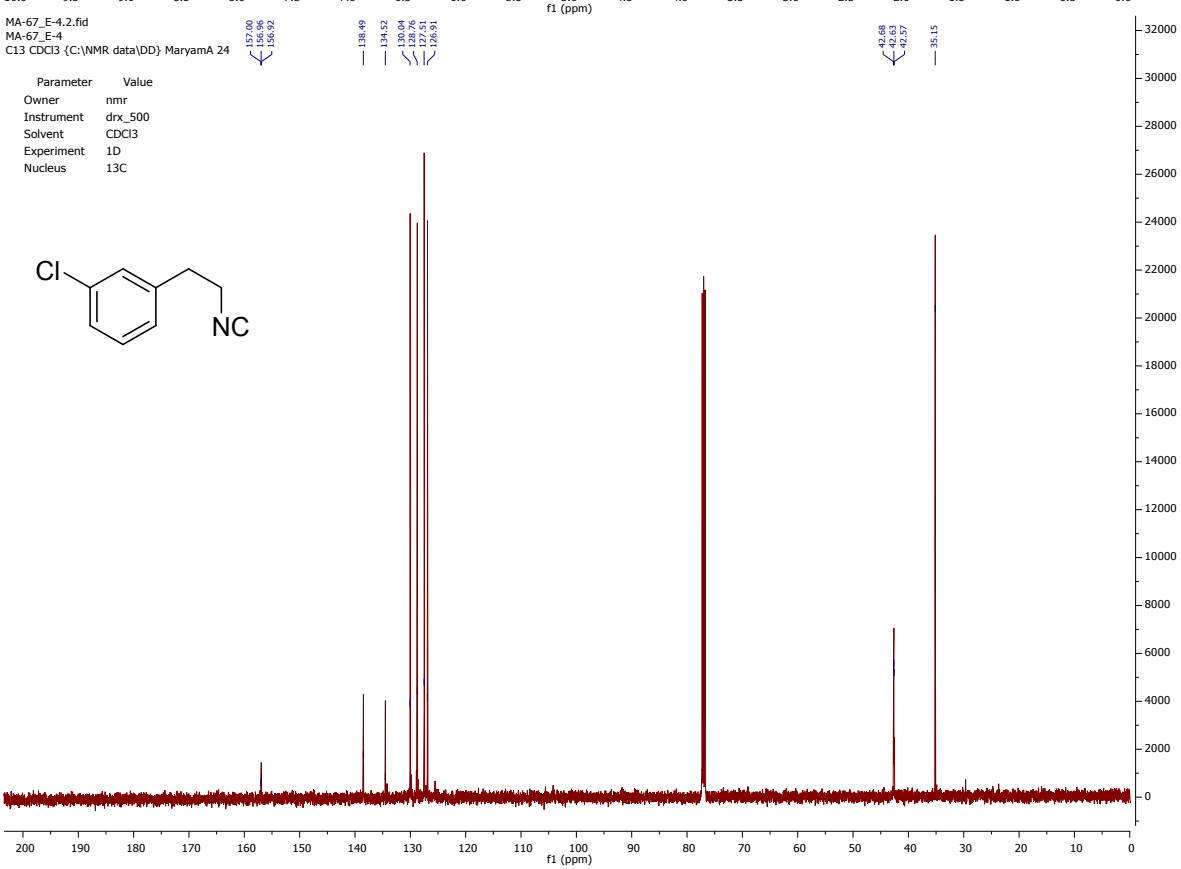
E-3: 2,4-Difluoro-1-(isocyanomethyl)benzene



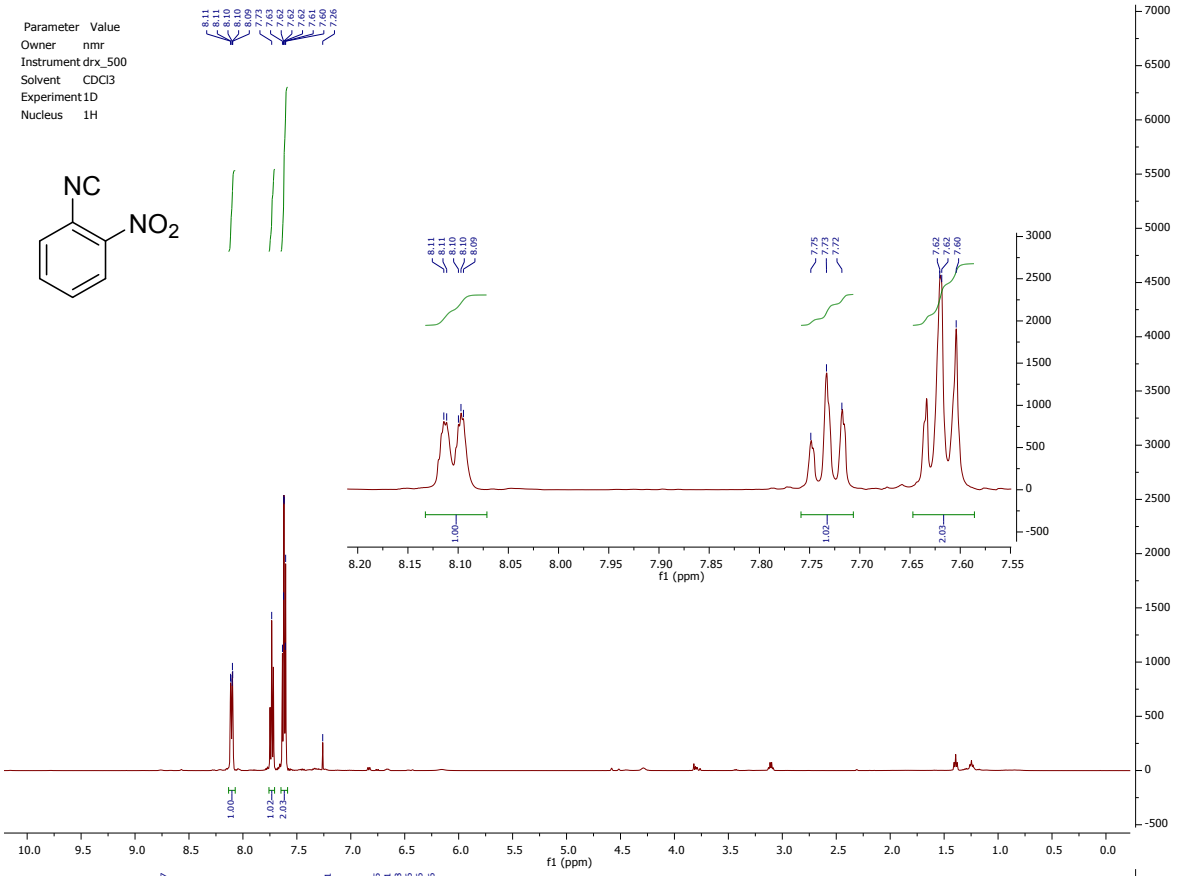


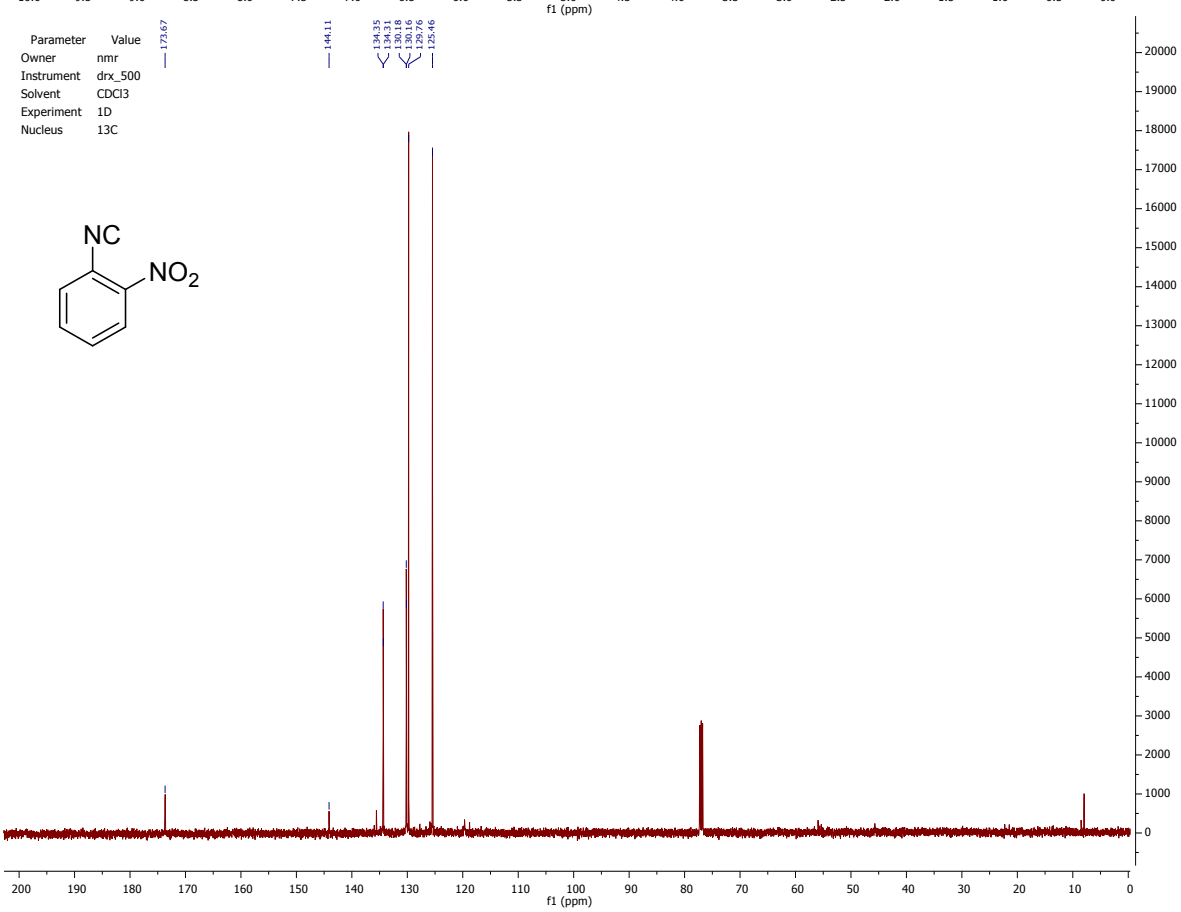
E-4: 1-Chloro-3-(2-isocyanoethyl)benzene



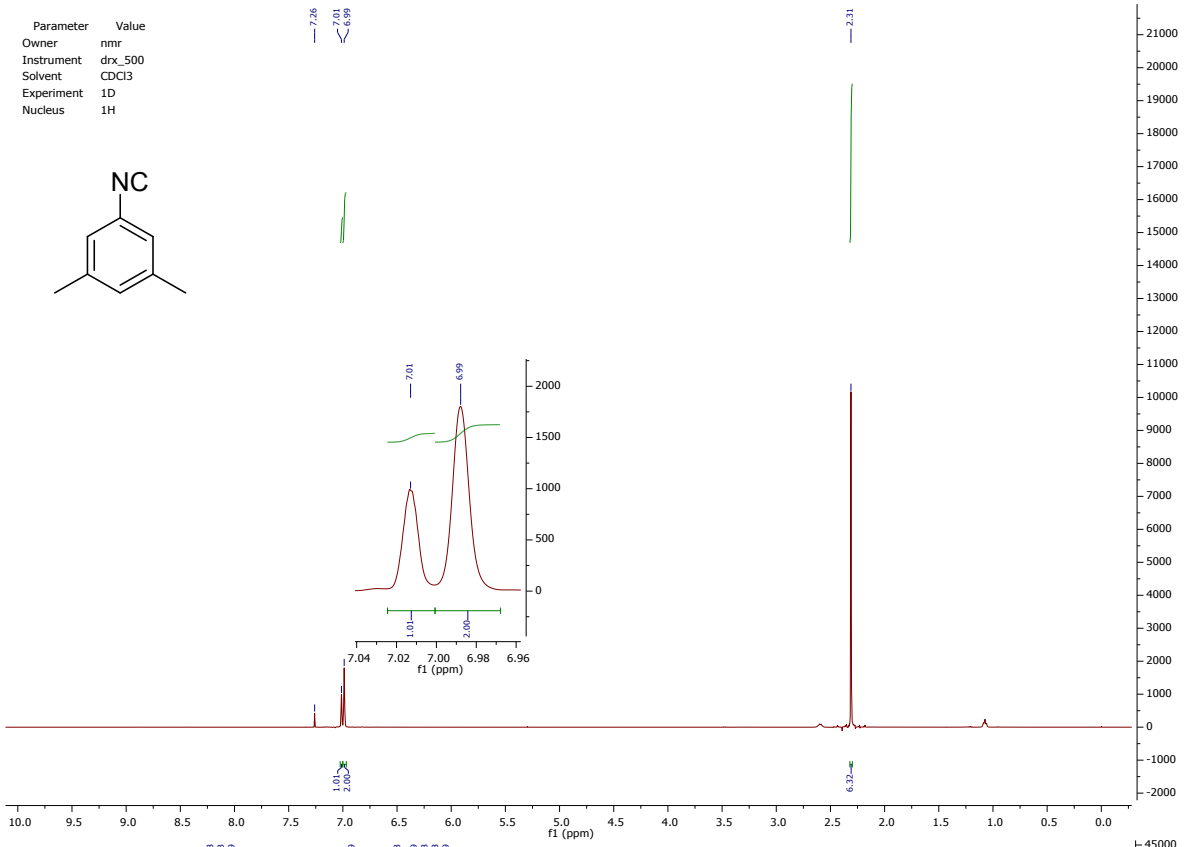


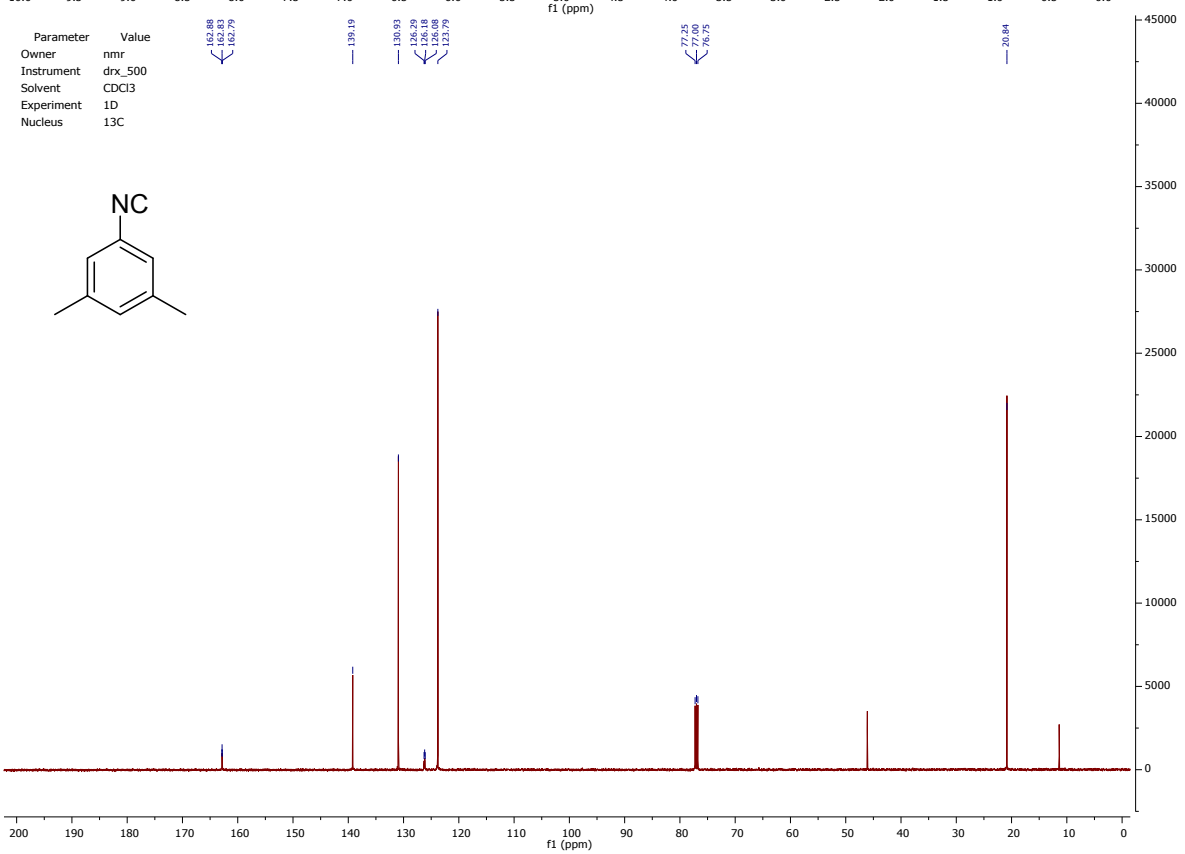
E-5 / I-32: 1-Isocyano-2-nitrobenzene



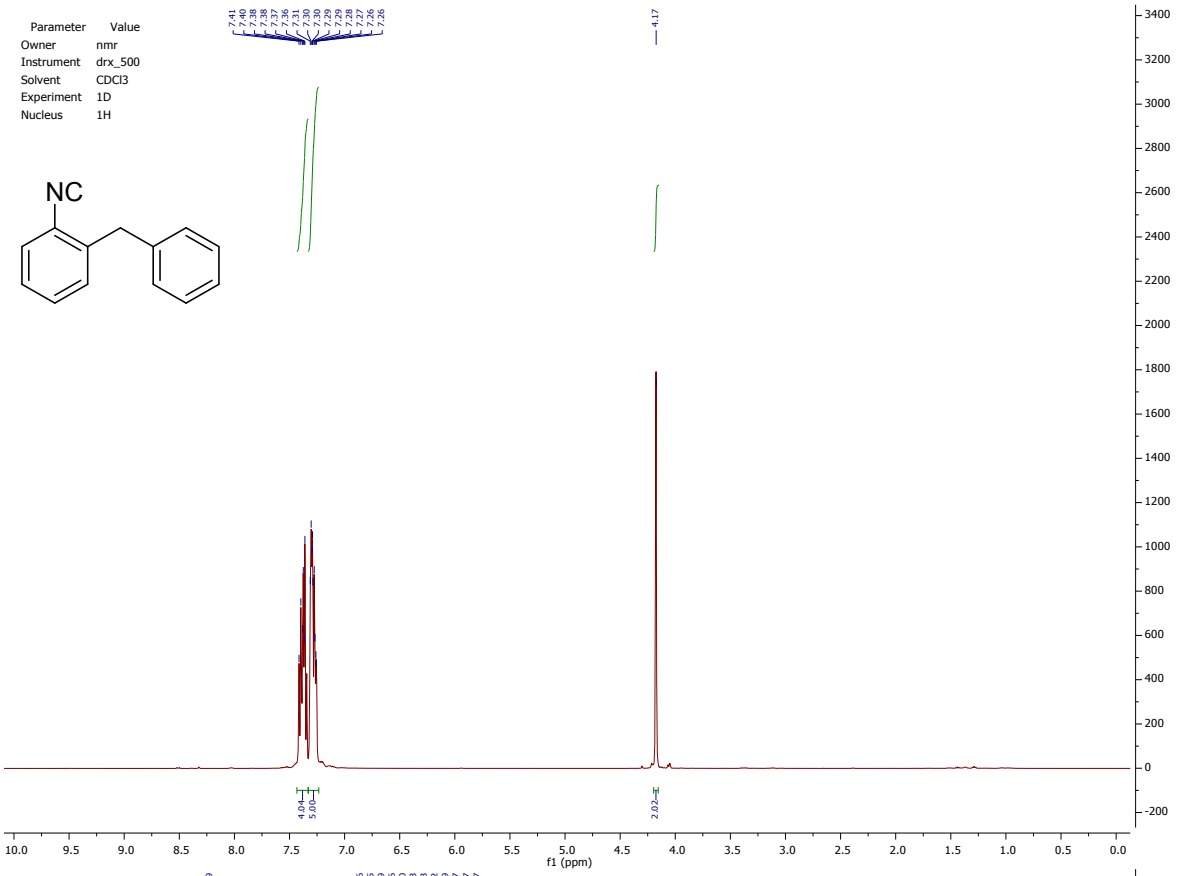


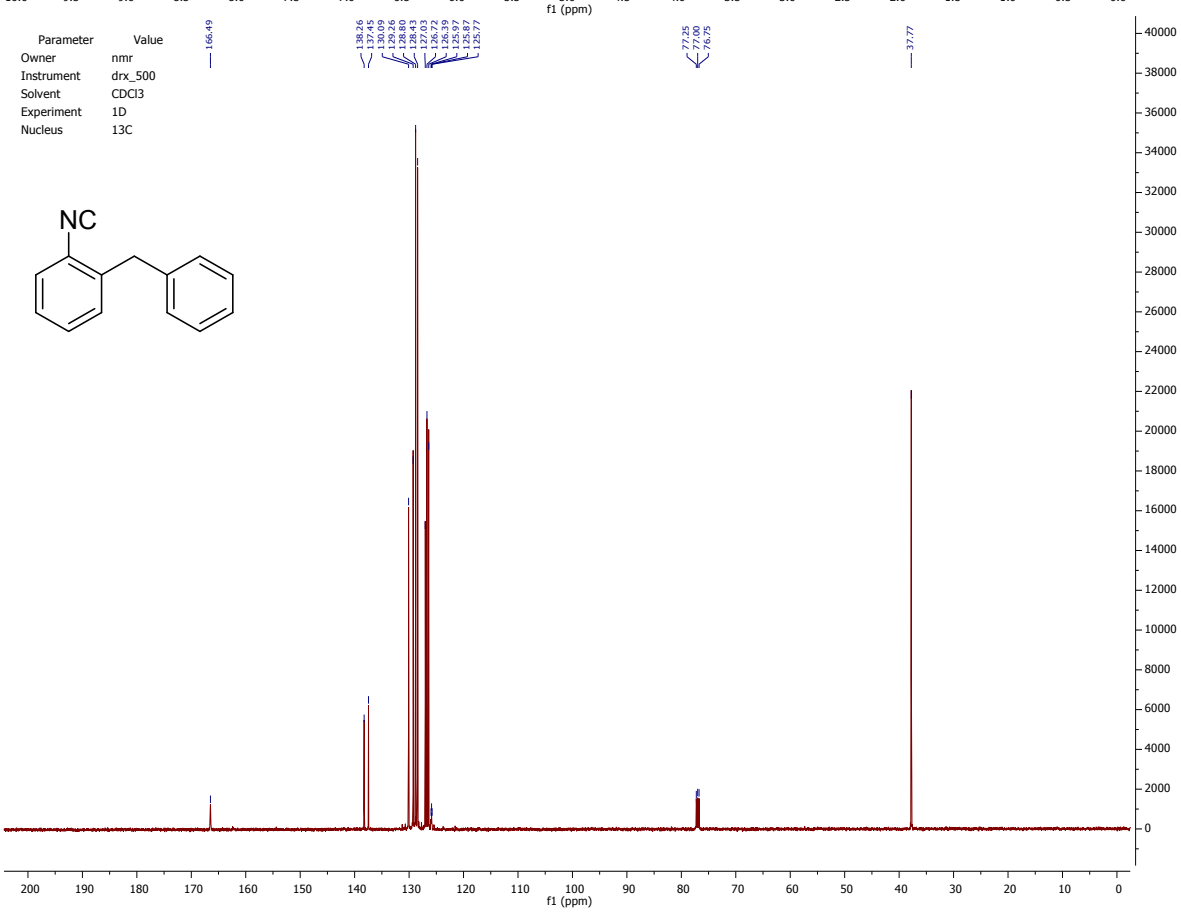
E-6: 1-Isocyano-3,5-dimethylbenzene



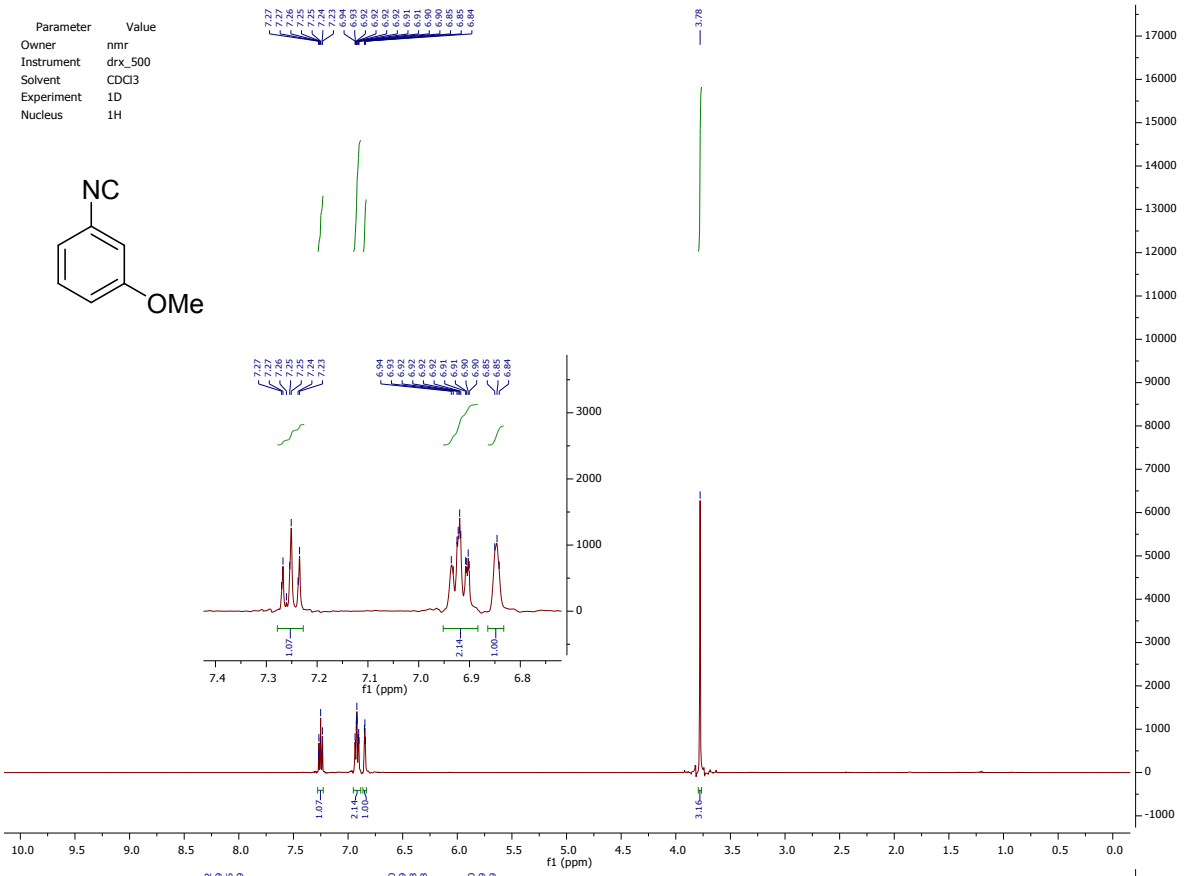


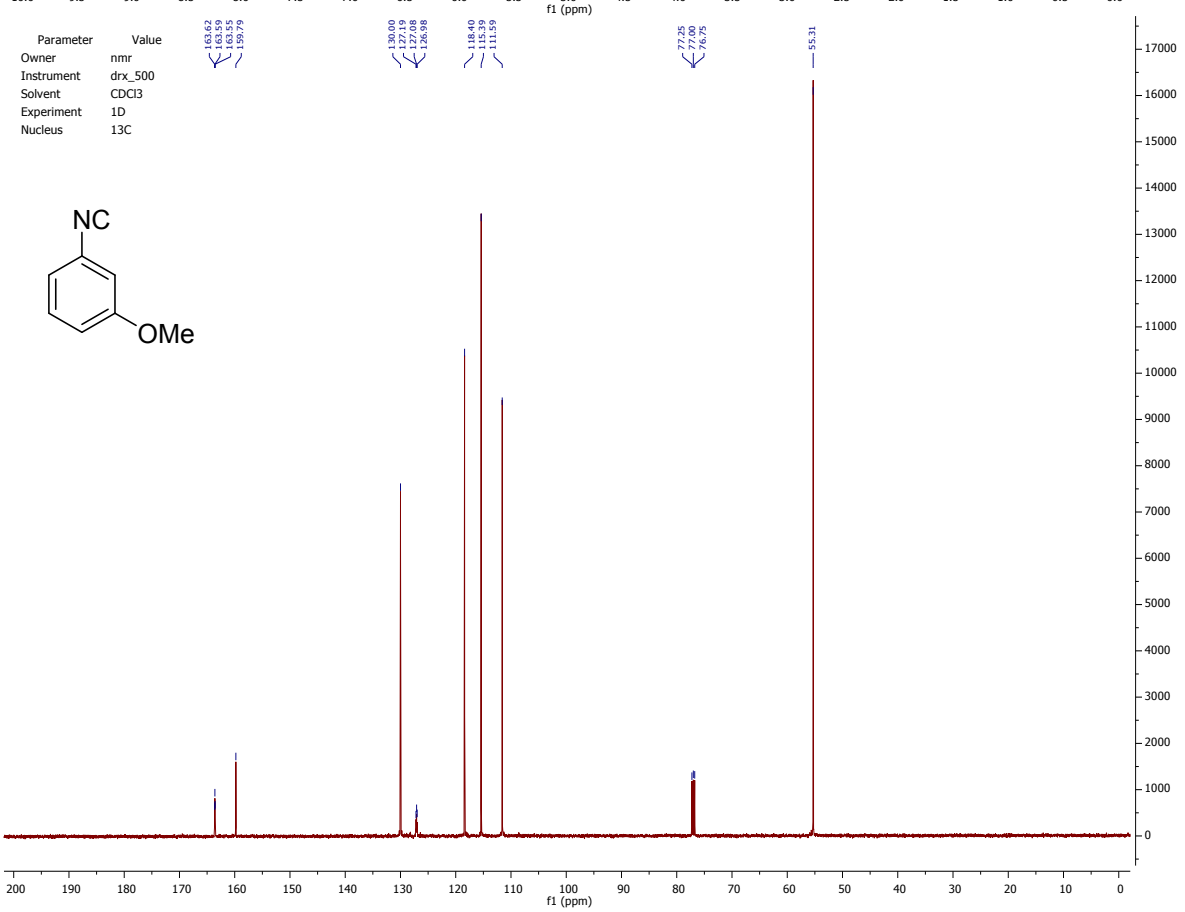
E-7 / I-28: 1-Benzyl-2-isocyanobenzene



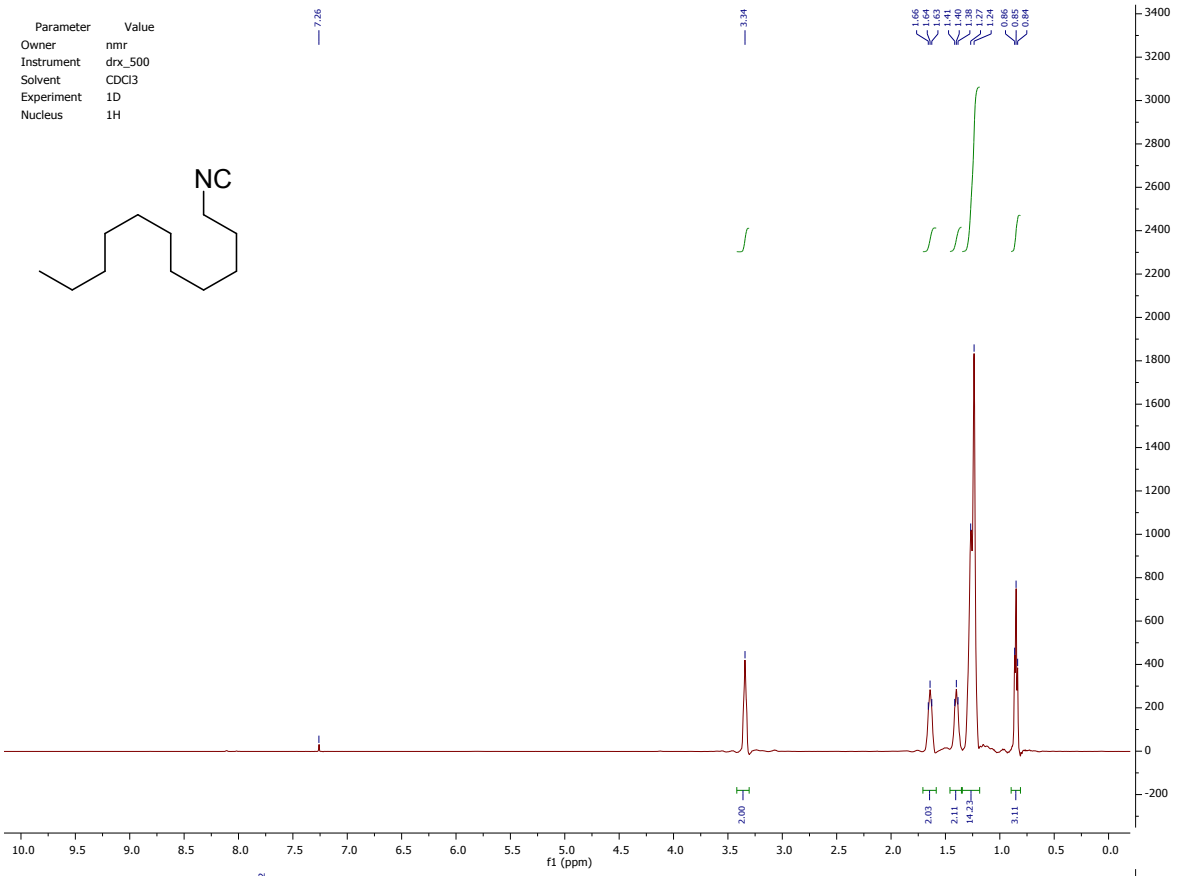


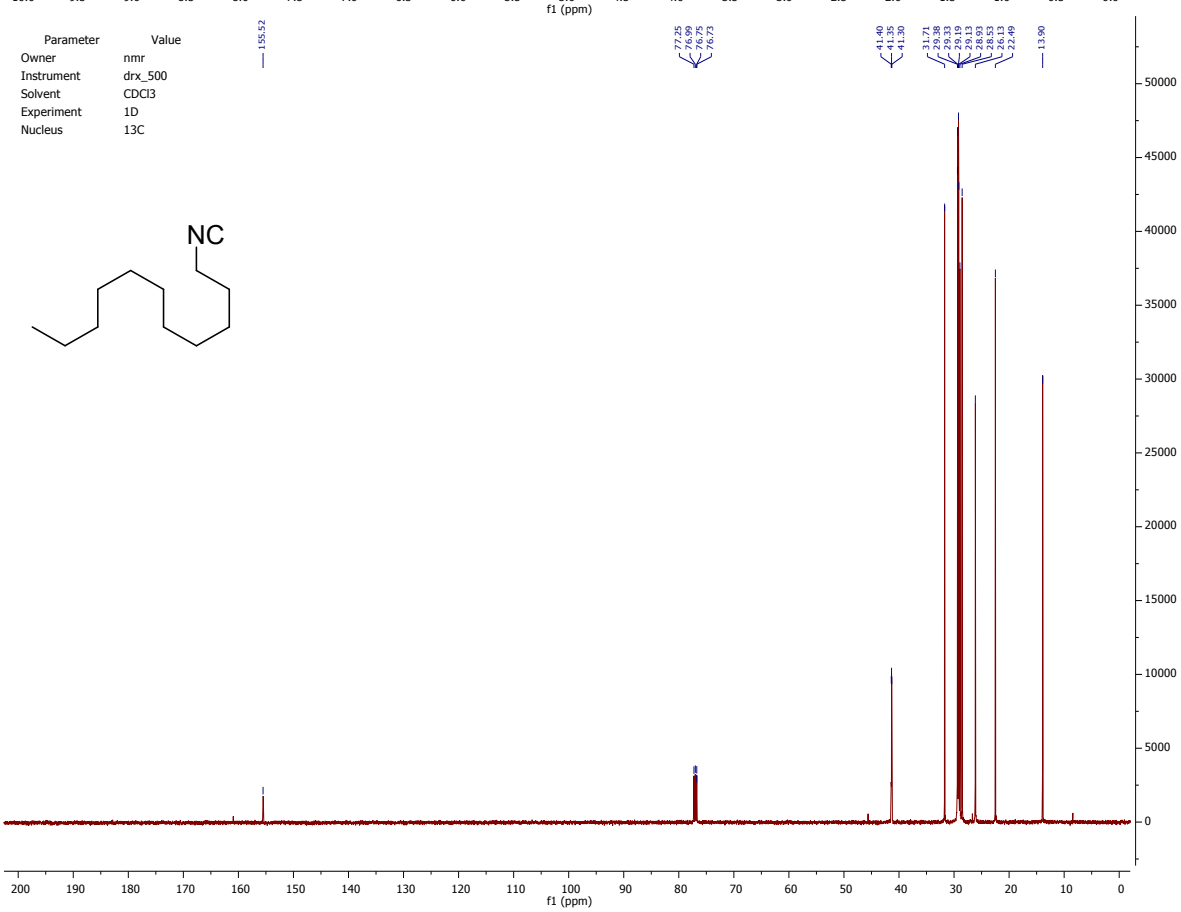
E-8 / I-31: 1-Isocyano-3-methoxybenzene



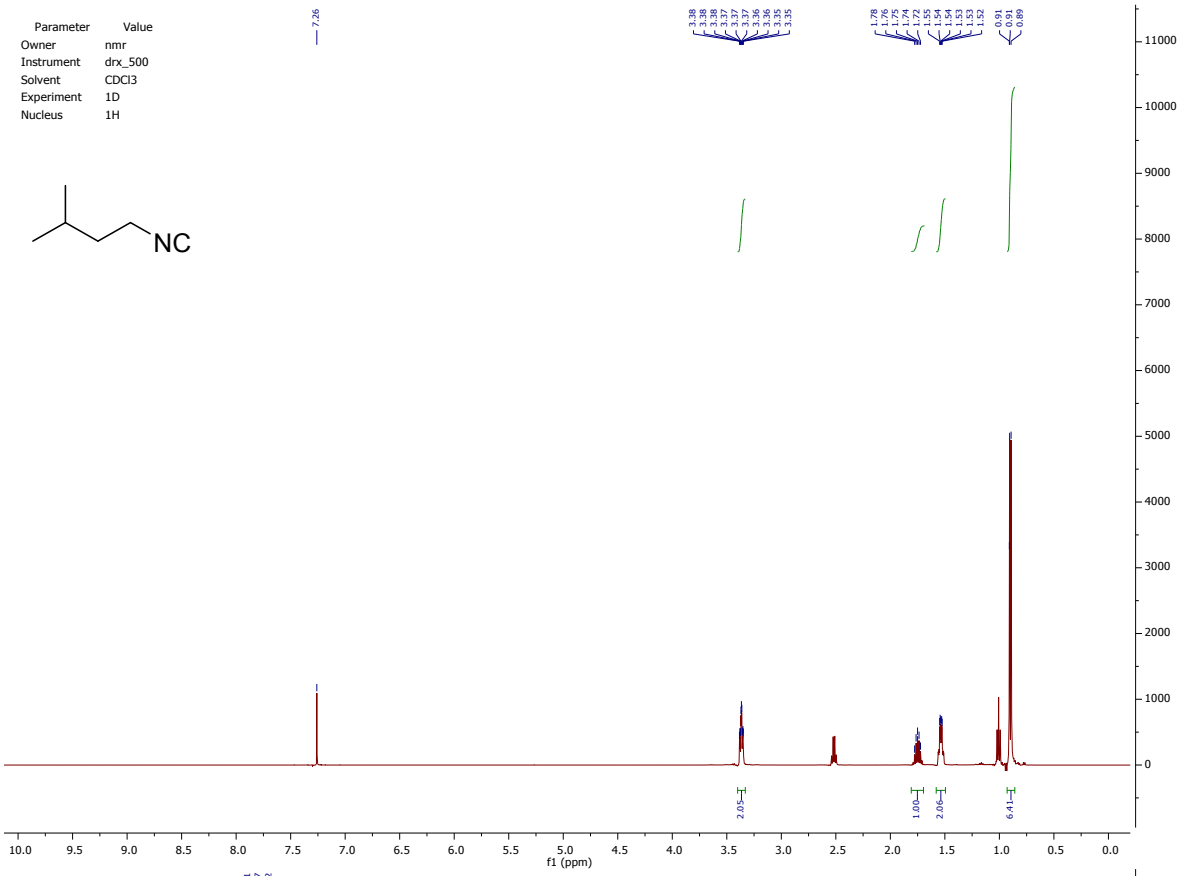


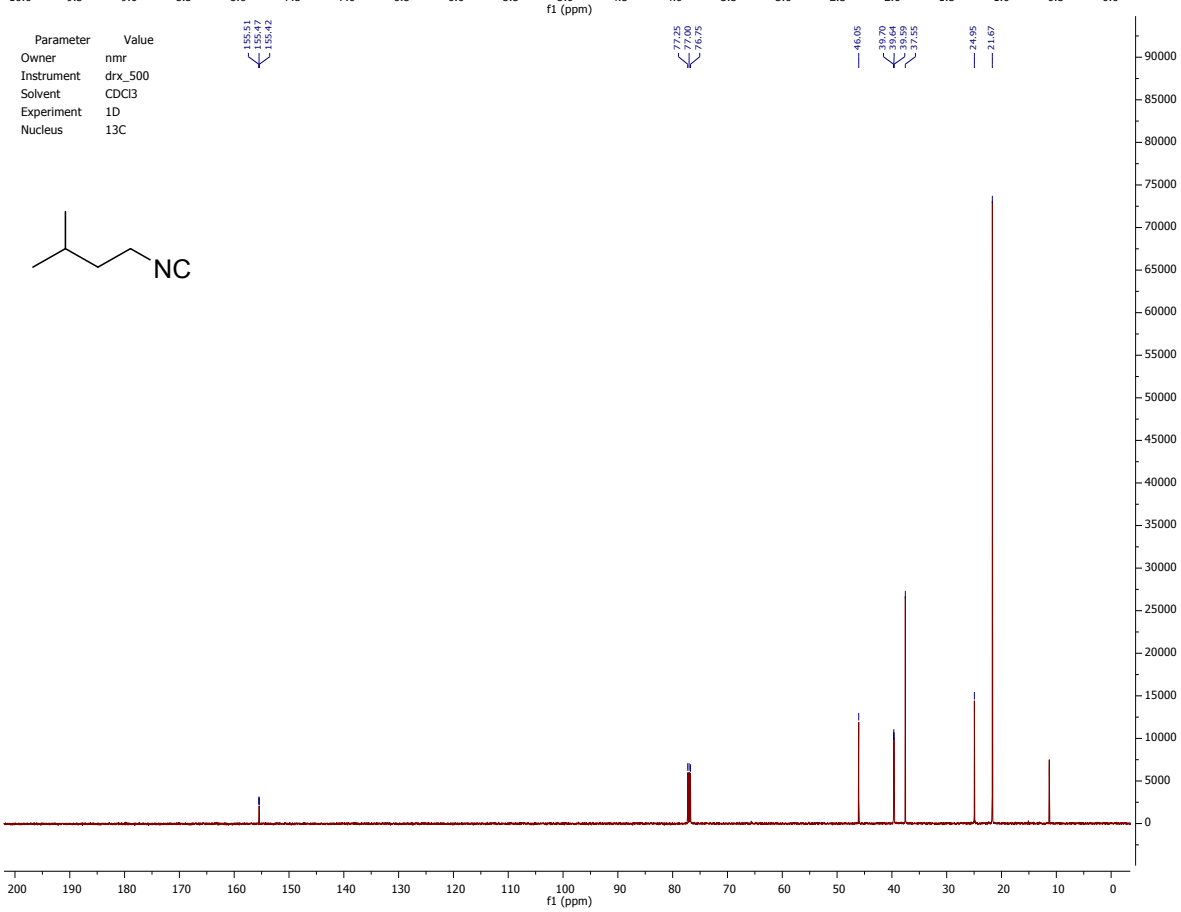
E-9 / I-39: 1-Isocyanoundecane



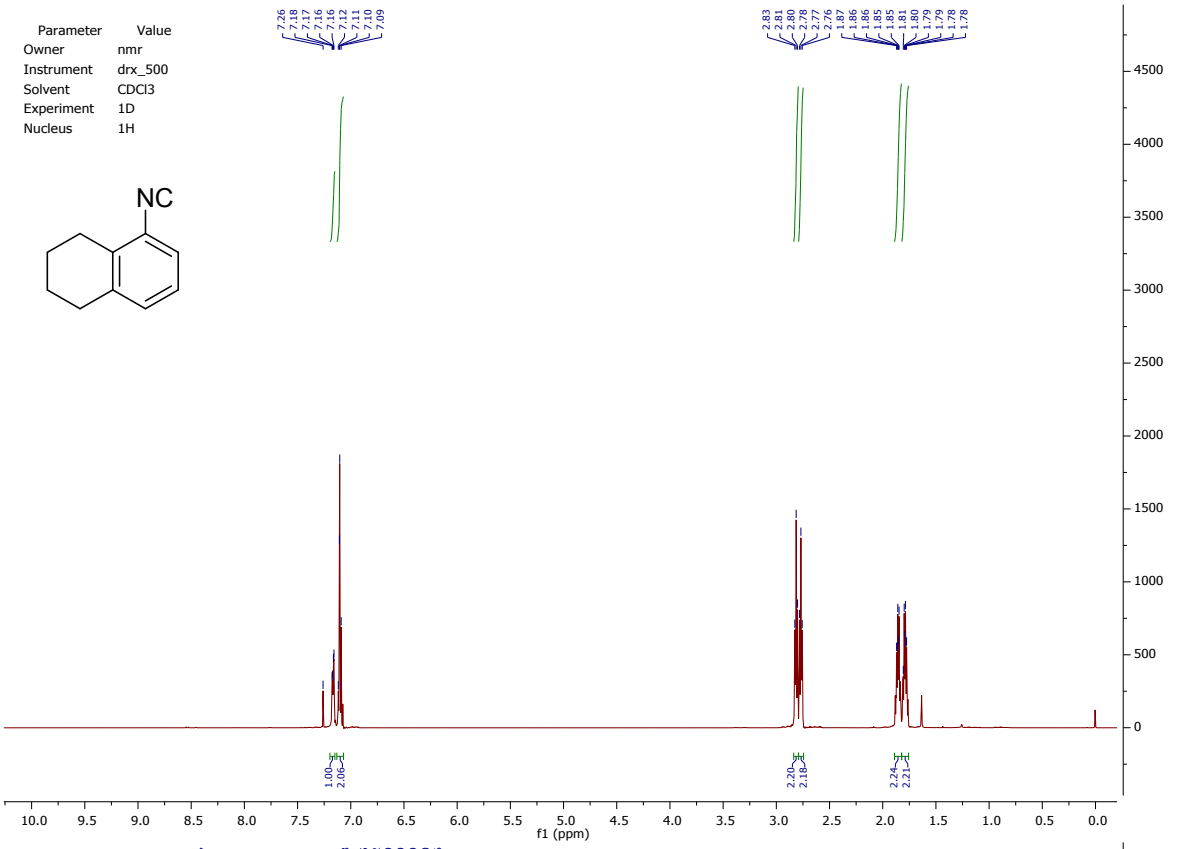


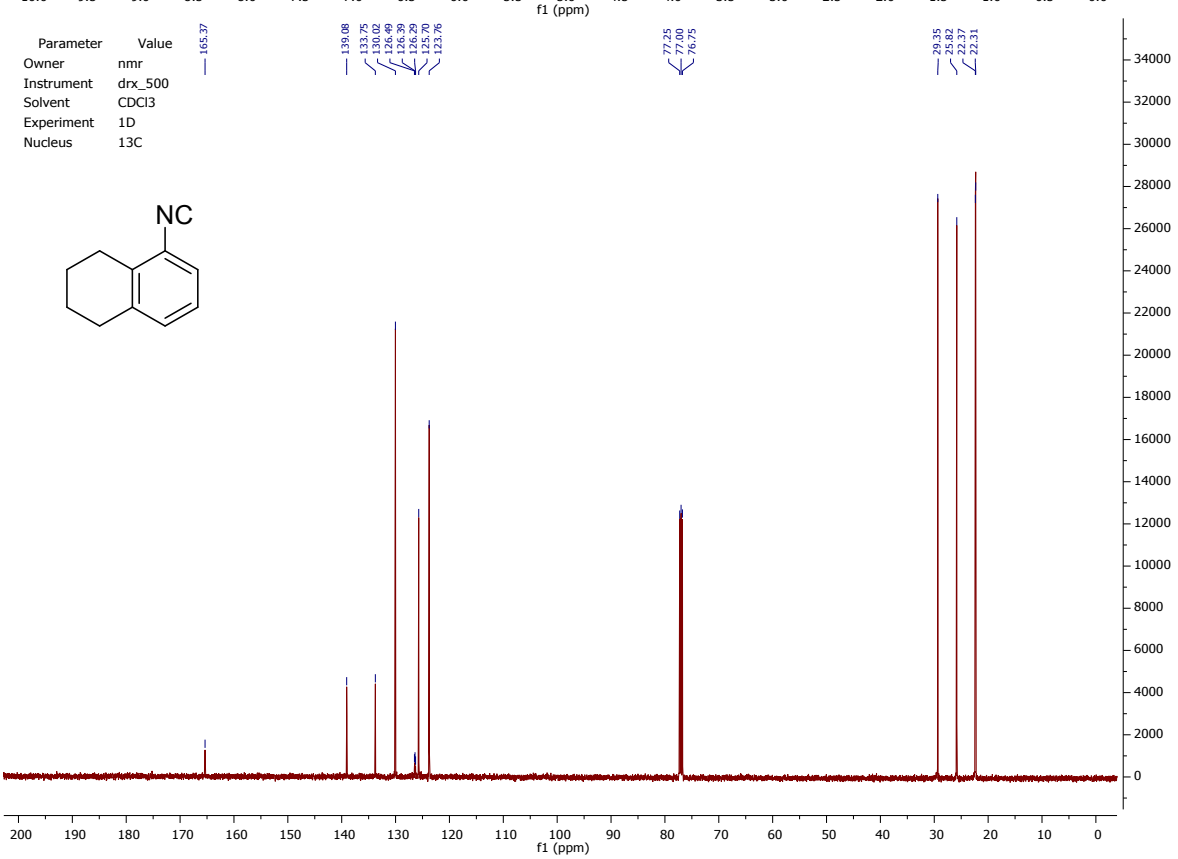
E-10 / I-47: 1-Isocyano-3-methylbutane



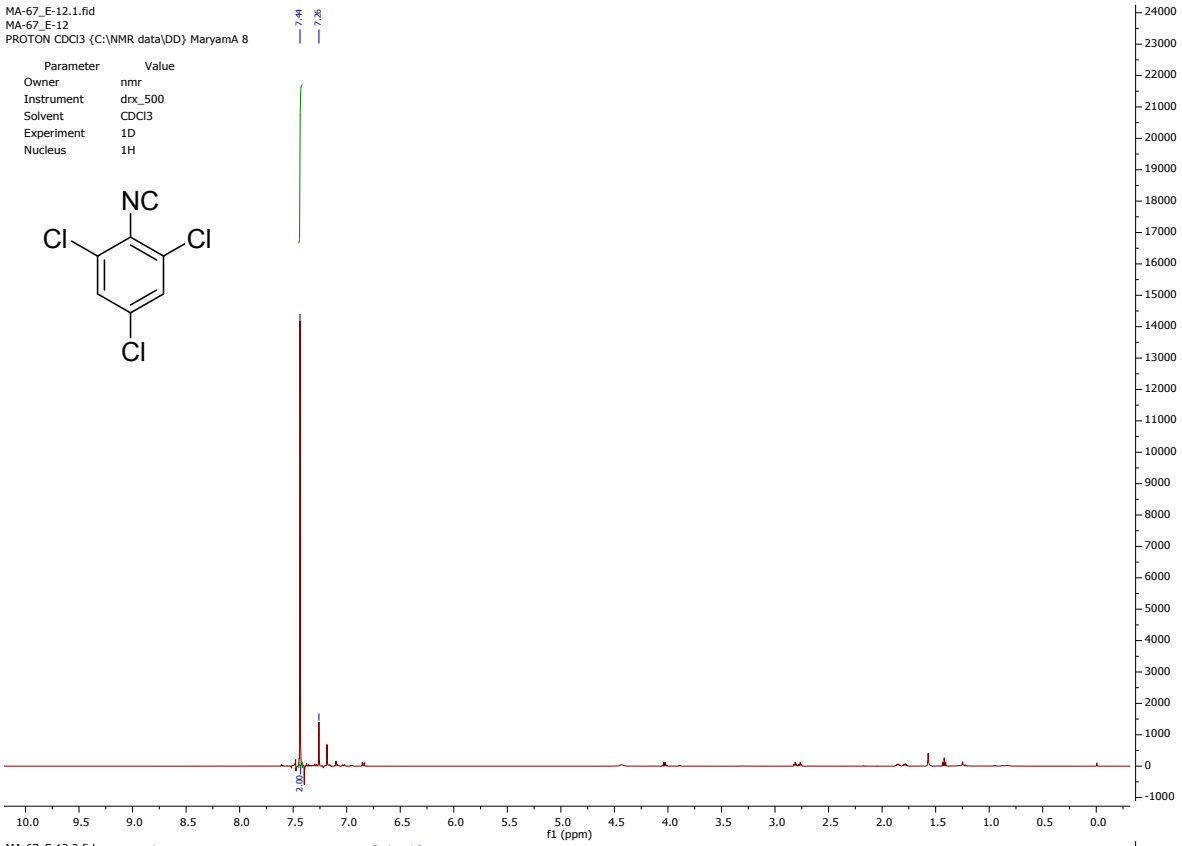


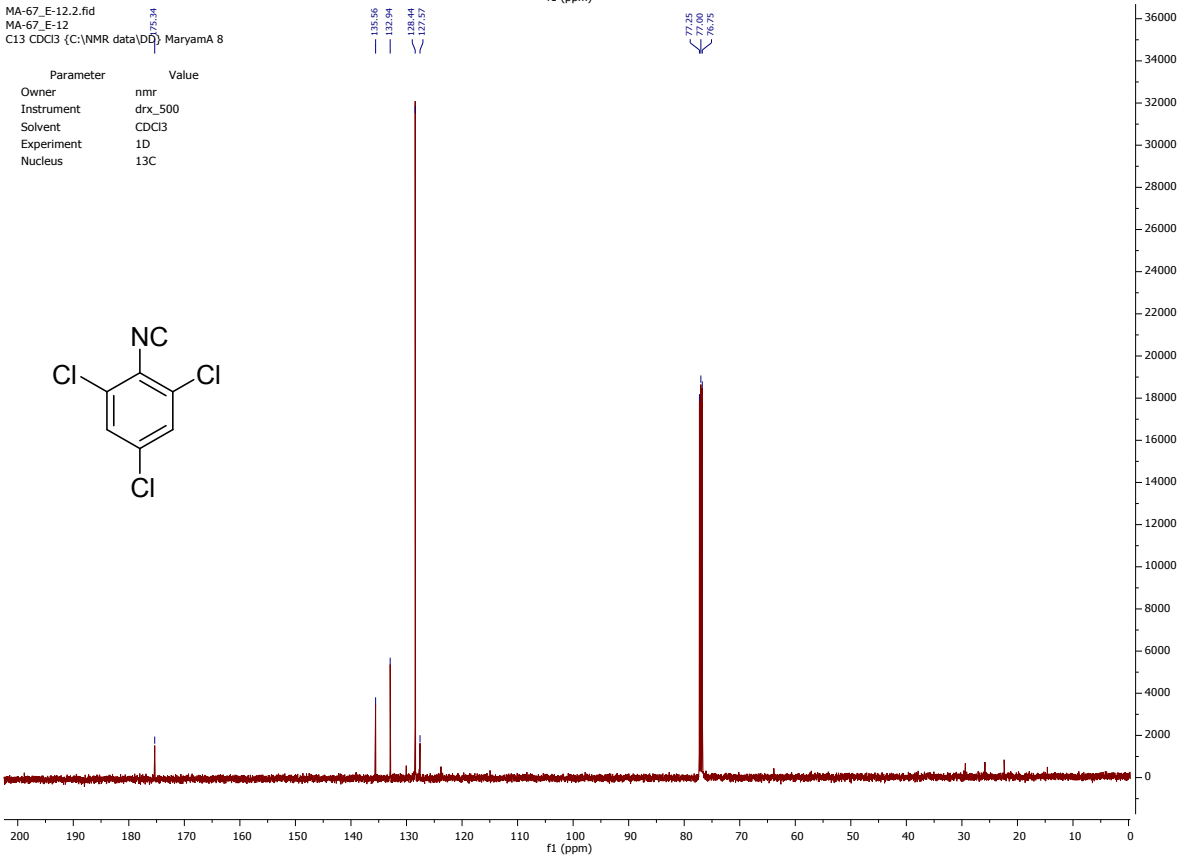
E-11: 5-Isocyano-1,2,3,4-tetrahydronaphthalene



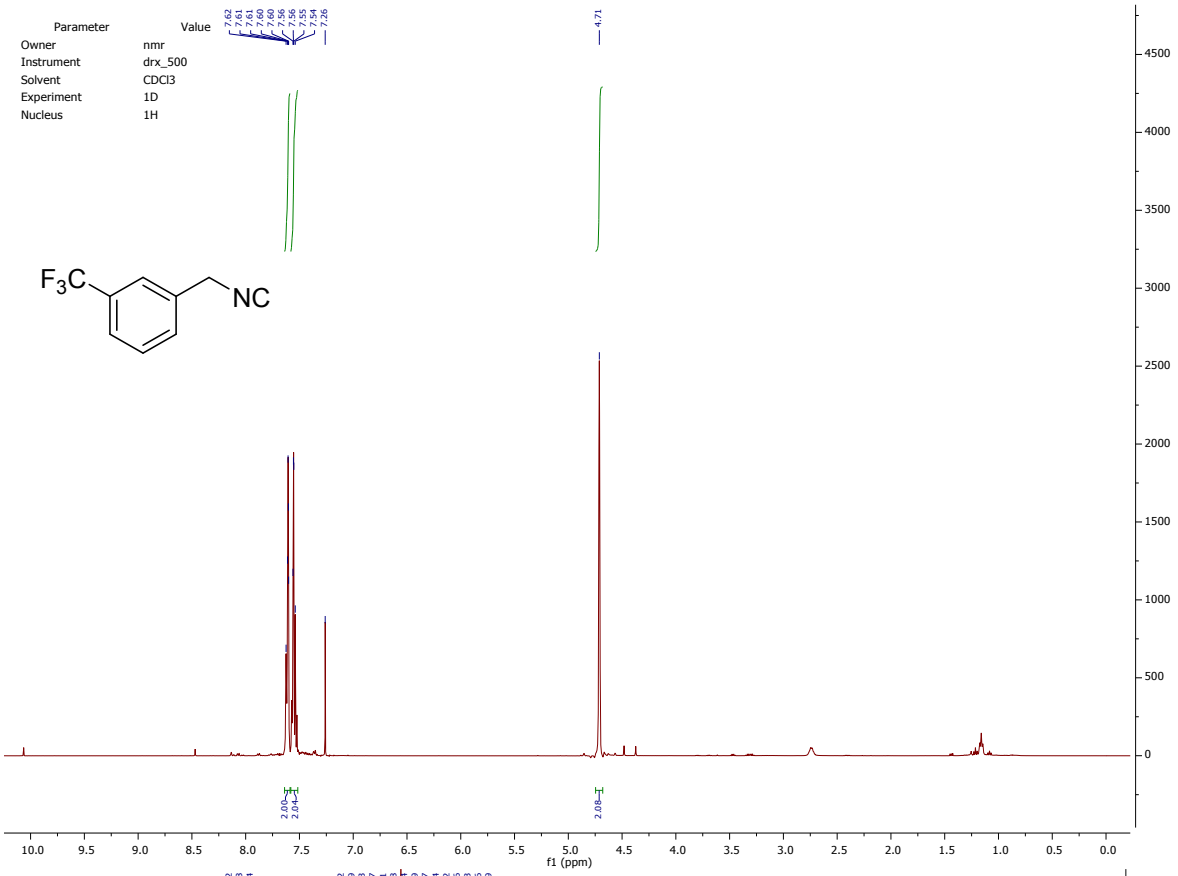


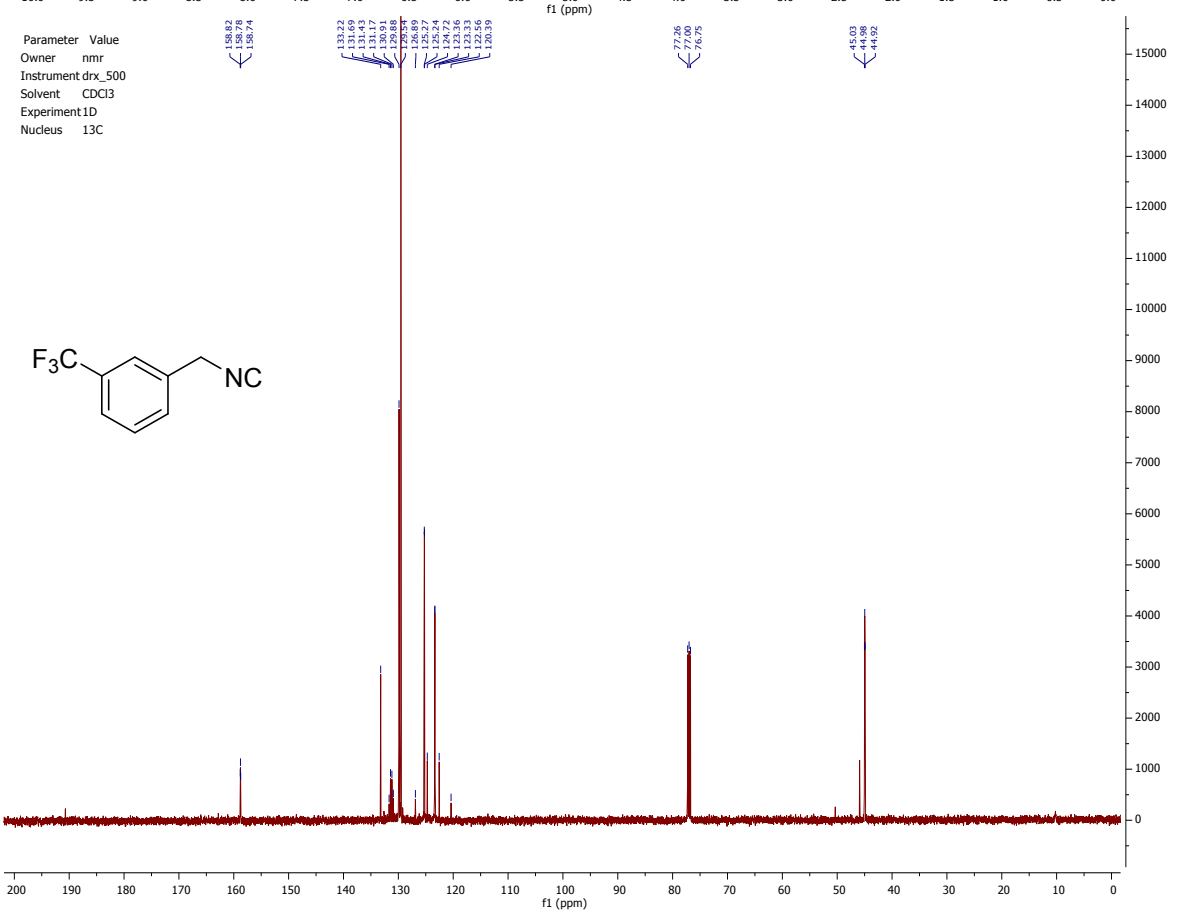
E-12: 1,3,5-Trichloro-2-isocyanobenzene



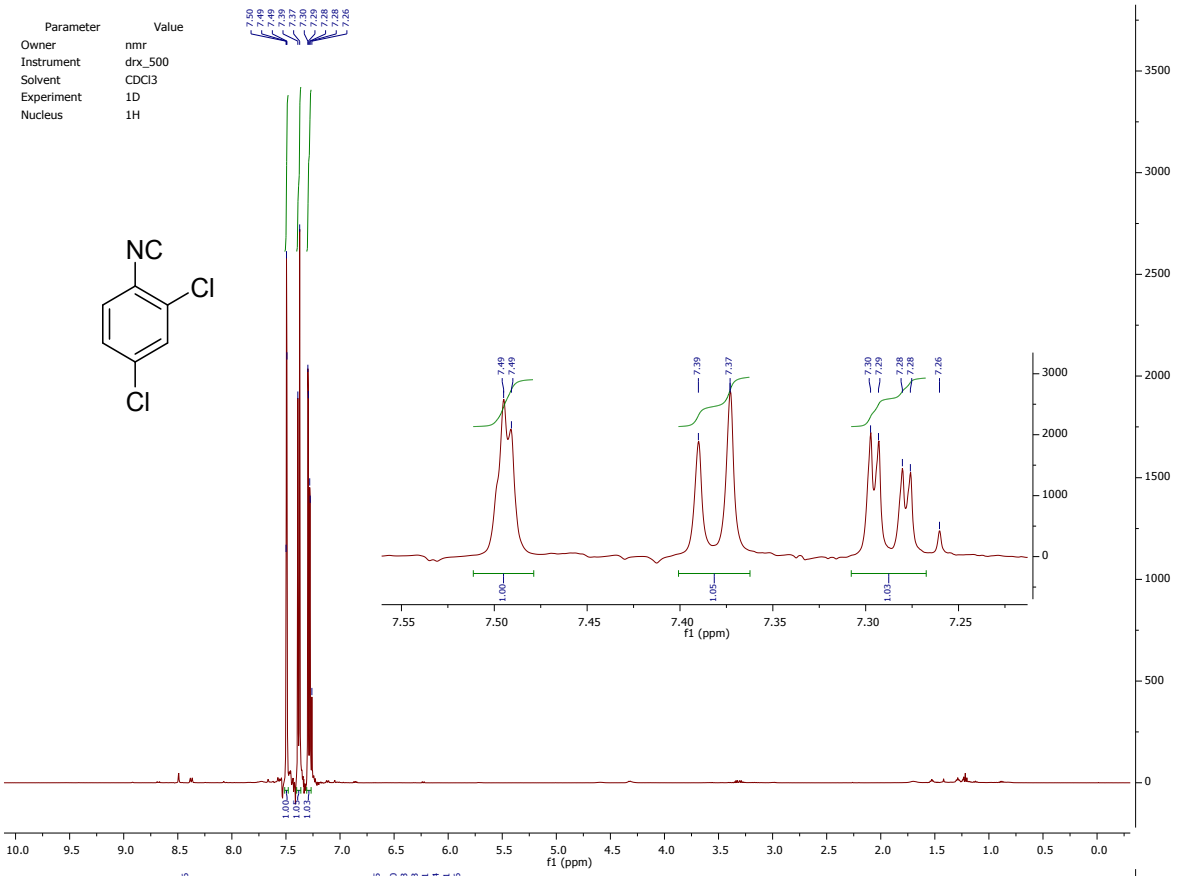


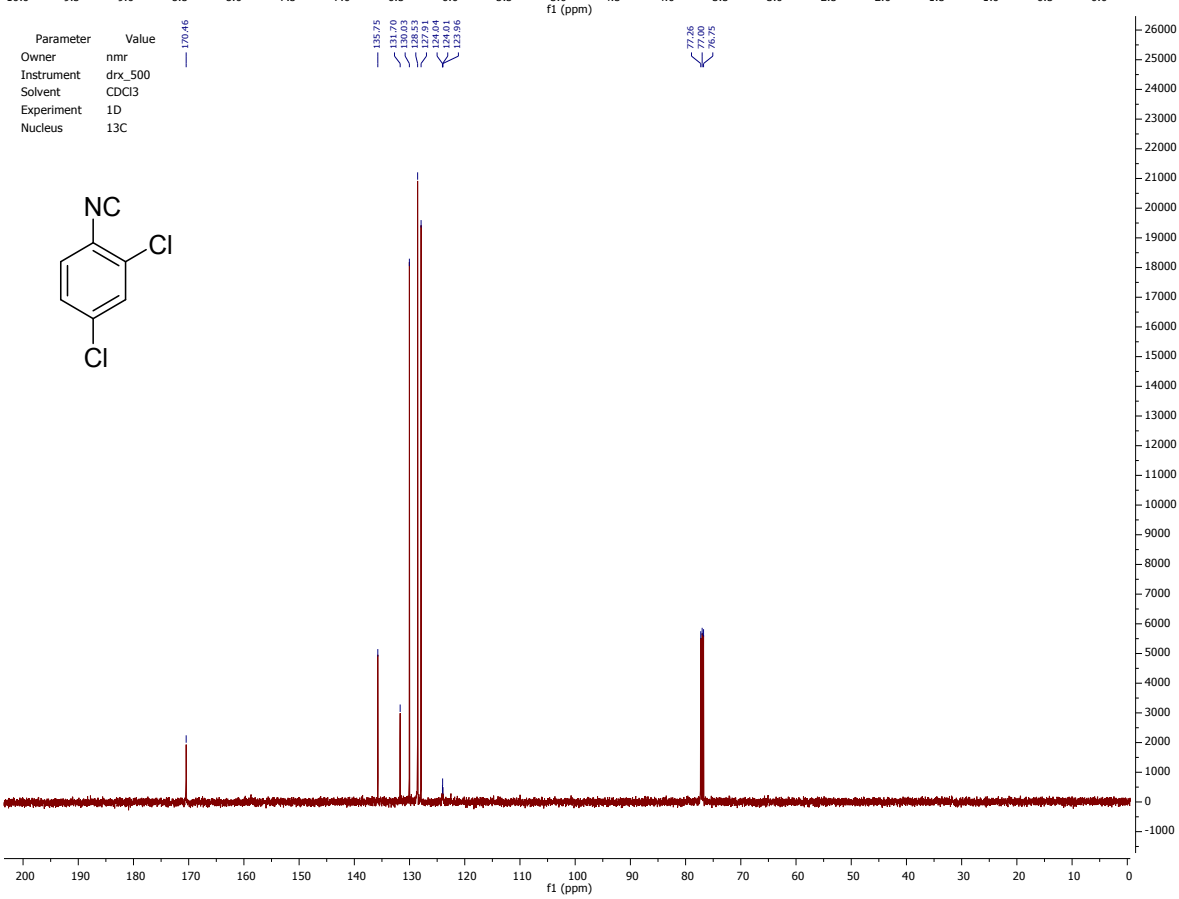
F-1 / I-4: 1-(Isocyanomethyl)-3-(trifluoromethyl)benzene



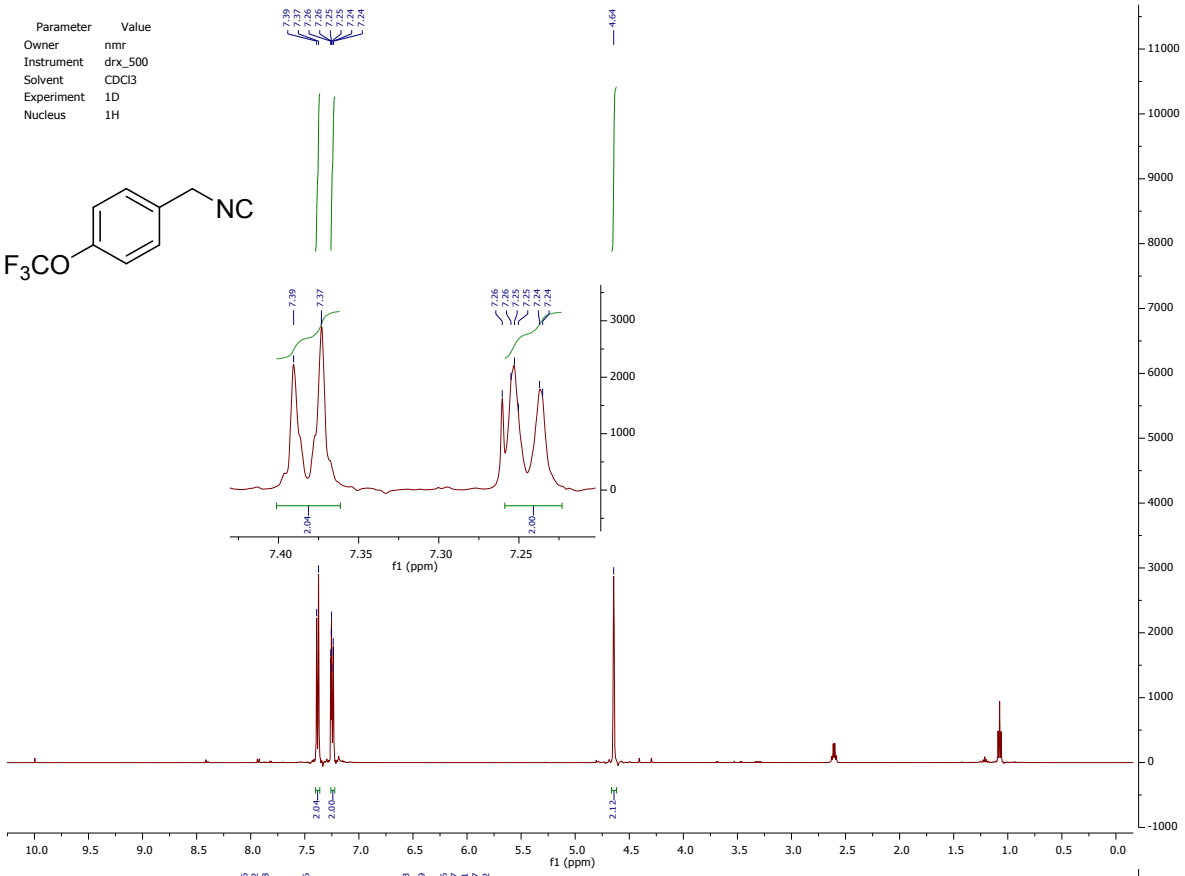


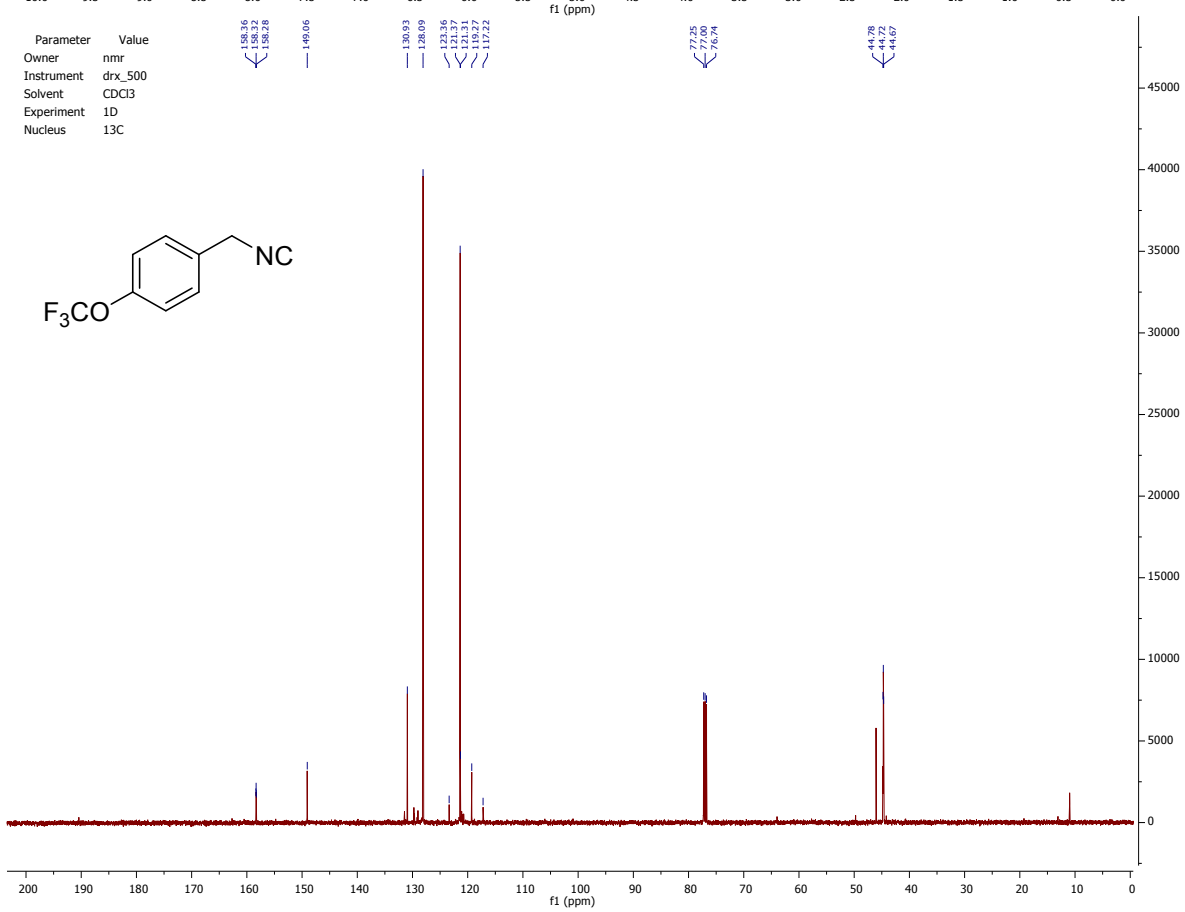
F-2 / I-9: 2,4-Dichloro-1-isocyanobenzene



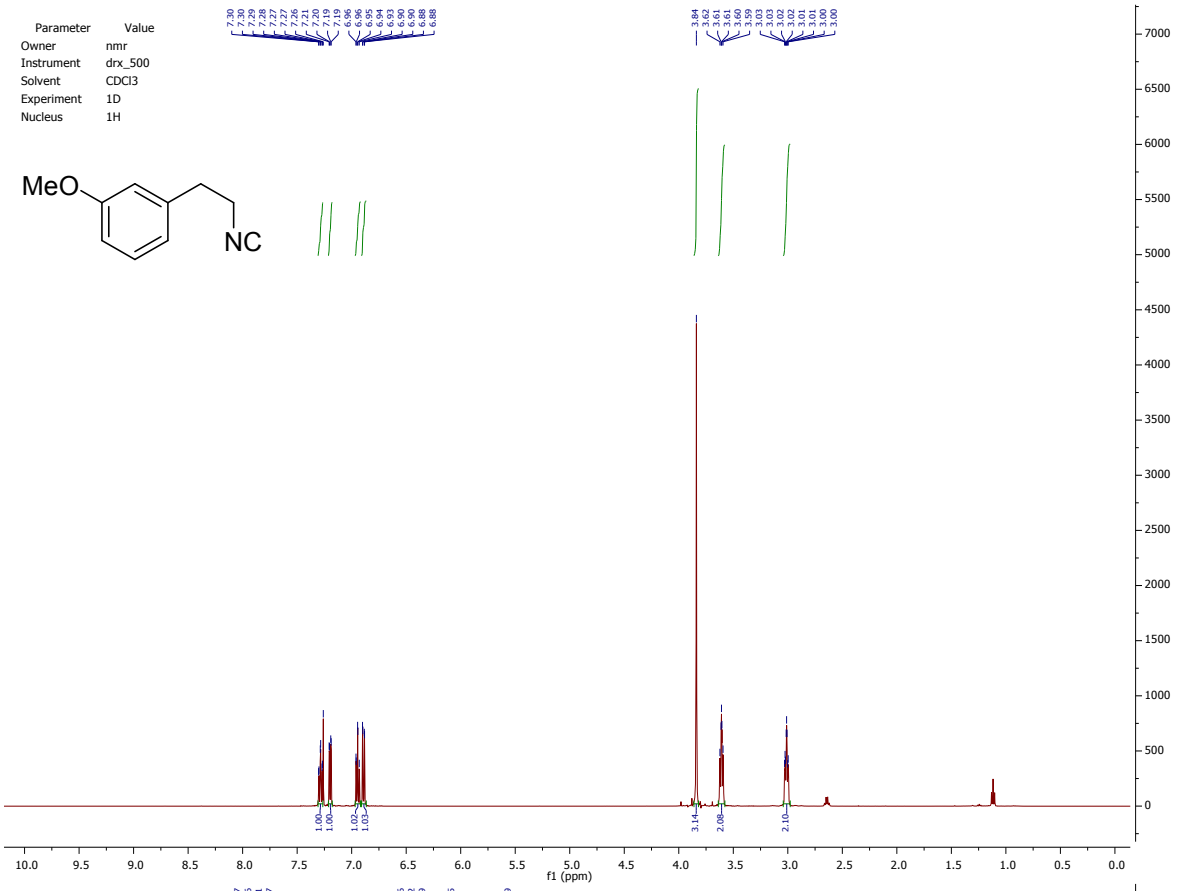


F-3 / I-12: 1-(Isocyanomethyl)-4-(trifluoromethoxy)benzene

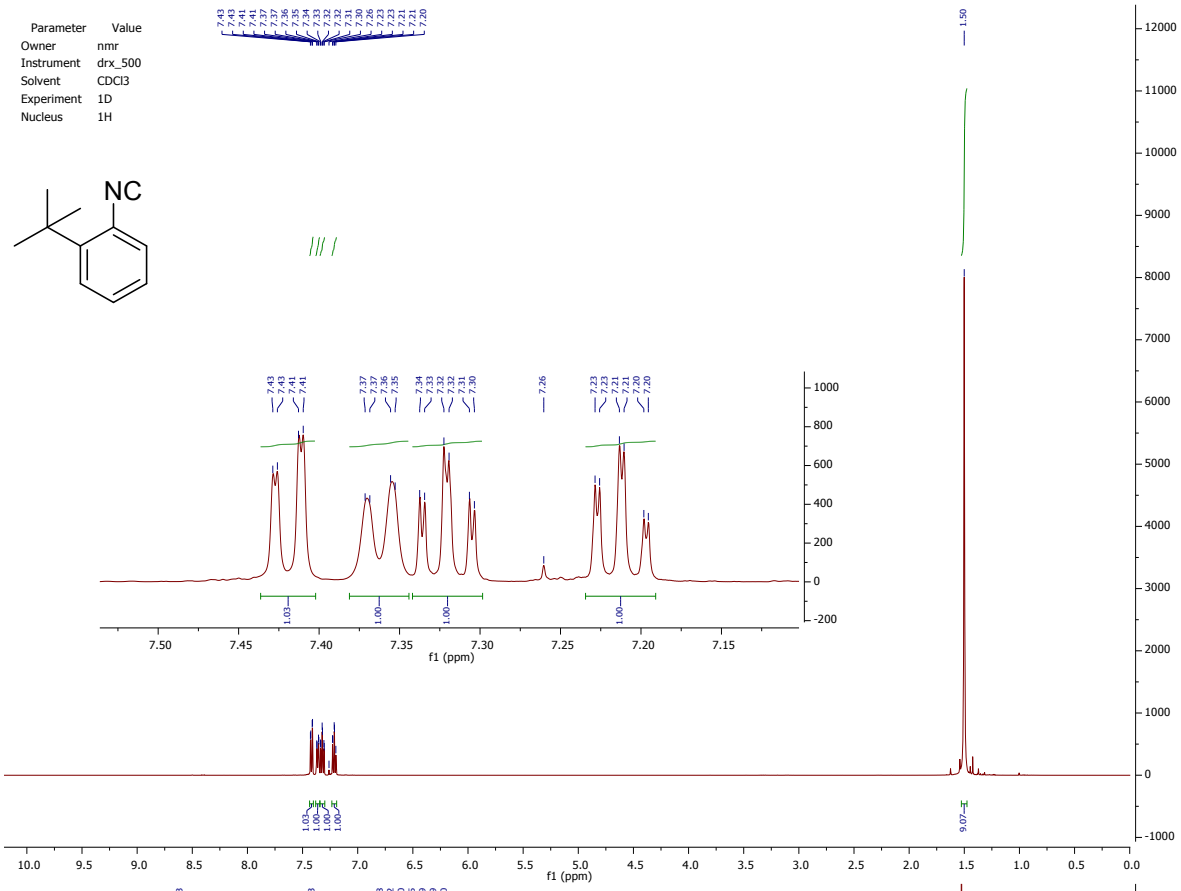


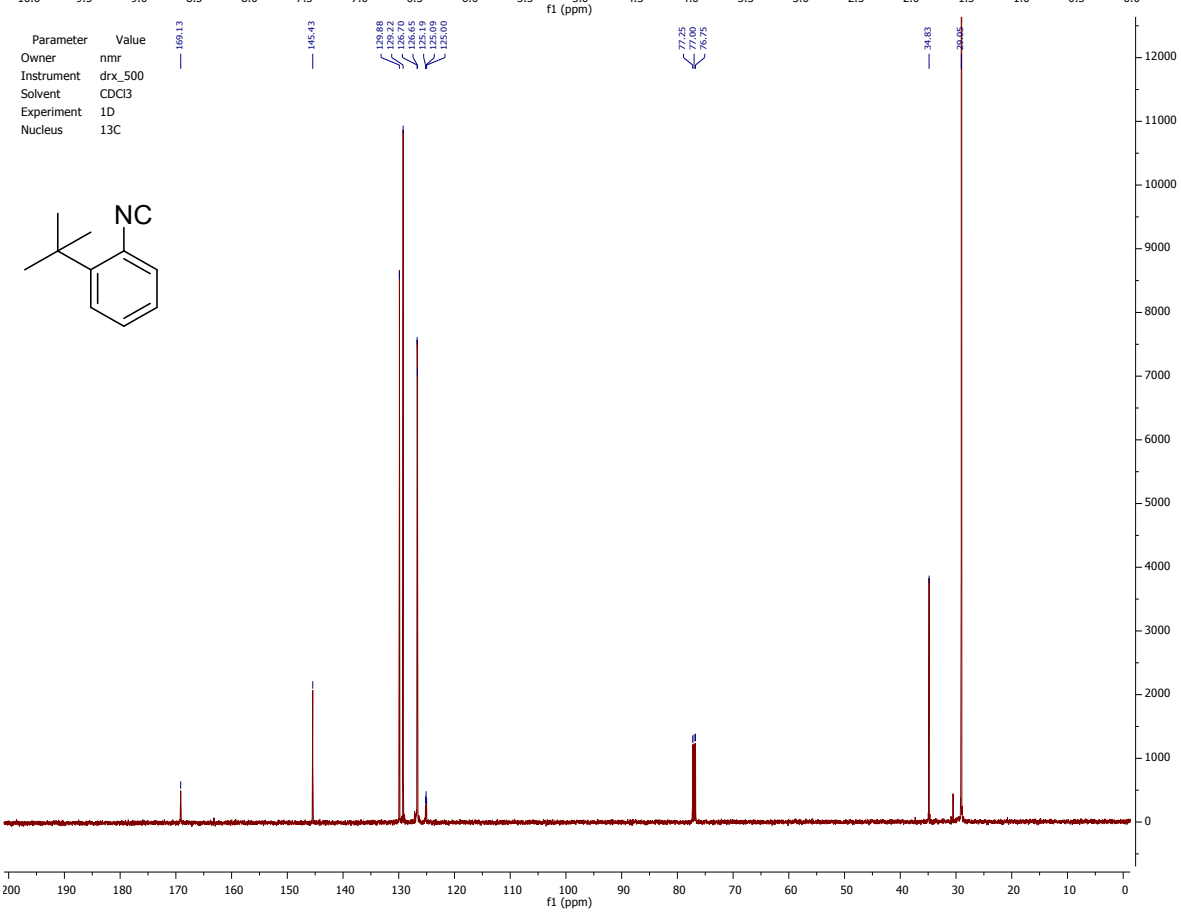


F-4 / I-18: 1-(2-Isocyanoethyl)-3-methoxybenzene

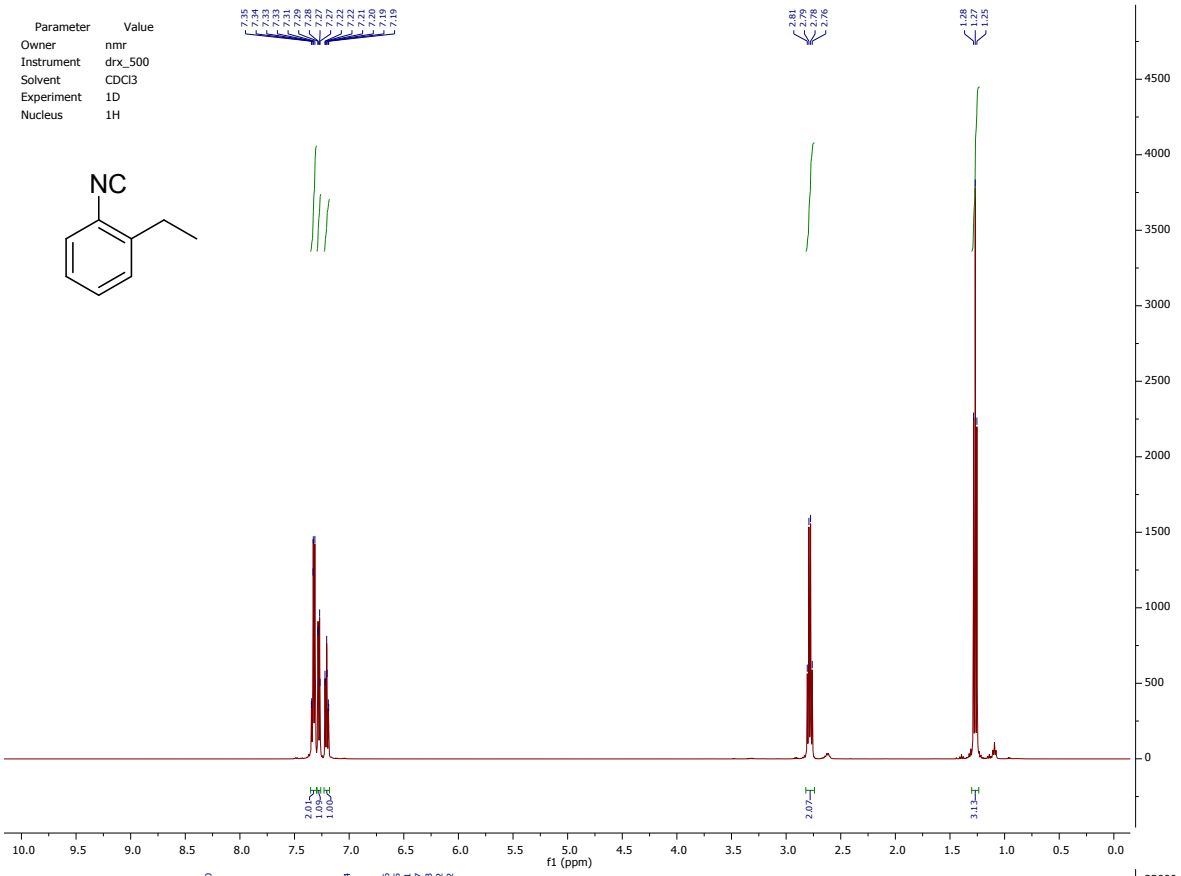


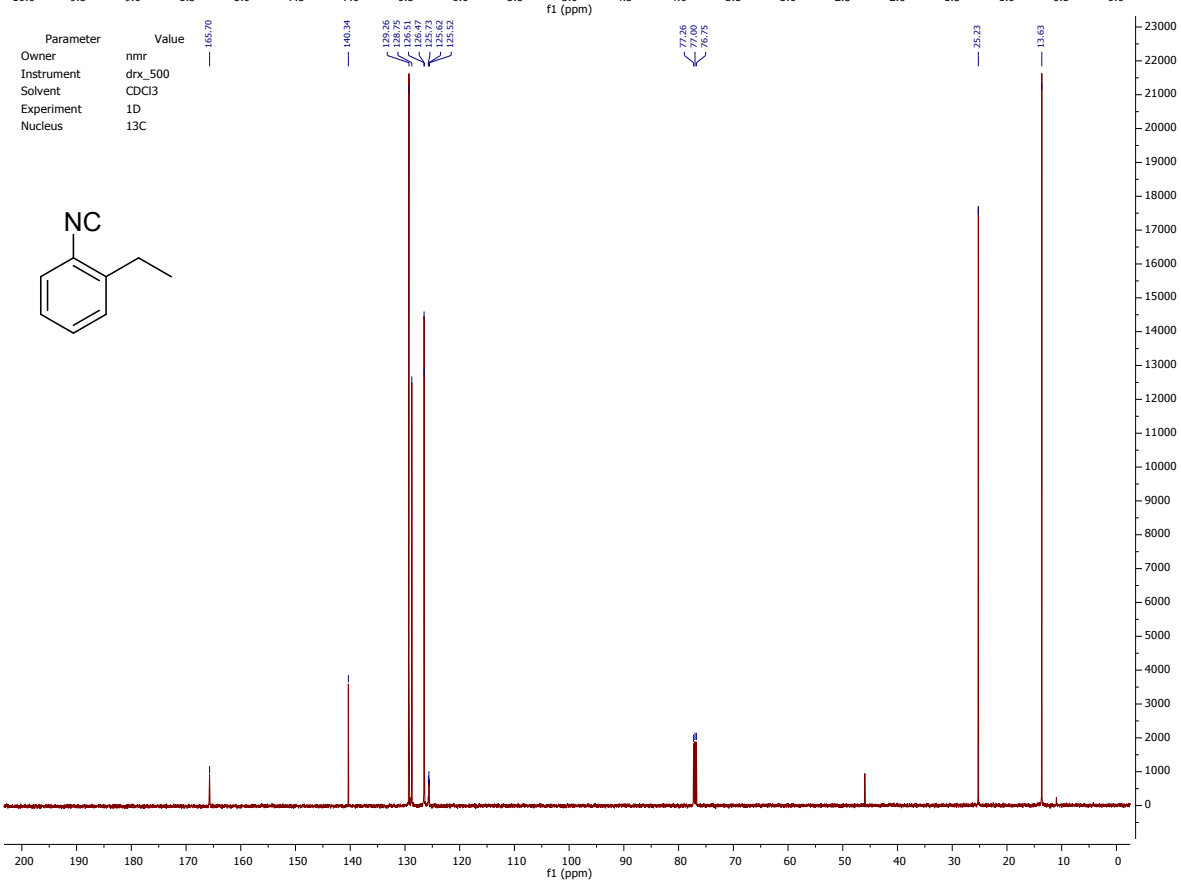
F-5 / I-22: 1-(*Tert*-butyl)-2-isocyanobenzene



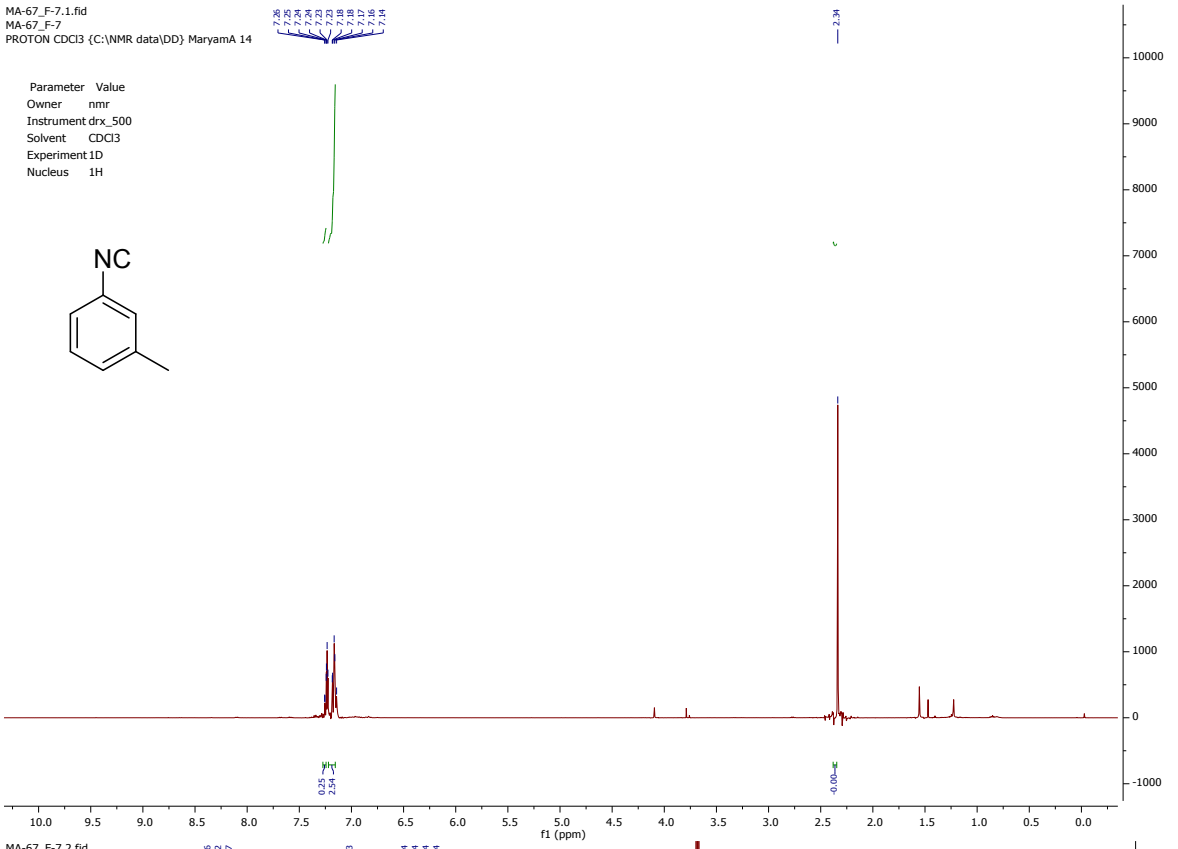


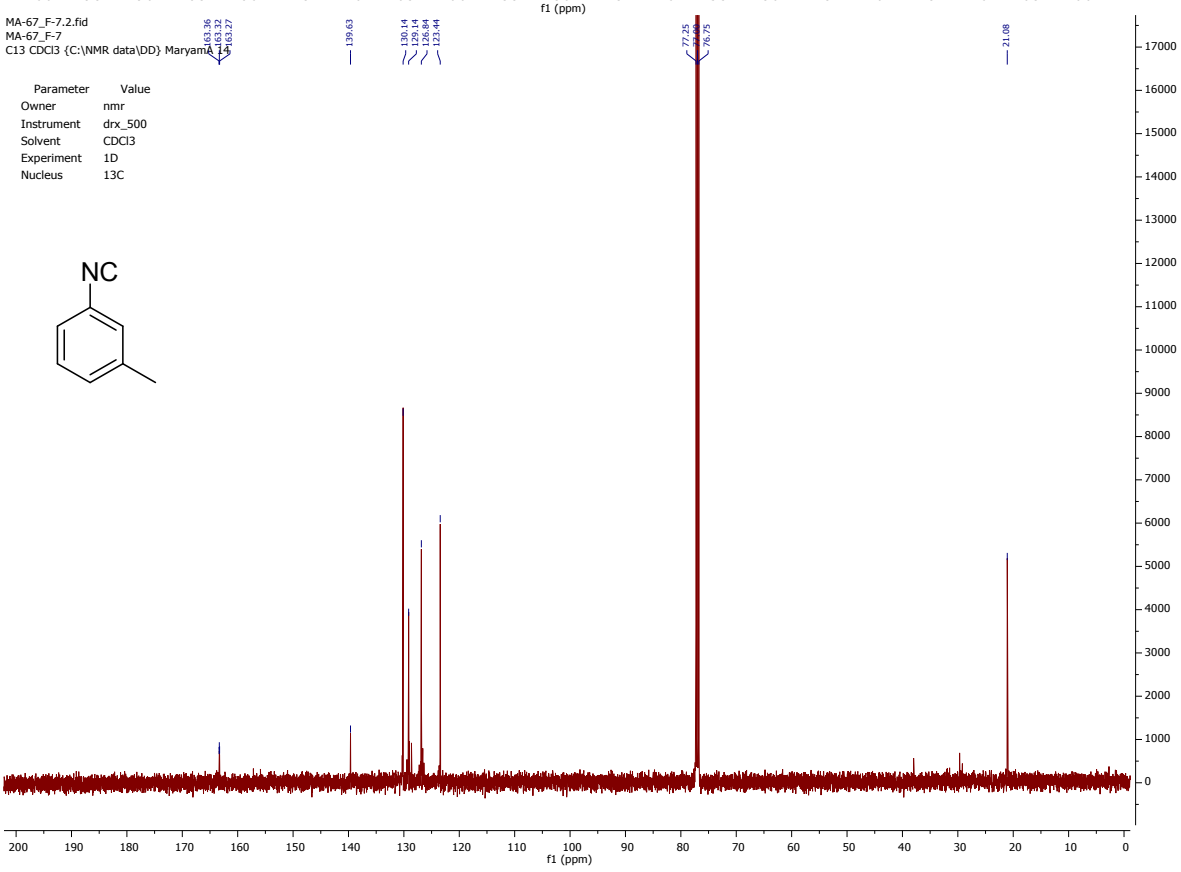
F-6 / I-26: 1-Ethyl-2-isocyanobenzen



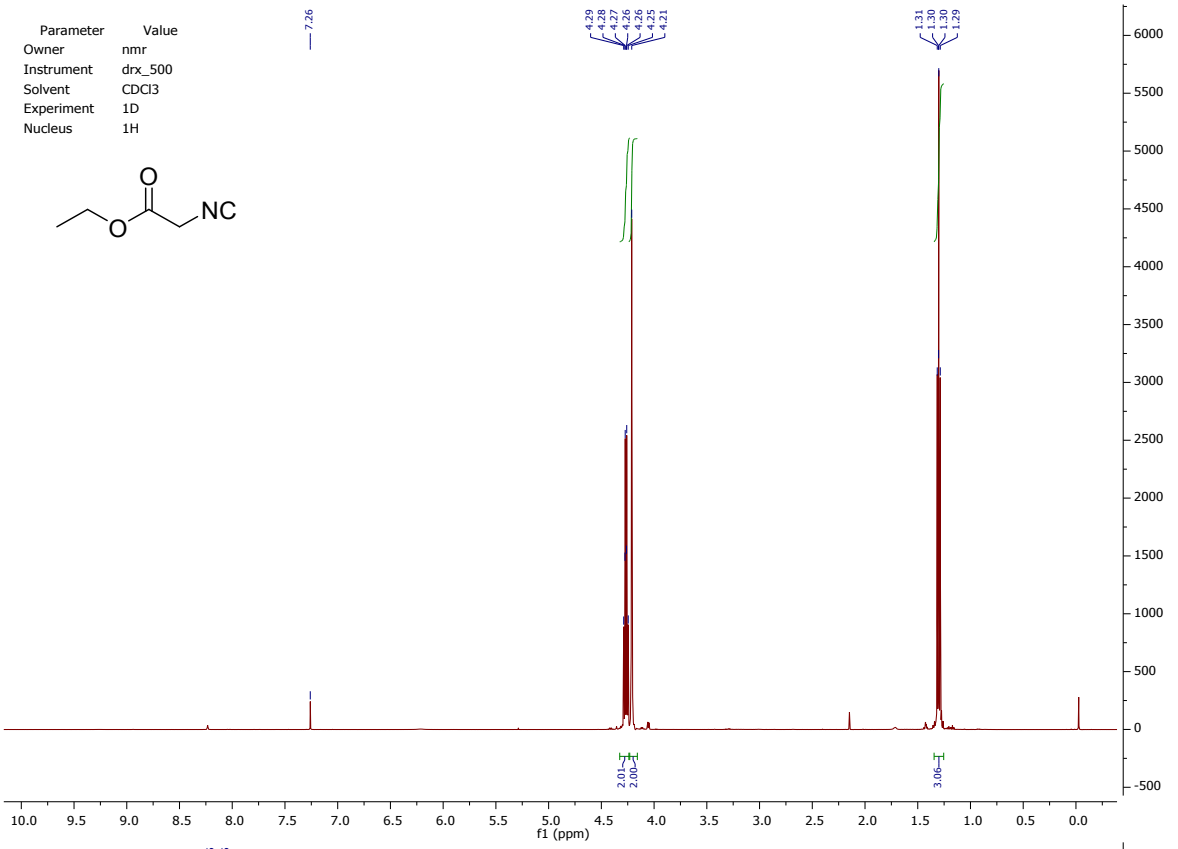


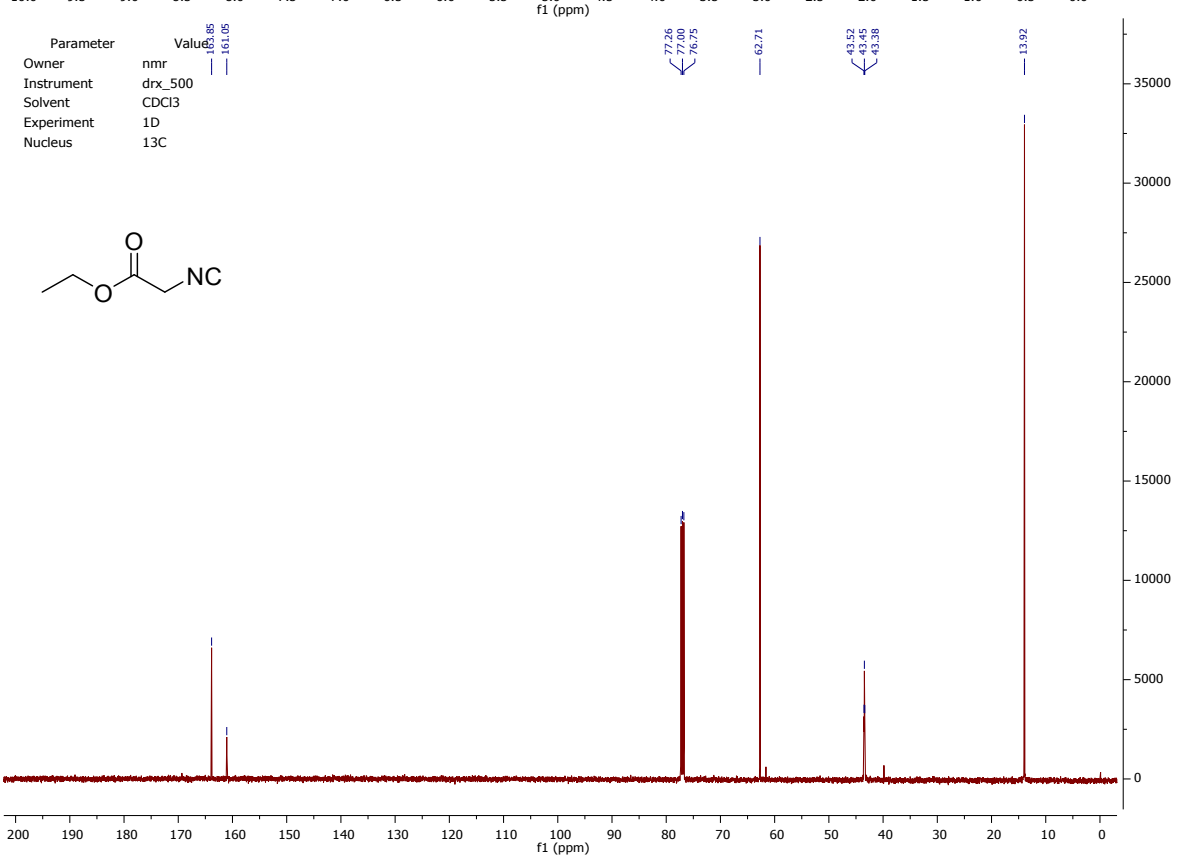
F-7: 1-Isocyano-3-methylbenzene



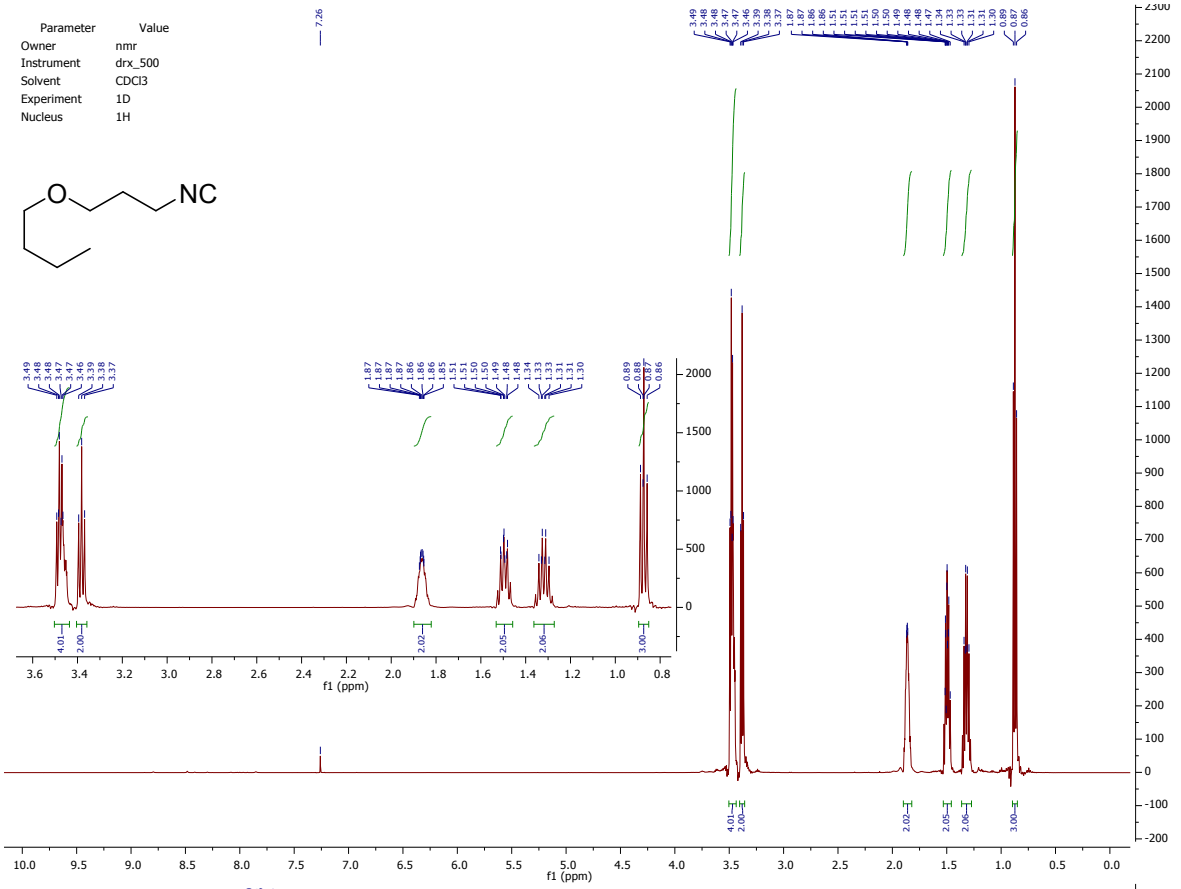


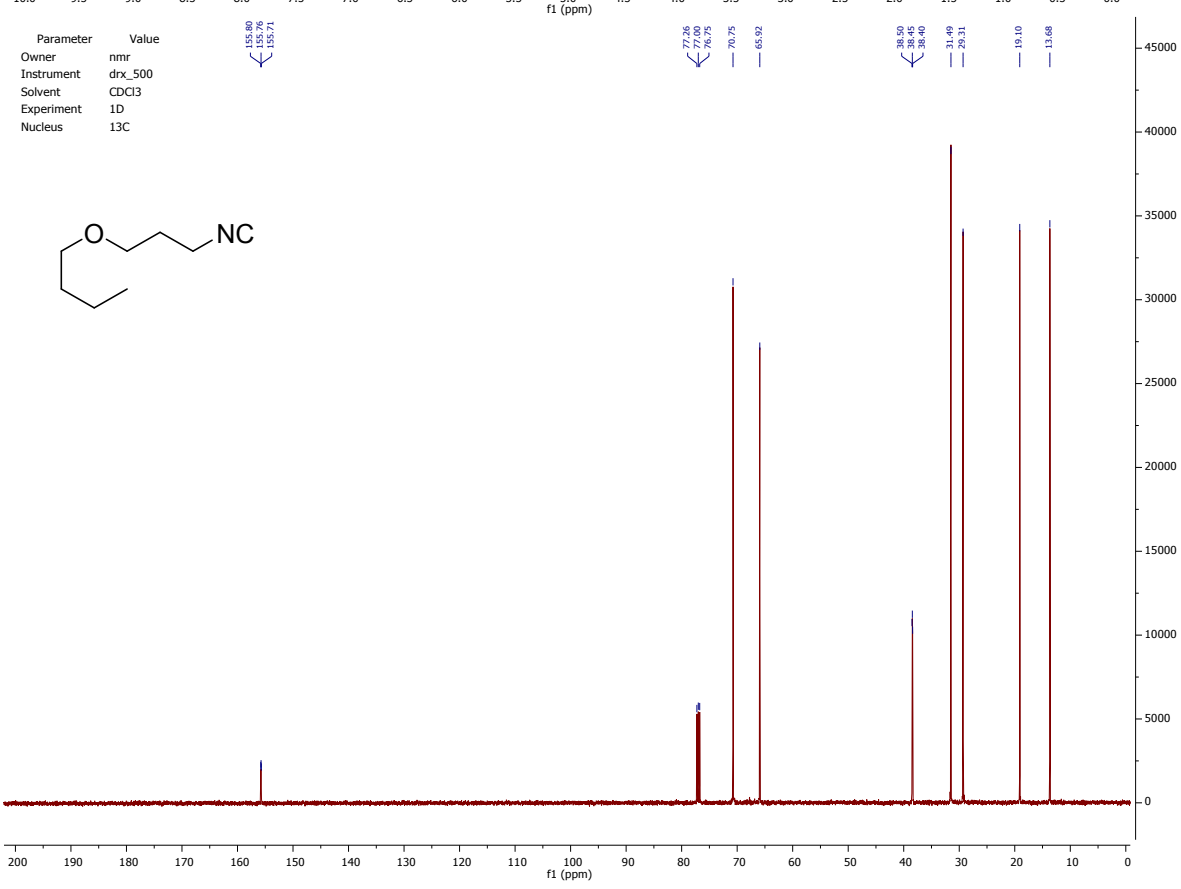
F-8: Ethyl 2-isocyanoacetate



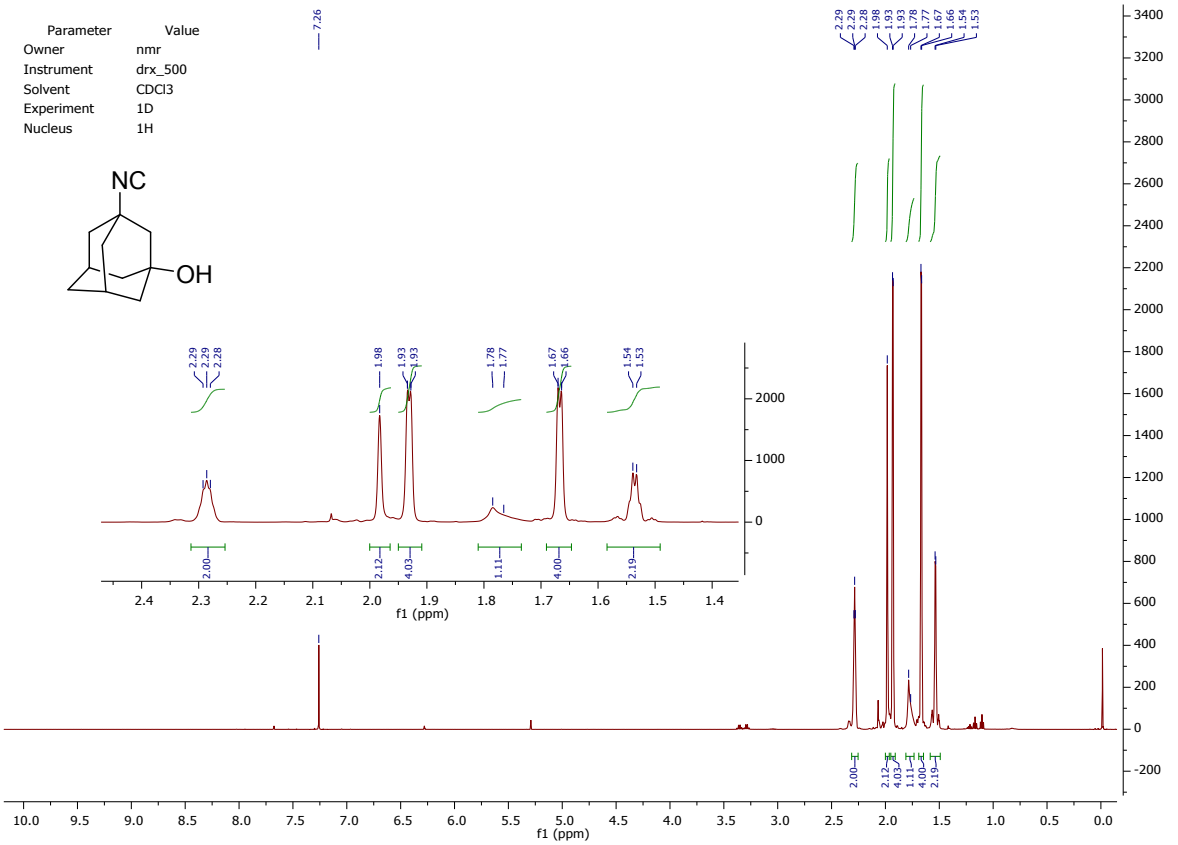


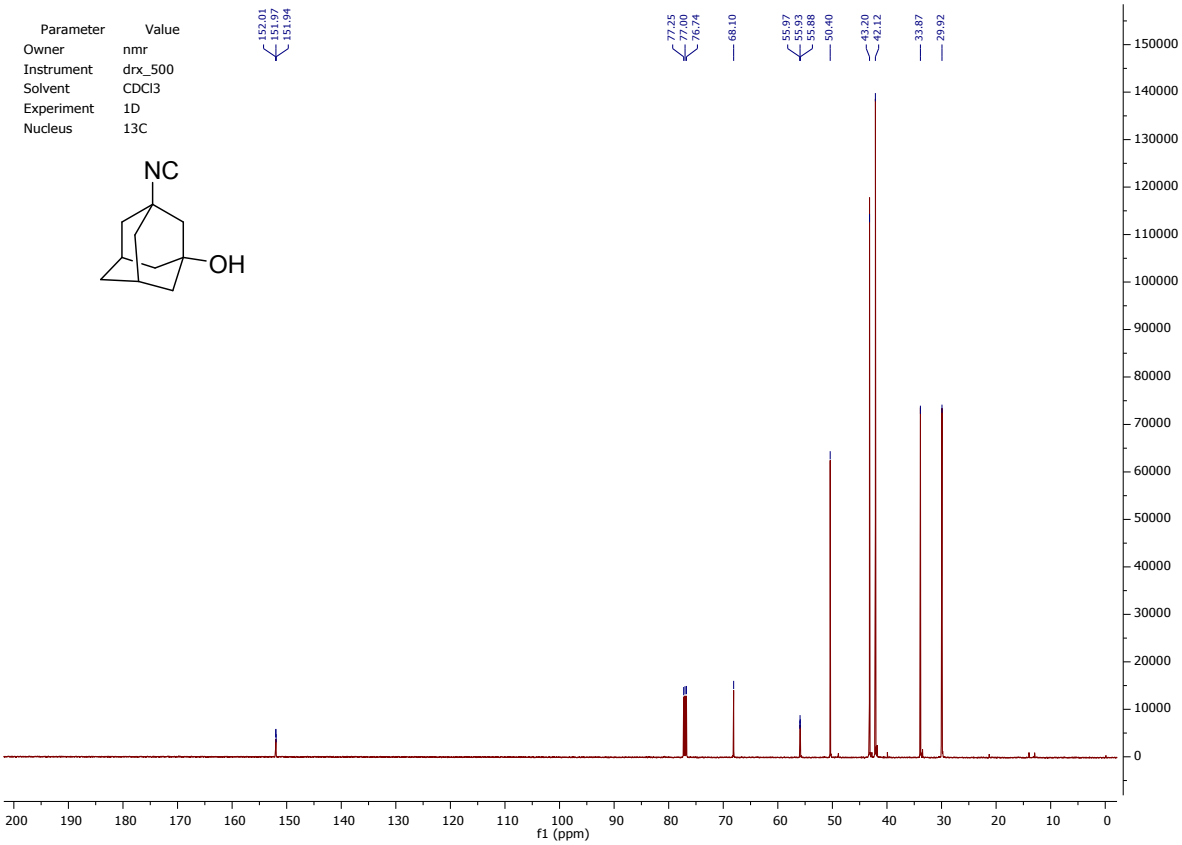
F-9 / I-40: 1-(3-Isocyanopropoxy)butane



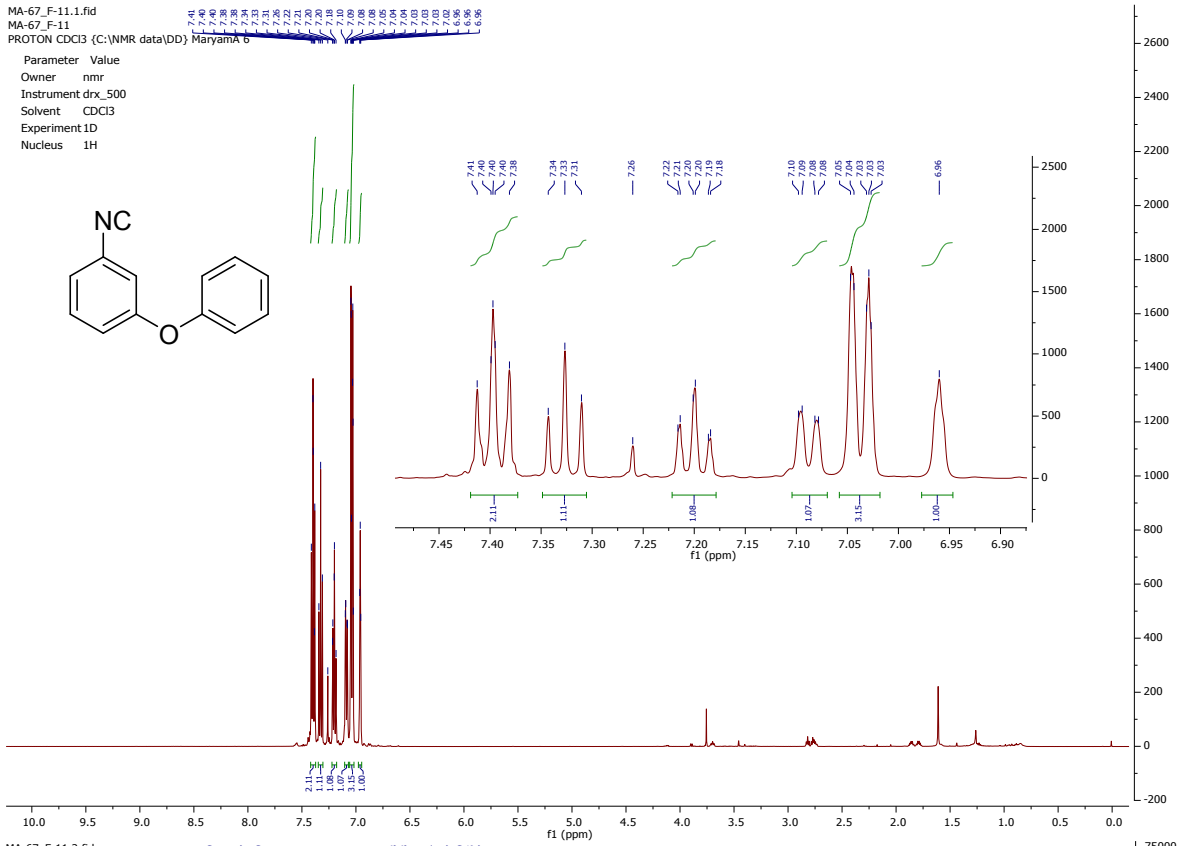


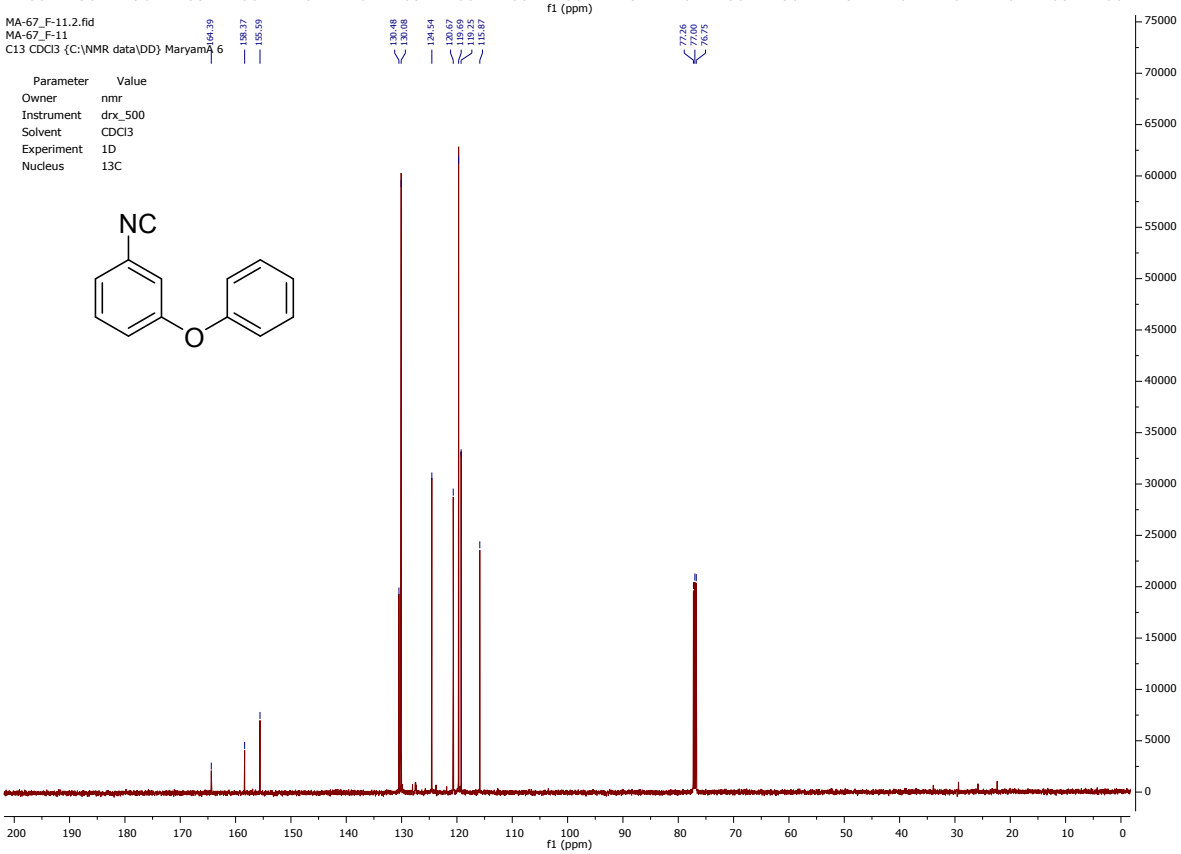
F-10 / I-50: (1*s*,3*r*,5*R*,7*S*)-3-Isocyanoadamantan-1-ol



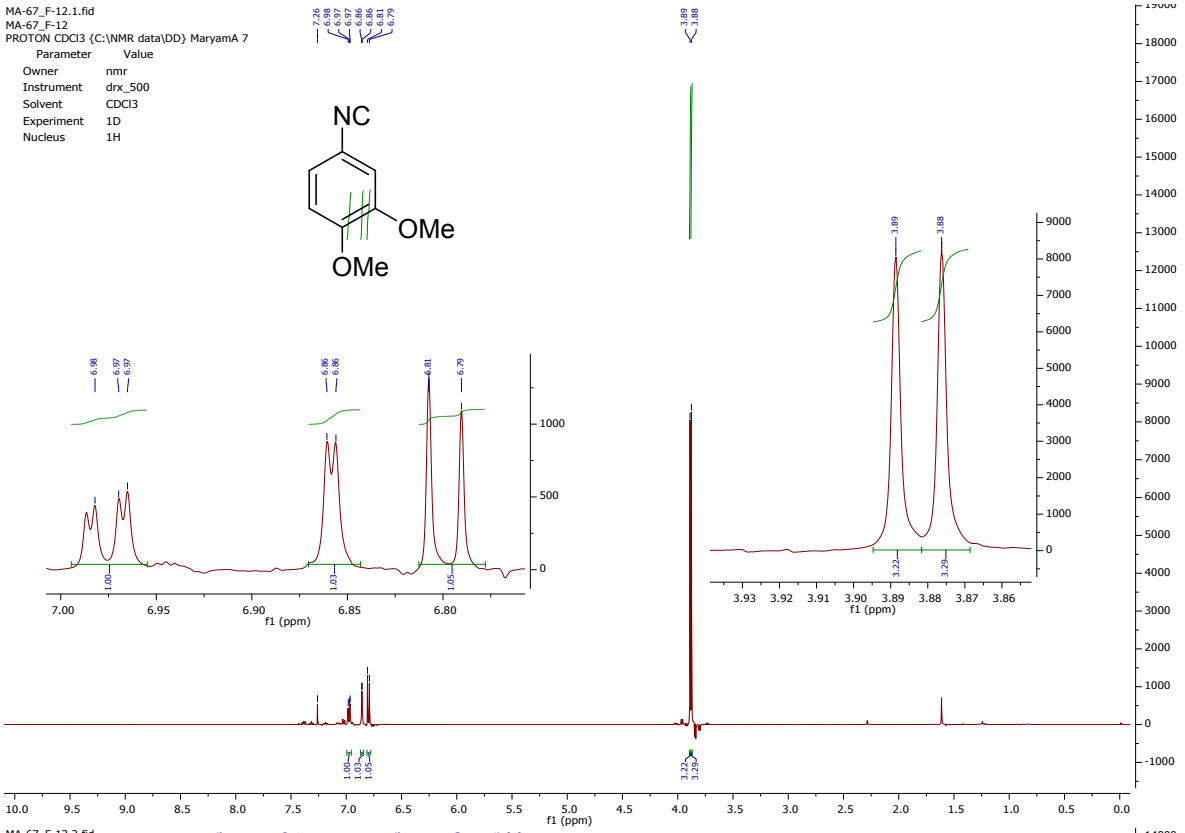


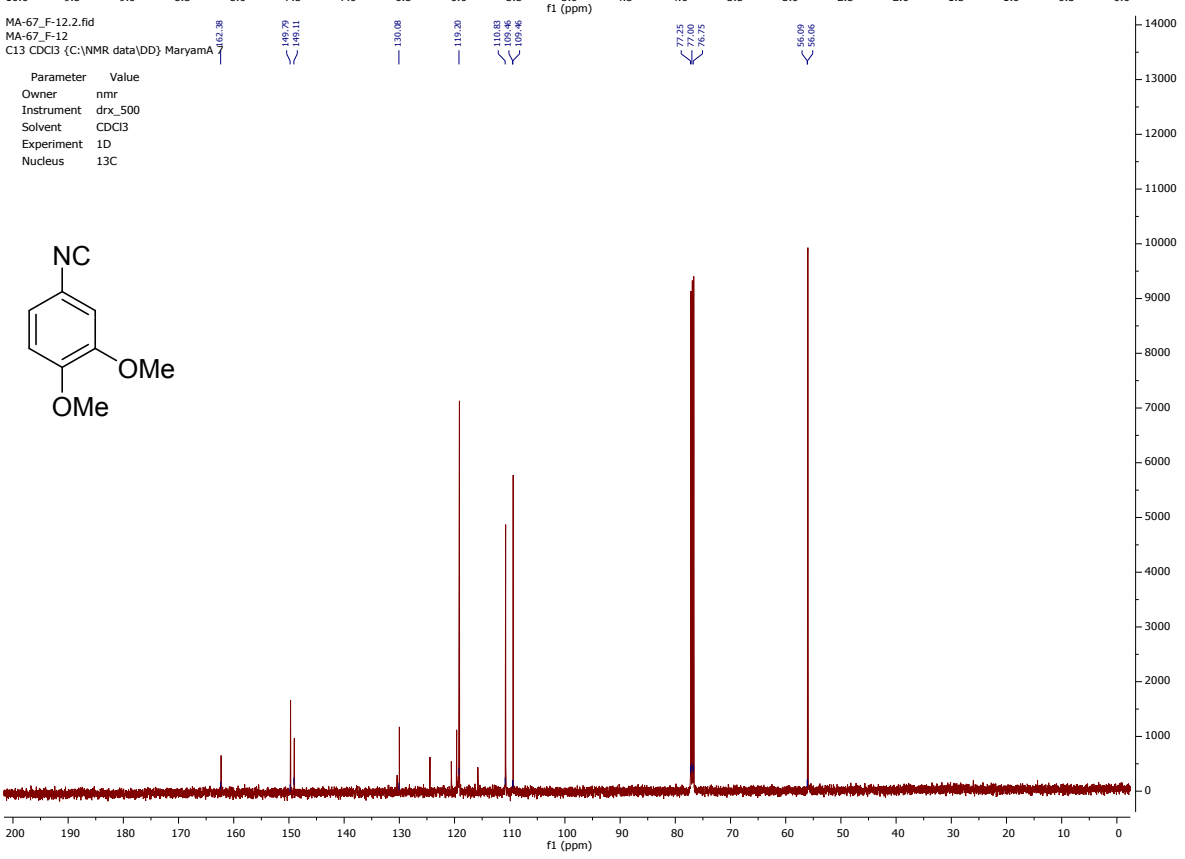
F-11: 1-Isocyano-3-phenoxybenzene



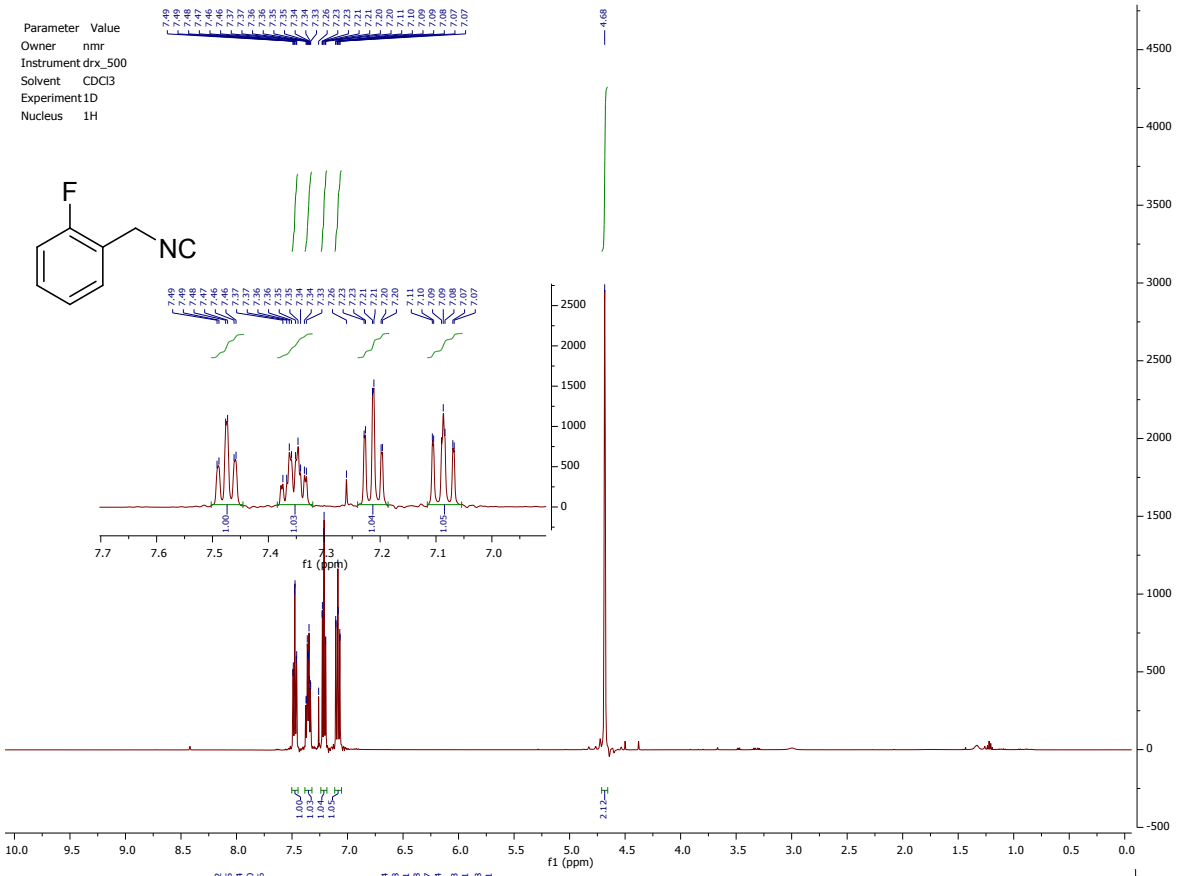


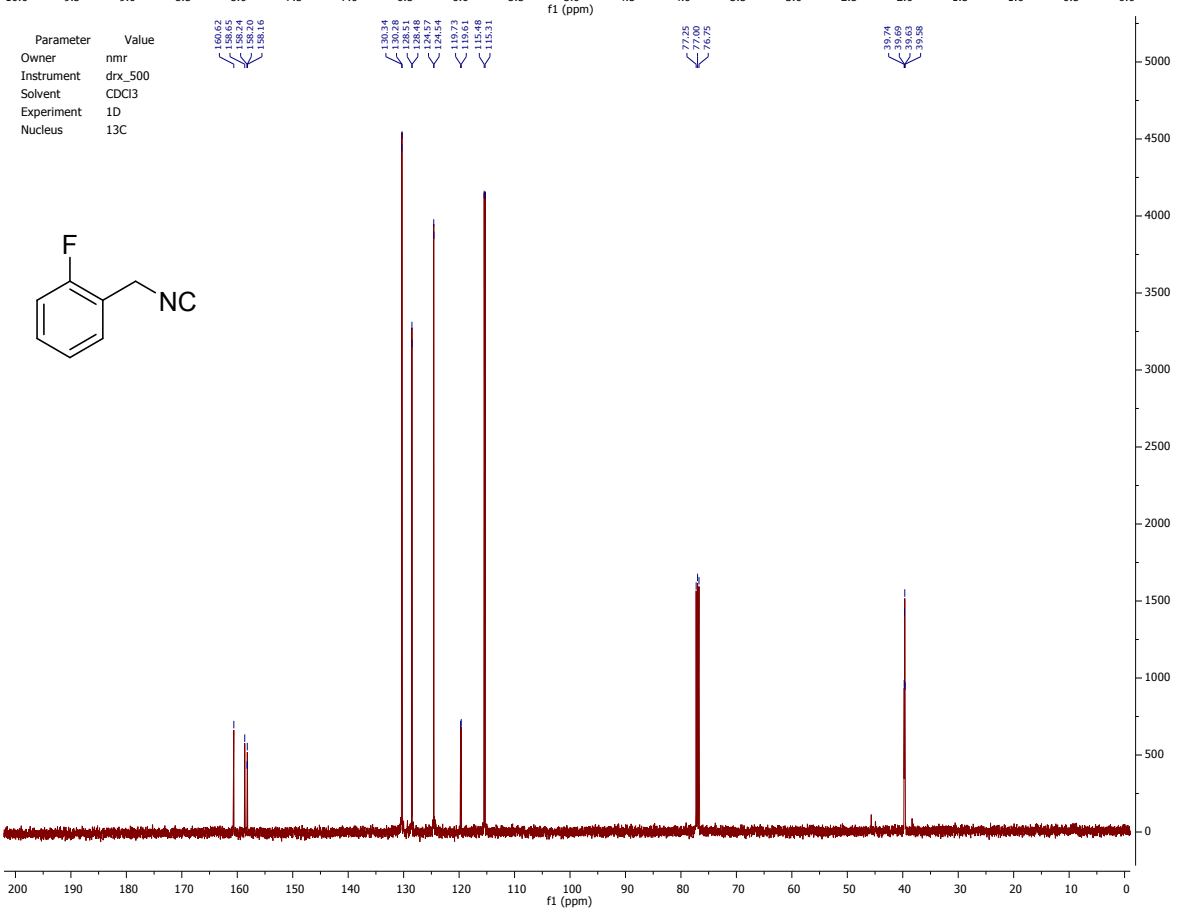
F-12: 4-Isocyano-1,2-dimethoxybenzene



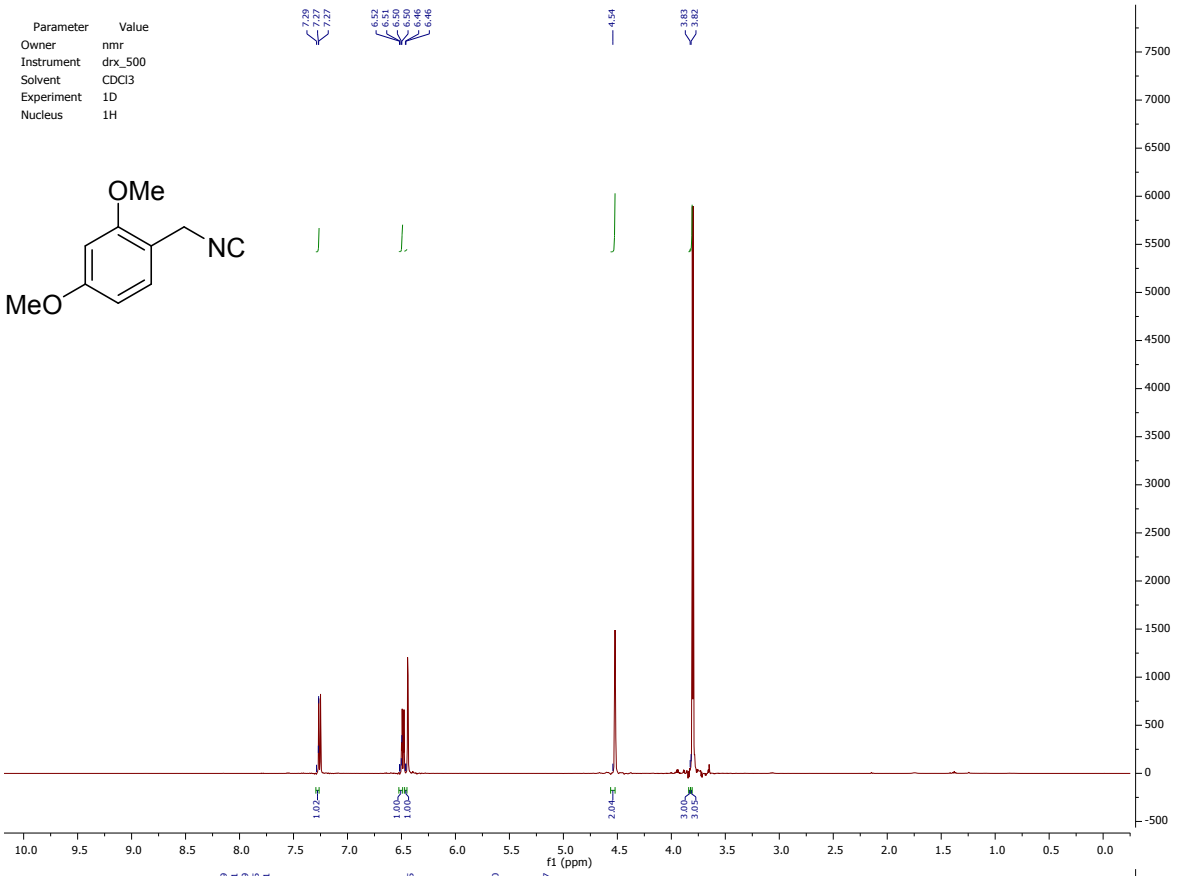


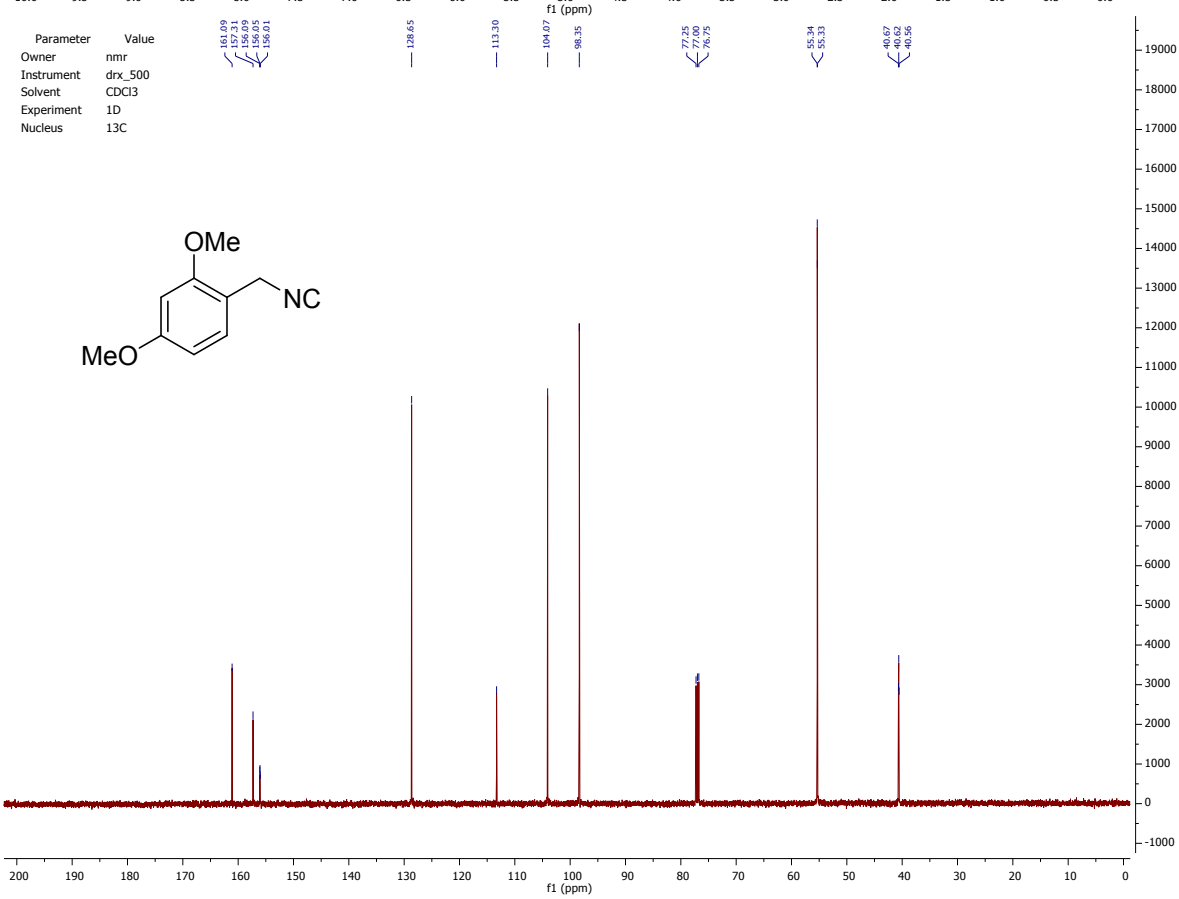
G-1 / I-5: 1-Fluoro-2-(isocyanomethyl)benzene



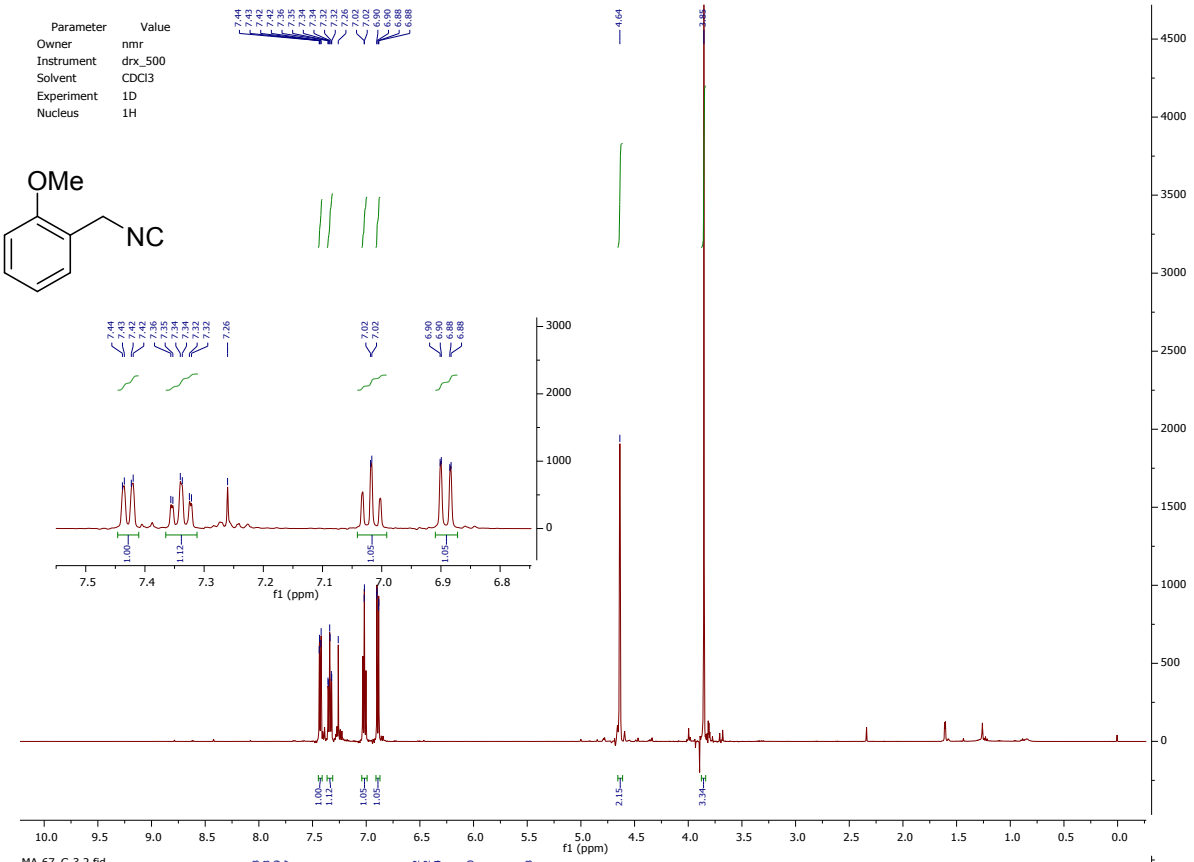


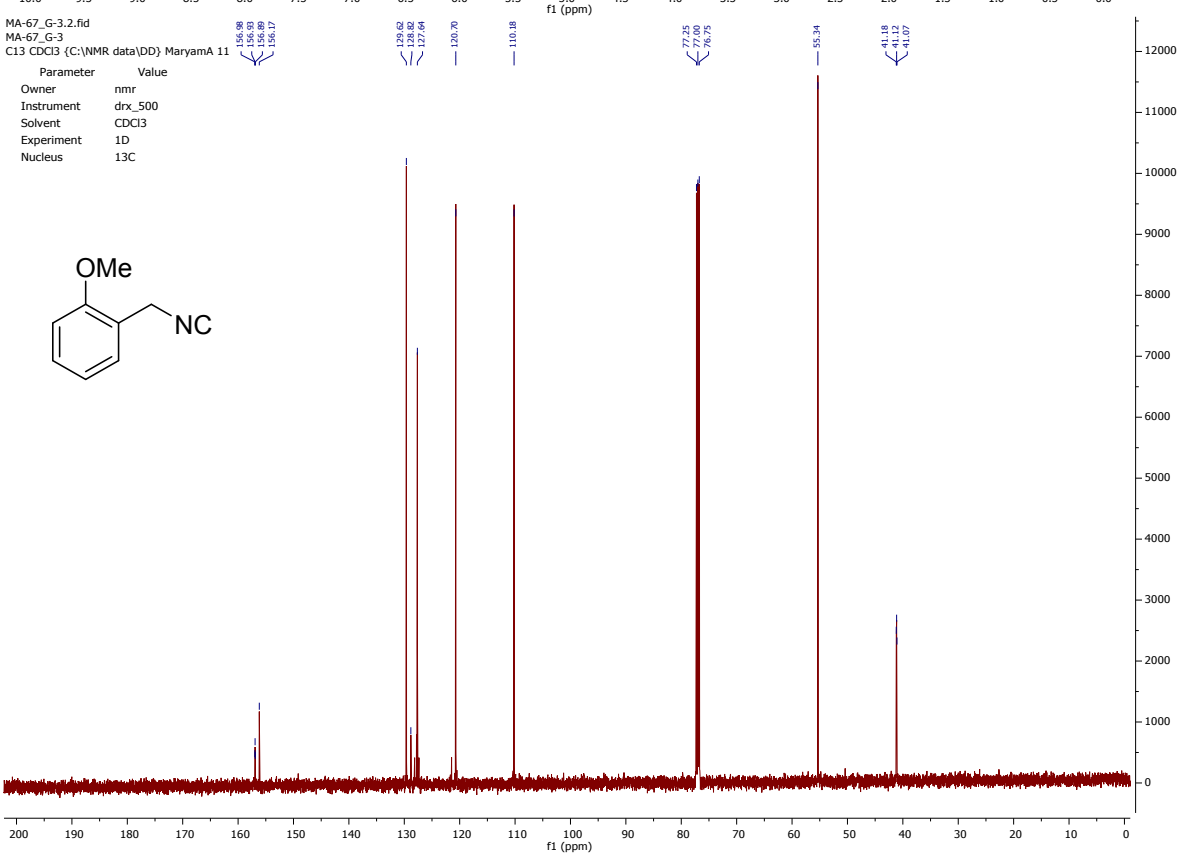
G-2 / I-10: 1-(Isocyanomethyl)-2,4-dimethoxybenzene



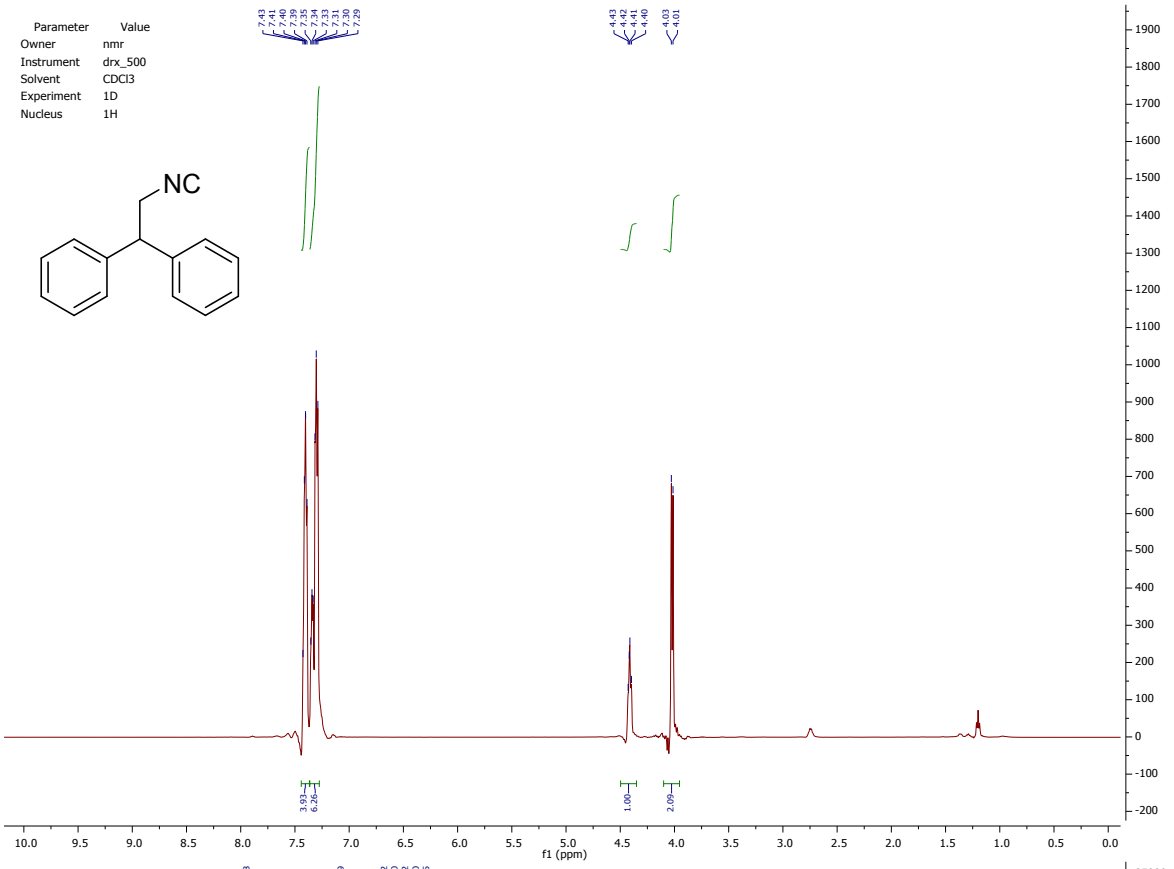


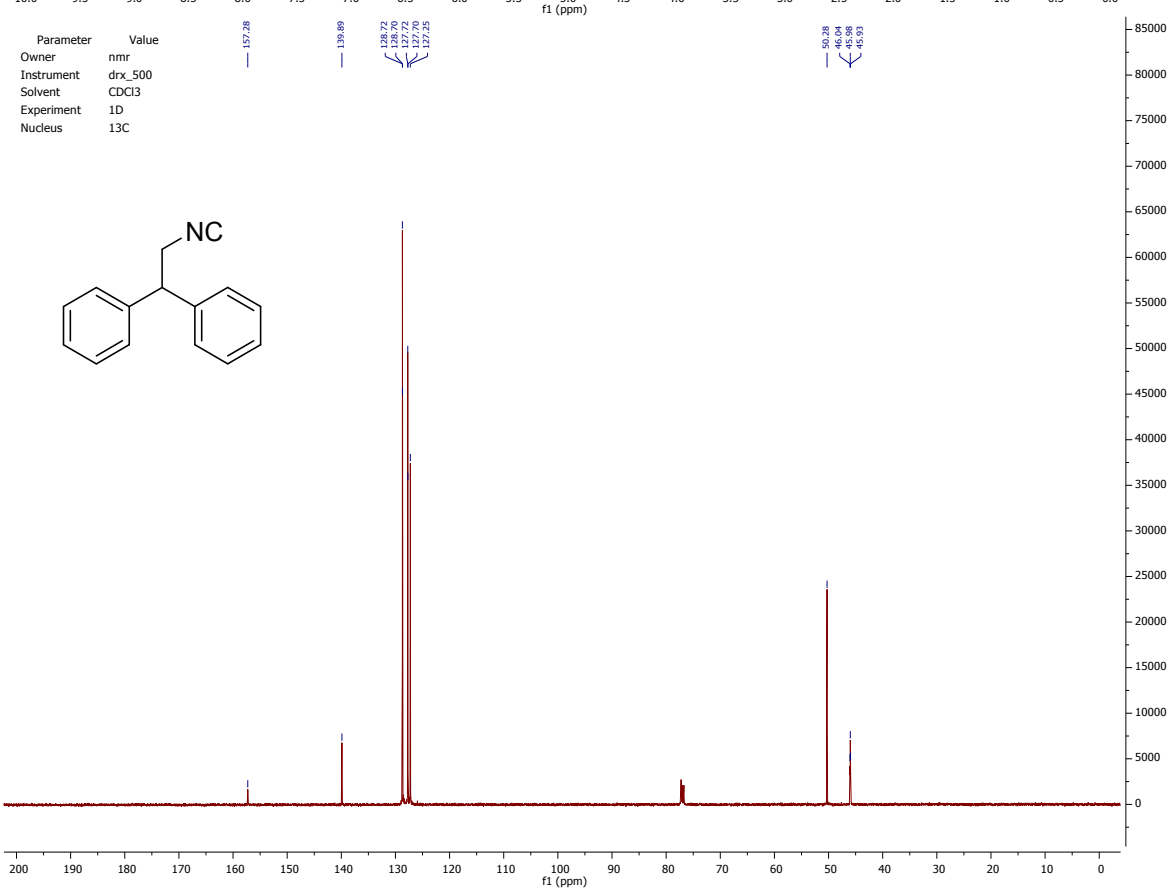
G-3: 1-(Isocyanomethyl)-2-methoxybenzene



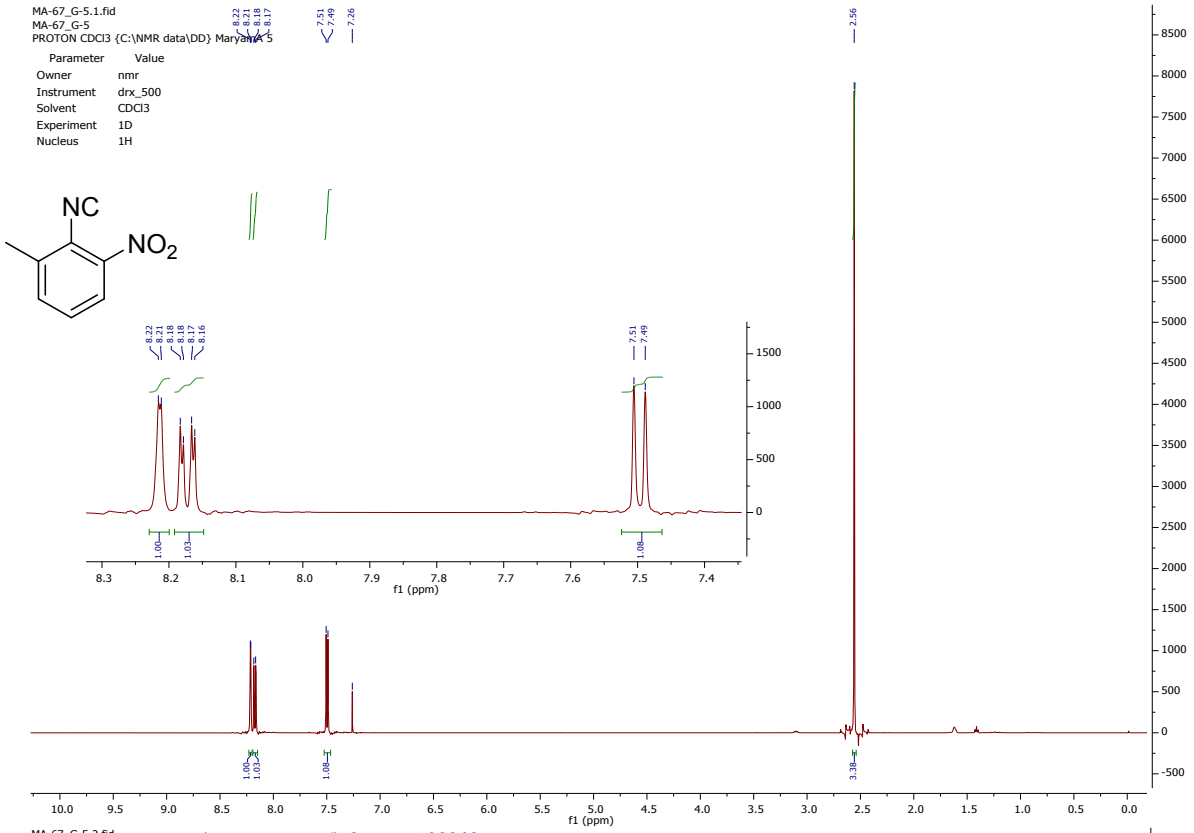


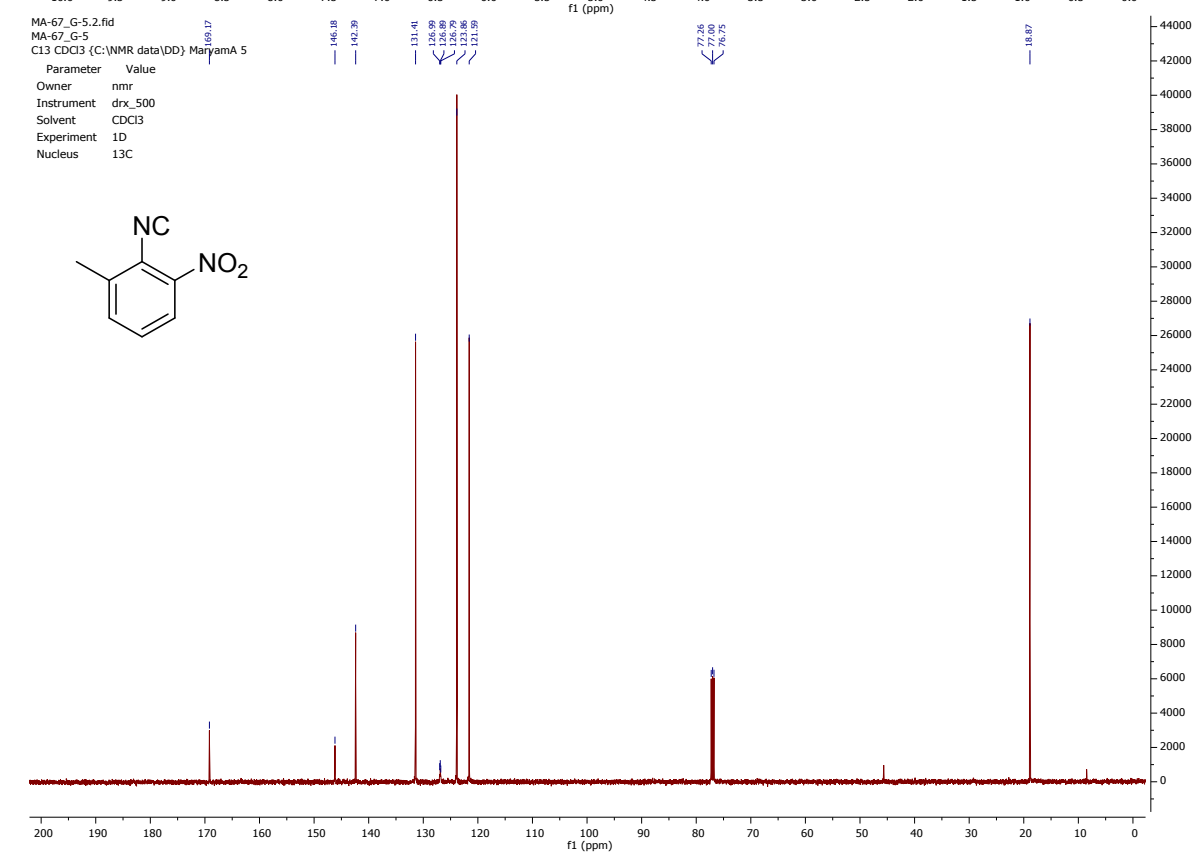
G-4 / I-19: (2-Isocyanoethane-1,1-diyl)dibenzene



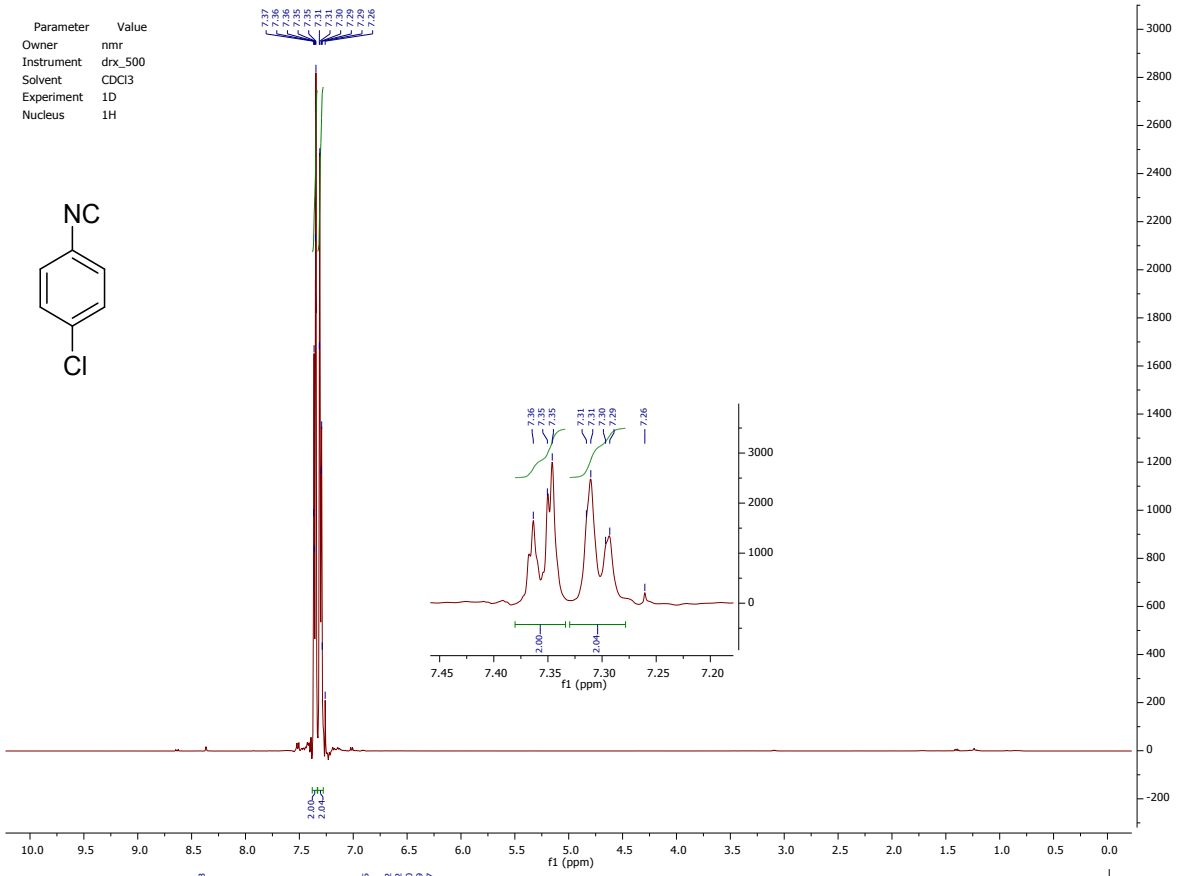


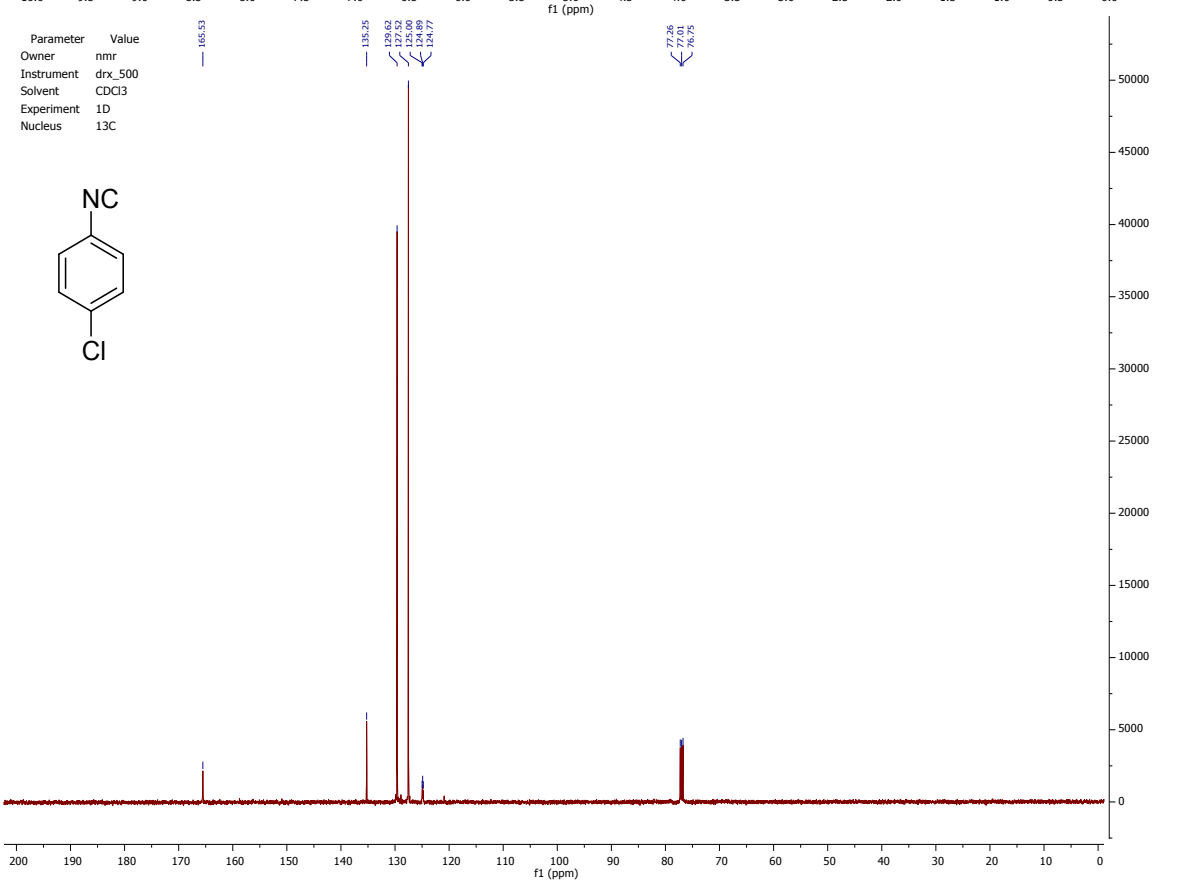
G-5: 2-Isocyano-1-methyl-3-nitrobenzene



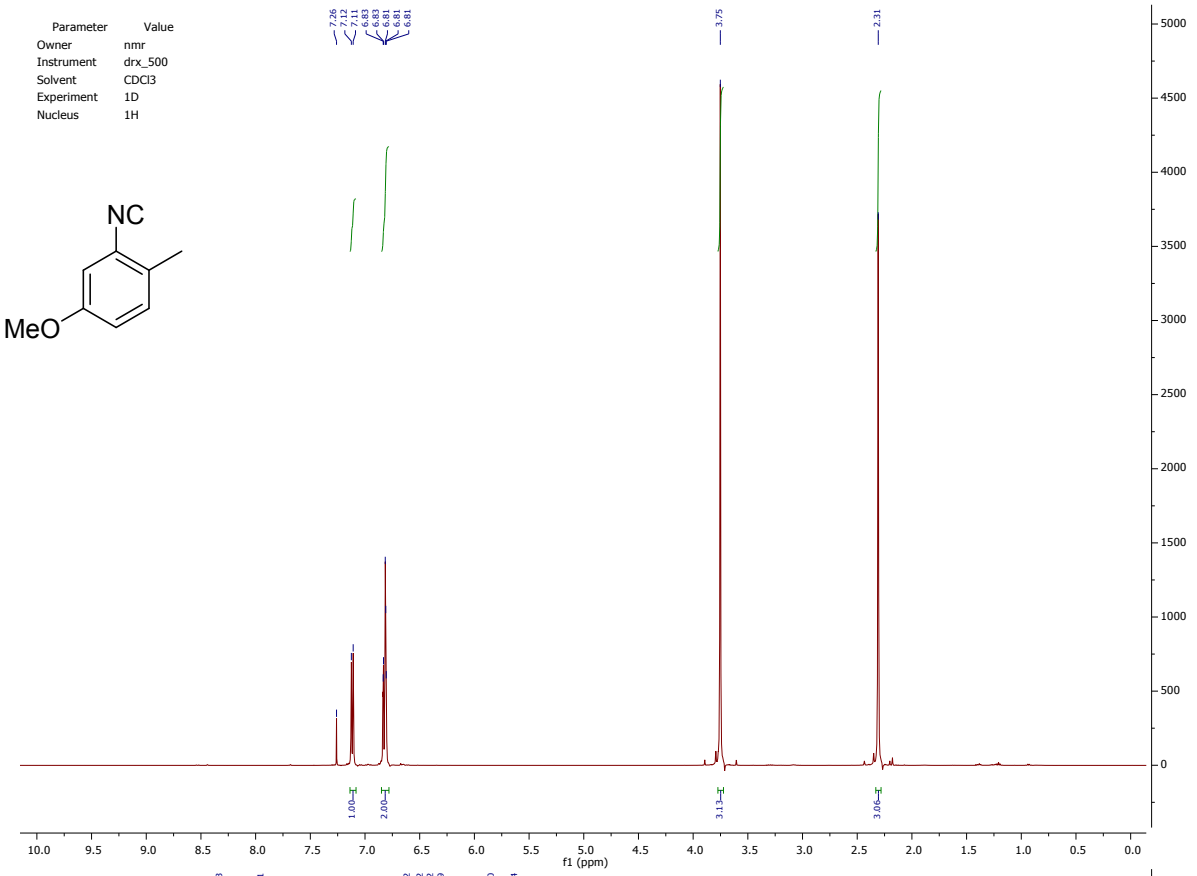


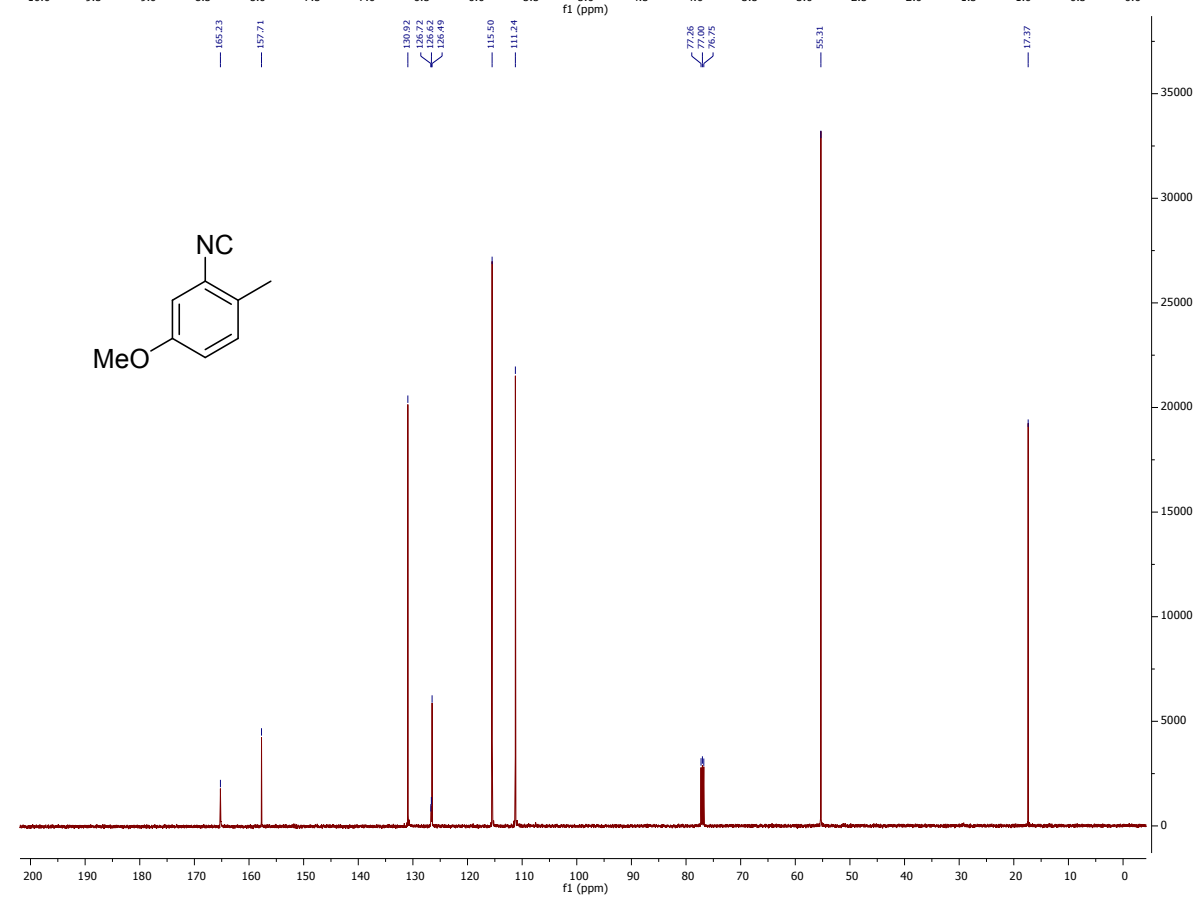
G-6 / I-27: 1-Chloro-4-isocyanobenzene



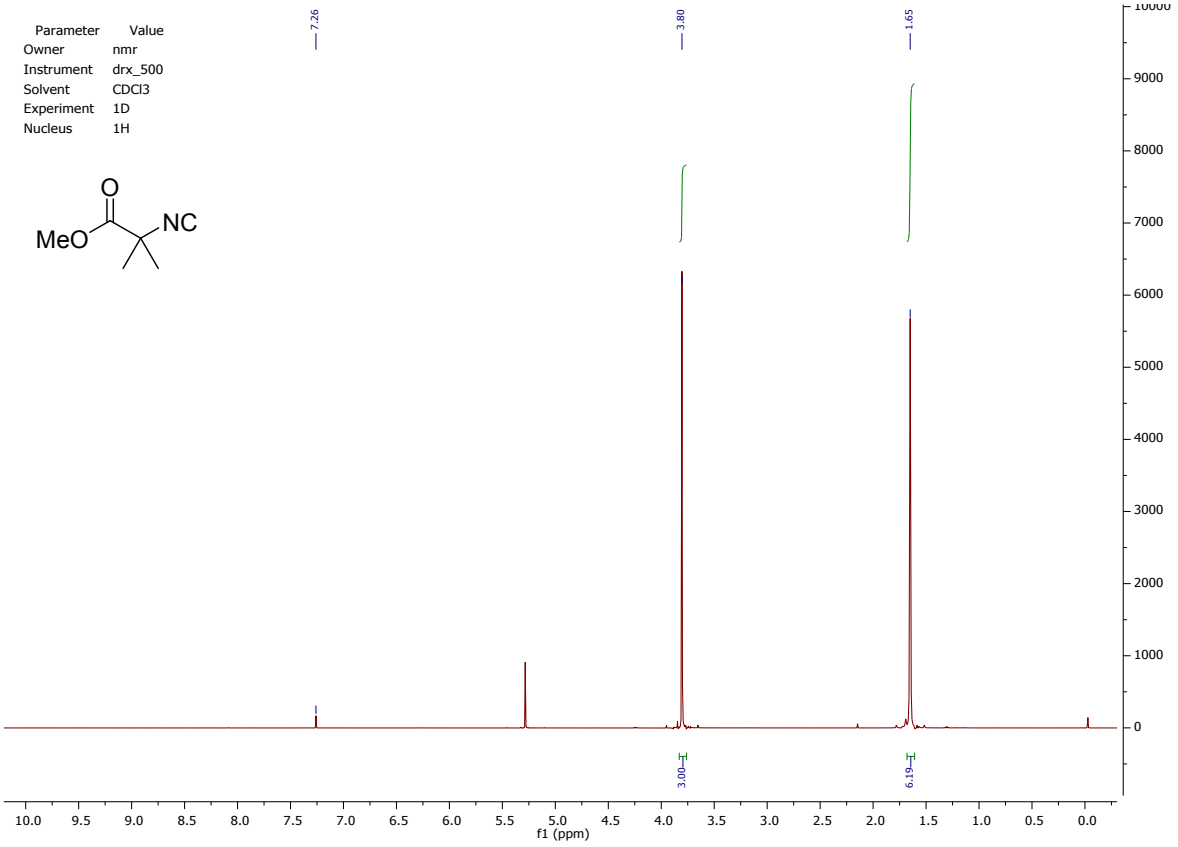


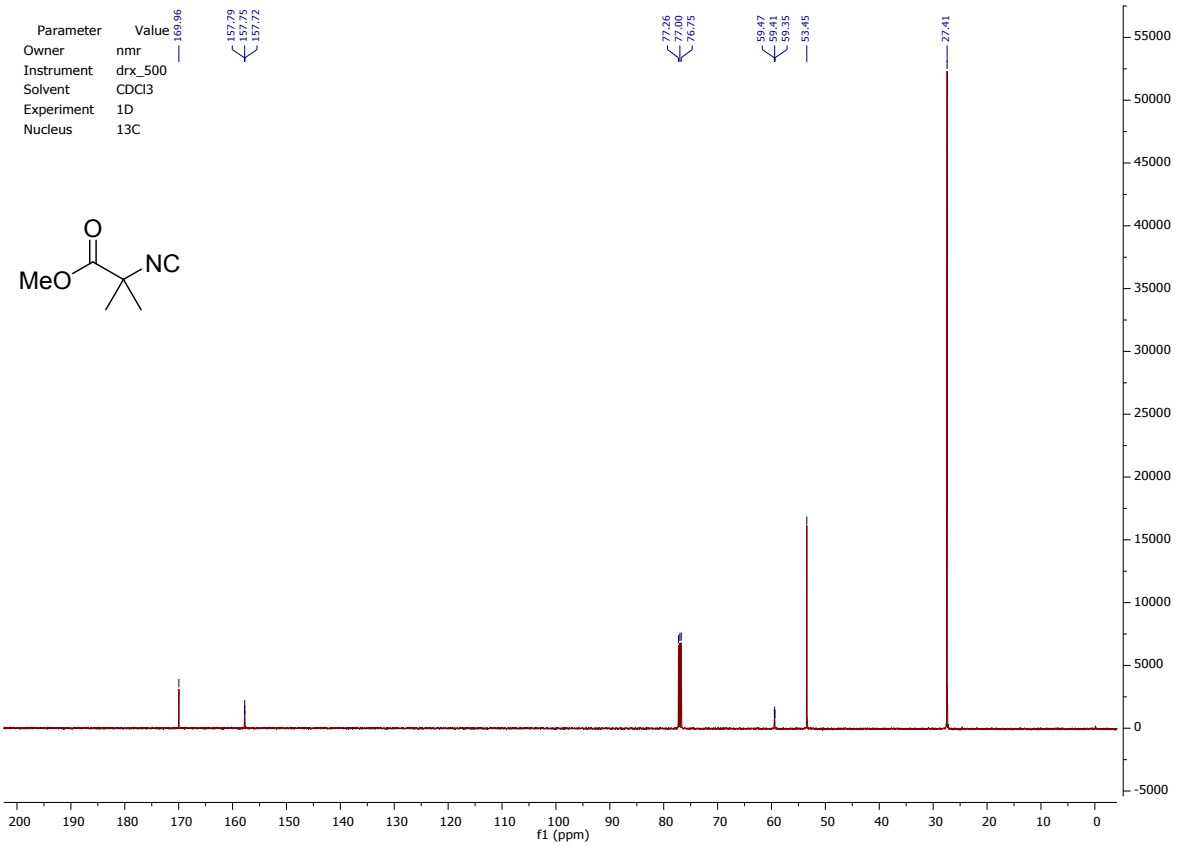
G-7 / I-29: 2-Isocyano-4-methoxy-1-methylbenzene



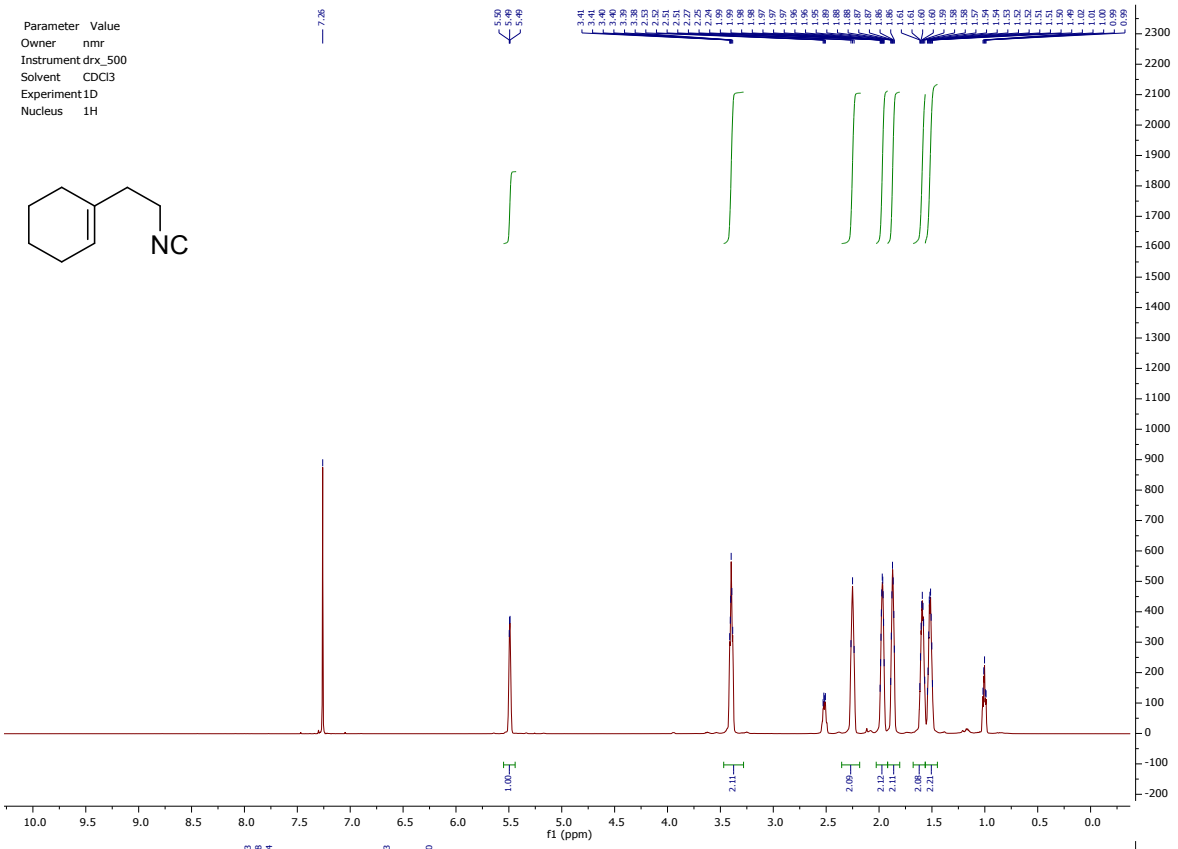


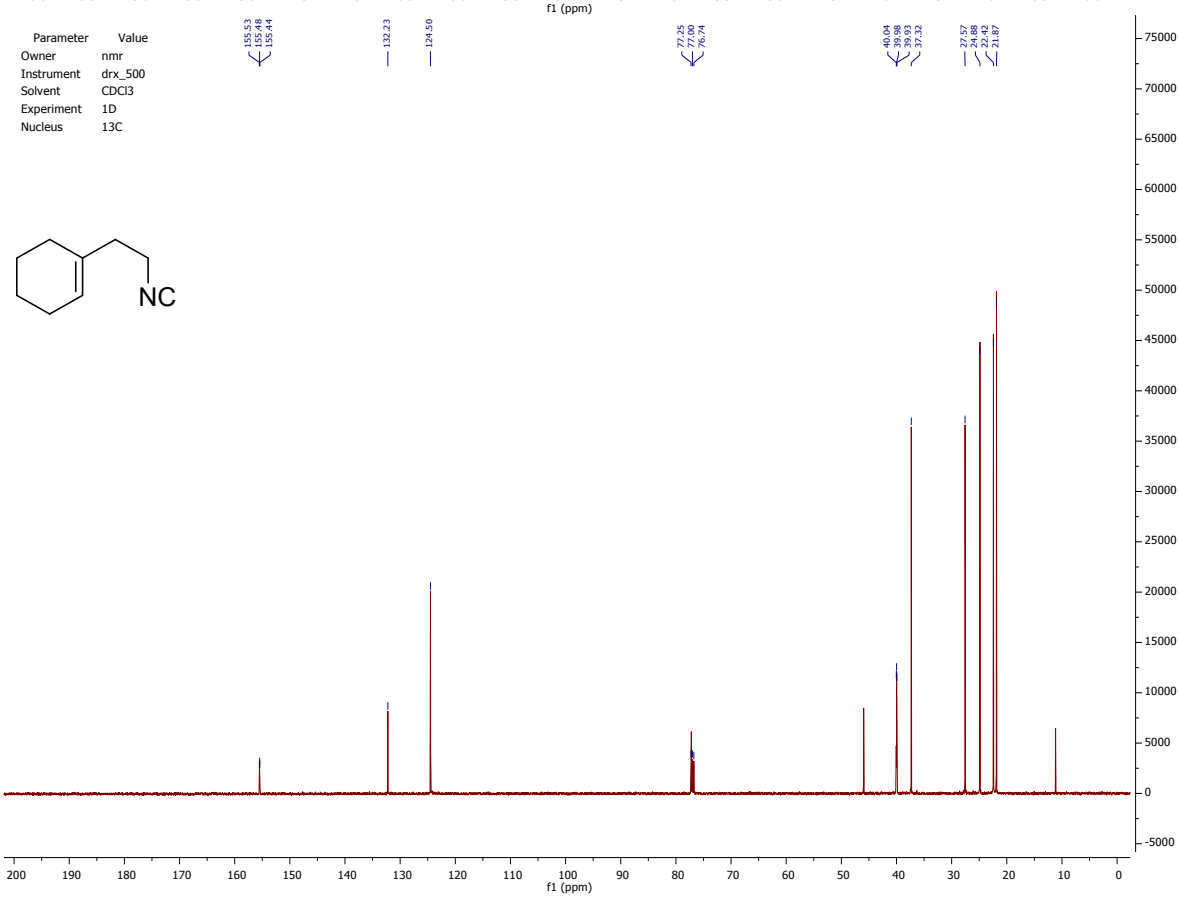
G-8: Ethyl 2-isocyano-2-methylpropanoate



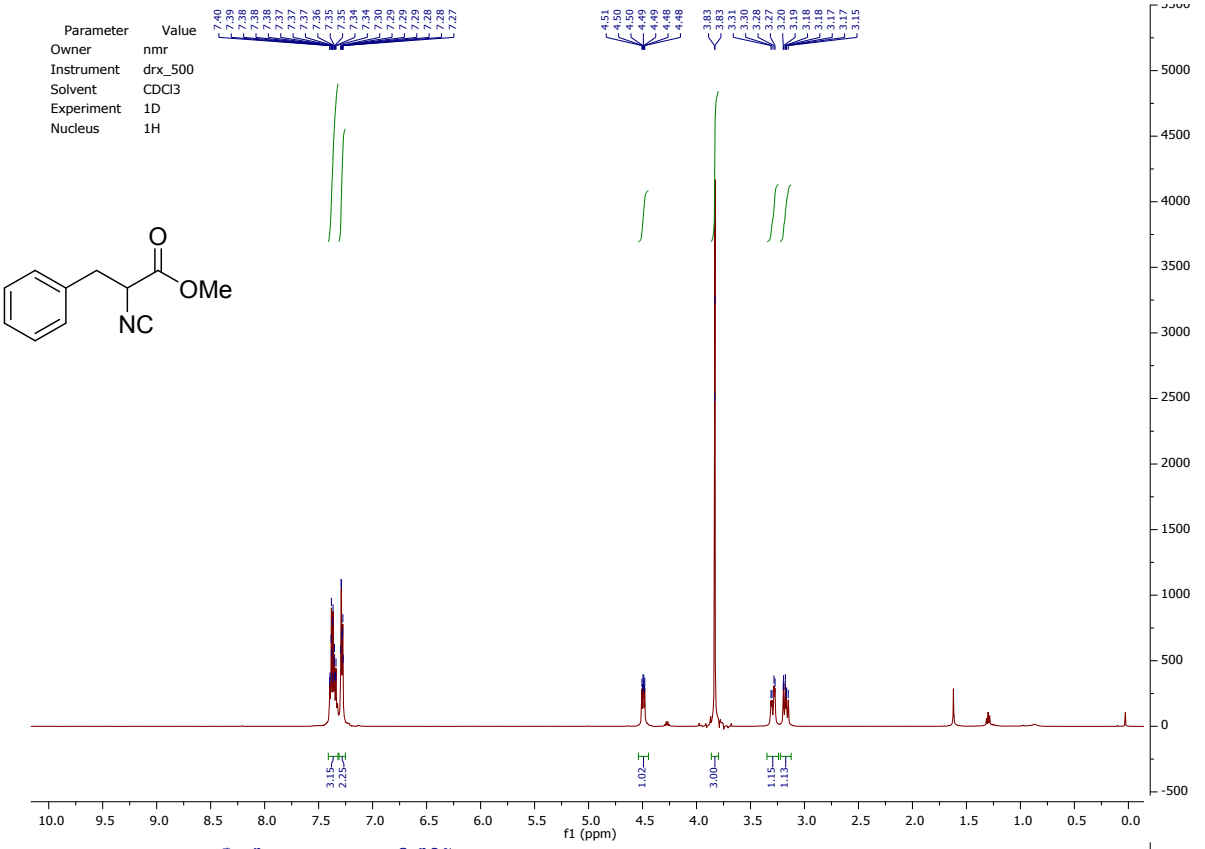


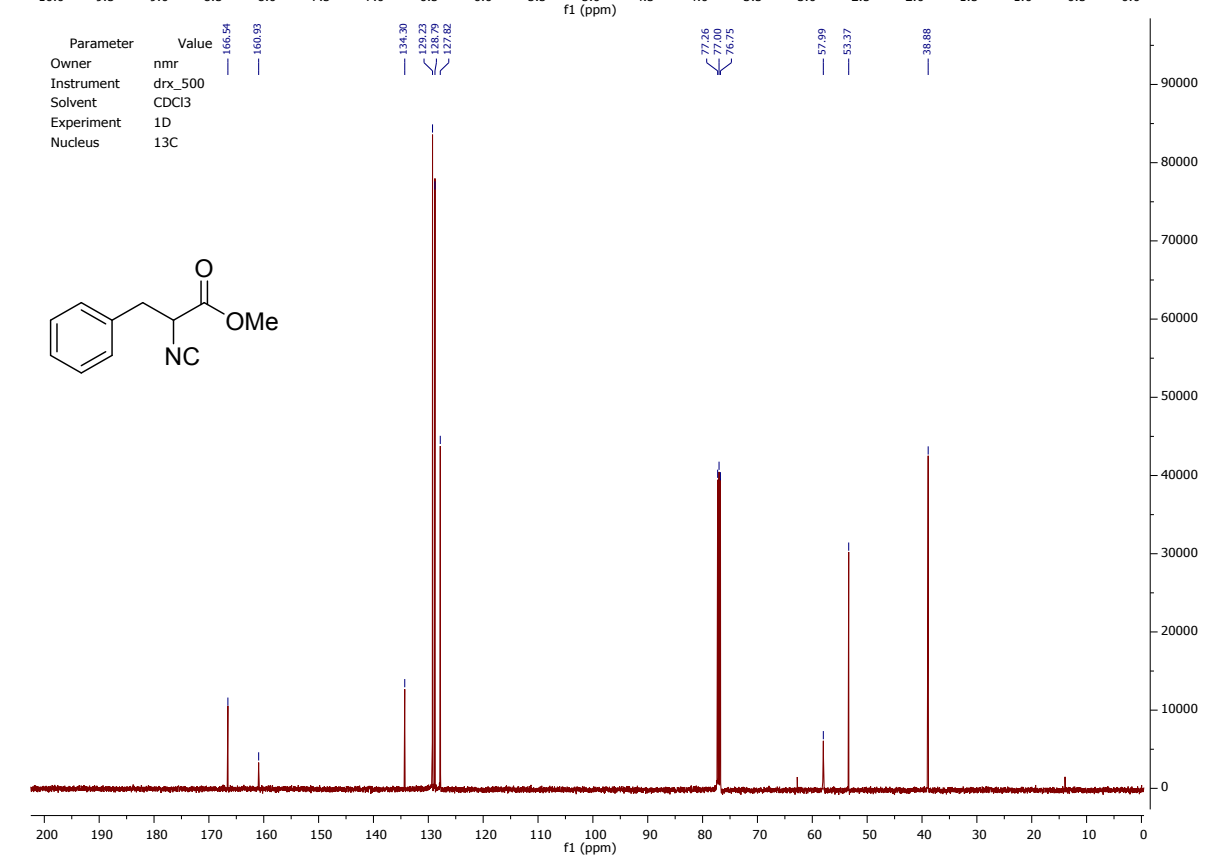
G-9 / I-41: 1-(2-Isocyanoethyl)cyclohex-1-ene



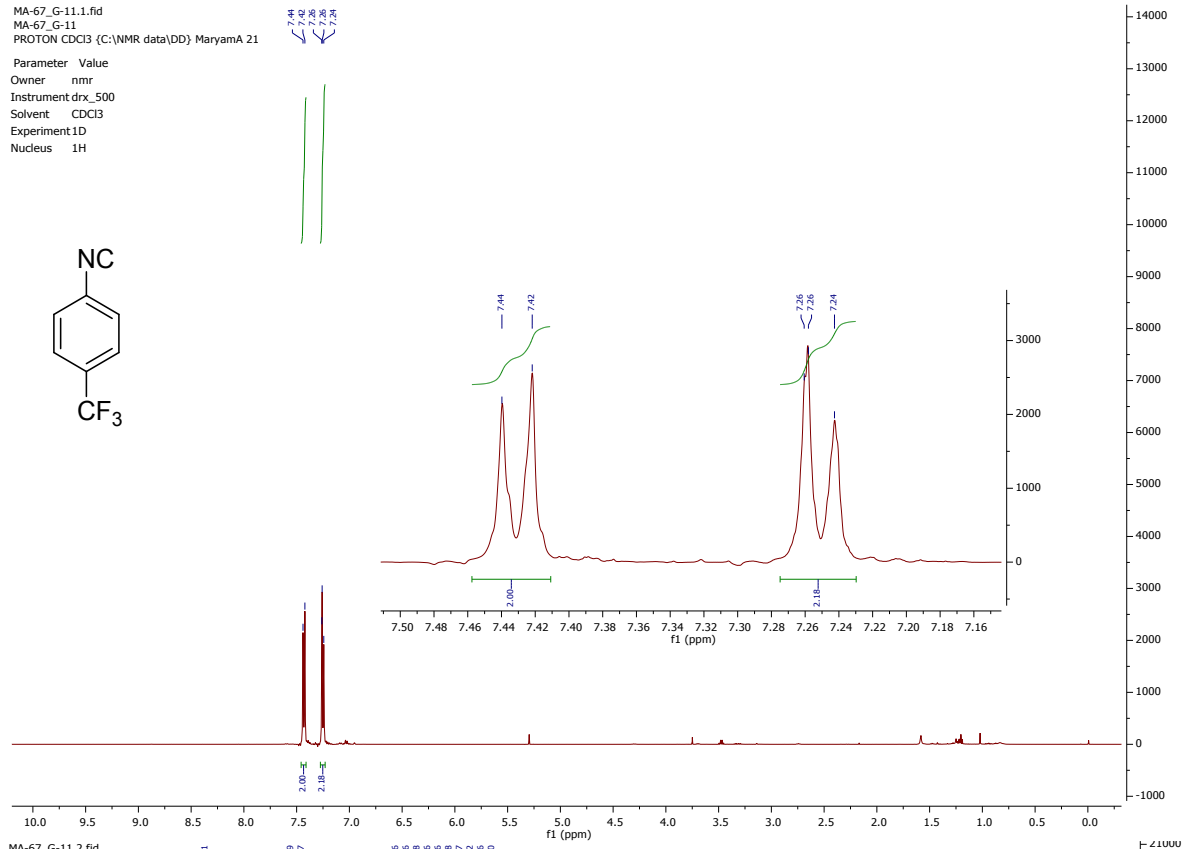


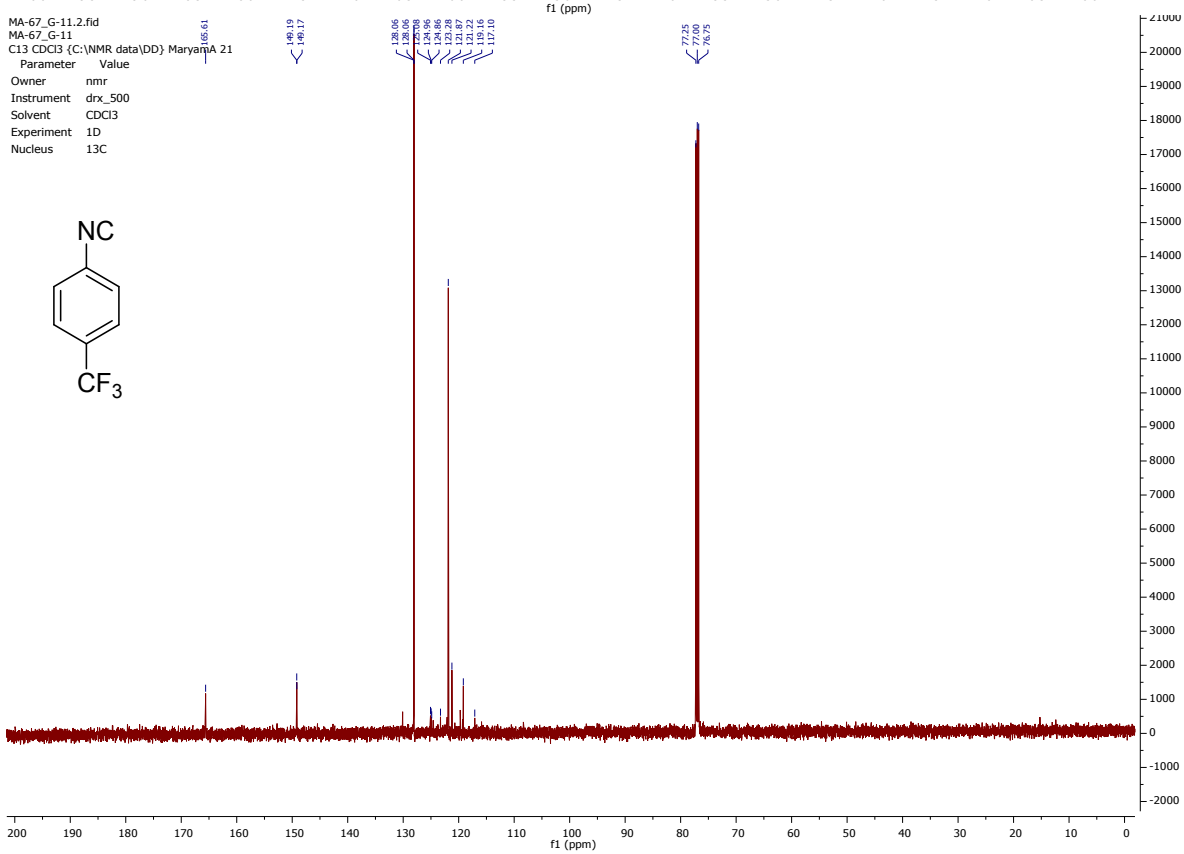
G-10: Methyl 2-isocyano-3-phenylpropanoate



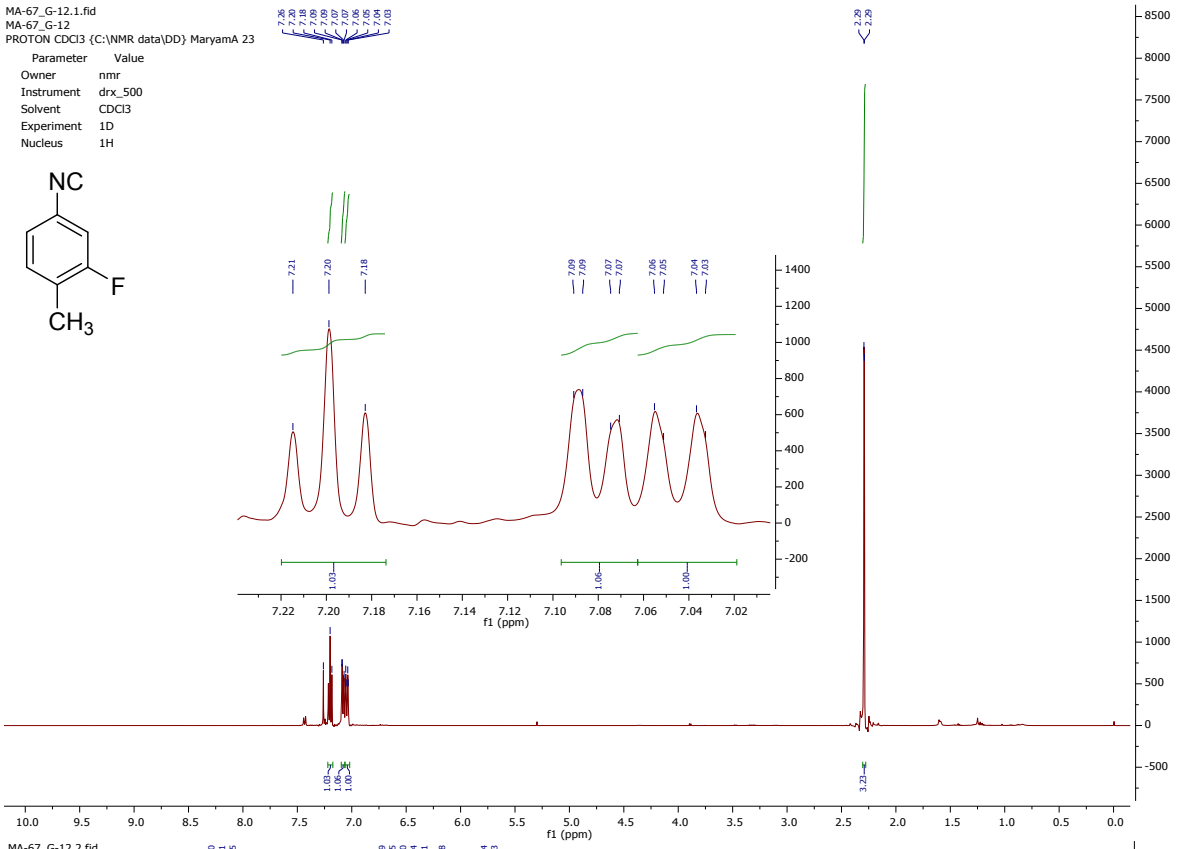


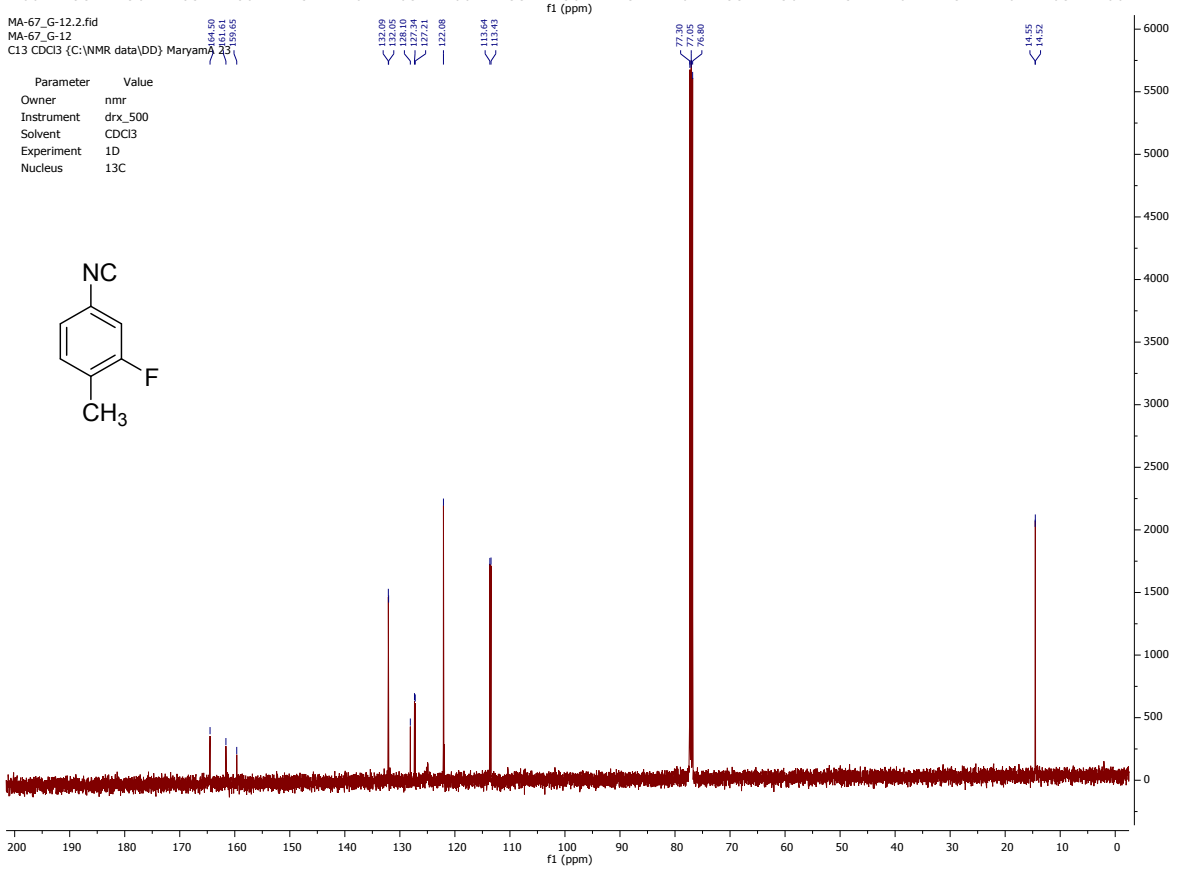
G-11: 1-Isocyano-4-(trifluoromethyl)benzene



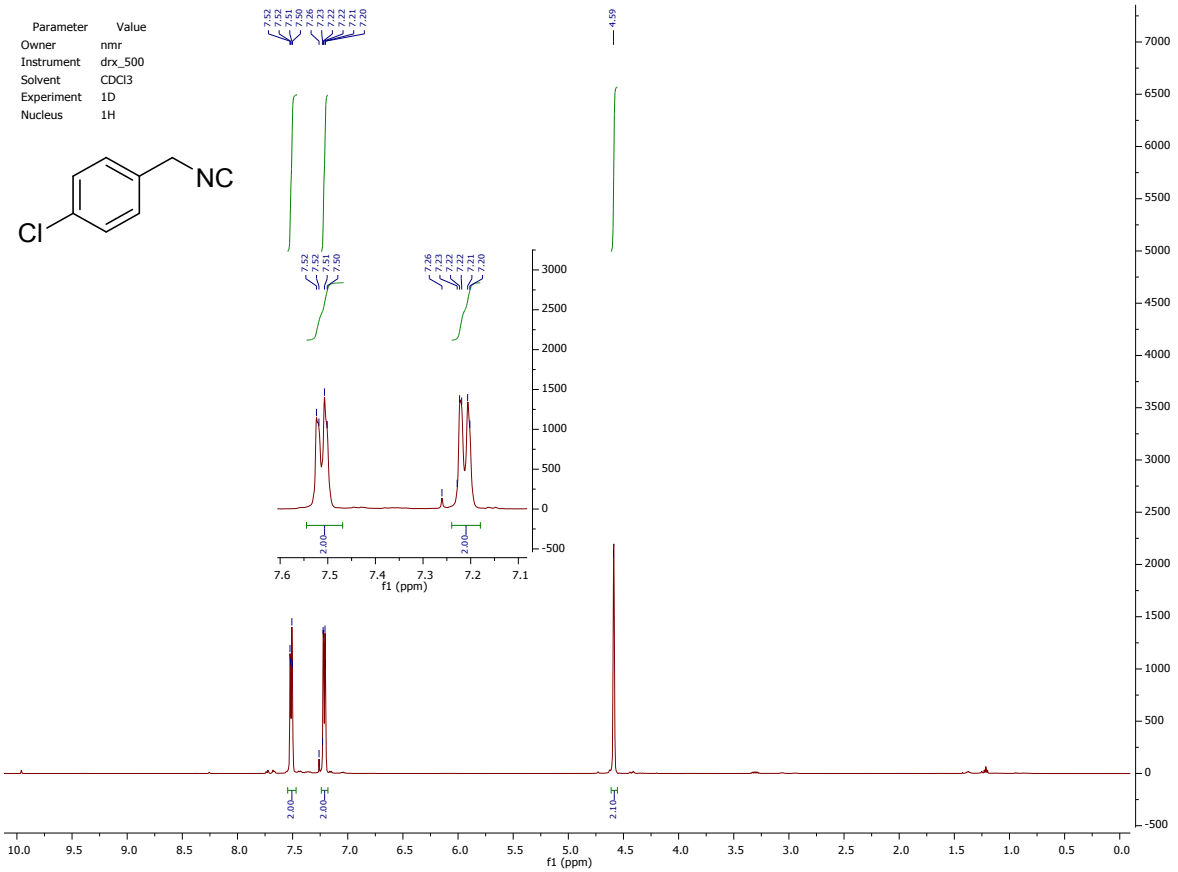


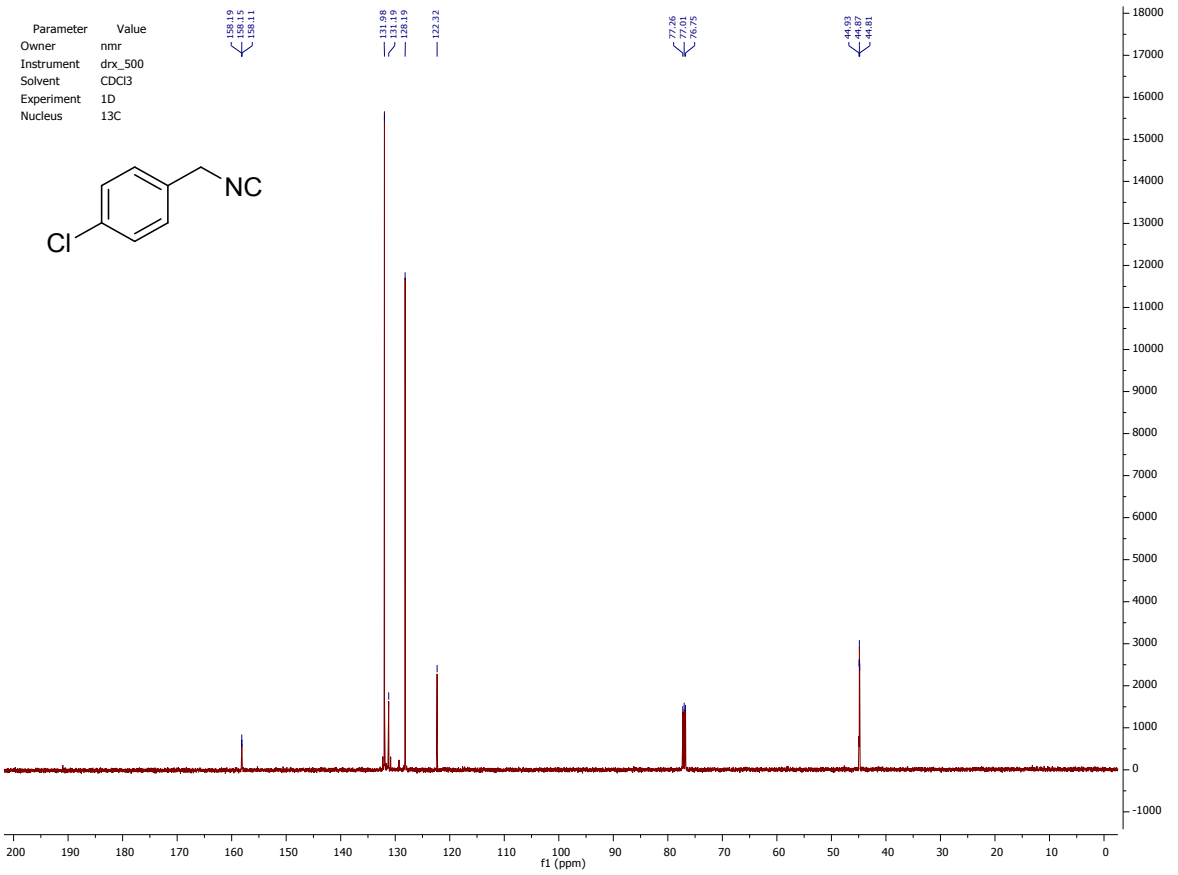
G-12: 2-Fluoro-4-isocyano-1-methylbenzene



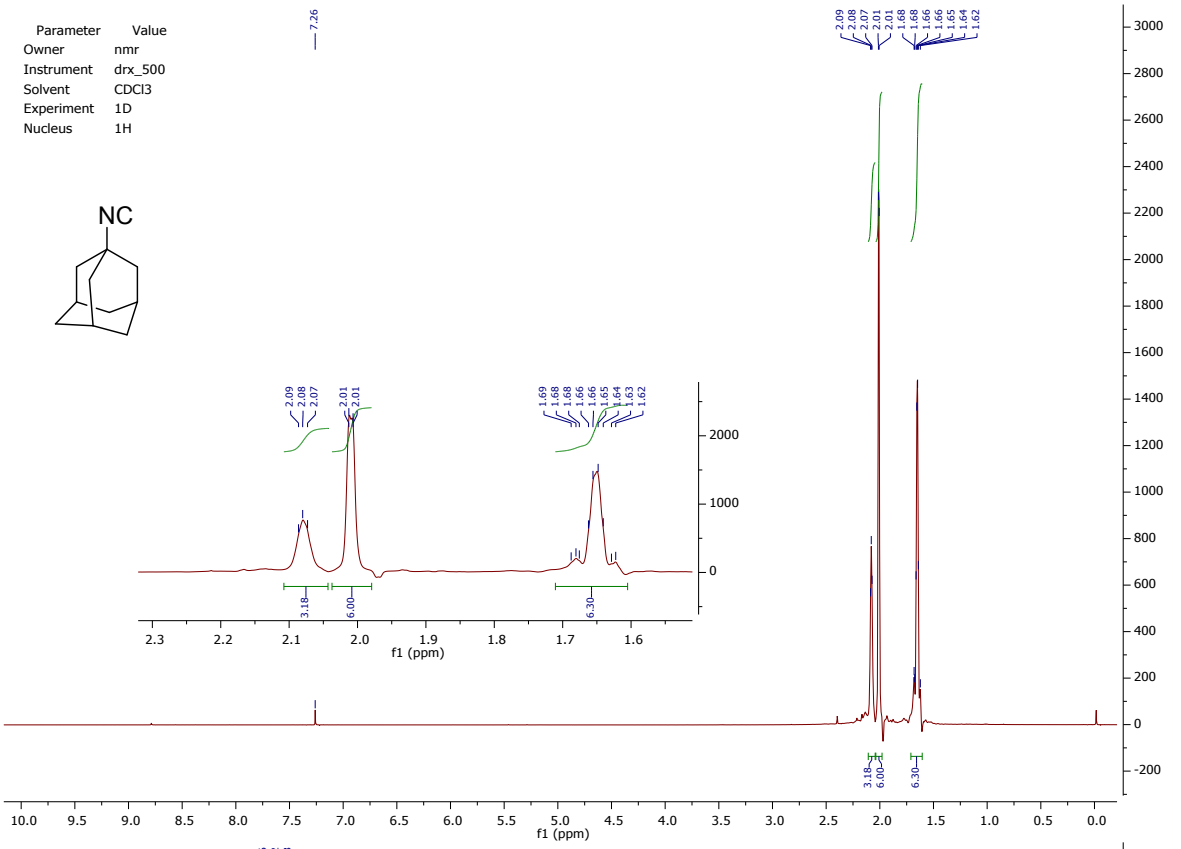


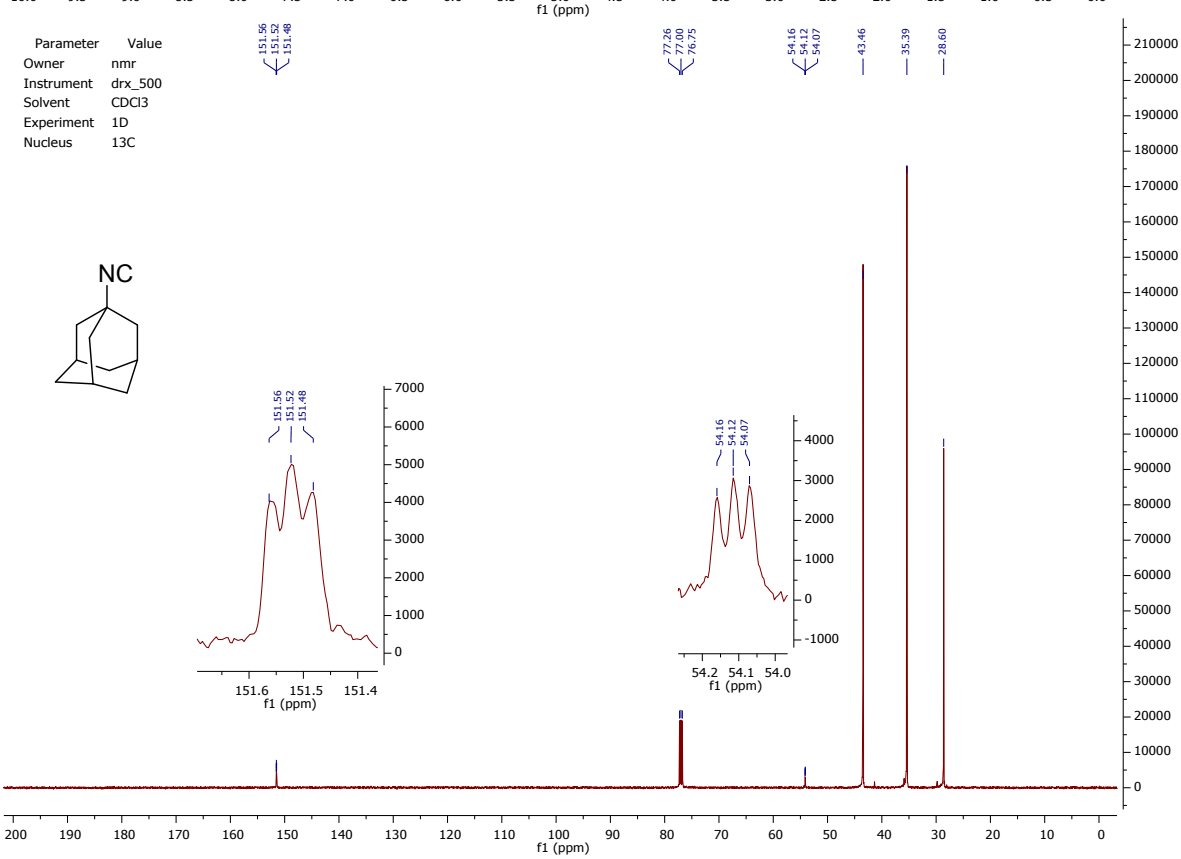
H-1 / I-6: 1-Chloro-4-(isocyanomethyl)benzene



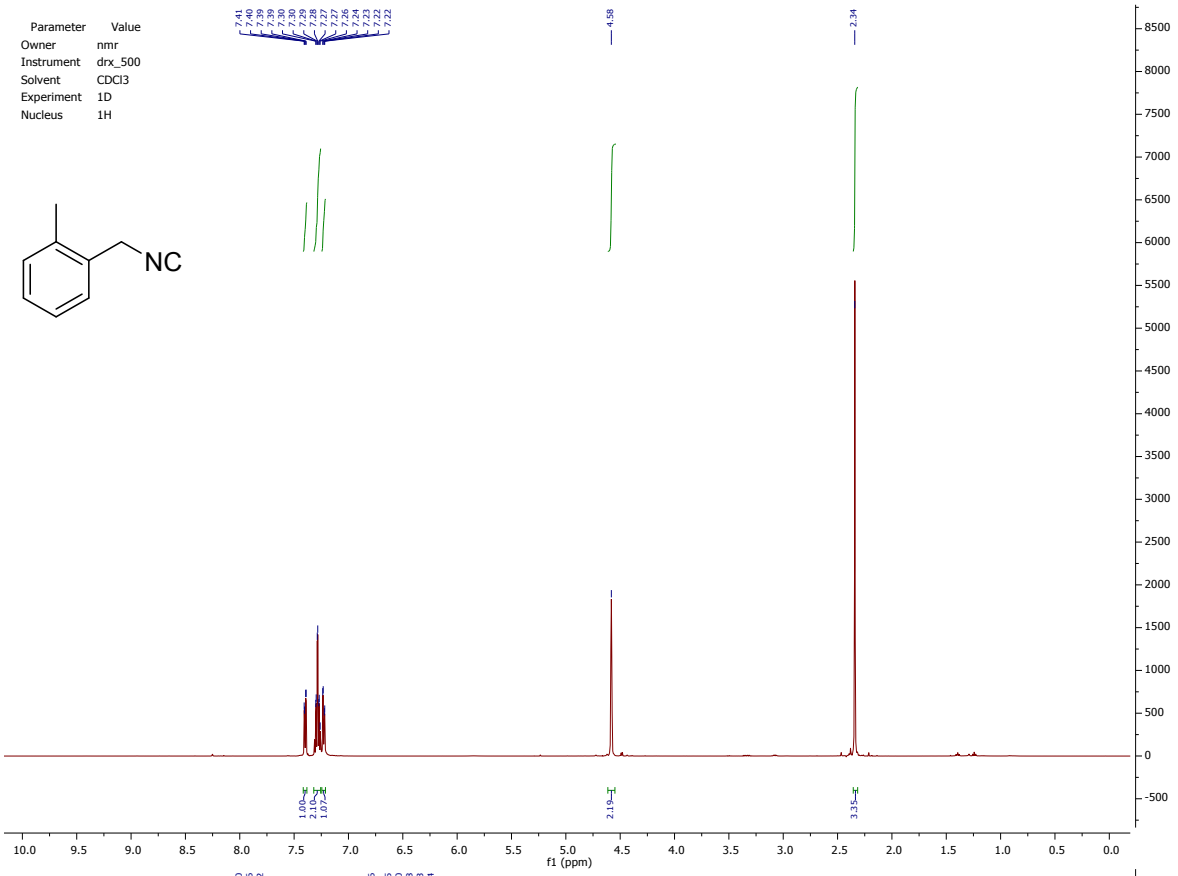


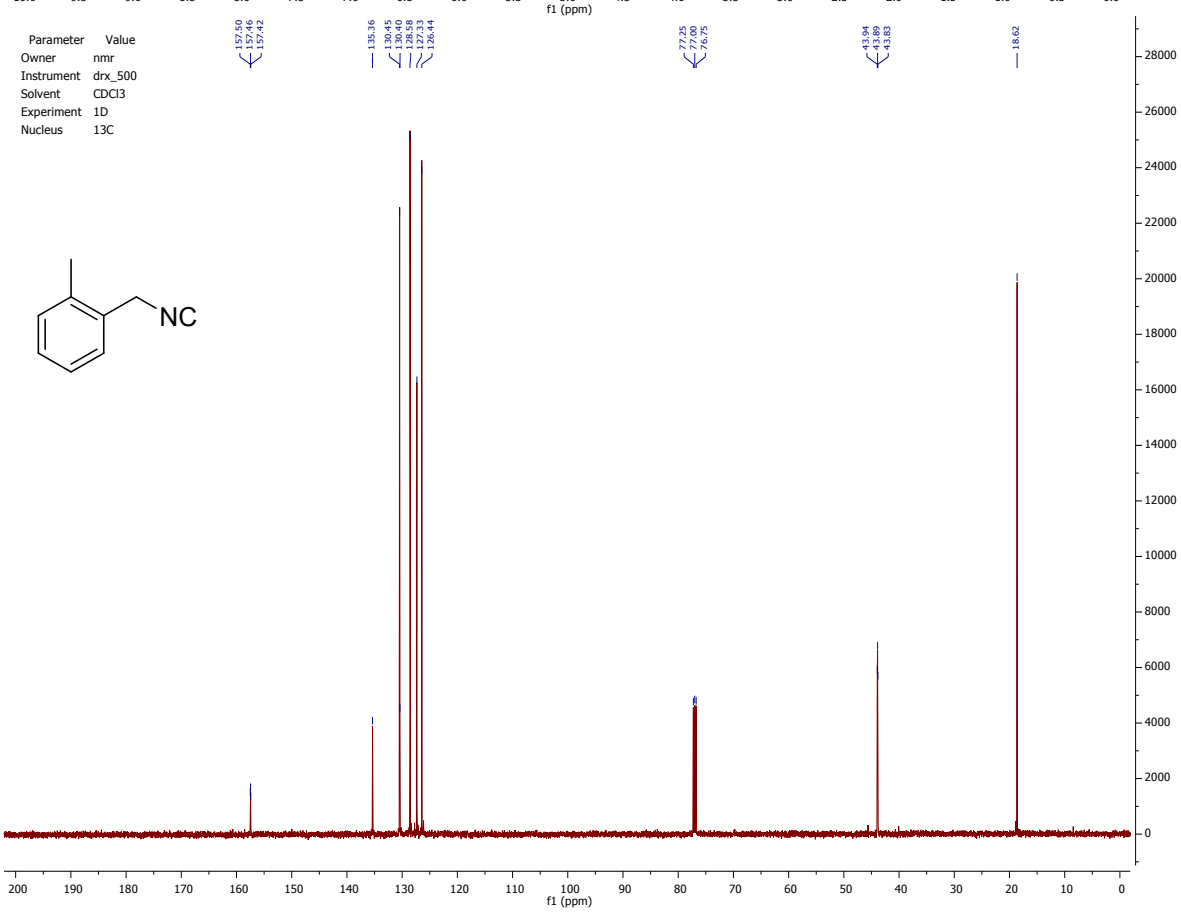
H-2 / I-49: (3*s*,5*s*,7*s*)-1-Isocyanoadamantane



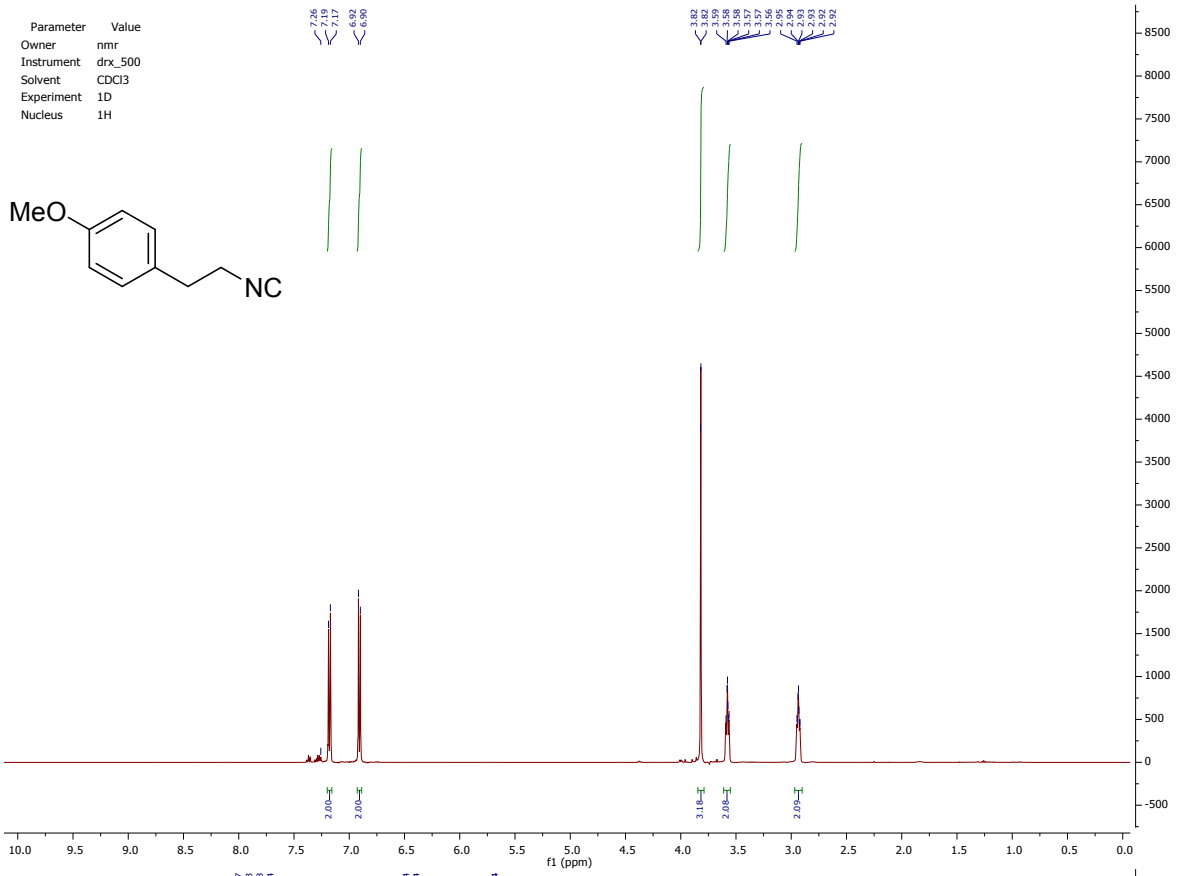


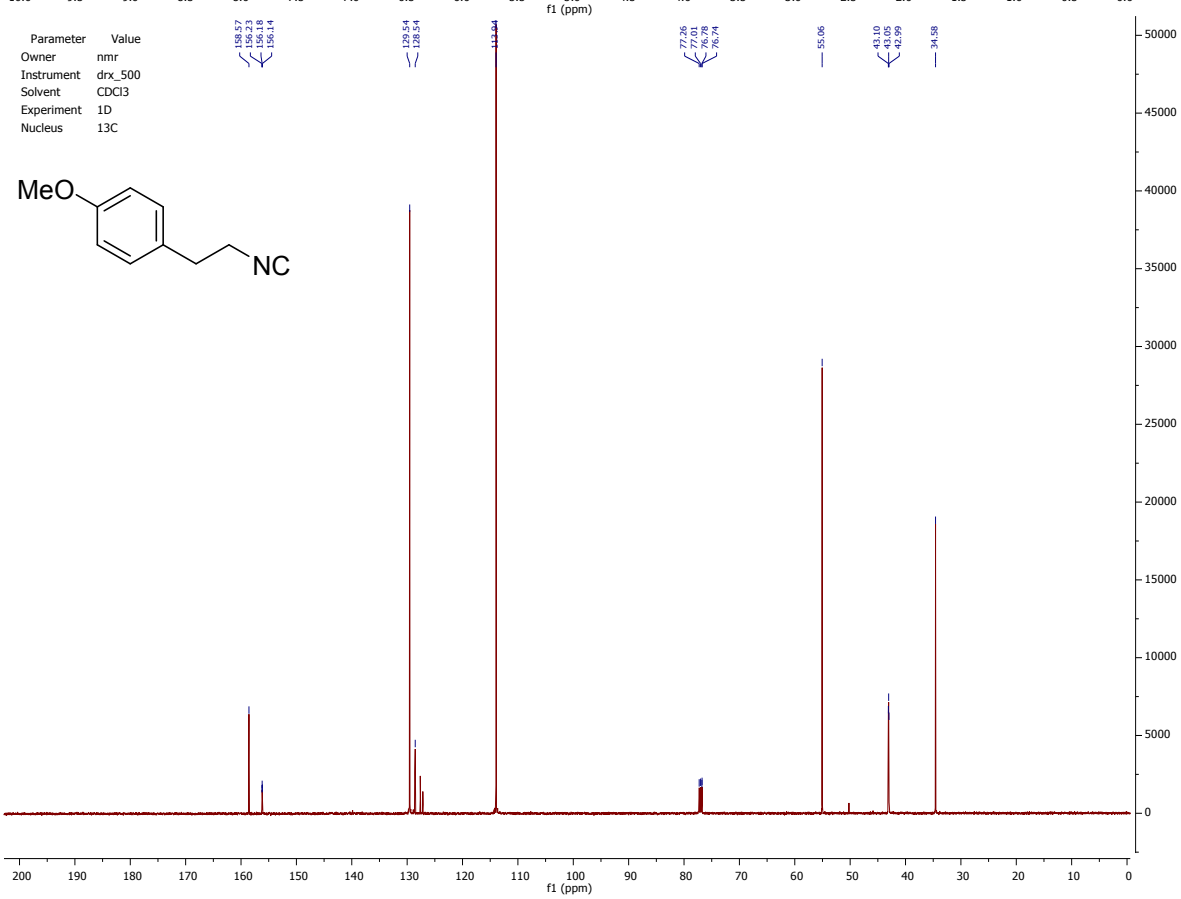
H-3 / I-13: 1-(isocyanomethyl)-2-methylbenzene



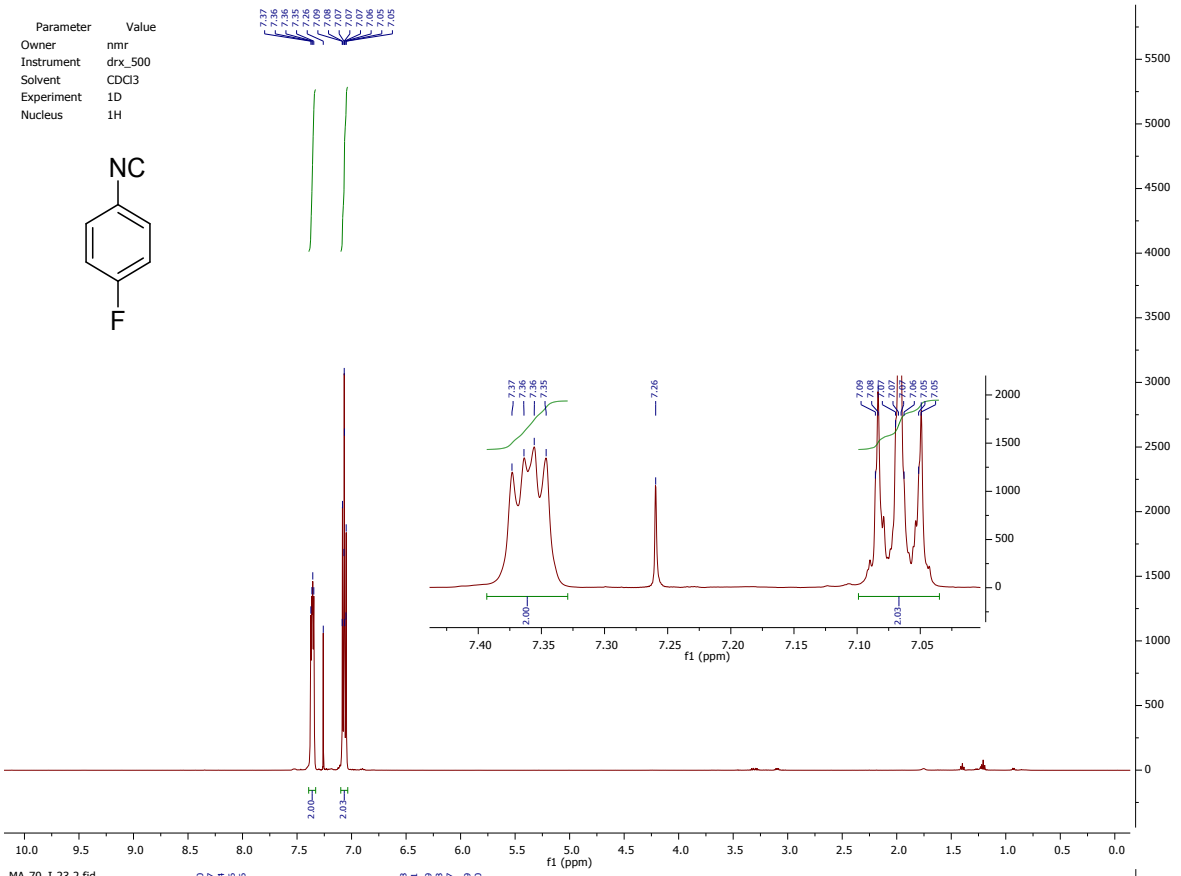


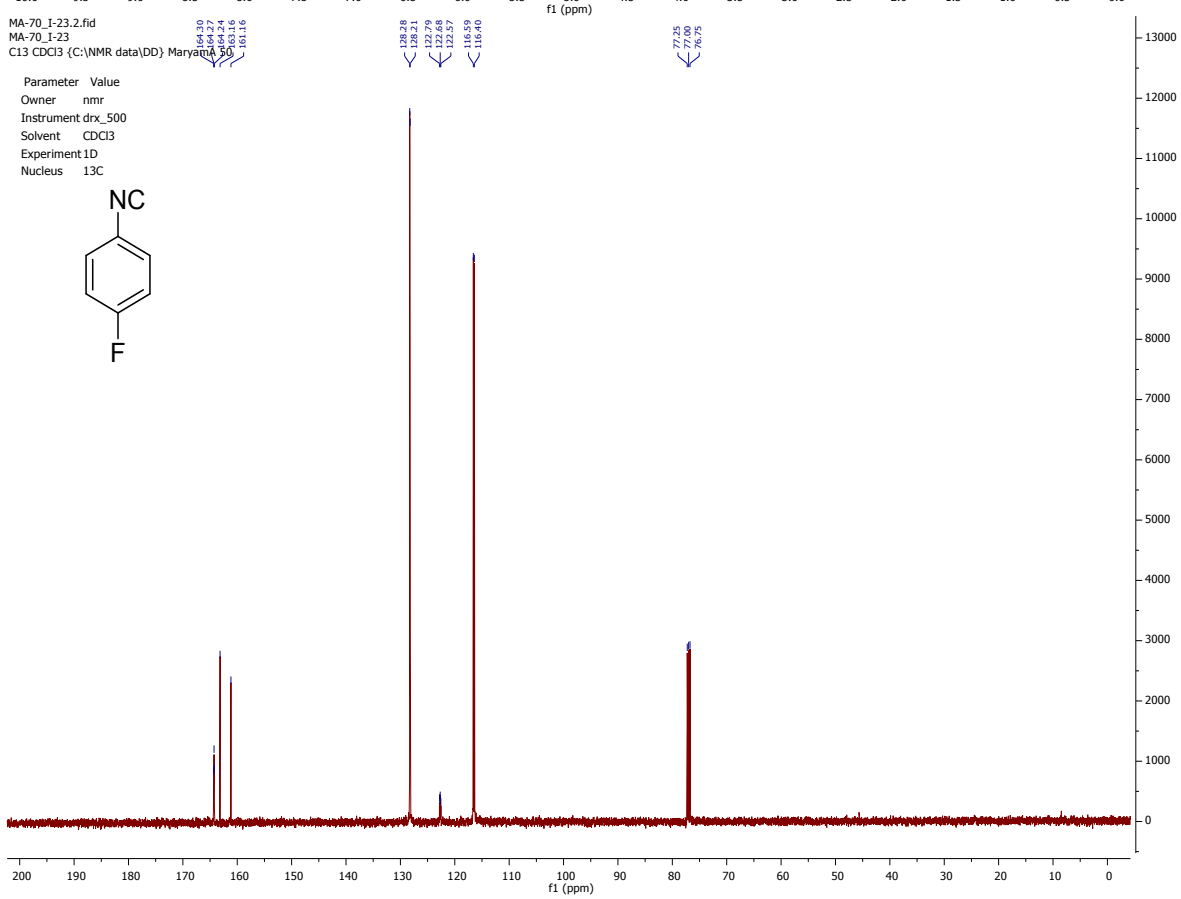
H-4 / I-20: 1-(2-Isocyanoethyl)-4-methoxybenzene



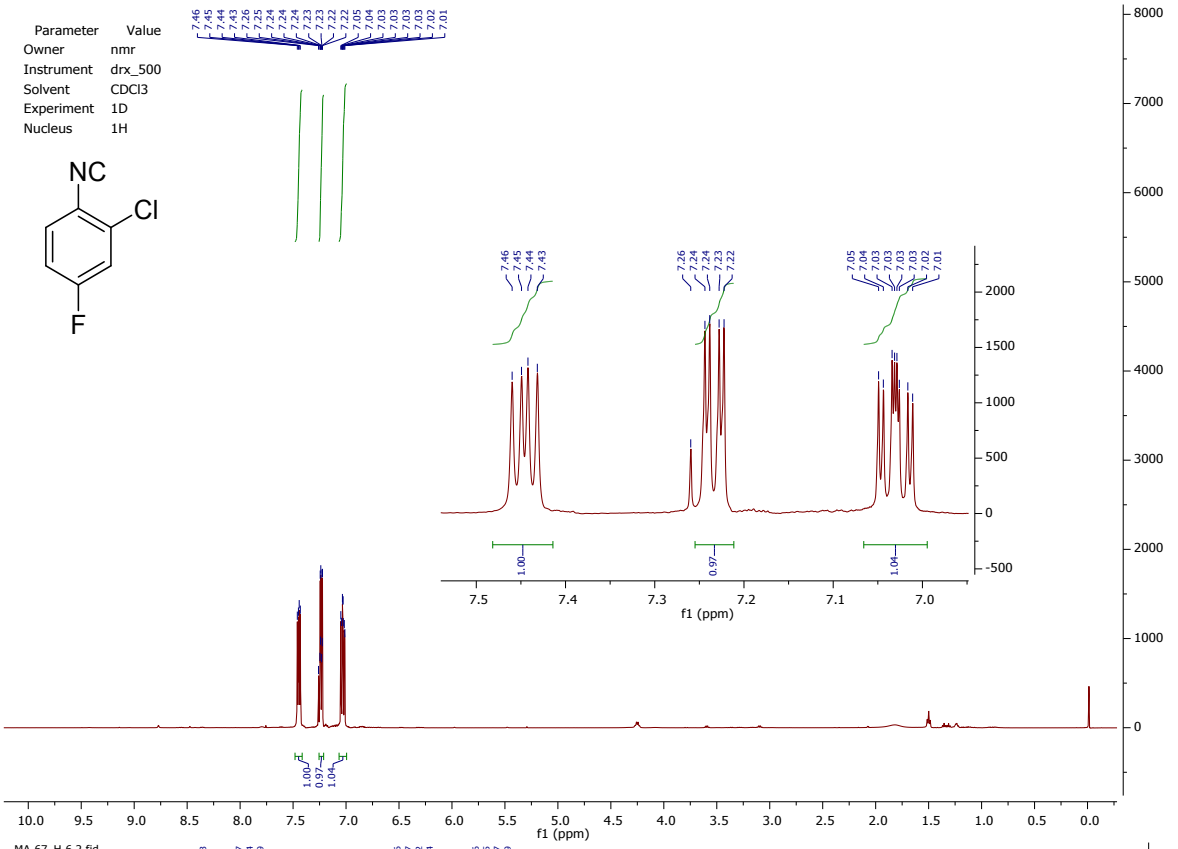


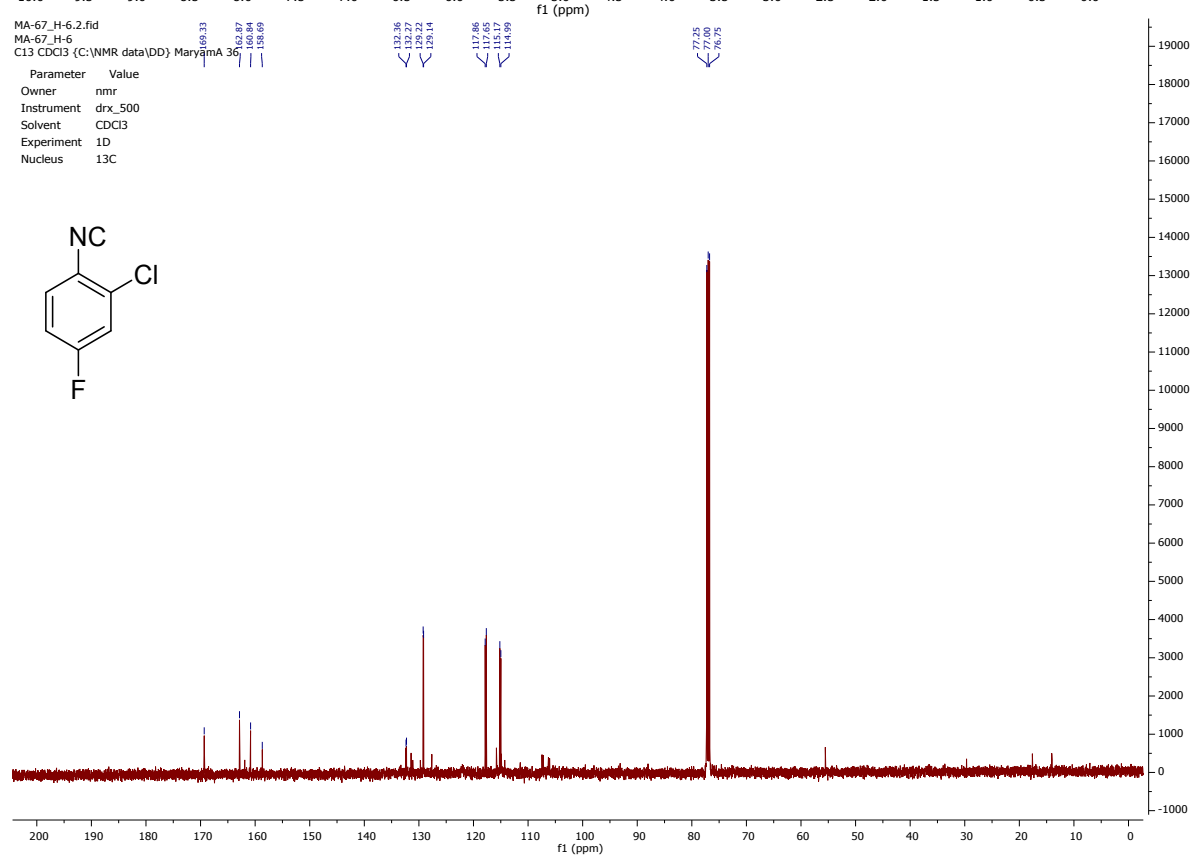
H-5 / I-23: 1-Fluoro-4-isocyanobenzene



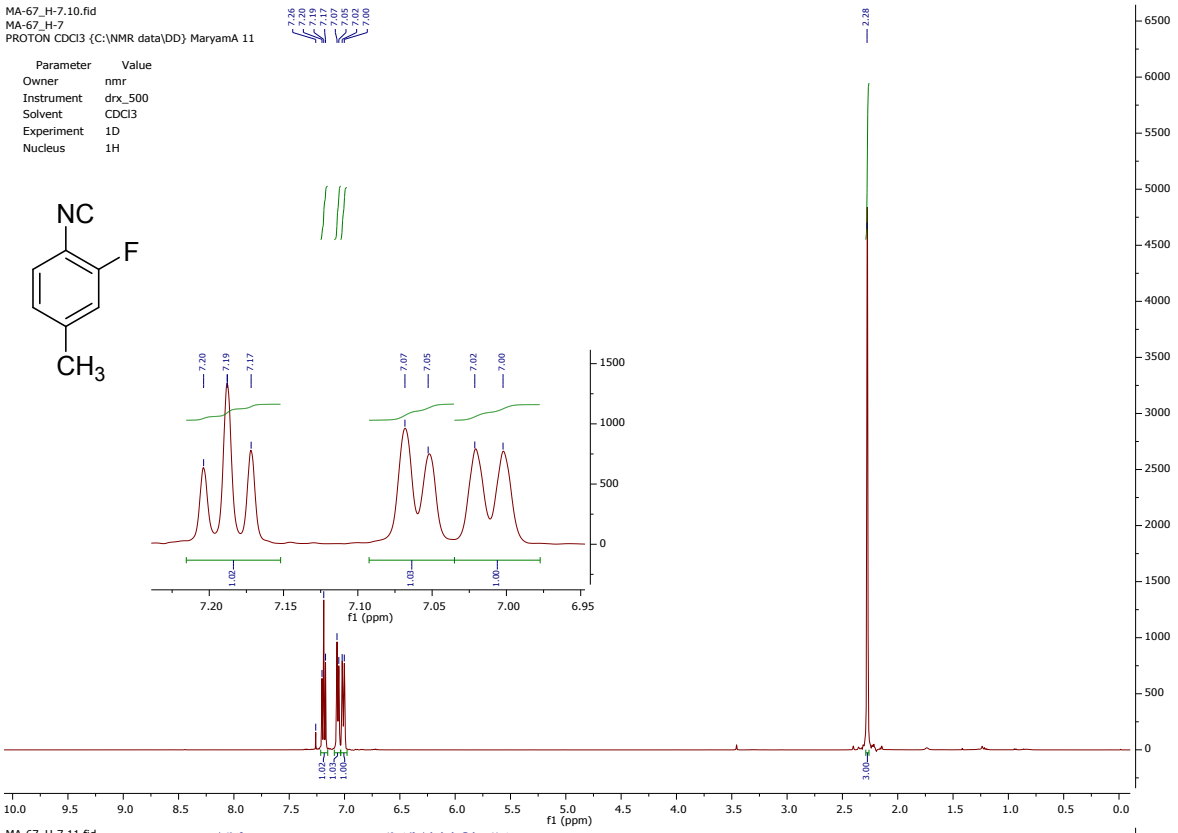


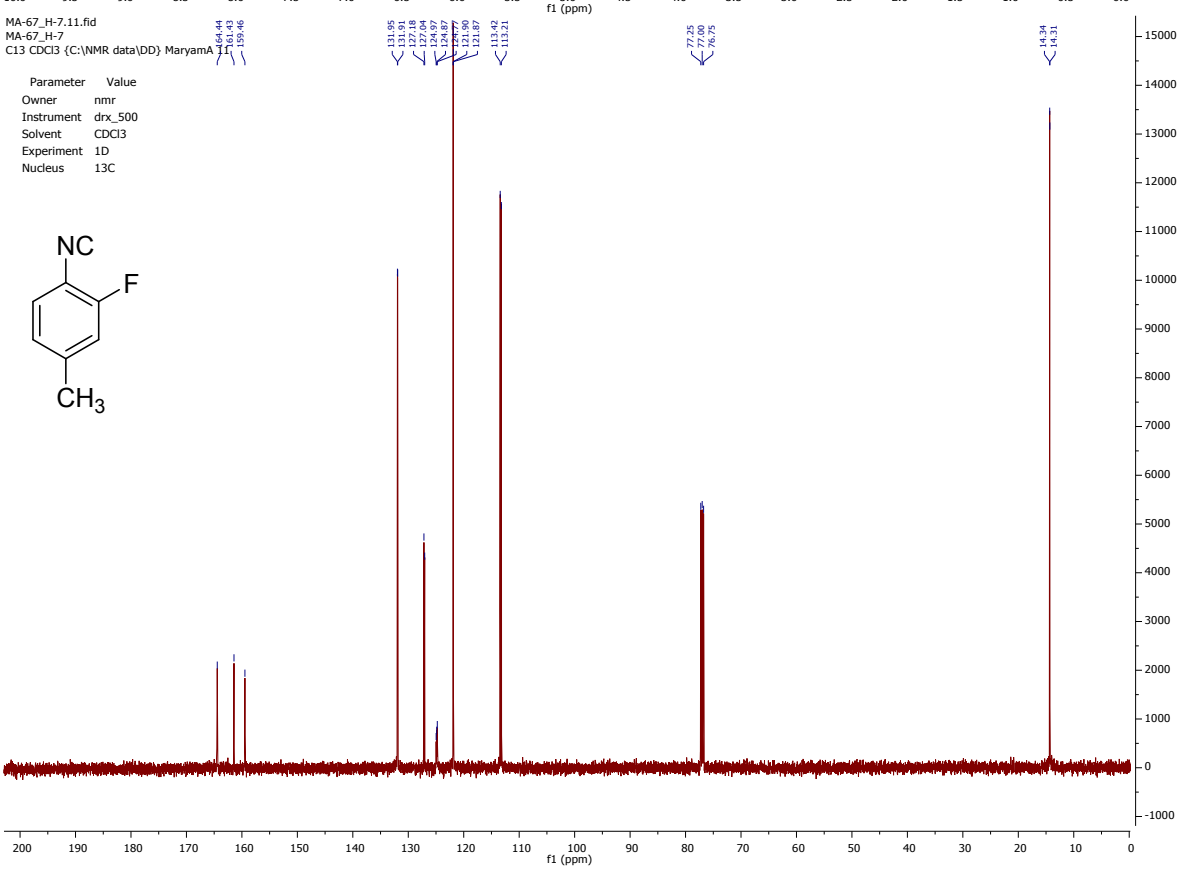
H-6: 2-Chloro-4-fluoro-1-isocyanobenzene



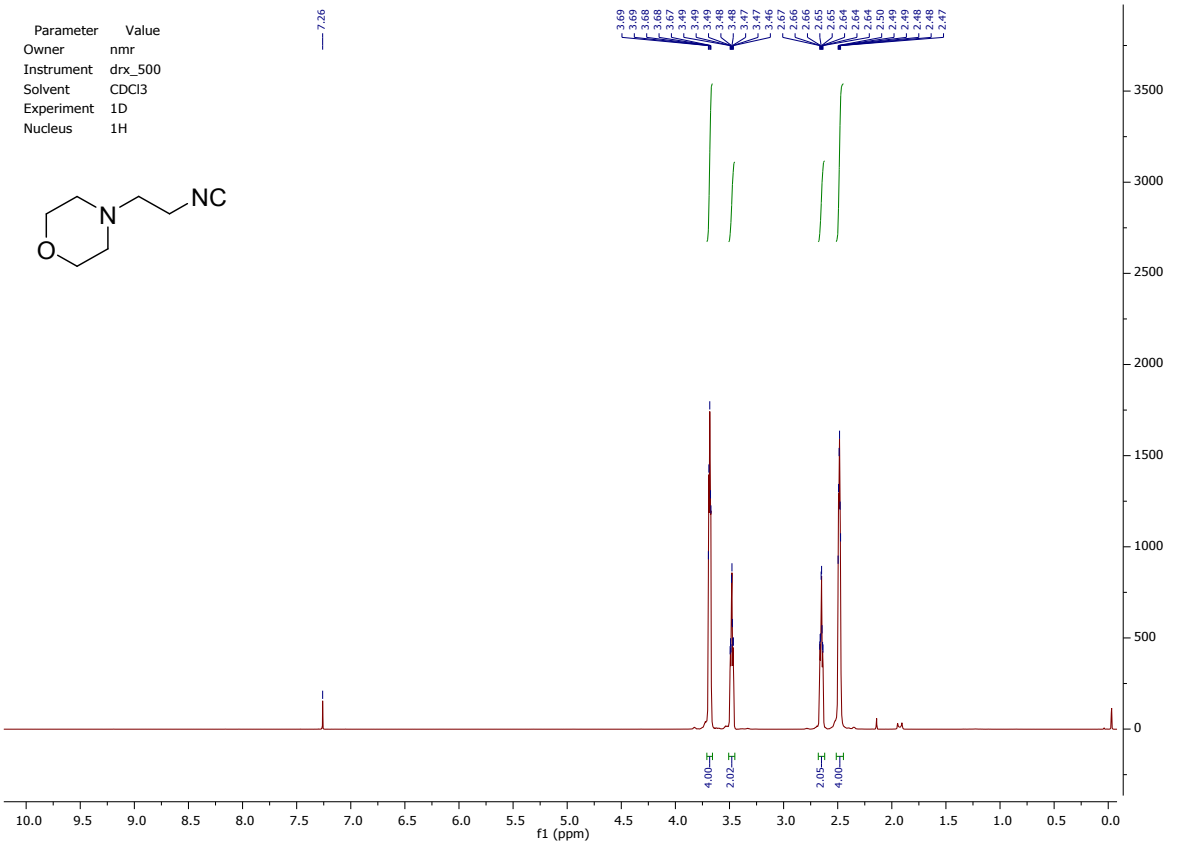


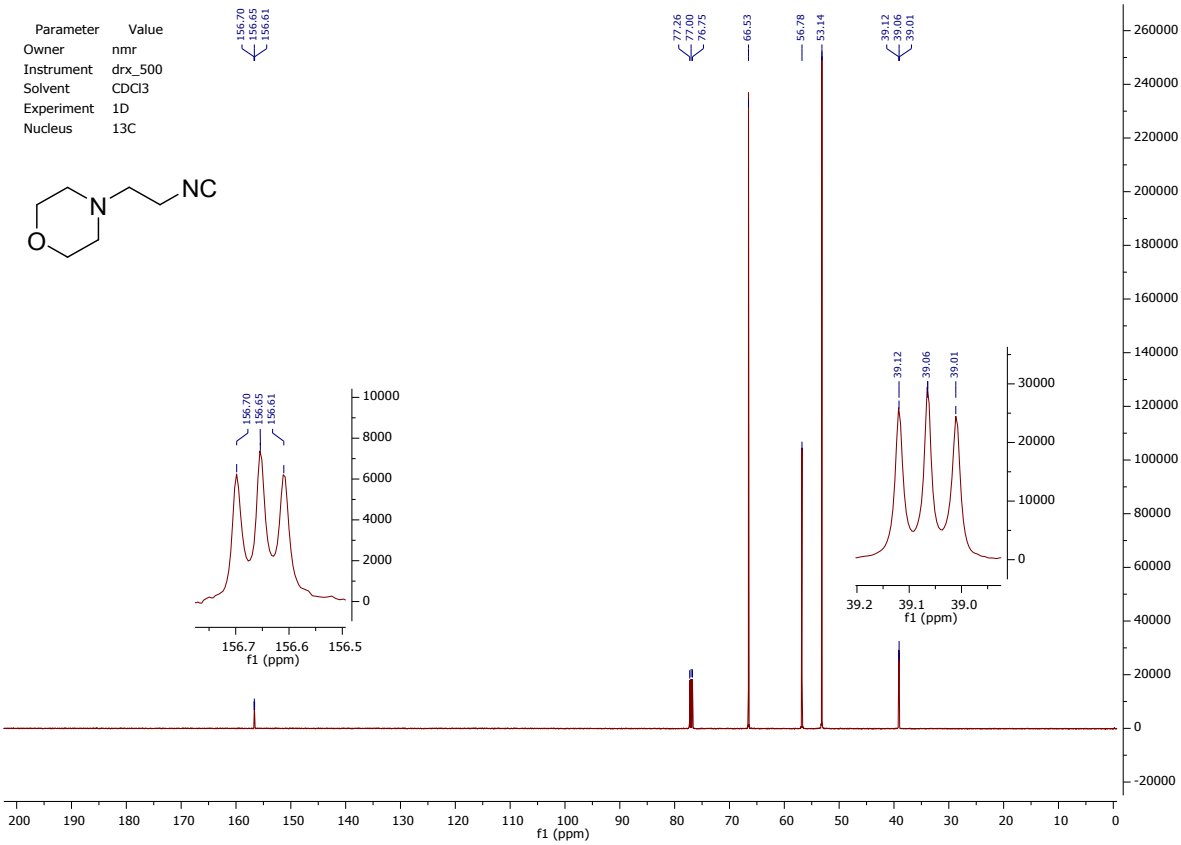
H-7: 2-Fluoro-1-isocyano-4-methylbenzene



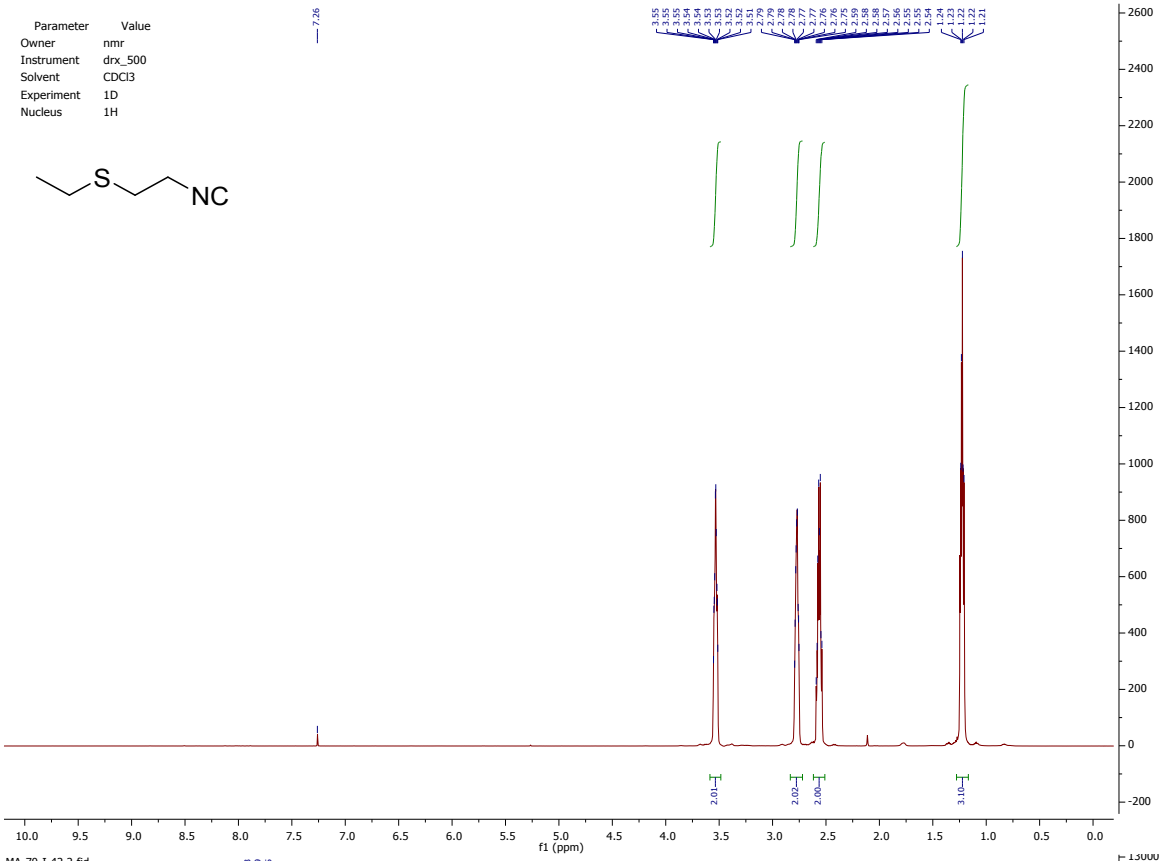


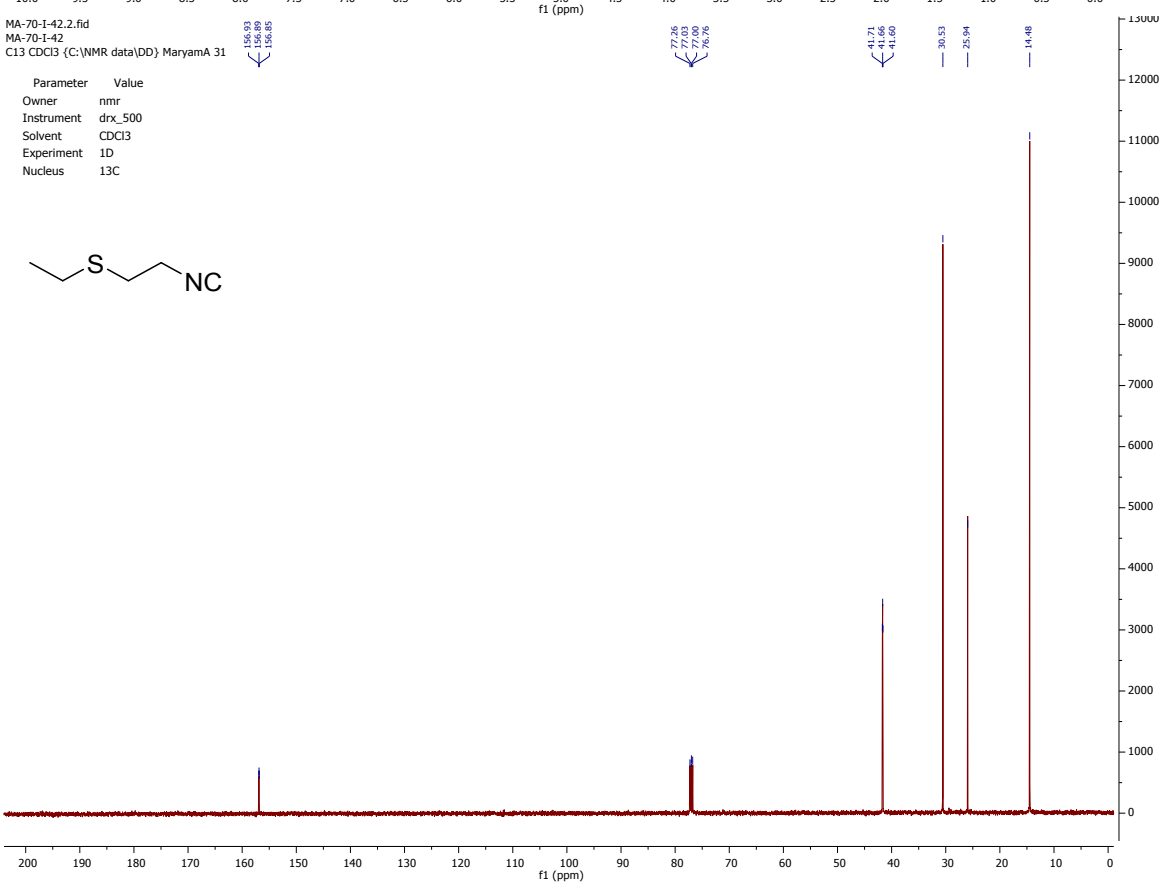
H-8 / I-59: 4-(2-Isocyanoethyl)morpholine



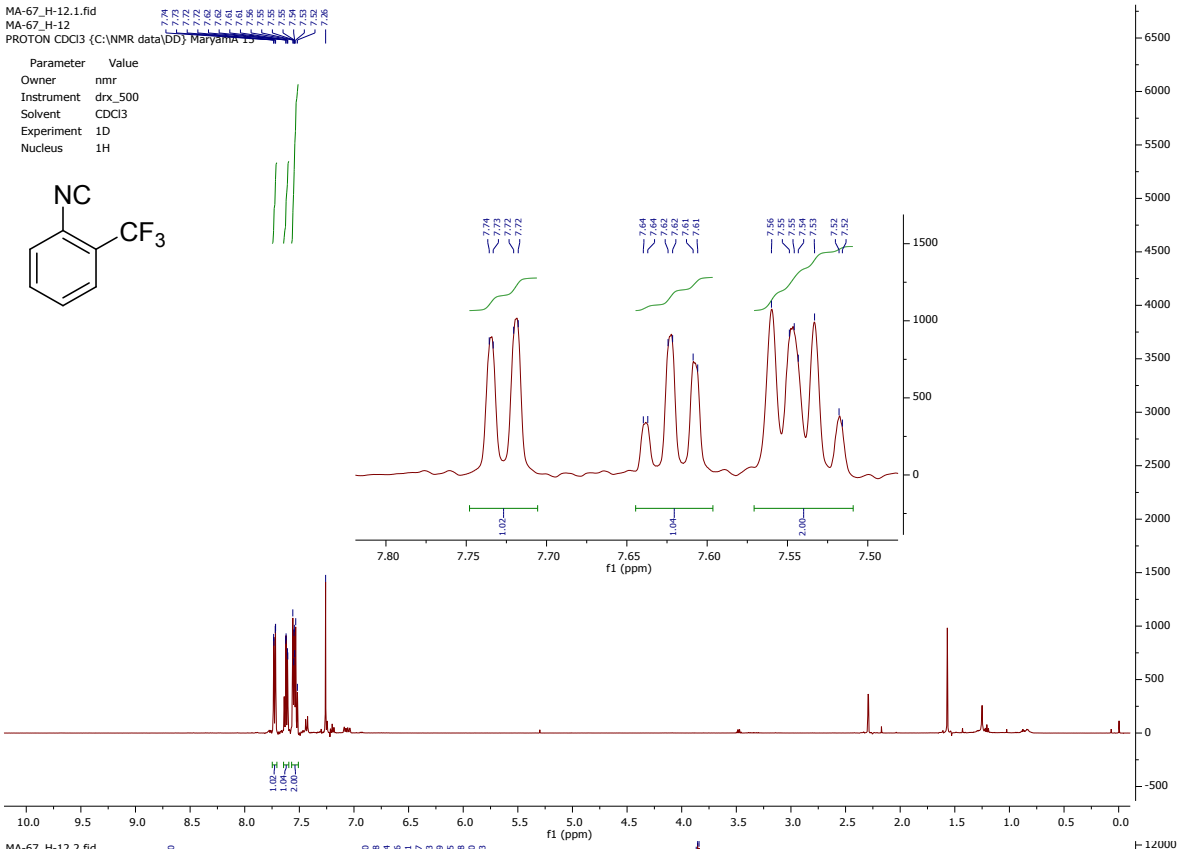


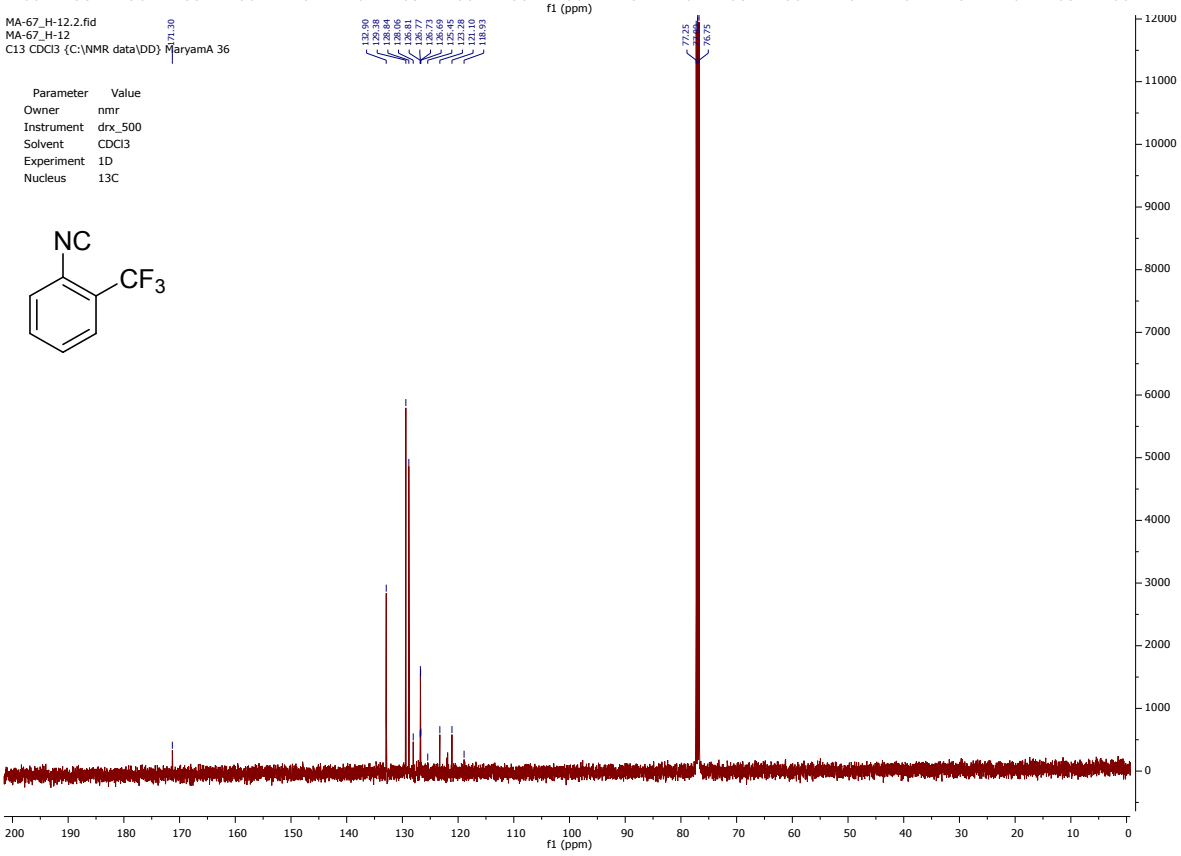
H-9 / I-42: Ethyl(2-isocyanoethyl)sulfane



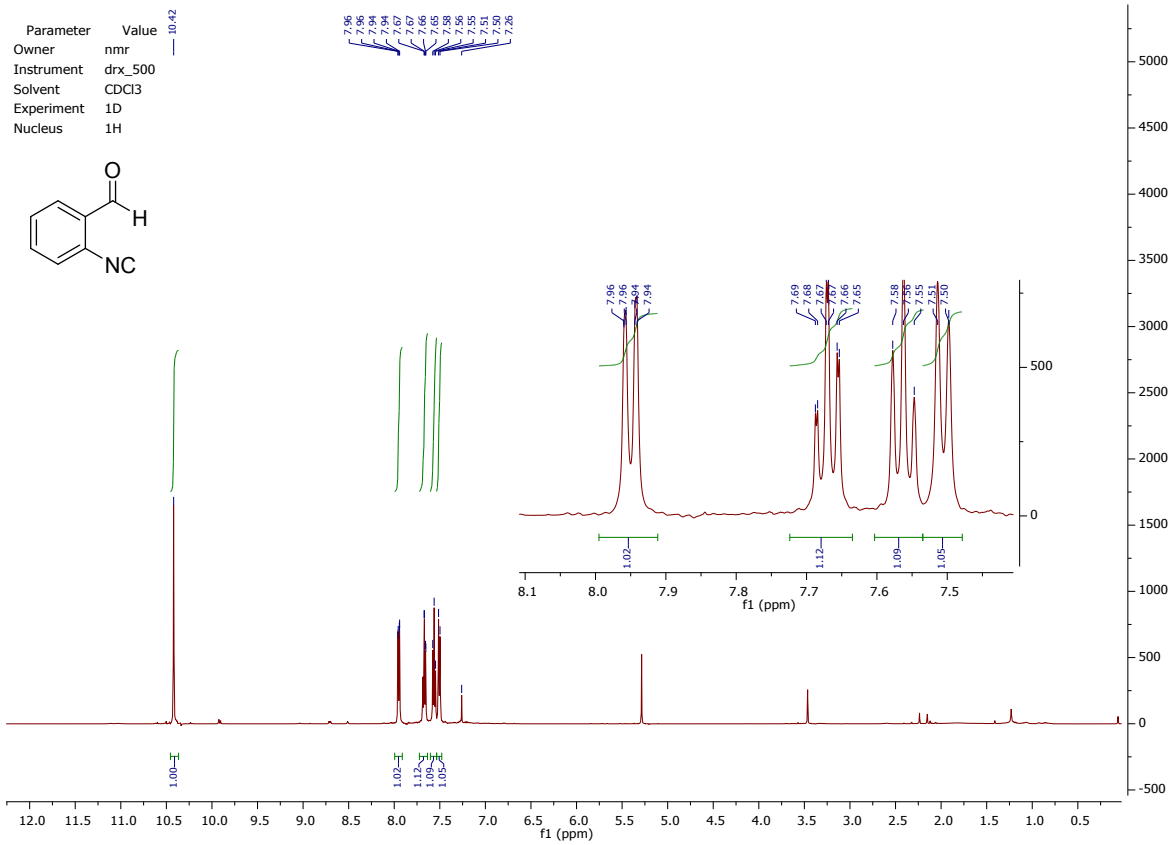


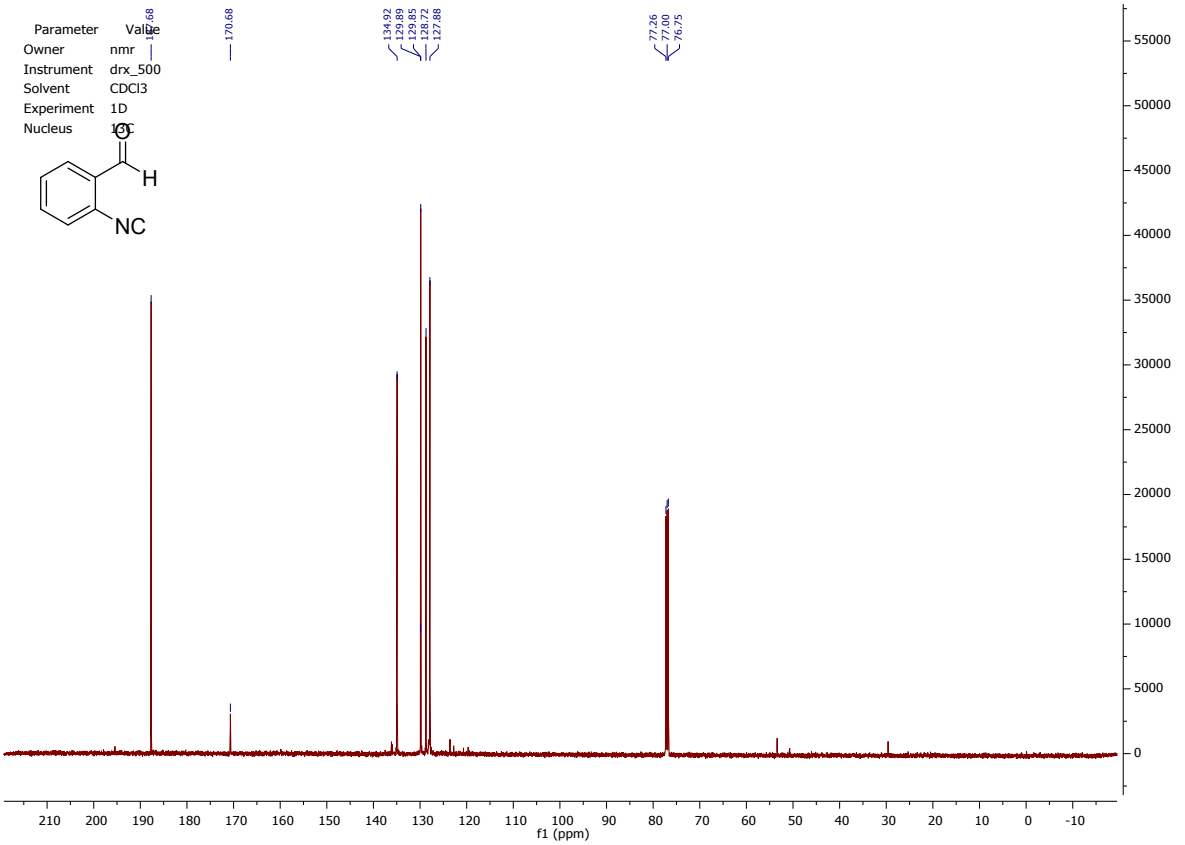
H-12: 1-Isocyano-2-(trifluoromethyl)benzene



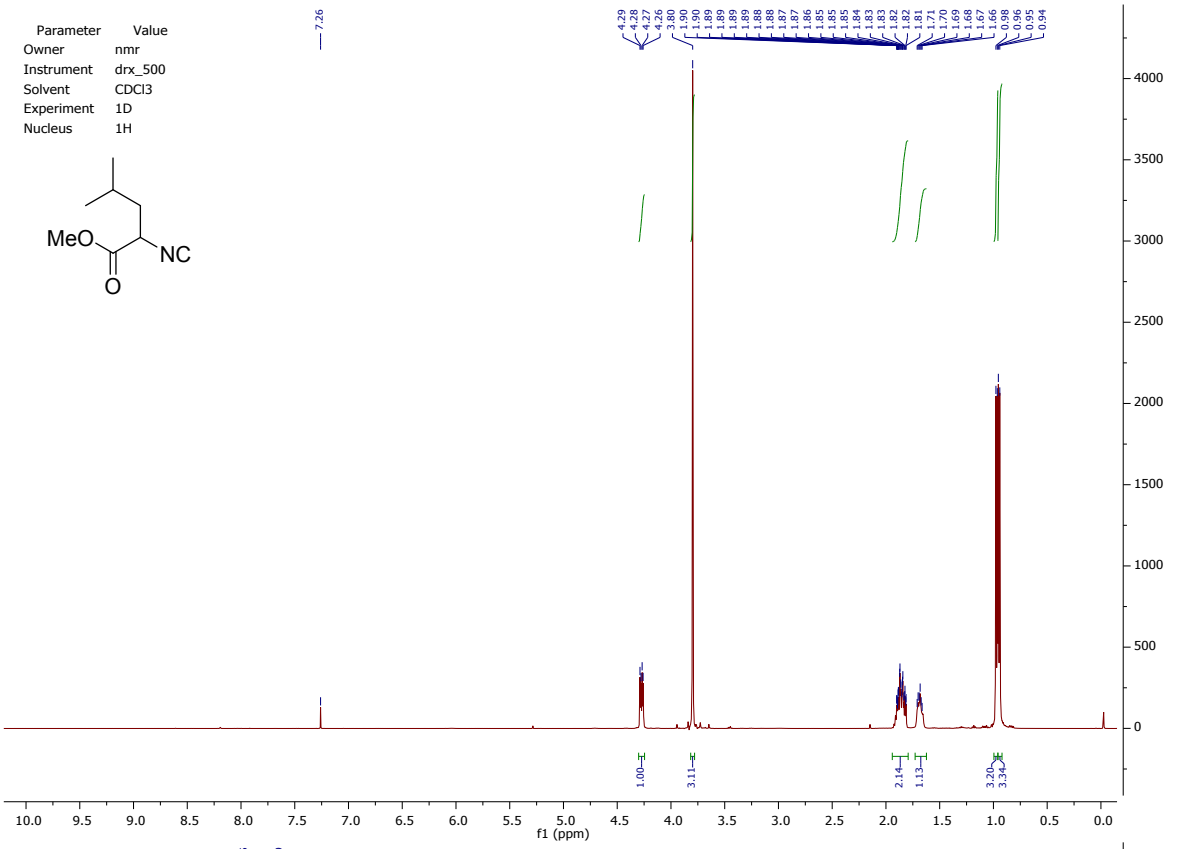


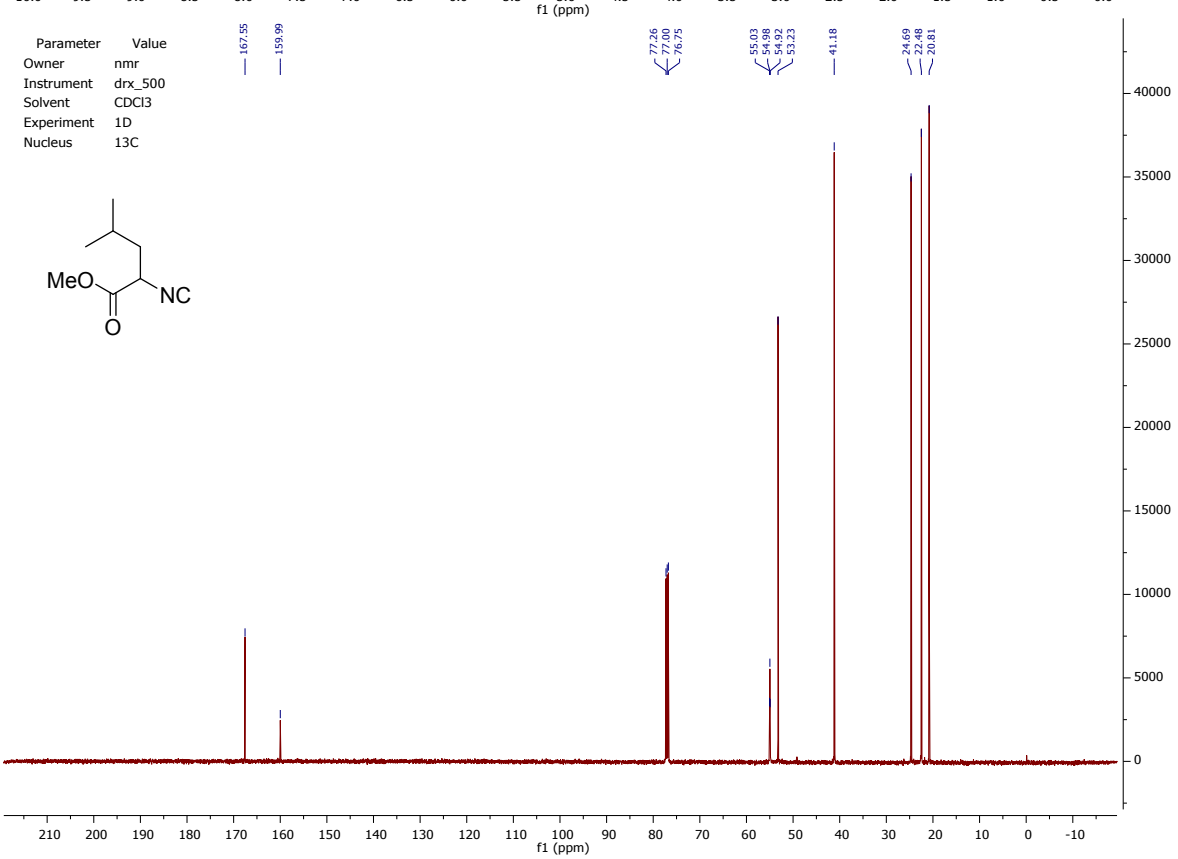
I-51: 2-Isocyanobenzaldehyde



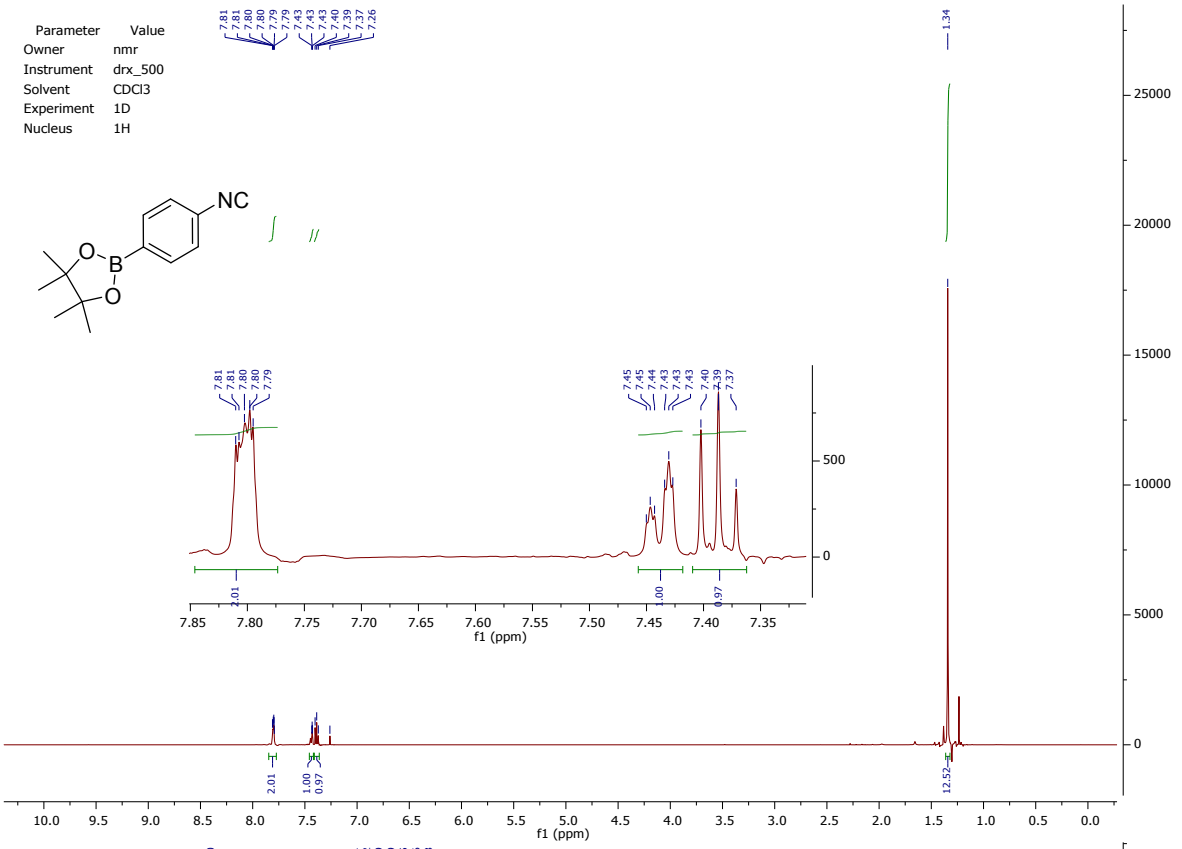


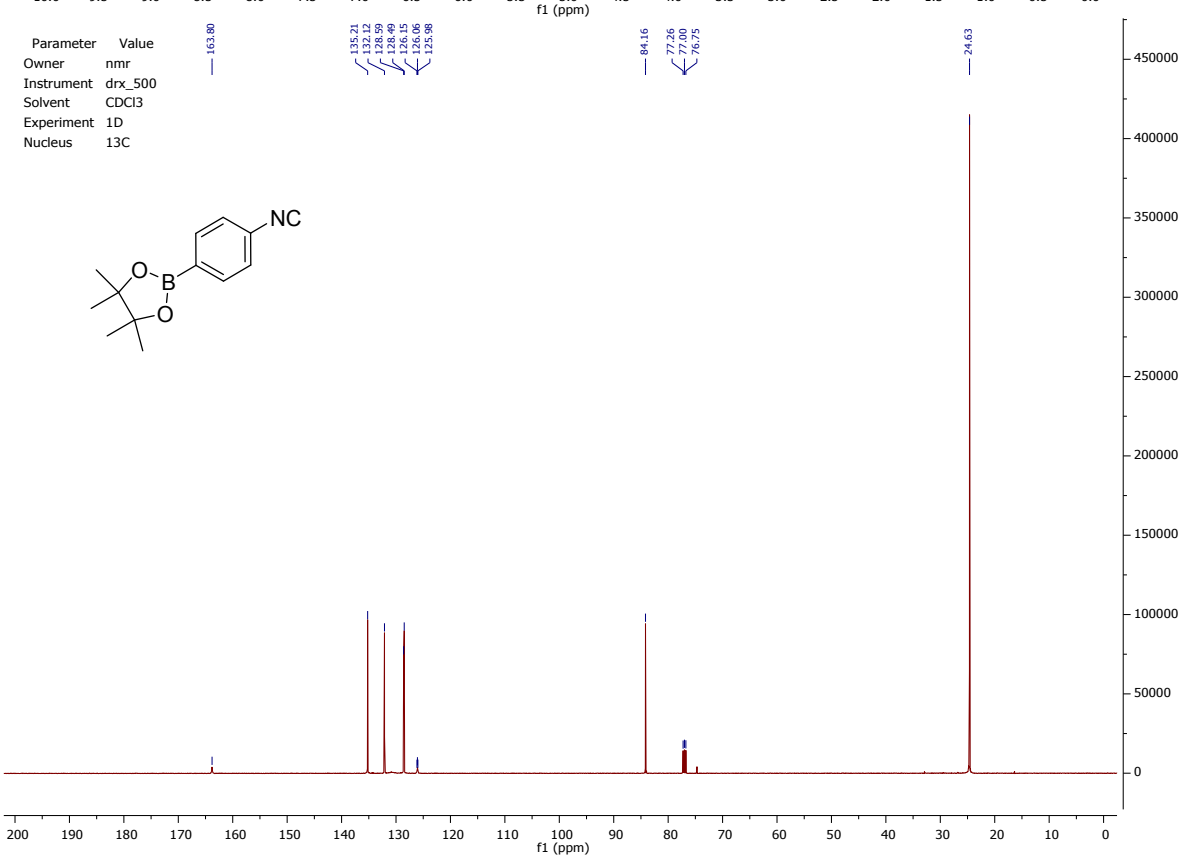
I-52: Methyl 2-isocyano-4-methylpentanoate



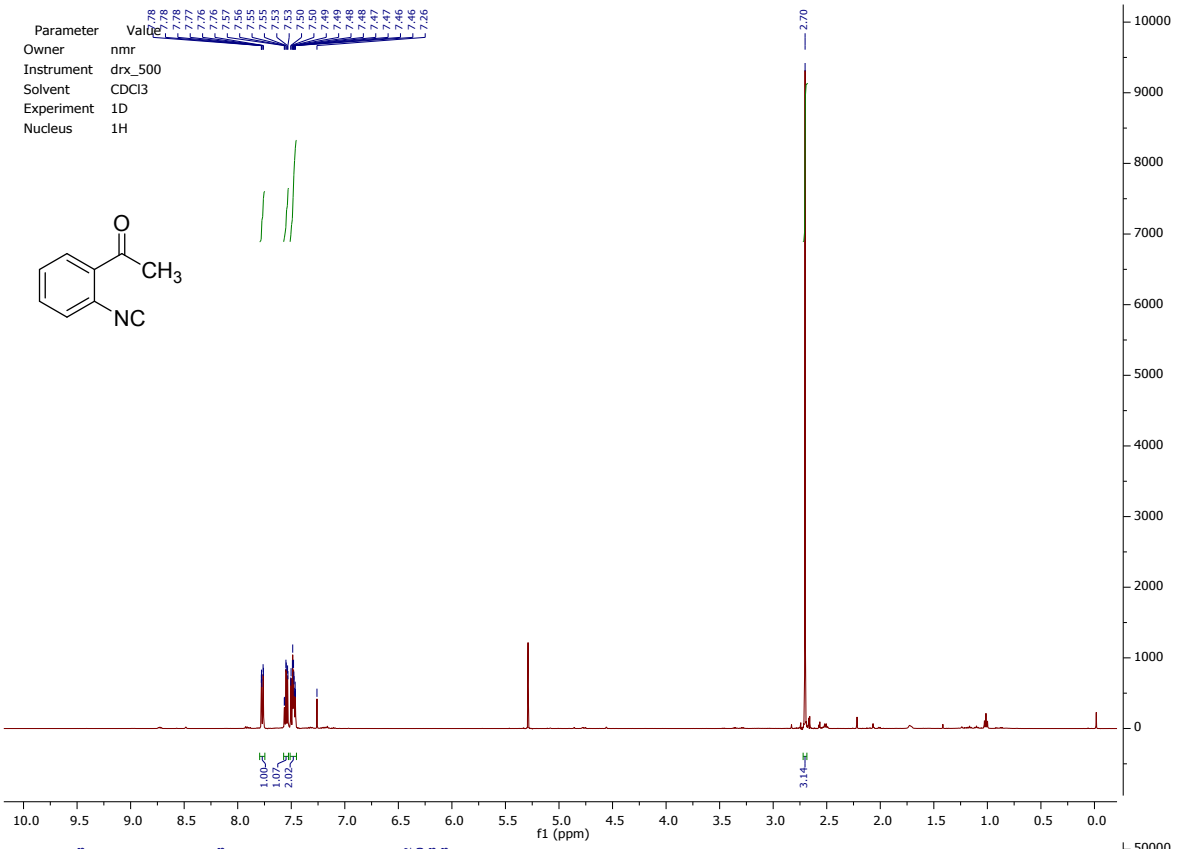


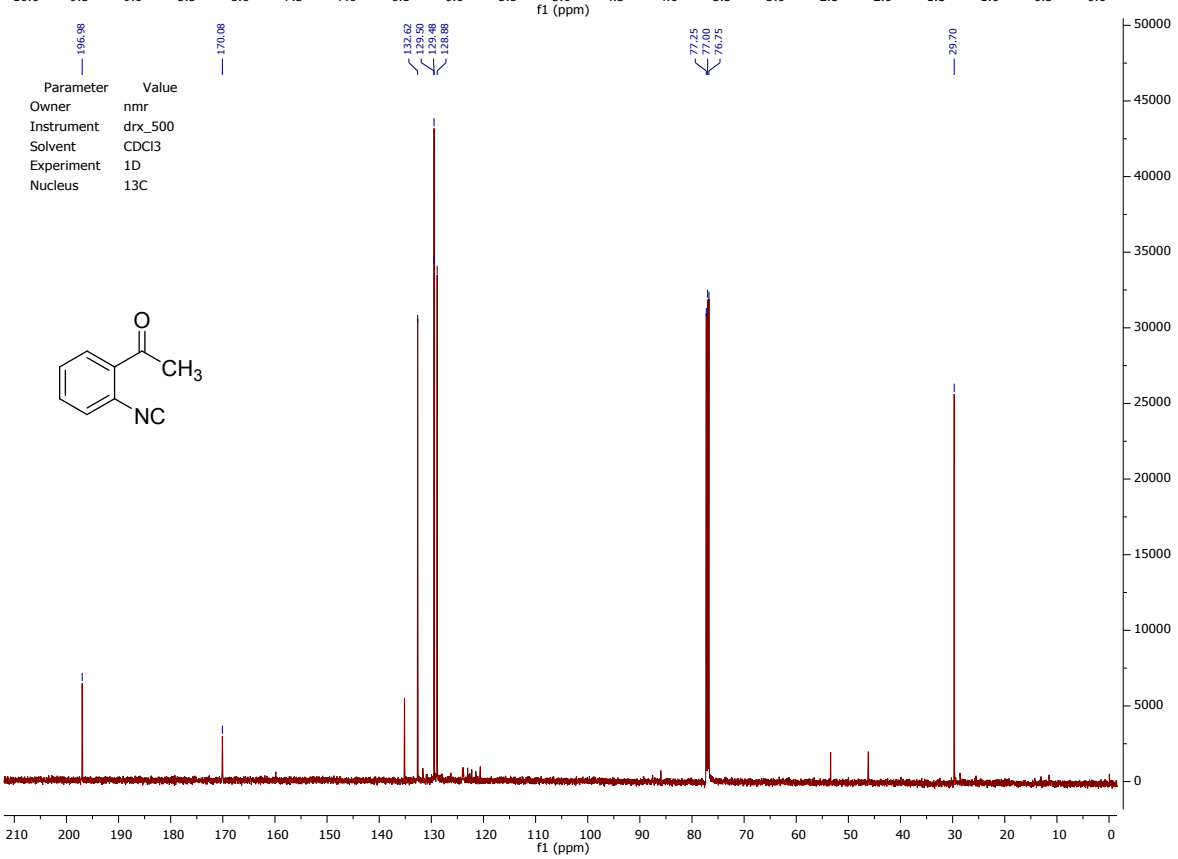
I-53: 2-(4-Isocyanophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane



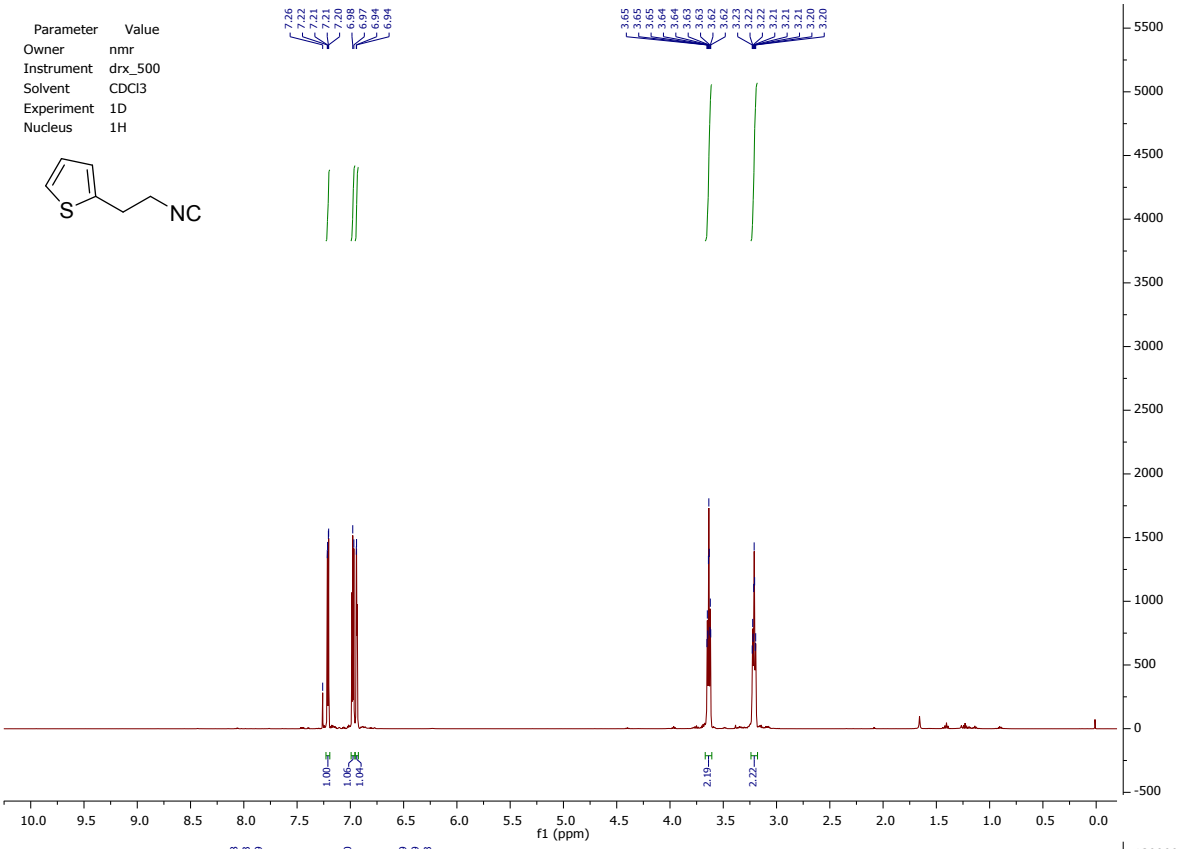


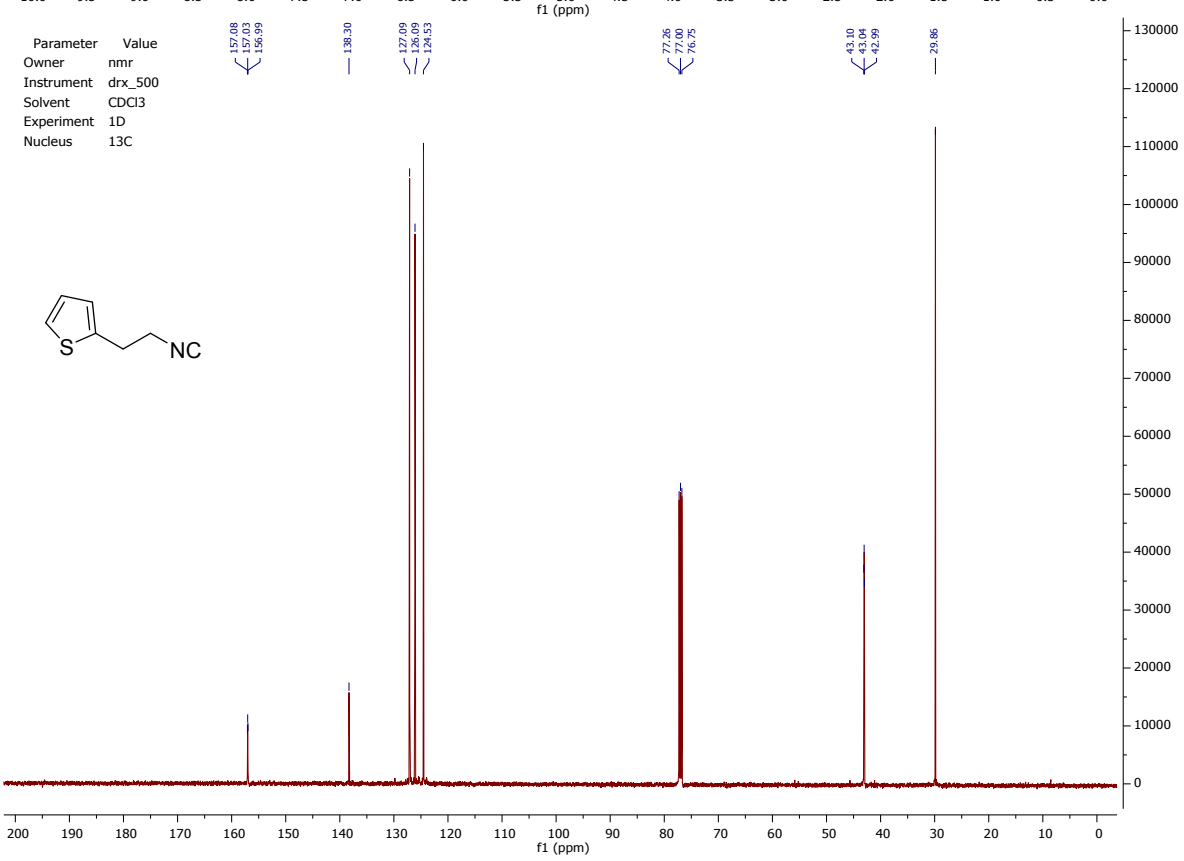
I-54: 1-(2-Isocyanophenyl)ethan-1-one



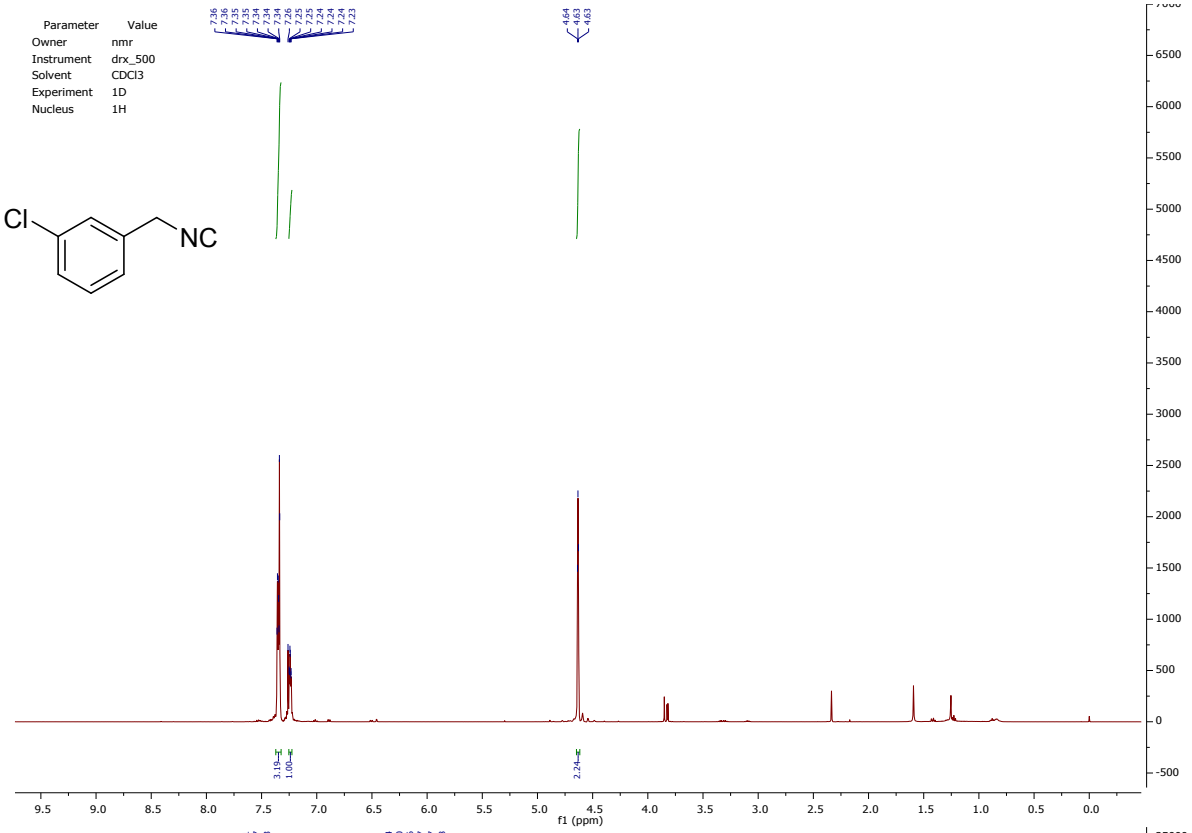


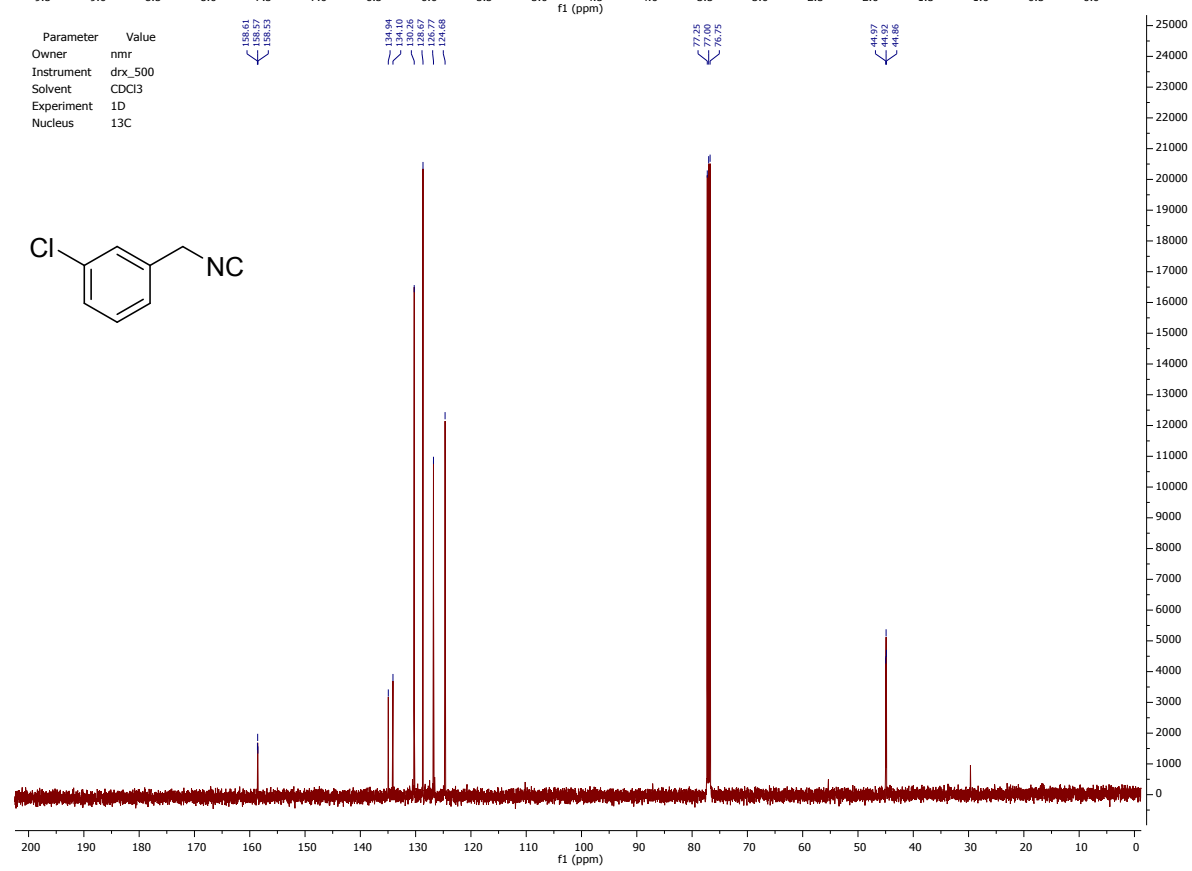
I-55: 2-(2-Isocyanoethyl)thiophene



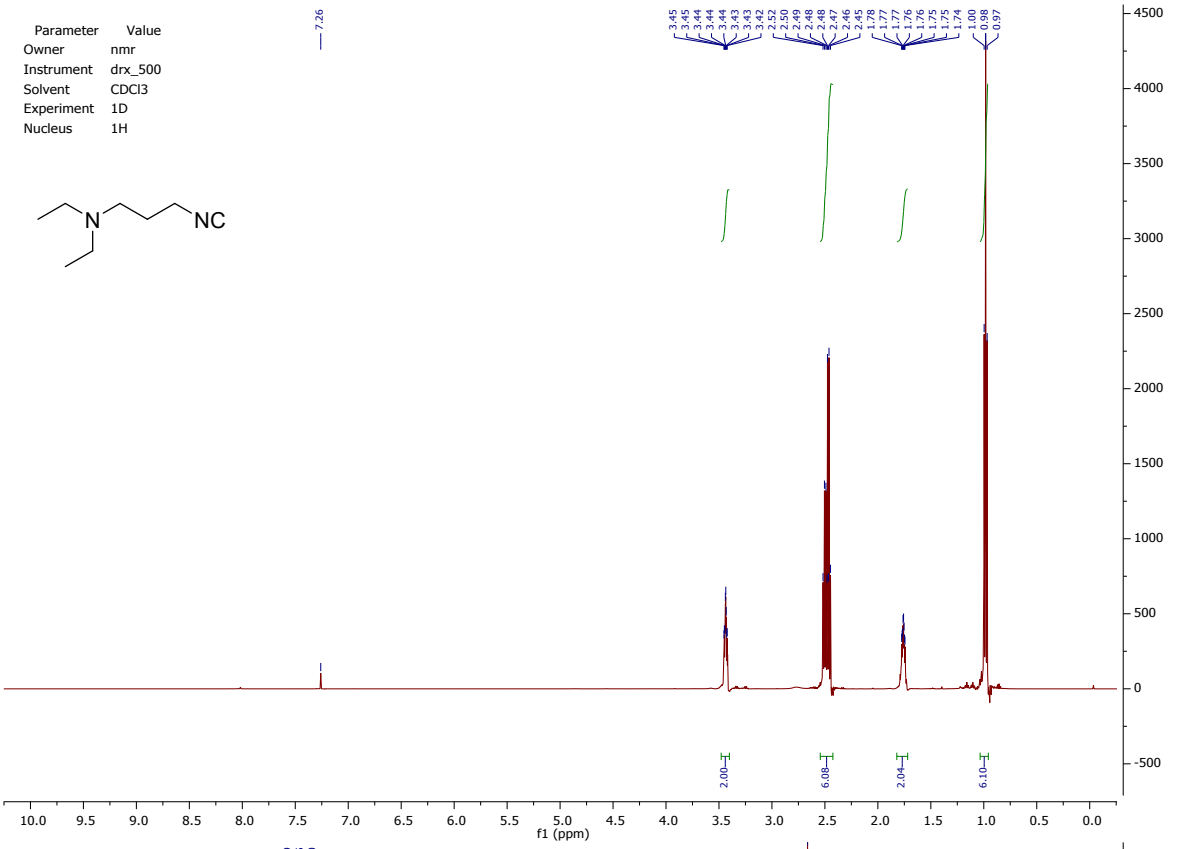


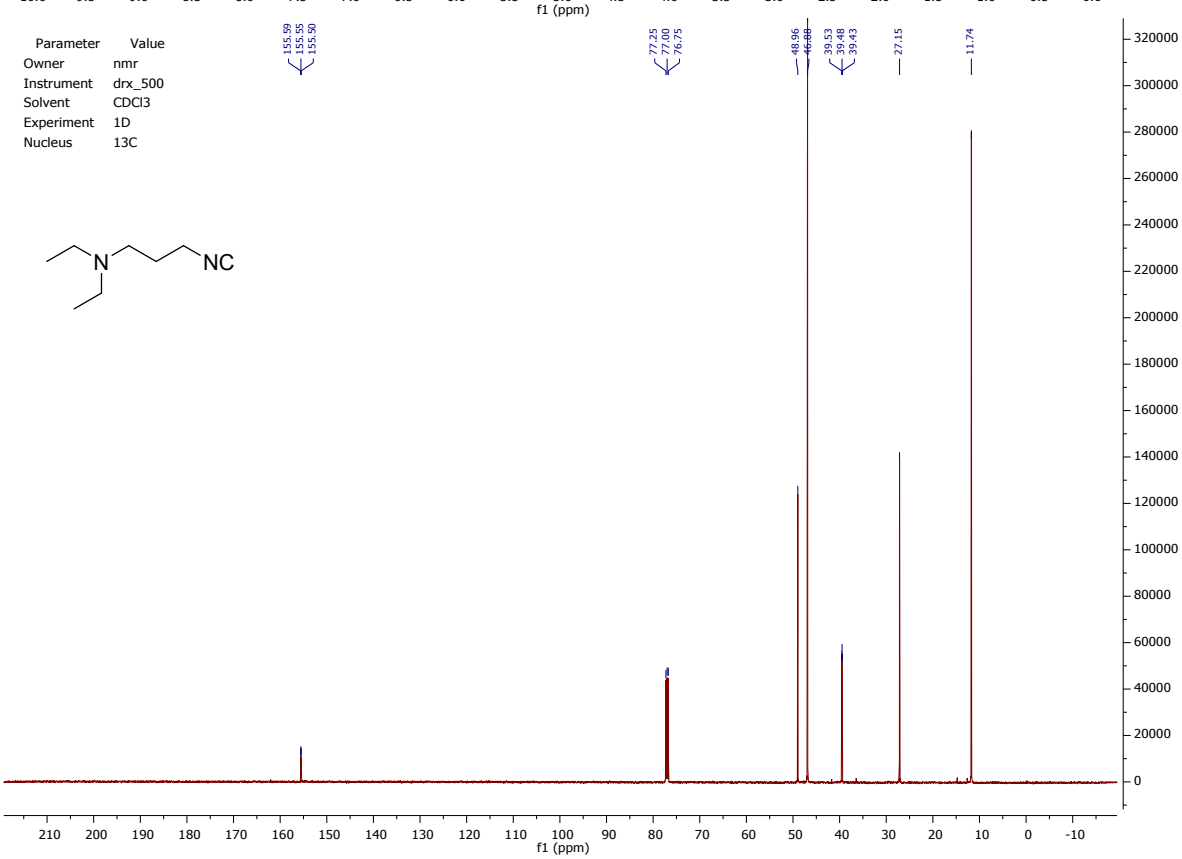
I-56: 1-Chloro-3-(isocyanomethyl)benzene



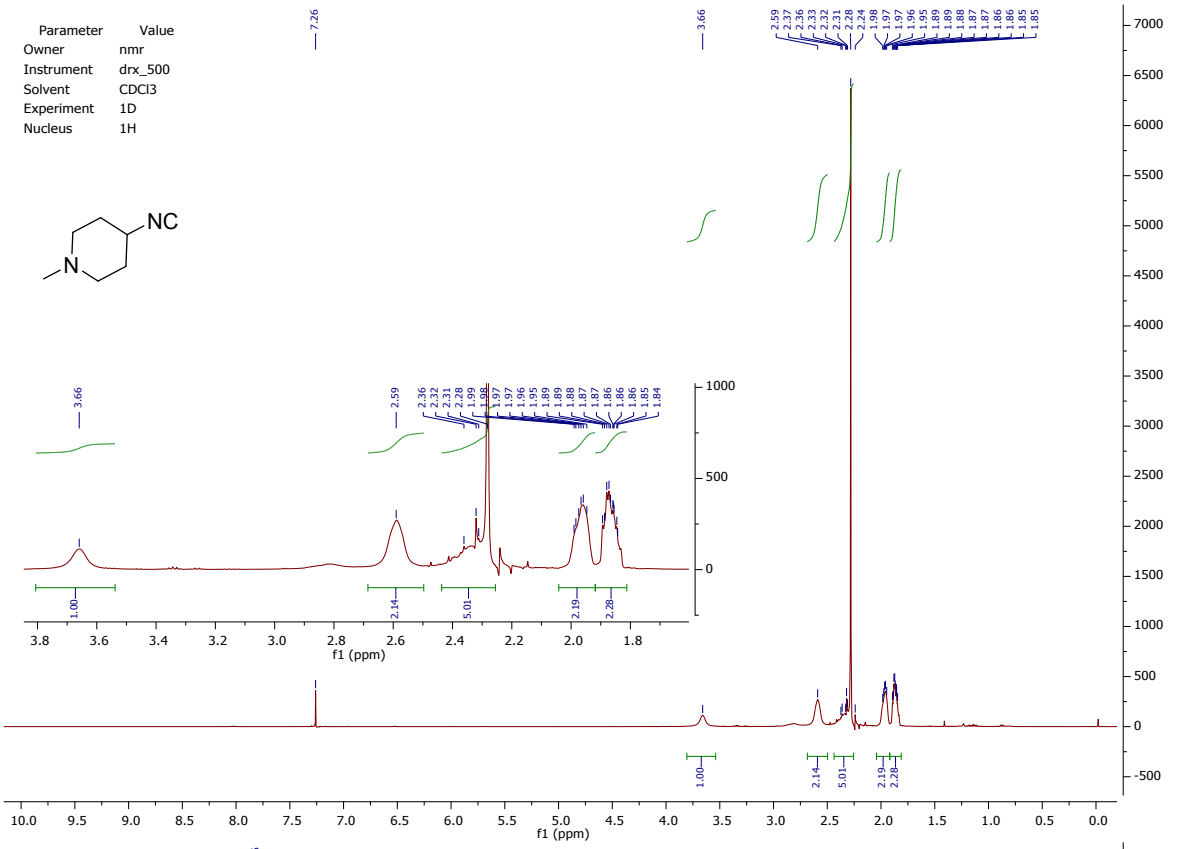


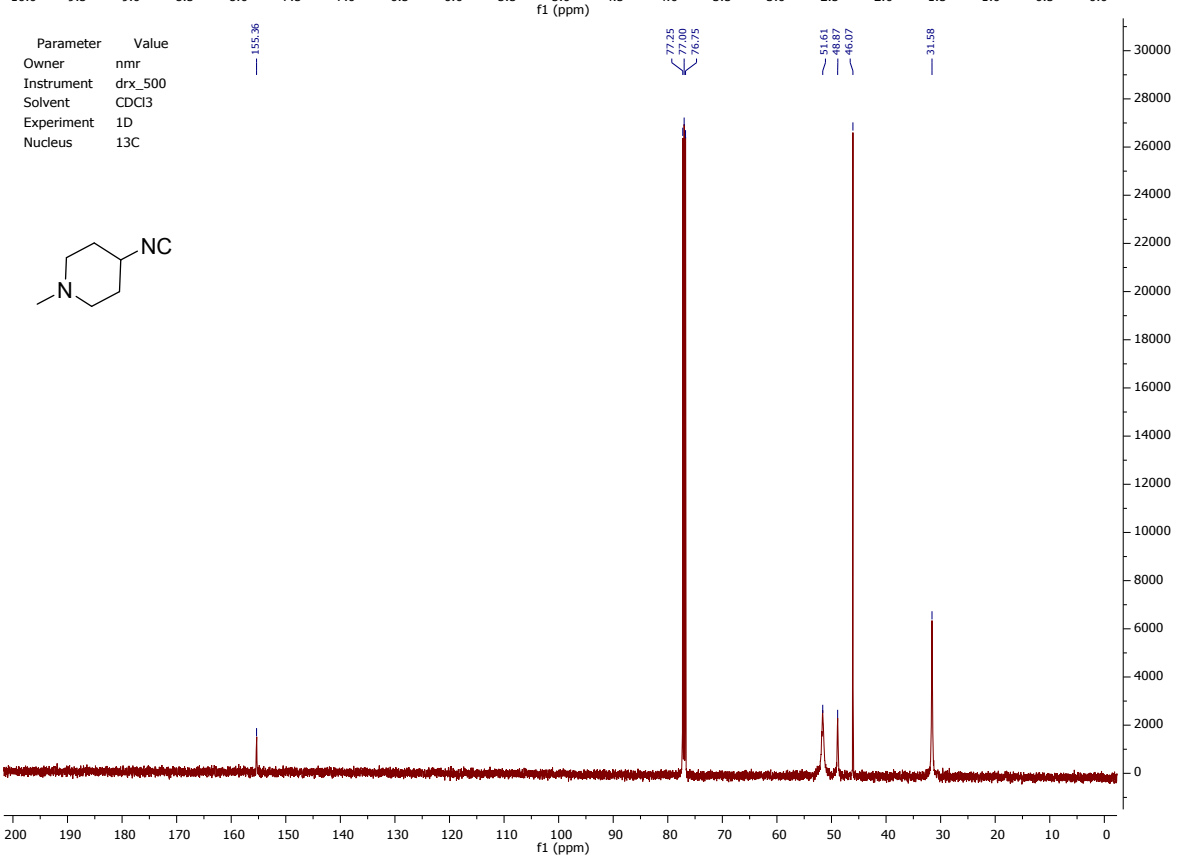
I-57: N,N-Diethyl-3-isocyanopropan-1-amine



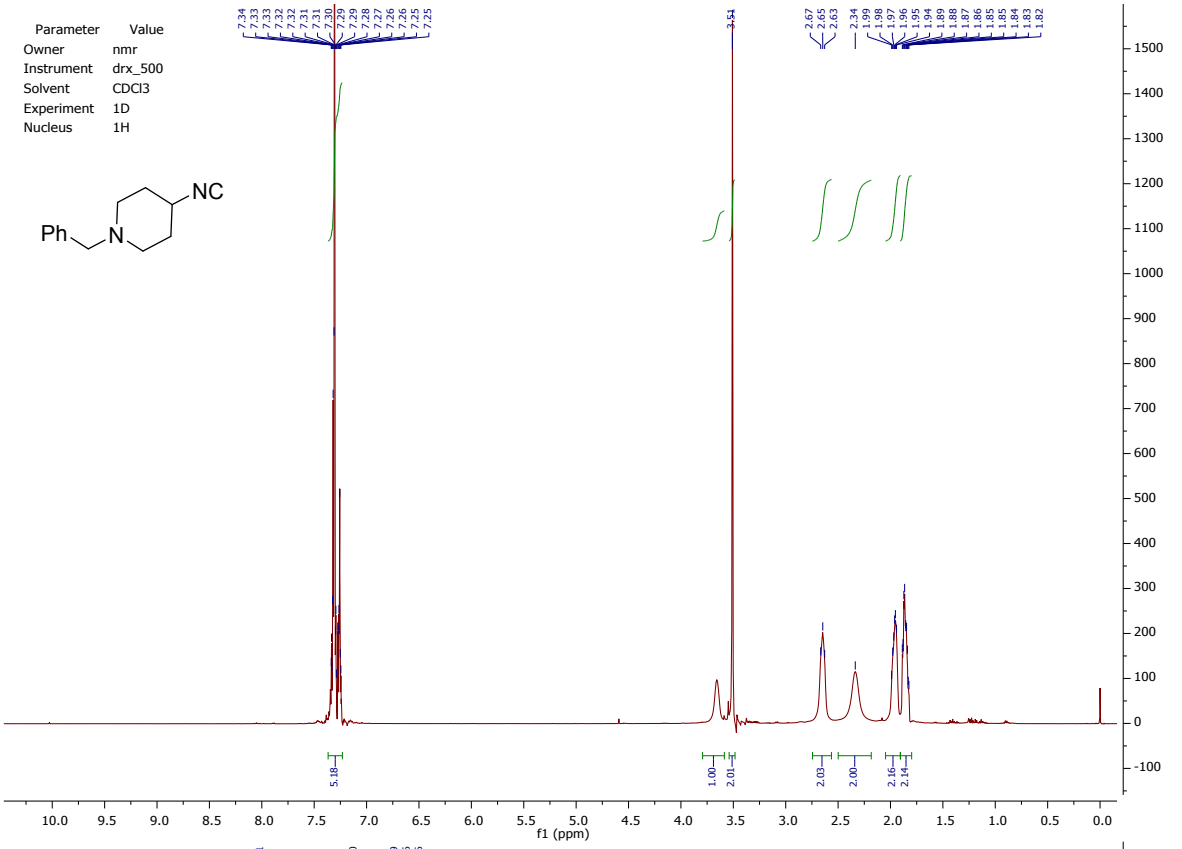


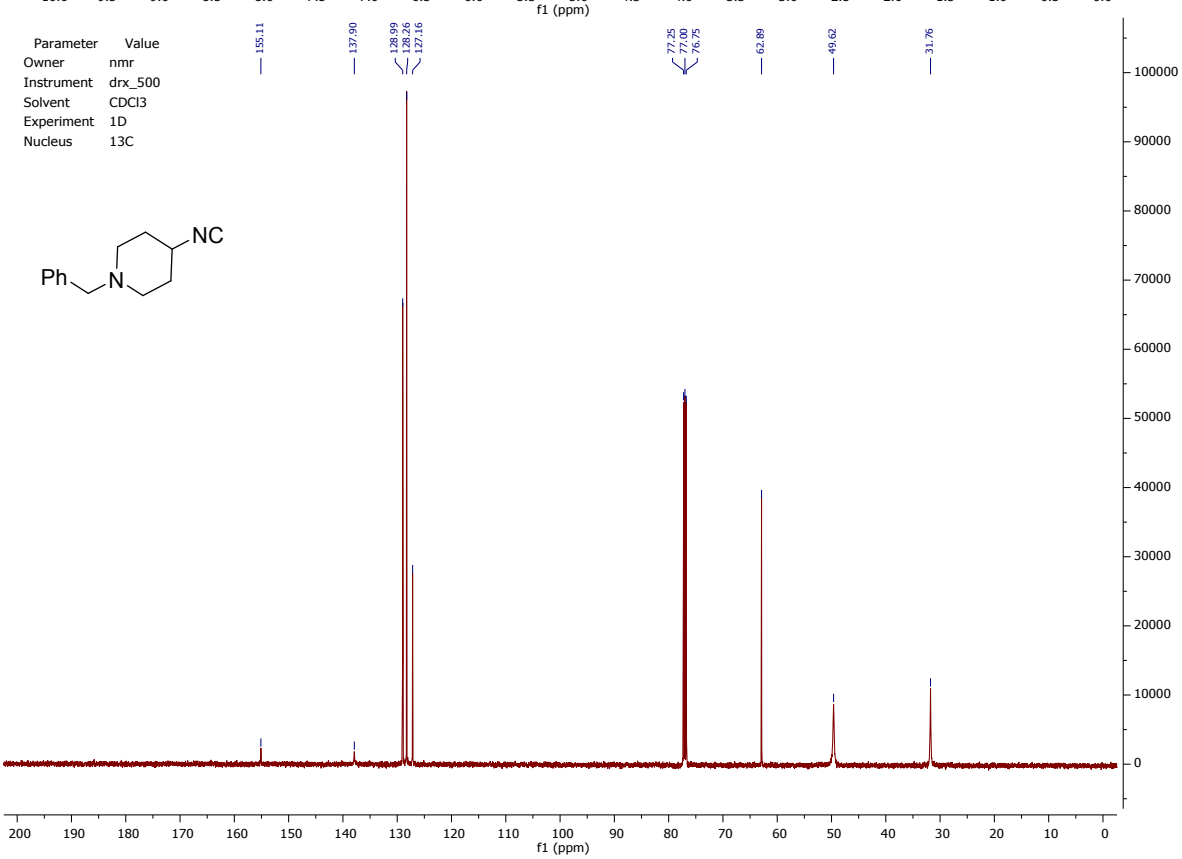
I-60: 4-Isocyano-1-methylpiperidine



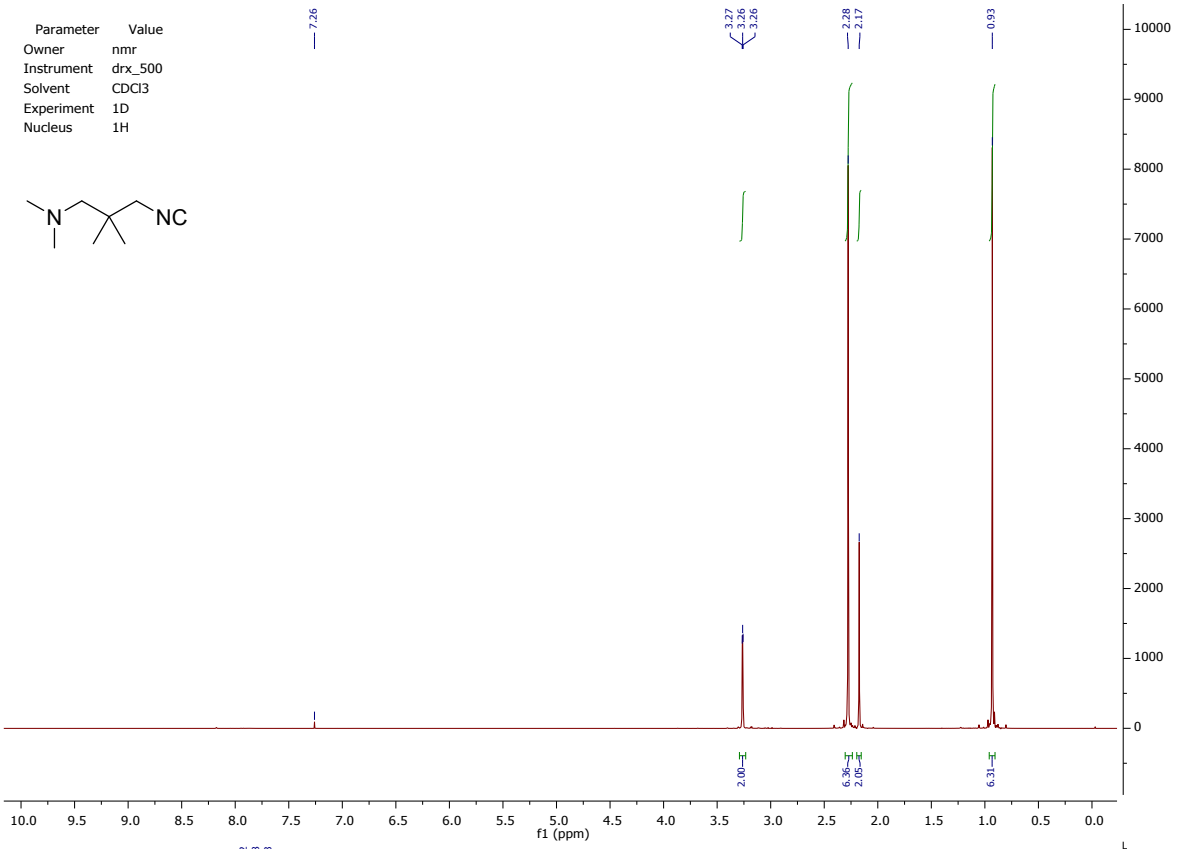


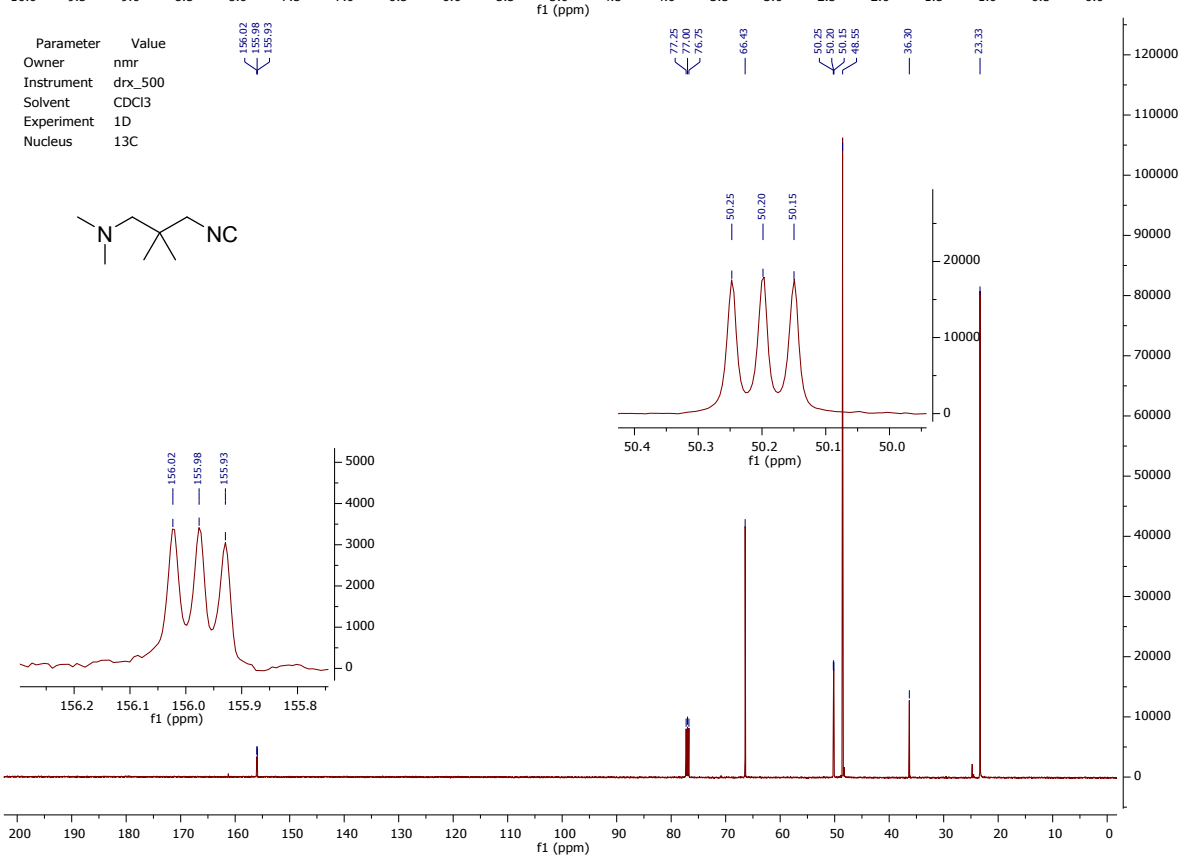
I-61: 1-Benzyl-4-isocyanopiperidine



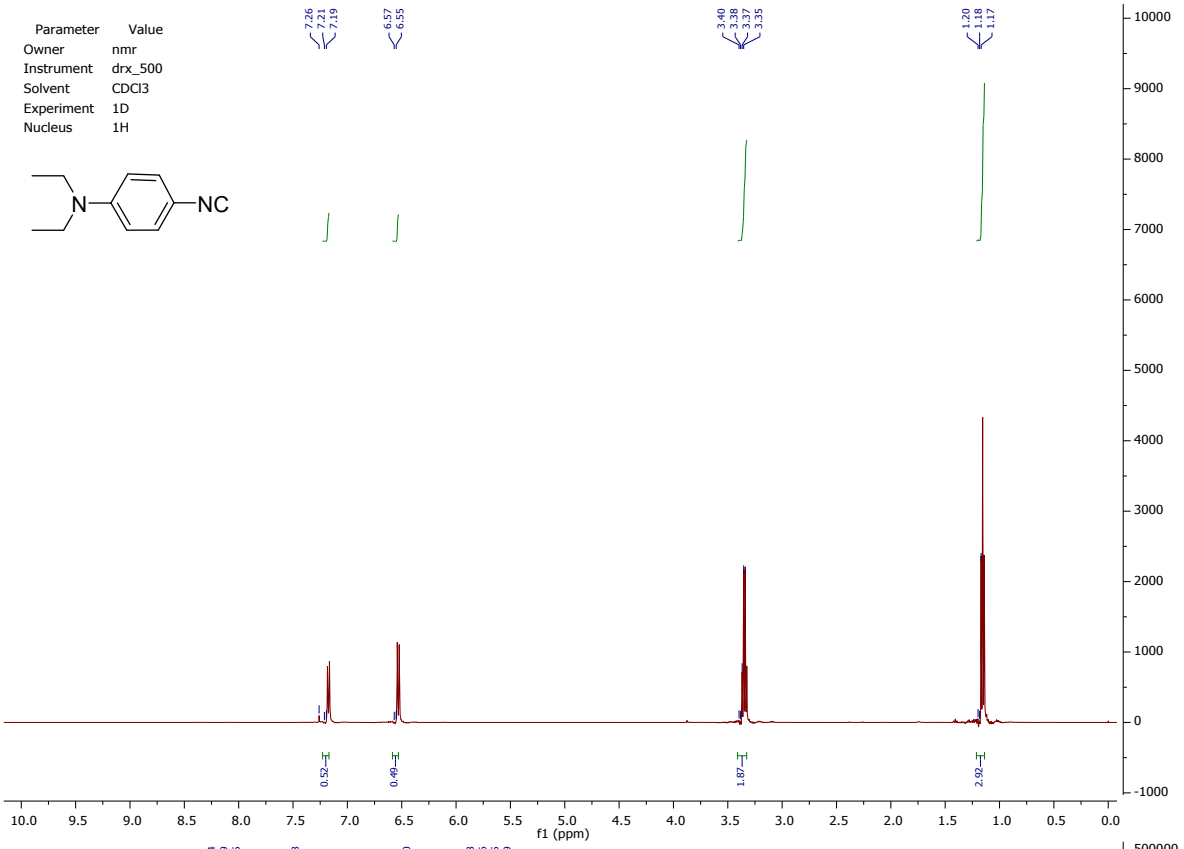


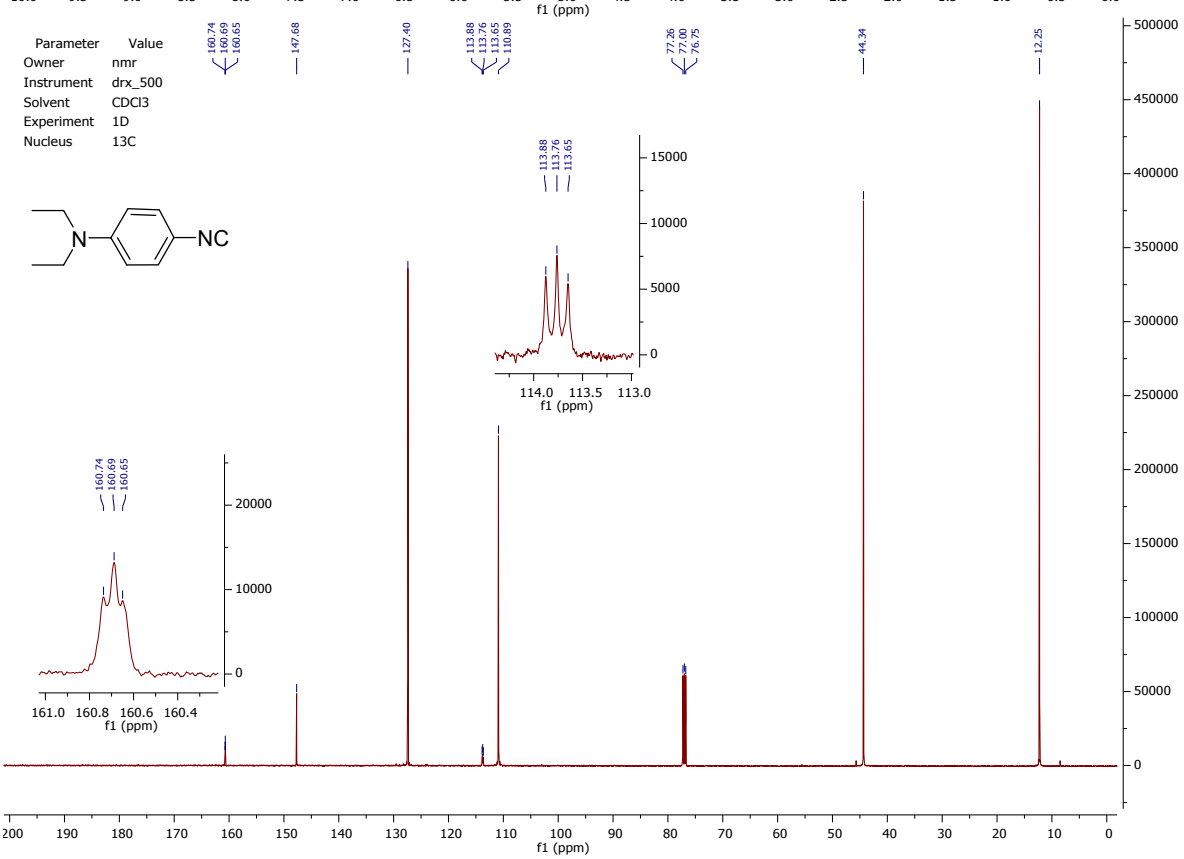
I-62: 3-Isocyano-N,N,2,2-tetramethylpropan-1-amine



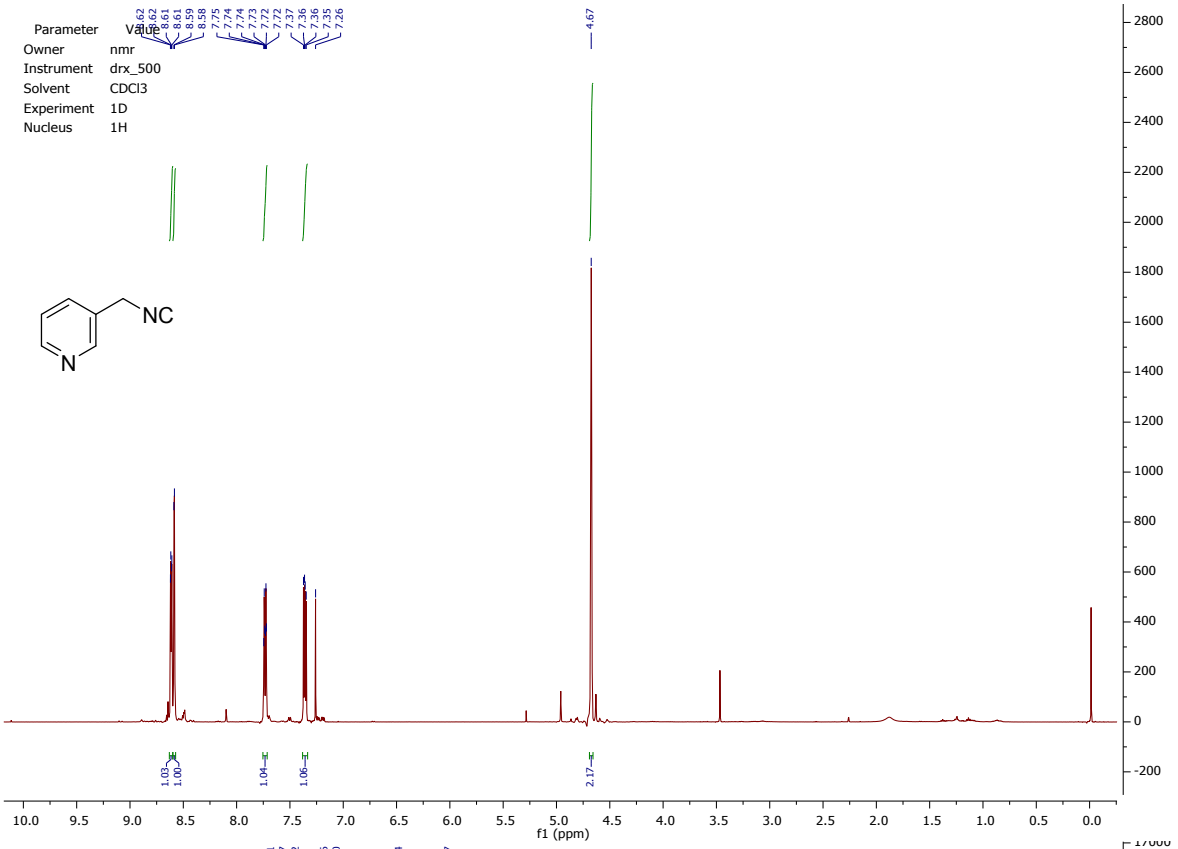


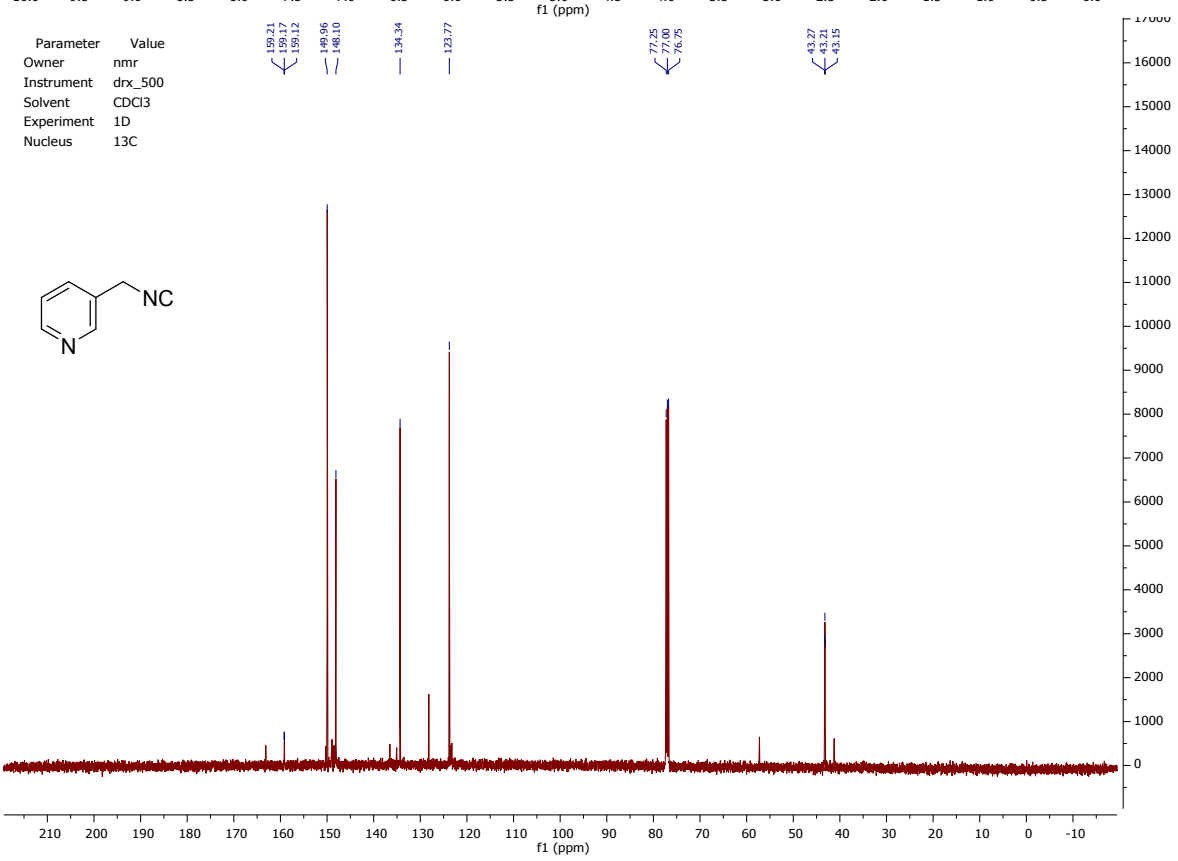
I-63: N,N-Diethyl-4-isocyanoaniline



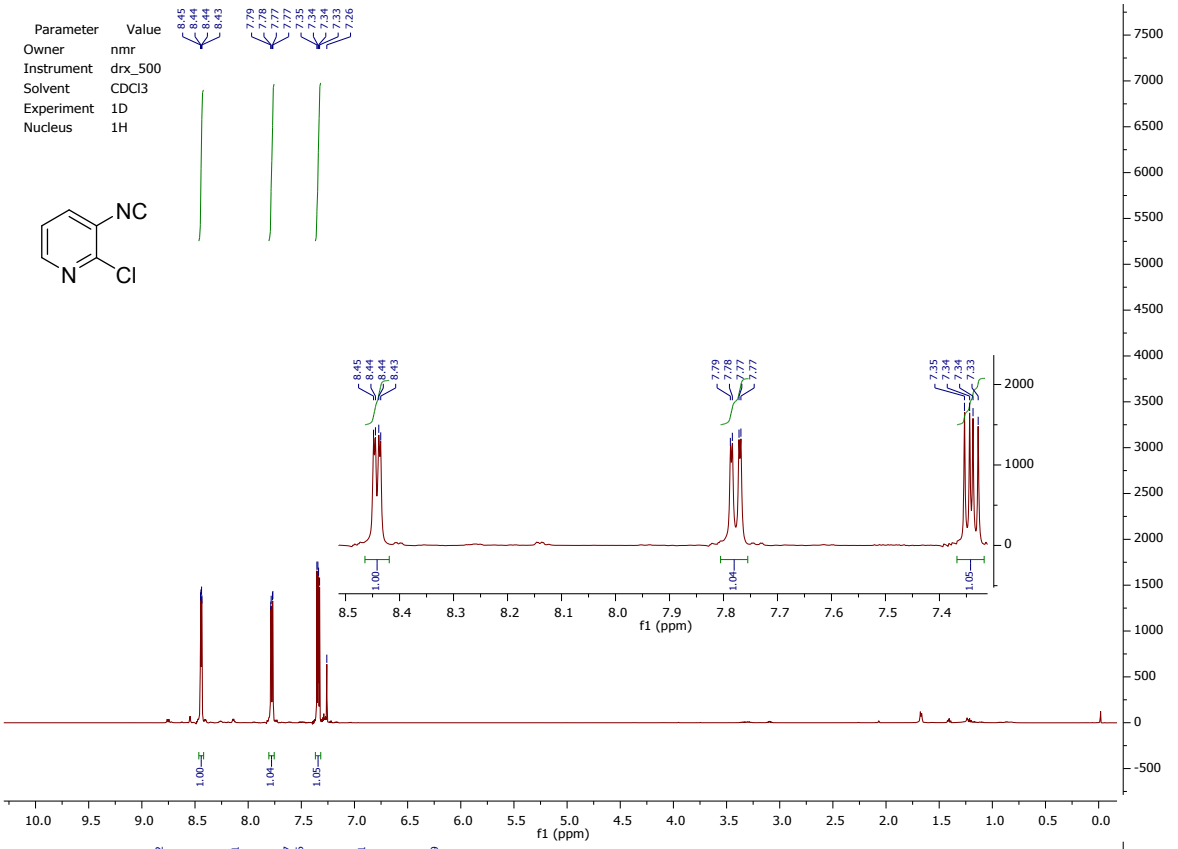


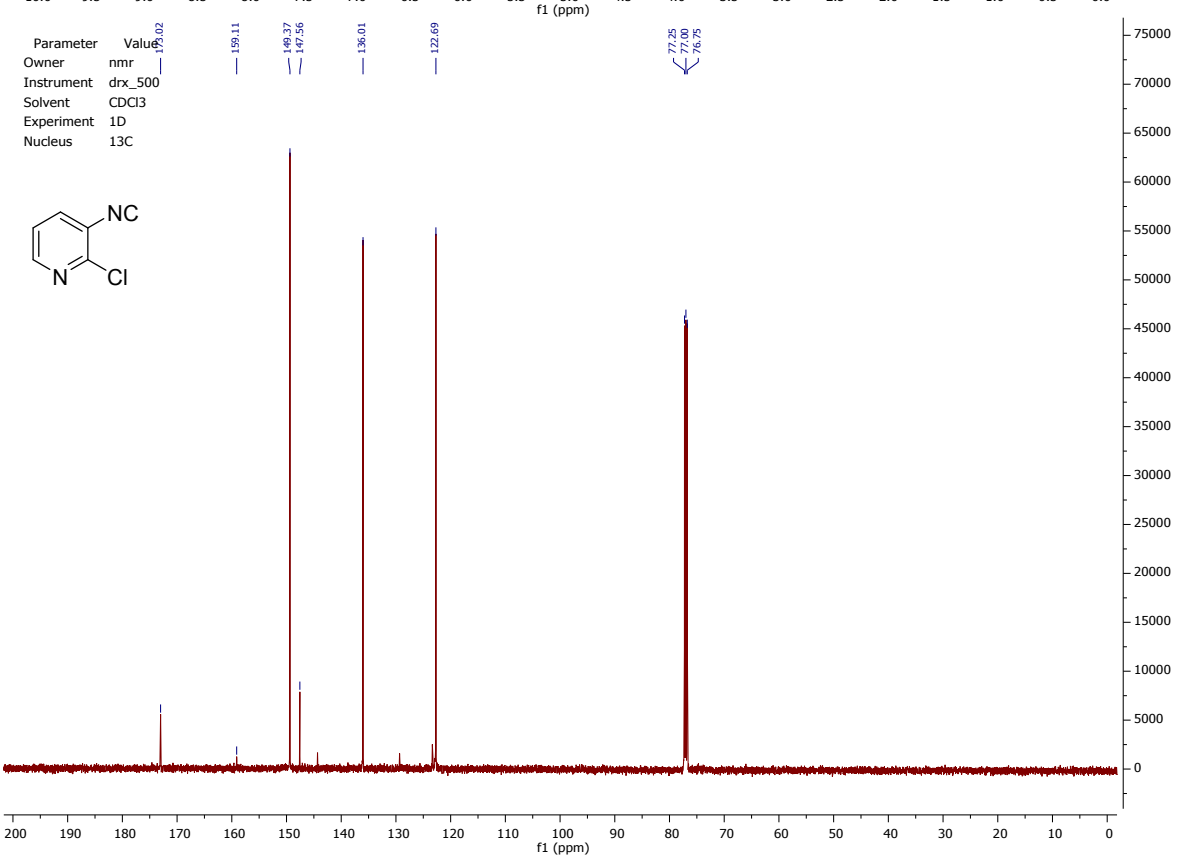
I-64: 3-(Isocyanomethyl)pyridine



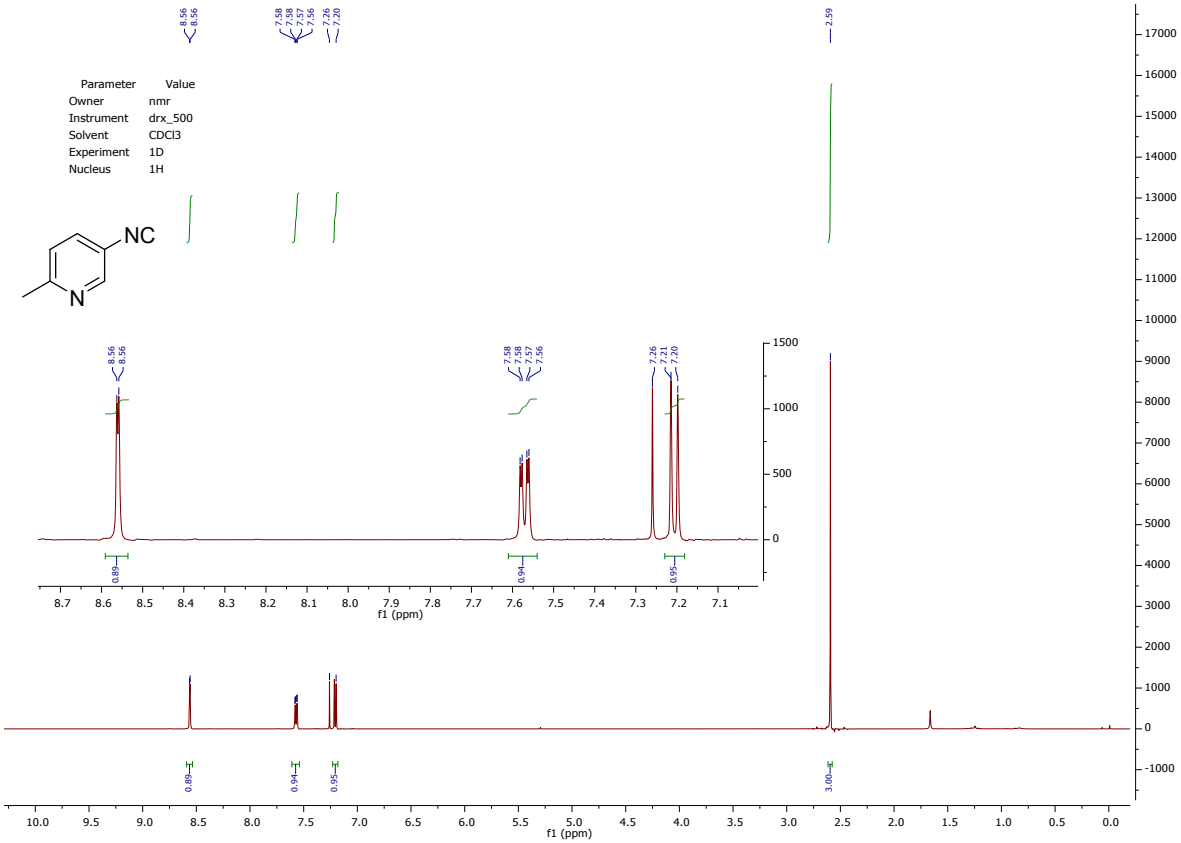


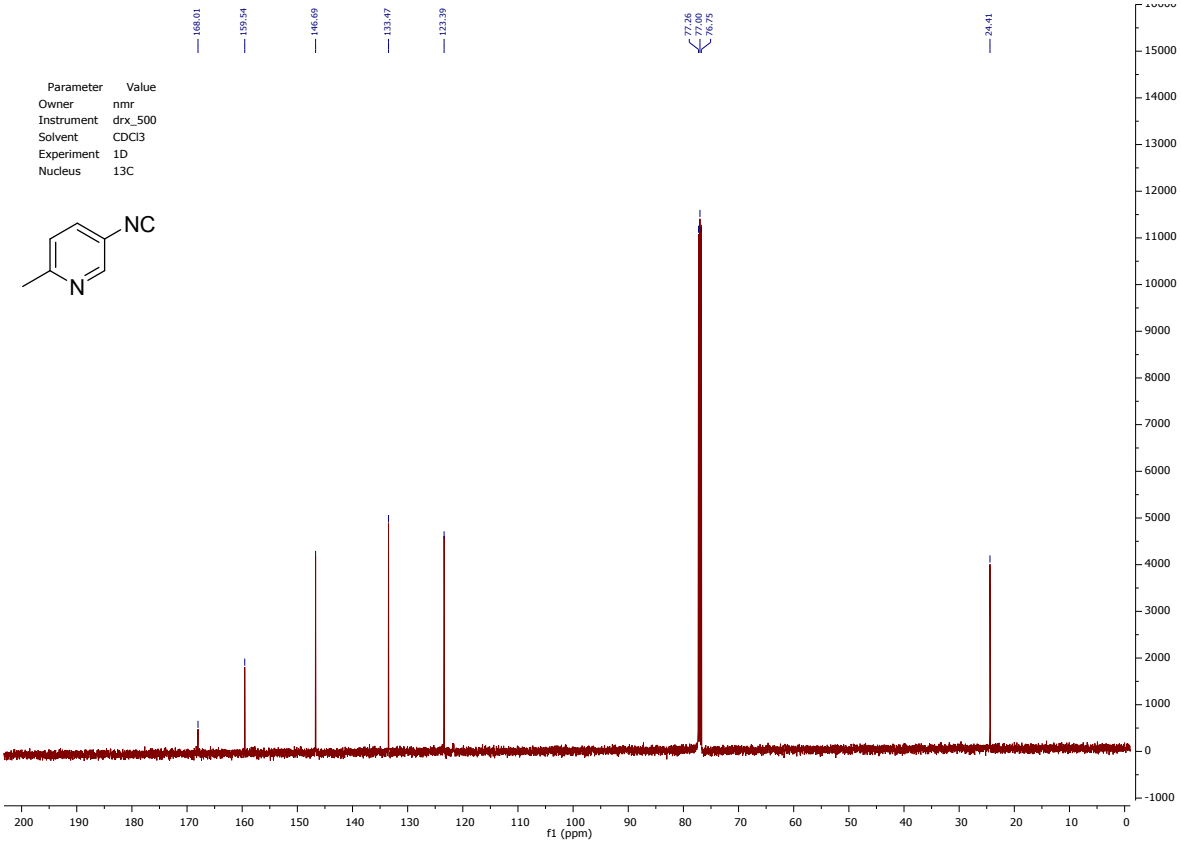
I-66: 2-Chloro-3-isocyanopyridine



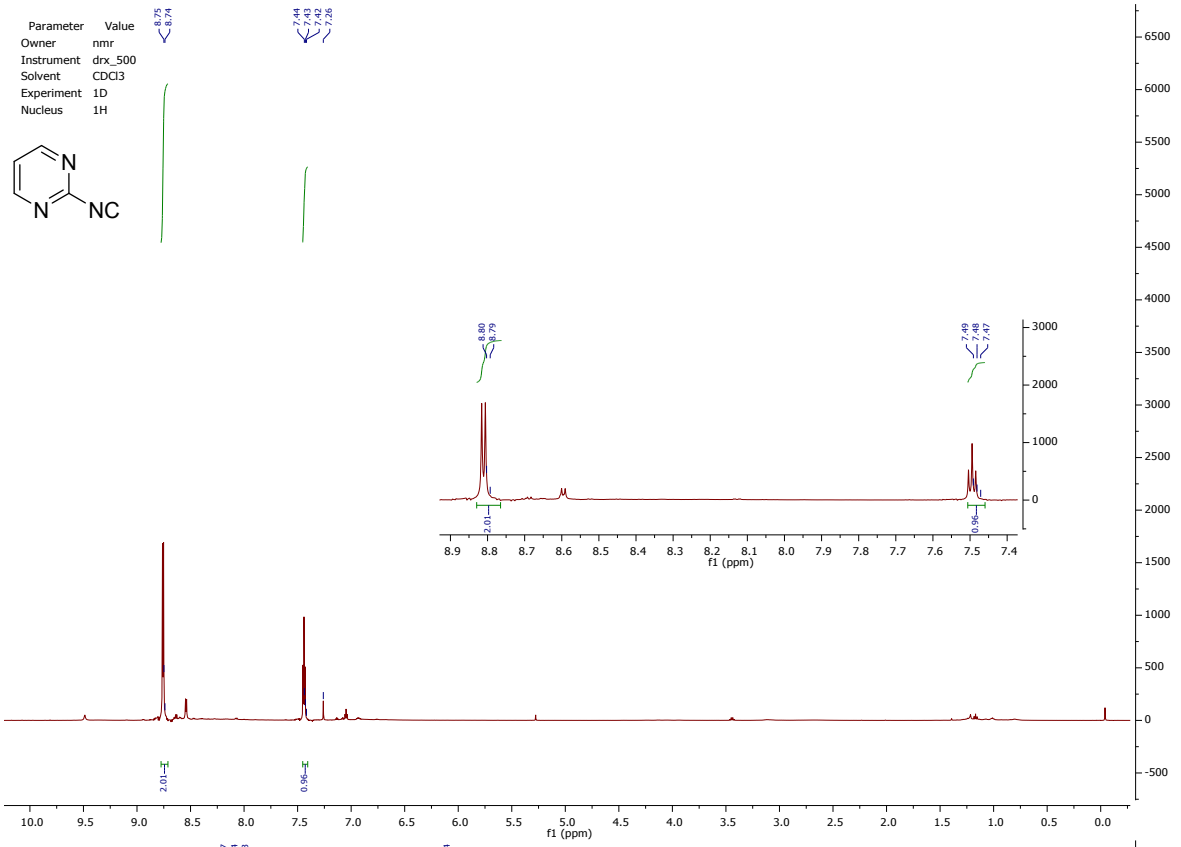


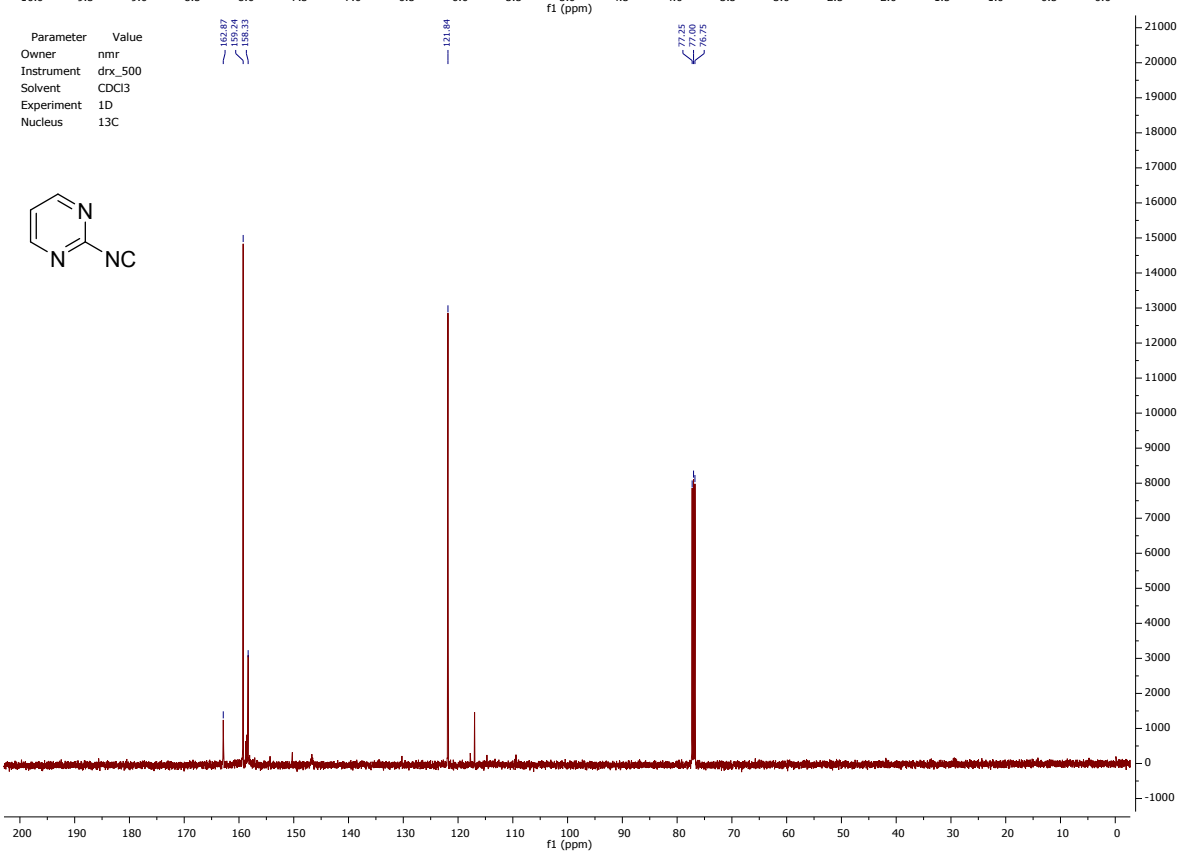
I-67: 5-Isocyano-2-methylpyridine



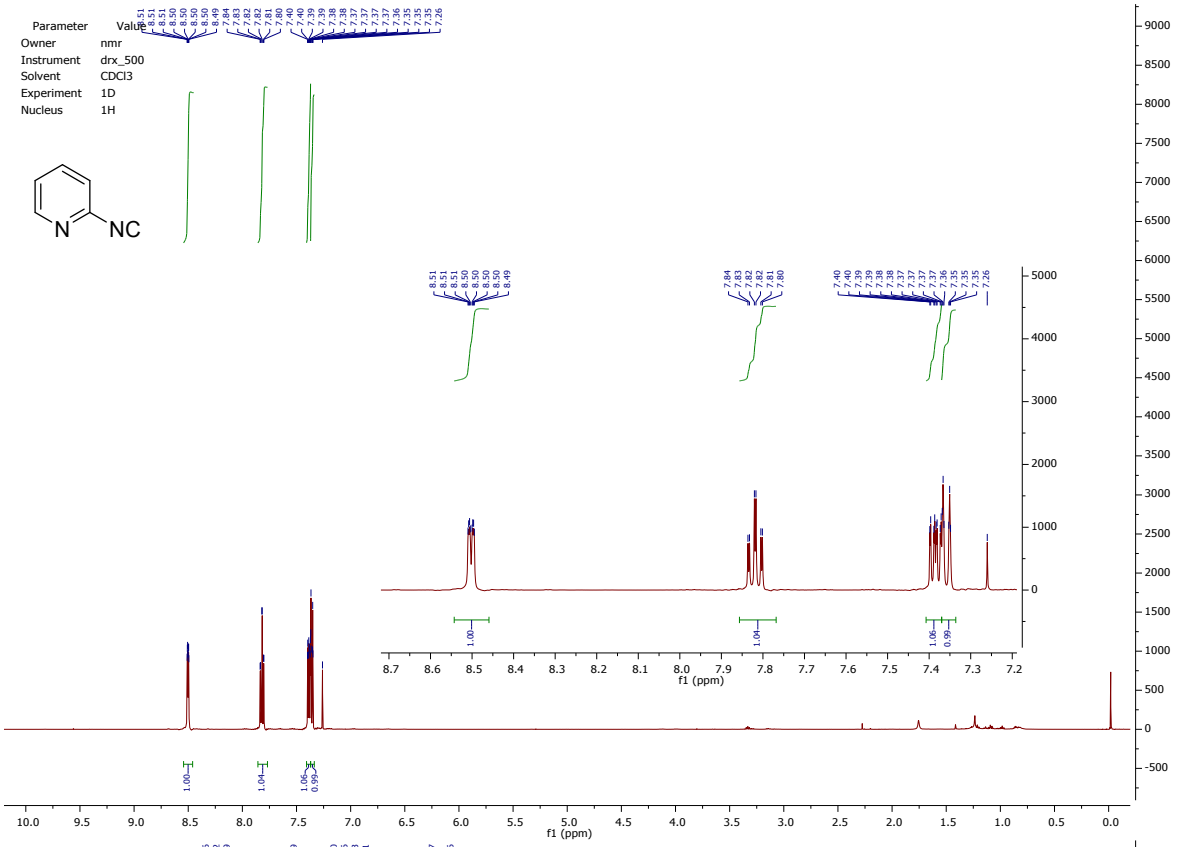


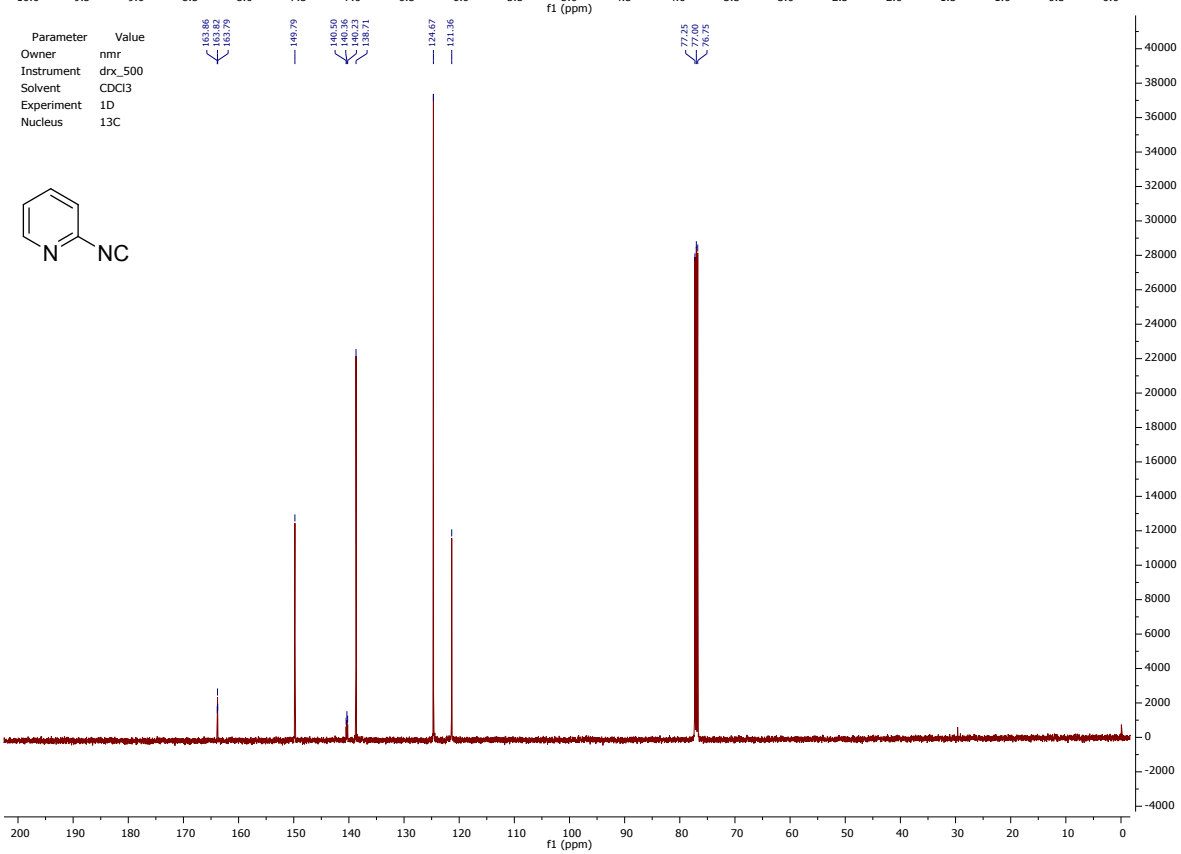
I-68: 2-Isocyanopyrimidine



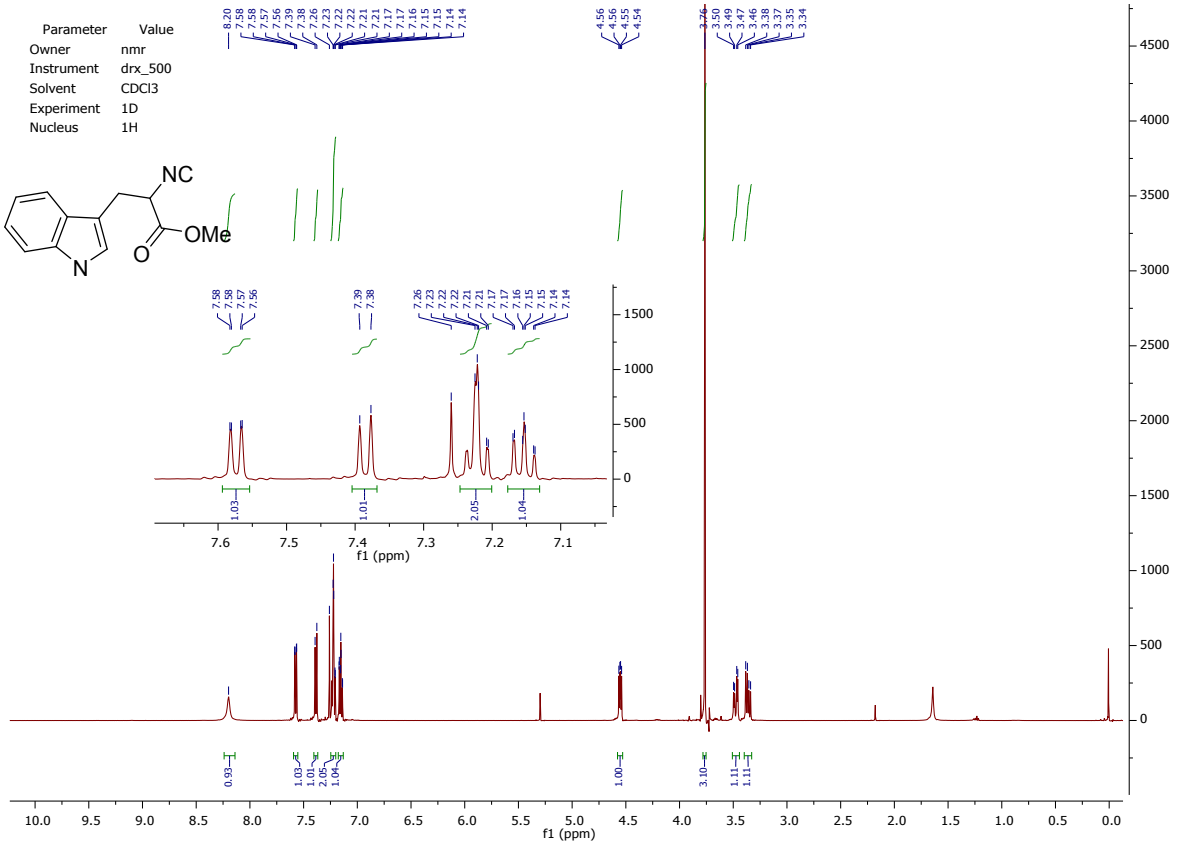


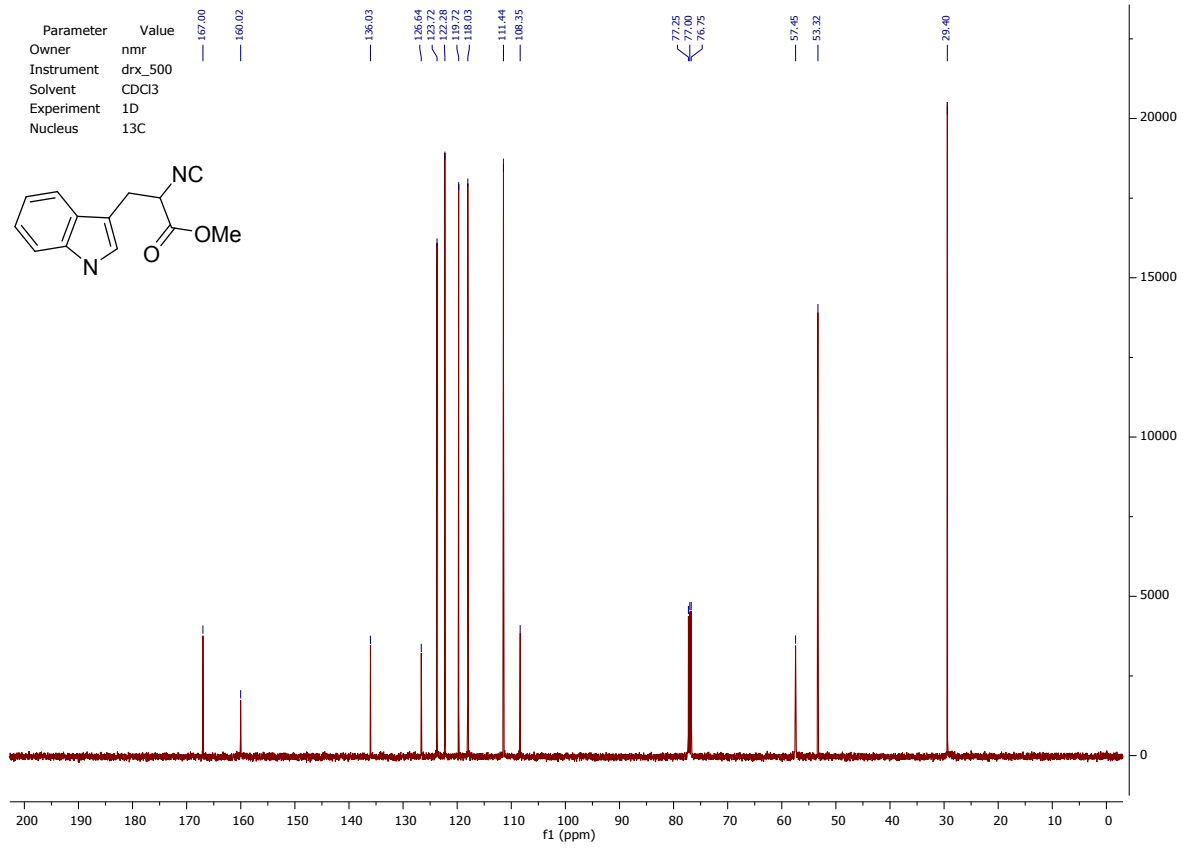
I-69: 2-Isocyanopyridine



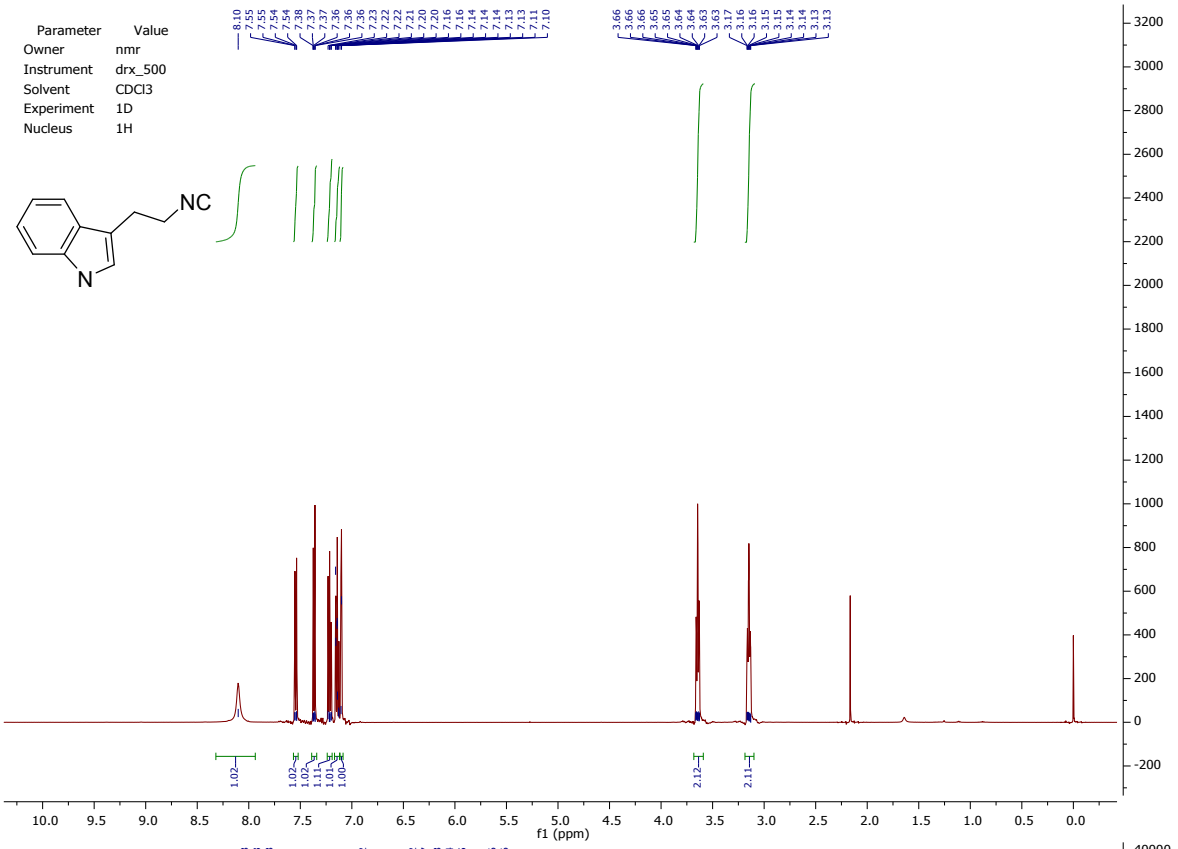


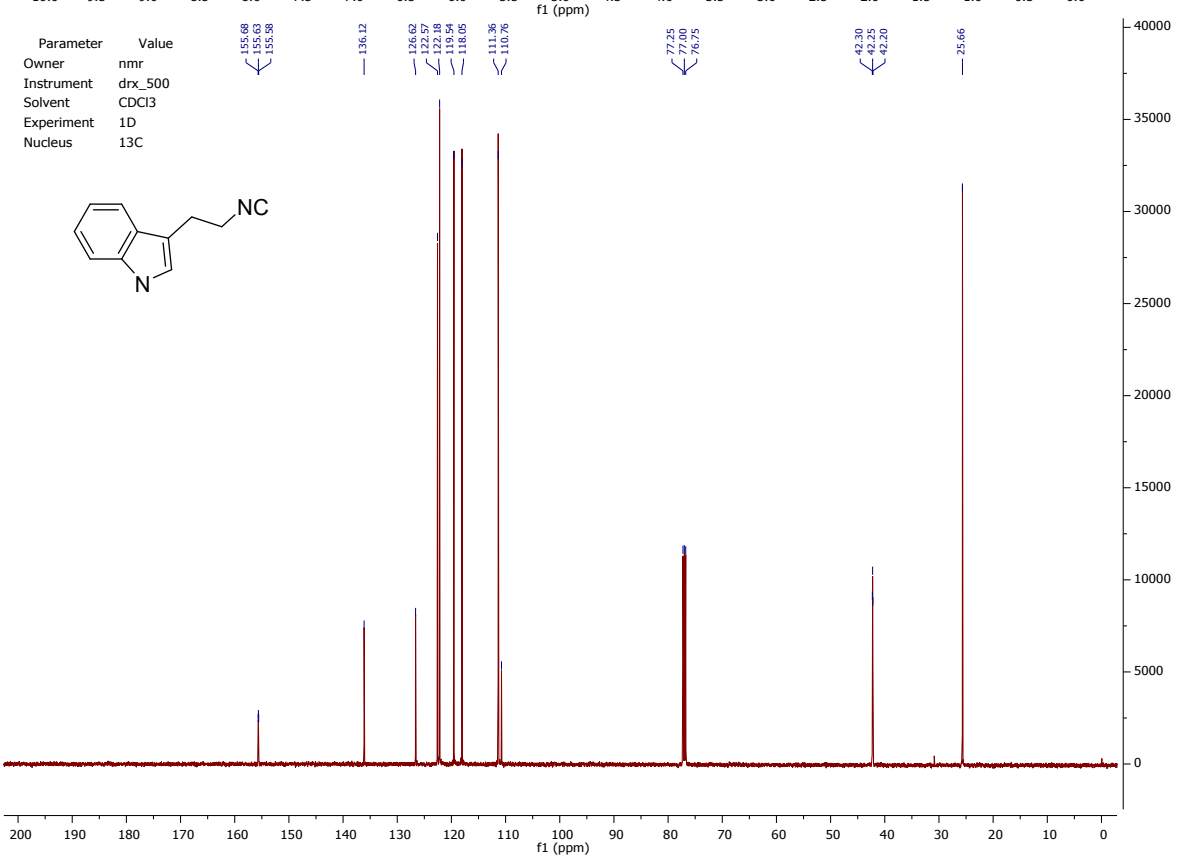
I-72: Methyl 3-(1H-indol-3-yl)-2-isocyanopropanoate



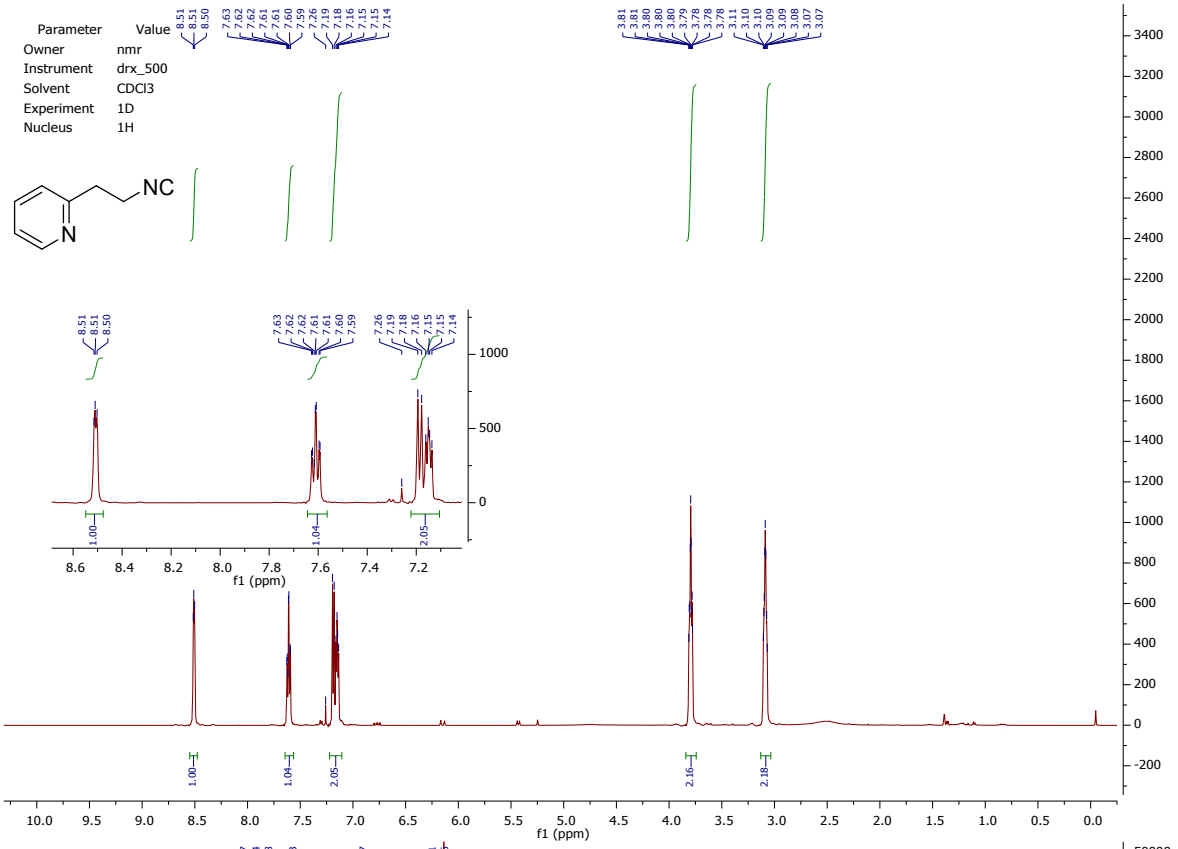


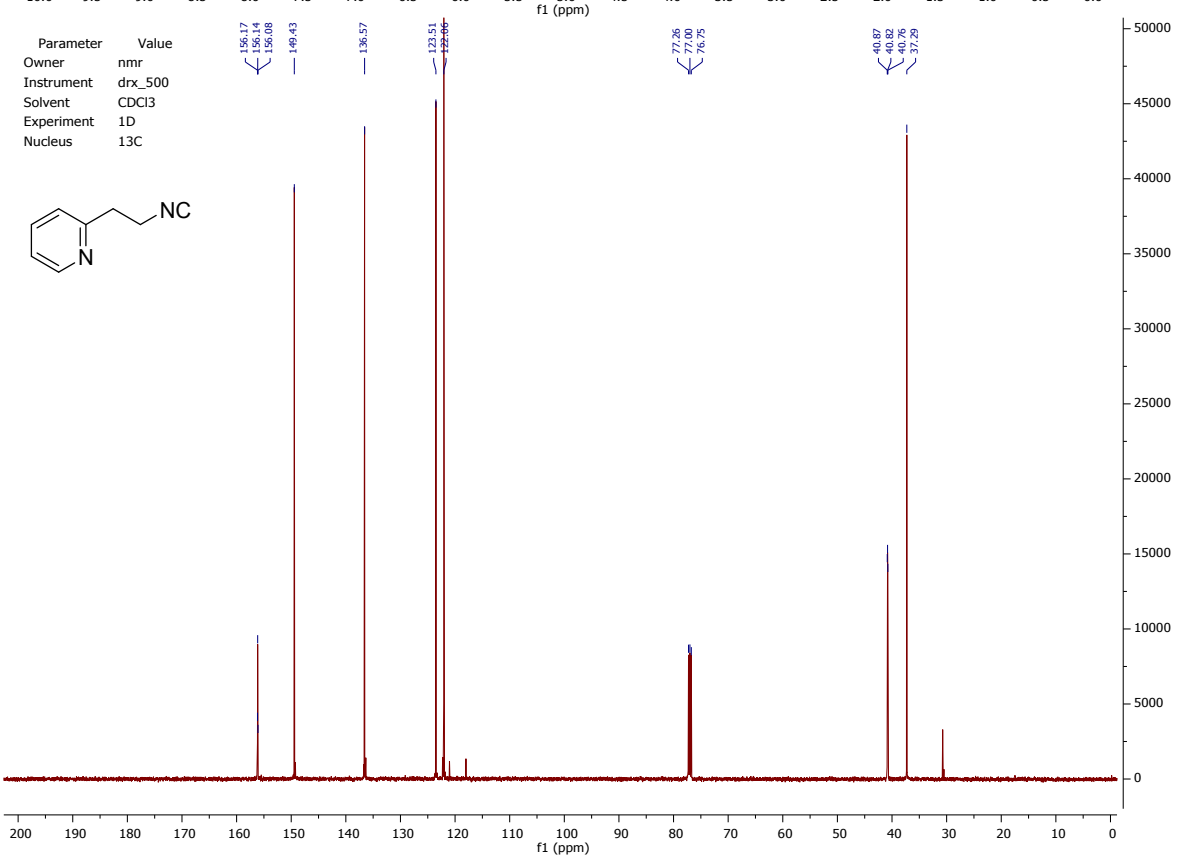
I-73: 3-(2-Isocyanoethyl)-1H-indole



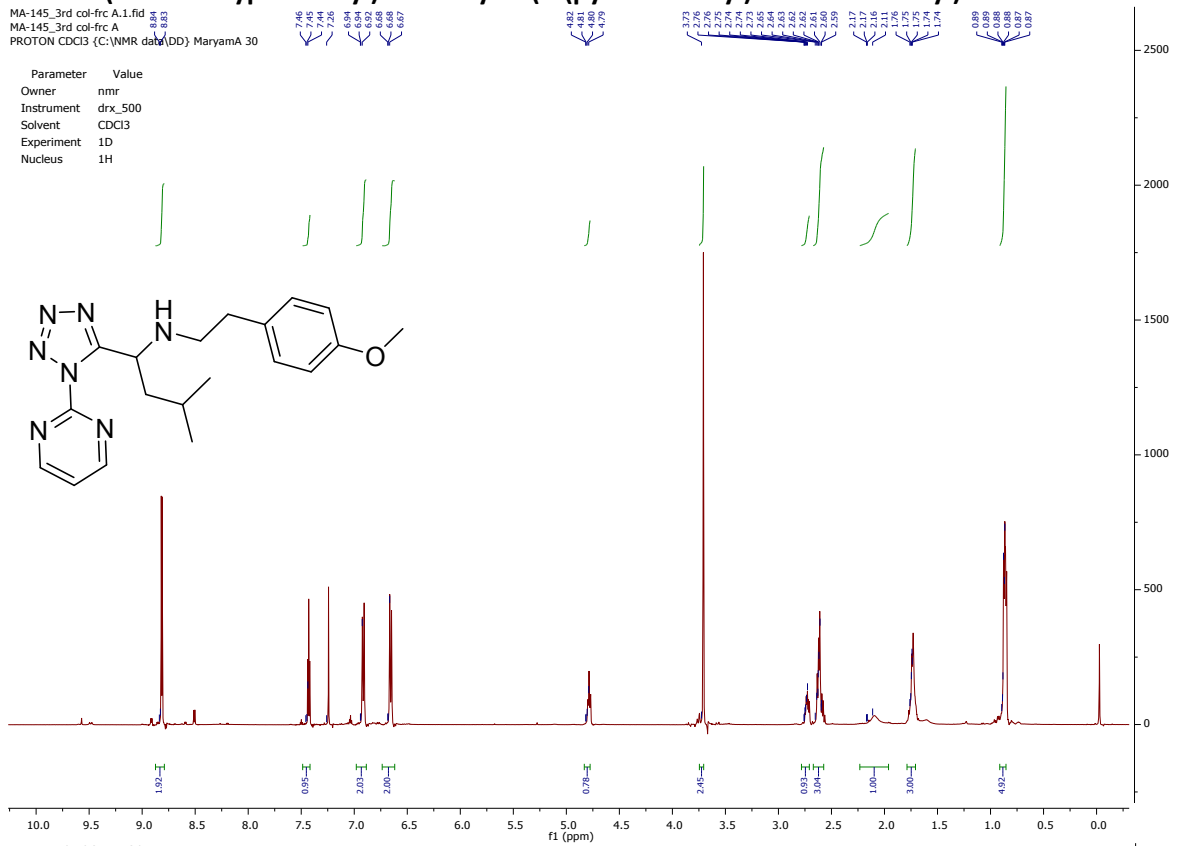


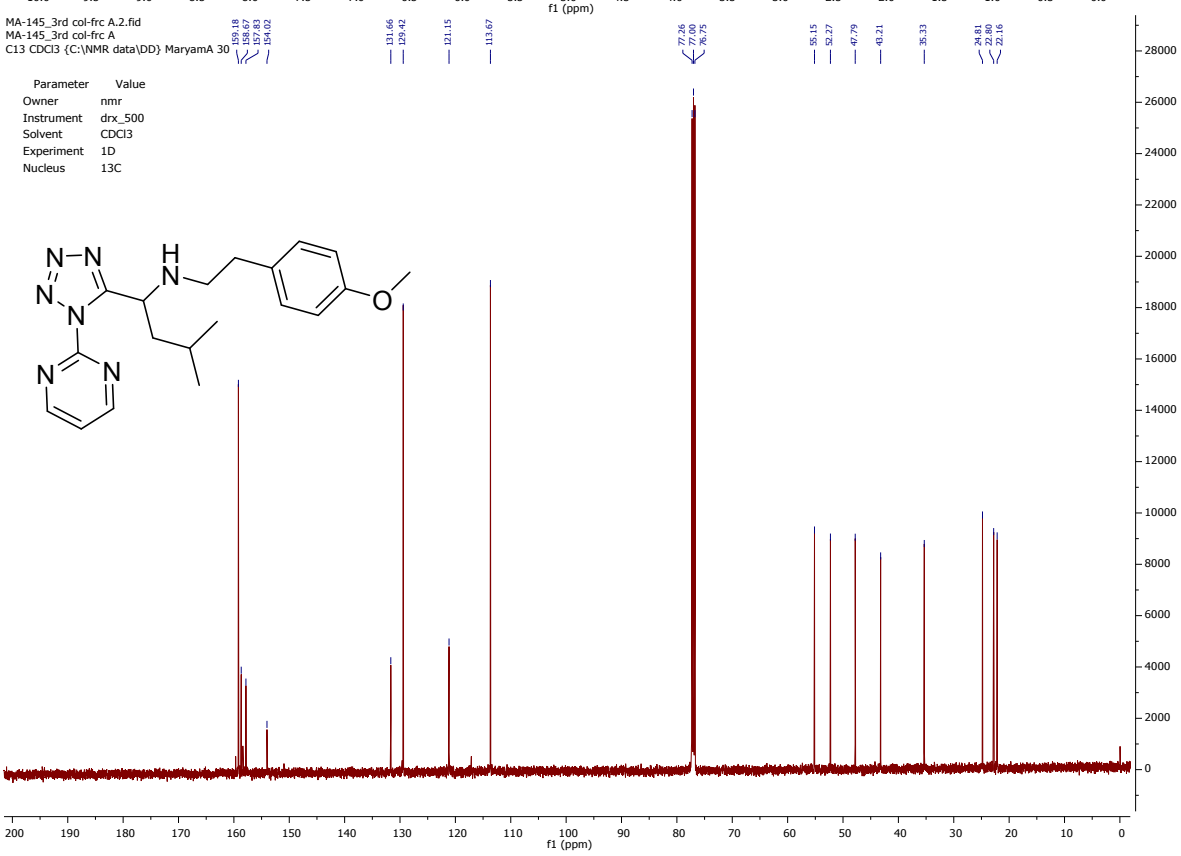
I-74: 2-(2-Isocyanoethyl)pyridine



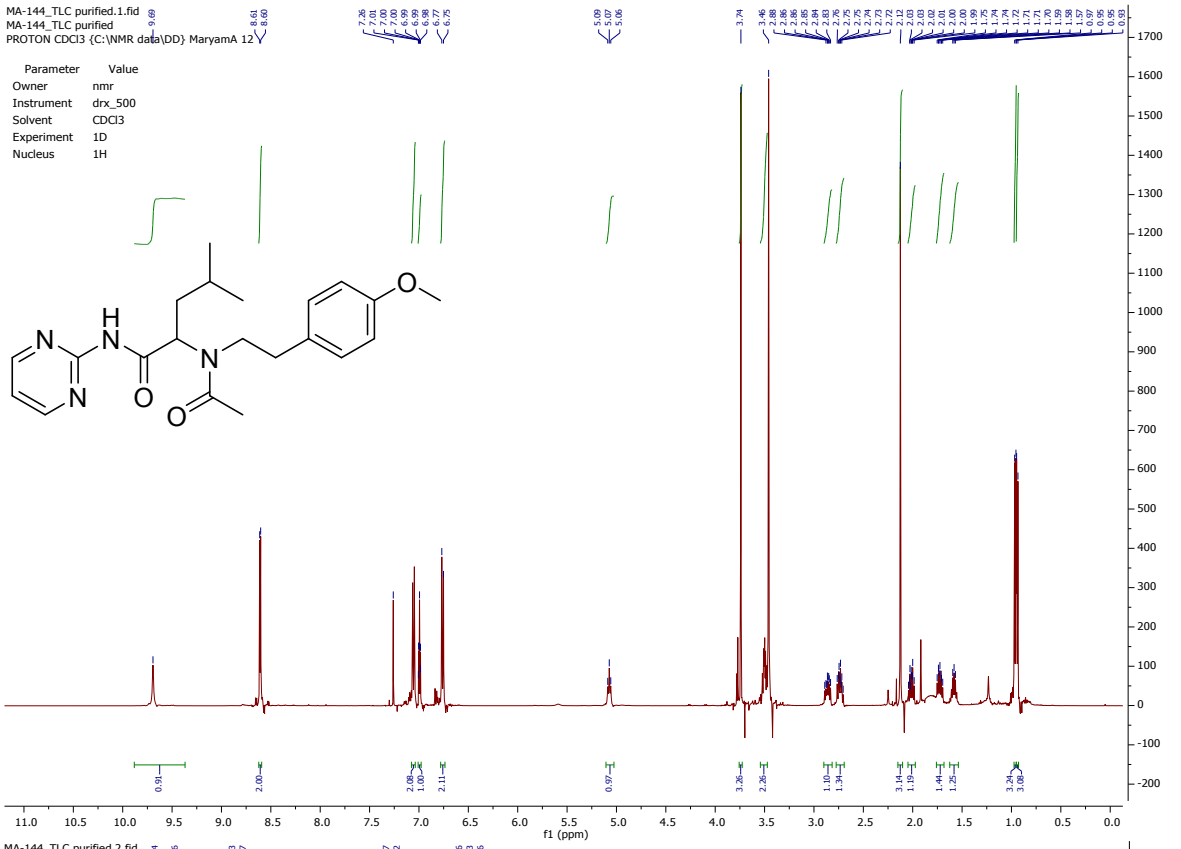


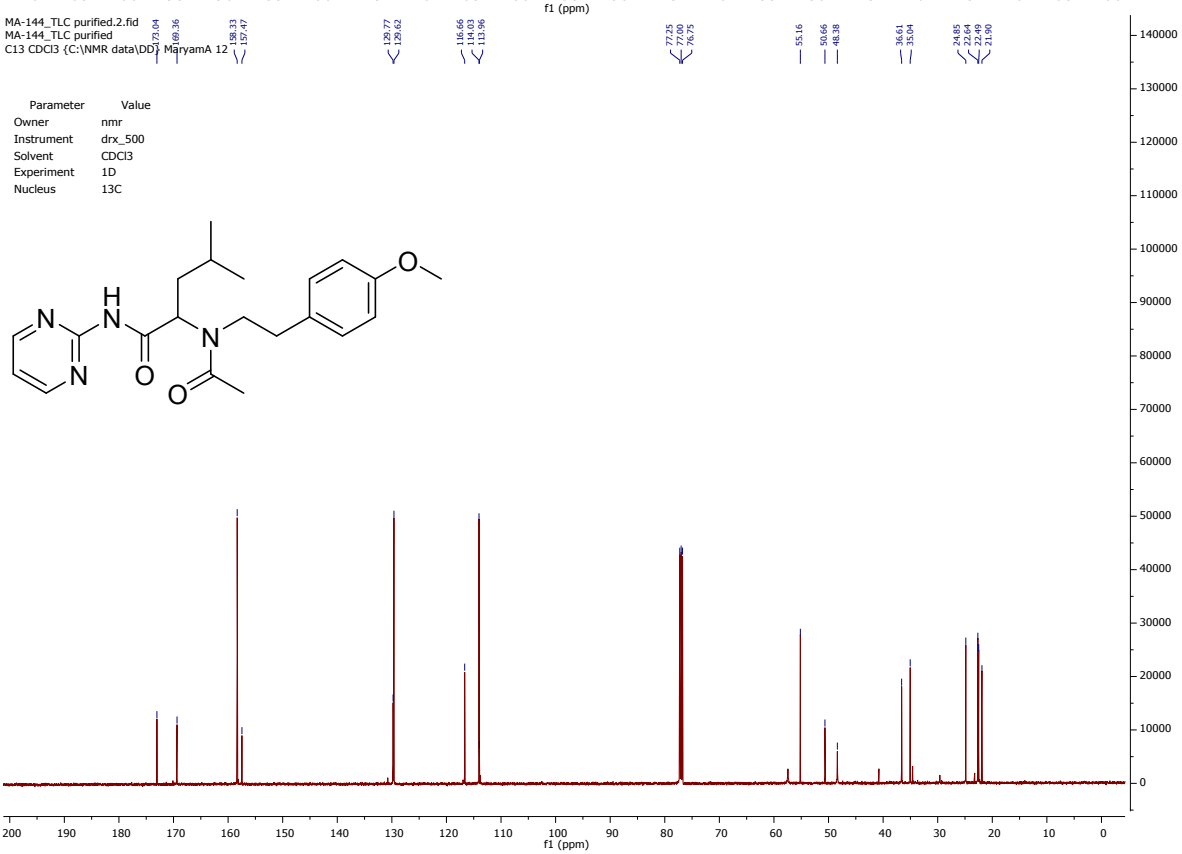
UT-1: *N*-(4-Methoxyphenethyl)-3-methyl-1-(1-(pyrimidin-2-yl)-1*H*-tetrazol-5-yl)butan-1-amine.





U-1: 2-(*N*-(4-Methoxyphenethyl)acetamido)-4-methyl-*N*-(pyrimidin-2-yl)pentanamide.





Comparisons of various parameters for literature reported synthesis of phenylethyl isocyanide with the current method:

Here we compare different parameters of literature reported procedures for the synthesis of phenylethylisocyanide using $POCl_3$.[27, 74-77] However, not all procedures were reported on a 100 mmol scale: 1. Porcal-2014: 30 mmol; 2. Pirali-2009: 70 mmol; 3. Andeana-2018: 70 mmol; 4. Domling-2009: 100 mmol; 5. Goldeman-2015: 150 mmol; 6. our method: 100 mmol. Clearly the differences to 100 mmol are not large and are therefore comparable. Thus, we calculate these values for solvents amount from literature by scaling them to 100 mmol scale. Moreover, we count the number of operations, reaction time, reaction workup time amount of dichloromethane used, aqueous waste generated during the reaction until isolating the pure product in the all procedures summarized in the Table S1. For comparison, we consider the factor of 100 mmol scale to summarized following table as reported in the actual reports.

Table S1: Comparison of various parameters for 100 mmol synthesis of phenylethyl isocyanide (C-2) useful for production of Praziquantel drug.

	Porcal,[74] 2014	Pirali,[75] 2009	Andreana,[76] 2018	Domling,[77] 2009	Goldeman,[27] 2015	This Method
CH_2Cl_2 used for the reaction, (mL)	250	220	220	100	400	50
Aq. waste generated, (mL)	500	400	400	300	300	0
% yield	99	77	95	65	45	97
Reaction time, (h)	3	3	3	5	3	0.2
Workup time, (h)	2	2	2	2	2	0
Number of operations	7	7	7	9	9	3
Temperature	-10^{o}C	-10^{o}C	-78^{o}C	0^{o}C 2h+3 hr rt	0^{o}C 1h+2hr rt	0^{o}C 10 min

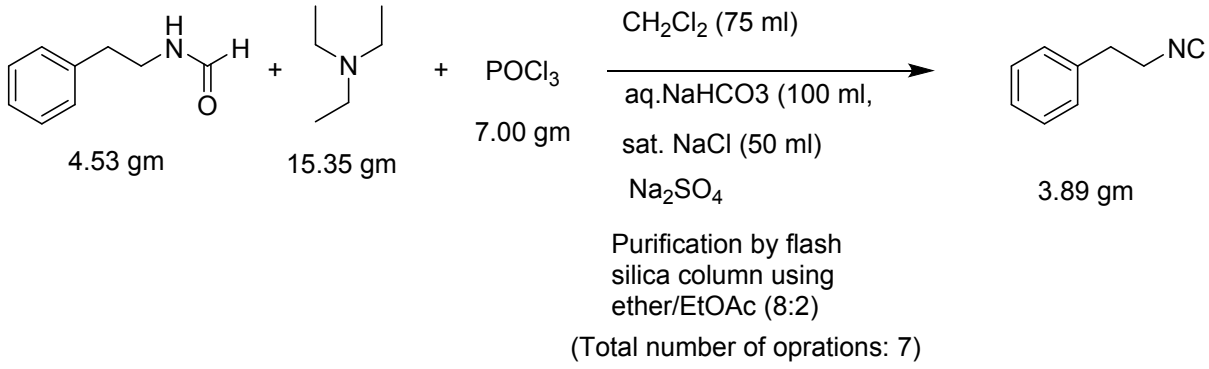
Environmental factor (E-factor) Calculations:

The reaction conditions of phenylethyl isocyanide synthesis using $POCl_3$ were taken from literature.[27, 74-77] While calculating the E-factors, we didn't consider the amount of silica gel used for flash column chromatography as it is generally not reported. However, if we consider the typical amount of silica gel used for other literature known methods synthesis, then in the first three reports which are using chromatography, E-factors will even increase. In our case for a 100 mmol scale reaction we used 140 gm of 100 -200 mesh size silica for the filtration process. Thus inclusion of silica gel waste would considerably increase the difference in E-factor between our and previous work.

Calculation of E-factor values for various phenylethyl isocyanide synthesis by using $POCl_3$ systems:

E-factor = Kg (waste)/Kg (product)

1) M. Ingold, G. V. López, **W. Porcal**, *ACS Sustain. Chem. Eng.,* **2014**, *2*, 1093-1097.[74]



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 4.53 gm

Mass (Triethylamine) = 15.35 gm

Mass ($POCl_3$) = 7.00 gm

Mass (Dichloromethane assuming 90% recovery): 75 ml x (1.33 g/ml) x 10% = 9.975 gm

Mass (Aq. $NaHCO_3$, (calculated by weight) (100 ml)) = 106.7 gm

Mass (Sat. NaCl sol. (calculated by weight): (50ml)) = 60.75 gm

Purification by flash silica column solvent (8:2 ether/EtOAc) for 4.53 gm assuming as 500 ml used and 90% recovery):

Mass (Ether (assuming as 90% recovery)): 400ml x (0.706 g/ml) x 10% = 28.24 gm

Mass (EtOAc (assuming as 90% recovery)): 100 ml x (0.902 gm/ml) x 10% = 9.02 gm

Mass (Na_2SO_4 used for drying (assuming two tea spoon)) = 5.0 gm

(Silica have been excluded from this calculation)

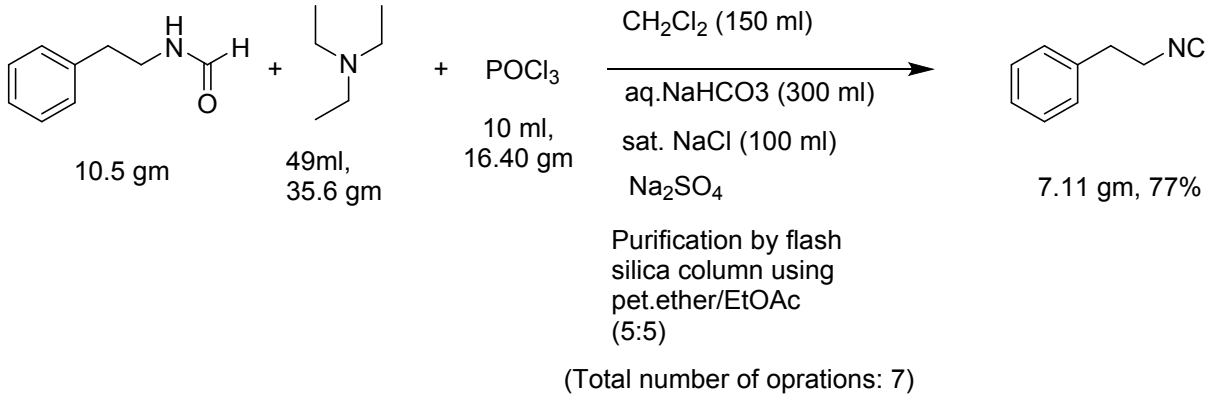
Total mass of Reactants waste: (4.53 gm + 15.35 gm + 7.00 gm + 9.975 gm + 106.7 gm + 60.75 gm + 28.24 gm + 9.02 gm + 5.0 gm) = 246.565 gm = **246.57 gm**

Amount of product = 3.89 gm

E-Factor = Amount of waste/Amount of product = 246.57 gm/3.89 gm = 63.39

E-factor = 63.39

2) A. A. Grolla, V. Podesta, M. G. Chini, S. Di Micco, A. Vallario, A. A. Genazzani, P. L. Canonico, G. Bifulco, G. C. Tron, G. Sorba, **T. Pirali**, *J. Med. Chem.,* **2009**, *52*, 2776-2785.[75]



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 10.5 gm

Mass (Triethylamine) = 35.6 gm

Mass (Dichloromethane (assuming 90% recovery)): 150 ml x (1.33 g/ml) x 10% = 19.95 gm

Mass ($POCl_3$) = 16.40 gm

Mass (Aq. $NaHCO_3$, (calculated by weight) (3 x 100 ml)) = 320.1 gm

Mass (Sat. NaCl sol. (calculated by weight): (100ml)) = 121.5 gm

Purification by flash silica column solvent (5:5 ether/EtOAc) for 10.5 gm assuming as 800 ml used and 90% recovery):

Mass (Pet. ether (assuming as 90% recovery)): 400ml x (0.64 g/ml) x 10% = 25.6 gm

Mass (EtOAc (assuming as 90% recovery)): 400 ml x (0.902 gm/ml) x 10% = 36.08 gm

Mass (Na_2SO_4 used for drying (assuming 3 tea spoon)) = 7.5 gm

(Silica have been excluded from this calculation)

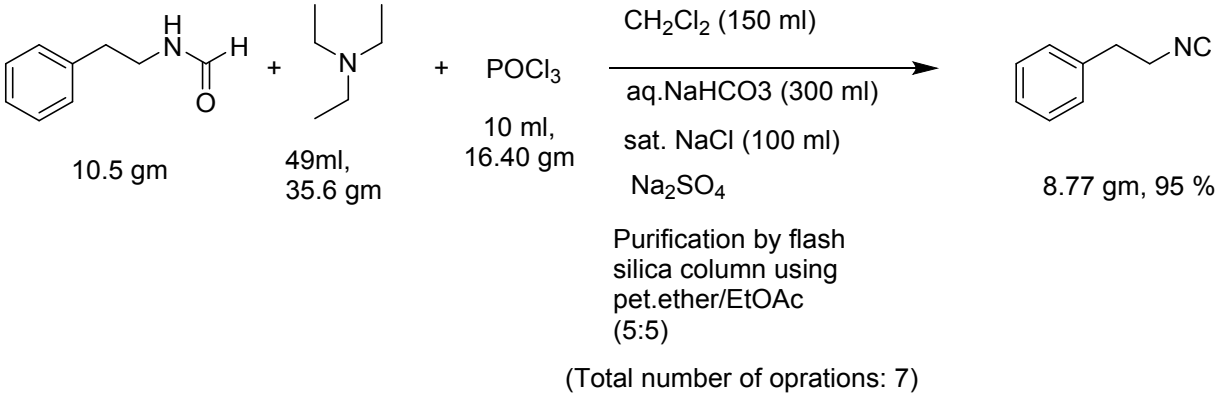
Total mass of Reactants waste: (10.5 gm + 35.6 gm + 19.95 gm + 16.40 gm + 320.1 gm + 121.5 gm + 25.6 gm + 36.08 gm + 7.5 gm) = **593.23 gm**

Amount of product = 7.11 gm

E-Factor = Amount of waste/Amount of product = 593.23 gm/7.11 gm = 83.44

E-factor = 83.44

3) N. Esmati, A. Maddirala, N. Hussein, H. Amawi, A. Tiwari, **P. Andreana**, *Org. Biomol. Chem.,* **2018**, *16*, 5332-5342.[76] [Note that these authors referred the above (*J. Med. Chem.,* **2009**, *52*, 2776-2785) manuscript for synthesis, and reported the yield 95% of phenyl ethyl isocyanide]



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 10.5 gm

Mass (Triethylamine) = 35.6 gm

Mass ($POCl_3$) = 16.40 gm

Mass (Dichloromethane (assuming 90% recovery)): 150 ml x (1.33 g/ml) x 10% = 19.95 gm

Mass (Aq. $NaHCO_3$, (calculated by weight) (3 x 100 ml)) = 320.1 gm

Mass (Sat. NaCl sol. (calculated by weight): (100ml)) = 121.5 gm

Purification by flash silica column solvent (5:5 ether/EtOAc) for 10.5 gm assuming as 800 ml used and 90% recovery):

Mass (Pet. ether (assuming as 90% recovery)): 400ml x (0.64 g/ml) x 10% = 25.6 gm

Mass (EtOAc (assuming as 90% recovery)): 400 ml x (0.902 gm/ml) x 10% = 36.08 gm

Mass (Na_2SO_4 used for drying (assuming 3 tea spoon)) = 7.5 gm

(Silica have been excluded from this calculation)

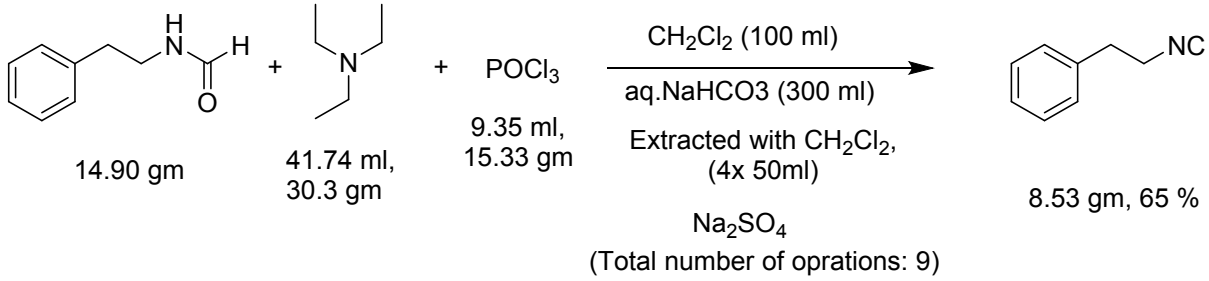
Total mass of Reactants waste: (10.5 gm + 35.6 gm + 19.95 gm + 16.40 gm + 320.1 gm + 121.5 gm + 25.6 gm + 36.08 gm + 7.5 gm) = **593.23 gm**

Amount of product = 8.77 gm

E-Factor = Amount of waste/Amount of product = 593.23 gm/8.77 gm = 67.64

E-factor = 67.64

4) **A. Doemling**, Preparation of praziquantel, 2009, PCT Int. Appl., 2009115333, WO2009115333.[77]



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 14.90 gm

Mass (Triethylamine) = 30.3 gm

Mass ($POCl_3$) = 15.33 gm

Mass (Dichloromethane (assuming 90% recovery)): 300 ml x (1.33 g/ml) x 10% = 39.9 gm

Mass (Water +Aq. $NaHCO_3$, (calculated by weight) (300ml)) = 320.1 gm

Mass (Na_2SO_4 used for drying (assuming 4 tea spoon)) = 10 gm

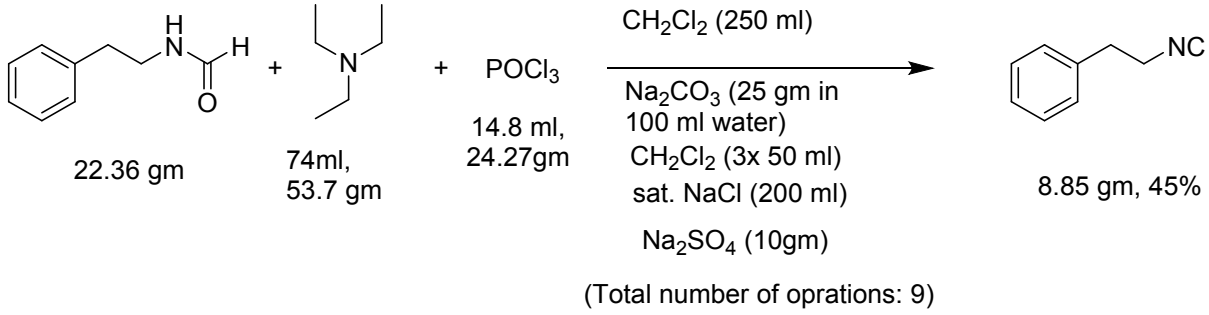
Total mass of Reactants waste: (14.90 gm + 30.3 gm + 15.33 gm + 39.9 gm + 320.1 gm + 10 gm) = **430.53 gm**

Amount of product = 8.53 gm

E-Factor = Amount of waste/Amount of product = 443.83 gm/ 8.53 = 50.47

E-factor = 50.47

5) **W. Goldeman**, A. Nasulewicz-Goldeman, *Tetrahedron* **2015**, *71*, 3282-3289.[27]



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 22.36 gm

Mass (Triethylamine) = 53.7 gm

Mass (Dichloromethane (assuming 90% recovery)): 400 ml x (1.33 g/ml) x 10% = 54.37 gm

Mass ($POCl_3$) = 24.27 gm

Mass (Na_2CO_3 Mass) = 25.0 gm

Mass (Water (100 ml)) = 100.0 gm

Mass (Sat. NaCl sol. (calculated by weight): (200ml)) = 243.0 gm

Mass (Na_2SO_4 used for drying (assuming 4 tea spoon)) = 10.0 gm

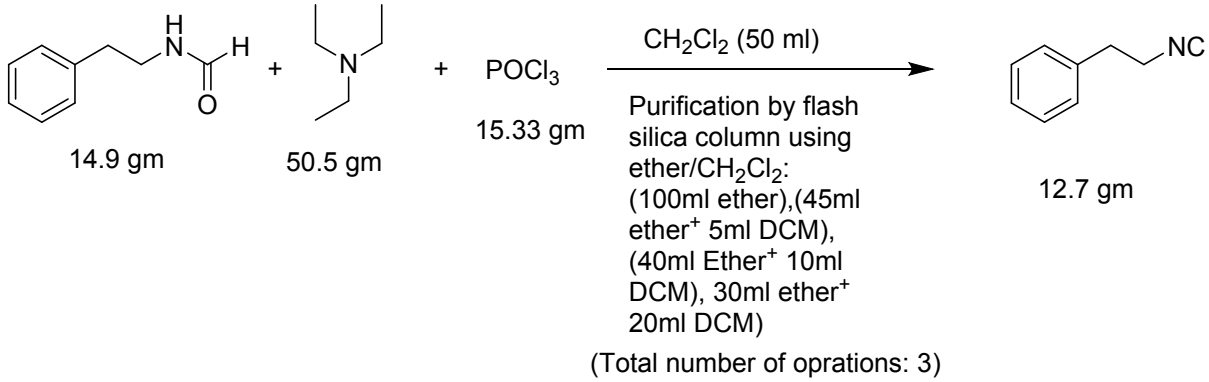
Total mass of Reactants waste: (22.36 gm + 53.7 gm + 54.37 gm + 24.27 gm + 25.0 gm + 100 gm + 243.0 gm + 10.0 gm) = **532.7 gm**

Amount of product = 8.85 gm

E-Factor = Amount of waste/Amount of product = 532.7 gm/8.85 gm = 60.19

E-factor = 60.19

6) E-factor calculation for our current work:



Amount of total amount of Reactants:

Mass (*N*-(2-phenylethyl) formamide) = 14.9 gm

Mass (Triethylamine) = 50.5 gm

Mass ($POCl_3$) = 15.33 gm

Mass (Dichloromethane (assuming 90% recovery)): 85 ml x (1.33 g/ml) x 10% = 11.31 gm

Mass (Diethyl ether (assuming 90% recovery)): 215 ml x (0.706 g/ml) x 10% = 15.18 gm

(Silica (140.0 gm) have been excluded from this calculation, as in all above mention references, we excluded silica.)

Total mass of Reactants waste: (14.9 gm + 50.5 gm + 15.33 gm + 11.31gm + 15.18 gm = **107.22 gm**

Amount of product = 12.7 gm

E-Factor = Amount of waste/Amount of product = 107.22 gm/12.7 gm = 8.44

E-factor = 8.44

Thus, herein we summarized the all E-factor calculations of the various literature process of phenylethyl isocyanides synthesis using $POCl_3$.

Process	E-Factor

Porcal-2014	63.39
Pirali-2009	83.44
Andreana-2018	67.64
Dömling-2009	50.47
Goldeman-2015	60.19
Present work	**8.44**

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