

Supporting Information

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Note on the Importance of Stirring and Solvent Ratio

In order for this procedure to be successful for the cyanation of (hetero)aryl halides, efficient stirring is absolutely essential. All 1 mmol scale reactions were performed using a stir plate set to 900 rpm. Deviations in reaction vessel size, stir bar size, and reaction scale may require optimization of stirring efficiency to guarantee best results. Additionally, deviation from a 1:1 organic:water solvent mixture can result in incomplete conversions. It is important to make sure no solvent can escape the vessel or be absorbed by the septum to ensure optimal yields.

General Reagent Information

Commercial materials were used as received unless otherwise noted. 1,4-dioxane (anhydrous, 99.8%), cyclohexane (anhydrous, 99.5%) and potassium carbonate (anhydrous, 99%) were purchased from Aldrich. Potassium acetate (99%) was purchased from Sigma. Potassium hexacyanoferrate(II) trihydrate (ReagentPlus, 98.5%) was purchased from Aldrich and ground into a fine powder using a mortar and pestle prior to use. [(allyl)PdCl]₂ was received as a gift from Johnson Matthey. Pd(OAc)₂ was purchased from Johnson Matthey. Pd₂dba₃, SPhos, XPhos, and

RuPhos, P(*o*-tol)₃, and PCy₃ were purchased from Strem. PPh₃, dppf, and P(*t*-Bu)₃ were purchased from Aldrich. BrettPhos was a gift from Aldrich. *t*-BuXPhos was received as a gift from Amgen. DavePhos was received as a gift from Saltigo. *t*-BuBrettPhos,^[1] precatalysts,^[2] and (COD)Pd(CH₂TMS)₂^[3] were synthesized according to literature procedures.

(Hetero)aryl halides:

4-chloroanisole (99%), 2-chloro-*m*-xylene (97%), 4-chloroacetophenone (97%), 3-chloroaniline (99%), 4-chlorobenzyl alcohol (98%), 4-chlorophenol (99%), 6-chloroquinoxaline (97%), 3-chloro-6-methoxypyridazine (95%), 3-chlorothiophene (98%), ethyl 4-bromopyrrole-2-carboxylate (97%), and 5-chlorobenzotriazole (99%) were purchased from Aldrich. Ethyl 4-chlorobenzoate (98%) and 4-chlorobenzonitrile (99%) were purchased from Avocado. 4-chlorobenzamide (98%), 4-chlorosulfonamide (98%), 7-chloroindole (98%), 2-acetyl-4-chlorothiophene (97%), and 2-chlorobenzimidazole (97%) were purchased from Alfa. 3-bromoquinoline (98%) and 3-chloroindazole (99%) were purchased from Acros. 4-bromothiazole (97%) was purchased from Oakwood. 3-bromopyrazole (95%) was purchased from Frontier. 4-bromopyrazole (98%), 4-chloro-7-azaindole (98%), and 4-bromoimidazole (98%) was purchased from CombiBlocks. 4-chloro-7-azaindole was recrystallized from toluene prior to use. 1-Chloro-4-fluorobenzene (98%) was purchased from Aldrich. Prior to use in stoichiometric palladium complex formation, 1-chloro-4-fluorobenzene was passed through a plug of basic alumina and degassed by sonication under vacuum.

Preparation of Degassed Aqueous Solutions

Performing a freeze/pump/thaw of aqueous solutions is time consuming and not necessary for highly efficient cyanation reactions. Degassed water can be prepared in less than 30 s by sonication under vacuum. A 100 mL round bottom flask was filled with deionized water and fitted with a rubber septum. The flask was placed into a water-filled sonication bath, vacuum was applied for 5 s, and the vessel was refilled with nitrogen gas. This process was repeated for a total of five cycles. The degassed water was then added via syringe to a volumetric flask under a nitrogen atmosphere equipped with a Teflon-lined screw-cap septum containing base (e.g., KOAc, K₂CO₃).

General Analytical Information

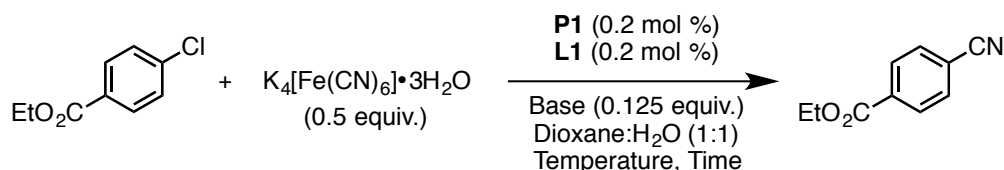
All compounds were characterized by ¹H NMR, ¹³C NMR, IR spectroscopy, and, for most, elemental analysis. Nuclear Magnetic Resonance spectra were recorded on Varian XL 300 NMR or Varian Inova 500 MHz instruments. Copies of the ¹H and ¹³C spectra can be found at the end of the Supporting Information. All ¹H NMR experiments were reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.24 ppm), methanol (3.31 ppm), dichloromethane (5.32 ppm), or DMSO (2.50 ppm) in the deuterated solvent. All ¹³C NMR spectra are reported

in ppm relative to deuteriochloroform (77.23 ppm), deuteromethanol (49.15 ppm), deuteriodichloromethane (54.00 ppm), or d⁶-DMSO (39.51 ppm) and all were obtained with ¹H decoupling. All IR spectra were obtained on a Thermo Scientific Nicolet iS5 spectrometer (iD5 ATR, diamond). GC analyses were performed on an Agilent 7980A chromatograph with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.). GC-MS analyses were performed on an Agilent 6850 chromatograph with an Agilent 5965 inert mass selective detector using an HP-5MS column (30 m, 0.25 mm I.D.). HPLC analyses were performed on an Agilent chromatograph using an Eclipse XDB-C18 column (5 uL, 4.6 x 150 mm) eluting with a solvent gradient of 60:40–90:10 (Methanol:0.1 % trifluoroacetic acid in H₂O). Powder X-ray diffraction patterns were recorded on a Bruker Advance D8 diffractometer using Nickel-filtered Cu-K α radiation (λ = 1.5418 Å) with accelerating voltage 40 kV and a current of 40 mA. ESI-MS spectra were recorded on a Bruker Daltonics APEXIV 4.7 Tesla Fourier transform ion cyclotron resonance mass spectrometer (FT-ICR-MS). Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. Flash chromatography was performed using Silicycle Silia P60 silica gel. Thin-layer chromatography was performed on EMD Silica Gel 60 F254 TLC plates and visualized using UV or/and ceric ammonium molybdate (CAM), potassium permanganate (KMnO₄), or ninhydrin stain.

Safety Considerations

While K₄[Fe(CN)₆]•3H₂O and Prussian Blue are non-toxic, crude reaction mixtures and aqueous phases from extractions should still be treated with caution. **NEVER** expose the crude reaction mixture or the aqueous layer to acidic conditions as formation of hydrogen cyanide is possible. All waste from crude reaction mixtures and aqueous workups should be disposed using accepted protocols in a basic aqueous solution (pH >12).^[4] Finally, always wear appropriate personal protective equipment (gloves, etc) to avoid the possibility of contact with cyanide.

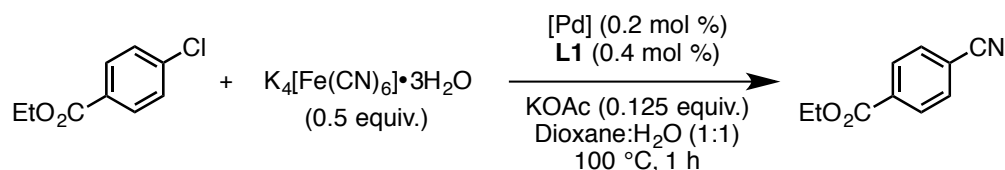
Experimental Procedure for Figure 1



To each of six screw-top test tubes equipped with a magnetic stir bar was added K₄[Fe(CN)₆]•3H₂O (211 mg, 0.5 equiv.). To a separate screw-top test tube equipped with a magnetic stir bar was added **P1** (14.7 mg) and **L1** (7.6 mg) (enough for 8 reactions at 0.2 mol % Pd loading, 1:2 Pd:L ratio). After sealing with a Teflon-lined screw-cap septum, all vessels were evacuated and backfilled with nitrogen (this process was repeated for a total of three cycles). Dioxane (20 mL) was added to the precatalyst/ligand tube via syringe, and the solution was stirred until all solids dissolved. Ethyl 4-chlorobenzoate (156 μ L, 184 mg, 1 mmol), Pd/L (2.5 mL) solution, and 0.05 M base in degassed water (2.5 mL) were then added via syringe to the reaction tube containing K₄[Fe(CN)₆]•3H₂O. The test tube was placed in an oil bath preheated to the

specified temperature. After stirring for the designated amount of time, the reaction mixture was then cooled to room temperature. EtOAc (10 mL), brine (10 mL), and dodecane (50 μ L) were added to each reaction vessel. The reaction vessels were sealed and shaken. A portion of the organic layer from each was filtered through a plug of silica gel, which was eluted with EtOAc. The eluents were then analyzed by GC.

Experimental Procedure for Figure 2

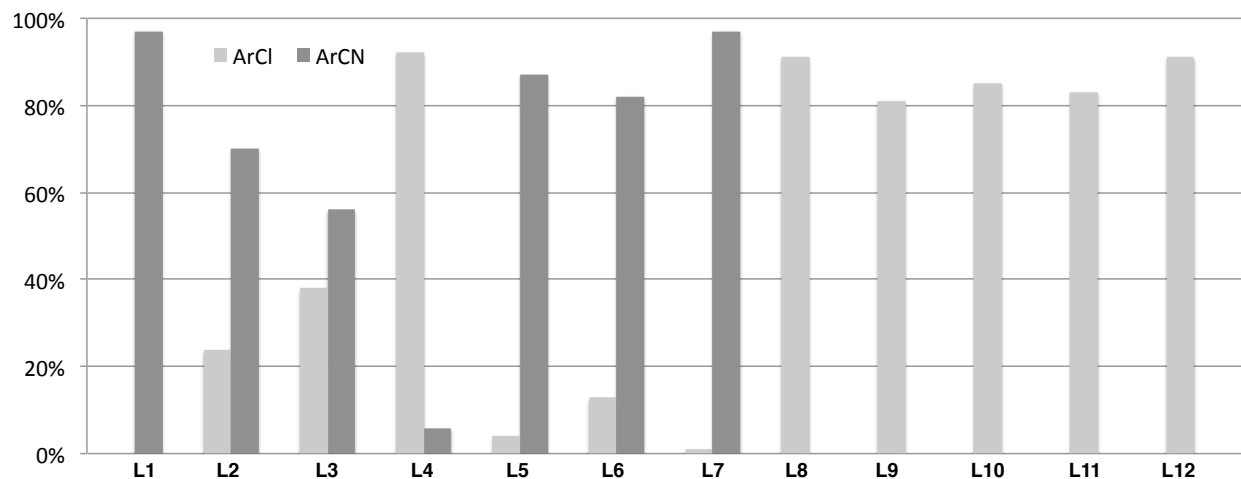
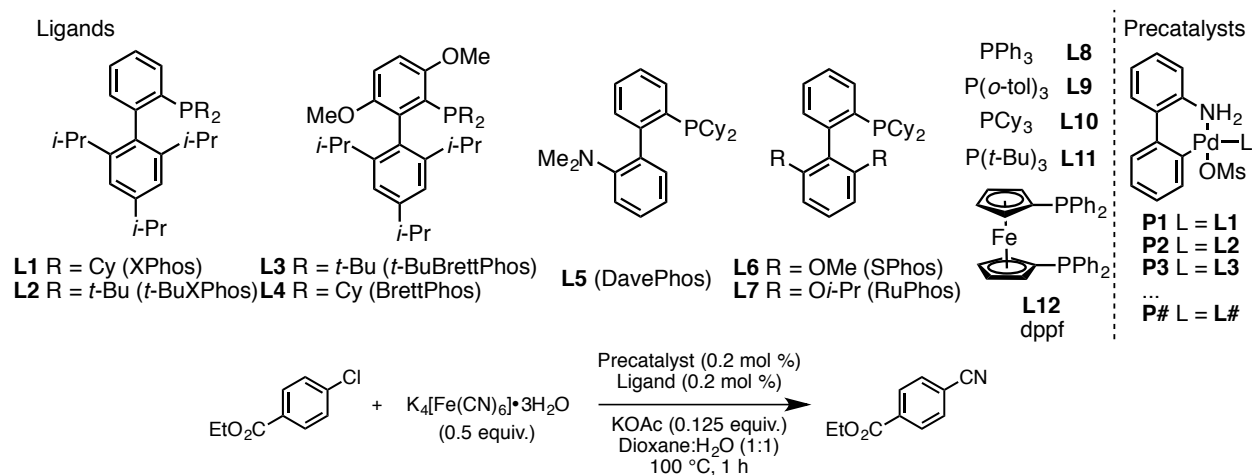


To each of five screw-top test tubes equipped with a magnetic stir bar was added $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$ (211 mg, 0.5 equiv.). To a separate screw-top test tube equipped with a magnetic stir bar was added palladium source and **L1** (enough for 4 reactions at 0.2 mol % Pd loading, 1:2 Pd:L ratio). After sealing with a Teflon-lined screw-cap septum, all vessels were evacuated and backfilled with nitrogen (this process was repeated for a total of three cycles). Dioxane (10 mL) was added to the Pd/**L1** tube via syringe, and the solution was stirred until all solids dissolved. For the Pd_2dba_3 preincubation run, the Pd/**L1** solution was stirred in an oil bath preheated to 120 $^\circ\text{C}$ for 3 min and cooled to room temperature. Ethyl 4-chlorobenzoate (156 μ L, 184 mg, 1 mmol), Pd/L solution (2.5 mL), and 0.05 M KOAc in degassed water (2.5 mL) were then added via syringe to the reaction tube containing $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$. The test tube was placed in an oil bath preheated to 100 $^\circ\text{C}$. After stirring for 1 h, the reaction mixture was then cooled to room temperature. EtOAc (10 mL), brine (10 mL), and dodecane (50 μ L) were added to each reaction vessel. The reaction vessels were sealed and shaken. A portion of the organic layer from each was filtered through a plug of silica gel, which was eluted with EtOAc. The eluents were then analyzed by GC.

Ligand Screen

To each of fifteen screw-top test tubes equipped with a magnetic stir bar was added $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$ (211 mg, 0.5 equiv.). To a separate screw-top test tube equipped with a magnetic stir bar was added precatalyst and ligand (enough for 4 reactions at 0.2 mol % Pd loading, 1:2 Pd:L ratio). For reactions utilizing **L10** and **L11**, precatalyst and ligand was weighed out in a nitrogen-filled glove box due to the oxygen-sensitive nature of these ligands. After sealing with a Teflon-lined screw-cap septum, all vessels were evacuated and backfilled with nitrogen (this process was repeated for a total of three cycles). Dioxane (10 mL) was added to each precatalyst/ligand tube via syringe, and the solution was stirred until all solids dissolved. Ethyl 4-chlorobenzoate (156 μ L, 184 mg, 1 mmol), Pd/L solution (2.5 mL), and 0.05 M KOAc in degassed water (2.5 mL) were then added via syringe to the reaction tube containing $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$. The test tube was placed in an oil bath preheated to 100 $^\circ\text{C}$. After 1 h of stirring at 100 $^\circ\text{C}$, the reaction mixture was then cooled to room temperature. EtOAc (10 mL), brine (10 mL), and

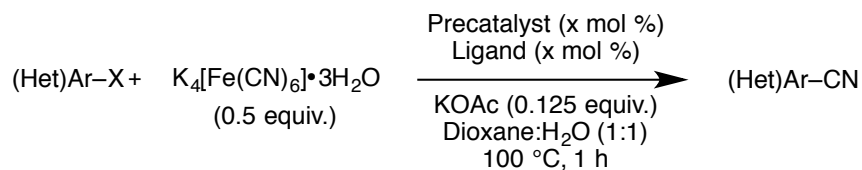
dodecane (50 μ L) were added to each reaction vessel. The reaction vessels were sealed and shaken. A portion of the organic layer from each was filtered through a plug of silica gel, which was eluted with EtOAc. The eluents were then analyzed by GC.



Regarding Ligand Rearrangement

Recently, our group^[5] and others^[6] reported the dearomative rearrangement of di-*tert*-butyl biaryl phosphine ligands. As both *t*-BuXPhos (**L2**) and *t*-BuBrettPhos (**L3**) were used in this study, we conducted preliminary investigations on select examples to see whether a rearrangement was occurring in this reaction as well. In the cyanation of 3-chloroindazole, a total of 8 mol % **L2** was used (Table 2, entry **2k**). 30 mg of **L2** was recovered from the reaction, representing 88% ligand recovery. Recovery of **L3** or derivatives thereof from the cyanation of 4-bromo-1-benzylimidazole was not successful, however spiking the crude reaction with additional **L3** showed only one peak via ³¹P NMR. In light of this data, we believe that ligand rearrangement does not occur to a significant extent in this reaction.

General Experimental Procedure for Tables 1 and 2



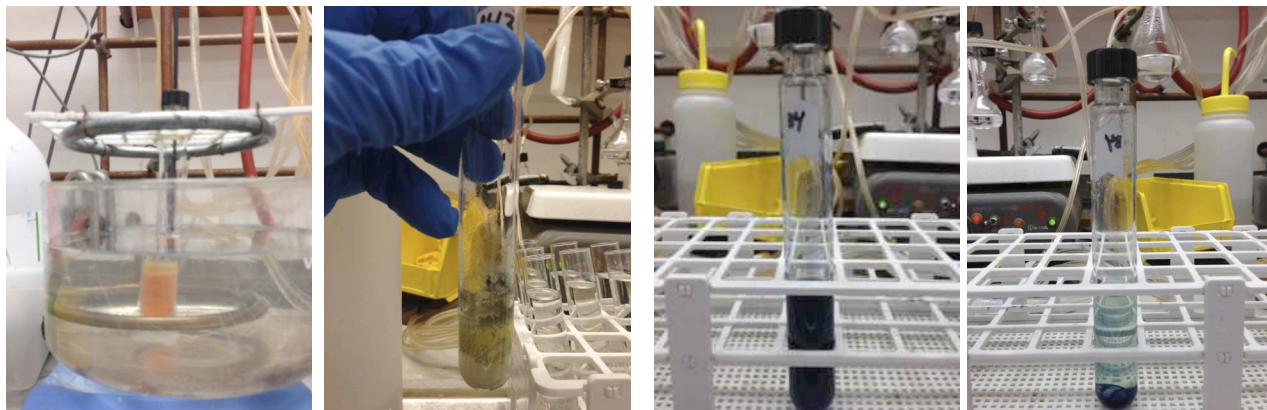
All reactions were set up on the bench top open to the air and all reagents for these processes were weighed and added to the reaction tube in the air.

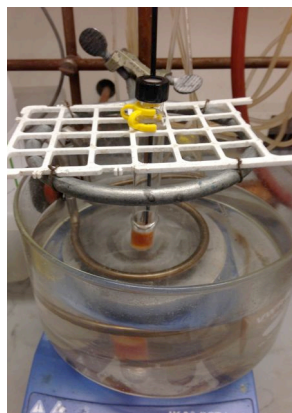
To a screw-top test tube equipped with a magnetic stir bar was added precatalyst, ligand, $\text{K}_4[\text{Fe}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$ (211 mg, 0.5 equiv.), and (if solid) (hetero)aryl halide (1 mmol). After sealing with a Teflon-lined screw-cap septum, the vessel was evacuated and backfilled with nitrogen (this process was repeated for a total of three cycles). (Hetero)aryl halide (if liquid) (1 mmol), dioxane (2.5 mL), and 0.05 M KOAc in degassed water (2.5 mL) were then added to the reaction tube via syringe. The test tube was placed in an oil bath preheated to 100 °C and stirred for 1 h. Upon initial stirring, a clear, yellow solution was observed. During the course of the reaction, a yellow or green precipitate formed on the walls of the reaction vessel. After 1 h of stirring at 100 °C, the reaction mixture was then cooled to room temperature. The contents of the test tube were transferred to a separatory funnel using EtOAc (15 mL) and brine (15 mL), and the organic layer was separated from the aqueous layer. If the reaction was successful, during the extraction process the color of the aqueous layer turns dark blue. This is a colloidal suspension of insoluble fine particles. Isolation and PXRD analysis revealed this solid to be Prussian Blue. The aqueous layer was further extracted with EtOAc (total 2 x 15 mL). The combined organic layers were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The resulting mixture was adsorbed onto silica gel, dried *in vacuo*, and purified via column chromatography to yield the product.

Notes:

- 1) In order for this procedure to be successful for the cyanation of (hetero)aryl halides, efficient stirring is absolutely essential. All 1 mmol scale reactions were performed using a stir plate set to 900 rpm. Deviations in reaction vessel size, stir bar size, and reaction scale may require optimization of stirring efficiency to guarantee best results.
- 2) Deviation from a 1:1 organic:water solvent mixture can result in incomplete conversions. It is important to make sure no solvent can escape the vessel or be absorbed by the septum to ensure optimal yields.

Pictures of Reactions

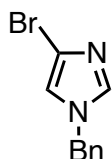




- | | | | |
|------------|-----|-----|-----|
| (1)
(5) | (2) | (3) | (4) |
|------------|-----|-----|-----|
- 1) Top down view of early reaction progress
 - 2) Reaction progresses, yellow precipitate begins to form
 - 3) Completed crude reaction, large amount of yellow precipitate on walls of reaction vessel
 - 4) Aqueous layer of reaction workup
 - 5) Aqueous layer of reaction workup, colloidal blue solid allowed to settle

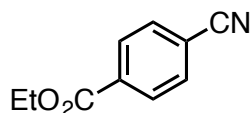
Note: Pictures are only given as examples and not every reaction will look exactly the same. These are not all pictures of the same reaction.

Preparation of 1-Benzyl-4-bromo-1H-imidazole

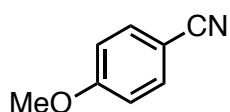


To a 100 mL round bottom flask equipped with a magnetic stir bar was added 4-bromo-1H-imidazole (2 g, 13.6 mmol, 1 equiv.), anhydrous K_2CO_3 (2.07 g, 15.0 mmol, 1.1 equiv.), acetone (40 mL), and benzyl bromide (1.8 mL, 2.59 g, 15.1 mmol, 1.1 equiv.). The vessel was capped and the reaction mixture was stirred at room temperature for 22 h. The reaction mixture was poured onto EtOAc (80 mL), washed with deionized water (2x80 mL), and brine (80 mL). 1H NMR of the crude reaction mixture showed an 82:18 mixture of 4-bromo and 5-bromo isomers. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting mixture was adsorbed onto silica gel, dried *in vacuo*, and purified via column chromatography (silica gel, 80:20 to 50:50 hexanes:EtOAc gradient, visualized with UV and $KMnO_4$) to yield the product as a white solid (2.19 g, 68%), **mp** = 92–93 °C (lit. 91–93 °C).^[7] 1H NMR (300 MHz, $CDCl_3$): δ 7.45–7.28 (m, 4H), 7.19–7.11 (m, 2H), 6.84 (d, J = 1.6 Hz, 1H), 5.04 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 137.0, 135.3, 129.2, 128.6, 127.6, 118.6, 115.6, 51.4. IR (neat, cm^{-1}): 3144, 3109, 3024, 1496, 1391, 1236, 1106, 944.

Characterization Data for Table 1

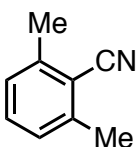


Ethyl 4-cyanobenzoate (1a). Following a modification of the general procedure with ethyl 4-chlorobenzoate (156 μ L, 184 mg, 1 mmol). **P1** (0.2 mol %) and **L1** (0.2 mol %) were added to the reaction vessel via syringe as a solution in dioxane (due to low catalyst loading). The product was purified by column chromatography (silica gel, 95:5 to 85:15 hexanes:EtOAc gradient, visualized with UV and $KMnO_4$) to yield ethyl 4-cyanobenzoate as a white solid. (168 mg, 96%), **mp** = 53–54 °C (lit. 54 °C).^[8] 1H NMR (300 MHz, $CDCl_3$): δ 8.17–8.08 (m, 2H), 7.76–7.68 (m, 2H), 4.39 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 164.9, 134.3, 132.2, 130.0, 118.0, 116.2, 61.8, 14.2. IR (neat, cm^{-1}): 2230, 1715, 1366, 1276, 1185, 1107, 1022, 873. **Anal.** Cald. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18. Found: C, 68.77; H, 5.28.

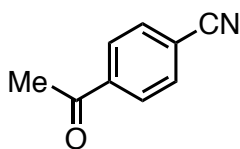


4-Methoxybenzonitrile (1b). Following the general procedure with 1-chloro-4-methoxybenzene (122 μ L, 142 mg, 1 mmol), **P1** (3.7 mg, 0.4 mol %), and **L1** (1.9 mg, 0.4 mol %). The product was purified by

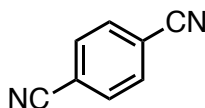
column chromatography (silica gel, 95:5 to 80:20 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 4-methoxybenzonitrile as a white solid. (126 mg, 95%), **mp** = 58–59 °C (lit. 57–59 °C).^[9] $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.52 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 9.0 Hz, 2H), 3.80 (s, 3H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 162.9, 134.0, 119.3, 114.8, 103.9, 55.6. **IR** (neat, cm^{-1}): 2216, 1604, 1506, 1255, 1174, 1020, 827, 682. **Anal.** Cald. for $\text{C}_8\text{H}_7\text{NO}$: C, 72.16; H, 5.30. Found: C, 72.10; H, 5.43.



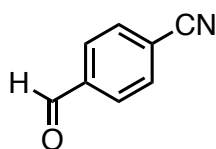
2,6-Dimethylbenzonitrile (1c). Following the general procedure with 2-chloro-1,3-dimethylbenzene (133 μL , 141 mg, 1 mmol), **P1** (5.5 mg, 0.6 mol %), and **L1** (2.9 mg, 0.6 mol %). The product was purified by column chromatography (silica gel, 100:0 to 97:3 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 2,6-dimethylbenzonitrile as a white solid. (113 mg, 86%), **mp** = 89–90 °C (lit. 89–91 °C).^[10] $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.32 (t, J = 7.7 Hz, 1H), 7.10 (d, J = 7.7 Hz, 2H), 2.51 (s, 6H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 142.1, 132.2, 127.4, 117.3, 113.4, 20.8. **IR** (neat, cm^{-1}): 2949, 2922, 2215, 1596, 1472, 1380, 1174, 1037. **Anal.** Cald. for $\text{C}_9\text{H}_9\text{N}$: C, 82.41; H, 6.92. Found: C, 82.21; H, 6.96.



4-Acetylbenzonitrile (1d). Following the general procedure with 1-(4-chlorophenyl)ethanone (130 μL , 155 mg, 1 mmol), **P1** (2.8 mg, 0.3 mol %), and **L1** (1.4 mg, 0.3 mol %). The product was purified by column chromatography (silica gel, 95:5 to 85:15 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 4-acetylbenzonitrile as a white solid. (138 mg, 95%), **mp** = 58–59 °C (lit. 57–58 °C).^[11] $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 8.02 (dt, J = 7.9, 0.9 Hz, 2H), 7.75 (dt, J = 8.1, 1.0 Hz, 2H), 2.62 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 196.5, 139.8, 132.4, 128.6, 117.9, 116.1, 26.7. **IR** (neat, cm^{-1}): 2229, 1686, 1401, 1354, 1261, 958. **Anal.** Cald. for $\text{C}_9\text{H}_7\text{NO}$: C, 74.47; H, 4.86. Found: C, 74.50; H, 4.86.

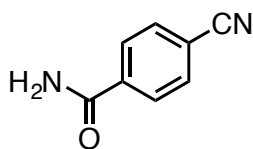


Terephthalonitrile (1e). Following the general procedure with 4-chlorobenzonitrile (138 mg, 1 mmol), **P2** (6.4 mg, 0.8 mol %), and **L2** (3.4 mg, 0.8 mol %). The product was purified by column chromatography (silica gel, 90:10 to 70:30 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield terephthalonitrile as a white solid. (120 mg, 94%), **mp** = 225–226 °C (lit. 225–227 °C).^[12] $^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.78 (s, 4H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3): δ 133.0, 117.2, 116.9. **IR** (neat, cm^{-1}): 3097, 3053, 2232, 1505, 1401, 1277, 1201, 1167. **Anal.** Cald. for $\text{C}_8\text{H}_4\text{N}_2$: C, 74.99; H, 3.15. Found: C, 74.76; H, 3.18.

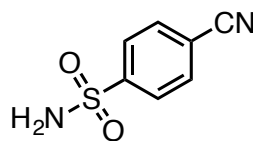


4-Formylbenzonitrile (1f). Following a modification of the general procedure with 4-chlorobenzaldehyde (141 mg, 1 mmol), **P2** (14.3 mg, 1.8 mol %), and **L2** (7.6 mg, 1.8 mol %). The reaction was stirred in an oil bath preheated to 70 °C for 12 hours. The product was purified by column chromatography (silica gel, 95:5 to 80:20 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 4-formylbenzonitrile as a pale yellow solid. (109 mg, 83%), **mp** = 98–99 °C (lit. 96–98 °C).^[13] $^1\text{H NMR}$ (300

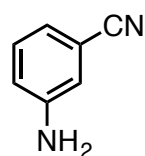
MHz, CDCl₃): δ 10.07 (s, 1H), 8.01–7.94 (m, 2H), 7.88–7.79 (m, 2H). **¹³C NMR (126 MHz, CDCl₃)**: δ 190.8, 138.7, 132.9, 129.9, 117.8, 117.5. **IR (neat, cm⁻¹)**: 3093, 3046, 2229, 1699, 1385, 1296, 1201, 1172. **Anal.** Cald. for C₈H₅NO : C, 73.27; H, 3.84. Found: C, 73.17; H, 3.81.



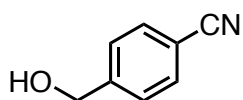
4-Cyanobenzamide (1g). Following the general procedure with 4-chlorobenzamide (156 mg, 1 mmol), **P2** (6.4 mg, 0.8 mol %), and **L2** (3.4 mg, 0.8 mol %). The product was purified by column chromatography (silica gel, 1:1 to 1:7 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 4-cyanobenzamide as a white solid. (133 mg, 91%), **mp** = 226–227 °C (lit. 222.1–223.3 °C).^[14] **¹H NMR (300 MHz, d⁶-DMSO)**: δ 8.22 (br s, 1H), 8.06–7.99 (m, 2H), 7.98–7.90 (m, 2H), 7.69 (br s, 1H). **¹³C NMR (126 MHz, d⁶-DMSO)**: δ 166.5, 138.3, 132.4, 128.3, 118.4, 113.7. **IR (neat, cm⁻¹)**: 3440, 3165, 2230, 1695, 1616, 1561, 1411, 770. **Anal.** Cald. for C₈H₆N₂O : C, 65.75; H, 4.14. Found: C, 65.74; H, 4.09.



4-Cyanobenzenesulfonamide (1h). Following the general procedure with 4-chlorobenzenesulfonamide (156 mg, 1 mmol), **P2** (5.7 mg, 0.7 mol %), and **L2** (3.0 mg, 0.7 mol %). The product was purified by column chromatography (silica gel, 70:30 to 50:50 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 4-cyanobenzenesulfonamide as a white solid. (165 mg, 91%), **mp** = 169–170 °C (lit. 168 °C).^[15] **¹H NMR (300 MHz, CD₃OD)**: δ 8.09–8.02 (m, 2H), 7.96–7.89 (m, 2H). **¹³C NMR (126 MHz, CD₃OD)**: δ 149.2, 134.2, 128.1, 118.7, 116.7. **IR (neat, cm⁻¹)**: 3340, 3253, 2228, 1490, 1335, 1096, 1091, 901. **Anal.** Cald. for C₇H₆N₂O₂S : C, 46.14; H, 3.32. Found: C, 46.17; H, 3.44.

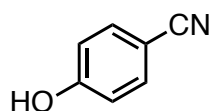


3-Aminobenzonitrile (1i). Following the general procedure with 3-chloroaniline (106 μ L, 128 mg, 1 mmol), **P2** (6.4 mg, 0.8 mol %), and **L2** (3.4 mg, 0.8 mol %). The product was purified by column chromatography (silica gel, 80:20 to 65:35 hexanes:EtOAc gradient, visualized with UV and ninhydrin) to yield 3-aminobenzonitrile as an off-white solid. (107 mg, 91%), **mp** = 47–48 °C (lit. 49–50 °C).^[16] **¹H NMR (300 MHz, CDCl₃)**: δ 7.19 (ddd, *J* = 8.2, 7.6, 0.6 Hz, 1H), 6.98 (ddd, *J* = 7.6, 1.5, 1.0 Hz, 1H), 6.91–6.78 (m, 2H), 3.88 (br s, 2H). **¹³C NMR (126 MHz, CDCl₃)**: δ 147.2, 130.0, 121.7, 119.4, 119.3, 117.3, 112.6. **IR (neat, cm⁻¹)**: 3469, 3375, 2222, 1625, 1577, 1447, 1298, 867. **Anal.** Cald. for C₇H₆N₂ : C, 71.17; H, 5.12. Found: C, 71.07; H, 5.28.



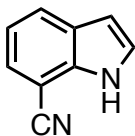
4-(Hydroxymethyl)benzonitrile (1j). Following the general procedure with (4-chlorophenyl)methanol (143 mg, 1 mmol), **P2** (3.9 mg, 0.5 mol %), and **L2** (2.1 mg, 0.5 mol %). The product was purified by column chromatography (silica gel, 60:40 to 50:50 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 4-(hydroxymethyl)benzonitrile as a white solid. (125 mg, 94%), **mp** = 43–44 °C (lit. 42–44 °C).^[17] **¹H NMR (300 MHz, CDCl₃)**: δ 7.64–7.53 (m, 2H), 7.49–7.38 (m, 2H), 4.73 (d, *J* = 5.6 Hz, 2H), 2.33 (t, *J* = 5.7 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃)**: δ 146.7, 132.2, 127.0,

118.9, 110.5, 63.7. **IR** (neat, cm^{-1}): 3317 (br), 2232, 1610, 1508, 1415, 1346, 1209, 1018. **Anal.** Cald. for $\text{C}_8\text{H}_7\text{NO}$: C, 72.16; H, 5.30. Found: C, 71.93; H, 5.47.

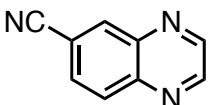


4-hydroxybenzonitrile (1k). Following the general procedure with 4-chlorophenol (129 mg, 1 mmol), **P2** (23.8 mg, 3 mol %), and **L2** (12.7 mg, 3 mol %). The product was purified by column chromatography (silica gel, 90:10 to 75:25 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 4-hydroxybenzonitrile as a white solid. (101 mg, 85%), **mp** = 110–111 °C (lit. 109–110 °C).^[18] **^1H NMR (300 MHz, CDCl_3):** δ 7.61–7.48 (m, 2H), 6.97–6.85 (m, 2H), 6.38 (br s, 1H). **^{13}C NMR (126 MHz, CDCl_3):** δ 160.5, 134.5, 119.5, 116.7, 103.1. **IR** (neat, cm^{-1}): 3266 (br), 2232, 1601, 1586, 1508, 1248, 1220, 1165. **Anal.** Cald. for $\text{C}_7\text{H}_5\text{NO}$: C, 70.58; H, 4.23. Found: C, 70.52; H, 4.46.

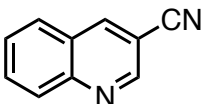
Characterization Data for Table 2



1H-Indole-7-carbonitrile (2a). Following the general procedure with 7-chloro-1H-indole (152 mg, 1 mmol), **P1** (6.4 mg, 0.7 mol %), and **L1** (3.3 mg, 0.7 mol %). The product was purified by column chromatography (silica gel, 100:0 to 80:20 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield 1H-indole-7-carbonitrile as a white solid. (134 mg, 94%), **mp** = 102–103 °C (lit. 96 °C).^[19] **^1H NMR (300 MHz, CDCl_3):** δ 9.12 (br s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.51 (dt, J = 7.4, 0.5 Hz, 1H), 7.33 (t, J = 2.4 Hz, 1H), 7.15 (t, J = 7.7 Hz, 1H), 6.63 (dd, J = 3.3, 2.0 Hz, 1H). **^{13}C NMR (126 MHz, CDCl_3):** δ 136.4, 128.8, 126.5, 126.3, 126.2, 119.5, 117.9, 103.4, 94.0. **IR** (neat, cm^{-1}): 3307 (br), 3105, 2221, 1609, 1447, 1348, 1334, 1113. **Anal.** Cald. for $\text{C}_9\text{H}_6\text{N}_2$: C, 76.04; H, 4.25. Found: C, 75.84; H, 4.19.

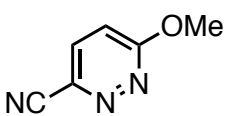


Quinoxaline-6-carbonitrile (2b). Following the general procedure with 6-chloroquinoxaline (165 mg, 1 mmol), **P2** (7.9 mg, 1 mol %), and **L2** (4.2 mg, 1 mol %). The product was purified by column chromatography (silica gel, 80:20 to 50:50 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield quinoxaline-6-carbonitrile as a white solid. (149 mg, 96%), **mp** = 181–182 °C (lit. 176–178 °C).^[20] **^1H NMR (300 MHz, CDCl_3):** δ 8.96 (s, 2H), 8.49 (dd, J = 1.8, 0.6 Hz, 1H), 8.21 (dd, J = 8.7, 0.6 Hz, 1H), 7.92 (dd, J = 8.7, 1.8 Hz, 1H). **^{13}C NMR (126 MHz, CDCl_3):** δ 147.5, 146.9, 144.4, 142.1, 135.7, 131.3, 130.9, 117.9, 113.8. **IR** (neat, cm^{-1}): 3063, 2229, 1498, 1418, 1374, 1302, 1131, 1018. **HRMS-ESI** (m/z) [$\text{M} + \text{H}$]⁺ calcd for $\text{C}_9\text{H}_5\text{N}_3$, 156.0556; found, 156.0557.

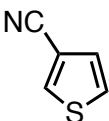


Quinoline-3-carbonitrile (2c). Following the general procedure with 3-bromoquinoline (136 μL , 208 mg, 1 mmol), **P2** (15.6 mg, 2 mol %), and **L2** (8.5 mg, 2 mol %). The product was purified by column chromatography (silica gel, 90:10 to 80:20 hexanes:EtOAc gradient, visualized with UV and KMnO_4) to yield quinoline-3-carbonitrile as a white solid. (142 mg, 92%), **mp** = 107–108 °C (lit. 106–107 °C).^[21] **^1H NMR (300 MHz, CDCl_3):** δ 9.02 (d, J = 2.1 Hz, 1H), 8.53 (dd, J = 2.1, 0.8 Hz, 1H), 8.16 (dq, J = 9.0, 0.8 Hz, 1H), 7.95–7.81 (m, 2H), 7.68 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H). **^{13}C NMR (126 MHz, CDCl_3):** δ 150.4, 149.4, 142.1, 133.5, 130.5, 129.2, 129.0, 126.8, 117.8, 107.1. **IR** (neat, cm^{-1}): 3036,

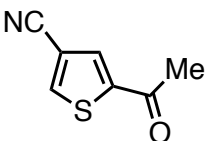
2228, 1619, 1567, 1489, 1371, 1130, 981. **Anal.** Calcd. for C₁₀H₆N₂ : C, 77.91; H, 3.92. Found: C, 77.84; H, 3.87.



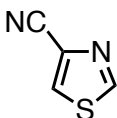
6-methoxypyridazine-3-carbonitrile (2d). Following a modification of the general procedure with 3-chloro-6-methoxypyridazine (145 mg, 1 mmol), **P2** (31.8 mg, 4 mol %), and **L2** (17 mg, 4 mol %). A 0.2 M solution of KOAc in degassed water (2.5 mL, 0.5 equiv. KOAc) was used. The product was purified by column chromatography (silica gel, 90:10 to 75:25 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 6-methoxypyridazine-3-carbonitrile as a white solid. (90 mg, 67%), **mp** = 93–94 °C (lit. 92–93.5 °C).^[22] **¹H NMR (300 MHz, CDCl₃):** δ 7.66 (d, *J* = 9.1 Hz, 1H), 7.07 (d, *J* = 9.2 Hz, 1H), 4.21 (s, 3H). **¹³C NMR (126 MHz, CDCl₃):** δ 165.4, 135.2, 132.5, 117.2, 115.8, 56.1. **IR (neat, cm⁻¹):** 3067, 2246, 1575, 1469, 1395, 1336, 1298, 1103. **Anal.** Calcd. for C₆H₅N₃O : C, 53.33; H, 3.73. Found: C, 53.50; H, 3.80.



Thiophene-3-carbonitrile (2e). Following a modification of the general procedure with 3-chlorothiophene (93 μL, 119 mg, 1 mmol), **P2** (12.7 mg, 1.6 mol %), and **L2** (6.8 mg, 1.6 mol %). During workup, the extraction was performed with Et₂O. The product was purified by column chromatography (silica gel, 95:5 to 80:20 pentane:Et₂O gradient, visualized with UV and KMnO₄) to yield thiophene-3-carbonitrile as a clear liquid. (77 mg, 71%). **¹H NMR (300 MHz, CDCl₃):** δ 7.93 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.41 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.29 (dd, *J* = 5.1, 1.2 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃):** δ 135.6, 128.9, 127.5, 115.3, 110.8. **IR (neat, cm⁻¹):** 3110, 2229, 1404, 1368, 1223, 1154, 930, 874. **HRMS-ESI (*m/z*) [M + H]⁺** calcd for C₅H₃NS, 110.0059; found, 110.0065.

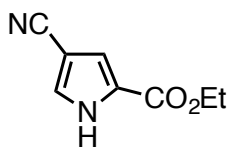


5-Acetylthiophene-3-carbonitrile (2f). Following the general procedure with 1-(4-chlorothiophen-2-yl)ethanone (120 μL, 160 mg, 1 mmol), **P2** (31.8 mg, 4 mol %), and **L2** (17 mg, 4 mol %). The product was purified by column chromatography (silica gel, 95:5 to 80:20 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 5-acetylthiophene-3-carbonitrile as an off-white solid. (137 mg, 91%), **mp** = 81–82 °C (lit. 78.5–80 °C).^[23] **¹H NMR (300 MHz, CDCl₃):** δ 8.14 (d, *J* = 1.3 Hz, 1H), 7.80 (d, *J* = 1.3 Hz, 1H), 2.57 (s, 3H). **¹³C NMR (126 MHz, CDCl₃):** δ 189.7, 146.2, 142.0, 133.0, 114.1, 111.5, 26.8. **IR (neat, cm⁻¹):** 3092, 2228, 1659, 1528, 1415, 1268, 1219, 1149. **Anal.** Calcd. for C₇H₅NOS : C, 55.61; H, 3.33. Found: C, 56.17; H, 3.56.

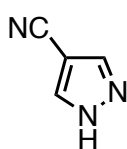


Thiazole-4-carbonitrile (2g). Following a modification of the general procedure with 4-bromothiazole (90 μL, 165 mg, 1 mmol), **P2** (31.8 mg, 4 mol %), and **L2** (17 mg, 4 mol %). During workup, the extraction was performed with Et₂O. The product was purified by column chromatography (silica gel, 80:20 to 33:64 pentane:Et₂O gradient, visualized with UV and KMnO₄) to yield thiazole-4-carbonitrile as a white solid. (98 mg, 89%), **mp** = 59–60 °C (lit. 55–56 °C).^[24] **¹H NMR (300 MHz, CDCl₃):** δ 8.89 (d, *J* = 2.0 Hz, 1H), 8.08 (d, *J* = 2.0 Hz, 1H). **¹³C NMR (126 MHz, CDCl₃):** δ 154.8, 130.7, 127.7, 113.9. **IR (neat, cm⁻¹):** 3118, 3090,

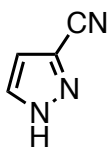
2236, 1422, 1298, 1218, 1130, 892. **Anal.** Calcd. for C₄H₂N₂S : C, 43.62; H, 1.83. Found: C, 43.79; H, 2.01.



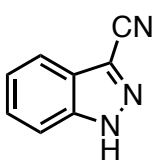
Ethyl 4-cyano-1H-pyrrole-2-carboxylate (2h). Following the general procedure with ethyl 4-bromo-1H-pyrrole-2-carboxylate (218 mg 1 mmol), **P2** (11.1 mg, 1.4 mol %), and **L2** (5.9 mg, 1.4 mol %). The product was purified by column chromatography (silica gel, 85:15 to 70:30 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield ethyl 4-cyano-1H-pyrrole-2-carboxylate as a white solid. (152 mg, 93%), **mp** = 84–85 °C **¹H NMR (300 MHz, CDCl₃):** δ 10.17 (s, 1H), 7.40 (dd, *J* = 3.2, 1.5 Hz, 1H), 7.11 (dd, *J* = 2.5, 1.5 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). **¹³C NMR (126 MHz, CDCl₃):** δ 160.6, 129.5, 124.2, 117.8, 115.6, 94.7, 61.5, 14.3. **IR (neat, cm⁻¹):** 3259, 3131, 2228, 1691, 1566, 1383, 1269, 1205. **Anal.** Calcd. for C₈H₈N₂O₂ : C, 58.53; H, 4.91. Found: C, 58.66; H, 4.88.



1H-Pyrazole-4-carbonitrile (2i). Following the general procedure with 4-bromo-1H-pyrazole (147 mg, 1 mmol), **P2** (7.9 mg, 1 mol %), and **L2** (4.2 mg, 1 mol %). The product was purified by column chromatography (silica gel, 2:1 to 1:2 hexanes:EtOAc gradient, visualized with CAM) to yield 1H-pyrazole-4-carbonitrile as a white solid. (84 mg, 90%), **mp** = 90–91 °C (lit. 91–92 °C). **¹H NMR (300 MHz, CD₃OD):** δ 8.13 (s, 2H). **¹³C NMR (126 MHz, CD₃OD):** δ 139.6, 114.9, 92.6. **IR (neat, cm⁻¹):** 3126, 2925, 2852, 2909, 2235, 1514, 1385, 1155. **Anal.** Calcd. for C₄H₃N₃ : C, 51.61; H, 3.25. Found: C, 51.63; H, 3.27.

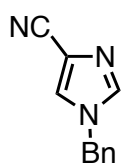


1H-pyrazole-3-carbonitrile hydrochloride (2j). Following a modification of the general procedure with 3-bromo-1H-pyrazole (147 mg, 1 mmol), **P3** (42.7 mg, 5 mol %), and **L3** (24.2 mg, 5 mol %). The product was purified by column chromatography (silica gel, 99:1 to 96:4 CH₂Cl₂:MeOH, visualized with CAM) to yield a light brown solid. The solid was dissolved in Et₂O (5 mL) and passed through a PTFE syringe filter. The filter was washed with Et₂O (2 mL), and the combined Et₂O solution was dried *in vacuo*. The solid was dissolved in Et₂O (1 mL) and 2 M HCl in Et₂O (0.6 mL) was added. Pentane (12 mL) was layered onto the solution. After 2 h, a solid was observed. The pentane layer was decanted, and the solid was washed with pentane (2x8mL). Drying *in vacuo* afforded 1H-pyrazole-3-carbonitrile hydrochloride as a light brown solid (95:5 mixture of 1H-pyrazole-3-carbonitrile hydrochloride:3-bromo-1H-pyrazole hydrochloride) (86 mg, 63%). **¹H NMR (300 MHz, d⁶-DMSO):** δ 13.73 (br s, 1H), 8.03 (d, *J* = 2.5 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H). **¹³C NMR (126 MHz, d⁶-DMSO):** δ 130.8, 123.3, 115.0, 110.6. **IR (neat, cm⁻¹):** 3268, 3147, 2245, 1508, 1456, 1348, 1271, 1176. **HRMS-ESI (*m/z*) [M]⁺** calcd for C₄H₃N₃, 93.0327; found, 93.0703.

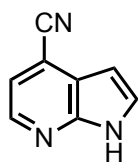


1H-indazole-3-carbonitrile (2k). Following the general procedure with 3-chloro-1H-indazole (153 mg, 1 mmol), **P2** (31.8 mg, 4 mol %), and **L2** (17 mg, 4 mol %). The product was purified by column chromatography (silica gel, 85:15 to 65:35 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 1H-indazole-3-carbonitrile as a white solid. (132 mg,

92%), **mp** = 140–141 °C (lit. 140 °C).^[26] **¹H NMR (300 MHz, CD₃OD)**: δ 7.78 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.66 (dt, *J* = 8.5, 0.9 Hz, 1H), 7.49 (ddd, *J* = 8.5, 6.9, 1.1 Hz, 1H), 7.34 (ddd, *J* = 8.2, 6.9, 0.9 Hz, 1H). **¹³C NMR (126 MHz, CD₃OD)**: δ 141.6, 129.0, 125.4, 124.6, 119.6, 119.5, 114.9, 112.3. **IR (neat, cm⁻¹)**: 3234 (br), 2239, 1622, 1470, 1344, 1251, 1170, 1073. **Anal.** Cald. for C₈H₅N₃: C, 67.12; H, 3.52. Found: C, 67.09; H, 3.65.

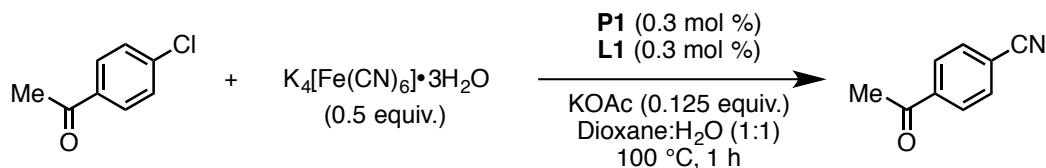


1-Benzyl-1*H*-imidazole-4-carbonitrile (2I). Following the general procedure with 1-benzyl-4-bromo-1*H*-imidazole (237 mg, 1 mmol), **P3** (12.8 mg, 1.5 mol %), and **L3** (7.3 mg, 1.5 mol %). The product was purified by column chromatography (silica gel, 70:30 to 40:60 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 1-benzyl-1*H*-imidazole-4-carbonitrile as a pale pink oil. (181 mg, 99%). **¹H NMR (300 MHz, CDCl₃)**: δ 7.54 (d, *J* = 1.3 Hz, 1H), 7.42 (d, *J* = 1.3 Hz, 1H), 7.40–7.33 (m, 3H), 7.19–7.13 (m, 2H), 5.13 (s, 2H). **¹³C NMR (126 MHz, CDCl₃)**: δ 138.8, 134.4, 129.3, 128.9, 127.9, 127.7, 114.9, 114.4, 51.5. **IR (neat, cm⁻¹)**: 3116, 2230, 1533, 1496, 1455, 1230, 1146, 976. **Anal.** Cald. for C₁₁H₉N₃: C, 72.11; H, 4.95. Found: C, 71.84; H, 4.92.



1*H*-pyrrolo[2,3-*b*]pyridine-4-carbonitrile Following the general procedure with 4-chloro-1*H*-pyrrolo[2,3-*b*]pyridine (153 mg, 1 mmol), **P2** (12.7 mg, 1.6 mol %), and **L2** (6.8 mg, 1.6 mol %). The product was purified by column chromatography (silica gel, 2:1 to 1:3 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 1*H*-pyrrolo[2,3-*b*]pyridine-4-carbonitrile as a white solid. (108 mg, 72%, 95:5 mixture of 1*H*-pyrrolo[2,3-*b*]pyridine-4-carbonitrile:4-chloro-1*H*-pyrrolo[2,3-*b*]pyridine). **¹H NMR (300 MHz, DMSO)**: δ ¹H NMR (300 MHz, DMSO-*d*₆) δ 12.38 (s, 1H), 8.40 (d, *J* = 4.9 Hz, 1H), 7.83 (d, *J* = 3.5 Hz, 1H), 7.55 (d, *J* = 4.9 Hz, 1H), 6.65 (d, *J* = 3.4 Hz, 1H). **¹³C NMR (126 MHz, DMSO)**: δ 148.5, 142.4, 130.3, 119.59, 118.2, 116.9, 108.9, 98.3. **IR (neat, cm⁻¹)**: 3129, 3069, 2909, 2233, 1599, 1326, 1277, 1121. **Anal.** Cald. for C₈H₅N₃: C, 67.12; H, 3.52. Found: C, 66.81; H, 3.74.

Experimental Procedure for a Reaction on a 10 mmol Scale



To a Schlenk tube equipped with a magnetic stir bar was added K₄[Fe(CN)₆]·3H₂O (2.11 g, 0.5 equiv.). Separately, to a 25 mL screw-cap volumetric flask was added **P1** (27.6 mg, 0.3 mol %) and **L1** (14.3 mg, 0.3 mol %). After sealing the vessels with a plug valve (Schlenk tube) or Teflon-lined screw-cap (volumetric flask), both vessels were evacuated and backfilled with nitrogen (this process was repeated for a total of three

cycles). 1-(4-chlorophenyl)ethanone (1.3 mL, 1.55 g, 10 mmol) was added via syringe to the Schlenk tube. Dioxane (25 mL) was added via syringe to the volumetric flask to obtain a clear precatalyst and ligand solution. Subsequently, the precatalyst and ligand solution was added to the Schlenk tube via cannula, followed by 0.05 M KOAc in degassed water (25 mL). The Schlenk tube was sealed with a Teflon plug valve, placed in an oil bath preheated to 100 °C, and stirred for 1 h. Upon initial stirring, a clear, yellow solution is observed. During the course of the reaction, a yellow precipitate forms on the walls of the reaction vessel. After 1 h of stirring at 100 °C, the reaction mixture was then cooled to room temperature. EtOAc (50 mL) and brine (50 mL) was added to the Schenk tube. The solution was transferred to a separatory funnel, and the organic layer was separated from the dark blue aqueous layer. The aqueous layer was further extracted with EtOAc (total 2 x 50 mL). The combined organic layers were dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting mixture was adsorbed onto silica gel, dried *in vacuo*, and purified via column chromatography (silica gel, 95:5 to 75:25 hexanes:EtOAc gradient, visualized with UV and KMnO₄) to yield 4-acetylbenzonitrile as a white solid (1.4 g, 96%). Analytical data was as is described for the experiment carried out on a 1 mmol scale (*vide supra*).

Preparation of Oxidative Addition Complex 6



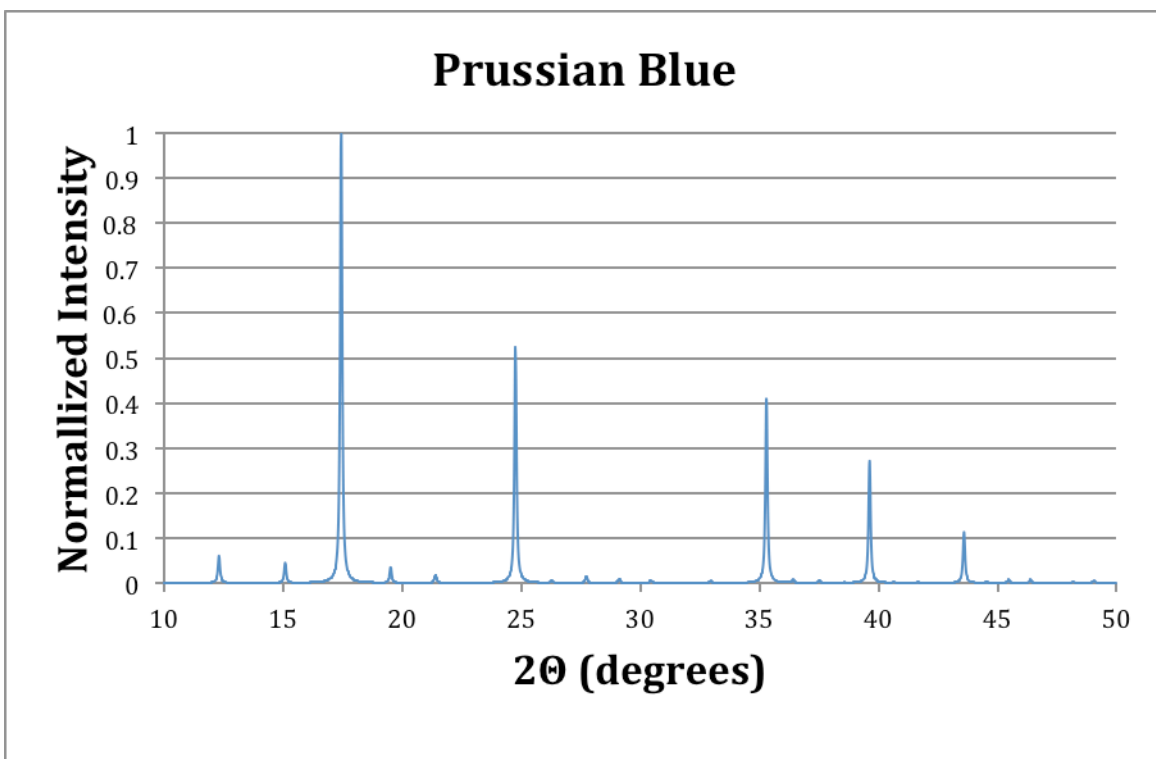
In a nitrogen-filled glove box, to an oven-dried screw-top reaction vial containing a magnetic stirbar was added **L2** (467 mg, 1.1 mmol, 1.1 equiv.), 1-chloro-4-fluoro-benzene (0.53 mL, 650 mg, 6 mmol, 5 equiv.) and cyclohexane (1 mL). The reaction mixture was stirred until **L2** had completely dissolved to yield a clear solution. (COD)Pd(CH₂TMS)₂ (389 mg, 1 mmol, 1 equiv.) was added to the solution, the vessel was sealed with a screw cap, and the reaction was stirred at room temperature for 18 h, during which time a yellow precipitate formed. Pentane (2 mL) was

added, and the vial was transferred to a -20 °C freezer and left for for 2 h. The cold suspension was then filtered and washed with cold pentane (4x2mL). Drying *in vacuo* afforded complex **6** as a yellow solid (451 mg, 68%). During characterization, approx. 4% dearomative rearrangement product was observed via ³¹P and ¹⁹F NMR. ¹H NMR (500 MHz, CD₂Cl₂): δ 7.99 (td, *J* = 6.1, 3.0 Hz, 1H), 7.46–7.34 (m, 2H), 7.08 (s, 2H), 7.02 (ddd, *J* = 8.8, 5.9, 1.7 Hz, 2H), 6.79 (dt, *J* = 5.9, 3.4 Hz, 1H), 6.66 (t, *J* = 9.1 Hz, 2H), 3.01 (hept, *J* = 6.9 Hz, 1H), 2.54 (hept, *J* = 6.7 Hz, 2H), 1.57 (d, *J* = 6.8 Hz, 6H), 1.39 (d, *J* = 14.0 Hz, 18H), 1.36 (d, *J* = 7.0 Hz, 6H), 0.90 (d, *J* = 6.7 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃): δ 162.0, 160.1, 157.8, 152.8, 147.9, 147.8, 138.7, 138.7, 138.7, 138.7, 136.9, 136.6, 135.8, 134.9, 134.8, 134.8, 130.7, 130.6, 127.7, 127.7, 127.6, 126.3, 126.3, 125.1, 125.0, 113.4, 113.4, 113.3, 113.3, 39.8, 39.7, 35.1, 31.9, 31.9, 31.9, 25.8, 25.0, 24.9. Observed complexity is due to C–P and C–F coupling. ¹⁹F NMR (471 MHz, CD₂Cl₂): δ -124.8. ³¹P NMR (121 MHz, CD₂Cl₂): δ 52.7. IR (neat, cm⁻¹): 2962, 2929, 2864, 1608, 1474, 1213, 1045, 1008.

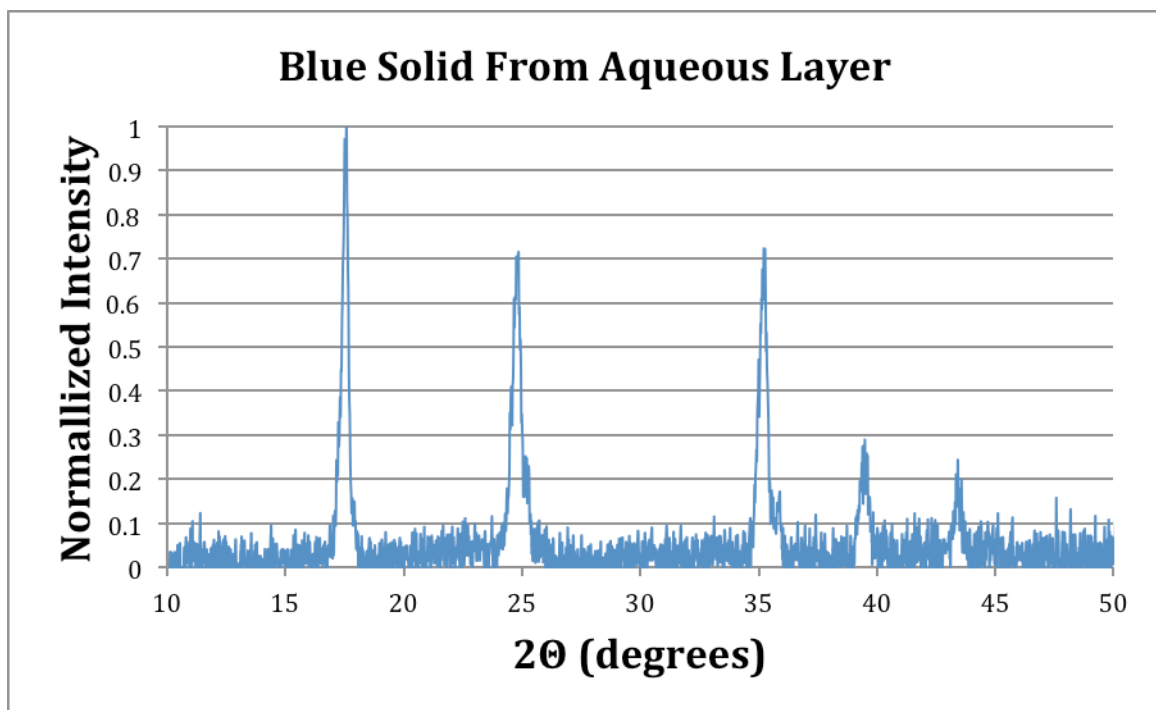
General Procedure for Table 3

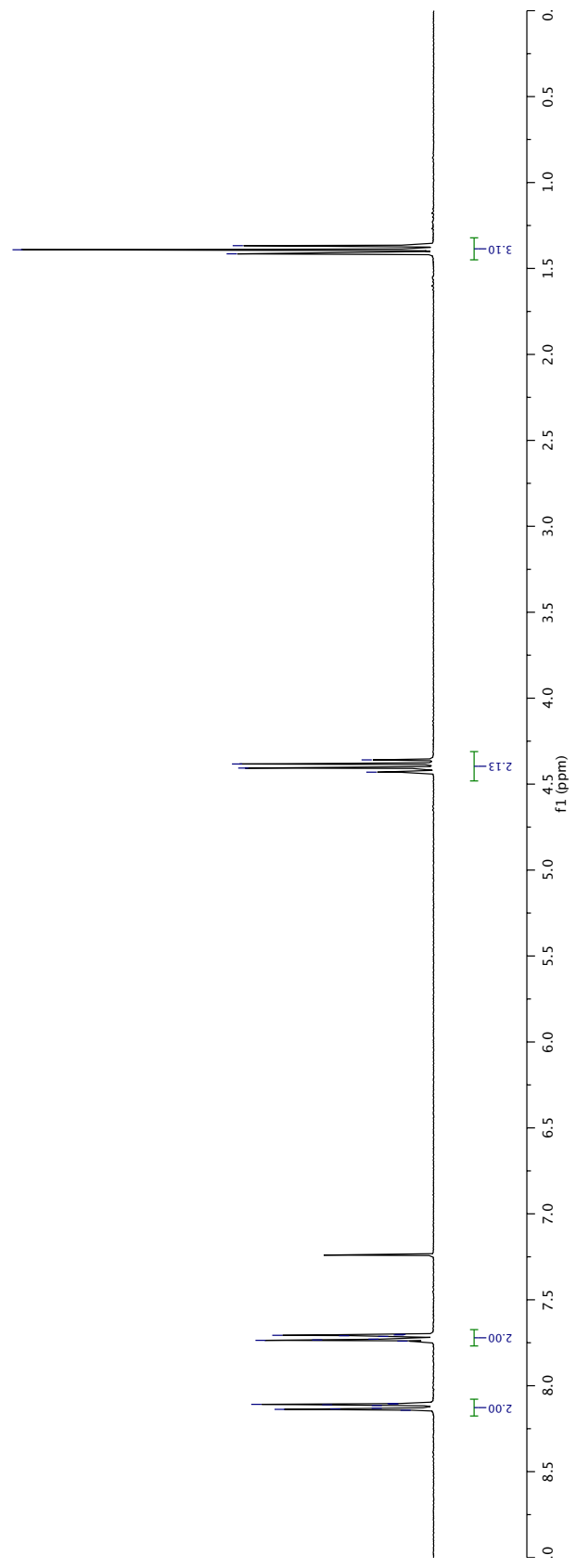
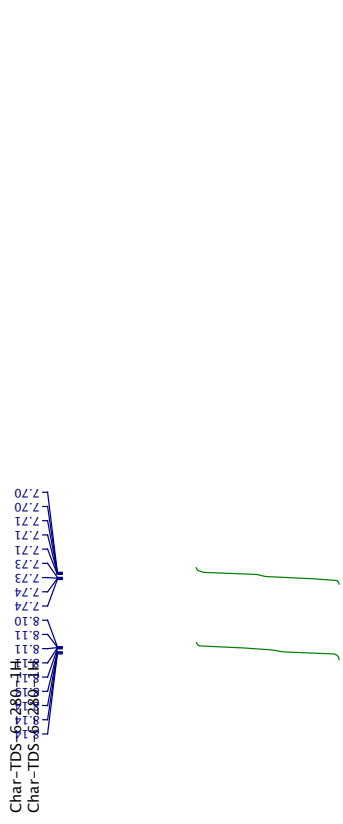
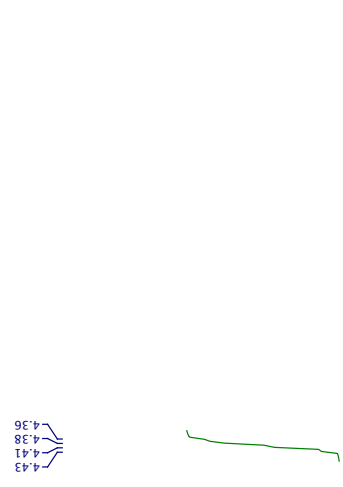
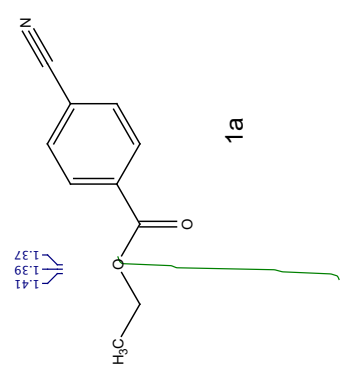
In a nitrogen-filled glove box, to an oven-dried screw-top reaction vial containing a magnetic stirbar was added oxidative addition complex **6** (15 mg, 0.023 mmol, 1 equiv.). The vessel was sealed with a screw-cap and removed from the glove box. 1-fluoronaphthalene (2.9 μ L, 3.3 mg, 0.022 mmol, 1 equiv.) and organic solvent (1 mL) were added via syringe. The reaction mixture was stirred, and a degassed aqueous solution of 0.023 M cyanide source and 0.023 M base (1 mL, 0.023 mmol, 1 equiv.) was added via syringe. For the 100 °C trial, the vial was then transferred to an oil bath preheated to 100 °C. The reaction mixture was stirred for the allotted period of time. At the end of this period, (after cooling to room temperature for the 100 °C trial), Et₂O (1 mL) was added to the reaction vessel via syringe and the vial was shaken. A portion of each organic layer was removed via syringe, filtered through a plug of silica gel, and eluted with Et₂O (0.3 mL). The eluents were then analyzed via ¹⁹F NMR.

PXRD Spectra

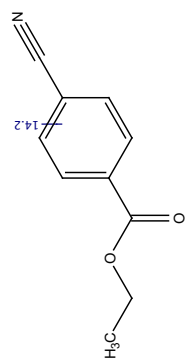


Extrapolated from Buser, H.J.; Schwarzenbach, D.; Petter, W.; Ludi, A. *Inorg. Chem.* **1977**, *16*, 2704-2710.

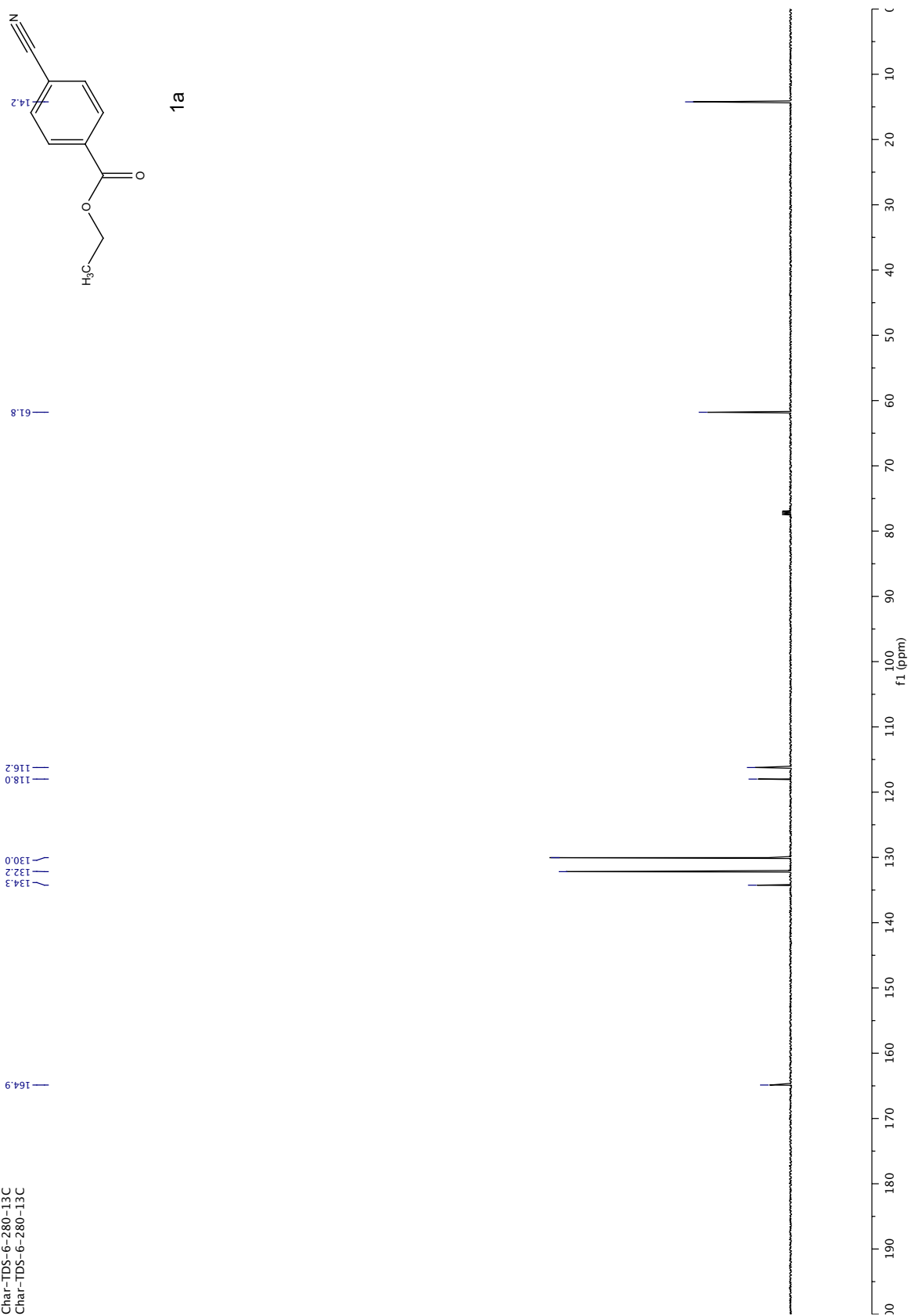


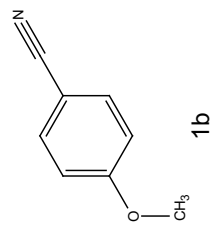


Char-TDS-6-280-13C
Char-TDS-6-280-13C

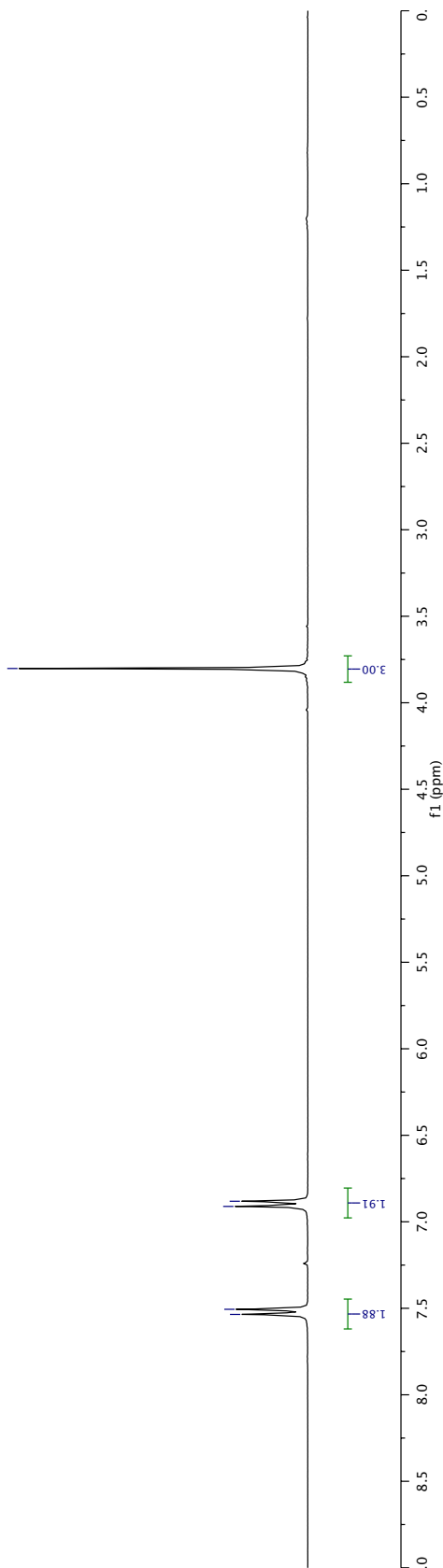


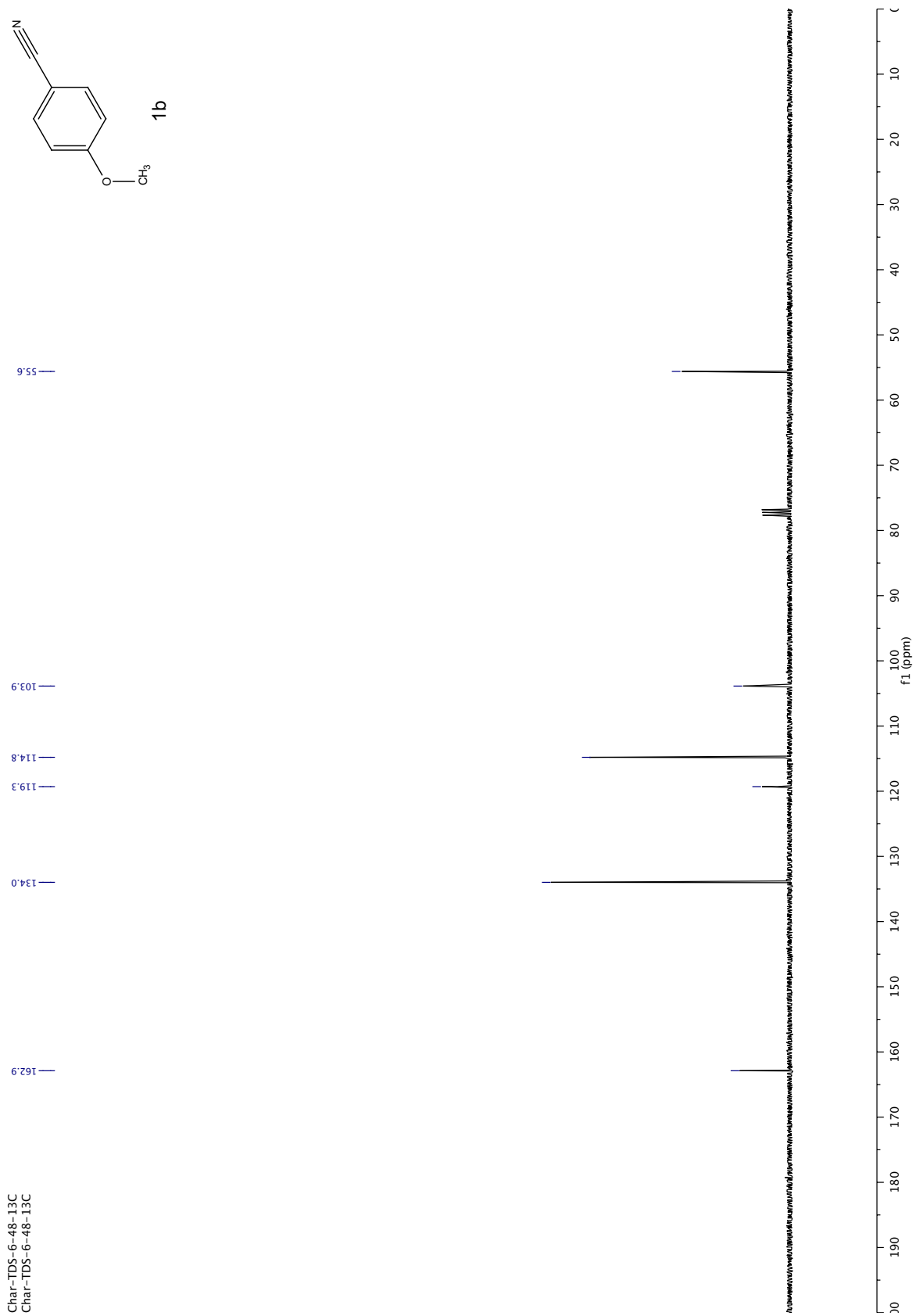
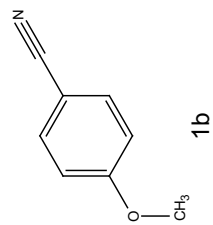
1a





Char-TDS-6-48-1H
Char-TDS-6-48-1H

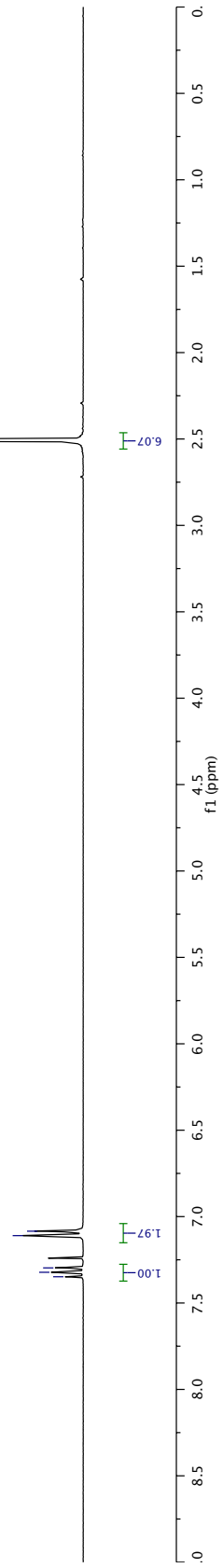
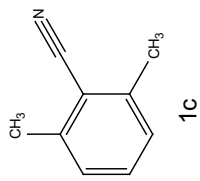




Char-TDS-6-150-1H
Char-TDS-6-150-1H

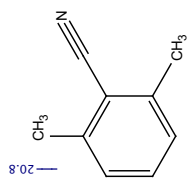
7.35
7.32
7.30
7.11
7.08

2.51

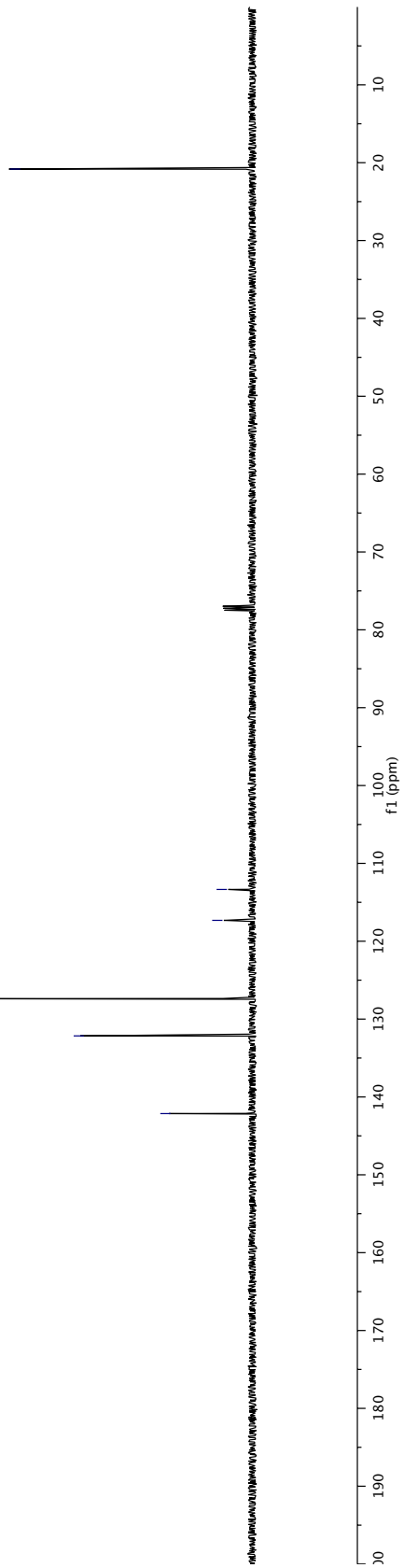


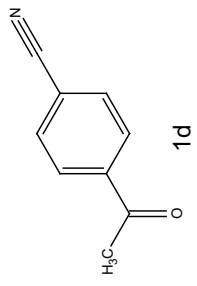
Char-TDS-6-150-13C
Char-TDS-6-150-13C

142.1
132.2
127.4
117.3
113.4

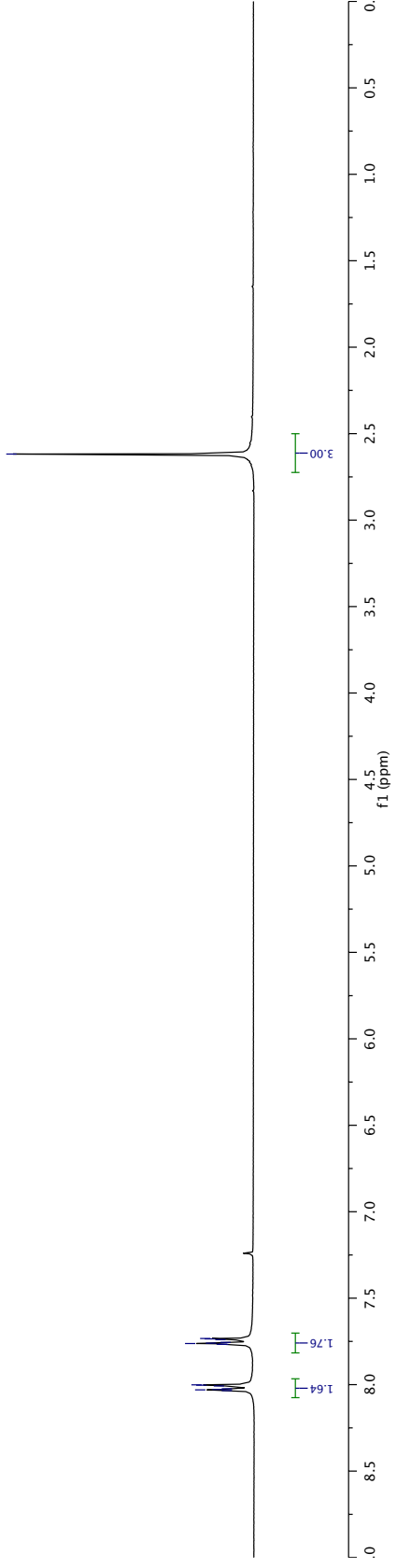
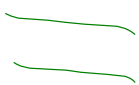


1C



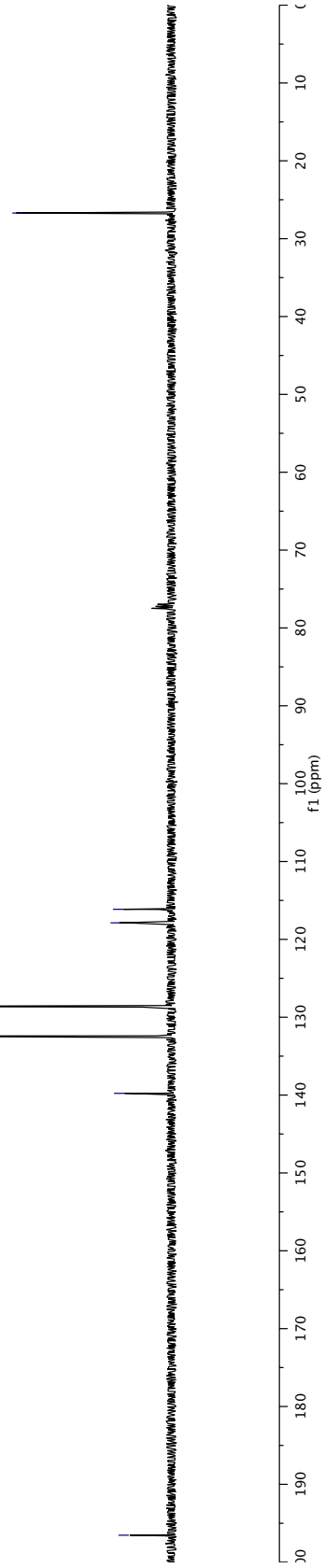
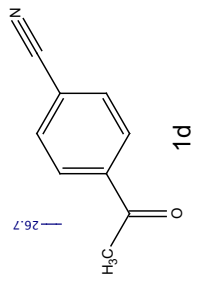


Char-TDS-6-151-11
Char-TDS-6-151-11



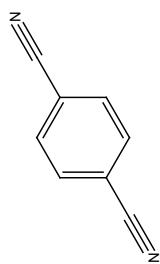
Char-TDS-6-151-13C
Char-TDS-6-151-13C

139.8
132.4
128.6
117.9
116.1

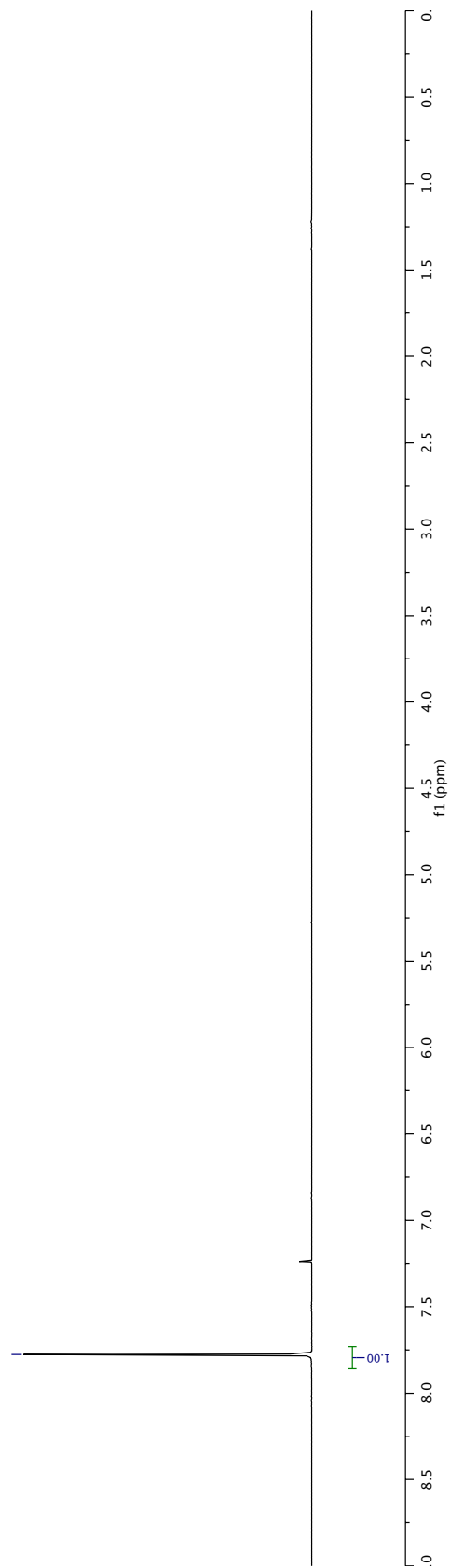


Char-TDS-6-210-1H
Char-TDS-6-210-1H

7.78

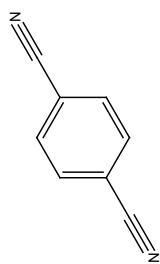


1e

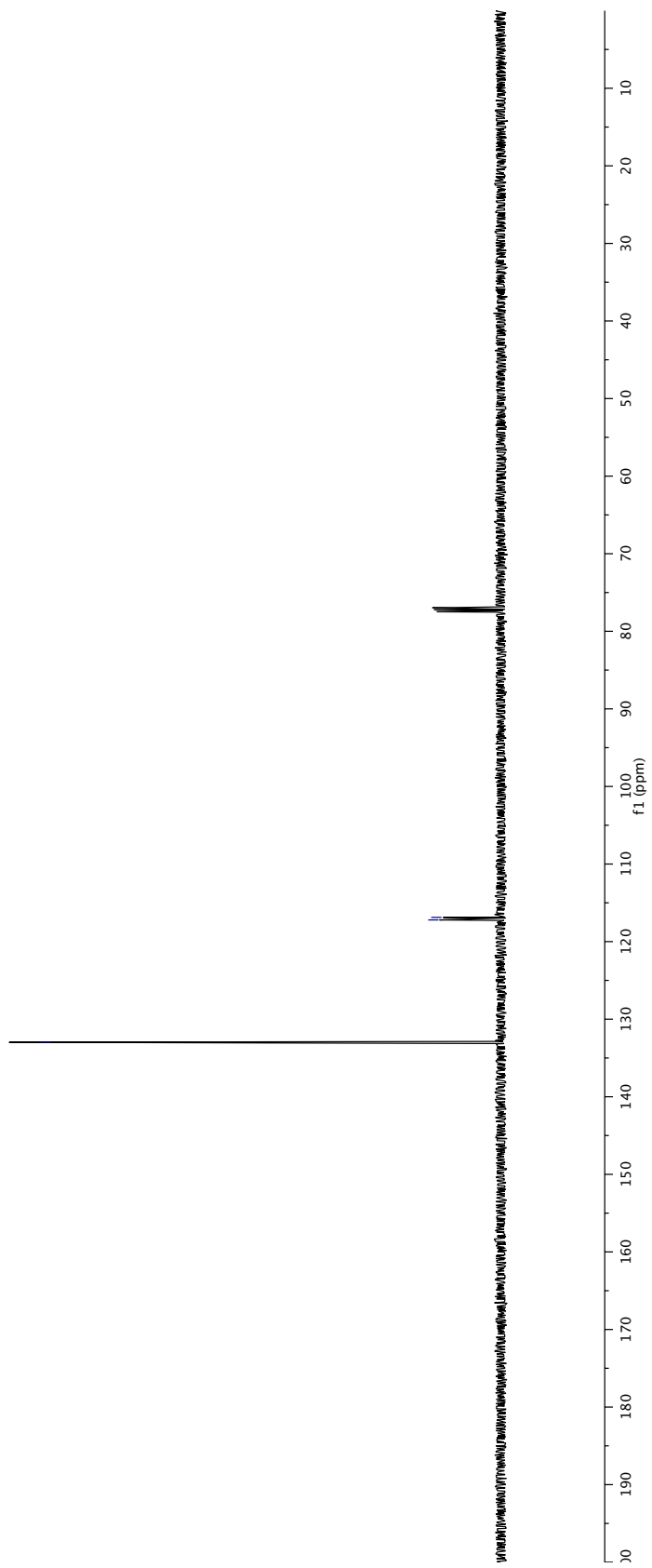


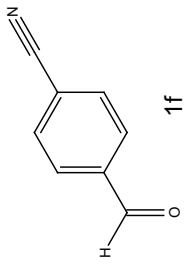
Char-TDS-6-210-13C
Char-TDS-6-210-1H

133.0
117.2
116.9



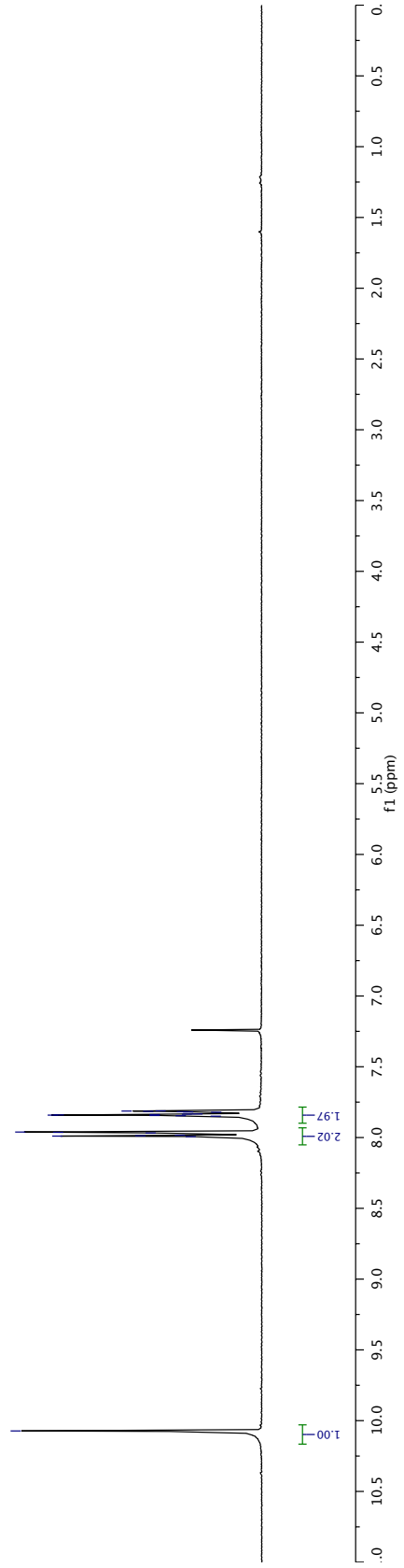
1e

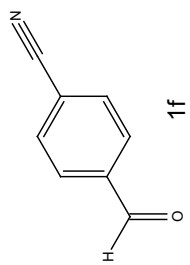




7.81
7.81
7.82
7.82
7.82
7.82
7.83
7.83
7.84
7.84
7.84
7.85
7.85
7.96
7.96
7.97
7.98
7.99
7.99

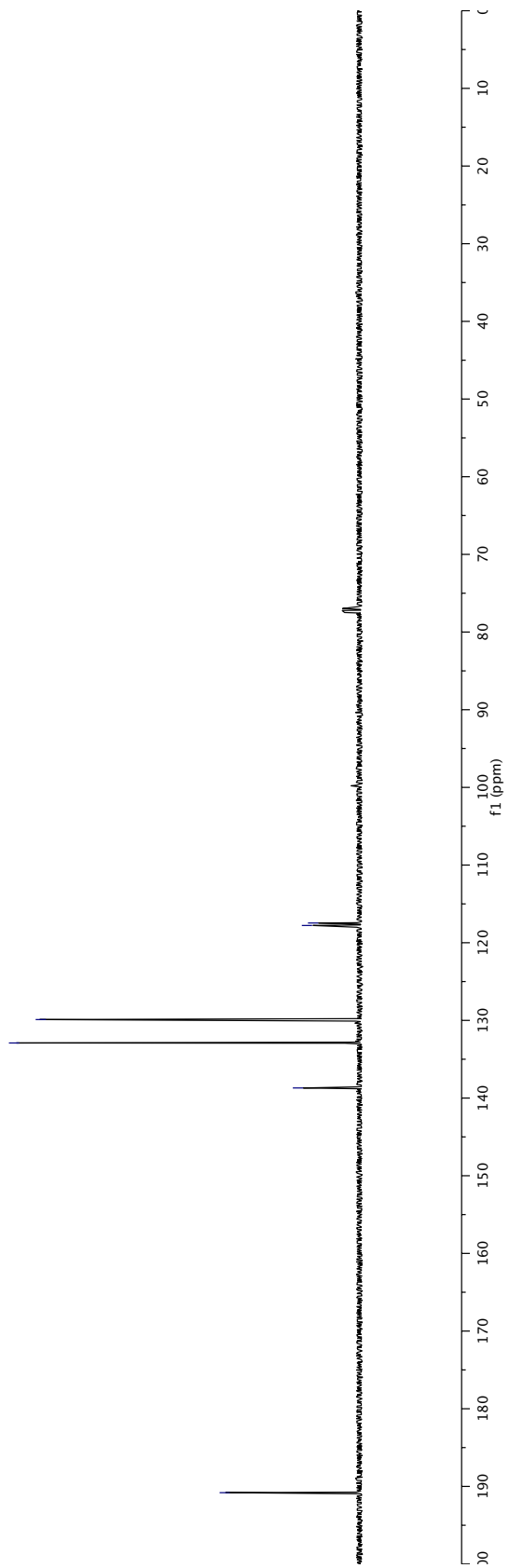
Char-TDS-6-153-H
Char-TDS-6-153-H

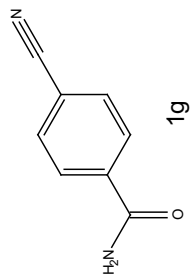




Char-TDS-6-153-13C
Char-TDS-6-153-13C

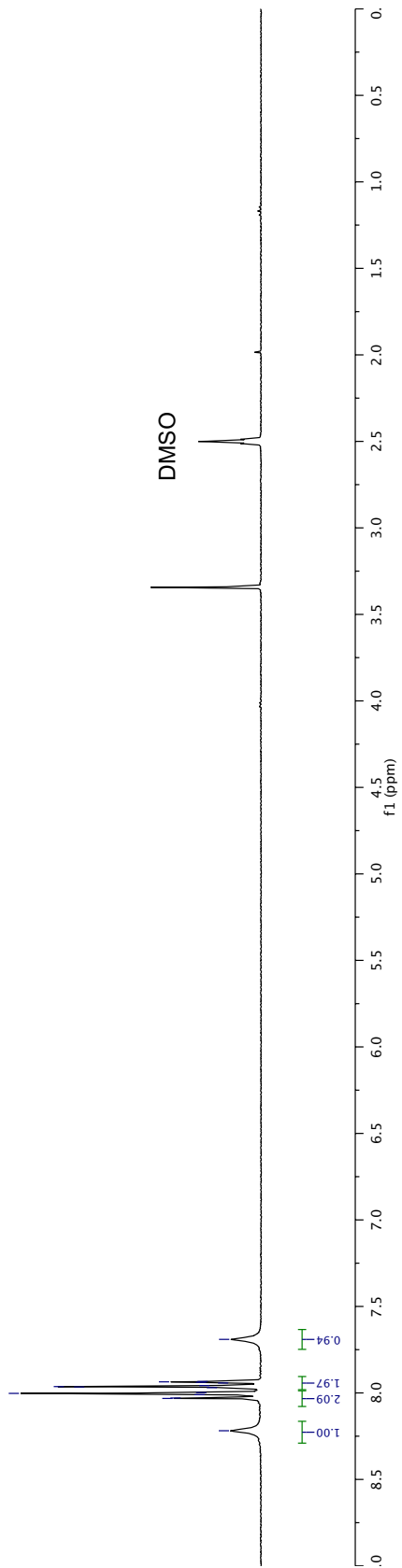
138.7
132.9
129.9
117.8
117.5





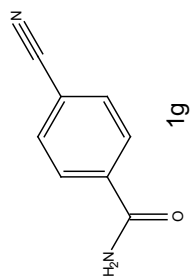
Char-TDS-6-147-1H
Char-TDS-6-147-1H

7.98
7.96
7.97
8.00
8.03

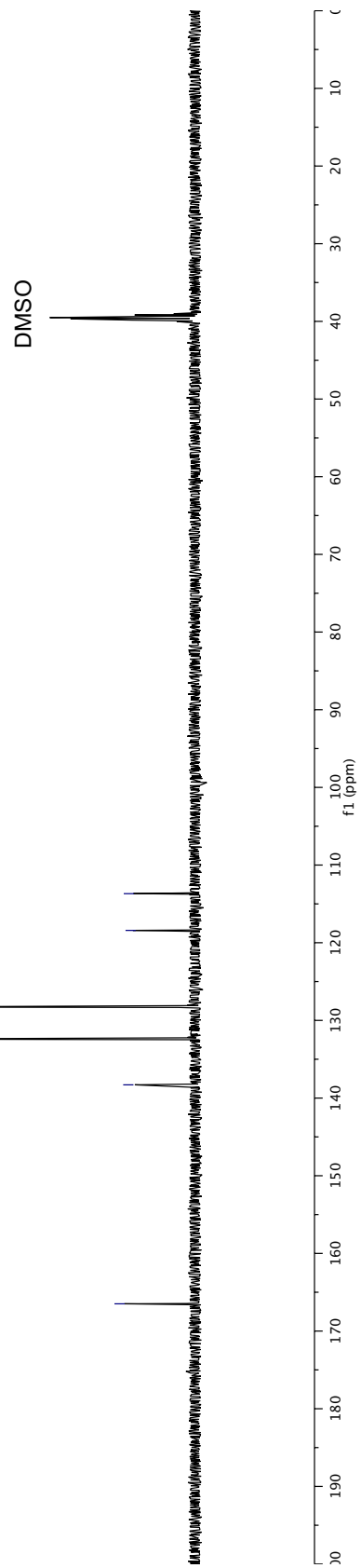


Char-TDS-6-147-13C
Char-TDS-6-147-13C

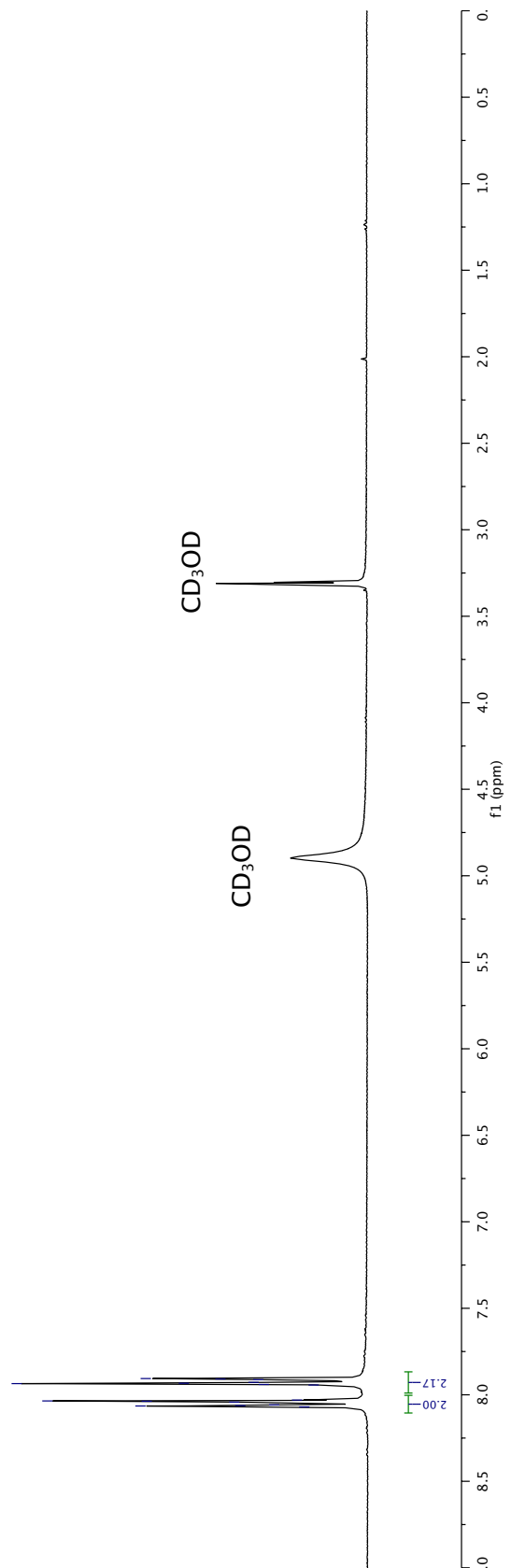
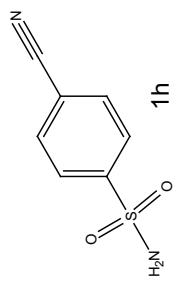
166.5
138.3
132.4
128.3
118.4
113.7



DMSO

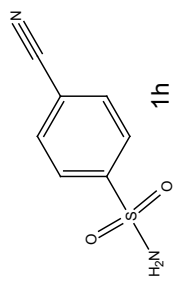


Char-TDS
Char-TDS

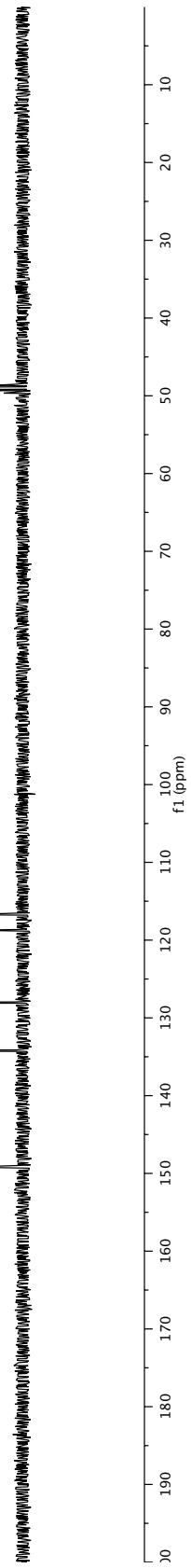


Char-TDS-6-155-13C
Char-TDS-6-155-13C

149.2
134.2
128.1
118.7
116.7



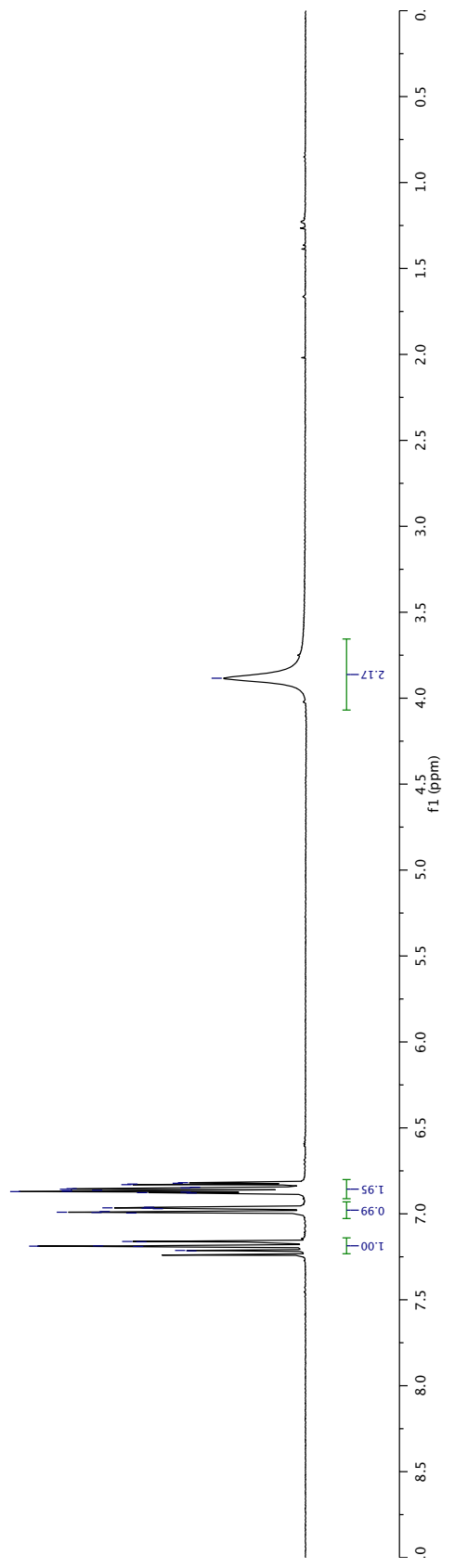
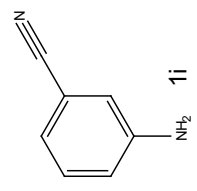
CD₃OD



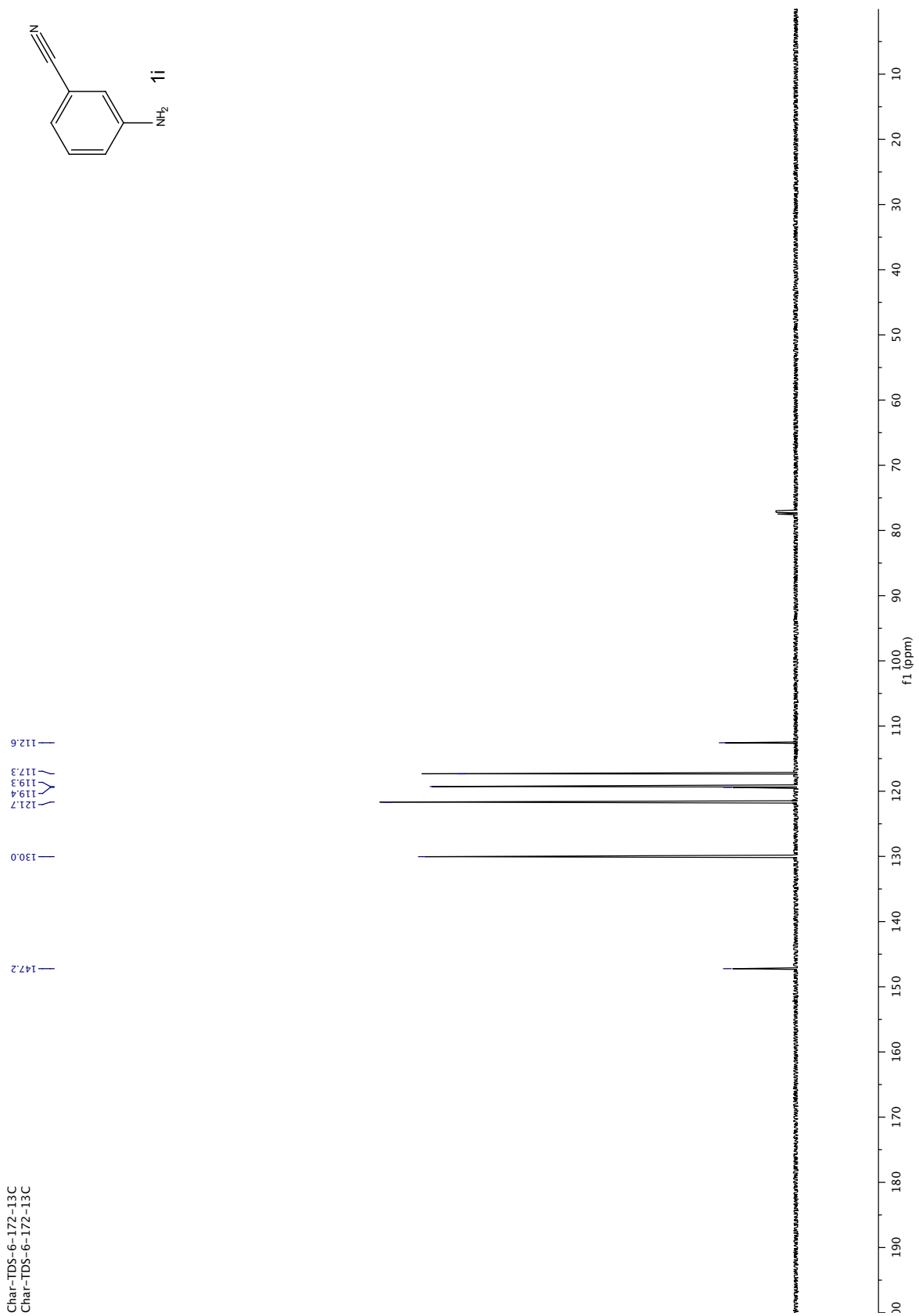
Char-TDS-6-172-1H
Char-TDS-6-172-1H

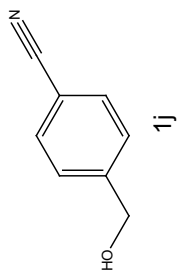
7.22
7.21
7.21
7.19
7.19
7.16
7.16
7.00
6.99
6.99
6.99
6.97
6.97
6.96
6.88
6.88
6.87
6.87
6.87
6.86
6.85
6.85
6.83
6.83
6.82

3.88



Char-TDS-6-172-13C
Char-TDS-6-172-13C

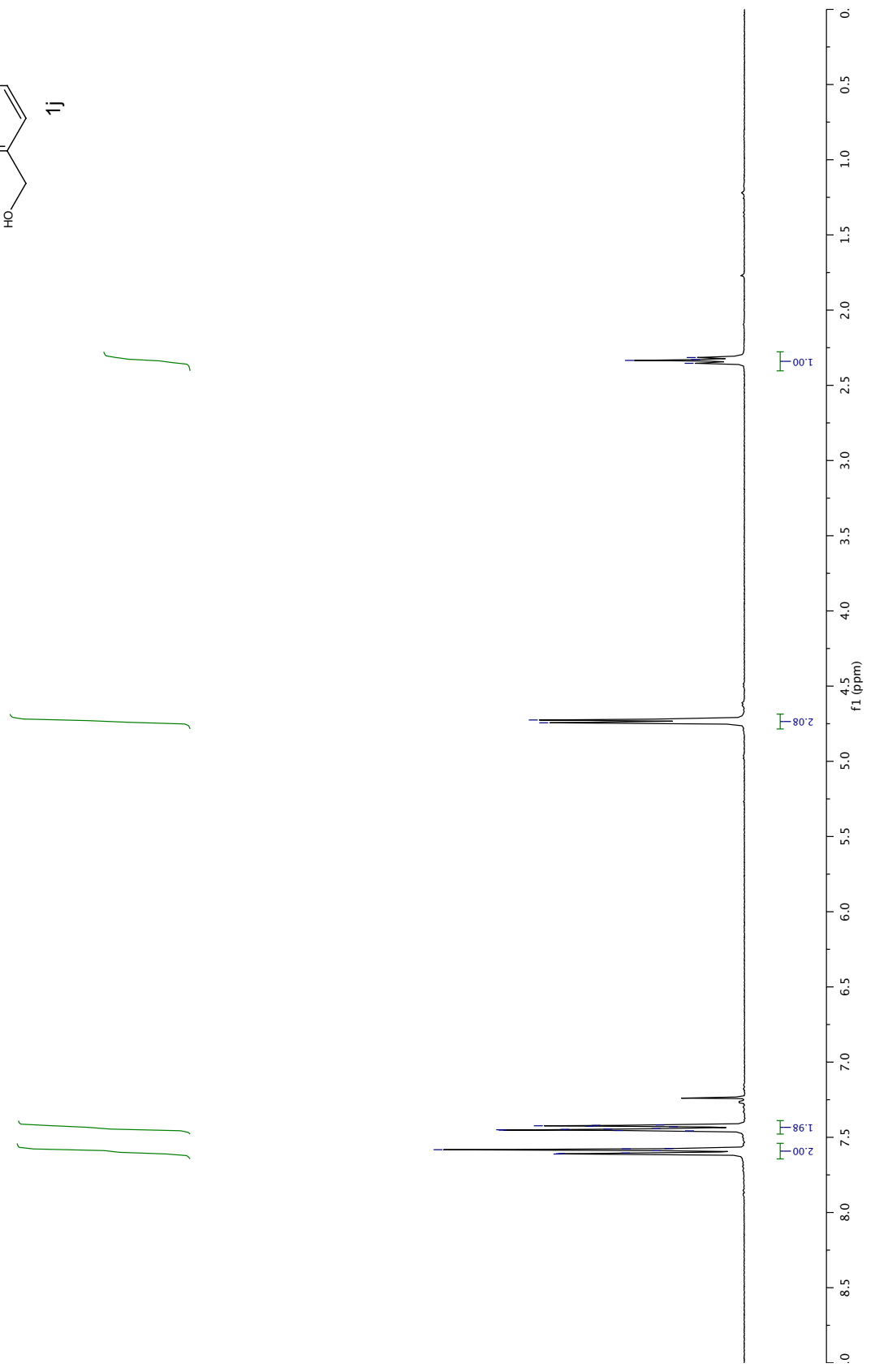




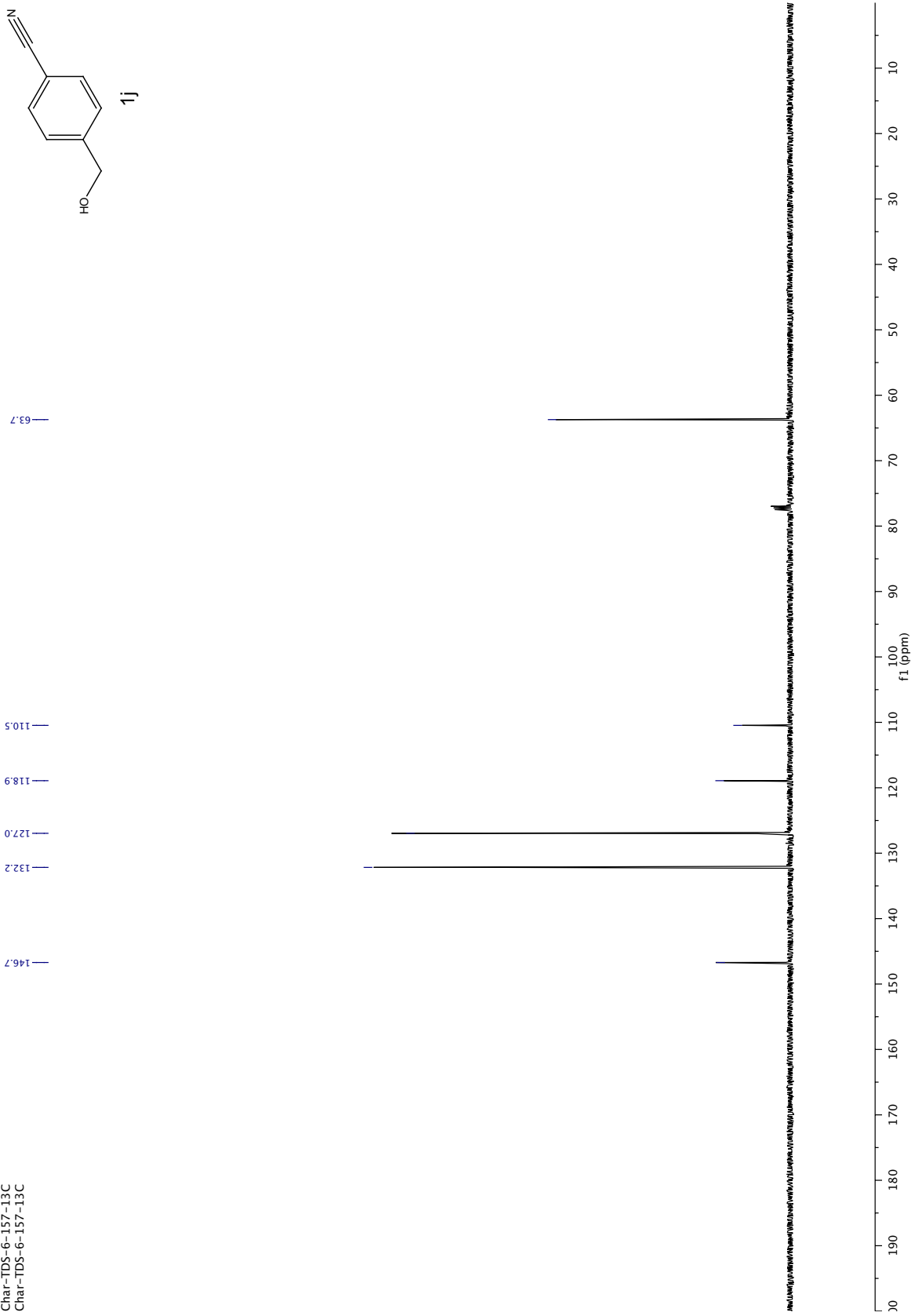
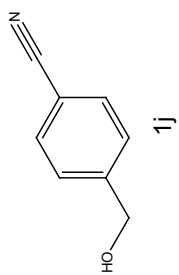
2.35
2.33
2.33
2.32

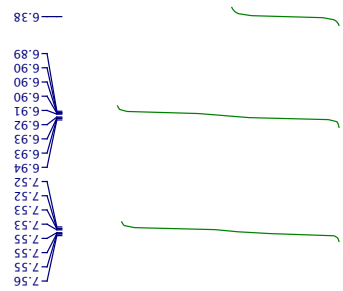
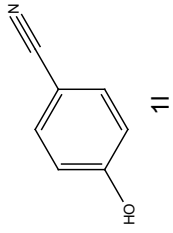
4.74
4.73

7.61
7.60
7.59
7.58
7.58
7.57
7.46
7.45
7.45
7.44
7.43
7.43
7.42
7.42

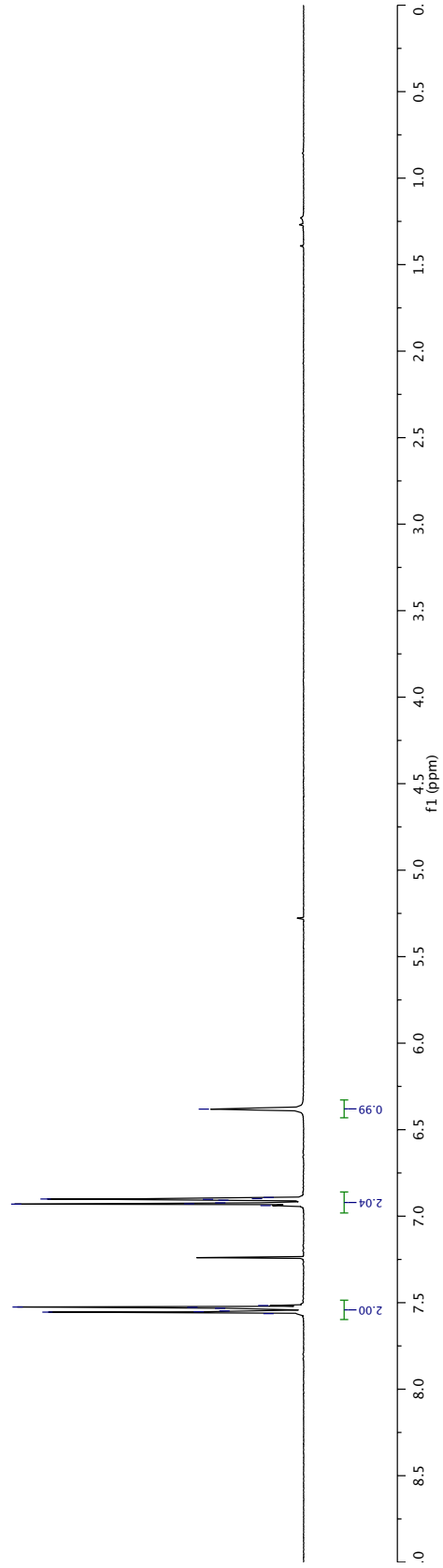


Char-TDS-6-157-13C
Char-TDS-6-157-13C



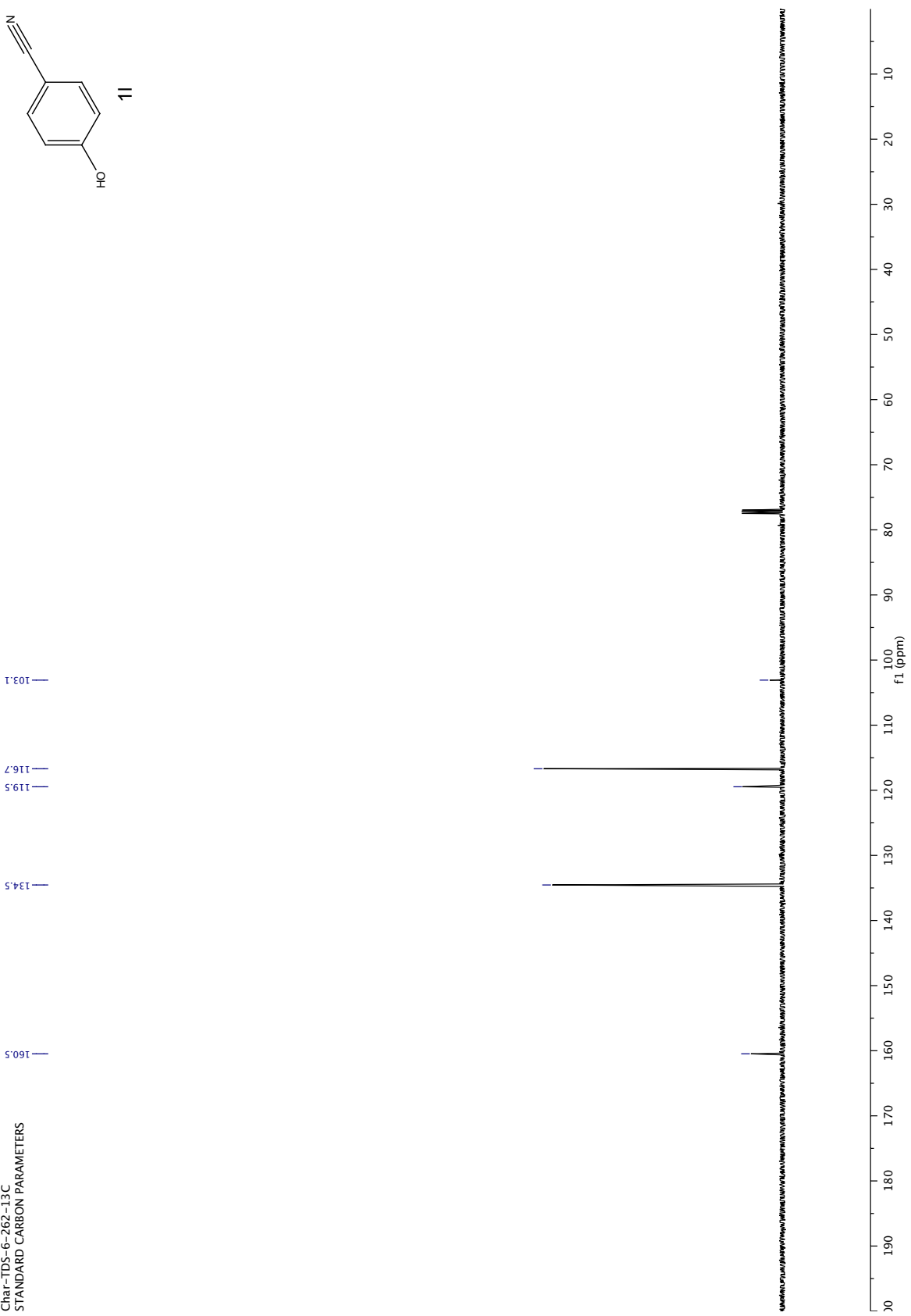
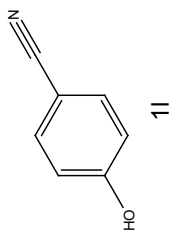


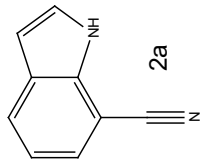
Char-TDS-6-262-1H
Char-TDS-6-262-1H



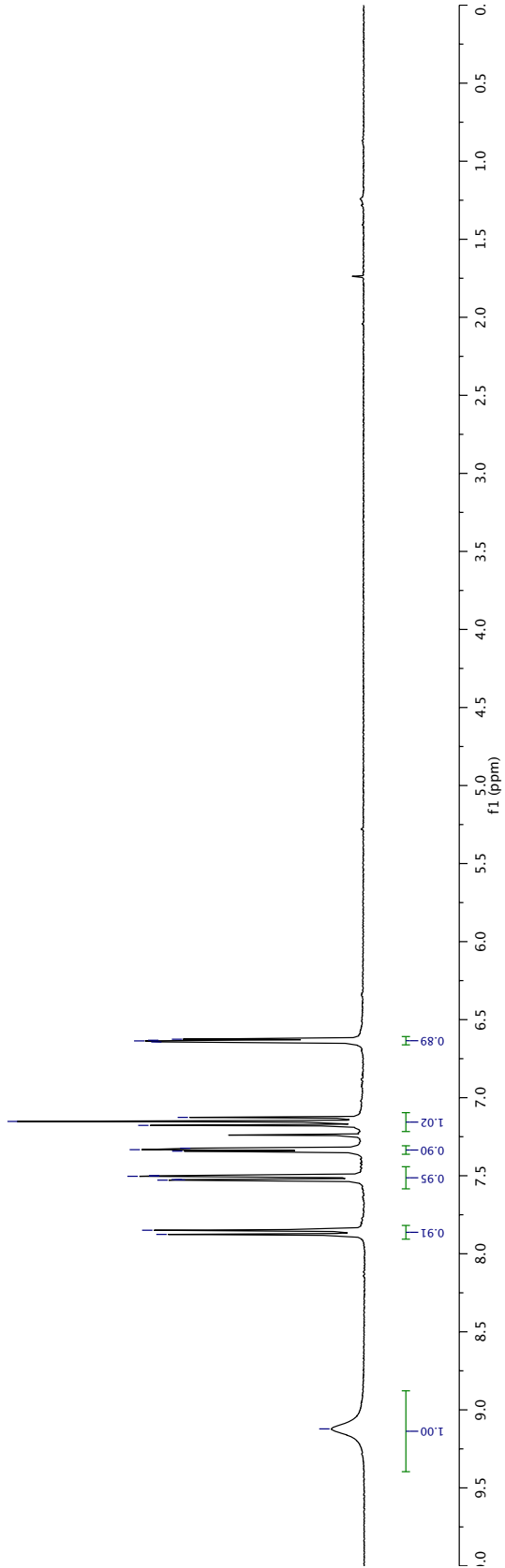
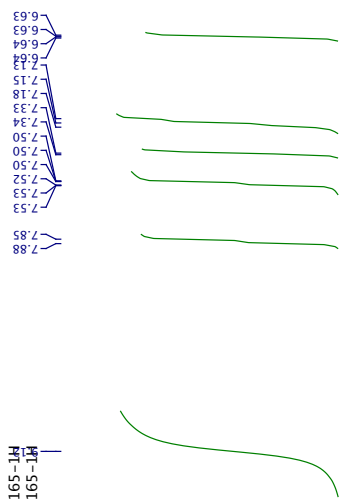
Char-TDS-6-262-13C
STANDARD CARBON PARAMETERS

160.5
134.5
119.5
116.7
103.1

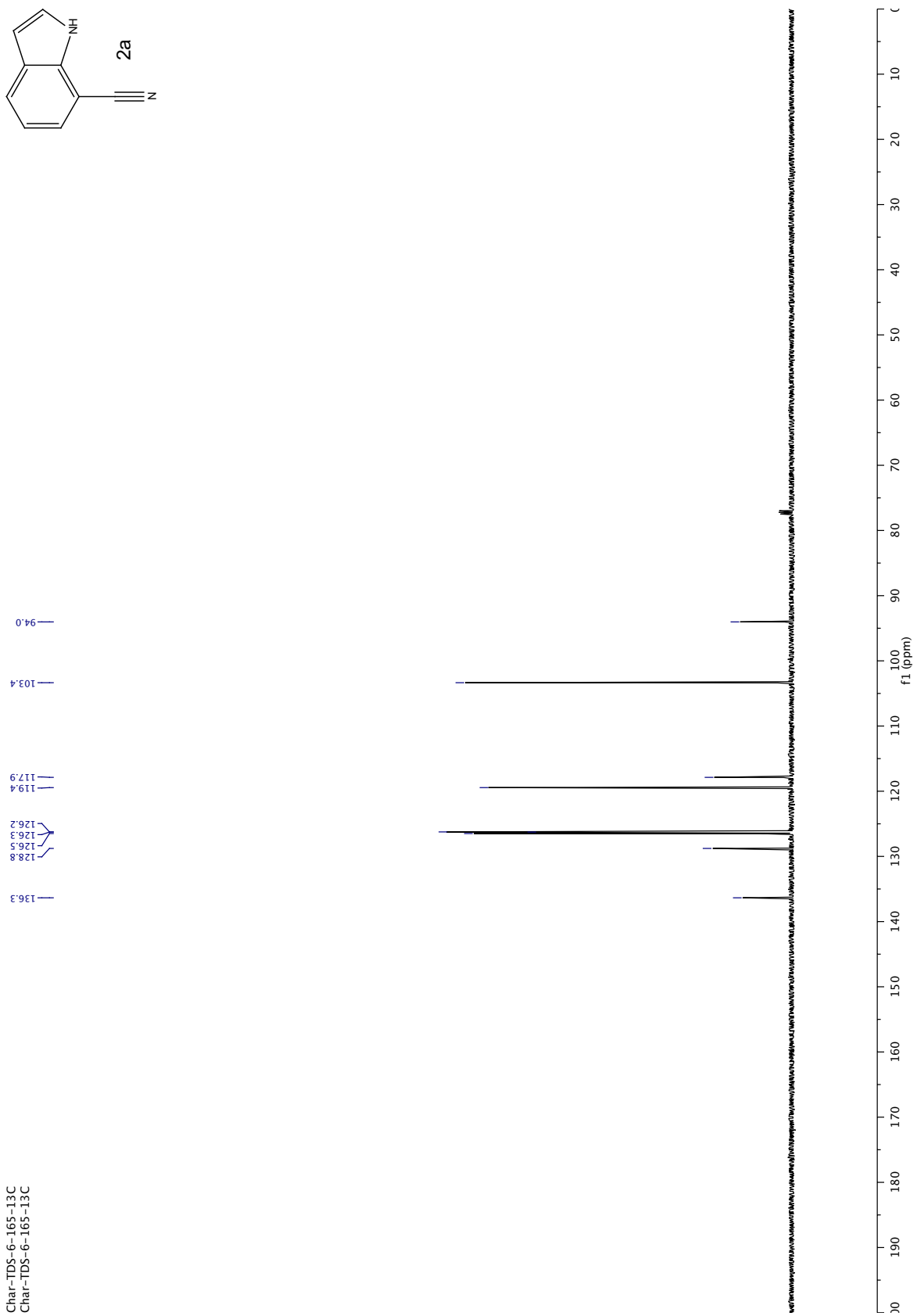
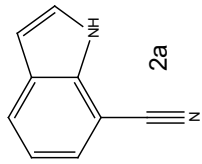


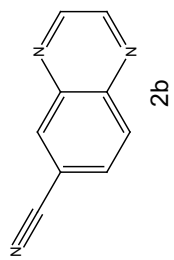


Char-TDS-6-165-1H
 Char-TDS-6-165-1H



Char-TDS-6-165-13C
Char-TDS-6-165-13C

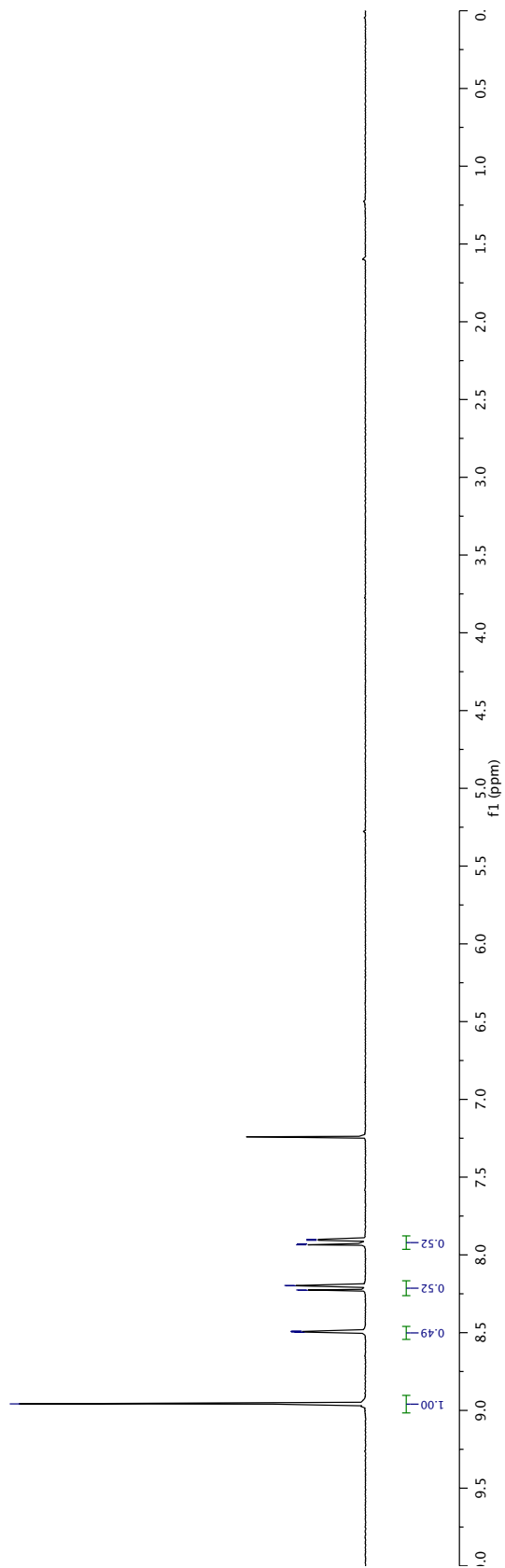


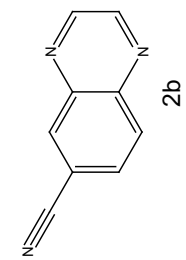


Char-TDS-6-86-1H
 Char-TDS-6-86-1H

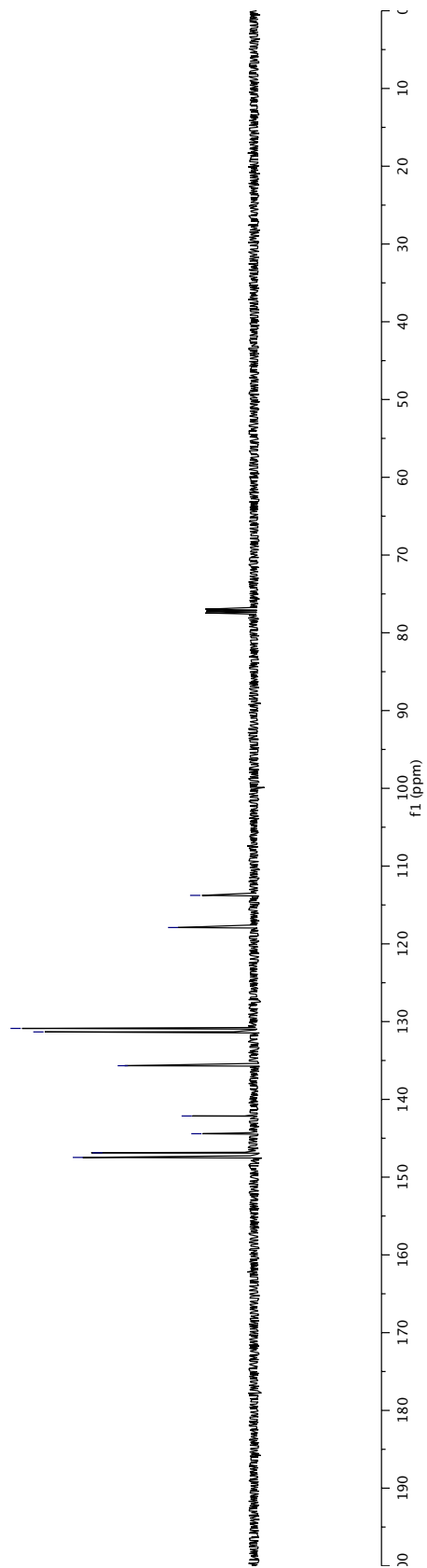
8.50
8.49
8.49
8.23
8.20
7.92
7.91
7.90

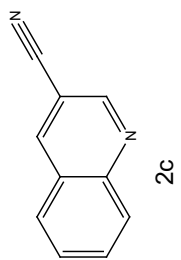
8.96



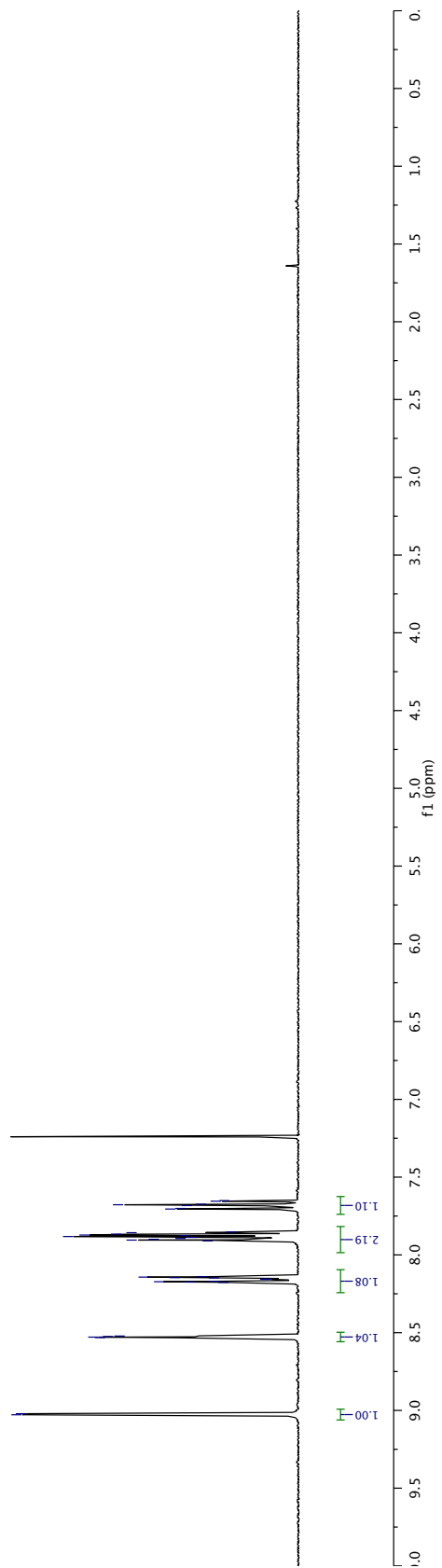
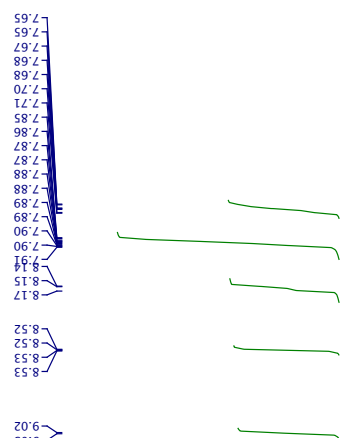


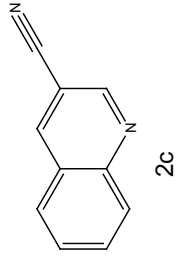
Char-TDS-6-86-1-13C
Char-TDS-6-86-1-13C



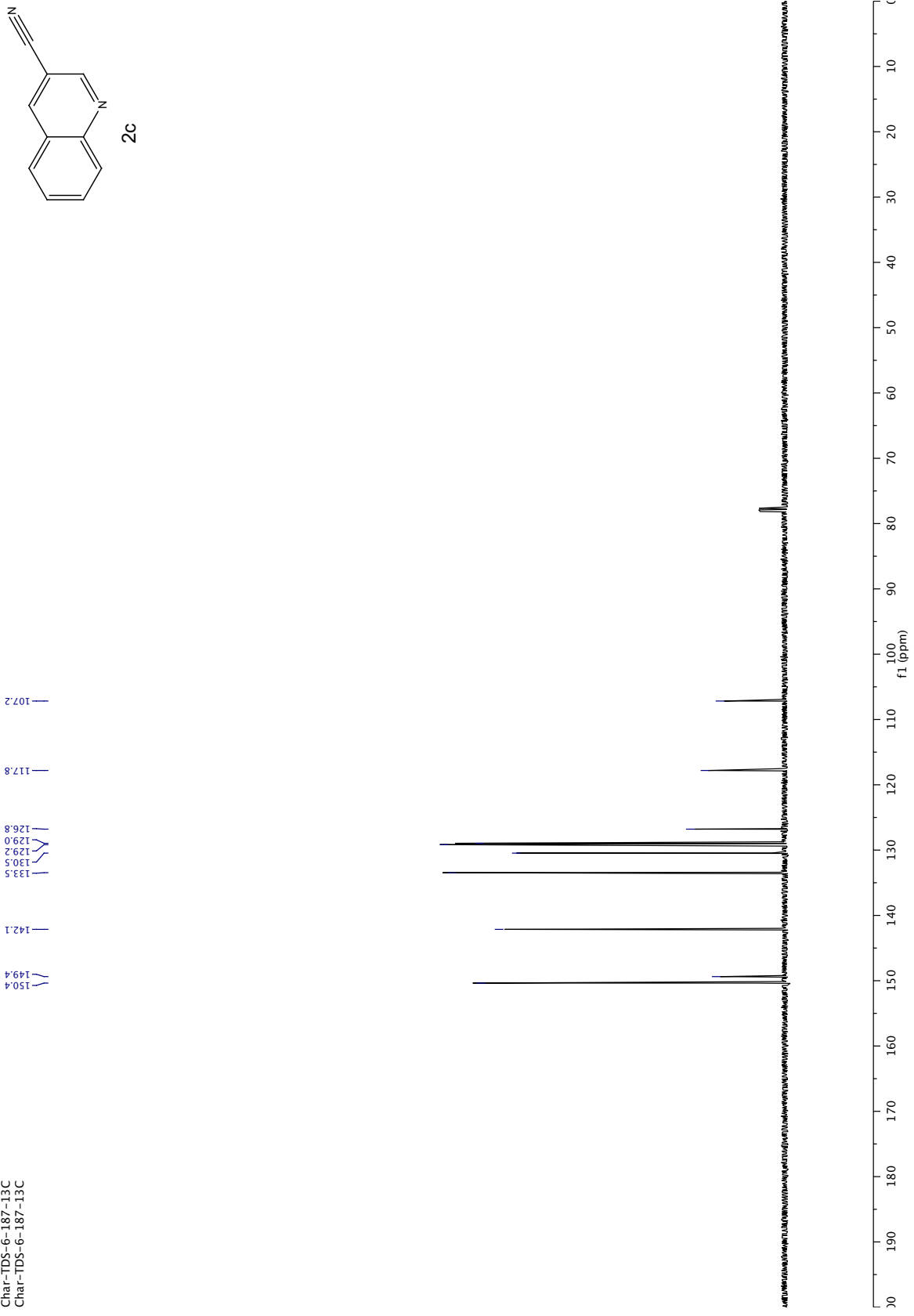


Char-TDS-6-187-1H
 Char-TDS-6-187-1H





Char-TDS-6-187-13C
Char-TDS-6-187-13C

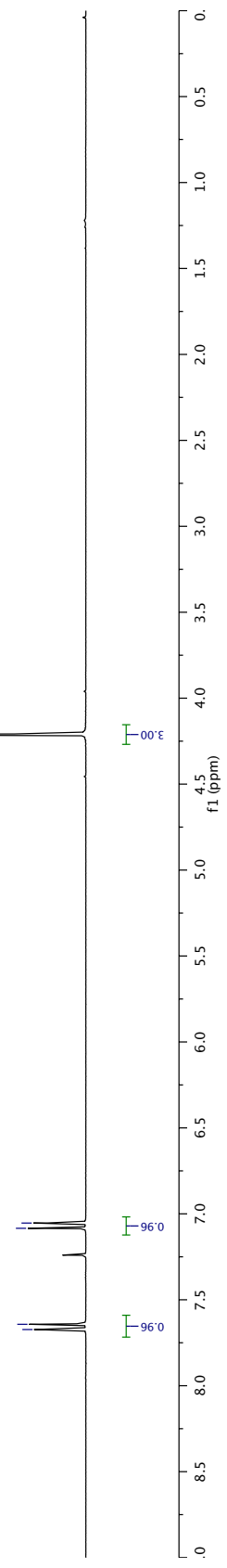
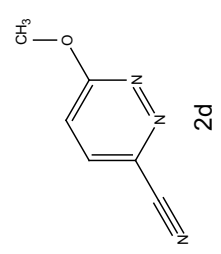


Char-TDS-6-100-1H
Char-TDS-6-100-1H

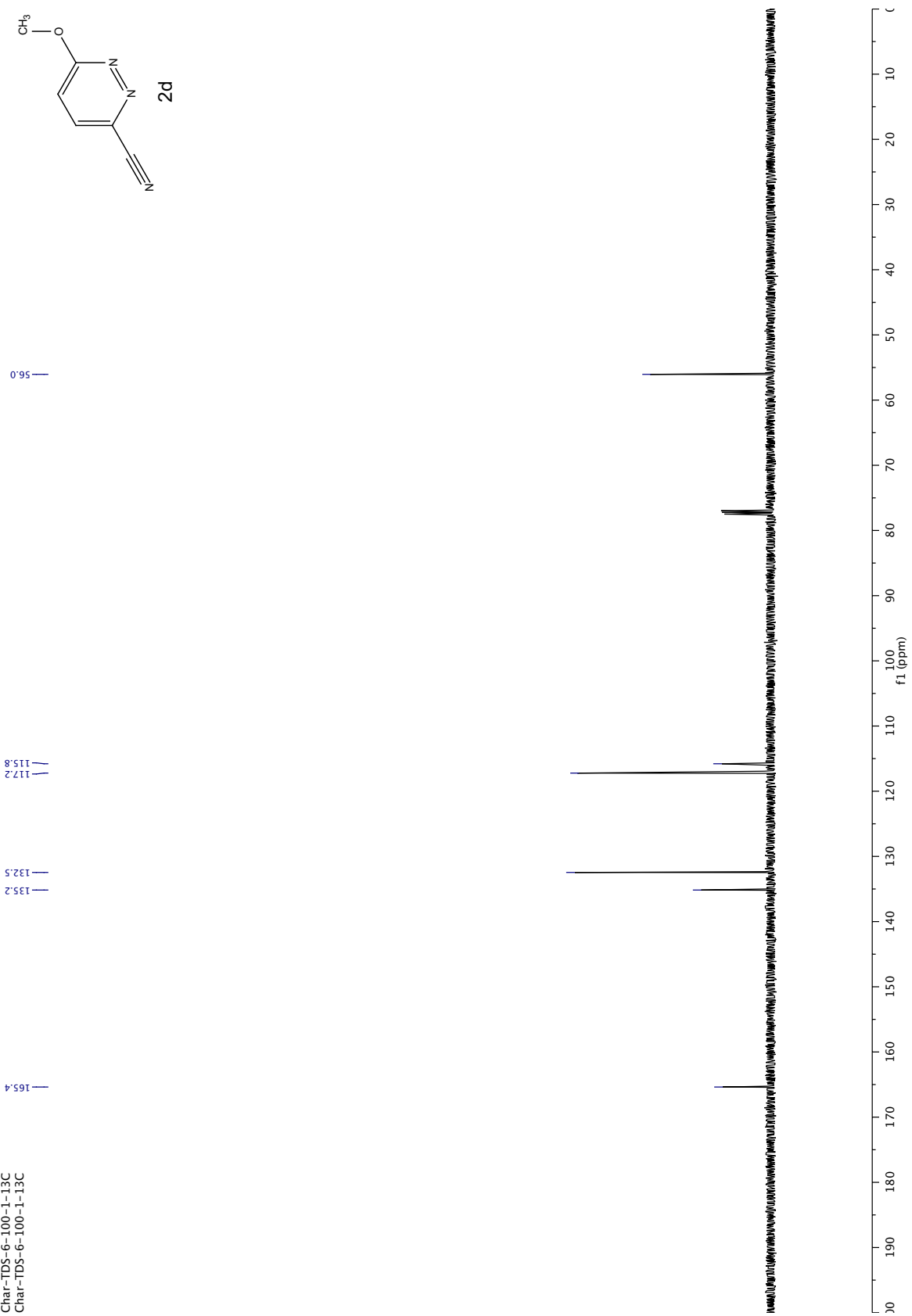
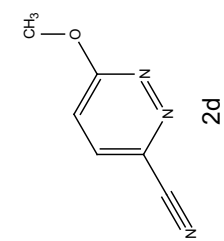
7.67

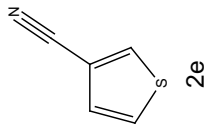
7.08

4.21



Char-TDS-6-100-1-1-13C
Char-TDS-6-100-1-1-13C

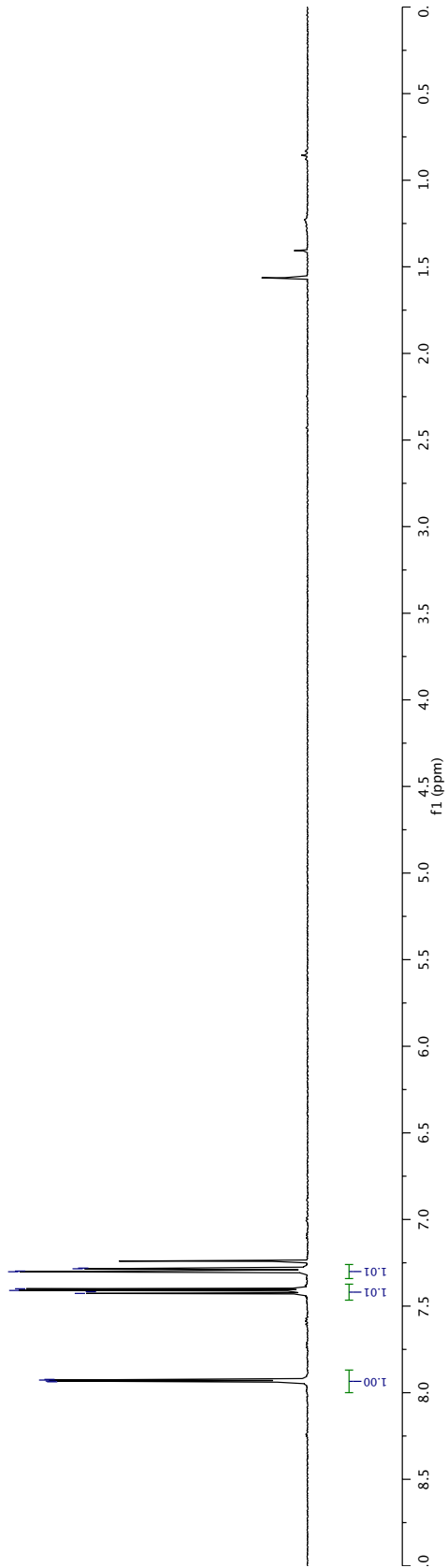
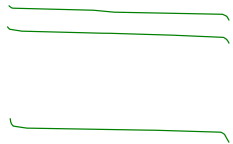




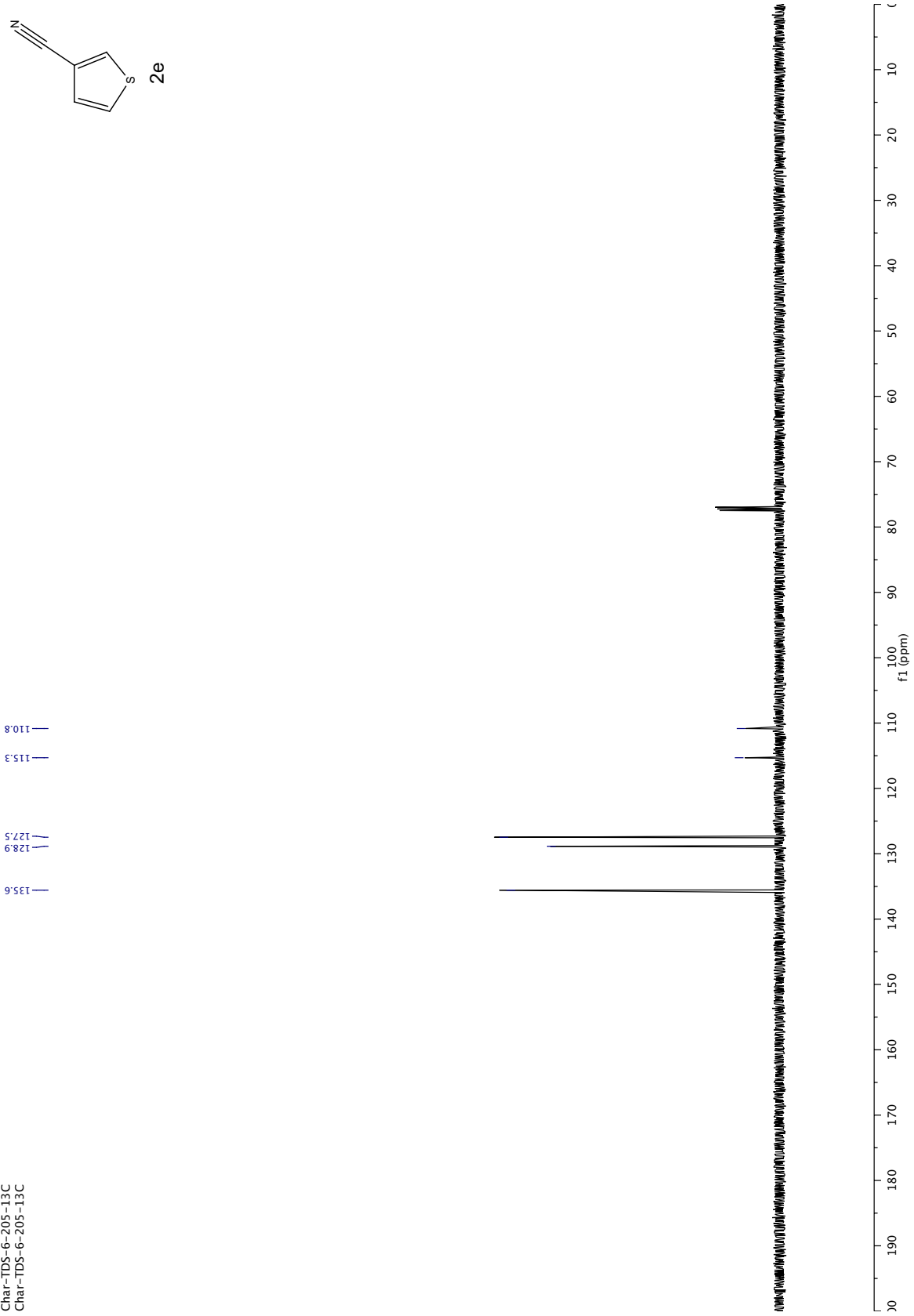
Char-TDS-6-205-1H
Char-TDS-6-205-1H

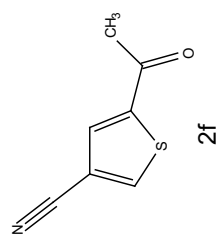
7.94
7.93
7.92

7.43
7.42
7.41
7.40
7.30
7.30
7.28



Char-TDS-6-205-13C
Char-TDS-6-205-13C



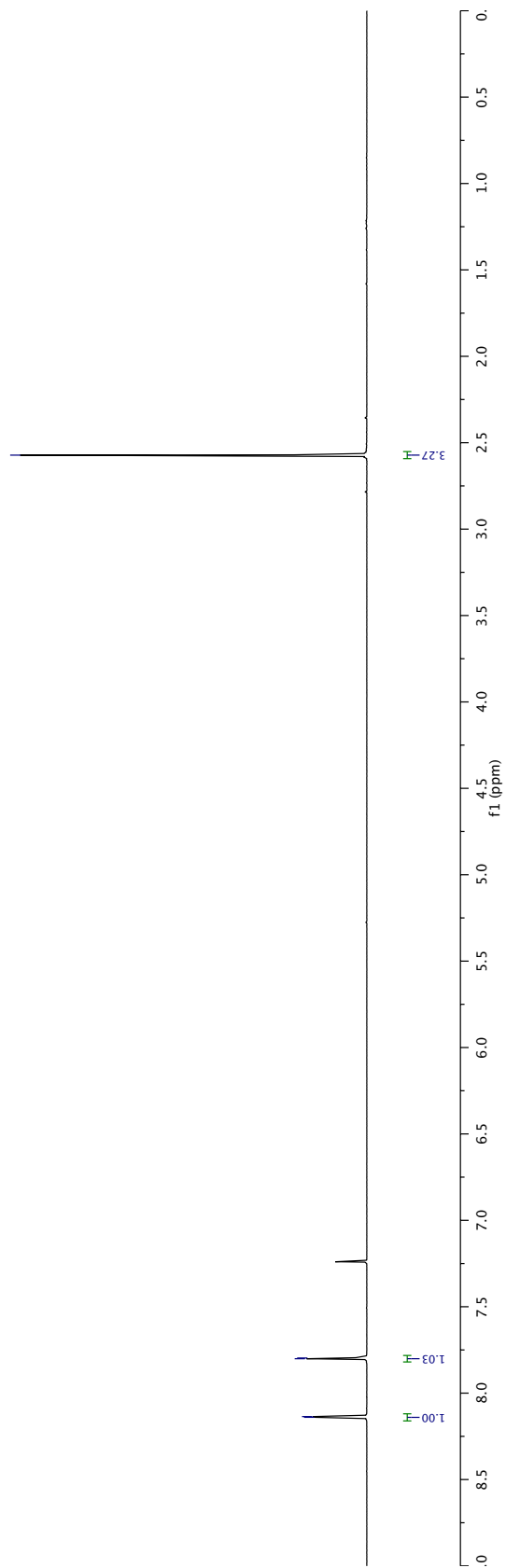


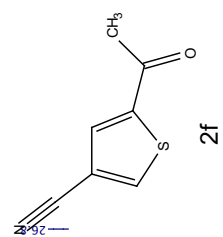
2.57

7.80

8.14

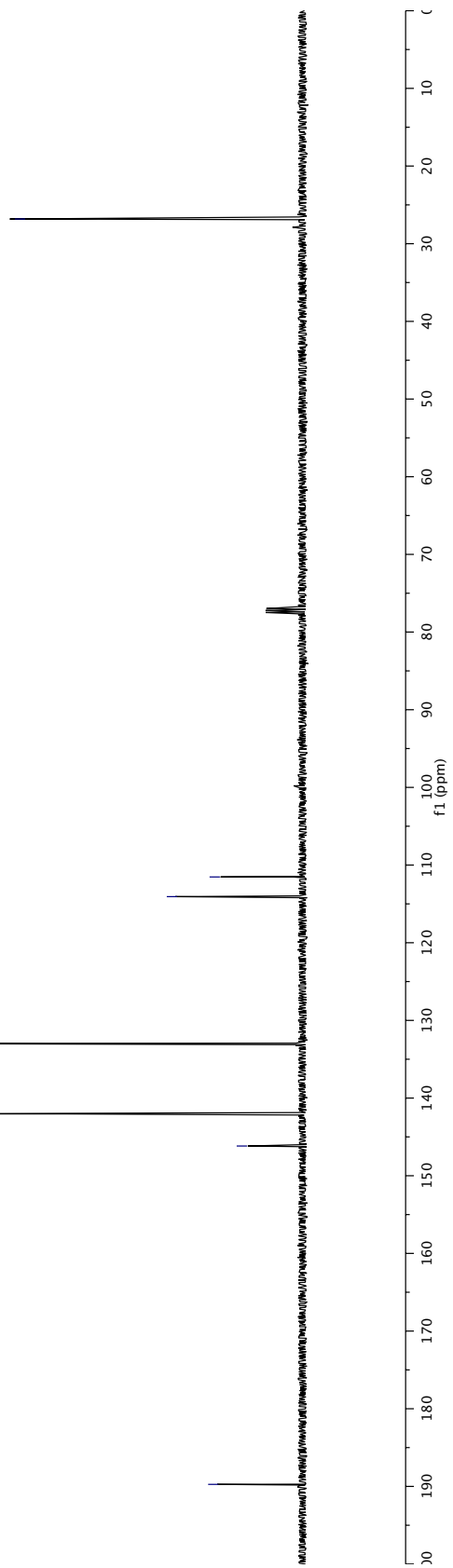
Char-TDS-6-245
Char-TDS-6-245

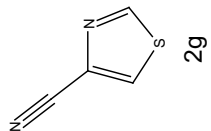




Char-TDS-6-245-13C
 Char-TDS-6-245-13C

111.5
 114.1
 133.0
 142.0
 146.2

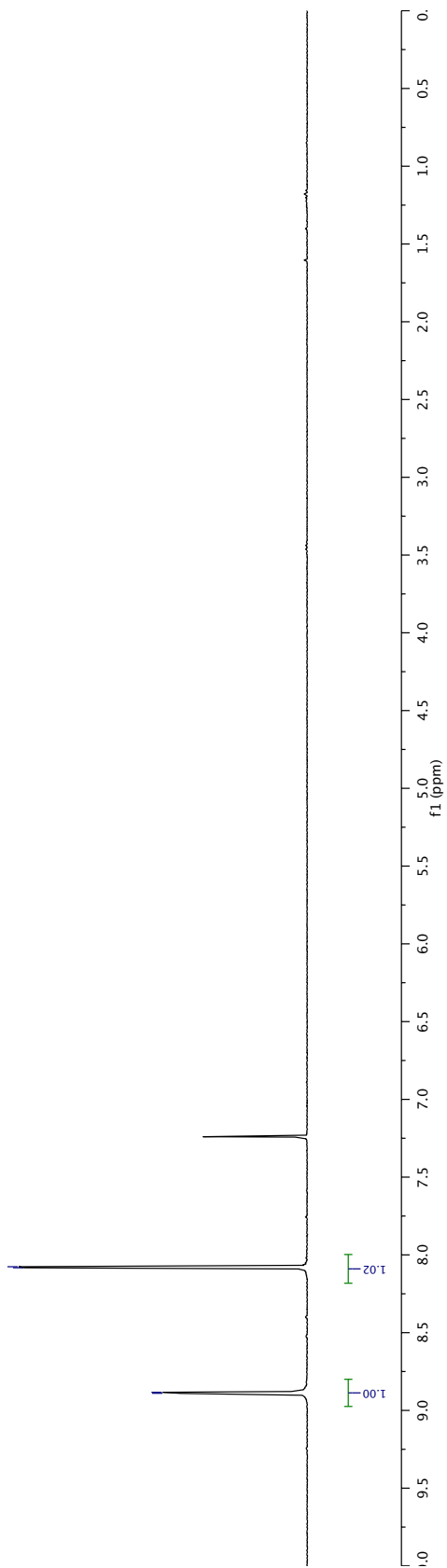


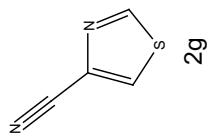


80.8
80.8

68.8
68.8

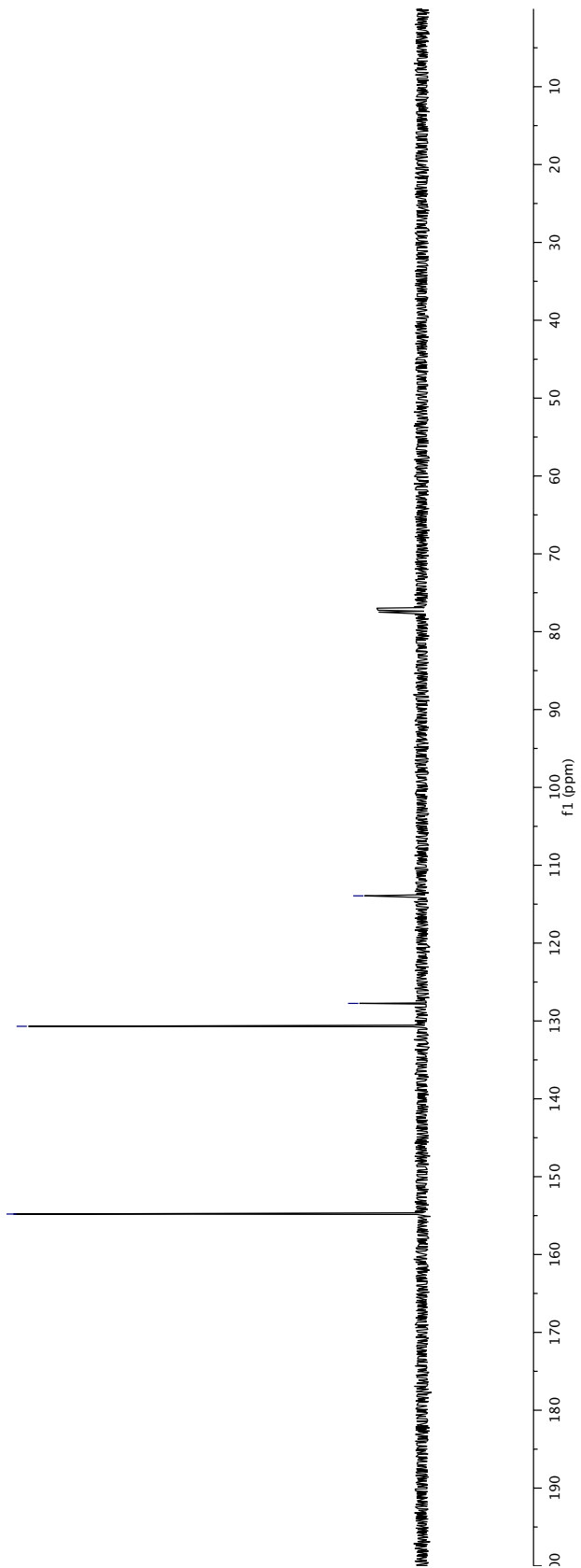
Char-TDS-6-170-1H
Char-TDS-6-170-1H

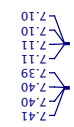
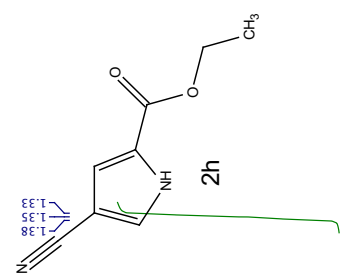




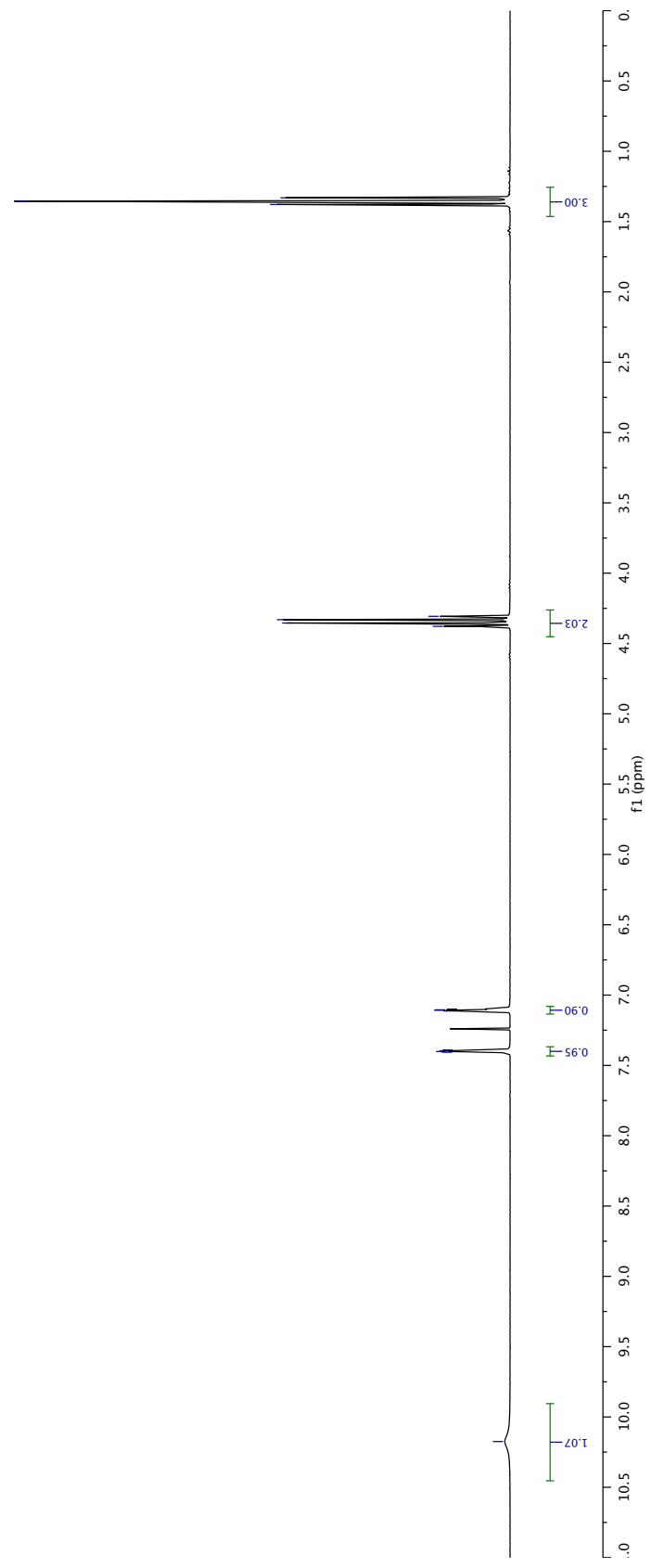
Char-TDS-6-170-13C
Char-TDS-6-170-13C

113.9
127.7
130.7
154.8

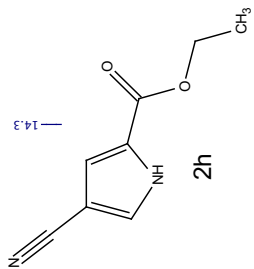




Char-TDS-6-184-1H
Char-TDS-6-184-1H



Char-TDS-6-184-13C
Char-TDS-6-184-13C



61.5

94.7

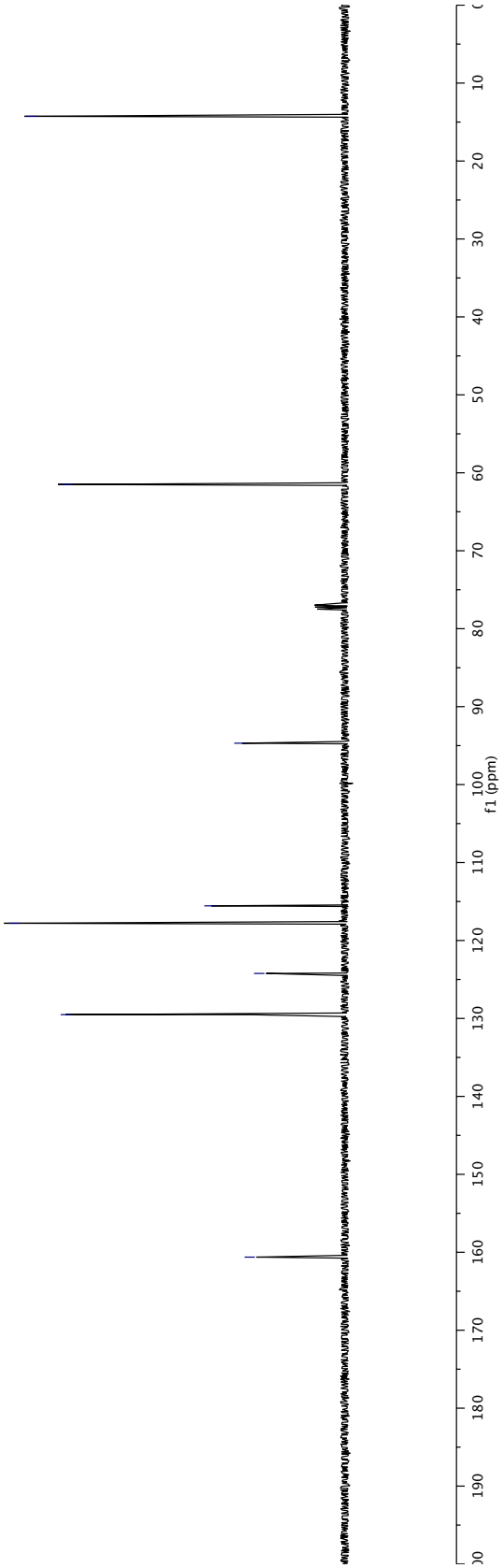
115.6

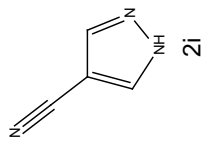
117.8

124.2

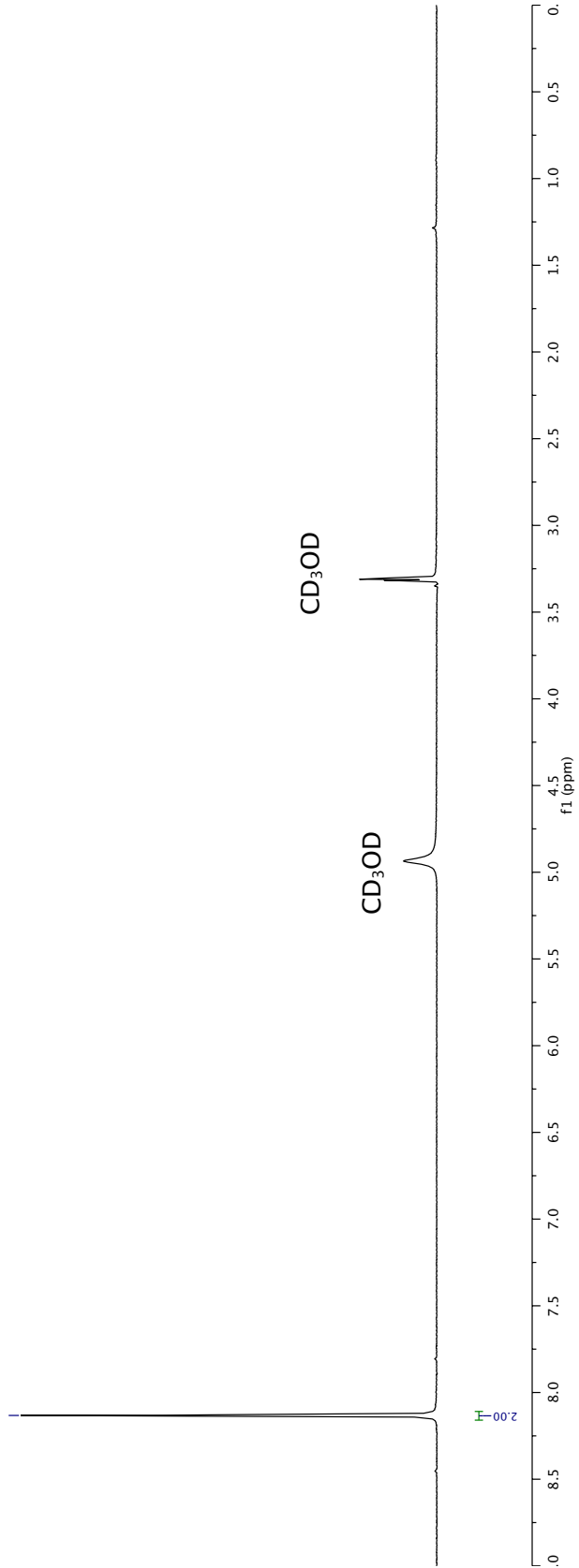
129.5

160.6

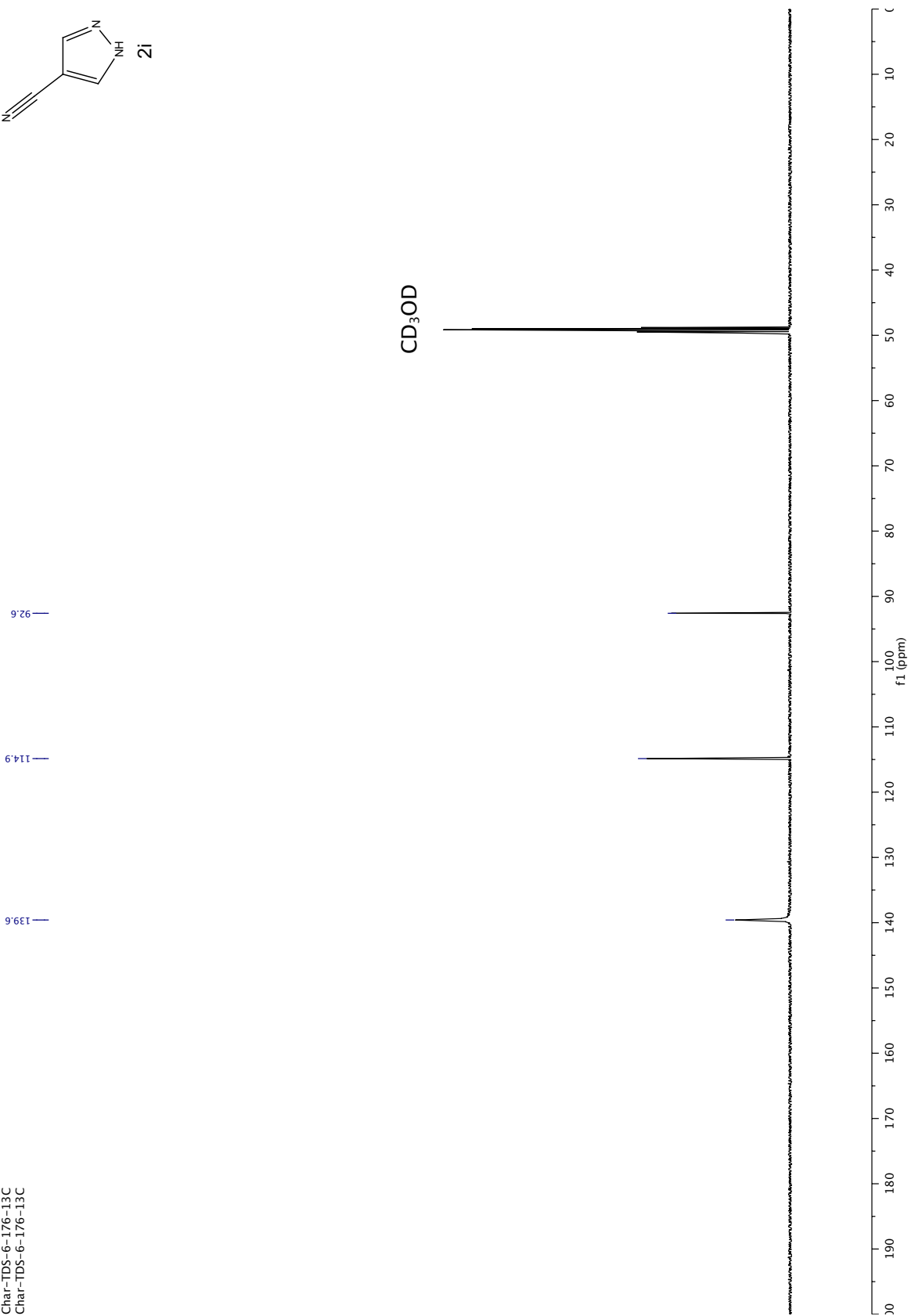
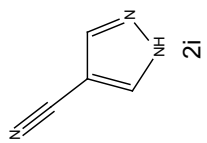


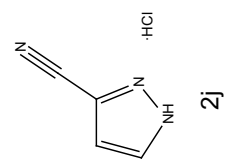


Char-TDS-6-176-1H
Char-TDS-6-176-1H



Char-TDS-6-176-13C
Char-TDS-6-176-13C

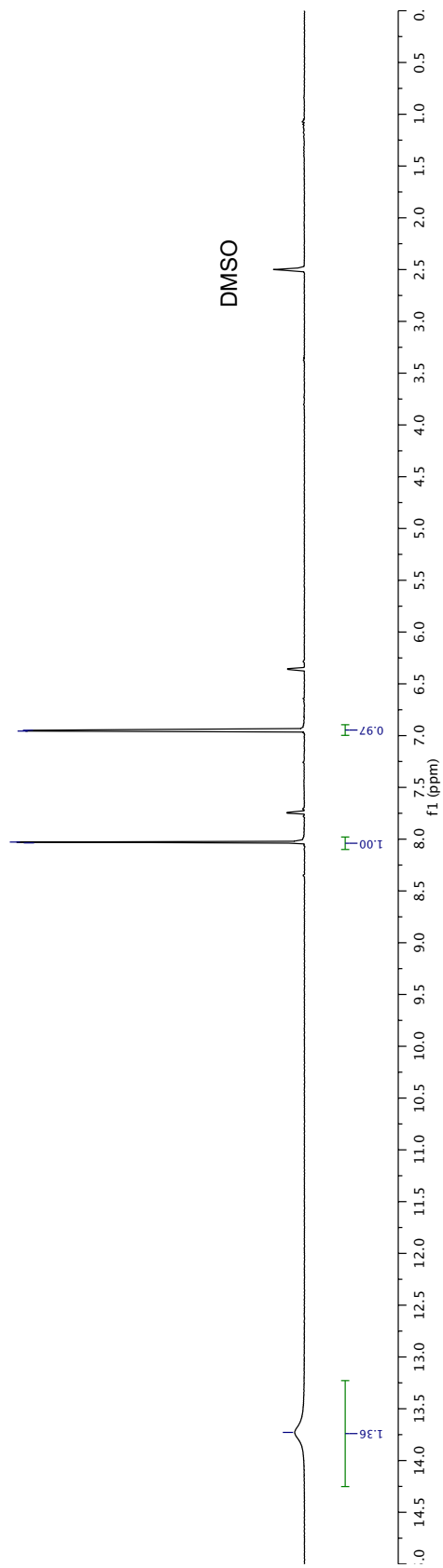
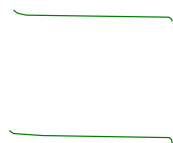




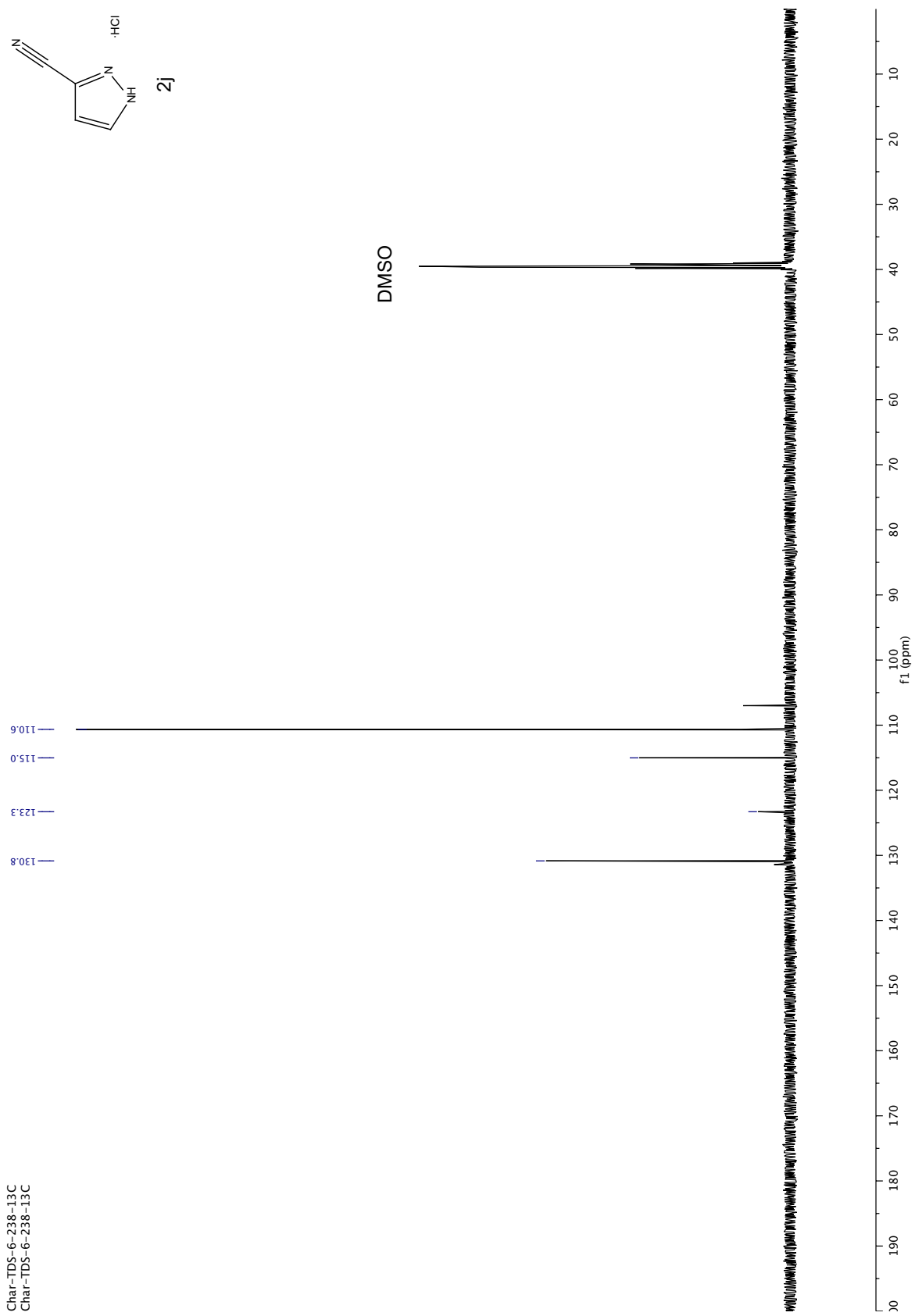
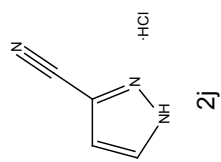
8.04

6.99

Char-TDS-6-238-1H
Char-TDS-6-238-1H

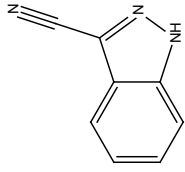


Char-TDS-6-238-13C
Char-TDS-6-238-13C



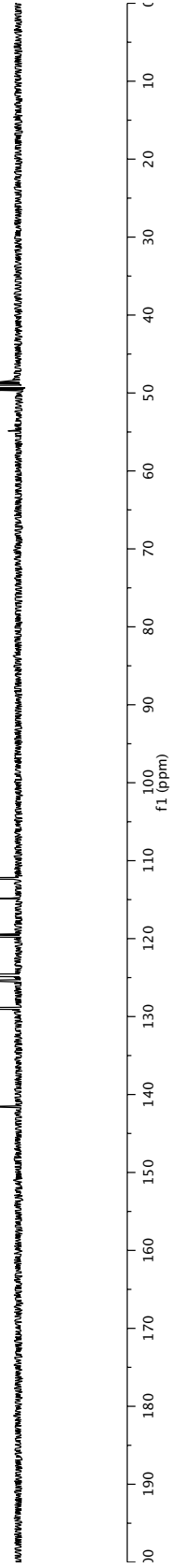
Char-TDS-6-136-13C
STANDARD CARBON PARAMETERS

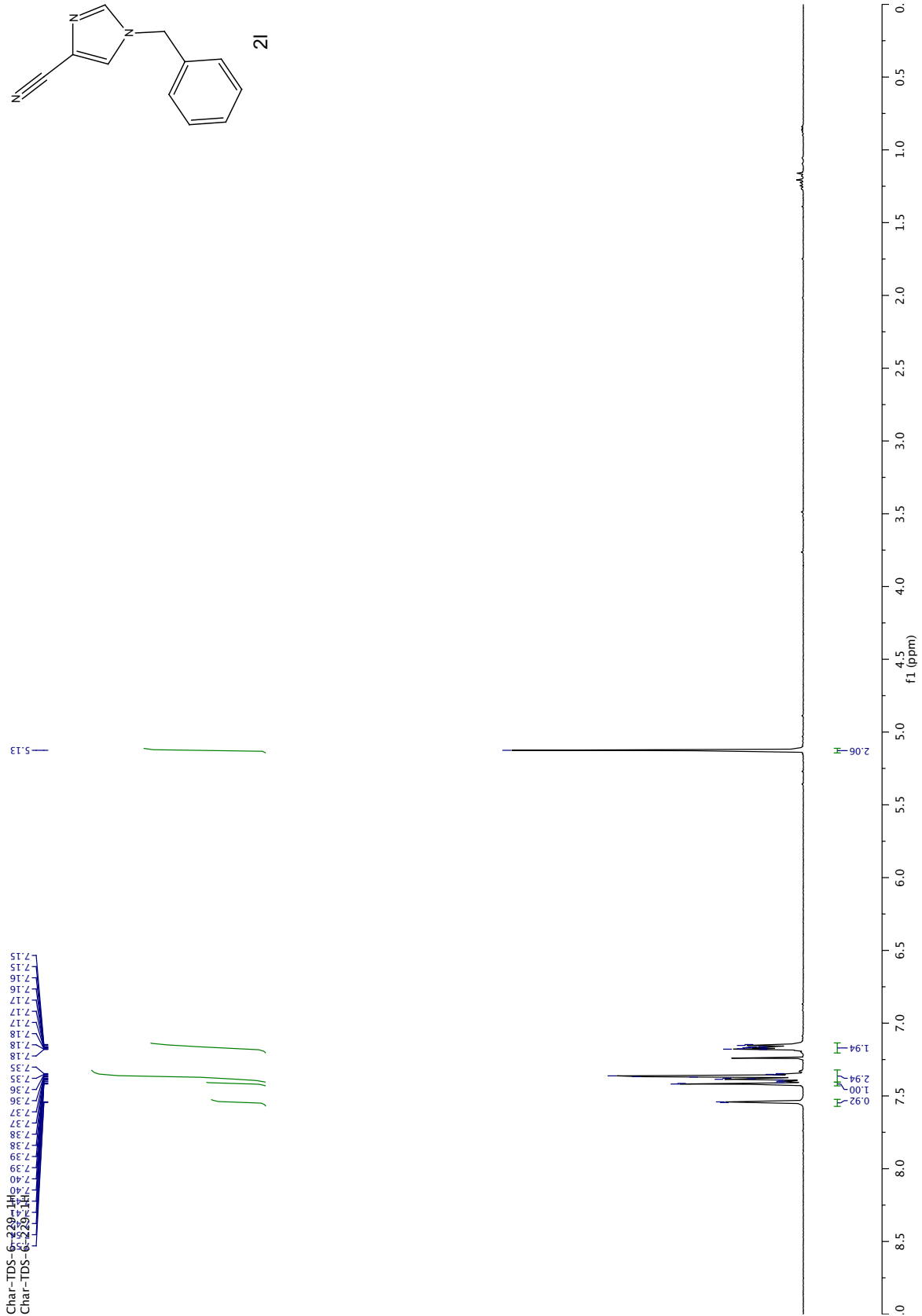
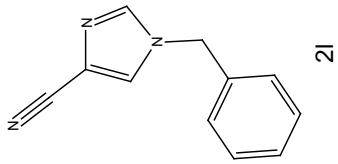
141.5
129.0
125.4
124.6
119.6
119.5
114.9
112.3

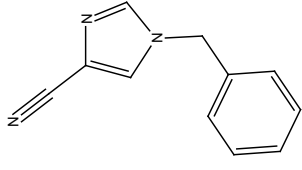


2k

CD₃OD

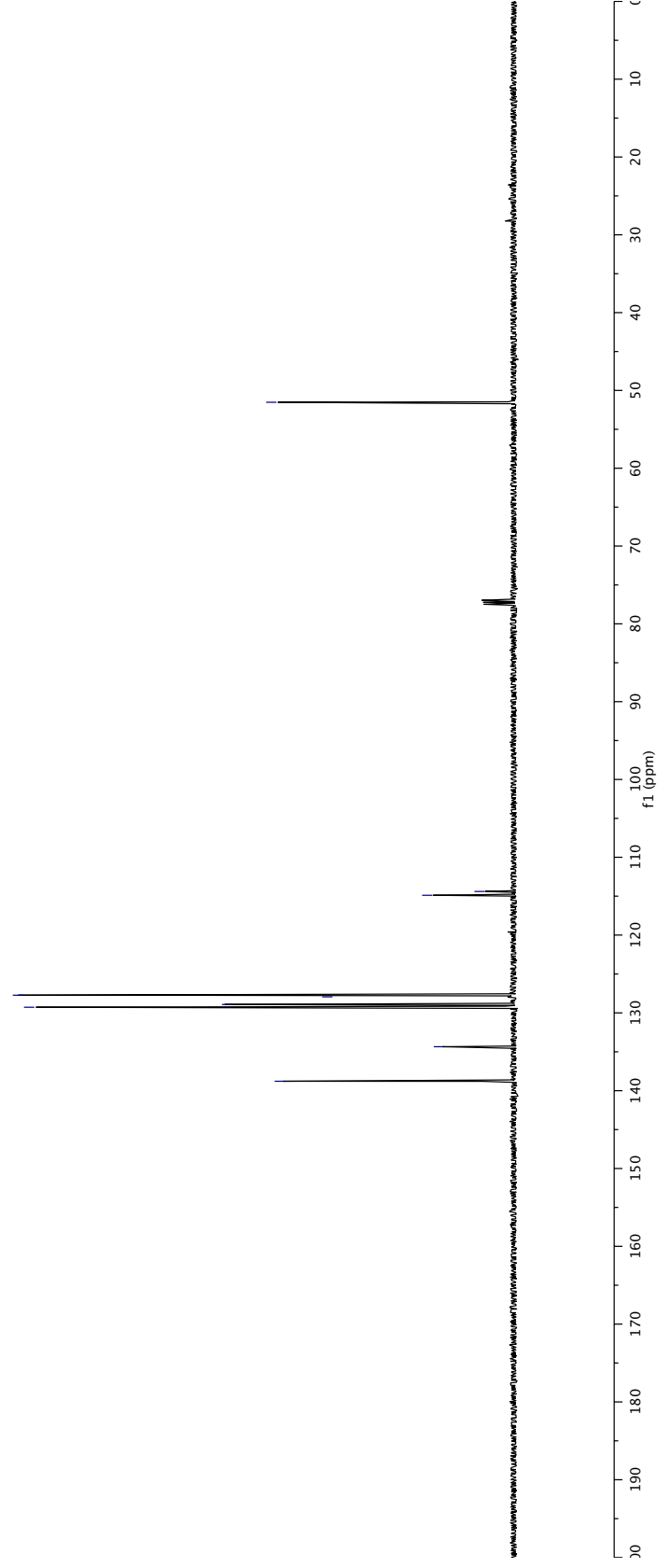


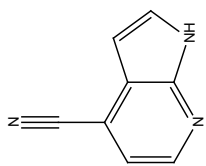




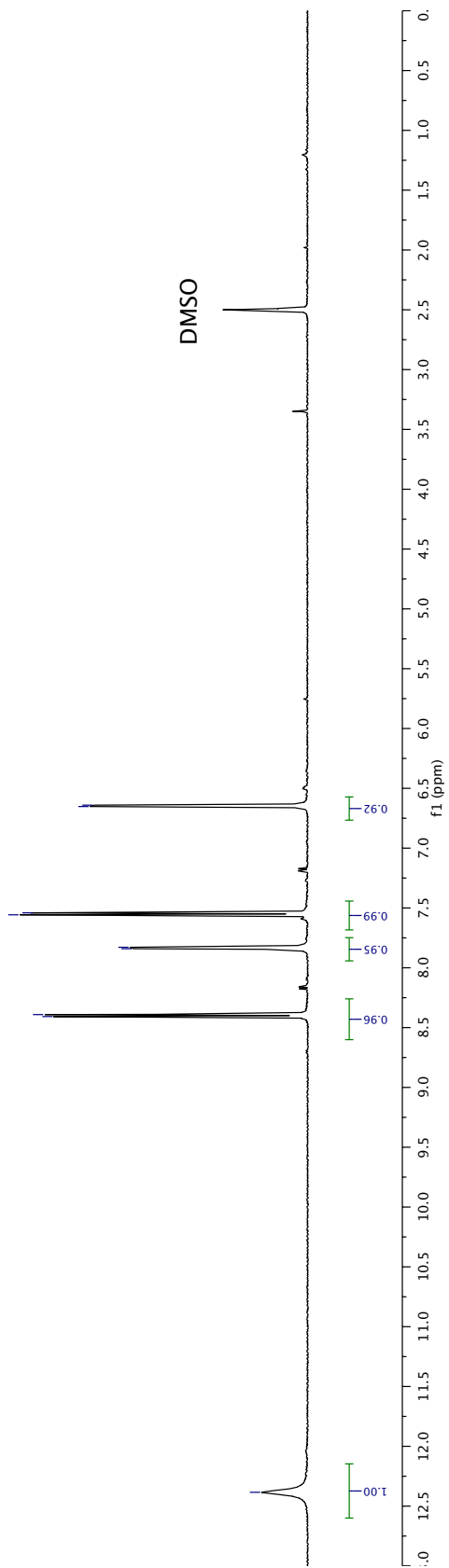
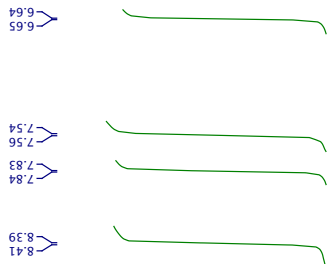
Char-TDS-6-229-13C
Char-TDS-6-229-13C

138.8
134.3
129.3
128.9
127.9
114.9
114.4
51.5

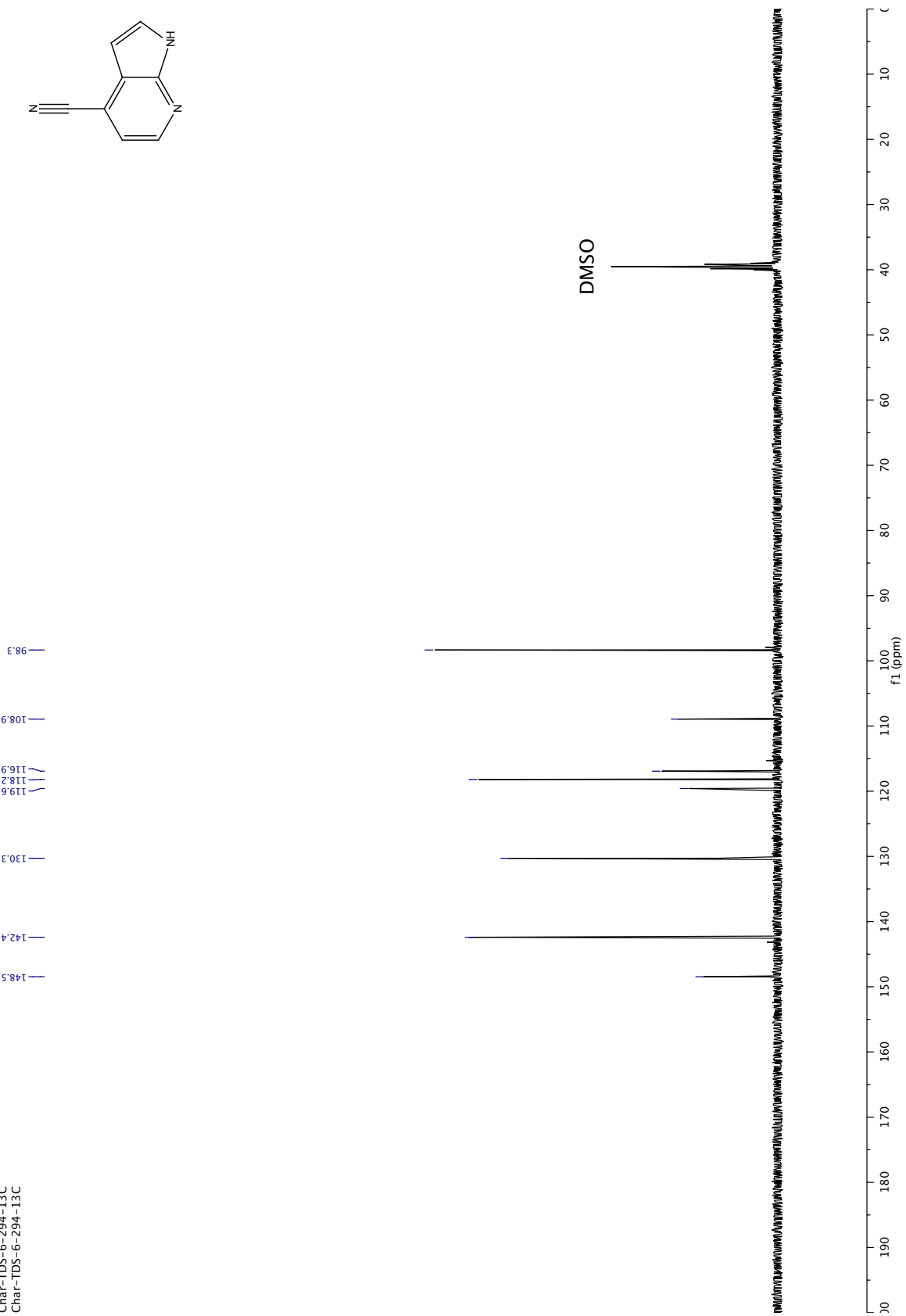




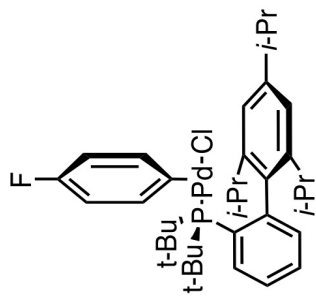
TDS-6-294
TDS-6-294



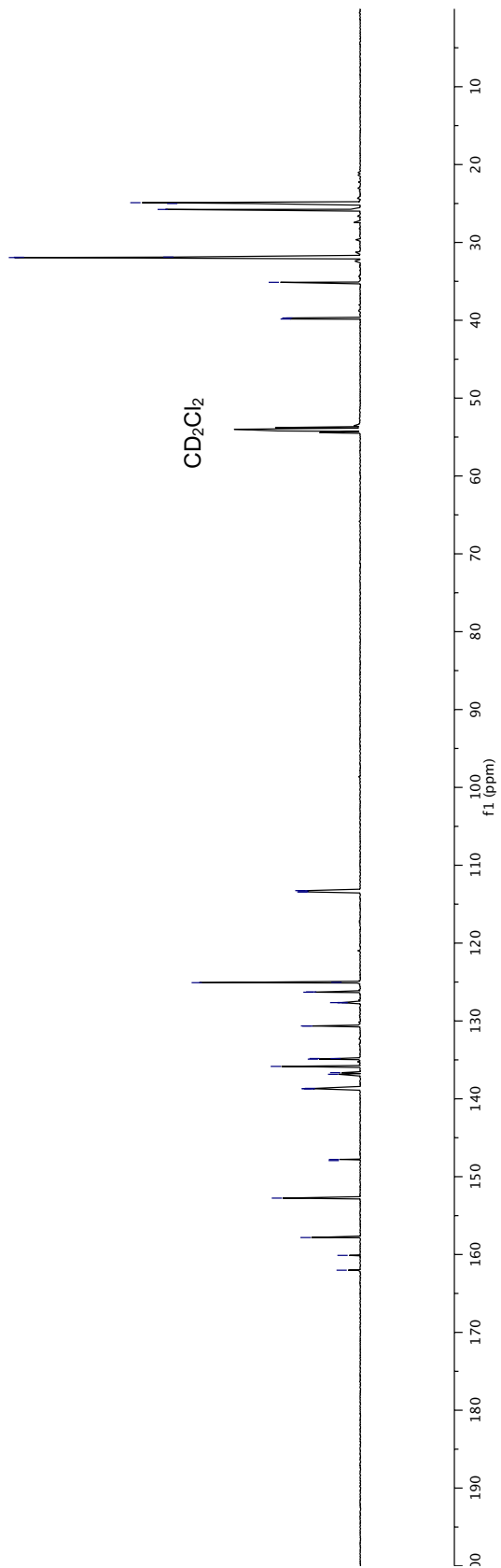
Char-TDS-6-294-13C
Char-TDS-6-294-13C



Char-TDS-6-298-13C
Char-TDS-6-298-13C

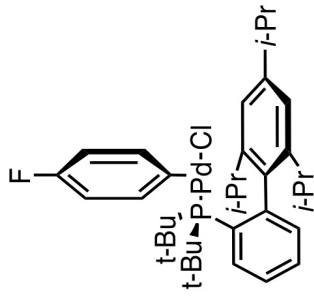


6

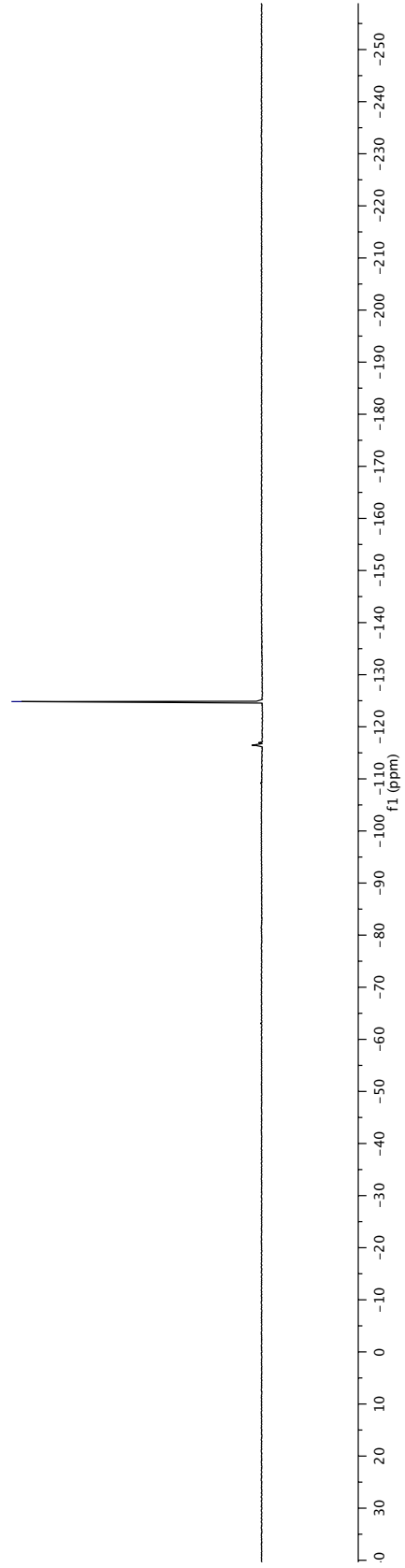


Char-TDS-6-298-19F-500MHz
Char-TDS-6-298-19F-500MHz

—124.83

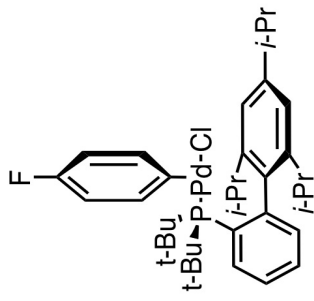


6

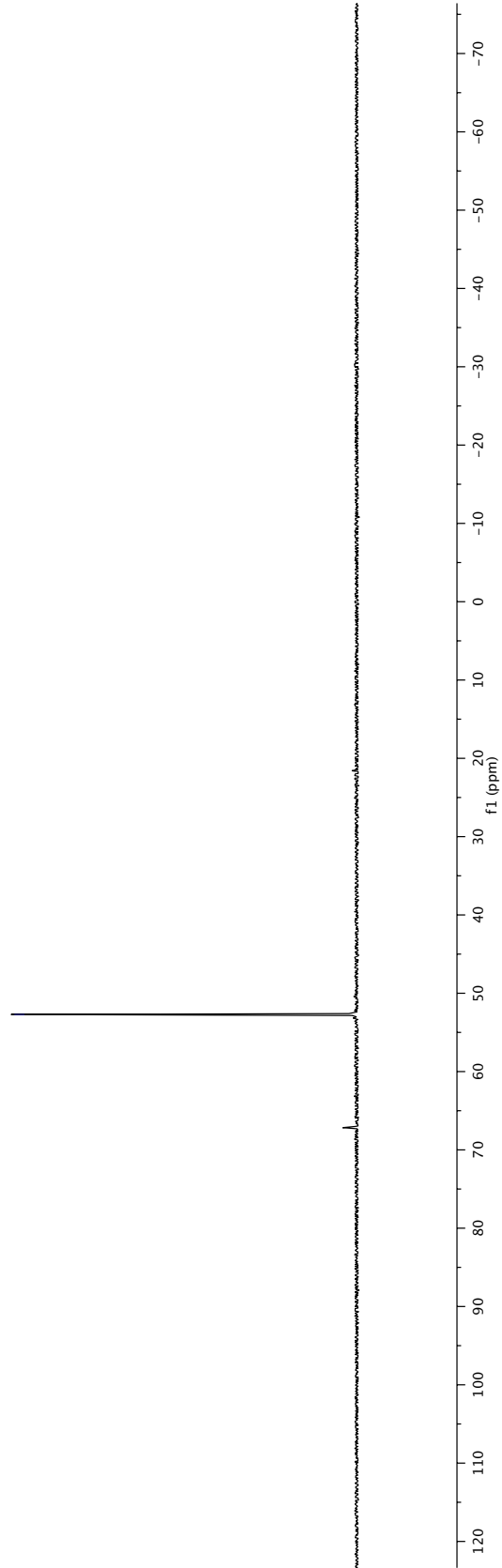


Char-TDS-6-298-31P
Char-TDS-6-298-31P

52.22



6



References

- [1] a) B. P. Fors, K. Dooleweerd, Q. Zeng, S. L. Buchwald, *Tetrahedron* **2009**, *65*, 6576-6583; b) N. Hoshiya, S. L. Buchwald, *Adv. Synth. Catal.* **2012**, *354*, 2031-2037.
- [2] a) N. C. Bruno, M. T. Tudge, S. L. Buchwald, *Chem. Sci.* **2013**, *4*, 916-920; b) N. C. Bruno, S. L. Buchwald, *Org. Lett.* **2013**, *15*, 2876-2879.
- [3] J. R. McAtee, S. E. S. Martin, D. T. Ahneman, K. A. Johnson, D. A. Watson, *Angew. Chem. Int. Ed.* **2012**, *51*, 3663-3667.
- [4] E. Gail, S. Gos, R. Kulzer, J. Lorösch, A. Rubo, M. Sauer, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, **2000**.
- [5] a) T. J. Maimone, P. J. Milner, T. Kinzel, Y. Zhang, M. K. Takase, S. L. Buchwald, *J. Am. Chem. Soc.* **2011**, *133*, 18106-18109; b) P. J. Milner, T. J. Maimone, M. Su, J. Chen, P. Müller, S. L. Buchwald, *J. Am. Chem. Soc.* **2012**, *134*, 19922-19934.
- [6] a) A. M. Allgeier, B. J. Shaw, T.-L. Hwang, J. E. Milne, J. S. Tedrow, C. N. Wilde, *Organometallics* **2012**, *31*, 519-522; b) D. K. Nielsen, A. G. Doyle, *Angew. Chem. Int. Ed.* **2011**, *50*, 6056-6059.
- [7] M. Begtrup, P. Larsen, *Acta Chem. Scand.* **1990**, *44*, 1050-1057.
- [8] H. Rupe, F. Bernstein, *Helv. Chim. Acta* **1930**, *13*, 457-473.
- [9] D. Mauleon, R. Granados, C. Minguillon, *J. Org. Chem.* **1983**, *48*, 3105-3106.
- [10] R. R. Herr, T. Enkoji, J. P. Dailey, *J. Am. Chem. Soc.* **1957**, *79*, 4229-4232.
- [11] W. K. Detweiler, E. D. Amstutz, *J. Am. Chem. Soc.* **1950**, *72*, 2882-2884.
- [12] Y. Ren, W. Wang, S. Zhao, X. Tian, J. Wang, W. Yin, L. Cheng, *Tetrahedron Lett.* **2009**, *50*, 4595-4597.
- [13] B. R. Kim, H.-G. Lee, E. J. Kim, S.-G. Lee, Y.-J. Yoon, *J. Org. Chem.* **2009**, *75*, 484-486.
- [14] M. A. Schade, G. Manolikakes, P. Knochel, *Org. Lett.* **2010**, *12*, 3648-3650.
- [15] K. Ishifuku, H. Sakurai, H. Okamoto, S. Satoh, *Yakugaku Zasshi* **1949**, *69*, 417-418.
- [16] R. J. Rahaim, R. E. Maleczka, *Org. Lett.* **2005**, *7*, 5087-5090.
- [17] M. R. Naimi-Jamal, J. Mokhtari, M. G. Dekamin, G. Kaupp, *Eur. J. Org. Chem.* **2009**, *2009*, 3567-3572.
- [18] A. Yasuhara, A. Kasano, T. Sakamoto, *J. Org. Chem.* **1999**, *64*, 4211-4213.
- [19] H. Singer, W. Shive, *J. Am. Chem. Soc.* **1955**, *77*, 5700-5702.
- [20] J. K. Landquist, *J. Chem. Soc.* **1953**, 2816-2821.
- [21] R. C. Fuson, J. J. Miller, *J. Am. Chem. Soc.* **1957**, *79*, 3477-3480.
- [22] M. Iwao, T. Kuraishi, *J. Heterocycl. Chem.* **1979**, *16*, 689-698.
- [23] P. J. Newcombe, R. K. Norris, *Aust. J. Chem.* **1981**, *34*, 1879-1886.
- [24] G. D. Hartman, L. M. Weinstock, *Synthesis* **1976**, *1976*, 681-682.
- [25] S. Trofimenko, *J. Org. Chem.* **1963**, *28*, 2755-2758.
- [26] R. Pschorr, G. Hoppe, *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 2543-2552.