

SUPPORTING INFORMATION

Mechanochemistry frees the thiourea dioxide (TDO) from the 'veils' of the solvent, exposing all its reactivity

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1. General information

Commercially available reagents were purchased from Acros, Aldrich, Strem Chemicals, Alfa-Aesar, TCI Europe, and used as received. All reactions were monitored by thin-layer chromatography (TLC) performed on glass-backed silica gel 60 F254, 0.2 mm plates (Merck), and compounds were visualized under UV light (254 nm) or using cerium ammonium molybdate solution with subsequent heating. The eluents were technical grade. Mechanochemical reactions were carried out using a Retsch MM500 Vario apparatus. The reagents were milled using a stainless-steel grinding jar (10 mL) equipped with two balls ($\phi = 7.0$ mm, 2.67 g) of the same material. These parameters were applied if not stated otherwise. ^1H and ^{13}C liquid NMR spectra were recorded on a Varian 600 MHz and Bruker Avance III HD 600 MHz NMR spectrometer at 298 K and were calibrated using trimethylsilane (TMS). Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referred to the residual hydrogen in the solvent (CHCl_3 , 7.27 ppm or DMSO 2.54 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, bs = broad singlet, and combination of thereof), coupling constant (J) in Hertz (Hz) and integration. Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvent (CDCl_3 , δ 77.0 ppm or δ DMSO- d_6 δ 39.5 ppm). Deuterated NMR solvents were obtained from Aldrich. Samples were analyzed using an Agilent 5977B MS interfaced to the GC 7890B equipped with a DB-5ms column (J & W), injector temperature at 230 °C, detector temperature at 280 °C, helium carrier gas flow rate of 1 ml/min. The GC oven temperature program was 60 °C initial temperature with 4 min hold time and ramping at 15°C/min to a final temperature of 270°C with 7 min hold time. 1 μL of each sample was injected in split (1:20) mode. After a solvent delay of 3 minutes mass spectra were acquired in full scan mode using 2.28 scans/s with a mass range of 50–500 Amu. Retention times of different compounds were determined by injecting pure compound under identical conditions. All the experiments were carried out in duplicate to ensure reproducibility of the experimental data. Yields refer to pure isolated materials.

2. Mechanochemical synthesis of **3a-j**, **3o-p**, **3s** and **4d-n**, **4o**, **4q-r**

General procedure A for anilines and *o*-phenylenediamines **3a-j**, **3o-p**, **3s** synthesis from 2-nitroanilines **2a-j**, **2o-p**, **2s**

A 10 mL stainless steel jar equipped with 2 stainless steel milling balls (7 mm diameter, 2.67 g) was filled with nitrobenzenes **2a-j**, **2o-p**, **2s** (1.00 mmol), NaOH (6.00 mmol), **1** (3.00 mmol) and 250 μ L of distilled water. The vessel was then closed and the mechanochemical reaction was conducted, ranging from 60 to 180 min at a frequency of 30 Hz. Whenever necessary, further purification through flash column chromatography has been made. Lastly, the solvent was removed under reduced pressure to afford the pure anilines **3a-j**, **3o-p**, **3s**.

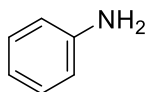
General procedure B for heterocycles **4l-n**, **4q-r** synthesis from *o*-phenylenediamines **3l-n**, **3q-r**

A 10 mL stainless steel jar equipped with 2 stainless steel milling balls (7.0 mm diameter, 2.67 g) was filled with *o*-phenylenediamines **3l-n**, **3q-r** (1.00 mmol), **1** (3.00 mmol) and 200 μ L of distilled water. The vessel was then closed, and the mechanochemical reaction was conducted, ranging from 60 min to 180 min at a frequency of 30 Hz. At the end of the reaction, an additional silica pad (SiO₂, heptane/ethyl acetate/methanol = 1:1:0 \rightarrow 6:3:1) was made to purify the reaction mixture. Lastly, the solvent was removed under reduced pressure to afford the pure heterocycle **4l-n**, **4q-r**.

General procedure C for heterocycles **4d-k**, **4o** synthesis from 2-nitroanilines **2d-k**, **2o**

A 10 mL stainless steel jar equipped with 2 stainless steel milling balls (7.0 mm diameter, 2.67 g) was filled with 2-nitroanilines **2d-k**, **2o** (1.00 mmol), NaOH (6.00 mmol), **1** (3.00 mmol) and 250 μ L of distilled water. The vessel was then closed and the mechanochemical reaction was conducted, ranging from 60 to 180 min at a frequency of 30 Hz. At the end of the reaction, it was made an additional refill of **1** (3.00 mmol) and 60 μ L of distilled water and the mechanochemical reaction was run ranging from 60 to 180 min at a frequency of 30 Hz. At the end of the reaction, an additional silica pad (SiO₂, hexane/ethyl acetate/methanol = 1:1:0 \rightarrow 6:3:1) was made to purify the reaction mixture. Lastly, the solvent was removed under reduced pressure to afford the pure heterocycle **4d-k**, **4o**.

Aniline **3a**



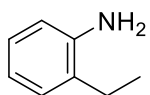
The title compound was synthesized according to the general procedure A. **2a** (123.11 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3a** as a colorless liquid (90.34 mg, 0.97 mmol, 97%).

¹H NMR (600 MHz, CDCl₃) δ = 7.20 (t, *J* = 9.0 Hz, 2H), 6.81 (t, 1H), 6.71 (d, *J* = 9.0 Hz, 2H), 3.65 (bs, 2H).

¹³C NMR (151 MHz, CDCl₃) δ = 146.5, 129.3, 118.6, 115.2.

The spectroscopic data closely match the ones previously reported in the literature.[1]

2-Ethylaniline **3b**



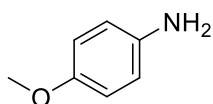
The title compound was synthesized according to the general procedure **A**. **2b** (151.2 mg, 1.0 mmol), NaOH (239.98 mg, 6.0 mmol), **1** (324.36 mg, 3.0 mmol), and 250 μ L of distilled water were used, to afford **3b** as a colourless liquid (117.54 mg, 0.97 mmol, 97%).

¹H NMR (600 MHz, CDCl₃) δ = 7.10 – 7.07 (m, 1H), 7.05 (td, J = 7.6, 1.6 Hz, 1H), 6.76 (td, J = 7.6, 1.6 Hz, 1H), 6.69 (dd, J = 7.9, 1.3 Hz, 1H), 3.62 (s, 2H), 2.53 (q, J = 7.5 Hz, 2H), 1.26 (t, J = 7.5 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ = 144.1, 128.5, 128.2, 126.9, 119.0, 115.5, 24.1, 13.1.

The spectroscopic data closely match the ones previously reported in the literature.[2]

4-Methoxyaniline **3c**



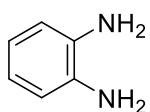
The title compound was synthesized according to the general procedure **A**. **2a** (153.14 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3a** as a colorless liquid (118.23 mg, 0.96 mmol, 96%).

¹H NMR (600 MHz, CDCl₃) δ = 6.75 (d, J = 8.8 Hz, 2H), 6.65 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H), 3.35 (bs, 2H).

¹³C NMR (151 MHz, CDCl₃) δ = 152.9, 140.1, 116.5, 114.9, 55.8.

The spectroscopic data closely match the ones previously reported in the literature.[2]

Benzene-1,2-diamine **3d**



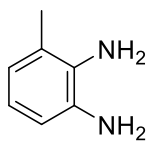
The title compound was synthesized according to the general procedure **A**. **2d** (138.13 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3d** as a light brown solid (105.98 mg, 0.98 mmol, 98%).

¹H NMR (600 MHz, CDCl₃ + DMSO-*d*₆) δ = 6.58 (dt, J = 6.0, 3.4 Hz, 2H), 6.51 (dd, J = 6.0, 4.9, 3.4 Hz, 2H).

¹³C NMR (151 MHz, CDCl₃ + DMSO-*d*₆) δ = 134.5, 118.5, 115.5, 115.4.

The spectroscopic data closely match the previously reported in the literature[3].

3-Methylbenzene-1,2-diamine **3e**



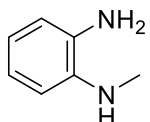
The title compound was synthesized according to the general procedure **A**. **2e** (152.2 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol) and 250 μ L of distilled water were used, to afford **3e** as a brownish solid (118.50 mg, 0.97 mmol, 97%).

^1H NMR (600 MHz, CDCl_3) δ = 6.67 – 6.71 (m, 3H), 3.38 (bs, 4H), 2.21 (s, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ = 134.0, 133.6, 123.5, 122.2, 119.2, 115.2, 17.5.

The spectroscopic data closely match the ones previously reported in the literature [4].

N-Methylbenzene-1,2-diamine **3f**



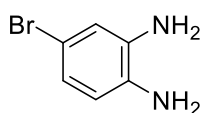
The title compound was synthesized according to the general procedure **A**. **2f** (152.15 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol) and 250 μ L of distilled water were used, to afford **3f** as a black liquid (117.28 mg, 0.96 mmol, 96%).

^1H NMR (600 MHz, CDCl_3) δ = 6.96 (ddd, J = 7.8, 6.7, 2.2, Hz, 1H), 6.82 – 6.72 (m, 3H), 3.41 (s, 3H), 2.91 (bs, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ = 138.9, 134.1, 120.7, 118.3, 116.2, 110.9, 30.9.

The spectroscopic data closely match the ones previously reported in the literature [5].

4-Bromobenzene-1,2-diamine **3g**



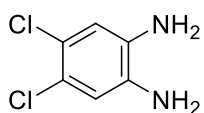
The title compound was synthesized according to the general procedure **A**. **2a** (217.02 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3a** as a yellowish solid (181.43 mg, 0.97 mmol, 97%).

^1H NMR (600 MHz, CDCl_3) δ = 6.74 – 6.69 (m, 3H), 3.28 (bs, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ = 134.9, 120.4, 116.9.

The spectroscopic data closely match the ones previously reported in the literature [6].

4,5-Dichlorobenzene-1,2-diamine **3h**



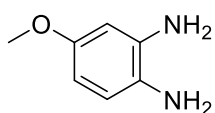
The title compound was synthesized according to the general procedure **A**. **2h** (207.01 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3h** as a yellow solid (168.18 mg, 0.95 mmol, 95%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 6.62 (s, 2H), 4.85 (bs, 4H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 135.6, 117.3, 114.3.

The spectroscopic data closely match the ones previously reported in the literature [7].

4-Methoxybenzene-1,2-diamine **3i**



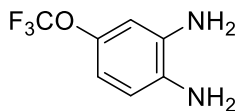
The title compound was synthesized according to the general procedure **A. 2i** (168.15 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3i** as a dark red solid (105.01 mg, 0.76 mmol, 76%).

¹H NMR (600 MHz, CDCl₃) δ = 6.63 (d, *J* = 8.4 Hz, 1H), 6.32 (d, *J* = 2.8 Hz, 1H), 6.26 (dd, *J* = 8.4, 2.7 Hz, 1H), 3.72 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ = 154.6, 137.1, 127.4, 118.3, 104.1, 103.0, 55.6.

The spectroscopic data closely match the ones previously reported in the literature [8].

4-(Trifluoromethoxy) benzene-1,2-diamine **3j**



The title compound was synthesized according to the general procedure **A. 2j** (222.12 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3j** as a yellow solid (178.69 mg, 0.93 mmol, 93%).

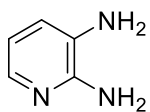
¹H NMR (600 MHz, CDCl₃) δ = 6.65 (d, *J* = 8.1 Hz, 1H), 6.58 – 6.56 (m, 2H), 3.40 (bs, 4H).

¹³C NMR (151 MHz, CDCl₃) δ = 142.9, 136.0, 133.2, 121.6, 119.9, 117.0, 112.4, 109.6.

¹⁹F NMR (565 MHz, CDCl₃) δ = -58.19.

HRMS: calculated for C₇H₇F₃N₂O: 193.0589 [*M*+*H*]⁺; found: 193.0580.

Pyridine-2,3-diamine **3o**



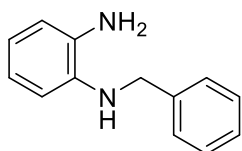
The title compound was synthesized according to the general procedure **A. 2o** (139.11 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used, to afford **3o** as a yellow solid (103.67 mg, 0.95 mmol, 95%).

¹H NMR (600 MHz, CDCl₃) δ = 7.65 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.88 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.62 (dd, *J* = 7.5, 5.0 Hz, 1H), 4.26 (bs, 2H), 3.31 (bs, 2H).

^{13}C NMR (151 MHz, CDCl_3) δ = 149.4, 138.9, 129.2, 122.6, 115.8.

The spectroscopic data closely match the ones previously reported in the literature [6].

N^1 -Benzylbenzene-1,2-diamine **3p**



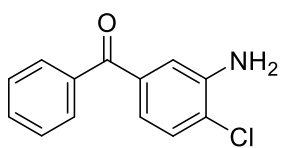
The title compound was synthesized according to the general procedure A. **2p** (228.25 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μL of distilled water were used, to afford **3p** as a white solid (158.62 mg, 0.80 mmol, 80%).

^1H NMR (600 MHz, CDCl_3) δ = 7.42 – 7.40 (m, 2H), 7.36 (dd, J = 8.4, 6.8 Hz, 2H), 7.30 (d, J = 7.3 Hz, 1H), 6.81 (td, J = 7.5, 1.6 Hz, 1H), 6.75 (dd, J = 7.6, 1.6 Hz, 1H), 6.72 – 6.68 (m, 2H), 4.33 (s, 2H), 3.47 (bs, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ = 139.6, 137.9, 134.3, 128.8, 127.9, 127.4, 120.9, 119.0, 116.7, 112.2, 48.8.

The spectroscopic data closely match the ones previously reported in the literature [9].

(3-Amino-4-chlorophenyl) (phenyl)methanone **3s**



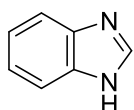
The title compound was synthesized according to the general procedure A. **2s** (261.66 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μL of distilled water were used, to afford **3s** as a yellowish solid (220.10 mg, 0.94 mmol, 94%).

^1H NMR (600 MHz, CDCl_3) δ = 7.79 – 7.77 (m, 2H), 7.60 – 7.57 (m, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.34 (d, J = 8.2 Hz, 1H), 7.22 (d, J = 2.0 Hz, 1H), 7.07 (dd, J = 8.2, 2.0 Hz, 1H), 4.21 (bs, 2H).

^{13}C NMR (151 MHz, CDCl_3) δ = 196.1, 143.1, 137.6, 137.2, 132.6, 130.1, 129.3, 128.4, 123.6, 120.9, 116.9.

HRMS: calculated for $\text{C}_{13}\text{H}_{10}\text{ClNO}$: 232.0529 $[M+H]^+$; found: 232.0523.

1H-Benzo[d]imidazole **4d**



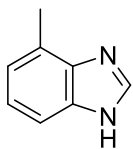
The title compound was synthesized according to the general procedure C. **2d** (138.13 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μL of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μL of distilled water were added. Lastly, an additional silica pad was made to afford **4d** as a white solid (111.05 mg, 0.94 mmol, 94%).

^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ = 12.42 (bs, 1H), 8.20 (s, 1H), 7.58 (s, 2H), 7.19 – 7.17 (m, 2H).

^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ = 141.9, 122.1, 121.3, 119.0, 111.6.

The spectroscopic data closely match the ones previously reported in the literature [10].

4-Methyl-1H-benzo[d]imidazole **4e**



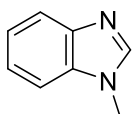
The title compound was synthesized according to the general procedure C. **2e** (152.15 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4e** as a white solid (120.27 mg, 0.91 mmol, 91%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 12.44 (bs, 1H), 8.17 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 2.52 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 141.3, 122.0, 121.7, 16.8.

The spectroscopic data closely match the ones previously reported in the literature [11].

4-Methyl-1H-benzo[d]imidazole **4f**



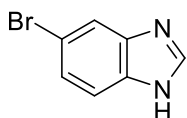
The title compound was synthesized according to the general procedure C. **2f** (152.15 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol) and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made for affording **4f** as a white solid (122.92 mg, 0.93 mmol, 93%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.17 (bs, 1H), 7.67 – 7.63 (m, 1H), 7.55 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H), 7.21 (td, *J* = 7.5, 1.2 Hz, 1H), 3.83 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 144.5, 143.3, 134.6, 122.2, 121.4, 119.3, 110.1, 30.6.

The spectroscopic data closely match the ones previously reported in the literature [11].

4-Methyl-1H-benzo[d]imidazole **4g**



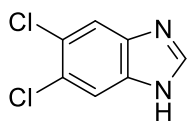
The title compound was synthesized according to the general procedure C. **2g** (217.02 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4g** as a white solid (181.28 mg, 0.92 mmol, 92%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 12.61 (s, 1H), 8.25 (s, 1H), 7.79 (s, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.32 (dd, *J* = 8.5, 1.9 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 143.3, 124.7, 114.1.

The spectroscopic data closely match the ones previously reported in the literature [12].

5,6-Dichloro-1H-benzo[d]imidazole **4h**



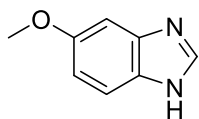
The title compound was synthesized according to the general procedure **C. 2h** (207.01 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol) and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made for affording **4h** as a white solid (168.32 mg, 0.90 mmol, 90%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.33 (s, 1H), 7.86 (s, 2H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 144.8, 124.3, 116.6.

The spectroscopic data closely match the ones previously reported in the literature [13].

5-Methoxy-1H-benzo[d]imidazole **4i**



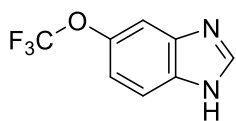
The title compound was synthesized according to the general procedure **C. 2i** (168.15 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4i** as a reddish solid (100.76 mg, 0.68 mmol, 68%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.10 (d, *J* = 5.1 Hz, 1H), 7.47 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.08 (t, *J* = 2.9 Hz, 1H), 6.81 (dd, *J* = 8.7, 2.7 Hz, 1H), 3.77 (s, 3H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 155.6, 141.5, 116.4, 111.4, 97.5, 55.4.

The spectroscopic data closely match the ones previously reported in the literature [11].

5-(Trifluoromethoxy)-1H-benzo[d]imidazole **4j**



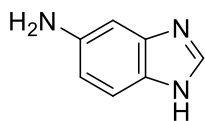
The title compound was synthesized according to the general procedure **C. 2j** (222.12 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4j** as a brownish solid (185.97 mg, 0.92 mmol, 92%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 12.69 (s, 1H), 8.34 (s, 1H), 7.67 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 2.3 Hz, 1H), 7.18 (dd, *J* = 8.7, 2.3 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 144.2, 143.6, 122.9, 121.3, 119.6, 115.6.

The spectroscopic data closely match the ones previously reported in the literature [14].

1H-Benzo[d]imidazol-5-amine **4k**



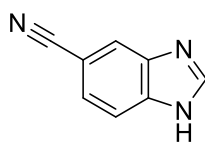
The title compound was synthesized according to the general procedure **C**. **2k** (153.14 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4k** as a brownish solid (59.9 mg, 0.45 mmol, 45%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 7.85 (s, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 6.66 (s, 1H), 6.56 (s, 2H), 6.51 (dd, *J* = 8.5, 2.1 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 144.6, 139.1, 134.6, 118.9, 111.3, 94.8.

The spectroscopic data closely match the ones previously reported in the literature [10].

1H-Benzo[d]imidazole-5-carbonitrile **4l**



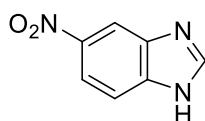
The title compound was synthesized according to the general procedure **B**. **3l** (133.15 mg, 1.00 mmol), **1** (324.36 mg, 3.00 mmol), and 200 μ L of distilled water were used. Lastly, an additional silica pad was made to afford **4l** as a brownish solid (35.79 mg, 0.25 mmol, 25%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.46 (s, 1H), 8.15 (m, 1H), 7.75 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.58 (dd, *J* = 8.3, 1.5 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 145.3, 125.3, 121.4, 120.0, 116.0, 103.8.

The spectroscopic data closely match the ones previously reported in the literature [15].

5-Nitro-1H-benzo[d]imidazole **4m**



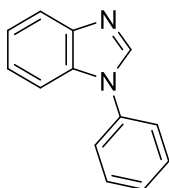
The title compound was synthesized according to the general procedure **B**. **3m** (153.14 mg, 1.00 mmol), **1** (324.36 mg, 3.00 mmol), and 200 μ L of distilled water were used. Lastly, an additional silica pad was made to afford **4m** as a brownish solid (16.31 mg, 0.10 mmol, 10%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.54 (s, 1H), 8.50 (t, *J* = 1.7 Hz, 1H), 8.11 – 8.09 (m, 1H), 7.76 (dd, *J* = 8.8, 1.3 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 146.8, 142.7, 117.6, 115.0, 112.8.

The spectroscopic data closely match the ones previously reported in the literature [10].

1-Phenyl-1H-benzo[d]imidazole **4n**



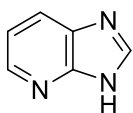
The title compound was synthesized according to the general procedure **B**. **3n** (184.24 mg, 1.00 mmol), **1** (324.36 mg, 3.00 mmol), and 200 μ L of distilled water were used. Lastly, an additional silica pad was made to afford **4n** as a pink solid (23.31 mg, 0.12 mmol, 12%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.55 (s, 1H), 7.82 – 7.76 (m, 1H), 7.67 – 7.63 (m, 2H), 7.62 – 7.56 (m, 3H), 7.49 – 7.45 (m, 1H), 7.33 – 7.28 (m, 2H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 143.9, 143.3, 136.0, 133.1, 130.1, 127.8, 123.7, 123.5, 122.5, 120.0, 110.7.

The spectroscopic data closely match the ones previously reported in the literature [11].

3H-Imidazo[4,5-*b*]pyridine **4o**



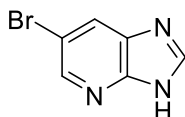
The title compound was synthesized according to the general procedure **C**. **2o** (139.11 mg, 1.00 mmol), NaOH (239.98 mg, 6.00 mmol), **1** (324.36 mg, 3.00 mmol), and 250 μ L of distilled water were used. After that, **1** (324.36 mg, 3.00 mmol) and 60 μ L of distilled water were added. Lastly, an additional silica pad was made to afford **4o** as a white solid (66.71 mg, 0.56 mmol, 56%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 12.95 (bs, 1H), 8.52 – 8.29 (m, 2H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.23 (dd, *J* = 8.0, 4.7 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 143.9, 143.7, 139.6, 117.8, 116.6, 114.4.

The spectroscopic data closely match the ones previously reported in the literature [14].

6-Bromo-3H-imidazo[4,5-*b*]pyridine **4q**



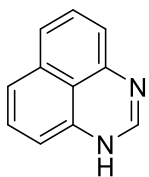
The title compound was synthesized according to the general procedure **B**. **3n** (188.03 mg, 1.00 mmol), **1** (324.36 mg, 3.00 mmol), and 200 μ L of distilled water were used. Lastly, an additional silica pad was made to afford **4n** as a pink solid (21.78 mg, 0.11 mmol, 11%).

¹H NMR (600 MHz, DMSO-*d*₆) δ = 8.48 (s, 1H), 8.43 (d, *J* = 2.2 Hz, 1H), 8.29 (d, *J* = 2.2 Hz, 1H).

¹³C NMR (151 MHz, DMSO-*d*₆) δ = 146.0, 144.6, 126.7, 113.2.

The spectroscopic data closely match the ones previously reported in the literature [16].

1H-Perimidine **4r**



The title compound was synthesized according to the general procedure **B**. **3r** (158.20 mg, 1.00 mmol), **1** (324.36 mg, 3.00 mmol), and 200 μ L of distilled water were used. Lastly, an additional silica pad was made to afford **4r** as a purple solid (100.92 mg, 0.60 mmol, 60%).

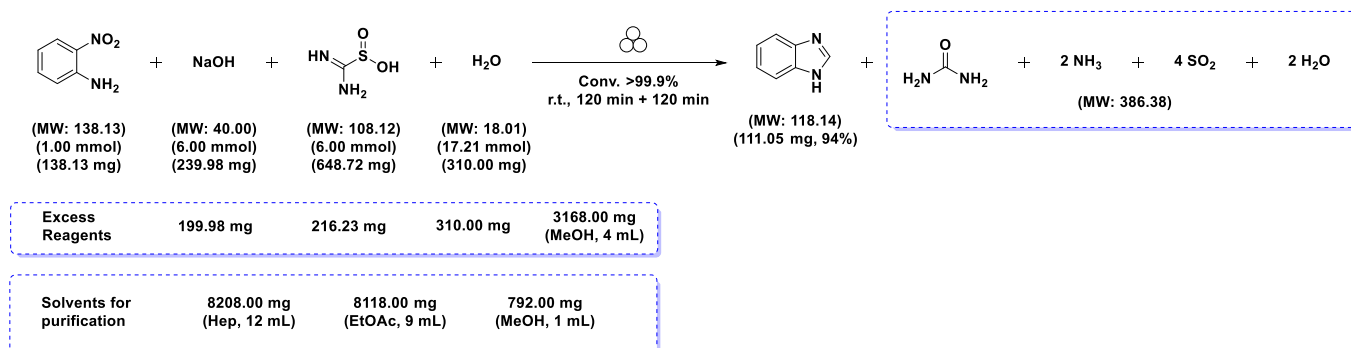
^1H NMR (600 MHz, DMSO- d_6) δ = 7.29 (s, 1H), 7.07 (t, J = 7.9 Hz, 2H), 6.97 (d, J = 8.3 Hz, 2H), 6.48 – 6.30 (m, 2H).

^{13}C NMR (151 MHz, DMSO- d_6) δ = 146.5, 135.4, 128.4, 123.0, 118.4.

The spectroscopic data closely match the ones previously reported in the literature [17].

3. Green Metrics calculations

Calculation of the Green Chemistry Metrics for the Mechanochemical Preparation of **4d**



Scheme M1. Mechanochemical preparation of **4d**.

Calculation of Green Chemistry Metrics

$$\text{Atom Economy} = \frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{118.14}{138.13 + 40.00 + 108.12 + 18.01} \times 100 = 38.8\%$$

$$\text{Environmental Factor} = \frac{\text{Mass of total waste}}{\text{Mass of desired product}} = \frac{199.98 + 216.23 + 310.00 + 386.38 + 3168.00 + 17118.00}{111.05} = 192.7$$

$$\text{Reaction Mass Efficiency} = \frac{\text{actual mass of desired product}}{\text{mass of reactants}} \times 100 = \frac{111.05}{138.13 + 239.98 + 648.72 + 310.00} \times 100 = 8.31\%$$

DOZN™ score for the mechanochemical synthesis of 4d

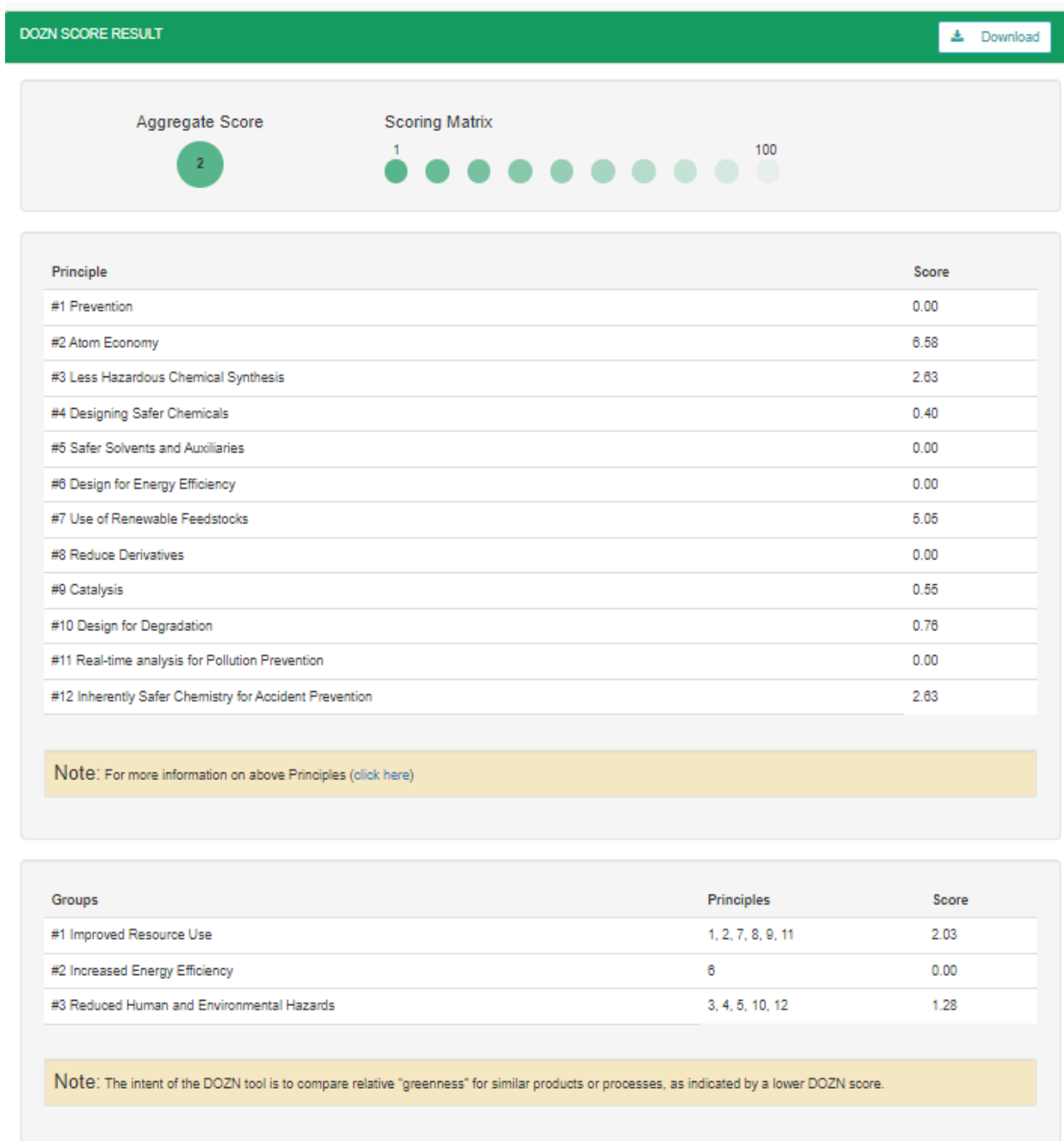
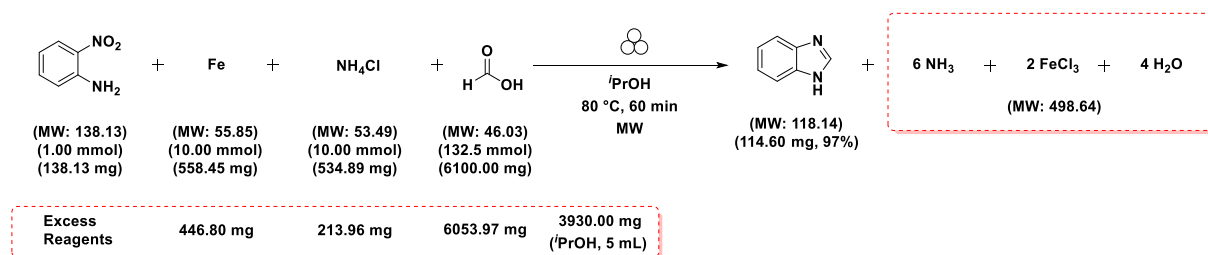


Figure S1

Calculation of the Green Chemistry Metrics for the microwave preparation of **4d**



Scheme M2. Microwave preparation of benzimidazole **4d** [18].

To the total amount of waste, the following quantities must be added:

- 1) 10 mL of 2-propanol (**7860.00 mg**) used for diluting the reaction mixture at the end of the reaction;
- 2) 20 mL of dichloromethane (**26600.00 mg**) and 5 mL of sat. aq NaHCO₃. With regards to the quantity of NaHCO₃, we based our calculations on the solubility of NaHCO₃ in water:

Solubility of NaHCO₃ in water = 96 mg/mL

Quantity of NaHCO₃ in a 5 mL sat. solution = 96 mg/mL * 5 mL = 480 mg NaHCO₃

Weight of a 5 mL sat. aq NaHCO₃ = 1,00 mg/mL * 5 mL + 480 mg NaHCO₃ = **5480 mg**

- 3) 100 mL of dichloromethane (**133000.00 mg**) for extracting the compound from the aqueous phase.
- 4) Quantity of MgSO₄ used for drying the organic mixture (NO DATA). In this case, we postulated it by considering as follows:

The quantity of water that can be found in dichloromethane is generally not higher than the 0.24% of the entire mass considered [19]. So, we assigned the quantity of anhydrous MgSO₄ used based on such data. Herein, we report all the calculi.

$$159600.00 \text{ mg CH}_2\text{Cl}_2 : 100 = X \text{ mg of H}_2\text{O dissolved in 120 mL of CH}_2\text{Cl}_2 : 0.24$$

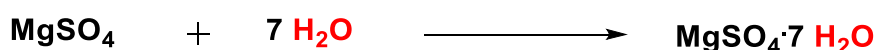
$$X = 383.04 \text{ mg of H}_2\text{O dissolved in 120 mL of CH}_2\text{Cl}_2$$

Now we estimate the moles of H₂O dissolved in 120 mL CH₂Cl₂.

$$18.00 \text{ mg H}_2\text{O} : 1.00 \text{ mmol} = 383.04 \text{ mg of H}_2\text{O dissolved in 120 mL of CH}_2\text{Cl}_2 : X \text{ mmol of H}_2\text{O dissolved in 120 mL of CH}_2\text{Cl}_2$$

$$X = 21.28 \text{ mmol of H}_2\text{O dissolved in 120 mL of CH}_2\text{Cl}_2$$

Considering the drying capacity of anhydrous MgSO₄ (1 mol of MgSO₄ is able to complex 7 mol of H₂O [19]), we can then evaluate the mg of anhydrous MgSO₄ necessary for the drying step:



Scheme M₃. MgSO₄ drying ability (CIT.)

1.00 mmol of MgSO₄ : 7.00 mmol of H₂O = X mmol of MgSO₄ required : 21.28 mmol of H₂O
dissolved in 120 mL of CH₂Cl₂

X= 3.04 mmol of MgSO₄ required

1.00 mmol of MgSO₄ : 120.37 mg of MgSO₄ = 3.04 mmol of MgSO₄ required : X mg of MgSO₄
required

X= 365.92 mg of MgSO₄ required

Calculation of Green Chemistry Metrics

$$\text{Atom Economy} = \frac{\text{Mass of desired useful product}}{\text{Total Mass of all reactants}} \times 100 = \frac{118.14}{138.13 + 55.85 + 53.49 + 46.03} \times 100 = 40.3\%$$

$$\text{Environmental Factor} = \frac{\text{Mass of total waste}}{\text{Mass of desired product}}$$

$$\text{EF} = \frac{446.80 + 213.96 + 6053.97 + 3930.00 + 498.64 + 7860 + 26600 + 5480 + 133000 + 365.92}{114.60} = 1609.5$$

$$\text{Reaction Mass Efficiency} = \frac{\text{actual mass of desired product}}{\text{mass of reactants}} \times 100$$

$$\text{RME} = \frac{114.60}{138.13 + 558.45 + 534.89 + 6100} \times 100 = 1.6\%$$

DOZN™ score for the microwave synthesis of 4d

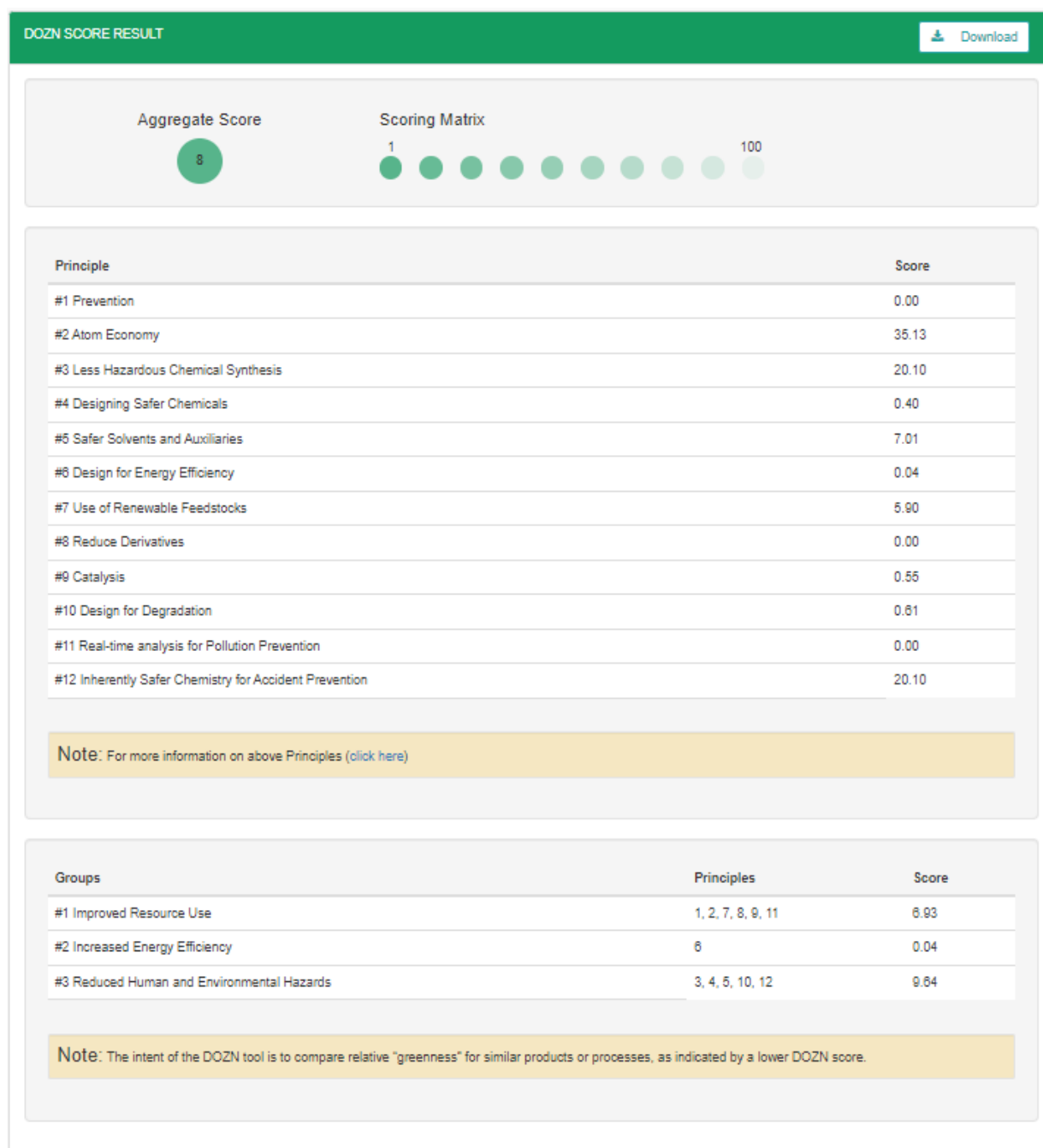
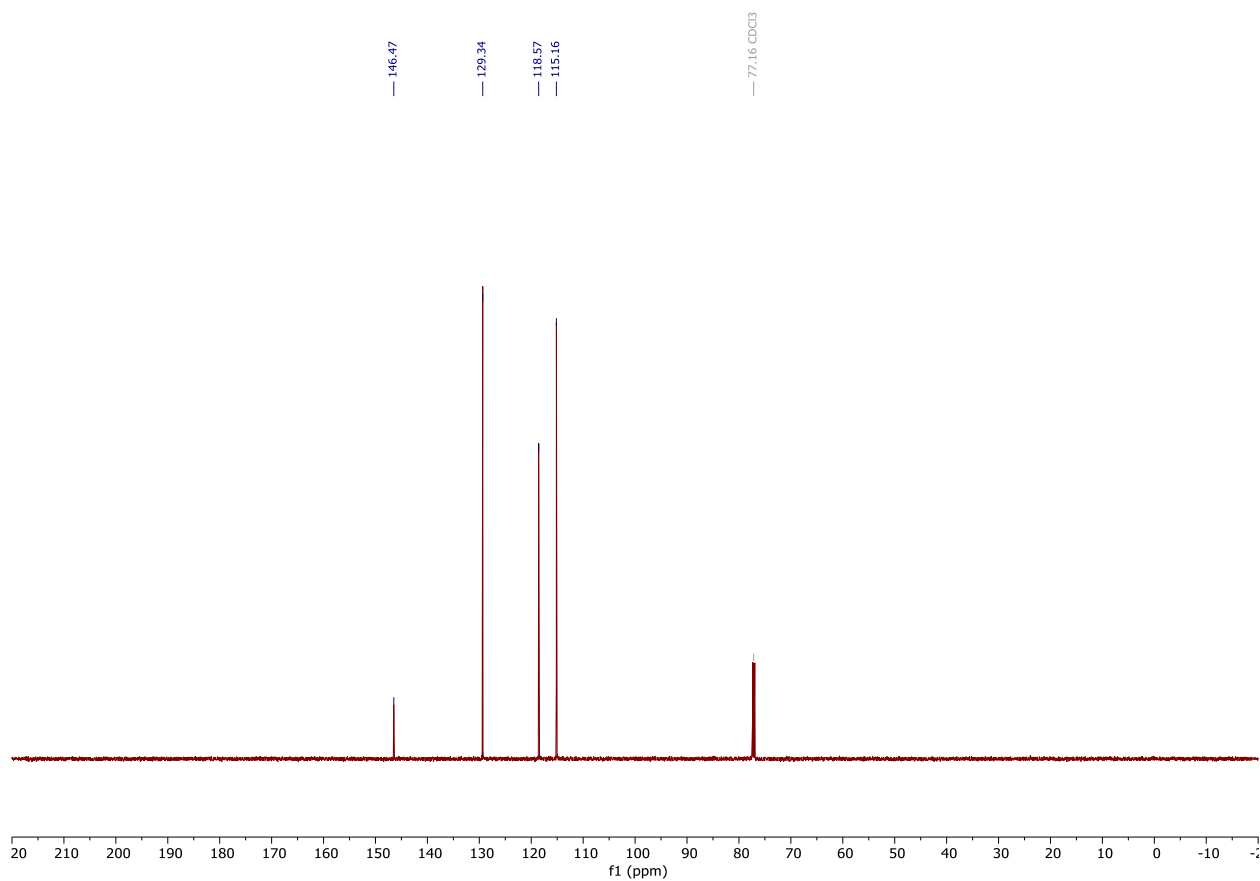
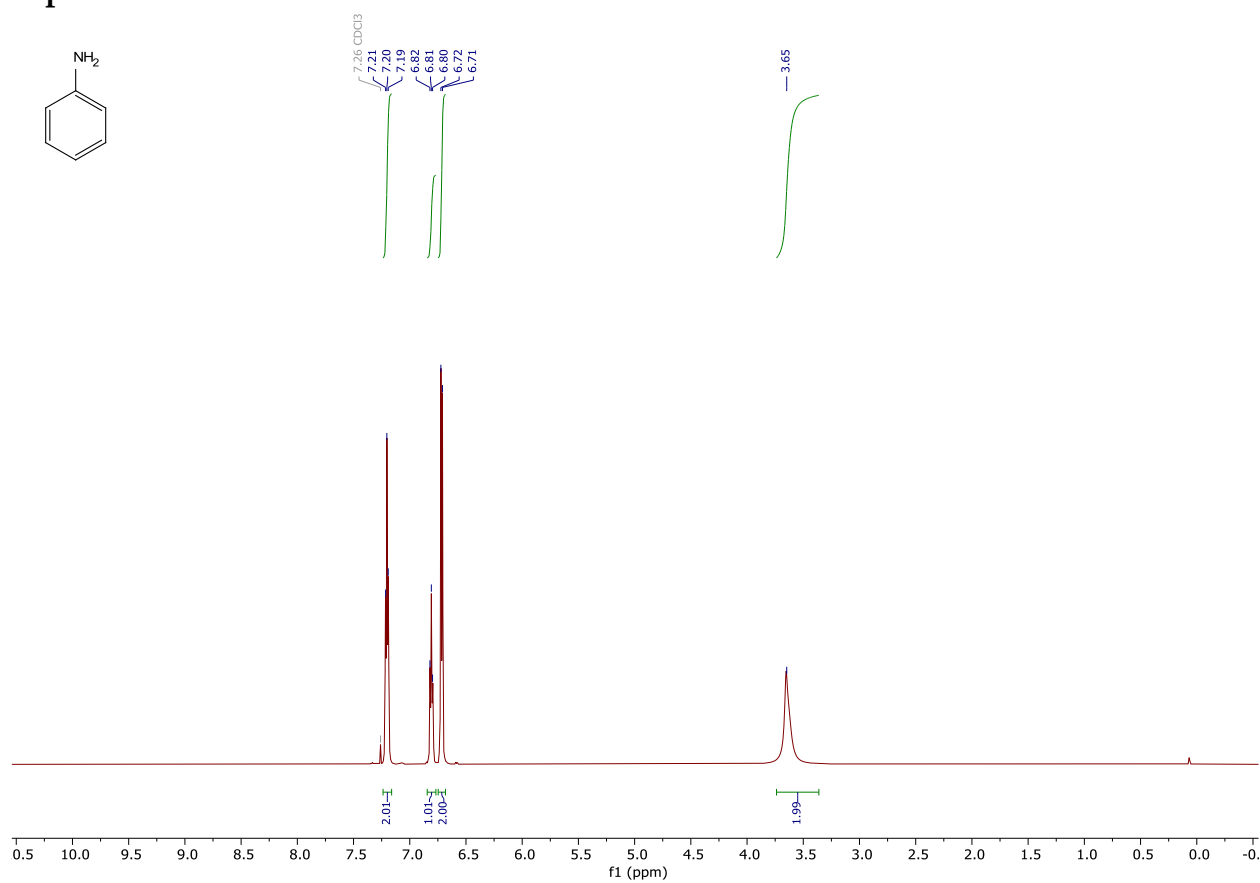
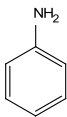
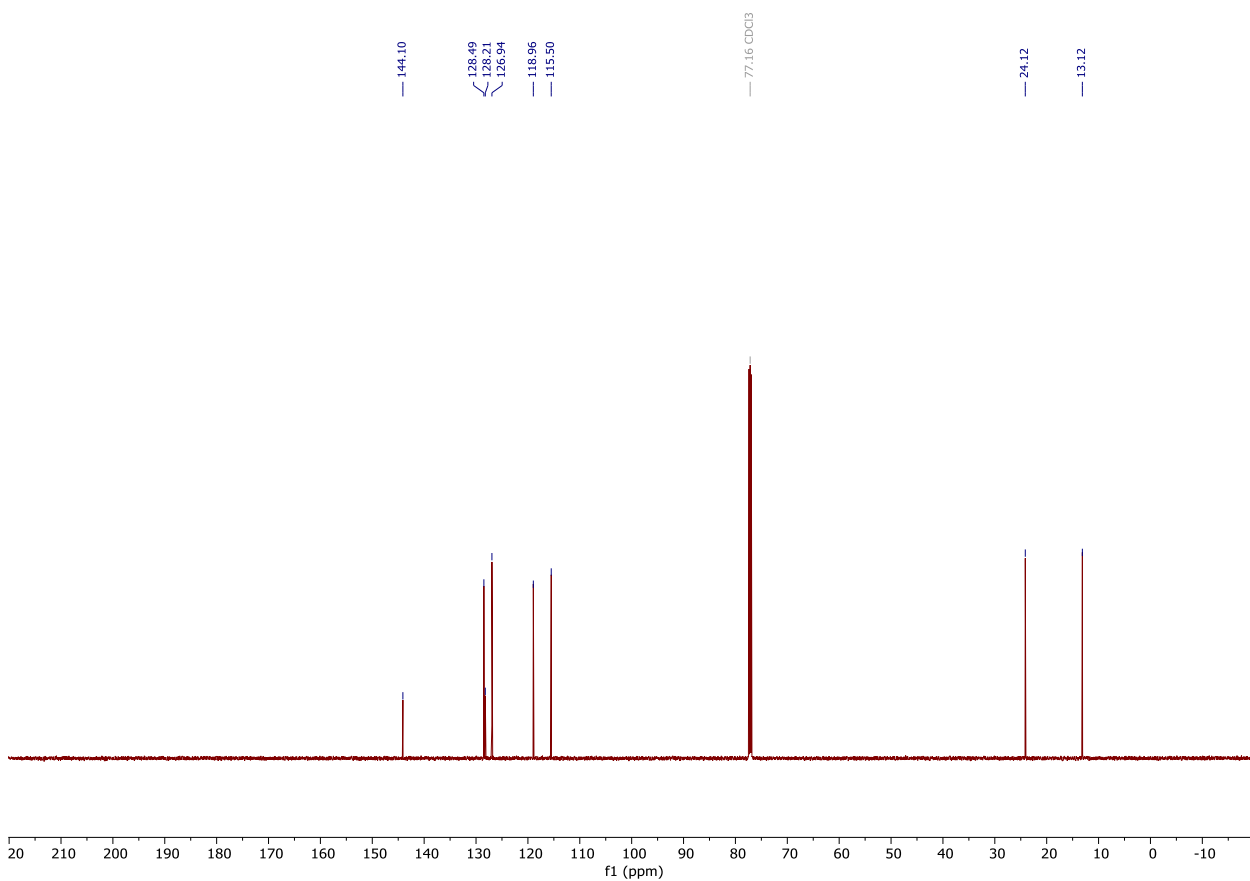
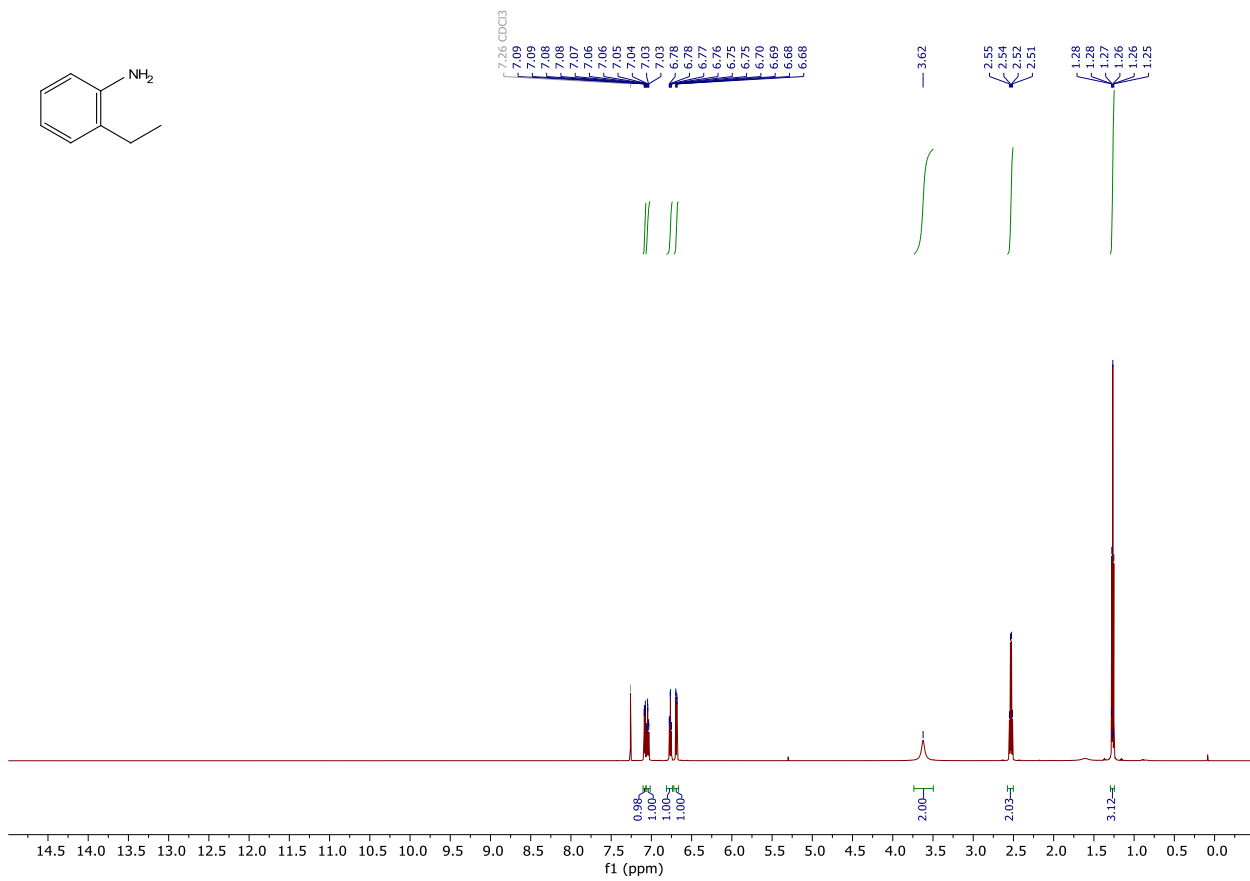
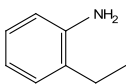
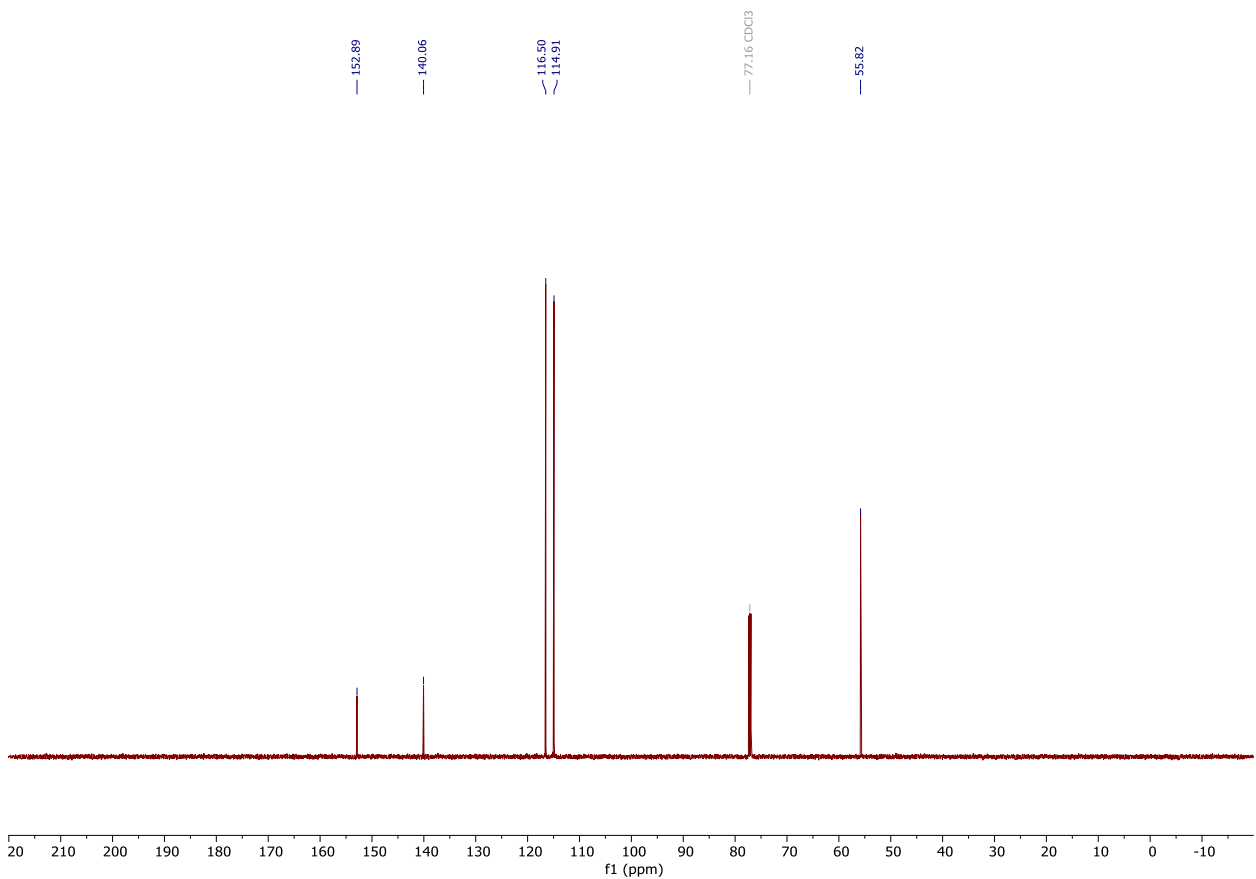
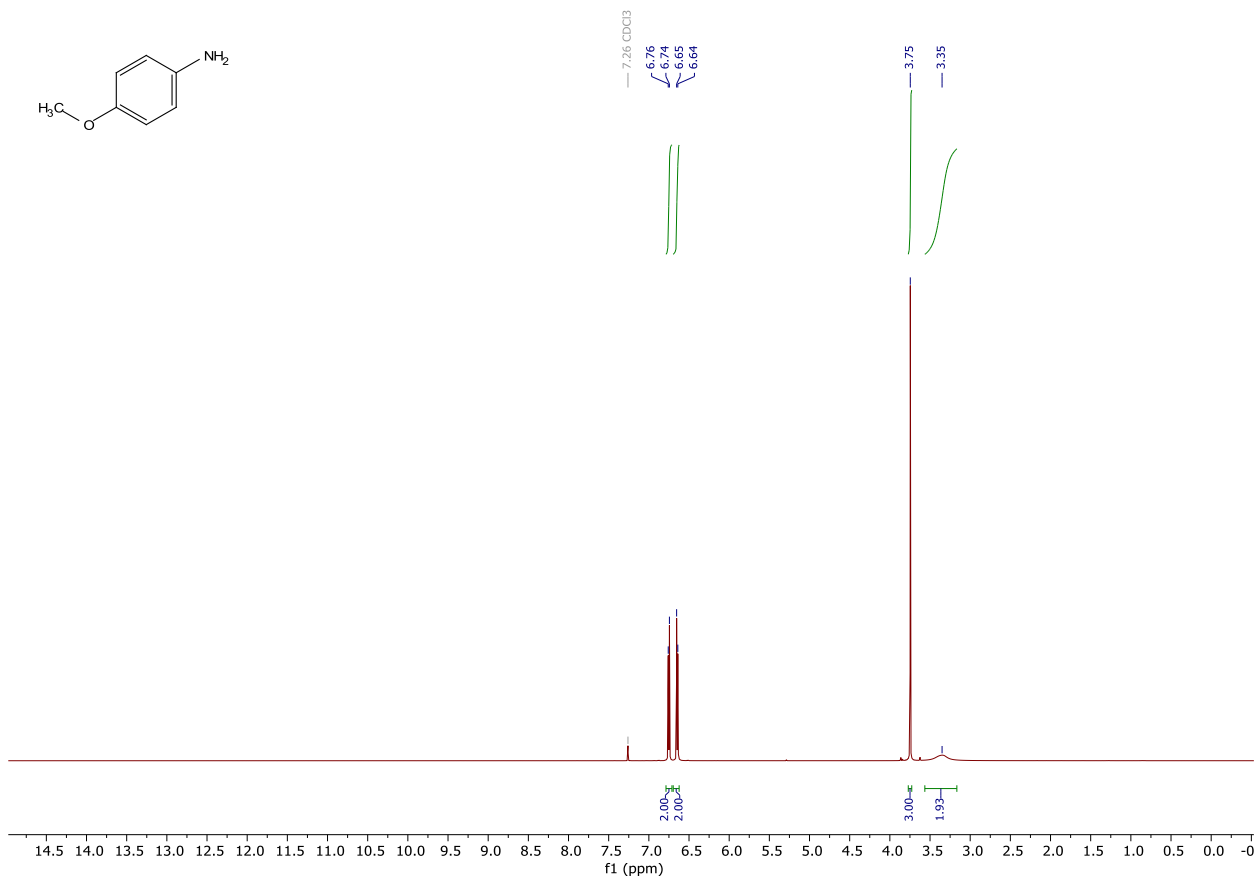
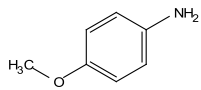


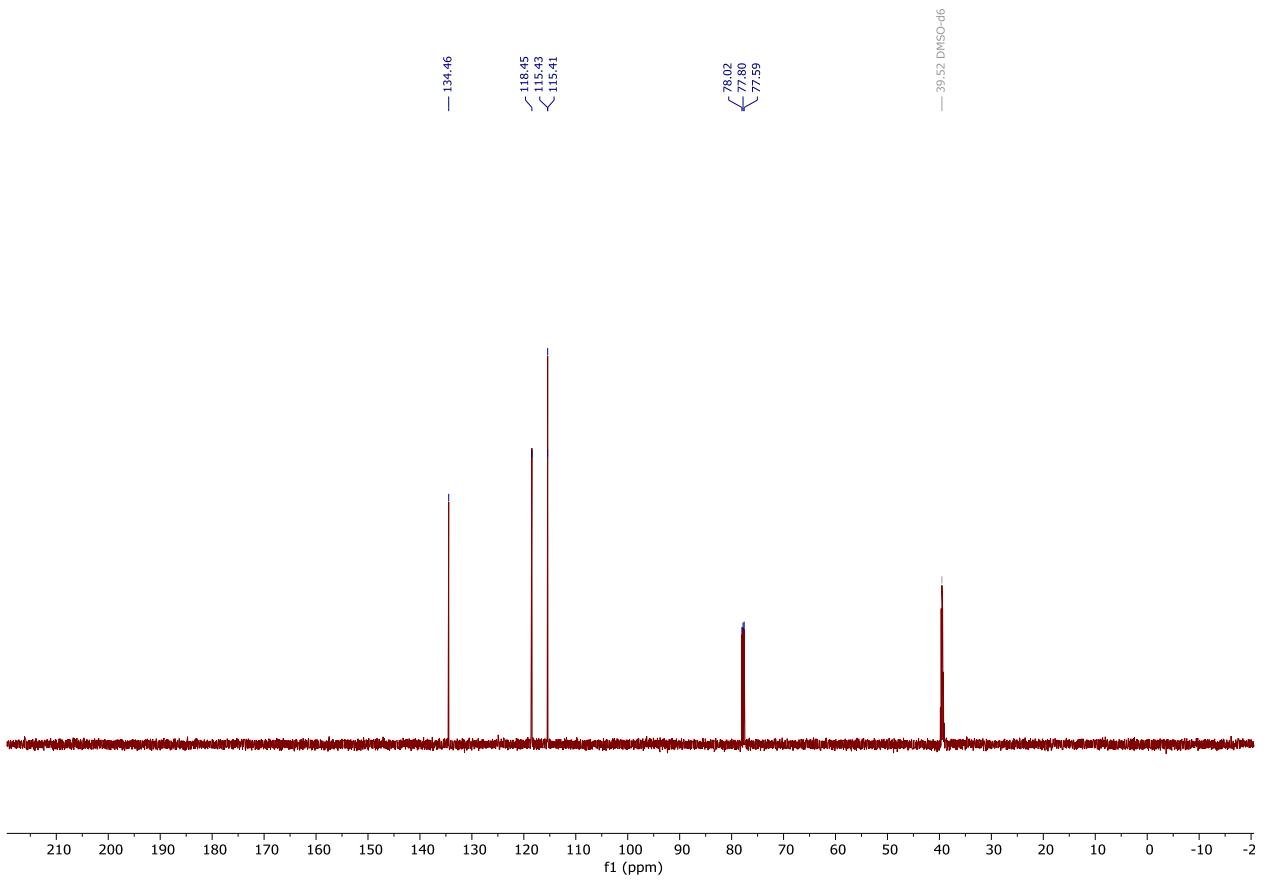
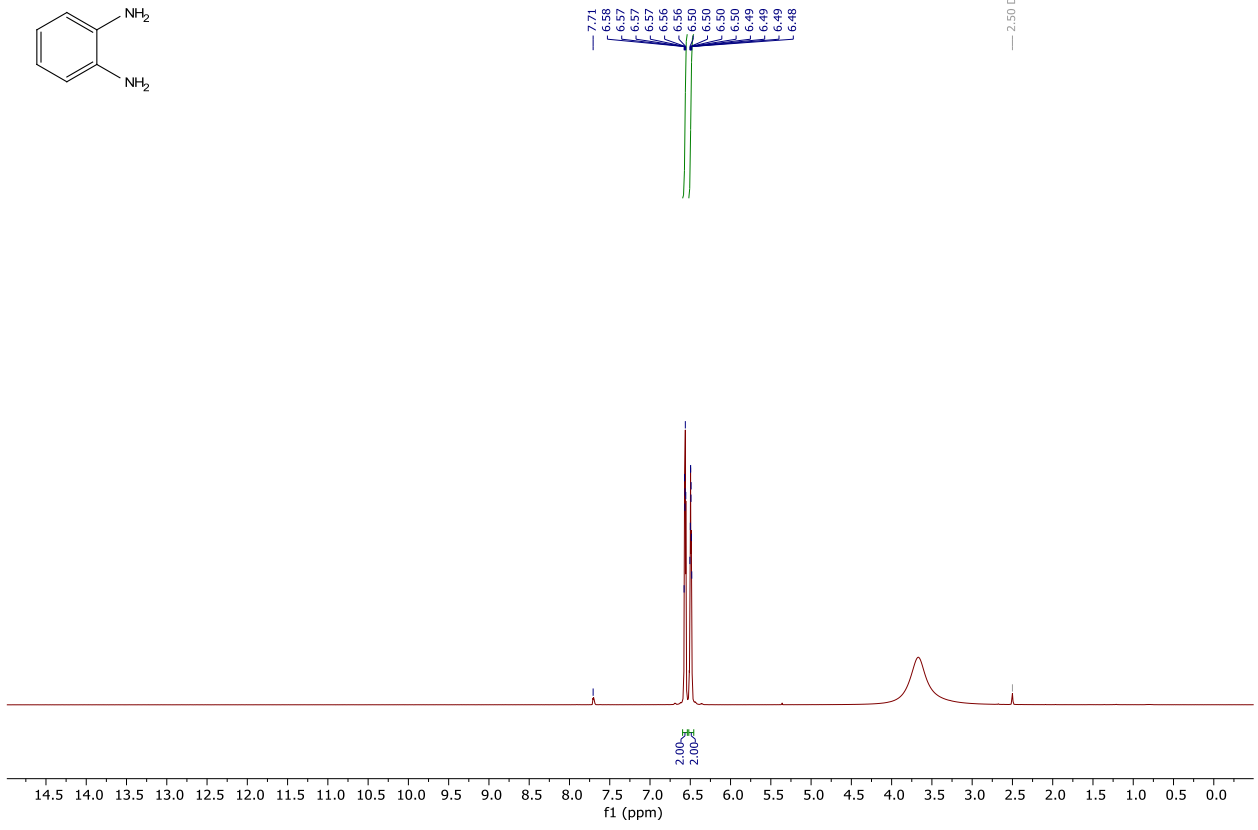
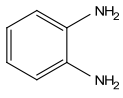
Figure S2

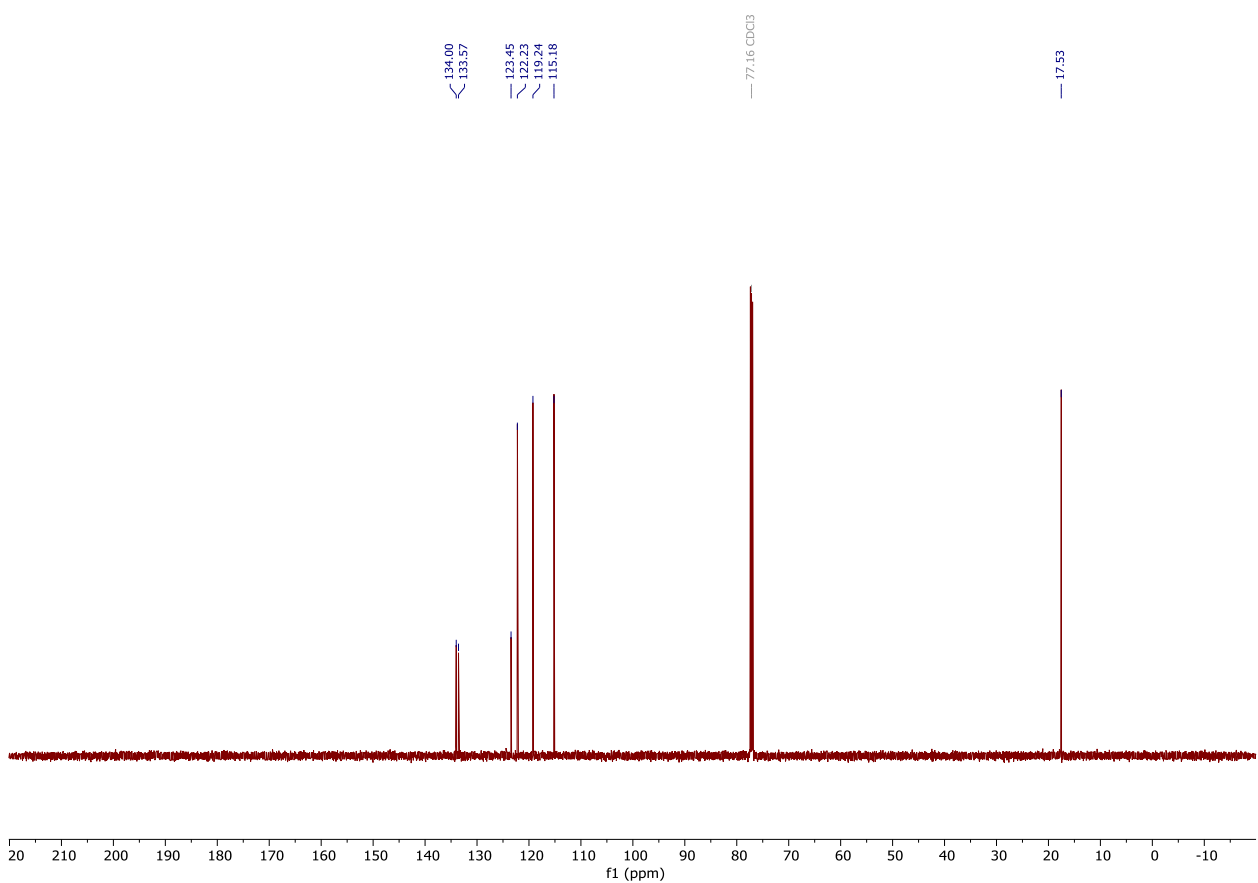
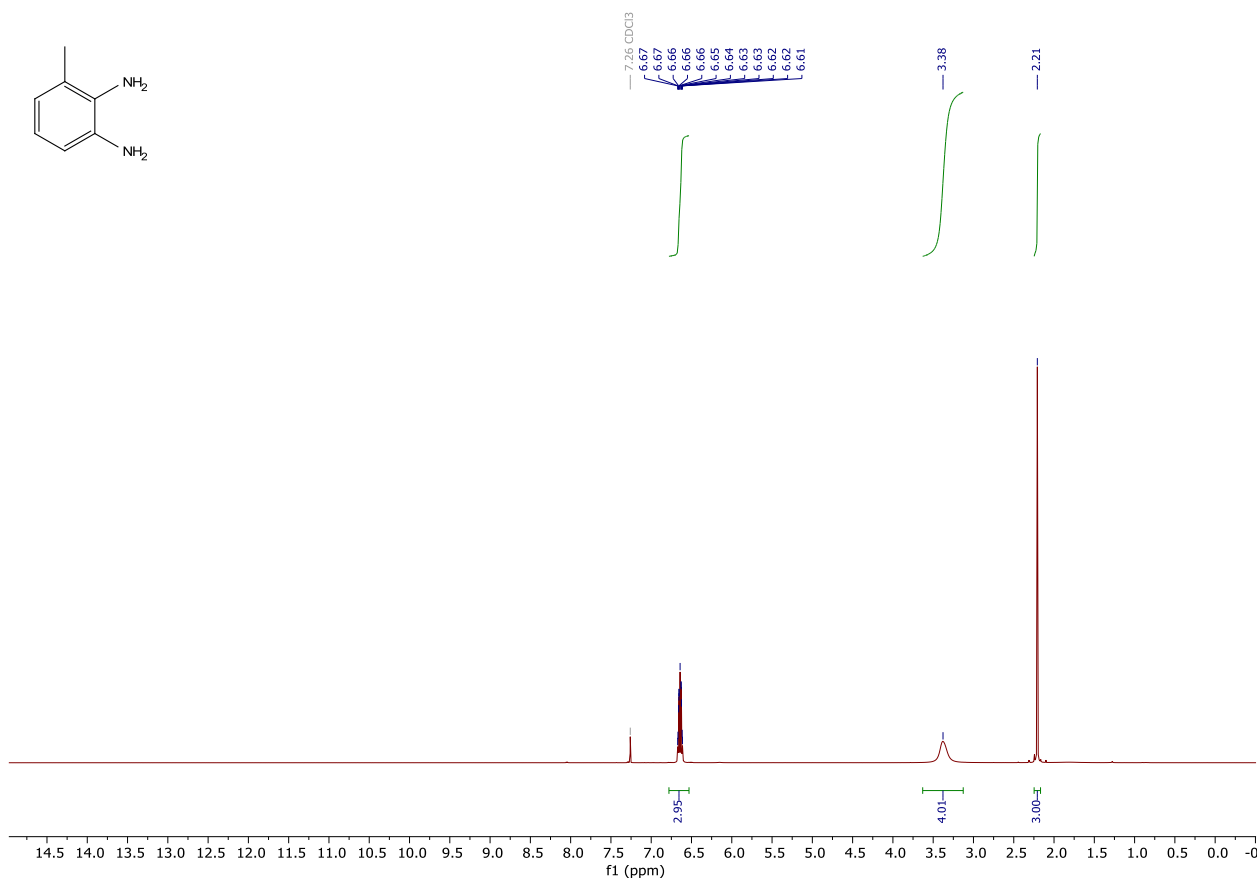
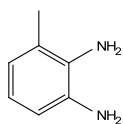
4. Spectra

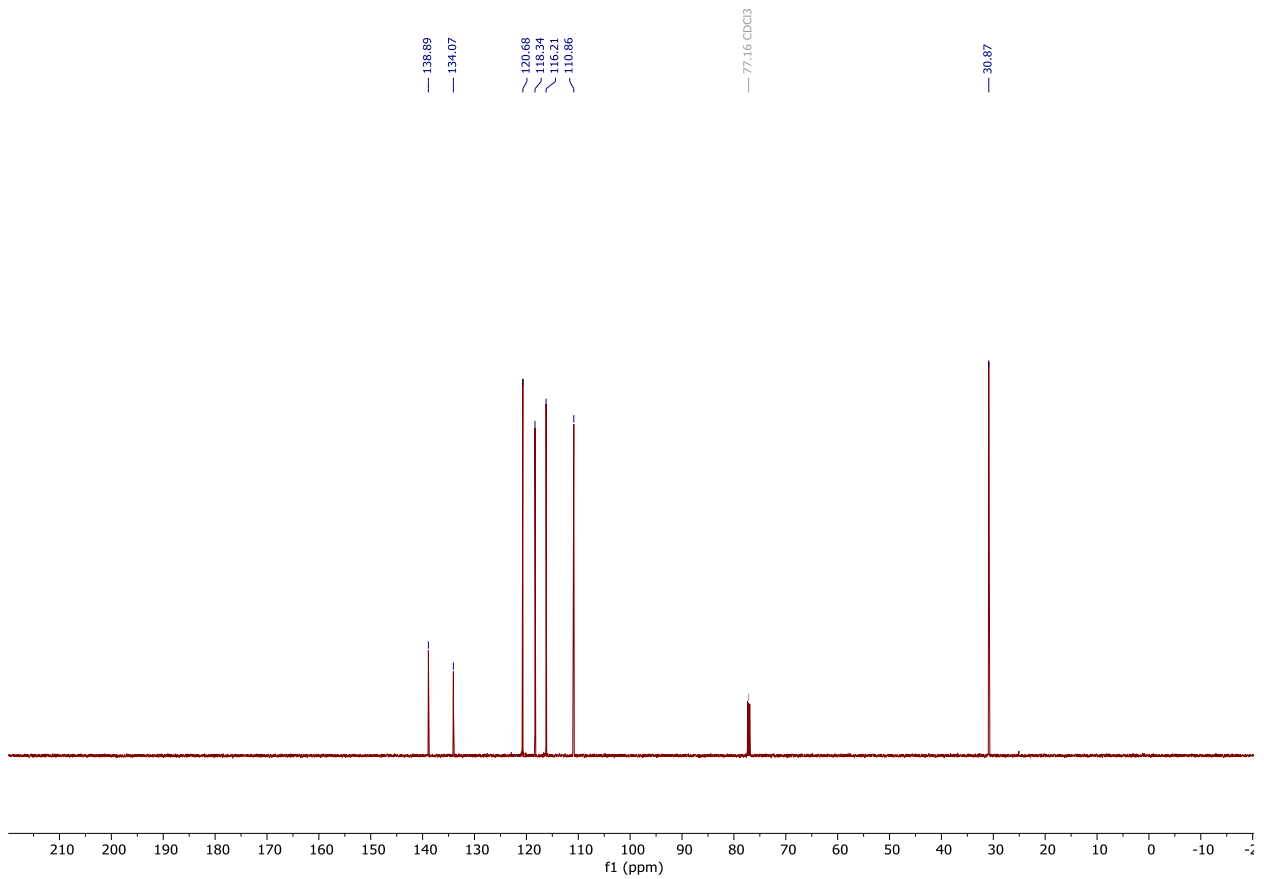
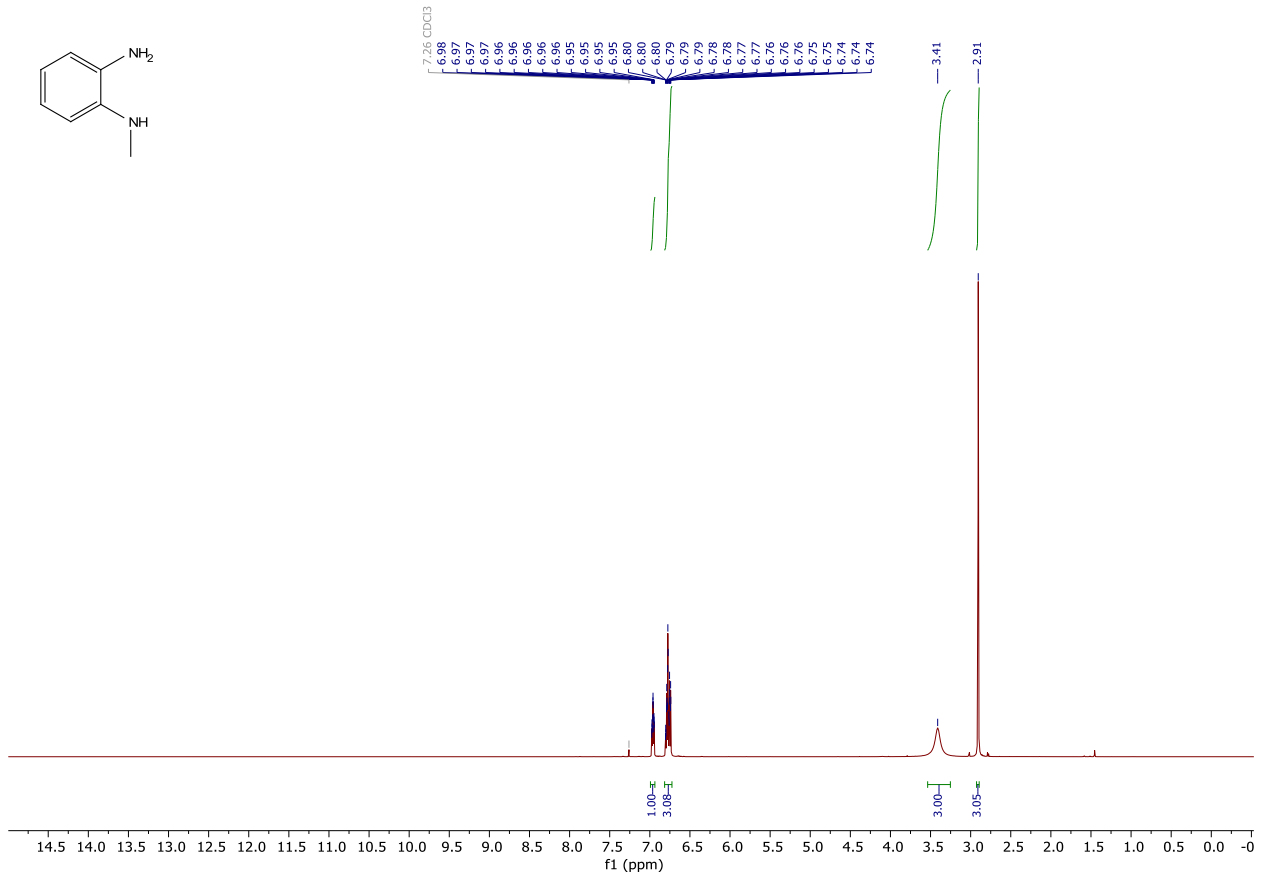
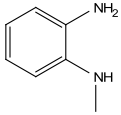


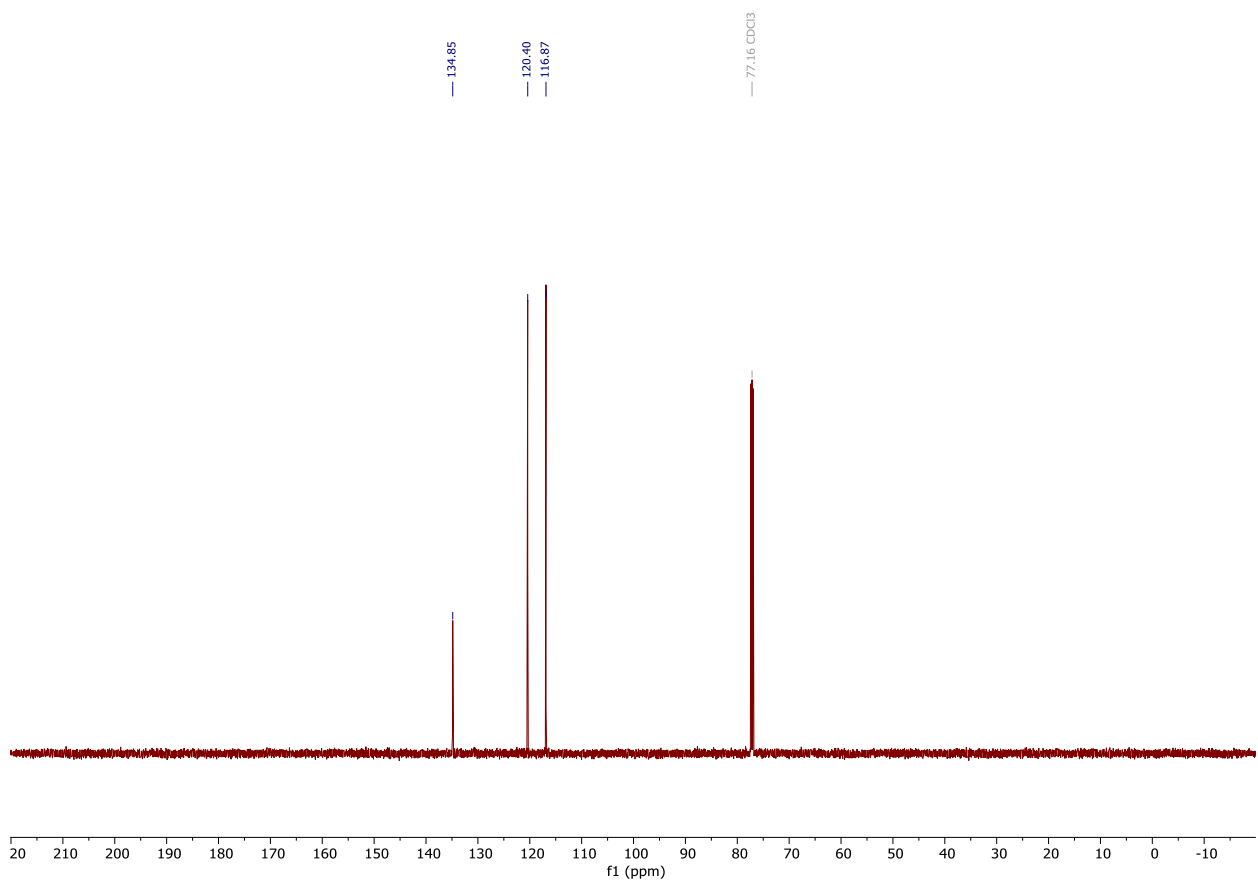
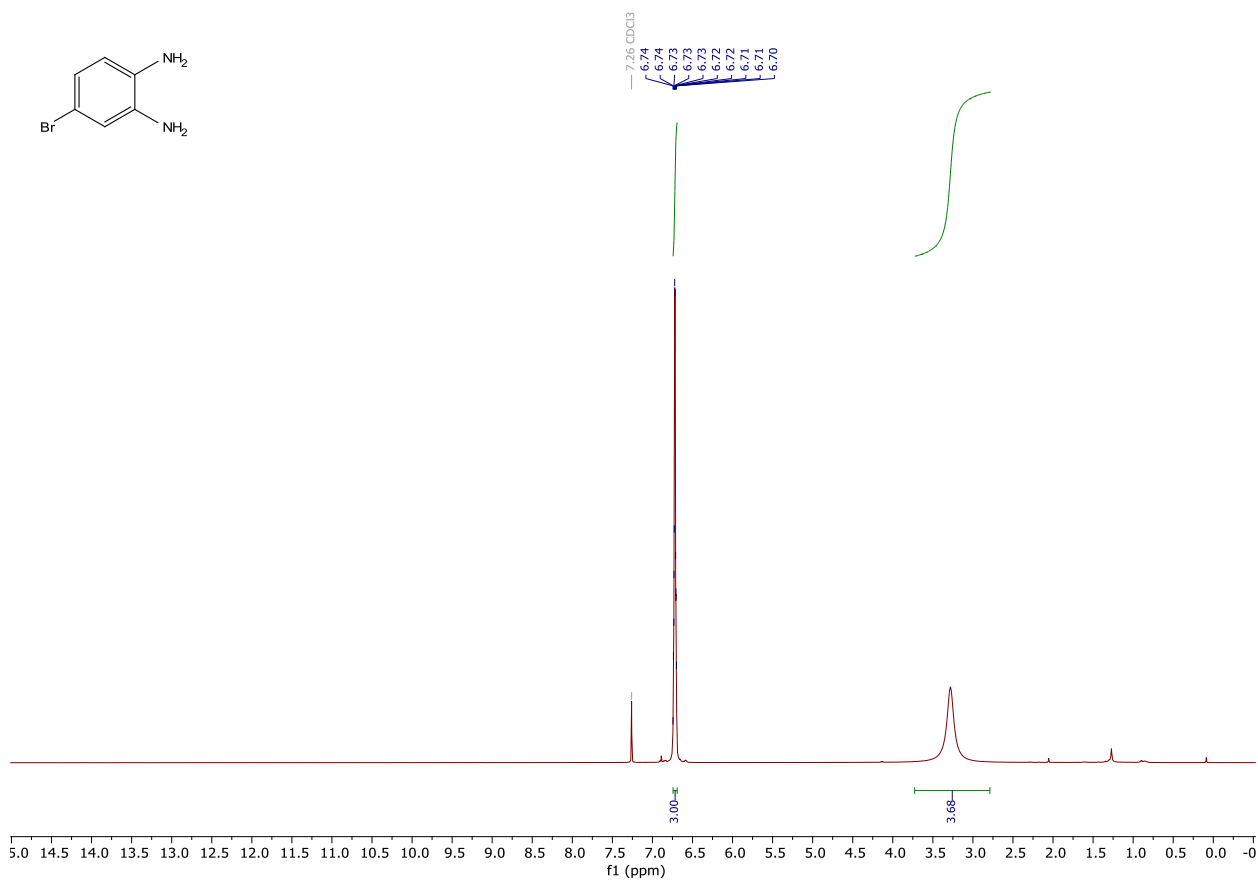
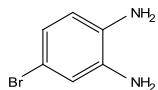


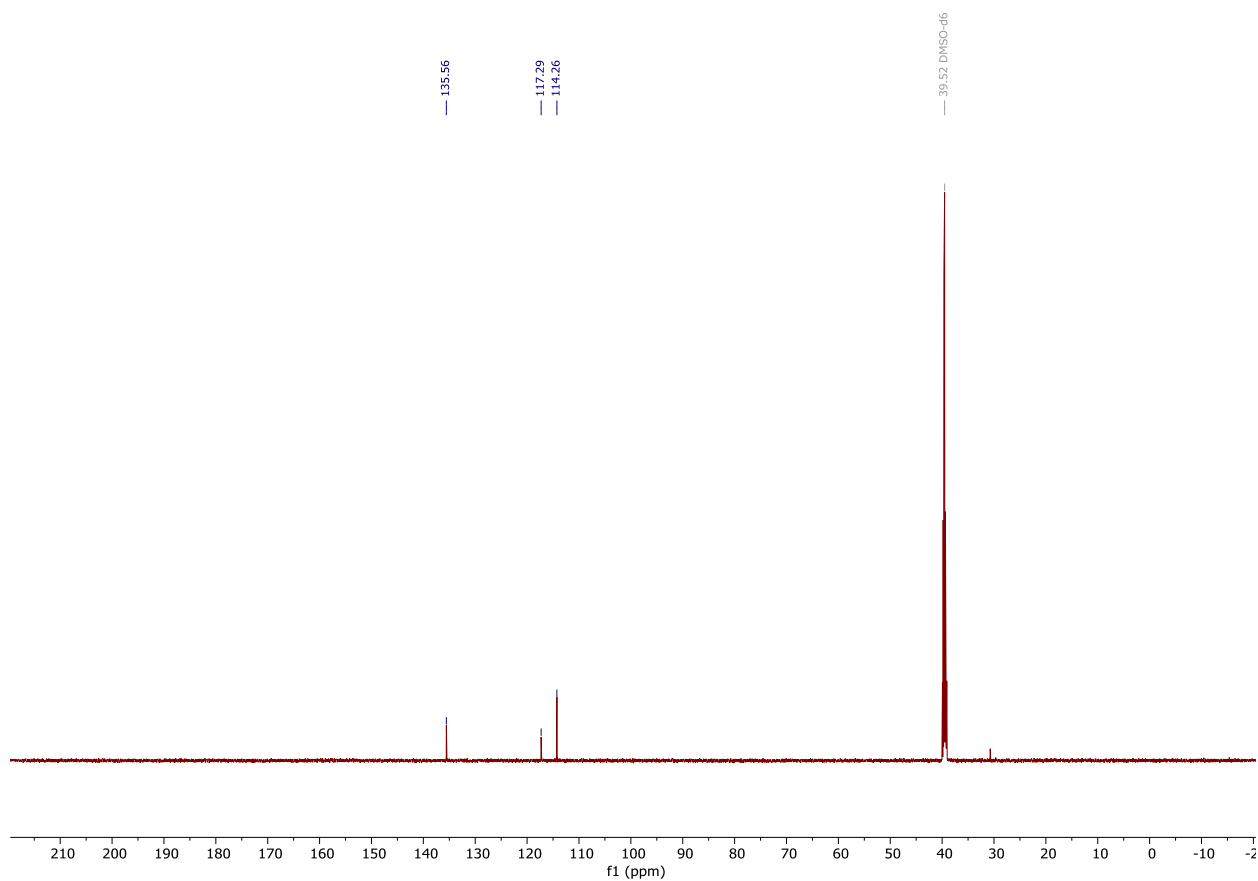
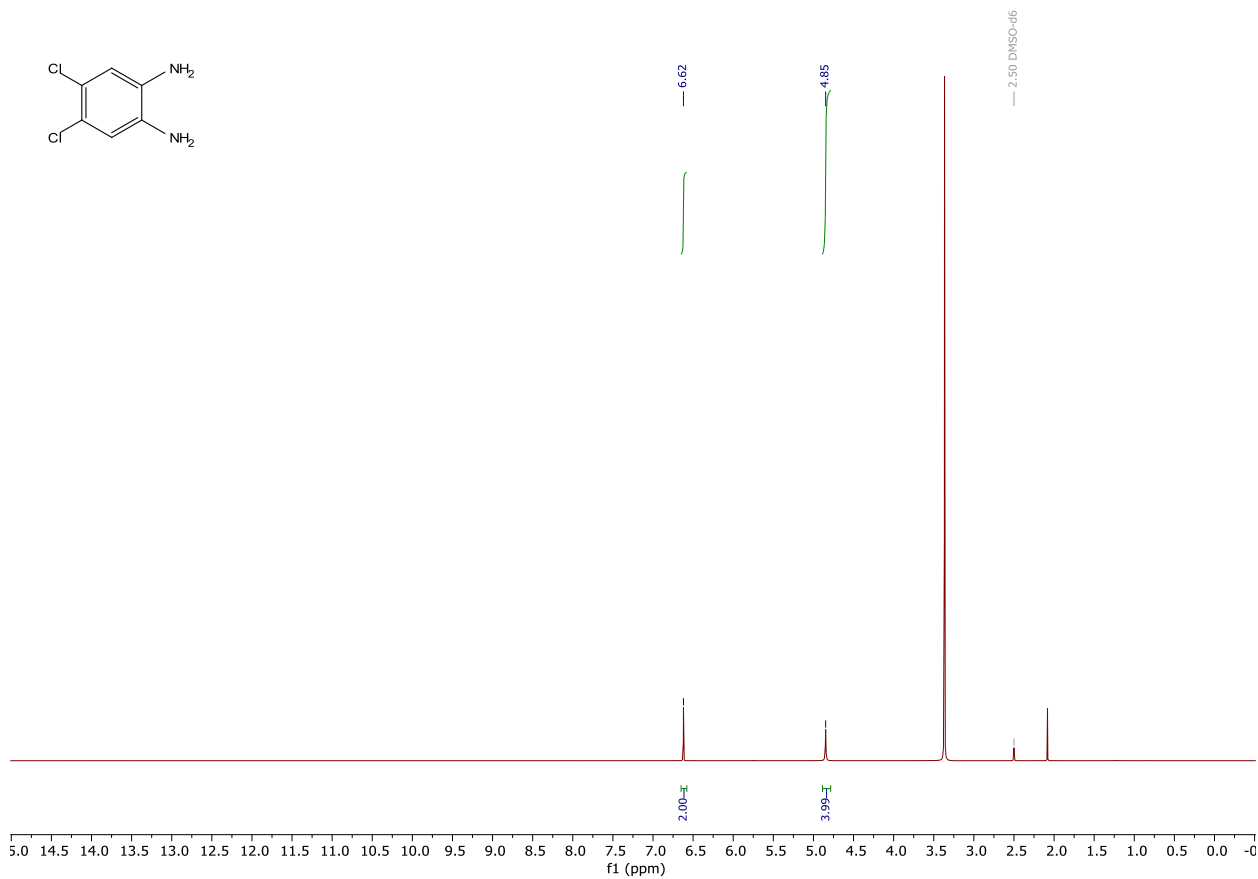
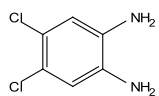


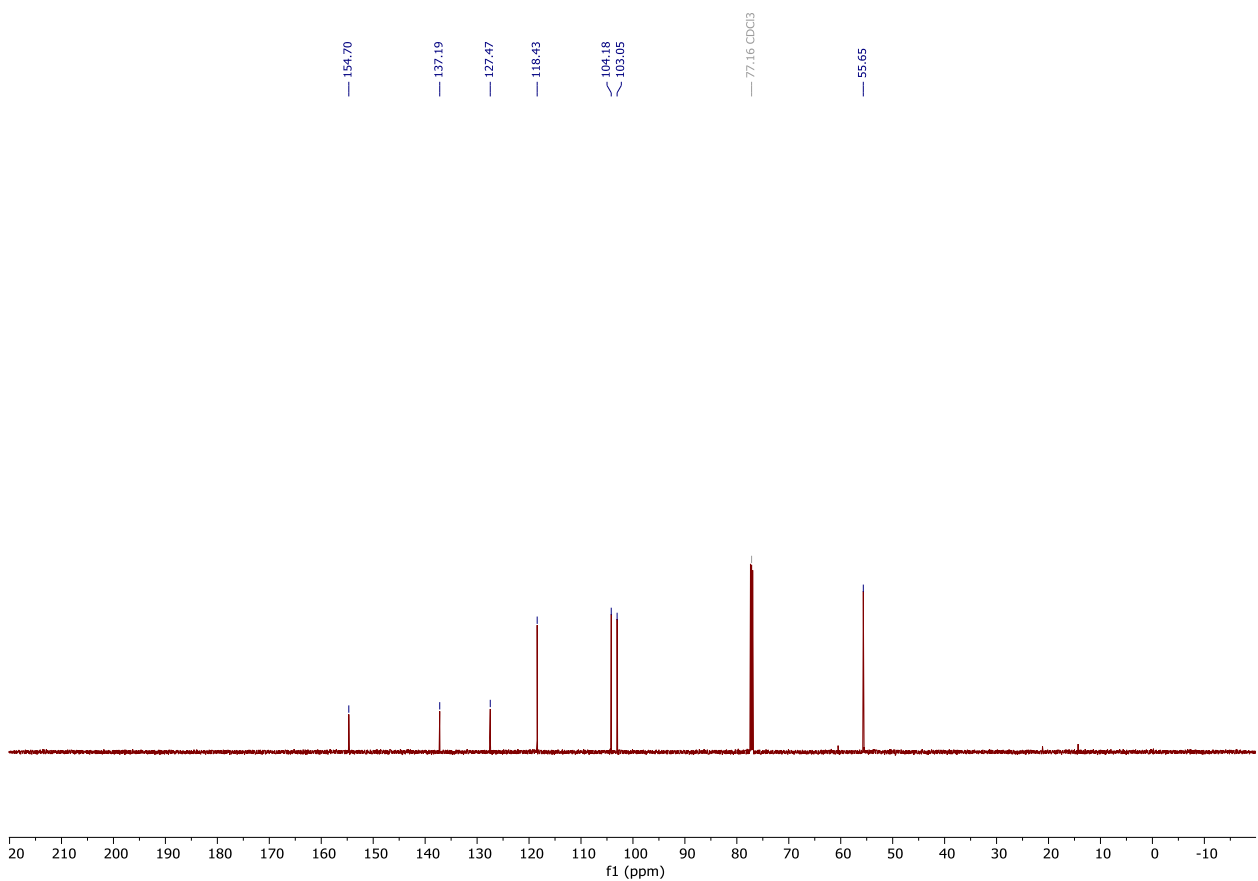
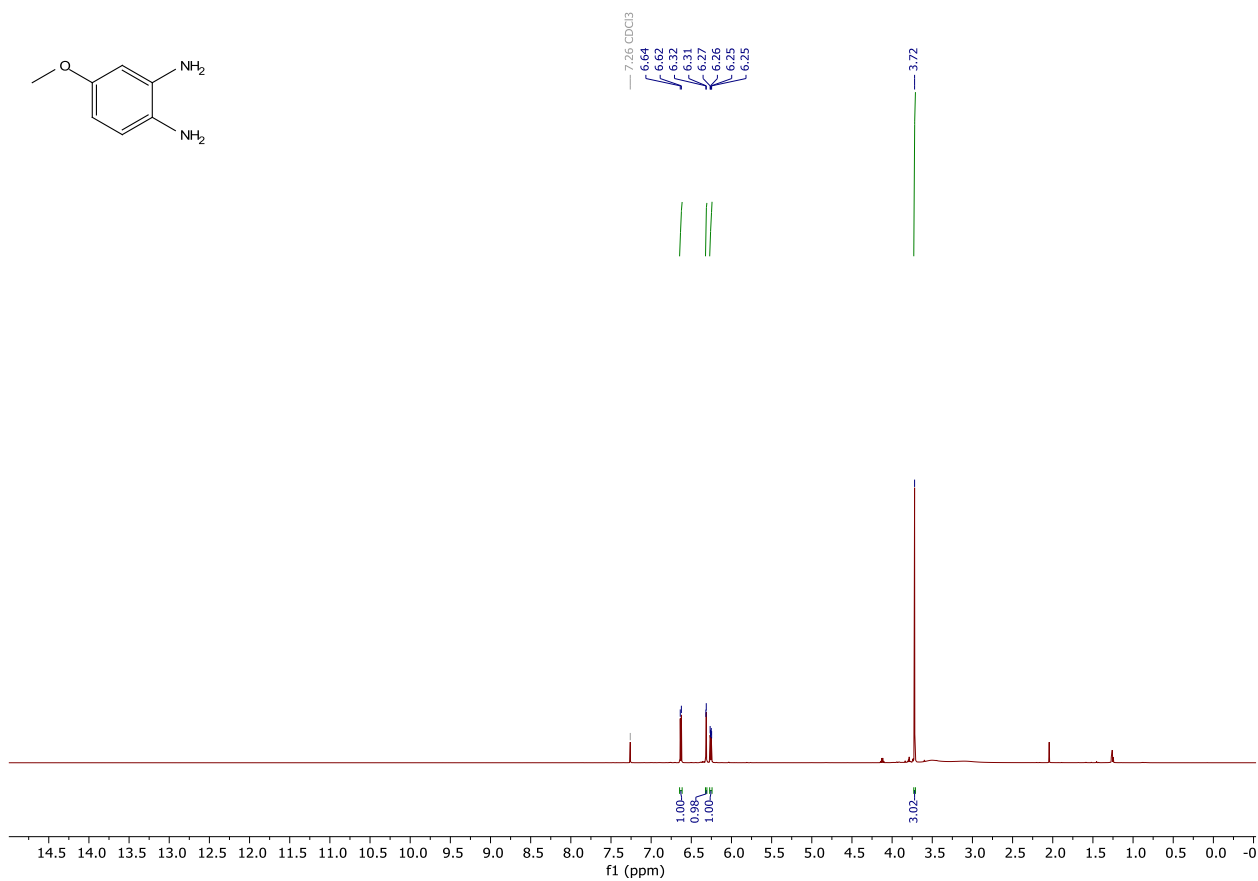
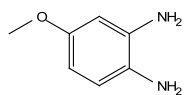


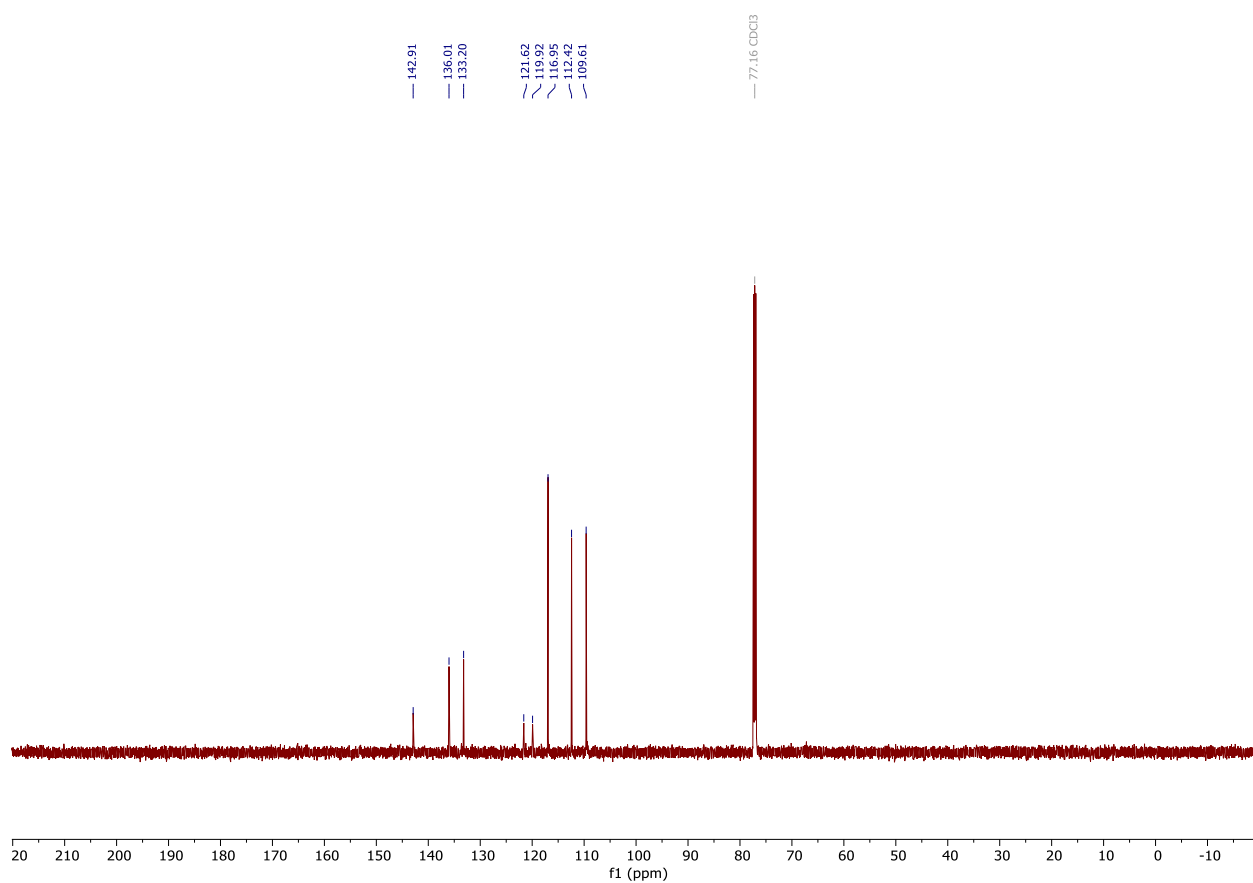
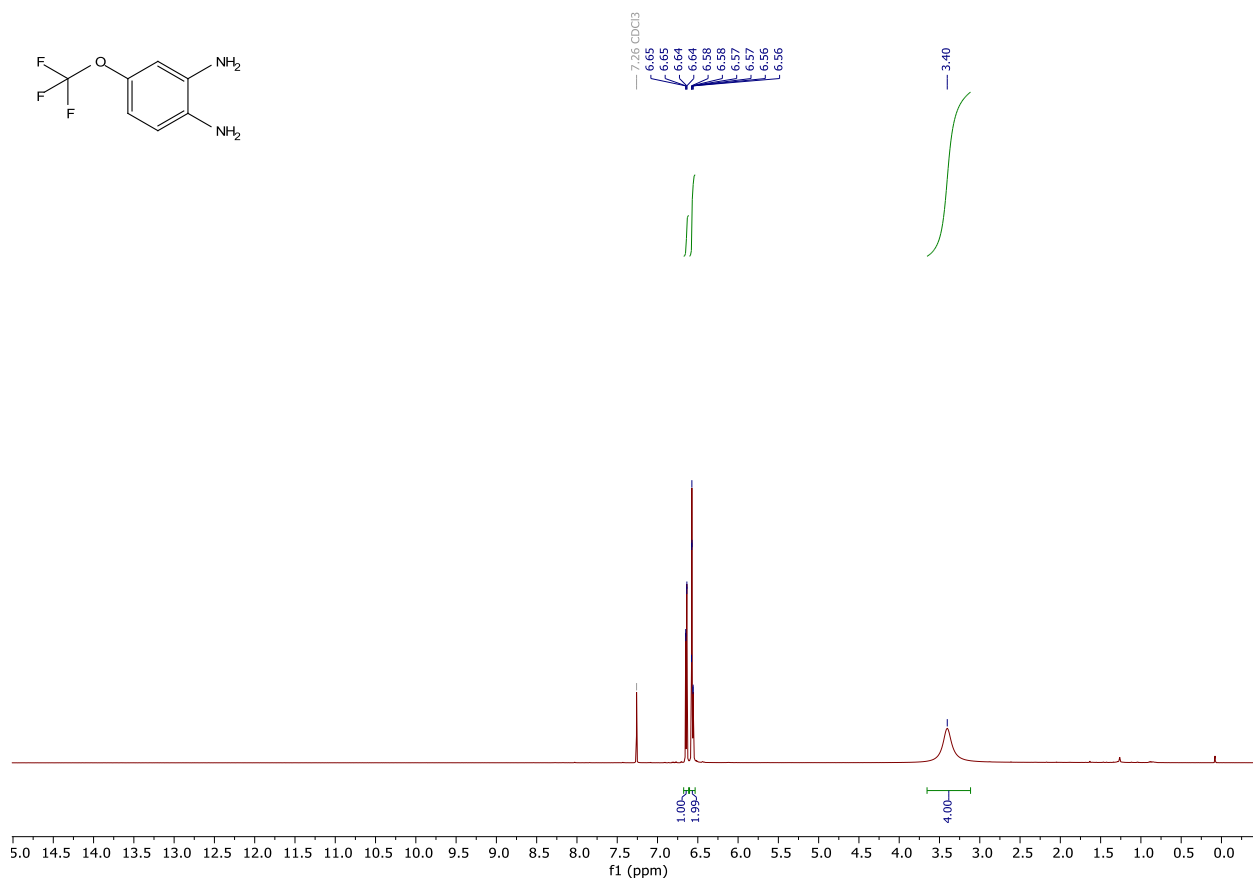
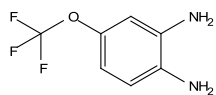


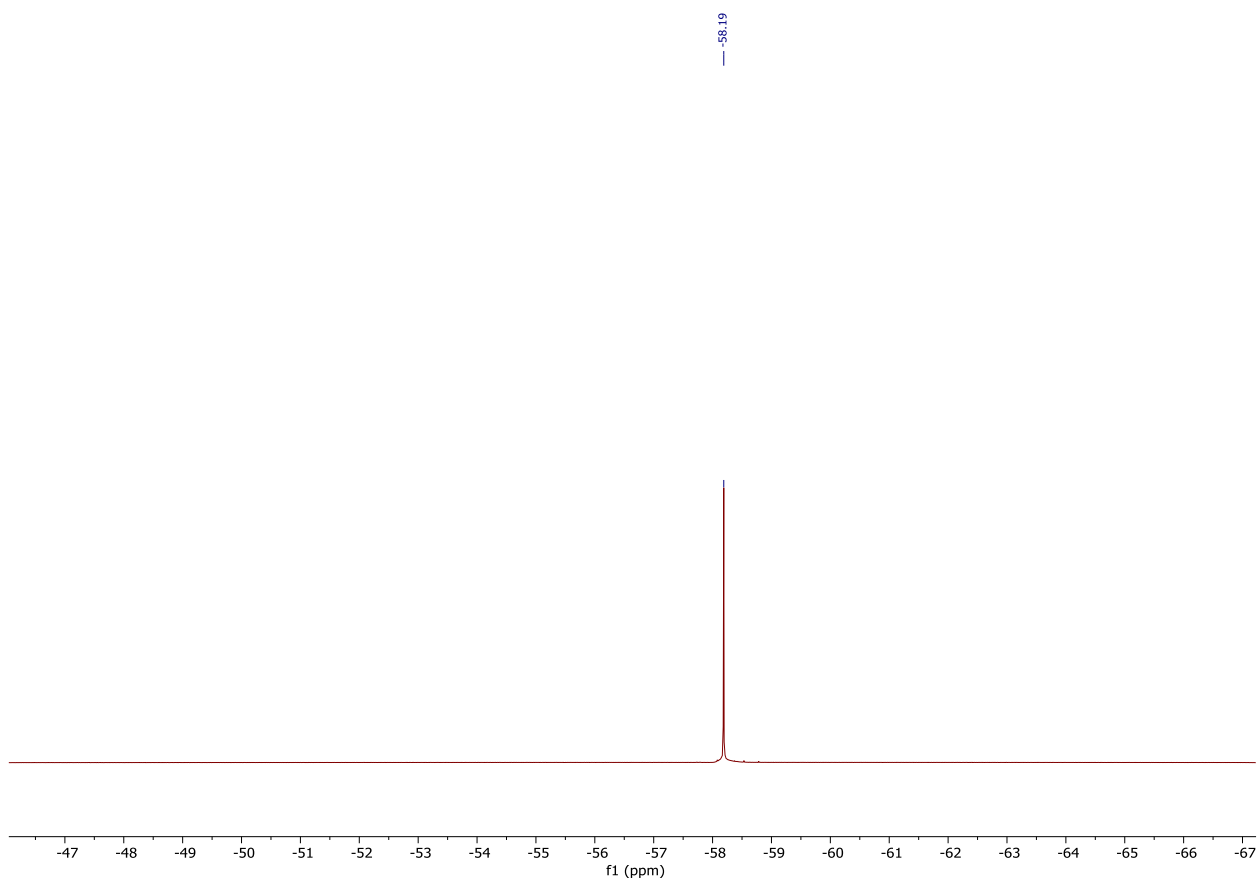


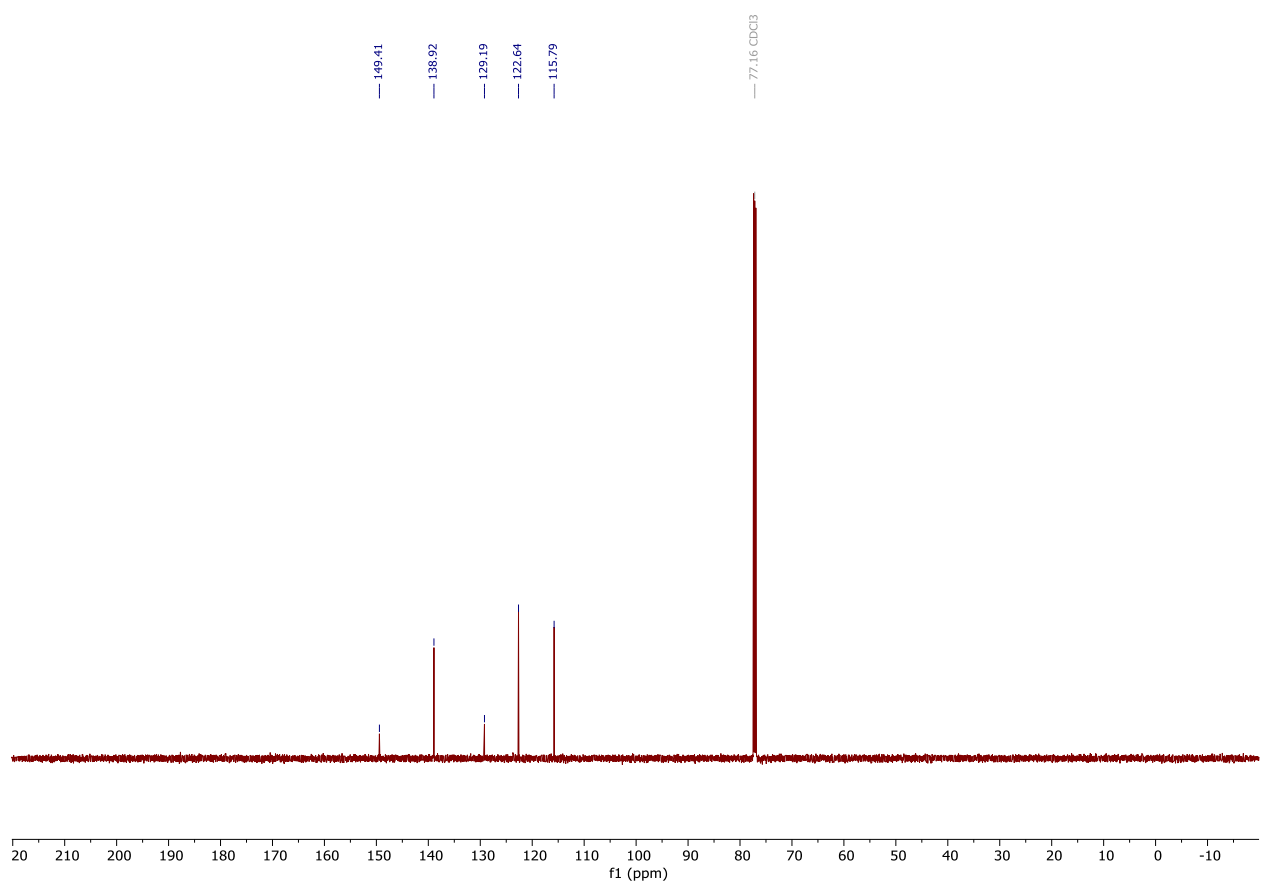
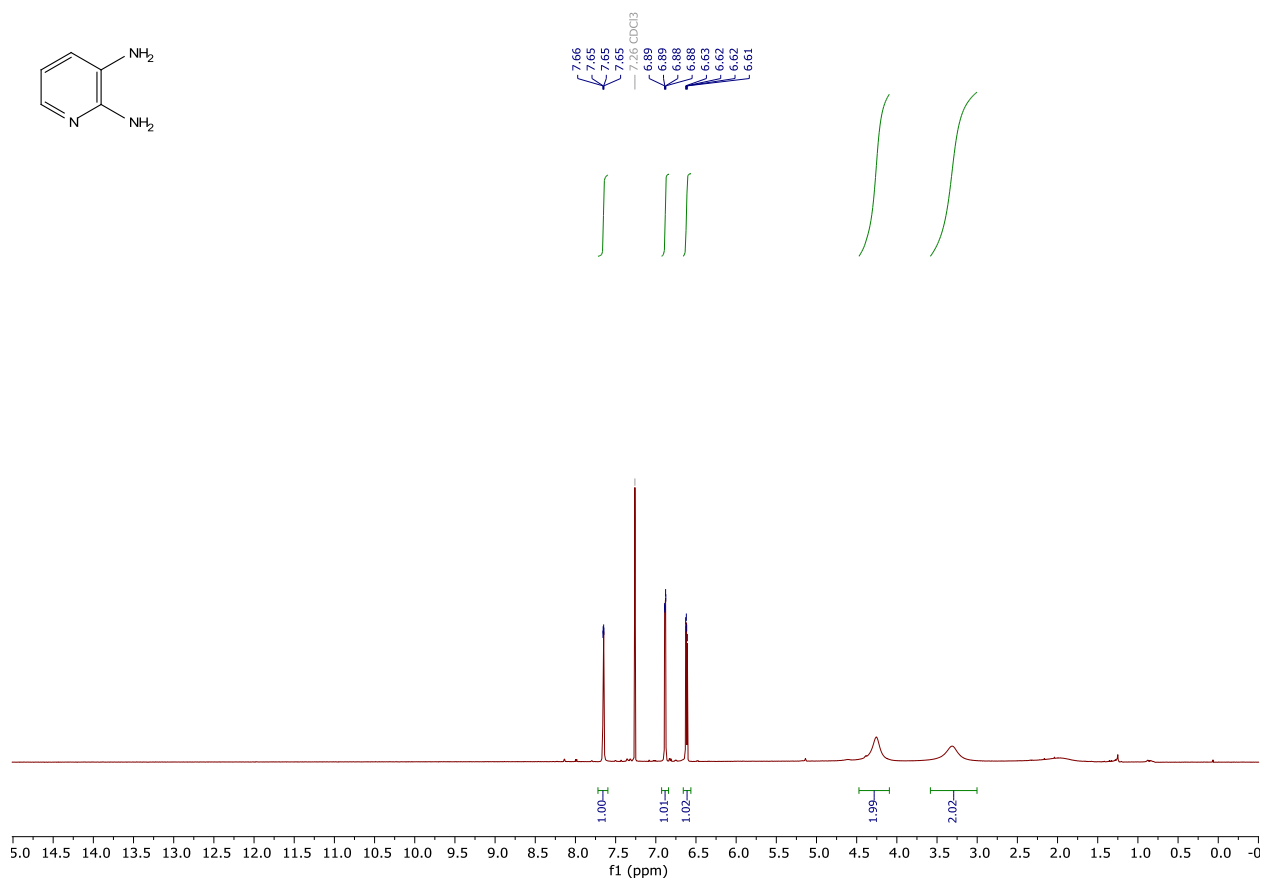
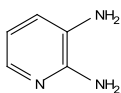


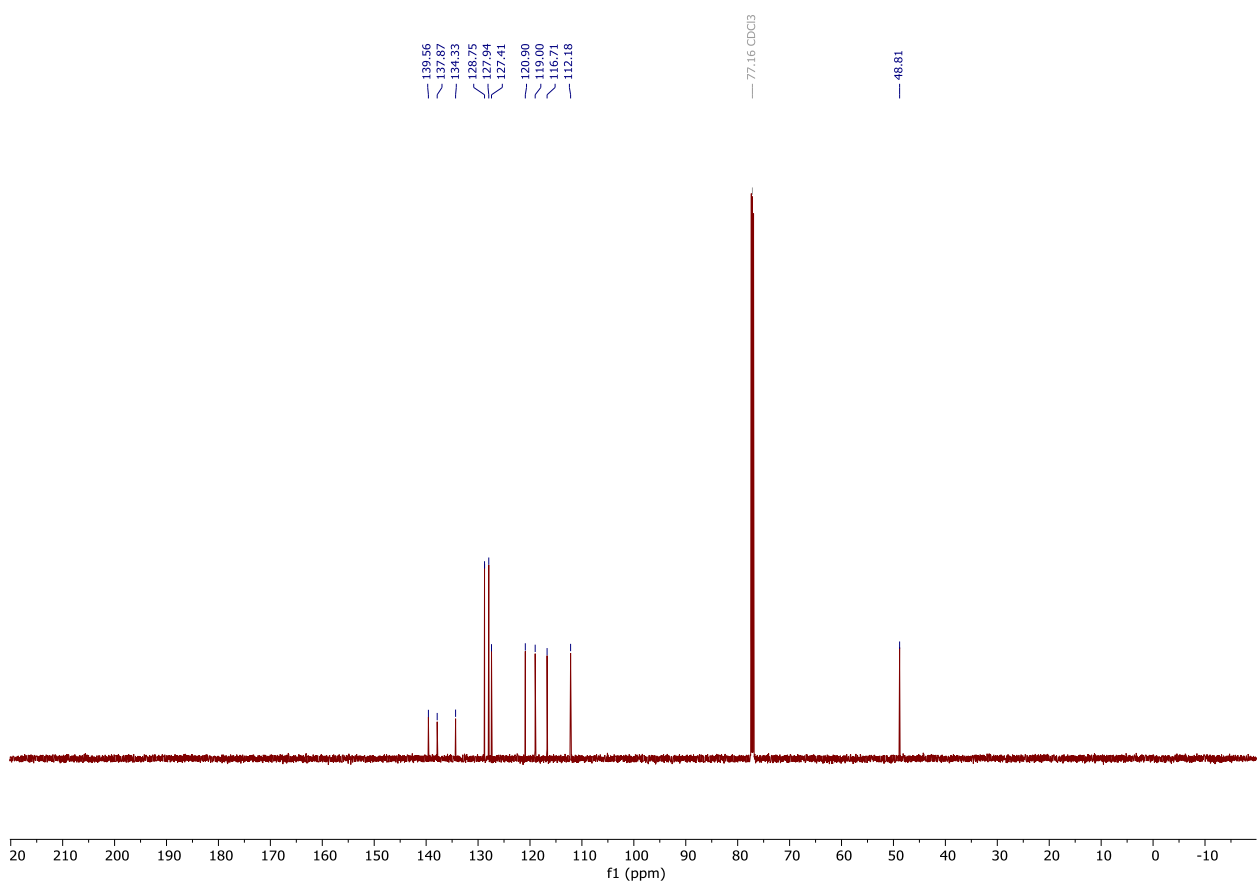
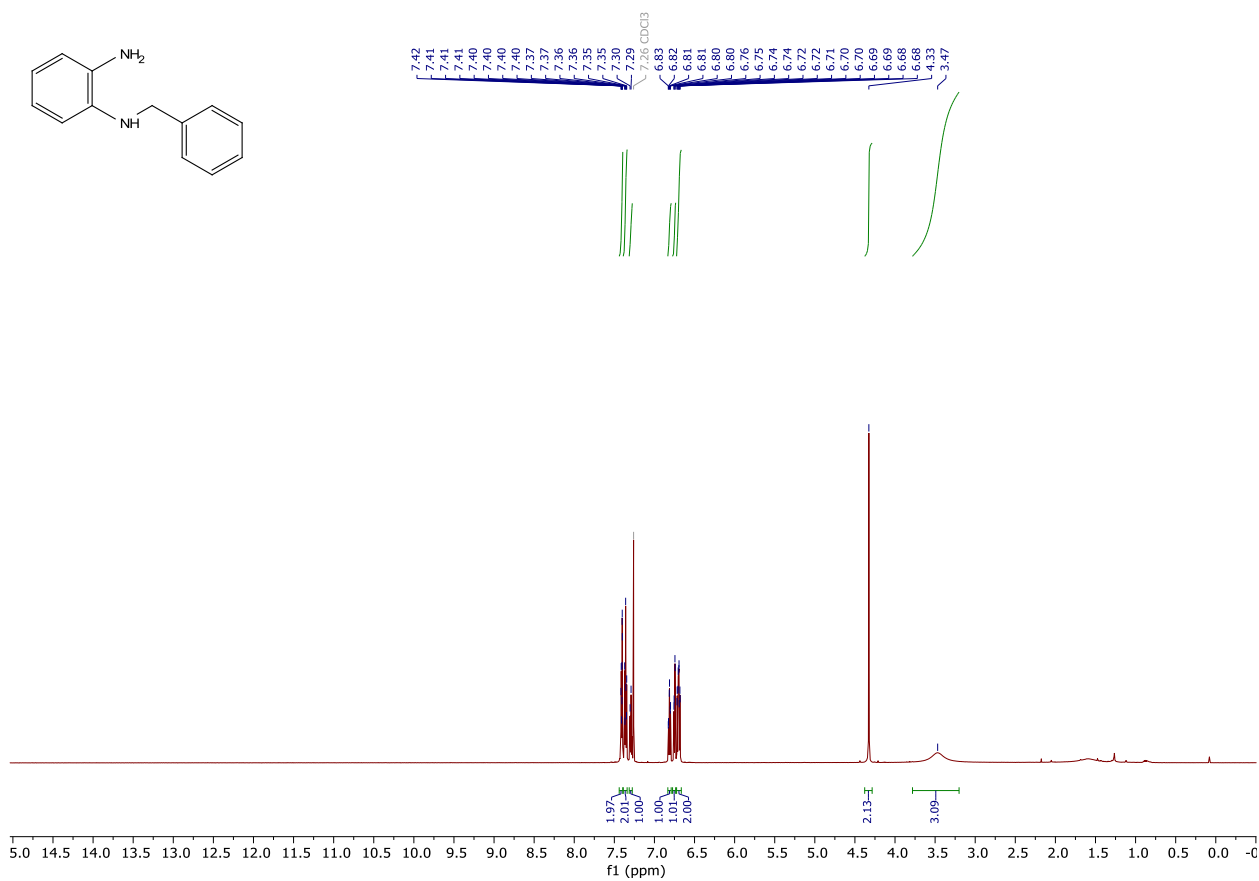
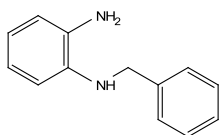


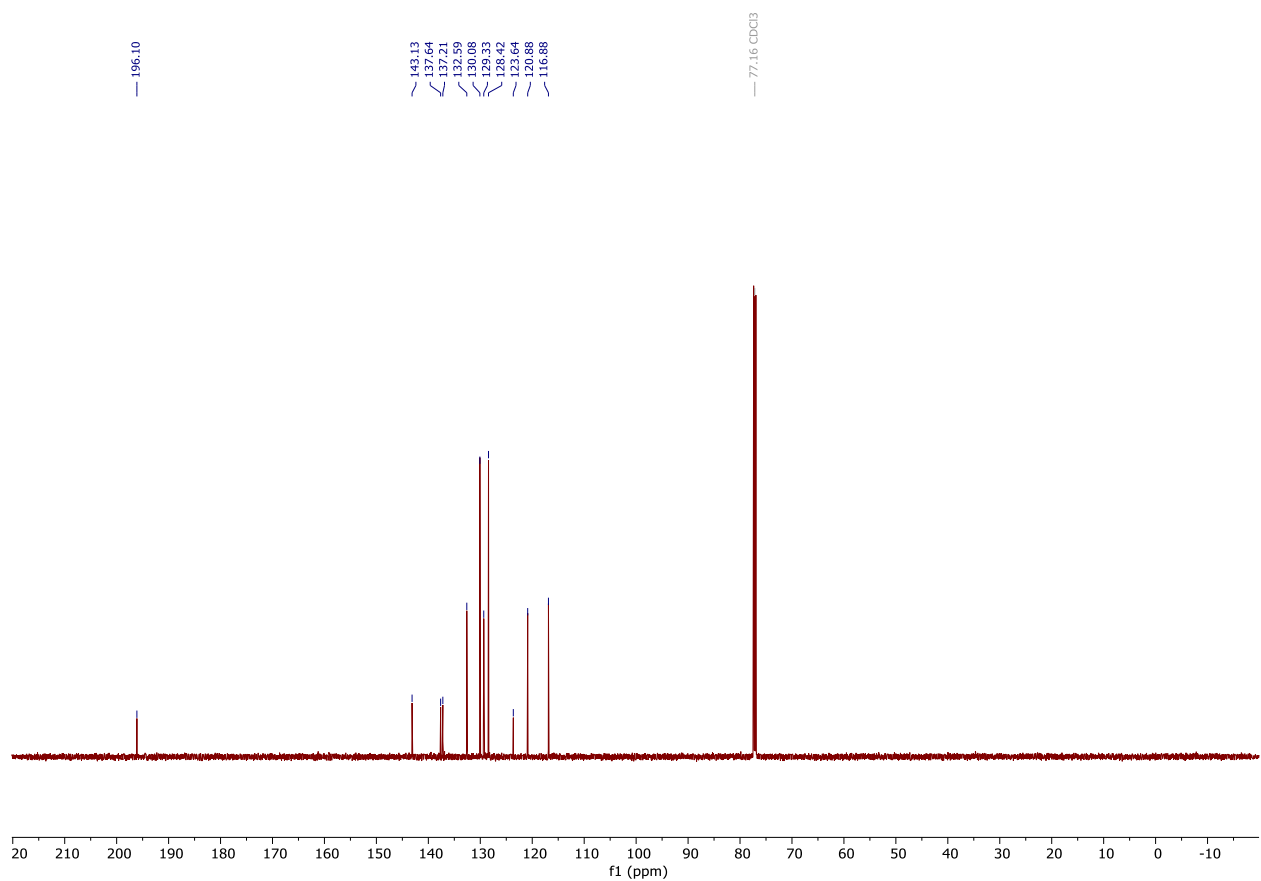
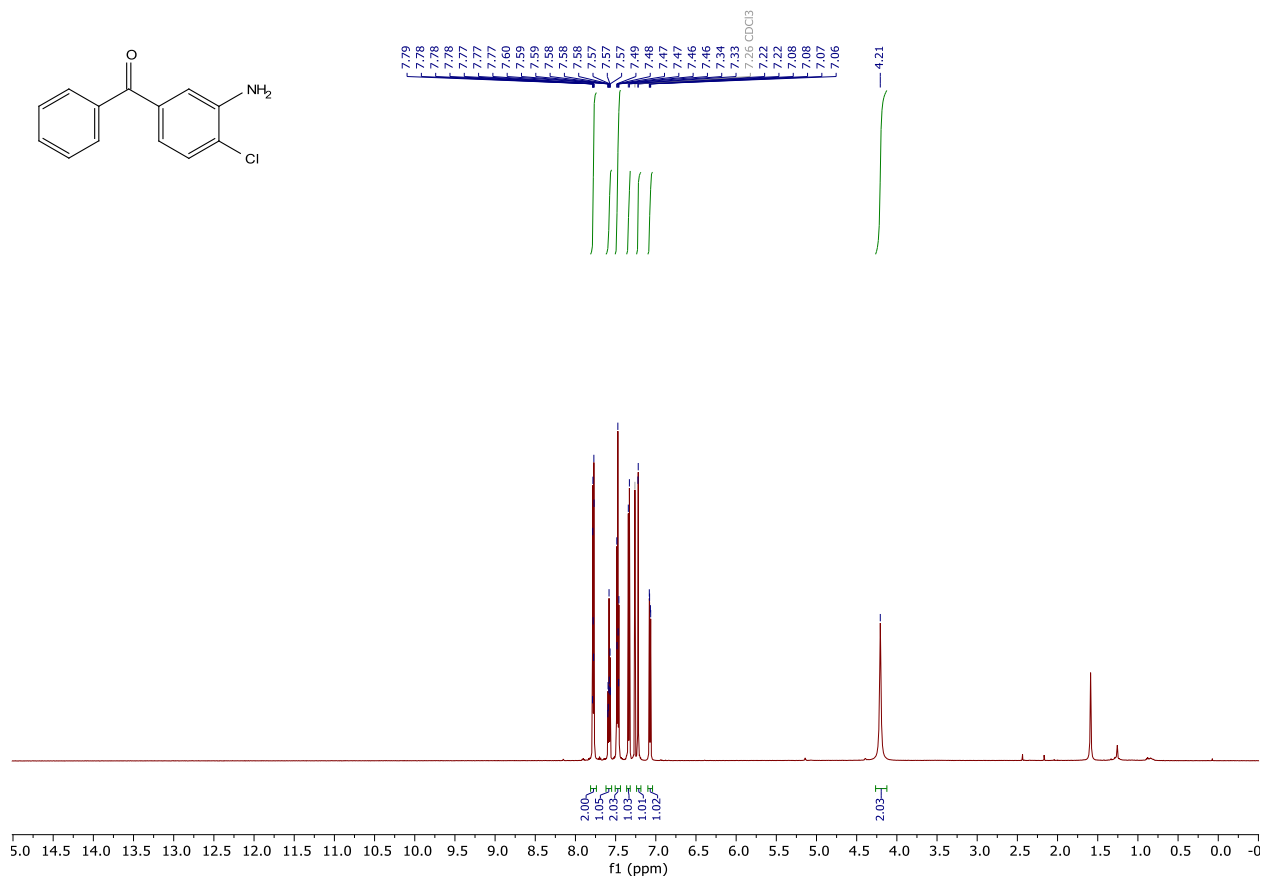
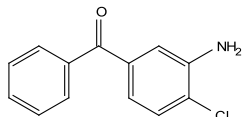


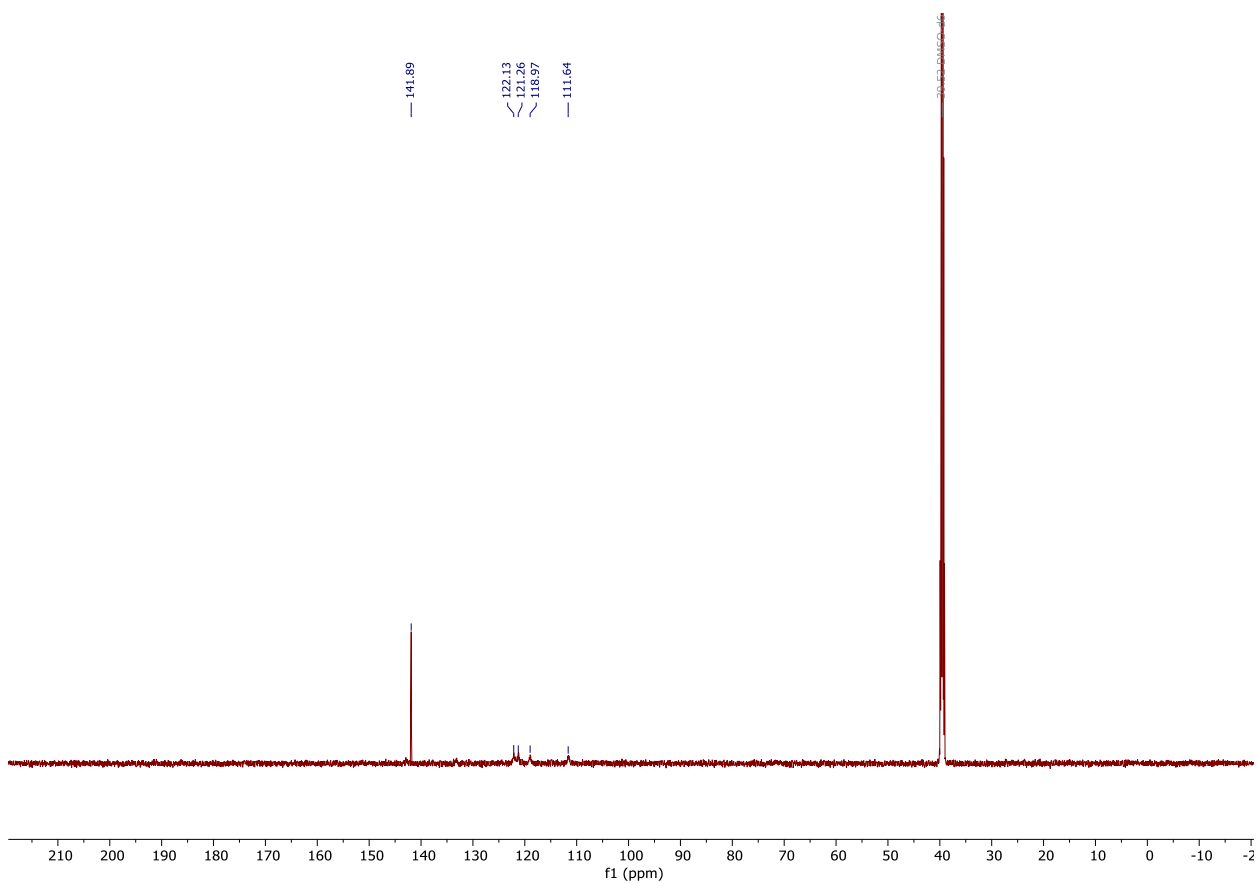
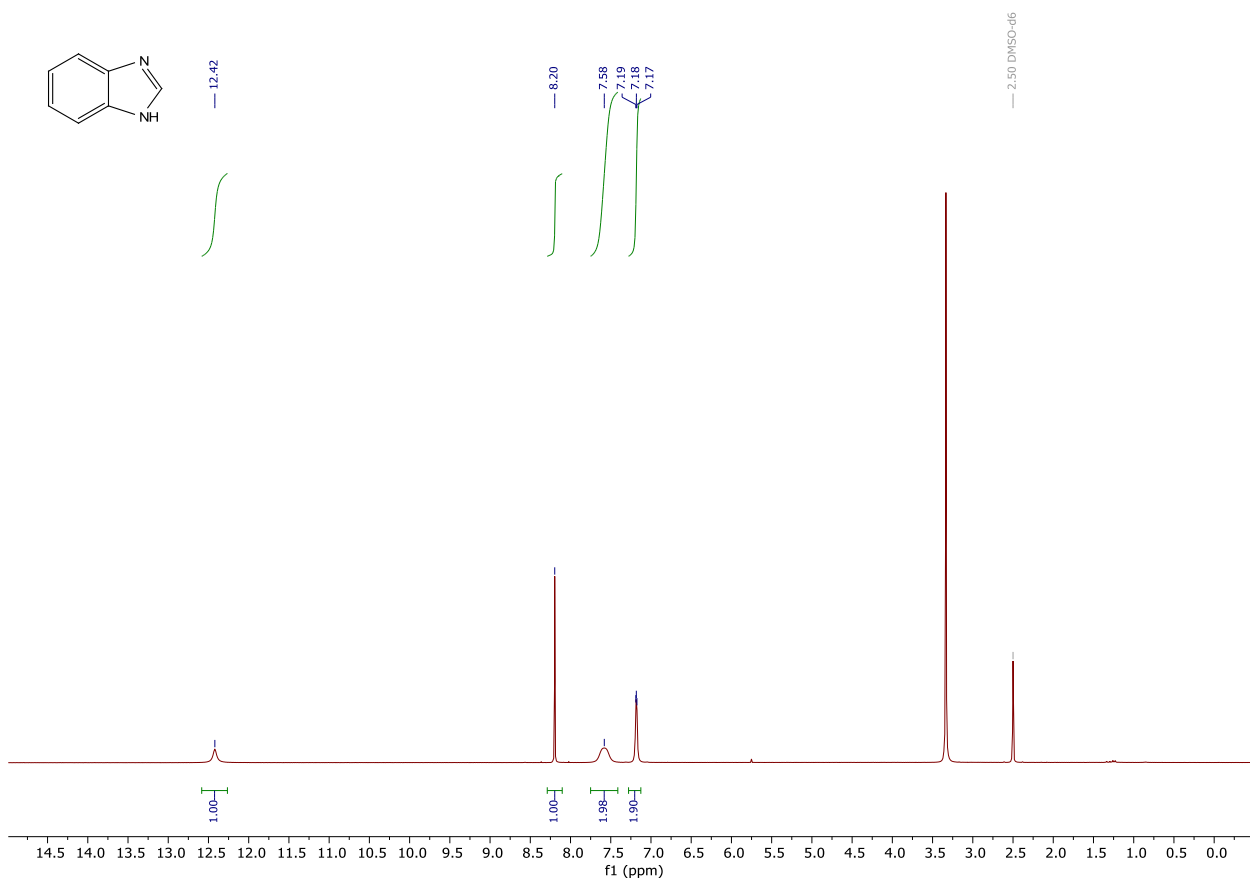


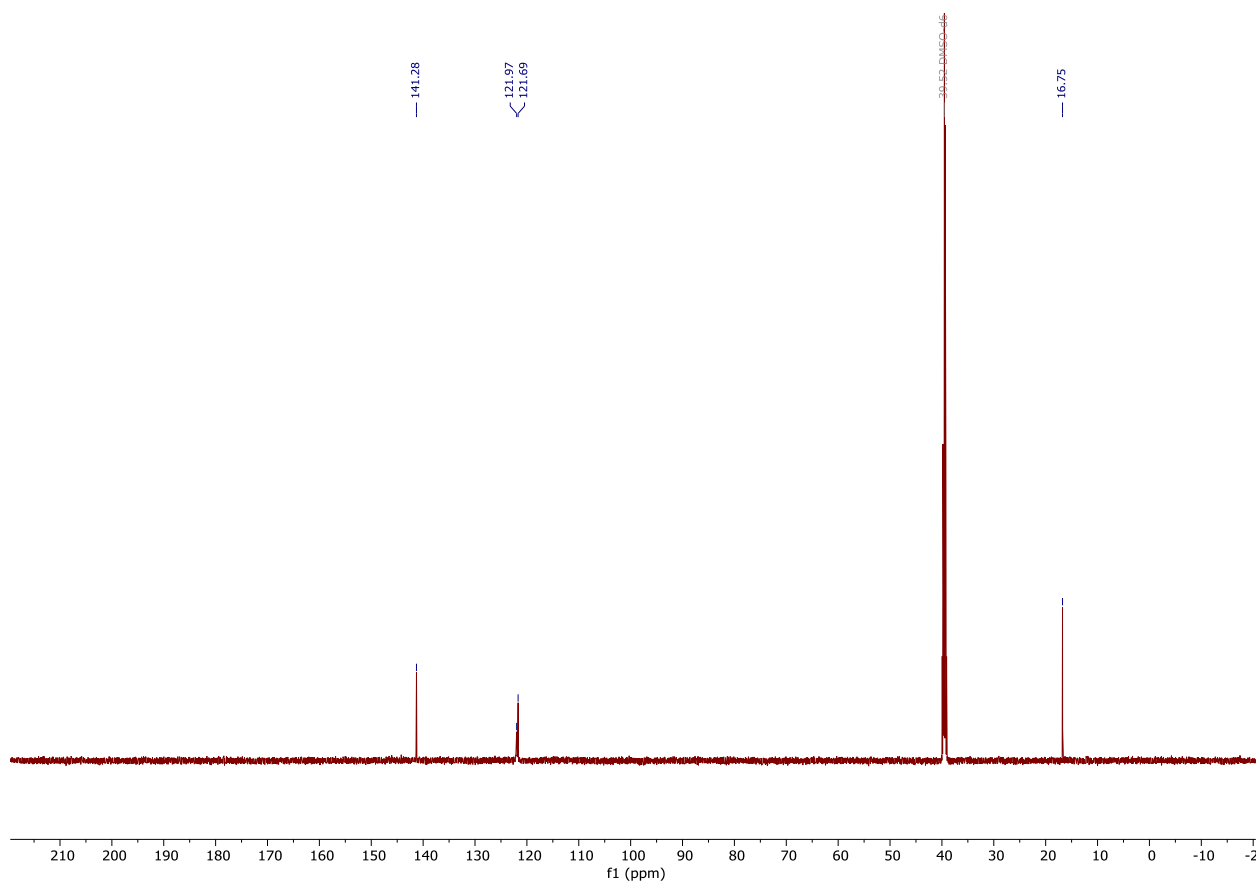
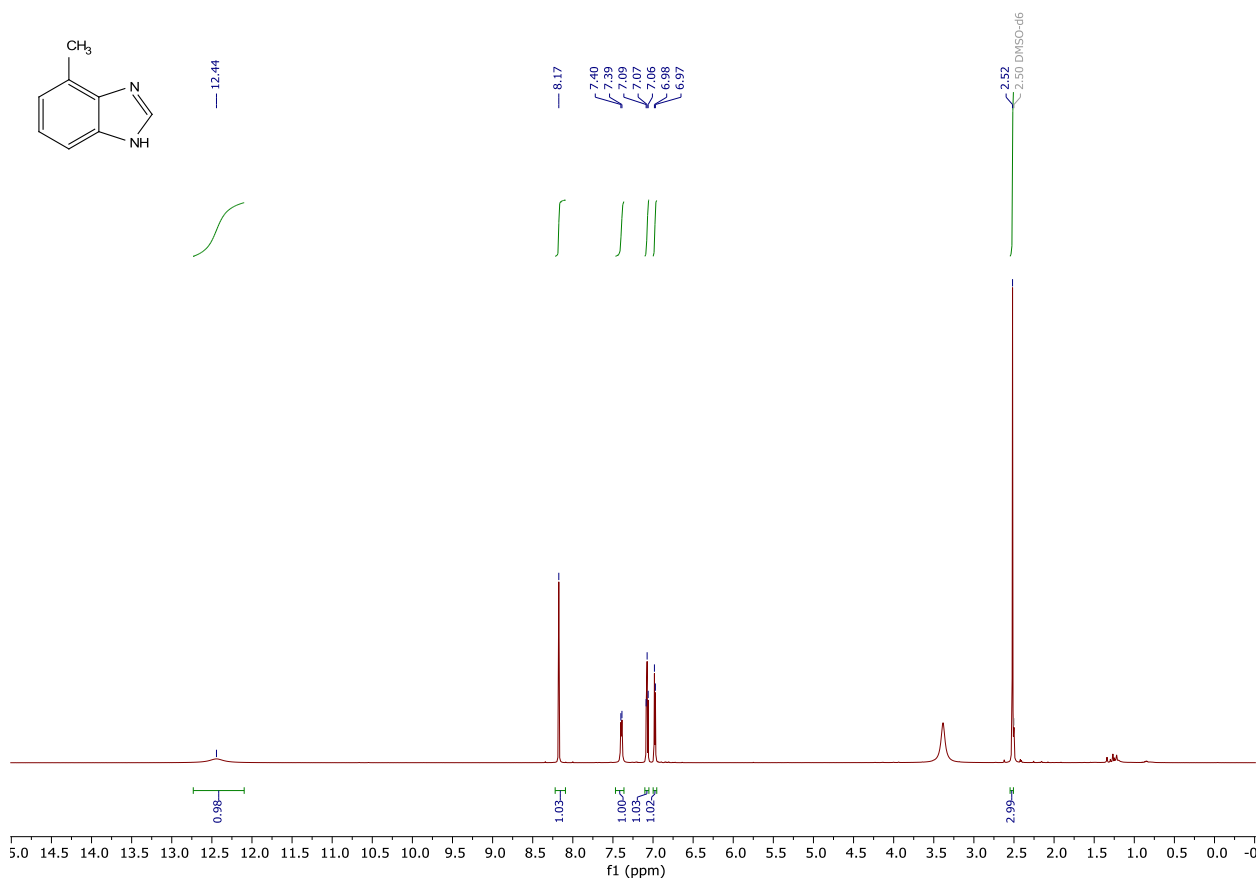


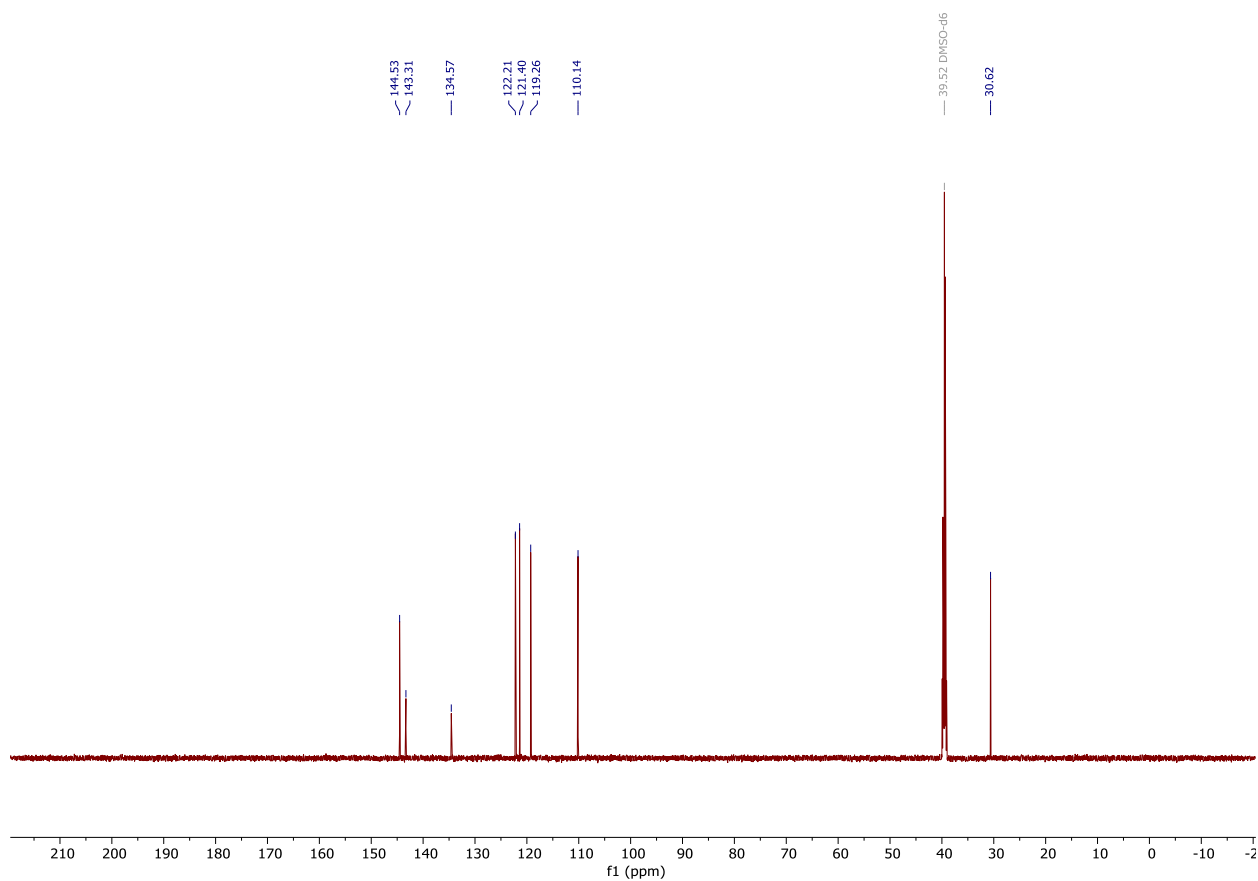
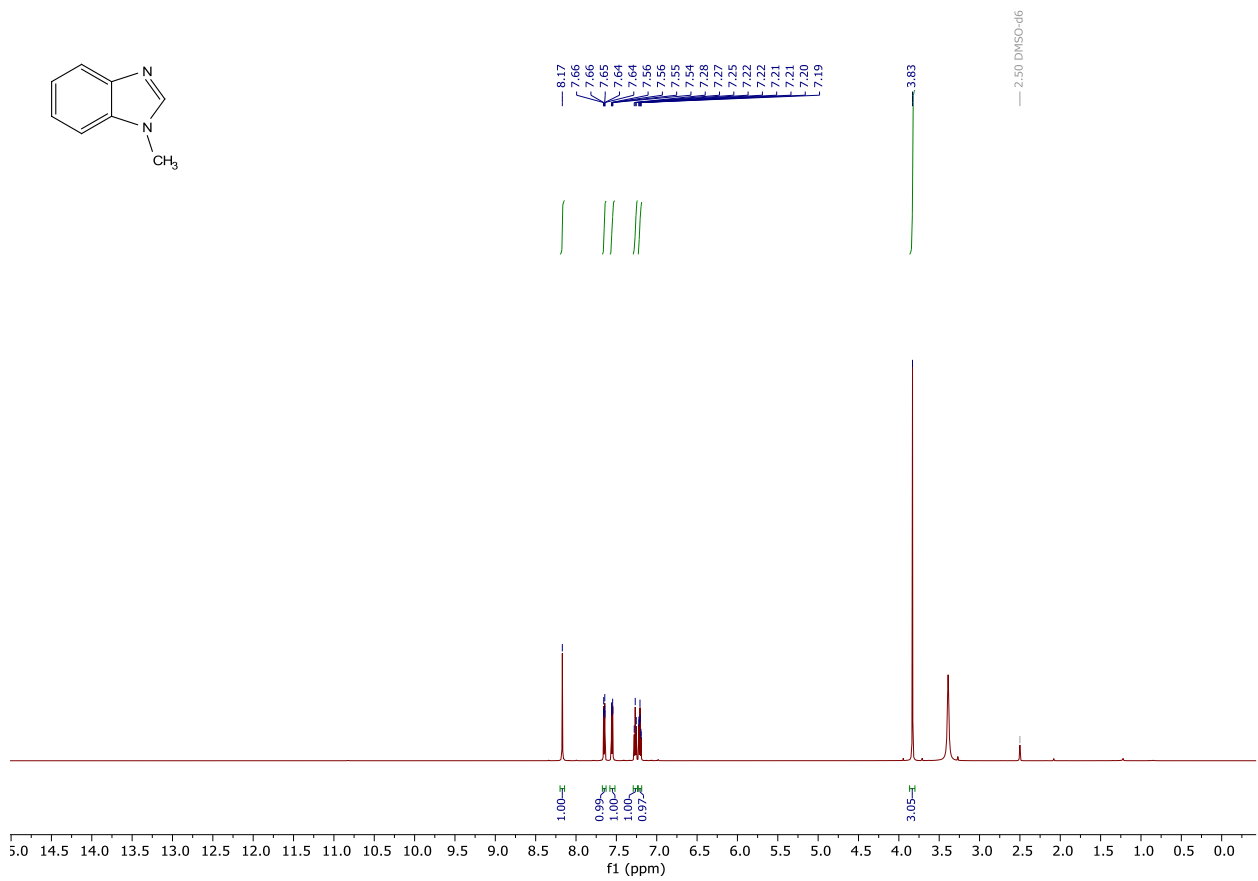


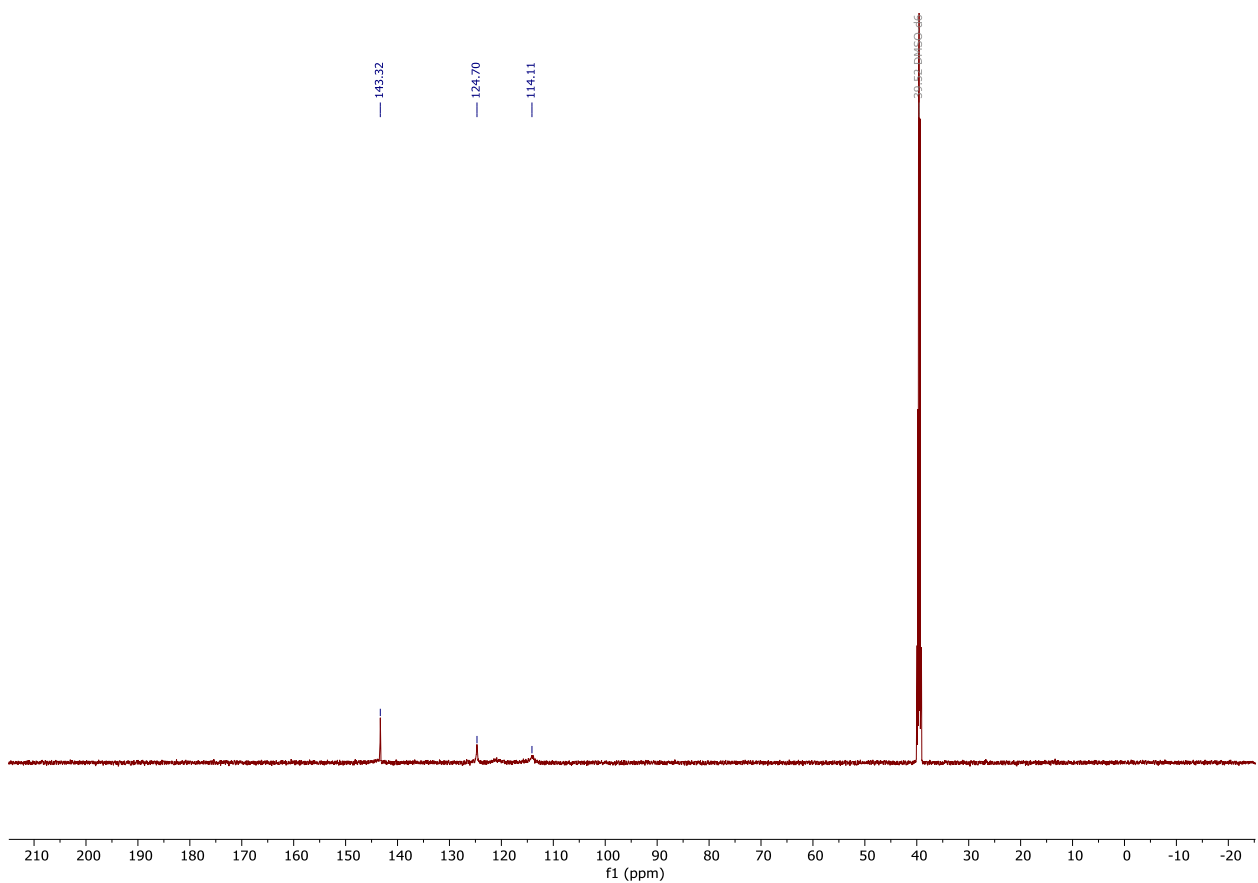
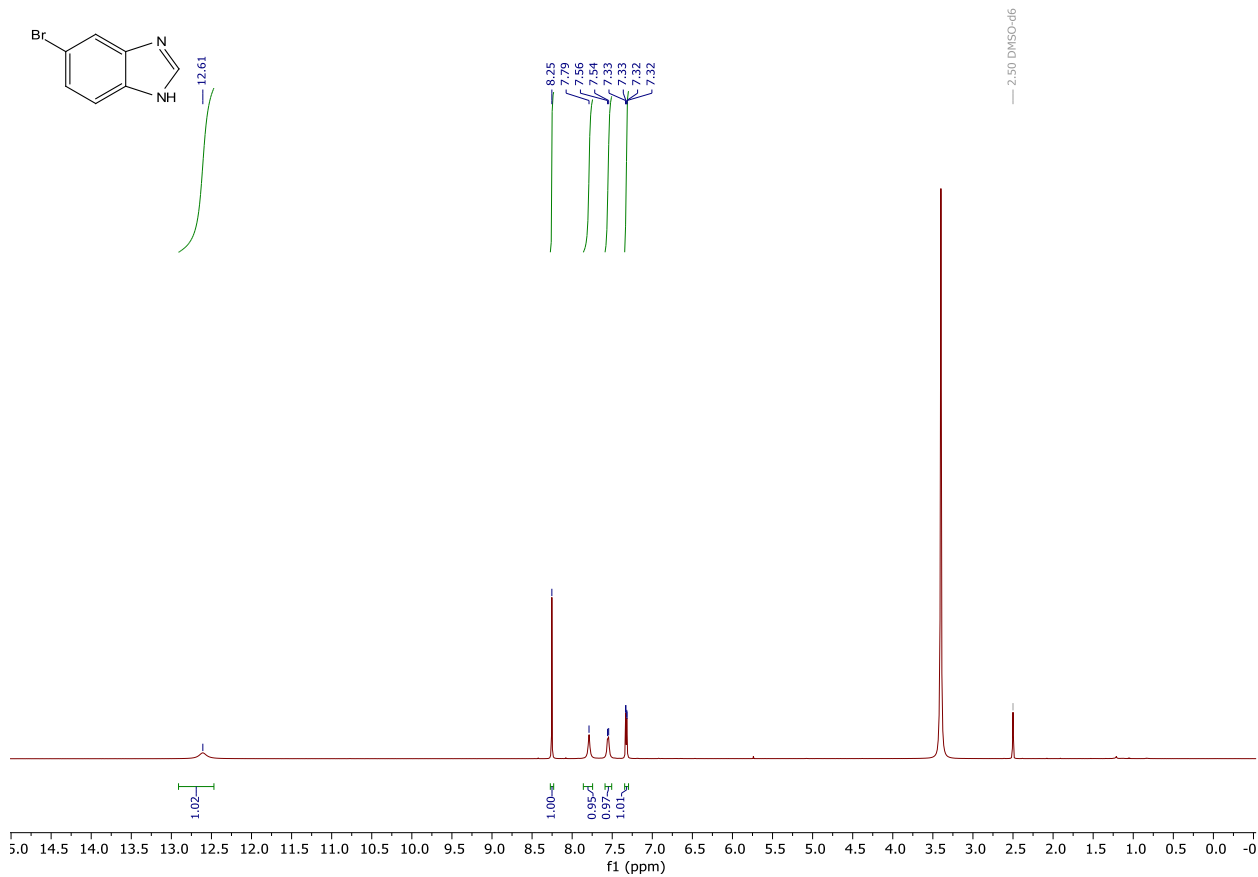


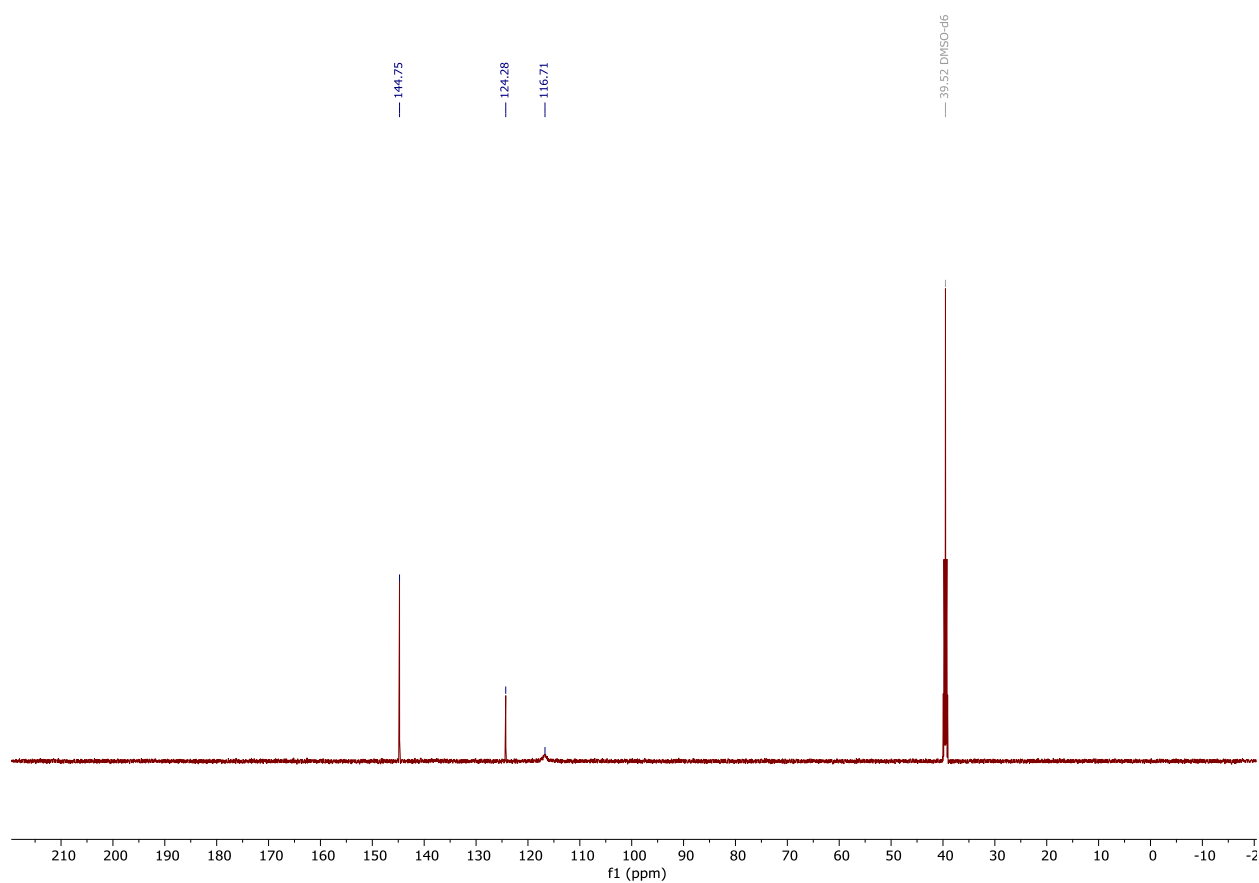
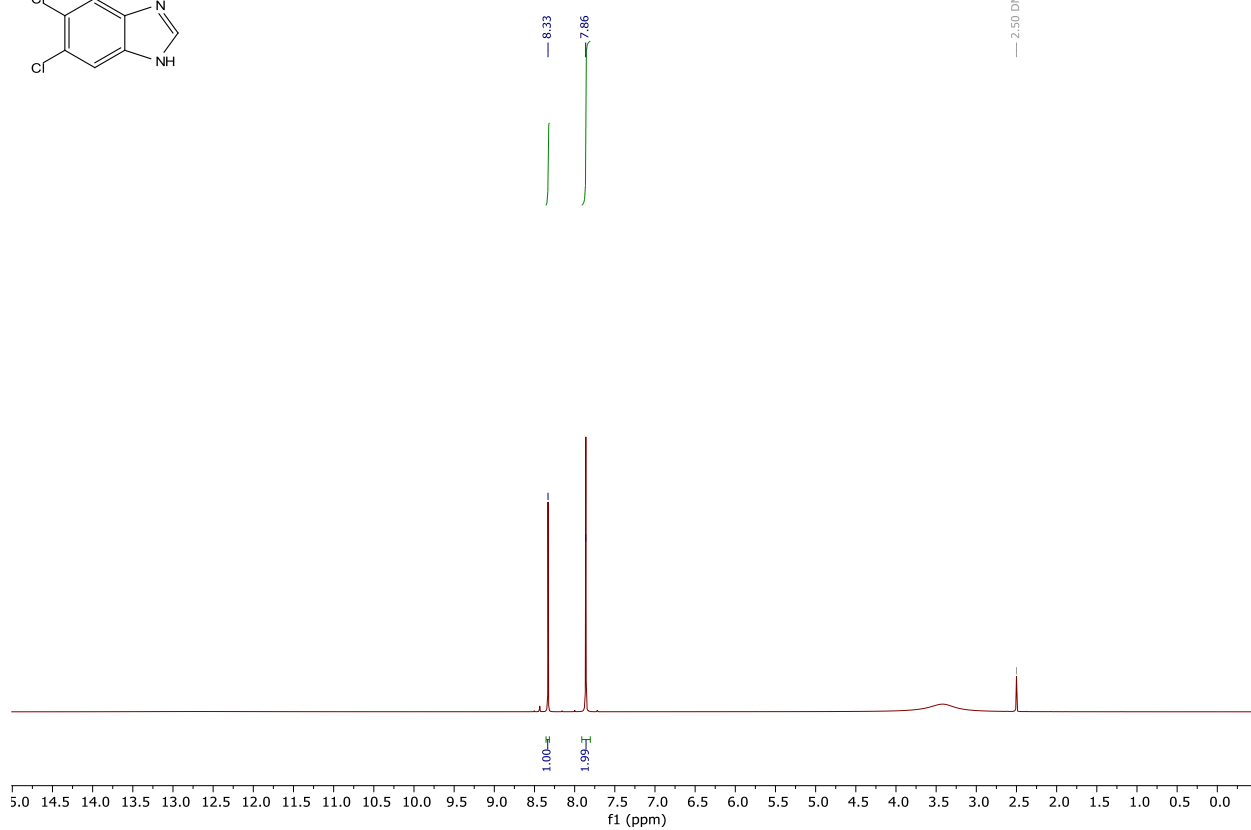
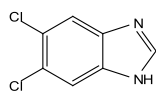


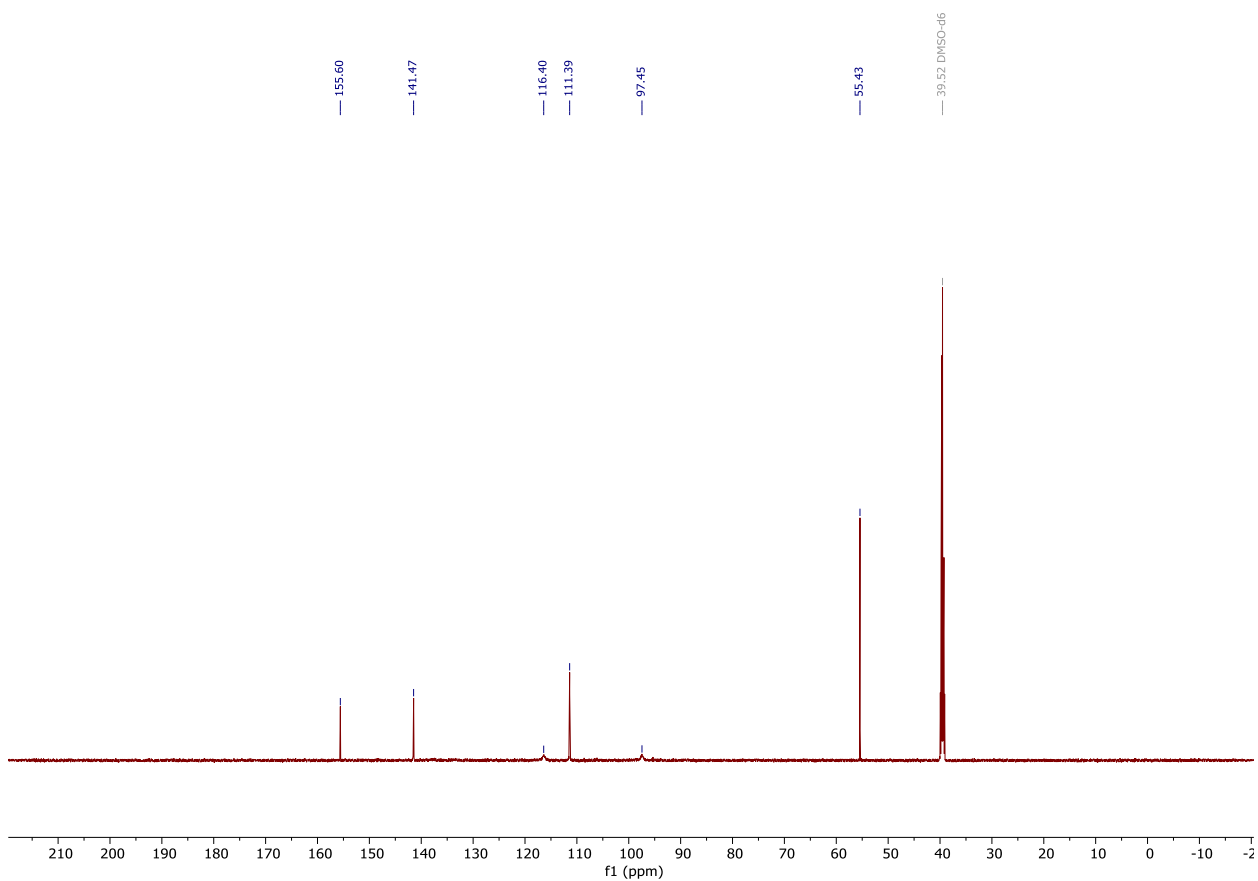
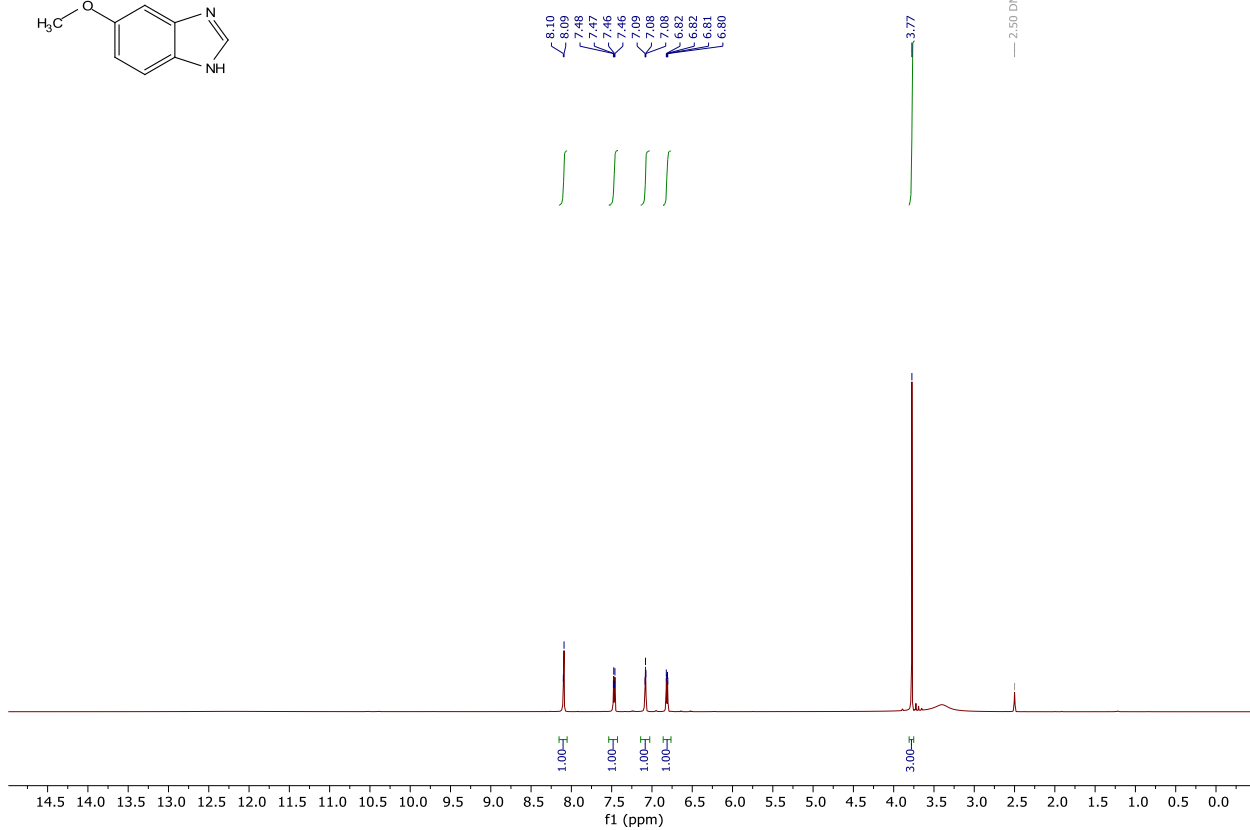
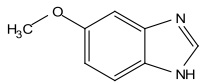


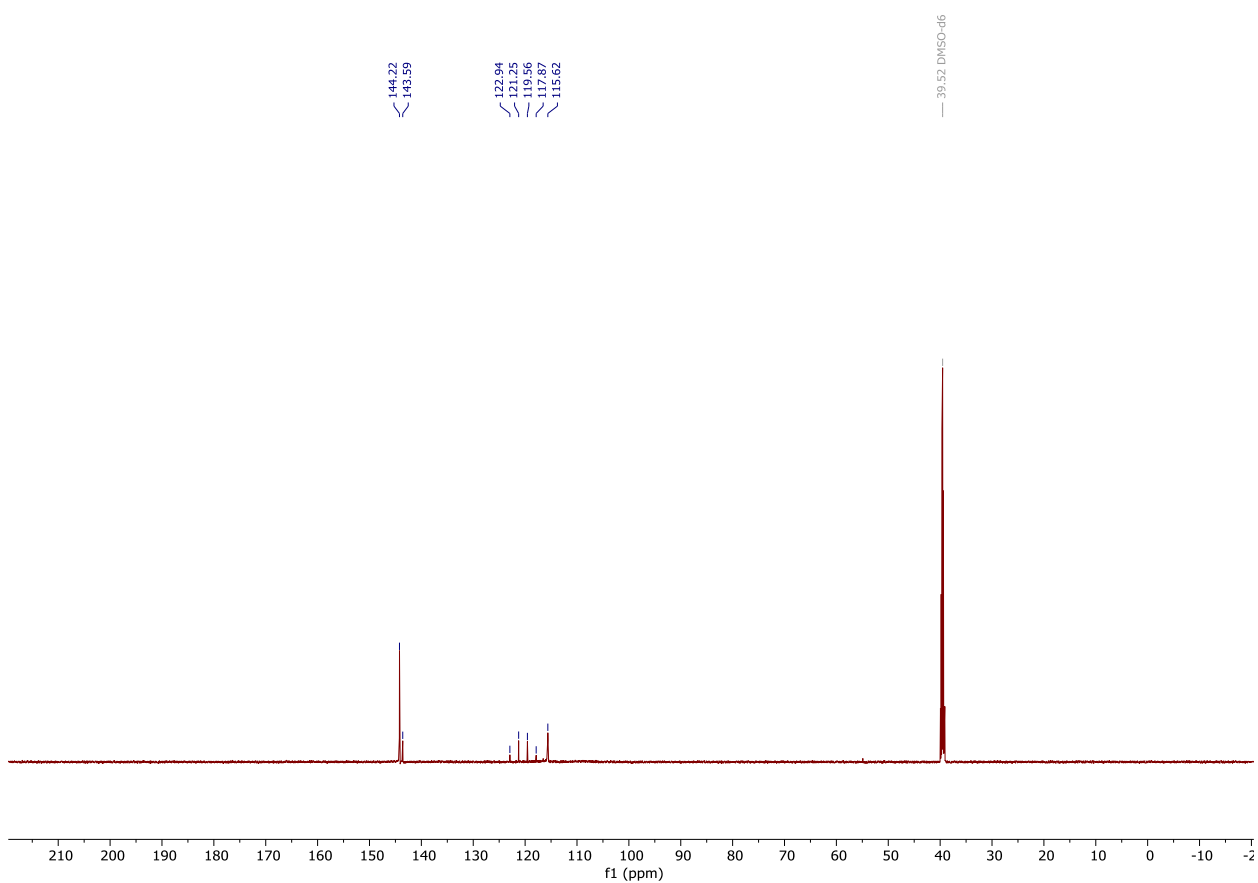
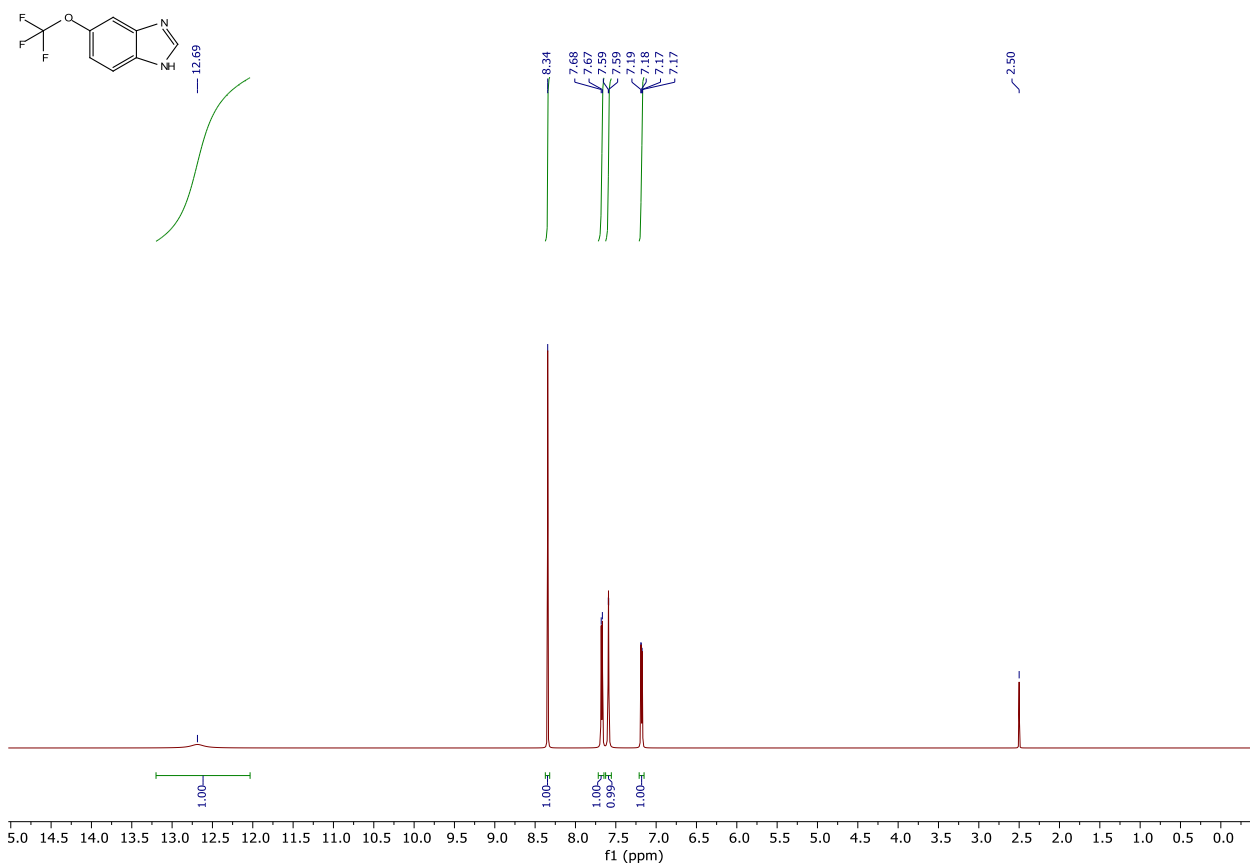


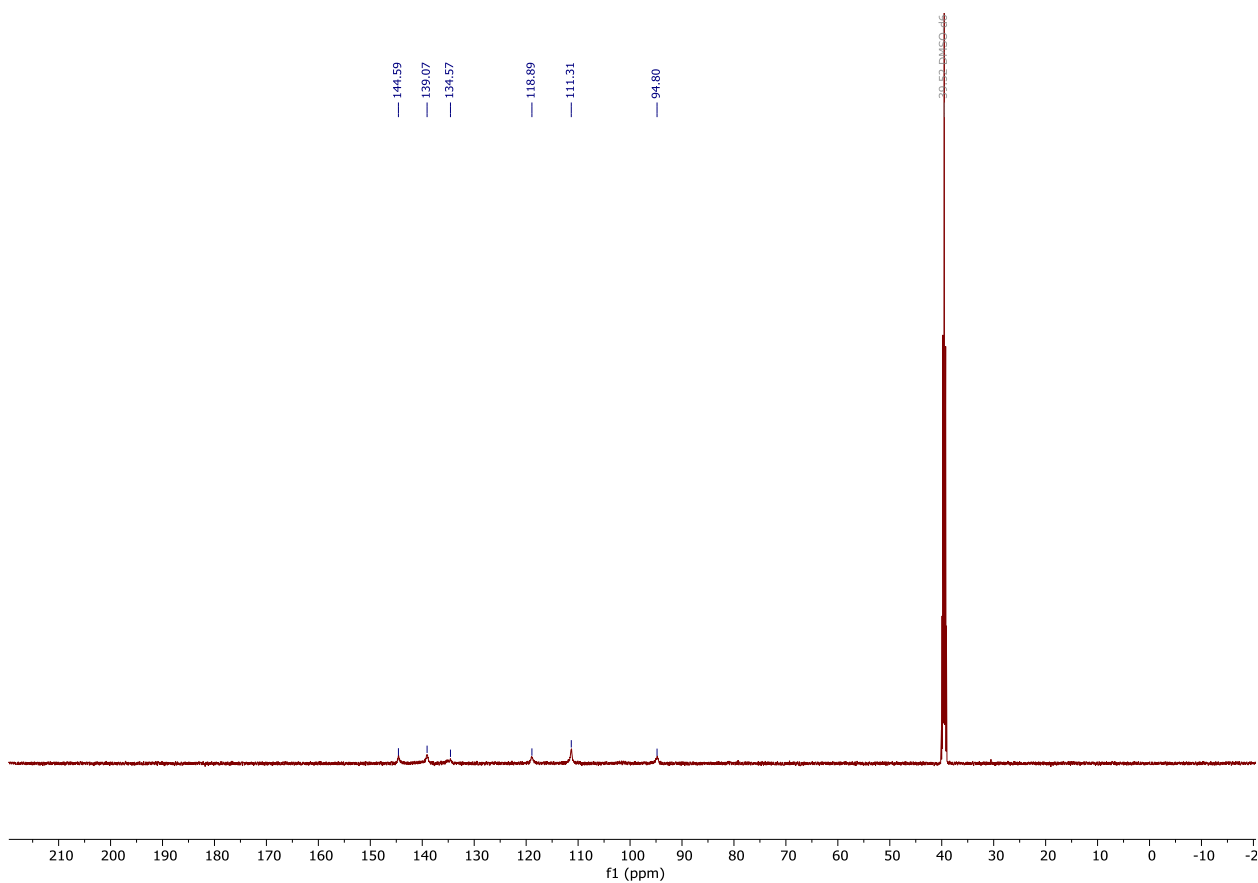
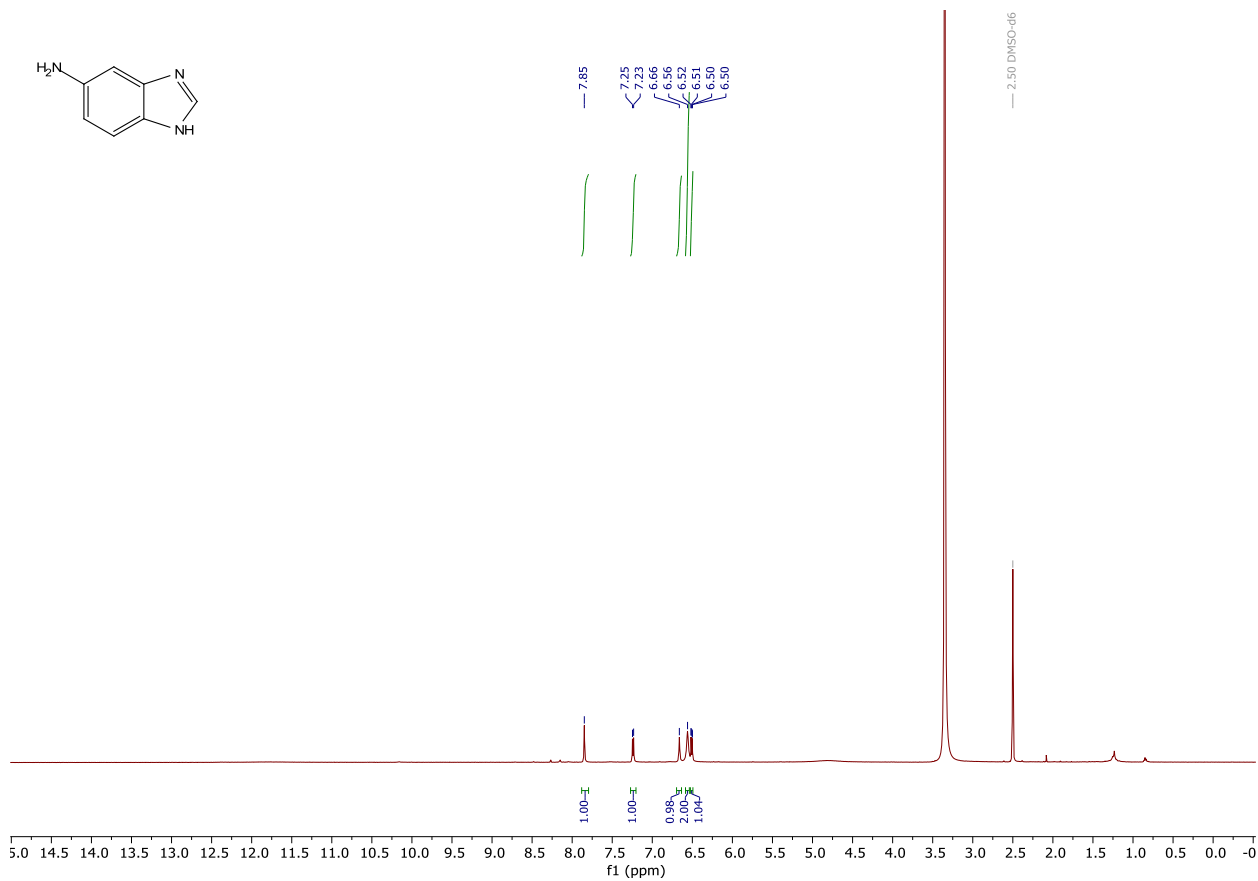


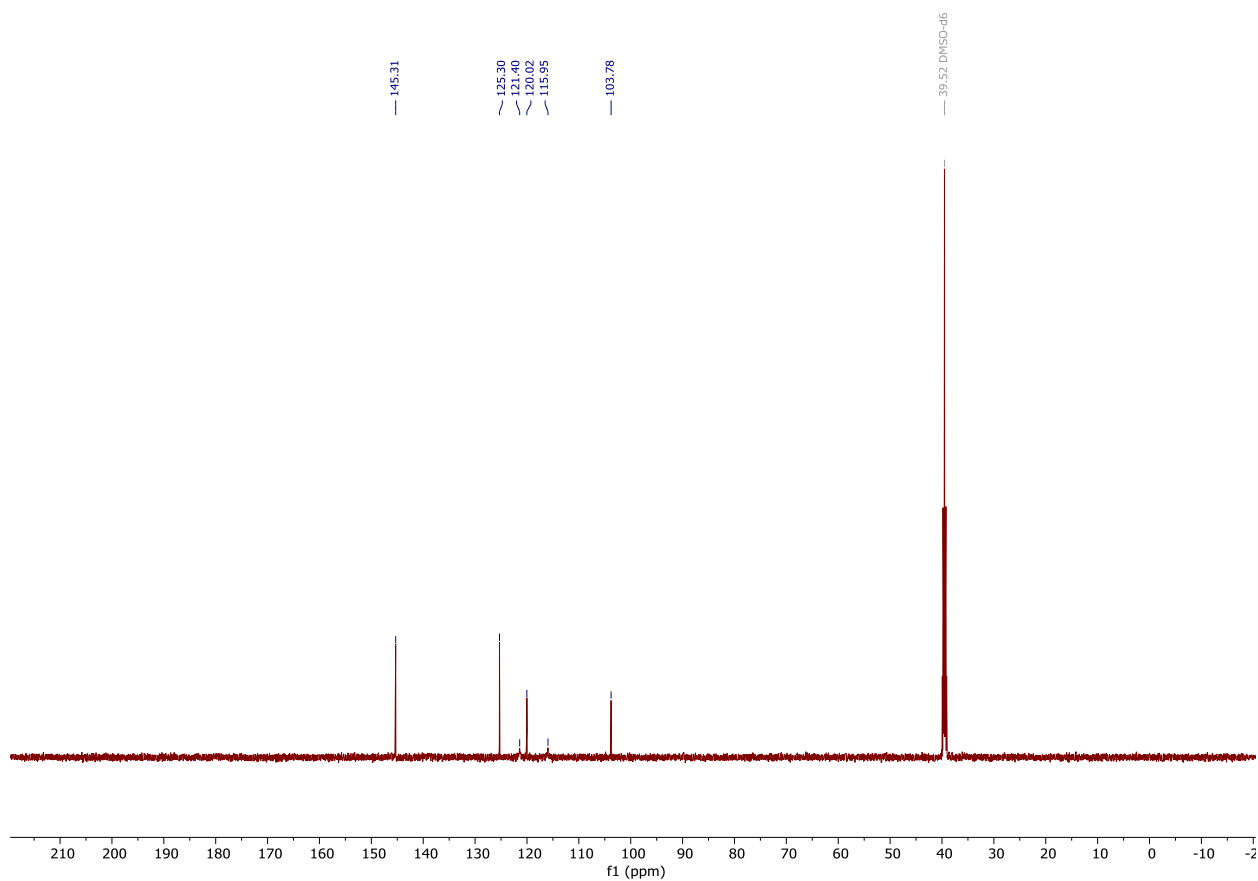
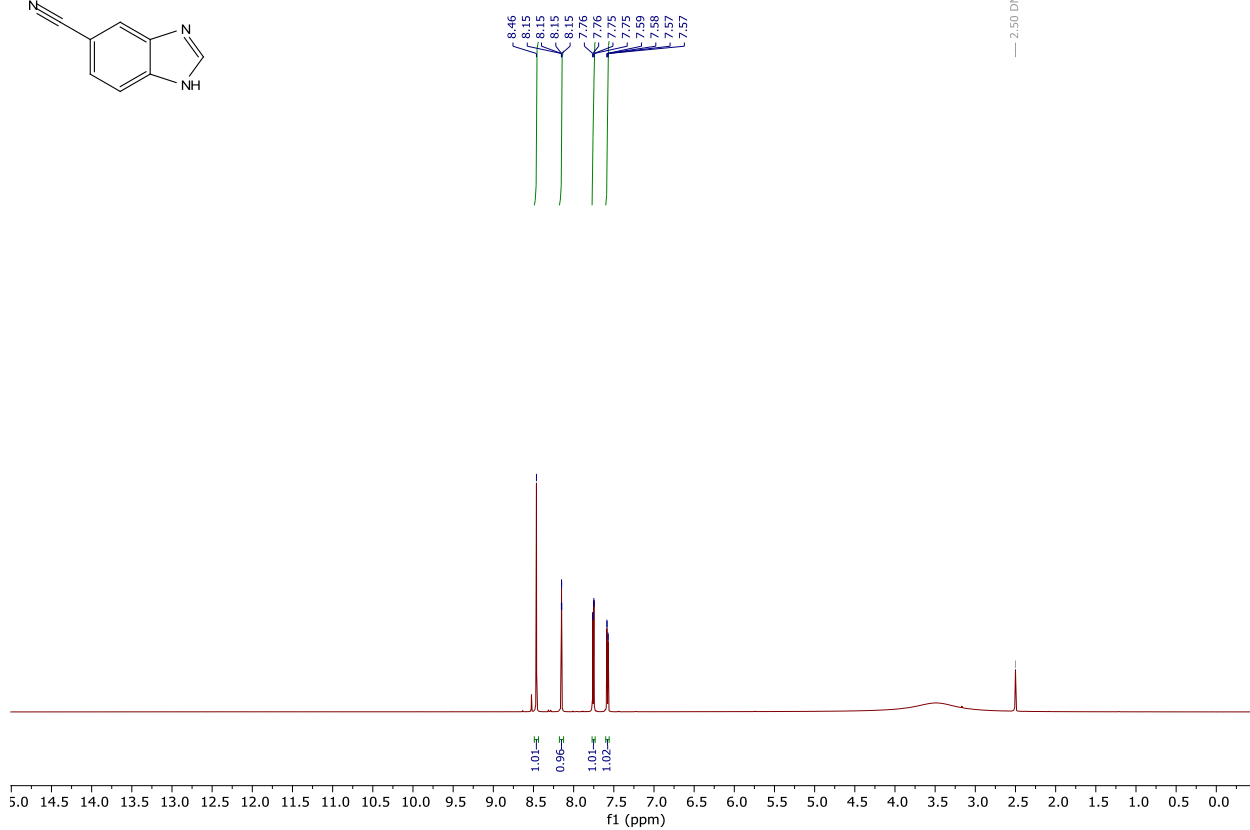
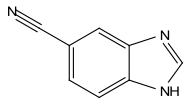


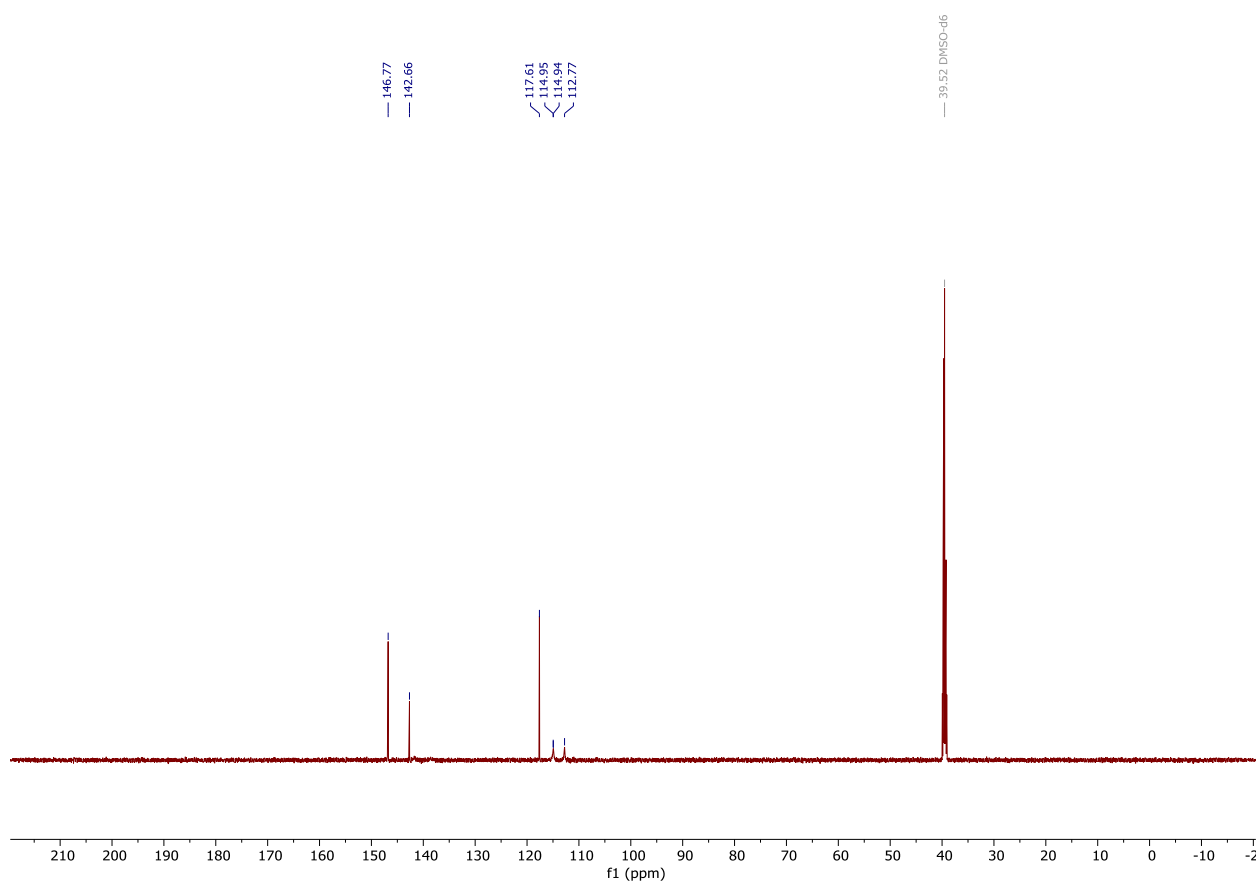
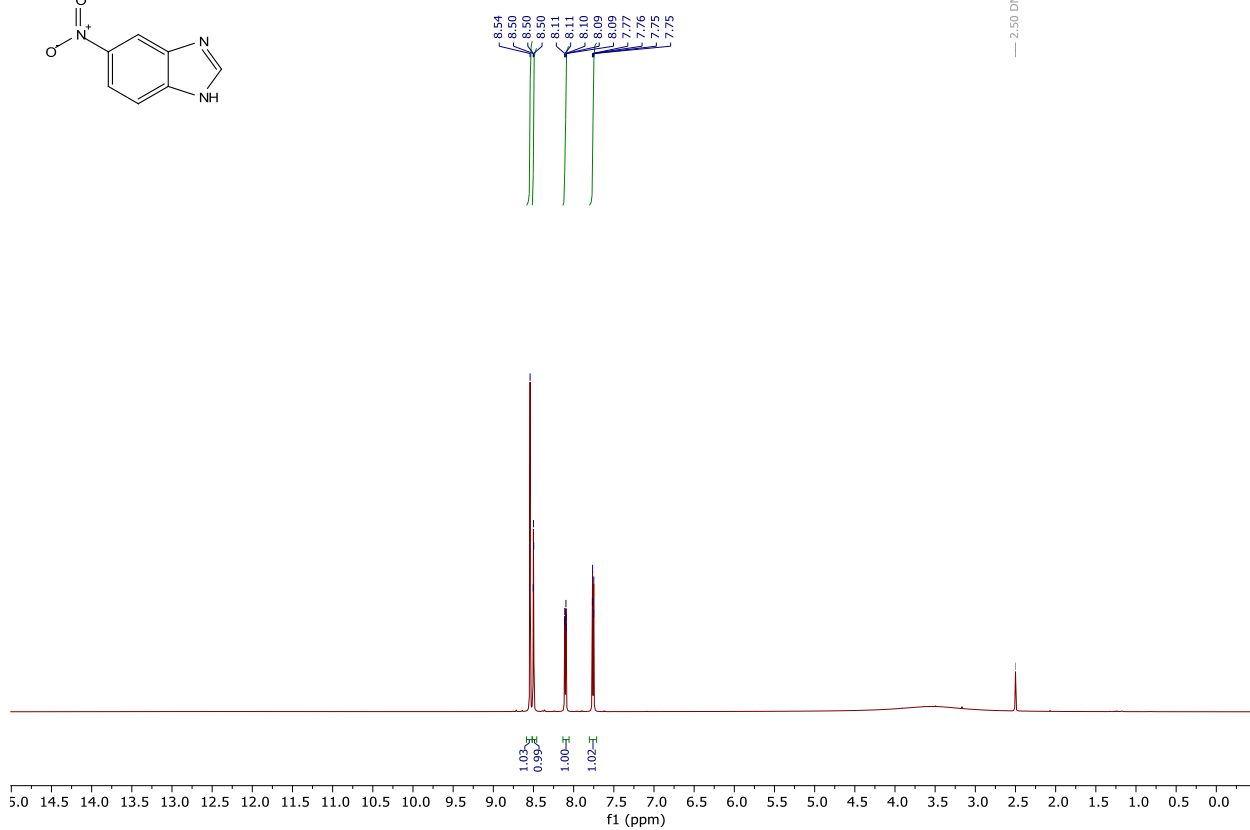
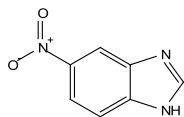


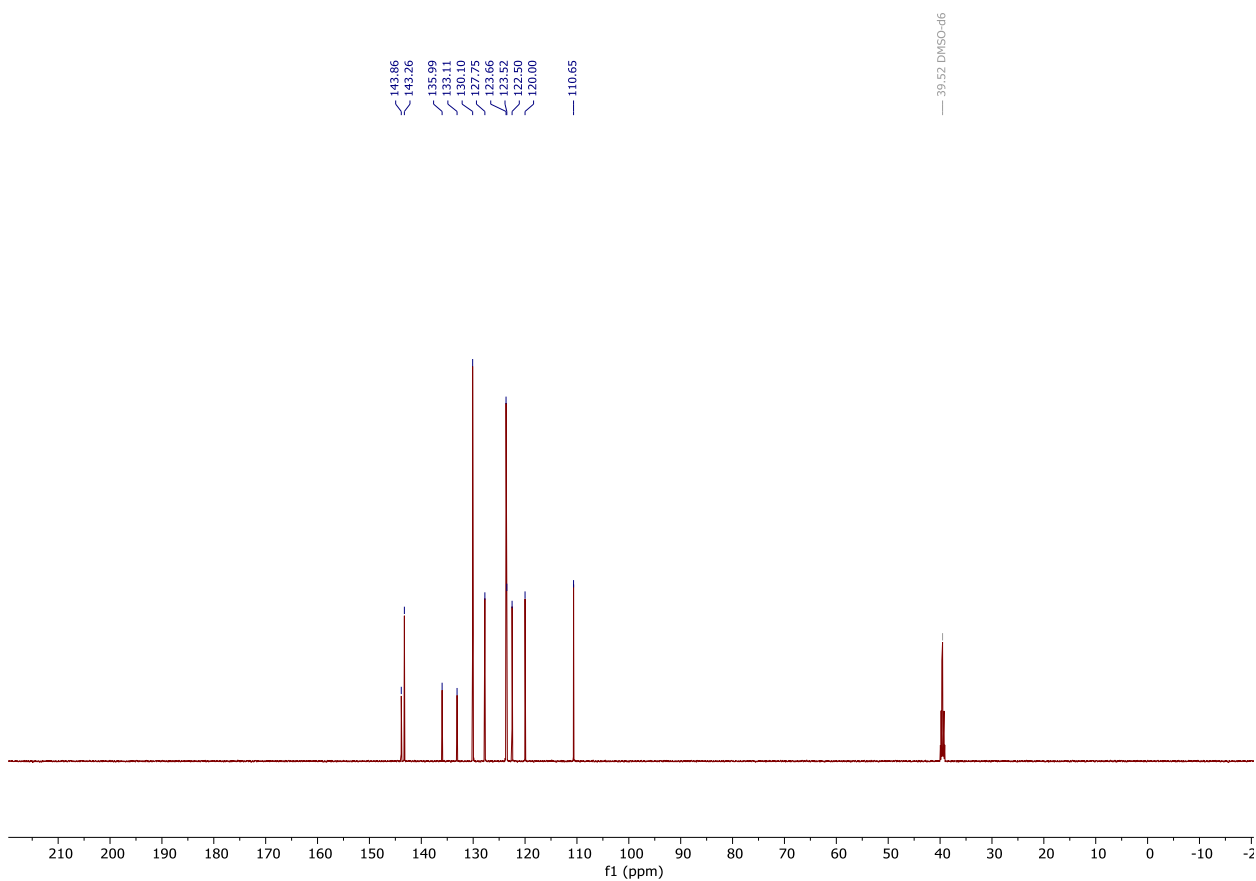
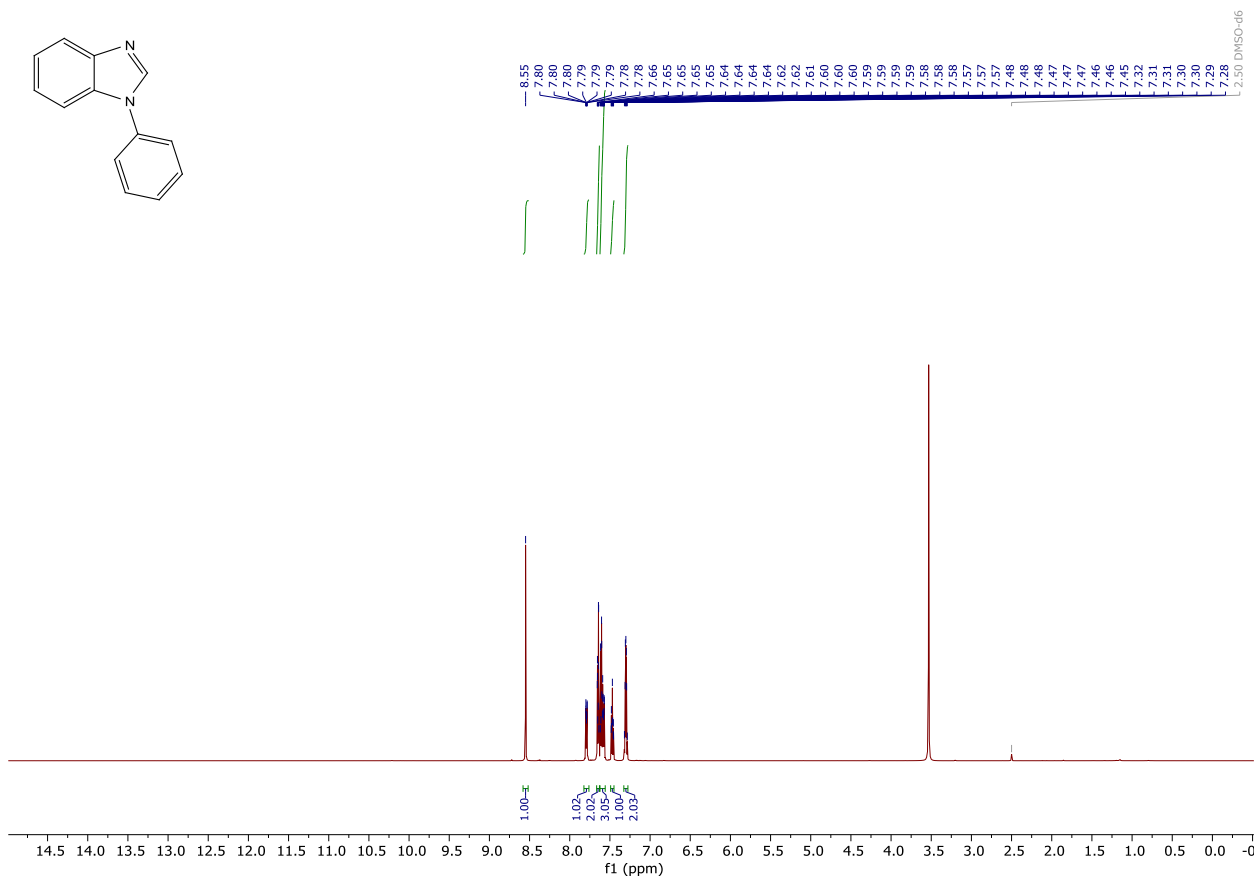
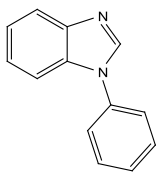


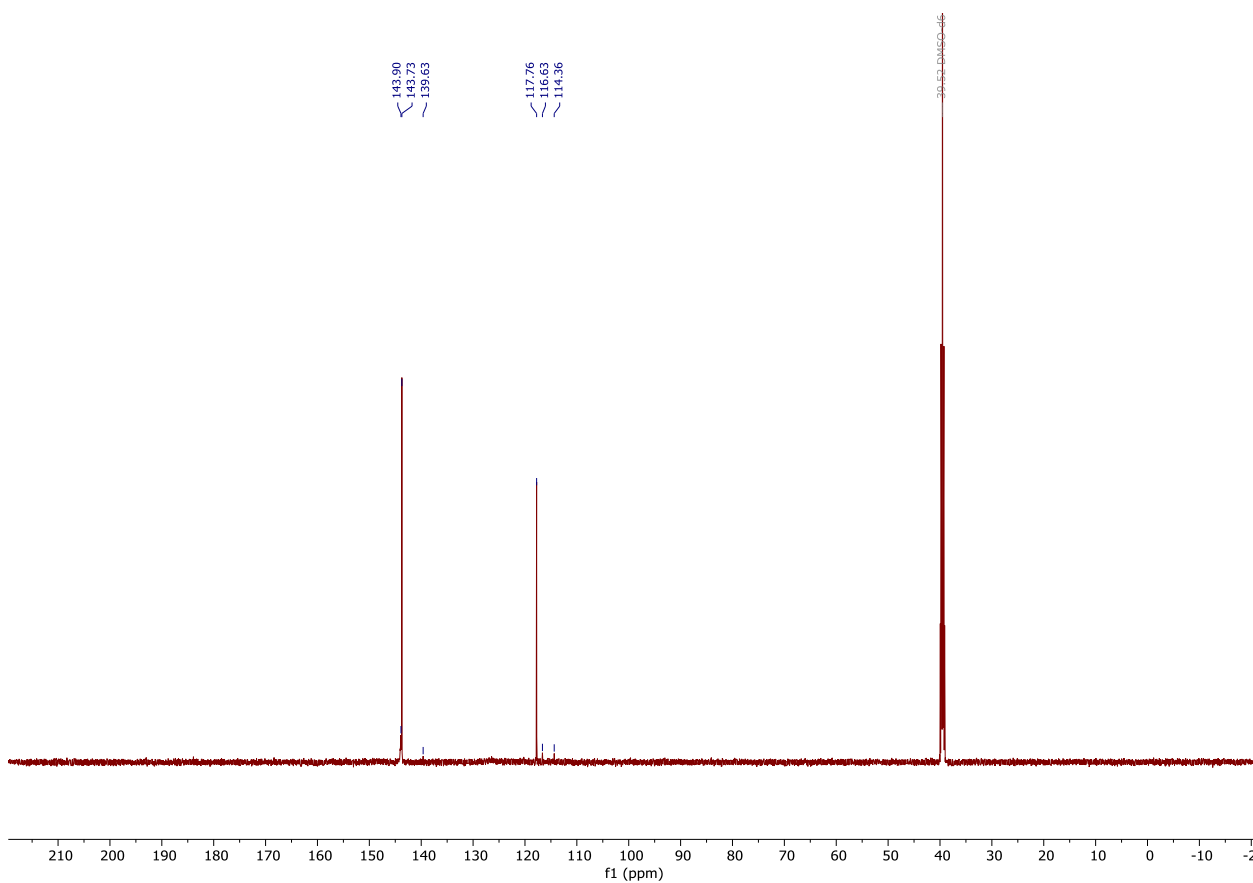
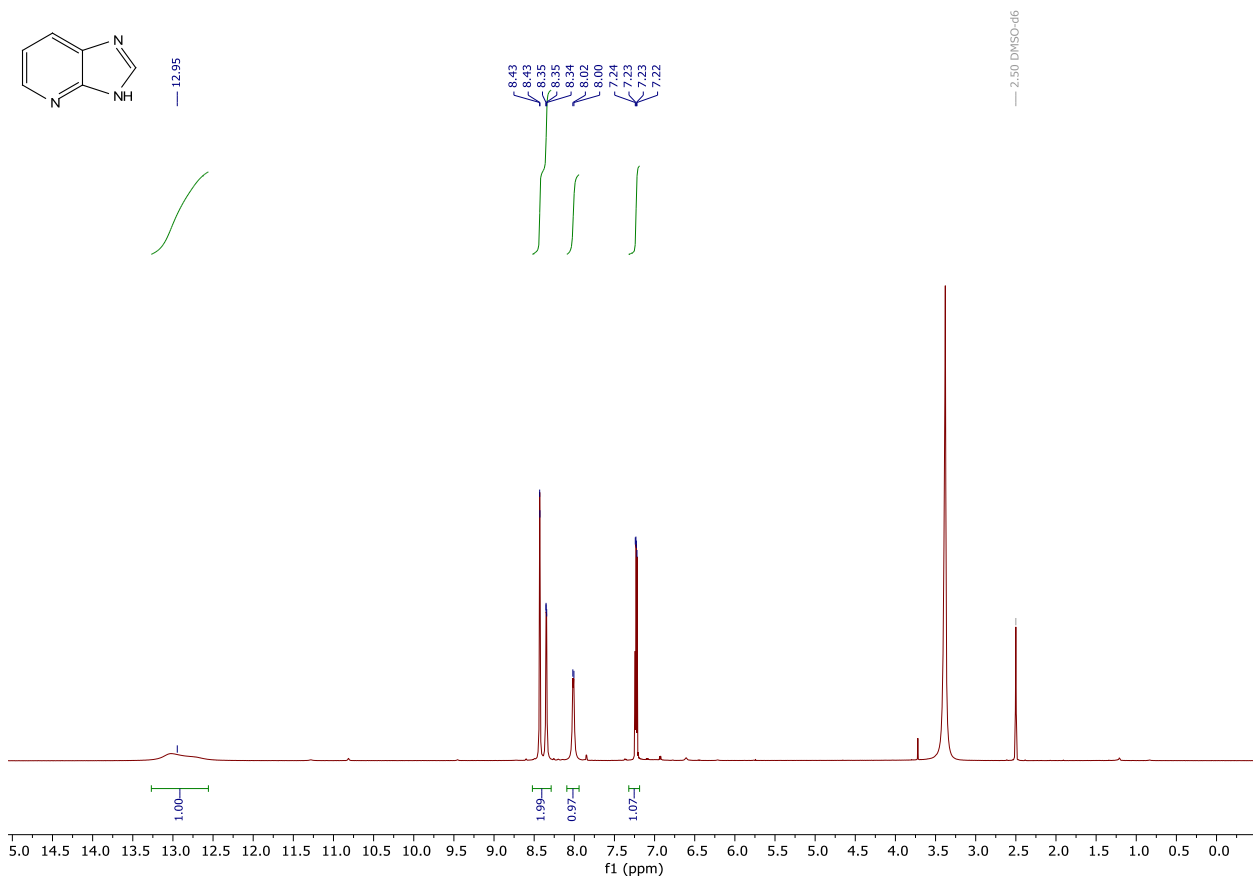


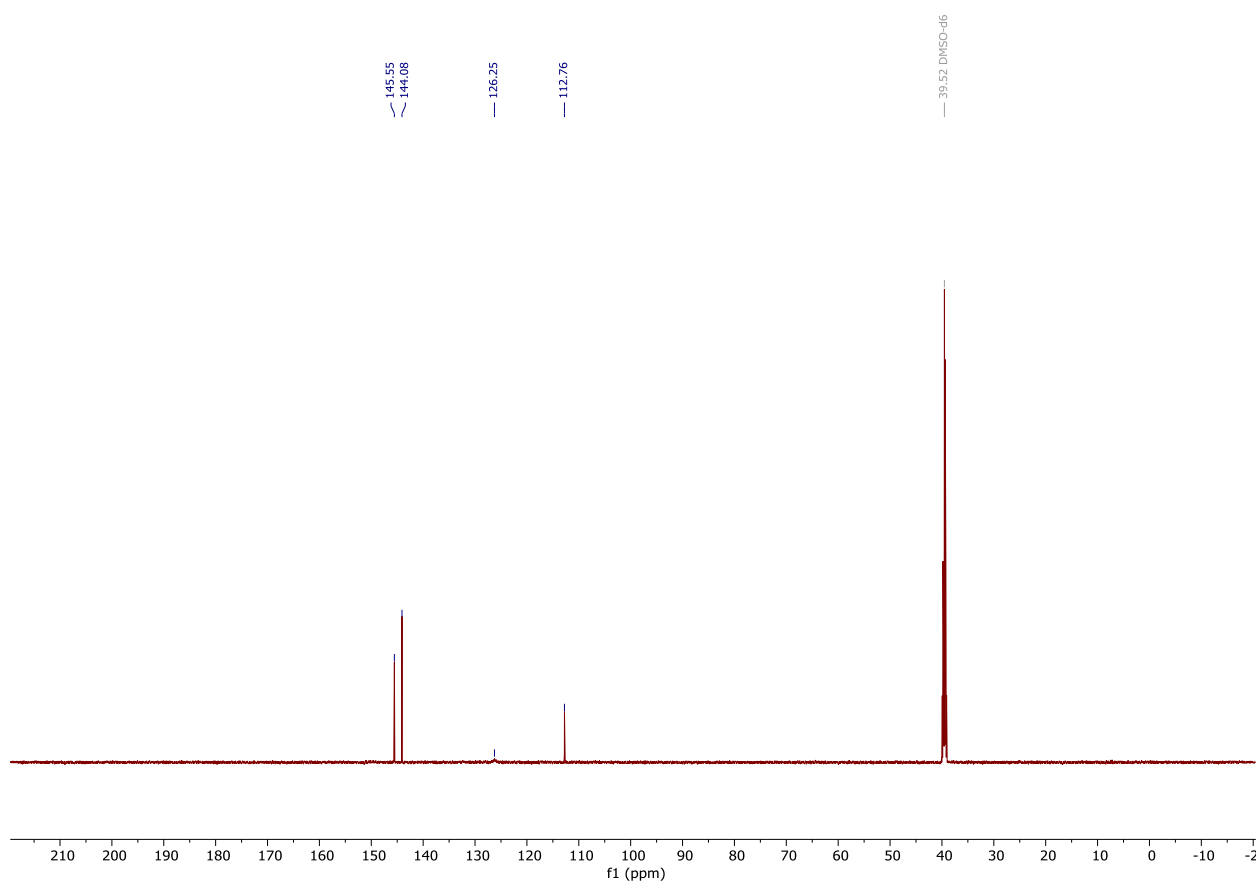
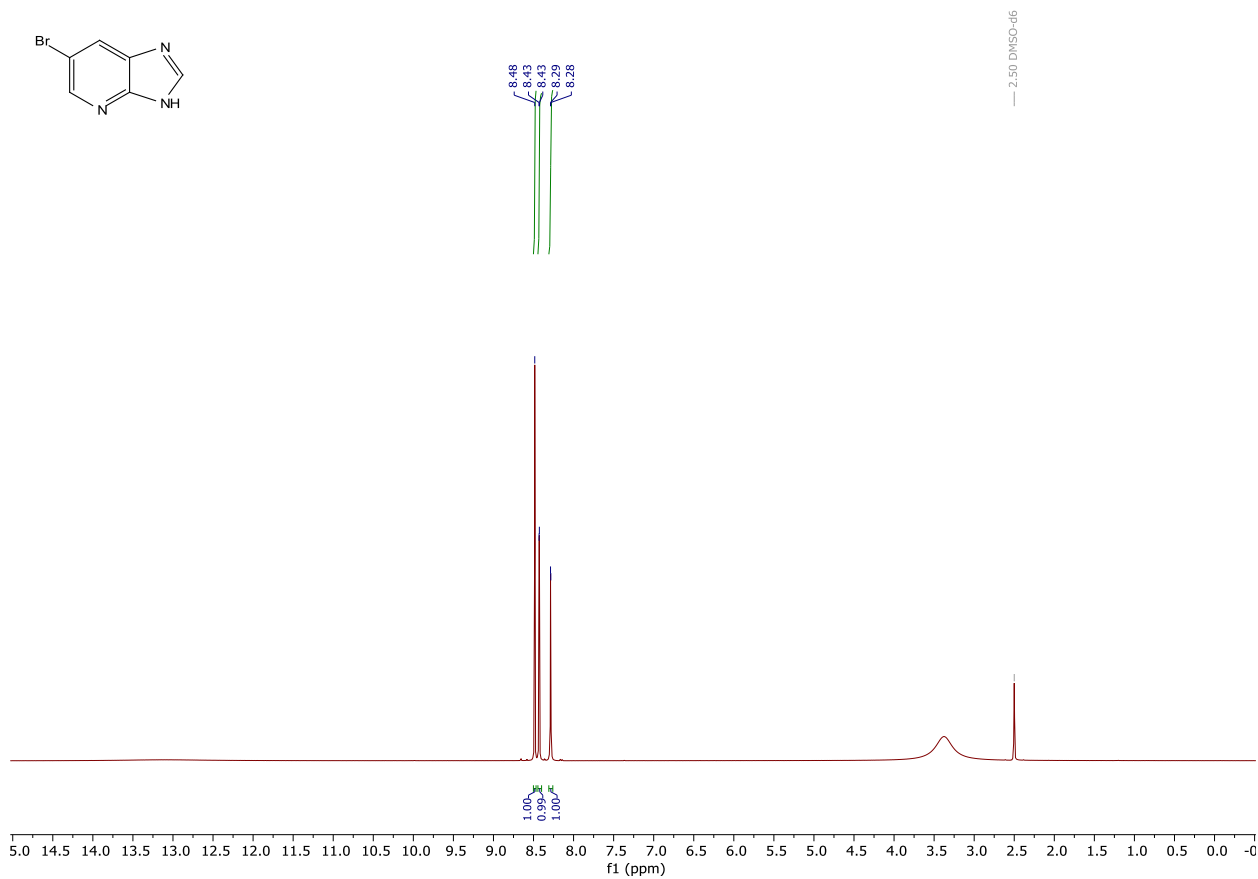


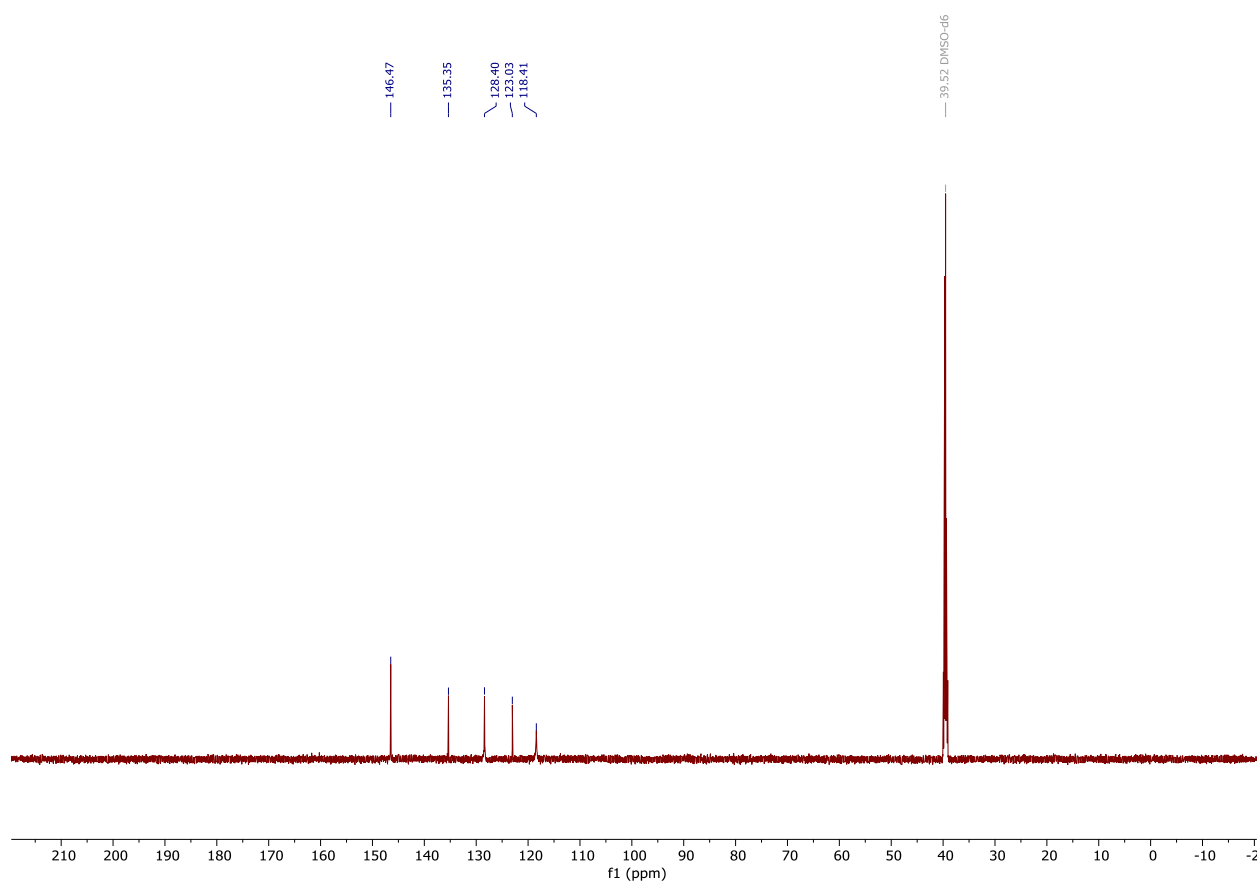
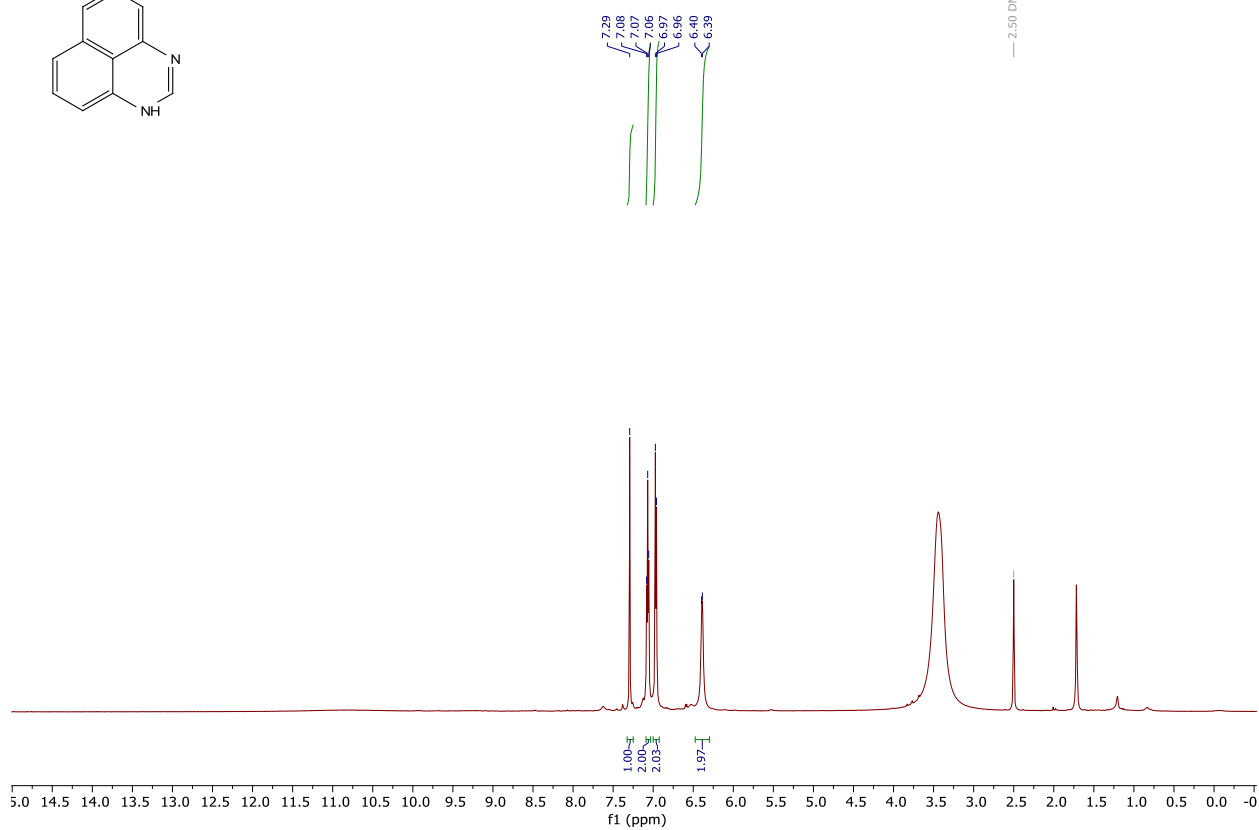
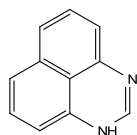












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