catalysts

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*Supplementary material on:*

# Microwave-assisted regioselective Suzuki coupling of 2,4-dichloropyrimidines with aryl boronic acids

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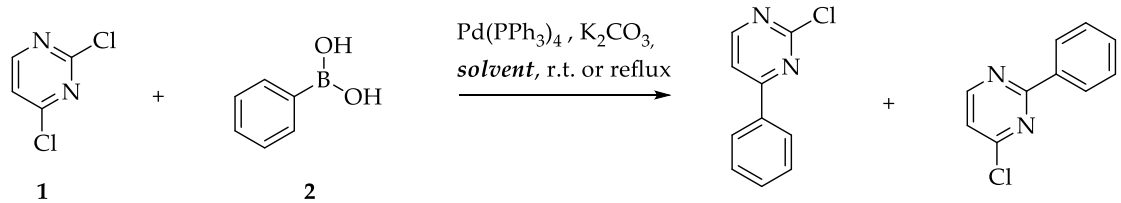
# 1 Additional description of optimization procedure

## 1.1 Solvent screening

2,4-dichloropyrimidine **1** (75 mg, 0.50 mmol) was dissolved/suspended in the selected *solvent* (3.5 mL), where the air (oxygen) was displaced with argon before use. Then potassium carbonate (207 g, 1.50 mmol), phenylboronic acid **2** (61 mg, 0.50 mmol), and 5 mol% of tetrakis(triphenylphosphine)palladium(0) (29 mg, 0.025 mmol) was added and stirred under argon atmosphere at room or other selected temperature (i.e. 60, 80 or 100 °C).

After 1 h, 2 h and 24 h, 50 μL of reaction mixture was taken and diluted with 950 μL of internal standard solution (prepared by 102 mg of acetanilide in 100 mL of acetonitrile). The sample was further diluted (1/10) with acetonitrile and filtered to obtain the final sample for LC-MS analysis.

**Table S1.** Solvent screening of Suzuki coupling between **1** and **2**.




**1** **2** **3** **4**

| Entry | Solvent | Temperature (°C) | Yield (%)[1,2] 1 h | 2 h | 24 h | Selectivity ratio 3:4[3] |
|---|---|---|---|---|---|---|
| 1 | $H_2O$ | r.t. | 4 | 4 | 4 | ND[4] |
| 2 | $H_2O$ | 100 | 6 | 6 | 4 | ND[4] |
| 3 | MeOH | r.t. | 2 | 3 | 11 | ND[4] |
| 4 | MeOH | 60 | 6 | 13 | 39 | >100 |
| 5 | THF | r.t. | 3 | 10 | 10 | ND[4] |
| 6 | THF | 60 | 7 | 15 | 38 | 14 |
| 7 | DMF | r.t. | 4 | 4 | 14 | >100 |
| 8 | DMF | 100 | 34 | 36 | 42 | 15 |
| 9 | 1,4-dioxane | r.t. | 6 | 7 | 32 | 43 |
| 10 | 1,4-dioxane | 100 | 29 | 41 | 72 | 9 |
| 11 | isopropanol | r.t. | 4 | 5 | 57 | 57 |
| 12 | isopropanol | 80 | 28 | 34 | 64 | 32 |
| 13 | ethylene glycol | r.t. | 6 | 6 | 14 | 7 |
| 14 | ethylene glycol | 100 | 5 | 12 | 26 | 13 |

[1] Reaction conditions: **1** (75 mg, 0.50 mmol), ***solvent*** (3.5 mL), $K_2CO_3$ (207 g, 1.50 mmol), **2** (61 mg, 0.50 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), room temperature (r.t.) or 60/80/100 °C, 1–24 h.

[2] Determined by LC-MS.

[3] Determined by LC-MS after 24 h reaction time.

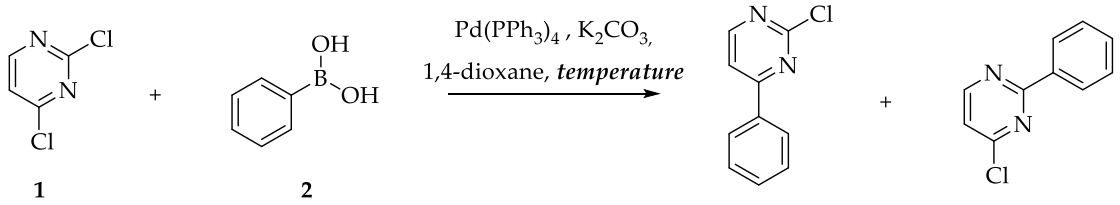
[4] The ratio cannot be determined due to really low reaction yield.

### 1.2 Temperature screening

**1** (75 mg, 0.50 mmol) was dissolved in 1,4-dioxane (3.5 mL), where the air (oxygen) was displaced with argon before use. Then $K_2CO_3$ (207 g, 1.50 mmol), **2** (61 mg, 0.50 mmol), and 5 mol% of $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) was added and stirred under argon atmosphere at selected temperature (i.e. 25, 50, 70 or 100 °C).

After 1, 2 and 24 h, 50 μL of reaction mixture was taken and diluted with 950 μL of internal standard solution (prepared by 102 mg of acetanilide in 100 mL of acetonitrile). The sample was further diluted (1/10) with acetonitrile and filtered to obtain the final sample for LC-MS analysis.

**Table S2.** Temperature screening of Suzuki coupling between **1** and **2**.




**1** + **2** → **3** + **4**

| Entry | Temperature (°C) | Yield (%)[1,2] | | | Selectivity ratio 3 : 4[3] |
|---|---|---|---|---|---|
| | | 1 h | 2 h | 24 h | |
| 1 | 25 | 5 | 7 | 15 | 3 |
| 2 | 50 | 5 | 8 | 26 | 26 |
| 3 | 70 | 6 | 11 | 28 | 9 |
| 4 | 100 | 29 | 41 | 72 | 9 |

[1] Reaction conditions: **1** (75 mg, 0.50 mmol), 1,4-dioxane (3.5 mL), $K_2CO_3$ (207 g, 1.50 mmol), **2** (61 mg, 0.50 mmol), $Pd(PPh_3)_4$ (29 mg, 0.025 mmol), ***temperature***, 1–24 h.

[2] Determined by LC-MS.

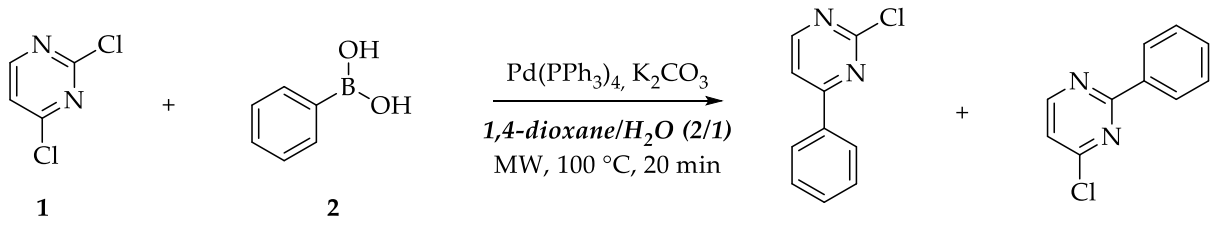
[3] Determined by LC-MS after 24 h reaction time.

### 1.3 Screening of the solvent volume for microwave-assisted Suzuki coupling between 1 and 2

**1** (75 mg, 0.50 mmol) was dissolved in a mixture of 1,4-dioxane and water in the ratio 2:1 (i.e. total volume of 1.8, 3, 4.5 and 6 mL), where the air (oxygen) was displaced with argon before use. Then $K_2CO_3$ (207 mg, 1.50 mmol), **2** (61 mg, 0.50 mmol), and 3 mol% of $Pd(PPh_3)_4$ (17.3 mg, 0.015 mmol) was added and stirred under argon atmosphere. The reaction mixture was then stirred for 20 min at 100 °C in a microwave reactor.

50 μL of reaction mixture was diluted with 950 μL of internal standard solution (prepared by 102 mg of acetanilide in 100 mL of $CH_3CN$). The sample was further diluted (1/10) with $CH_3CN$ and filtered to obtain the final sample for LC-MS analysis.

**Table S1.** Solvent volume screening for Suzuki coupling between **1** and **2**.




**1** **2** **3** **4**

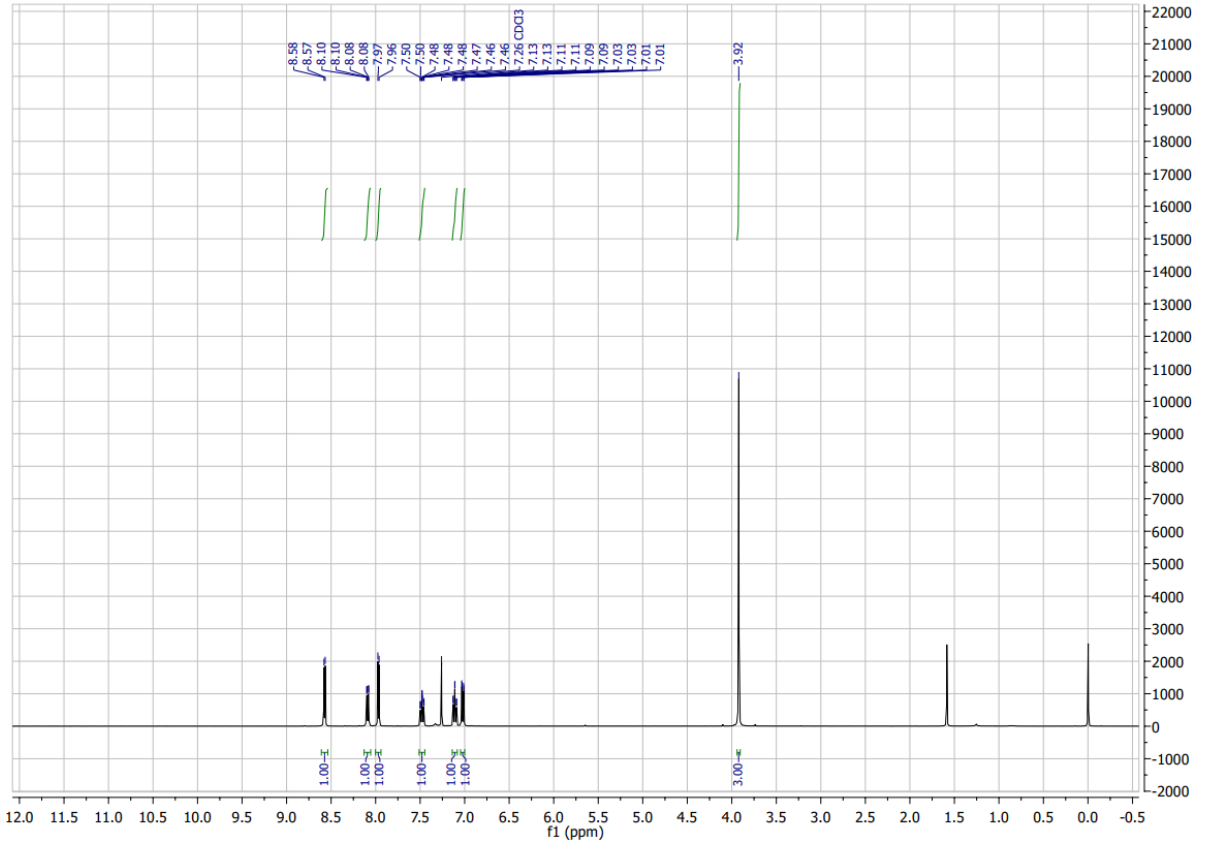
| Entry | 1,4-dioxane volume [mL] | $H_2O$ volume [mL] | Yield (%)[1,2] |
|---|---|---|---|
| 1 | 4 | 2 | 80 |
| 2 | 3 | 1.5 | 76 |
| 3 | 2 | 1 | 69 |
| 4 | 1.2 | 0.6 | 43 |

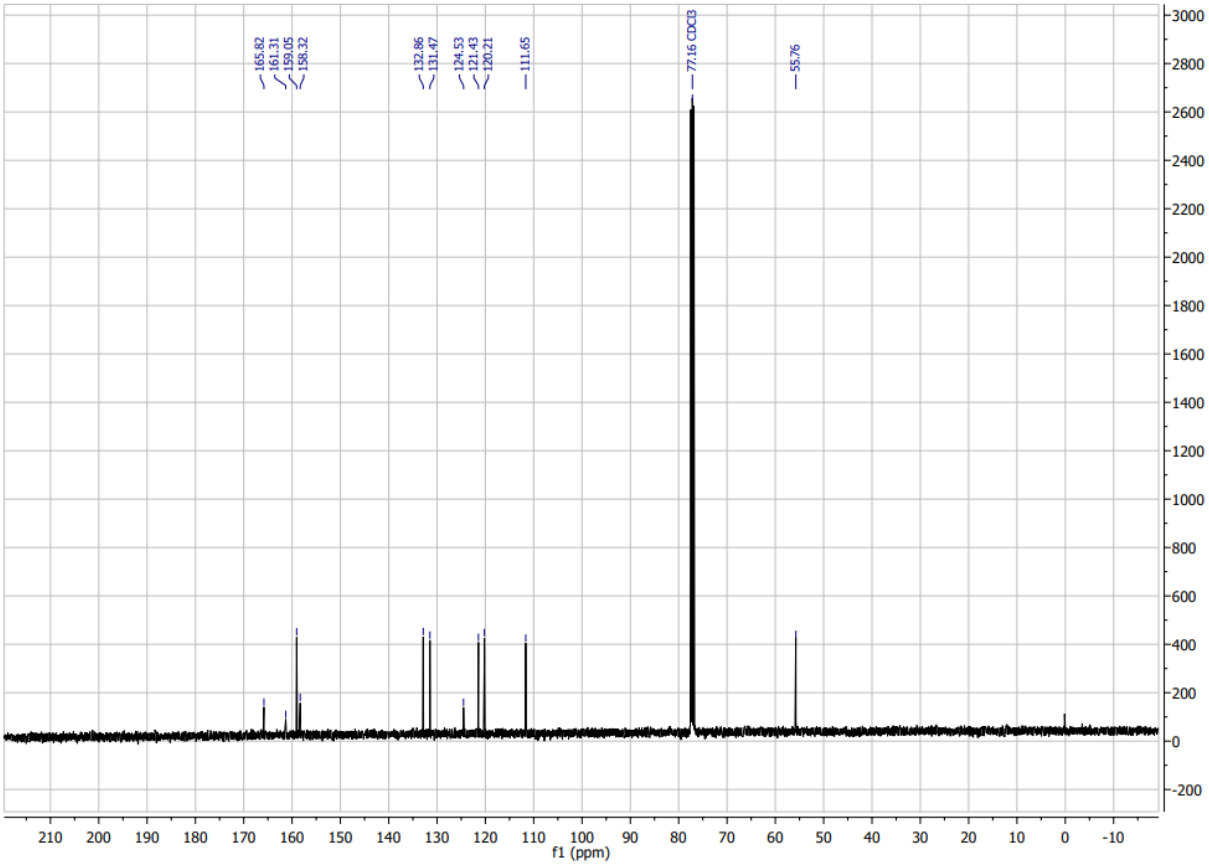
[1] Reaction conditions: **1** (75 mg, 0.50 mmol), ***1,4-dioxane/ $H_2O$ (2/1)***, $K_2CO_3$ (207 mg, 1.50 mmol), **2** (61 mg, 0.50 mmol), $Pd(PPh_3)_4$ (17.3 mg, 0.015 mmol), MW, 100 °C, 20 min.

[2] Yield for **3**, determined by LC-MS.

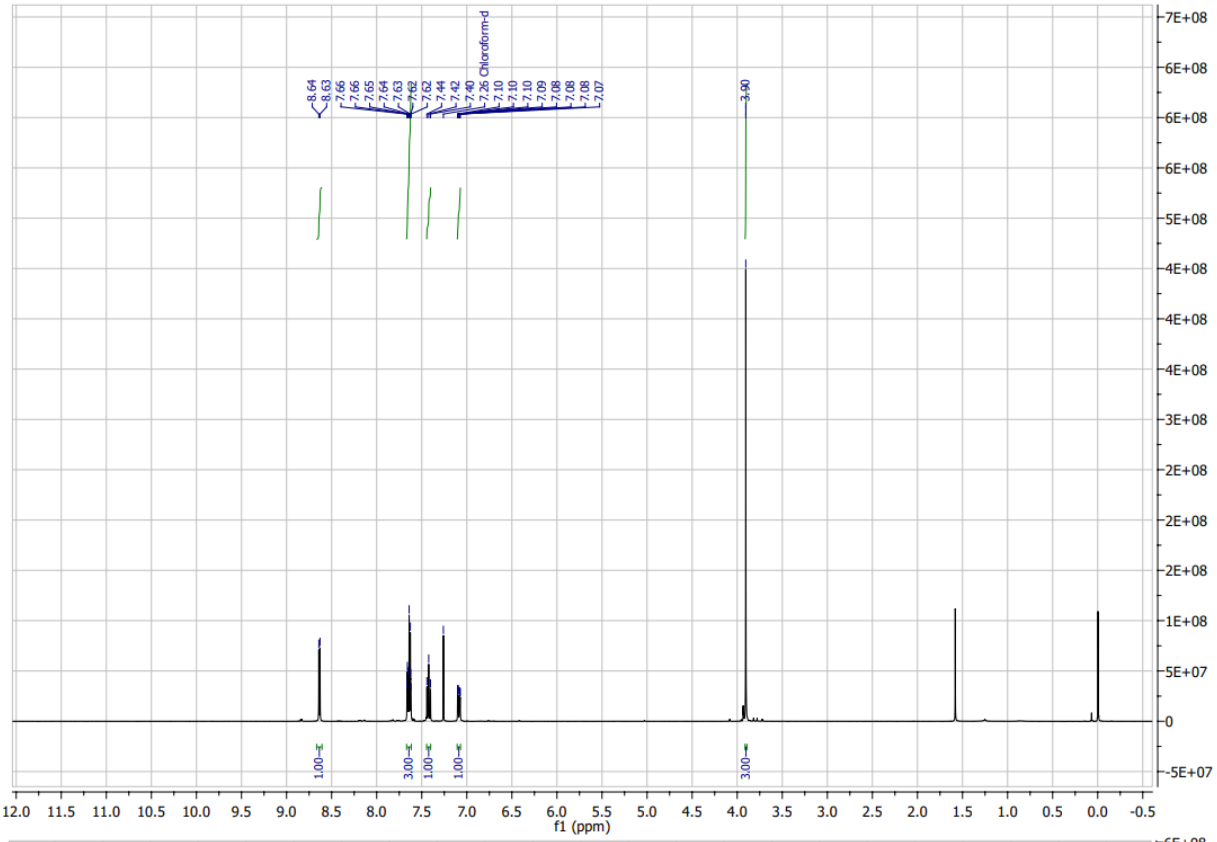
## 2 $^{1}$H NMR and $^{13}$C NMR spectra of compounds

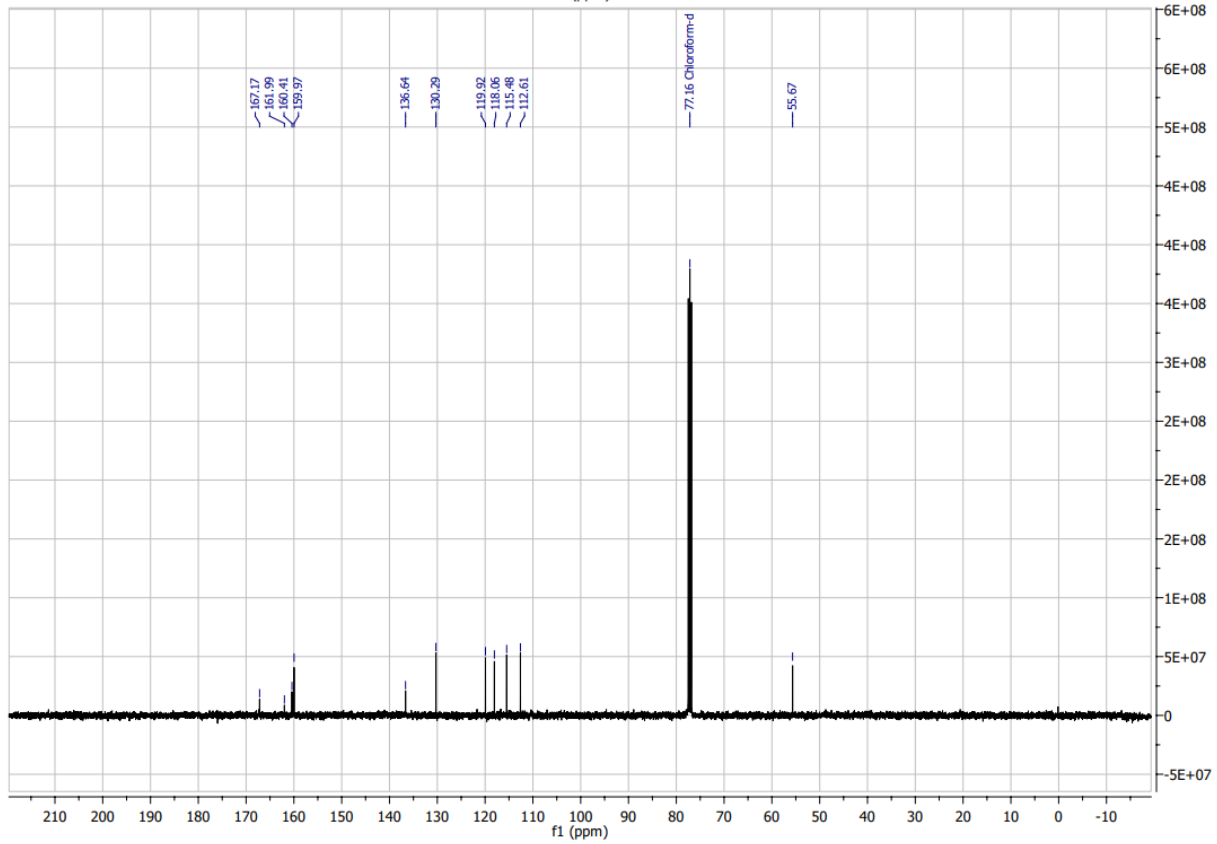
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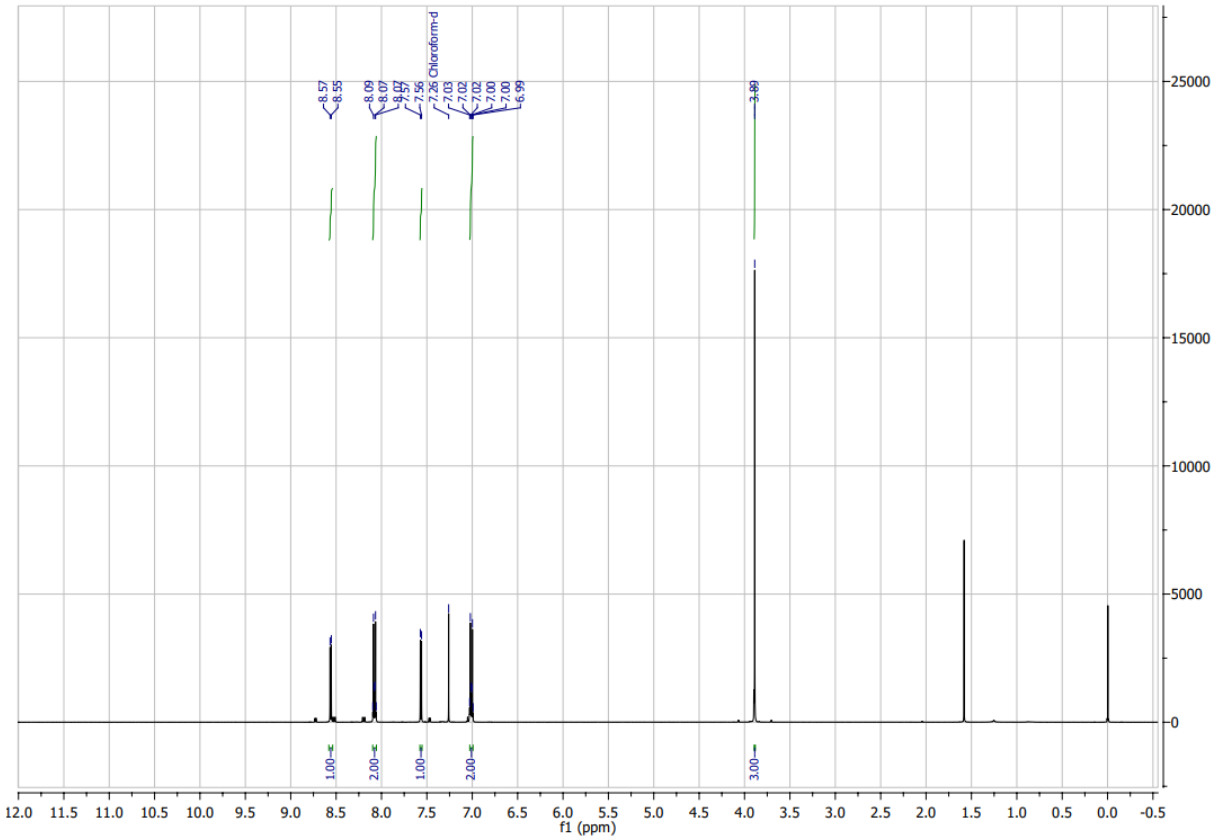



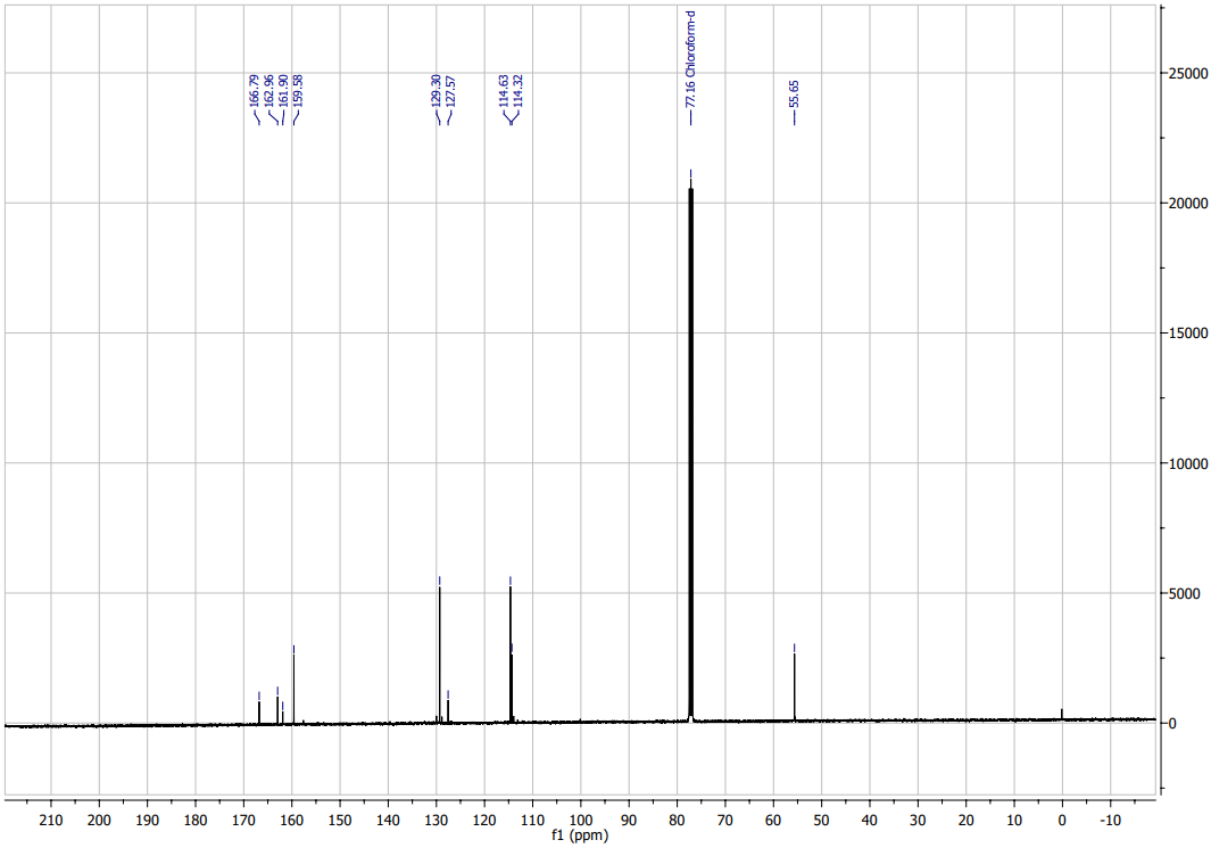
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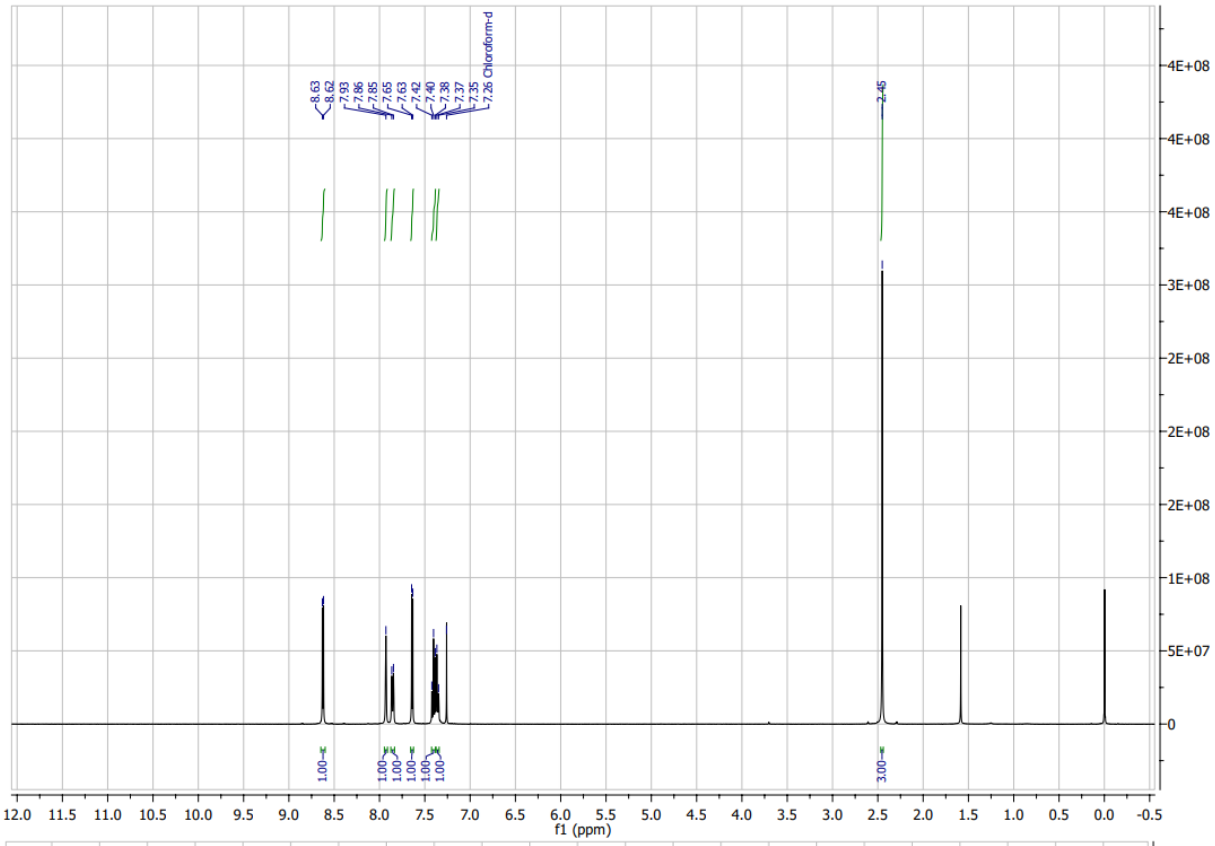



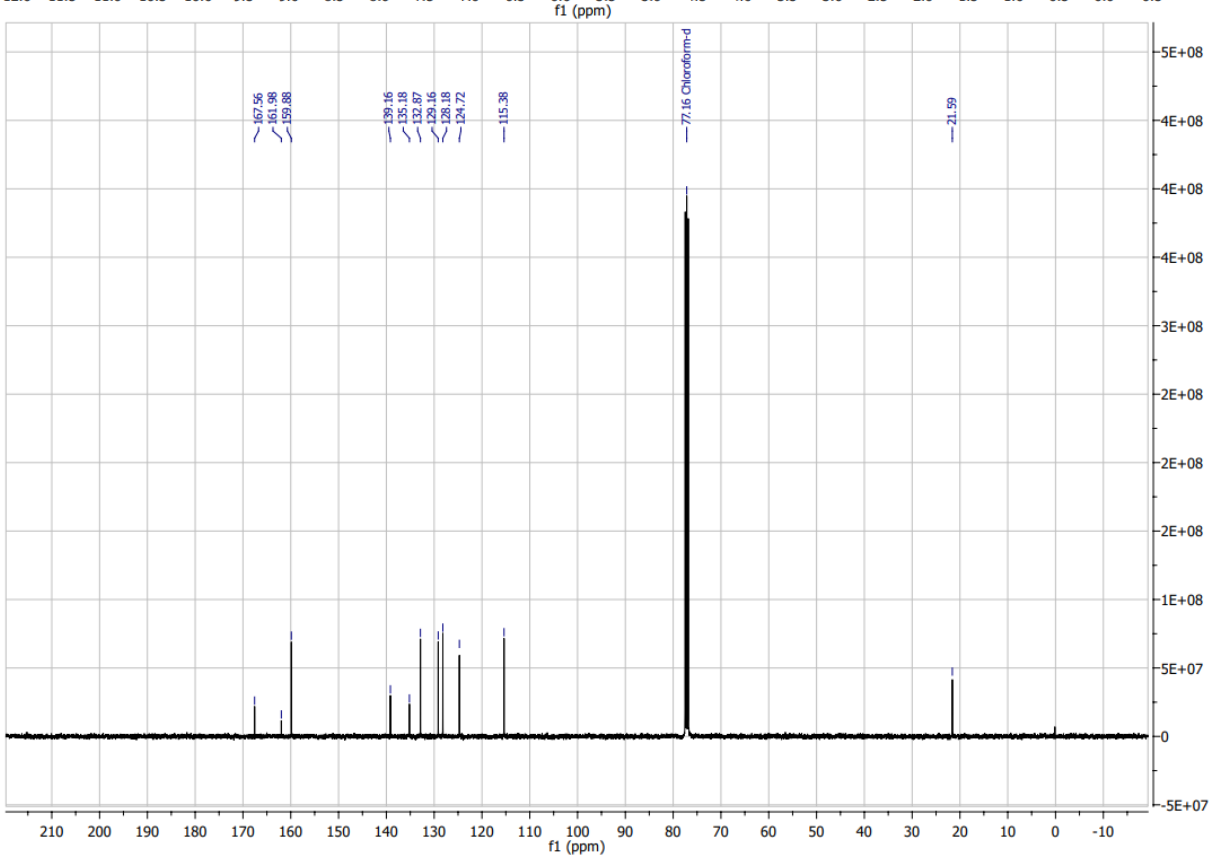
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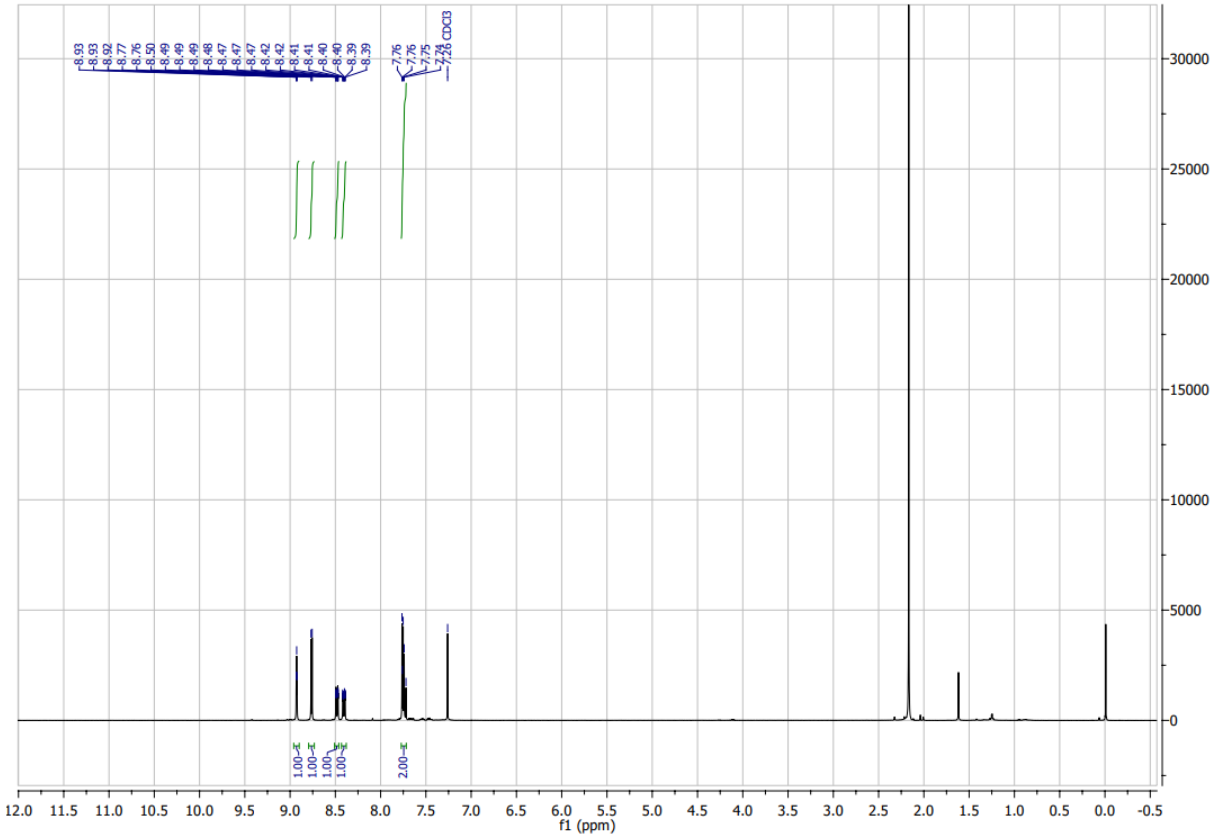



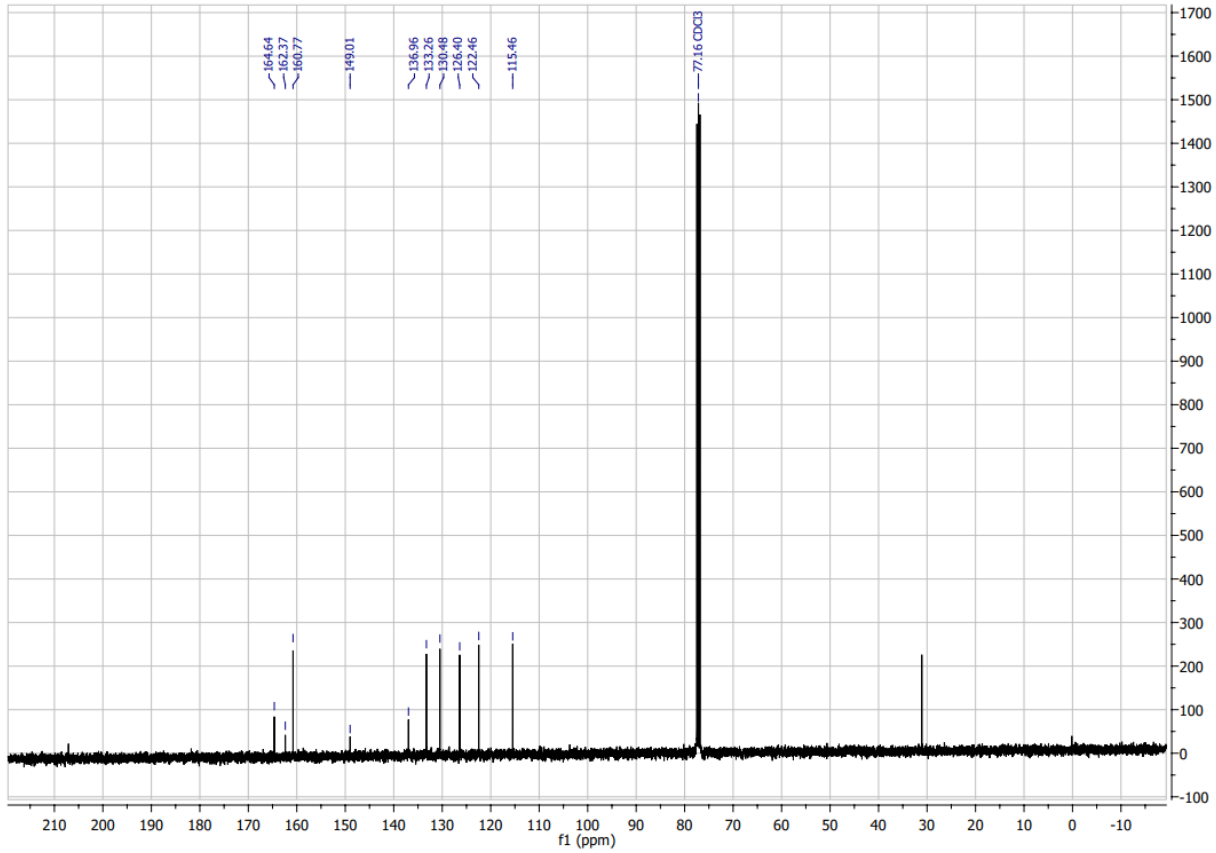
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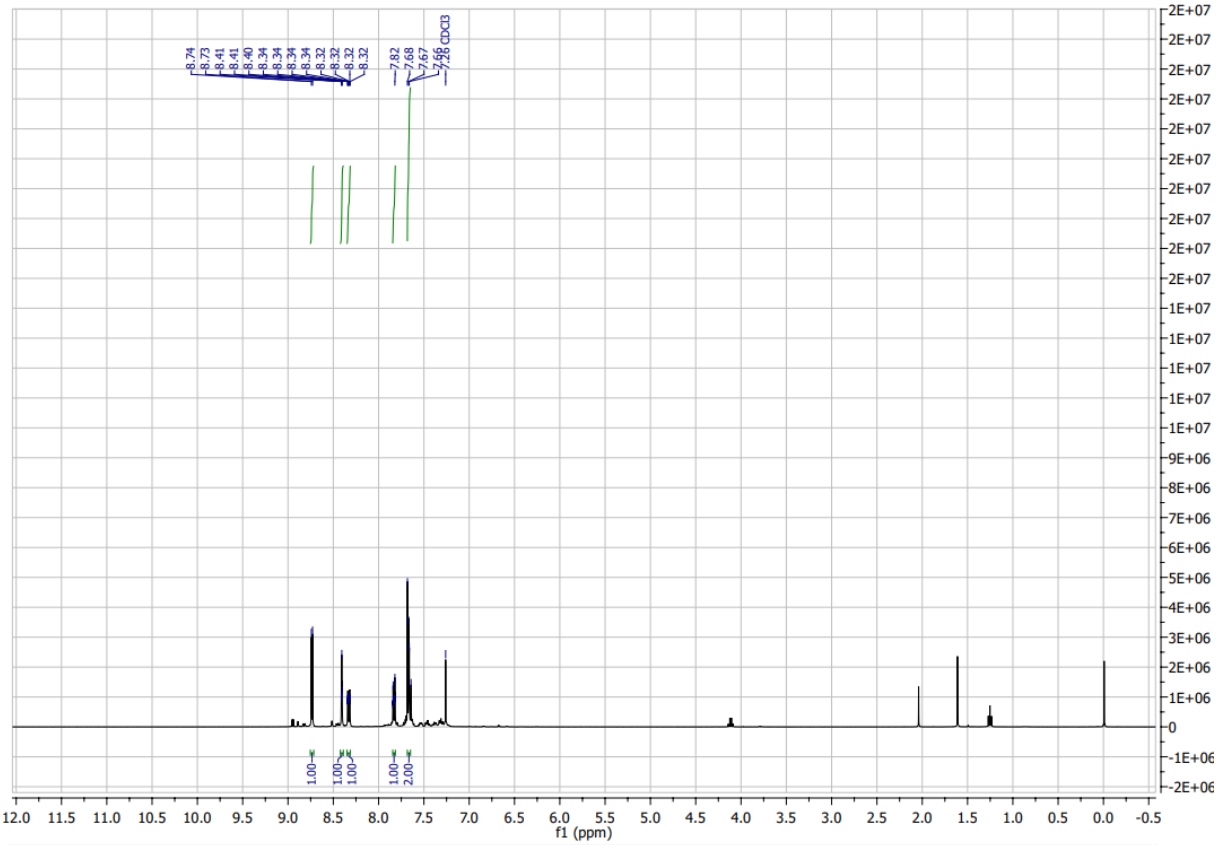



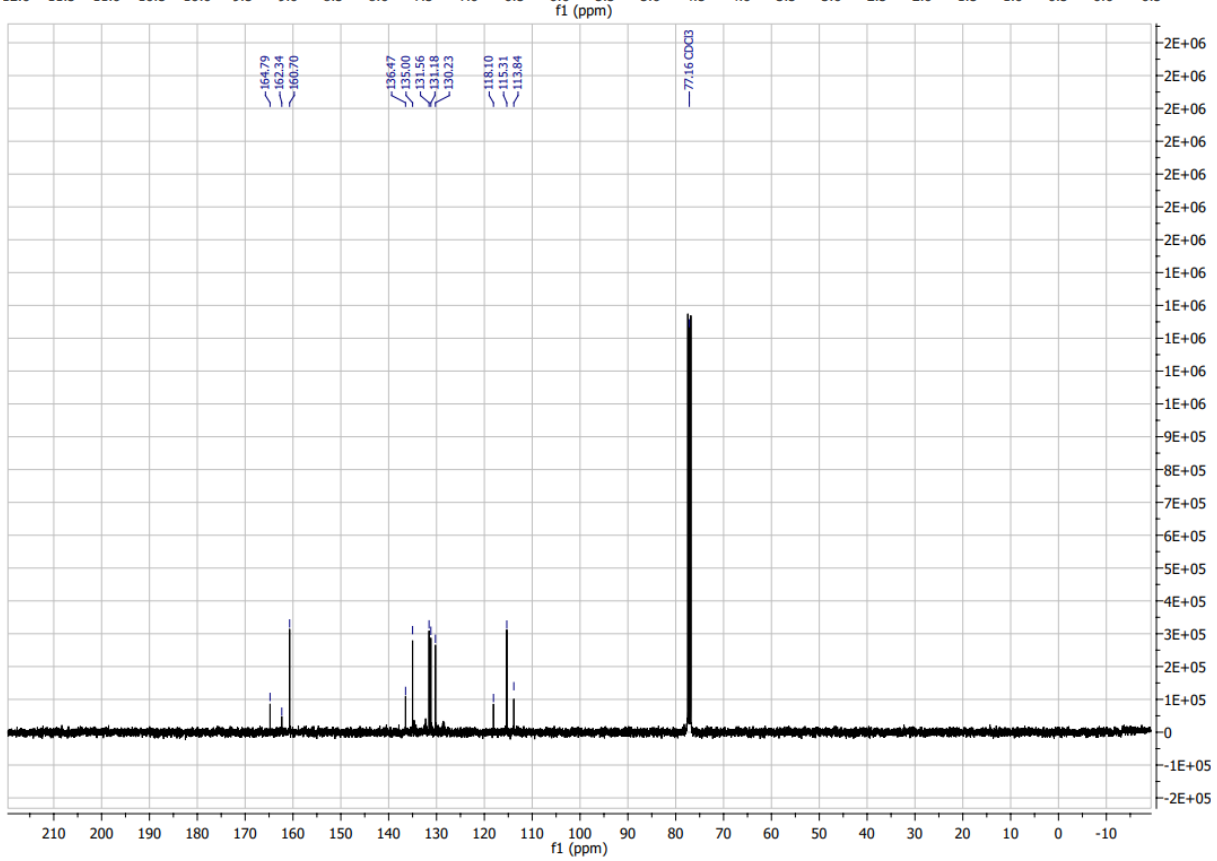
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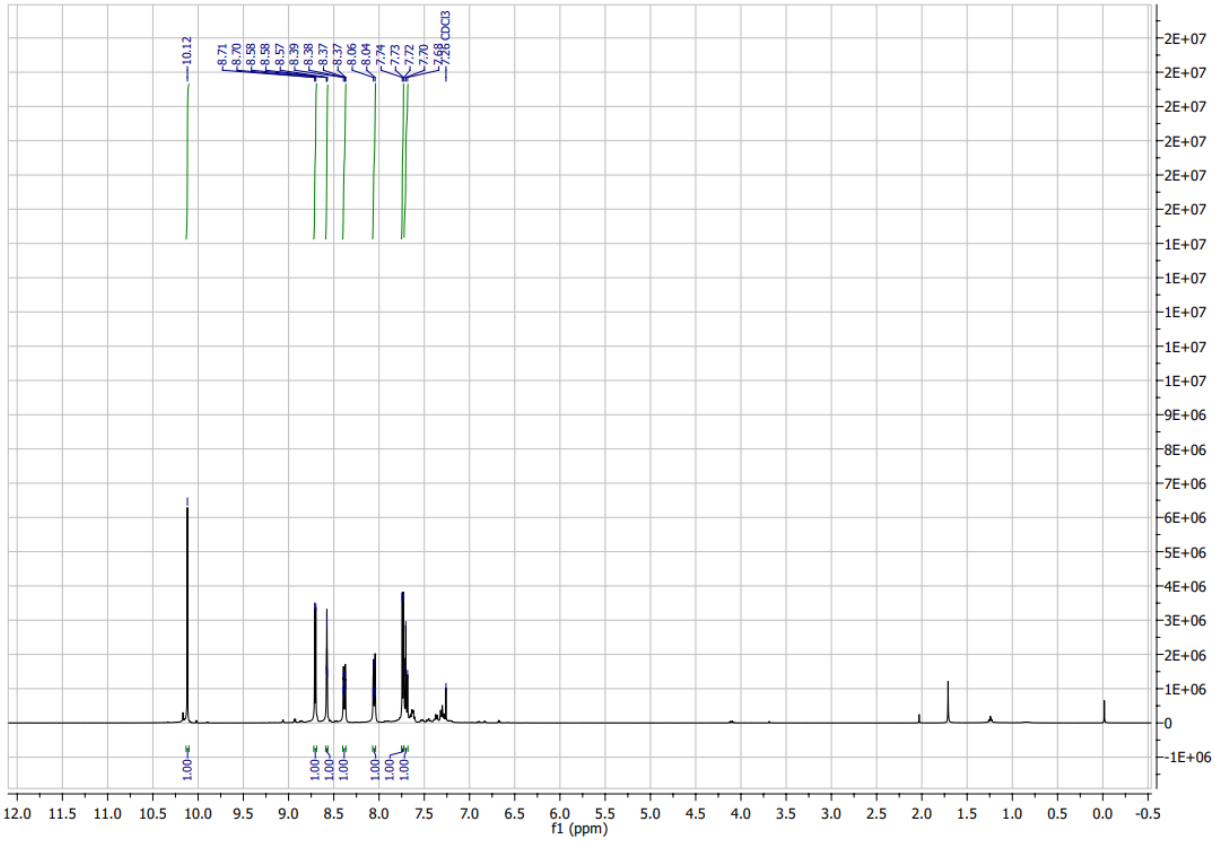



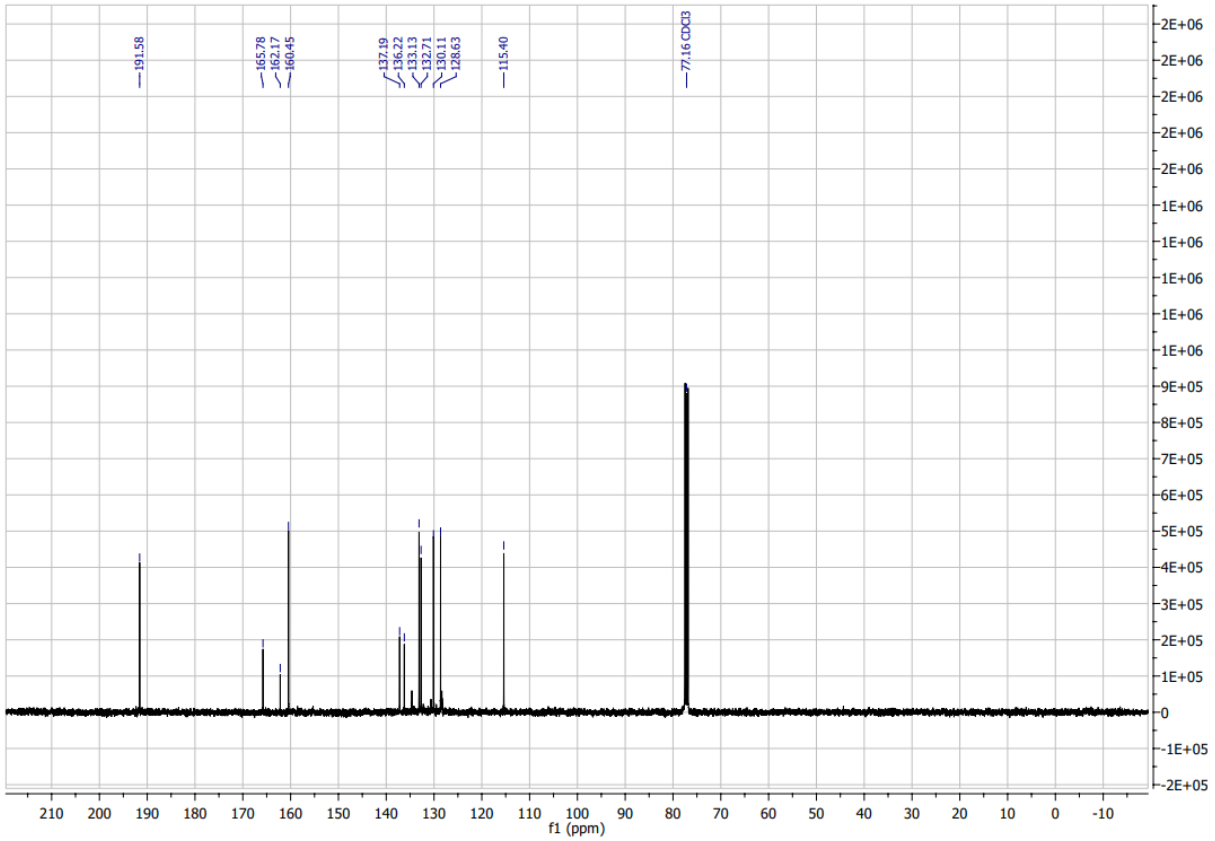
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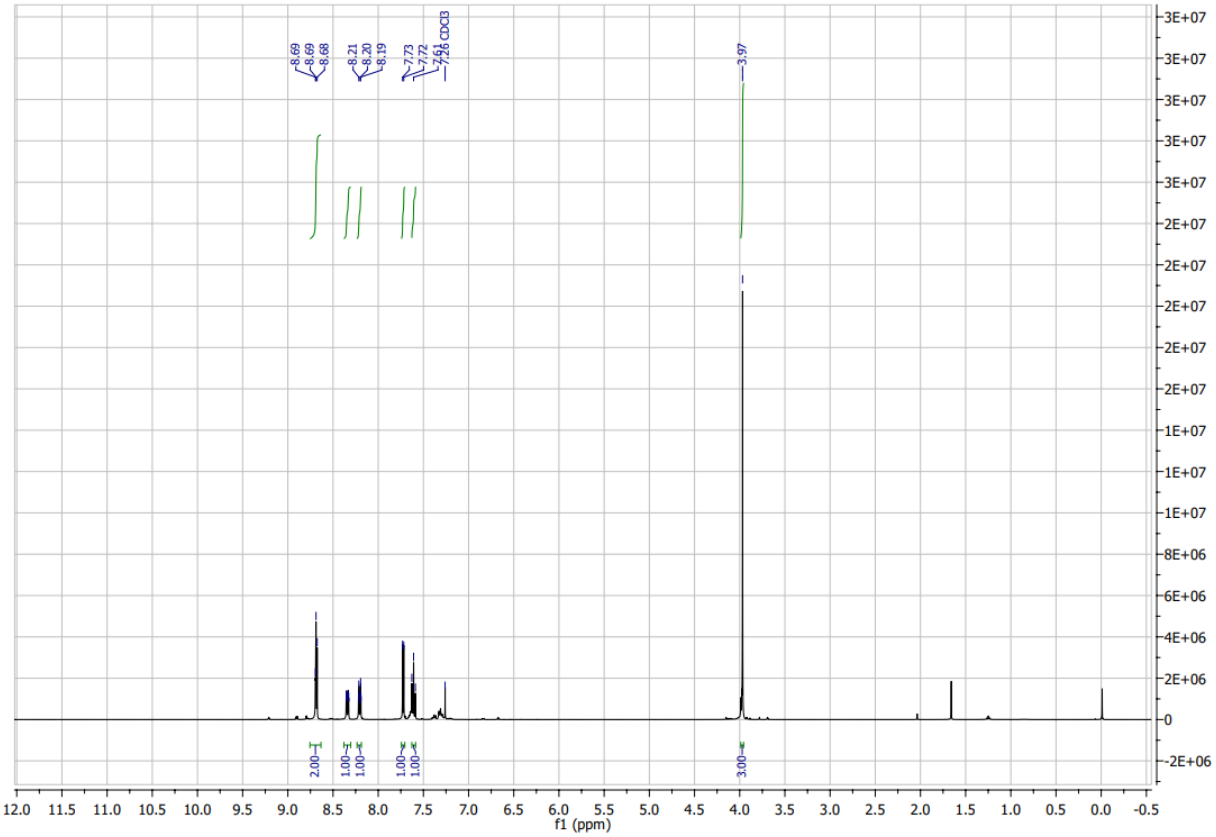



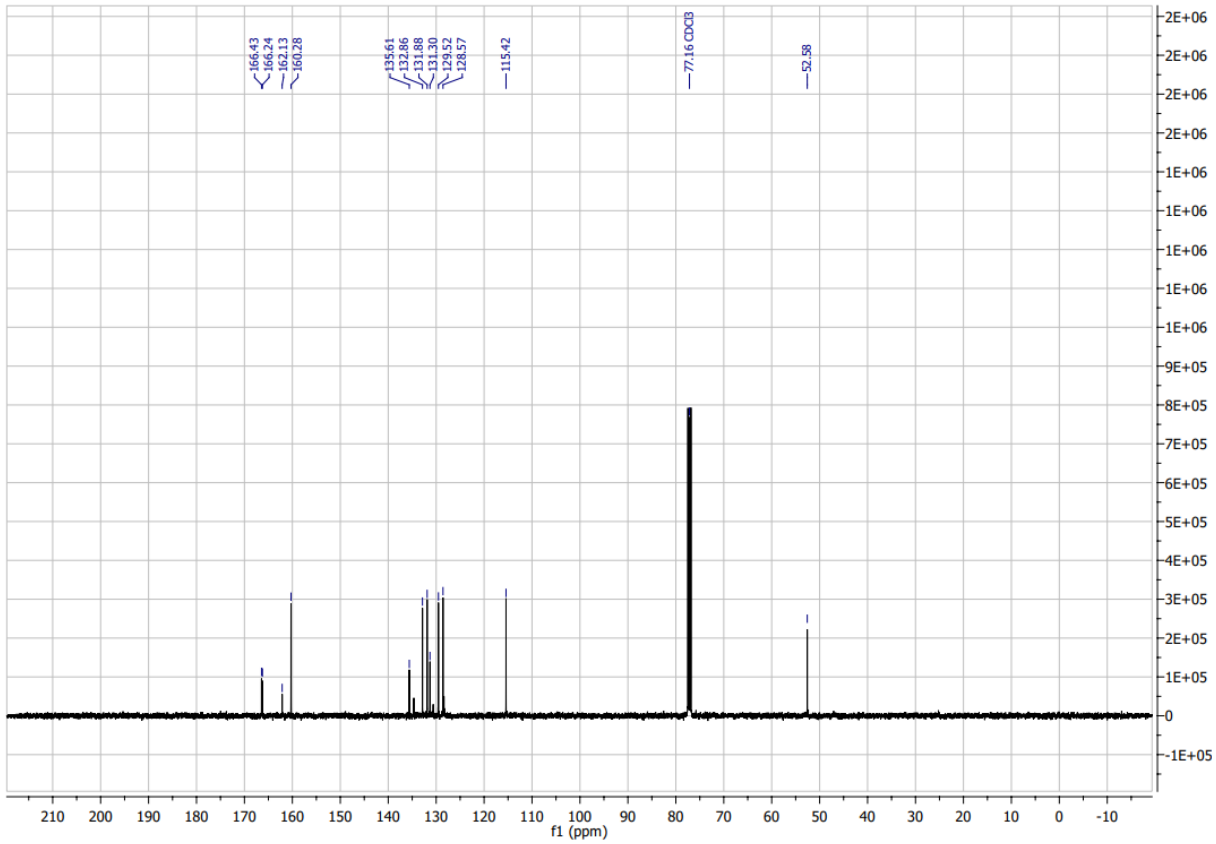
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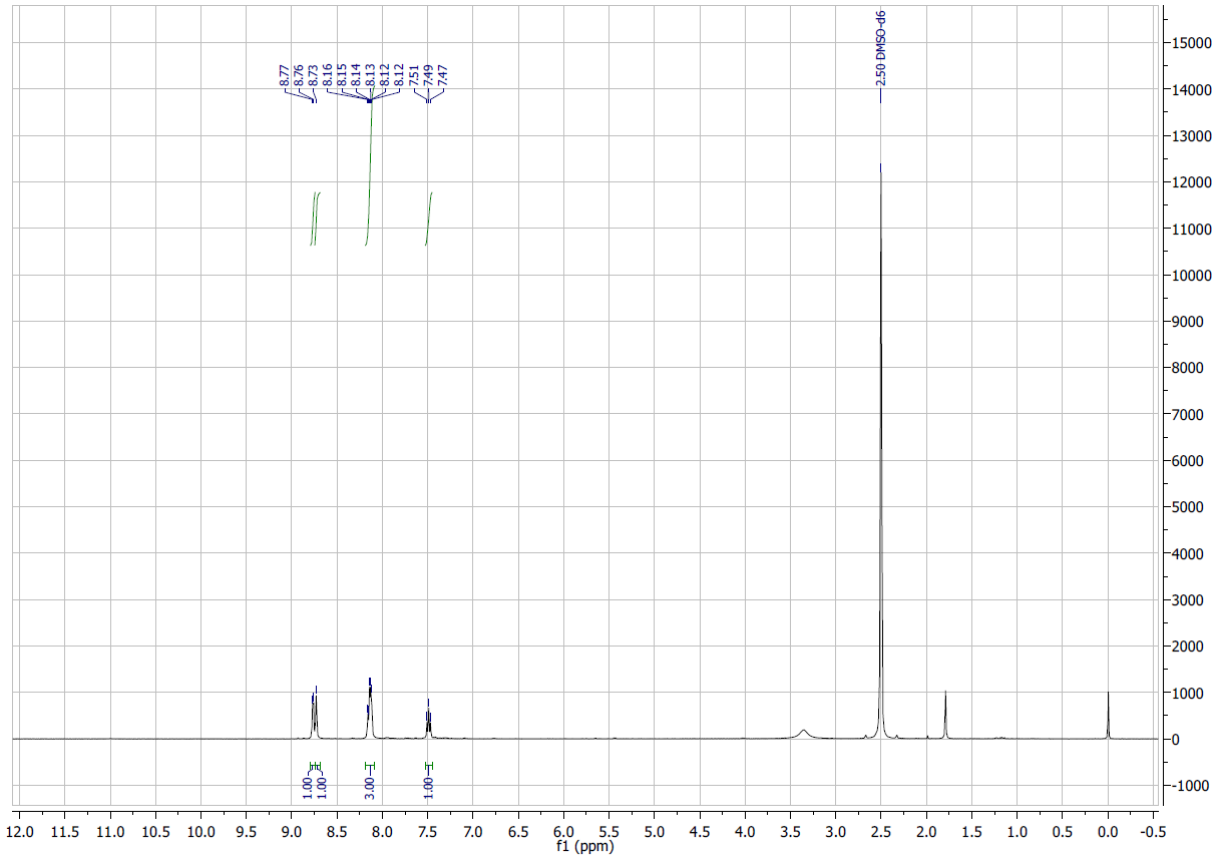



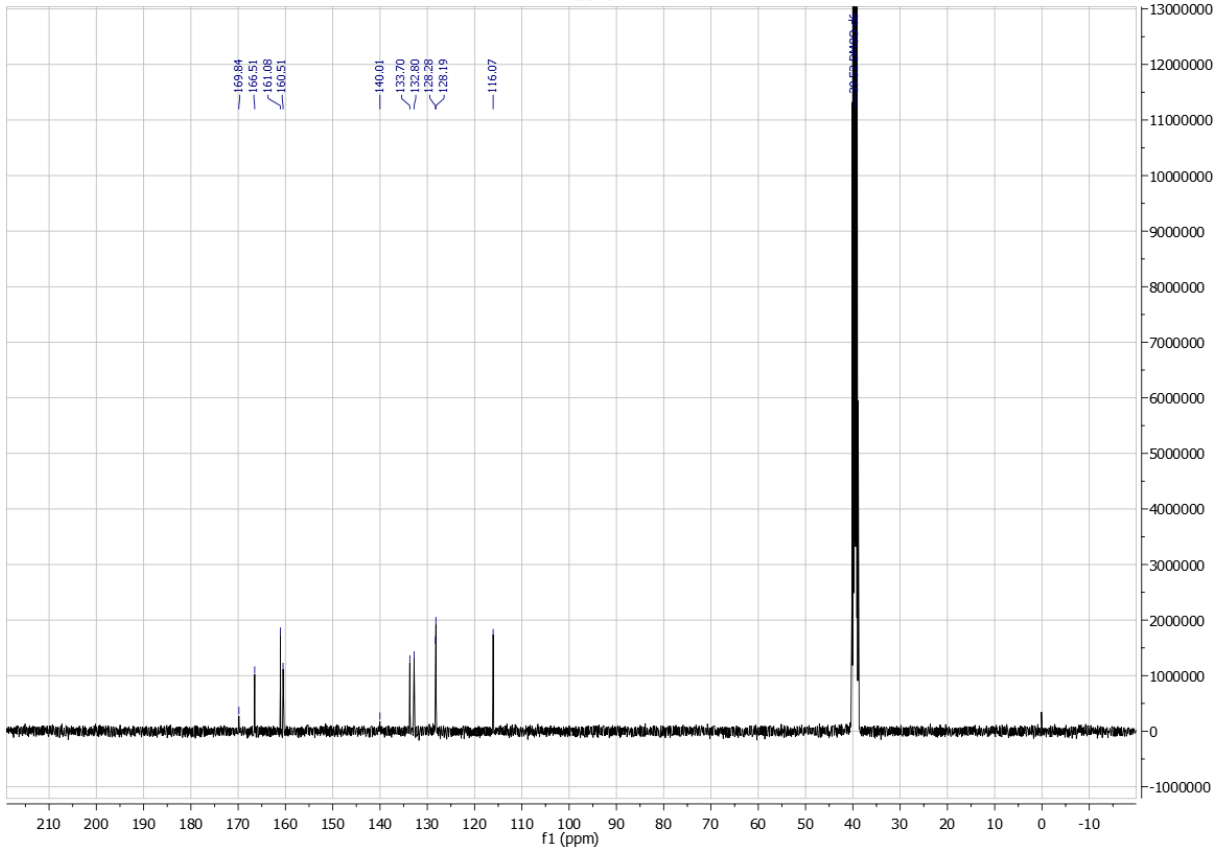
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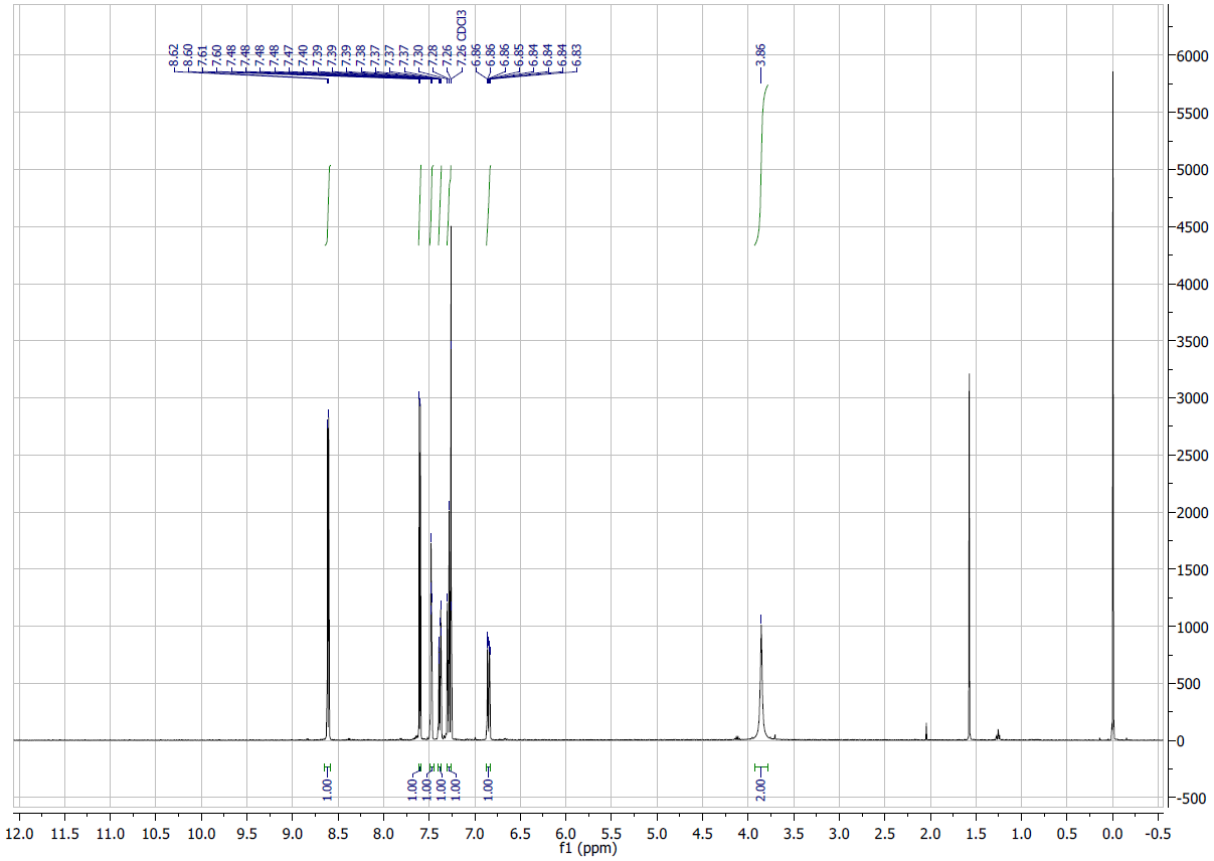



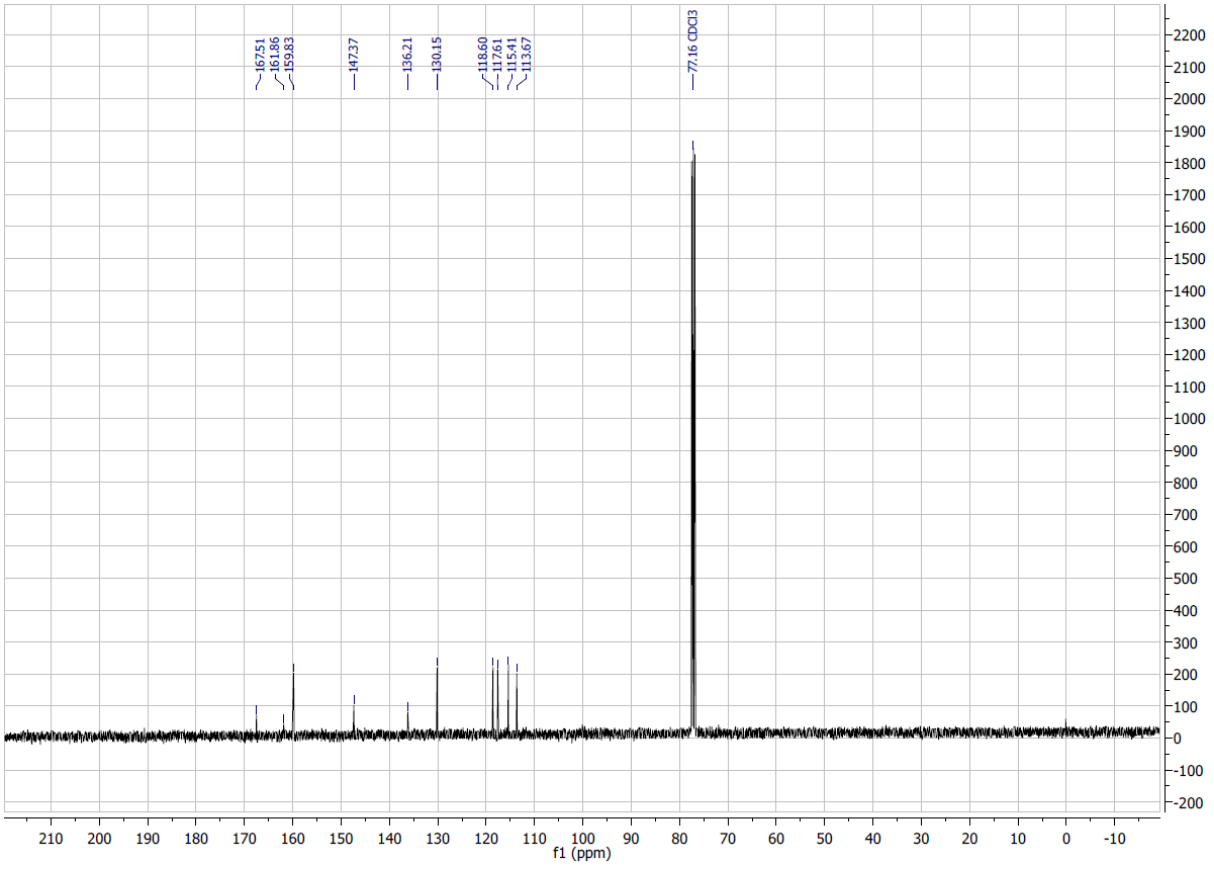
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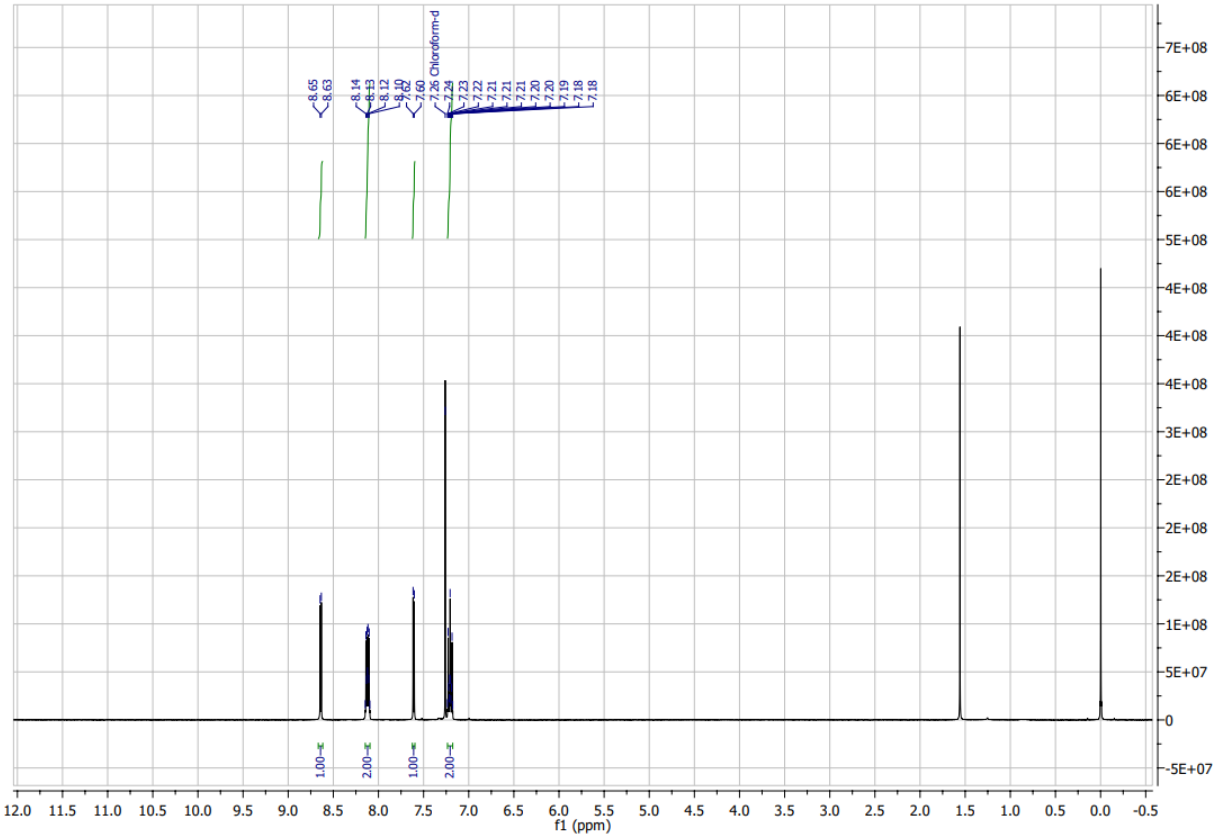



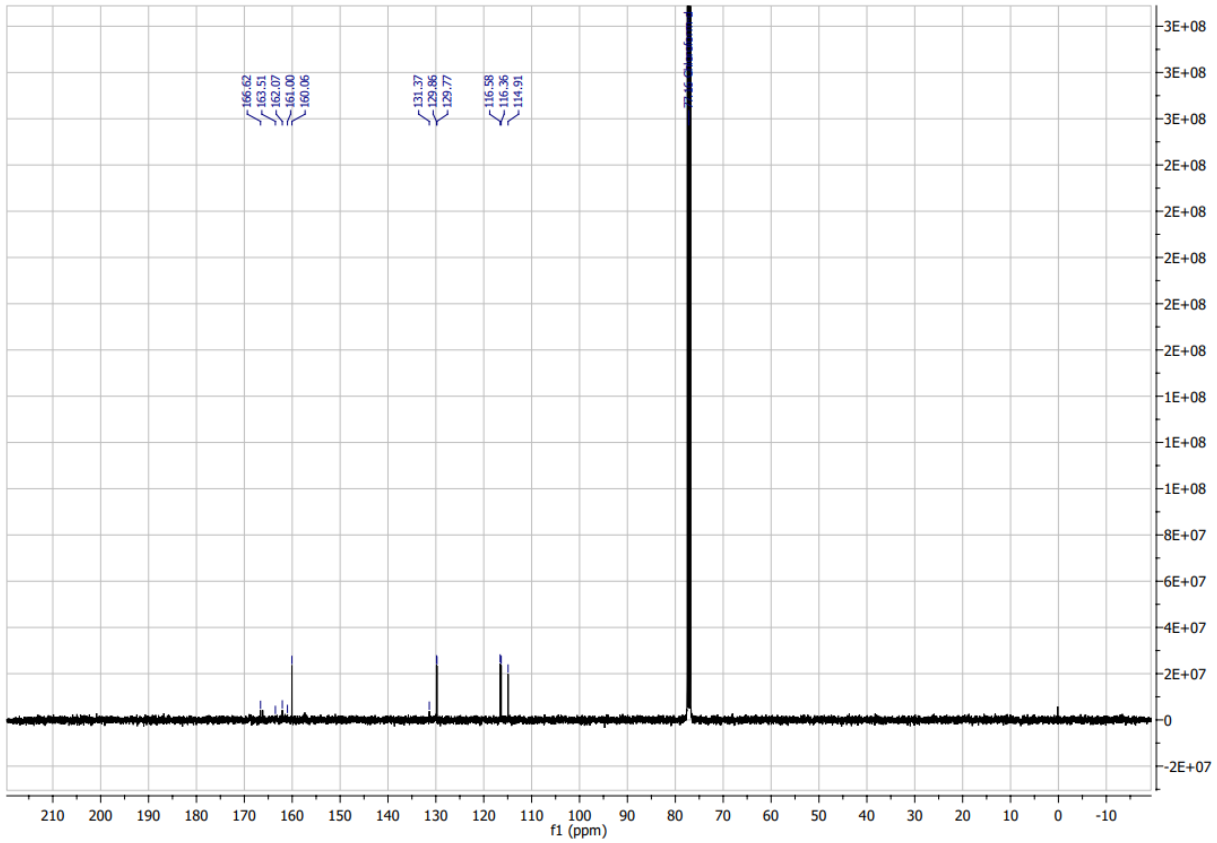
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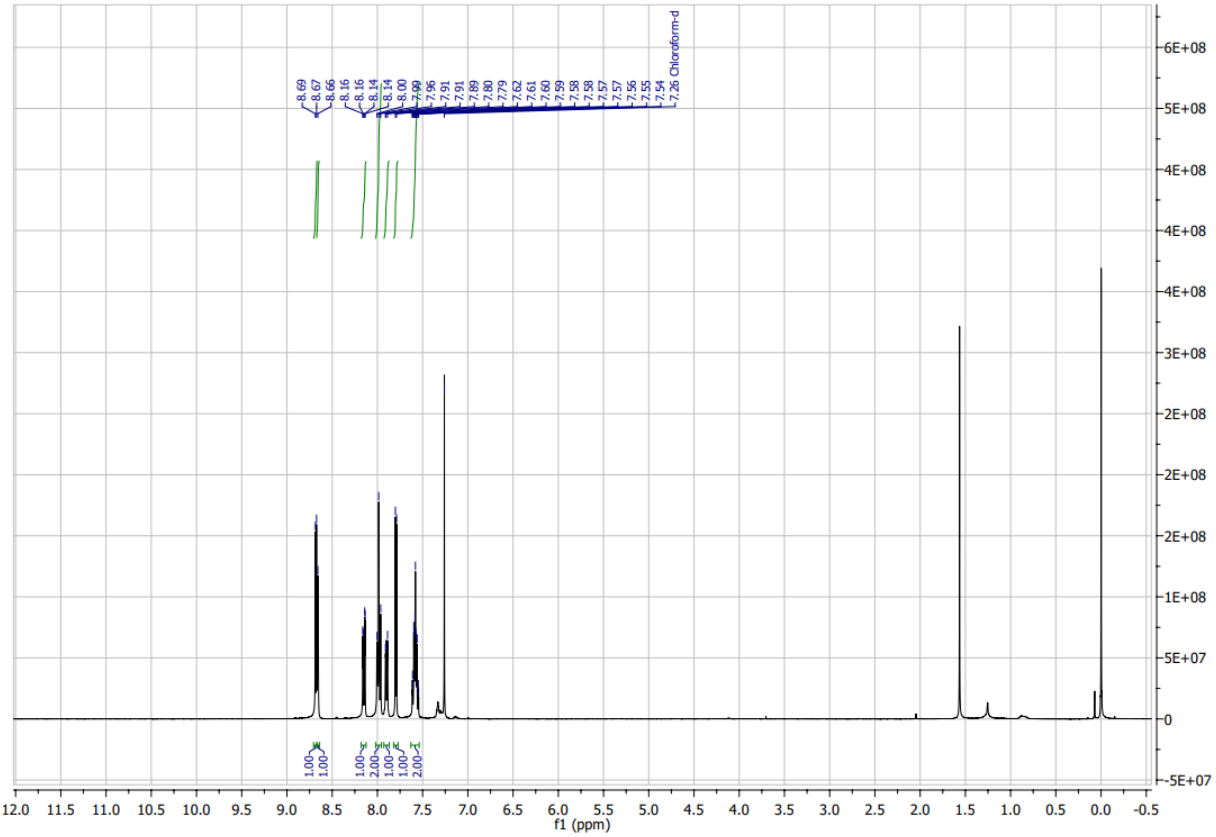



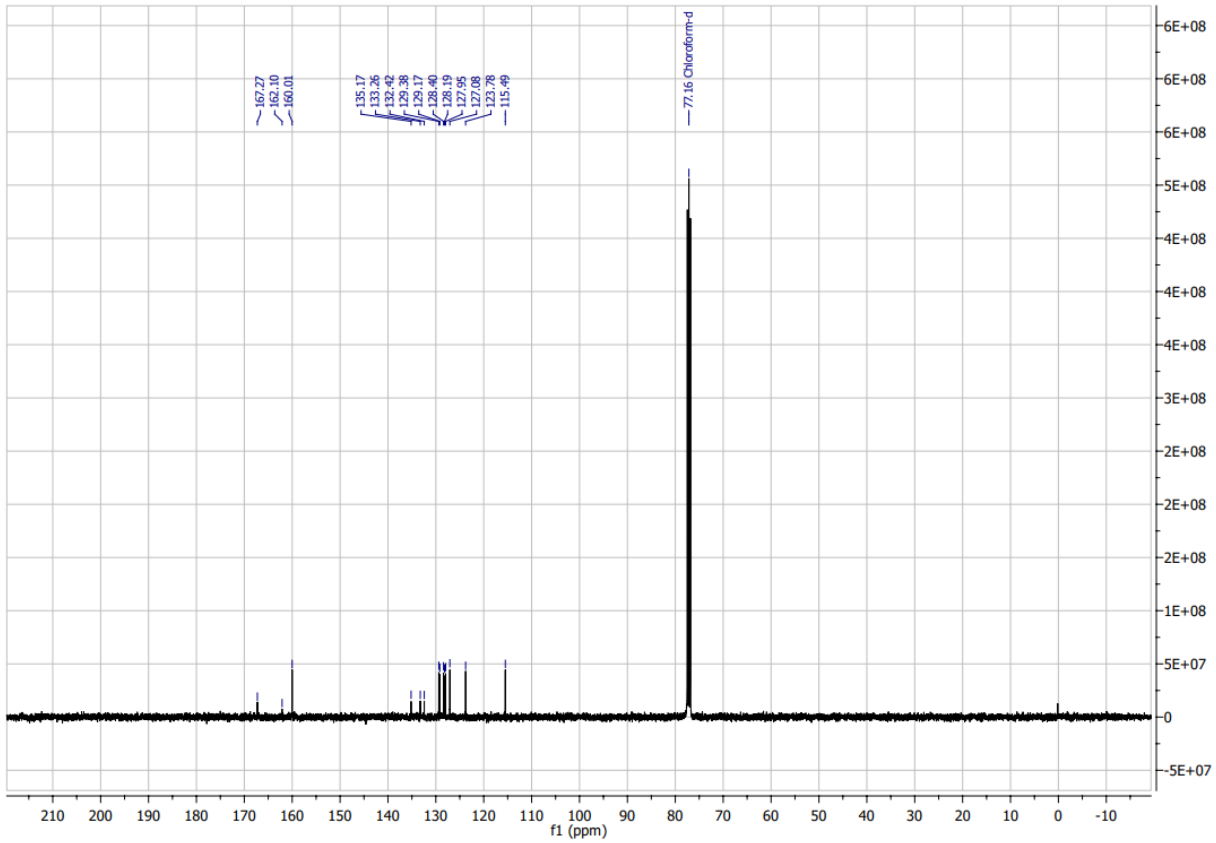
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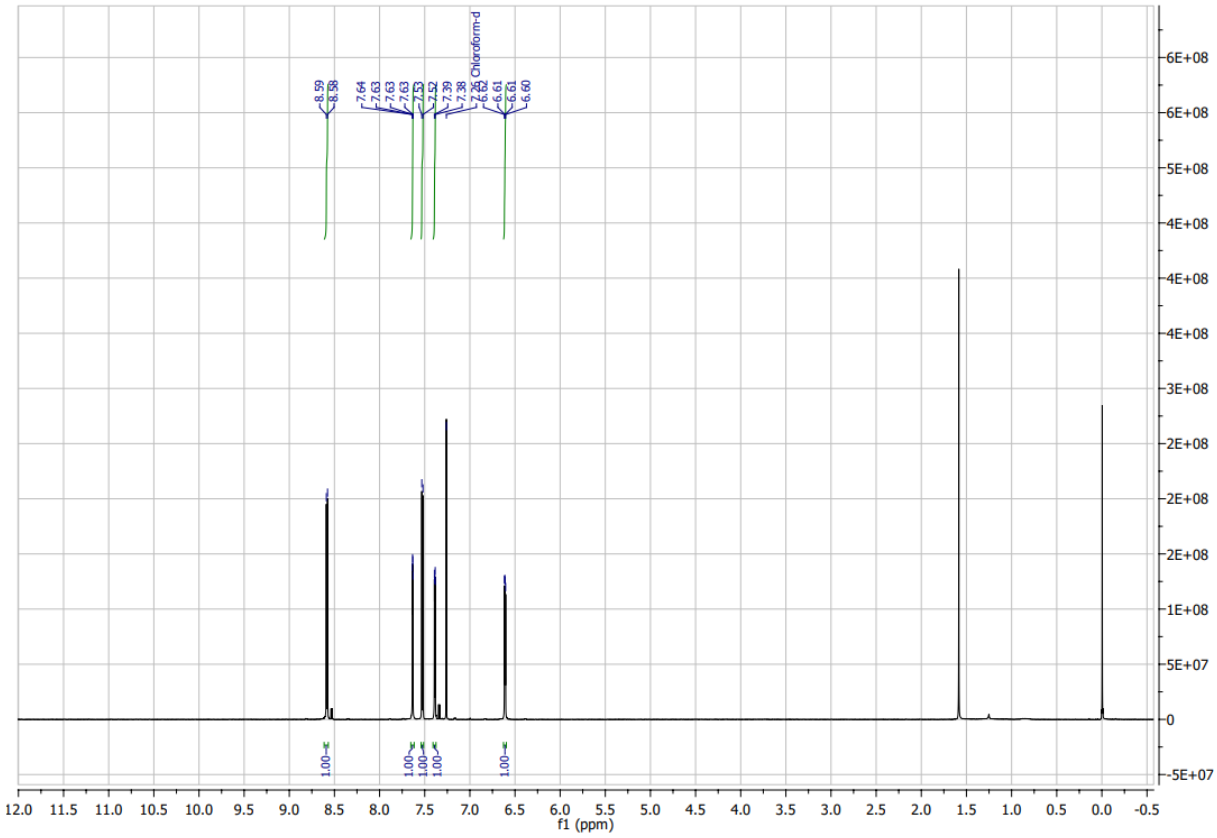



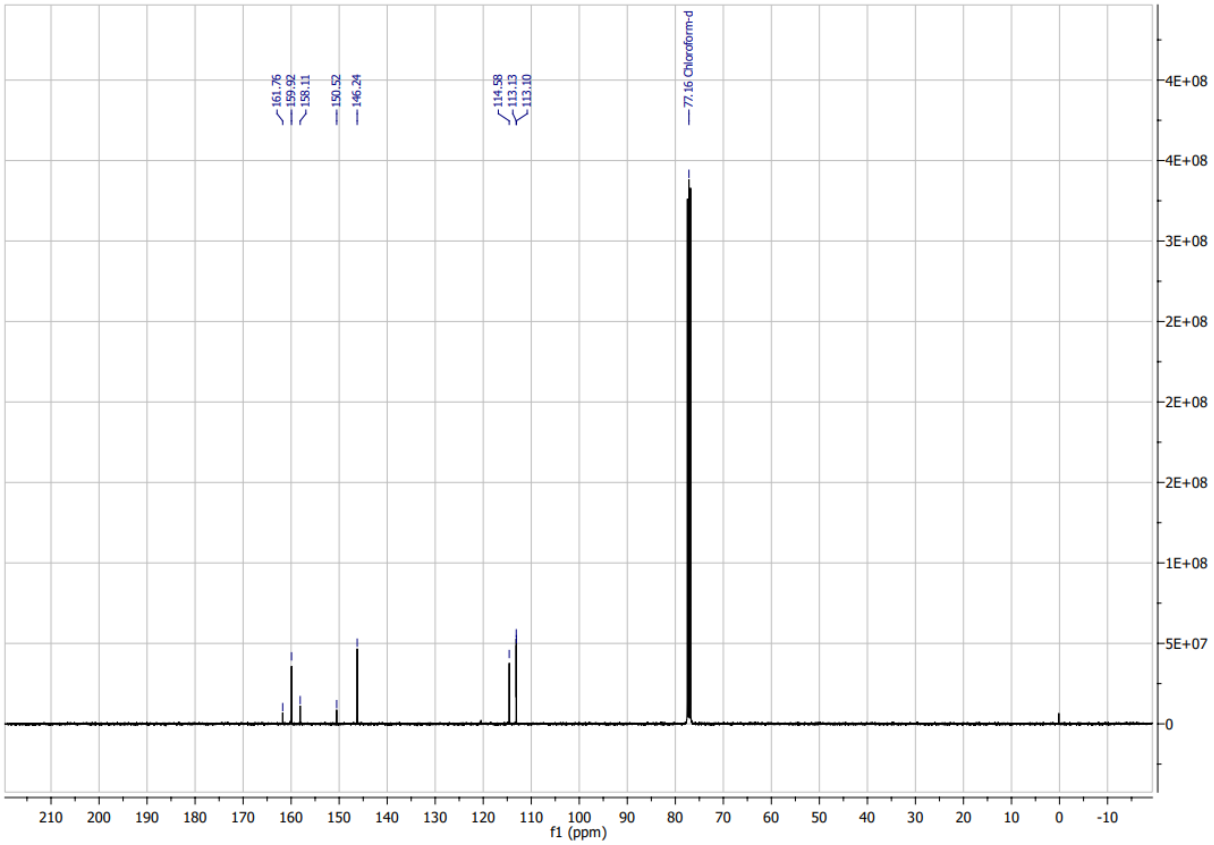
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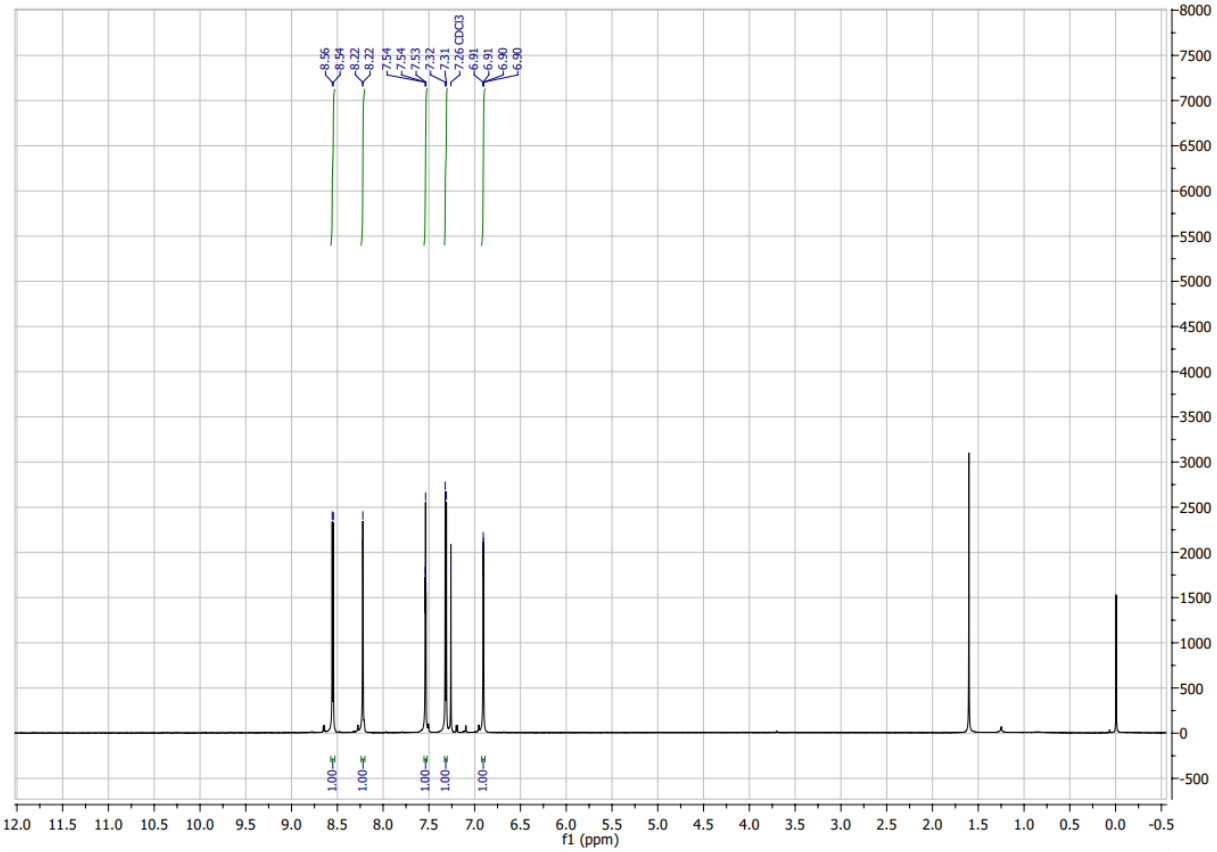



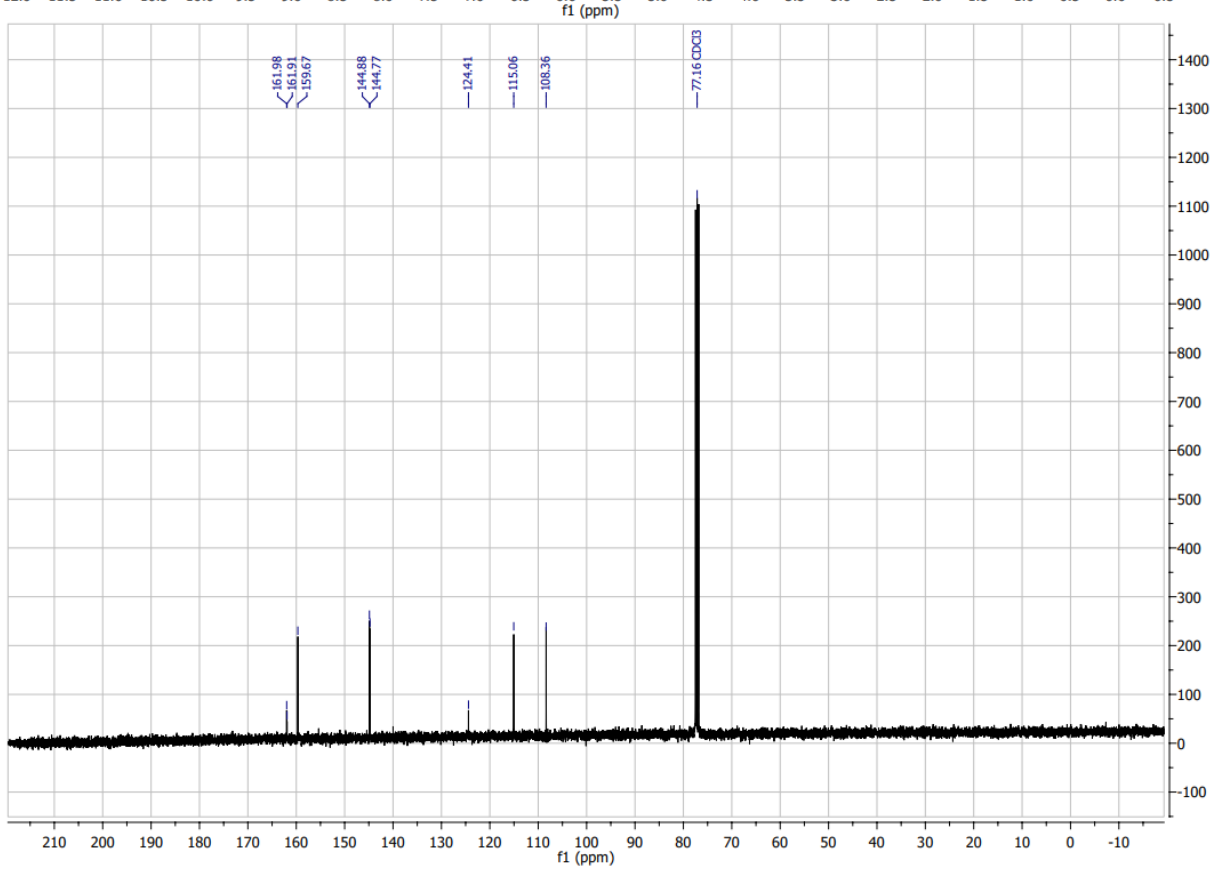
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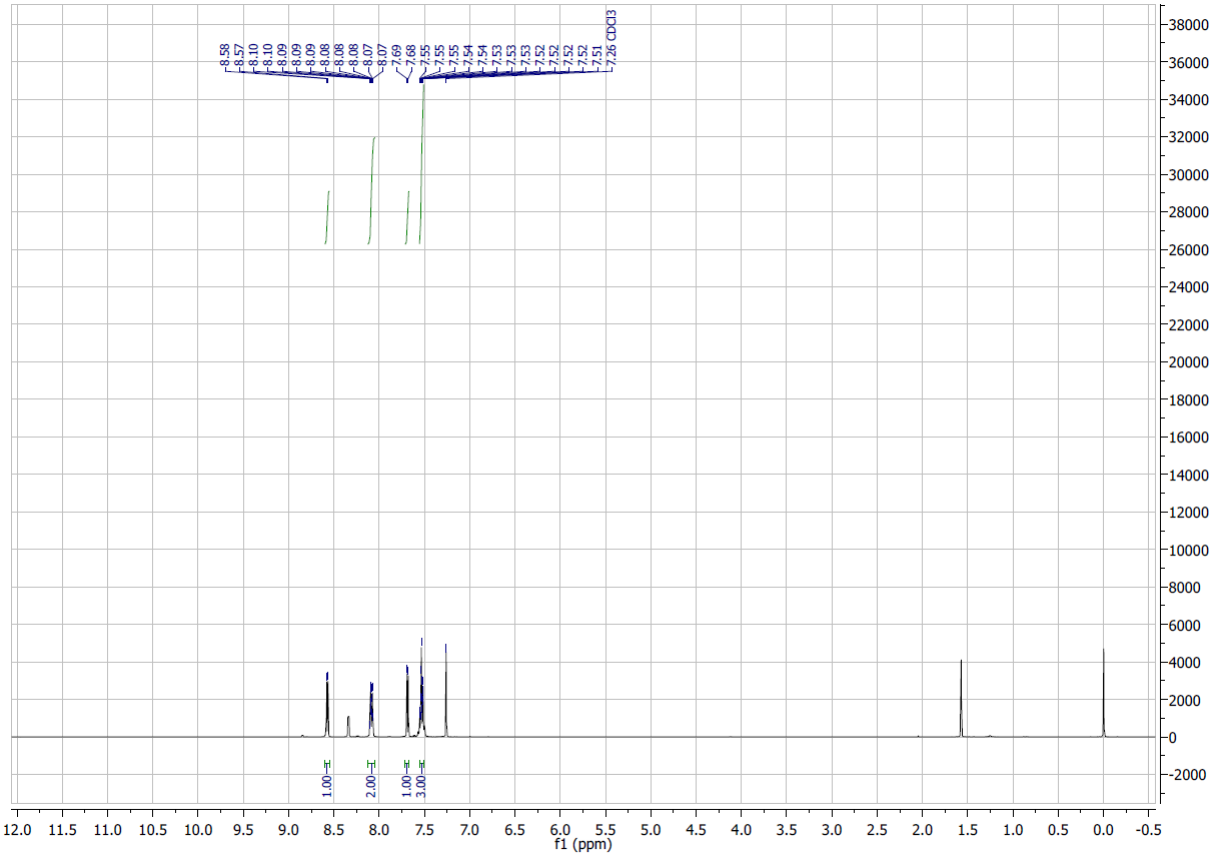



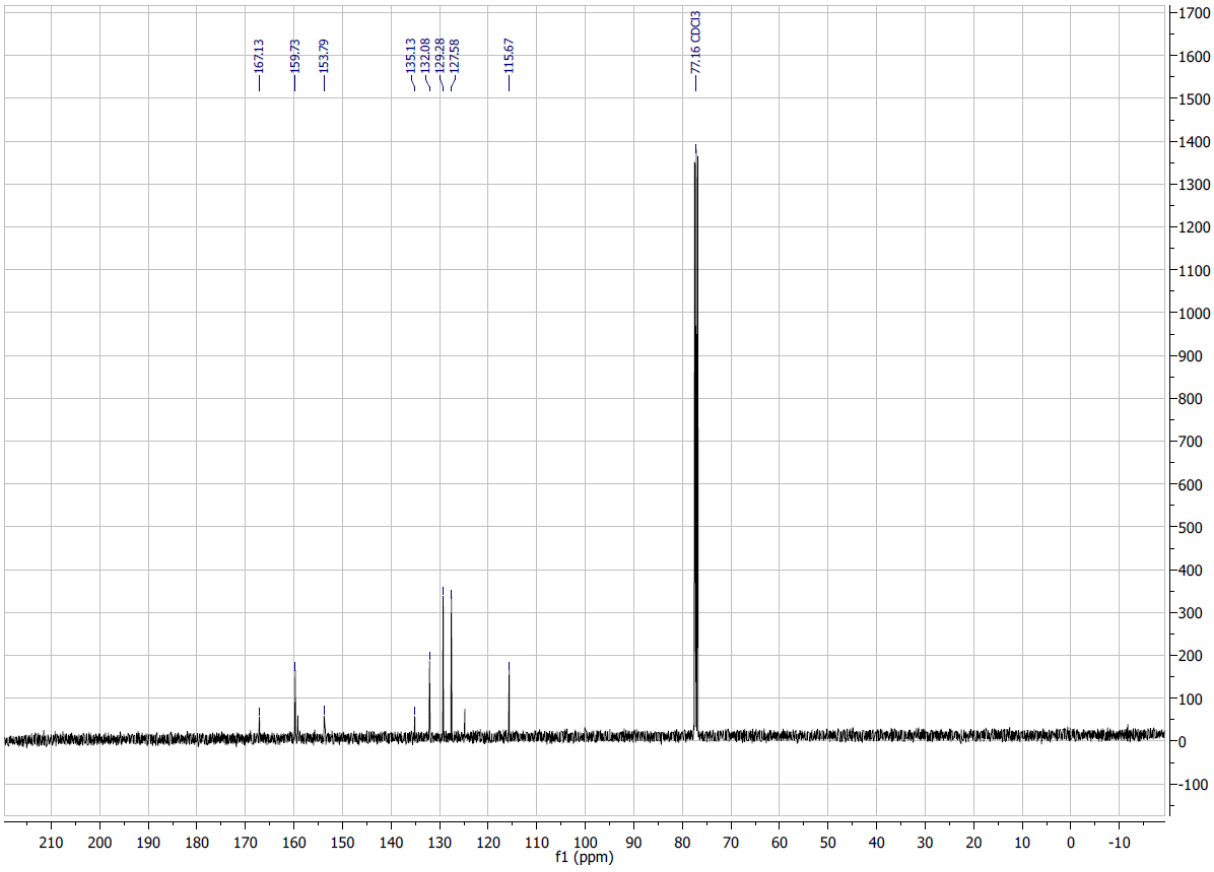
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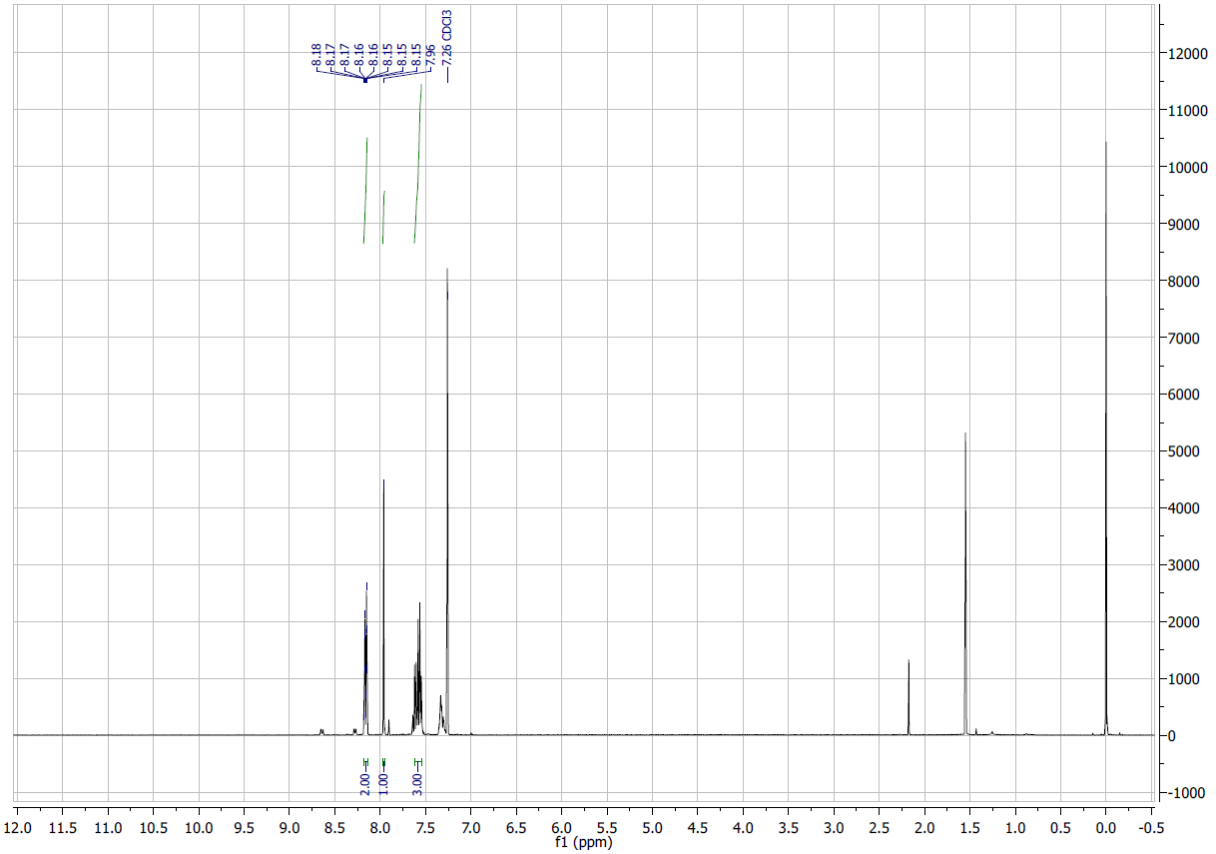



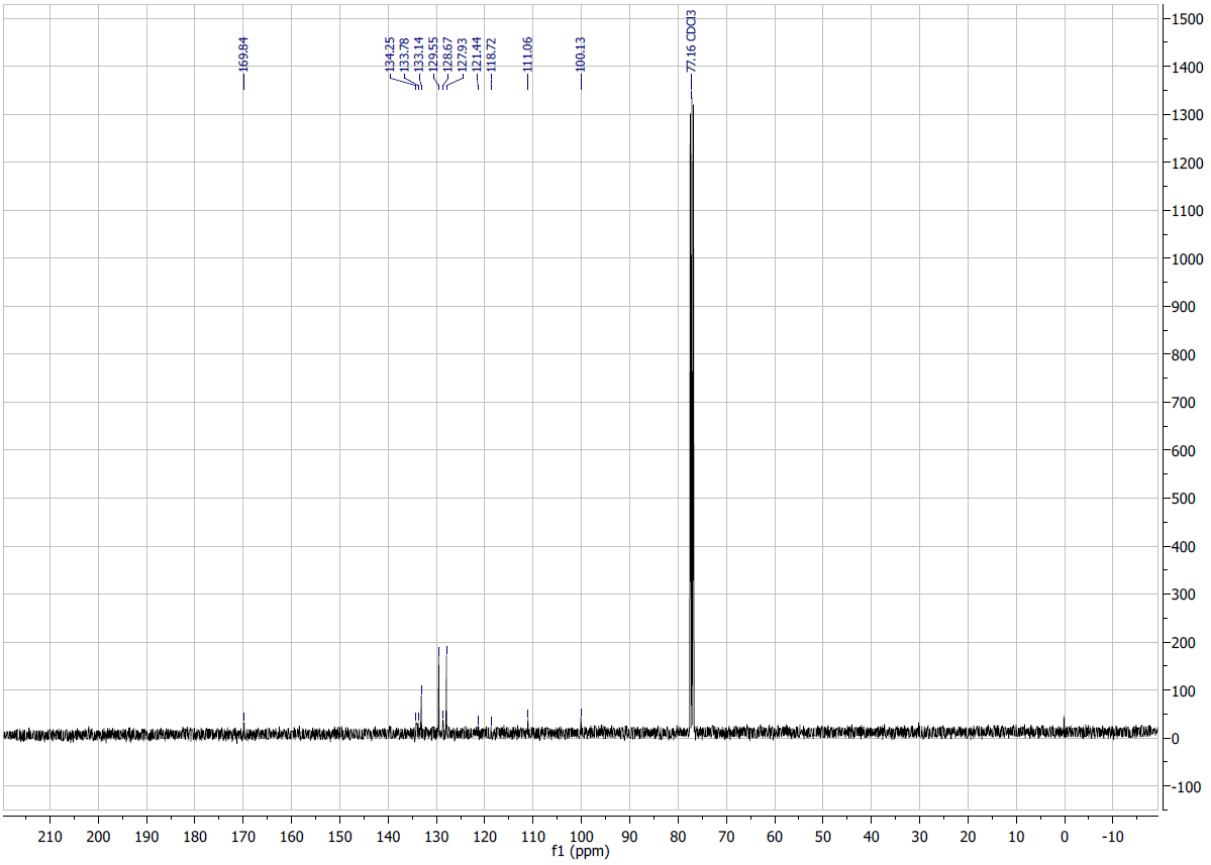
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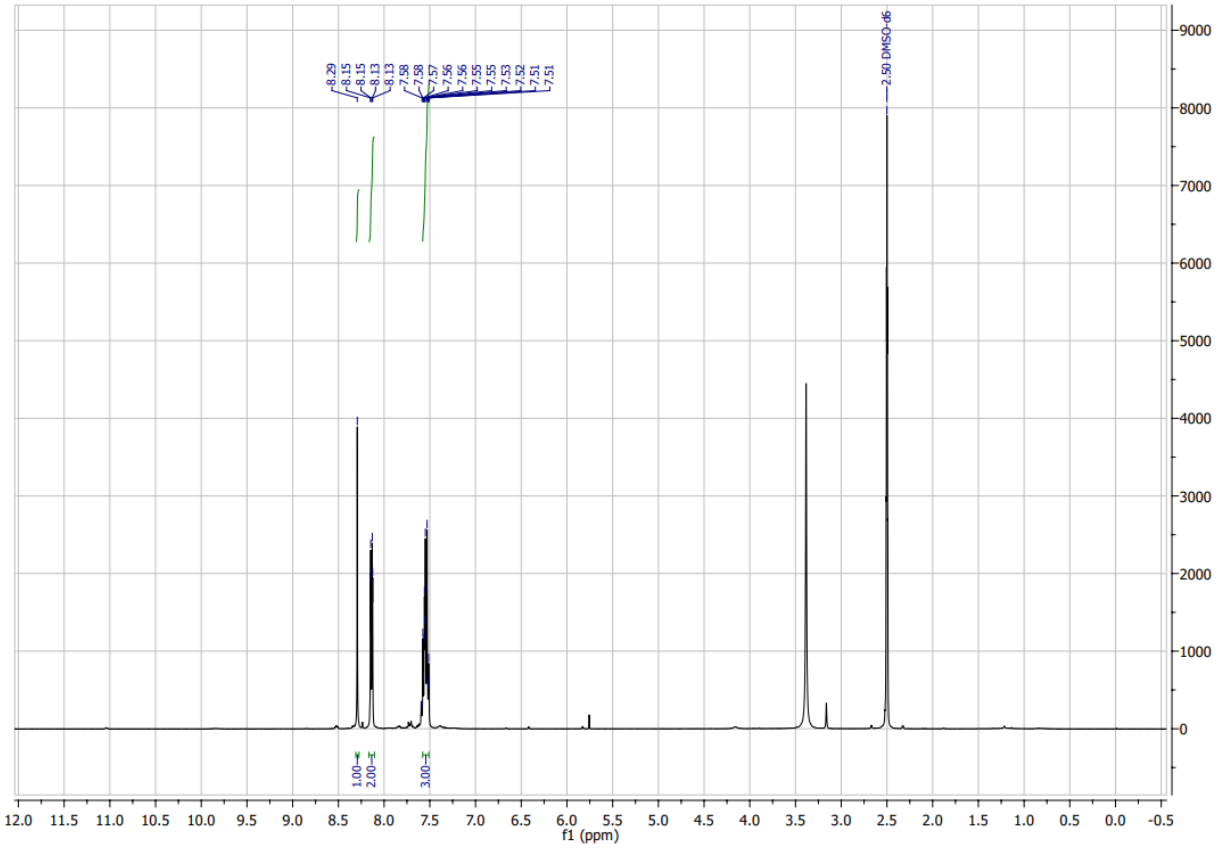



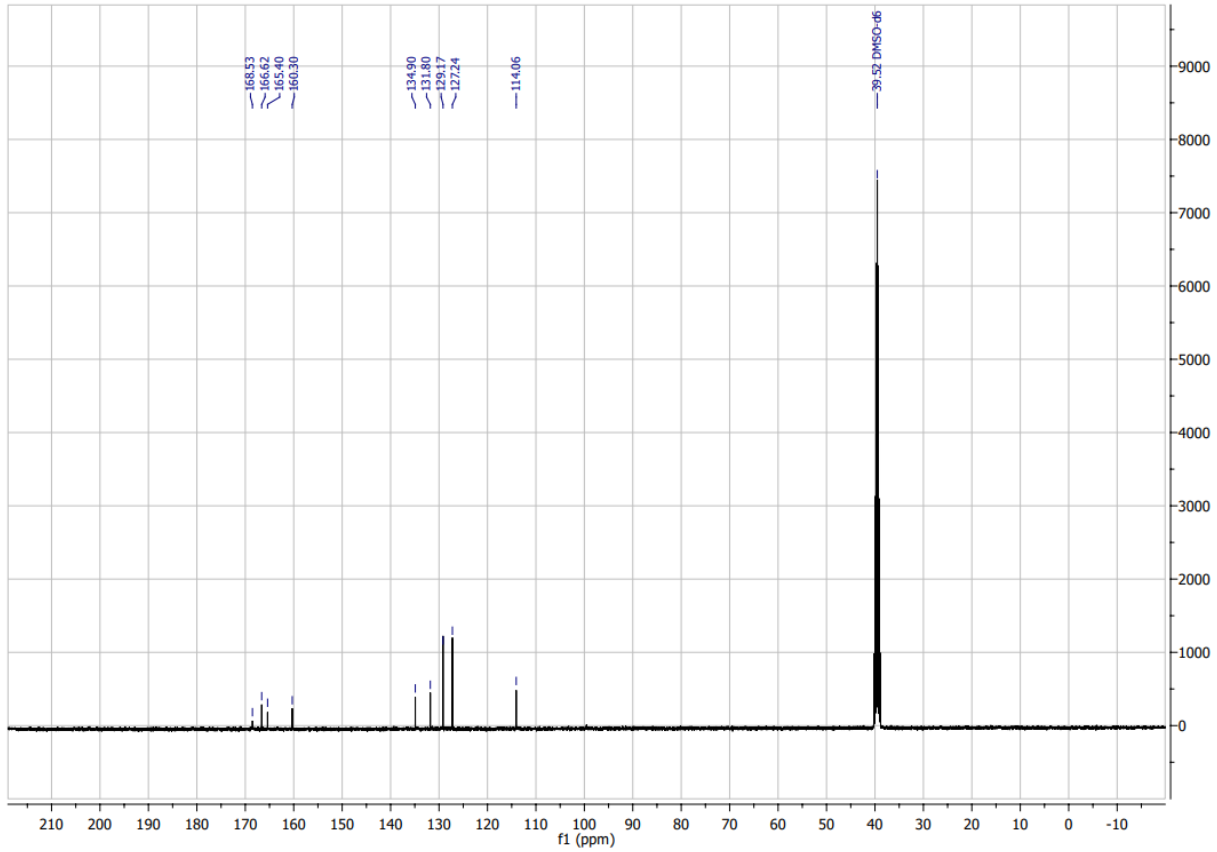
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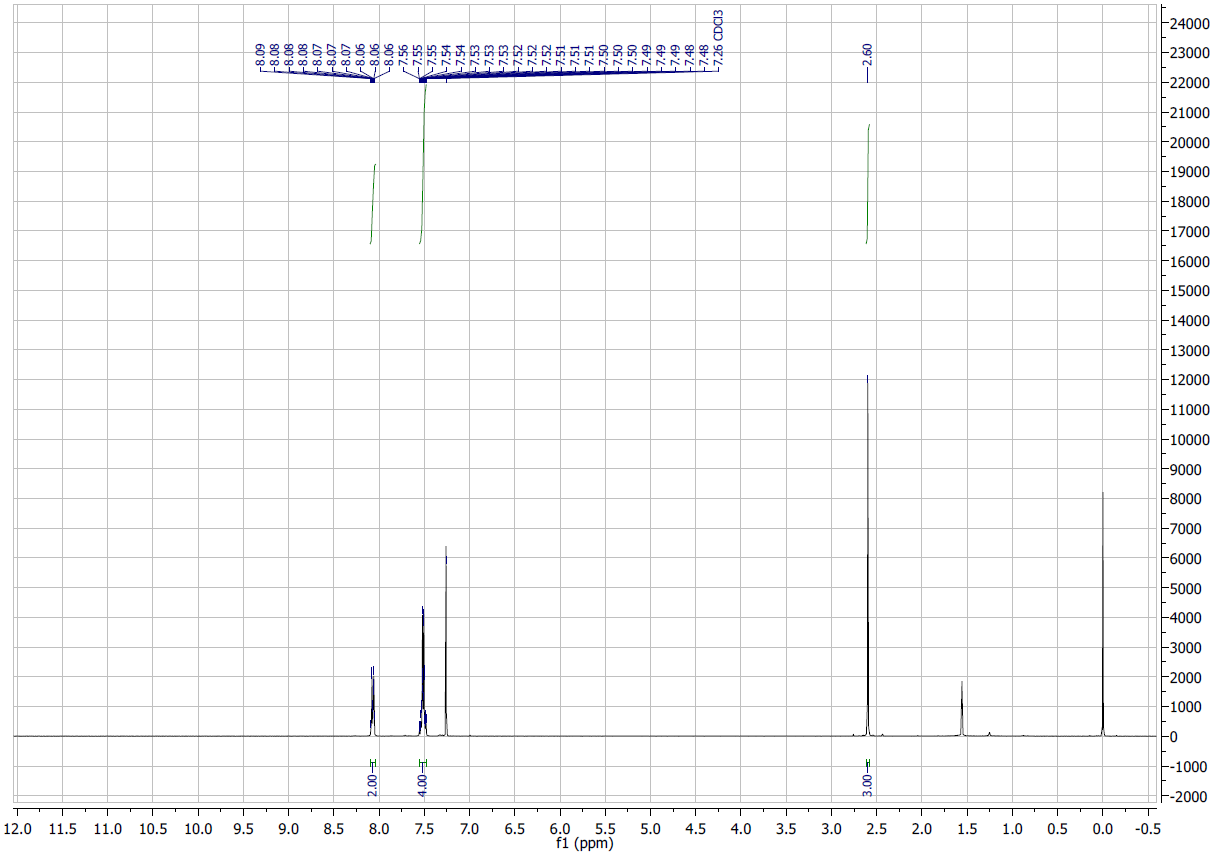



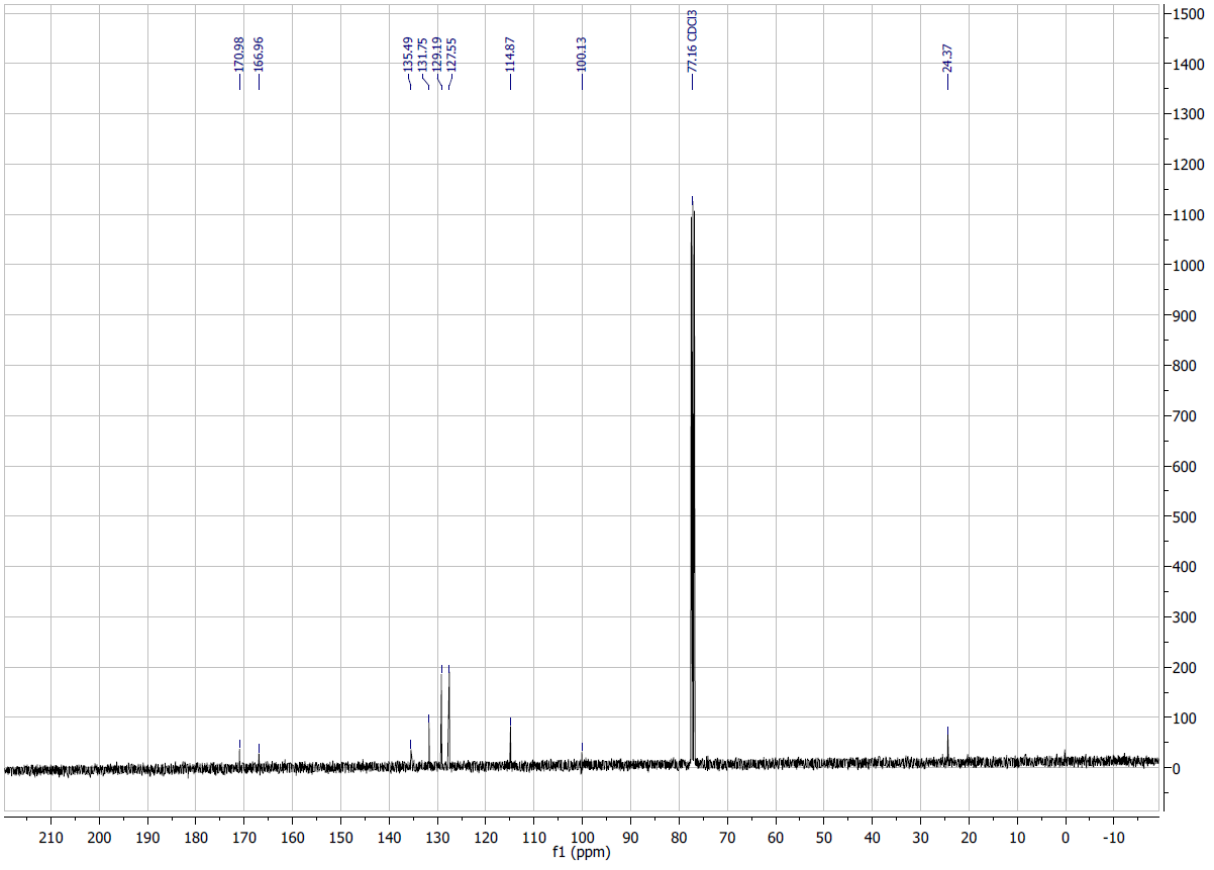
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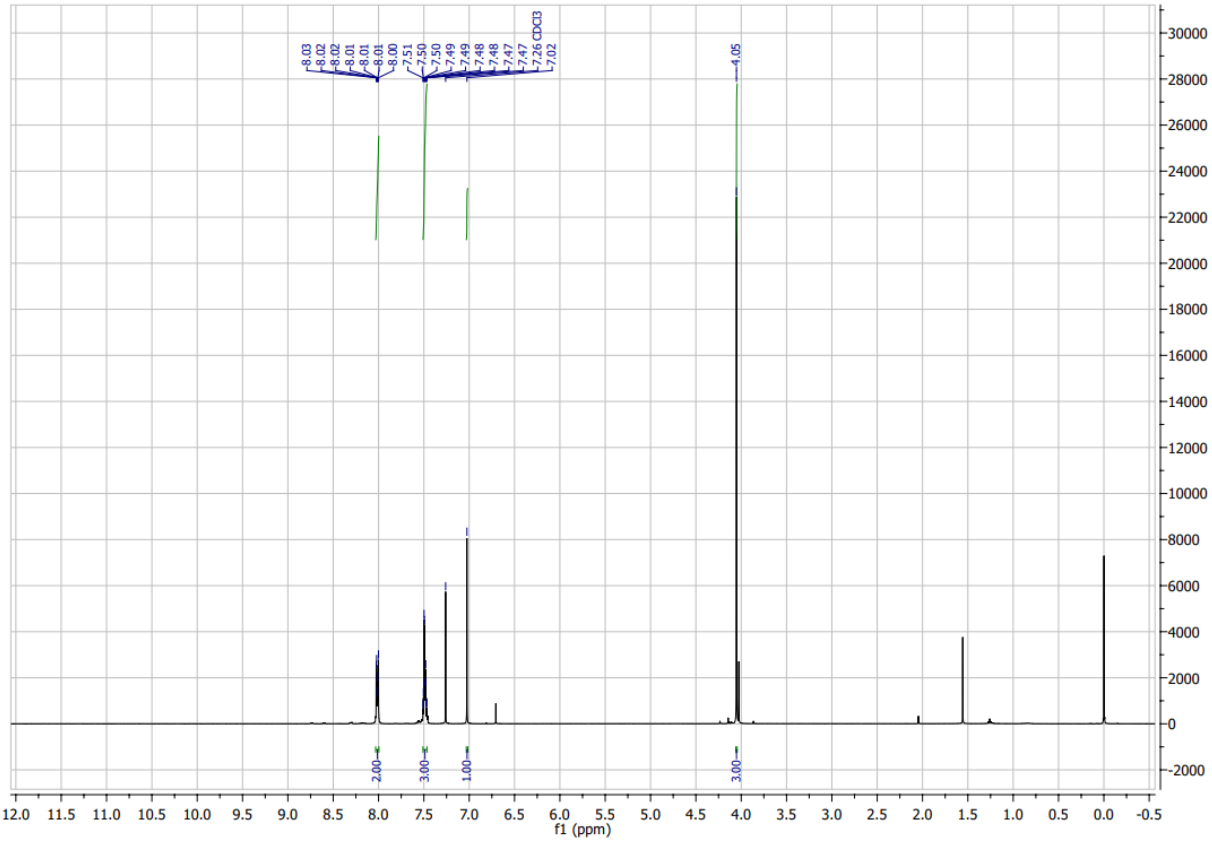



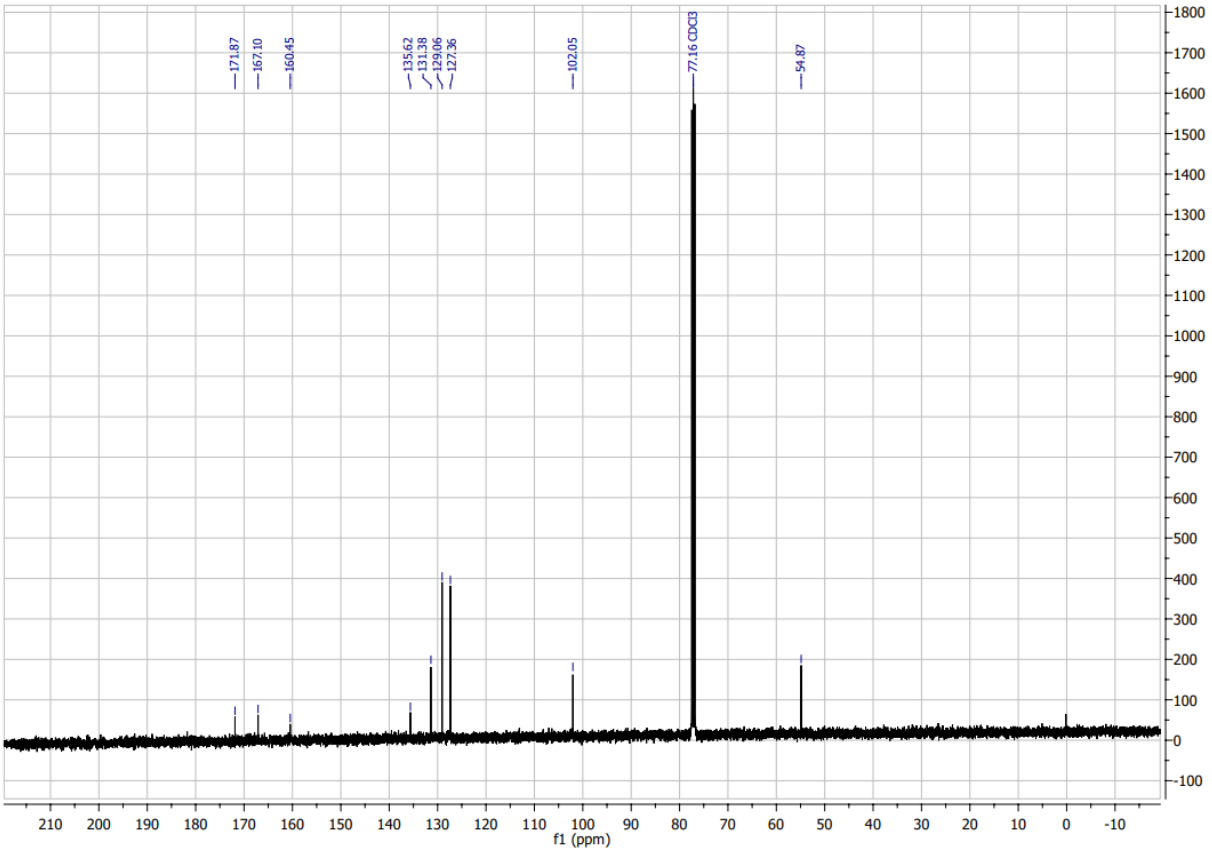
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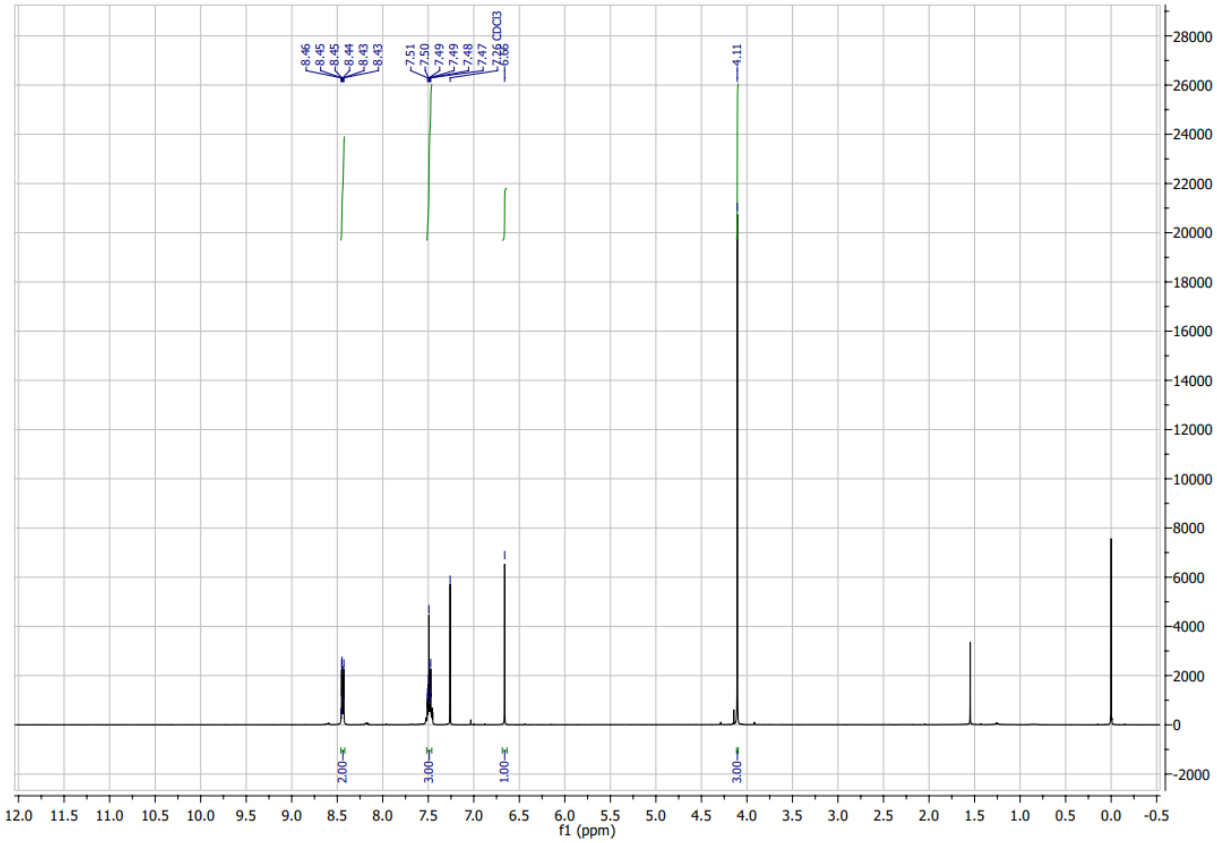



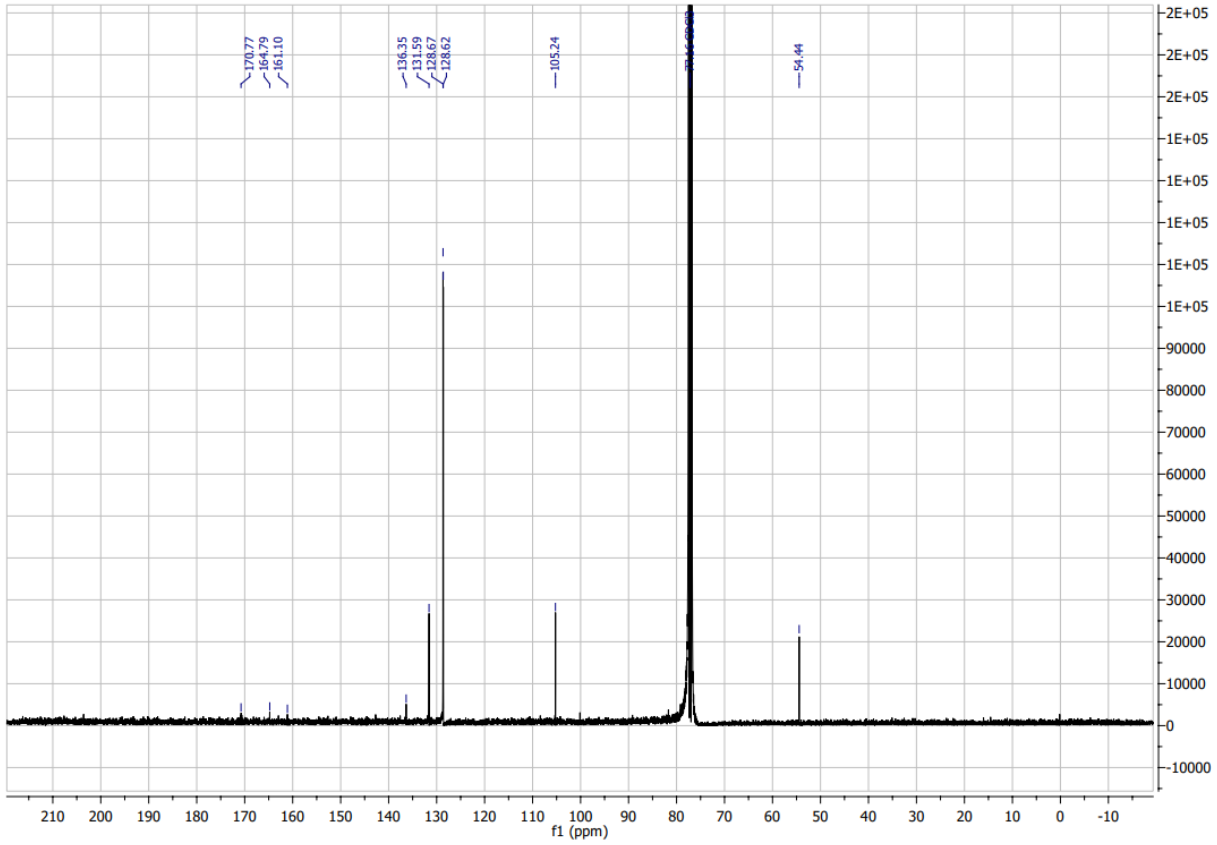
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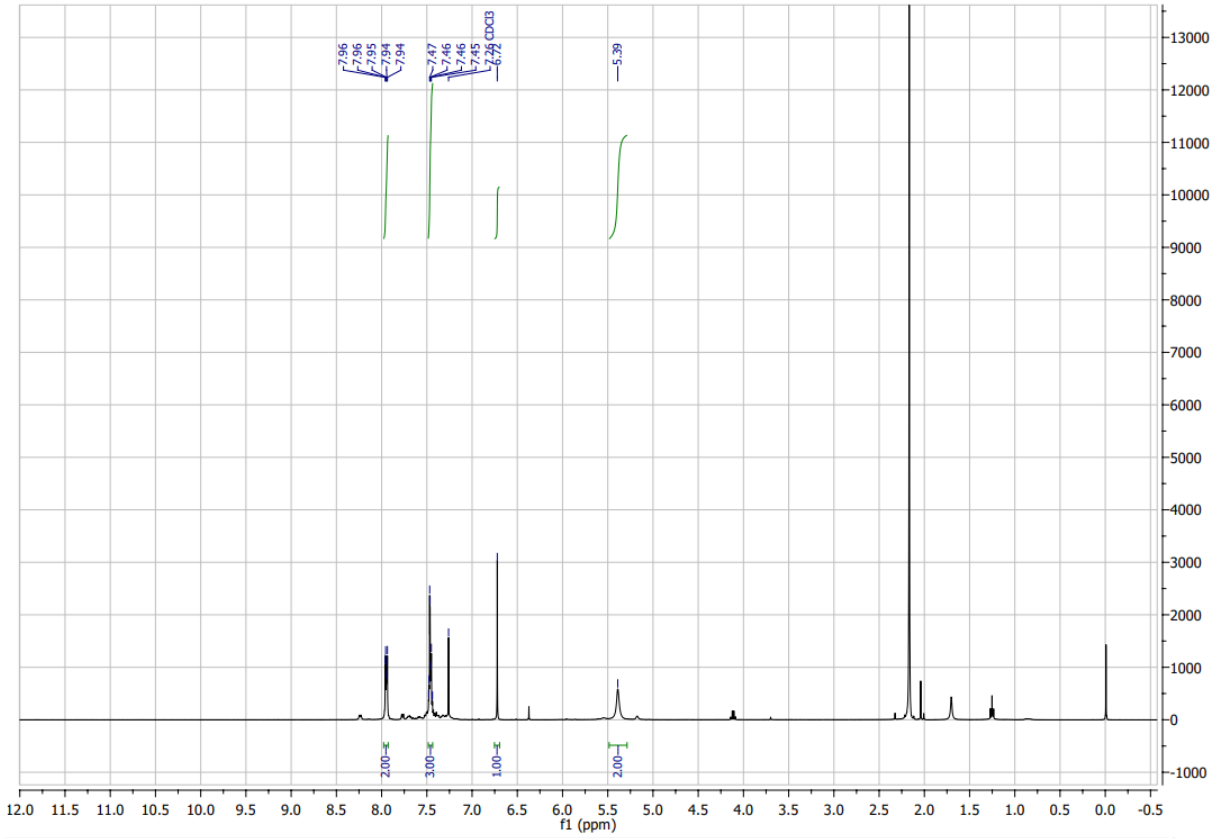



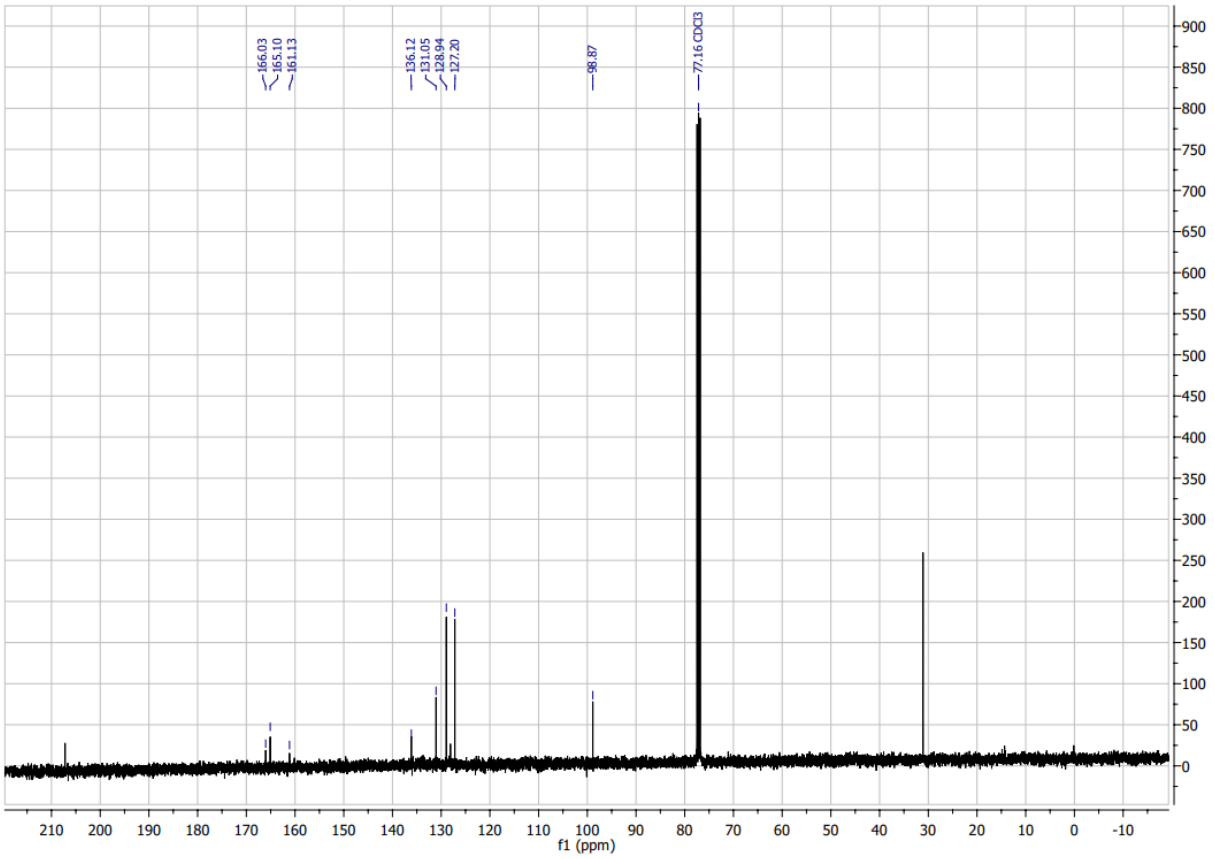
## 2.20 Compound 44B



## 2.21 Compound 45



## 2.22 Compound 46

