

# **2-Oxoester Phospholipase A<sub>2</sub> Inhibitors With Enhanced Metabolic Stability**

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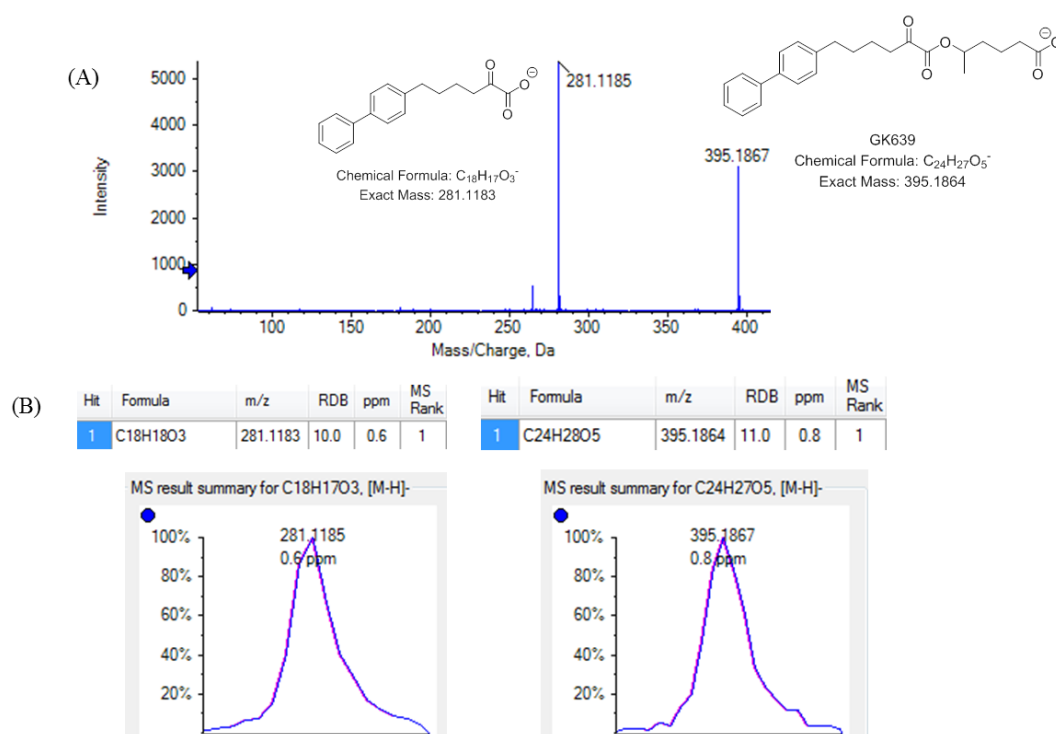
**SUPPLEMENTARY MATERIALS**

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## Plasma Stability of 2-Oxoester Inhibitors

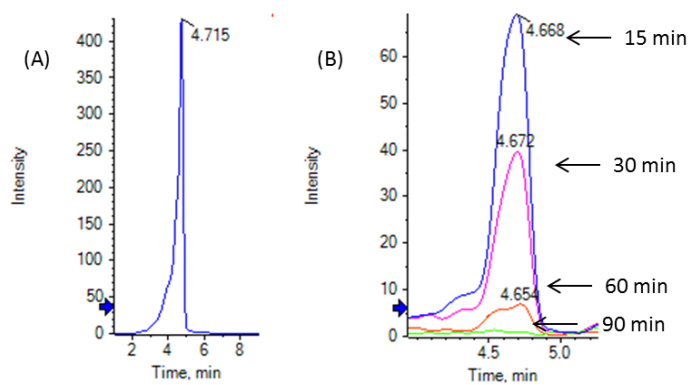
The *in vitro* stabilities of the 2-oxoester inhibitors were studied in human plasma. The reactions were initiated by the addition of test compound to a 250  $\mu\text{L}$  of preheated plasma solution to yield a final concentration of 1 mg/L. Samples (50  $\mu\text{L}$ ) were obtained at 0, 15, 30, 60 and 90 min and acetonitrile (200  $\mu\text{L}$ ) was added. The samples were subjected to vortex mixing for 1 min and then centrifugation for 10 min. The clear supernatants were analyzed by LC-HRMS/MS.

As an example, the full scan ESI-HRMS spectrum of inhibitor GK639 is depicted in Figure 1. The chemical formulas of the parent and the fragment ions were also identified using the Formula Finder tab from Peak View 2.1. The MS Rank values, as well as the RDB values, for the elemental compositions of the two ions are presented in Figure 1. The MS Rank order is based on the MS data using a combination of mass accuracy and match to the theoretical isotope pattern. The RDB value is a formal calculation of the sum of the number of rings and double bonds present in the formula.



**Supporting Figure 1.** Full scan ESI-HRMS spectrum of GK639 (A) and mass spectral data for the parent and the fragment ions (B).

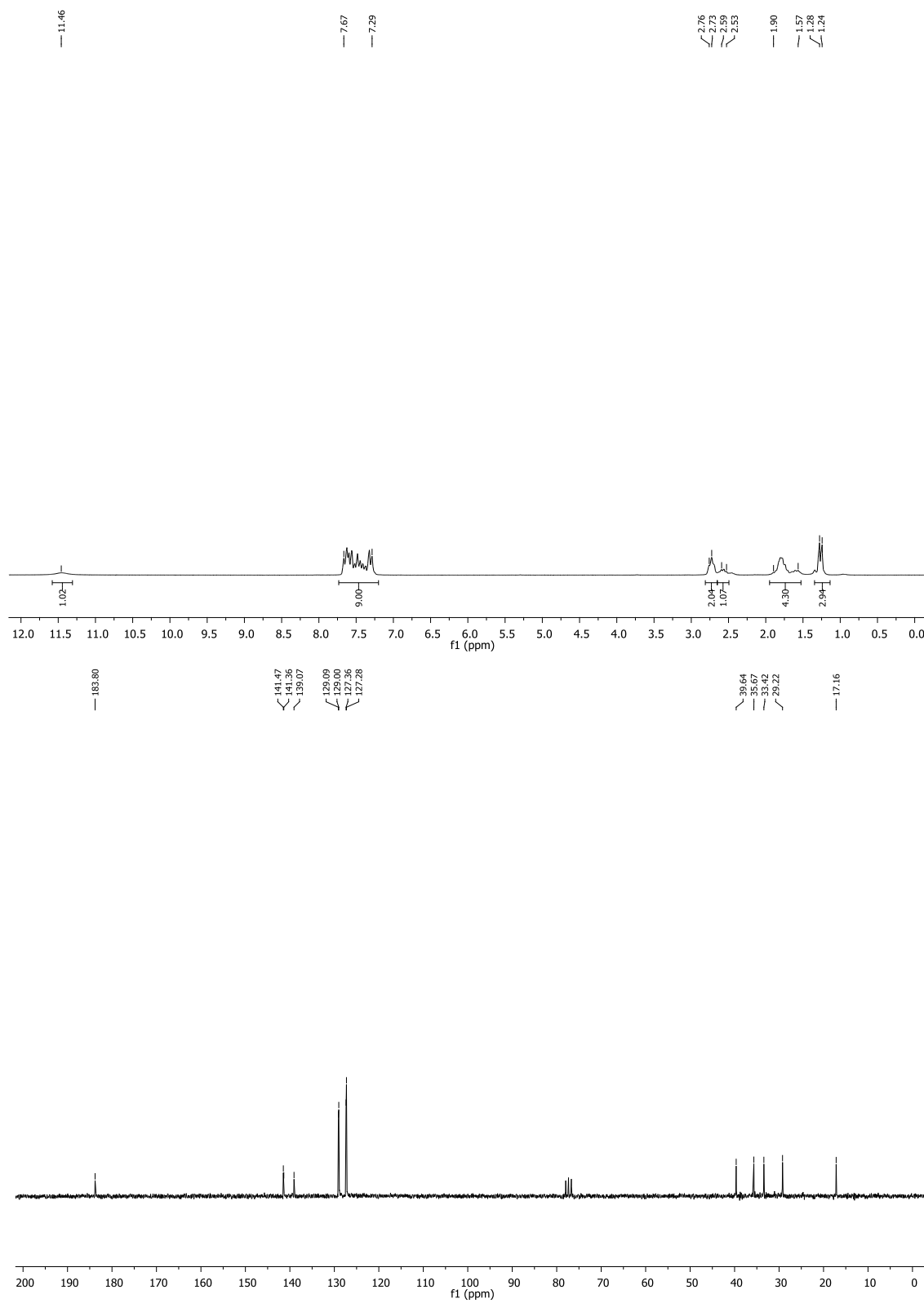
The extracted ion chromatograms (EICs) of a standard GK639 sample (1 mg/L) and plasma samples that contain inhibitor GK639, taken at 15, 30, 60, 90 min, are shown in Figure 2.



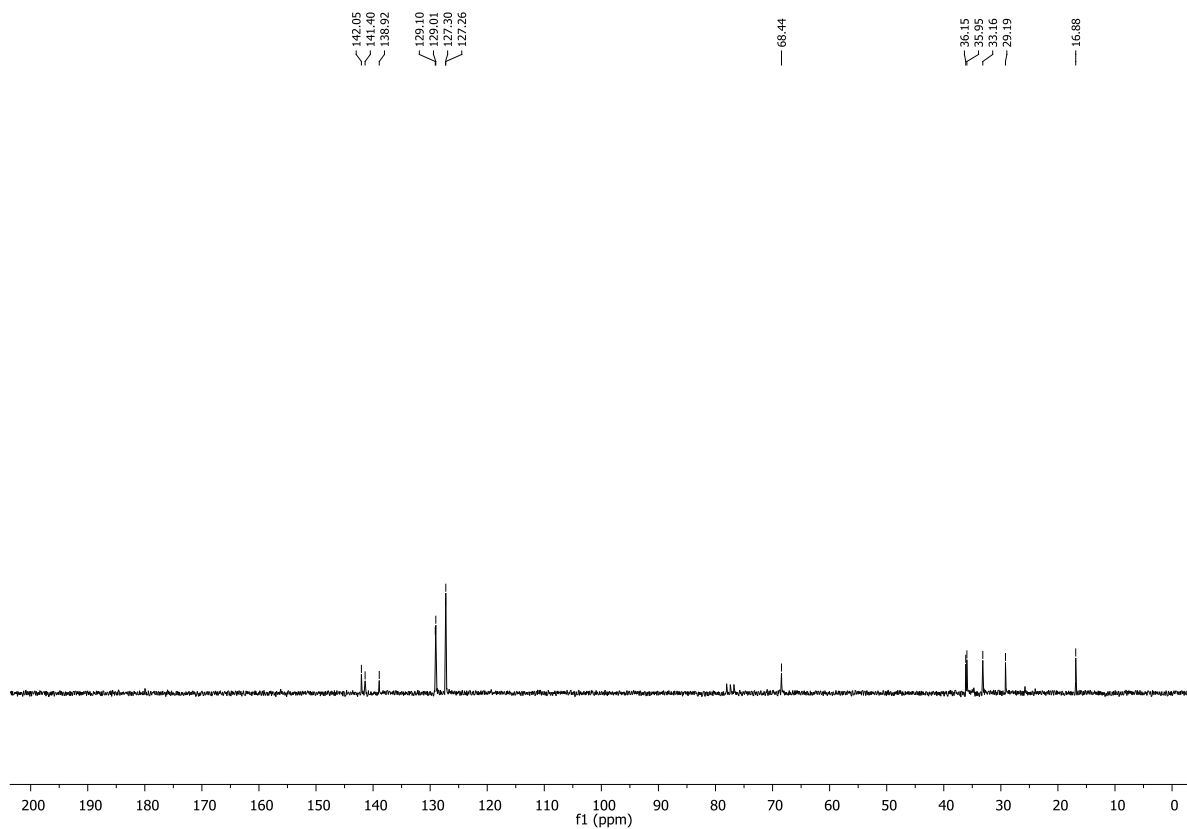
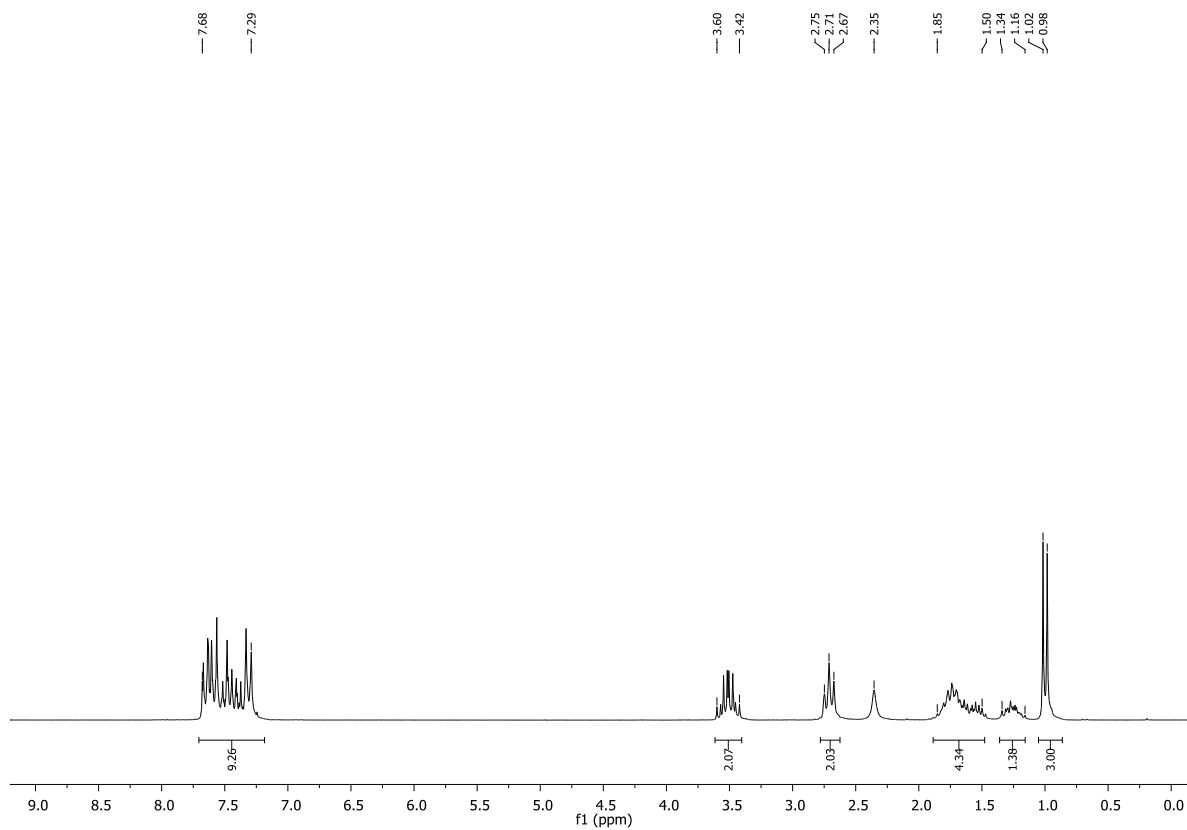
**Supporting Figure 2.** Extracted ion chromatograms (EICs) of a standard GK639 sample (1 mg/L) (A) and plasma samples that contain GK639, taken at 15, 30, 60, 90 min (B).

## NMR Spectra

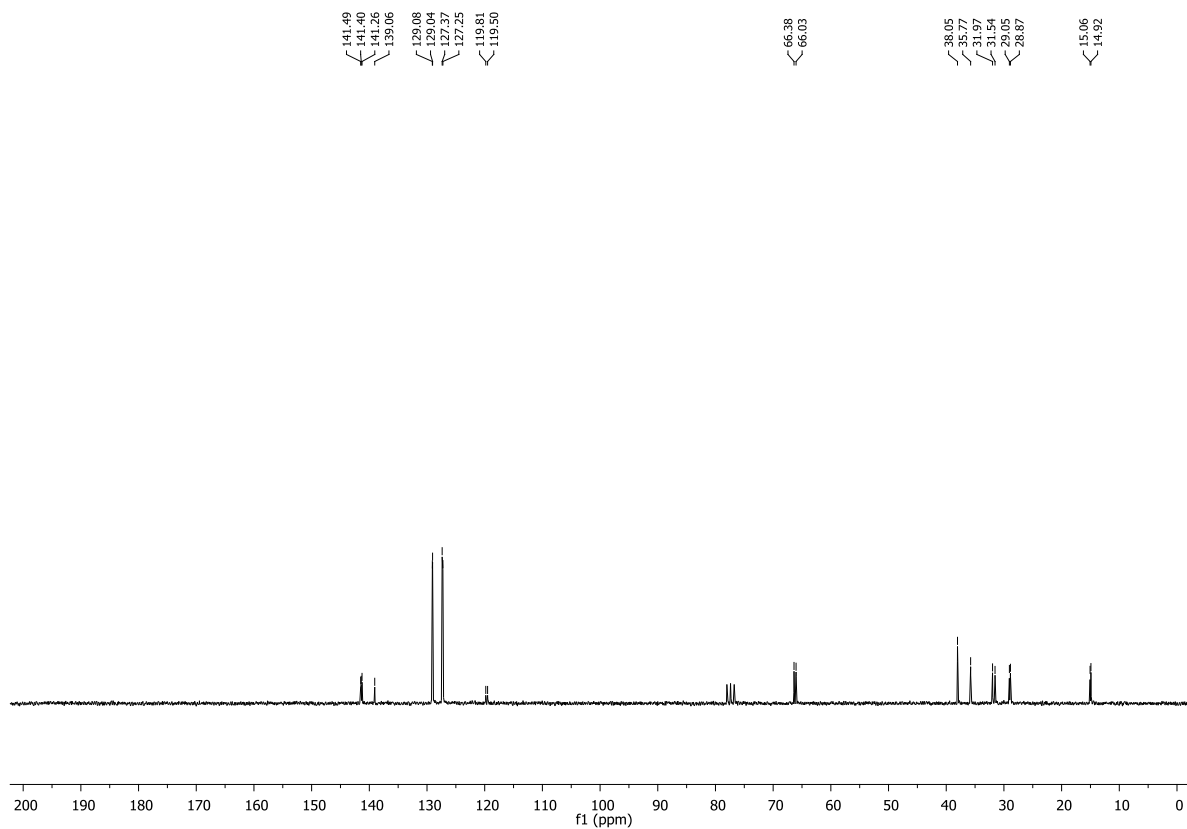
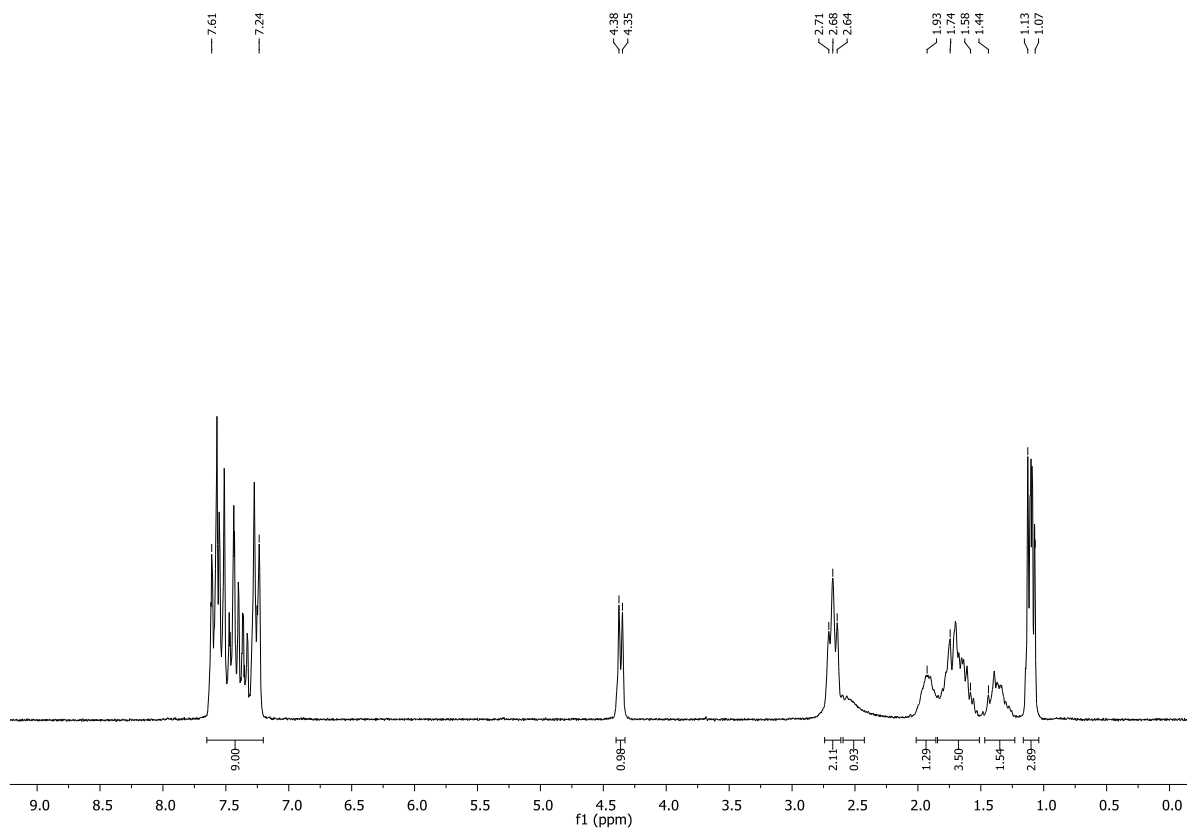
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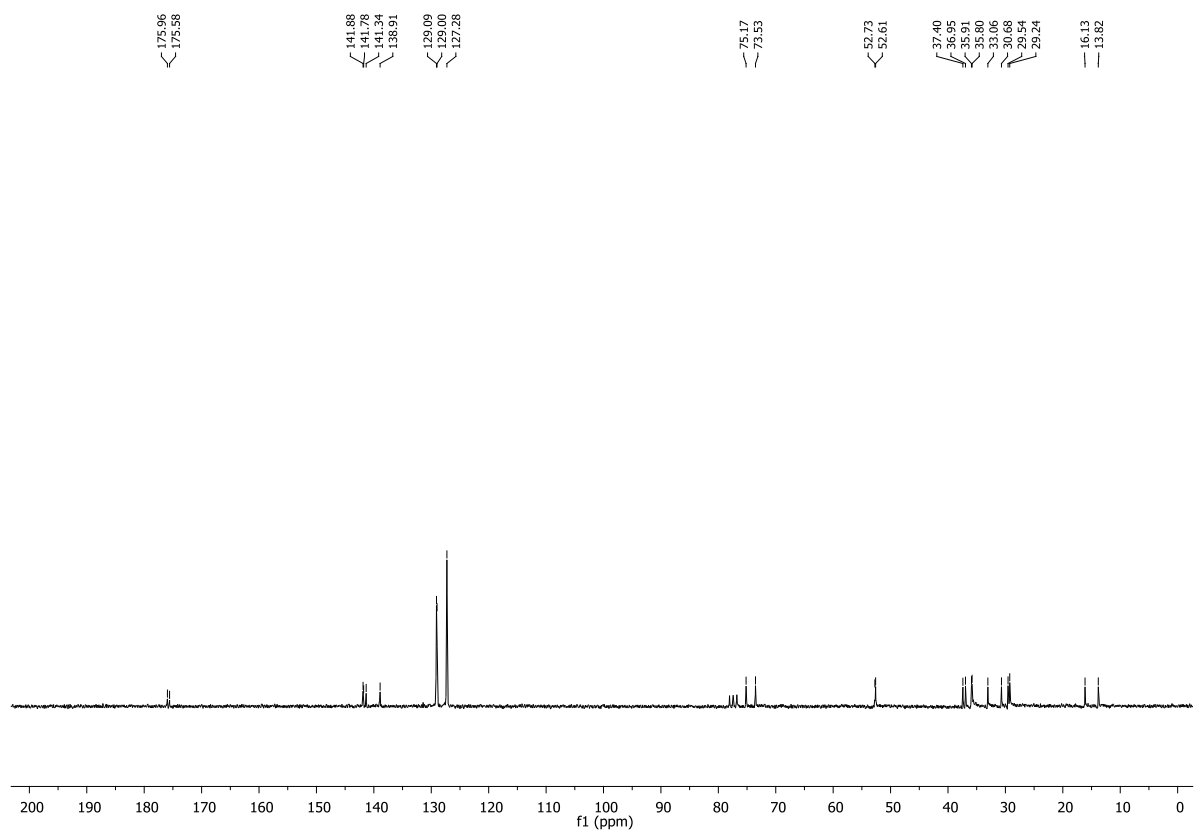
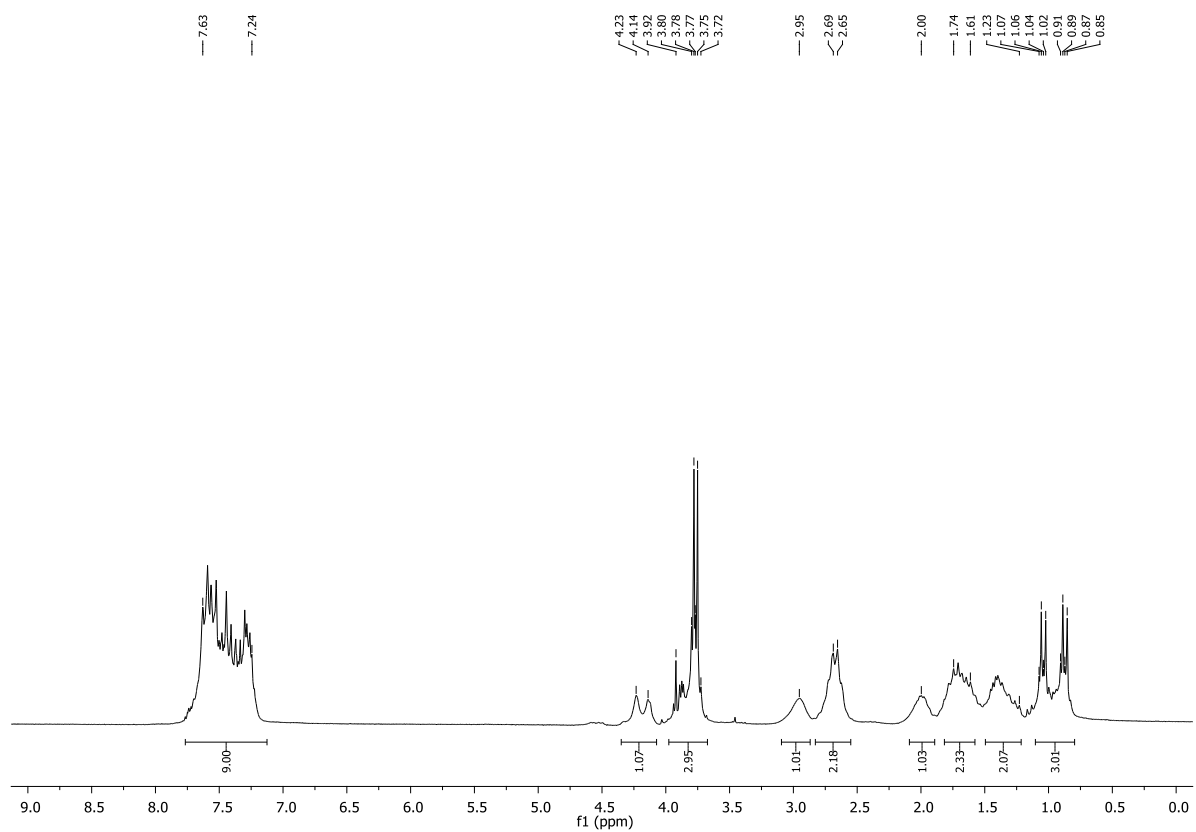
(5)



(7)

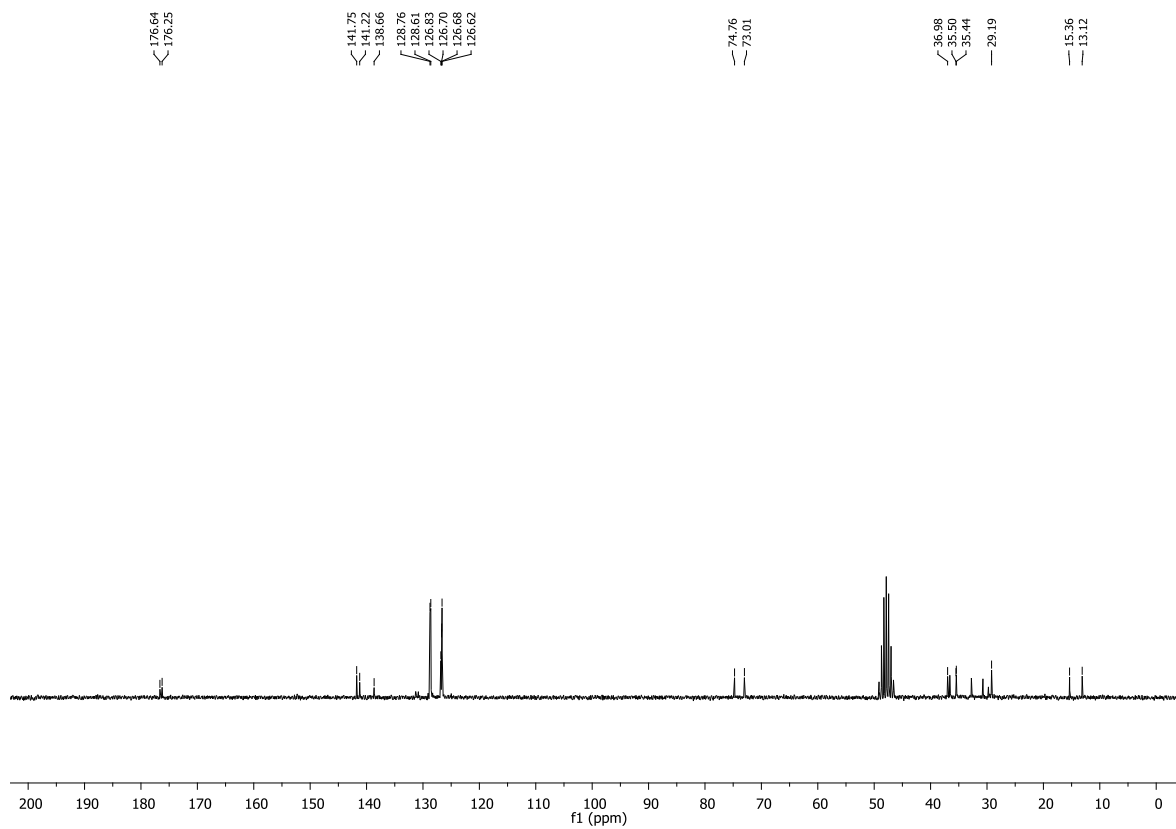
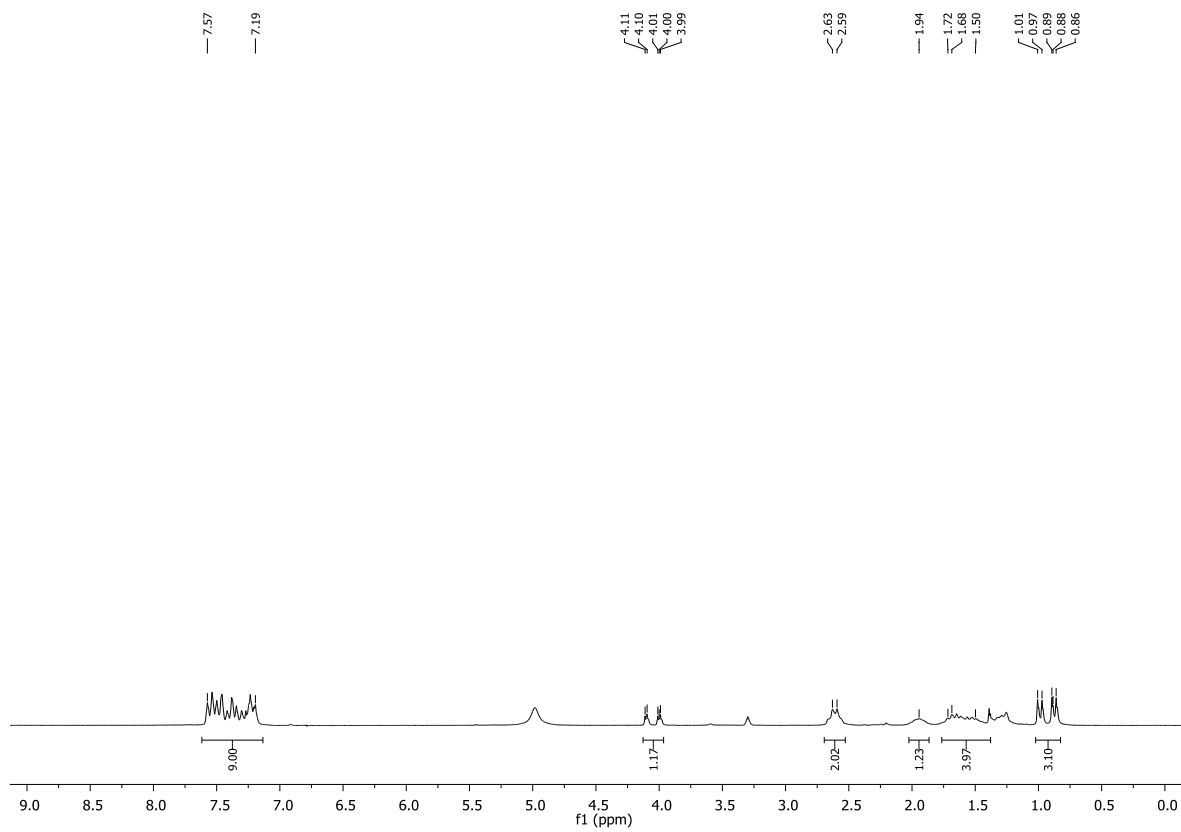


(8)

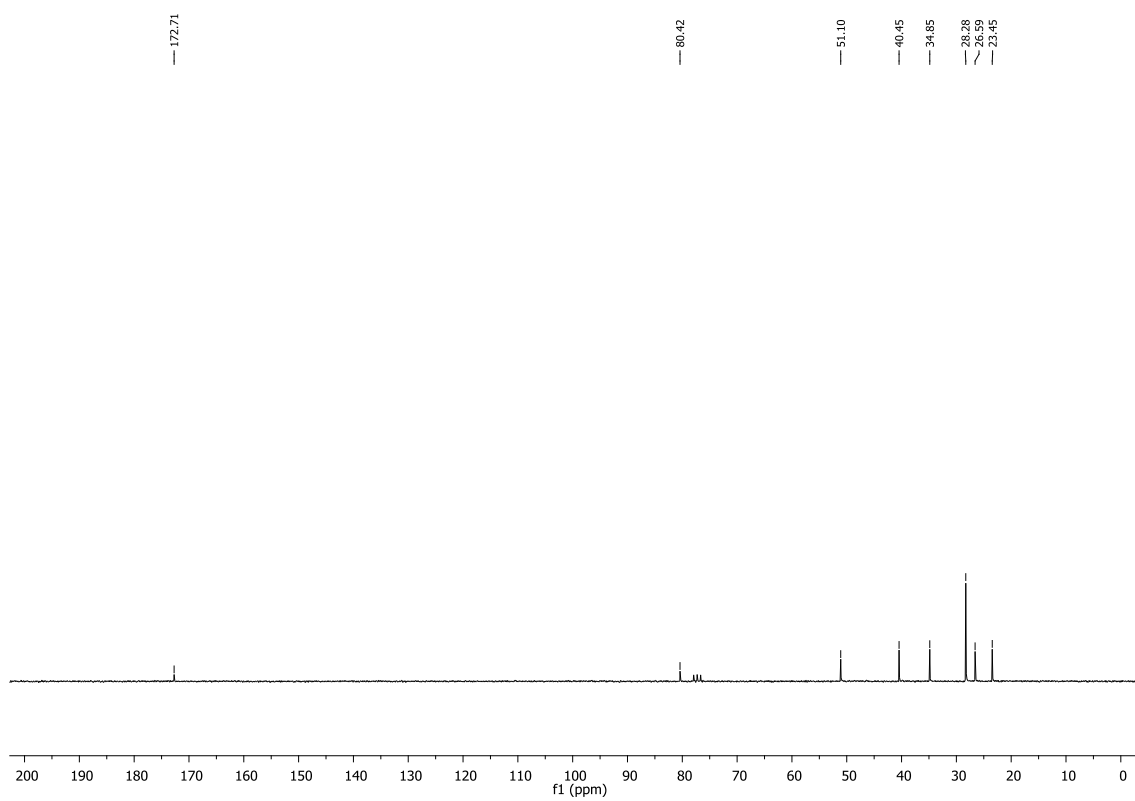
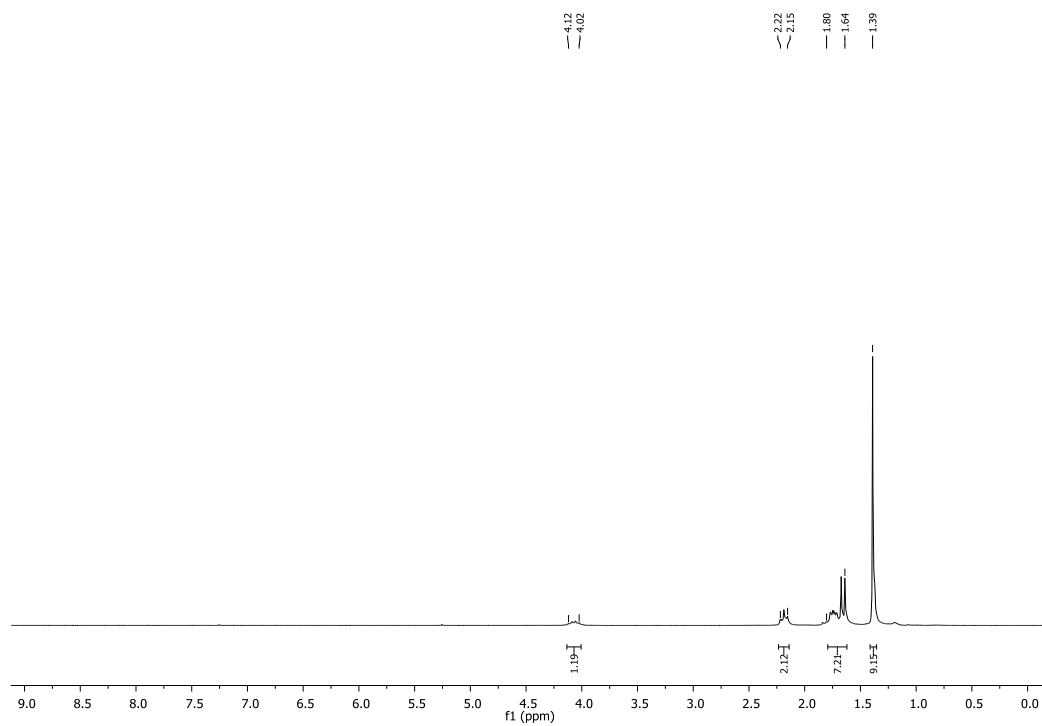


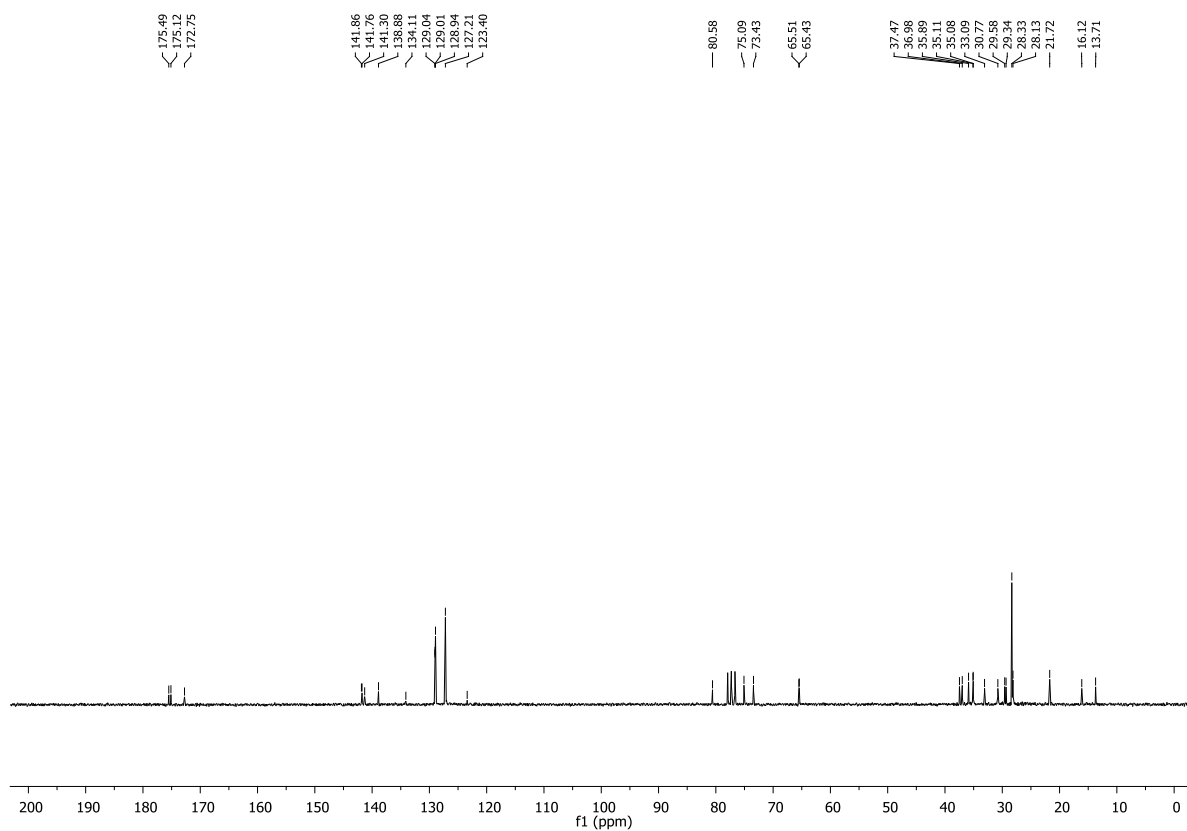
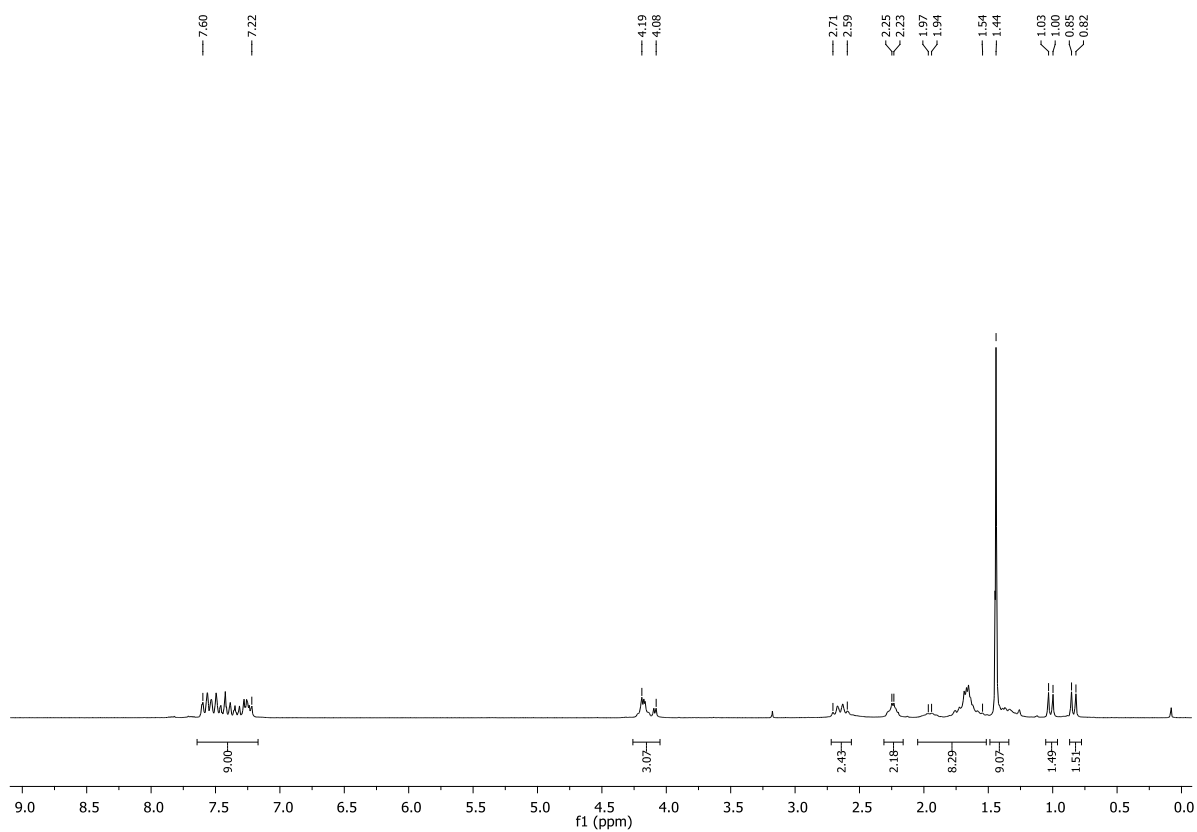


(9)

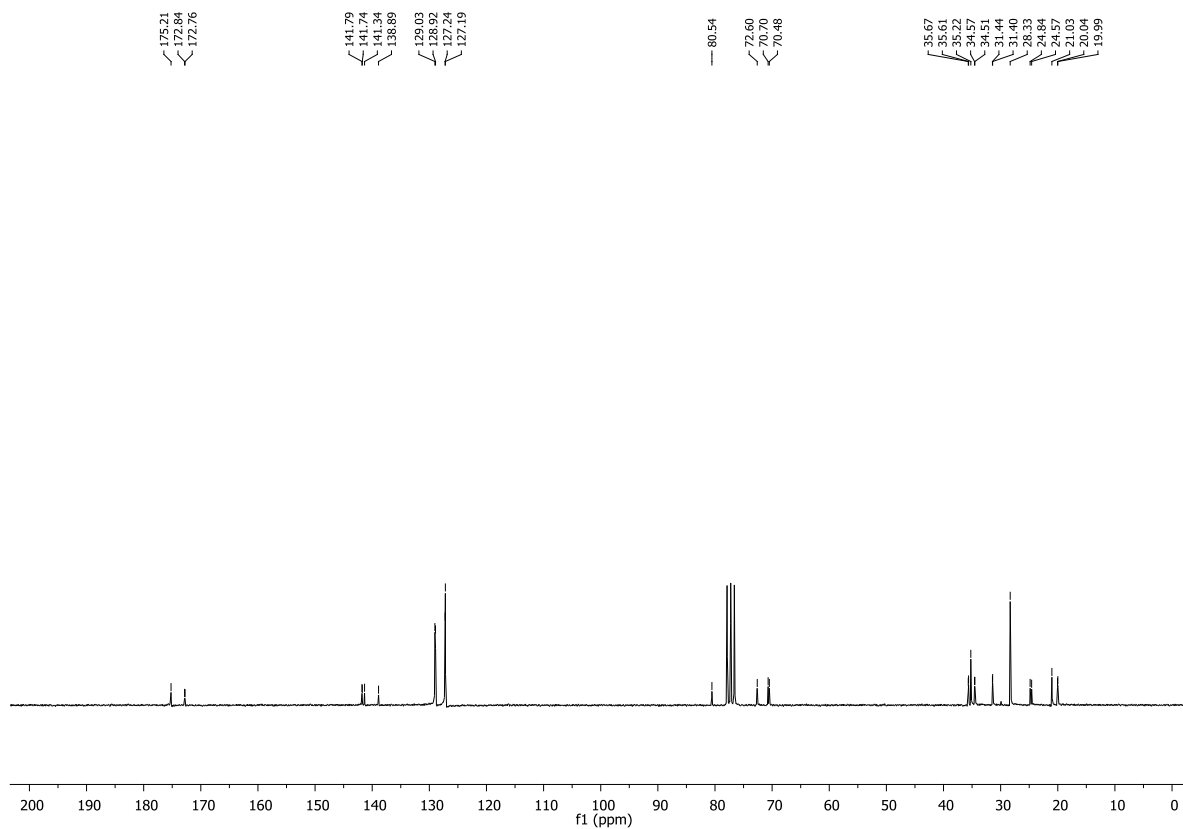
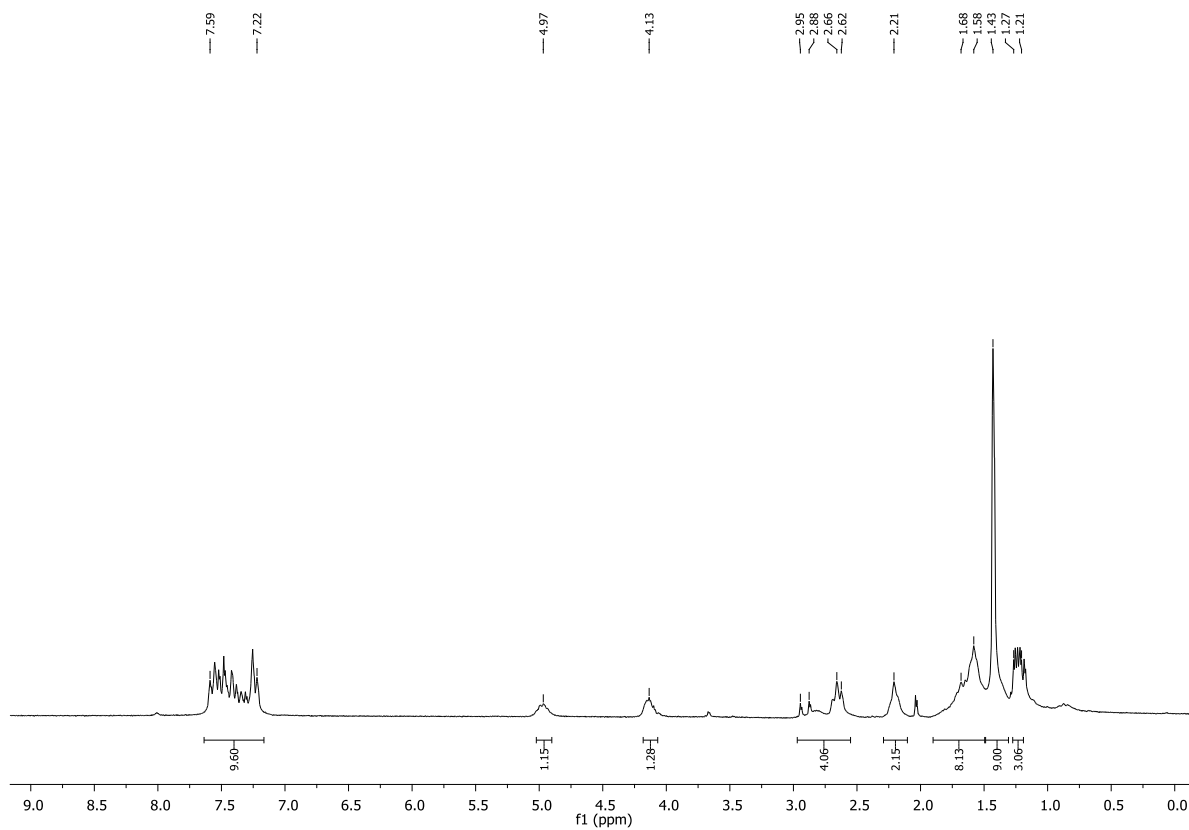


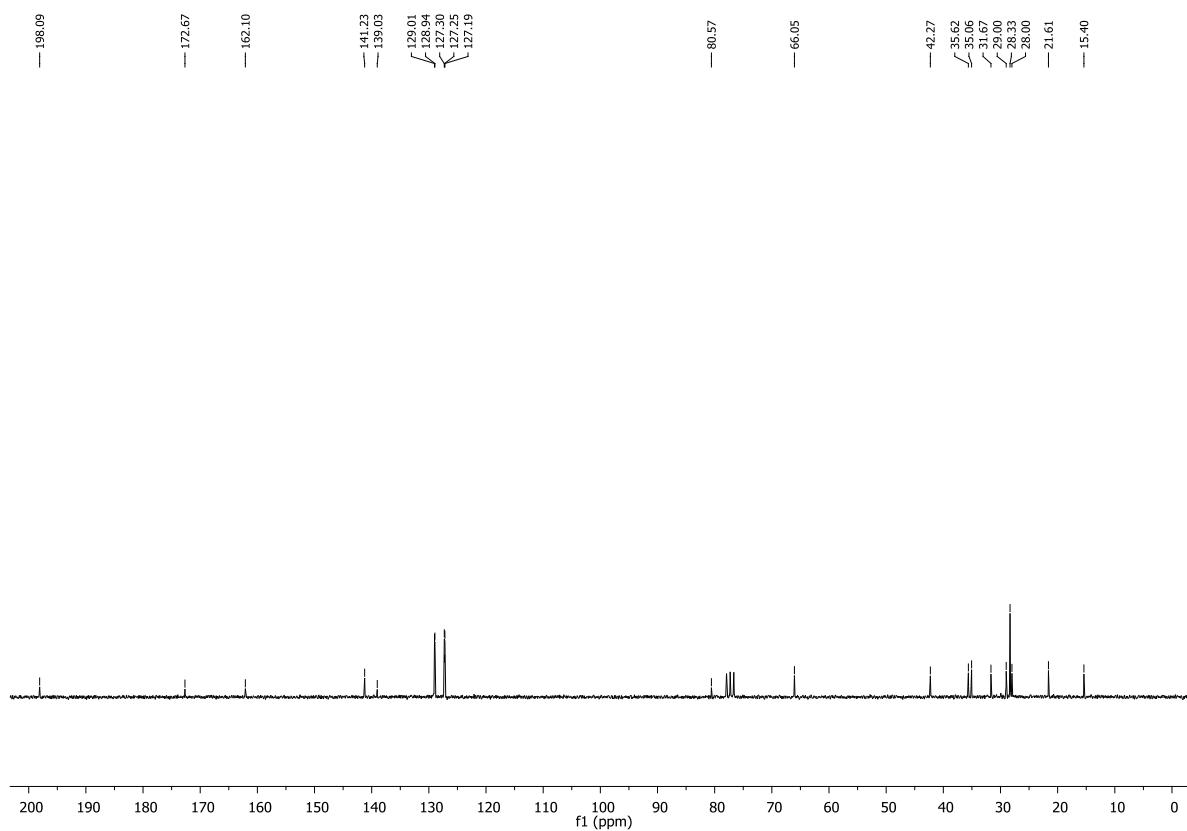
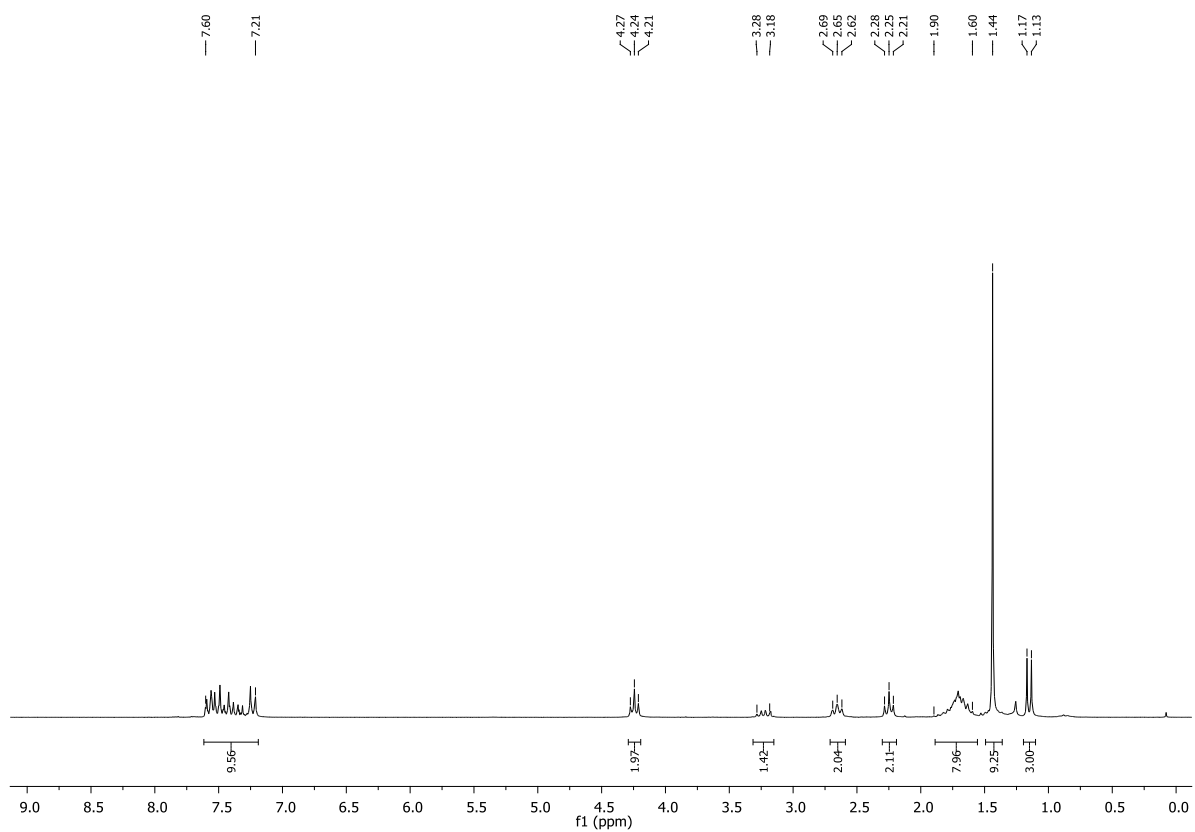
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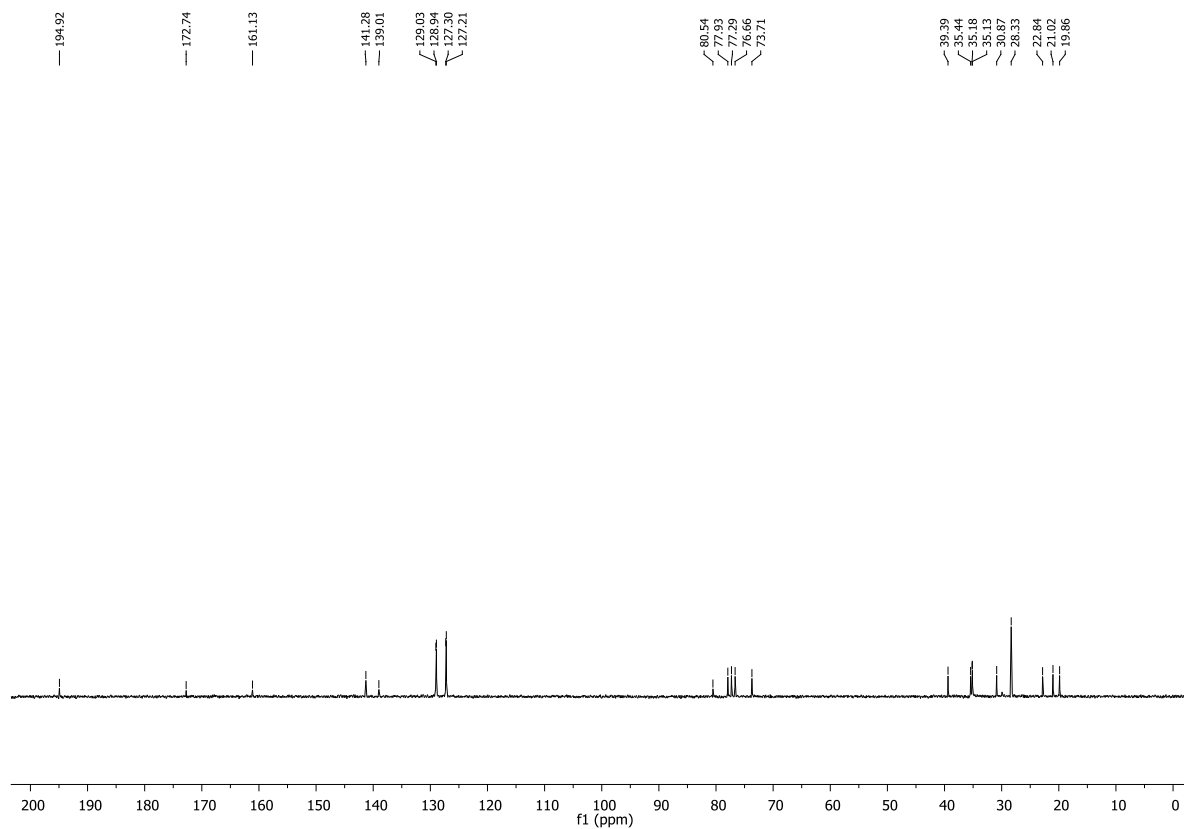
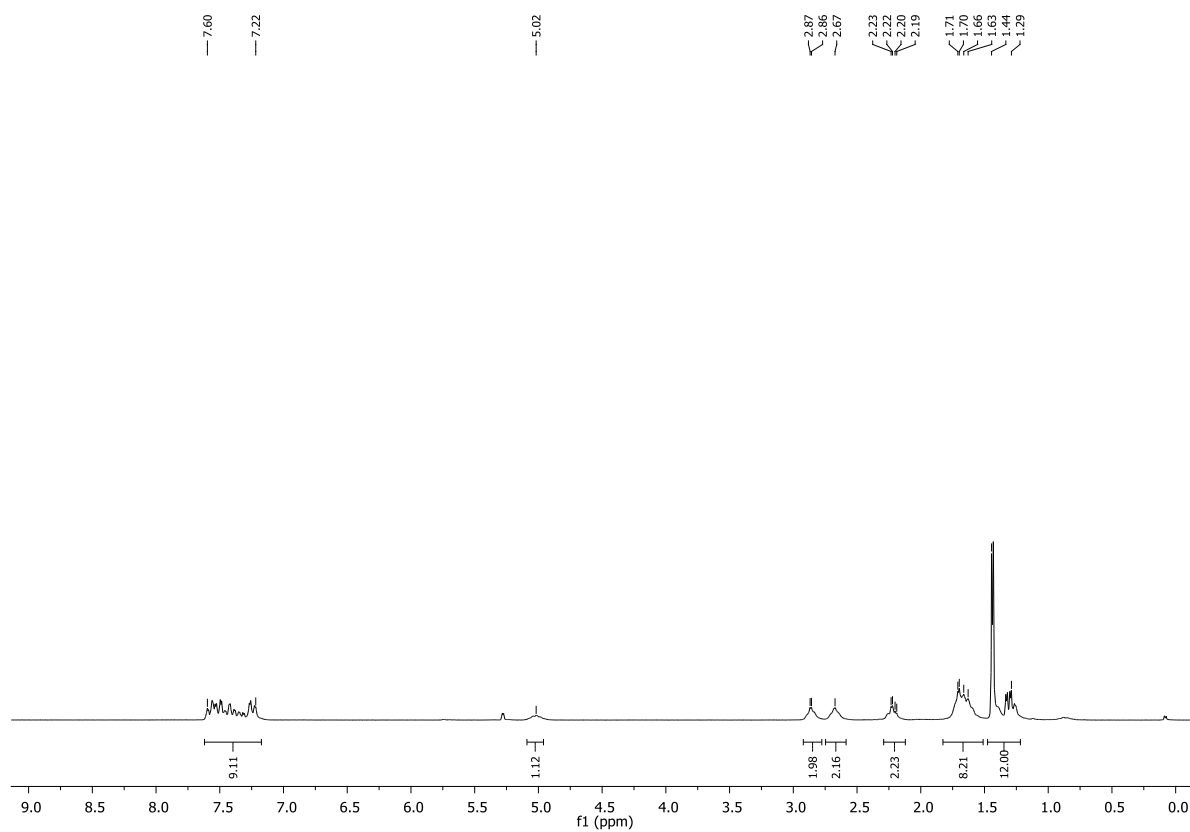


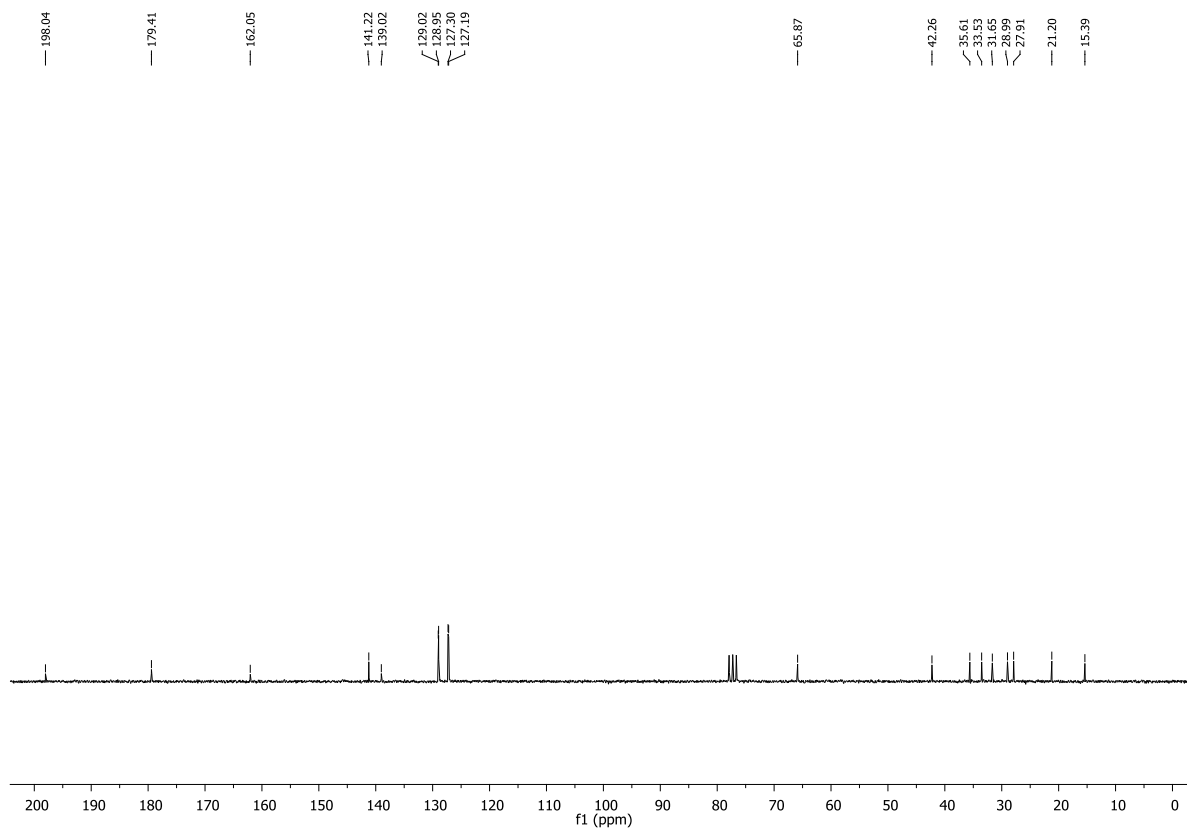
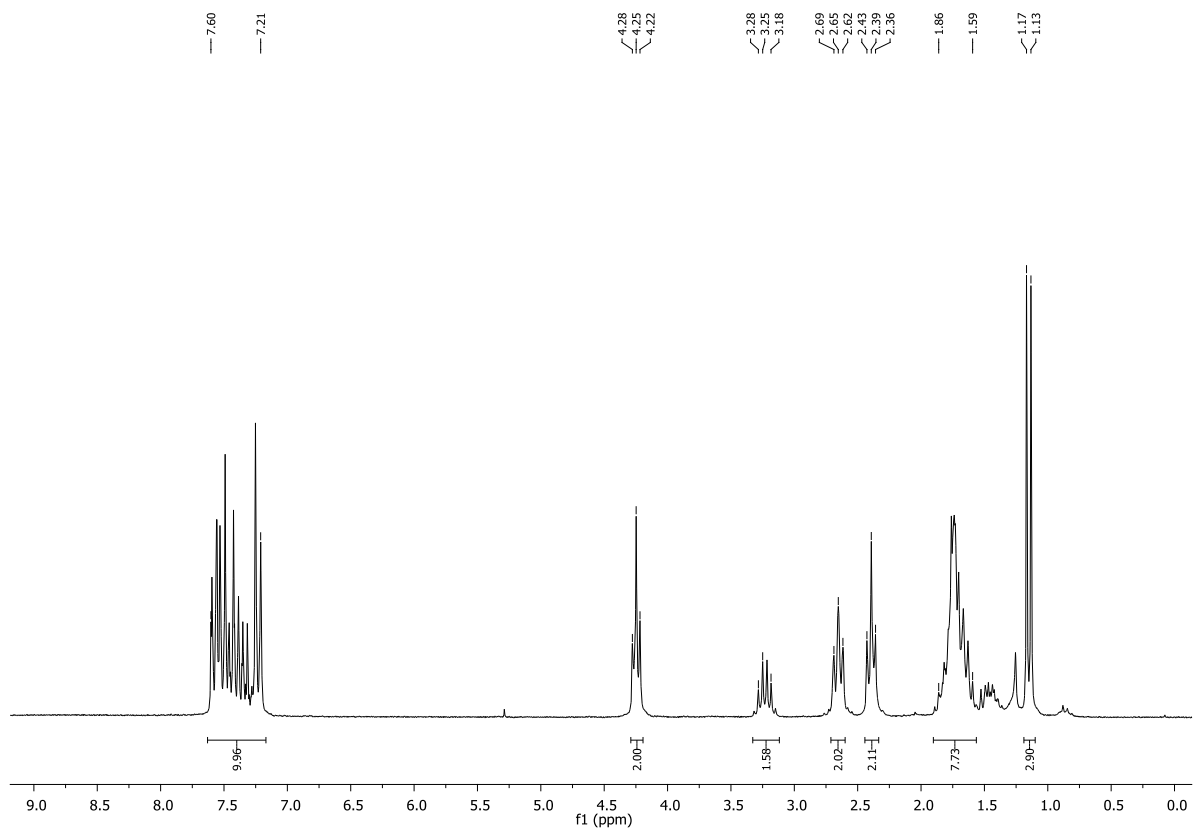
**(15a)**

## (15b)



**(16a)**

**(16b)**

**(17a)**

## (17b)

