Inhibition of *Acinetobacter nosocomialis* Twitching Motility by Quinolones Produced by *Pseudomonas aeruginosa*

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General information

All solvents and reagents were of reagent grade quality (Acros, Aldrich or Sigma) and used without further purification. For flash chromatography, Sigma-Aldrich silica gel, high-purity grade, pore size 60 Å, 230–400 mesh particle size, 40–63 µm was used. TLC was performed using Merck TLC silica gel 60 F254 glass plates (20 × 20 cm), detected by UV (λ = 254 nm), or stained using potassium permanganate and heated at 150 °C. All compounds MS analyses were performed using an LCQ Fleet mass spectrometer (Thermo Fisher Scientific) with an ESI source, or using a Q-Exactive Orbitrap (Thermo) high-resolution mass spectrometer. Spectra were collected in positive ion mode and analyzed by Xcalibur software (Thermo Fisher Scientific). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 and 500 MHz spectrometers. Chemical shifts are reported in δ ppm relative to TMS or residual solvent peak. NMR data were analyzed using MestReNova 6.0.2. Optical density and spectroscopic measurements were performed on a Varioskan Flash Spectral Scanning Multimode Plate Reader (Thermo Fisher Scientific) and SpectraMax M2 Microplate reader (Molecular Devices). Bacterial migration was observed and quantified using ImageJ software by measuring the migration area.

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Biological procedures

Strain information

The *A. nosocomialis* M2 (wild-type) strain was used in all biological assays.

Twitching motility assay

The twitching motility of *A. nosocomialis* was assessed using several established methods [1,2,3], with a primary focus on the protocol developed by the Blackwell group, albeit with minor modifications[4]. *A. nosocomialis* M2 was grown on LB bacto agar and incubated at 37°C for 16-24 hours. A single colony was then transferred into 10-15 mL of LB medium and incubated overnight at 37°C with shaking at 150-180 rpm. The optical density at 600 nm (OD_{600}) of the culture was adjusted to 1.2 using LB medium, and 5 µL of this adjusted culture was applied to the surface of 0.3% LB Eiken agar in a 100 mm Petri dish. After allowing the bacterial suspension to dry and absorb into the agar for a few hours, the plate was incubated at 37°C for 12-16 hours. Bacterial migration was subsequently observed and quantified using ImageJ software by measuring the migration area[5].

Concentration-dependent motility and SAR assays

The tested compound was incorporated into the 0.3% LB Eiken agar medium after it had cooled but before it solidified, at the specified concentration. The standard motility procedure was then employed to assess the compound's impact on bacterial migration. The concentration of DMSO in the medium did not exceed 0.2%.

Static growth assay

Acinetobacter nosocomialis M2 was cultured on LB bacto agar and incubated at 37°C for 16-24 hours. A single colony was then transferred to 10-15 mL of LB medium and incubated overnight at 37°C with shaking at 150-180 rpm. To evaluate the effect of the tested compounds, 100 µL of a 2x concentration of each compound, diluted with fresh LB, was added to a 96-well plate. The optical density at 600 nm (OD_{600}) of the overnight bacterial culture was adjusted to 1.2 using LB, followed by a 1:100 dilution with LB. Subsequently, 100 µL of the diluted bacterial culture was added to each well of the plate, which was then covered and incubated at 37°C for 24 hours without shaking. Bacterial

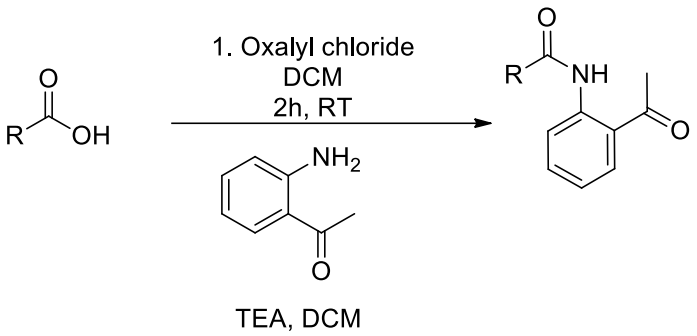
growth was assessed by observing turbidity in the wells and quantified by measuring the OD_{600}[4].

Kinetic growth assay

Acinetobacter nosocomialis M2 was grown on LB bacto agar and incubated at 37°C for 16-24 hours. A single colony was then transferred to 10-15 mL of LB medium and incubated overnight at 37°C with shaking at 150-180 rpm. In a 96-well plate, 100 µL of two-fold serial dilutions of the tested compounds were prepared by diluting with fresh LB. The optical density at 600 nm (OD_{600}) of the overnight bacterial culture was adjusted to 1.2 using LB, followed by a 1:100 dilution with LB. Next, 100 µL of the diluted bacterial culture was added to each well of the plate, which was then covered and incubated at 37°C for 24 hours with shaking. Kinetic OD_{600} readings were taken at 20 minutes intervals over the 24-hour incubation period.

Quinolones synthesis

HHQ and analogues



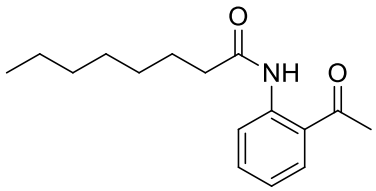
Scheme 1. General synthesis of precursors to a focused quinolone library

General Procedure A[6]:

Step 1: To a solution of the corresponding acid (0.20 g, 1.1 mmol) in 10 mL of dichloromethane, oxalyl chloride (0.423 g, 3.3 mmol) and a drop of DMF were added. The reaction was stirred at room temperature for 2 hours. After the solvents were removed by evaporation, the resulting acid chloride was used in the subsequent step.

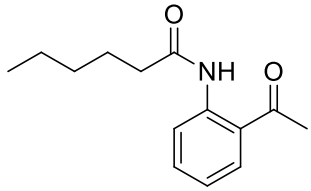
Step 2: In a separate flask, amino acetophenone (0.22 g, 1.66 mmol) was dissolved in 10 mL of dichloromethane, and triethylamine (0.33 g, 3.3 mmol) was added. The mixture was cooled to 0–5 °C, followed by the addition of the acid chloride from Step 1, and the reaction was stirred at room temperature for 2 hours. The mixture was then treated with 20 mL of 0.1 N HCl and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed successively with 30 mL of saturated aqueous $NaHCO_3$ and 30 mL of brine. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude product was used in the next step without further purification.

***N*-(2-acetylphenyl)octanamide-(1a)**



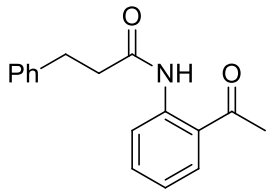
Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (bs, 1H), 8.78 (d, *J* = 8.57 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.11-7.07 (m, 1H), 2.65 (s, 3H), 2.42 (t, *J* = 7.36 Hz, 2H), 1.76-1.72 (m, 2H), 1.38-1.26 (m, 9H), 0.87 (t, *J* = 6.69 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.93, 172.93, 141.28, 135.28, 131.73, 122.27, 121.78, 120.86, 38.92, 31.80, 29.30, 29.11, 28.72, 25.66, 22.72, 14.18. MS (ESI) HRMS m/z calcd for $C_{16}H_{23}NNaO_2^+$ $(M+Na)^+$ 284.1621; m/z found $(M+Na)^+$ 284.1618.

_N_-(2-acetylphenyl)hexanamide-(3a)[7]



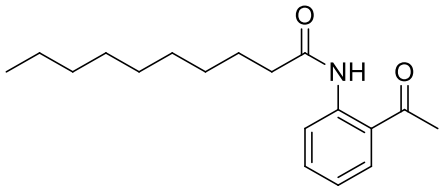
Yield: 17%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.94 Hz, 1H), 7.57-7.53 (m, 1H), 7.13-7.08 (m, 1H), 2.66 (s, 3H), 2.45-2.41 (m, 2H), 1.77-1.74 (m, 2H), 1.38-1.35 (m, 4H), 0.91 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.99, 172.97, 141.32, 135.32, 131.76, 122.30, 121.82, 120.90, 38.90, 31.49, 28.75, 25.35, 22.52, 14.05.

_N_-(2-acetylphenyl)-3-phenylpropanamide-(4a)



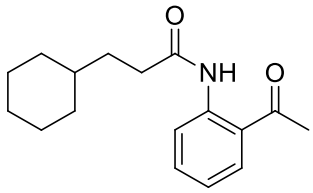
Yield: 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80-8.78 (m, 1H), 7.92-7.89 (m, 1H), 7.60-7.55 (m, 1H), 7.34-7.27 (m, 5H), 7.15-7.11 (m, 1H), 3.10 (t, *J* = 7.44 Hz, 2H), 2.80-2.76 (m, 2H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.91, 171.67, 141.09, 140.74, 135.27, 131.72, 128.64, 128.50, 126.33, 122.42, 121.85, 120.91, 40.37, 31.51, 28.69. MS (ESI) HRMS m/z calcd for $C_{17}H_{18}NO_2^+$ $(M+H)^+$ 268.1332; m/z found $(M+H)^+$ 268.1326.

***N*-(2-acetylphenyl)decanamide-(5a)**



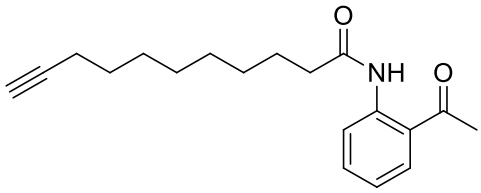
Yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76-8.74 (m, 1H), 7.87-7.85 (m, 1H), 7.54-7.48 (m, 1H), 7.09-7.04 (m, 1H), 2.64 (s, 3H), 2.43-2.38 (m, 2H), 1.74-1.71 (m, 2H), 1.32-1.24 (m, 12H), 0.84 (t, *J* = 5.3 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.85, 172.86, 141.23, 135.20, 131.68, 122.21, 121.71, 120.79, 38.85, 31.92, 29.50, 29.39, 29.32, 28.64, 25.60, 22.72, 14.15. MS (ESI) HRMS m/z calcd for $C_{18}H_{28}NO_2^+$ $(M+H)^+$ 290.2115; m/z found $(M+H)^+$ 290.2112.

***N*-(2-acetylphenyl)-3-cyclohexylpropanamide-(6a)**



Yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.69 (bs, 1H), 8.75-8.72 (m, 1H), 7.86-7.84 (m, 1H), 7.52-7.50 (m, 1H), 7.07-7.06 (m, 1H), 2.62 (s, 3H), 2.42-2.41 (m, 2H), 1.75-1.60 (m, 7H), 1.28-1.13 (m, 4H), 0.96-0.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.80, 173.03, 141.21, 135.14, 131.65, 122.14, 121.63, 120.70, 37.26, 36.28, 33.07, 32.91, 28.60, 26.57, 26.26, 26.16. MS (ESI) HRMS m/z calcd for $C_{17}H_{24}NO_2^+$ $(M+H)^+$ 274.1802; m/z found $(M+H)^+$ 274.1794.

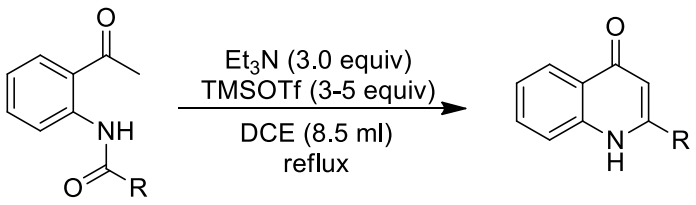
***N*-(2-acetylphenyl)undec-10-ynamide-(14a)**



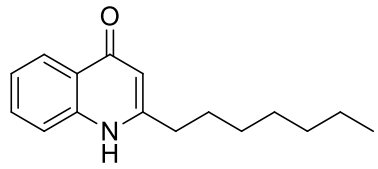
Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.70 (bs, 1H), 8.77 (d, *J* = 8.5 Hz, 1H), 7.90-7.87 (m, 1H), 7.56-7.52 (m, 1H), 7.11-7.08 (m, 1H), 2.66 (s, 3H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.18-2.14 (m, 2H), 1.92 (t, *J* = 2.7 Hz, 1H), 1.76-1.72 (m, 2H), 1.53-1.49 (m, 2H), 1.40-1.30 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.95, 172.85, 141.27, 135.29, 131.74, 122.28, 121.77, 120.85, 84.86, 68.21, 38.87, 29.28, 29.24, 29.14, 29.02, 28.78, 28.74, 28.55, 25.60, 18.48. MS (ESI) HRMS m/z calcd for $C_{19}H_{26}NO_2^+$ $(M+H)^+$ 300.1958; m/z found $(M+H)^+$ 300.1951.

General procedure (cyclization) B[8]:

A solution of *o*-amidoacetophenone (0.8 mmol, 1.0 equiv) in 8.5 mL of DCE was prepared, to which Et_3N (3.0 equiv) was added, followed by the addition of TMSOTf (6.0 equiv). The reaction mixture was heated to 95 °C under an argon atmosphere for 3 days. After cooling to room temperature, the remaining TMSOTf was quenched by the gradual addition of 5 mL of MeOH. All volatile components were removed under reduced pressure, and the residual material was partitioned between 50 mL of EtOAc and 30 mL of 2 M NaOH. The organic layer was separated and washed with an additional 2 x 30 mL of 2 M NaOH. The aqueous layer was back-extracted with 2 x 30 mL of EtOAc, and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was then purified by flash column chromatography (SiO_2, 5% MeOH in CH_2Cl_2) to yield HHQ.

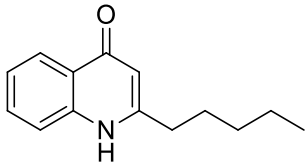


2-heptylquinolin-4(1*H*)-one (HHQ) (1)[8]



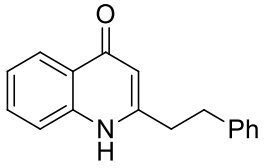
Yield: 78%; ^{1}H NMR (400 MHz, CDCl3) δ 8.37 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 1H), 7.60-7.56 (m, 1H), 7.34-7.31 (t, *J* = 7.6 Hz, 1H), 6.25 (s, 1H), 2.7 (t, *J* = 7.8 Hz, 2H), 1.75-1.67 (m, 2H), 1.27-1.13 (m, 8H), 0.80 (t, *J* = 6.5 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ 179.02, 155.68, 140.89, 131.89, 125.29, 125.08, 123.69, 118.82, 108.19, 34.51, 31.77, 29.31, 29.10, 22.69, 14.15. MS (ESI) HRMS m/z calcd for $C_{16}H_{22}NO^{+}$ $(M+H)^{+}$ 244.1696; m/z found $(M+H)^{+}$ 244.1695.

2-Pentylquinolin-4(1*H*)-one (3)[9]**:**



Yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 1H), 7.61-7.57 (m, 1H), 7.33 (t, *J* = 7.5 Hz, 1H) 6.27 (s, 1H), 2.71 (t, *J* = 8.0 Hz, 2H), 1.75-1.68 (m, 2H), 1.26-1.19 (m, 4H), 0.78 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.99, 155.91, 140.96, 131.85, 125.15, 125.04, 123.67, 118.94, 108.07, 34.39, 31.42, 28.97, 22.42, 13.95.

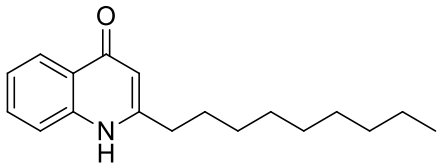
2-Phenethylquinolin-4(1*H*)-one (4)[10]**:**



Yield: 35%; ^{1}H NMR (400 MHz, CD_3OD) δ 8.21-8.18 (m, 1H), 7.70-7.65 (m, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.40-7.36 (m, 1H) 7.27-7.15 (m, 5H), 6.20 (s, 1H), 3.08-3.04 (m, 2H), 3.02-2.98

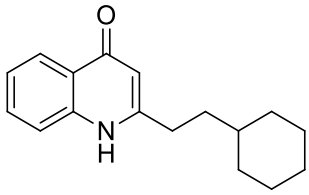
(m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.61, 155.98, 141.58, 141.33, 133.41, 129.57, 129.46, 127.49, 125.97, 125.51, 125.09, 119.08, 109.23, 36.93, 36.13.

2-Nonylquinolin-4(1*H*)-one (5)[11]:



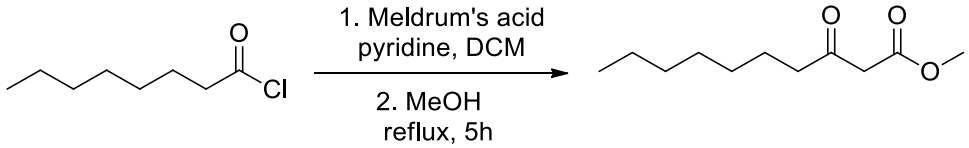
Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.1 Hz, 1H), 7.9 (d, *J* = 8.3 Hz, 1H), 7.6 (t, J = 7.2 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.30 (s, 1H), 2.74 (t, *J* = 7.8 Hz, 2H), 1.78-1.71 (m, 2H), 1.27-1.19 (m, 12H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.92, 155.91, 140.94, 131.81, 125.13, 125.00, 123.63, 118.92, 108.03, 34.44, 31.89, 29.51, 29.41, 29.33, 22.69, 14.15.

2-(2-Cyclohexylethyl)quinolin-4(1*H*)-one (6)



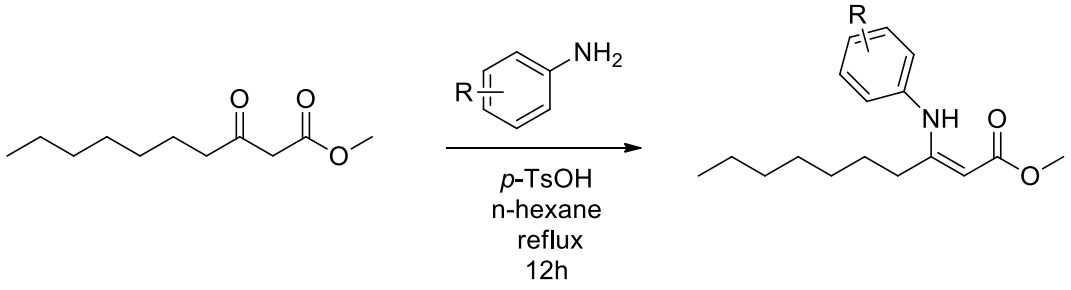
Yield: 7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.59-7.55 (m, 1H), 7.34-7.30 (m, 1H), 6.24 (s, 1H), 2.70-2.66 (m, 2H), 1.60-1.54 (m, 7H), 1.13-1.04 (m, 4H), 0.80-0.74 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.02, 156.14, 140.94, 131.86, 125.25, 125.07, 123.66, 118.84, 108.09, 37.38, 36.81, 33.04, 31.93, 26.56, 26.24. MS (ESI) HRMS m/z calcd for $C_{17}H_{21}NNaO^+$ $(M+Na)^+$ 278.1515; m/z found $(M+Na)^+$ 278.1511.

Methyl 3-oxodecanoate (29)[8]



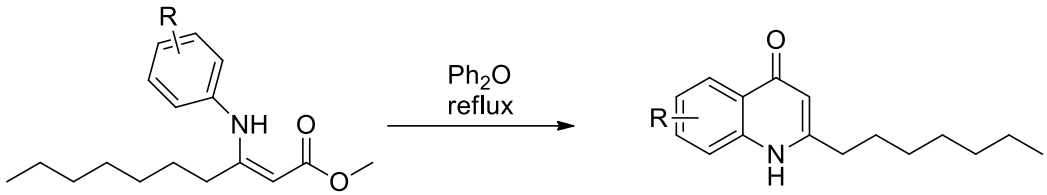
2,2-Dimethyl-1,3-dioxane-4,6-dione (5.04 g, 34.9 mmol) was dissolved in 50 mL of dichloromethane and cooled to 0°C. Pyridine (5.5 mL, 68.1 mmol) was then introduced, and after maintaining the temperature at 0°C for 20 minutes, octanoyl chloride (6.0 mL, 35.15 mmol) was gradually added dropwise. The resulting orange mixture was stirred at 0°C for 1 hour, followed by an additional hour at room temperature. The reaction mixture was then washed with 5% hydrochloric acid (3 x 60 mL), distilled water (2 x 60 mL), and brine (2 x 60 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The resulting brown oil was dissolved in 100 mL of methanol and refluxed for 5 hours. After the solvent was evaporated, the residue was purified by silica gel column chromatography using a 4:1 hexane/ethyl acetate mixture. The final product was obtained as a colorless oil (4.5 g, 64%), with a R_f of 0.62 (hexane/ethyl acetate 4:1). ^{1}H-NMR ($CDCl_3$ 400 MHz) δ (ppm): 3.75 (s, 1H), 3.46 (s, 1H), 2.54 (t, *J* = 7.2 Hz, 2H), 1.63-1.58 (m, 2H), 1.29 (bs, 9H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$ 100 MHz) δ (ppm): ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.01, 167.85, 88.79, 77.48, 77.16, 76.84, 52.45, 49.15, 43.22, 31.76, 29.09, 23.60, 14.18.

General procedure C-for the Enamine synthesis[8]



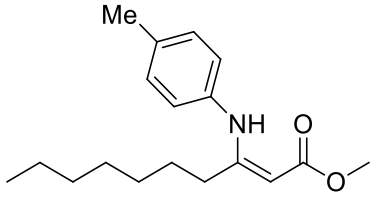
β-Ketoester 29 (9.7 g, 48.4 mmol) was dissolved in 150 mL of *n*-hexane, and aniline (4.0 g, 43 mmol) along with *p*-toluenesulfonic acid (0.16 g, 0.92 mmol) were added to the solution. The mixture was then refluxed for 12 hours. After allowing the reaction to cool to room temperature, the solvent was evaporated. The resulting residue was purified by column chromatography on silica gel using an *n*-hexane/ethyl acetate mixture. The final product was obtained as a yellow oil.

General procedure D-for HHQ analogues[8]



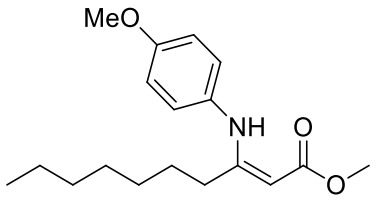
Methyl-3-anilino-2-decenoate derivative (3 g, 10.9 mmol) was added dropwise to 15 mL of diphenyl ether at reflux temperature, and the mixture was kept under reflux for 6 hours. After the reaction was allowed to cool to room temperature, the mixture was added dropwise to *n*-hexane. The resulting precipitate was filtered and washed with *n*-hexane. The final product was obtained as a white solid.

Methyl 3-(*p*-tolylamino)dec-2-enoate (7a)



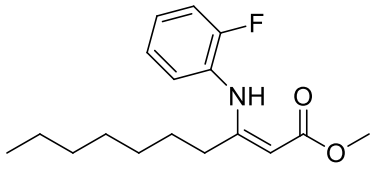
Yield: 32%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 7.8 Hz, 2H), 7.0 (d, *J* = 8.2 Hz, 2H), 4.7 (s, 1H), 3.69 (s, 3H), 2.35 (s, 3H), 2.25 (t, *J* = 7.8 Hz, 2H), 1.43-1.39 (m, 3H), 1.31-1.19 (m, 7H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.18, 164.40, 136.65, 135.31, 129.78, 125.49, 83.93, 50.34, 32.30, 31.68, 29.16, 28.92, 28.09, 22.69, 21.03, 14.16. MS (ESI) HRMS m/z calcd for $C_{18}H_{28}NO_2^+$ $(M+H)^+$ 290.2115; m/z found $(M+H)^+$ 290.2108.

Methyl 3-((4-methoxyphenyl)amino)dec-2-enoate (8a)



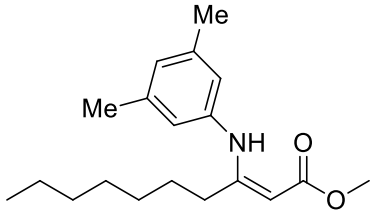
Yield: 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 4.66 (s, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 2.16 (t, *J* = 7.7 Hz, 2H), 1.28-1.24 (m, 5H), 1.17-1.12 (m, 5H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.23, 164.91, 157.77, 132.10, 127.51, 114.35, 83.44, 55.55, 50.29, 32.29, 31.68, 29.17, 28.91, 28.08, 22.69, 14.14. MS (ESI) HRMS m/z calcd for $C_{18}H_{28}NO_3^+$ $(M+H)^+$ 306.2064; m/z found $(M+H)^+$ 306.2055.

Methyl 3-((2-fluorophenyl)amino)dec-2-enoate (9a)



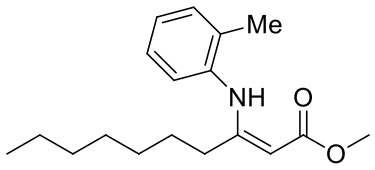
Yield: 56%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (bs, 1H), 7.18-7.15 (m, 1H), 7.14-7.13 (m, 1H), 7.12-7.07 (m, 2H), 4.79 (s, 1H), 3.69 (s, 3H), 2.21 (t, *J* = 7.6 Hz, 2H), 1.41-1.37 (m, 2H), 1.17-1.16 (m, 8H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.11, 163.78, 158.32, 155.87, 127.54, 126.99 (d, J_{CF} = 7.7 Hz), 124.37(d, J_{CF} = 3.8 Hz), 116.40 (d, J_{CF} = 20.1 Hz), 85.75, 50.49, 32.38, 31.66, 29.10, 28.90, 27.89, 22.67, 14.14. MS (ESI) HRMS m/z calcd for $C_{17}H_{25}FNO_2^+$ $(M+H)^+$ 294.1864; m/z found $(M+H)^+$ 294.1857.

Methyl 3-((3,5-dimethylphenyl)amino)dec-2-enoate (10a)



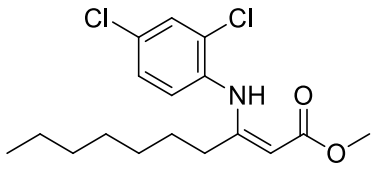
Yield: 35%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (s, 1H), 6.72 (s, 2H), 4.70 (s, 1H), 3.68 (s, 3H), 2.3 (s, 6H), 1.46-1.40 (m, 2H), 1.27-1.16 (m, 10H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.10, 164.15, 139.18, 138.82, 127.04, 122.86, 84.20, 50.33, 32.32, 31.71, 29.16, 28.92, 28.19, 22.70, 21.36, 14.16. MS (ESI) HRMS m/z calcd for $C_{19}H_{30}NO_2^+$ $(M+H)^+$ 304.2271; m/z found $(M+H)^+$ 304.2262.

Methyl 3-(*o*-tolylamino)dec-2-enoate (11a)



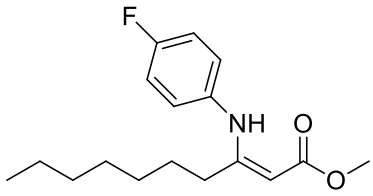
Yield: 39%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (bs, 1H), 7.28-7.24 (m, 1H), 7.19-7.15 (m, 2H), 7.10-7.08 (d, *J* = 7.9 Hz, 1H), 4.75 (s, 1H), 3.71 (s, 3H), 2.29 (s, 3H), 2.16 (t, *J* = 7.6 Hz, 2H), 1.38-1.34 (m, 2H), 1.24-1.16 (m, 8H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.31, 164.73, 137.98, 134.44, 130.83, 127.03, 126.48, 126.33, 83.88, 50.34, 32.32, 31.66, 29.11, 28.89, 27.91, 22.68, 18.16, 14.15. MS (ESI) HRMS m/z calcd for $C_{18}H_{28}NO_2^+$ $(M+H)^+$ 290.2115; m/z found $(M+H)^+$ 290.2106.

Methyl 3-((2,4-dichlorophenyl)amino)dec-2-enoate (12a)



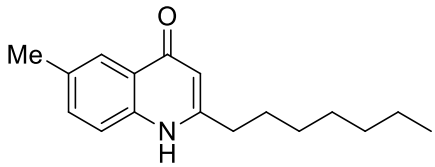
Yield: 69%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.45 (m, 1H), 7.24-7.21 (m, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 4.85 (s, 1H), 3.71 (s, 3H), 2.22 (t, *J* = 7.3 Hz, 2H), 1.40-1.37 (m, 3H), 1.28-1.19 (m, 7H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.94, 162.51, 135.66, 131.18, 130.90, 129.95, 127.50, 87.12, 50.64, 32.36, 31.67, 29.03, 28.92, 27.88, 22.68, 14.16. MS (ESI) HRMS m/z calcd for $C_{17}H_{24}Cl_2NO_2^+$ $(M+H)^+$ 344.1179; m/z found $(M+H)^+$ 344.1176.

Methyl 3-((4-fluorophenyl)amino)dec-2-enoate (15a)



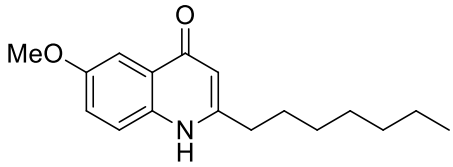
Yield: 62%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (bs, 1H), 7.09-7.01 (m, 4H), 4.73 (s, 1H), 3.69 (s, 3H), 2.21 (t, *J* = 7.5 Hz, 2H), 1.43-1.35 (m, 2H), 1.28-1.18 (m, 8H), 0.85 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.17, 164.06, 161.89, 159.46, 135.35 (d, J_{CF} = 3.8 Hz), 127.54 (d, J_{CF} = 7.6 Hz), 116.10 (d, J_{CF} = 20.1 Hz), 84.62, 50.40, 32.25, 31.66, 29.14, 28.90, 28.04, 22.67, 14.13.MS (ESI) HRMS m/z calcd for $C_{17}H_{25}FNO_2^+$ $(M+H)^+$ 294.1864; m/z found $(M+H)^+$ 294.1855.

2-Heptyl-6-methylquinolin-4(1*H*)-one (7)[11]



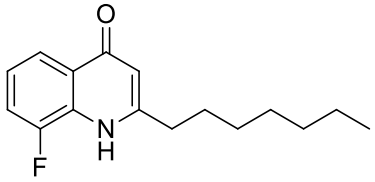
Yield: 43%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.70-7.69 (m, 1H), 7.40-7.38 (m, 1H), 6.21 (s, 1H), 2.67 (t, *J* = 7.8 Hz, 2H), 2.42 (s, 3H), 1.72-1.65 (m, 2H), 1.24-1.14 (m, 8H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.79, 155.19, 138.97, 133.42, 124.98, 124.46, 118.70, 107.87, 34.43, 31.77, 29.31, 29.11, 22.68, 21.32, 14.13.

2-Heptyl-6-methoxyquinolin-4(1*H*)-one (8)[11]



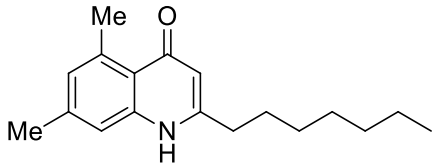
Yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 3.0 Hz, 1H), 7.74-7.21 (m, 1H), 6.23 (s, 1H), 3.79 (s, 3H), 2.69 (t, *J* = 7.7 Hz, 2H), 1.74-1.66 (m, 2H), 1.28-1.12 (m, 8H), 0.80 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.21, 156.44, 154.40, 135.66, 126.02, 123.09, 120.41, 107.39, 103.99, 55.62, 34.38, 31.77, 29.33, 29.32, 29.10, 22.68, 14.12.

8-Fluoro-2-heptylquinolin-4(1*H*)-one (9)[12]



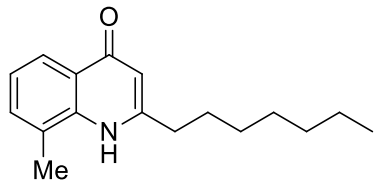
Yield: 59%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.2 Hz, 1H), 7.33-7.28 (m, 1H), 7.24-7.19 (m, 1H), 6.22 (s, 1H), 2.71 (t, *J* = 7.4 Hz, 2H), 1.75-1.69 (m, 2H), 1.36-1.30 (m, 2H), 1.29-1.19 (m, 6H), 0.80 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.24, 154.06, 153.07, 150.60, 127.13, 122.74 (d, J_{CF} = 7.1 Hz), 121.37 (d, J_{CF} = 3.8 Hz), 116.21(d, J_{CF} = 16.7 Hz), 109.56, 34.37, 31.77, 29.22, 29.08, 28.95, 22.69, 14.14.

2-Heptyl-5,7-dimethylquinolin-4(1*H*)-one (10)



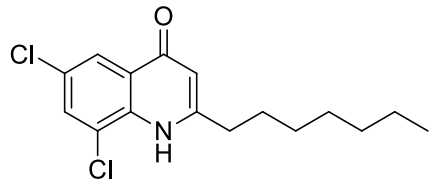
Yield: 46%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.35 (s, 1H), 7.31 (d, *J* = 12.4 Hz, 1H), 7.41 (d, *J* = 6.8 Hz, 1H), 6.86 (s, 1H), 6.08 (s, 1H), 2.97 (s, 3H), 2.57 (t, *J* = 7.7 Hz, 2H), 2.35 (s, 3H), 1.68-1.61 (m, 2H), 1.23-1.17 (m, 8H), 0.82 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.52, 152.98, 142.62, 141.39, 140.03, 127.93, 121.65, 116.12, 109.76, 33.90, 31.81, 29.30, 29.15, 29.08, 23.79, 22.71, 21.54, 14.15. MS (ESI) HRMS m/z calcd for $C_{18}H_{26}NO^{+}$ $(M+H)^{+}$ 272.2009; m/z found $(M+H)^{+}$ 272.2001.

2-Heptyl-8-methylquinolin-4(1*H*)-one (11)



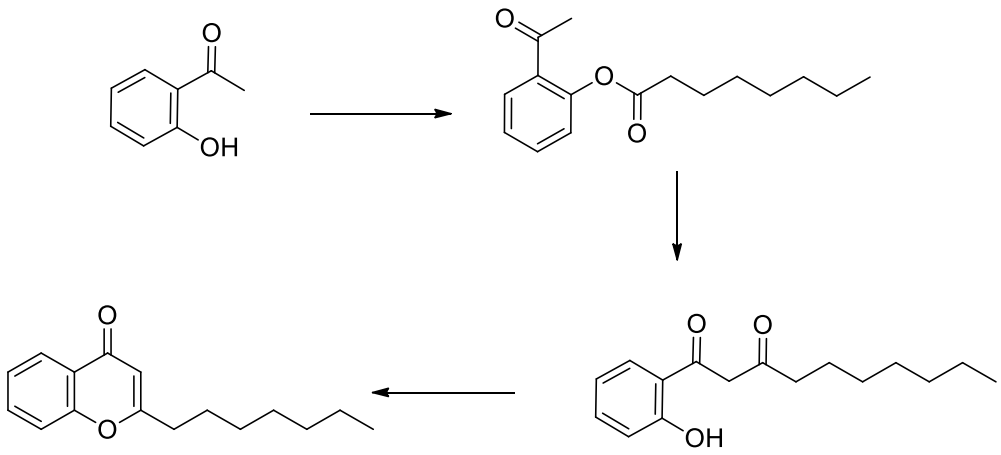
Yield: 57%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.20 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 6.8 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.16 (s, 1H), 2.71 (t, *J* = 7.8 Hz, 2H), 2.59 (s, 3H), 1.73-1.65 (m, 2H), 1.29-1.19 (m, 8H), 0.80 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.14, 154.11, 139.02, 132.83, 125.51, 125.33, 123.84, 123.12, 108.74, 34.36, 31.78, 29.26, 29.16, 29.10, 22.67, 17.50, 14.14. MS (ESI) HRMS m/z calcd for $C_{17}H_{24}NO^{+}$ $(M+H)^{+}$ 258.1852; m/z found $(M+H)^{+}$ 258.1846.

6,8-Dichloro-2-heptylquinolin-4(1*H*)-one (12)

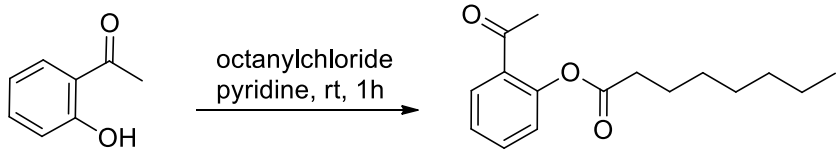


Yield: 41%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.22 (s, 1H), 7.61 (s, 1H), 6.18 (s, 1H), 2.67 (t, *J* = 7.7 Hz, 2H), 1.77-1.69 (m, 2H), 1.39-1.27 (m, 8H), 0.87 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.17, 153.06, 134.89, 131.56, 129.07, 126.95, 124.89, 122.22, 109.86, 34.57, 31.75, 29.11, 29.05, 28.36, 22.70, 14.16. MS (ESI) HRMS m/z calcd for $C_{16}H_{20}Cl_2NO^{+}$ $(M+H)^{+}$ 312.0916; m/z found $(M+H)^{+}$ 312.0912.

Synthesis of 1-O-HHQ (13)

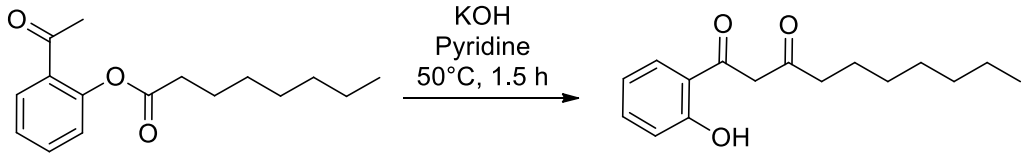


Synthesis of 2-acetylphenyl octanoate (13a)[8]



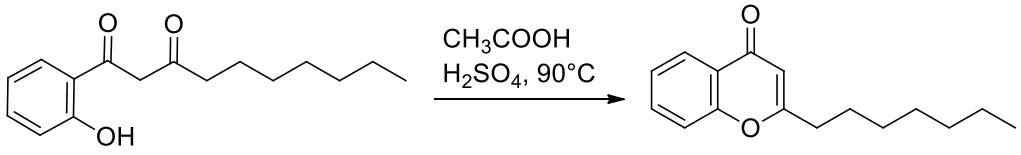
2-Hydroxyacetophenone (5 mL, 36.7 mmol) and octanoyl chloride (7.16 mL, 35.2 mmol) were combined with dry pyridine (7.34 mL) and stirred for 1 hour at room temperature. The reaction mixture was then transferred to a separatory funnel containing crushed ice (70 g) and 1 M HCl (180 mL). Ether was introduced, and the organic layer was separated. The aqueous layer was further extracted twice with ether, and the combined organic layers were dried over $MgSO_4$ and concentrated. The resulting product was purified via column chromatography on silica gel with a hexane/ethyl acetate ratio of 9:1, yielding a colorless oil (9 g, 93%). ^{1}H-NMR ($CDCl_3$ 400 MHz) δ (ppm): 7.80 (dd, *J* = 1.7, 7.7 Hz, 1H), 7.54-7.50 (m, 1H), 7.32-7.28 (m, 1H), 7.11 (dd, *J* = 1.2, 8.1 Hz, 1H), 2.61 (t, *J* = 7.4 Hz, 2H), 2.54 (s, 3H),1.78-1.74 (m, 2H), 1.42-1.30 (m, 8H), 0.89 (t, *J* = 7.1 Hz, 3H)^{13}C-NMR ($CDCl_3$ 100 MHz) δ (ppm): 197.80, 172.36, 149.23, 133.43, 131.12, 130.26, 126.03, 123.93, 34.48, 31.77, 29.58, 29.20, 29.05, 24.68, 22.71, 14.17.

Synthesis of 3-hydroxy-1-(2-hydroxyphenyl)-dec-2-en-1-one (13b)[8]



Ester **13a** (5 g, 19.1 mmol) was dissolved in 20 mL of anhydrous pyridine and the solution was heated to 50°C. Potassium hydroxide (1.71 g, 30.5 mmol) was then added rapidly in one portion. The mixture was kept at 50°C for 1.5 hours, then allowed to cool to ambient temperature. A 10% acetic acid solution (30 mL) was introduced, and the mixture was extracted with ether. The combined organic layers were dried over magnesium sulfate, filtered, and the solvent was evaporated. The resulting product was purified via column chromatography on silica gel using a hexane/ethyl acetate ratio of 9:1. The isolated red solid, comprising a mixture of isomers (3.295 g, 66%), had an R_f value of 0.45 (hexane/ethyl acetate 9:1). The principal compound was characterized as 3-hydroxy-1-(2-hydroxyphenyl)-dec-2-en-1-one. ^{1}H-NMR (CDCl3 400 MHz) δ (ppm): 7.67-7.64 (m, 1H), 7.47-7.42 (m, 1H), 6.99-6.97 (m, 1H), 6.93-6.87 (m, 1H), 6.18 (s, 1H), 4.10 (s, 1H), 2.39-2.35 (t, *J* = 7.5 Hz, 2H), 1.71-1.67 (m, 2H), 1.41-1.29 (m, 8H), 0.91 (t, *J* = 6.7 Hz, 3H). Representative peak for the keto isomer: 2.59 (t), 7.53-7.49 (m). 13C-NMR (CDCl3 100.61 MHz) δ (ppm): 195.63, 186.78, 137.24, 135.76, 130.97, 128.62, 119.09, 118.80, 94.81, 36.65, 31.79, 29.27, 29.11, 26.64, 22.73, 14.18. Representative peak for the keto isomer: 162.61, 119.42, 53.91, 43.61, 23.59.

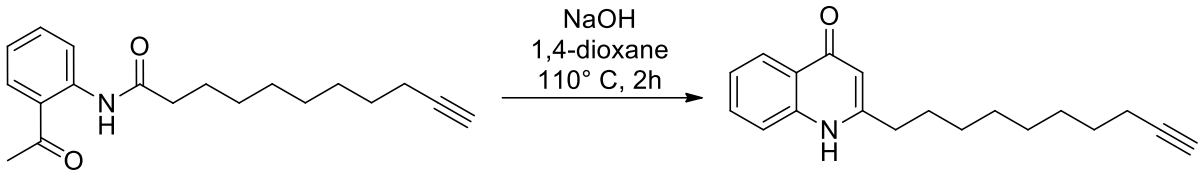
Synthesis of 2-heptyl-chromen-4-one, 1-O-HHQ (13)[8]



1.00 g of compound **13b** (3.8 mmol) was dissolved in 5 mL of glacial acetic acid. Concentrated sulfuric acid (0.2 mL) was added to the solution, which was then heated at

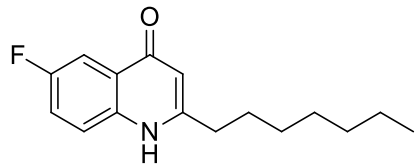
90°C for 1.5 hours. After heating, the hot solution was poured over 25 g of crushed ice, with stirring maintained until the ice was fully melted. The mixture was extracted four times with ether, and the combined organic extracts were dried over magnesium sulfate, filtered, and concentrated. The resulting product was purified by column chromatography on silica gel using a hexane/ethyl acetate mixture (9:1). The final product was obtained as a yellow crystalline solid (0.699 g, 75%). ^{1}H-NMR ($CDCl_3$ 400 MHz) δ (ppm): 8.16-8.12 (m, 1H), 7.62-7.56 (m, 1H), 7.42-7.29 (m, 1H), 6.16-6.12 (m, 1H), 20.62-2.54 (m, 2H), 1.72-1.65 (m, 2H), 1.34-1.24 (m, 8H), 0.87-0.82 (m, 3H). ^{13}C-NMR ($CDCl_3$ 100.61 MHz) δ (ppm): 178.38, 169.88, 156.56, 133.45, 125.67, 124.91, 123.79, 117.91, 109.83, 34.36, 31.72, 29.00, 26.85, 22.66, 14.12.

2-(Dec-9-yn-1-yl)quinolin-4(1*H*)-one (14)[8]:



To a solution of N-(2-acetylphenyl)undec-10-ynamide (0.720 g, 2.4 mmol) in 15.0 mL of 1,4-dioxane, sodium hydroxide (288 mg, 7.2 mmol) was added. The mixture was heated to 110°C under an argon atmosphere for 3 hours. Upon cooling to room temperature, the volatiles were removed under reduced pressure, and the residue was purified by column chromatography on silica gel using 3% methanol in dichloromethane. The desired compound was obtained as a pale-yellow solid with a yield of 29% (0.196 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.61-7.57 (m, 1H), 7.33 (t, *J* = 7.09 Hz, 1H), 6.26 (s, 1H), 2.72 (t, *J* = 7.8 Hz 2H), 2.13-2.09 (m, 2H), 1.91 (t, *J* = 2.3 Hz, 1H), 1.76-1.68 (m, 2H), 1.47-1.39 (m, 2H), 1.32-1.24 (m, 4H), 1.20-1.18 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.00, 155.73, 140.93, 131.89, 125.23, 125.07, 123.69, 118.88, 108.15, 84.74, 68.31, 34.48, 29.28, 29.02, 28.73, 28.48, 18.45. MS (ESI) HRMS m/z calcd for $C_{19}H_{24}NO^{+}$ $(M+H)^{+}$ 282.1852; m/z found $(M+H)^{+}$ 282.1846.

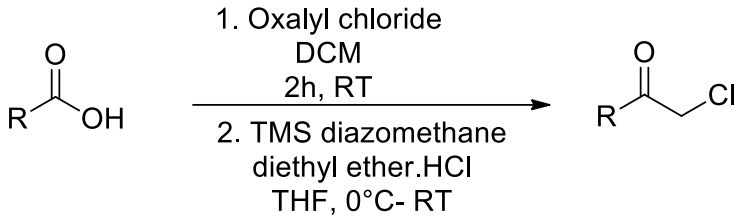
6-Fluoro-2-heptylquinolin-4(1*H*)-one (15)[12]:



Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.96 (m, 1H), 7.90-7.86 (m, 1H), 7.39-7.35 (m, 1H), 6.24 (s, 1H), 2.72 (t, *J* = 6.8 Hz, 2H), 1.73-1.71 (m, 2H), 1.28-1.17 (m, 8H), 0.80 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.10, 160.62, 158.19, 156.04, 137.53, 126.19 (d, J_{CF} = 7.1 Hz), 121.14, 120.88, 109.57 (d, J_{CF} = 22.4 Hz), 107.47, 34.53, 31.76, 29.36, 29.09, 22.67, 14.10.

Synthesis of PQS analogues

Typical procedure for the preparation of substrates[13,14]

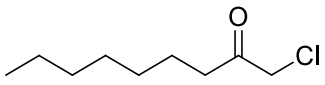


Scheme 1. Synthesis of small molecule probes library.

General Procedure 1:

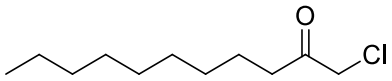
To a solution of the appropriate acid (0.23 g, 1.27 mmol) in 10 mL of dichloromethane, oxalyl chloride (0.486 g, 3.83 mmol) and a drop of DMF were added. The mixture was stirred at room temperature for 2 hours. After evaporating the volatiles, the acid chloride was dissolved in 10 mL of THF and cooled to 0°C. A 2M solution of TMS-diazomethane in hexane (1.9 mL, 3.83 mmol) was then added slowly over 10 minutes. The resulting yellow solution was allowed to stand at room temperature for 12 hours. The solution was concentrated, and the residue was dissolved in 5 mL of THF and gradually treated with 5 mL of 4N HCl in ether. The mixture was stirred at 24°C for 3 hours. After concentration under reduced pressure, the residue was purified by column chromatography on silica gel using a hexane/dichloromethane gradient to yield the desired product.

1-Chlorononan-2-one (2a)[13]



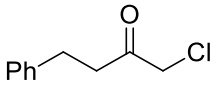
Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 2H), 2.57 (t, *J* = 7.3 Hz, 2H), 1.62–1.59 (m, 2H), 1.30–1.24 (m, 8H), 0.87 (t, *J* = 6.49, 3H), 5.49 (d, *J* = 8.0 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.94, 48.33, 39.85, 31.74, 29.15, 29.10, 23.73, 22.70, 14.16.

1-Chloroundecan-2-one (16a)



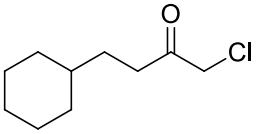
Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 2H), 2.56 (t, *J* = 7.43 Hz, 2H), 1.61-1.58 (m, 2H), 1.26-1.24 (m, 12H), 0.86 (t, *J* = 5.34 Hz, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.88, 77.48, 77.16, 76.84, 48.32, 39.83, 31.95, 29.49, 29.43, 29.34, 29.17, 23.72, 22.76, 14.19. MS (ESI) HRMS m/z calcd for $C_{11}H_{21}ClNaO^+$ $(M+Na)^+$ 227.1173; m/z found $(M+Na)^+$ 227.1174.

1-Chloro-4-phenylbutan-2-one (17a)



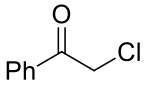
Yield: 42%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2H), 7.24-7.19 (m, 3H), 4.04 (s, 2H), 2.97-2.90 (m, 4H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.87, 140.38, 128.68, 128.39, 126.44, 48.38, 41.36, 29.65. MS (ESI) HRMS m/z calcd for $C_{10}H_{11}ClNaO^+$ $(M+Na)^+$ 205.0391; m/z found $(M+Na)^+$ 205.0391.

1-Chloro-4-cyclohexylbutan-2-one (18a)



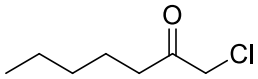
Yield: 53%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.05 (s, 2H), 2.58–2.54 (m, 2H), 1.67-1.59 (m, 5H), 1.51-1.54 (m, 2H), 1.23-1.08 (m, 4H), 0.90-0.85 (m, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.08, 48.25, 37.36, 37.20, 33.09, 30.97, 26.53, 26.25. MS (ESI) HRMS m/z calcd for $C_{10}H_{17}ClNaO^+$ $(M+Na)^+$ 211.0860; m/z found $(M+Na)^+$ 211.0861.

2-Chloro-1-phenylethanone (19a)[13]



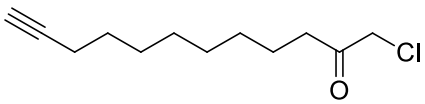
Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.60-7.56 (m, 1H), 7.48-7.43 (m, 2H), 4.69 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.08, 134.01, 128.89, 128.47, 46.16.

1-Chloroheptan-2-one (20a)[14]



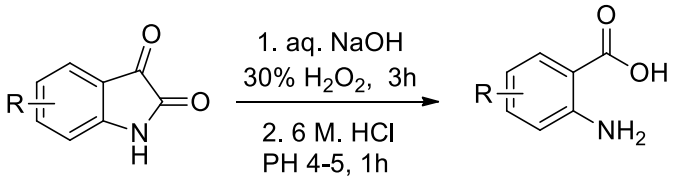
Yield: 67%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 2H), 2.57 (d, *J* = 7.39 Hz, 2H), 1.64-1.59 (m, 2H), 1.34-1.24 (m, 4H), 0.88 (m, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.93, 77.48, 77.16, 76.84, 48.33, 39.79, 31.33, 23.40, 22.48, 13.97.

1-Chlorododec-11-yn-2-one (22a)



Yield: 45%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (s, 1H), 2.57 (t, *J* = 7.21 Hz, 2H), 2.18-2.14 (m, 2H), 1.92 (t, *J* = 2.53 Hz, 1H), 1.61-1.58 (m, 2H), 1.52-1.48 (m, 2H), 1.39-1.29 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.88, 84.80, 68.24, 48.32, 39.79, 29.27, 29.09, 28.97, 28.74, 28.52, 23.66, 18.48. MS (ESI) HRMS m/z calcd for $C_{12}H_{19}ClNaO^{+}$ $(M+Na)^{+}$ 237.1017; m/z found $(M+Na)^{+}$ 237.1020.

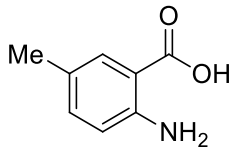
General procedure 2-for the synthesis of Anthralinic acid[15]



The compound was prepared using a standard procedure[15]. Indoline-2,3-dione (1, 5.0 g, 34.0 mmol) was dissolved in a NaOH solution (67 mL, 1 mol/L). Hydrogen peroxide (7.3 mL, 30%) was then added dropwise to the solution at 0°C. The mixture was stirred at 30–

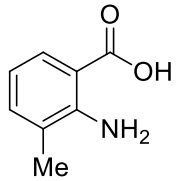
40°C for 3 hours. Afterward, the reaction mixture was neutralized to pH 7.5 using hydrochloric acid (3 mol/L). Activated carbon was then added, and the mixture was stirred for an additional 30 minutes. The resulting precipitate was filtered out, and the filtrate was acidified to pH 4–5 while stirring continued for 1 hour. The mixture was filtered again, and the filter cake was combined with the initial precipitate and dried in a vacuum oven to obtain the crude product. The crude product was then purified by flash column chromatography using a dichloromethane/methanol mixture, resulting in 2-Aminobenzoic acid as a solid.

2-Amino-5-methylbenzoic acid (23b)



Yield: 66%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.65 (s, 1H), 7.11 (d, *J* = 8.42 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 170.26, 150.69, 135.98, 131.85, 124.65, 117.52, 110.37, 20.24. MS (ESI) HRMS m/z calcd for $C_8H_9NNaO_2^+$ $(M+Na)^+$ 174.0525; m/z found $(M+Na)^+$ 174.0526.

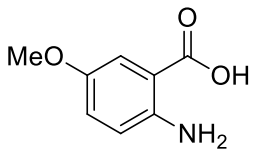
2-amino-3-methylbenzoic acid (24b)



Yield: 37%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.78-7.76 (m, 1H), 7.21-7.19 (m, 1H), 6.55-6.52 (m, 1H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 170.66, 150.96, 135.58,

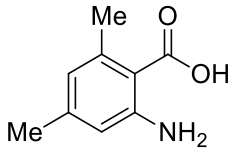
130.28, 123.92, 115.58, 110.26, 17.61. MS (ESI) HRMS m/z calcd for $C_8H_9NNaO_2^+$ $(M+Na)^+$ 174.0525; m/z found $(M+Na)^+$ 174.0526.

2-amino-5-methoxybenzoic acid (25b)



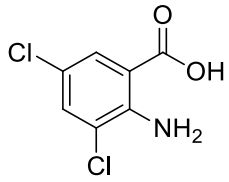
Yield: 49%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.35-7.30 (m, 1H), 7.70-6.99 (m, 1H), 6.81-6.77 (m, 1H), 3.72 (s, 3H). (excess peaks are due to rotamers) ^{13}C NMR (100 MHz, Acetone-d_6) δ 169.85, 154.52, 147.47, 124.57, 123.99, 119.10, 118.89, 114.15, 111.99, 55.93. (excess peaks are due to rotamers). MS (ESI) HRMS m/z calcd for $C_8H_9NNaO_3^+$ $(M+Na)^+$ 190.0475; m/z found $(M+Na)^+$ 190.0473.

2-amino-4,6-dimethylbenzoic acid (26b)



Yield: 38%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 6.47 (s, 1H), 6.29 (s, 1H), 2.4 (s, 3H), 2.15 (s, 3H). (excess peaks are due to rotamers) ^{13}C NMR (100 MHz, Acetone-d_6) δ 171.10, 163.30, 152.17, 149.38, 145.61, 143.38, 142.84, 141.21, 123.96, 121.43, 115.49, 114.49, 110.68, 108.89, 23.65, 22.43, 21.58, 21.28. (excess peaks are due to rotamers). MS (ESI) HRMS m/z calcd for $C_9H_{11}NNaO_2^+$ $(M+Na)^+$ 188.0682; m/z found $(M+Na)^+$ 188.0682.

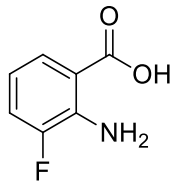
2-amino-3,5-dichlorobenzoic acid (27b)



Yield: 87%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.82 (s, 1H), 7.52 (s, 1H), 6.77 (bs, 1H), 3.72 (s, 3H). (excess peaks are due to rotamers) ^{13}C NMR (100 MHz, Acetone-d_6) δ 168.73,

147.41, 134.22, 130.74, 121.42, 119.55, 113.10. (excess peaks are due to rotamers). HRMS m/z calcd for $C_7H_6Cl_2NO_2^+$ $(M+H)^+$ 205.9771; m/z found $(M+H)^+$ 205.9766.

2-Amino-3-fluorobenzoic acid (28b)[16]

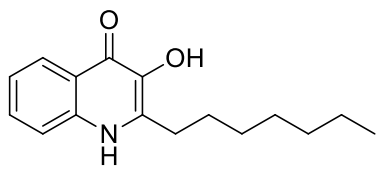


Yield: 49%; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.68 (bs, 1H), 7.19 (bs, 1H), 6.58 (bs, 1H), 6.36 (bs, 2H). ^{13}C NMR (100 MHz, Acetone-d_6) δ 169.47, 153.49, 127.71, 119.29 (d, J_{CF} = 18.5 Hz), 114.88 (d, J_{CF} = 7.2 Hz), 113.02.

General procedure 3[17]**: preparation of PQS and analogues using microwave irridation**

Diisopropylethylamine (1.2 equivalents) and the corresponding α-chloro ketone (1.0 equivalent) were sequentially introduced to a solution of the substituted anthranilic acid (0.15 g, 1.0 equivalent) in anhydrous NMP (2.25 mL) contained in a 10 mL microwave vial. The mixture was then heated under microwave irradiation at 200°C for 30 to 60 minutes. After cooling to room temperature, the solution was added to an ice-water mixture and allowed to settle for 20 minutes. The resulting precipitate was filtered, dried under high vacuum overnight, and the crude product was purified by recrystallization.

2-Heptyl-3-hydroxyquinolin-4(1H)-one (2)[17]

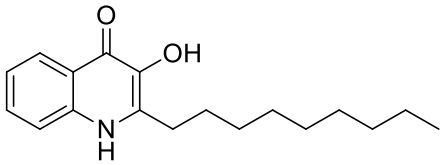


2-heptyl-3-hydroxyquinolin-4(1H)-one (PQS) was prepared by a known procedure.

Spectral data were found to be identical to literature values.

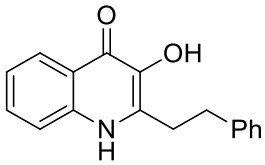
Yield: 60%; ^{1}H NMR (400 MHz, DMSO-d6) δ 8.10 (d, *J* = 7.9 Hz, 1H), 7.54-7.53 (m, 2H), 7.23-7.19 (m, 1H), 2.73 (t, *J* = 7.08 Hz, 3H), 1.66 (m, 2H), 1.31-1.24 (m, 8H), 0.84 (t, *J* = 6.6, 3H). 13C NMR (100 MHz, DMSO-d6) δ 168.86, 137.82, 137.36, 135.50, 129.95, 124.47, 122.19, 121.48, 117.76, 31.18, 28.78, 28.46, 28.12, 27.81, 22.05, 13.91.

3-Hydroxy-2-nonylquinolin-4(1H)-one (16)[17]



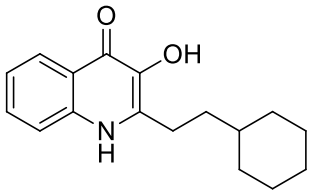
Yield: 43%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 8.2 Hz, 1H), 7.53 (s, 2H), 7.21 (m, 1H), 2.73 (s, 2H), 1.30-1.22 (m, 12H), 0.83 (t, *J* = 6.5, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.88, 137.87, 137.37, 135.53, 129.94, 124.48, 122.19, 121.49, 117.78, 31.25, 28.90, 28.80, 28.65, 28.12, 27.79, 22.07, 13.92.

3-Hydroxy-2-phenethylquinolin-4(1H)-one (17)[17]



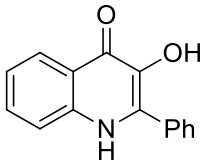
Yield: 39%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (d, *J* = 8.0 Hz, 1H), 7.55 (bs, 2H), 7.31-7.17 (m, 7H), 3.03-3.01 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.06, 140.86, 138.03, 137.40, 134.72, 130.10, 128.43, 128.21, 126.14, 124.56, 122.32, 121.63, 117.83, 33.49, 30.19.

2-(2-Cyclohexylethyl)-3-hydroxyquinolin-4(1H)-one (18)



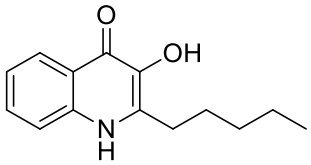
Yield: 52%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.54 (bs, 2H), 7.21 (t, *J* = 6.9 Hz, 1H), 2.74 (t, *J* = 7.0 Hz, 2H), 1.78-1.75 (m, 2H), 1.67-1.54 (m, 5H), 1.26-1.13 (m, 4H), 0.93 (t, *J* = 10.9 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.84, 137.75, 137.40, 135.90, 129.95, 124.47, 122.19, 121.50, 117.77, 37.10, 35.36, 32.62, 26.12, 25.75. MS (ESI) HRMS m/z calcd for $C_{17}H_{22}NO_2^+$ $(M+H)^+$ 272.1645; m/z found $(M+H)^+$ 272.1637.

3-Hydroxy-2-phenylquinolin-4(1H)-one-(19)[17]



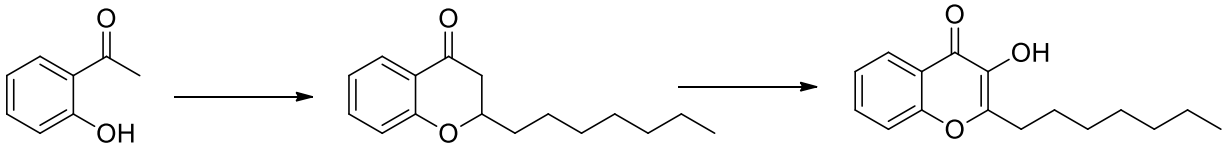
Yield: 41%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 6.9, 2H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.62-7.52 (m, 4H), 7.28 (t, J = 7.5Hz, 1H), 0.86 (t, *J* = 6.4, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.03, 138.04, 137.80, 132.35, 131.46, 130.54, 129.24, 128.29, 124.45, 121.88, 118.44.

3-Hydroxy-2-pentylquinolin-4(1H)-one (20)[17]



Yield: 40%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.54 (s, 2H), 2.73 (t, J = 7.6 Hz, 2H), 1.67 (bs, 2H), 1.32 (bs, 4H), 0.86 (t, *J* = 6.4, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.89, 137.86, 137.37, 135.59, 129.97, 124.49, 122.21, 121.53, 117.79, 31.01, 28.08, 27.49, 21.90, 13.88.

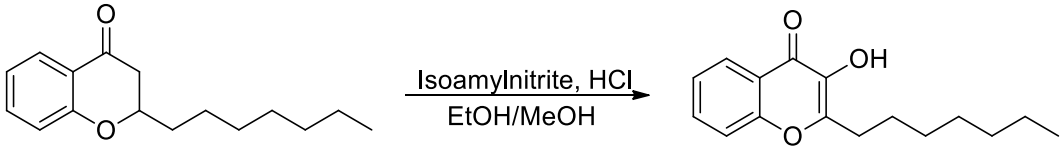
Synthesis of 2-heptyl-3-hydroxy-Chromen-4-one, 1-O-PQS (21)[8]



21a **21**

The compound was prepared using a previously established method[8]. Octanal (0.26 mL, 1.66 mmol) and pyrrolidine (0.067 mL, 0.82 mmol) were dissolved in 5 mL of dry toluene under a nitrogen atmosphere, with molecular sieve added for extra dryness. After 10 minutes, 2'-hydroxyacetophenone (0.226 g, 1.66 mmol) was introduced into the mixture. The initially white solution was stirred at room temperature for 30 minutes until it became clear. The solution was then heated to 110°C and refluxed for 3 hours. Upon cooling to room temperature, the mixture was diluted with diethyl ether. It was then washed sequentially with saturated $NaHCO_3$, saturated NH_4Cl, water, and brine. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. The resulting product **(21a)** was purified by column chromatography on silica gel using a 3:1 mixture of n-hexane and dichloromethane, yielding a colorless oil (0.109 g, 27%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 4.74–4.66 (m, 1H), 4.41 (dd, *J* = 16.6, 8.7 Hz, 1H), 4.31 (dd, *J* = 10.4, 8.2 Hz, 1H), 2.58–2.49 (m, 1H), 2.46–2.36 (m, 1H), 2.17 (td, *J* = 7.3, 2.6 Hz, 2H), 2.13–2.06 (m, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.91–1.84 (m, 1H), 1.74–1.68 (m, 1H), 1.61 (s, 6H), 1.52–1.41 (m, 4H), 1.38 (s, 9H), 1.26-1.18 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.10, 173.55 (2C), 83.93, 68.61, 67.05, 63.13, 53.42, 51.55, 32.35, 30.30, 29.50, 28.87, 28.34 (3C), 28.09, 27.82, 26.68, 25.78, 22.92, 18.18.

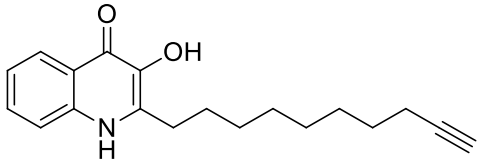
Synthesis of 2-heptyl-3-hydroxy-chromen-4-one, 1-O-PQS (21)[8]



Under a nitrogen atmosphere, 95 mg (0.386 mmol) of compound **(21a)** was dissolved in a 5:4 mixture of ethanol and methanol, and isoamyl nitrite (0.15 mL, 1.10 mmol) was added carefully. The resulting yellow solution was cooled to 0°C, and concentrated HCl

(0.23 mL) was added dropwise. After 10 minutes on ice, the solution turned orange, and the mixture was stirred at room temperature for 1 hour. The temperature was then increased to 80°C, and the reaction was continued for an additional 45 minutes. Once cooled to room temperature, the mixture was poured into water. It was then extracted three times with diethyl ether, and the combined organic layers were washed with brine and dried over magnesium sulfate. The product was separated from most byproducts via column chromatography on silica gel with a hexane/ethyl acetate (5:1) mixture, followed by further purification using dichloromethane/methanol (20:1) on silica gel. The final product **21** was obtained as a gray solid (15 mg, 15%). The R_f value was 0.71 in dichloromethane. Unreacted starting material was recovered during the initial chromatography with hexane/ethyl acetate (5:1) (22 mg, 23%). ^{1}H-NMR (CDCl3 400.13 MHz) δ (ppm): 0.88 (t, *J* = 7.0 Hz, 3H, H15), 1.22 – 1.47 (m, 8H, H-11-14), 1.77 (quint., *J* = 7.5 Hz, 2H, H-10), 2.84 (t, *J* = 7.7 Hz, 2H, H-9), 6.23 (s, 1H, -OH), 7.37 (t, J = 7.3 Hz, 1H, H-6), 7.47 (d, *J* = 8.5 Hz, 1H, H-8), 7.64 (t, *J* = 7.7 Hz, 1H, H-7), 8.22 (d, *J* = 7.8 Hz, 1H, H-5). 13C-NMR (CDCl3 100.61 MHz) δ (ppm): 14.2, 22.7, 26.8, 29.1, 29.1, 29.3, 31.8, 118.3, 121.6, 124.4, 125.6, 133.1, 138.3 , 152.6, 155.8, 172.6. ESI-MS: m/z = 260.9 [M+H]+ , calc. for C16H20O3 + H+ = 261.2.

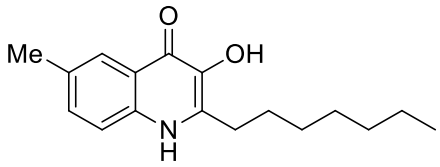
2-(Dec-9-yn-1-yl)-3-hydroxyquinolin-4(1H)-one (22)



Yield: 31%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 7.8 Hz, 1H), 7.53 (bs, 2H), 7.22-7.16 (m, 1H), 2.72-2.71 (m, 2H), 2.30 (t, *J* = 7.6 Hz, 1H), 2.12 (bs, 2H), 1.66 (bs, 2H), 1.41-1.27 (m, 10H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.87, 137.84, 137.36, 135.49, 129.95, 124.48,

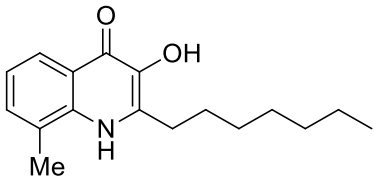
122.19, 121.49, 117.76, 84.53, 71.08, 28.75, 28.69, 28.37, 28.09, 27.91, 27.77, 17.64. MS (ESI) HRMS m/z calcd for $C_{19}H_{24}NO_2^+$ $(M+H)^+$ 298.1802; m/z found $(M+H)^+$ 298.1792.

2-Heptyl-3-hydroxy-6-methylquinolin-4(1H)-one (23)



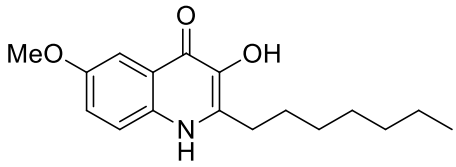
Yield: 59%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (bs, 1H), 7.46-7.43 (m, 1H), 7.37-7.35 (m, 1H), 2.71 (t, *J* = 7.64 Hz, 2H), 2.39 (s, 3H), 1.67-1.62 (m, 2H), 1.32-1.25 (m, 8H), 0.84 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.52, 137.70, 135.60, 135.19, 131.61, 130.60, 123.42, 122.13, 117.72, 31.18, 28.78, 28.45, 28.13, 27.81, 22.04, 20.71, 13.91. MS (ESI) HRMS m/z calcd for $C_{17}H_{24}NO_2^+$ $(M+H)^+$ 274.1802; m/z found $(M+H)^+$ 274.1796.

2-Heptyl-3-hydroxy-8-methylquinolin-4(1H)-one (24)



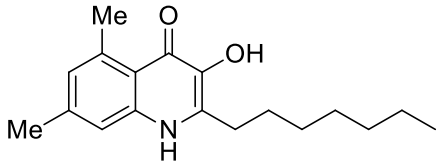
Yield: 56%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99 (d, J = 7.6Hz, 1H), 7.38 (d, *J* = 6.7 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 2.83 (t, *J* = 6.91 Hz, 2H), 2.52 (s, 3H), 1.64 (bs, 2H), 1.32-1.25 (m, 7H), 0.84 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.15, 137.83, 136.19, 136.05, 130.85, 125.78, 122.57, 122.48, 121.32, 31.27, 28.98, 28.56, 28.24, 27.82, 22.06, 17.70, 13.92. MS (ESI) HRMS m/z calcd for $C_{17}H_{24}NO_2^+$ $(M+H)^+$ 274.1802; m/z found $(M+H)^+$ 274.1795.

2-Heptyl-3-hydroxy-6-methoxyquinolin-4(1H)-one (25)[17]



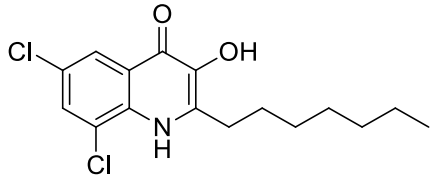
Yield: 66%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45 (bs, 2H), 7.19 (s, 1H), 3.82 (s, 3H), 1.66 (bs, 2H), 1.31-1.24 (m, 9H), 0.84 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.88, 154.38, 137.35, 134.87, 132.35, 122.92, 121.30, 119.60, 102.85, 55.25, 31.18, 28.79, 28.45, 28.16, 27.85, 22.04, 13.91.

2-Heptyl-3-hydroxy-5,7-dimethylquinolin-4(1H)-one (26)



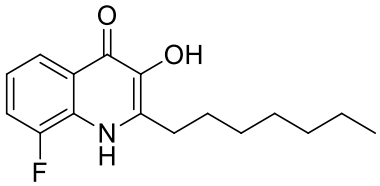
Yield: 52%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.11 (s, 1H), 6.72 (s, 1H), 2.82 (s, 3H), 2.67 (t, *J* = 7.58 Hz, 2H), 2.31 (s, 3H), 1.62-1.64 (bs, 2H), 1.30-1.24 (m, 8H), 0.84 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.91, 139.22, 139.06, 138.44, 138.25, 132.38, 125.48, 118.05, 115.08, 31.19, 28.70, 28.46, 27.78, 27.70, 22.71, 22.05, 21.04, 13.91. MS (ESI) HRMS m/z calcd for $C_{18}H_{26}NO_2^+$ $(M+H)^+$ 288.1958; m/z found $(M+H)^+$ 288.1947.

6,8-Dichloro-2-heptyl-3-hydroxyquinolin-4(1H)-one (27)



Yield: 59%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (bs, 1H), 8.05 (d, *J* = 2.4 Hz 1H), 7.87 (s, 1H), 2.87 (t, J = 7.5 Hz, 2H), 1.62 (bs, 2H), 1.32-1.25 (m, 8H), 0.85 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.48, 138.88, 137.86, 132.55, 129.86, 125.77, 124.67, 124.25, 122.85, 31.22, 28.91, 28.48, 28.08, 27.65, 22.04, 13.91. MS (ESI) HRMS m/z calcd for $C_{16}H_{20}Cl_2NO_2^+$ $(M+H)^+$ 328.0866; m/z found $(M+H)^+$ 328.0863.

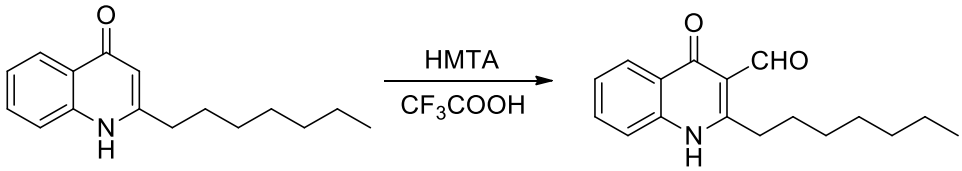
8-Fluoro-2-heptyl-3-hydroxyquinolin-4(1*H*)-one (28)



Yield: 34%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (bs, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 10.3 Hz, 1H), 7.21-7.17 (m, 1H), 2.80 (t, *J* = 6.85 Hz, 2H), 1.63 (s, 2H), 1.31-1.24 (m, 8H), 0.84 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.34, 150.27, 138.58, 136.52, 126.83 (J_{CF} = 13.1 Hz), 124.48, 121.05, 120.33, 114.29 (d, J_{CF} = 16.5 Hz), 31.22, 28.87, 28.47, 28.04, 27.74, 22.06, 13.91. MS (ESI) HRMS m/z calcd for $C_{16}H_{21}FNO_2^+$ $(M+H)^+$ 278.1551; m/z found $(M+H)^+$ 278.1544.

<u>Synthesis of C3-subtituted quinolones</u>

2-Heptyl-4-oxo-1,4-dihydroquinoline-3-carbaldehyde (29)[18]

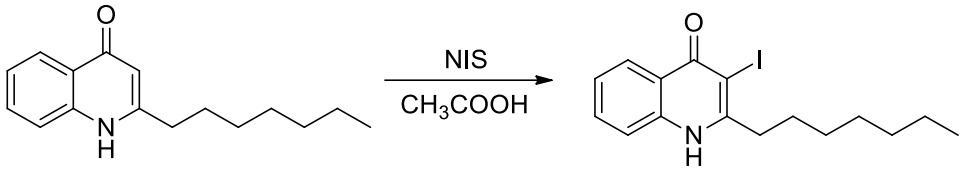


HHQ **(1)** (1.03 g, 4.26 mmol) and hexamethylenetetramine (0.3 g, 2.14 mmol) were stirred under a nitrogen atmosphere for 15 minutes. Trifluoroacetic acid (1.65 mL) was added, and the reaction vessel was again purged with nitrogen. The mixture was heated to reflux overnight, with additional trifluoroacetic acid (2 × 2.5 mL) added at 2-hour and 4-hour intervals. After adding 10 mL of distilled water and 10 mL of methanol, the reaction continued to reflux for 2.5 hours. Then, 6 mL of 2M HCl was introduced, and reflux was

maintained for another 1.5 hours. The mixture was allowed to cool, and the precipitate was filtered and washed with 15 mL of acetone. The crude product was triturated with 5 mL of acetone and filtered to yield compound **29** as a white powder (0.7 g, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (s, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 3.03 (t, *J* = 7.4 Hz, 2H), 1.62-1.58 (m, 2H), 1.37-1.25 (m, 8H), 0.84 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ190.76, 178.05, 160.02, 139.16, 133.05, 126.19, 124.95, 118.68, 113.35, 31.52, 31.12, 28.99, 28.84, 28.33, 22.03, 13.89.

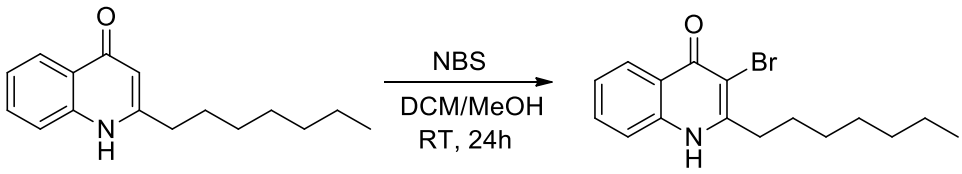
2-Heptyl-3-iodoquinolin-4(1*H*)-one (30)[18]



To a stirred solution of HHQ **(1)** (0.150 g, 0.6164 mmol) in 5 mL of glacial acetic acid, N-iodosuccinimide (0.141 g, 0.6287 mmol) was added gradually. The reaction progress was monitored using TLC. After 2 hours, the precipitate was filtered off and washed with acetic acid and acetonitrile. The product was purified by column chromatography on silica gel using a gradient of 80:20 ethyl acetate/hexane, increasing to 100% ethyl acetate. The final product **30** was obtained as a white-yellow solid (0.115 g, 51% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 2.92 (t, *J* = 7.6 Hz, 2H), 1.70-1.68 (m, 2H), 1.41-1.28 (m, 8H), 0.87 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.16, 154.52, 139.00, 131.94, 125.47, 123.80, 120.60, 117.74, 85.79, 31.10, 28.66, 28.32, 27.94, 22.02, 13.93.

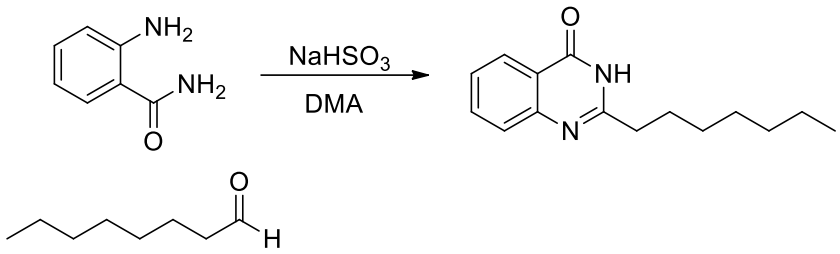
3-Bromo-2-heptylquinolin-4(1*H*)-one (31)[18]



A solution of HHQ **(1)** (0.2 g, 0.8219 mmol) in 2.5 mL of dichloromethane and 10.0 mL of methanol was stirred, and N-bromosuccinimide (0.117 g, 0.6575 mmol) was added gradually. The mixture was maintained at room temperature and stirred for 24 hours. The solvent was then evaporated under reduced pressure, and the crude product was purified by recrystallization from ethanol, yielding **31** as a yellow solid (0.089 g, 42% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.9 Hz, 1H), 7.67 (t, *J* = 7.0 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 2.86 (t, *J* = 7.2 Hz, 2H), 1.75-1.67 (m, 2H), 1.36-1.25 (m, 8H), 0.85 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.27, 152.02, 138.71, 131.90, 125.26, 123.65, 122.73, 117.95, 105.56, 34.56, 31.09, 28.66, 28.31, 27.67, 22.02, 13.91.

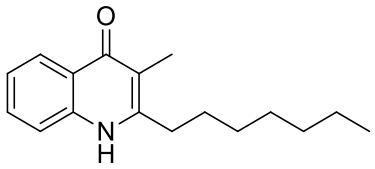
2-Heptylquinazolin-4(3*H*)-one (32)[18]



A mixture of anthranilamide (1.0 g, 7.3447 mmol), n-octanal (0.942 g, 7.3447 mmol), and sodium bisulfite (1.15 g, 11.0172 mmol) in 10 mL of dimethylacetamide was stirred at 150°C for 2 hours. The progress of the reaction was tracked by TLC. After completion, the reaction mixture was poured into 200 mL of water, and the resulting precipitate was collected by filtration. The precipitate was then recrystallized from ethanol, resulting in the product as an off-white crystalline solid (1.2 g, 67% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.9 Hz, 1H), 7.78-7.69 (m, 2H), 7.46 (t, *J* = 7.3 Hz, 1H), 2.81 (t, *J* = 7.4 Hz, 2H), 1.91-1.88 (m, 2H), 1.46-1.28 (m, 8H), 0.86 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.71, 157.33, 149.64, 134.88, 127.30, 126.39, 126.32, 120.58, 36.07, 31.78, 29.35, 29.05, 27.74, 22.73, 14.17.

2-Heptyl-3-methylquinolin-4(1*H*)-one (33)[18]



Following the standard procedure, a solution of N-(2-propionylphenyl)octanamide (220 mg, 0.8 mmol), TMSOTf (1.1 g, 4.8 mmol), and NEt_3 (0.334 mL, 0.243 g, 2.4 mmol) in 1,2-DCE (8.5 mL) was heated to 95°C for 3 days. After completion, the mixture was purified by flash column chromatography on silica gel with 5% MeOH in CH2Cl2, yielding 0.92 g (45%) of compound **33** as a yellow solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.55-7.53 (m, 1H), 7.31-7.27 (m, 1H), 2.79 (t, *J* = 7.8 Hz, 2H), 2.25 (s, 3H), 1.67-1.63 (m, 2H), 1.24-1.14 (m, 8H), 0.83 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.04, 151.88, 139.84, 131.15, 125.50, 123.74, 123.13, 118.52, 115.07, 33.01, 31.81, 29.69, 29.16, 22.69, 14.17, 11.07.

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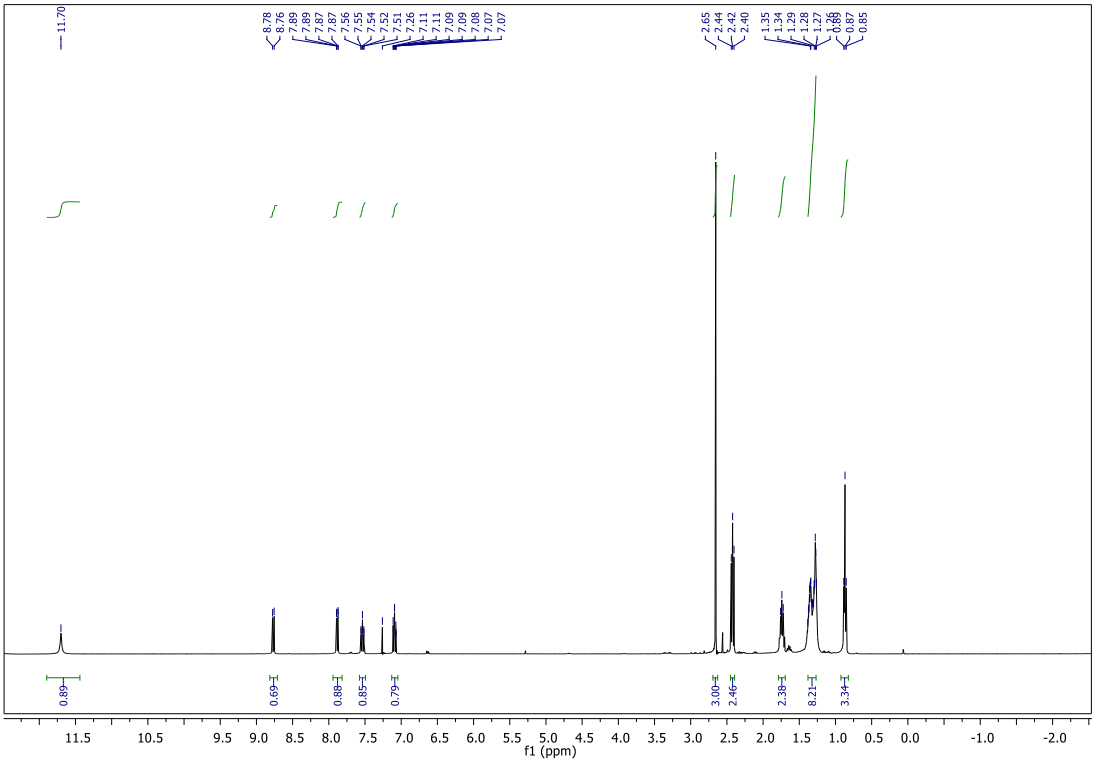
1a)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2.42
2.40
1.35
1.34
1.29
1.28
1.27
1.26
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0.89
0.69
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0.85
0.79
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2.46
2.38
8.21
3.34
11.5
10.5
9.5
9.0
8.5
8.0
7.5
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6.0
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4.0
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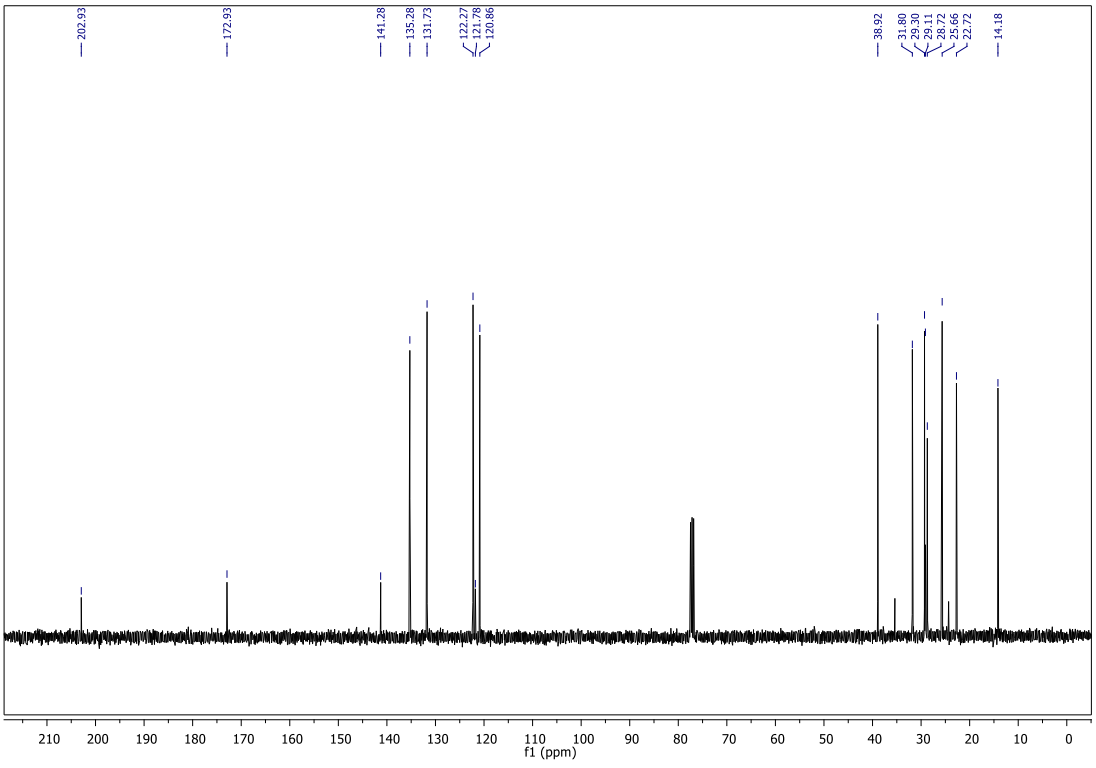
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31.80
29.30
29.11
28.72
25.66
22.72
14.18
210
200
190
180
170
160
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140
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110
100
90
80
70
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50
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30
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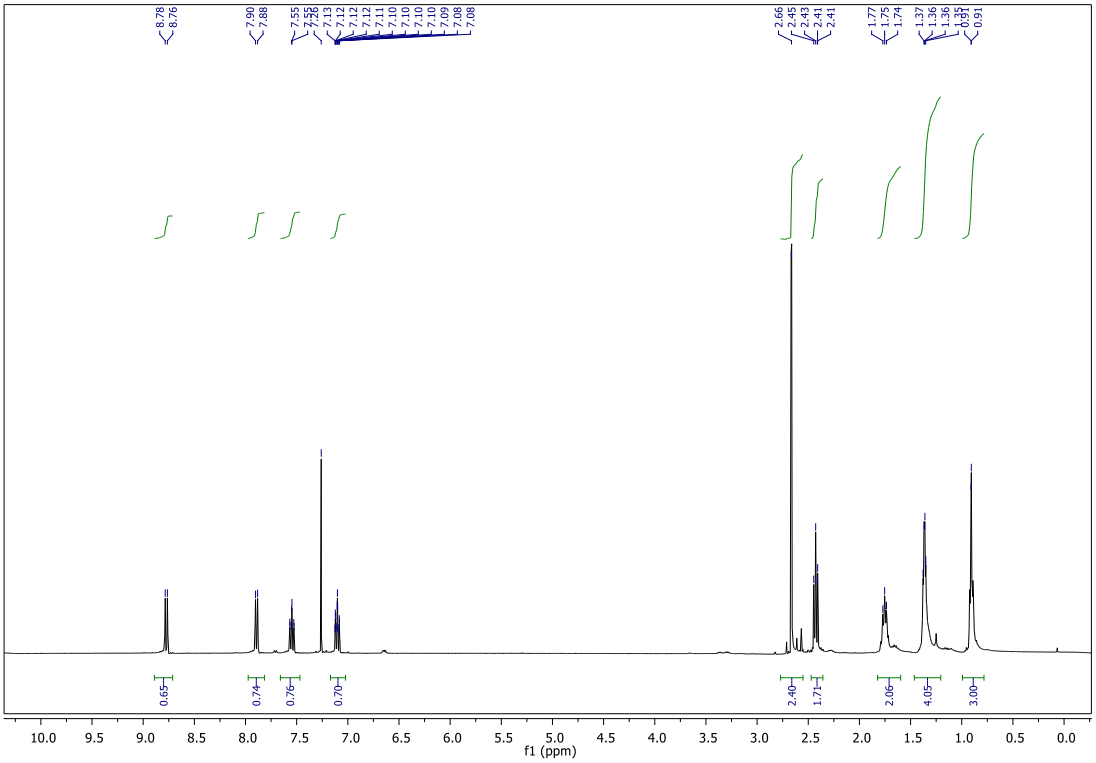
f1 (ppm)

3a)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7.10
7.10
7.10
7.09
7.08
7.08
2.66
2.45
2.43
2.41
2.41
1.77
1.75
1.74
1.37
1.36
1.36
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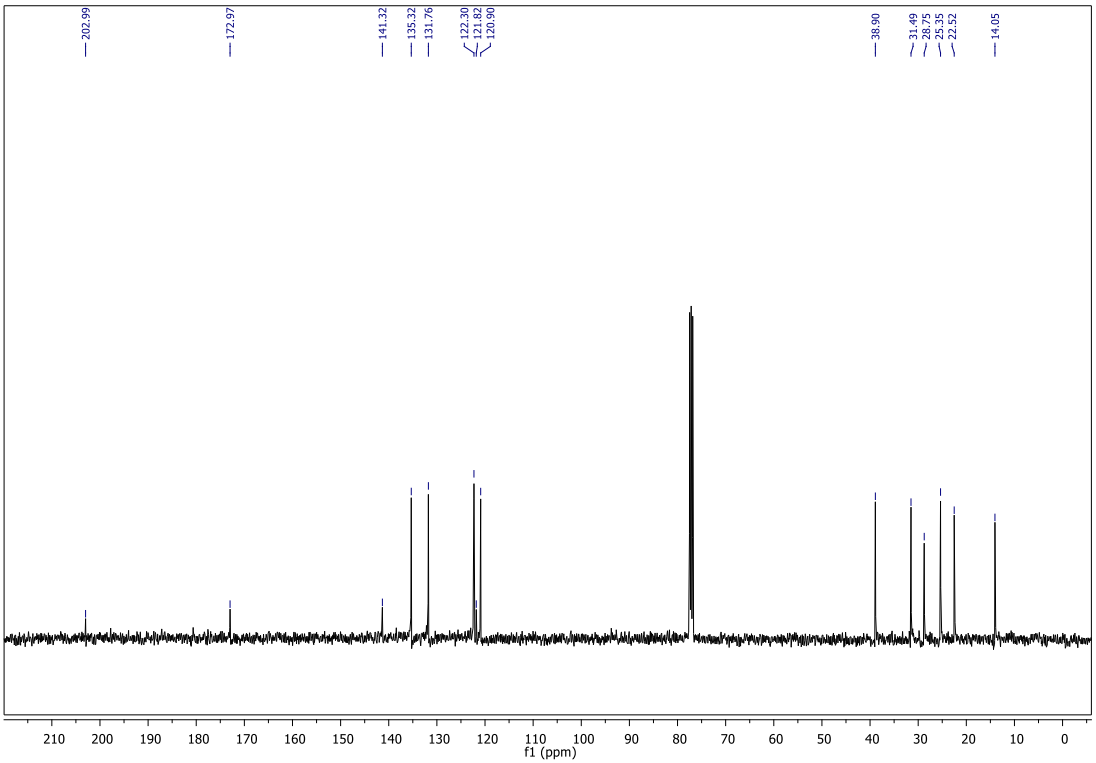
f1 (ppm)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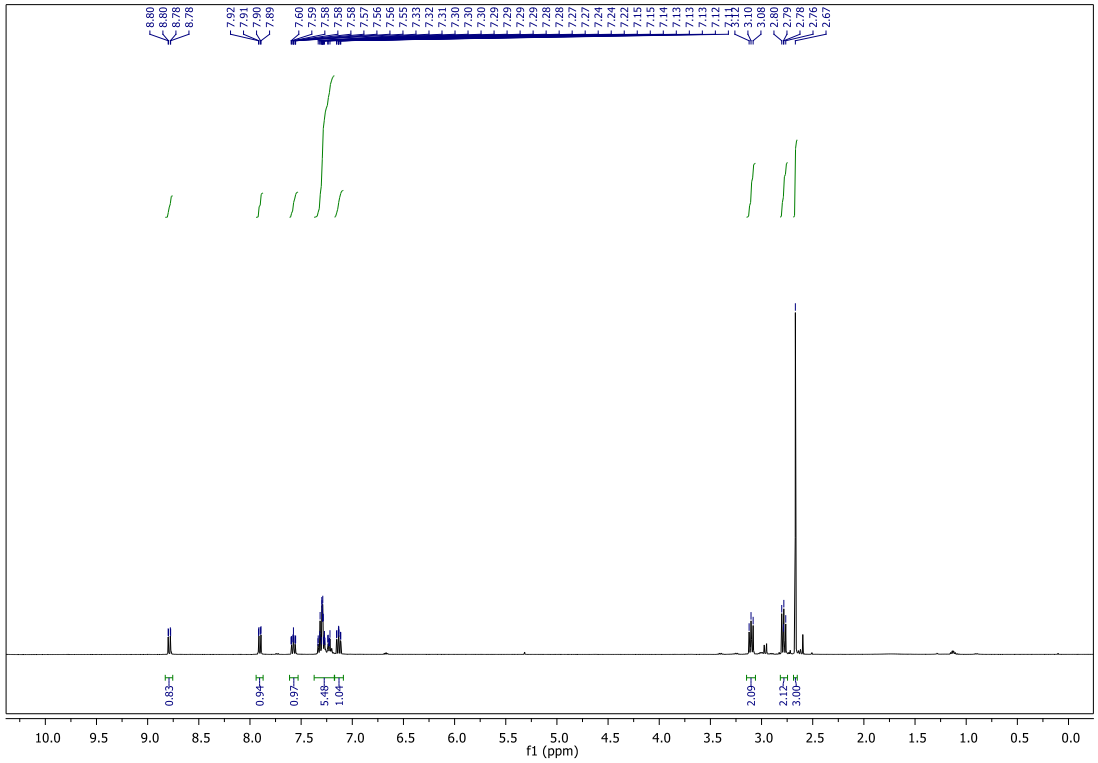
f1 (ppm)

4a)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7.56
7.56
7.55
7.33
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7.29
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7.27
7.27
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7.13
7.13
7.12
3.11
3.10
3.08
2.80
2.79
2.78
2.76
2.67
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0.94
0.97
5.48
1.04
2.09
2.12
3.00
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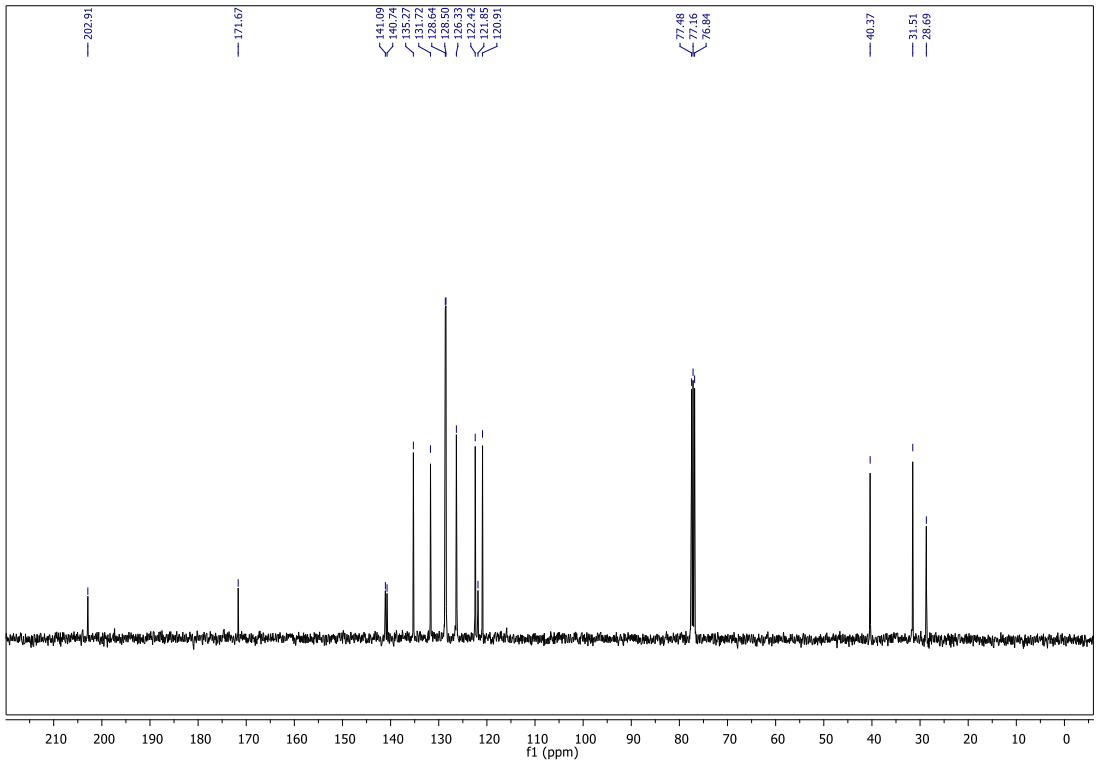
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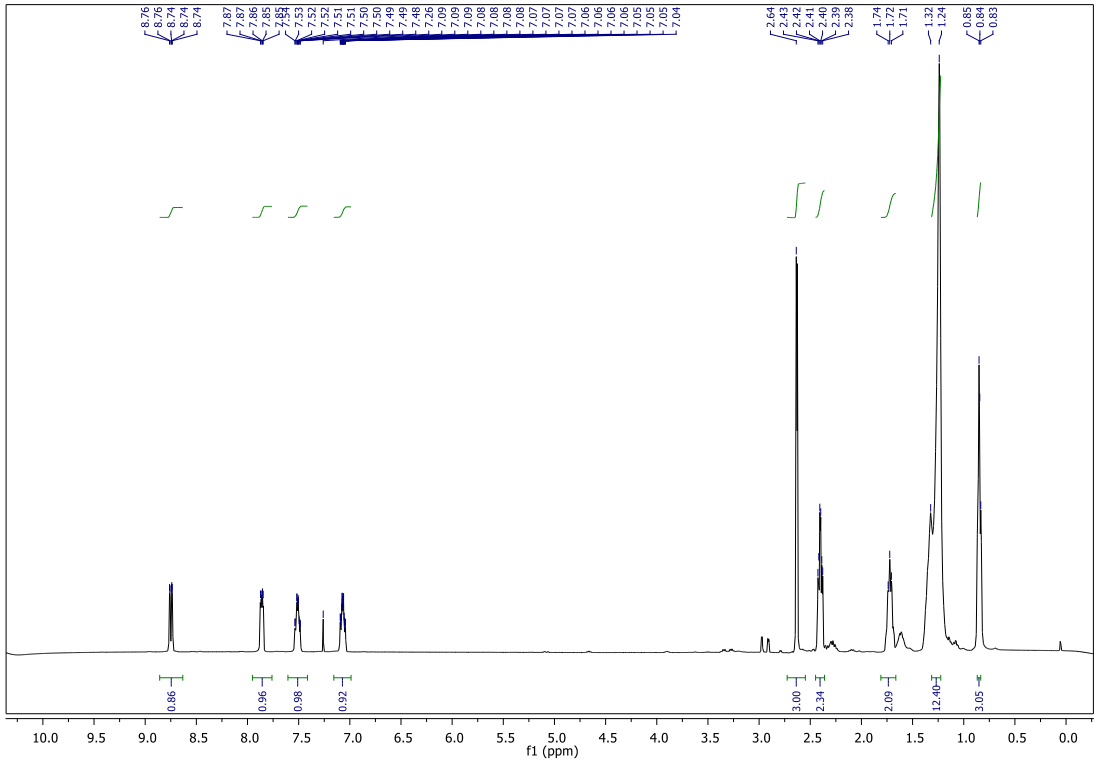
122.42
121.85
120.91
77.48
77.16
76.84
40.37
31.51
28.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

5a)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7.51
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7.50
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2.64
2.43
2.42
2.41
2.40
2.39
2.38
1.74
1.72
1.71
1.32
1.24
0.85
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0.83
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0.92
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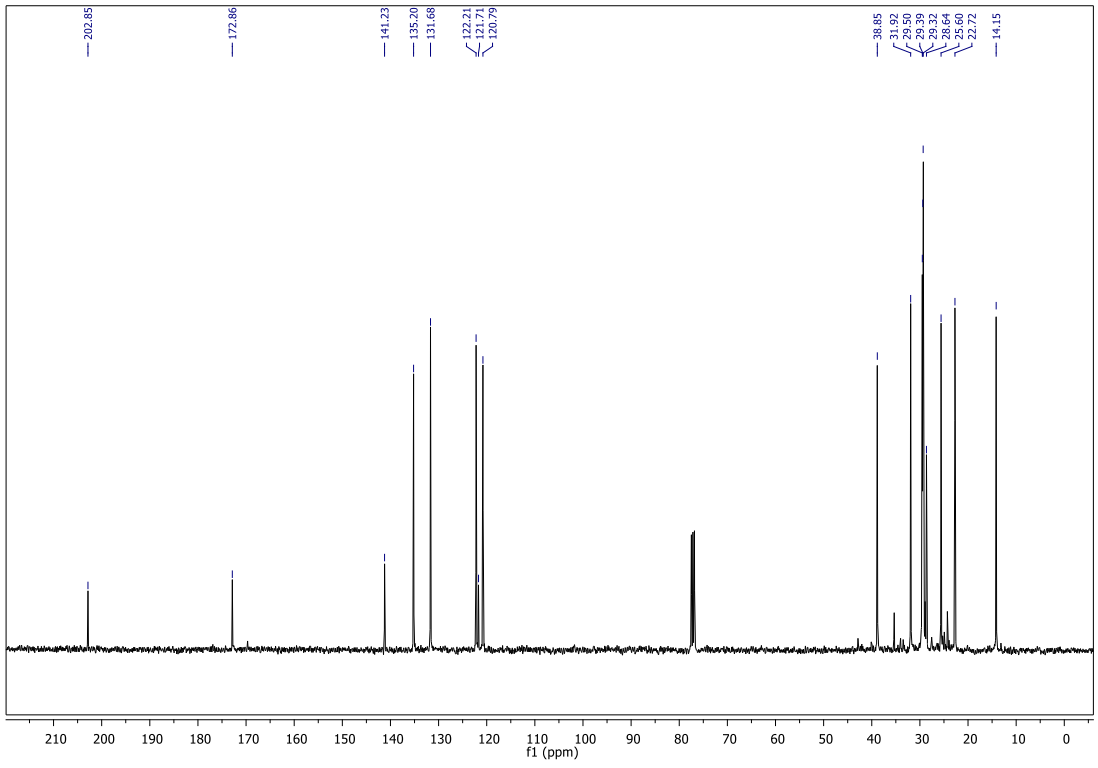
2.34
2.09
12.40
3.05
f1 (ppm)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29.32
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22.72
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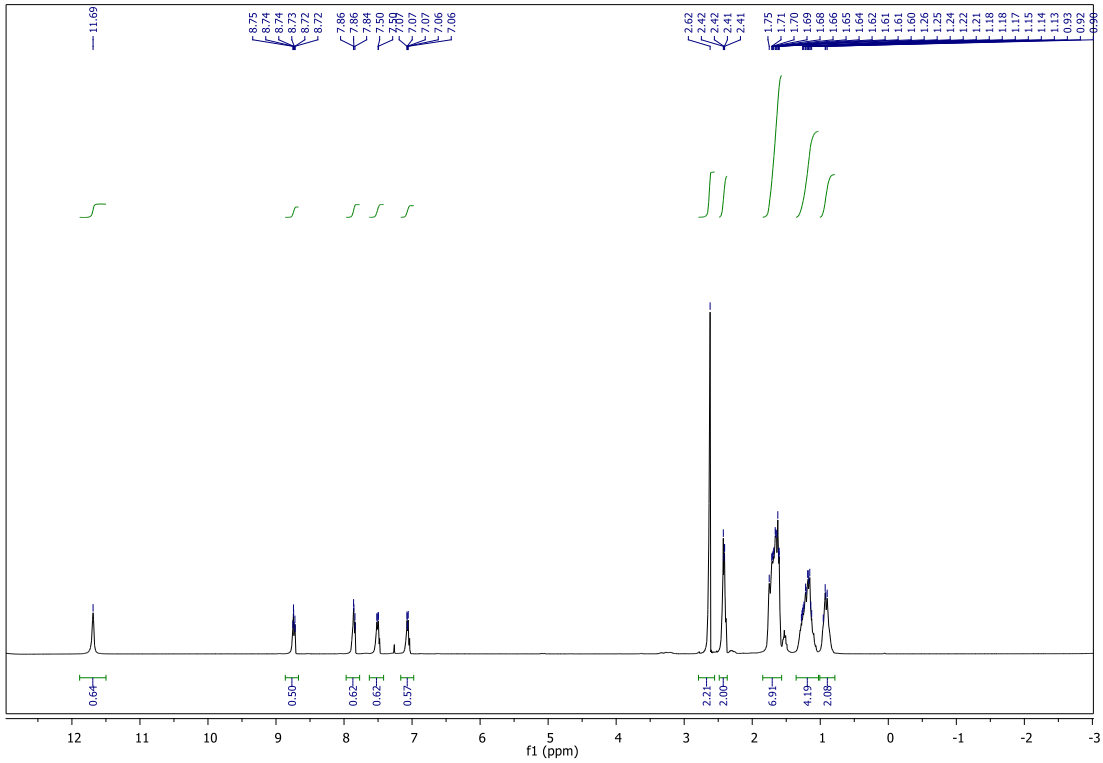
f1 (ppm)

6a)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7.06
7.06
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1.25
1.24
1.22
1.21
1.18
1.18
1.17
1.15
1.14
1.13
0.93
0.92
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0.62
0.62
0.57
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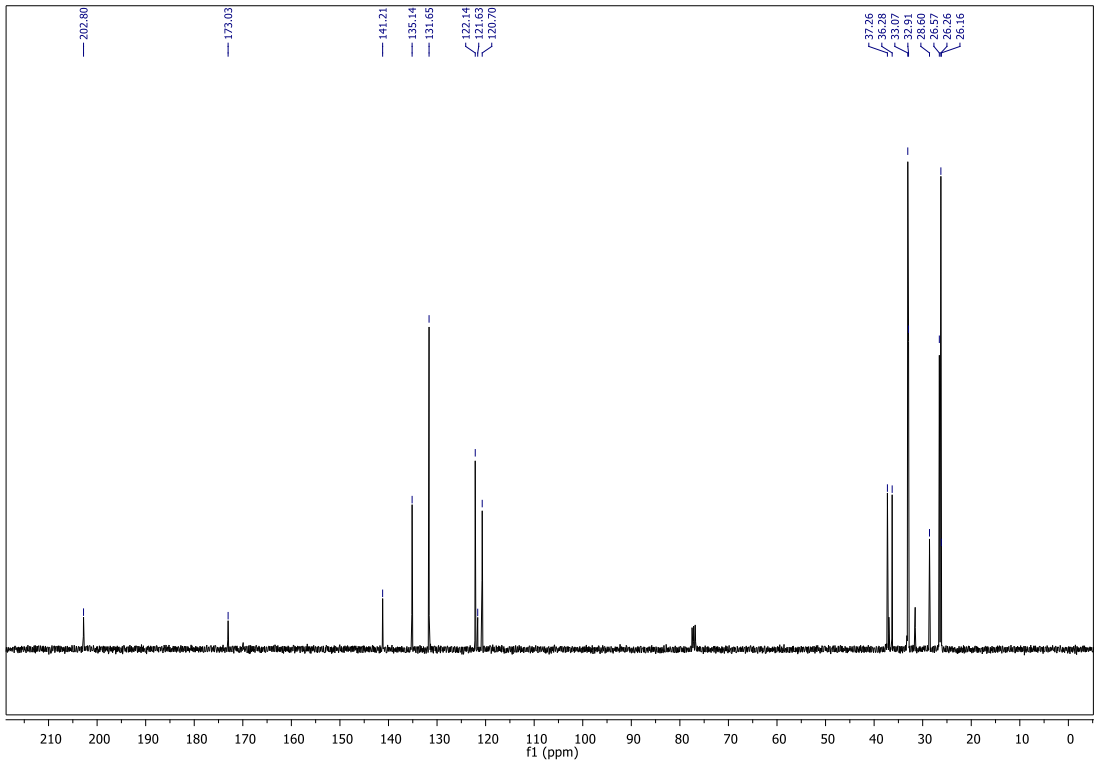
2.08
f1 (ppm)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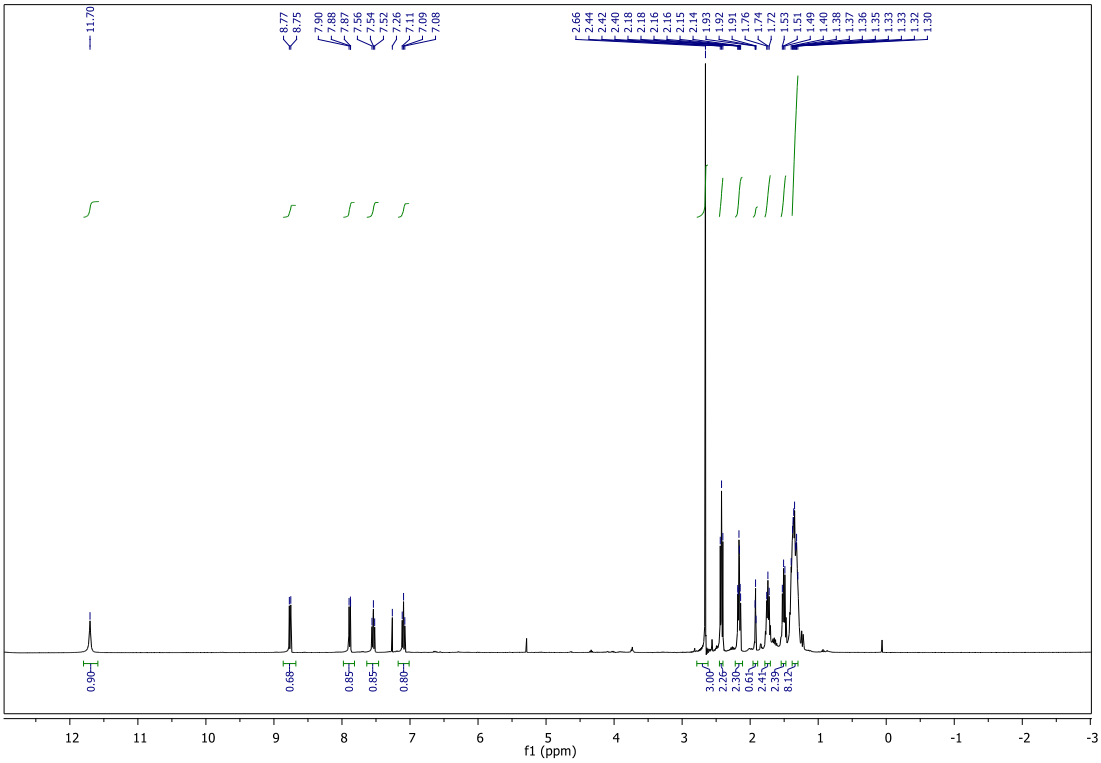
26.16
f1 (ppm)

14a)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2.16
2.15
2.14
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1.33
1.32
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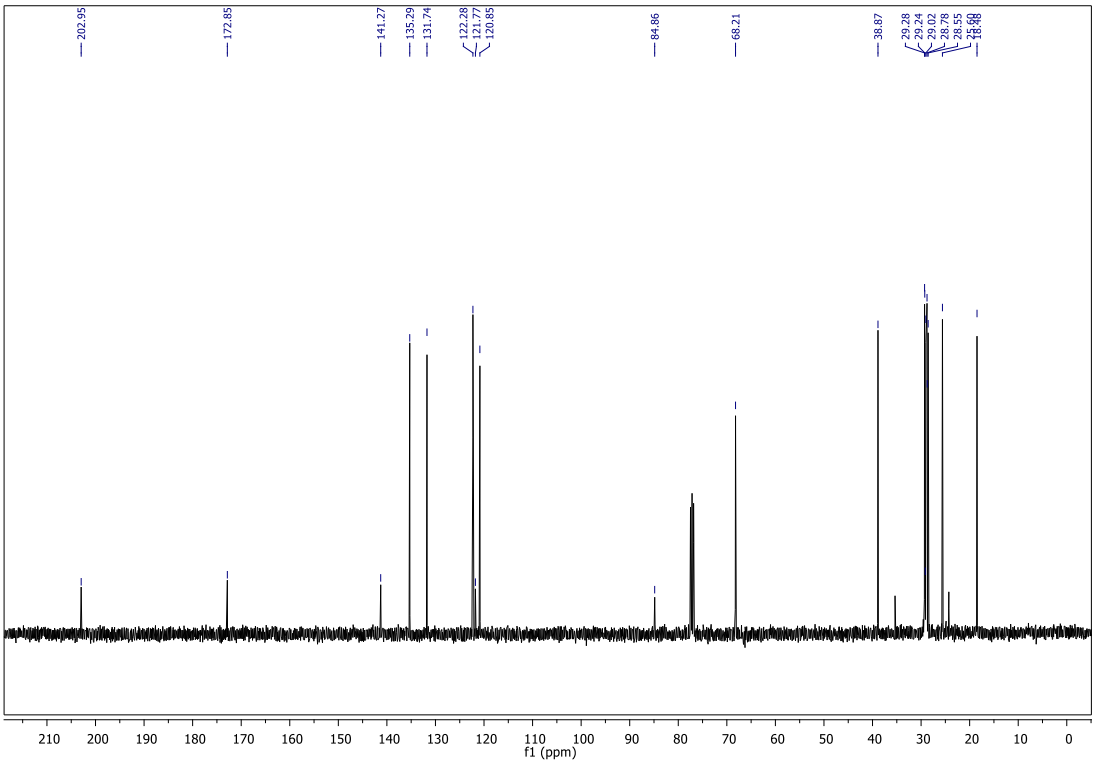
f1 (ppm)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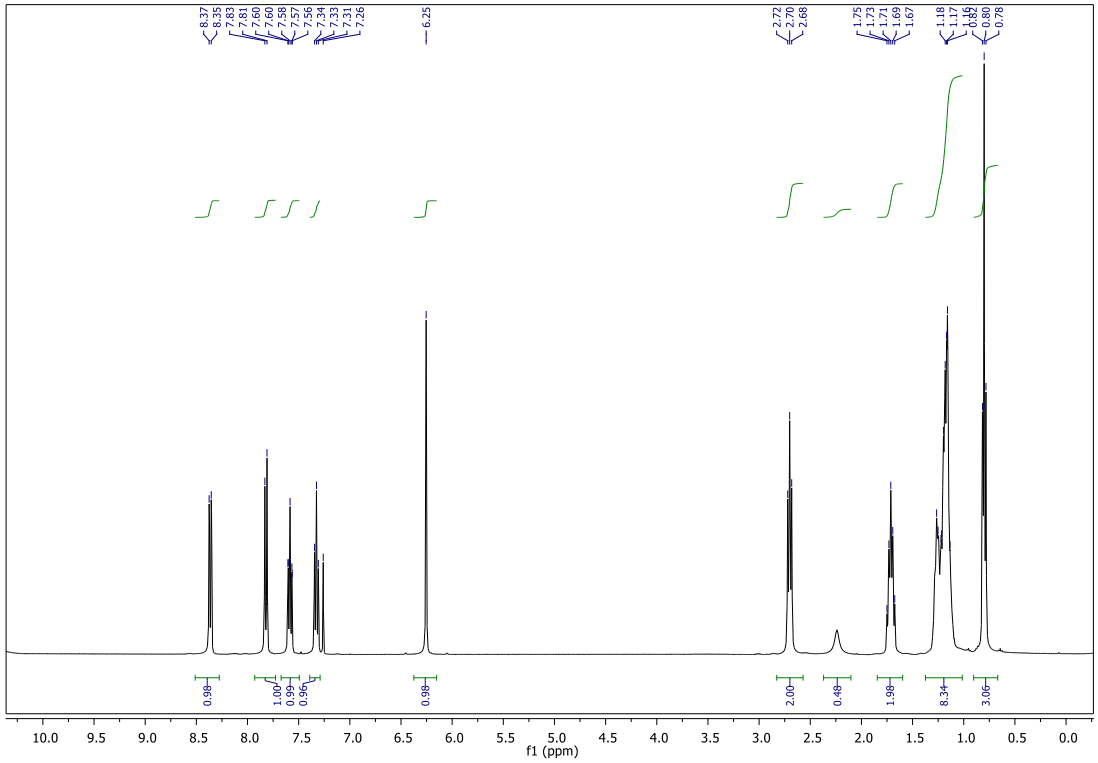
f1 (ppm)

1)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2.68
1.75
1.73
1.71
1.69
1.67
1.18
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1.16
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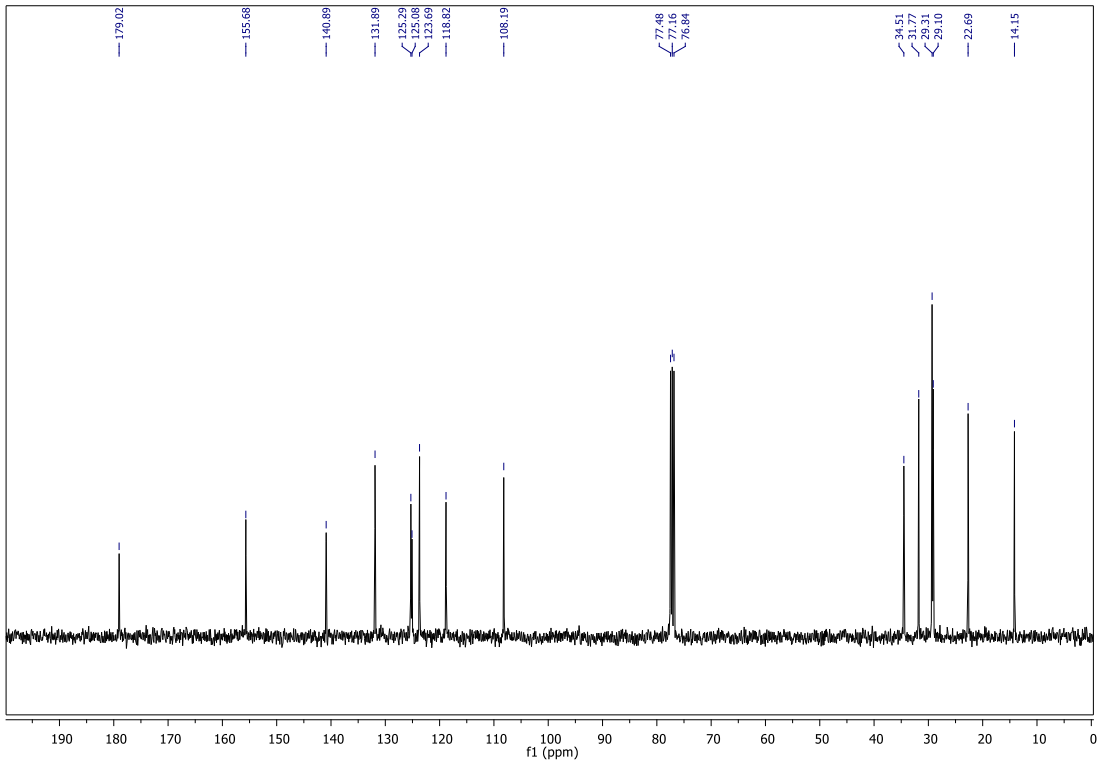
0.80
0.78
0.98
1.00
0.99
0.96
0.98
2.00
0.48
1.98
8.34
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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108.19
77.48
77.16
76.84
34.51
31.77
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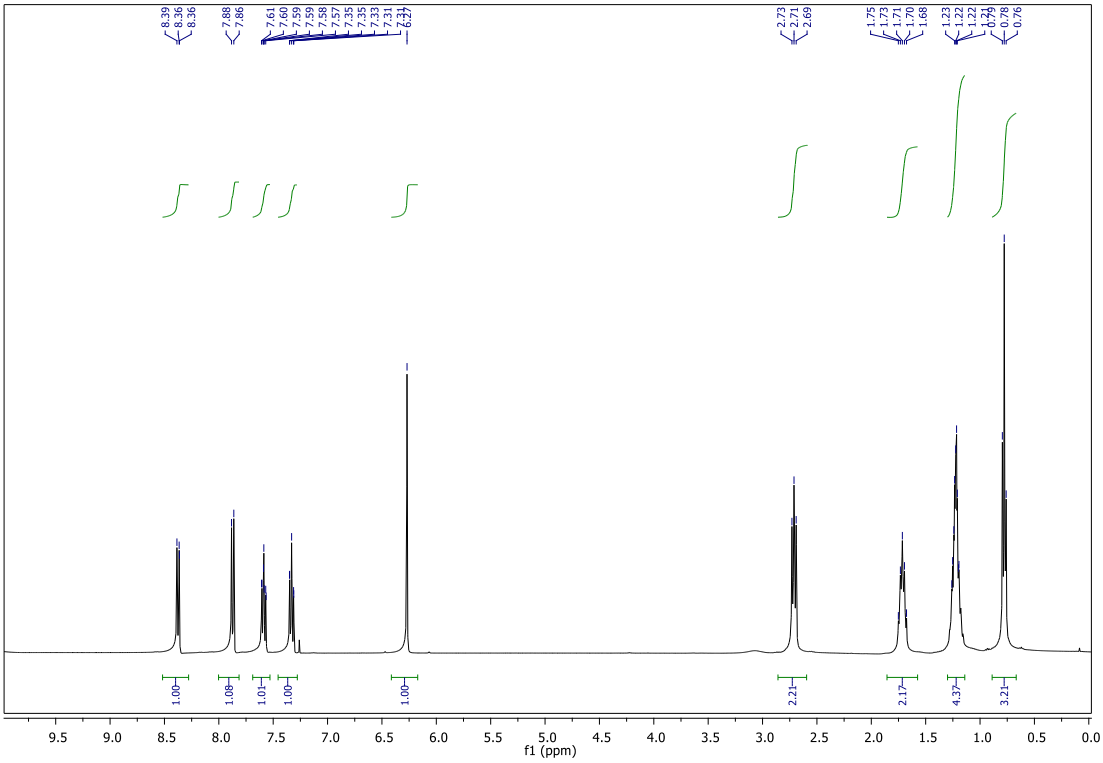
29.10
22.69
14.15
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

3)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7.57
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7.33
7.31
2.73
2.71
2.69
1.75
1.73
1.71
1.70
1.68
1.23
1.22
1.22
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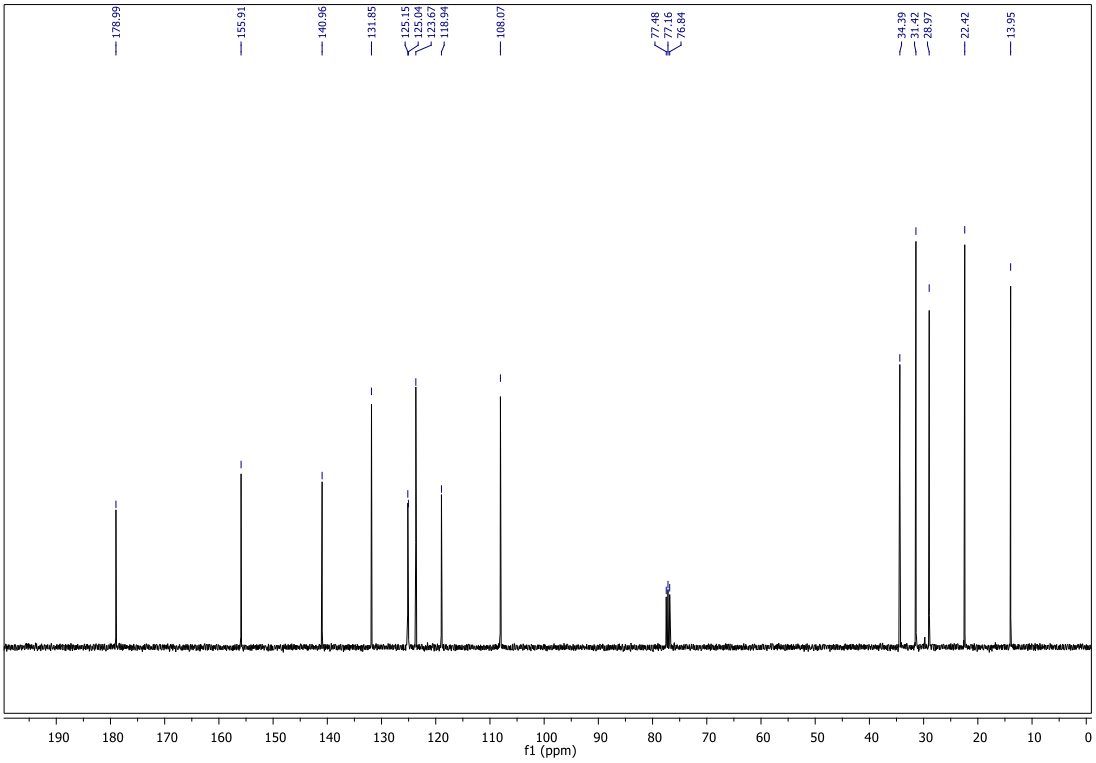
1.08
1.01
1.00
1.00
2.21
2.17
4.37
3.21
f1 (ppm)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22.42
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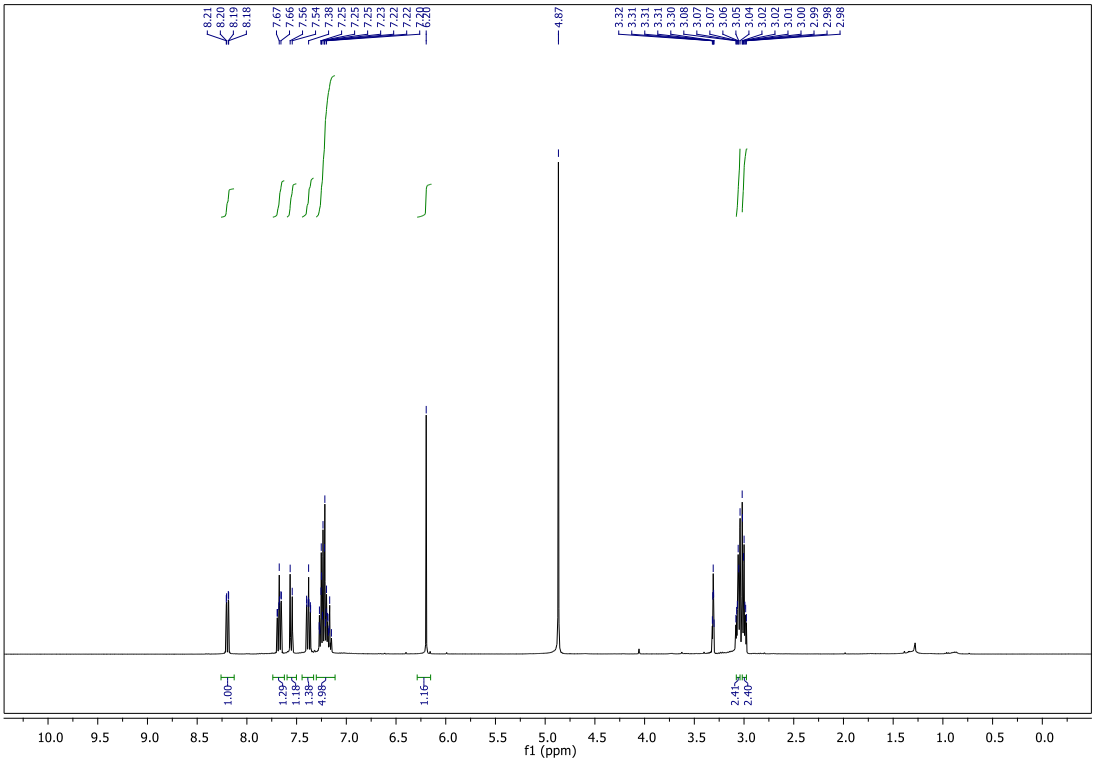
f1 (ppm)

4)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7.54
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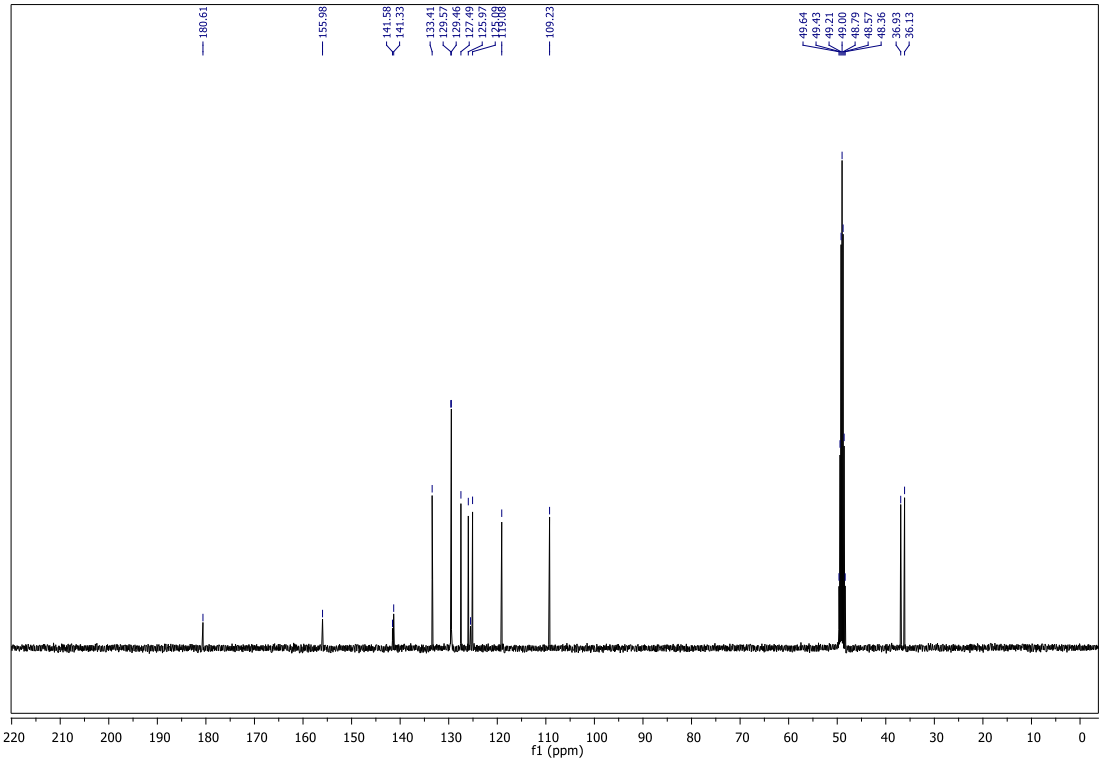
7.25
7.25
7.25
7.23
7.22
7.22
7.20
6.20
4.87
3.32
3.31
3.31
3.31
3.30
3.08
3.07
3.07
3.06
3.05
3.04
3.02
3.01
3.00
2.99
2.98
2.98
1.00
1.29
1.18
1.38
4.98
1.16
2.41
2.40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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127.49
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125.08
119.08
109.23
49.64
49.43
49.21
49.00
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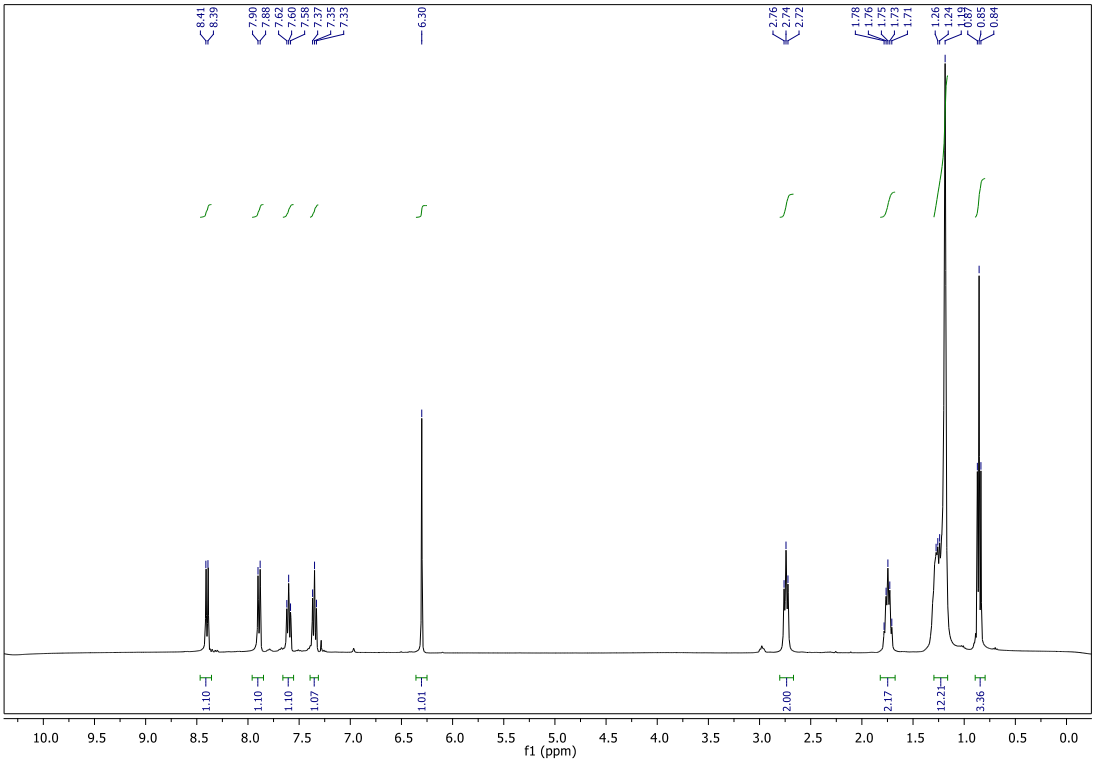
36.93
36.13
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

5)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2.74
2.72
1.78
1.76
1.75
1.73
1.71
1.26
1.24
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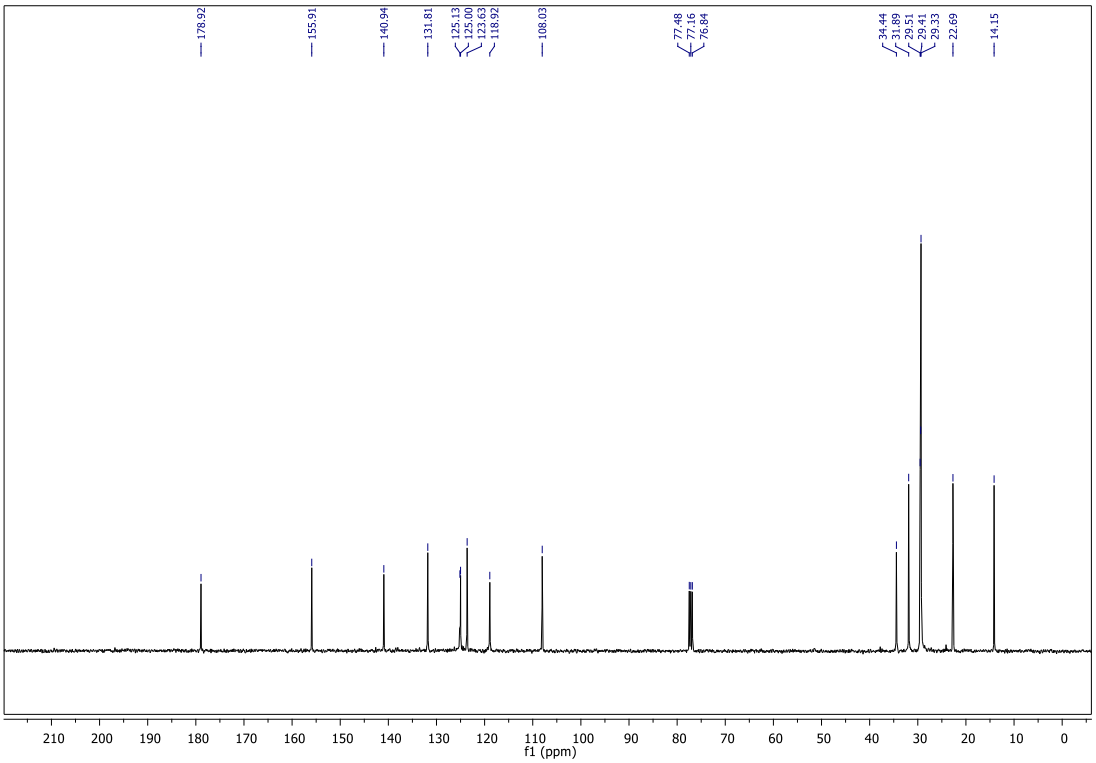
1.10
1.10
1.07
1.01
2.00
2.17
12.21
3.36
f1 (ppm)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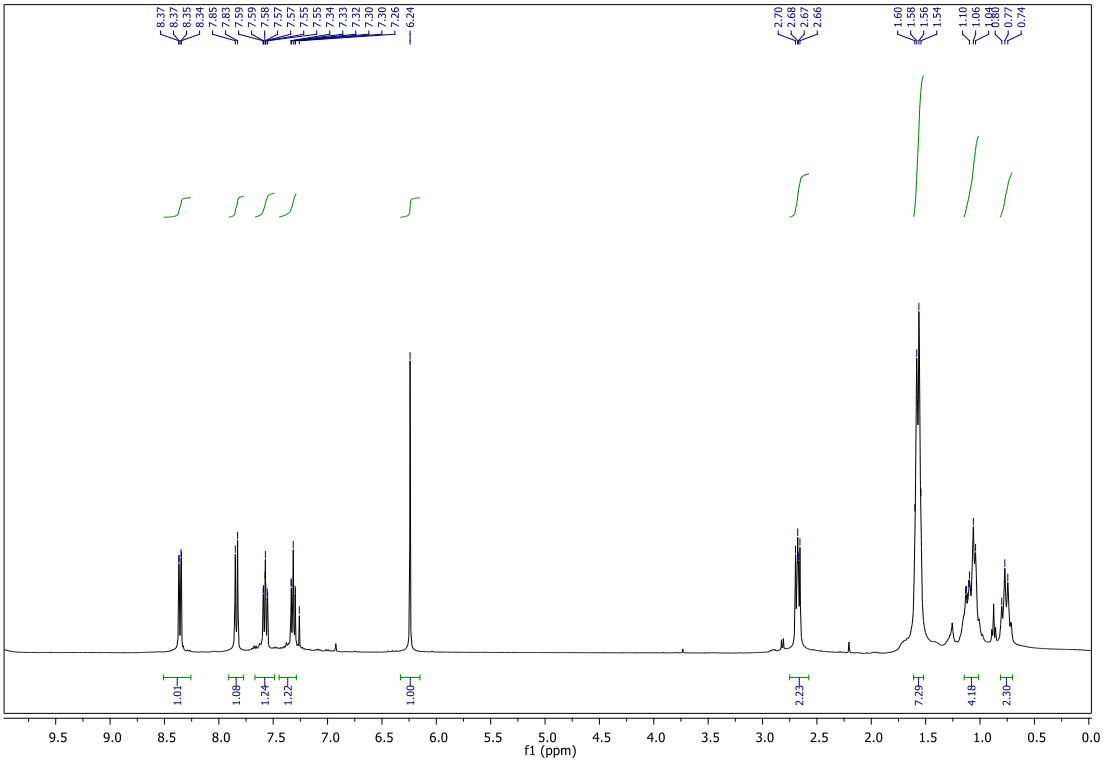
29.41
29.33
22.69
14.15
f1 (ppm)

6)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7.57
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7.55
7.34
7.33
7.32
7.30
7.26
6.24
2.70
2.68
2.67
2.66
1.60
1.58
1.56
1.54
1.10
1.06
0.88
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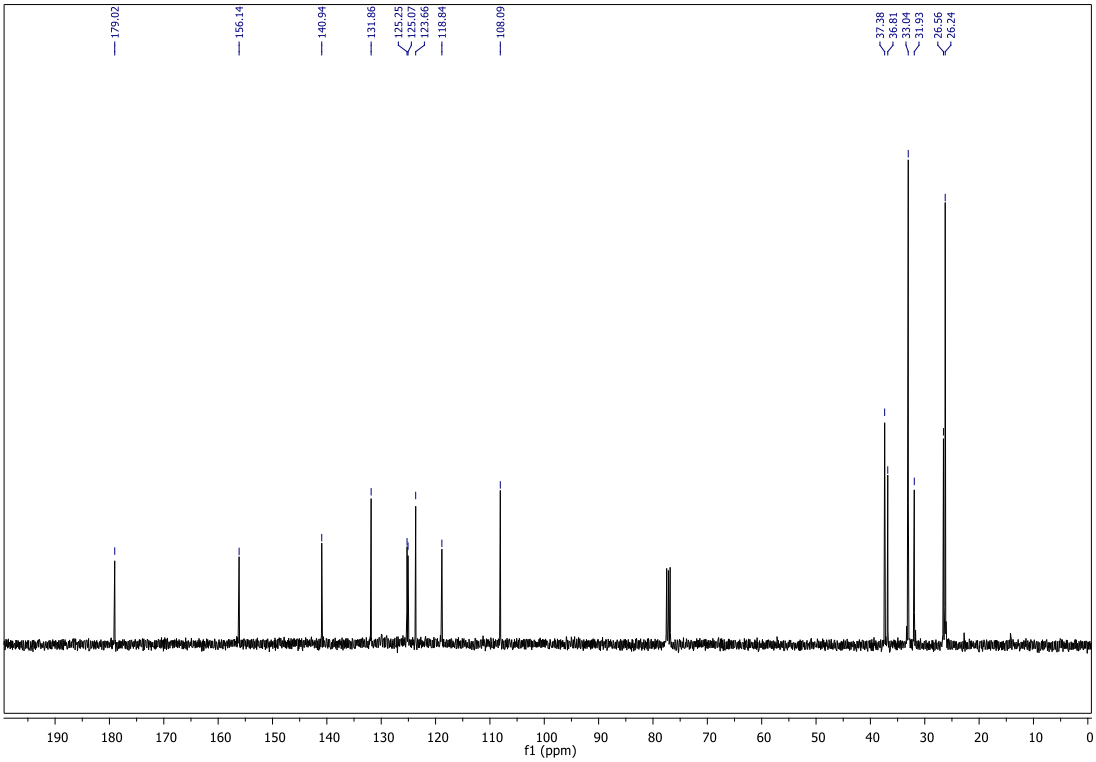
1.08
1.24
1.22
1.00
2.23
7.29
4.18
2.30
f1 (ppm)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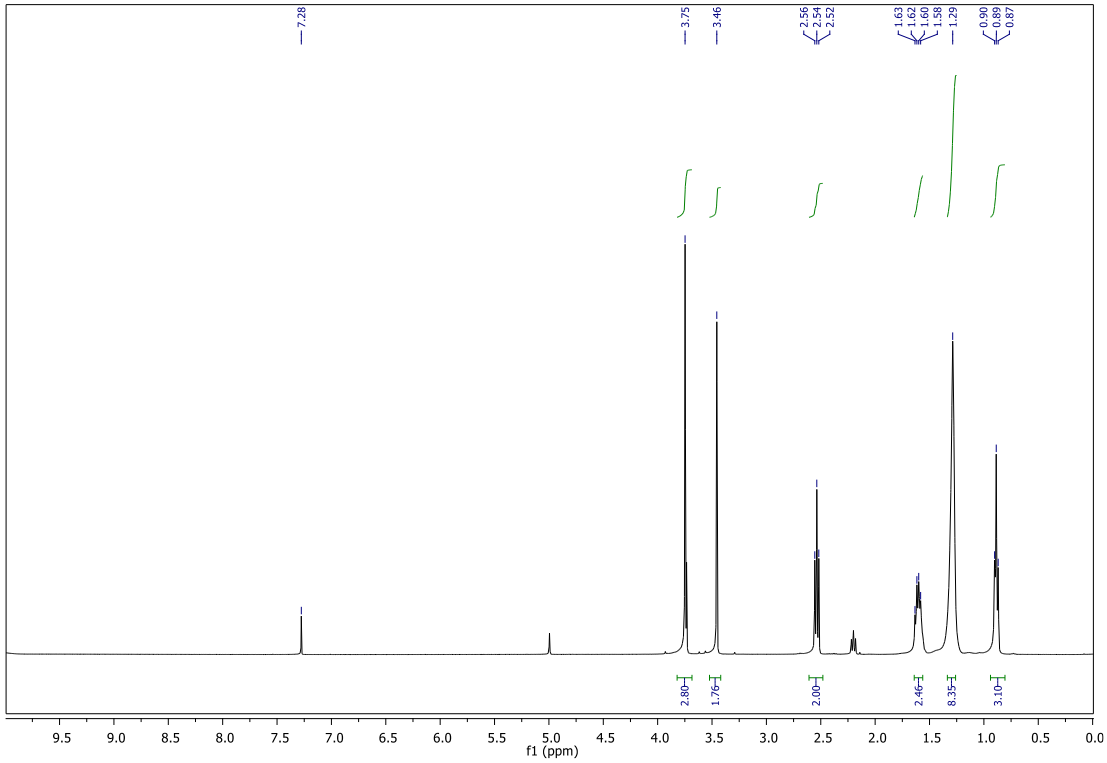
26.56
26.24
f1 (ppm)

29)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1.63
1.62
1.60
1.58
1.29
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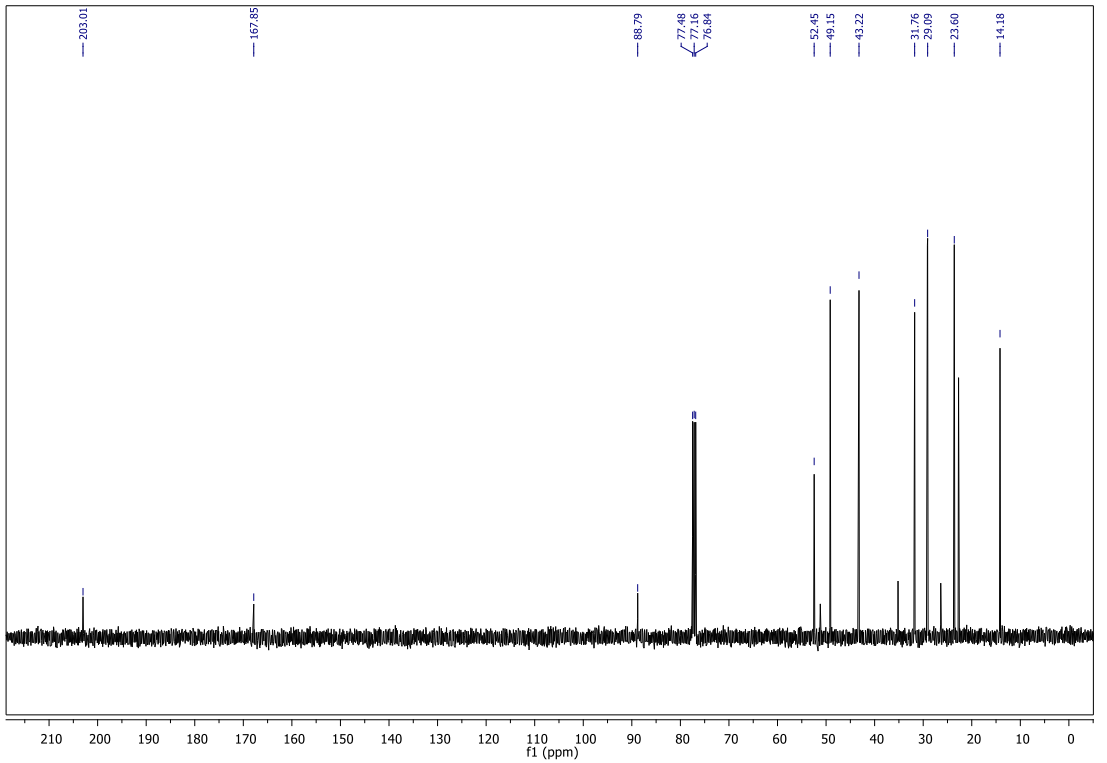
0.89
0.87
2.80
1.76
2.00
2.46
8.35
3.10
f1 (ppm)


203.01
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88.79
77.48
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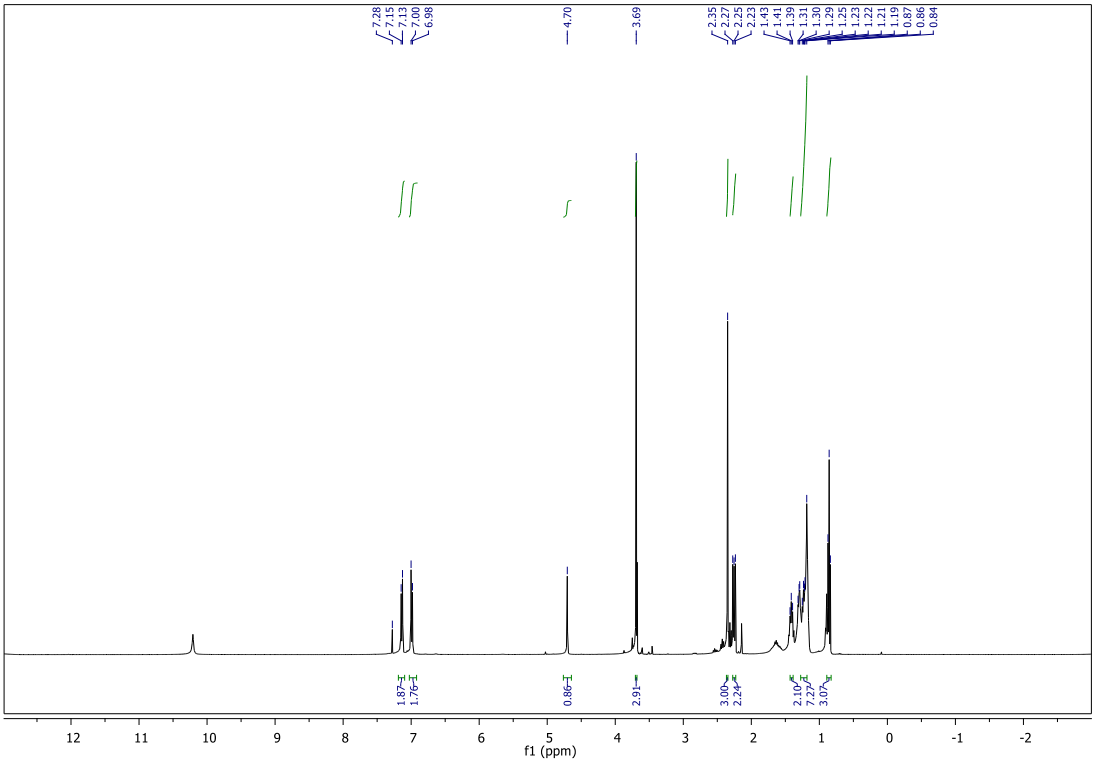
52.45
49.15
43.22
31.76
29.09
23.60
14.18
f1 (ppm)

7a)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2.35
2.27
2.25
2.23
1.43
1.41
1.39
1.31
1.30
1.29
1.25
1.23
1.22
1.21
1.19
0.87
0.86
0.84
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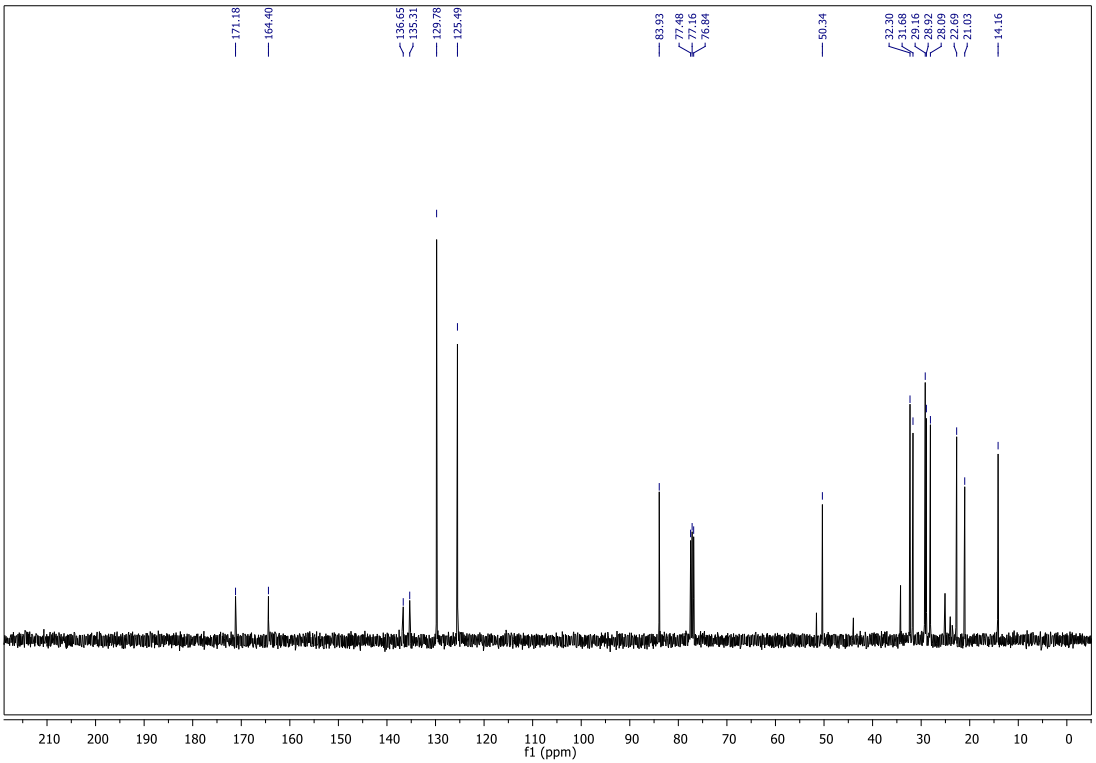
1.76
0.86
2.91
3.00
2.24
2.10
7.22
3.07
f1 (ppm)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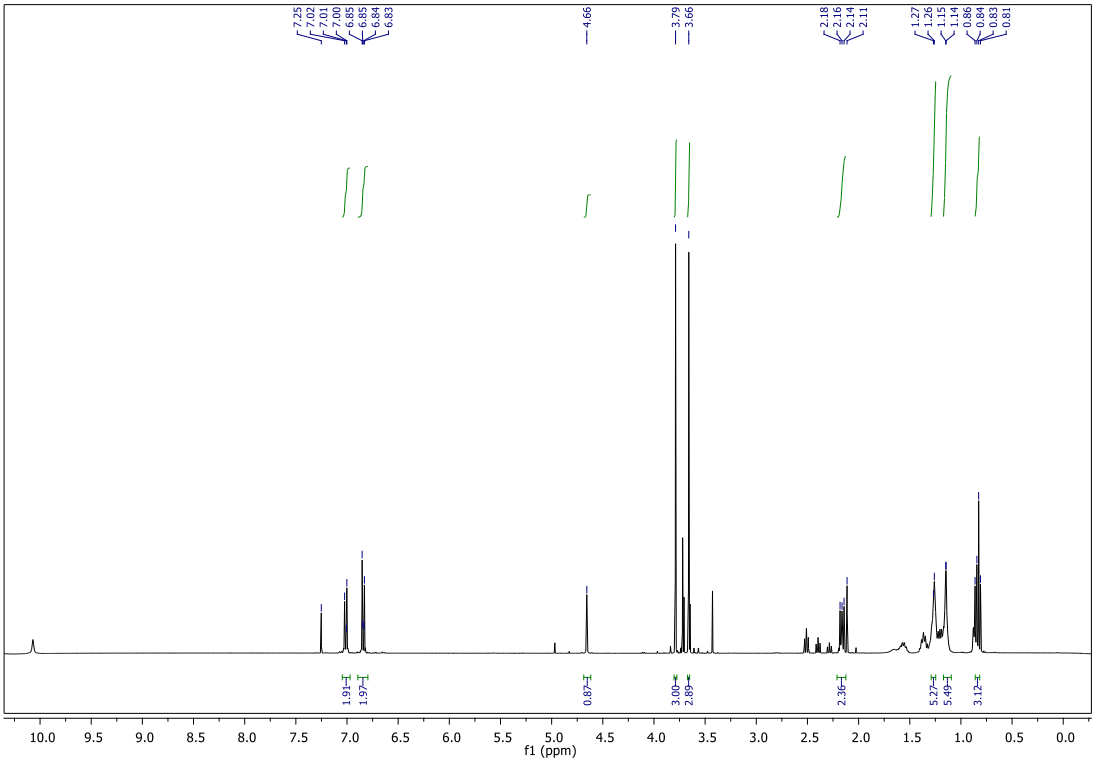
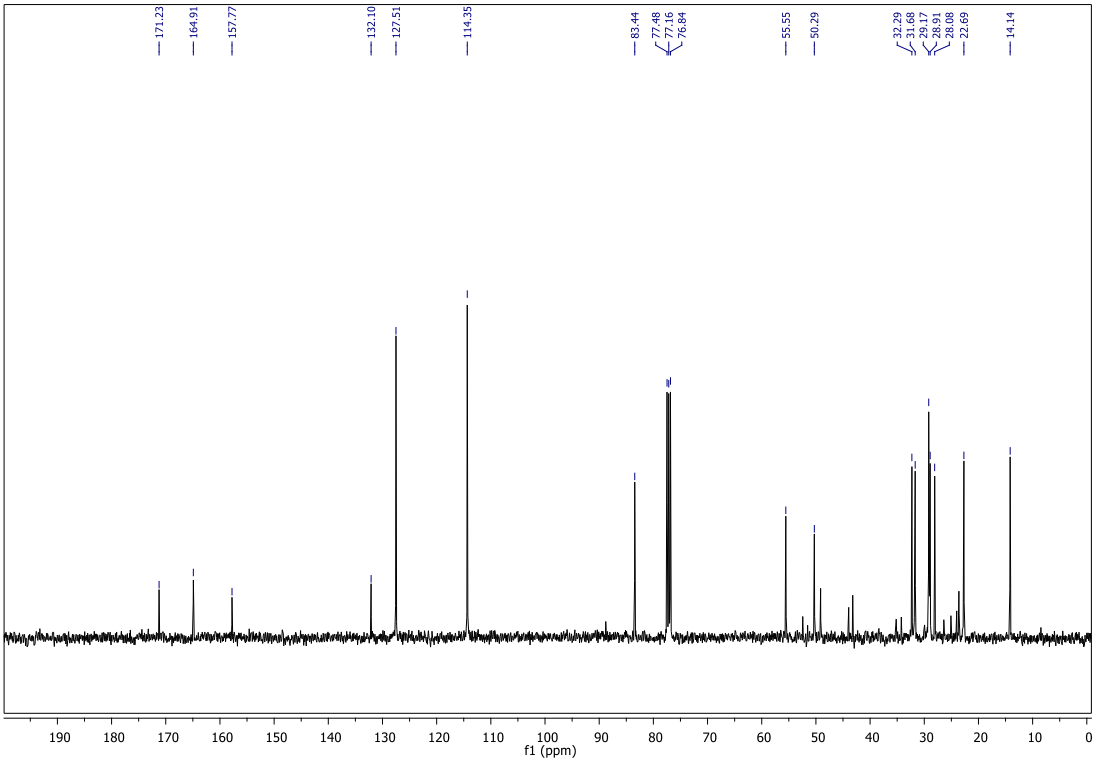
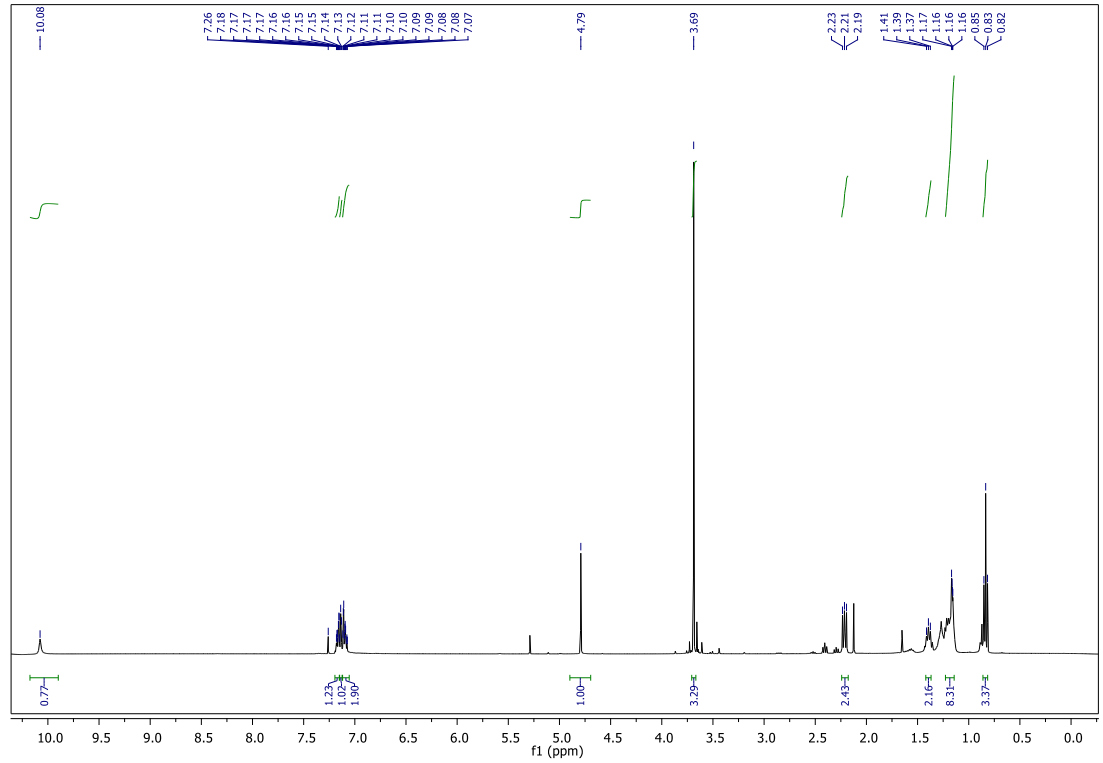
135.31
129.78
125.49
83.93
77.48
77.16
76.84
50.34
32.30
31.68
29.15
28.92
28.09
22.69
21.03
14.16
f1 (ppm)

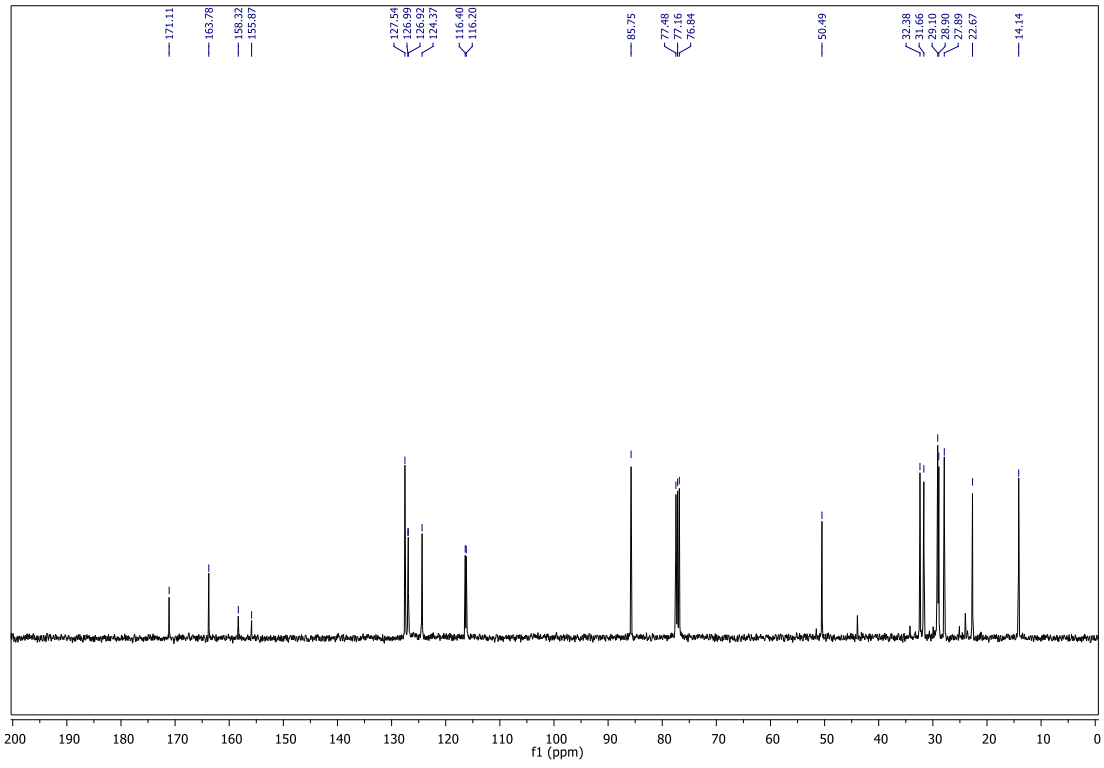
8a)


7.25
7.02
7.01
7.00
6.85
6.84
6.83
4.66
3.79
3.66
2.18
2.16
2.14
2.11
1.27
1.26
1.15
1.14
0.86
0.84
0.83
0.81
1.91
1.97
0.87
3.00
2.89
2.36
5.27
5.49
3.12
f1 (ppm)


171.23
164.91
157.77
132.10
127.51
114.35
83.44
77.48
77.16
76.84
55.55
50.29
32.29
31.68
29.17
28.91
28.08
22.69
14.14
f1 (ppm)

9a)


10.08
7.26
7.18
7.17
7.17
7.17
7.16
7.16
7.15
7.15
7.14
7.13
7.12
7.11
7.11
7.10
7.10
7.09
7.09
7.08
7.08
7.07
4.79
3.69
2.23
2.21
2.19
1.41
1.39
1.37
1.17
1.16
1.16
0.85
0.83
0.82
0.77
1.23
1.02
1.90
1.00
3.29
2.43
2.16
8.31
3.37
f1 (ppm)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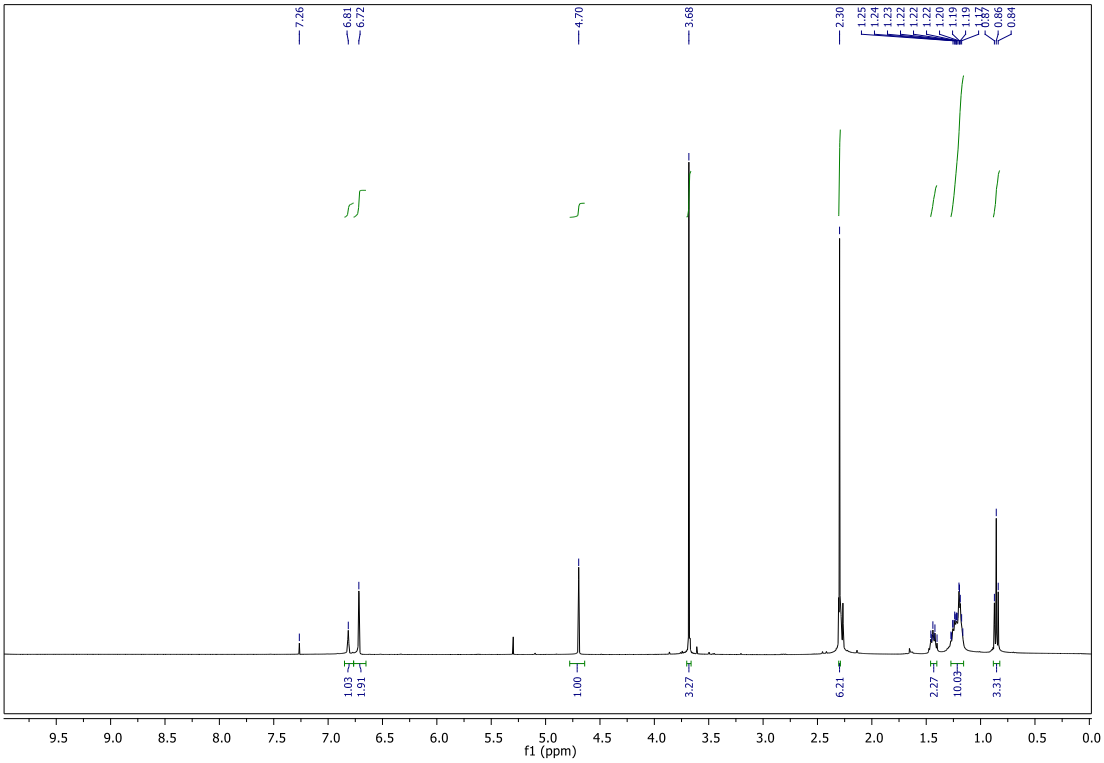
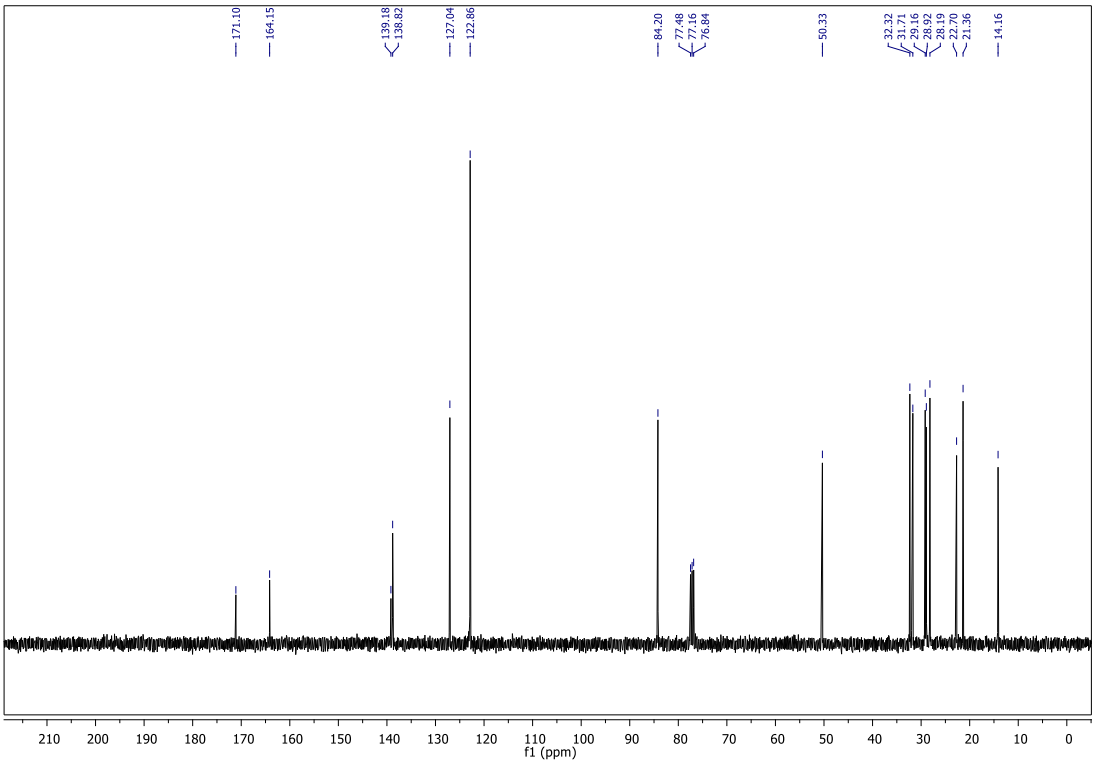
163.78
158.32
155.87
127.54
126.99
126.92
124.37
116.40
116.20
85.75
77.48
77.16
76.84
50.49
32.38
31.66
29.10
28.90
27.89
22.67
14.14
f1 (ppm)

10a)


7.26
6.81
6.72
4.70
3.68
2.30
1.25
1.24
1.23
1.22
1.22
1.20
1.19
1.19
0.87
0.86
0.84
1.03
1.91
1.00
3.27
6.21
2.27
10.03
3.31
f1 (ppm)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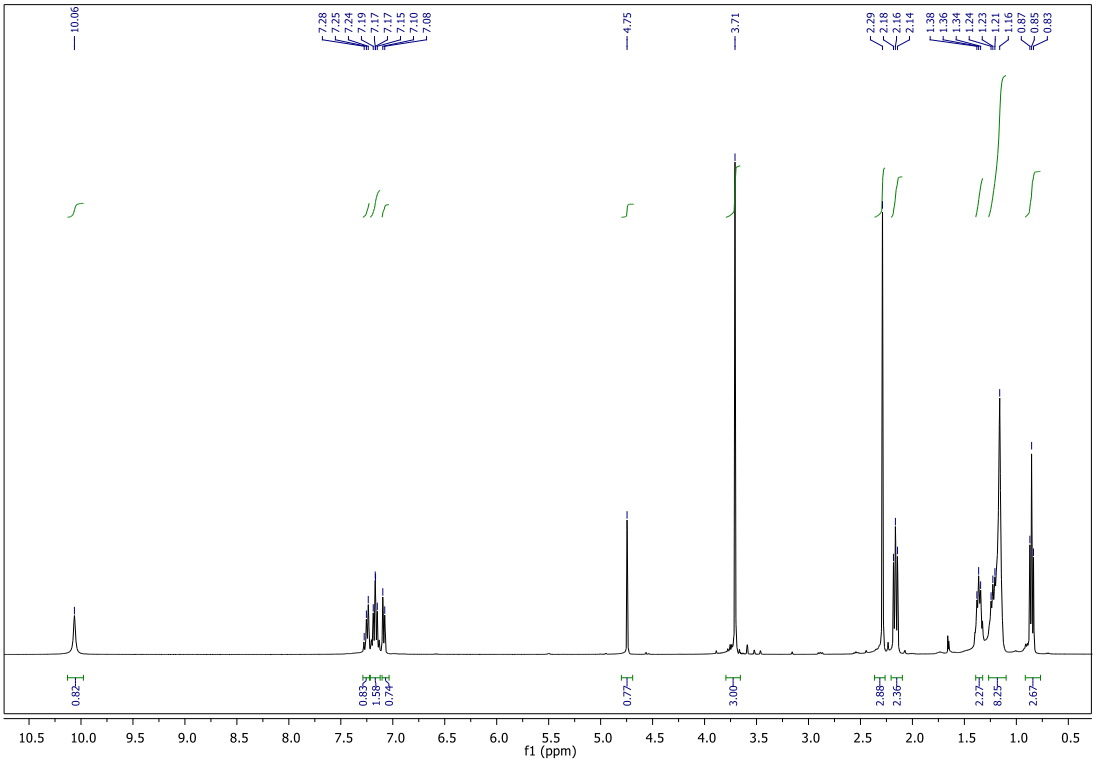
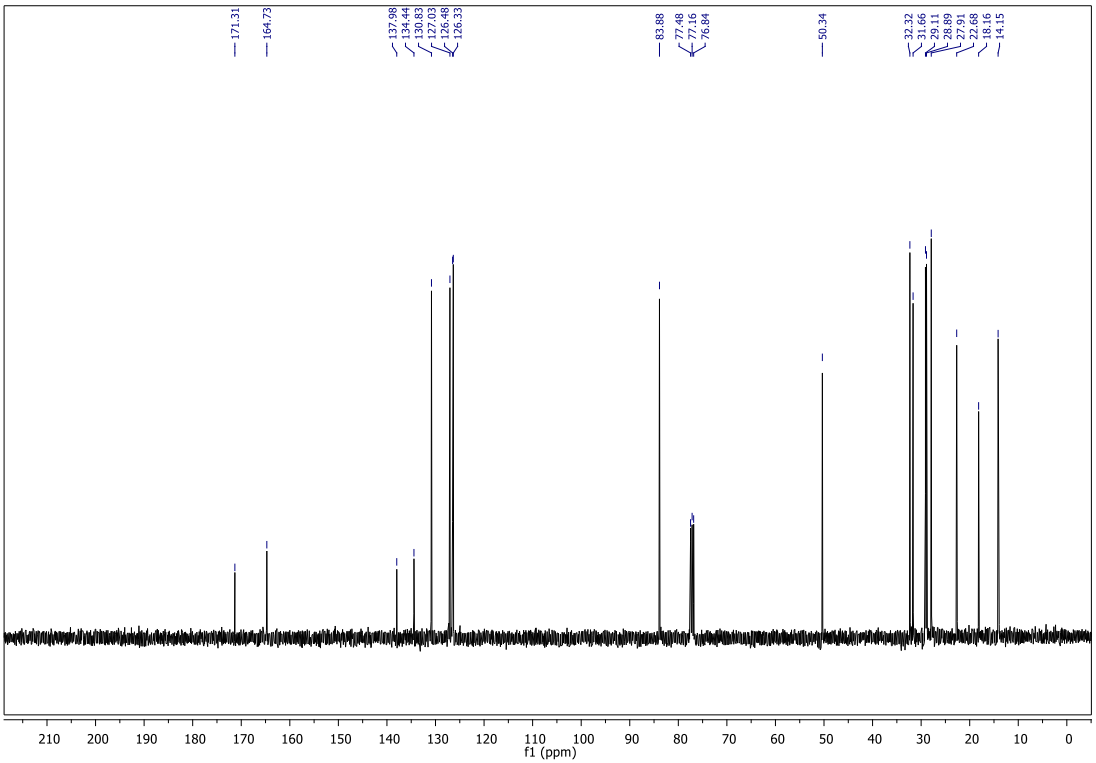
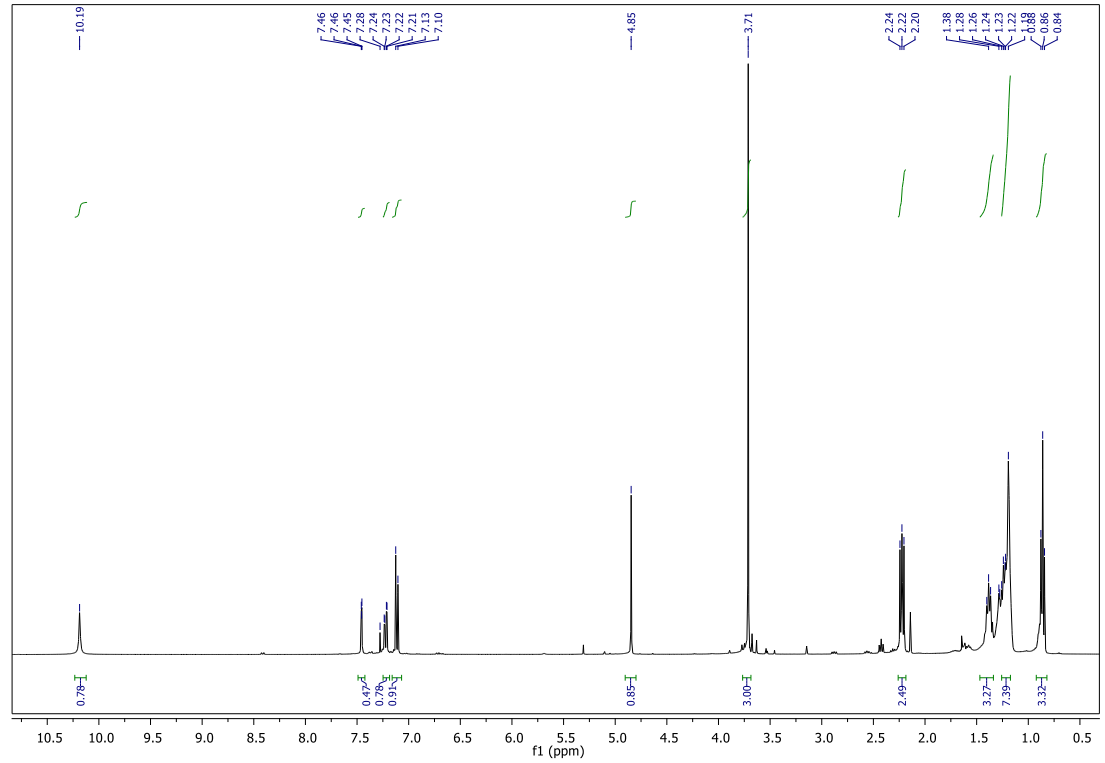
164.15
139.18
138.82
127.04
122.86
84.20
77.48
77.16
76.84
50.33
32.32
31.71
29.16
28.92
28.19
22.70
21.36
14.16
f1 (ppm)

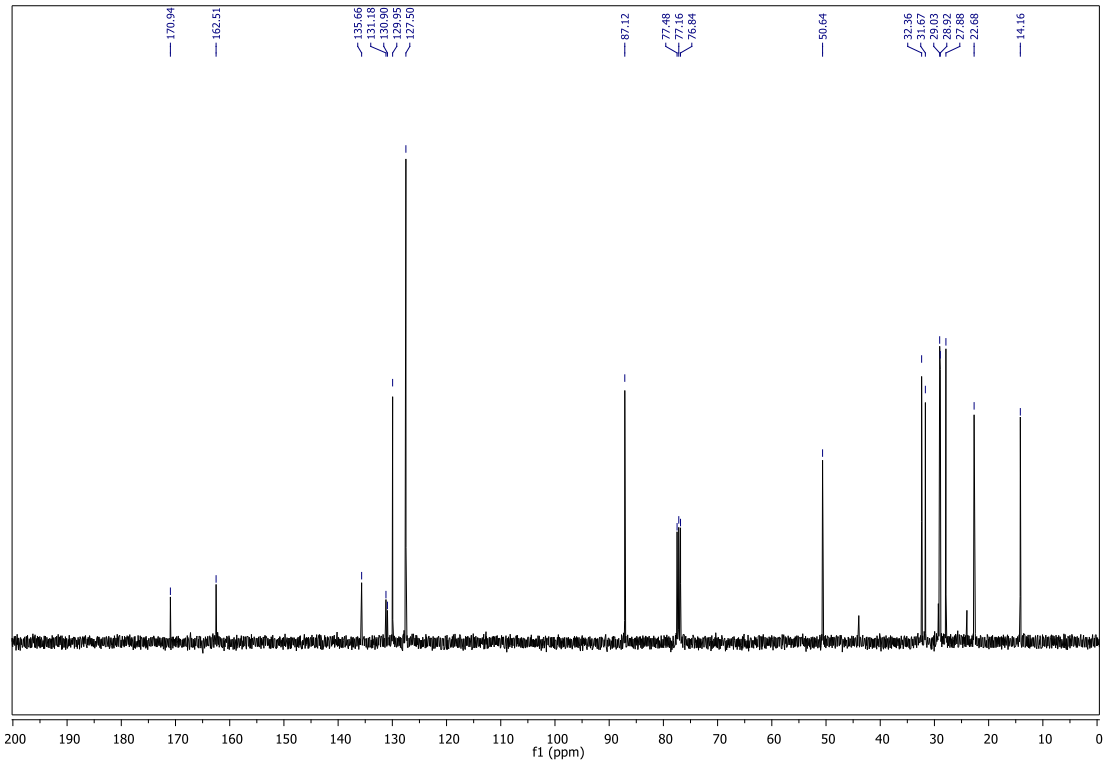
11a)


10.06
7.28
7.25
7.24
7.19
7.17
7.17
7.15
7.10
7.08
4.75
3.71
2.29
2.18
2.16
2.14
1.38
1.36
1.34
1.24
1.23
1.21
1.16
0.87
0.85
0.83
0.82
0.83
1.58
0.74
0.77
3.00
2.88
2.36
2.27
8.25
2.67
f1 (ppm)

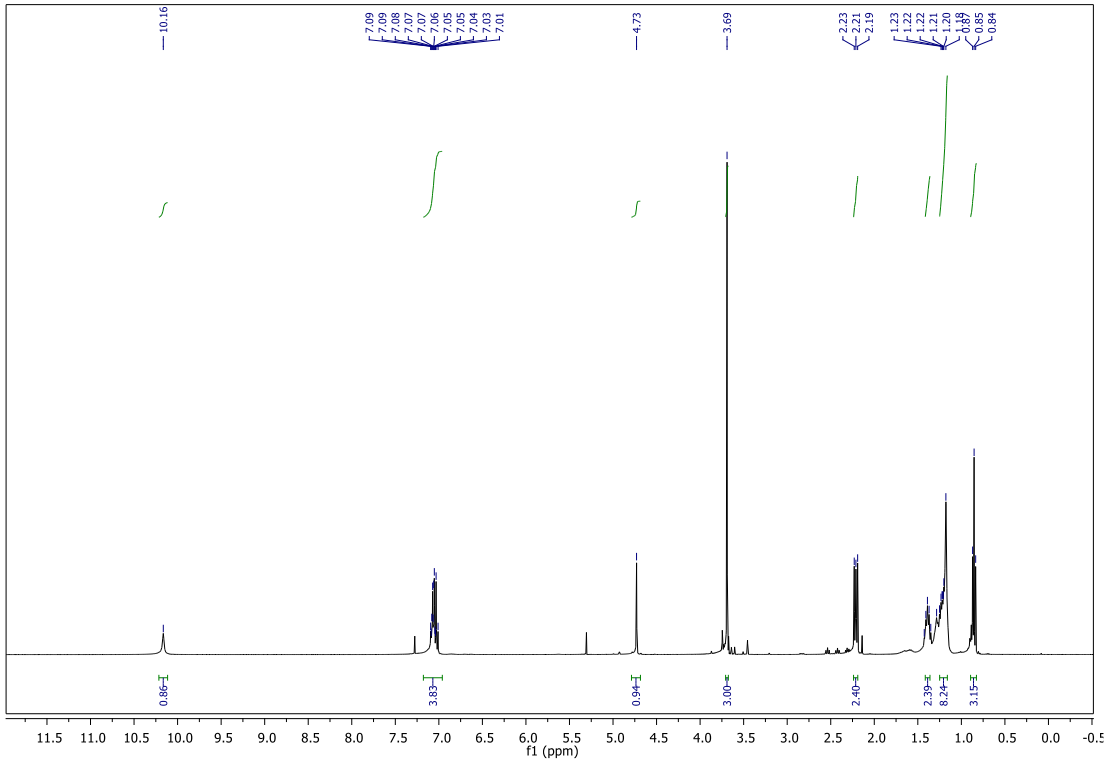

171.31
164.73
137.98
134.44
130.83
127.03
126.48
126.33
83.88
77.48
77.16
76.84
50.34
32.32
31.66
29.11
28.89
27.91
22.68
18.16
14.15
f1 (ppm)

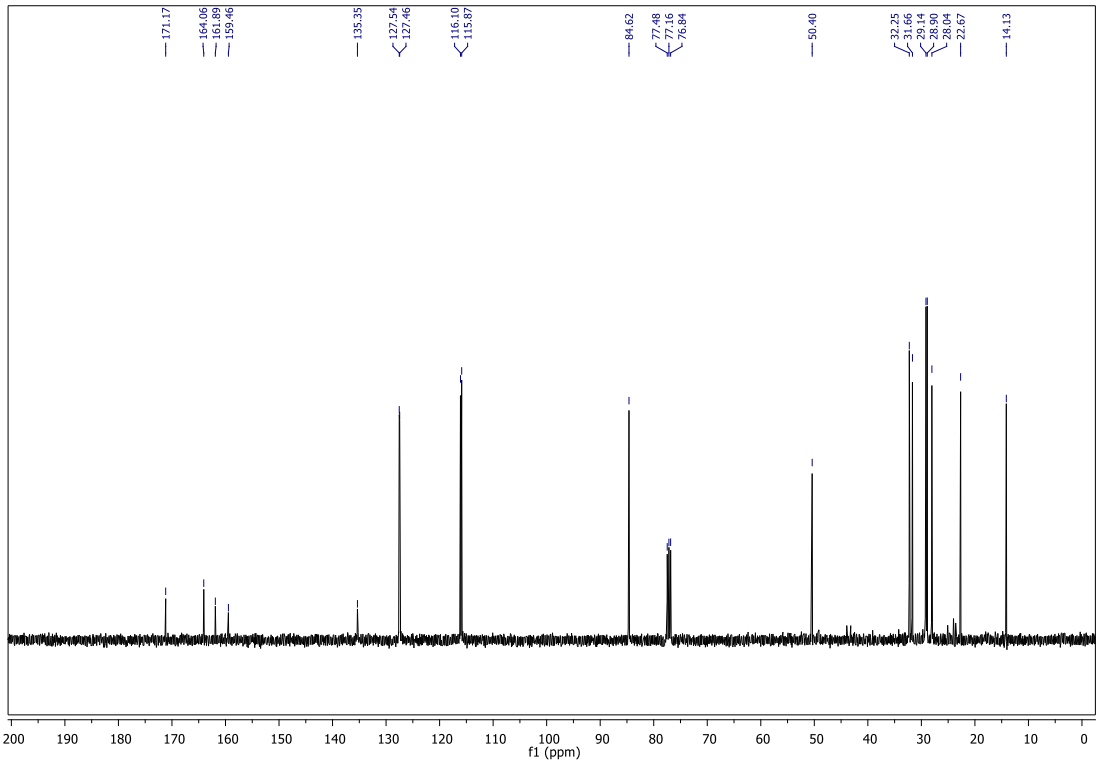
12a)


10.19
7.46
7.46
7.45
7.28
7.24
7.23
7.22
7.21
7.13
7.10
4.85
3.71
2.24
2.22
2.20
1.38
1.28
1.26
1.24
1.23
1.22
0.88
0.86
0.84
0.78
0.47
0.78
0.91
0.85
3.00
2.49
3.27
7.39
3.32
f1 (ppm)

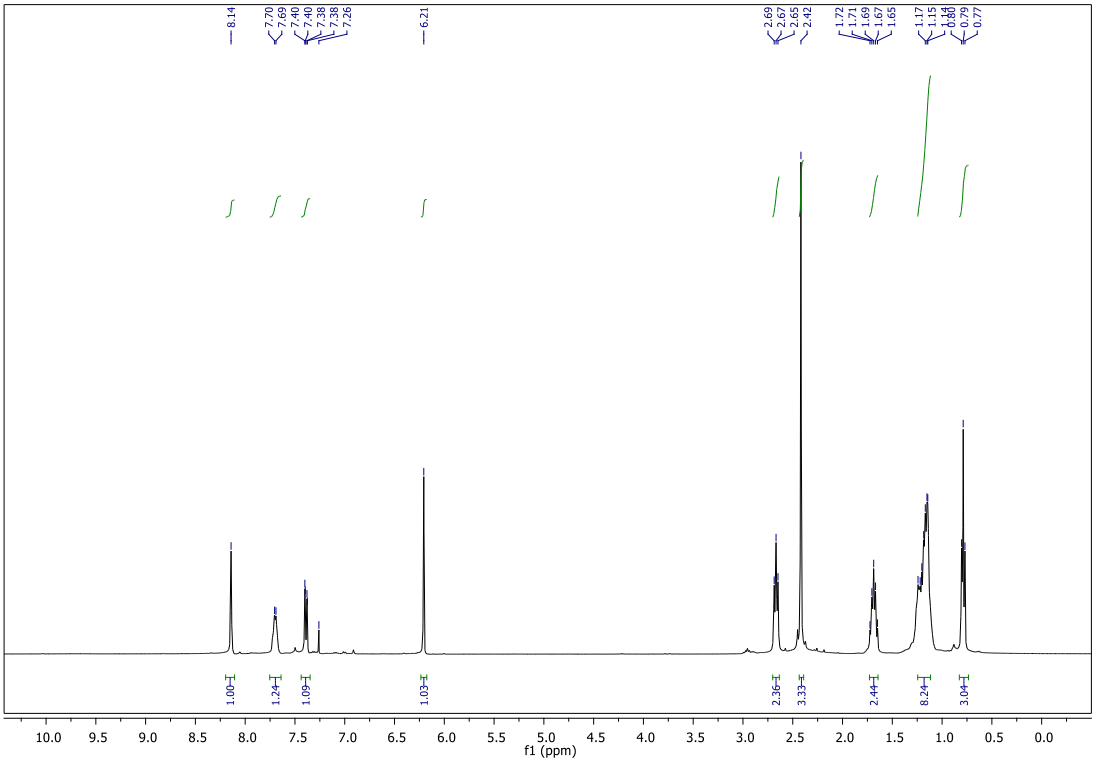

170.94
162.51
135.66
131.18
130.90
129.95
127.50
87.12
77.48
77.16
76.84
50.64
32.36
31.67
29.03
28.92
27.88
22.68
14.16
f1 (ppm)

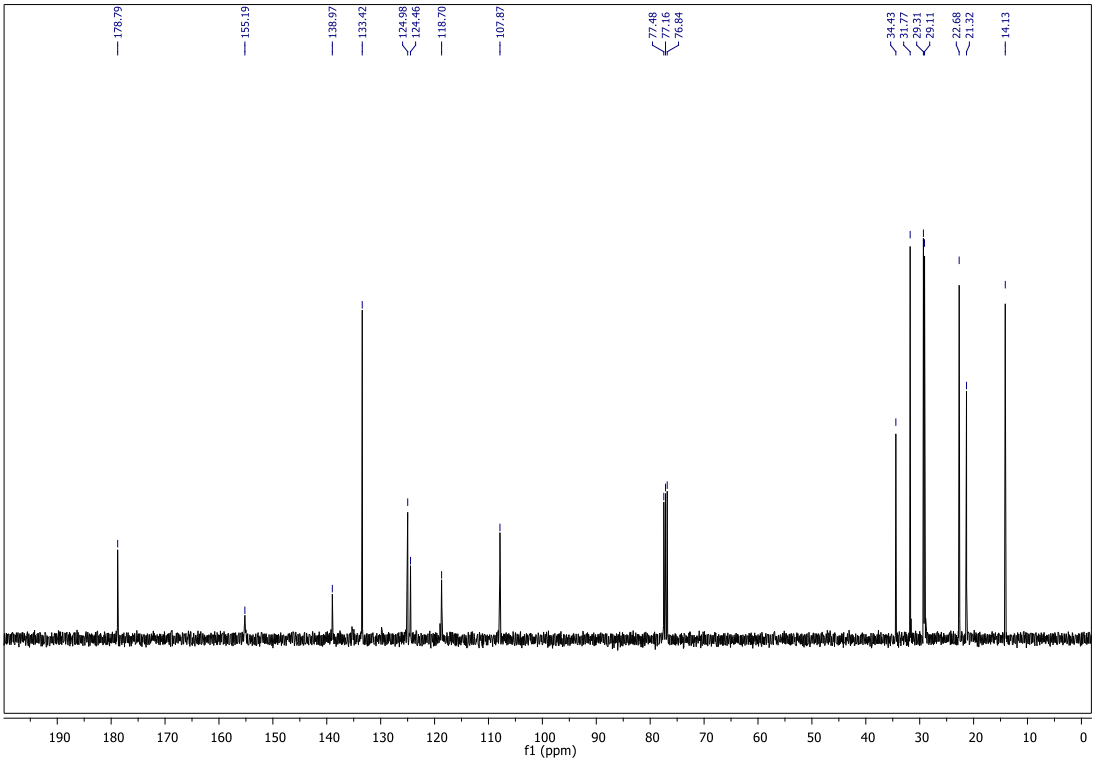
15a)


10.16
7.09
7.09
7.08
7.07
7.07
7.06
7.05
7.05
7.04
7.03
7.01
4.73
3.69
2.23
2.21
2.19
1.23
1.22
1.22
1.21
1.20
0.87
0.85
0.84
0.86
3.83
0.94
3.00
2.40
2.39
8.24
3.15
f1 (ppm)

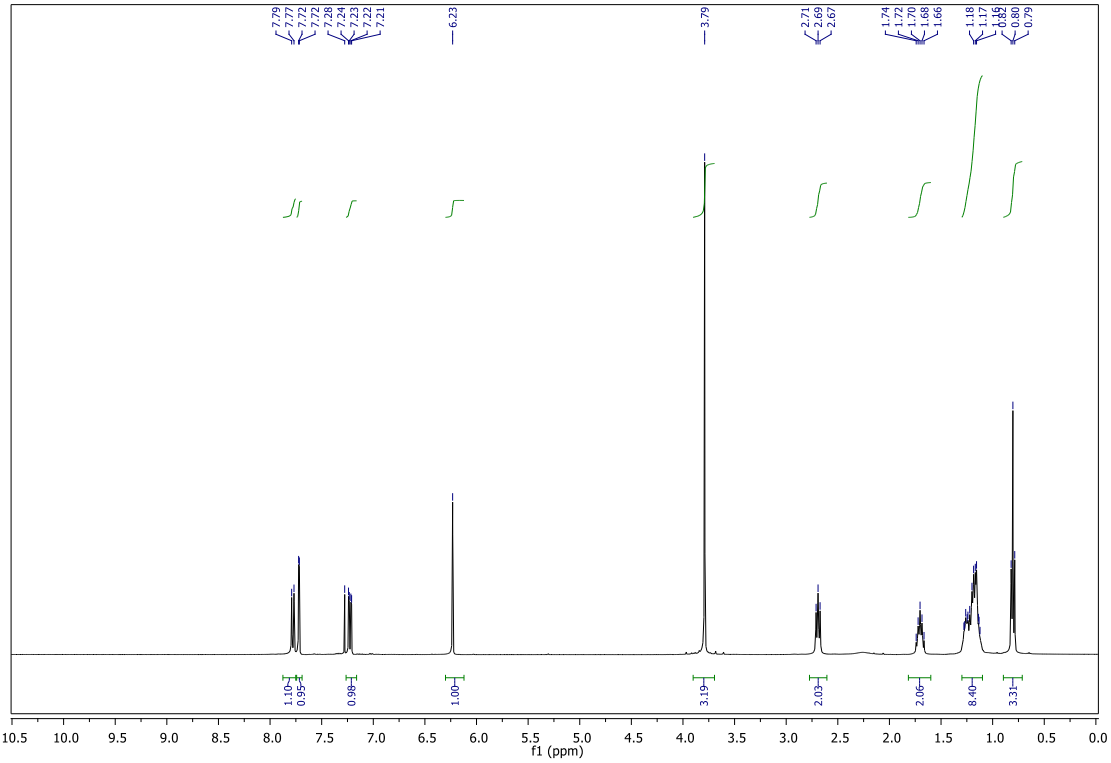

171.17
164.06
161.89
159.46
135.35
127.54
127.46
116.10
115.87
84.62
77.48
77.16
76.84
50.40
32.25
31.66
29.14
28.90
28.04
22.67
14.13
f1 (ppm)

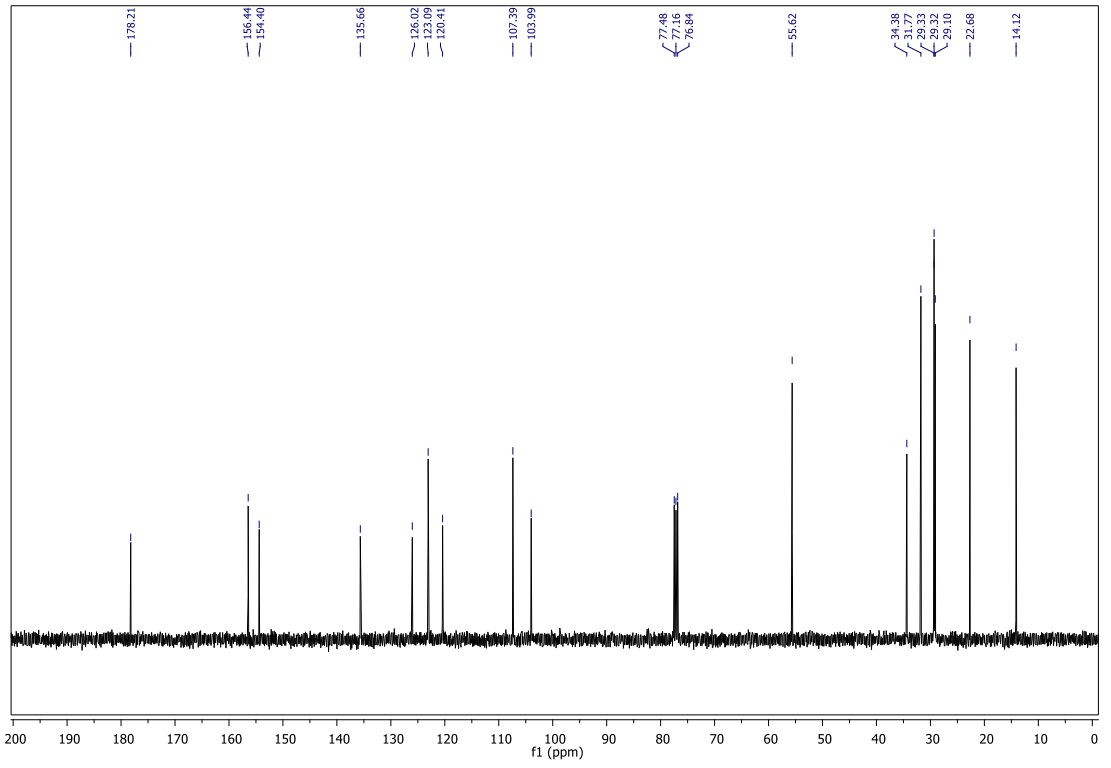
7)


8.14
7.70
7.69
7.40
7.40
7.38
7.38
7.26
6.21
2.69
2.67
2.65
2.42
1.72
1.71
1.69
1.67
1.65
1.17
1.15
0.81
0.79
0.77
1.00
1.24
1.09
1.03
2.36
3.33
2.44
8.24
3.04
f1 (ppm)

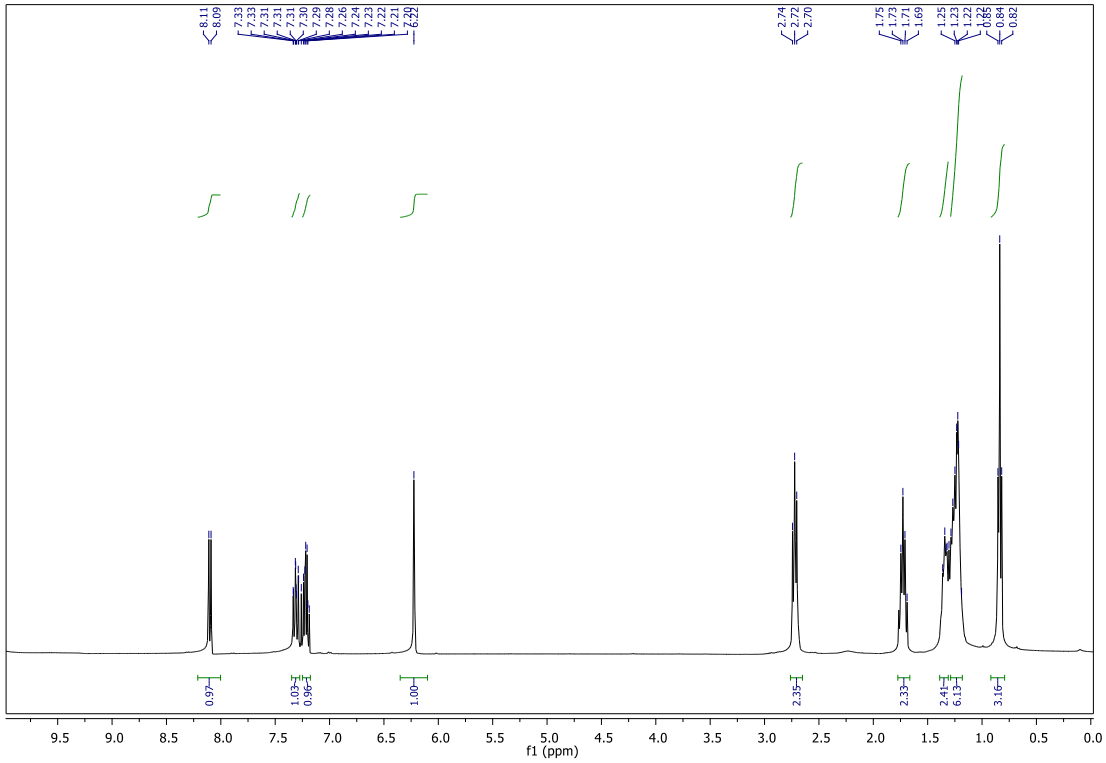

178.79
155.19
138.97
133.42
124.98
124.46
118.70
107.87
77.48
77.16
76.84
34.43
31.77
29.31
29.11
22.68
21.32
14.13
f1 (ppm)

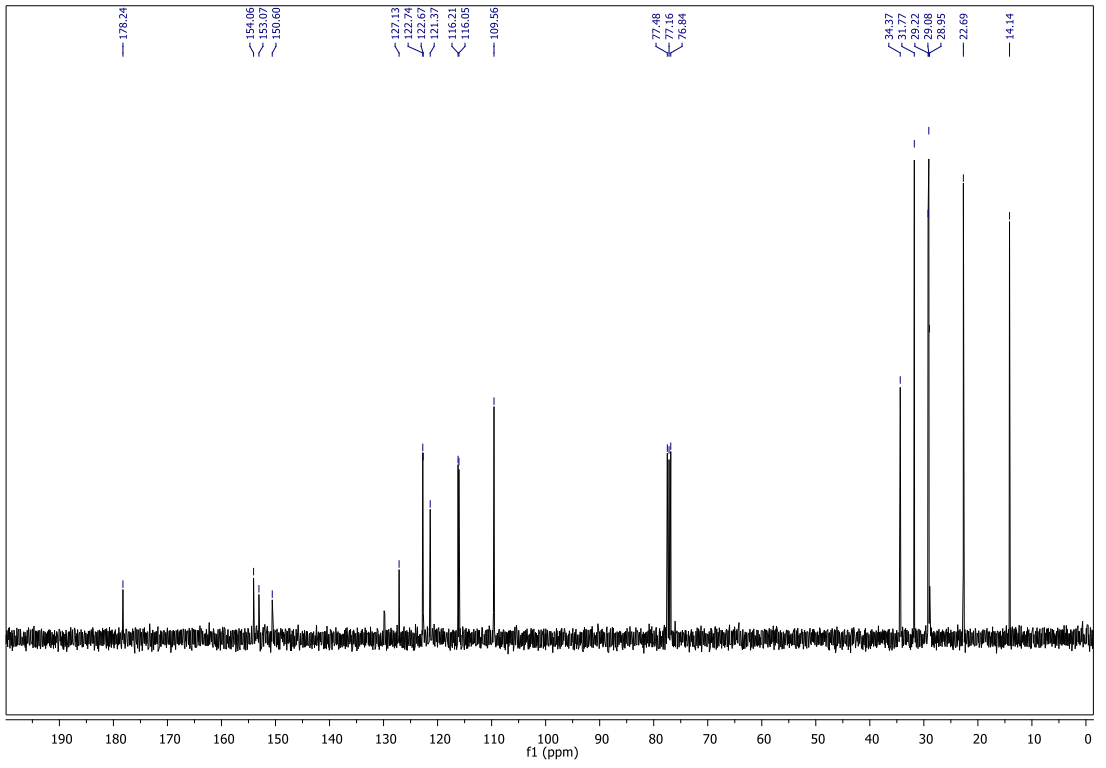
8)


7.79
7.77
7.72
7.72
7.28
7.24
7.23
7.22
7.21
6.23
3.79
2.71
2.69
2.67
1.74
1.72
1.70
1.68
1.66
1.18
1.17
0.80
0.79
1.10
0.95
0.98
1.00
3.19
2.03
2.06
8.40
3.31
f1 (ppm)

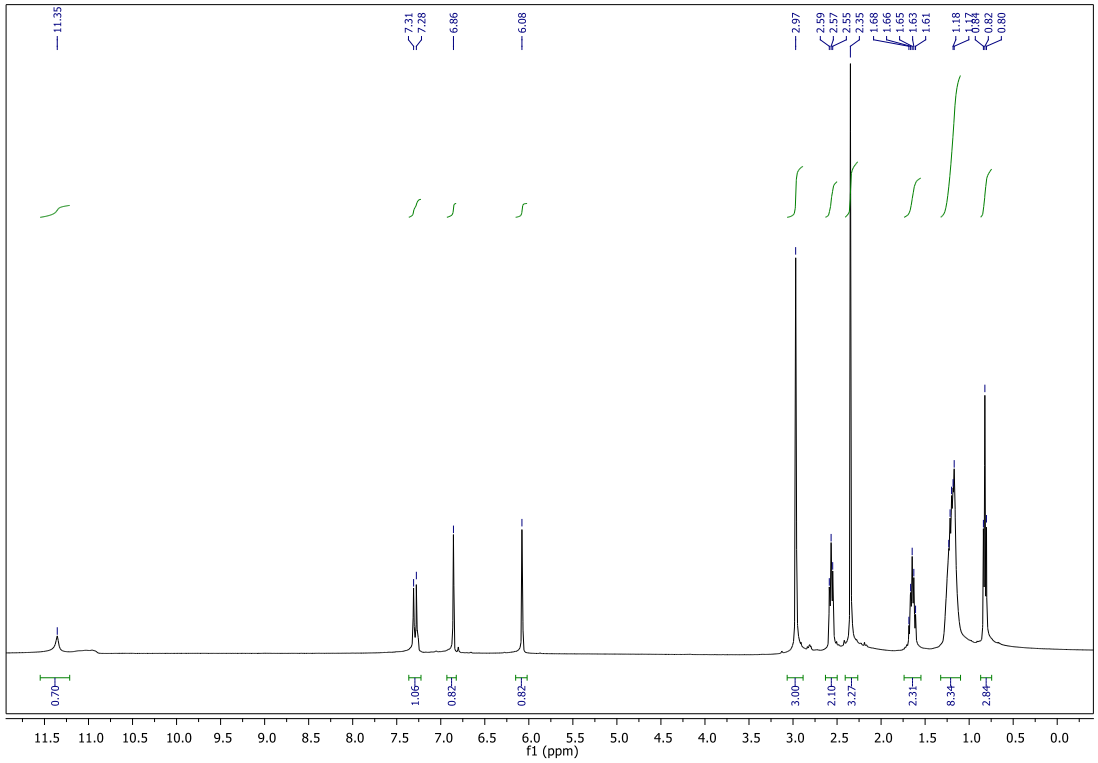

178.21
156.44
154.40
135.66
126.02
123.09
120.41
107.39
103.99
77.48
77.16
76.84
55.62
34.38
31.77
29.33
29.32
29.10
22.68
14.12
f1 (ppm)

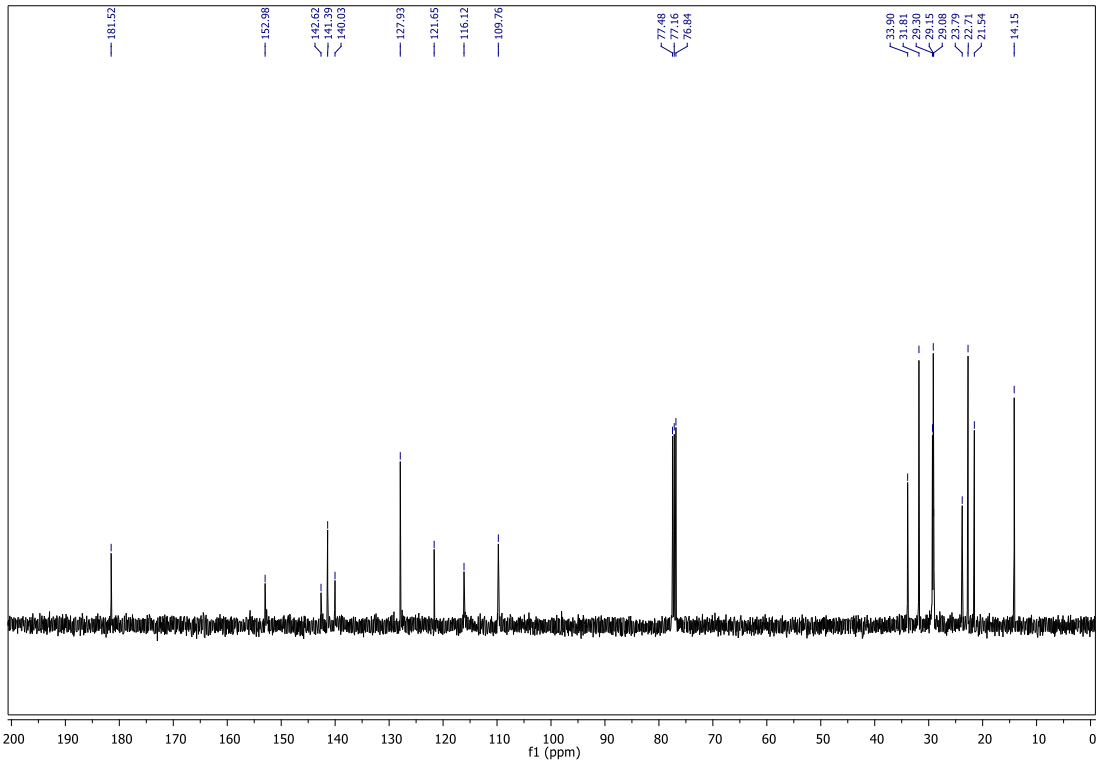
9)


8.11
8.09
7.33
7.33
7.31
7.31
7.31
7.30
7.29
7.28
7.26
7.24
7.23
7.22
7.21
7.20
6.22
2.74
2.72
2.70
1.75
1.73
1.71
1.69
1.25
1.23
1.22
0.85
0.84
0.82
0.97
1.03
0.96
1.00
2.35
2.33
2.41
6.13
3.16
f1 (ppm)


178.24
154.06
153.07
150.60
127.13
122.74
122.67
121.37
116.21
116.05
109.56
77.48
77.16
76.84
34.37
31.77
29.22
29.08
28.95
22.69
14.14
f1 (ppm)

10)


11.35
7.31
7.28
6.86
6.08
2.97
2.59
2.57
2.55
2.35
1.68
1.66
1.65
1.63
1.61
1.18
1.17
0.84
0.82
0.80
0.70
1.06
0.82
0.82
3.00
2.10
3.27
2.31
8.34
2.84
f1 (ppm)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152.98
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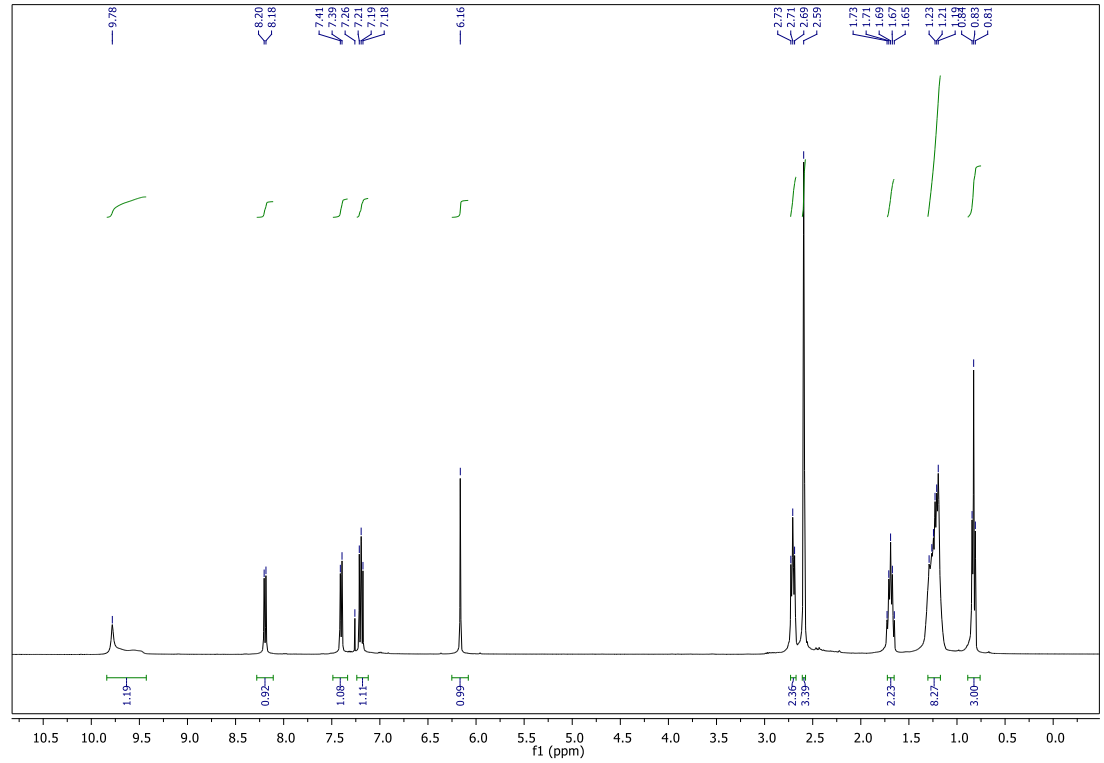
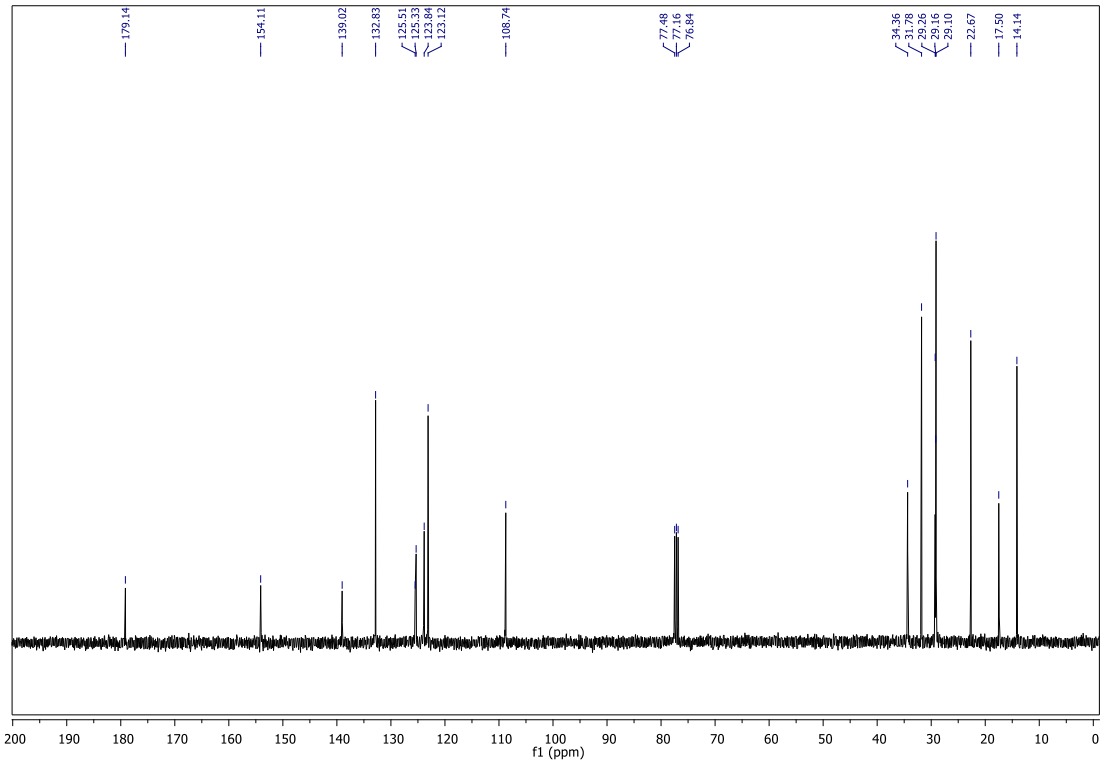
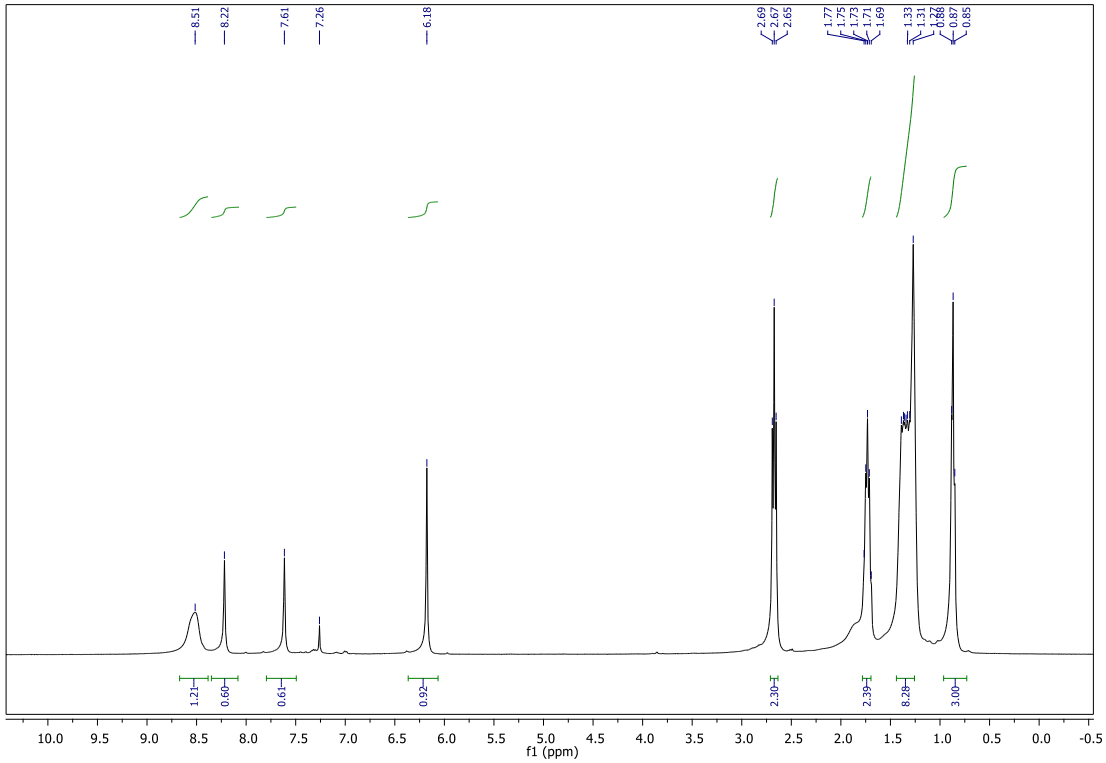
141.39
140.03
127.93
121.65
116.12
109.76
77.48
77.16
76.84
33.90
31.81
29.30
29.15
29.08
23.79
22.71
21.54
14.15
f1 (ppm)

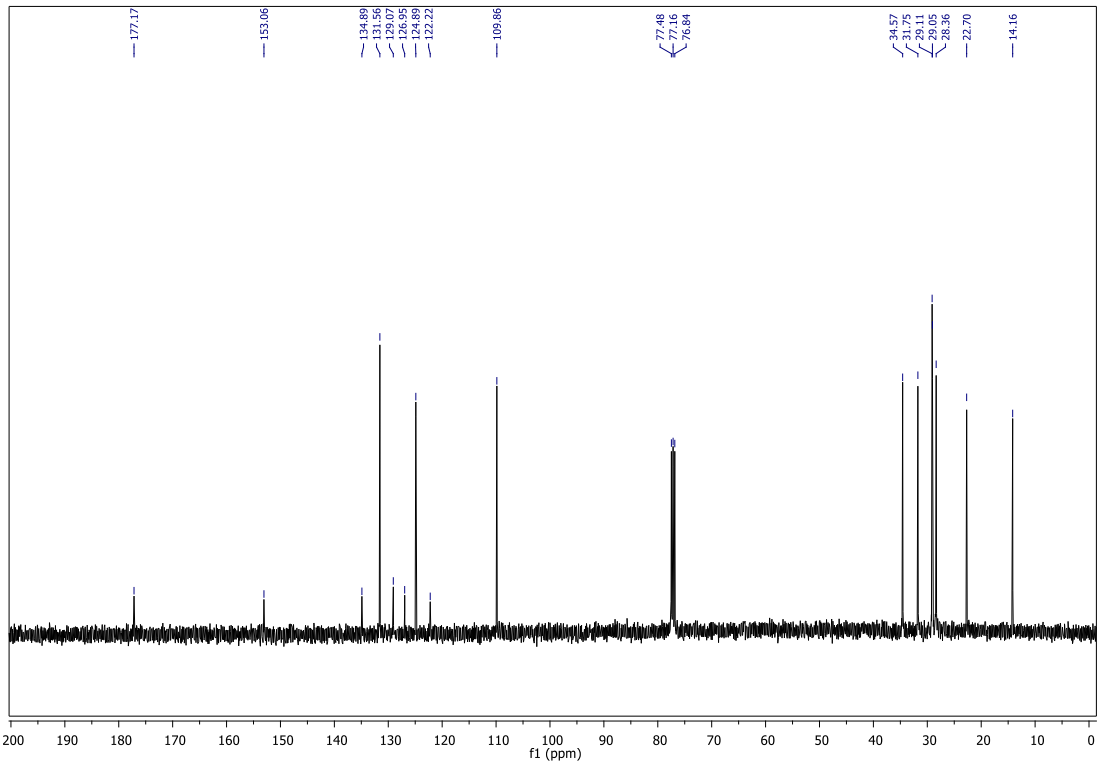
11)


9.78
8.20
8.18
7.41
7.39
7.26
7.21
7.19
7.18
6.16
2.73
2.71
2.69
2.59
1.73
1.71
1.69
1.67
1.65
1.23
1.21
0.85
0.83
0.81
1.19
0.92
1.08
1.11
0.99
2.36
3.39
2.23
8.27
3.00
f1 (ppm)

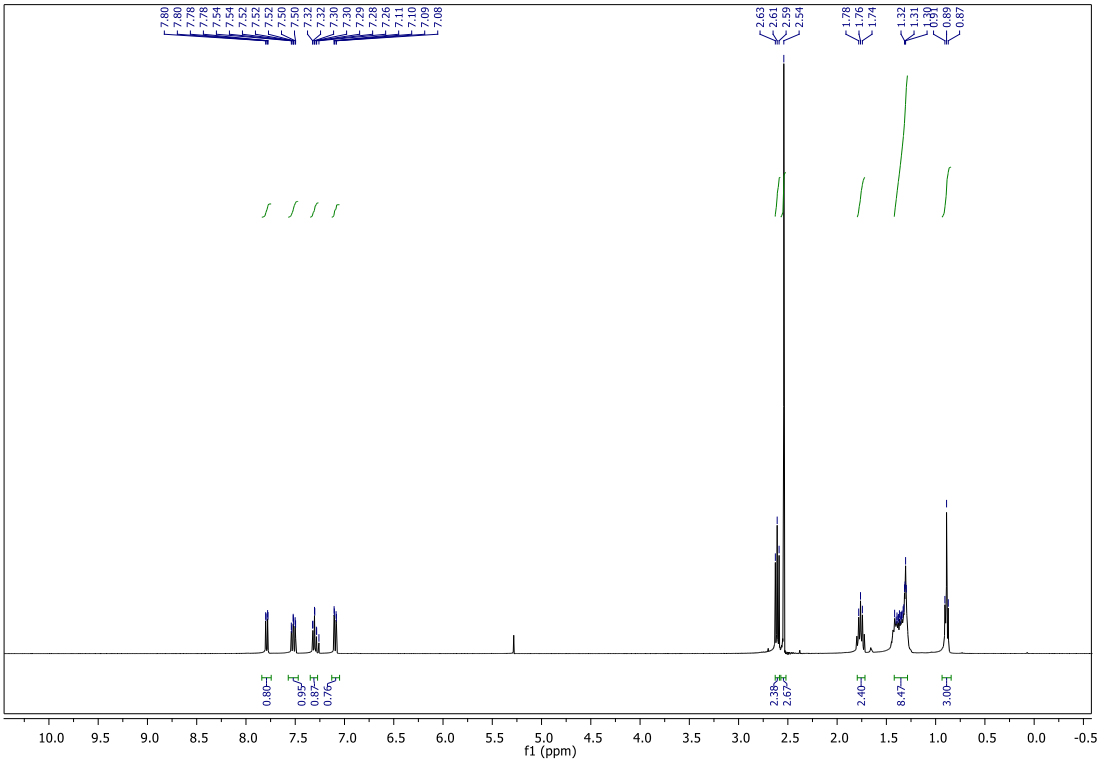

179.14
154.11
139.02
132.83
125.51
125.33
123.84
123.12
108.74
77.48
77.16
76.84
34.36
31.78
29.26
29.16
29.10
22.67
17.50
14.14
f1 (ppm)

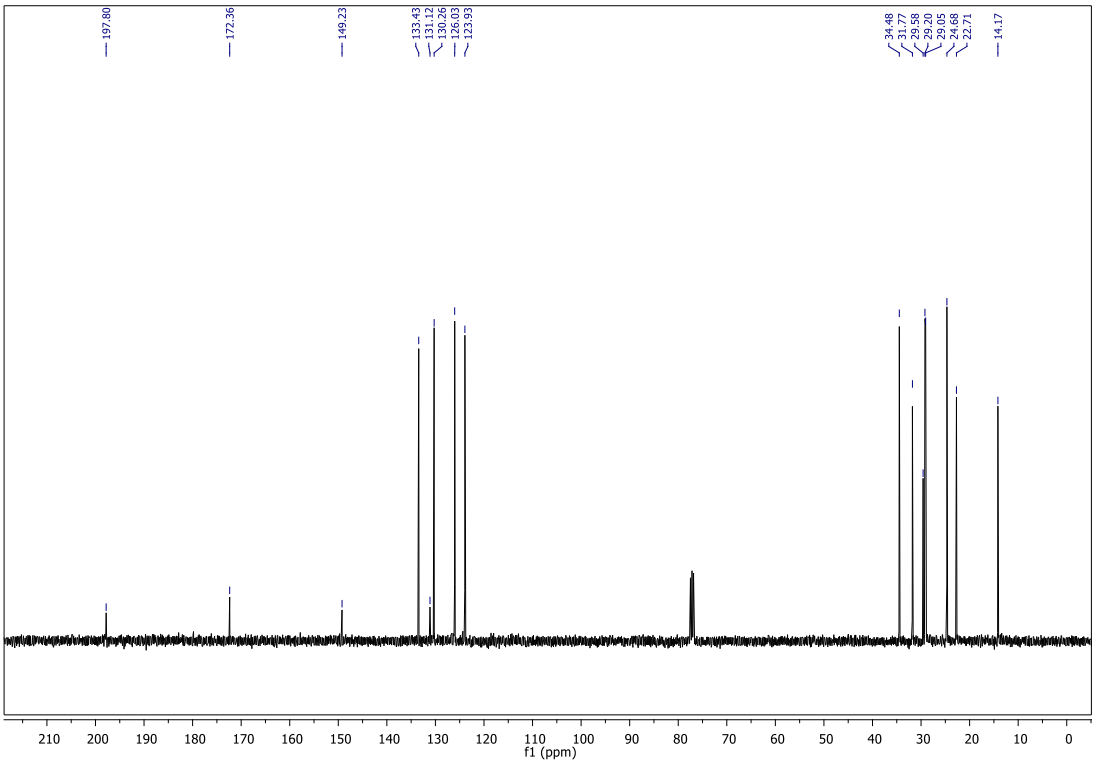
12)


8.51
8.22
7.61
7.26
6.18
2.69
2.67
2.65
1.77
1.75
1.73
1.71
1.69
1.33
1.31
0.88
0.87
0.85
1.21
0.60
0.61
0.92
2.30
2.39
8.28
3.00
f1 (ppm)

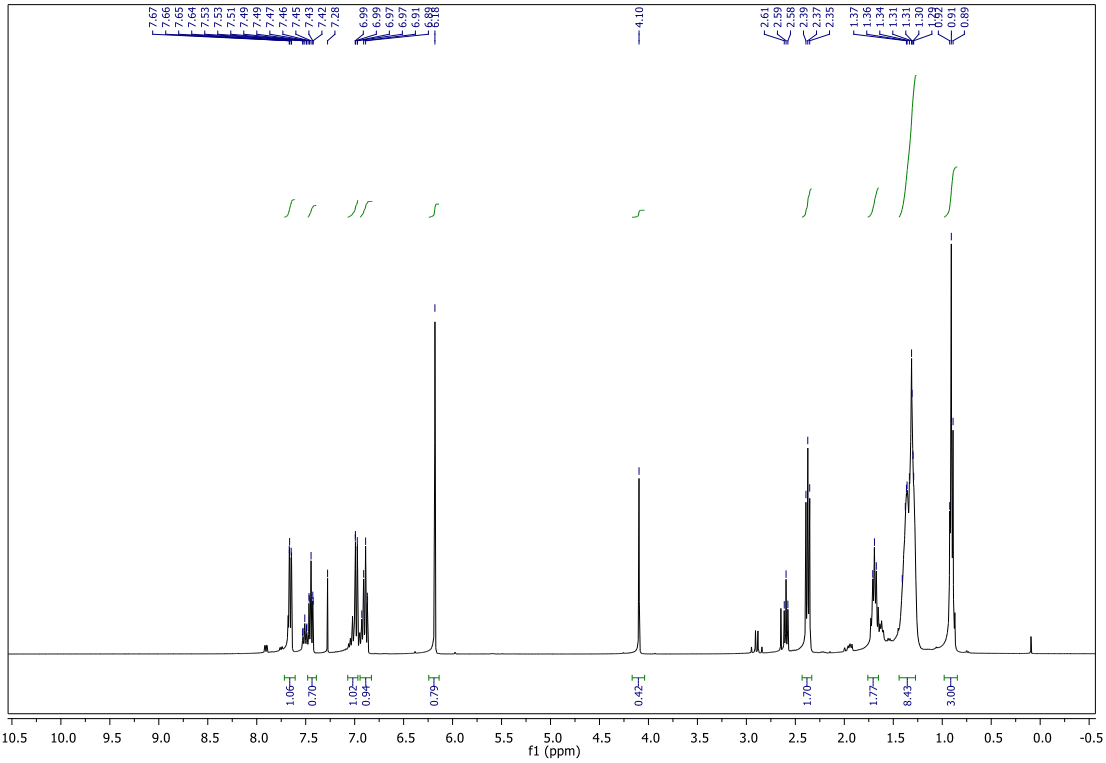

177.17
153.06
134.89
131.56
129.07
126.65
124.89
122.22
109.86
77.48
77.16
76.84
34.57
31.75
29.11
29.05
28.36
22.70
14.16
f1 (ppm)

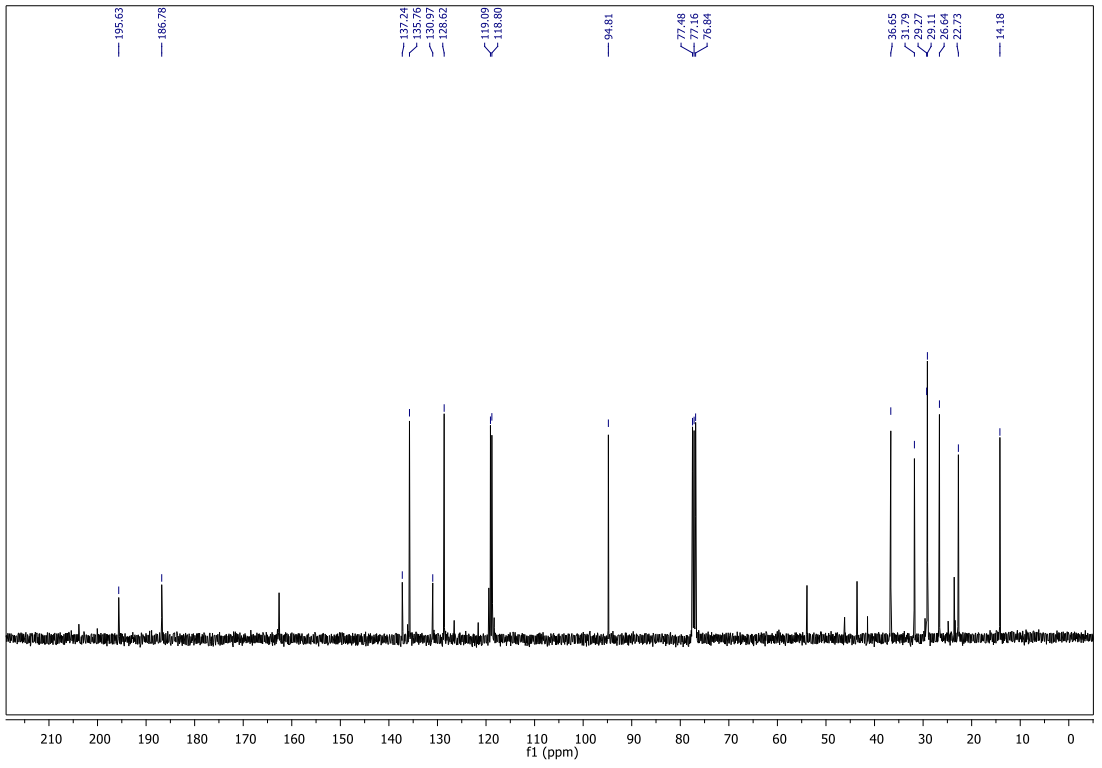
13a)


7.80
7.80
7.78
7.78
7.54
7.54
7.52
7.52
7.50
7.50
7.32
7.32
7.30
7.30
7.29
7.28
7.26
7.11
7.10
7.09
7.08
2.63
2.61
2.59
2.54
1.78
1.76
1.74
1.32
1.31
1.30
0.91
0.89
0.87
0.80
0.95
0.97
0.76
2.38
2.67
2.40
8.47
3.00
f1 (ppm)

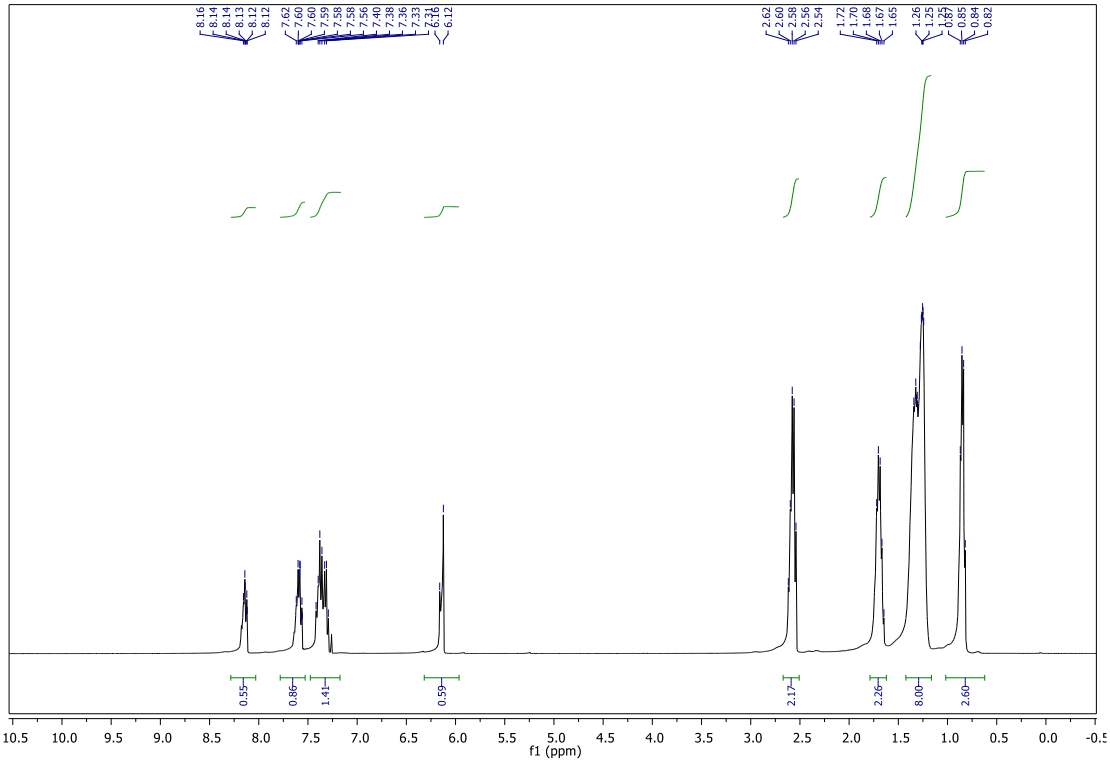

197.80
172.36
149.23
133.43
131.12
130.26
126.03
123.93
34.48
33.77
29.58
29.20
29.05
24.68
22.71
14.17
f1 (ppm)

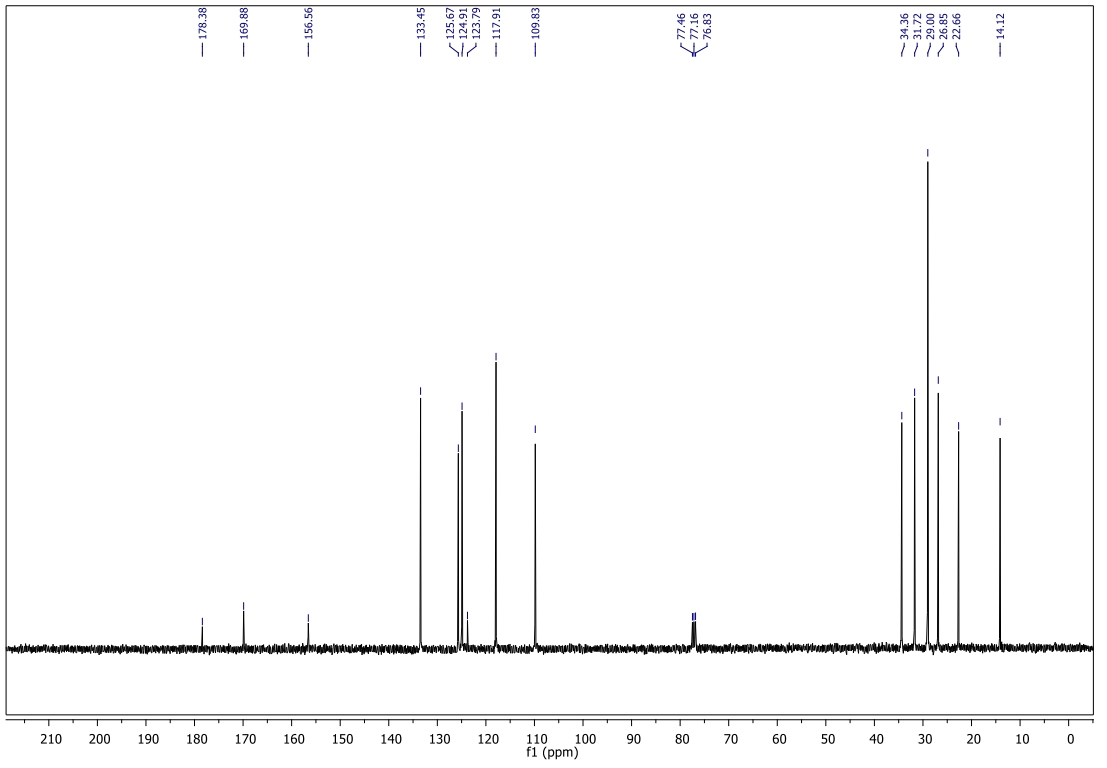
13b)


7.67
7.66
7.65
7.64
7.53
7.51
7.49
7.49
7.47
7.46
7.45
7.43
7.42
7.28
6.99
6.99
6.97
6.97
6.91
6.88
4.10
2.61
2.59
2.58
2.39
2.37
2.35
1.37
1.36
1.34
1.31
1.31
1.30
1.29
0.92
0.91
0.89
1.06
0.70
1.02
0.94
0.79
0.42
1.70
1.77
8.43
3.00
f1 (ppm)

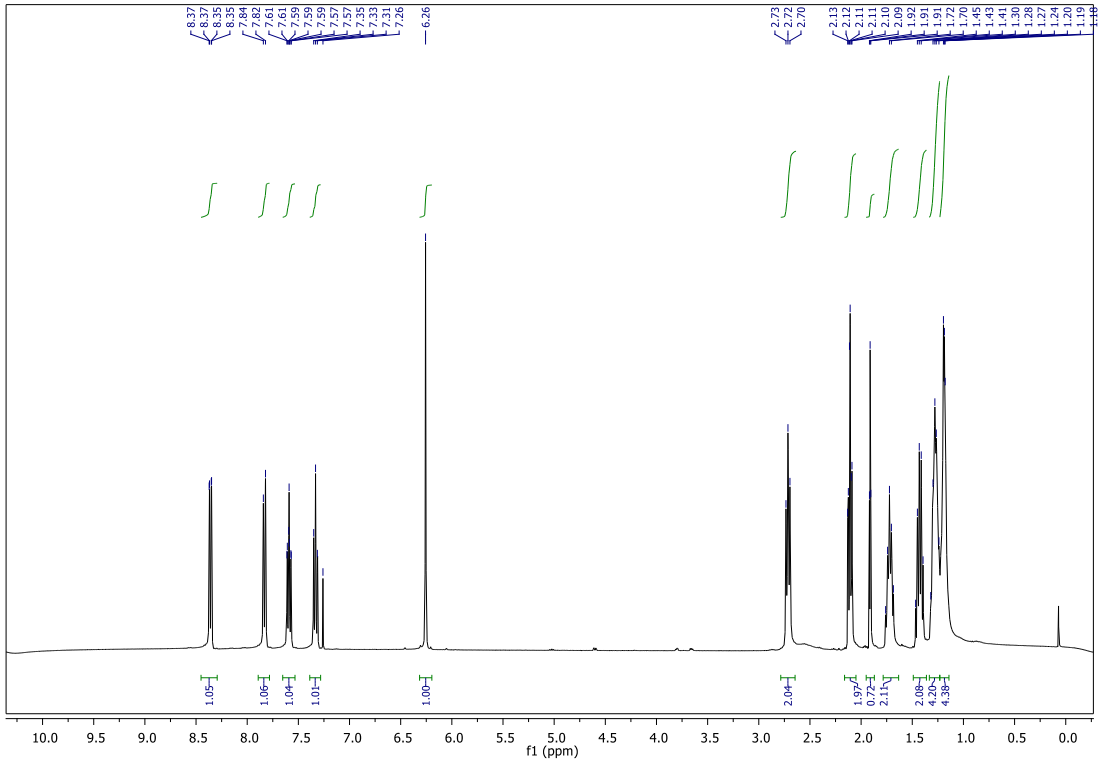

195.63
186.78
137.24
135.76
130.97
128.62
119.09
118.80
94.81
77.48
77.16
76.84
36.65
31.79
29.27
29.11
26.64
22.73
14.18
f1 (ppm)

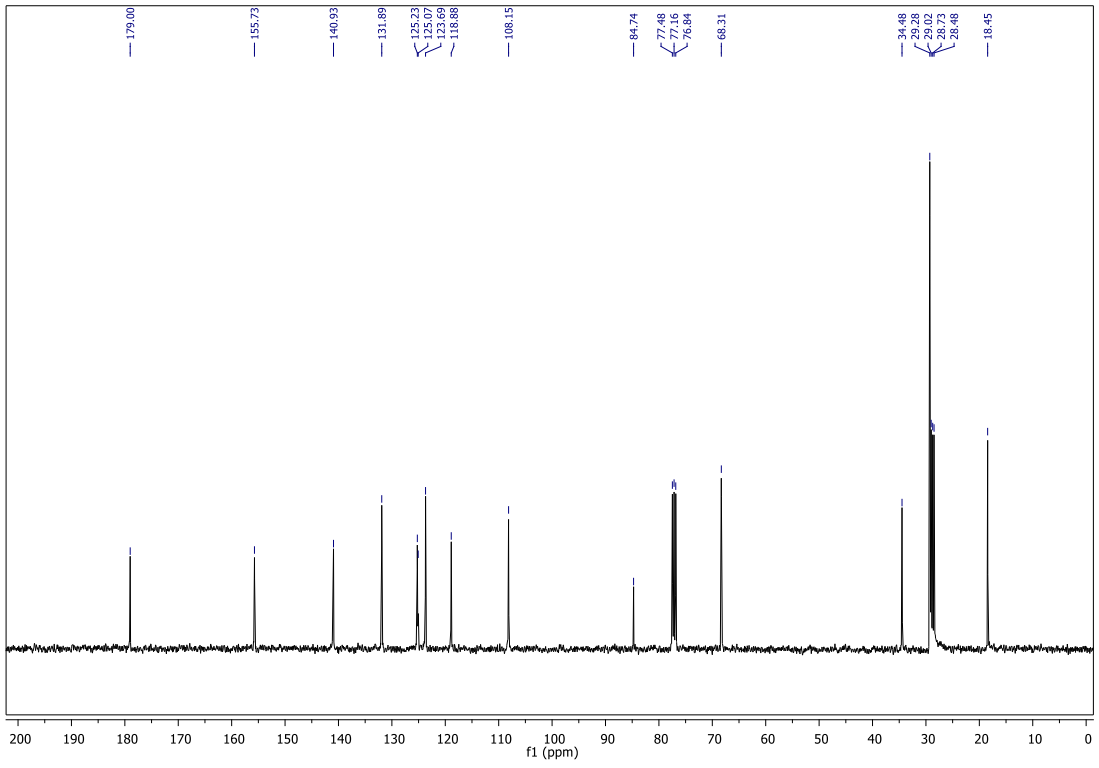
13)


8.16
8.14
8.14
8.13
8.12
8.12
7.62
7.60
7.60
7.59
7.58
7.58
7.56
7.40
7.38
7.36
7.33
7.31
6.16
6.12
2.62
2.60
2.58
2.56
2.54
1.72
1.70
1.68
1.67
1.65
1.26
1.25
1.25
0.85
0.84
0.82
0.55
0.86
1.41
0.59
2.17
2.26
8.00
2.60
f1 (ppm)

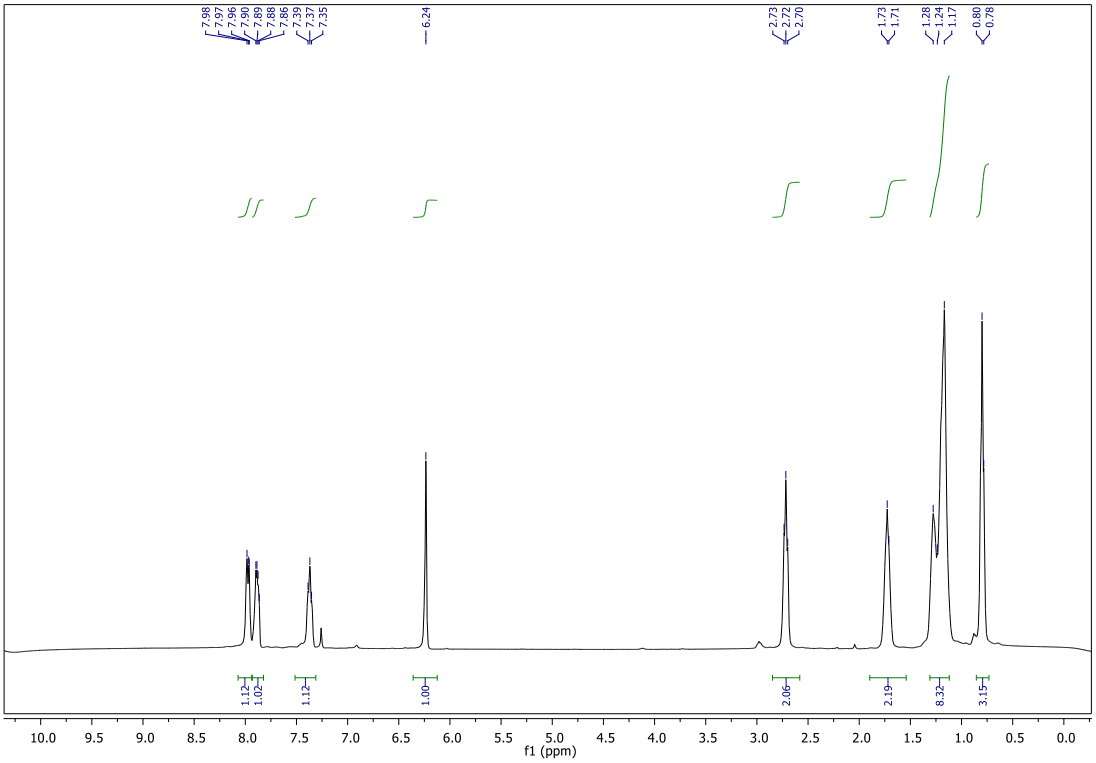

178.38
169.88
156.56
133.45
125.67
124.91
123.79
117.91
109.83
77.46
77.16
76.83
34.36
31.72
29.00
26.85
22.66
14.12
f1 (ppm)

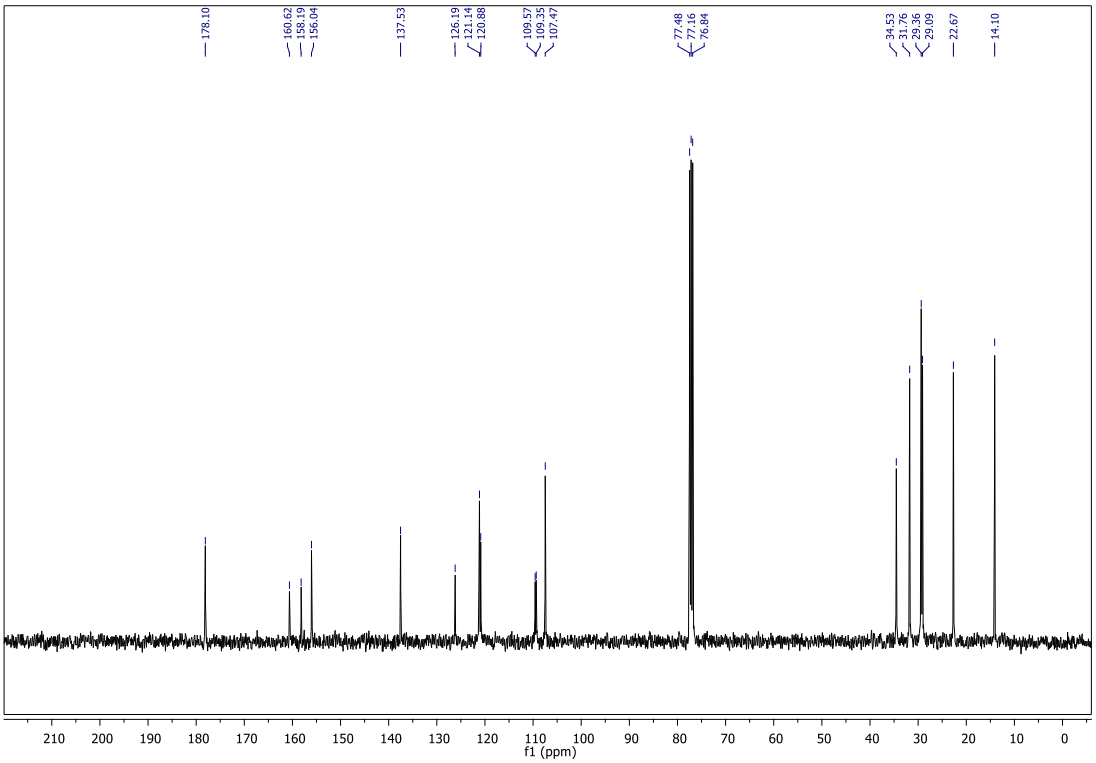
14)


8.37
8.37
8.35
8.35
7.84
7.82
7.61
7.61
7.59
7.59
7.59
7.57
7.57
7.35
7.33
7.31
7.26
6.26
2.73
2.72
2.70
2.13
2.12
2.11
2.11
2.10
2.09
1.92
1.91
1.91
1.72
1.70
1.45
1.43
1.41
1.30
1.28
1.27
1.24
1.20
1.19
1.05
1.06
1.04
1.01
1.00
2.04
1.97
0.72
2.11
2.08
4.20
4.38
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

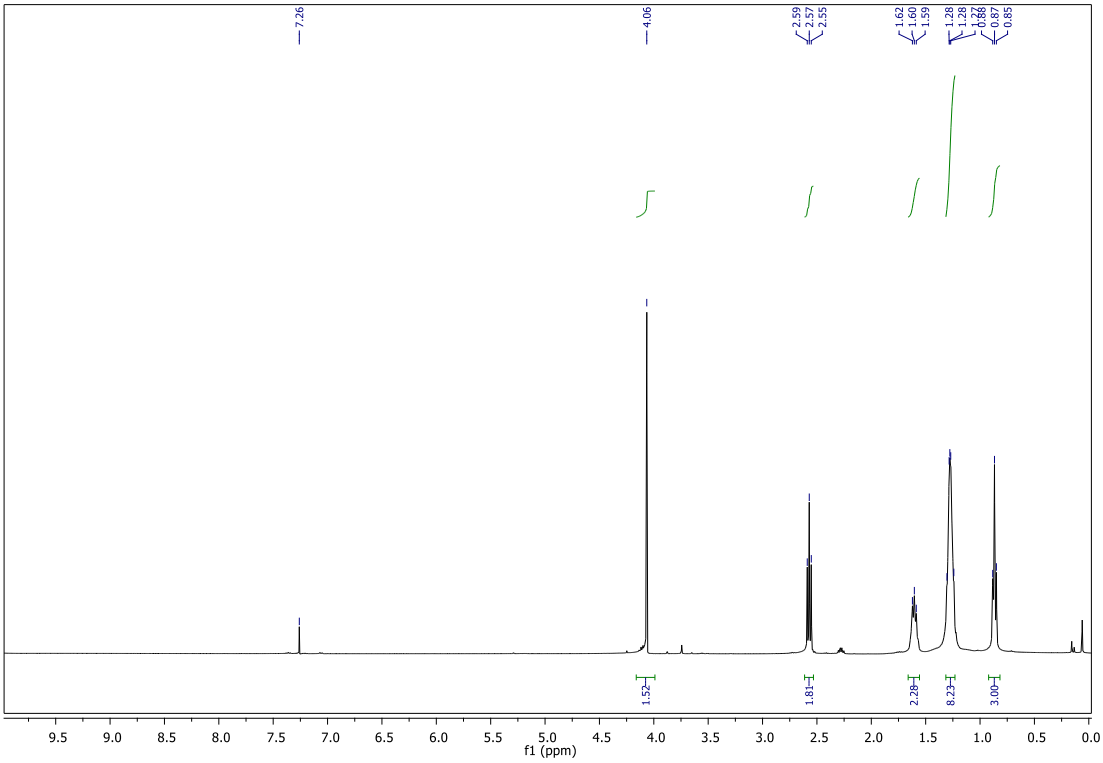

179.00
155.73
140.93
131.89
125.23
125.07
123.69
118.88
108.15
84.74
77.48
77.16
76.84
68.31
34.48
29.28
29.02
28.73
28.48
18.45
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

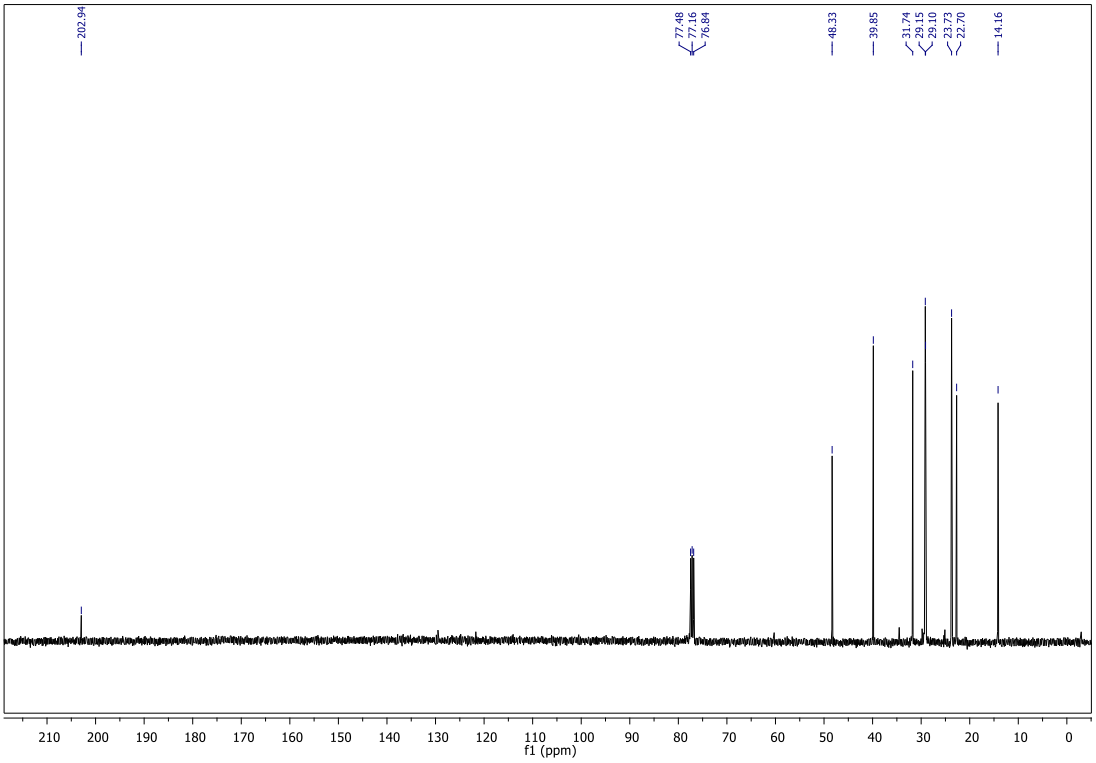
15)


7.98
7.97
7.96
7.90
7.89
7.88
7.86
7.39
7.37
7.35
6.24
2.73
2.72
2.70
1.73
1.71
1.28
1.24
1.17
0.80
0.78
1.12
1.02
1.12
1.00
2.06
2.19
8.32
3.15
f1 (ppm)

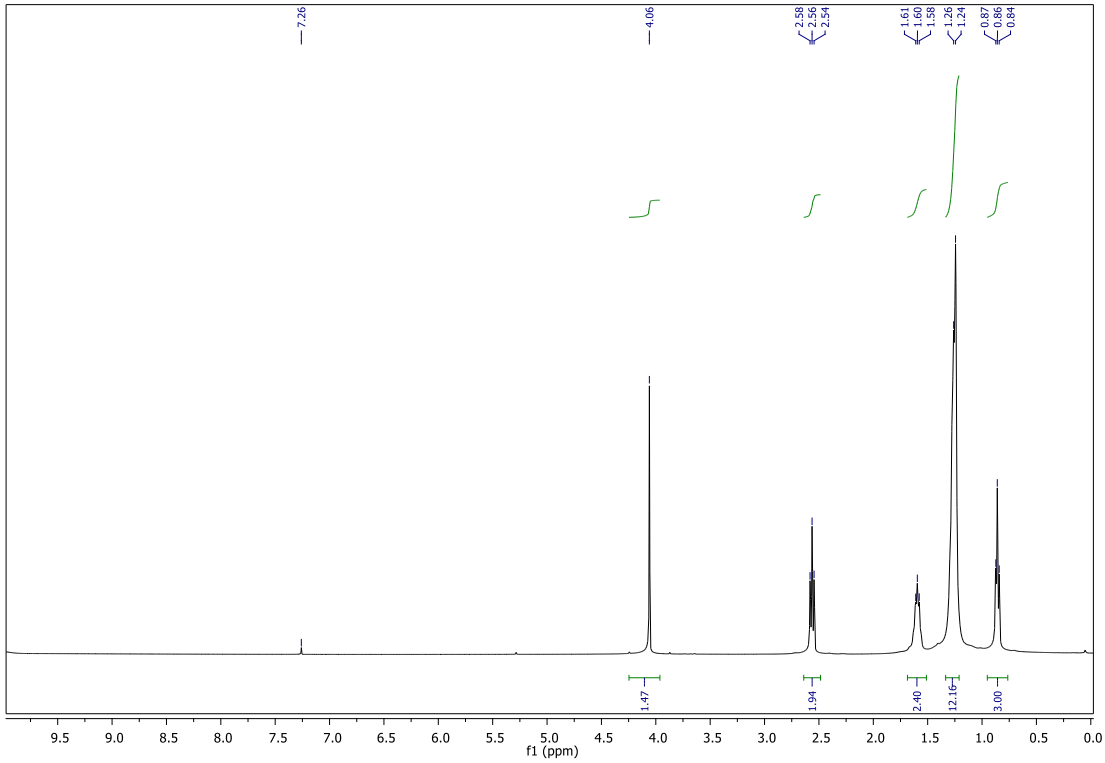

178.10
160.62
158.19
156.04
137.53
126.19
121.14
120.88
109.57
109.35
107.47
77.48
77.16
76.84
34.53
31.76
29.36
29.09
22.67
14.10
f1 (ppm)

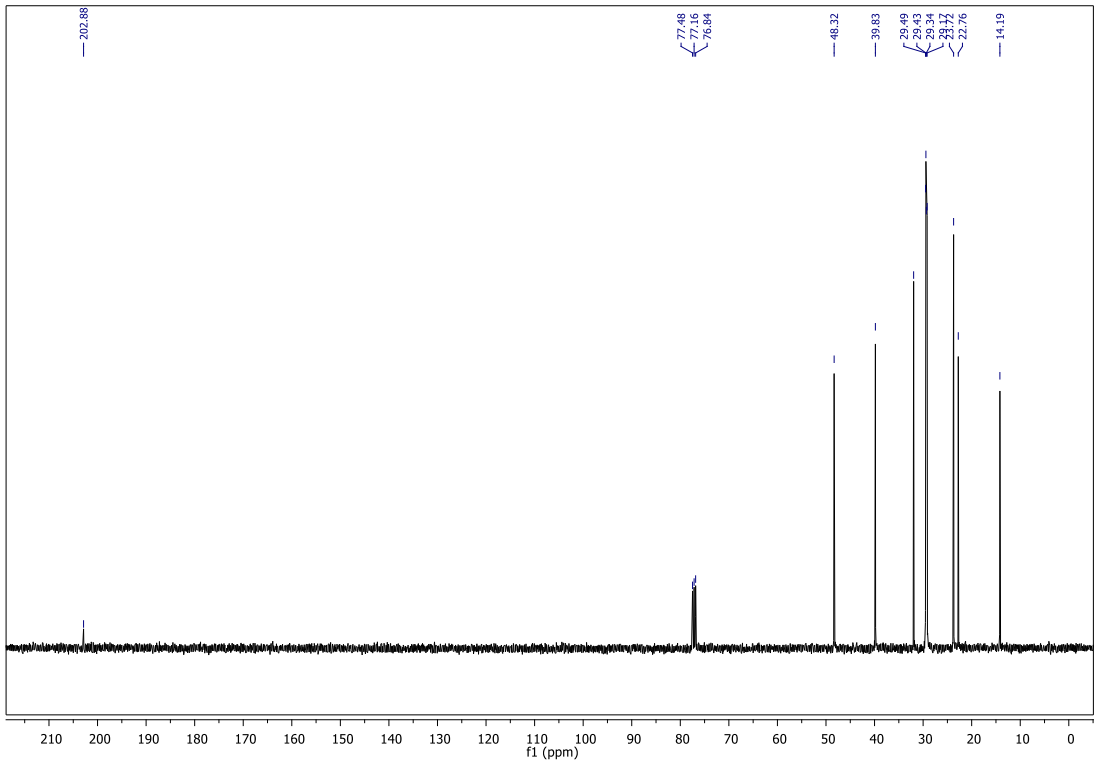
2a)


7.26
4.06
2.59
2.57
2.55
1.62
1.60
1.59
1.28
1.28
0.88
0.87
0.85
1.52
1.81
2.28
8.23
3.00
f1 (ppm)

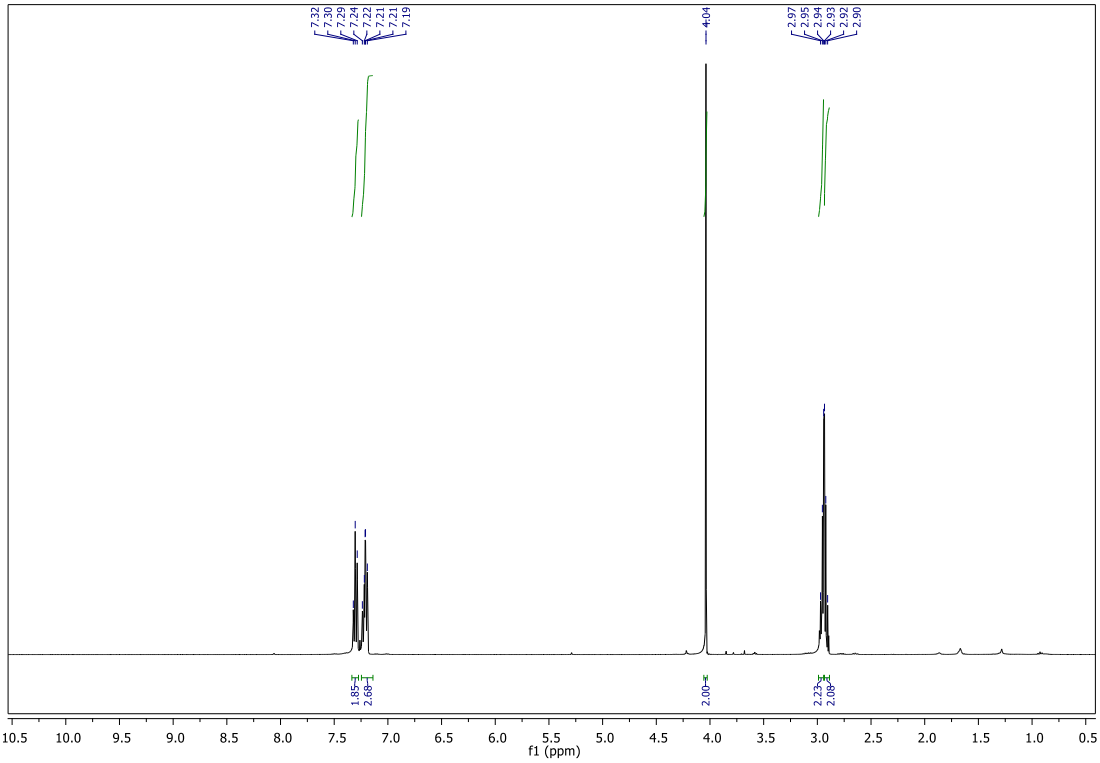

202.94
77.48
77.16
76.84
48.33
39.85
31.74
29.15
29.10
23.73
22.70
14.16
f1 (ppm)

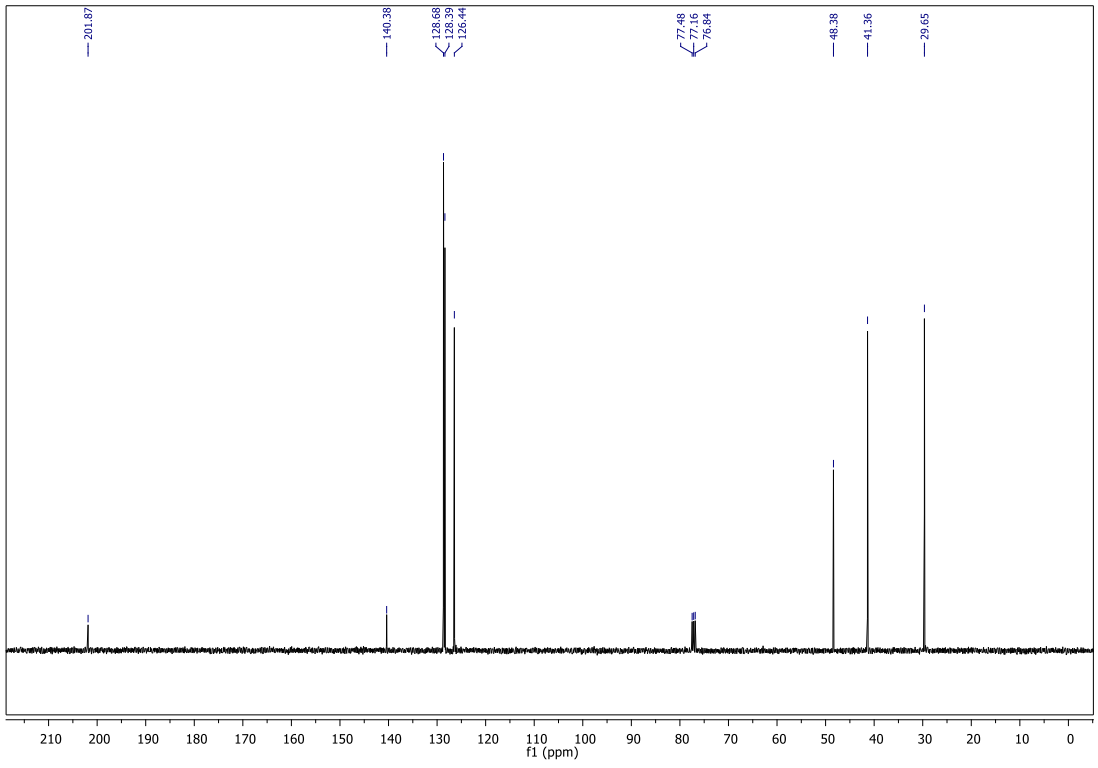
16a)


7.26
4.06
2.58
2.56
2.54
1.61
1.60
1.58
1.26
1.24
0.87
0.86
0.84
1.47
1.94
2.40
12.16
3.00
f1 (ppm)

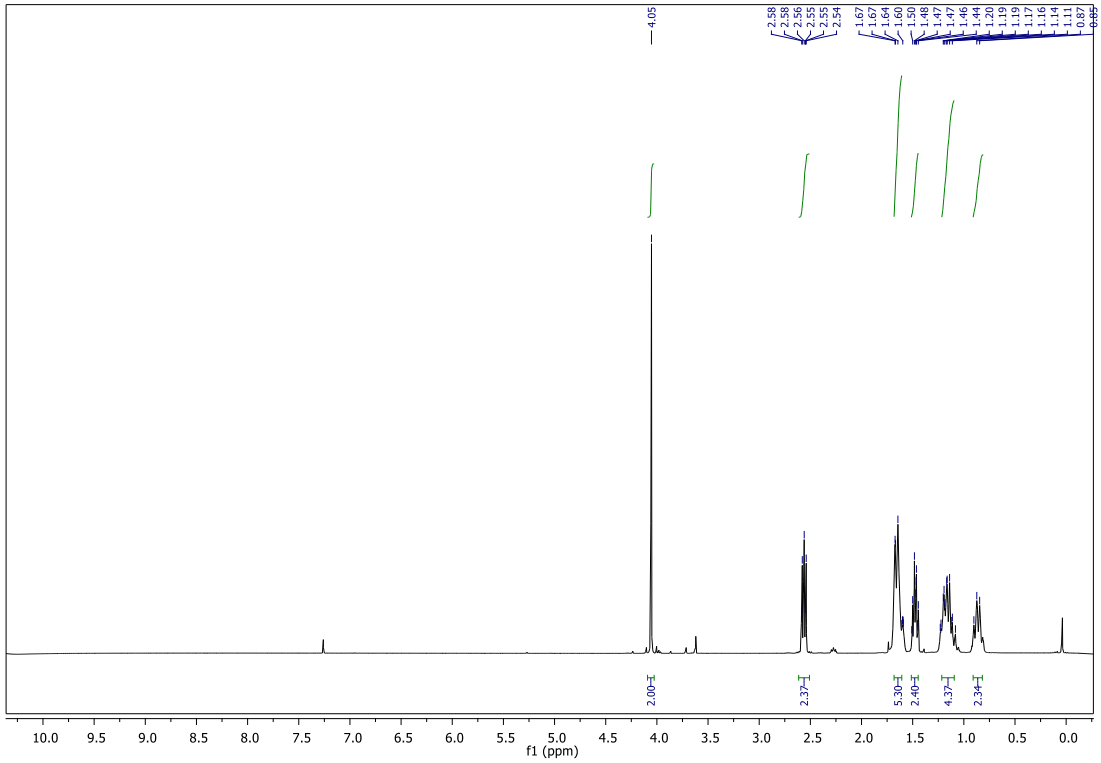

202.88
77.48
77.16
76.84
48.32
39.83
29.49
29.43
29.34
23.72
22.76
14.19
f1 (ppm)

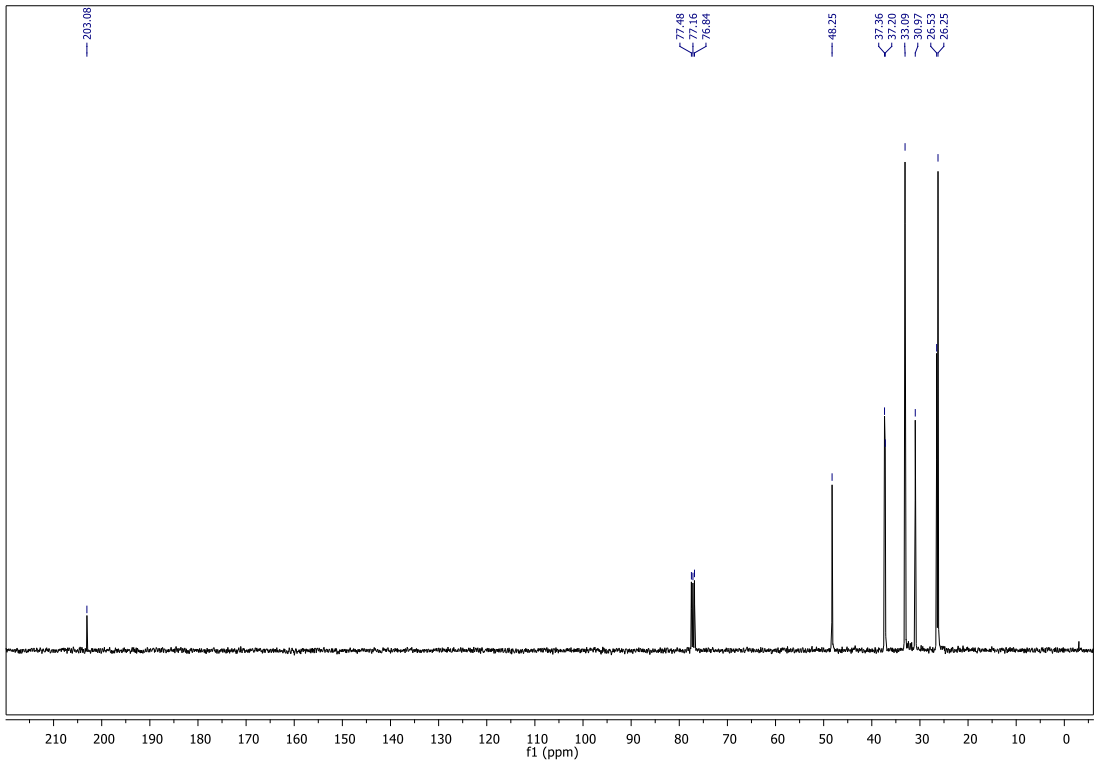
17a)


7.32
7.30
7.29
7.24
7.22
7.21
7.21
7.19
4.04
2.97
2.95
2.94
2.93
2.92
2.90
1.85
2.69
2.00
2.23
2.08
f1 (ppm)

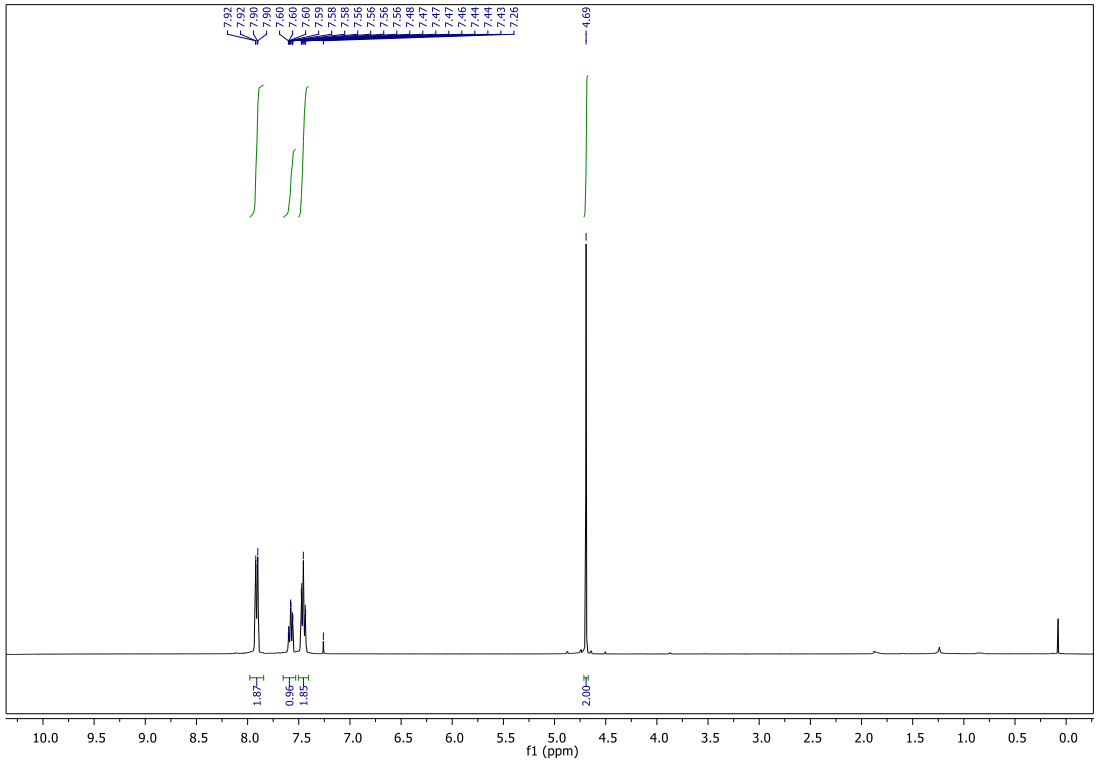

201.87
140.38
128.68
128.39
126.44
77.48
77.16
76.84
48.38
41.36
29.65
f1 (ppm)

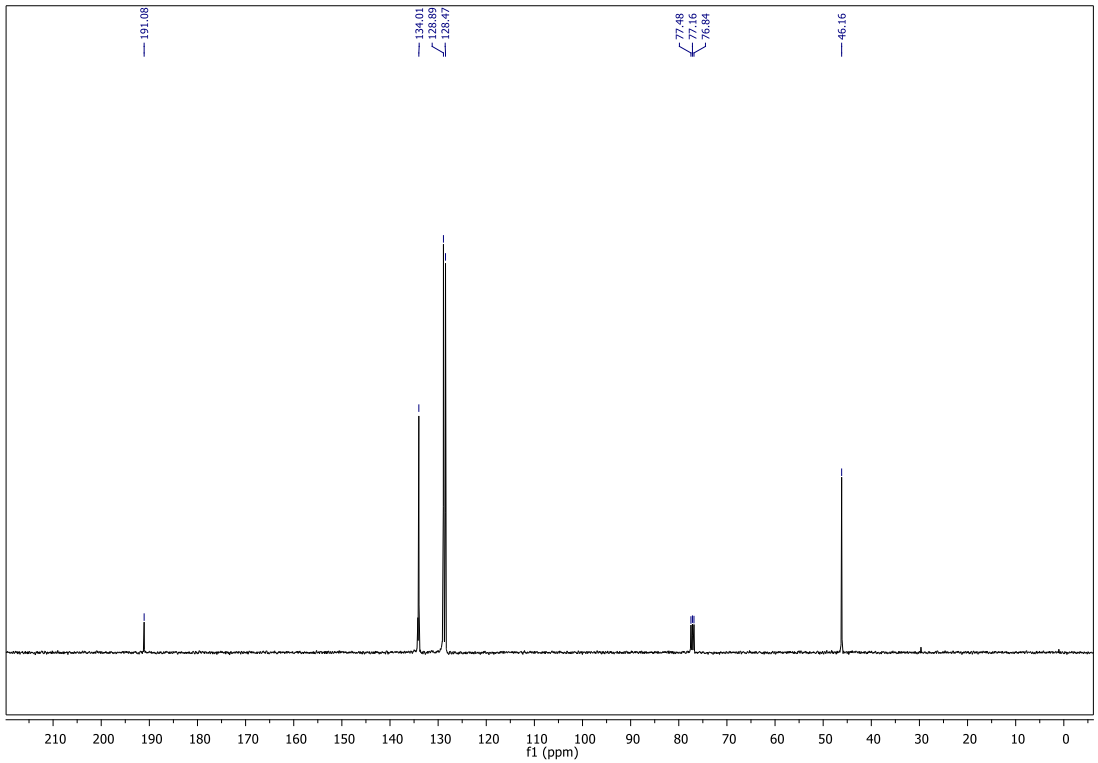
18a)


4.05
2.58
2.58
2.56
2.55
2.55
2.54
1.67
1.67
1.64
1.60
1.50
1.48
1.47
1.47
1.46
1.44
1.20
1.19
1.19
1.17
1.16
1.14
1.11
0.87
0.85
2.00
2.37
5.30
2.40
4.37
2.34
f1 (ppm)

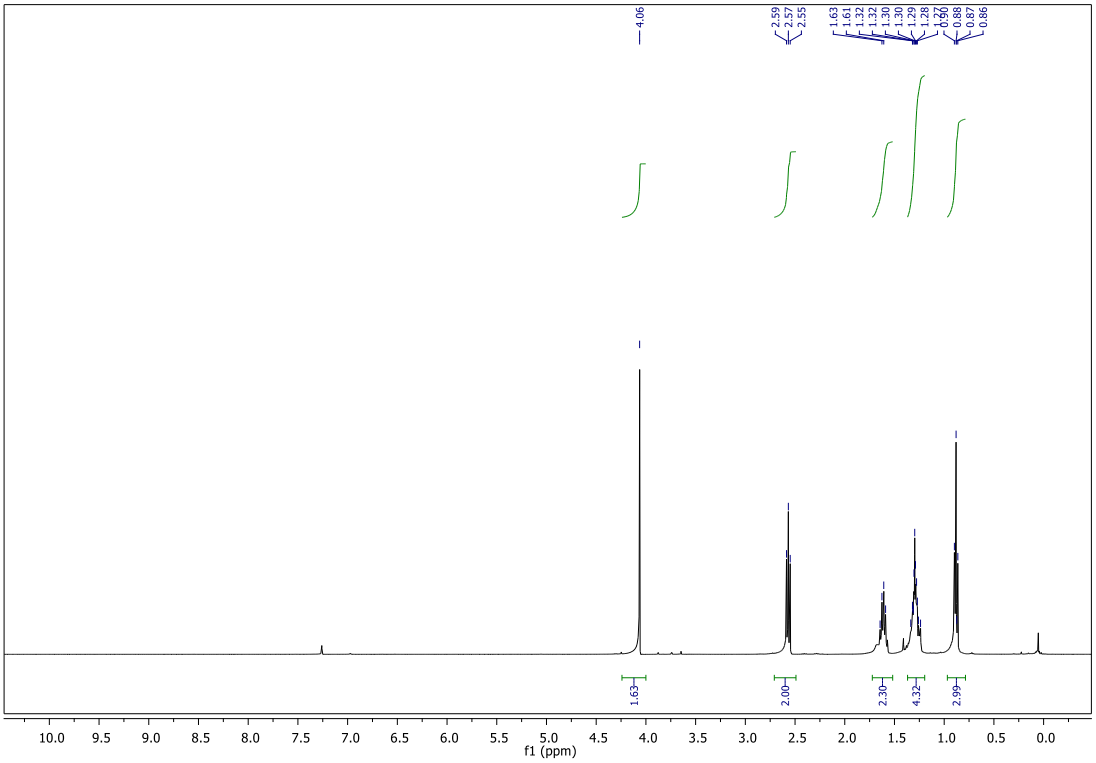

203.08
77.48
77.16
76.84
48.25
37.36
37.20
33.09
30.97
26.53
26.25
f1 (ppm)

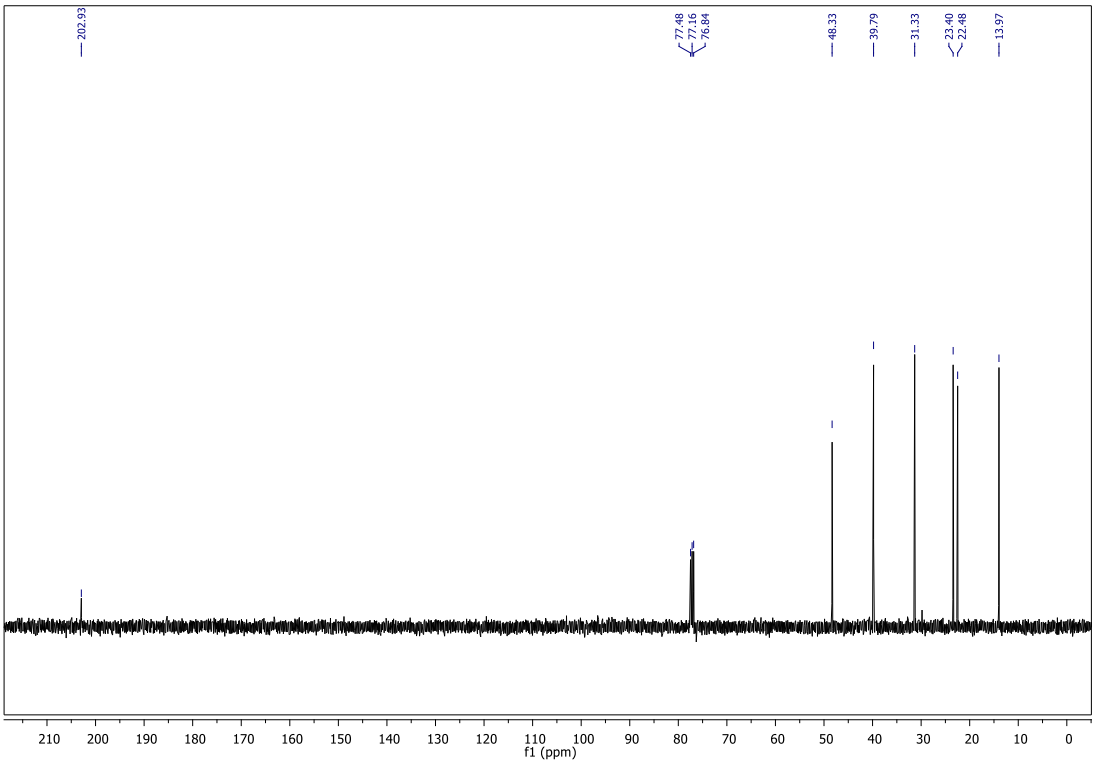
19a)


7.92
7.92
7.90
7.90
7.60
7.60
7.59
7.58
7.58
7.56
7.56
7.56
7.48
7.47
7.47
7.47
7.46
7.44
7.44
7.43
7.26
4.69
1.87
0.96
1.85
2.00
f1 (ppm)

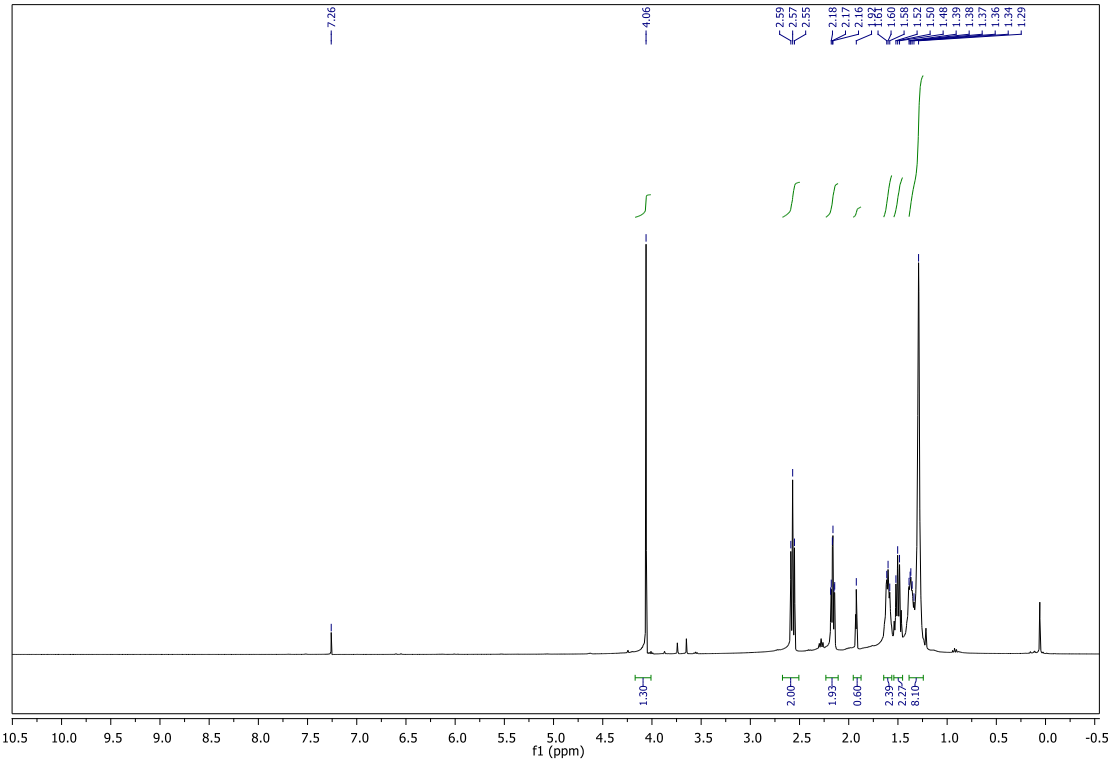

191.08
134.01
128.89
128.47
77.48
77.16
76.84
46.16
f1 (ppm)

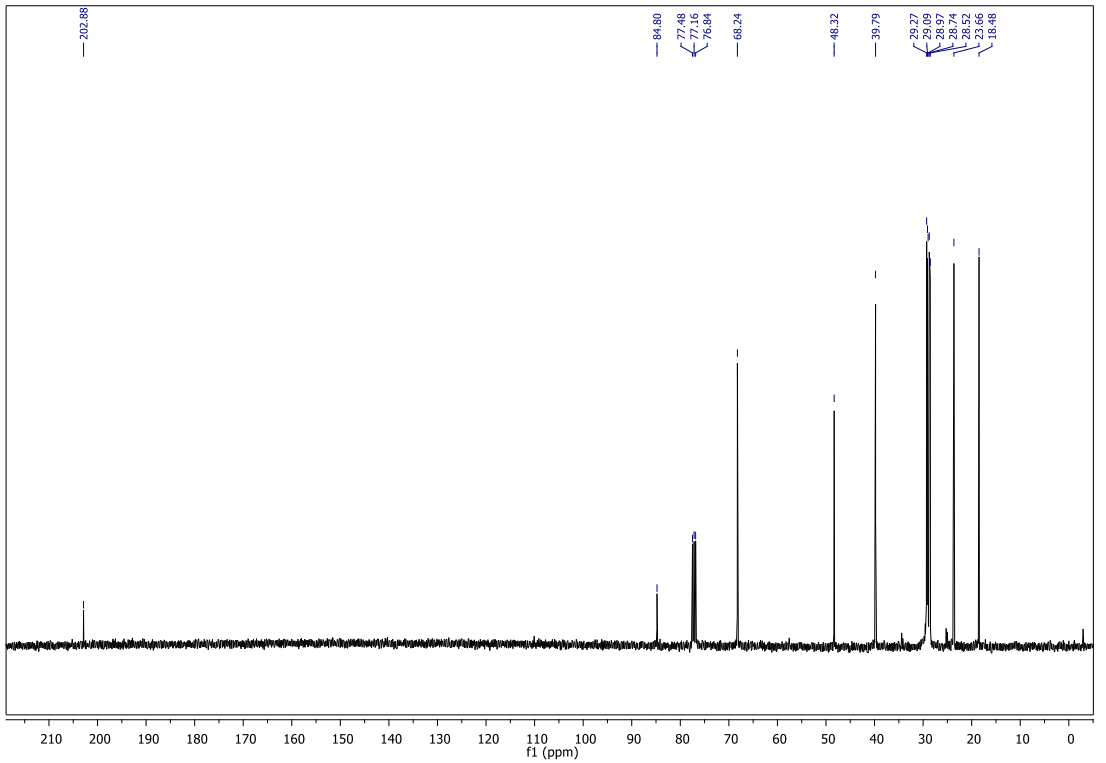
20a)


4.06
2.59
2.57
2.55
1.63
1.61
1.32
1.30
1.29
1.28
0.88
0.87
0.86
1.63
2.00
2.30
4.32
2.99
f1 (ppm)

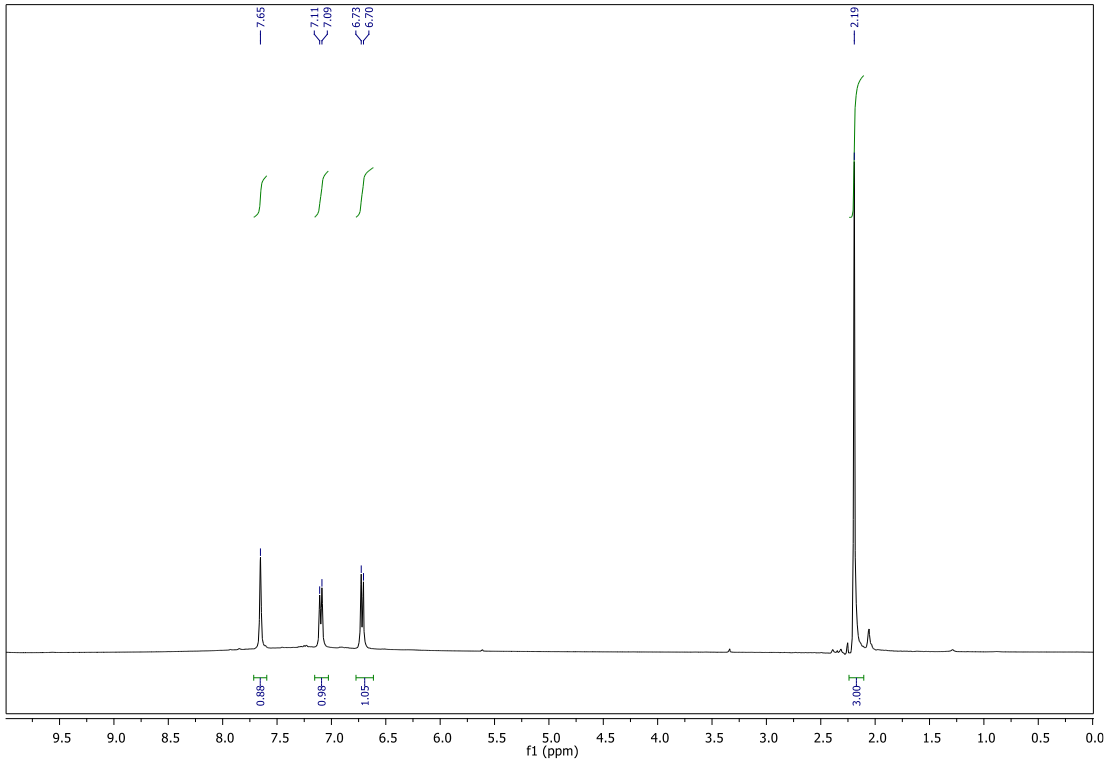

202.93
77.48
77.16
76.84
48.33
39.79
31.33
23.40
22.48
13.97
f1 (ppm)

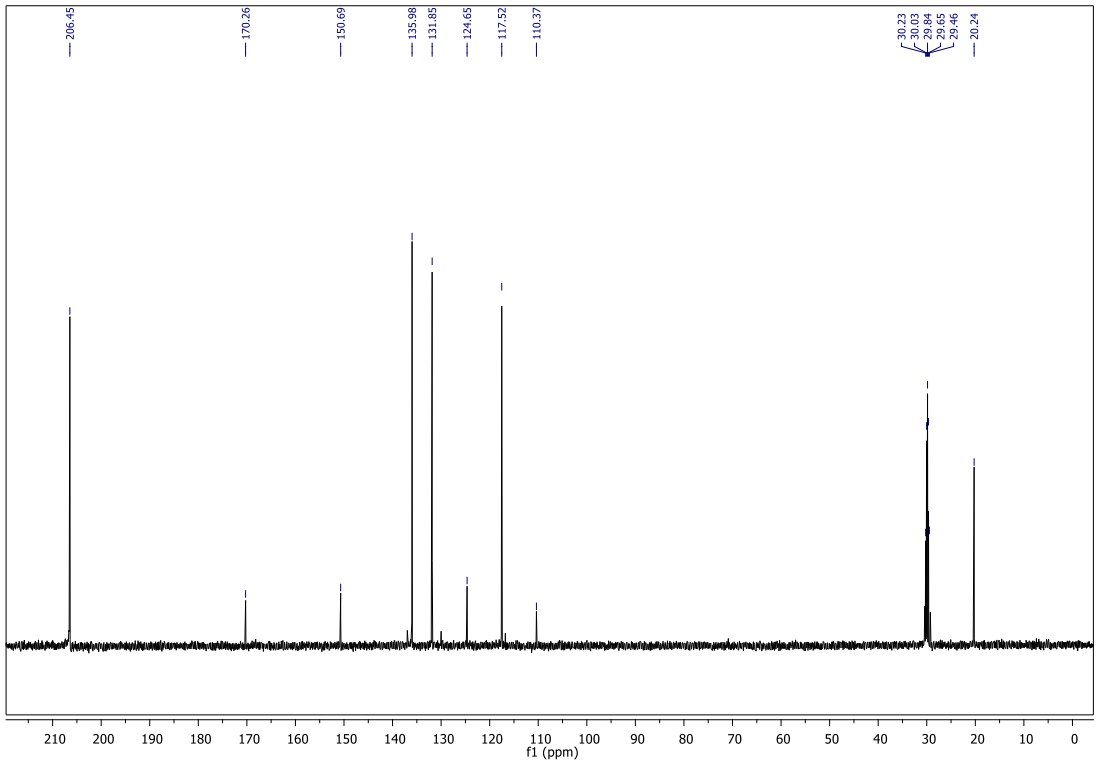
22a)


7.26
4.06
2.59
2.57
2.55
2.18
2.17
2.16
1.62
1.60
1.58
1.52
1.50
1.48
1.39
1.38
1.37
1.36
1.34
1.29
1.30
2.00
1.93
0.60
2.39
2.27
8.10
f1 (ppm)

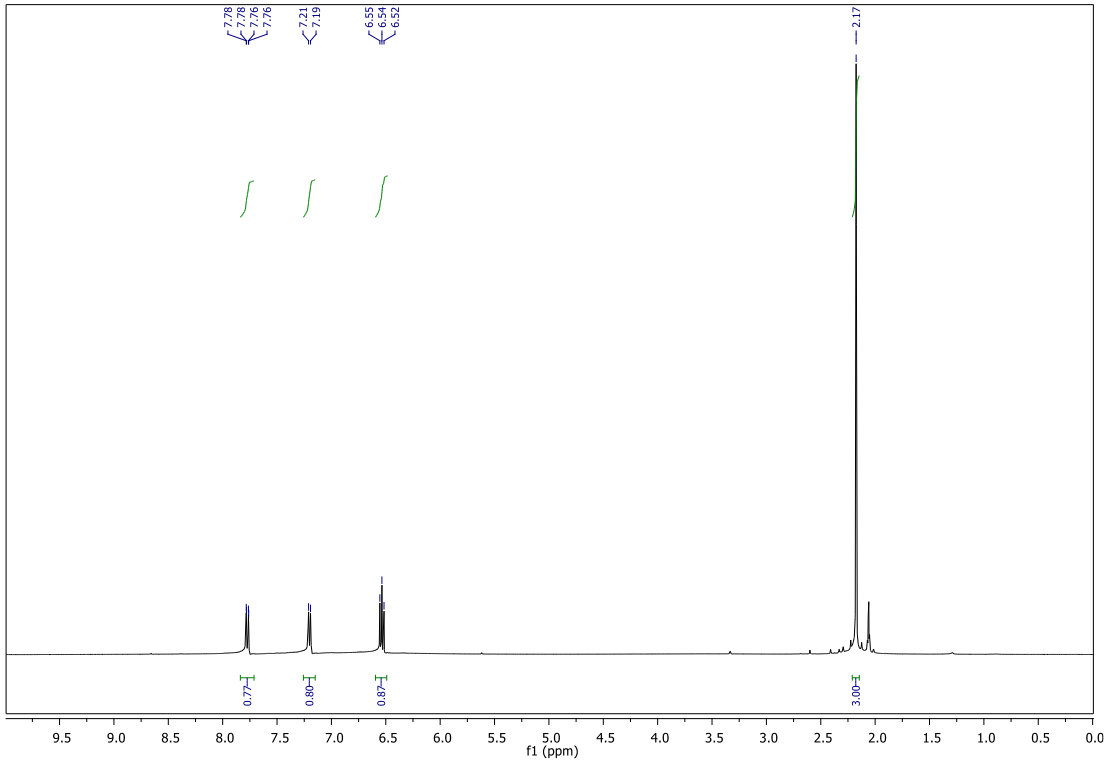

202.88
84.80
77.48
77.16
76.84
68.24
48.32
39.79
29.27
29.09
28.97
28.74
28.52
23.66
18.48
f1 (ppm)

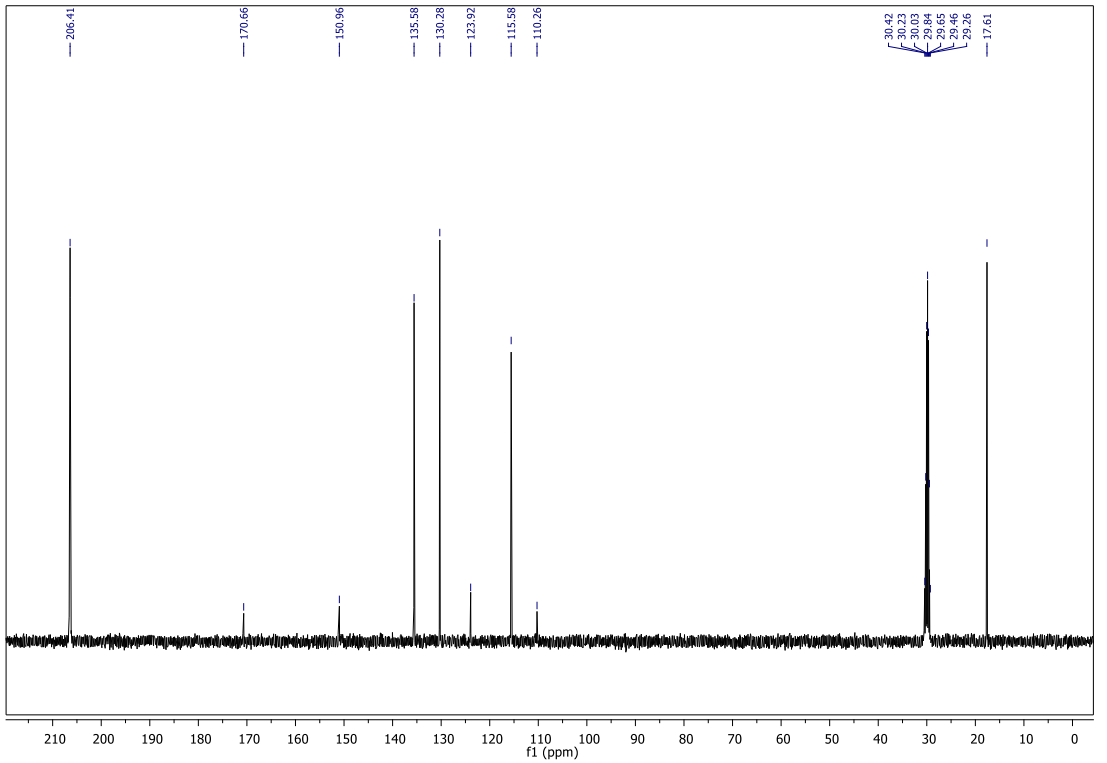
23b)


7.65
7.11
7.09
6.73
6.70
2.19
0.89
0.98
1.05
3.00
f1 (ppm)

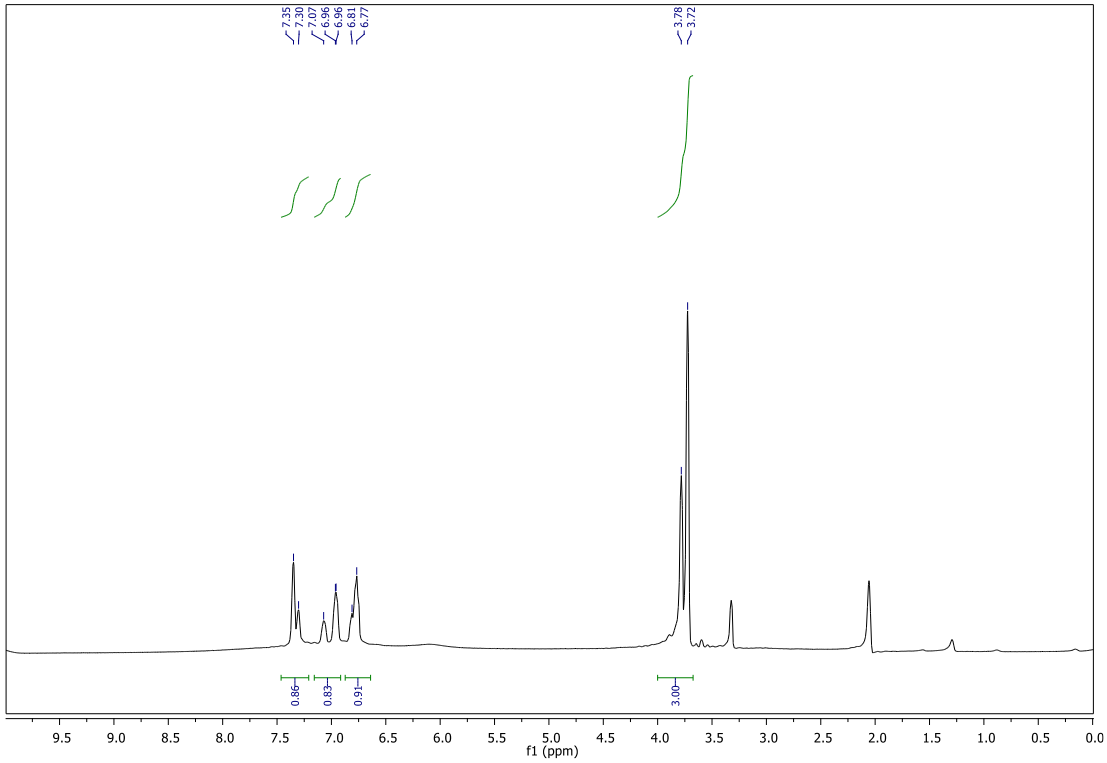

206.45
170.26
150.69
135.98
131.85
124.65
117.52
110.37
30.23
30.03
29.84
29.65
29.46
20.24
f1 (ppm)

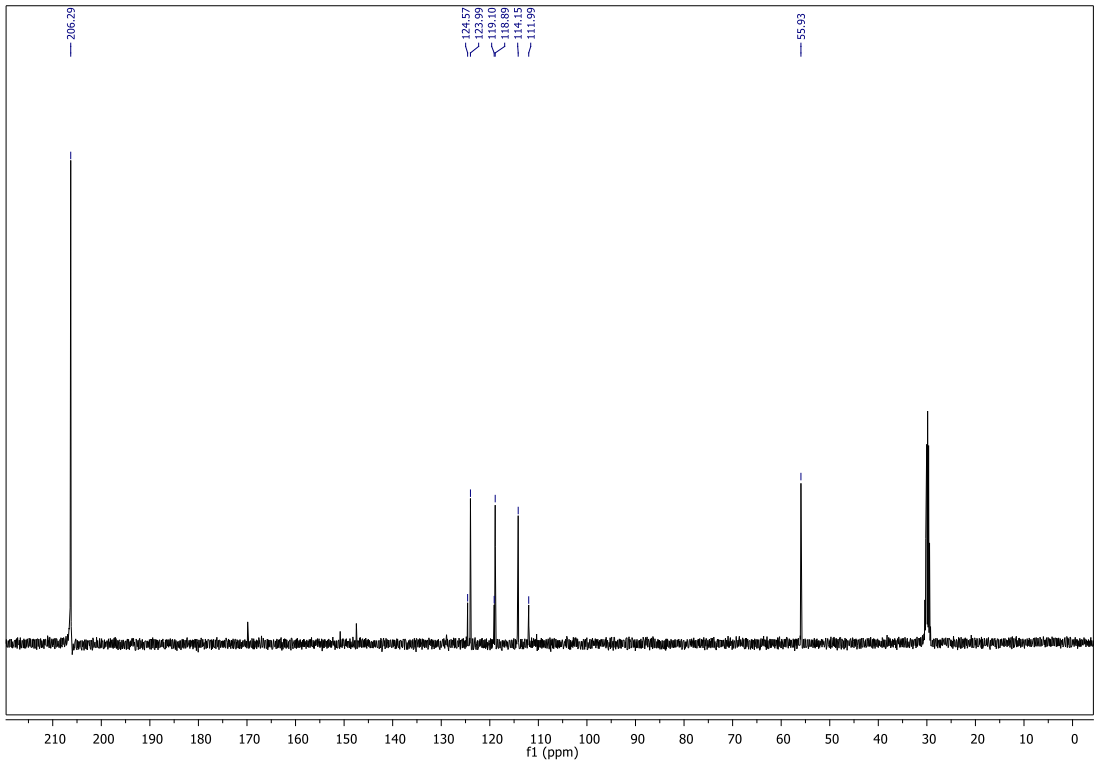
24b)


7.78
7.78
7.76
7.76
7.21
7.19
6.55
6.54
6.52
2.17
0.77
0.80
0.87
3.00
f1 (ppm)

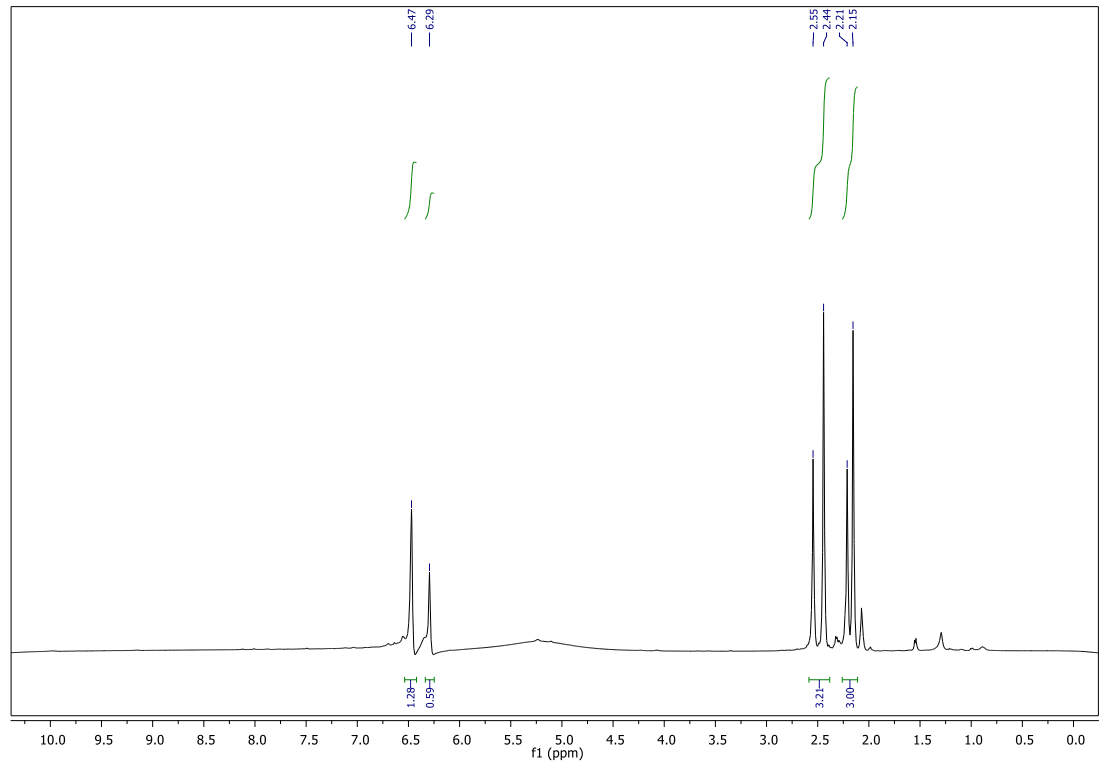

206.41
170.66
150.96
135.58
130.28
123.92
115.58
110.26
30.42
30.23
30.03
29.84
29.65
29.46
29.26
17.61
f1 (ppm)

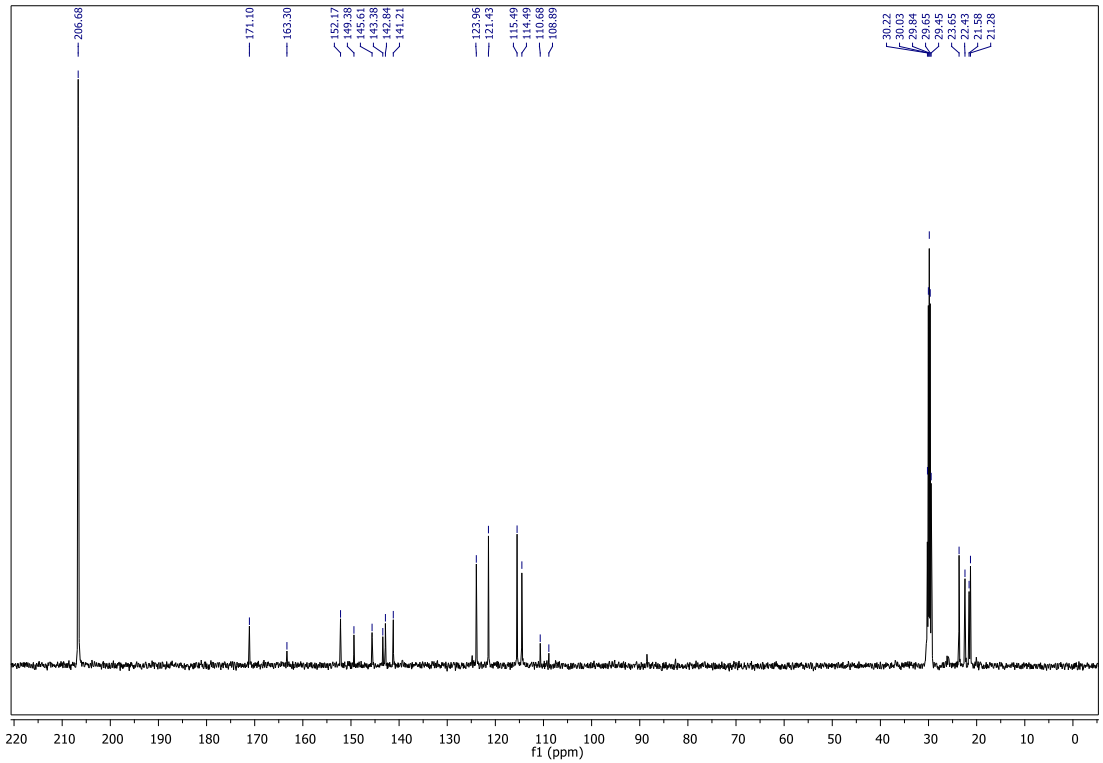
25b)


7.35
7.30
7.07
6.96
6.96
6.81
6.77
3.78
3.72
0.86
0.83
0.91
3.00
f1 (ppm)

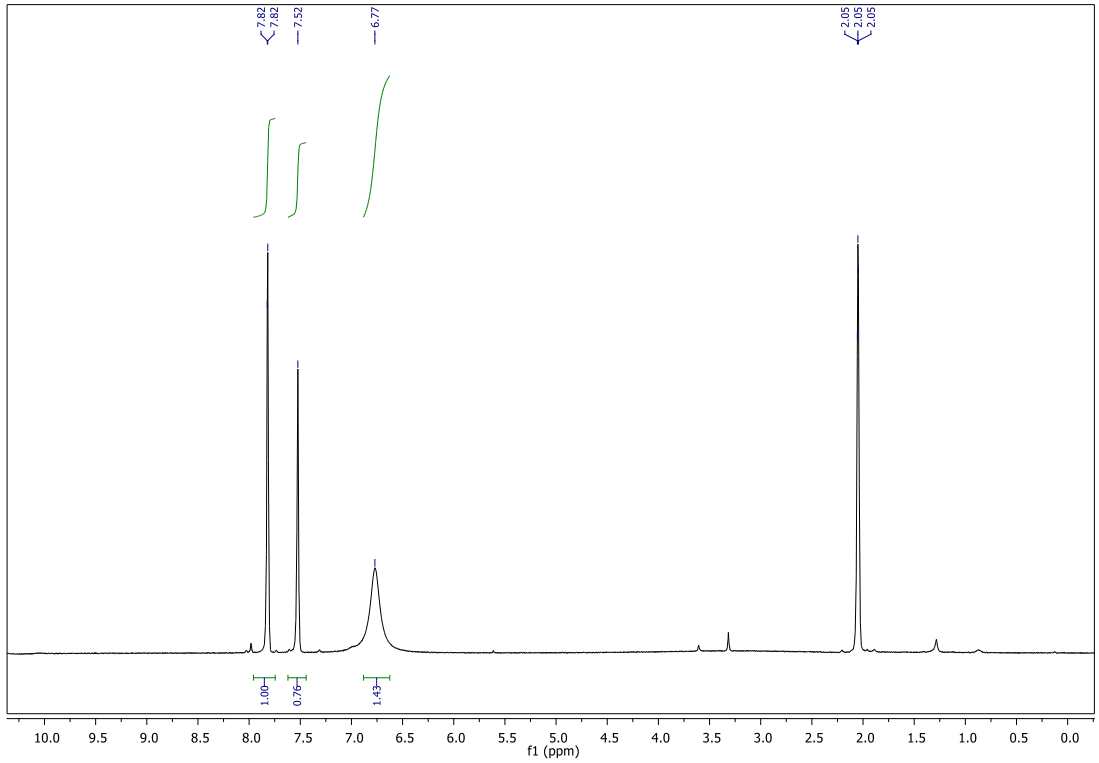

206.29
124.57
123.99
119.10
118.89
114.15
111.99
55.93
f1 (ppm)

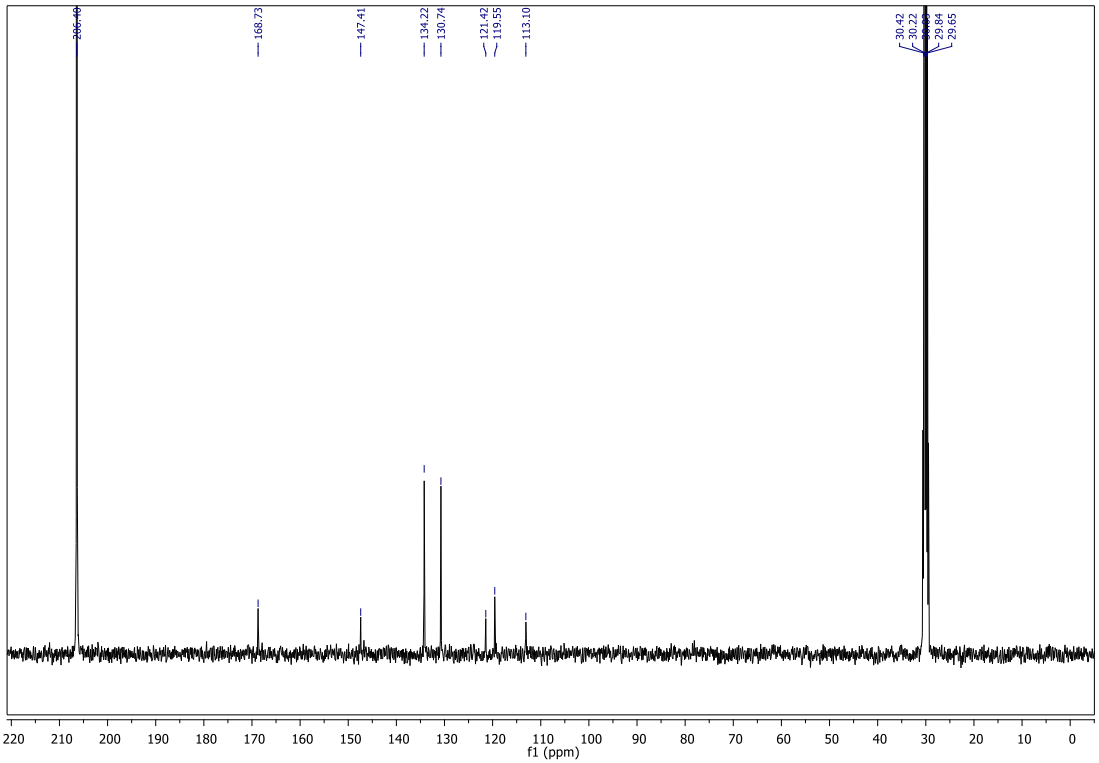
26b)


6.47
6.29
2.55
2.44
2.21
2.15
1.28
0.59
3.21
3.00
f1 (ppm)

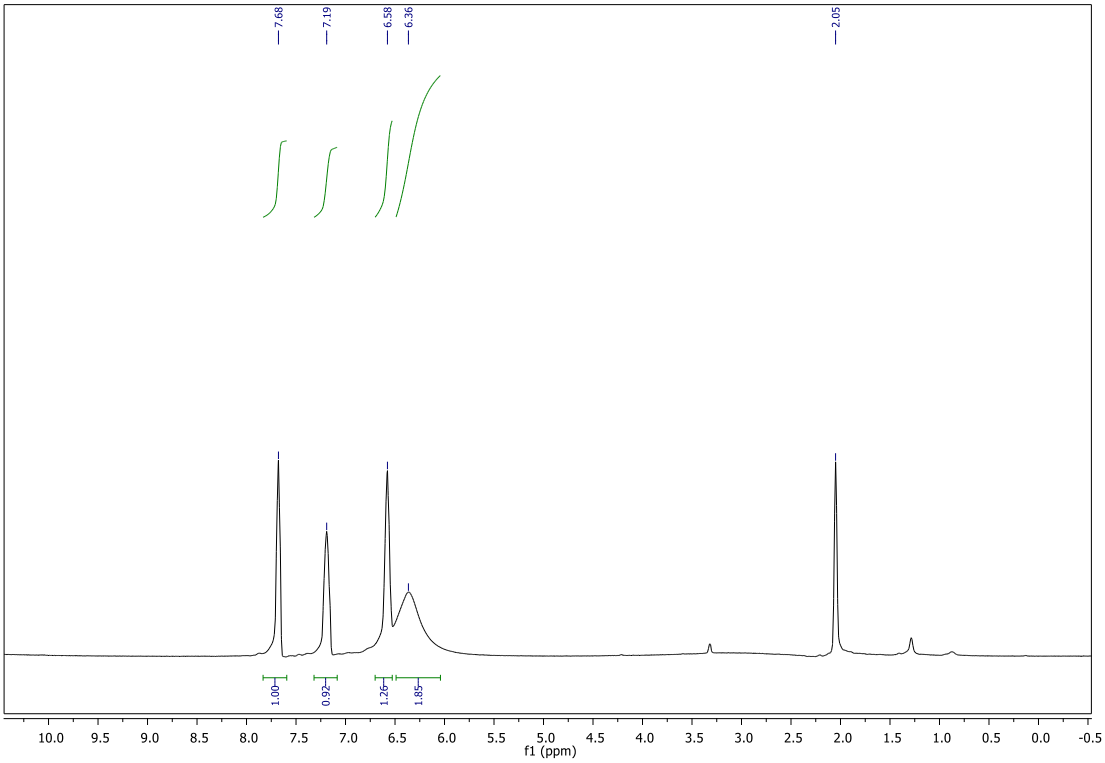

206.68
171.10
163.30
152.17
149.38
145.61
143.38
142.84
141.21
123.96
121.43
115.49
114.49
110.68
108.89
30.22
30.03
29.84
29.65
29.45
23.65
22.43
21.58
21.28
f1 (ppm)

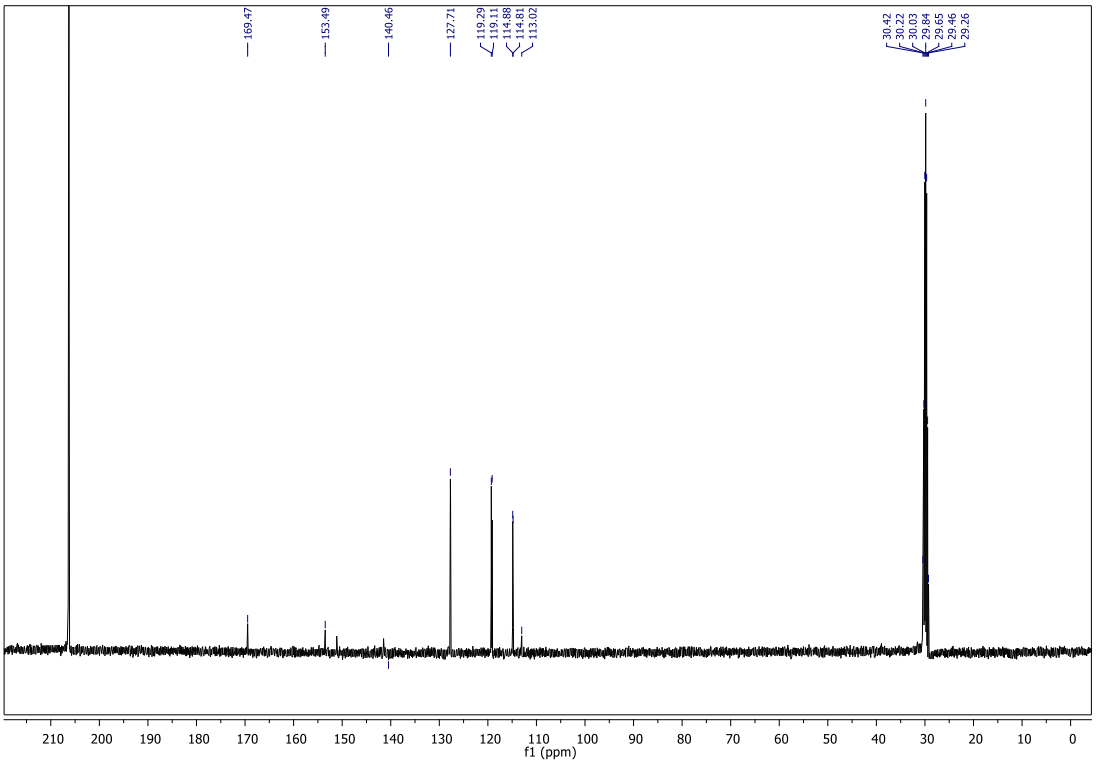
27b)


7.82
7.82
7.52
6.77
2.05
2.05
2.05
1.00
0.76
1.43
f1 (ppm)

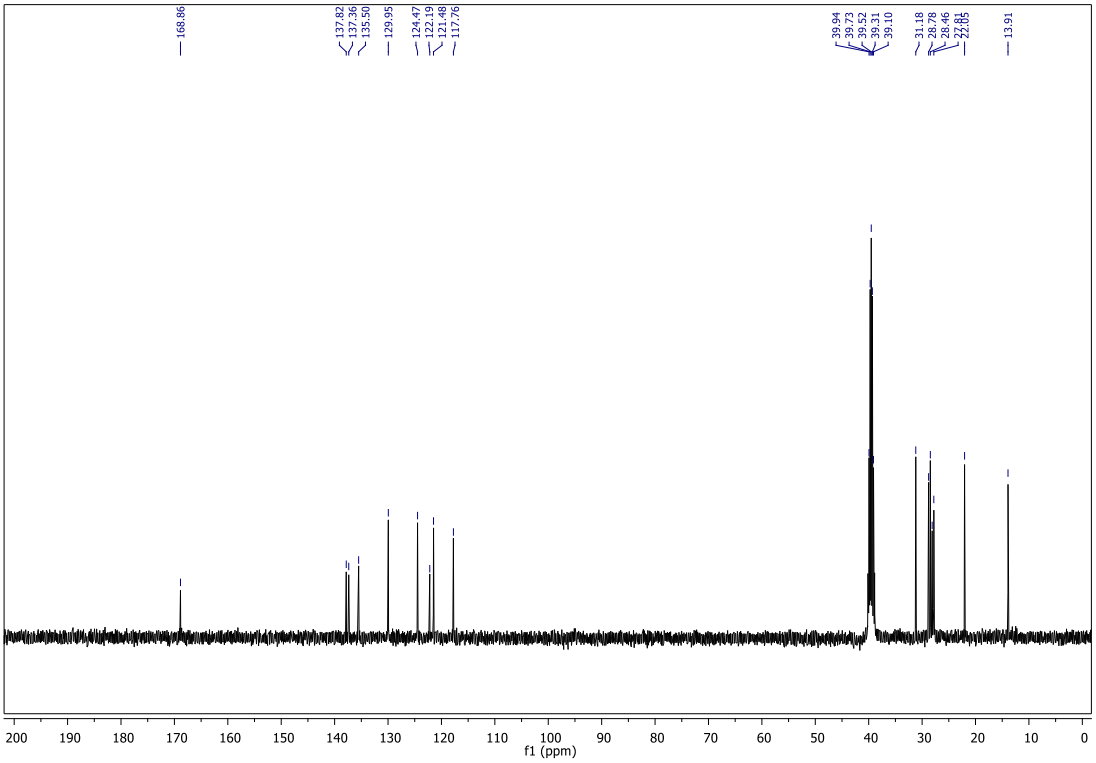

168.73
147.41
134.22
130.74
121.42
119.55
113.10
30.42
30.22
29.84
29.65
f1 (ppm)

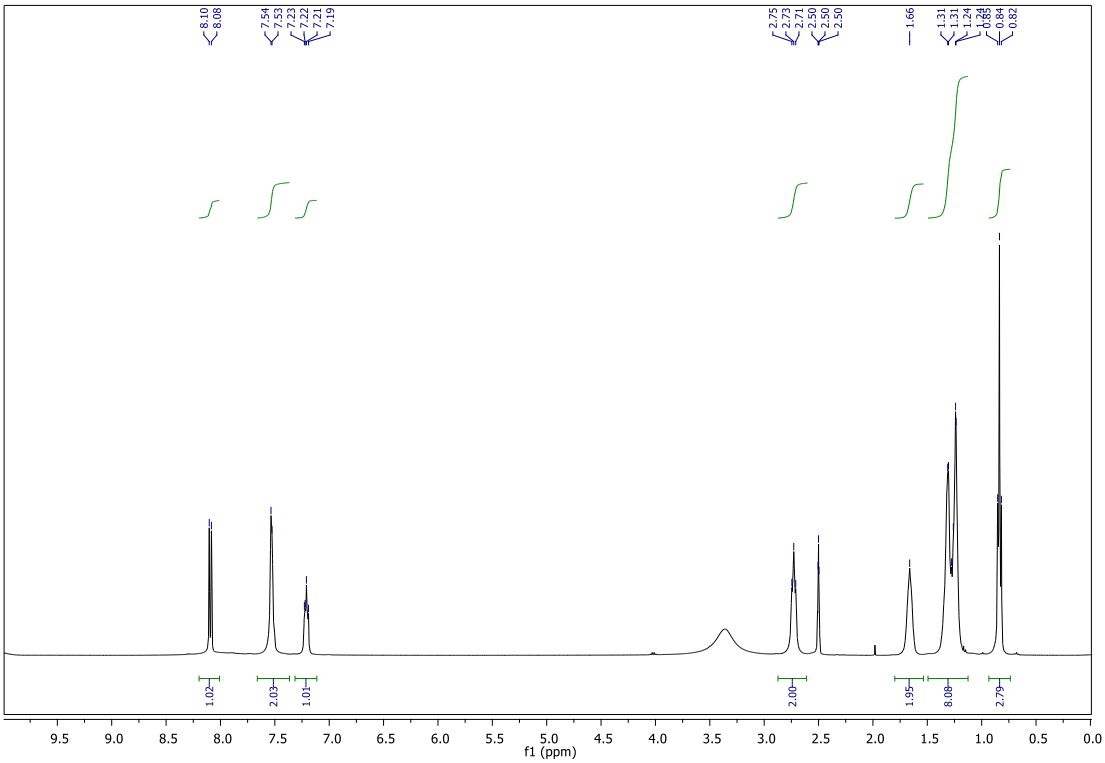
28b)


7.68
7.19
6.58
6.36
2.05
1.00
0.92
1.26
1.85
f1 (ppm)

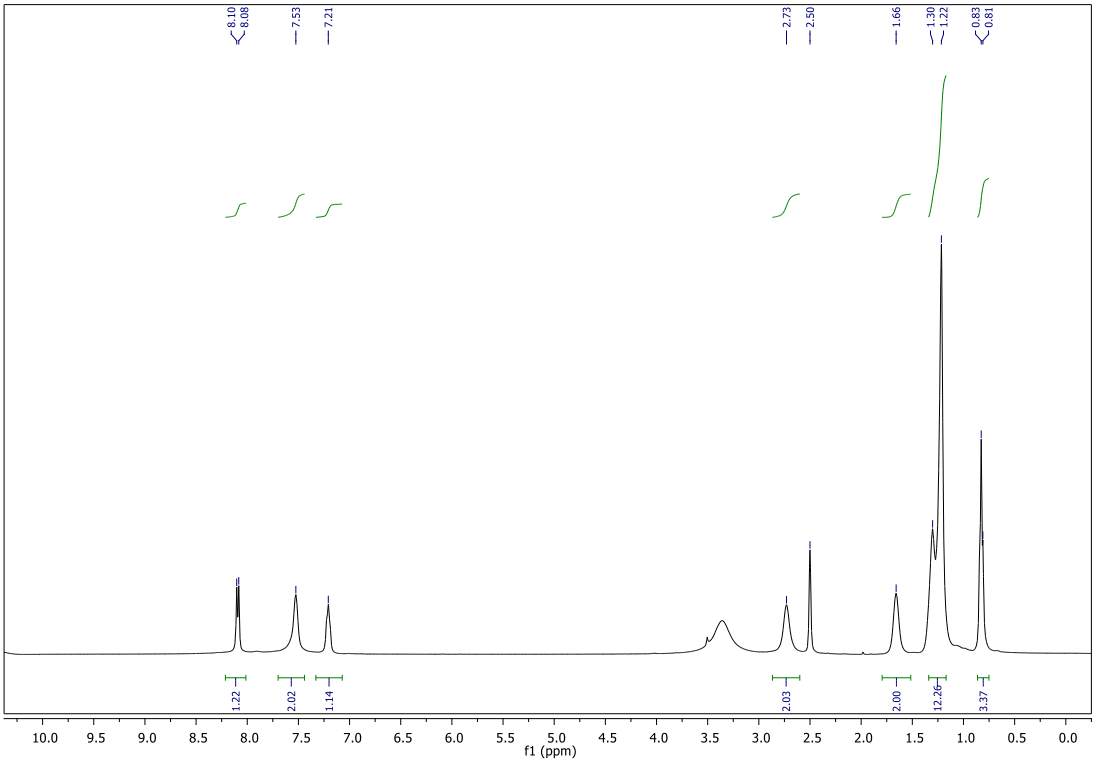

169.47
153.49
140.46
127.71
119.29
119.11
114.88
114.81
113.02
30.42
30.22
30.03
29.84
29.65
29.46
29.26
f1 (ppm)

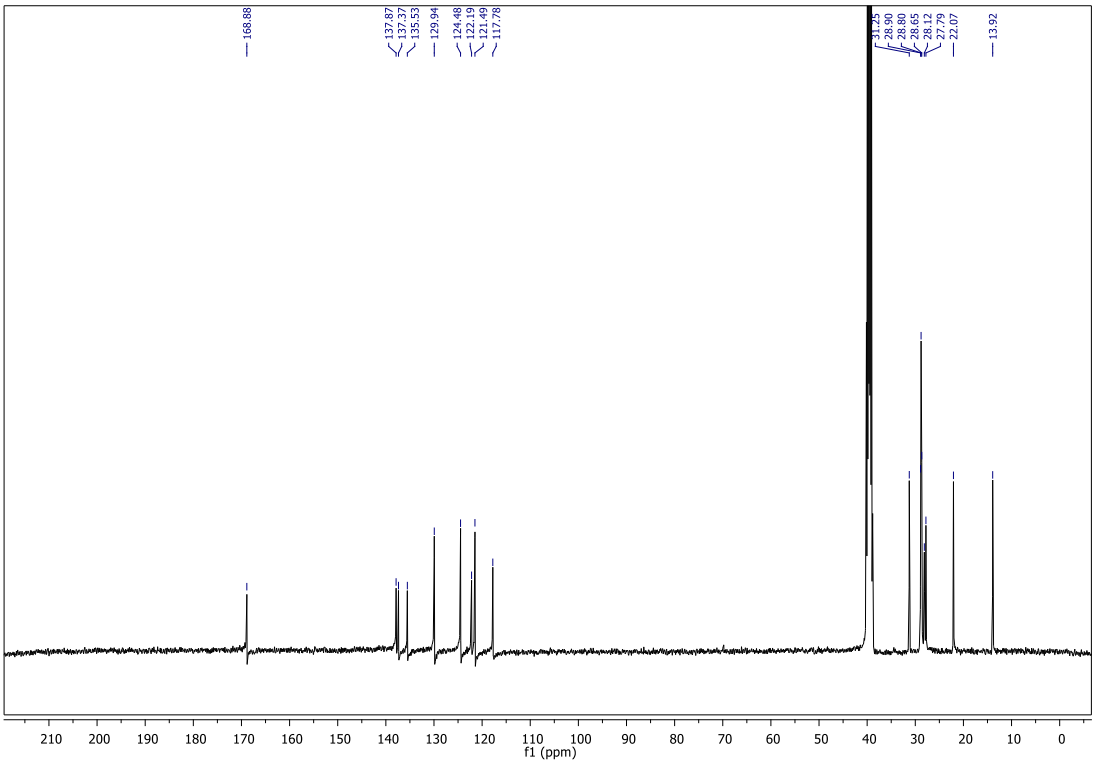
2)


168.86
137.82
137.36
135.50
129.95
124.47
122.19
121.48
117.76
39.94
39.73
39.52
39.31
39.10
31.18
28.78
28.46
22.81
13.91
f1 (ppm)

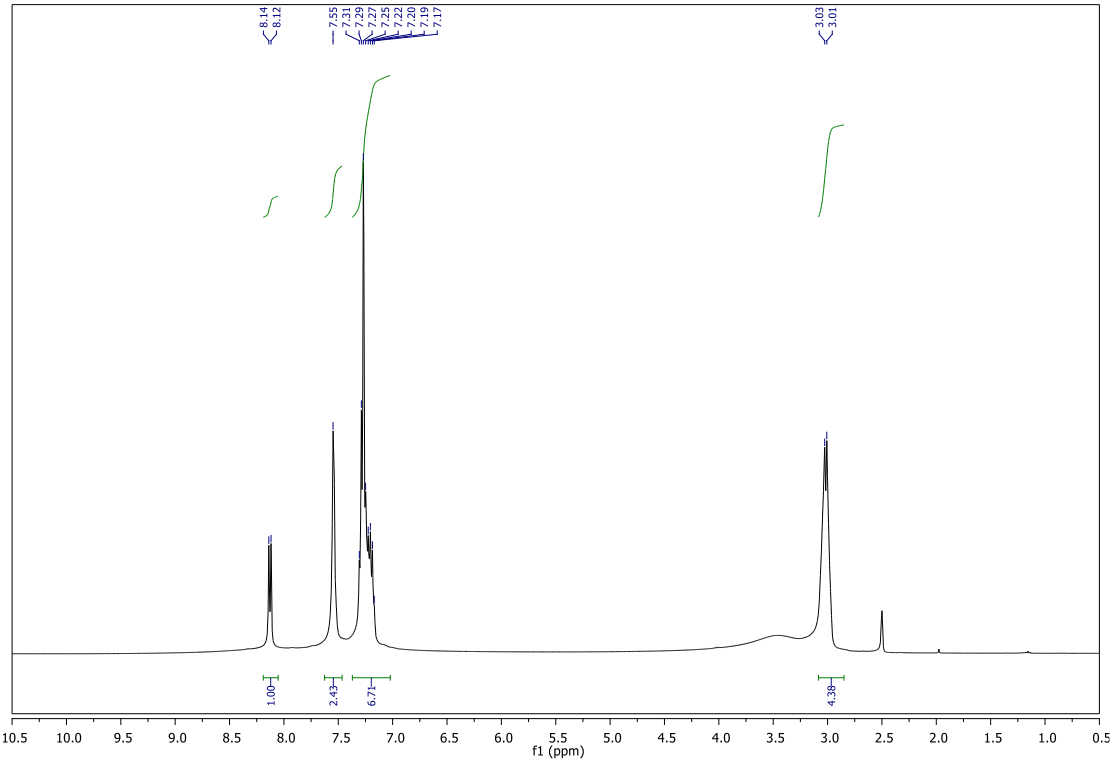

8.10
8.08
7.54
7.53
7.23
7.22
7.21
7.19
2.75
2.73
2.71
2.50
2.50
2.50
1.66
1.31
1.31
1.24
0.85
0.84
0.82
1.02
2.03
1.01
2.00
1.95
8.08
2.79
f1 (ppm)

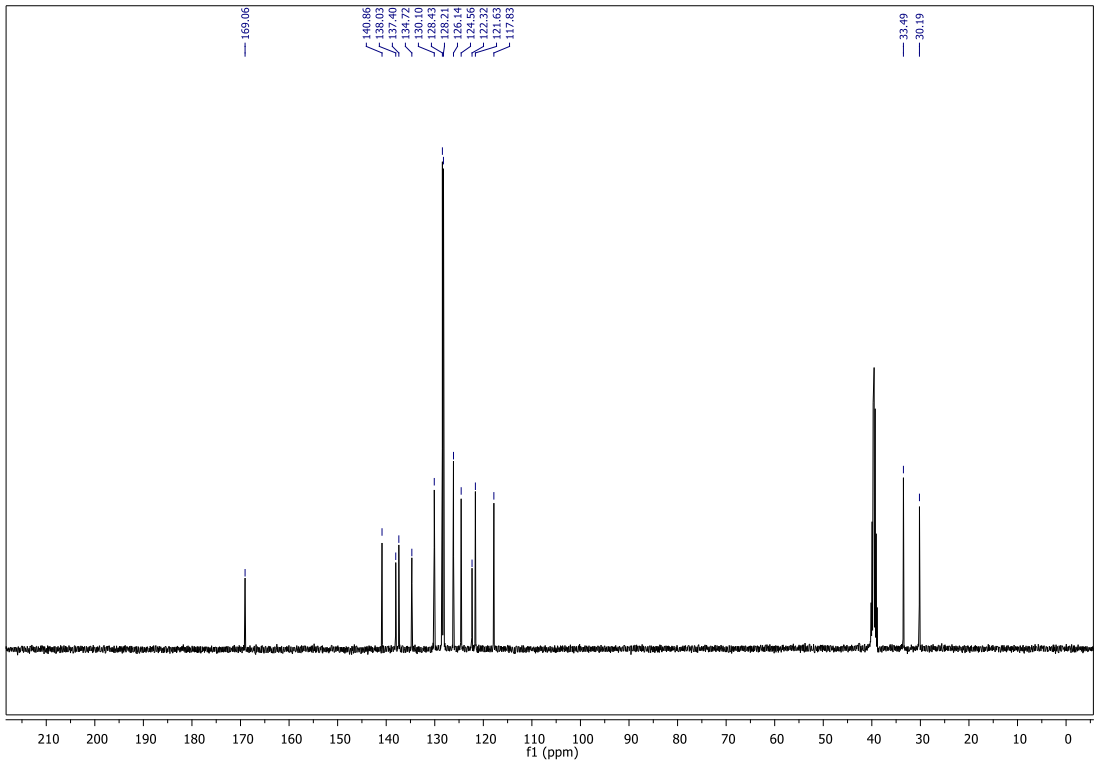
16)


8.10
8.08
7.53
7.21
2.73
2.50
1.66
1.30
1.22
0.83
0.81
1.22
2.02
1.14
2.03
2.00
12.26
3.37
f1 (ppm)


168.88
137.87
137.37
135.53
129.94
124.48
122.19
121.49
117.78
31.25
28.90
28.80
28.65
28.12
27.79
22.07
13.92
f1 (ppm)

17)


8.14
8.12
7.55
7.31
7.29
7.27
7.25
7.22
7.20
7.19
7.17
3.03
3.01
1.00
2.43
6.71
4.38
f1 (ppm)


169.06
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138.03
137.40
134.72
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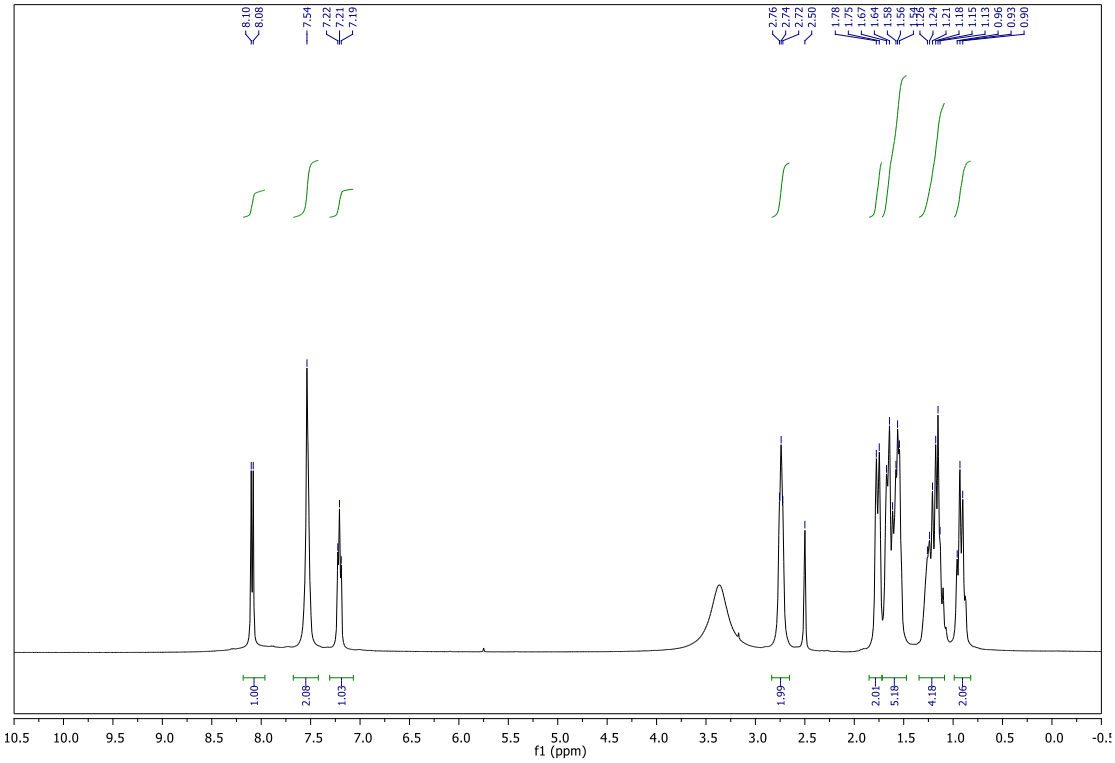
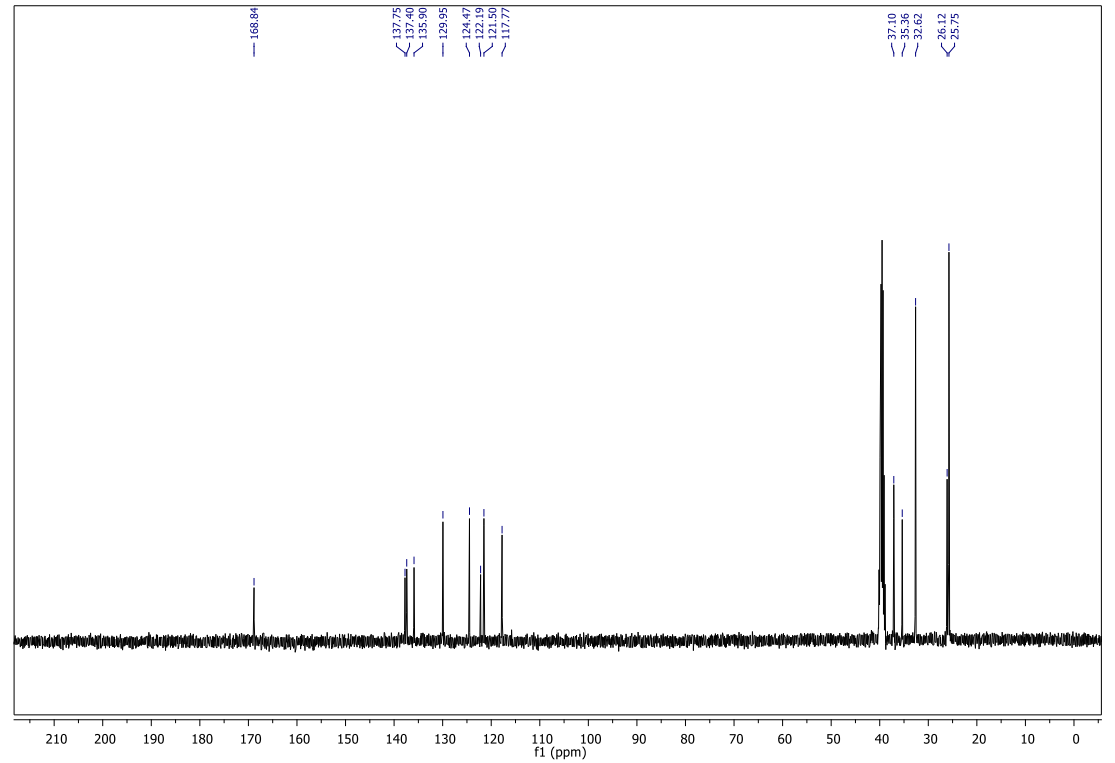
128.43
128.21
126.14
125.56
122.32
121.63
117.83
33.49
30.19
f1 (ppm)

18)


8.10
8.08
7.54
7.22
7.21
7.19
2.76
2.74
2.72
2.50
1.78
1.75
1.67
1.64
1.58
1.56
1.24
1.21
1.18
1.15
1.13
0.96
0.93
0.90
1.00
2.08
1.03
1.99
2.01
5.18
4.18
2.06
f1 (ppm)


168.84
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129.95
124.47
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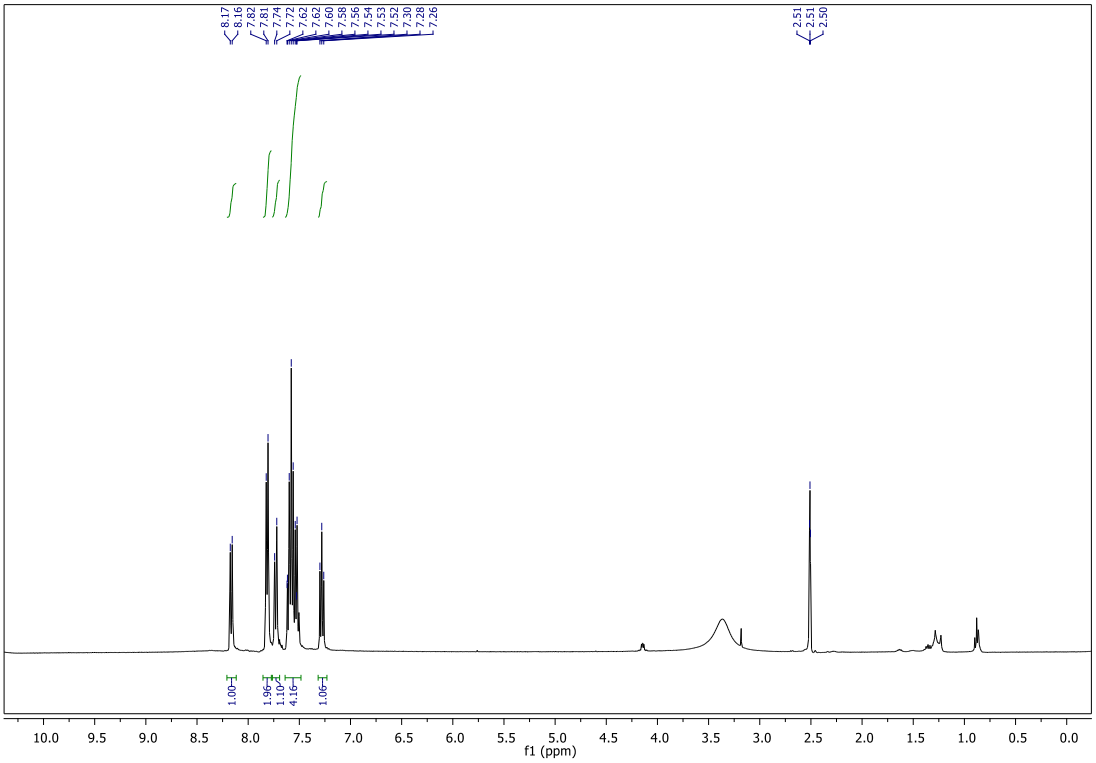
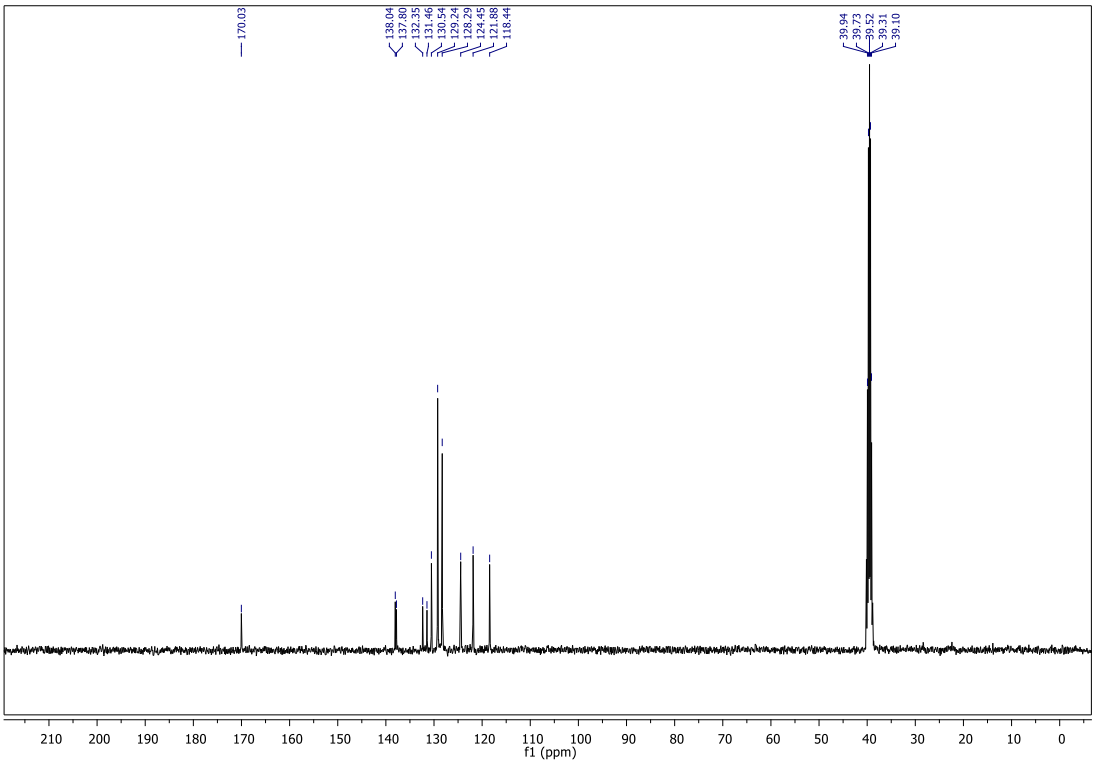
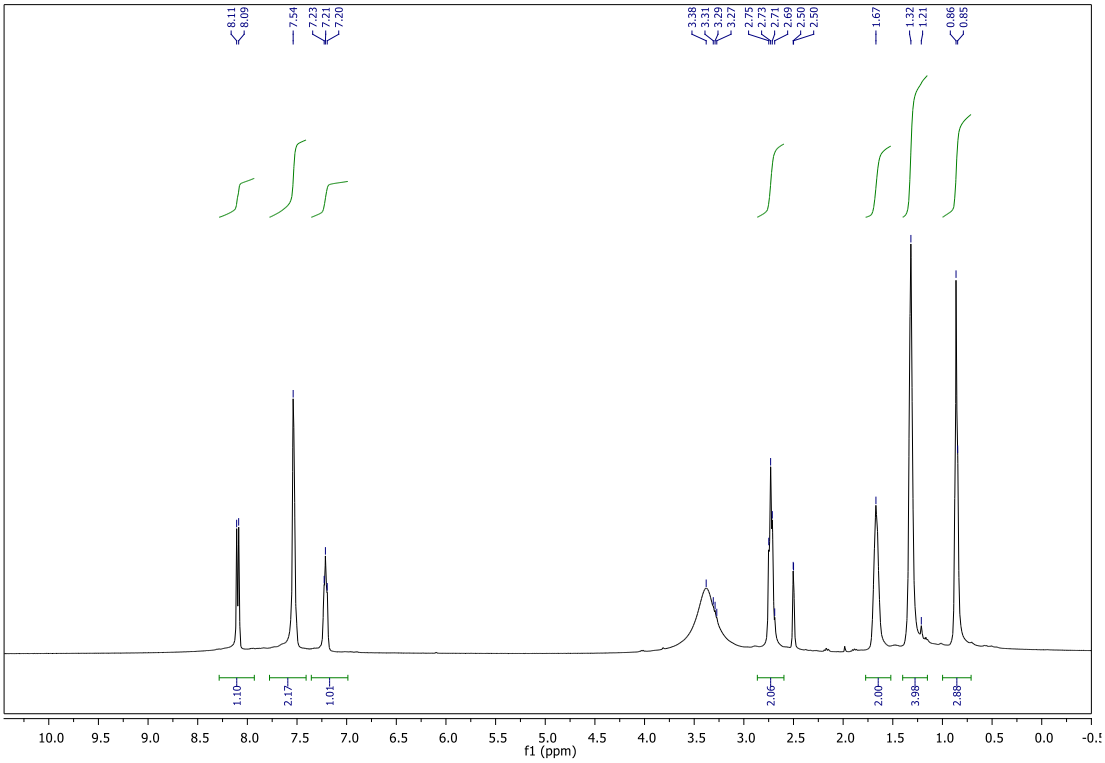
121.50
117.77
37.10
35.36
32.62
26.12
25.75
f1 (ppm)

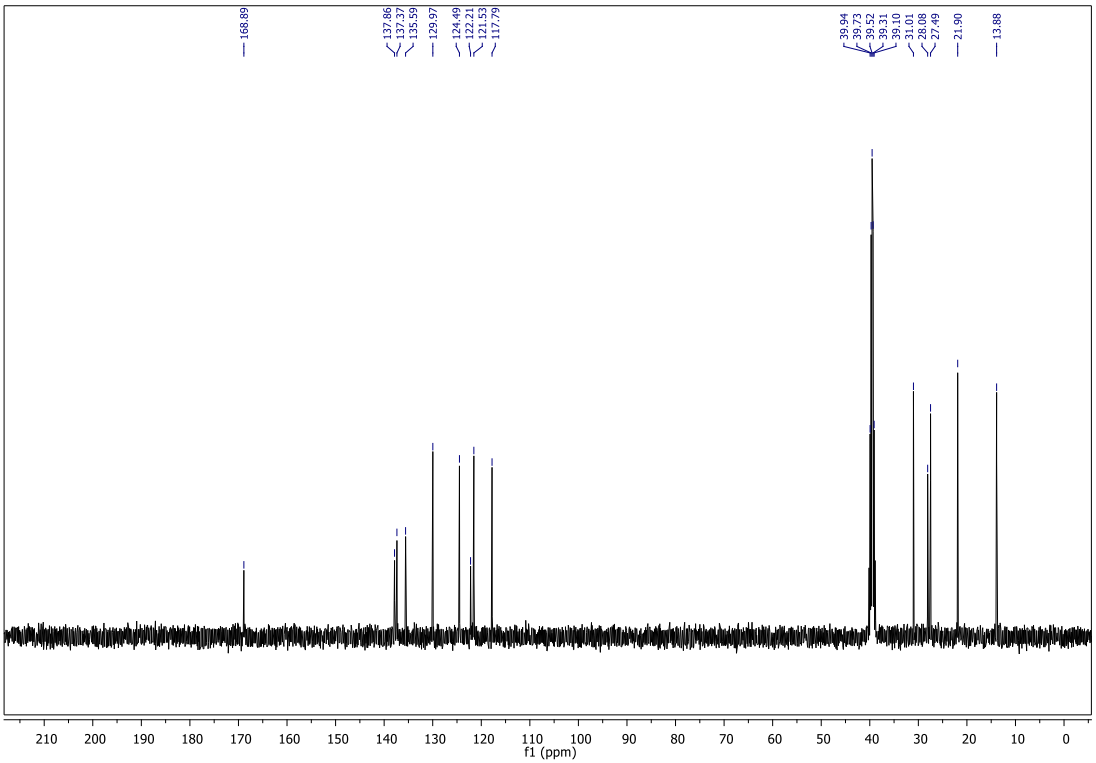
19)


8.17
8.16
7.82
7.81
7.74
7.72
7.62
7.62
7.60
7.58
7.56
7.54
7.53
7.52
7.30
7.28
7.26
2.51
2.51
2.50
1.00
1.96
1.10
4.16
1.06
f1 (ppm)


170.03
138.04
137.80
132.35
131.46
130.54
129.24
129.09
124.45
121.88
118.44
39.94
39.73
39.52
39.31
39.10
f1 (ppm)

20)


8.11
8.09
7.54
7.23
7.21
7.20
3.38
3.31
3.29
3.27
2.75
2.73
2.71
2.69
2.50
2.50
1.67
1.32
1.21
0.86
0.85
1.10
2.17
1.01
2.06
2.00
3.98
2.88
f1 (ppm)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137.37
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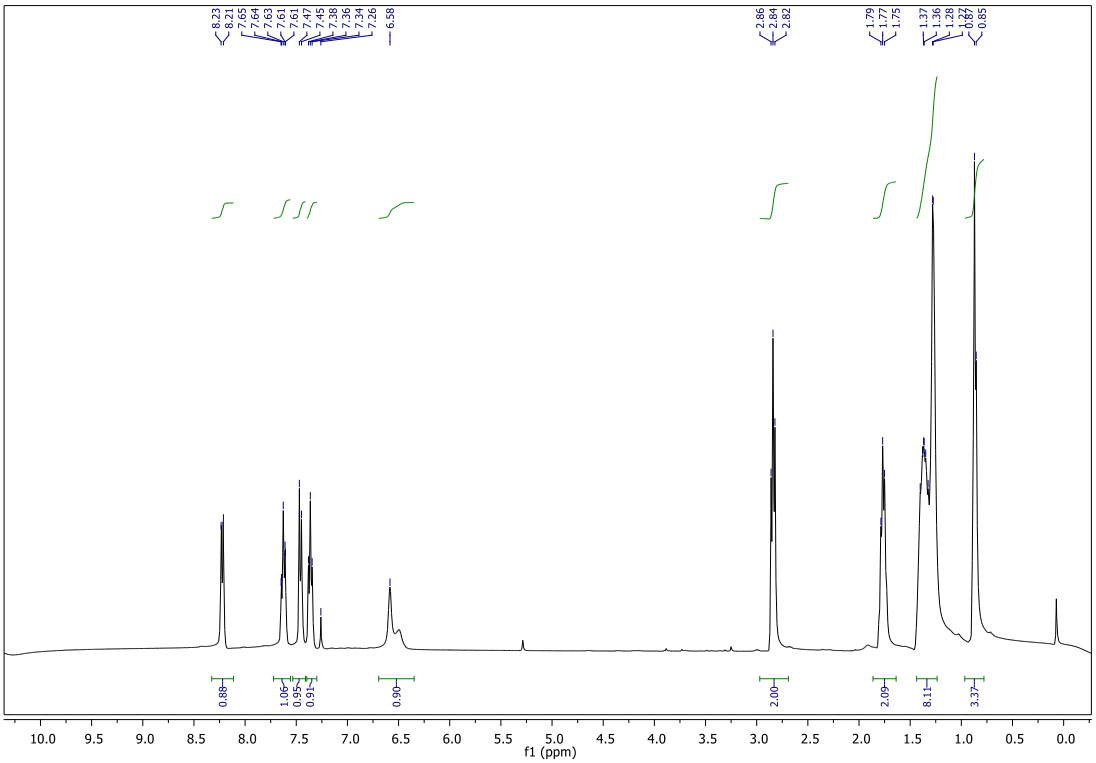
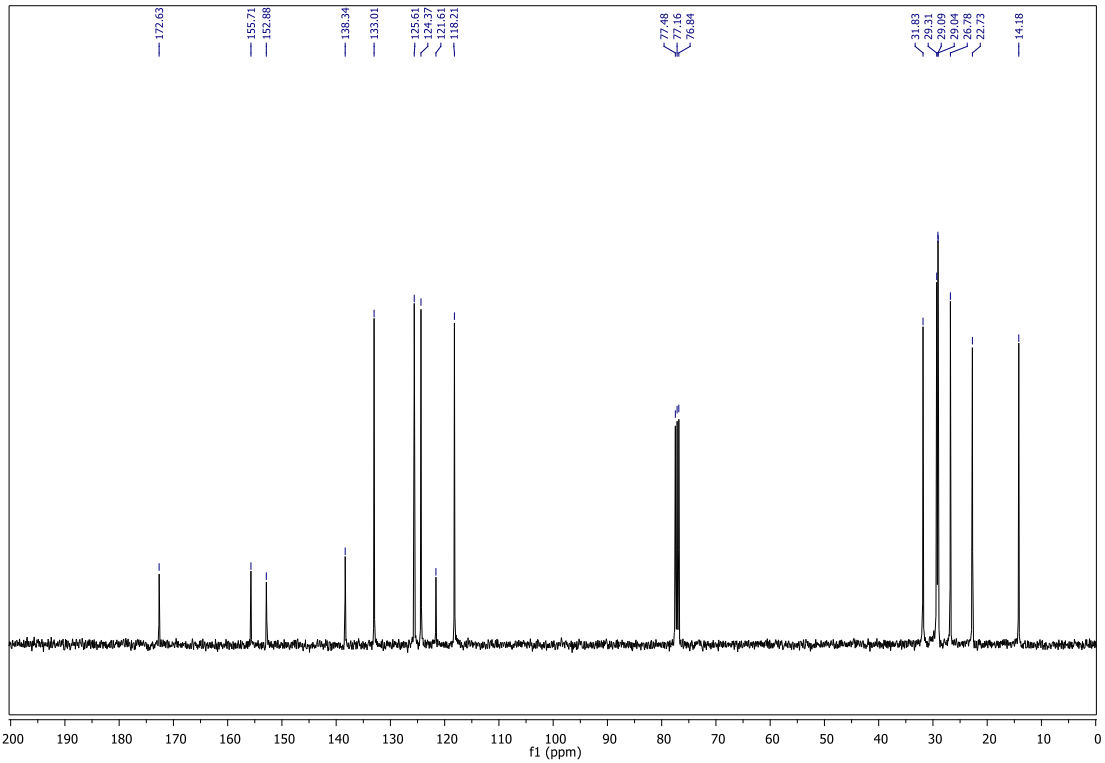
124.49
122.21
121.53
117.79
39.94
39.73
39.52
39.31
39.10
31.01
28.08
27.49
21.90
13.88
f1 (ppm)

21)


8.23
8.21
7.65
7.64
7.63
7.61
7.61
7.47
7.45
7.38
7.36
7.34
7.26
6.58
2.86
2.84
2.82
1.79
1.77
1.75
1.37
1.36
1.28
0.87
0.85
0.88
1.06
0.95
0.91
0.90
2.00
2.09
8.11
3.37
f1 (ppm)


172.63
155.71
152.88
138.34
133.01
125.61
124.37
121.61
118.21
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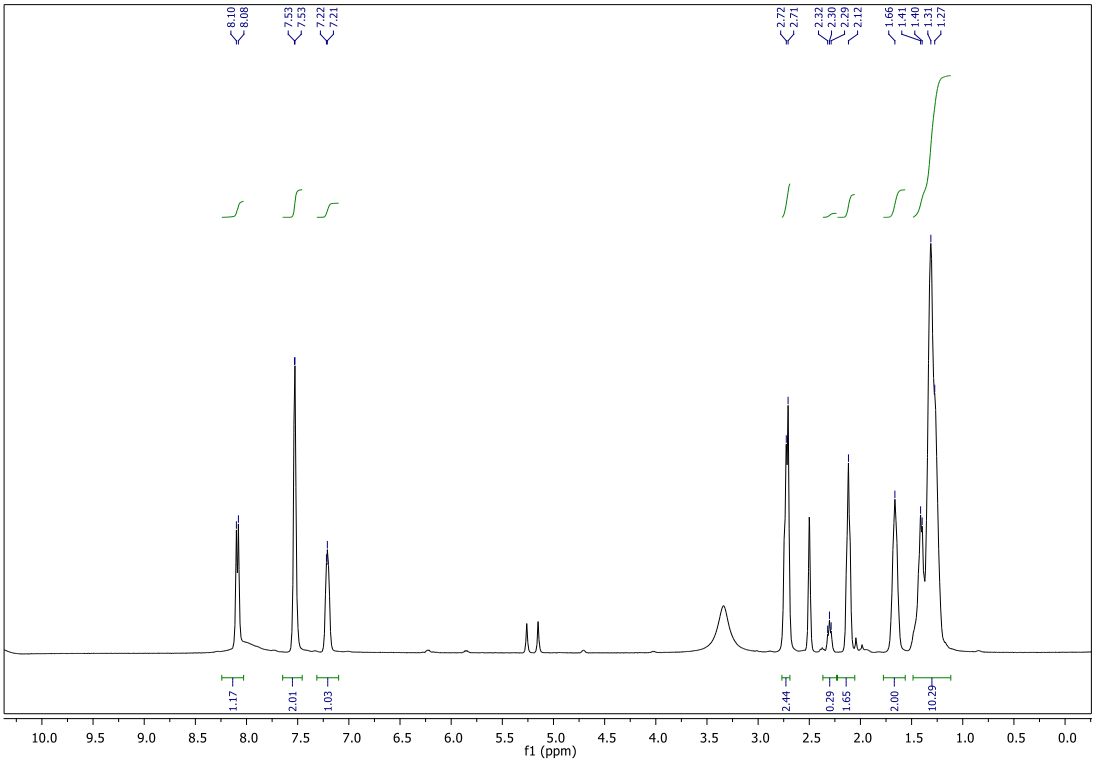
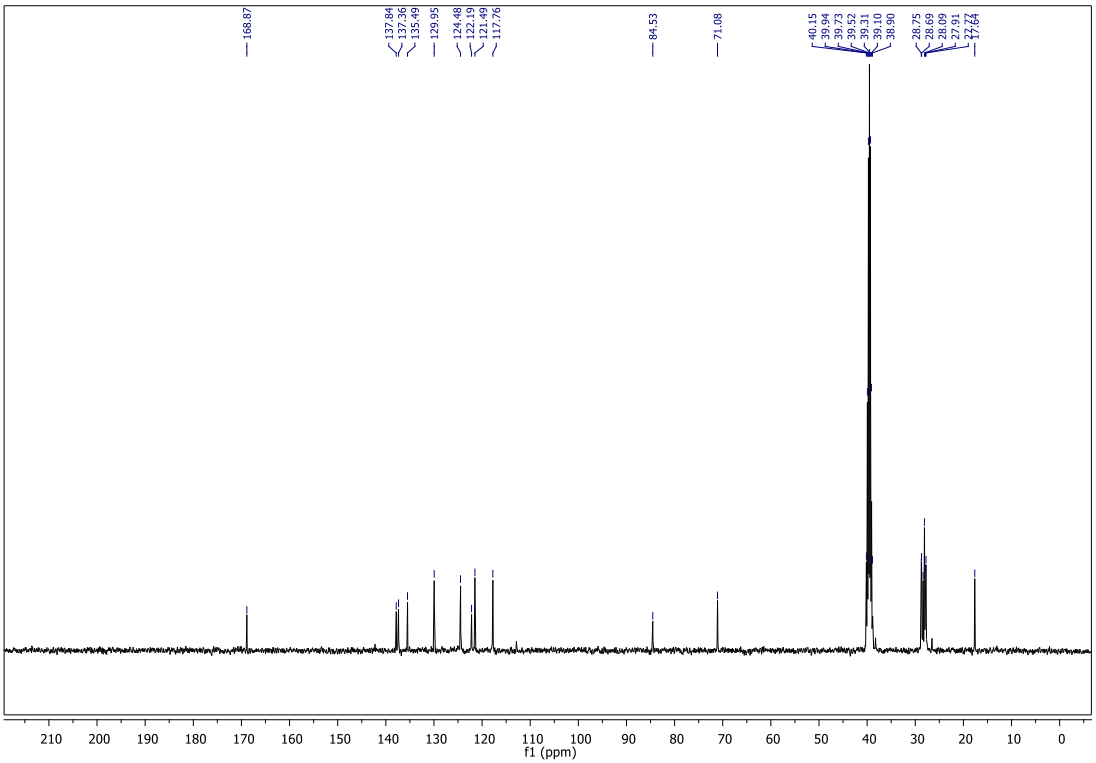
77.16
76.84
31.83
29.31
29.09
29.04
26.78
22.73
14.18
f1 (ppm)

22)


8.10
8.08
7.53
7.53
7.22
7.21
2.72
2.71
2.32
2.30
2.29
2.12
1.66
1.41
1.40
1.31
1.27
1.17
2.01
1.03
2.44
0.29
1.65
2.00
10.29
f1 (ppm)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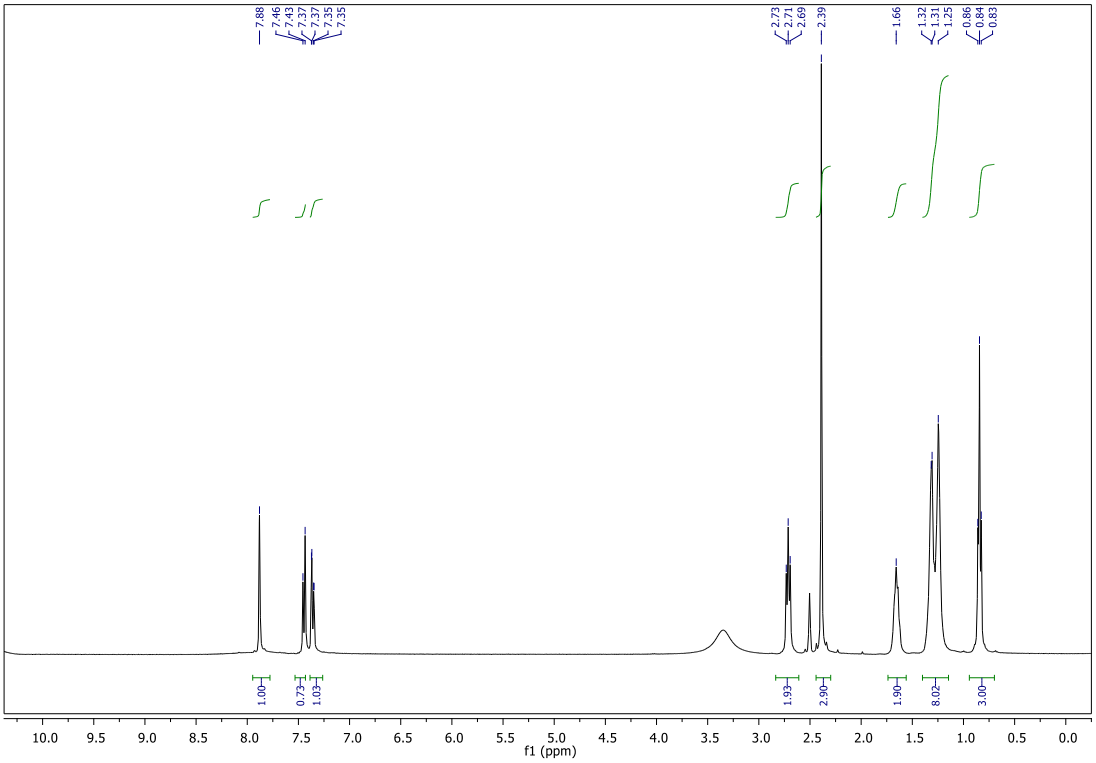
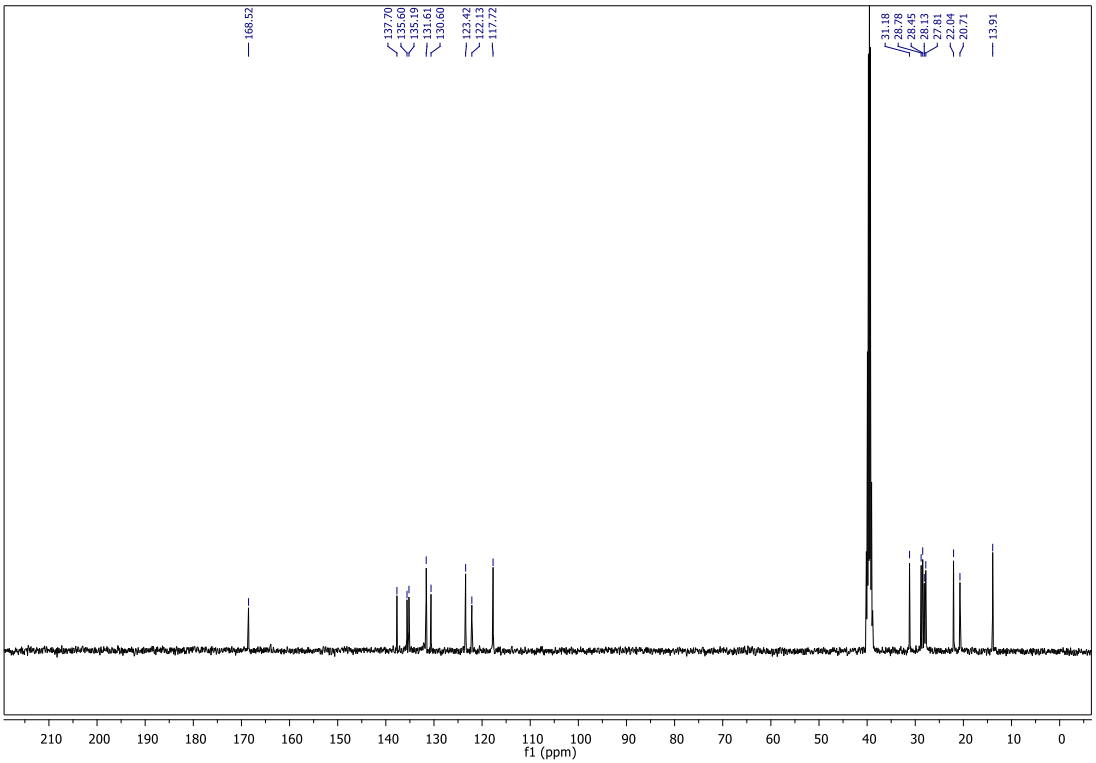
137.84
137.36
135.49
129.95
124.48
122.19
121.49
117.76
84.53
71.08
40.15
39.94
39.73
39.52
39.31
39.10
38.90
28.75
28.69
28.09
27.91
17.77
17.64
f1 (ppm)

23)


7.88
7.46
7.43
7.37
7.37
7.35
7.35
2.73
2.71
2.69
2.39
1.66
1.32
1.31
1.25
0.86
0.84
0.83
1.00
0.73
1.03
1.93
2.90
1.90
8.02
3.00
f1 (ppm)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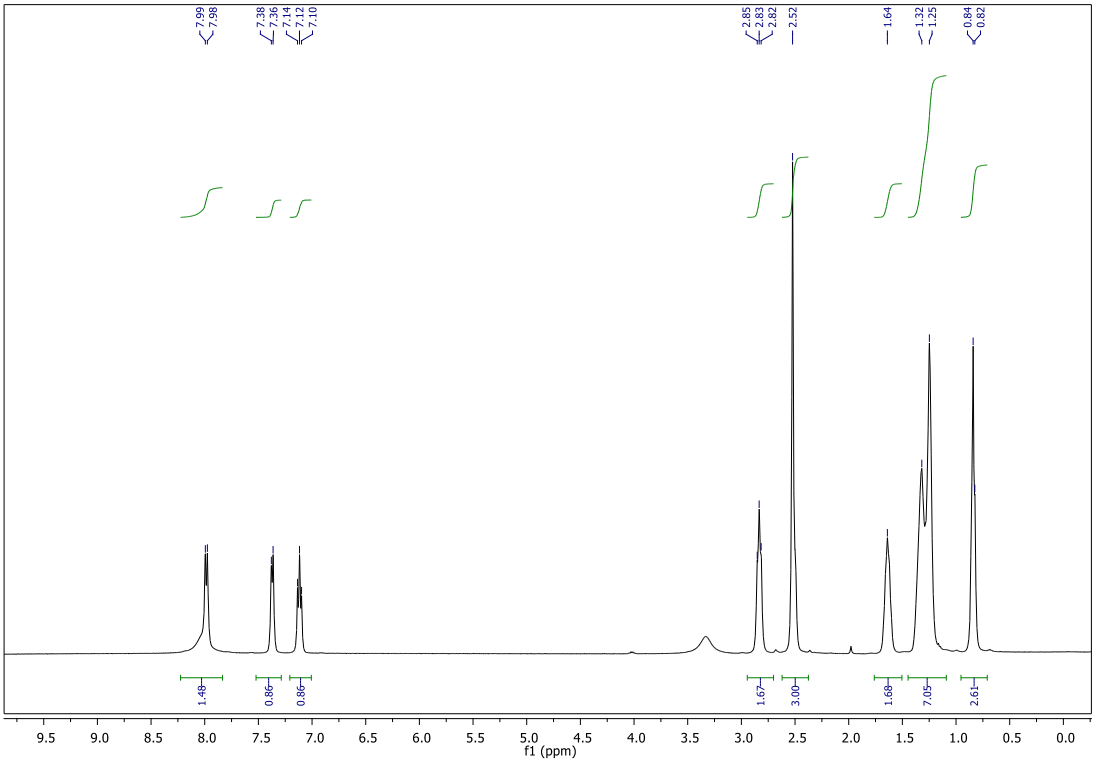
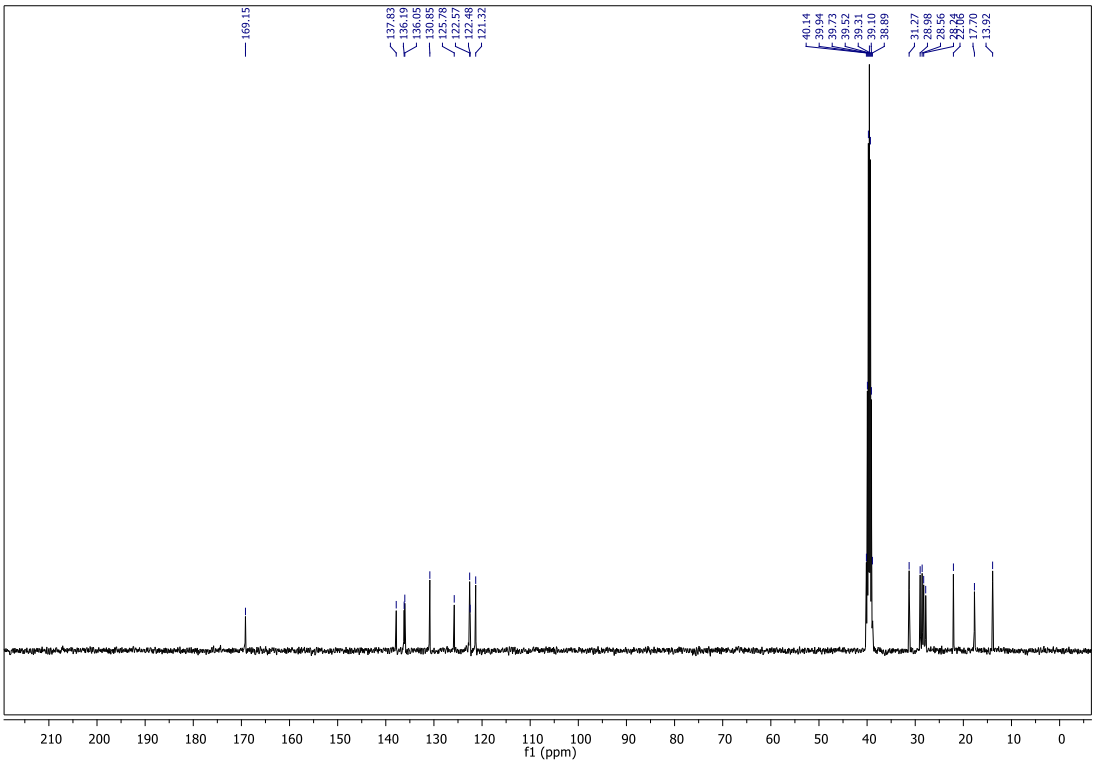
135.60
135.19
131.61
130.60
123.42
122.13
117.72
31.18
28.78
28.45
28.13
27.81
22.04
20.71
13.91
f1 (ppm)

24)


7.99
7.98
7.38
7.36
7.14
7.12
7.10
2.85
2.83
2.82
2.52
1.64
1.32
1.25
0.84
0.82
1.48
0.86
0.86
1.67
3.00
1.68
7.05
2.61
f1 (ppm)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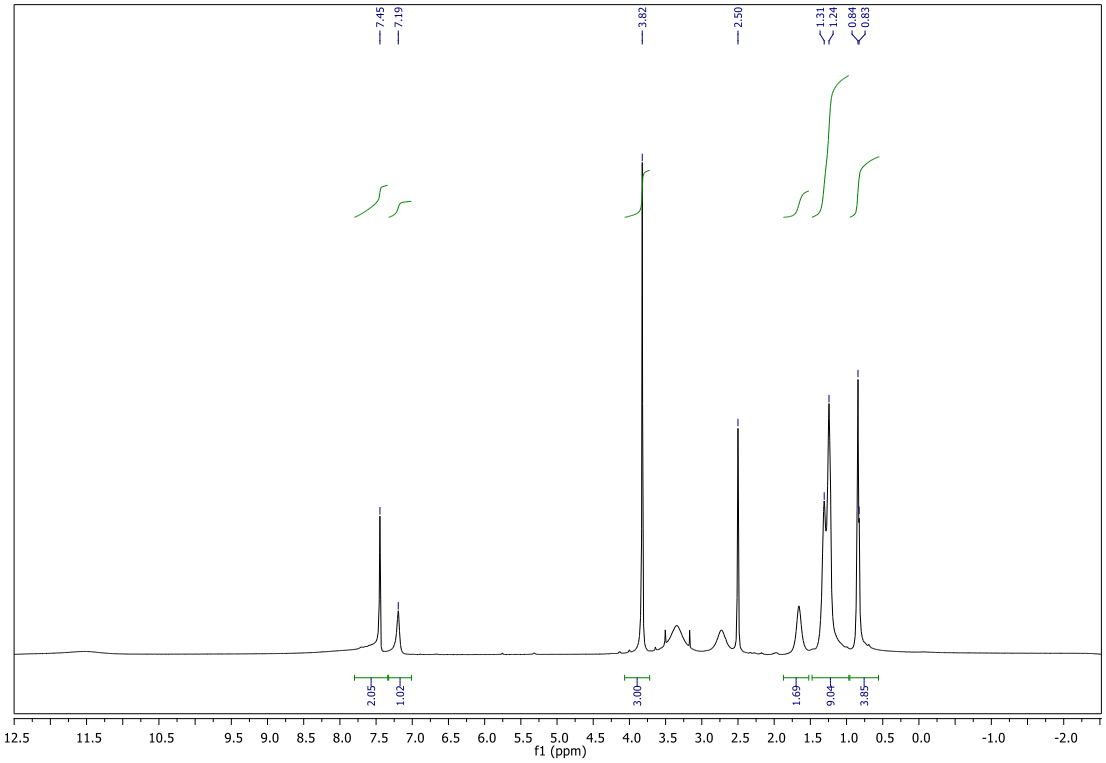
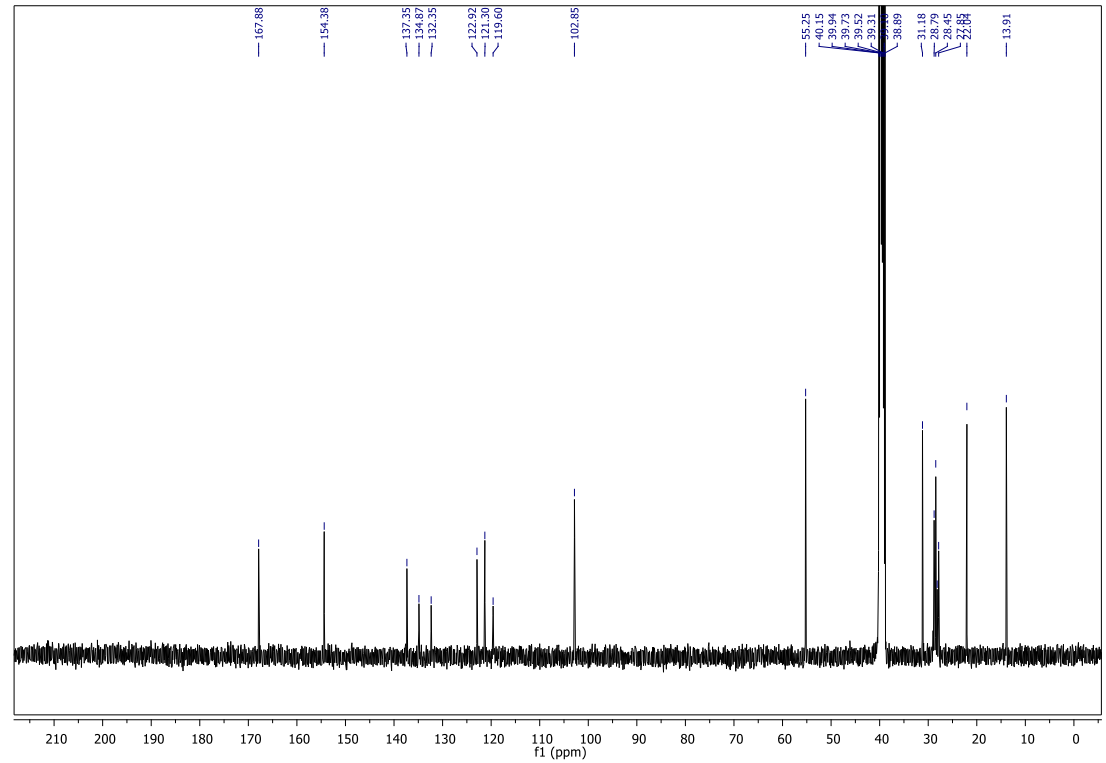
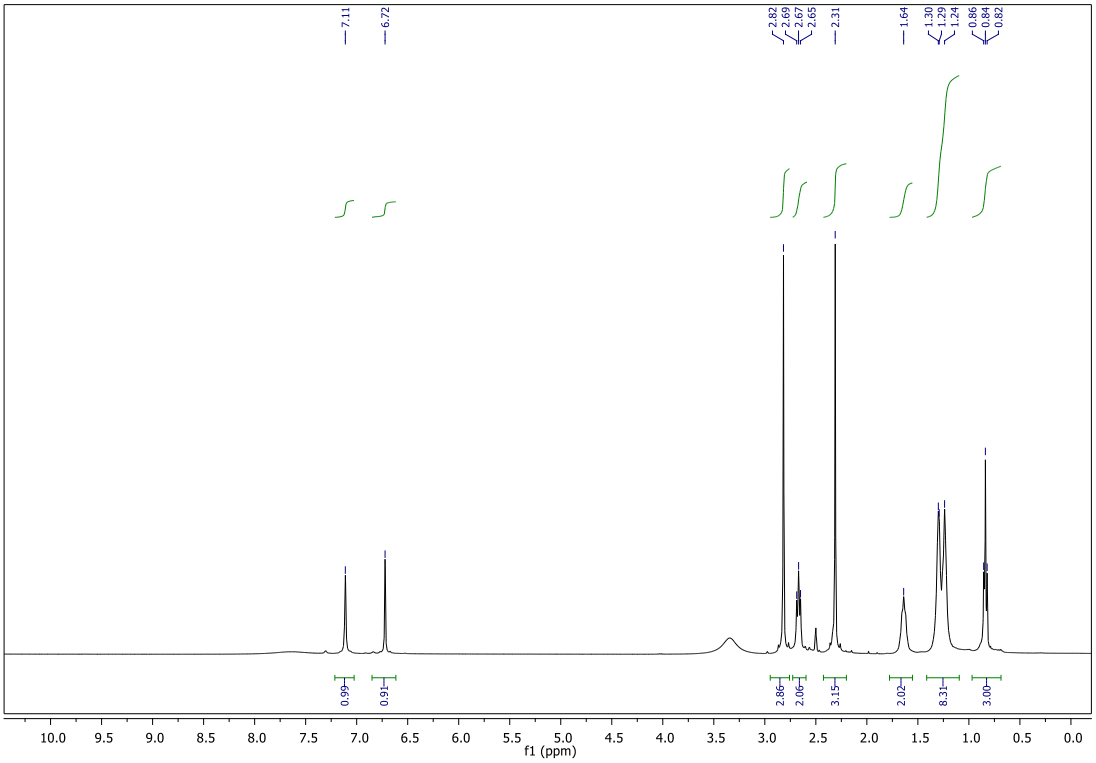
137.83
136.19
136.05
130.85
125.78
122.57
122.48
121.32
40.14
39.94
39.73
39.52
39.31
39.10
38.89
31.27
28.98
28.56
28.24
22.06
17.70
13.92
f1 (ppm)

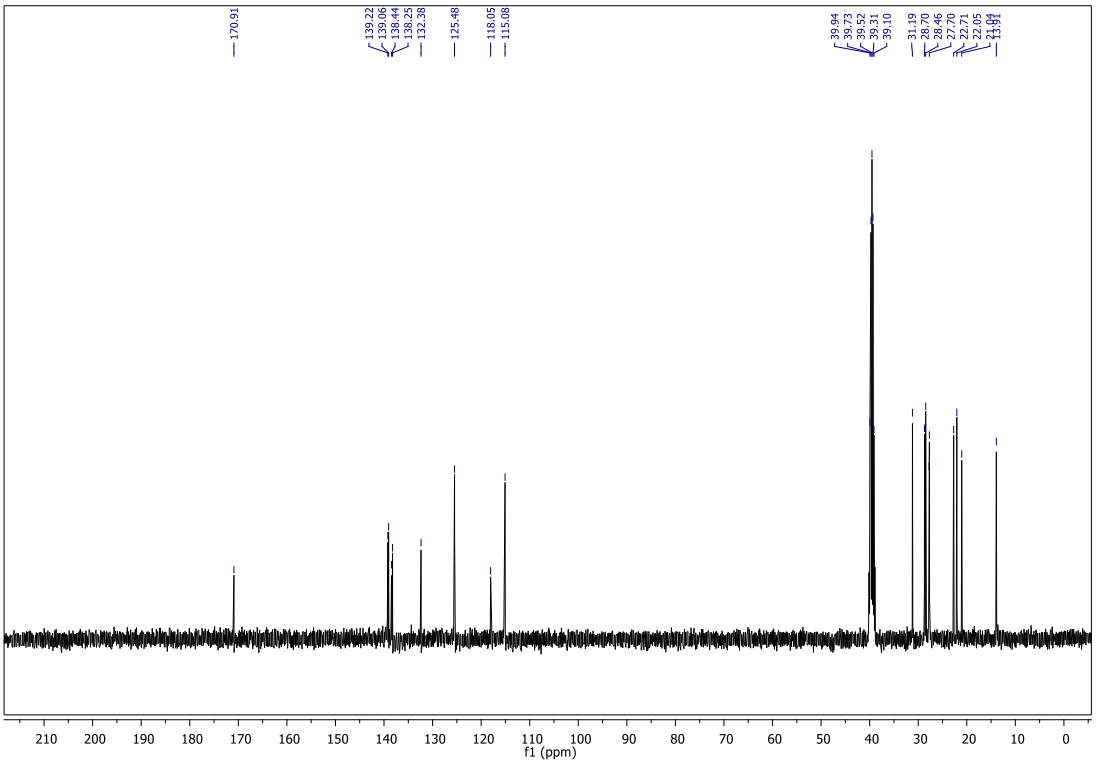
25)


7.45
7.19
3.82
2.50
1.31
1.24
0.84
0.83
2.05
1.02
3.00
1.69
9.04
3.85
f1 (ppm)


167.88
154.38
137.35
134.87
132.35
122.92
121.30
119.60
102.85
55.25
40.15
39.94
39.73
39.52
39.31
38.89
31.18
28.79
28.45
22.84
13.91
f1 (ppm)

26)


7.11
6.72
2.82
2.69
2.67
2.65
2.31
1.64
1.30
1.29
1.24
0.86
0.84
0.82
0.99
0.91
2.86
2.06
3.15
2.02
8.31
3.00
f1 (ppm)


170.91
139.22
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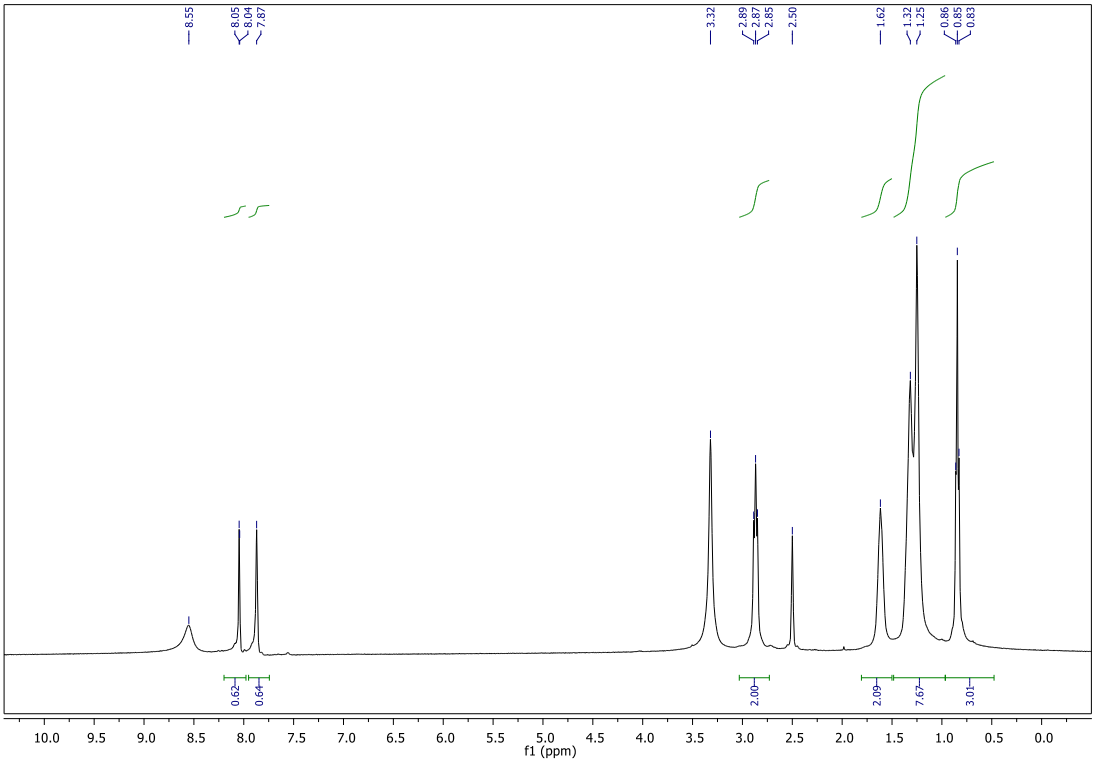
138.44
138.25
132.38
125.48
118.05
115.08
39.94
39.73
39.52
39.31
39.10
31.19
28.70
28.46
27.70
22.71
22.05
13.94
13.91
f1 (ppm)

27)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2.89
2.87
2.85
2.50
1.62
1.32
1.25
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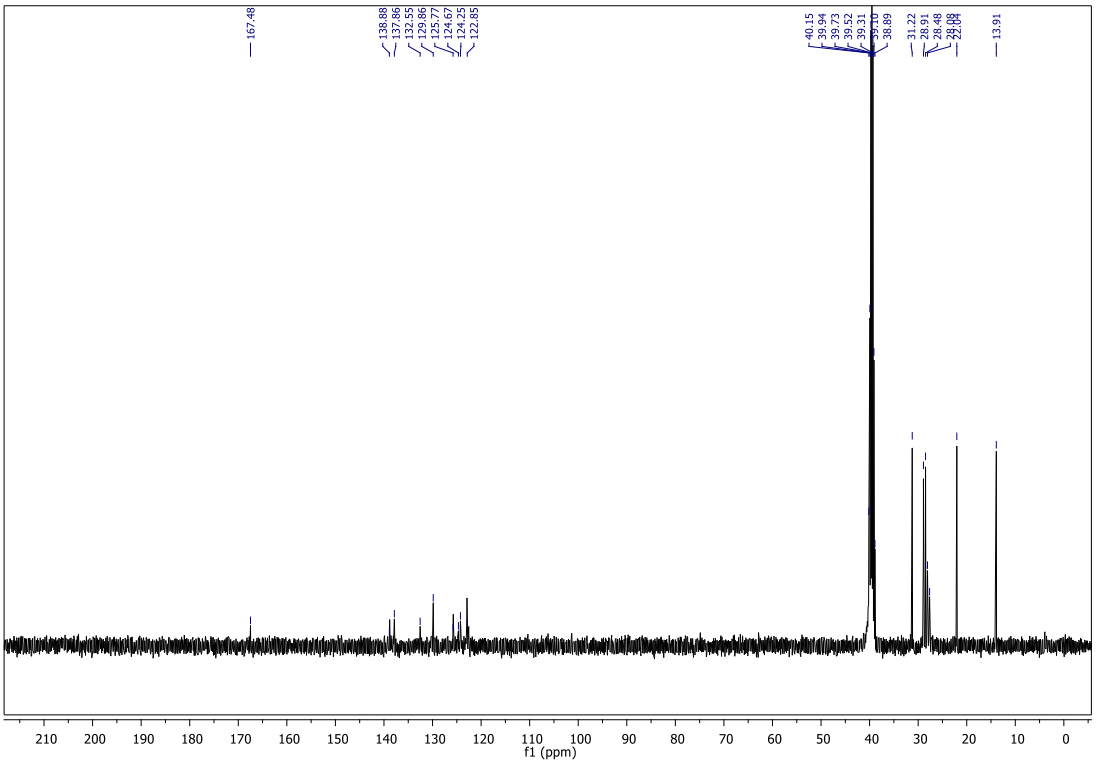
0.85
0.83
0.62
0.64
2.00
2.09
7.67
3.01
f1 (ppm)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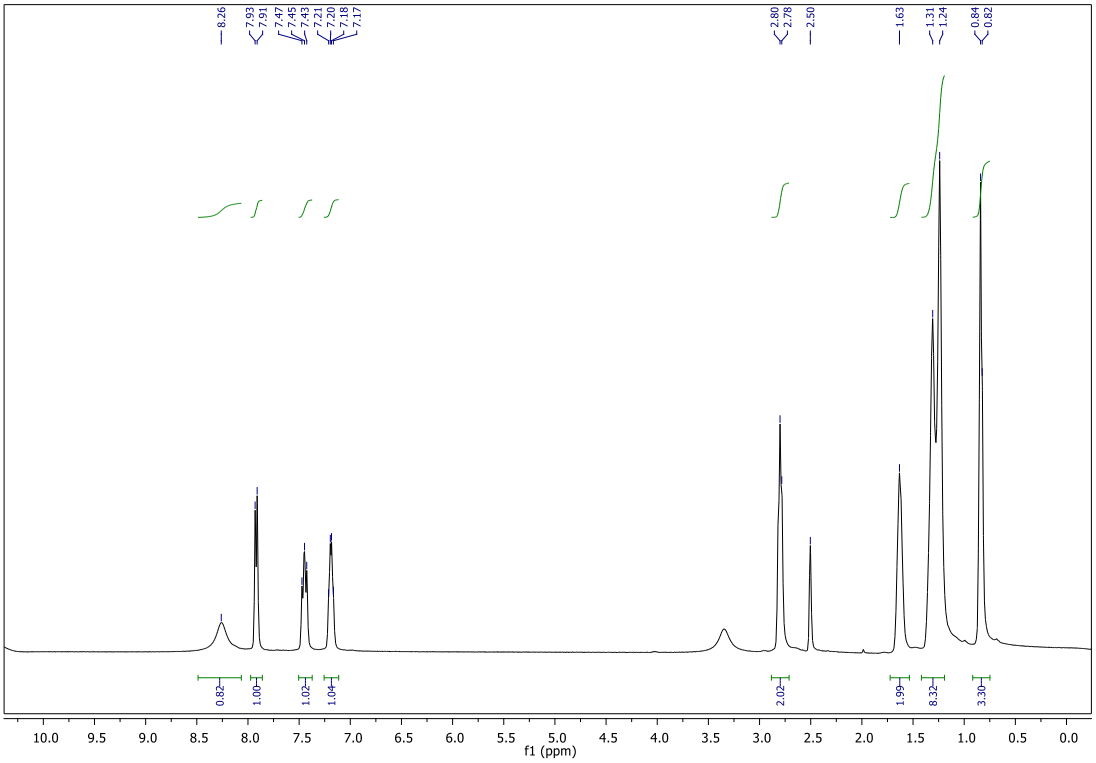
132.55
129.86
125.77
124.67
124.25
122.85
40.15
39.94
39.73
39.52
39.31
39.10
38.89
31.22
28.91
28.48
22.04
13.91
f1 (ppm)

28)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7.93
7.91
7.47
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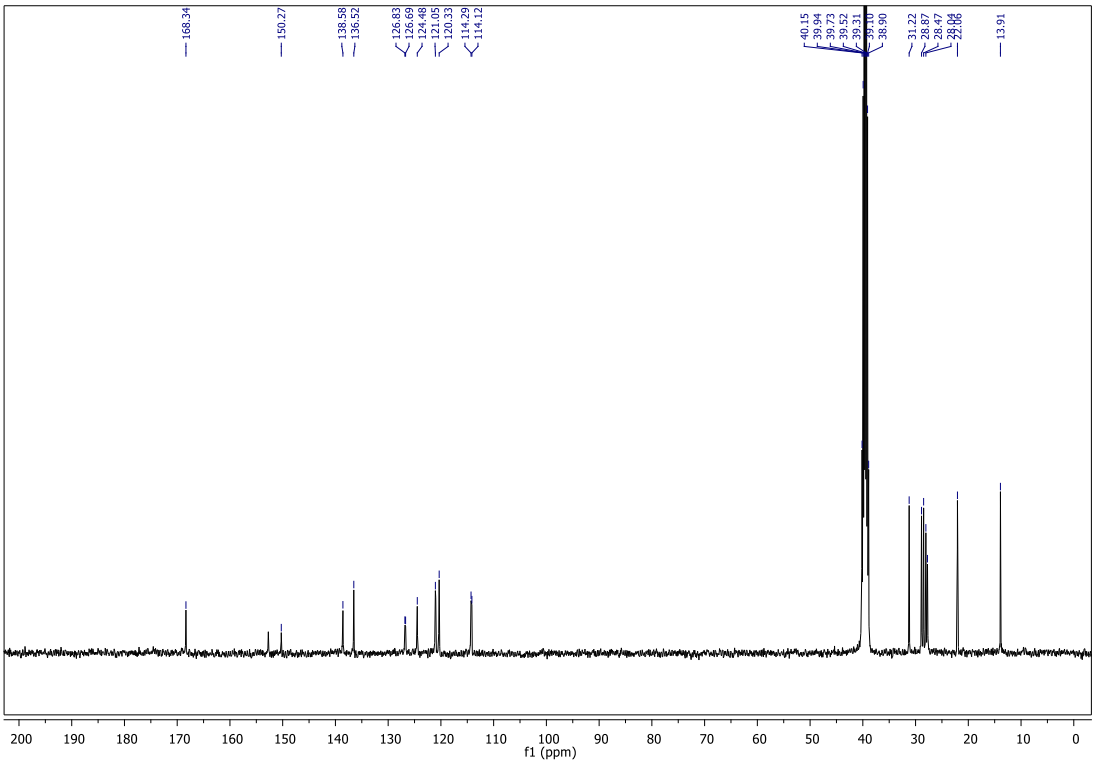
7.43
7.21
7.20
7.18
7.17
2.80
2.78
2.50
1.63
1.31
1.24
0.84
0.82
0.82
1.00
1.02
1.04
2.02
1.99
8.32
3.30
f1 (ppm)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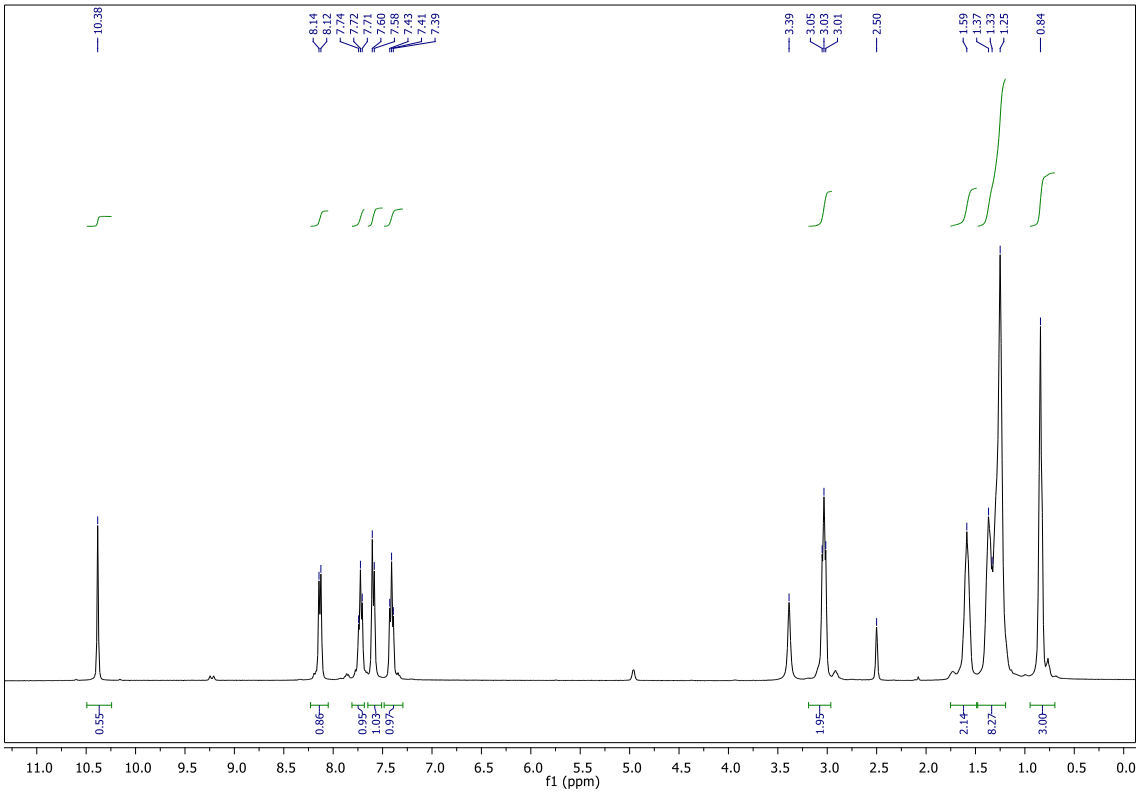
126.69
124.48
121.05
120.33
114.29
114.12
40.15
39.94
39.73
39.52
39.31
39.10
38.90
31.22
28.87
28.47
22.08
13.91
f1 (ppm)

29)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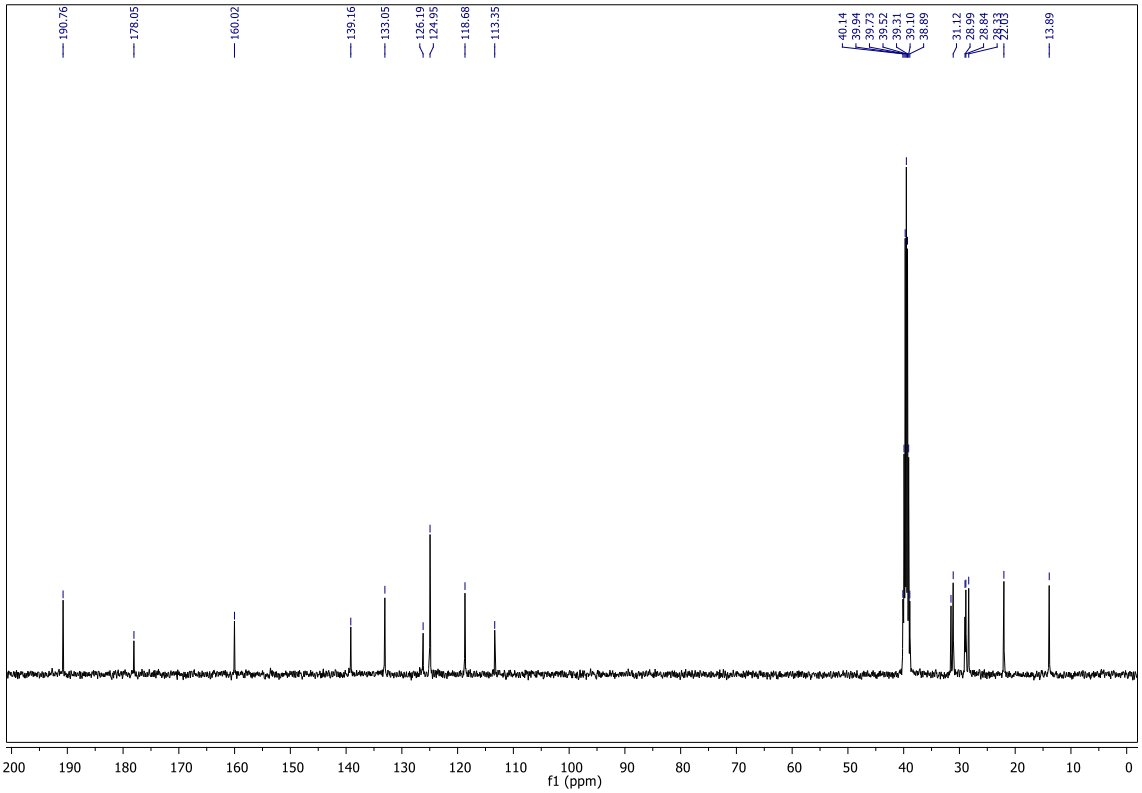
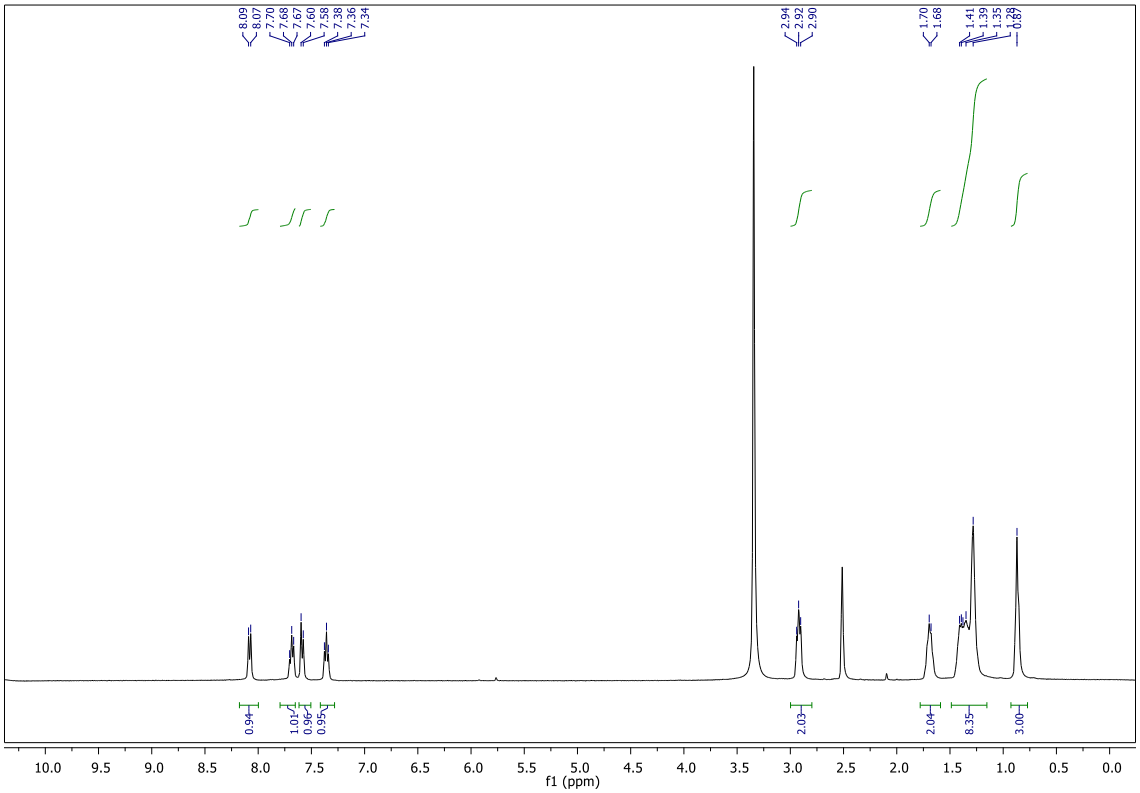
7.71
7.60
7.58
7.43
7.41
7.39
3.39
3.05
3.03
3.01
2.50
1.59
1.37
1.33
1.25
0.84
0.55
0.86
0.95
1.03
0.97
1.95
2.14
8.27
3.00
f1 (ppm)


190.76
178.05
160.02
139.16
133.05
126.19
124.95
118.68
113.35
40.14
39.94
39.73
39.52
39.31
39.10
38.89
31.12
28.99
28.84
28.33
22.03
13.89
f1 (ppm)

30)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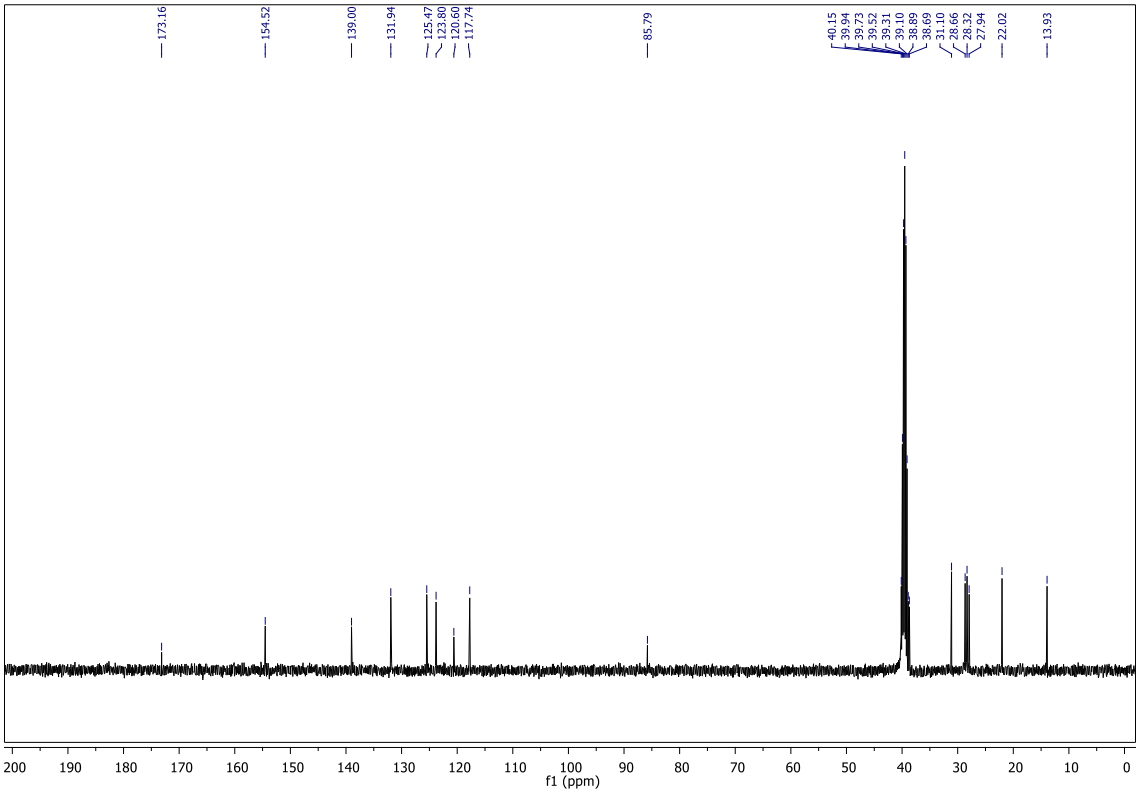
7.60
7.58
7.38
7.36
7.34
2.94
2.92
2.90
1.70
1.68
1.41
1.39
1.35
1.28
0.87
0.94
1.01
0.96
0.95
2.03
2.04
8.35
3.00
f1 (ppm)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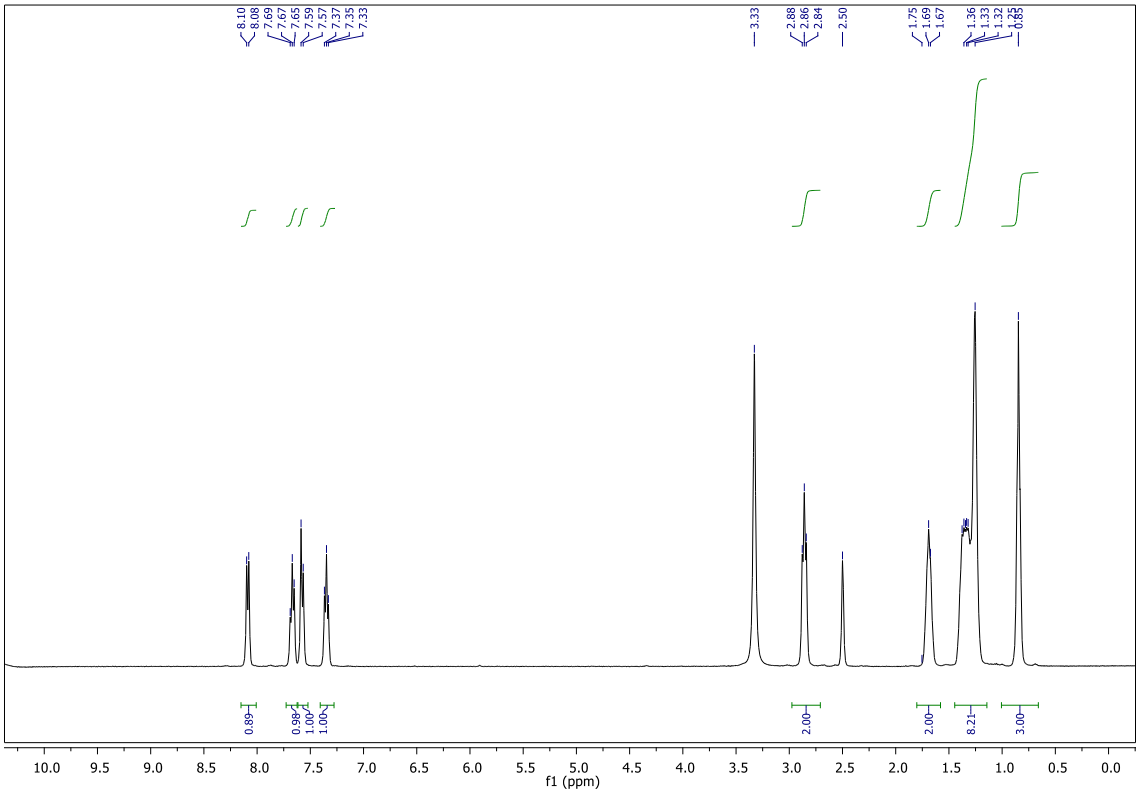
125.47
123.80
120.60
117.74
85.79
40.15
39.94
39.73
39.52
39.31
39.10
38.89
38.69
31.10
28.66
28.32
27.94
22.02
13.93
f1 (ppm)

31)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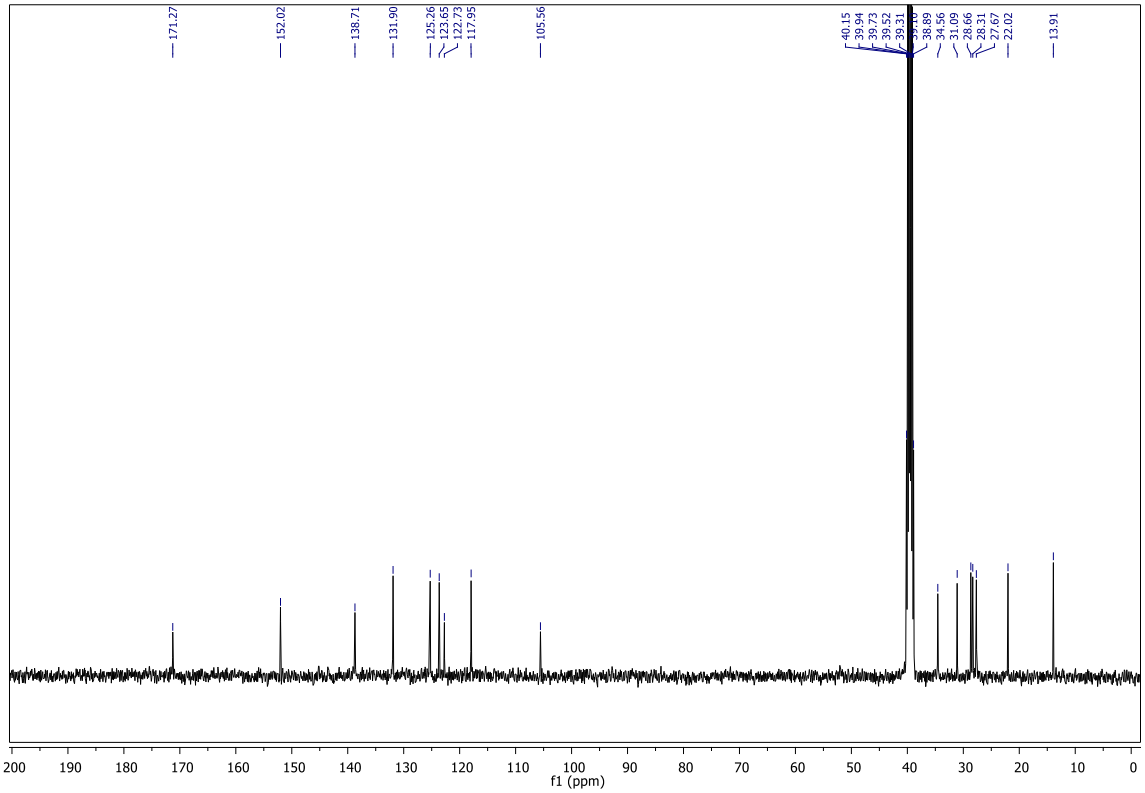
7.69
7.67
7.65
7.59
7.57
7.37
7.35
7.33
3.33
2.88
2.86
2.84
2.50
1.75
1.69
1.67
1.36
1.33
1.32
1.25
0.85
0.89
0.98
1.00
1.00
2.00
2.00
8.21
3.00
f1 (ppm)


171.27
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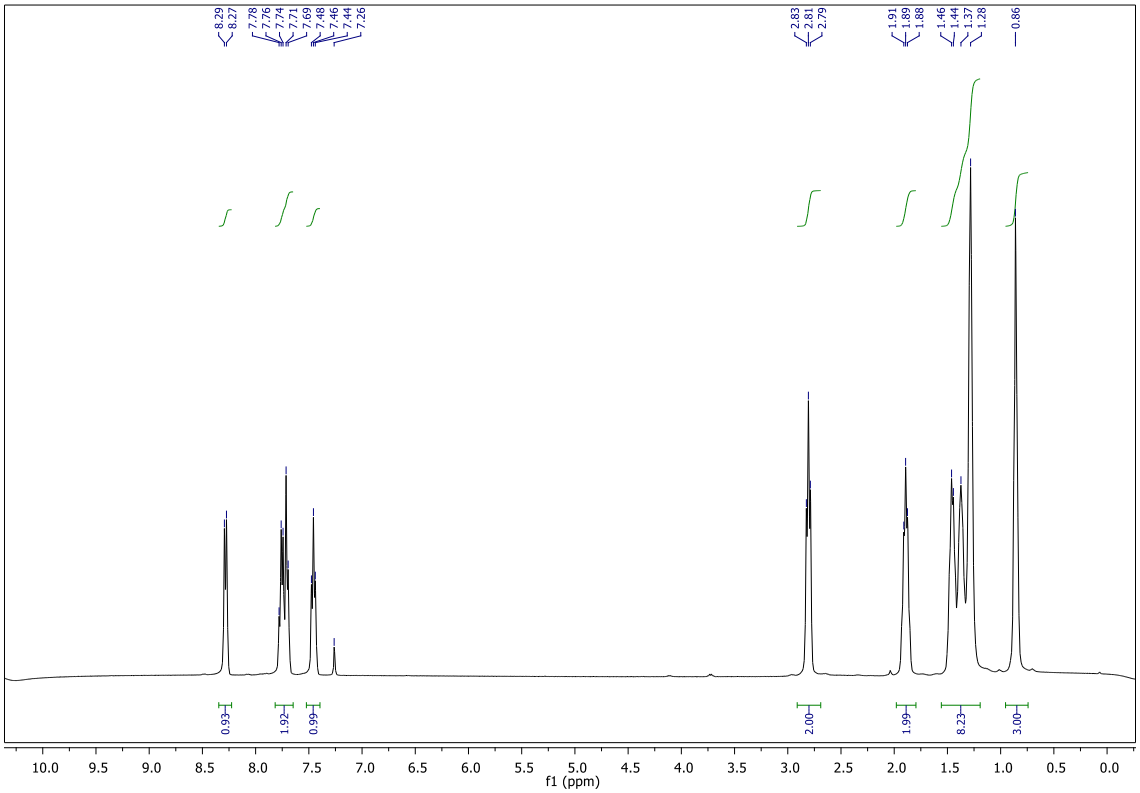
138.71
131.90
125.26
123.65
122.73
117.95
105.56
40.15
39.94
39.73
39.52
39.31
38.89
34.56
31.09
28.66
28.31
27.67
22.02
13.91
f1 (ppm)

32)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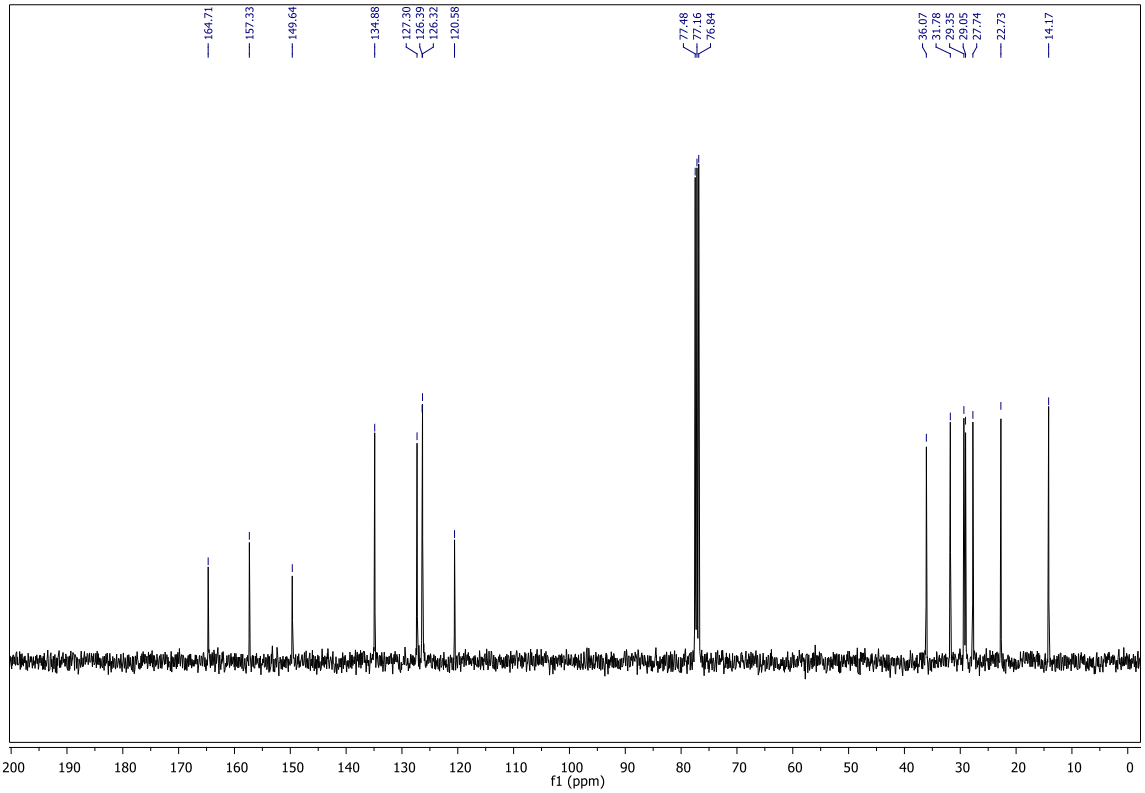
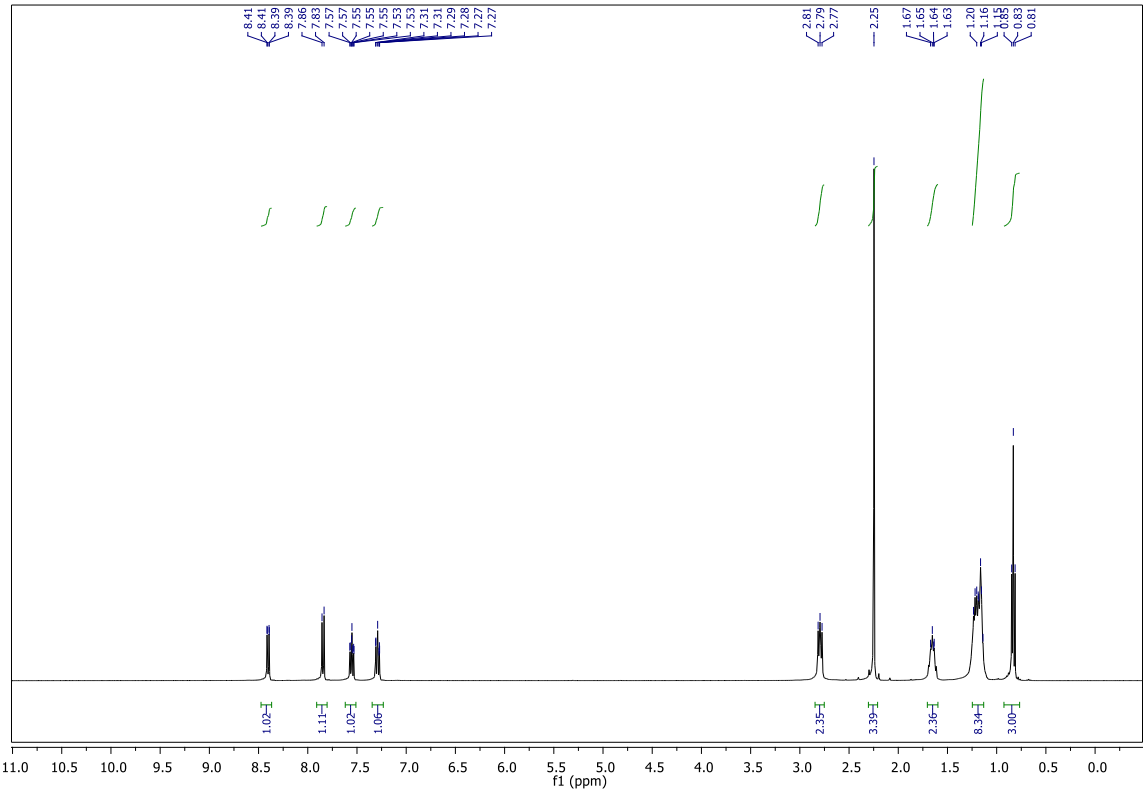
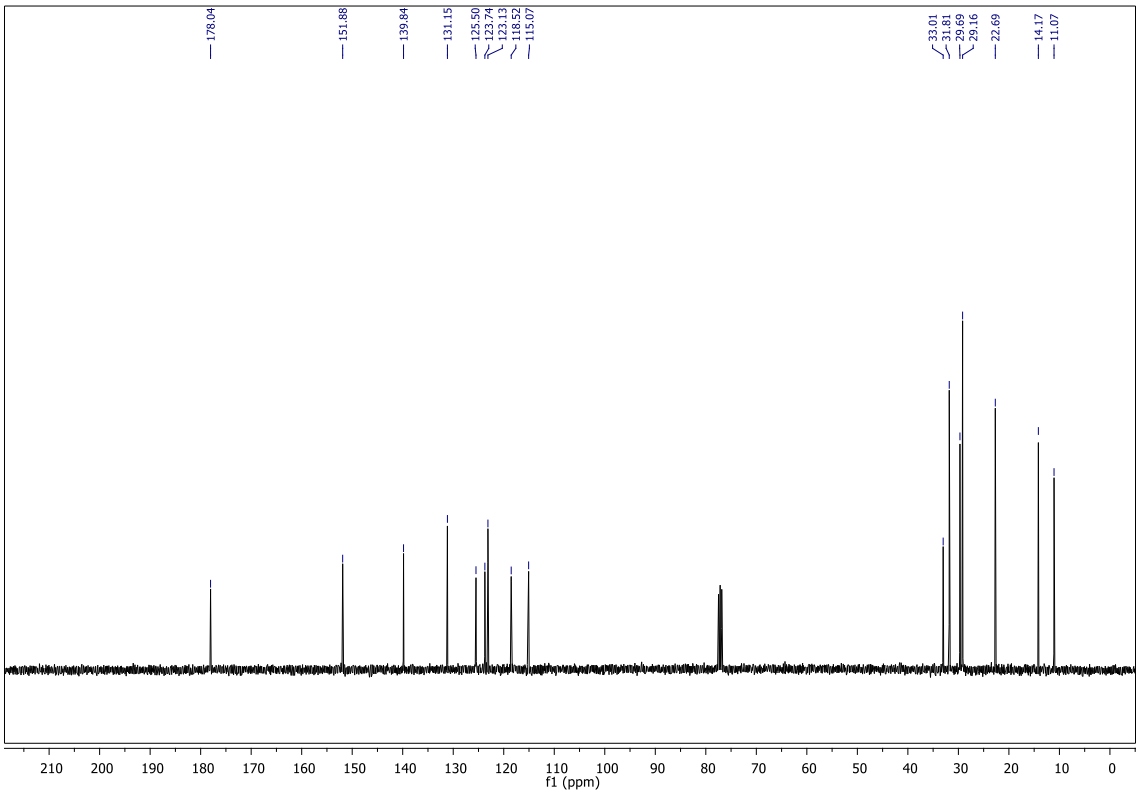
8.27
7.78
7.76
7.74
7.71
7.69
7.48
7.46
7.44
7.26
2.83
2.81
2.79
1.91
1.89
1.88
1.46
1.44
1.37
1.28
0.86
0.93
1.92
0.99
2.00
1.99
8.23
3.00
f1 (ppm)


164.71
157.33
149.64
134.88
127.30
126.39
126.32
120.58
77.48
77.16
76.84
36.07
31.78
29.35
29.05
27.74
22.73
14.17
f1 (ppm)

33)


8.41
8.41
8.39
8.39
7.86
7.83
7.57
7.57
7.55
7.55
7.55
7.53
7.53
7.31
7.31
7.29
7.28
7.27
7.27
2.81
2.79
2.77
2.25
1.67
1.65
1.64
1.63
1.20
1.16
0.85
0.83
0.81
1.02
1.11
1.02
1.06
2.35
3.39
2.36
8.34
3.00
f1 (ppm)


178.04
151.88
139.84
131.15
125.50
123.74
123.13
118.52
115.07
33.01
31.81
29.69
29.16
22.69
14.17
11.07
f1 (ppm)