Electronic Supplementary Information

PEGylated N-heterocyclic carbene-gold(I) complex: an efficient catalyst for cyclization reaction in water

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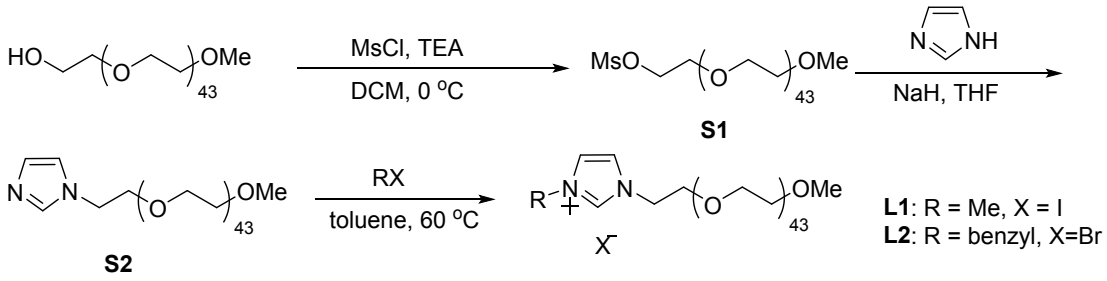
1. Experimental section

1.1 General information

Commercially available reagents were used without purification. 4-Pentynoic acid (**1b**), 2-ethynylbenzoic acid (**1f**) and 5-hexynoic acid (**1l**) are commercially available chemicals. 1,2-Dichloromethane (ACS Reagent grade), hexanes (AR grade), ethyl acetate (AR grade), diethyl ether (AR) were used without further purification. Anhydrous dichloromethane and tetrahydrofuran were obtained from solvent purification system. Deionized water was used in all reactions. Reactions were monitored by thin layer chromatography (TLC) using silica gel plates. Column chromatography was performed over Merck silica gel 60. ^{1}H and ^{13}C NMR spectra were measured on Bruker DPX-400 MHz, DPX-500 MHz and Bruker Avance 600 MHz spectrometers at 298 K. Chemical shifts are reported in ppm, and the residual solvent or tetramethylsilane (TMS) peak was used as internal standard. Mass spectra of new products were recorded on a Finnigan MAT 95 mass spectrometer. Matrix-assisted laser desorption/ionization time-of-flight (MOLDI-TOF) mass analysis were conducted on a Bruker Daltonics flexAnalysis using α-cyano-4-hydroxycinnamic acid matrix.

1.2 Synthesis of PEGylated-imidazolium salts

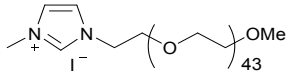


Scheme S1. Synthetic route 1 for PEGylated-imidazolium salts.

Ligands **L1** and **L2** were synthesized according to the known procedure with modification.[1]

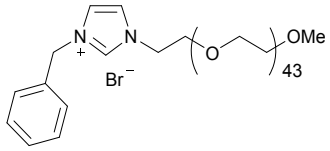
Synthesis of mPEG$_{2000}$-OMs (S1): MeO-PEG$_{2000}$OH (5 mmol) and triethylamine (10 mmol) were dissolved in 300 mL dry DCM at an ice-water bath, followed by adding dropwise a solution of methanesulfonyl chloride (MsCl) in 200 mL dry DCM. The mixture was warmed to room temperature and stirred for 24 h. The reaction was quenched with 500 mL ice water and adjusted to pH 7 using 10% NaOH solution. Then the organic layer was separated, dried with Na_2SO_4 and concentrated *in vacuo*. The residual was precipitated with diethyl ether to afford MeO-PEG$_{2000}$-OMs as a white solid (10 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 – 4.35 (m, 2H), 3.64 (s, 174H), 3.38 (s, 3H), 3.09 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 71.83, 70.46, 69.20, 68.92, 58.92, 37.64.

Synthesis of mPEG$_{2000}$-imidazole (S2): To a solution of imidazole (5.6 mol) in 50 mL dry THF was added NaH (60% in mineral oil, 10 mol) at room temperature. The mixture was then heated to 40 °C and stirred for 1 h. After that, mPEG$_{2000}$-OMs (2 mol) was added and the reaction mixture was refluxed for 24 h. Upon completion, the resultant suspension was filtered through celite, concentrated *in vacuo* and precipitated with Et_2O to afford mPEG$_{2000}$-imidazole as a white solid (2.9 g, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.03 (s, 1H), 7.00 (s, 1H), 4.11 (t, J = 5.2 Hz, 2H), 3.79 – 3.49 (m, 174H), 3.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.48, 129.15, 119.38, 71.88, 70.51, 58.97, 46.99.

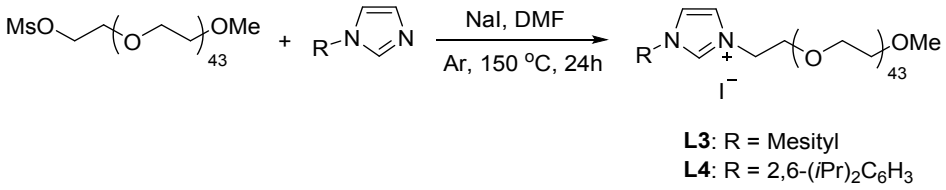


Synthesis of 1-methylimidazole-mPEG$_{2000}$ (L1): Iodomethane (0.5 mL) was added dropwise to a solution of mPEG$_{2000}$-imidazole (0.5 mol) in toluene (15 mL) under argon. The mixture was heated to 60 °C and stirred overnight. After that, the mixture was concentrated and the resulting imidazolium salt was isolated by precipitation with Et_2O (1.04 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.72 (s, 1H), 7.45 (s, 1H), 4.60 – 4.51 (m, 2H), 4.02 (d, J = 2.7 Hz, 3H), 3.93 – 3.38 (m, 174H), 3.35 (d, J = 5.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.24, 123.63, 123.10, 71.91, 70.52, 70.32, 70.23, 70.20, 68.82,

59.01, 49.83, 36.71. MALDI–TOF–MS *m/z*: $[M\text{-}I]^+$ calcd. for $C_{93}H_{185}N_2O_{44}$, 2035.2334; found, 2036.1598.



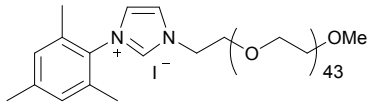
Synthesis of 1-benzylimidazole-mPEG$_{2000}$ (L2): Benzyl bromide (0.5 mL) was added dropwise to a solution of mPEG$_{2000}$-imidazole (0.5 mol) in toluene (15 mL). The mixture was heated to 100 °C and stirred overnight. After that, the mixture was concentrated and precipitated with Et_2O to afford 1-benzylimidazole-mPEG$_{2000}$ as a light yellow solid (1.06 g, 96 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.40 (s, 1H), 7.75 (s, 1H), 7.47 – 7.45 (m, 2H), 7.45 – 7.39 (m, 3H), 7.31 (s, 1H), 5.54 (s, 2H), 4.63 – 4.61 (m, 2H), 3.93 – 3.91 (m, 2H, CH_2), 3.66 – 3.49 (m, 172H), 3.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.07, 133.17, 129.26, 128.96, 128.76, 123.72, 121.27, 71.77, 70.38, 70.18, 70.13, 70.11, 68.84, 58.88, 53.12, 49.67. MALDI–TOF–MS *m/z*: $[M\text{-}Br]^+$ calcd. for $C_{99}H_{189}N_2O_{44}$, 2111.2647; found, 2111.0342.



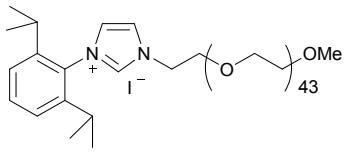
L3: R = Mesityl
L4: R = 2,6-(*i*Pr)$_2$C$_6$H$_3$

Scheme S2. Synthetic route 2 for PEGylated-imidazolium salts.

Ligands **L3** and **L4** were synthesized according to the reaction as shown in **Scheme S2**.

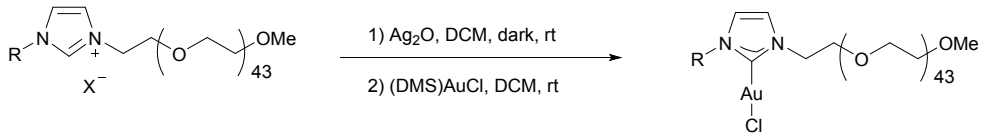


Synthesis of 1-mesityl imidazole-mPEG$_{2000}$ (L3): 1-Mesityl-1H-imidazole (6 mmol) and the above-described mPEG$_{2000}$-OMs (4 mmol) were dissolved in 10 mL DMF, followed by adding NaI (8 mmol). The mixture was refluxed for 24 h. After completion, the mixture was cooled to room temperature, washed with water, extracted with DCM and dried with Na_2SO_4. Then the organic layer was concentrated under reduced pressure and precipitated with diethyl ether to afford a yellow solid (8.62 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.17 (s, 1H), 7.19 (s, 1H), 7.02 (s, 2H), 4.95 – 4.92 (m, 2H), 4.02 – 4.00 (m, 2H), 3.83 – 3.45 (m, 172H), 3.38 (s, 3H), 2.36 (s, 3H), 2.09 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.77, 141.07, 137.35, 134.16, 130.55, 129.60, 124.50, 122.55, 71.70, 70.33, 70.13, 70.08, 70.02, 69.97, 68.73, 58.79, 50.02, 20.90, 17.47. MALDI–TOF–MS *m/z*: $[M\text{-}I]^+$ calcd. for $C_{101}H_{193}N_2O_{44}$, 2139.2960; found, 2140.9884.

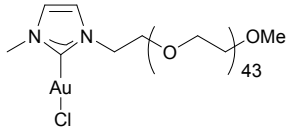


Synthesis of 1-(2,6-diisopropylphenyl) imidazole-mPEG$_{2000}$ (L4): The procedure is the same as that for **L3** except for use of 1-(2,6-diisopropylphenyl)-1H- imidazole. The yield of the resulting yellow solid: 97%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.35 (s, 1H), 7.55 (t, J = 7.8 Hz, 1H), 7.32 (d, J = 7.8 Hz, 2H), 7.19 (t, J = 1.8 Hz, 1H), 5.12 – 4.95 (m, 2H), 4.07 – 3.96 (m, 2H), 3.81 – 3.48 (m, 172H), 3.38 (s, 3H), 2.32 (p, J = 6.8 Hz, 2H), 1.24 (d, J = 6.8 Hz, 6H), 1.17 (d, J = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.33, 137.53, 131.83, 130.05, 124.68, 124.56, 123.55, 71.79, 70.42, 70.36, 70.32, 70.23, 70.17, 70.15, 70.10, 70.03, 68.91, 58.88, 50.16, 28.53, 24.21, 24.19. MALDI–TOF–MS *m/z*: $[M\text{-}I]^+$ calcd. for $C_{104}H_{199}N_2O_{44}$, 2181.3429; found, 2183.6780.

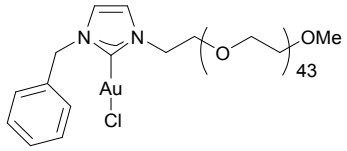
1.3 Synthesis of PEGylated NHC-gold(I) complexes



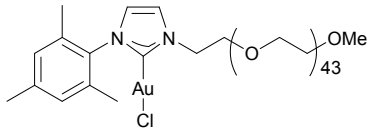
Silver oxide (2 mmol) was added to a solution of PEGylated-imidazolium salts (1 mmol) in dry DCM (20 mL) under argon at room temperature. The mixture was stirred overnight in dark. Upon completion, the suspension liquid was filtered through celite into a solution of (DMS)AuCl (1.2 mmol) in 15 mL DCM. The mixture was bubbled with N_2 for 0.5 h and continued to be stirred for 24 h. Then the suspension solution was filtered through celite, concentrated under reduced pressure and precipitated with diethyl ether to afford a yellow solid. All PEGylated NHC-gold(I) complexes have good solubility in water. Their solubility in water has been measured to be 423 g/L for L1AuCl, 356 g/L for L2AuCl, 302 g/L for L3AuCl and 283 g/L for L4AuCl, respectively.



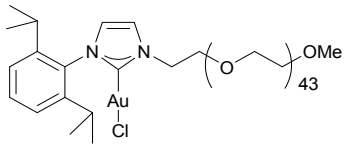
1-Methylimidazole-mPEG$_{2000}$-AuCl (L1AuCl): yellow solid. Yield: 92%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H), 6.93 (s, 1H), 4.36 – 4.34 (m, 2H), 3.83 01 (s, 3H), 3.82 – 3.49 (m, 174H), 3.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.62, 122.43, 121.26, 71.86, 70.48, 70.39, 70.31, 70.28, 58.96, 51.06, 38.14. MALDI–TOF–MS *m/z*: $[M\text{-}Cl]^+$ calcd. for $C_{93}H_{184}N_2O_{44}Au$, 2231.1921; found, 2230.9059; calcd. for dimer $C_{186}H_{368}N_4O_{88}Au$, 4265.4177; found, 4261.9402.



1-Benzylimidazole-mPEG$_{2000}$-AuCl (L2AuCl): yellow solid. Yield: 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 7.20 (s, 1H), 6.85 (s, 1H), 5.33 (s, 2H), 4.35 (t, J = 4.9 Hz, 2H), 3.82 – 3.43 (m, 174H), 3.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.26, 135.00, 128.89, 128.52, 127.90, 122.83, 119.89, 71.75, 70.35, 70.21, 70.12, 58.86, 54.92, 51.09. MALDI–TOF–MS *m/z*: $[M\text{-}Cl]^+$ calcd. for $C_{99}H_{188}N_2O_{44}Au$, 2307.2234; found, 2311.7653.



1-Mesityl imidazole-mPEG$_{2000}$-AuCl (L3AuCl): yellow solid. Yield: 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 6.95 (s, 2H), 6.86 (s, 1H), 4.50 – 4.47 (m, 2H), 3.92 – 3.89 (m, 2H), 3.82 – 3.45 (m, 172H), 3.38 (s, 3H), 2.33 (s, 3H), 2.00 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.48, 139.50, 134.76, 134.69, 129.30, 122.35, 121.57, 71.85, 70.46, 70.33, 58.95, 51.17, 21.02, 17.72. MALDI–TOF–MS *m/z*: $[M\text{-}Cl]^+$ calcd. for $C_{101}H_{192}N_2O_{44}Au$, 2334.2547; found 2337.0323; calcd. for dimer $C_{202}H_{384}N_4O_{88}Au$, 4473.5429; found, 4478.2901.

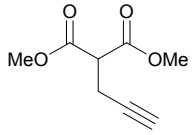


1-(2,6-Diisopropylphenyl) imidazole-mPEG$_{2000}$-AuCl (L4AuCl): yellow solid. Yield: 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 2H), 7.25 (s, 1H), 7.23 (s, 1H), 6.90 (d, J = 1.8 Hz, 1H), 4.54 – 4.46 (m, 2H), 3.96 – 3.89 (m, 2H), 3.83 – 3.45 (m, 172H), 3.38 (s, 3H), 2.38 (p, J = 6.9 Hz, 2H), 1.28 (d, J = 6.8 Hz, 6H), 1.12 (d, J = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.53, 145.68, 134.16, 130.48, 124.16, 122.89, 122.06, 71.89, 70.51, 70.41, 70.37, 58.99, 51.20, 28.35, 24.33, 24.31. MALDI–TOF–MS *m/z*: $[M\text{-}Cl]^+$ calcd. for $C_{104}H_{198}N_2O_{44}Au$, 2377.3017; found, 2377.5142.

1.4 Preparation of alkynoic acids

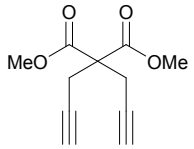
General procedure **A** (for the alkylation of malonate): based on the known method.[2] Dimethyl malonate (50 mmol, 5.74 mL) and propargyl bromide (50 mmol, 5.45 mL) were added to a solution of K_2CO_3 (100 mmol, 13.8 g) in acetone (100 mL). The mixture was stirred for 24 h at room temperature. Then it was quenched with saturated ammonium chloride solution (50 mL) and extracted with DCM (3×50 mL). The combined organic layer was dried with sodium sulfate and concentrated under reduced pressure. The oil residue was purified with column chromatography (hexane/EA: 50:1 v/v) to give dimethyl-2-propargyl malonate as a colourless oil (5.78 g, 68%) and dimethyl 2,2-di(prop-2-yn-1-yl) malonate as a white solid (1.12 g, 10%).

Dimethyl-2-propargyl malonate (S3)[2]



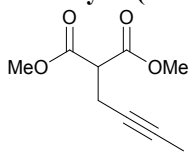
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (d, J = 1.2 Hz, 6H), 3.63 (t, J = 7.7 Hz, 1H), 2.80 (d, J = 7.7 Hz, 2H), 2.03 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 168.5, 80.0, 70.7, 53.0, 51.1, 18.7.

Dimethyl 2,2-di(prop-2-yn-1-yl)malonate (S4)[3]



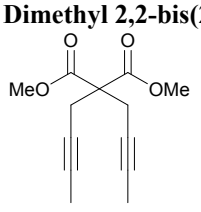
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 6H), 3.01 (s, 4H), 2.05 (s, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 169.01, 78.24, 71.76, 56.38, 53.15, 22.61.

Dimethyl 2-(but-2-yn-1-yl)malonate (S5)[4]



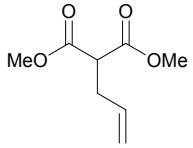
Following the general procedure **A**, dimethyl 2-(but-2-yn-1-yl) malonate was obtained as a colourless oil (2.36 g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 6H), 3.46 (t, J = 7.7 Hz, 1H), 2.74 – 2.72 (m, 2H), 1.76 (t, J = 2.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.60, 77.92, 74.51, 52.68, 51.46, 18.87, 3.43.

Dimethyl 2,2-bis(2-butynyl)malonate (S6)[5]



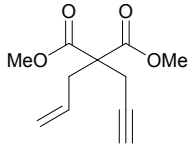
Following the general procedure **A**, dimethyl 2,2-bis(2-butynyl) malonate was obtained as a white solid in above reaction (370 mg, 5%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (s, 6H), 2.91 (q, J = 2.5 Hz, 4H), 1.75 (t, J = 2.5 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.74, 78.99, 73.09, 57.08, 52.87, 22.98, 3.50.

Dimethyl 2-allylmalonate (S7)[2]



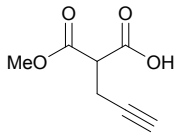
Following the general procedure **A**, dimethyl 2-allylmalonate was obtained as a colourless oil (6.86 g, 71.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 – 5.69 (m, 1H), 5.19 – 4.98 (m, 2H), 3.78 – 3.67 (m, 6H), 3.47 (td, *J* = 7.6, 4.8 Hz, 1H), 2.70-2.58 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.27, 133.90, 117.65, 52.49, 51.38, 32.85.

Dimethyl 2-allyl-2-(prop-2-yn-1-yl)malonate (S8)[6]



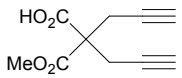
General procedure **B** (for the synthesis of dimethyl 2-allyl-2-(prop-2-yn-1-yl)malonate): according to the reported methods.[6] In a 50 mL two-neck flask, NaH (60% in mineral oil) (22 mmol, 440 mg) was suspended in 20 mL dry THF and cooled to 0 °C. Then dimethyl 2-allylmalonate (20 mmol, 3.44 g) was added dropwise. The mixture was warmed to room temperature and stirred for 30 min. Subsequently, propargyl bromide (22 mmol, 2.62 g) was added and the mixture was stirred at room temperature overnight. The reaction was quenched with 50 mL water and extracted with Et_2O (3×50 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. It was further purified through column chromatography (hexane/EA: 8:1 v/v) to give dimethyl 2-allyl-2-(prop-2-yn-1-yl) malonate as a colourless oil (3.36 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 – 5.52 (m, 1H), 5.16 (dd, *J* = 20.8, 13.5 Hz, 2H), 3.74 (d, *J* = 2.6 Hz, 6H), 2.85 – 2.74 (m, 4H), 2.03 (t, *J* = 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.14, 131.61, 119.94, 78.73, 71.46, 56.86, 52.77, 36.50, 22.67.

General procedure **C** (for the mono-saponification of malonates): **2-(methoxycarbonyl)pent-4-ynoic acid[2] (1a)**



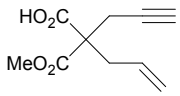
Dimethyl-2-propargyl malonate (2.5 g, 15 mmol) was dissolved in MeOH (30 mL) and potassium hydroxide (924 mg, 16.5 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. Afterwards, the solvent was removed under reduced pressure. The residue was diluted with 20 mL water and extracted with Et_2O (2×20 mL) to remove unreacted starting material. The aqueous layer was acidified with 5 M HCl solution and extracted with ethyl acetate (3×20 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a colourless solid (1.68 g, 72%) without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 3.81 (s, 3H), 3.66 (t, *J* = 7.6 Hz, 1H), 2.84 – 2.78 (m, 2H), 2.07 (t, *J* = 2.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.98, 168.05, 79.40, 70.76, 53.00, 50.74, 18.28.

2-(Methoxycarbonyl)-2-(prop-2-yn-1-yl)pent-4-ynoic acid[7] (1c)



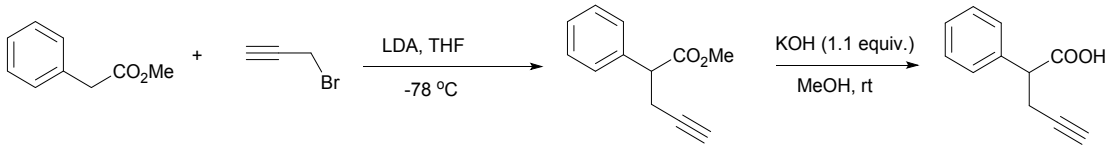
Following the general procedure **C**, **1c** was obtained as a white solid (428 mg, 74 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 3.00 (d, *J* = 2.6 Hz, 4H), 2.06 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.19, 168.85, 78.00, 72.00, 56.39, 53.34, 22.61.

2-(Methoxycarbonyl)-2-(prop-2-yn-1-yl)pent-4-enoic acid[7] (1d)



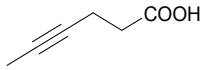
Following the general procedure **C**, **1d** was obtained as a white solid (1.35 g, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 5.65 (dq, *J* = 17.3, 7.6 Hz, 1H), 5.18 (dd, *J* = 22.1, 13.4 Hz, 2H), 3.77 (s, 3H), 2.88 – 2.73 (m, 4H), 2.05 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.72, 170.14, 131.26, 120.25, 78.43, 71.75, 56.92, 53.00, 36.67, 22.80.

2-Phenylpent-4-ynoic acid[8] (1e)



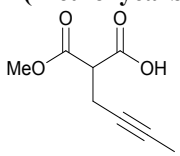
1e was synthesized in two steps. The first step was propargylation of methyl 2-phenylacetate following the reported procedure.[9] To a solution of methyl 2-phenylacetate (3.0 g, 20 mmol) in dry THF (15 mL) was added dropwise LDA (2 M in THF, 30 mmol) at -78 °C. After stirring for 5 h at this temperature, propargyl bromide (1.87 mL, 24 mmol) was added. The reaction mixture was warmed to room temperature and stirred overnight. Subsequently, the mixture was treated with saturated NH_4Cl solution and extracted with Et_2O (3×30 mL). After concentrating the organic layer, the residue was purified through column chromatography (hexane/EA: 30:1 v/v) to give **1e** as a pale-yellow oil (3.2 g, 85%). The second step refers to the general procedure **C** to give 2-phenylpent-4-ynoic acid as an off-white solid (1.13 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 3.83 (t, *J* = 7.7 Hz, 1H), 2.93 (ddd, *J* = 16.8, 8.1, 2.6 Hz, 1H), 2.65 (ddd, *J* = 16.8, 7.2, 2.6 Hz, 1H), 1.96 (t, *J* = 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.21, 136.78, 129.36, 128.81, 128.63, 128.01, 127.85, 81.00, 70.19, 50.60, 22.55.

4-Hexynoic acid[10] (1g)



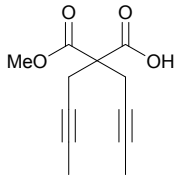
5-Hexynoic acid (5 mmol, 560 mg) and KO*t*Bu (10 mmol, 1.12g) were dissolved in DMSO (20 mL). The mixture was stirred at room temperature for 3 h. Then it was quenched with 2 M HCl solution (10 mL) and extracted with ethyl ether (3×10 mL). The organic layer was separated, dried and evaporated under reduced pressure to yield a colourless oil (524.7 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.57-2.54 (m, 2H), 2.47- 2.43 (m, 2H), 1.77-1.76 (t, *J* = 2.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 178.15, 76.96, 76.73, 33.82, 14.52, 3.53.

2-(Methoxycarbonyl)hex-4-ynoic acid[10] (1h)



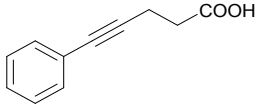
Following the general procedure **C**, **1h** was obtained as a colourless oil (1.10 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.59 (t, *J* = 7.4 Hz, 1H), 2.83 – 2.69 (m, 2H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.83, 168.58, 78.29, 74.18, 52.91, 51.23, 18.82, 3.42.

2-(But-2-yn-1-yl)-2-(methoxycarbonyl)hex-4-ynoic acid[5] (1i)



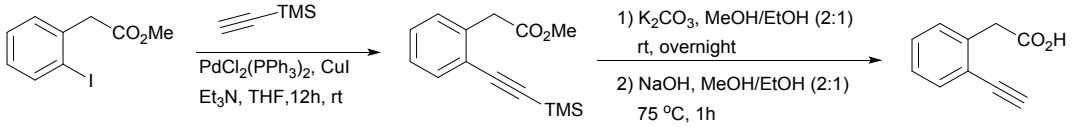
Following the general procedure **C**, **1f** was obtained as a white solid (241 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (s, 1H), 3.78 (s, 3H), 2.91 (d, J = 2.4 Hz, 4H), 1.76 (t, J = 2.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.17, 169.68, 79.30, 72.81, 57.08, 53.08, 23.07, 3.45.

5-Phenylpent-4-ynoic acid[11] (1j)



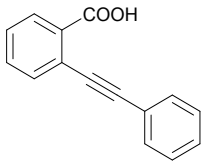
The synthesis route for **1j** is according to the reported method with minor modification.[11] $SOCl_2$ (120 mmol, 8.7 mL) was added dropwise to a solution of 4-pentynoic acid (15 mmol, 1.47 g) in ethanol (30 mL) at 0 °C. The mixture was heated to reflux for 4 h and then concentrated. The residue was dissolved in ethyl acetate and washed with $NaHCO_3$ aqueous solution, water and brine. The organic layer was separated, dried over Na_2SO_4 and concentrated to give crude ethyl pent-4-ynoate (1.74 g, 92%).
Then it was used in the general procedure **D** for Sonogashira coupling reaction. To a solution of ethyl pent-4-ynoate (10 mmol) in dry DMF (5 mL) and Et_3N (5 mL) was added $PdCl_2(PPh_3)_2$ (0.5 mmol), CuI (1 mmol) and iodobezene (10 mmol). The resulting mixture was then stirred at room temperature for 8 h. Afterwards, it was quenched with water (80 mL) and extracted with EA (3×30 mL). The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was then purified through column chromatography to give ethyl 5-phenylpent-4-yonate (1.71 g, 85%).
Afterwards, to a solution ethyl 5-phenylpent-4-yonate (1.5 mmol) in water/MeOH (1:9 v/v, 10 mL) was added NaOH (30 mmol). The mixture was heated to 40 °C and stirred for 1 h. Then it was evaporated, added saturated $NaHCO_3$ aqueous solution (15 mL) and washed with dichloromethane (2×15 mL). The aqueous layer was separated and acidified with 5 M HCl solution until no bubble occurred. Finally, it was extracted with EA (3×20 mL), dried and concentrated under reduced pressure to give a yellow solid (227 mg, 87%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H), 7.39 – 7.33 (m, 5H), 2.63 (t, J = 6.9 Hz, 2H), 2.57 – 2.48 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.38, 131.71, 129.04, 128.50, 123.48, 90.00, 80.97, 33.53, 15.22.

2-(2-Ethynylphenyl)acetic acid[12] (1k)



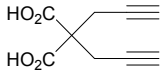
1k was synthesized by three steps.[12] First, Sonogashira reaction was carried out by using methyl 2-(2-iodophenyl)acetate (6 mmol) and trimethylsilylacetylene (6 mmol) according to the general procedure **D** to afford methyl 2-(2-((trimethylsilyl)ethynyl)phenyl)acetate. Then, it was further dissolved in 6 mL MeOH/EtOH (2:1 v/v) and added a catalytic quantity of K_2CO_3. After stirring in air overnight, the mixture was concentrated under reduced pressure and dissolved in DCE. The organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. Solvent was removed in *vacuo*. The resulting oil was dissolved in 6 mL MeOH/EtOH (2:1 v/v) again. 5% NaOH (1.3 equiv.) was added and the mixture was stirred at 75 °C for 1 h. The solution was then concentrated and diluted with water (20 mL), washed with Et_2O (2×15 mL). Subsequently, the aqueous layer was acidified to pH 1-2, extracted with EA (3×15 mL), dried and concentrated in *vacuo* to give a white solid (800 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 7.6 Hz, 1H), 7.35 – 7.23 (m, 4H), 3.89 (s, 2H), 3.28 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.19, 136.02, 132.95, 130.04, 129.18, 127.51, 122.69, 81.99, 81.57, 39.50.

2-(Phenylethynyl)benzoic acid (1m)



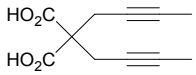
The synthesis of **1m** was according to general procedure **D** for Sonogashira coupling and procedure **C** for mono-saponification. Yellow solid. Yield: 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 7.9, 1.1 Hz, 1H), 7.69 (dd, J = 7.8, 0.9 Hz, 1H), 7.62 – 7.50 (m, 3H), 7.42 (td, J = 7.7, 1.3 Hz, 1H), 7.30 (dtd, J = 9.1, 4.5, 1.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.38, 171.35, 134.17, 132.56, 131.74, 131.35, 130.54, 128.58, 128.35, 127.94, 124.39, 123.13, 95.34, 88.02.

2,2-Di(prop-2-ynyl)malonic acid[7] (1n)



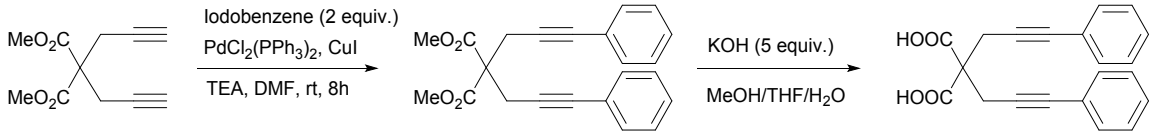
General procedure **E** (for di-saponification): Dimethyl 2,2-di(prop-2-yn-1-yl)malonate (3 mmol) was dissolved in 9 mL mixture solvent (MeOH/THF/H_2O: 1:1:1 v/v/v). The reaction solution was added KOH (15 mmol) and stirred overnight at room temperature in open air. Then the mixture was concentrated under reduced pressure and added 10 mL saturated $NaHCO_3$ solution. The aqueous solution was washed with Et_2O (3×10 mL). Subsequently, the aqueous layer was acidified 1 M HCl solution and extracted with ethyl acetate (3×20 mL). The organic layer was dried with anhydrous Na_2SO_4 and concentrated to give white solid without further purification (328 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.03 (d, J = 2.3 Hz, 4H), 2.38 (s, 2H), 2.10 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.46, 79.68, 74.48, 55.91, 22.51.

2,2-Di(but-2-yn-1-yl)malonic acid[13] (1o)



Following the general procedure **E**, **1o** was obtained as a white solid (536 mg, 98%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.02 (s, 2H), 2.70 (s, 4H), 1.72 (s, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.98, 79.10, 74.76, 56.50, 22.95, 3.67. HRMS (EI) for $C_{11}H_{12}O_4$ calcd. 208.0736, found 208.0689.

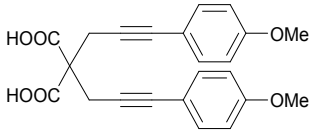
2,2-Bis(3-phenylprop-2-yn-1-yl)malonic acid[14] (1p)



1p

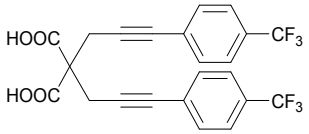
To a solution of dimethyl 2,2-di(prop-2-yn-1-yl)malonate (6 mmol) in dry DMF (6 mL) and Et_3N (6 mL) was added $PdCl_2(PPh_3)_2$ (0.3 mmol), CuI (0.6 mmol) and iodobezene (12 mmol). The mixture was then stirred at room temperature for 8 h. After the reaction completed, it was quenched with water (80 mL) and extracted with EA (3×30 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified through column chromatography to give a colourless oil (1.856 g, 86%). The intermediate product was subjected to the general procedure **E** to give a white solid **1p** (983 mg, 87%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.37 (s, 2H), 7.36 (s, 10H), 3.10 (s, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.82, 131.93, 129.19, 128.97, 123.03, 85.94, 83.57, 56.84, 23.81. HRMS (EI) for $C_{21}H_{16}O_4$, calcd. 332.1049, found 332.0991.

2,2-Bis(3-(4-methoxyphenyl)prop-2-yn-1-yl)malonic acid (1q)



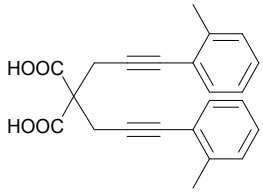
1q was prepared following the similar procedure carried out for **1p**. Yield: 85%. Yellow solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.30 (s, 2H), 7.31 (d, J = 8.7 Hz, 4H), 6.91 (d, J = 8.8 Hz, 4H), 3.76 (s, 6H), 3.05 (s, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.83, 159.64, 133.31, 114.92, 114.68, 84.09, 83.33, 56.79, 55.69, 23.69. HRMS (EI) for $C_{23}H_{20}O_6$, calcd. 392.1260, found 392.1256.

2,2-Bis(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)malonic acid (1r)



1r was prepared following the similar procedure carried out for **1p**. Yield: 89%. White solid. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.71 (d, J = 8.0 Hz, 4H), 7.58 (d, J = 8.0 Hz, 4H), 3.14 (s, 4H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 170.30, 132.29, 128.61 (q, J = 32.3 Hz), 126.83, 125.68 (q, J = 3.9 Hz), 124.11 (q, J = 272.1 Hz), 88.60, 81.98, 56.29, 23.53. HRMS (EI) for $C_{23}H_{14}F_6O_4$, calcd. 468.0796, found 468.0715.

2,2-Bis(3-(o-tolyl)prop-2-yn-1-yl)malonic acid (1s)

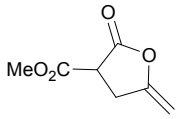


1s was synthesized following the similar procedure carried out for **1p**. White solid. Yield: 97%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.34 (d, J = 7.5 Hz, 2H), 7.25 (d, J = 4.1 Hz, 4H), 7.16 (dt, J = 8.2, 4.3 Hz, 2H), 3.16 (s, 4H), 2.35 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.81, 140.03, 132.05, 129.96, 128.80, 126.28, 122.74, 89.58, 82.19, 56.65, 23.99, 20.71. HRMS (EI) for $C_{23}H_{20}O_4$, calcd. 360.1362, found 360.1297.

1.5 General procedure for gold(I)-catalysed cyclization of alkynoic acid into enol lactones

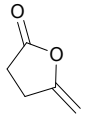
Alkynoic acid (0.3 mmol), **L4AuCl** (0.0015 mmol) and water (2 mL) were added in a reaction tube. The reaction was stirred at room temperature and monitored by TLC (a small amount of sample was taken from the reaction mixture and was extracted with dichloromethane; then the organic product in the dichloromethane extract was detected by TLC). Upon completion, the reaction mixture was extracted with Et_2O (4×3 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified through column chromatography.

Methyl 5-methylene-2-oxotetrahydrofuran-3-carboxylate[10] (2a)



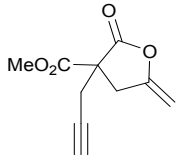
Colourless oil. Yield: 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 – 4.77 (m, 1H), 4.44 – 4.37 (m, 1H), 3.81 (s, 3H), 3.76 (dd, J = 10.4, 7.7 Hz, 1H), 3.29 (ddt, J = 16.6, 7.6, 2.0 Hz, 1H), 3.09 (ddt, J = 16.6, 10.4, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.52, 167.31, 153.12, 89.90, 53.39, 46.23, 29.34.

5-Methylenedihydrofuran-2(3H)-one[7] (2b)



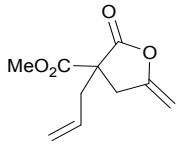
Colourless oil. Yield: 88%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.70 (dd, J = 4.4, 2.1 Hz, 1H), 4.28 (dd, J = 4.0, 1.9 Hz, 1H), 2.85 (ddd, J = 6.7, 5.9, 1.8 Hz, 2H), 2.69 – 2.60 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.87, 155.60, 88.61, 27.90, 24.98.

Methyl 5-methylene-2-oxo-3-(prop-2-yn-1-yl)tetrahydrofuran-3-carboxylate[7] (2c)



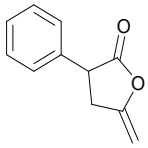
Pale yellow oil. Yield: 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 – 4.81 (m, 1H), 4.44 (t, *J* = 1.8 Hz, 1H), 3.82 (s, 3H), 3.36 – 3.17 (m, 2H), 2.94 – 2.86 (m, 2H), 2.10 (t, *J* = 2.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.43, 168.57, 152.55, 89.88, 77.73, 72.47, 54.55, 53.76, 34.83, 23.89.

Methyl 3-allyl-5-methylene-2-oxotetrahydrofuran-3-carboxylate[7] (2d)



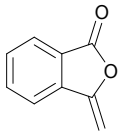
Yellow oil. Yield: 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 – 5.59 (m, 1H), 5.24 – 5.14 (m, 2H), 4.78 (t, *J* = 2.3 Hz, 1H), 4.36 (t, *J* = 2.4 Hz, 1H), 3.78 (s, 3H), 3.28 (dt, *J* = 16.8, 1.8 Hz, 1H), 2.90 (dt, *J* = 16.7, 2.1 Hz, 1H), 2.76 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.66 (dd, *J* = 14.0, 7.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.24, 169.36, 152.70, 131.09, 121.17, 89.73, 54.95, 53.49, 38.35, 34.44.

5-Methylene-3-phenyldihydrofuran-2(3H)-one[15] (2e)



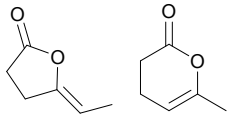
Colourless oil. Yield: 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 5H), 4.86 – 4.79 (m, 1H), 4.45 – 4.38 (m, 1H), 3.98 (dd, *J* = 10.0, 7.9 Hz, 1H), 3.33 (ddt, *J* = 16.5, 10.1, 1.8 Hz, 1H), 3.00 (ddt, *J* = 16.4, 7.7, 1.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.06, 154.15, 136.71, 129.21, 128.08, 127.63, 89.29, 46.11, 34.56.

3-Methyleneisobenzofuran-1(3H)-one[16] (2f)



Yellow solid. Yield: 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.73 (d, *J* = 3.9 Hz, 2H), 7.59 (dt, *J* = 7.9, 4.0 Hz, 1H), 5.24 (dd, *J* = 5.8, 2.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.89, 151.86, 139.03, 134.48, 130.48, 125.32, 125.15, 120.60, 91.27.

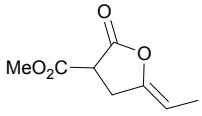
(Z)-5-Ethylidenedihydrofuran-2(3H)-one[10] (2g-*exo*)
6-Methyl-3,4-dihydro-2H-pyran-2-one[17] (2g-*endo*)



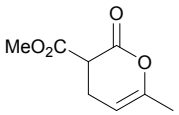
2g-*exo* **2g-*endo***

Colourless oil. Yield: 85% (**2g-*exo***:**3g-*endo***/20:1) ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (td, *J* = 4.4, 1.3 Hz, 1H, **2g-*endo***), 4.60 (qt, *J* = 6.9, 1.8 Hz, 1H, **2g-*exo***), 2.83 – 2.79 (m, 2H, **2g-*exo***), 2.66 – 2.62 (m, 2H, **2g-*exo***), 2.58 (t, *J* = 7.6 Hz, 2H, **2g-*endo***), 2.29 (tdd, *J* = 7.6, 4.4, 2.0 Hz, 2H, **2g-*endo***), 1.89 (q, *J* = 1.8 Hz, 3H, **2g-*endo***), 1.67 (dt, *J* = 6.9, 1.9 Hz, 3H, **2g-*exo***). ^{13}C NMR of **2g-*exo*** (126 MHz, $CDCl_3$) δ 175.33, 148.44, 99.30, 28.14, 25.05, 10.48.

Methyl (Z)-5-ethylidene-2-oxotetrahydrofuran-3-carboxylate[10] (2h-*exo*)
Methyl 6-methyl-2-oxo-3,4-dihydro-2H-pyran-3-carboxylate[10] (2h-*endo*)



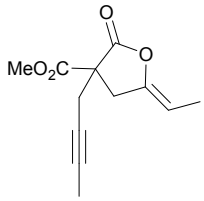
2h-*exo*



2h-*endo*

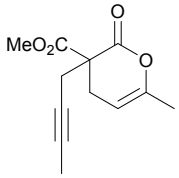
Colourless oil. Yield: 99% (**2h-*exo***:**2h-*endo***/ 5:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.03 (s, 1H, **2h-*endo***), 4.72 (q, *J* = 6.8 Hz, 1H, **2h-*exo***), 3.82 (s, 3H, **2h-*exo***), 3.80 (s, 3H, **2h-*endo***), 3.74 (dd, *J* = 10.1, 8.1 Hz, 1H, **2h-*exo***), 3.56 (t, *J* = 7.8 Hz, 1H, **2h-*endo***), 3.23 (dd, *J* = 16.0, 7.8 Hz, 1H, **2h-*exo***), 3.04 (dd, *J* = 15.8, 10.6 Hz, 1H, **2h-*exo***), 2.77 – 2.71 (m, 1H, **2h-*endo***), 2.57 – 2.40 (m, 2H, **2h-*endo***), 1.90 (s, 3H, **2h-*endo***), 1.69 (d, *J* = 6.8 Hz, 3H, **2h-*exo***). ^{13}C NMR of **2h-*exo*** (101 MHz, $CDCl_3$) δ 169.76, 167.58, 145.84, 100.38, 53.21, 46.18, 29.22, 10.40. ^{13}C NMR of **2h-*endo*** (101 MHz, $CDCl_3$) δ 169.76, 168.66, 150.26, 98.66, 52.87, 45.42, 22.36, 18.41.

Methyl (Z)-3-(but-2-yn-1-yl)-5-ethylidene-2-oxotetrahydrofuran-3-carboxylate[18] (2i-*exo*)



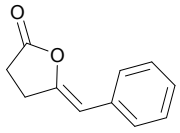
Colourless oil. Yield: 86% (**10**:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (qt, *J* = 6.9, 1.7 Hz, 1H), 3.78 (s, 3H), 3.18 (tdq, *J* = 18.2, 16.3, 1.8 Hz, 2H), 2.90 – 2.74 (m, 2H), 1.75 (t, *J* = 2.5 Hz, 3H), 1.71 (dt, *J* = 6.9, 1.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 169.03, 145.41, 99.89, 79.76, 72.43, 54.68, 53.40, 34.66, 24.31, 10.42, 3.42.

Methyl 3-(but-2-yn-1-yl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-3-carboxylate[18] (2i-*endo*)



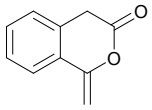
Colourless oil. Yield: 86% (10:**1**) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.01 (ddd, *J* = 6.1, 2.7, 1.3 Hz, 1H), 3.76 (s, 3H), 2.90 – 2.80 (m, 1H), 2.80 – 2.71 (m, 2H), 2.62 (dp, *J* = 17.0, 2.5 Hz, 1H), 1.88 (dt, *J* = 2.5, 1.2 Hz, 3H), 1.77 (t, *J* = 2.5 Hz, 3H).

(Z)-5-Benzylidenedihydrofuran-2(3H)-one[10] (2j)



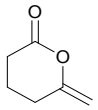
White solid. Yield: 99%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (s, 2H), 7.31 (d, *J* = 5.5 Hz, 2H), 7.20 (d, *J* = 5.8 Hz, 1H), 5.54 (s, 1H), 3.01 (s, 2H), 2.69 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.07, 148.28, 134.06, 128.58, 128.42, 126.84, 105.00, 27.06, 26.43.

1-Methyleneisochroman-3-one[19] (2k)

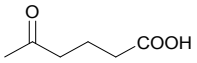


Brown oil. Yield: 23%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.35 (tt, *J* = 12.6, 6.4 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 1H), 5.13 (d, *J* = 2.4 Hz, 1H), 5.03 (d, *J* = 2.4 Hz, 1H), 3.84 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.20, 153.77, 130.05, 128.62, 127.92, 127.41, 127.25, 124.79, 95.03, 34.92.

6-Methylenetetrahydro-2H-pyran-2-one[7] (2l) and 5-Oxohexanoic acid[20] (3l)



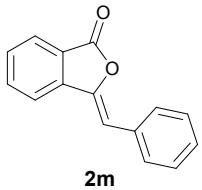
2l



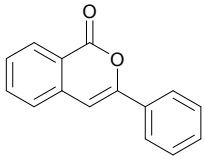
3l

Colourless oil. Yield: 95% (**2l**:**3l**/ 61:34) ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.65 – 4.62 (m, 1H, **2l**), 4.29 (dd, *J* = 2.5, 1.2 Hz, 1H, **2l**), 2.63 (t, *J* = 6.8 Hz, 2H, **2l**), 2.53 (t, *J* = 7.2 Hz, 2H, **3l**), 2.50 – 2.44 (m, 2H, **2l**), 2.39 (t, *J* = 7.2 Hz, 2H, **3l**), 2.14 (s, 3H, **3l**), 1.95 – 1.81 (m, 4H, **2l** and **3l**). ^{13}C NMR of **2l** (101 MHz, $CDCl_3$) δ 93.75, 42.28, 32.80, 30.25, 26.73, 18.56.

(Z)-3-Benzylideneisobenzofuran-1(3H)-one (2m) and 3-Phenyl-1H-isochromen-1-one (3m)[17]



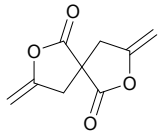
2m



3m

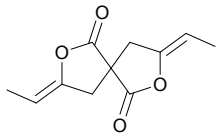
Pale yellow solid. 82%. The (*Z*)-5-*exo*-*dig* and 6-*endo*-*dig* isomers were obtained in a 20:80 ratio. Signals corresponding to **3m**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.2 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.53 – 7.37 (m, 5H), 6.94 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.30, 153.64, 137.53, 134.87, 131.98, 129.97, 129.66, 128.83, 128.15, 125.98, 125.26, 120.56, 101.81. Representative signals corresponding to **2m**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H), 6.41 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.48, 133.10, 130.13, 129.77, 128.77, 128.42, 125.57, 119.82, 107.06.

3,8-Dimethylene-2,7-dioxaspiro[4.4]nonane-1,6-dione[7] (2n)



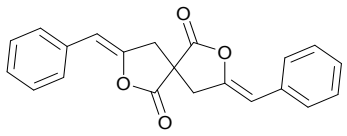
Colourless oil. Yield: 97%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (s, 2H), 4.50 (s, 2H), 3.46 (d, *J* = 16.6 Hz, 2H), 2.94 (d, *J* = 16.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.81, 151.26, 91.11, 51.92, 36.34.

(3Z,8Z)-3,8-Diethylidene-2,7-dioxaspiro[4.4]nonane-1,6-dione (2o)



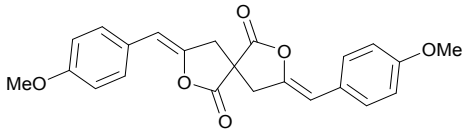
White solid. Yield: 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.78 (qt, *J* = 6.9, 1.6 Hz, 2H), 3.39 (dt, *J* = 16.1, 1.6 Hz, 2H), 2.85 (dt, *J* = 16.1, 1.8 Hz, 2H), 1.72 (dt, *J* = 6.9, 1.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.30, 144.31, 101.71, 51.69, 36.61, 10.62. HRMS (EI) for C_{11} H_{12} O_4, calcd. 208.0736, found 208.0730.

3-((Z)-Benzylidene)-8-((Z)-cyclohexa-2,4-dien-1-ylidenemethyl)-2,7-dioxaspiro[4.4]nonane-1,6-dione (2p)



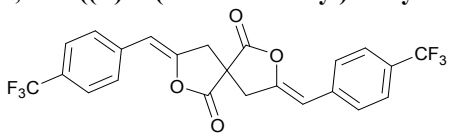
White solid. Yield: 93% ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 4H), 7.35 (t, *J* = 7.7 Hz, 4H), 7.25 (t, *J* = 7.2 Hz, 2H), 5.69 (s, 2H), 3.64 (dd, *J* = 16.6, 1.0 Hz, 2H), 3.12 (dd, *J* = 16.6, 1.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.82, 143.35, 132.91, 128.67, 128.59, 127.49, 107.04, 49.96, 37.81. HRMS (EI) for $C_{21}H_{16}O_4$, calcd. 332.1049, found 332.1056

3,8-Bis((Z)-4-methoxybenzylidene)-2,7-dioxaspiro[4.4]nonane-1,6-dione (2q)



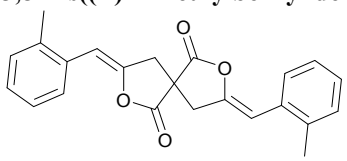
White solid. Yield: 97%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.8 Hz, 4H), 6.88 (d, *J* = 8.9 Hz, 4H), 5.63 (s, 2H), 3.82 (d, *J* = 2.1 Hz, 6H), 3.62 (dd, *J* = 16.5, 1.5 Hz, 2H), 3.10 (dd, *J* = 16.5, 1.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.12, 158.98, 141.80, 130.08, 125.79, 114.11, 106.64, 55.40, 50.22, 37.95. HRMS (EI) for $C_{23}H_{20}O_6$, calcd. 392.1260, found 392.1249.

3,8-Bis((Z)-4-(trifluoromethyl)benzylidene)-2,7-dioxaspiro[4.4]nonane-1,6-dione (2r)



White solid. Yield: 96%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.2 Hz, 4H), 7.60 (d, *J* = 8.3 Hz, 4H), 5.76 (s, 2H), 3.70 (d, *J* = 16.9 Hz, 2H), 3.20 (d, *J* = 16.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.22, 145.17, 136.25, 129.19 (q, *J* = 32.9 Hz), 128.75, 125.48 (q, *J* = 3.8 Hz), 124.04 (q, *J* = 272.2 Hz), 105.87, 49.69, 37.60. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.59. HRMS (EI) for $C_{23}H_{14}F_6O_4$, calcd. 468.0796, found 468.0795.

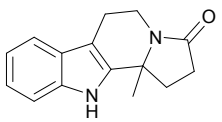
3,8-Bis((Z)-2-methylbenzylidene)-2,7-dioxaspiro[4.4]nonane-1,6-dione (2s)



White solid. Yield: 84% ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.5 Hz, 2H), 7.24 – 7.13 (m, 6H), 5.84 (s, 2H), 3.65 (dd, *J* = 16.6, 1.5 Hz, 2H), 3.15 (dd, *J* = 16.6, 1.7 Hz, 2H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.89, 143.74, 135.54, 131.54, 130.14, 129.23, 127.58, 126.13, 104.42, 50.31, 37.71, 20.20. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.59. HRMS (EI) for $C_{23}H_{20}O_4$, calcd. 360.1362, found 360.1347.

1.6 General procedure for gold(I)-catalysed synthesis of fused polycyclic indoles

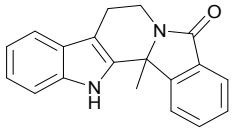
11B-methyl-1,2,5,6,11,11b-hexahydro-3H-indolizino[8,7-b]indol-3-one[21] (7a)



To a round-bottomed flask, 4-pentynoic acid (0.3 mmol) and **L4**AuCl (0.0015 mmol) was added in water (2 mL). After stirring at room temperature for half hour, tryptamine (0.3 mmol) was added. Then the mixture was heated to 60 °C and stirred for 15 h. The resulting white solid was filtered and purified via

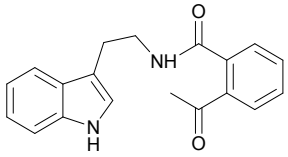
flash column chromatography. White solid. Yield: 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.08 – 7.00 (m, 1H), 6.99 – 6.90 (m, 1H), 4.18 (dd, J = 13.1, 5.6 Hz, 1H), 3.03 (td, J = 12.1, 4.4 Hz, 1H), 2.69 (dd, J = 15.2, 4.3 Hz, 1H), 2.64 – 2.51 (m, 2H), 2.33 – 2.16 (m, 2H), 2.10 – 1.95 (m, 1H), 1.52 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.45, 139.53, 136.51, 126.85, 121.56, 119.15, 118.54, 111.70, 105.23, 59.45, 34.83, 33.15, 30.64, 25.53, 21.46.

13B-methyl-7,8,13,13b-tetrahydro-5H-benzo[1,2]indolizino[8,7-b]indol-5-one[11] (7b)



To a round-bottomed flask, 2-ethynylbenzoic acid (0.3 mmol) and **L4**AuCl (0.0015 mmol) was added in water (2 mL). After stirring at room temperature for 1 h, tryptamine (0.3 mmol) and a catalytic amount of TFA were added. The mixture was heated to 60 °C and stirred for 15 h. The resulting white solid was extracted with DCM, dried over with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified via flash column chromatography. White solid. Yield: 74%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.31 (s, 1H), 8.29 (d, J = 7.8 Hz, 1H), 7.69 (dd, J = 6.7, 4.6 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.0 Hz, 2H), 7.07 (t, J = 7.5 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H), 4.51 (dd, J = 13.2, 5.5 Hz, 1H), 3.38 (td, J = 12.6, 4.5 Hz, 1H), 2.77 (dd, J = 15.3, 4.1 Hz, 1H), 2.72 – 2.60 (m, 1H), 1.83 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.63, 149.79, 136.65, 135.64, 132.65, 130.72, 129.04, 126.44, 123.62, 123.21, 122.05, 119.33, 118.77, 111.65, 106.80, 62.46, 35.87, 26.35, 21.89.

N-(2-(1H-indol-3-yl)ethyl)-2-acetylbenzamide[22] (6b)

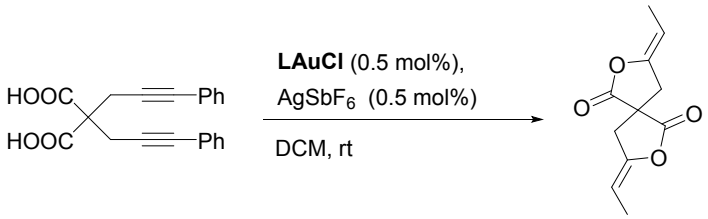


White solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.83 (s, 1H), 7.71 – 7.60 (m, 4H), 7.55 – 7.49 (m, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 2.6 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.02 (t, J = 7.3 Hz, 1H), 6.34 (s, 1H), 3.77 – 3.51 (m, 2H), 3.22 – 2.95 (m, 2H), 1.60 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.74, 149.10, 136.27, 131.97, 130.70, 128.98, 127.17, 122.72, 122.14, 121.91, 120.93, 118.28, 111.82, 111.40, 87.86, 39.04, 24.89.

1.7 Procedure for recycling PEGylated NHC-gold(I) catalyst for cyclization of alkynoic acid into enol lactones

1a (0.5 mmol), **L4AuCl** (0.005 mmol) and water (2 mL) were added in a reaction tube. The reaction was stirred at room temperature and was monitored by TLC. Upon completion of the reaction, the reaction mixture was extracted with Et_2O (5×2 mL). The combined organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo.* Yield was determined by ^{1}H NMR with trimethoxyphenylsilane as internal standard. The aqueous layer containing recycled gold catalyst was used for consecutive reactions under identical condition.

1.8 Catalytic comparison of L4AuCl and other gold catalysts for cyclization of alkynoic acid



1o **2o**

Entry	Catalyst	Silver salt	Solvent	Time (h)	Yield of **2o** (%)
1	**L4**AuCl	--	H_2O	1.5	96
2	IPrAuCl	$AgSbF_6$	DCM	2.0	36
3	JohnPhosAuCl	$AgSbF_6$	DCM	2.0	15

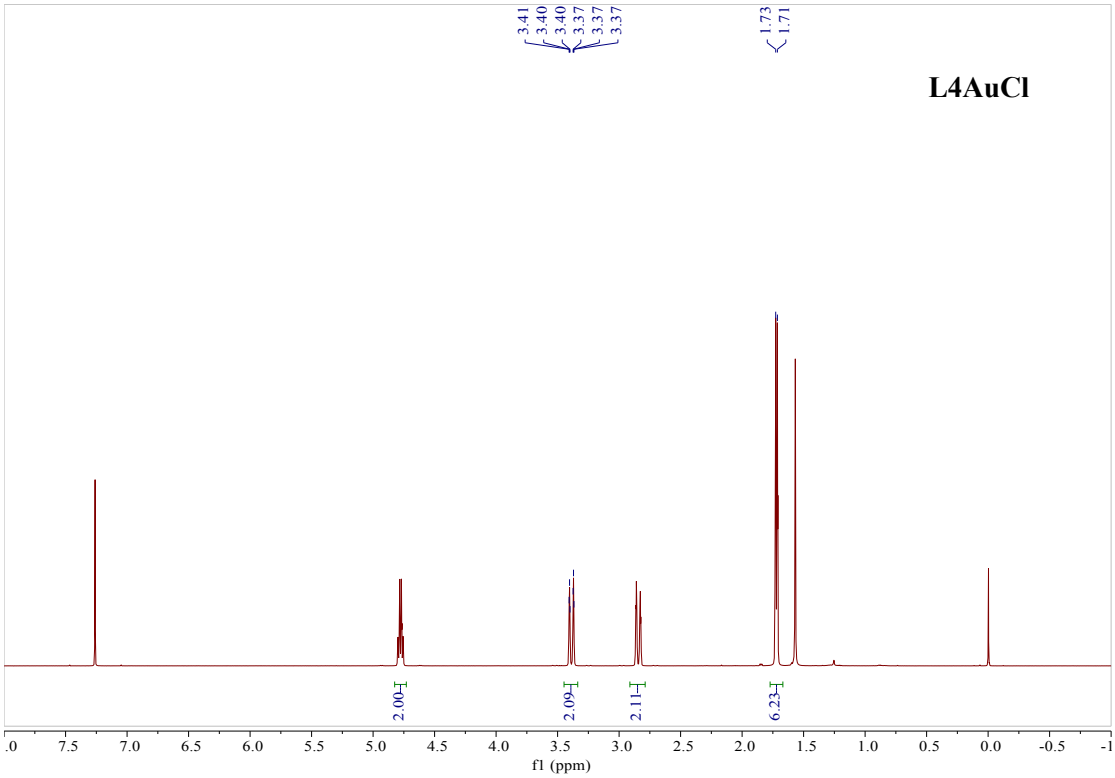


Fig. S1. ^{1}H NMR spectrum of **2o** obtained by **L4AuCl** as catslyst.

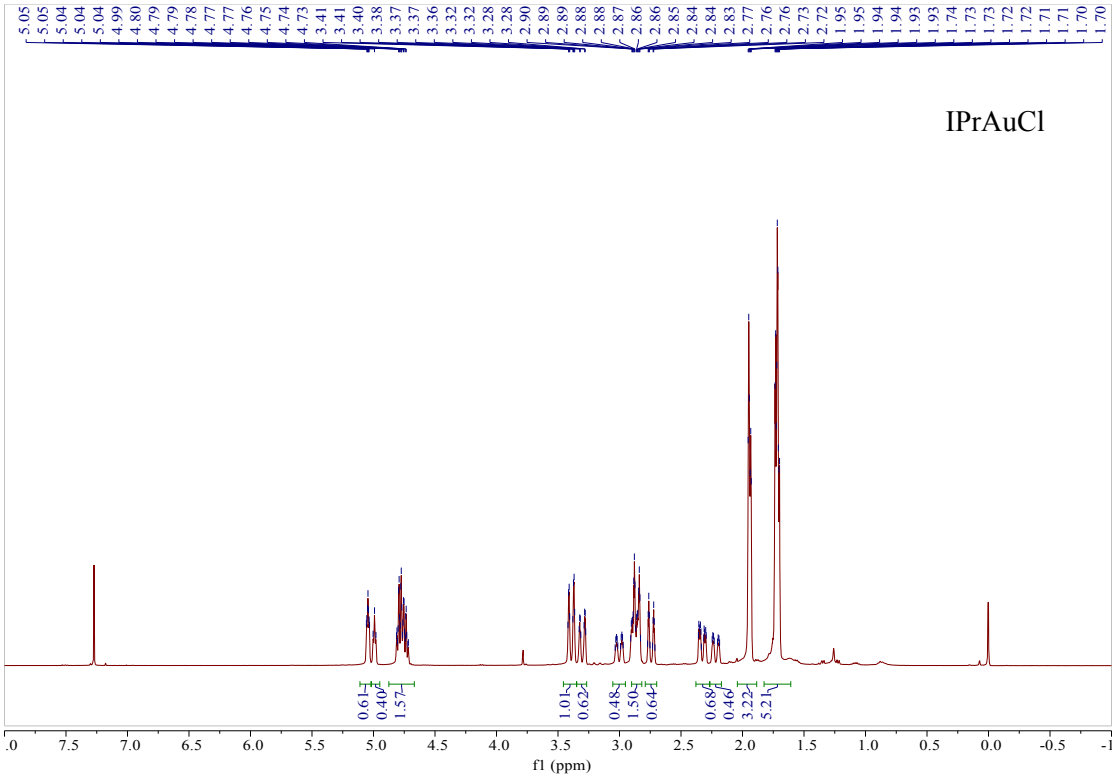


Fig. S2. ^{1}H NMR spectrum of a mixture of products obtained by IPrAuCl as catalyst.

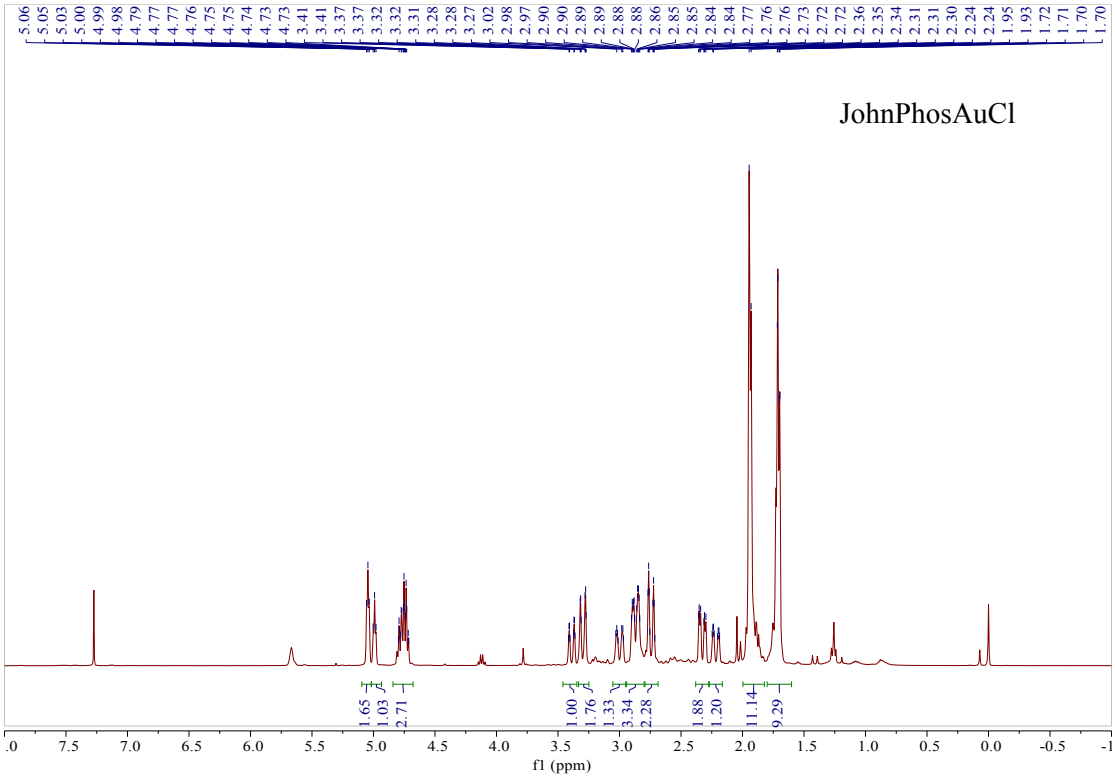


Fig. S3. ^{1}H NMR spectrum of a mixture of products obtained by JohnPhosAuCl as catalyst.

1.9 Detection of gold nanoparticles in reaction solution

The colourless reaction solution was found to turn to pink during the reaction. This observation is indicative of the formation of gold nanoparticles according to literature.[23] To further demonstrate the formation of gold nanoparticles, we examined the reaction solution by UV-visible absorption spectroscopy revealing the formation of an absorption band at around 520 nm, which is the absorption of gold nanoparticles (Fig. S4).[23] Absorbance of UV-Vis increased with increasing concentration of the solution. No absorption of UV-Vis for L4 and fresh **L4AuCl** was observed. Transmission electron microscope (TEM) also showed that there are gold nanoparticles around 20-50 nm in reaction solution (Fig. S7). In order to probe the stability of **L4AuCl** in water, $2x10^{-4}$ mol/mL water solution of **L4AuCl** was tested at different time. UV-visible absorption spectroscopy (Fig. S5) showed that there was no gold nanoparticle formed at the beginning. Slight absorption band for gold nanoparticles occurred after 1.5 h and became higher as time went. But even the solution was kept under air for 2 days (Fig. S5, 2 d), the absorption band was lower than that of used **L4AuCl** (Fig. S4, green line). This indicated that substate or cyclization reaction would promote the formation of gold nanoparticles. We also compared the stability of **L1-L4AuCl** in water. UV-Vis tests of $2x10^{-4}$ mol/mL water solutions of **L1-L4AuCl** were performed after keeping under air for 24 h. It showed that **L1AuCl** and **L4AuCl** are more stable than **L3AuCl** (Fig. S6). The water solution of **L2AuCl** became turbid after 24 h, indicating decomposition of **L2AuCl**.

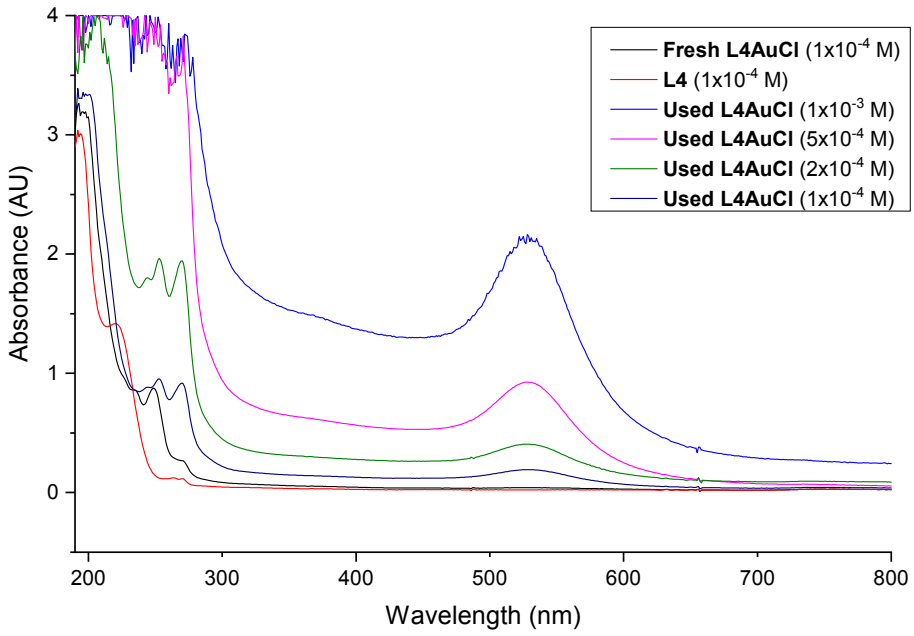


Fig. S4. UV-Vis spectra of blank **L4AuCl**, **L4** and used **L4AuCl** water solution in different concentrations.

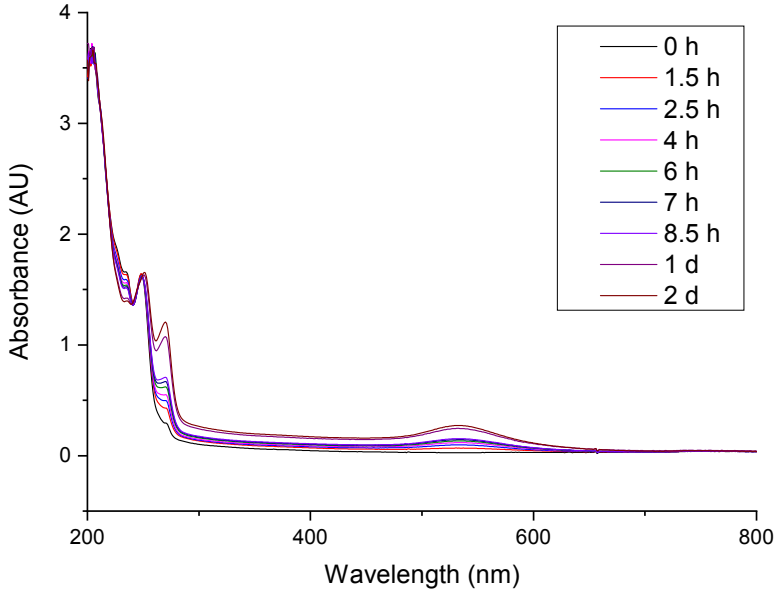


Fig. S5. UV-Vis spectra of $2x10^{-4}$ mol/mL **L4AuCl** water solution in open air at different time.

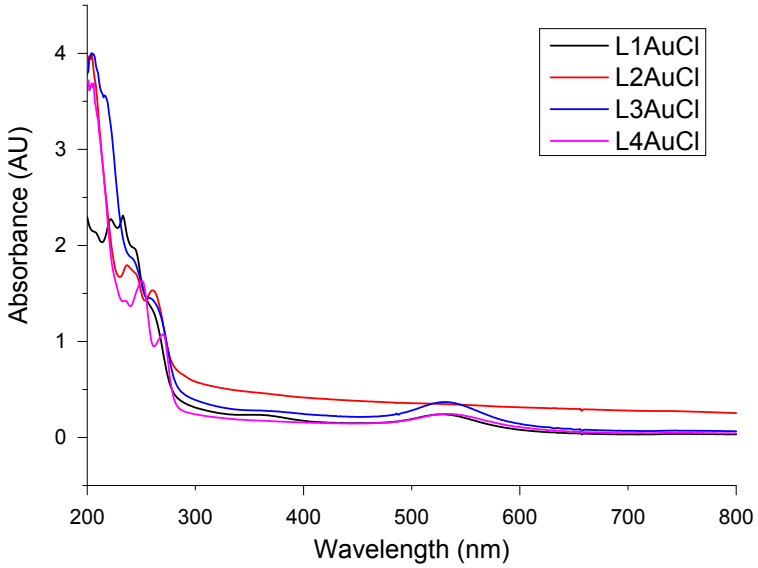


Fig. S6. UV-Vis spectra of $2x10^{-4}$ mol/L **L1-L4AuCl** water solution in open air for 24 h.

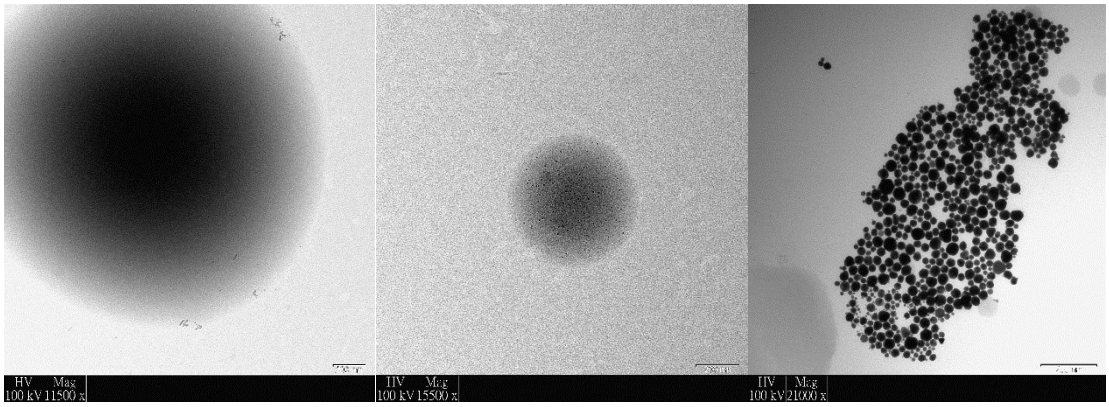


Fig. S7. TEM images of ligand **L4** (left), gold complex **L4AuCl** (middle) and used **L4AuCl** (right).

2. References

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14. S. Li, W. Jia and N. Jiao, *Adv. Synth. Catal.*, 2009, **351**, 569-575.
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23. V. Amendola and M. Meneghetti, *J. Phys. Chem. C*, 2009, **113**, 4277-4285.

3. ^{1}H NMR and MOLDI-TOF mass spectra of PEGylated NHC ligands and gold complexes

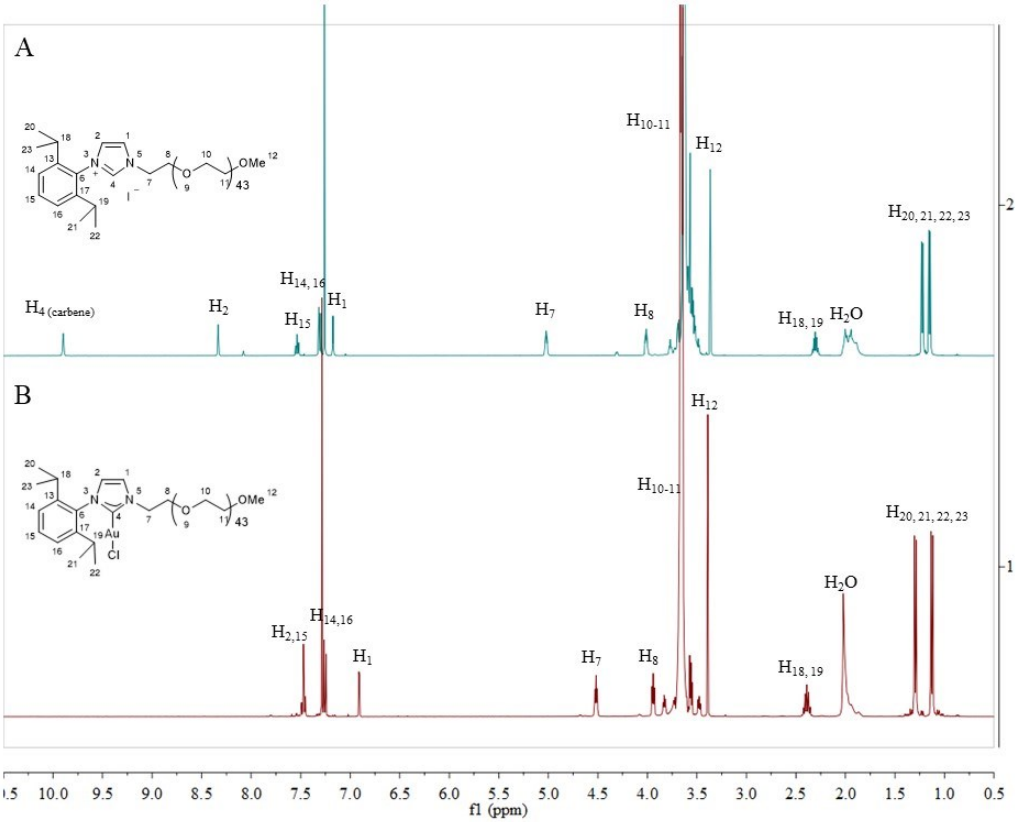


Fig. S8. ^{1}H NMR spectrum of **L4** and **L4AuCl**.

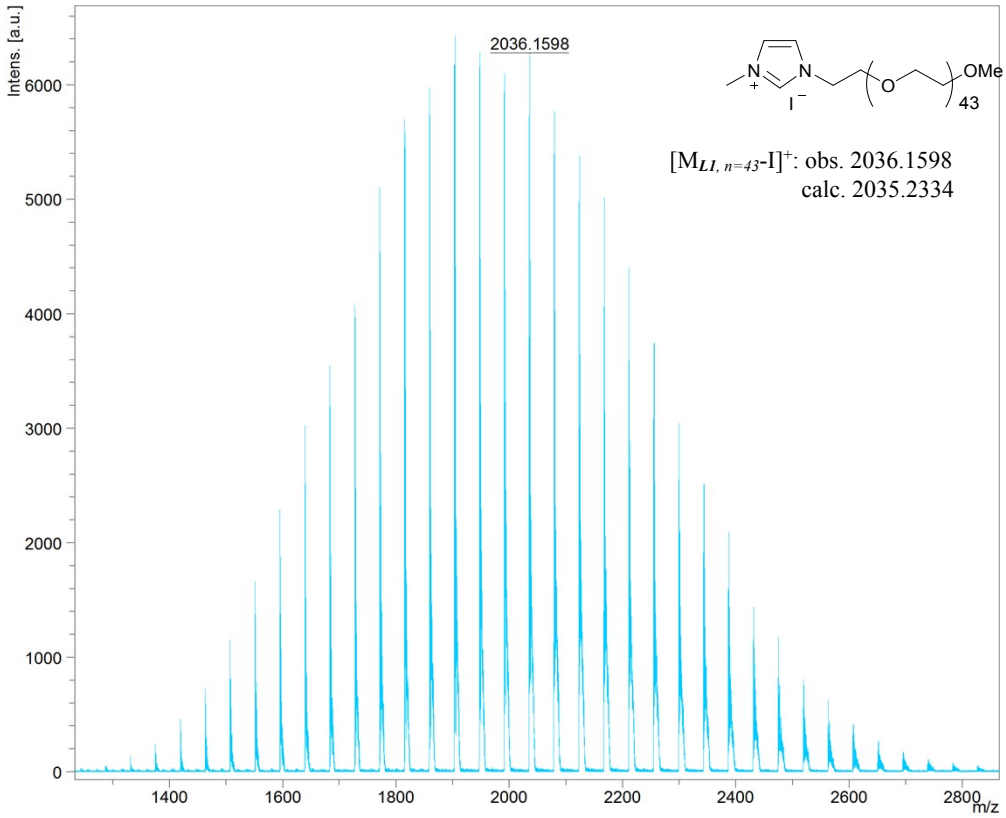


Fig. S9. MALDI-TOF mass spectrum of 1-methylimidazole-mPEG$_{2000}$ (**L1**).

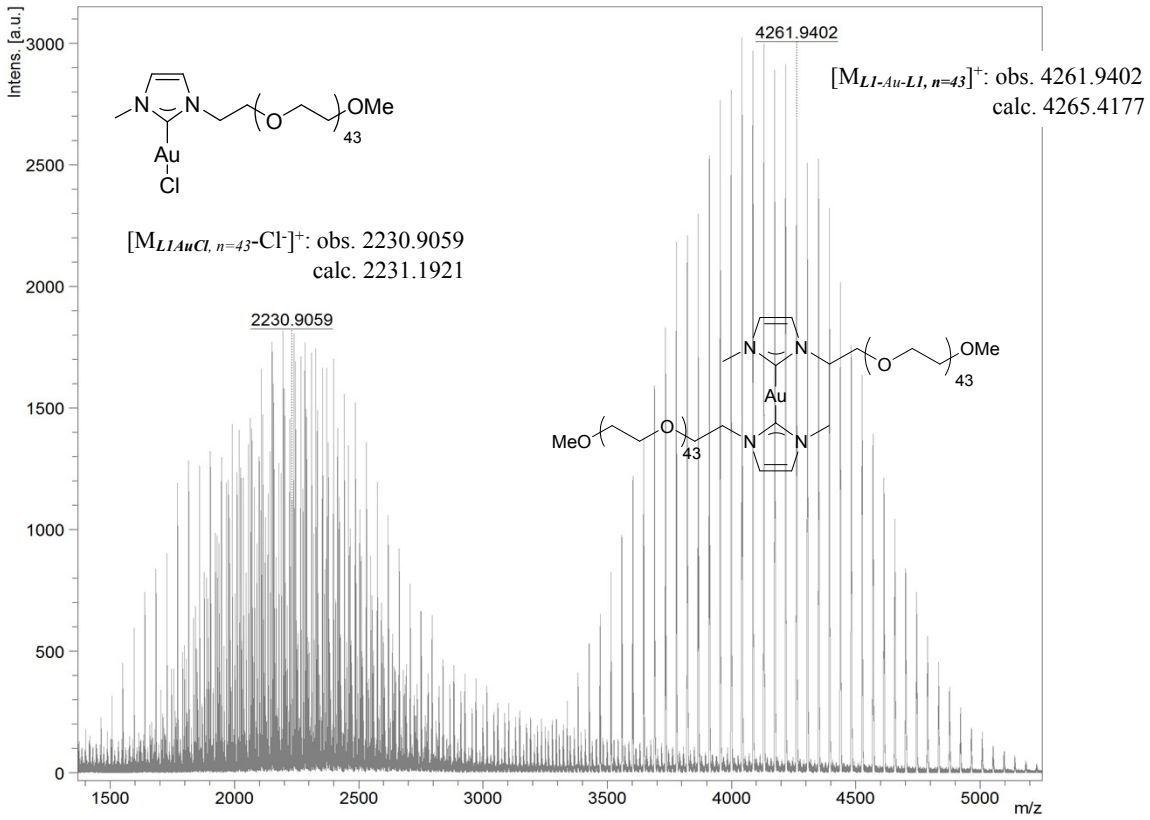


Fig. S10. MALDI-TOF mass spectrum of 1-methylimidazole-mPEG$_{2000}$-AuCl (**L1AuCl**) and dimer (**L1-Au-L1**).

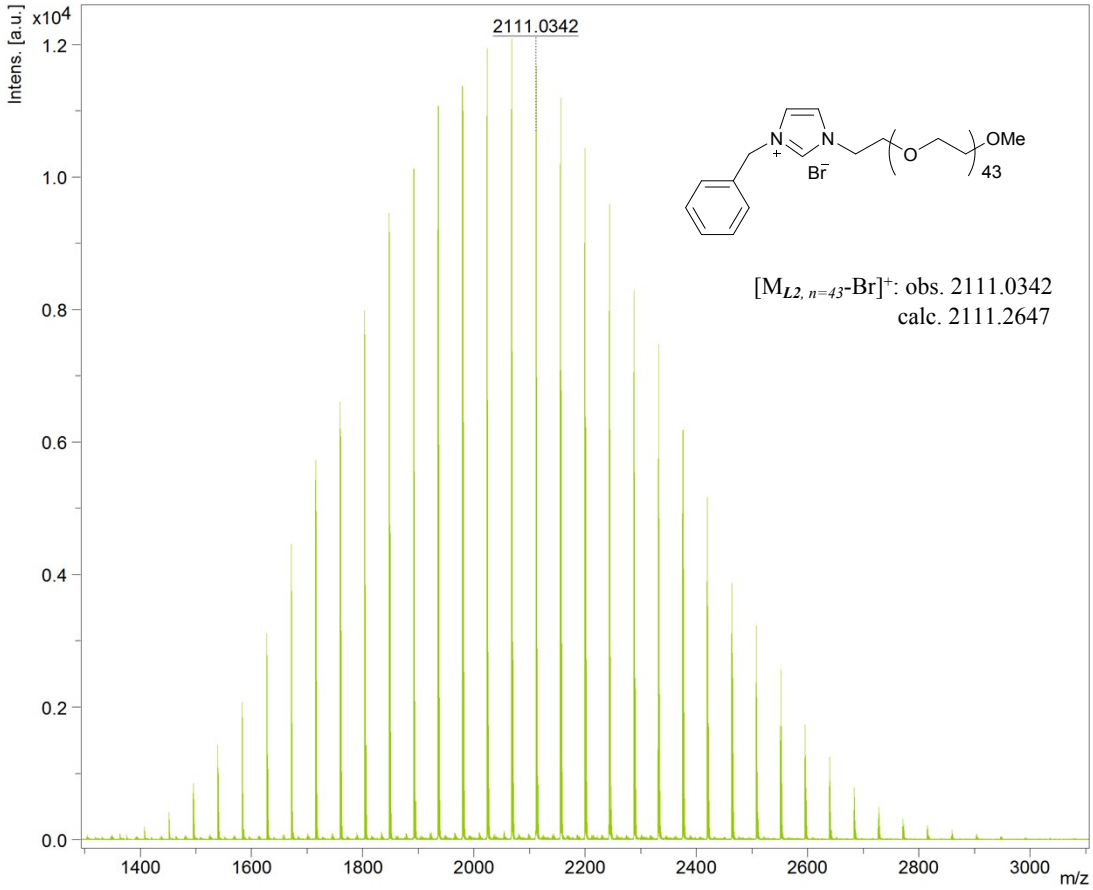


Fig. S11. MALDI-TOF mass spectrum of 1-benzylimidazole-mPEG$_{2000}$ (**L2**).

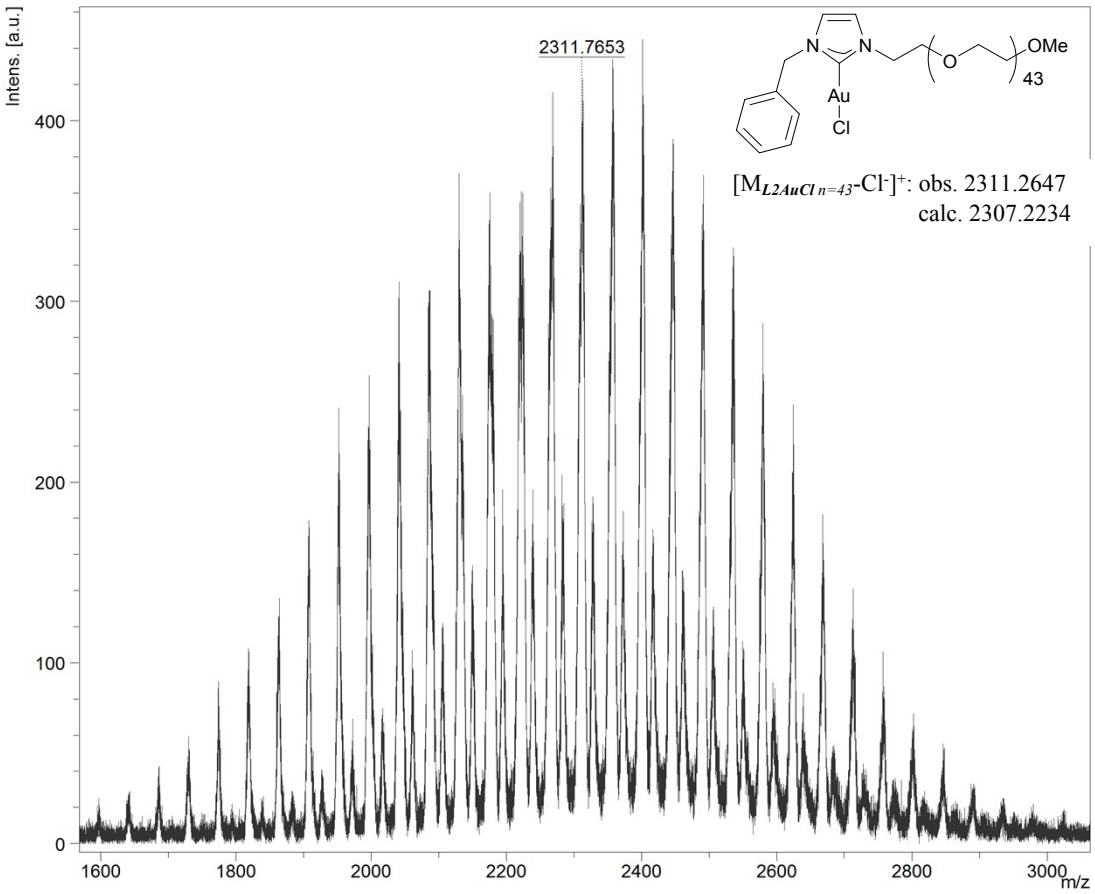


Fig. S12. MALDI-TOF mass spectrum of 1-benzylimidazole-mPEG$_{2000}$-AuCl (**L2AuCl**).

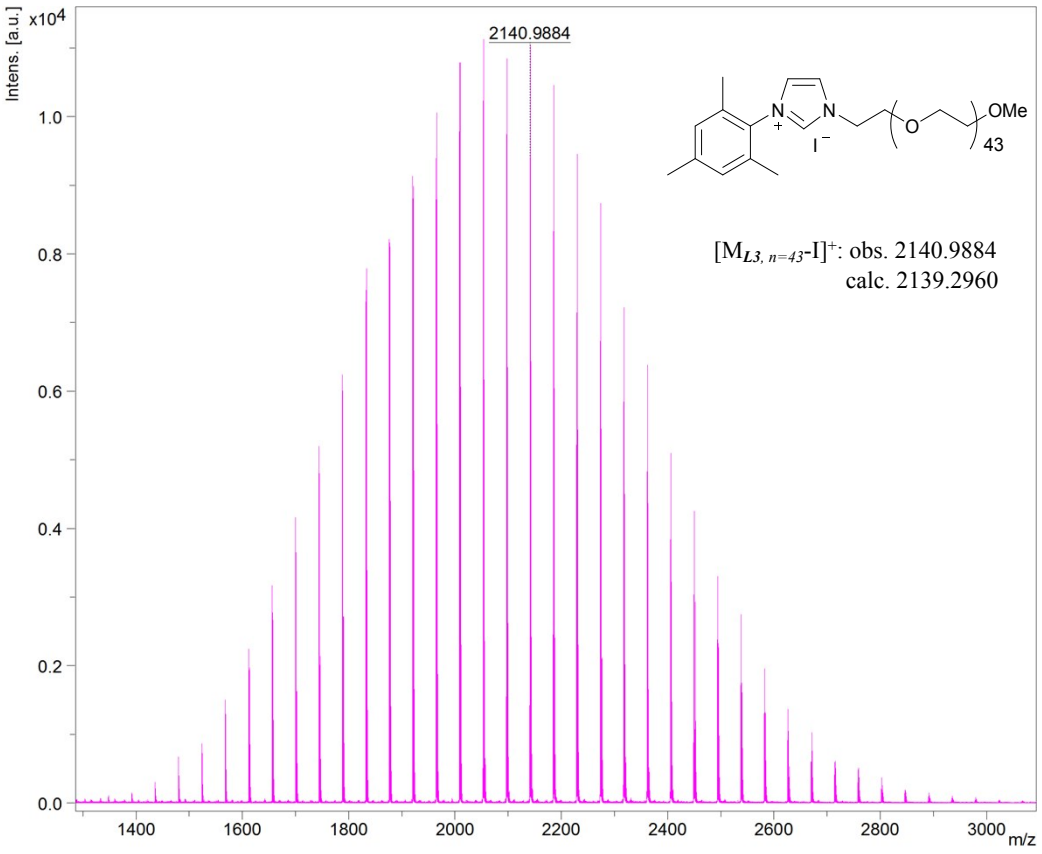


Fig. S13. MALDI-TOF mass spectrum of 1-mesityl imidazole-mPEG$_{2000}$ (**L3**).

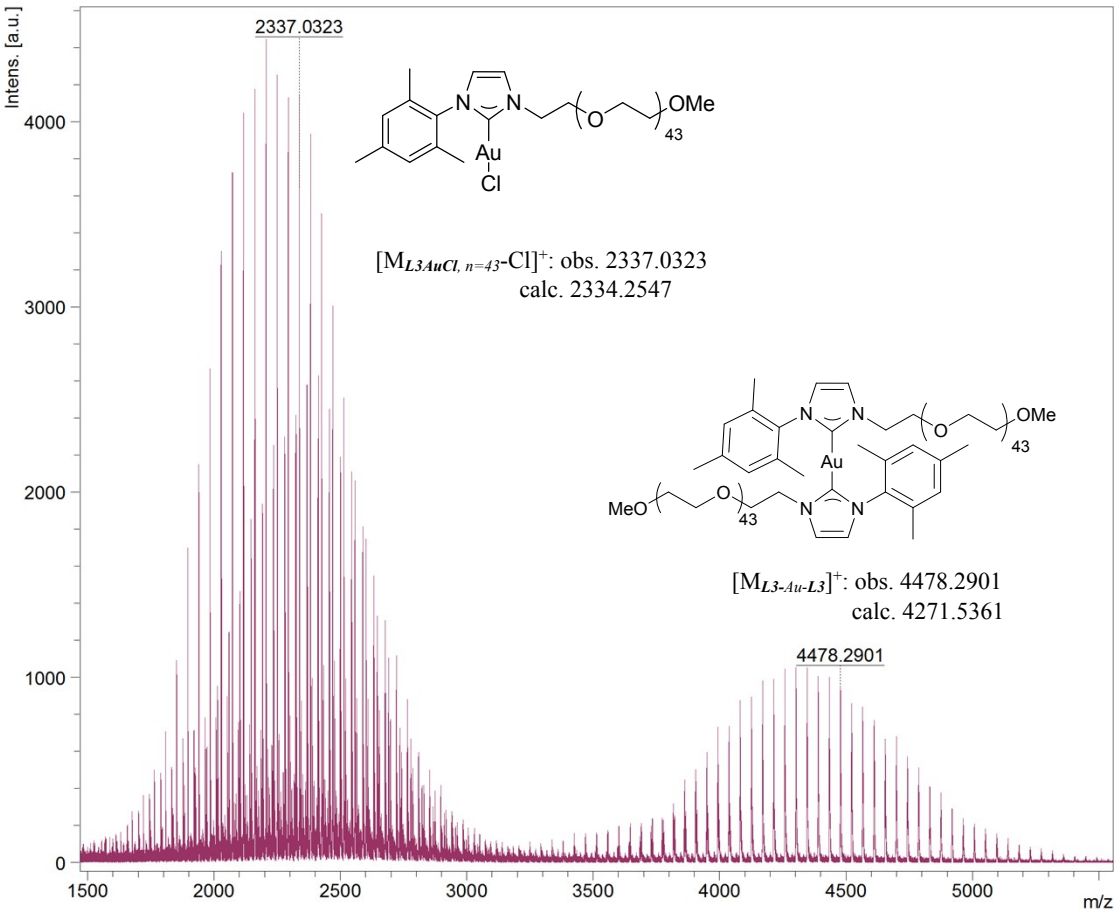


Fig. S14. MALDI-TOF mass spectrum of 1-mesityl imidazole-mPEG$_{2000}$-AuCl (**L3AuCl**) and dimer (**L3-Au-L3**).

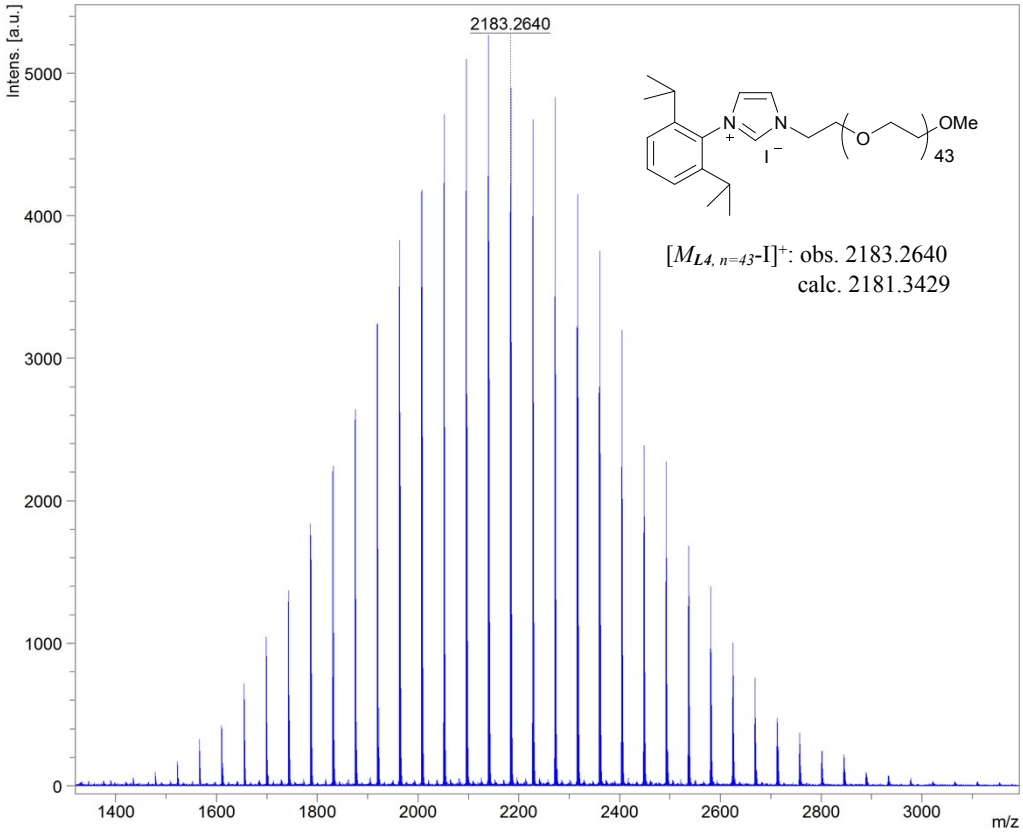


Fig. S15. MALDI-TOF mass spectrum of 1-(2,6-diisopropylphenyl) imidazole-mPEG$_{2000}$ (**L4**).

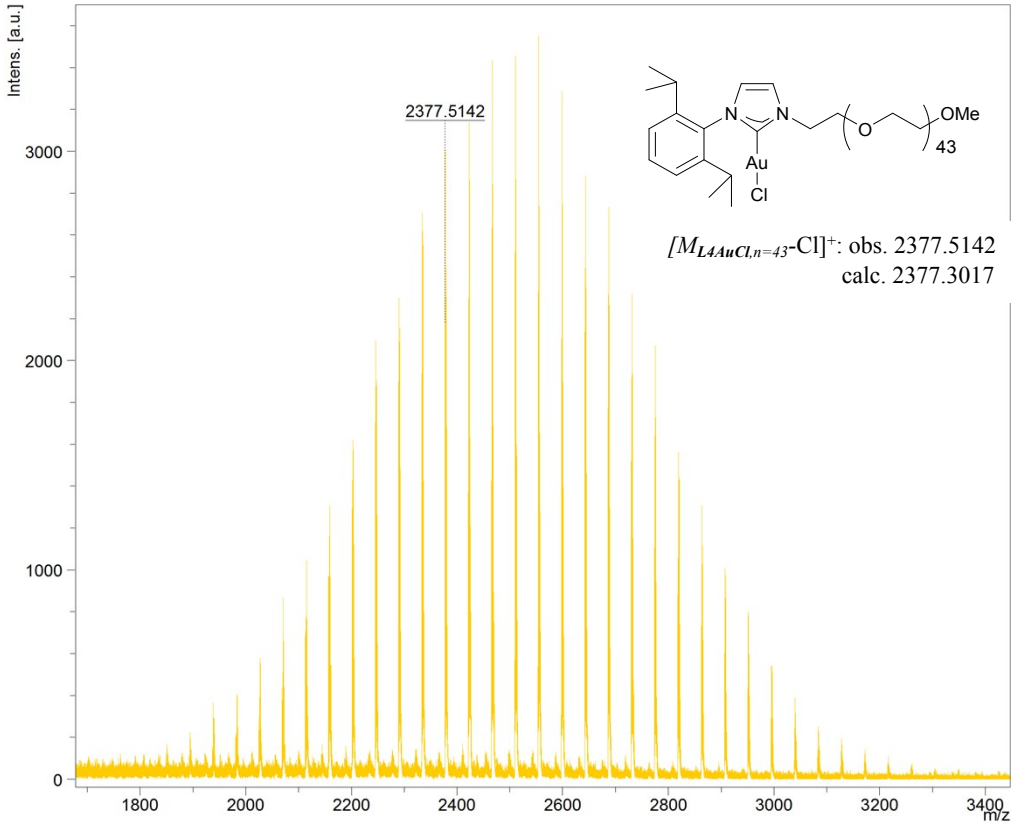
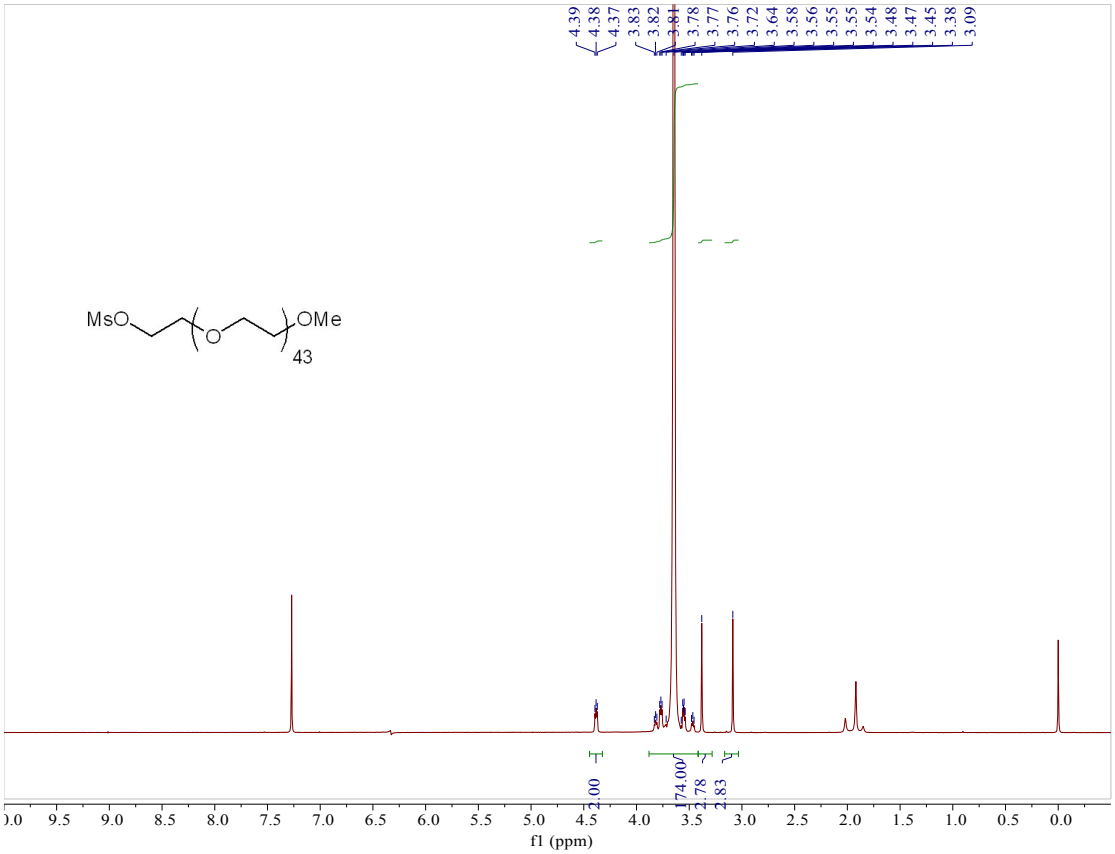
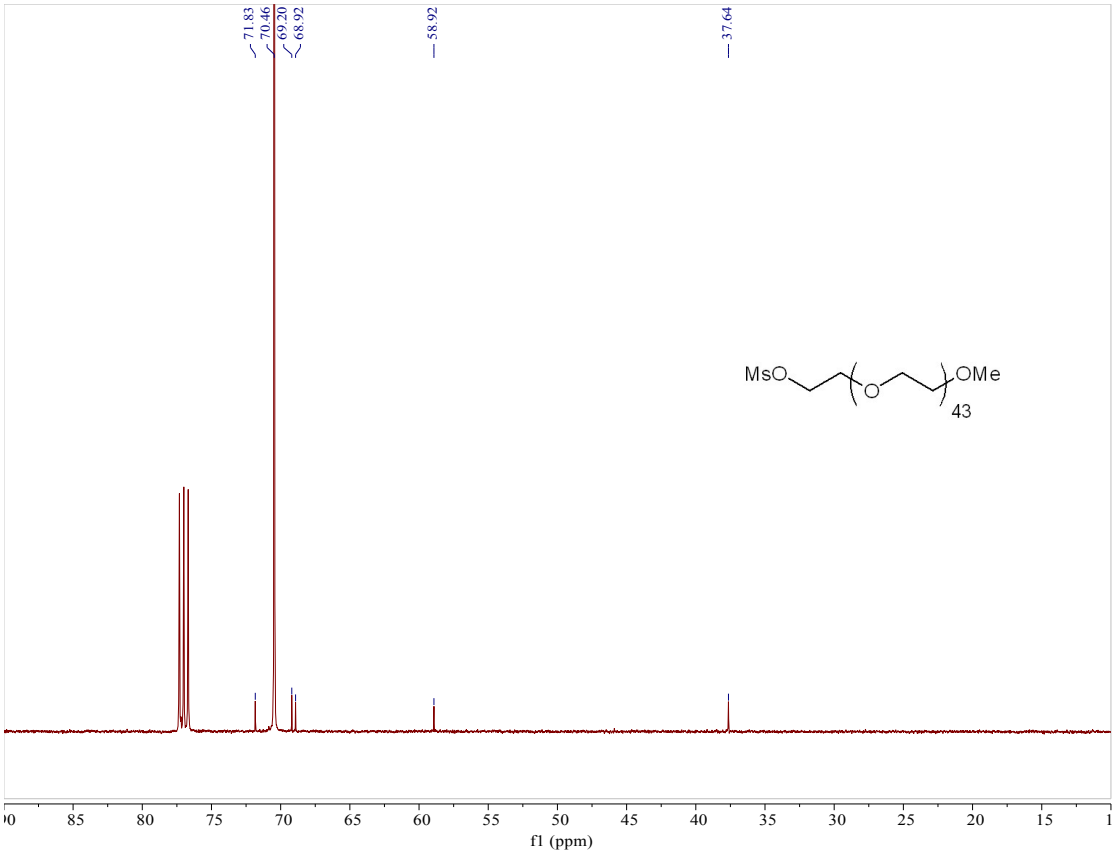
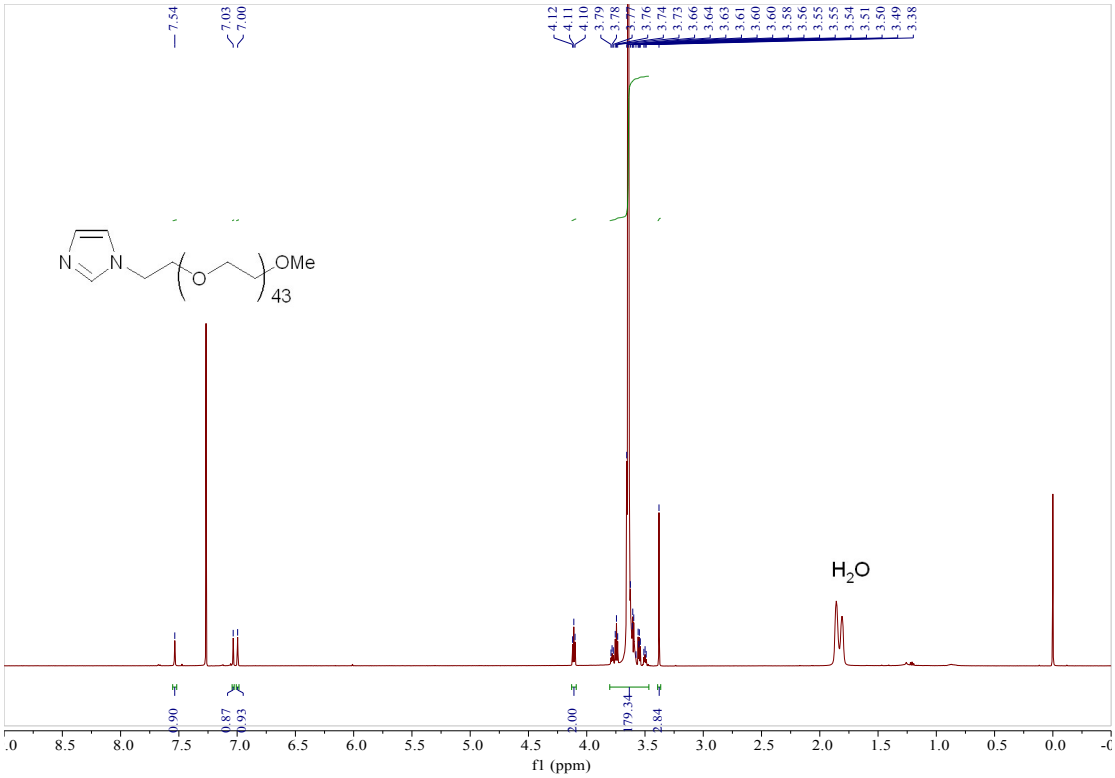


Fig. S16. MALDI-TOF mass spectrum of 1-(2,6-diisopropylphenyl) imidazole-mPEG$_{2000}$-AuCl (**L4AuCl**).

4. ^{1}H and ^{13}C NMR spectra



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3.60
3.60
3.58
3.56
3.55
3.55
3.54
3.51
3.50
3.49
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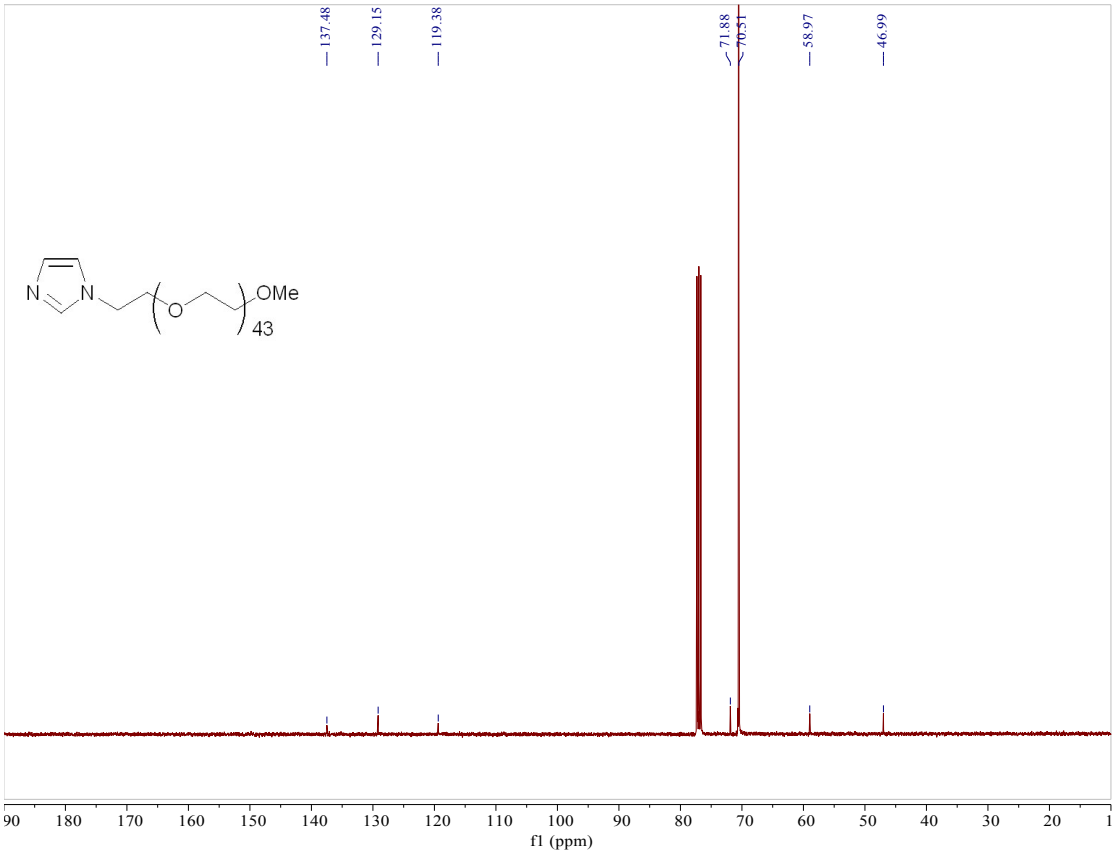
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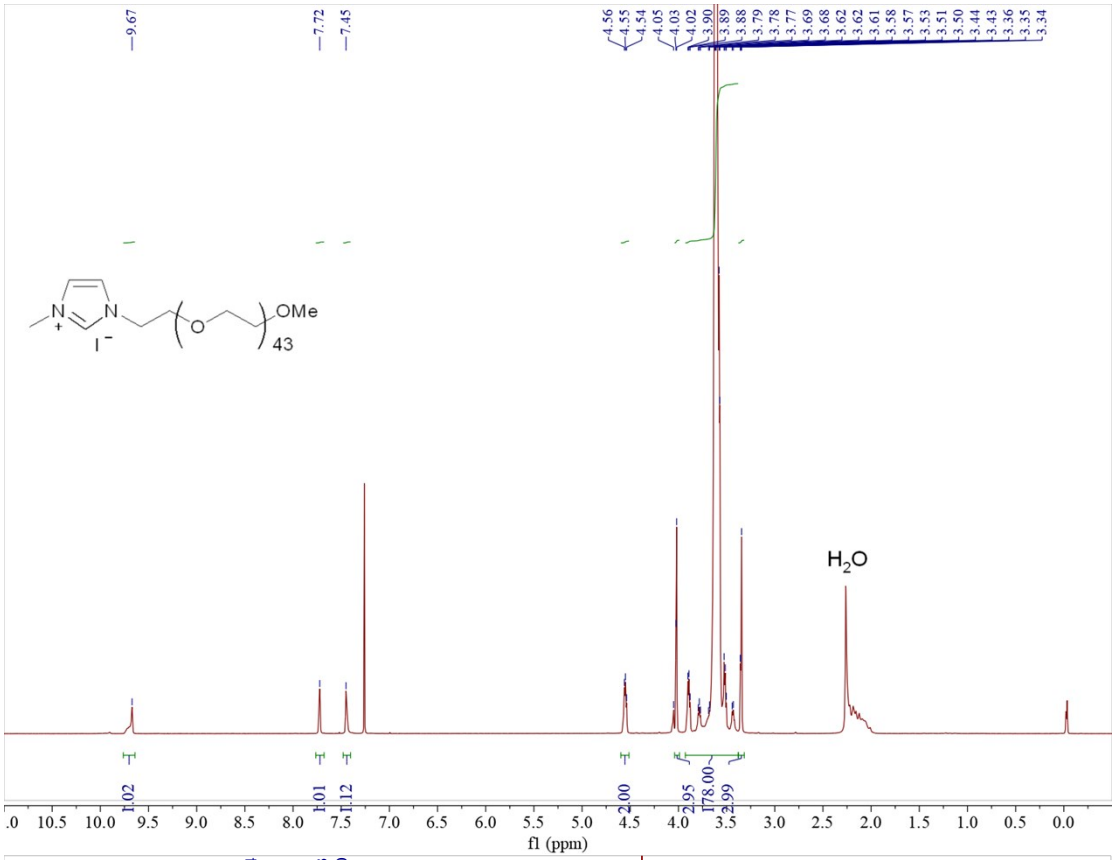
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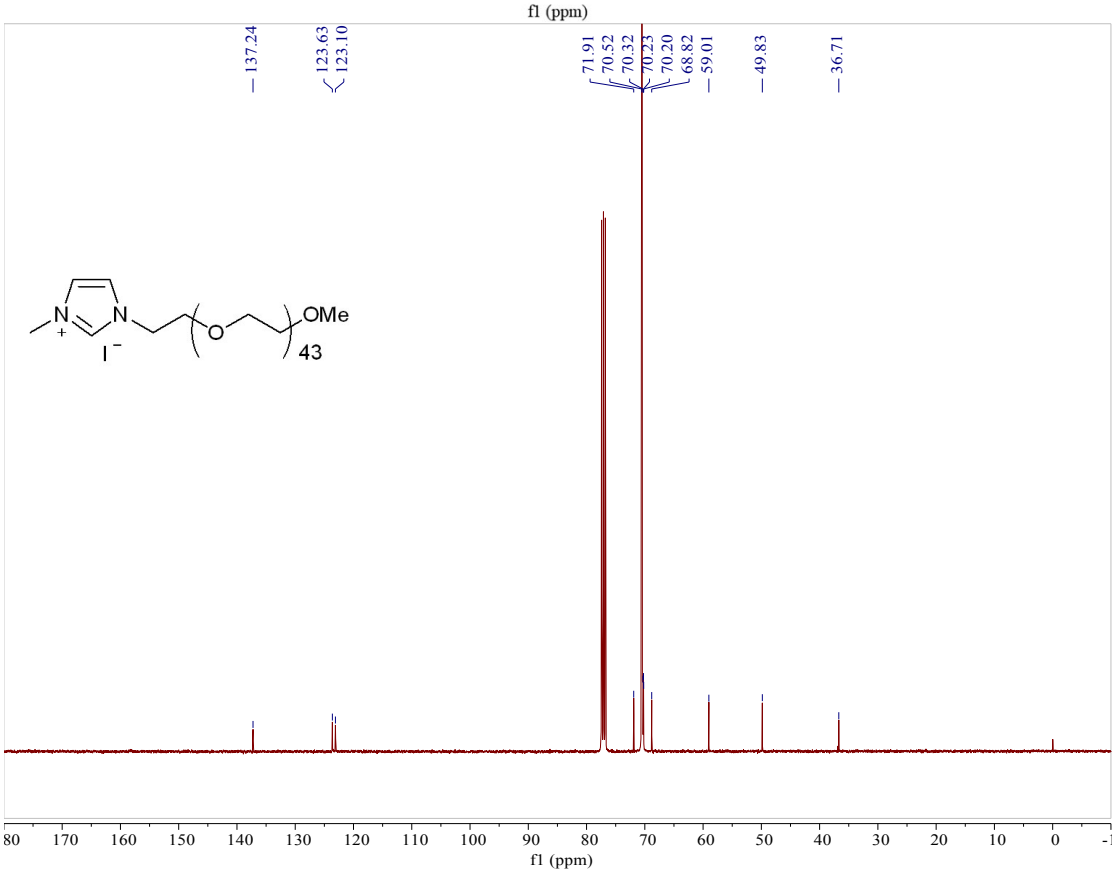
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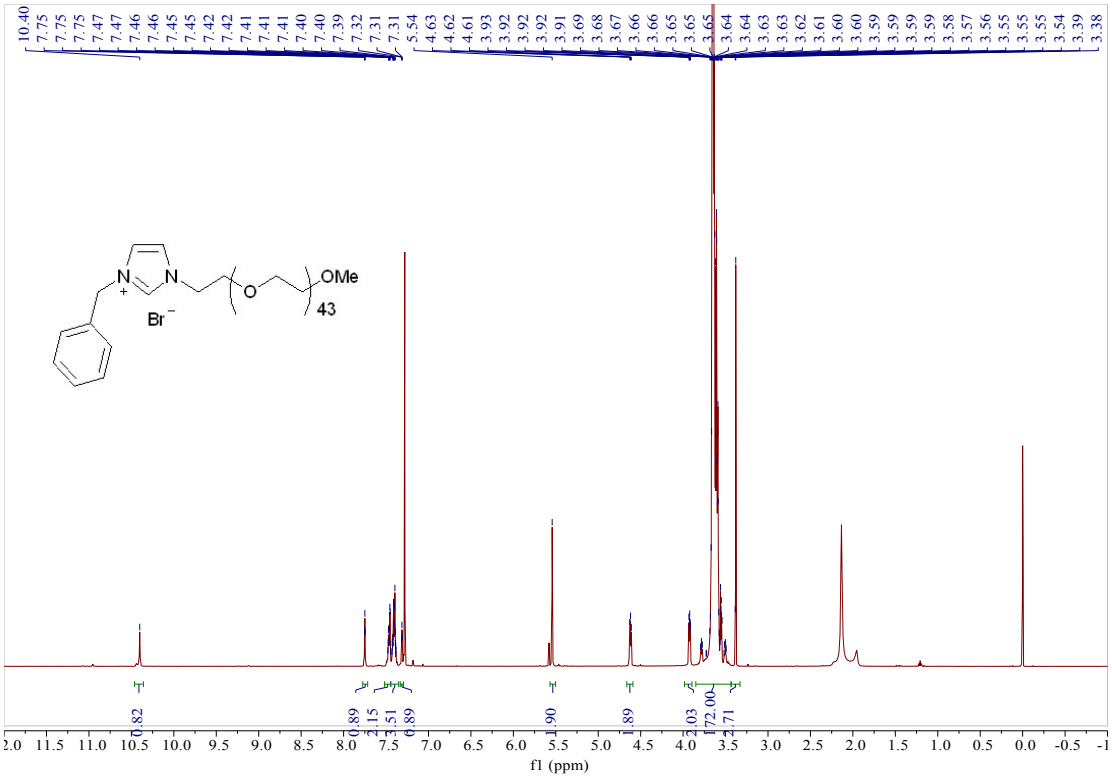
I⁻
f1 (ppm)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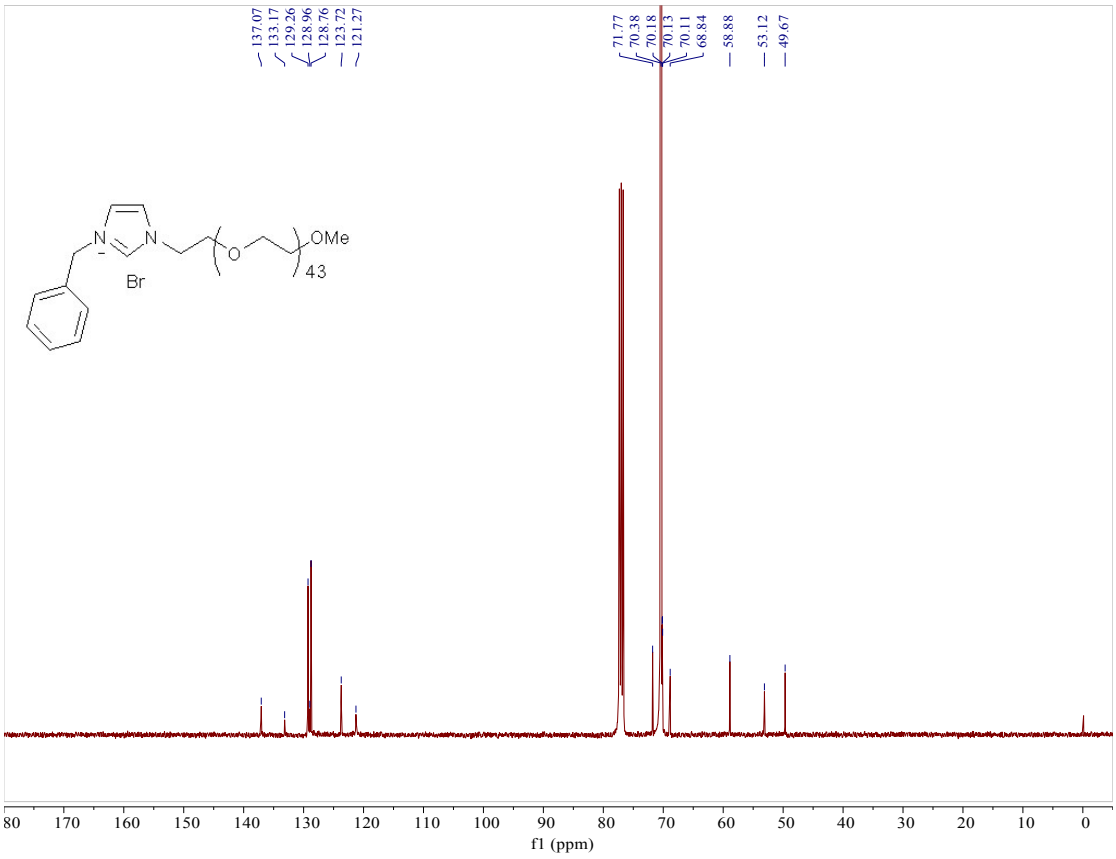
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N
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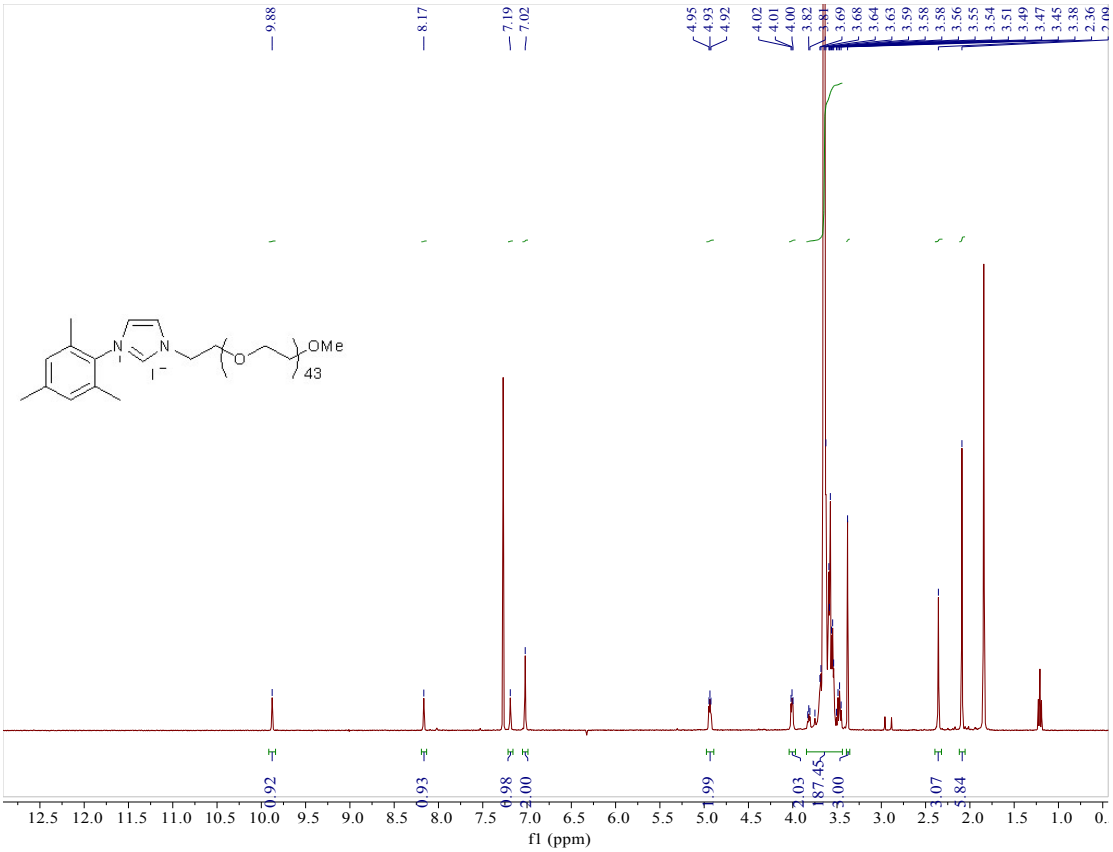
Br
f1 (ppm)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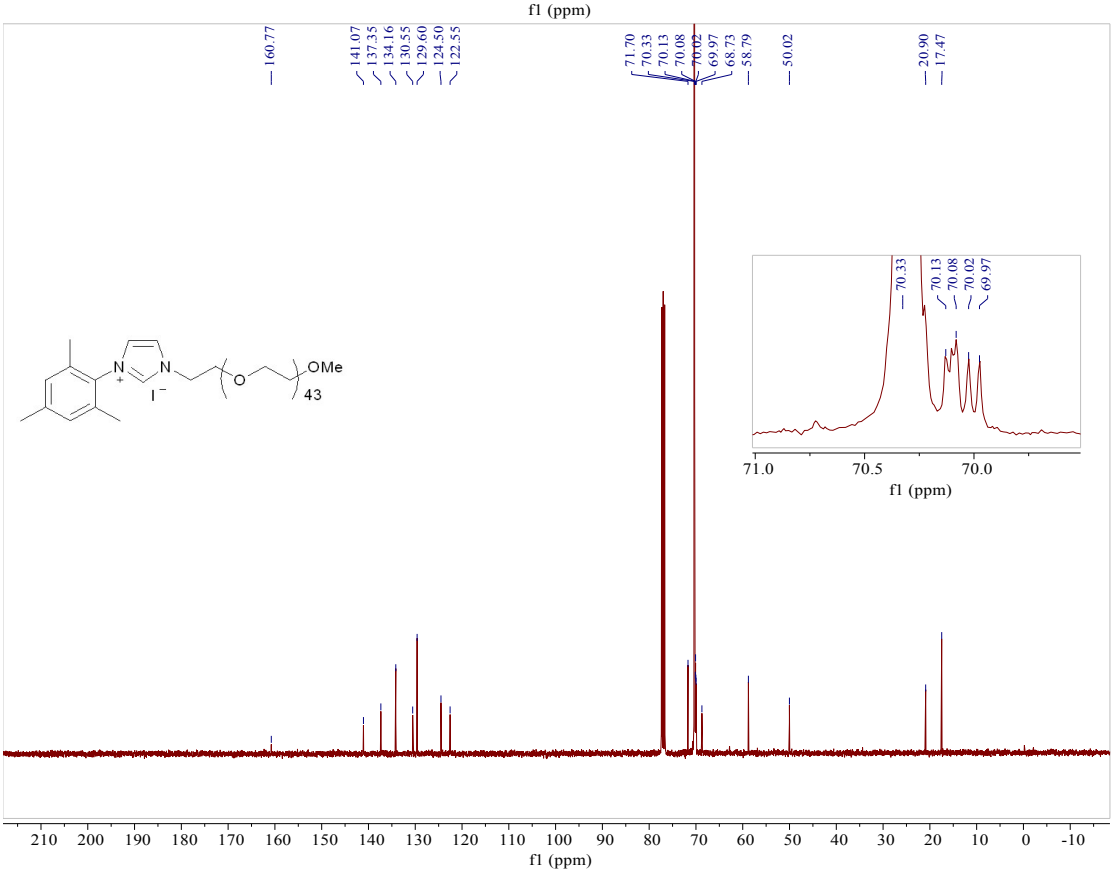
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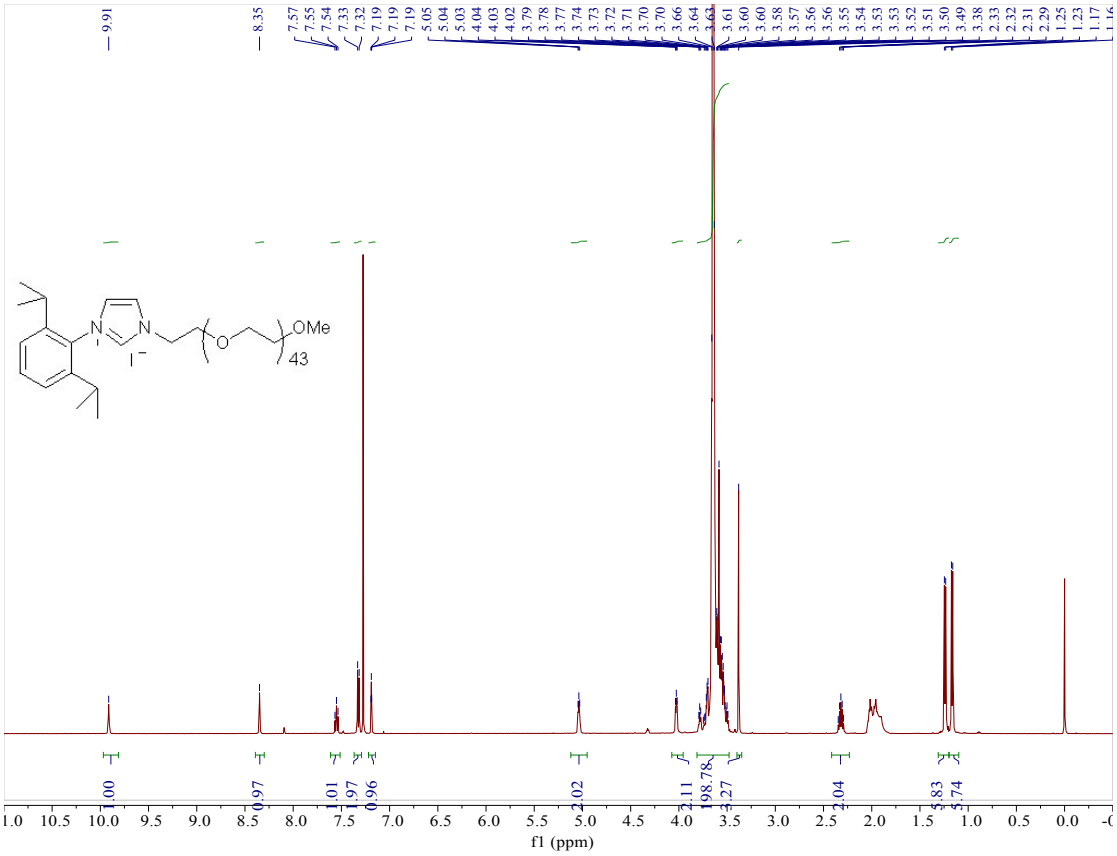
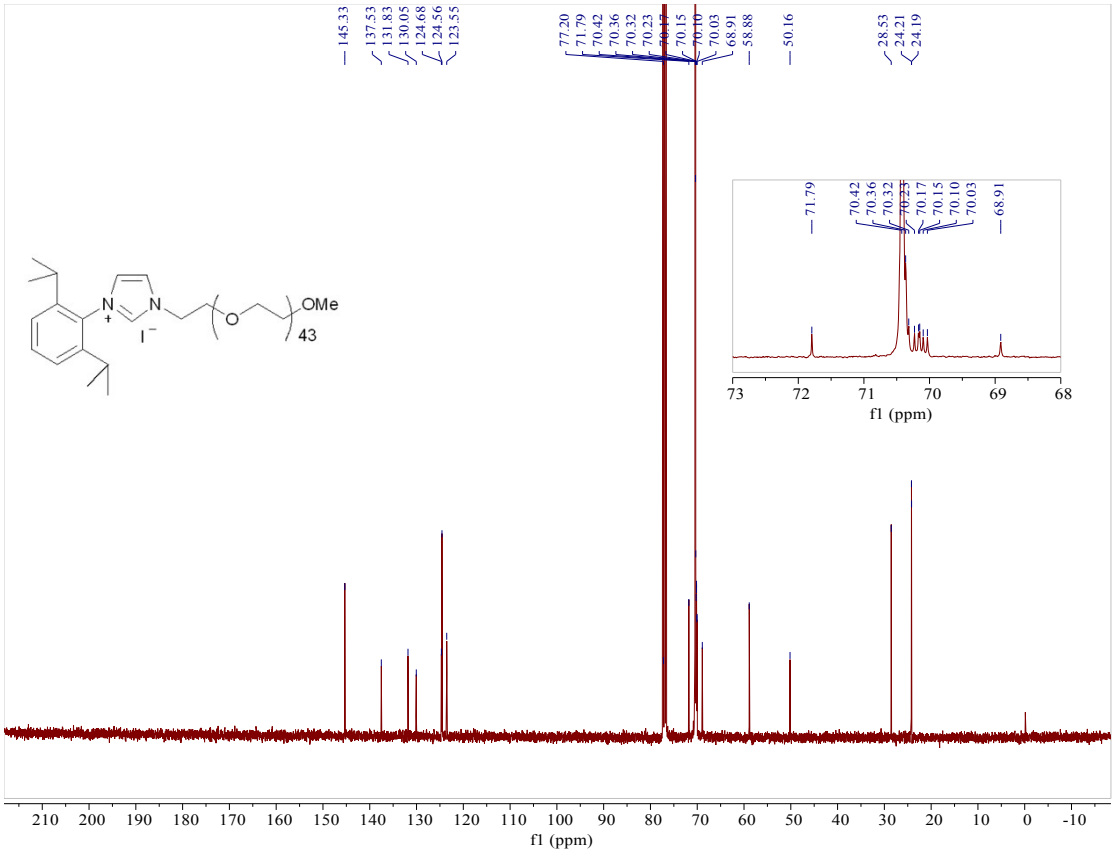
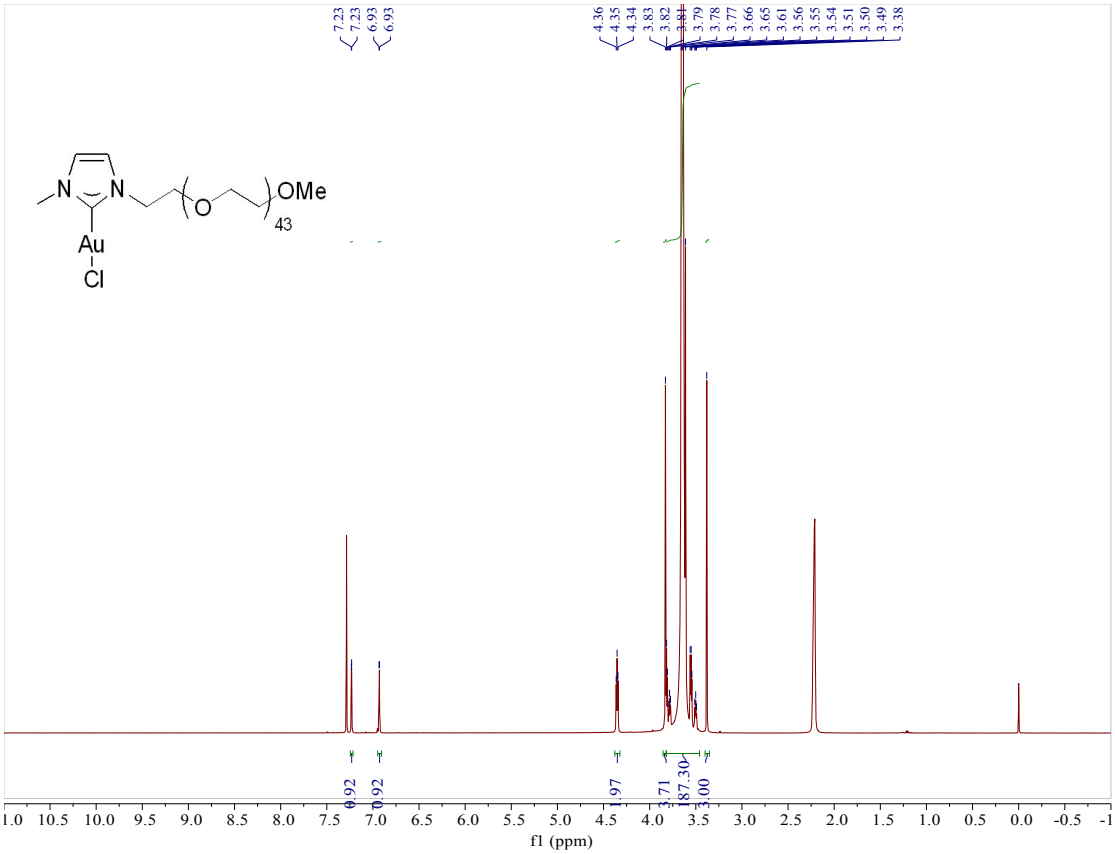
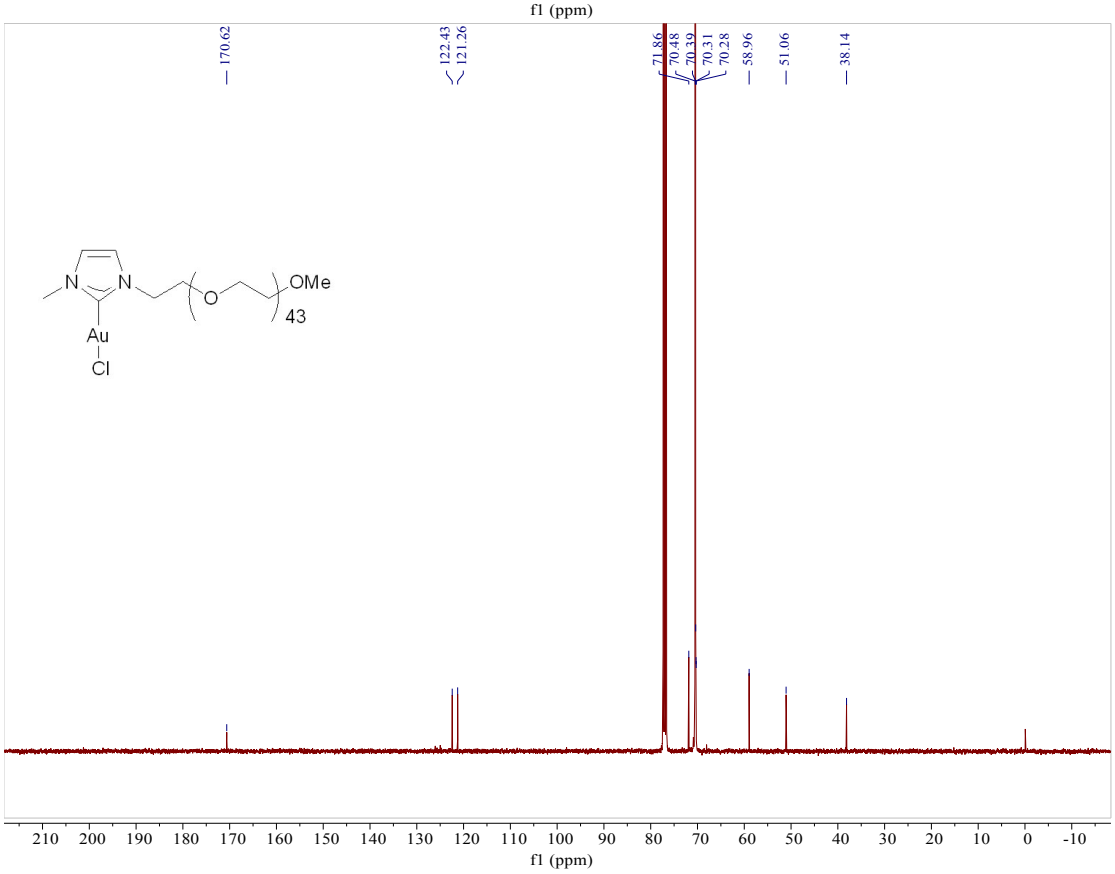
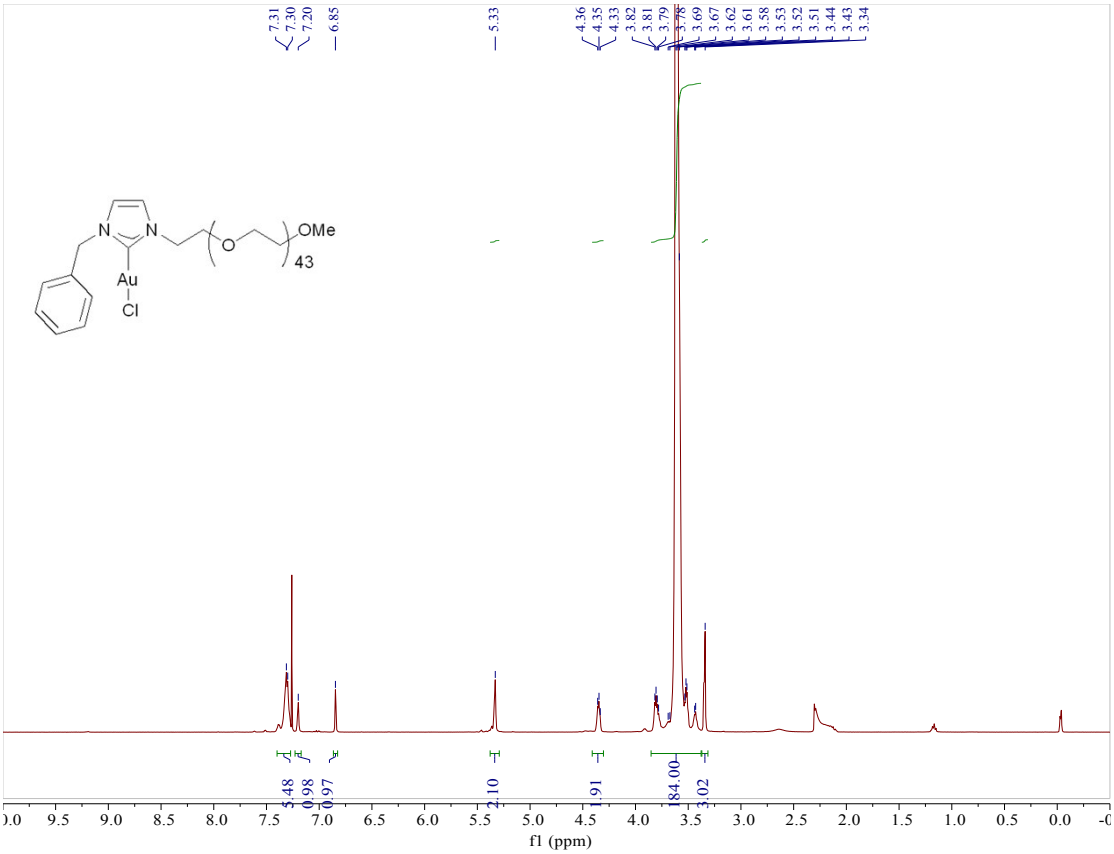
58.79
50.02
20.90
17.47
OMe
43
I⁻
f1 (ppm)

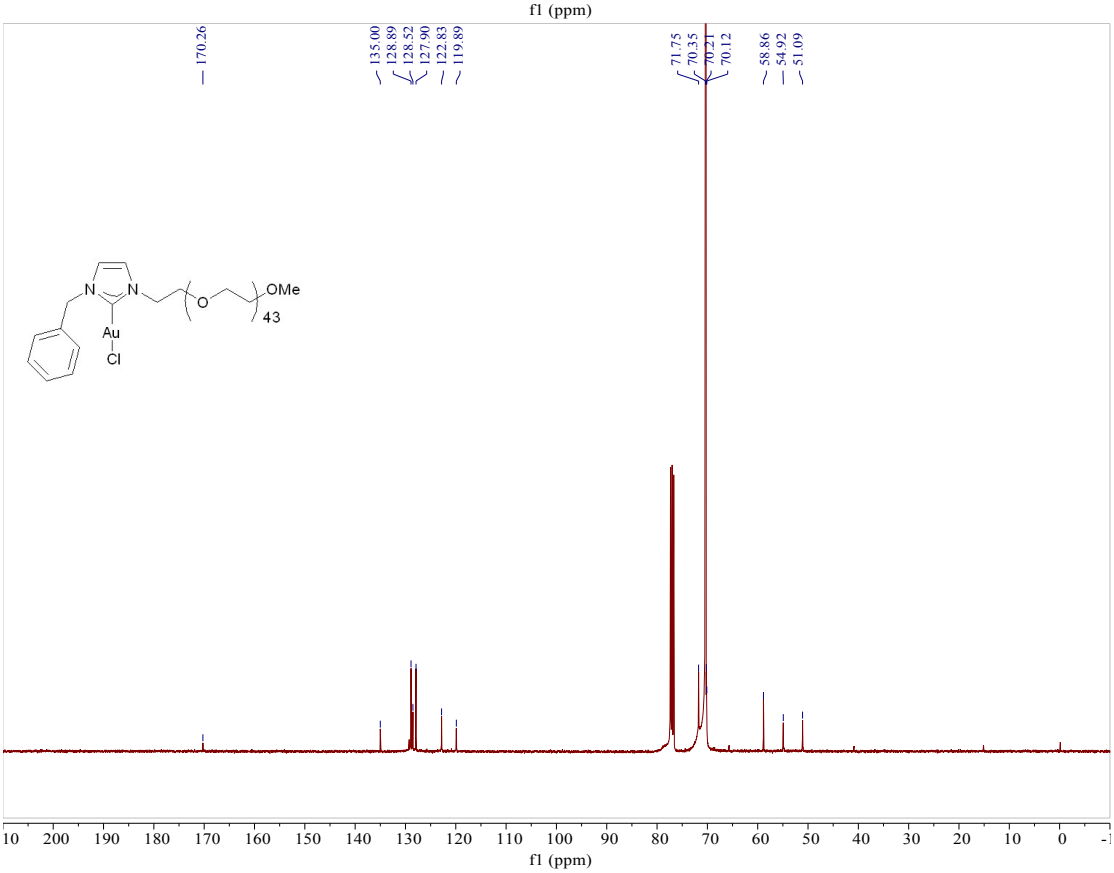

9.91
8.35
7.57
7.55
7.54
7.33
7.32
7.19
7.19
7.19
5.05
5.04
5.03
4.04
4.03
4.02
3.79
3.78
3.77
3.74
3.73
3.72
3.71
3.70
3.70
3.66
3.64
3.63
3.61
3.60
3.60
3.58
3.57
3.56
3.56
3.55
3.54
3.53
3.53
3.52
3.51
3.50
3.49
3.38
2.33
2.32
2.31
2.29
1.25
1.23
1.17
OMe
43
I⁻
1.00
0.97
1.01
1.97
0.96
2.02
2.11
198.78
3.27
2.04
3.83
3.74
f1 (ppm)

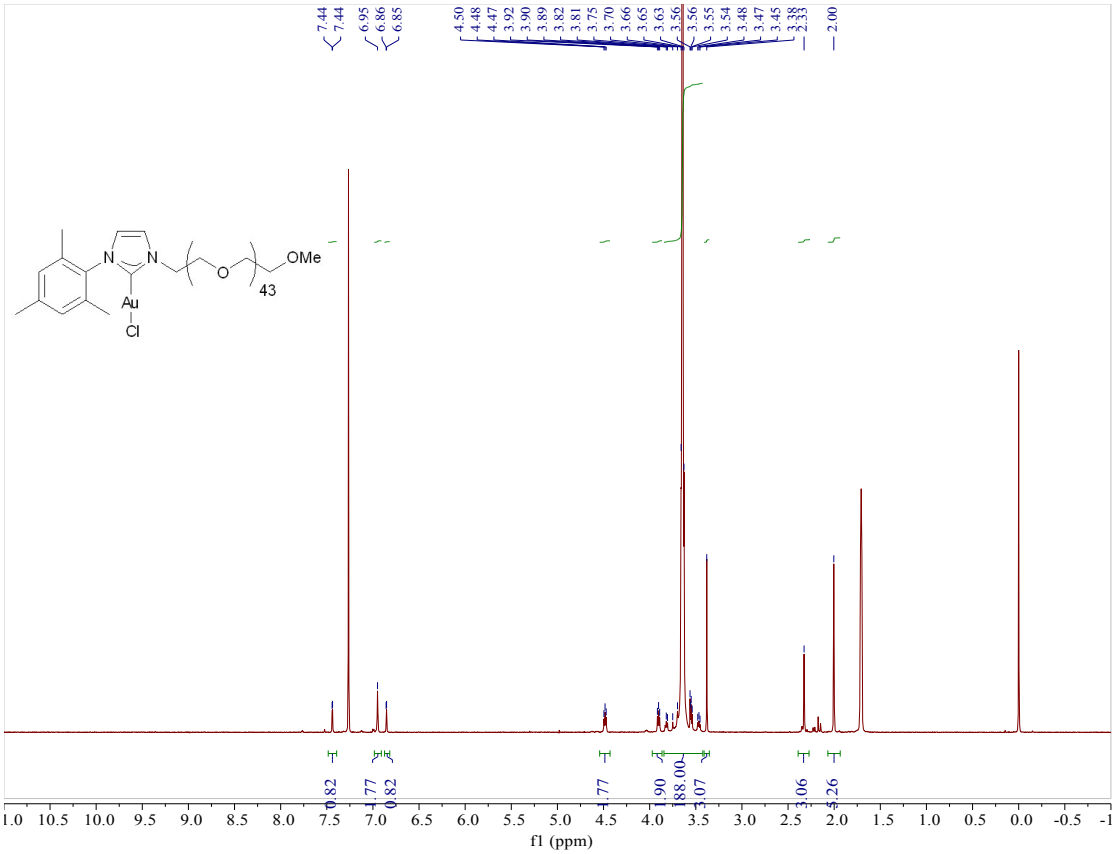

145.33
137.53
131.83
130.05
124.68
124.56
123.55
77.20
71.79
70.42
70.36
70.32
70.23
70.17
70.15
70.10
70.03
68.91
58.88
50.16
28.53
24.21
24.19
OMe
43
I⁻
f1 (ppm)

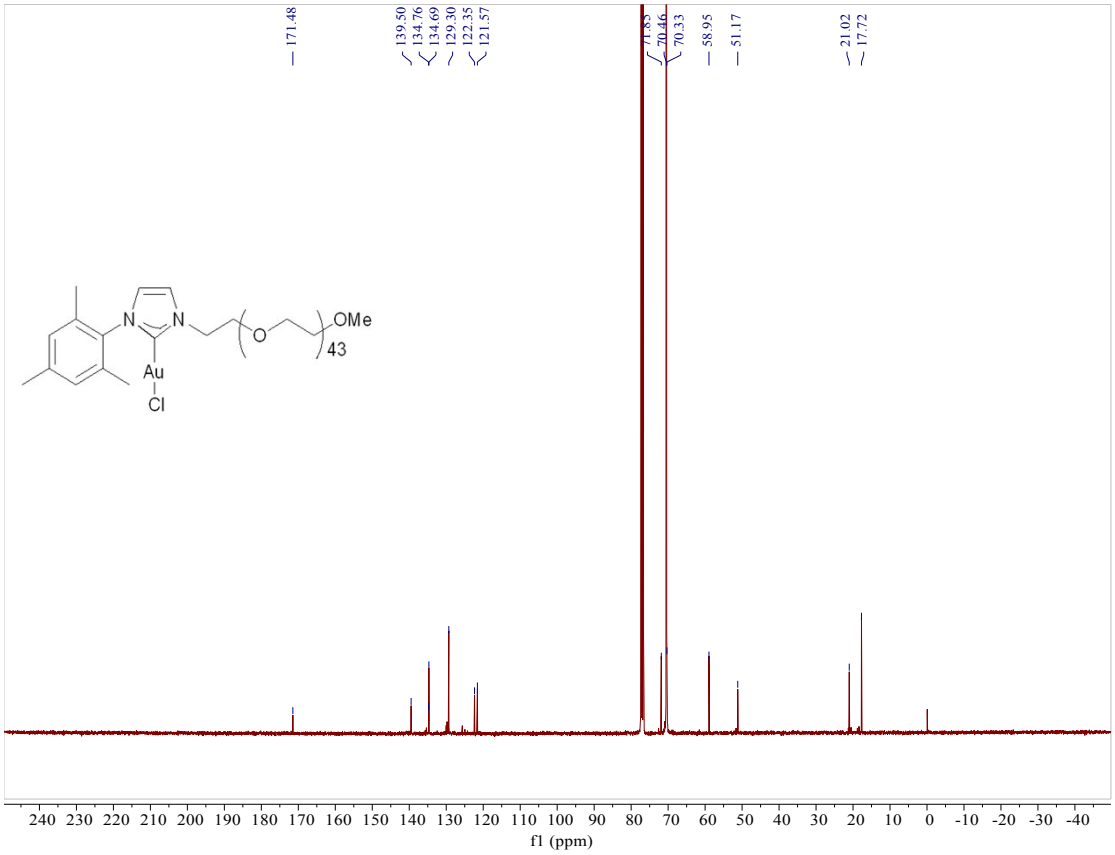

7.23
7.23
6.93
6.93
4.36
4.35
4.34
3.83
3.82
3.81
3.79
3.78
3.77
3.66
3.65
3.61
3.56
3.55
3.54
3.51
3.50
3.49
3.38
N
N
O
OMe
43
Au
Cl
0.92
0.92
1.97
3.71
7.30
3.00
f1 (ppm)

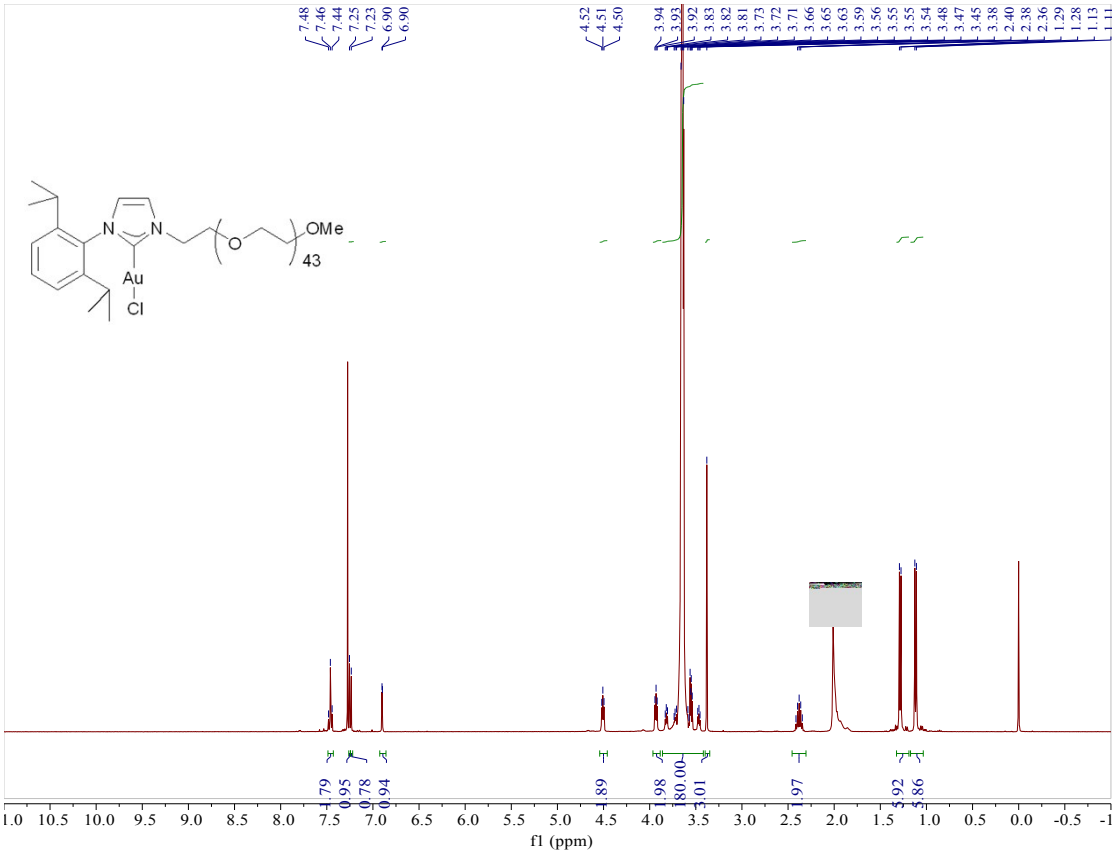

170.62
122.43
121.26
71.86
70.48
70.39
70.31
70.28
58.96
51.06
38.14
N
N
O
OMe
43
Au
Cl
f1 (ppm)

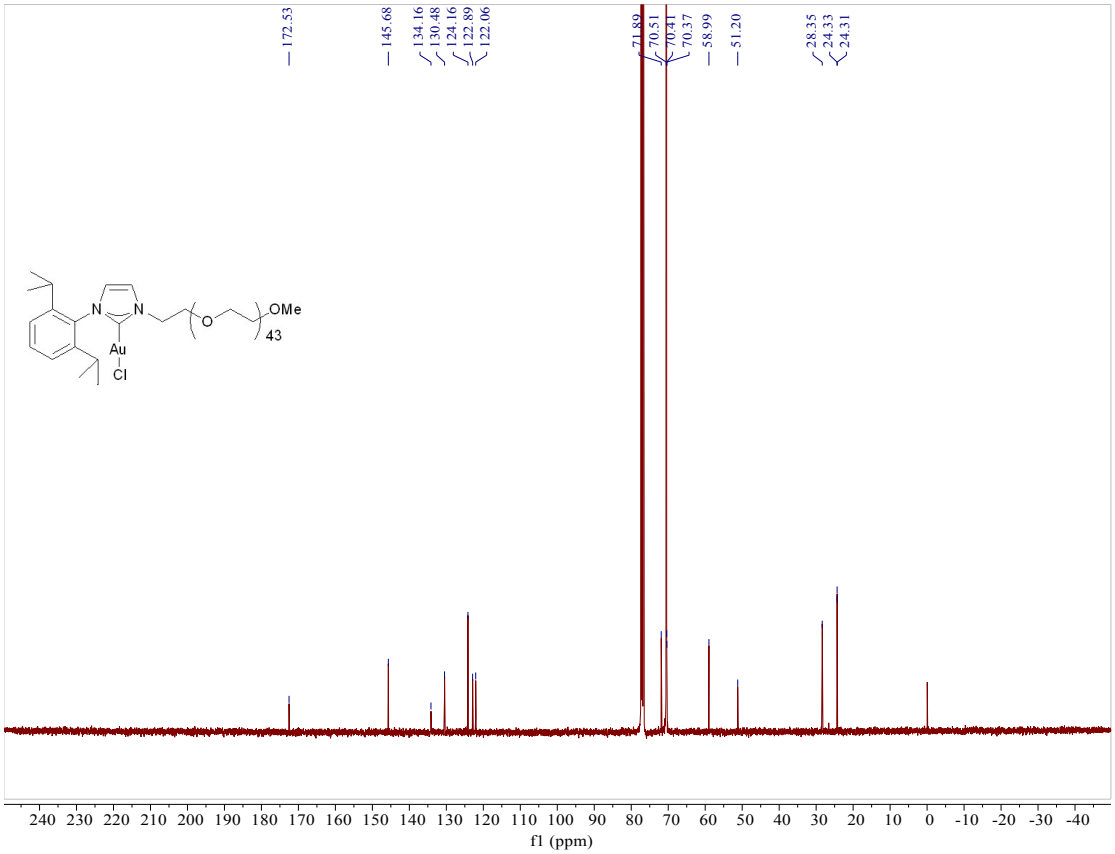

7.31
7.30
7.20
6.85
5.33
4.36
4.35
4.33
3.82
3.81
3.79
3.78
3.69
3.67
3.62
3.61
3.58
3.53
3.52
3.51
3.44
3.43
3.34
OMe
43
Au
Cl
3.48
0.98
0.97
2.10
1.91
84.00
3.02
f1 (ppm)

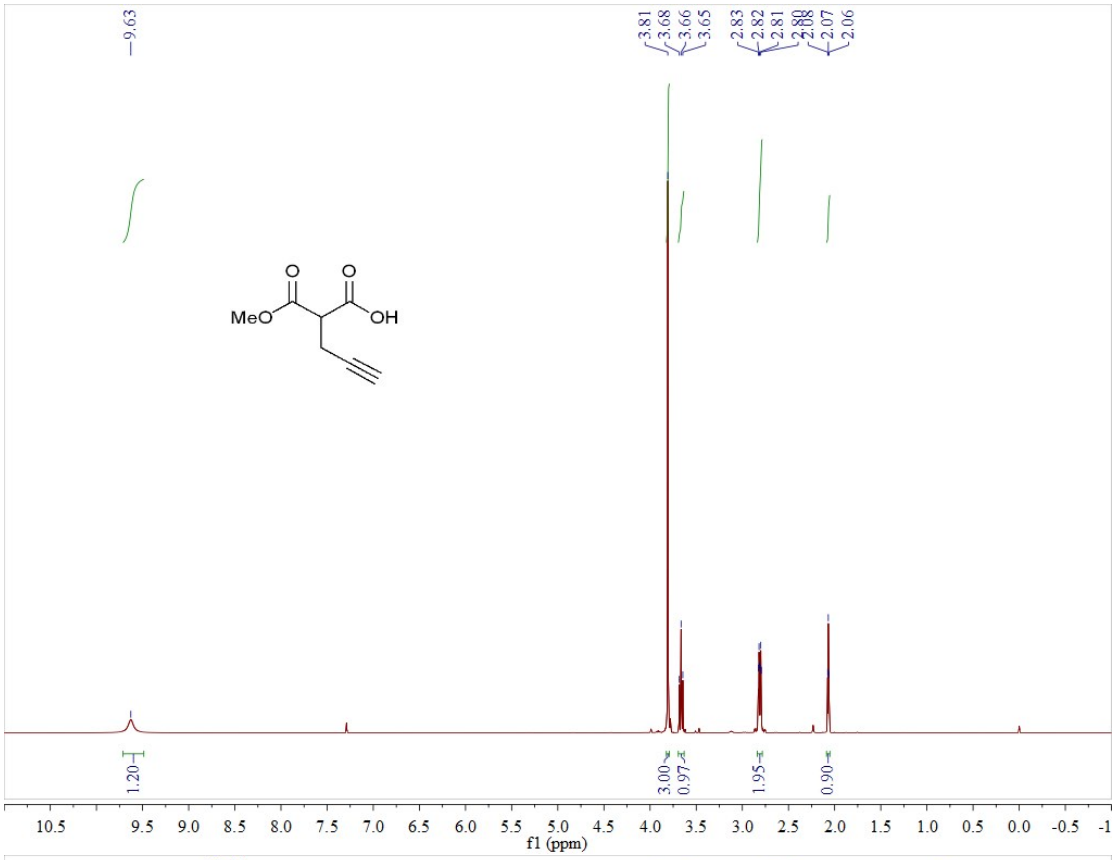

170.26
135.00
128.89
128.52
127.90
122.83
119.89
71.75
70.35
70.21
70.12
58.86
54.92
51.09
OMe
43
Au
Cl
f1 (ppm)

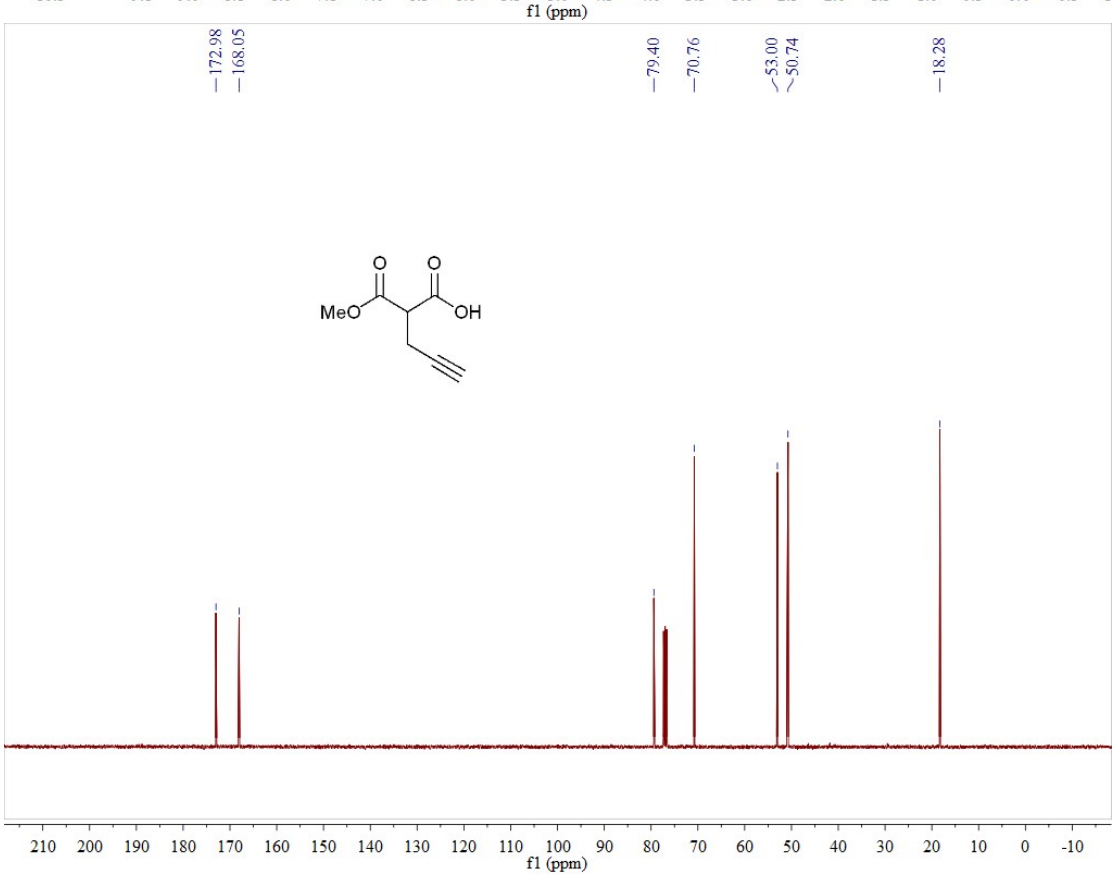

7.44
7.44
6.95
6.86
6.85
4.50
4.48
4.47
3.92
3.90
3.89
3.82
3.81
3.75
3.70
3.66
3.65
3.63
3.56
3.55
3.54
3.48
3.47
3.45
3.38
3.33
2.00
N
N
O
OMe
43
Au
Cl
0.82
1.77
0.82
1.77
1.90
18.00
3.07
3.06
3.26
f1 (ppm)

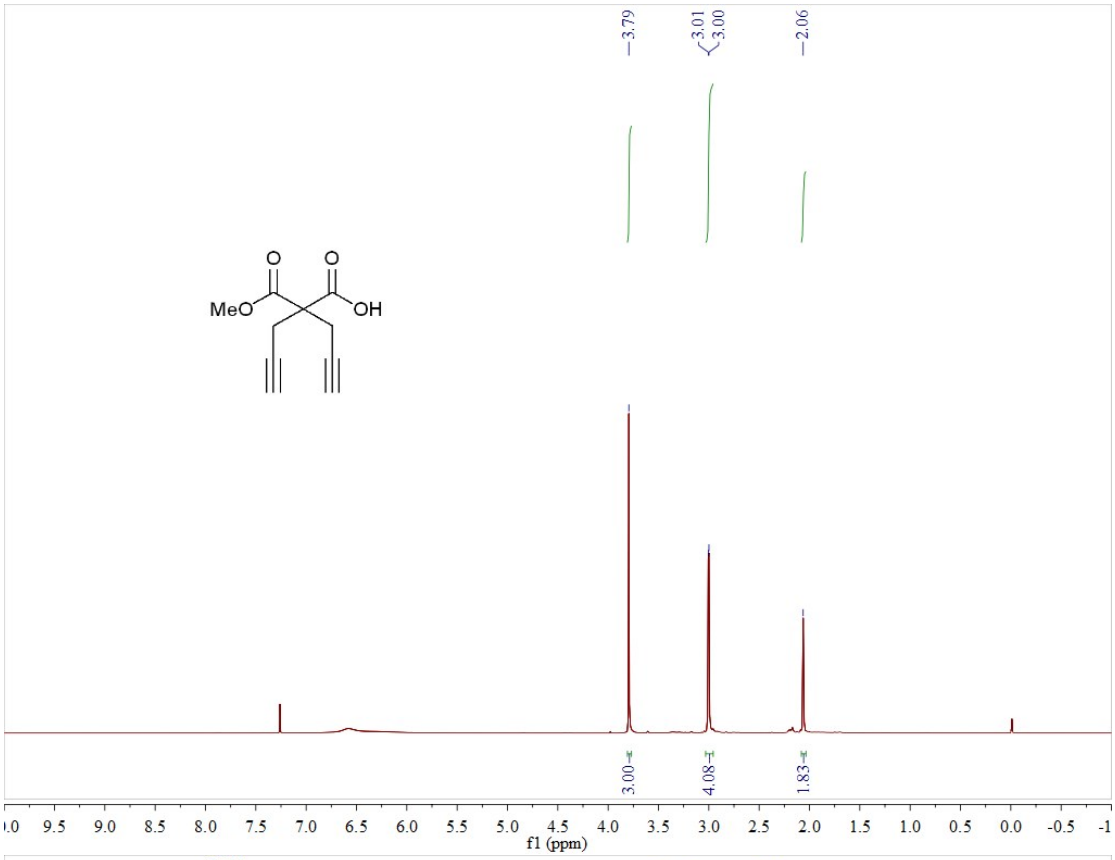

171.48
139.50
134.76
134.69
129.30
122.35
121.57
71.85
70.46
70.33
58.95
51.17
21.02
17.72
N
N
O
OMe
43
Au
Cl
f1 (ppm)

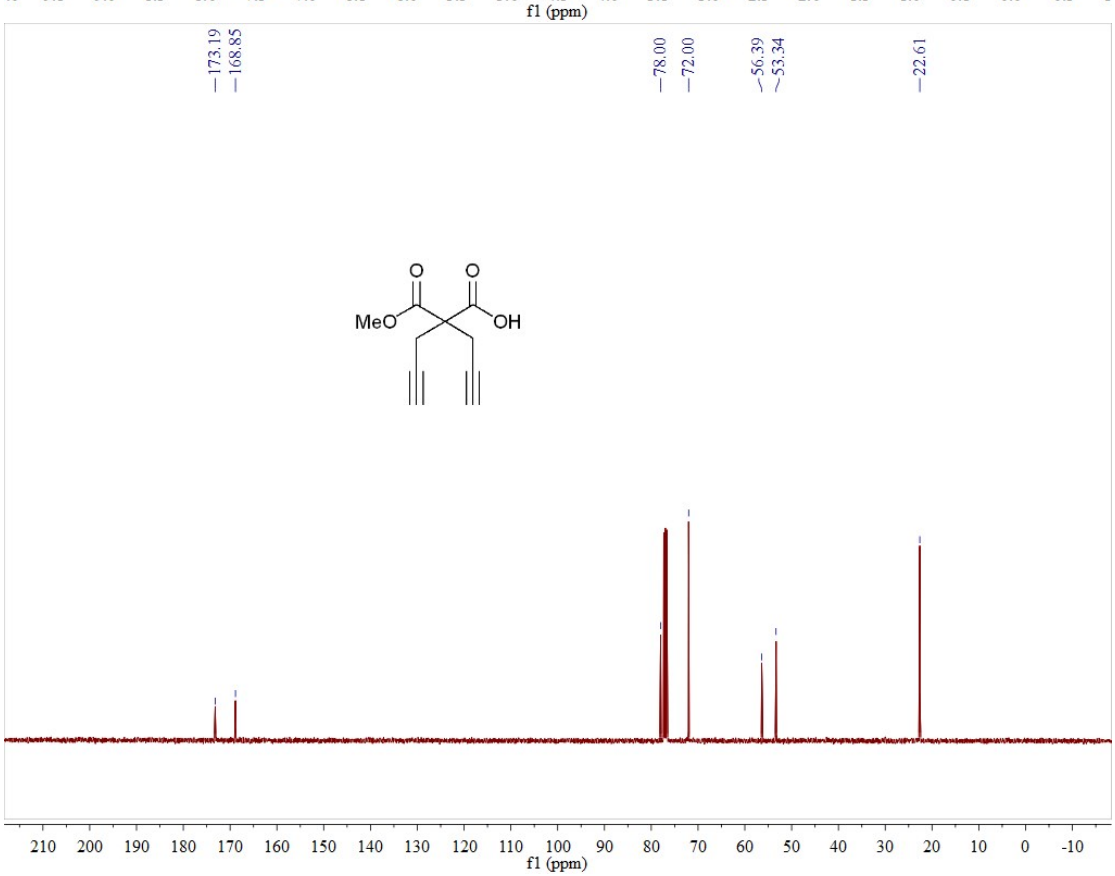

7.48
7.46
7.44
7.25
7.23
6.90
6.90
4.52
4.51
4.50
3.94
3.93
3.92
3.83
3.82
3.81
3.73
3.72
3.71
3.66
3.65
3.63
3.59
3.56
3.55
3.55
3.54
3.48
3.47
3.45
3.38
2.40
2.38
2.36
1.29
1.28
1.13
1.11
N
N
O
OMe
43
Au
Cl
1.79
0.95
0.78
0.94
1.89
1.98
80.00
3.01
1.97
3.92
3.86
f1 (ppm)

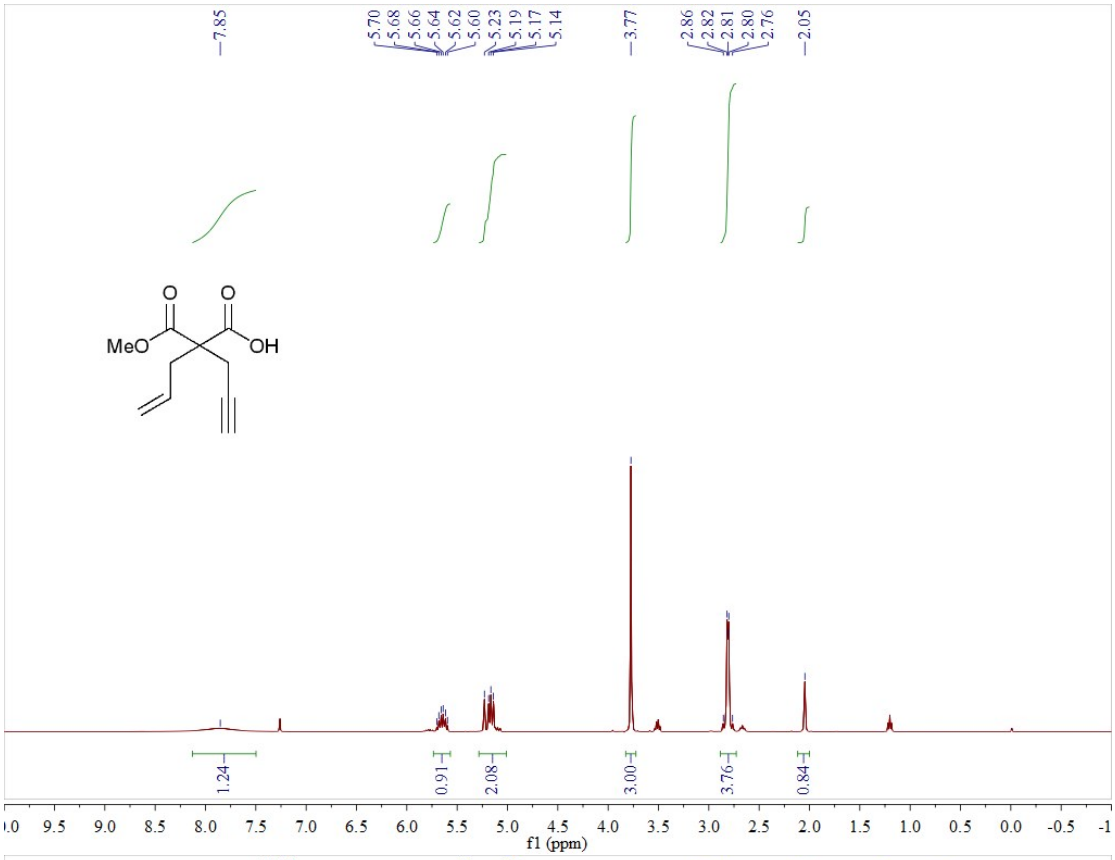

172.53
145.68
134.16
130.48
124.16
122.89
122.06
71.89
70.51
70.41
70.37
58.99
51.20
28.35
24.33
24.31
N
N
O
OMe
43
Au
Cl
f1 (ppm)

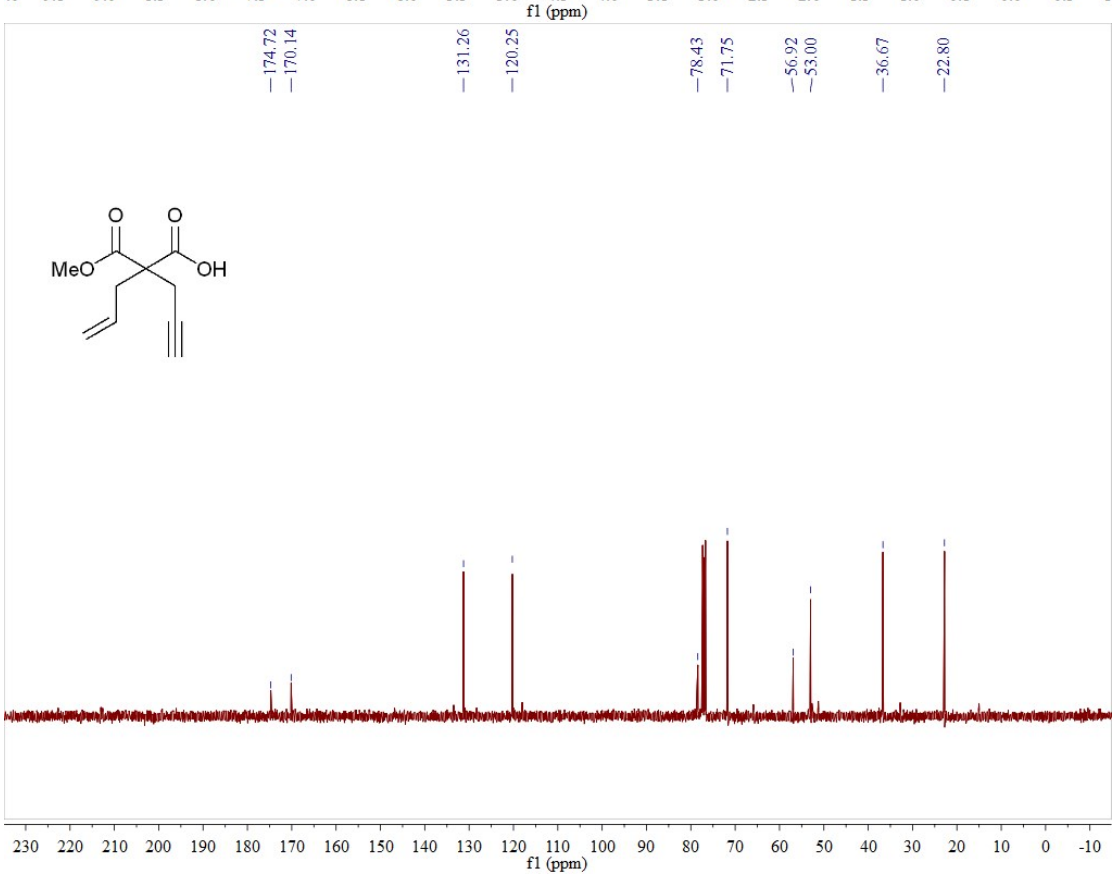

9.63
3.81
3.68
3.66
3.65
2.83
2.82
2.81
2.07
2.06
MeO
OH
1.20
3.00
0.97
1.95
0.90
f1 (ppm)

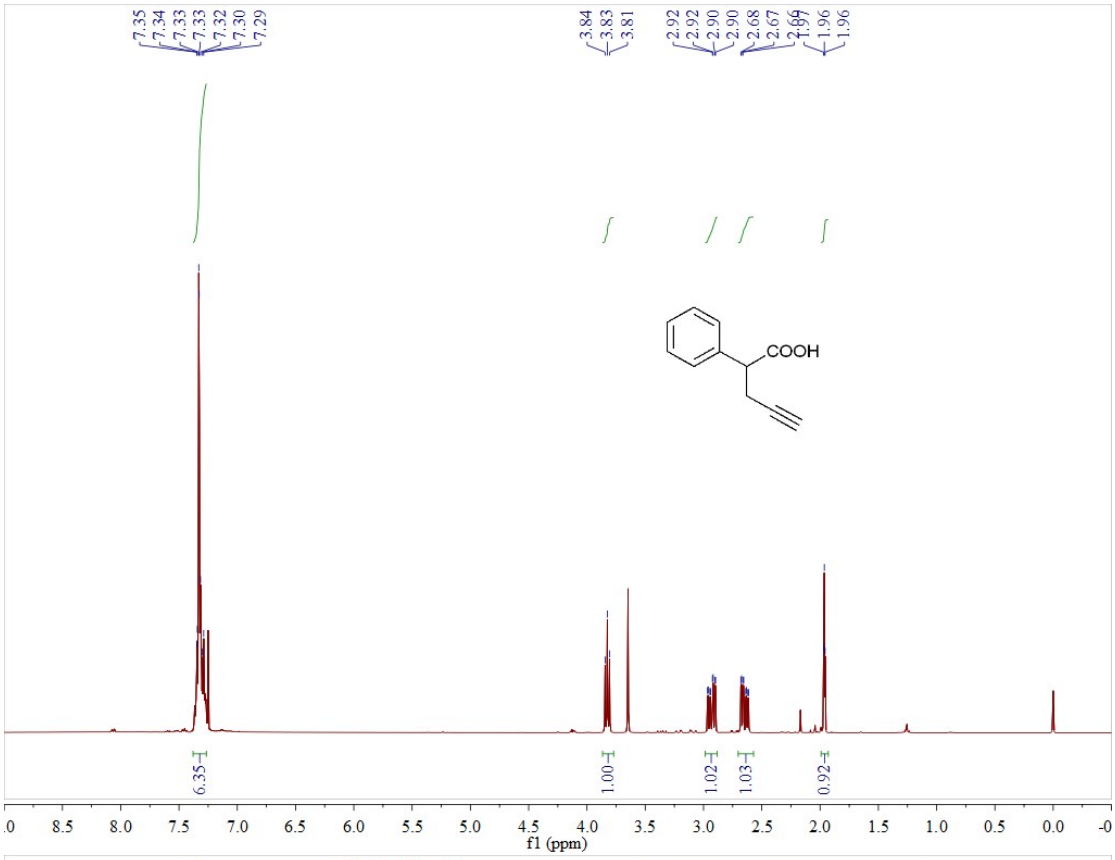

172.98
168.05
79.40
70.76
53.00
50.74
18.28
MeO
OH
f1 (ppm)

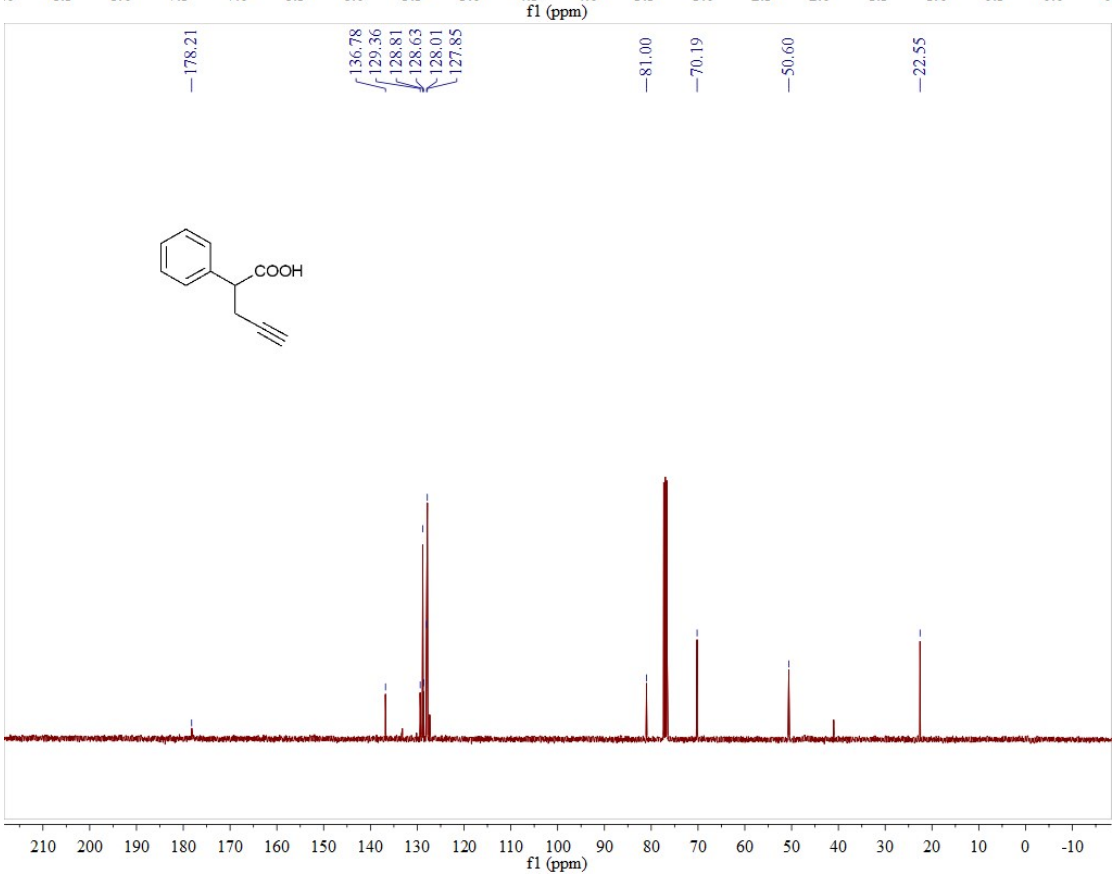

3.79
3.01
3.00
2.06
MeO
OH
3.00
4.08
1.83
f1 (ppm)

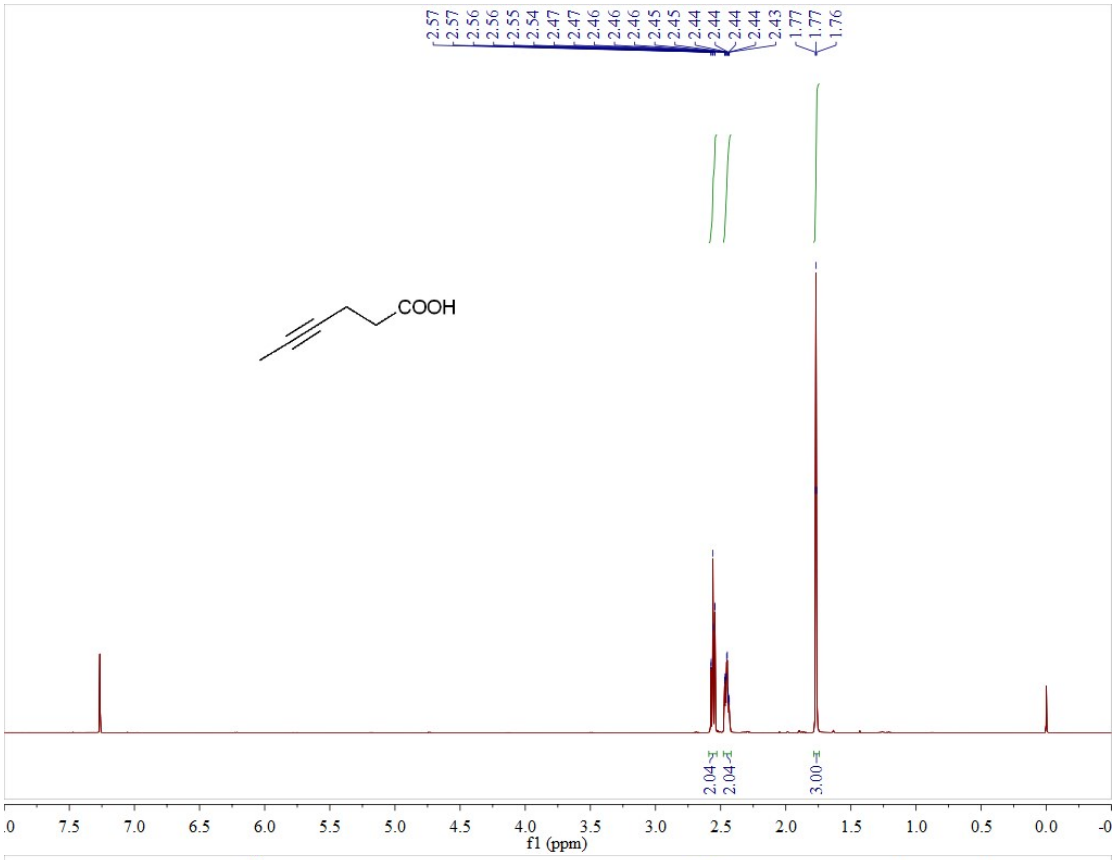

173.19
168.85
78.00
72.00
56.39
53.34
22.61
MeO
OH
f1 (ppm)

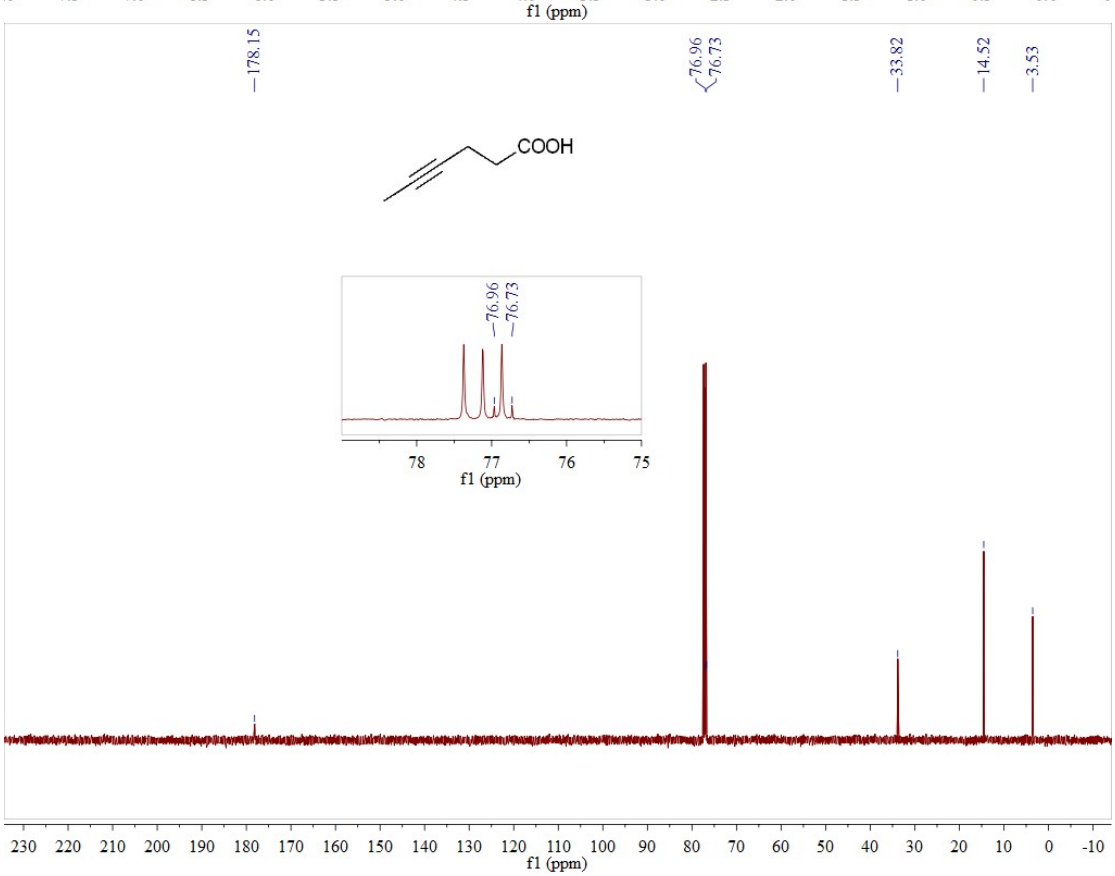

7.85
5.70
5.68
5.66
5.64
5.62
5.60
5.23
5.19
5.17
5.14
3.77
2.86
2.82
2.81
2.80
2.76
2.05
MeO
OH
1.24
0.91
2.08
3.00
3.76
0.84
f1 (ppm)

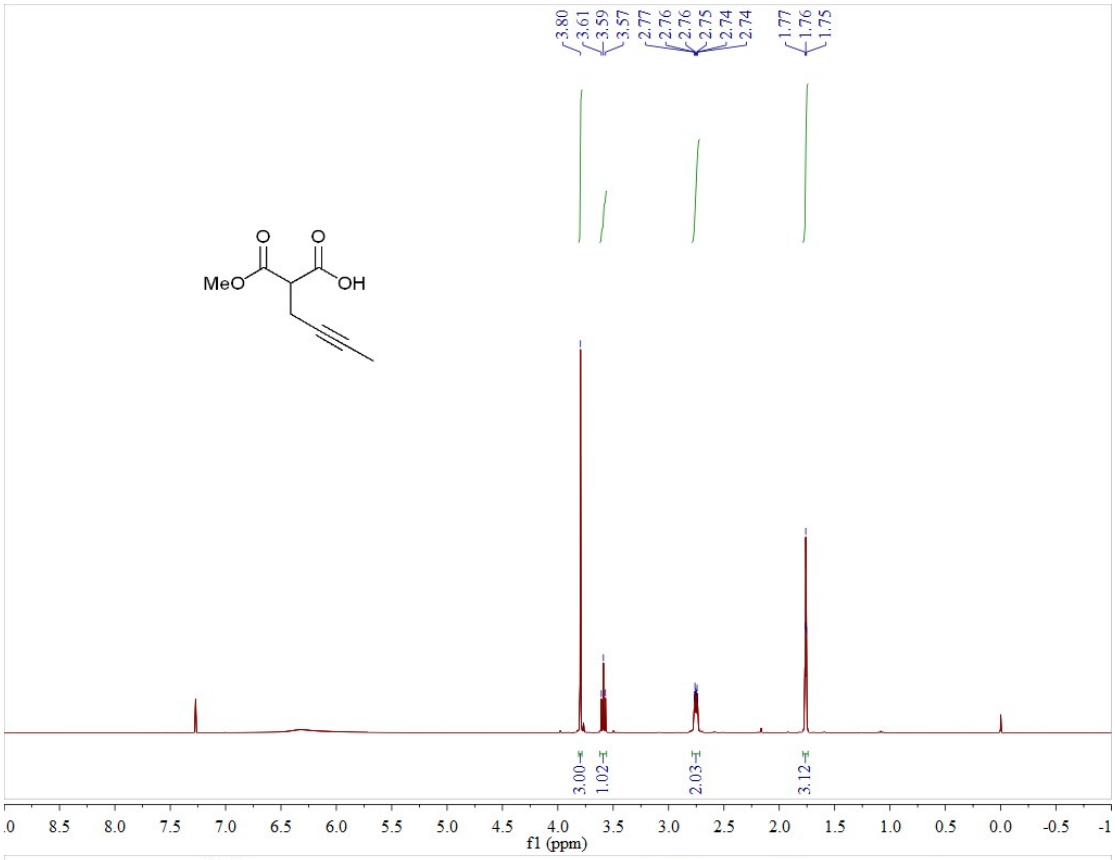

174.72
170.14
131.26
120.25
78.43
71.75
56.92
53.00
36.67
22.80
MeO
OH
f1 (ppm)

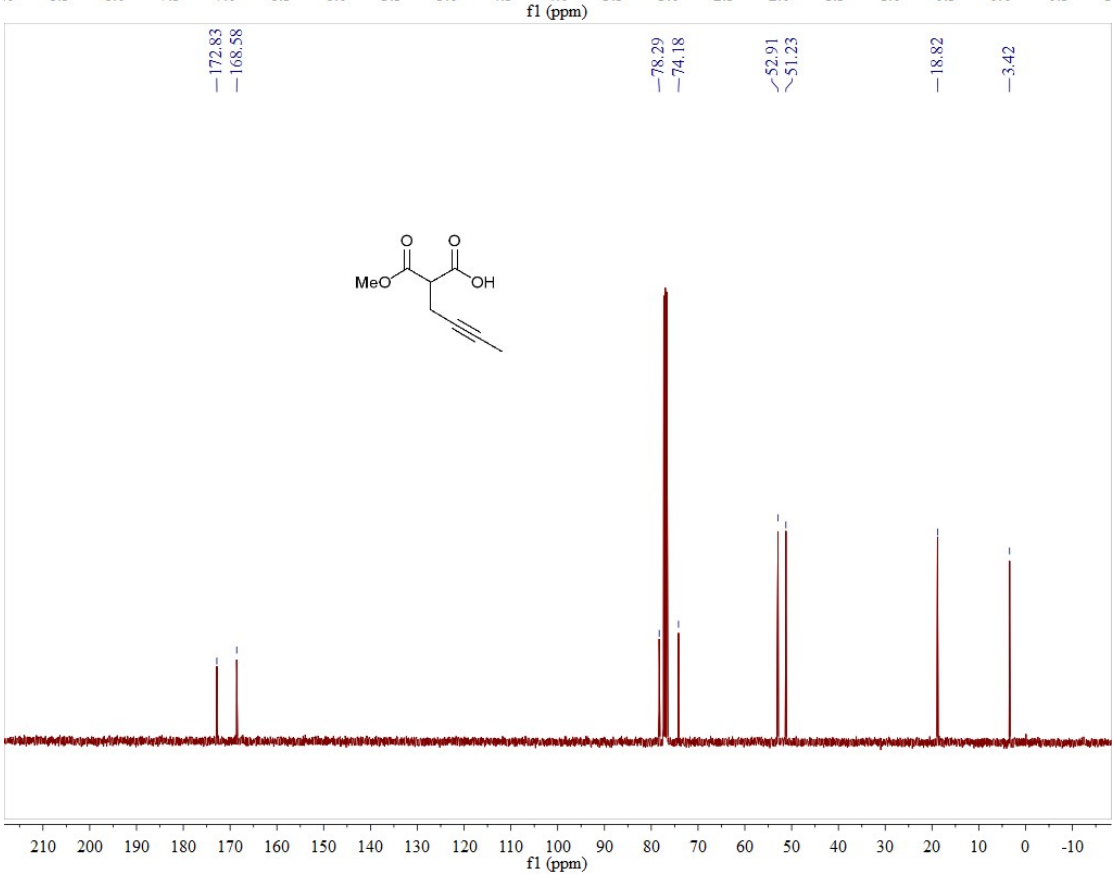

7.35
7.34
7.33
7.33
7.32
7.30
7.29
3.84
3.83
3.81
2.92
2.92
2.90
2.90
2.68
2.67
1.96
1.96
COOH
6.35
1.00
1.02
1.03
0.92
f1 (ppm)

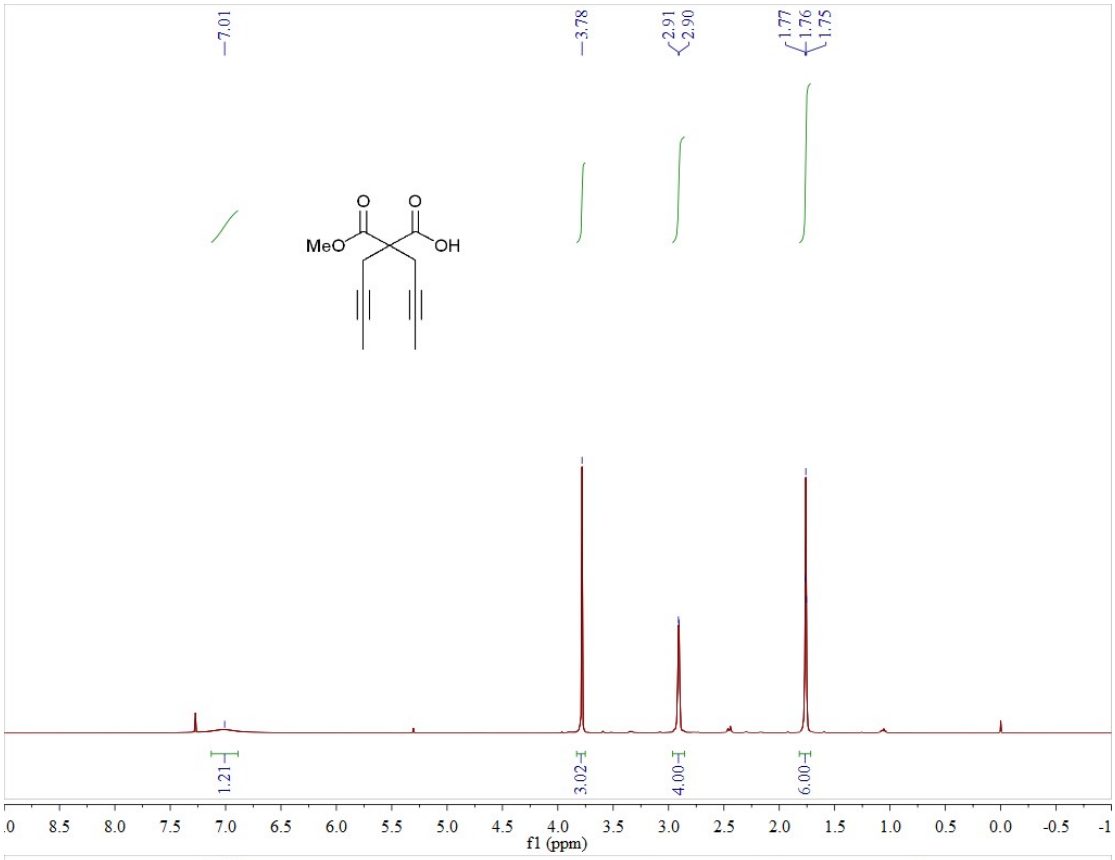

178.21
136.78
129.36
128.81
128.63
128.01
127.85
81.00
70.19
50.60
22.55
COOH
f1 (ppm)

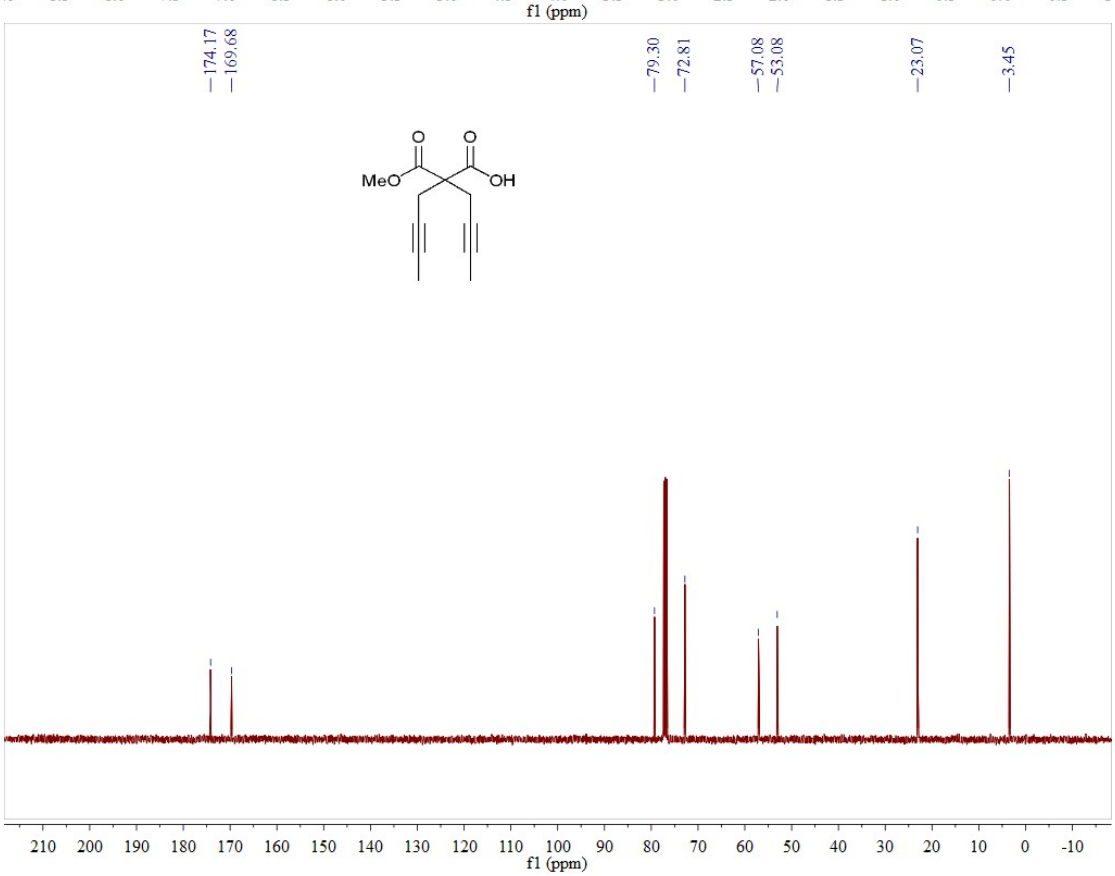

2.57
2.57
2.56
2.56
2.55
2.54
2.47
2.47
2.46
2.46
2.46
2.45
2.45
2.44
2.44
2.44
2.44
2.43
1.77
1.77
1.76
COOH
2.04
2.04
3.00
f1 (ppm)

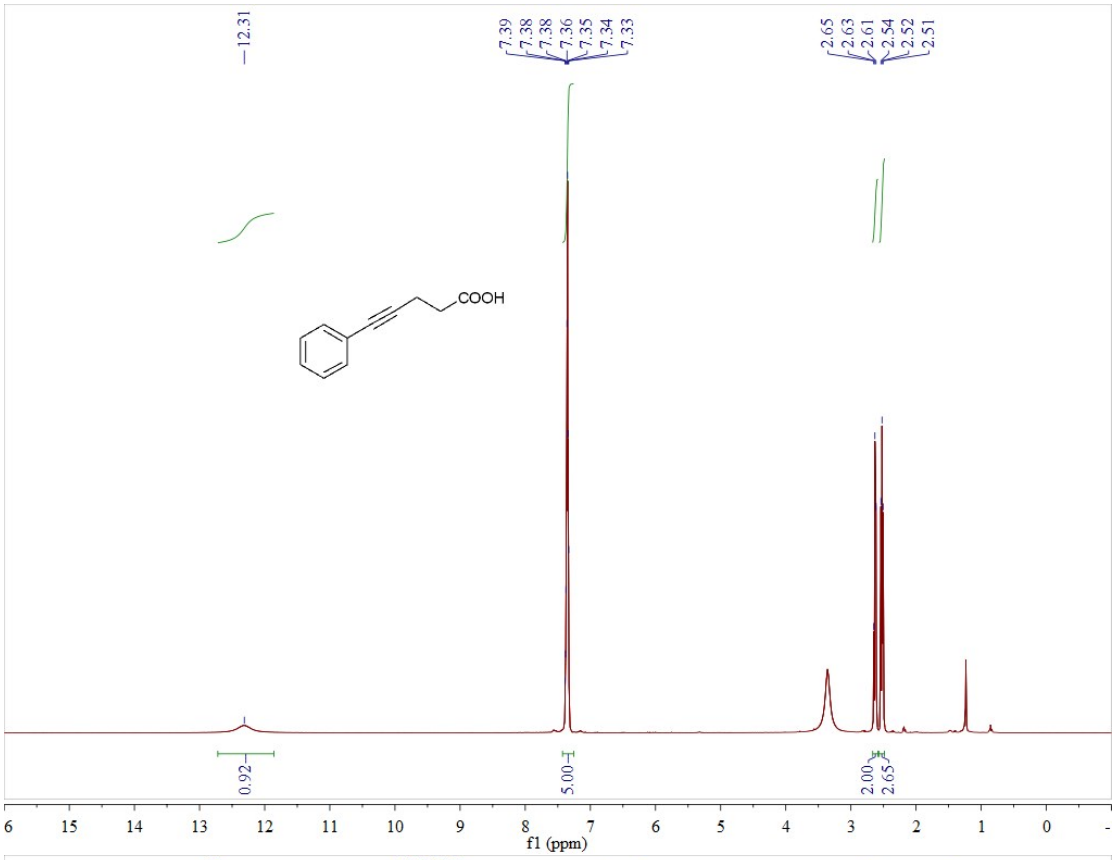

178.15
76.96
76.73
33.82
14.52
3.53
COOH
76.96
76.73
f1 (ppm)
f1 (ppm)

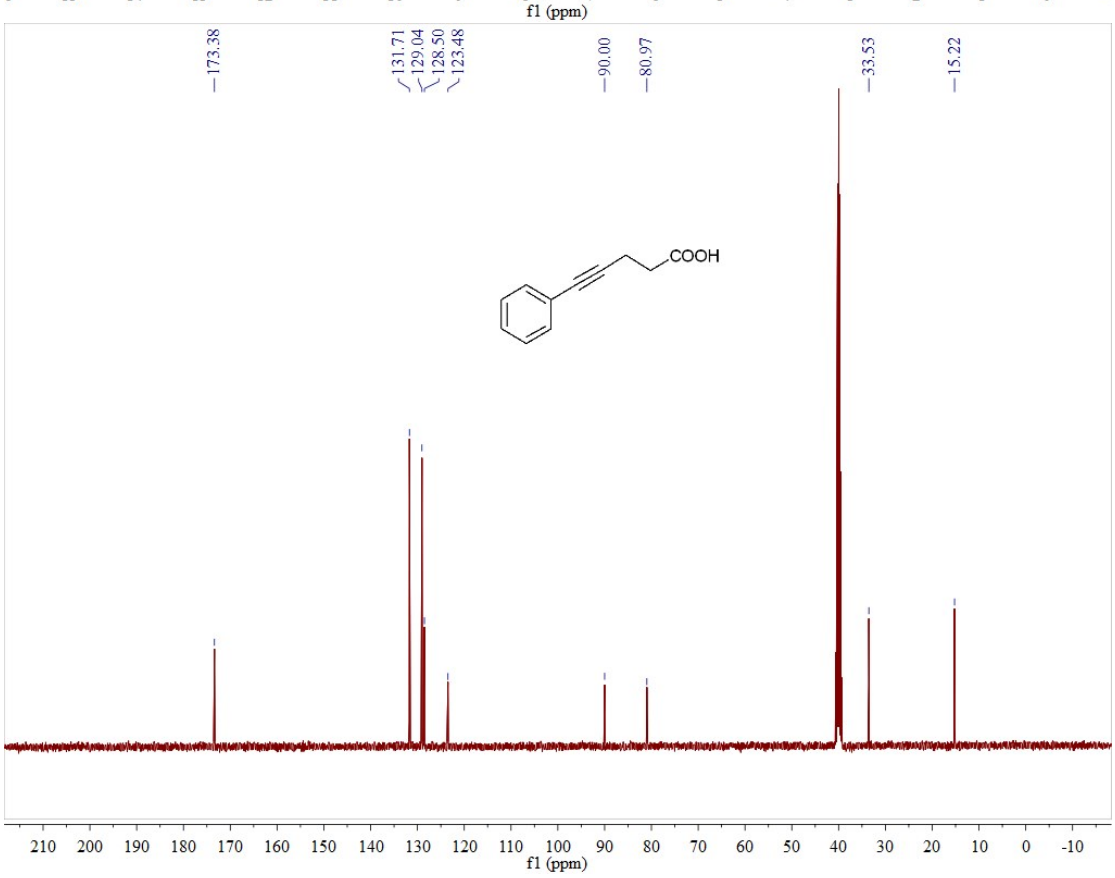

3.80
3.61
3.59
3.57
2.77
2.76
2.76
2.75
2.74
2.74
1.77
1.76
1.75
MeO
OH
3.00
1.02
2.03
3.12
f1 (ppm)

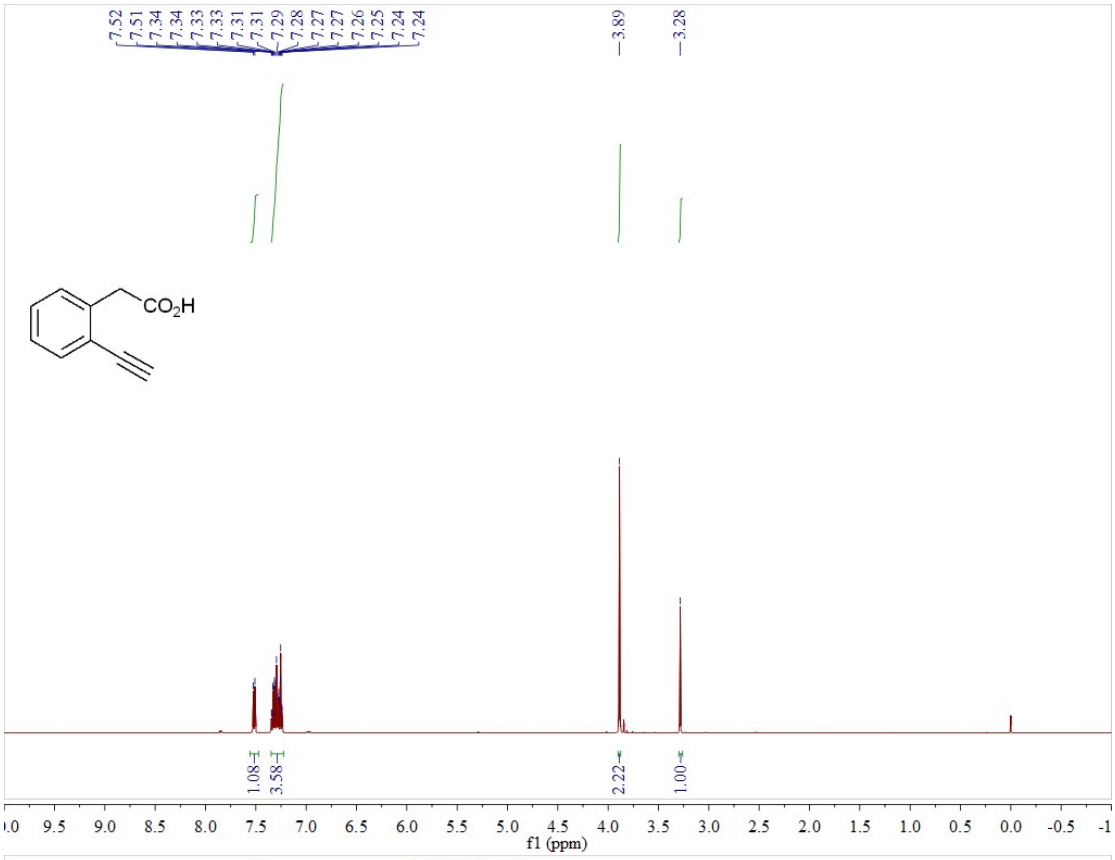

172.83
168.58
78.29
74.18
52.91
51.23
18.82
3.42
MeO
OH
f1 (ppm)

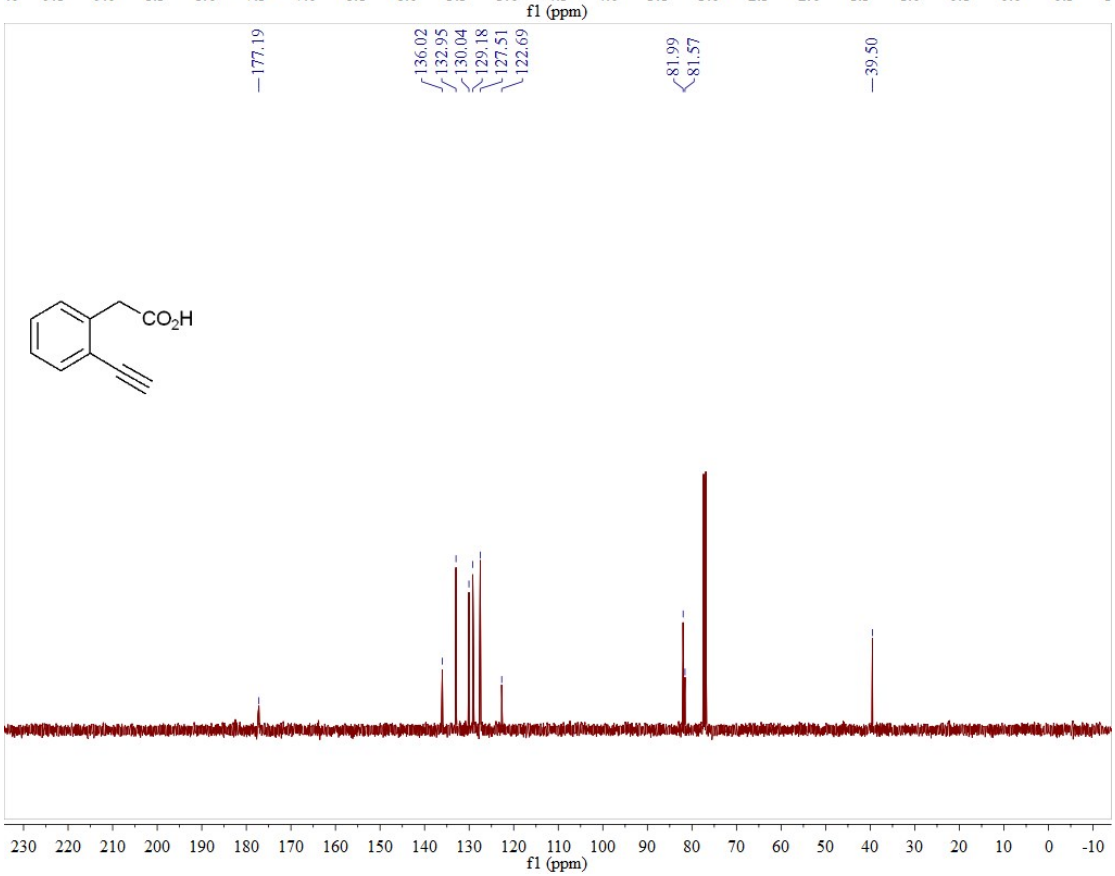

7.01
3.78
2.91
2.90
1.77
1.76
1.75
MeO
O
O
OH
1.21
3.02
4.00
6.00
f1 (ppm)


174.17
169.68
79.30
72.81
57.08
53.08
23.07
3.45
MeO
O
O
OH
f1 (ppm)


12.31
7.39
7.38
7.38
7.36
7.35
7.34
7.33
2.65
2.63
2.61
2.54
2.52
2.51
COOH
0.92
5.00
2.00
2.65
f1 (ppm)


173.38
131.71
129.04
128.50
123.48
90.00
80.97
33.53
15.22
COOH
f1 (ppm)


7.52
7.51
7.34
7.34
7.33
7.33
7.31
7.31
7.29
7.28
7.27
7.27
7.26
7.25
7.24
7.24
3.89
3.28
CO2H
1.08
3.58
2.22
1.00
f1 (ppm)


177.19
136.02
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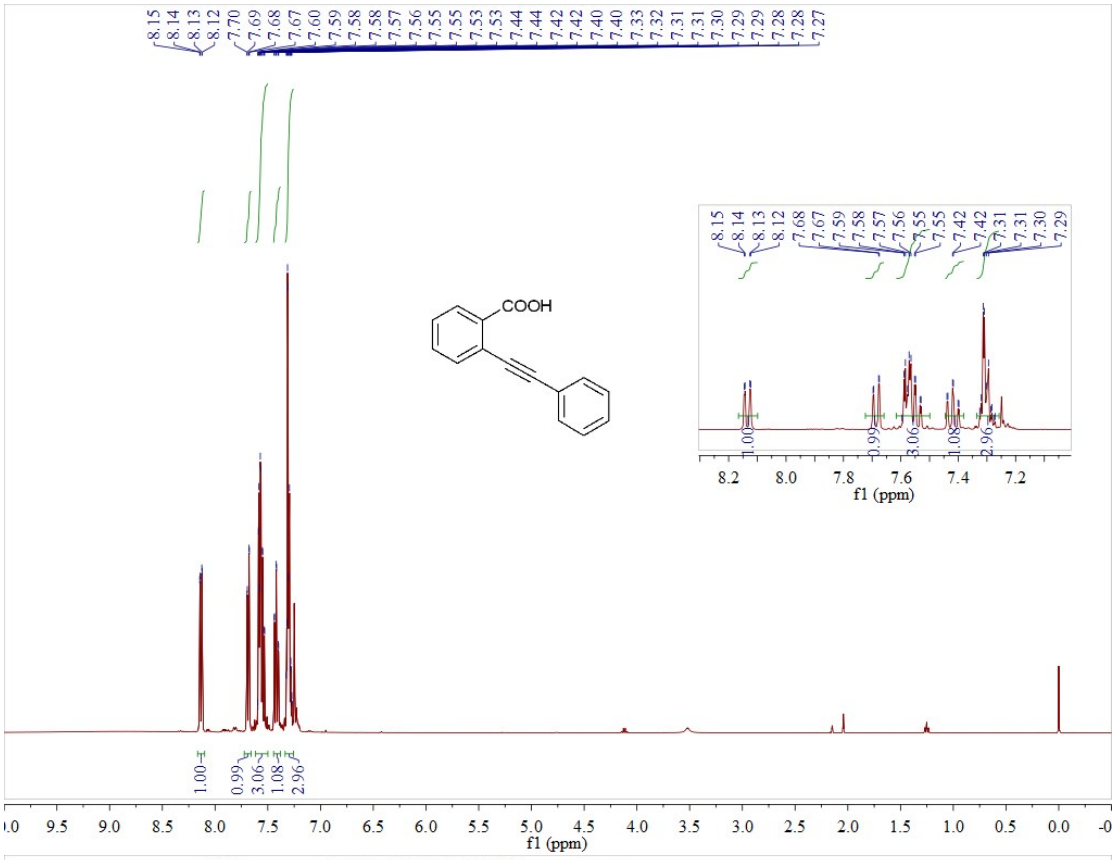
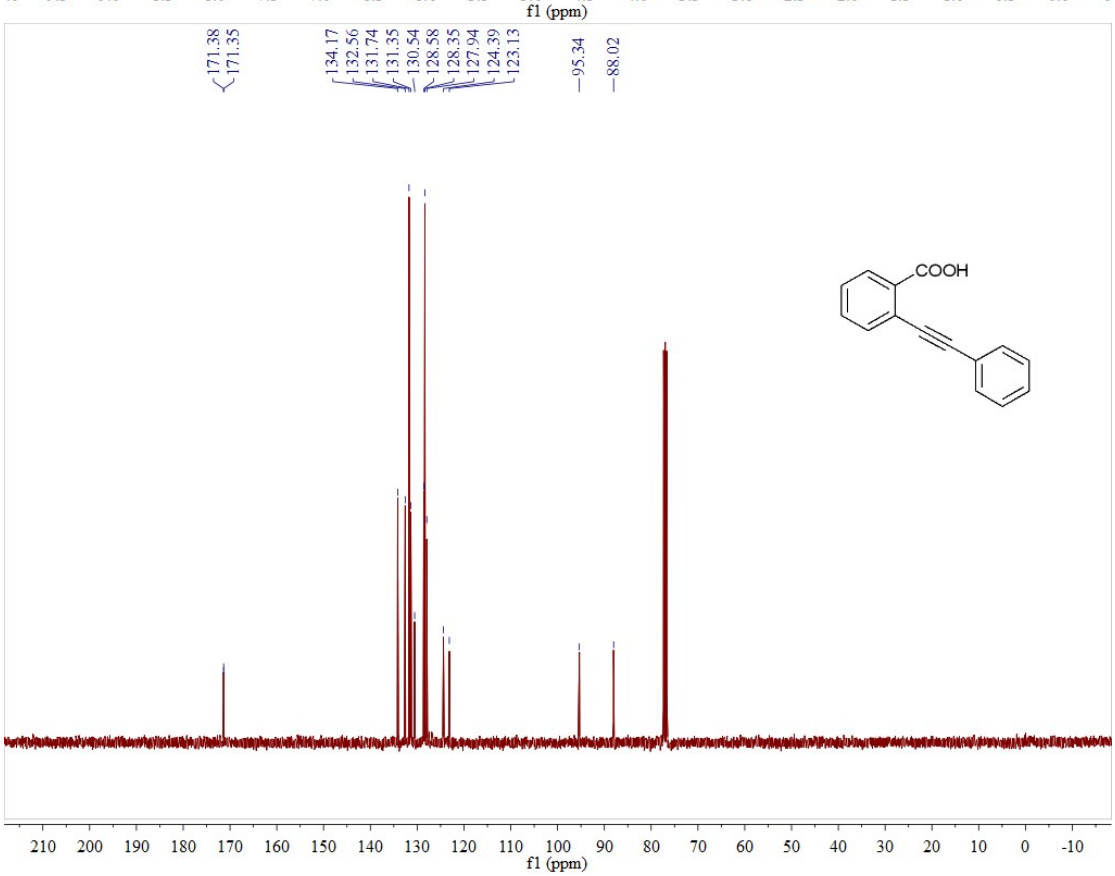
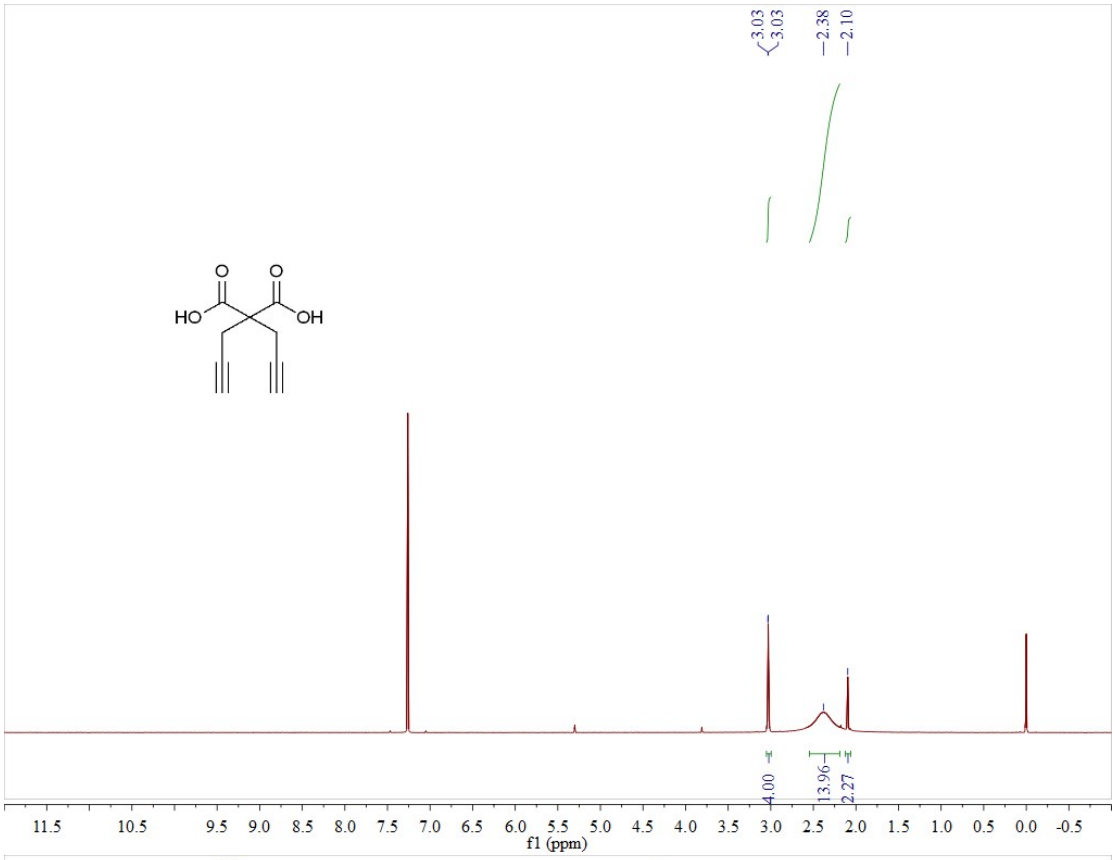
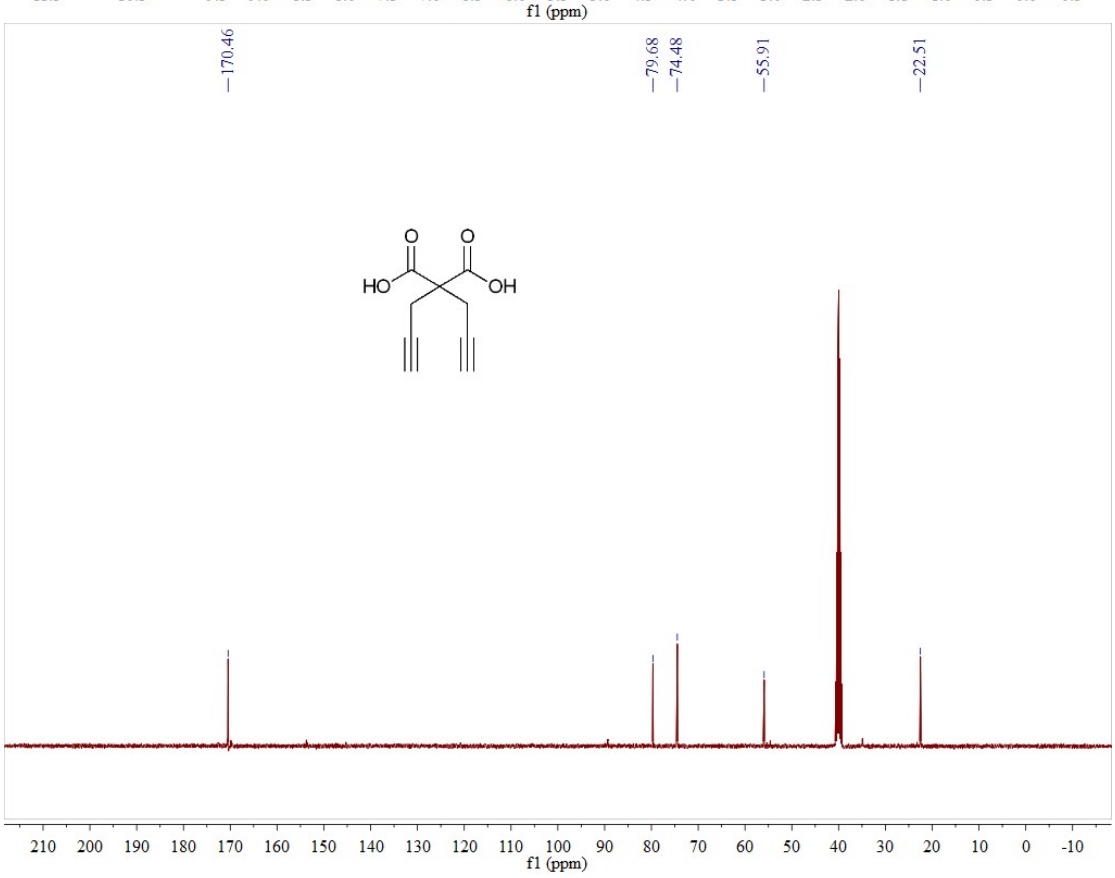
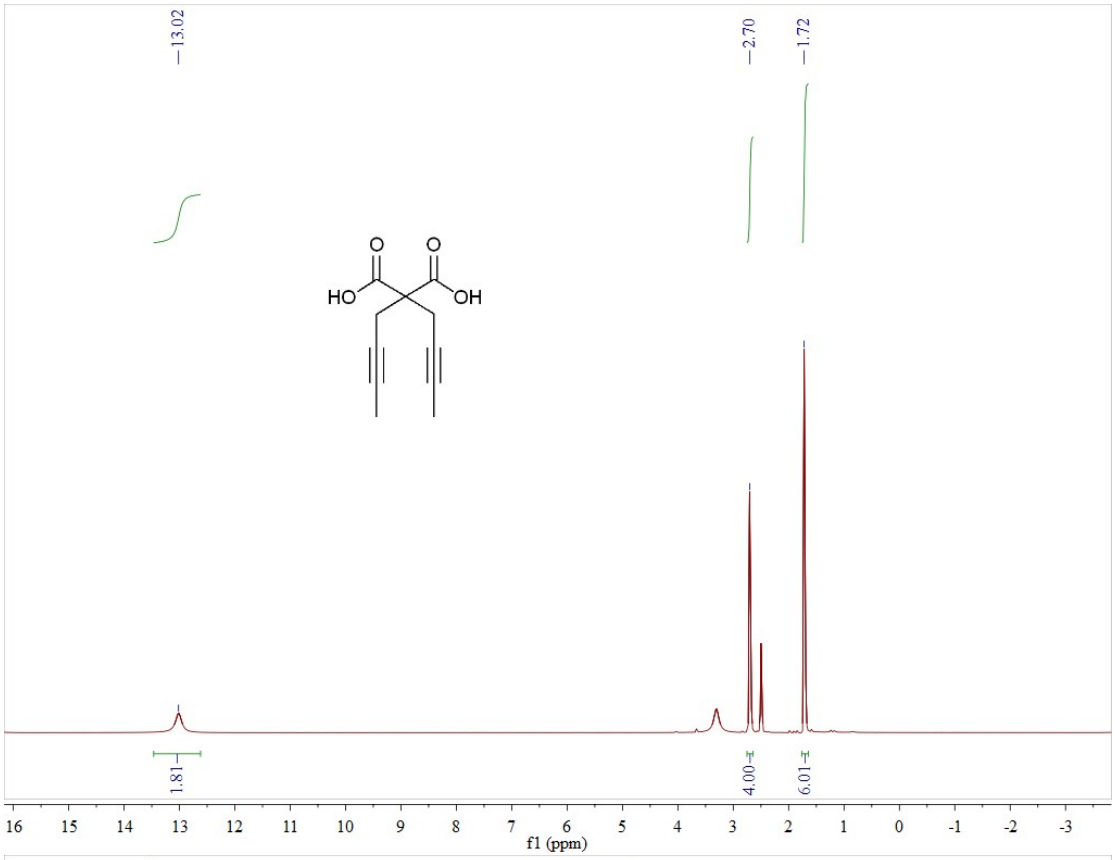
130.04
129.18
127.51
122.69
81.99
81.57
39.50
CO2H
f1 (ppm)

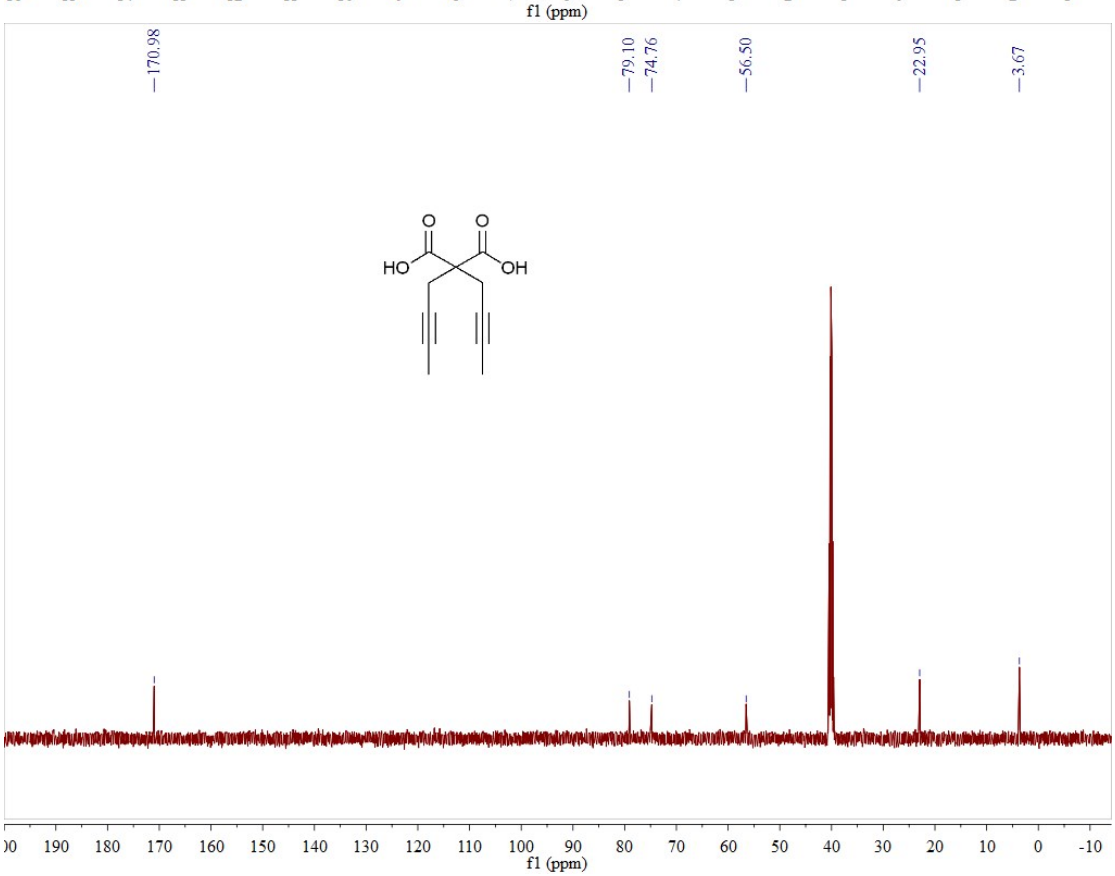

8.15
8.14
8.13
8.12
7.70
7.69
7.68
7.67
7.60
7.59
7.58
7.58
7.57
7.56
7.55
7.55
7.53
7.53
7.44
7.44
7.42
7.42
7.40
7.40
7.33
7.32
7.31
7.31
7.30
7.29
7.29
7.28
7.28
7.27
COOH
1.00
0.99
3.06
1.08
2.96
f1 (ppm)

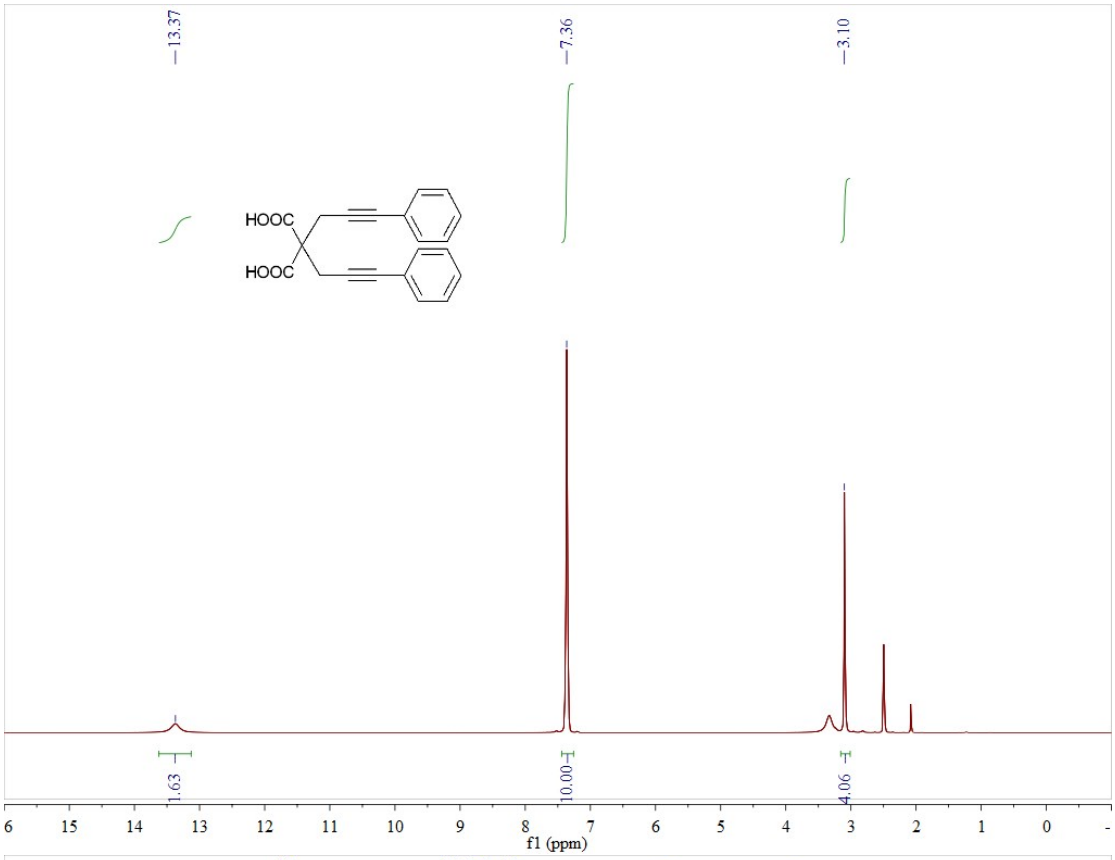

171.38
171.35
134.17
132.56
131.74
131.35
130.54
128.58
128.35
127.94
124.39
123.13
95.34
88.02
COOH
f1 (ppm)

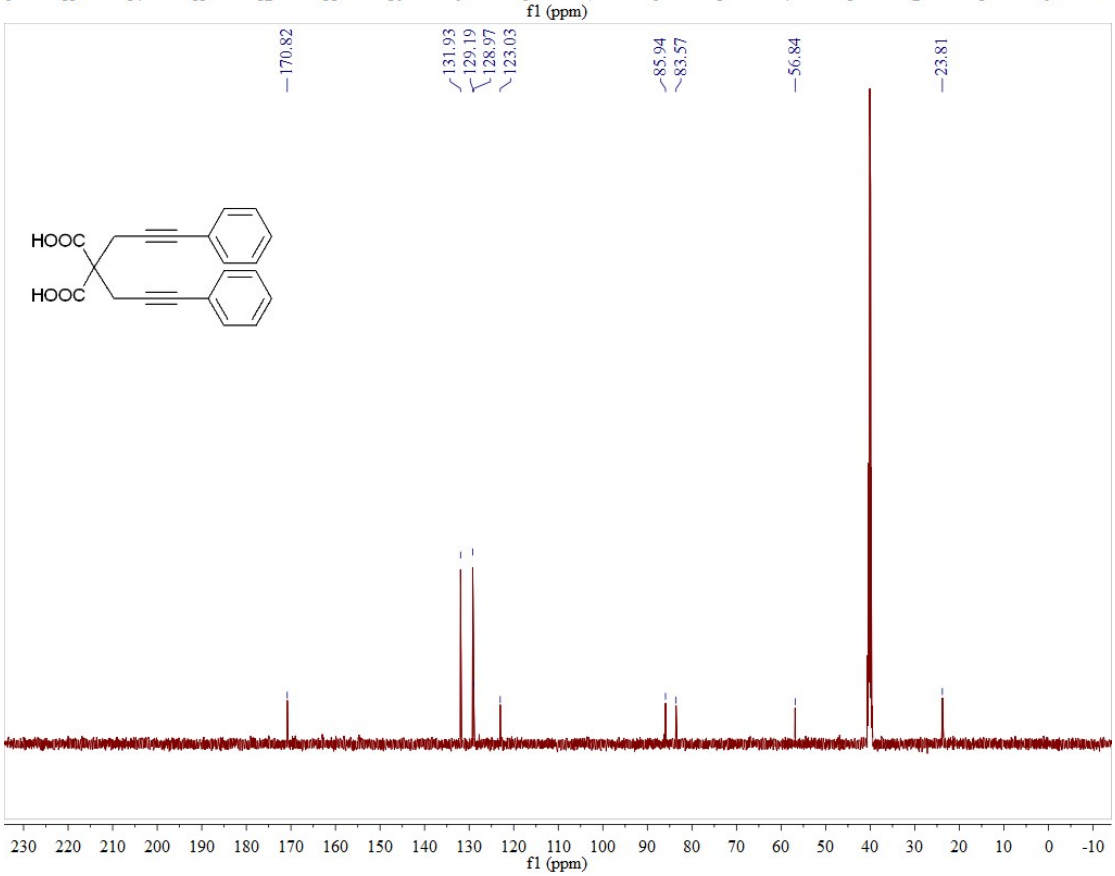

3.03
3.03
2.38
2.10
HO
O
O
OH
4.00
13.96
2.27
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

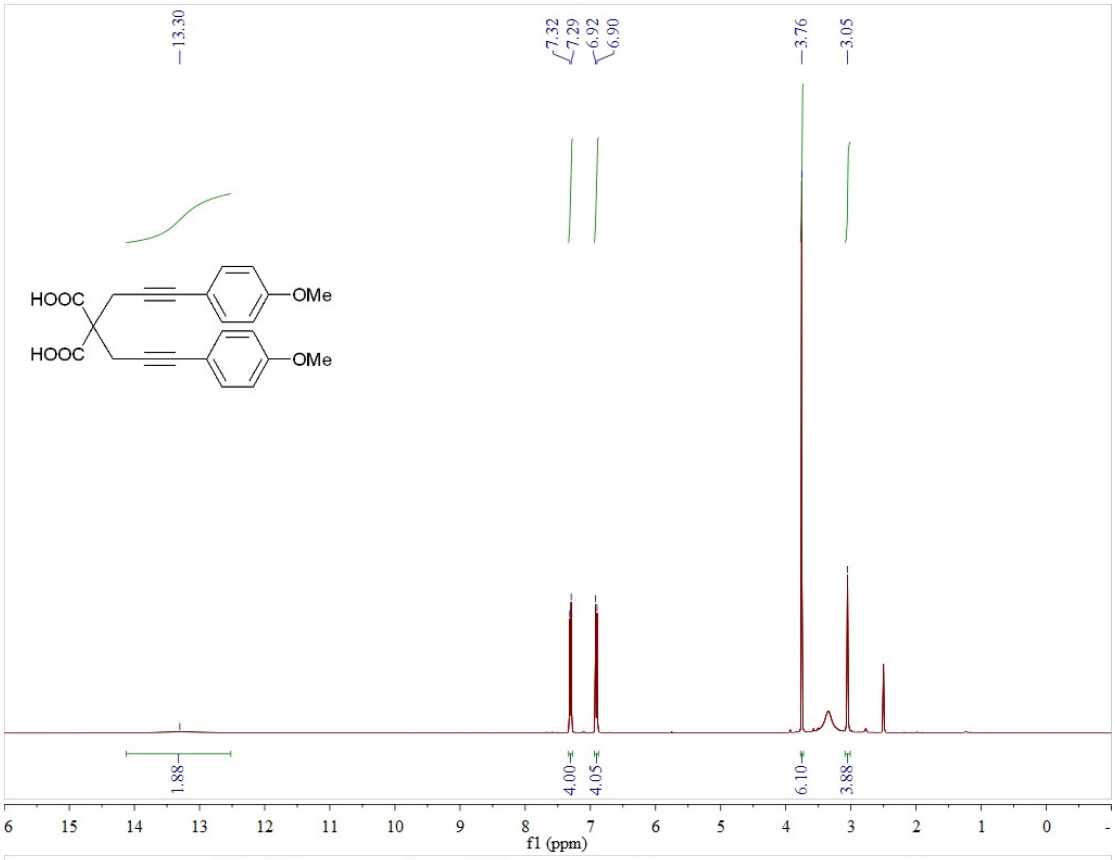

170.46
79.68
74.48
55.91
22.51
HO
O
O
OH
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

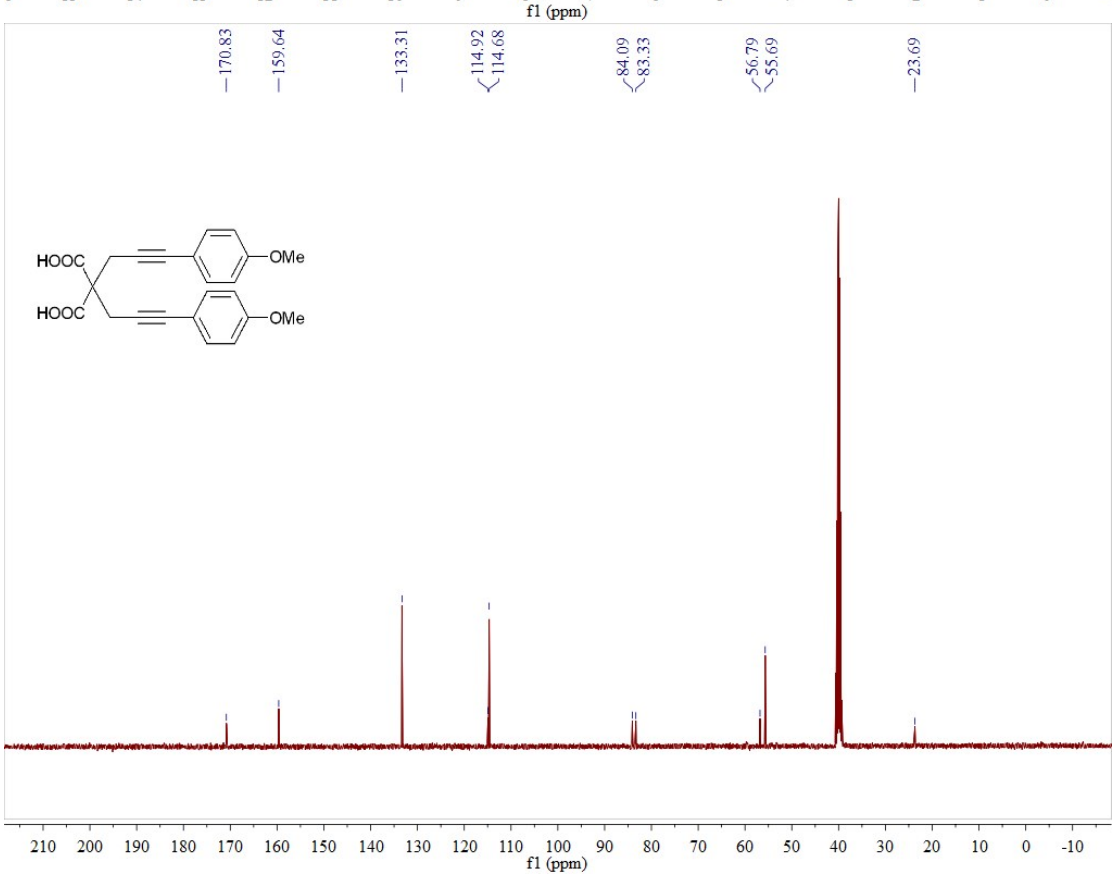

13.02
2.70
1.72
HO
O
O
OH
1.81
4.00
6.01
f1 (ppm)

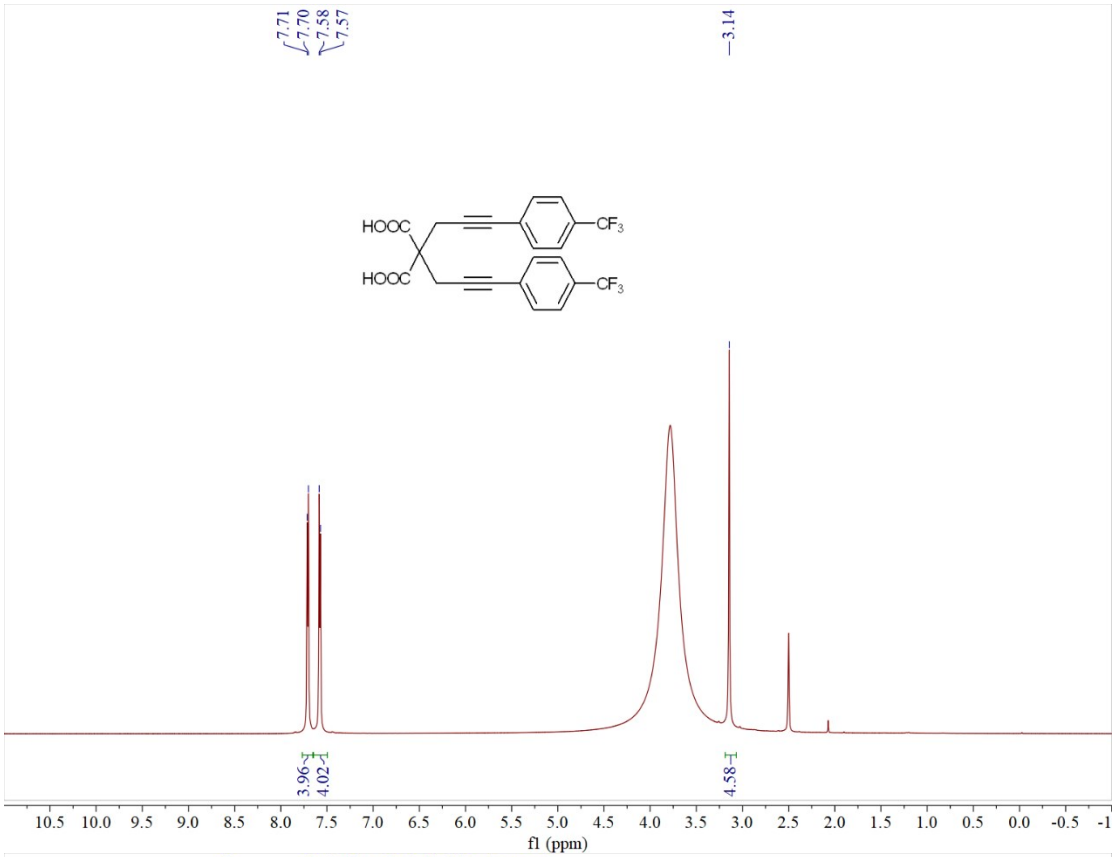

170.98
79.10
74.76
56.50
22.95
3.67
HO
O
O
OH
f1 (ppm)

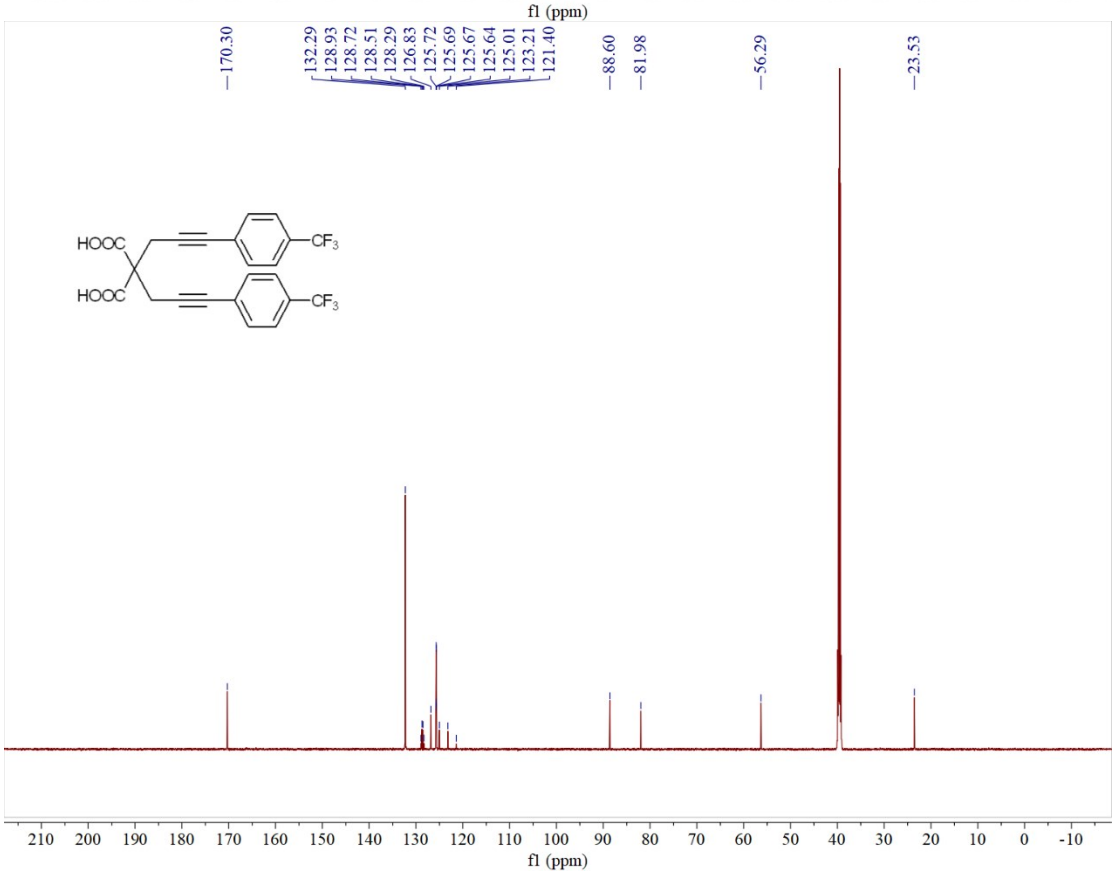

13.37
7.36
3.10
HOOC
HOOC
1.63
10.00
4.06
f1 (ppm)

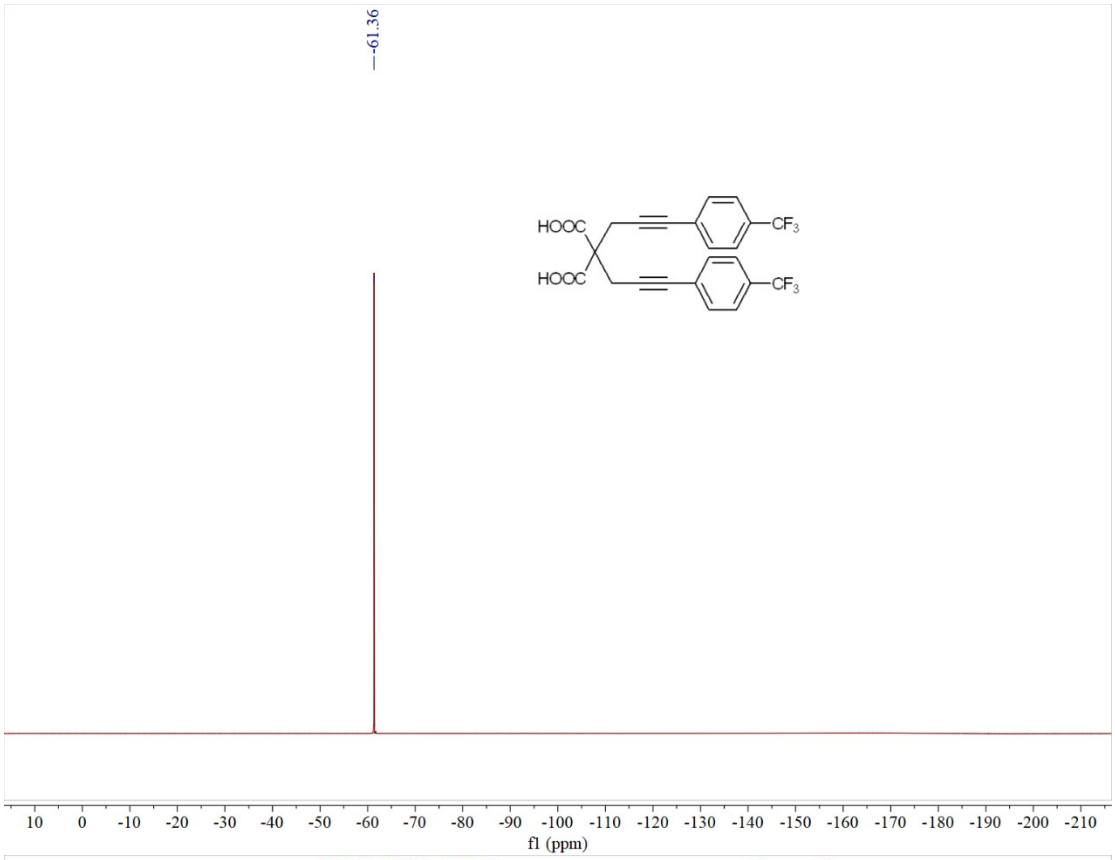

170.82
131.93
129.19
128.97
123.03
85.94
83.57
56.84
23.81
HOOC
HOOC
f1 (ppm)

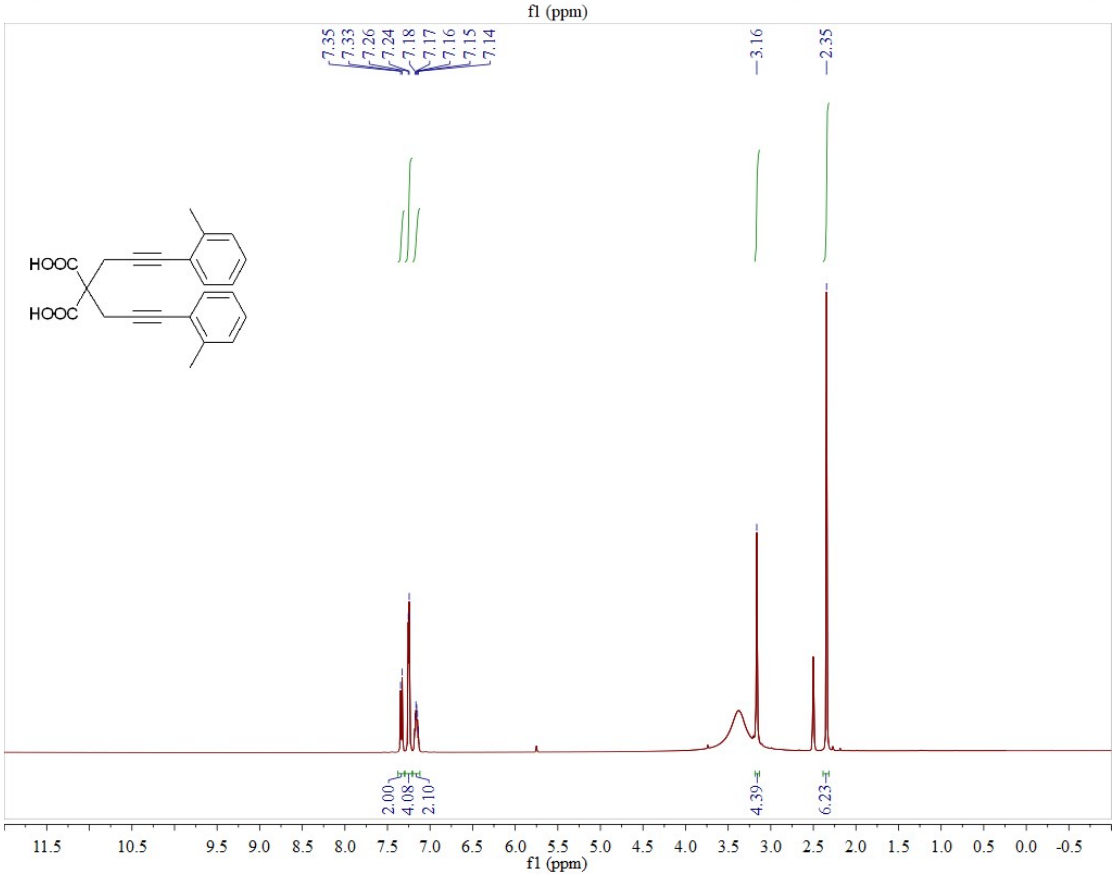

13.30
7.32
7.29
6.92
6.90
3.76
3.05
HOOC
HOOC
OMe
OMe
1.88
4.00
4.05
6.10
3.88
f1 (ppm)

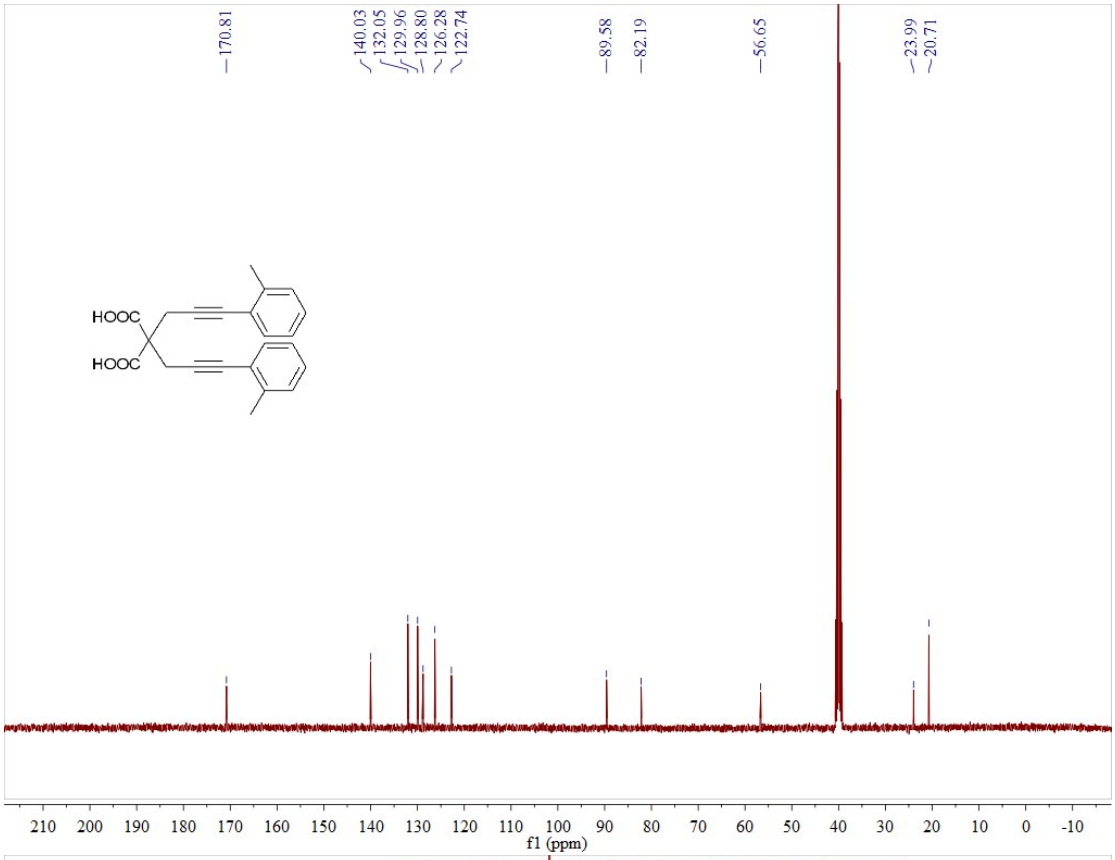

170.83
159.64
133.31
114.92
114.68
84.09
83.33
56.79
55.69
23.69
HOOC
HOOC
OMe
OMe
f1 (ppm)

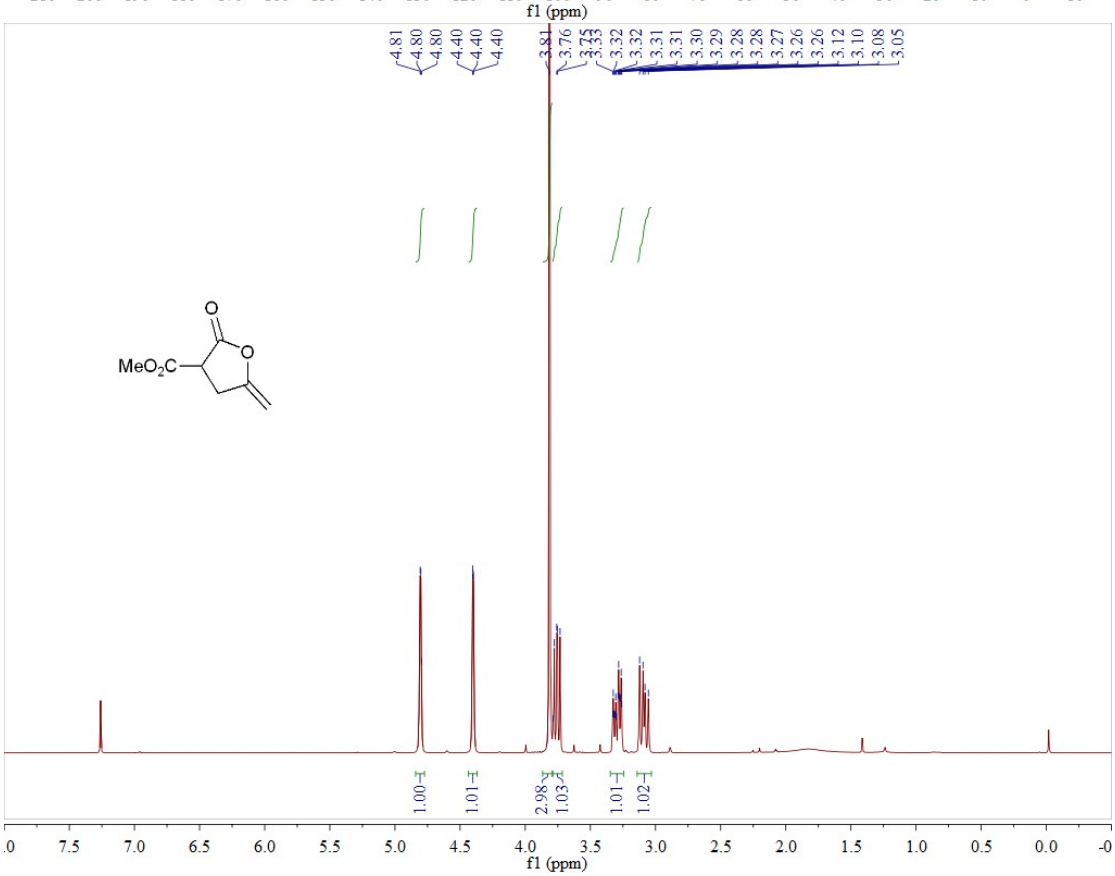

7.71
7.70
7.58
7.57
3.14
HOOC
HOOC
CF3
CF3
3.96
4.02
4.58
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

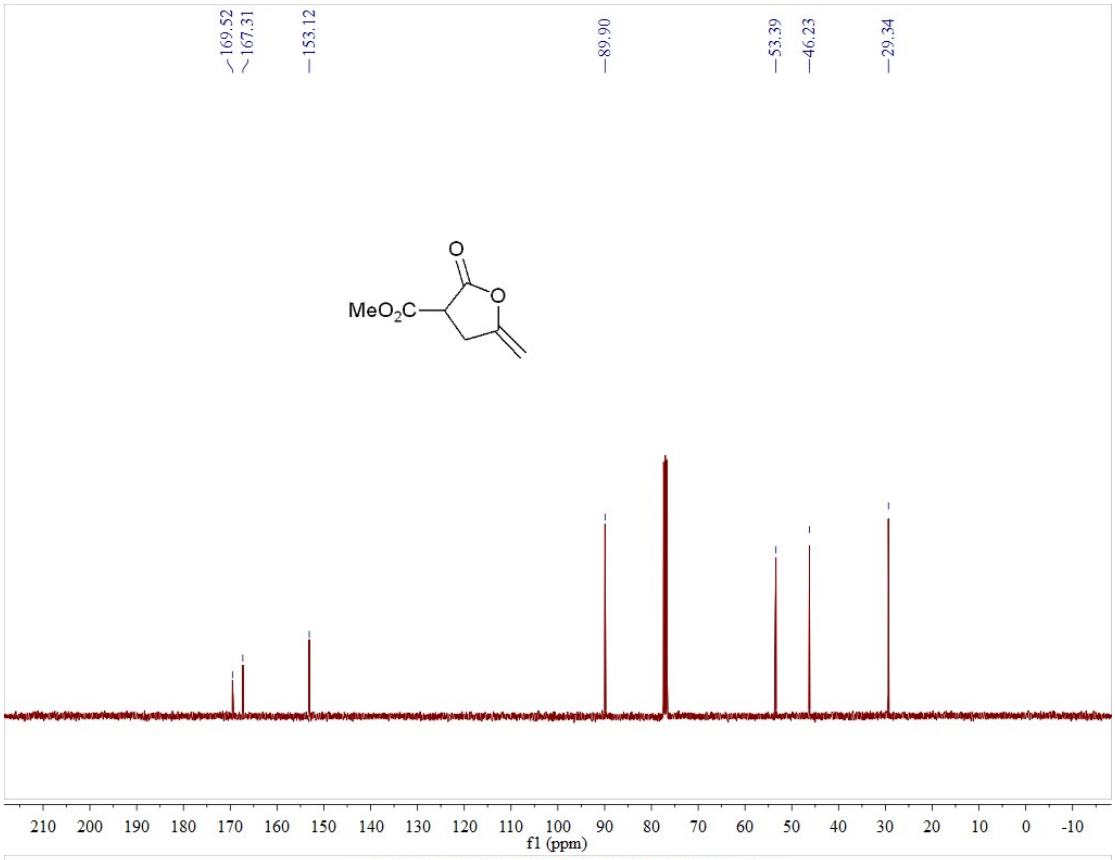

170.30
132.29
128.93
128.72
128.51
128.29
126.83
125.72
125.69
125.67
125.64
125.01
123.21
121.40
88.60
81.98
56.29
23.53
HOOC
HOOC
CF3
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

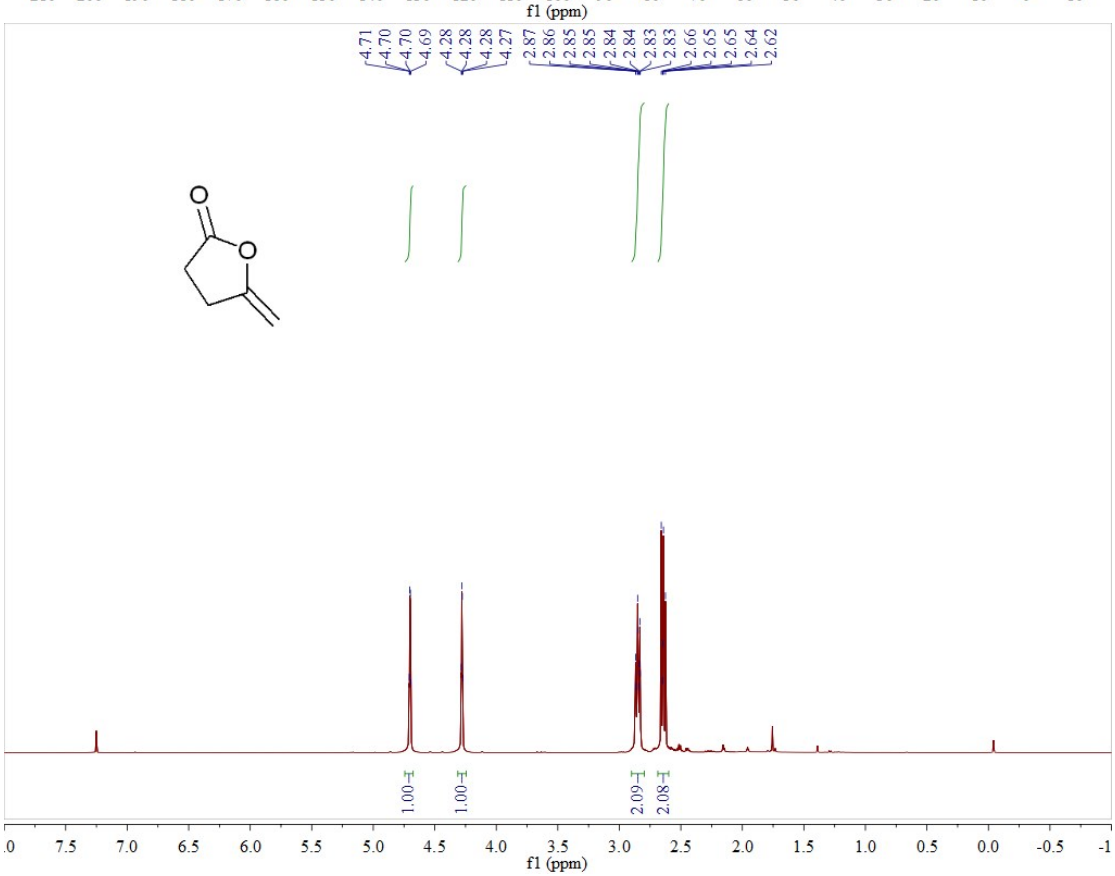

-61.36
HOOC
HOOC
CF3
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

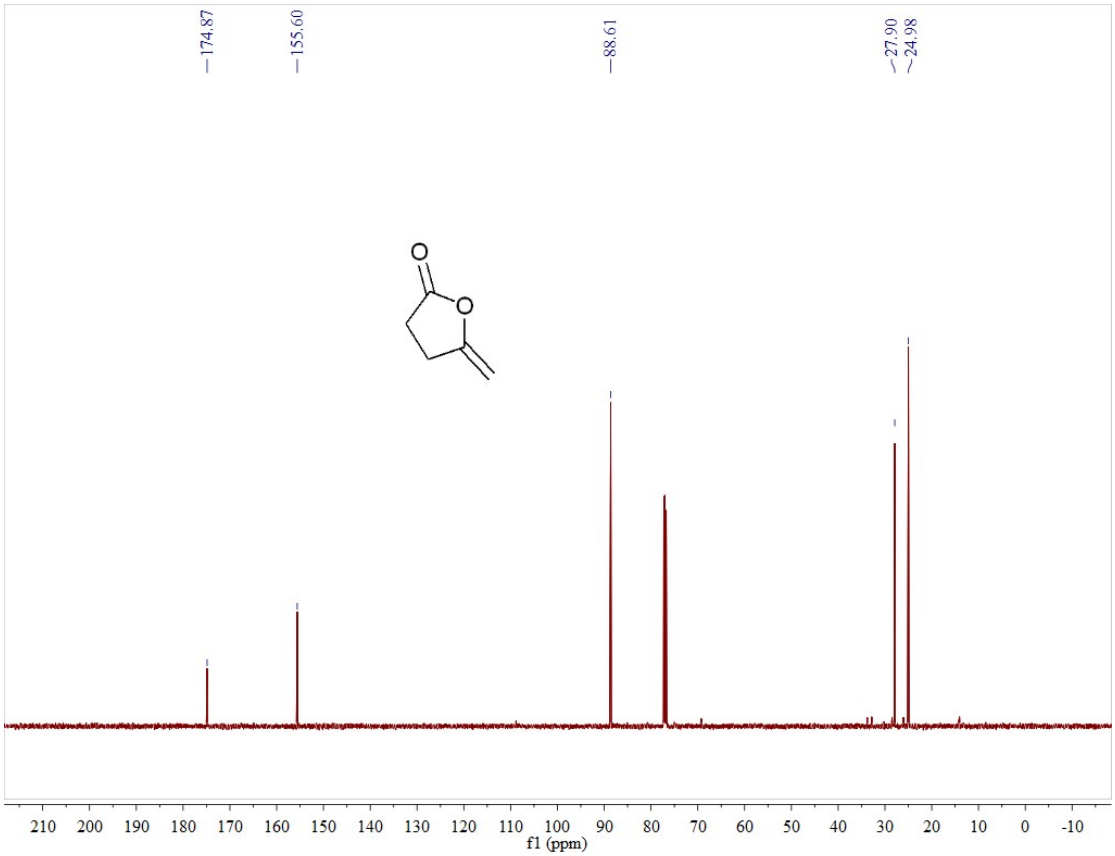

7.35
7.33
7.26
7.24
7.18
7.17
7.16
7.15
7.14
3.16
2.35
HOOC
HOOC
2.00
4.08
2.10
4.39
6.23
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

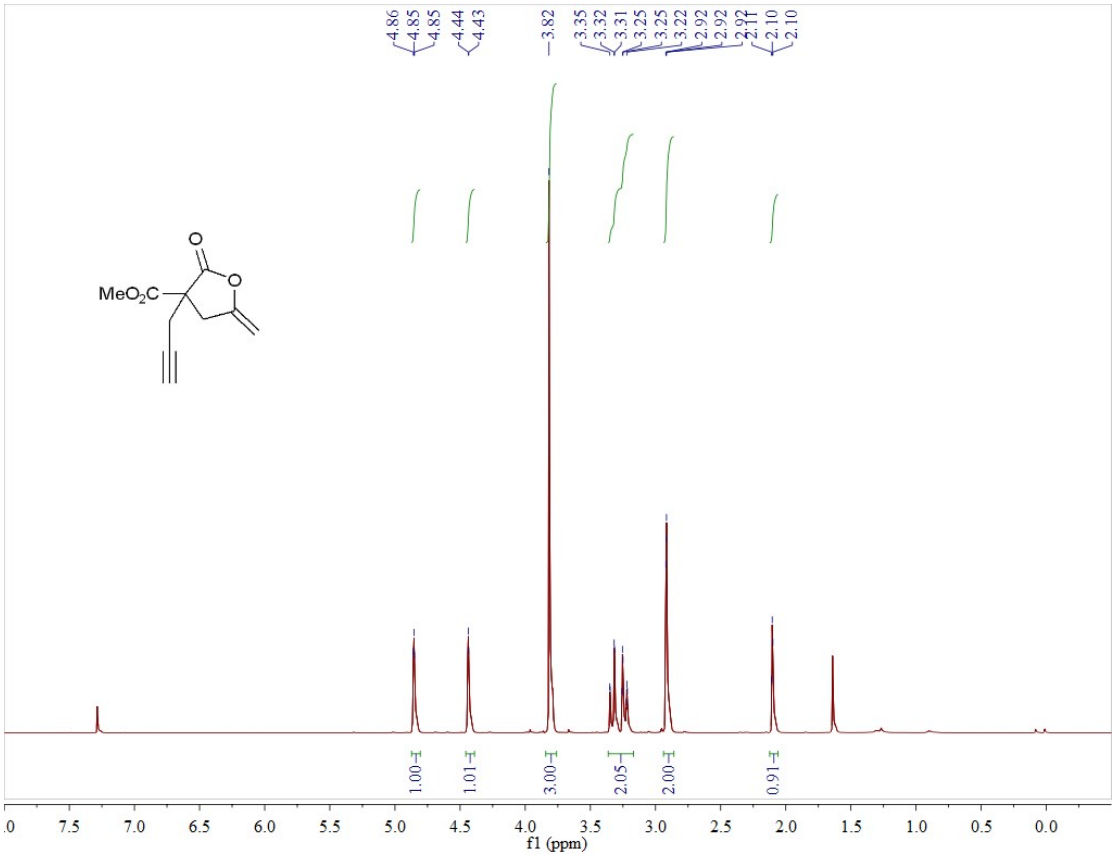

170.81
140.03
132.05
129.96
128.80
126.28
122.74
89.58
82.19
56.65
23.99
20.71
HOOC
HOOC
f1 (ppm)

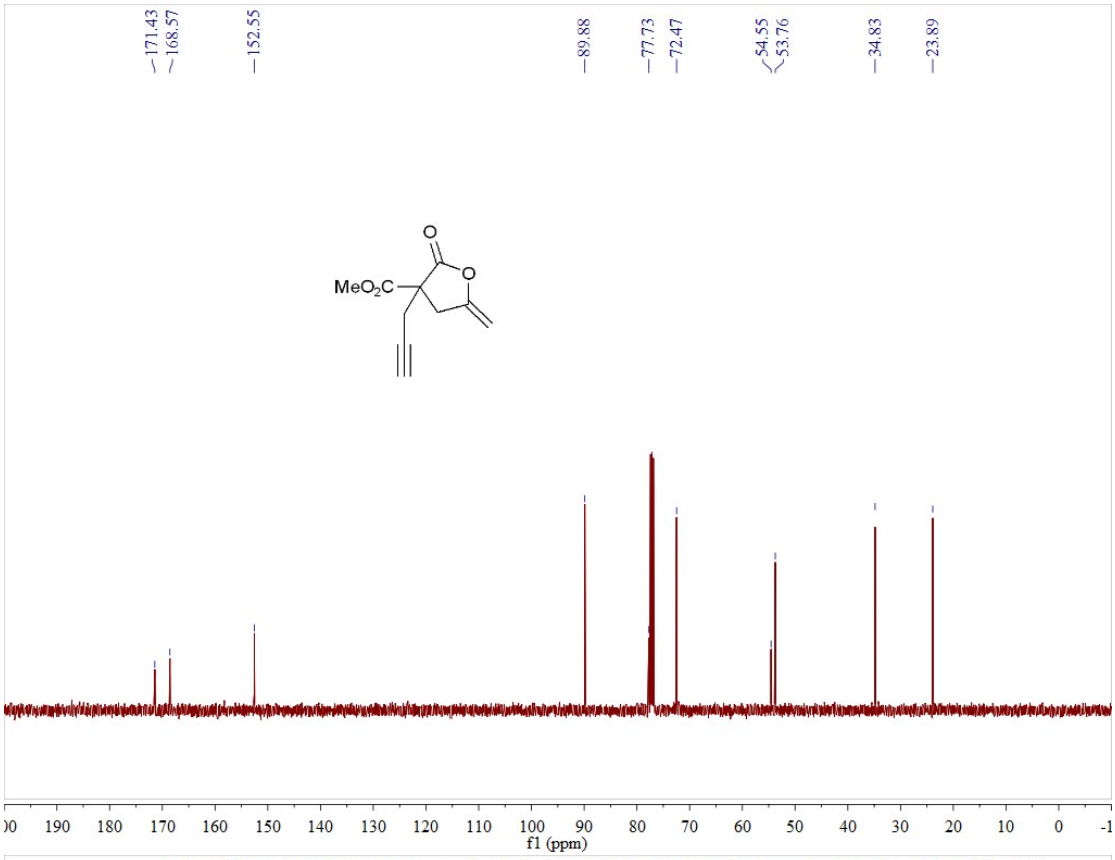

4.81
4.80
4.80
4.40
4.40
4.40
3.81
3.76
3.75
3.33
3.32
3.32
3.31
3.31
3.30
3.29
3.28
3.28
3.27
3.26
3.26
3.12
3.10
3.08
3.05
MeO2C
O
O
1.00
1.01
2.98
1.03
1.01
1.02
f1 (ppm)

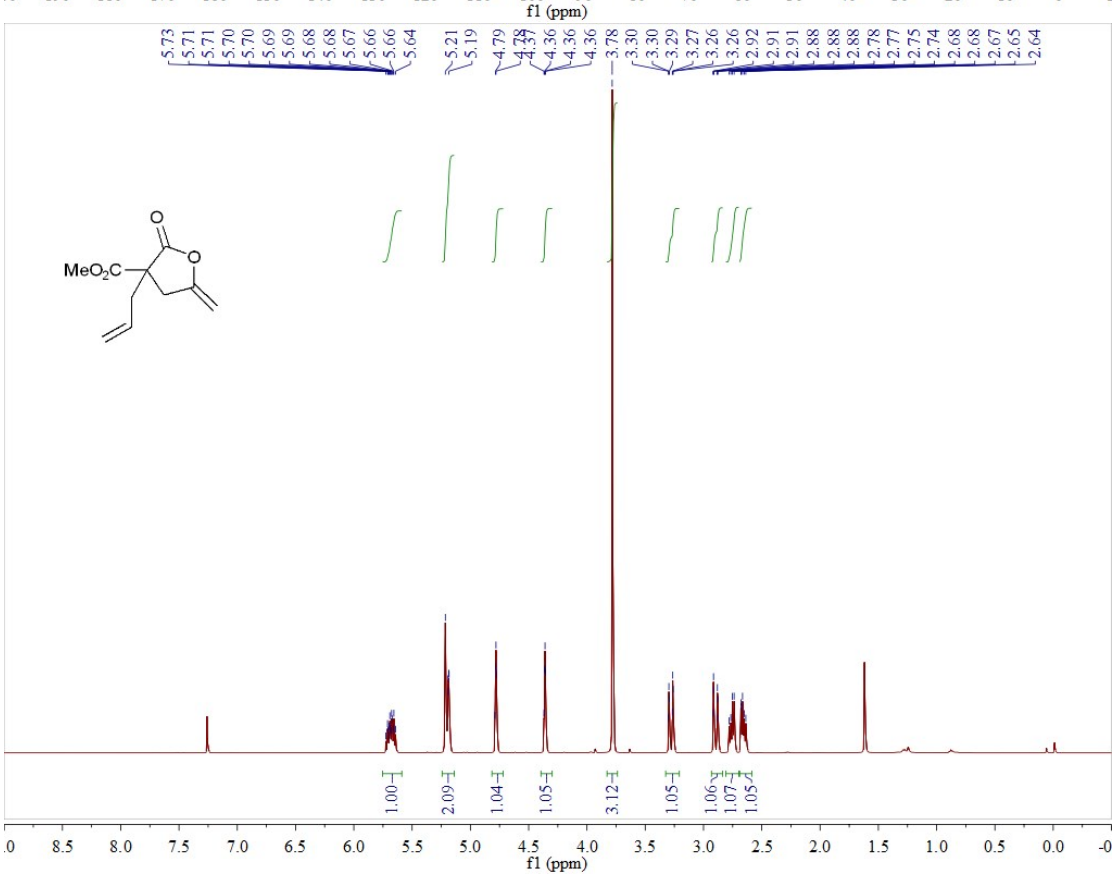

169.52
167.31
153.12
89.90
53.39
46.23
29.34
MeO2C
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

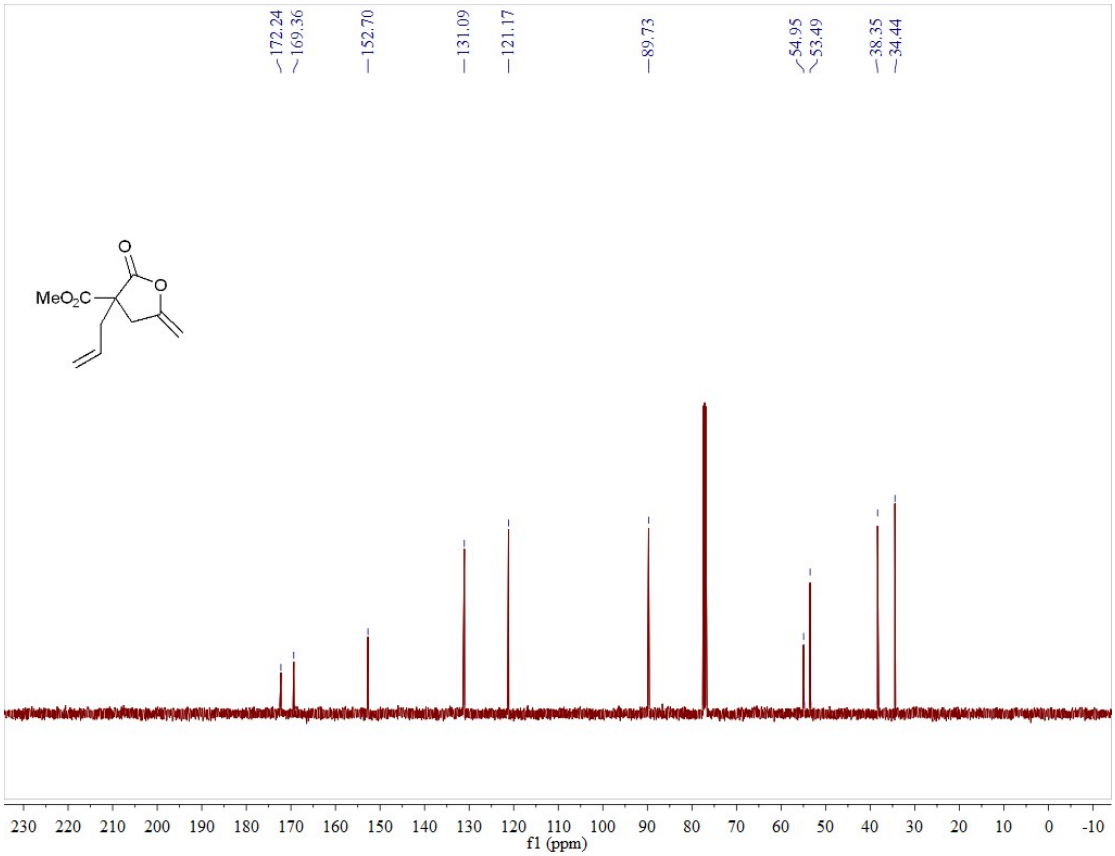

4.71
4.70
4.70
4.69
4.28
4.28
4.28
4.27
2.87
2.86
2.85
2.85
2.84
2.84
2.83
2.83
2.66
2.65
2.65
2.64
2.62
O
O
1.00
1.00
2.09
2.08
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

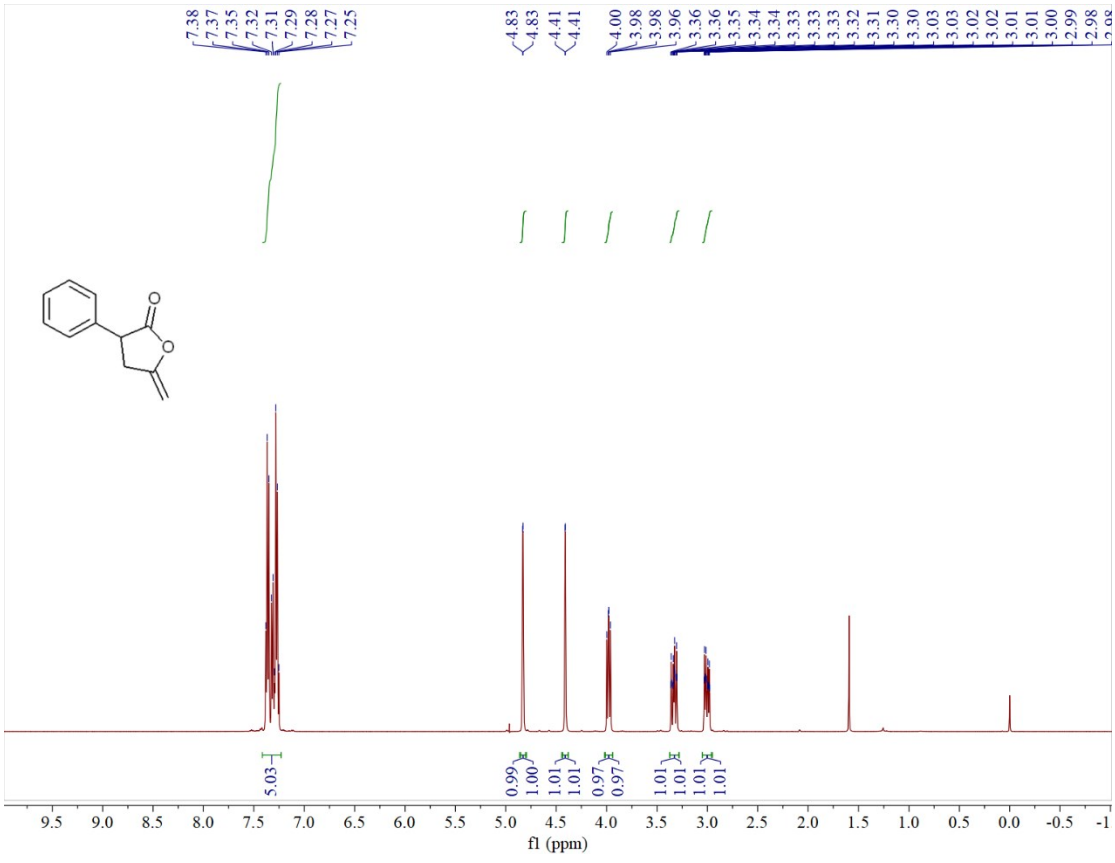

174.87
155.60
88.61
27.90
24.98
O
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

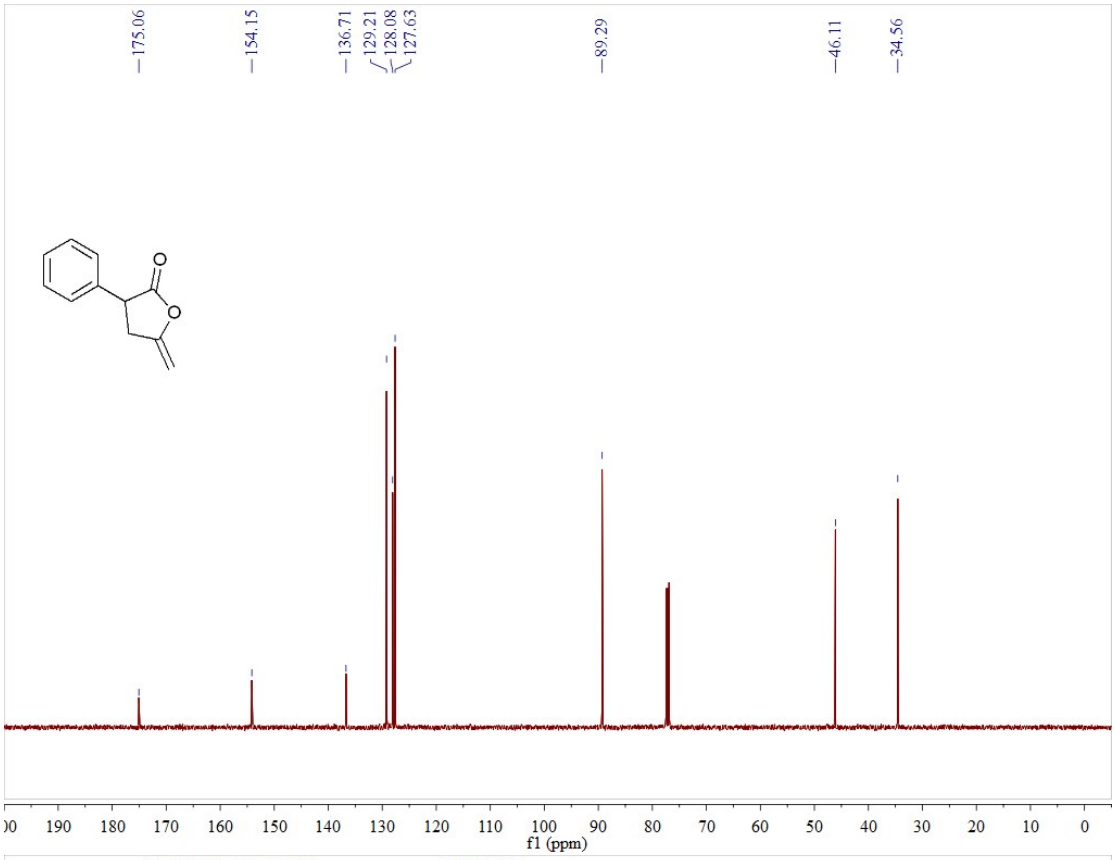

4.86
4.85
4.85
4.44
4.43
3.82
3.35
3.32
3.31
3.25
3.25
3.22
2.92
2.92
2.92
2.10
2.10
MeO2C
O
O
1.00
1.01
3.00
2.05
2.00
0.91
.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

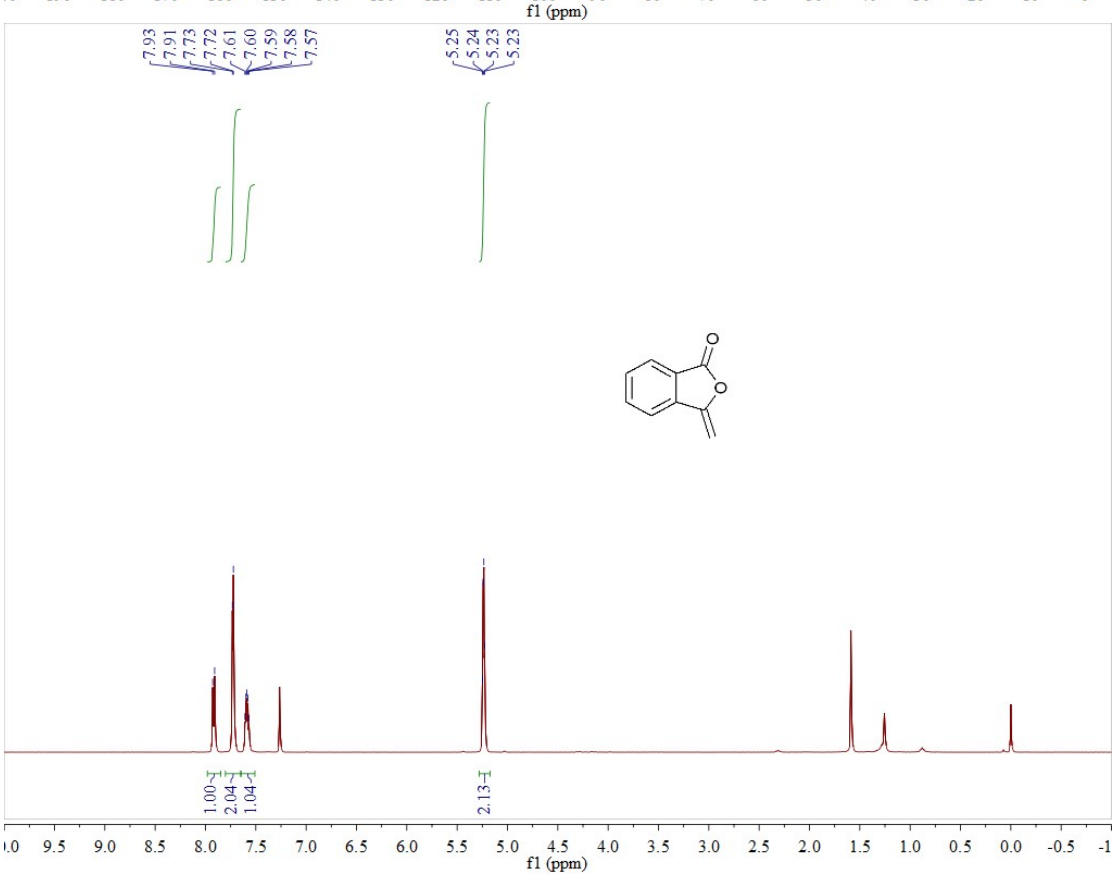

171.43
168.57
152.55
89.88
77.73
72.47
54.55
53.76
34.83
23.89
MeO2C
O
O
f1 (ppm)

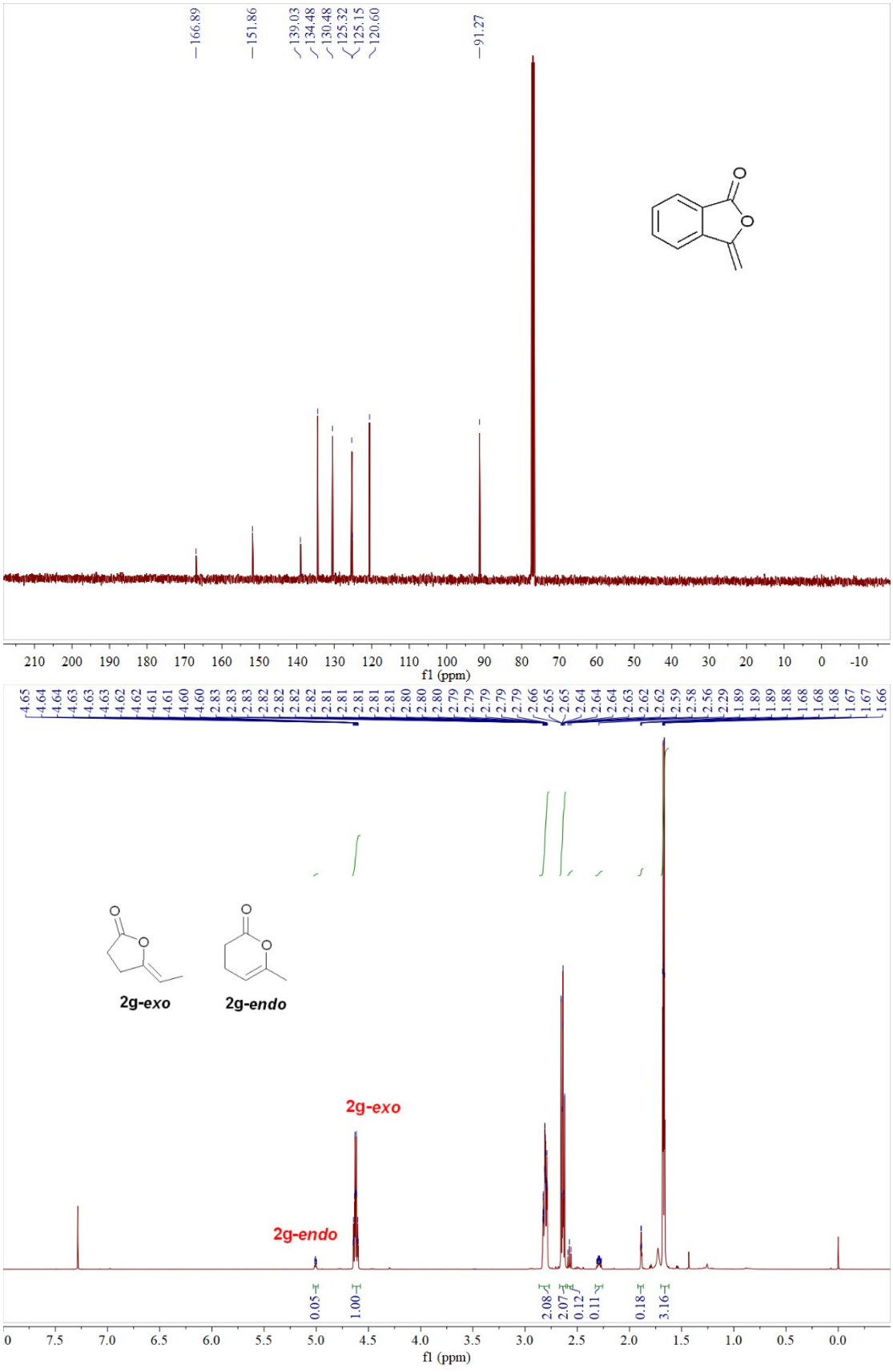

5.73
5.71
5.71
5.70
5.70
5.69
5.69
5.68
5.68
5.67
5.66
5.66
5.64
5.21
5.19
4.79
4.36
4.36
4.36
3.78
3.30
3.30
3.29
3.27
3.26
3.26
2.92
2.91
2.91
2.88
2.88
2.88
2.78
2.77
2.75
2.74
2.68
2.68
2.67
2.65
2.64
1.00
2.09
1.04
1.05
3.12
1.05
1.06
1.07
1.05
MeO2C
O
O
f1 (ppm)

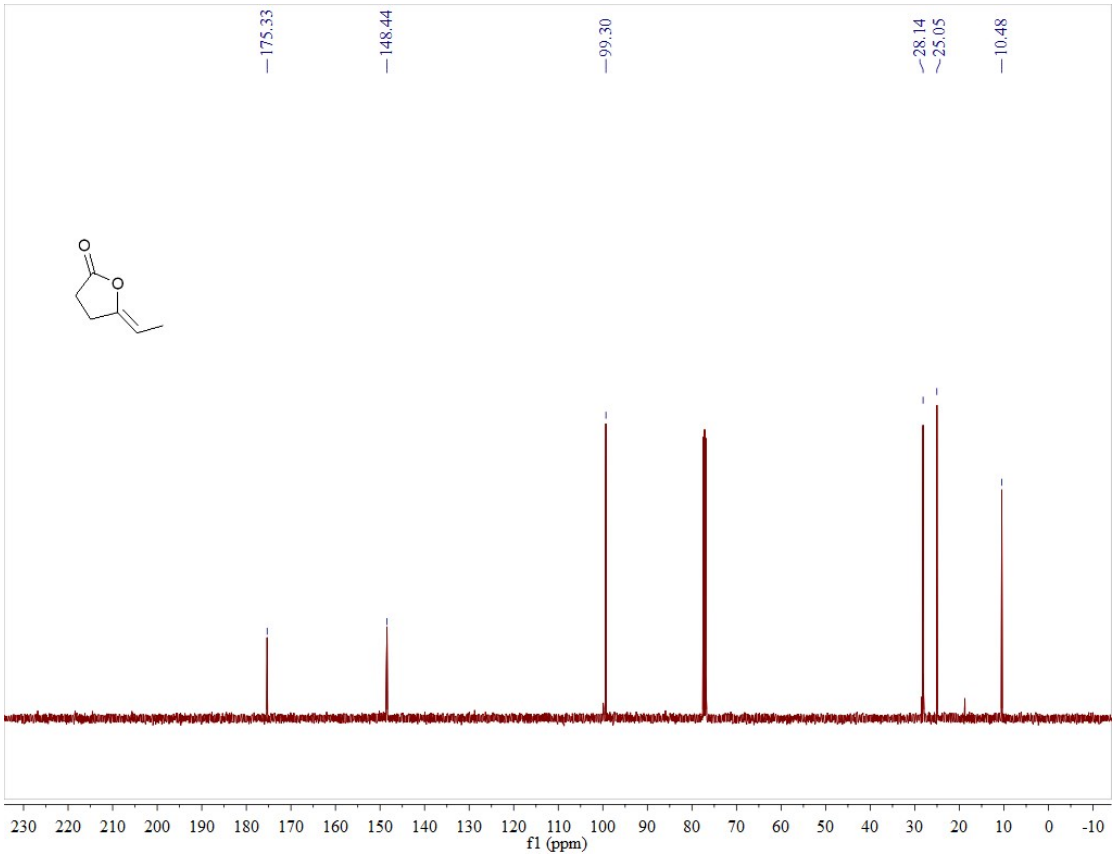

172.24
169.36
152.70
131.09
121.17
89.73
54.95
53.49
38.35
34.44
MeO2C
O
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

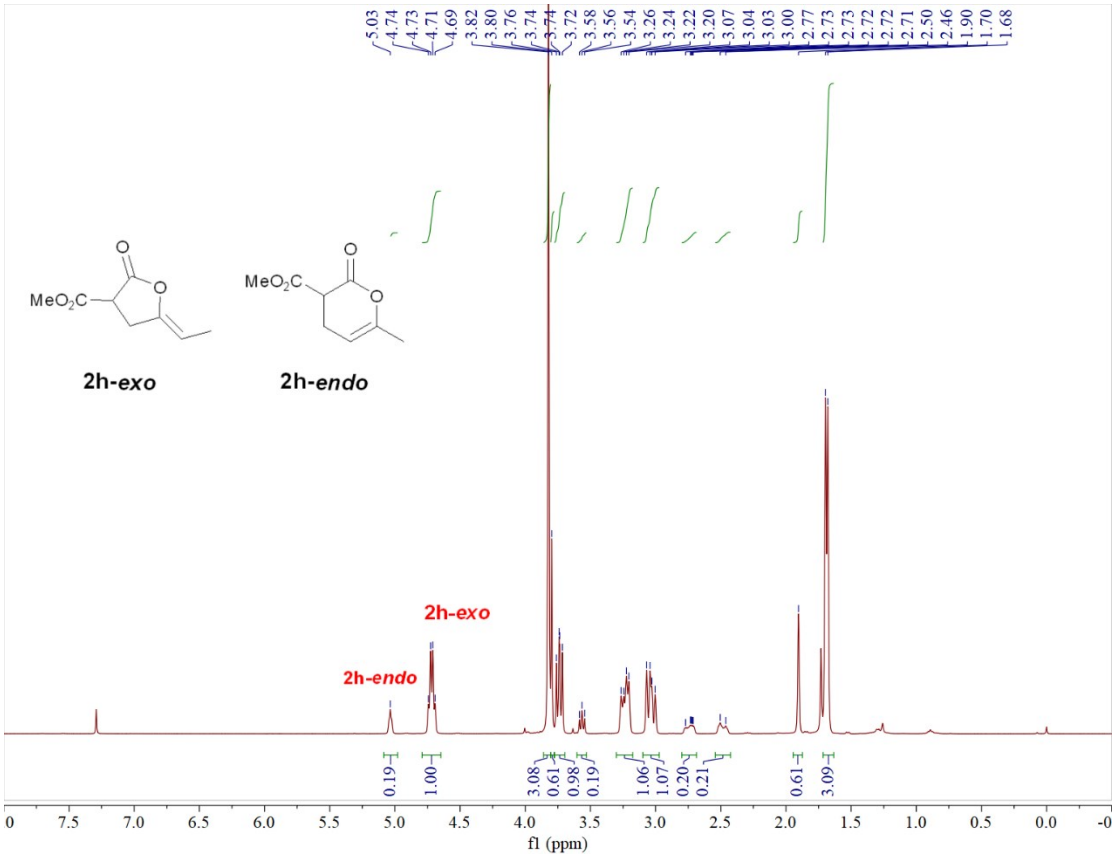

7.38
7.37
7.35
7.32
7.31
7.29
7.28
7.27
7.25
4.83
4.83
4.41
4.41
4.00
3.98
3.98
3.96
3.36
3.36
3.35
3.34
3.34
3.33
3.33
3.33
3.32
3.31
3.30
3.30
3.03
3.03
3.02
3.02
3.01
3.01
3.00
2.99
2.98
O
O
5.03
0.99
1.00
1.01
1.01
0.97
0.97
1.01
1.01
1.01
1.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

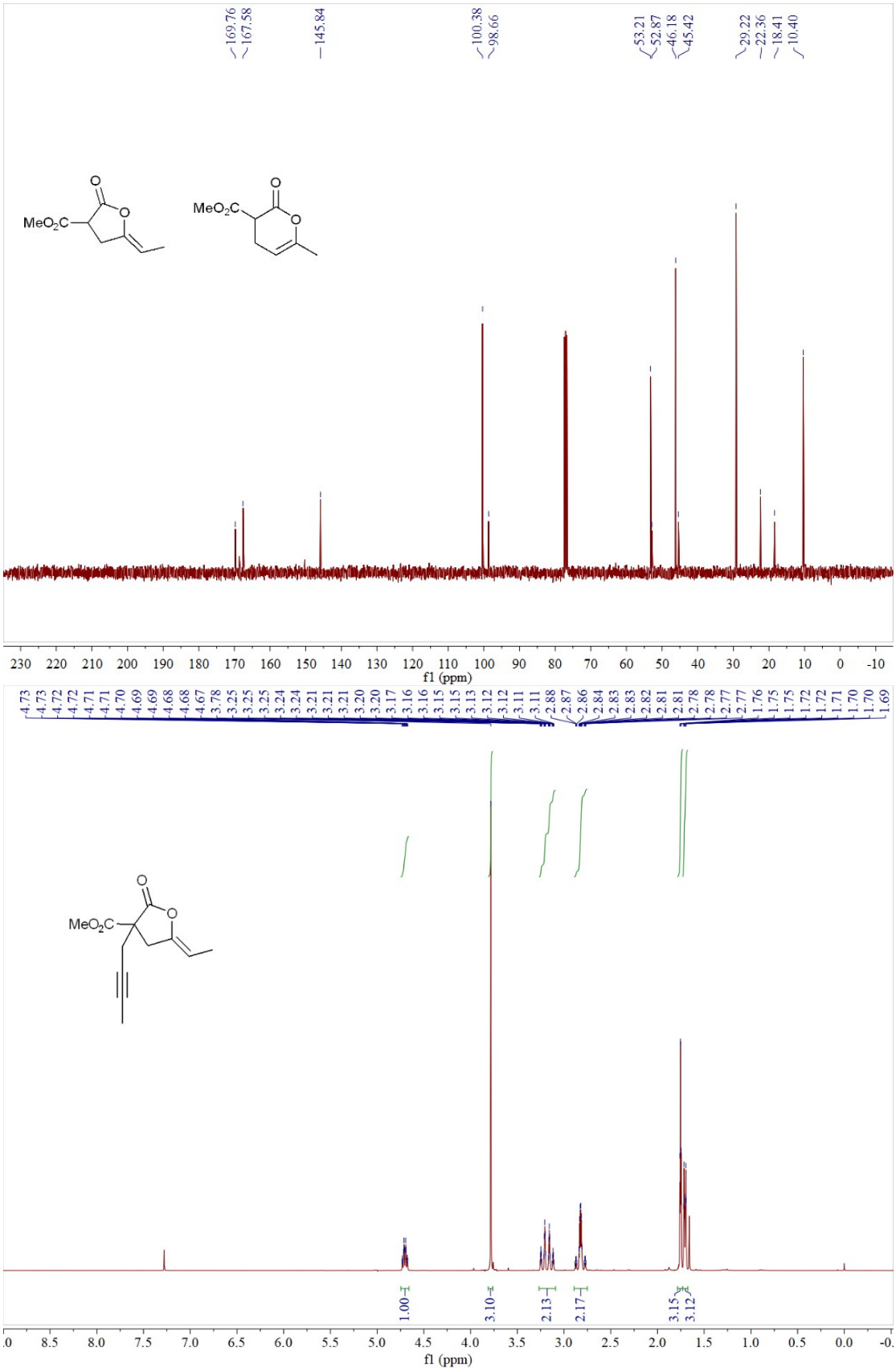

175.06
154.15
136.71
129.21
128.08
127.63
89.29
46.11
34.56
f1 (ppm)

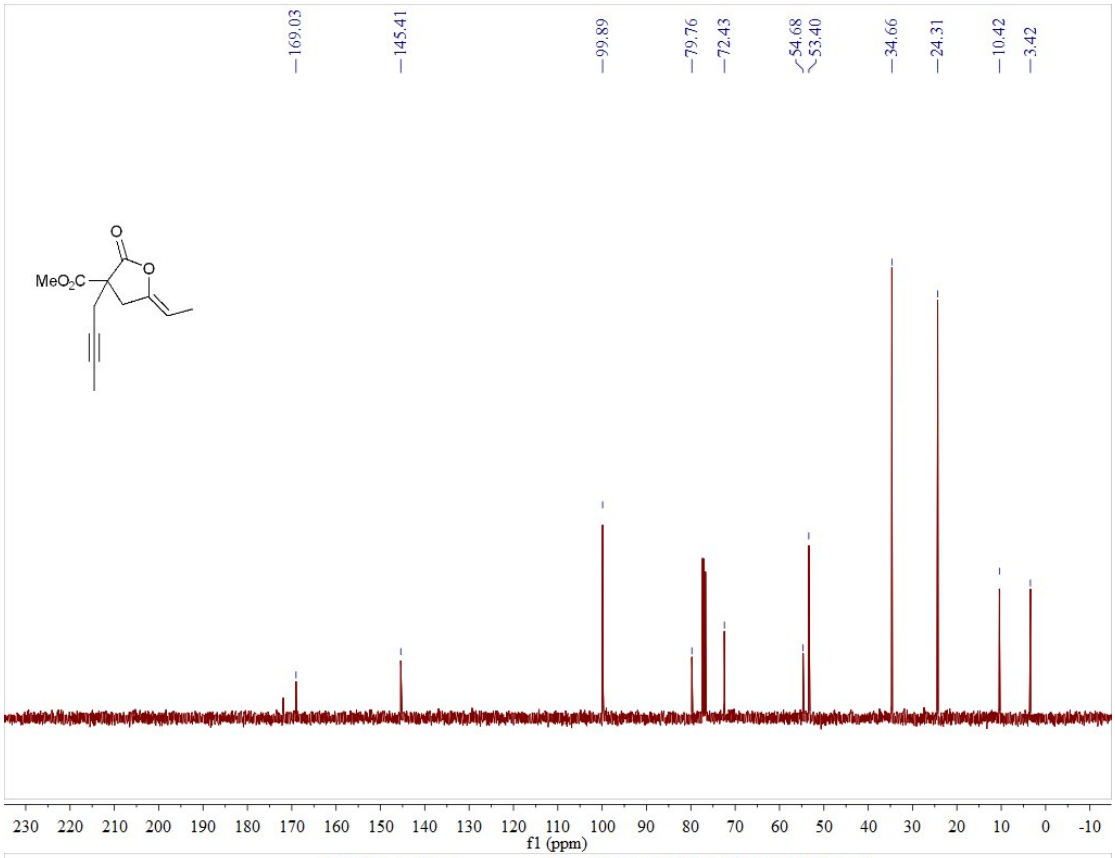

7.93
7.91
7.73
7.72
7.61
7.60
7.59
7.58
7.57
5.25
5.24
5.23
5.23
1.00
2.04
1.04
2.13
f1 (ppm)

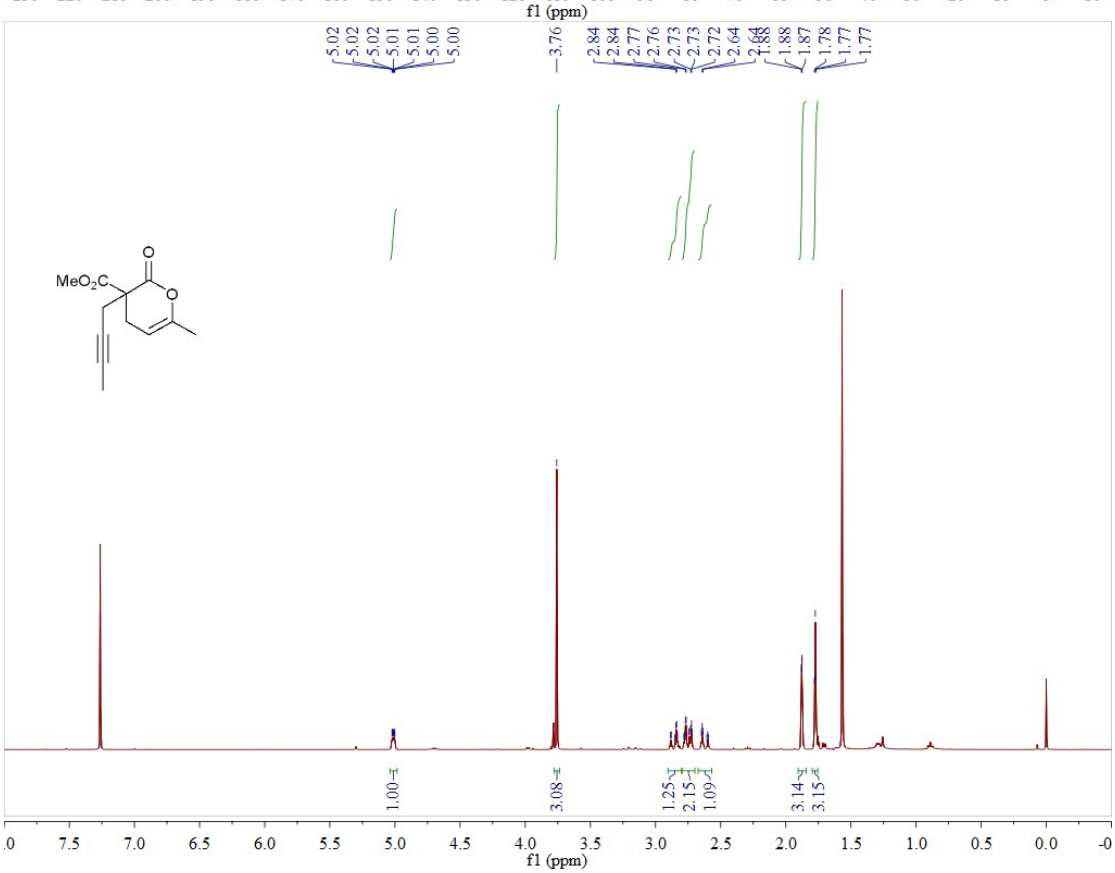

166.89
151.86
139.03
134.48
130.48
125.32
125.15
120.60
91.27
f1 (ppm)
2g-exo
2g-endo
2g-exo
2g-endo
0.05
1.00
2.08
2.07
0.12
0.11
0.18
3.16
f1 (ppm)

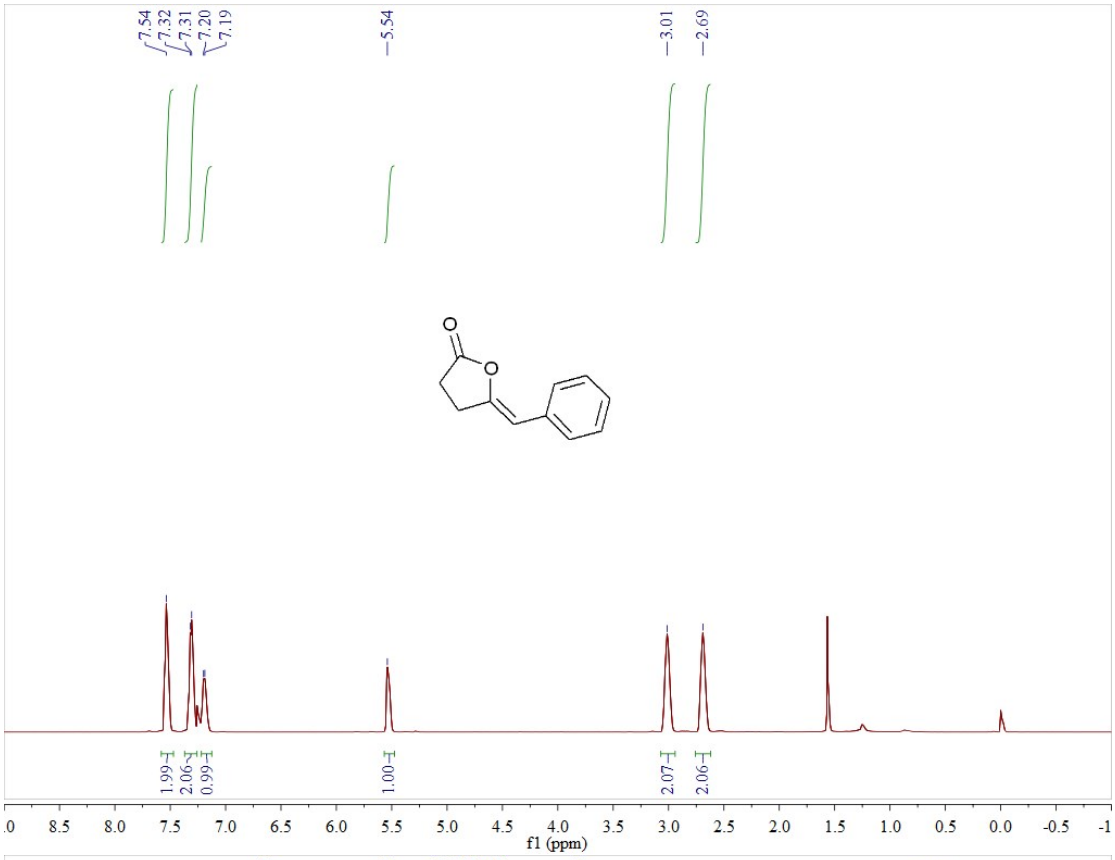

175.33
148.44
99.30
28.14
25.05
10.48
f1 (ppm)

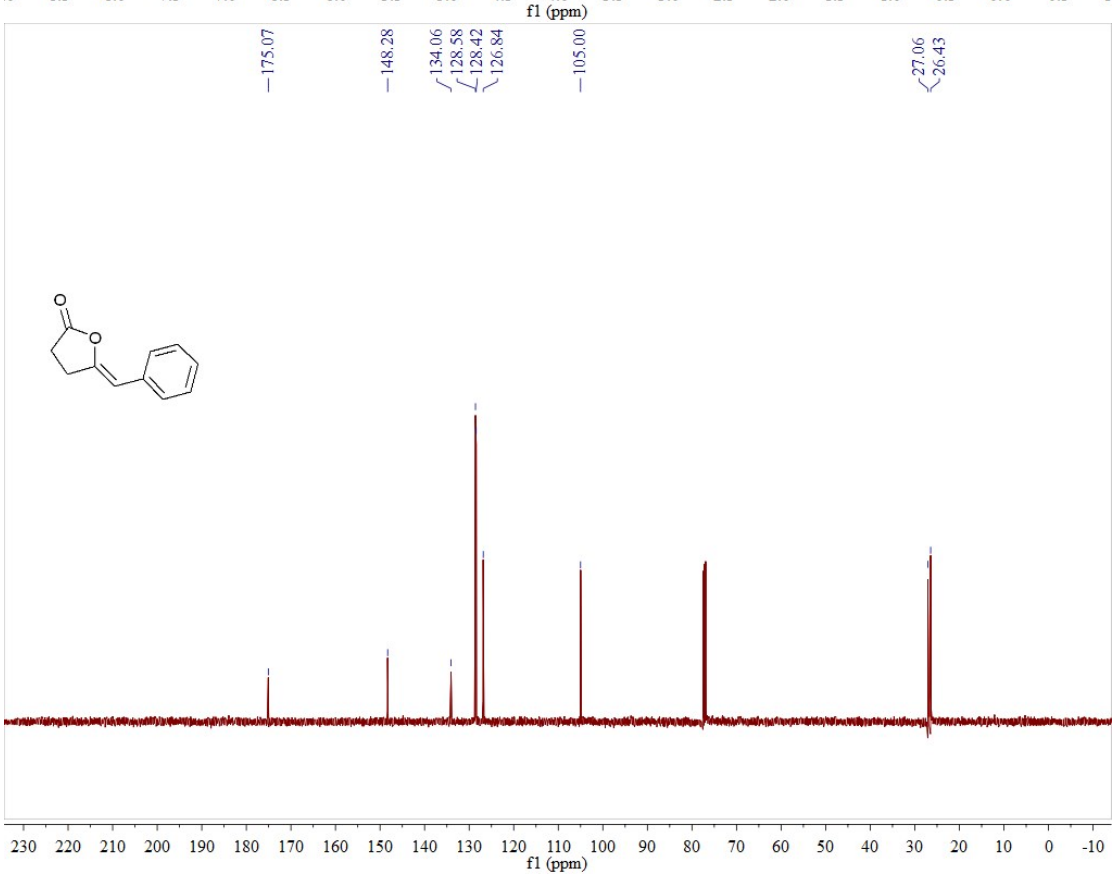

MeO2C
2h-exo
MeO2C
2h-endo
2h-exo
2h-endo
f1 (ppm)

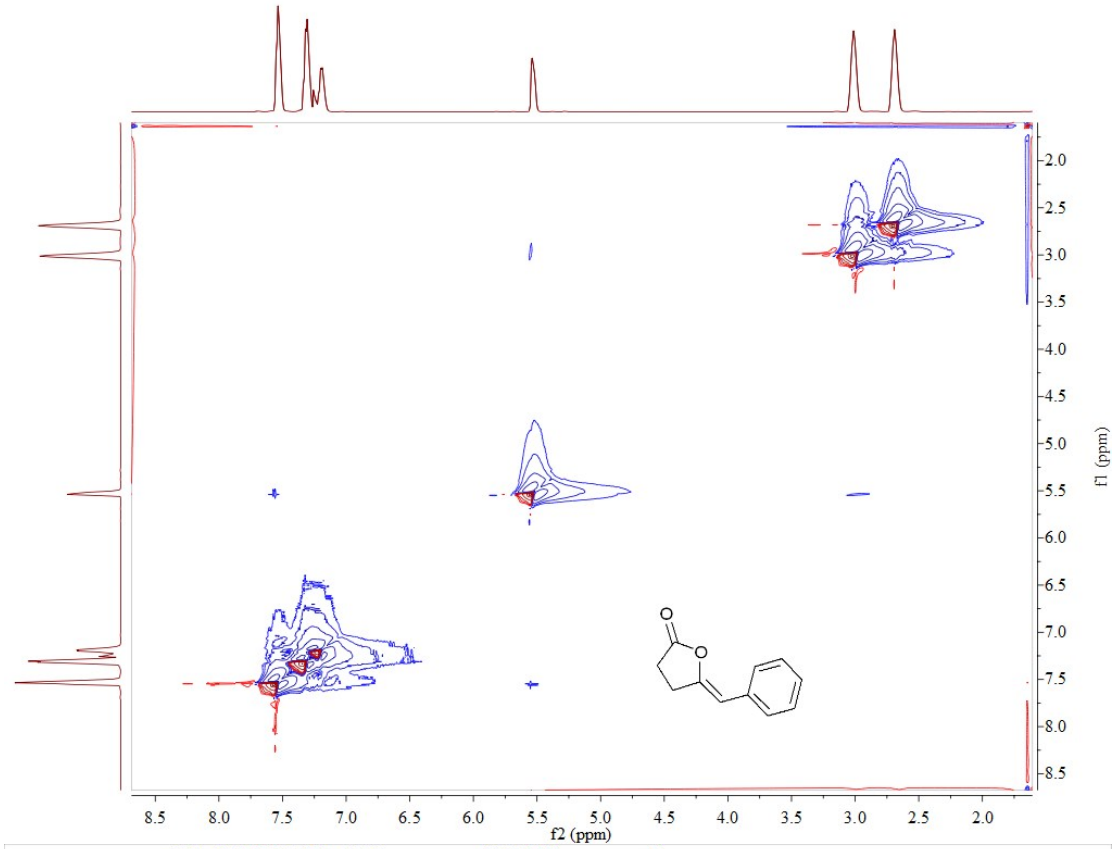

169.76
167.58
145.84
100.38
98.66
53.21
52.87
46.18
45.42
29.22
22.36
18.41
10.40
MeO2C
MeO2C
f1 (ppm)
MeO2C
1.00
3.10
2.13
2.17
3.15
3.12
f1 (ppm)

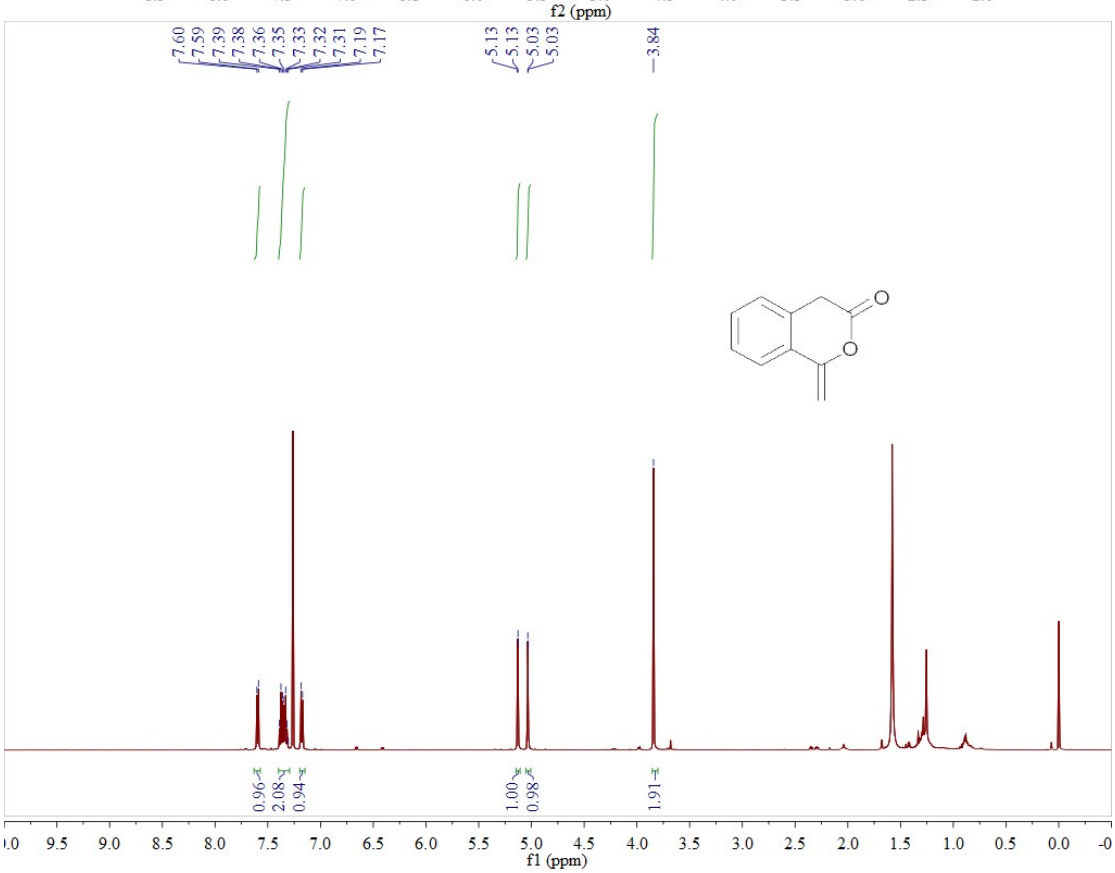

169.03
145.41
99.89
79.76
72.43
54.68
53.40
34.66
24.31
10.42
3.42
MeO2C
f1 (ppm)

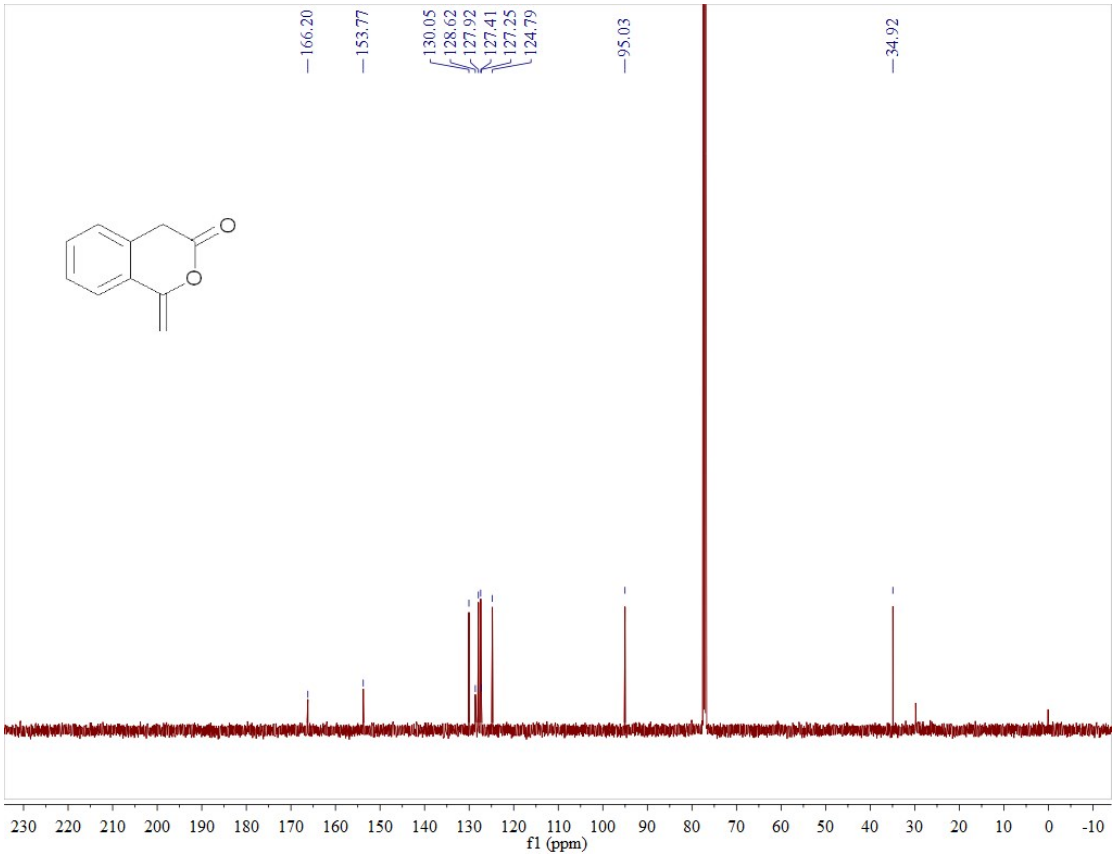

5.02
5.02
5.02
5.01
5.01
5.00
5.00
3.76
2.84
2.84
2.77
2.76
2.73
2.73
2.72
2.64
1.88
1.87
1.78
1.77
1.77
MeO2C
1.00
3.08
1.25
2.15
1.09
3.14
3.15
f1 (ppm)

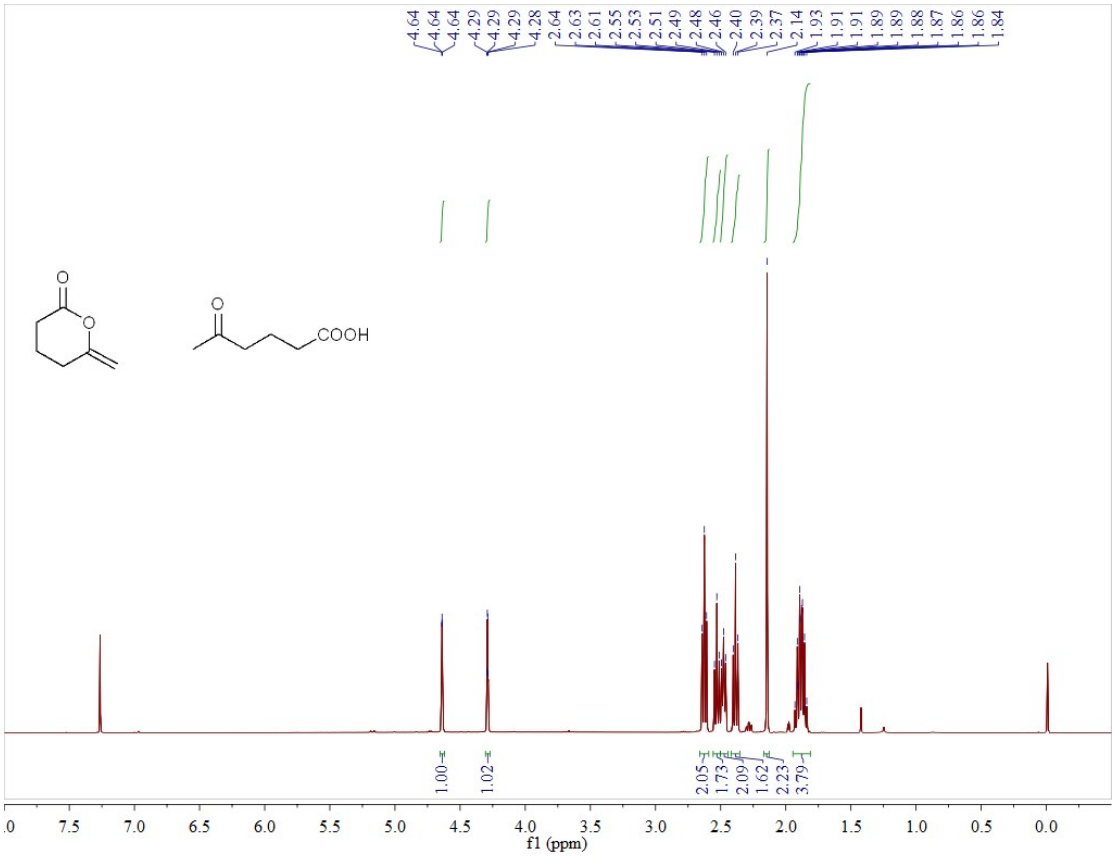

7.54
7.32
7.31
7.20
7.19
5.54
3.01
2.69
1.99
2.06
0.99
1.00
2.07
2.06
f1 (ppm)


175.07
148.28
134.06
128.58
128.42
126.84
105.00
27.06
26.43
f1 (ppm)


f2 (ppm)
f1 (ppm)


7.60
7.59
7.39
7.38
7.36
7.35
7.33
7.32
7.31
7.19
7.17
5.13
5.13
5.03
5.03
3.84
0.96
2.08
0.94
1.00
0.98
1.91
f1 (ppm)


166.20
153.77
130.05
128.62
127.92
127.41
127.25
124.79
95.03
34.92
O
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


4.64
4.64
4.64
4.29
4.29
4.29
4.28
2.64
2.63
2.61
2.55
2.53
2.51
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2.48
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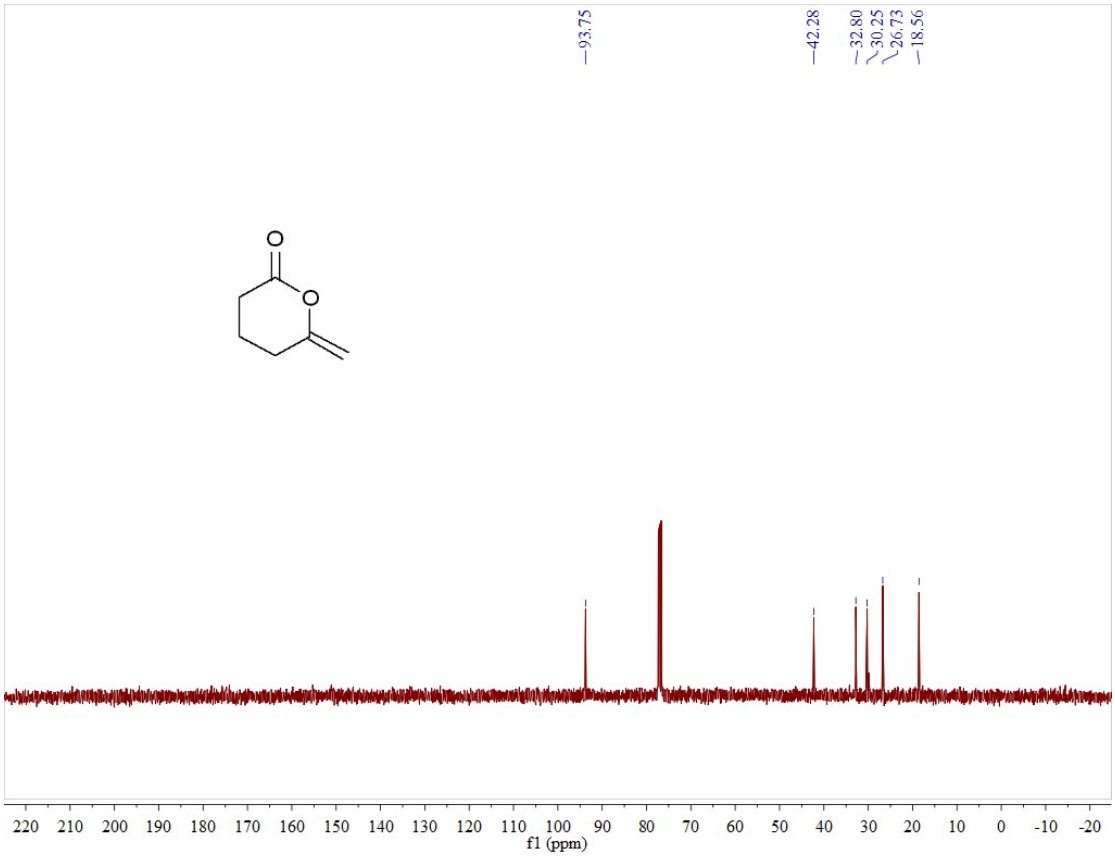
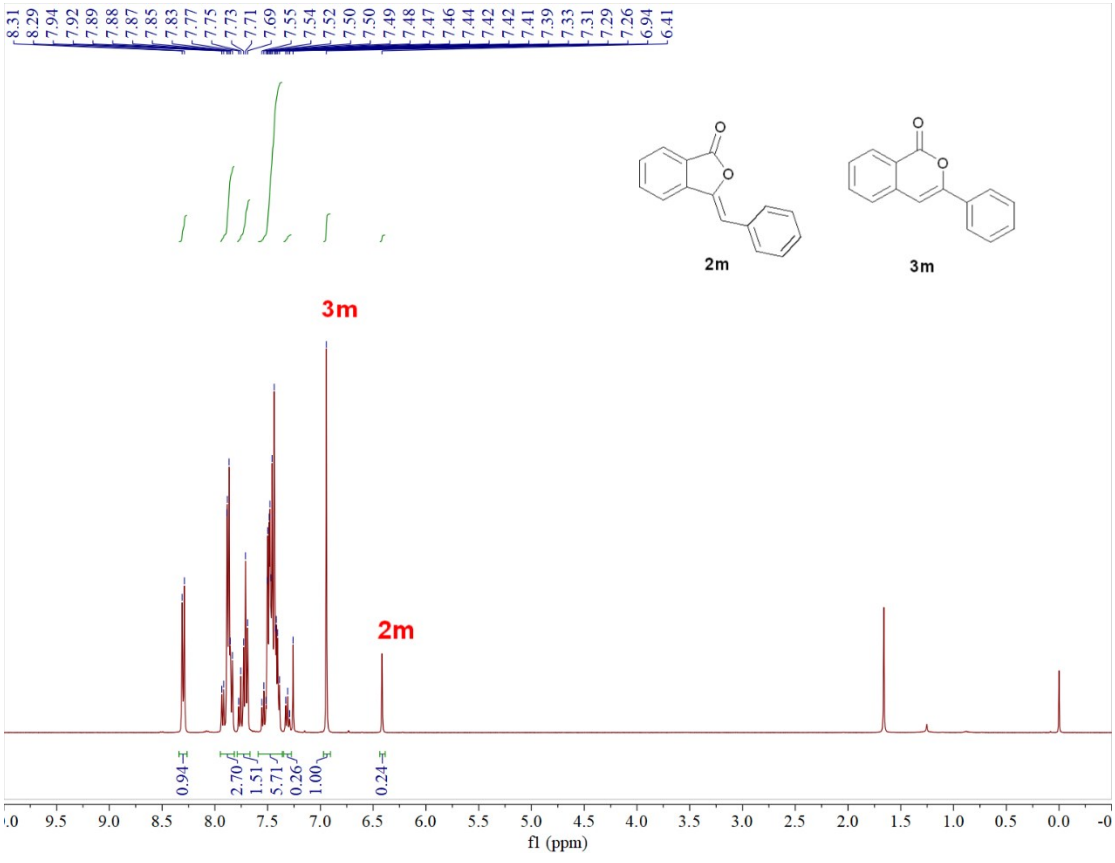
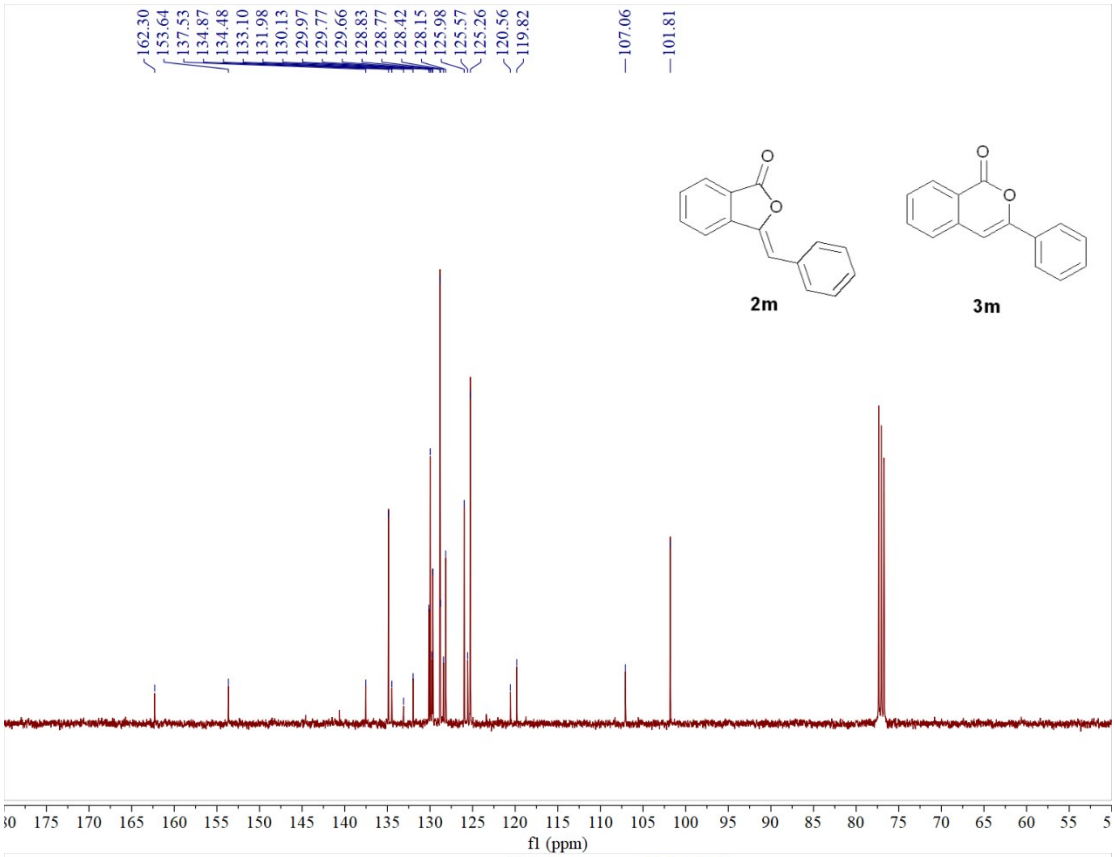
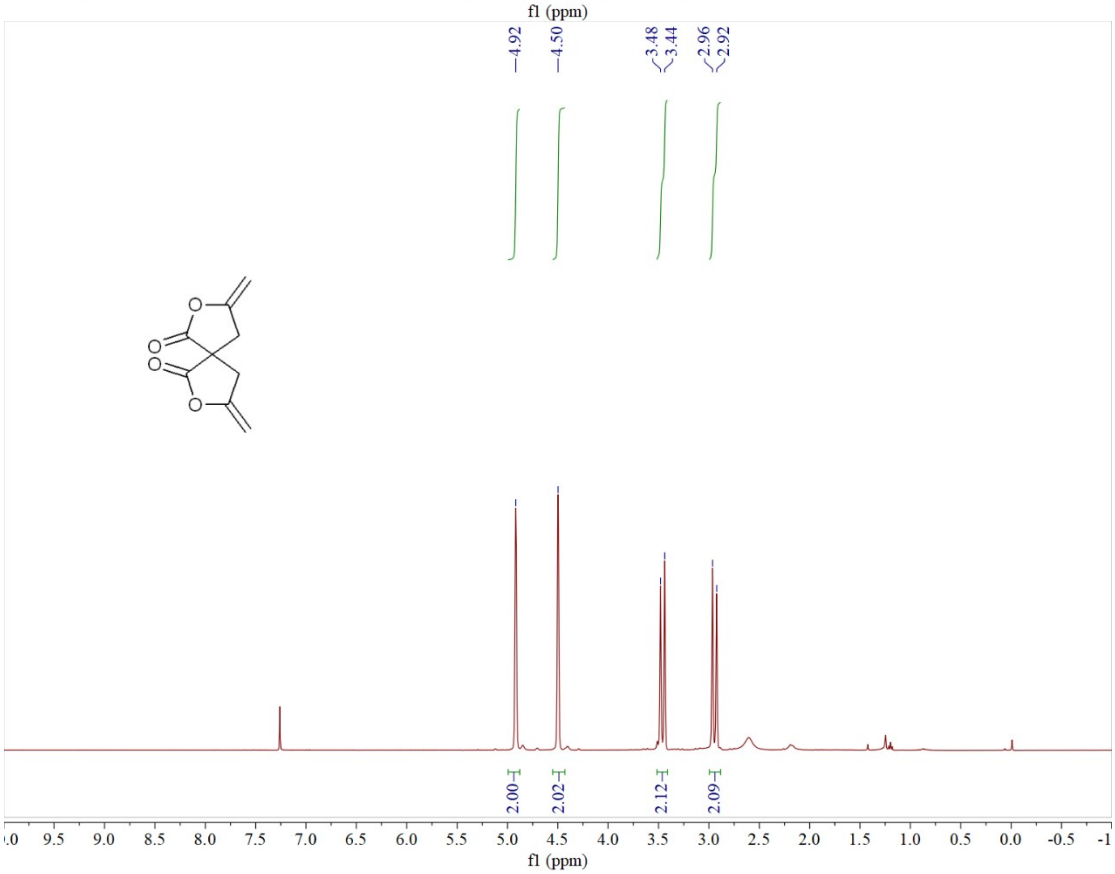
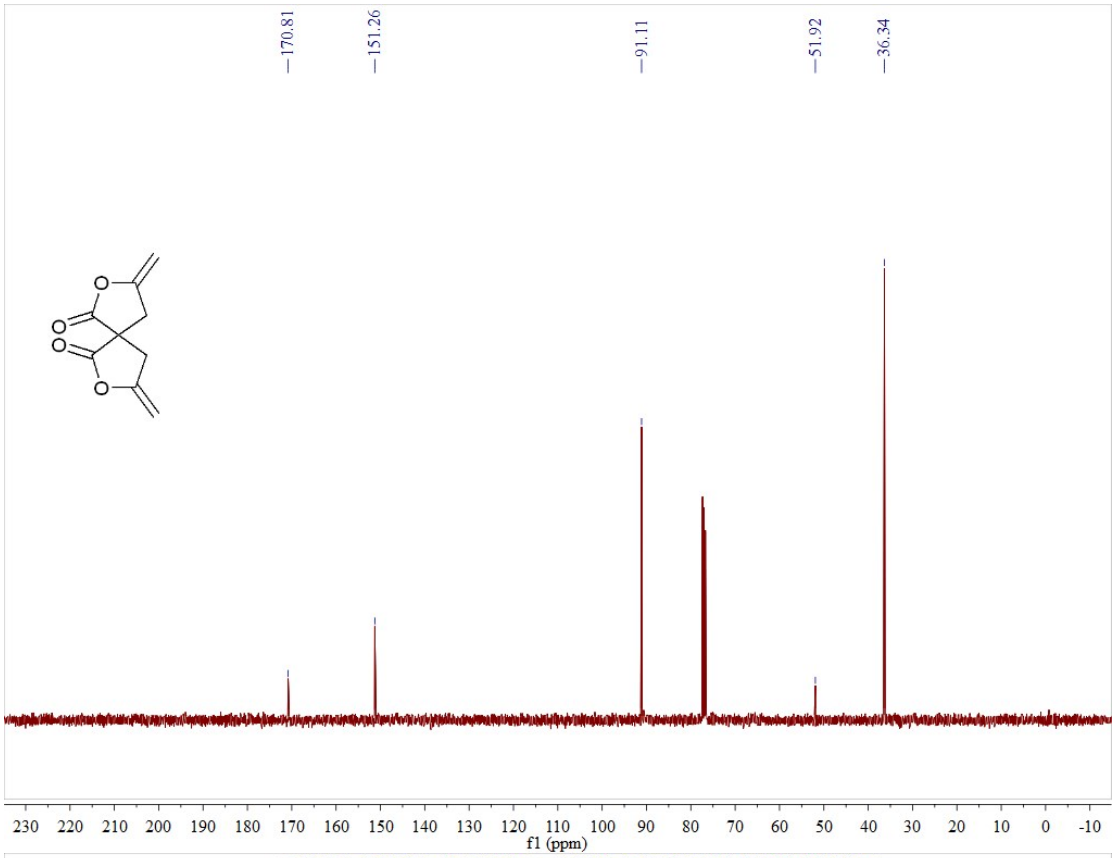
2.40
2.39
2.37
2.14
1.93
1.91
1.91
1.89
1.89
1.88
1.87
1.86
1.86
1.84
O
O
O
COOH
1.00
1.02
2.05
1.73
2.09
1.62
2.23
3.79
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

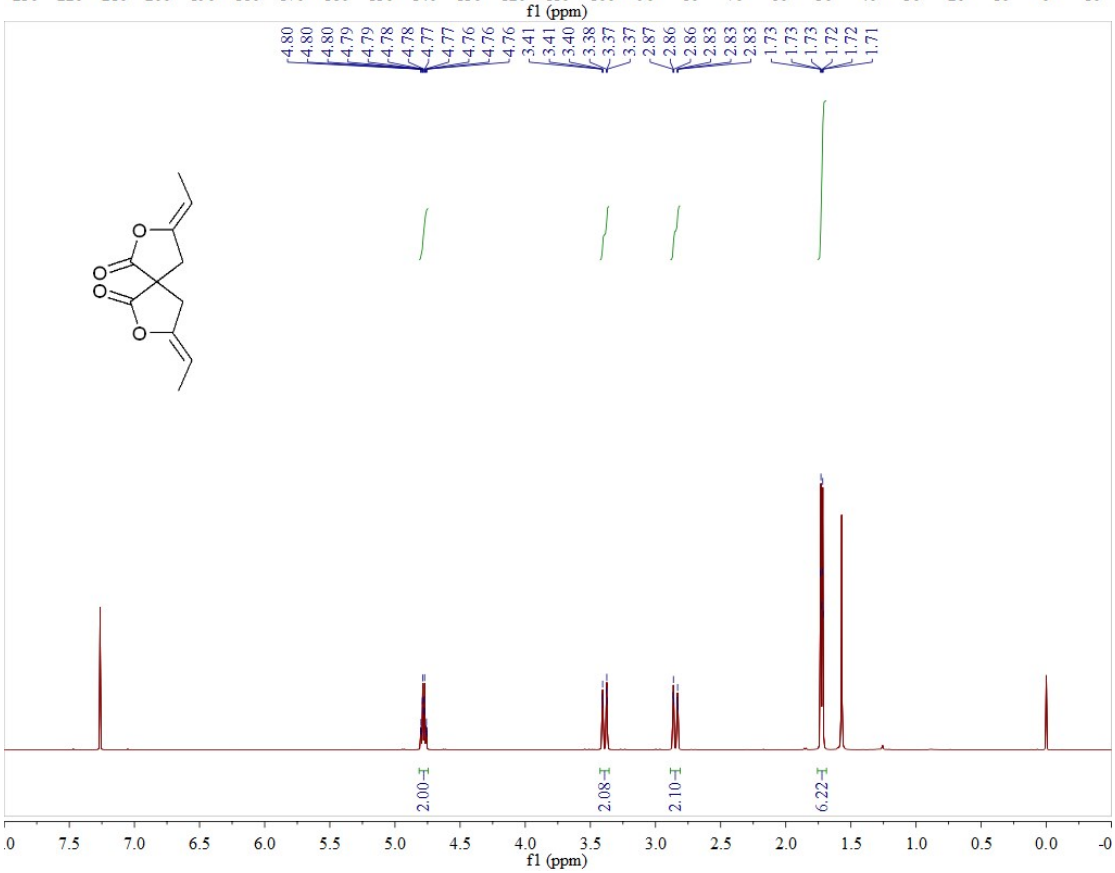

93.75
42.28
32.80
30.25
26.73
18.56
f1 (ppm)

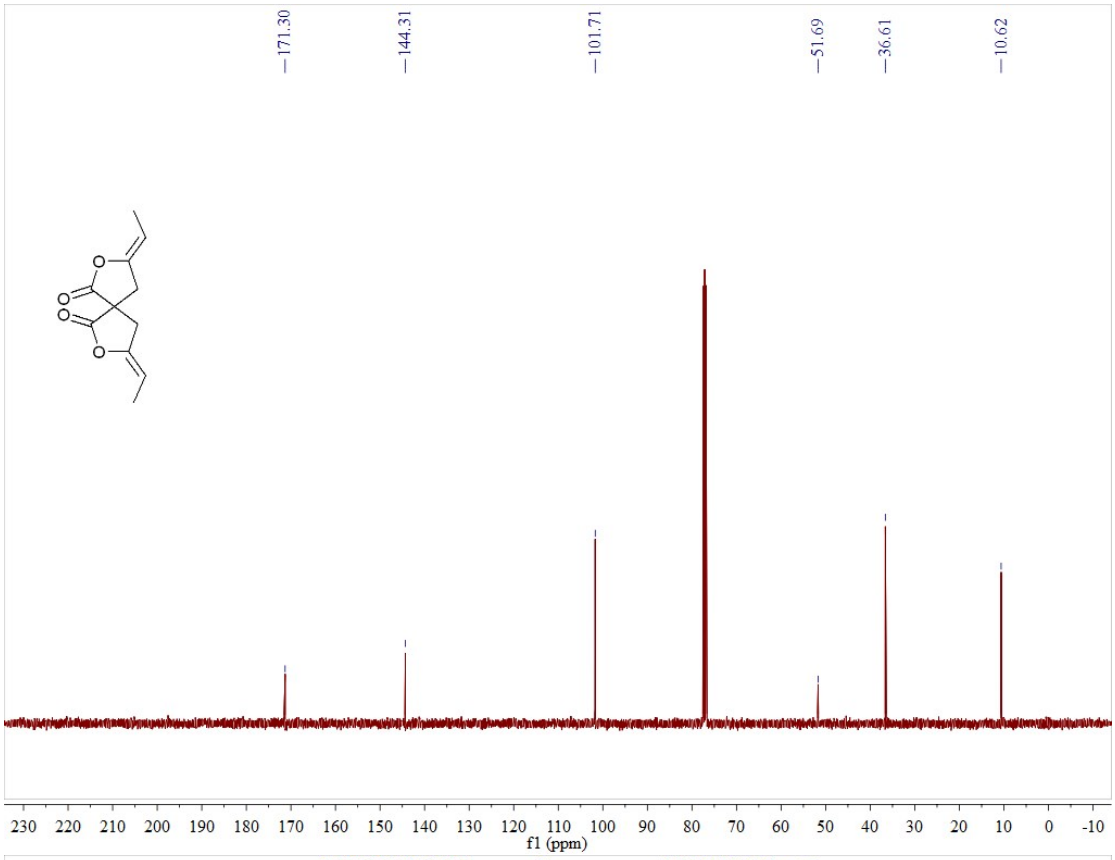

2m
3m
3m
2m
f1 (ppm)

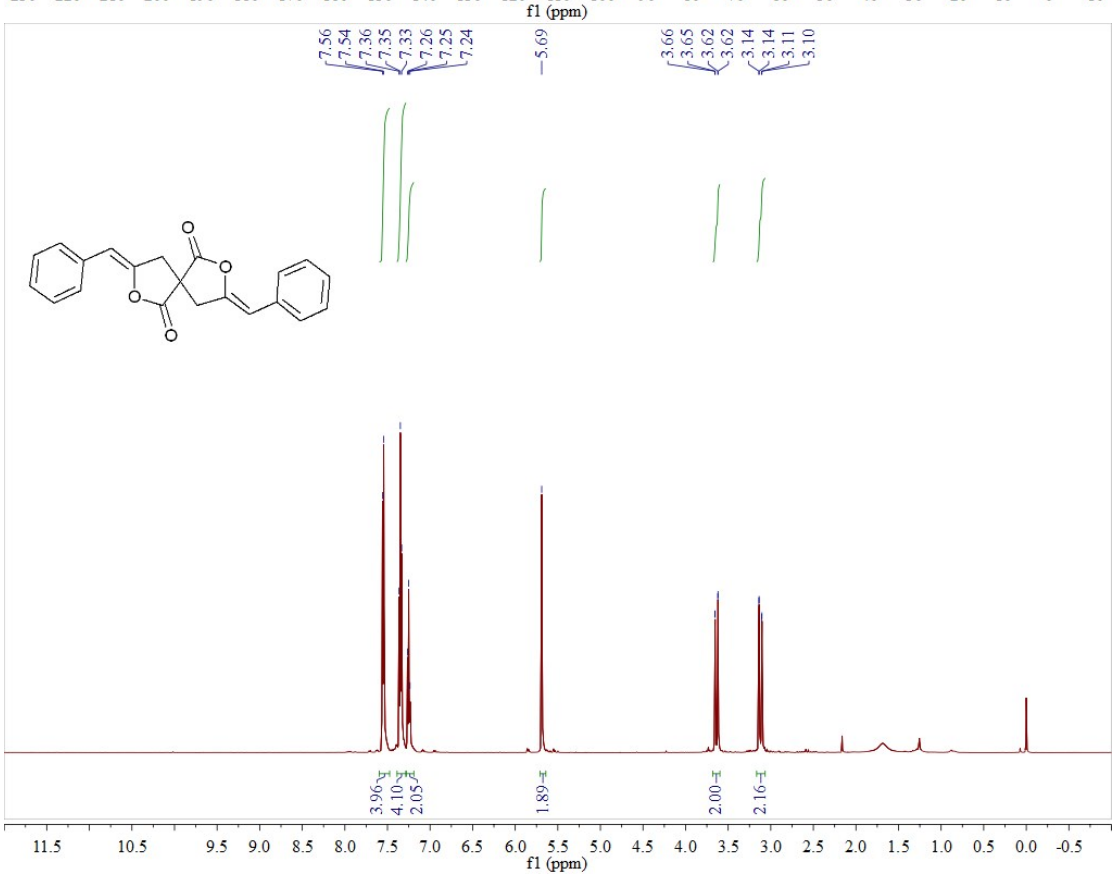

162.30
153.64
137.53
134.87
134.48
133.10
131.98
130.13
129.97
129.77
129.66
128.83
128.77
128.42
128.15
125.98
125.57
125.26
120.56
119.82
107.06
101.81
2m
3m
fl (ppm)


4.92
4.50
3.48
3.44
2.96
2.92
2.00
2.02
2.12
2.09
fl (ppm)


170.81
151.26
91.11
51.92
36.34
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


4.80 4.80 4.80 4.79 4.79 4.78 4.78 4.77 4.77 4.76 4.76 4.76
3.41 3.41 3.40 3.38 3.37 3.37
2.87 2.86 2.86 2.83 2.83 2.83
1.73 1.73 1.73 1.72 1.72 1.71
2.00 2.08 2.10 6.22
.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 -0
f1 (ppm)


171.30
144.31
101.71
51.69
36.61
10.62
f1 (ppm)


7.56
7.54
7.36
7.35
7.33
7.26
7.25
7.24
5.69
3.66
3.65
3.62
3.62
3.14
3.14
3.11
3.10
3.96
4.10
2.05
1.89
2.00
2.16
f1 (ppm)

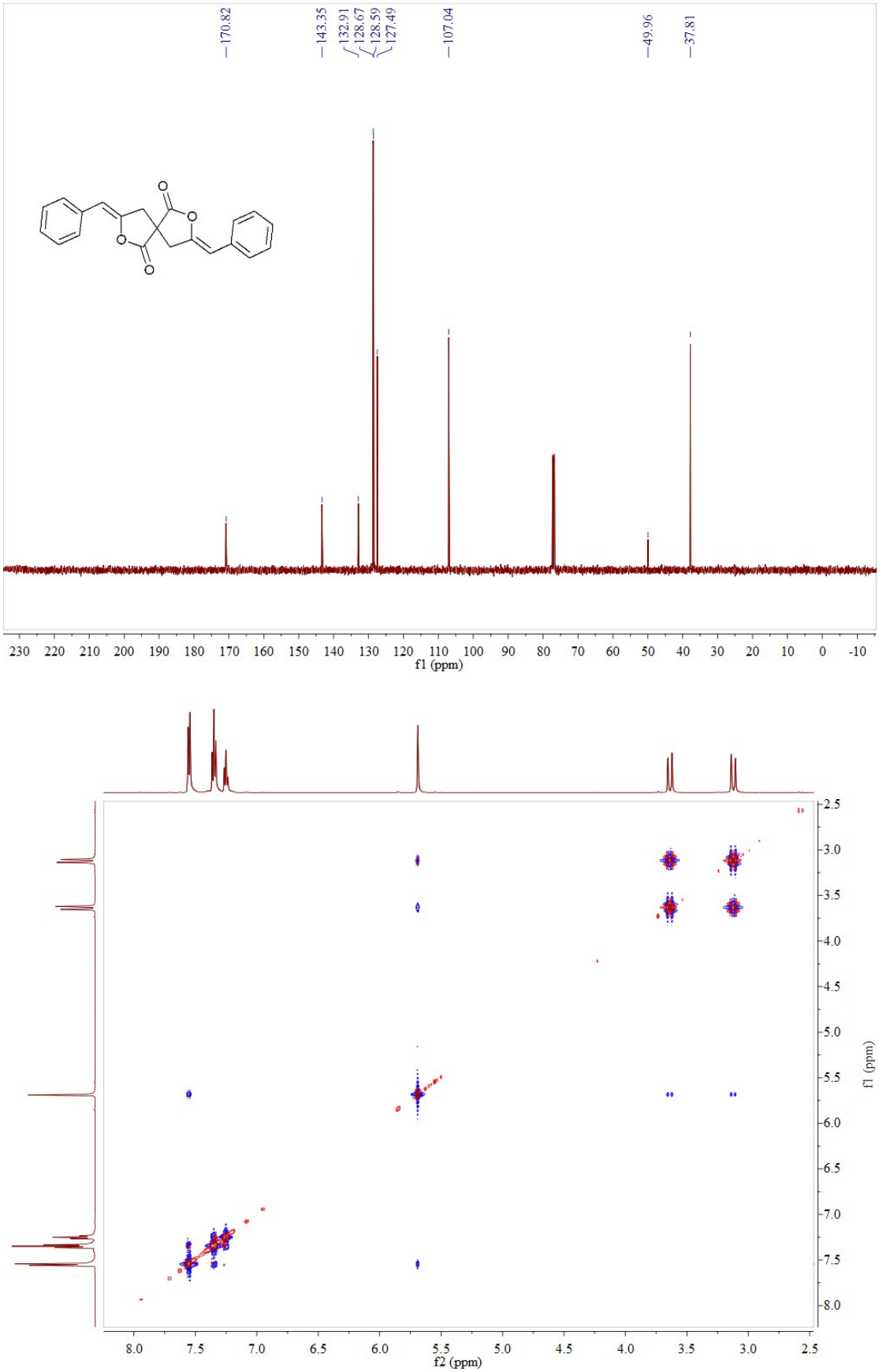


Fig. S17 H-H Noesy experiment of **2p**

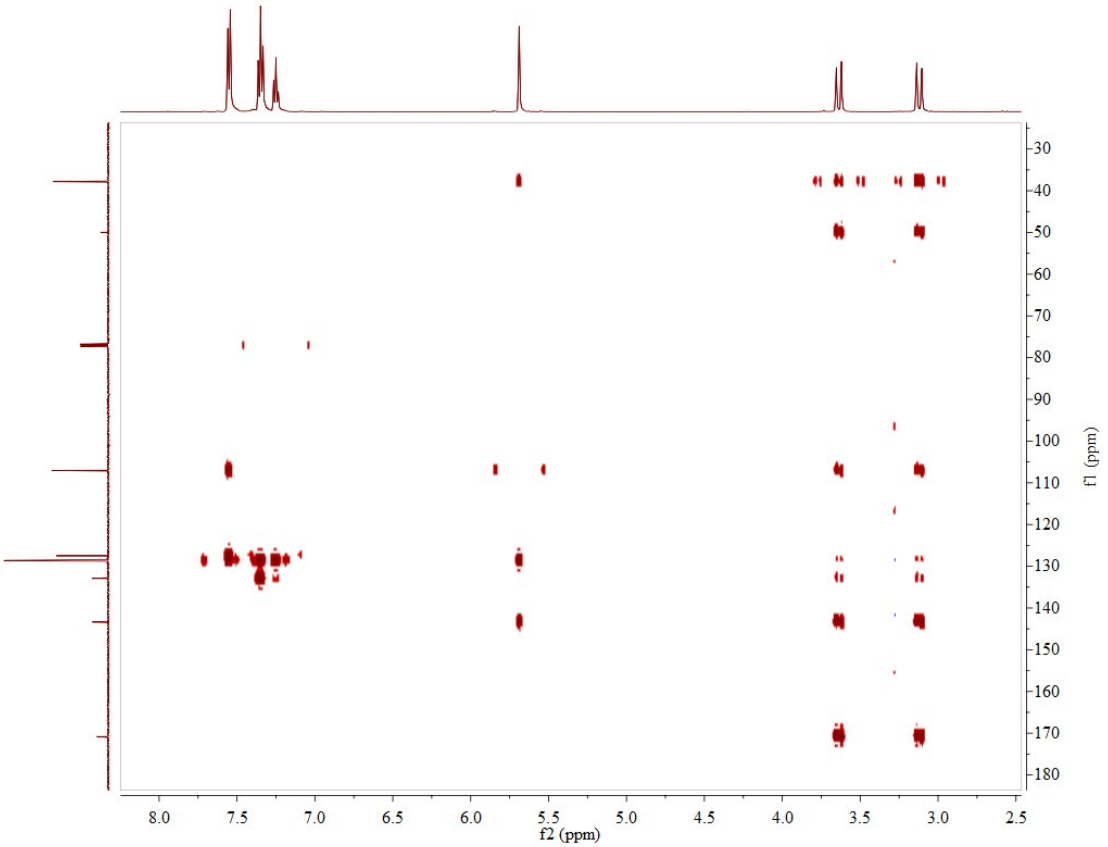
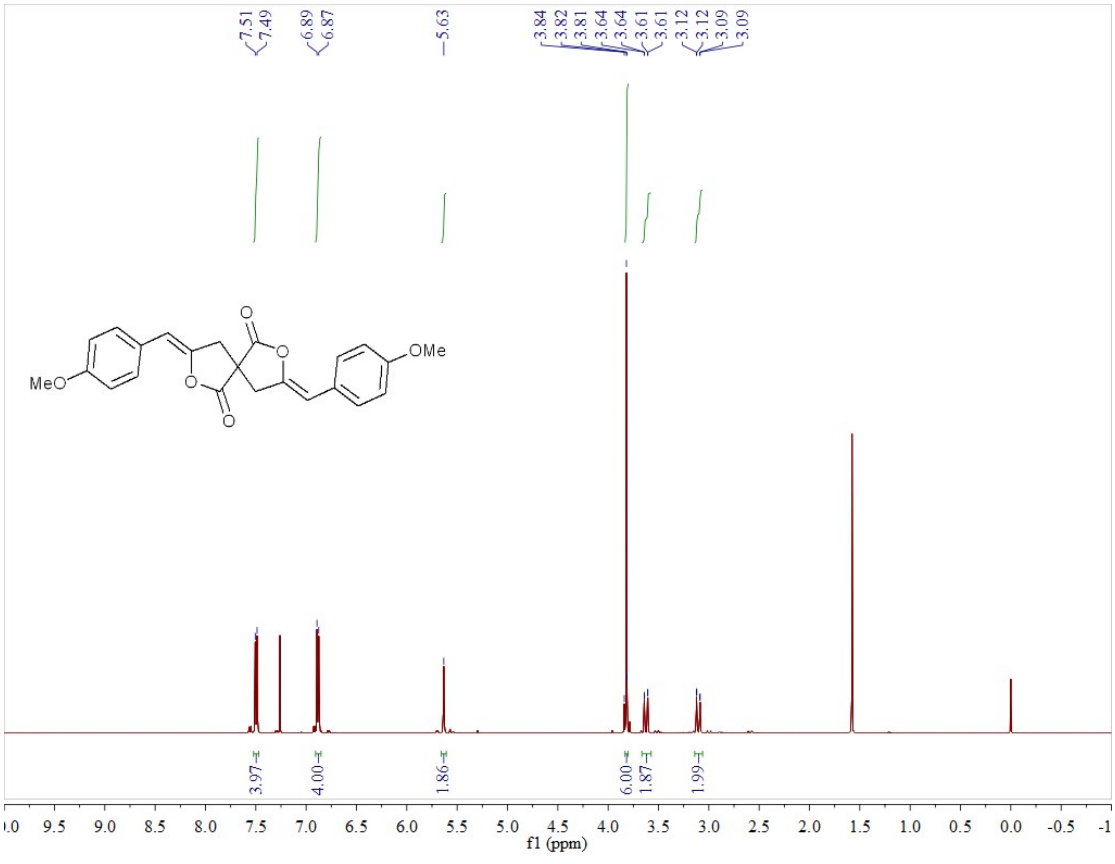
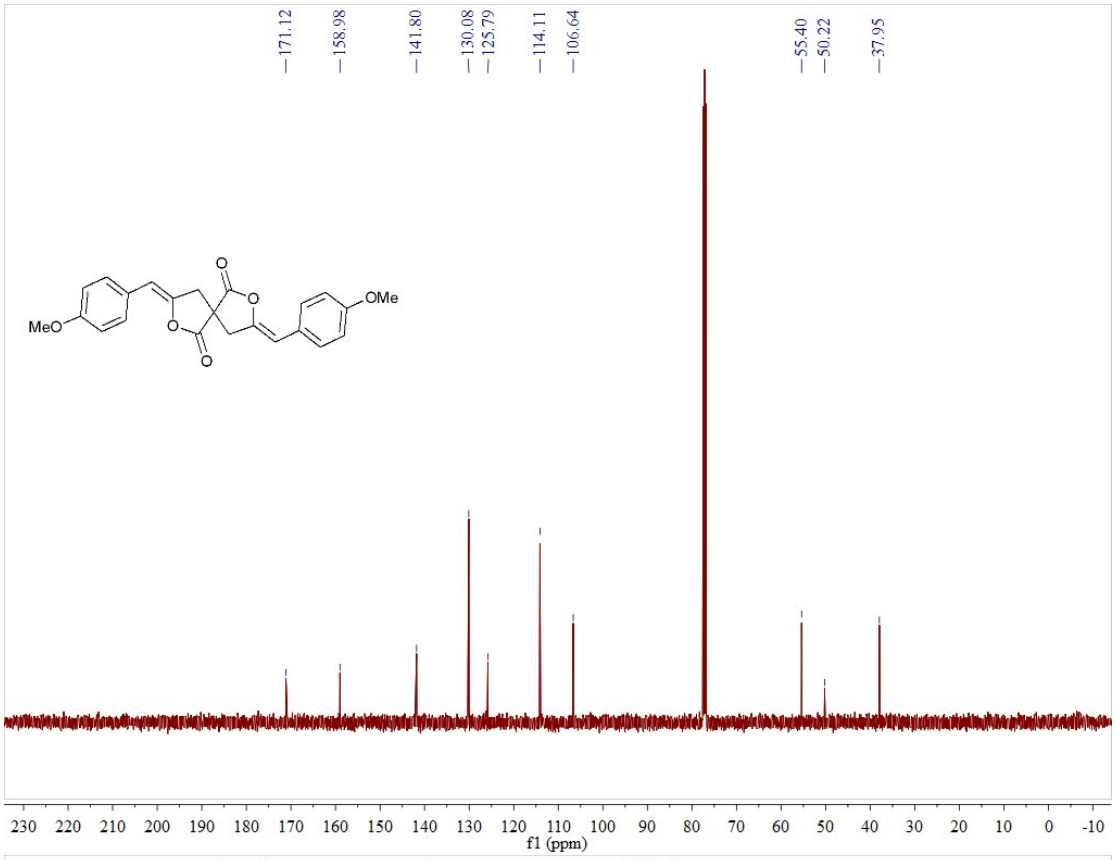
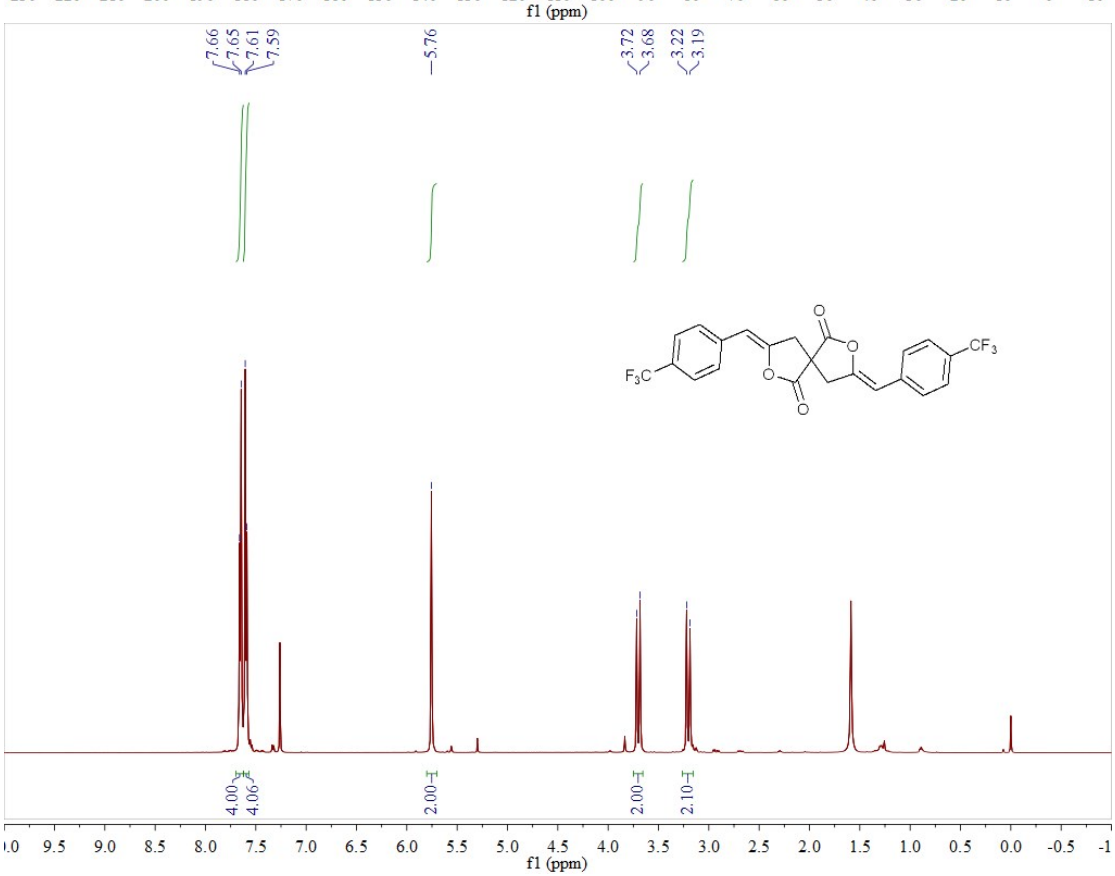
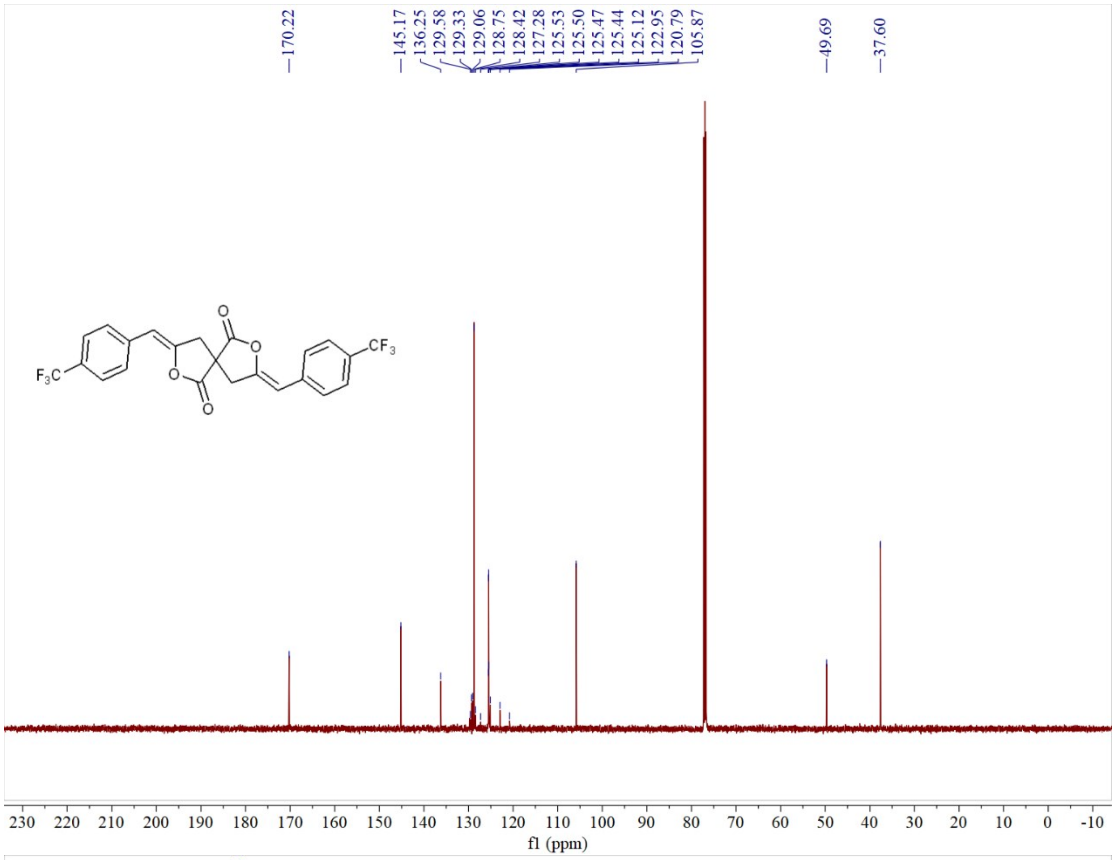


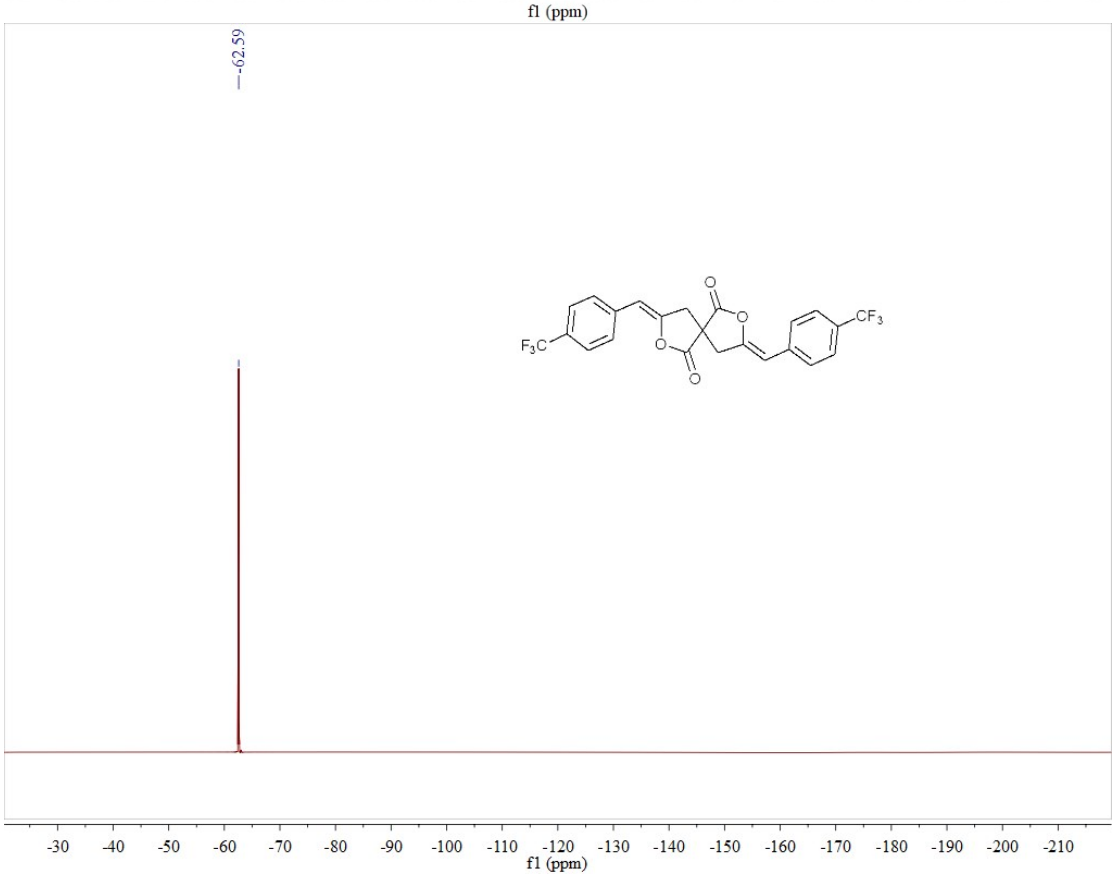
Fig. S18 H-C HMBC experiment of **2p**

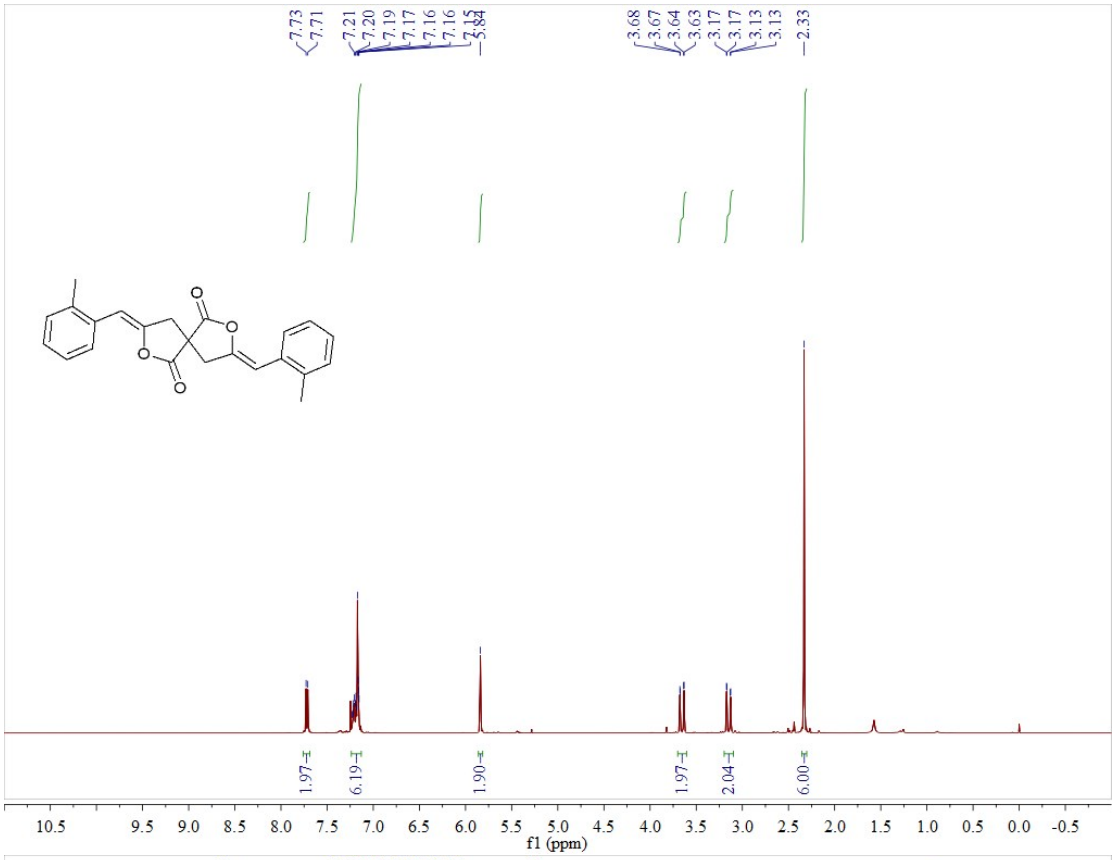


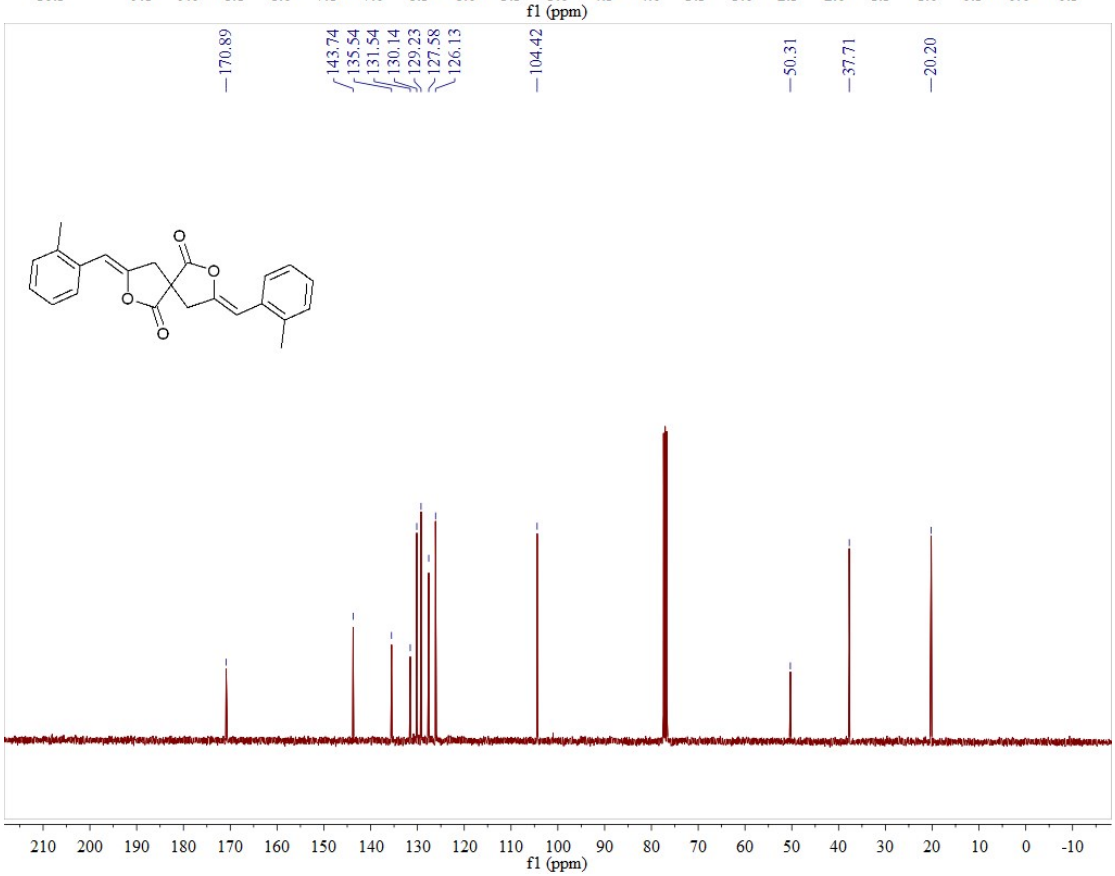

171.12
158.98
141.80
130.08
125.79
114.11
106.64
55.40
50.22
37.95
MeO
OMe
O
O
O
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.66
7.65
7.61
7.59
5.76
3.72
3.68
3.22
3.19
F3C
CF3
O
O
O
O
4.00
4.06
2.00
2.00
2.10
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 -0.5 -1
f1 (ppm)


170.22
145.17
136.25
129.58
129.33
129.06
128.75
128.42
127.28
125.53
125.50
125.47
125.44
125.12
122.95
120.79
105.87
49.69
37.60
F3C
CF3
O
O
O
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-62.59
F3C
CF3
O
O
O
O
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


7.73
7.71
7.21
7.20
7.19
7.17
7.16
7.16
7.15
7.14
5.84
3.68
3.67
3.64
3.63
3.17
3.17
3.13
3.13
2.33
1.97
6.19
1.90
1.97
2.04
6.00
f1 (ppm)


170.89
143.74
135.54
131.54
130.14
129.23
127.58
126.13
104.42
50.31
37.71
20.20
f1 (ppm)

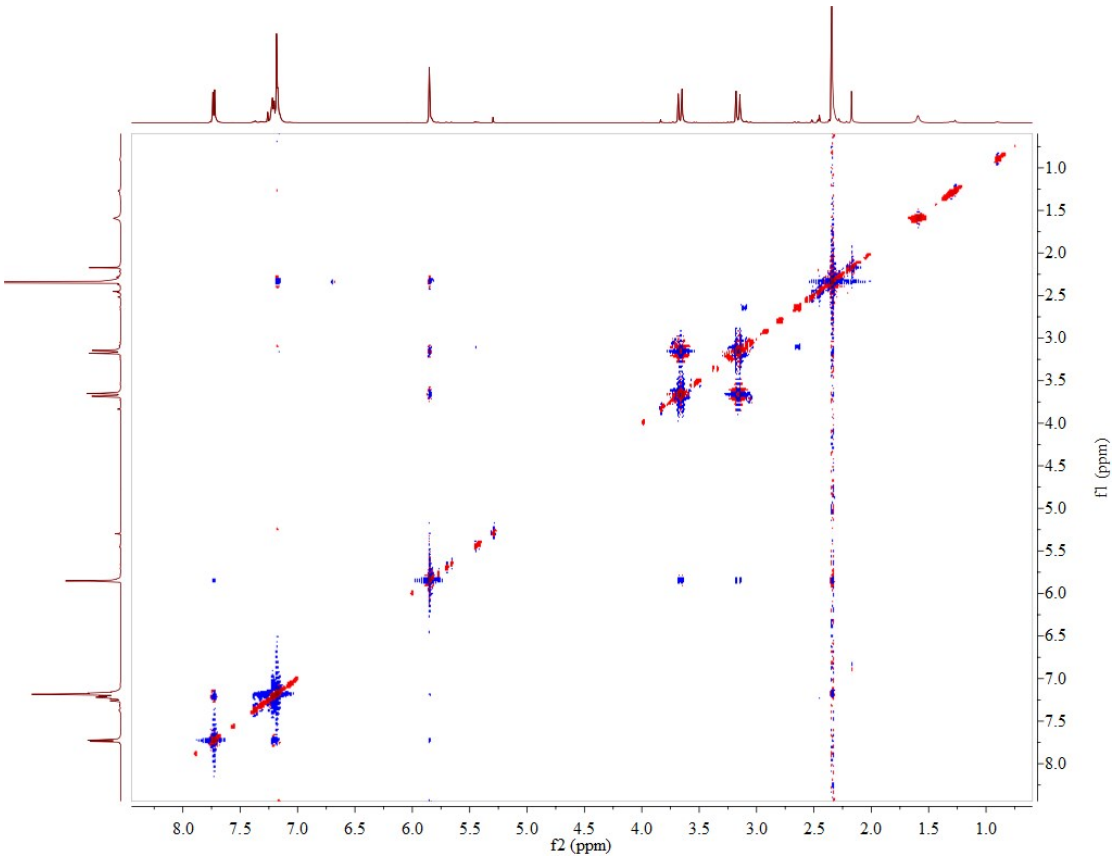


Fig. S19 H-H Noesy experiment of **2s**

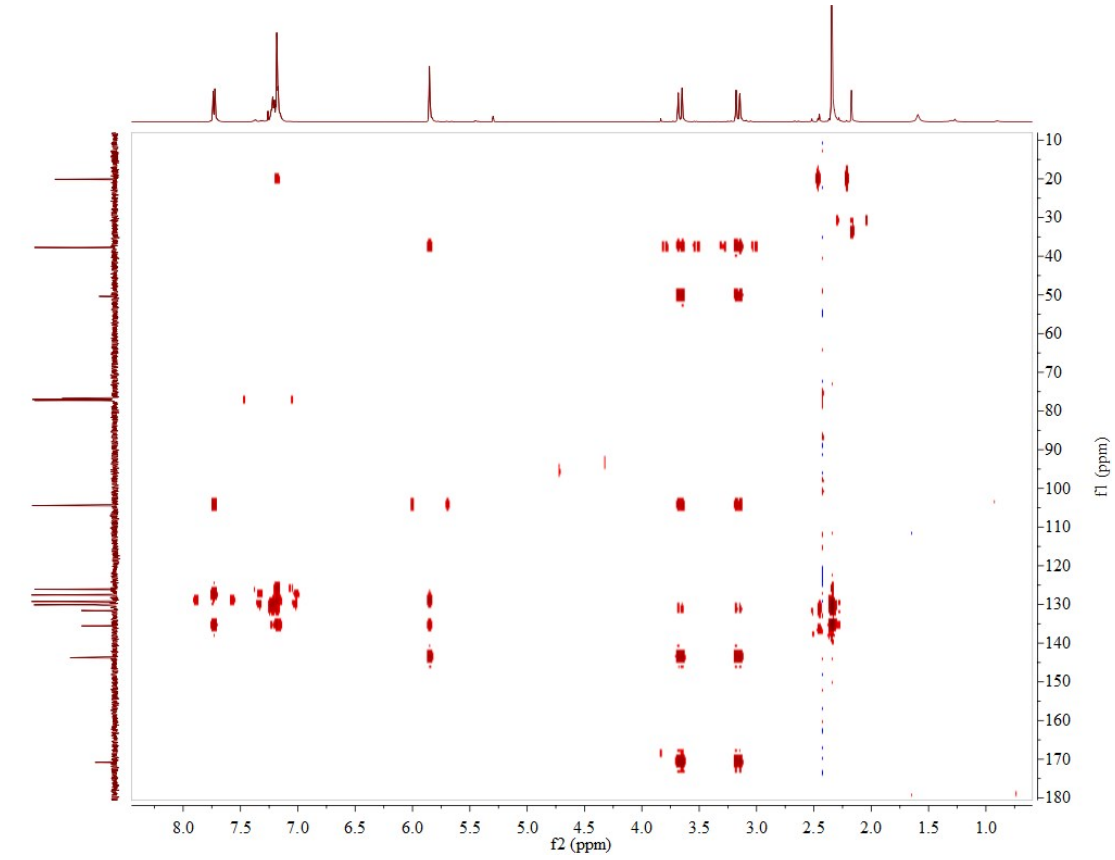
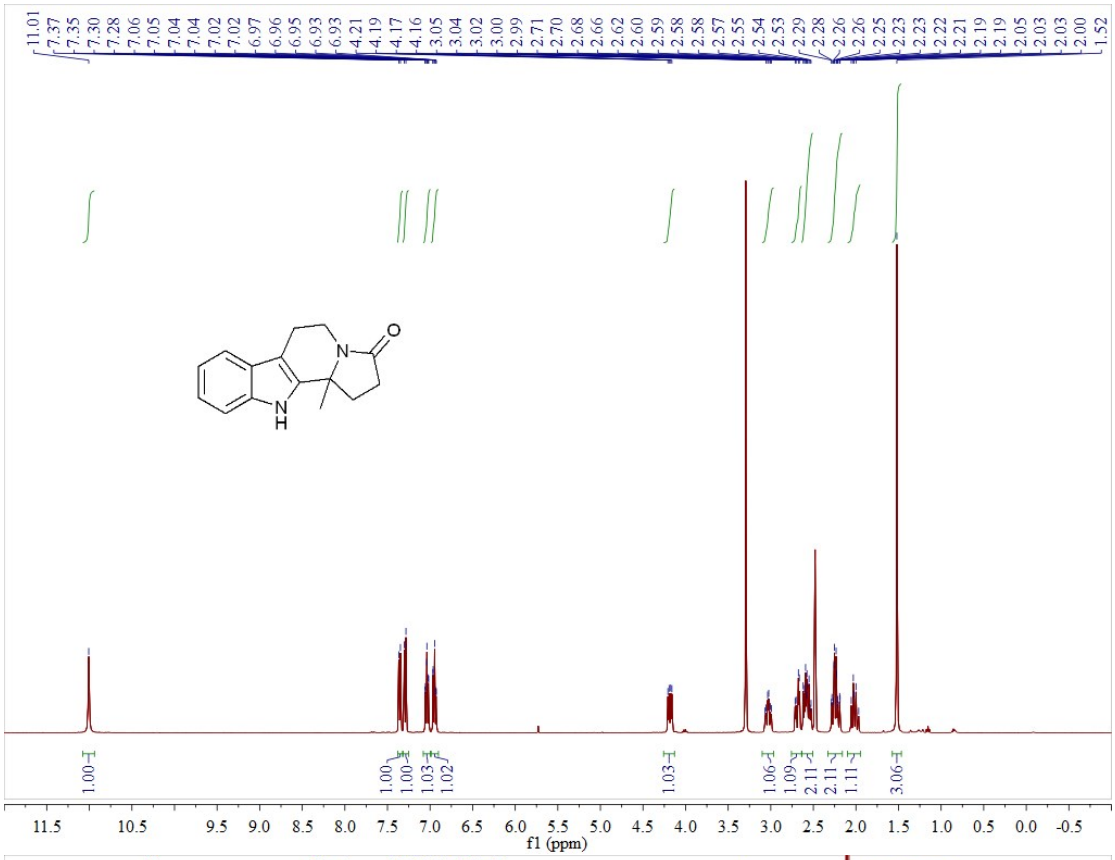
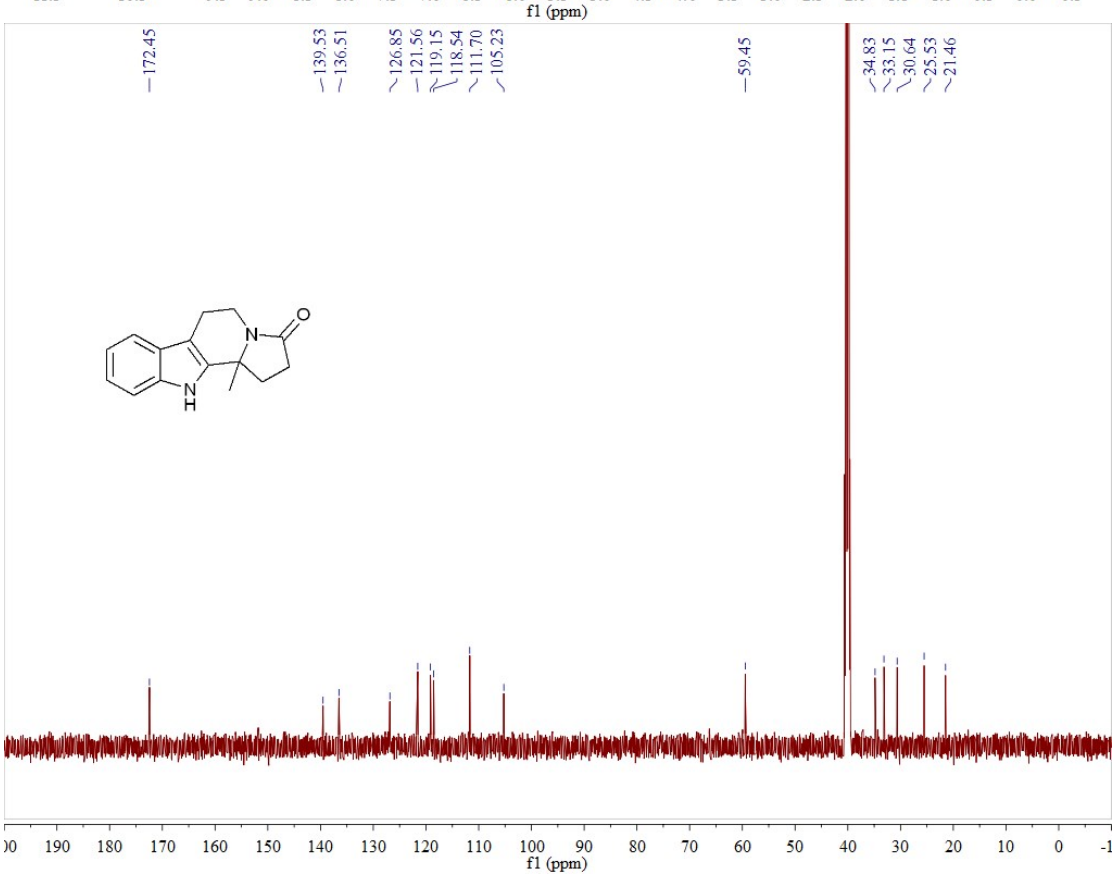
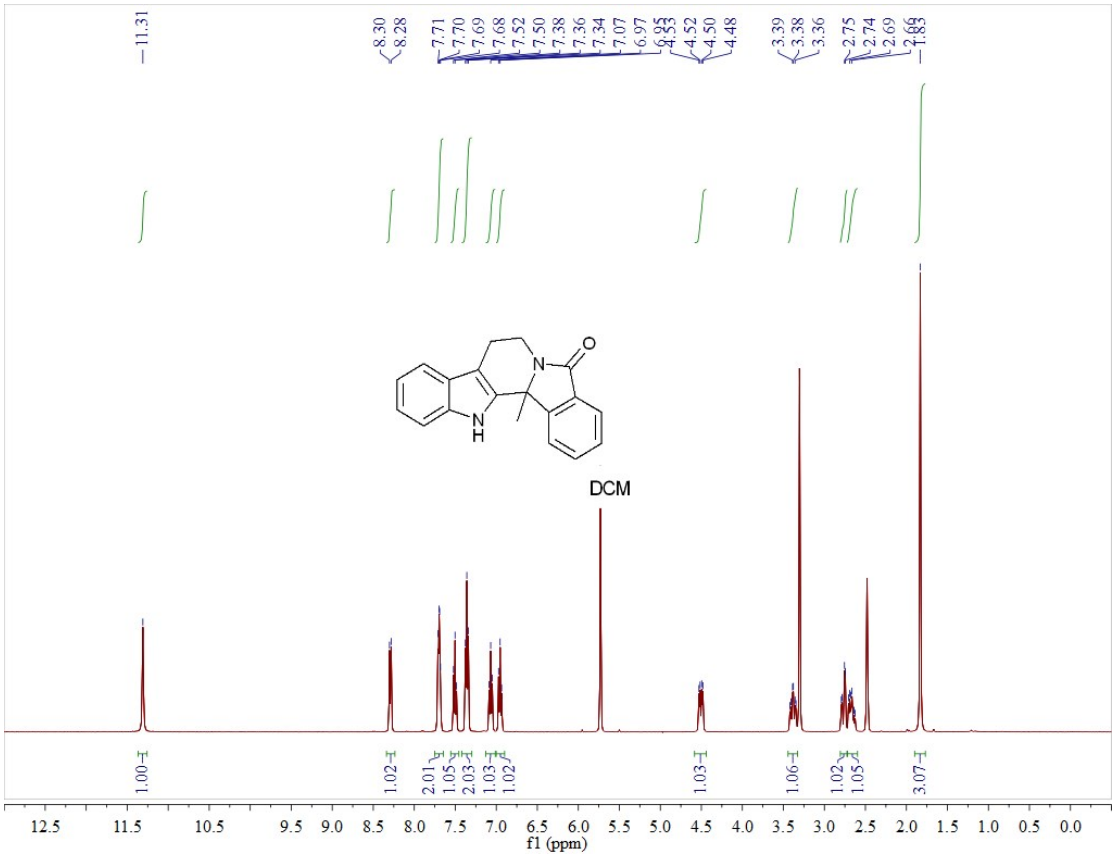
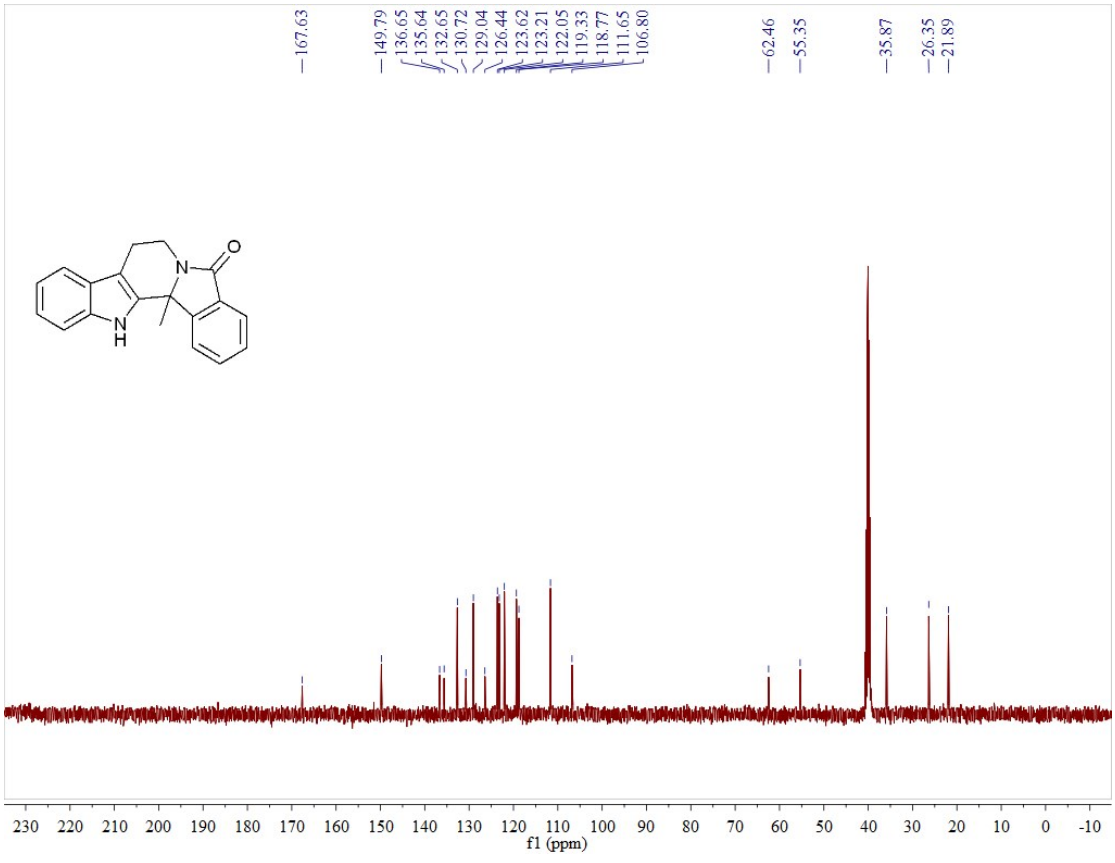


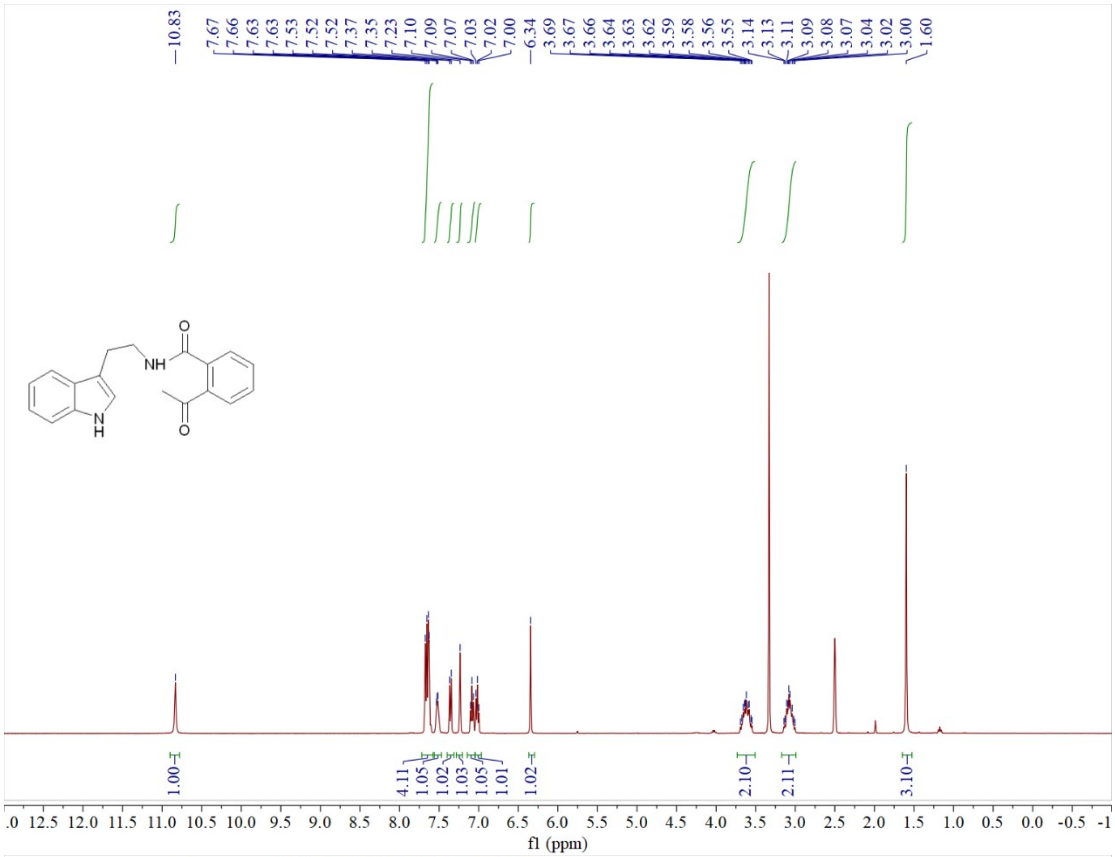
Fig. S20 H-C HMBC experiment of **2s**

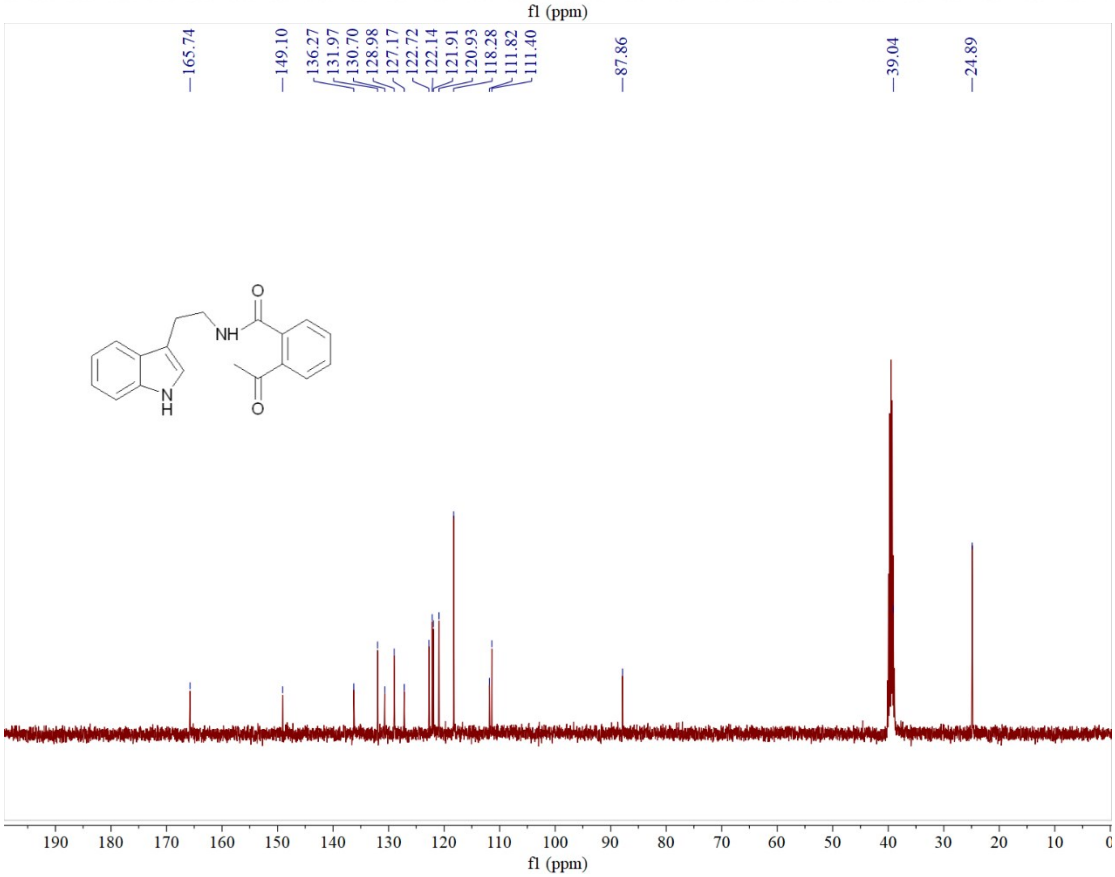

11.01
7.37
7.35
7.30
7.28
7.06
7.05
7.04
7.04
7.02
7.02
6.97
6.96
6.95
6.93
6.93
4.21
4.19
4.17
4.16
3.05
3.04
3.02
3.00
2.99
2.71
2.70
2.68
2.66
2.62
2.60
2.59
2.58
2.58
2.57
2.55
2.54
2.53
2.29
2.28
2.26
2.26
2.25
2.23
2.23
2.22
2.21
2.19
2.19
2.05
2.03
2.03
2.00
1.52
1.00
1.00
1.00
1.03
1.02
1.03
1.06
1.09
2.11
2.11
1.11
3.06
O
N
H
11.5
10.5
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
-0.5
f1 (ppm)


172.45
139.53
136.51
126.85
121.56
119.15
118.54
111.70
105.23
59.45
34.83
33.15
30.64
25.53
21.46
O
N
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


11.31
8.30
8.28
7.71
7.70
7.69
7.68
7.52
7.50
7.38
7.36
7.34
7.07
6.97
4.52
4.50
4.48
3.39
3.38
3.36
2.75
2.74
2.69
1.83
DCM
1.00
1.02
2.01
1.05
2.03
1.03
1.02
1.03
1.06
1.02
1.05
3.07
f1 (ppm)


167.63
149.79
136.65
135.64
132.65
130.72
129.04
126.44
123.62
123.21
122.05
119.33
118.77
111.65
106.80
62.46
55.35
35.87
26.35
21.89
f1 (ppm)


10.83
7.67
7.66
7.63
7.63
7.53
7.52
7.52
7.37
7.35
7.23
7.10
7.09
7.07
7.03
7.02
7.00
6.34
3.69
3.67
3.66
3.64
3.63
3.62
3.59
3.58
3.56
3.55
3.14
3.13
3.11
3.09
3.08
3.07
3.04
3.02
3.00
1.60
NH
O
O
N
H
1.00
4.11
1.05
1.02
1.03
1.05
1.01
1.02
2.10
2.11
3.10
fl (ppm)


165.74
149.10
136.27
131.97
130.70
128.98
127.17
122.72
122.14
121.91
120.93
118.28
111.82
111.40
87.86
39.04
24.89
NH
O
O
N
H
fl (ppm)