Difunctionalization of alkenes proceeding with radical 1,2-alkynyl migration in batch and continuous-flow modes

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Context

1. General Information

Commercially available reagents and solvents were of reagent grade quality without any further purification. Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates (HSGF 254) and visualized using a UV lamp (254 nm). Flash column chromatography was performed using silicycle silica gel (200-300 mesh). 1H NMR and 13C NMR were recorded on magnet system 400’54 ascend purchased from Bruker Biospin AG. ESI-MS spectra were recorded on Agilent Q-TOF 6520.

Electrosynthesis of α-alkynyl ketones was carried out in an undivided cell equipped with a carbon cloth anode and a platinum plate cathode under the open air. The carbon cloth, graphite rod (⌀ 6 mm) and platinum plate were purchased from Shanghai Jing Chong Electronic Technology Development Co., Ltd. And, electrolysis was conducted under an AXIOMET AX3003P potentiostat in constant current mode. Cyclic voltammogram experiments were investigated using a Metrohm Autolab PGSTAT204 workstation and Nova 2.0 software.

2. Batch and continuous-flow electrochemical reactor

Figure 1 Batch reactor device

Figure 2 Microfluidic reactor device

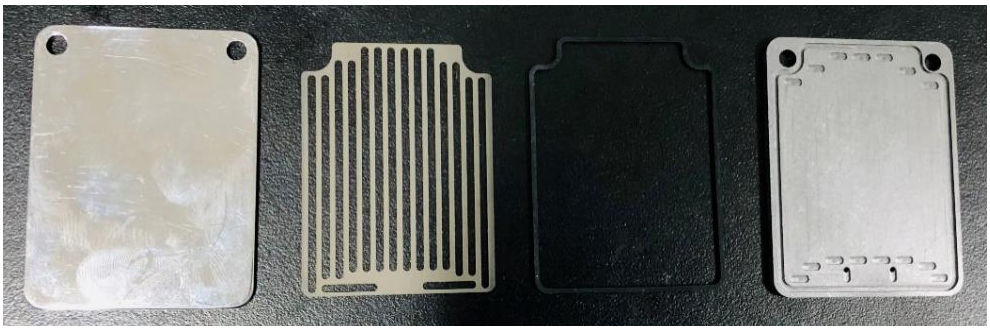
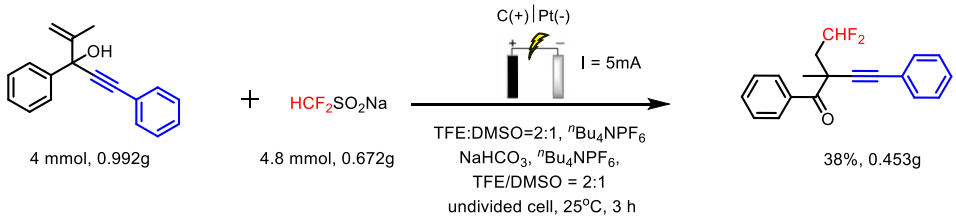


Figure 3 Diagram of continuous-flow electrochemical reactor

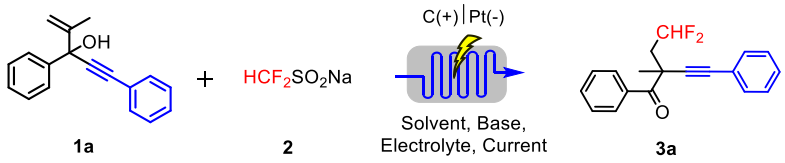
3. Gram-Scale Synthesis of 3 in batch



Scheme S1 Scale up investigations in batch

4. Select Optimization Results

Table S1: Selected optimization results synthetic compound **3a** in the continuous-flow electrosynthesis reactor

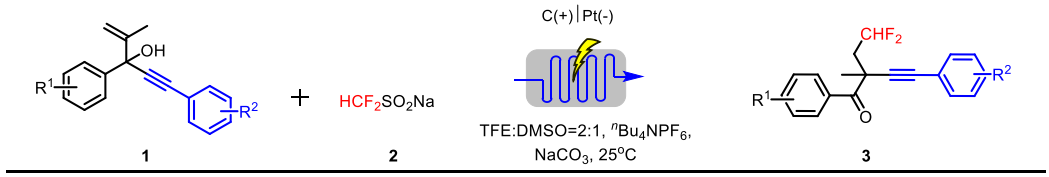


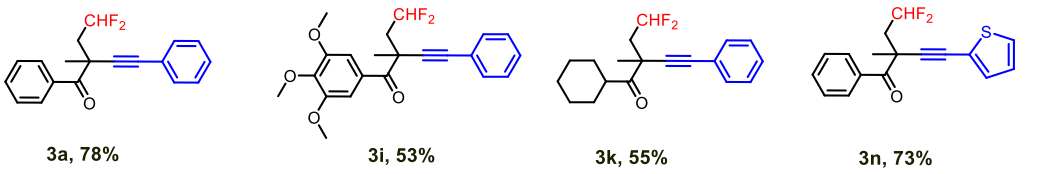
Entry	Variation from the "standard conditions"	Yield[b] (%)
1	None	78
2	5 mA, 15 mA, 20 mA instead of 10mA	46, 70, 62
3	Flow rate 225 = μL/ min, Residence time = 1 min	39
4	Flow rate 113 = μL/ min, Residence time = 2 min	52
5	Flow rate 75 = μL/ min, Residence time = 3 min	66
6	Flow rate 45 = μL/ min, Residence time = 5 min	69

[a] Reaction conditions: C anode (50 × 40 mm), Pt (SS 316 L platinum-coated) cathode (50 × 40 mm), **1a** (0.6 mmol), HCF_2SO_2Na (0.72 mmol), $NaHCO_3$ (0.9 mmol), $^nBu_4NPF_6$ (0.02 mol/L), TFE/DMSO (12 mL, v/v = 2/1), constant current 10 mA, flow rate 56 μL/ min, residence time 4 min, 25℃. [b] Yields are determined by high-performance liquid chromatography analysis with **3a** as the external standard.

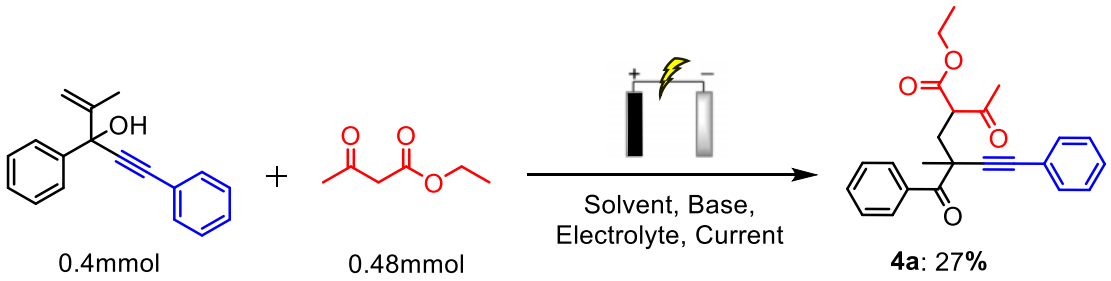
5. Synthesis of some *α*-alkynyl ketones

Table S2: Substrate scope for the continuous-flow electrosynthesis of **3**





3a, 78% **3i, 53%** **3k, 55%** **3n, 73%**

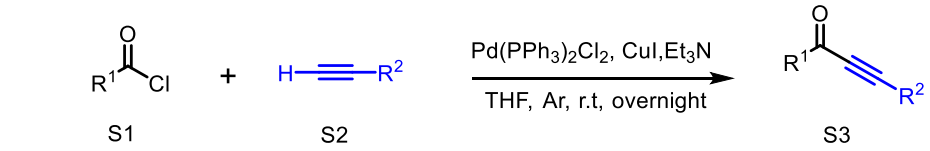


Scheme S2 Synthesis of compound **4a**[a]

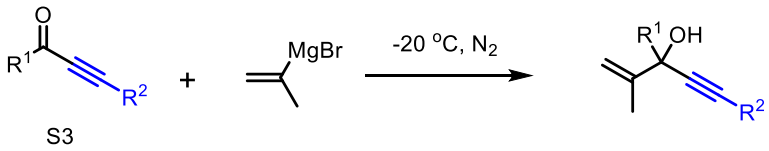
[a] Reaction conditions, see Table 1, entry 5, isolated yield.

6. Synthesis of Substrates

Step 1:



Step 2:



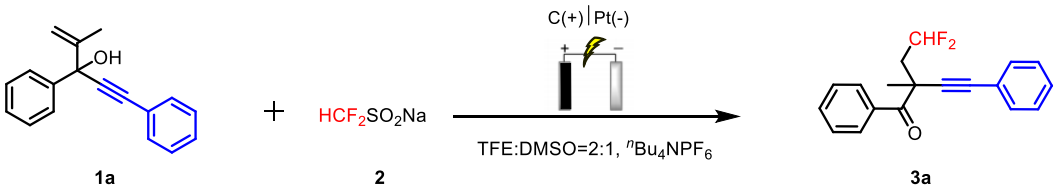
Step 1: [1]

A mixture of $Pd(PPh_3)Cl_2$ (2 mol%, 0.2 mmol), CuI (4 mol%, 0.4 mmol), Et_3N (1.5 equiv, 15 mmol) and acyl chloride **S1** (1.2 equiv, 12 mmol) were dissolved in 20 mL anhydrous tetrahydrofuran (THF) and stirred for 10 minutes at room temperature under argon conditions. Then, terminal alkyne **S2** (1.0 equiv, 10 mmol) was added to the reaction vial by dropwise and stirred for overnight. Then, the reaction solution was diluted with ethyl acetate (150 mL) and washed with brine (150 mL) and H_2O (150 mL). The separated organic layer was dried with anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude product, which was separated by column chromatography (eluent: petroleum ether 100/1) to give the desired product **S3**.

Step 2: [1]

Compound **S3** was dissolved in 10 mL anhydrous tetrahydrofuran. Then, isopropenylmagnesium bromide (10 mL, 1 mol/L in THF) was added to the solution above dropwise at -20 °C and stirred for 10 mins under argon. The reaction was then moved to room temperature for another 6 hours. After the completion of the reaction determined by TLC, the reaction mixture was quenched by adding aqueous saturated solution of NH_4Cl (80 mL) and extracted with ethyl acetate (2×60 mL). The organic phase was dried over Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to obtain a crude product, which was separated by column chromatography (eluent: petroleum ether 5/1) to give the desired product.

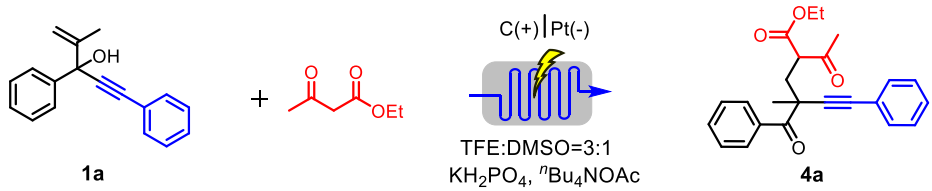
7. General Procedure for the Synthesis of Compounds 3



Example for the synthesis of **3a**:

In an undivided cell equipped with a carbon cloth (30 × 15 mm) anode and a Pt (10 × 10 × 0.1 mm) cathode, **1a** (0.4 mmol), HCF_2SO_2Na (0.48 mmol), $NaHCO_3$ (0.6 mmol), $^nBu_4NPF_6$ (0.6 mmol) were dissolved in 8 mL TFE and 4 mL DMSO. The mixture above was stirred and electrolyzed at a constant current of 5 mA for 3 h under the open air. The reaction solution was diluted with ethyl acetate (50 mL) and washed with H_2O (50 mL). The separated organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate: 50/1 to 5/1) to obtain the desired product.

8. General Procedure for the Synthesis of Compounds 4

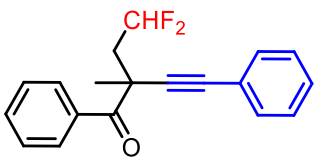


1a **4a**

Example for the synthesis of **4a**

The continuous-flow electrosynthesis reactors was assembled with a carbon cloth (50 × 40 mm) anode and a Pt (SS 316 L platinum-coated, 10 × 10 × 0.1 mm) cathode, and the volume of electrolytic cell was 225 μL. **1a** (0.2 mmol), EAA (0.24 mmol), KH_2PO_4 (0.3 mmol), $^nBu_4NOAc$ (0.02 mol/L) were dissolved in the mixture of TFE (6 mL) and DMSO (2 mL) in a 25 mL beaker. The mixture above was stirred and filtered, and then the reaction mixture was pumped into the continuous-flow electrochemical reactor with an injection pump at a flow rate of 75 μL/min and residence time of 3 min. Meanwhile, the current was adjusted to a constant 15 mA at the control module, and the electrolytic reaction was carried out at 25°C. After the reaction was stabilized, the reaction effluent was collected. The reaction solution was diluted with ethyl acetate (25 mL) and washed with H_2O (25 mL). The separated organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated under reduced pressure to give the crude product, which was purified by column chromatographic separation (petroleum ether/ethyl acetate: 15/1 to 3/1) to obtain the desired product.

9. Characterization Data for Final Products

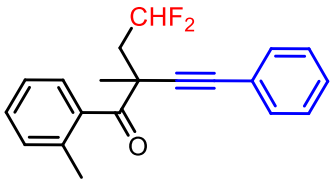


3a

2-(2,2-difluoroethyl)-2-methyl-1,4-diphenylbut-3-yn-1-one (3a)

Yellow oil (89.4 mg, 75%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.35 (m, 2H), 7.34 – 7.30 (m, 3H), 6.34-6.04 (m, 1H), 2.82 – 2.68 (m, 1H), 2.42-2.30 (m, 1H), 1.75 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.16 (d, *J* = 23.1 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.92, 134.88, 132.92, 131.41, 129.73, 128.66, 128.40, 128.19, 122.39, 118.81, 116.44, 114.06, 89.55, 87.61, 43.46, 43.27, 43.24, 43.16, 43.02, 26.88; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{16}F_2ONa$ 321.1061; found: 321.1073.

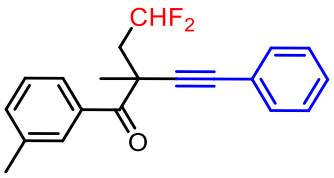


3b

2-(2,2-difluoroethyl)-2-methyl-4-phenyl-1-(o-tolyl)but-3-yn-1-one (3b)

Yellow oil (87.4 mg, 70%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.7 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.28 (m, 6H), 7.22 (t, *J* = 7.6 Hz, 1H), 6.28 – 5.99 (m, 1H), 2.83 – 2.67 (m, 1H), 2.36 (s, 3H), 2.35 – 2.24 (m, 1H), 1.66 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.06 (d, *J* = 6.2 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.48, 136.62, 135.38, 130.33, 130.10, 129.25, 127.53, 127.30, 126.15, 123.58, 121.30, 117.75, 115.38, 113.00, 87.96, 86.34, 44.02, 43.97, 43.92, 41.71, 41.49, 41.27, 25.67, 19.19; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{20}H_{18}F_2ONa$ 335.1218; found: 335.1236.

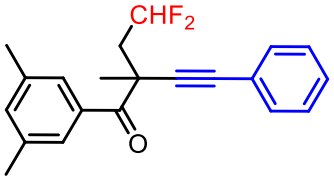


3c

2-(2,2-difluoroethyl)-2-methyl-4-phenyl-1-(m-tolyl)but-3-yn-1-one (3c)

Yellow oil (88.6 mg, 71%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.2 Hz, 1H), 7.98 (s, 1H), 7.31 – 7.27 (m, 4H), 7.25 – 7.22 (m, 3H), 6.21 – 5.92 (m, 1H), 2.70 – 2.62 (m, 1H), 2.33 (s, 3H), 2.30 – 2.24 (m, 1H), 1.66 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.20 (d, *J* = 24.9 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.10, 136.95, 133.83, 132.62, 130.31, 129.25, 127.58, 127.35, 126.92, 125.83, 121.39, 117.80, 115.42, 113.05, 88.64, 86.46, 42.39, 42.23, 42.17, 42.12, 41.94, 25.90, 20.43; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{20}H_{18}F_2ONa$ 335.1218; found: 335.1241.

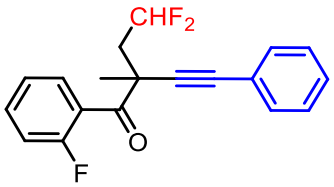


3d

2-(2,2-difluoroethyl)-1-(3,5-dimethylphenyl)-2-methyl-4-phenylbut-3-yn-1-one (3d)

Yellow oil (90.0 mg, 70%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 2H), 7.29 (d, *J* = 1.8 Hz, 2H), 7.24 – 7.19 (m, 3H), 7.11 (s, 1H), 6.25 – 5.95 (m, 1H), 2.73 – 2.60 (m, 1H), 2.28 (s, 6H), 2.25 – 2.23 (m, 1H), 1.65 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.18 (d, *J* = 18.6 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.40, 137.73, 135.05, 134.52, 133.03, 131.37, 131.31, 128.60, 128.41, 127.49, 124.46, 122.55, 118.89, 116.51, 114.13, 89.91, 87.48, 77.38, 77.06, 76.74, 43.49, 43.27, 43.05, 27.03, 21.51, 21.37; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{21}H_{20}F_2ONa$ 349.1374 ; found: 349.1397.

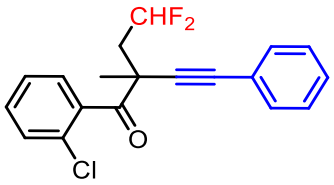


3e

2-(2,2-difluoroethyl)-1-(2-fluorophenyl)-2-methyl-4-phenylbut-3-yn-1-one (3e)

Yellow oil (102.4 mg, 81%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 – 7.47 (m, 1H), 7.42 – 7.34 (m, 2H), 7.21 – 7.16 (m, 5H), 7.16 – 7.10 (m, 2H), 7.08 – 7.03 (m, 1H), 6.20 – 5.91 (m, 1H), 2.77 – 2.64 (m, 1H), 2.27 – 2.15 (m, 1H), 1.61 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -108.92 (s, 1F), -113.80 (d, *J* = 18.5 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 199.98, 159.31, 156.82, 131.67, 131.59, 130.38, 128.51, 128.48, 127.52, 127.27, 127.19, 122.86, 121.21, 115.22, 114.93, 114.71, 112.84, 87.30, 85.47, 44.20, 44.14, 44.09, 41.95, 41.73, 41.51, 25.17; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{15}F_3ONa$ 339.0967; found:339.0976.

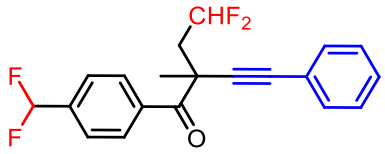


3f

1-(2-chlorophenyl)-2-(2,2-difluoroethyl)-2-methyl-4-phenylbut-3-yn-1-one (3f)

Yellow oil (102.3 mg, 77%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.36 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.30 (td, *J* = 7.7, 1.7 Hz, 1H), 7.25 – 7.15 (m, 6H), 6.22 – 5.93 (m, 1H), 2.72 – 2.57 (m, 1H), 2.35 – 2.20 (m, 1H), 1.61 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): -112.66 (d, *J* = 2.4 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.10, 137.46, 130.38, 129.83, 128.82, 127.61, 127.31, 126.87, 125.06, 121.11, 117.59, 115.21, 112.83, 87.04, 86.21, 44.50, 41.16, 24.98; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{15}F_2ClONa$ 355.0672; found: 355.0689.

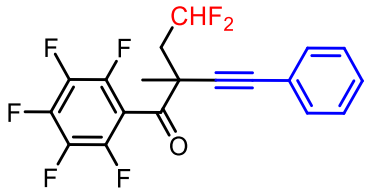


3g

2-(2,2-difluoroethyl)-1-(4-(difluoromethyl)phenyl)-2-methyl-4-phenylbut-3-yn-1-one (3g)

Yellow oil (87.7 mg, 63%); Eluent: petroleum ether/ethyl acetate 80:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.4 Hz, 1H), 8.01 (d, *J* = 8.6 Hz, 1H), 7.82 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.57 –7.52 (m, 1H), 7.38 – 7.30 (m, 5H), 6.36 – 6.00(m, 1H), 2.81 – 2.65 (m, 1H), 2.44 – 2.28 (m, 1H), 1.74 (d, *J* = 13.3 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.22 (d, *J* = 9.1 Hz, 2F), -112.34 (d, *J* = 19.3 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.04, 137.52, 134.04, 133.86, 131.79, 131.41, 131.25, 131.16, 129.79, 128.88, 128.83, 128.75, 128.48, 128.45, 128.09, 122.63, 122.26, 122.13, 118.67, 116.38, 116.29, 113.91, 101.00, 92.87, 89.36, 89.14, 88.61, 87.90, 43.20, 43.15, 31.46, 30.21, 26.89, 26.84; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{20}H_{16}F_4ONa$ 371.1029; found: 371.1038.

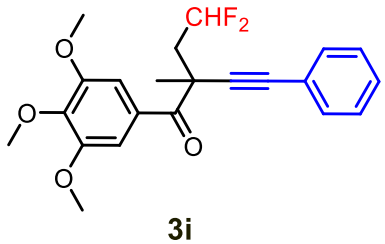


3h

2-(2,2-difluoroethyl)-2-methyl-1-(perfluorophenyl)-4-phenylbut-3-yn-1-one (3h)

Yellow oil (111.8 mg, 72%); Eluent: petroleum ether/ethyl acetate 80:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.25 (m, 5H), 6.32 – 5.99 (m, 1H), 2.79 – 2.66 (m, 1H), 2.42 – 2.26 (m, 1H), 1.67 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.49 – -113.79 (m, 2F), -137.09 – -137.30 (m, 2F), -150.11 – -150.38 (m, 1F), -159.95 – -160.58 (m, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.83, 144.06, 141.65, 141.01, 138.72, 136.18, 131.49, 129.05, 128.50, 121.49, 118.09, 115.70, 113.32, 87.15, 86.12, 46.63, 46.58, 46.52, 42.20, 41.97, 41.74, 25.76; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{11}F_7ONa$ 411.0590; found: 411.0613.



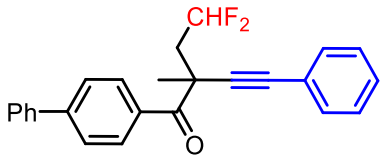
3i

2-(2,2-difluoroethyl)-2-methyl-4-phenyl-1-(3,4,5-trimethoxyphenyl)but-3-yn-1-one (3i)

Yellow oil (76.1 mg, 49%); Eluent: petroleum ether/ethyl acetate 6:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 2H), 7.38 (dd, *J* = 7.4, 1.9 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 3H), 6.34 – 6.05 (m, 1H), 3.93 (s, 3H), 3.86 (s, 6H), 2.83 – 2.69 (m, 1H), 2.44 – 2.30 (m, 1H), 1.76 (s,

3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.00 (d, *J* = 14.0 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.18, 152.58, 142.49, 131.38, 129.41, 128.79, 128.63, 128.50, 122.21, 118.79, 116.41, 114.03, 107.62, 107.51, 89.88, 87.74, 60.97, 56.32, 56.21, 43.71, 43.49, 43.27, 43.08, 43.02, 42.97, 27.29; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{22}H_{22}F_2O_4Na$ 411.1378; found: 411.1384.

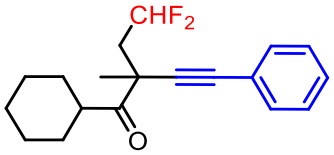


3j

1-([1,1'-biphenyl]-4-yl)-2-(2,2-difluoroethyl)-2-methyl-4-phenylbut-3-yn-1-one (3j)

Yellow oil (88.3 mg, 59%); Eluent: petroleum ether/ethyl acetate 60:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 7.7 Hz, 2H), 7.82 – 7.40 (m, 12H), 6.68 – 5.95 (m, 1H), 2.92 – 2.68 (m, 1H), 2.57 – 2.28 (m, 1H), 1.76 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.15 (d, *J* = 22.3 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.93, 141.48, 140.22, 134.90, 132.97, 131.86, 129.76, 128.92, 128.24, 127.79, 127.09, 121.25, 118.85, 116.47, 90.20, 87.52, 43.50, 43.30, 26.92; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{25}H_{20}F_2ONa$ 397.1374; found: 397.1388.

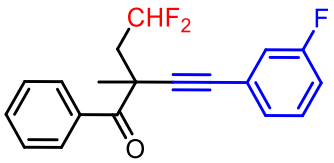


3k

1-cyclohexyl-2-(2,2-difluoroethyl)-2-methyl-4-phenylbut-3-yn-1-one (3k)

Yellow oil (52.3 mg, 43%); Eluent: petroleum ether/ethyl acetate 150:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.33 (m, 2H), 7.29 – 7.24 (m, 3H), 6.14 – 5.86 (m, 1H), 3.17 (tt, *J* = 11.3, 3.2 Hz, 1H), 2.49 – 2.38 (m, 1H), 2.05 (dtd, *J* = 19.1, 14.3, 4.8 Hz, 1H), 1.85 (t, *J* = 12.2 Hz, 2H), 1.76 – 1.72 (m, 2H), 1.66 – 1.59 (m, 2H), 1.41 (s, 3H), 1.39 – 1.31 (m, 2H), 1.19 (d, *J* = 8.1 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -113.63 (d, *J* = 24.9 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 210.22, 132.03, 130.47, 127.56, 127.43, 121.41, 117.70, 115.32, 112.94, 87.68, 84.81, 46.50, 44.71, 43.59, 43.54, 43.48, 41.12, 40.90, 40.68, 28.66, 25.05, 24.67, 24.63, 24.58; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{22}F_2ONa$ 327.1531; found: 327.1558.



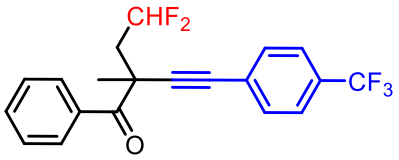
3l

2-(2,2-difluoroethyl)-4-(3-fluorophenyl)-2-methyl-1-phenylbut-3-yn-1-one (3l)

Yellow oil (96.1 mg, 76%); Eluent: petroleum ether/ethyl acetate 100:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 – 8.19 (m, 2H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz,

2H), 7.42 – 7.26 (m, 4H), 6.33 – 6.02 (m, 1H), 2.87 – 2.69 (m, 1H), 2.37 (qd, *J* = 14.5, 5.4 Hz, 1H), 1.76 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -110.14 (s, 1F), -112.31 (d, *J* = 27.7 Hz, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.52, 134.60, 133.19, 133.02, 130.44, 130.36, 129.84, 129.07, 128.20, 126.74, 124.02, 123.99, 94.68, 81.27, 43.34, 43.30, 43.08, 42.86, 26.86; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{19}H_{15}F_3ONa$ 339.0967; found: 339.0989.

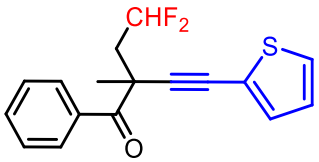


3m

2-(2,2-difluoroethyl)-2-methyl-1-phenyl-4-(4-(trifluoromethyl)phenyl)but-3-yn-1-one (3m)

Yellow oil (114.2 mg, 78%); Eluent: petroleum ether/ethyl acetate 80:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, *J* = 7.3 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 3H), 7.47 (t, *J* = 7.8 Hz, 4H), 6.26 – 5.97 (m, 1H), 2.76 (tdd, *J* = 17.6, 14.6, 3.7 Hz, 1H), 2.38 (qd, *J* = 14.6, 5.6 Hz, 1H), 1.77 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.90 (s, 3F), -112.22 (s, 2F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.47, 134.72, 133.10, 131.70, 129.64, 128.26, 125.37, 125.33, 118.56, 116.18, 113.80, 92.14, 86.29, 43.23, 43.19, 26.82; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{20}H_{15}F_5ONa$ 389.0935; found:389.0944.

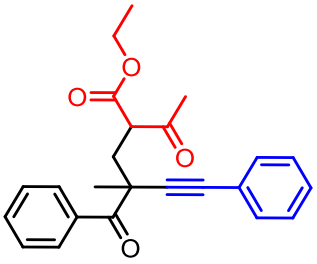


3n

2-(2,2-difluoroethyl)-2-methyl-1-phenyl-4-(thiophen-2-yl)but-3-yn-1-one (3n)

Yellow oil (79.2 mg, 65%); Eluent: petroleum ether/ethyl acetate 80:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.26 – 7.23 (m, 1H), 7.18 – 7.13 (m, 1H), 6.96 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.26 – 5.95 (m, 1H), 2.80 – 2.65 (m, 1H), 2.34 (td, *J* = 14.7, 5.7 Hz, 1H), 1.74 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -112.19 (q, *J* = 15.4, 14.9 Hz, 1F), -112.34 (q, *J* = 15.3 Hz, 1F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.61, 134.83, 132.97, 132.08, 129.67, 128.24, 127.43, 127.05, 122.22, 118.66, 116.29, 113.91, 93.32, 81.09, 43.51, 43.46, 43.40, 43.36, 43.14, 42.91, 26.75; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{17}H_{14}F_2ONa$ 327.0626; found: 327.0653.

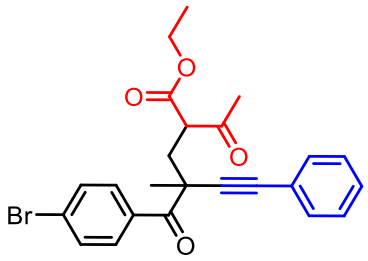


4a

ethyl 2-acetyl-4-benzoyl-4-methyl-6-phenylhex-5-ynoate (4a)

Yellow oil (54.2 mg, 72%); Eluent: petroleum ether/ethyl acetate 15:1;

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 – 8.18 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.39 – 7.30 (m, 5H), 4.13 – 3.96 (m, 2H), 3.92 – 3.83 (m, 1H), 2.73 (ddd, J = 16.1, 9.8, 6.2 Hz, 1H), 2.31 – 2.21 (m, 4H), 1.62 (s, 3H), 1.10 (dt, J = 17.7, 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 202.83, 202.75, 198.71, 198.51, 169.70, 169.64, 135.06, 135.03, 133.58, 131.47, 129.84, 129.29, 129.13, 129.07, 128.80, 122.34, 122.32, 91.41, 91.32, 87.13, 87.10, 61.60, 56.66, 56.55, 45.82, 45.73, 36.78, 36.50, 29.66, 29.44, 26.49, 26.25, 14.22, 14.16; HRMS (ESI) m/z [M+Na]$^+$ Calcd for $C_{24}H_{24}O_4Na$ 399.1567; found: 399.1588.

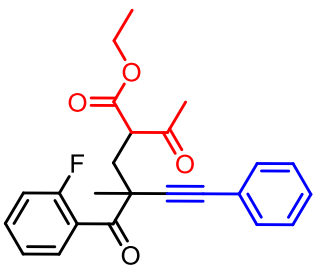


4b

ethyl 2-acetyl-4-(4-bromobenzoyl)-4-methyl-6-phenylhex-5-ynoate (4b)

Yellow oil (57.2 mg, 63%); Eluent: petroleum ether/ethyl acetate 15:1;

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.26 – 8.18 (m, 2H), 7.67 – 7.52 (m, 5H), 7.36 – 7.32 (m, 2H), 4.12 – 3.98 (m, 2H), 3.90 (m, 1H), 2.73 (ddd, J = 14.2, 10.6, 6.2 Hz, 1H), 2.27 (d, J = 22.9 Hz, 4H), 1.63 (s, 3H), 1.12 (dt, J = 18.4, 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 202.88, 202.81, 198.42, 198.25, 169.76, 169.68, 134.92, 133.82, 133.67, 132.30, 131.26, 130.49, 129.83, 128.85, 124.49, 122.04, 92.97, 85.53, 61.63, 56.54, 56.49, 45.82, 45.72, 40.58, 40.37, 40.17, 39.96, 39.75, 39.54, 39.33, 29.65, 29.44, 26.39, 26.16, 14.23, 14.18; HRMS (ESI) m/z [M+Na]$^+$ Calcd for $C_{24}H_{23}O_4BrNa$ 477.0672; found: 477.0679.

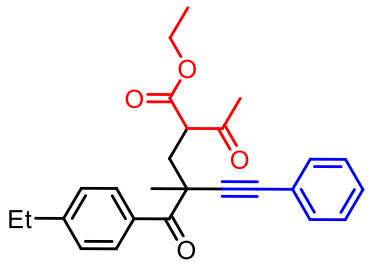


4c

ethyl 2-acetyl-4-(2-fluorobenzoyl)-4-methyl-6-phenylhex-5-ynoate (4c)

Yellow oil (59.9 mg, 76%); Eluent: petroleum ether/ethyl acetate 15:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 7.2 Hz, 2H), 7.55 (dd, *J* = 7.9, 3.1 Hz, 3H), 7.49 – 7.40 (m, 4H), 4.23 – 3.98 (m, 2H), 3.76 (q, *J* = 5.4 Hz, 1H), 2.91 – 2.83 (m, 1H), 2.51 – 2.40 (m, 1H), 2.36 – 2.23 (m, 3H), 1.70 (d, *J* = 2.3 Hz, 3H), 1.27 – 1.13 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.88 (s, 1F). ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.12, 203.09, 202.40, 202.33, 169.53, 169.22, 138.85, 138.70, 131.89, 131.36, 131.32, 130.75, 130.72, 130.39, 130.33, 129.85, 128.50, 128.30, 127.69, 127.62, 126.08, 126.05, 122.34, 89.45, 89.02, 87.05, 87.02, 76.75, 61.76, 61.67, 57.12, 56.66, 48.49, 48.31, 35.90, 35.66, 29.77, 29.07, 25.88, 25.85, 13.98, 13.93; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{24}H_{23}O_4FNa$ 417.1473; found: 417.1491.

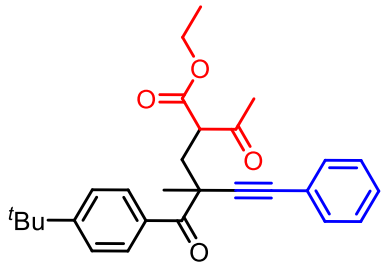


4d

ethyl 2-acetyl-4-(4-ethylbenzoyl)-4-methyl-6-phenylhex-5-ynoate (4d)

Yellow oil (55.01 mg, 68%); Eluent: petroleum ether/ethyl acetate 20:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 7.9 Hz, 2H), 7.54 (t, *J* = 6.9 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.28 – 7.24 (m, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 4.23 – 3.98 (m, 2H), 3.86 – 3.76 (m, 1H), 2.85 (ddd, *J* = 13.8, 7.7, 5.3 Hz, 1H), 2.62 (q, *J* = 7.6 Hz, 2H), 2.48 – 2.38 (m, 1H), 2.37 – 2.24 (m, 3H), 1.66 (s, 3H), 1.26 – 1.12 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.74, 198.59, 169.69, 144.98, 135.01, 132.88, 131.36, 129.93, 128.13, 127.92, 119.72, 90.21, 87.51, 77.39, 77.08, 76.76, 61.67, 57.17, 45.94, 37.09, 29.56, 28.81, 26.91, 15.40, 14.02; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{26}H_{28}O_4Na$ 427.1880; found: 427.1892.



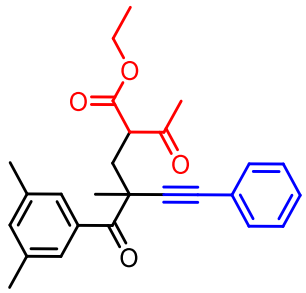
4e

ethyl 2-acetyl-4-(4-(tert-butyl)benzoyl)-4-methyl-6-phenylhex-5-ynoate (4e)

Yellow oil (61.4 mg, 71%); Eluent: petroleum ether/ethyl acetate 20:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 7.2 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.33 (m, 2H), 7.31 – 7.27 (m, 3H), 4.20 – 3.97 (m, 2H), 3.81 (q, *J* = 5.7 Hz, 1H), 2.92 – 2.81 (m, 1H), 2.43 (dd, *J* = 14.3, 5.8 Hz, 1H), 2.38 – 2.23 (m, 3H), 1.67 (s, 3H), 1.34 (d, *J* = 1.4 Hz, 9H), 1.25 – 1.11 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.78, 202.51, 197.77, 197.63, 169.72, 169.57, 156.70, 156.66, 132.12, 132.06, 131.42, 131.36, 130.01, 129.99, 128.47, 128.35, 128.32, 125.15, 125.12,

122.67, 91.19, 90.86, 87.14, 87.09, 77.43, 77.11, 76.79, 61.65, 61.53, 57.23, 57.17, 45.84, 45.72, 37.10, 36.97, 35.13, 31.08, 29.55, 29.47, 26.97, 26.88, 14.02, 13.91; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{28}H_{32}O_4Na$ 455.2193; found: 455.2202.

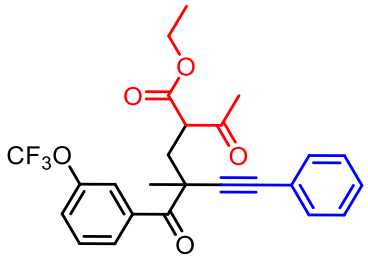


4f

ethyl 2-acetyl-4-(3,5-dimethylbenzoyl)-4-methyl-6-phenylhex-5-ynoate (4f)

Yellow oil (53.4 mg, 66%); Eluent: petroleum ether/ethyl acetate 20:1;

^1H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 2H), 7.26 (dd, *J* = 7.6, 3.2 Hz, 2H), 7.21 (dd, *J* = 5.4, 2.0 Hz, 3H), 7.11 (s, 1H), 4.14 – 3.92 (m, 2H), 3.77 – 3.66 (m, 1H), 2.77 (dt, *J* = 14.2, 5.0 Hz, 1H), 2.36 – 2.33 (m, 1H), 2.31 – 2.25 (m, 8H), 2.17 (s, 1H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.11 (dt, *J* = 37.0, 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.74, 198.95, 169.71, 137.66, 135.12, 134.49, 131.27, 128.45, 128.34, 127.69, 122.71, 90.99, 87.19, 61.54, 57.17, 46.07, 36.97, 29.41, 27.02, 21.36, 14.01; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{26}H_{28}O_4Na$ 427.1880; found: 427.1889.

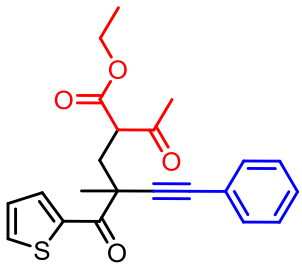


4g

ethyl 2-acetyl-4-methyl-6-phenyl-4-(3-(trifluoromethoxy)benzoyl)hex-5-ynoate (4g)

Yellow oil (77.3 mg, 84%); Eluent: petroleum ether/ethyl acetate 12:1;

^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 7.7 Hz, 1H), 8.18 (s, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.32 (m, 3H), 7.31 (s, 2H), 4.24 – 4.08 (m, 2H), 3.80 (q, *J* = 5.2 Hz, 1H), 2.85 (dd, *J* = 14.3, 5.3 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.31 (d, *J* = 38.8 Hz, 3H), 1.67 (s, 3H), 1.19 (dt, *J* = 38.6, 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$): δ -57.92 (s, 3F); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.41, 196.96, 169.54, 149.00, 136.63, 131.36, 131.31, 129.68, 128.71, 128.39, 128.28, 125.32, 122.37, 122.18, 90.14, 87.85, 61.76, 57.05, 46.00, 36.77, 29.36, 26.74, 13.95; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{25}H_{23}O_5F_3Na$ 483.1390; found: 483.1396.

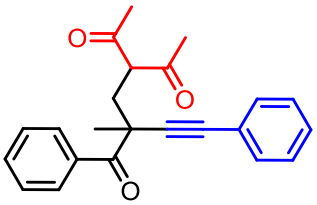


4h

ethyl 2-acetyl-4-methyl-6-phenyl-4-(thiophene-2-carbonyl)hex-5-ynoate (4h)

Yellow oil (53.5 mg, 70%); Eluent: petroleum ether/ethyl acetate 15:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.21 (m, 1H), 7.12 (d, *J* = 3.6 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.23 – 4.03 (m, 2H), 3.76 (t, *J* = 5.6 Hz, 1H), 2.90 – 2.81 (m, 1H), 2.46 – 2.38 (m, 1H), 2.31 (d, *J* = 39.4 Hz, 3H), 1.66 (d, *J* = 2.0 Hz, 3H), 1.21 (dt, *J* = 35.5, 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.52, 202.25, 198.13, 198.00, 169.56, 169.44, 134.91, 134.86, 132.98, 132.95, 131.95, 131.92, 129.84, 129.81, 128.19, 128.18, 127.26, 127.00, 126.98, 122.40, 94.68, 94.42, 80.87, 61.74, 61.65, 57.09, 57.06, 46.18, 36.81, 29.49, 29.41, 26.76, 26.63, 14.02, 13.93; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{22}H_{22}O_4SNa$ 405.1331; found: 405.1348.

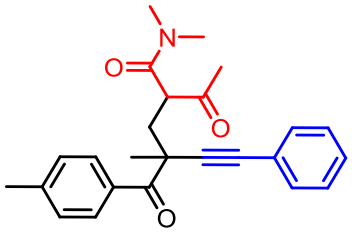


4i

4-acetyl-2-methyl-1-phenyl-2-(phenylethynyl)hexane-1,5-dione (4i)

Yellow oil (42.9 mg, 62%); Eluent: petroleum ether/ethyl acetate 30:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 7.3 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.34 – 7.29 (m, 5H), 3.97 (dd, *J* = 6.1, 4.8 Hz, 1H), 2.79 (dd, *J* = 14.1, 4.6 Hz, 1H), 2.47 – 2.42 (m, 1H), 2.32 (s, 3H), 2.17 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6): δ 204.12, 203.90, 198.74, 135.08, 133.59, 131.41, 129.86, 129.30, 129.18, 128.81, 122.31, 91.83, 87.09, 64.31, 46.09, 36.45, 30.30, 30.15, 26.39; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{23}H_{22}O_3Na$ 369.1461; found: 369.1484.



4j

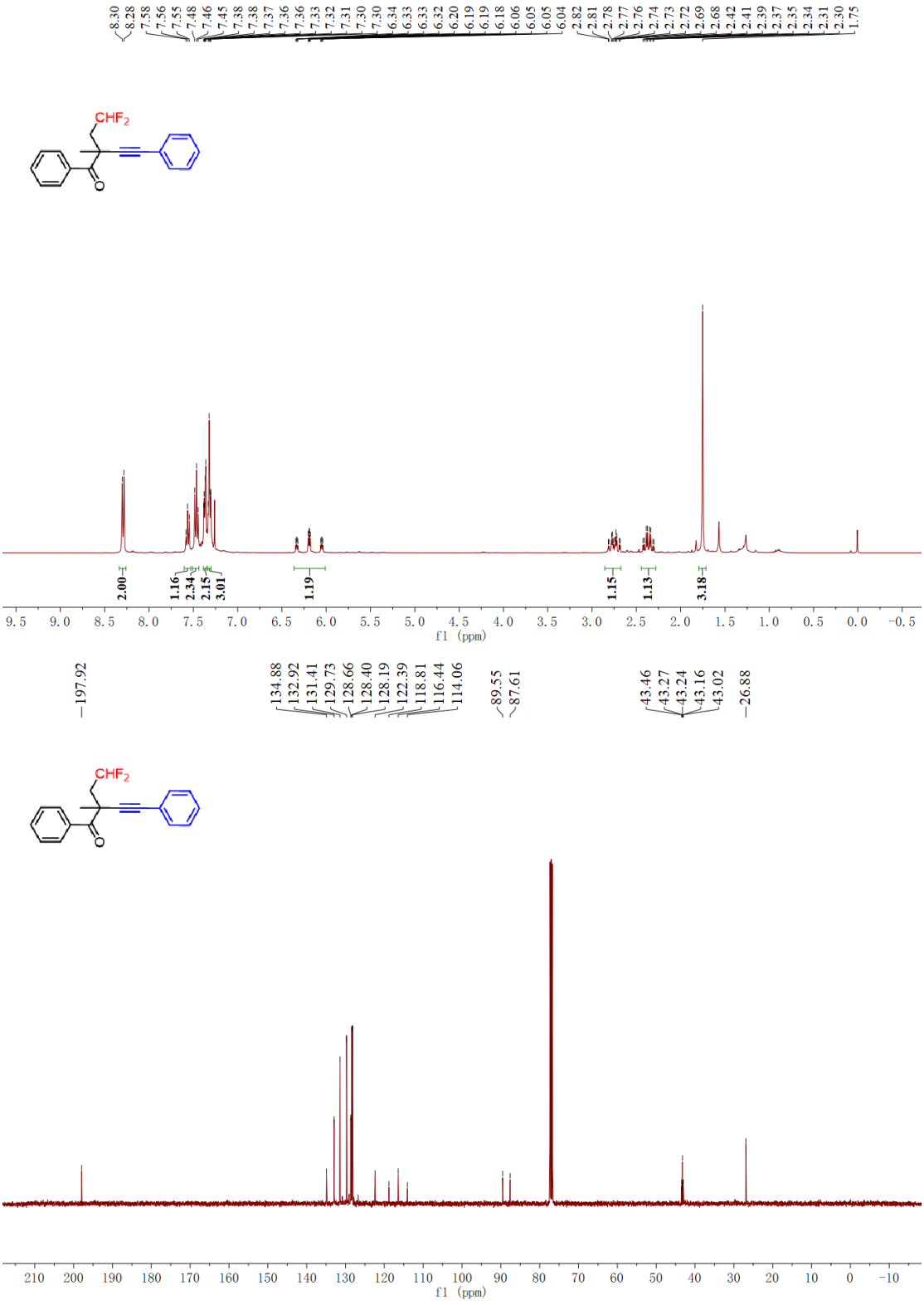
2-acetyl-N,N,4-trimethyl-4-(4-methylbenzoyl)-6-phenylhex-5-ynamide (4j)

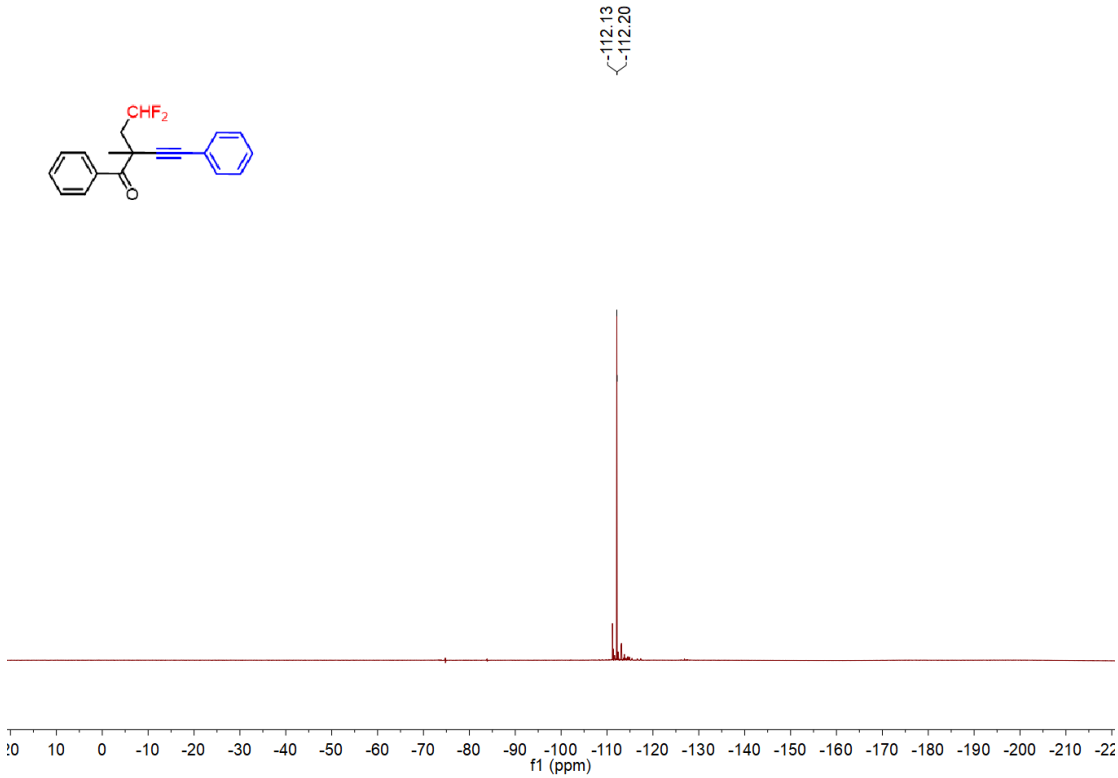
Yellow oil (63.1 mg, 81%); Eluent: petroleum ether/ethyl acetate 2:1;

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (t, *J* = 7.8 Hz, 2H), 7.39 – 7.23 (m, 7H), 4.08 – 3.92 (m, 1H), 3.12 (s, 1.27H), 3.07 – 2.86 (m, 4H), 2.81 (s, 1.75H), 2.78 – 2.54 (m, 1H), 2.40 (d, *J* = 2.5 Hz, 3H), 2.30 – 2.17 (m, 3H), 1.75 – 1.60 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.97, 198.04, 169.14, 143.79, 132.21, 131.29, 130.08, 128.84, 128.48, 128.34, 122.61, 90.96, 87.00, 55.43, 46.04, 37.85, 37.63, 36.18, 27.35, 27.29, 21.66; HRMS (ESI) m/z $[M+Na]^+$ Calcd for $C_{25}H_{27}NO_3Na$ 412.1883; found: 412.1904.

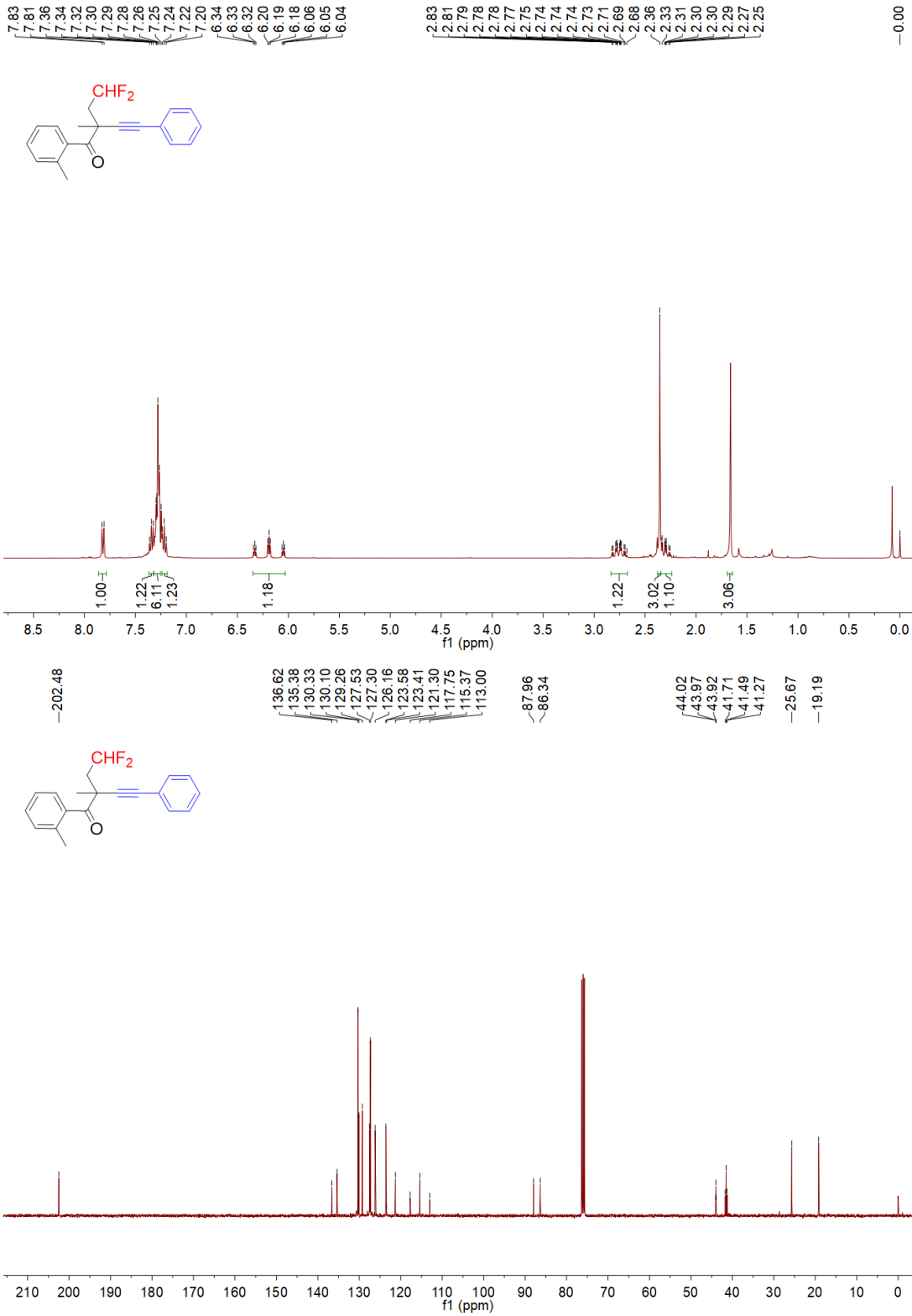
10. NMR Spectra for Final Products

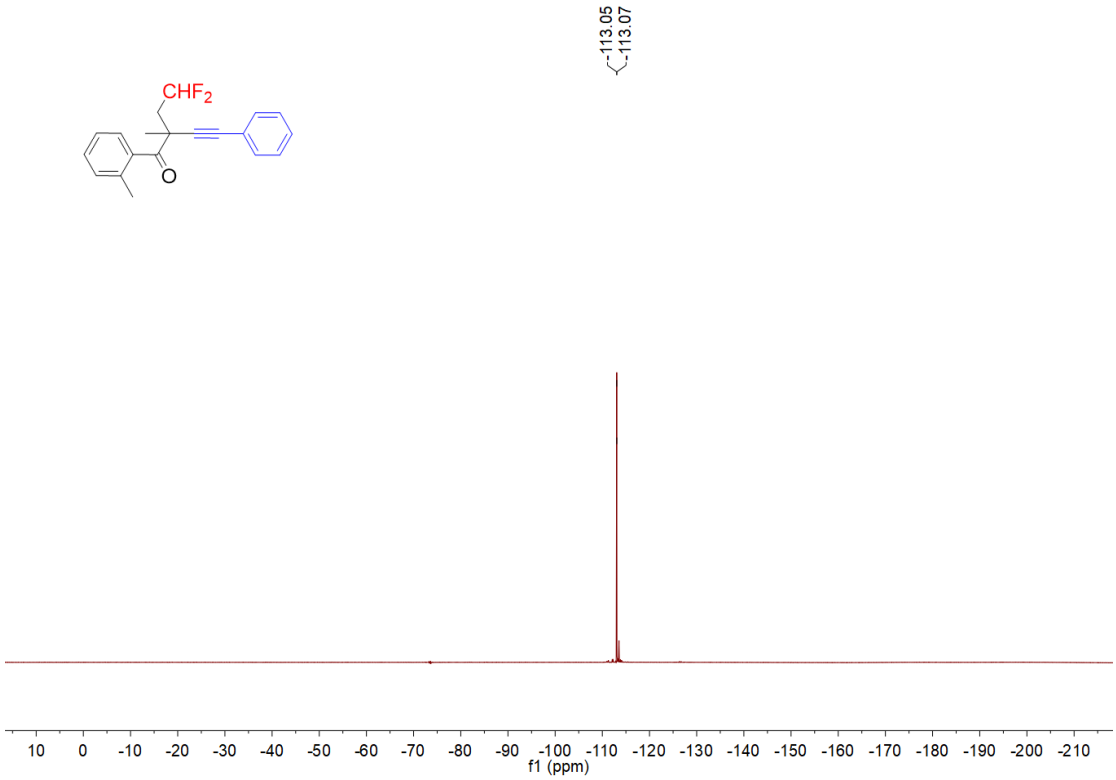
3a




-112.13
-112.20
CHF2
O
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)

3b


7.83 7.81 7.36 7.34 7.32 7.30 7.29 7.28 7.26 7.25 7.24 7.22 7.20 6.34 6.33 6.32 6.20 6.19 6.18 6.06 6.05 6.04
2.83 2.81 2.79 2.78 2.78 2.77 2.75 2.74 2.74 2.74 2.73 2.71 2.69 2.68 2.36 2.33 2.31 2.30 2.30 2.29 2.27 2.25
0.00
CHF2
O
1.00 1.22 6.11 1.23 1.18 1.22 3.02 1.10 3.06
f1 (ppm)
202.48
136.62 135.38 130.33 130.10 129.26 127.53 127.30 126.16 123.58 123.41 121.30 117.75 115.37 113.00
87.96 86.34
44.02 43.97 43.92 41.71 41.49 41.27
25.67 19.19
CHF2
O
f1 (ppm)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O
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-113.07
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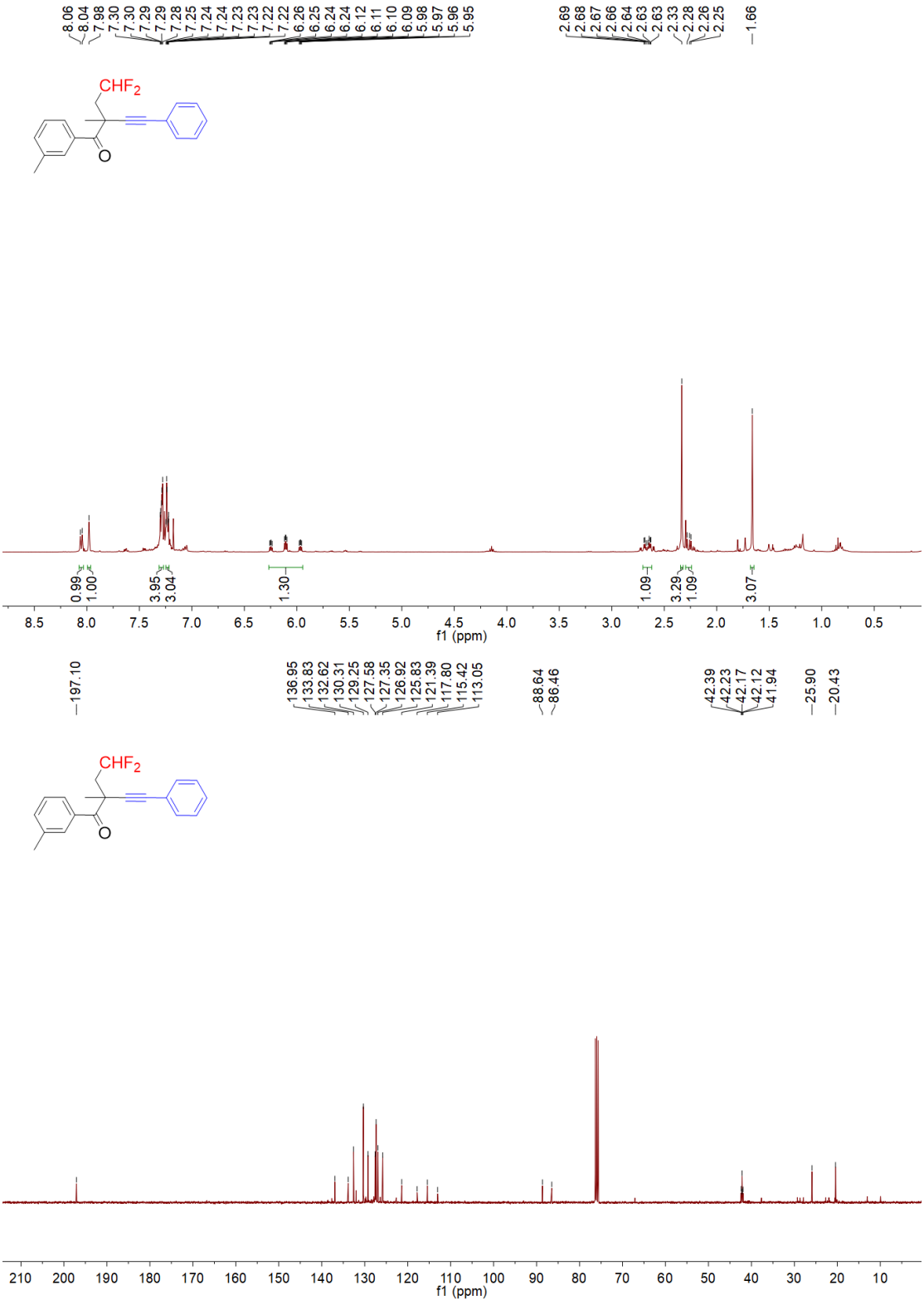
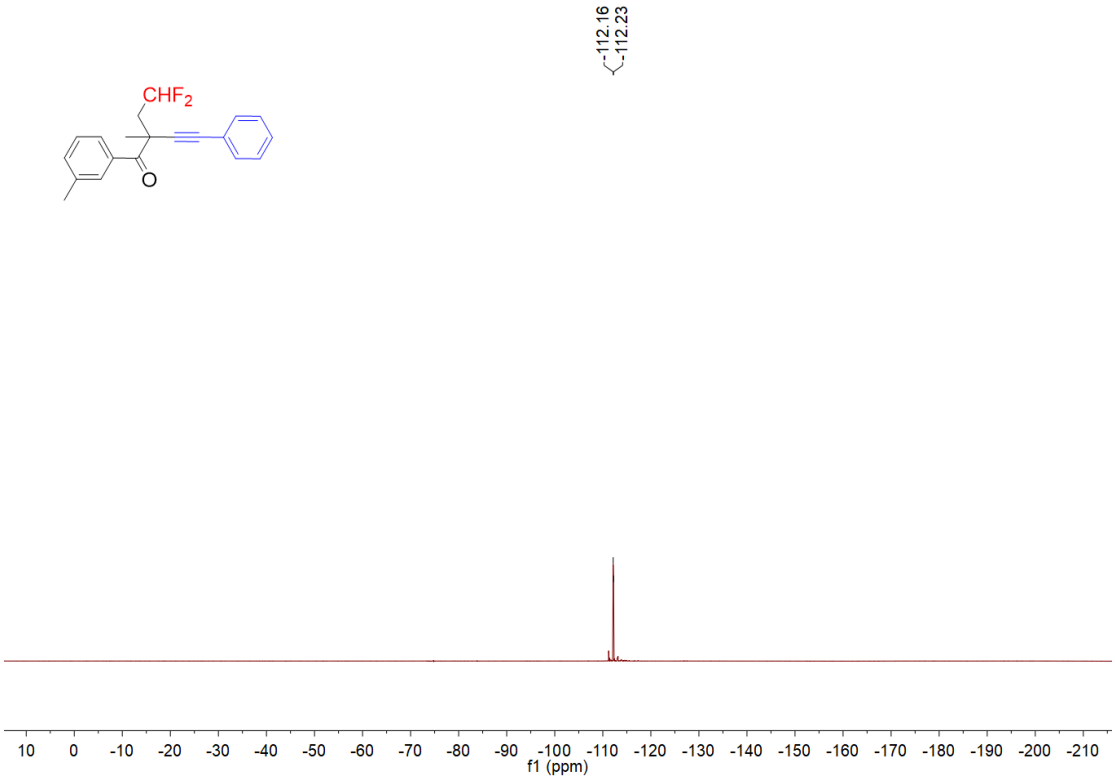
f1 (ppm)

3c


8.06
8.04
7.98
7.30
7.29
7.29
7.28
7.25
7.24
7.24
7.23
7.23
7.22
7.22
6.26
6.25
6.24
6.24
6.12
6.11
6.10
6.09
5.98
5.97
5.96
5.95
2.69
2.68
2.67
2.66
2.64
2.63
2.63
2.33
2.28
2.26
2.25
1.66
CHF2
O
0.99
1.00
3.95
3.04
1.30
1.09
3.29
1.09
3.07
f1 (ppm)
197.10
136.95
133.83
132.62
130.31
129.25
127.58
127.35
126.92
125.83
121.39
117.80
115.42
113.05
88.64
86.46
42.39
42.23
42.17
42.12
41.94
25.90
20.43
CHF2
O
f1 (ppm)

CHF2
O


-112.16
-112.23
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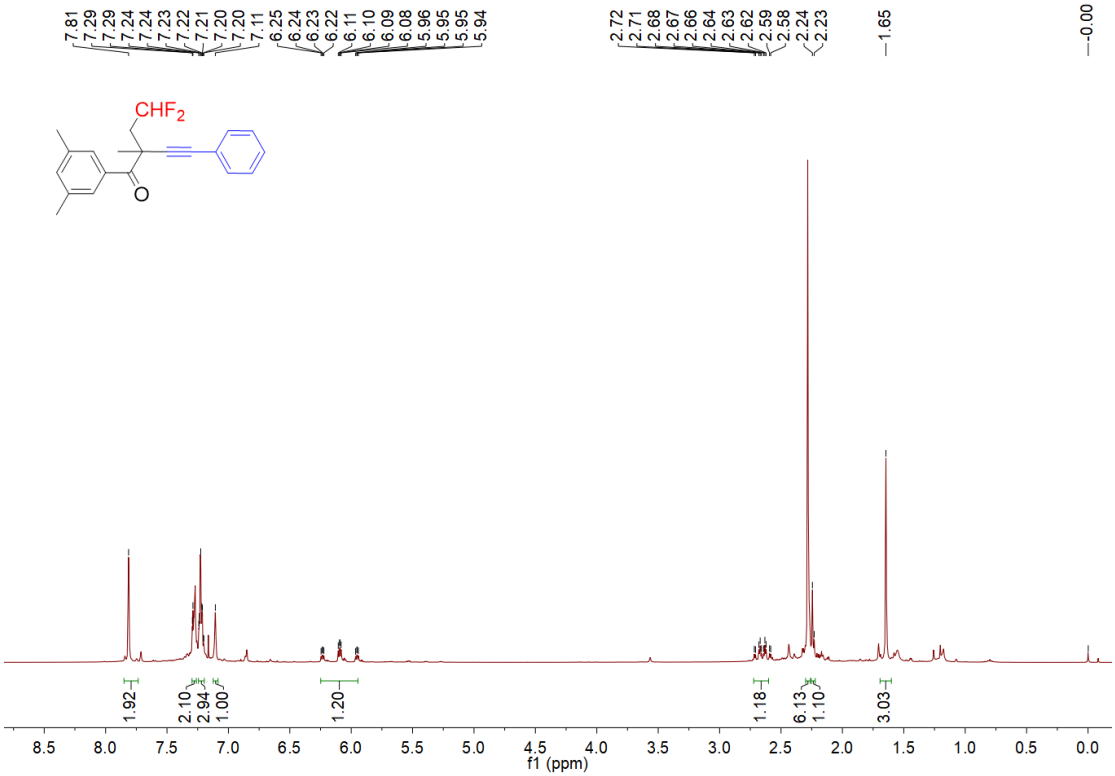
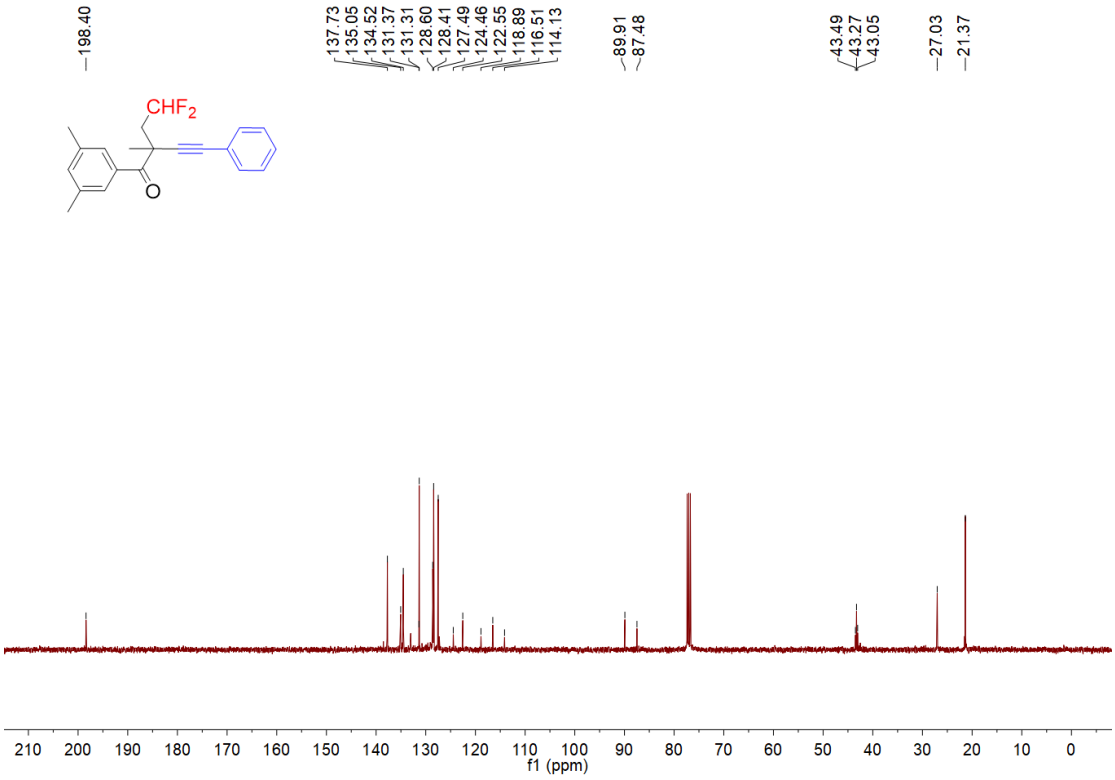
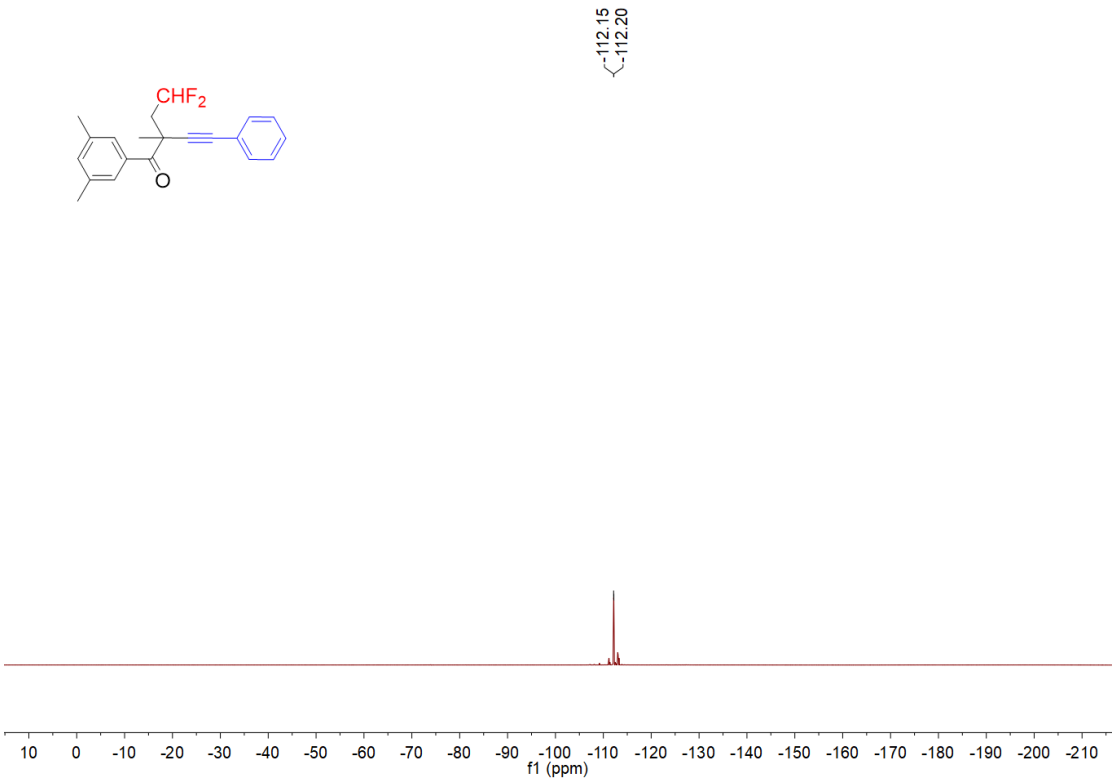
f1 (ppm)

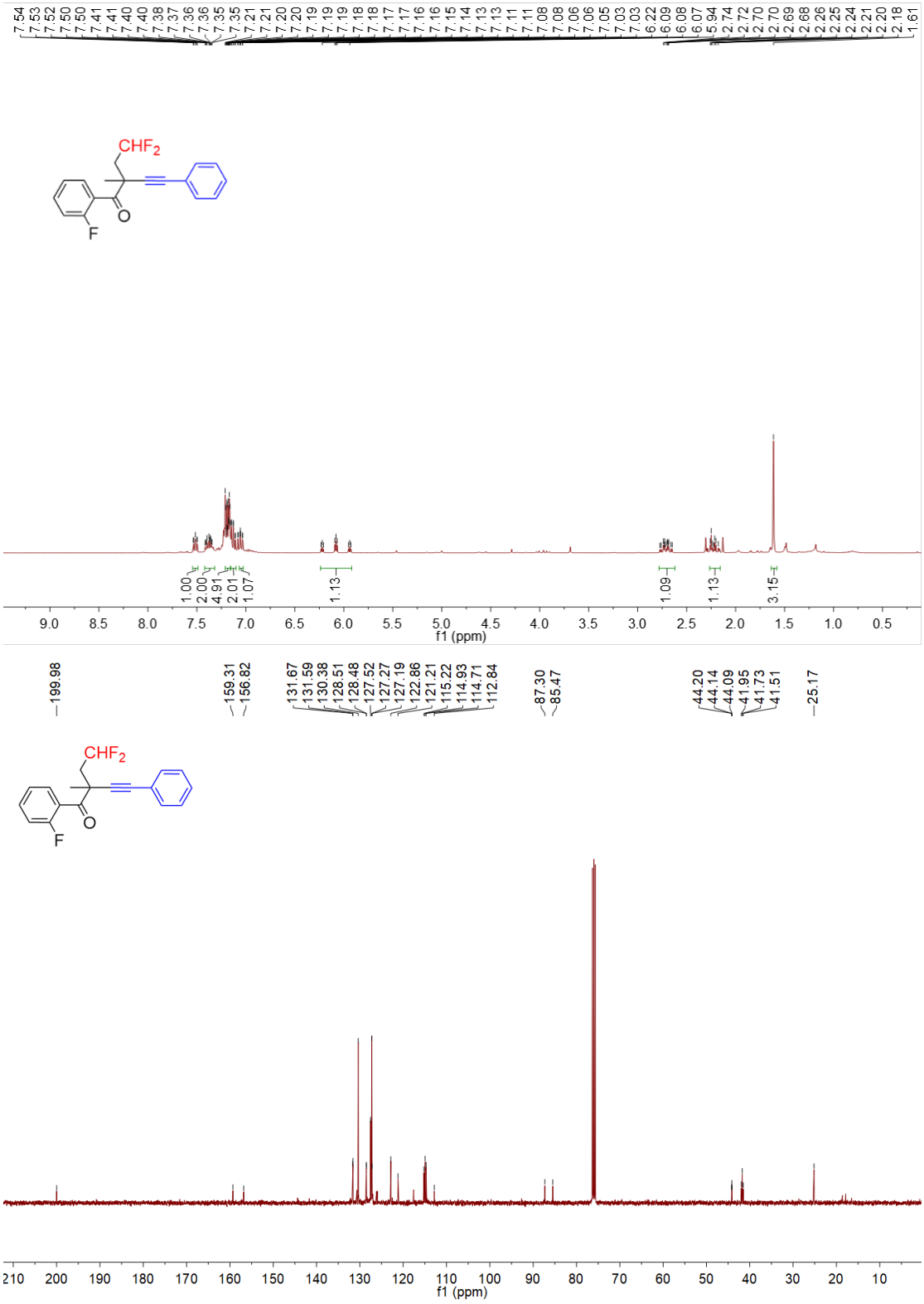
3d

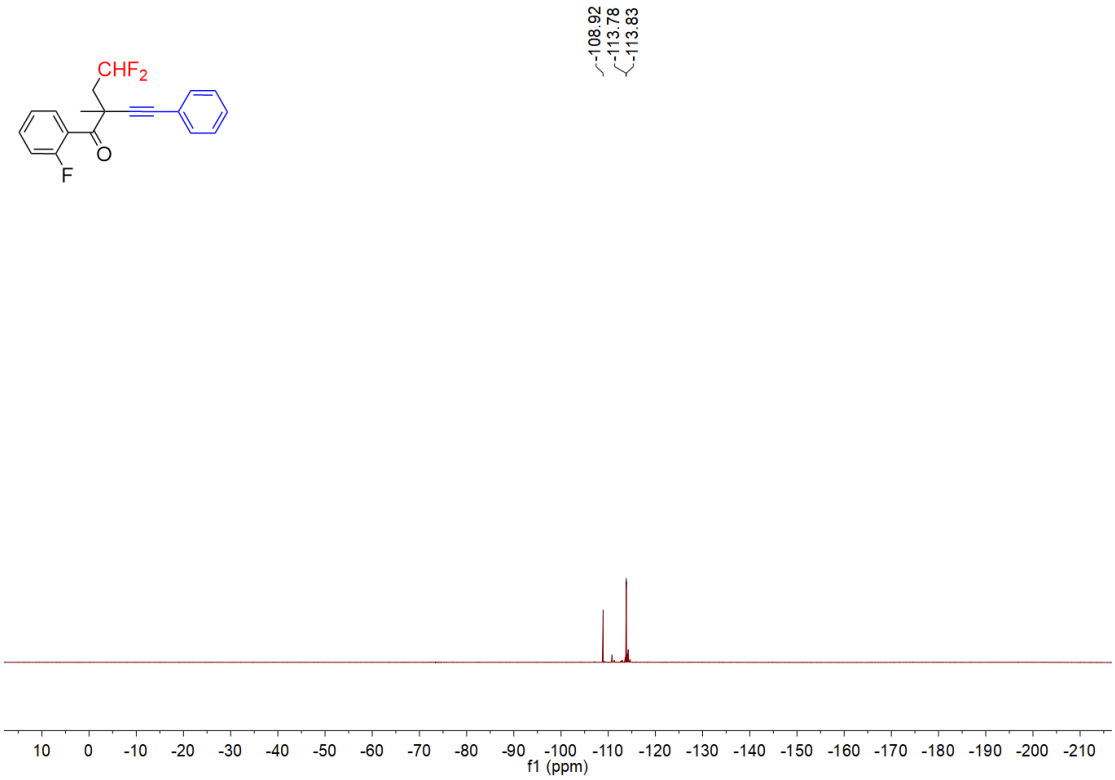

7.81
7.29
7.29
7.24
7.24
7.23
7.22
7.21
7.20
7.20
7.11
6.25
6.24
6.23
6.22
6.11
6.10
6.09
6.08
5.96
5.95
5.95
5.94
2.72
2.71
2.68
2.67
2.66
2.64
2.63
2.62
2.59
2.58
2.24
2.23
1.65
0.00
CHF2
O
1.92
2.10
2.94
1.00
1.20
1.18
6.13
1.10
3.03
f1 (ppm)


198.40
137.73
135.05
134.52
131.37
131.31
128.60
128.41
127.49
124.46
122.55
118.89
116.51
114.13
89.91
87.48
43.49
43.27
43.05
27.03
21.37
CHF2
O
f1 (ppm)

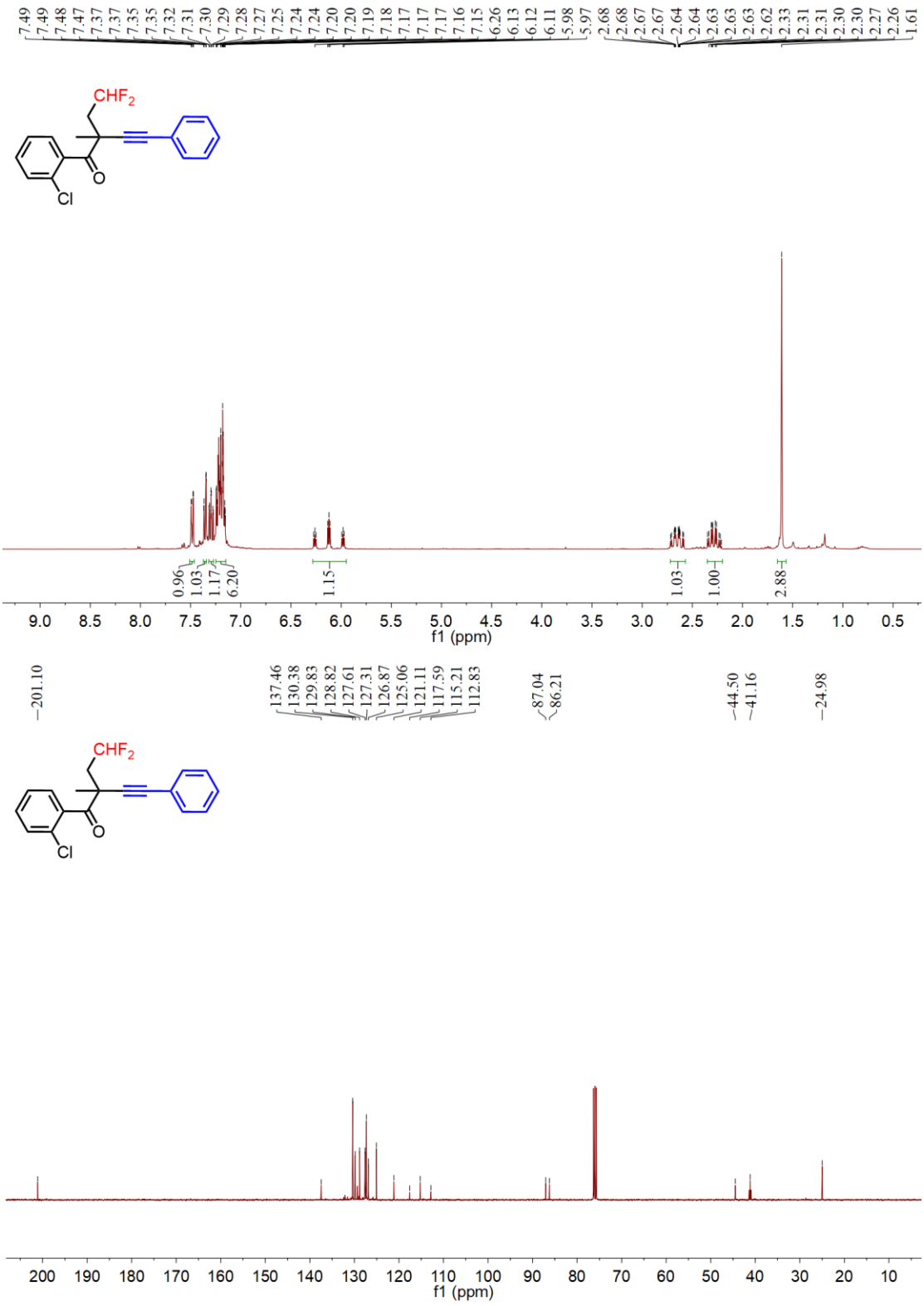

CHF2
O
-112.15
-112.20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

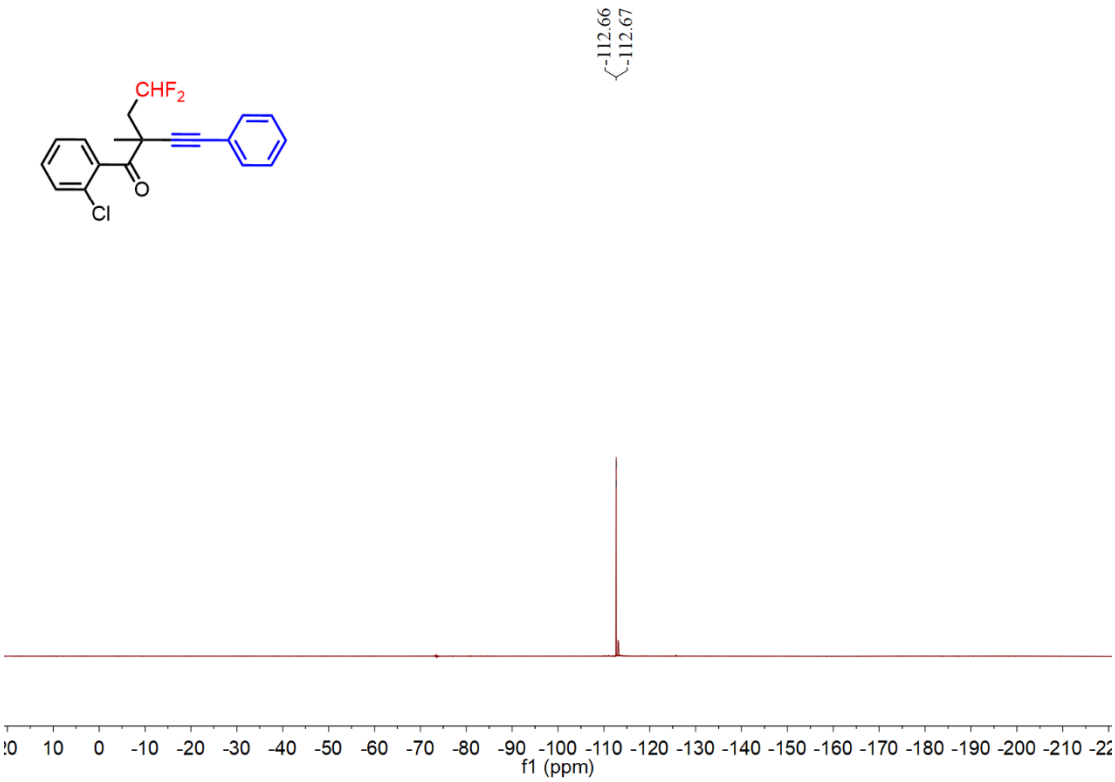
3e


7.54 7.53 7.52 7.50 7.50 7.41 7.40 7.40 7.38 7.37 7.36 7.36 7.35 7.35 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.18 7.17 7.17 7.16 7.16 7.15 7.14 7.13 7.13 7.11 7.11 7.08 7.08 7.06 7.06 7.05 7.03 7.03 6.22 6.09 6.08 6.07 5.94 2.74 2.72 2.70 2.70 2.69 2.68 2.26 2.25 2.24 2.21 2.20 2.18 1.61
CHF2
O
F
1.00 2.00 4.91 2.01 1.07 1.13 1.09 1.13 3.15
f1 (ppm)
199.98 159.31 156.82 131.67 131.59 130.38 128.51 128.48 127.52 127.27 127.19 122.86 121.21 115.22 114.93 114.71 112.84 87.30 85.47 44.20 44.14 44.09 41.95 41.73 41.51 25.17
CHF2
O
F
f1 (ppm)


CHF2
O
F
-108.92
-113.78
-113.83
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)

3f


7.49 7.49 7.48 7.47 7.37 7.37 7.35 7.35 7.32 7.31 7.30 7.29 7.28 7.27 7.25 7.24 7.24 7.20 7.20 7.19 7.18 7.17 7.17 7.17 7.16 7.15 6.26 6.13 6.12 6.11 5.98 5.97 2.68 2.68 2.67 2.67 2.64 2.64 2.63 2.63 2.63 2.62 2.33 2.31 2.31 2.30 2.30 2.27 2.26 1.61
CHF2
O
Cl
0.96 1.03 1.17 6.20 1.15 1.03 1.00 2.88
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
f1 (ppm)
201.10 137.46 130.38 129.83 128.82 127.61 127.31 126.87 125.06 121.11 117.59 115.21 112.83 87.04 86.21 44.50 41.16 24.98
CHF2
O
Cl
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


CHF2
O
Cl
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-112.67
10
0
-10
-20
-30
-40
-50
-60
-70
-80
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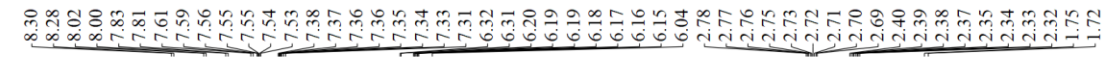
-160
-170
-180
-190
-200
-210
f1 (ppm)

3g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7.81
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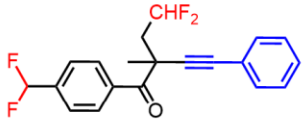
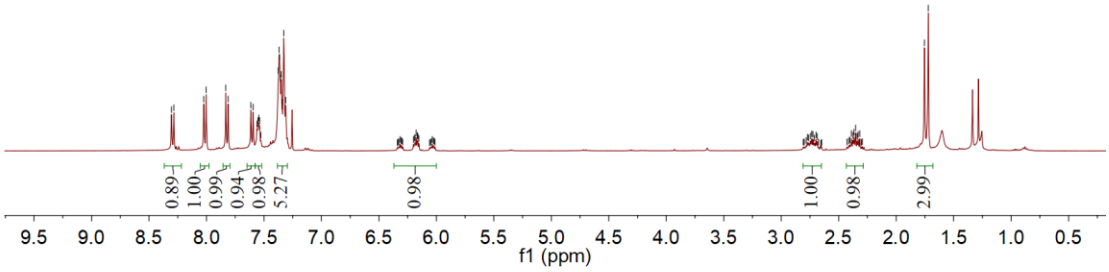
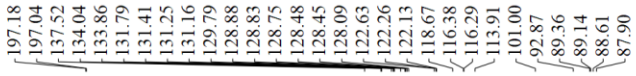
7.55
7.54
7.53
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.31
6.32
6.31
6.20
6.19
6.19
6.18
6.17
6.16
6.15
6.04
2.78
2.77
2.76
2.75
2.73
2.72
2.71
2.70
2.69
2.40
2.39
2.38
2.37
2.35
2.34
2.33
2.32
1.75
1.72


CHF2
F
F
O


0.89
1.00
0.99
0.94
0.98
5.27
0.98
1.00
0.98
2.99
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
f1 (ppm)


197.18
197.04
137.52
134.04
133.86
131.79
131.41
131.25
131.16
129.79
128.88
128.83
128.75
128.48
128.45
128.09
122.63
122.26
122.13
118.67
116.38
116.29
113.91
101.00
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89.36
89.14
88.61
87.90
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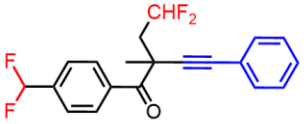
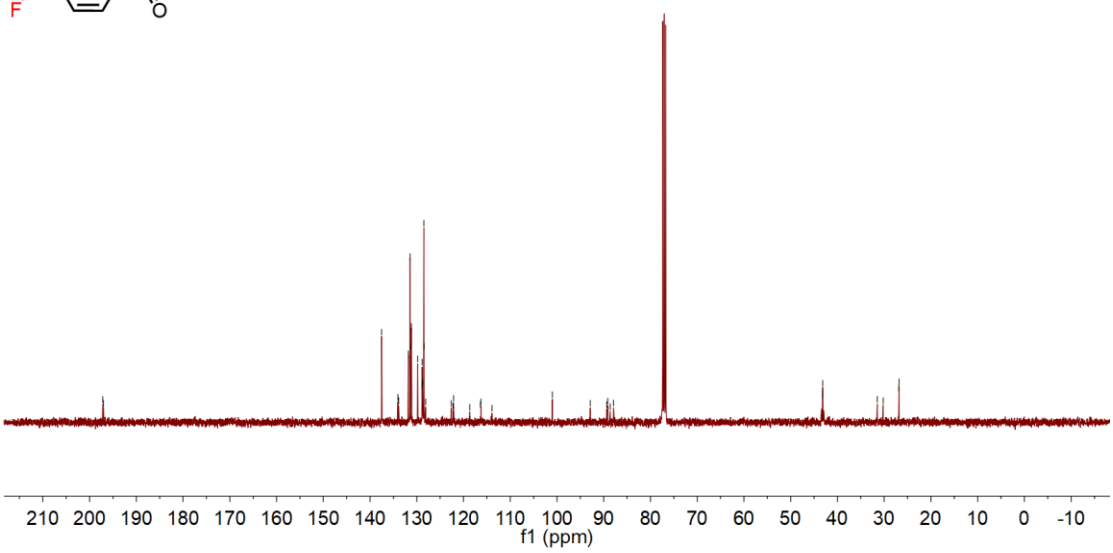
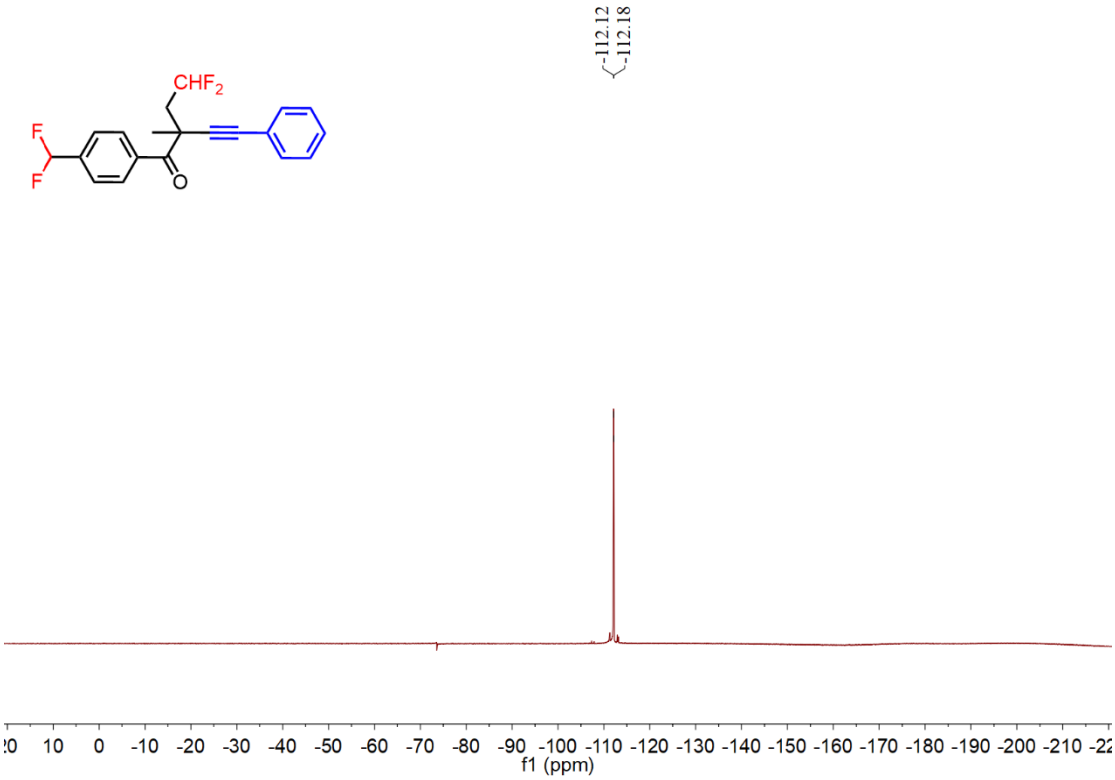
43.15
31.46
30.21
26.89
26.84


CHF2
F
F
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)


CHF2
F
F
O
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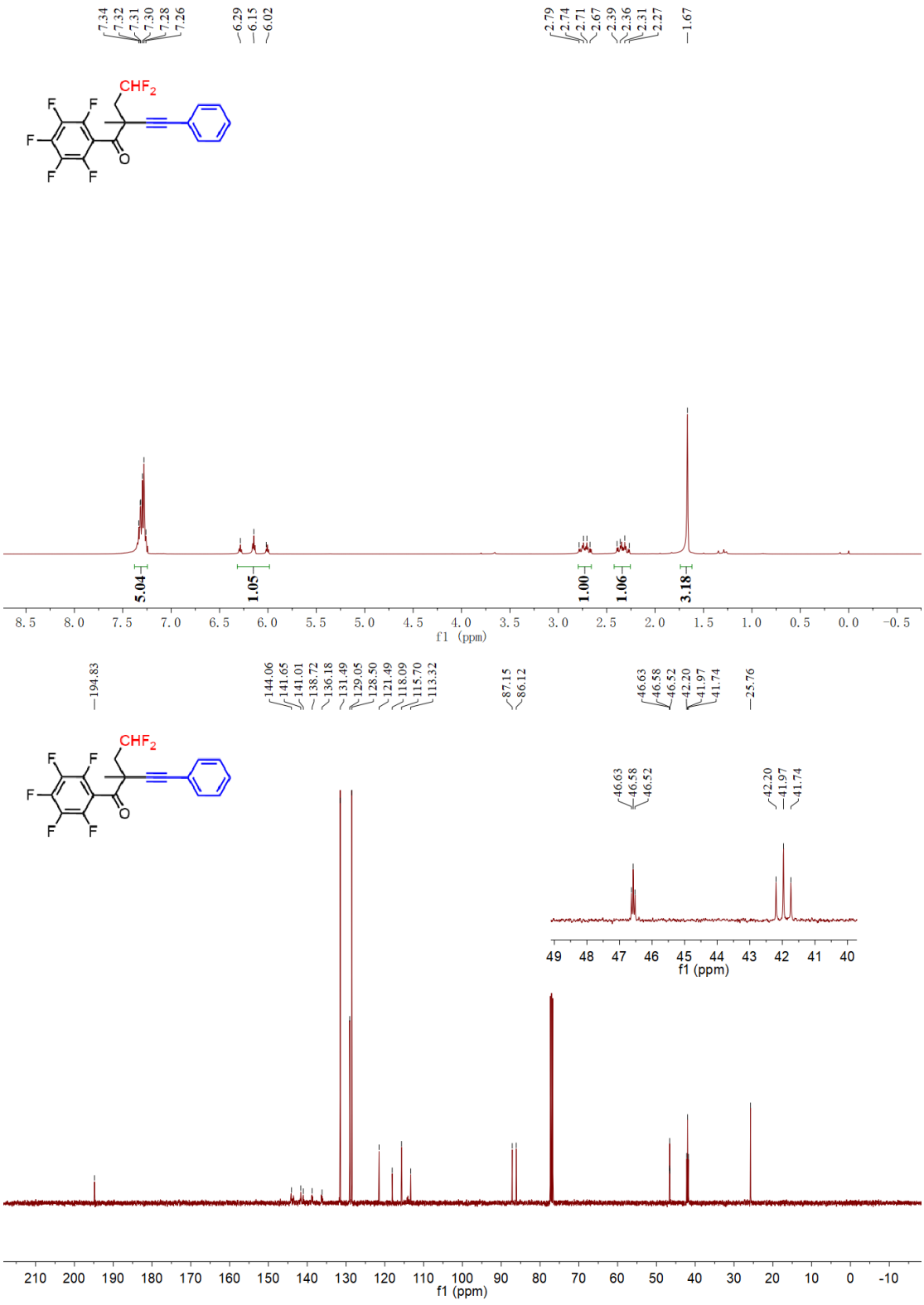
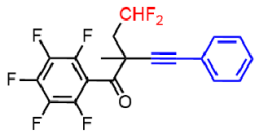
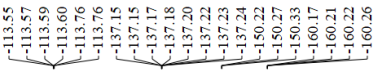
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

3h


7.34
7.32
7.31
7.30
7.28
7.26
6.29
6.15
6.02
2.79
2.74
2.71
2.67
2.39
2.36
2.31
2.27
1.67
CHF2
F
F
F
F
F
O
5.04
1.05
1.00
1.06
3.18
f1 (ppm)
194.83
144.06
141.65
141.01
138.72
136.18
131.49
129.05
128.50
121.49
118.09
115.70
113.32
87.15
86.12
46.63
46.58
46.52
42.20
41.97
41.74
25.76
f1 (ppm)


CHF2
F
F
F
F
F
O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-137.15
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-137.18
-137.20
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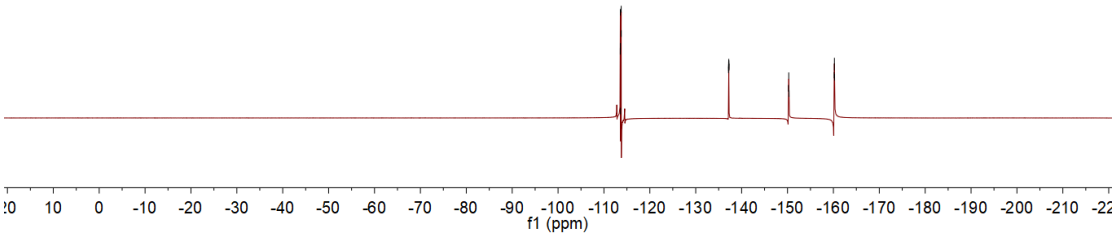
-150.22
-150.27
-150.33
-160.17
-160.21
-160.22
-160.26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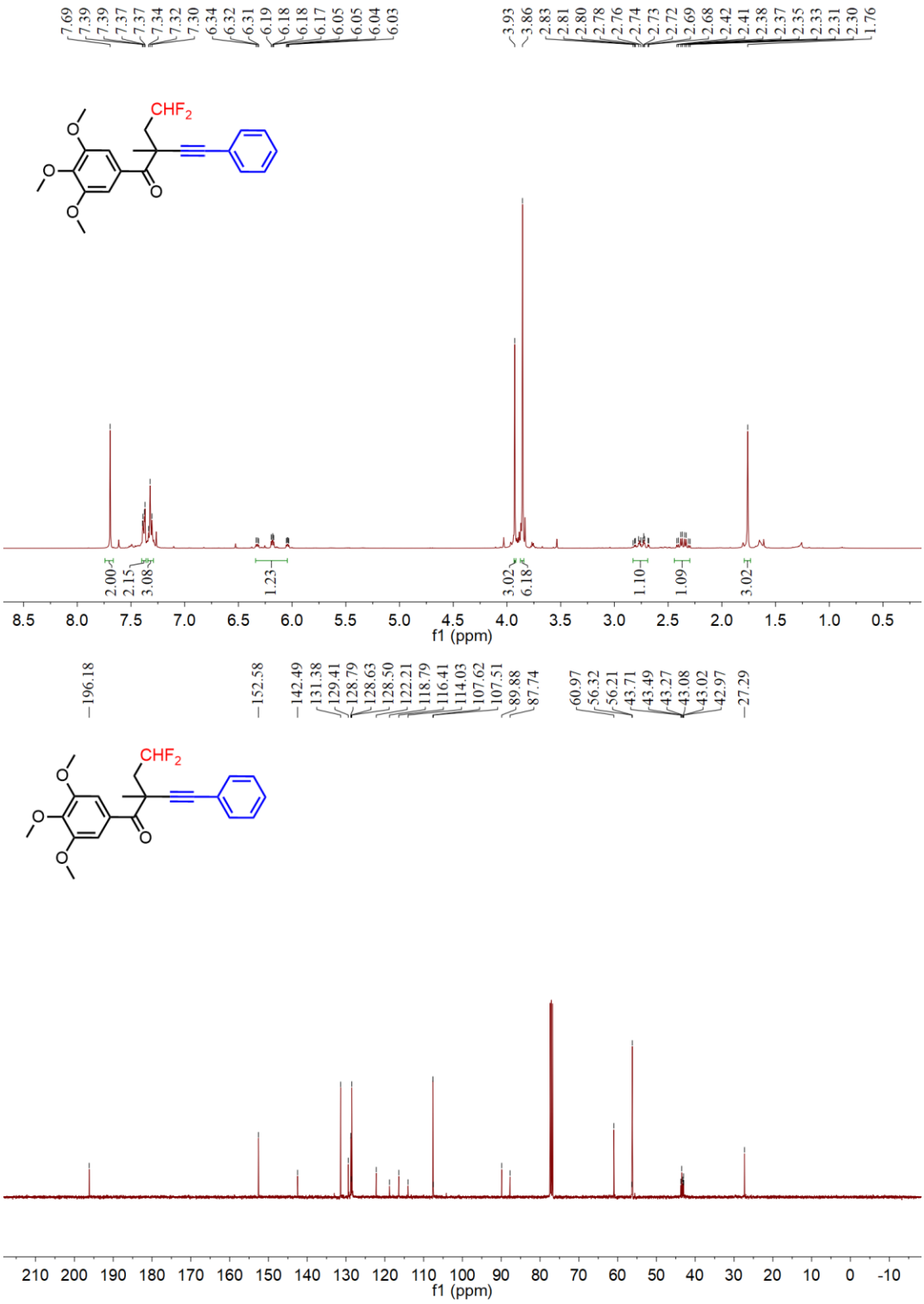
f1 (ppm)

3i


7.69
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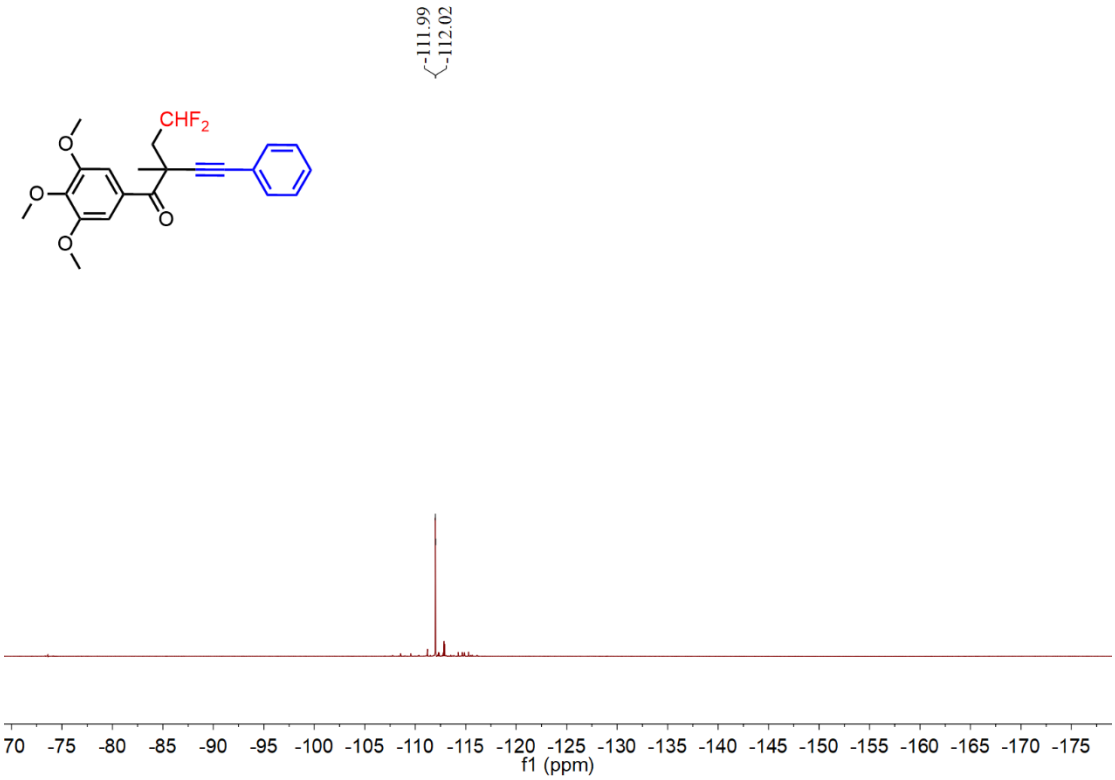
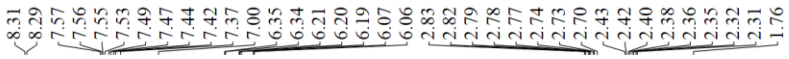
7.39
7.37
7.37
7.34
7.32
7.30
6.34
6.32
6.31
6.19
6.18
6.18
6.17
6.05
6.05
6.04
6.03
3.93
3.86
2.83
2.81
2.80
2.78
2.76
2.74
2.73
2.72
2.69
2.68
2.42
2.41
2.38
2.37
2.35
2.33
2.31
2.30
1.76
CHF2
O
O
O
O
2.00
2.15
3.08
1.23
3.02
6.18
1.10
1.09
3.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
196.18
152.58
142.49
131.38
129.41
128.79
128.63
128.50
122.21
118.79
116.41
114.03
107.62
107.51
89.88
87.74
60.97
56.32
56.21
43.71
43.49
43.27
43.08
43.02
42.97
27.29
CHF2
O
O
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)


-111.99
-112.02
CHF2
O
O
O
O
70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175
f1 (ppm)

3j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8.29
7.57
7.56
7.55
7.53
7.49
7.47
7.44
7.42
7.37
7.00
6.35
6.34
6.21
6.20
6.19
6.07
6.06
2.83
2.82
2.79
2.78
2.77
2.74
2.73
2.70
2.43
2.42
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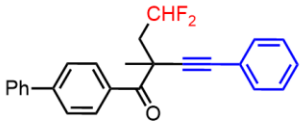
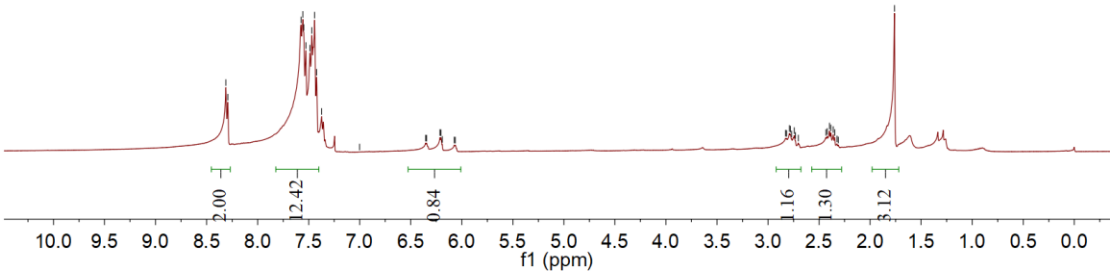
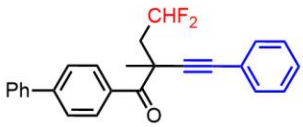
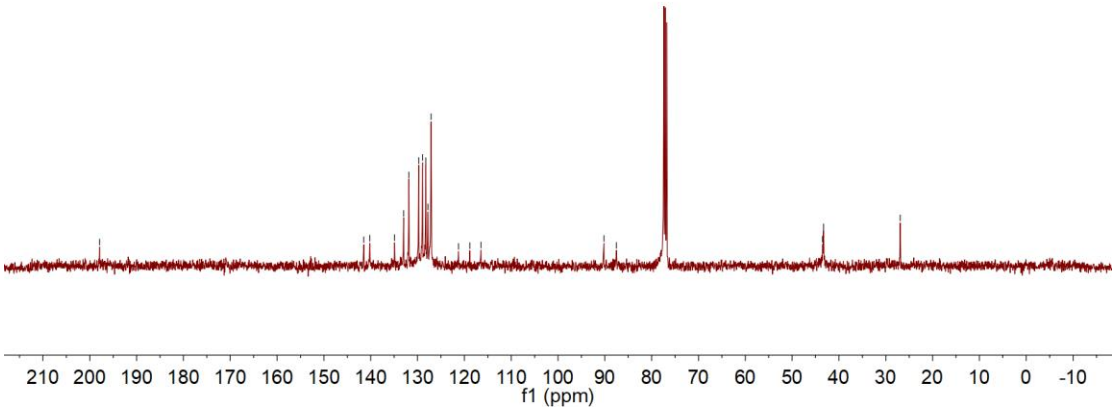
2.38
2.36
2.35
2.32
2.31
1.76

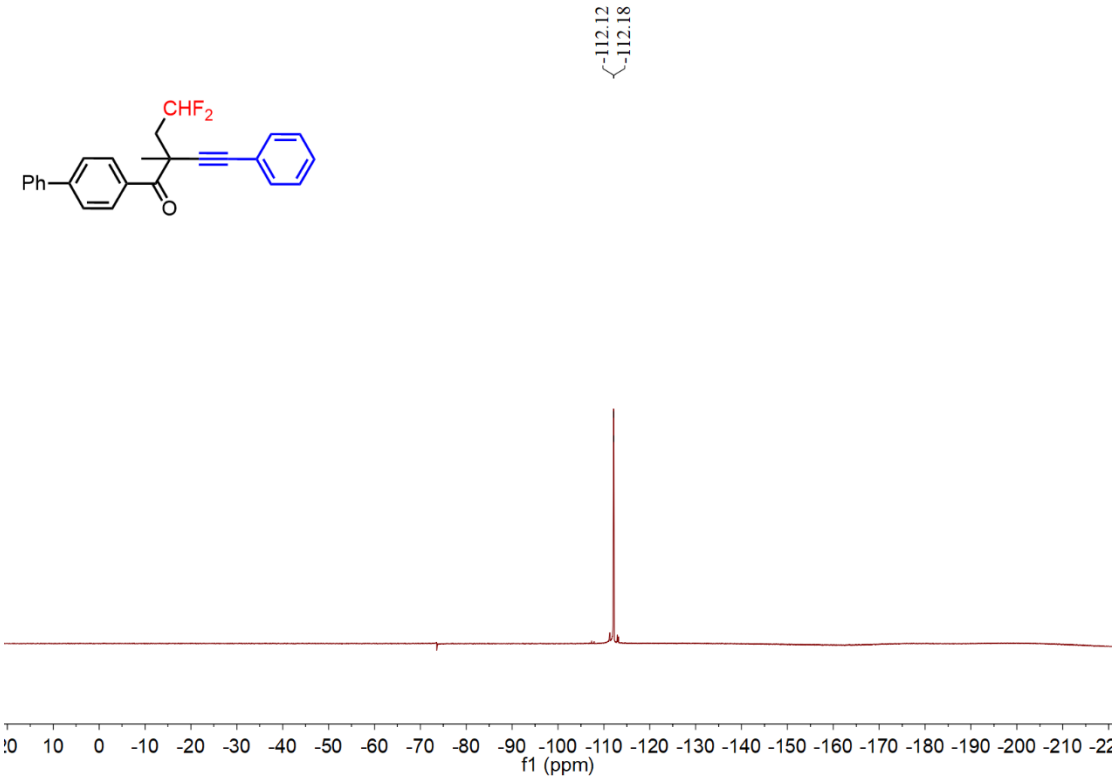

CHF2
Ph
O


2.00
12.42
0.84
1.16
1.30
3.12
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

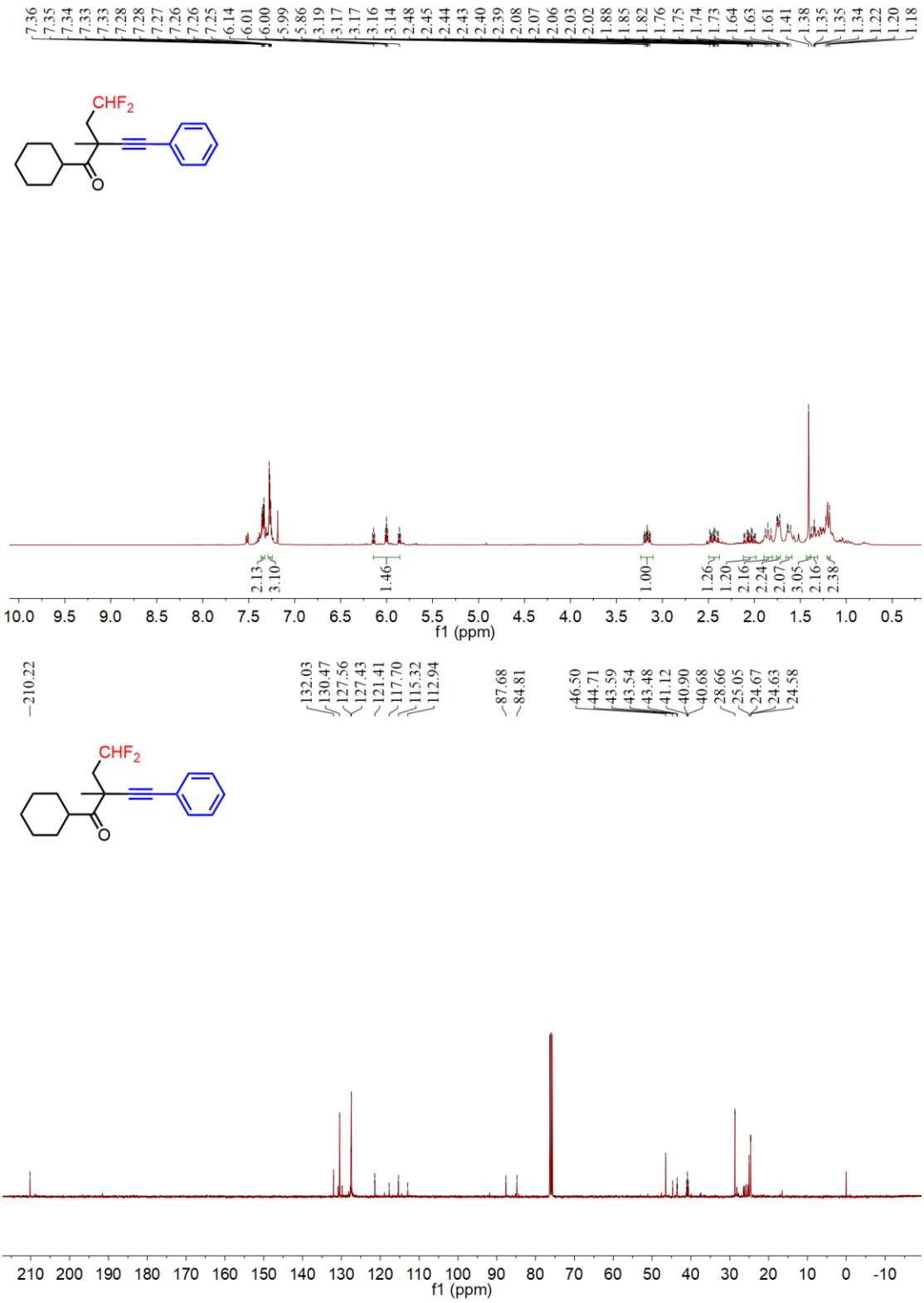

197.93
141.48
140.22
134.90
132.97
131.86
129.76
128.92
128.24
127.79
127.09
121.25
118.85
116.47
90.20
87.52
43.50
43.30
26.92

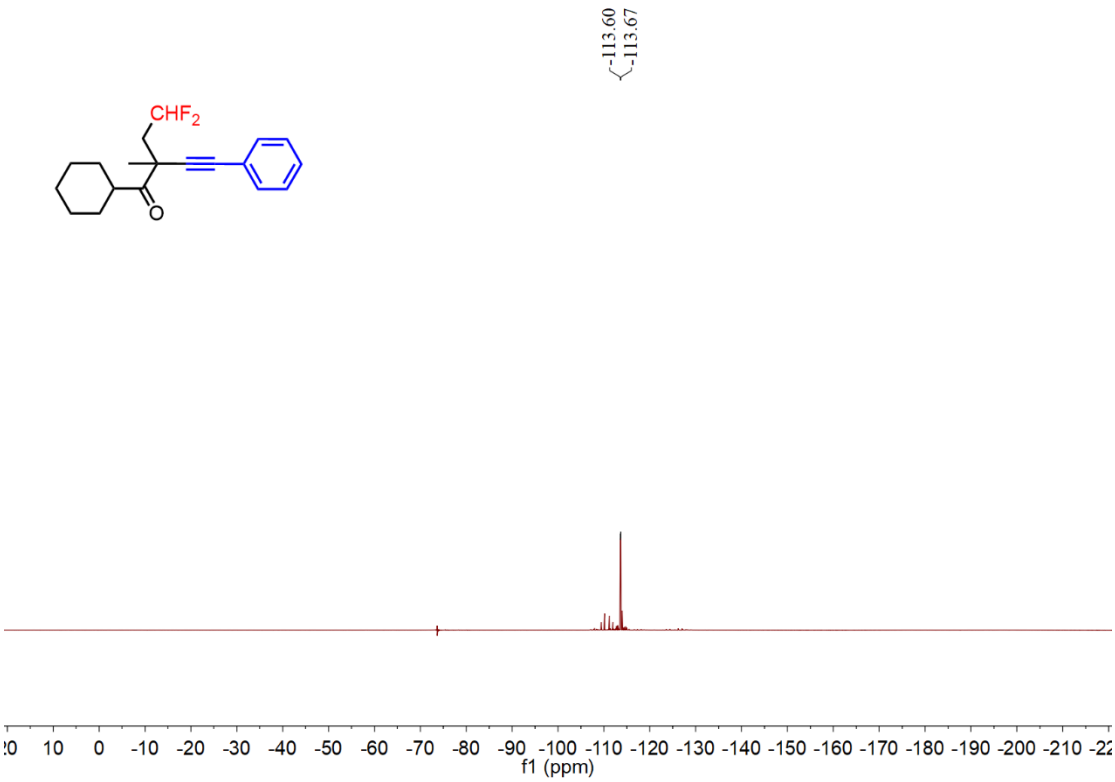

CHF2
Ph
O


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)

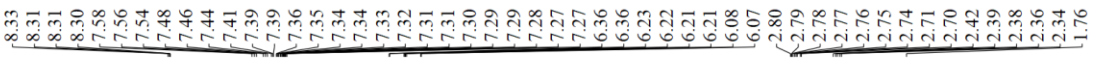

-112.12
-112.18
CHF2
Ph
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

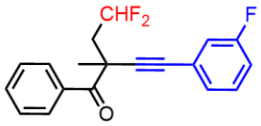
3k

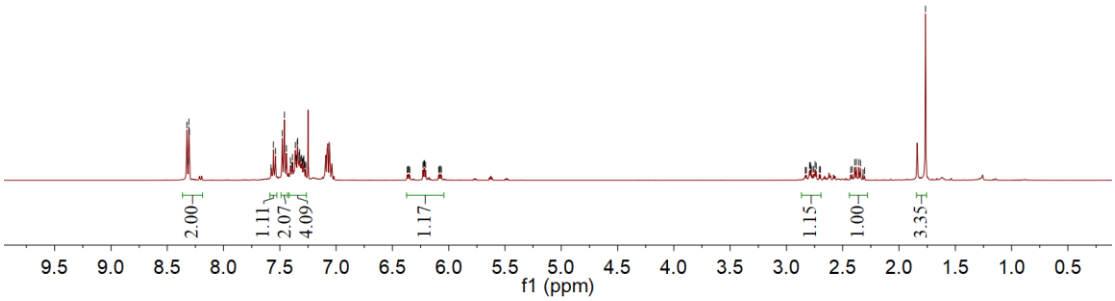

7.36 7.35 7.34 7.33 7.33 7.28 7.28 7.27 7.26 7.26 7.25 6.14 6.01 6.00 5.99 5.86 3.19 3.17 3.17 3.16 3.14 2.48 2.45 2.44 2.43 2.40 2.39 2.08 2.07 2.06 2.03 2.02 1.88 1.85 1.82 1.76 1.75 1.74 1.73 1.64 1.63 1.61 1.41 1.38 1.35 1.35 1.34 1.22 1.20 1.18
CHF2
O
2.13 3.10 1.46 1.00 1.26 1.20 2.16 2.24 2.07 3.05 2.16 2.38
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
210.22
132.03 130.47 127.56 127.43 121.41 117.70 115.32 112.94
87.68 84.81
46.50 44.71 43.59 43.54 43.48 41.12 40.90 40.68 28.66 25.05 24.67 24.63 24.58
CHF2
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)

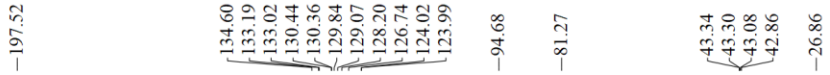

-113.60
-113.67
CHF2
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

3l


8.33 8.31 8.31 8.30 7.58 7.56 7.54 7.48 7.46 7.44 7.41 7.39 7.39 7.36 7.35 7.34 7.34 7.33 7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.27 7.27 6.36 6.36 6.23 6.22 6.21 6.21 6.08 6.07 2.80 2.79 2.78 2.77 2.76 2.75 2.74 2.71 2.70 2.42 2.39 2.38 2.36 2.34 1.76


CHF2
F
O


2.00
1.11
2.07
4.09
1.17
1.15
1.00
3.35
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
f1 (ppm)


197.52
134.60
133.19
133.02
130.44
130.36
129.84
129.07
128.20
126.74
124.02
123.99
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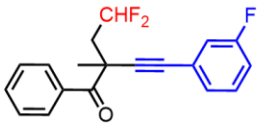
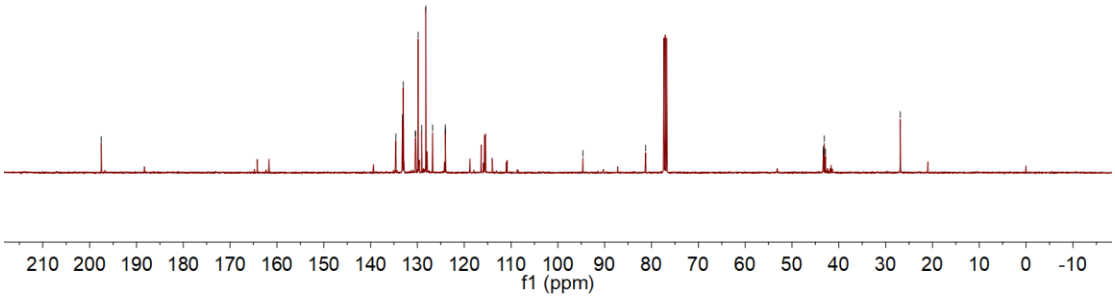
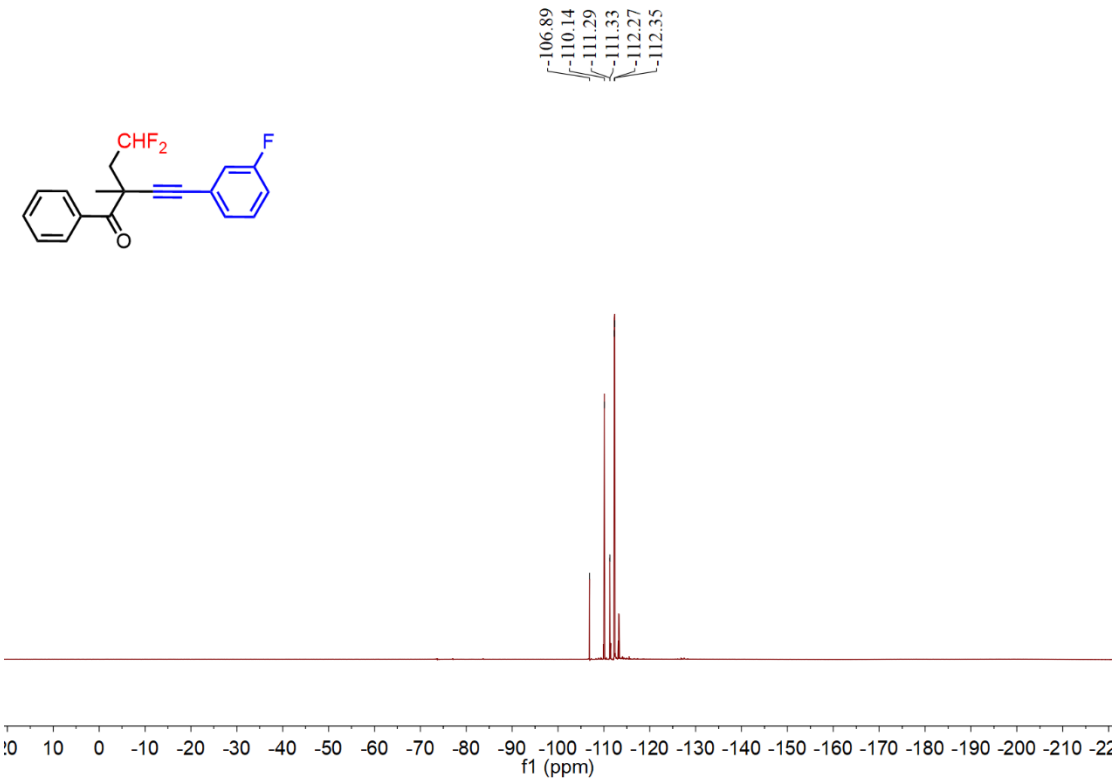
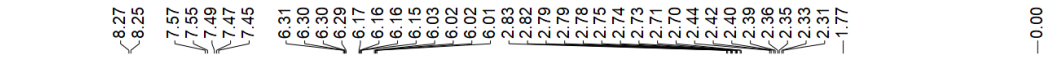
81.27
43.34
43.30
43.08
42.86
26.86


CHF2
F
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)


-106.89
-110.14
-111.29
-111.33
-112.27
-112.35
CHF2
F
O
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)

3m


8.27
8.25
7.57
7.55
7.49
7.47
7.45
6.31
6.30
6.30
6.29
6.17
6.16
6.16
6.15
6.03
6.02
6.02
6.01
2.83
2.82
2.79
2.79
2.78
2.75
2.74
2.73
2.71
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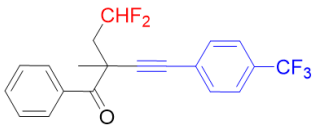
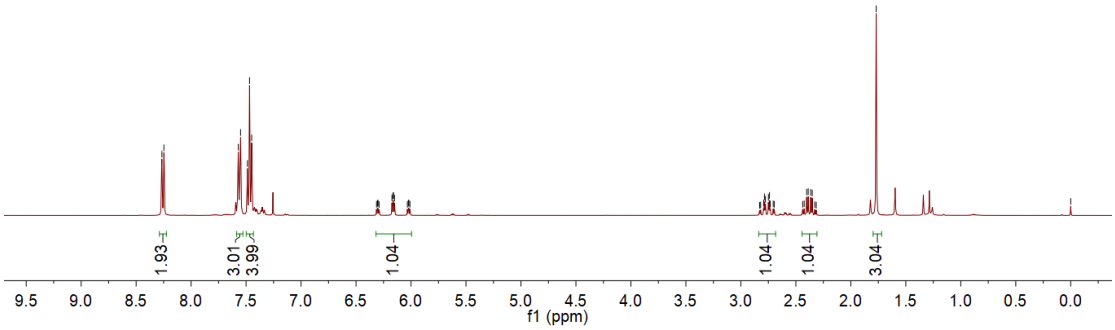
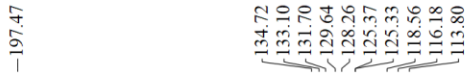
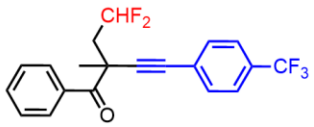
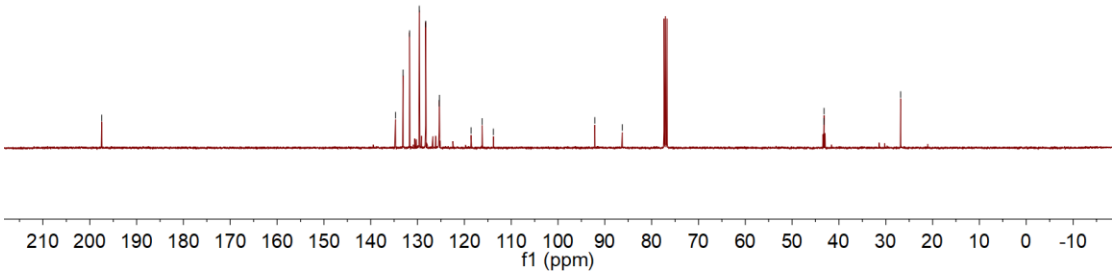
2.36
2.35
2.33
2.31
1.77
0.00

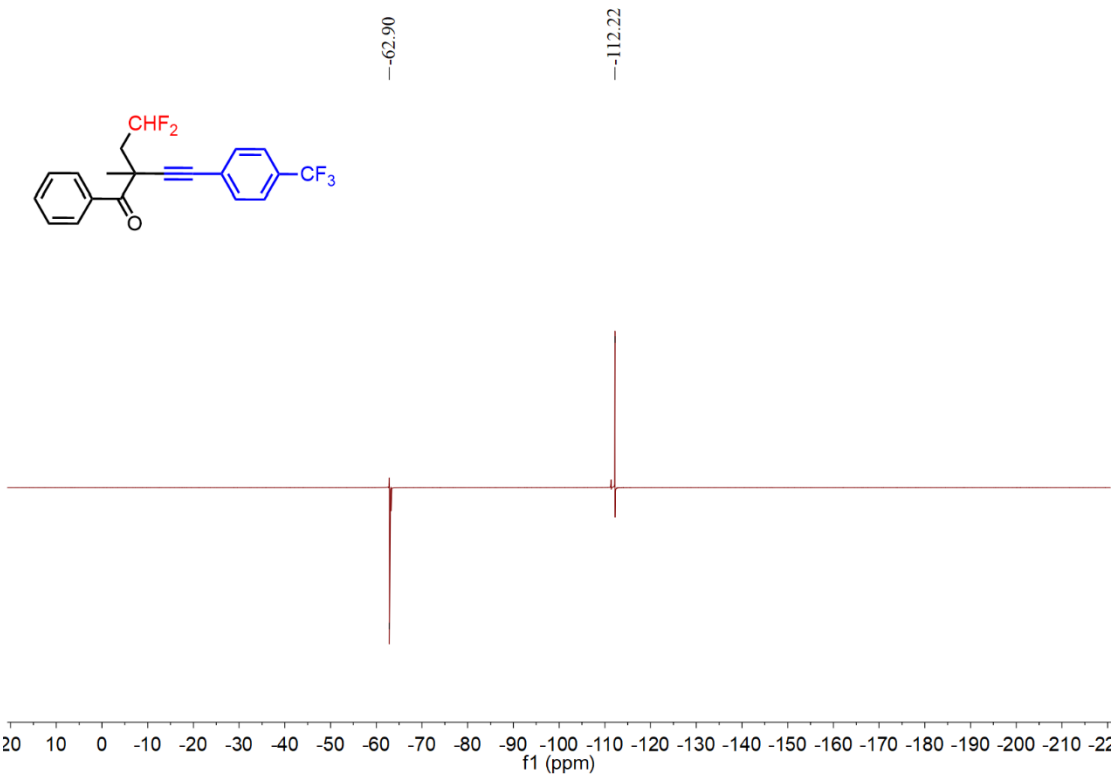

CHF2
CF3
O


1.93
3.01
3.99
1.04
1.04
1.04
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

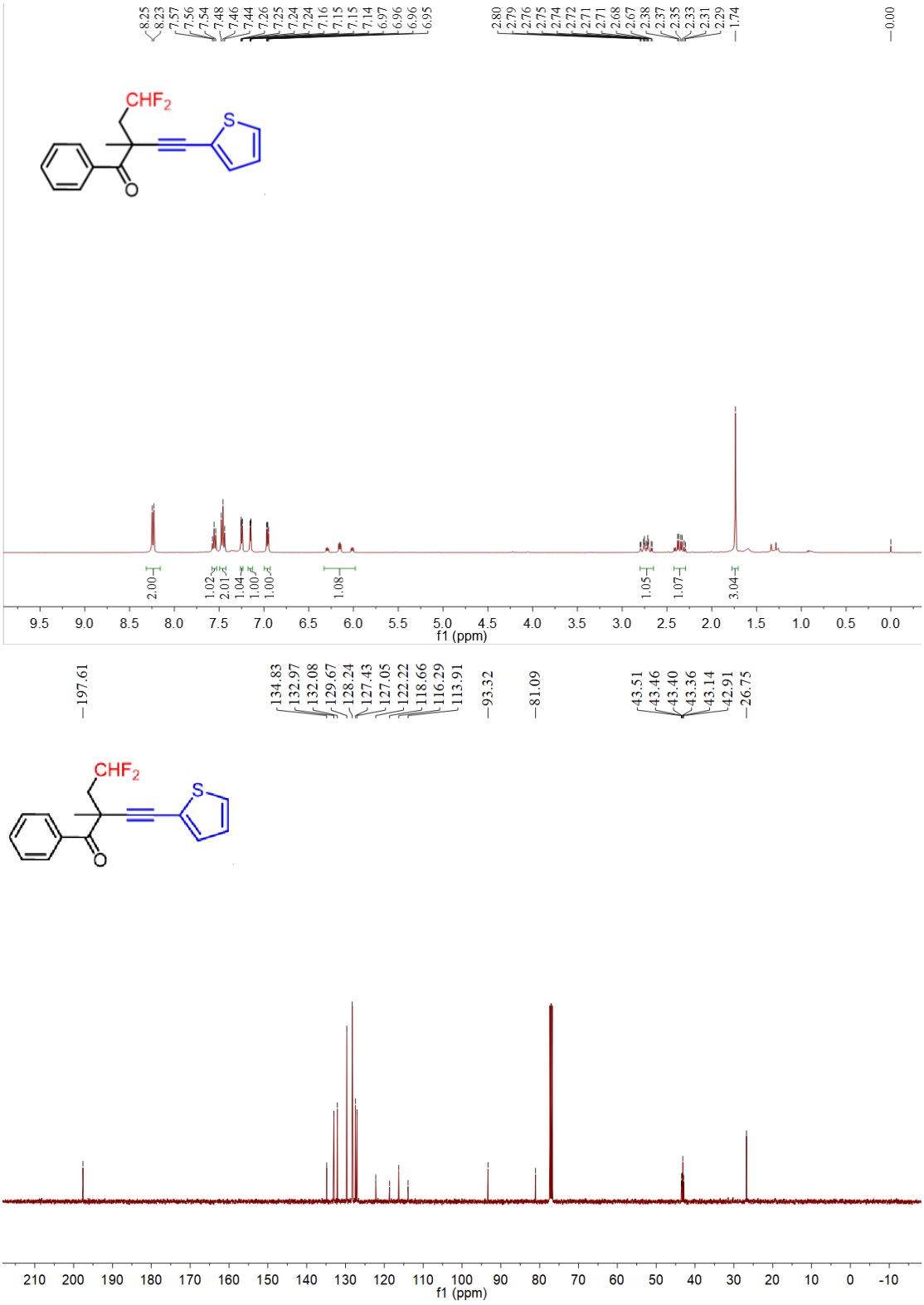

197.47
134.72
133.10
131.70
129.64
128.26
125.37
125.33
118.56
116.18
113.80
92.14
86.29
43.23
43.19
26.82

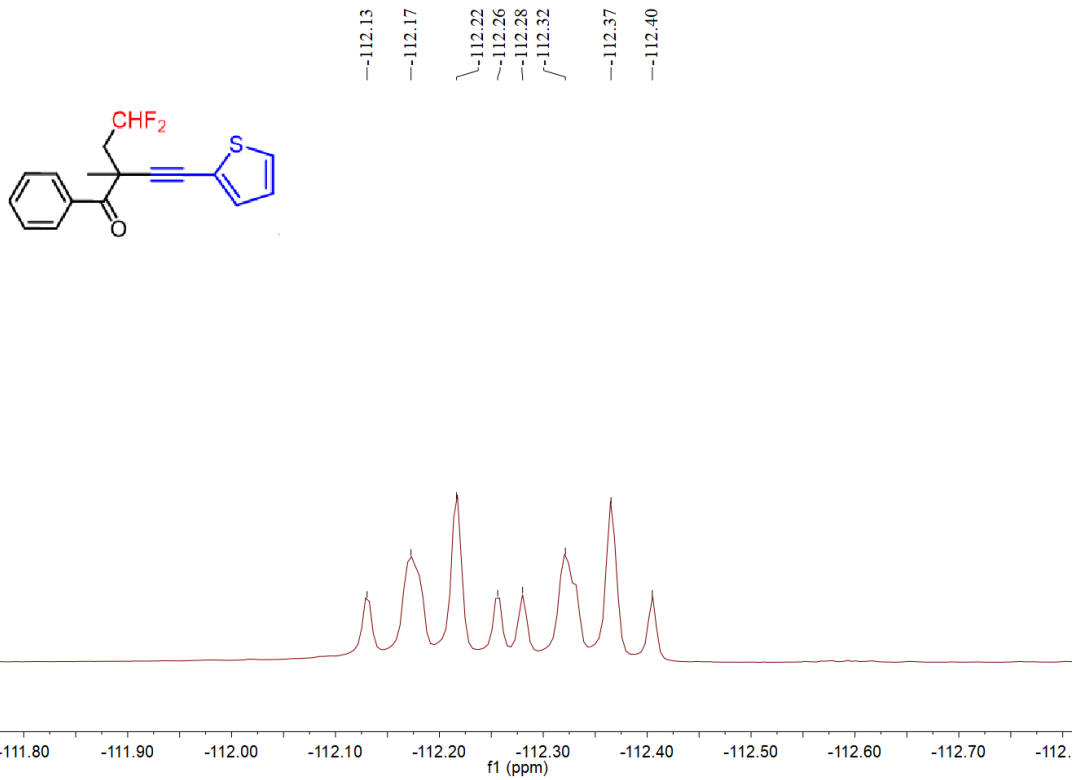

CHF2
CF3
O


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)

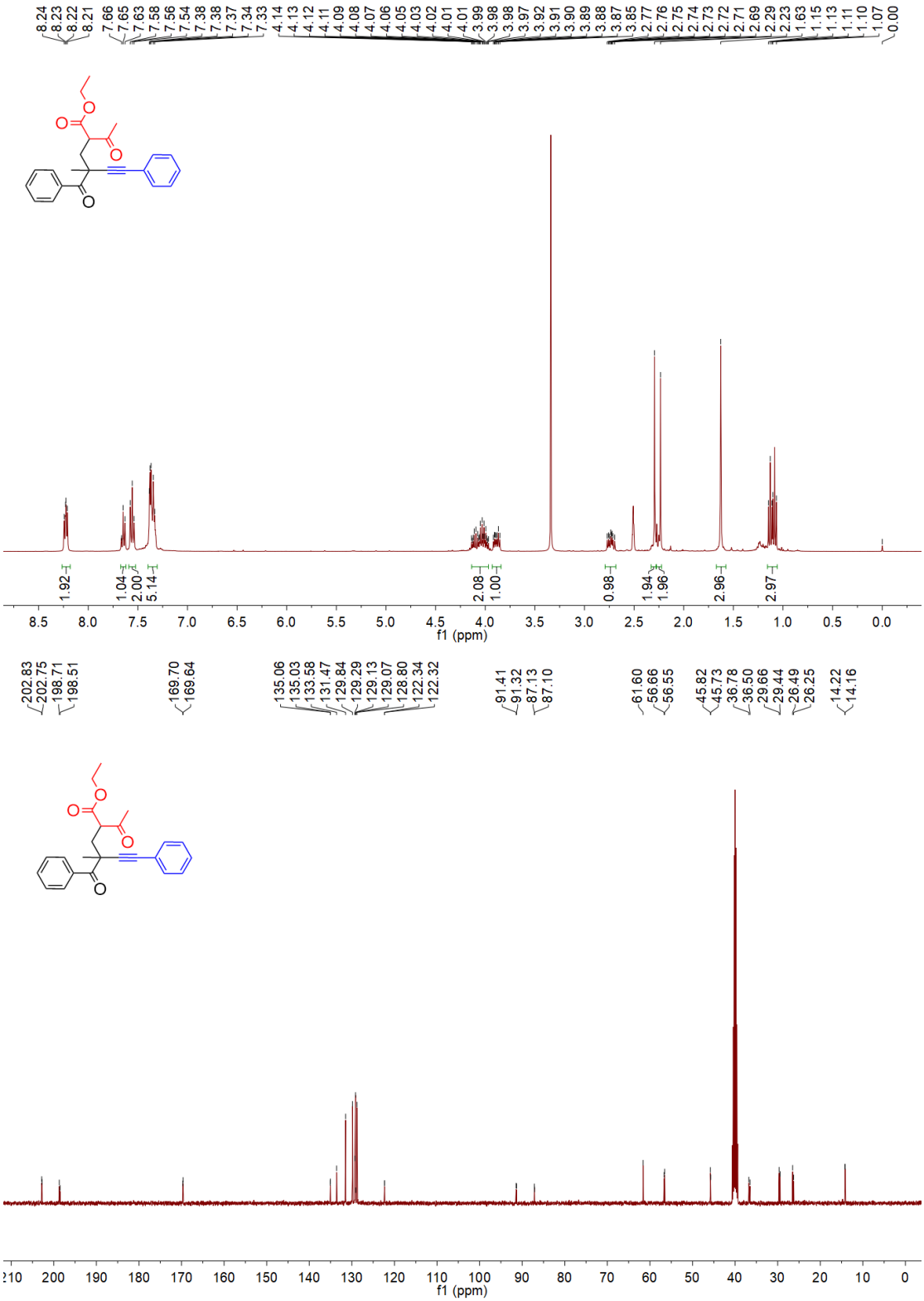

-62.90
-112.22
CHF2
CF3
O
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -22
f1 (ppm)

3n

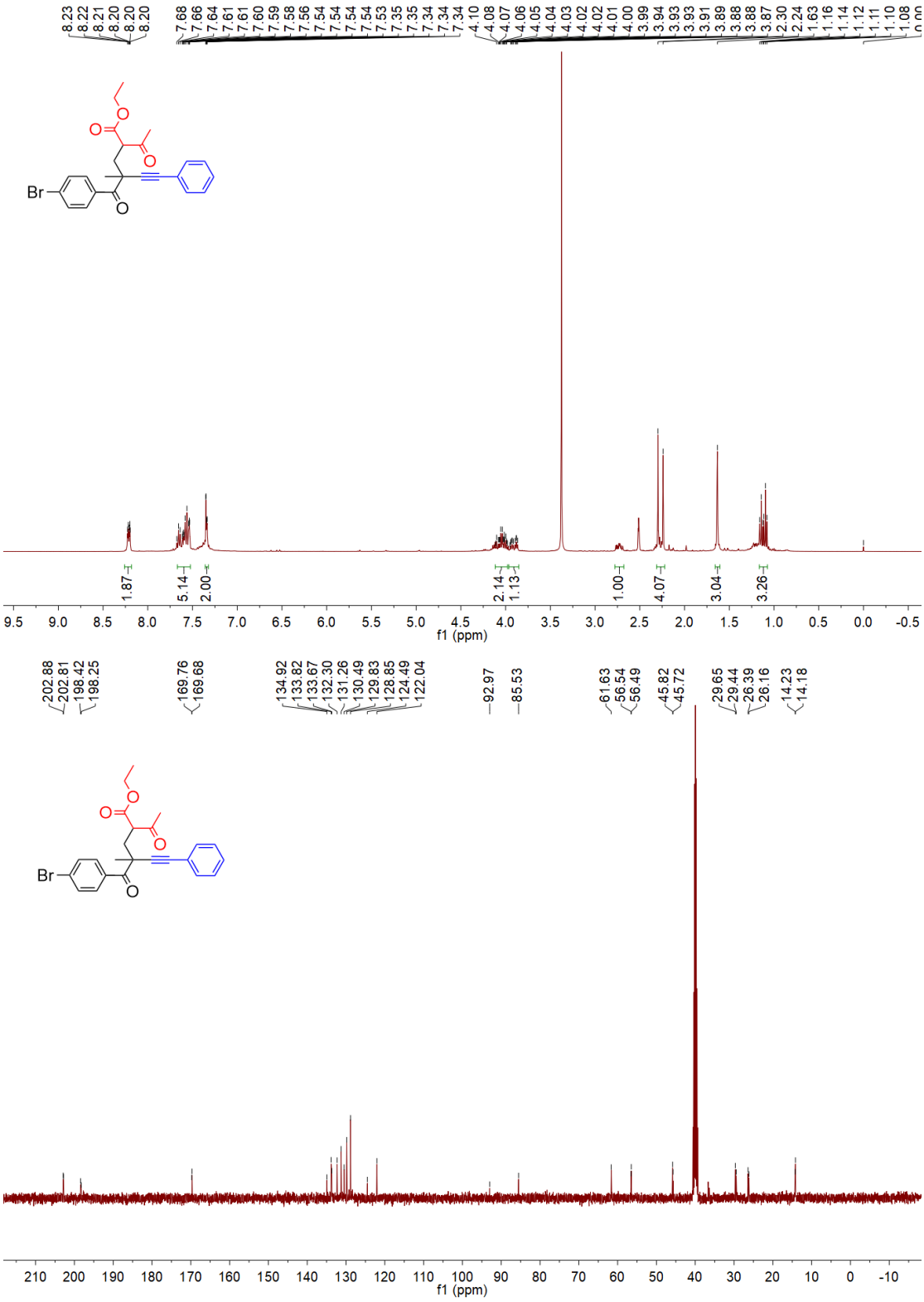

8.25
8.23
7.57
7.56
7.54
7.48
7.46
7.44
7.26
7.25
7.24
7.24
7.16
7.15
7.15
7.14
6.97
6.96
6.96
6.95
2.80
2.79
2.76
2.75
2.74
2.72
2.71
2.71
2.68
2.67
2.38
2.37
2.35
2.33
2.31
2.29
1.74
0.00
CHF2
S
O
2.00
1.02
2.01
1.04
1.00
1.00
1.08
1.05
1.07
3.04
f1 (ppm)
197.61
134.83
132.97
132.08
129.67
128.24
127.43
127.05
122.22
118.66
116.29
113.91
93.32
81.09
43.51
43.46
43.40
43.36
43.14
42.91
26.75
CHF2
S
O
f1 (ppm)


-112.13
-112.17
-112.22
-112.26
-112.28
-112.32
-112.37
-112.40
CHF2
S
O
-111.80
-111.90
-112.00
-112.10
-112.20
-112.30
-112.40
-112.50
-112.60
-112.70
-112.
f1 (ppm)

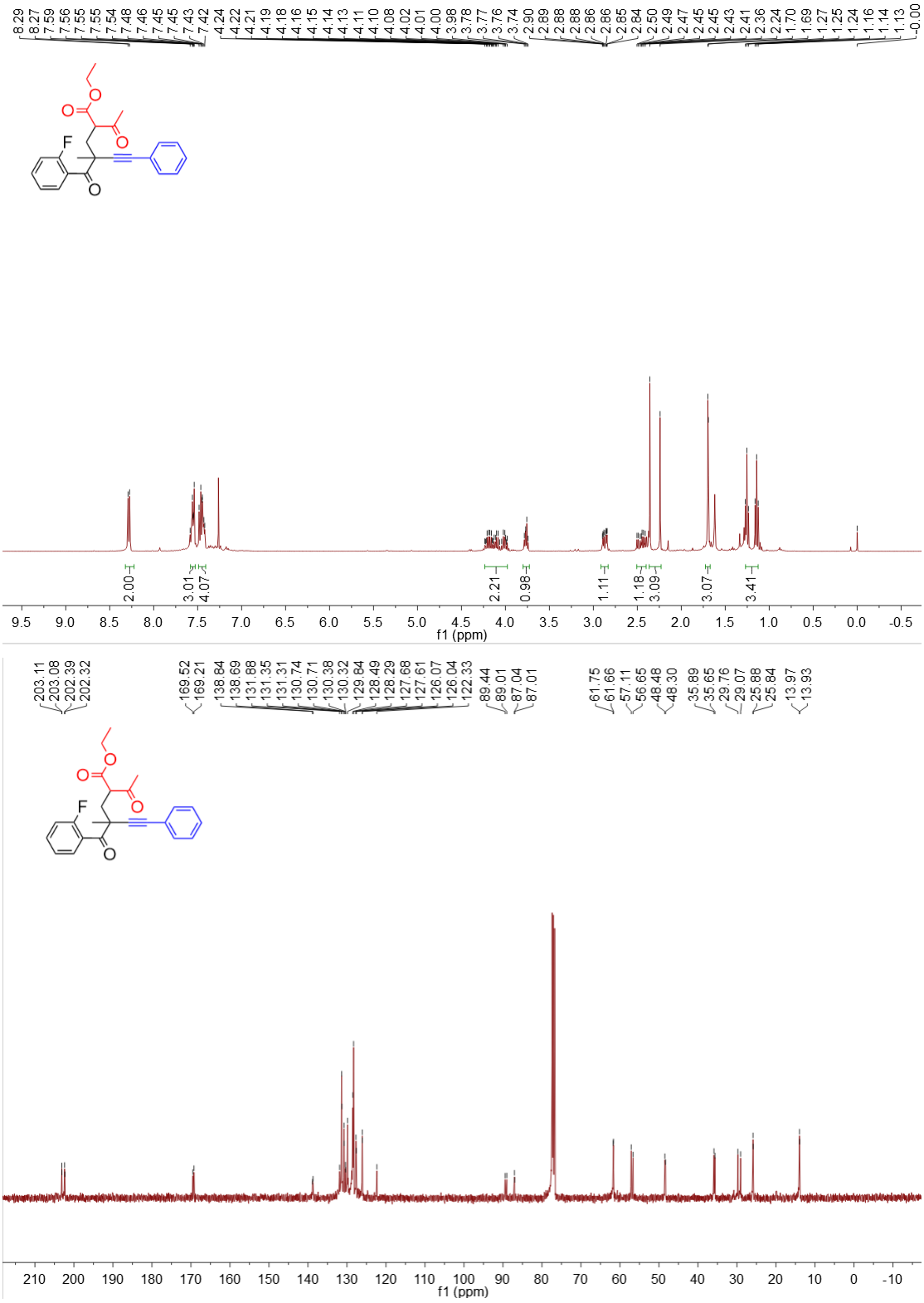
4a

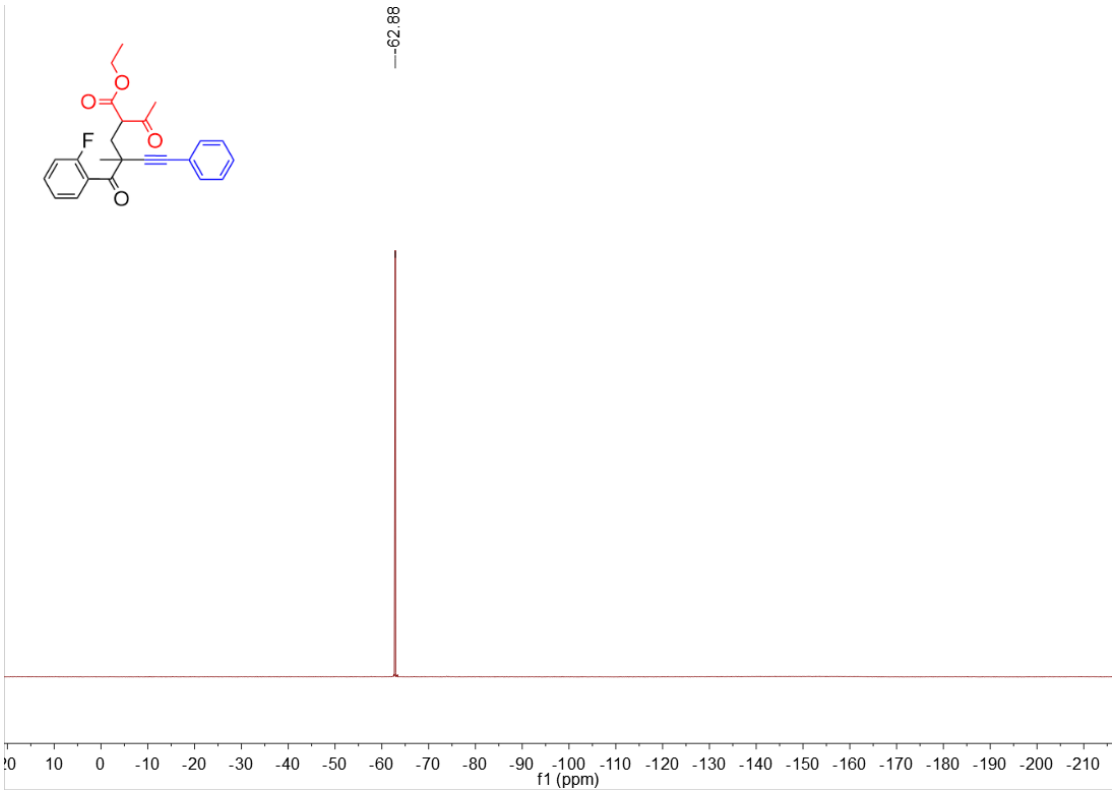

8.24 8.23 8.22 8.21 7.66 7.65 7.63 7.58 7.56 7.54 7.38 7.38 7.37 7.34 7.33 4.14 4.13 4.12 4.11 4.09 4.08 4.07 4.06 4.05 4.03 4.02 4.01 4.01 3.99 3.98 3.98 3.97 3.92 3.91 3.90 3.89 3.88 3.87 3.85 2.77 2.76 2.75 2.74 2.73 2.72 2.71 2.69 2.29 2.23 1.63 1.15 1.13 1.11 1.10 1.07 0.00
1.92 1.04 2.00 5.14 2.08 1.00 0.98 1.94 1.96 2.96 2.97
f1 (ppm)
202.83 202.75 198.71 198.51 169.70 169.64 135.06 135.03 133.58 131.47 129.84 129.29 129.13 129.07 128.80 122.34 122.32 91.41 91.32 87.13 87.10 61.60 56.66 56.55 45.82 45.73 36.78 36.50 29.66 29.44 26.49 26.25 14.22 14.16
f1 (ppm)

4b

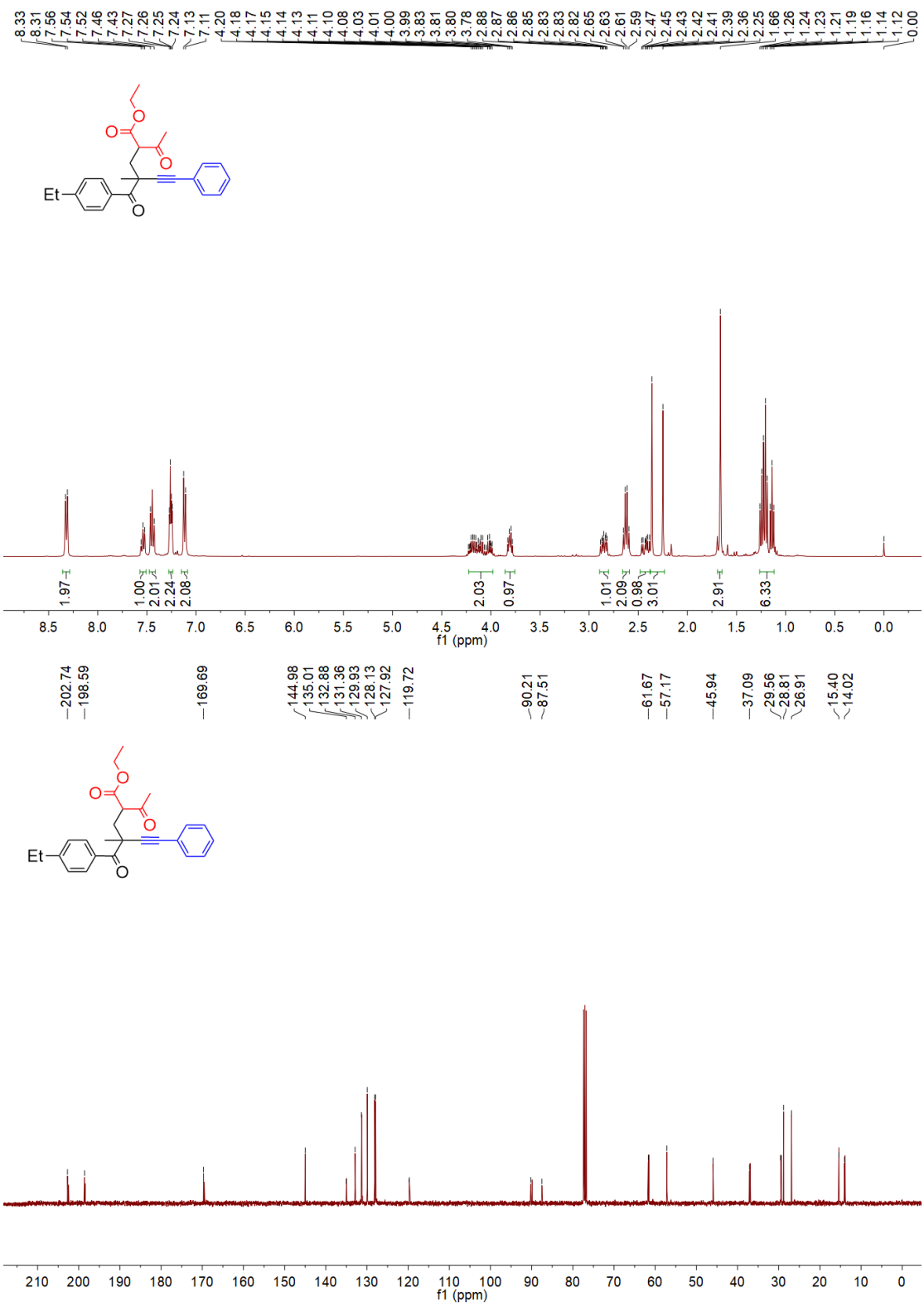

8.23 8.22 8.21 8.20 8.20 8.20
7.68 7.66 7.64 7.61 7.61 7.60 7.59 7.58 7.56 7.54 7.54 7.54 7.54 7.53 7.35 7.35 7.34 7.34 7.34
4.10 4.08 4.07 4.06 4.05 4.04 4.03 4.02 4.02 4.01 4.00 3.99 3.94 3.93 3.93 3.91 3.89 3.88 3.88 3.87 2.30 2.24 1.63 1.16 1.14 1.12 1.11 1.10 1.08
Br
O
O
O
O
1.87 5.14 2.00 2.14 1.13 1.00 4.07 3.04 3.26
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)
202.88 202.81 198.42 198.25 169.76 169.68 134.92 133.82 133.67 132.30 131.26 130.49 129.83 128.85 124.49 122.04 92.97 85.53 61.63 56.54 56.49 45.82 45.72 29.65 29.44 26.39 26.16 14.23 14.18
Br
O
O
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)

4c


8.29 8.27 7.59 7.56 7.55 7.55 7.54 7.48 7.46 7.45 7.45 7.43 7.42 4.24 4.22 4.21 4.19 4.18 4.16 4.15 4.14 4.13 4.11 4.10 4.08 4.02 4.01 4.00 3.98 3.78 3.77 3.76 3.74 2.90 2.89 2.88 2.88 2.86 2.86 2.85 2.84 2.50 2.49 2.47 2.45 2.45 2.43 2.41 2.36 2.24 1.70 1.69 1.27 1.25 1.24 1.16 1.14 1.13 0.00
F
O
O
O
O
2.00 3.01 4.07 2.21 0.98 1.11 1.18 3.09 3.07 3.41
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)
203.11 203.08 202.39 202.32 169.52 169.21 138.84 138.69 131.88 131.35 131.31 130.74 130.71 130.38 130.32 129.84 128.49 128.29 127.68 127.61 126.07 126.04 122.33 89.44 89.01 87.04 87.01 61.75 61.66 57.11 56.65 48.48 48.30 35.89 35.65 29.76 29.07 25.88 25.84 13.97 13.93
F
O
O
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)


-62.88
O
O
F
O
O
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)

4d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7.27
7.26
7.25
7.24
7.13
7.11
4.20
4.18
4.17
4.15
4.14
4.13
4.11
4.10
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2.87
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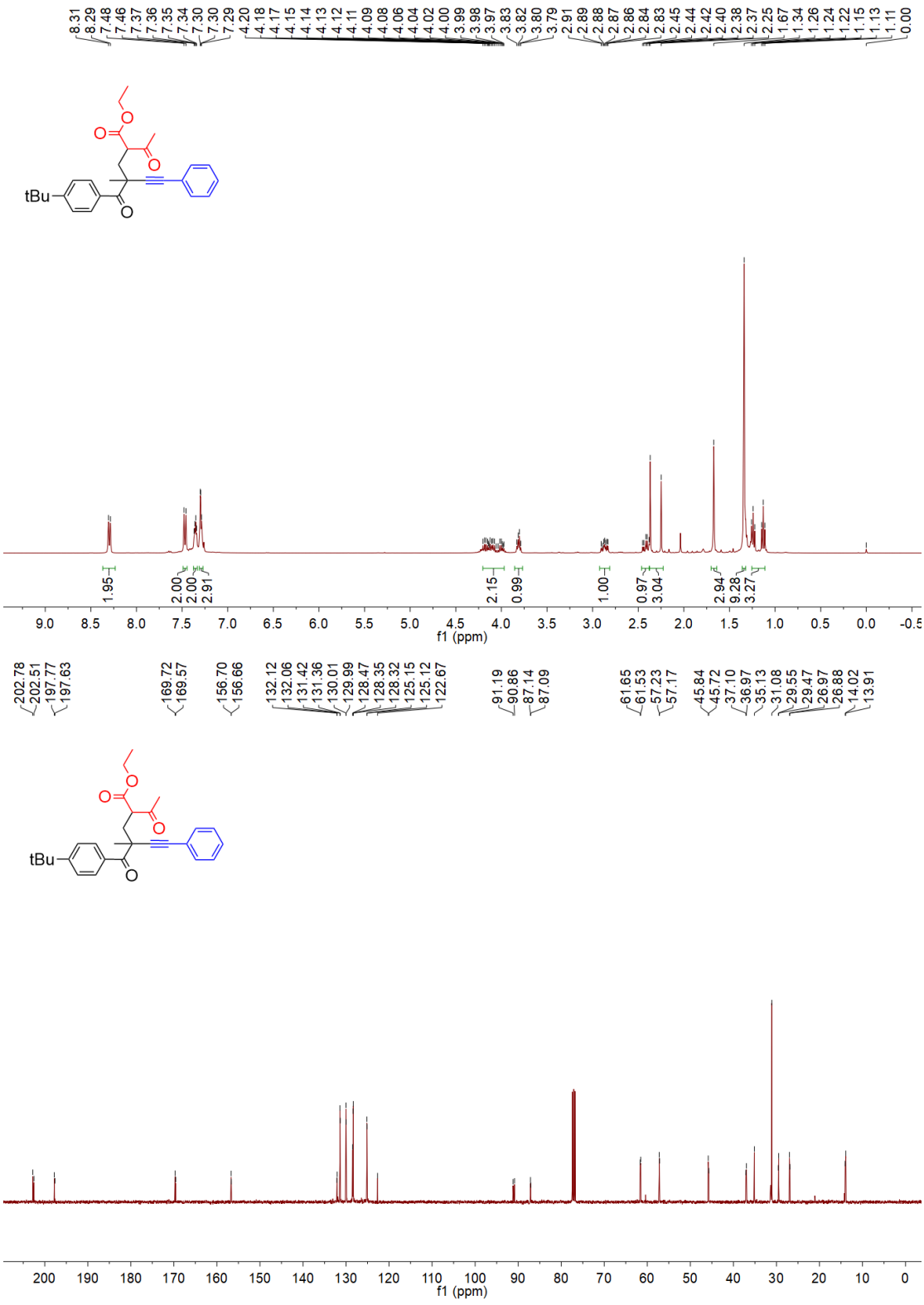
2.82
2.65
2.63
2.61
2.59
2.47
2.45
2.43
2.42
2.41
2.39
2.36
2.25
1.66
1.26
1.24
1.23
1.21
1.19
1.16
1.14
1.12
0.00
Et
1.97
1.00
2.01
2.24
2.08
2.03
0.97
1.01
2.09
0.98
3.01
2.91
6.33
f1 (ppm)
202.74
198.59
169.69
144.98
135.01
132.88
131.36
129.93
128.13
127.92
119.72
90.21
87.51
61.67
57.17
45.94
37.09
29.56
28.81
26.91
15.40
14.02
Et
f1 (ppm)

4e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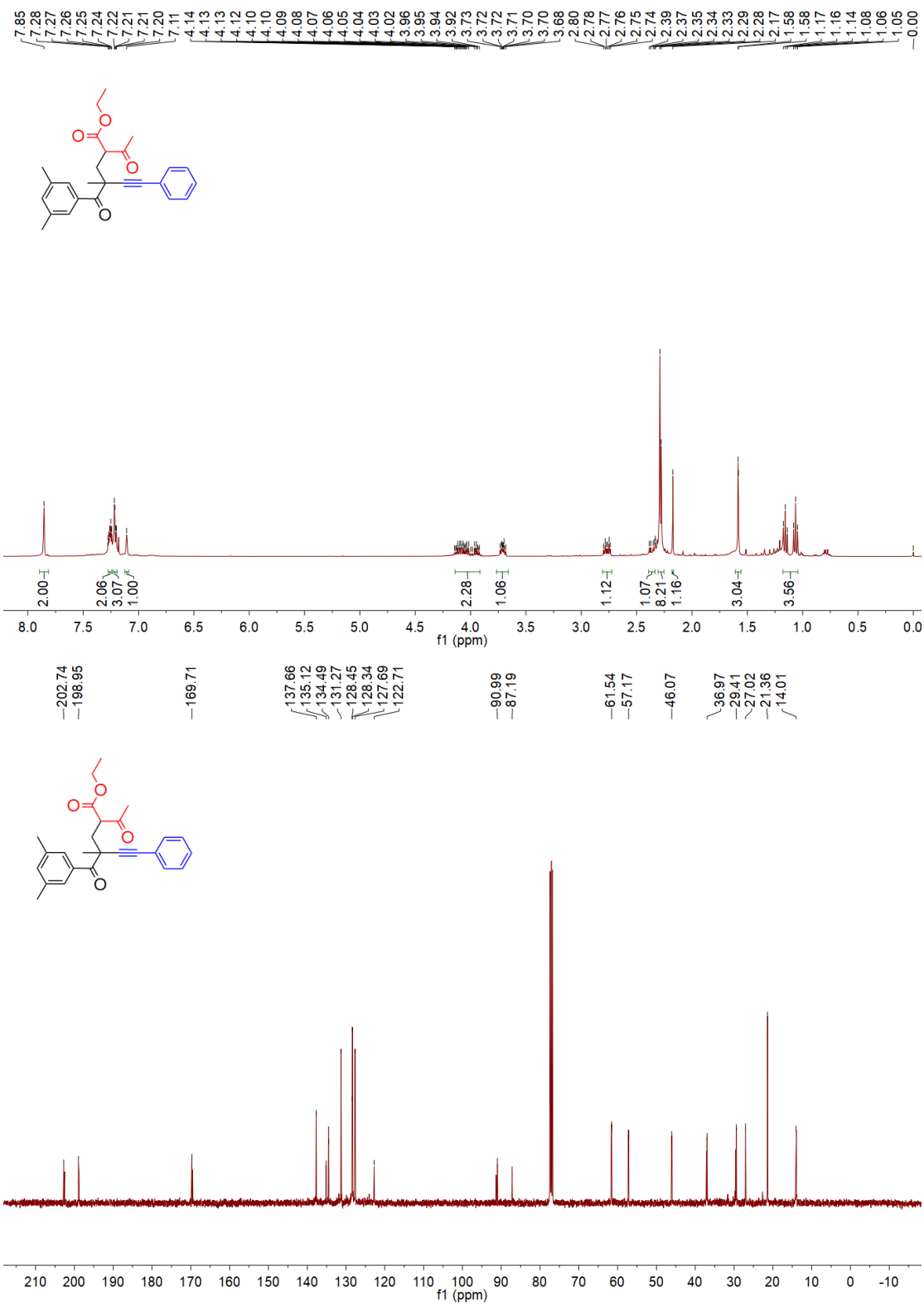
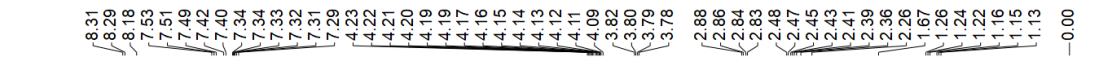
tBu
1.95 2.00 2.00 2.91 2.15 0.99 1.00 0.97 3.04 2.94 9.28 3.27
f1 (ppm)
202.78 202.51 197.77 197.63 169.72 169.57 156.70 156.66 132.12 132.06 131.42 131.36 130.01 129.99 128.47 128.35 128.32 125.15 125.12 122.67 91.19 90.86 87.14 87.09 61.65 61.53 57.23 57.17 45.84 45.72 37.10 36.97 35.13 31.08 29.55 29.47 26.97 26.88 14.02 13.91
tBu
f1 (ppm)

4f


7.85 7.28 7.27 7.26 7.25 7.24 7.22 7.21 7.21 7.20 7.11 4.14 4.13 4.13 4.12 4.10 4.10 4.09 4.08 4.07 4.06 4.05 4.04 4.03 4.02 3.96 3.95 3.94 3.92 3.73 3.72 3.72 3.71 3.70 3.70 3.68 2.80 2.78 2.77 2.76 2.75 2.74 2.39 2.37 2.35 2.34 2.33 2.29 2.28 2.17 1.58 1.58 1.17 1.16 1.14 1.08 1.06 1.05 0.00
2.00 2.06 3.07 1.00 2.28 1.06 1.12 1.07 8.21 1.16 3.04 3.56
f1 (ppm)
202.74 198.95 169.71 137.66 135.12 134.49 131.27 128.45 128.34 127.69 122.71 90.99 87.19 61.54 57.17 46.07 36.97 29.41 27.02 21.36 14.01
f1 (ppm)

4g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7.34
7.34
7.33
7.32
7.31
7.29
4.23
4.22
4.21
4.20
4.19
4.19
4.17
4.16
4.15
4.14
4.13
4.12
4.11
4.09
3.82
3.80
3.79
3.78
2.88
2.86
2.84
2.83
2.48
2.47
2.45
2.43
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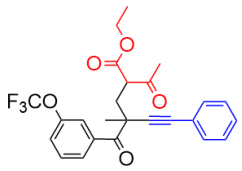
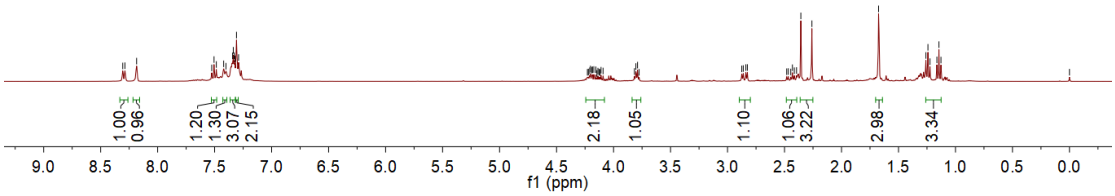
1.22
1.16
1.15
1.13
0.00


F3CO
O
O
O
O
O


1.00
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1.20
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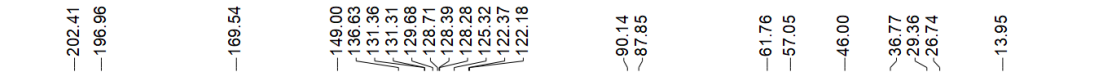
3.07
2.15
2.18
1.05
1.10
1.06
3.22
2.98
3.34
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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136.63
131.36
131.31
129.68
128.71
128.39
128.28
125.32
122.37
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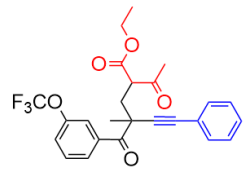
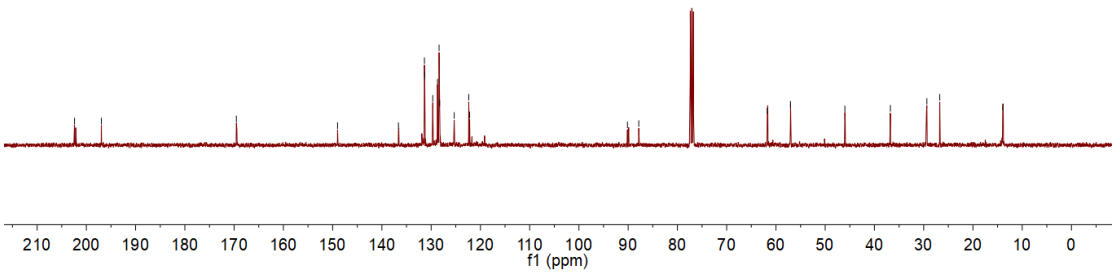
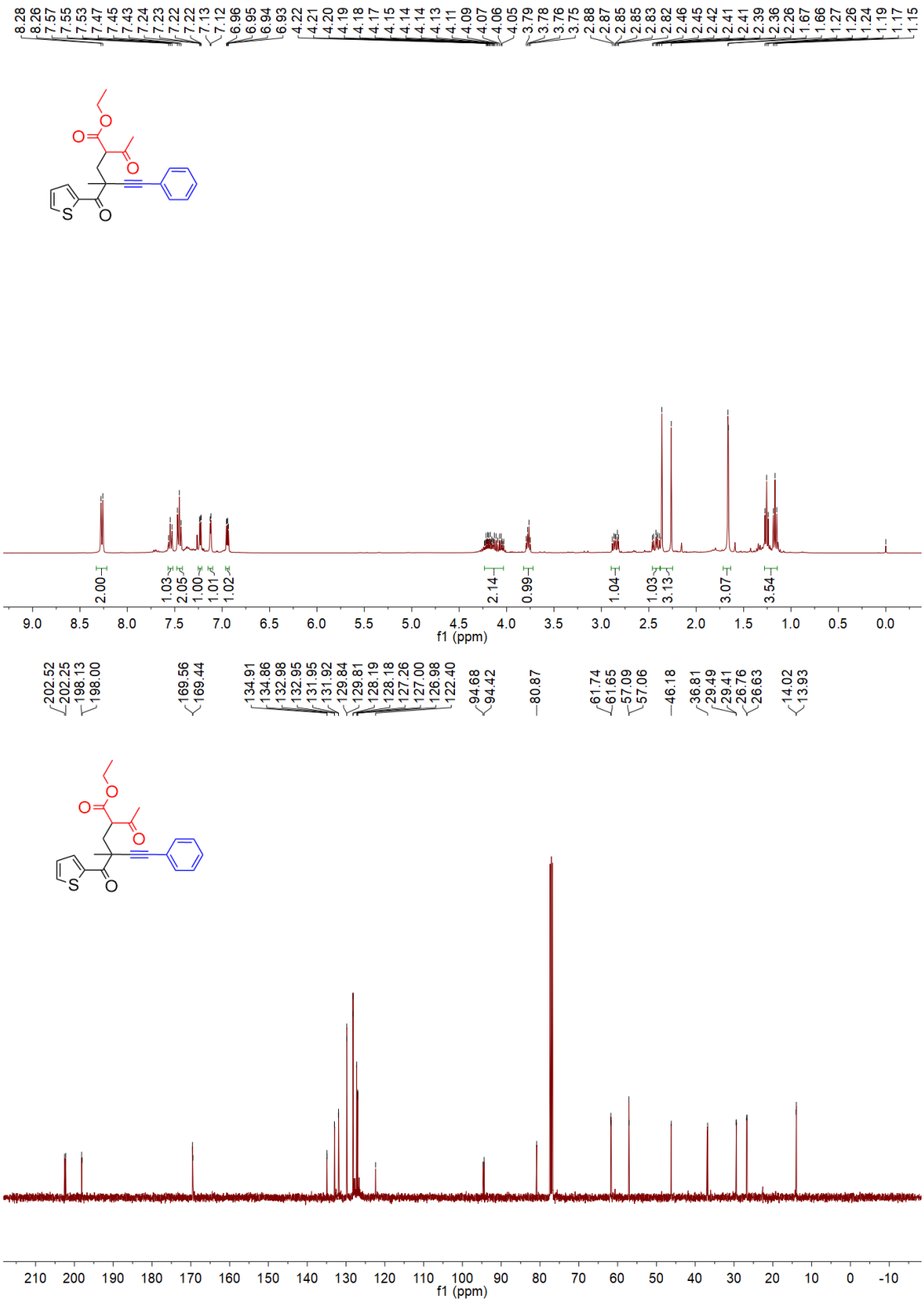
90.14
87.85
61.76
57.05
46.00
36.77
29.36
26.74
13.95

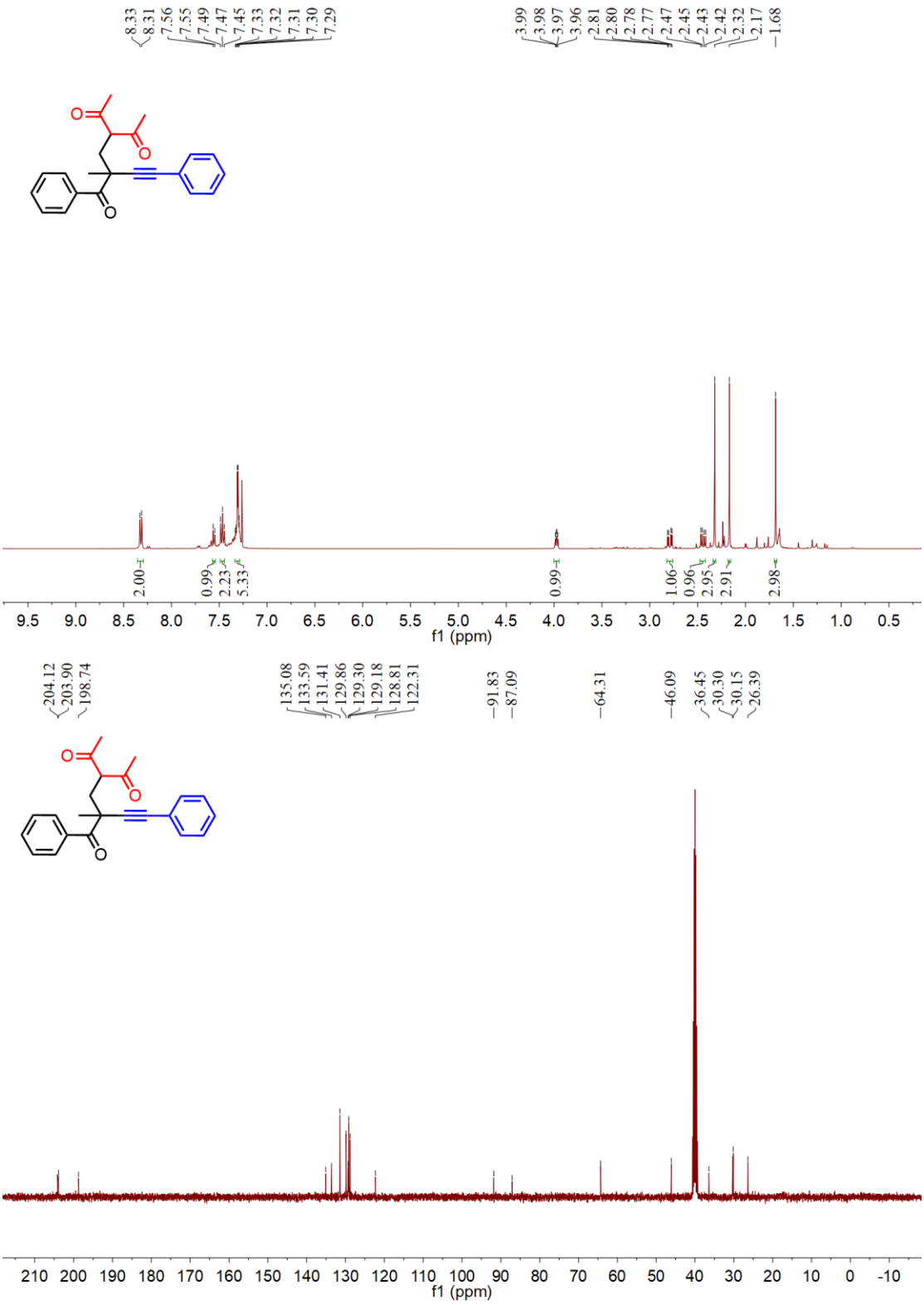

F3CO
O
O
O
O
O


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

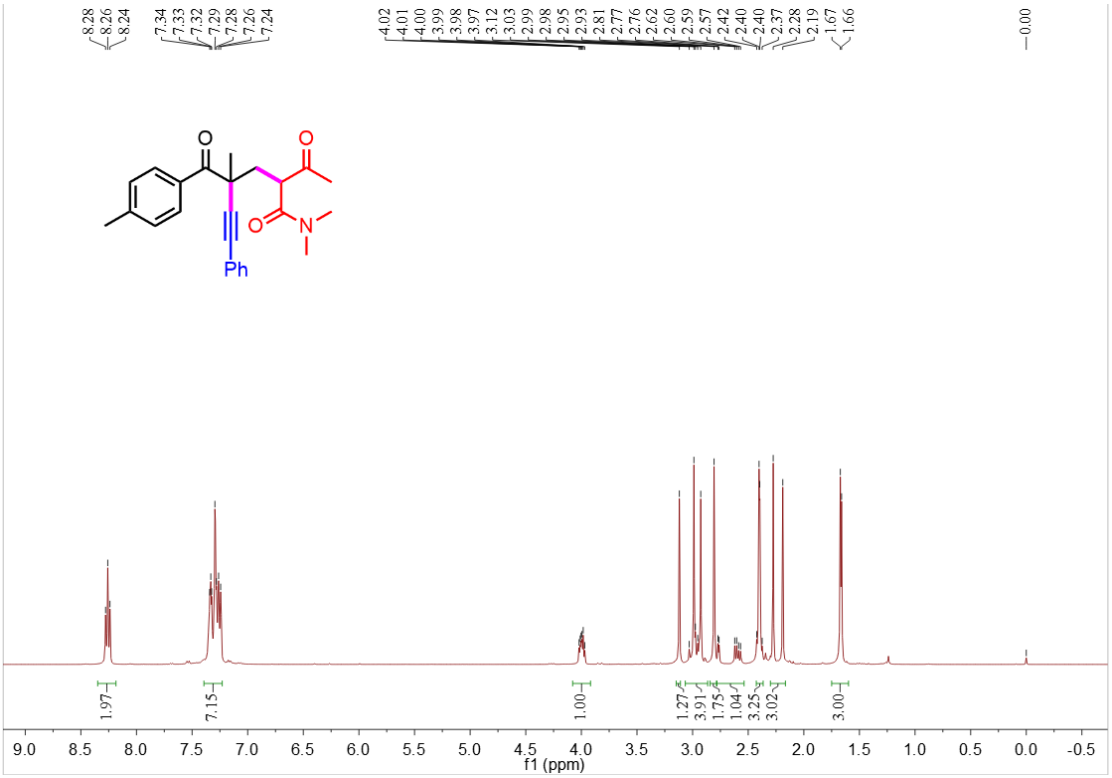
4h

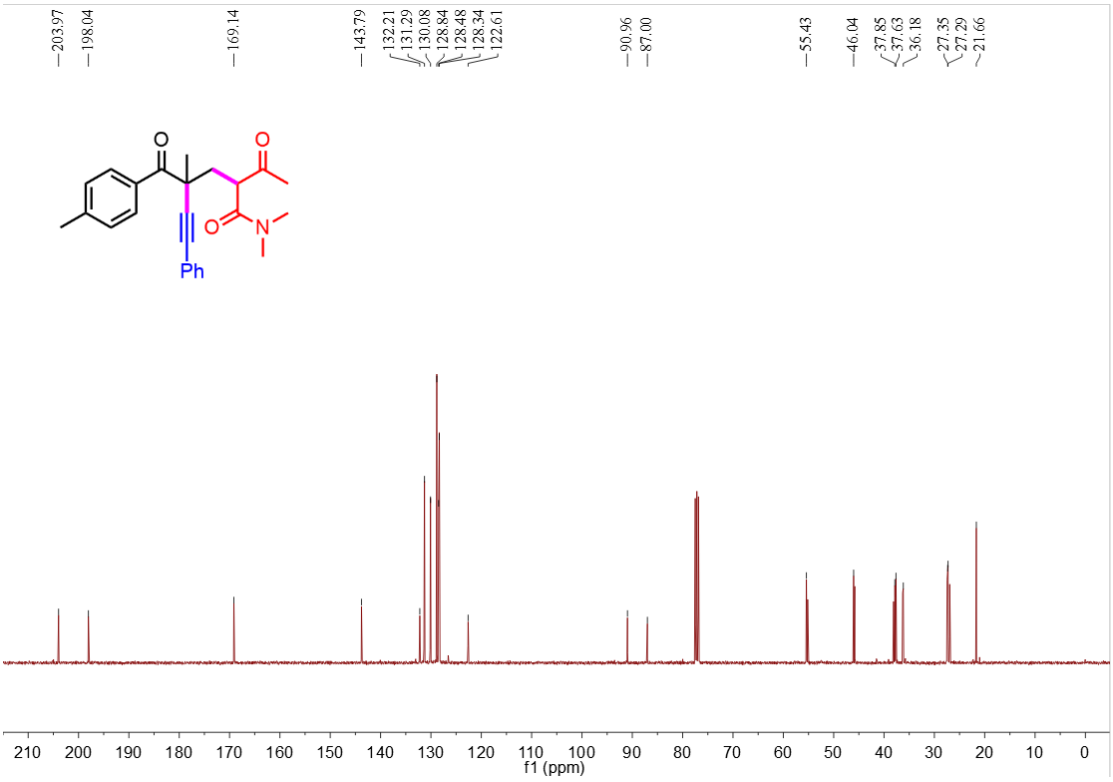

8.28 8.26 7.57 7.55 7.53 7.47 7.45 7.43 7.24 7.23 7.22 7.22 7.13 7.12 6.96 6.95 6.94 6.93 4.22 4.21 4.20 4.19 4.18 4.17 4.15 4.14 4.14 4.13 4.11 4.09 4.07 4.06 4.05 3.79 3.78 3.76 3.75 2.88 2.87 2.85 2.85 2.83 2.82 2.46 2.45 2.42 2.41 2.41 2.39 2.36 2.26 1.67 1.66 1.27 1.26 1.24 1.19 1.17 1.15
O
O
O
S
O
2.00 1.03 2.05 1.00 1.01 1.02 2.14 0.99 1.04 1.03 3.13 3.07 3.54
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
202.52 202.25 198.13 198.00 169.56 169.44 134.91 134.86 132.98 132.95 131.95 131.92 129.84 129.81 128.19 128.18 127.26 127.00 126.98 122.40 94.68 94.42 80.87 61.74 61.65 57.09 57.06 46.18 36.81 29.49 29.41 26.76 26.63 14.02 13.93
O
O
O
S
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)

4i


8.33
8.31
7.56
7.55
7.49
7.47
7.45
7.33
7.32
7.31
7.30
7.29
3.99
3.98
3.97
3.96
2.81
2.80
2.78
2.77
2.47
2.45
2.43
2.42
2.32
2.17
1.68
2.00
0.99
2.23
5.33
0.99
1.06
0.96
2.95
2.91
2.98
f1 (ppm)
204.12
203.90
198.74
135.08
133.59
131.41
129.86
129.30
129.18
128.81
122.31
91.83
87.09
64.31
46.09
36.45
30.30
30.15
26.39
f1 (ppm)

4j


8.28
8.26
8.24
7.34
7.33
7.32
7.29
7.28
7.26
7.24
4.02
4.01
4.00
3.99
3.98
3.97
3.12
3.03
2.99
2.98
2.95
2.93
2.81
2.77
2.76
2.62
2.60
2.59
2.57
2.42
2.40
2.40
2.37
2.28
2.19
1.67
1.66
0.00
O
O
O
N
Ph
1.97
7.15
1.00
1.27
3.91
1.75
1.04
3.25
3.02
3.00
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)


203.97
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143.79
132.21
131.29
130.08
128.84
128.48
128.34
122.61
90.96
87.00
55.43
46.04
37.85
37.63
36.18
27.35
27.29
21.66
O
O
O
N
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

11. References

1. Q. Zhao, X. S. Ji, Y. Y. Gao, W. J. Hao, K. Y. Zhang, S. J. Tu and B. Jiang, *Organic Letters*, 2018, **20**, 3596-3600.