Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information

Recyclable Cellulose-Palladium Nanoparticles for Clean Cross-Coupling Chemistry

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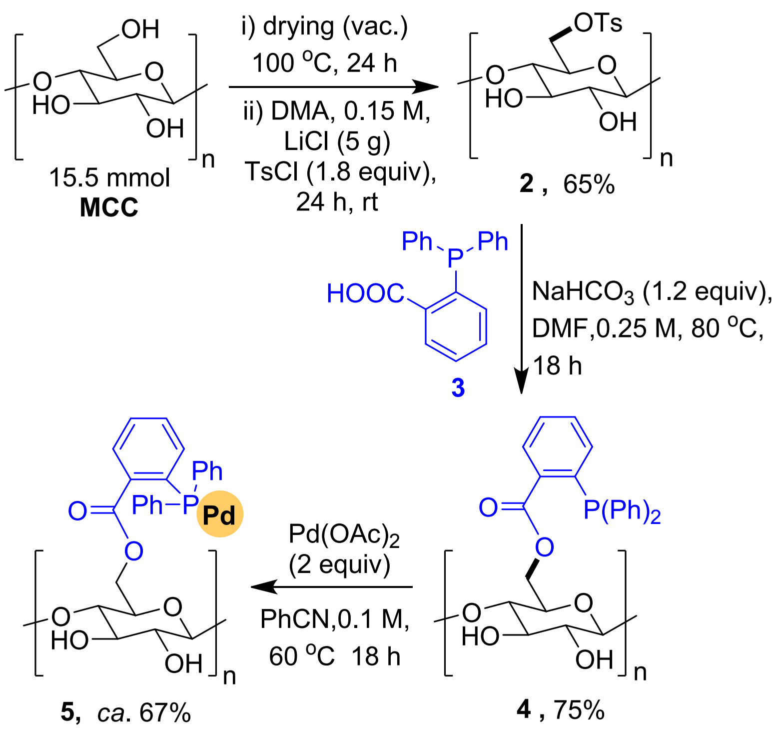
Section 1. General experimental details

^1H and ^{31}P NMR spectra were recorded at 400 and 162 MHz respectively, using $CDCl_3$ or DMSO as a solvent. The chemical shifts are reported in δ (ppm) values relative to $CHCl_3$ (δ 7.26 ppm for ^1H NMR), multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. All air and/or moisture sensitive reactions were carried out under argon atmosphere.

Solvents (tetrahydrofuran, ether, dichloromethane) were chemically dried using a commercial solvent purification system, DMA was purchased from Millipore-Sigma. Cellulose microcrystalline (MCC) was from Alfa Aesar and dried at 100°C under vacumm for 24 h. Anhydrous LiCl was purchased from Alfa Aesar and then dried at 130°C for 2 h under vacuum. Single Element ICP and ICP/MS Certified Palladium Reference Standards was purchased from BDH® ARISTAR®. All other reagents and solvents were employed without further purification. The products were purified using a CombiFlash system. TLC was developed on Merck silica gel 60 F254 aluminum sheets. All NMR solvents were purchased from Cambridge Isotope Laboratories, Inc. Other chemicals including metal catalysts were purchased from Aldrich, Alfa Aesar or Strem.

SAVANT SPEED VAC SVC 200H was used for Centrifugation. The centrifugal force, applied by the rotor spinning at up to 1760 RPM, concentrates all the precipitate at the bottom of the vial. Thermo X-Series Collision-Cell ICP-MS with New Wave 213nm Laser Ablation System and Microsampler was applied for the assay of Pd residue in product. Thermogravimetric analysis (TGA) was measured in N_2 atmosphere with SDT Q600 V20.9 Build 20. Most of the products formed in these reactions have been reported in the literature (references are found in the manuscript), hence we only used ^1H NMR to confirm the identity of those known compound's.

Section 2. Synthesis of MCC-OOCPhPPh$_2$-Pd



Scheme S1. Synthetic protocol of Cellulose-Pd NPs

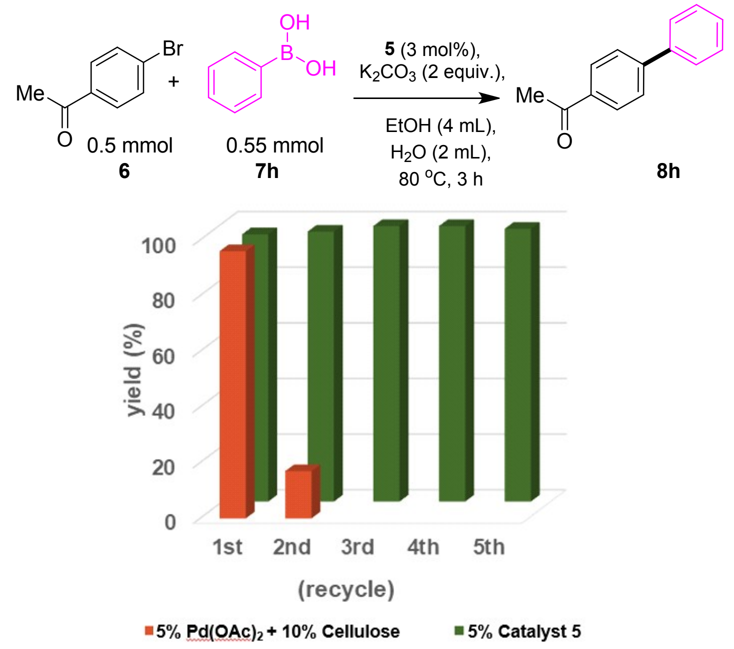
Experiment procedure: The dried MCC (2.5 g, 15.5 mmol) was suspended in 100 mL of dry DMA and stirred at 130°C for 2 hours. After the slurry had been allowed to cool to 100°C, 5 g of anhydrous LiCl were added. By cooling to room temperature and stirring the cellulose dissolves completely. To the above solution, a mixture of 6.5 mL (46.5 mmol) triethylamine and 5mL DMA was added under stirring. After cooling to about 8 °C and stirring, a solution of 5.32 g (27.9 mmol) p-toluenesulfonyl chloride in 8 mL DMA was added dropwise within 30 min. The homogeneous reaction mixture was stirred for 24 hours at room temperature, and then slowly poured into 700 mL of ice water. The precipitate was filtered off, washed carefully with about 2 L of distilled water and 250 mL of ethanol, suspended in 125 mL of acetone and reprecipitated into 400 mL of distilled water. After filtration and washing with ethanol, the sample was dried at 50 °C under vacuum for 3 hours to afford MCC-OTs **2** (3.2 g, 65.1%) and it was assayed with IR. found:1353 (Vas SO_2), 1373 (Vs SO_2).

A 20-mL vial containing 8 mL DMF was charged with MCC-OTs **2** (0.634 g, 2 mmol), sodium bicarbonate (0.202 g, 2.4 mmol) and 2-(Diphenylphosphino)benzoic acid **3** (0.695 g, 2.2 mmol). The mixture was stirred at 70 °C overnight. Precipitation occurred when it was poured into 30 mL ice water. Filtered and washed the remnant with 50 mL deionized water, 20 mL ethanol. The remnant was then dried at room temperature under vacuum for 2 hours to afford compound MCC-OOCPhPPh$_2$ **4** (0.68 g, 75.6%).

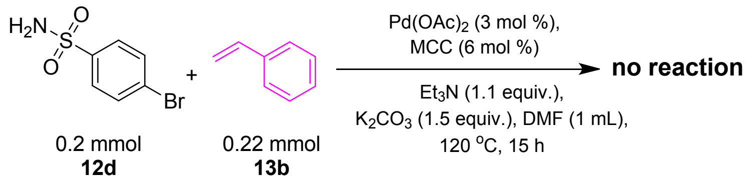
A 20-mL vial containing 10 mL benzonitrile was charged with MCC-OOCPhPPh$_2$ **4** (0.45 g, 1 mmol) and palladium acetate (0.449 g, 2 mmol) under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 20 hours. After cooling to room temperature, the mixture was stirred for another 10 hours. The precipitate was filtered off and washed carefully with toluene, and diethyl ether. The collected solid product was vacuum dried at room temperature to give MCC-OOCPhPPh$_2$-Pd **5** (0.373 g, 67.1%).

Section 3. Catalyst recycling with control experiment

a) Suzuki-Miyaura coupling with grafted catalyst 5 and ungrafted Pd



b) Heck reaction with ungrafted Pd



Scheme S2. Catalyst recycling with control experiment.

The recycling test was studied using the Suzuki–Miyaura reaction and yield was calculated with GC-MS. After completion of the reaction, the mixture was centrifuged, and the liquid phase was decanted. 1 mL water was added to the remnant and the result mixture was centrifuged and decanted to remove the salt. This process was repeated twice to fully remove the salt. Ethanol (2 mL) was added and removed after centrifugation to get rid of the organic remnants on the catalyst. The recovered catalyst was directly applied to the next reaction round with fresh portions of reactants. As shown in Scheme S2a, no obvious catalytic activity loss was observed even with five successive reactions (Green bar). A control experiment was also conducted with $Pd(OAc)_2$ and Cellulose employing the same recycling procedure, the reaction yield decreased sharply to 17% with the loss of $Pd(OAc)_2$ (blue bar). The extension of reaction time didn't improve the reaction yield.

Control experiment with Heck reaction (Scheme S2b): An 8-mL vial fitted with a stirring bar was charged with 4-Bromobenzenesulfonamide (0.2 mmol), styrene (0.22 mmol), triethylamine (0.22 mmol), K_2CO_3 (0.3mmol). 3% $Pd(OAc)_2$ (1.5 mg), 6% MCC (2 mg). 1 mL dry DMF was added and the mixture was flushed with argon for 1min. The reaction was stirred at 120 ^{o}C for 15 h and then monitored with GC-MS.

Section 4. STEM and XPS data from fresh catalyst and recycled catalyst

Transmission electron microscopy (TEM) was performed using a field emission gun FEI Tecnai F20 electron microscope at an accelerating voltage of 200 kV. Scanning TEM (STEM) Z-contrast images were collected in the nanoprobe mode, with a 1 nm electron probe and a Fischione High-Angle Annular Dark Filed Detector (HAADFD). X-ray photoelectron spectroscopy (XPS) was used to study the valance states of palladium and to measure their relative concentrations. This was done using a VG Scientific MultiLab 3000 ultra-high vacuum surface analysis system, equipped with a CLAM4 hemispherical electron energy analyzer and a dual-anode (Mg/Al) X-ray source. XPS spectra were acquired at the base pressure of ~10-9 Torr using a non-monochromatic Al Kα (hν = 1486.6 eV) X-ray radiation at a take-off angle of 54.7o. For the analysis, the binding energy of the spectrum was first calibrated using an intrinsic C1s peak at 284.5 eV, which then was followed by the spectrum deconvolution. Shirley model function was used for the background fitting and XPS peaks were fitted using combinations of Gaussian functions.

STEM images from the fresh catalyst (ZLU-327) and the recycled catalyst (after 5 round of reaction) (ZLU-286) are shown in Figure S1. In both samples, high concertation of Pd nanoparticles (appearing as bright spots) was observed on the surface of carbon support particles (Figure S1 a,d). However, there is a clear difference in the Pd nanoparticle size distribution between these two samples. For the fresh catalyst, a bi-modal size distribution is evident with many nanoparticles having ~1 nm diameter and with remaining nanoparticles in the size range of about 3-4 nm (Figure S1b). On the other hand, the recycled catalyst has almost all particles in the 3-4 nm (Figure S1e). XPS analysis of these two catalysts shows the change of the Pd valance state. As indicated by the analysis of the Pd3d line, both catalyst show Pd(II) and Pd(0) states . The relative concertation between these valance states changes a little bit from 0.44 for the fresh catalyst (Figure S1c) to 0.39 in the recycled catalyst, which helps explain why the catalyst still reserve the catalytic efficiency (Figure S1f)

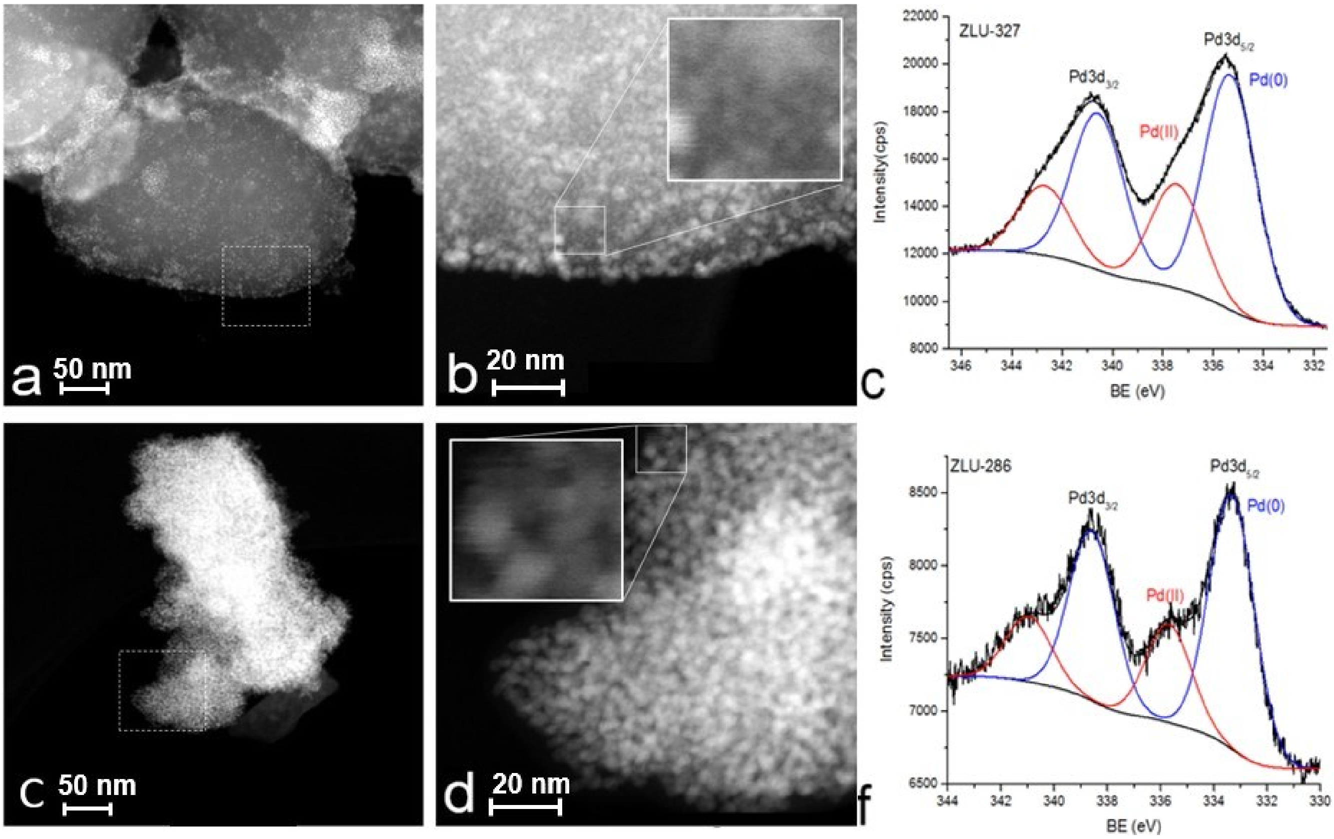


Figure S1. STEM and XPS data from fresh catalyst (ZLU-327) and five-times recycled catalyst (ZLU-286): (a), (d) Low-magnification STEM images; (b), (e) Higher-magnification STEM images of regions marked in panels a and d; (c), (f) Deconvoluted high-resolution Pd3d XPS spectra.

Section 5. TGA data of the catalyst.

Thermogravimetric analysis (TGA) was measured in N_2 atmosphere with SDT Q600 V20.9 Build 20 to evaluate the stability of the catalyst at high temperature. As shown in Figure S2, the catalyst system showed high thermal stability in nitrogen with decomposition at around 225 ^{o}C. This result demonstrated that this catalyst was considerably stable for most of the existed cross coupling reactions.

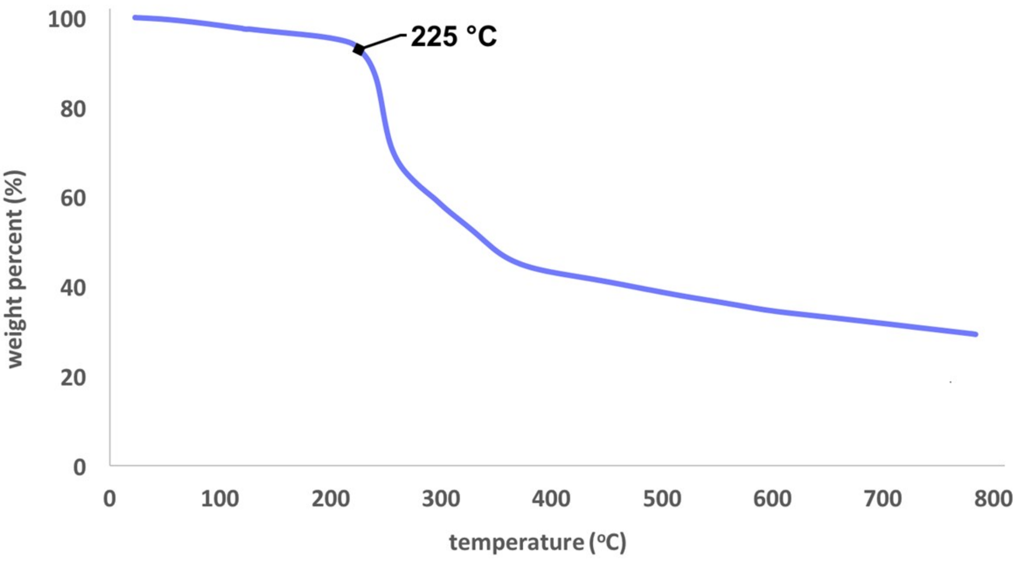
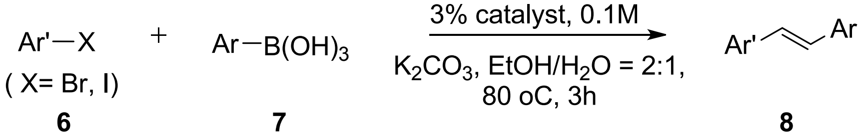


Figure S2. TGA Spectra for catalyst **5**.

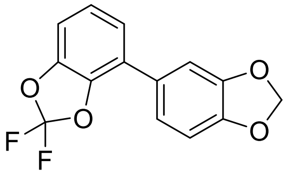
Section 6. General procedure for coupling reactions

6.1 Suzuki–Miyaura reaction



6 **7** **8**

An 8-mL vial fitted with a stirring bar was charged with aryl halide (0.2 mmol), K_2CO_3 (0.4 mmol), boronic acid (0.22mmol), 3% catalyst MCC-OOCPhPPh$_2$-Pd **5** (4 mg). 3 mL mixed solvent (Ethanol: DI water = 2:1) was added and the mixture was flushed with argon for 1min. The reaction was heated to 80 ^{o}C and stirred at 500 r/min for 2 hours. Monitored with GC-MS. The mixture was poured into 30 mL EtOAc which was washed with 10mL water, brine and the organic layer was dried over Na_2SO_4. filtered and the filtrate was concentrated. The result crude was purified with flash chromatography.

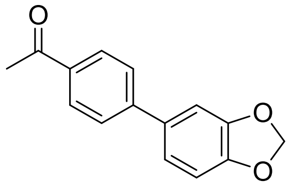


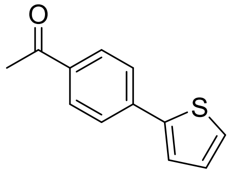
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 2H), 7.06 (d, *J* = 6.9 Hz, 1H), 6.96 (s, 2H), 6.86 (d, *J* = 7.2 Hz, 1H), 6.00 (s, 2H).

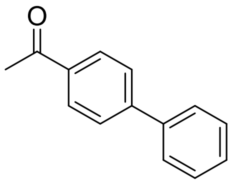
^{13}C NMR (100 MHz, $CDCl_3$) δ 148.22, 147.36, 144.17, 142.85, 137.54, 134.29, 134.21, 131.67, 122.11, 120.63, 109.44, 108.63, 108.26, 107.58, 101.28.

^{19}F NMR (376 MHz, $CDCl_3$) δ -50.04.

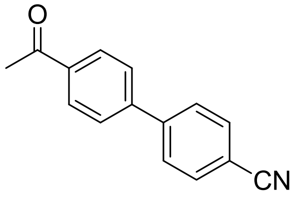
HRMS: (LDI) [M] cal. for $C_{14}H_8F_2O_4$: 278.0391; found: 278.0380



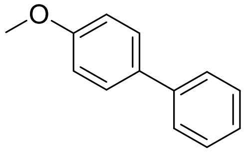


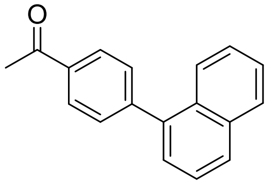


The NMR data obtained were in agreement with those reported in the literature. [1]

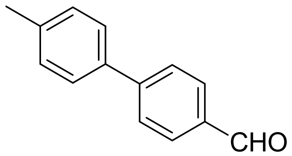


The NMR data obtained were in agreement with those reported in the literature.[2]

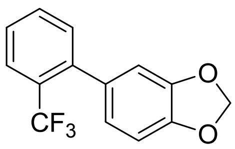




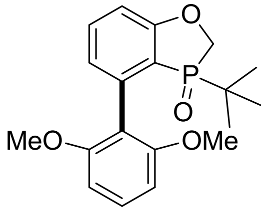
The NMR data obtained were in agreement with those reported in the literature.[3]



The NMR data obtained were in agreement with those reported in the literature.[4]

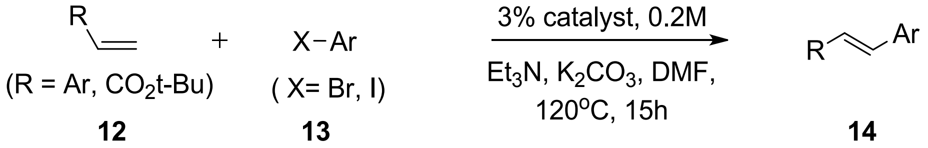


The NMR data obtained were in agreement with those reported in the literature. [5]

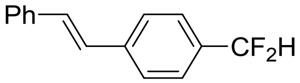


The NMR data obtained were in agreement with those reported in the literature.[6]

6.2 Heck reaction



An 8-mL vial fitted with a stirring bar was charged with aryl halide (0.2 mmol), alkene (0.22 mmol), triethylamine (0.22 mmol), K_2CO_3 (0.3mmol), 3% catalyst MCC-OOCPhPPh$_2$-Pd **5** (4 mg). 1 mL dry DMF was added and the mixture was flushed with argon for 1min. The reaction was stirred at 120 °C for 15 h and then monitored with GC-MS. The mixture was poured into 30 mL EtOAc which was washed with 10 mL 5% LiCl aqueous solution, brine and the organic layer was dried over Na_2SO_4. Filtered and the filtrate was concentrated. The result crude was purified with flash chromatography.

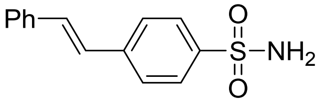


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.9 Hz, 2H), 7.51 (dd, *J* = 13.9, 8.0 Hz, 4H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.15 (q, *J* = 16.4 Hz, 2H), 6.65 (t, *J* = 56.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 139.77, 136.82, 133.48, 133.26, 133.03, 130.42, 128.74, 128.06, 127.53, 126.67, 126.63, 125.99, 125.93, 125.87, 117.03, 114.65, 112.28.

^{19}F NMR (376 MHz, $CDCl_3$) δ -110.30, -110.45.

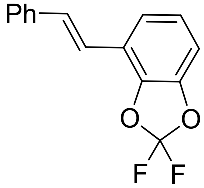
GCMS: (EI) [M] cal. for $C_{15}H_{12}F_2$: 230.1; found: 230.2.



^{1}H NMR (400 MHz, d_6-DMSO) δ 7.77 (q, *J* = 8.4 Hz, 4H), 7.62 (d, *J* = 7.4 Hz, 2H), 7.39 (dd, *J* = 15.4, 6.0 Hz, 3H), 7.35 – 7.25 (m, 4H).

^{13}C NMR (100 MHz, d_6-DMSO) δ 143.11, 140.84, 136.96, 131.52, 129.22, 128.67, 127.39, 127.24, 127.12, 126.53.

HRMS: (LDI) [M] cal. for $C_{14}H_{13}NO_2S$: 259.0667; found: 259.0657.

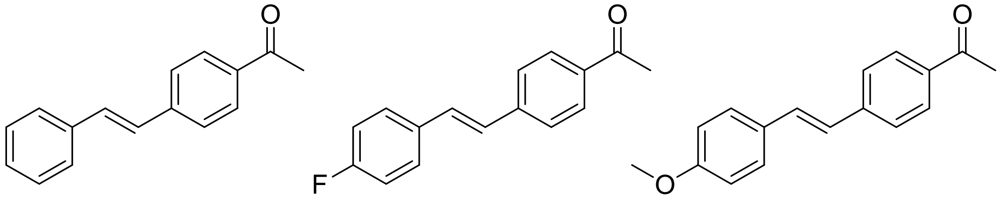


^{1}H NMR (400 MHz, CDCl$_3$) δ 7.49 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 9.8 Hz, 2H), 7.02 (d, *J* = 6.7 Hz, 3H).

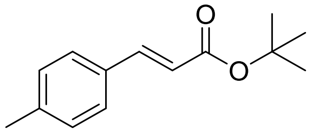
^{13}C NMR (100 MHz, CDCl$_3$) δ 144.32, 143.08, 136.74, 136.49, 134.17, 133.97, 131.63, 129.08, 128.74, 127.92, 127.26, 126.50, 122.60, 122.51, 109.68, 109.44, 108.48, 106.56.

^{19}F NMR (376 MHz, CDCl$_3$) δ -49.96, -50.20.

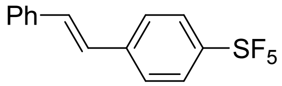
GCMS: (EI) [M] cal. for $C_{15}H_{10}F_2O_2$: 260.1; found: 260.2.



The NMR data obtained were in agreement with those reported.[7]

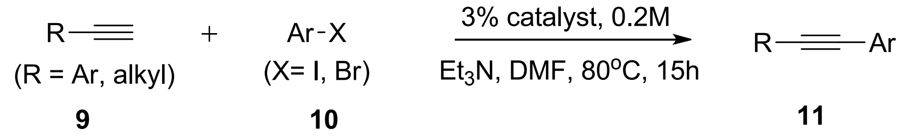


The NMR data obtained were in agreement with those reported.[8]

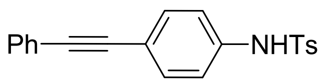


The NMR data obtained were in agreement with those reported.[9]

6.3 Sonagashira reaction



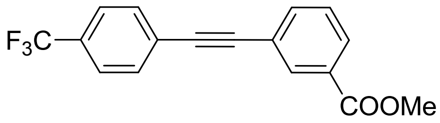
An 8-mL vial fitted with a stirring bar was charged with aryl halide (0.2mmol), triethylamine (0.4 mmol), alkyne (0.22mmol), CuI (2.0 mg, 5 mol %) and 3% catalyst MCC-OOCPhPPh2-Pd **5** (4 mg). 1 mL dry DMF was added and the mixture was flushed with argon for 1min. The reaction was then heated to 80 °C and stirred at 500 r/min for 15 hours. Monitored with GC-MS. The mixture was poured into 30 mL EtOAc which was washed with 10 mL 5% LiCl aqueous solution, brine and the organic layer was dried over Na_2SO_4. filtered and the filtrate was concentrated. The result crude was purified with flash chromatography.



<u>^{1}H NMR</u> (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.53 – 7.47 (m, 2H), 7.33 (d, *J* = 2.6 Hz, 3H), 7.28 – 7.16 (m, 5H), 7.08 (d, *J* = 11.6 Hz, 2H), 2.37 (s, 3H).

<u>^{13}C NMR</u> (100 MHz, $CDCl_3$) δ 144.09, 136.72, 135.83, 131.62, 129.76, 129.33, 128.49, 128.43, 128.36, 127.24, 124.42, 123.97, 122.83, 121.03, 90.09, 88.44, 21.54.

<u>HRMS:</u> (LDI) [M] cal. for $C_{21}H_{17}NO_2S$: 347.0980; found: 347.0972.

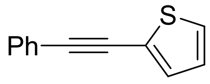


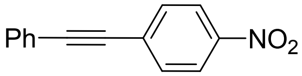
<u>^{1}H NMR</u> (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.61 (t, *J* = 5.5 Hz, 4H), 7.44 (t, *J* = 7.8 Hz, 1H), 3.93 (s, 3H).

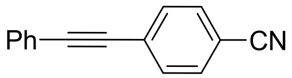
<u>^{13}C NMR</u> (100 MHz, $CDCl_3$) δ 166.24, 135.72, 132.87, 131.85, 130.55, 129.71, 128.58, 126.66, 125.32, 125.28, 123.01, 90.56, 88.74, 52.30.

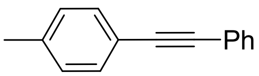
<u>^{19}F NMR</u> (376 MHz $CDCl_3$) δ -62.88.

<u>HRMS:</u> (ESI+) [M+Na] cal. for $C_{17}H_{11}F_3O_2Na$: 327.0603; found: 327.0612.

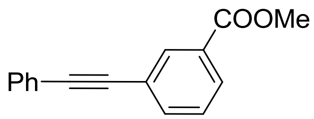


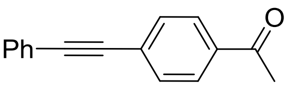


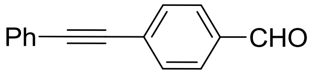




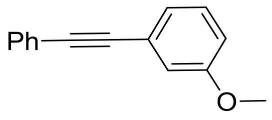
The NMR data obtained were in agreement with those reported in the literature. [10]



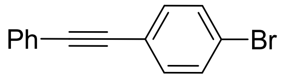




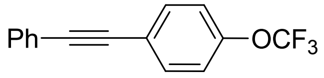
The NMR data obtained were in agreement with those reported in the literature. [11]



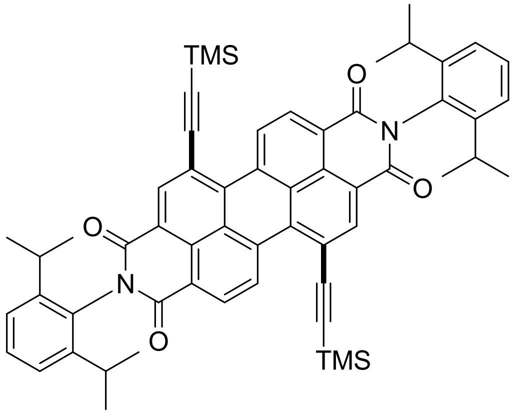
The NMR data obtained were in agreement with those reported in the literature.[12]



The NMR data obtained were in agreement with those reported in the literature.[13]



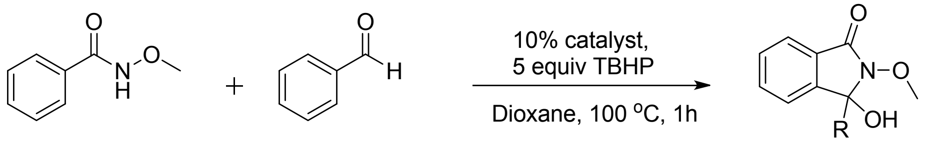
The NMR data obtained were in agreement with those reported in the literature.[14]



The NMR data obtained were in agreement with those reported in the literature.[15]

6.4 C—H activation

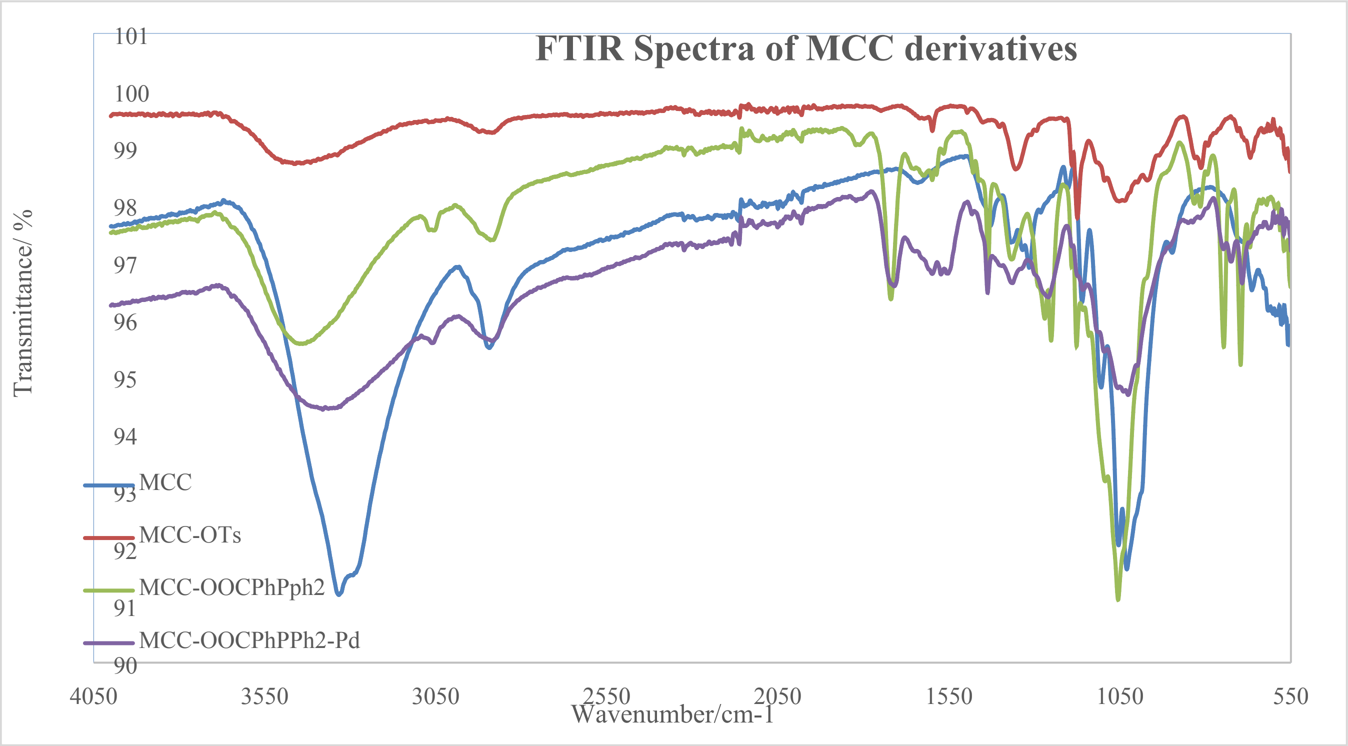
A solution of amide (0.5 mmol), aldehyde (1.5 mmol), catalyst (10 mol%) and TBHP (40% in H2O, 2.5 mmol) in 1,4-dioxane (2.5 mL) was heated at reflux under air for 1 hour. After the reaction was completed, the reaction mixture was allowed to cool down to room temperature and EtOAc (20 mL) was added. The resulting mixture was washed with saturated aqueous $Na_2S_2O_3$ (20 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure to provide the crude product. The purification was performed by flash column chromatography on silica gel to give hydroxyl isoindolone. The NMR data obtained were in agreement with those reported.[16]

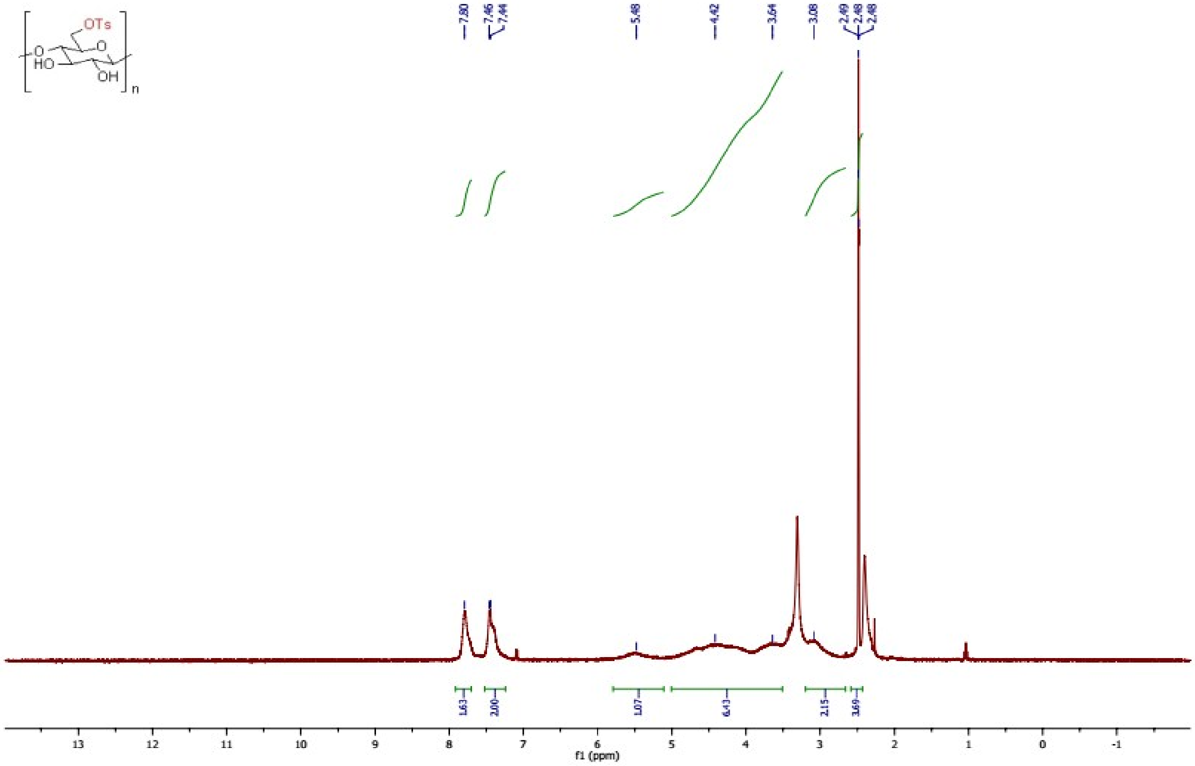


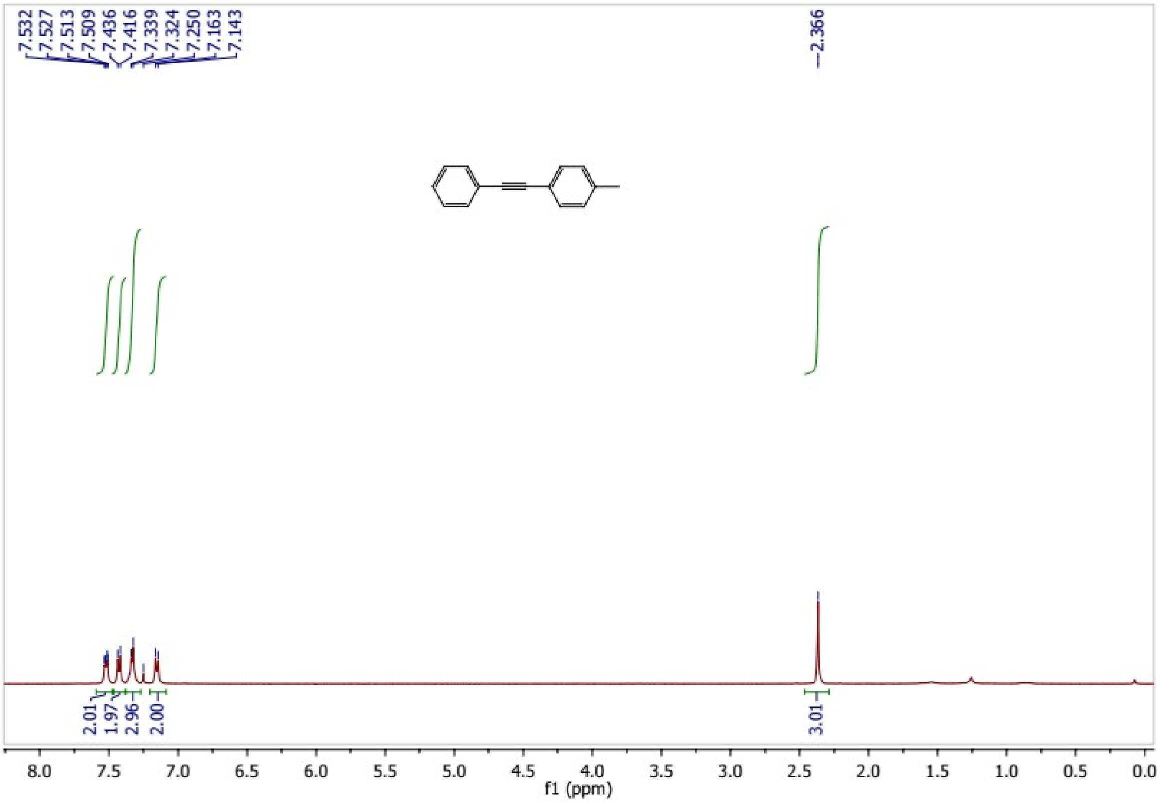
15 **16**

17a: R= Ph, 92%
17b: R=4-BrPh, 84%

Section 7. Spectral Analyses of a Catalyst and Coupling Products



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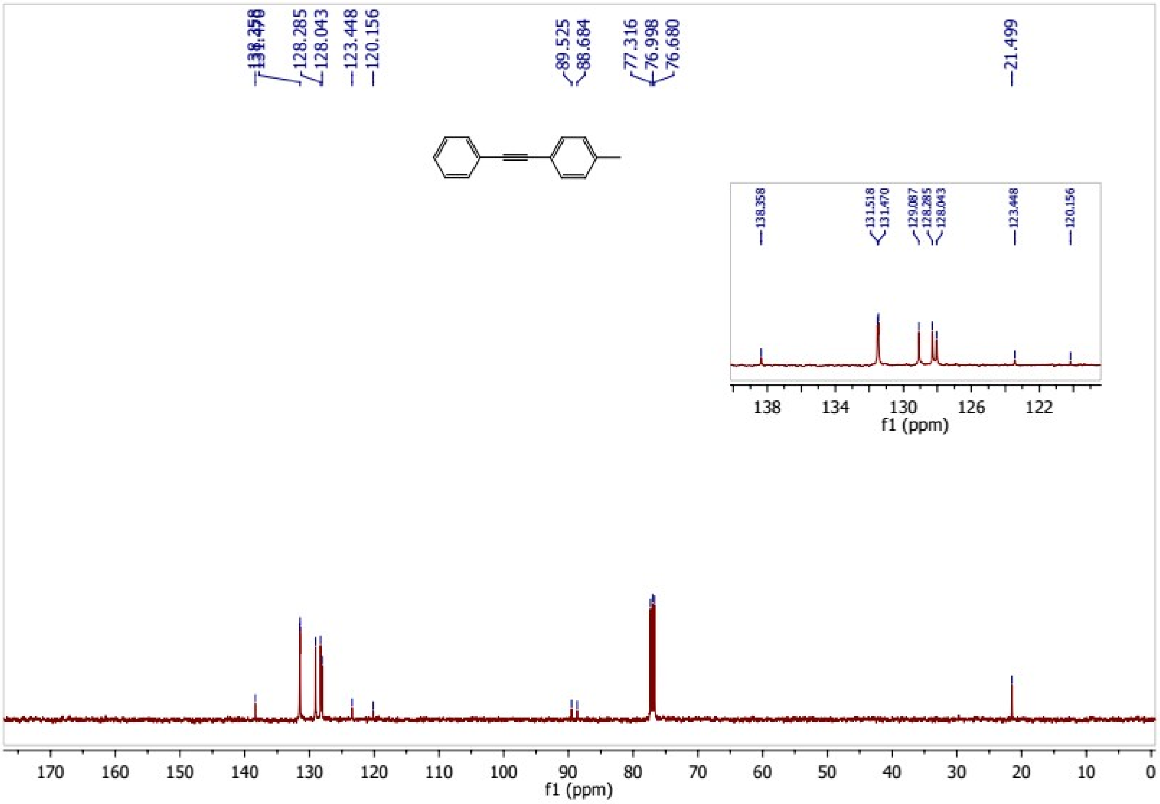
7.513
7.509
7.436
7.416
7.339
7.324
7.250
7.163
7.143
2.366
2.01
1.97
2.96
2.00
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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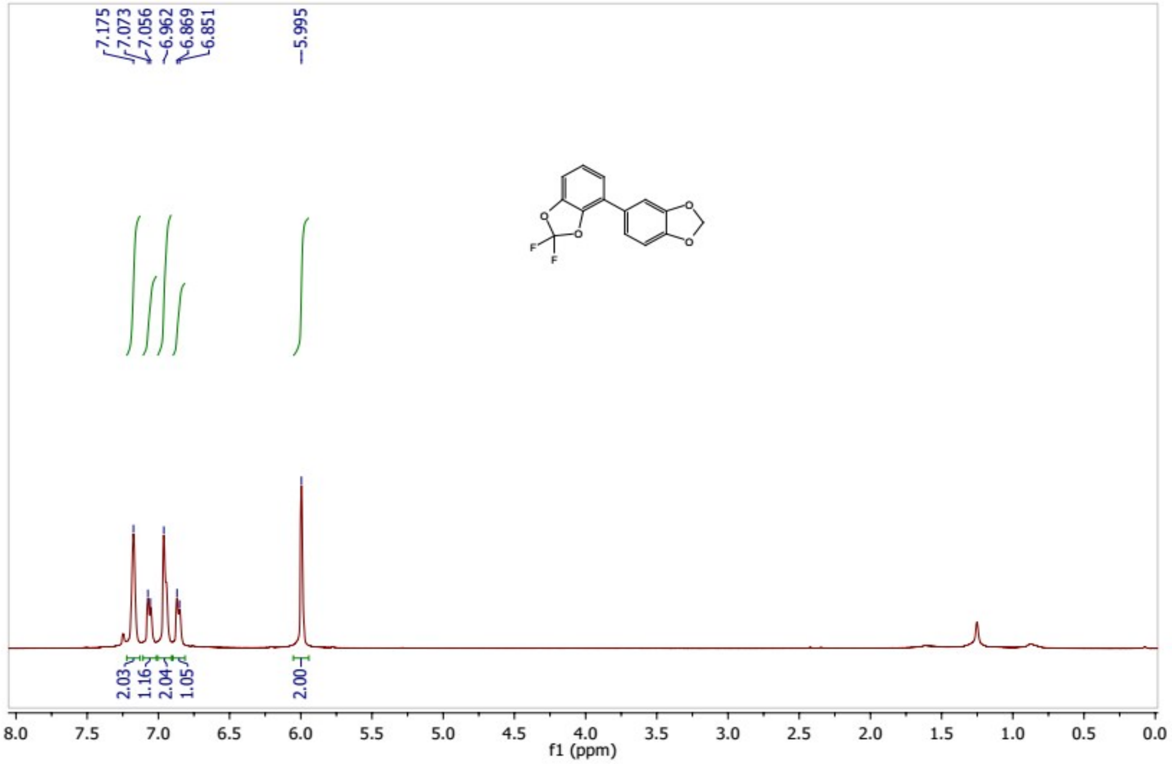
131.470
128.285
128.043
123.448
120.156
89.525
88.684
77.316
76.998
76.680
21.499
138.358
131.518
131.470
129.087
128.285
128.043
123.448
120.156
138
134
130
126
122
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.073
7.056
6.962
6.869
6.851
5.995
O
O
O
O
F
F
2.03
1.16
2.04
1.05
2.00
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
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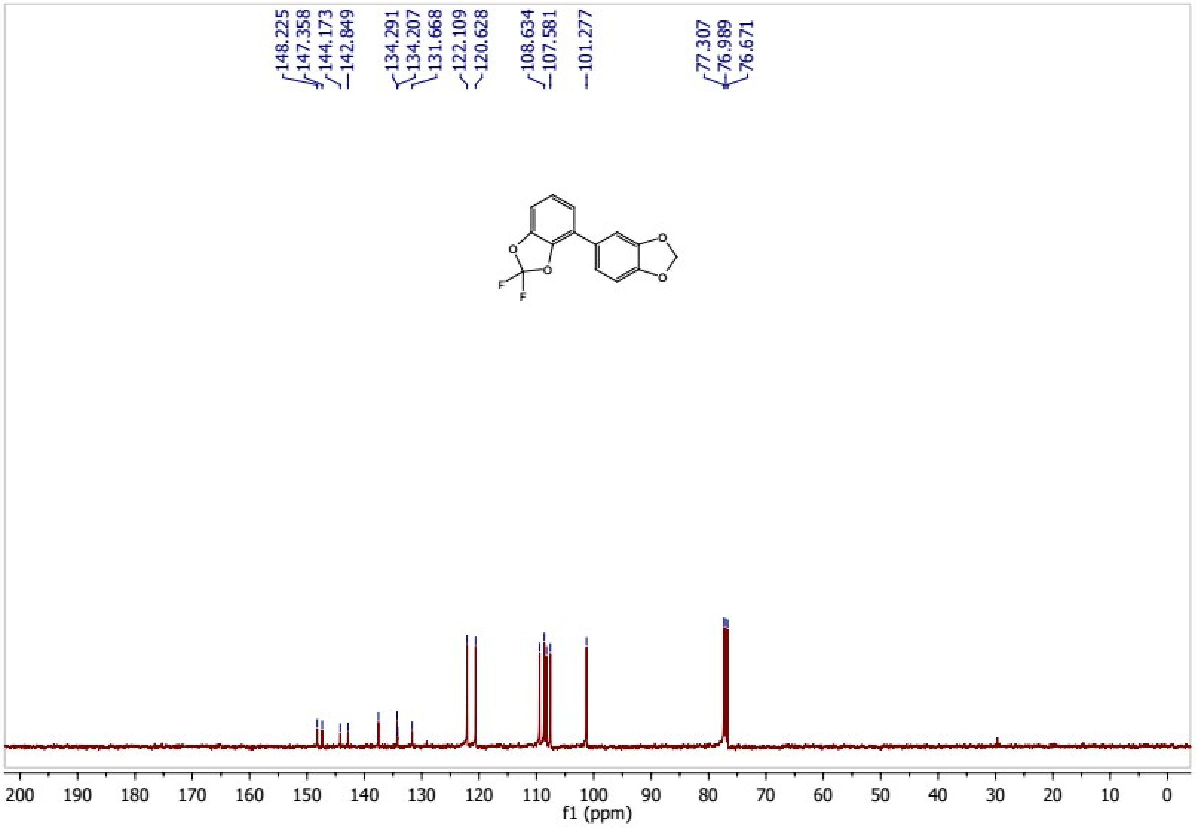
0.0
f1 (ppm)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147.358
144.173
142.849
134.291
134.207
131.668
122.109
120.628
108.634
107.581
101.277
77.307
76.989
76.671
O
O
O
O
F
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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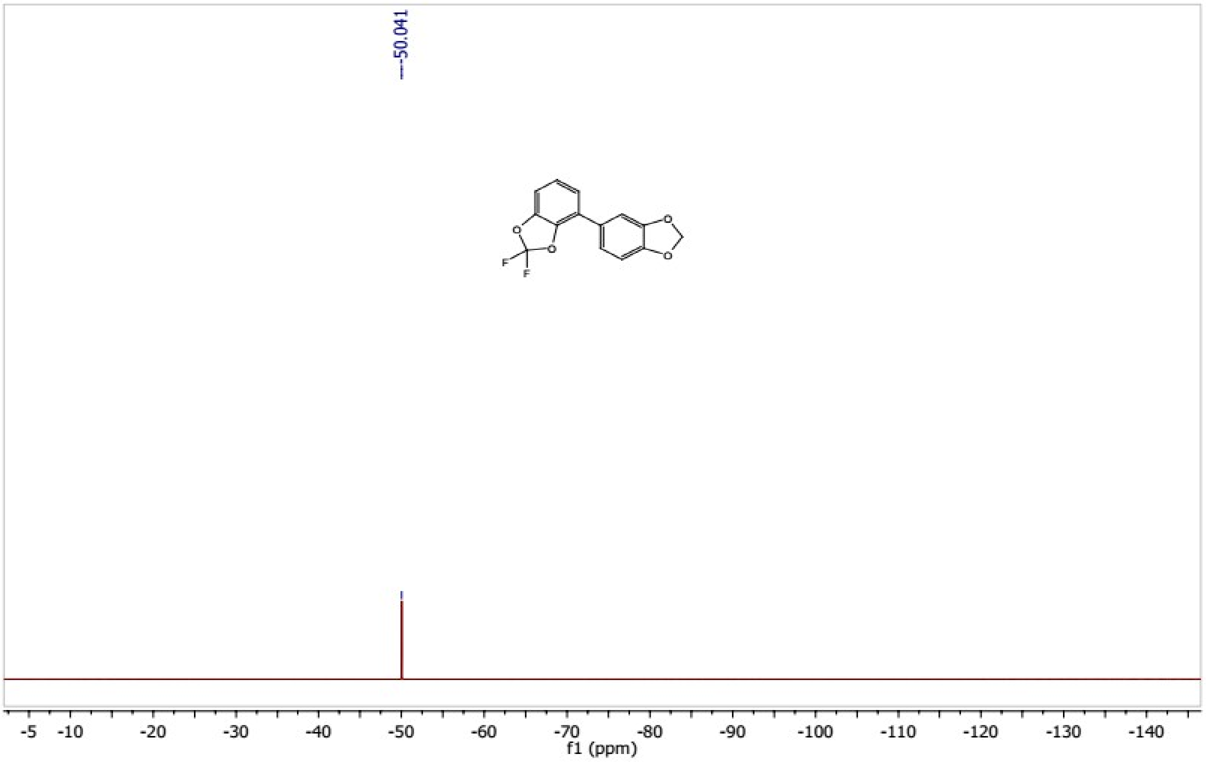
50
40
30
20
10
0
f1 (ppm)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-5
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-70
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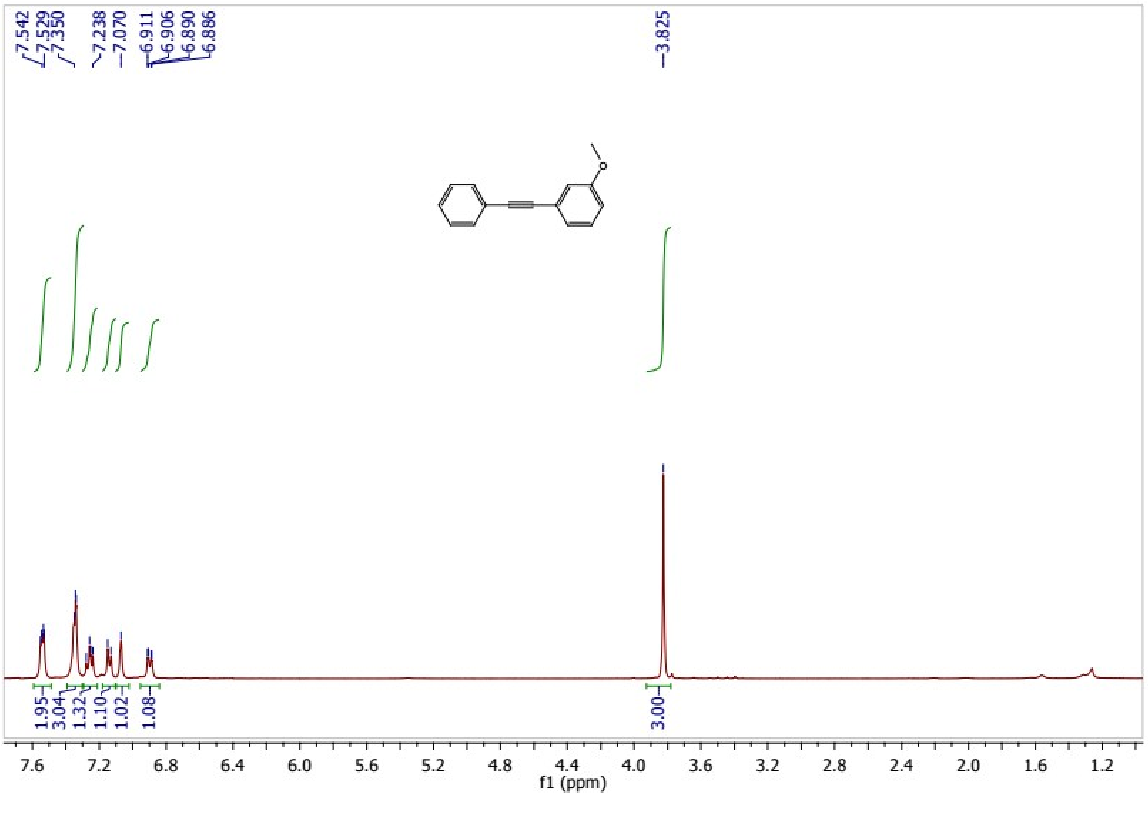
-120
-130
-140
f1 (ppm)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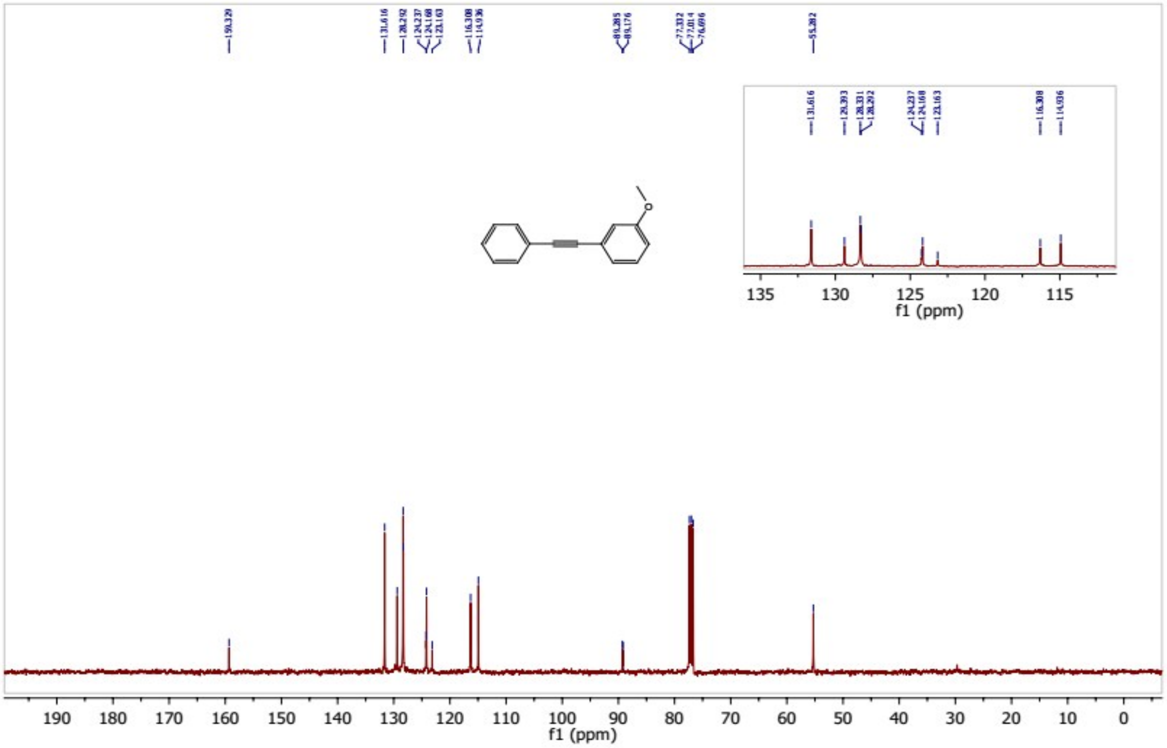
7.529
7.350
7.238
7.070
6.911
6.906
6.890
6.886
3.825
O
1.95
3.04
1.32
1.10
1.02
1.08
3.00
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
f1 (ppm)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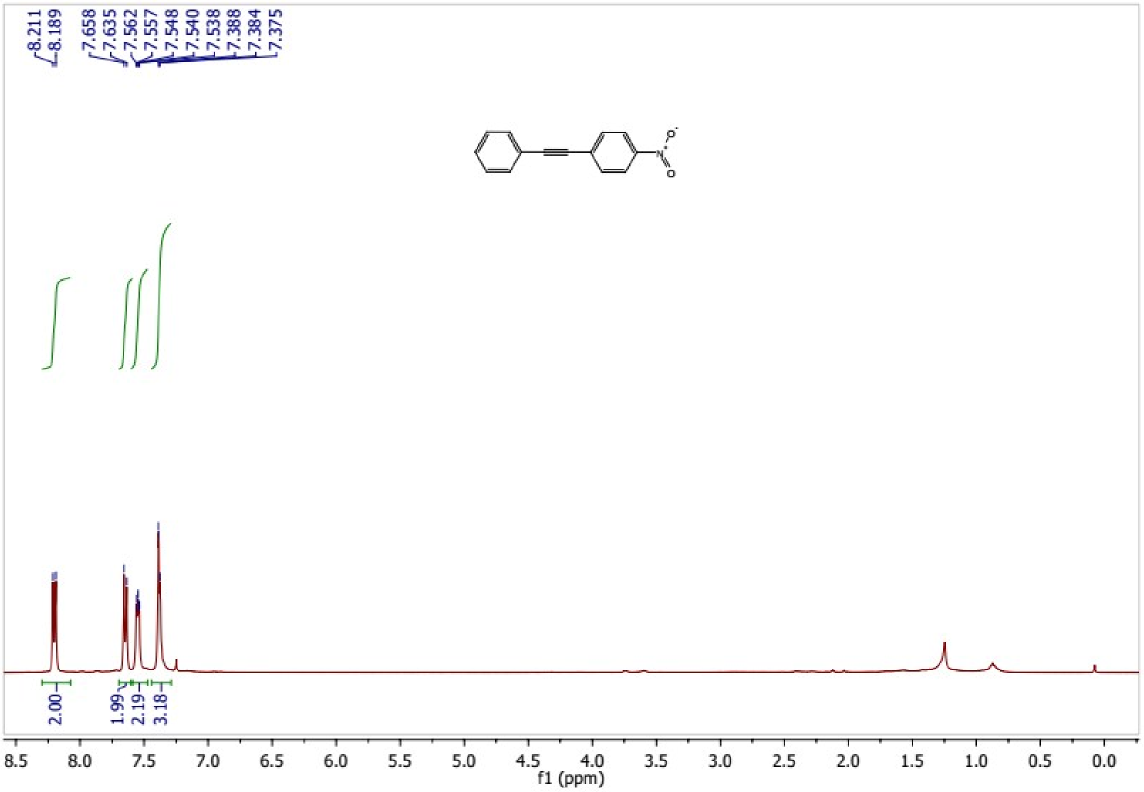
124.237
124.168
123.163
116.308
114.936
89.285
89.176
77.332
77.014
76.696
55.282
131.616
129.393
128.331
128.292
124.237
124.168
123.163
116.308
114.936
135
130
125
120
115
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.635
7.562
7.557
7.548
7.540
7.538
7.388
7.384
7.375
2.00
1.99
2.19
3.18
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
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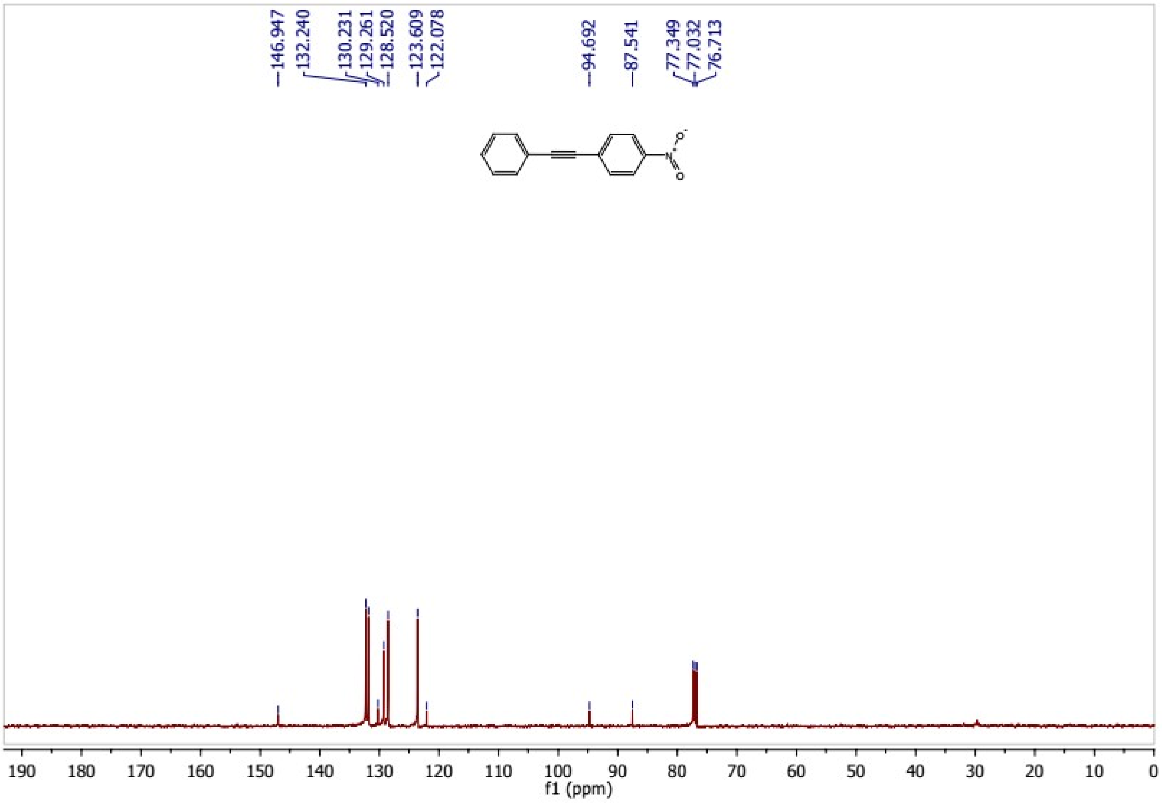
0.0
f1 (ppm)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130.231
129.261
128.520
123.609
122.078
94.692
87.541
77.349
77.032
76.713
190
180
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160
150
140
130
120
110
100
90
80
70
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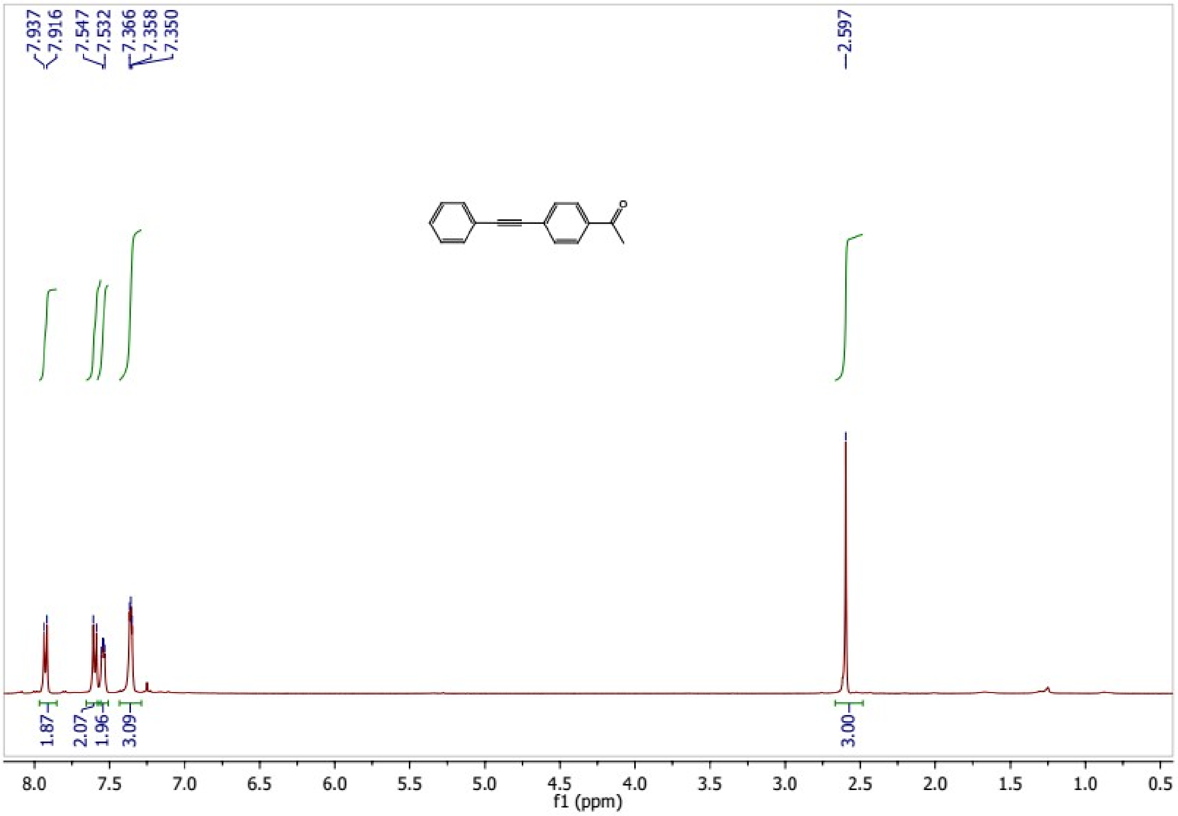
50
40
30
20
10
0
f1 (ppm)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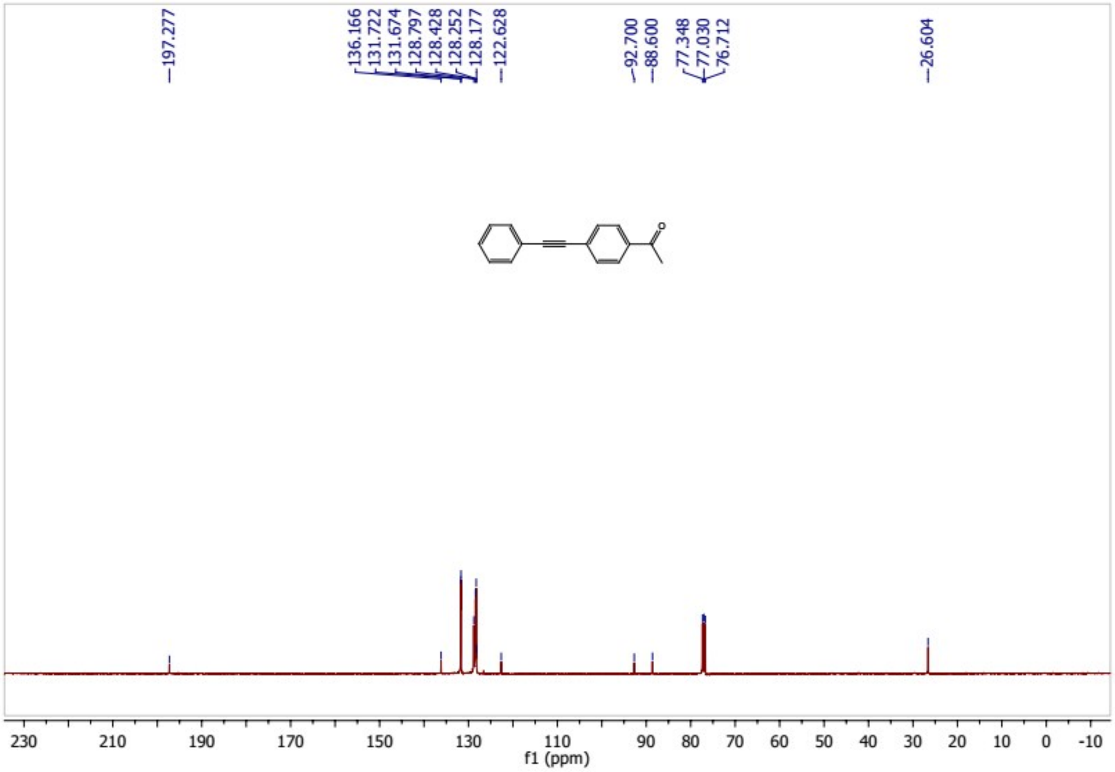
2.07
1.96
3.09
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
O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128.428
128.252
128.177
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92.700
88.600
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77.030
76.712
26.604
230
210
190
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150
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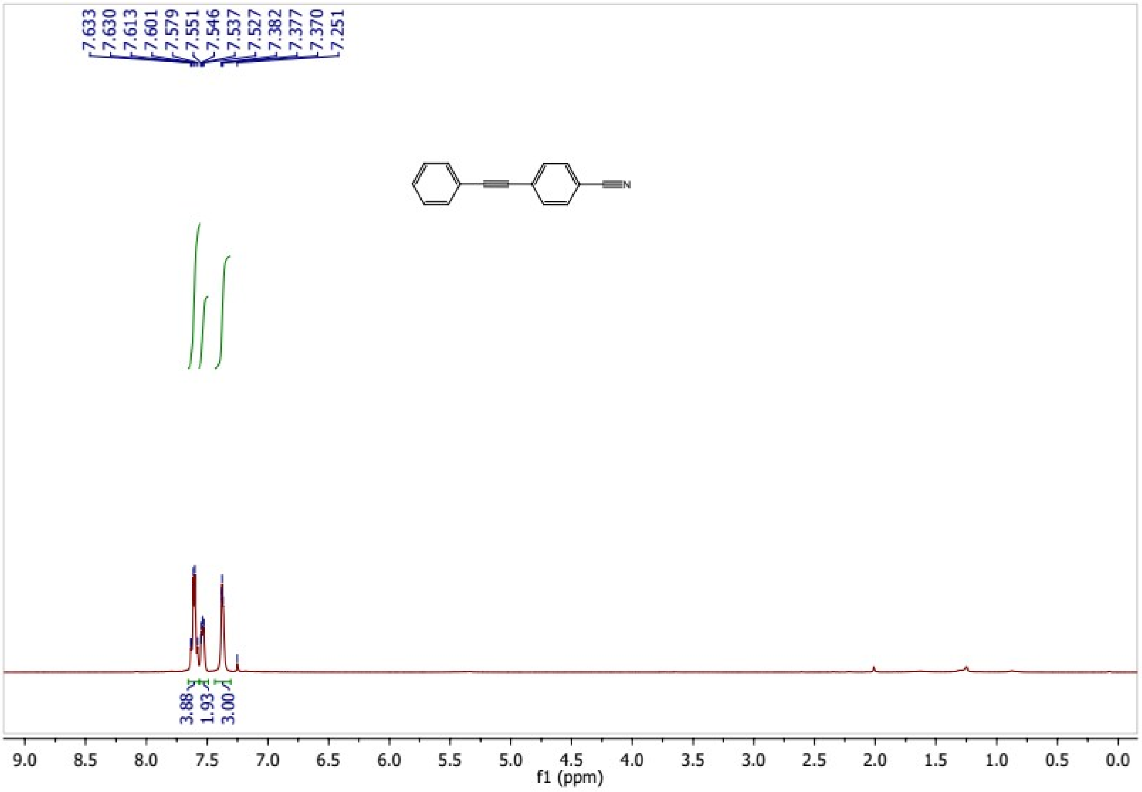
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
O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7.537
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7.382
7.377
7.370
7.251
N
3.88
1.93
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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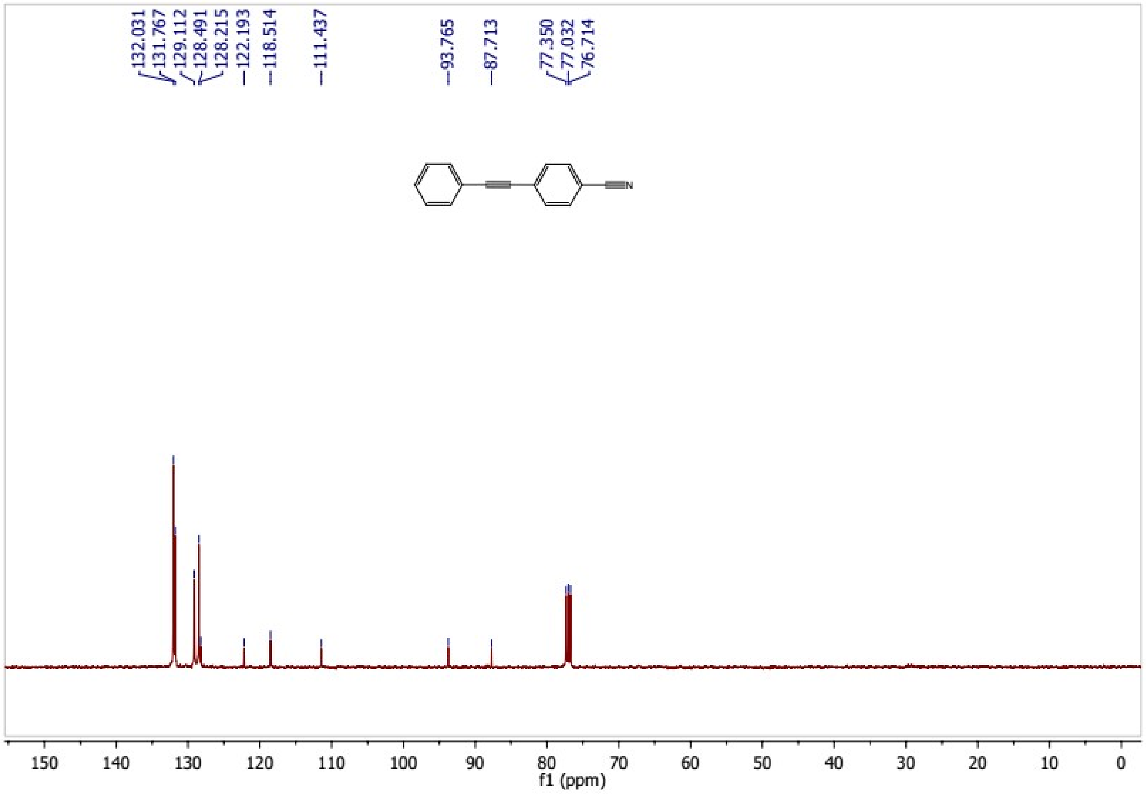
0.0
f1 (ppm)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111.437
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30
20
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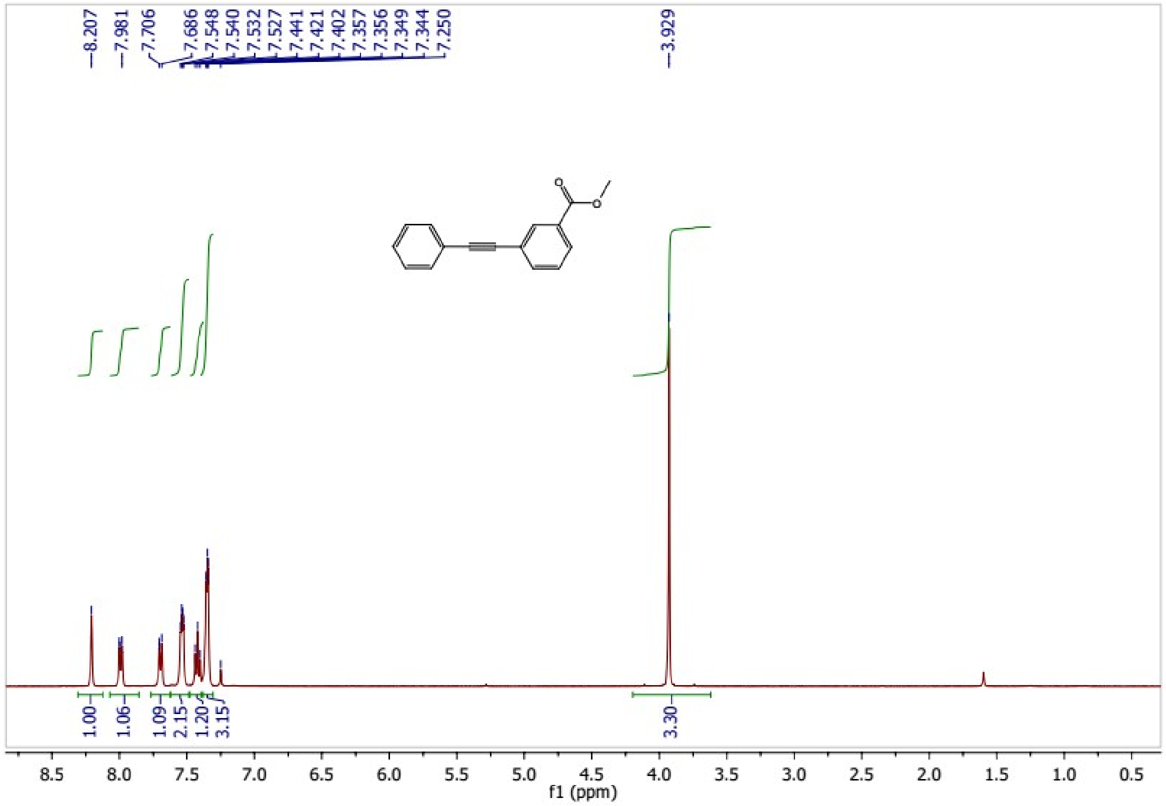
f1 (ppm)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7.527
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7.421
7.402
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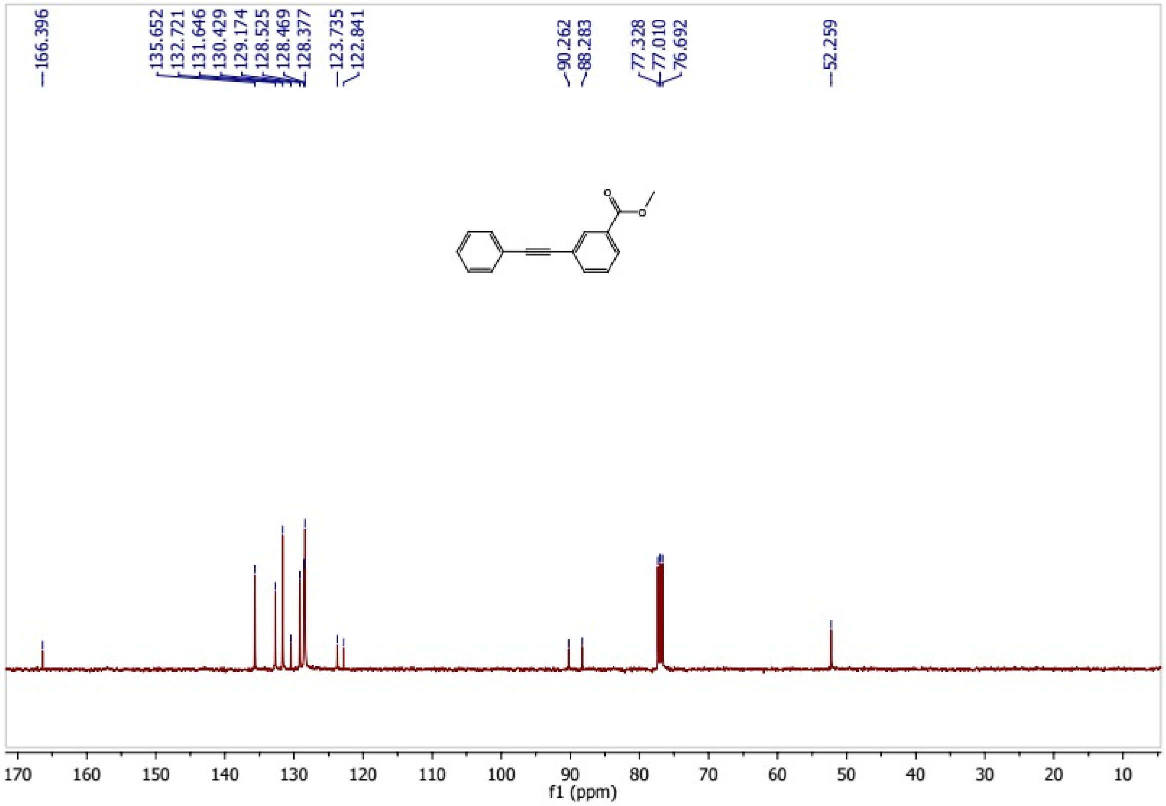
7.356
7.349
7.344
7.250
3.929
1.00
1.06
1.09
2.15
1.20
3.15
3.30
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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130.429
129.174
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128.469
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123.735
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77.328
77.010
76.692
52.259
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150
140
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120
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100
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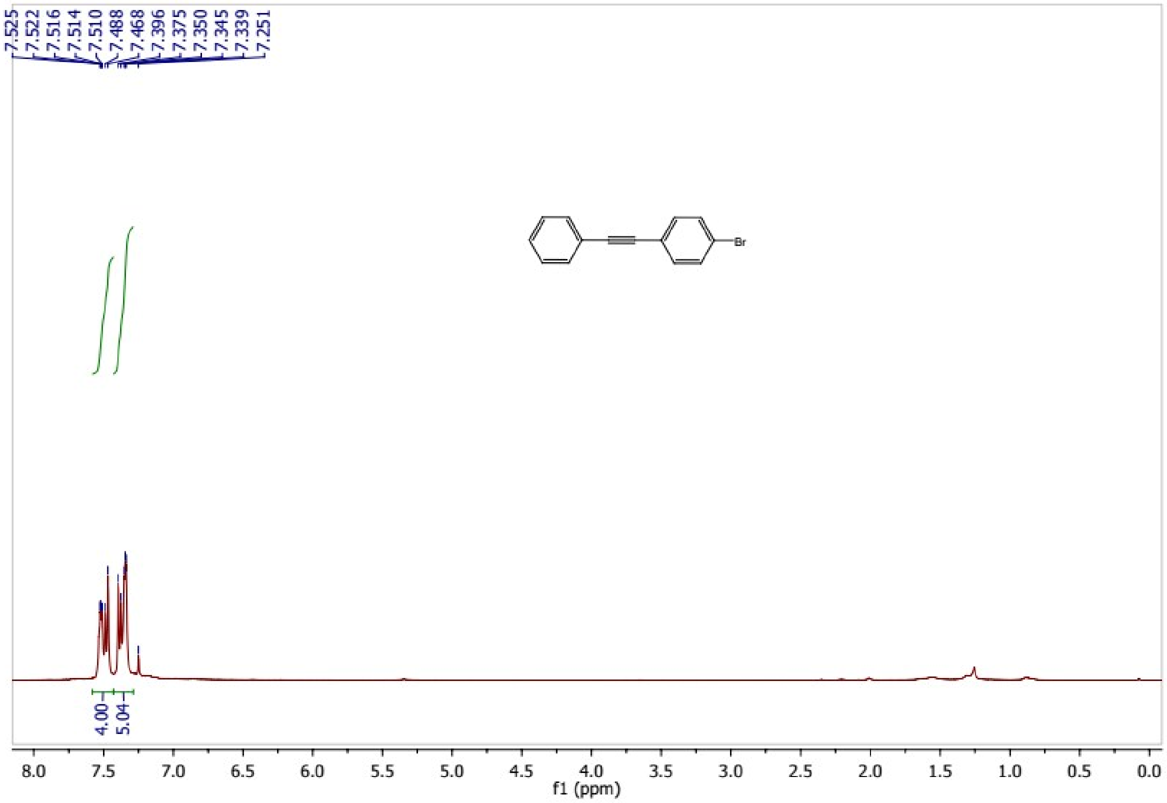
80
70
60
50
40
30
20
10
f1 (ppm)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7.514
7.510
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7.375
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7.345
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7.251
Br
4.00
5.04
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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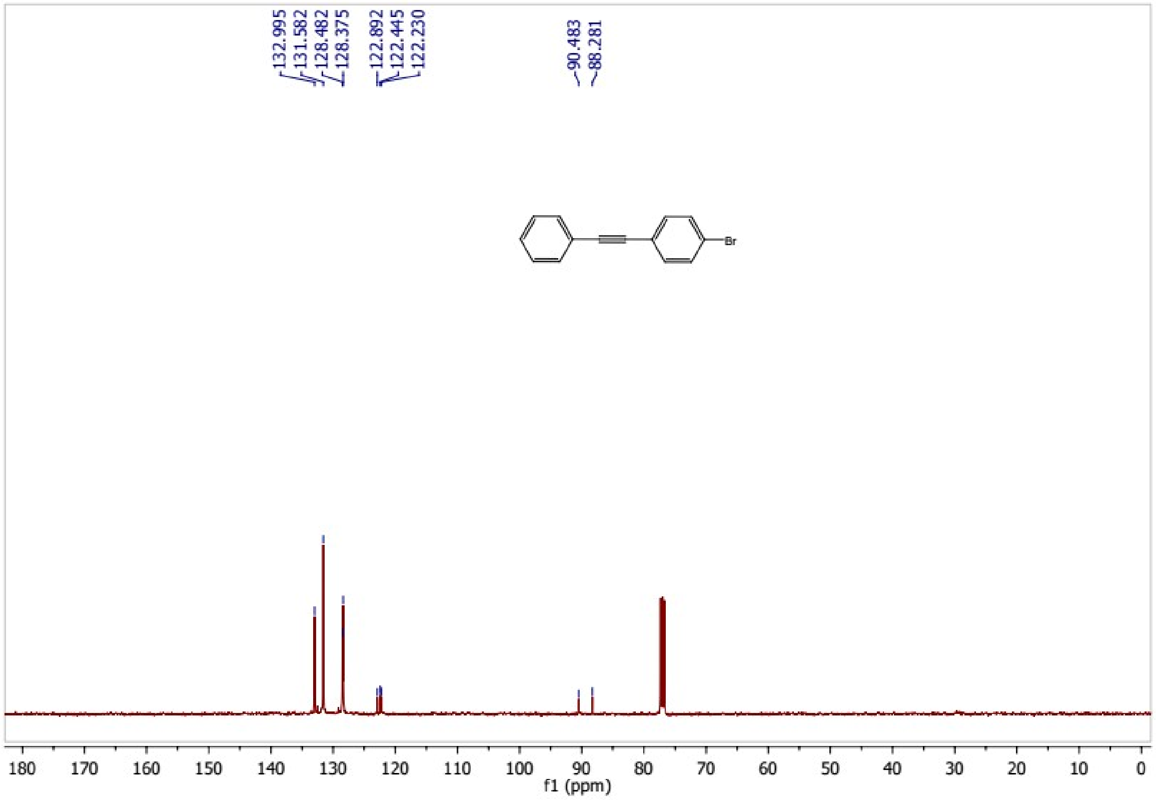
0.0
f1 (ppm)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Br
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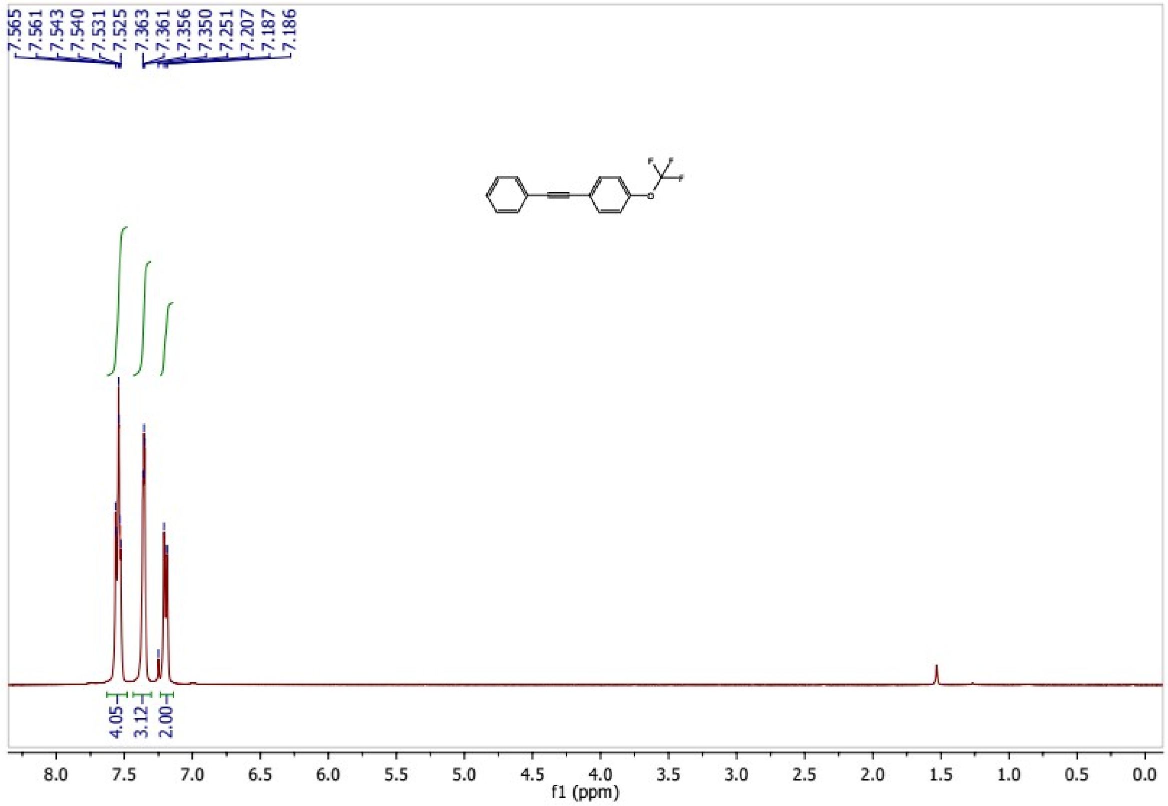
20
10
0
f1 (ppm)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7.361
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7.251
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7.187
7.186
F
F
F
O
4.05
3.12
2.00
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
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2.5
2.0
1.5
1.0
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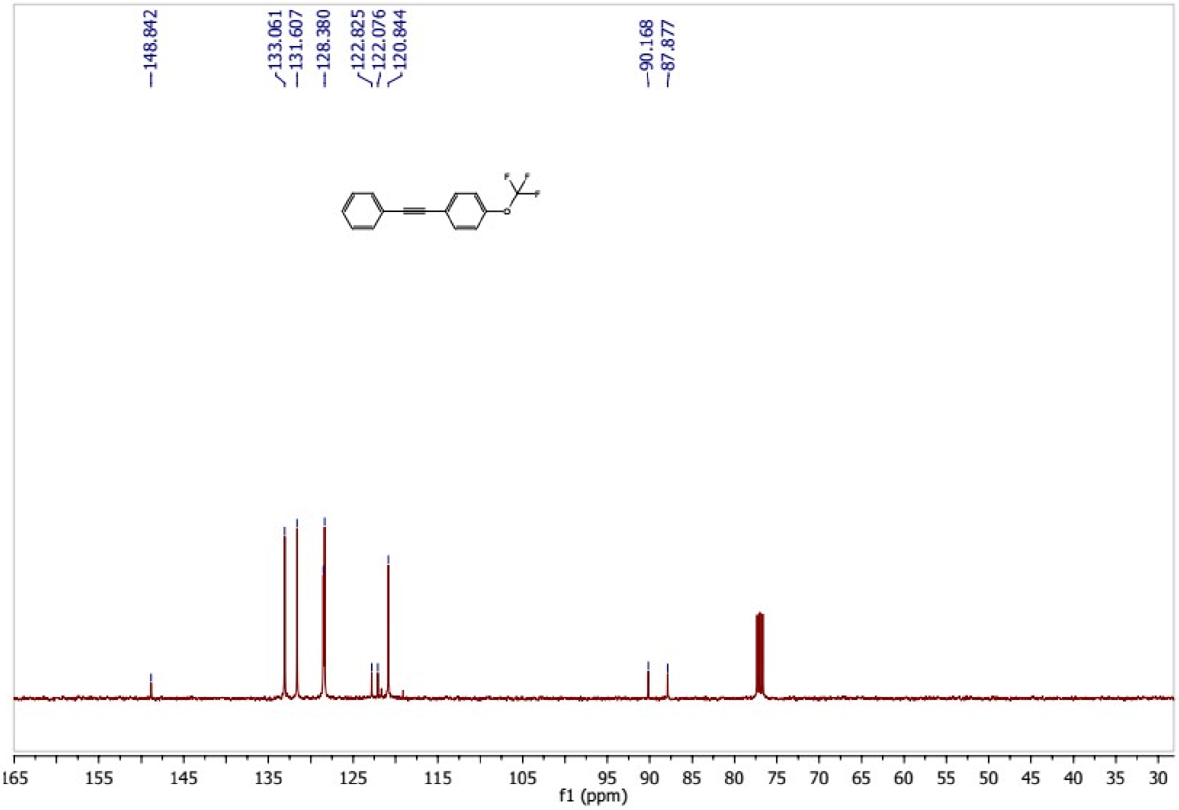
f1 (ppm)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90.168
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F
F
O
165
155
145
135
125
115
105
95
90
85
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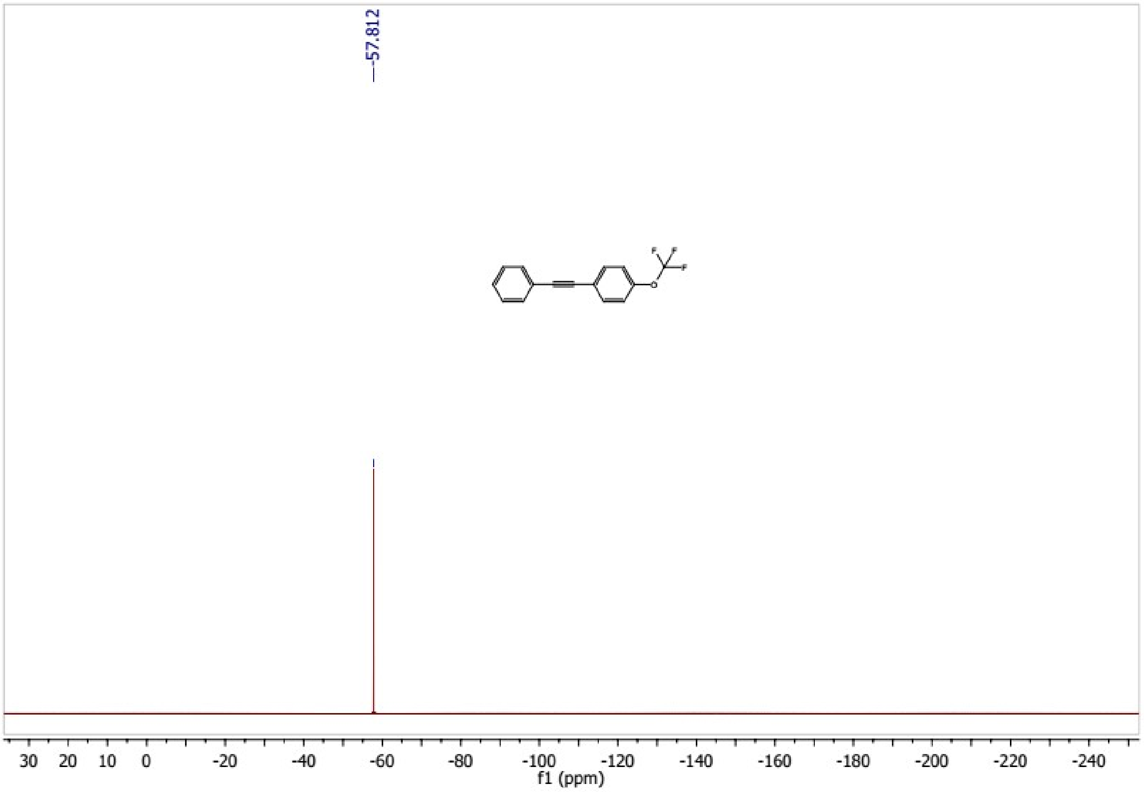
75
70
65
60
55
50
45
40
35
30
f1 (ppm)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F
O
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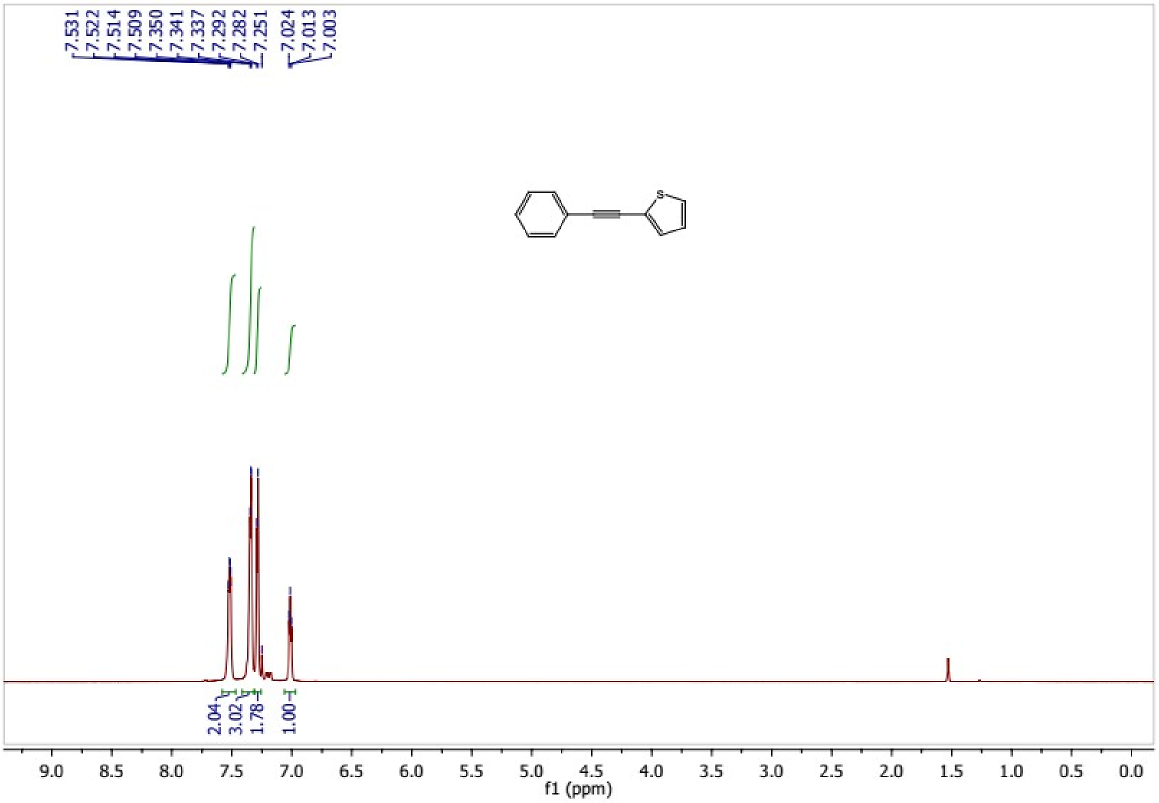
-240
f1 (ppm)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7.350
7.341
7.337
7.292
7.282
7.251
7.024
7.013
7.003
S
2.04
3.02
1.78
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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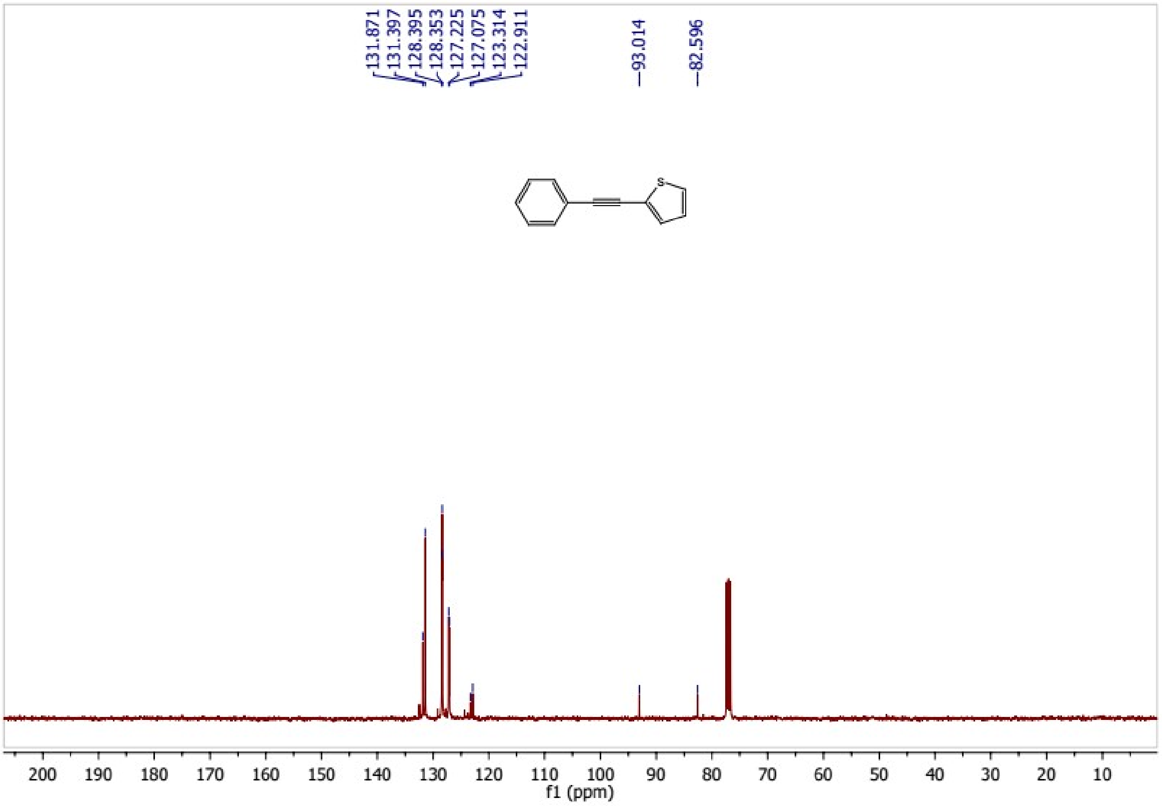
0.0
f1 (ppm)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82.596
S
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190
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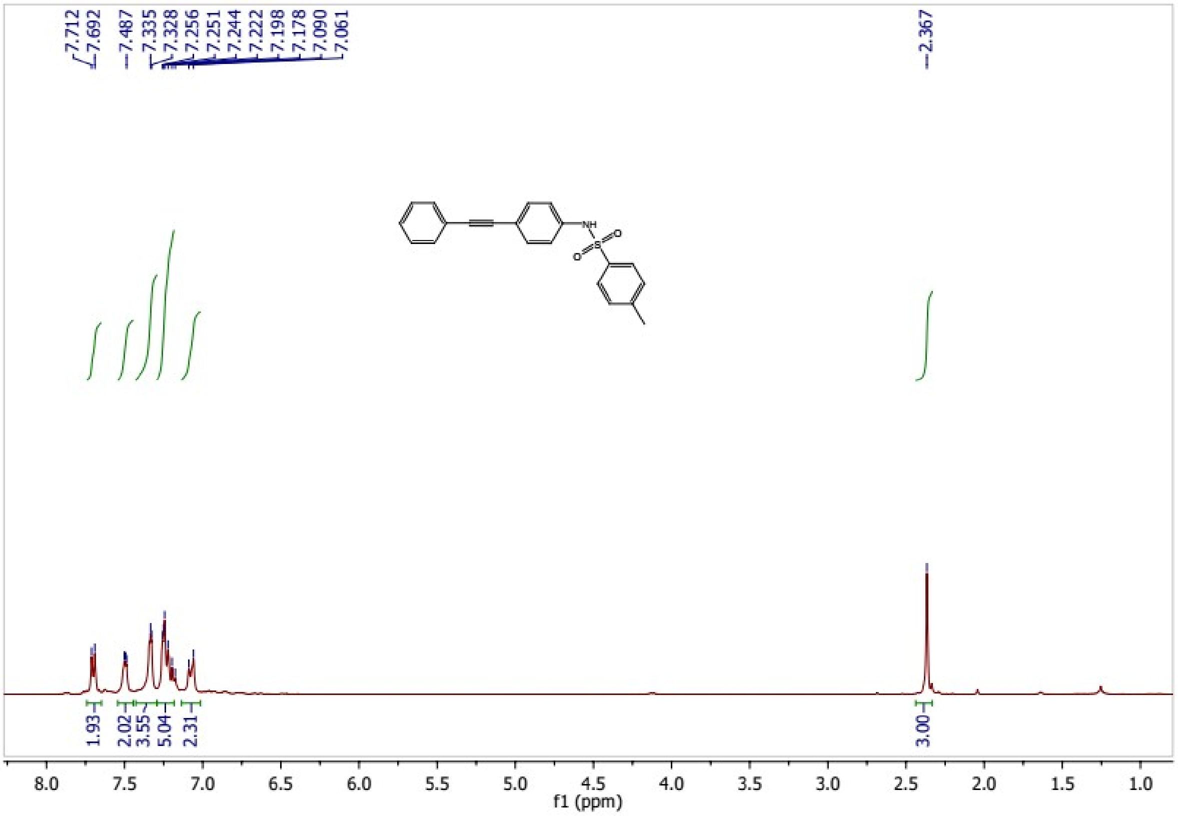
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.328
7.256
7.251
7.244
7.222
7.198
7.178
7.090
7.061
2.367
NH
S
O
O
1.93
2.02
3.55
5.04
2.31
3.00
8.0
7.5
7.0
6.5
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3.5
3.0
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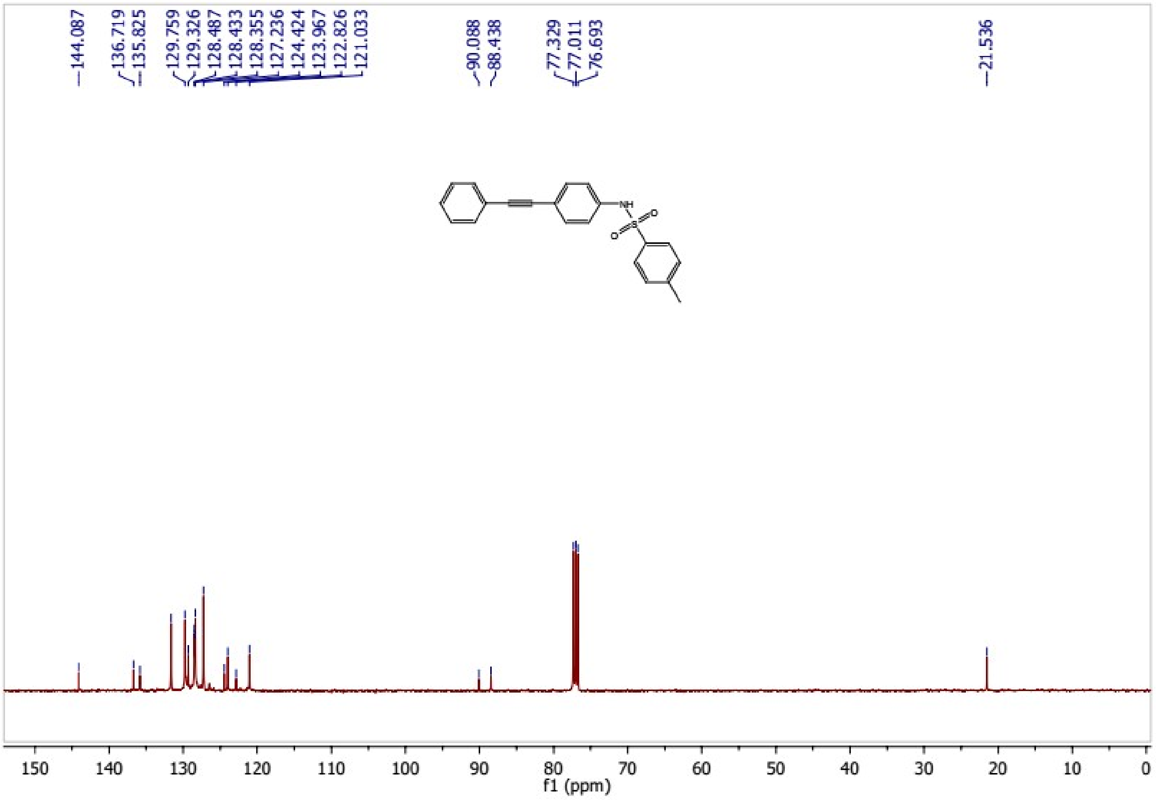
2.0
1.5
1.0
f1 (ppm)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128.355
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124.424
123.967
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121.033
90.088
88.438
77.329
77.011
76.693
21.536
NH
S
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90
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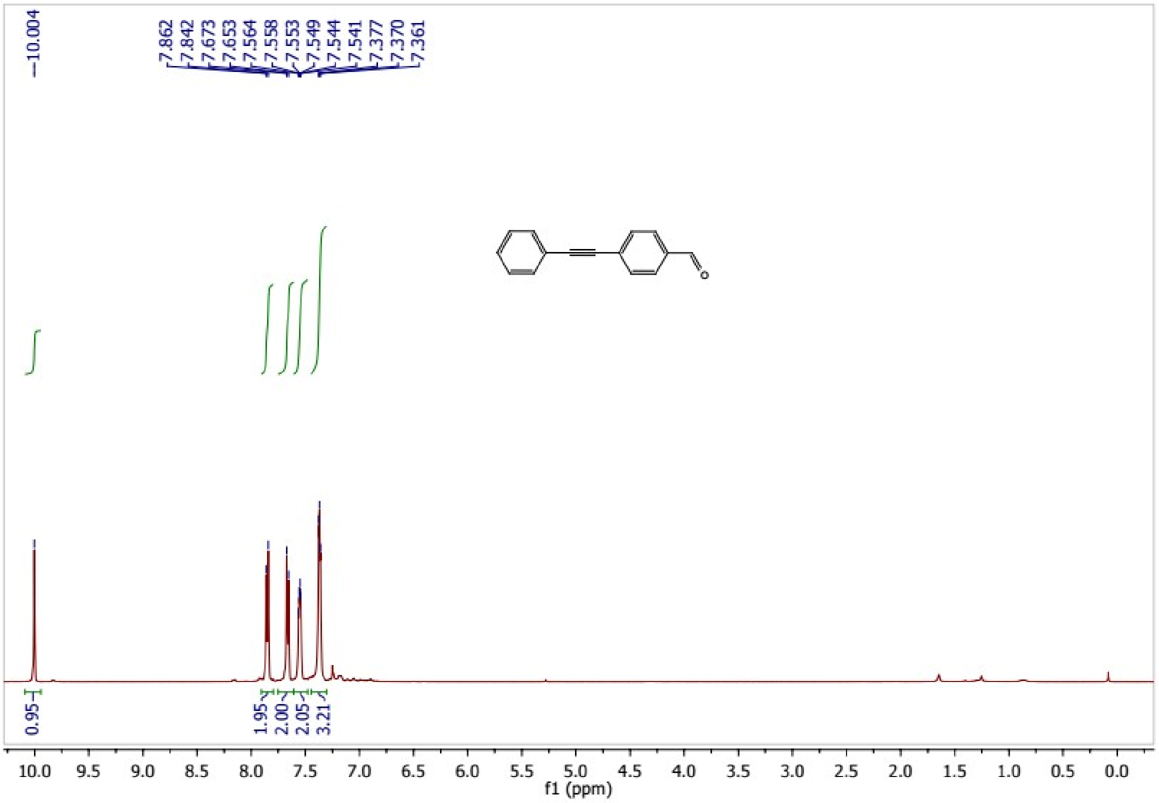
50
40
30
20
10
0
f1 (ppm)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7.541
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7.370
7.361
O
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1.95
2.00
2.05
3.21
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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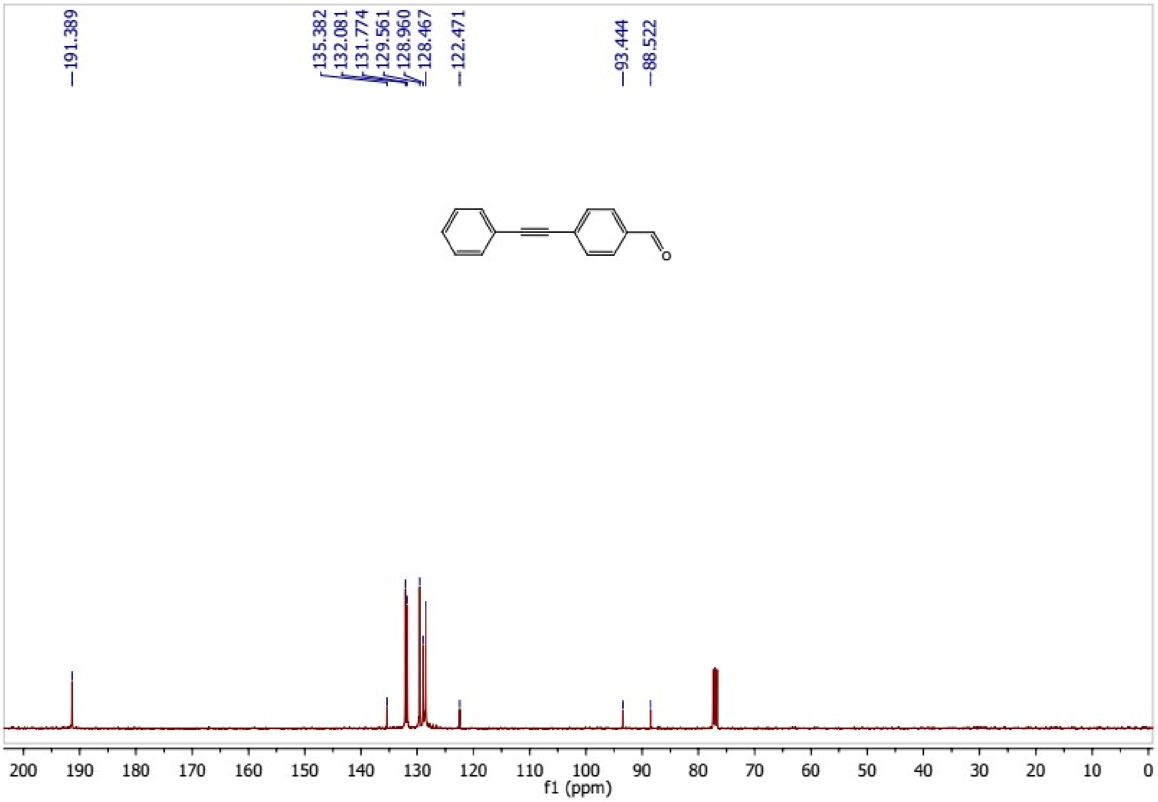
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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O
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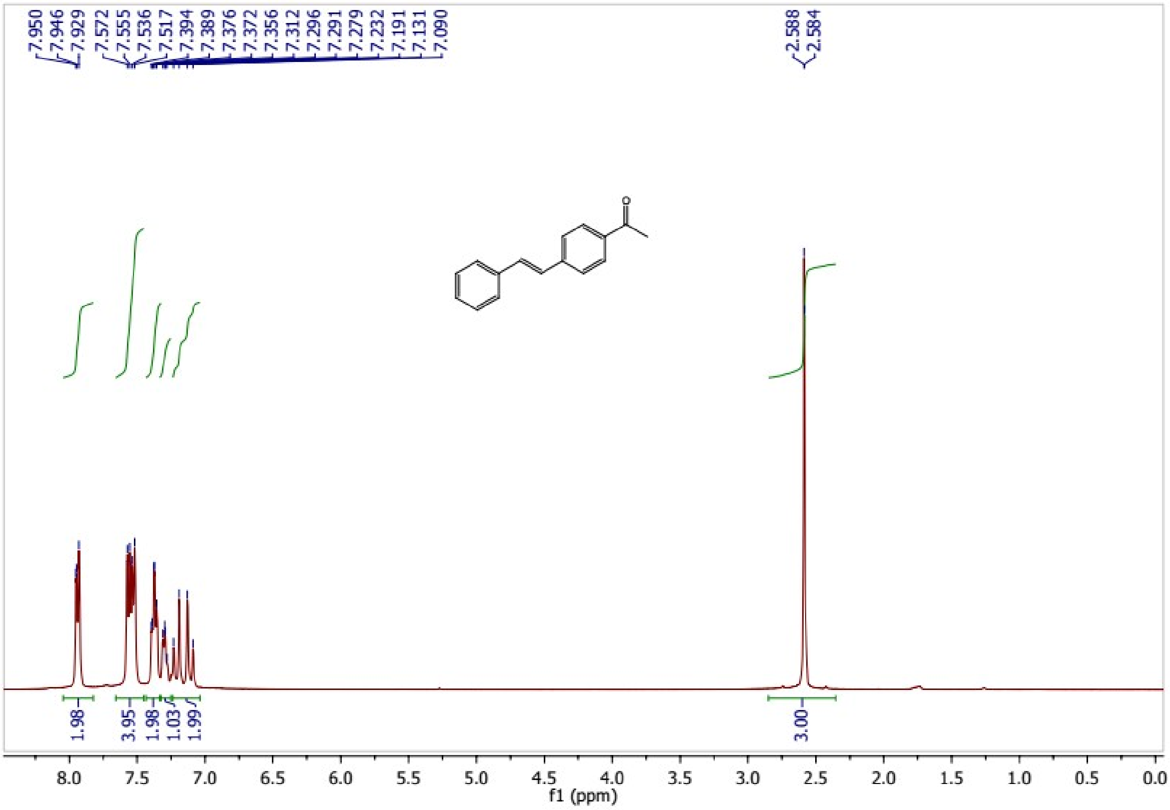
f1 (ppm)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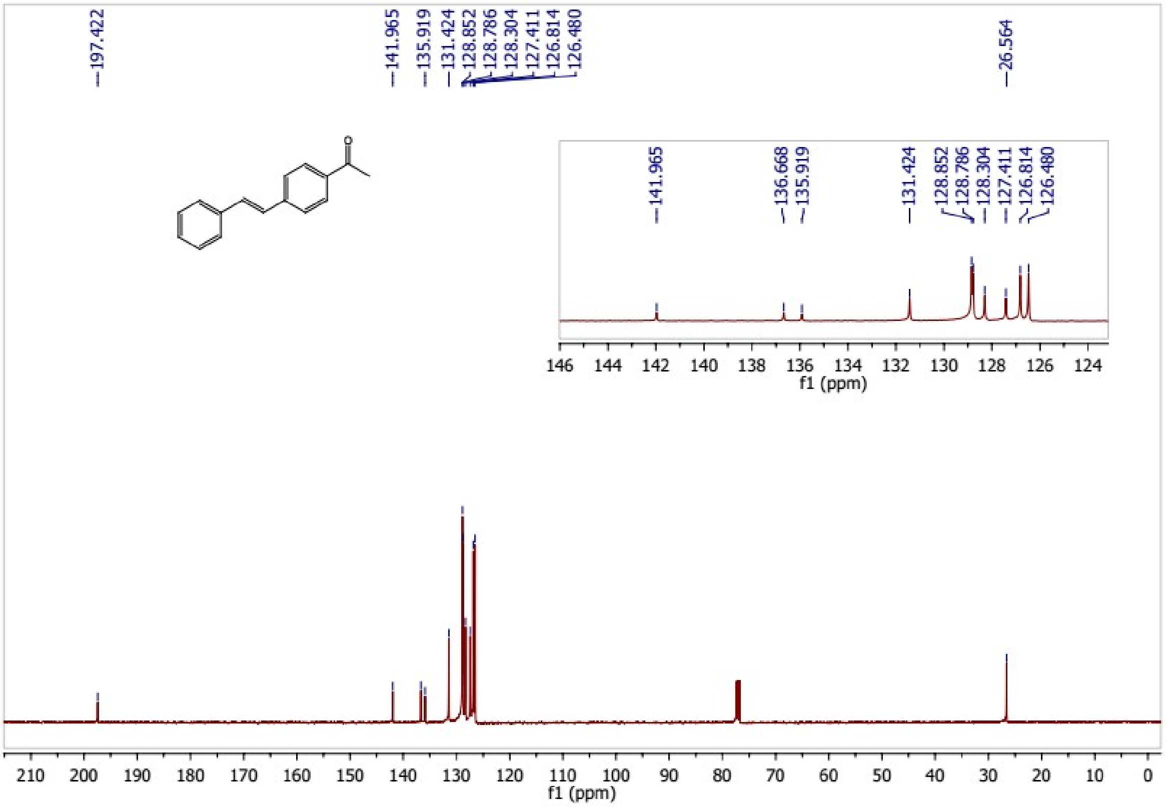
7.394
7.389
7.376
7.372
7.356
7.312
7.296
7.291
7.279
7.232
7.191
7.131
7.090
2.588
2.584
O
1.98
3.95
1.98
1.03
1.99
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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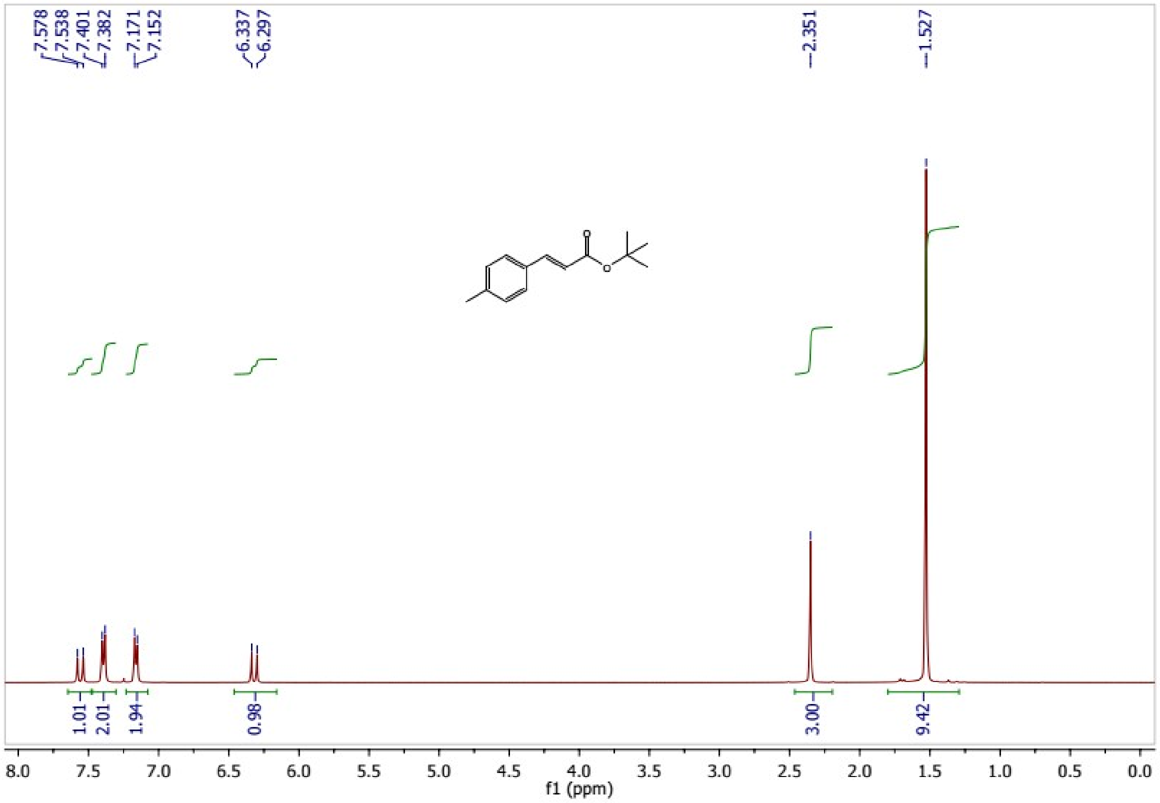
135.919
131.424
128.852
128.786
128.304
127.411
126.814
126.480
26.564
141.965
136.668
135.919
131.424
128.852
128.786
128.304
127.411
126.814
126.480
146 144 142 140 138 136 134 132 130 128 126 124
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.538
7.401
7.382
7.171
7.152
6.337
6.297
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1.527
1.01
2.01
1.94
0.98
3.00
9.42
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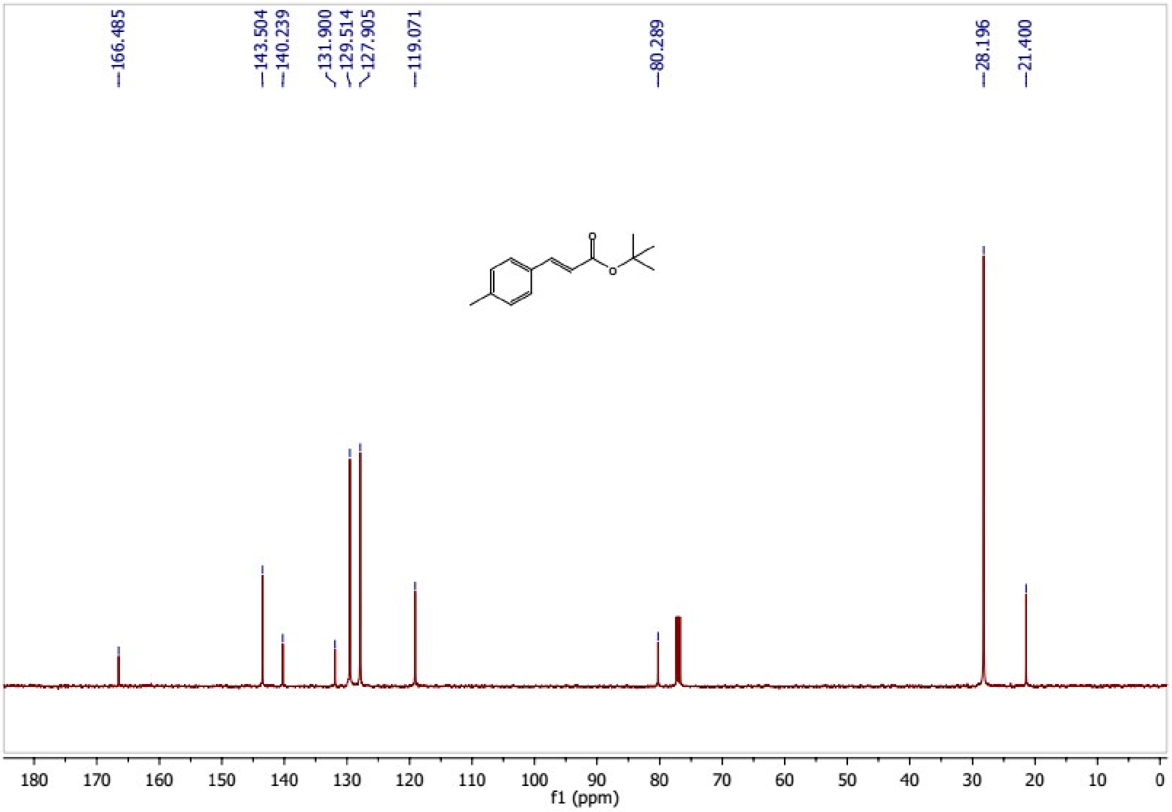
f1 (ppm)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143.504
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131.900
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127.905
119.071
80.289
28.196
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O
O
180
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150
140
130
120
110
100
90
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50
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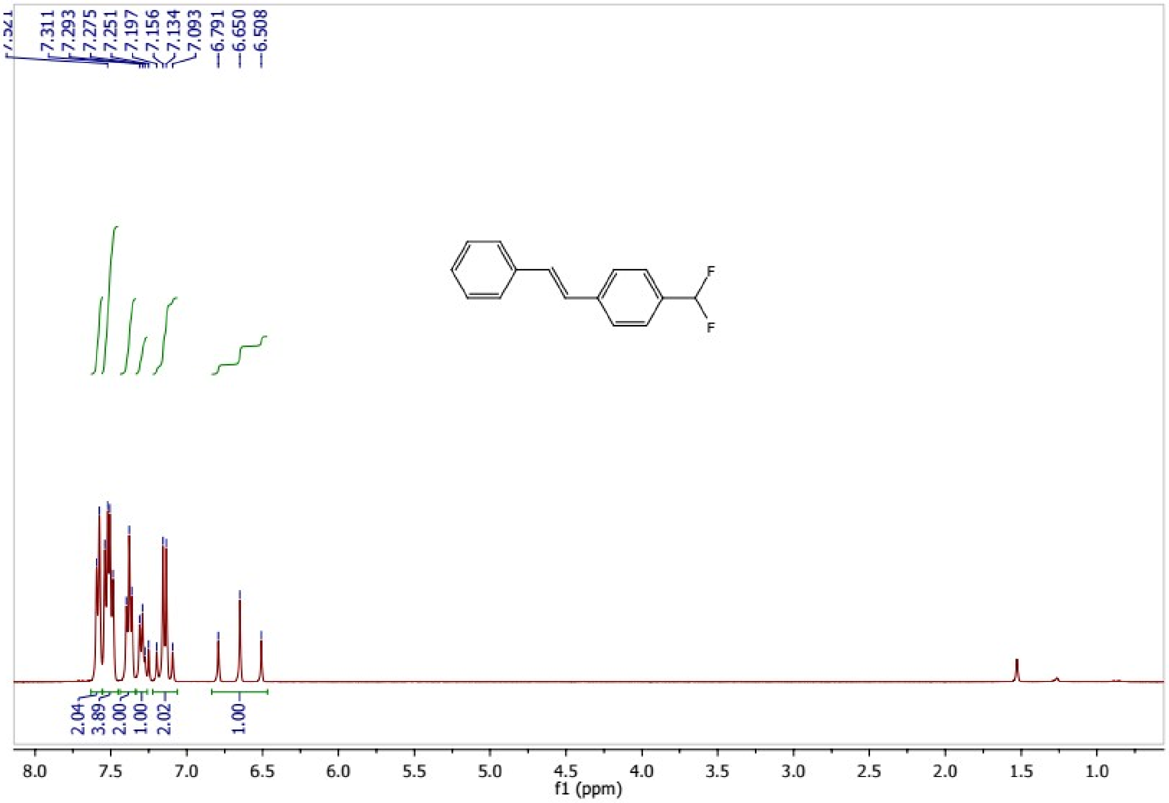
20
10
0
f1 (ppm)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7.293
7.275
7.251
7.197
7.156
7.134
7.093
6.791
6.650
6.508
F
F
2.04
3.89
2.00
1.00
2.02
1.00
8.0
7.5
7.0
6.5
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5.0
4.5
4.0
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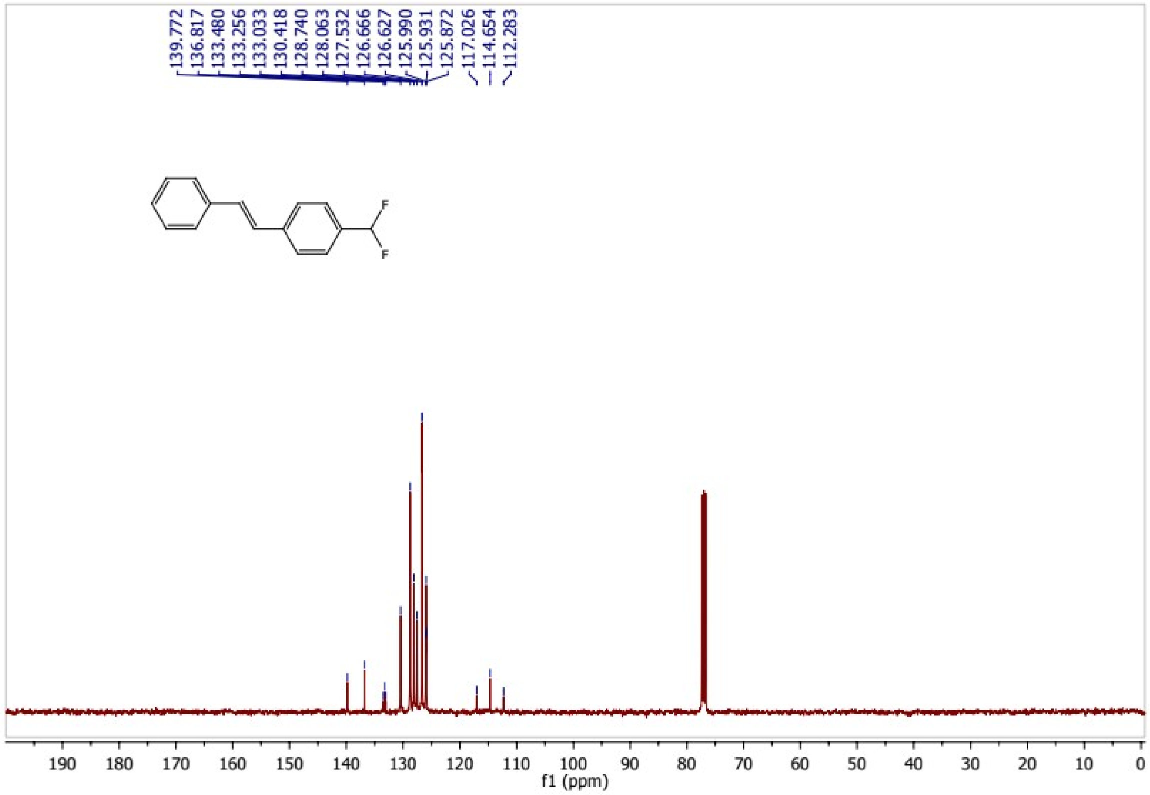
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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136.817
133.480
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133.033
130.418
128.740
128.063
127.532
126.666
126.627
125.990
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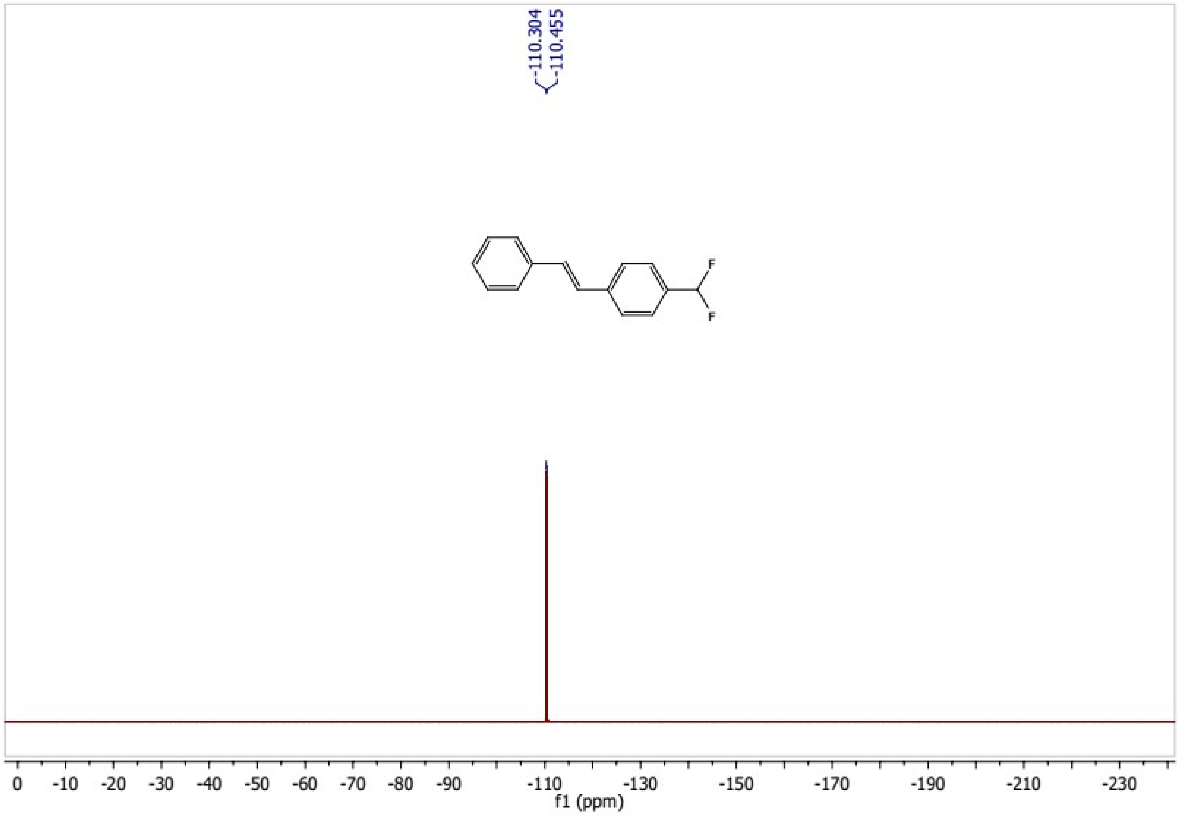
125.872
117.026
114.654
112.283
F
F
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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F
F
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150 -170 -190 -210 -230
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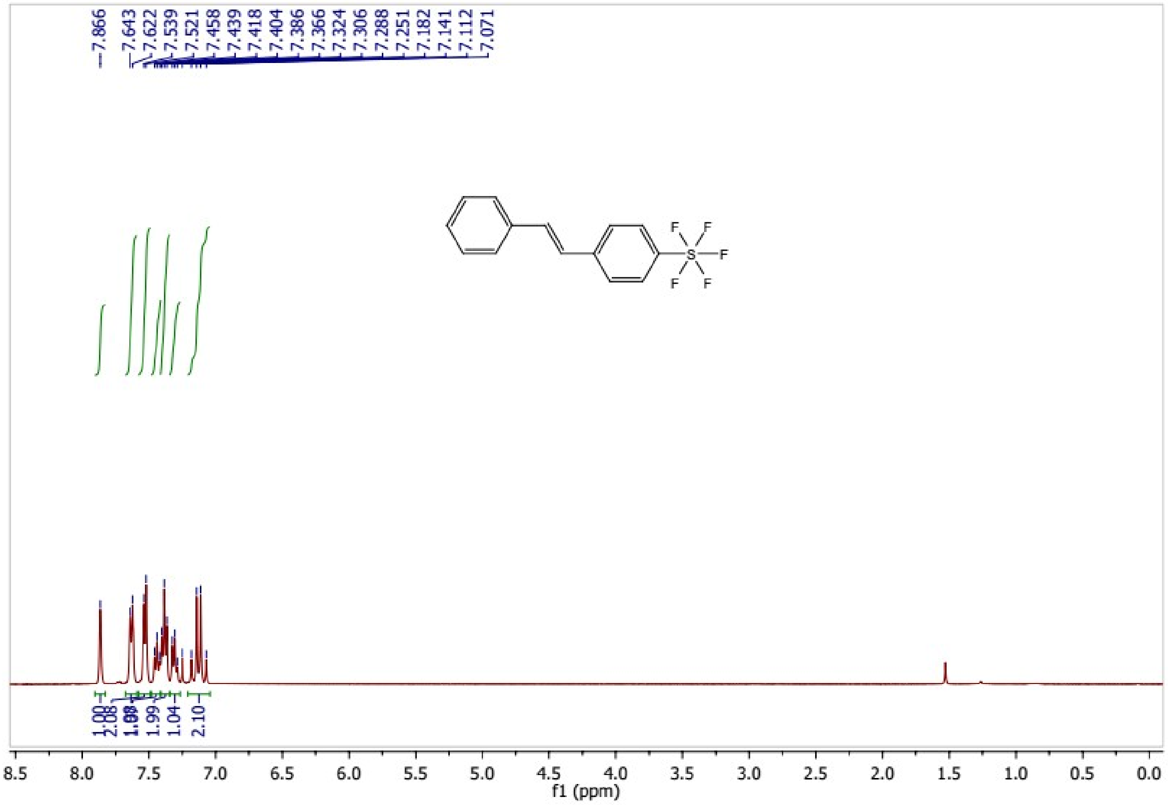
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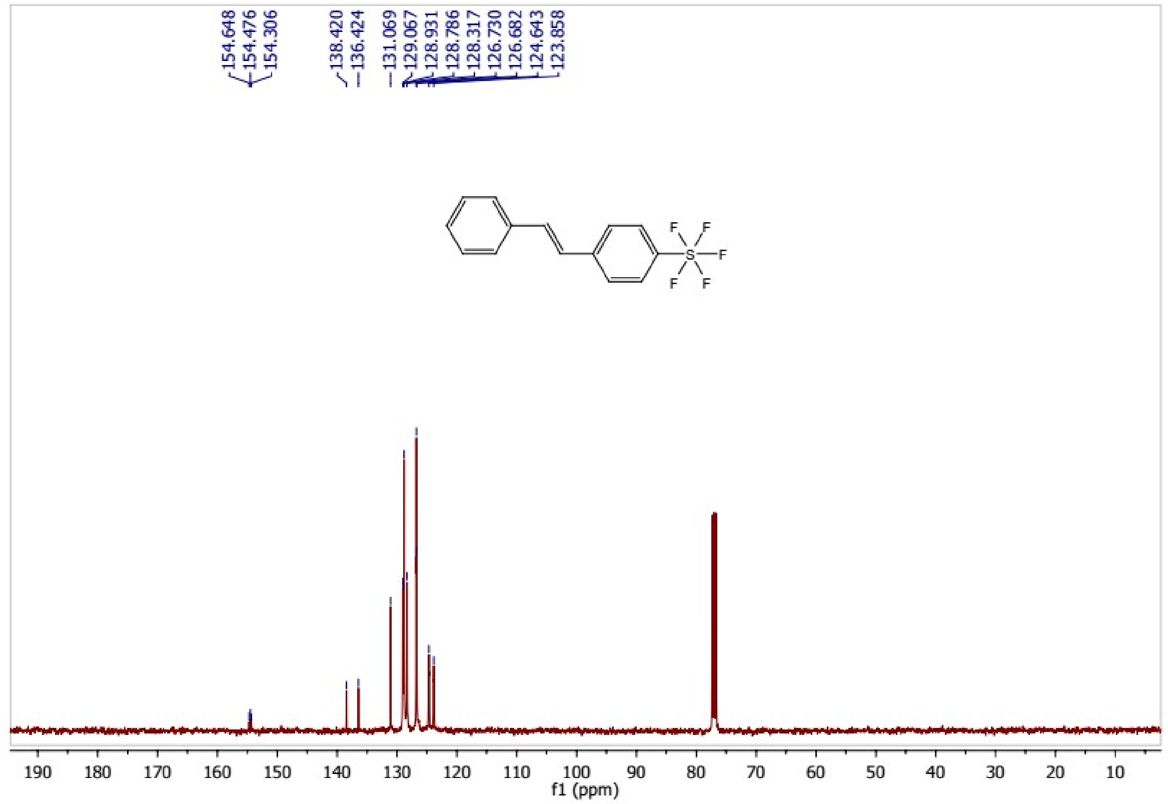
7.622
7.539
7.521
7.458
7.439
7.418
7.404
7.386
7.366
7.324
7.306
7.288
7.251
7.182
7.141
7.112
7.071
F
F
S
F
F
F
1.00
2.08
1.99
1.04
2.10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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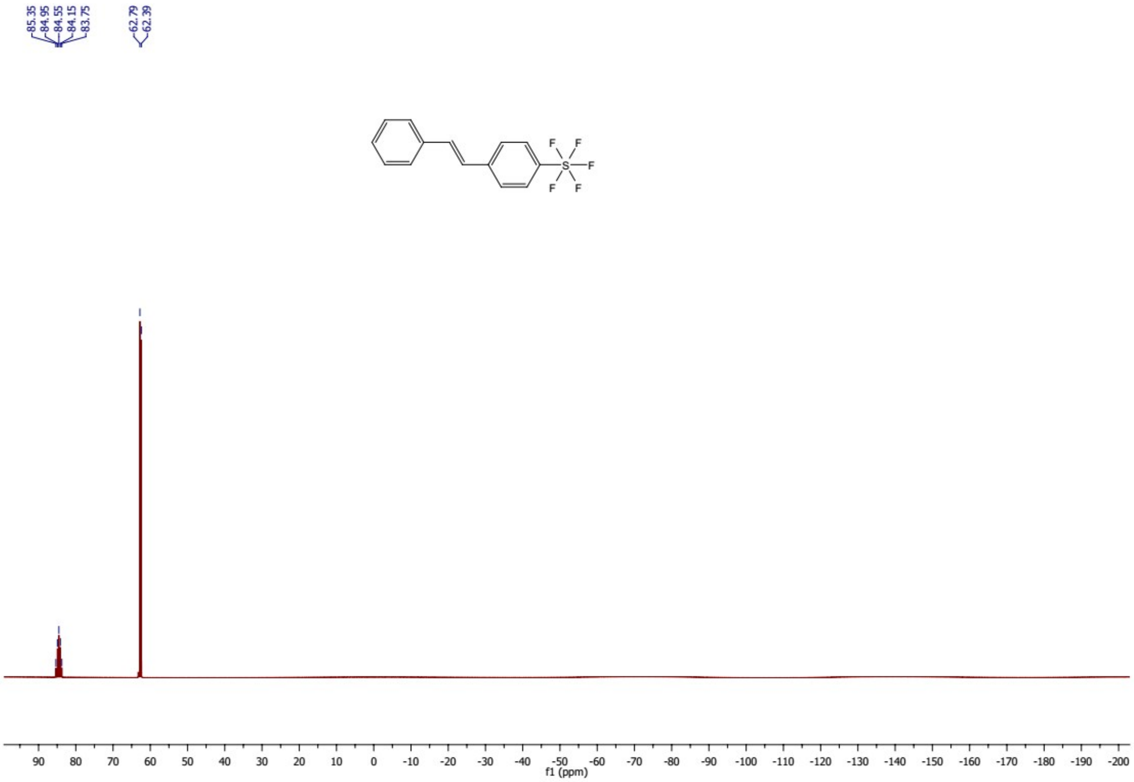
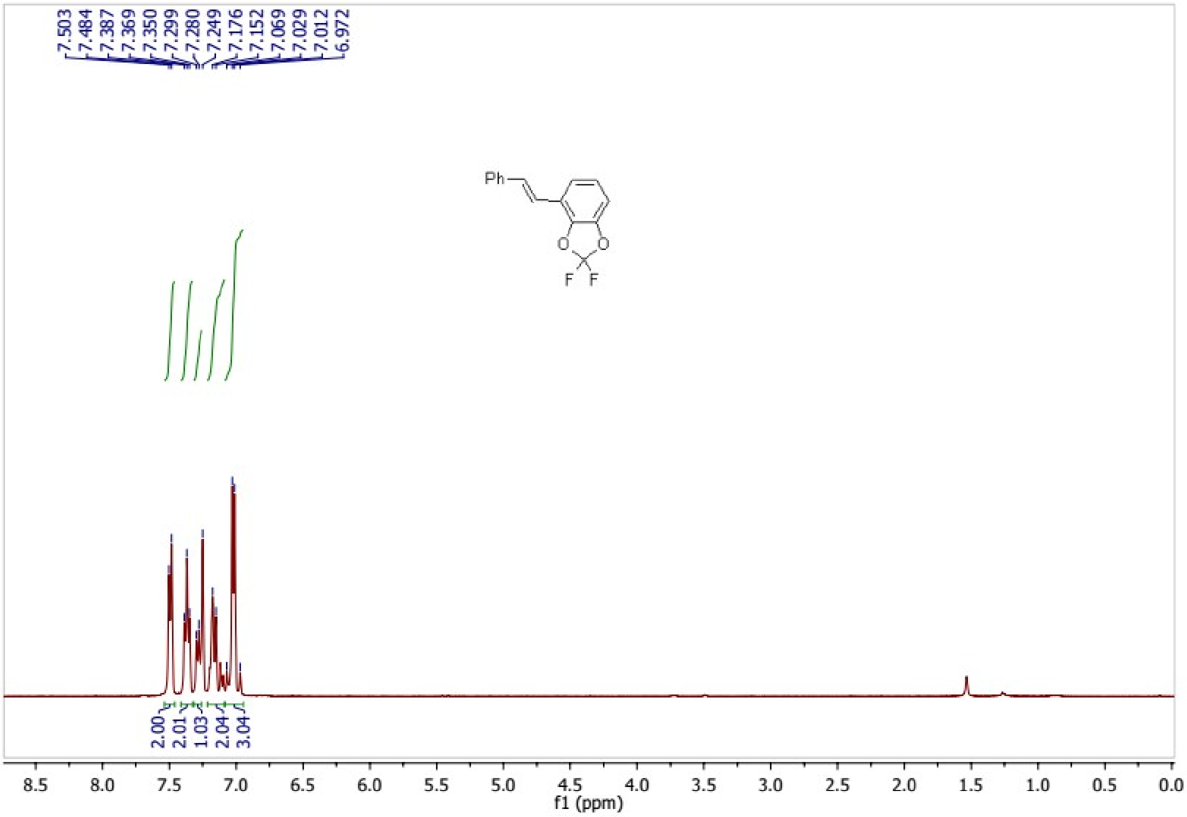
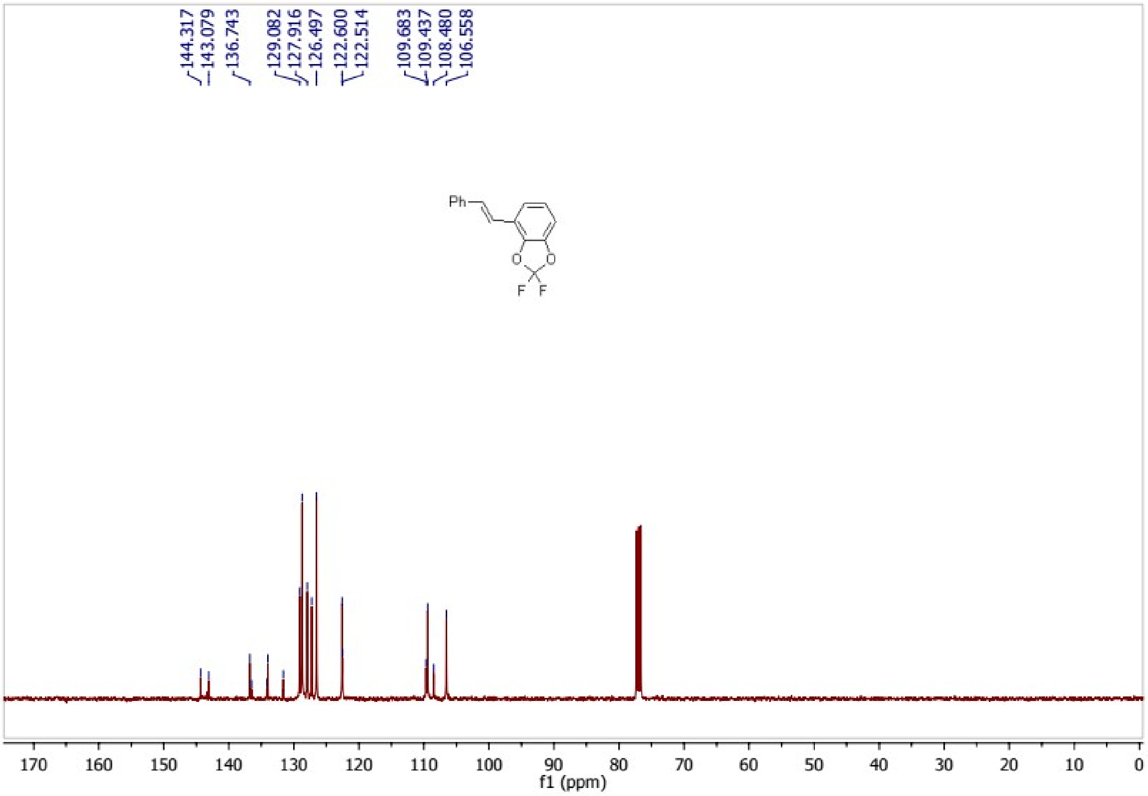
154.476
154.306
138.420
136.424
131.069
129.067
128.931
128.786
128.317
126.730
126.682
124.643
123.858
F
F
S
F
F
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


85.35
84.95
84.55
84.15
83.75
62.79
62.39
F
F
S
F
F
F
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


7.503
7.484
7.387
7.369
7.350
7.299
7.280
7.249
7.176
7.152
7.069
7.029
7.012
6.972
Ph
O
O
F F
2.00
2.01
1.03
2.04
3.04
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)


144.317
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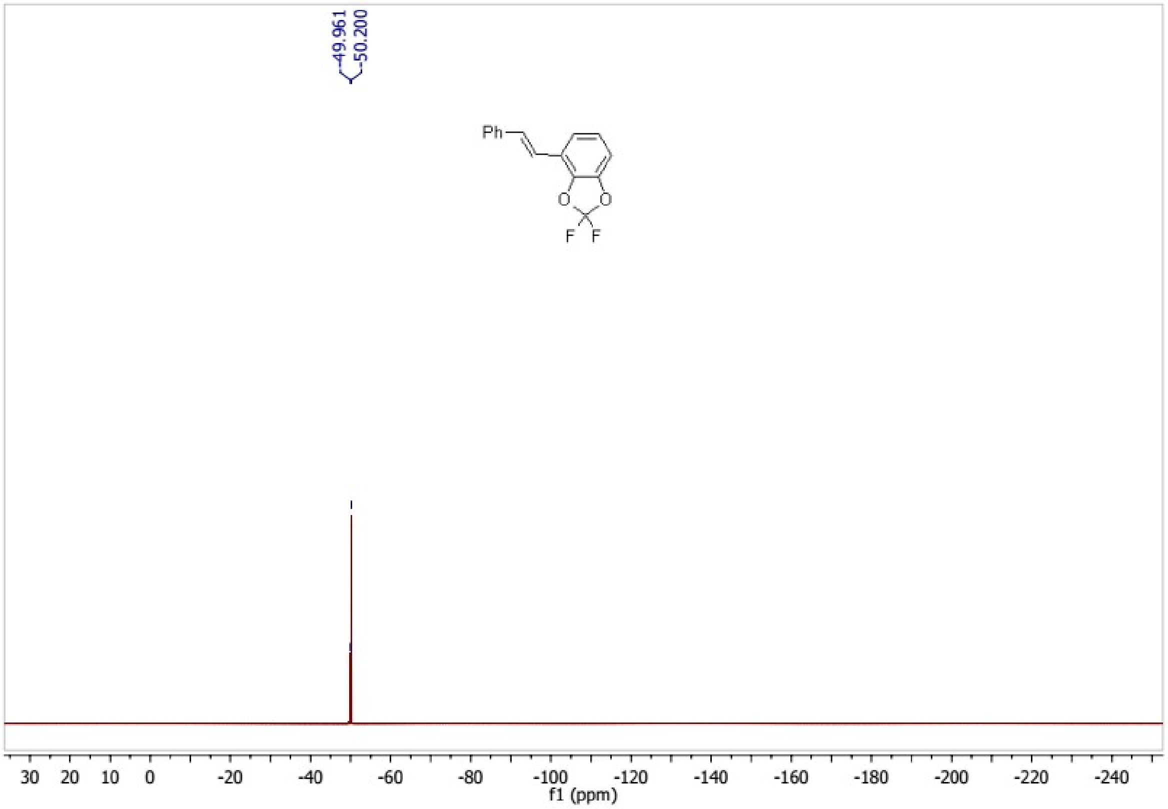
136.743
129.082
127.916
126.497
122.600
122.514
109.683
109.437
108.480
106.558
Ph
O
O
F
F
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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-50.200
Ph
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O
F
F
30
20
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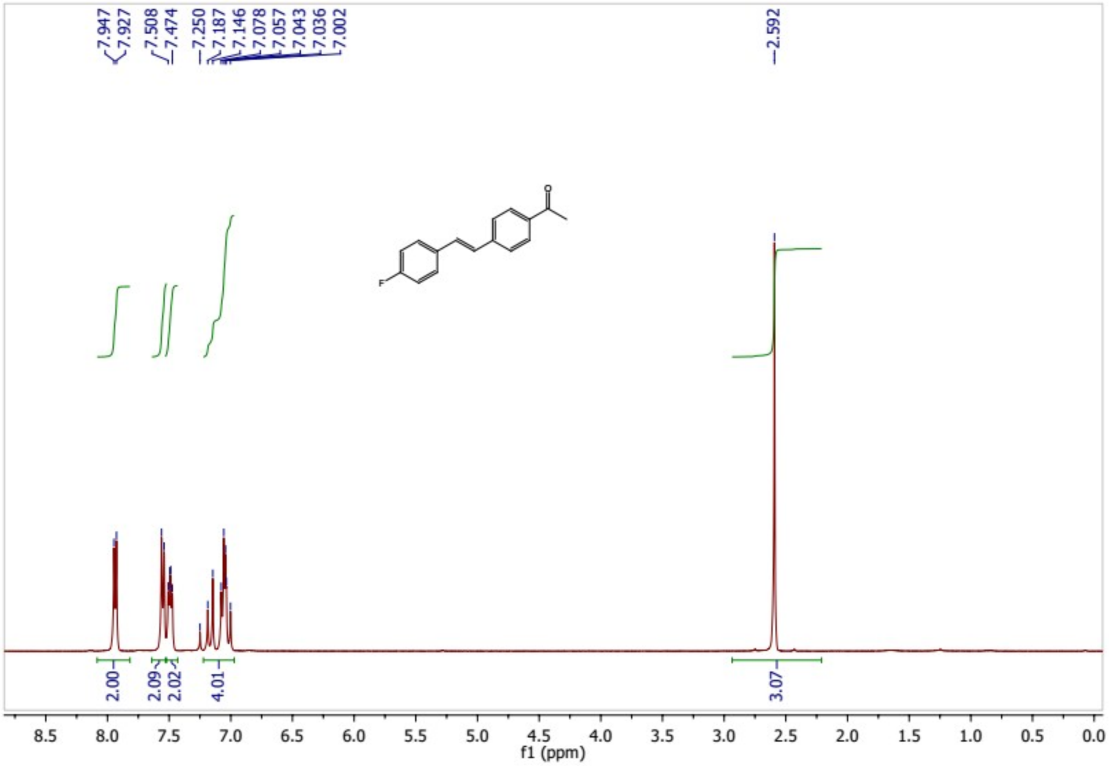
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm)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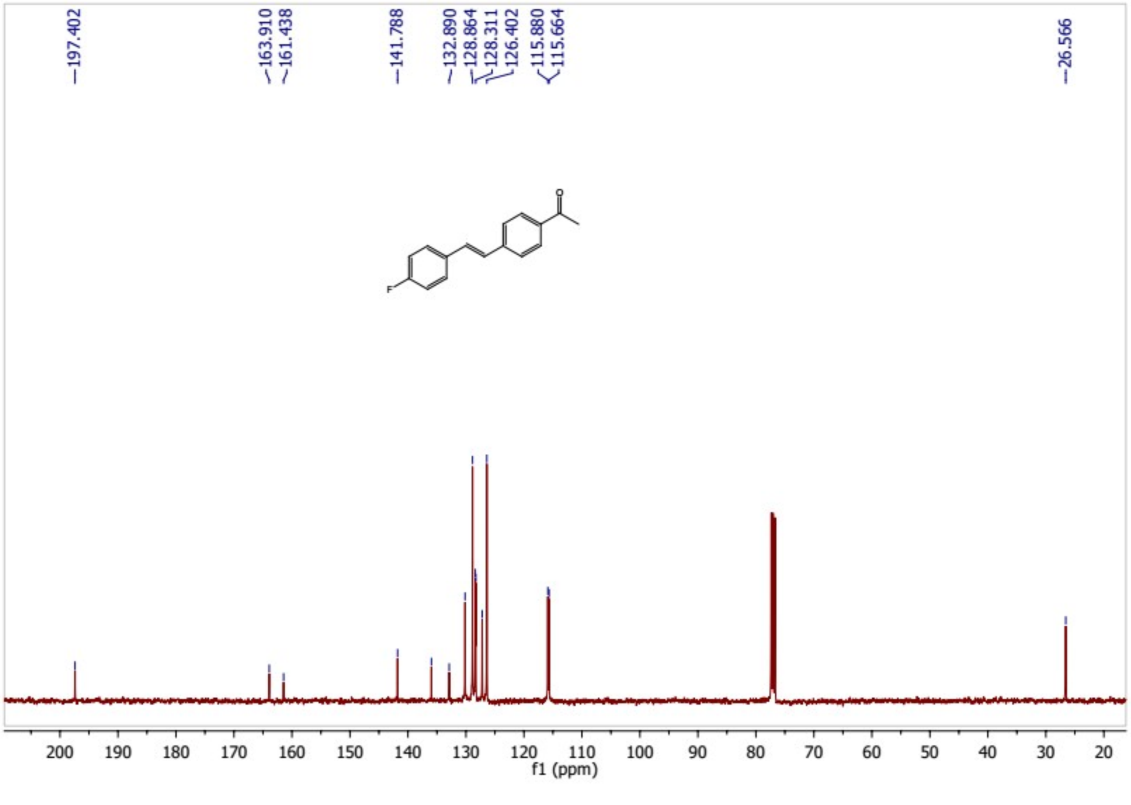
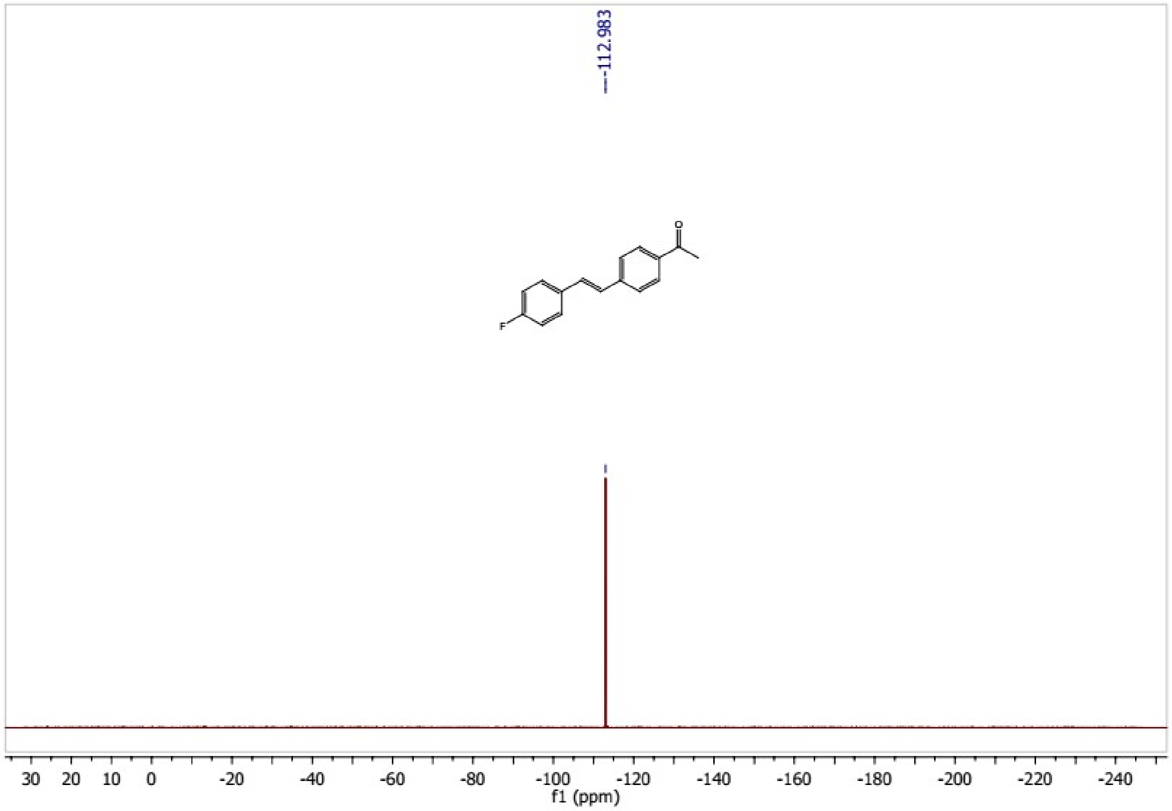
7.187
7.146
7.078
7.057
7.043
7.036
7.002
2.592
F
O
2.00
2.09
2.02
4.01
3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


197.402
163.910
161.438
141.788
132.890
128.864
128.311
126.402
115.880
115.664
26.566
F
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)



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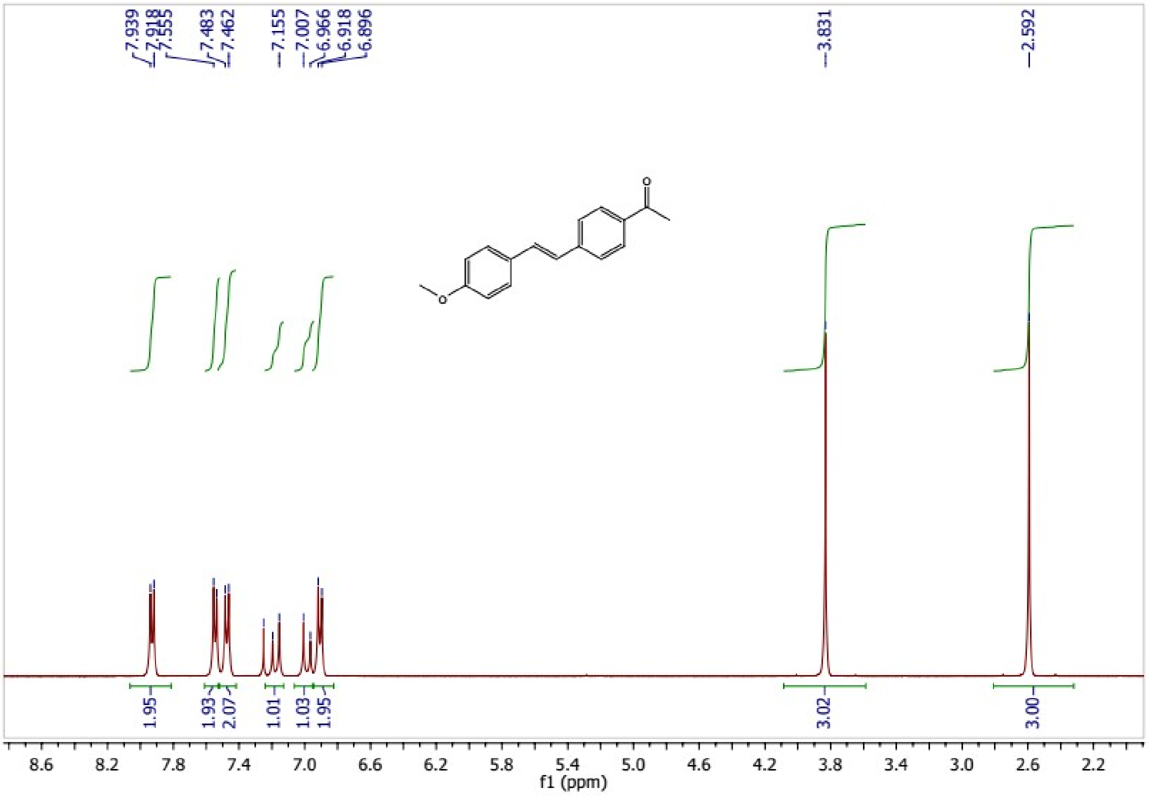
O
F
30
20
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm)



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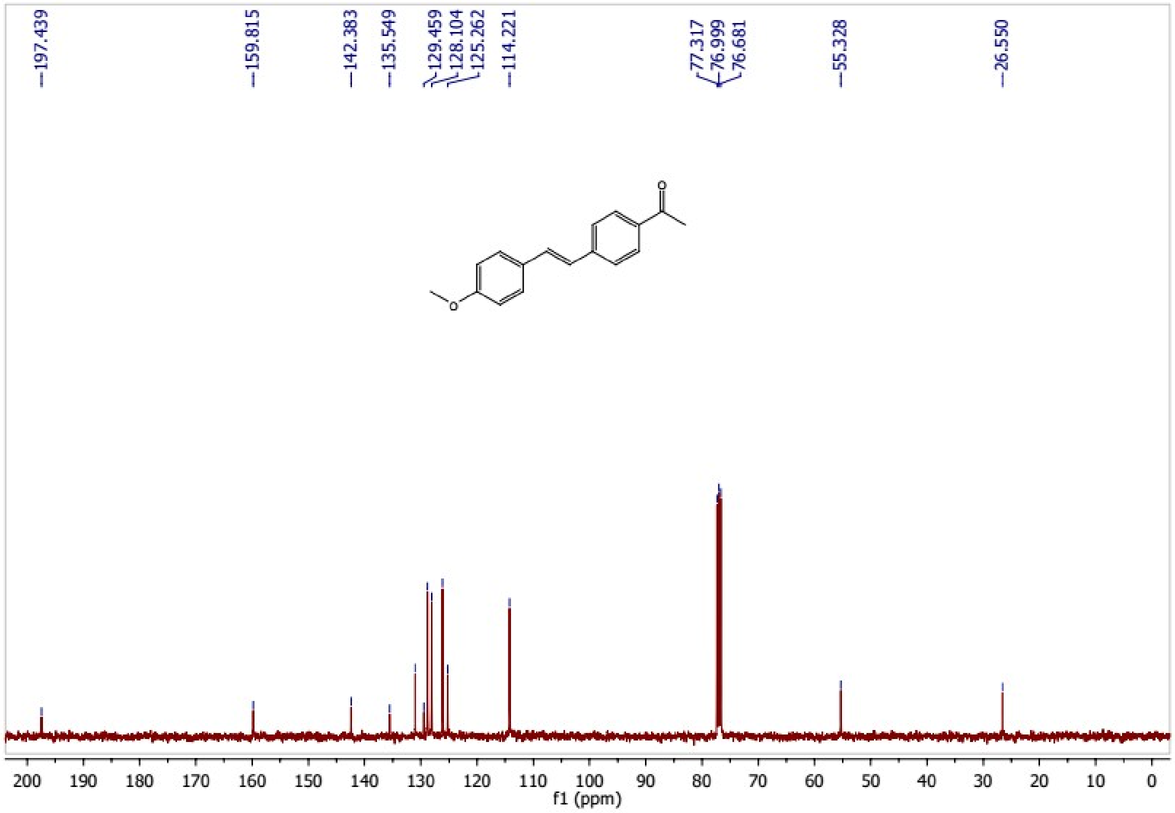
7.483
7.462
7.155
7.007
6.966
6.918
6.896
3.831
2.592
O
O
1.95
1.93
2.07
1.01
1.03
1.95
3.02
3.00
8.6
8.2
7.8
7.4
7.0
6.6
6.2
5.8
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
f1 (ppm)



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142.383
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125.262
114.221
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55.328
26.550
O
O
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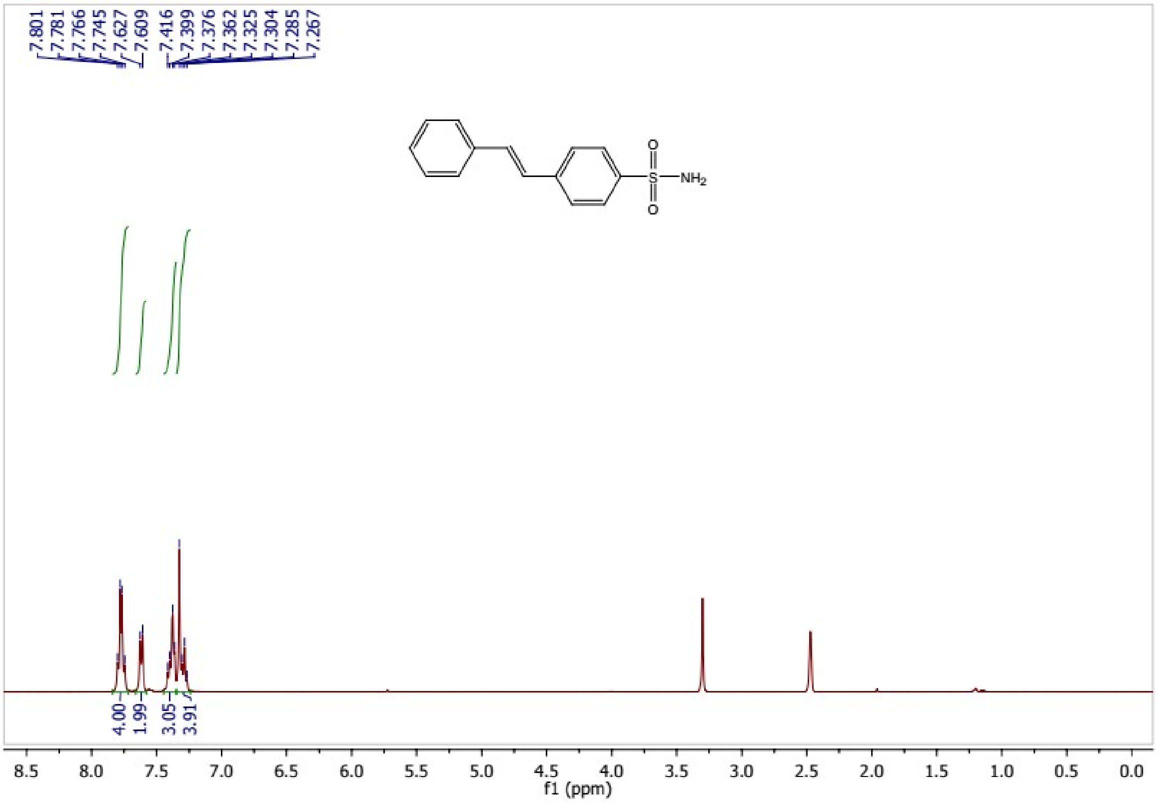
f1 (ppm)



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7.609
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7.362
7.325
7.304
7.285
7.267
O
S
NH2
O
4.00
1.99
3.05
3.91
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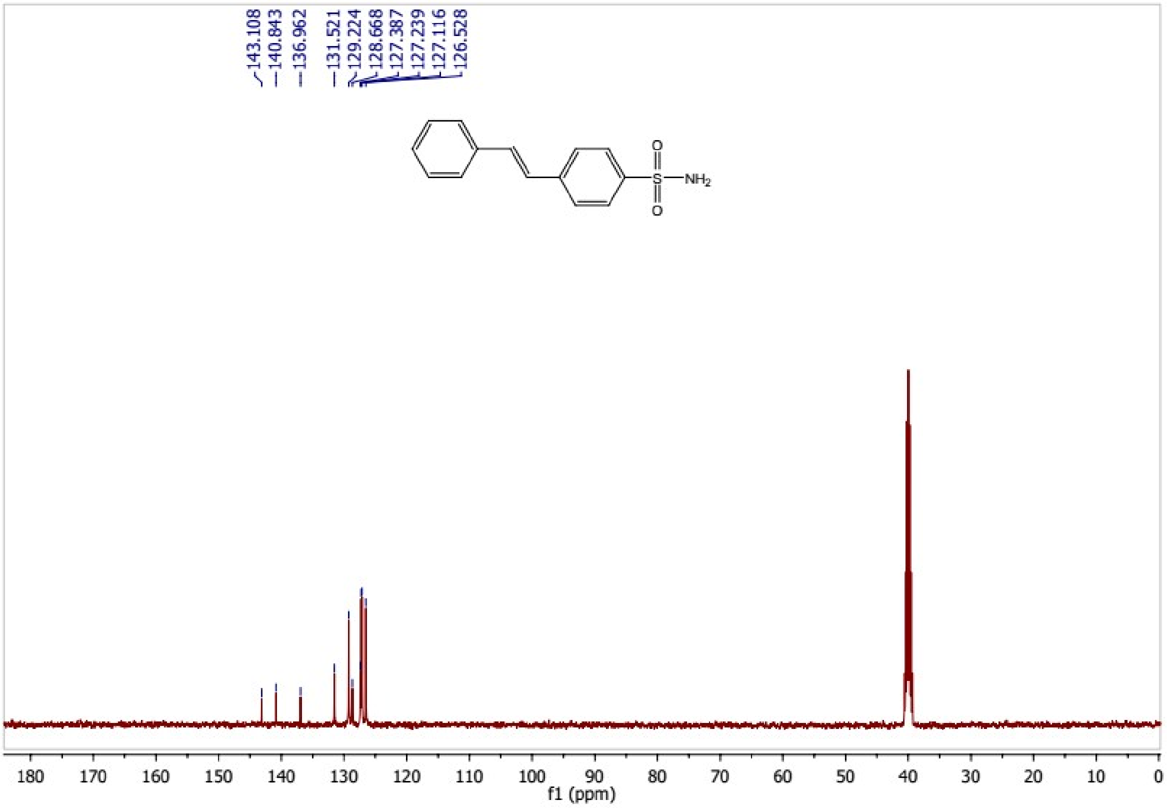
f1 (ppm)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S
NH2
O
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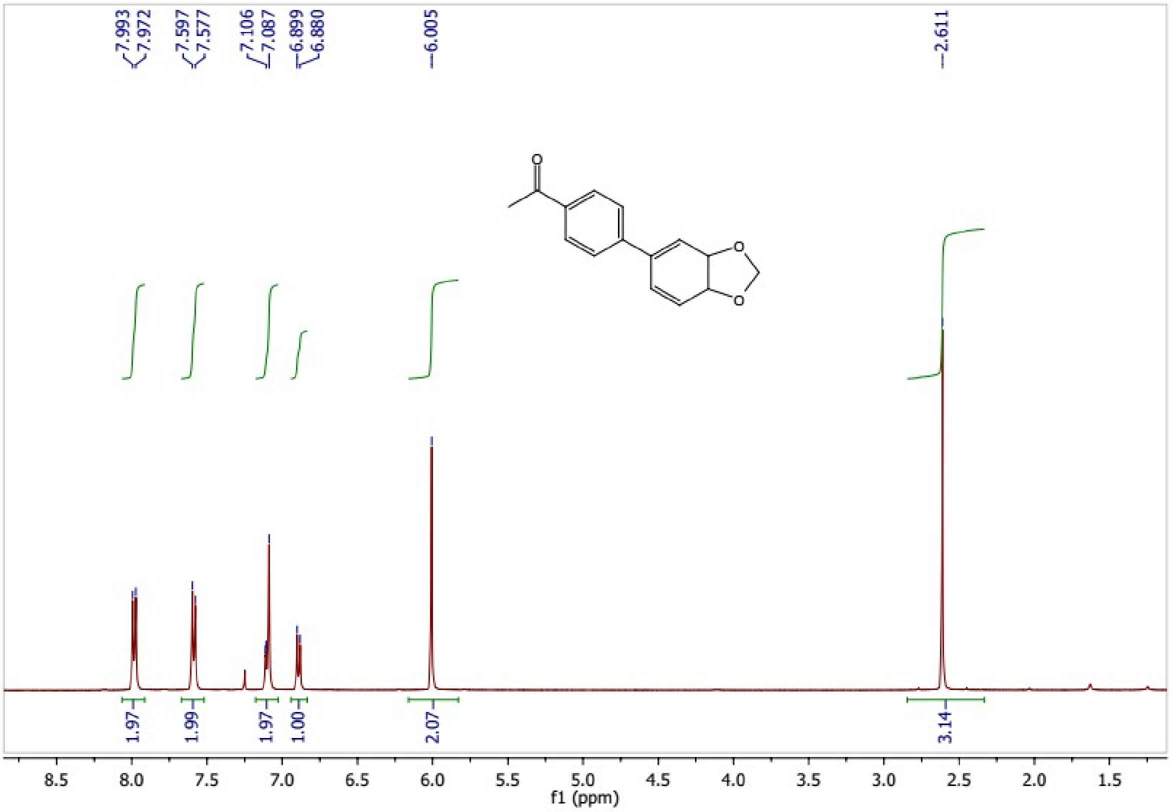
f1 (ppm)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6.880
6.005
2.611
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O
O
1.97
1.99
1.97
1.00
2.07
3.14
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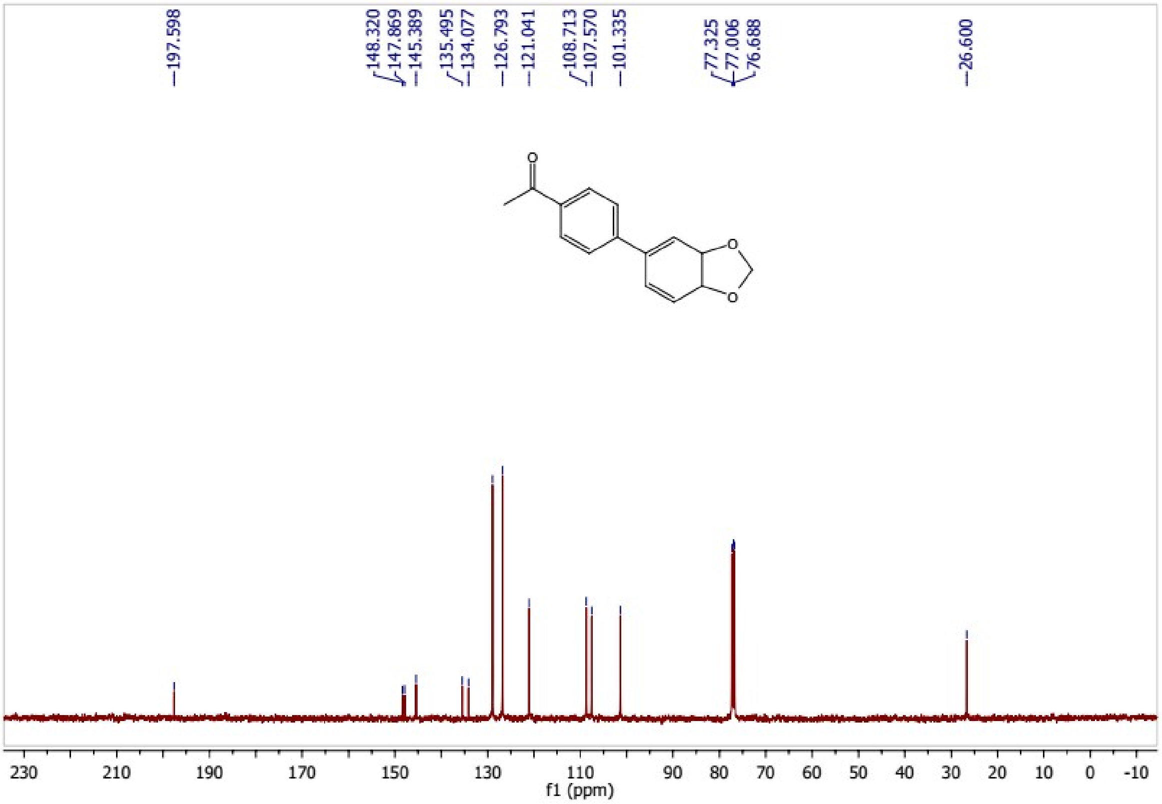
f1 (ppm)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145.389
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134.077
126.793
121.041
108.713
107.570
101.335
77.325
77.006
76.688
26.600
O
O
O
230
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190
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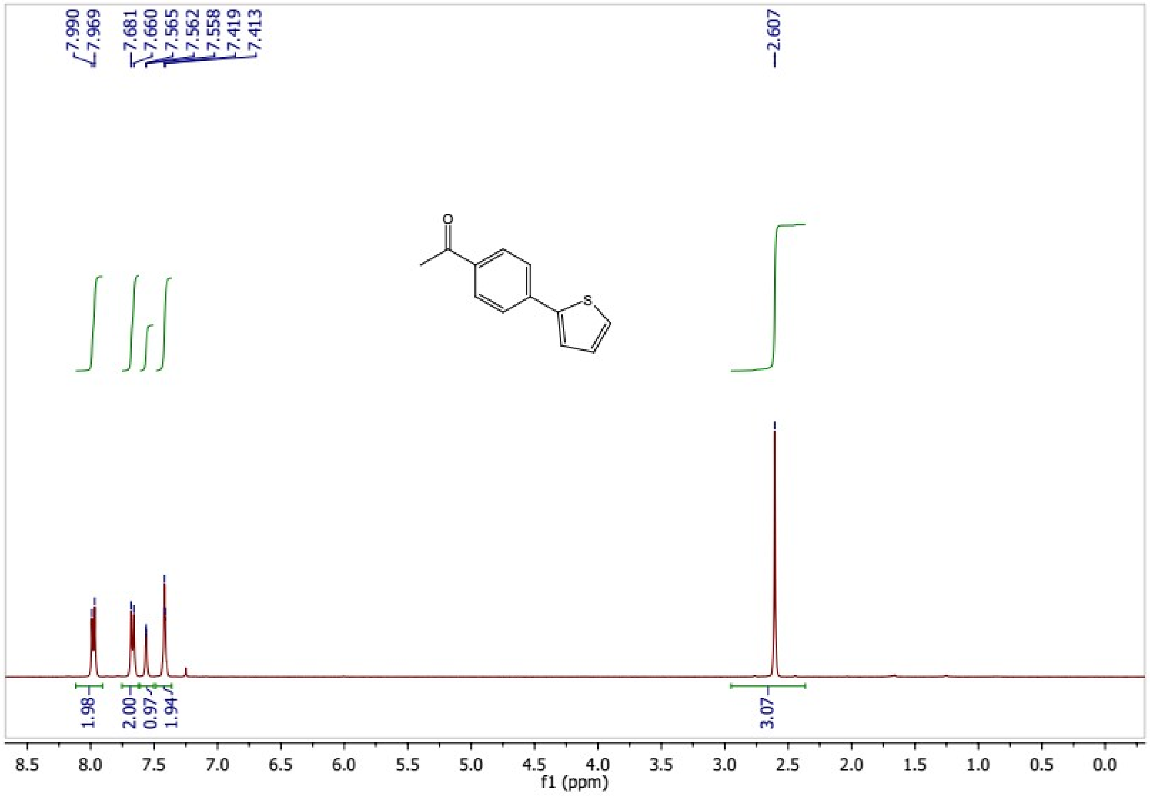
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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2.607
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2.00
0.97
1.94
3.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
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2.5
2.0
1.5
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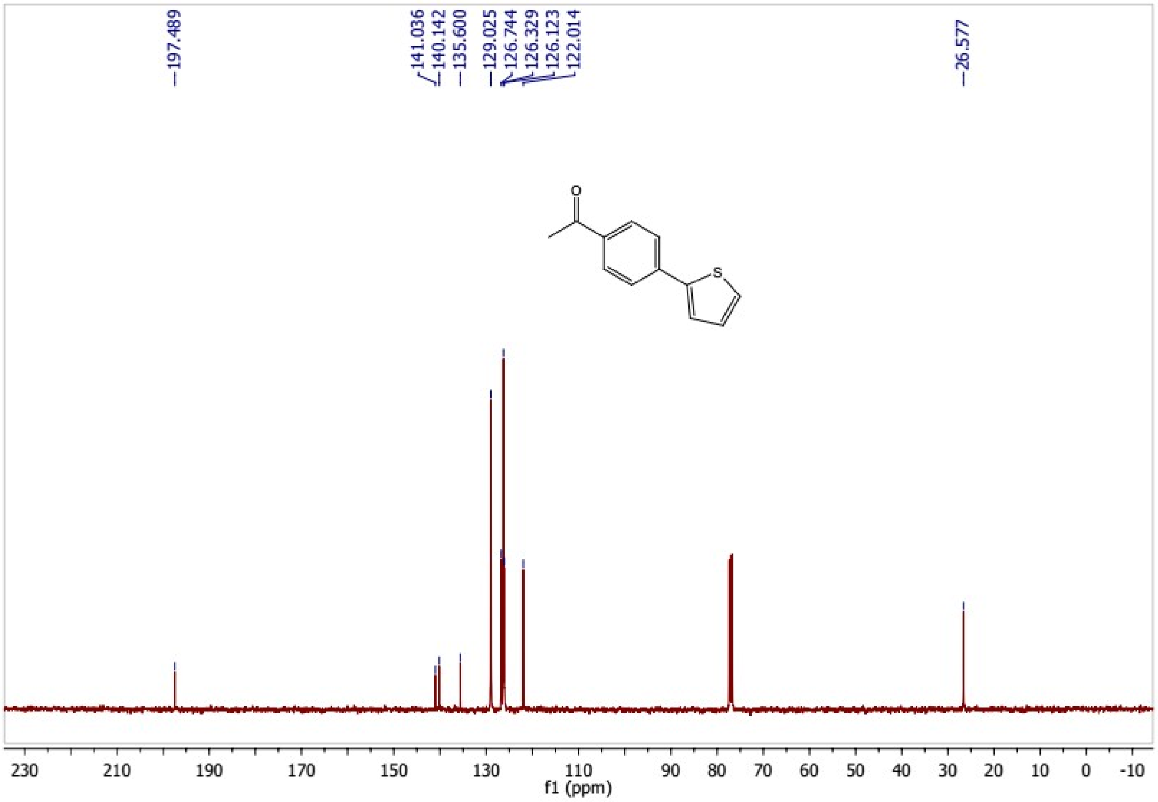
f1 (ppm)



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26.577
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150
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110
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80
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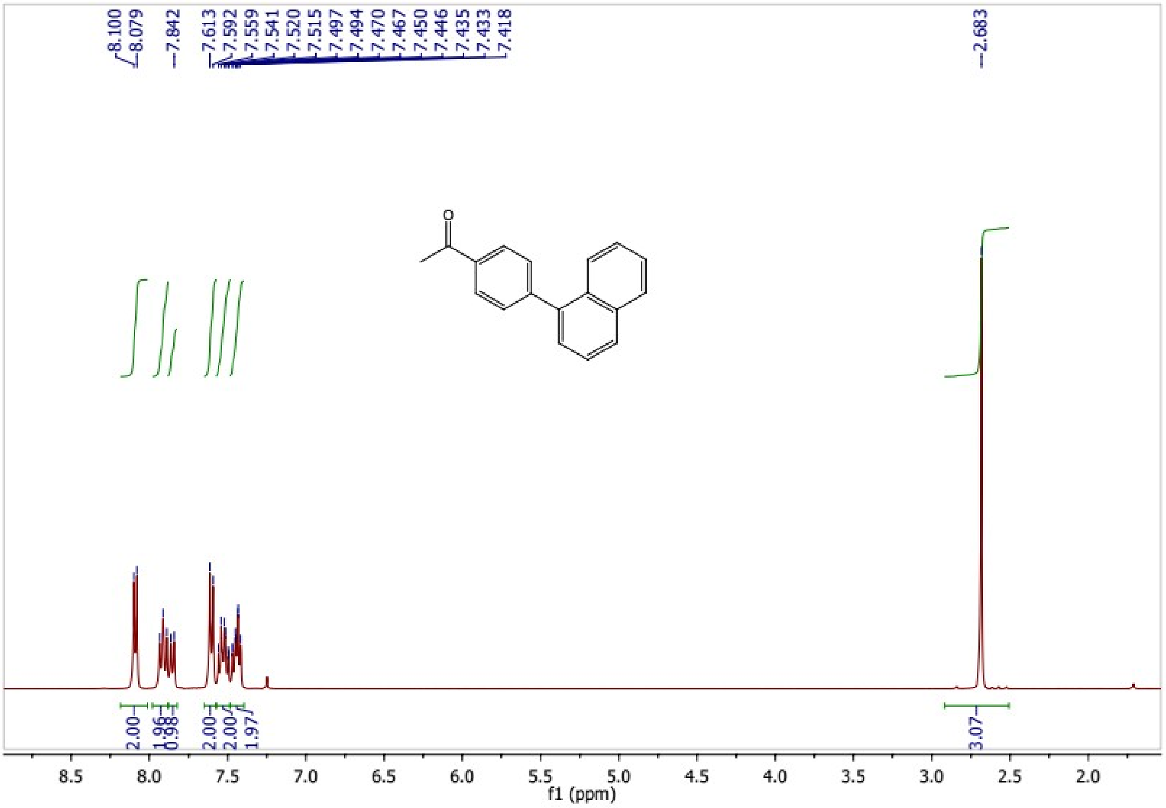
60
50
40
30
20
10
0
-10
f1 (ppm)



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7.520
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7.467
7.450
7.446
7.435
7.433
7.418
2.683
O
2.00
1.96
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2.00
2.00
1.97
3.07
8.5
8.0
7.5
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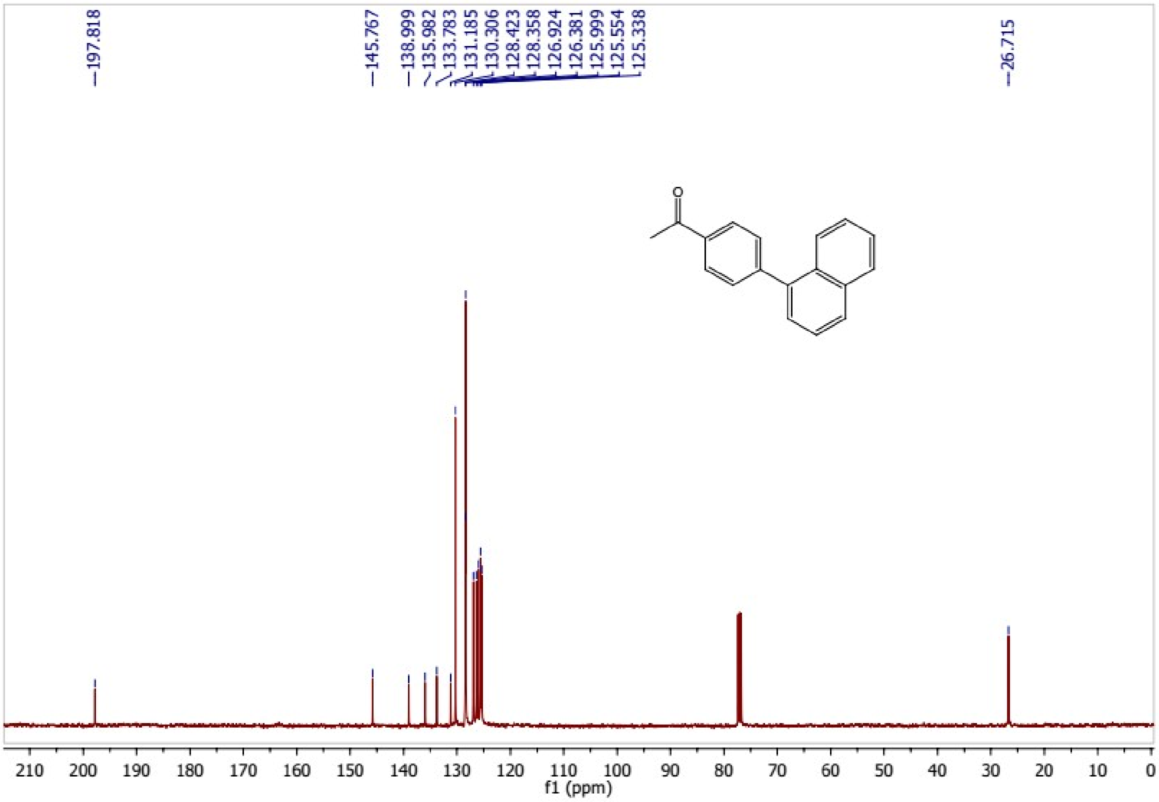
2.5
2.0
f1 (ppm)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125.554
125.338
26.715
O
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200
190
180
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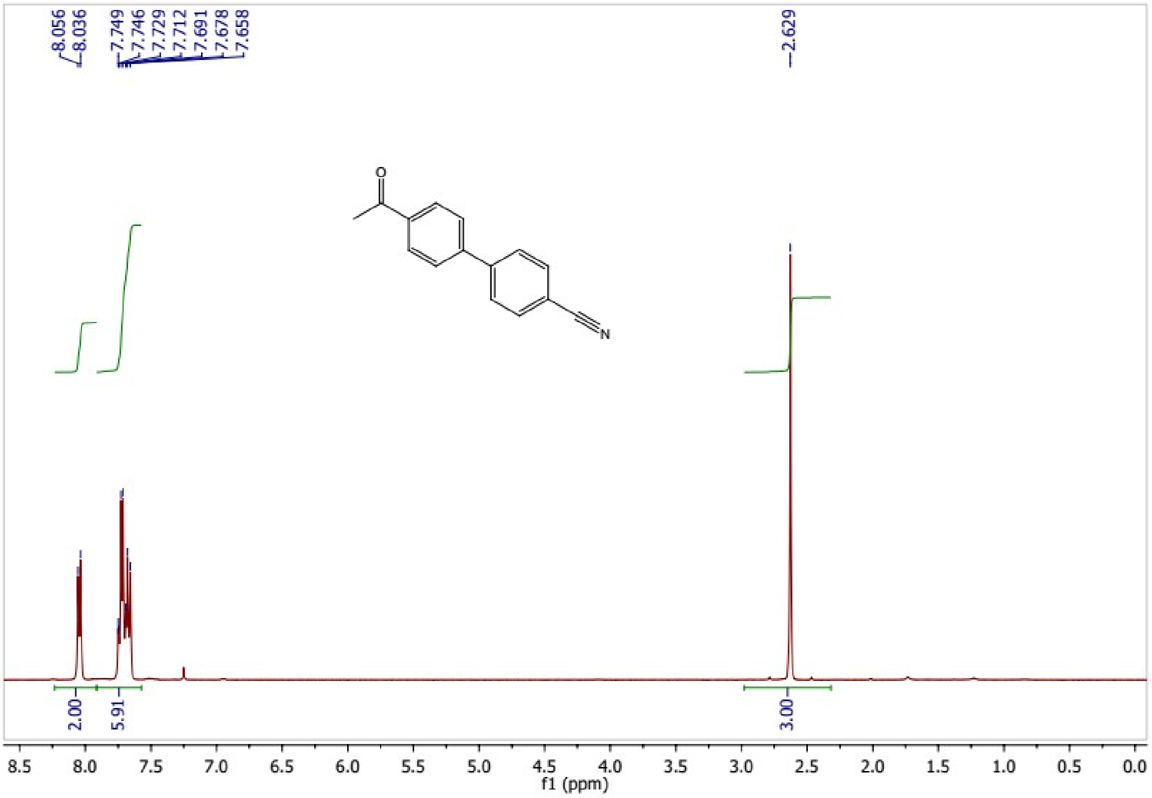
f1 (ppm)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2.00
5.91
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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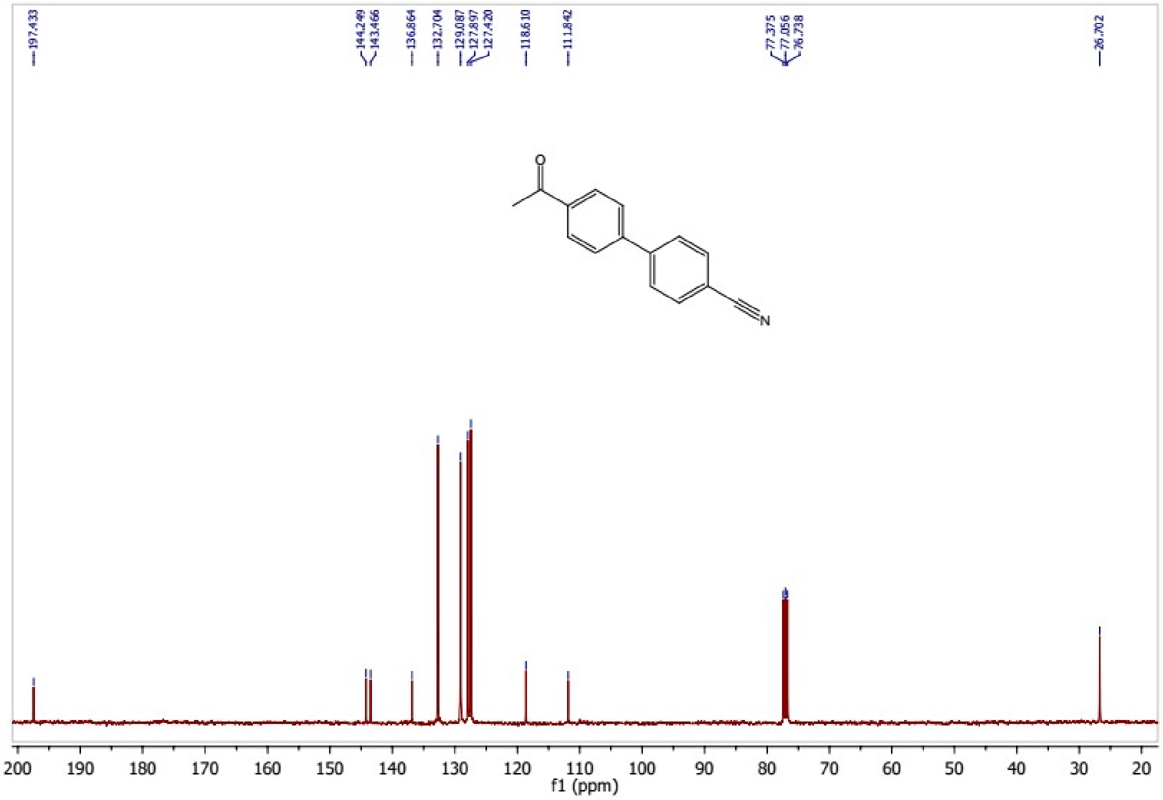
f1 (ppm)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127.897
127.420
118.610
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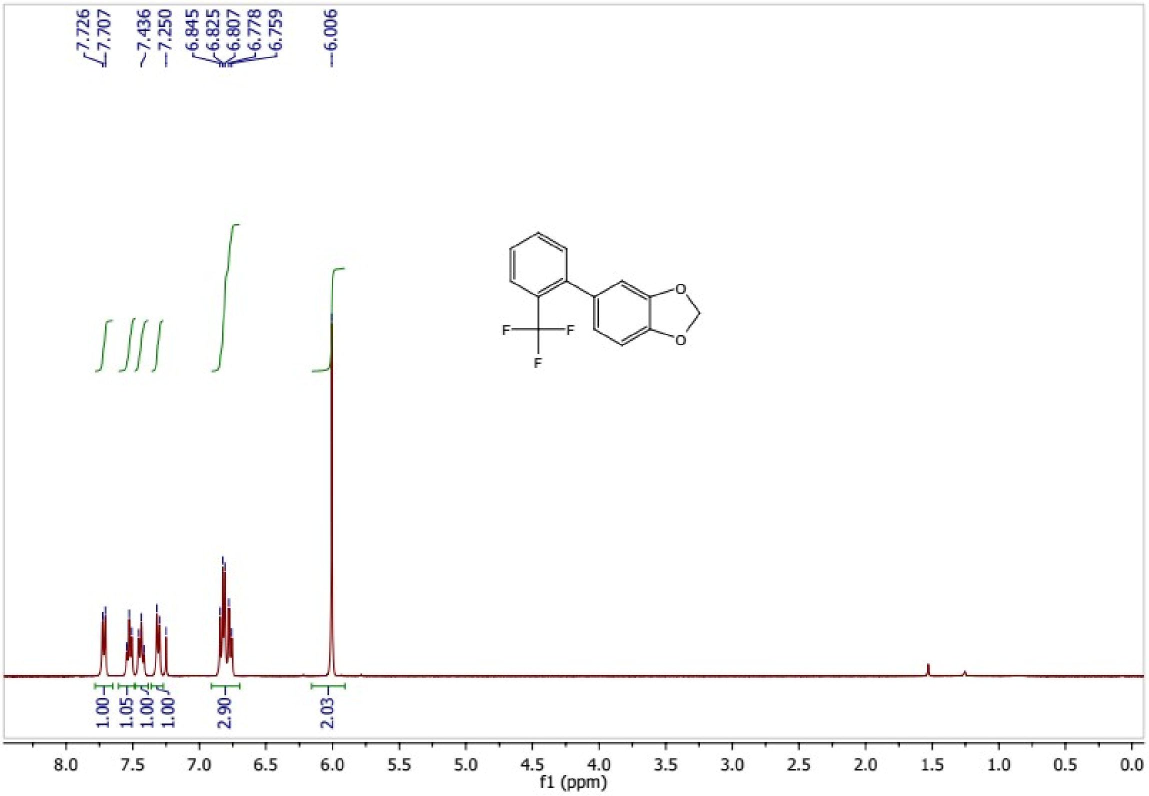
76.738
26.702
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)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6.006
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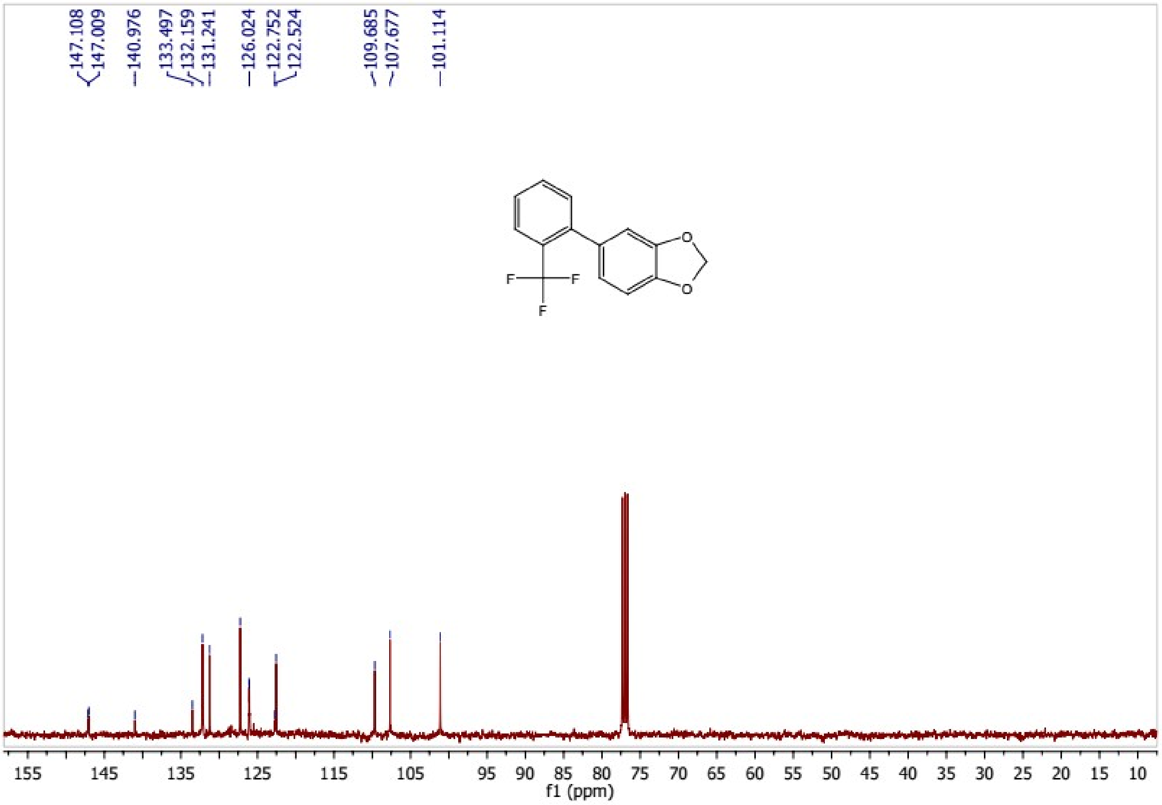
F
O
O
1.00
1.05
1.00
1.00
2.90
2.03
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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107.677
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F
F
F
O
O
155
145
135
125
115
105
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55
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45
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35
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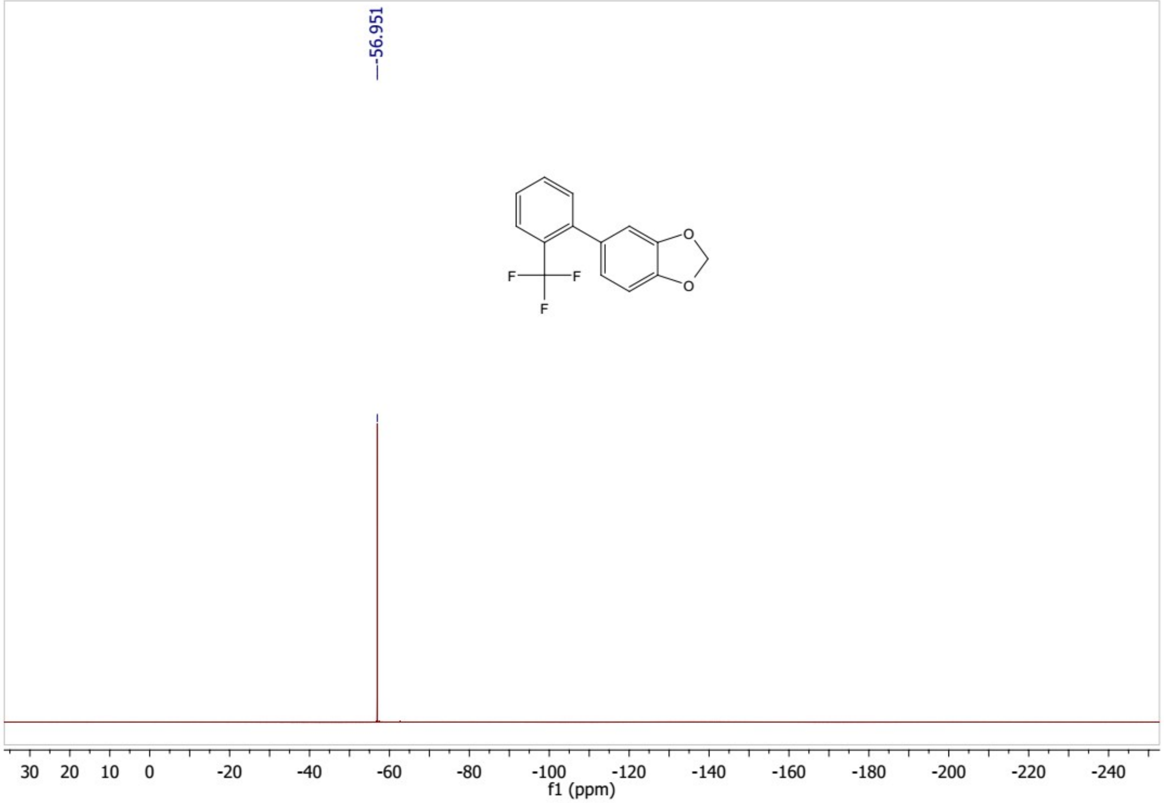
15
10
f1 (ppm)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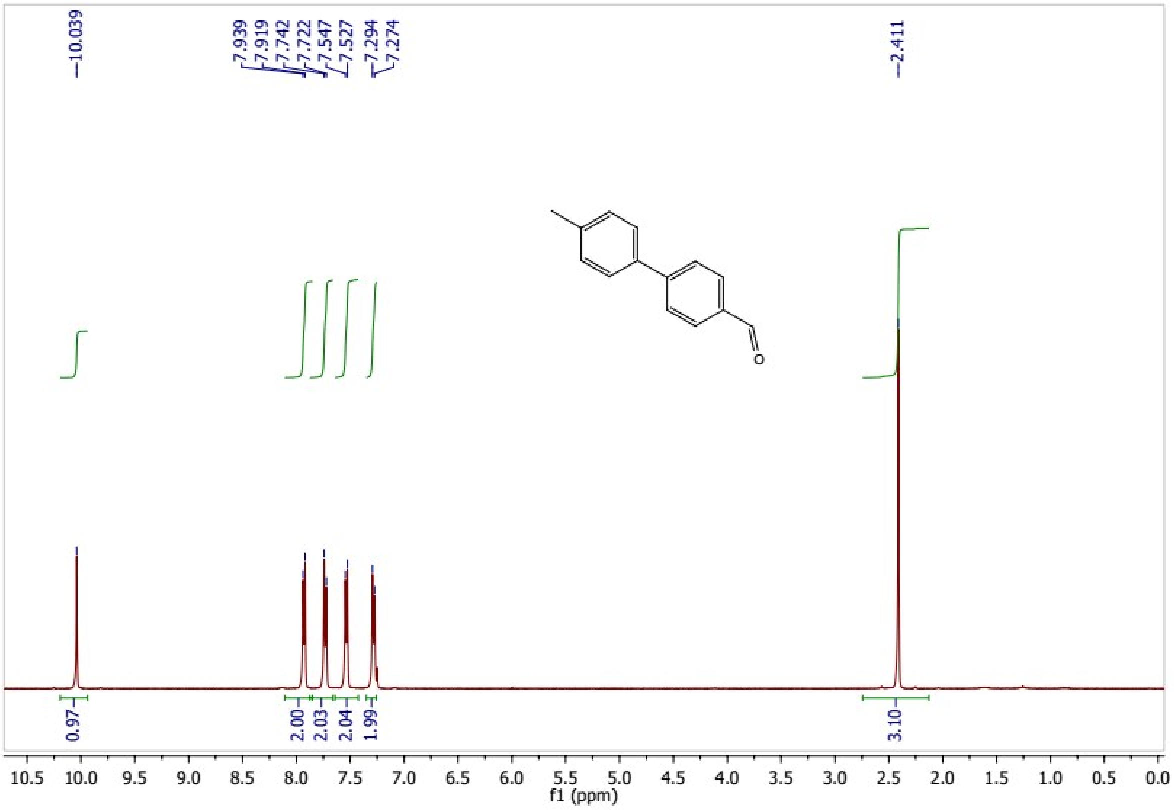
-200
-220
-240
f1 (ppm)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7.722
7.547
7.527
7.294
7.274
2.411
O
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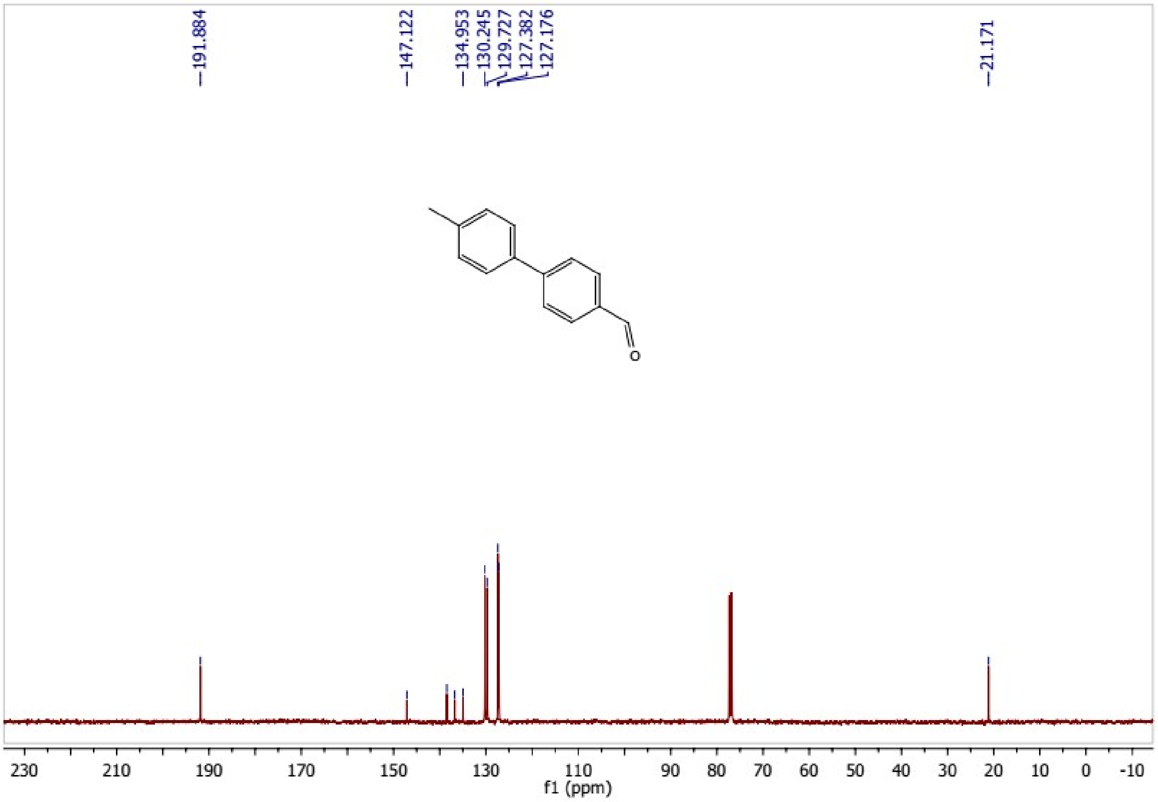
2.00
2.03
2.04
1.99
3.10
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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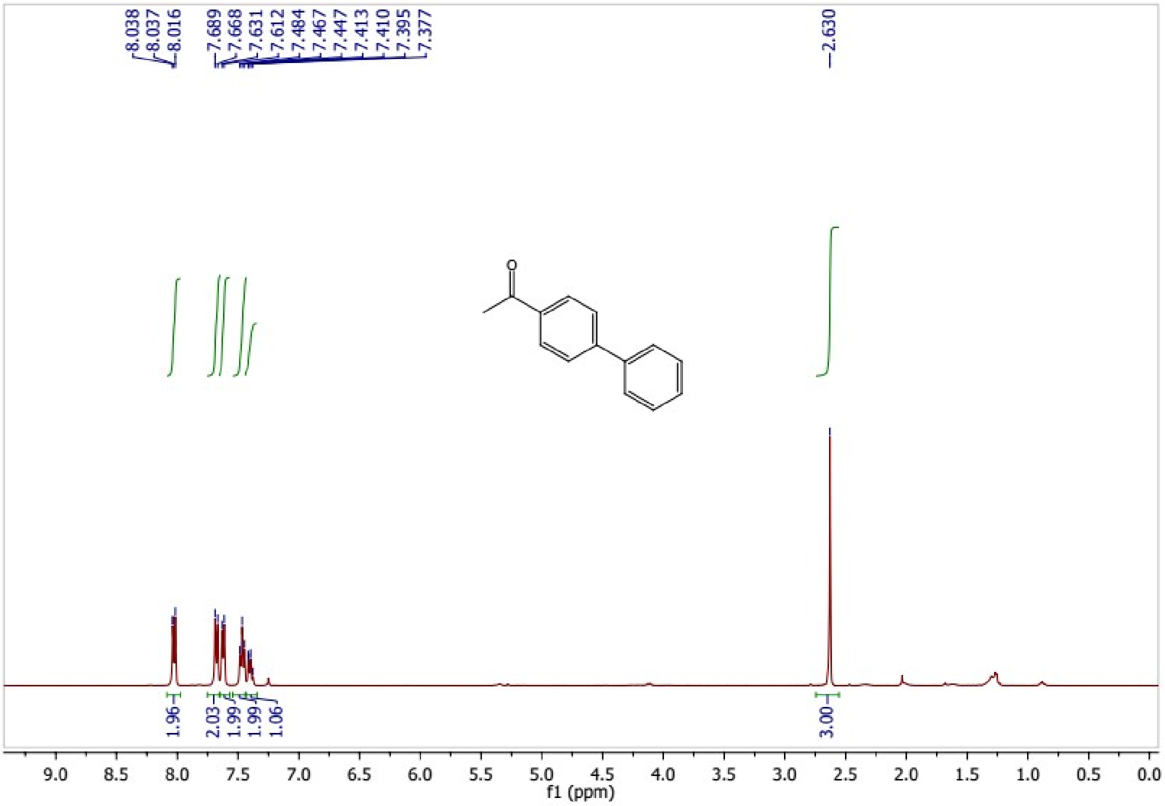
129.727
127.382
127.176
21.171
O
230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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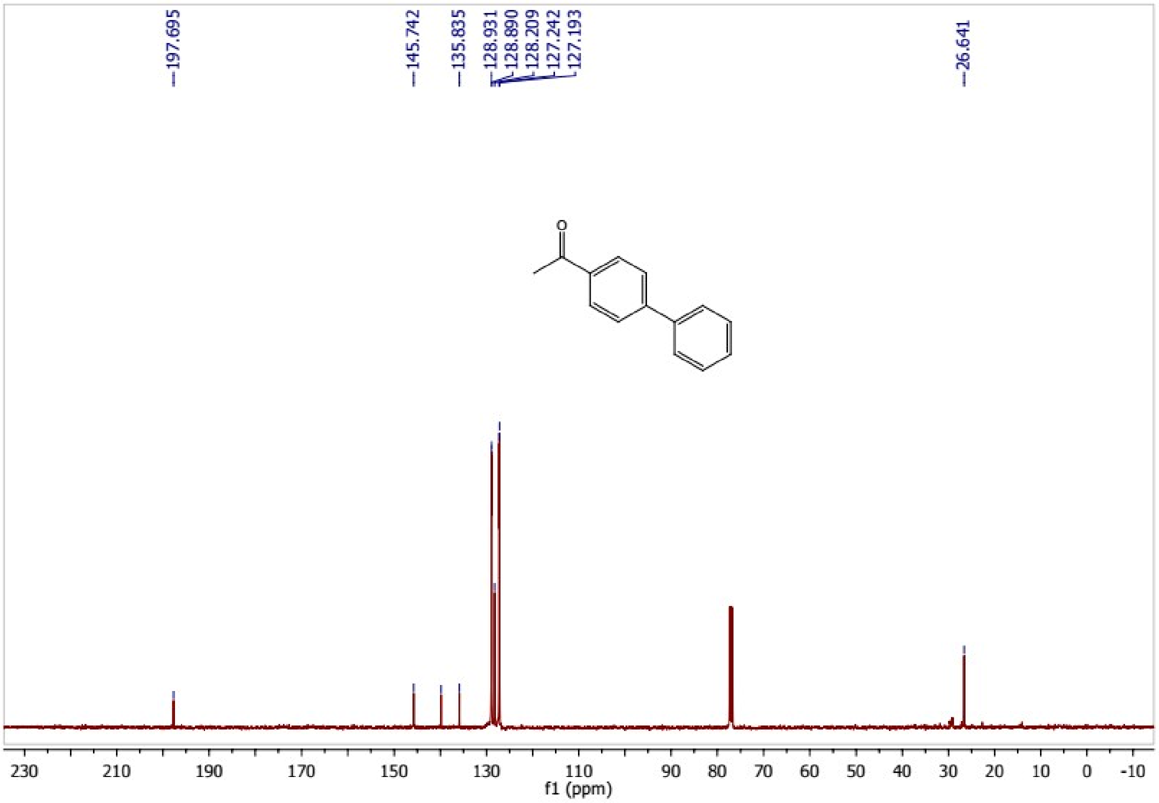
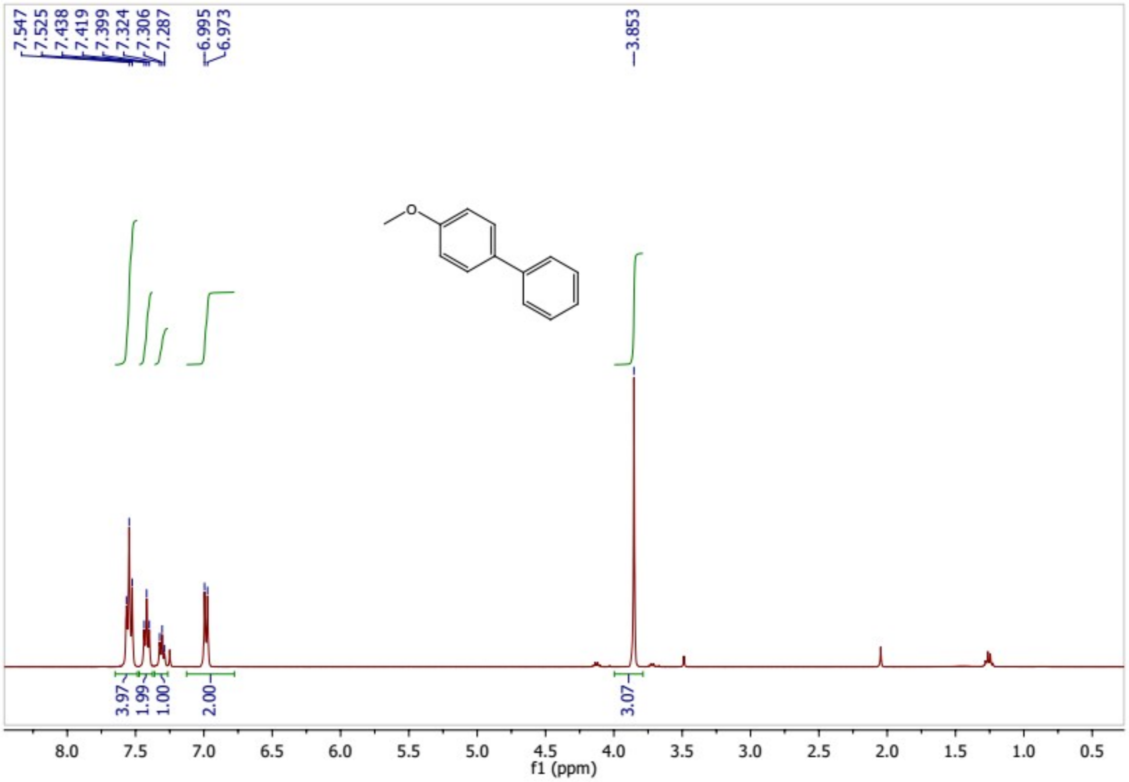
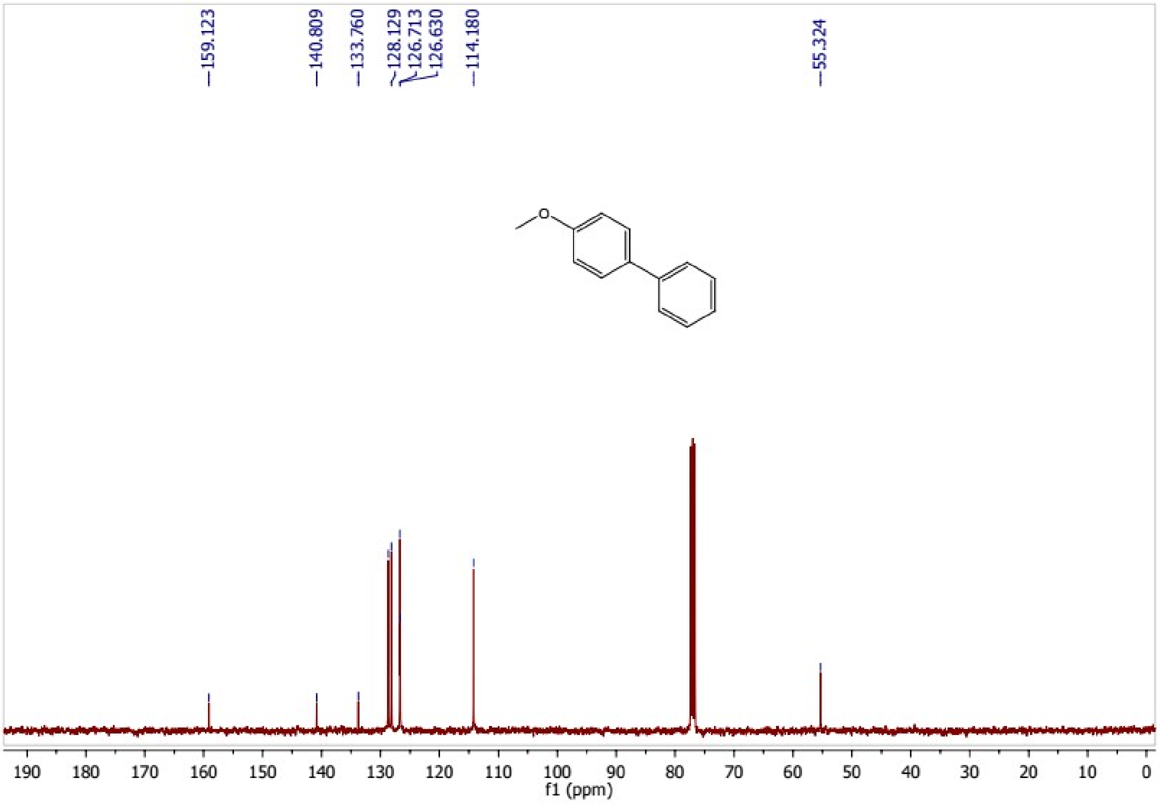
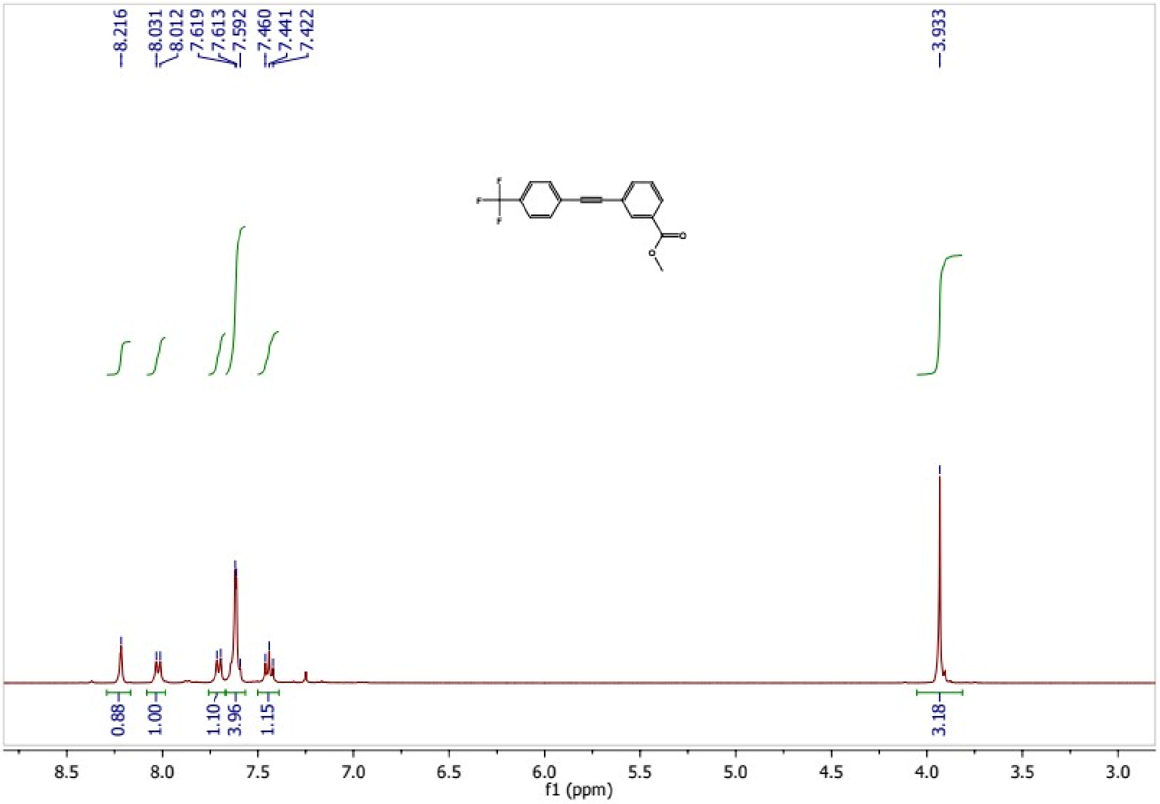
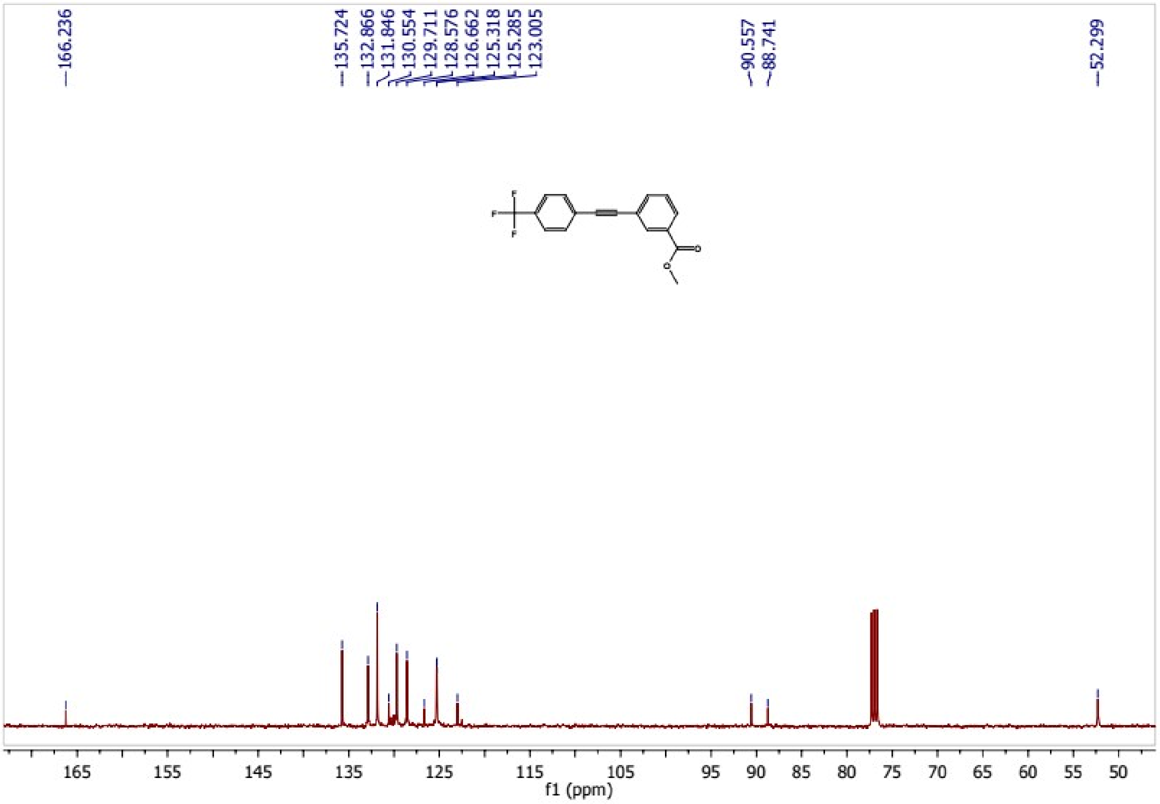
8.037
8.016
7.689
7.668
7.631
7.612
7.484
7.467
7.447
7.413
7.410
7.395
7.377
2.630
O
1.96
2.03
1.99
1.99
1.06
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

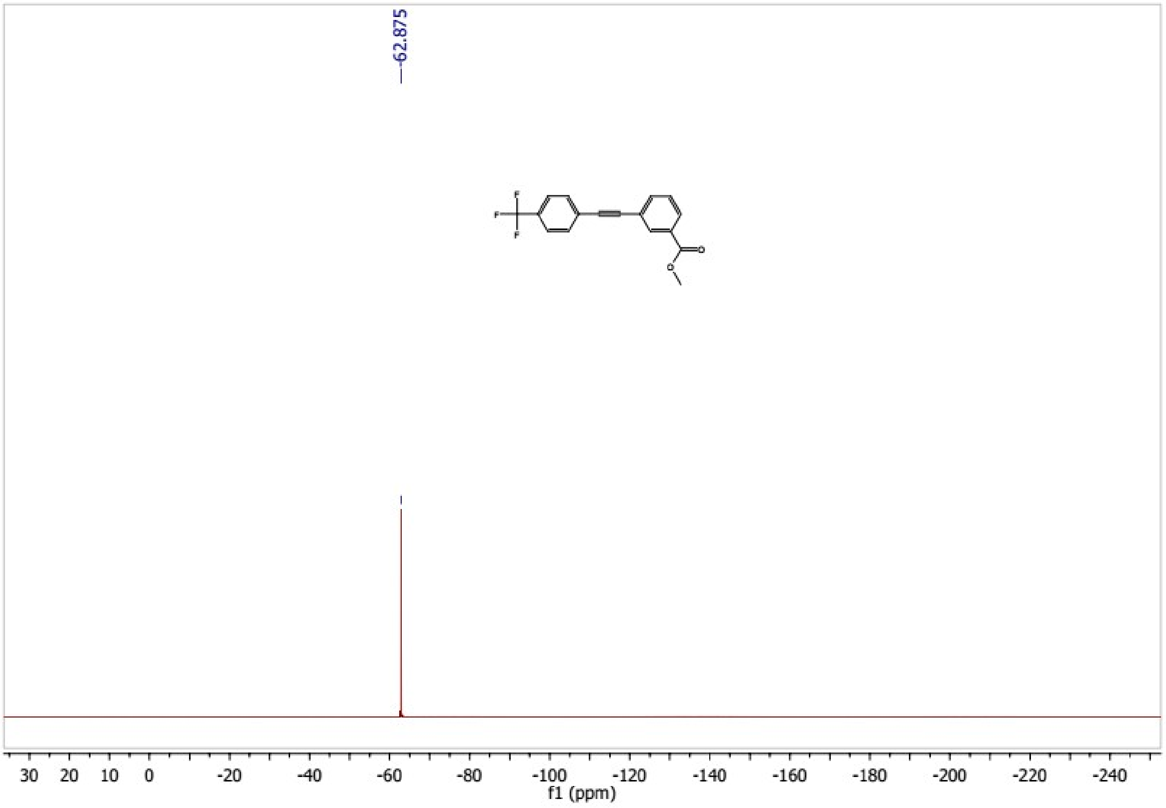

197.695
145.742
135.835
128.931
128.890
128.209
127.242
127.193
26.641
O
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.547
7.525
7.438
7.419
7.399
7.324
7.306
7.287
6.995
6.973
3.853
3.97
1.99
1.00
2.00
3.07
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)
O

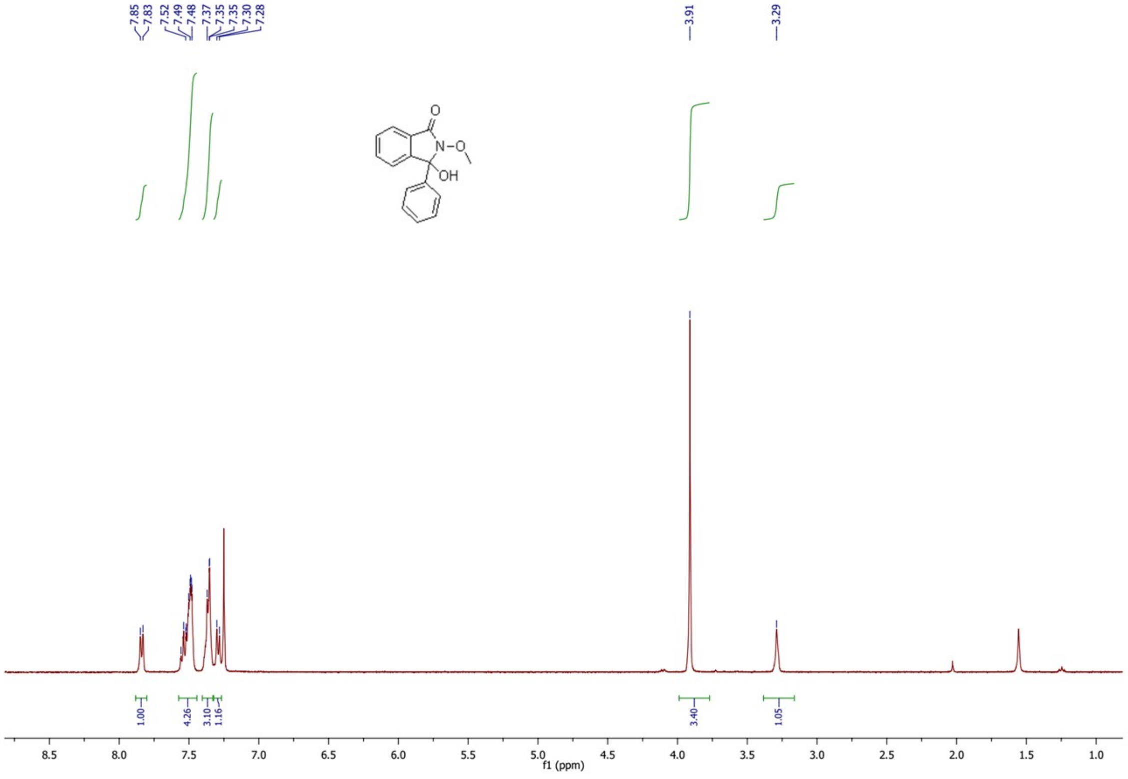

159.123
140.809
133.760
128.129
126.713
126.630
114.180
55.324
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O


8.216
8.031
8.012
7.619
7.613
7.592
7.460
7.441
7.422
3.933
F
F
F
O
O
0.88
1.00
1.10
3.96
1.15
3.18
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)

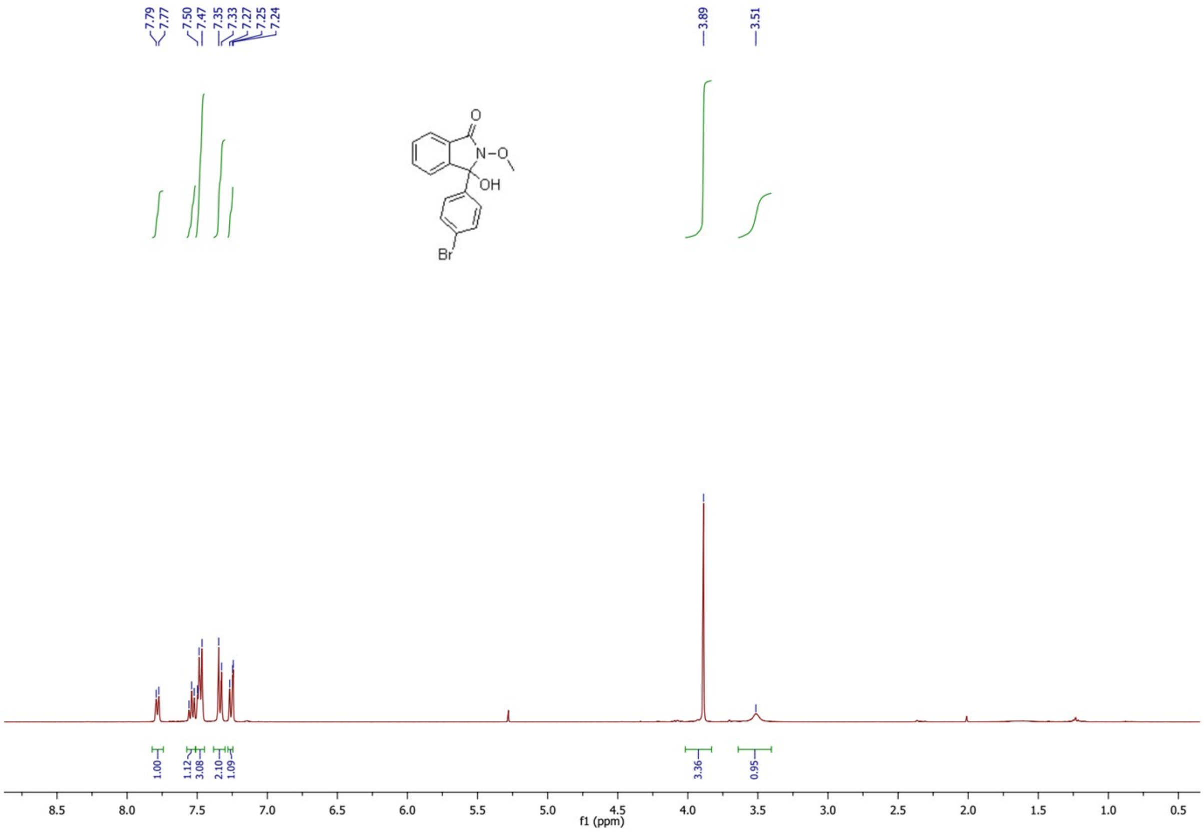

166.236
135.724
132.866
131.846
130.554
129.711
128.576
126.662
125.318
125.285
123.005
90.557
88.741
52.299
F
F
F
O
O
165
155
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
f1 (ppm)

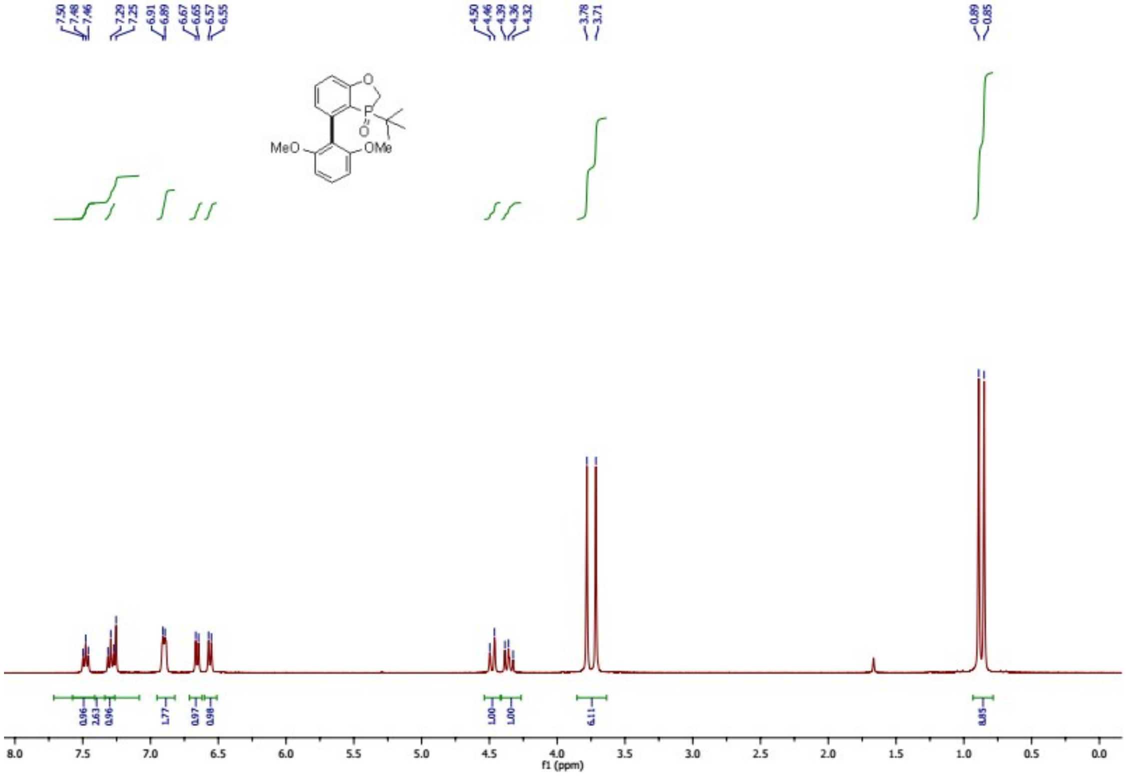


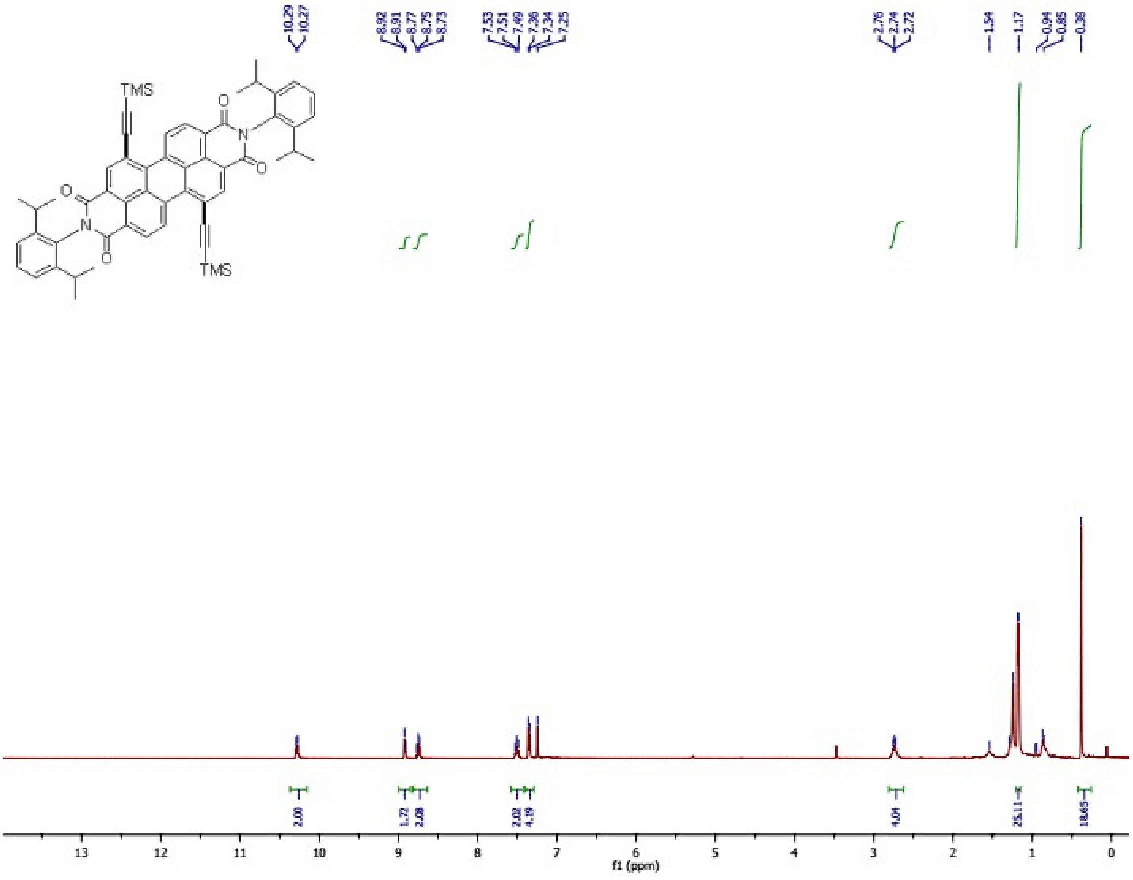
-62.875
F
F
F
O
O
30
20
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm)



7.85
7.83
7.52
7.49
7.48
7.37
7.35
7.35
7.30
7.28
3.91
3.29
O
N
O
OH
1.00
4.26
3.10
1.16
3.40
1.05
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
f1 (ppm)


7.79
7.77
7.50
7.47
7.35
7.33
7.27
7.25
7.24
3.89
3.51
O
N–O
OH
Br
1.00
1.12
3.08
2.10
1.09
3.36
0.95
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)


7.50
7.48
7.46
7.29
7.25
6.91
6.89
6.67
6.65
6.57
6.55
4.50
4.46
4.39
4.36
4.32
3.78
3.71
0.89
0.85
O
P
O
MeO
OMe
0.96
2.63
0.96
1.77
0.97
0.98
1.00
1.00
6.11
8.85
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)



Section 8. References

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