Expanding the Scope of the Gold (I) Catalyzed Rautenstrauch Rearrangement: Protic Additives

Cédric Bürki, Andrew Whyte, Sebastian Arndt, A. Stephen K. Hashmi and Mark Lautens*
<mlautens@chem.utoronto.ca>

Department of Chemistry, University of Toronto, 80 St. George Street,
Toronto, Ontario, M5S 3H6, Canada

Supporting Information

Table of Contents

1 General Considerations 3
2 Optimization of the Rautenstrauch Rearrangment 4
  2.1 Catalyst Loading 4
  2.2 Control Experiments 5
  2.3 Stability of Enol Esters 6
3.0 General Procedures 7
  3.1 Synthesis of **7a** and **8a** 11
  3.2 Synthesis of **7b** and **8b** 13
  3.3 Synthesis of **7c** and **8c** 15
  3.4 Synthesis of **7d** and **8d** 18
  3.5 Synthesis of **7e** and **8e** 21
  3.6 Synthesis of **7f** and **8f** 24
  3.7 Synthesis of **7g** and **8g** 26
  3.8 Synthesis of **7h** and **8h** 28
  3.9 Synthesis of **7i** and **8i** 30
  3.10 Synthesis of **7j** and **8j** and **17** 33
    3.10.1 Synthesis of **18**, Palladium catalyzed conjugate addition 38
    3.10.2 Synthesis of **17**, Benzylation of with trichloroacetimidate 51
  3.11 Synthesis of **7k** and **8k** 52
  3.12 Synthesis of **7l** and **8l** 56
  3.13 Synthesis of **7m** and **8m** 58
  3.14 Synthesis of **7n** and **8n** 60
  3.15 Synthesis of **7o** and **8o** 62
  3.16 Synthesis of **7p** and **8p** 64
  3.17 Synthesis of **21a** and **22a** 66
    3.17.1 Enantioselective Synthesis of **22a** 68
  3.18 Synthesis of **21b** and **22b** 70
    3.18.1 Enantioselective Synthesis of **22b** 72
  3.19 Unsuccessful Substrates in the Rautenstrauch Rearrangement 74
4.0 References 75
5.0 NMR Spectra 76

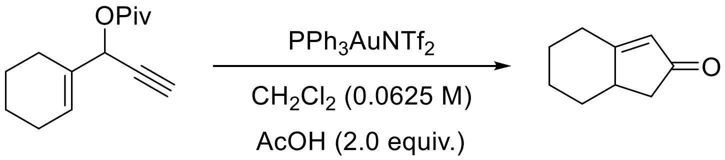
1 General Considerations

Catalytic reactions were run under inert atmosphere using glassware that was dried under a vacuum. All workups and isolations were carried out on the benchtop using standard techniques. The reactions were monitored using thin-layer chromatography (TLC) on EMD Silica Gel 60 F254 plates and were visualized under UV light (254 nm) or using a $KMnO_4$ stain. Purification of products were done using flash chromatography in the indicated solvent using 230-400 mesh silica gel. Dichloromethane, 1,2-dichloroethane, acetonitrile, and toluene were distilled over CaH_2. Tetrahydrofuran and dioxane were distilled over Na/benzophenone. All other chemicals were used as received from Sigma-Aldrich, Strem, and Combi-Blocks. NMR spectra were taken on a Bruker Avance III 400 MHz, Varian Mercury 400 MHz or a Varian Mercury 300 MHz. Shifts are reported in ppm and referenced relative to $CHCl_3$. Infrared spectra were obtained using a Shimadzu FTIR 8400S on a NaCl plate and are reported in cm^{-1}. High-resolution mass spectroscopy was performed in DART mode with a time-of-flight detector. X-Ray crystallography was performed by Dr. Alan Lough.

2 Optimization of the Rautenstrauch Rearrangment

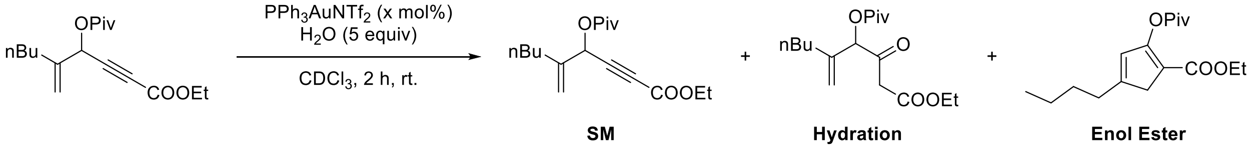
Reactions were run in dry 20 mL vials on a 0.25 mmol scale. The catalyst was added in to the vial followed by half the indicated amount of solvent (either 0.5 mL or 2 mL) with the proton source (either water or acetic acid). Water was added using a microsyringe. Acetic acid was added from a premade solution in the solvent. The starting material was dissolved in the second half of solvent and added dropwise to the catalyst solution. It was found that a dropwise addition gave cleaner reactions and better yields, likely due to the decreased concentration of reactive enol ester in the reaction solution. The reaction was monitored by TLC until completion (typically 1 h). The reaction was poured over a silica plug washing with EtOAc. The filtrate was concentrated and TMB was added as an NMR standard.

2.1 Catalyst Loading



Catalyst Loading	**NMR Yield**
1 mol%	81%
2.5 mol%	81%
5 mol%	91%

2.2 Control Experiments

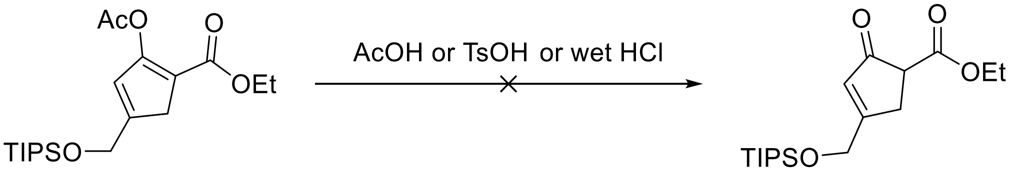


Gold mol%	SM	Hydration	Enol Ester
0	96%	0%	0%
1	0%	83%	18%

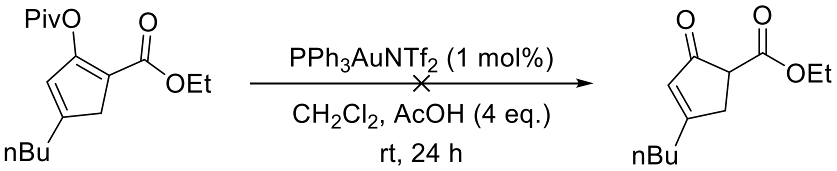
TMB was added as internal standard in crude mixture and NMR was run directly. Reaction requires gold catalyst. Hydration byproduct is gold catalyzed.

2.3 Stability of Enol Esters

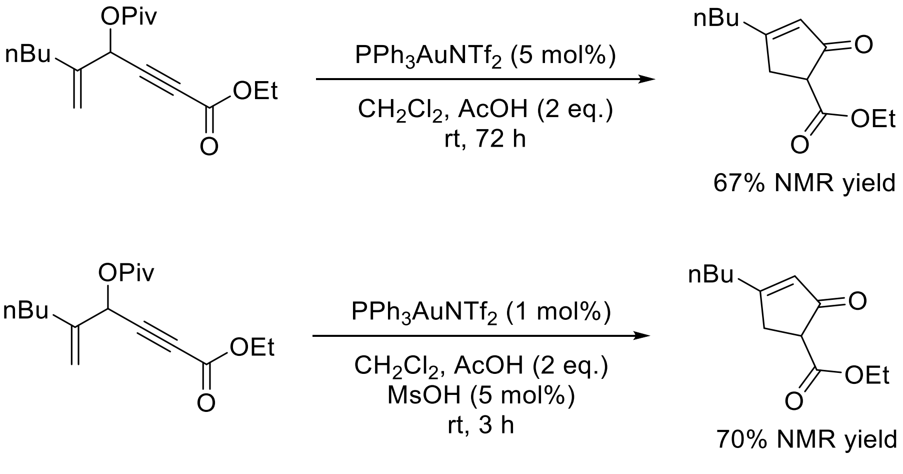
The enol ester intermediate could be isolated using flash column chromatography. It was found that it would not readily hydrolyze in a variety of acids.



It was also found that it would not hydrolyze if resubjected to the reaction conditions. In this case since there is no alkyne to initiate the catalytic cycle, the NTf_2 anion is still bound to the gold catalyst.

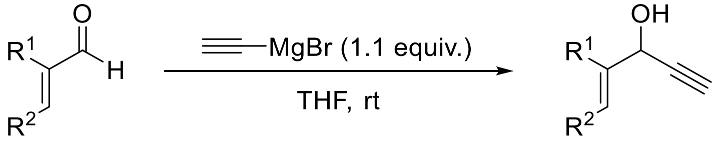


We proposed that the NTf_2 anion is responsible for hydrolyzing the enol ester, implying a strong acid is required to catalyze the hydrolysis. Either by using an increased catalyst loading (thereby increasing the amount of NTf_2 anion) or by adding a catalytic amount of an external strong acid lead to ketone formation. Dry HCl was used to quench the stable enol esters in the end; TfOH led to degradation of silyl protected alcohols and HCl could not coexist with the catalyst as the chlorine anion deactivated the gold catalyst.

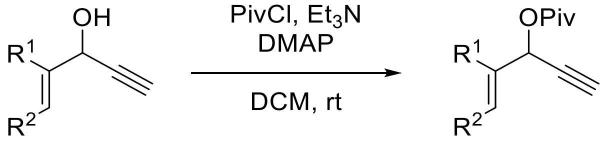


3.0 General Procedures

General Procedure 1: Two pot synthesis of Starting Materials

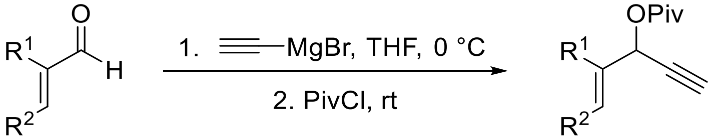


A flame-dried Schlenk flask with a magnetic stir bar was charged with the aldehyde (1.0 equiv.) in THF (1.0 equiv.). Then ethynylmagnesium bromide (0.5M in THF, 1.1 equiv.) was added and the reaction mixture was stirred at room temperature until TLC showed full conversion. The reaction was quenched with saturated solution of $NaHCO_3$. The aqueous phase was extracted with dichloromethane (3 x 100 mL) and the organic extracts were dried over anhydrous $MgSO_4$, filtered and the solvent was removed under reduced pressure. If necessary the crude was purified by flash column chromatography before being subjected to the second step. Aldehydes were commercially available unless otherwise shown.



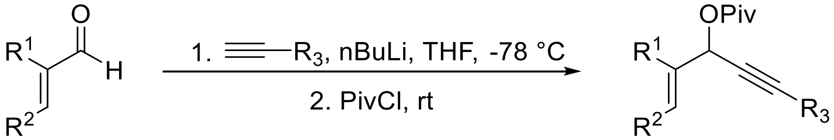
A flame dried Schlenk flask equipped with a magnetic stir bar was charged with the propargyl alcohol (1.0 equiv.) in anhydrous dichloromethane (0.5 M). Then pivaloyl chloride (1.05 equiv.) and trimethylamine (1.05 equiv.) was added followed by catalytic amounts of DMAP. The reaction was stirred at room temperature until TLC showed full conversion. Quenched with an aqueous solution of $NaHCO_3$ and was extracted with dichloromethane (3 x 20 mL). Combined organic layers were dried over anhydrous $MgSO_4$, filtered and rotovapped. Crude was purified by flash column chromatography or Kugelrohr distillation.

General Procedure 2: One pot synthesis of starting materials



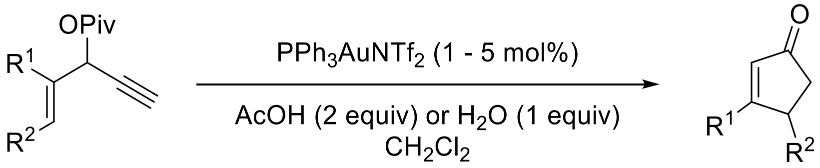
A round bottom flask equipped with a magnetic stir bar was dried under vacuum with a heat gun. The aldehyde (1.0 equiv.) was added in THF (1.0 M). The solution was stirred in an ice-water bath at 0 °C. Ethynylmagnesium bromide (0.5 M in THF, 1.1 equiv.) was added dropwise. Stirred at 0 °C and monitored by TLC until the aldehyde disappeared (typically 1 h, additional Grignard added if needed). Added pivaloyl chloride (1.5 equiv.) dropwise and the reaction was allowed to warm to room temperature. Stirred until the alkoxide intermediate disappeared by TLC (typically 1 h). Reaction quenched with 1 M NH_4OH. Diluted in EtOAc and washed with NH_4OH three times, then brine. The organic layer was dried over anhydrous sodium sulfate, filtered, and rotovapped to give crude. The crude was purified by flash column chromatography. It was important to completely convert the aldehyde as residual starting material often co-eluted with the propargyl ester product. Aldehydes were commercially available unless otherwise shown.

General Procedure 3: Synthesis for Aryl or Ester Substituted Alkynes



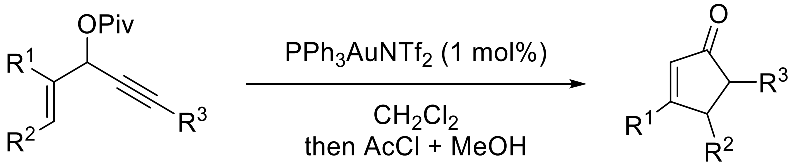
In a typical procedure a 100 mL dry flask was added with diisopropylamine (0.28 mL, 1.98 mmol, 1.2 eq) in anh. THF (8.2 mL) and flask was immersed in acetone-dry ice bath at -78 °C. nBuLi (0.73 mL, 1.82 mmol, 1.1 eq.) was added dropwise. Stirred for 30 min. Then added alkyne (1.65 mmol, 1.0 eq.) dropwise. Stirred for 30 min. Then added aldehyde (1.65 mmol, 1.0 eq.) in anhydrous THF (5.5 mL). Stirred for 1 h then added pivaloyl chloride (0.27 mL, 2.15 mmol, 1.3 eq.) dropwise. Warmed to rt stirring for 1 h. Quenched with 1 M NH_4OH. Diluted in EtOAc and washed with NH_4OH (3 x 100 mL). Washed with brine and dried over anhydrous sodium sulfate. Rotovapped to obtain crude. Isolated using column chromatography.

General Procedure 4 - For Unstable Enol Esters



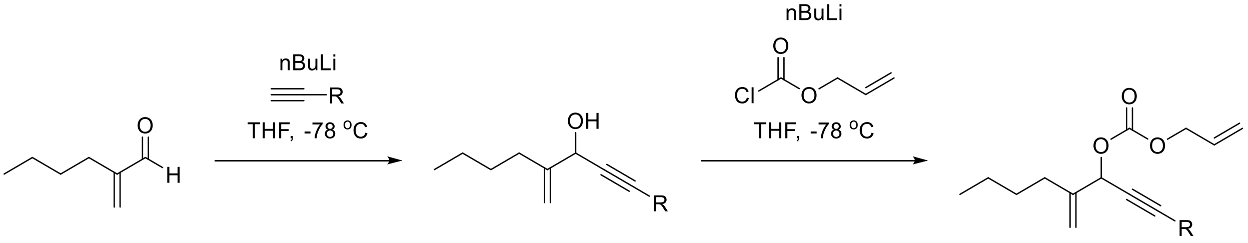
All reactions were run under the following conditions unless otherwise stated. A 20 mL vial equipped with a stir bar was dried under vacuum with a heat gun. Then PPh_3AuNTf_2 (1 mol% or 5 mol%) and anhydrous dichloromethane (2.0 mL) was added. Either water (1.0 equiv.) or acetic acid (2.0 equiv.) was added. The starting material (0.25 mmol) was added in anhydrous dichloromethane (2 mL) dropwise. The reaction was monitored by TLC until starting material was consumed. The reaction was quenched with 1 M NH_4OH and extracted with dichloromethane (3 x 4 mL). The organic extracts were dried with anhydrous sodium sulfate, filtered, and rotovapped. The crude was purified via SiO_2 column chromatography.

General Procedure 5 – For Stable Enol Esters



A 20 mL vial equipped with a stir bar was dried under vacuum with a heat gun. Then PPh_3AuNTf_2 (1.8 mg, 2.5 µmol, 1 mol%) and anhydrous dichloromethane (2.0 mL) was added. The starting material (0.25 mmol) was added in anhydrous dichloromethane (2 mL) dropwise. The reaction was monitored by TLC until starting material was consumed. Then added 6 drops of methanol and 3 drops of acetyl chloride and stirred for 30 min. The reaction was quenched with 1 M NH_4OH and extracted with dichloromethane (3 x 4 mL). The organic extracts were dried with anhydrous sodium sulfate, filtered, and rotovapped. The crude was purified via SiO_2 column.

General Procedure 6 – Two Step Method to Propargyl Allyl Carbonates

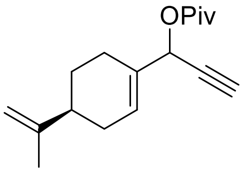


To a clean and dry 250 mL rb flask added alkyne (19.61 mmol, 1.1 equiv.) and anh. THF (98 mL). Cooled to -78 °C then added n-BuLi (7.5 mL, 18.7 mmol, 1.05 equiv., 2.5 M in hexanes) dropwise. Stirred for 30 min. Added aldehyde (17.83 mmol, 1.0 equiv.) in THF (60 mL) dropwise. Stirred for 2 h. Quenched with water. Diluted in EtOAc and washed with water (2 x 200 mL) then brine (200 mL). Dried over anhydrous Na_2SO_4 and filtered. Concentrated under reduced pressure and purified on column chromatography.

The alcohol (5.0 mmol) was dissolved in anh. THF (50 mL) in a dry 150 mL rb flask. Cooled to -78 °C then added n-BuLi (2.0 mL, 5.0 mmol, 1.0 equiv., 2.5 M in hexanes) dropwise. Stirred for 30 min then added allyl chloroformate (0.59 mL, 5.5 mmol, 1.1 equiv.) dropwise and stirred until TLC showed no alcohol remaining. Quenched with water and warmed to rt. Diluted in EtOAc and washed with water (3 x 100 mL) then brine (100 mL). Dried over anhydrous Na_2SO_4 and filtered. Concentrated under reduced pressure and purified on column chromatography.

3.1 Synthesis of **7a** and **8a**

Synthesis of 1-((S)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)prop-2-yn-1-yl pivalate (7a)



7a

Mixture of diastereomers

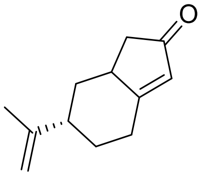
Synthesized by General Procedure 1 on 2.84 mmol scale

^{1}H NMR (300 MHz, CDCl3) δ = 6.01 (s, 1H), 5.78 (s, 1H), 4.74 (s, 1H), 4.72 (s, 1H), 2.49 (t, *J*=2.2, 1H), 2.33 – 1.92 (m, 4H), 1.87 (ddt, *J*=10.1, 5.0, 2.2, 1H), 1.74 (s, 3H), 1.60 – 1.41 (m, 2H), 1.23 (s, 9H)

^{13}C NMR (100 MHz, CDCl3) δ = 177.1, 149.4, 133.1, 126.9, 109.0, 80.1, 74.3, 67.1, 40.8, 38.9, 30.6, 27.4, 27.1, 24.9, 20.8

Isolated: Distilled on Kugelrohr (164 °C) as a clear colourless oil (544 mg, 74%)

Synthesis of (6S)-6-(prop-1-en-2-yl)-1,4,5,6,7,7a-hexahydro-2H-inden-2-one (8a)



8a

Synthesized with General Procedure 4 using **7a** (65 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a pale yellow oil (33 mg, 75%).

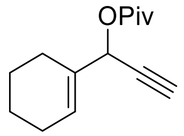
Characterization matched previously reported data[1]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.85 (m, 1H), 5.04 – 4.93 (m, 1H), 4.75 – 4.70 (m, 1H), 2.91 – 2.80 (m, 1H), 2.79 – 2.34 (m, 4H), 2.34 – 2.26 (m, 1H), 2.24 – 2.16 (m, 1H), 2.09 – 1.91 (m, 1H), 1.77 (s, 3H), 1.72 – 1.61 (m, 1H), 1.46 – 1.33 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.1, 185.5, 148.4, 127.0, 111.5, 44.2, 42.3, 39.7, 37.2, 31.9, 28.7, 22.6

3.2 Synthesis of **7b** and **8b**

Synthesis of 1-(cyclohex-1-en-1-yl)prop-2-yn-1-yl pivalate (7b)



7b

Characterization matched previously reported data[2]

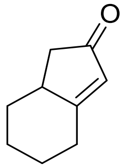
Synthesized by General Procedure 1 on 0.29 mmol scale (64%) or General Procedure 2 on 9.1 mmol scale (86%) as a yellow oil.

^{1}H- NMR (400 MHz, CDCl3) δ = 5.98 (s,1H), 5.74 (s, 1H), 2.48 (d, *J*=2.2, 1H), 2.20 – 1.96 (m, 4H), 1.62 (m, 4H), 1.22 (s, 9H)

^{13}C NMR (100 MHz, CDCl3) δ = 177.1, 133.1, 127.1, 80.0, 74.0, 67.3, 38.8, 27.0, 25.0, 24.3, 22.3, 22.0

Isolated: 5% EtOAc/Hex as a yellow oil (1.72 g, 86%)

Synthesis of 1,4,5,6,7,7a-hexahydro-2H-inden-2-one (8b)



8b

Synthesized with General Procedure 4 using **7b** (55 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a yellow oil (26 mg, 76%).

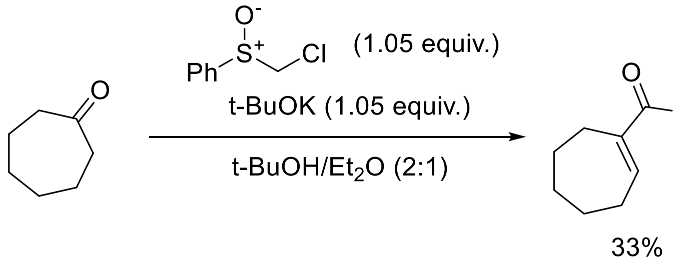
Characterization matched previously reported data[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.84 (s, 1H), 2.87 – 2.77 (m, 1H), 2.71 – 2.51 (m, 2H), 2.33 – 2.12 (m, 2H), 2.08 – 1.92 (m, 2H), 1.90 –1.80 (m, 1H), 1.59 – 1.32 (m, 2H), 1.13 (qt, *J*=12.7, 3.2, 1H)

^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.2, 185.0, 126.6, 42.3, 41.7, 35.0, 30.9, 27.0, 25.2

3.3 Synthesis of **7c** and **8c**

Synthesis of cyclohept-1-ene-1-carbaldehyde



Followed previous literature procedure[3] on a 8.9 mmol scale

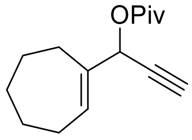
Characterization matched previously reported data[3,4]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.33 (s, 1H), 6.86 (t, *J* = 6.3 Hz, 1H), 2.51 – 2.37 (m, 4H), 1.85 – 1.74 (m, 2H), 1.60 (m, 2H), 1.54 – 1.44 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 157.0, 147.5, 31.7, 29.9, 26.1, 26.0, 23.8.

Isolated: 5% EtOAc/Hex as a clear oil (365 mg, 33%)

Synthesis of 1-(cyclohept-1-en-1-yl)prop-2-yn-1-yl pivalate (7c)



7c

Synthesized by General Procedure 2 on a 0.81 mmol scale

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.04 (t, *J* = 6.5 Hz, 1H), 5.65 (d, *J* = 2.2 Hz, 1H), 2.40 (d, *J* = 2.2 Hz, 1H), 2.21 – 2.16 (m, 2H), 2.13 – 2.07 (m, 2H), 1.72 – 1.65 (m, 2H), 1.50 – 1.40 (m, 4H), 1.15 (s, 9H).

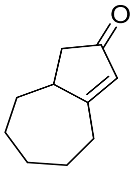
^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 139.2, 132.6, 80.2, 73.9, 68.6, 38.8, 32.4, 29.2, 28.3, 27.0, 26.9, 26.5.

IR ($CDCl_3$, *ν*) 401.21, 410.85, 416.64, 432.07, 449.43, 1145.75, 1735.99, 2860.53, 2933.83, 2974.33, 3292.6 cm^{-1}

HRMS (DART) calculated for $C_{15}H_{26}NO_2$ [M+NH_4] 252.19581, measured 252.19595

Isolated: 10% EtOAc/Hex as a yellow liquid (172 mg, 91%)

Synthesis of 4,5,6,7,8,8a-hexahydroazulen-2(1H)-one (8c)



8c

Synthesized with General Procedure 4 using **7c** (59 mg, 0.25 mmol), PPh_3AuNTf_2 (5 mol%), water (4.5 µL, 1.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a yellow oil (28 mg, 74%).

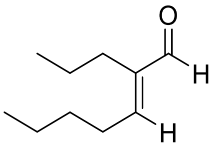
Characterization matched previously reported data[1]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.86 (q, *J* = 1.5 Hz, 1H), 2.99 – 2.88 (m, 1H), 2.80 – 2.69 (m, 1H), 2.73 – 2.60 (m, 2H), 2.00 (dd, *J* = 18.2, 2.9 Hz, 1H), 2.00 – 1.88 (m, 1H), 1.90 – 1.77 (m, 1H), 1.81 – 1.63 (m, 3H), 1.55 – 1.31 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 187.9, 129.8, 44.5, 44.4, 34.3, 32.7, 30.3, 28.5, 26.4.

3.4 Synthesis of **7d** and **8d**

Synthesis of (E)-2-propylhept-2-enal

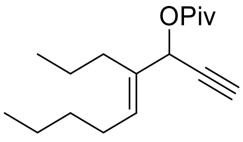


Followed previous literature procedure[5]

A round-bottom flask equipped with a magnetic stirrer bar was charged with an aqueous solution of sodium hydroxide (1.00 M) and 2.00 equivalents of the aldehyde were added drop wise over a period of 1 h. The reaction mixture was then heated to 50°C and upon complete conversion (monitored by TLC) the aqueous layer was extracted with diethyl ether. The organic phases were combined dried with anhydrous magnesium sulfate, filtered and the solvent was evaporated under reduced pressure to afford the desired product. If needed, the crude product was purified by flash column chromatography on silica gel.

Characterization matched previously reported data[6]

Synthesis of (E)-4-propylnon-4-en-1-yn-3-yl pivalate (7d)



7d

Synthesized by General Procedure 1 on 5.88 mmol scale

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.77 (s, 1H), 5.73 (t, *J*=7.2, 1H), 2.48 – 2.45 (m, 1H), 2.14 – 2.00 (m, 2H), 1.45 (tt, *J*=13.8, 6.7, 2H), 1.37 – 1.25 (m, 6H), 1.18 (s, 9H), 0.88 (m, 6H)

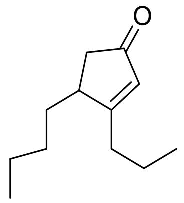
^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.0, 134.2, 131.9, 74.3, 67.5, 38.7, 34.2, 31.5, 29.9, 27.5, 26.9, 22.3, 22.1, 14.2, 13.9

HRMS (DART) calculated for $C_{17}H_{32}NO_2$ [M+NH$_4$] 282.24275, measured 282.24361

IR (neat, ν) = 3314, 3295, 2961, 2934, 2874, 1736, 1479, 1460, 1275, 1144 cm^{-1}

Isolated: 2% EtOAc/Hex as a clear oil (1.17 g, 75%)

Synthesis of 4-butyl-3-propylcyclopent-2-en-1-one (8d)



8d

Synthesized with General Procedure 4 using **7d** (66 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 15% EtOAc/Hex as a slightly yellow oil (37 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.85 (q, *J*=1.4, 1H), 2.76 – 2.69 (m, 1H), 2.47 (dd, *J*=18.6, 6.5, 1H), 2.40 – 2.29 (m, 1H), 2.25 – 2.14 (m, 1H), 2.03 (dd, *J*=18.6, 2.2, 1H), 1.77 – 1.64 (m, 1H), 1.63 – 1.45 (m, 2H), 1.34 – 1.18 (m, 5H), 0.91 (t, *J*=7.4, 3H), 0.84 (t, *J*=7.1, 3H)

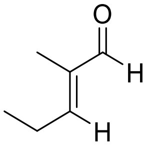
^{13}C NMR (100 MHz, $CDCl_3$) δ = 209.4, 129.3, 77.2, 43.3, 41.6, 33.3, 32.6, 29.3, 27.1, 22.8, 20.5, 14.1, 14.0

IR ($CDCl_3$, ν) 2959, 2932, 2874, 2862, 1716, 1699, 1612, 1458, 1412, 1186 cm^{-1}

HRMS (DART) calculated for $C_{12}H_{21}O$ [M+H] 181.15869, measured 181.15921

3.5 Synthesis of **7e** and **8e**

Synthesis of (E)-2-methylpent-2-enal

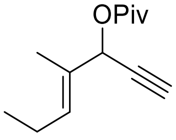


Followed previous literature procedure[5]

A round-bottom flask equipped with a magnetic stirrer bar was charged with an aqueous solution of sodium hydroxide (1.00 M) and 2.00 equivalents of the aldehyde were added drop wise over a period of 1 h. The reaction mixture was then heated to 50°C and upon complete conversion (monitored by TLC) the aqueous layer was extracted with diethyl ether. The organic phases were combined dried with anhydrous magnesium sulfate, filtered and the solvent was evaporated under reduced pressure to afford the desired product. If needed, the crude product was purified by flash column chromatography on silica gel.

Characterization matched previously reported data[7]

Synthesis of (E)-4-methylhept-4-en-1-yn-3-yl pivalate (7e)



7e

Synthesized by General Procedure 1 on a 8.72 mmol scale

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.74 (d, *J*=1.9, 1H), 5.72 – 5.64 (m, 1H), 2.49 (d, *J*=2.2, 1H), 2.13 – 2.01 (p, *J*=7.5, 2H), 1.73 – 1.69 (s, 3H), 1.22 (s, 9H), 0.99 (t, *J*=7.5, 3H)

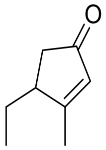
^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.0, 132.4, 129.7, 80.1, 74.0, 68.6, 38.8, 27.0, 21.03, 13.54, 12.19

HRMS (DART) calculated for $C_{13}H_{24}NO_2$ [M+NH$_4$] 226.18015, measured 226.18081

IR (neat, ν) = 3295, 2969, 2934, 2876, 1736, 1479, 1460, 1397, 1273, 1144 cm^{-1}

Isolated: 2% EtOAc/Hex (373 mg, 21%)

Synthesis of 4-ethyl-3-methylcyclopent-2-en-1-one (8e)



8e

Synthesized with General Procedure 4 using **7e** (52 mg, 0.25 mmol), PPh_3AuNTf_2 (5 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 15% EtOAc/Hex as a yellow oil (25 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.94 – 5.91 (m, 1H), 2.80 – 2.67 (m, 1H), 2.54 (dd, *J*=18.6, 6.6, 1H), 2.11 – 2.09 (overlayed dd, *J*=18.8, 1H), 2.09 (s, 3H), 1.84 (ddq, *J*=14.9, 7.4, 3.6, 1H), 1.40 – 1.27 (m, 1H), 0.90 (t, *J*=7.4, 3H)

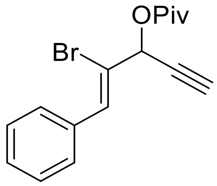
^{13}C NMR (100 MHz, $cdcl_3$) δ 209.2, 181.5, 131.0, 45.4, 41.1, 25.1, 17.3, 10.8

IR ($CHCl_3$, ν) 1614, 1402, 1370, 1350, 1333, 1310, 1182 cm^{-1}

HRMS (DART) calculated for $C_8H_{13}O$ [M+H] 125.09664, measured 125.09651

3.6 Synthesis of **7f** and **8f**

Synthesis of (Z)-2-bromo-1-phenylpent-1-en-4-yn-3-yl pivalate (7f)



7f

Synthesized by General Procedure 2 on 4.74 mmol scale

^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.59 – 7.49 (m, 2H), 7.32 – 7.16 (m, 4H), 6.07 (dd, *J*=2.2, 0.9, 1H), 2.58 (d, *J*=2.2, 1H), 1.17 (s, 9H)

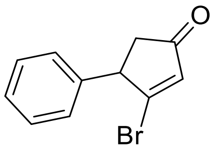
^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.6, 134.4, 132.4, 129.3, 128.9, 128.3, 119.8, 78.4, 76.1, 68.4, 38.9, 27.0

IR (KBr, ν) = 3293, 3027, 2128, 1737, 1479, 1453, 1396, 1366, 1272, 1130, 1030 cm^{-1}

HRMS (EI(+)) fragments detected, calculated for $C_{16}H_{17}O_2$ [M-Br], 241.12231, measured 241.12419, calculated for $C_{11}H_8O^{79/81}Br$ [M-OPiv] 218.98039/220.97834, measured 218.98218/220.98086

Isolated: pure petroleum ether -> 2% EtOAc/petroleum ether as a yellow oil (1.50 g, 99%)

Synthesis of 3-bromo-4-phenylcyclopent-2-en-1-one (8f)



8f

Synthesized with General Procedure 4 using **7f** (80 mg, 0.25 mmol), PPh_3AuNTf_2 (5 mol%), water (4.5 µL, 1.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% EtOAc/petroleum ether as white solid (47 mg, 80%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.41 – 7.28 (m, 3H), 7.19 – 7.12 (m, 2H), 6.57 (d, *J*=1.8, 1H), 4.23 (dt, *J*=7.2, 2.0, 1H), 3.05 (dd, *J*=18.7, 7.3, 1H), 2.58 (dd, *J*=18.7, 2.4, 1H)

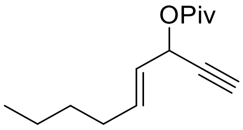
^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.3, 164.9, 139.6, 136.3, 129.2, 128.0, 127.6, 53.7, 46.6

IR (KBr, ν) = 3404, 3080, 3026, 2967, 2924, 1706, 1578, 1494, 1455, 1402, 1328, 1265, 1244, 1218, 1166, 1146, 1076, 1031, 1004 cm^{-1}

HRMS (EI(+)) calculated for $C_{11}H_9{}^{79/81}BrO$ [M] 235.98313/237.98108, measured 235.98387/237.98192

3.7 Synthesis of **7g** and **8g**

Synthesis of (E)-non-4-en-1-yn-3-yl pivalate (7g)



7g

Synthesized by General Procedure 1 on a 2.01 mmol scale

Characterization matched previously reported data[2]

^{1}H NMR (300 MHz, CDCl3) δ = 5.99 (dtd, *J*=15.0, 6.8, 1.1, 1H), 5.81 (ddd, *J*=6.4, 2.1, 1.1, 1H), 5.52 (ddt, *J*=15.3, 6.4, 1.5, 1H), 2.52 (d, *J*=2.2, 1H), 2.08 (q, *J*=7.0, 2H), 1.45 – 1.24 (m, 4H), 1.21 (s, 9H), 0.90 (t, *J*=7.1, 3H)

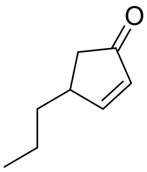
^{13}C NMR (100 MHz, cdcl3) δ = 177.0, 136.3, 124.8, 80.1, 63.8, 38.6, 34.0, 26.9, 21.8, 13.5

IR (neat, ν) 3296, 2962, 2934, 2874, 1736, 1480, 1460, 1479, 1275, 1146 cm^{-1}

HRMS (DART) calculated for $C_{13}H_{24}NO_2$ [M+NH$_4$] 226.18070, measured 226.18036

Isolated: Kugelrohr distillation (110 °C) as a colourless clear oil (93 mg, 23%)

Synthesis of 4-propylcyclopent-2-en-1-one (8g)



8g

Synthesized with General Procedure 4 using **7g** (56 mg, 0.25 mmol), PPh_3AuNTf_2 (5 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 15% EtOAc/Hex as yellow oil (23 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 5.6, 2.5 Hz, 1H), 6.14 (dd, *J* = 5.7, 2.0 Hz, 1H), 2.96 – 2.86 (m, 1H), 2.53 (dd, *J* = 18.8, 6.3 Hz, 1H), 2.00 (dd, *J* = 18.8, 2.2 Hz, 1H), 1.65 – 1.52 (m, 2H), 1.46 – 1.23 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H).

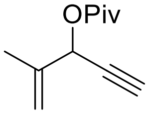
^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.1, 168.6, 133.5, 41.4, 41.0, 34.4, 29.8, 22.6, 13.9

IR ($CHCl_3$, ν) 2957, 2928, 2872, 2859, 1713, 1460, 1287, 1275, 1202, 1184 cm^{-1}

HRMS (DART) calculated for $C_9H_{15}O$ [M+H] 139.11229, measured 139.11233

3.8 Synthesis of **7h** and **8h**

Synthesis of 2-methylpent-1-en-4-yn-3-yl pivalate (7h)



7h

Synthesized by General Procedure 1 on a 34.4 mmol scale

^{1}H NMR (400 MHz, CDCl3) δ = 5.71 (s, 1H), 5.17 (s, 1H), 4.94 (s, 1H), 2.43 (d, *J*=2.2, 1H), 1.77 (s, 3H), 1.16 (s, 9H)

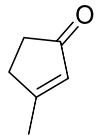
^{13}C NMR (100 MHz, CDCl3) δ = 176.9, 140.0, 114.7, 79.6, 74.2, 66.5, 38.8, 26.9, 18.2

IR (neat, ν) 3296, 2978, 2936, 2876, 1738, 1479, 1460, 1397, 1275, 1144 cm^{-1}

HRMS (DART) calculated for $C_{11}H_{20}NO_2$ [M+NH$_4$] 198.14885, measured 198.14889

Isolated: Crude was stirred in 1 M KOH for 3 h then extracted with Et_2O (3 x 20 mL), dried over $MgSO_4$ and evaporated. The product was purified by Kugelrohr as a clear oil (1.89 g, 30%)

Synthesis of 3-methylcyclopent-2-en-1-one (8h)



8h

Synthesized with General Procedure 4 using **7h** (45 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Rotovapped under reduced pressure at 0 °C. Yield measured relative to 1,3,5-trimethoxybenzene, product is volatile. Appeared as a clear oil (18 mg, 74%)

Characterization matched previously reported data[8]

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.95 (q, *J*=1.4, 1H), 2.61 – 2.52 (m, 2H), 2.46 – 2.38 (m, 2H), 2.13 (s, 3H)

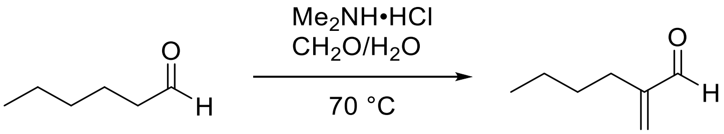
^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.3, 178.9, 130.7, 35.7, 33.0, 19.4

IR ($CDCl_3$, ν) 2956, 2862, 1703, 1697, 1605, 1479, 1460, 1206, 1152, 1067 cm^{-1}

HRMS (DART) calculated for C_6H_9O [M+H] 97.06534, measured 97.06492

3.9 Synthesis of **7i** and **8i**

Synthesis of 2-Methylenehexanal



Followed previous literature procedure[9]

A 100 mL rb flask was equppied with a water condenser and a stir bar. Added dimethylamine hydrochloride (9.20 g, 112.3 mmol, 1.2 equiv.), formaldehyde solution (9.1 mL, 112.3 mmol, 1.2 equiv., 37% soln. in water), and hexanal (11.5 mL, 93.6 mmol, 1.0 equiv.). Heated to 70 °C and stirred vigorously overnight. Quenched reaction with 100 mL of a saturated NH_4Cl soln. Extracted with Et_2O (3 x 100 mL). Organic extracts were combined and washed with NH_4Cl (100 mL), $NaHCO_3$ (100 mL) and brine (100 mL). Dried over anhydrous sodium sulfate and filtered. Rotovapped to give product. Dried under high vacuum. Product is volatile (48%-79%).

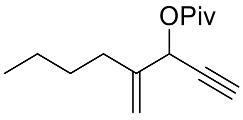
Characterization matched previously reported data[9]

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 6.24 (q, *J* = 1.2 Hz, 1H), 5.98 (d, *J* = 0.8 Hz, 1H), 2.24 (t, *J* = 7.4 Hz, 2H), 1.52 – 1.38 (m, 2H), 1.38 – 1.26 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 150.4, 133.8, 29.9, 27.4, 22.3, 13.8

Isolated: Can be purified on column if needed, 2% EtOAc/Hex, appears as a clear oil (48% - 79%)

Synthesis of 4-methyleneoct-1-yn-3-yl pivalate (7i)



7i

Can be synthesized with General Procedure 1 on 34.4 mmol scale (1.29 g, 29%) or General Procedure 2 on 20 mmol scale (44% - 63%)

^{1}H NMR (400 MHz, CDCl3) δ = 5.82 (s, 1H), 5.38 – 5.29 (m, 1H), 5.08 – 4.99 (m, 1H), 2.50 (d, *J*=2.3, 1H), 2.21 – 2.12 (m, 2H), 1.56 – 1.42 (m, 2H), 1.36 (dt, *J*=15.0, 7.3, 2H), 1.23 (s, 9H), 0.92 (t, *J*=7.3, 3H)

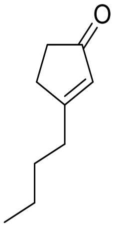
^{13}C NMR (100 MHz, CDCl3) δ = 177.0, 144.2, 113.5, 79.9, 74.3, 66.0, 38.8, 31.6, 29.7, 27.0, 22.4, 13.9

IR (neat, ν) = 3314, 3295, 2961, 2933, 2874, 1738, 1479, 1460, 1275, 1144 cm^{-1}

HRMS (DART) calculated for $C_{14}H_{26}NO_2$ [M+NH$_4$] 240.19635, measured 240.19566

Isolated: 2% EtOAc/Hex (29%-63%)

Synthesis of 3-butylcyclopent-2-en-1-one (8i)



8i

Synthesized with General Procedure 4 using **7i** (56 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a yellow oil (29 mg, 80%).

Characterization matched previously reported data[10]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.94 (p, *J*=1.5, 1H), 2.60 – 2.55 (m, 2H), 2.43 – 2.37 (m, 4H), 1.61 – 1.50 (m, 2H), 1.43 – 1.33 (m, 2H), 0.93 (t, *J*=7.3, 3H)

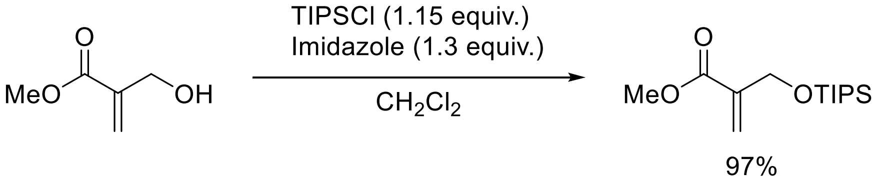
^{13}C NMR (100 MHz, $CDCl_3$) δ = 210.2, 183.2, 129.4, 35.3, 33.2, 31.5, 29.2, 22.4, 13.8

IR ($CDCl_3$, ν) 2956, 2930, 2870, 2862, 1709, 1672, 1614, 1439, 1408, 1231 cm^{-1}

HRMS (DART) calculated for $C_9H_{15}O$ [M+H] 139.11174, measured 139.11184

3.10 Synthesis of **7j** and **8j** and **17**

Synthesis of Methyl 2-(((triisopropylsilyl)oxy)methyl)acrylate



Followed previous literature procedure[11] on 19.5 mmol scale

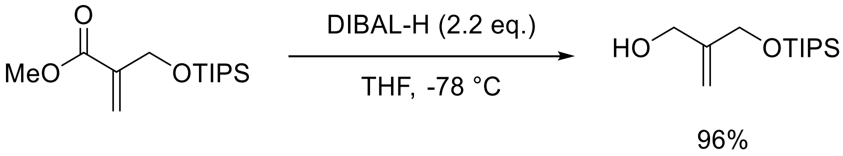
Characterization matched previously reported data[12]

^{1}H NMR (400 MHz, CDCl$_3$) δ 6.27 (q, *J* = 2.1 Hz, 1H), 6.00 (q, *J* = 2.2 Hz, 1H), 4.45 (t, *J* = 2.2 Hz, 2H), 3.75 (s, 3H), 1.18 – 1.03 (m, 21H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 166.4, 139.6, 123.7, 61.6, 51.6, 18.0, 12.0.

Isolated: 5% EtOAc/Hex as a yellow oil (5.15 g, 97%)

Synthesis of 2-(((triisopropylsilyl)oxy)methyl)prop-2-en-1-ol



Followed previous literature procedure[11] on 18 mmol scale

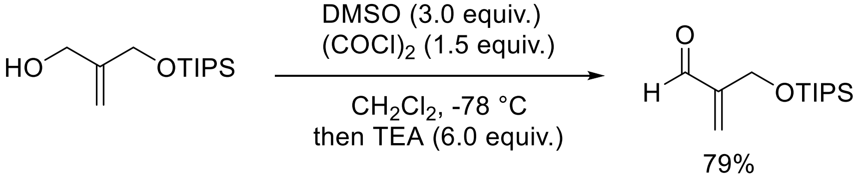
Characterization matched previously reported data[11]

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.12 (q, *J* = 1.6, 1H), 5.08 (q, *J* = 1.3 Hz, 1H), 4.34 (s, 2H), 4.19 (d, *J* = 4.3 Hz, 2H), 2.04 (s, 1H), 1.14 – 1.01 (m, 21H).

^{13}C NMR (100 MHz, CDCl$_3$) δ 147.4, 111.0, 65.5, 64.9, 18.0, 11.9.

Isolated: Carried forward without further purification as a slightly cloudy oil

Synthesis of 2-(((triisopropylsilyl)oxy)methyl)acrylaldehyde



Followed previous literature procedure[13] on 5.1 mmol scale

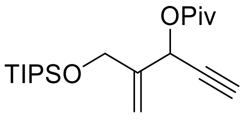
Characterization matched previously reported data[14]

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 6.61 – 6.58 (m, 1H), 6.12 (q, *J* = 2.0 Hz, 1H), 4.49 (t, *J* = 2.1 Hz, 2H), 1.07 (m, 21H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.7, 149.7, 132.8, 59.9, 18.0, 11.9.

Isolated: 50% DCM/Hex as a yellow oil (980 mg, 79%)

Synthesis of 2-(((triisopropylsilyl)oxy)methyl)pent-1-en-4-yn-3-yl pivalate (7j)



7j

Synthesized by General Procedure 2 on 2.1 mmol scale

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.95 – 5.90 (m, 1H), 5.45 (t, *J* = 1.4 Hz, 1H), 5.44 – 5.40 (m, 1H), 4.42 – 4.27 (m, 2H), 2.51 (d, *J* = 2.3 Hz, 1H), 1.22 (s, 9H), 1.15 – 1.04 (m, 21H).

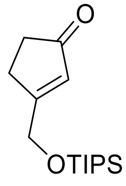
^{13}C NMR (100 MHz, CDCl$_3$) δ 176.7, 143.4, 113.2, 79.3, 74.6, 63.7, 62.6, 38.7, 26.9, 17.9, 11.9.

IR (CDCl$_3$, ν) 401.21, 414.71, 636.53, 659.68, 682.82, 881.5, 1122.61, 1141.9, 1458.23, 1741.78, 2341.66, 2360.95, 2868.24, 2893.32, 2943.47, 2960.83, 3313.82 cm^{-1}

HRMS (DART) calculated for $C_{20}H_{37}O_3Si$ [M+H] 353.25120, measured 353.25138

Isolated: 5% EtOAc/Hex as a yellow oil (89% - 93%)

Synthesis of 3-(((triisopropylsilyl)oxy)methyl)cyclopent-2-en-1-one (8j)



8j

Synthesized with General Procedure 4 using **7j** (88 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 20% EtOAc/Hex as a yellow oil (48 mg, 72%).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.23 – 6.18 (m, 1H), 4.54 (s, 2H), 2.59 – 2.52 (m, 2H), 2.45 – 2.39 (m, 2H), 1.32 – 1.01 (m, 21H).

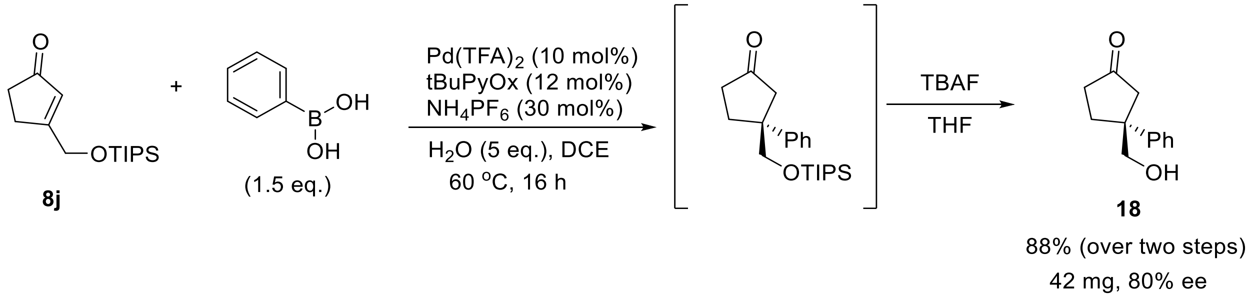
^{13}C NMR (100 MHz, cdcl$_3$) δ 209.2, 181.6, 128.3, 63.7, 35.0, 27.8, 17.9, 11.9

IR ($CDCl_3$, ν) 663.53, 684.75, 790.84, 839.06, 881.5, 1068.6, 1089.82, 1145.75, 1259.56, 1464.02, 1626.05, 1712.85, 2866.32, 2943.47

HRMS (DART) calculated for $C_{15}H_{29}O_2Si$ [M+H] 269.19368, measured 269.19378

3.10.1 Synthesis of **18**, Palladium catalyzed conjugate addition

Synthesis of (S)-3-(hydroxymethyl)-3-phenylcyclopentan-1-one (18)



Based on previous literature procedure[15]

A 1 dr vial was equipped with a magnetic stir bar. Added t-BuPyOX (6.1 mg, 0.03 mmol, 0.12 equiv.), $Pd(TFA)_2$ (8.3 mg, 0.025 mmol, 0.1 equiv.), NH_4PF_6 (12.2 mg, 0.075 mmol, 0.3 equiv.) and phenylboronic acid (46 mg, 0.35 mmol, 1.5 equiv.) then anhydrous DCE (0.75 mL) and water (22.5 µL, 1.25 mmol, 5.0 equiv.) to vial and stirred for 10 min. Added cyclopentenone (67 mg, 0.25 mmol, 1.0 equiv.) in anhydrous DCE (0.75 mL) dropwise. Stirred at 60 °C for 16 h. Eluted through silica plug with DCM and rotovapped. Continued to next step with no further purification.

Crude solution was dissolved in anhydrous THF (2.0 mL) and stirred at 0 °C. A solution of TBAF (0.33 mL, 0.33 mmol, 1.3 equiv., 1.0 M in THF) was added dropwise and the reaction was stirred for 1 h. Filtered reaction through silica plug with EtOAc then concentrated the filtrate. Purified by flash column chromatography with 20% -> 50% EtOAc/Hex and collected product as a white solid, 42 mg, 88% yield, 80% ee.

Product could be recrystallized by vapour diffusion in 1:1 acetone/ether with pentane then filtered with cold ether. Obtained 97% ee.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.31 – 7.25 (m, 3H), 3.70 – 3.60 (m, 2H), 2.72 (d, *J* = 18.0 Hz, 1H), 2.62 (d, *J* = 18.6 Hz, 1H), 2.59 – 2.51 (m, 1H), 2.49 – 2.39 (m, 1H), 2.38 – 2.30 (m, 1H), 2.25 (dt, *J* = 11.9, 8.8 Hz, 1H), 1.45 (t, *J* = 6.0 Hz, 1H).

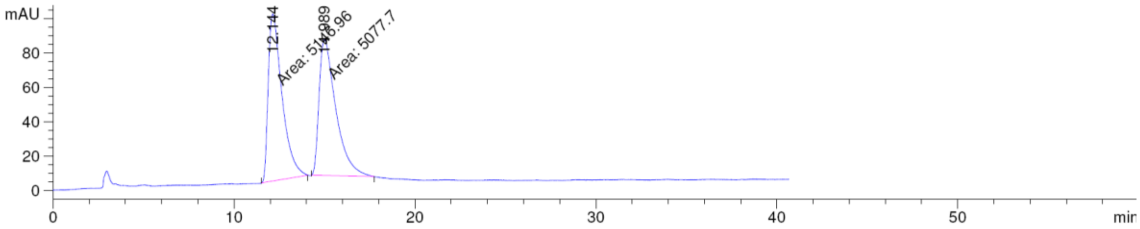
^{13}C NMR (100 MHz, $CDCl_3$) δ 218.2, 144.4, 128.7, 127.0, 126.6, 70.4, 49.5, 47.3, 36.7, 30.6.

IR ($CDCl_3$, ν) 705, 751, 1058, 1159, 1731, 2870, 2919, 2938, 2952, 3409

HRMS (DART) calculated for $C_{12}H_{18}NO_2$ [M+NH_4] 208.13375, measured 208.13320

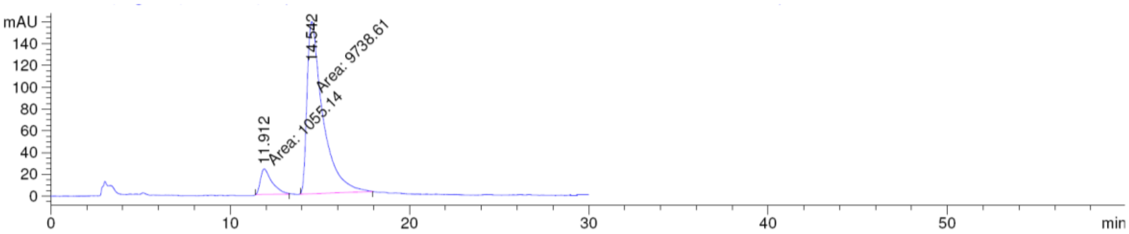
Chiral HPLC: OJ column, 1 mL/min, 20% IPA/Hex. 80% ee after reaction, 97% ee after two recrystallizations

Racemic Sample



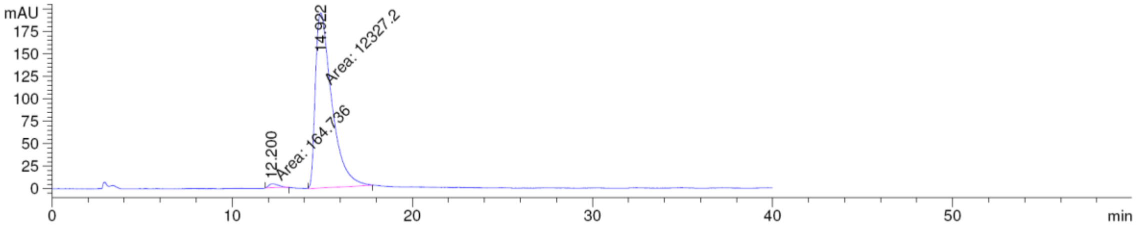
```
Signal 1: DAD1 A, Sig=210,6 Ref=360,40

Peak RetTime Type  Width     Area       Height     Area  
  #   [min]        [min]   [mAU*s]      [mAU]        %   
----|-------|----|-------|----------|----------|--------|
   1  12.144 MM    0.8822 5146.95703   97.23611  50.3387
   2  14.989 MM    1.0714 5077.69971   78.98862  49.6613

Totals :                  1.02247e4  176.22473
```

Sample After Reaction



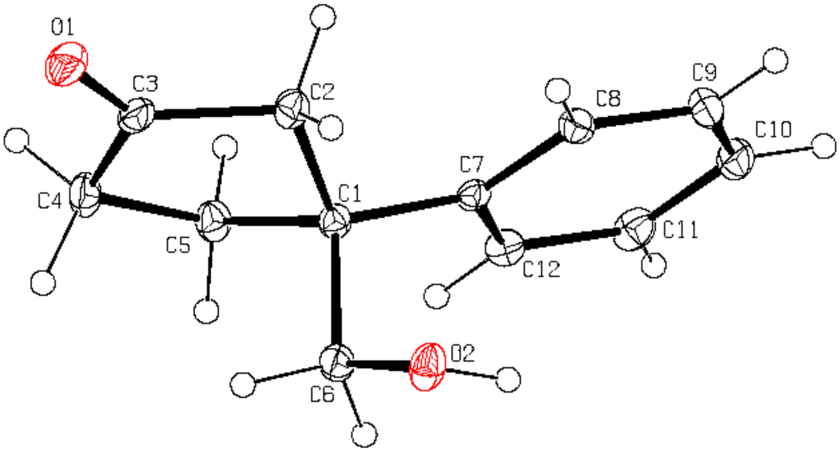
```
Signal 1: DAD1 A, Sig=210,6 Ref=360,40

Peak RetTime Type  Width     Area       Height     Area  
  #   [min]        [min]   [mAU*s]      [mAU]        %   
----|-------|----|-------|----------|----------|--------|
   1  11.912 MM    0.7482 1055.14441   23.50309   9.7755
   2  14.542 MM    1.0269 9738.60840  158.05536  90.2245

Totals :                  1.07938e4  181.55844
```

Sample After Recrystallization



```
Signal 1: DAD1 A, Sig=210,6 Ref=360,40

Peak RetTime Type  Width     Area       Height     Area  
  #   [min]        [min]   [mAU*s]      [mAU]        %   
----|-------|----|-------|----------|----------|--------|
   1  12.200 MM    0.6180  164.73650    4.44258   1.3187
   2  14.922 MM    1.0555 1.23272e4  194.64838  98.6813

Totals :                  1.24919e4  199.09095
```

X-Ray Crystallography: Absolute stereochemistry determined by X-Ray



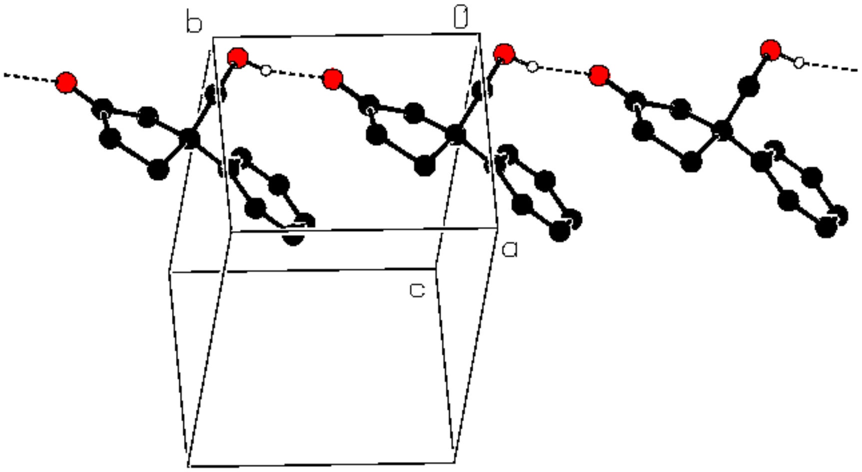


Table 1. Crystal data and structure refinement for d15151.

Identification code	d15151	
Empirical formula	C12 H14 O2	
Formula weight	190.23	
Temperature	147(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.1020(2) Å	a= 90°.
	b = 7.0956(3) Å	b= 90.988(2)°.
	c = 11.5895(5) Å	g = 90°.
Volume	501.72(3) Å^3	
Z	2	
Density (calculated)	1.259 Mg/m^3	
Absorption coefficient	0.676 mm^{-1}	
F(000)	204	
Crystal size	0.230 x 0.170 x 0.040 mm^3	
Theta range for data collection	3.814 to 67.413°.	
Index ranges	-7<=h<=7, -8<=k<=8, -13<=l<=13	
Reflections collected	14226	
Independent reflections	1785 [R(int) = 0.0360]	
Completeness to theta = 67.413°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7529 and 0.6901	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1785 / 1 / 131	
Goodness-of-fit on F^2	1.068	
Final R indices [I>2sigma(I)]	R1 = 0.0296, wR2 = 0.0781	
R indices (all data)	R1 = 0.0299, wR2 = 0.0784	
Absolute structure parameter	-0.01(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.320 and -0.140 e.Å^{-3}	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3)
for d15151. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	12(3)	5202(2)	1843(1)	36(1)
O(2)	-195(2)	-1127(2)	1058(1)	29(1)
C(1)	2686(3)	730(3)	2066(2)	18(1)
C(2)	979(3)	2101(3)	2541(2)	24(1)
C(3)	1321(4)	3924(3)	1888(2)	26(1)
C(4)	3514(3)	3881(3)	1321(2)	28(1)
C(5)	4614(3)	2073(3)	1770(2)	24(1)
C(6)	1808(3)	-140(3)	927(2)	25(1)
C(7)	3306(3)	-836(3)	2896(2)	18(1)
C(8)	1802(3)	-1535(3)	3677(2)	22(1)
C(9)	2325(4)	-3036(3)	4403(2)	28(1)
C(10)	4377(4)	-3866(3)	4361(2)	29(1)
C(11)	5892(3)	-3194(3)	3582(2)	28(1)
C(12)	5362(3)	-1699(3)	2856(2)	23(1)

Table 3. Bond lengths [Å] and angles [°] for d15151.

O(1)-C(3)	1.209(3)
O(2)-C(6)	1.419(2)
O(2)-H(2O)	0.85(4)
C(1)-C(7)	1.514(3)
C(1)-C(2)	1.534(3)
C(1)-C(6)	1.545(3)
C(1)-C(5)	1.557(3)
C(2)-C(3)	1.515(3)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.501(3)
C(4)-C(5)	1.535(3)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-H(6A)	0.9900
C(6)-H(6B)	0.9900
C(7)-C(8)	1.392(3)
C(7)-C(12)	1.398(3)
C(8)-C(9)	1.391(3)
C(8)-H(8A)	0.9500
C(9)-C(10)	1.385(3)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.388(3)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.389(3)
C(11)-H(11A)	0.9500
C(12)-H(12A)	0.9500
C(6)-O(2)-H(2O)	107(2)
C(7)-C(1)-C(2)	113.69(15)
C(7)-C(1)-C(6)	109.22(16)
C(2)-C(1)-C(6)	109.40(16)

C(7)-C(1)-C(5)	114.08(15)
C(2)-C(1)-C(5)	102.18(16)
C(6)-C(1)-C(5)	107.94(16)
C(3)-C(2)-C(1)	105.23(17)
C(3)-C(2)-H(2A)	110.7
C(1)-C(2)-H(2A)	110.7
C(3)-C(2)-H(2B)	110.7
C(1)-C(2)-H(2B)	110.7
H(2A)-C(2)-H(2B)	108.8
O(1)-C(3)-C(4)	126.1(2)
O(1)-C(3)-C(2)	124.5(2)
C(4)-C(3)-C(2)	109.42(18)
C(3)-C(4)-C(5)	104.87(16)
C(3)-C(4)-H(4A)	110.8
C(5)-C(4)-H(4A)	110.8
C(3)-C(4)-H(4B)	110.8
C(5)-C(4)-H(4B)	110.8
H(4A)-C(4)-H(4B)	108.8
C(4)-C(5)-C(1)	104.99(16)
C(4)-C(5)-H(5A)	110.7
C(1)-C(5)-H(5A)	110.7
C(4)-C(5)-H(5B)	110.7
C(1)-C(5)-H(5B)	110.7
H(5A)-C(5)-H(5B)	108.8
O(2)-C(6)-C(1)	113.06(17)
O(2)-C(6)-H(6A)	109.0
C(1)-C(6)-H(6A)	109.0
O(2)-C(6)-H(6B)	109.0
C(1)-C(6)-H(6B)	109.0
H(6A)-C(6)-H(6B)	107.8
C(8)-C(7)-C(12)	117.95(17)
C(8)-C(7)-C(1)	120.96(17)
C(12)-C(7)-C(1)	120.99(17)
C(9)-C(8)-C(7)	121.26(18)
C(9)-C(8)-H(8A)	119.4
C(7)-C(8)-H(8A)	119.4

C(10)-C(9)-C(8)	120.16(19)
C(10)-C(9)-H(9A)	119.9
C(8)-C(9)-H(9A)	119.9
C(9)-C(10)-C(11)	119.30(19)
C(9)-C(10)-H(10A)	120.4
C(11)-C(10)-H(10A)	120.4
C(10)-C(11)-C(12)	120.40(19)
C(10)-C(11)-H(11A)	119.8
C(12)-C(11)-H(11A)	119.8
C(11)-C(12)-C(7)	120.92(19)
C(11)-C(12)-H(12A)	119.5
C(7)-C(12)-H(12A)	119.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x 10^3) for d15151. The anisotropic displacement factor exponent takes the form: $-2p^2$[h^2 $a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	49(1)	23(1)	36(1)	-1(1)	-2(1)	9(1)
O(2)	31(1)	22(1)	33(1)	4(1)	-12(1)	-7(1)
C(1)	18(1)	18(1)	19(1)	1(1)	-1(1)	-2(1)
C(2)	26(1)	19(1)	26(1)	2(1)	0(1)	3(1)
C(3)	38(1)	18(1)	21(1)	-3(1)	-7(1)	1(1)
C(4)	34(1)	21(1)	27(1)	5(1)	-6(1)	-9(1)
C(5)	23(1)	23(1)	26(1)	2(1)	0(1)	-6(1)
C(6)	32(1)	22(1)	20(1)	2(1)	-5(1)	-4(1)
C(7)	22(1)	17(1)	17(1)	-3(1)	-4(1)	-2(1)
C(8)	22(1)	22(1)	21(1)	0(1)	0(1)	0(1)
C(9)	35(1)	26(1)	21(1)	4(1)	2(1)	-5(1)
C(10)	41(1)	22(1)	24(1)	3(1)	-9(1)	2(1)
C(11)	27(1)	24(1)	33(1)	-2(1)	-7(1)	6(1)
C(12)	22(1)	24(1)	24(1)	-2(1)	-1(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for d15151.

	x	y	z	U(eq)
H(2A)	-523	1613	2404	29
H(2B)	1212	2295	3380	29
H(4A)	4391	5004	1538	33
H(4B)	3339	3844	471	33
H(5A)	5528	2338	2465	29
H(5B)	5550	1510	1172	29
H(6A)	1588	878	352	30
H(6B)	2921	-1017	623	30
H(8A)	390	-976	3716	26
H(9A)	1273	-3494	4929	33
H(10A)	4744	-4884	4861	35
H(11A)	7299	-3761	3544	33
H(12A)	6412	-1257	2323	28
H(2O)	130(50)	-2210(50)	1330(30)	47(9)

Table 6. Torsion angles [°] for d15151.

C(7)-C(1)-C(2)-C(3)	155.48(15)
C(6)-C(1)-C(2)-C(3)	-82.14(19)
C(5)-C(1)-C(2)-C(3)	32.1(2)
C(1)-C(2)-C(3)-O(1)	163.71(18)
C(1)-C(2)-C(3)-C(4)	-16.4(2)
O(1)-C(3)-C(4)-C(5)	173.2(2)
C(2)-C(3)-C(4)-C(5)	-6.6(2)
C(3)-C(4)-C(5)-C(1)	26.8(2)
C(7)-C(1)-C(5)-C(4)	-159.65(16)
C(2)-C(1)-C(5)-C(4)	-36.51(19)
C(6)-C(1)-C(5)-C(4)	78.77(19)
C(7)-C(1)-C(6)-O(2)	66.0(2)
C(2)-C(1)-C(6)-O(2)	-59.0(2)
C(5)-C(1)-C(6)-O(2)	-169.43(16)
C(2)-C(1)-C(7)-C(8)	30.9(2)
C(6)-C(1)-C(7)-C(8)	-91.5(2)
C(5)-C(1)-C(7)-C(8)	147.60(18)
C(2)-C(1)-C(7)-C(12)	-152.87(17)
C(6)-C(1)-C(7)-C(12)	84.7(2)
C(5)-C(1)-C(7)-C(12)	-36.2(2)
C(12)-C(7)-C(8)-C(9)	0.5(3)
C(1)-C(7)-C(8)-C(9)	176.78(17)
C(7)-C(8)-C(9)-C(10)	0.2(3)
C(8)-C(9)-C(10)-C(11)	-0.6(3)
C(9)-C(10)-C(11)-C(12)	0.4(3)
C(10)-C(11)-C(12)-C(7)	0.3(3)
C(8)-C(7)-C(12)-C(11)	-0.7(3)
C(1)-C(7)-C(12)-C(11)	-176.99(18)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for d15151 [Å and °].

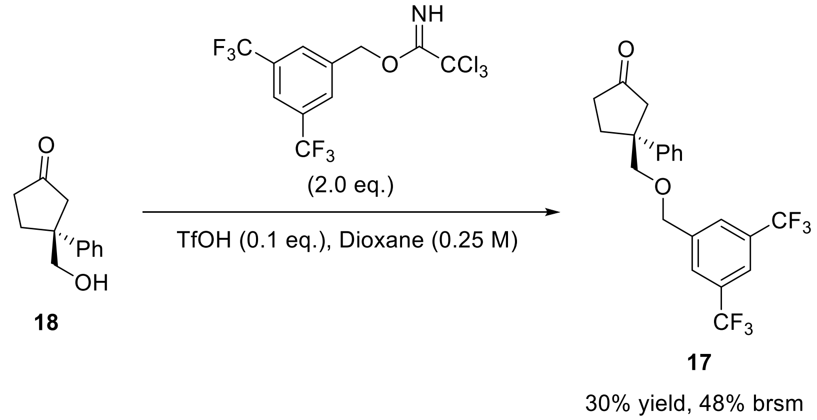
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(4)-H(4B)...O(2)#1	0.99	2.59	3.393(2)	138.3
O(2)-H(2O)...O(1)#2	0.85(4)	1.93(4)	2.762(2)	164(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y+1/2,-z #2 x,y-1,z

3.10.2 Synthesis of **17**, Benzylation of with trichloroacetimidate

Synthesis of (S)-3-(((3,5-bis(trifluoromethyl)benzyl)oxy)methyl)-3-phenylcyclopentan-1-one (17)



Based on previous literature procedure[16]

Characterization matched previously reported data[17]

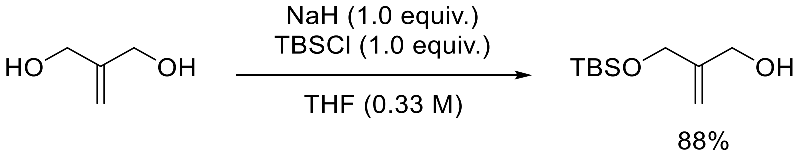
Added the alcohol starting material (48 mg, 0.25 mmol, 1.0 equiv.) to a 1 dr vial with a magnetic stir bar. Added the trichloroacetimidate (194 mg, 0.50 mmol, 2.0 equiv.) in dioxane (1.0 mL) and stirred until the alcohol was fully dissolved. Added triflic acid (2 drops, ~ 0.1 equiv.) and stirred at rt. Stopped at 6 h and diluted in to EtOAc (6 mL). Washed with water (3 x 6 mL) and concentrated the organic layer. Purified on flash column, 10% -> 40% EtOAc/Hex. Obtained 36 mg of product as a yellow oil, and 8 mg of SM (30% yield, 46% brsm)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (s, 1H), 7.61 (s, 2H), 7.38 – 7.33 (m, 2H), 7.31 – 7.24 (m, 3H), 4.53 (s, 2H), 3.63 – 3.52 (m, 2H), 2.77 (d, *J* = 17.8 Hz, 1H), 2.68 (d, *J* = 17.7 Hz, 1H), 2.61 – 2.29 (m, 4H).

^{13}C NMR (100 MHz, cdcl$_3$) δ 217.3, 144.5, 140.7, 131.5, 128.0, 128.5, 127.0, 126.9, 126.4, 121.5, 79.2, 71.9, 48.4, 47.9, 36.8, 31.6.

3.11 Synthesis of **7k** and **8k**

Synthesis of 2-(((tert-butyldimethylsilyl)oxy)methyl)prop-2-en-1-ol



Followed previous literature procedure[18] on a 24.5 mmol scale

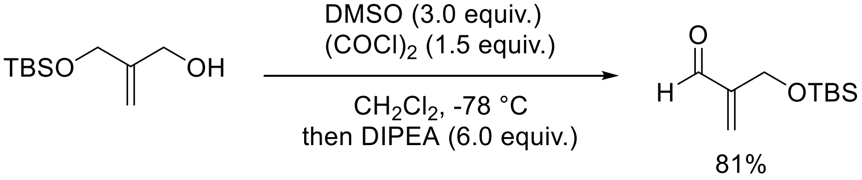
Characterization matched previously reported data[18]

^{1}H NMR (300 MHz, Chloroform-*d*) δ 5.10 (s, 1H), 5.08 (s, 1H), 4.24 (s, 2H), 4.17 (d, *J* = 5.6 Hz, 2H), 1.93 (t, *J* = 5.9 Hz, 1H), 0.91 (s, 9H), 0.09 (s, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 110.9, 65.0, 64.4, 25.9, 18.3, -5.4.

Isolated: 20% EtOAc/Hex as a colourless oil (4.38 g, 88%)

Synthesis of 2-(((tert-butyldimethylsilyl)oxy)methyl)acrylaldehyde



Followed previous literature procedure[13] on 1 mmol scale

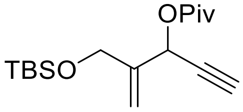
Characterization matched previously reported data[13]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.61 (s, 1H), 6.52 (td, *J* = 2.1, 1.2 Hz, 1H), 6.10 (td, *J* = 2.0, 1.1 Hz, 1H), 4.40 (d, *J* = 0.9 Hz, 2H), 0.92 (s, 9H), 0.08 (s, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 149.5, 132.6, 59.5, 25.8, 18.3, -5.6.

Isolated: Carried forward with no further purification, can be purified if needed, 15% EtOAc/Hex appears as a yellow oil (162 mg, 81%)

Synthesis of 2-(((tert-butyldimethylsilyl)oxy)methyl)pent-1-en-4-yn-3-yl pivalate (7k)



7k

Synthesized by General Procedure 1 on 7.9 mmol scale

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (s, 1H), 5.44 (t, *J* = 1.4 Hz, 1H), 5.35 (s, 1H), 4.34 – 4.17 (m, 2H), 2.51 (d, *J* = 2.3 Hz, 1H), 1.23 (s, 9H), 0.91 (s, 9H), 0.07 (s, 6H)

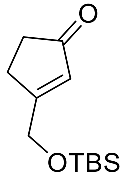
^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 143.4, 113.4, 79.3, 74.6, 63.6, 62.5, 38.8, 27.0, 25.9, 18.3, -5.5

IR ($CDCl_3$, ν) 426.28, 439.78, 478.36, 543.94, 669.32, 777.34, 839.06, 1089.82, 1118.75, 1141.9, 1257.63, 1473.66, 1739.85, 2360.95, 2931.9, 2958.9, 3313.82 cm^{-1}

HRMS (DART) calculated for $C_{17}H_{31}O_3Si$ [M+H] 311.20425, measured 311.20467

Isolated: Kugelrohr distillation appeared as a milky oil (1.75 g, 75%)

Synthesis of 3-(((tert-butyldimethylsilyl)oxy)methyl)cyclopent-2-en-1-one (8k)



8k

Synthesized with General Procedure 4 using **7k** (78 mg, 0.25 mmol), PPh_3AuNTf_2 (5 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M). Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 20% EtOAc/Hex as a yellow oil (34 mg, 60%).

Characterization matched previously reported data[19]

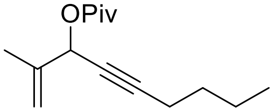
^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.16 (t, *J* = 1.7 Hz, 1H), 4.45 (s, 2H), 2.58 – 2.51 (m, 2H), 2.46 – 2.41 (m, 2H), 0.91 (s, 9H), 0.08 (s, 6H).

^{13}C NMR (100 MHz, cdcl$_3$) δ 209.2, 181.4, 128.3, 63.2, 35.0, 27.8, 25.7, 18.2, -5.5.

HRMS (DART) calculated for $C_{12}H_{23}O_2Si$ [M+H] 227.14673, measured 227.14615

3.12 Synthesis of **7l** and **8l**

Synthesis of 2-methylnon-1-en-4-yn-3-yl pivalate (7l)



7l

Synthesized by general method 3 on a 6 mmol scale.

^{1}H NMR (399 MHz, Chloroform-*d*) δ 5.77 (s, 1H), 5.19 (q, *J* = 1.1 Hz, 1H), 4.95 (td, *J* = 1.6, 0.8 Hz, 1H), 2.22 (td, *J* = 7.0, 2.1 Hz, 2H), 1.81 (s, 3H), 1.53 – 1.44 (m, 2H), 1.43 – 1.34 (m, 2H), 1.22 (s, 9H), 0.90 (t, *J* = 7.2 Hz, 3H).

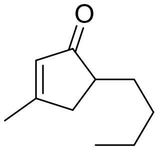
^{13}C NMR (100 MHz, cdcl$_3$) δ 177.1, 141.2, 113.8, 87.0, 76.1, 67.3, 38.8, 30.5, 27.0, 21.8, 18.4, 18.3, 13.5.

IR (CDCl$_3$, *ν*) 422, 912, 934, 982, 1032, 1142, 1275, 156, 1479, 1736, 2874, 2934, 2961

HRMS (DART) calculated for $C_{15}H_{28}NO_2$ [M+NH$_4$] 254.21200, measured 254.21214

Isolated: 20% -> 40% DCM/Hex as a clear oil (900 mg, 63%)

Synthesis of 5-butyl-3-methylcyclopent-2-en-1-one (8l)



8l

Synthesized with General Procedure 4 using **7l** (59 mg, 0.25 mmol), PPh_3AuNTf_2 (1 mol%), AcOH (30 µL, 2.0 equiv), in anhydrous dichloromethane (4.0 mL, 0.0625 M) for 90 min. Crude was quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 20% EtOAc/Hex as a clear oil (28 mg, 74%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.83 (q, *J* = 1.5 Hz, 1H), 2.67 (ddd, *J* = 18.5, 6.7, 0.9 Hz, 1H), 2.31 (s, 0H), 2.18 (d, *J* = 18.5 Hz, 1H), 2.05 (s, 2H), 1.81 – 1.65 (m, 1H), 1.36 – 1.18 (m, 5H), 0.87 – 0.79 (m, 3H).

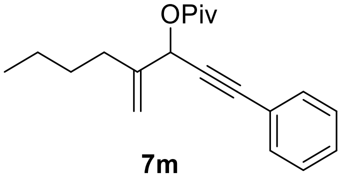
^{13}C NMR (101 MHz, $CDCl_3$) δ 212.34, 177.29, 130.00, 46.76, 39.85, 31.14, 29.49, 22.70, 19.43, 13.99.

IR ($CDCl_3$, ν) 444, 667, 1179, 1431, 1626, 1699, 2342, 2359, 2859, 2930, 2957

HRMS (DART) calculated for $C_{10}H_{17}O_1$ [M+H] 153.12794 measured 153.12825

3.13 Synthesis of **7m** and **8m**

Synthesis of 4-methylene-1-phenyloct-1-yn-3-yl pivalate (7m)



7m

Synthesized with General Procedure 3 on 3.2 mmol scale

^{1}H NMR (399 MHz, $CDCl_3$) δ 7.46 – 7.42 (m, 2H), 7.34 – 7.28 (m, 3H), 6.07 (s, 1H), 5.36 (s, 1H), 5.05 (s, 1H), 2.22 (m, 2H), 1.56 – 1.49 (m, 2H), 1.38 (m, 2H), 1.25 (s, 9H), 0.93 (t, *J* = 7.3 Hz, 3H).

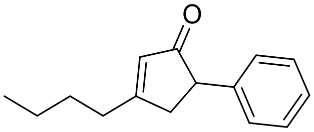
^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 144.8, 131.8, 128.6, 128.2, 122.4, 113.4, 85.9, 85.3, 66.8, 38.9, 31.8, 29.8, 27.1, 22.4, 13.9.

IR ($CDCl_3$, ν) 691, 756, 918, 975, 1032, 1140, 1366, 1397, 1444, 1460, 1479, 1491, 1735, 2871, 2933, 2960

HRMS (DART) calculated for $C_{20}H_{30}NO_2$ [M+NH4] 316.22711, measured 316.22765

Isolated: 10% -> 40% DCM/Hex as a clear oil (553 mg, 58%)

Synthesis of 3-butyl-5-phenylcyclopent-2-en-1-one (8m)



8m

Synthesized with General Procedure 5 using **7m** (75 mg, 0.25 mmol) and PPh_3AuNTf_2 (1 mol%) in anhydrous dichloromethane (4.0 mL, 0.0625 M). When complete, added dry HCl then quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a yellow oil (42 mg, 78%).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 7.31 (t, *J* = 7.3 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 6.9 Hz, 1H), 6.03 (s, 1H), 3.61 (dd, *J* = 7.2, 2.8 Hz, 1H), 3.12 (dd, *J* = 18.7, 7.2 Hz, 1H), 2.69 (d, *J* = 18.7, 1H), 2.49 (t, *J* = 7.4 Hz, 2H), 1.69 – 1.57 (m, 2H), 1.42 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

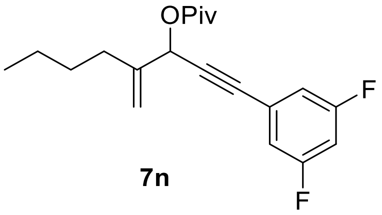
^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 182.3, 139.9, 128.8, 128.5, 127.5, 126.8, 52.2, 41.3, 33.2, 29.2, 22.5, 13.8

IR ($CDCl_3$, ν) 700, 753, 847, 919, 1033, 1076, 1170, 1235, 1278, 1337, 1380, 1431, 1454, 1496, 1616, 1699, 2868, 2930, 2957, 3029

HRMS (DART) calculated for $C_{15}H_{19}O$ [M+H] 215.14359, measured 215.14338

3.14 Synthesis of **7n** and **8n**

Synthesis of 1-(3,5-difluorophenyl)-4-methyleneoct-1-yn-3-yl pivalate (7n)



7n

Synthesized with General Procedure 3 on 0.8 mmol scale

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 – 6.90 (m, 2H), 6.79 (m, *J* = 8.9, 2.4 Hz, 1H), 6.03 (s, 1H), 5.34 (s, 1H), 5.06 (s, 1H), 2.20 (t, *J* = 7.6 Hz, 2H), 1.57 – 1.46 (m, 2H), 1.37 (ddd, *J* = 8.7, 7.6, 6.9 Hz, 2H), 1.25 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H).

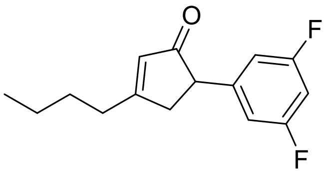
^{13}C NMR (100 MHz, Chloroform-*d*) δ 177.0, 162.6 (dd, *J* = 249.5, 12.8 Hz), 144.3, 125.0, 114.7 (dd, *J* = 19, 7.4 Hz), 113.7, 104.8 (t, *J* = 25.2 Hz), 87.4, 83.7, 66.4, 38.9, 31.8, 29.8, 27.0, 22.4, 13.9.

IR ($CDCl_3$, *ν*) 672, 859, 991, 1052, 1124, 1139, 1276, 1431, 1458, 1588, 1618, 1738, 2872, 2931, 2960

HRMS (DART) calculated for $C_{20}H_{28}F_2NO_2$ [M+NH$_4$] 352.20826, measured 352.20906

Isolated: 20% DCM/Hex as a clear oil (192 mg, 71%)

Synthesis of 3-butyl-5-(3,5-difluorophenyl)cyclopent-2-en-1-one (8n)



8n

Synthesized with General Procedure 5 using **7n** (84 mg, 0.25 mmol) and PPh_3AuNTf_2 (1 mol%) in anhydrous dichloromethane (4.0 mL, 0.0625 M). When complete, added dry HCl then quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 5% -> 20% EtOAc/Hex as a clear oil (48 mg, 76%).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 6.72 – 6.64 (m, 3H), 6.02 (s, 1H), 3.58 (dd, *J* = 7.3, 2.9 Hz, 1H), 3.12 (dd, *J* = 19.6, 7.3 Hz, 1H), 2.65 (d, *J* = 18.7 Hz, 1H), 2.48 (t, *J* = 7.6 Hz, 2H), 1.62 (m, 2H), 1.42 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H)

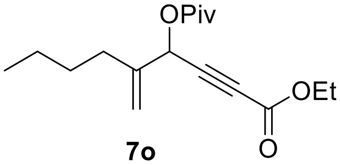
^{13}C NMR (100 MHz, Chloroform-*d*) δ 207.2, 182.3, 163.2 (dd, *J* = 248.7, 13.1 Hz), 143.3 (t, *J* = 9.2 Hz), 128.3, 110.6 (dd, *J* = 18.6, 6.8 Hz), 102.4 (t, *J* = 25.2 Hz), 51.6, 40.7, 33.2, 29.1, 22.5, 13.8.

IR ($CDCl_3$, *ν*) 685, 750, 853, 983, 1000, 1118, 1171, 1235, 1290, 1333, 1381, 1432, 1459, 1595, 1621, 1703, 2870, 2933, 2959

HRMS (DART) calculated for $C_{15}H_{17}F_2O$ [M+H] 251.12475, measured 251.12449

3.15 Synthesis of **7o** and **8o**

Synthesis of ethyl 5-methylene-4-(pivaloyloxy)non-2-ynoate (7o)



7o

Synthesized with General Procedure 3 on 4.9 mmol scale

^{1}H NMR (399 MHz, Chloroform-*d*) δ 5.92 (s, 1H), 5.30 (s, 1H), 5.06 (s, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.15 (t, *J* = 7.6 Hz, 2H), 1.54 – 1.41 (m, 2H), 1.41 – 1.33 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.23 (s, 9H), 0.91 (t, *J* = 7.3 Hz, 3H).

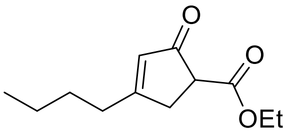
^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 153.0, 143.1, 114.6, 82.6, 65.5, 62.2, 38.9, 31.7, 29.6, 27.0, 22.3, 14.0, 13.9.

IR ($CDCl_3$, *ν*) 751, 767, 916, 1014, 1031, 1133, 1247, 1367, 1397, 1463, 1480, 1717, 1740, 2245, 2863, 2872, 2935

HRMS (DART) calculated for $C_{17}H_{30}NO_4$ [M+NH_4] 312.21693, measured 312.21748

Isolated: 50% -> 75% DCM/Hex as a yellow oil (608 mg, 46%)

Synthesis of ethyl 4-butyl-2-oxocyclopent-3-ene-1-carboxylate (8o)



8o

Synthesized with General Procedure 5 using **7o** (74 mg, 0.25 mmol) and PPh_3AuNTf_2 (1 mol%) in anhydrous dichloromethane (4.0 mL, 0.0625 M). When complete, added dry HCl then quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% -> 20% EtOAc/Hex of a slightly yellow oil (42 mg, 80%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.88 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.42 (dd, *J* = 7.1, 2.8 Hz, 1H), 2.97 (d, *J* = 18.4 Hz, 1H), 2.75 (dd, *J* = 18.4, 7.1 Hz, 1H), 2.44 (t, *J* = 7.7Hz, 2H), 1.58 (p, *J* = 7.5 Hz, 2H), 1.38 (sextet, *J* = 7.3 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H).

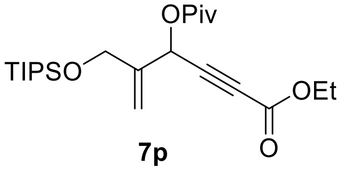
^{13}C NMR (100 MHz, Chloroform-*d*) δ 202.2, 183.2, 169.1, 127.4, 61.6, 52.3, 35.5, 33.1, 29.0, 22.4, 14.2, 13.7.

IR ($CDCl_3$, *ν*) 850, 1023, 1098, 1150, 1203, 1250, 1323, 1369, 1466, 1618, 1706, 1736, 2871, 2933, 2959

HRMS (DART) calculated for $C_{12}H_{19}O_3$ [M+H] 211.13287, measured 211.13342

3.16 Synthesis of **7p** and **8p**

Synthesis of ethyl 4-(pivaloyloxy)-5-(((triisopropylsilyl)oxy)methyl)hex-5-en-2-ynoate (7p)



7p

Synthesized using General Procedure 3 on 1.65 mmol

^{1}H NMR (399 MHz, Chloroform-*d*) δ 6.05 (s, 1H), 5.46 – 5.42 (m, 2H), 4.36 (d, *J* = 14.5 Hz, 1H), 4.28 (d, *J* = 14.4 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.22 (s, 9H), 1.18 – 1.03 (m, 21H).

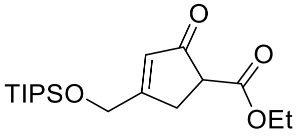
^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 152.9, 142.4, 114.2, 82.1, 77.7, 63.1, 62.7, 62.2, 38.8, 27.0, 17.9, 14.0, 11.9.

IR ($CDCl_3$, ν) 684, 751, 811, 883, 992, 1019, 1130, 1248, 1367, 1394, 1465, 1719, 1744, 2245, 2868, 2949

HRMS (DART) calculated for $C_{23}H_{41}O_5Si$ [M+H] 425.27233, measured 425.27209

Isolated: 50% -> 80% DCM/Hex as a yellow oil (413 mg, 59%)

Synthesis of ethyl 2-oxo-4-(((triisopropylsilyl)oxy)methyl)cyclopent-3-ene-1-carboxylate (8p)



8p

Synthesized with General Procedure 5 using **7p** (106 mg, 0.25 mmol) and PPh_3AuNTf_2 (1 mol%) in anhydrous dichloromethane (4.0 mL, 0.0625 M). When complete, added dry HCl then quenched with 1M NH_4OH and extracted with dichloromethane (3 x 4 mL). Product was purified using column chromatography in 10% EtOAc/Hex as a clear oil (64 mg, 75%).

^{1}H NMR (399 MHz, Chloroform-*d*) δ 6.17 (s, 1H), 4.62 (d, *J* = 18.5 Hz, 1H), 4.55 (d, *J* = 18.2 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.46 (dd, *J* = 7.2, 2.8 Hz, 1H), 2.95 (d, *J* = 19.4 Hz, 1H), 2.75 (dd, *J* = 18.4, 7.2 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.11 – 1.00 (m, 21H).

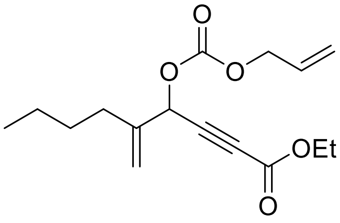
^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 181.7, 168.9, 126.3, 63.5, 61.7, 52.0, 31.9, 17.9, 14.1, 11.9.

IR ($CDCl_3$, *ν*) 684, 793, 837, 883, 1015, 1069, 1094, 1139, 1203, 1253, 1313, 1369, 1465, 1629, 1709, 1737, 2867, 2945

HRMS (DART) calculated for $C_{18}H_{33}O_4Si$ [M+H] 341.21426, measured 341.21468

3.17 Synthesis of **21a** and **22a**

Synthesis of ethyl 4-(((allyloxy)carbonyl)oxy)-5-methylenenon-2-ynoate (21a)



21a

Followed General Procedure 6 on 7.5 mmol scale

^{1}H NMR (399 MHz, Chloroform-*d*) δ 5.93 (ddt, *J* = 17.2, 10.4, 5.8 Hz, 1H), 5.79 (s, 1H), 5.40 – 5.34 (m, 2H), 5.31 – 5.27 (m, 1H), 5.10 (s, 1H), 4.66 (dt, *J* = 5.8, 1.4 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.20 – 2.14 (m, 2H), 1.52 – 1.44 (m, 2H), 1.40 – 1.33 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H).

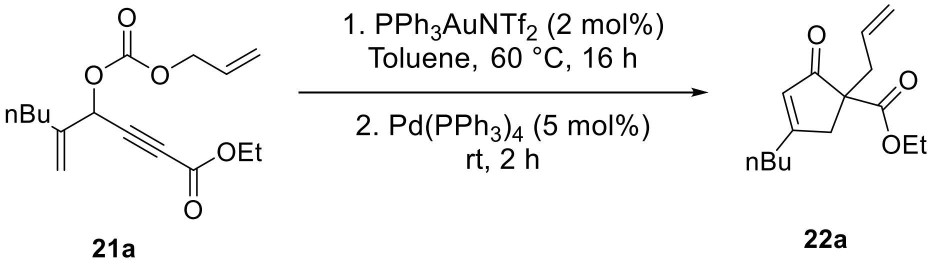
^{13}C NMR (100 MHz, cdcl$_3$) δ 153.8, 152.8, 142.4, 131.1, 131.1, 119.3, 115.5, 81.6, 78.5, 69.8, 69.1, 62.3, 31.4, 29.5, 22.3, 13.9, 13.9.

IR (CDCl$_3$, ν) 750.33, 786.98, 918.15, 937.44, 974.08, 1014.59, 1080.17, 1095.6, 1234.48, 1367.58, 1448.59, 1465.95, 1716.7, 1755.28, 2245.22, 2933.83, 2958.9

HRMS (DART) calculated for $C_{16}H_{26}NO_5$ [M+NH$_4$] 312.18055, measured 312.18098

Isolated: 30% -> 50% DCM/Hex as a yellow oil (778 mg, 35% over two steps)

Racemic Two-Step One-Pot Synthesis of ethyl 1-allyl-4-butyl-2-oxocyclopent-3-ene-1-carboxylate (22a)



To a dried 2 dr vial added PPh_3AuNTf_2 (3.7 mg, 2 mol%) and dissolved in 1 mL of toluene. Added **21a** (74 mg, 0.25 mmol) in 1 mL toluene. Capped vial with Teflon cap and stirred at 60 °C for 16 h. Reaction does work at rt, but it is very slow. The enol ester intermediate can be purified on a column with 40 -> 60% DCM/Hex with 1% TEA. After consumption of SM monitored by TLC, added $Pd(PPh_3)_4$ (14 mg, 5 mol%) and stirred under argon for 2 h at rt. Put reaction crude directly on column and purified with 5% EtOAc/Hex to get product as a yellow oil (45 mg 73%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.82 (s, 1H), 5.61 – 5.49 (m, 1H), 5.04 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.02 – 4.97 (m, 1H), 4.09 (qd, *J* = 7.1, 2.8 Hz, 2H), 3.01 (dd, *J* = 18.5, 1.0 Hz, 1H), 2.65 (dd, *J* = 13.9, 7.6 Hz, 1H), 2.49 – 2.41 (m, 2H), 2.37 (t, *J* = 7.6 Hz, 2H), 1.56 – 1.46 (m, 2H), 1.31 (m, 2H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H).

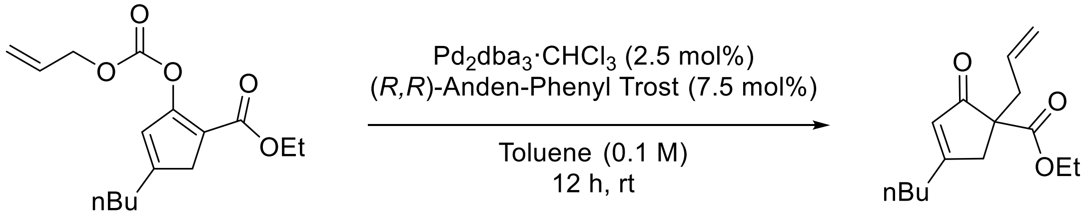
^{13}C NMR (101 MHz, $CDCl_3$) δ 204.7, 182.7, 170.6, 132.9, 127.0, 119.0, 61.6, 58.7, 40.9, 38.6, 33.0, 29.0, 22.3, 14.1, 13.8.

IR ($CDCl_3$, *ν*) 856.42, 920.08, 997.23, 1020.38, 1053.17, 1097.53, 1147.68, 1184.33, 1242.2, 1282.71, 1338.64, 1365.65, 1425.44, 1620.26, 1641.48, 1705.13, 1741.78, 2933.83, 2958.9

HRMS (DART) calculated for $C_{15}H_{22}O_3$ [M+H] 251.16472 measured 251.16445

3.17.1 Enantioselective Synthesis of 22a

Enantioselective Synthesis of ethyl 1-allyl-4-butyl-2-oxocyclopent-3-ene-1-carboxylate (22a)

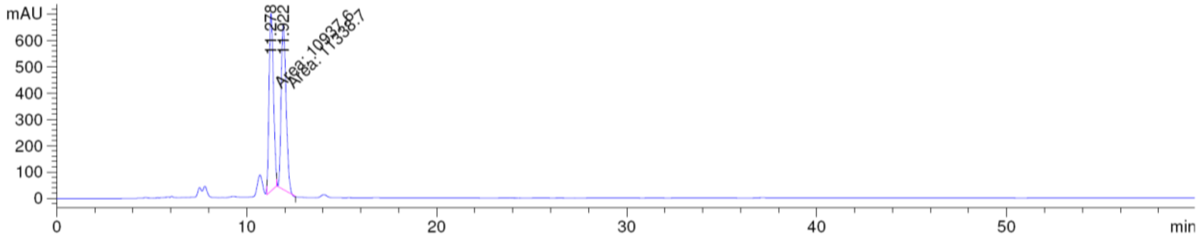


22a

To a dried 2 dr vial added $Pd_2dba_3 \cdot CHCl_3$ (6.1 mg, 2.5 mol%) and (*R,R*)-Anden-Phenyl Trost (6.1 mg, 7.5 mol%). Added 0.5 mL of anhydrous toluene and premixed for 30 min. Added the enol carbonate (29 mg, 0.1 mmol) in 0.5 mL of anhydrous toluene dropwise. Stirred for 12 h at rt. Filtered through silica pad with 10% EtOAc/Hex. Concentrated the filtrate under reduced pressure. 59% yield measured by NMR with 1,3,5-trimethoxybenzene in internal standard.

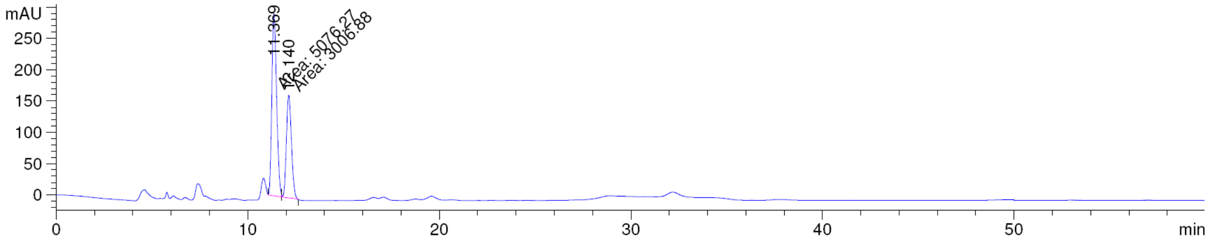
Chiral HPLC: OD-H column, 1 mL/min, 1% IPA/Hex, 26% ee

Racemic Sample



```
Signal 2: DAD1 B, Sig=220,2 Ref=360,40

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.278 MM    0.2699 1.09376e4  675.44434  49.0997
   2  11.922 MM    0.3006 1.13387e4  628.73041  50.9003

Totals :                  2.22763e4 1304.17474
```

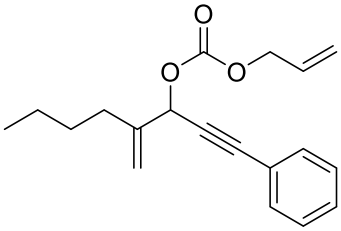
Chiral Sample



```
Signal 2: DAD1 B, Sig=220,2 Ref=360,40

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  11.369 MM    0.2905 5076.26904  291.28693  62.8006
   2  12.140 MM    0.3053 3006.88354  164.16991  37.1994

Totals :                  8083.15259  455.45683
```

3.18 Synthesis of **21b** and **22b**

Synthesis of allyl (4-methylene-1-phenyloct-1-yn-3-yl) carbonate (21b)



21b

Followed General Procedure 6 on 5.8 mmol scale

^{1}H NMR (399 MHz, Chloroform-*d*) δ 7.48 – 7.43 (m, 2H), 7.34 – 7.27 (m, 3H), 6.01 – 5.90 (overlap, m, 1H), 5.94 (overlap, s, 1H), 5.42 – 5.35 (overlap, m, 1H), 5.40 (overlap, s, 1H), 5.28 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.09 (s, 1H), 4.68 (dt, *J* = 5.8, 1.4 Hz, 2H), 2.32 – 2.18 (m, 2H), 1.59 – 1.49 (m, 2H), 1.43 – 1.33 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

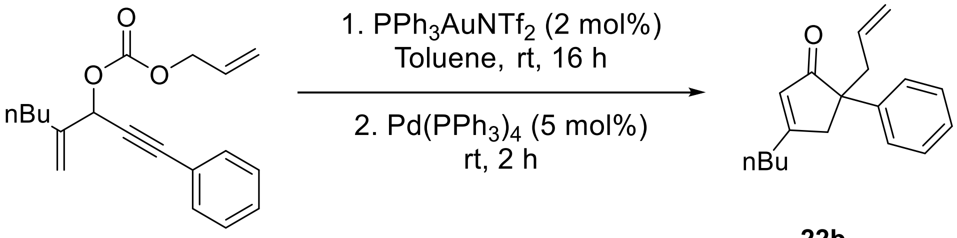
^{13}C NMR (100 MHz, cdcl$_3$) δ 154.2, 144.2, 131.9, 131.4, 128.8, 128.2, 122.1, 119.0, 114.3, 87.2, 84.3, 71.3, 68.8, 31.4, 29.8, 22.4, 13.9.

IR (CDCl$_3$, ν) 756.12, 788.91, 912.36, 931.65, 968.3, 1244.13, 1292.35, 1323.21, 1367.58, 1489.1, 1749.49, 2224, 2872.1, 2929.97, 2956.97 cm^{-1}

HRMS (DART) calculated for $C_{19}H_{26}N_1O_3$ [M+NH4] 316.19127, measured 316.19093

Isolated: 10% DCM/Hex as a yellow oil (480 mg, 28% over two steps)

Racemic Two-Step One-Pot Synthesis of 5-allyl-3-butyl-5-phenylcyclopent-2-en-1-one (22b)



21b

22b

To a dried 2 dr vial added PPh_3AuNTf_2 (3.7 mg, 2 mol%) and dissolved in 1 mL of toluene. Added **21b** (75 mg, 0.25 mmol) in 1 mL toluene. Capped vial with Teflon cap and stirred at rt for 16 h. The enol ester intermediate can be purified on a column with 20 -> 30% DCM/Hex with 1% TEA. After consumption of SM monitored by TLC, added $Pd(PPh_3)_4$ (14 mg, 5 mol%) and stirred under argon for 2 h at rt. Put reaction crude directly on column and purified with 5% EtOAc/Hex to get product as a yellow oil (45 mg, 71%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.19 (m, 4H), 7.18 – 7.09 (m, 1H), 5.89 (t, *J* = 1.6 Hz, 1H), 5.53 (dddd, *J* = 16.7, 10.1, 7.9, 6.5 Hz, 1H), 5.03 (dq, *J* = 17.0, 1.6 Hz, 1H), 5.01 – 4.93 (m, 1H), 2.83 (s, 1H), 2.64 (ddt, *J* = 13.6, 6.5, 1.4 Hz, 1H), 2.58 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.35 (t, *J* = 7.6 Hz, 2H), 1.51 (p, *J* = 7.5 Hz, 1H), 1.38 – 1.24 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H).

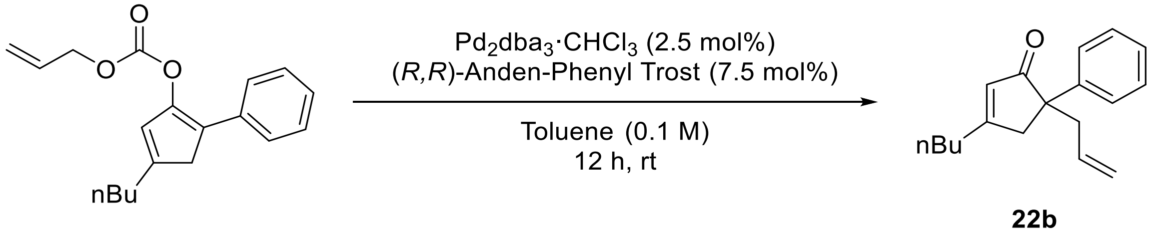
^{13}C NMR (101 MHz, $CDCl_3$) δ 210.4, 181.3, 142.8, 133.7, 128.5, 128.3, 126.6, 126.3, 118.6, 55.0, 45.6, 42.5, 33.1, 29.2, 22.5, 13.8.

IR ($CDCl_3$, *ν*) 750.33, 786.98, 918.15, 937.44, 974.08, 1014.59, 1080.17, 1095.6, 1234.48, 1367.58, 1448.59, 1465.95, 1716.7, 1755.28, 2245.22, 2933.83, 2958.9

HRMS (DART) calculated for $C_{18}H_{22}O_1$ [M+H] 255.17489, measured 255.17433

3.18.1 Enantioselective Synthesis of 22b

Enantioselective Synthesis of 5-allyl-3-butyl-5-phenylcyclopent-2-en-1-one (22b)

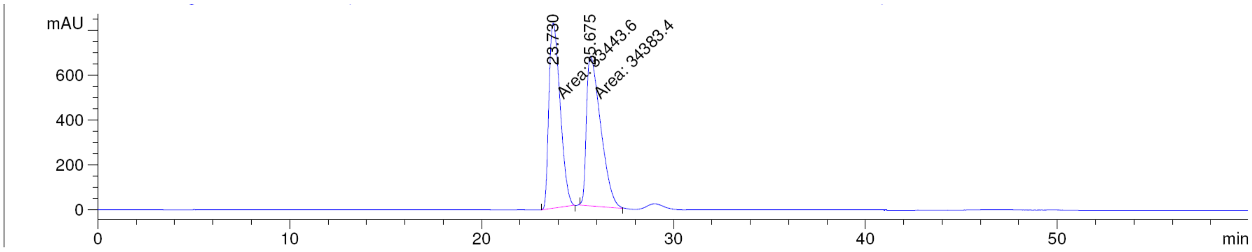


22b

To a dried 2 dr vial added $Pd_2dba_3 \cdot CHCl_3$ (6.1 mg, 2.5 mol%) and (*R*,*R*)-Anden-Phenyl Trost (6.1 mg, 7.5 mol%). Added 0.5 mL of anhydrous toluene and premixed for 30 min. Added the enol carbonate (30 mg, 0.1 mmol) in 0.5 mL of anhydrous toluene dropwise. Stirred for 12 h at rt. Filtered through silica pad with 10% EtOAc/Hex. Concentrated the filtrate under reduced pressure. 69% yield measured by NMR with 1,3,5-trimethoxybenzene in internal standard.

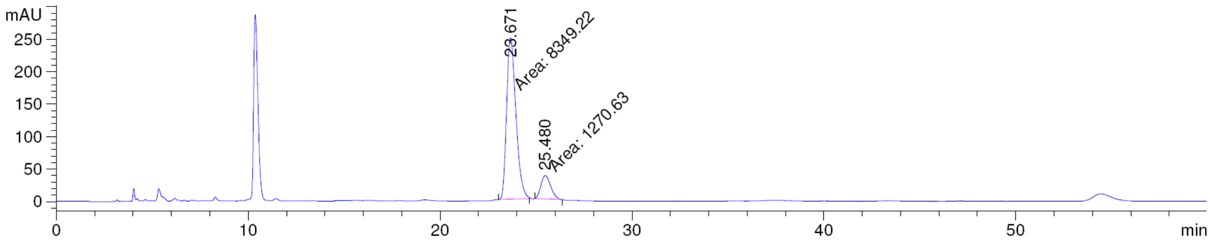
Chiral HPLC: AD-H column, 1 mL/min, 0.5% IPA/Hex, 74% ee

Racemic Sample



```
Signal 2: DAD1 B, Sig=220,2 Ref=360,40

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.730 MM    0.6764 3.34436e4   824.05969  49.3072
   2  25.675 MM    0.8604 3.43834e4   666.06671  50.6928

Totals :                  6.78271e4  1490.12640
```

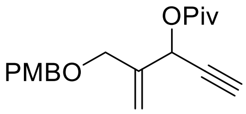
Chiral Sample

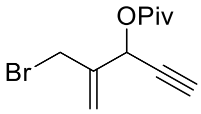


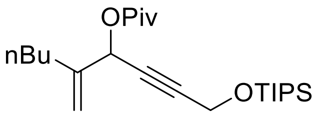
```
Signal 2: DAD1 B, Sig=220,2 Ref=360,40

Peak RetTime Type  Width     Area       Height      Area
  #    [min]        [min]    [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.671 MM    0.5604 8349.22461  248.32071  86.7916
   2  25.480 MM    0.5883 1270.63379   35.99833  13.2084

Totals :                  9619.85840  284.31904
```

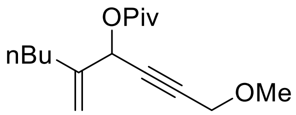
Peak at 10.4 min is 1,3,5-trimethoxybenzene from NMR.

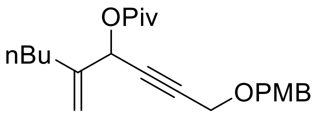
3.19 Unsuccessful Substrates in the Rautenstrauch Rearrangement











Allylic and propargyl alcohols were unsuccessful giving messy reactions. Primary bromide likely inactivated the catalyst.

4.0 References

(1) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802.

(2) Brancour, C.; Fukuyama, T.; Ohta, Y.; Ryu, I.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Chem. Commun. (Camb).* **2010**, *46*, 5470.

(3) Molnar, I. G.; Tanzer, E. M.; Daniliuc, C.; Gilmour, R. *Chem. - A Eur. J.* **2014**, *20*, 794.

(4) Ohata, K.; Terashima, S. *Chem. Pharm. Bull.* **2009**, *57*, 920.

(5) Wang, A.; Fraga, R. P. A.; Hörmann, E.; Pfaltz, A. *Chem. - An Asian J.* **2011**, *6*, 599.

(6) Zheng, S.; Zhang, J.; Shen, Z. *Adv. Synth. Catal.* **2015**, *357*, 2803.

(7) Robert, F.; Héritier, J.; Quiquerez, J.; Simian, H.; Blank, I. *J. Agric. Food Chem.* **2004**, *52*, 3525.

(8) Shing, T. K. M.; Yeung; Su, P. L. *Org. Lett.* **2006**, *8*, 3149.

(9) Ragoussis, V.; Giannikopoulos, A.; Skoka, E.; Grivas, P. *J. Agric. Food Chem.* **2007**, *55*, 5050.

(10) Li, Z.; Moser, W. H.; Deng, R.; Sun, L. *J. Org. Chem.* **2007**, *72*, 10254.

(11) Sickert, M.; Weinstabl, H.; Peters, B.; Hou, X.; Lautens, M. *Angew. Chemie Int. Ed.* **2014**, *53*, 5147

(12) Liu, J.; De Brabander, J. K. *J. Am. Chem. Soc.* **2009**, *131*, 12562.

(13) Brass, S.; Chan, N.-S.; Gerlach, C.; Luksch, T.; Böttcher, J.; Diederich, W. E. *J. Organomet. Chem.* **2006**, *691*, 5406.

(14) Bassetti, M.; D'Annibale, A.; Fanfoni, A.; Minissi, F. *Org. Lett.* **2005**, *7*, 1805.

(15) Kikushima, K.; Holder, J. C.; Gatti, M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2011**, *133*, 6902.

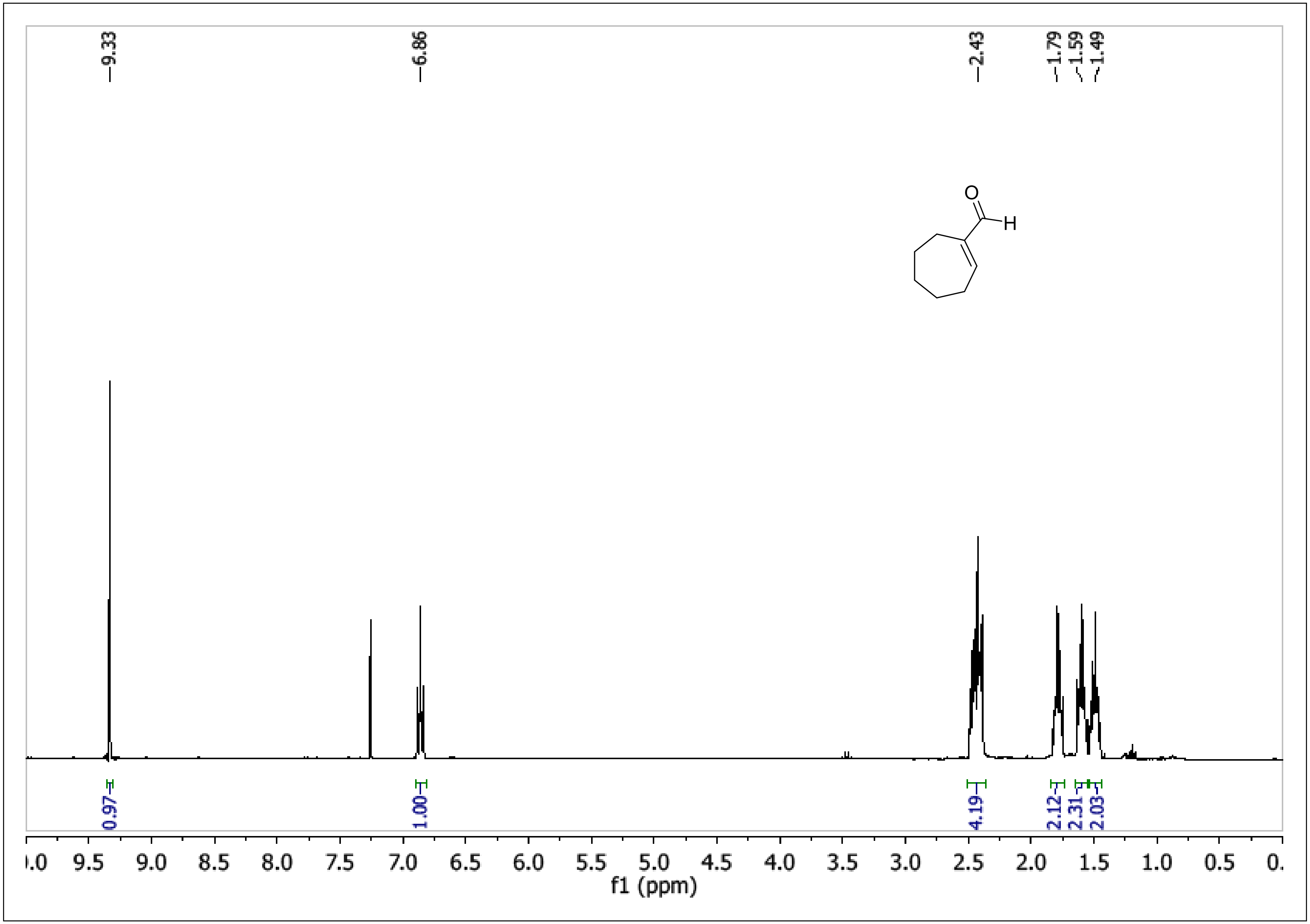
(16) Yang, F.; Feng, L.; Wang, N.; Liu, X.; Li, J.; Shen, Y. *Tetrahedron* **2013**, *69*, 9463.

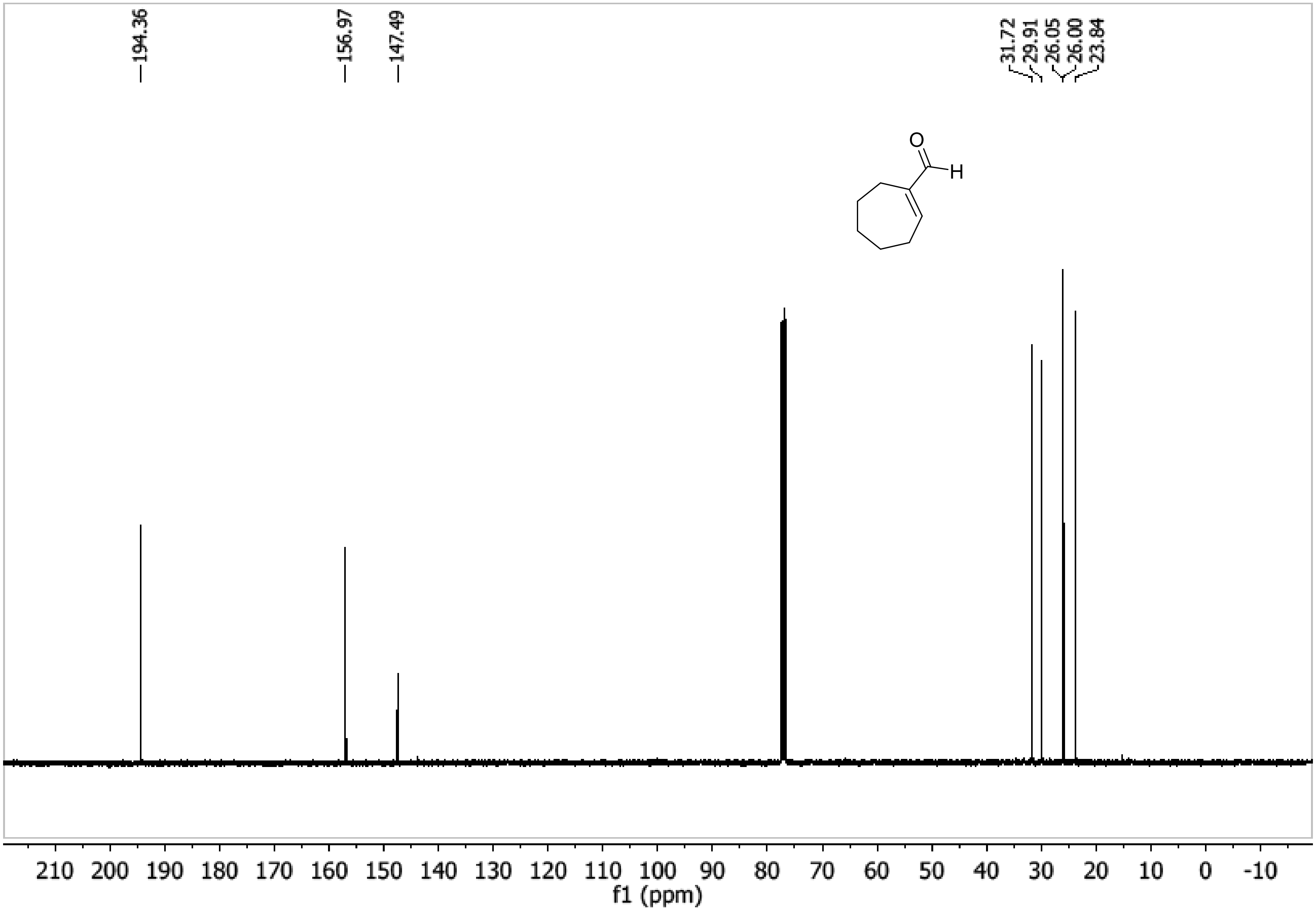
(17) Wu, Y. J.; He, H.; Bertekap, R.; Westphal, R.; Lelas, S.; Newton, A.; Wallace, T.; Taber, M.; Davis, C.; MacOr, J. E.; Bronson, J. *Bioorganic Med. Chem.* **2013**, *21*, 2217.

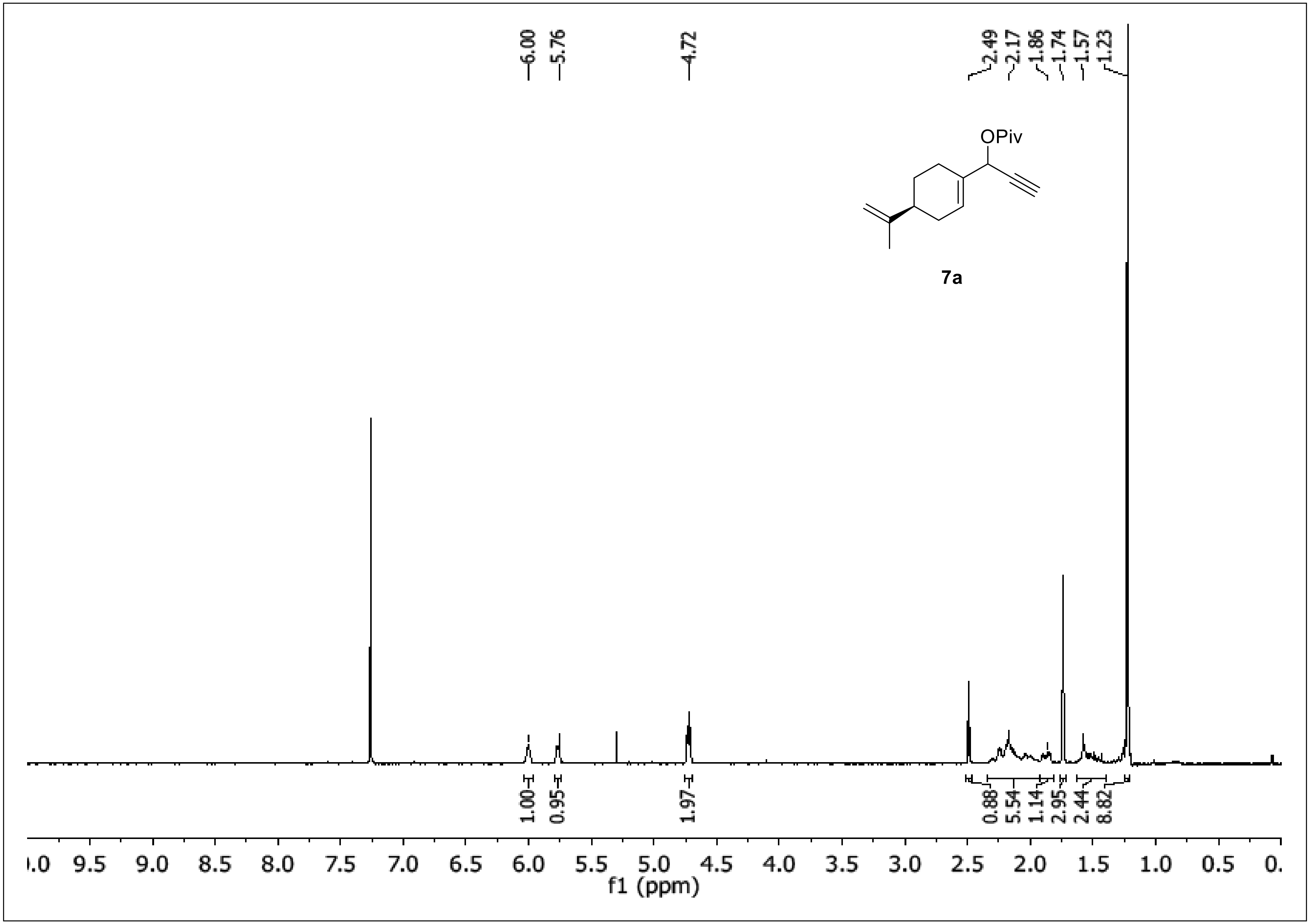
(18) Senter, T. J.; Fadeyi, O. O.; Lindsley, C. W. *Org. Lett.* **2012**, *14*, 1869.

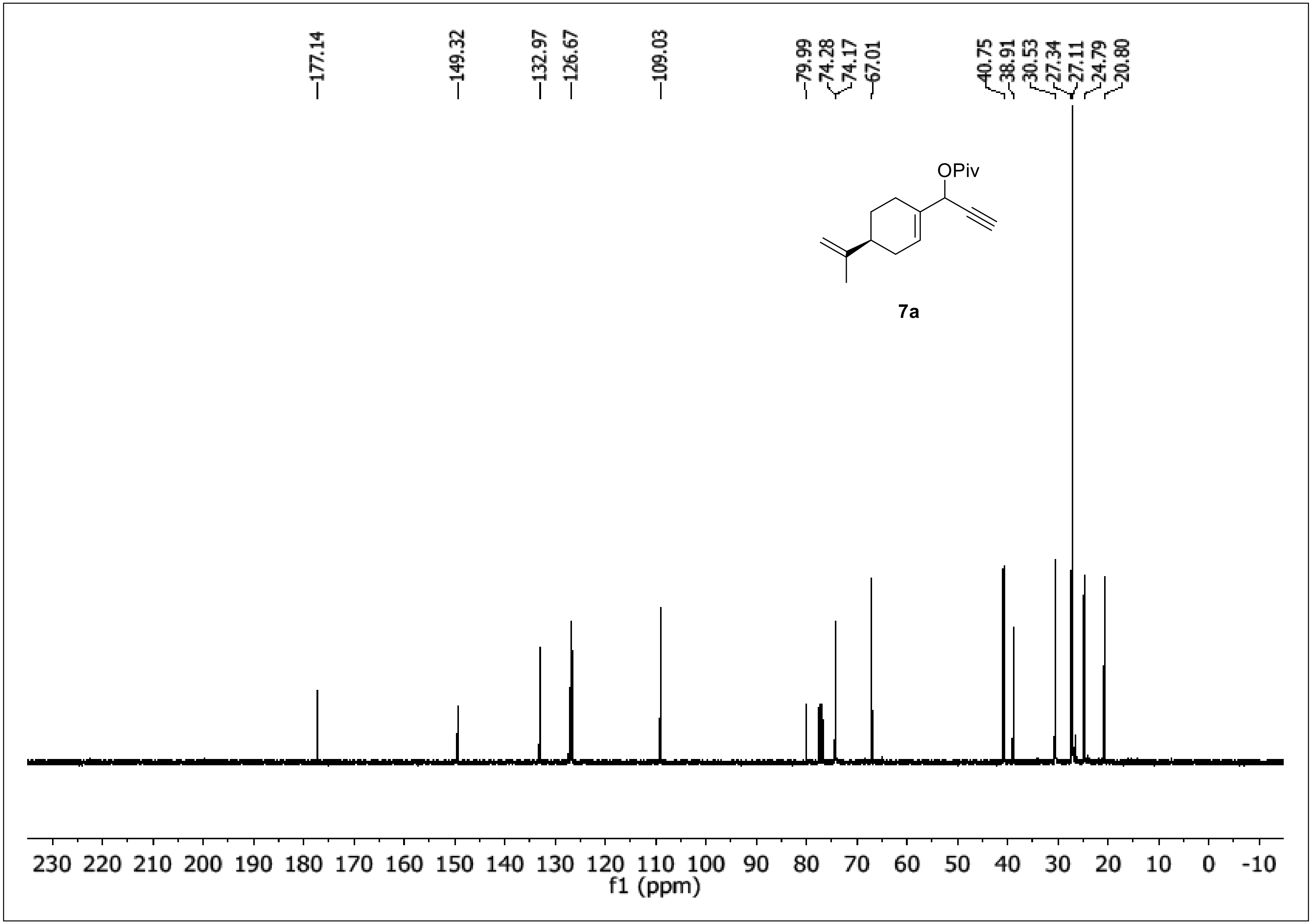
(19) Hudon, J.; Cernak, T. A.; Ashenhurst, J. A.; Gleason, J. L. *Angew. Chemie - Int. Ed.* **2008**, *47*, 8885.

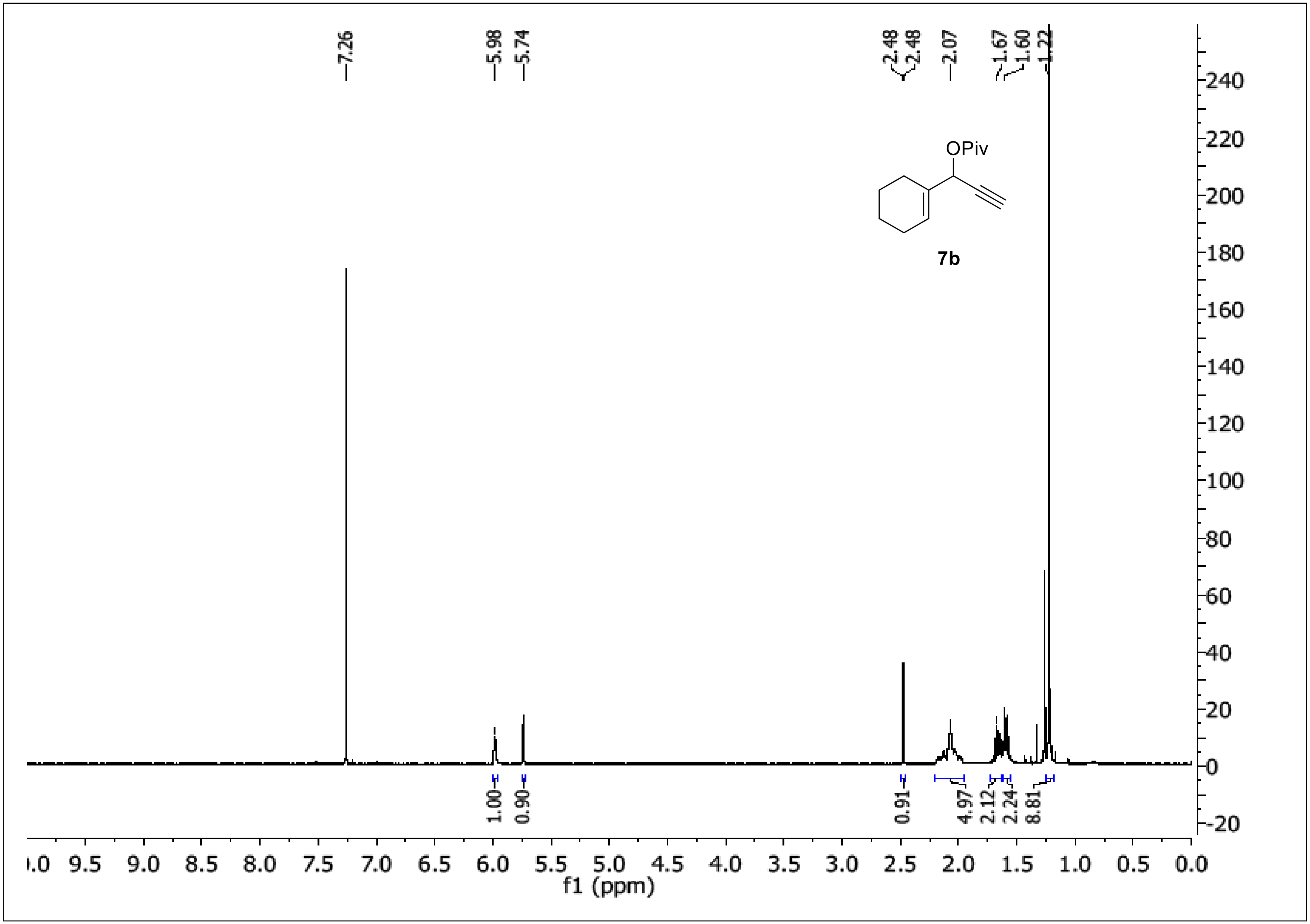
5.0 NMR Spectra


9.33
6.86
2.43
1.79
1.59
1.49
O
H
0.97
1.00
4.19
2.12
2.31
2.03
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.
f1 (ppm)

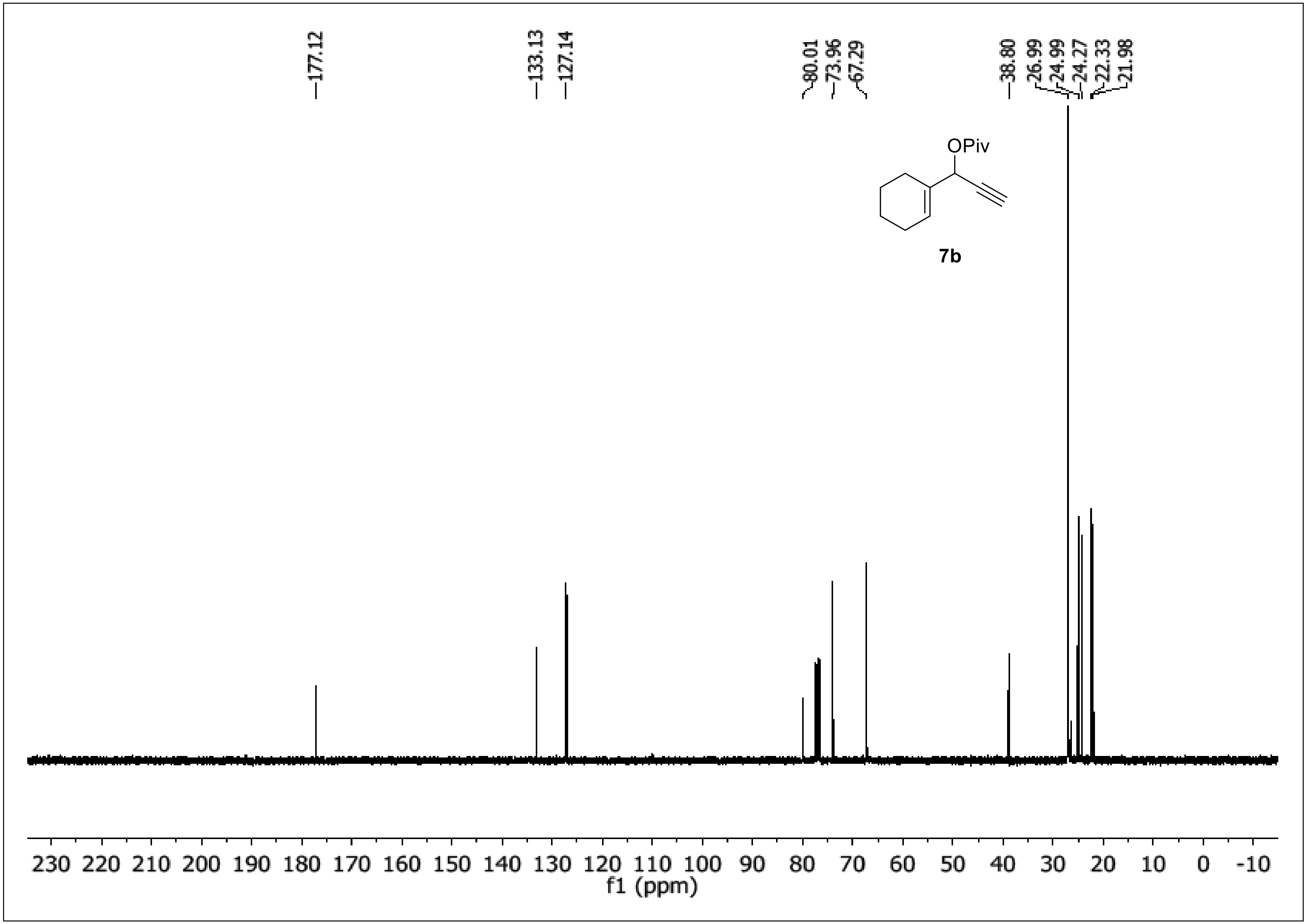

194.36
156.97
147.49
31.72
29.91
26.05
26.00
23.84
O
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

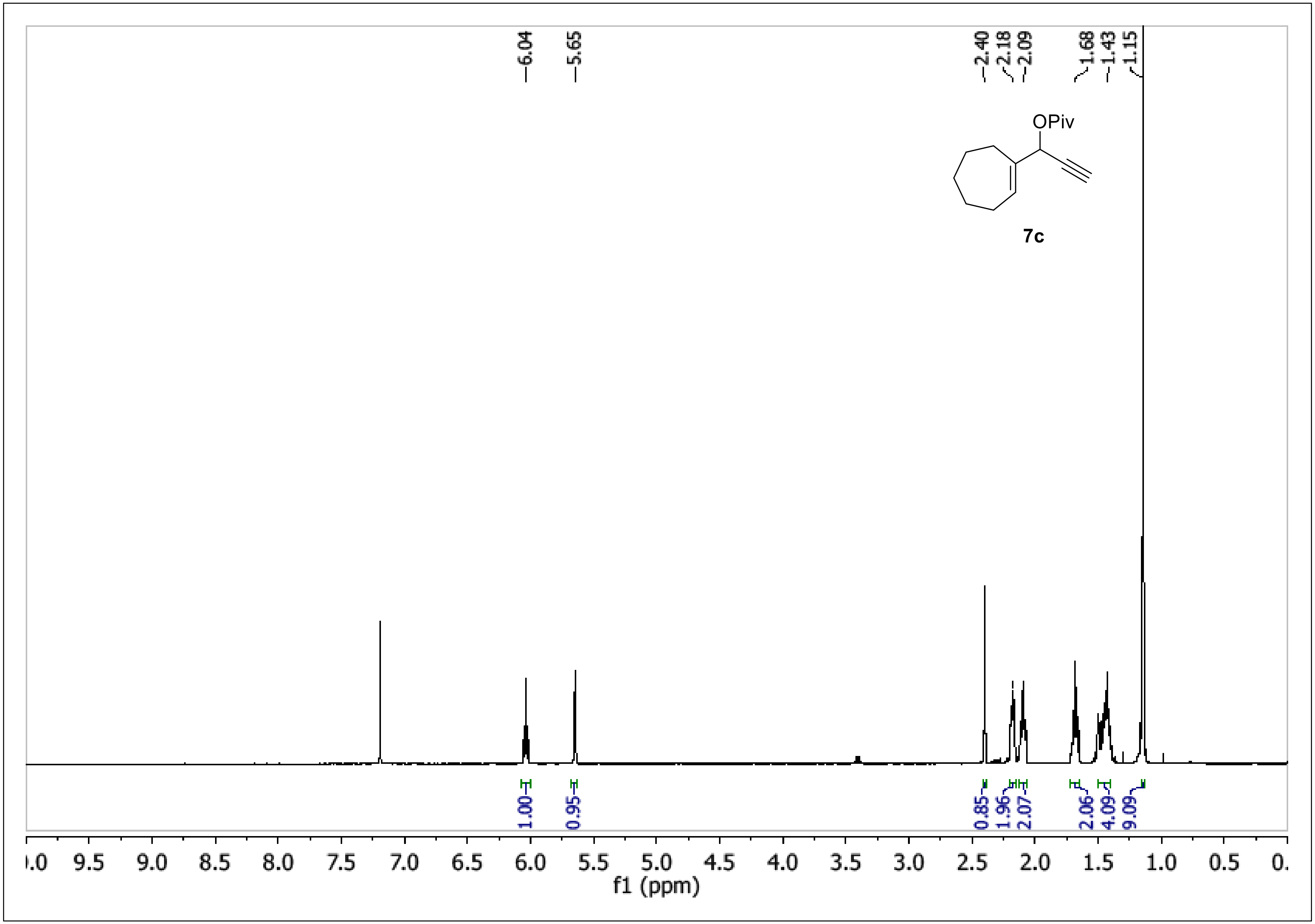

6.00
5.76
4.72
2.49
2.17
1.86
1.74
1.57
1.23
OPiv
7a
1.00
0.95
1.97
0.88
5.54
1.14
2.95
2.44
8.82
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


177.14
149.32
132.97
126.67
109.03
79.99
74.28
74.17
67.01
40.75
38.91
30.53
27.34
27.11
24.79
20.80
OPiv
7a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

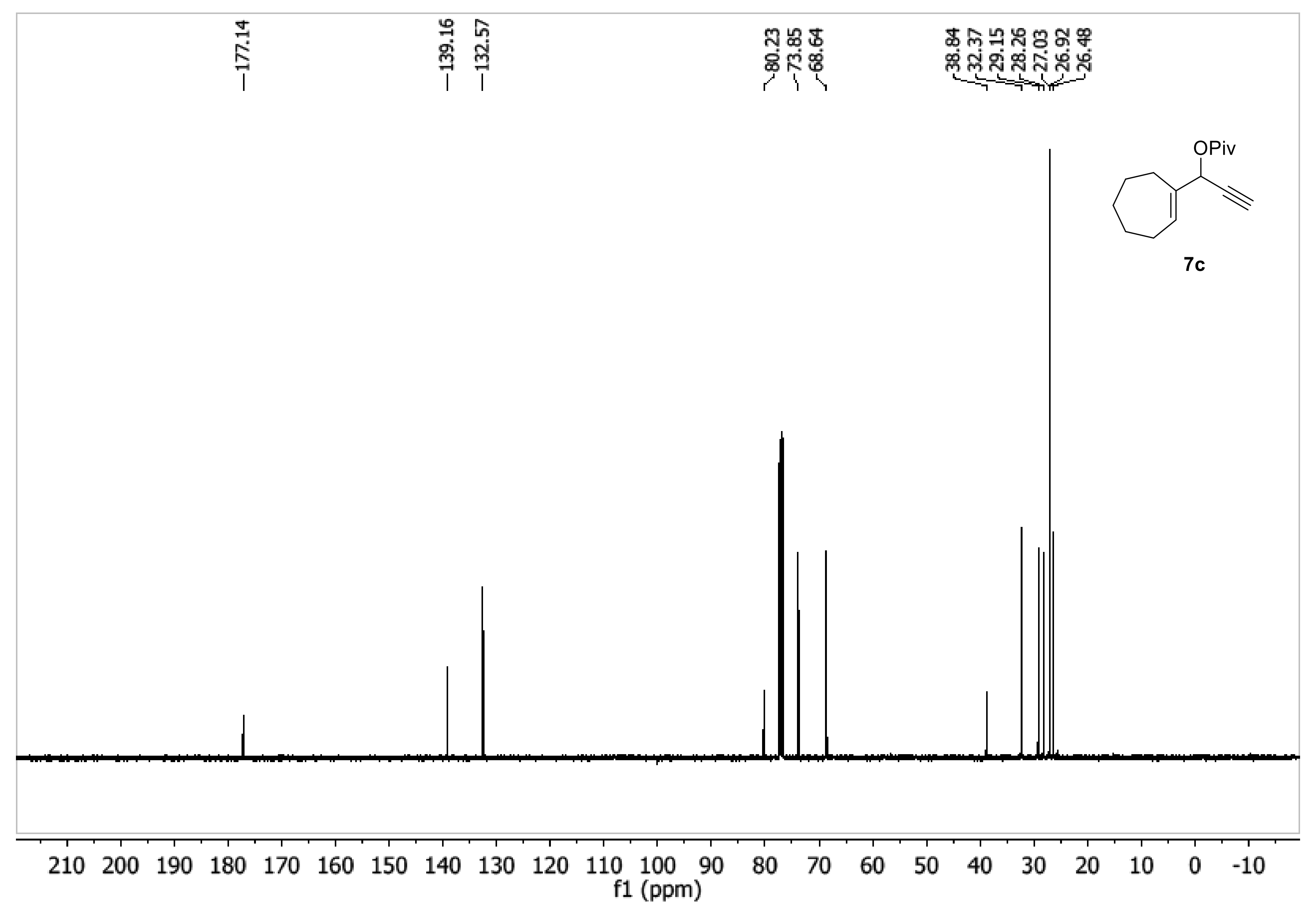


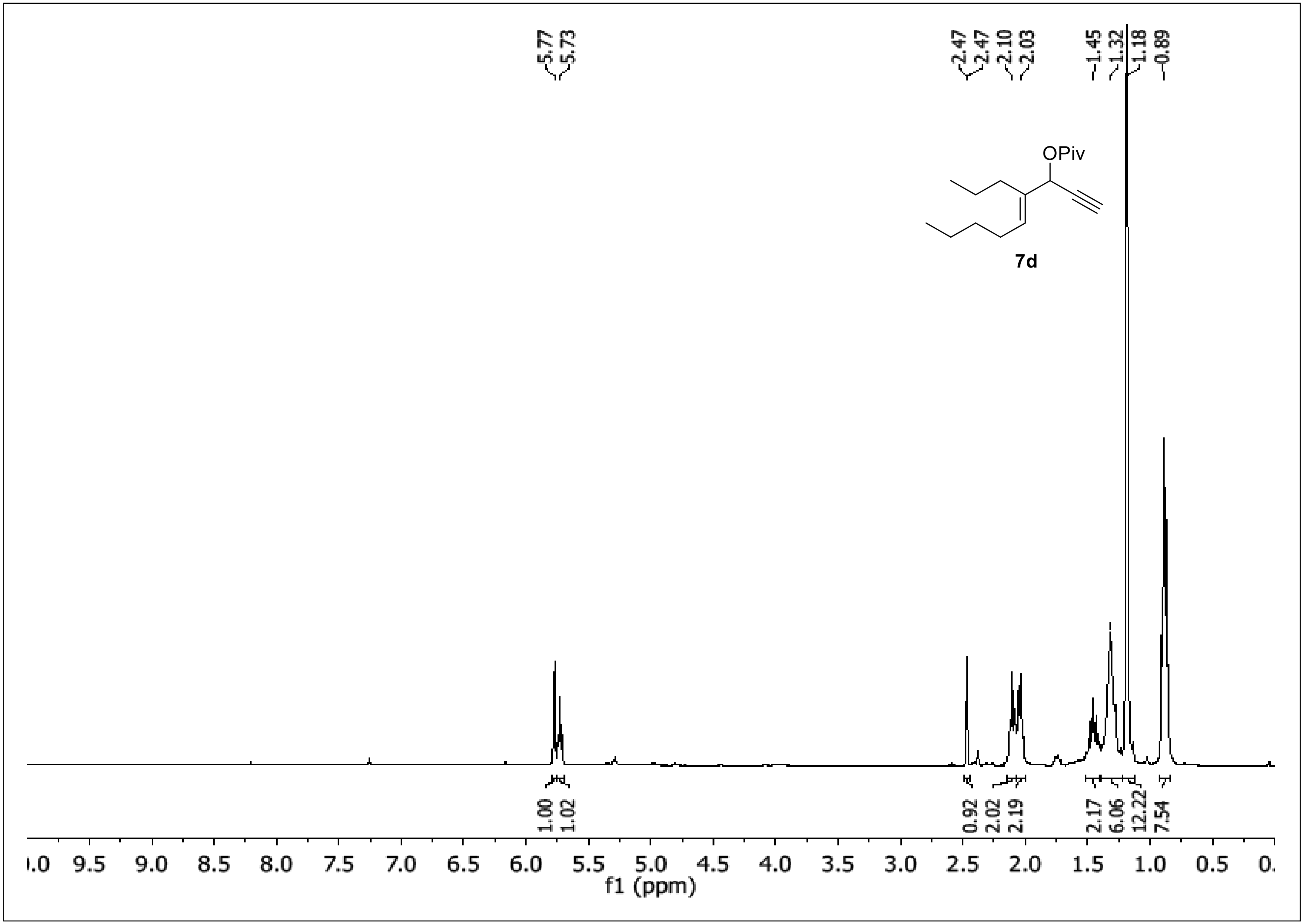
7.26
5.98
5.74
2.48
2.48
2.07
1.67
1.60
1.22
OPiv
7b
1.00
0.90
0.91
4.97
2.12
2.24
8.81
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

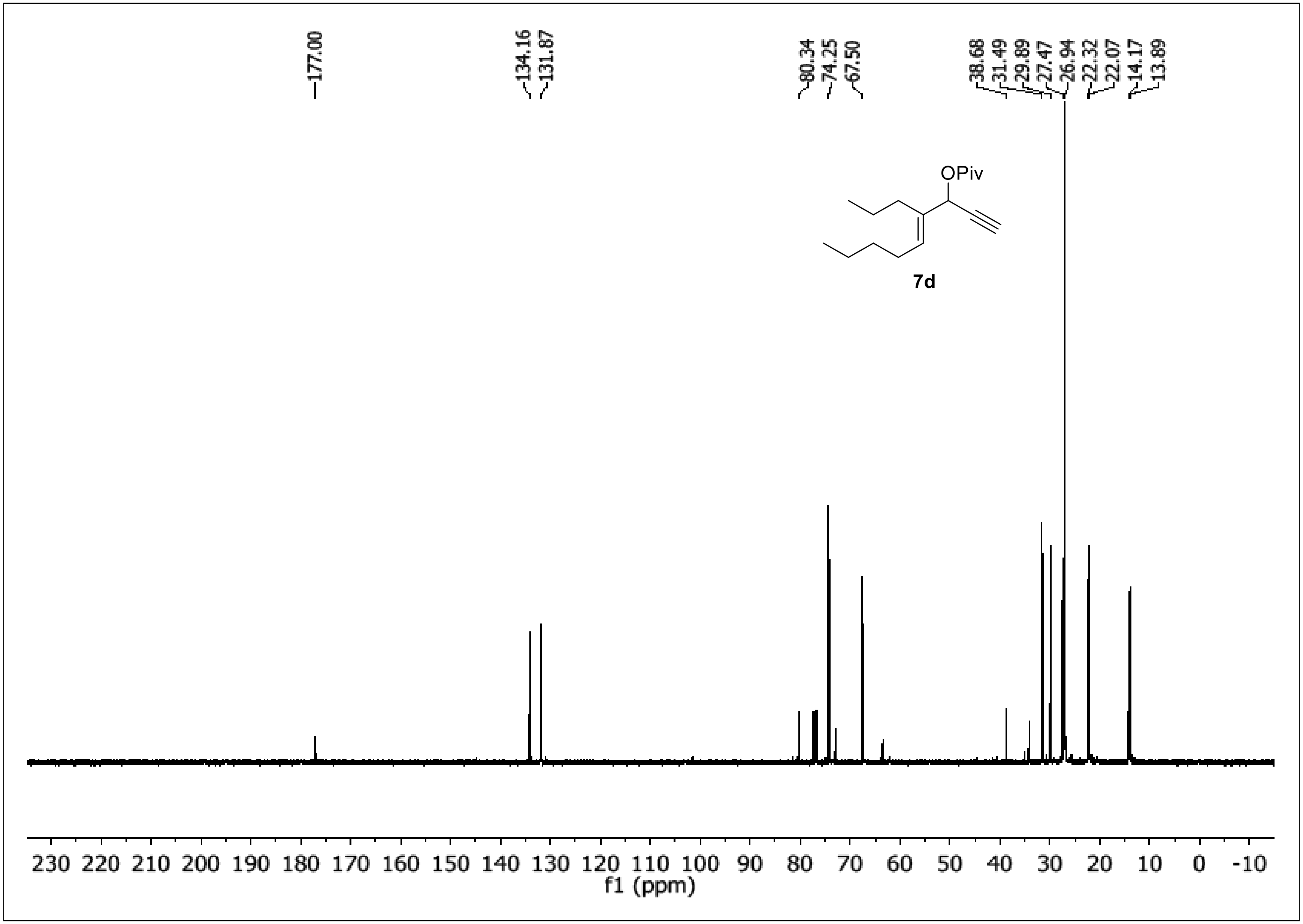

177.12
133.13
127.14
80.01
73.96
67.29
38.80
26.99
24.99
24.27
22.33
21.98
OPiv
7b
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

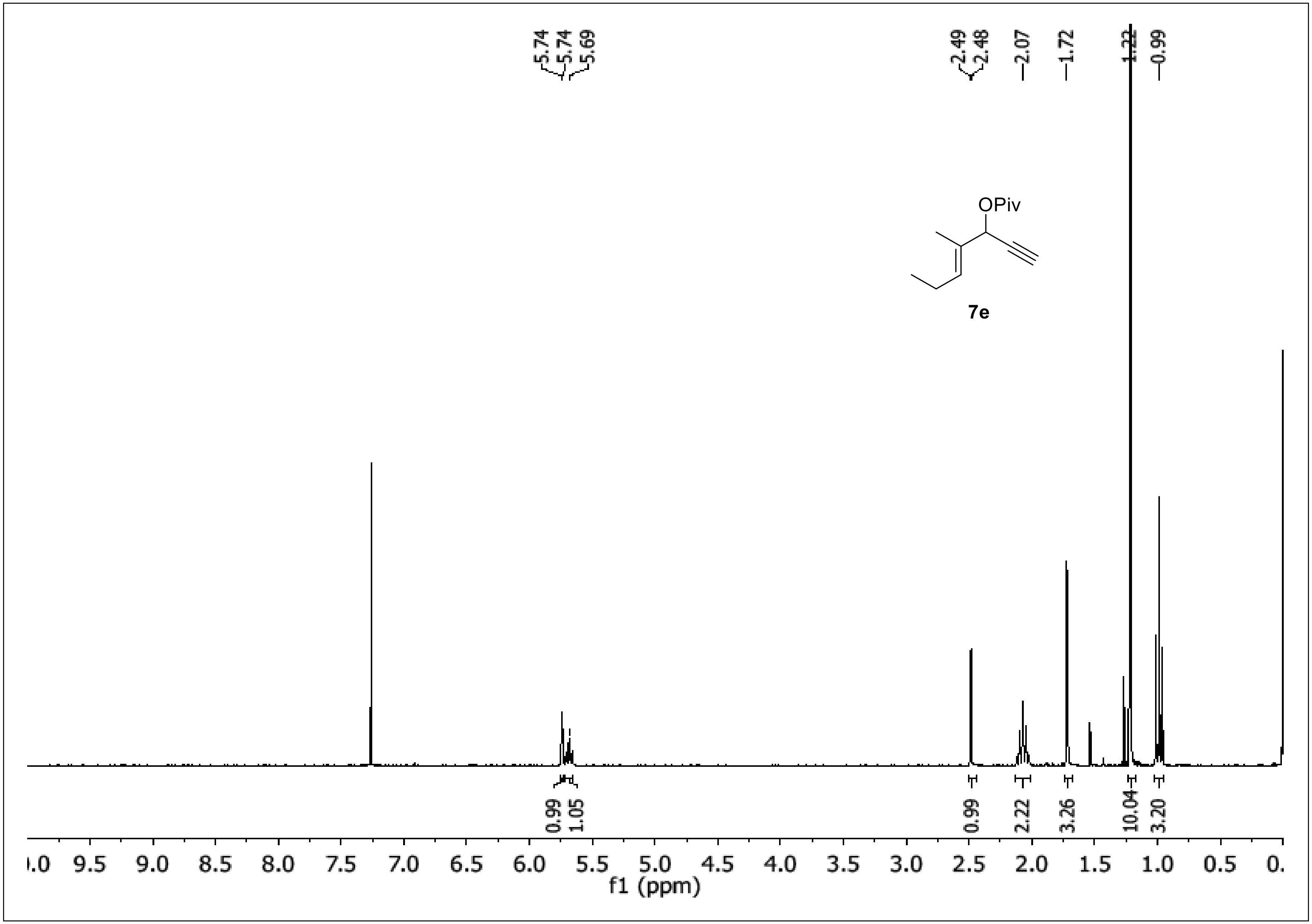

7c

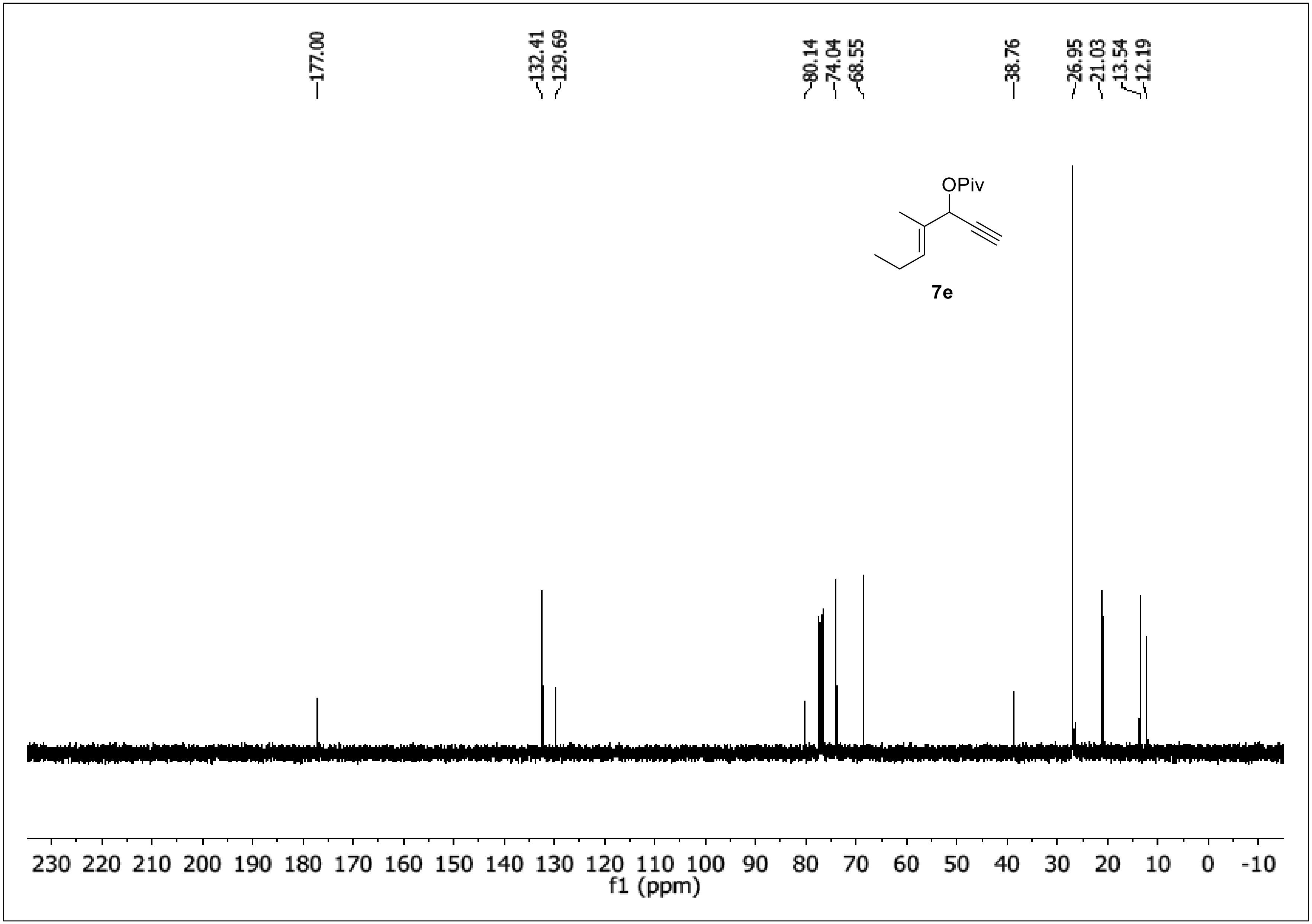
6.04
5.65
2.40
2.18
2.09
1.68
1.43
1.15
OPiv
1.00
0.95
0.85
1.96
2.07
2.06
4.09
9.09
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

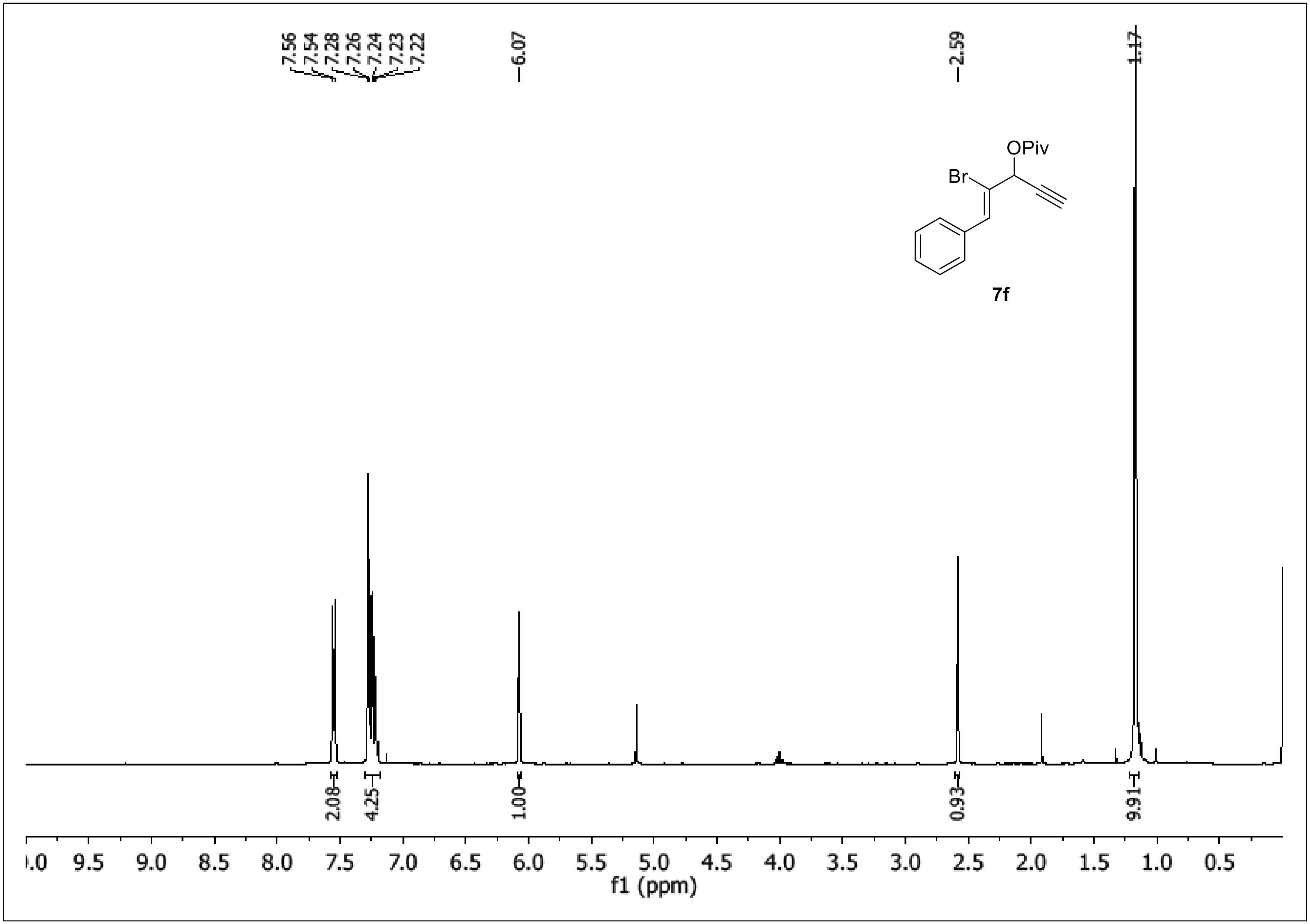

177.14
139.16
132.57
80.23
73.85
68.64
38.84
32.37
29.15
28.26
27.03
26.92
26.48
OPiv
7c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

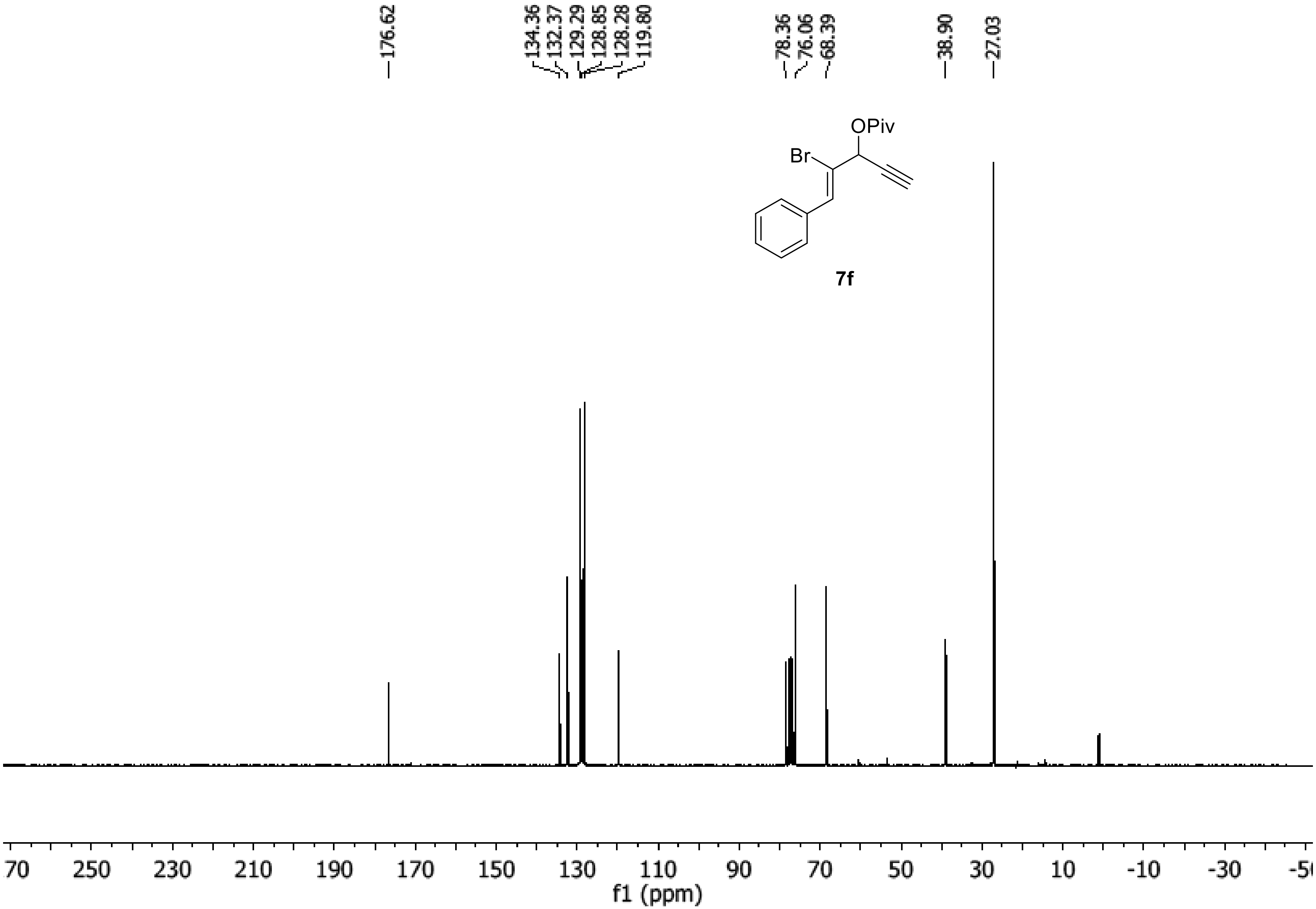

5.77
5.73
2.47
2.47
2.10
2.03
1.45
1.32
1.18
0.89
OPiv
7d
1.00
1.02
0.92
2.02
2.19
2.17
6.06
12.22
7.54
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

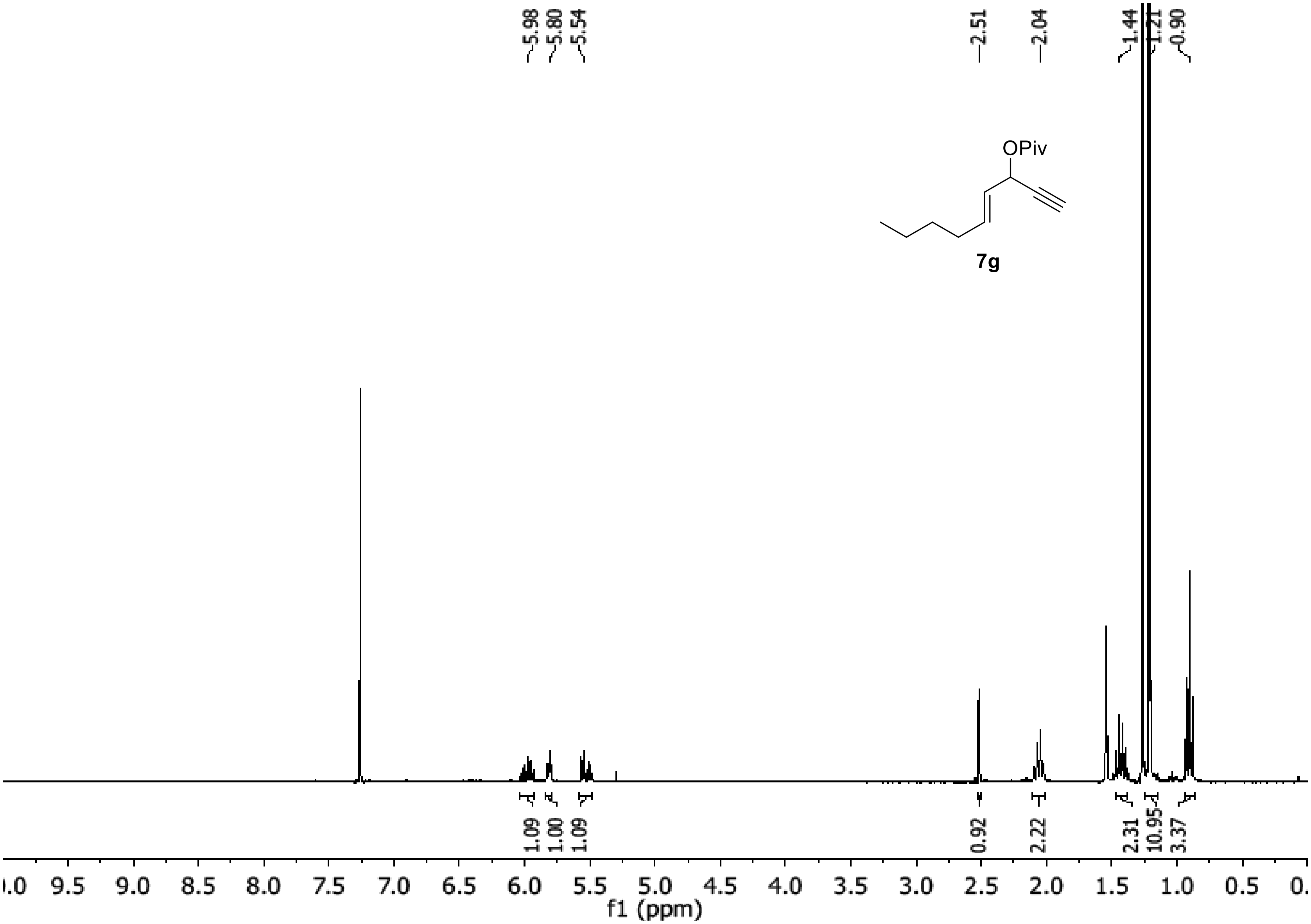

177.00
134.16
131.87
80.34
74.25
67.50
38.68
31.49
29.89
27.47
26.94
22.32
22.07
14.17
13.89
OPiv
7d
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


5.74
5.74
5.69
2.49
2.48
2.07
1.72
1.22
0.99
OPiv
7e
0.99
1.05
0.99
2.22
3.26
10.04
3.20
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)

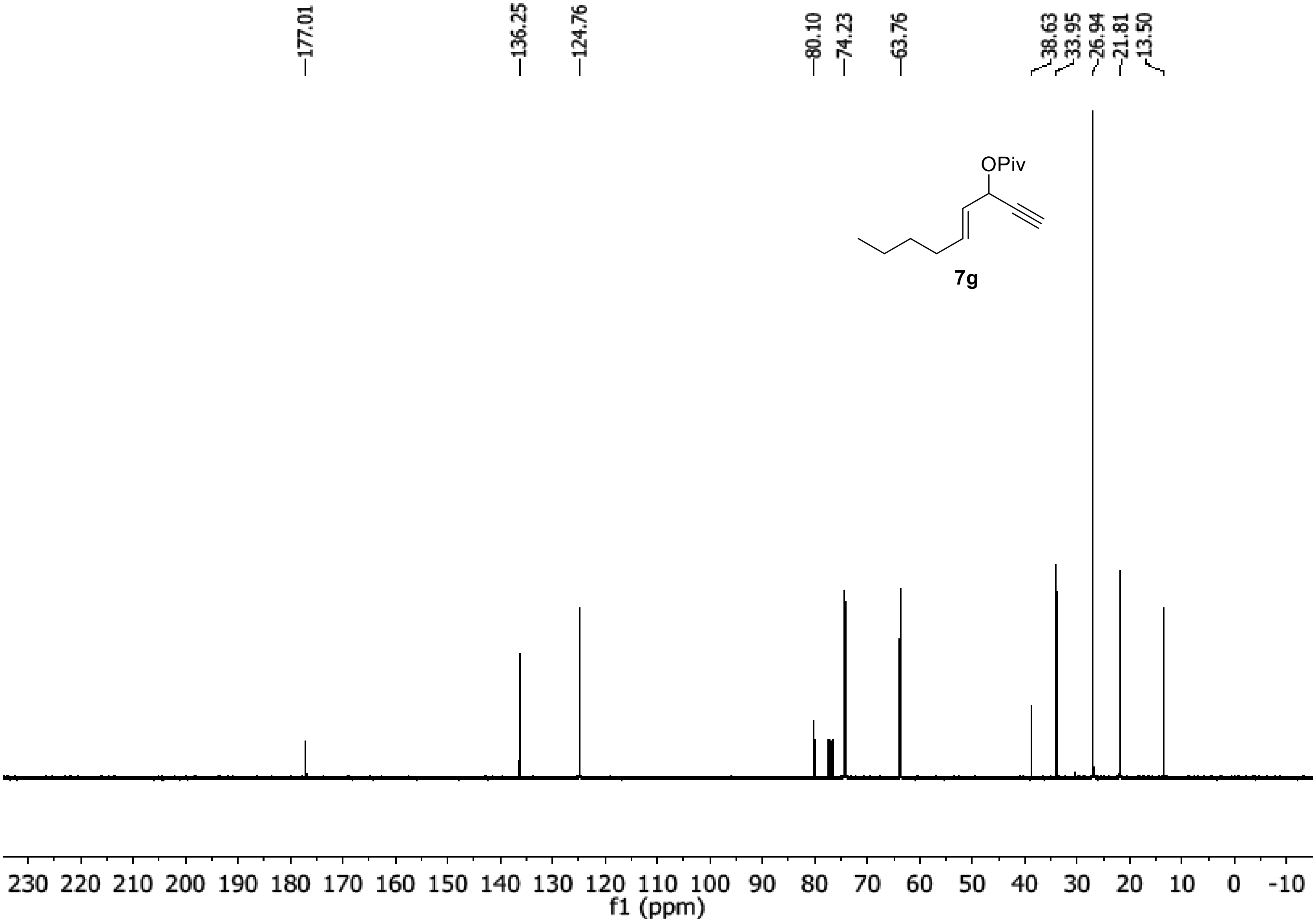

177.00
132.41
129.69
80.14
74.04
68.55
38.76
26.95
21.03
13.54
12.19
OPiv
7e
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.56
7.54
7.28
7.26
7.24
7.23
7.22
6.07
2.59
1.17
OPiv
Br
7f
2.08
4.25
1.00
0.93
9.91
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)

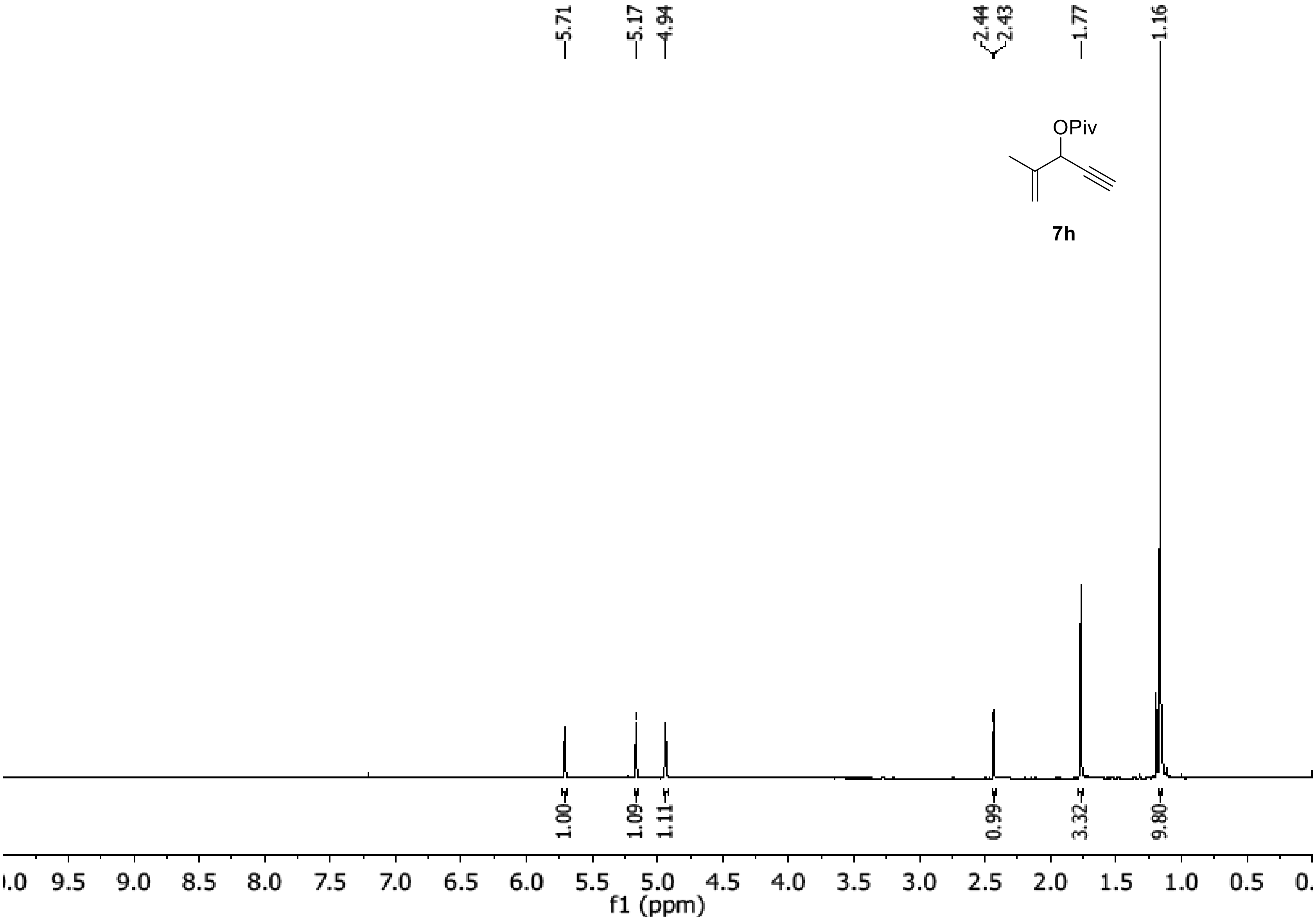

176.62
134.36
132.37
129.29
128.85
128.28
119.80
78.36
76.06
68.39
38.90
27.03
OPiv
Br
7f
70
250
230
210
190
170
150
130
110
90
70
50
30
10
-10
-30
-5
f1 (ppm)

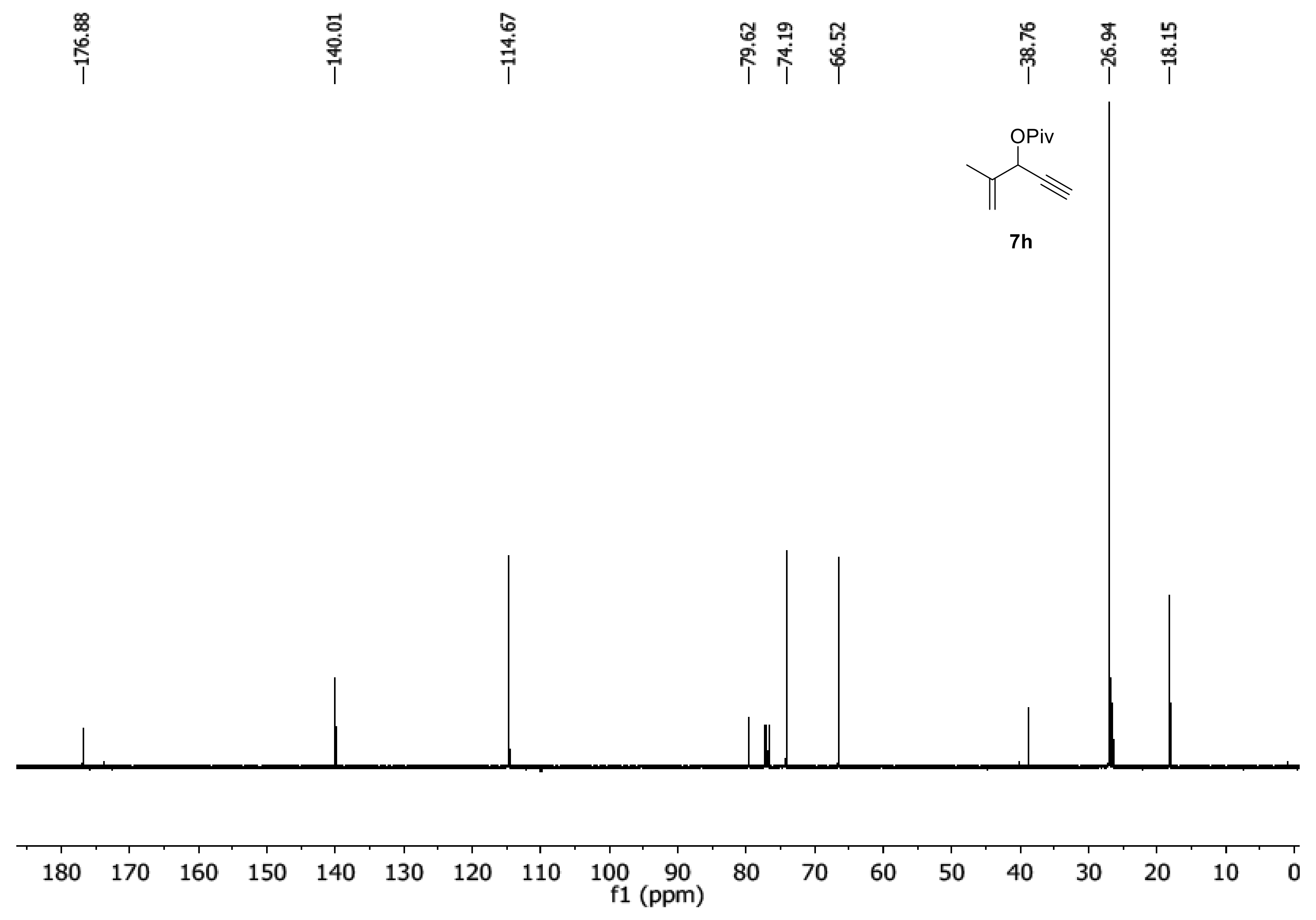


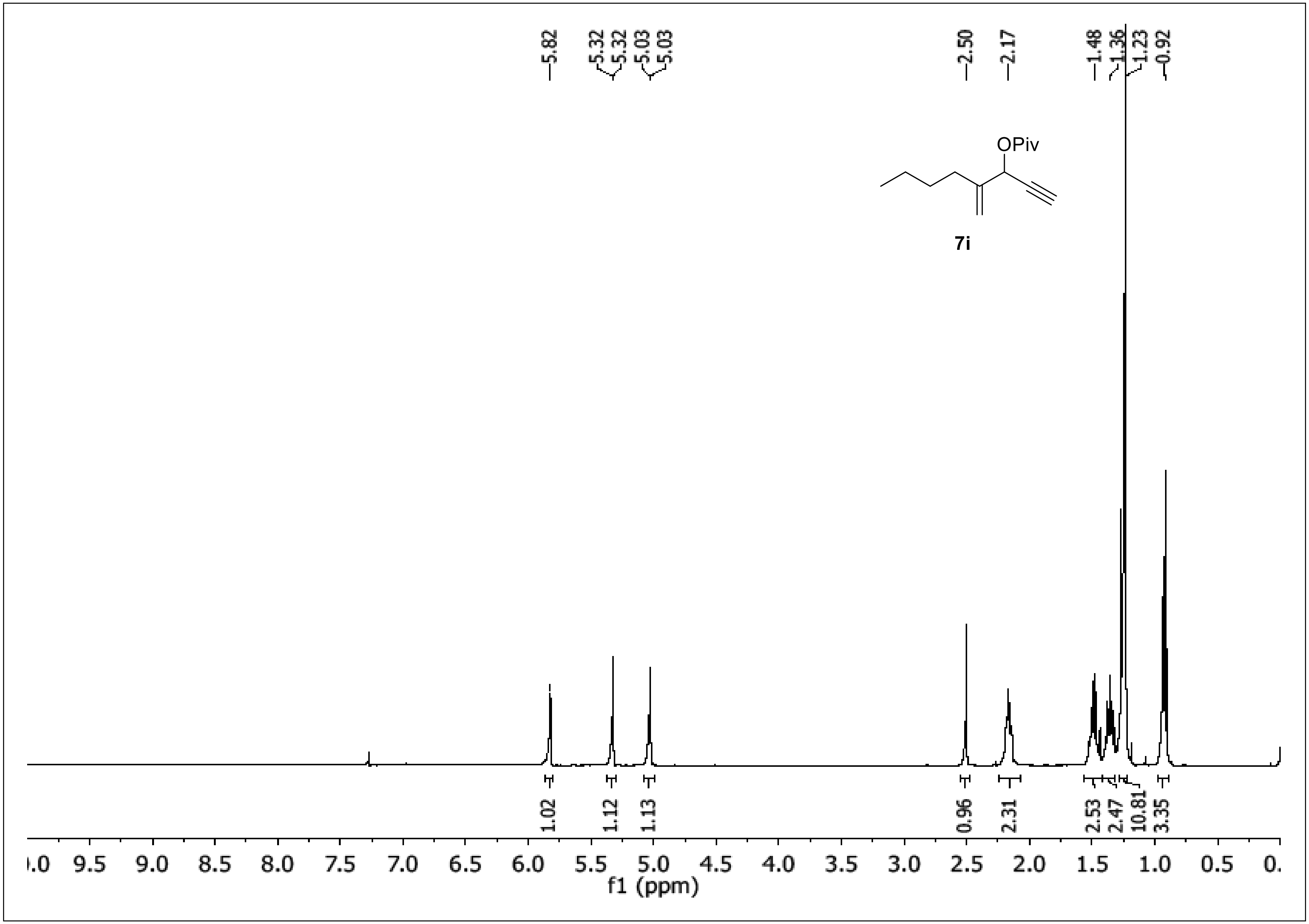
5.98
5.80
5.54
2.51
2.04
1.44
1.21
0.90
OPiv
7g
1.09
1.00
1.09
0.92
2.22
2.31
10.95
3.37
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

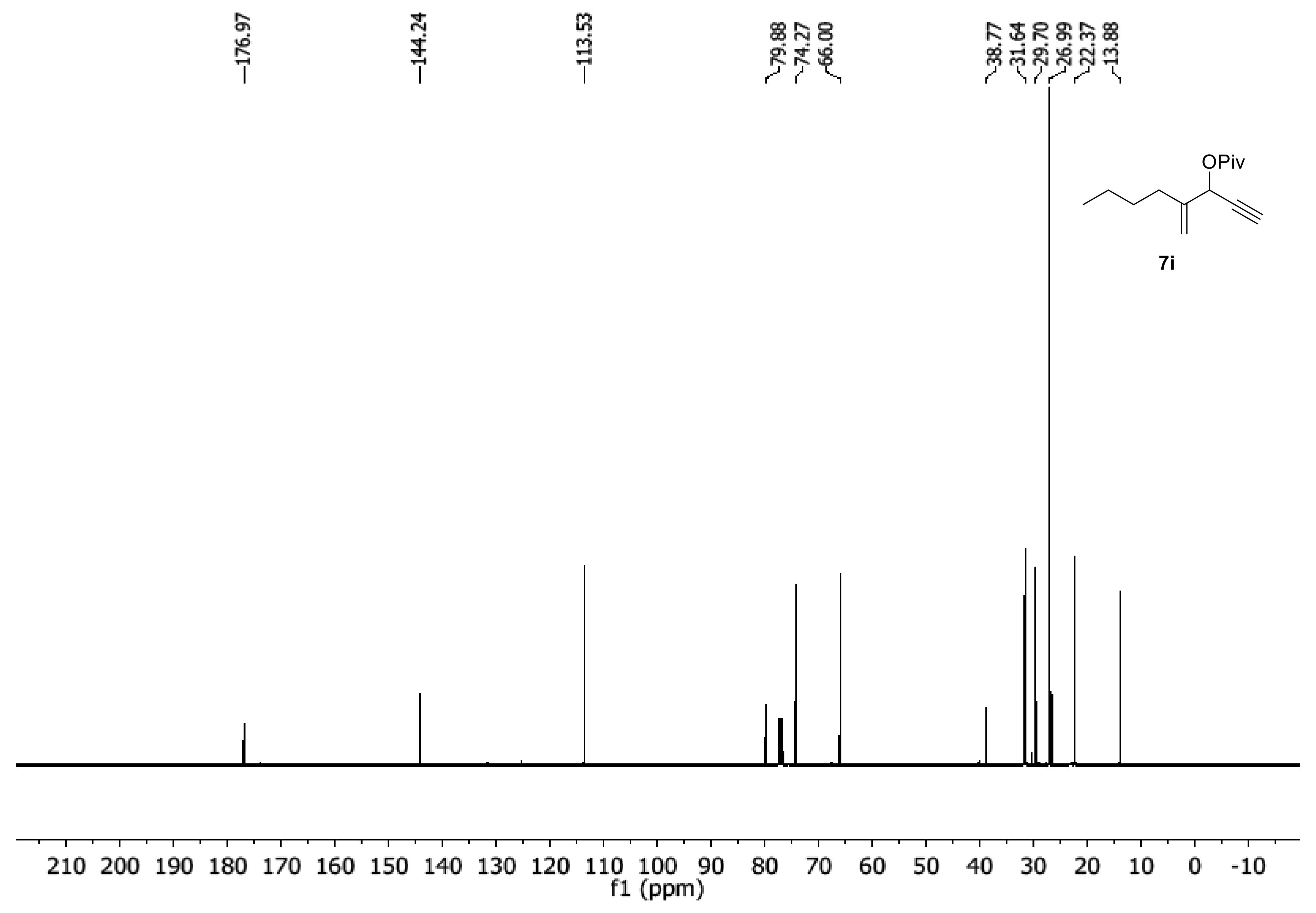


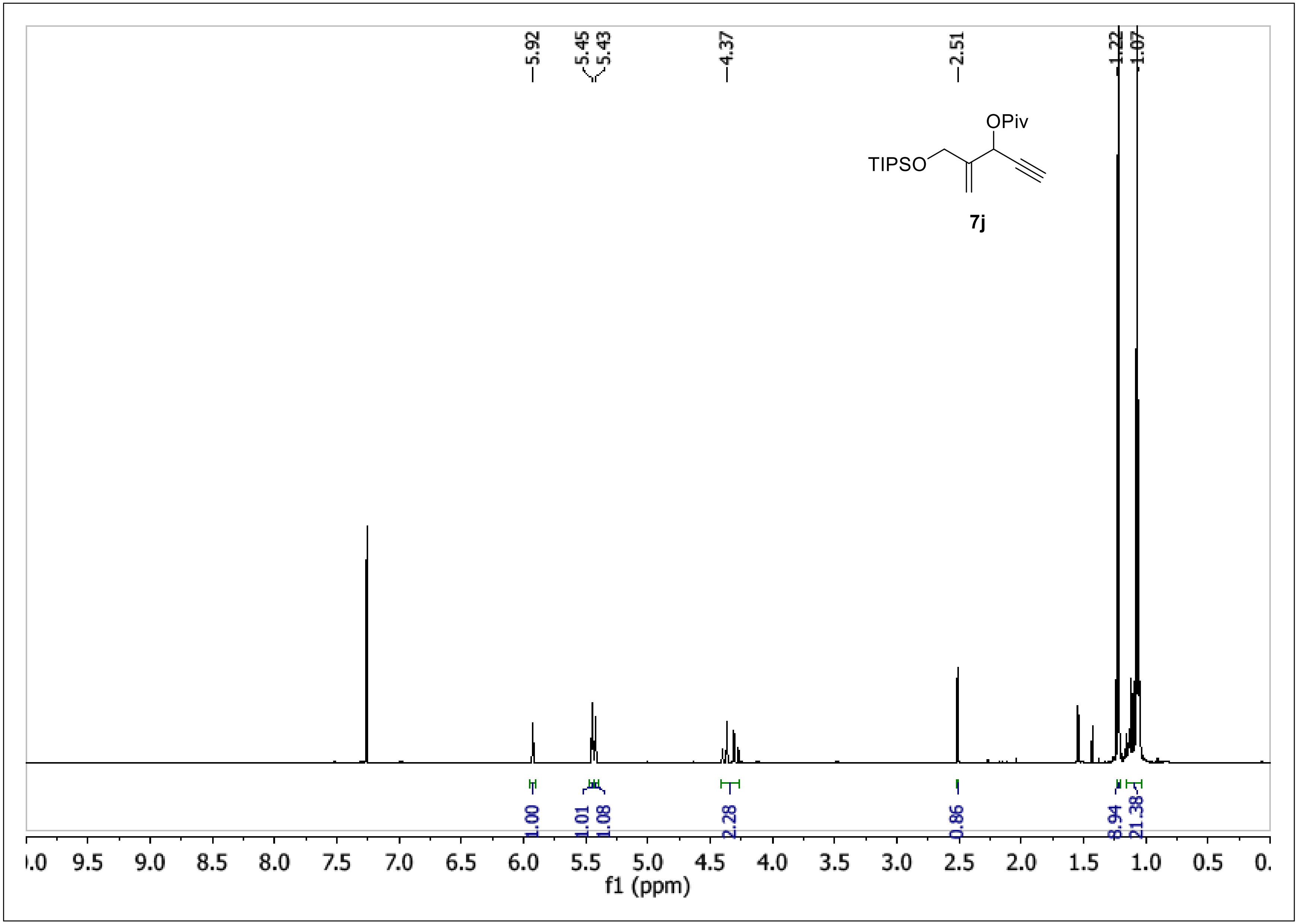
177.01
136.25
124.76
80.10
74.23
63.76
38.63
33.95
26.94
21.81
13.50
OPiv
7g
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

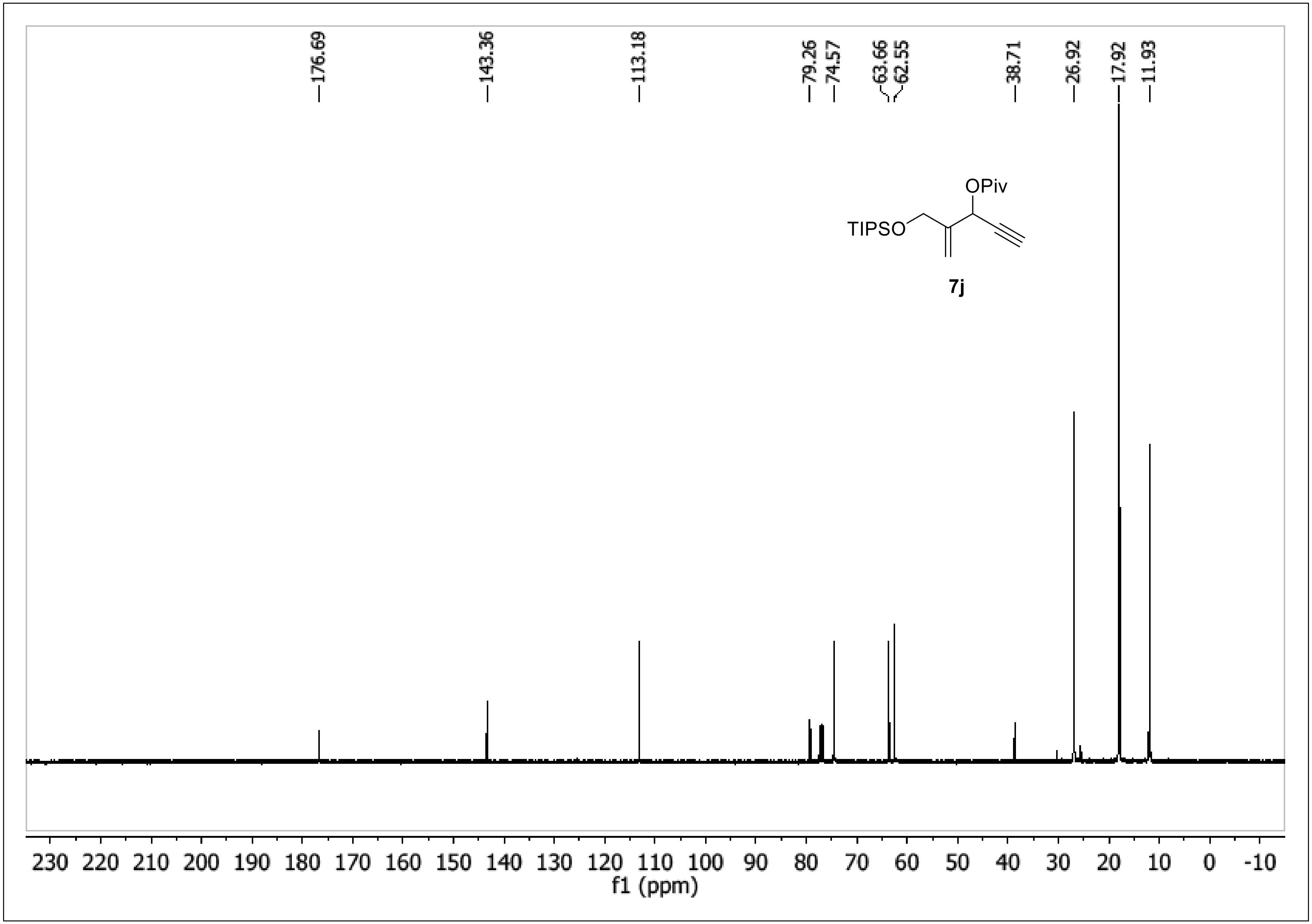

5.71
5.17
4.94
2.44
2.43
1.77
1.16
OPiv
7h
1.00
1.09
1.11
0.99
3.32
9.80
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

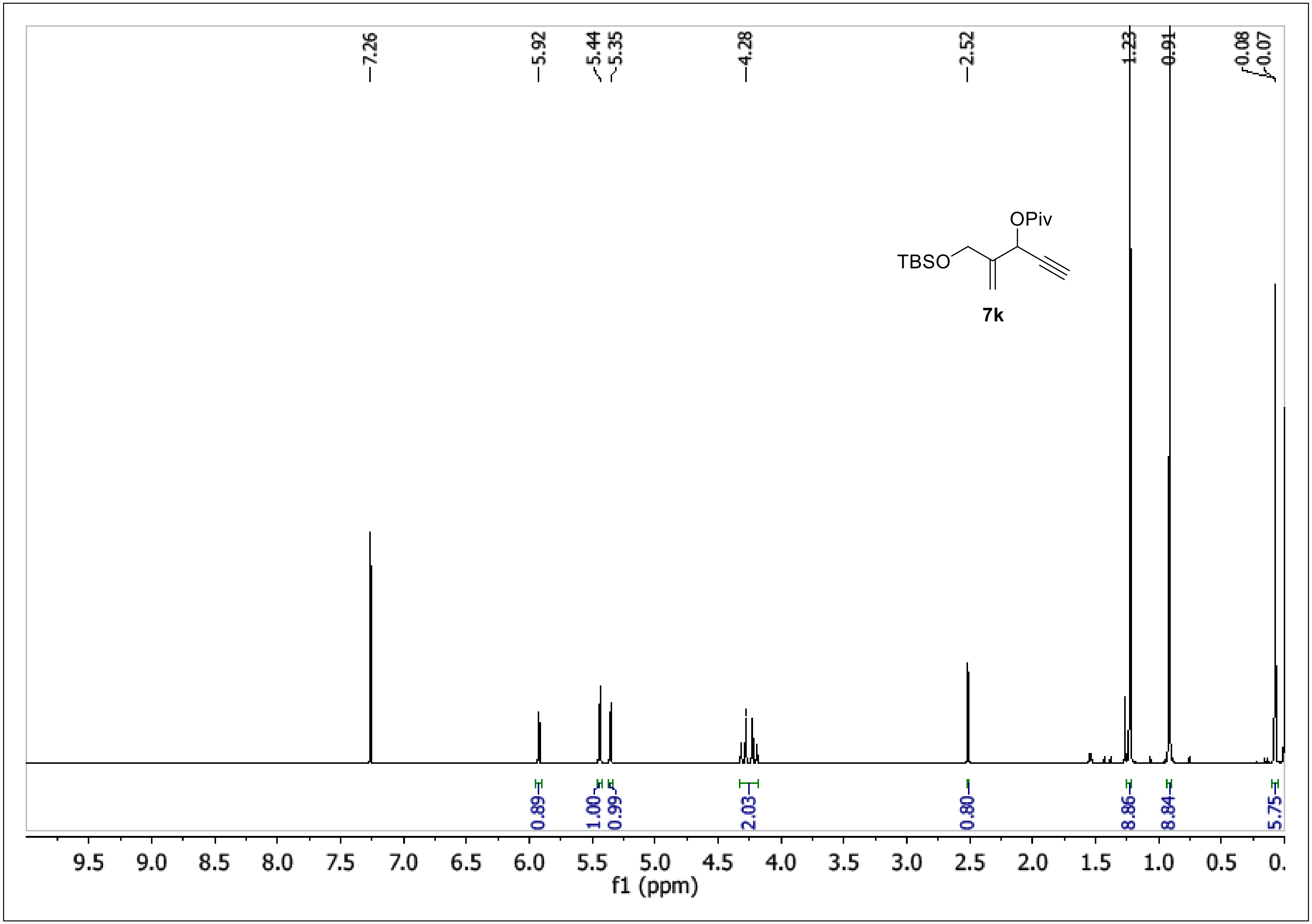

176.88
140.01
114.67
79.62
74.19
66.52
38.76
26.94
18.15
OPiv
7h
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


5.82
5.32
5.32
5.03
5.03
2.50
2.17
1.48
1.36
1.23
0.92
OPiv
7i
1.02
1.12
1.13
0.96
2.31
2.53
2.47
10.81
3.35
.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.
f1 (ppm)


176.97
144.24
113.53
79.88
74.27
66.00
38.77
31.64
29.70
26.99
22.37
13.88
OPiv
7i
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)

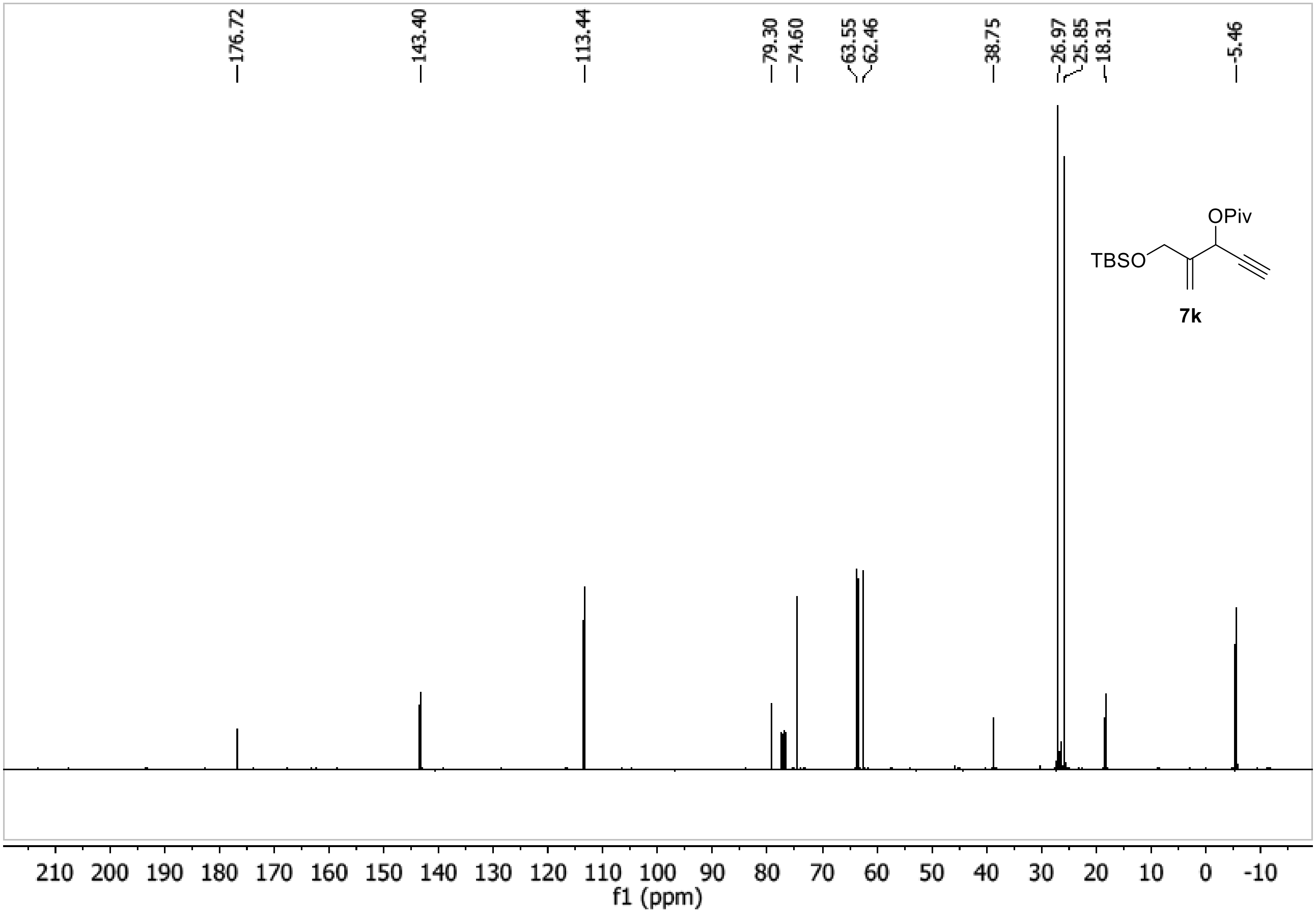

5.92
5.45
5.43
4.37
2.51
1.22
1.07
OPiv
TIPSO
7j
1.00
1.01
1.08
2.28
0.86
8.94
21.38
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


176.69
143.36
113.18
79.26
74.57
63.66
62.55
38.71
26.92
17.92
11.93
OPiv
TIPSO
7j
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

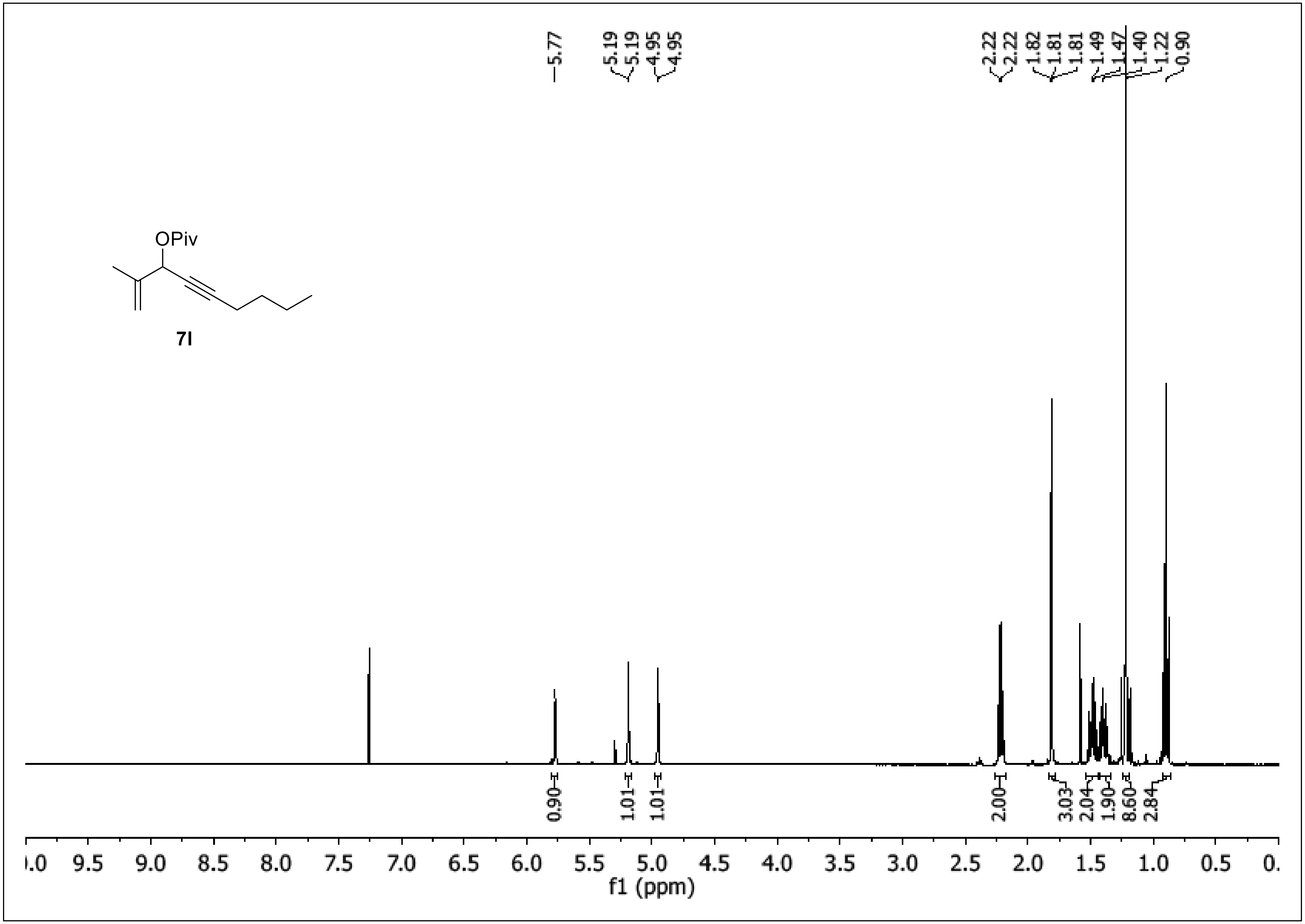


7k

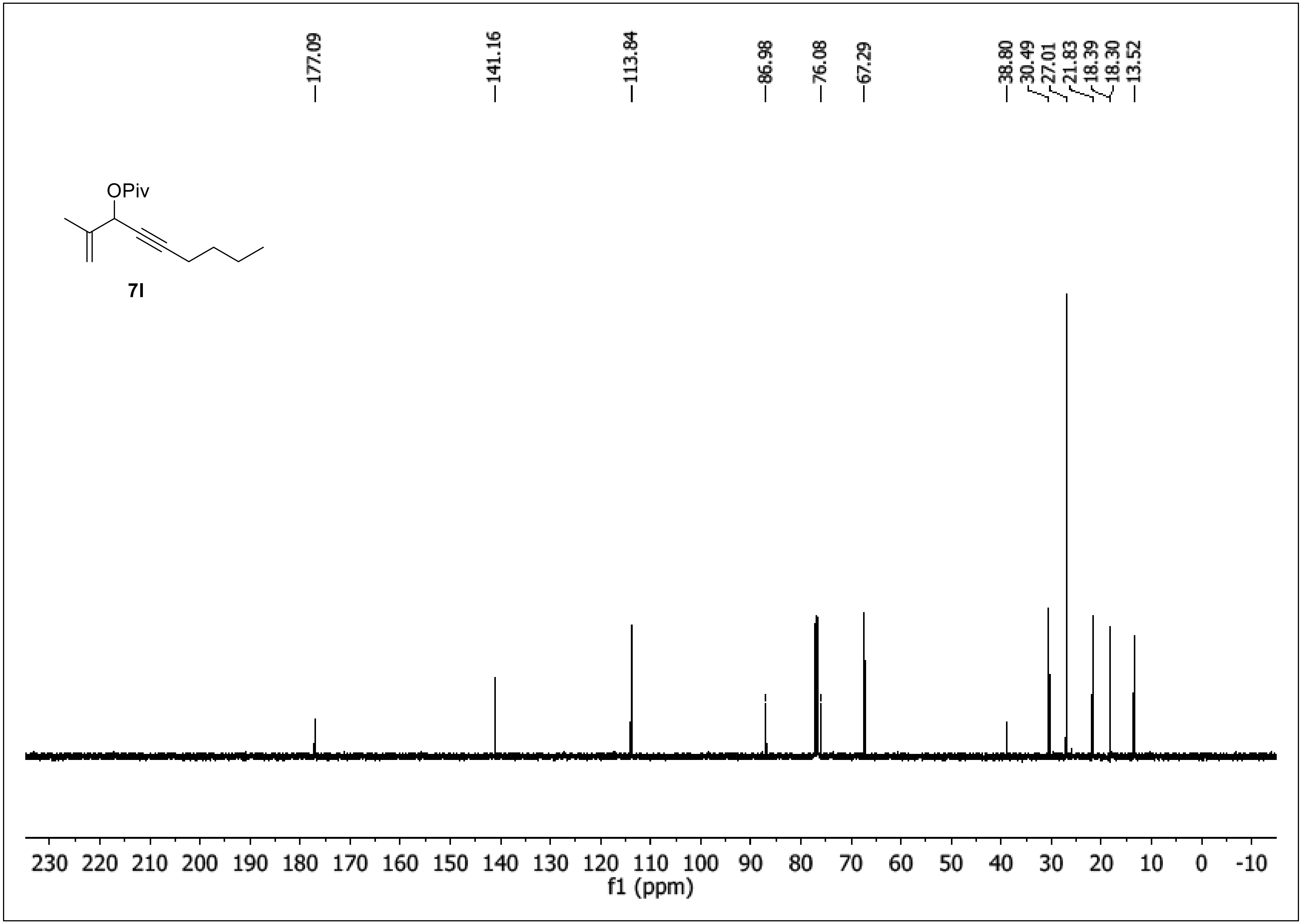
7.26
5.92
5.44
5.35
4.28
2.52
1.23
0.91
0.08
0.07
OPiv
TBSO
0.89
1.00
0.99
2.03
0.80
8.86
8.84
5.75
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

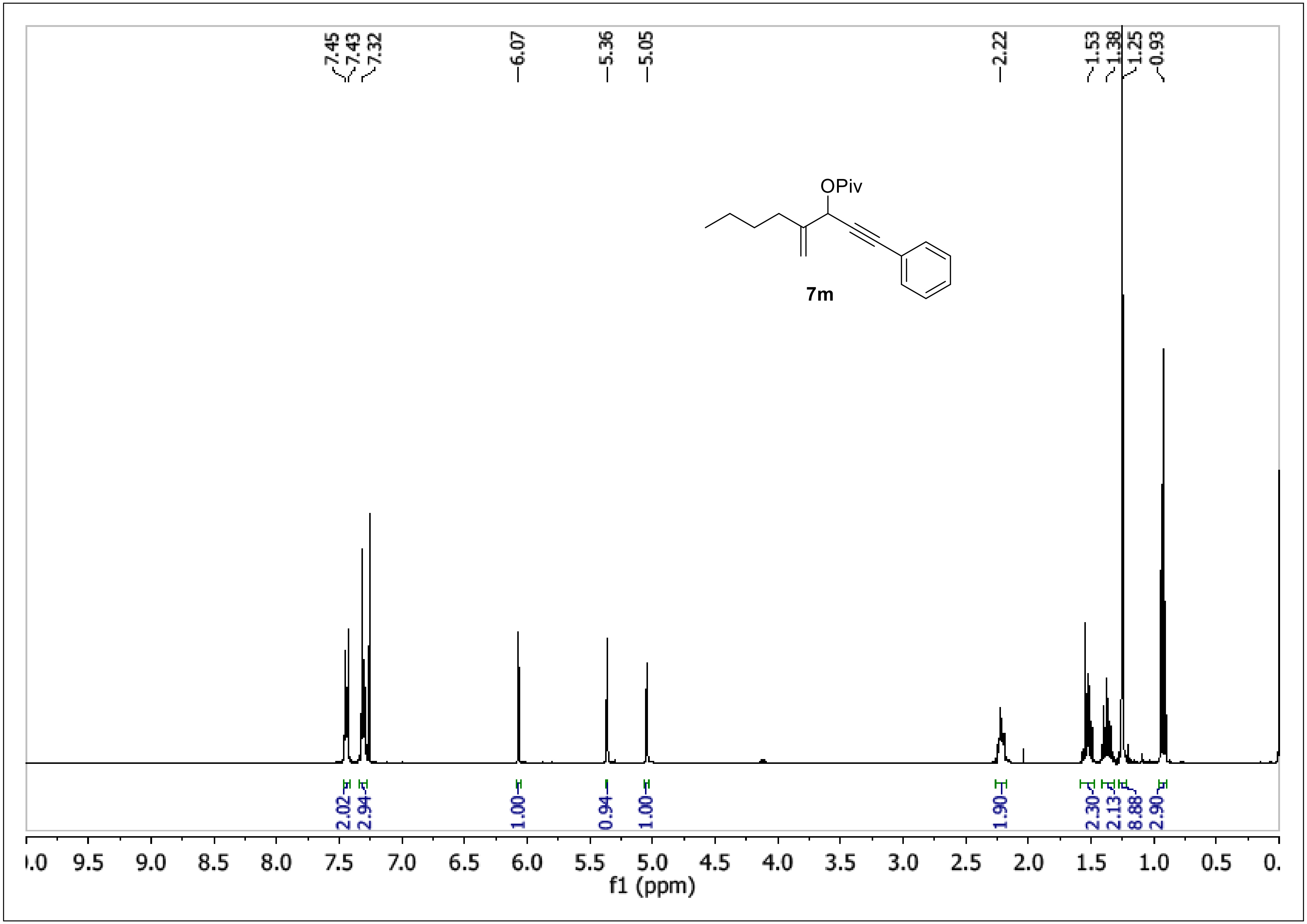

176.72
143.40
113.44
79.30
74.60
63.55
62.46
38.75
26.97
25.85
18.31
-5.46
OPiv
TBSO
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

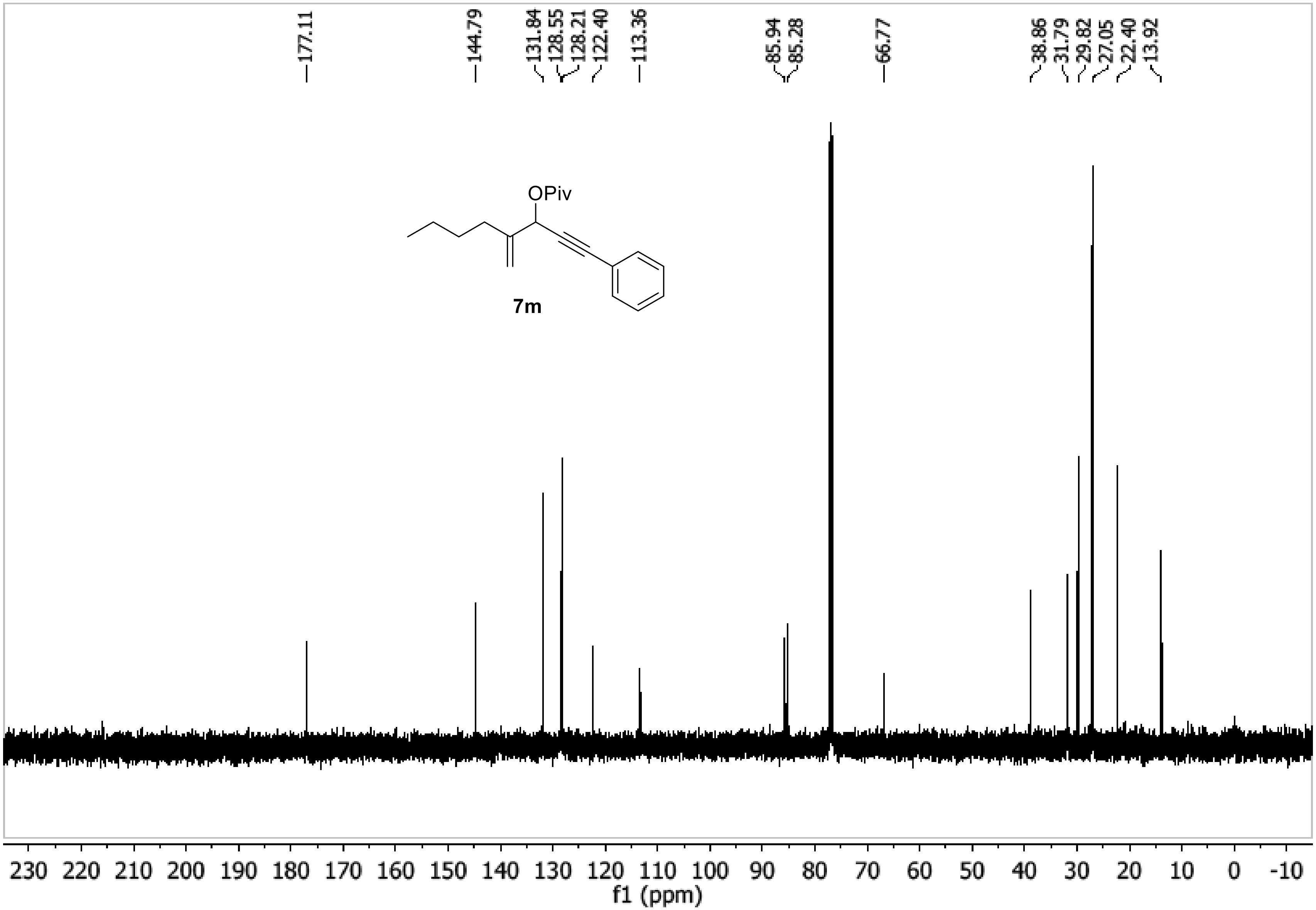
7k


OPiv
5.77
5.19
5.19
4.95
4.95
2.22
2.22
1.82
1.81
1.81
1.49
1.47
1.40
1.22
0.90
0.90
1.01
1.01
2.00
3.03
2.04
1.90
8.60
2.84
.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.
f1 (ppm)

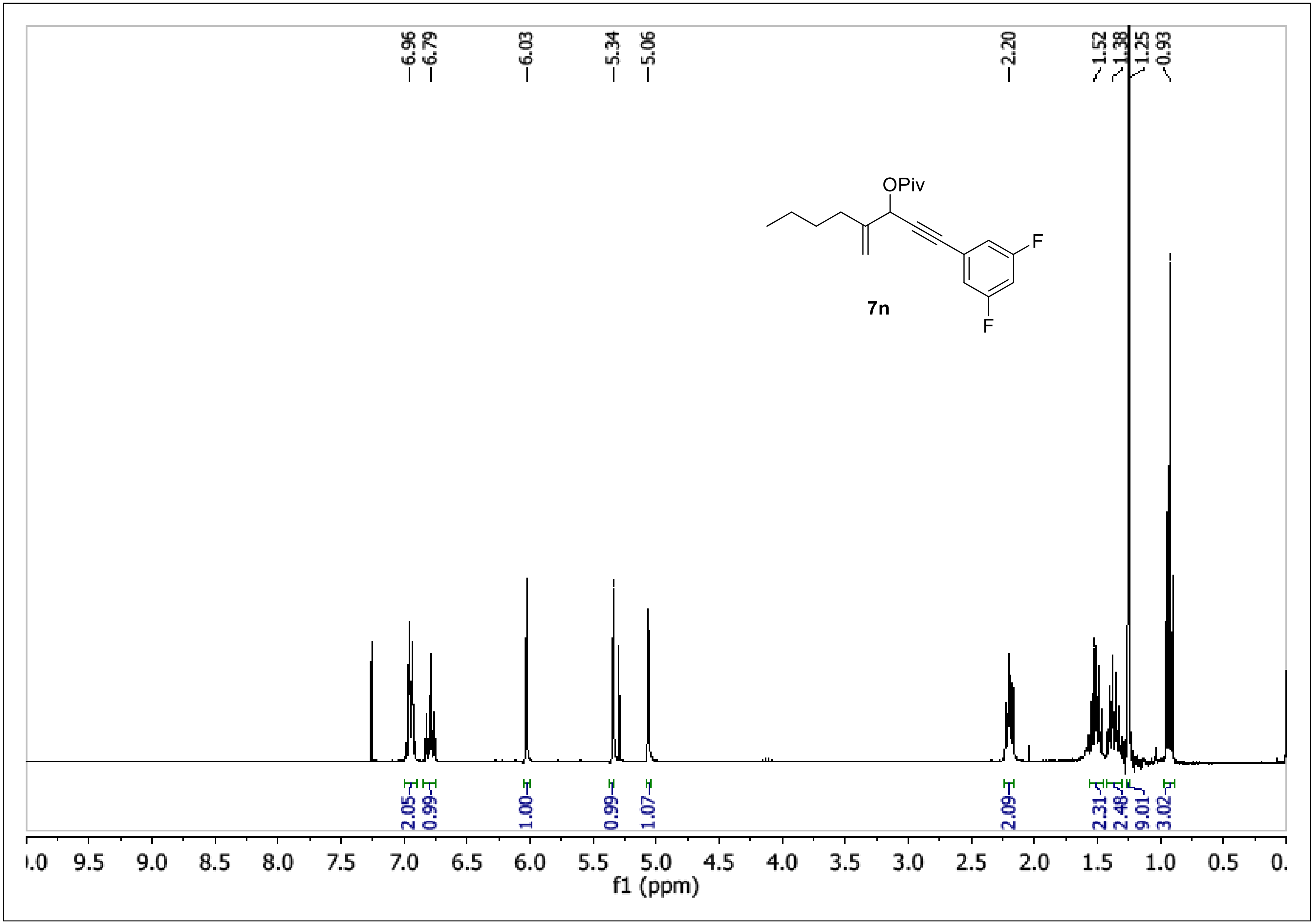
7l

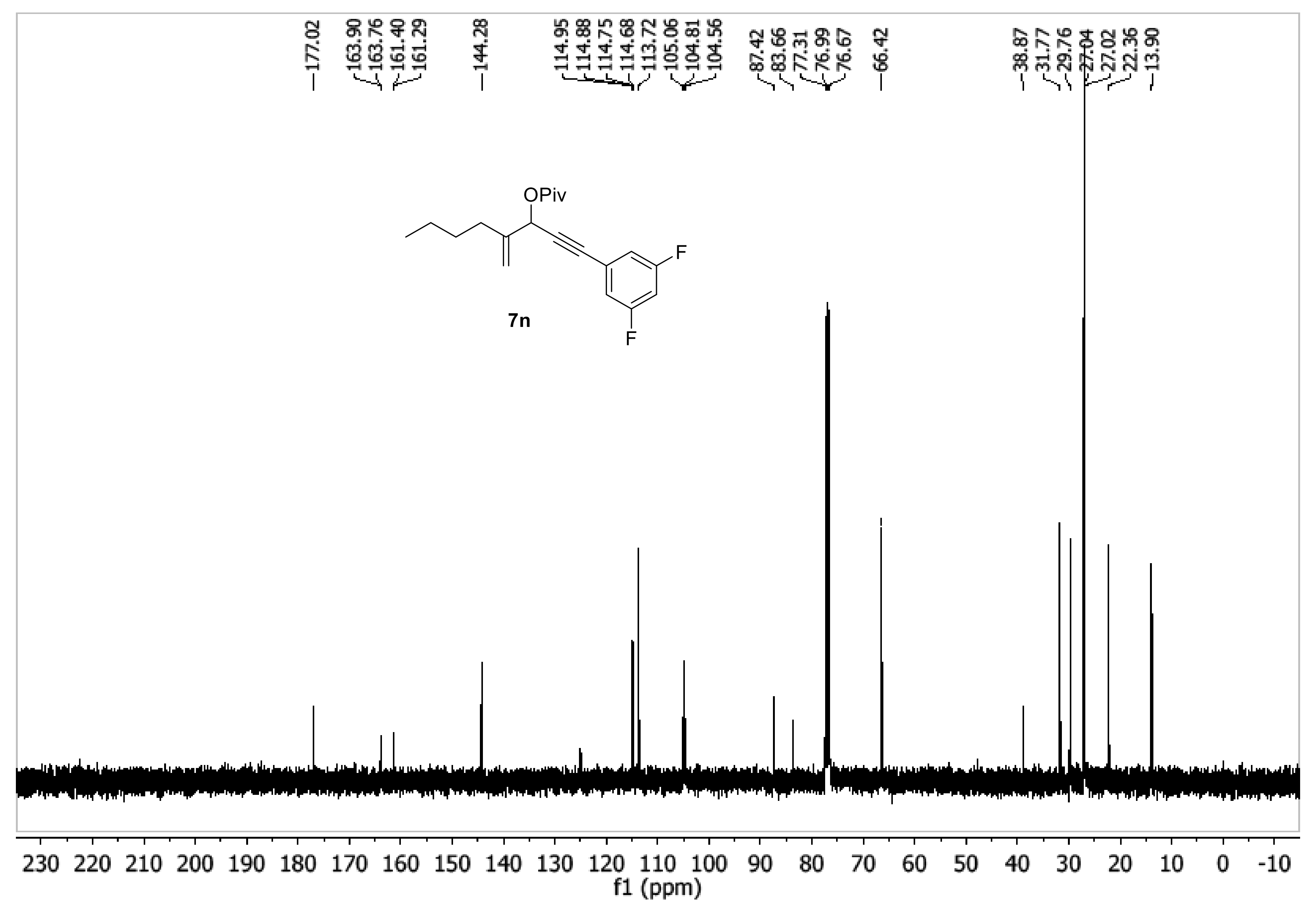

177.09
141.16
113.84
86.98
76.08
67.29
38.80
30.49
27.01
21.83
18.39
18.30
13.52
OPiv
7l
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

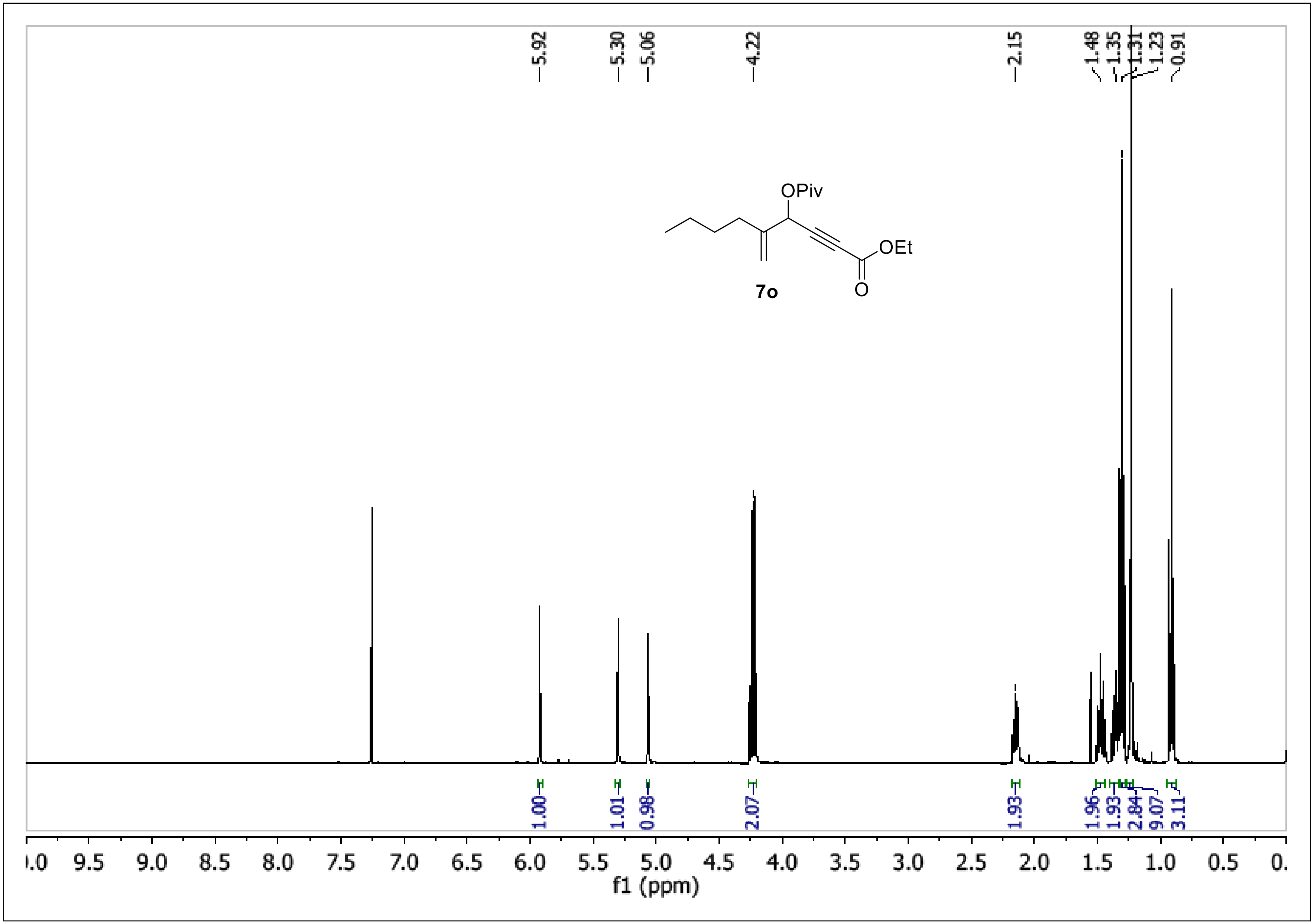

7.45
7.43
7.32
6.07
5.36
5.05
2.22
1.53
1.38
1.25
0.93
OPiv
7m
2.02
2.94
1.00
0.94
1.00
1.90
2.30
2.13
8.88
2.90
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

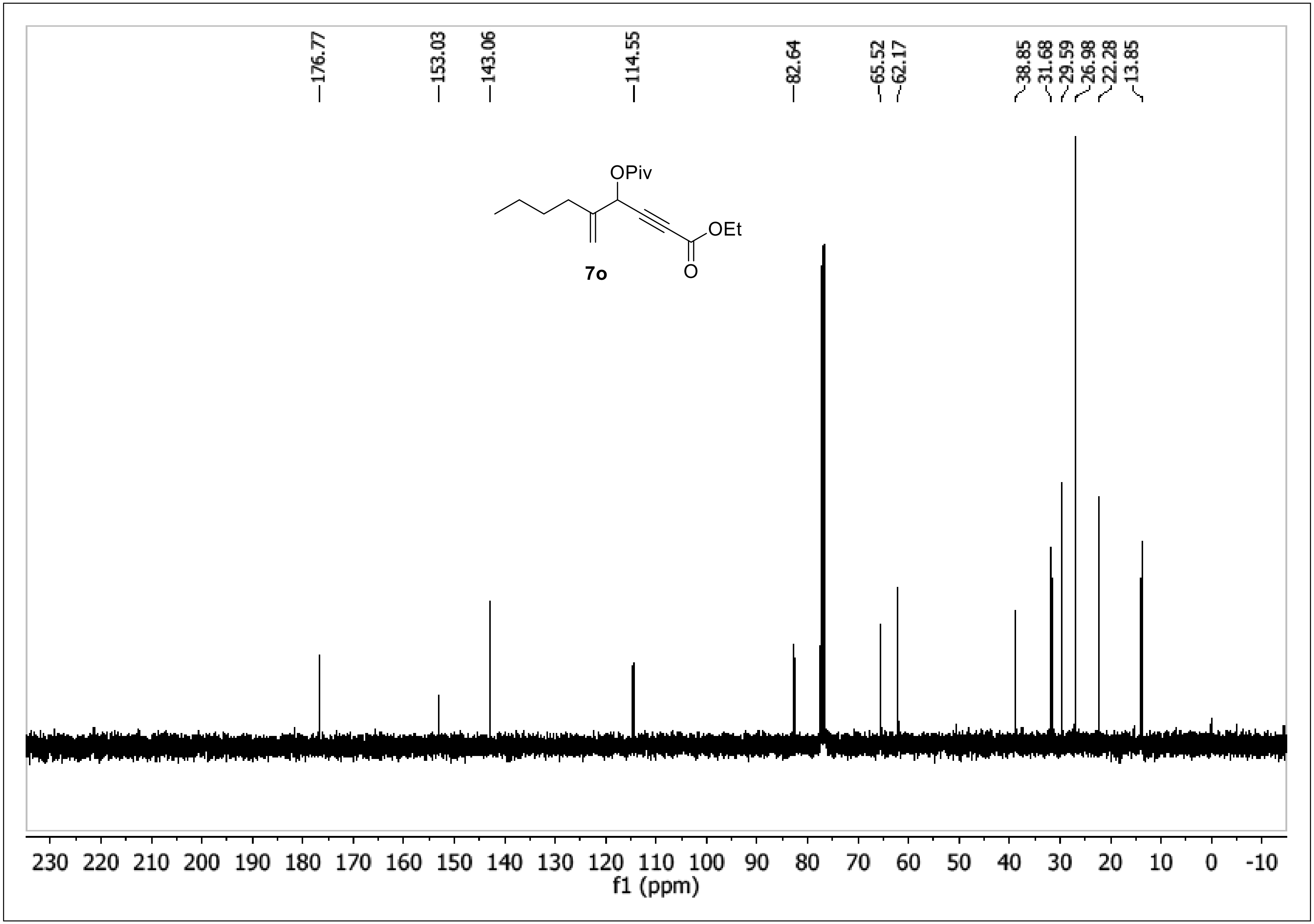


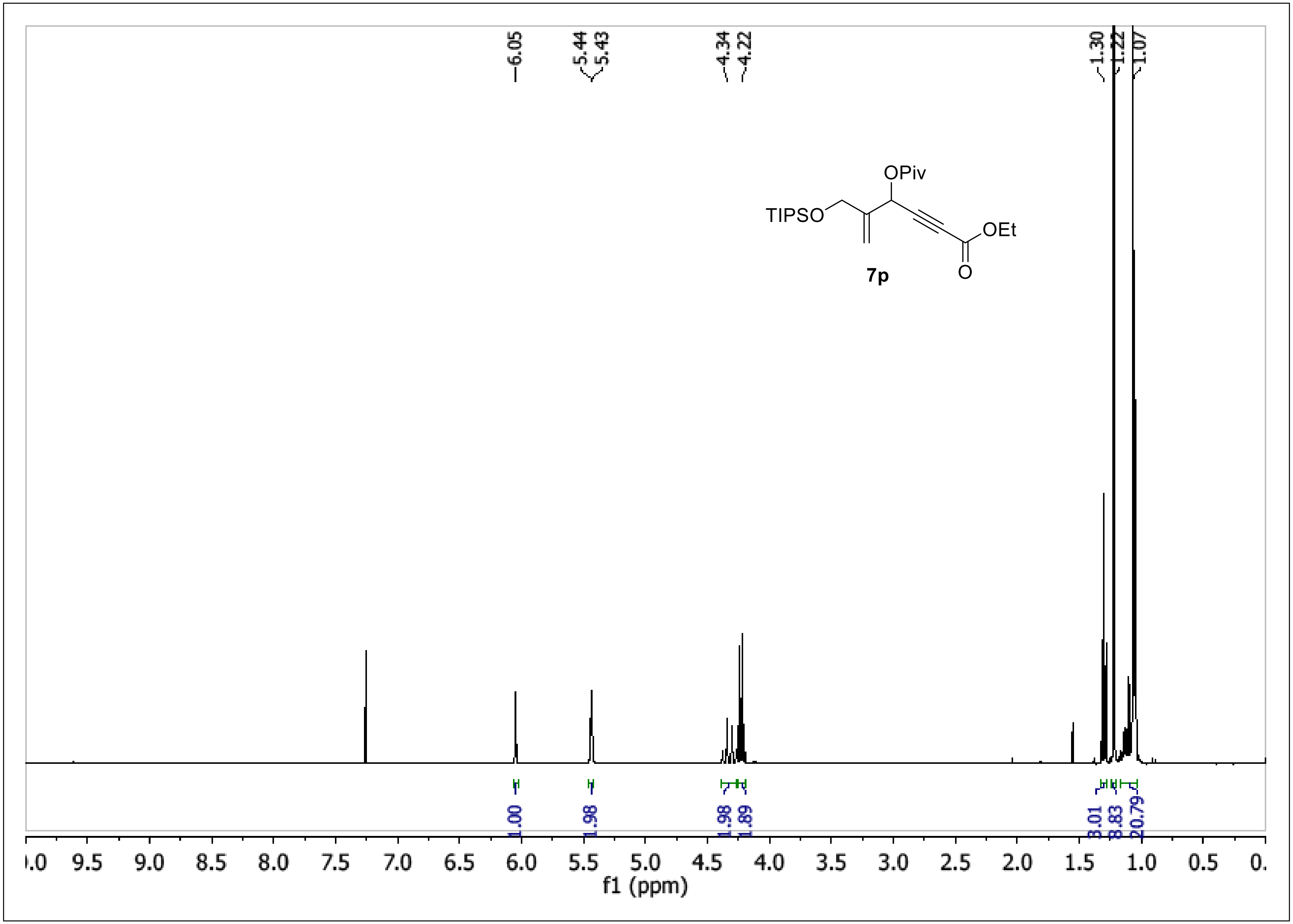
177.11
144.79
131.84
128.55
128.21
122.40
113.36
85.94
85.28
66.77
38.86
31.79
29.82
27.05
22.40
13.92
OPiv
7m
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

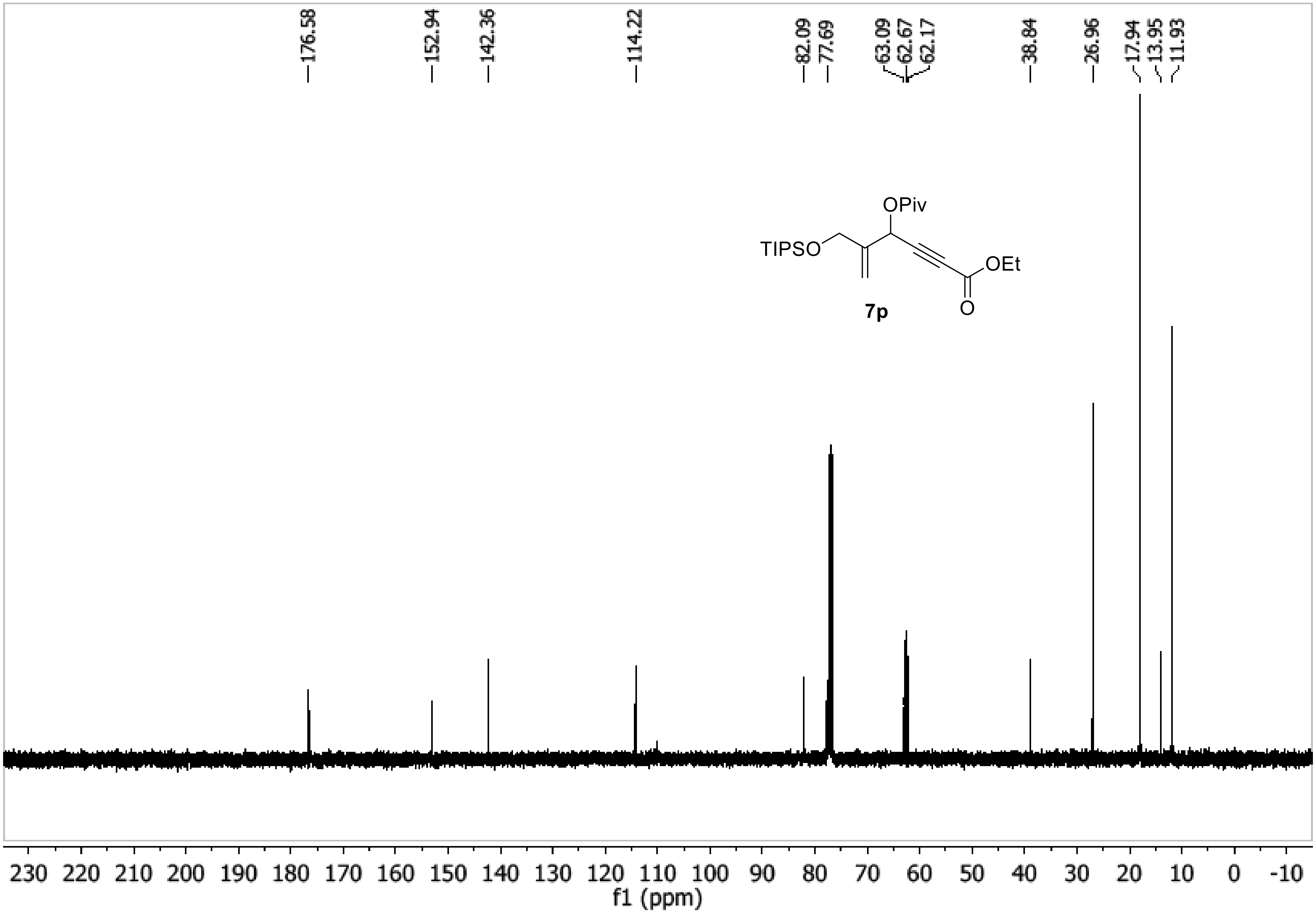

6.96
6.79
6.03
5.34
5.06
2.20
1.52
1.38
1.25
0.93
OPiv
F
F
7n
2.05
0.99
1.00
0.99
1.07
2.09
2.31
2.48
9.01
3.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

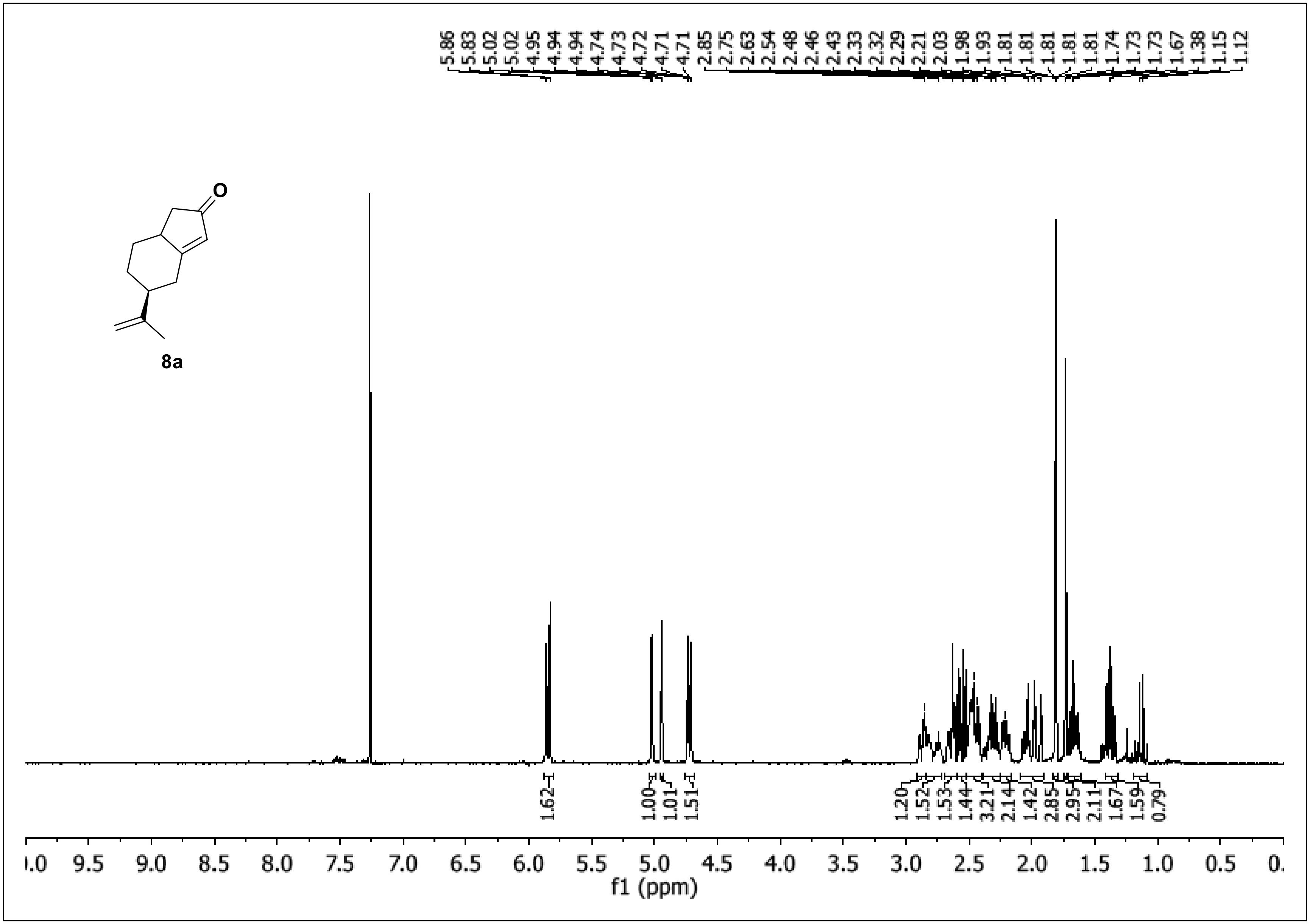

177.02
163.90
163.76
161.40
161.29
144.28
114.95
114.88
114.75
114.68
113.72
105.06
104.81
104.56
87.42
83.66
77.31
76.99
76.67
66.42
38.87
31.77
29.76
27.04
27.02
22.36
13.90
OPiv
F
F
7n
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

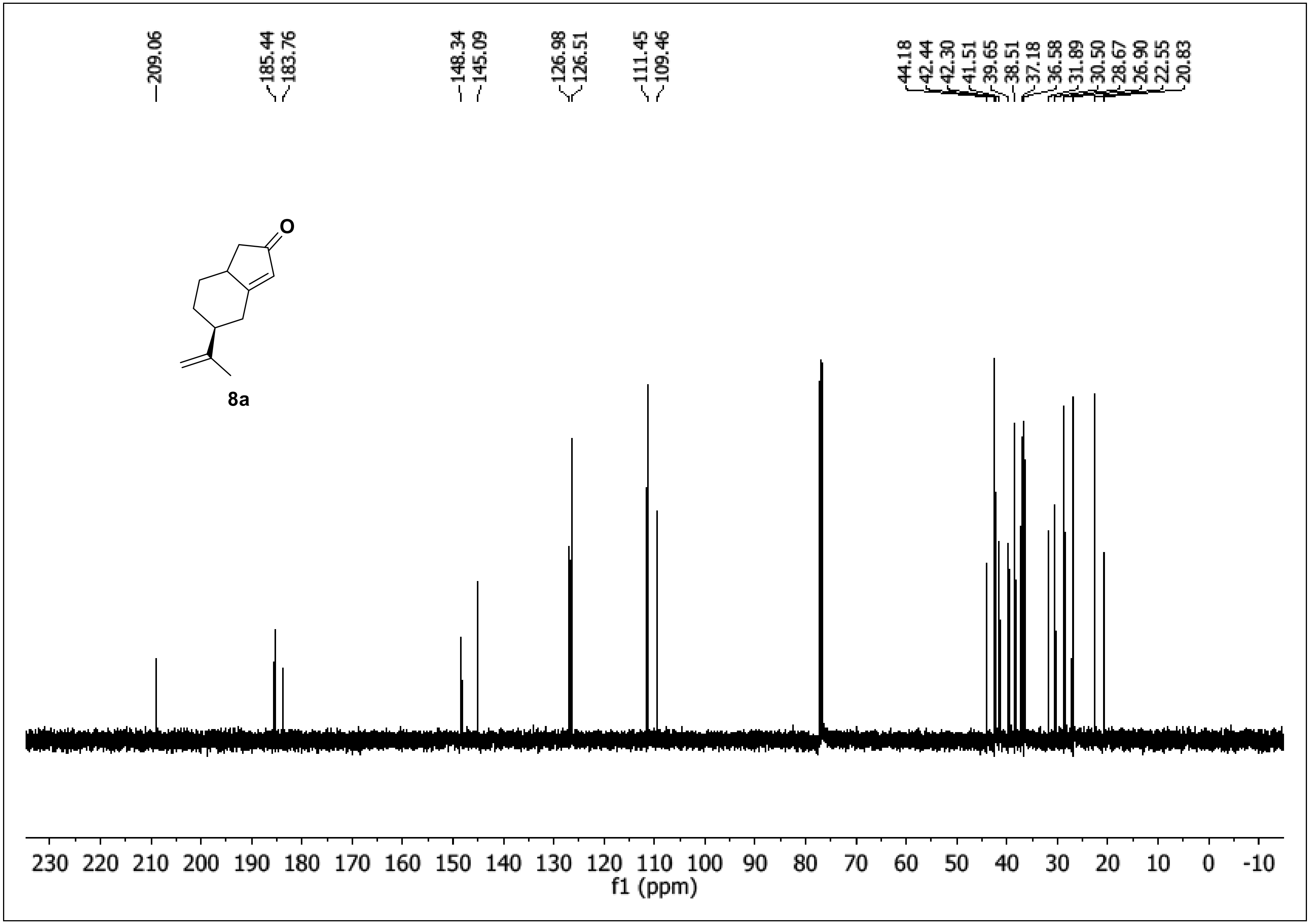

5.92
5.30
5.06
4.22
2.15
1.48
1.35
1.31
1.23
0.91
OPiv
OEt
O
7o
1.00
1.01
0.98
2.07
1.93
1.96
1.93
2.84
9.07
3.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

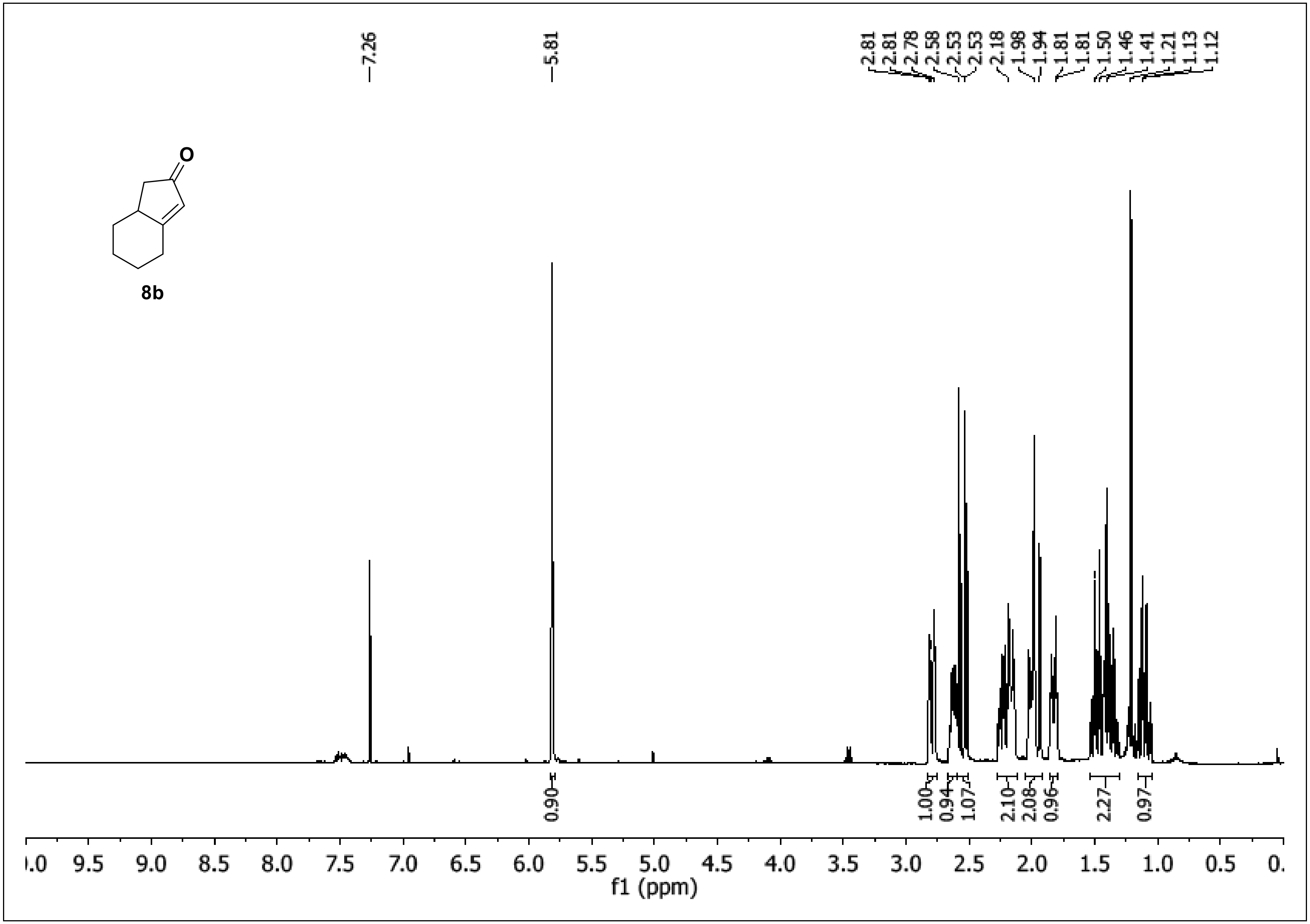

7o
176.77
153.03
143.06
114.55
82.64
65.52
62.17
38.85
31.68
29.59
26.98
22.28
13.85
OPiv
OEt
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

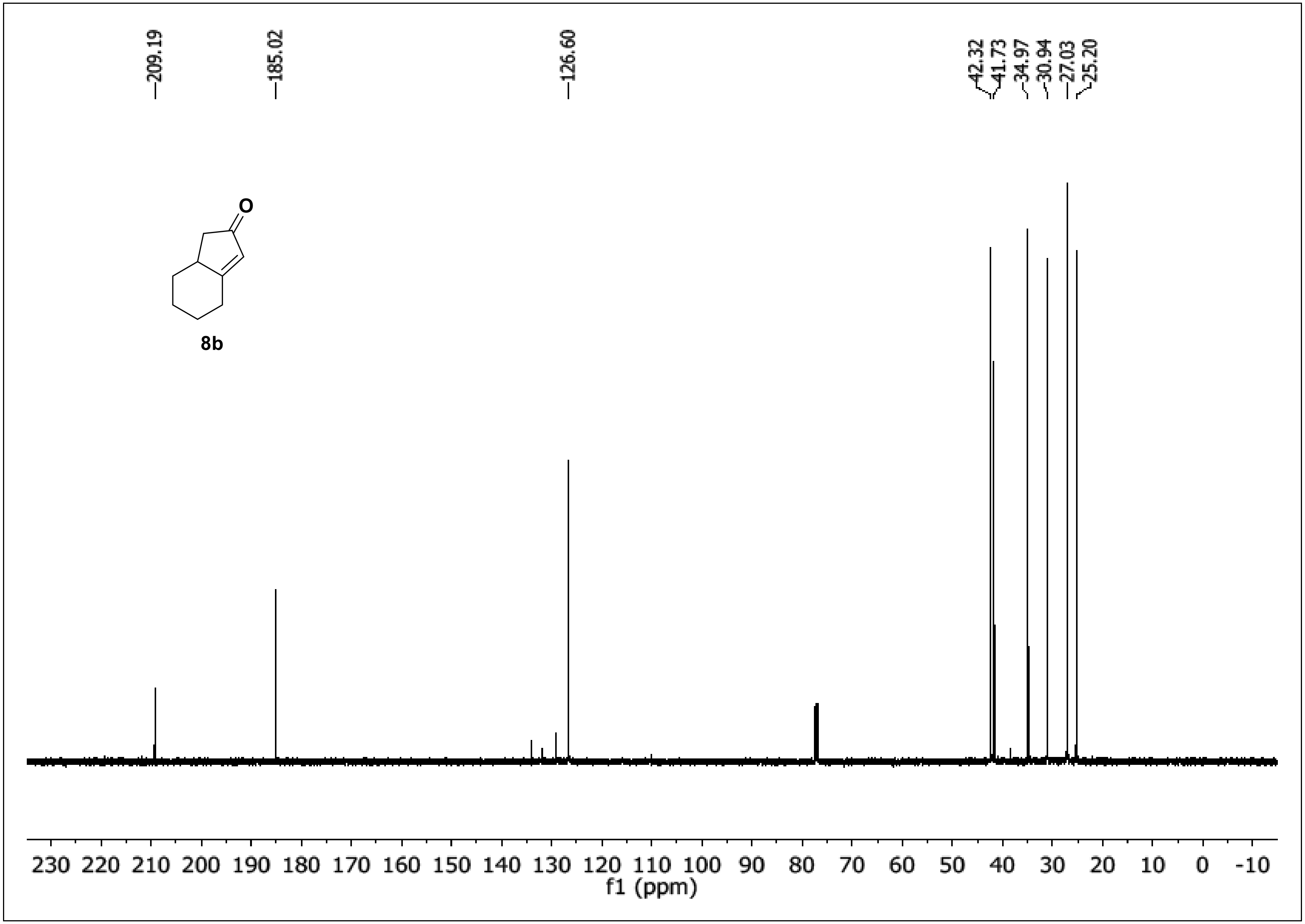

6.05
5.44
5.43
4.34
4.22
1.30
1.22
1.07
OPiv
TIPSO
OEt
O
7p
1.00
1.98
1.98
1.89
3.01
8.83
20.79
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


176.58
152.94
142.36
114.22
82.09
77.69
63.09
62.67
62.17
38.84
26.96
17.94
13.95
11.93
OPiv
TIPSO
OEt
O
7p
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


5.86
5.83
5.02
5.02
4.95
4.94
4.94
4.74
4.73
4.72
4.71
4.71
2.85
2.75
2.63
2.54
2.48
2.46
2.43
2.33
2.32
2.29
2.21
2.03
1.98
1.93
1.81
1.81
1.81
1.81
1.81
1.74
1.73
1.73
1.67
1.38
1.15
1.12
O
8a
1.62
1.00
1.01
1.51
1.20
1.52
1.53
1.44
3.21
2.14
1.42
2.85
2.95
2.11
1.67
1.59
0.79
.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.
f1 (ppm)

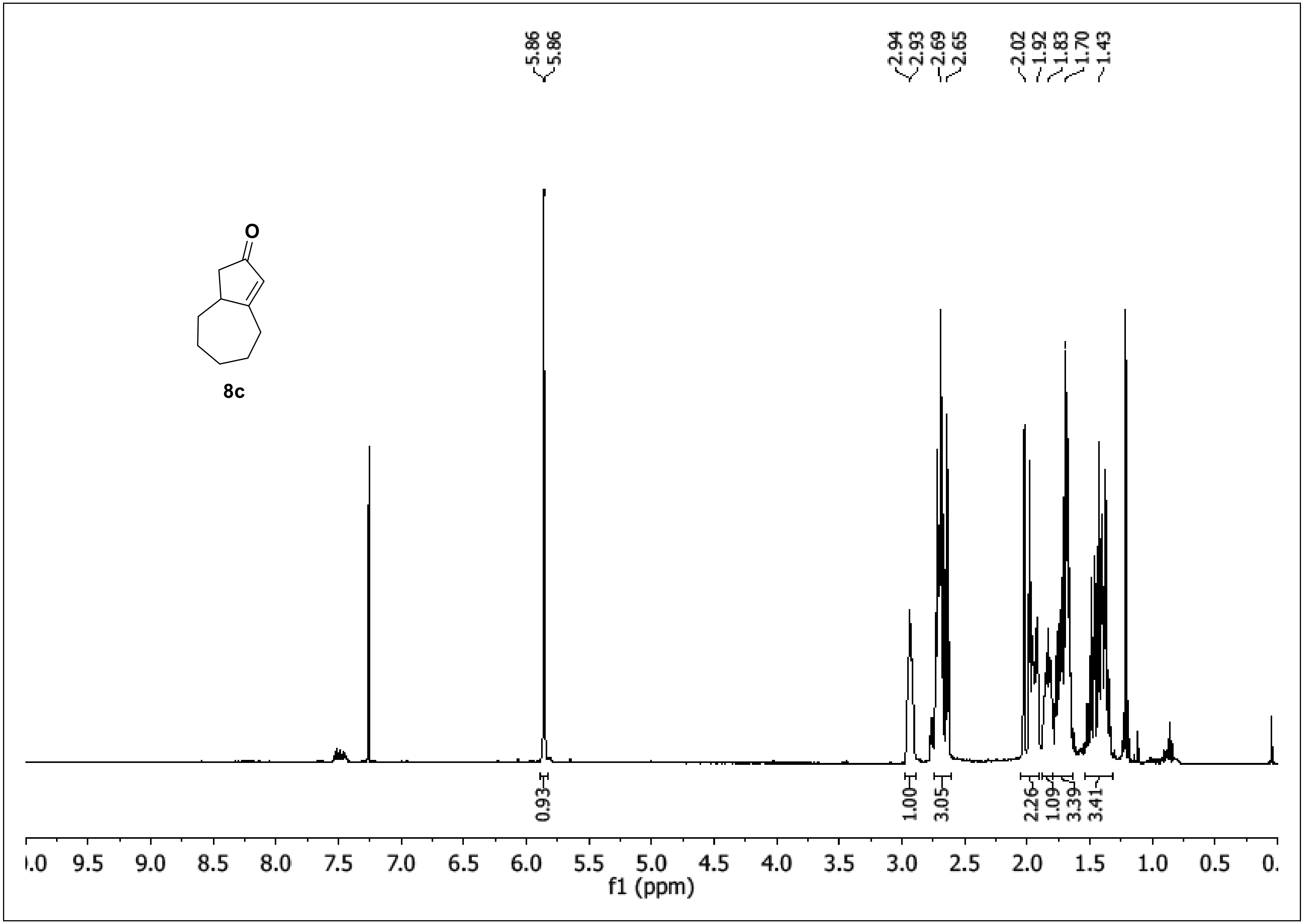

209.06
185.44
183.76
148.34
145.09
126.98
126.51
111.45
109.46
44.18
42.44
42.30
41.51
39.65
38.51
37.18
36.58
31.89
30.50
28.67
26.90
22.55
20.83
O
8a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

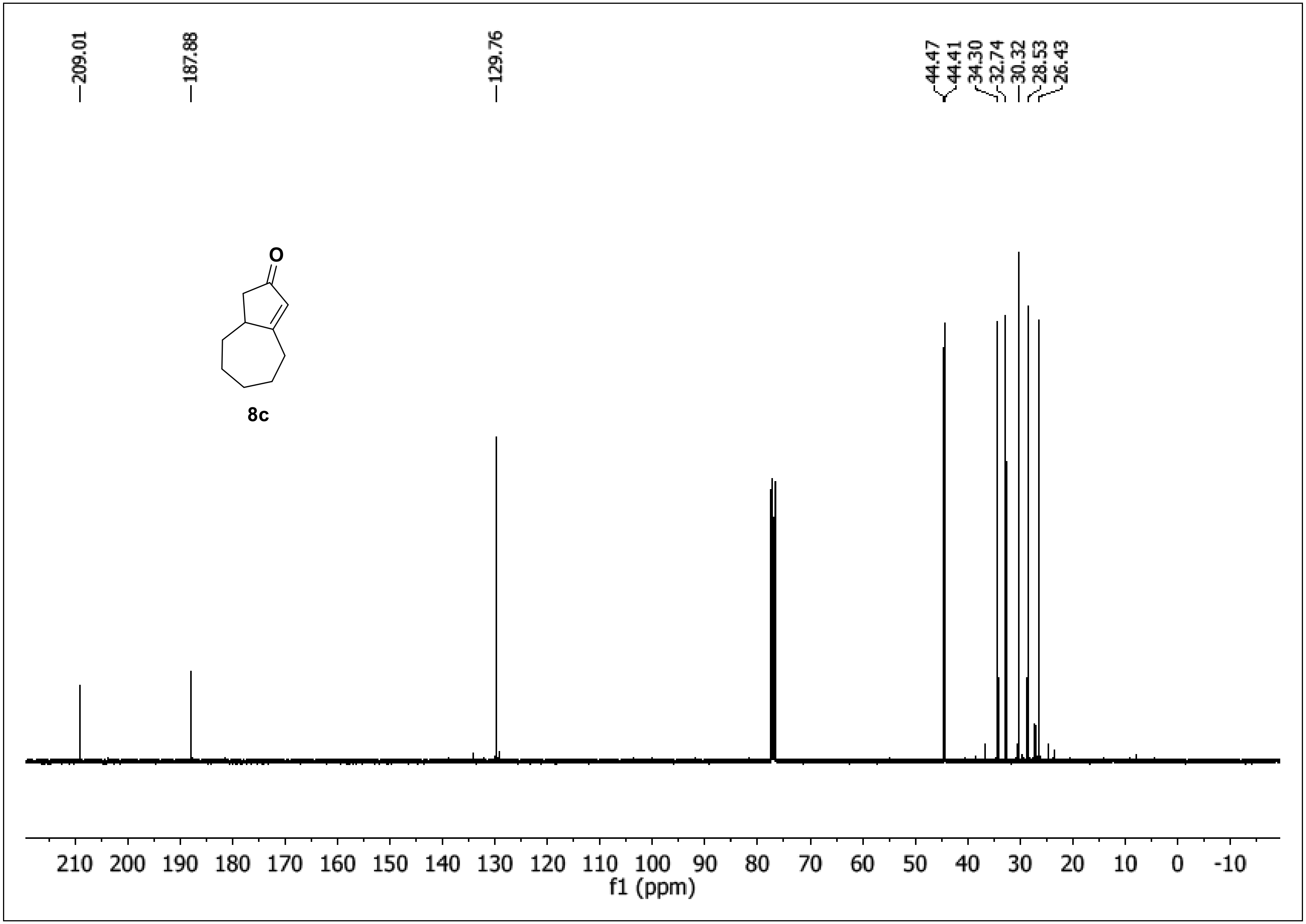

7.26
5.81
2.81
2.81
2.78
2.58
2.53
2.53
2.18
1.98
1.94
1.81
1.81
1.50
1.46
1.41
1.21
1.13
1.12
O
8b
0.90
1.00
0.94
1.07
2.10
2.08
0.96
2.27
0.97
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)



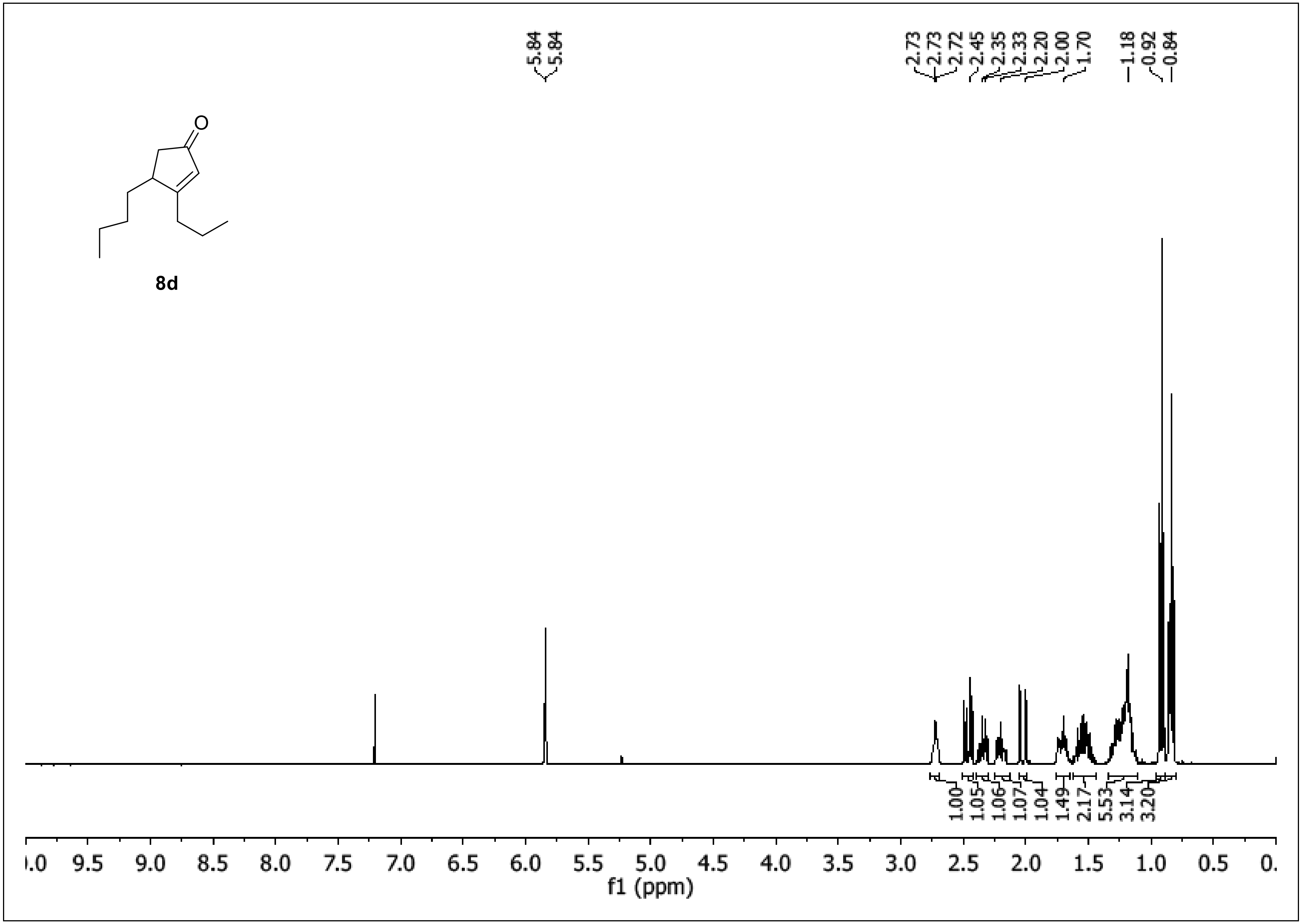
8b

209.19
185.02
126.60
42.32
41.73
34.97
30.94
27.03
25.20
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

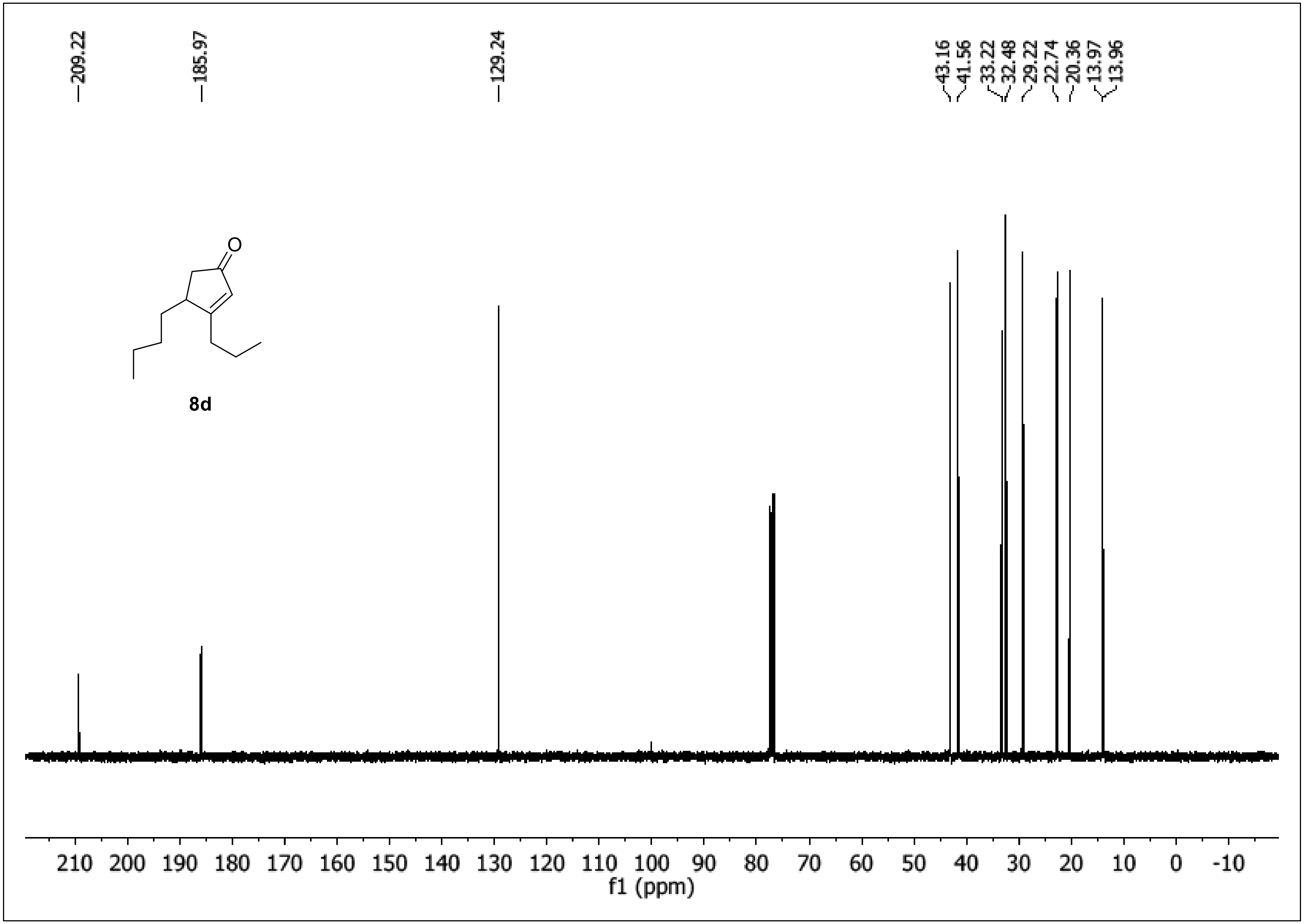

5.86
5.86
2.94
2.93
2.69
2.65
2.02
1.92
1.83
1.70
1.43
O
8c
0.93
1.00
3.05
2.26
1.09
3.39
3.41
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

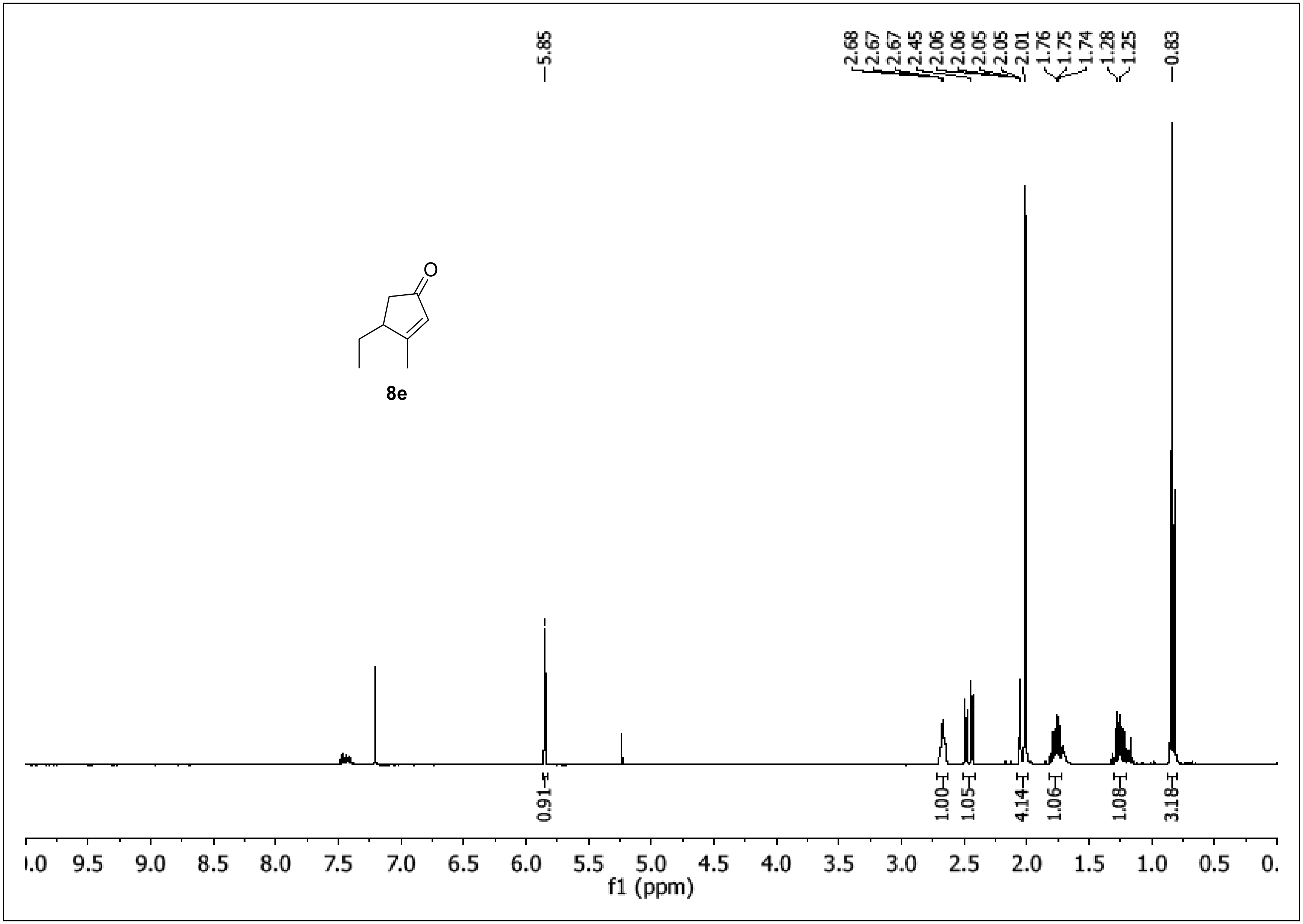

209.01
187.88
129.76
44.47
44.41
34.30
32.74
30.32
28.53
26.43
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

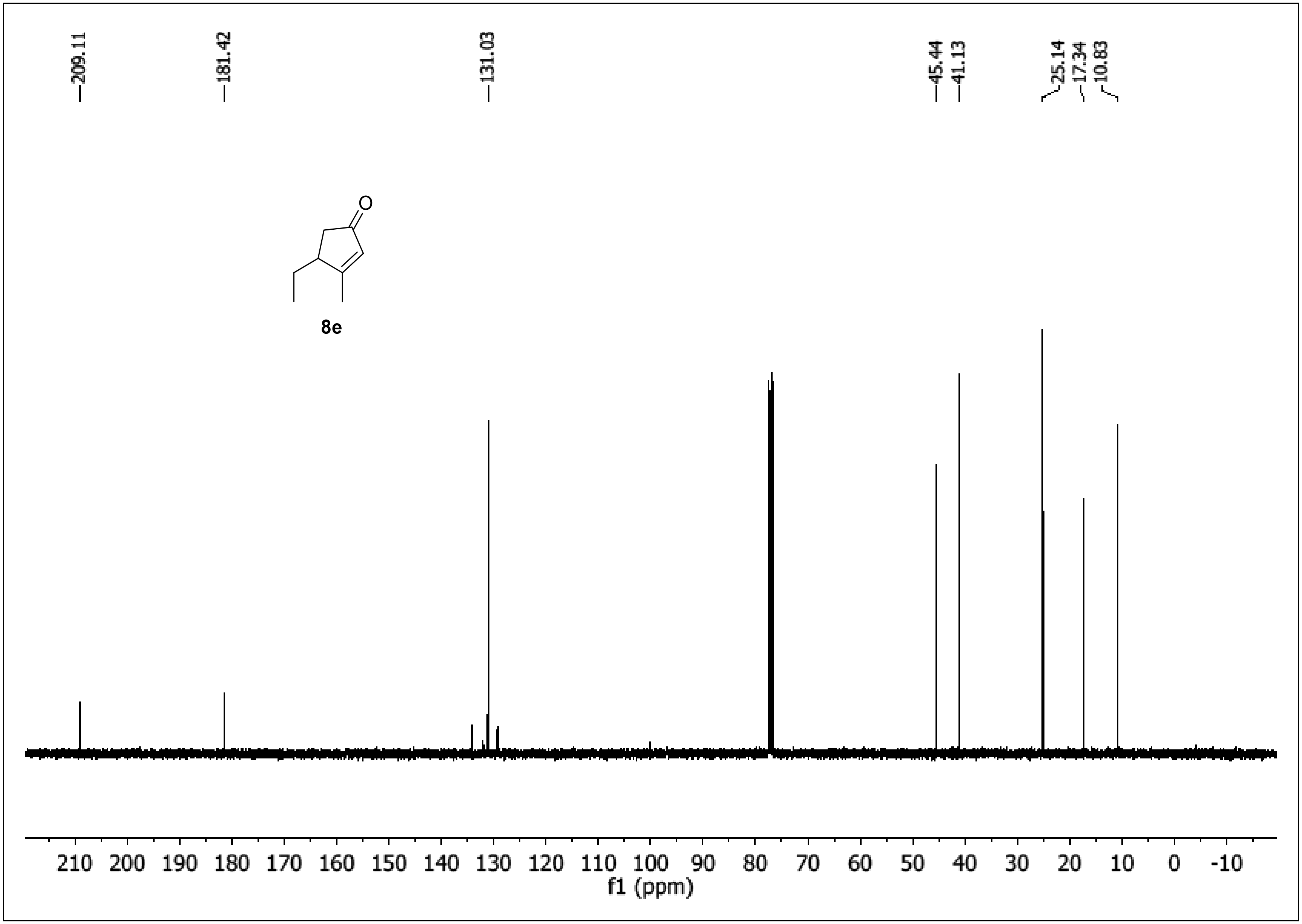
8c



8d
5.84
5.84
2.73
2.73
2.72
2.45
2.35
2.33
2.20
2.00
1.70
1.18
0.92
0.84
1.00
1.05
1.06
1.07
1.04
1.49
2.17
5.53
3.14
3.20
.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.
f1 (ppm)

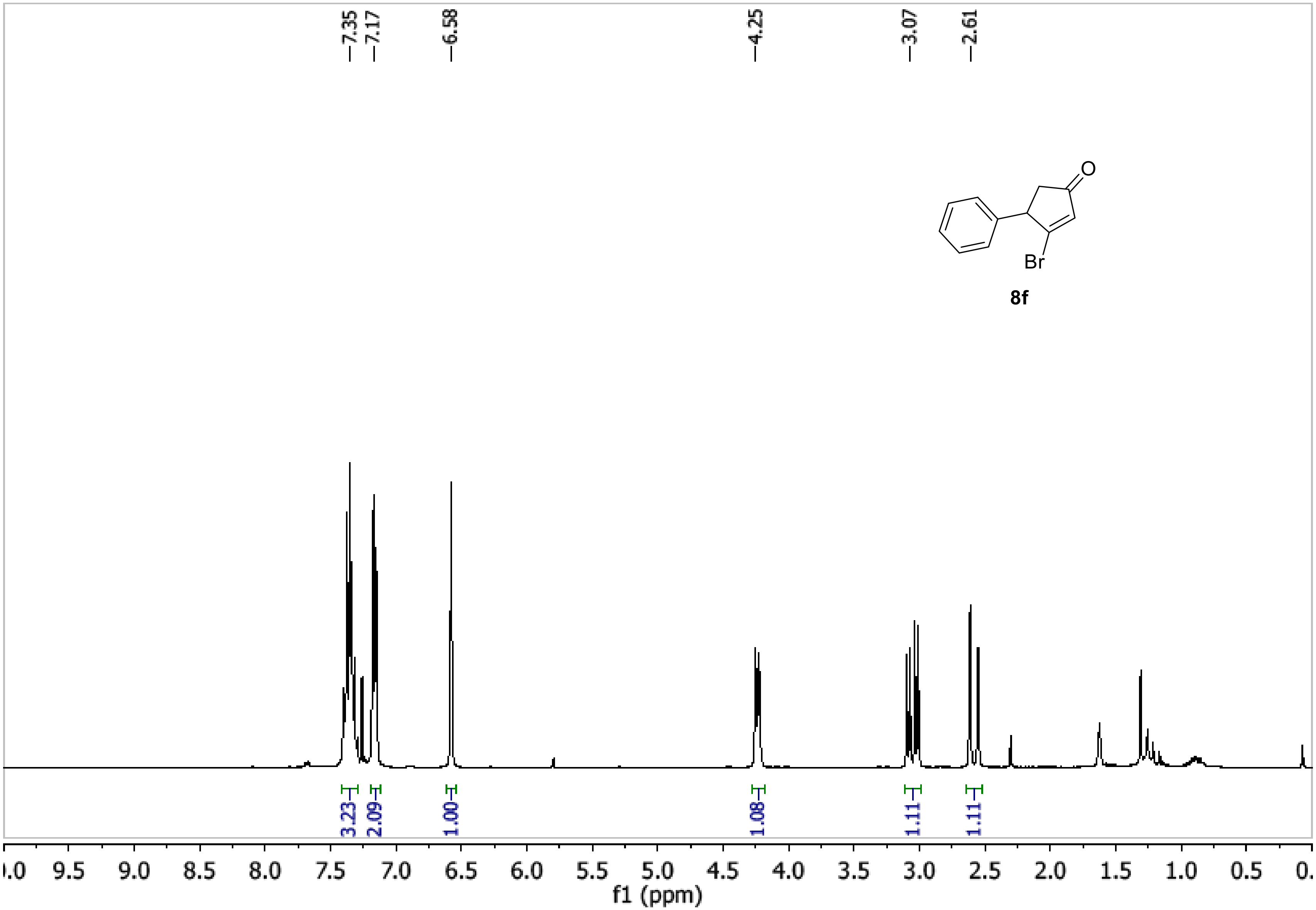

209.22
185.97
129.24
43.16
41.56
33.22
32.48
29.22
22.74
20.36
13.97
13.96
O
8d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


5.85
2.68
2.67
2.67
2.45
2.06
2.06
2.05
2.05
2.01
1.76
1.75
1.74
1.28
1.25
0.83
O
8e
0.91
1.00
1.05
4.14
1.06
1.08
3.18
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)

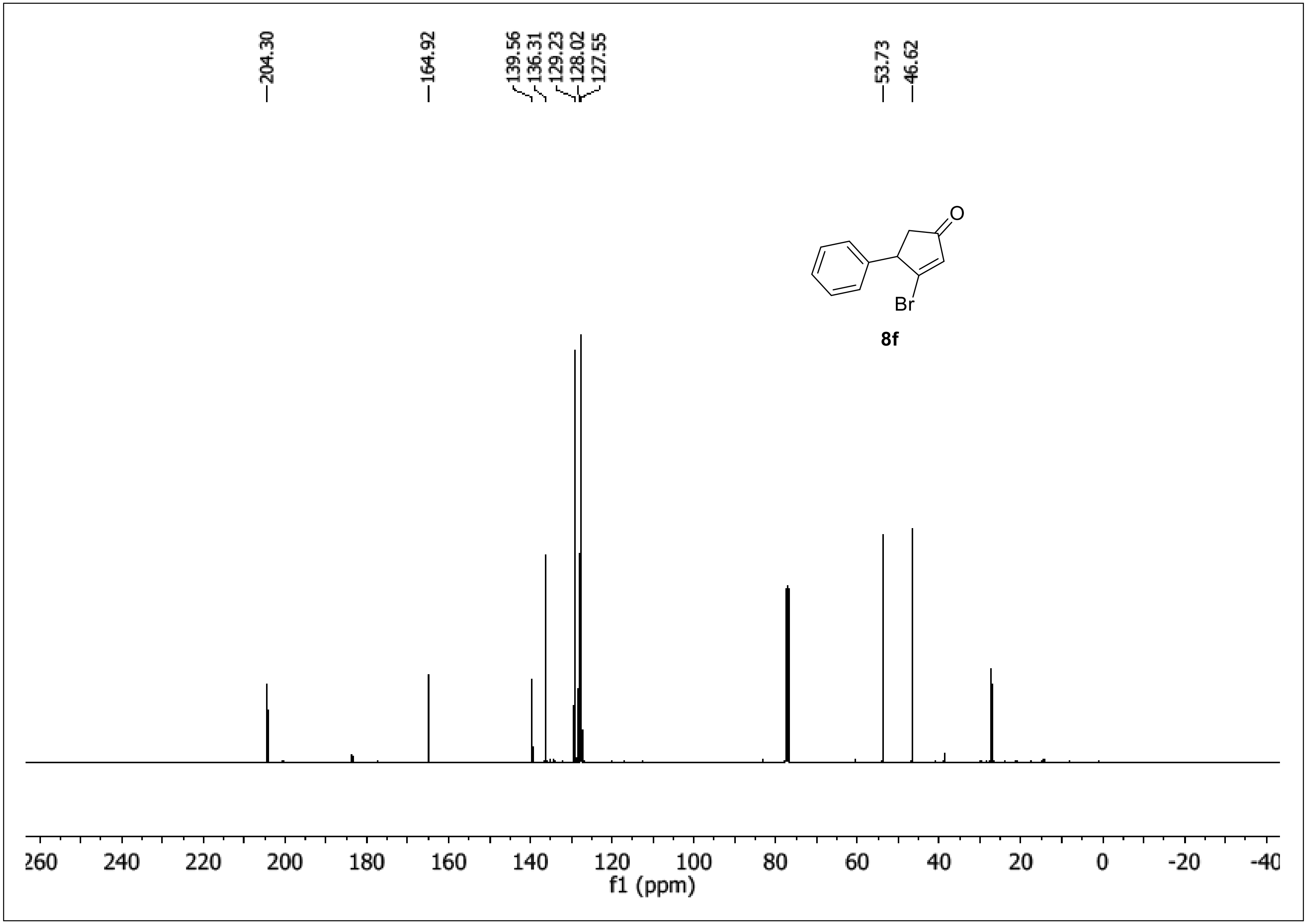


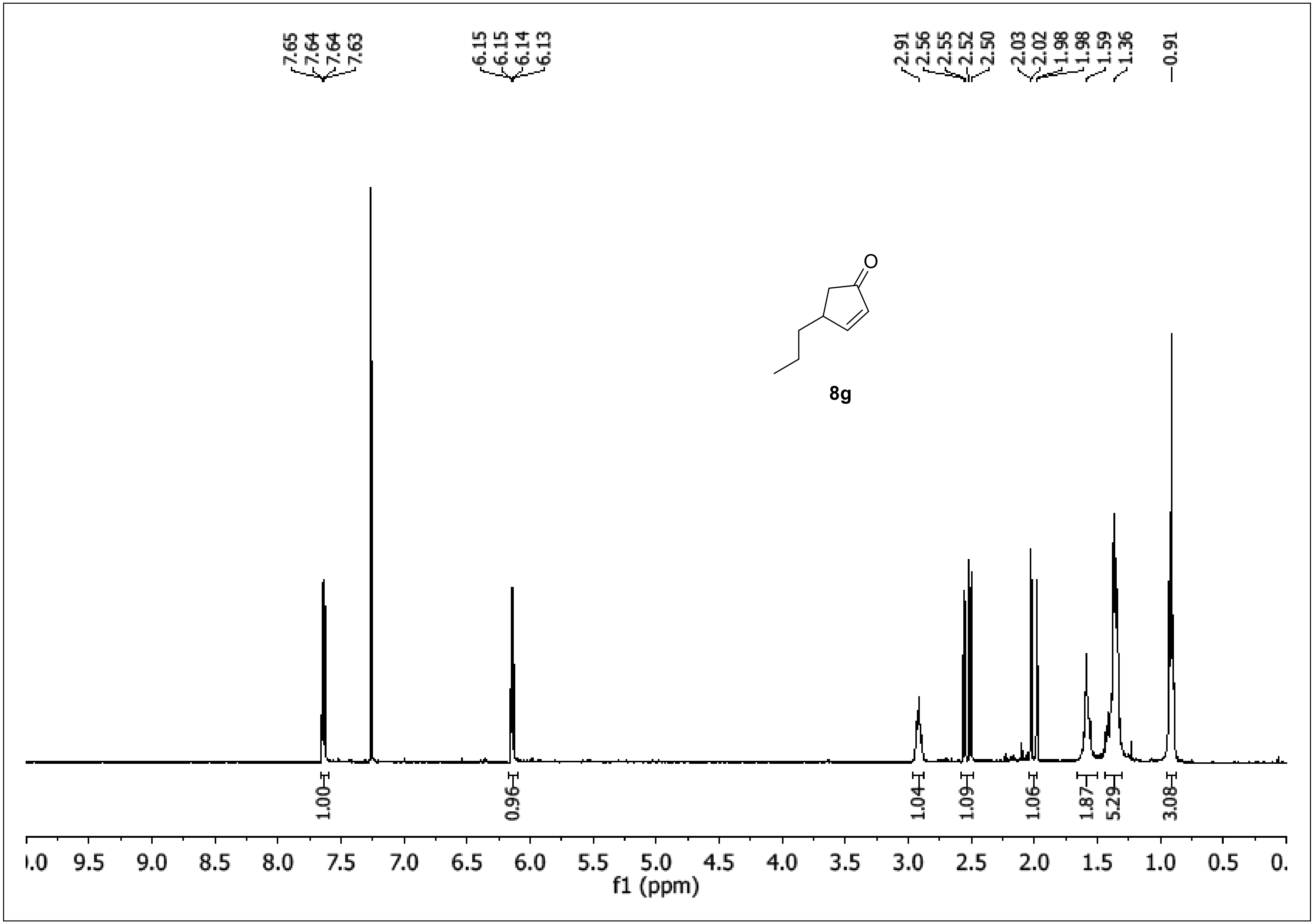
8e

209.11
181.42
131.03
45.44
41.13
25.14
17.34
10.83
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)

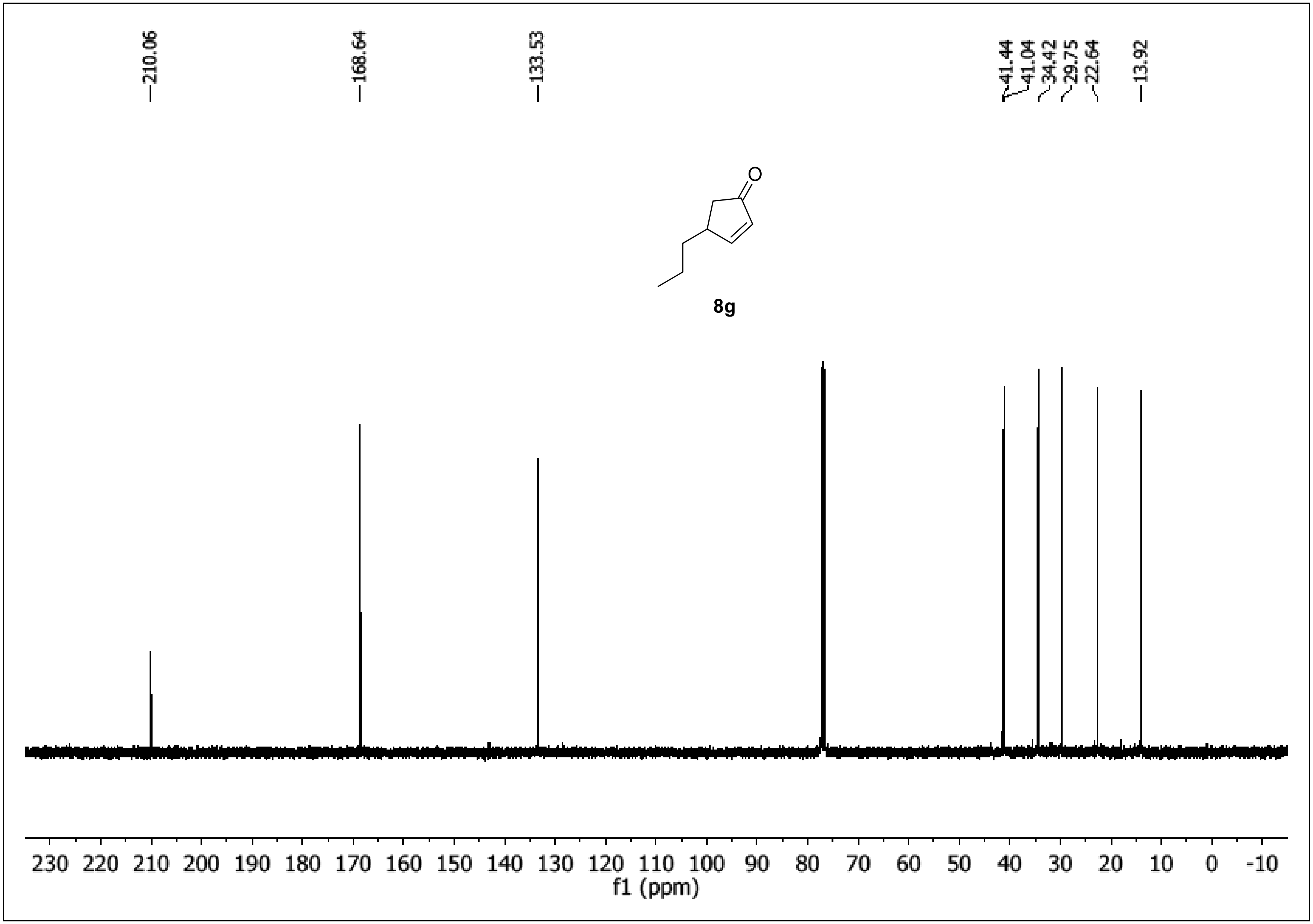

7.35
7.17
6.58
4.25
3.07
2.61
O
Br
3.23
2.09
1.00
1.08
1.11
1.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

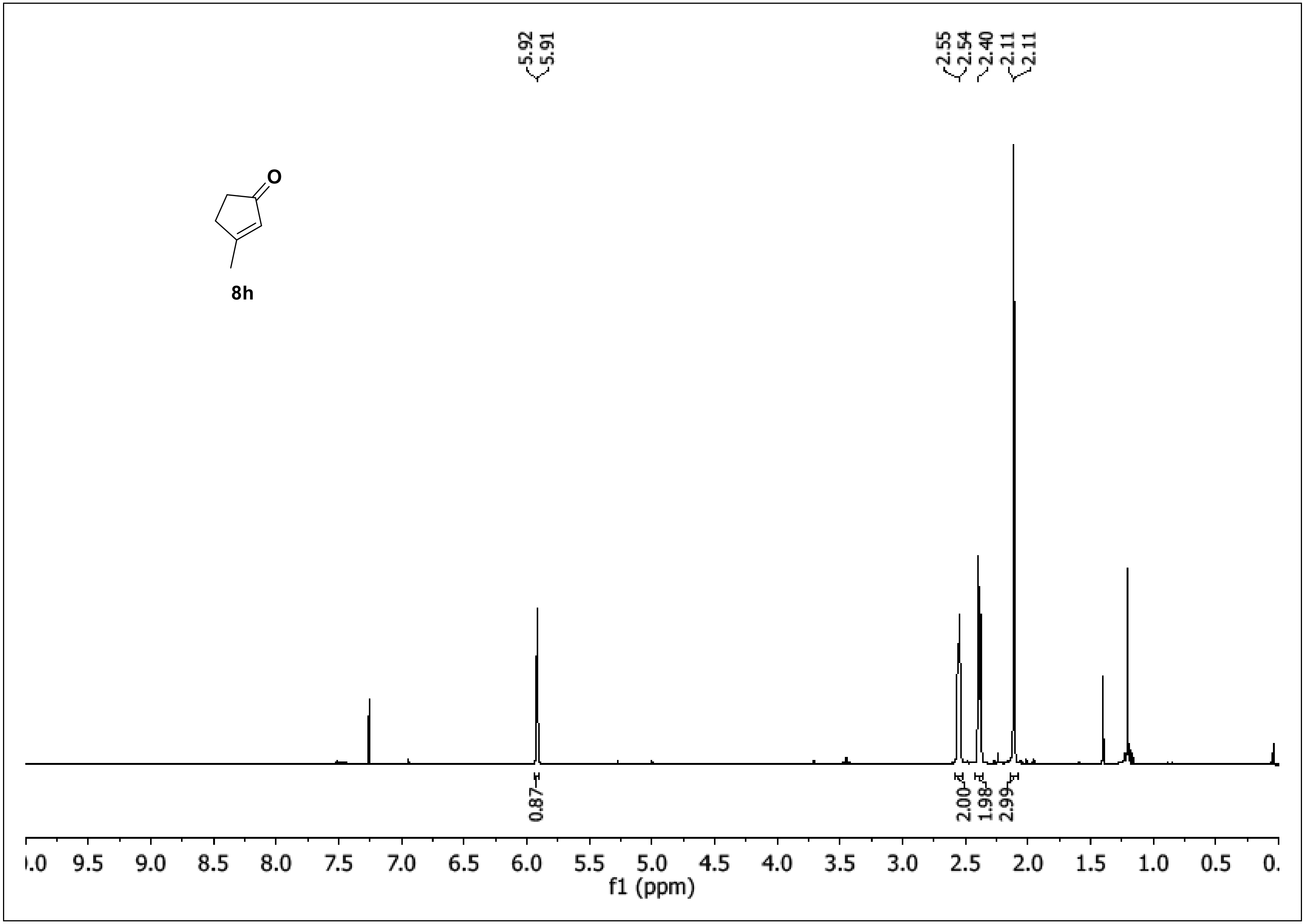
8f


204.30
164.92
139.56
136.31
129.23
128.02
127.55
53.73
46.62
O
Br
8f
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
f1 (ppm)

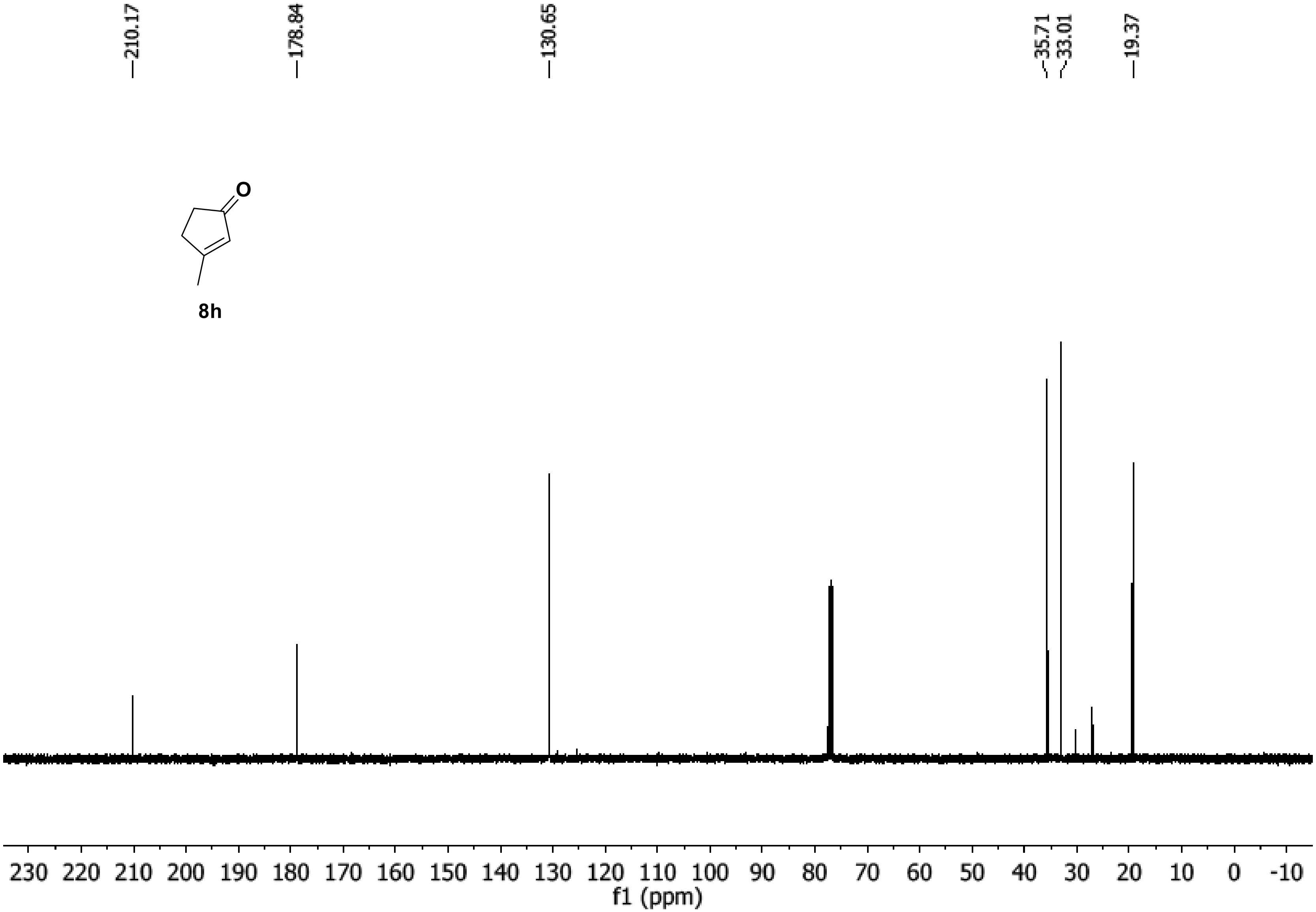

7.65
7.64
7.64
7.63
6.15
6.15
6.14
6.13
2.91
2.56
2.55
2.52
2.50
2.03
2.02
1.98
1.98
1.59
1.36
0.91
O
1.00
0.96
1.04
1.09
1.06
1.87
5.29
3.08
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

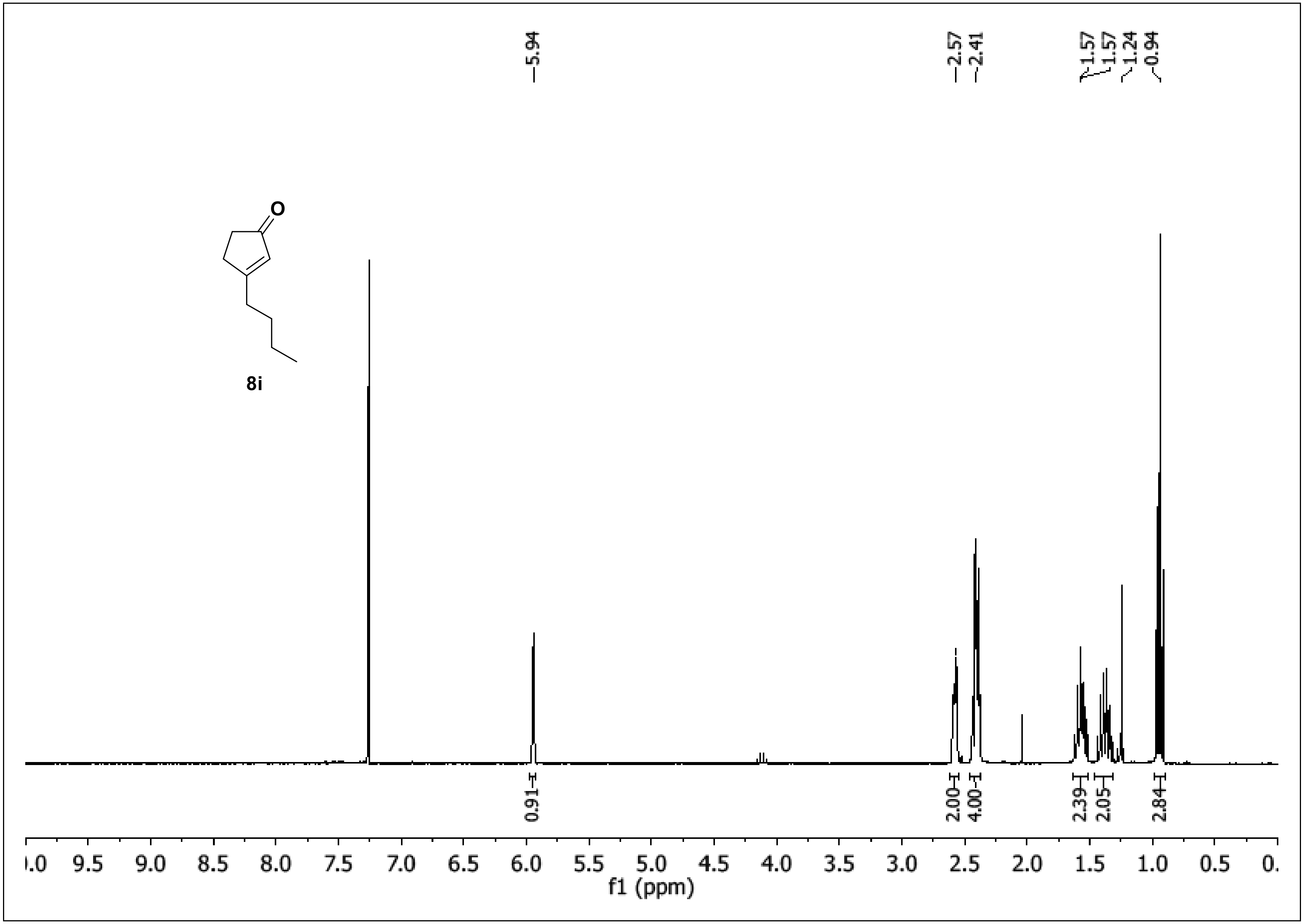
8g

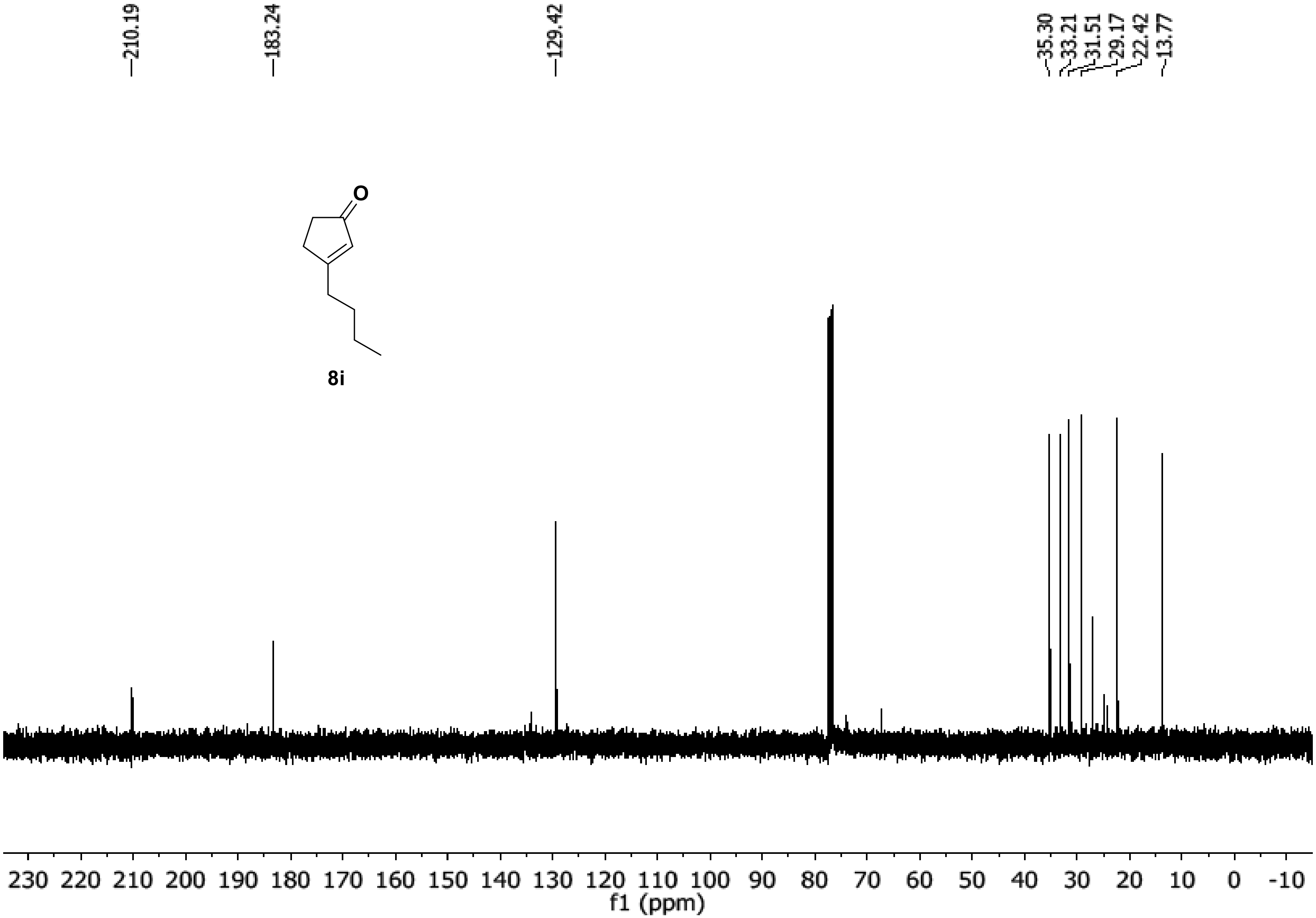

210.06
168.64
133.53
41.44
41.04
34.42
29.75
22.64
13.92
O
8g
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8h

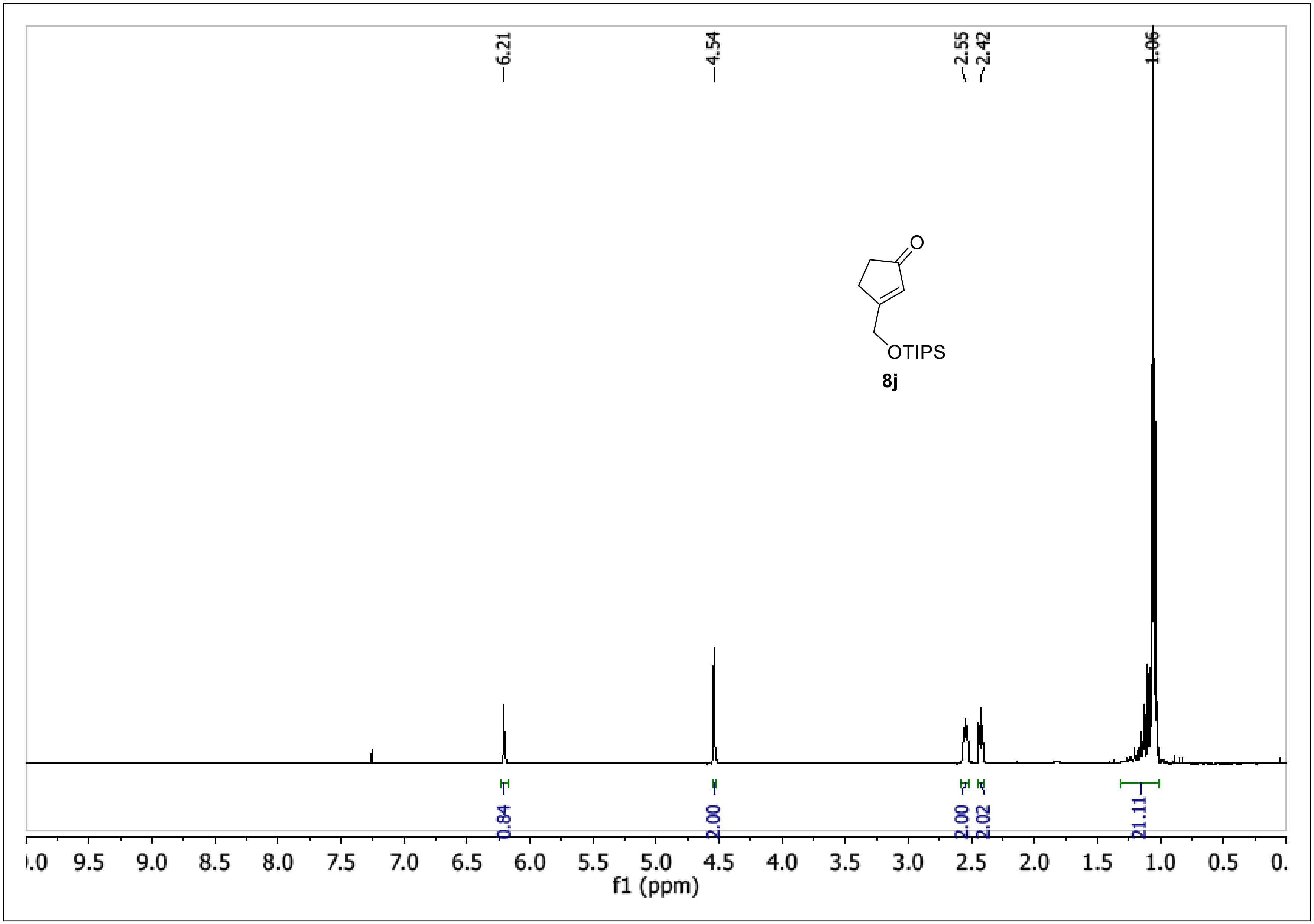
O
5.92
5.91
2.55
2.54
2.40
2.11
2.11
0.87
2.00
1.98
2.99
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

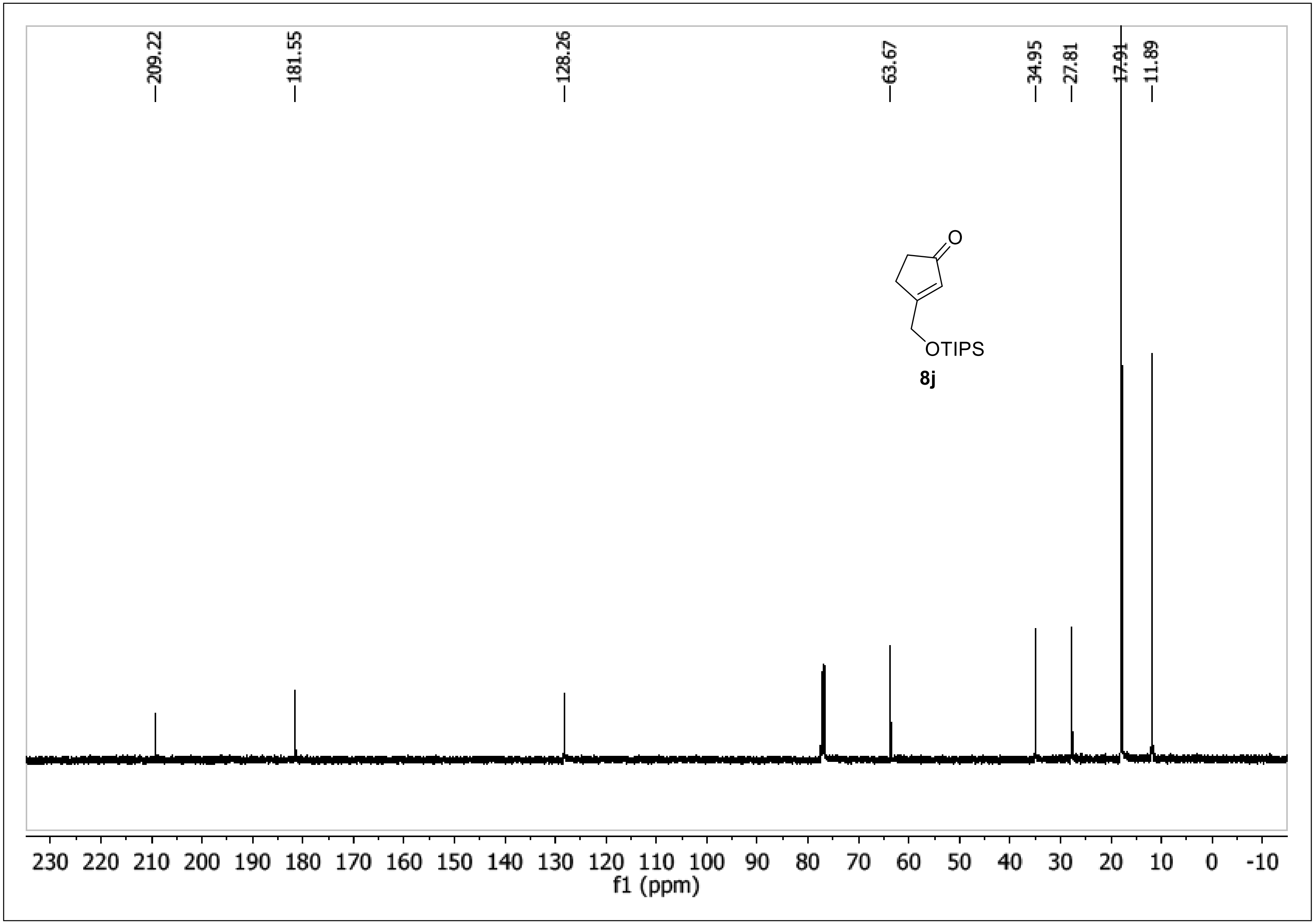

210.17
178.84
130.65
35.71
33.01
19.37
O
8h
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


5.94
2.57
2.41
1.57
1.57
1.24
0.94
O
8i
0.91
2.00
4.00
2.39
2.05
2.84
.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.
f1 (ppm)

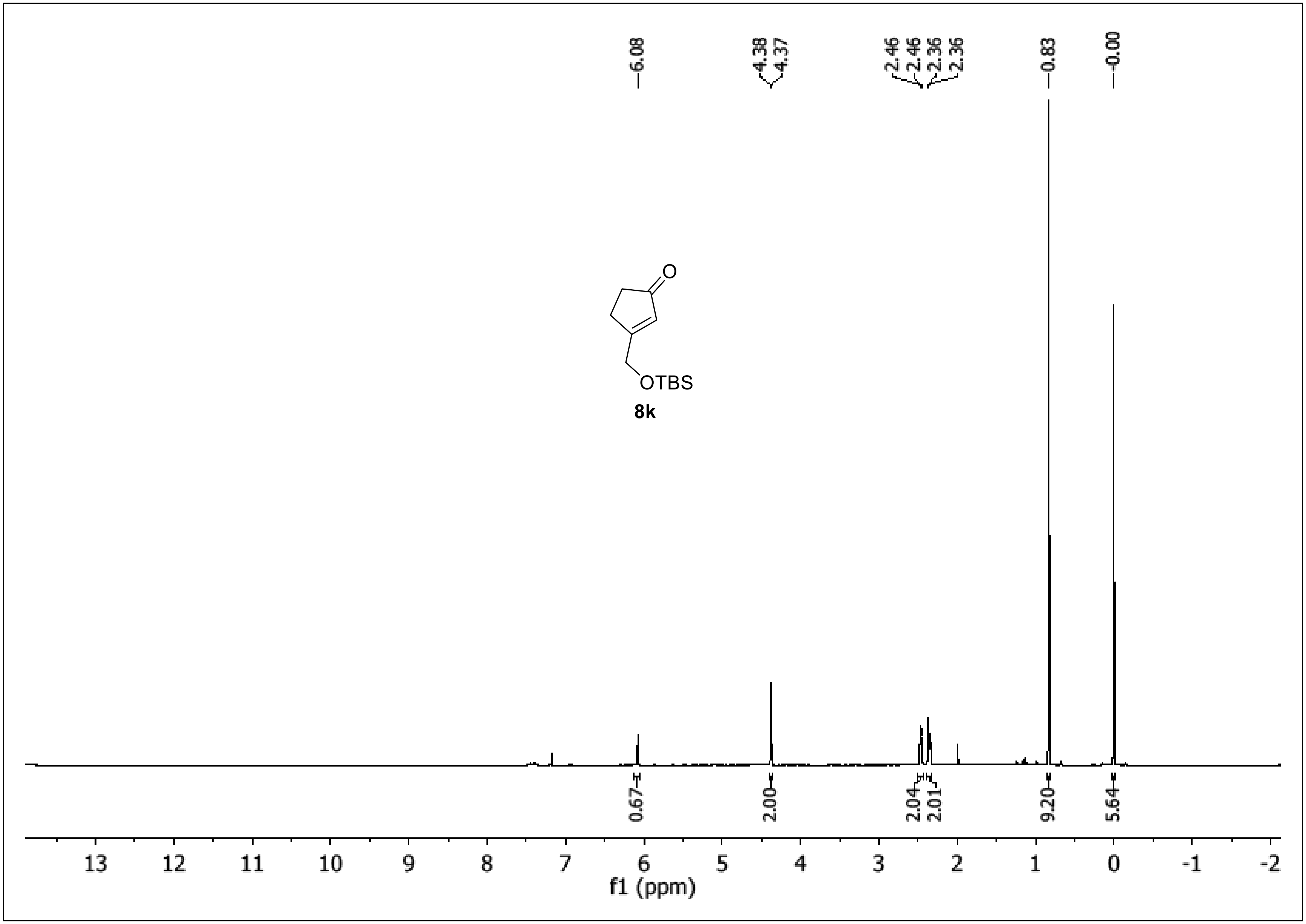


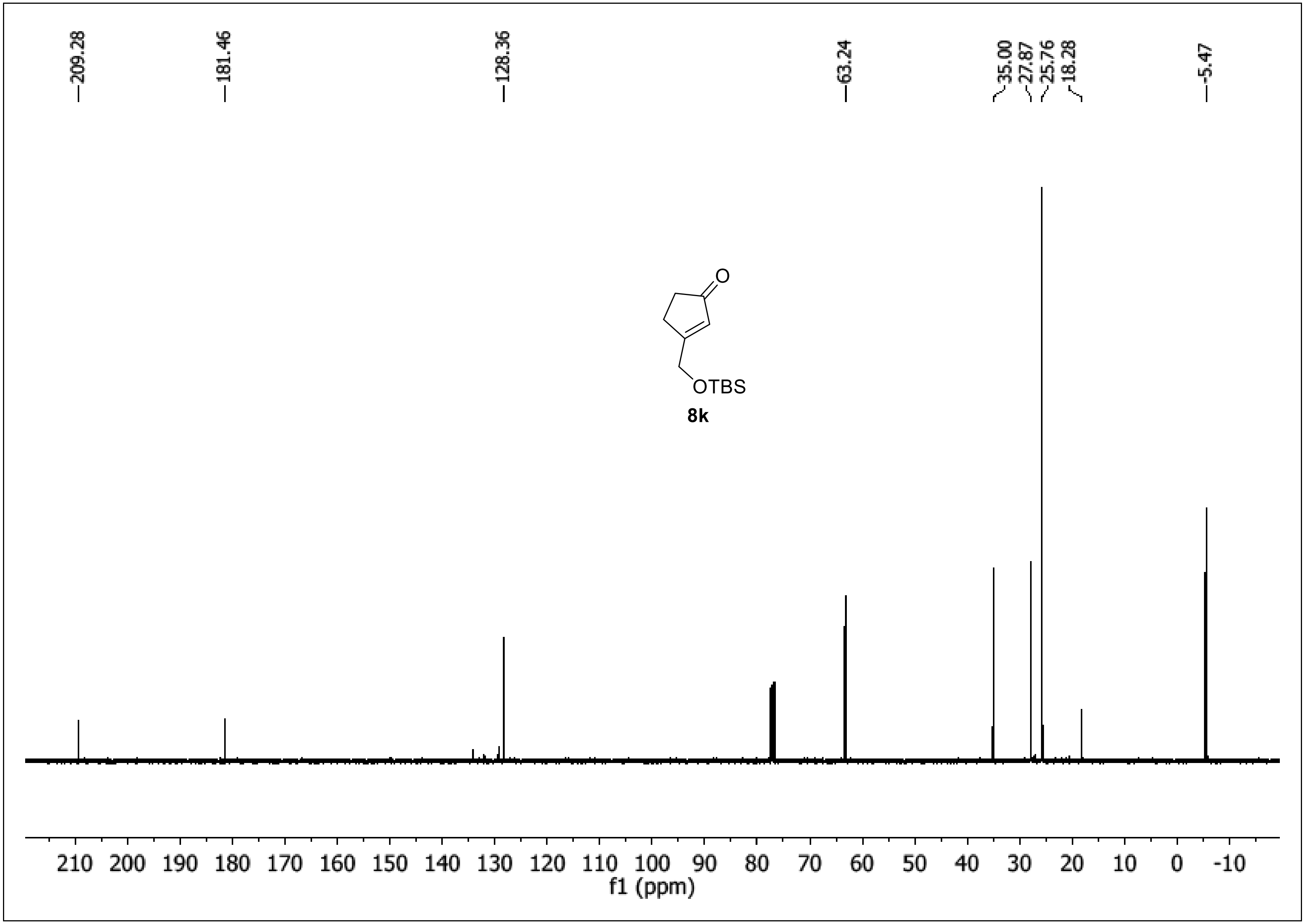
210.19
183.24
129.42
35.30
33.21
31.51
29.17
22.42
13.77
O
8i
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

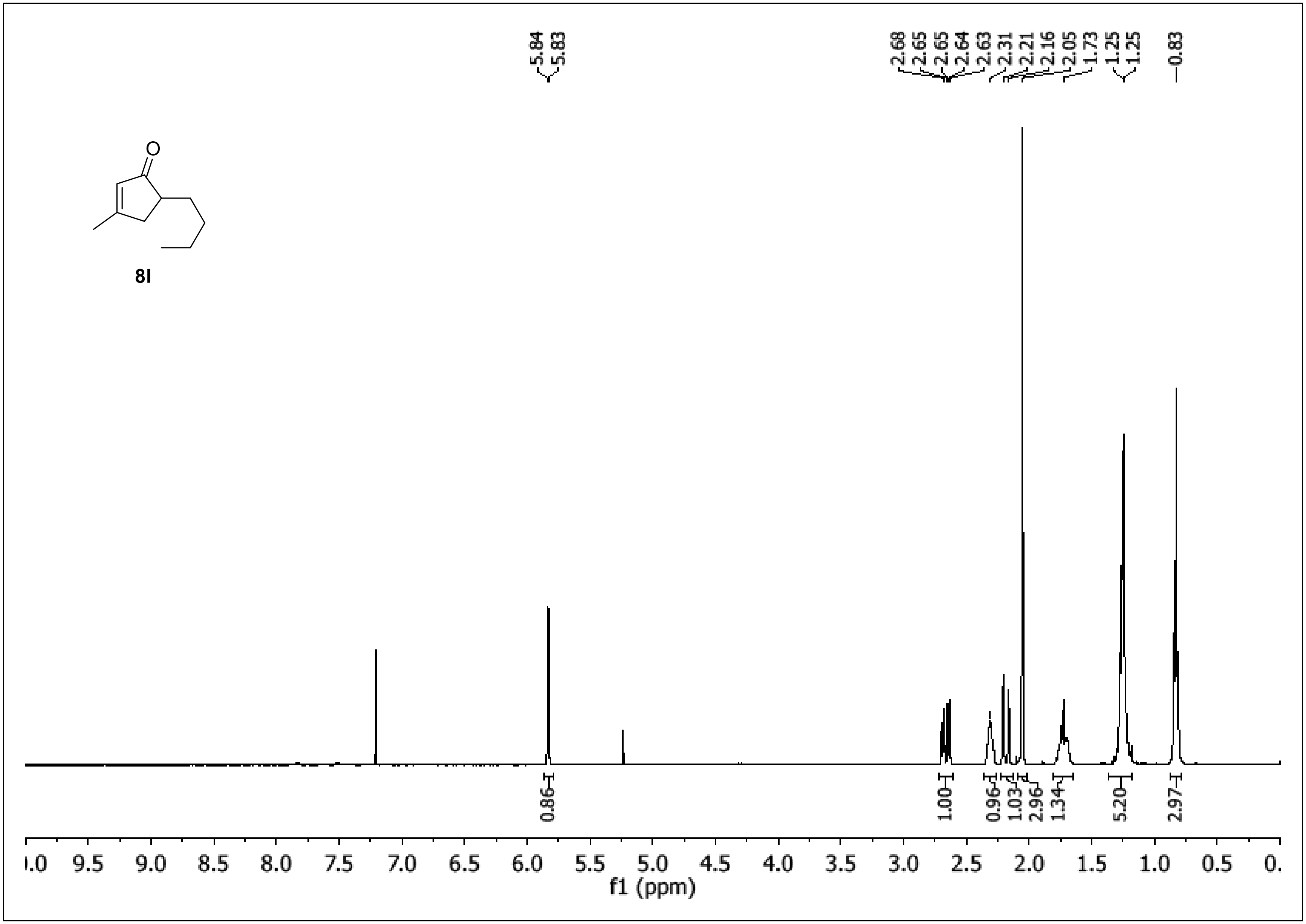

6.21
4.54
2.55
2.42
1.06
O
OTIPS
8j
0.84
2.00
2.00
2.02
21.11
.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

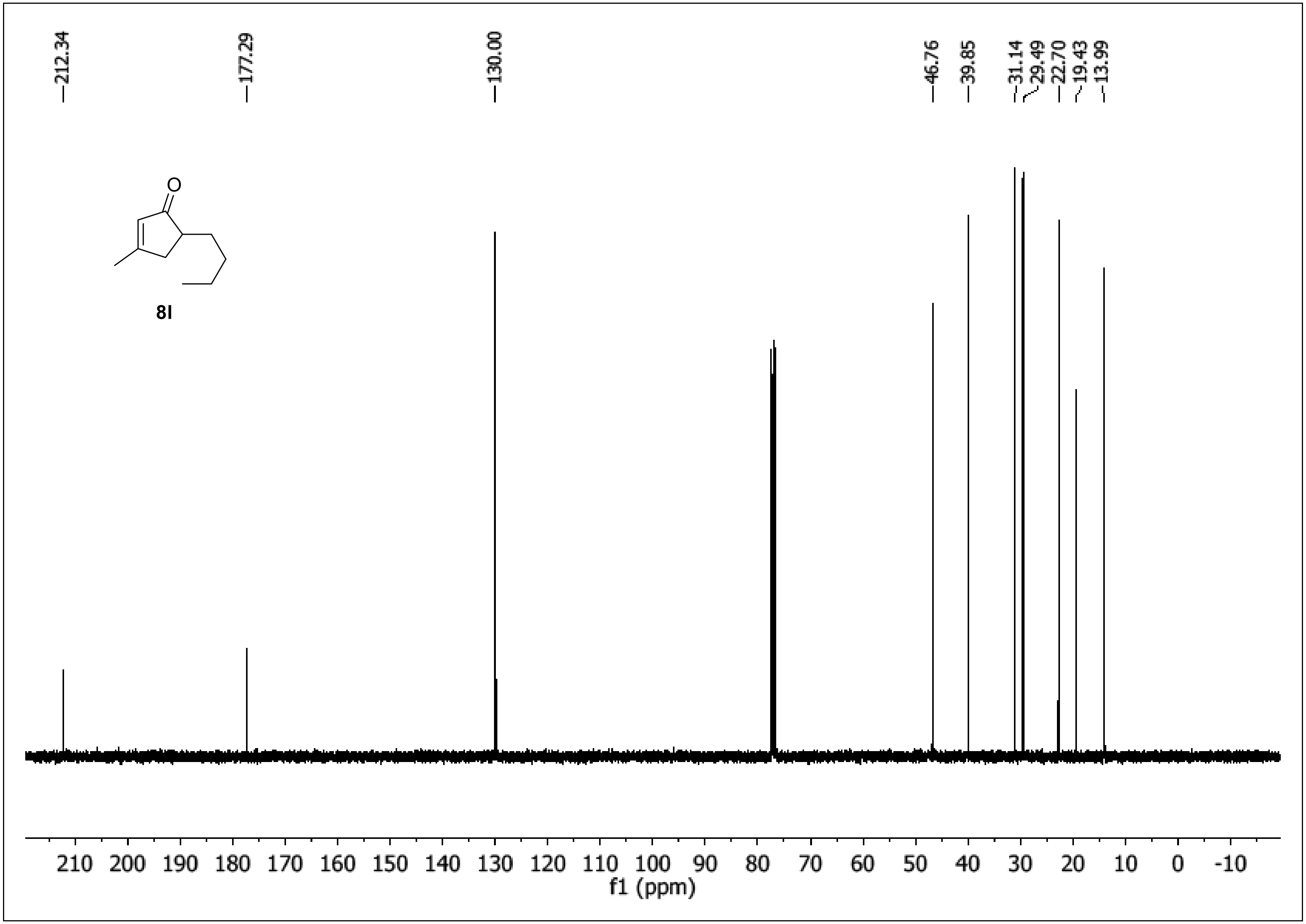

209.22
181.55
128.26
63.67
34.95
27.81
17.91
11.89
O
OTIPS
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

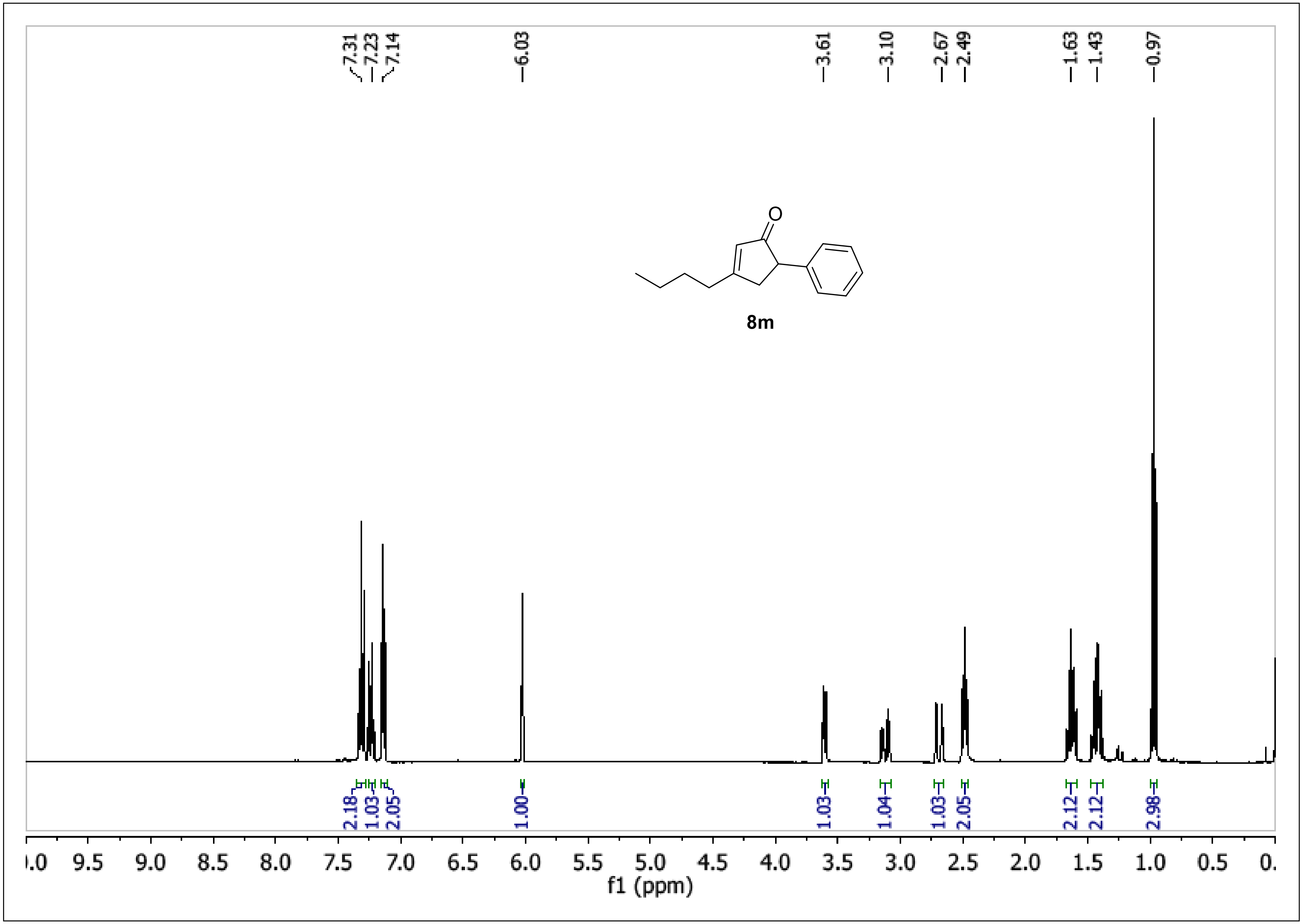
8j


6.08
4.38
4.37
2.46
2.46
2.36
2.36
0.83
-0.00
O
OTBS
8k
0.67
2.00
2.04
2.01
9.20
5.64
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)

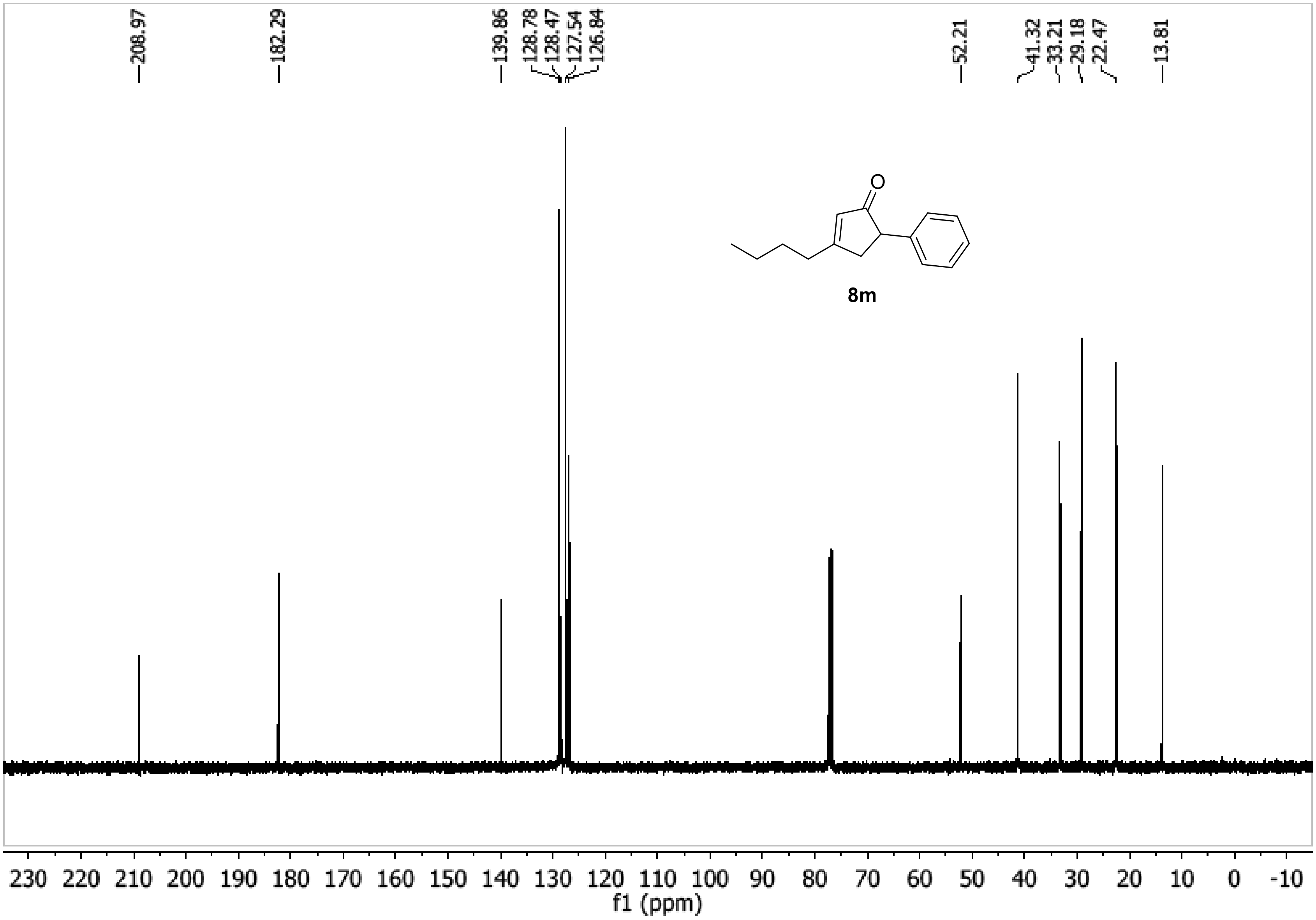

209.28
181.46
128.36
63.24
35.00
27.87
25.76
18.28
-5.47
O
OTBS
8k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8l
O
5.84
5.83
2.68
2.65
2.65
2.64
2.63
2.31
2.21
2.16
2.05
1.73
1.25
1.25
0.83
0.86
1.00
0.96
1.03
2.96
1.34
5.20
2.97
.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.
f1 (ppm)

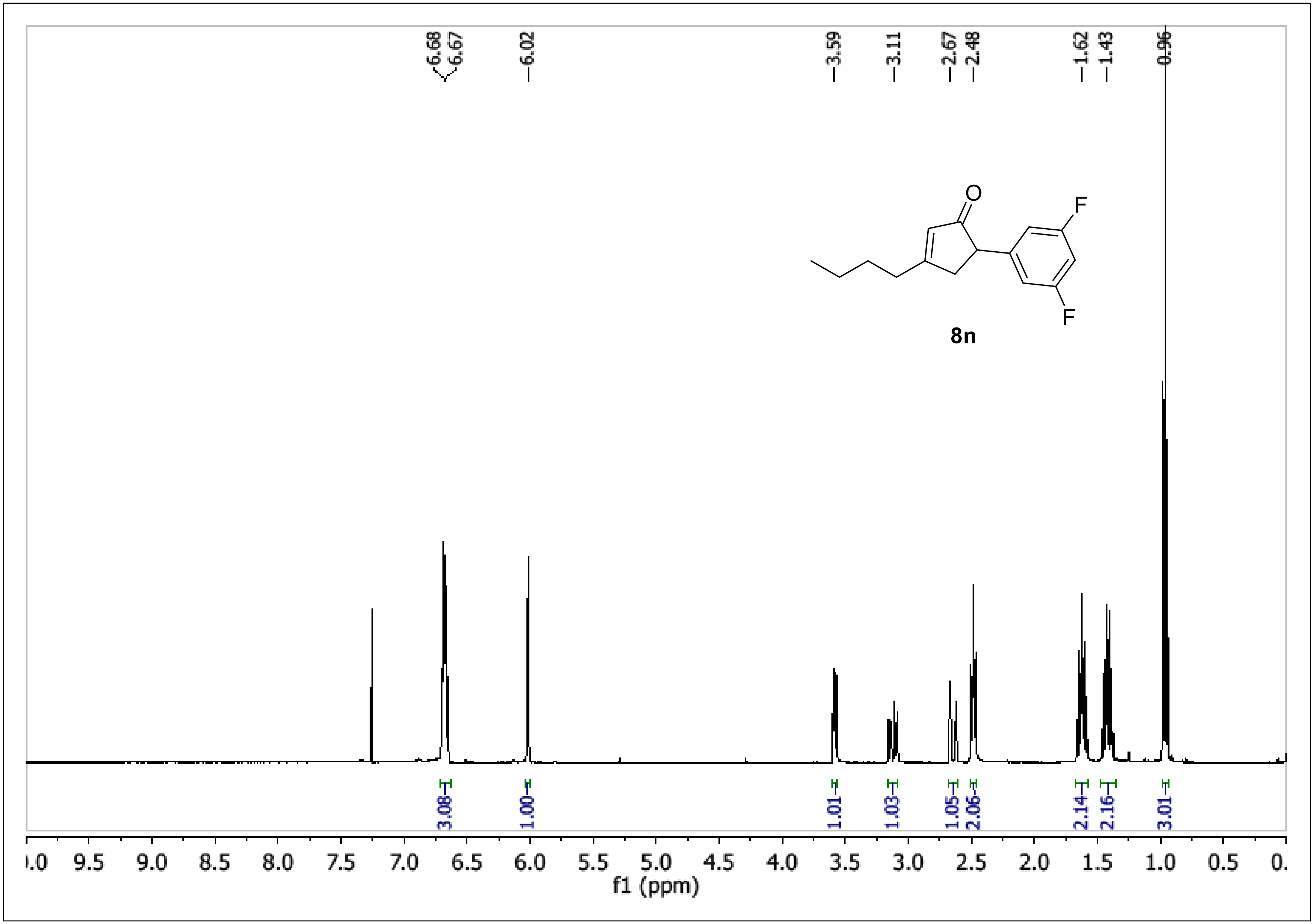

212.34
177.29
130.00
46.76
39.85
31.14
29.49
22.70
19.43
13.99
O
8l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.31
7.23
7.14
6.03
3.61
3.10
2.67
2.49
1.63
1.43
0.97
O
2.18
1.03
2.05
1.00
1.03
1.04
1.03
2.05
2.12
2.12
2.98
.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.
f1 (ppm)

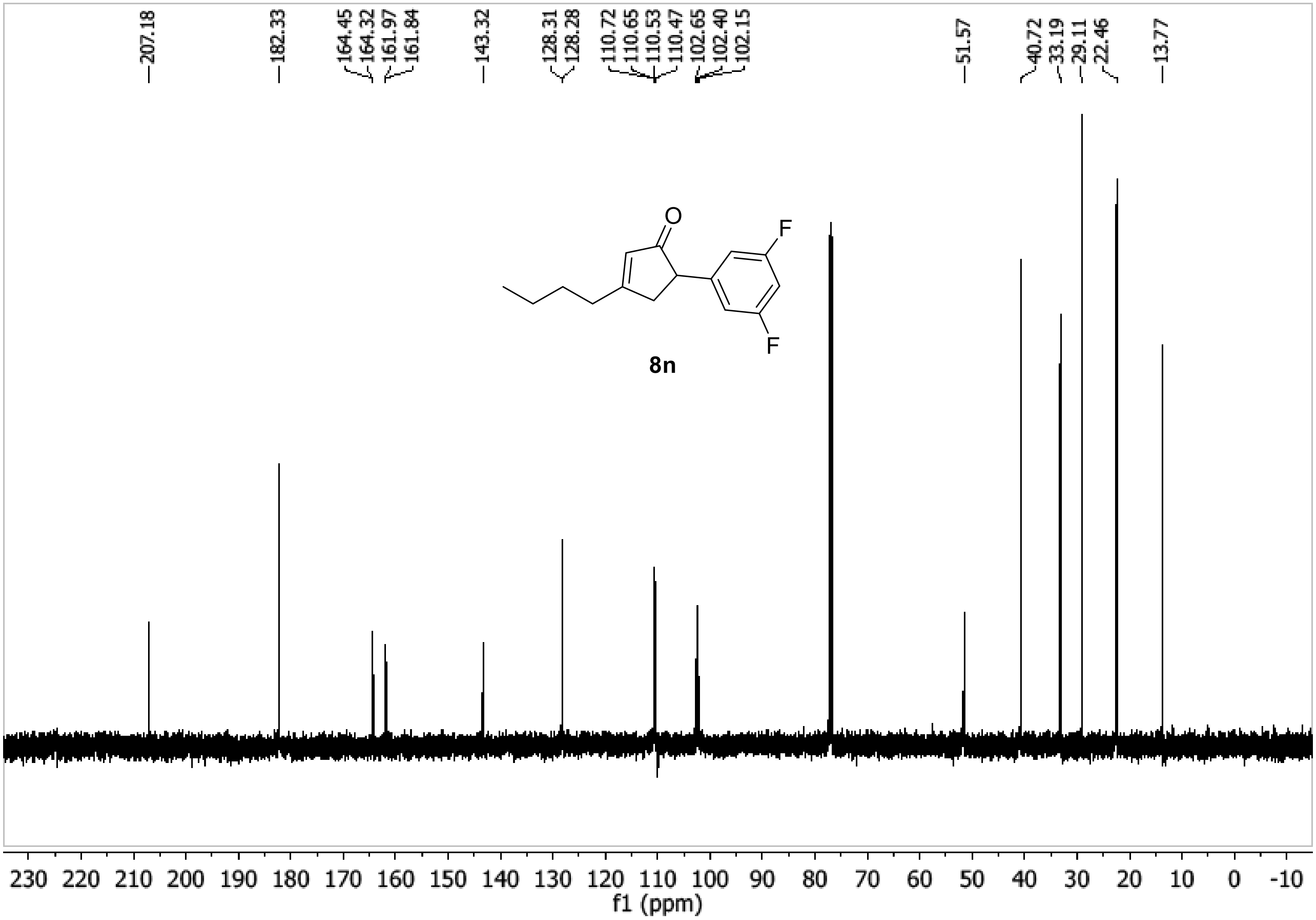
8m

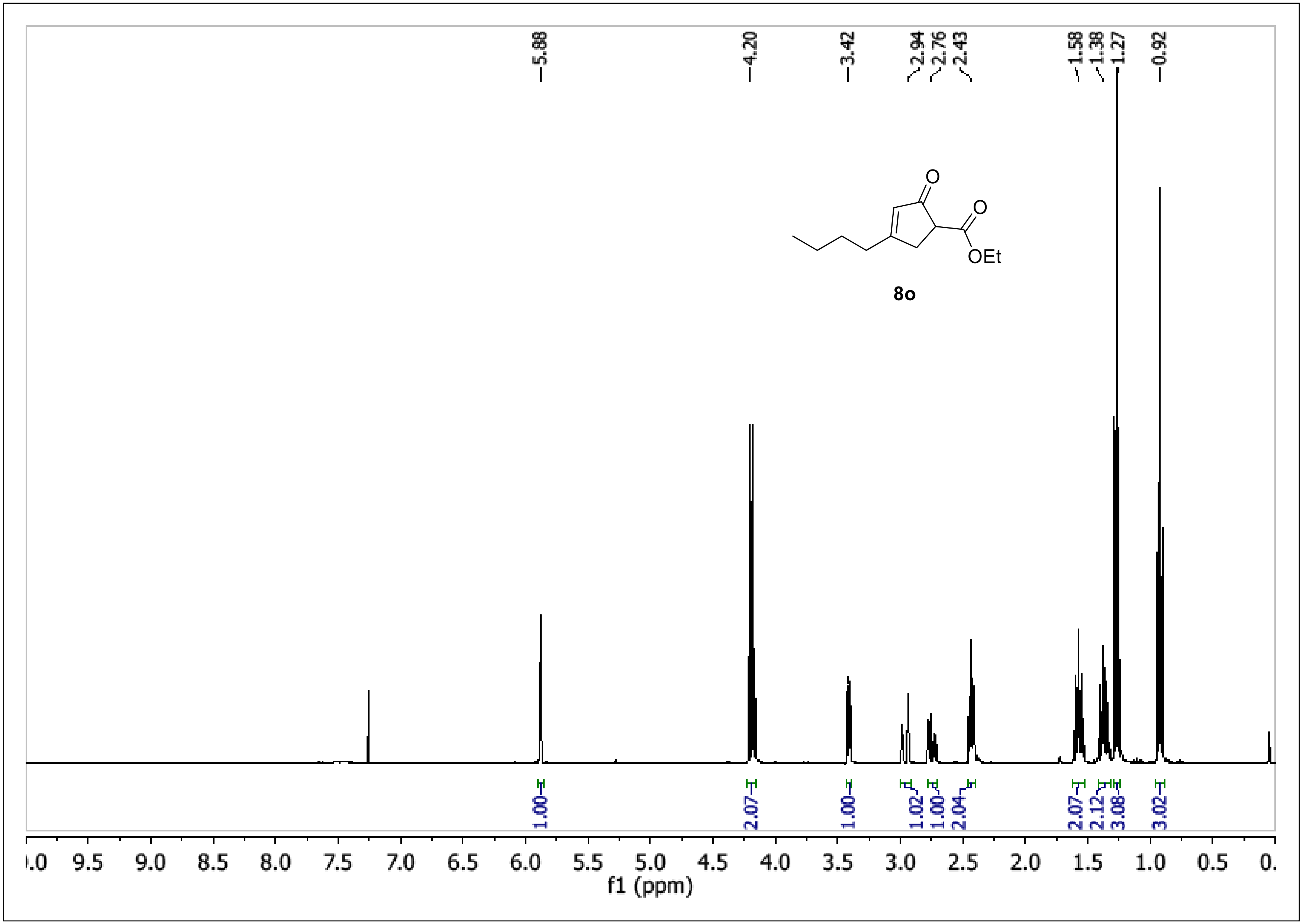


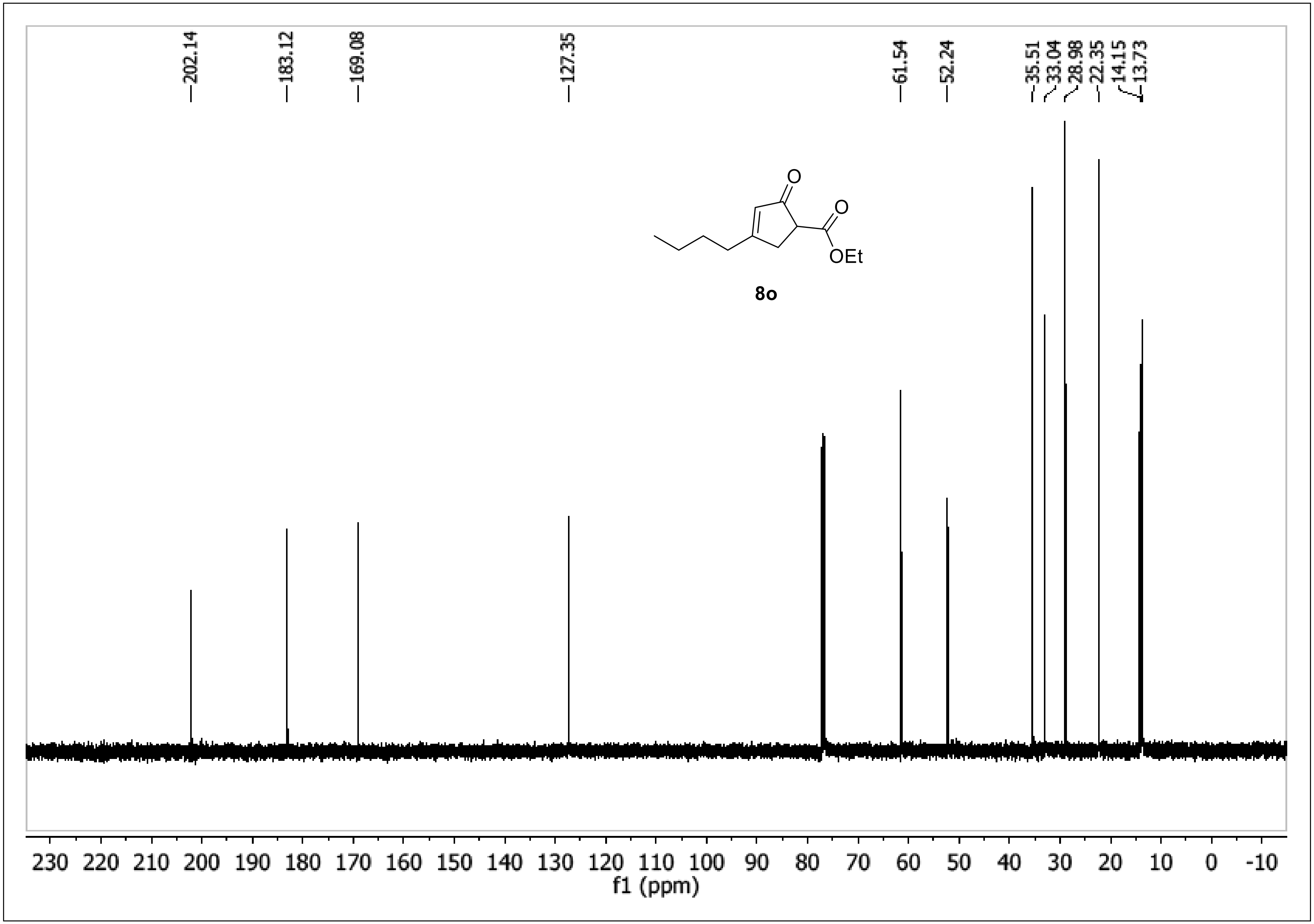
208.97
182.29
139.86
128.78
128.47
127.54
126.84
52.21
41.32
33.21
29.18
22.47
13.81
O
8m
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8n

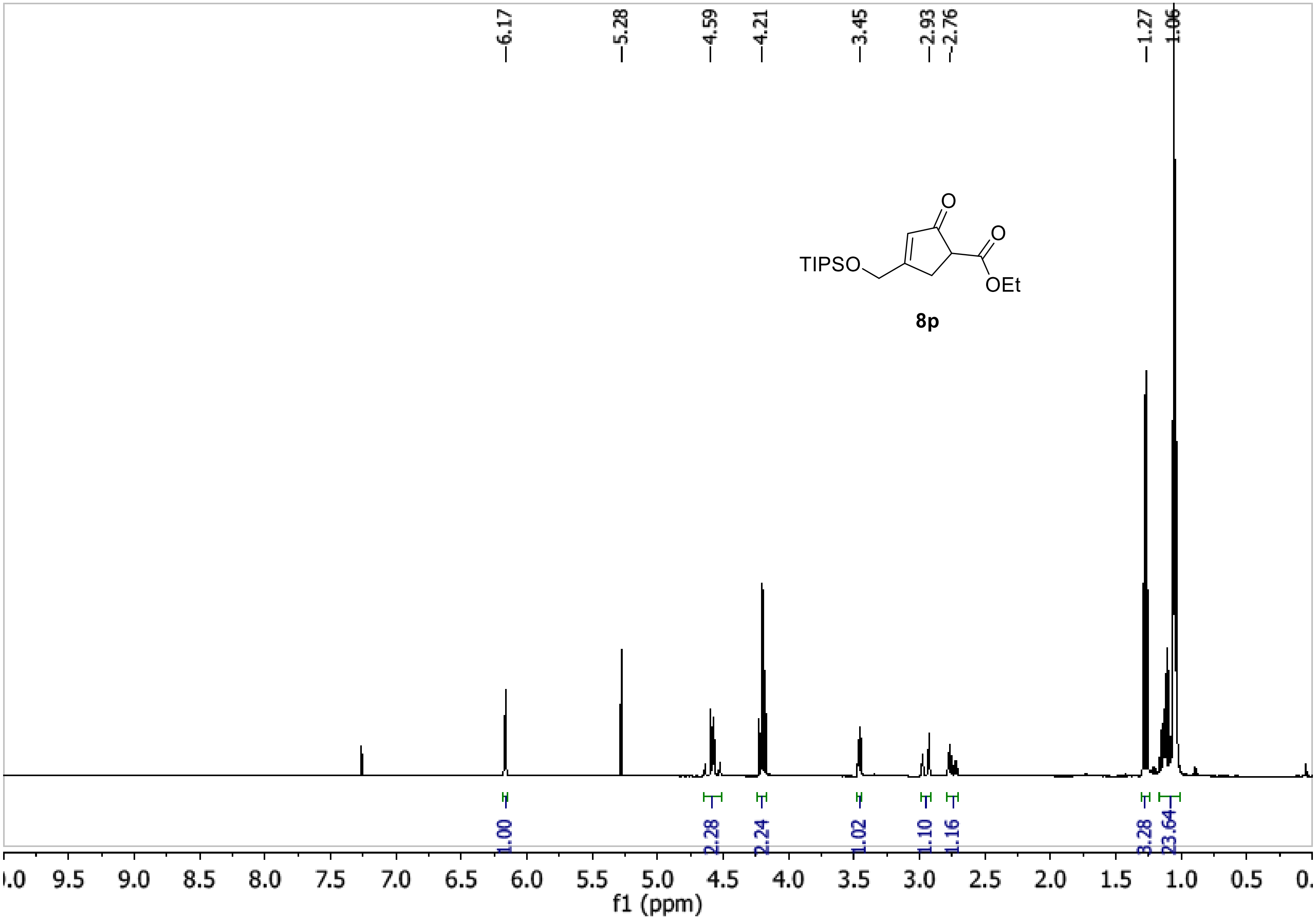
6.68
6.67
6.02
3.59
3.11
2.67
2.48
1.62
1.43
0.96
3.08
1.00
1.01
1.03
1.05
2.06
2.14
2.16
3.01
O
F
F
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


207.18
182.33
164.45
164.32
161.97
161.84
143.32
128.31
128.28
110.72
110.65
110.53
110.47
102.65
102.40
102.15
51.57
40.72
33.19
29.11
22.46
13.77
O
F
F
8n
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

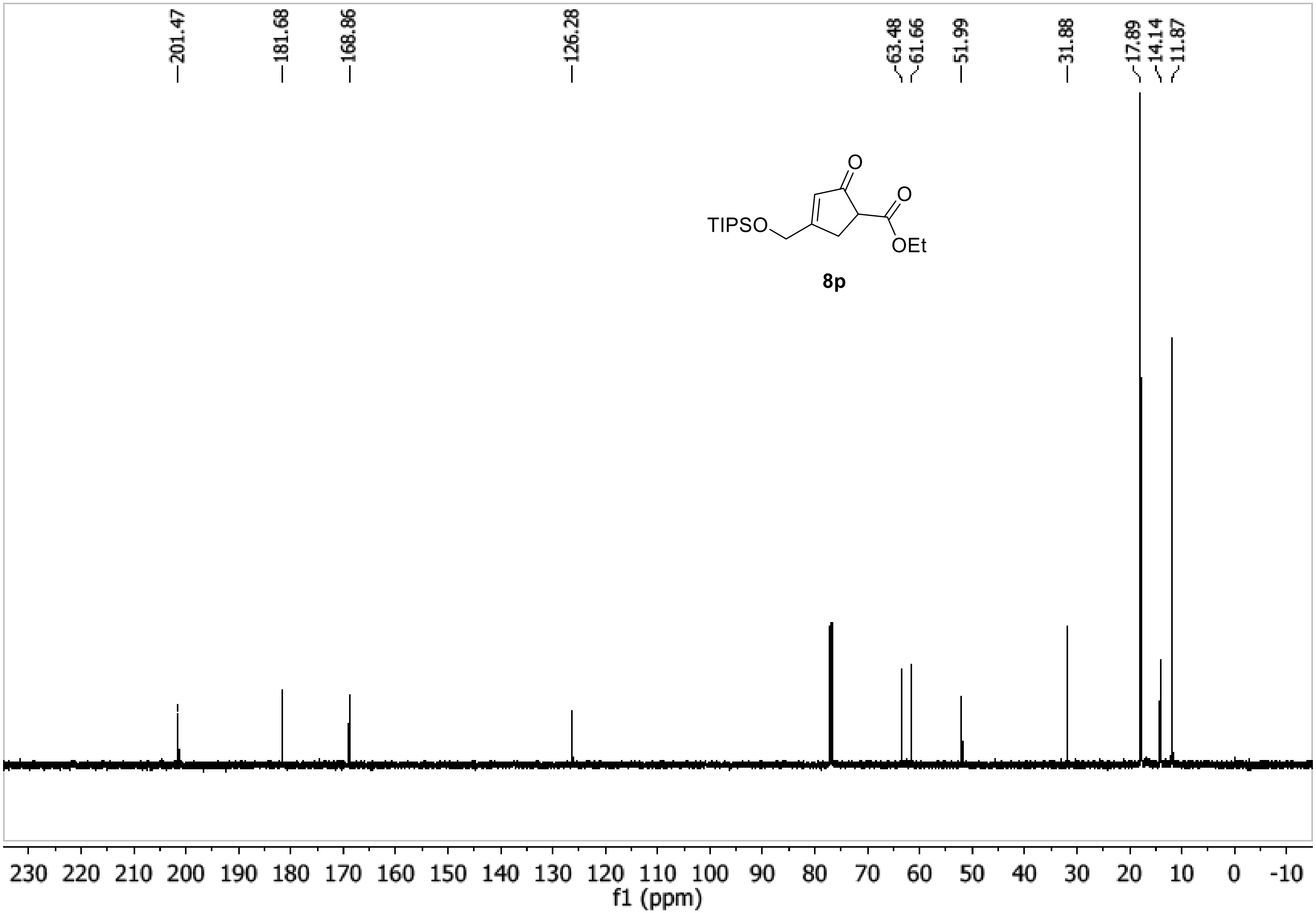

8o
5.88
4.20
3.42
2.94
2.76
2.43
1.58
1.38
1.27
0.92
O
O
OEt
1.00
2.07
1.00
1.02
1.00
2.04
2.07
2.12
3.08
3.02
.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)


202.14
183.12
169.08
127.35
61.54
52.24
35.51
33.04
28.98
22.35
14.15
13.73
O
O
OEt
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

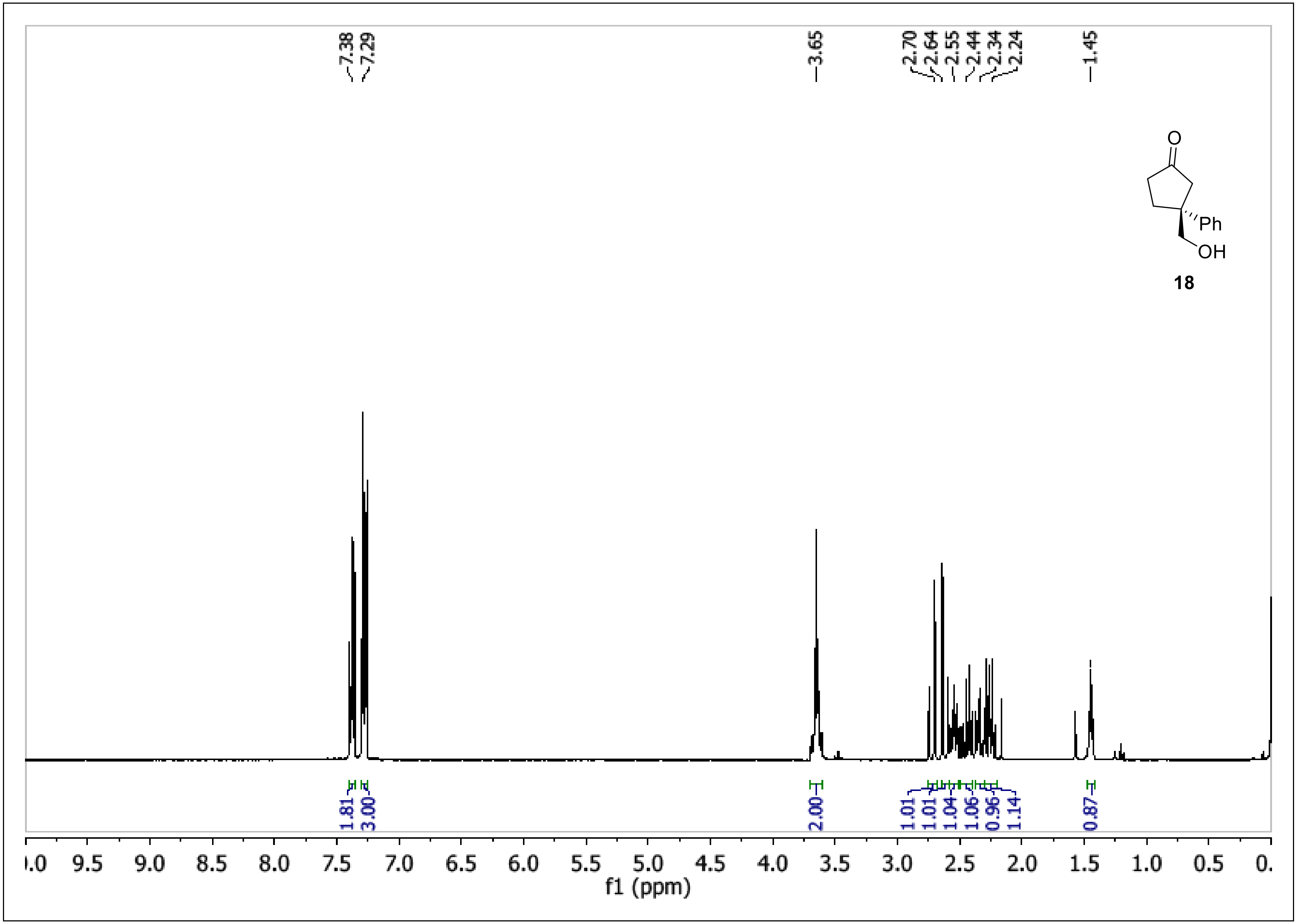
8o

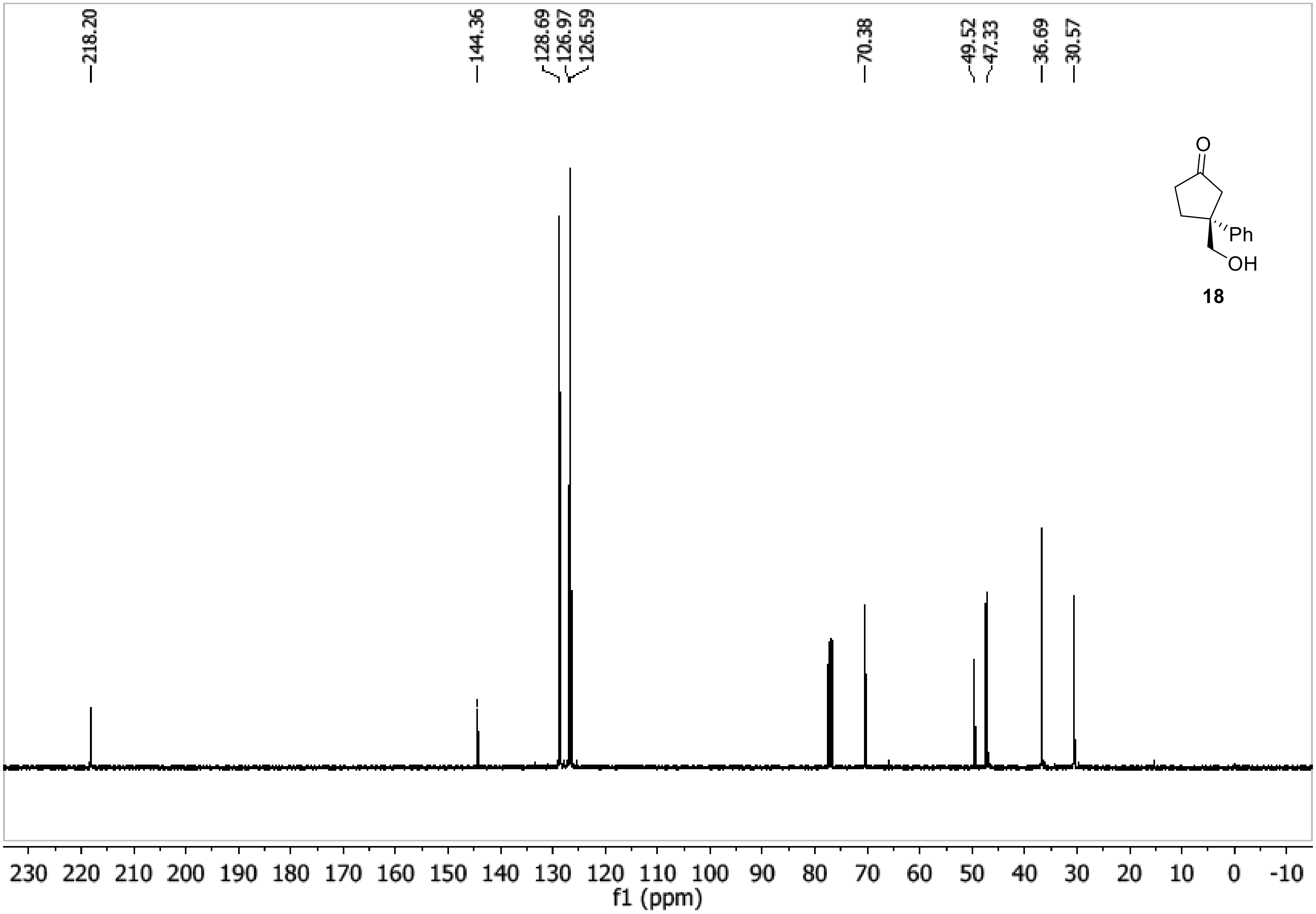

6.17
5.28
4.59
4.21
3.45
2.93
2.76
1.27
1.06
TIPSO
O
O
OEt
1.00
2.28
2.24
1.02
1.10
1.16
3.28
23.64
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

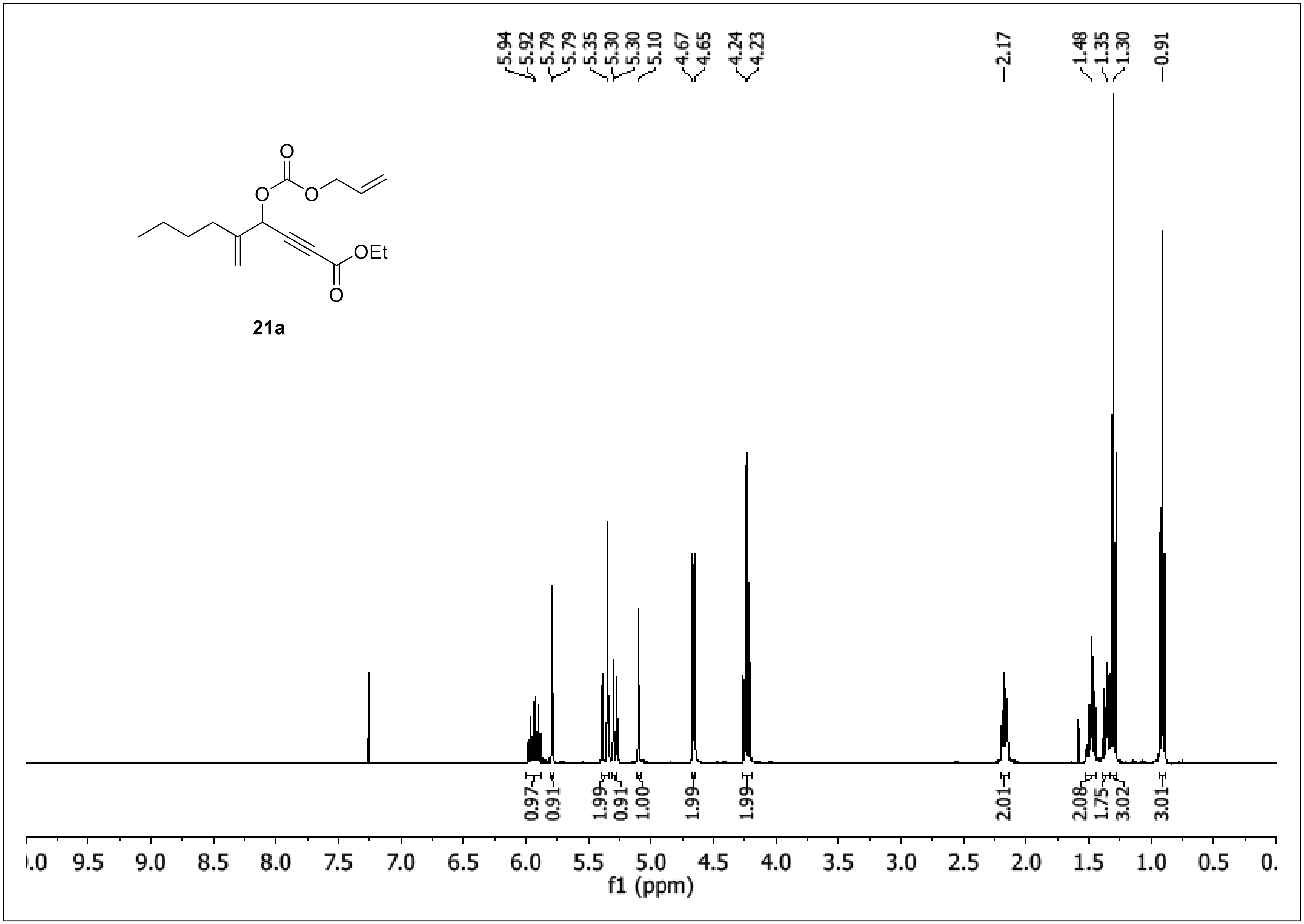
8p

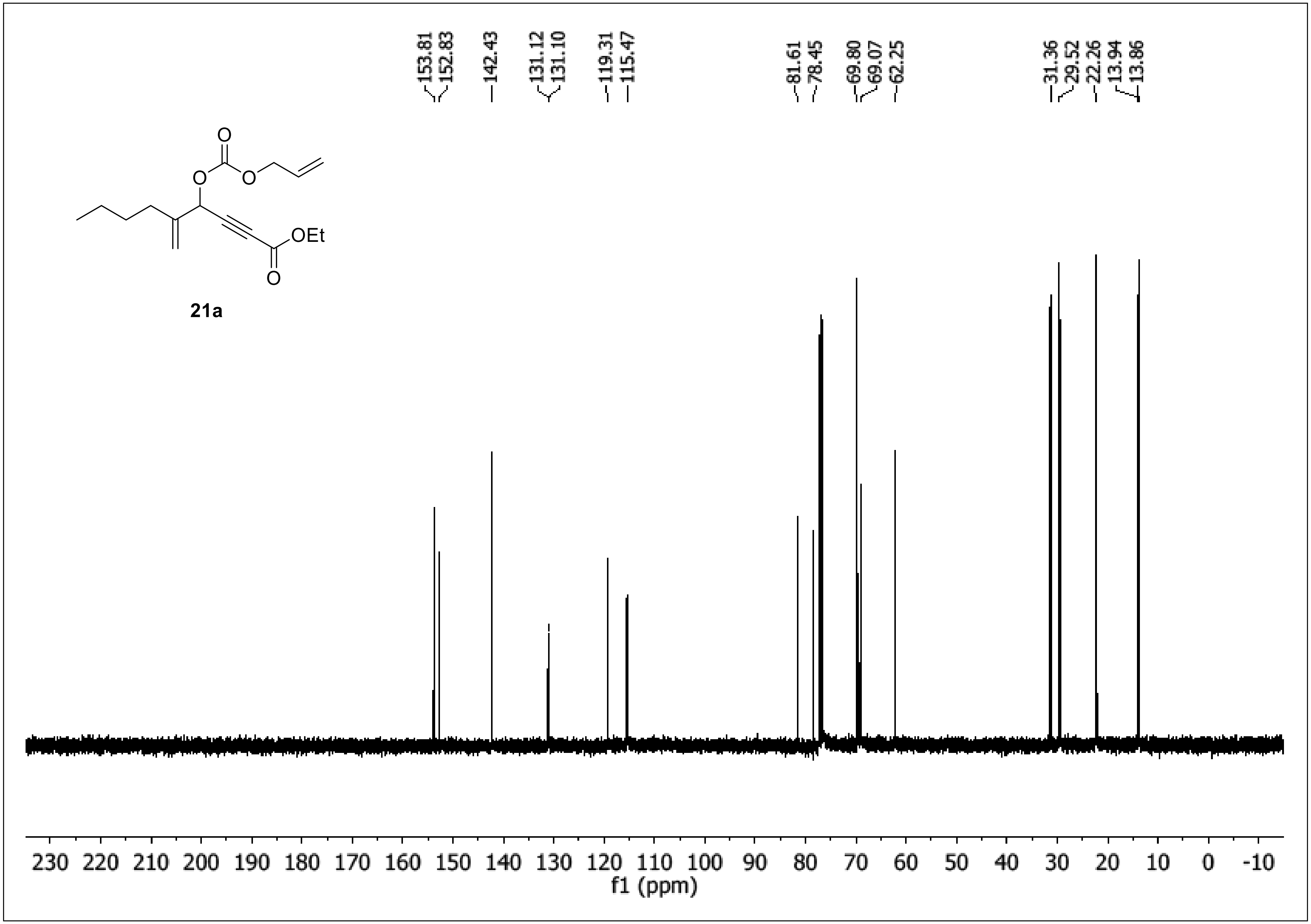

201.47
181.68
168.86
126.28
63.48
61.66
51.99
31.88
17.89
14.14
11.87
TIPSO
O
O
OEt
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

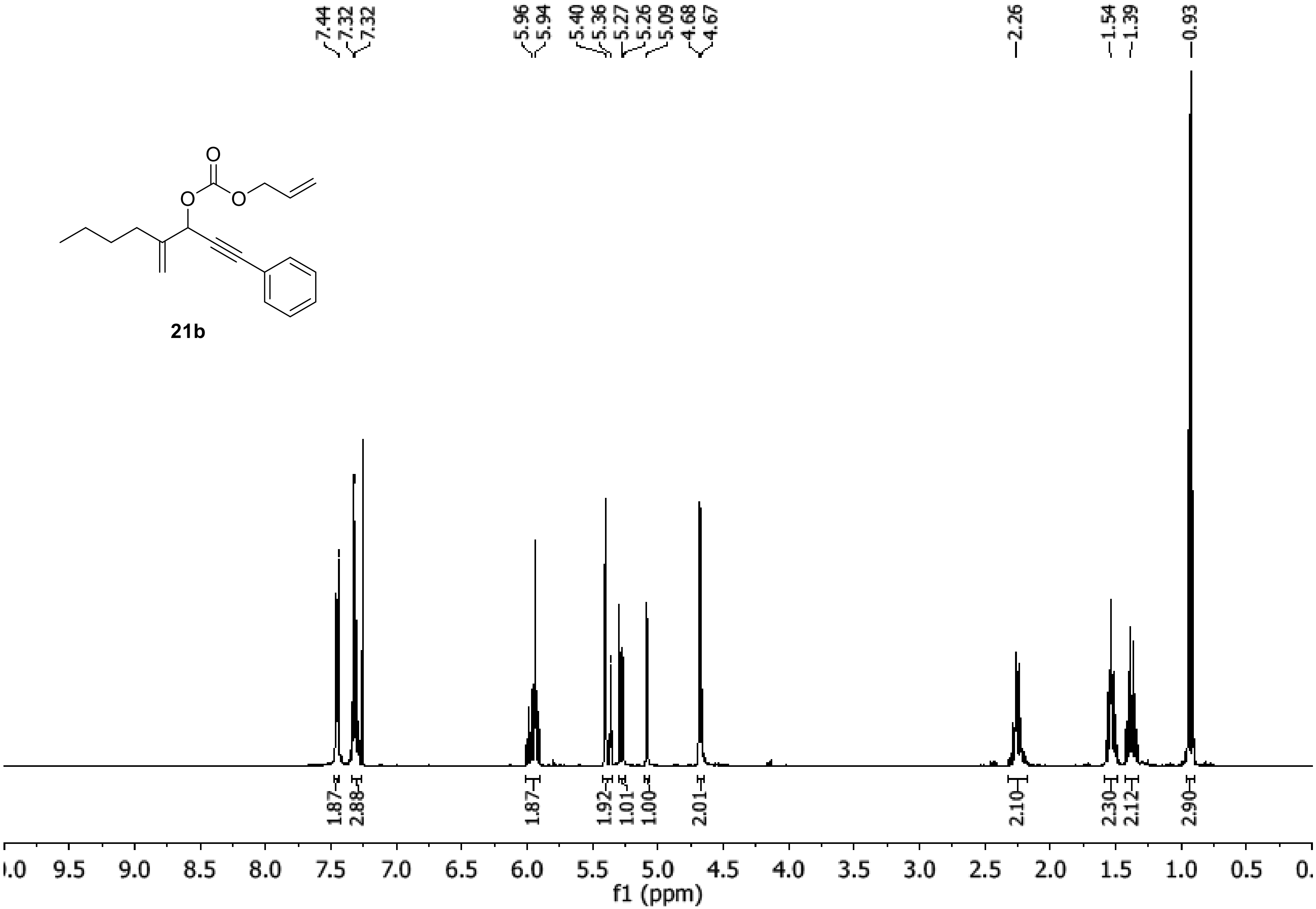
8p


7.38
7.29
3.65
2.70
2.64
2.55
2.44
2.34
2.24
1.45
O
Ph
OH
18
1.81
3.00
2.00
1.01
1.01
1.04
1.06
0.96
1.14
0.87
.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.
f1 (ppm)


218.20
144.36
128.69
126.97
126.59
70.38
49.52
47.33
36.69
30.57
O
Ph
OH
18
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

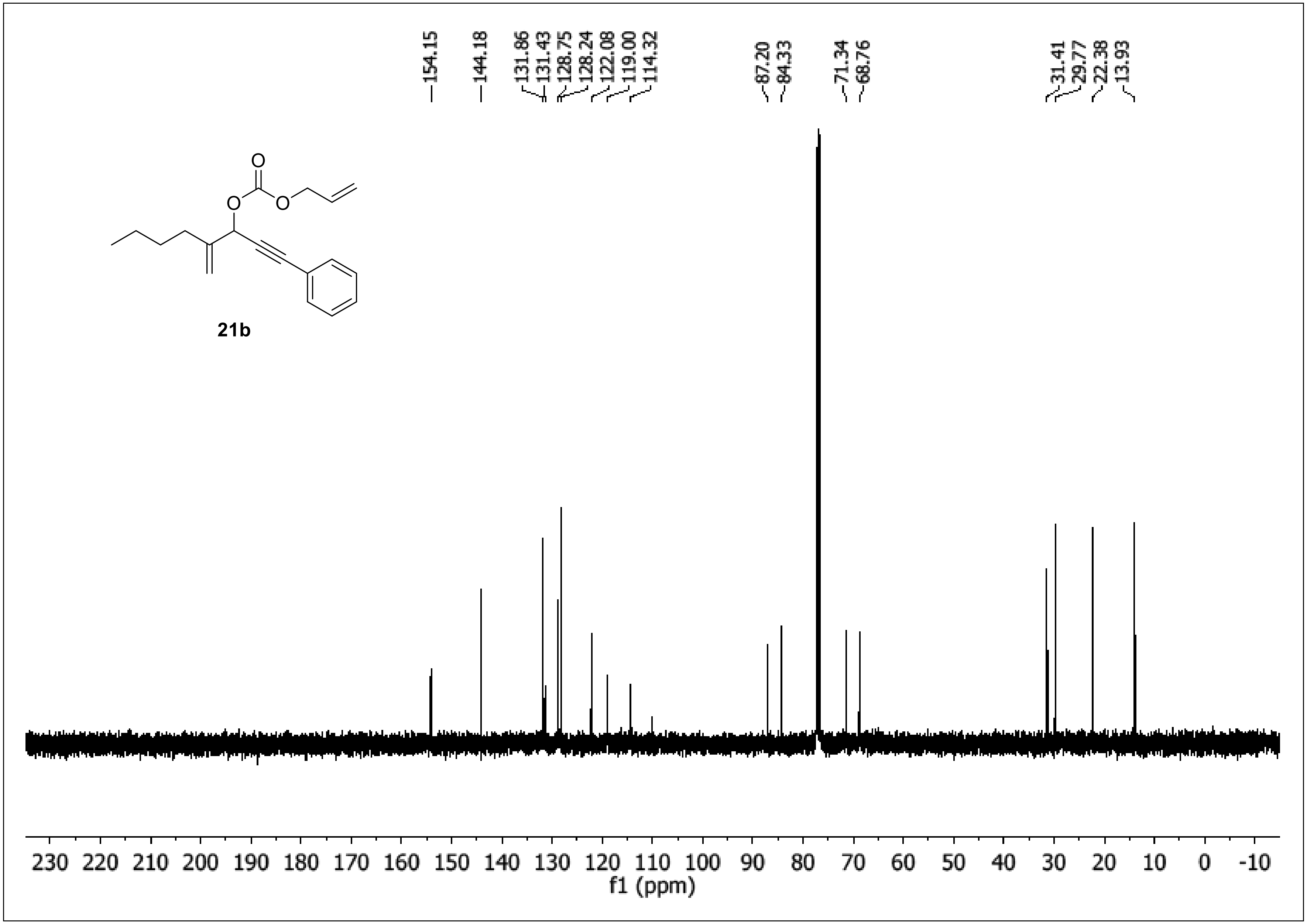

5.94
5.92
5.79
5.79
5.35
5.30
5.30
5.10
4.67
4.65
4.24
4.23
2.17
1.48
1.35
1.30
0.91
0.97
0.91
1.99
0.91
1.00
1.99
1.99
2.01
2.08
1.75
3.02
3.01
O
O
O
OEt
O
21a
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

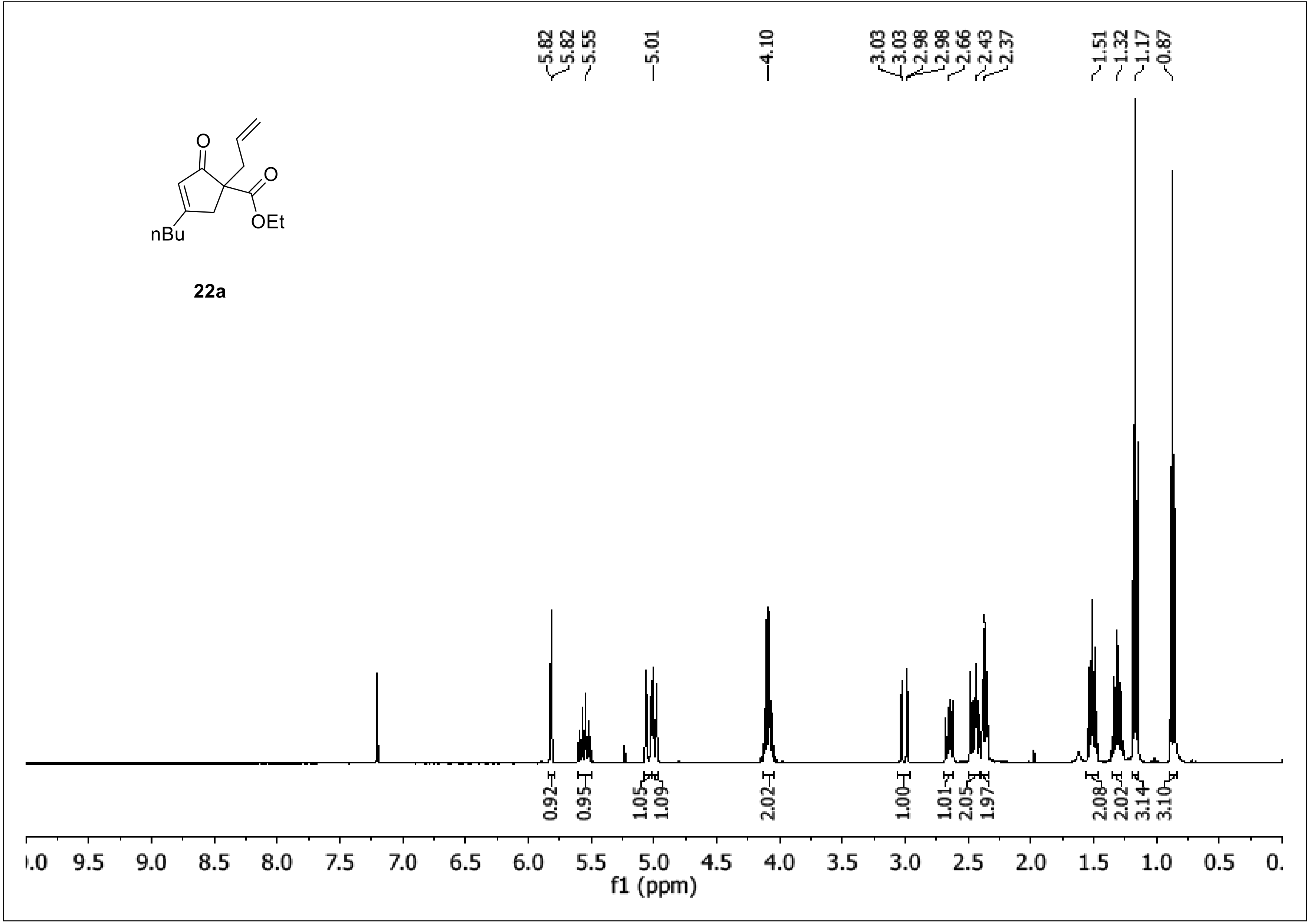

153.81
152.83
142.43
131.12
131.10
119.31
115.47
81.61
78.45
69.80
69.07
62.25
31.36
29.52
22.26
13.94
13.86
O
O
O
OEt
O
21a
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



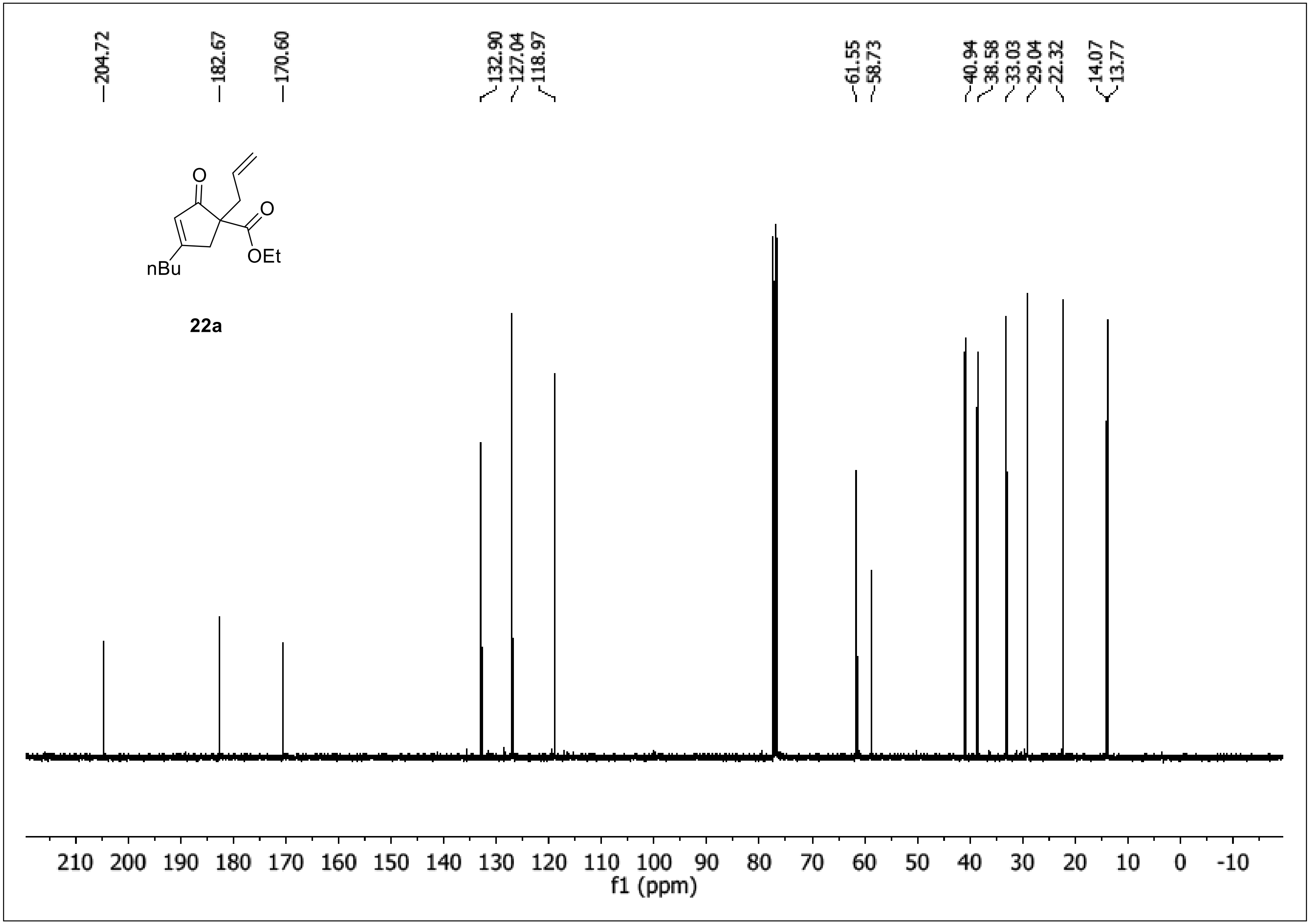
21b

7.44
7.32
7.32
5.96
5.94
5.40
5.36
5.27
5.26
5.09
4.68
4.67
2.26
1.54
1.39
0.93
1.87
2.88
1.87
1.92
1.01
1.00
2.01
2.10
2.30
2.12
2.90
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.
f1 (ppm)

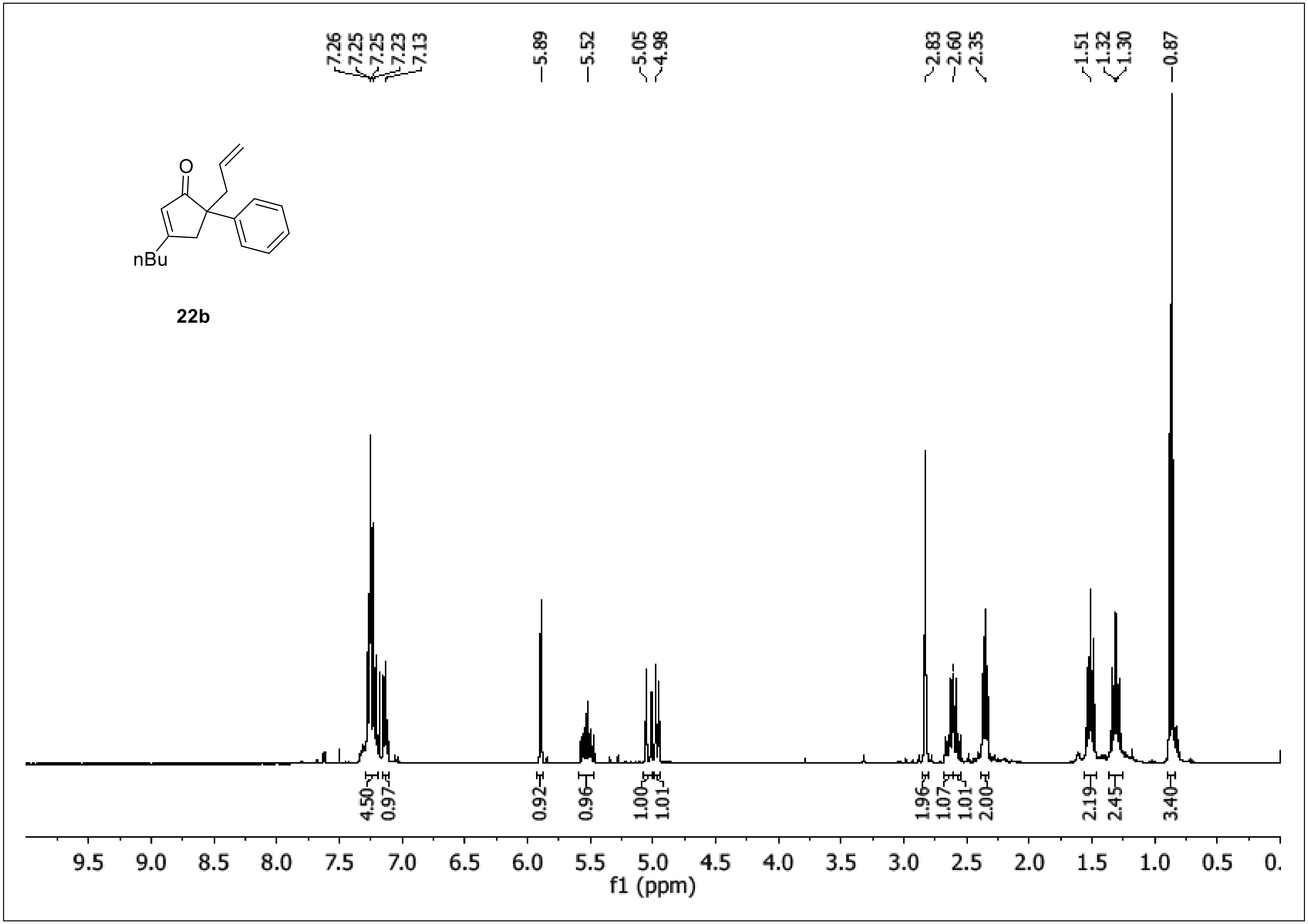

154.15
144.18
131.86
131.43
128.75
128.24
122.08
119.00
114.32
87.20
84.33
71.34
68.76
31.41
29.77
22.38
13.93
O
O
O
21b
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


5.82
5.82
5.55
5.01
4.10
3.03
3.03
2.98
2.98
2.66
2.43
2.37
1.51
1.32
1.17
0.87
O
O
OEt
nBu
0.92
0.95
1.05
1.09
2.02
1.00
1.01
2.05
1.97
2.08
2.02
3.14
3.10
.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.
f1 (ppm)

22a

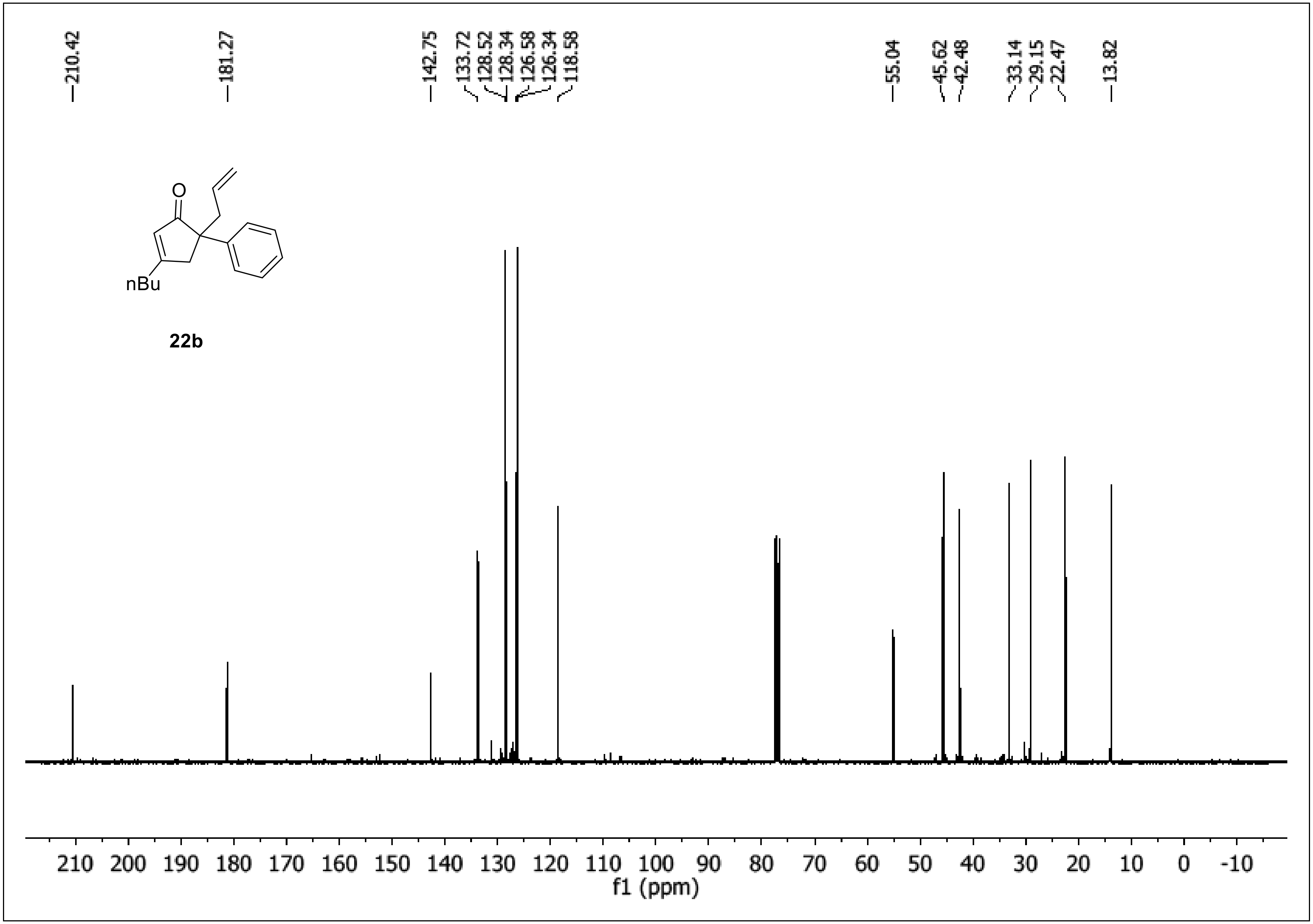


204.72
182.67
170.60
132.90
127.04
118.97
61.55
58.73
40.94
38.58
33.03
29.04
22.32
14.07
13.77
O
O
OEt
nBu
22a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



22b

O
nBu
7.26
7.25
7.25
7.23
7.13
5.89
5.52
5.05
4.98
2.83
2.60
2.35
1.51
1.32
1.30
0.87
4.50
0.97
0.92
0.96
1.00
1.01
1.96
1.07
1.01
2.00
2.19
2.45
3.40
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.
f1 (ppm)


210.42
181.27
142.75
133.72
128.52
128.34
126.58
126.34
118.58
55.04
45.62
42.48
33.14
29.15
22.47
13.82
O
nBu
22b
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)