Supplementary Materials for

# Scalable, Electrochemical Oxidation of Unactivated C–H Bonds

Yu Kawamata,[†] Ming Yan,[†] Zhiqing Liu,[‡] Deng-Hui Bao,[‡] Jinshan Chen,[¶] Jeremy T. Starr,[¶] and Phil S. Baran*[,†]

†Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, United States

‡Asymchem Life Science (Tianjin), Tianjin Economic-Technological Development Zone, Tianjin 300457, China

¶ Discovery Sciences, Medicine Design, Pfizer Global Research and Development, 445 Eastern Point Rd, Groton, CT 06340, United States

Correspondence to: pbaran@scripps.edu

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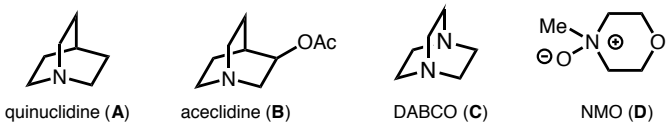
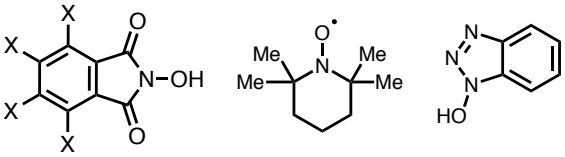
# General Methods

Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Dry tetrahydrofuran (THF) and *N*,*N*-dimethylformamide (DMF) were obtained by passing the previously degassed solvent through an activated alumina column. Yields refer to chromatographically and spectroscopically ($^1$H NMR) homogeneous material, unless otherwise stated. Reactions were monitored by LC-MS or thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using shortwave UV light and $KMnO_4$ for visualization. Flash column chromatography was performed using E. Merck silica gel (60, particle size 0.043 – 0.063 mm). NMR spectra were recorded on Bruker AVIII-600 instruments and were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: 7.26 ppm $^1$HNMR, 77.2 ppm $^{13}$C NMR. The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad. High–resolution mass spectra (HRMS) were recorded on an Agilent LCMS TOF mass spectrometer using electrospray ionization time-of-flight (ESI-TOF) reflectron experiments.

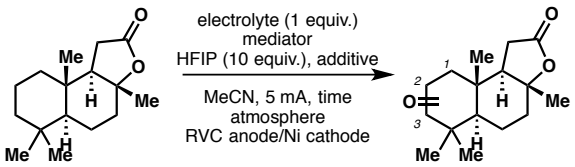
# Optimization and Present Limitations

### Mediators used in optimization



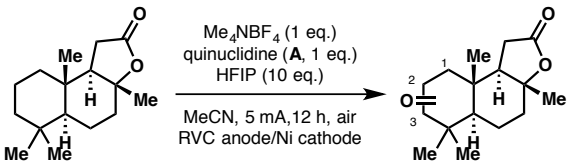

### Initial optimization




| Entry | Electrolyte (eq.) | Mediator (eq.) | Additive(eq.) | Atmosphere | Time (h) | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | $Bu_4NBF_4$ (1) | **A** (0.4) | pyridine (1) | $O_2$ | 12 | 19 |
| 2 | $Bu_4NBF_4$ (1) | **B** (0.4) | pyridine (1) | $O_2$ | 12 | 15 |
| 3 | $Et_4NClO_4$ (1) | **A** (1) | none | air | 12 | 57 |
| 4 | $Et_4NClO_4$ (1) | **A** (2) | none | air | 12 | 60 |
| 5 | $Et_4NClO_4$ (1) | none | none | air | 18 | < 5 |
| 6 | $Me_4NBF_4$ (1) | **A** (1) | none | air | 12 | 51 |
| 7 | $LiClO_4$ (1) | **A** (1) | none | air | 12 | < 5 |

**Note:** Tetramethylammonium tetrafluoroborate was chosen for further screening due to its better safety profile compared to the perchlorate salt.

**Effect of reaction parameters**




| | Entry | Deviation from standard conditions | Yield (%) |
|---|---|---|---|
| Mediators | 1 | **B** as a mediator | 39 |
| | 2 | **C** as a mediator | 9 |
| | 3 | **D** as a mediator | 19 |
| | 4 | **E**, **F**, **G**, **H** as a mediator | < 5 |
| | 5 | quinuclidine N-oxide as a mediator | 9 |
| Cathode | 6 | Pb as cathode | 40 |
| | 7 | Al as cathode | 36 |
| | 8 | Sn as cathode | 39 |
| | 9 | Cu as cathode | 45 |
| | 10 | stainless steel as cathode | 49 |
| | 11 | Mg as cathode | 49 |
| Other parameters | 12 | no **A** | < 5 |
| | 13 | 0.4 equiv. of **A** | 30 |
| | 14 | no HFIP | < 5 |
| | 15 | TFA (1.0 eq.) instead of HFIP | < 5 |
| | 16 | AcOH (2.0 eq.) instead of HFIP | 15 |
| | 17 | under Ar | < 5 |
| | 18 | 10 mA, 6 h | 39 |
| | 19 | portionwise addition of **A** (0.5 eq x2) | 42 |
| | 20 | constant potential (3.5 V without reference electrode) | 37 |
| | 21 | MS 4 Å as an additive | 41 |

**Note:** ***1)*** Under the optimized conditions, a current of 5 mA is passed over 12 h, meaning 11 equiv. of electricity is required to oxidize 1 equiv. of substrate. This is putatively because under the reaction conditions, the quinuclidine mediator is oxidized anodically to quinuclidine *N*-oxide which was reduced back to quinuclidine. This process could have consumed extra electrons. Additionally, the redox cycle between $O_2$ and $O_2^-$ may also consume electricity.

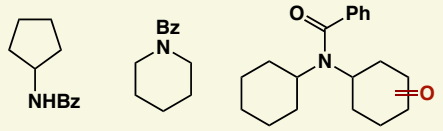
***2)*** The working potential of the reaction was measured to be + 1.8 V (v.s. Ag/AgCl) while the cyclic voltammogram of quinuclidine in the presence of HFIP showed an oxidation peak at *ca.* + 1.1 V (*vide infra*, page S39). This difference can be attributed to the fact that different electrodes (in terms of materials and surface area) have been used in the two measurements. Glassy carbon disc working electrode and platinum counter electrode were used for cyclic voltammetry while RVC anode and Ni foam cathode were used in the reaction setup.

***3)*** Some reactions (including the oxidation of sclareolide in the table above) are taken to partial completion as prolonged electrolysis led to the decomposition of products and lower yields.

***4)*** In the cases of unsuccessful mediators, the starting materials were recovered as they were not capable of homolytically cleaving aliphatic C–H bonds.

**Limitations of the reaction in its present scope**

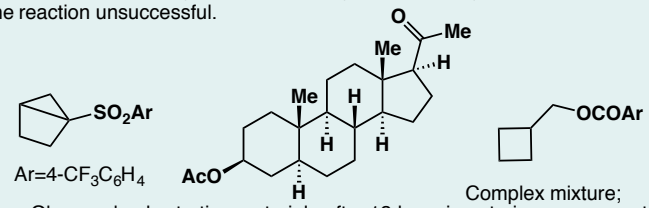
**A.** Oxidation of α–hydrogen possibly caused substrate decomposition.




Complex mixture after 12 h of electrolysis

31% mixture of isomers (12% dioxygenation)

**B.** The lack of sterically accessible methylene units may have rendered the reaction unsuccessful.



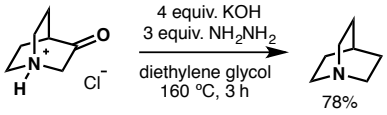

Observed only starting materials after 12 h; prolonged electrolysis led to complex mixtures

Complex mixture; ring strain may account for the failure to oxidize.

# Substrate Synthesis and Characterization

**Synthesis of quinuclidine**

Note: quinuclidine is available from Sigma Aldrich and other suppliers.




A 2L four-neck round-bottom flask equipped with a mechanical stirrer, thermometer, and a Dean-Stark apparatus was charged diethylene glycol (700 mL), KOH (139.3g, 2.483mol, 4 equiv.), and quinuclidin-3-one hydrochloride (100g, 620.9 mmol, 1.0 equiv.). Hydrazine hydrate (93.3g, 1.86mol, 3 equiv.) was added dropwise at room temperature under vigorous stirring. The reaction mixture was heated to reflux (internal temperature, 120–130°C) over 2–3 hours and was stirred under reflux for an additional hour when *ca.* 50 mL of water was collected in the Dean-Stark apparatus. The internal reaction temperature was increased to 145–155 ºC; heating was continued to maintain this temperature until no more liquid was collected in the Dean-Stark apparatus (5–6 hours). The resulting residue was subsequently cooled to 20–30 °C and was then distilled under vacuum. Quinuclidine was collected as a white solid at 60–70 °C (58g, 84% yield).

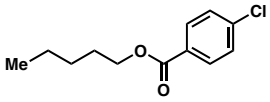
**Synthesis of substrates and characterization**

Sclareolide, valerophenone, 1-methylcyclohexanol, tetrahydropyran, pregnenolone acetate were purchased from Aldrich and used for experiments without further purification. Valencene was purchased from Aldrich and purified by column chromatography (hexanes) before use.

*Preparation of 4-chlorobenzoate esters*

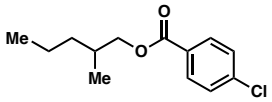
To a stirred solution of alcohol (3.0 mmol, 1.0 equiv.) and DMAP (20 mg, 0.16 mmol, 0.05 equiv.) in $CH_2Cl_2$ were added $Et_3N$ (4.0 mmol, 0.56 mL, 1.3 equiv.) and 4-chlorobenzoyl chloride (3.0 mmol, 0.48 g, 1.0 equiv.) at ambient temperature. After 2 h, a white precipitate was observed; the resulting mixture was filtered and the filtrate was concentrated *in vacuo*. The crude material was purified by column chromatography to afford the desired ester.

***n*-Pentyl-4-chlorobenzoate (S1)**



Spectra data matched values reported in the literature.[1]

**2-Methylpentyl 4-chlorobenzoate (S2)**



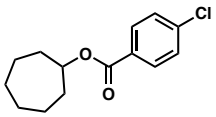
**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.97 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 4.20 (dd, *J* = 10.7, 5.8 Hz, 1H), 4.10 (dd, *J* = 10.7, 6.8 Hz, 1H), 1.87 – 1.90 (m, 1H), 1.46 – 1.38 (m, 2H), 1.38 – 1.31 (m, 1H), 1.25 – 1.20 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H);

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 165.92, 139.36, 131.04, 129.11, 128.81, 70.25, 35.82, 32.56, 20.12, 17.11, 14.39;

**HRMS (ESI-TOF):** calc'd for $C_{13}H_{18}ClO_2$ $[M+H]^+$ 241.099; found 241.0989;

$R_f$ = 0.5 (hexanes:EtOAc = 10:1).

**Cycloheptyl 4-chlorobenzoate (S3)**



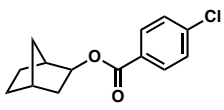
**$^1$H NMR (600 MHz, Chloroform-*d* ):** δ 7.97 (d, 2H), 7.40 (d, 2H), 5.18 (tt, *J* = 8.3, 4.4 Hz, 1H), 2.02 – 1.97 (m, 2H), 1.84 – 1.78 (m, 2H), 1.74 – 1.70 (m, 2H), 1.62 – 1.60 (m, 4H), 1.55 – 1.49 (m, 2H);

**$^{13}$C NMR (151 MHz, Chloroform-*d* ):** δ 165.19, 139.18, 131.04, 129.61, 128.71, 77.37, 77.16, 76.95, 76.14, 33.95, 28.44, 23.06;

**HRMS (ESI-TOF):** calc'd for $C_{14}H_{18}ClO_2$ $[M+H]^+$ 253.099; found 253.0989;

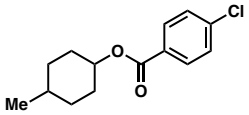
$R_f$ = 0.5 (hexanes:EtOAc = 10:1).

***exo*-Norbornyl 4-chlorobenzoate (S4)**



Spectra data matched with values reported in the literature.[2]

**4-Methylcyclohexyl 4-chlorobenzoate (S5)**



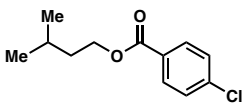
**$^1$H NMR (600 MHz, Chloroform-*d*, mixture of *cis* and *trans* isomers**): δ 7.99 – 7.95 (m, 2.56H), 7.42 – 7.38 (m, 2.56H), 5.24 – 5.22 (m, 0.28H), 4.90 (tt, *J* = 11.2, 4.4 Hz, 1H), 2.08 – 2.06 (m, 2H), 1.99 – 1.96 (m, 0.56H), 1.80 – 1.77 (m, 2H), 1.65 – 1.57 (m, 1.56H), 1.54 – 1.31 (m, 2H), 1.10 (tdd, *J* = 13.5, 11.6, 3.4 Hz, 4.40H), 0.96 (d, *J* = 6.5 Hz, 0.84H), 0.92 (d, *J* = 6.5 Hz, 3H);

**$^{13}$C NMR (151 MHz, Chloroform-*d* ):** δ 165.38, 165.20, 139.22, 139.21, 131.07, 131.03, 129.70, 129.52, 128.78, 128.70, 74.52, 70.90, 33.14, 31.86, 31.82, 31.60, 29.85, 29.83, 22.30, 21.97;

**HRMS (ESI-TOF):** calc'd for $C_{14}H_{18}ClO_2$ $[M+H]^+$ 253.099; found 253.0992;

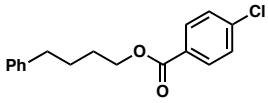
$R_f$ = 0.5 (hexanes:EtOAc = 10:1)

**3-Methylbutyl 4-chlorobenzoate (S6)**



Spectra data matched with values reported in the literature.[3]

**4-Phenylbutyl 4-chlorobenzoate (S7)**



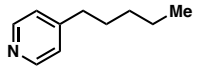
**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.30 (m, 2H), 7.21 – 7.19 (m, 3H), 4.34 (t, *J* = 6.3 Hz, 2H), 2.70 (t, *J* = 7.1 Hz, 2H), 1.84 – 1.76 (m, 4H);

**$^{13}$C NMR (151 MHz, Chloroform-*d* ):** δ 165.89, 142.07, 139.42, 131.07, 128.99, 128.81, 128.52, 128.51, 126.02, 65.22, 35.60, 28.41, 27.92;

**HRMS (ESI-TOF):** calc'd for $C_{17}H_{18}ClO_2$ $[M+H]^+$ 289.099; found 289.0993;

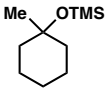
$R_f$ = 0.5 (hexanes:EtOAc = 15:1).

**4-Pentylpyridine (S8)**



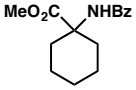
Prepared by following the literature protocol.[4] Spectra data matched with values reported in the literature.[4]

**Trimethyl((1-methylcyclohexyl)oxy)silane (S9)**



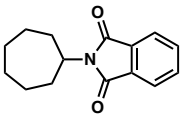
Prepared by following the literature protocol.[5] Spectra data matched with values reported in the literature.[5]

**Methyl 1-benzamidecyclohexanecarboxylate (S10)**



To a stirred solution of 1-aminocyclohexanecarboxylic acid (3 mmol, 0.43 g, 1.0 equiv.) in MeOH (10 mL) was added $SOCl_2$ (6 mmol, 0.44 mL, 2.0 equiv.) slowly at ambient temperature (*note: this addition was very exothermic*). The solution was heated to reflux and stirred for another 2 h at this temperature. Methanol was removed *in vacuo* and the crude material was dissolved in $CH_2Cl_2$ (15 mL). $Et_3N$ (4 mmol, 0.56 mL, 1.3 equiv.), DMAP (20 mg, 0.16 mmol, 0.05 equiv.), and benzoyl chloride (3.3 mmol, 0.39 mL, 1.1 equiv.) were added to this solution; the resulting mixture was stirred at ambient temperature for 2 h. After removal of the solvent *in vacuo*, the crude material was purified by column chromatography (hexanes:EtOAc = 1:1, $R_f$ = 0.5) to afford the desired product (0.55 g, 70% yield). The spectra data matched with values reported in the literature.[6]

***N*-Cycloheptylphthalimide (S11)**



To a stirred solution of cycloheptanol (4 mmol, 0.48 mL, 1.0 equiv.), $PPh_3$ (4.3 mmol, 1.12 g, 1.075 equiv.) and phthalimide (4.4 mmol, 0.65 g, 1.1 equiv.) in 15 mL THF was added diisopropyl azodicarboxylate (4.2 mmol, 0.87 mL, 1.05 equiv.) under Ar atmosphere at ambient temperature. After 3 h, the solvent was removed *in vacuo* and the residue was purified by column chromatography (hexanes:EtOAc = 10:1) to give the desired product as a white solid (650 mg, 67% yield).

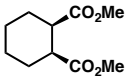
**$^1$H NMR (600 MHz, Chloroform-*d* )**: $^1$H NMR (600 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.26 (tt, *J* = 10.8, 3.7 Hz, 1H), 2.29 – 2.22 (m, 2H), 1.84 – 1.78 (m, 4H), 1.69 – 1.59 (m, 4H), 1.54 – 1.48 (m, 2H);

**$^{13}$C NMR (151 MHz, Chloroform-*d* ):** δ 168.37, 133.84, 132.27, 123.12, 52.92, 32.83, 27.72, 25.63.

**HRMS (ESI-TOF):** calc'd for $C_{15}H_{18}NO_2$ $[M+H]^+$ 244.1332; found 244.1334;

$R_f$ = 0.5 (hexanes:EtOAc = 2:1).

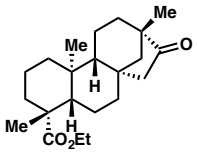
**Dimethyl *cis*-1,2-cyclohexanedicarboxylate (S12)**




To a stirred solution of *cis*-1,2-cyclohexanedicarboxylic anhydride (5 mmol, 0.77 g) in MeOH (15 mL) was added conc. $H_2SO_4$ (50 μL) at ambient temperature. The resulting mixture was stirred at 60 °C overnight after which the reaction mixture was poured onto sat. aq. $NaHCO_3$. The organic layer was extracted with a mixture of hexanes:EtOAc (3:1) three times. The combined organic phase was dried over anhydrous $Na_2SO_4$ and concentrated *in vacuo*. The resulting pale yellow oil (hexanes:EtOAc = 5:1) was found to be essentially pure without further purification (quantitative yield).

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 3.65 (s, 6H), 2.80 – 2.74 (br, 2H), 2.00 – 1.96 (m, 2H), 1.76 – 1.73 (m, 2H), 1.52 – 1.47 (m, 2H), 1.40 – 1.35 (m, 2H);
**$^{13}$C NMR (151 MHz, Chloroform-*d* ):** δ 174.26, 51.73, 42.72, 26.32, 23.83;
**HRMS (ESI-TOF):** calc'd for $C_{10}H_{17}NO_4$ $[M+H]^+$ 201.1121; found 201.1121;
$R_f$ = 0.4 (hexanes:EtOAc = 5:1).

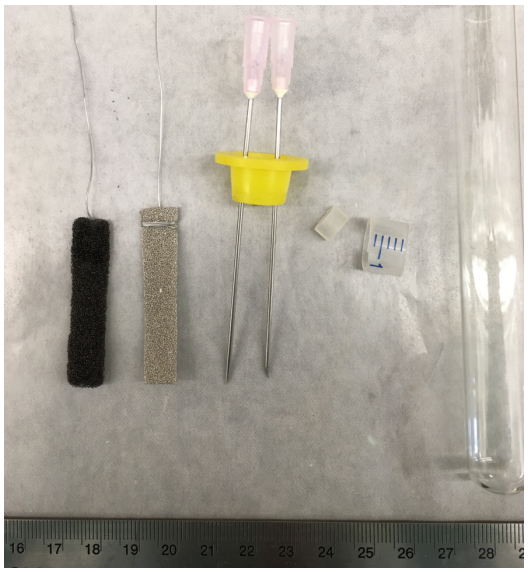
**Isosteviol ethyl ester (S13)**




Isosteviol was obtained by hydrolysis of stevia extract (purchased from Whole Foods Market) with 1N HCl at 80 °C for 2h. Esterification was performed following the reported protocol.[7] Spectra data matched with values reported in the literature.[8]

# Graphical Guide for the Assembly of a Hand-made Electrochemical Cell

**(The entire process takes *ca.* 15 minutes.)**



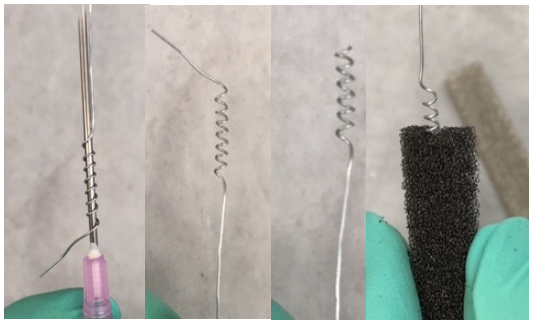
While this electrochemical C–H oxidation may be conducted using a variety of electrochemical cells, depicted here is our standard setup for 0.10–0.40 mmol scale experiments that makes use of readily available materials in a laboratory setting.

***Step 0. Overview of materials used.***

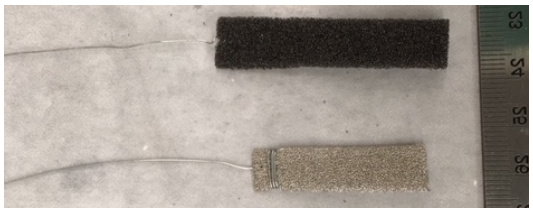
*From left to right:* ***1)*** RVC anode attached to a stainless-steel wire; ***2)*** Ni foam cathode attached to a stainless-steel wire; ***3)*** a yellow cap (diameter at the bottom: 14 mm) pierced with two pink needles (18 G); ***4)*** plastic insulator (a small plastic piece); ***5)*** holder (a cross-section of a disposable syringe); ***6)*** test tube (16 × 125 mm). The rest of this section depicts the construction of these individual units and the assembly thereof into the electrochemical cell.

***Step 1. Preparation of the electrodes.***

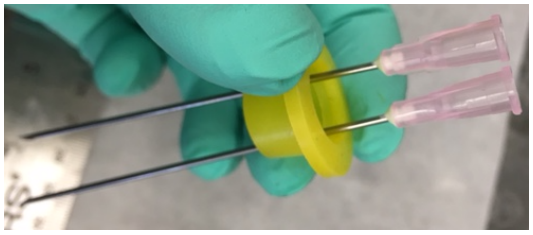
*From left to right:* ***1)*** Stainless steel wire used was purchased from Home Depot; ***2)*** The RVC electrode (1 cm × 5 cm) was furnished from commercial RVC sheet (100 mm × 100 mm 100 PPI 3%, purchased from KRReynolds, $15.75/sheet); ***3)*** Ni foam electrode (1 cm × 4 cm) was furnished from Nickel Foam (1.5 mm x 100 mm x 250 mm for Battery, Electric Capacity etc. purchased from eBay). A razor blade was used to cut the electrodes into the desired dimensions; the lengths of the electrodes may be varied so long as the connection to the steel wire attached is above the reaction solution.



*From left to right:* ***1)*** the stainless-steel wire was wrapped around an 18 G needle; ***2)*** the needle was removed; ***3)*** the tip of the wire was cut off; ***4)*** the resulting wire was screwed into the RVC electrode.



*From top to bottom:* ***1)*** the RVC electrode attached to stainless-steel wire; ***2)*** the nickel foam electrode was encircled with stainless steel wire.



***Step 2. Assembly of the cell cap.***

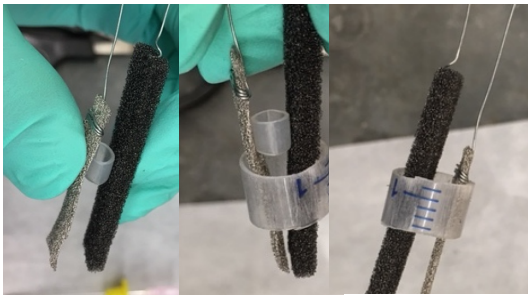
Two 18 G pink needles were inserted into a yellow cap. The use of longer needles (9 cm) is recommended to keep the electrodes apart in the cell.

***Step 3. Preparation of the insulator and holder.***

*From left to right:* ***1)*** a plastic insulator was obtained from a needle case; ***2)*** the said insulator was compressed by hand or a hammer to ease subsequent assembly.

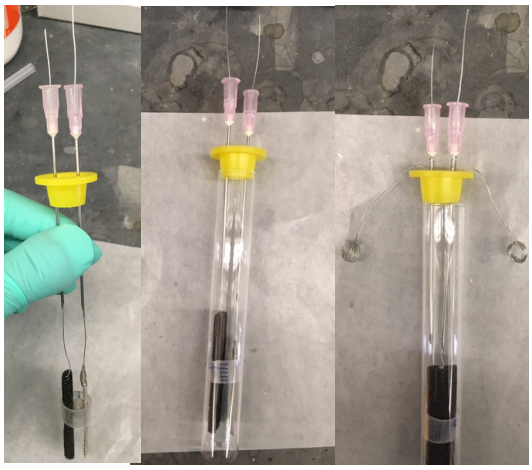
Aside from the plastic insulator described herein, cotton could also serve as the insulator.

The cell holder (*ca.* 1 cm in length) was furnished from a 6.0 mL disposable syringe.



***Step 4. Assembly of the individual components.***

*From left to right:* 1) The insulator was placed between the RVC and nickel foam electrodes which were aligned at the bottom; ***2)*** and ***3)*** the assembly consisting of the electrodes and the insulator was inserted into the holder.



*From left to right:* ***1)*** the stainless-steel wires attached to the RVC and nickel foam electrodes were inserted into the pink needles on the left and right side of the cell cap respectively; ***2)*** the "electrode assembly" thus prepared can be fitted into a test tube (16 mm x 125 mm) which serves as the reaction vessel; ***3)*** when needed, additional stainless steel wires could be wrapped around the pink needles to connect the electrodes to the potentiostat.

# General Procedure for Electrochemical Oxidation of Unactivated C–H bonds

**General procedure for small scale electrolysis (See page S16 for a graphical guide)**

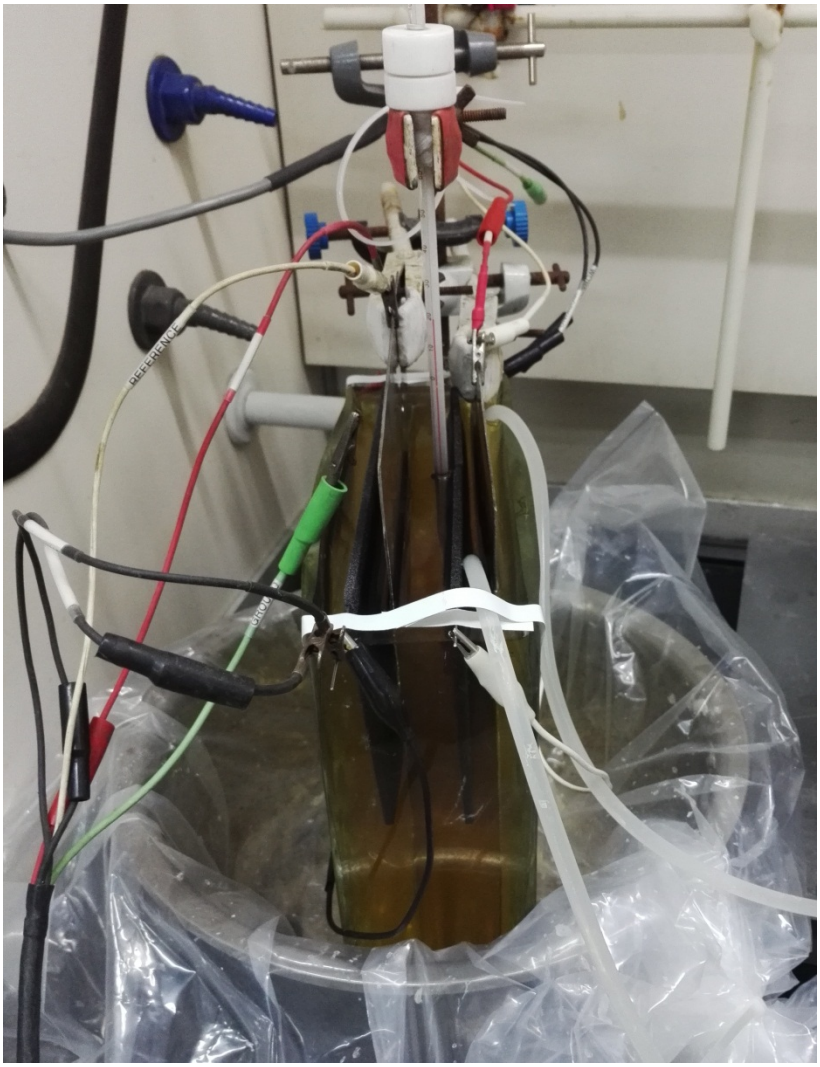
With no precautions to exclude air or moisture, a test tube was charged with a stir bar, tetramethylammonium tetrafluoroborate ($Me_4NBF_4$) (0.2 mmol, 32 mg, 1.0 equiv.) and quinuclidine (0.2 mmol, 22 mg, 1.0 equiv.). Solid substrates were added in at this point. MeCN (1.8 mL) and HFIP (2.0 mmol, 0.21 mL, 10 equiv.) were added (liquid substrates were added at this point), the anode (RVC) and cathode (Ni foam) separated by an insulator in a holder (see page S11) are placed in the solution, and the reaction mixture was electrolyzed under a constant current of 5 mA (25 mA/mmol, potentiostat: EZstat-Pro) until the complete consumption of the starting material as judged by TLC or NMR of an aliquot. The reaction mixture was transferred to a 25 mL flask and the solvent was removed *in vacuo*. The residue was re-dissolved in a small amount of $CH_2Cl_2$ and passed through a short silica-gel plug with EtOAc to remove the electrolyte. The solution was concentrated and the crude material was purified by either column chromatography or preparative thin-layer chromatography (PTLC) to furnish the desired product.

Note: Teraethylammonium or tetrabutylammonium tetrafluoroborate can also be used as the electrolyte.

**Procedure of 50 gram scale reaction**

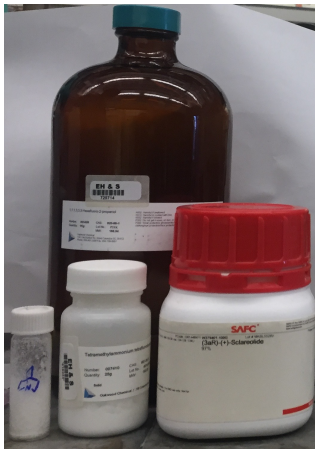
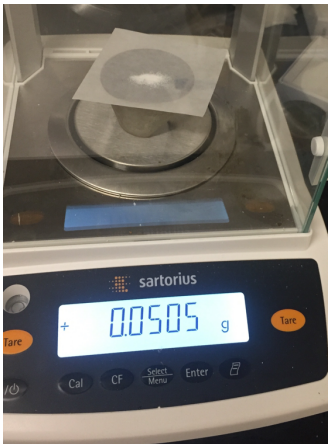
To a 3.5 L cell were added sclareolide (200 mmol, 50 g, 1.0 equiv.), $Bu_4NBF_4$ (200 mmol, 65.8 g, 1.0 equiv.), quinuclidine (200 mmol, 22 g, 1.0 equiv.), HFIP (2 mol, 336 g, 10 equiv.) and MeCN (3 L). RVC anode (area: 150 $cm^2 \times 2$) and 304 stainless steel cathode (area: 150 $cm^2 \times 2$) were inserted to this solution and electrolysis was conducted at a constant current (1.5 A, potentiostat: EZstat-Pro); air was bubbled into the reaction mixture. The applied cell voltage was measured to be between 2.5 and 5.6 V (in the absence of a reference electrode). Extra electrolyte $Bu_4NBF_4$ (20 mmol, 6.6 g, 0.1 equiv.) was added to the mixture when cell voltage was over 5.6 V. The electrolysis was stopped after 108 h; the solution was transferred to a 5 L round bottom flask and concentrated *in vacuo*. The resulting residue was passed through a short silica-gel plug (hexanes:EtOAc = 1:2) to remove the electrolyte; the filtrate was concentrated *in vacuo*. The crude material was purified by flash column chromatography (hexanes:EtOAc=2:1) to afford the desired product in 47% yield with 26% of recovered starting material.

Photo of the 50 gram scale reaction set up:

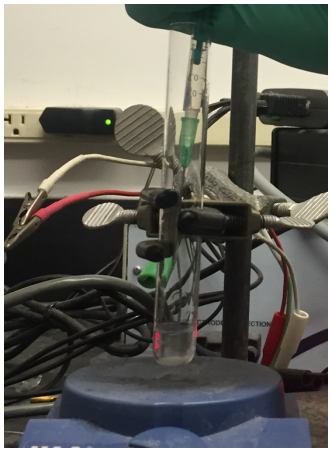
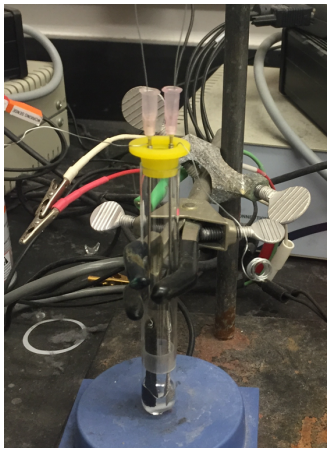


# Graphical Guide for Electrochemical Oxidation of Unactivated C-H bonds

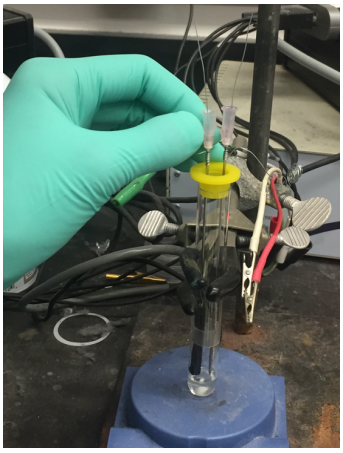
**Photos used are from the oxidation of sclareolide.**

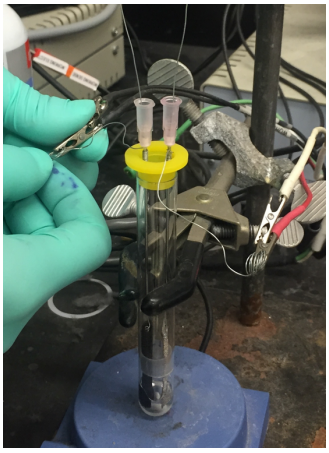




*From left to right:* ***1)*** Materials used in the reaction (quinuclidine was synthesized in house); ***2)*** Solids (sclareolide, quinuclidine, $Me_4N•BF_4$) were weighed on a balance (shown in the picture is sclareolide); ***2)*** solids were transferred to a 16 × 125 mm test tube charged with a stir bar.

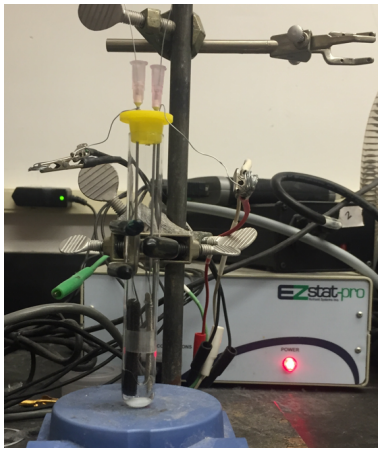



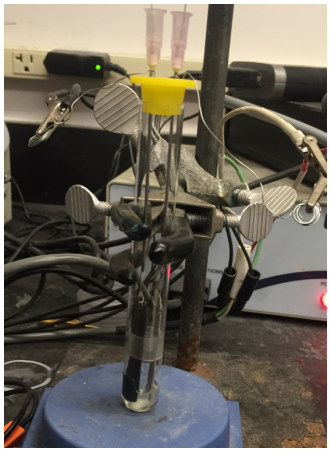
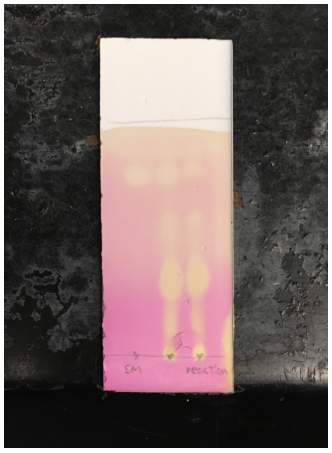
*From left to right:* ***1)*** MeCN was added under stirring; ***2)*** HFIP was added to the reaction mixture *via* a syringe; ***3)*** the electrode assembly described in the preceding section (see page S11) was fitted on top of the reaction vessel.





*From left to right:* ***1)*** the height of the electrodes was adjusted to maximize surface submerged under the reaction mixture while keeping a little space for stirring; ***2)*** *the final position of the electrodes;* ***3)*** the RVC electrode was connected to the anode (the black wire) of a potentiostat and the nickel foam was connected to the cathode (the red wire), each via a crocodile clip.

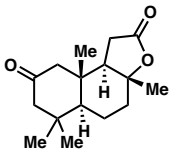



*From left to right:* ***1)*** the reaction mixture was subjected to constant current electrolysis (I = 5.0 mA) using an EZstat-Pro potentiostat; ***2)*** the reaction mixture after 12 h of electrolysis; ***3)*** TLC of the reaction mixture (left-lane: starting material; middle lane: co-spot of starting material and reaction mixture; right lane: reaction mixture).

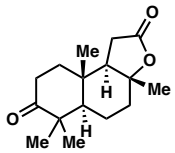
# Characterization Data of Oxidation Products

### 2-Oxosclareolide (2)



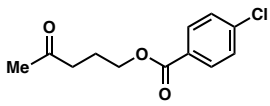
Sclareolide (0.2 mmol, 50 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by PTLC ($CH_2Cl_2$:$Et_2O$ = 5:1, $R_f$ = 0.4) to give the 2-oxosclareolide as a white solid (22 mg, 42% yield). The spectra data matched with values reported in the literature.[9]

### 3-Oxosclareolide (2, 3-oxo product)



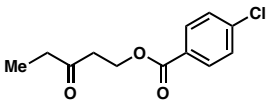
3-oxosclareolide was obtained as a white solid from the purification of 2-oxosclareolide ($CH_2Cl_2$:$Et_2O$ = 5:1, $R_f$ = 0.5, 4.5 mg, 9% yield). The spectra data matched with values reported in the literature.[9]

### 4-Oxopentyl 4-chlorobenzoate (3, δ-oxo product)



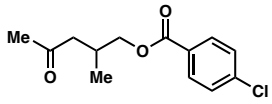
*n*-pentyl 4-chlorobenzoate (0.2 mmol, 45.3 mg) was electrolyzed for 21 h following the general procedure. The crude material was purified by PTLC (hexanes:EtOAc=5:1, $R_f$ = 0.2) to give the titled compound as a colorless liquid (26 mg, 54% yield). The spectra data matched with values reported in the literature.[10]

### 3-Oxopentyl 4-chlorobenzoate (3, γ-oxo product)



The γ-oxo product was obtained as a colorless liquid from the purification of δ-oxo product (hexanes:EtOAc=5:1, $R_f$ = 0.3) (8.7 mg, 18% yield). The spectra data matched with values reported in the literature.[10]

**2-Methyl-4-oxopentyl 4-chlorobenzoate (4, δ-oxo product)**



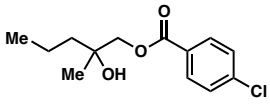
2-methylpentyl 4-chlorobenzoate (0.2 mmol, 48 mg) was electrolyzed for 15 h following the general procedure. The crude material was purified by PTLC ($CH_2Cl_2$) to afford the titled compound as a colorless liquid (22 mg, 43% yield).

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.95 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 2H), 4.21 (dd, *J* = 10.8, 5.7 Hz, 1H), 4.14 (dd, *J* = 10.8, 6.4 Hz, 1H), 2.60 (dd, *J* = 16.5, 5.8 Hz, 1H), 2.54 (td, *J* = 12.6, 6.2 Hz, 1H), 2.39 (dd, *J* = 16.4, 7.0 Hz, 1H), 2.15 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H);

**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 207.49, 165.77, 139.61, 131.07, 128.91, 128.73, 69.37, 47.56, 30.68, 28.99, 17.18;

**HRMS (ESI-TOF):** calc'd for $C_{13}H_{16}ClO_3$ $[M+H]^+$ 255.0782; found 255.0780;

***R*$_f$** = 0.5 ($CH_2Cl_2$).



**2-hydroxy-2-methylpentyl 4-chlorobenzoate (4, β-oxidation product)**

The β-hydroxy product was obtained as a colorless liquid from the purification of δ-oxo product (6.2 mg, 13% yield).

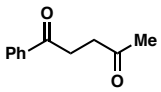
**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.99 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 4.24 (d, *J* = 11.2 Hz, 1H), 4.20 (d, *J* = 11.2 Hz, 1H), 1.59 – 1.57 (m, 2H), 1.47 – 1.41 (m, 2H), 1.28 (s, 3H), 0.96 (t, *J* = 7.3 Hz, 3H);

**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 165.88, 139.80, 131.15, 128.98, 128.56, 72.15, 71.82, 41.72, 24.16, 17.05, 14.79;

**HRMS (ESI-TOF):** calc'd for $C_{13}H_{18}ClO_3$ $[M+H]^+$ 257.0939; found 257.0940;

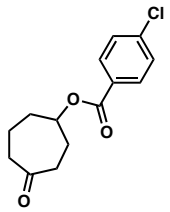
***R*$_f$** = 0.2 ($CH_2Cl_2$).

**1-Phenylpentan-1,4-dione (5)**



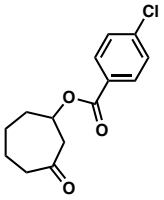
Valerophenone (0.2 mmol, 32 mg) was electrolyzed for 18 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 3:1, $R_f$ = 0.4) to afford the titled compound as a white solid (20 mg, 58% yield). The spectra data matched with values reported in the literature.[11]

**4-Oxocycloheptyl 4-chlorobenzoate (6, δ-oxo product)**



Cycloheptyl 4-chlorobenzoate (0.2 mmol, 50 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by PTLC ($CH_2Cl_2$, $R_f$ = 0.4) to give the titled compound as a colorless liquid (29 mg, 54% yield). The spectra data matched with values reported in the literature.[10]

**3-Oxocycloheptyl 4-chlorobenzoate (6, γ-oxo product)**

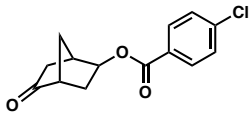


The γ-oxo product was obtained as a colorless liquid from the purification of the δ-oxo product ($CH_2Cl_2$, $R_f$ = 0.5) (13 mg, 24% yield). The spectra data matched with values reported in the literature.[10]

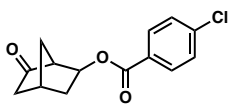
**Scale-up C-H oxidation of Cycloheptyl 4-chlorobenzoate**

To a test tube (15 cm, ø = 2.2 cm) were added Cycloheptyl 4-chlorobenzoate (4.0 mmol, 1.1 g), $Me_4NBF_4$ (2 mmol, 0.32 g, 0.1 M), quinuclidine (4.0 mmol, 0.44 g, 1.0 equiv.), HFIP (20 mmol, 2.1 mL, 5 equiv.) and MeCN (18 mL). RVC anode (5.5 cm × 1.5 cm) and Ni foam cathode (5.5 cm × 1.5 cm) were inserted to this solution and electrolysis was conducted at a constant current (30 mA, potentiostat: EZstat-Pro) for 40 h  The crude material was purified by column chromatography (hexanes:EtOAc = 10:1 to 3:1) to give the titled compound as a colorless liquid (881 mg, 83% yield).

**(1*R*,4*R*)-5-Oxobicyclo[2.2.1]heptan-2-yl 4-chlorobenzoate (7, δ-oxo product)**



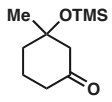
*exo*-Norbornyl 4-chlorobenzoate (0.2 mmol, 50 mg) was electrolyzed for 14 h following the general procedure. The crude material was purified by PTLC ($CH_2Cl_2$, $R_f$ = 0.4) to afford the titled compound as a white solid (19 mg, 37% yield). The spectra data matched with values reported in the literature.[10]



**(1*S*,4*R*)-6-Oxobicyclo[2.2.1]heptan-2-yl 4-chlorobenzoate (7, γ-oxo product)**

The γ-oxo product was obtained as a white solid from the purification of δ-oxo product ($CH_2Cl_2$, $R_f$ = 0.5) (10 mg, 19% yield). The spectra data matched with values reported in the literature.[10]

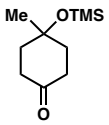
**3-Methyl-3-trimethylsiloxycyclohexanone (8, γ-oxo product)**




Trimethyl((1-methylcyclohexyl)oxy)silane (0.2 mmol, 37 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 10:1 to 5:1) to give the titled compound as a mixture with δ-oxo product in (21 mg, 52% yield, 3-oxo:4-oxo = 2.4:1 by $^1$H NMR). Although separation of the isomers was difficult by column chromatography, an analytical sample of the titled compound could be obtained from the mixture by PTLC (hexanes:$Et_2O$ = 3:1).

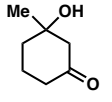
**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 2.45 (dt, *J* = 13.8, 2.1 Hz, 1H), 2.32 (m, 2H), 2.19 (dddd, *J* = 14.4, 11.1, 6.2, 1.3 Hz, 1H), 2.05 – 1.97 (m, 1H), 1.86 – 1.82 (m, 1H), 1.81 – 1.76 (m, 1H), 1.70 – 1.66 (m, 1H), 1.34 (s, 3H), 0.10 (s, 9H);
**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 210.52, 55.95, 40.64, 39.06, 29.82, 21.45, 2.52;
**HRMS (ESI-TOF):** calc'd for $C_{10}H_{21}O_2Si$ $[M+H]^+$201.1305; found 201.1306;
***R*$_f$** = 0.5 (hexanes:$Et_2O$ = 3:1).

**4-Methyl-4-trimethylsiloxycyclohexanone (8, δ-oxo product)**




The titled compound was separated from 3-oxo compound by PTLC (hexane:$Et_2O$ = 3:1, $R_f$ = 0.6). The spectra data matched with values reported in the literature.[12]

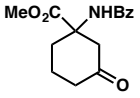
**3-Hydroxy-3-methylcyclohexanone (9, γ-oxo product)**




1-methylcyclohexanol (0.2 mmol, 23 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc= 1:2 to 1:4) to give the titled compound as an inseparable mixture with 4-oxo (δ-oxo) product (25

mg, 80% yield, γ:δ = 4:1 by $^{1}$H NMR). The spectra data of the major isomer matched with values reported in the literature.[13]

**Methyl 1-benzamido-3-oxocyclohexane-1-carboxylate (10, γ-oxo product)**



Methyl 1-benzamidocyclohexane-1-carboxylate (0.2 mmol, 52 mg) was electrolyzed for 15 h following the general procedure. The crude material was purified by PTLC (hexanes:EtOAc = 1:3) to give the titled compound as a white solid (26 mg, 44% yield).

**$^1$H NMR (600 MHz, Chloroform-*d*)**: δ 7.74 (d, *J* = 7.1 Hz, 2H), 7.51 (t, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 6.58 (br, 1H), 3.77 (s, 3H), 3.03 (d, *J* = 15.2 Hz, 1H), 2.91 (d, *J* = 15.0 Hz, 1H), 2.60 – 2.57 (m, 1H), 2.46 – 2.41 (m, 2H), 2.20 (dt, *J* = 13.6, 6.4 Hz, 1H), 1.98 – 1.93 (m, 2H);

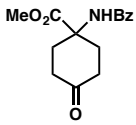
**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 207.49, 172.92, 167.19, 133.77, 132.16, 128.79, 127.18, 62.54, 53.16, 47.90, 40.25, 31.41, 21.12;

**HRMS (ESI-TOF):** calc'd for $C_{15}H_{18}NO_4$ $[M+H]^+$ 276.1236; found 276.1233;

***R*$_f$** = 0.4 (hexanes:EtOAc = 1:3);

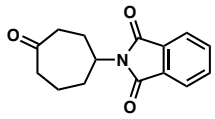
**Melting point:** 169 °C.

**Methyl 1-benzamido-4-oxocyclohexane-1-carboxylate (10, δ-oxo product)**



The δ-oxo product was obtained as colorless amorphous solid from the purification of γ-oxo product (hexanes:EtOAc = 1:3, $R_f$ = 0.5) (11 mg, 19% yield). The spectra data matched with values reported in the literature.[14]

***N*-(4-oxocycloheptyl)phthalimide (11, δ-oxo product)**



Methyl 1-benzamidocyclohexane-1-carboxylate (0.2 mmol, 49 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by PTLC (hexanes:EtOAc = 1:1) to afford the titled compound as a white solid (15 mg, 29% yield).

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H), 4.28-4.24 (m, 1H), 2.65 – 2.56 (m, 5H), 2.37 (q, *J* = 13.4, 12.7 Hz, 1H), 2.02 – 1.99 (m, 2H), 1.94 – 1.88 (m, 1H), 1.75 – 1.68 (m, 1H);

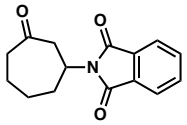
**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 213.32, 168.03, 134.15, 131.96, 123.36, 53.62, 43.49, 40.96, 34.03, 28.48, 22.20.

**HRMS (ESI-TOF):** calc'd for $C_{15}H_{16}NO_3$ $[M+H]^+$ 258.1125; found 258.1127;

$R_f$ = 0.4 (hexanes:EtOAc = 1:1);

**Melting point:** 98 °C.

**_N_-(3-oxocycloheptyl)phthalimide (11, γ-oxo product)**



The γ-oxo product was obtained as white solid from the purification of δ-oxo product (hexanes:EtOAc = 1:1) (11 mg, 21% yield).

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 7.83 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.0 Hz, 2H), 4.49 (tt, *J* = 11.9, 2.7 Hz, 1H), 3.65 (dd, *J* = 14.9, 12.1 Hz, 1H), 2.65 – 2.52 (m, 3H), 2.44 – 2.38 (m, 1H), 2.09 – 2.04 (m, 1H), 2.02 – 1.95 (m, 2H), 1.78 – 1.71 (m, 1H), 1.53 (dtt, *J* = 14.7, 12.1, 2.7 Hz, 1H);

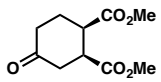
**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 210.76, 167.78, 134.22, 131.93, 123.45, 48.23, 48.12, 44.17, 35.49, 27.86, 23.80;

**HRMS (ESI-TOF):** calc'd for $C_{15}H_{16}NO_3$ $[M+H]^+$ 258.1125; found 258.1129;

$R_f$ = 0.5 (hexanes:EtOAc = 1:1).

**Melting point:** 113 °C

**Dimethyl *rac-cis*-4-oxocyclohexane-1,2-dicarboxylate (12)**



Dimethyl *cis*-cyclohexane-1,2-dicarboxylate (0.2 mmol, 40 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 1:1.5) to afford the titled compound as a colorless liquid (22 mg, 52% yield).

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 3.74 (s, 3H), 3.70 (s, 3H), 3.24 (q, *J* = 5.0 Hz, 1H), 3.14 (dt, *J* = 9.5, 5.0 Hz, 1H), 2.90 – 2.81 (m, 1H), 2.63 (dd, *J* = 15.4, 5.4 Hz, 1H), 2.46 – 2.32 (m, 3H), 2.05 (tq, *J* = 12.9, 4.5 Hz, 1H);

**$^{13}$C NMR (151 MHz, Chloroform-*d*)**: δ 208.93, 173.02, 172.67, 52.53, 52.42, 43.68, 41.39, 40.81, 38.38, 25.71;

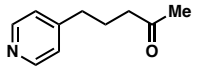
**HRMS (ESI-TOF):** calc'd for $C_{10}H_{15}O_5$ $[M+H]^+$ 215.0914; found 215.0916;

$R_f$ = 0.5 (hexanes:EtOAc = 1:1.5).

**500 mg scale C-H oxidation of Dimethyl *rac-cis*-4-oxocyclohexane-1,2-dicarboxylate**

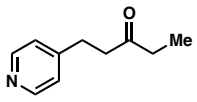
To a test tube (15 cm, ø = 2.2 cm) charged with a magnetic stirrer bar were added dimethyl *rac-cis*-4-oxocyclohexane-1,2-dicarboxylate (2.5 mmol, 0.5 g), $Me_4NBF_4$ (1.4 mmol, 0.22 g, 0.1 M), quinuclidine (2.5 mmol, 0.28 g, 1.0 equiv.), HFIP (13 mmol, 1.4 mL, 5 equiv.) and MeCN (12 mL). RVC anode (5.5 cm × 1.5 cm) and Ni foam cathode (5.5 cm × 1.5 cm) were inserted to this solution and electrolysis was conducted at a constant current (30 mA, potentiostat: EZstat-Pro) for 37 h. The crude material was purified by column chromatography (hexanes:EtOAc = 1:1 to 1:3) to give the titled compound as a colorless liquid (328 mg, 61% yield).

**5-(pyridine-4-yl)-pent-2-one (13, δ-oxo product)**




4-pentylpyridine (0.2 mmol, 30 mg) was electrolyzed for 18 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 1:5, $R_f$ = 0.2) to give the titled compound as a pale brown liquid (9.5 mg, 29% yield). The spectra data matched with values reported in the literature.[4]

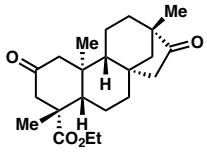
**5-(pyridine-4-yl)-pent-3-one (13, γ-oxo product)**




This product was obtained as pale brown liquid from the purification of δ-oxo product (hexanes:EtOAc = 1:5, $R_f$ = 0.3) (4.9 mg, 15% yield).

The spectra data matched with values reported in the literature.[4]

**2-Oxoisosteviol ethyl ester (14)**




Isosteviol ethyl ester (0.2 mmol, 69 mg) was electrolyzed for 9 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 1:1) to give the titled compound as a white solid (35 mg, 48% yield) along with recovered starting materiel (29% yield).

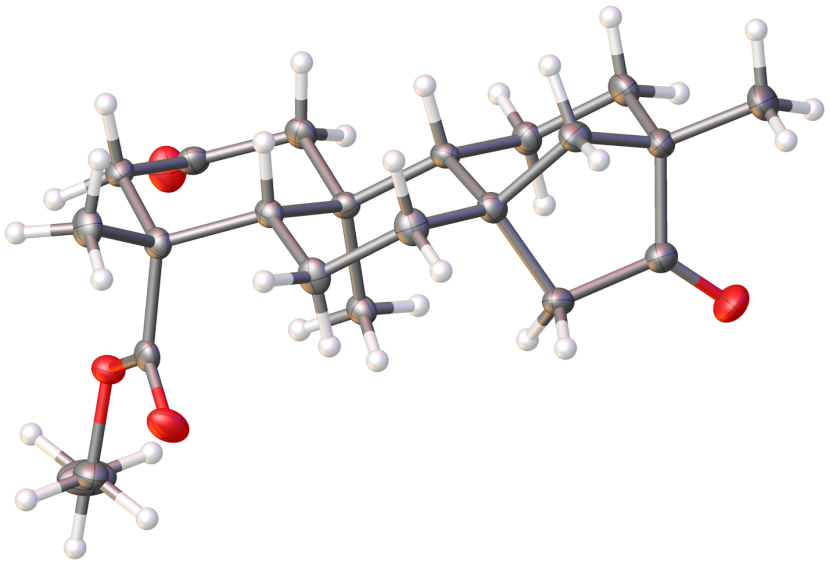
**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 4.09 (dq, *J* = 11.0, 7.2 Hz, 1H), 4.03 (dq, *J* = 11.0, 7.2 Hz, 1H), 2.92 (dd, *J* = 14.1, 2.3 Hz, 1H), 2.54 (dd, *J* = 18.6, 3.8 Hz, 1H), 2.44 (dd, *J* = 13.8, 2.3 Hz, 1H), 2.09 – 2.03 (m, 2H), 1.94 (d, *J* = 13.7 Hz, 1H), 1.81 (d, *J* = 18.6 Hz, 1H), 1.75 – 1.54 (m, 7H), 1.45 – 1.37 (m, 6H), 1.28 – 1.21(m, 4H), 0.98 (s, 3H), 0.73 (s, 3H);

**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 221.58, 207.90, 175.45, 61.14, 56.20, 55.38, 54.19, 54.04, 51.45, 48.74, 47.94, 47.91, 42.21, 40.92, 39.65, 37.10, 28.67, 21.58, 20.47, 19.90, 14.76, 13.97.

**HRMS (ESI-TOF):** calc'd for $C_{22}H_{33}O_4$ $[M+H]^+$ 361.2373; found 362.2372;

$R_f$ = 0.5 (hexanes:EtOAc = 1:1);

**Melting point:** 161 °C.

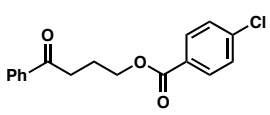


X-ray structure of 2-oxoisosteviol ethyl ester.

| | | |
|---|---|---|
| Empirical formula | C22 H32 O4 | |
| Molecular formula | C22 H32 O4 | |
| Formula weight | 360.47 | |
| Temperature | 100.0 K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Triclinic | |
| Space group | P1 | |
| Unit cell dimensions | a = 6.4628(3) Å | α= 70.4450(10)°. |
| | b = 12.4060(5) Å | β= 86.3930(10)°. |
| | c = 13.1362(6) Å | γ= 76.9130(10)°. |
| Volume | 966.61(7) $Å^3$ | |
| Z | 2 | |

| | |
|---|---|
| Density (calculated) | 1.239 $Mg/m^3$ |
| Absorption coefficient | 0.665 $mm^{-1}$ |
| F(000) | 392 |
| Crystal size | 0.4 x 0.25 x 0.06 $mm^3$ |
| Crystal color, habit | colorless plate |
| Theta range for data collection | 3.571 to 70.054°. |
| Index ranges | -7<=h<=7, -15<=k<=15, -15<=l<=15 |
| Reflections collected | 25233 |
| Independent reflections | 6975 [R(int) = 0.0380] |
| Completeness to theta = 67.500° | 98.4 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.5230 and 0.4194 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 6975 / 4 / 483 |
| Goodness-of-fit on $F^2$ | 1.052 |
| Final R indices [I>2sigma(I)] | R1 = 0.0292, wR2 = 0.0823 |
| R indices (all data) | R1 = 0.0293, wR2 = 0.0824 |
| Absolute structure parameter | -0.01(4) |
| Extinction coefficient | 0.0029(7) |
| Largest diff. peak and hole | 0.242 and -0.154 $e.Å^{-3}$ |

**4-Oxo-4-phenylbutyl 4-chlorobenzoate (15)**



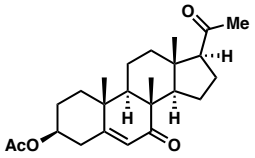
4-Phenylbutyl 4-chlorobenzoate (0.2 mmol, 58 mg) was electrolyzed for 7 h following the general procedure. The crude material was purified by PTLC (hexanes:EtOAc = 10:1) to afford the titled compound as a white solid (27 mg, 45% yield)

**$^1$H NMR (600 MHz, Chloroform-*d*)**: δ 8.04 – 7.86 (m, 4H), 7.62 – 7.51 (m, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 4.42 (t, *J* = 6.4 Hz, 2H), 3.14 (t, *J* = 7.1 Hz, 2H), 2.24 (p, *J* = 6.7 Hz, 2H).
**$^{13}$C NMR (151 MHz, Chloroform-*d*)** δ 199.03, 165.76, 139.47, 136.84, 133.28, 131.05, 128.79, 128.74, 128.10, 64.69, 35.00, 23.38;
**HRMS (ESI-TOF):** calc'd for $C_{17}H_{16}ClO_3$ $[M+H]^+$ 303.0782; found 303.078;
$R_f$ = 0.5 (hexanes:EtOAc = 10:1);
**Melting point:** 78 °C.

**δ-Valerolactone (16)**

Tetrahydropyran (0.2 mmol, 17 mg) was electrolyzed for 9 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 1:1, $R_f$ = 0.3) to give the titled compound as a colorless liquid (13 mg, 65% yield). The spectra data matched with values reported in the literature.[15]

**7-Oxo-pregnenolone acetate (17)**



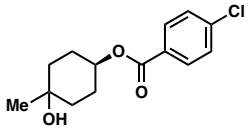
Pregnenolone acetate (0.2 mmol, 72 mg) was electrolyzed for 4 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 2:1, $R_f$ = 0.35) to give the titled compound as white needles in (69 mg, 91% yield). The spectra data matched with the literature value reported previously.[16]

**Nootokatone (18)**

Valencene (0.2 mmol, 41 mg) was electrolyzed for 4 h following the general procedure. The reaction gave complex mixture of oxidized products and attempts to isolate the desired compound was not successful.

**4-Hydroxy-4-methylcyclohexyl 4-chlorobenzoate (19)**

4-methylcyclohexyl 4-chlorobenzoate (0.2 mmol, 51 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by PTLC (hexane:AcOEt= 3:1) to give the top diastereomer in 33% (17.4 mg) and the bottom diastereomer in 23% yield (12.3 mg) both as white solid.




**$^1$H NMR (600 MHz, Chloroform-*d*, top diastereomer):** δ 7.97 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 4.97 (tt, *J* = 9.4, 4.6 Hz, 1H), 1.95 – 1.86 (m, 4H), 1.79 – 1.75 (m, 2H), 1.59 – 1.54 (m, 2H), 1.28 (s, 3H);

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 165.36, 139.36, 131.10, 129.34, 128.77, 72.99, 68.82, 36.73, 30.03, 27.44;

**HRMS (ESI-TOF):** calc'd for $C_{14}H_{18}ClO_3$ $[M+H]^+$ 269.0939; found 269.0940;

$R_f$ = 0.4 (hexanes:EtOAc = 3:2).

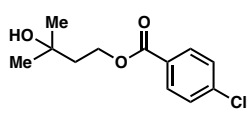
**$^1$H NMR (600 MHz, Chloroform-*d*, bottom diatereomer):** δ 7.96 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 5.20 (tt, *J* = 5.6, 3.2 Hz, 1H), 2.05 – 2.00 (m, 2H), 1.83 – 1.75 (m, 4H), 1.61 – 1.57 (m, 2H), 1.32 (s, 3H);

**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 165.27, 139.38, 131.03, 129.45, 128.83, 71.15, 69.49, 34.86, 30.23, 26.73;

**HRMS (ESI-TOF):** calc'd for $C_{14}H_{18}ClO_3$ $[M+H]^+$ 269.0939; found 269.0936;

$R_f$ = 0.3 (hexanes:EtOAc = 3:2).

**3-Hydroxy-3-methylbutyl 4-chlorobenzoate (20)**




3-methylbutyl 4-chlorobenzoate (0.2 mmol, 45 mg) was electrolyzed for 12 h following the general procedure. The crude material was purified by PTLC (hexanes:EtOAc = 2:1) to give the titled compound as a colorless liquid yield (29 mg, 62%).

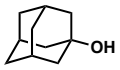
**$^{1}$H NMR (600 MHz, Chloroform-*d*):** δ 7.95 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 4.49 (t, *J* = 6.9 Hz, 2H), 1.97 (t, *J* = 6.9 Hz, 2H), 1.32 (s, 6H);

**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 166.03, 139.63, 131.06, 128.90, 128.75, 70.45, 62.32, 41.74, 29.84;

**HRMS (ESI-TOF):** calc'd for $C_{12}H_{16}ClO_3$ $[M+H]^+$ 243.0782; found 243.0784;

$R_f$ = 0.4 (hexanes:EtOAc = 2:1).

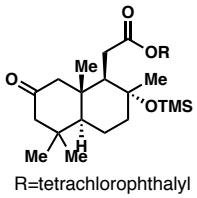
**1-Adamantanol (21)**




Adamantane (0.2 mmol, 27 mg) was electrolyzed for 6 h following the general procedure. The crude material was purified by column chromatography (hexanes:EtOAc = 3:1) to give the titled compound as a white solid (17 mg, 56% yield). The spectra data matched with values reported in the literature.[17]

# Synthesis of 2-oxo-yahazunone

**Compound 22**

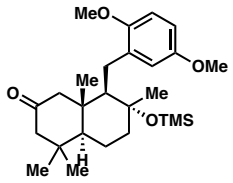


R=tetrachlorophthalyl

To a stirred solution of 2-oxo-sclareolide **2** (0.64 mmol, 167 mg, 1.0 equiv.) in MeOH (4 mL) was added aqueous 3 M KOH (4 mL) and the solution was refluxed for 2h. Then, 1N HCl was added to acidify the solution (pH = 1). This solution was partitioned between brine and EtOAc; the organic phase was dried over anhydrous $Na_2SO_4$ and was concentrated *in vacuo*. The residue was dissolved to 5 mL of $CH_2Cl_2$. Imidazole (4 mmol, 272 mg) and TMSCl (3 mmol, 0.38 mL) were added successively under an argon atmosphere. After stirring overnight at ambient temperature, the mixture was poured into water and extracted with a mixture of organic solvents (hexanes:EtOAc =5:1) twice. The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated. The crude product was re-dissolved in $CH_2Cl_2$ (4 mL) and was treated with *N*-hydroxytetrachlorophthalimide (0.7 mmol, 210 mg) and *N*,*N*'-diisopropylcarbodiimide (0.7 mmol, 0.11 mL) under argon atmosphere at ambient temperature. After stirring for 2 h, the reation mixture was concentrated *in vacuo* and the resulting residue was quickly passed through a short silica-gel plug with EtOAc as the eluent. Finally, this crude material was purified by recrystallization from $CH_2Cl_2$/MeOH to afford the desired redox active ester (190 mg, 48% yield) as pale yellow needles.

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 2.96 (dd, *J* = 16.9, 3.1 Hz, 1H), 2.47 (dd, *J* = 16.9, 6.8 Hz, 1H), 2.33 (d, *J* = 13.3 Hz, 1H), 2.34 – 2.26 (m, 3H), 2.16 (dd, *J* = 13.2, 1.9 Hz, 1H), 2.05 (dt, *J* = 12.6, 3.2 Hz, 1H), 1.85 – 1.81 (m, 1H), 1.76 (td, *J* = 12.9, 4.0 Hz, 1H), 1.67 (dd, *J* = 12.3, 2.4 Hz, 1H), 1.41 – 1.33 (m, 1H), 1.17 (s, 3H), 1.08 (s, 3H), 0.87 (s, 3H), 0.86 (s, 3H), 0.13 (s, 9H);
**$^{13}$C NMR (151 MHz, Chloroform-*d*):** δ 210.23, 170.31, 157.54, 141.03, 130.53, 124.92, 76.07, 57.70, 56.40, 55.13, 54.98, 43.54, 43.07, 38.96, 33.50, 27.00, 24.57, 22.99, 20.72, 16.64, 2.79;
**HRMS (ESI-TOF):** calc'd for $C_{27}H_{34}Cl_4NO_6Si$ $[M+H]^+$ 636.0904; found 636.0905;
$R_f$ = 0.2 (hexanes:EtOAc=10:1);
**Melting point:** 190 °C.

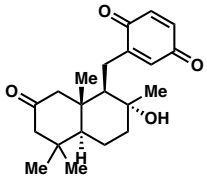
**Compound 23**



To an argon-purged test tube charged with redox active ester **22** (0.083 mmol, 53 mg, 1.0 equiv.) was added 0.55 mL of Ni catalyst stock solution (containing 0.030 M of $NiCl_2$•$6H_2O$ and 0.015 M 4,4'-di-tert-butylbypyridyl in DMF). To the resulting mixture was added arylzinc reagent (0.75 mL, prepared by adding 1.0 mL of 1.0 M anhydrous $ZnCl_2$ in THF to the corresponding Grignard reagent, which was prepared from 1.0 mmol of 1-bromo-2,5-dimethoxybenzene, 1.5 mmol of Mg turnings, and 2.0 mmol of LiCl in 2 mL of THF) at ambient temperature. The mixture was warmed up to 50 °C and stirred for 8 h. The reaction was then quenched with sat. aq. $NH_4Cl$, poured onto water, and extracted with a mixture of solvents (hexanes:EtOAc = 4:1) twice. The combined organic layer was dried over $Na_2SO_4$ and concentrated *in vacuo*. The crude material was purified by PTLC (hexanes:EtOAc = 5:1) to give the desired product (21 mg, 58% yield) as white needles.

**$^1$H NMR (600 MHz, Chloroform-*d*):** δ 6.94 (d, *J* = 3.1 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 6.63 (dd, *J* = 8.8, 3.1 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.86 (dd, *J* = 14.8, 7.3 Hz, 1H), 2.60 (dd, *J* = 14.8, 2.5 Hz, 1H), 2.23 (dd, *J* = 12.7, 2.3 Hz, 1H), 2.14 (d, *J* = 13.2 Hz, 1H), 2.06 – 2.02 (m, 2H), 1.92 (dd, *J* = 7.3, 2.6 Hz, 1H), 1.77 – 1.66 (m, 3H), 1.53 (dd, *J* = 12.3, 2.0 Hz, 1H), 1.39 – 1.32 (m, 1H), 1.25 (s, 3H), 1.02 (s, 3H), 0.94 (s, 3H), 0.84 (s, 3H), 0.10 (s, 9H);
**$^{13}$C NMR (151 MHz, $CDCl_3$):** δ 211.97, 153.71, 150.96, 134.77, 116.38, 111.36, 110.49, 77.13, 63.79, 56.37, 56.10, 55.80, 55.47, 54.96, 44.41, 44.15, 38.73, 33.63, 24.60, 23.10, 22.80, 20.75, 16.71, 2.96;
**HRMS (ESI-TOF):** calc'd for $C_{26}H_{43}O_4Si$ $[M+H]^+$ 447.2925; found 447.2924;
$R_f$ = 0.4 (hexanes:EtOAc = 5:1);
**Melting point:** 105 °C.

**2-Oxo-yahazunone 25**



Compound **23** (0.057 mmol, 25.4 mg, 1 equiv.) was dissolved in a minimal amount of DCM (0.1 mL). To this solution were added 6 mL of solvent mixture (DMF:MeCN:$H_2O$ = 2:2:1) and 2,6-pyridinedicarboxylic acid 1-oxide (**24**) (0.09 mmol, 16 mg, 1.58 equiv.). The mixture (compound **23** was found to precipitate partially in the solvent mixture) was cooled down to 0 °C when an aqueous solution of CAN (1 M, 0.17 mmol, 0.17 mL) was added immediately. Upon the complete consumption of starting material as judged by TLC

(usually within 5 minutes), the reaction was poured onto brine, and was extracted with $Et_2O$ three times. The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated *in vacuo*. The crude material was purified by PTLC (hexane:AcOEt = 1:1.5) to give the desired product (9.2 mg, 47% yield) as a viscous yellow liquid.

**$^1$H NMR (600 MHz, Chloroform-*d*)** δ 6.74 (d, *J* = 10.1 Hz, 1H), 6.68 (dd, *J* = 10.1, 2.5 Hz, 1H), 6.61 (d, *J* = 2.6 Hz, 1H), 2.62 (dd, *J* = 15.1, 7.0 Hz, 1H), 2.44 (dd, *J* = 15.1, 4.8 Hz, 1H), 2.34 (dd, *J* = 12.4, 2.2 Hz, 1H), 2.30 (d, *J* = 13.4 Hz, 1H), 2.17 (dd, *J* = 13.5, 2.3 Hz, 1H), 2.14 (d, *J* = 12.5 Hz, 1H), 1.94 (dt, *J* = 12.6, 3.2 Hz, 1H), 1.90 (dd, *J* = 7.0, 4.7 Hz, 1H), 1.81 – 1.78 (m, 1H), 1.54 – 1.49 (m, 2H), 1.39 (td, *J* = 13.0, 12.5, 3.1 Hz, 1H), 1.23 (s, 3H), 1.07 (s, 3H), 0.90 (s, 3H), 0.87 (s, 3H);
**$^{13}$C NMR (151 MHz, Chloroform-*d*)** δ 210.60, 188.01, 187.64, 151.57, 137.15, 136.43, 133.03, 73.86, 60.12, 56.23, 55.81, 55.49, 44.41, 44.30, 38.75, 33.63, 25.23, 23.65, 23.16, 20.62, 16.56;
**HRMS (ESI-TOF):** calc'd for $C_{21}H_{29}O_4$ $[M+H]^+$ 345.206; found 345.2059;
$R_f$ = 0.5 (hexanes:EtOAc = 1:2).

# TFDO Oxidation

**General Procedure**

TFDO (*ca.* 0.4 M in trifluoroacetone) was prepared by following the procedure reported in the literature[18] with slight modifications (The details are described in the Baran Laboratory Blog: http://openflask.blogspot.com/2014/01/tfdo-synthesis-procedure.html). This TFDO solution (0.3 mmol, 0.75 mL, 3.0 equiv.) was added to a stirred solution of a substrate (0.1 mmol, 1.0 equiv.) in $CH_2Cl_2$ (1.0 mL) at 0 °C and stirred for 6 h. The solvents were removed under reduced pressure and the crude material was purified by either PTLC or column chromatography.

**2-Methylpentyl 4-chlorobenzoate (S2)**

The crude material was purified by PTLC ($CH_2Cl_2$) to give the corresponding ketone (**4**) and alcohol (δ:β = 1.9:1, 60% yield).

**1-Methylcyclohexanol**

The crude material was purified by column chromatography (hexanes:EtOAc = 1:2) to give trace amount of the corresponding ketone (**9**, <5%).

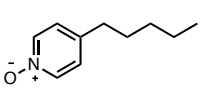
**Methyl 1-benzamidocyclohexane-1-carboxylate (S10)**

The crude material was purified by PTLC (hexanes:EtOAc = 1:3) to give the corresponding ketone (**10**) and alcohol (δ:γ = 1.1:1, 42% yield).

**4-Pentylpyridine (S8)**

The crude material was purified by PTLC (EtOAc:MeOH = 1:3) to give the corresponding *N*-oxide (**S14**) (10 mg, 63% yield) as colorless liquid.

**4-Pentylpyridine *N*-oxide (S14)**



**$^1$H NMR (600 MHz, Chloroform-*d*)** δ 8.17 – 8.05 (br, 2H), 7.13 – 6.99 (br, 2H), 2.66 – 2.47 (br, 2H), 1.66 – 1.45 (br, 2H), 1.39 – 1.20 (br, 4H), 0.93 – 0.78 (br, 3H).

**$^{13}$C NMR (151 MHz, $CDCl_3$)** δ 142.65, 138.86, 126.07, 34.46, 31.26, 29.96, 22.49, 14.04.

**HRMS (ESI-TOF):** calc'd for $C_{15}H_{10}NO$ $[M+H]^+$ 166.1226; found 166.1228;

$R_f$ = 0.2 (EtOAc:MeOH = 5:1).

**Sclareolide (1)**

The crude material was purified by column chromatography ($CH_2Cl_2$:$Et_2O$ = 5:1) to give the corresponding ketones (**2**, C2:C3 = 1:3.5, 47% yield).

# Cost Calculation for 50 gram Scale Sclareolide Oxidation

Prices of all reagents were obtained from Sigma Aldrich (accessed on Apr.8.2017)

The scale of the reaction is 0.2 mol (50 g).

**TFDO oxidation**

trifluoroacetone (T62804-100G, $237.50**)** Price for the reaction: $ 9120 (3840 g)

Calculation based on 3 equiv. of TFDO is required for the oxidation (this is consistent with Ref. 10) and the yield of TFDO is taken as 2% from trifluoroacetone. See Baran Laboratory Blog for details: http://openflask.blogspot.com/2014/01/tfdo-synthesis-procedure.html
$2.375/g × 0.20 mol × 3 equiv. × 128 g/mol (TFDO) ÷ 2% = $ 9120

**Iron catalysis[9]**

Fe(S,S-PDP) (730459-500MG, $399.50) $ 37,229 (25 mol%, 50 mmol, 46.5 g)
$799/g × 50 mmol × 931.9 g/mol ÷ 1000 = $37,229

**This work**

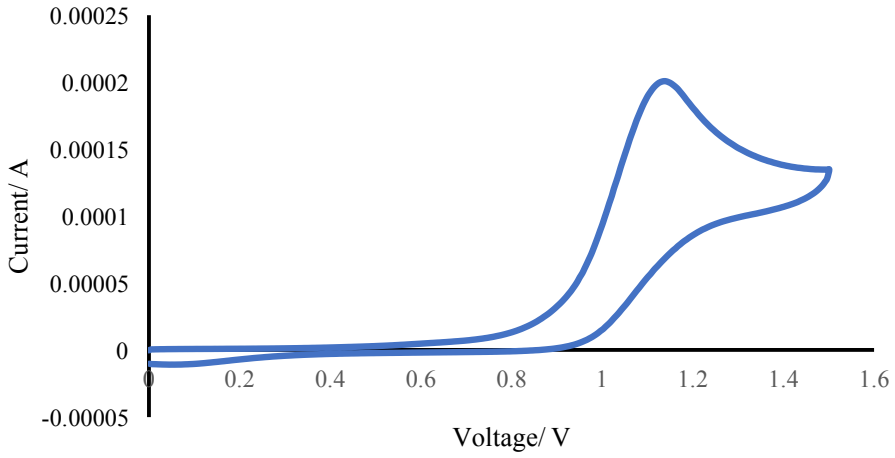
| | | Price for the reaction |
|---|---|---|
| Acetonitrile, ≥99.5%, ACS reagent (110086-4L)) | $ 362 | $271 (3 L) |
| HFIP(105228-2KG**)** | $1905 | $319 (336 g) |
| $Bu_4N•BF_4$ (217964-100G) | $ 359 | $236 (65.8 g) |
| quinuclidine (197602-10G) | $769 | $1691 (22 g) |
| Electricity (approximate cost for Tianjin, China) | $ 0.1/kW•h | $ 0.081 (108 h × 1.5 A × 5 V × $0.1 ÷ 1000) |
| | | $2517 |

The working potential of the 50 g scale electrochemical oxidation was kept between 2.5 V and 5.6 V during the reaction. 5.0 V is used for this calculation. Since no reference electrode was used, this number is an approximation. Nevertheless, it shows that the cost of electricity is insubstantial.

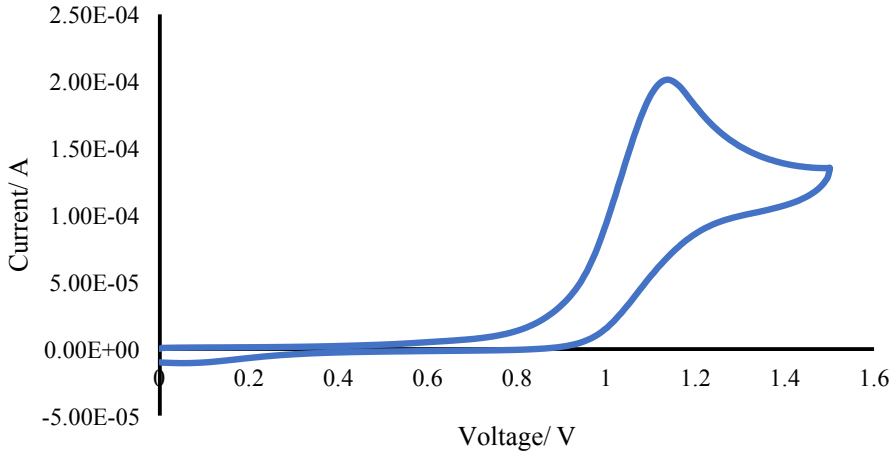
# Cyclic Voltammetry

Cyclic voltammetry was carried out in a glass cell with Pine WaveNow potentiostat. A glassy carbon disk electrode (diameter is 3.0 mm, PCTFE shroud) was used as a working electrode. A platinum wire was used as a counter electrode. Ag/AgCl electrode was used as a reference electrode. Electrolyte: 0.1 M $Me_4NBF_4$ in MeCN; Concentration of a sample: 0.05 M

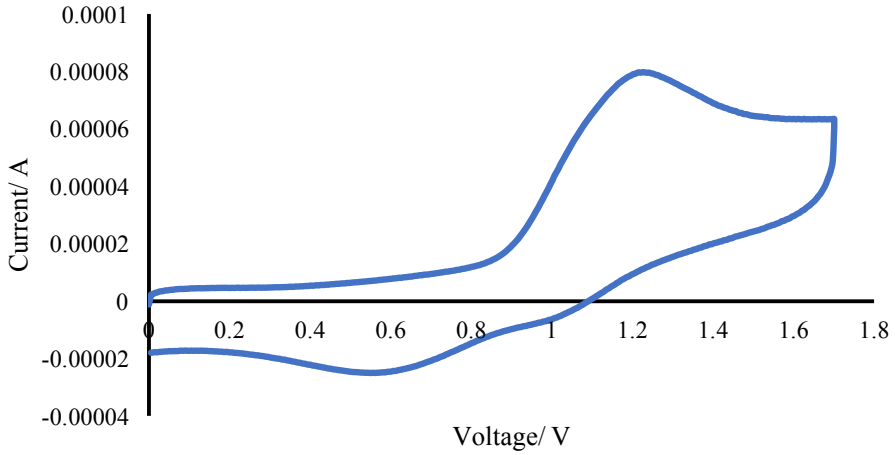
**Quinuclidine**



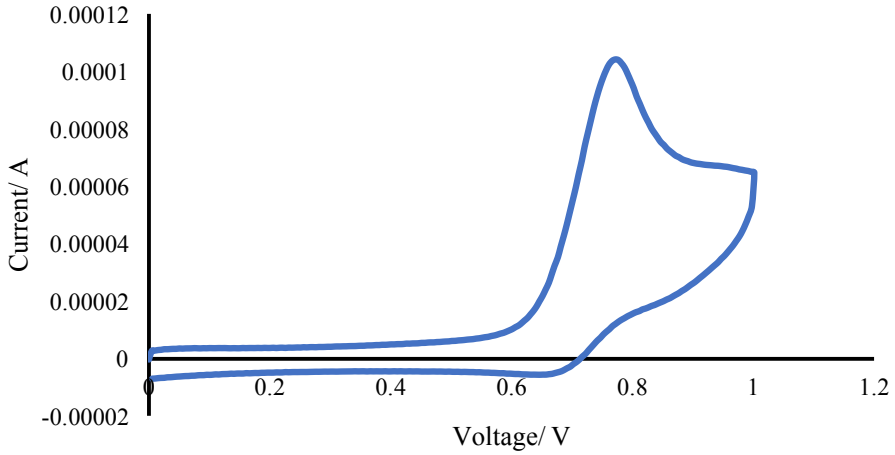

**Quinuclidine + HFIP (10 equiv.)**



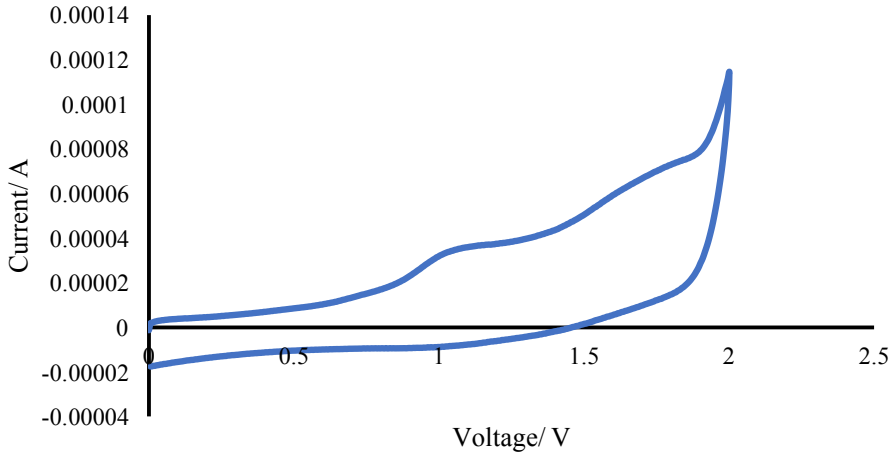
**Aceclidine + HFIP (10 equiv.)**



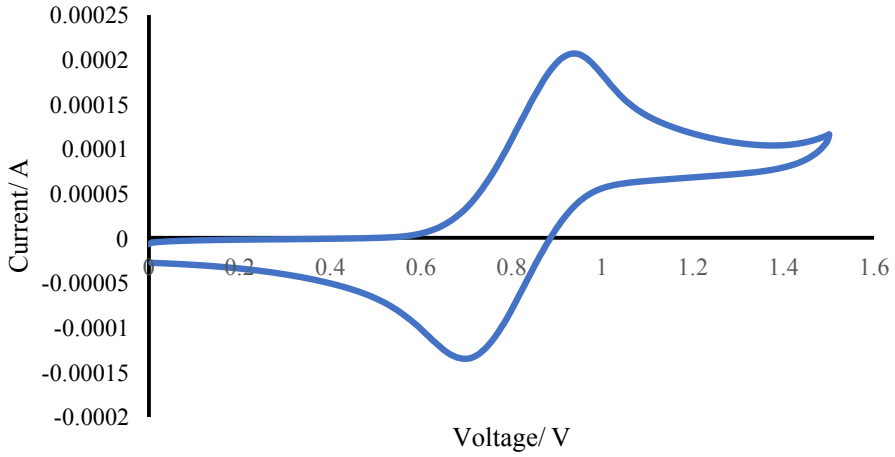

**DABCO + HFIP (10 equiv.)**



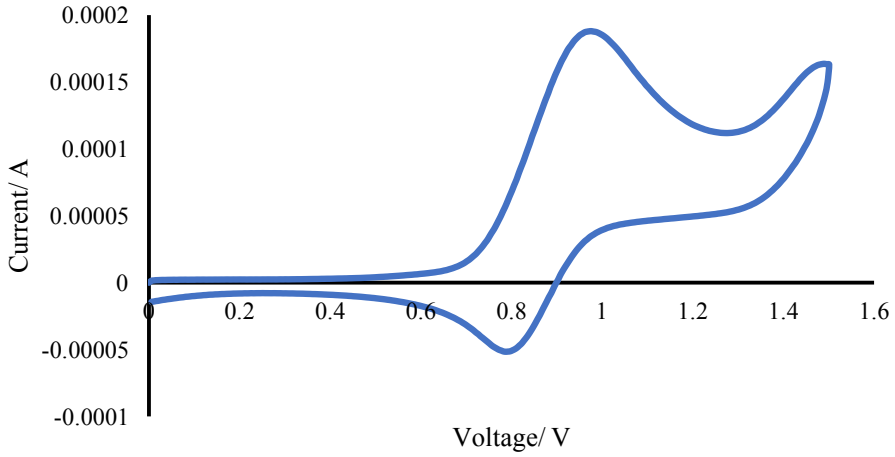
**NMO**



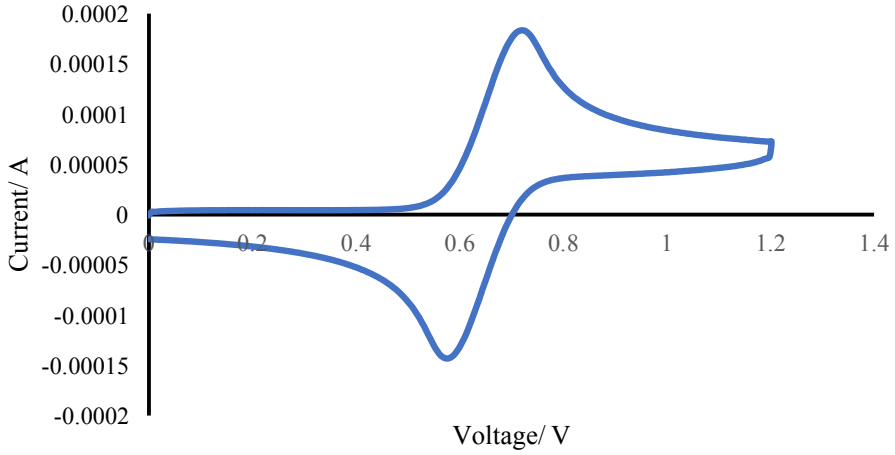

**NHPI + 2,6-lutidine (1.0 equiv.)**



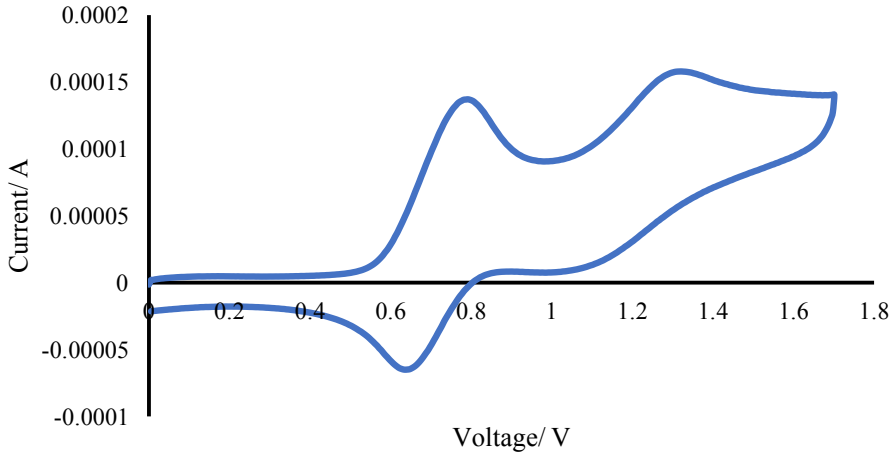
**TCNHPI + 2,6-lutidine (1.0 equiv.)**




**TEMPO**



**HOBT + 2,6-lutidine (1.0 equiv.)**



## Trouble shooting & FAQ

Q. What can I do when the yield of the reaction was not reproducible?

A. Check the voltage of the reaction. From our experiences, if the voltage is too high (roughly above 5 V at 5 mA on 0.2 mmol scale without reference electrode), this reaction does not proceed well. Normal operational voltage is around 2.5V–4V for this reaction.

When a high voltage is noted:
• Ensure there is sufficient contact between the electrode and attached wire to avoid undesired increase of the resistance in the entire circuit.
• Increasing the amount of electrolyte also helps to reduce the resistance of the cell.

If the reaction voltage is not likely to be the cause of irreproducibility, make sure that the wire attached to the RVC anode is well above the solution to avoid the corrosion of the wire. Please note that the wire can still be in contact with the solution even if it looks there is no apparent contact during set-up of an experiment, as RVC soaks up the solution quite well.

Q. What are the suitable current values for reactions on different scales?

A. The reaction is usually run at 25 mA/mmol. For instance, the suitable current will be 1.5-2.5 mA for 0.1 mmol scale, while 5-10 mA will be suitable for 0.4 mmol scale.

Q. We don’t have Ni foam; are there any alternative materials we can use for the reaction?

A. Ni foam is not crucial to the reaction. You can also use stainless steel, copper, aluminium etc.

Q. Aside from the stainless steel wires (from Home Depot) you described, can we use different wires?

A. Yes. Any conductive material can be used to connect the electrodes with the potentiostat.

Q. Is this reaction sensitive to water?

A. A small amount of water (10–20 mol%) does not significantly affect the outcome. Therefore, wet ammonium salt can be used as the electrolyte. However, large amount of water should be avoided since it slows down the reaction and sometimes inhibits.

Q. Does graphite or other carbon anode work for this reaction?

A. We have attempted using graphite during the very early stages of the study; lower conversions were observed. We thus strongly recommend RVC anode.

Q. Where can I get the materials to construct the electrochemical cell?

A. Materials used and their commercial sources have been detailed in the graphical guide for cell construction (page S11).

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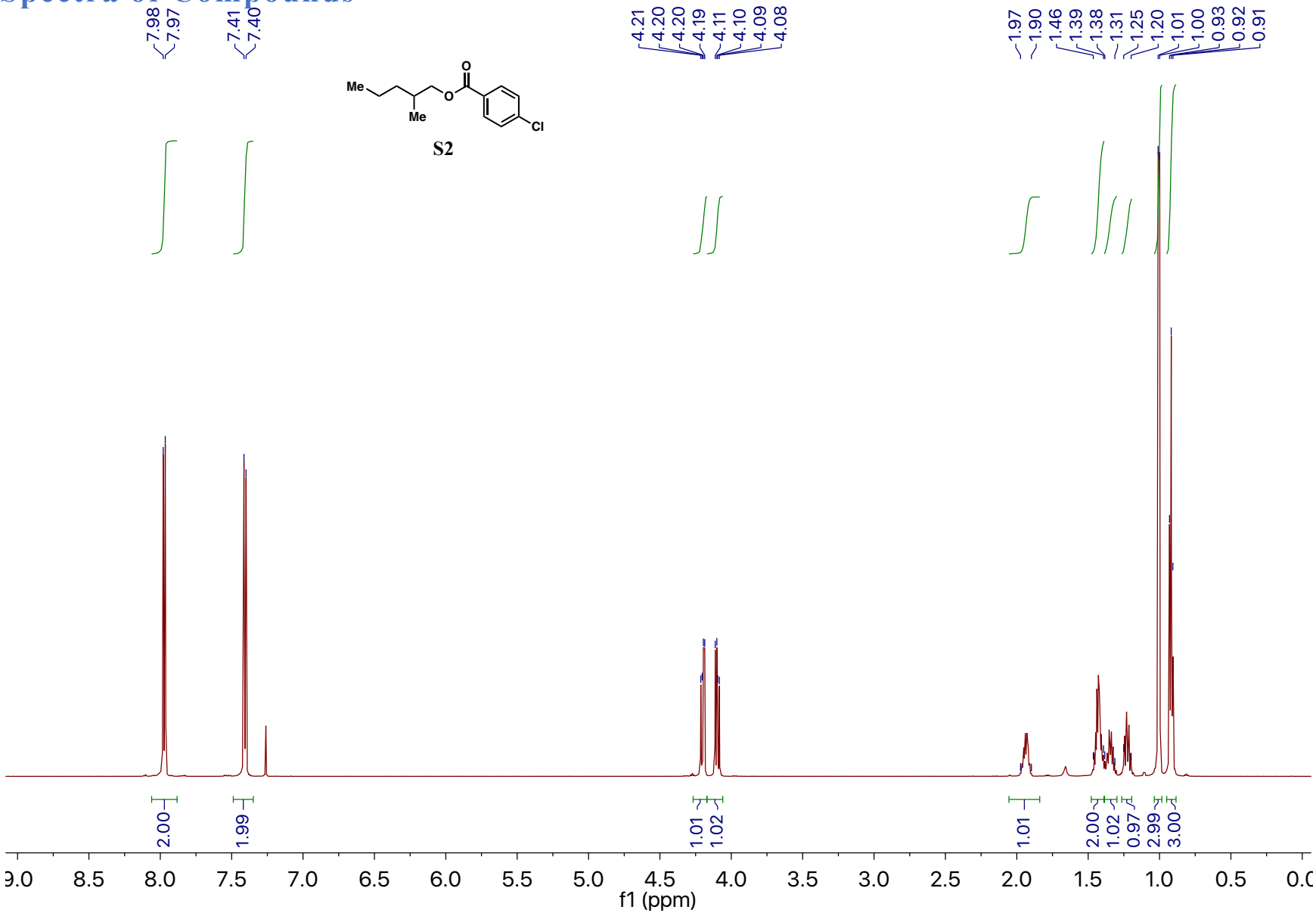
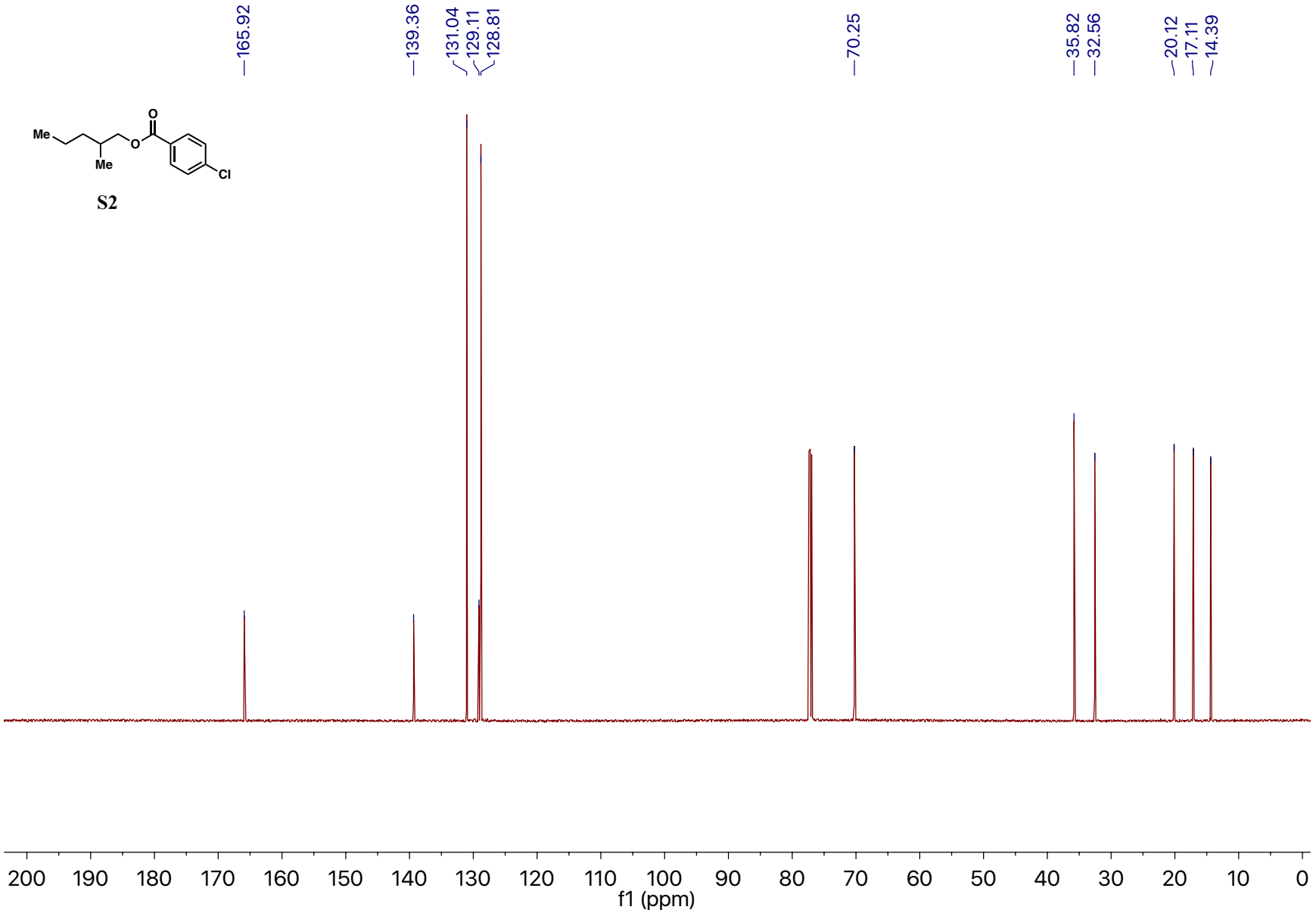
## Spectra of Compounds




**S2**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139.36
131.04
129.11
128.81
70.25
35.82
32.56
20.12
17.11
14.39
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Me
O
O
Cl
S2
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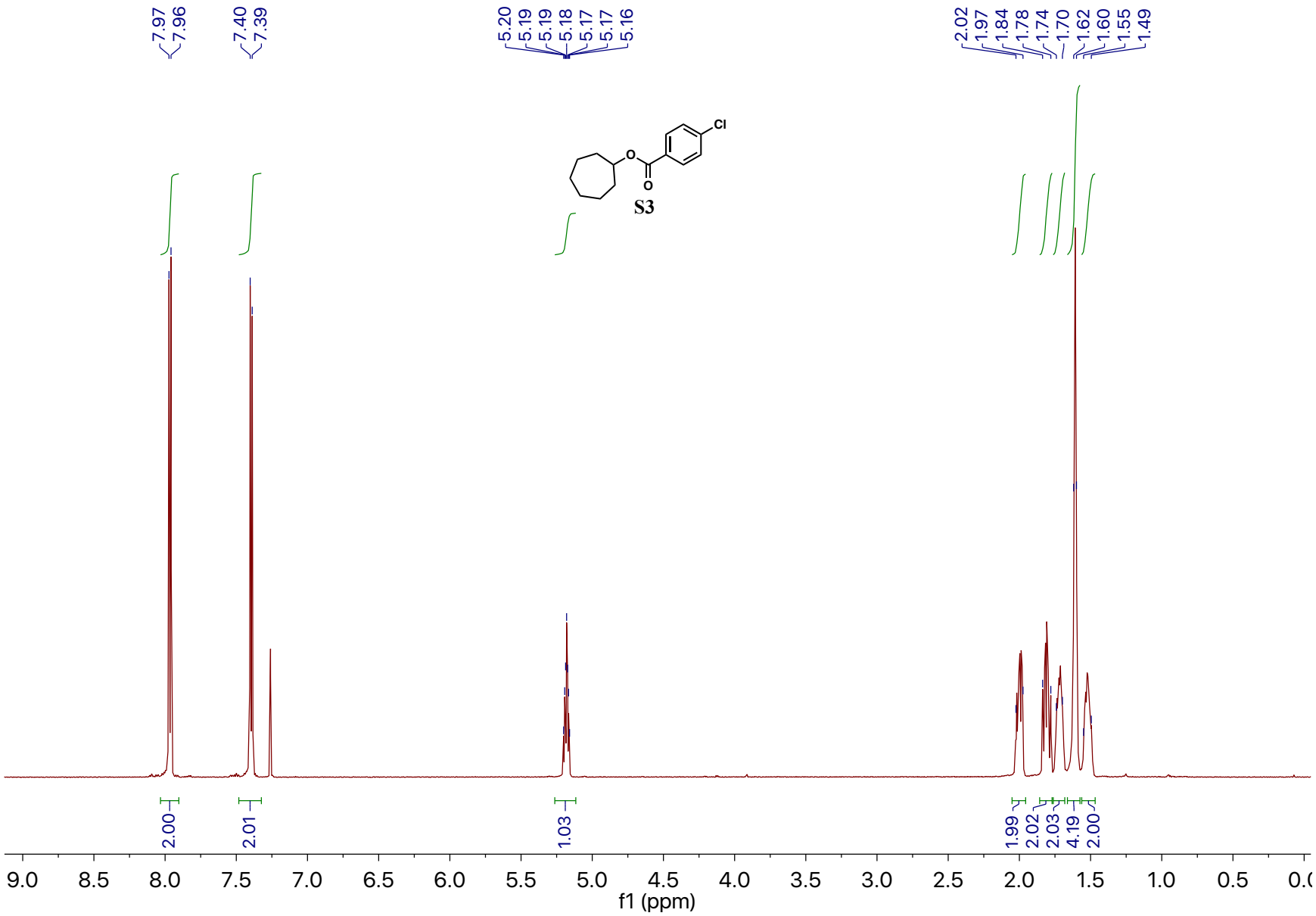
f1 (ppm)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7.96
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7.39
5.20
5.19
5.19
5.18
5.17
5.17
5.16
2.02
1.97
1.84
1.78
1.74
1.70
1.62
1.60
1.55
1.49
Cl
O
O
S3
2.00
2.01
1.03
1.99
2.02
2.03
4.19
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
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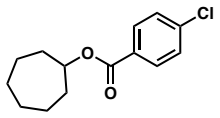
2.0
1.5
1.0
0.5
f1 (ppm)


Cl
O
O

**S3**


165.19
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131.04
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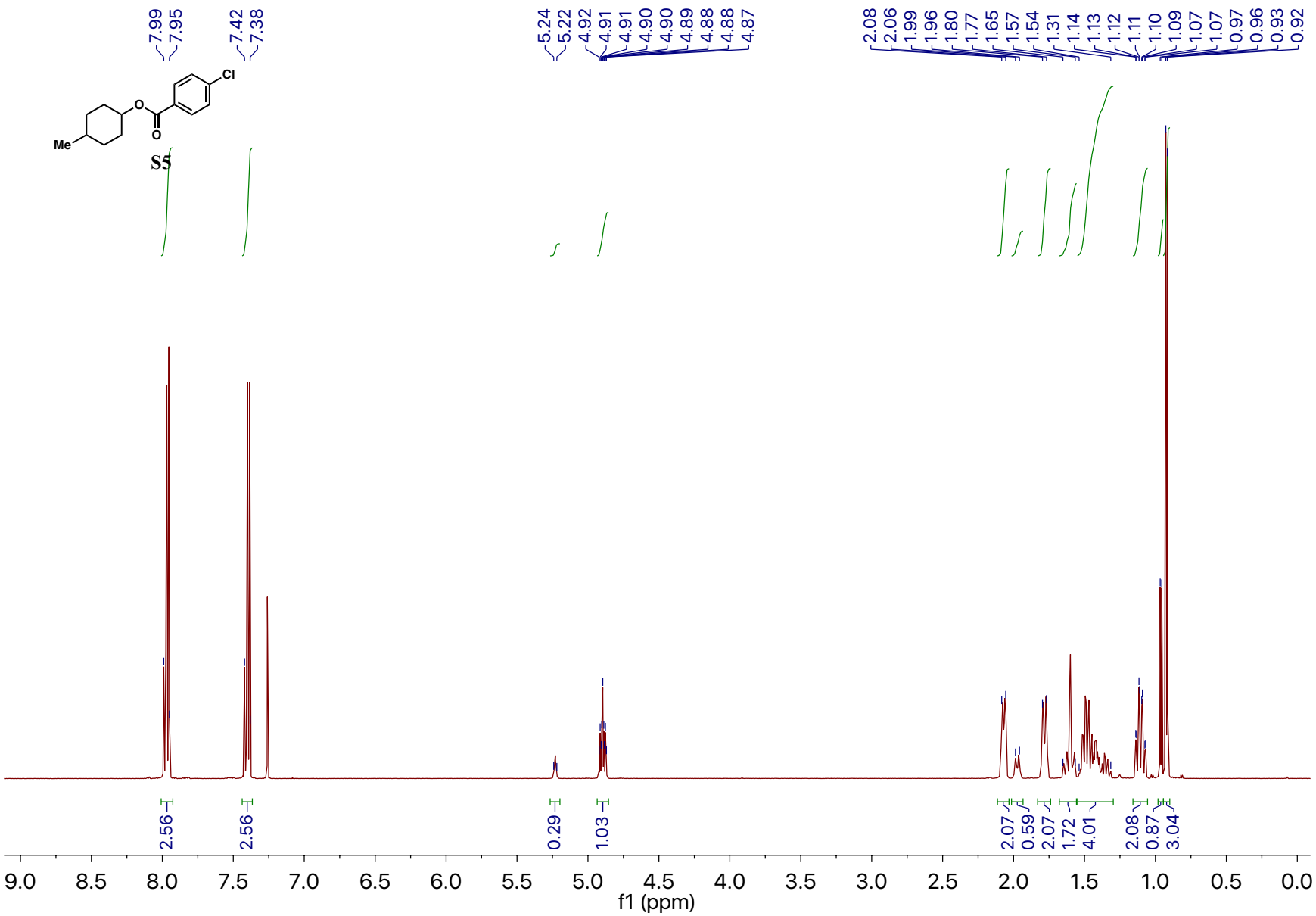
28.44
23.06
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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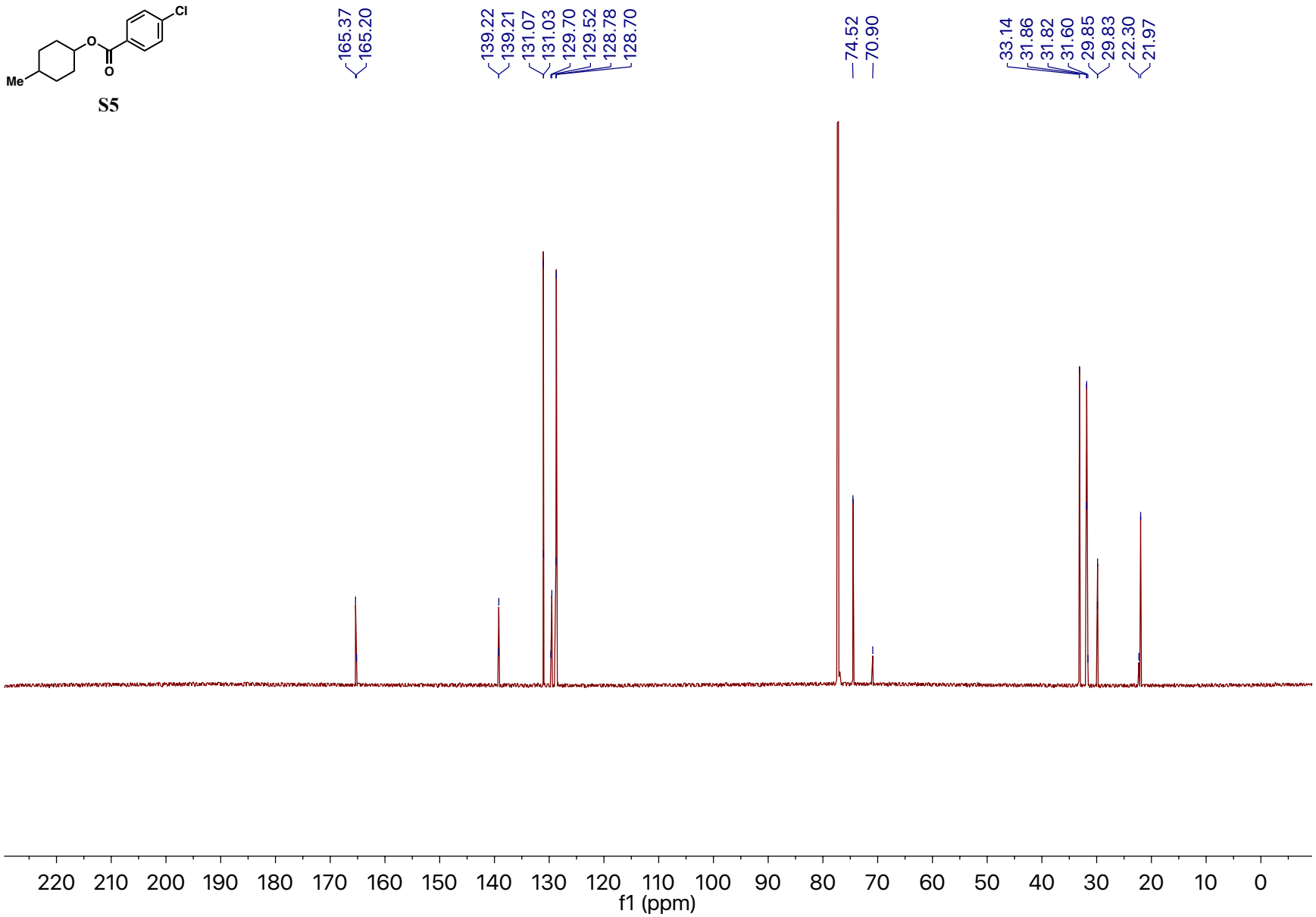
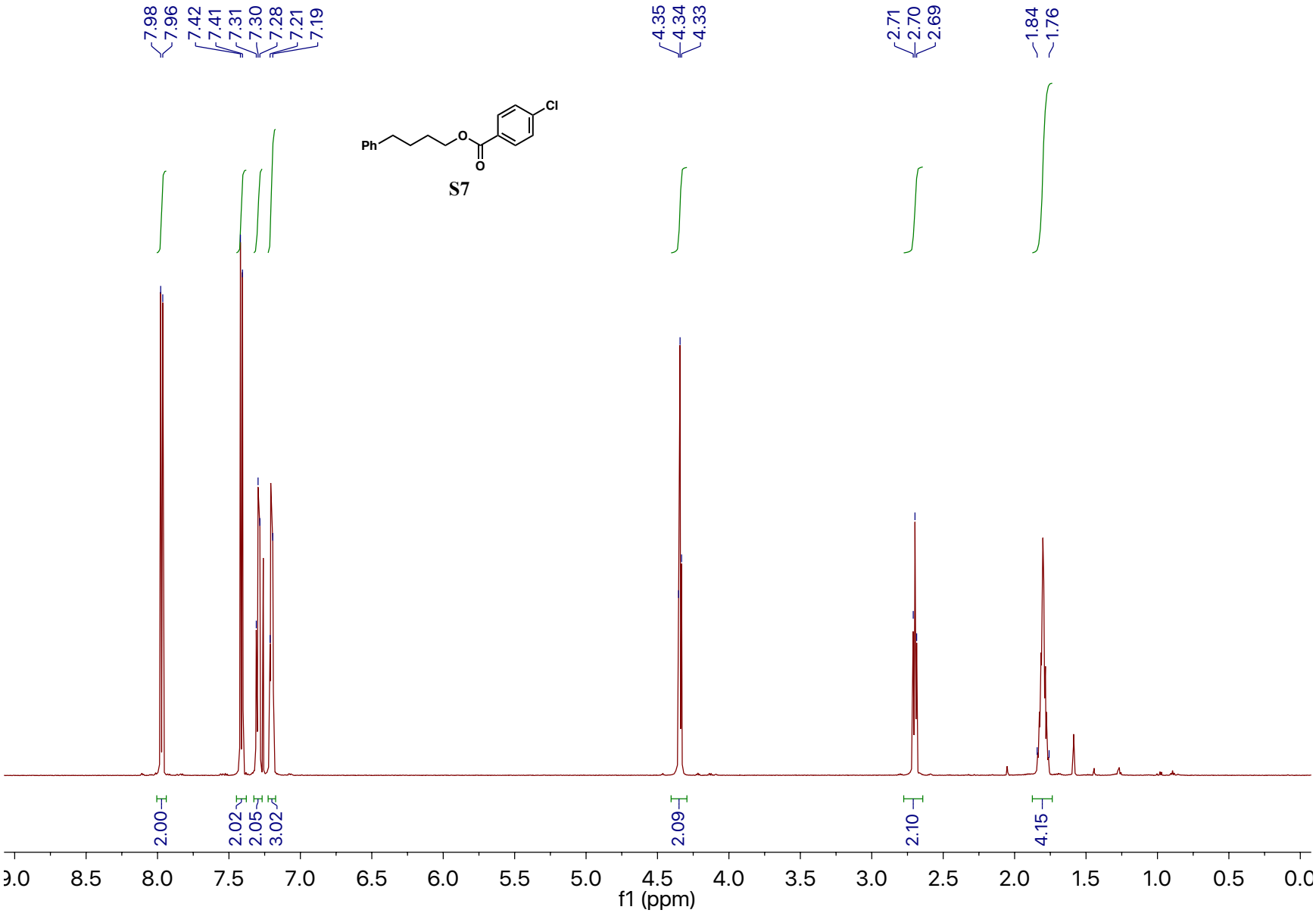
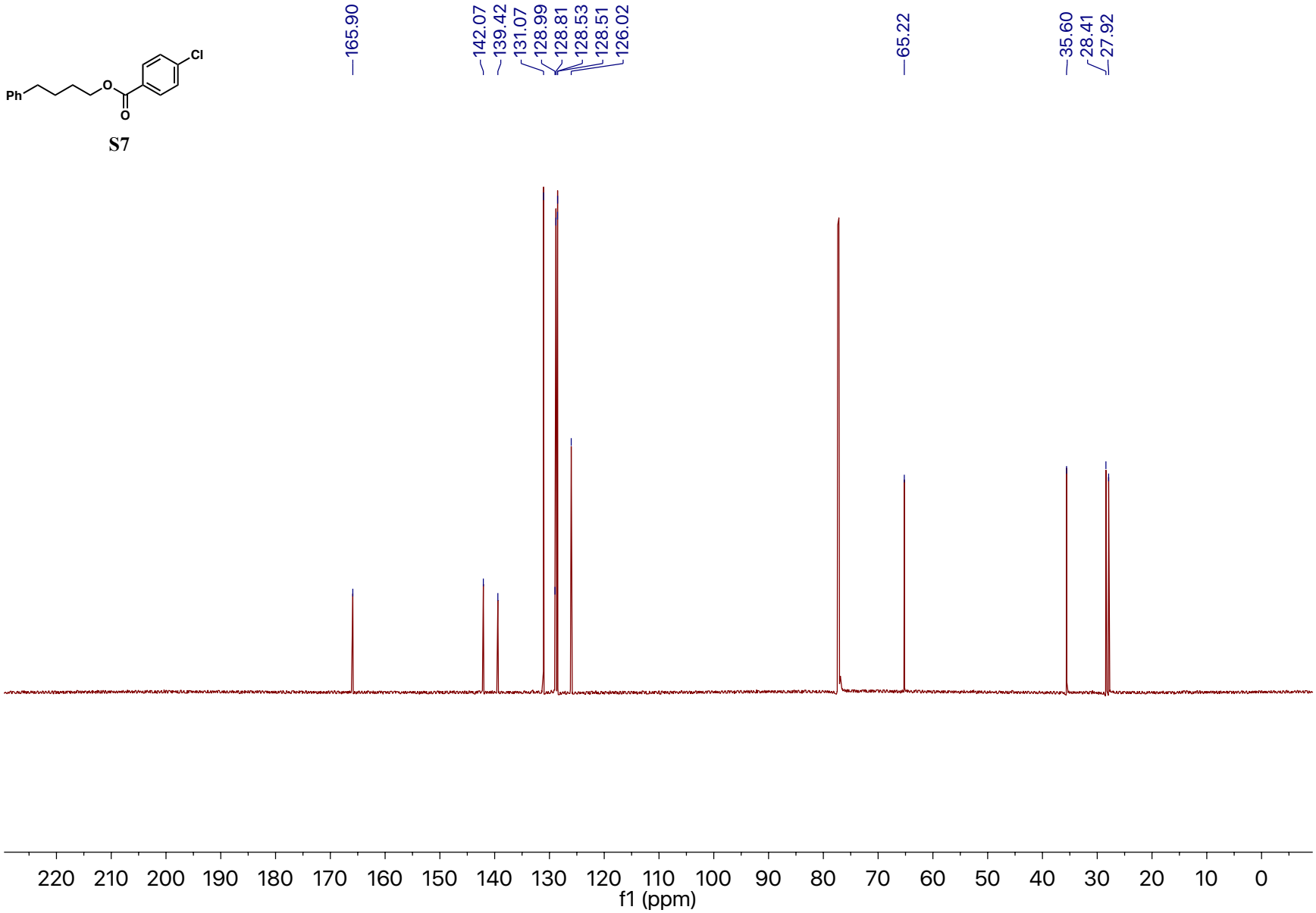
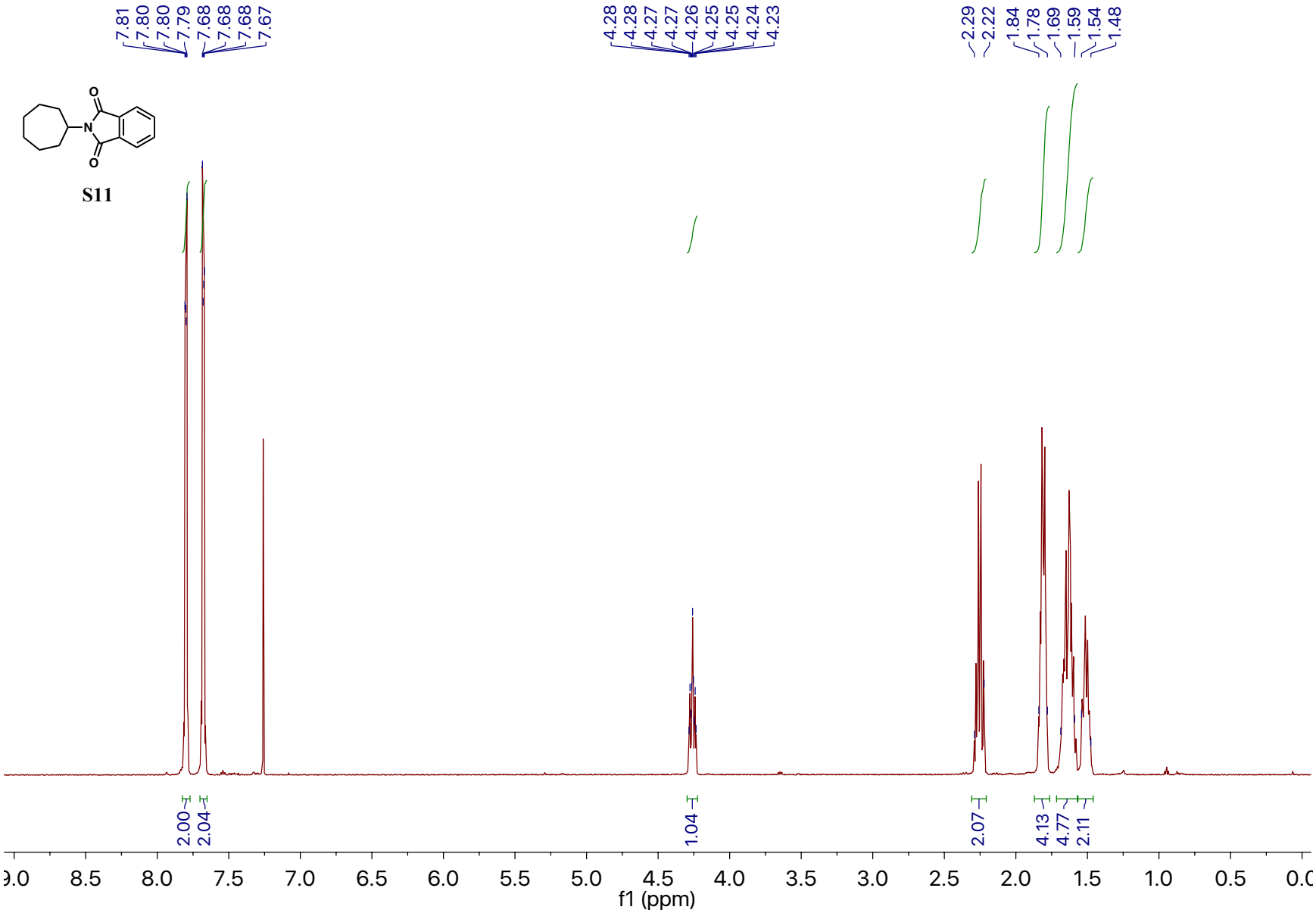
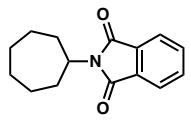
5.24
5.22
4.92
4.91
4.91
4.90
4.90
4.89
4.88
4.88
4.87
2.08
2.06
1.99
1.96
1.80
1.77
1.65
1.57
1.54
1.31
1.14
1.13
1.12
1.11
1.10
1.09
1.07
1.07
0.97
0.96
0.93
0.92
Cl
O
O
Me
S5
2.56
2.56
0.29
1.03
2.07
0.59
2.07
1.72
4.01
2.08
0.87
3.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Cl
O
O
Me
S5
165.37
165.20
139.22
139.21
131.07
131.03
129.70
129.52
128.78
128.70
74.52
70.90
33.14
31.86
31.82
31.60
29.85
29.83
22.30
21.97
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.98
7.96
7.42
7.41
7.31
7.30
7.28
7.21
7.19
4.35
4.34
4.33
2.71
2.70
2.69
1.84
1.76
Cl
Ph
O
O
S7
2.00
2.02
2.05
3.02
2.09
2.10
4.15
f1 (ppm)

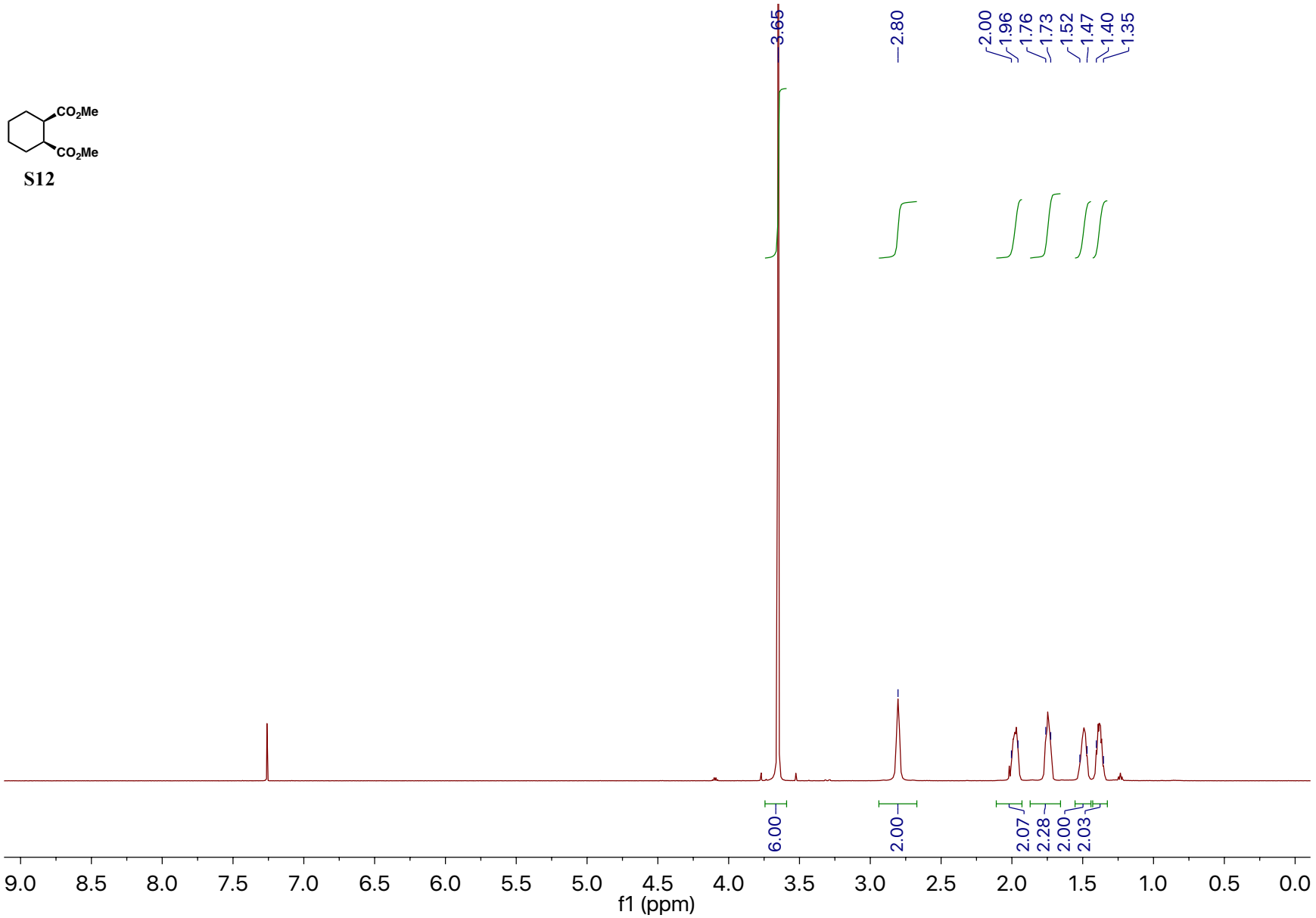

Ph
O
O
Cl
S7
165.90
142.07
139.42
131.07
128.99
128.81
128.53
128.51
126.02
65.22
35.60
28.41
27.92
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

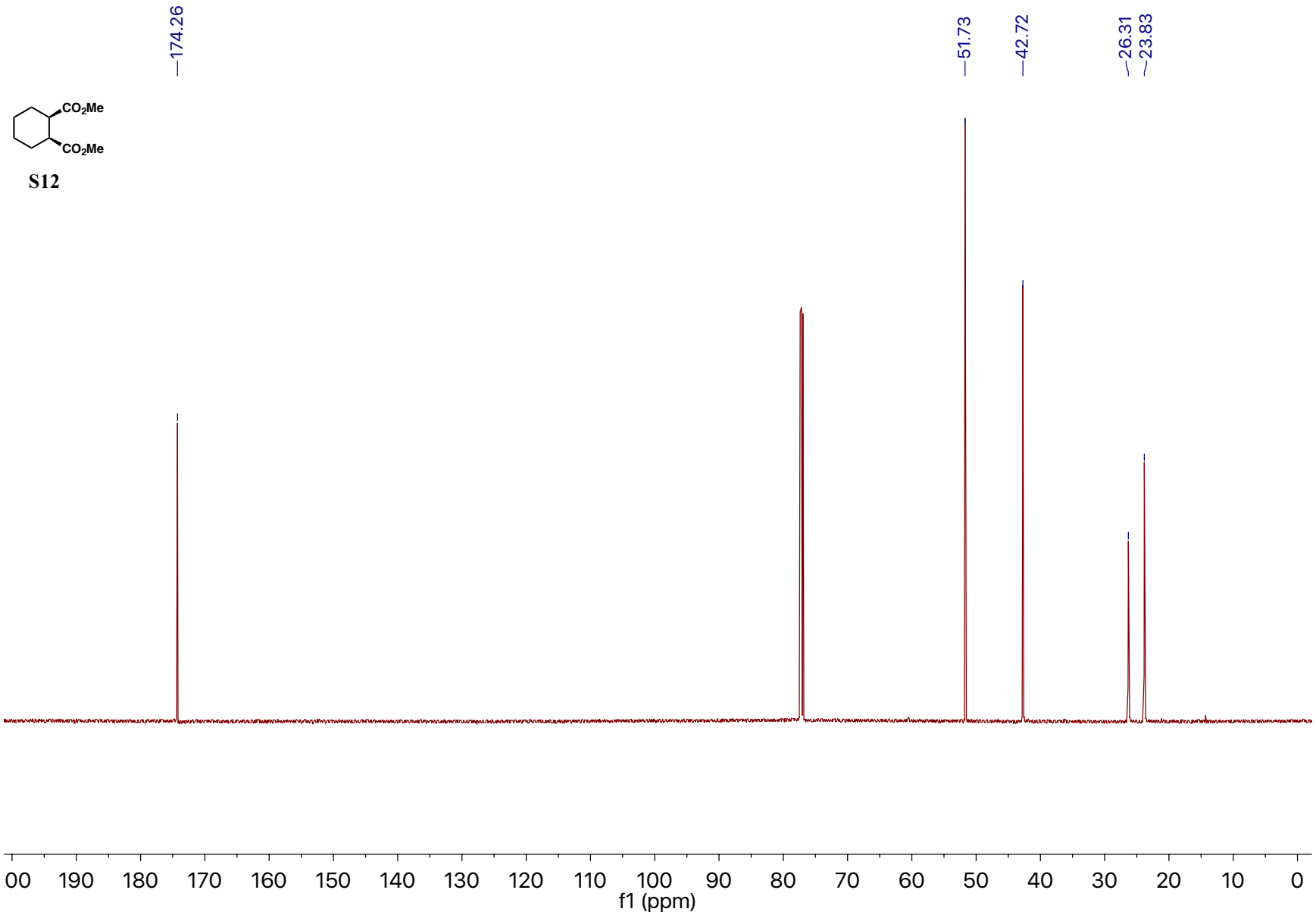

7.81
7.80
7.80
7.79
7.68
7.68
7.68
7.67
4.28
4.28
4.27
4.27
4.26
4.25
4.25
4.24
4.23
2.29
2.22
1.84
1.78
1.69
1.59
1.54
1.48
O
N
O
S11
2.00
2.04
1.04
2.07
4.13
4.77
2.11
f1 (ppm)

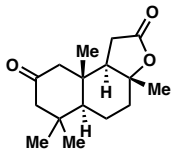


**S11**


168.37
133.84
132.27
123.12
52.92
32.83
27.72
25.63
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

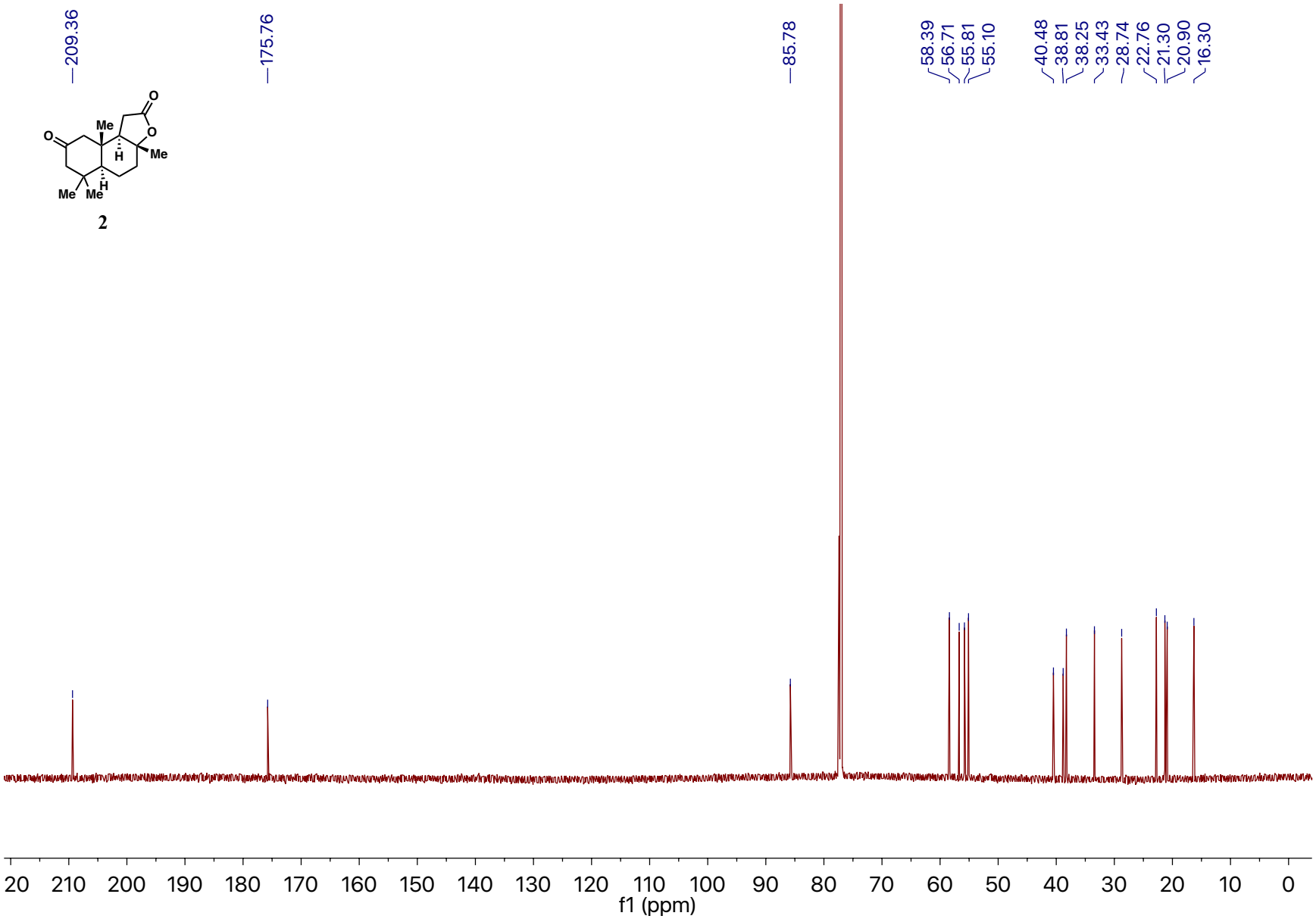

CO2Me
CO2Me
S12
3.65
2.80
2.00
1.96
1.76
1.73
1.52
1.47
1.40
1.35
6.00
2.00
2.07
2.28
2.00
2.03
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

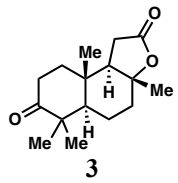

174.26
51.73
42.72
26.31
23.83
CO2Me
CO2Me
S12
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
O
Me
O
Me
H
H
Me
Me

**2**

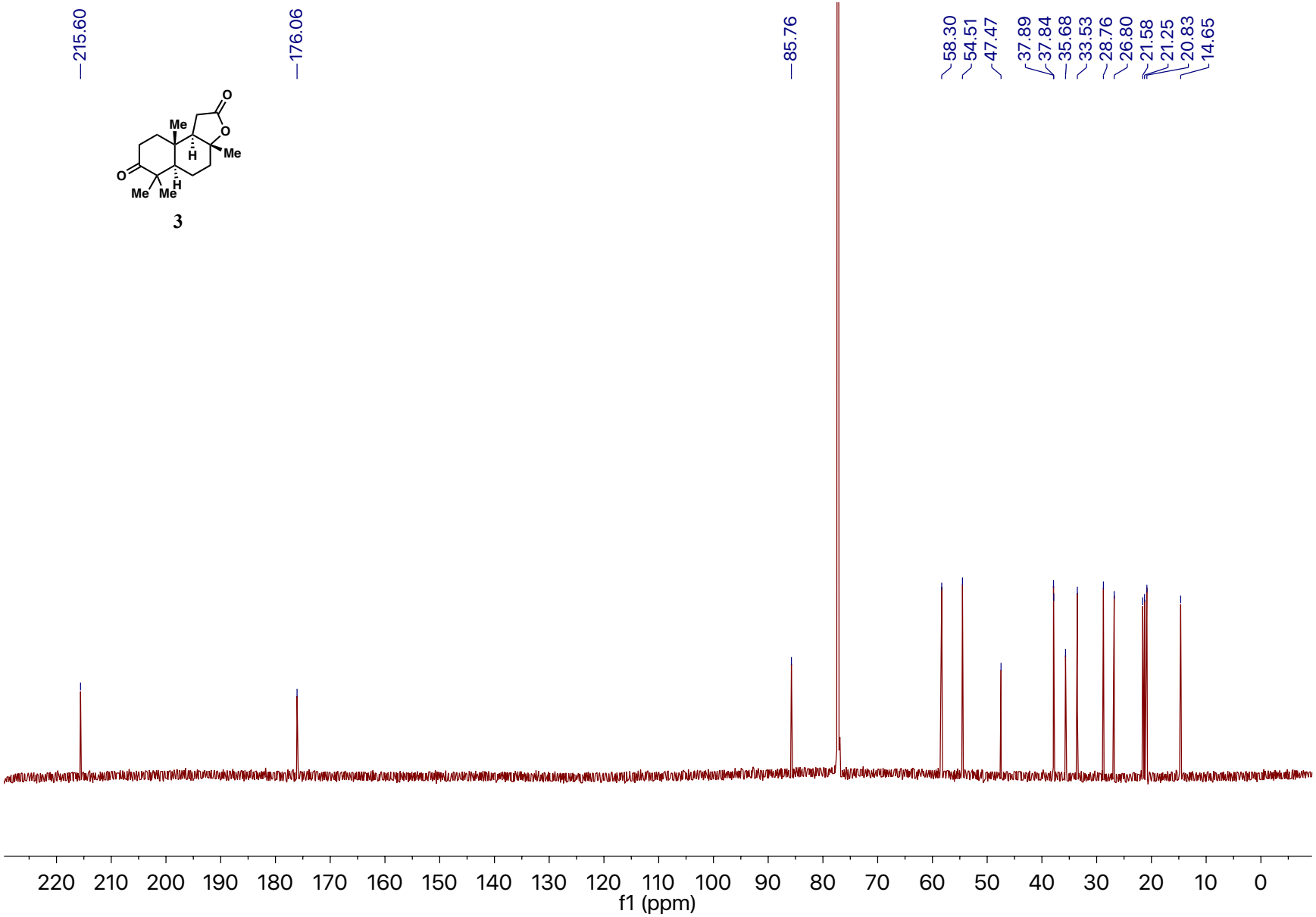

2.47 2.45 2.45 2.42 2.31 2.29 2.26 2.26 2.25 2.24 2.23 2.22 2.20 2.14 2.04 2.04 2.03 2.03 2.02 2.01 2.01 2.00 1.82 1.81 1.80 1.79 1.78 1.77 1.70 1.69 1.68 1.67 1.53 1.52 1.50 1.50 1.48 1.47 1.46 1.45 1.35 1.09 0.92
1.00 1.10 2.88 3.25 1.12 1.16 1.10 1.24 3.08 2.97 5.99
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

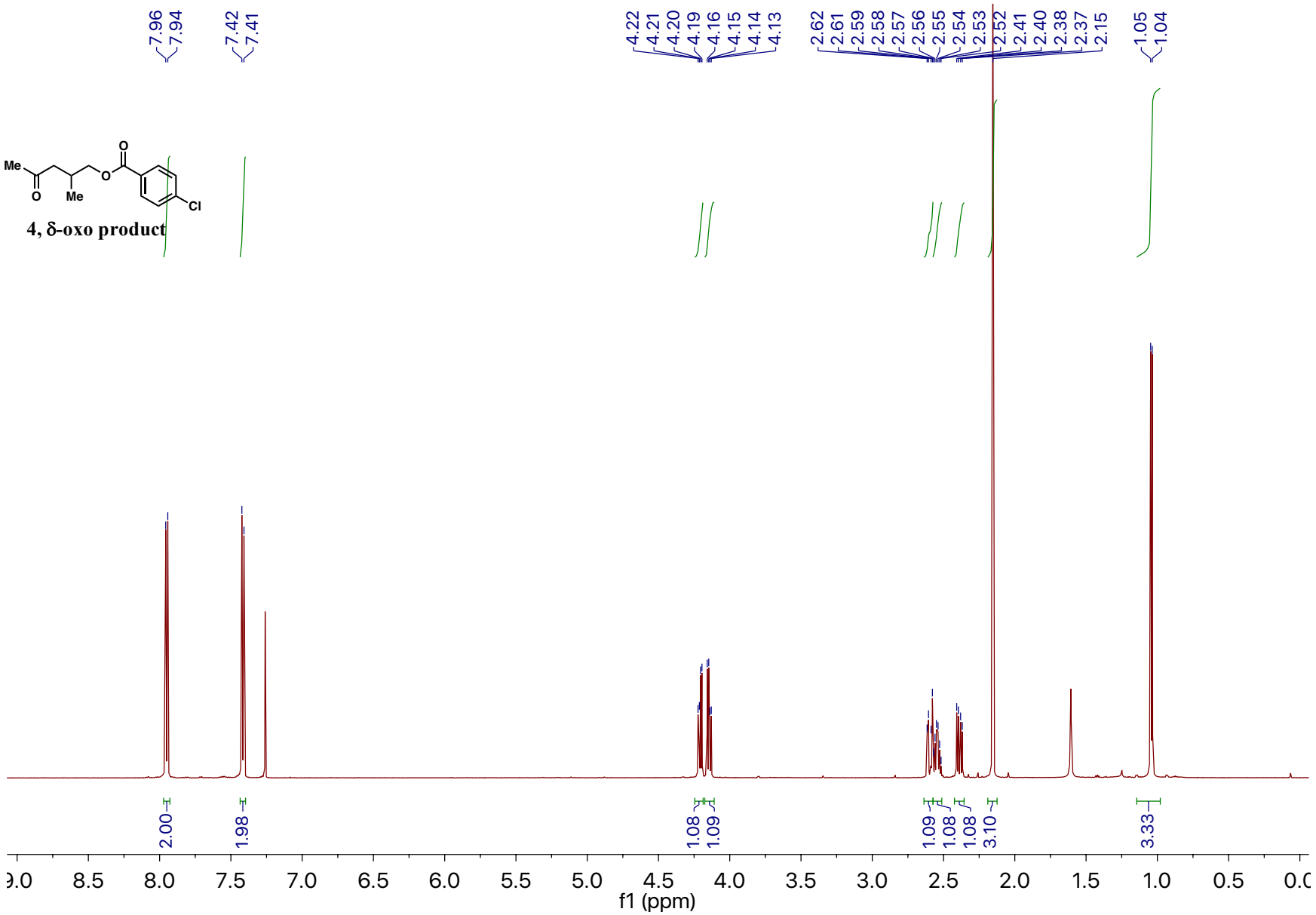

209.36
175.76
85.78
58.39
56.71
55.81
55.10
40.48
38.81
38.25
33.43
28.74
22.76
21.30
20.90
16.30
O
O
O
Me
Me
H
Me
H
Me
Me
2
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

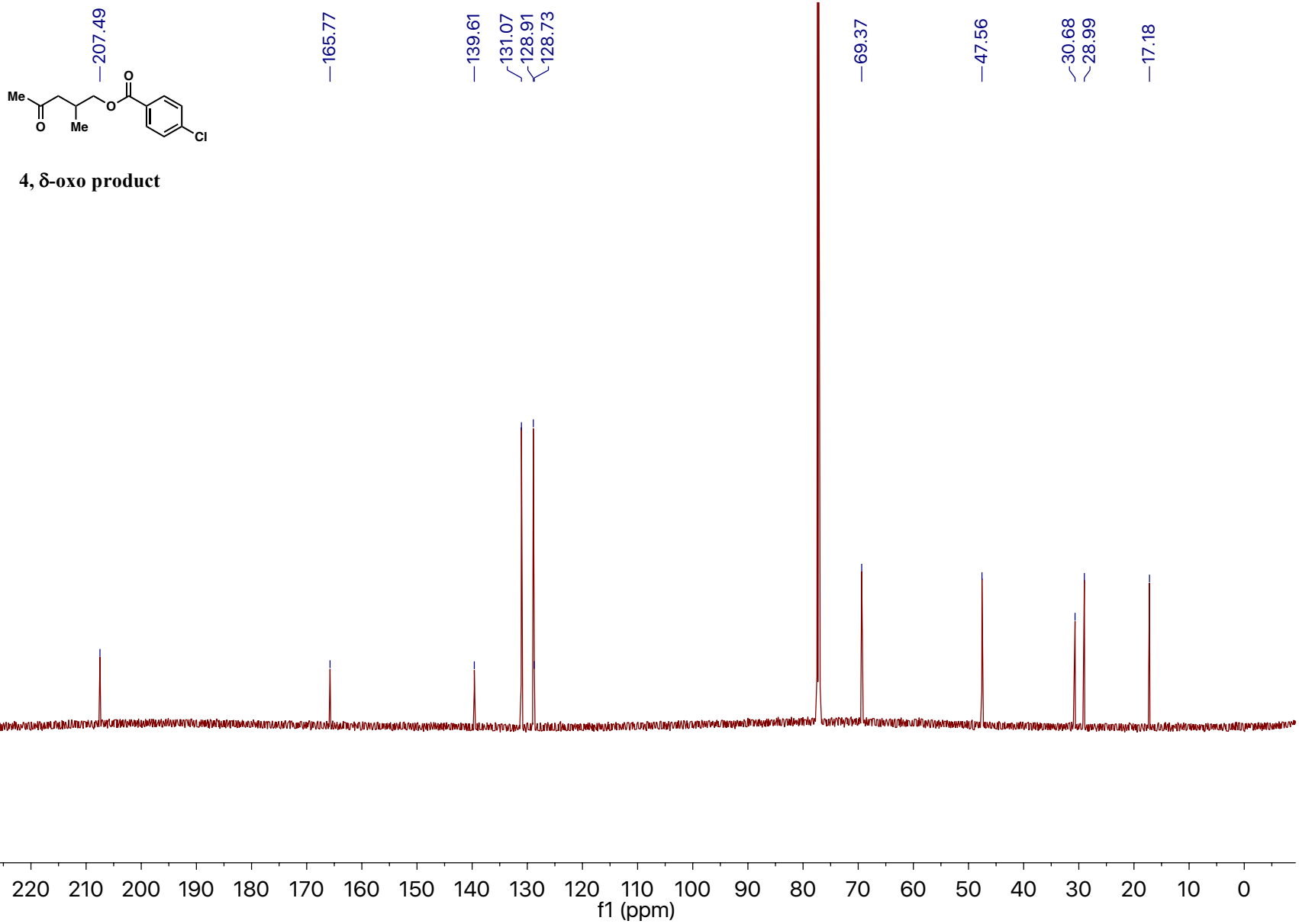

O
O
Me
H
Me
O
Me
Me
H

**3**

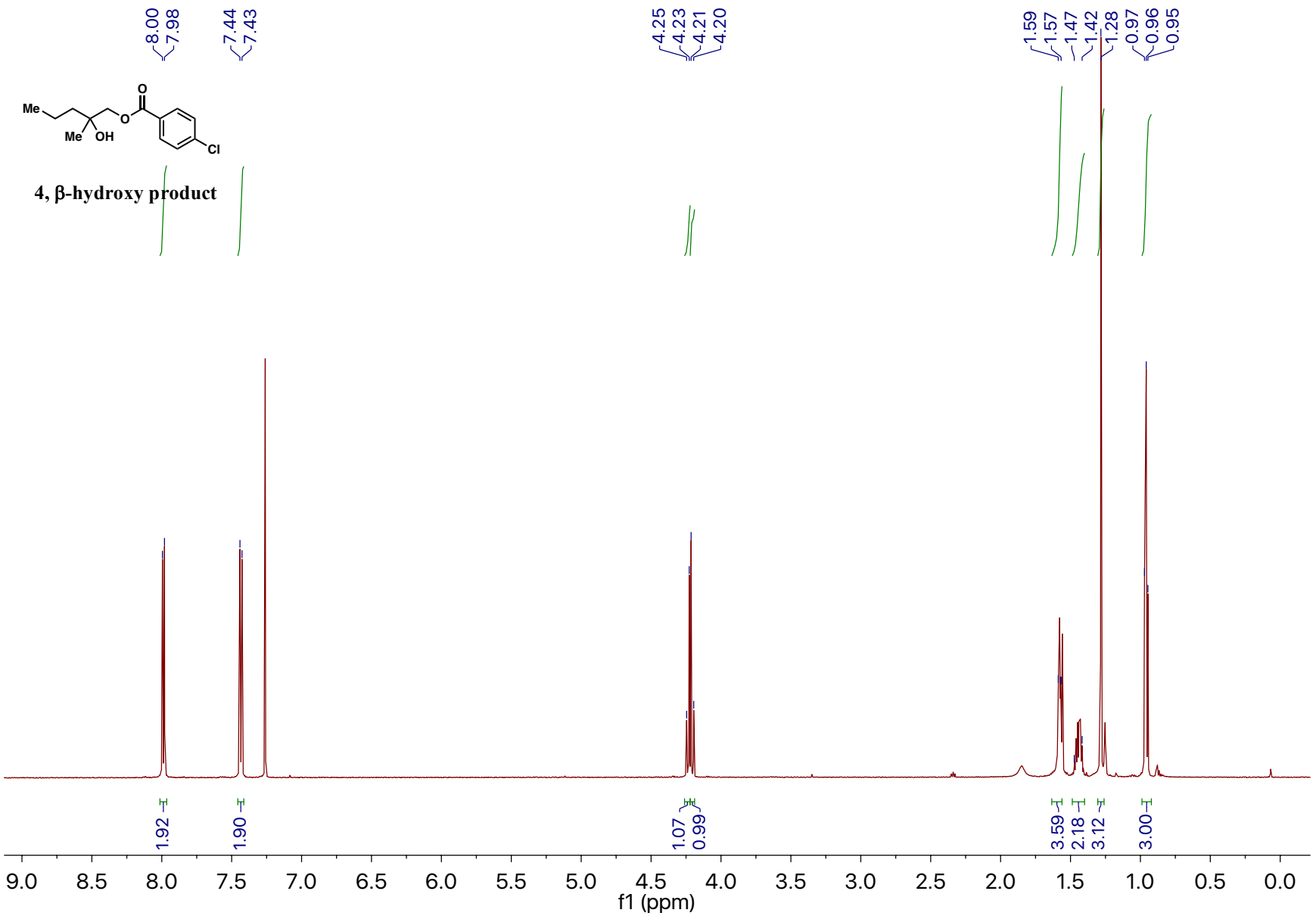

2.61
2.59
2.59
2.58
2.57
2.56
2.55
2.51
2.45
2.31
2.30
2.28
2.27
2.14
2.14
2.13
2.12
2.12
2.11
2.02
2.01
1.99
1.98
1.86
1.85
1.85
1.84
1.84
1.83
1.83
1.82
1.76
1.70
1.63
1.53
1.38
1.13
1.06
1.03
0.98
1.78
1.00
0.96
0.93
0.95
1.80
3.77
2.60
2.47
2.47
2.41
.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

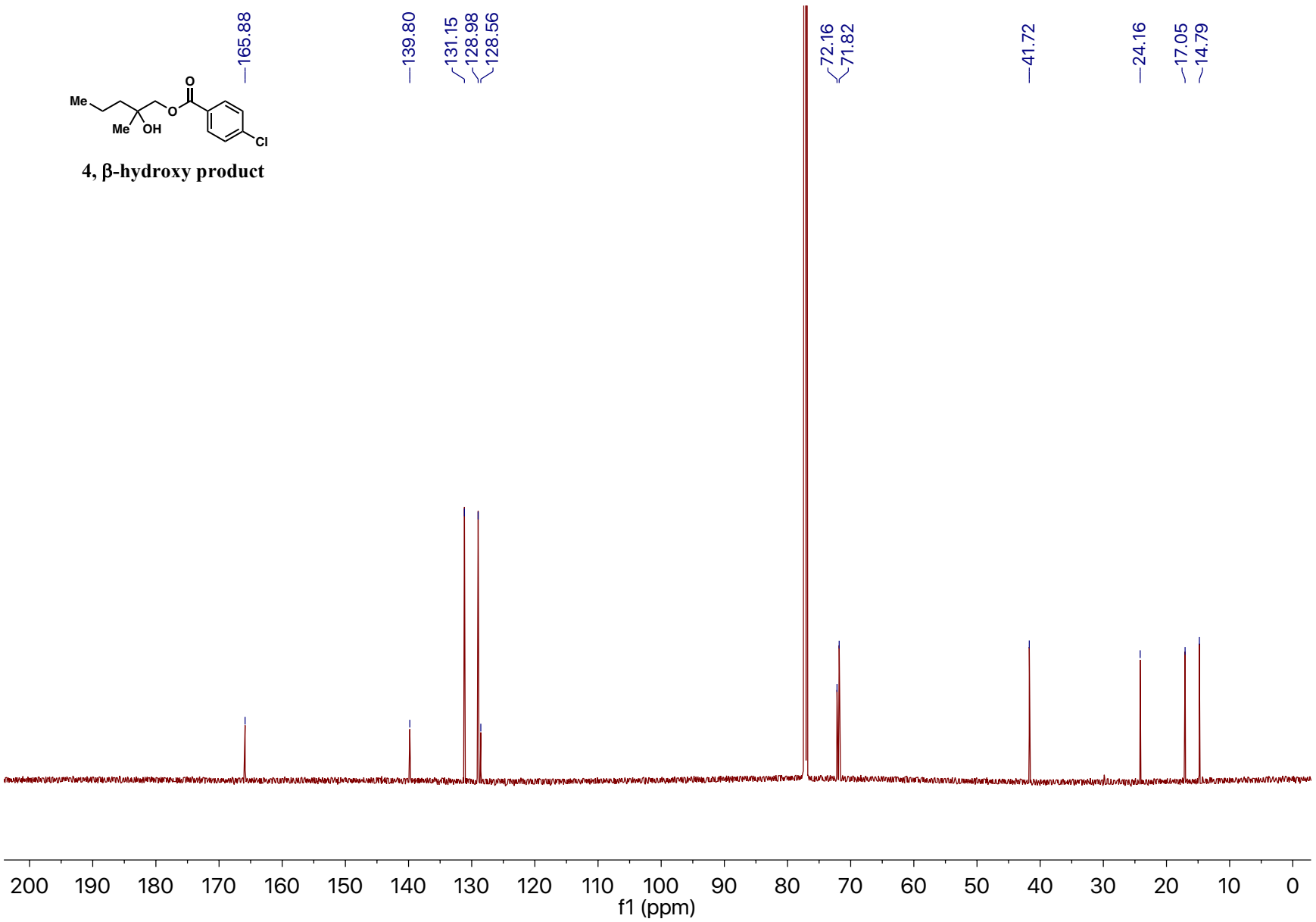

215.60
176.06
85.76
58.30
54.51
47.47
37.89
37.84
35.68
33.53
28.76
26.80
21.58
21.25
20.83
14.65
Me
Me
Me
Me
O
O
O
H
H
3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.96
7.94
7.42
7.41
4.22
4.21
4.20
4.19
4.16
4.15
4.14
4.13
2.62
2.61
2.59
2.58
2.57
2.56
2.55
2.54
2.53
2.52
2.41
2.40
2.38
2.37
2.15
1.05
1.04
Me
O
O
Me
O
Cl
4, δ-oxo product
2.00
1.98
1.08
1.09
1.09
1.08
1.08
3.10
3.33
f1 (ppm)

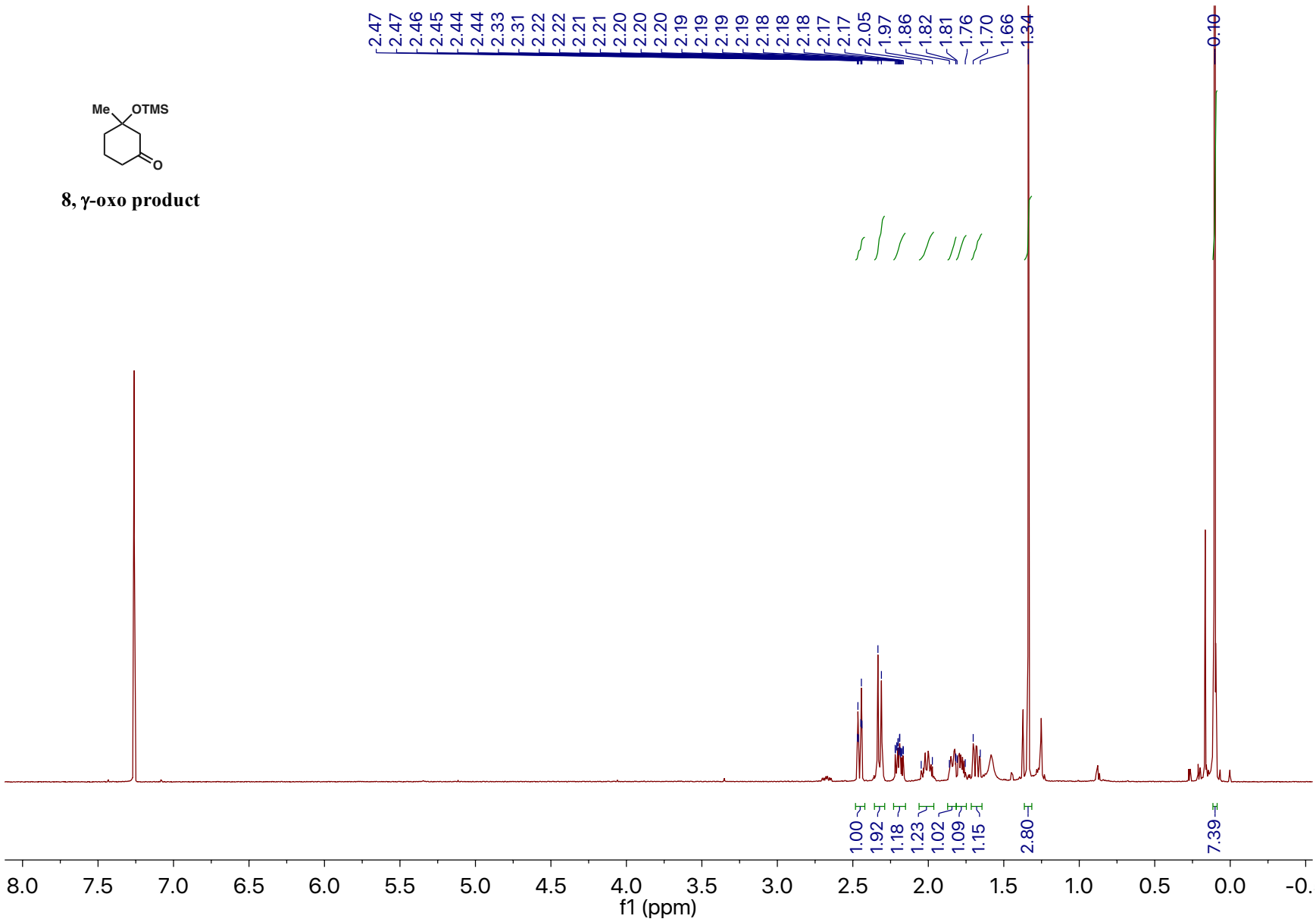


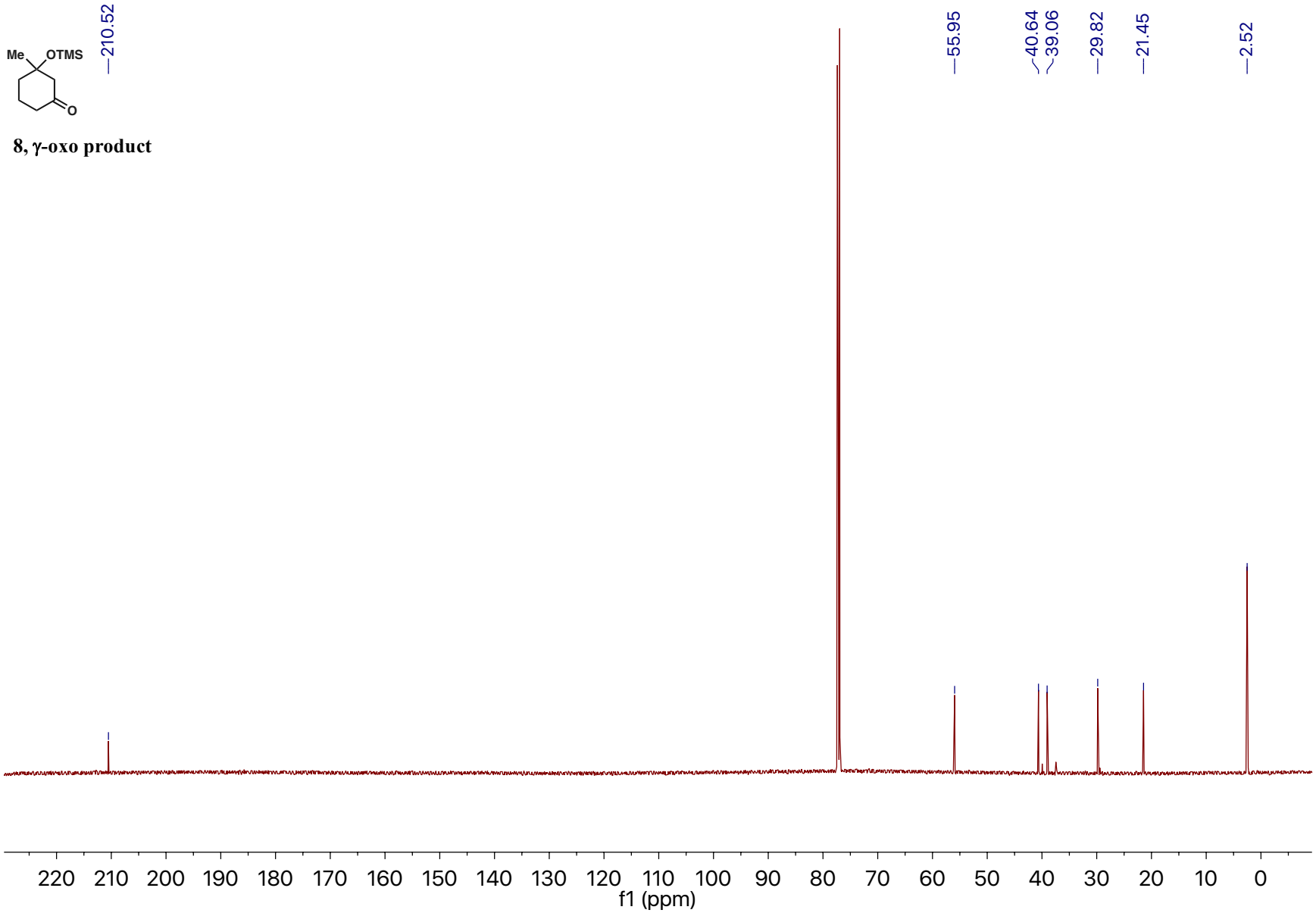

**4, δ-oxo product**


8.00
7.98
7.44
7.43
4.25
4.23
4.21
4.20
1.59
1.57
1.47
1.42
1.28
0.97
0.96
0.95
Me
Me
OH
O
O
Cl
4, β-hydroxy product
1.92
1.90
1.07
0.99
3.59
2.18
3.12
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

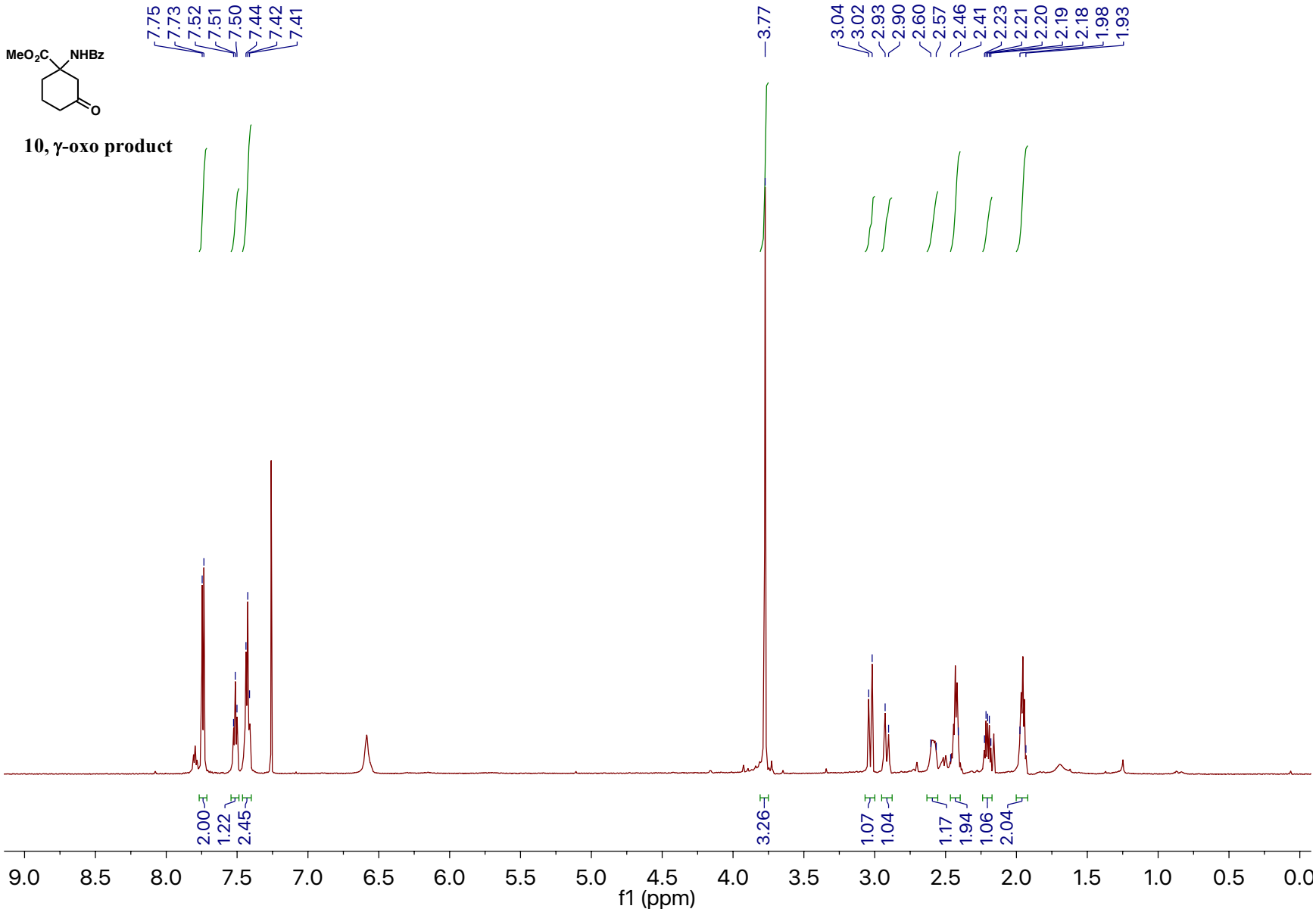


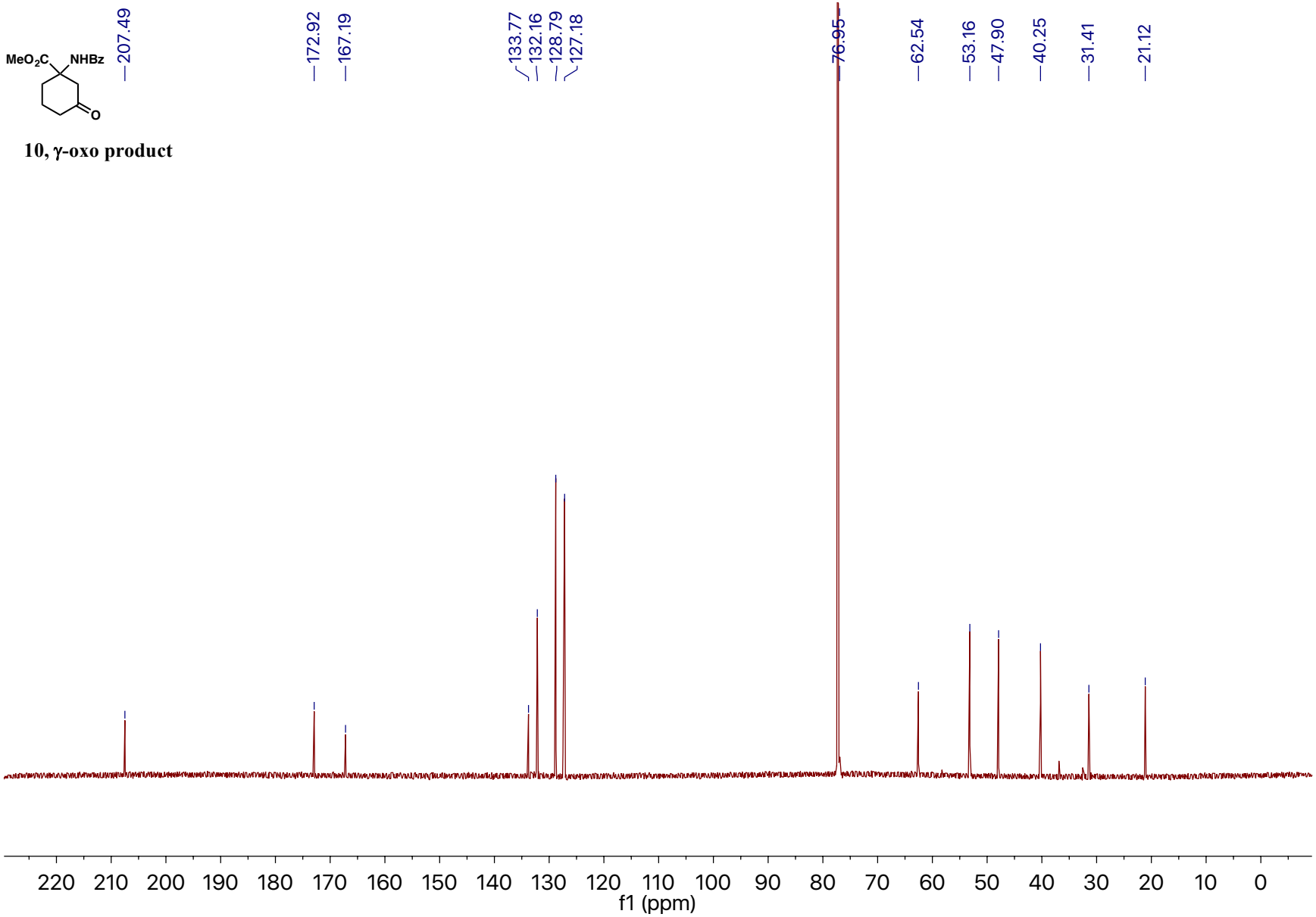

**4, β-hydroxy product**


Me
OTMS
O
8, γ-oxo product
2.47 2.47 2.46 2.45 2.44 2.44 2.33 2.31 2.22 2.22 2.21 2.21 2.20 2.20 2.20 2.19 2.19 2.19 2.19 2.18 2.18 2.18 2.17 2.17 2.05 1.97 1.86 1.82 1.81 1.76 1.70 1.66 1.34
0.10
1.00 1.92 1.18 1.23 1.02 1.09 1.15 2.80 7.39
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

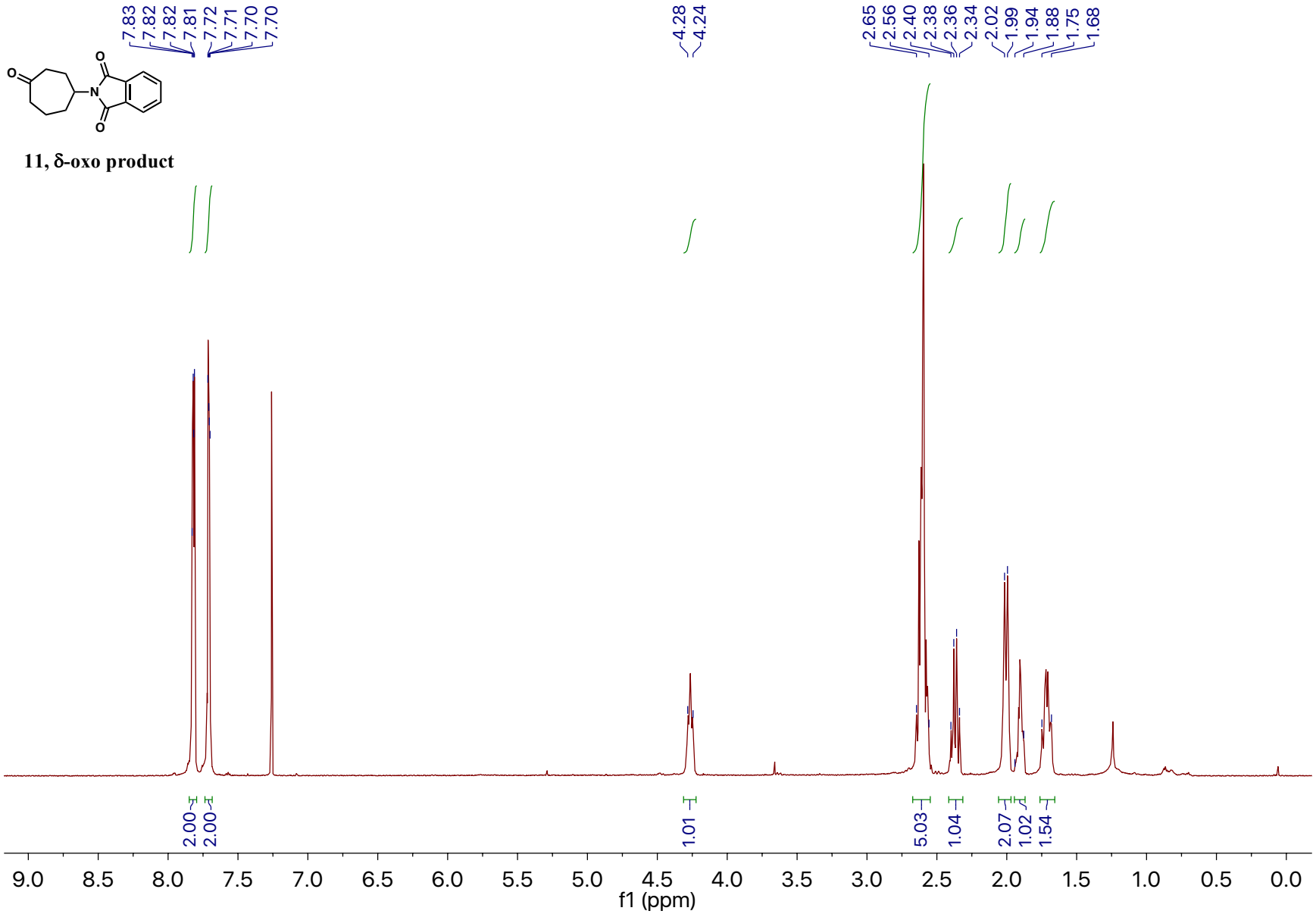



**8, γ-oxo product**

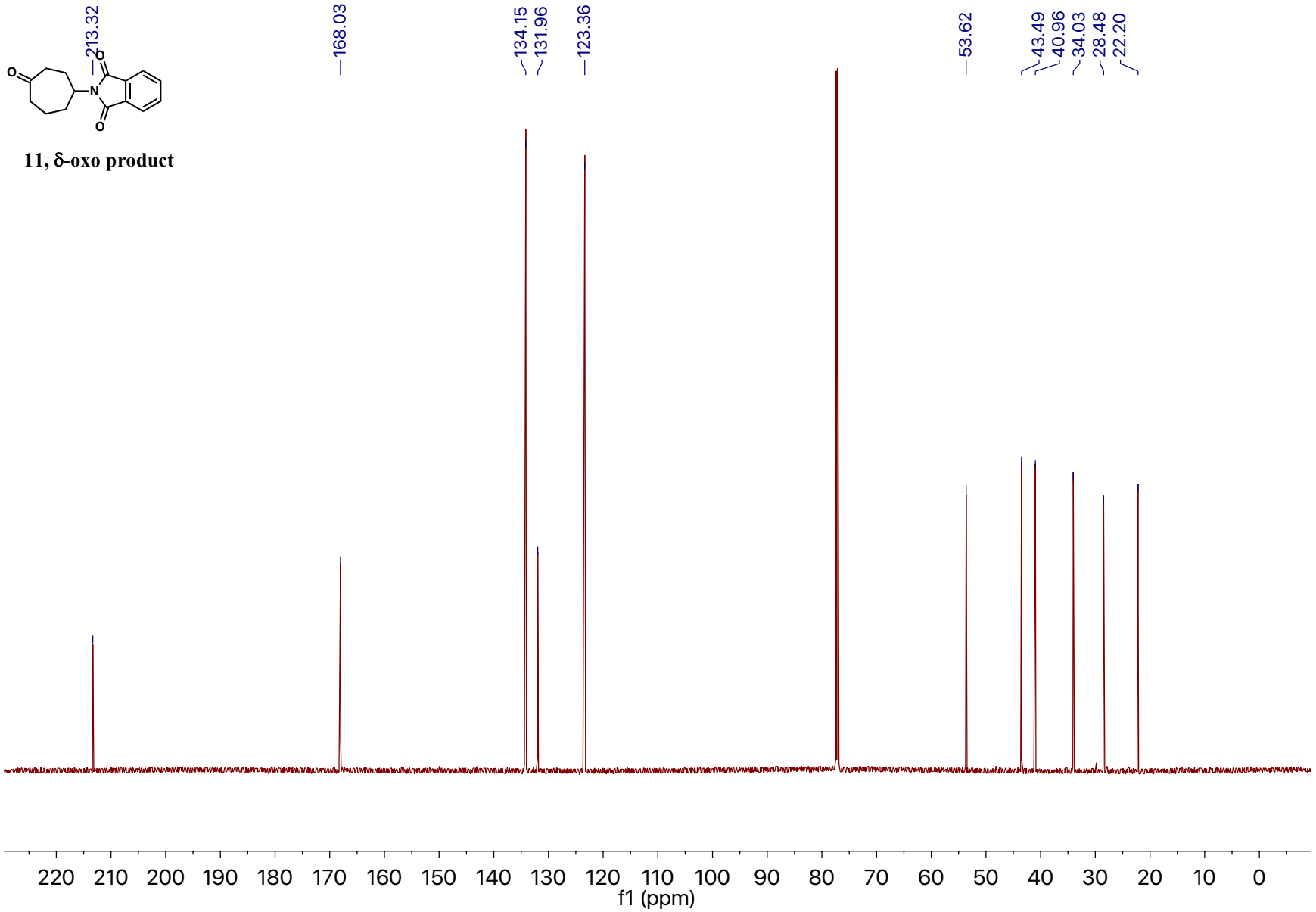

MeO2C
NHBz
O
10, γ-oxo product
7.75
7.73
7.52
7.51
7.50
7.44
7.42
7.41
3.77
3.04
3.02
2.93
2.90
2.60
2.57
2.46
2.41
2.23
2.21
2.20
2.19
2.18
1.98
1.93
2.00
1.22
2.45
3.26
1.07
1.04
1.17
1.94
1.06
2.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



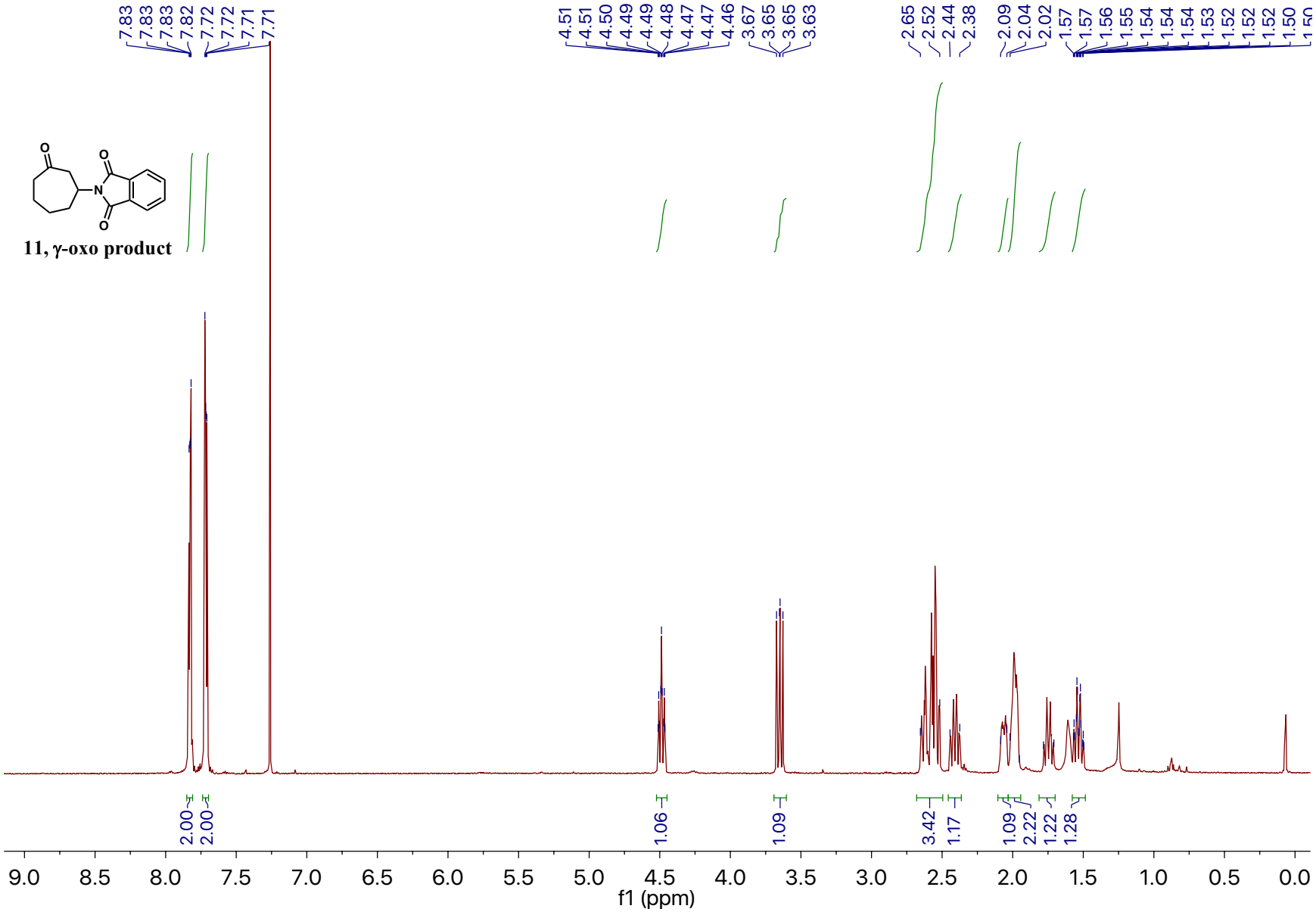

**10, γ-oxo product**

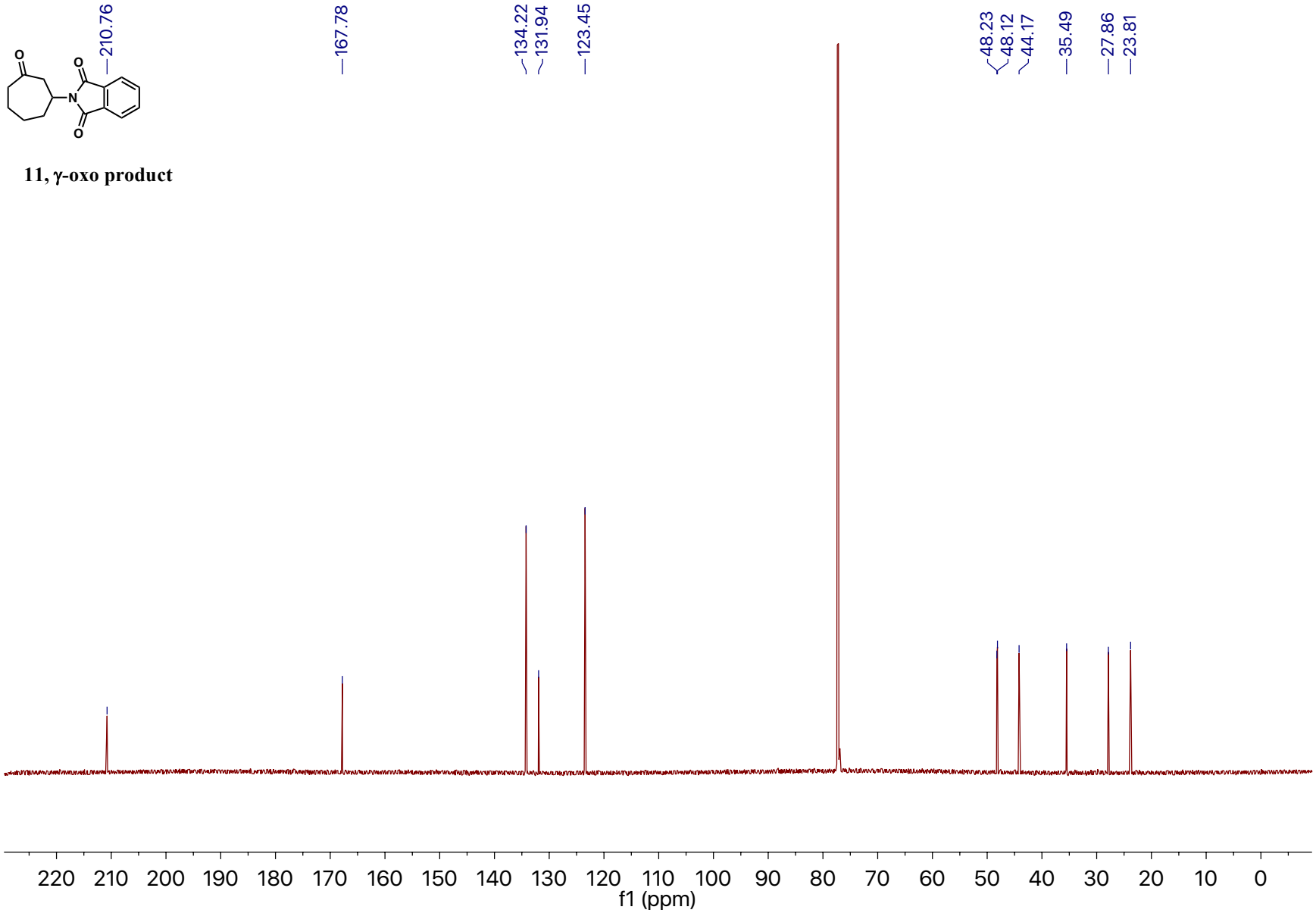



**11, δ-oxo product**

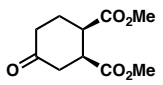



**11, δ-oxo product**


11, γ-oxo product
f1 (ppm)

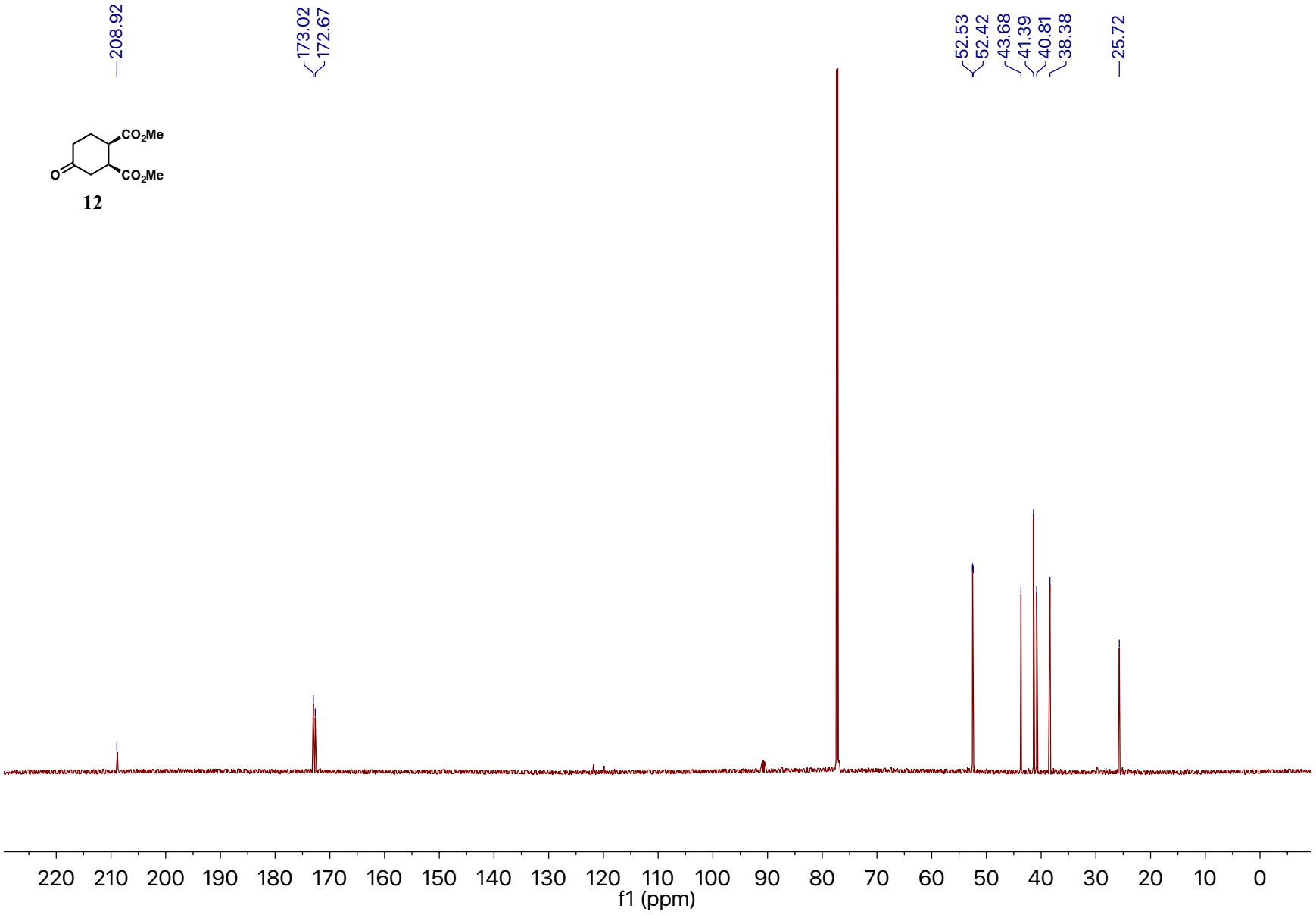


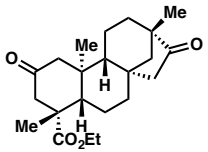

**11, γ-oxo product**


CO2Me
O
CO2Me

**12**

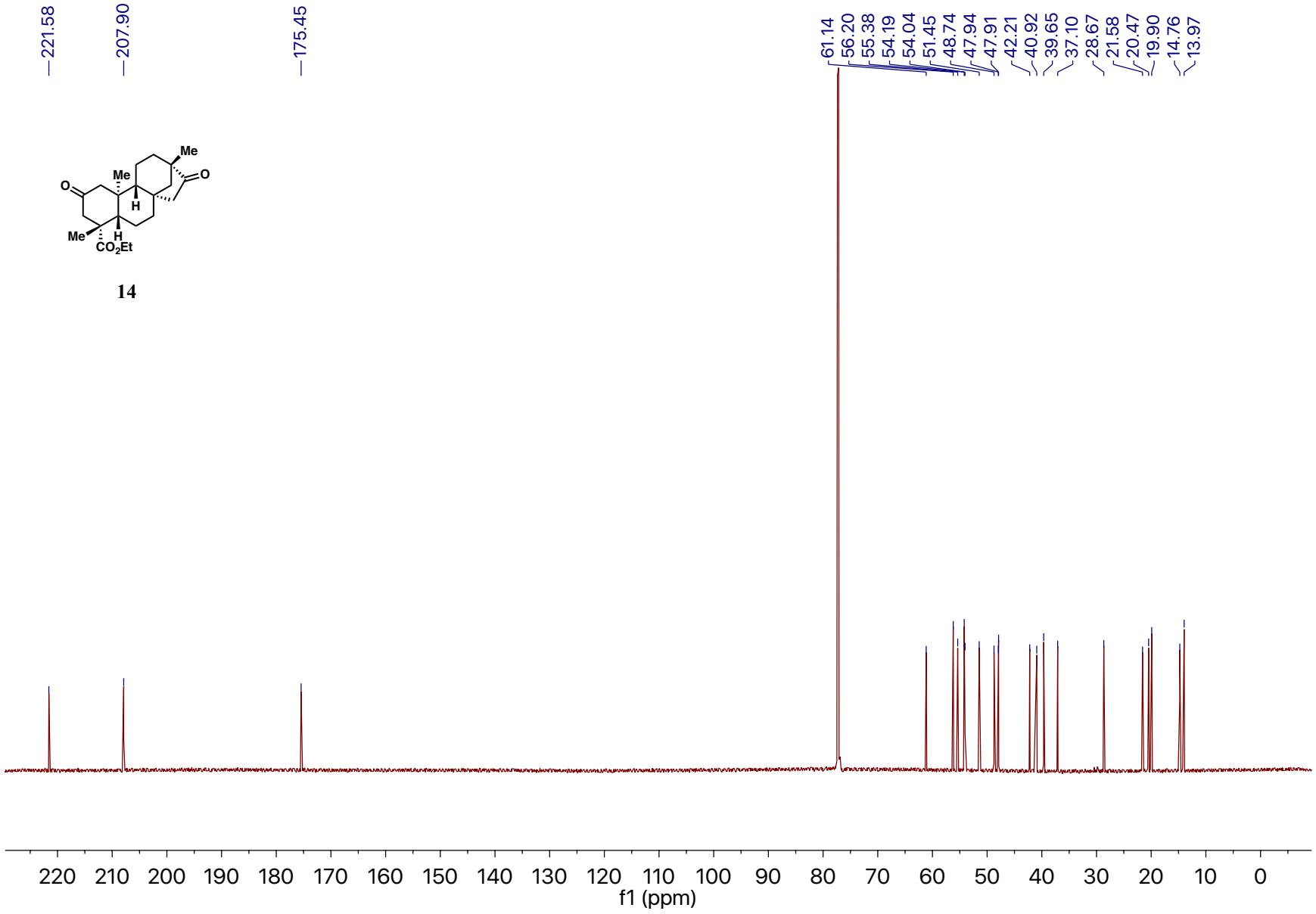

3.74
3.70
3.26
3.25
3.24
3.23
3.15
3.14
3.14
3.13
3.12
2.88
2.83
2.64
2.63
2.62
2.61
2.46
2.32
2.08
2.07
2.07
2.06
2.06
2.05
2.04
2.04
3.00
3.18
0.93
0.95
0.98
1.01
3.08
1.20
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


208.92
173.02
172.67
52.53
52.42
43.68
41.39
40.81
38.38
25.72
CO2Me
CO2Me
O
12
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

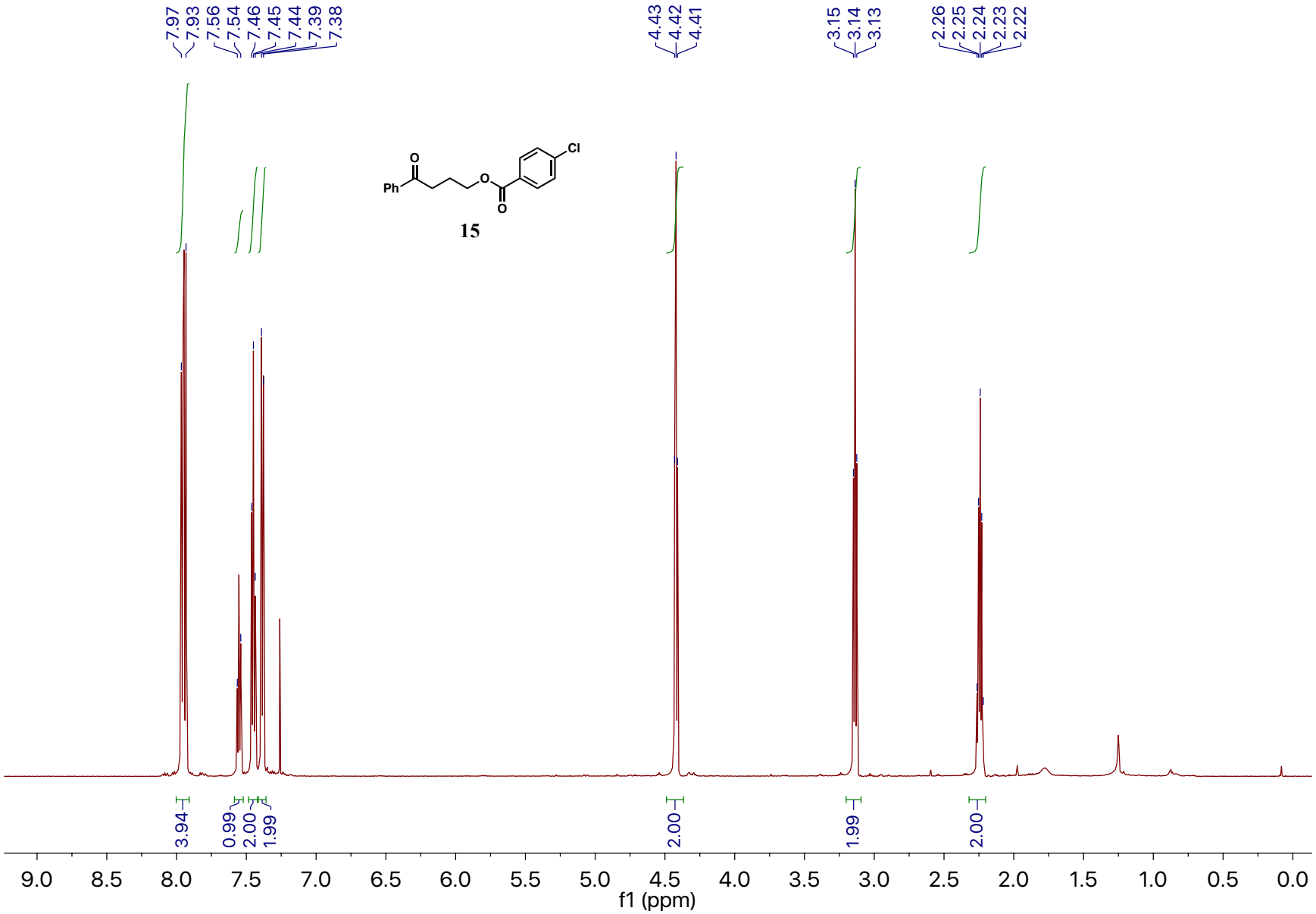

Me
Me
O
O
H
Me
H
CO2Et

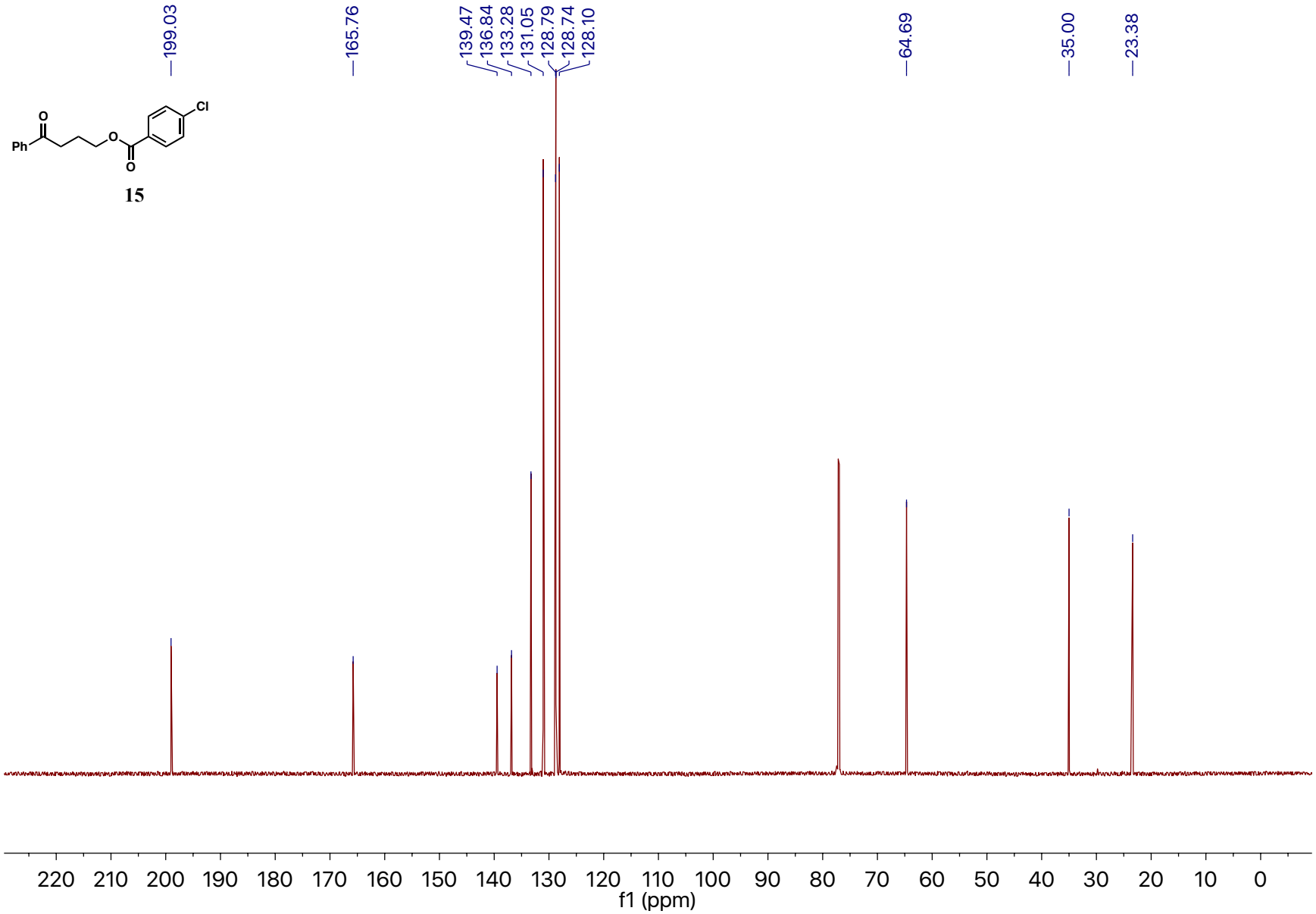
**14**

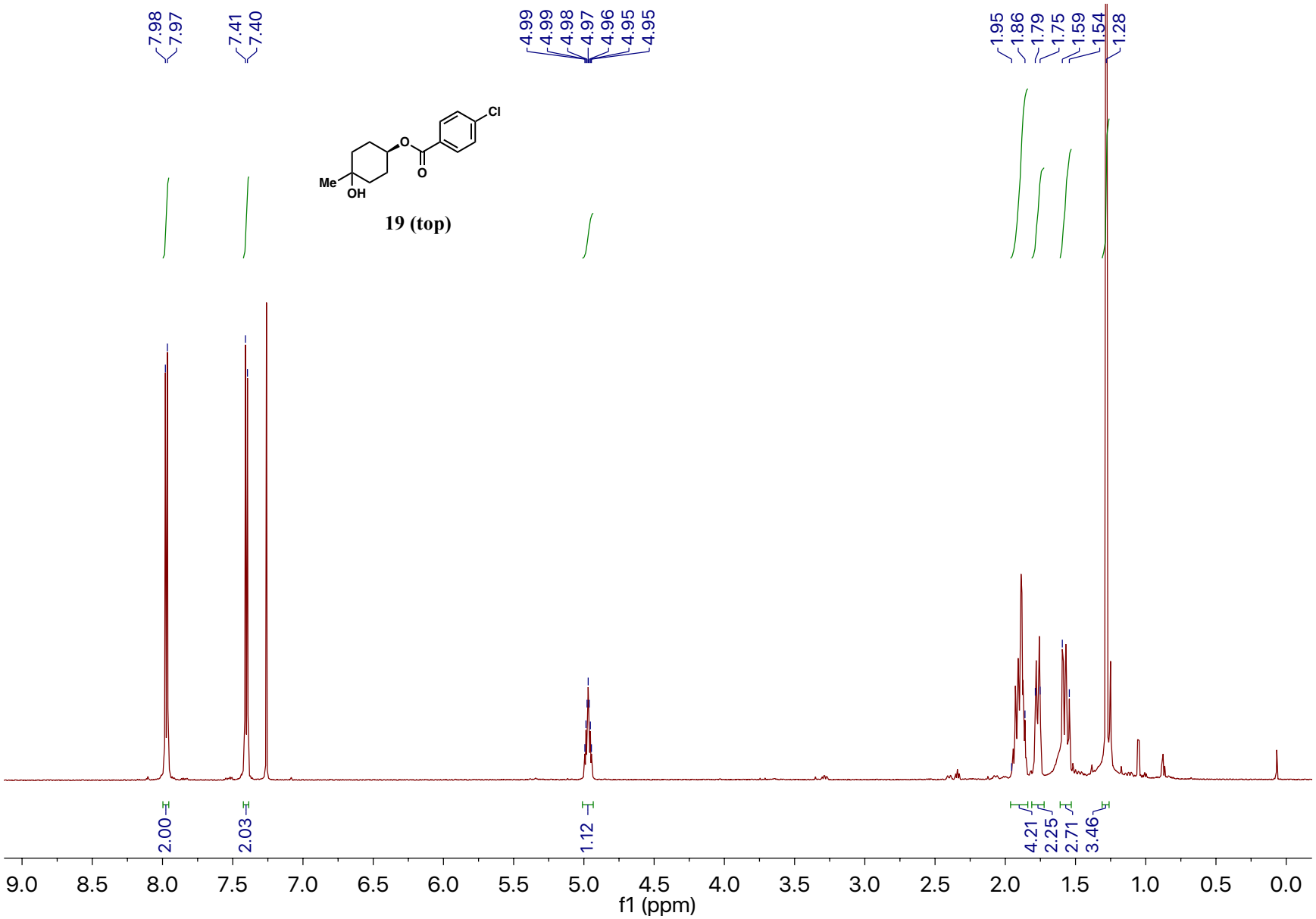

4.12
4.11
4.10
4.10
4.09
4.08
4.08
4.07
4.05
4.05
4.04
4.03
4.03
4.02
4.01
2.93
2.93
2.91
2.90
2.55
2.55
2.52
2.52
2.46
2.45
2.43
2.43
2.09
2.03
1.95
1.93
1.83
1.80
1.75
1.45
1.37
0.98
1.12
1.00
1.06
1.07
1.08
2.16
1.10
1.14
8.14
6.20
4.80
3.07
2.95
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

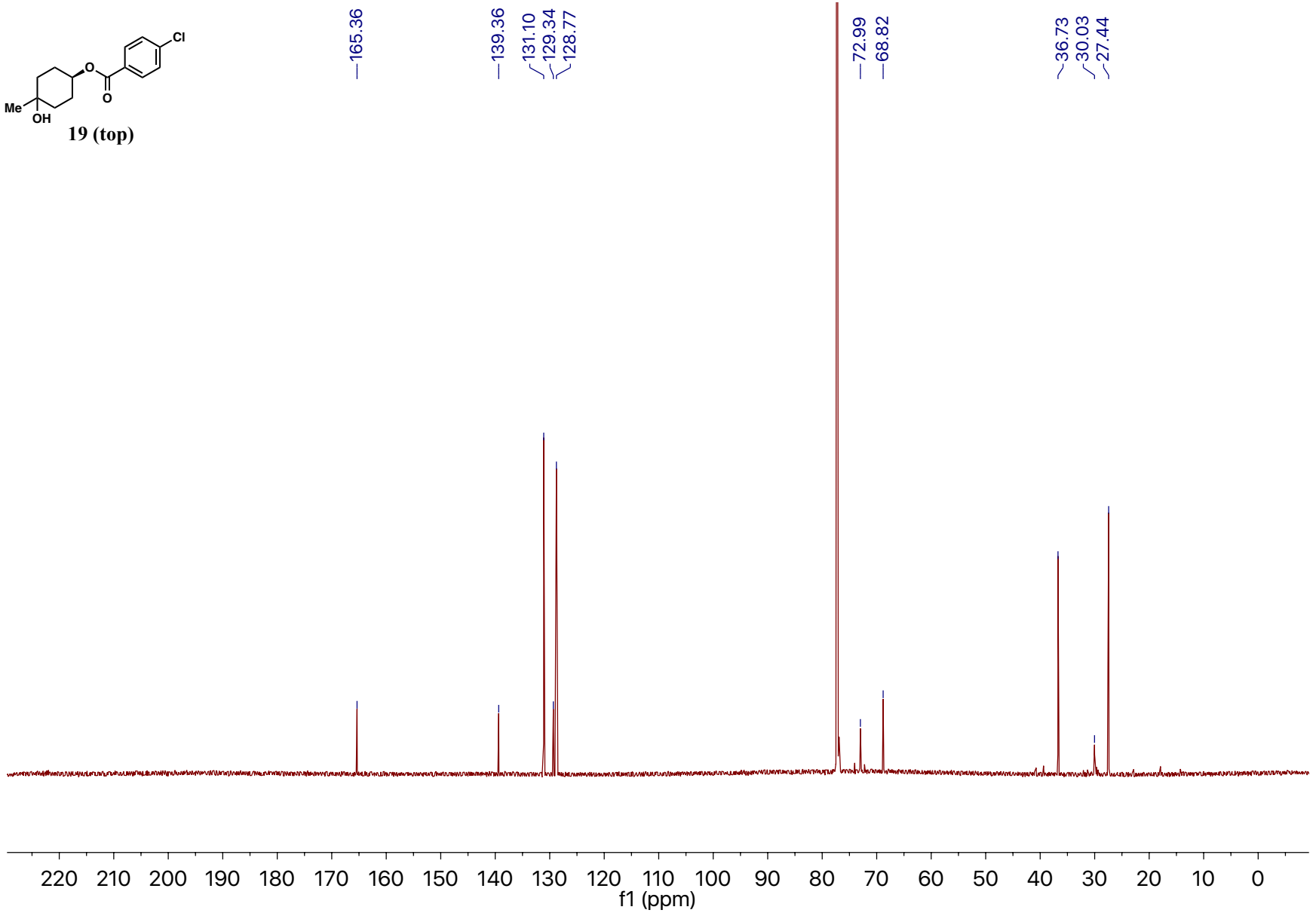

221.58
207.90
175.45
61.14
56.20
55.38
54.19
54.04
51.45
48.74
47.94
47.91
42.21
40.92
39.65
37.10
28.67
21.58
20.47
19.90
14.76
13.97
Me
Me
O
O
H
Me
H
CO2Et
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

**14**

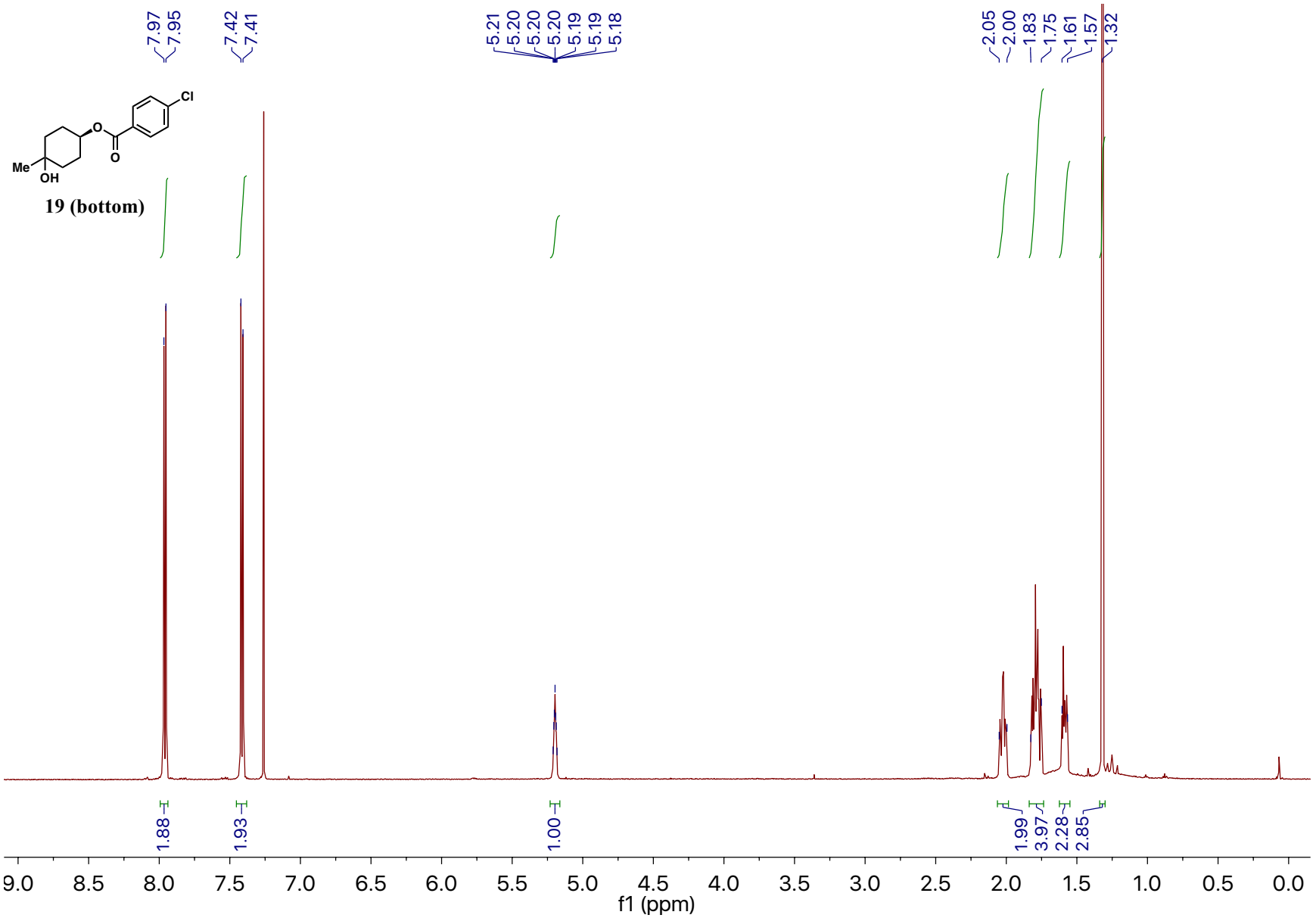

7.97
7.93
7.56
7.54
7.46
7.45
7.44
7.39
7.38
4.43
4.42
4.41
3.15
3.14
3.13
2.26
2.25
2.24
2.23
2.22
O
Ph
O
O
Cl
15
3.94
0.99
2.00
1.99
2.00
1.99
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

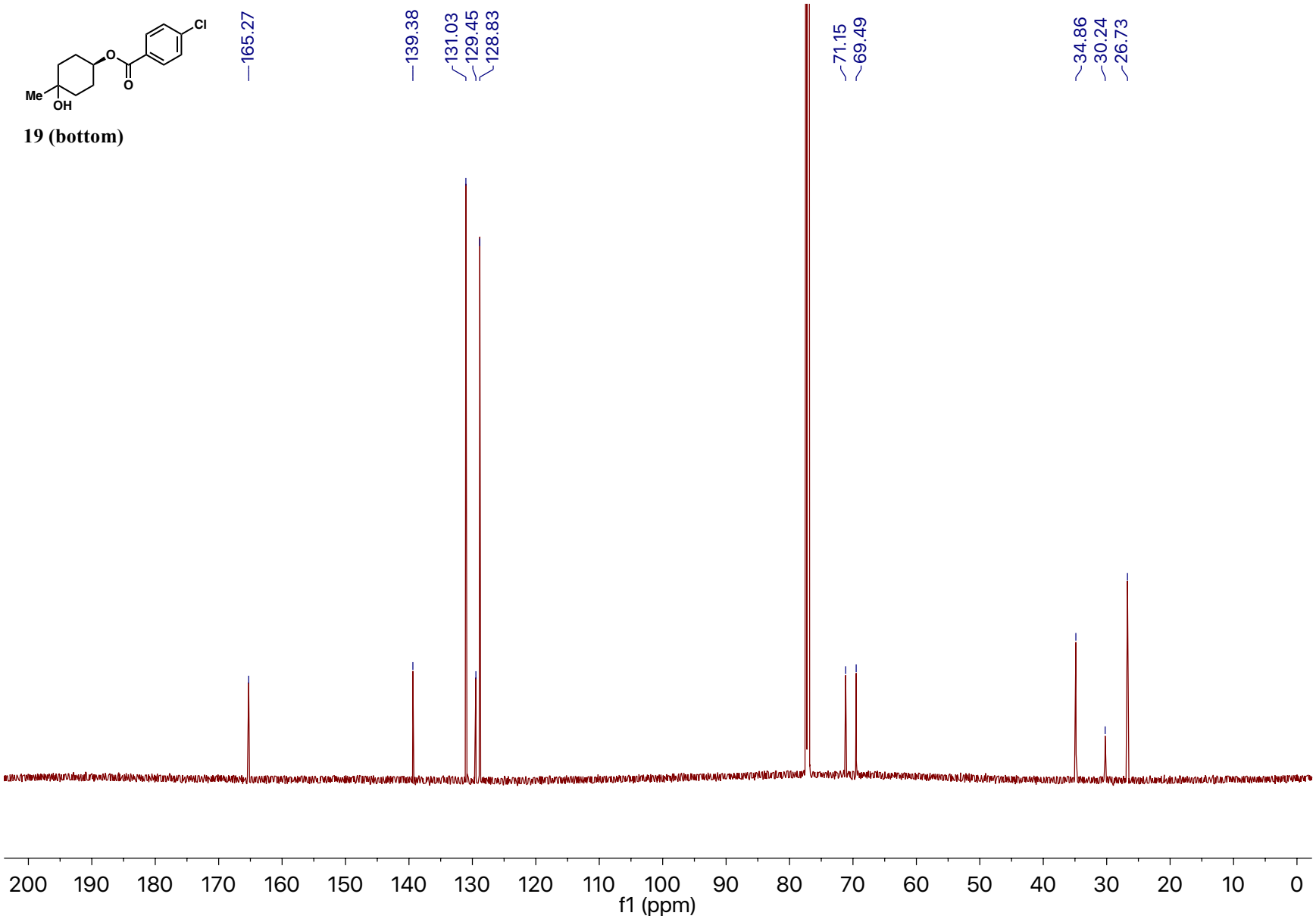

199.03
165.76
139.47
136.84
133.28
131.05
128.79
128.74
128.10
64.69
35.00
23.38
O
Ph
O
O
Cl
15
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.98
7.97
7.41
7.40
4.99
4.99
4.98
4.97
4.96
4.95
4.95
1.95
1.86
1.79
1.75
1.59
1.54
1.28
Cl
O
O
Me
OH
19 (top)
2.00
2.03
1.12
4.21
2.25
2.71
3.46
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)

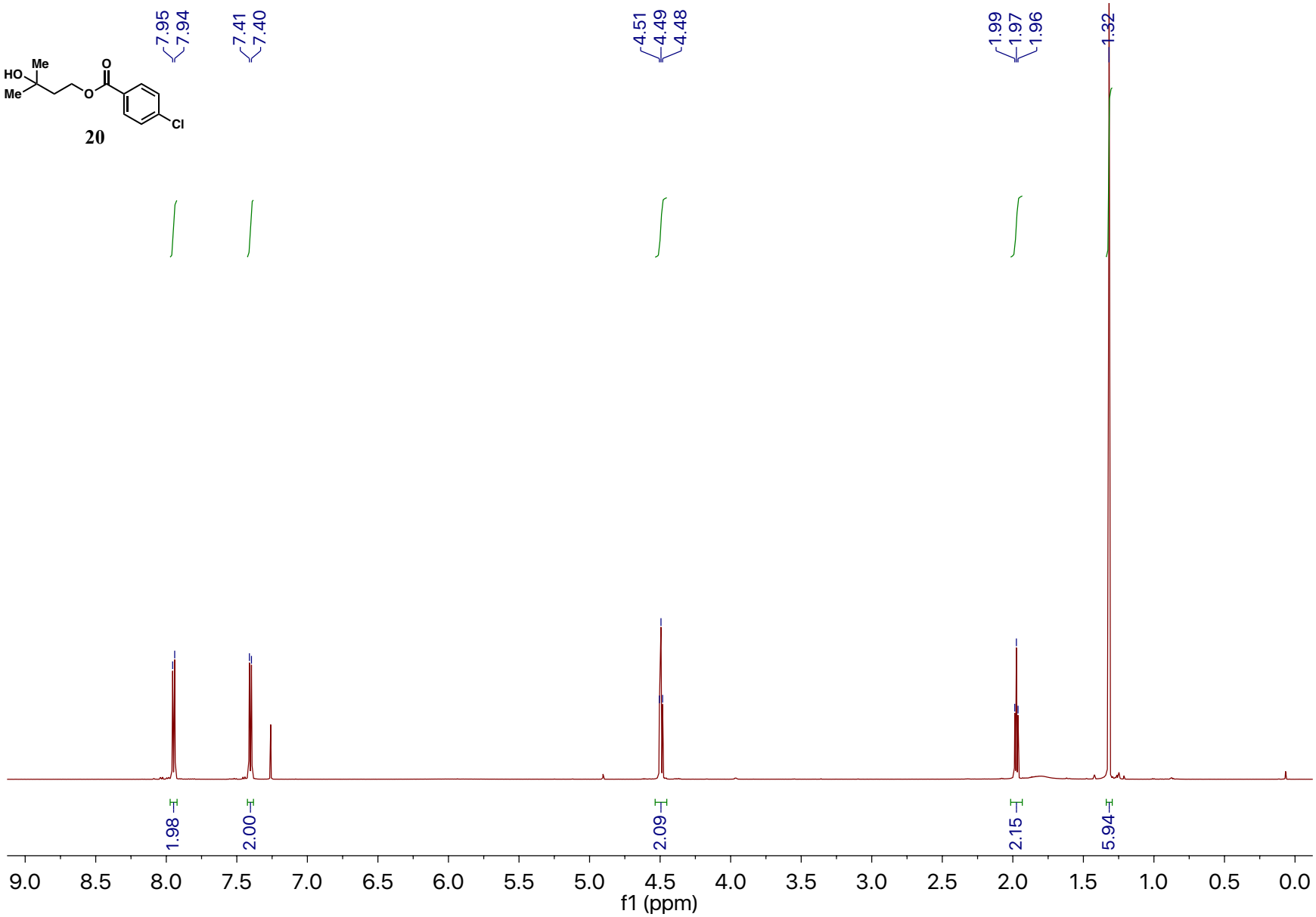

Cl
O
O
Me
OH
165.36
139.36
131.10
129.34
128.77
72.99
68.82
36.73
30.03
27.44
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

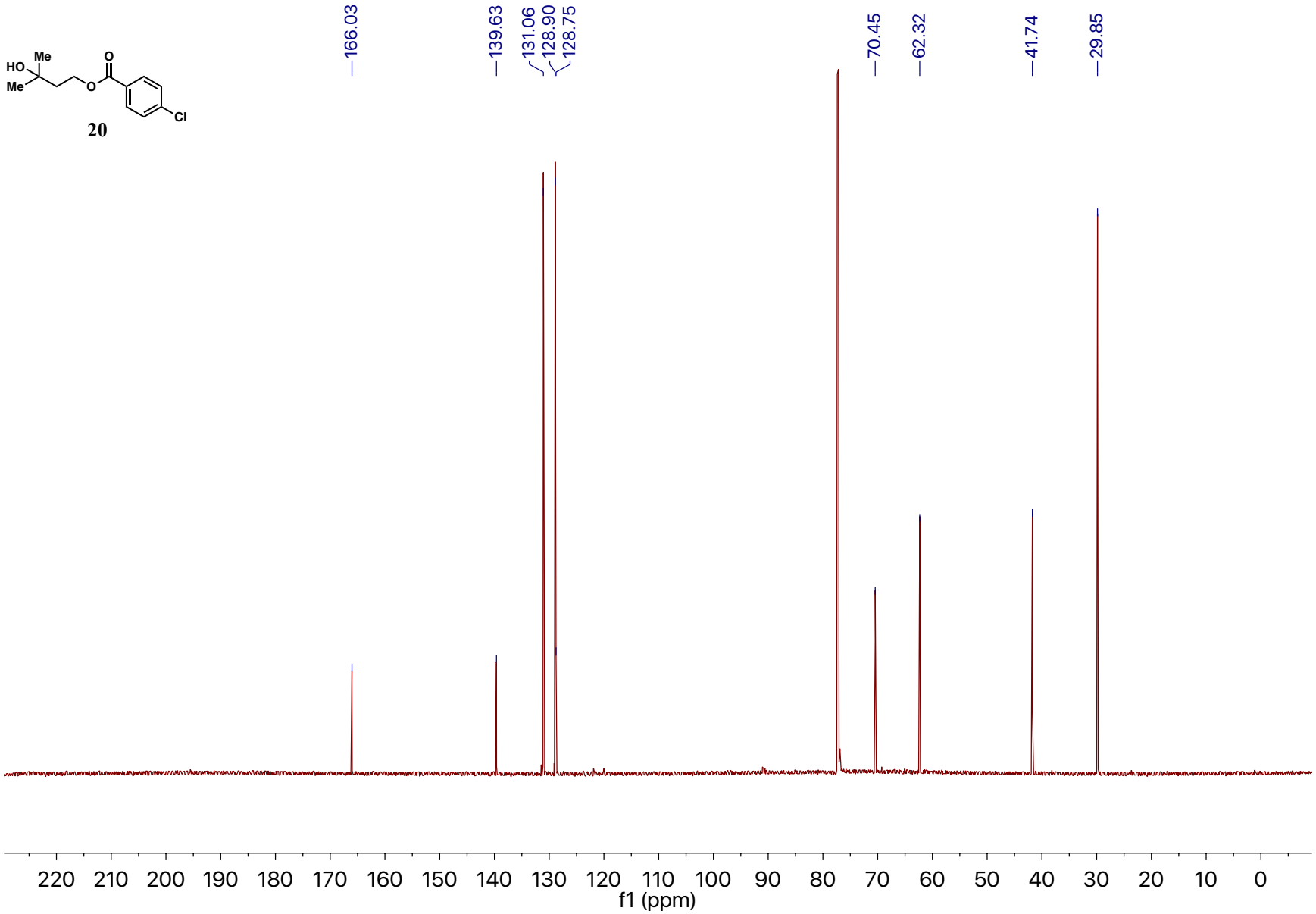
**19 (top)**

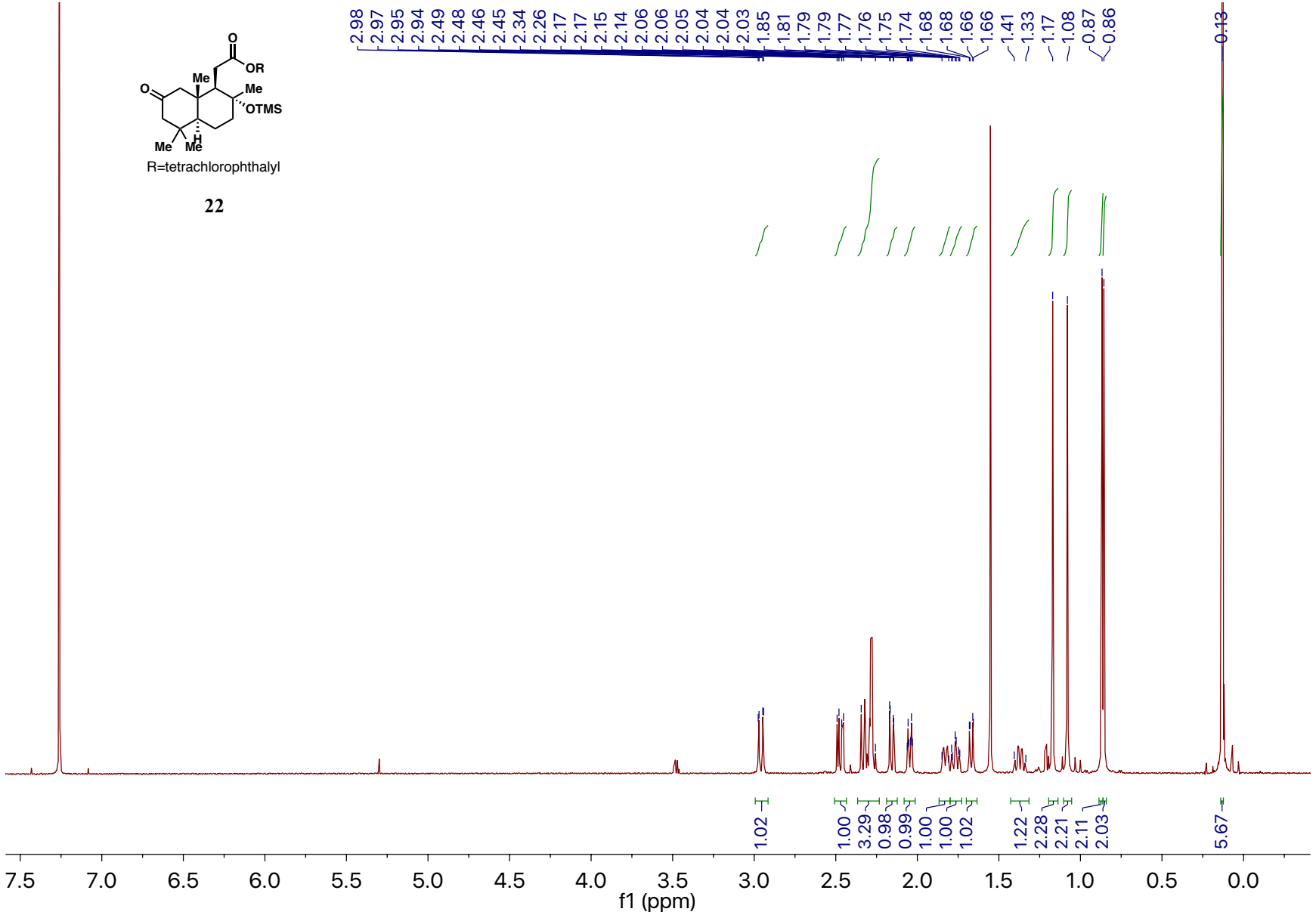

7.97
7.95
7.42
7.41
5.21
5.20
5.20
5.20
5.19
5.19
5.18
2.05
2.00
1.83
1.75
1.61
1.57
1.32
Cl
O
O
Me
OH
19 (bottom)
1.88
1.93
1.00
1.99
3.97
2.28
2.85
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

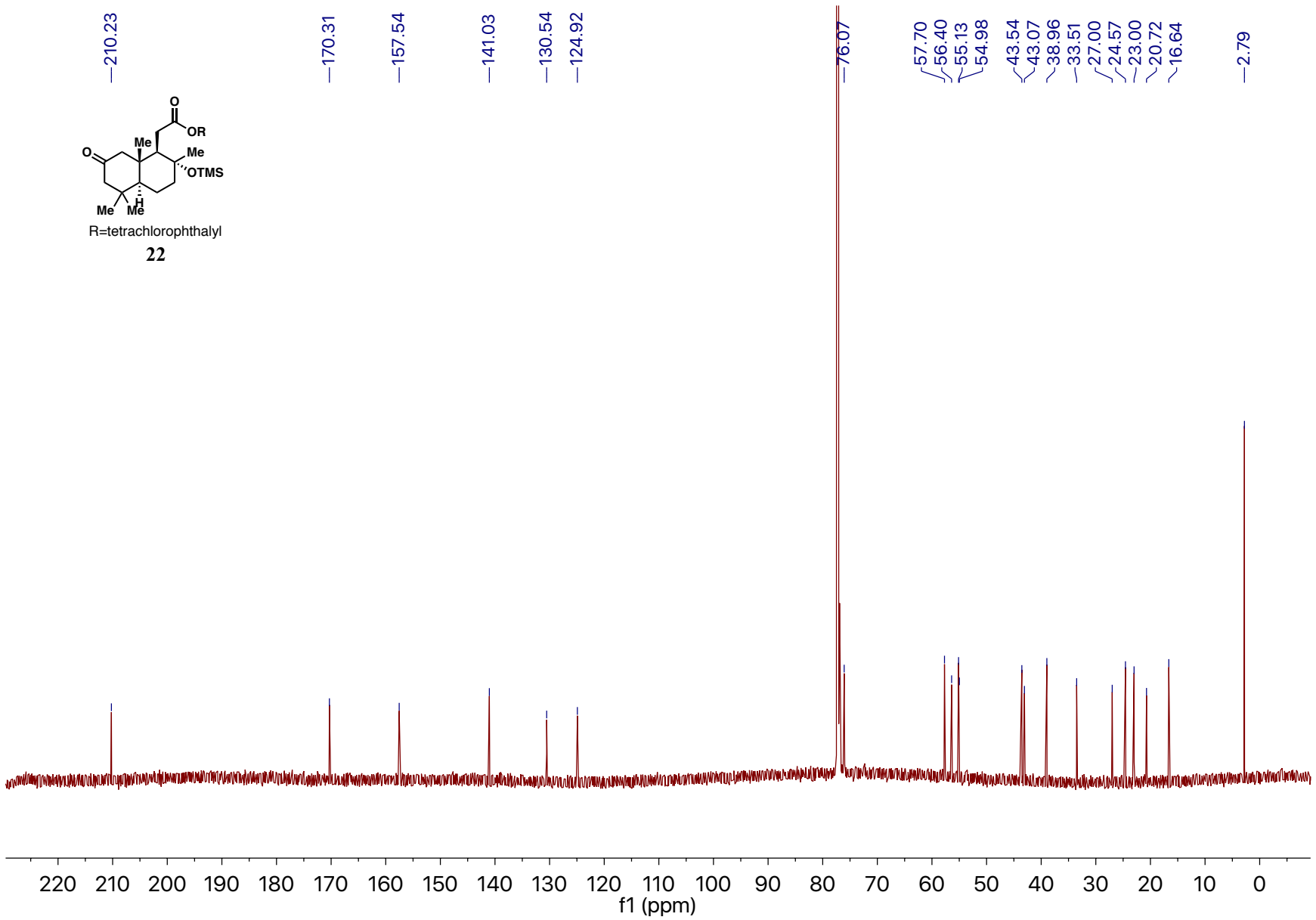

Cl
O
O
Me
OH
165.27
139.38
131.03
129.45
128.83
71.15
69.49
34.86
30.24
26.73
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

**19 (bottom)**


7.95
7.94
7.41
7.40
4.51
4.49
4.48
1.99
1.97
1.96
1.32
HO
Me
Me
O
O
Cl
20
1.98
2.00
2.09
2.15
5.94
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)

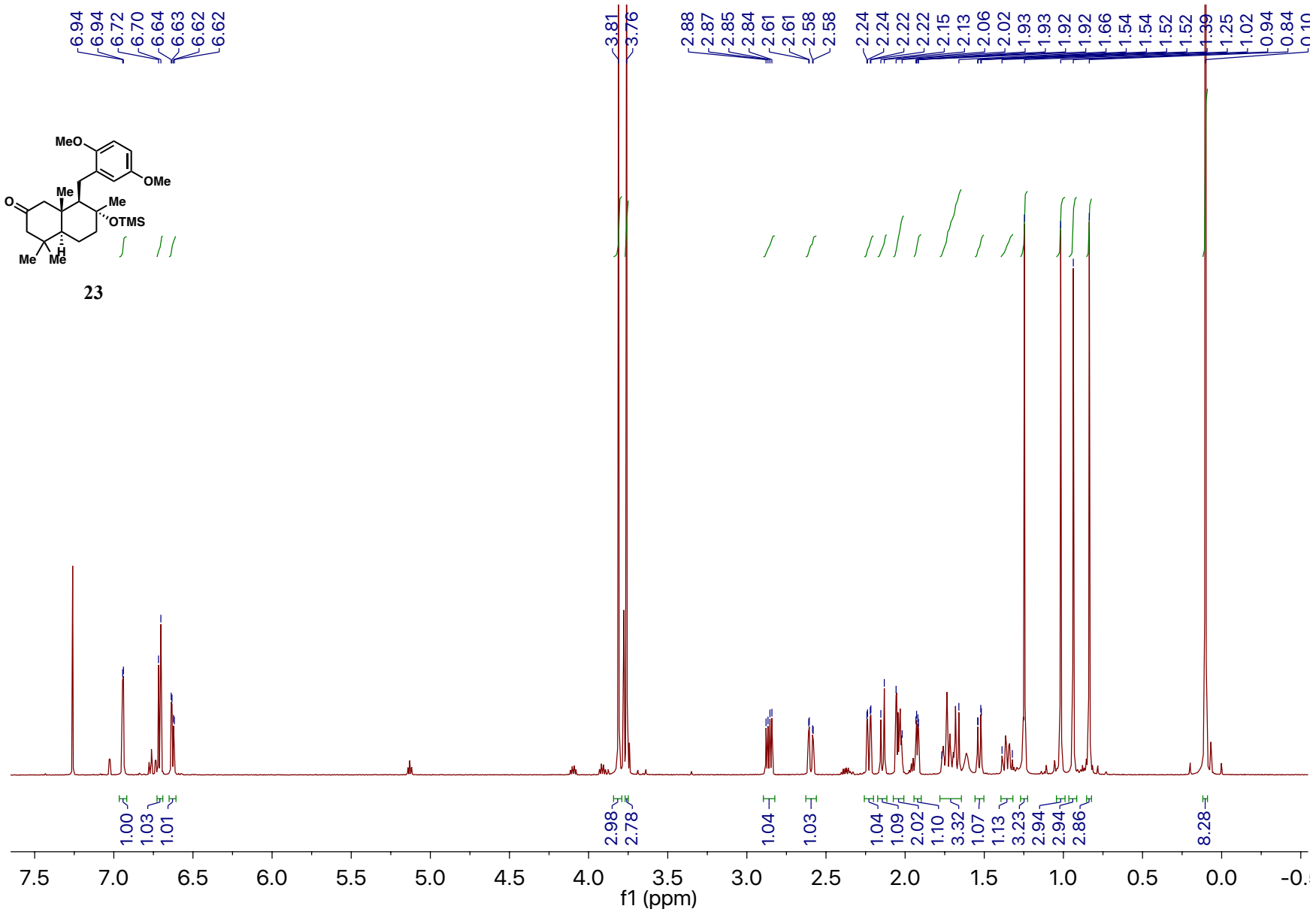

166.03
139.63
131.06
128.90
128.75
70.45
62.32
41.74
29.85
HO
Me
Me
O
O
Cl
20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


O
OR
Me
O
Me
OTMS
Me
Me
H
R=tetrachlorophthalyl
22
2.98 2.97 2.95 2.94 2.49 2.48 2.46 2.45 2.34 2.26 2.17 2.17 2.15 2.14 2.06 2.06 2.05 2.04 2.04 2.03 1.85 1.81 1.79 1.79 1.77 1.76 1.75 1.74 1.68 1.68 1.66 1.66 1.41 1.33 1.17 1.08 0.87 0.86
0.13
1.02 1.00 3.29 0.98 0.99 1.00 1.00 1.02 1.22 2.28 2.21 2.11 2.03 5.67
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)

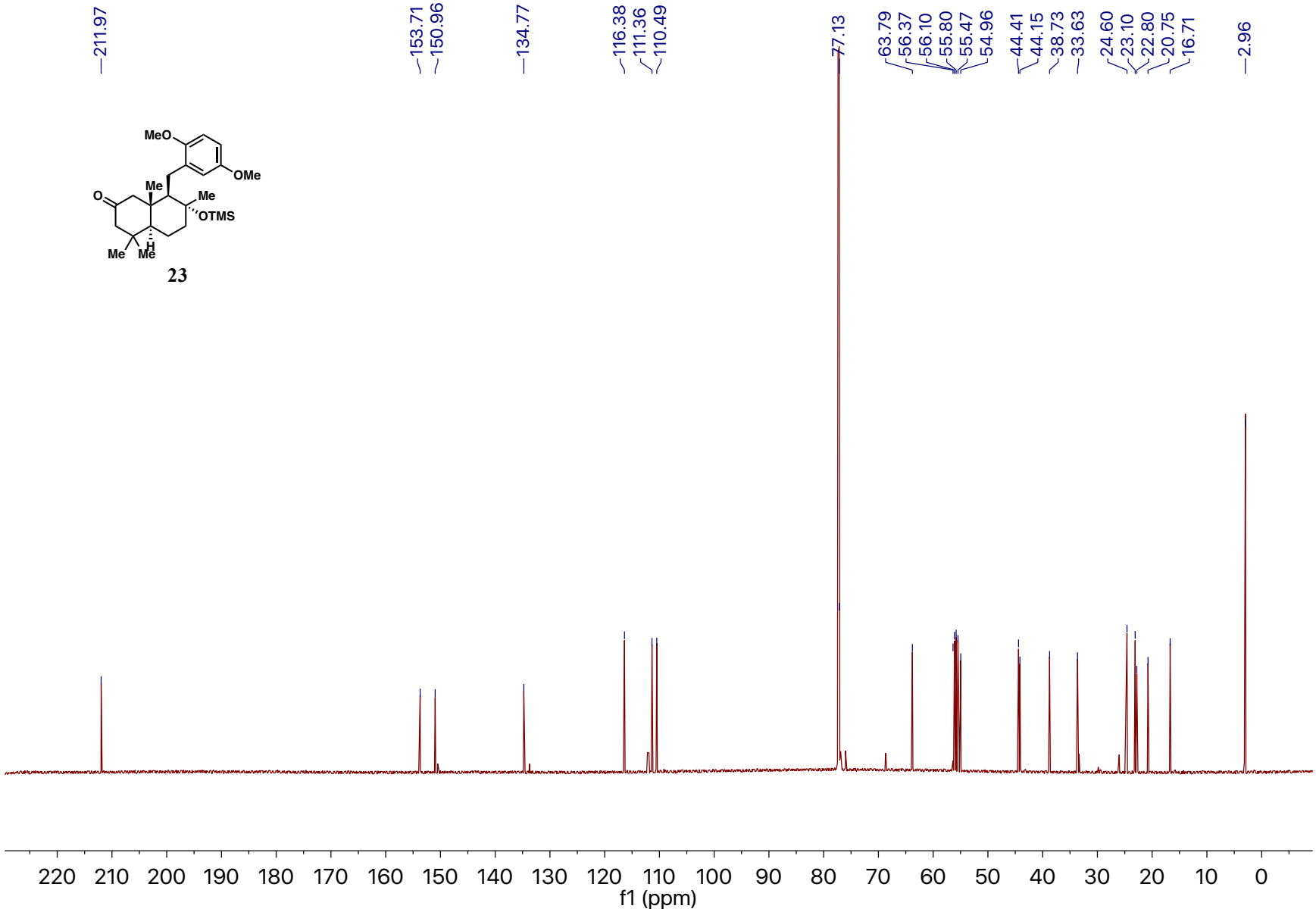


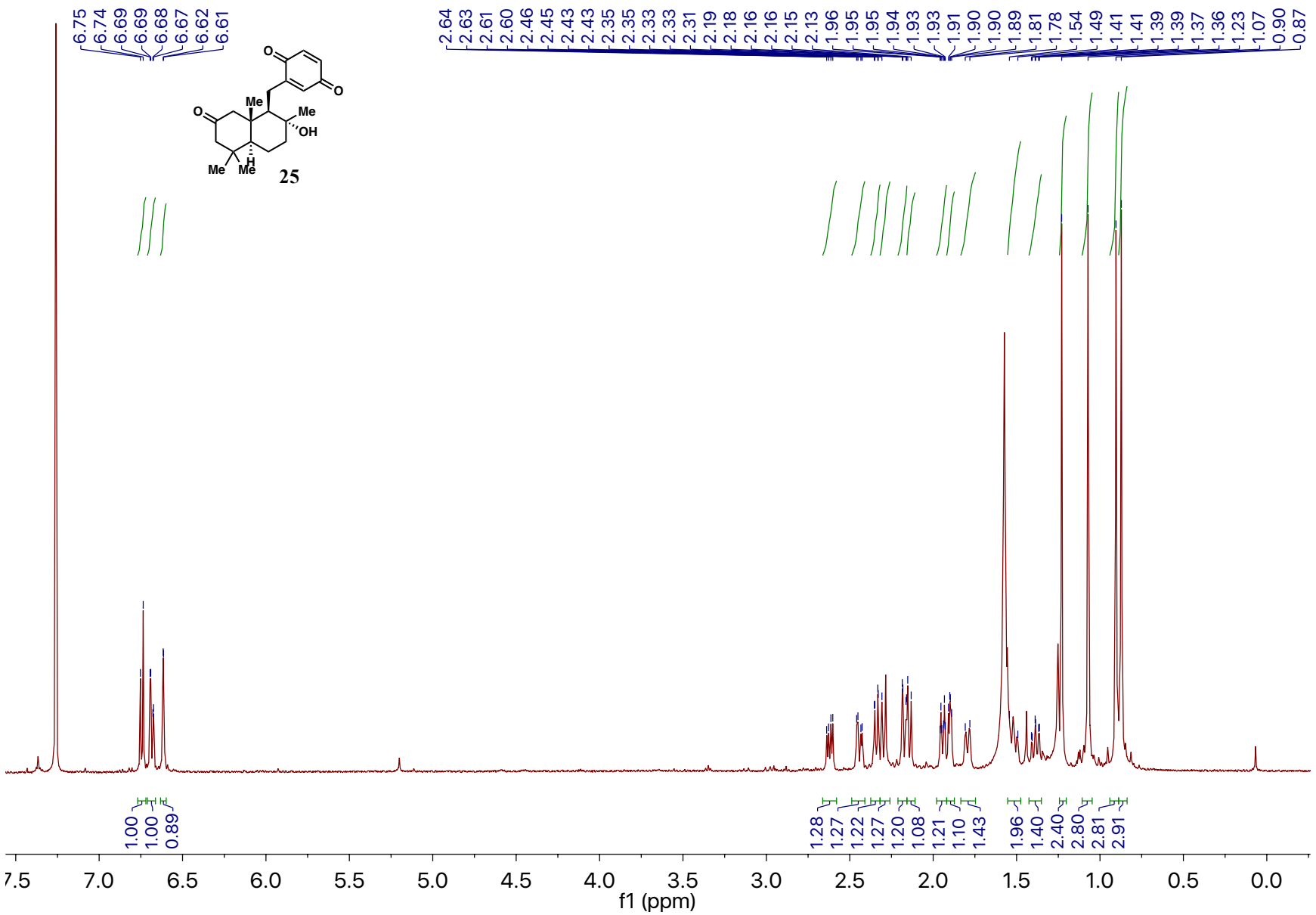

R=tetrachlorophthalyl

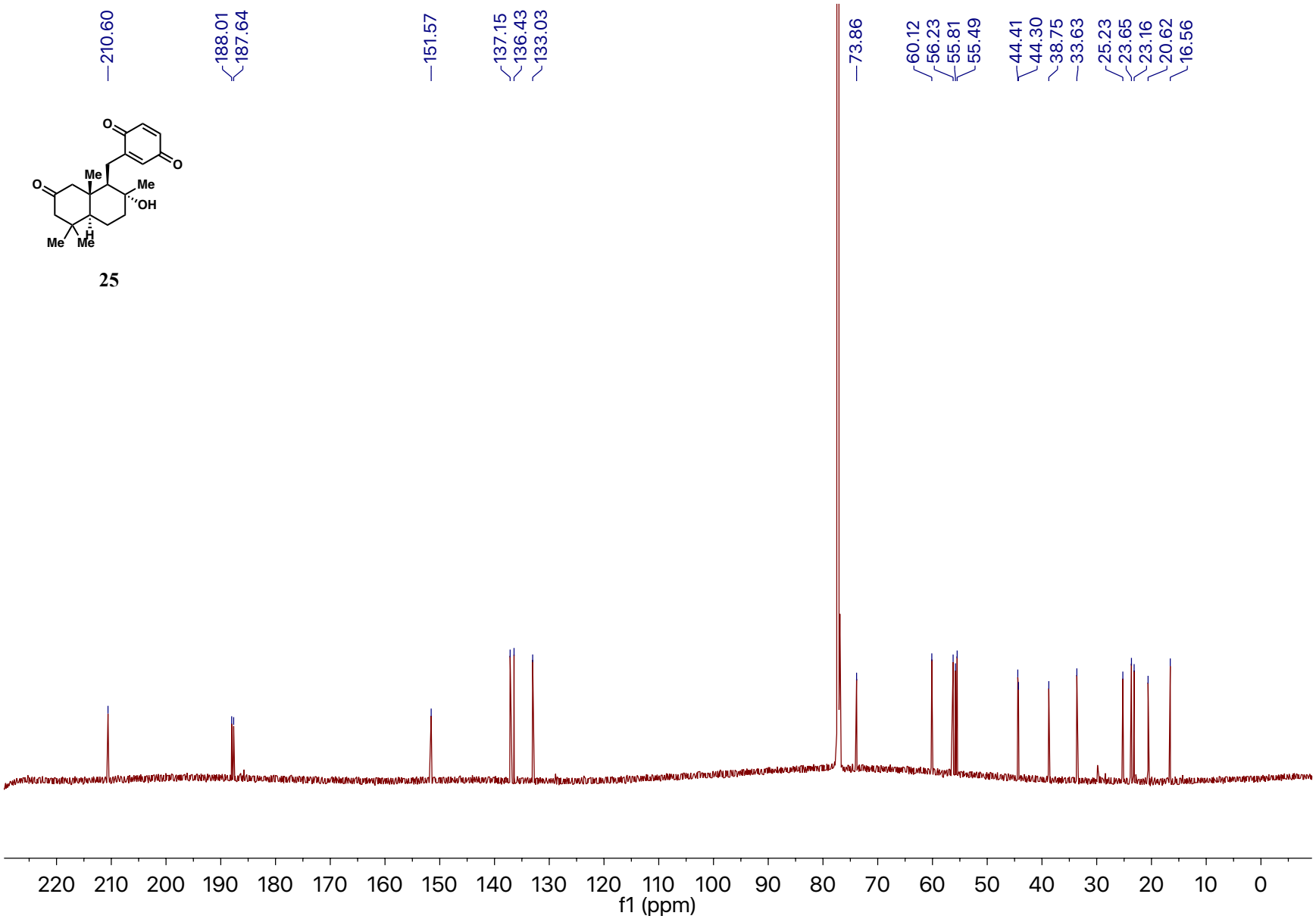
**22**


6.94
6.94
6.72
6.70
6.64
6.63
6.62
6.62
3.81
3.76
2.88
2.87
2.85
2.84
2.61
2.61
2.58
2.58
2.24
2.24
2.22
2.22
2.15
2.13
2.06
2.02
1.93
1.93
1.92
1.92
1.66
1.54
1.54
1.52
1.52
1.39
1.25
1.02
0.94
0.84
MeO
OMe
Me
Me
OTMS
O
Me
Me
H
1.00
1.03
1.01
2.98
2.78
1.04
1.03
1.04
1.09
2.02
1.10
3.32
1.07
1.13
3.23
2.94
2.94
2.86
8.28
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)

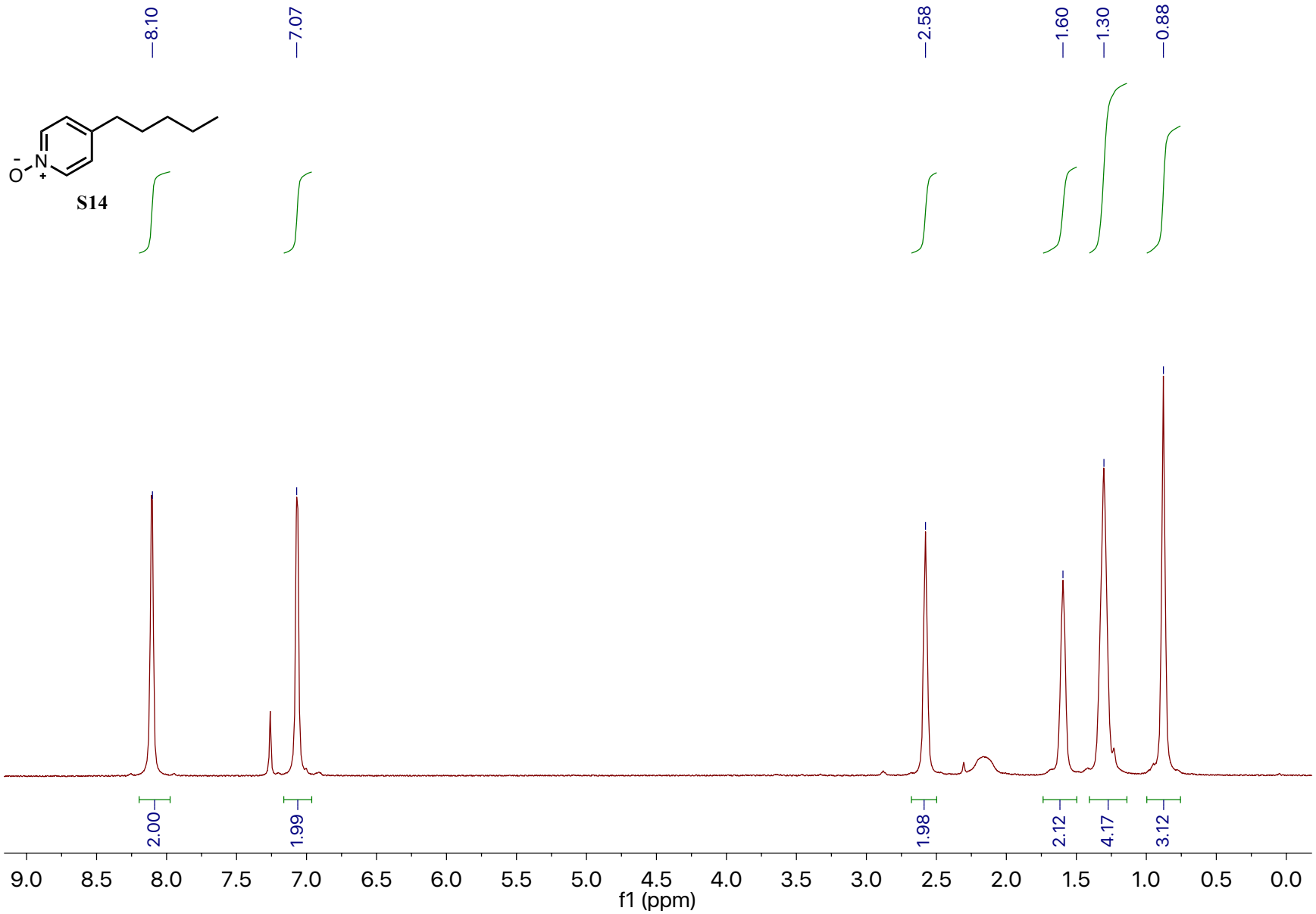
**23**


211.97
153.71
150.96
134.77
116.38
111.36
110.49
77.13
63.79
56.37
56.10
55.80
55.47
54.96
44.41
44.15
38.73
33.63
24.60
23.10
22.80
20.75
16.71
2.96
MeO
OMe
O
Me
Me
OTMS
Me
Me
H
23
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

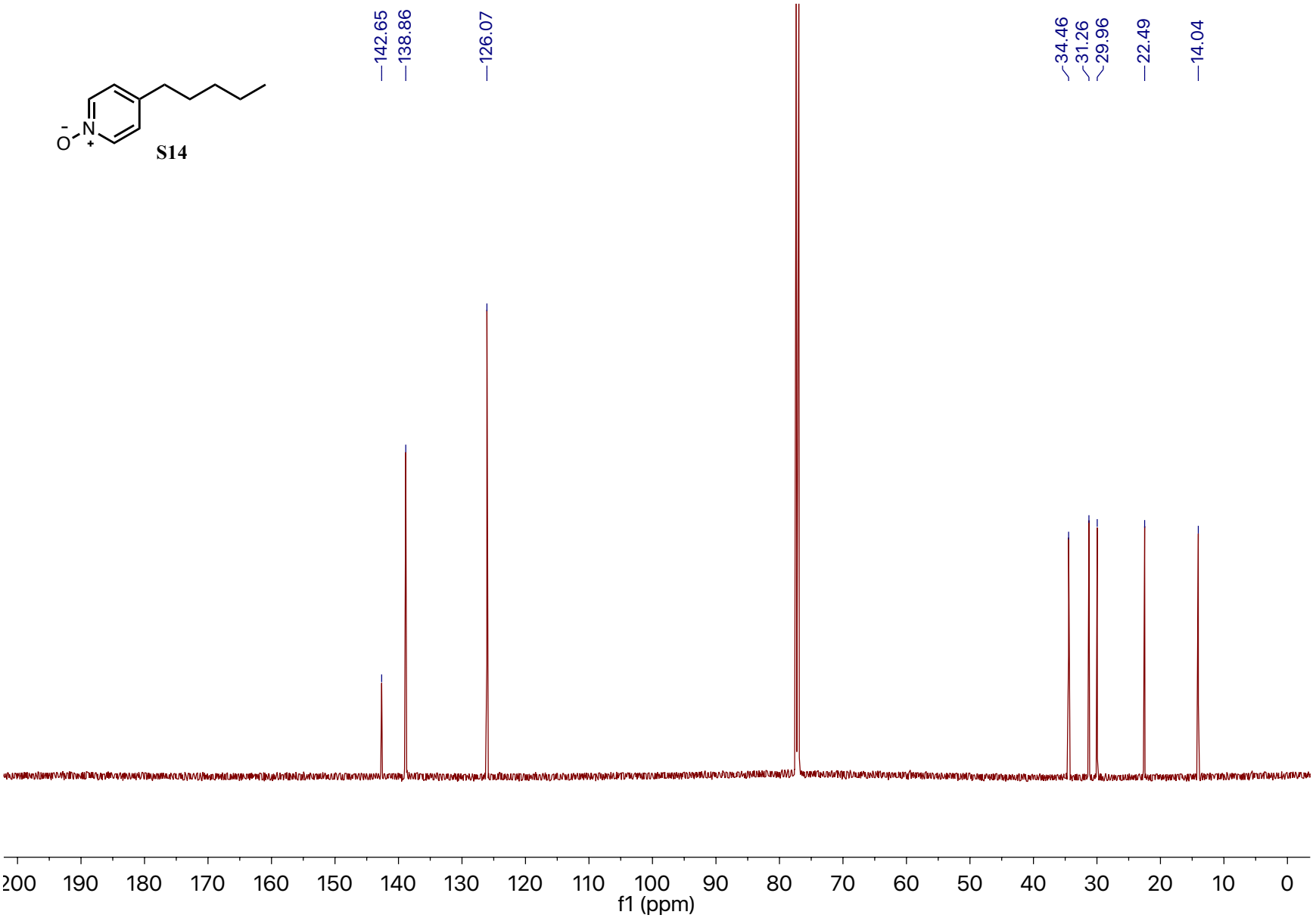

6.75
6.74
6.69
6.69
6.68
6.67
6.62
6.61
2.64
2.63
2.61
2.60
2.46
2.45
2.43
2.43
2.35
2.35
2.33
2.33
2.31
2.19
2.18
2.16
2.16
2.15
2.13
1.96
1.95
1.95
1.94
1.93
1.93
1.91
1.90
1.90
1.89
1.81
1.78
1.54
1.49
1.41
1.41
1.39
1.39
1.37
1.36
1.23
1.07
0.90
0.87
O
O
O
Me
Me
OH
Me
Me
H
25
1.00
1.00
0.89
1.28
1.27
1.22
1.27
1.20
1.08
1.21
1.10
1.43
1.96
1.40
2.40
2.80
2.81
2.91
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)


210.60
188.01
187.64
151.57
137.15
136.43
133.03
73.86
60.12
56.23
55.81
55.49
44.41
44.30
38.75
33.63
25.23
23.65
23.16
20.62
16.56
O
O
O
Me
Me
OH
H
Me
Me
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

**25**


8.10
7.07
2.58
1.60
1.30
0.88
2.00
1.99
1.98
2.12
4.17
3.12
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)

**S14**


142.65
138.86
126.07
34.46
31.26
29.96
22.49
14.04
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

**S14**