# Total Synthesis of Proposed Elgonene C and its (4R,5R)-Diastereomer

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## Table of contents



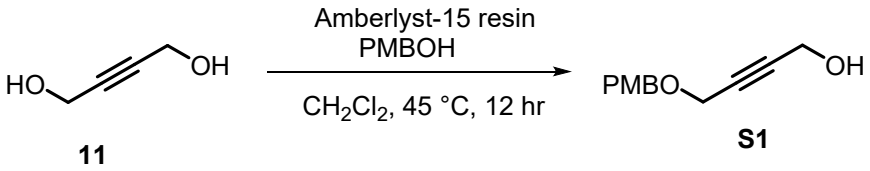
## 1. General Experimental Procedure:

All moisture-sensitive reactions were performed in an oven or flame-dried glassware with Teflon coated magnetic stirring bar under argon atmosphere using dry, freshly distilled solvents unless otherwise noted. Air- and moisture-sensitive liquids were transferred *via* a gastight syringe and a stainless-steel needle. Reactions were monitored by thin-layer chromatography (TLC, Silica gel 60 $F_{254}$) plates with UV light, ethanolic anisaldehyde (with 1% AcOH and 3.3% conc. $H_2SO_4$)-heat and phosphomolybdic acid as developing agents. All workup and purification procedures were carried out with reagent-grade solvents under ambient atmosphere unless otherwise stated. Column chromatography was performed using silica gel 60-120 mesh, 100-200 mesh. Yields are mentioned as chromatographically and spectroscopically homogeneous materials unless otherwise stated. Optical rotations were measured only for pure compounds and not for mixtures using sodium (589, D line; Anton Paar MCP 200 system) lamp and are reported as follows: $[\alpha]_D^{25}$ ($c$ = g/100 mL, solvent). HRMS were taken using Quadruple-TOF (Q-TOF) micro MS system using electrospray ionization (ESI) technique. $^{1}$H

NMR spectra were recorded on 400, 700 MHz spectrometers in appropriate solvents and calibrated using residual undertreated solvent as an internal reference, and the chemical shifts are shown in ppm scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved lines), etc. $^{13}C$ spectra were recorded on 100 MHz spectrometers.

**2. Experimental procedure:**

**4-((4-Methoxybenzyl)oxy)but-2-yn-1-ol (S1)**




*Procedure adapted from a literature procedure.*[1]

To a stirred solution of butyne-1,4-diol **11** (10.0 g, 116.3 mmol) and a catalytic amount of Amberlyst-15 resin (1.0 g, 10% w/w) in anhydrous $CH_2Cl_2$ (100 mL) was added 4-methoxybenzyl alcohol (16.0 g, 89.5 mmol) at room temperature and the reaction mixture was heated to reflux at 45 °C for 12 h. After completion of the reaction (monitored by TLC), it was filtered through a pad of Celite. The filtrate was washed with $CH_2Cl_2$ (2 × 50 mL), the combined organic layer was dried over anhydrous $Na_2SO_4$, concentrated under reduced pressure to obtain a brown oil, which was purified by silica gel column chromatography (30% ethyl acetate in hexanes) afforded the title compound **S1** (15.5 g, 86%).

**Physical State:** colourless oil.

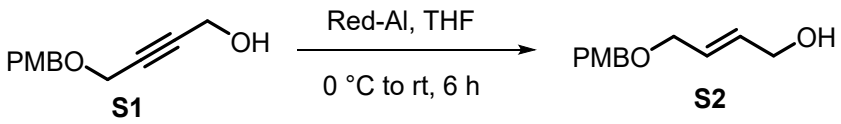
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.30 (d, *J* = 8.4 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 2H), 4.54 (s, 2H), 4.33 (s, 2H), 4.19 (s, 2H), 3.82 (s, 3H), 2.13 (br, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 159.4, 129.7, 129.3, 113.9, 84.8, 81.7, 71.4, 57.0, 55.3, 51.0.

**HRMS (ESI-TOF):** calc'd for $C_{12}H_{14}O_3$ [M+$Na^+$]: 229.0841, found: 229.0838.

**TLC:** $R_f$ = 0.2 (25% EtOAc in hexanes, phosphomolybdic acid staining).

**(*E*)-4-((4-methoxybenzyl)oxy)but-2-en-1-ol (S2)**




*Procedure adapted from a literature procedure.*[1]

Red-Al (31.4 mL, 109.2 mmol, 70% in toluene) was added to a solution of compound **S1** (9.0 g, 43.7 mmol) in anhydrous THF (70 mL) at 0 °C and the reaction mixture was allowed to stir at room temperature for 6 h. After complete consumption of the starting material (monitored by TLC), it was quenched with a saturated solution of sodium potassium tartrate (100 mL) at 0 °C and diluted with ethyl acetate (100 mL). The organic layer was separated and the aqueous

layer was extracted with ethyl acetate (2 × 75 mL). The combined organic layers were washed with brine, dried over anhydrous $Na_2SO_4$, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (30% ethyl acetate in hexanes) to furnish the desired compound **S2** (7.7 g, 85%).

**Physical State:** colorless oil.

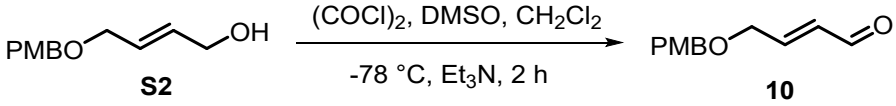
**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.28 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 5.95 – 5.77 (m, 2H), 4.47 (s, 2H), 4.14 (s, 2H), 4.02 (d, *J* = 5.3 Hz, 2H), 3.81 (s, 3H), 2.10 (br, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 159.2, 132.3, 130.2, 129.4, 127.7, 113.8, 72, 69.8, 62.8, 55.3.

**HRMS (ESI-TOF):** calc'd for $C_{12}H_{16}O_3$ [M+$Na^+$]: 231.0997, found: 231.0995.

**TLC:** $R_f$ = 0.2 (30% EtOAc in hexanes, phosphomolybdic acid staining).

(*E*)-4-((4-methoxybenzyl)oxy)but-2-enal (**10**)




*Procedure adapted from a literature procedure.*[1]

To a stirred solution of oxalyl chloride (4.1 mL, 48.1 mmol) in $CH_2Cl_2$ (40 mL), was added DMSO (6.8 mL, 96.1 mmol) at −78 °C. After 20 min, alcohol **S2** (5.0 g, 24.0 mmol) in $CH_2Cl_2$ (40 mL) was added to the reaction mixture at −78 °C and stirred for 45 min. Then triethylamine (26.7 mL, 192.3 mmol) was added to the reaction mixture and the reaction mixture was stirred at the same temperature for a further 45 min. After completion of the reaction (monitored by TLC), the reaction was quenched with a saturated aqueous $NH_4Cl$ (50 mL) solution and the organic layer was separated. The aqueous layer was extracted with $CH_2Cl_2$ (2 × 75 mL). The combined organic layer was washed with water (30 mL) and brine (20 mL), dried over anhydrous $Na_2SO_4$ and concentrated, evaporated to dryness, and then purified by silica gel column chromatography (20% ethyl acetate in hexanes) to obtain the desired product **10** (4.2 g, 86%).

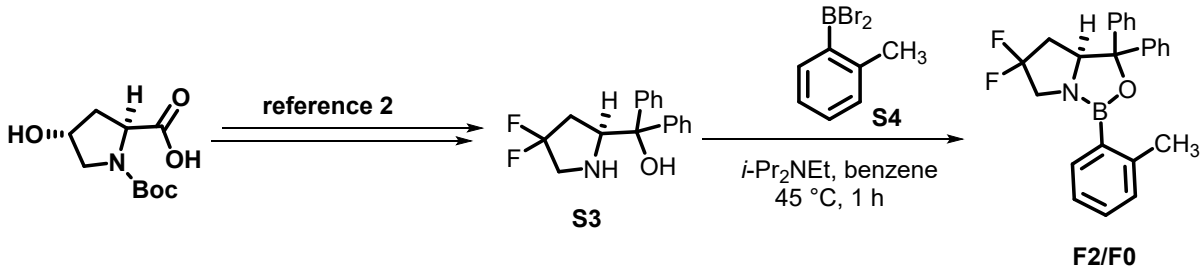
**Physical State:** colourless oil.

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 9.59 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.86 (dt, *J* = 15.8, 4.1 Hz, 1H), 6.40 (ddt, *J* = 15.7, 7.9, 1.8 Hz, 1H), 4.54 (s, 2H), 4.27 (dd, *J* = 4.1, 1.9 Hz, 2H), 3.82 (s, 3H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 193.3, 159.5, 153.2, 131.8, 129.5, 129.4, 113.9, 72.7, 68.3, 55.3.

**HRMS (ESI-TOF):** calc'd for $C_{12}H_{14}O_3$ [M+$Na^+$]: 229.0835, found:229.0837.

(*S*)-5,5-difluoro-3,3-diphenyl-1-(o-tolyl)tetrahydro-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaborole (**F2/F0**)




Compound **S3** was prepared by following standard literature procedure.[2] The physical and spectral data were identical to those previously reported for compound **S3**.[2]

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.49 (d, *J* = 7.3 Hz, 2H), 7.38 (d, *J* = 7.3 Hz, 2H), 7.32 – 7.05 (m, 6H), 4.50 – 4.40 (m, 1H), 3.24 (dd, *J* = 16.8, 10.0 Hz, 2H), 2.29 – 2.07 (m, 1H), 1.94 – 1.77 (m, 1H).

**$^{13}$C NMR (100 MHz, $CDCl_3$)** δ 146.0, 143.9, 128.6, 128.3, 127.1, 126.9, 125.8, 125.2, 76.5, 63.1 (m), 54.0 (m), 35.8 (m).

**$^{19}$F NMR (377 MHz, $CDCl_3$)** δ -95.4 (m), -99.2 (m).

**M. P.;** 76 °C (Lit.74-75 °C)

$[\alpha]_D^{25}$ = –91.0 (c =1.34, $CHCl_3$), {Lit–90.7 (c =1.34, $CHCl_3$) for >99% ee}.

**HRMS (ESI-TOF):** calc'd for $C_{12}H_{20}O_5$ [M+$Na^+$]: 290.1356, found: 290.1365.

(*S*)-5,5-difluoro-3,3-diphenyl-1-(o-tolyl)tetrahydro-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaborole (**F2/F0**)

**F2/F0** precatalyst was prepared from the known literature procedure[2]: Compound **S3** (290 mg, 1.15 mmol) was placed in a 25 mL oven- and flame-dried round bottom flask together with anhydrous benzene (15 mL) and diisopropylethylamine (0.44 mL, 2.53 mmol) under nitrogen at 23 °C. A solution of dibromo(*o*-tolyl)borane **S4**[2] (300 mg; 1.15 mmol) in anhydrous benzene (3 mL) was added *via* syringe over 30 min at 23 °C. After the addition was complete, the resulting white suspension was heated at 45 °C for 1 h. Stirring was stopped and the solids were allowed to settle at the bottom of the flask at room temperature. The supernatant solution was used directly for the Diels–Alder experiments. The supernatant solution was concentrated under reduced pressure on a Schlenk line to afford a pale-yellow oil which was pure by NMR.

***Notes:***

1. After preparation of the pre-catalyst, supernatant solutions were kept in a freezer at –20 °C under rigorous exclusion of moisture.
2. For the Diels–Alder experiments, concentration of the pre-catalyst solution should be done in a freshly oven- and flame-dried flask under rigorous exclusion of moisture.
3. For analytical purposes, NMR solvents should be rigorously dried and oven-dried NMR tubes should be used to obtain spectroscopically intact samples.

The spectral data for pre-catalyst **F2/F0** was in good agreement with literature values.[2]

**$^1$H NMR (400 MHz, $CDCl_3$)** δ 7.52 – 7.47 (m, 3H), 7.41 – 7.34 (m, 2H), 7.29 – 7.23 (m, 4H), 7.22 – 7.10 (m, 5H), 4.79 (dd, *J* = 10.7, 5.9 Hz, 1H), 3.71 (dd, *J* = 24.1, 12.6 Hz, 1H), 3.49 (dt, *J* = 17.1, 12.1 Hz, 1H), 2.54 (s, 3H), 2.18 – 2.06 (m, 1H), 1.65 – 1.45 (m, 1H).

**References:**


1. B. Thirupathi and D. K. Mohapatra, *Organic & biomolecular chemistry.*, 2016, **14**, 6212-6224.
2. K. Mahender Reddy, E. Bhimireddy, B. Thirupathi, S. Breitler, S. Yu and E. J. Corey, *Journal of the American Chemical Society*, 2016, **138**, 2443-2453.


**Table 1. Comparison of $^1$H NMR spectral data between natural and synthetic elgonene C.**

| Position | Natural Elgonene C ($^1$H 500MHz, $CDCl_3$) | Synthetic compounds ($^1$H 700MHz, $CDCl_3$) | | Δδ (synthetic-natural) ppm | |
|---|---|---|---|---|---|
| | Data reported by Stadler | **1** | **1a** | **1** | **1a** |
| 3 | 6.87 (br d, *J*=8.82 Hz) | 6.83 (br d, *J*= 8.7 Hz) | 6.83 (br d, *J*= 8.7 Hz) | −0.04 | −0.04 |
| 4 | 4.53 (dd, *J* = 8.82, 4.52 Hz) | 4.46 (dd, *J* = 8.7, 5.7 Hz) | 4.47 (dd, *J* = 8.7, 5.7 Hz) | −0.07 | −0.06 |
| 5 | 4.34 (d, *J* = 4.52 Hz) | 4.12 (d, *J* = 5.5 Hz) | 4.11 (d, *J* = 5.5 Hz) | −0.22 | −0.23 |
| 7 | 2.12 (m) | 2.16 (m) | 2.13 (m) | +0.04 | +0.01 |
| 8 | 1.49 (m), 1.84(m) | 1.56 (m), 1.84 (m) | 1.48 (m), 1.80 (m) | +0.07, 0.0 | −0.01, −0.04 |
| 9 | 1.98 (m), 2.04 (m) | 1.79 (m), 2.06 (m) | 1.99 (m), 2.08 (m) | -0.19, +0.02 | +0.01, +0.04 |
| 11 | 5.41 (m) | 5.41 (m) | 5.41 (m) | 0.0 | 0.0 |
| 12 | 1.99 (m), 2.08 (m) | 1.99 (m), 2.06 (m) | 1.99 (m), 2.08 (m) | 0.0, -0.02 | 0.0, 0.0 |
| 13 | 1.66 (s) | 1.67 (s) | 1.67 (s) | +0.01 | +0.01 |
| 14 | 5.07 (s), 5.22 (s) | 5.08 (s), 5.23 (s) | 5.09 (s), 5.23 (s) | +0.02, +0.02 | +0.02, +0.02 |
| 15 | 1.92 (s) | 1.93 (s) | 1.92 (s) | +0.01 | 0.0 |

**Table 2. Comparison of $^{13}$C NMR spectral data between natural and synthetic elgonene C.**

| Position | Natural Elgonene C ($^{13}$C 125 MHz, in CDCl3) | Synthetic Elgonene C (175 MHz, in $CDCl_3$ | | Δδ (synthetic-natural) ppm | |
|---|---|---|---|---|---|
| | | **1** | **1a** | **1** | **1a** |
| 1 | 170.6 | 172.2 | 172.0 | +1.6 | +1.4 |
| 2 | 130.3 | 130.0 | 130.0 | −0.3 | −0.3 |

| | | | | | |
|---|---|---|---|---|---|
| 3 | 140.1 | 141.1 | 141.0 | +1.0 | +0.9 |
| 4 | 69.9 | 70.6 | 70.6 | +0.7 | +0.7 |
| 5 | 76.4 | 76.6 | 76.5 | +0.2 | +0.1 |
| 6 | 152.7 | 153.5 | 153.2 | +0.8 | +0.5 |
| 7 | 36.8 | 37.3 | 37.3 | +0.5 | +0.5 |
| 8 | 29.6 | 28.6 | 29.3 | −1.0 | −0.3 |
| 9 | 30.6 | 30.7 | 30.5 | +0.1 | −0.1 |
| 10 | 133.7 | 134.0 | 133.7 | +0.3 | +0.0 |
| 11 | 120.5 | 120.3 | 120.4 | −0.2 | −0.1 |
| 12 | 31.6 | 32.8 | 31.6 | +1.2 | 0.0 |
| 13 | 23.4 | 23.4 | 23.4 | 0.0 | 0.0 |
| 14 | 111.3 | 111.0 | 111.4 | −0.3 | 0.1 |
| 15 | 13.0 | 13.0 | 13.0 | 0.0 | 0.0 |

**Table 3. Comparison of $^{13}C$ NMR spectral data between natural and synthetic elgonene C with traces $H_2O$ and TFA**

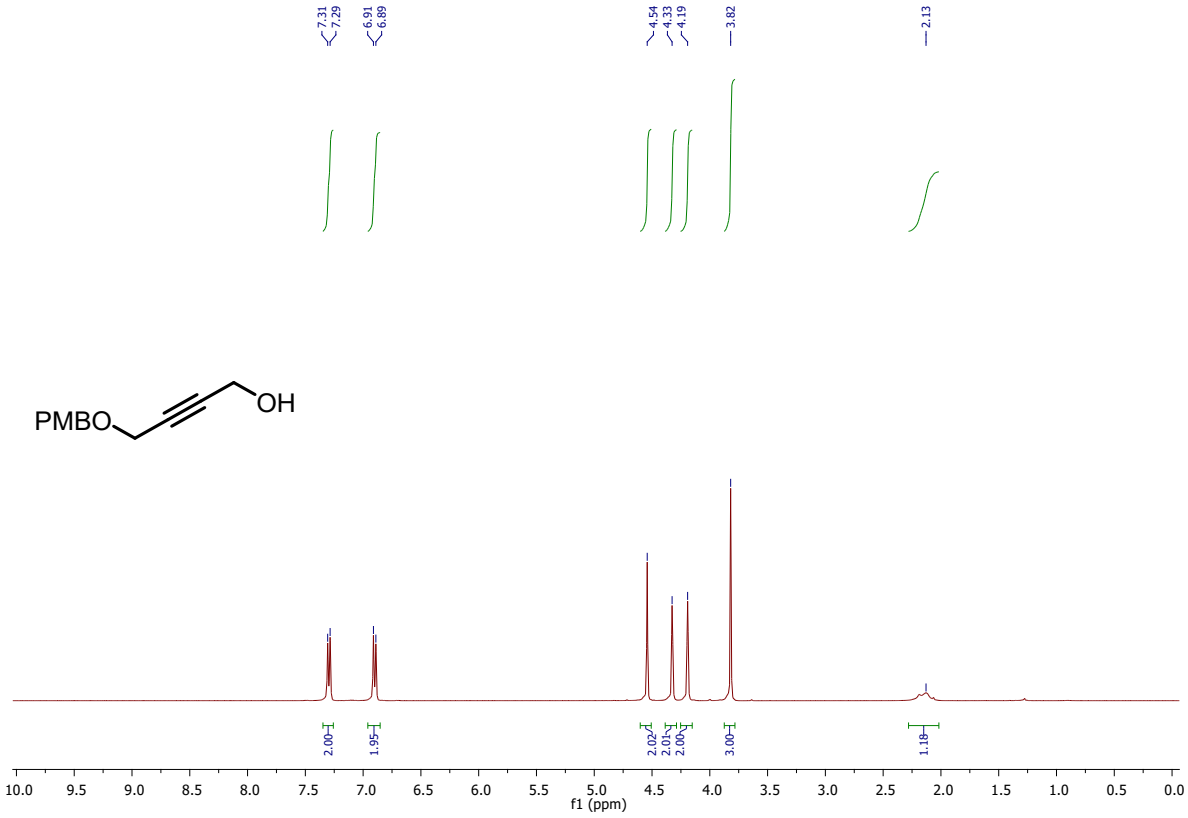
| Position | Natural Elgonene C ($^{13}C$ 125 MHz, in $CDCl_3$) | Synthetic Elgonene C 1 ($^{13}CNMR$, $CDCl_3$, 100 MHz) | | Δδ (synthetic-natural) ppm | |
|---|---|---|---|---|---|
| | | (With trace amount of $H_2O$) | (With traces amount of TFA) | (With traces amount of $H_2O$) | (With traces amount of TFA) |
| 1 | 170.6 | 171.0 | 171.0 | +0.4 | +0.4 |
| 2 | 130.3 | 130.0 | 130.0 | −0.3 | −0.3 |
| 3 | 140.1 | 140.9 | 141.0 | +0.8 | +0.9 |
| 4 | 69.9 | 70.7 | 70.7 | +0.7 | +0.8 |
| 5 | 76.4 | 76.6 | 76.6 | +0.2 | +0.2 |
| 6 | 152.7 | 153.7 | 153.7 | +1.0 | +1.0 |
| 7 | 36.8 | 37.4 | 37.4 | +0.6 | +0.6 |
| 8 | 29.6 | 28.7 | 28.7 | −0.9 | −0.9 |
| 9 | 30.6 | 30.8 | 30.8 | +0.1 | +0.2 |
| 10 | 133.7 | 134.1 | 134.1 | +0.4 | +0.4 |
| 11 | 120.5 | 120.4 | 120.4 | −0.2 | −0.1 |
| 12 | 31.6 | 32.9 | 32.9 | +1.3 | +1.3 |
| 13 | 23.4 | 23.4 | 23.4 | 0.0 | 0.0 |
| 14 | 111.3 | 111.0 | 111.1 | −0.3 | −0.2 |
| 15 | 13.0 | 13.2 | 13.2 | 0.1 | +0.2 |

**Table 4: Comparison table of $^{13}C$-NMR spectrum of compound 1 ($CDCl_3$, 100 MHz) with concentration variations**

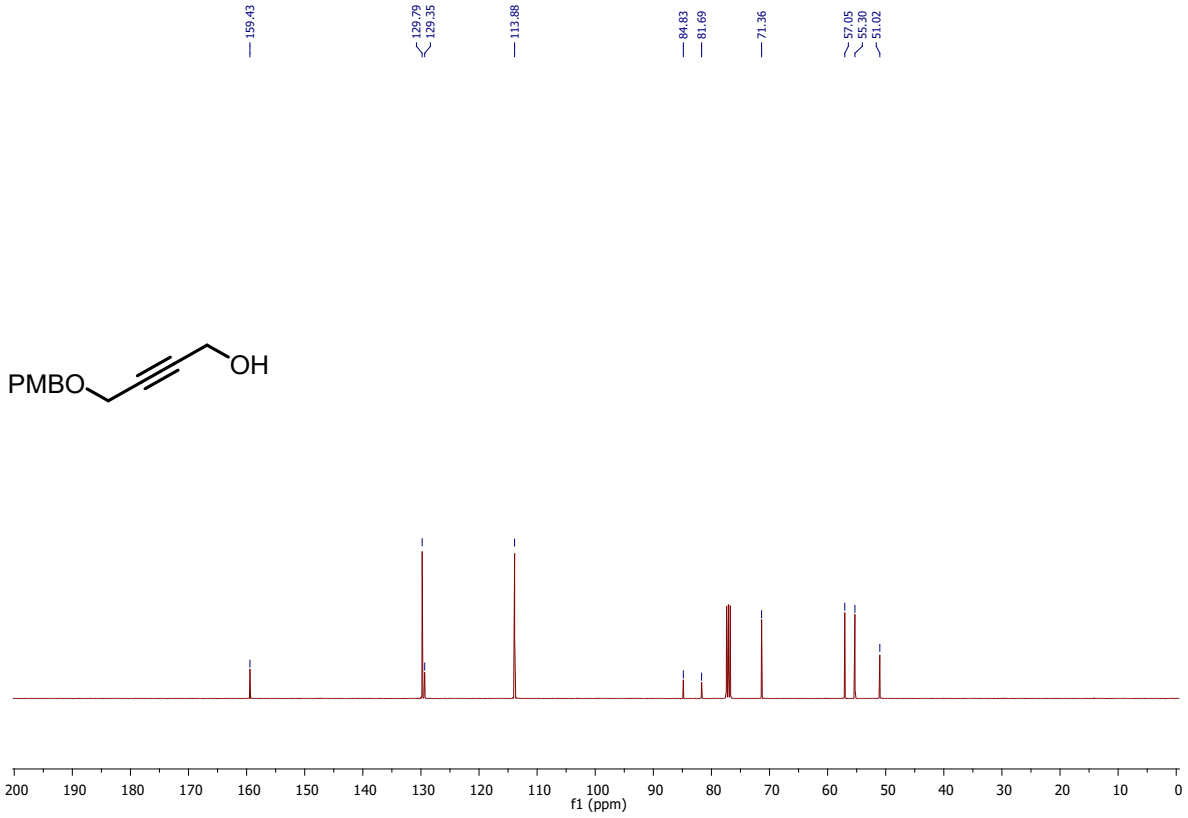
| Position | Natural Elgonene C ($^{13}C$ | Synthetic Elgonene C 1 ($^{13}C$ 100 MHz) |
|---|---|---|

| | **125 MHz, in $CDCl_3$)** | **(0.025 M $CDCl_3$)** | **(0.094 M $CDCl_3$)** | **(0.075 M $CDCl_3$)** |
|---|---|---|---|---|
| 1 | 170.6 | 171.6 | 172.3 | 172.1 |
| 2 | 130.3 | 130.0 | 130.1 | 130.1 |
| 3 | 140.1 | 141.0 | 141.1 | 141.1 |
| 4 | 69.9 | 70.7 | 70.6 | 70.6 |
| 5 | 76.4 | 76.6 | 76.5 | 76.5 |
| 6 | 152.7 | 153.7 | 153.6 | 153.6 |
| 7 | 36.8 | 37.4 | 37.3 | 37.3 |
| 8 | 29.6 | 28.7 | 28.7 | 28.7 |
| 9 | 30.6 | 30.8 | 30.7 | 30.7 |
| 10 | 133.7 | 134.1 | 134.1 | 134.1 |
| 11 | 120.5 | 120.4 | 120.4 | 120.4 |
| 12 | 31.6 | 32.9 | 32.8 | 32.8 |
| 13 | 23.4 | 23.5 | 23.5 | 23.5 |
| 14 | 111.3 | 111.1 | 111.1 | 111.1 |
| 15 | 13.0 | 13.2 | 13.1 | 13.1 |

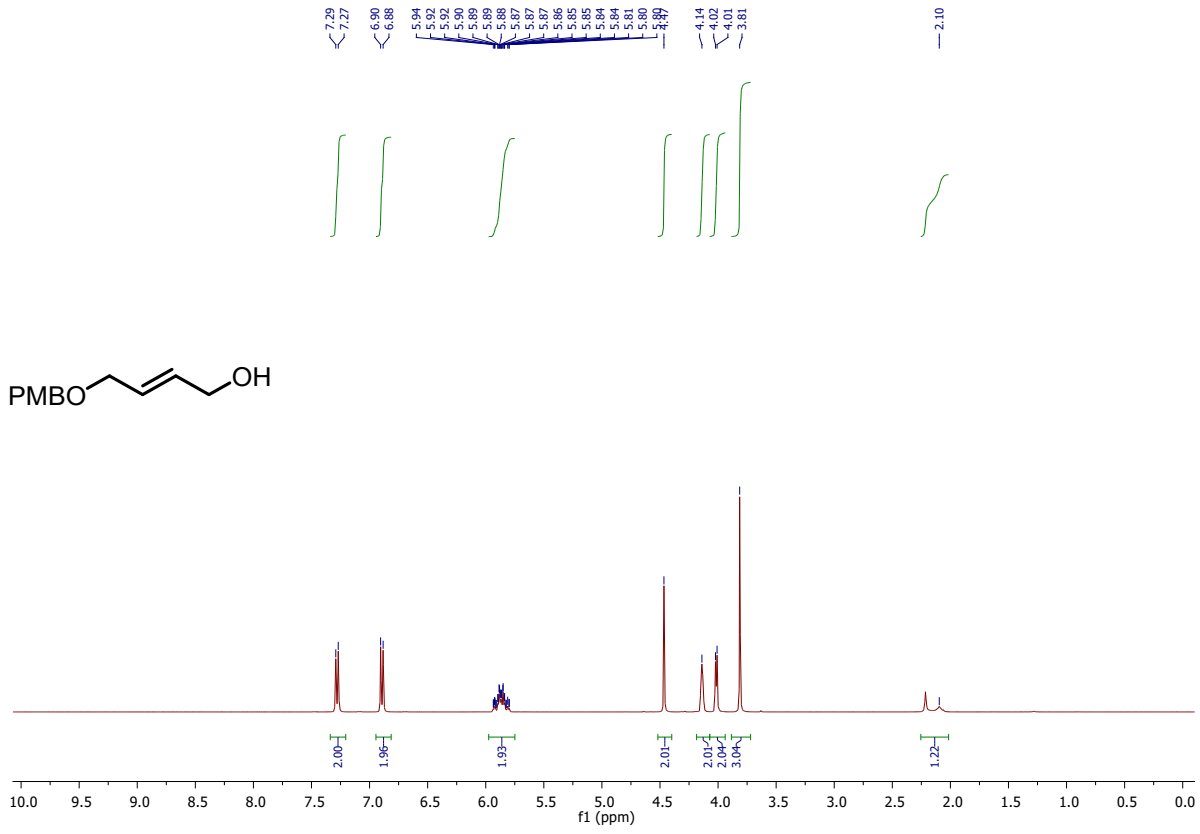
**$^1$H-NMR of intermediate S1 for compound 10 (400 MHz, $CDCl_3$):**



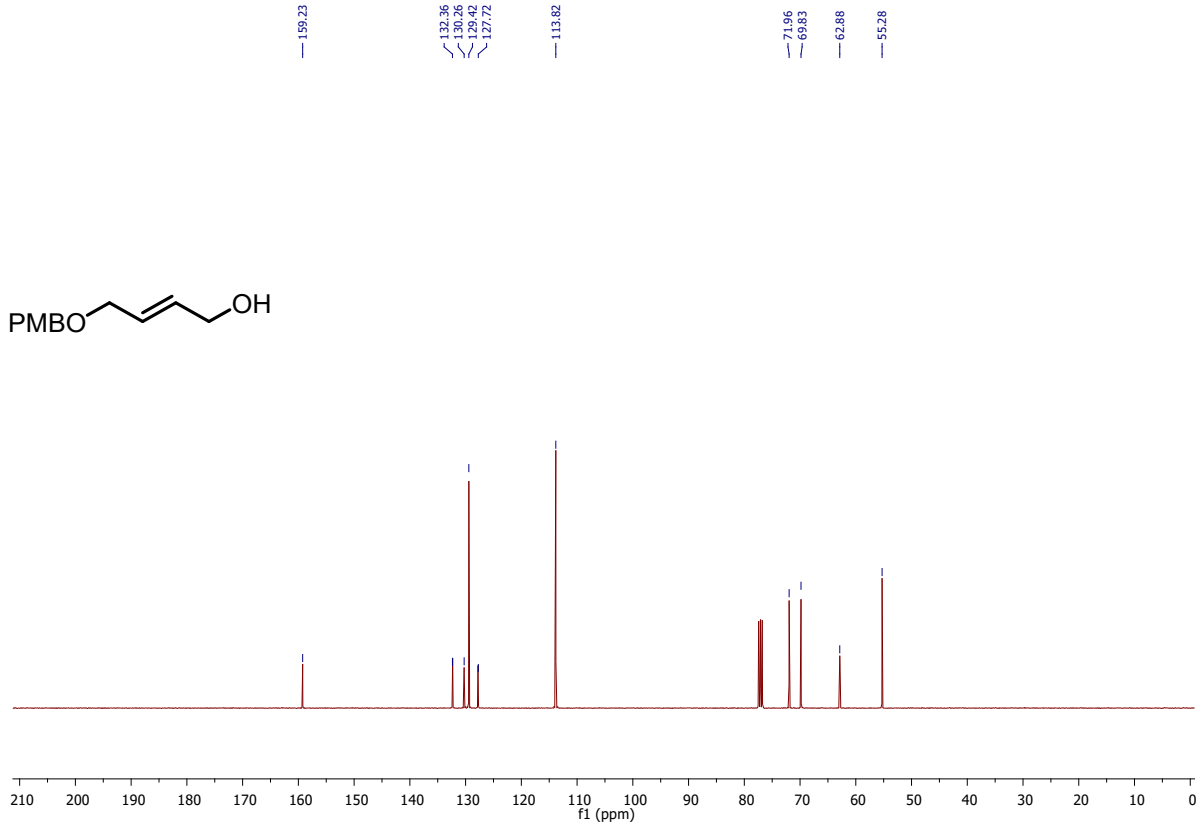
**$^{13}$C-NMR spectrum of intermediate S1 for compound 10 (100 MHz, $CDCl_3$):**



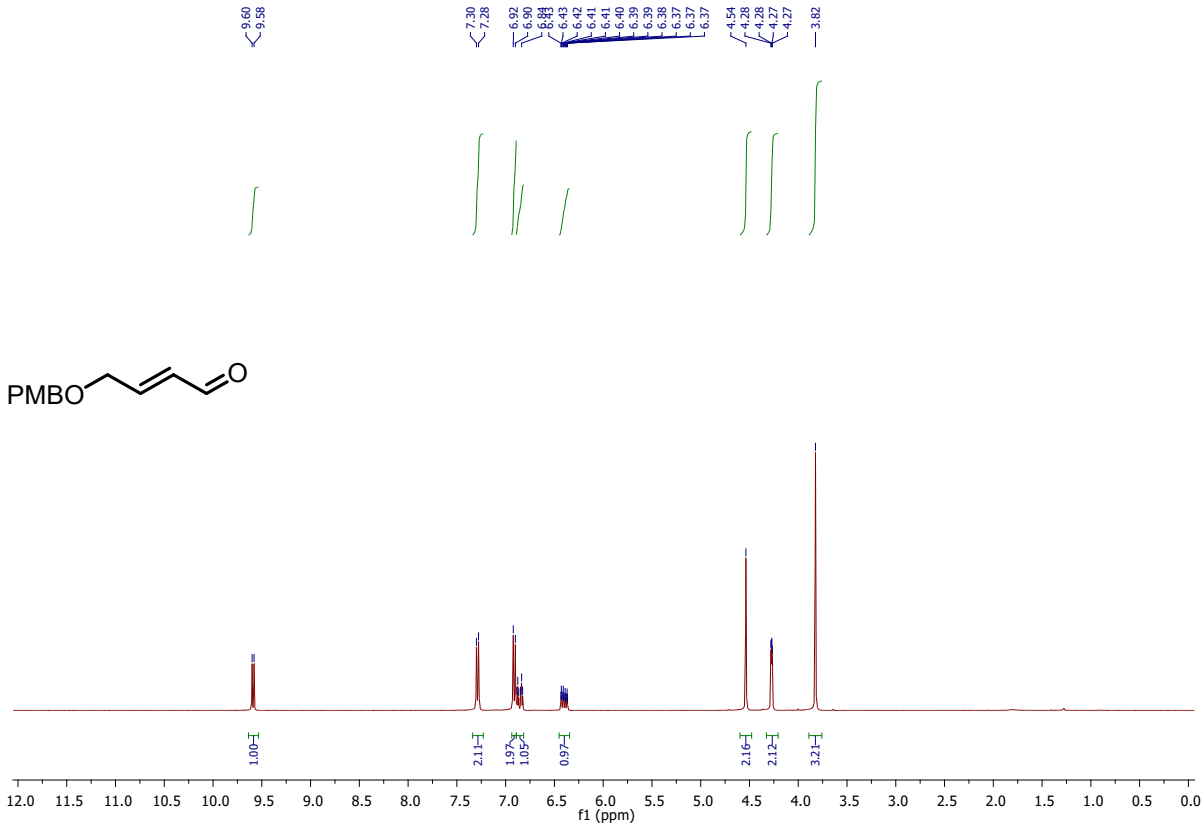

**$^{1}$H-NMR of intermediate S2 for compound 10 (400 MHz, $CDCl_3$):**



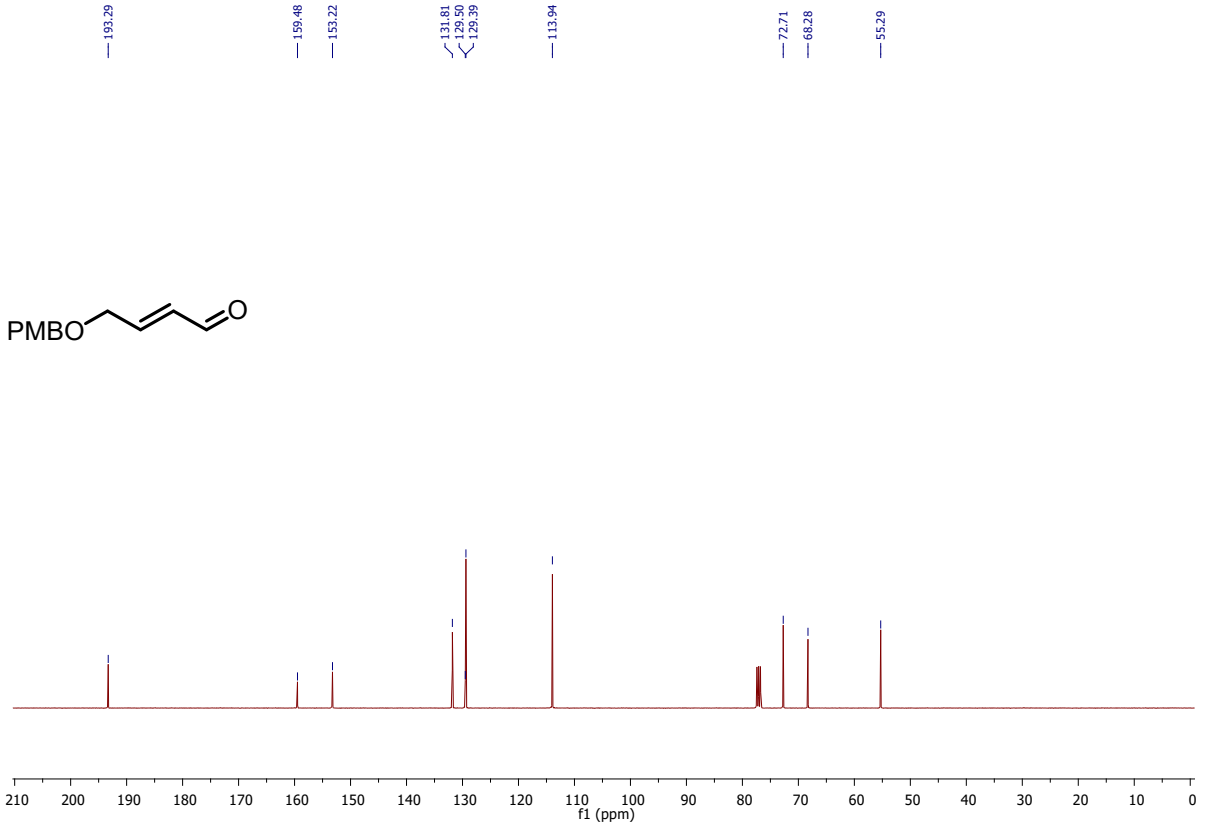
**$^{13}$C-NMR spectrum of intermediate S2 for compound 10 (100 MHz, $CDCl_3$):**



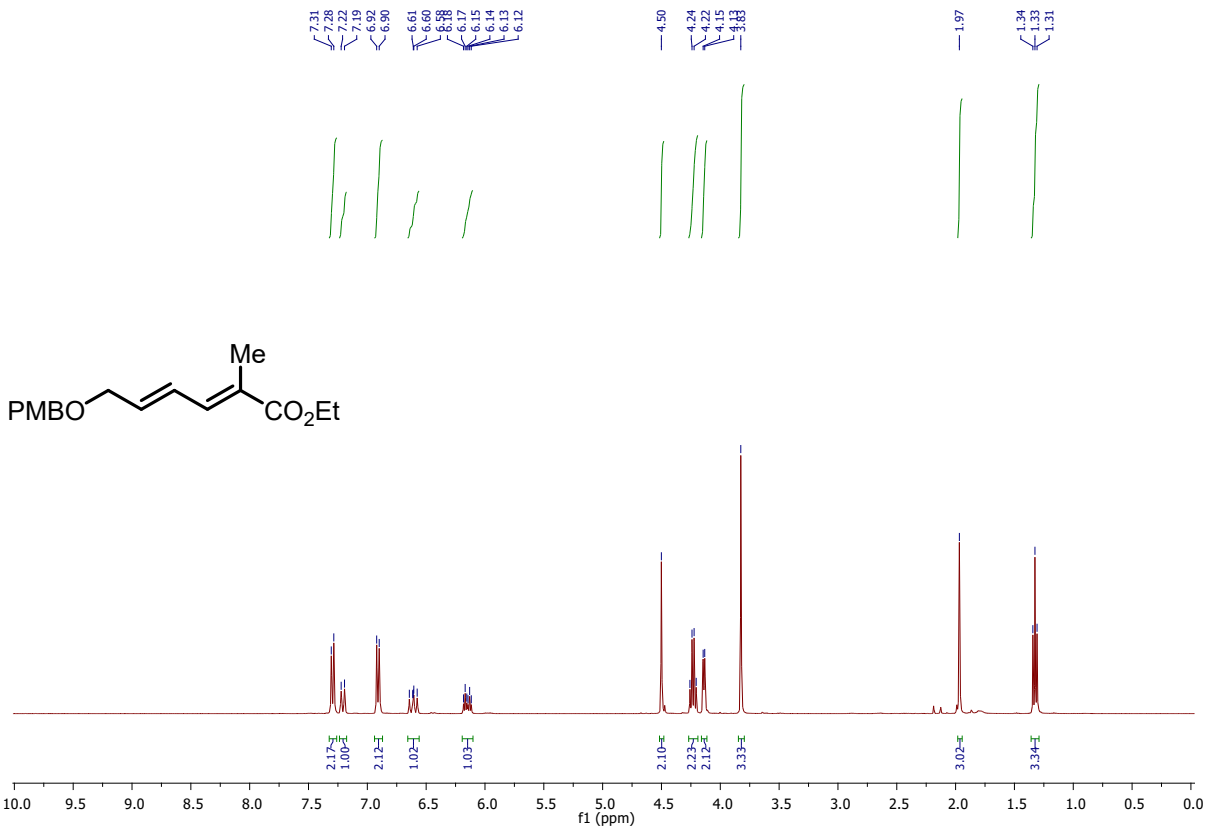

**$^{1}$H-NMR spectrum of compound 10 (400 MHz, $CDCl_3$):**



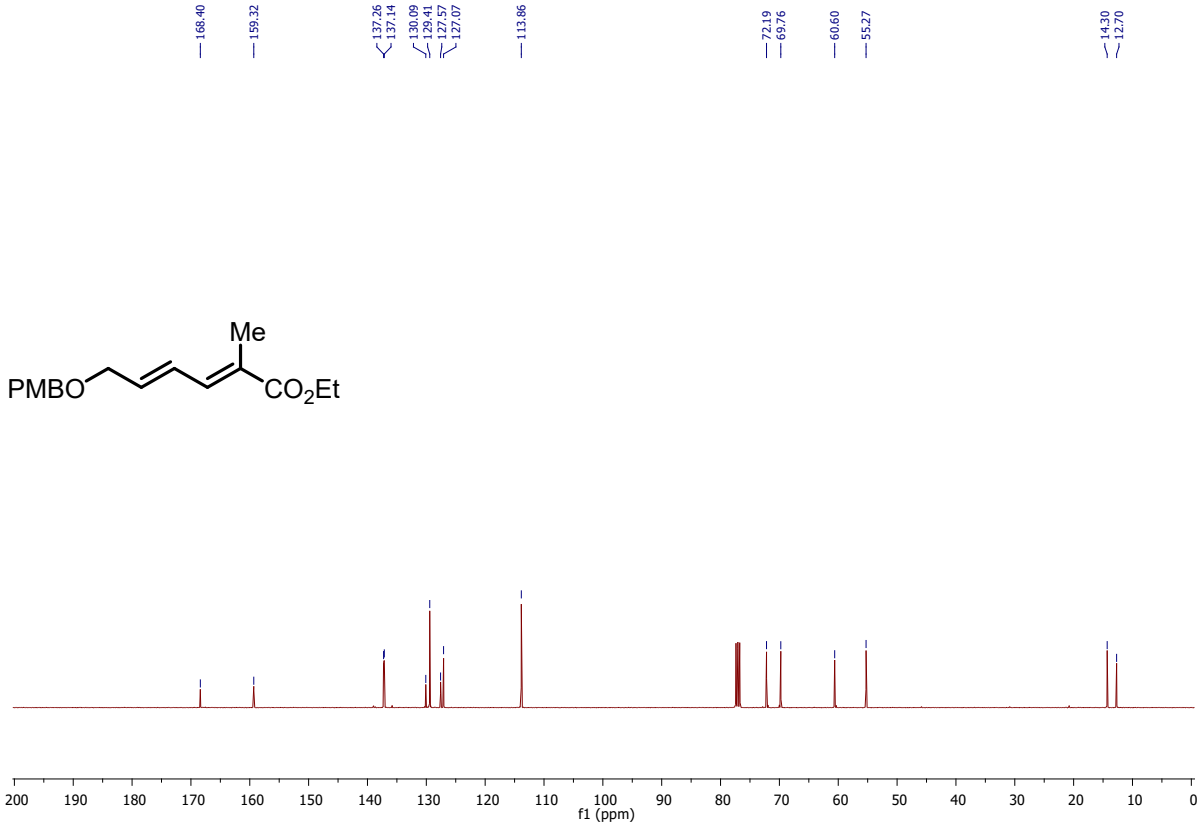
**$^{13}$C-NMR spectrum of compound 10 (100 MHz, $CDCl_3$):**



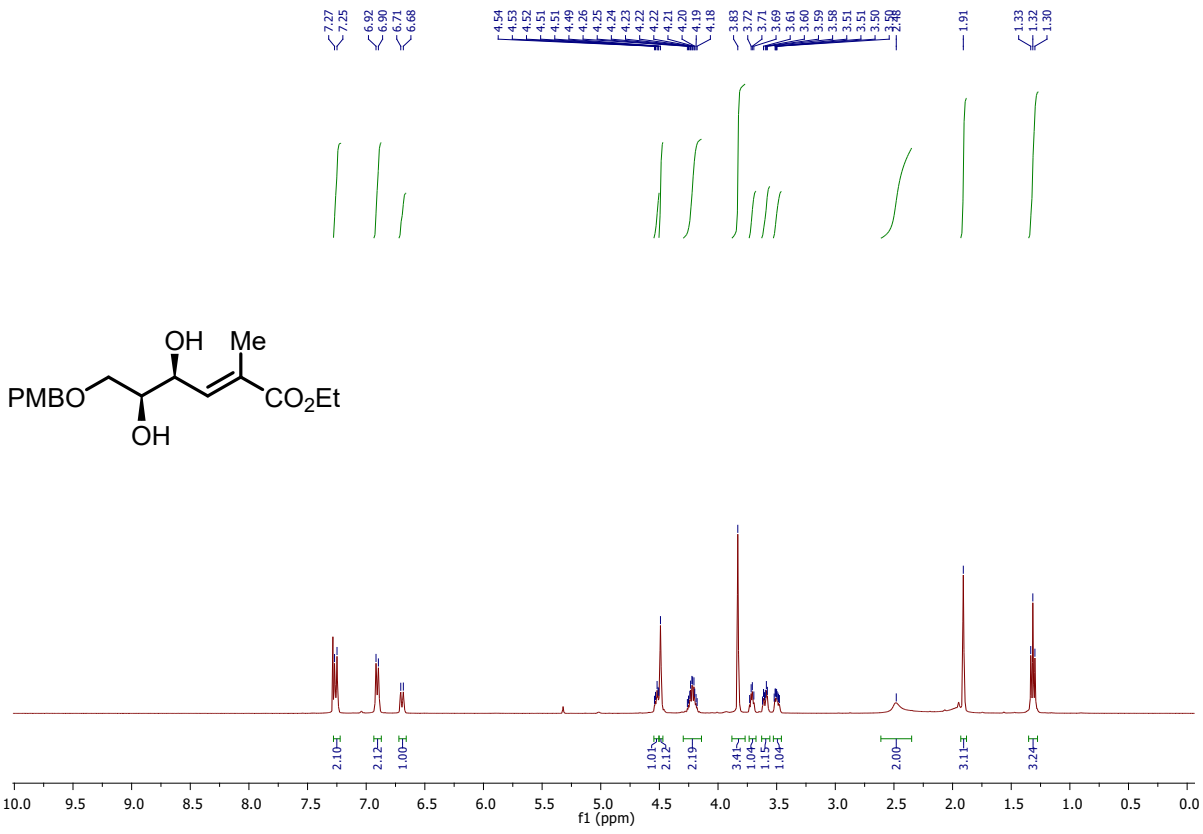

**$^{1}$H-NMR spectrum of compound 13 (400 MHz, $CDCl_3$):**



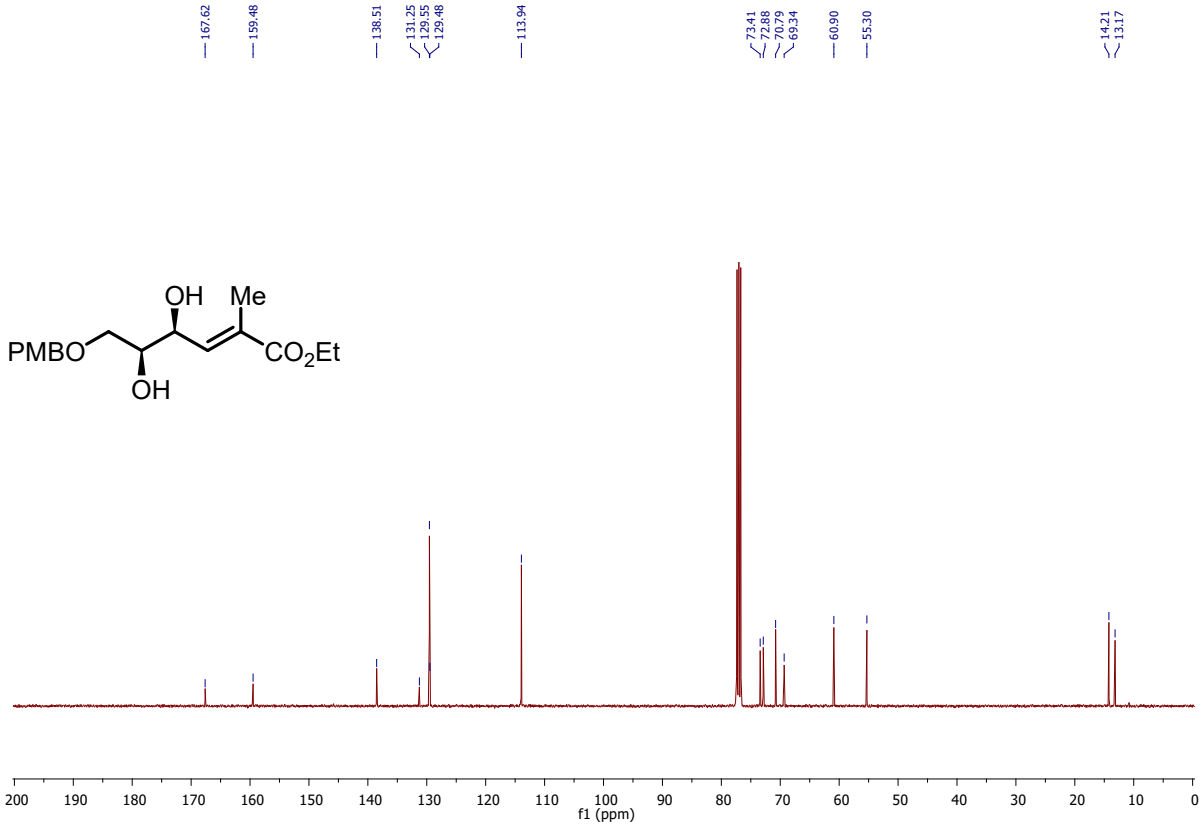
**$^{13}$C-NMR spectrum of compound 13 (100 MHz, $CDCl_3$):**




**$^{1}$H-NMR spectrum of compound 14 (400 MHz, $CDCl_3$):**

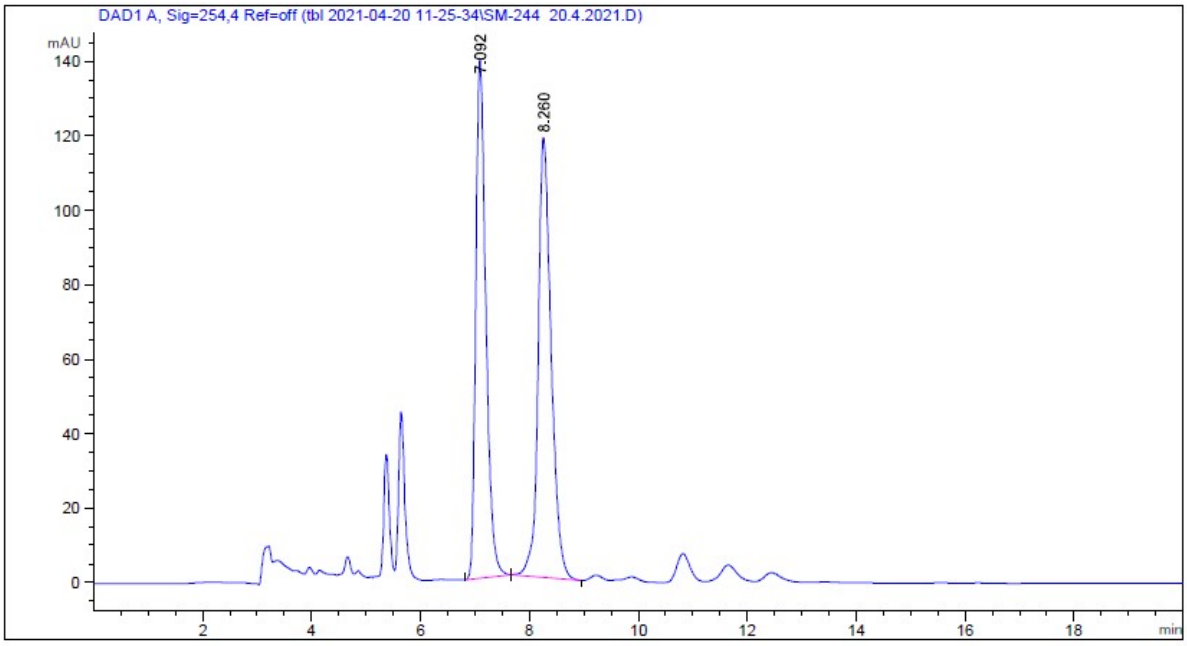


**$^{13}$C-NMR spectrum of compound 14 (100 MHz, $CDCl_3$):**




**Chiral HPLC:** Enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK@OJ-H (250×4.6mm, 5µm), hexanes/*i*-PrOH = 60/40, 1.0 mL/min, 254 nm), $t_{major}$ = 8.3 min, $t_{minor}$ =7.2 min; ee = 97%.

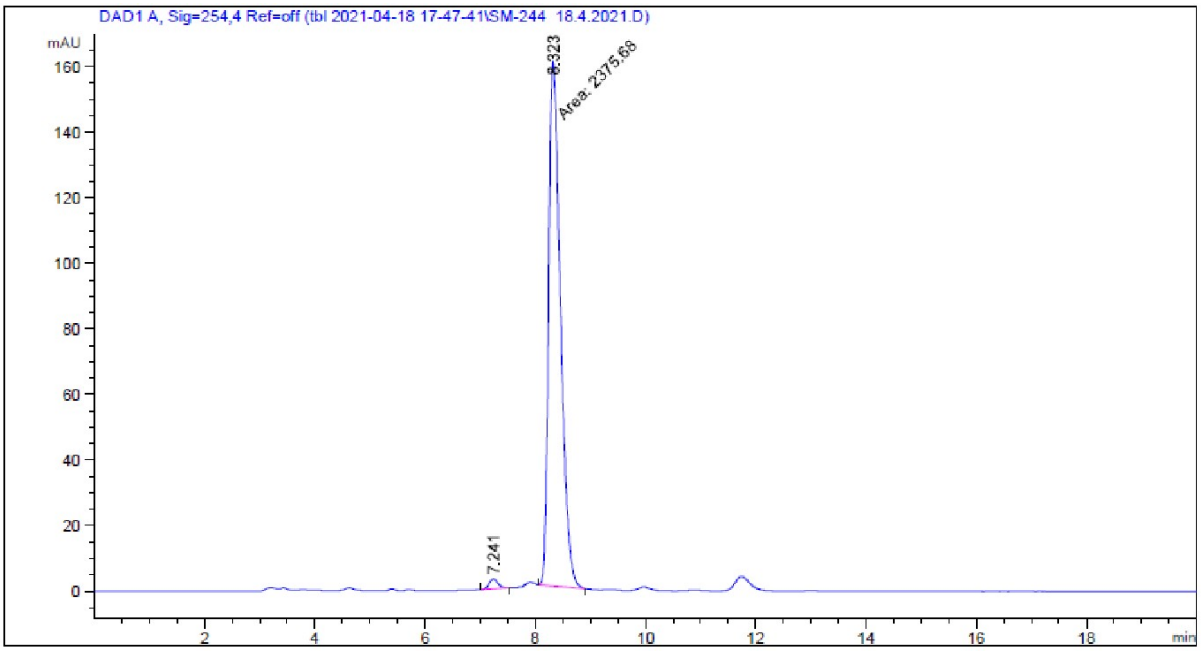
HPLC chromatogram of racemic compound **14:**



Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.092 | BB | 0.1960 | 1791.54810 | 139.34712 | 47.8075 |
| 2 | 8.260 | BB | 0.2490 | 1955.86951 | 118.23582 | 52.1925 |

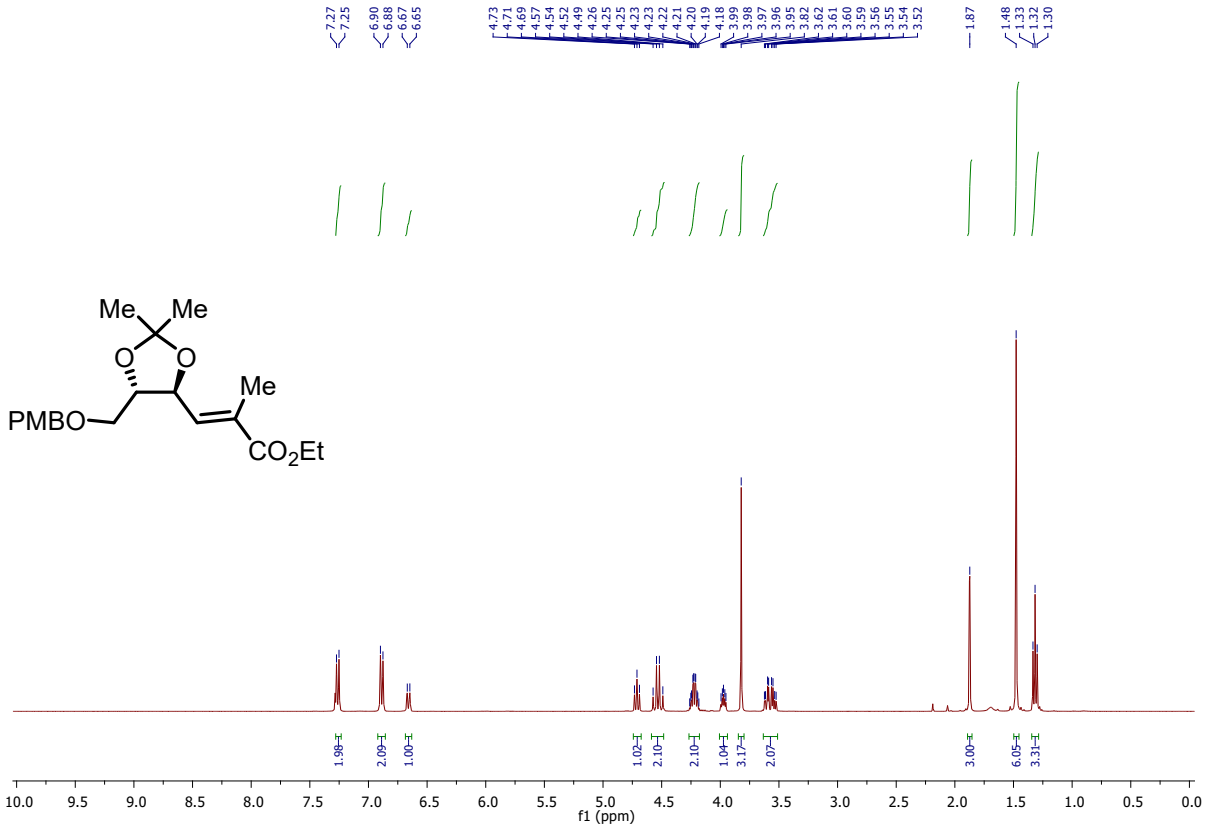
HPLC chromatogram of chiral compound **14:**



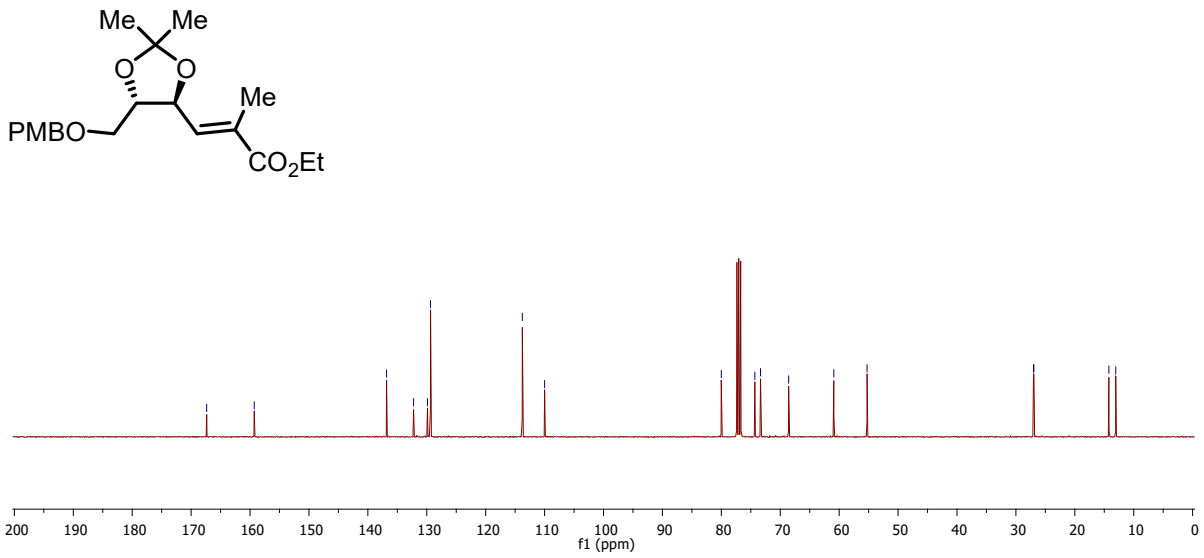

Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.241 | BB | 0.1749 | 34.08890 | 3.03759 | 1.4146 |
| 2 | 8.323 | MM | 0.2471 | 2375.67554 | 160.26422 | 98.5854 |

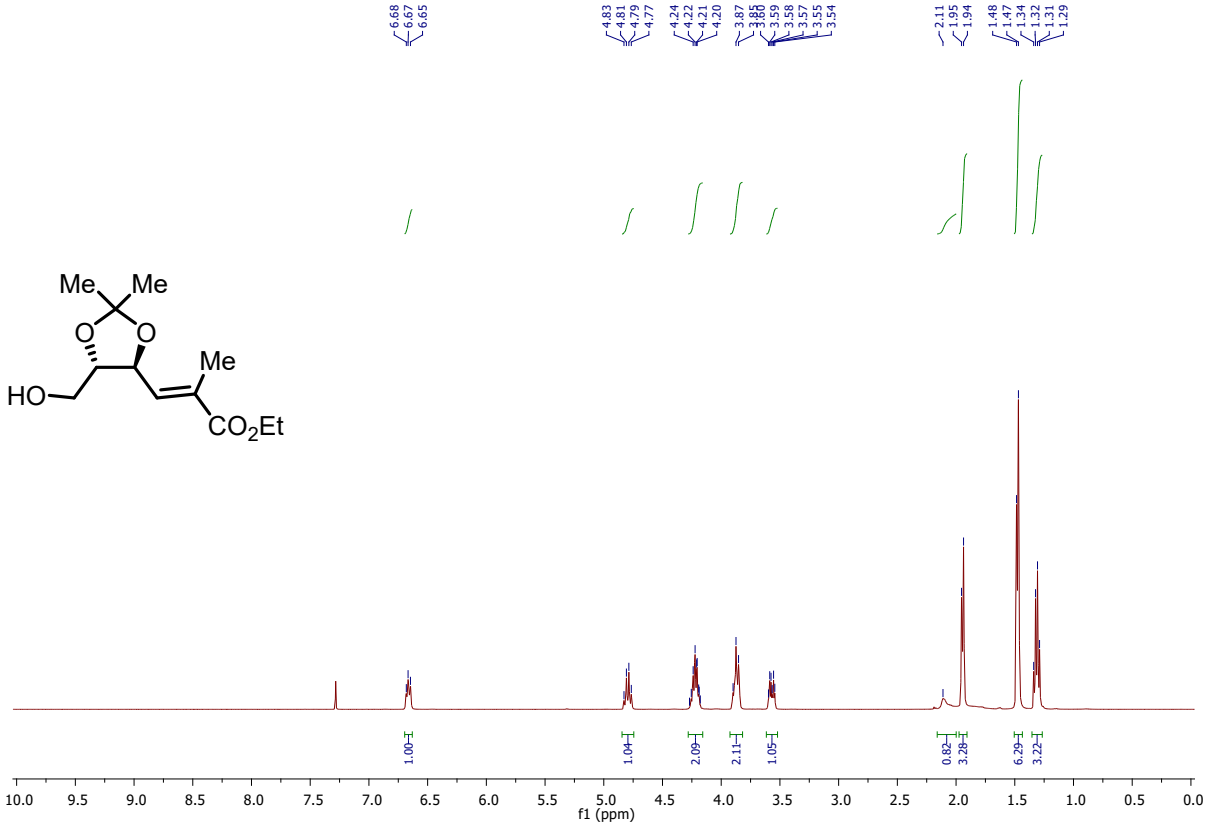
**$^{1}$H-NMR spectrum of compound 8 (400 MHz, $CDCl_3$):**



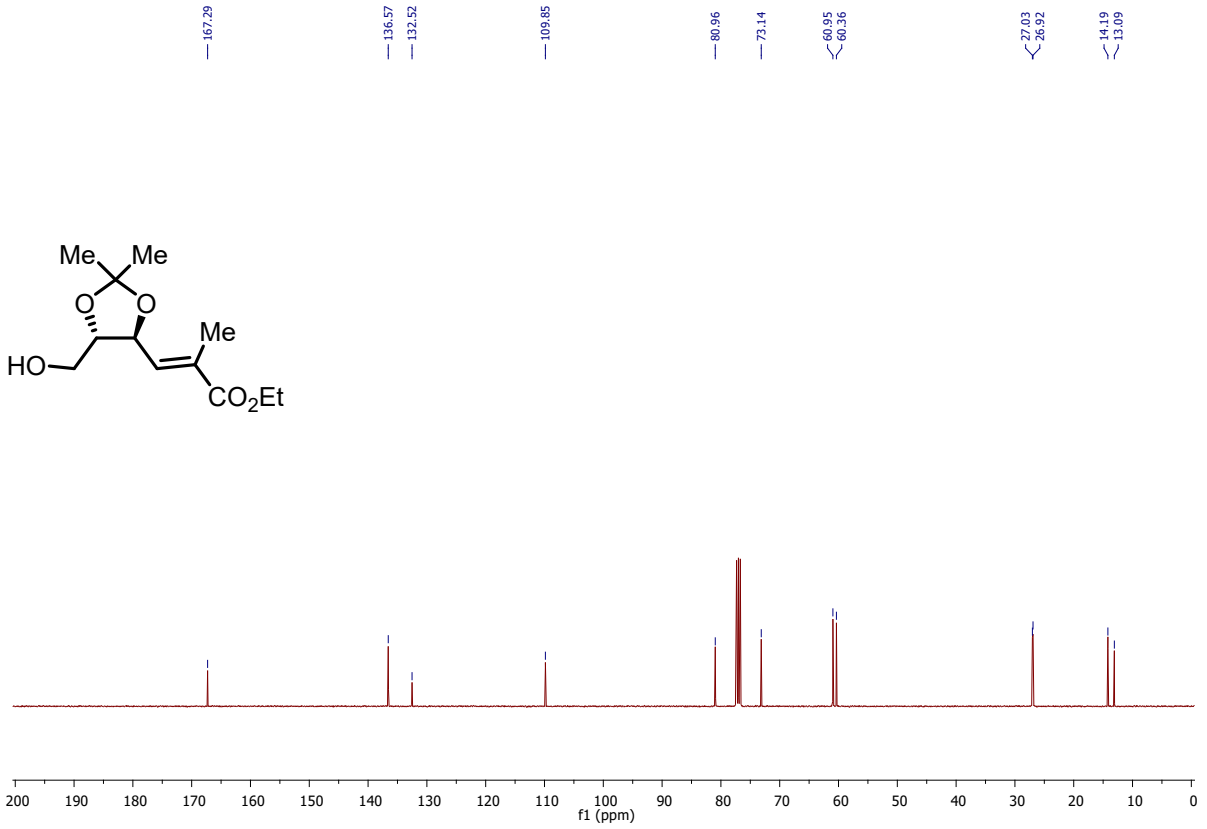

**$^{13}$C-NMR spectrum of compound 8 (100 MHz, $CDCl_3$):**



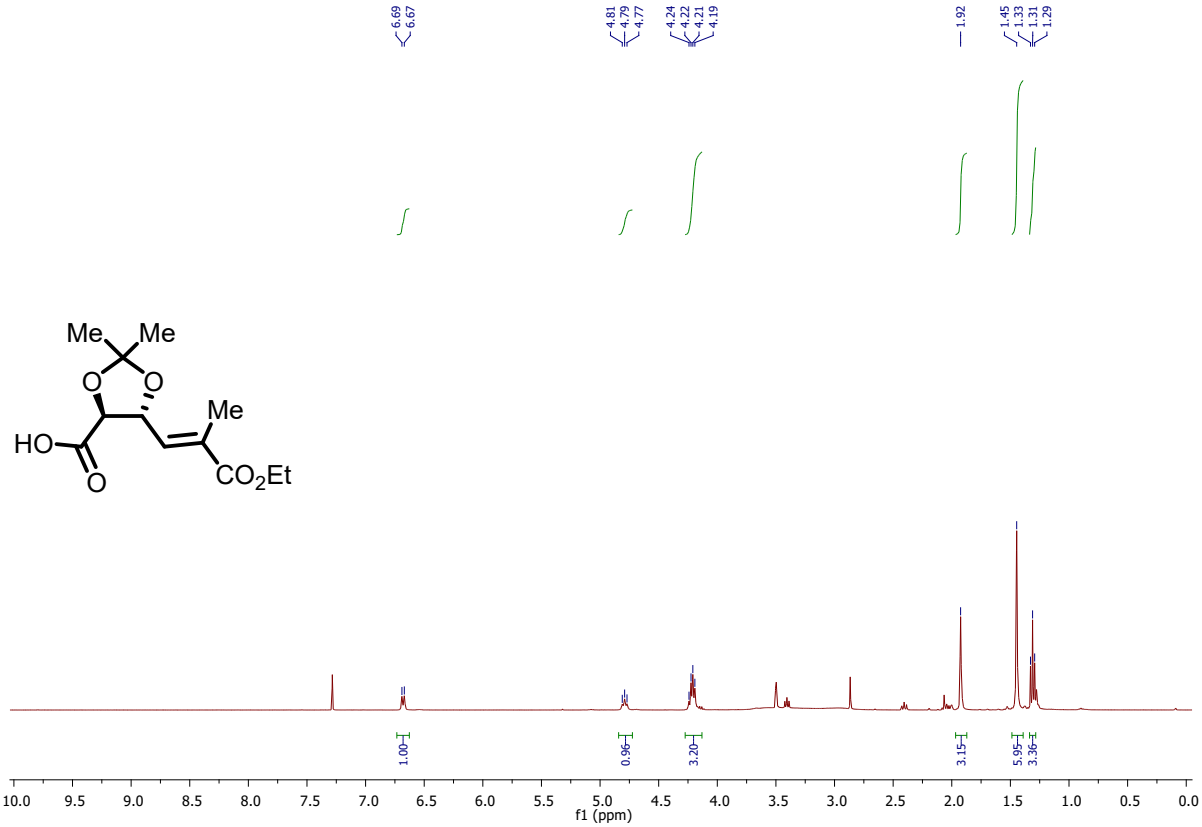
**$^{1}$H-NMR spectrum of compound 15 (400 MHz, $CDCl_3$):**



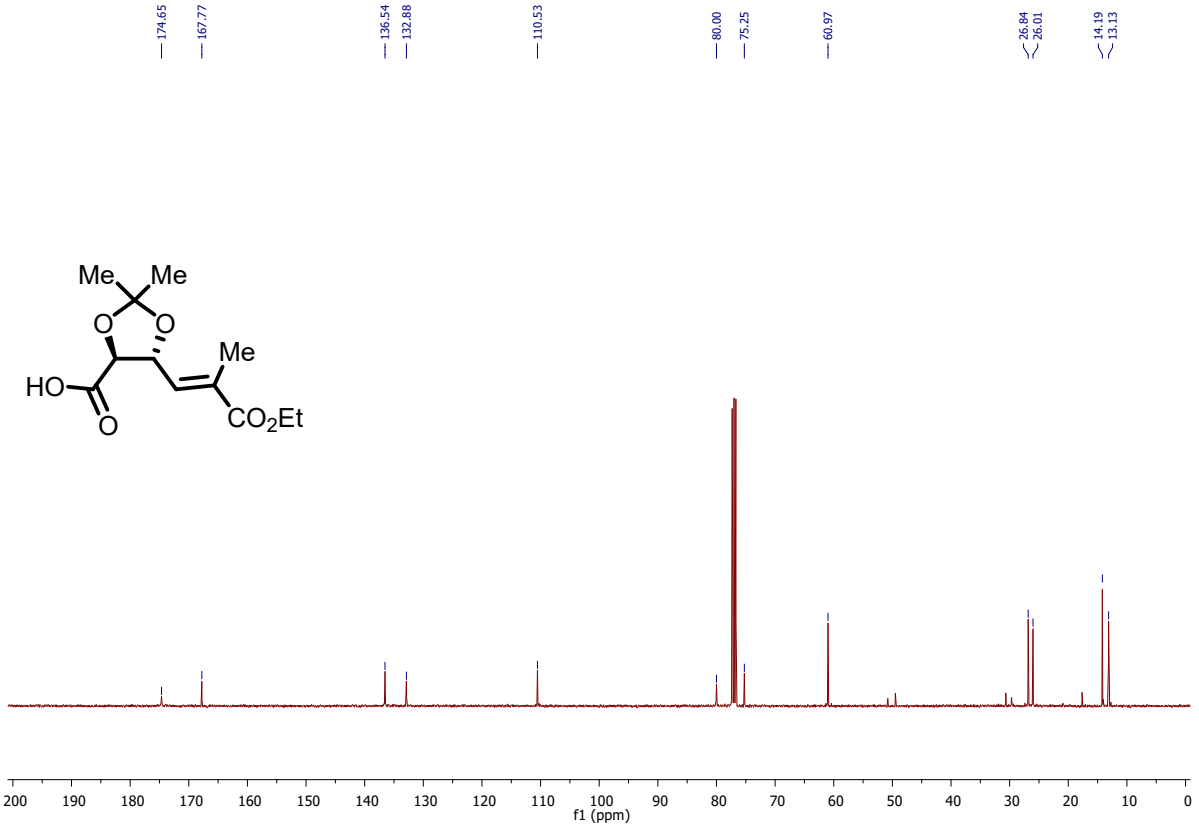

**$^{13}$C-NMR spectrum of compound 15 (100 MHz, $CDCl_3$):**



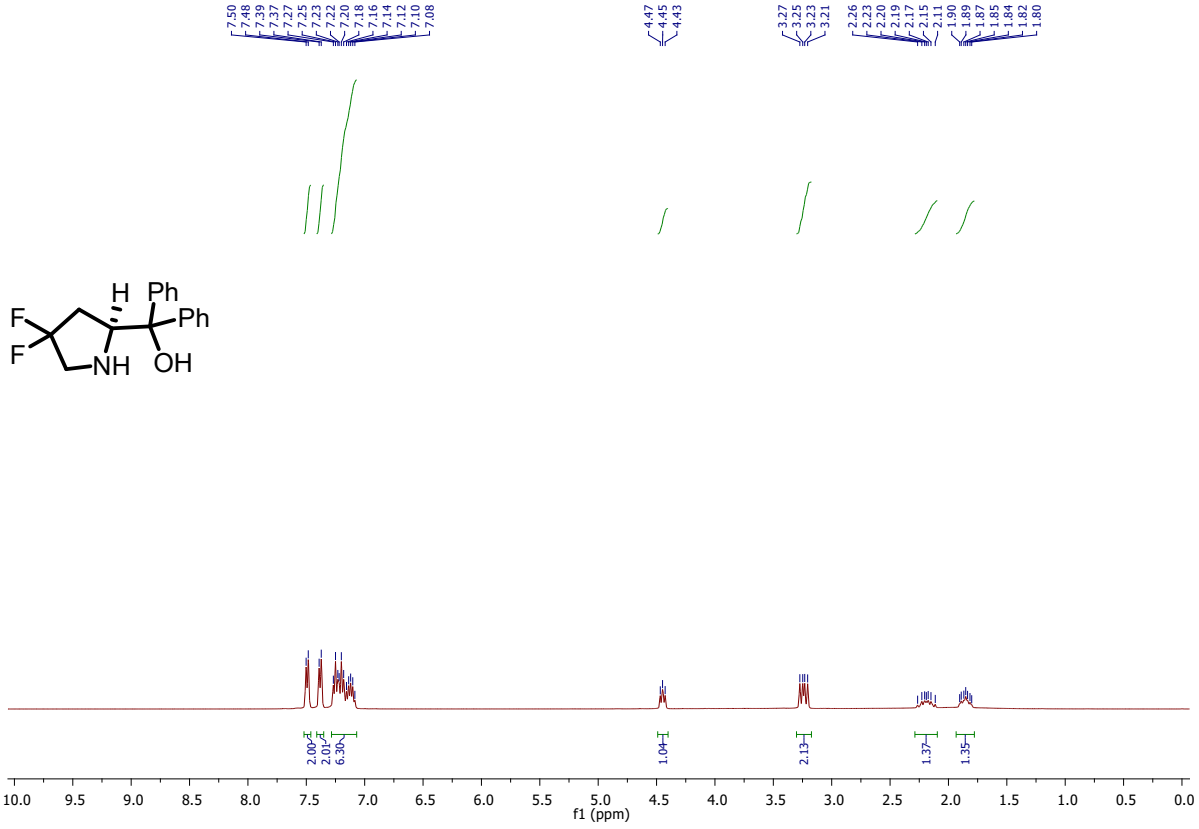

**$^{1}$H-NMR spectrum of compound 5 (400 MHz, $CDCl_3$):**



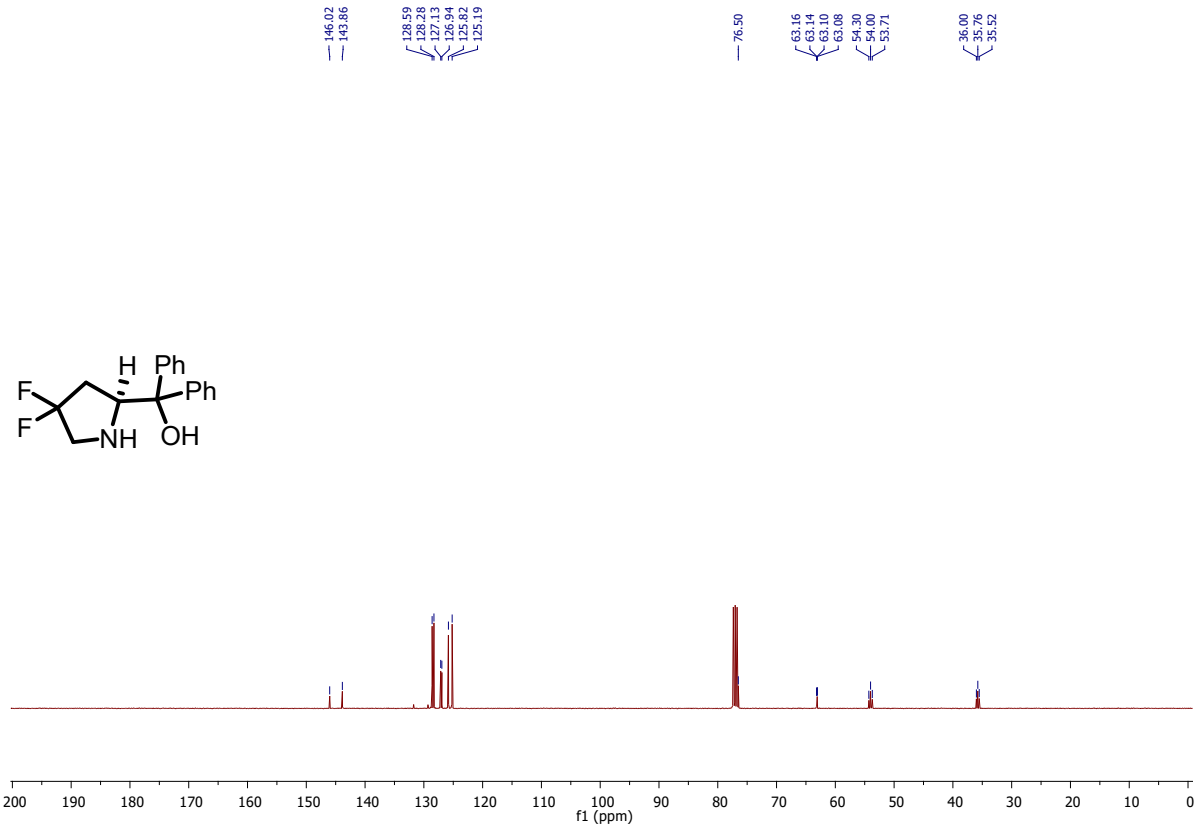

**$^{13}$C-NMR spectrum of compound 5 (100 MHz, $CDCl_3$):**



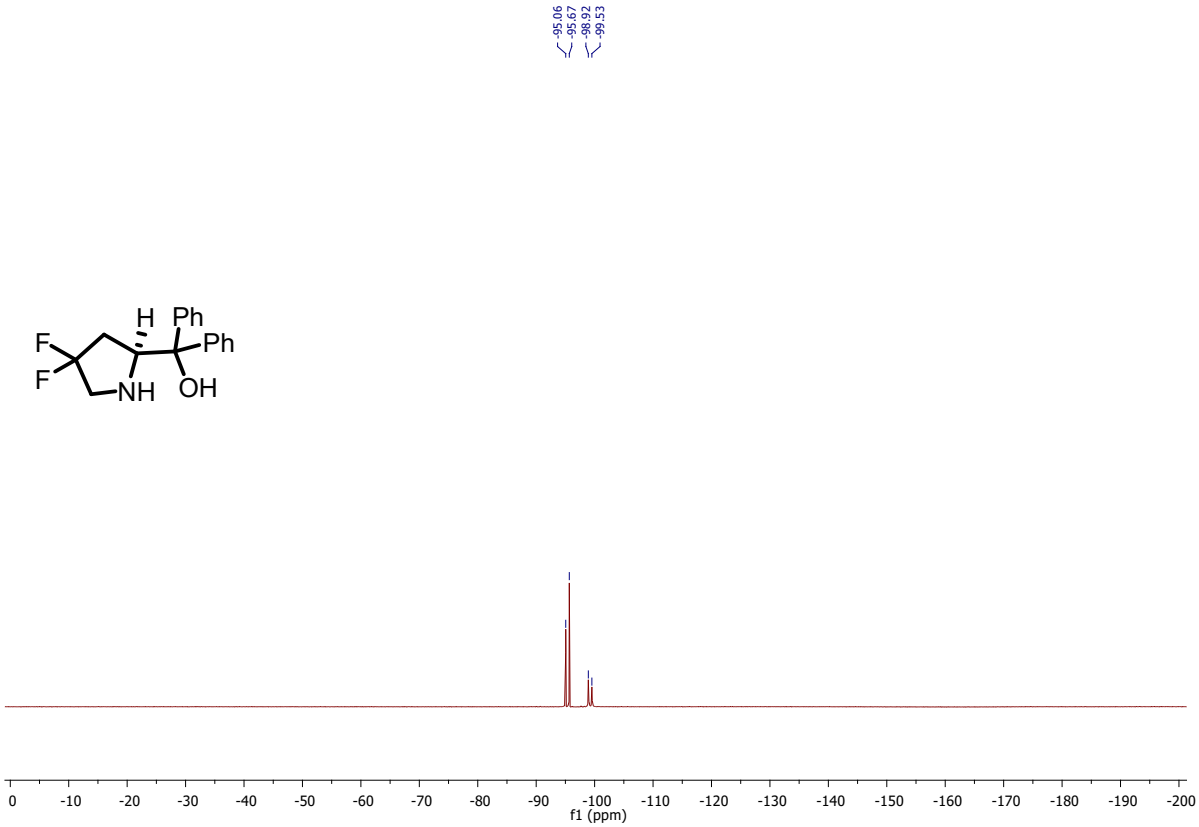
**$^{1}$H-NMR spectrum of compound S3 (400 MHz, $CDCl_3$):**



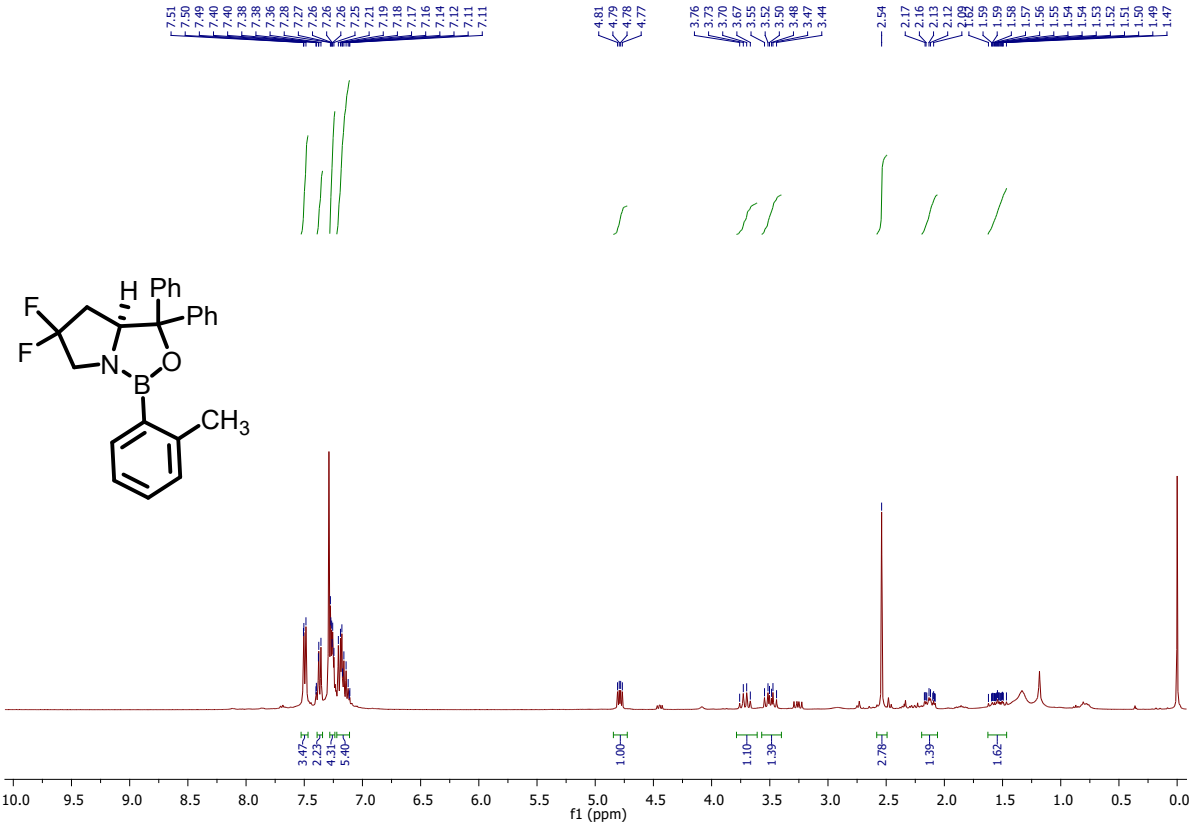

**$^{13}$C-NMR spectrum of compound S3 (100 MHz, $CDCl_3$):**



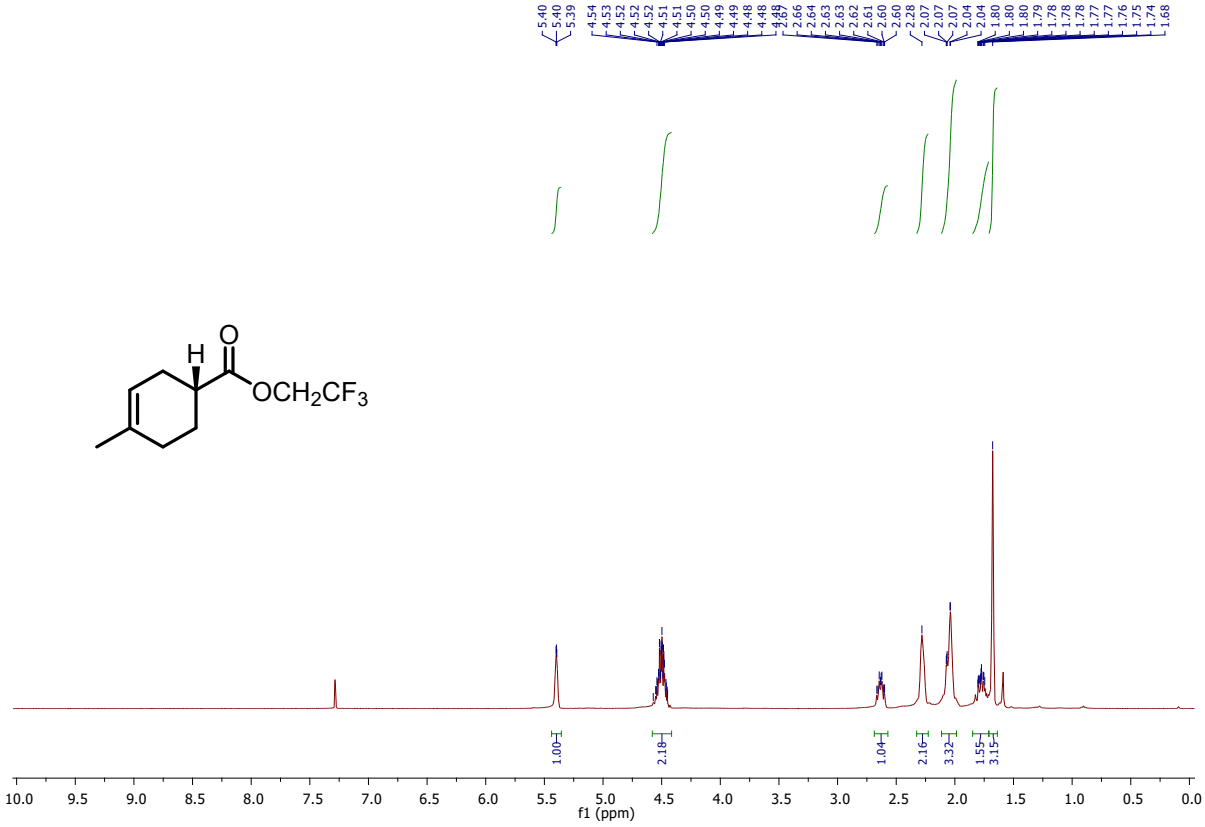
**$^{19}$F-NMR spectrum of compound S3 (400 MHz, $CDCl_3$):**



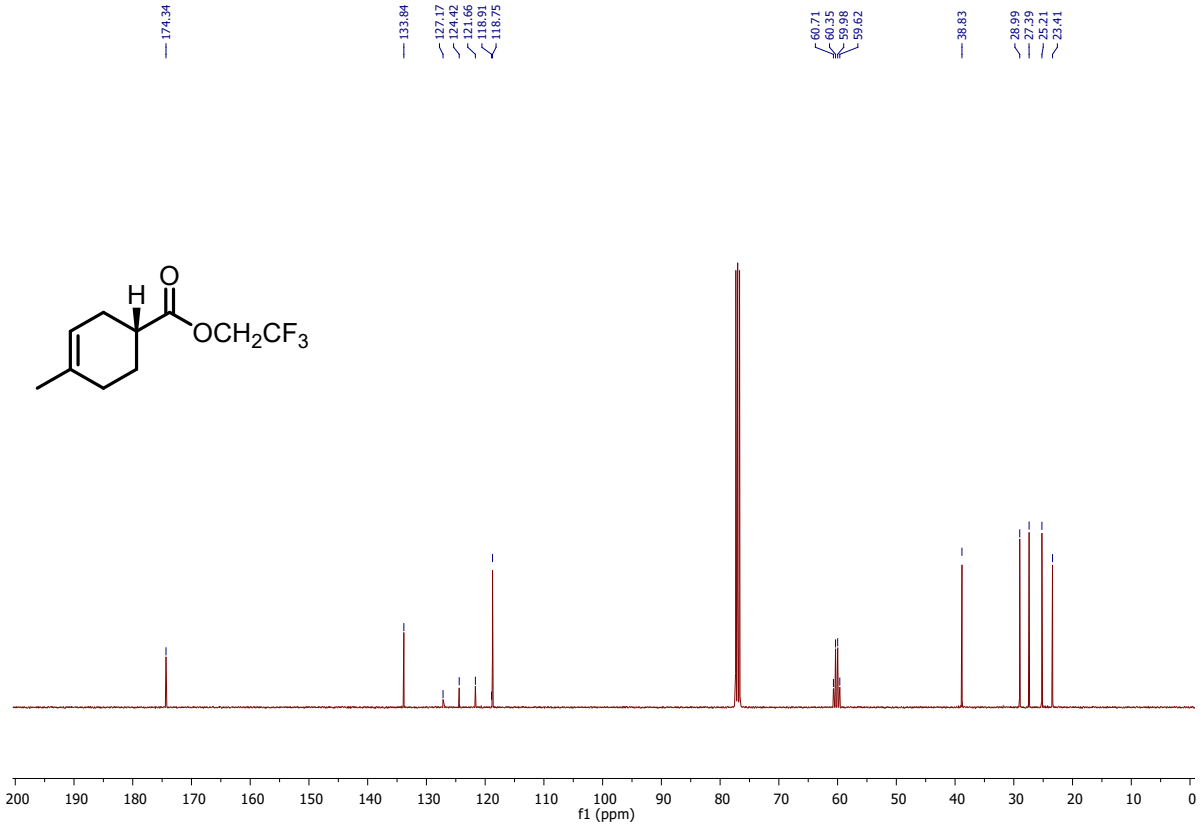

**$^{1}$H-NMR spectrum of compound F2/F0 (400 MHz, $CDCl_3$):**



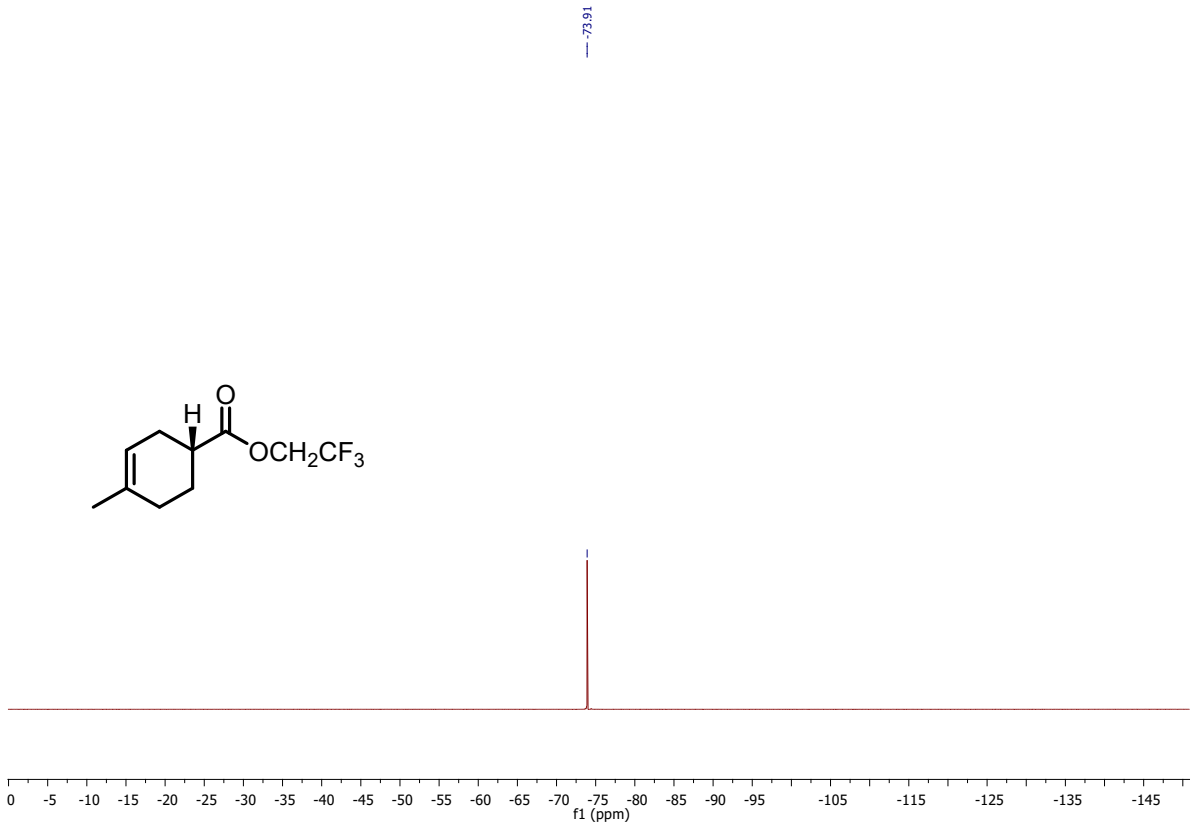
**$^{1}$H-NMR spectrum of compound 12 (400 MHz, $CDCl_3$):**



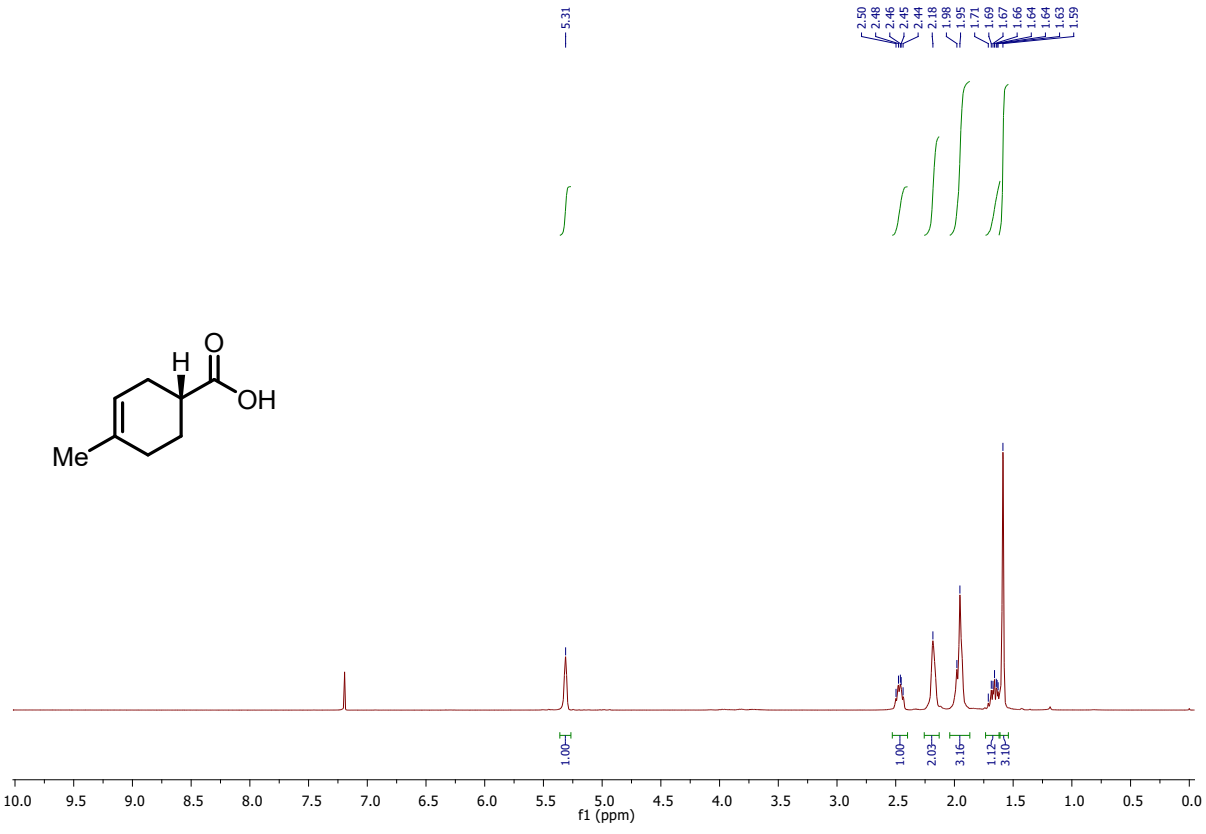

**$^{13}$C-NMR spectrum of compound 12 (100 MHz, $CDCl_3$):**



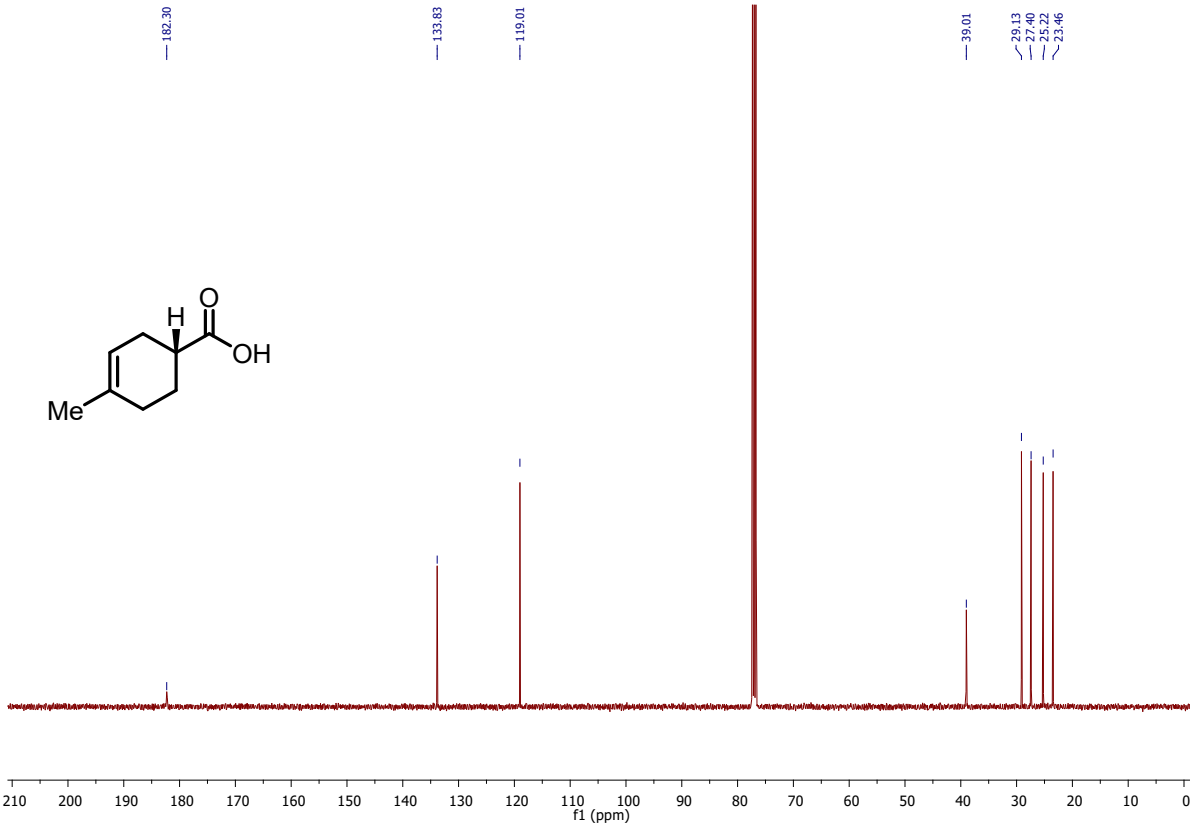

**$^{19}$F-NMR spectrum of compound 12 (400 MHz, $CDCl_3$):**



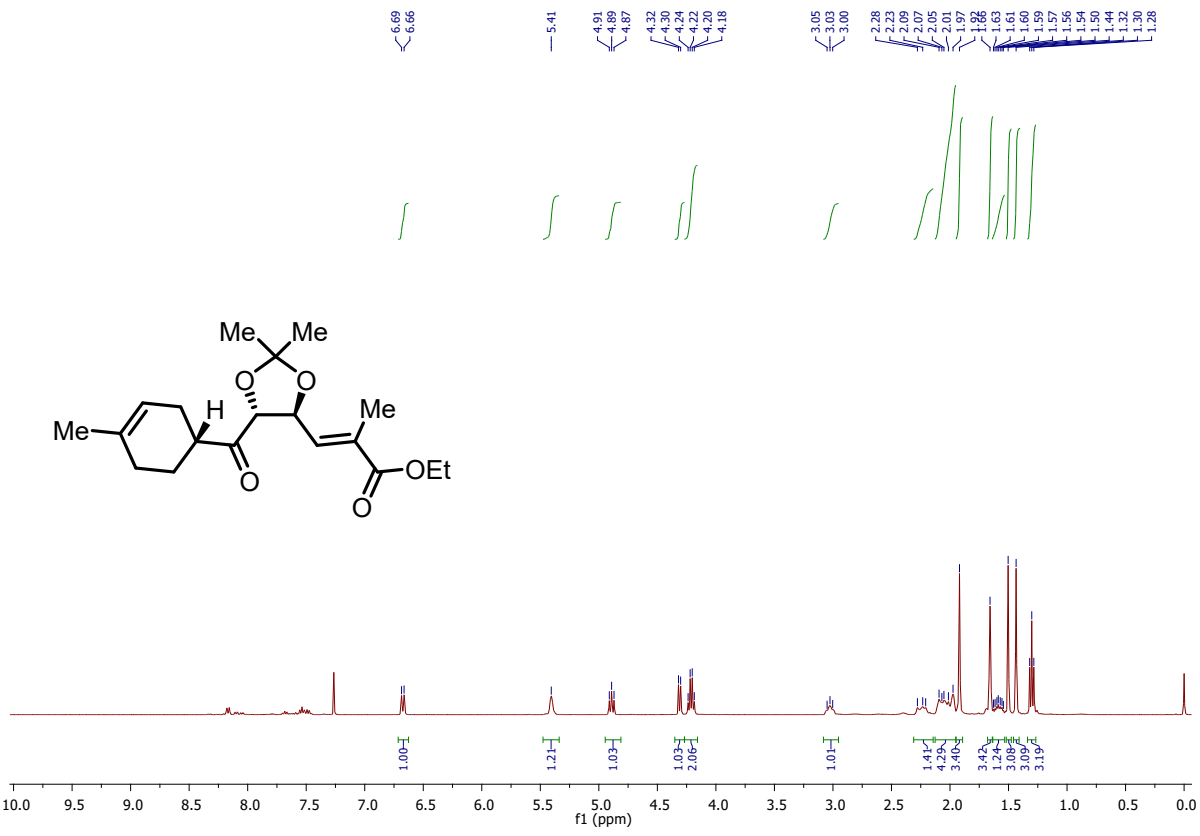

**$^{1}$H-NMR spectrum of compound 4 (400 MHz, $CDCl_3$):**



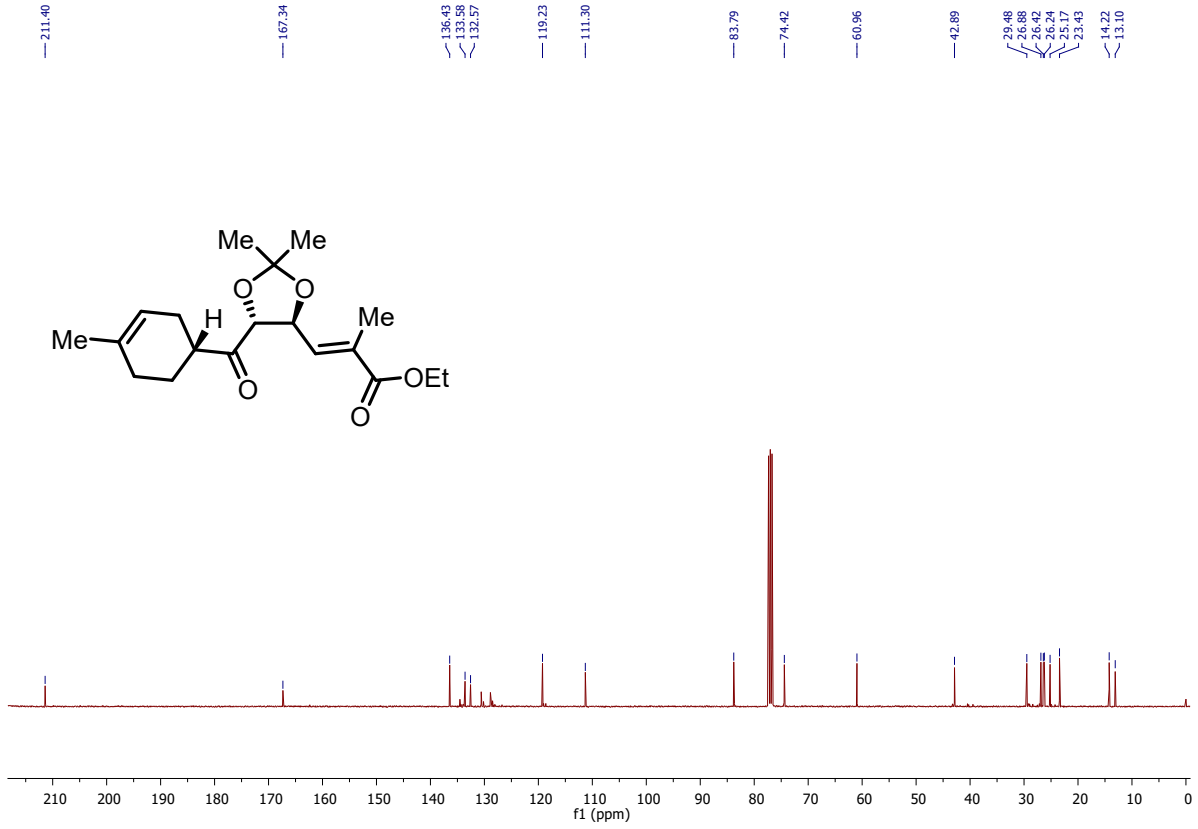
**$^{13}$C-NMR spectrum of compound 4 (100 MHz, $CDCl_3$):**



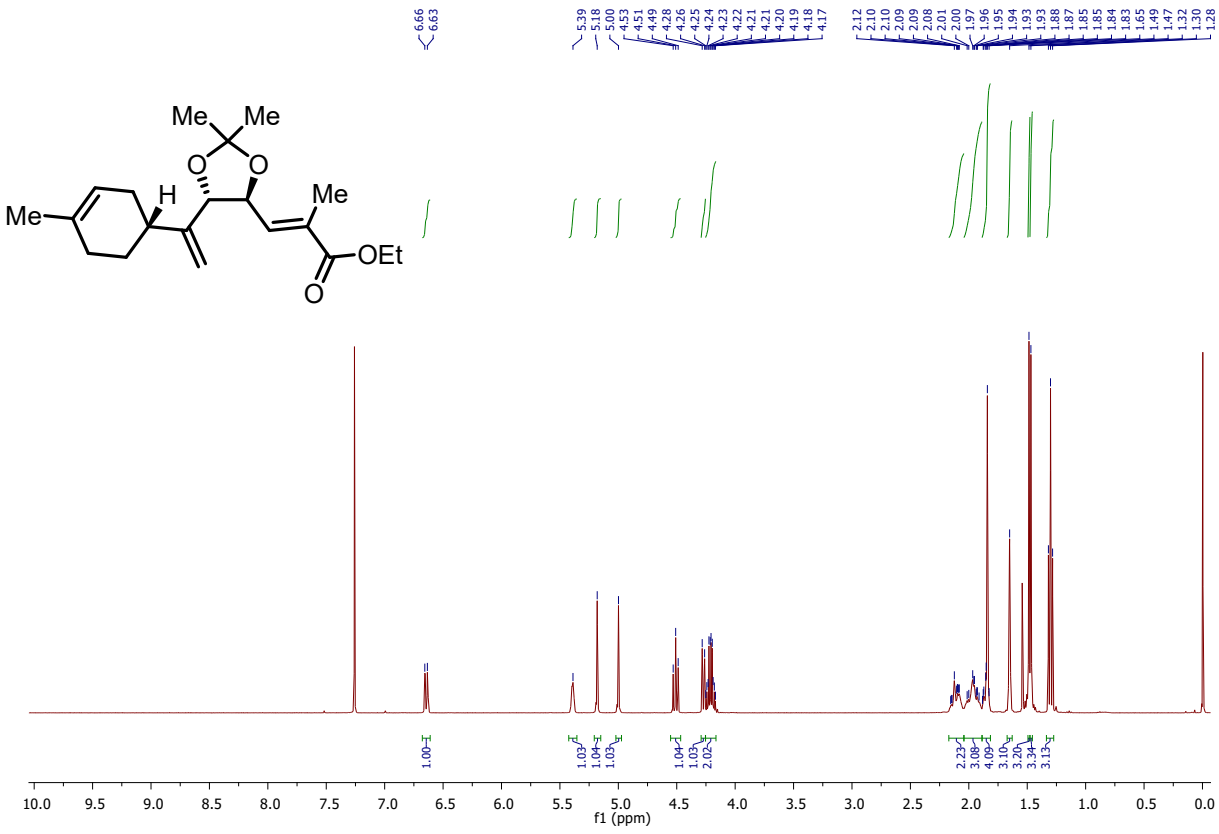

**$^{1}$H-NMR spectrum of compound 16 (400 MHz, $CDCl_3$):**



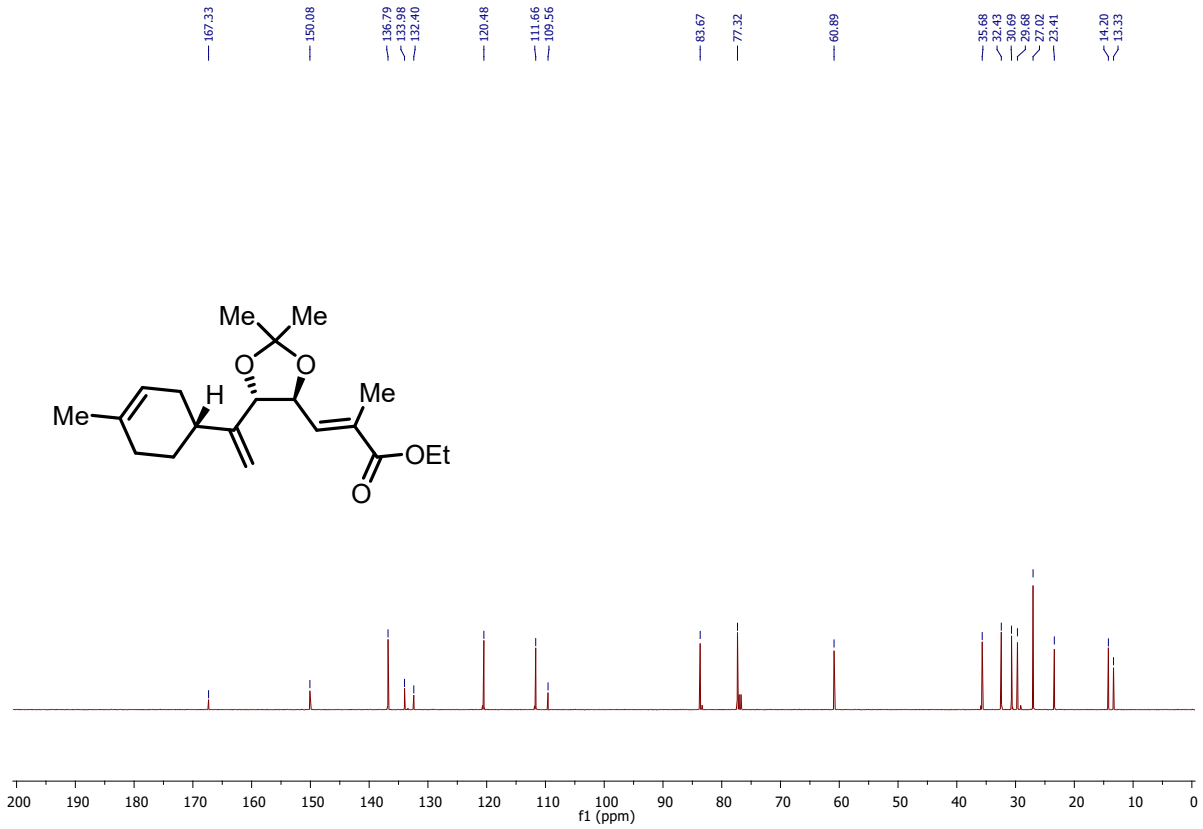
**$^{13}$C-NMR spectrum of compound 16 (100 MHz, $CDCl_3$):**



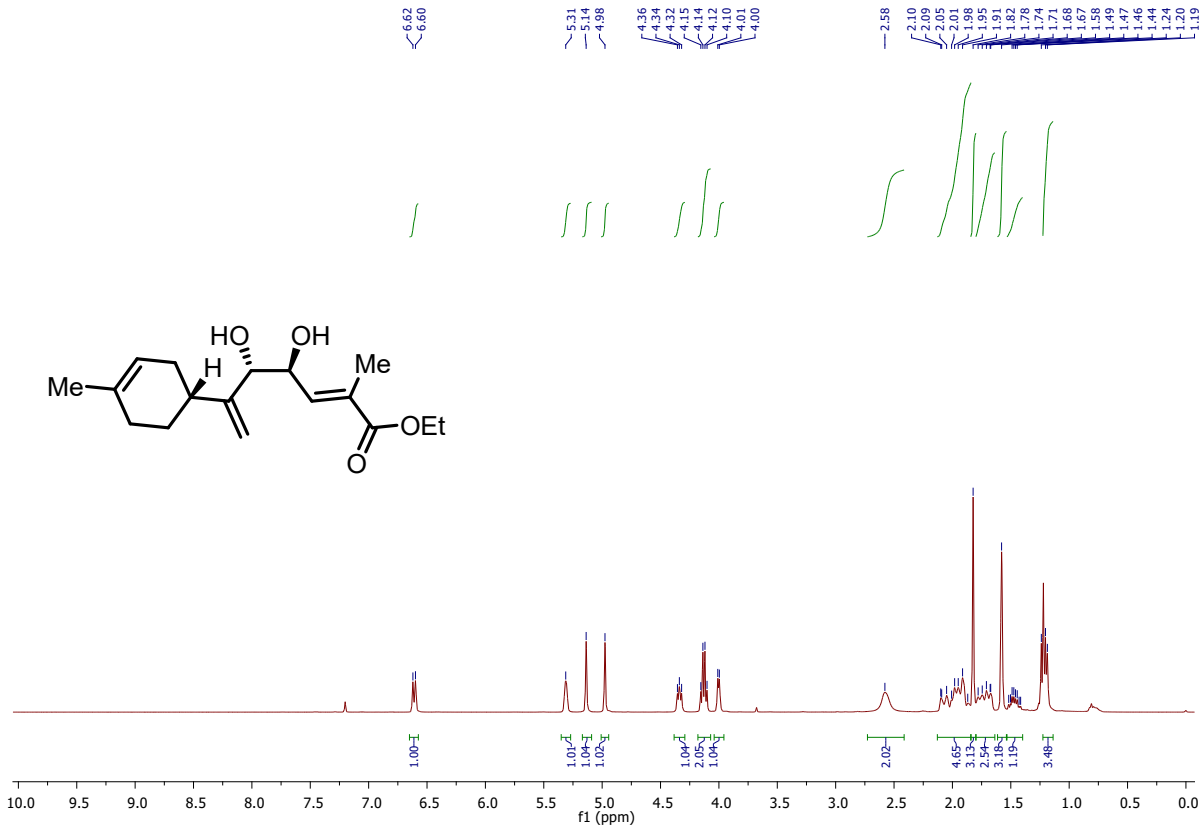

**$^{1}$H-NMR spectrum of compound 17 (400 MHz, $CDCl_3$):**



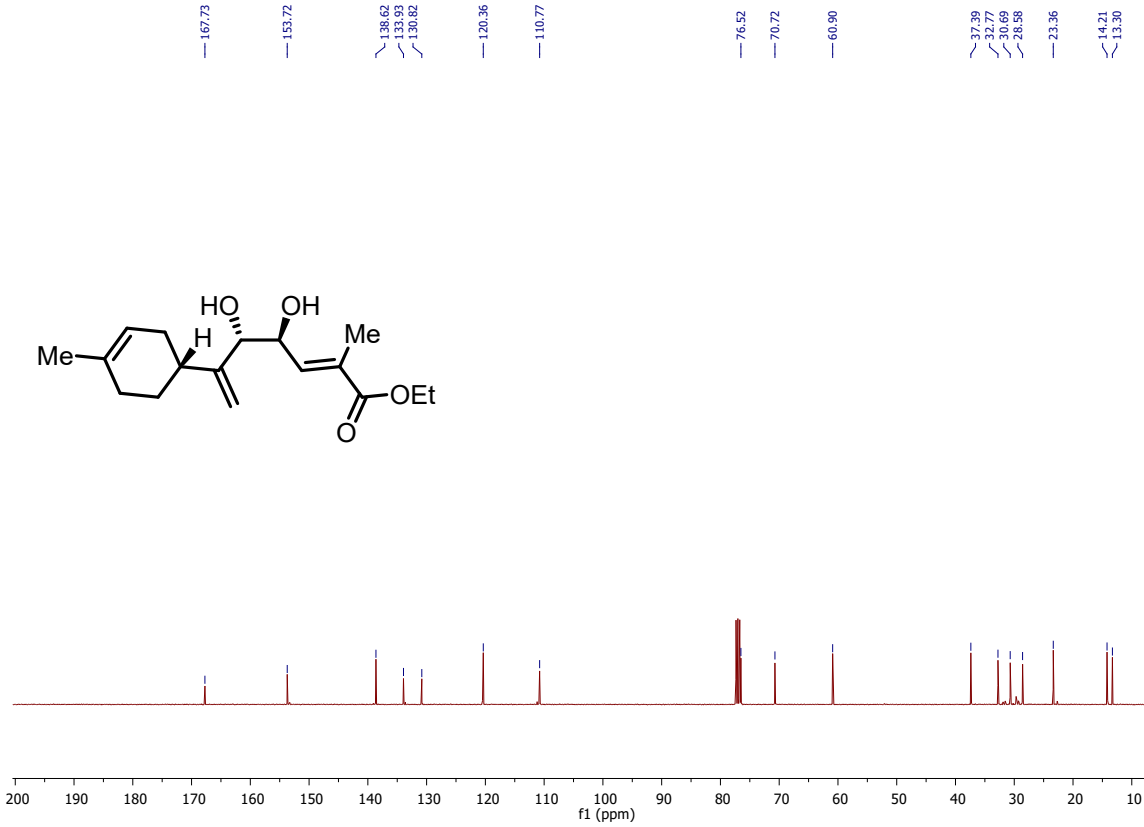
**$^{13}$C-NMR spectrum of compound 17 (100 MHz, $CDCl_3$):**



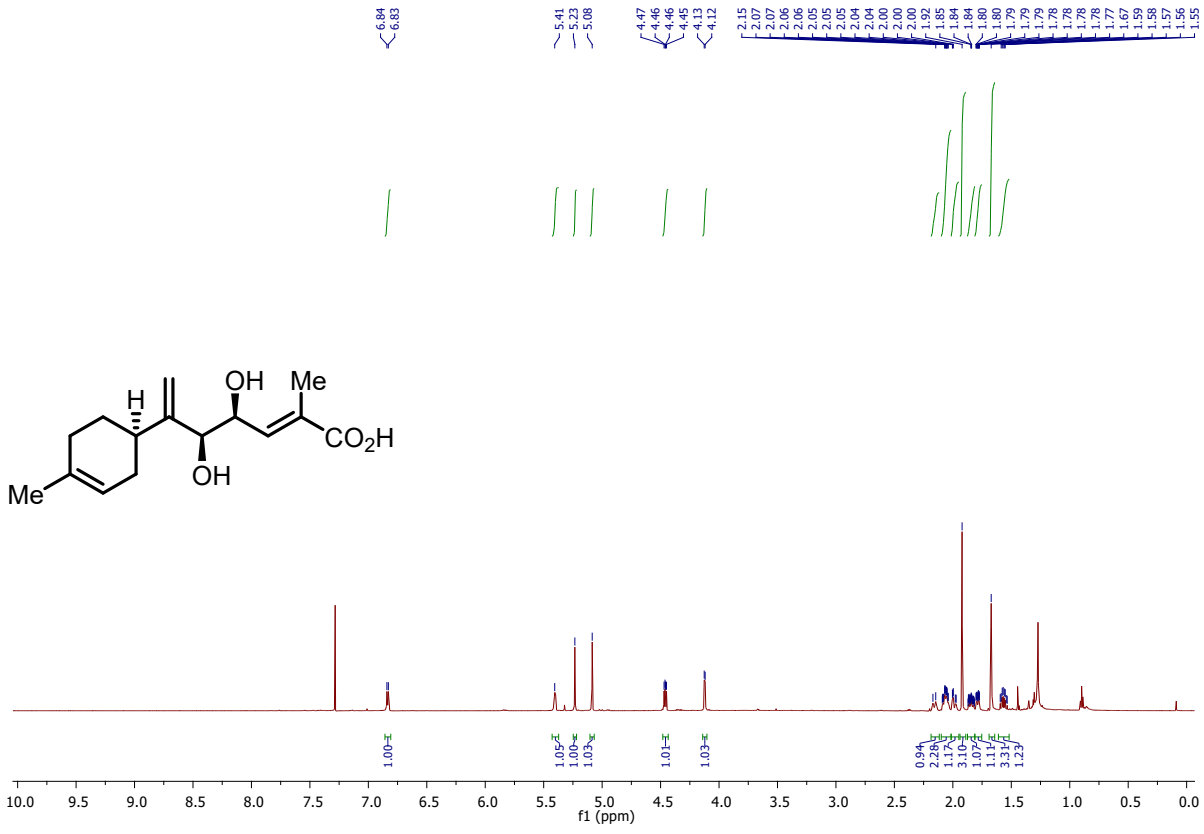

**$^{1}$H-NMR spectrum of compound 18 (400 MHz, $CDCl_3$):**



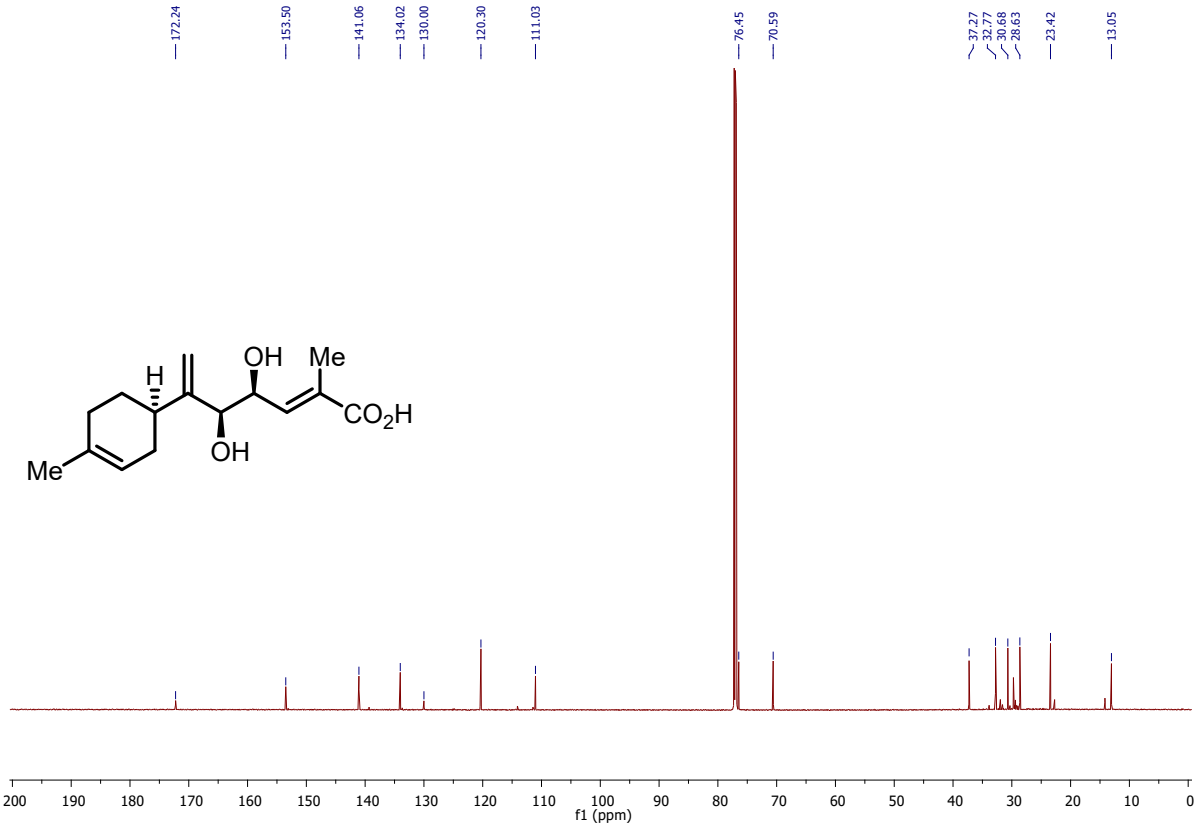
**$^{13}$C-NMR spectrum of compound 18 (100 MHz, $CDCl_3$):**



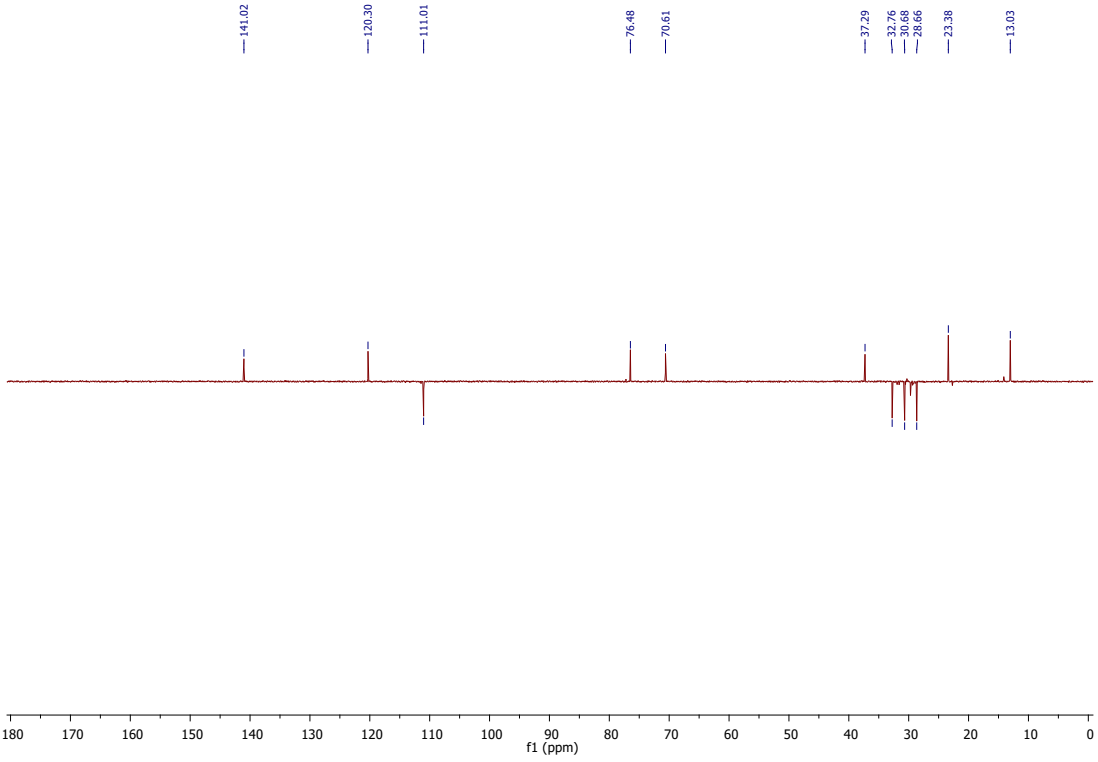

**$^{1}$H-NMR spectrum of compound 1 (700 MHz, $CDCl_3$):**



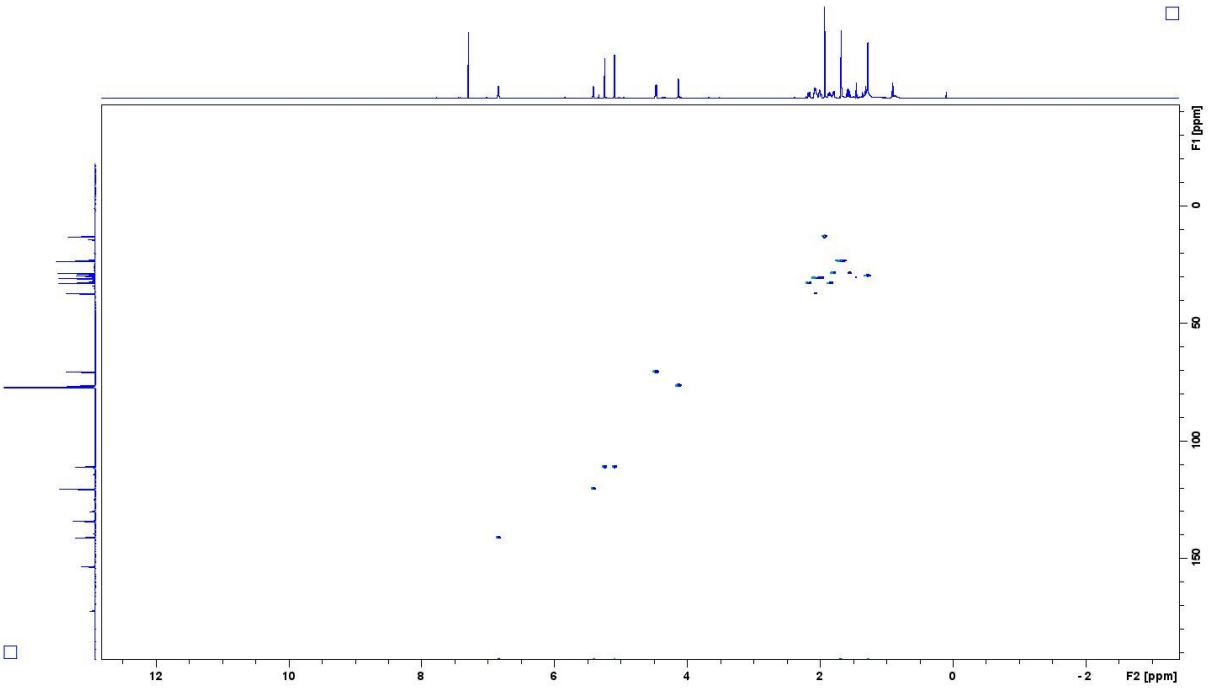
**$^{13}$C-NMR spectrum of compound 1 (175 MHz, $CDCl_3$):**



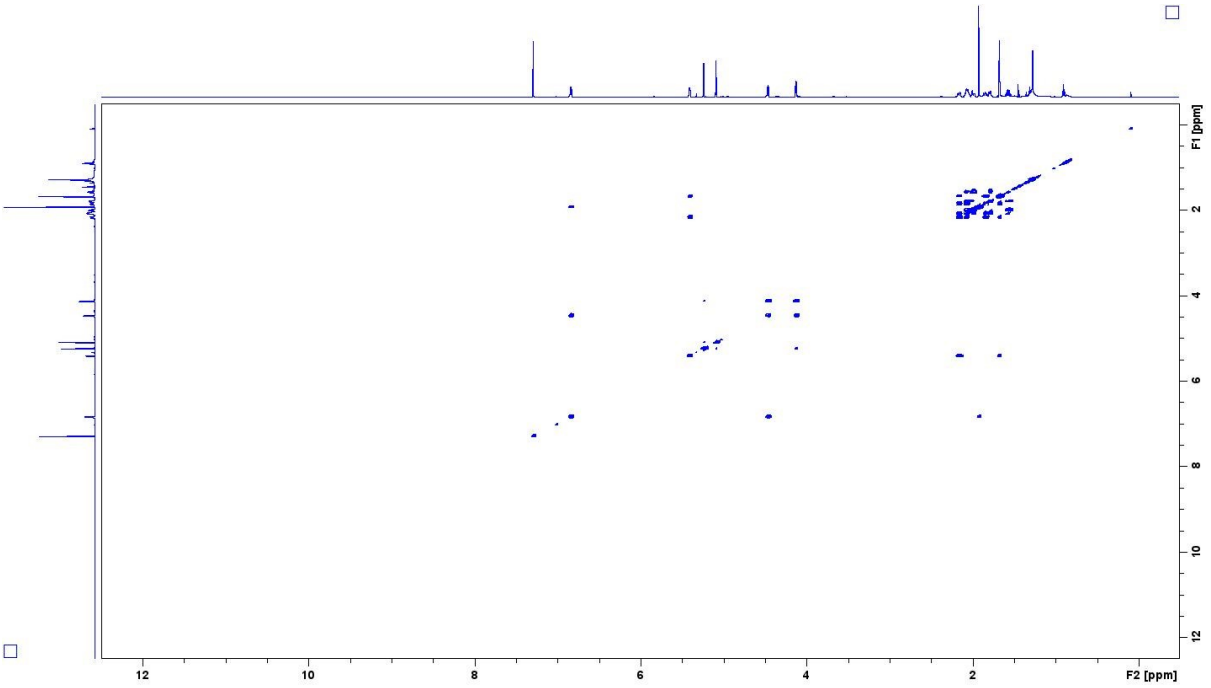

**DEPT-135 NMR spectrum of Compound 1 (100 MHz in $CDCl_3$)**



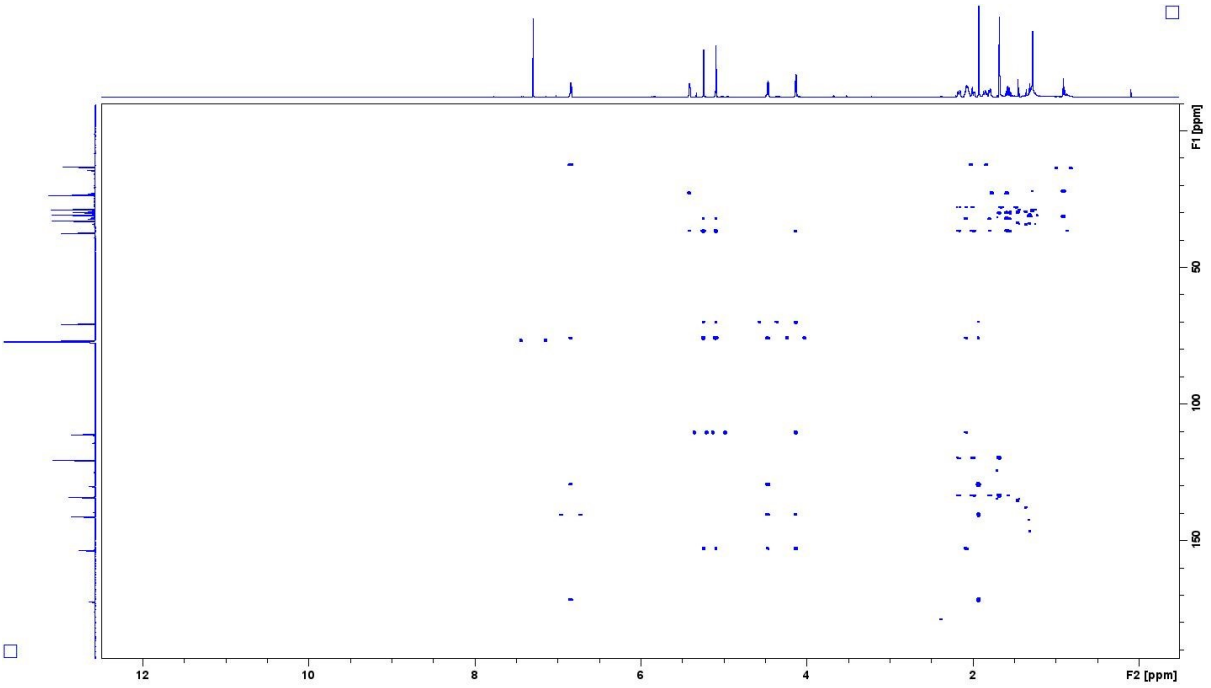
**$^{1}H$, $^{13}C$ HSQC NMR spectrum of Compound 1 (700 MHz, 175 MHz in $CDCl_3$)**



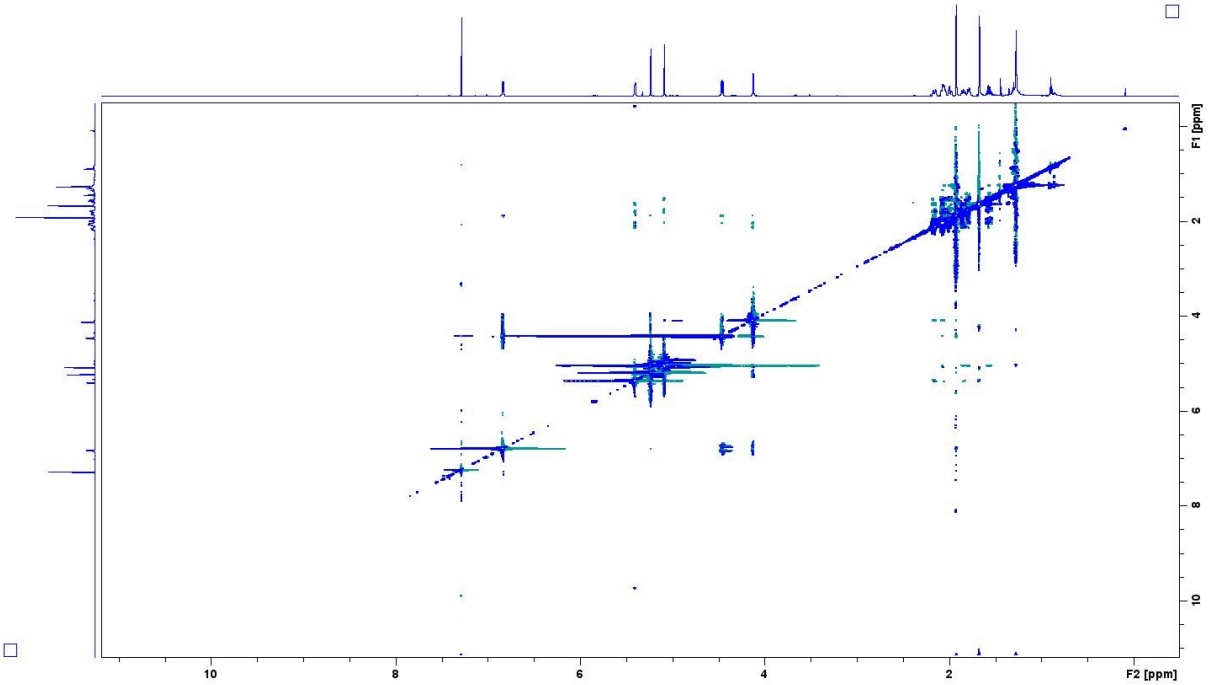

**$^{1}H$, $^{1}H$ COSY NMR spectrum of Compound 1 (700 MHz in $CDCl_3$)**



**$^{1}H$, $^{13}C$ HMBC NMR spectrum of Compound 1 (700 MHz, 175 MHz in $CDCl_3$)**




**$^{1}H$, $^{1}H$ ROESY NMR spectrum of Compound 1 (700 MHz in $CDCl_3$)**



## HRMS (ESI-TOF) Spectra of Compound 1:

**Elemental Composition Report** Page 1

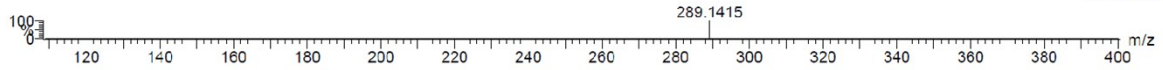
**Single Mass Analysis**
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
38 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 10-23 H: 10-30 O: 3-200 23Na: 0-1

TB
SM-237 11 (0.226) Cm (8:48)

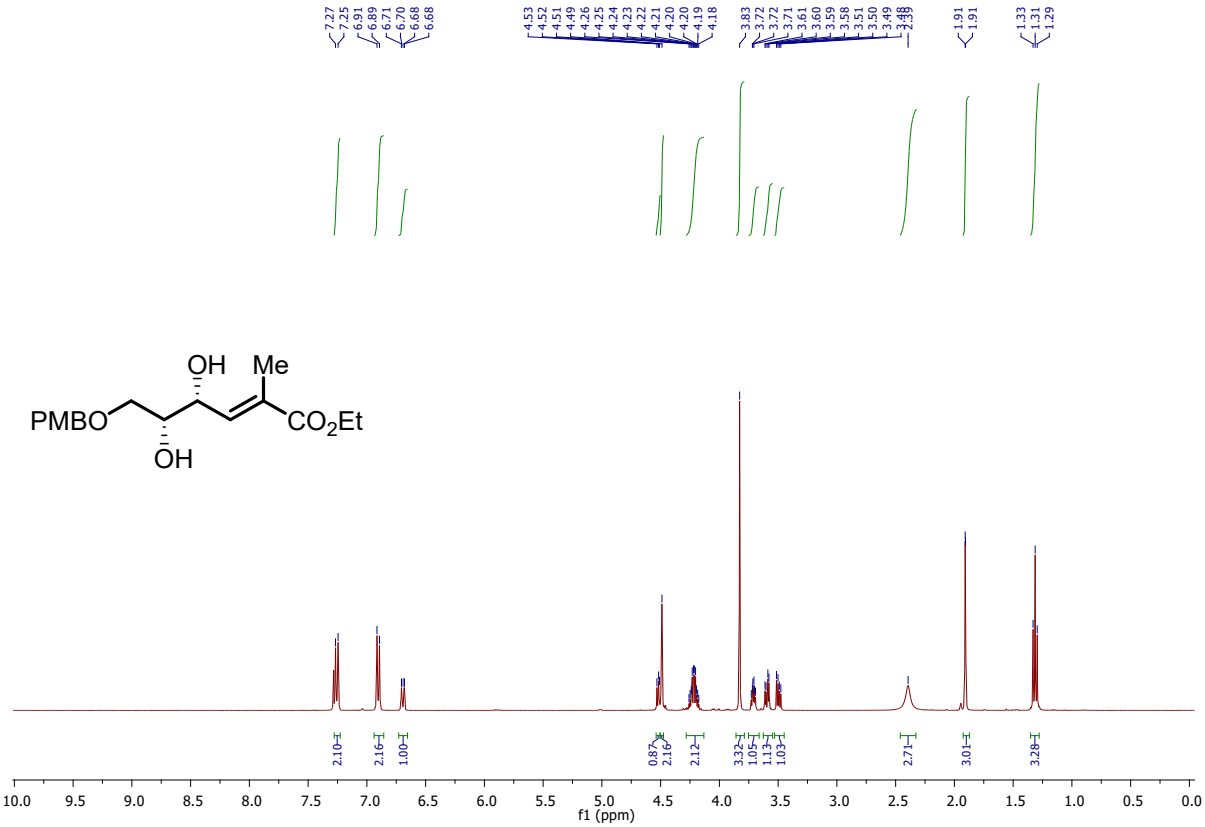
IISER Berhampur

1: TOF MS ES+
6.61e+006

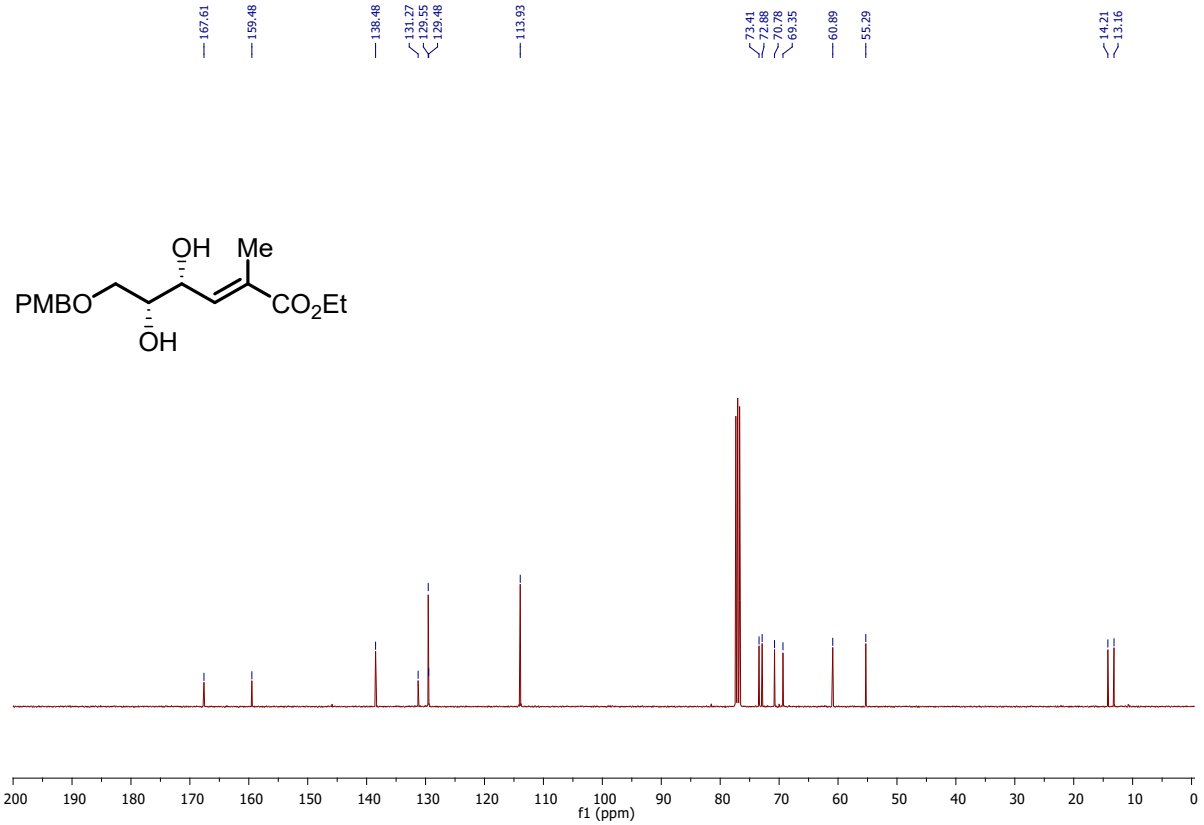



| | | | | | |
|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | |
| Maximum: | | 5.0 | 5.0 | 50.0 | |
| Mass | Calc. Mass | mDa | PPM | DBE | Formula |
| 289.1415 | 289.1416 | -0.1 | -0.3 | 4.5 | C15 H22 O4 23Na |

## $^{1}$H-NMR spectrum of compound 19 (400 MHz, $CDCl_3$):



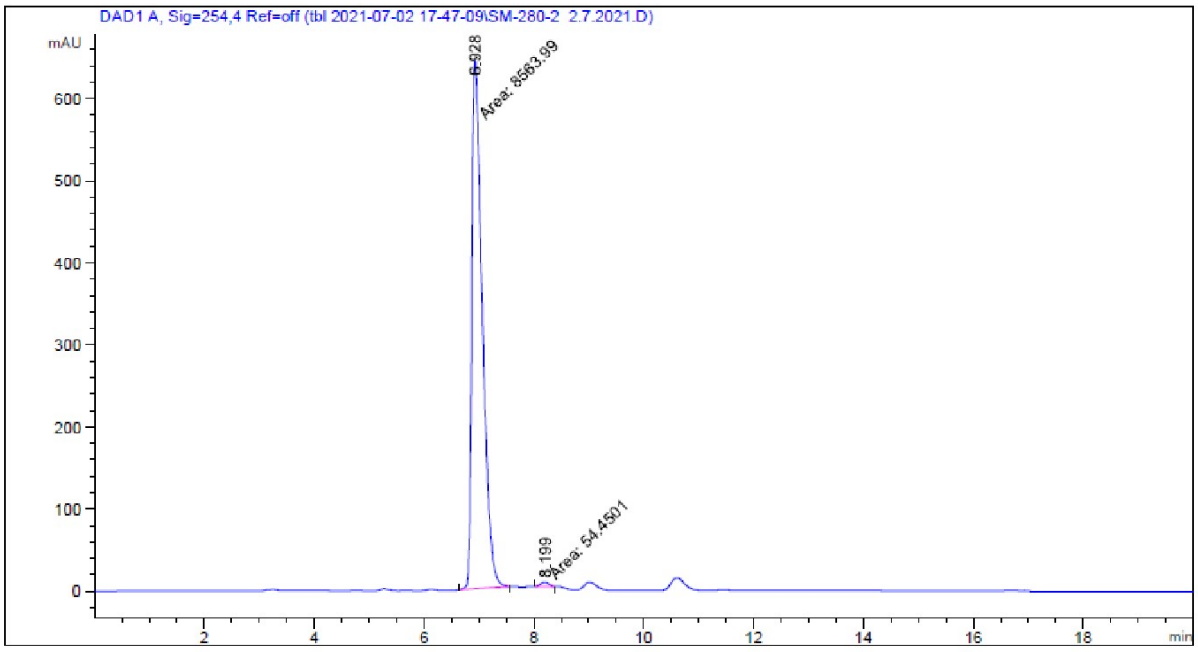
**$^{13}$C-NMR spectrum of compound 19 (100 MHz, $CDCl_3$):**




**Chiral HPLC:** Enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK@OJ-H (250×4.6mm, 5μm), hexanes/*i*-PrOH = 60/40, 1.0 mL/min, 254 nm), $t_{major}$ = 6.9 min, $t_{minor}$ =8.2 min; ee = 98.7%.

HPLC chromatogram of racemic compound **19**:

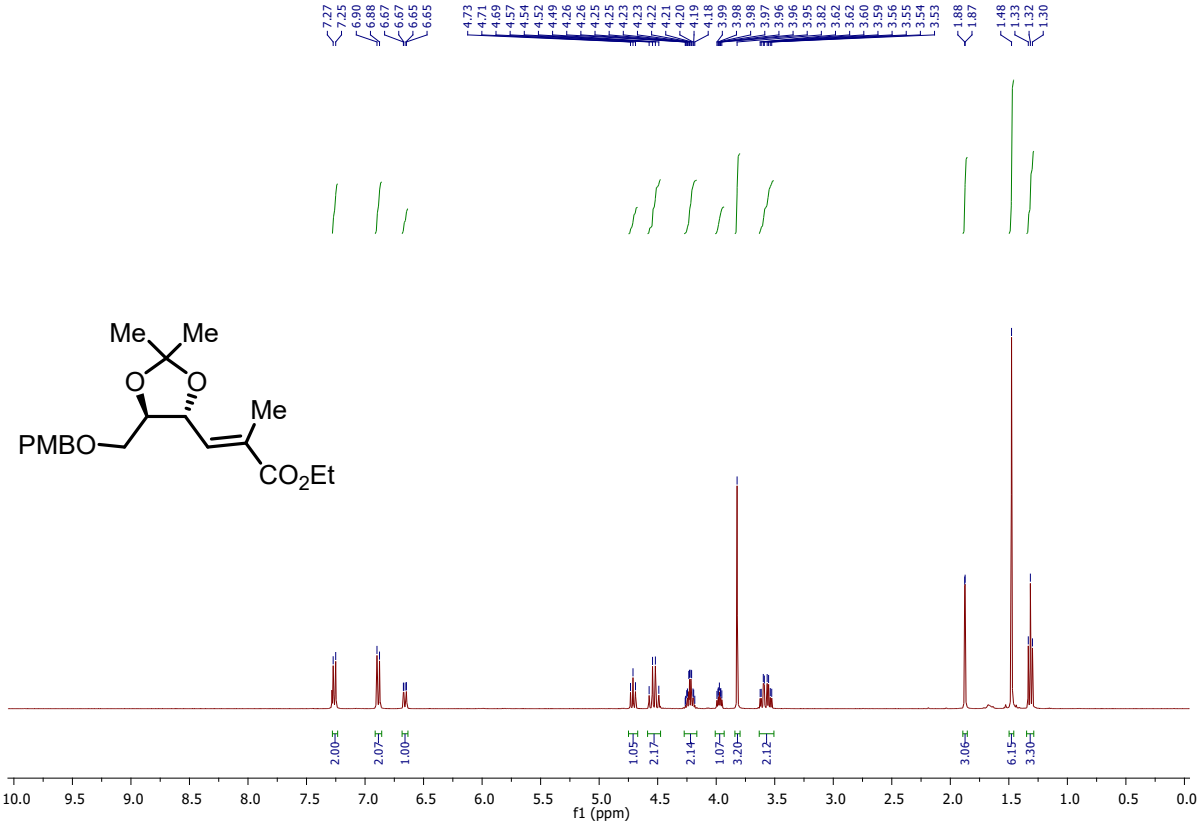
HPLC chromatogram of chiral compound **19**:



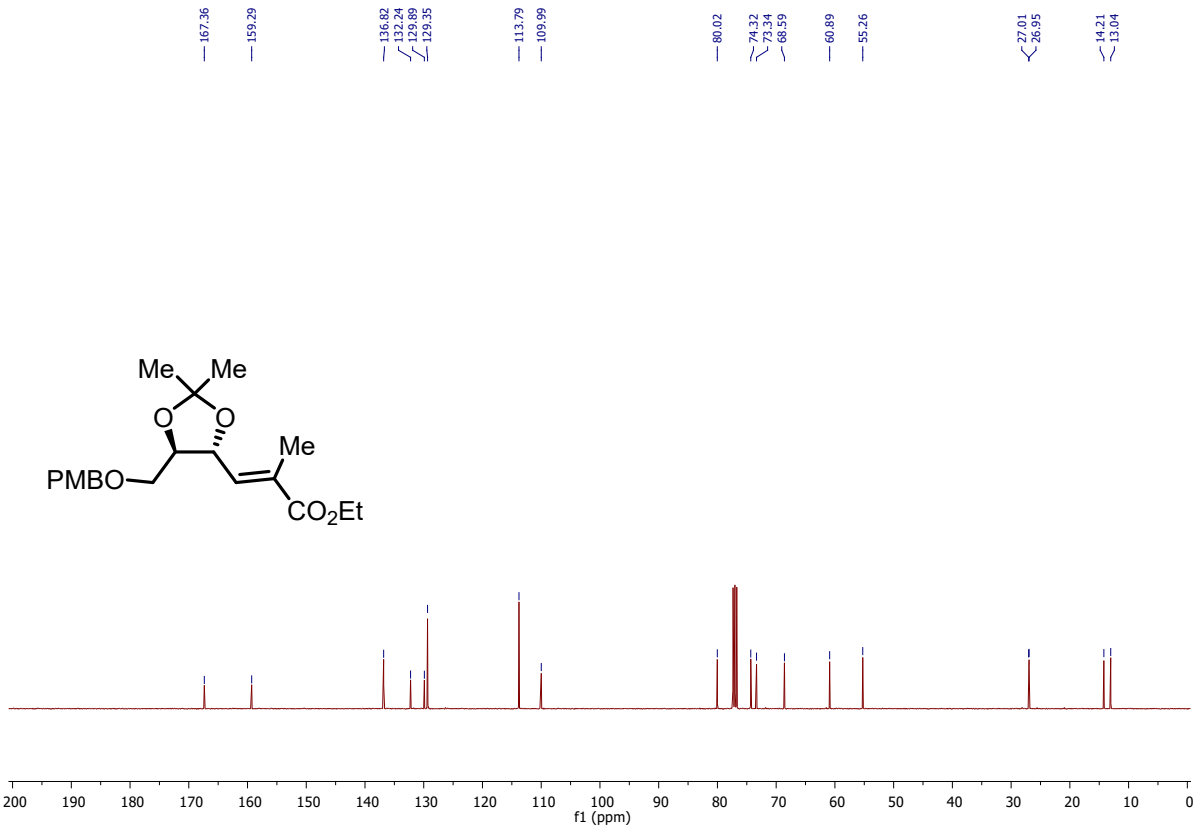

Signal 1: DAD1 A, Sig=254,4 Ref=off

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.928 | MM | 0.2219 | 8563.98828 | 643.21307 | 99.3682 |
| 2 | 8.199 | MM | 0.1781 | 54.45012 | 5.09442 | 0.6318 |

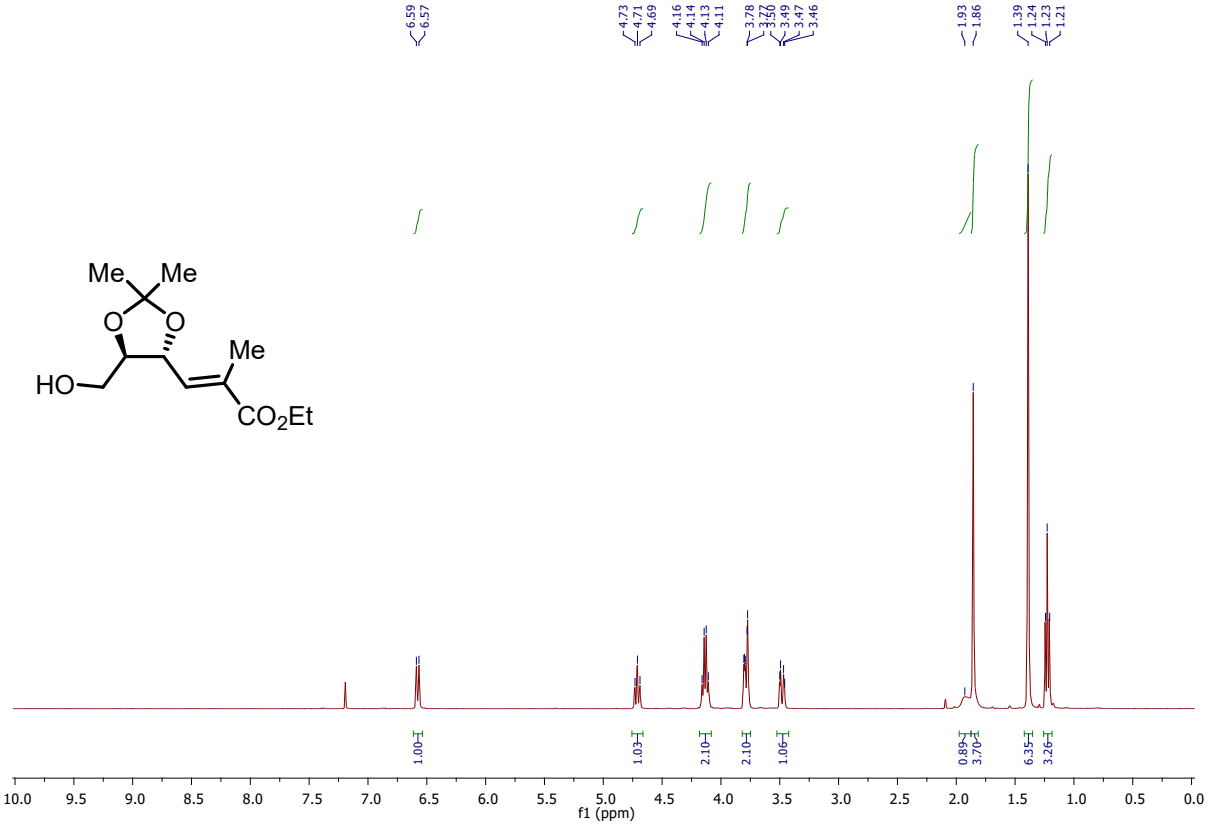
**$^{1}$H-NMR spectrum of compound 20 (400 MHz, $CDCl_3$):**



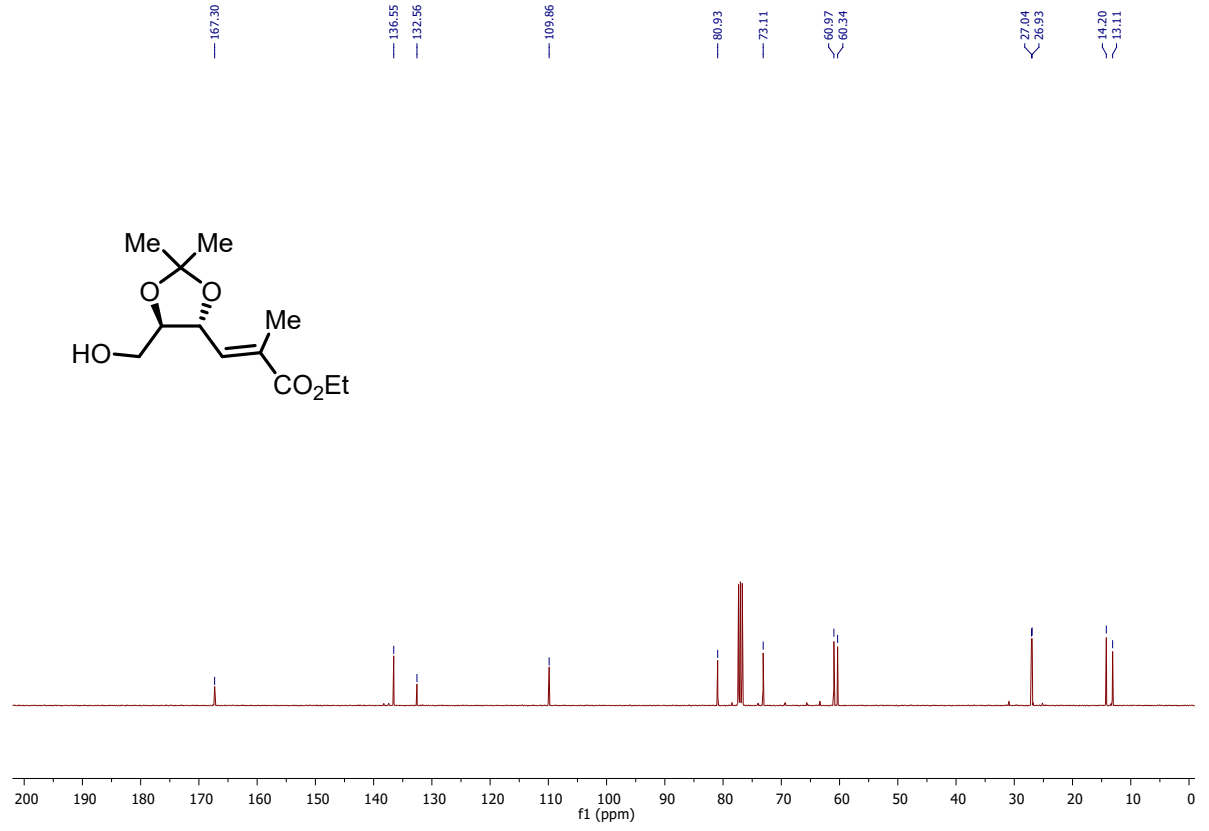

**$^{13}$C-NMR spectrum of compound 20 (100 MHz, $CDCl_3$):**



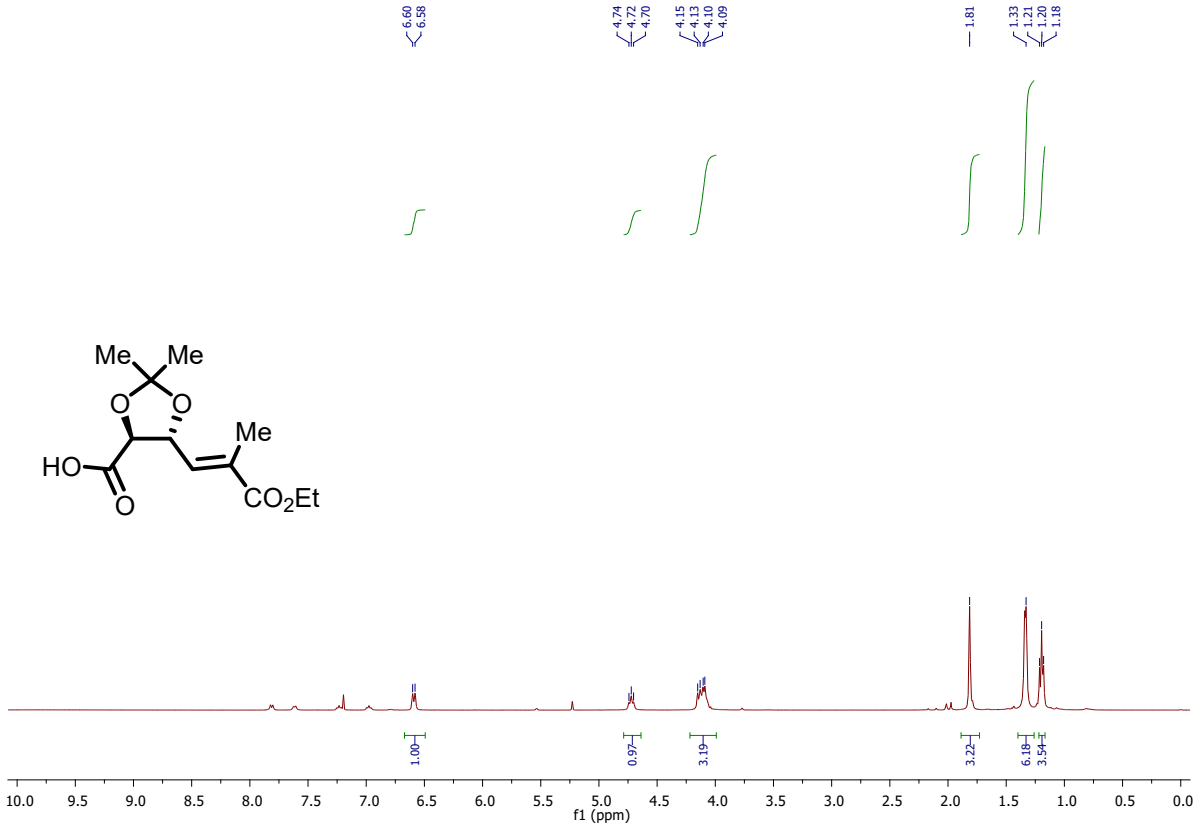
**$^{1}$H-NMR spectrum of compound 21 (400 MHz, $CDCl_3$):**



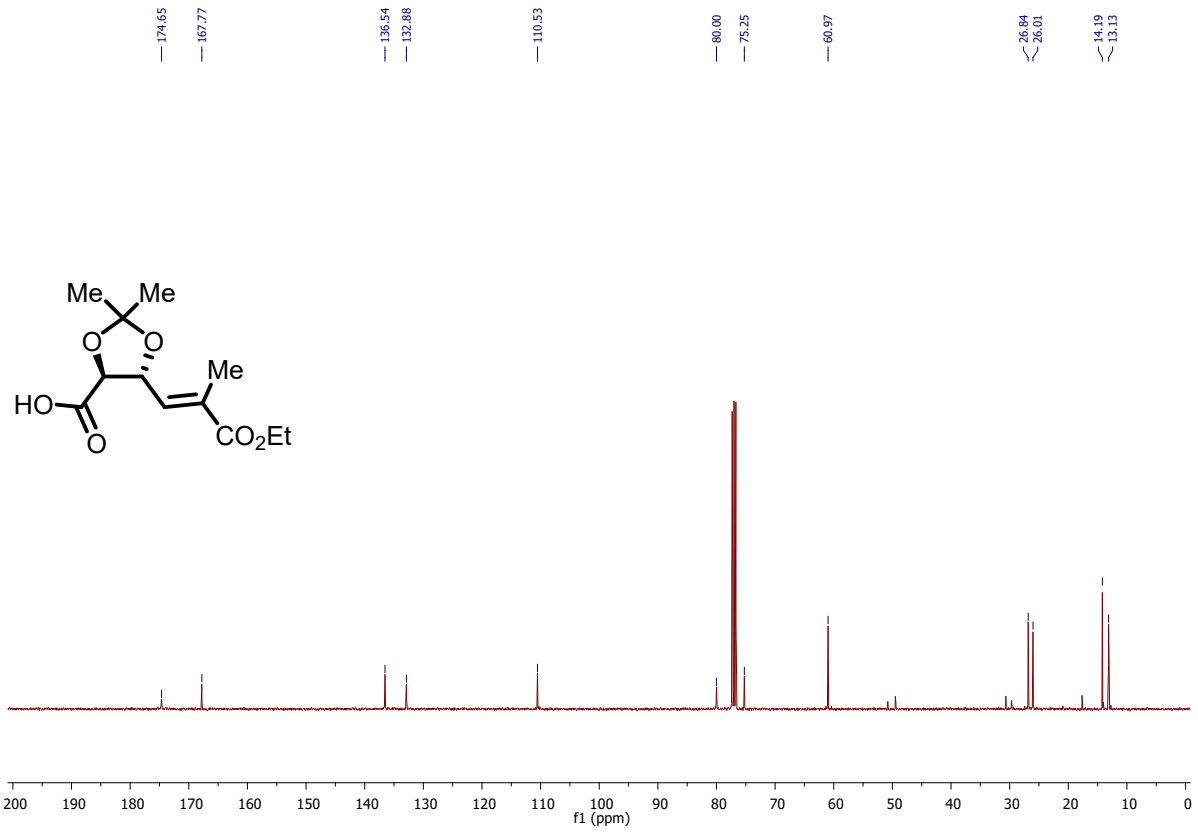

**$^{13}$C-NMR spectrum of compound 21 (100 MHz, $CDCl_3$):**



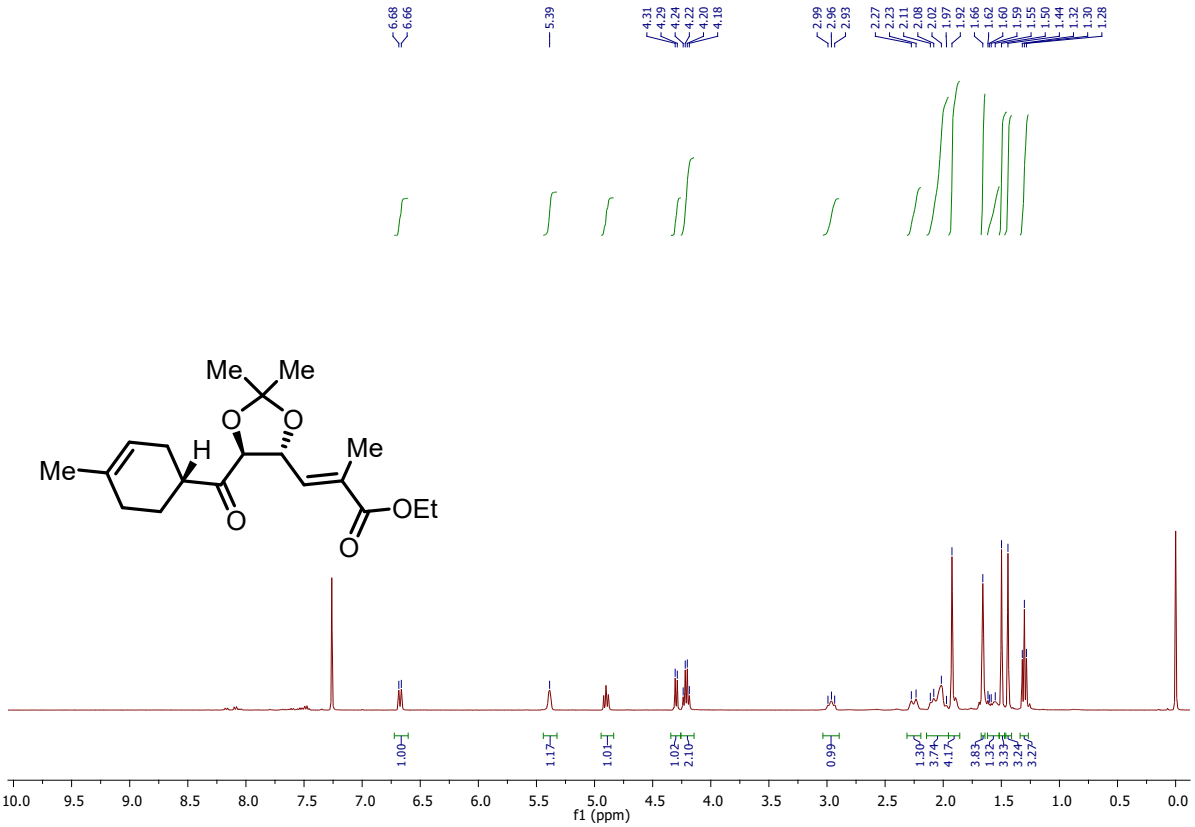
**$^{1}$H-NMR spectrum of compound 22 (400 MHz, $CDCl_3$):**



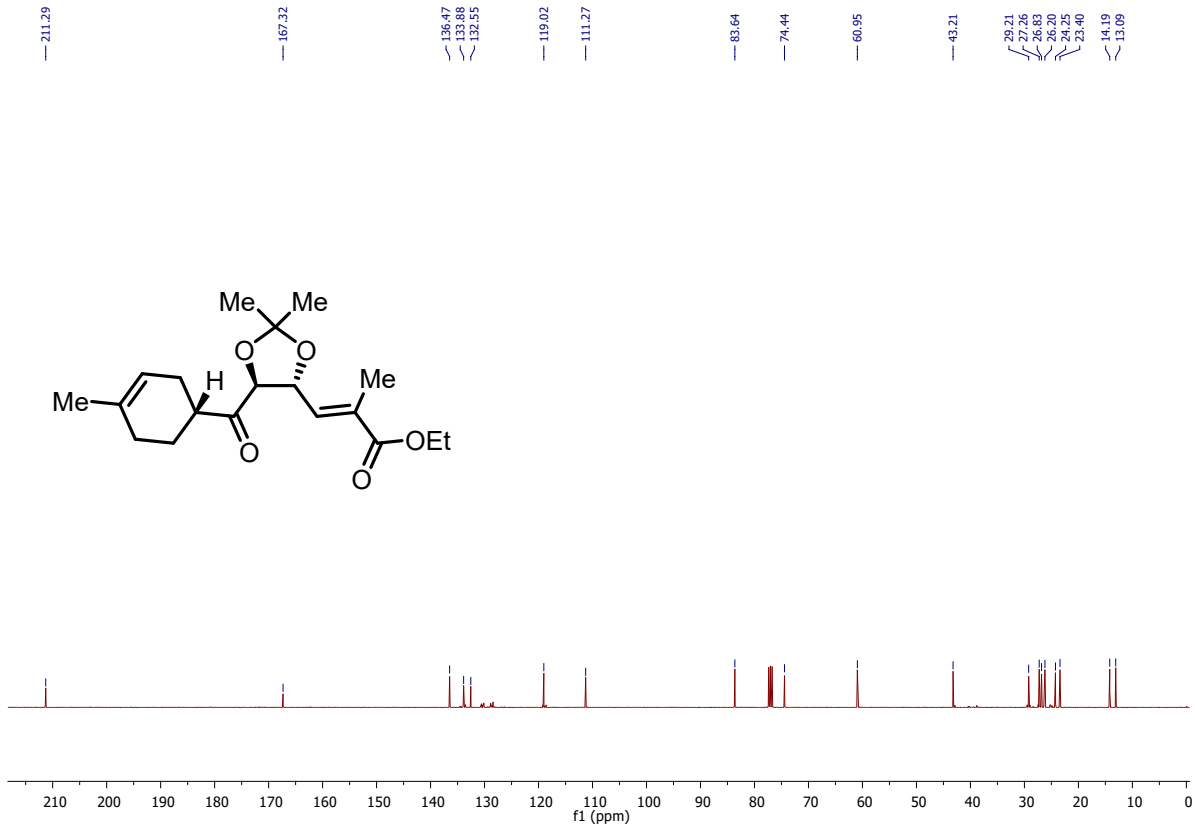

**$^{13}$C-NMR spectrum of compound 22 (100 MHz, $CDCl_3$):**



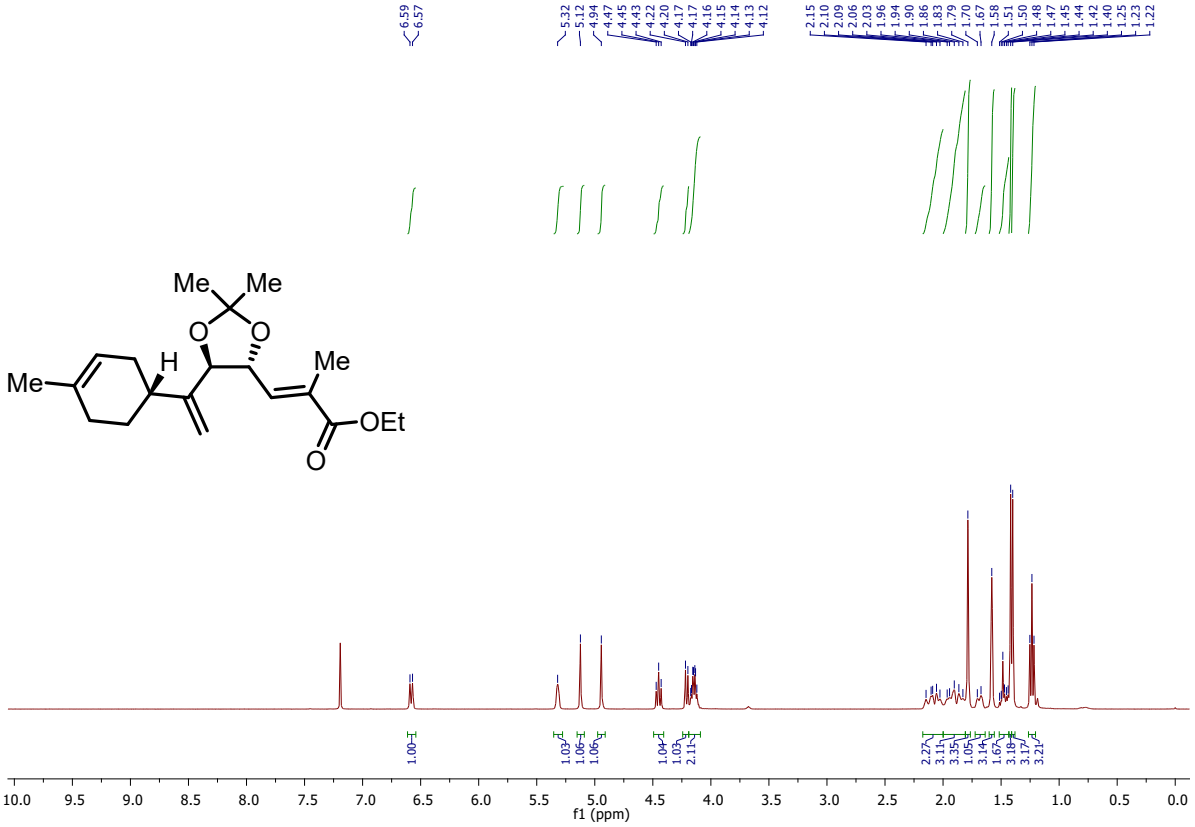
**$^{1}$H-NMR spectrum of compound 23 (400 MHz, $CDCl_3$):**



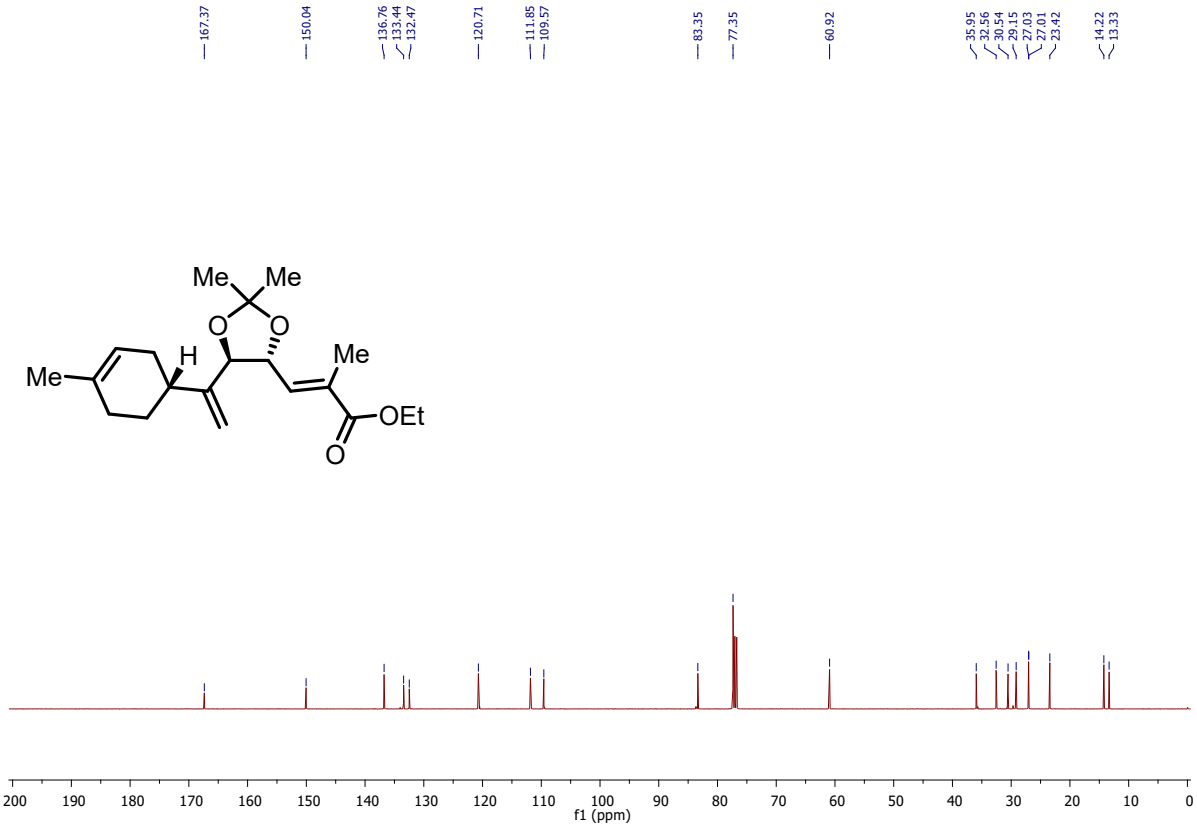

**$^{13}$C-NMR spectrum of compound 23 (100 MHz, $CDCl_3$):**



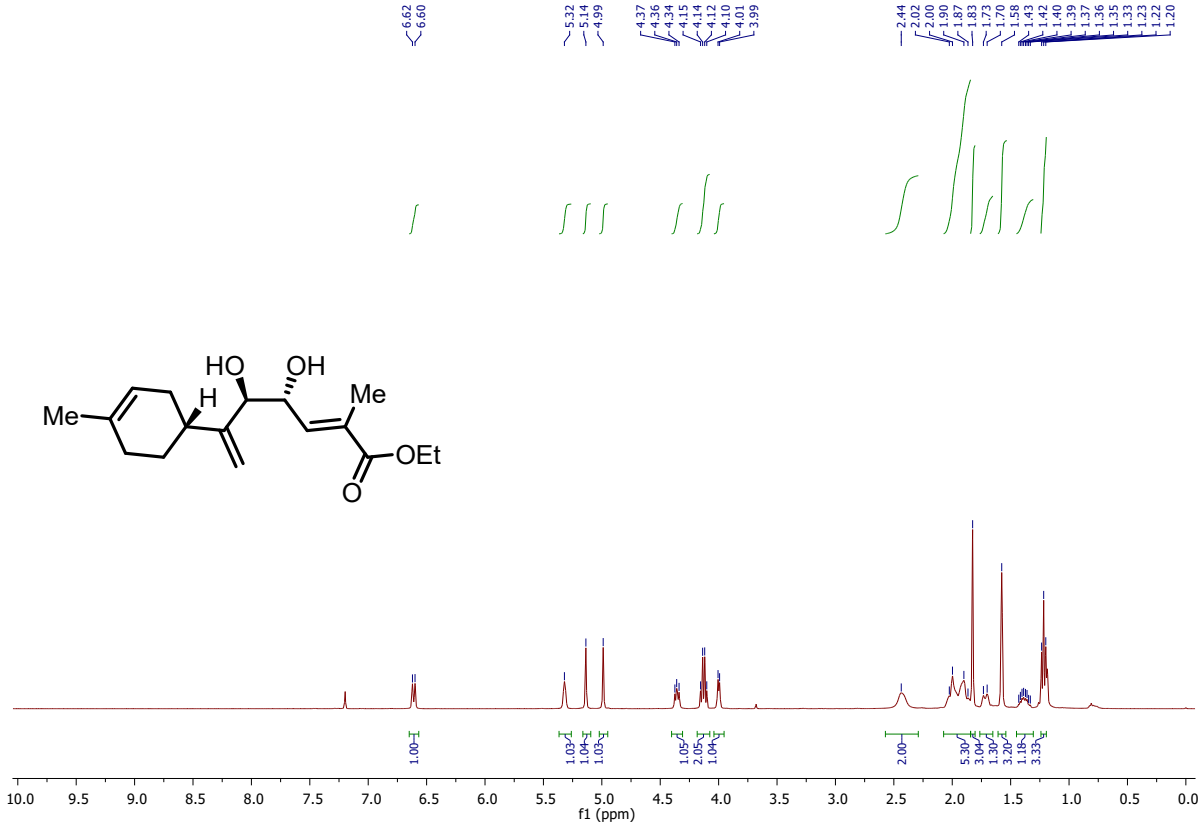
**$^{1}$H-NMR spectrum of compound 24 (400 MHz, $CDCl_3$):**



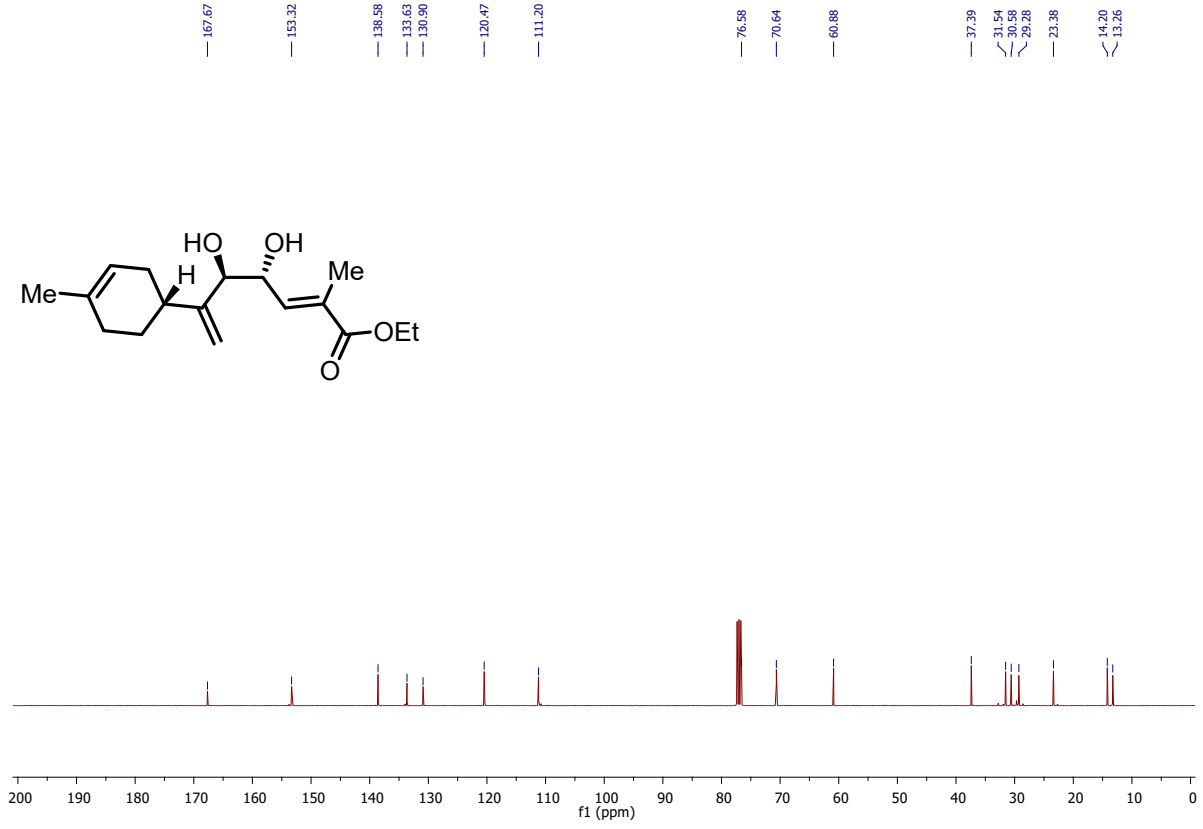

**$^{13}$C-NMR spectrum of compound 24 (100 MHz, $CDCl_3$):**



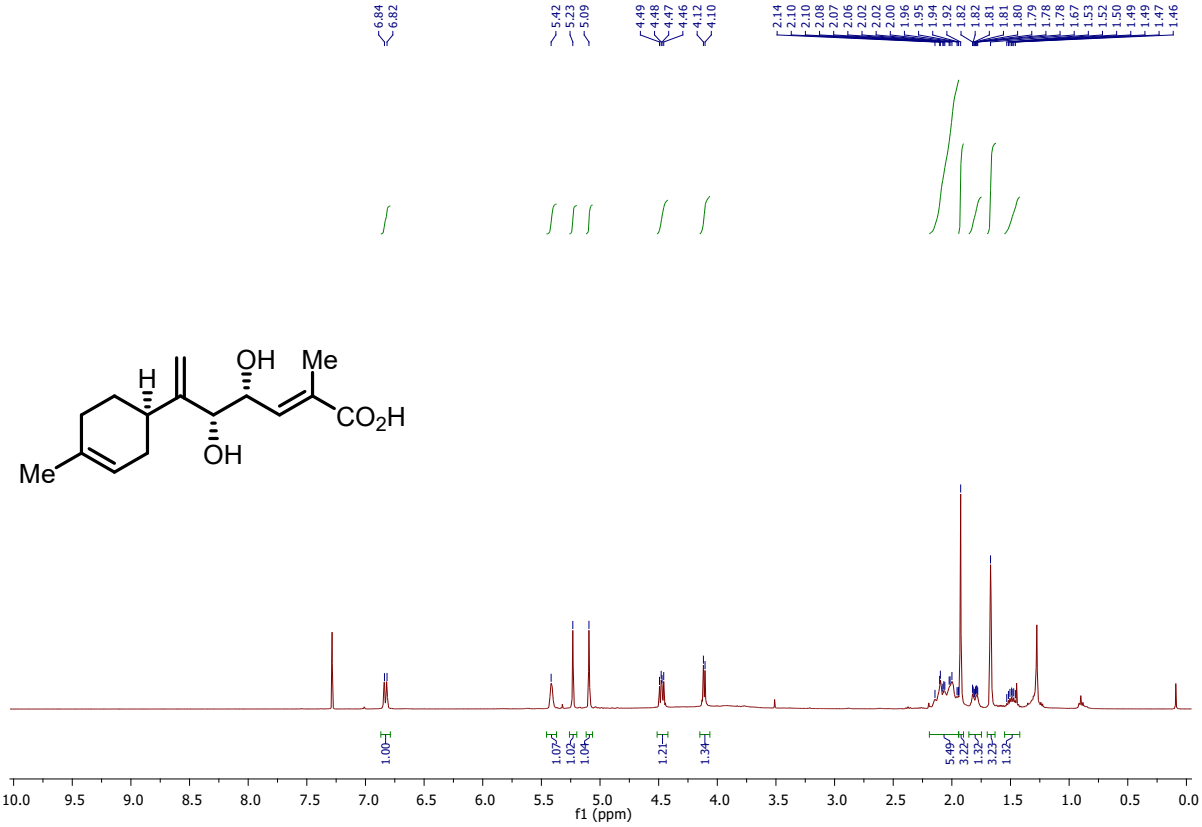
**$^{1}$H-NMR spectrum of compound 25 (400 MHz, $CDCl_3$):**



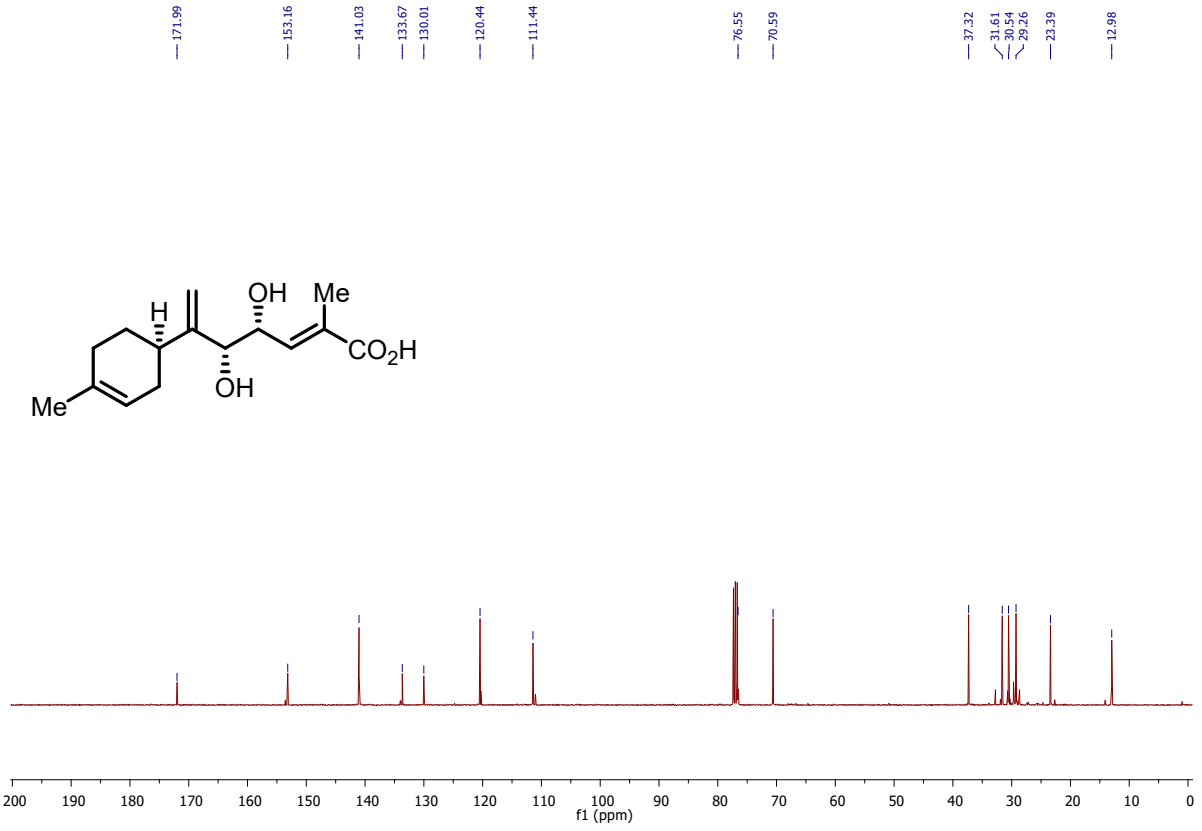

**$^{13}$C-NMR spectrum of compound 25 (100 MHz, $CDCl_3$):**



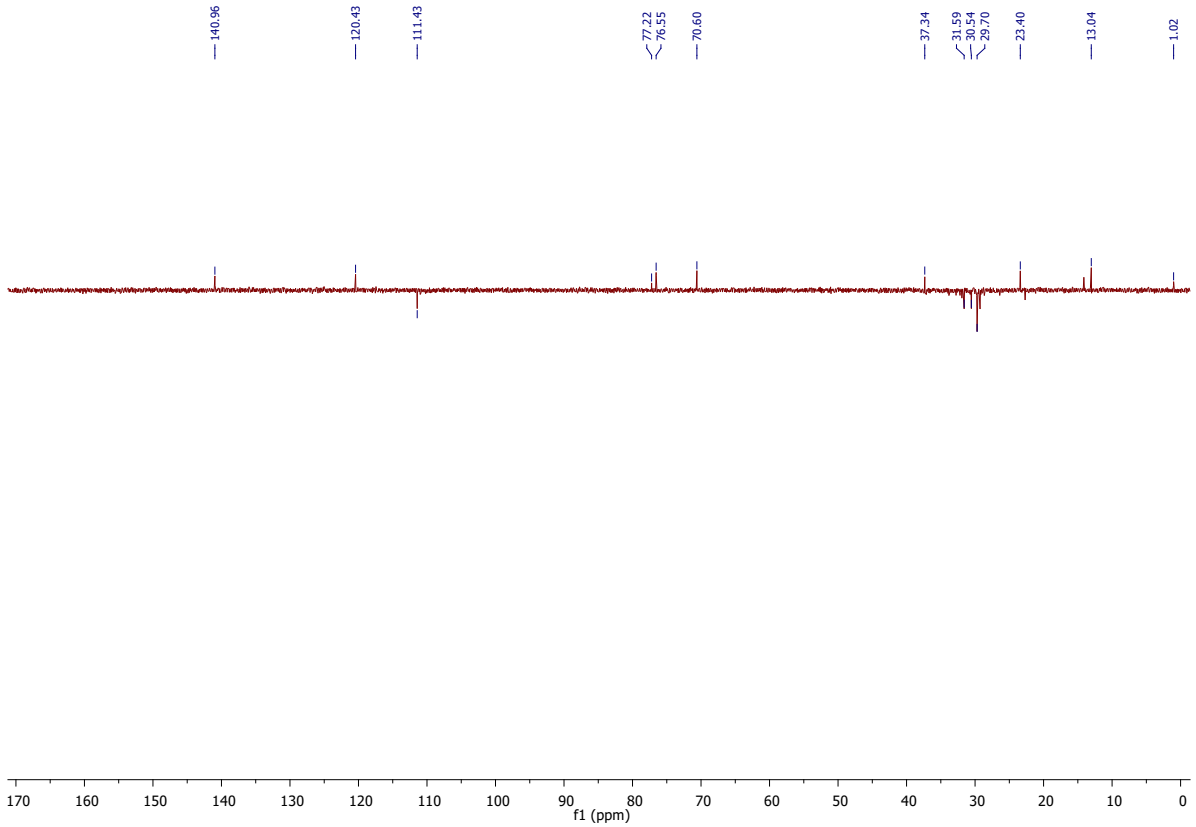
**$^{1}$H-NMR spectrum of compound 1a (400 MHz, $CDCl_3$):**



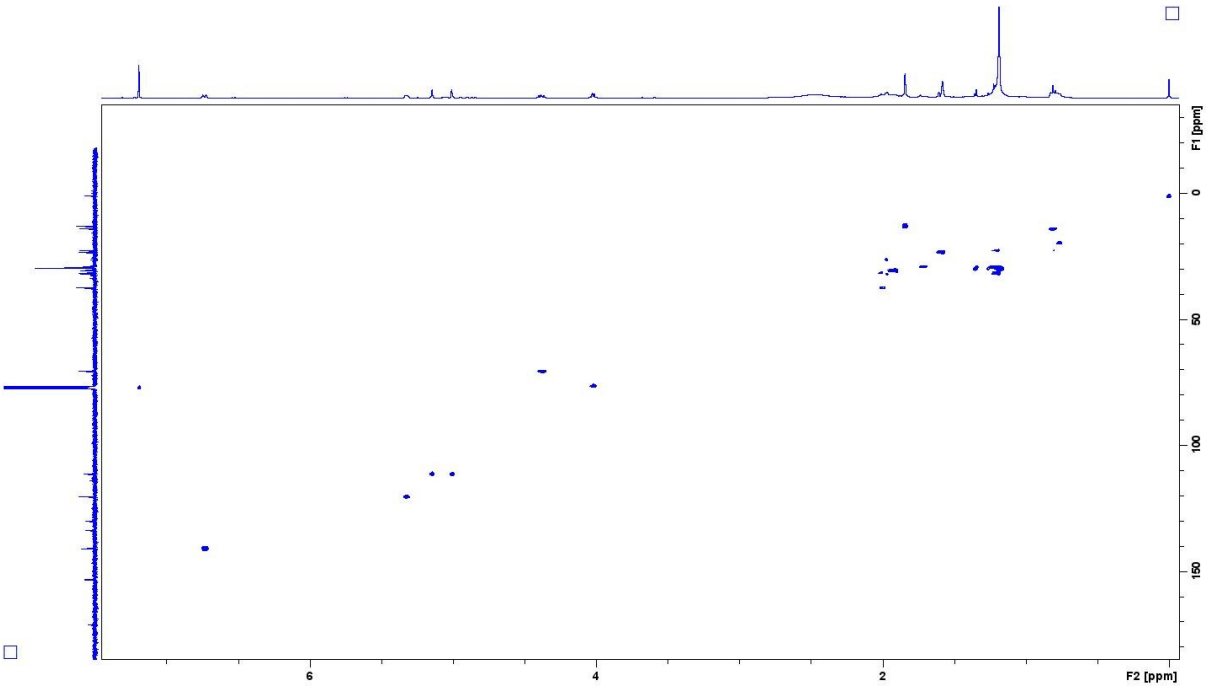

**$^{13}$C-NMR spectrum of compound 1a (100 MHz, $CDCl_3$):**



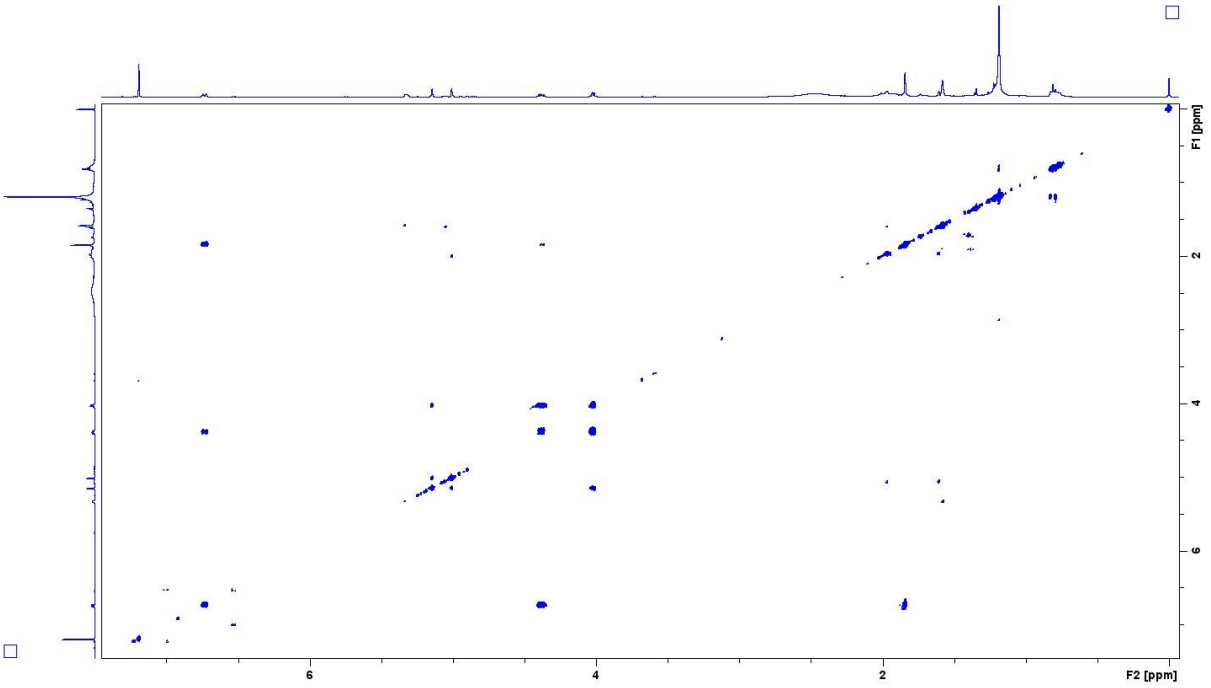
**DEPT-135 NMR spectrum of Compound 1 (100 MHz in $CDCl_3$)**



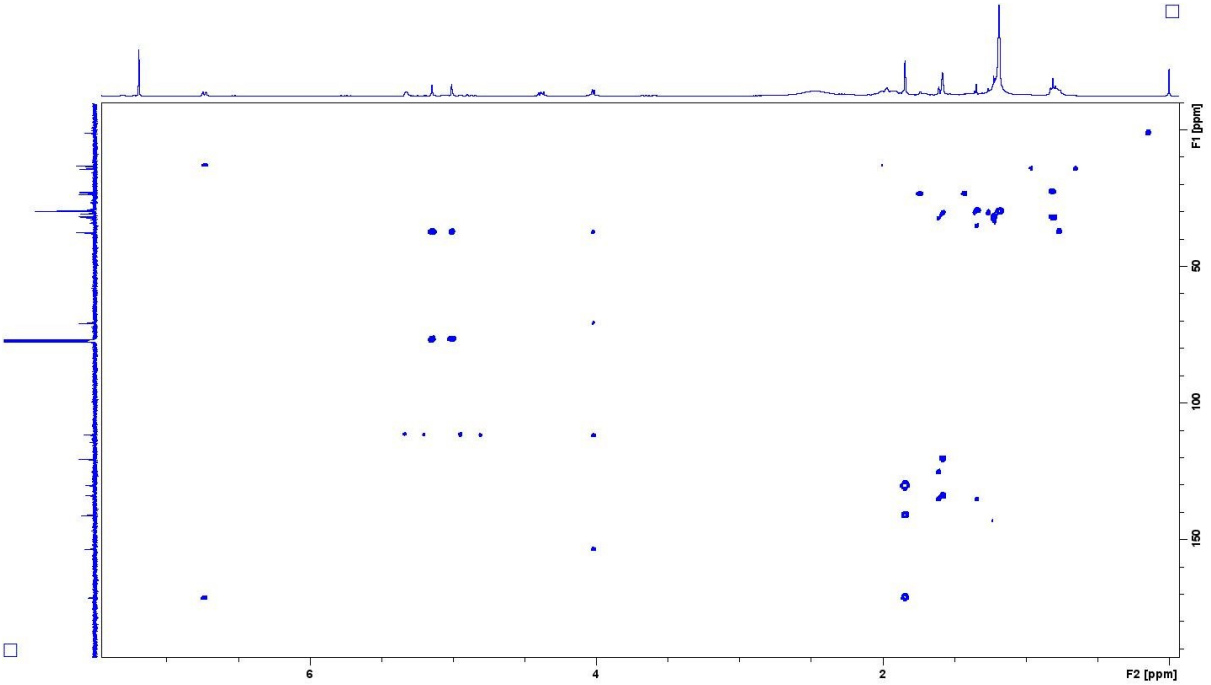

**$^{1}H$, $^{13}C$ HSQC NMR spectrum of Compound 1a (400 MHz, 100 MHz in $CDCl_3$)**



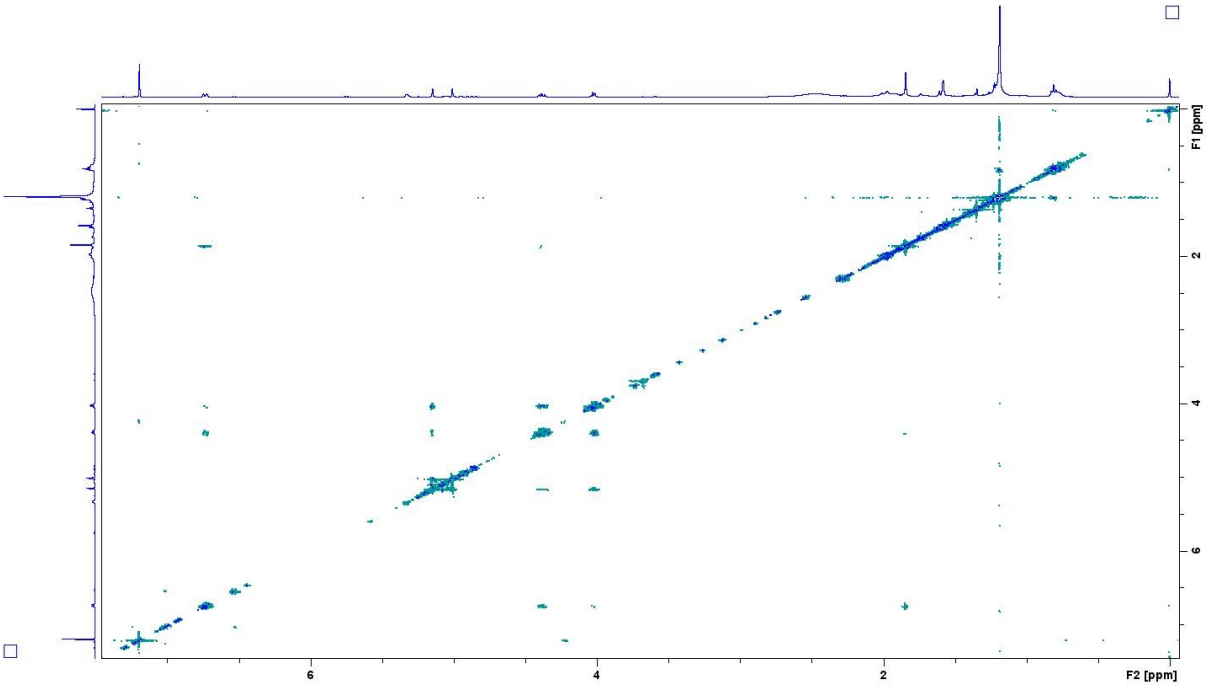
**$^{1}H$, $^{1}H$ COSY NMR spectrum of Compound 1a (400 MHz in $CDCl_3$)**




**$^{1}H$, $^{13}C$ HMBC NMR spectrum of Compound 1a (400 MHz, 100 MHz in $CDCl_3$)**



## $^{1}H$, $^{1}H$ ROESY NMR spectrum of Compound 1a (400 MHz in $CDCl_3$)




## HRMS (ESI-TOF) Spectra of Compound 1a:

**Elemental Composition Report** **Page 1**

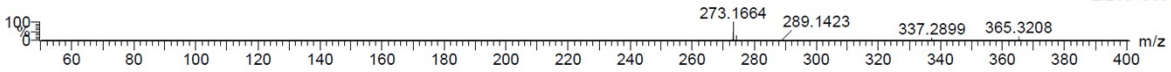
**Single Mass Analysis**
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
16 formula(e) evaluated with 1 results within limits (up to 1 closest results for each mass)
Elements Used:
C: 10-20 H: 22-40 O: 0-5 23Na: 0-1

TB
SM-299 7 (0.147) Cm (7:43)

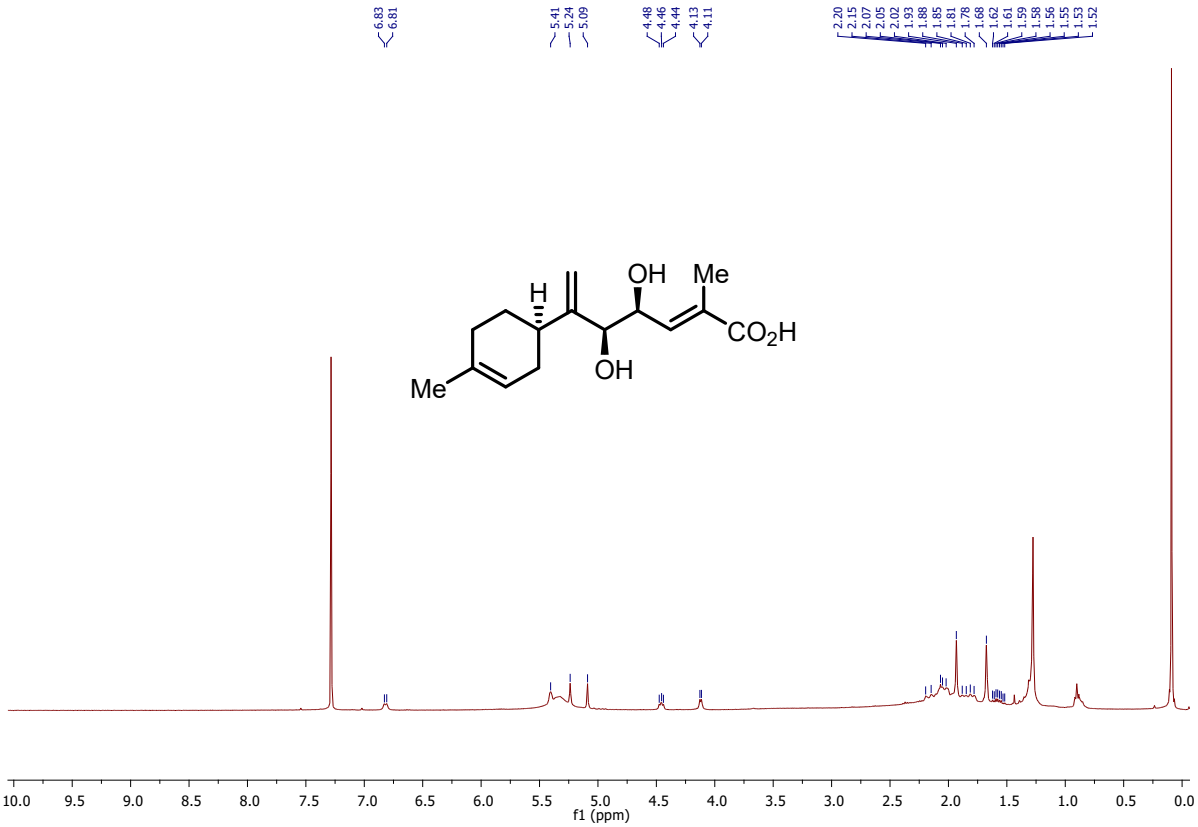
IISER Berhampur

04-Aug-202116:53:04
1: TOF MS ES+
2.21e+008

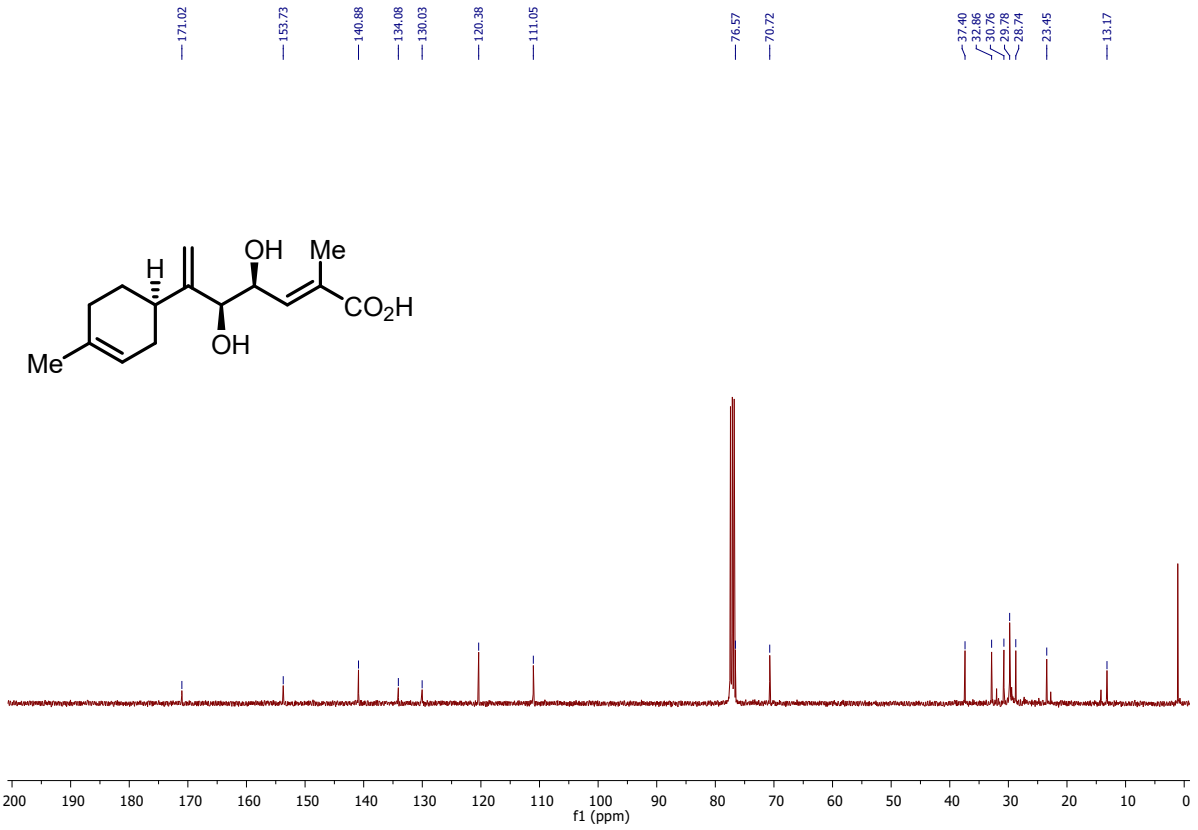



| | | | | | |
|---|---|---|---|---|---|
| Minimum: | | | | -1.5 | |
| Maximum: | | 5.0 | 10.0 | 50.0 | |
| Mass | Calc. Mass | mDa | PPM | DBE | Formula |
| 289.1423 | 289.1416 | 0.7 | 2.4 | 4.5 | C15 H22 O4 23Na |

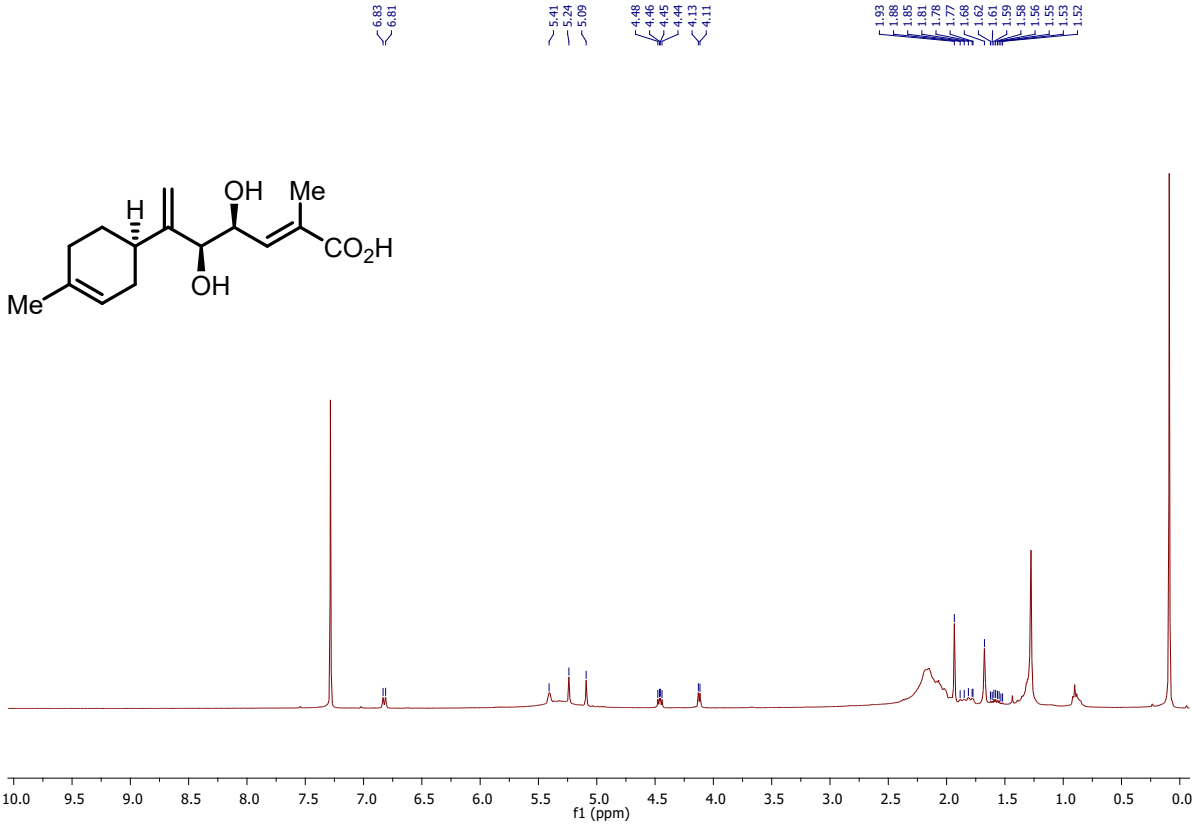
**$^{1}$H-NMR spectrum of compound 1 (400 MHz, in $CDCl_3$ and traces amount $H_2O$):**



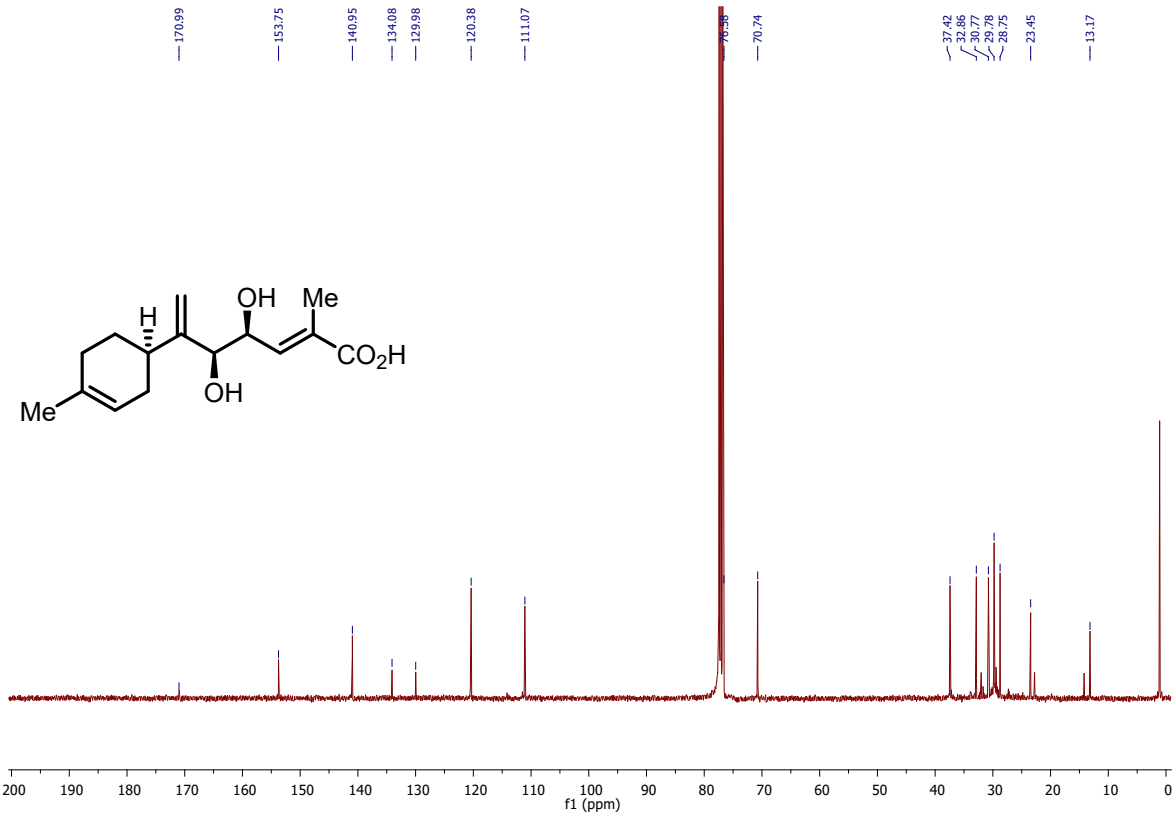

**$^{13}$C-NMR spectrum of compound 1 (100 MHz, in $CDCl_3$ and traces amount $H_2O$):**



**$^{1}$H-NMR spectrum of compound 1 (400 MHz, in $CDCl_3$ and traces amount TFA):**




**$^{13}$C-NMR spectrum of compound 1 (100 MHz, in $CDCl_3$ and traces amount TFA):**



**$^{13}$C-NMR spectrum of compound 1 ($CDCl_3$, 100 MHz) with concentration variations**