

**Supporting Information** Haug, Kirsch

## **Total synthesis of (+)-Chloriolide**

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**Supporting Information** Representative experimental procedures, and copies of  $^1\text{H}$  and  $^{13}\text{C}$  NMR of **1-11**, **13-15** and intermediates. Copies of HPLC traces used to determine enantiopurity for **5**.

**General experimental details:** All commercially available chemicals were used without further purification. (+)-COP-OAc was purchased from Aldrich and purified by column chromatography on silica (100%  $\text{CH}_2\text{Cl}_2$ ) prior to usage. All reactions were performed under argon.  $^1\text{H}$  NMR spectra were obtained on 500 MHz FT-NMR, 360 MHz FT-NMR and 250 MHz FT-NMR spectrometers.  $^{13}\text{C}$  NMR spectra were recorded at 90.6 MHz. Chemical shifts are reported in ppm relative to solvent signal. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); quin (quintet). High resolution mass spectra (EI) were determined on a Finnigan MAT 95S and MAT 8200. High resolution mass spectra (ESI) were recorded on a MAT 95 of the Department of chemistry at Ludwigs-Maximilians-Universität München. We thank Dr. Werner Spahl for help. Optical rotation values were determined on a Perkin-Elmer 241 MC. Flash chromatography was performed with E. Merck silica gel (43–60  $\mu\text{m}$ ). The eluent used is reported in parentheses (P = pentane). Thin-layer chromatography (TLC) was performed on precoated glass-backed plates (Merck Kieselgel 60 F254), and components were visualized by observation under UV light or by treating the plates with  $\text{KMnO}_4/\text{H}_2\text{SO}_4$  followed by heating. HPLC determination of enantiopurity was carried out on a Dionex using a Chiralcel® OH-J column (250 mm x 4.6 mm). All HPLC analyses used to determine enantiomeric purity were calibrated with samples of the racemate.

## Synthesis of (*S,E*)-methyl 4-hydroxyhexa-2,5-dienoate (2).

### (*Z*)-4-(4-methoxybenzyloxy)but-2-en-1-ol

To a suspension of 2.91 g (72.8 mmol, 1.50 eq) NaH (60%) in 56 mL DMF were slowly added 4.67 mL (5.00 g, 56.0 mmol, 1.00 eq) 1,4-butanediol at 0 °C and the resulting solution was stirred for 30 min. 13.0 g (85.0 mmol, 1.50 eq) PMB-Cl and 2.07 g (5.60 mmol, 0.1 eq) TBAI were added and the solution was allowed to warm to rt and stirred for 3.5 h. 100 mL water were added and the reaction mixture extracted with diethylether (3 x 50 mL). The combined organic layers were washed with sat. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was evaporated. Flash chromatography (P/EtOAc = 9/1) gave 6.55 g (31.0 mmol, 56%) of the product. The analytical data are identical to those reported elsewhere.<sup>1</sup>

<sup>1</sup>H NMR (360 MHz, CDCl<sub>3</sub>): δ = 7.27 – 7.24 (m, 2H), 6.92 – 6.84 (m, 2H), 5.92 – 5.64 (m, 2H), 4.46 (s, 2H), 4.22 – 4.13 (m, 2H), 4.11 – 4.01 (m, 2H), 3.80 (s, 3H), 1.83 (s, 1H).

<sup>13</sup>C NMR (90.6 MHz, CDCl<sub>3</sub>): δ = 55.6, 59.2, 65.8, 72.5, 114.2, 128.9, 129.8, 130.3, 132.6, 159.7.

### (*Z*)-4-(4-methoxybenzyloxy)but-2-enyl 2,2,2-trichloroacetimidate (4)

3.80 g (27.0 mmol, 1.00 eq) trichloroacetonitrile and 410 mg (2.70 mmol, 0.10 eq) DBU were added to a solution of 5.69 g (27.0 mmol, 1.00 eq) (*Z*)-4-(4-methoxybenzyloxy)but-2-en-1-ol in 135 mL dichloromethane. After 16 h, sat. aq NH<sub>4</sub>Cl solution (100 mL) was added and the solution extracted with diethylether (3 x 70 mL). The combined organic layers were washed with sat. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was evaporated. Flash chromatography (P/EtOAc = 9/1 to 8/2) gave 8.93 g (25.0 mmol, 94%) of the product 4. The analytical data are identical to those reported elsewhere.<sup>2</sup>

<sup>1</sup>H NMR (360 MHz, CDCl<sub>3</sub>): δ = 8.31 (s, 1H), 7.30 – 7.25 (m, 2H), 6.90 – 6.87 (m, 2H), 5.92 – 5.87 (m, 2H), 4.86 (d, *J* = 5.7 Hz, 2H), 4.46 (s, 2H), 4.15 (d, *J* = 5.9 Hz, 2H), 3.82 (s, 3H).

<sup>13</sup>C NMR (90.6 MHz, CDCl<sub>3</sub>): δ = 162.9, 159.7, 132.2, 130.5, 129.8, 126.0, 114.3, 72.5, 65.9, 65.5, 55.7.

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<sup>1</sup> B. M. Trost, J. D. Chisholm, S. T. Wroblewski, M. Jung, *J. Am. Chem. Soc.*, 2002, **124**, 12420.

<sup>2</sup> S. F. Kirsch, L. E. Overman, *J. Am. Chem. Soc.*, 2005, **127**, 2866.

### **(S)-1-(4-methoxybenzyloxy)but-3-en-2-yl benzoate (5)**

To a solution of 3.00 g (8.51 mmol, 1.00 eq) **4** in 6 mL CH<sub>2</sub>Cl<sub>2</sub> were added 154 mg (0.09 mmol, 0.01 eq) (+)-COP-OAc<sup>3</sup> and 3.11 g (25.5 mmol, 3.00 eq) benzoic acid. The solution was stirred for 16 h, poured into sat. aq. NaHCO<sub>3</sub> solution (10 mL) and extracted with diethylether (3 x 10 mL). The combined organic layers were washed with sat. aq. NaCl solution and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, flash chromatography (P/EtOAc = 95/5) yielded 2.51 g (8.05 mmol, 95%, 96% ee) of **5**. HPLC analysis indicated an enantiomeric excess of 96% [Daicel Chiralpak OJ-H column; flow: 1.0 mL/min; hexane/isopropanol = 9/1; 215 nm; minor enantiomer: t<sub>R</sub> = 28.14 min; major enantiomer: t<sub>R</sub> = 22.02 min]. See HPLC traces.

<sup>1</sup>H NMR (360 MHz, CDCl<sub>3</sub>): δ = 8.14 – 8.04 (m, 2H), 7.61 – 7.53 (m, 1H), 7.51 – 7.40 (m, 2H), 7.27 – 7.22 (m, 2H), 6.87 – 6.81 (m, 2H), 5.95 (ddd, *J* = 17.2, 10.6, 5.9 Hz, 1H), 5.77 – 5.67 (m, 1H), 5.41 (dt, *J* = 17.3, 1.3 Hz, 1H), 5.28 (dt, *J* = 10.6, 1.3 Hz, 1H), 4.62 – 4.42 (m, 2H), 3.79 (s, 3H), 3.72 – 3.65 (m, 2H).

<sup>13</sup>C NMR (90.6 MHz, CDCl<sub>3</sub>): δ = 165.9, 159.4, 133.6, 133.1, 130.5, 130.2, 129.9, 129.4, 128.5, 118.1, 114.0, 73.9, 73.0, 71.2, 55.4.

MS (EI, 70 eV), m/z (%): 312 [M<sup>+</sup>] (1), 282 (1), 242 (1), 226 (1), 160 (6), 136 (61), 121 (100), 105 (36).

HRMS (C<sub>19</sub>H<sub>20</sub>O<sub>4</sub>Na) found: 335.1255

calculated: 335.1259

Rotation value [α]<sub>D</sub><sup>20</sup> = -11.8 (c = 0.83, CH<sub>2</sub>Cl<sub>2</sub>)

### **(S)-1-(4-methoxybenzyloxy)but-3-en-2-ol**

A solution of 2.40 g (7.67 mmol, 1.00 eq) **5** and 10.6 g (76.7 mmol, 10.0 eq) K<sub>2</sub>CO<sub>3</sub> in 75 mL MeOH were stirred for 16 h. H<sub>2</sub>O (100 mL) was added and the solution extracted with diethylether (3x 50 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent evaporated. Flash chromatography (P/EtOAc = 9/1 to 5/5) gave 1.42 g (6.80 mmol, 89%) of (S)-1-(4-methoxybenzyloxy)but-3-en-2-ol. The analytical data are identical to those reported elsewhere.<sup>4</sup>

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<sup>3</sup> S. F. Kirsch, L. E. Overman, *J. Org. Chem.* 2005, **70**, 2859.

<sup>4</sup> P. A. Evans, D. K. Leahy, W. J. Andrews, D. Uraguchi, *Angew. Chem. Int. Ed.* 2004, **43**, 4788.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 7.32 – 7.21 (m, 2H), 6.99 – 6.81 (m, 2H), 5.83 (ddd, *J* = 17.2, 10.6, 5.6 Hz, 1H), 5.35 (dt, *J* = 17.3, 1.5, Hz, 1H), 5.19 (dt, *J* = 10.6, 1.5, Hz, 1H), 4.51 (s, 2H), 4.35 – 4.27 (m, 1H), 3.81 (s, 3H), 3.52 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.35 (dd, *J* = 9.6, 8.0 Hz, 1H), 2.40 (d, *J* = 3.4 Hz, 1H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 159.5, 136.7, 130.1, 129.6, 116.6, 114.0, 73.9, 73.2, 71.7, 55.4.

### **(*S*)-triisopropyl(1-(4-methoxybenzyloxy)but-3-en-2-yloxy)silane**

To a solution of 1.90 g (9.12 mmol, 1.00 eq) (*S*)-1-(4-methoxybenzyloxy)but-3-en-2-ol in 4.5 mL DMF were added 4.10 mL (11.9 mmol, 1.30 eq) TIPS-Cl and 930 mg (13.7 mmol, 1.50 eq) imidazole. The solution was stirred for 19 h, diluted with H<sub>2</sub>O (20 mL) and extracted with diethylether (3 x 20 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. Flash chromatography (P/EtOAc = 99/1 to 96/4) gave 3.19 g (8.76 mmol, 96%) of (*S*)-triisopropyl(1-(4-methoxybenzyloxy)but-3-en-2-yloxy). We were not able to obtain adequate MS data for this compound.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 7.27 – 7.23 (m, 2H), 6.89 – 6.84 (m, 2H), 5.91 (ddd, *J* = 17.2, 10.5, 5.8 Hz, 1H), 5.30 (dt, *J* = 17.3, 1.6, Hz, 1H), 5.14 (dt, *J* = 10.0, 1.5 Hz, 1H), 4.48 (s, 2H), 4.42 – 4.36 (m, 1H), 3.80 (s, 3H), 3.49 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.36 (dd, *J* = 9.6, 6.1 Hz, 1H), 1.10 – 0.99 (m, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 159.3, 139.6, 130.7, 129.4, 115.2, 113.9, 75.1, 73.2, 73.1, 55.4, 18.2, 12.5.

**Rotation value** [ $\alpha$ ]<sub>D</sub><sup>20</sup> = -15.9 (c = 1.1, CH<sub>2</sub>Cl<sub>2</sub>).

### **(*S*)-2-(triisopropylsilyloxy)but-3-en-1-ol (6)**

A solution of 711 mg (1.95 mmol, 1.00 eq) (*S*)-triisopropyl(1-(4-methoxybenzyloxy)but-3-en-2-yloxy)silane and 620 mg (2.73 mmol, 1.40 eq) DDQ in 11 mL dichloromethane and 11 mL pH7 buffer were stirred for 2 h. 20 mL sat. aq. NaHCO<sub>3</sub> were added and the aqueous phase extracted with dichloromethane (3 x 20 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. Flash chromatography (P/EtOAc = 9/1) yielded 472 mg (1.93 mmol, 99%) of the product **6**.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 5.84 (ddd, *J* = 17.1, 10.4, 6.6 Hz, 1H), 5.37 (tq, *J* = 17.3, 1.5 Hz, 2H), 4.40 – 4.27 (m, 1H), 3.65 – 3.45 (m, 2H), 1.98 (t, *J* = 6.5 Hz, 1H), 1.10 – 0.95 (m, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 138.7, 116.5, 74.8, 67.1, 18.2, 18.2, 12.5.

**MS** (EI, 70 eV), *m/z* (%): 201 [*M*<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (43), 159 (12), 157 (15), 131 (100), 117 (20), 103 (74).

**HRMS** (C<sub>10</sub>H<sub>21</sub>O<sub>2</sub>Si) found: 201.1312

calculated: 201.1311

**Rotation value** [*α*]<sub>D</sub><sup>20</sup> = +2.2 (*c* = 1.1, CH<sub>2</sub>Cl<sub>2</sub>)

### **(*S,E*)-methyl 4-(triisopropylsilyloxy)hexa-2,5-dienoate (7)**

A solution of 472 mg (1.93 mmol, 1.00 eq) **6** and 1.35 g (4.83 mmol, 2.50 eq) IBX in 6.4 mL EtOAc was heated to 80 °C for 5 h. It was cooled to rt and filtered. The filtrate was concentrated and the crude product was dissolved in 4 mL dichloromethane with 1.88 g (5.64 mmol, 2.90 eq) PPh<sub>3</sub>CHCOOMe and stirred for 18 h. Sat. aq. NH<sub>4</sub>Cl (20 mL) was added and the mixture extracted with diethylether (3 x 20 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. Flash chromatography (P/EtOAc = 95/5) gave 435 mg (1.50 mmol, 78%) of the product.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 6.89 (dd, *J* = 15.5, 4.6 Hz, 1H), 6.06 (dd, *J* = 15.5, 1.7 Hz, 1H), 5.76 (ddd, *J* = 17.1, 10.2, 6.1 Hz, 1H), 5.35 – 5.08 (m, 2H), 4.95 – 4.81 (m, 1H), 3.73 (s, 3H), 1.14 – 0.96 (m, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 167.2, 150.0, 138.7, 119.3, 115.5, 73.5, 51.7, 18.2, 18.1, 12.4.

**MS** (EI, 70 eV), *m/z* (%): 298 [*M*<sup>+</sup>] (5), 267 (6), 255 [*M*<sup>+</sup> – 43] (100), 145 (71), 117 (51).

**HRMS** (C<sub>16</sub>H<sub>30</sub>O<sub>3</sub>Si) found: 298.1966

calculated: 298.1964

**Rotation value** [*α*]<sub>D</sub><sup>20</sup> = +21.2 (*c* = 1.0, CH<sub>2</sub>Cl<sub>2</sub>)

### **(*S,E*)-methyl 4-hydroxyhexa-2,5-dienoate (2)**

50 mg (0.17 mmol, 1.00 eq) **7** in 700  $\mu$ L MeCN were mixed with 300  $\mu$ L HF (50% in water) and stirred for 4 h. The solution was diluted with sat. aq. NaHCO<sub>3</sub> (2 mL) and stirred for additional 30 min and then extracted with EtOAc (3 x 2 mL). The combined organic layers were washed with sat. NaCl solution and dried over Na<sub>2</sub>SO<sub>4</sub>. After evaporation of the solvent, flash chromatography (P/EtOAc = 9/1 to 8/2) gave 22 mg (0.15 mmol, 88%) of the product **2** as a colourless oil.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 6.92 (dd,  $J$  = 15.7, 4.8 Hz, 1H), 6.06 (dd,  $J$  = 15.7, 1.7 Hz, 1H), 5.93 – 5.78 (m, 1H), 5.31 (dt,  $J$  = 17.2, 1.2 Hz, 1H), 5.21 (dt,  $J$  = 10.3, 1.1 Hz, 1H), 4.83 – 4.76 (m, 1H), 3.73 (s, 3H), 2.33 (s, 1H, OH).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 167.0, 148.2, 137.6, 120.3, 116.8, 72.3, 51.8.

**MS** (EI, 70 eV),  $m/z$  (%): 124 [ $M^+$  - H<sub>2</sub>O] (5), 114 (9), 113 (72), 87 (71), 83 (70), 82 (36), 81 (35).

**HRMS** (C<sub>7</sub>H<sub>8</sub>O<sub>2</sub>) found: 124.0524

calculated: 124.0524

**Rotation value**  $[\alpha]_D^{20} = +63.6$  ( $c = 1.2$ , CH<sub>2</sub>Cl<sub>2</sub>)

### **Synthesis of (2*S*,6*R*)-6-hydroxyoct-7-en-2-yl acetate (3)**

#### **(*S*)-6-(benzyloxy)hex-4-yn-2-ol**

To a solution of 9.50 g (64.0 mmol, 1.90 eq) ((prop-2-ynyloxy)methyl)benzene in 170 mL THF were added 29 mL (72.5 mmol, 2.10 eq) *n*BuLi (2.50 M in THF) at -78 °C. After 50 min, 5.25 mL (41.4 mmol, 1.20 eq) BF<sub>3</sub>•OEt<sub>2</sub> were added at -78 °C, followed after 10 min by 2.40 mL (34.5 mmol, 1.00 eq) (*S*)-(-)-propylene oxide. The solution was stirred for 3 h at -78 °C. 100 mL H<sub>2</sub>O were added and the mixture extracted with Et<sub>2</sub>O (3x 50 mL). The combined organic layers were washed with sat. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. After removal of the solvents, flash chromatography (P/Et<sub>2</sub>O = 80/20) gave 6.54 g (31.0 mmol, 93%) of (*S*)-6-(benzyloxy)hex-4-yn-2-ol as a transparent liquid. The analytical data are identical to those reported elsewhere.<sup>5</sup>

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<sup>5</sup> R. W. Bates, T. B. Maiti, *Synth. Commun.* 2003, **33**, 633.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 1.27 (d, *J* = 6.2 Hz, 3H), 1.92 (s, 1H), 2.50 – 2.34 (m, 2H), 4.02 – 3.91 (m, 1H), 4.18 (t, *J* = 2.1 Hz, 2H), 4.60 (s, 2H), 7.27-7.32 (m, 5H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 22.5, 29.5, 57.8, 66.5, 71.7, 78.7, 83.5, 128.0, 128.2, 128.6, 137.6.

**(*S*)-6-(benzyloxy)hex-4-yn-2-yloxy)triisopropylsilane (8)**

2.30 g (33.8 mmol, 1.30 eq) imidazol and 9.80 mL (28.6 mmol, 1.10 eq) TIPS-Cl were added to a solution of 5.32 g (26.0 mmol, 1.00 eq) (*S*)-6-(benzyloxy)hex-4-yn-2-ol in 13 mL DMF. The reaction was stirred for 22 h, diluted with 50 mL H<sub>2</sub>O and extracted with Et<sub>2</sub>O (3 x 30 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent evaporated. Flash chromatography (P/Et<sub>2</sub>O = 95/5) gave 9.28 g (25.0 mmol, 98%) of the product **8**.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 7.41 – 7.28 (m, 5H), 4.59 (s, 2H), 4.20 – 4.13 (m, 2H), 4.13 – 4.00 (m, 1H), 2.58 – 2.26 (m, 2H), 1.30 (d, *J* = 6.0 Hz, 3H), 1.07 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 137.8, 128.5, 128.2, 127.9, 84.5, 77.7, 71.5, 67.7, 57.9, 30.1, 23.6, 18.2, 18.2, 12.5.

**MS** (EI, 70 eV), *m/z* (%): 317 [*M*<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (4), 287 (24), 221 (27), 201 (12), 169 (16).

**HRMS** (C<sub>19</sub>H<sub>29</sub>O<sub>2</sub>Si) found: 317.1938

calculated: 317.1937

**Rotation value** [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –7.1 (*c* = 0.9, CH<sub>2</sub>Cl<sub>2</sub>)

**(*S*)-5-(triisopropylsilyloxy)hexan-1-ol**

A solution of 200 mg (0.55 mmol, 1.00 eq) of **8** and 43 mg (0.03 mmol, 0.05 eq) of Pd/C (5%) in 5 mL ethanol was stirred for 4 h under a hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated. 163 mg (0.55 mmol, quant.) of the free alcohol were obtained as a transparent oil.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 4.00 – 3.90 (m, 1H), 3.65 (t, *J* = 6.6 Hz, 2H), 1.65 – 1.35 (m, 6H), 1.27 – 1.21 (m, 1H), 1.16 (d, *J* = 6.1 Hz, 3H), 1.05 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 68.6, 63.2, 39.8, 33.2, 27.1, 23.4, 21.6, 18.3, 12.7.

**MS** (EI, 70 eV), *m/z* (%): 231 [*M*<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (14), 213 (6), 201 (6), 175 (16), 157 (15), 149 (15), 133 (34), 131 (100), 103 (50).

**HRMS** (C<sub>12</sub>H<sub>27</sub>O<sub>2</sub>Si) found: 231.1779

calculated: 231.1780

**Rotation value**  $[\alpha]_{\text{D}}^{20} = +1.00$  (c = 0.796, CH<sub>2</sub>Cl<sub>2</sub>)

**(S)-5-(triisopropylsilyloxy)hexanal (9)**

To a solution of 1.11 mL (1.64 g, 12.9 mmol, 1.10 eq) oxalyl chloride in 32 mL dichloromethane were added 1.75 mL (2.02 g, 25.9 mmol, 2.20 eq) DMSO in 3.8 mL dichloromethane at -78 °C. After stirring for 30 min at -78 °C, 3.23 g (11.8 mmol, 1.00 eq) (S)-5-(triisopropylsilyloxy)hexan-1-ol in 3 mL dichloromethane were added. After additional 30 min, 8.2 mL (58.9 mmol, 5.00 eq) NEt<sub>3</sub> were added dropwise before the solution was slowly allowed to warm to room temperature and stirred for 1 h. H<sub>2</sub>O (50 mL) was added and the mixture extracted with dichloromethane (3 x 20 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, and filtered. After removal of the solvents, 3.03 g (11.1 mmol, 94%) of the aldehyde were isolated.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 9.77 (t, *J* = 1.8 Hz, 1H), 4.10 – 3.90 (m, 1H) 2.43 (td, *J* = 7.2, 1.6 Hz, 2H), 1.75 – 1.65 (m, 2H), 1.60 – 1.40 (m, 2H), 1.17 (d, *J* = 6.2 Hz, 3H), 1.06 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 202.8, 68.3, 44.2, 39.4, 23.5, 18.3, 18.3, 18.0, 12.7.

**MS** (EI, 70 eV), *m/z* (%): 229 [M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (100), 187 (58), 131 (83), 103 (83), 75 (77).

**HRMS** (C<sub>12</sub>H<sub>25</sub>O<sub>2</sub>Si) found: 229.1623

calculated: 229.1624

**Rotation value**  $[\alpha]_{\text{D}}^{20} = +2.8$  (c = 0.83, CH<sub>2</sub>Cl<sub>2</sub>)

**(S,Z)-methyl 7-(triisopropylsilyloxy)oct-2-enoate**

To a solution of 2.52 g (12.0 mmol, 1.30 eq) methyl (diphenylphosphono)acetate<sup>6</sup> in 44 mL THF were added 516 mg (12.9 mmol, 1.40 eq) NaH (60% in mineral oil) at 0 °C. After stirring for 30 min, the reaction was cooled to -78 °C and 3.00 g (9.23 mmol, 1.00 eq) of the aldehyde **9** were added slowly. The solution was allowed to warm to -20 °C over three hours. A saturated solution of ammonium chloride (50 mL) was added and the mixture extracted with Et<sub>2</sub>O (3x 30 mL). The combined organic layers were washed with sat. aq. NaCl solution,

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<sup>6</sup> K. Ando, *J. Org. Chem.* 1998, **63**, 8411.



dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. Flash chromatography (P/EtOAc = 99/1) gave 5.04 g (13.9 mmol, 75%) of (*S,Z*)-methyl 7-(triisopropylsilyloxy)oct-2-enoate.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 6.22 (dt, *J* = 11.5, 7.5 Hz, 1H), 5.77 (dt, *J* = 11.5, 1.7 Hz, 1H), 4.00 – 3.90 (m, 1H), 3.70 (s, 3H), 2.70 – 2.60 (m, 2H), 1.55 – 1.40 (m, 4H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.05 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 167.0, 150.9, 119.5, 68.4, 51.1, 39.6, 29.2, 24.9, 23.6, 18.3, 18.3, 12.7.

**MS** (EI, 70 eV), *m/z* (%): 285 [M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (100), 253 (53), 145 (66), 117 (35).

**HRMS** (C<sub>15</sub>H<sub>29</sub>O<sub>3</sub>Si) found: 285.1888  
calculated: 285.1886

**Rotation value** [α]<sub>D</sub><sup>20</sup> = –1.5 (c = 0.82, CH<sub>2</sub>Cl<sub>2</sub>)

#### **(*S,Z*)-7-(triisopropylsilyloxy)oct-2-en-1-ol**

At –78 °C, 6.30 mL (7.59 mmol, 3.00 eq) Dibal-H (1.2 M in Toluene) were added to a solution of 830 mg (2.53 mmol, 1.00 eq) (*S,Z*)-methyl 7-(triisopropylsilyloxy)oct-2-enoate in 25 mL THF. After stirring at –78 °C for 3 h, 20 mL of a 20% solution of K/Na-tartrate in H<sub>2</sub>O and 500 μL glycerine were added and the solution was stirred for 1 h and extracted with Et<sub>2</sub>O (3x 20 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub> and filtered. After removal of the solvents, flash chromatography (P/EtOAc = 9/1) gave 735 mg (2.44 mmol, 97%) of (*S,Z*)-7-(triisopropylsilyloxy)oct-2-en-1-ol as a transparent honey.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 5.65 – 5.49 (m, 2H), 4.19 (d, *J* = 6.1 Hz, 2H), 3.96 – 3.89 (m, 1H), 2.11 – 2.03 (m, 2H), 1.60 – 1.40 (m, 4H), 1.15 (d, *J* = 5.9 Hz, 3H), 1.05 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 133.2, 128.7, 68.5, 58.8, 39.6, 27.8, 25.4, 23.7, 23.6, 18.3, 12.7.

**MS** (EI, 70 eV), *m/z* (%): 257 [M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (16), 201 (8), 175 (8), 157 (9), 149 (21), 131 (90), 109 (100), 103 (50).

**HRMS** (C<sub>14</sub>H<sub>29</sub>O<sub>2</sub>Si) found: 257.1937  
calculated: 257.1937

**Rotation value** [α]<sub>D</sub><sup>20</sup> = +29.8 (c = 0.80, CH<sub>2</sub>Cl<sub>2</sub>)

**(S,Z)-7-(triisopropylsilyloxy)oct-2-enyl 2,2,2-trichloroacetimidate (10)**

56 mg (0.38 mmol, 1.00 eq) trichloroacetonitrile and 0.01 mL (0.033 mmol, 0.10 eq) DBU were added to a solution of 115 mg (0.38 mmol, 1.00 eq) (S,Z)-7-(triisopropylsilyloxy)oct-2-en-1-ol in 3.8 mL dichloromethane. After stirring for 18 h, the solution was diluted with sat. aq. NH<sub>4</sub>Cl (5 mL) and extracted with Et<sub>2</sub>O (3 x 5 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated. Flash chromatography (P/EtOAc = 95/5) gave 165 mg (0.37 mmol, 97%) of the product **10**.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 8.28 (s, 1H), 5.76-5.60 (m, 2H), 4.84 (d, *J* = 5.7 Hz, 2H), 3.86 – 3.89 (m, 1H), 2.15 (q, *J* = 7.0 Hz, 2H), 1.50 – 1.40 (m, 4H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.06 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 162.9, 136.3, 122.9, 77.4, 68.5, 65.4, 39.6, 28.1, 25.2, 23.7, 18.4, 18.3, 12.7.

**MS** (EI, 70 eV), *m/z* (%): 400 [M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>] (6), 294 (6), 292 (6), 276 (64), 274 (63), 141 (40), 109 (100).

**HRMS** (C<sub>16</sub>H<sub>29</sub>NO<sub>2</sub>Si<sup>35</sup>Cl<sub>3</sub>) found: 400.1023  
calculated: 400.1033

**Rotation value** [α]<sub>D</sub><sup>20</sup> = +2.4 (c = 0.80, CH<sub>2</sub>Cl<sub>2</sub>)

**(3R,7S)-7-(triisopropylsilyloxy)oct-1-en-3-yl 4-(4-methoxybenzyloxy)butanoate (11)**

To a solution of 54 mg (0.12 mmol, 1.00 eq) **10** and 45 mg (0.20 mmol, 1.50 eq) 4-(4-methoxy-benzyloxy)-butyric acid in 80 μL CH<sub>2</sub>Cl<sub>2</sub> were added 9 mg (0.006 mmol, 0.05 eq) (+)-COP-OAc and the solution was stirred in the dark for 16 h. Then further 15 mg of the acid were added. After stirring for 5 h, the solvents were removed *in vacuo* and the residue was purified by flash chromatography (P/EtOAc = 95/5 to 9/1) to yield 52 mg (0.10 mmol, 83%) of the product as a pure diastereoisomere. We were not able to obtain adequate MS data for this compound due to its instability.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 7.27 – 7.22 (m, 2H), 6.85 – 6.80 (m, 2H), 5.75 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H), 5.36 – 5.05 (m, 3H), 4.42 (s, 2H), 4.01 – 3.86 (m, 1H), 3.80 (s, 3H), 3.47 (t, *J* = 6.2 Hz, 2H), 2.42 (t, *J* = 7.5 Hz, 2H), 1.96 – 1.87 (m, 2H), 1.71 – 1.59 (m, 2H), 1.52 – 1.29 (m, 4H), 1.14 (d, *J* = 6.1 Hz, 3H), 1.05 (s, 21H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 172.9, 159.3, 136.8, 130.7, 129.4, 116.7, 113.9, 74.8, 72.7,

69.1, 68.5, 55.4, 39.8, 34.6, 31.5, 25.3, 23.6, 21.0, 18.3, 18.3, 12.7.

**(3*R*,7*S*)-7-hydroxyoct-1-en-3-yl 4-(4-methoxybenzyloxy)butanoate**

300  $\mu$ L HF (50% in H<sub>2</sub>O) were added to a solution of 72 mg (0.14 mmol, 1.00 eq) **11** in 1 mL MeCN and the mixture was stirred for 3 h. Sat. aq. NaHCO<sub>3</sub> (5 mL) was added and after 30 min, the solution was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent evaporated. Flash chromatography (P/EtOAc = 7/3) gave 39 mg (0.11 mmol, 79%) of the product (3*R*,7*S*)-7-hydroxyoct-1-en-3-yl 4-(4-methoxybenzyloxy)butanoate.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.27 – 7.23 (m, 2H), 6.87 (d,  $J$  = 8.7, 2H), 5.76 (ddd,  $J$  = 17.1, 10.5, 6.4 Hz, 1H), 5.24 – 5.08 (m, 3H), 4.42 (s, 2H), 3.90 - 3.65 (m, 4H), 3.48 (t,  $J$  = 6.2, 2H), 2.43 (t,  $J$  = 7.5 Hz, 2H), 2.00 – 1.82 (m, 2H), 1.75 – 1.58 (m, 2H), 1.49 – 1.25 (m, 4H), 1.18 (d,  $J$  = 6.2 Hz, 3H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 172.9, 159.3, 136.7, 130.7, 129.4, 116.8, 114.0, 74.7, 72.7, 69.1, 68.0, 55.4, 39.1, 34.3, 31.5, 25.3, 23.7, 21.4.

**HRMS** (C<sub>20</sub>H<sub>30</sub>O<sub>5</sub><sup>23</sup>Na) found: 373.1985

calculated: 373.1991

**Rotation value**  $[\alpha]_{\text{D}}^{20} = +1.3$  (c = 1.3, CH<sub>2</sub>Cl<sub>2</sub>)

**(3*R*,7*S*)-7-acetoxyoct-1-en-3-yl 4-(4-methoxybenzyloxy)butanoate**

To a solution of 62 mg (0.17 mmol, 1.00 eq) (3*R*,7*S*)-7-hydroxyoct-1-en-3-yl 4-(4-methoxybenzyl-oxy)butanoate in 170  $\mu$ L Ac<sub>2</sub>O were added 170  $\mu$ L pyridine and the solution was stirred for 3 h. Ice water (1 mL) was added and the aqueous phase was extracted with Et<sub>2</sub>O (3 x 1 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, and filtrated. After removal of the solvent, the residue was purified by flash chromatography (P/EtOAc = 95/5 to 9/1) to yield 53 mg (0.14 mmol, 83%) of the product (3*R*,7*S*)-7-acetoxyoct-1-en-3-yl 4-(4-methoxybenzyloxy)butanoate.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.30 – 7.23 (m, 2H), 6.98 – 6.83 (m, 2H), 5.83 – 5.65 (m, 1H), 5.28 – 5.10 (m, 3H), 4.89 – 4.81 (m, 1H), 4.42 (s, 2H), 3.80 (s, 3H), 3.47 (t,  $J$  = 6.2 Hz, 2H), 2.42 (t,  $J$  = 7.5 Hz, 2H), 2.02 (s, 3H), 1.92 (dt,  $J$  = 6.7, 13.6 Hz, 2H), 1.70 – 1.57 (m, 2H), 1.50 – 1.25 (m, 4H), 1.19 (d,  $J$  = 6.3 Hz, 3H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 172.9, 170.9, 159.3, 136.6, 130.7, 129.4, 116.9, 113.9, 74.6, 72.7, 70.8, 69.1, 55.4, 35.7, 34.1, 31.5, 25.3, 21.5, 21.1, 20.1.

**HRMS** (C<sub>22</sub>H<sub>32</sub>O<sub>6</sub><sup>23</sup>Na) found: 415.2090  
calculated: 415.2097

**Rotation value**  $[\alpha]_{\text{D}}^{20} = -0.631$  (c = 0.908, CH<sub>2</sub>Cl<sub>2</sub>).

### **(2*S*,6*R*)-6-hydroxyoct-7-en-2-yl acetate (3)**

To a solution of 50 mg (0.13 mmol, 1.00 eq) (3*R*,7*S*)-7-acetoxyoct-1-en-3-yl 4-(4-methoxybenzyl-oxy)butanoate in 720 μL CH<sub>2</sub>Cl<sub>2</sub> and 720 μL pH7 buffer were added 41 mg (0.18 mmol, 1.40 eq) DDQ and the solution was stirred for 3.5 h. Sat. aq. NaHCO<sub>3</sub> (3 mL) was added and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 2 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent evaporated. The residue was treated with 2 mg (0.017 mmol, 0.15 eq) KO*t*Bu in 2 mL THF for 5 min. The mixture was neutralized with 50 μL glacial acetic acid and extracted with EtOAc (2 x 5 mL). The combined organic layers were washed with sat. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated and the solvent evaporated. Flash chromatography (P/EtOAc = 9/1) gave 21 mg (0.11 mmol, 87%) of **3**.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 5.85 (ddd, *J* = 16.9, 10.4, 6.2 Hz, 1H), 5.22 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.10 (dt, *J* = 10.4, 1.2 Hz, 1H), 4.94 – 4.84 (m, 1H), 4.09 (m, 1H), 2.02 (s, 3H), 1.70 – 1.32 (m, 6H), 1.21 (d, *J* = 6.3 Hz, 3H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 170.9, 141.3, 114.9, 73.2, 71.0, 36.9, 35.9, 21.5, 21.4, 20.1.

**MS** (EI, 70 eV), *m/z* (%): 169 [M<sup>+</sup> – OH] (1), 130 (4), 126 (8), 115 (8), 111 (9).

**HRMS** (C<sub>10</sub>H<sub>17</sub>O<sub>2</sub>) found: 169.1248  
calculated: 169.1229

**Rotation value**  $[\alpha]_{\text{D}}^{20} = -3.22$  (c = 1.469, CH<sub>2</sub>Cl<sub>2</sub>)

### **Synthesis of (+)-chloriolide (1)**

#### **(*S,E*)-methyl-4-(((3*R*,7*S*)-7-acetoxyoct-1-en-3-yloxy)diisopropylsilyloxy)hexa-2,5-dienoate (12)**

To a solution of 650 mg (3.50 mmol, 10.0 eq) dichlorodiisopropylsilane in 3.5 mL pyridine were slowly added 50 mg (0.35 mmol, 0.10 eq) **2** in 3.5 mL pyridine.<sup>7</sup> After stirring for 19 h,

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<sup>7</sup> B. A. Harrison, G. L. Verdine, *Org. Lett.* 2001, **3**, 2157.

the solvent and the excess silane were removed *in vacuo* ( $10^{-2}$  mbar, 40 °C). 71 mg (0.42 mmol, 1.20 eq) **3** in 5 mL pyridine were added and the solution stirred for further 18 h. The solvents were removed *in vacuo* and the crude product was dissolved in water and Et<sub>2</sub>O. the aqueous phase was extracted with Et<sub>2</sub>O (3 x 10 mL) and the combined organic phases were washed with sat. aq. NaCl, dried over Na<sub>2</sub>SO<sub>4</sub>, and filtered. After removal of the solvent, flash chromatography (P/EtOAc = 95/5 to 9/1) gave 118 mg (0.27 mmol, 77%) of the product **12**.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 6.90 (dd, *J* = 15.5, 4.6 Hz, 1H), 6.06 (dd, *J* = 15.5, 1.7 Hz, 1H), 5.77 (ddd, *J* = 16.5, 10.3, 6.1 Hz, 2H), 5.28 (dt, *J* = 17.2, 1.3 Hz, 1H), 5.19 – 5.01 (m, 3H), 5.01 – 4.93 (m, 1H), 4.90 – 4.84 (m, 1H), 4.30 – 4.26 (m, 1H), 3.74 (s, 3H), 2.01 (s, 3H), 1.54 – 1.26 (m, 6H), 1.19 (d, *J* = 6.3 Hz, 3H), 1.11 – 0.89 (m, 14H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 170.9, 167.1, 149.5, 141.0, 138.2, 119.4, 115.6, 114.4, 73.7, 72.7, 71.0, 51.7, 37.9, 36.1, 21.5, 20.6, 20.0, 17.5, 12.8, 12.8.

**MS** (EI, 70 eV), *m/z* (%): 397 [*M*<sup>+</sup> – *iPr*] (3), 311 (21), 229 (38), 147 (45).

**HRMS** (C<sub>20</sub>H<sub>33</sub>O<sub>6</sub>Si) found: 397.2044

calculated: 397.2047

**Rotation value** [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +1.8 (*c* = 0.92, CH<sub>2</sub>Cl<sub>2</sub>)

**(*E*)-methyl-3-((4*S*,7*R*)-7-((*S*)-4-acetoxypentyl)-2,2-diisopropyl-4,7-dihydro-1,3,2-dioxasilepin-4-yl)acrylate**

A solution of 35 mg (0.079 mmol, 1.00 eq) **12** in 20 mL toluene was degassed (3 x freeze-pump-thaw), then 2.30 mg (0.003 mmol, 0.03 eq) Grubbs-II catalyst were added and the solution was degassed again. It was stirred at 70 °C for 18 h, before the solvent was removed *in vacuo* and the residue was purified by flash chromatography (P/EtOAc = 98/2 to 95/5). 28 mg (0.068 mmol, 86%) of (*E*)-methyl 3-((4*S*,7*S*)-7-((*R*)-4-acetoxypentyl)-2,2-diisopropyl-4,7-dihydro-1,3,2-dioxasilepin-4-yl)acrylate could be isolated.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>): δ = 6.98 (dd, *J* = 15.3, 3.8 Hz, 1H), 6.17 (dd, *J* = 15.3, 2.1 Hz, 1H), 5.54 (d, *J* = 0.6 Hz, 2H), 5.38 – 5.35 (m, 1H), 4.97 – 4.84 (m, 1H), 4.68 – 4.62 (m, 1H), 3.75 (s, 3H), 2.02 (s, 3H), 1.70 – 1.37 (m, 6H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.12 – 0.97 (m, 14H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>): δ = 170.9, 167.3, 148.8, 135.6, 130.2, 119.5, 71.1, 70.8, 70.4, 51.7, 37.8, 35.9, 21.5, 21.4, 20.1, 17.4, 12.5, 12.5.

**MS** (EI, 70 eV), *m/z* (%): 359 (2), 287 (6), 227 (14), 147 (54), 99 (100).



– 4.36 (m, 1H), 3.74 (s, 3H), 2.02 (s, 3H), 1.70 – 1.33 (m, 6H), 1.21 (d,  $J = 6.3$  Hz, 3H), 1.05 – 0.77 (m, 18H), 0.09 – 0.02 (m, 12H).

$^{13}\text{C}$  NMR (90.6 MHz,  $\text{CDCl}_3$ ):  $\delta = 170.8, 167.1, 149.0, 134.9, 129.2, 119.5, 70.9, 69.0, 68.7, 51.7, 38.3, 36.0, 26.0, 25.9, 21.5, 21.1, 20.0, 18.3, 18.3, -4.0, -4.3, -4.3, -4.4$ .

MS (EI, 70 eV),  $m/z$  (%): 528 [ $\text{M}^+$ ] (1), 471 (4), 439 (6), 399 (8), 337 (18), 205 (17), 145 (29), 117 (72).

Rotation value  $[\alpha]_{\text{D}}^{20} = +70.4$  ( $c = 1.02, \text{CH}_2\text{Cl}_2$ )

#### **(2E,4R,5Z,7R,11S)-4,7-bis(*tert*-butyldimethylsilyloxy)dodeca-2,5-diene-1,11-diol**

550  $\mu\text{L}$  (0.55 mmol, 5 eq) Dibal-H (1 M) was added to a solution of 55 mg (0.11 mmol, 1.00 eq) **13** in 1.1 mL  $\text{CH}_2\text{Cl}_2$  at  $-78$  °C. After stirring for 1.5 h, 1 mL of a solution of 20% K/Na-tartrate in  $\text{H}_2\text{O}$  and 200  $\mu\text{L}$  glycerine were added to the solution which was allowed to warm to rt. It was extracted with  $\text{Et}_2\text{O}$  (3 x 1 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over  $\text{Na}_2\text{SO}_4$ , filtrated, and the solvent evaporated. The residue was purified on a silica-gel column (P/EtOAc = 8/2 to 7/3). 51 mg (0.11 mmol, quant.) of (2E,4R,5Z,7R,11S)-4,7-bis(*tert*-butyldimethylsilyloxy)dodeca-2,5-diene-1,11-diol were obtained.

$^1\text{H}$  NMR (360 MHz,  $\text{CDCl}_3$ ):  $\delta = 5.94 - 5.62$  (m, 2H), 5.42 - 5.22 (m, 2H), 4.98 – 4.81 (m, 1H), 4.46 – 4.39 (m, 1H), 4.15 (d,  $J = 5.2$  Hz, 2H), 3.80 (d,  $J = 4.5$  Hz, 1H), 1.50 – 1.30 (m, 6H), 1.19 (d,  $J = 6.2$  Hz, 3H), 0.88 (d,  $J = 4.6$  Hz, 18H), 0.08 – –0.02 (m, 12H).

$^{13}\text{C}$  NMR (90.6 MHz,  $\text{CDCl}_3$ ):  $\delta = 133.9, 133.4, 130.7, 129.0, 69.5, 69.1, 68.2, 63.3, 39.5, 38.5, 26.0, 23.6, 21.6, 18.3, 18.3, -3.9, -4.0, -4.2, -4.3$ .

MS (EI, 70 eV),  $m/z$  (%): 401 [ $\text{M}^+ - \text{C}_4\text{H}_9$ ] 383 [ $\text{M}^+ - \text{C}_4\text{H}_9 - \text{H}_2\text{O}$ ] (6), 309 (12), 291 (4), 269 (30), 239 (14), 177 (15), 159 (22), 147 (23), 119 (32).

HRMS ( $\text{C}_{20}\text{H}_{41}\text{O}_4\text{Si}_2$ ) found: 401.2565

calculated: 401.2543

Rotation value  $[\alpha]_{\text{D}}^{20} = +25.6$  ( $c = 0.65, \text{CH}_2\text{Cl}_2$ )

#### **(2E,4S,5Z,7R,11S)-4,7-bis(*tert*-butyldimethylsilyloxy)-11-hydroxydodeca-2,5-dienoic acid (14)**

To a solution of 10 mg (0.022 mmol, 1.00 eq) (2E,4R,5Z,7R,11S)-4,7-bis(*tert*-butyldimethylsilyloxy)dodeca-2,5-diene-1,11-diol in 400  $\mu\text{L}$   $\text{CH}_2\text{Cl}_2$  were added 43 mg (0.49

mmol, 22 eq) MnO<sub>2</sub>. After stirring for 4 h, the solution was filtered through a pad of celite and the solvent was removed *in vacuo*. The residue was dissolved in 1 mL *t*BuOH and 500  $\mu$ L H<sub>2</sub>O, 15 mg (0.163 mmol, 7.50 eq) NaClO<sub>2</sub>, 25 mg (0.163 mmol, 7.50 eq) NaH<sub>2</sub>PO<sub>4</sub>, and 250  $\mu$ L 2-methyl-2-butene were added. After three hours, 1 mL sat. aq. NH<sub>4</sub>Cl was added and the mixture extracted with EtOAc (3 x 2 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was evaporated. 9 mg (0.019 mmol, 87%) of **14** were isolated.

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.01 (dd, *J* = 15.4, 4.4 Hz, 1H), 6.03 (dd, *J* = 15.4, 1.6 Hz, 1H), 5.54 – 5.36 (m, 1H), 5.22 (dd, *J* = 11.7, 8.3 Hz, 1H), 5.17 – 5.02 (m, 1H), 4.48 - 4.40 (m, 1H), 3.91 – 3.72 (m, 1H), 1.54 – 1.36 (m, 6H), 1.19 (d, *J* = 6.2 Hz, 3H), 0.92 – 0.86 (m, 18H), 0.09 – 0.02 (m, 12H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 171.0, 151.3, 135.1, 129.0, 119.0, 69.4, 68.7, 68.2, 39.4, 38.4, 26.0, 25.9, 23.6, 21.5, 18.3, 18.3, -4.0, -4.3, -4.3, -4.4.

**MS** (EI, 70 eV): 471 [M<sup>+</sup> – H] (34), 339 (9), 277 (23), 207 (43), 147 (54), 133 (23).

**HRMS** (C<sub>24</sub>H<sub>48</sub>O<sub>5</sub>NaSi<sub>2</sub>) found: 495.2933

calculated: 495.2938

**Rotation value** [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +72.5 (c = 0.27, CH<sub>2</sub>Cl<sub>2</sub>)

**(3*E*,5*S*,6*Z*,8*R*,12*S*)-5,8-bis(*tert*-butyldimethylsilyloxy)-12-methyloxacyclododeca-3,6-dien-2-one**

To a solution of 13 mg (0.027 mmol, 1.00 eq) **15** in 750  $\mu$ L THF were added 5  $\mu$ L (0.041 mmol, 1.50 eq) NEt<sub>3</sub> and 8  $\mu$ L (0.032 mmol, 1.20 eq) 2,4,6-trichlorobenzoylchloride.<sup>8</sup> The solution was stirred for 3 h. Meanwhile, 10 mg (0.089 mmol, 3.30 eq) DMAP in 30 mL benzene were stirred for 15 min. 20 mL benzene were added to the first THF solution, which was then slowly added to the DMAP solution and stirred for further 18 h. The solvents were removed *in vacuo*, and the residue was dissolved in 20 mL Et<sub>2</sub>O and 10 mL sat. NaHCO<sub>3</sub> and extracted with Et<sub>2</sub>O (3 x 20 mL). The combined organic layers were washed with sat. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent evaporated. The residue was purified by flash chromatography (P/EtOAc = 98/2). 8 mg (0.018 mmol, 65%) of (3*E*,5*S*,6*Z*,8*R*,12*S*)-5,8-bis(*tert*-butyldimethylsilyloxy)-12-methyloxacyclododeca-3,6-dien-2-one were obtained.

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<sup>8</sup> B. B. Snyder, J. Zhou, *Org. Lett.* 2006, **8**, 1283.



**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.41 – 7.28 (m, 1H), 6.13 (dd, *J* = 15.7, 2.4 Hz, 1H), 5.53 – 5.40 (m, 2H), 5.21 – 5.08 (m, 1H), 4.84 – 4.80 (m, 1H), 4.67 – 4.55 (m, 1H), 1.83 – 1.56 (m, 4H), 1.34 – 1.25 (m, 5H), 0.93 (s, 9H), 0.84 (s, 9H), 0.11 – 0.06 (m, 6H), 0.01 – -0.02 (m, 6H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 166.7, 154.0, 140.8, 125.6, 119.2, 73.7, 70.4, 68.5, 37.2, 34.3, 26.0, 26.0, 21.7, 19.8, 18.4, 18.2, -3.9, -4.4, -4.7, -4.9.

**MS** (EI, 70 eV), *m/z* (%): 454 [M<sup>+</sup>] (27), 397 [M<sup>+</sup> – 57] (27), 265 (10), 239 (14), 147 (71).

**HRMS** (C<sub>24</sub>H<sub>46</sub>O<sub>4</sub>Si<sub>2</sub>) found: 454.2938

calculated: 454.2935

### Chloriolide (1)

To a solution of 6 mg (0.013 mmol, 1.00 eq) (3*E*,5*S*,6*Z*,8*R*,12*S*)-5,8-bis(*tert*-butyldimethylsilyloxy)-12-methyloxacyclododeca-3,6-dien-2-one in 300  $\mu$ L MeCN were added 100  $\mu$ L HF (50% in H<sub>2</sub>O). After stirring for 2 h, sat. aq. NaHCO<sub>3</sub> (1 mL) was added and the stirring continued for 1 h. The mixture was extracted with EtOAc (3 x 2 mL). The combined organic layers were washed with sat. aq. NaCl solution, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and the solvent was evaporated. The residue was purified by flash chromatography (P/EtOAc = 1/1). 3 mg (0.013 mmol, quant.) of the product were obtained as a white powder. Characterization data for the synthetic (+)-chloriolide (<sup>1</sup>H NMR, <sup>13</sup>C NMR, LRMS, HRMS, optical rotation) was indistinguishable from that reported for the natural occurring material.<sup>9</sup>

**<sup>1</sup>H NMR** (360 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.30 (dd, *J* = 16.0, 2.9 Hz, 1H), 6.16 (dd, *J* = 16.0, 2.4 Hz, 1H), 5.73 (ddd, *J* = 11.7, 7.4, 1.2 Hz, 1H), 5.58 (dd, *J* = 11.8, 8.2 Hz, 1H), 5.20 – 5.08 (m, 1H), 4.89 (dt, *J* = 7.3, 2.5 Hz, 1H), 4.61 (br t, *J* = 9.3 Hz, 1H), 1.92 – 1.39 (m, 6H), 1.33 (d, *J* = 6.4 Hz, 3H).

**<sup>13</sup>C NMR** (90.6 MHz, CDCl<sub>3</sub>):  $\delta$  = 166.7, 152.7, 140.6, 126.8, 119.9, 74.0, 69.9, 68.2, 36.4, 34.4, 21.6, 19.8.

**MS** (EI, 70 eV), *m/z* (%): 208 [M<sup>+</sup> – H<sub>2</sub>O] (1), 182 (4), 165 (6), 154 (100), 125 (30), 99 (59), 84 (85).

**HRMS** (C<sub>12</sub>H<sub>16</sub>O<sub>3</sub>) found: 208.1100

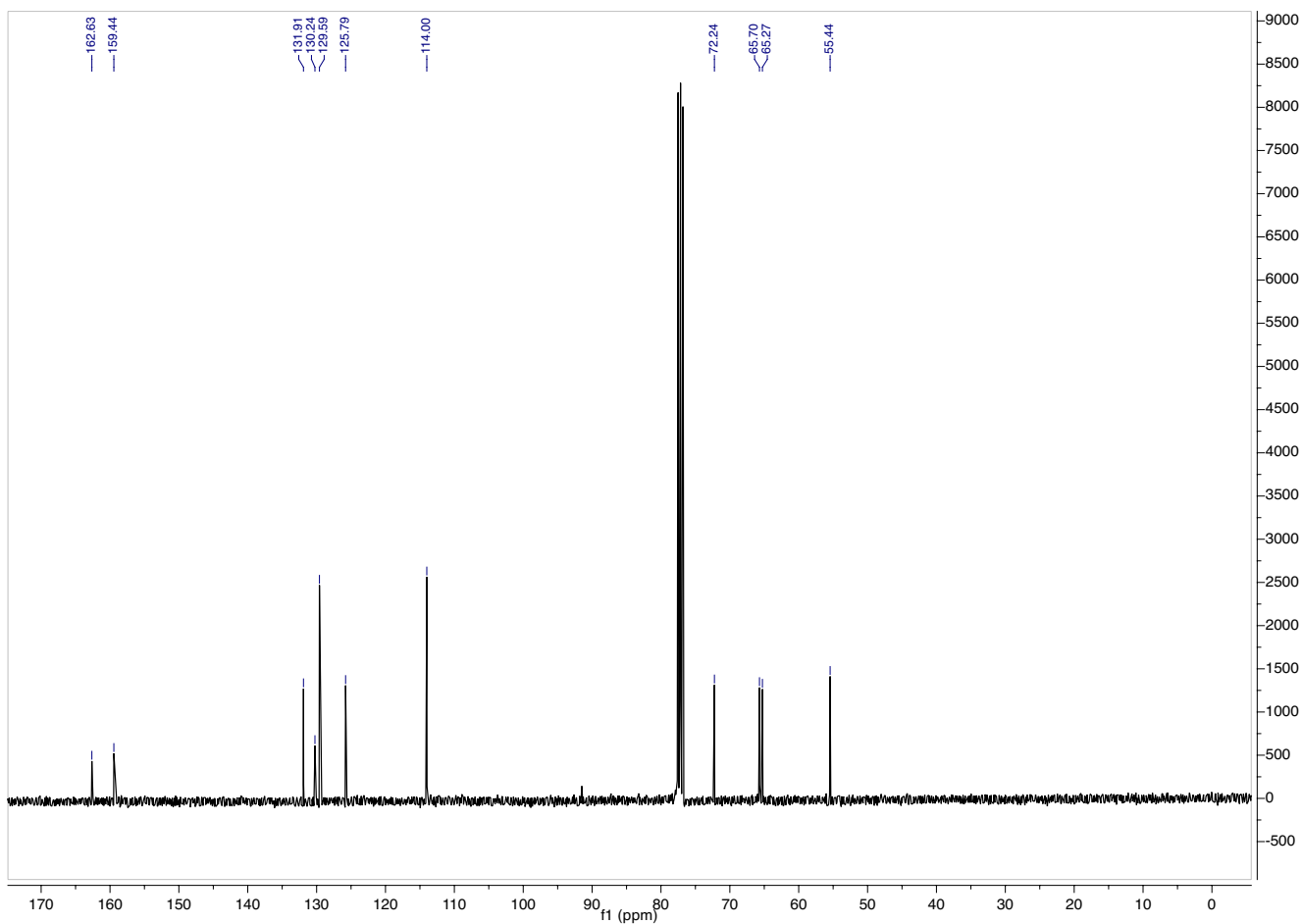
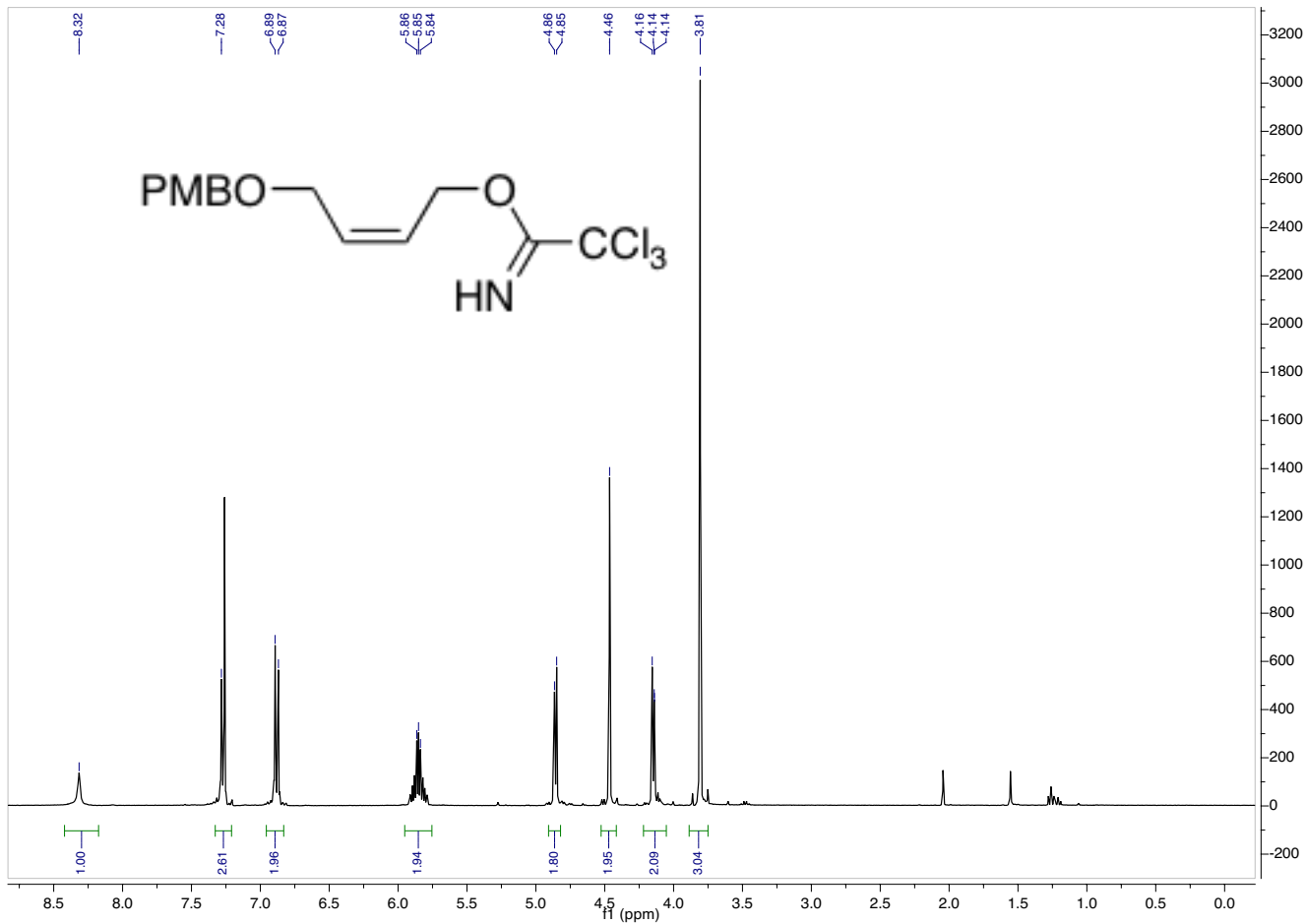
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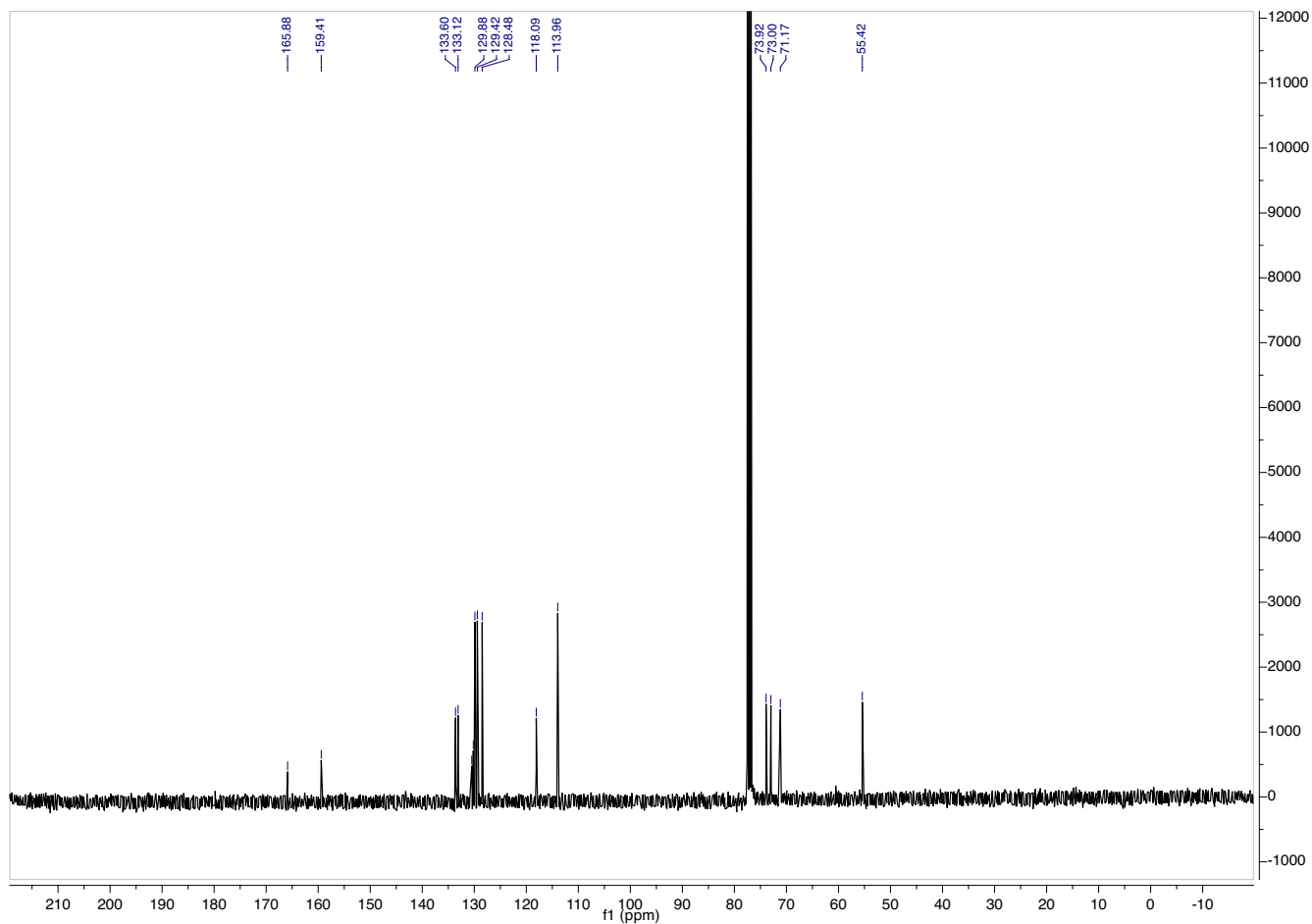
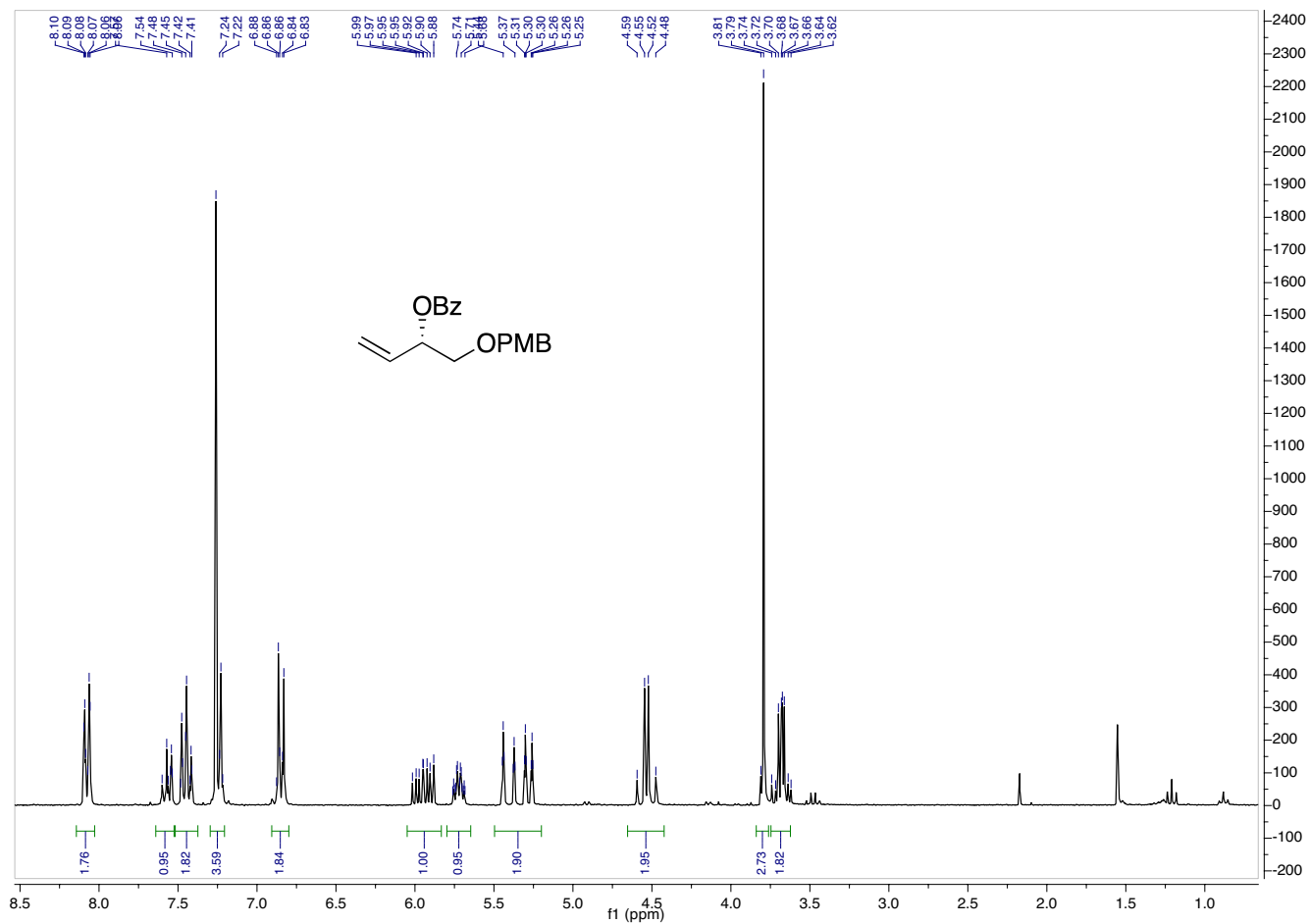
<sup>9</sup> P. Jiao, D. C. Swenson, J. B. Gloer, D. T. Wicklow, *J. Nat. Prod.* 2006, **69**, 636.

calculated: 208.1099

**Rotation value**  $[\alpha]_D^{20} = +101$  (c = 0.2, CH<sub>2</sub>Cl<sub>2</sub>) (Literature: +107 (c = 0.2, CH<sub>2</sub>Cl<sub>2</sub>)).

**T<sub>m</sub>** = 162.8 °C (decomp.).



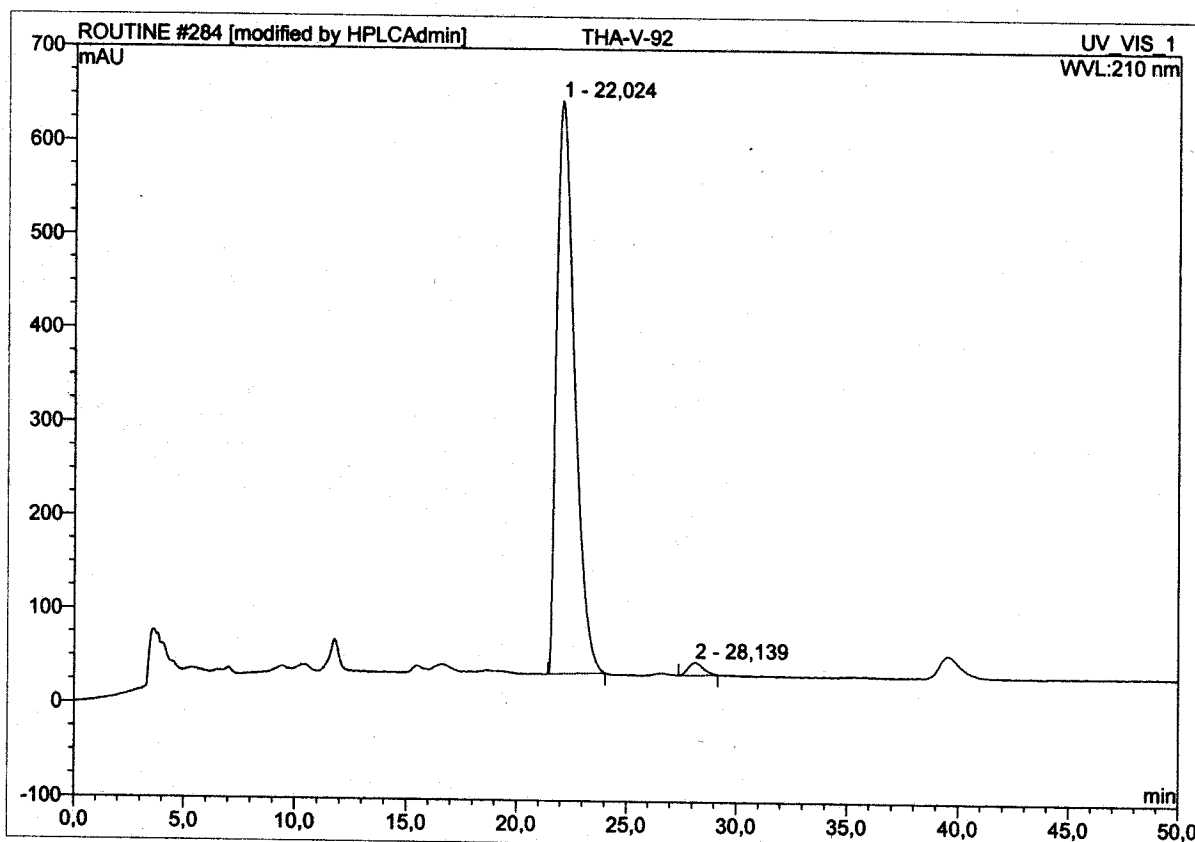


### 284 THA-V-92

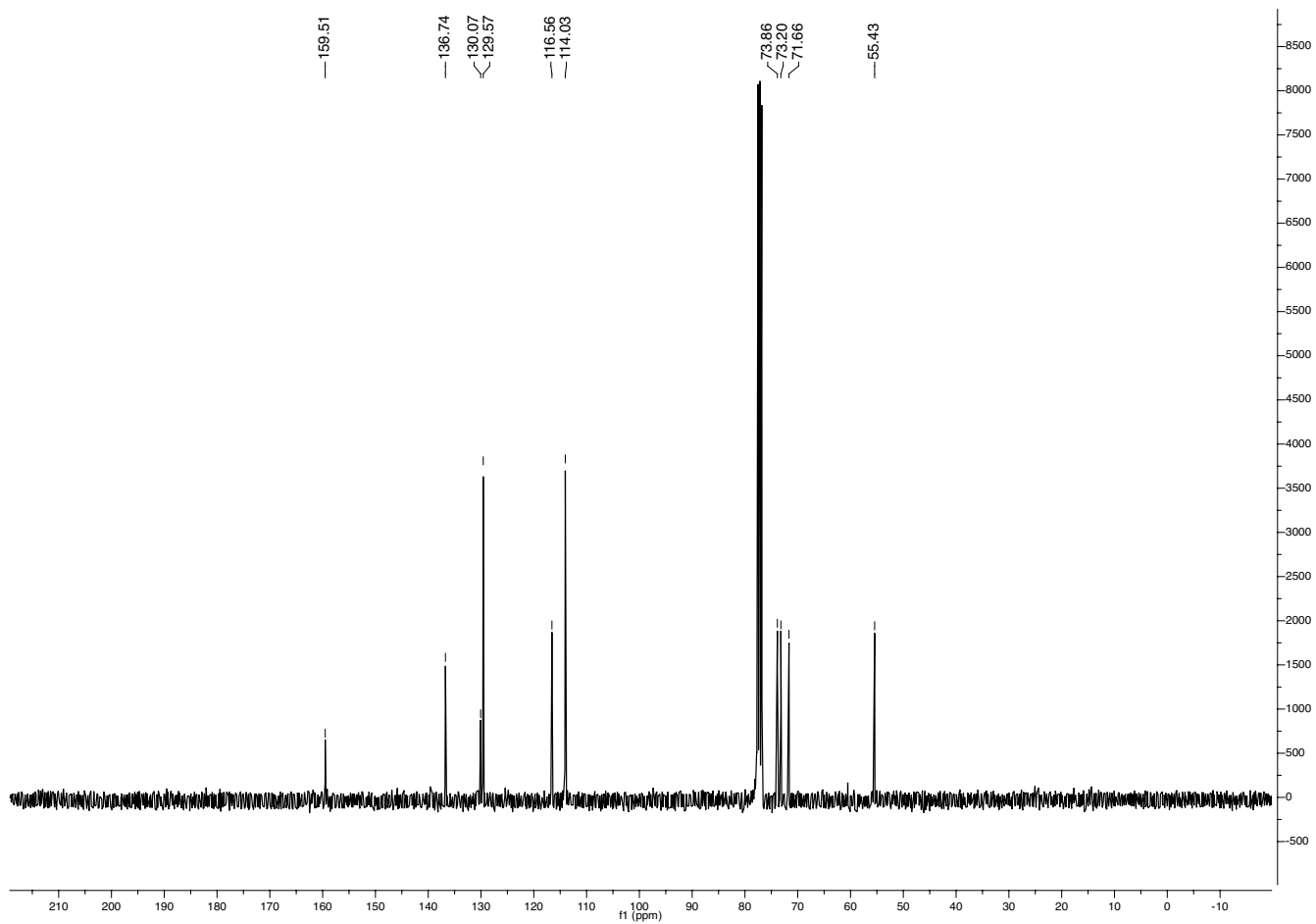
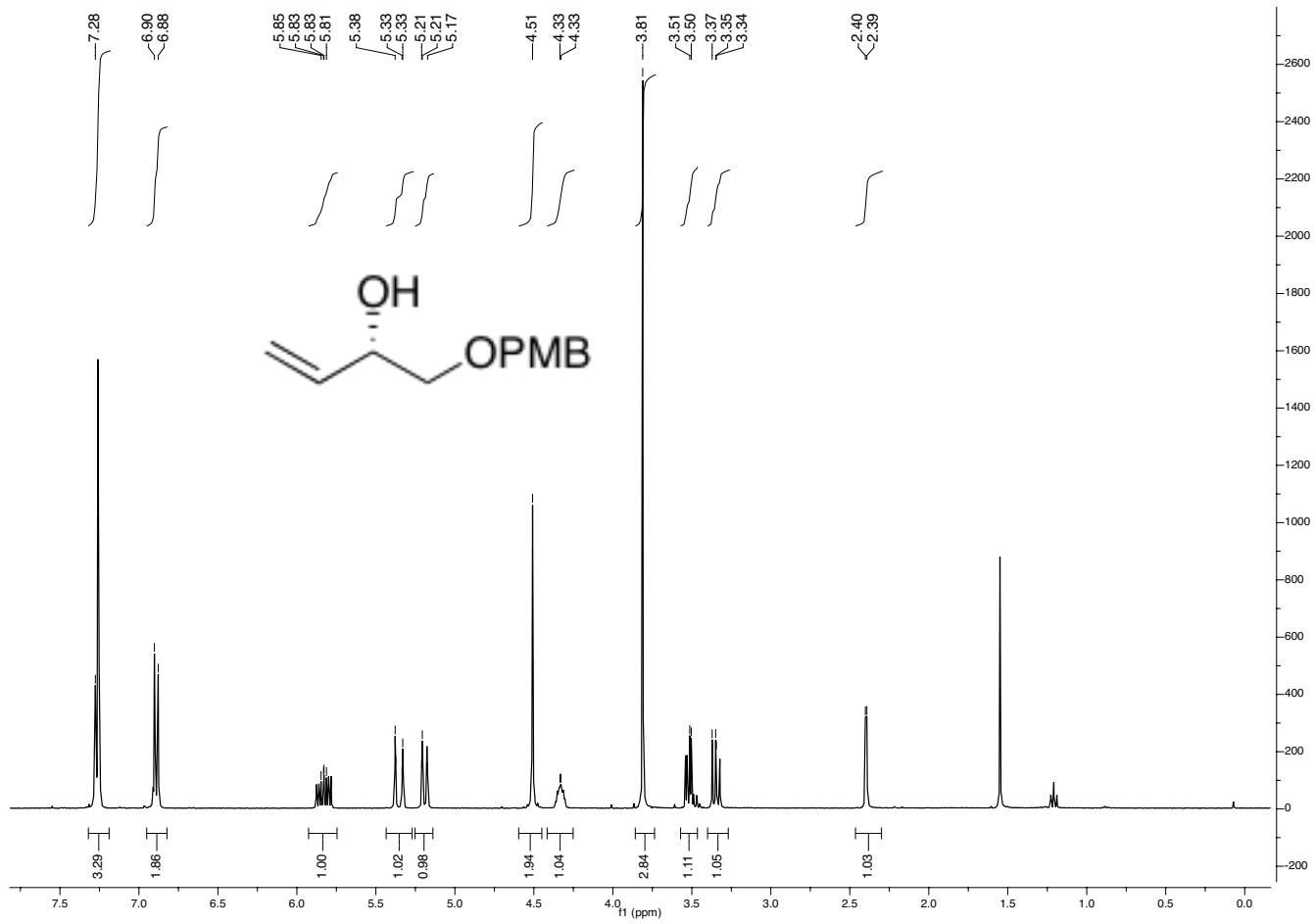


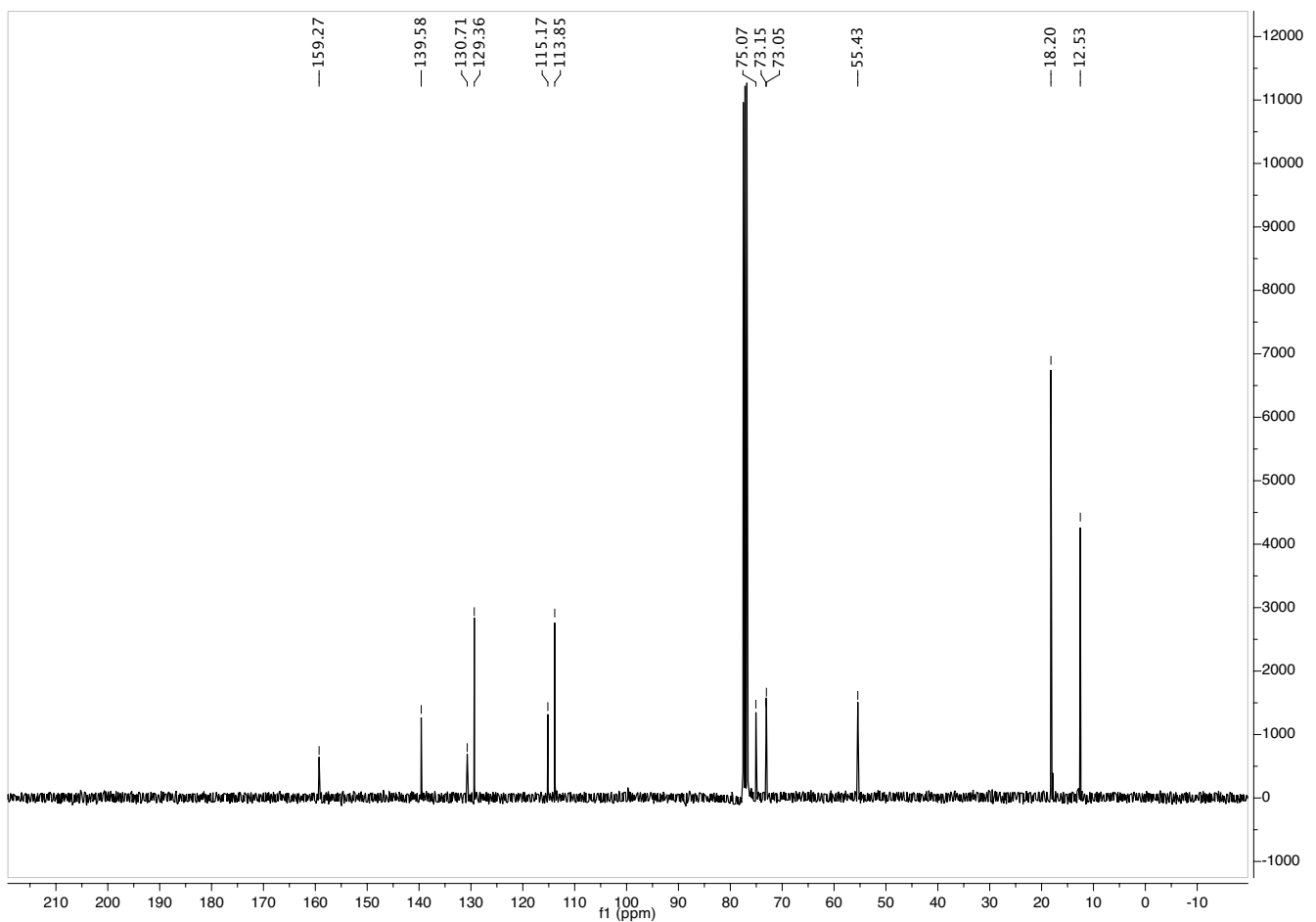
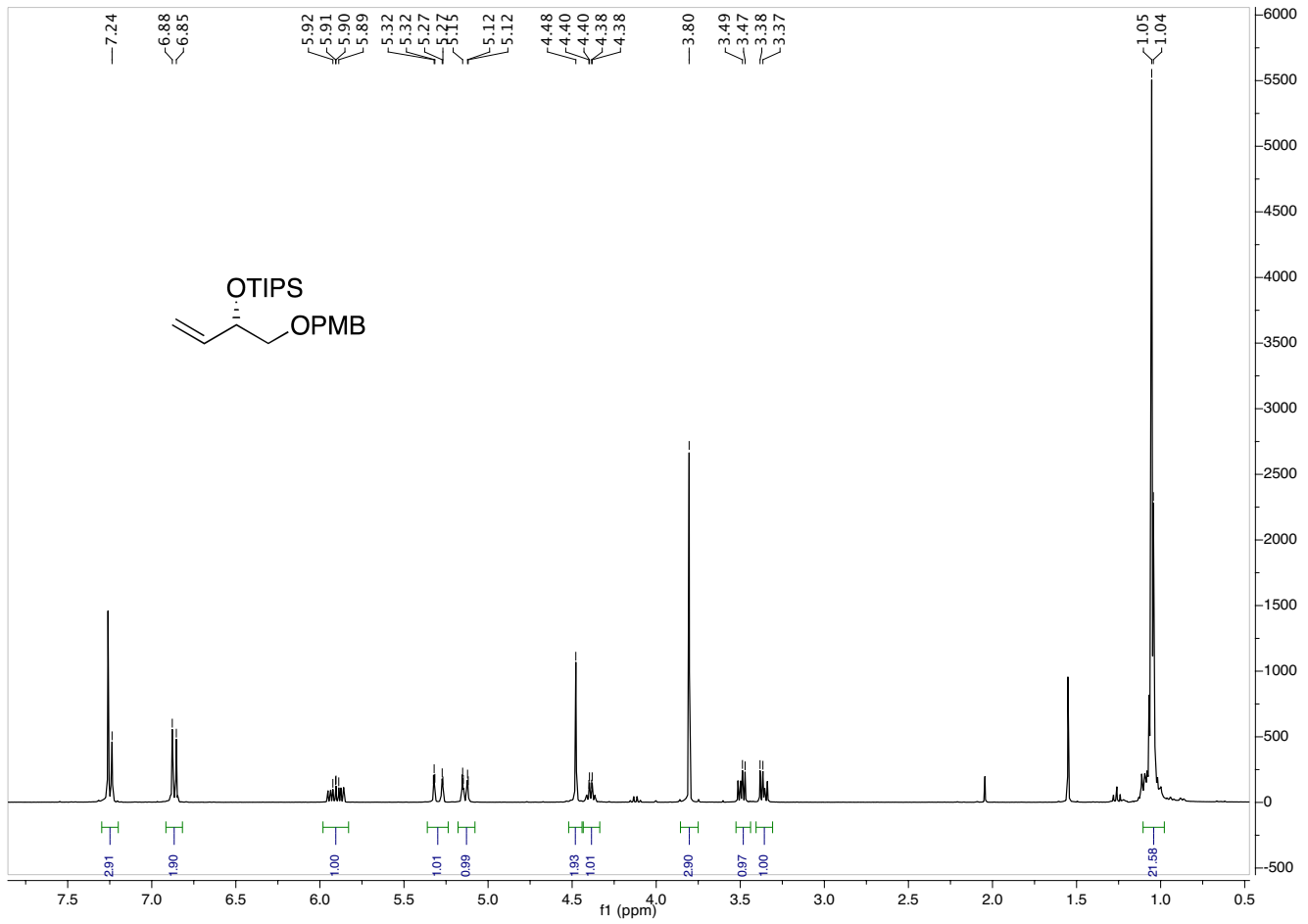
Daicel Chiralpak OJ-H, 250x4.6

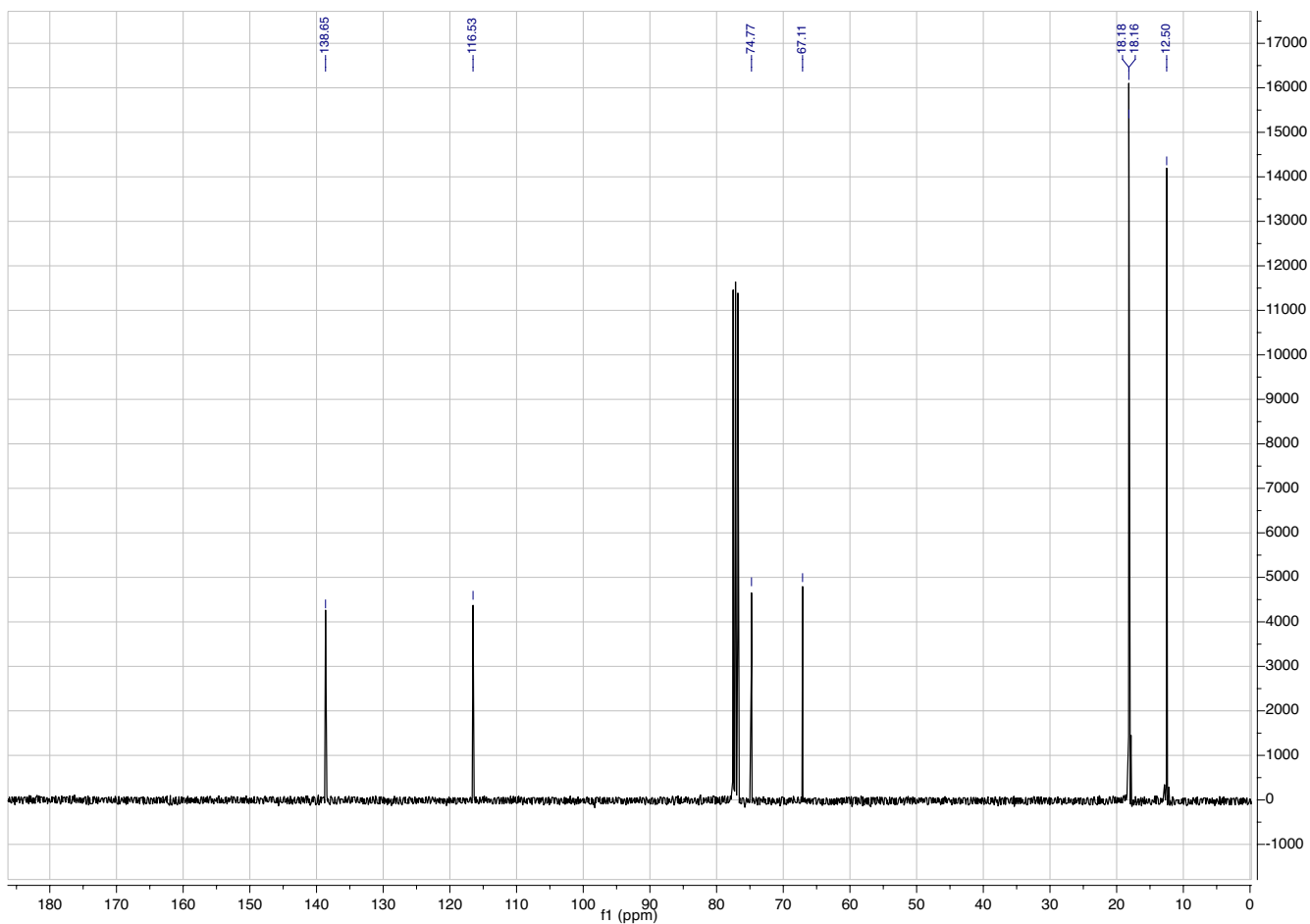
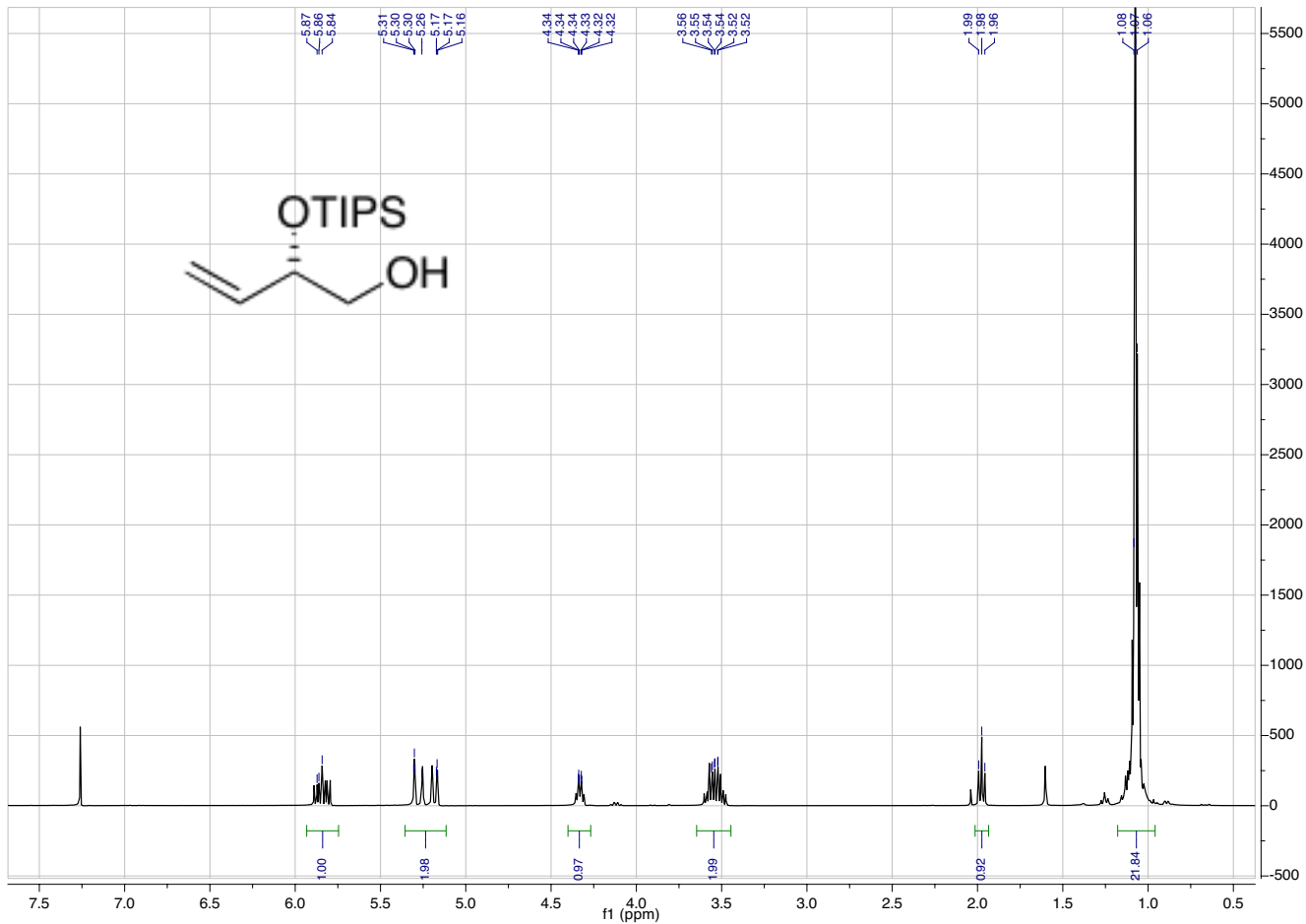
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Vial Number:	RA11	Channel:	UV_VIS_1
Sample Type:	unknown	Wavelength:	210
Control Program:	Säule2_NP_ISO_90_10_1_50_oV	Bandwidth:	1
Quantif. Method:	gradA	Dilution Factor:	1,0000
Recording Time:	22.4.2009 13:17	Sample Weight:	1,0000
Run Time (min):	50,00	Sample Amount:	1,0000



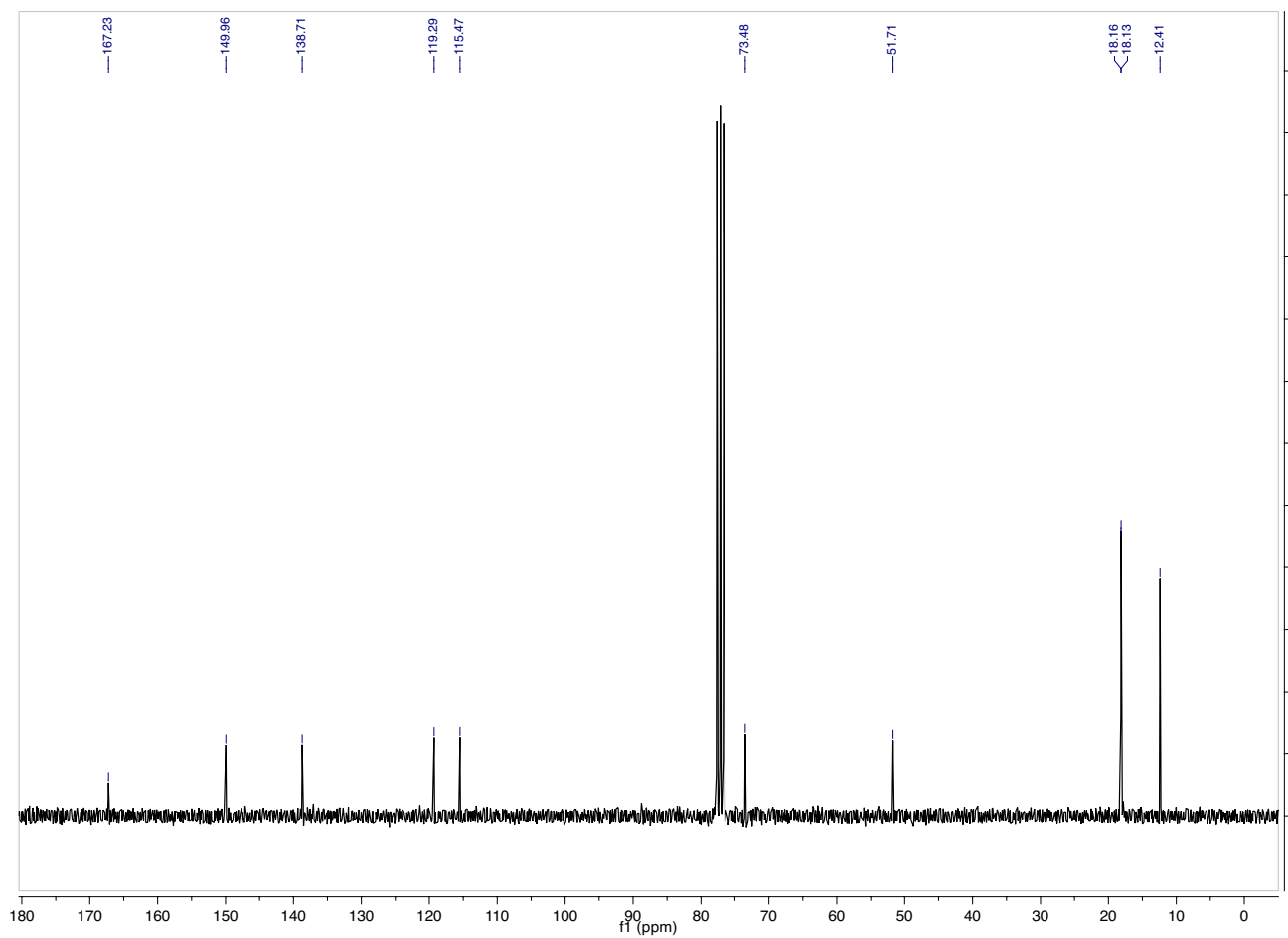
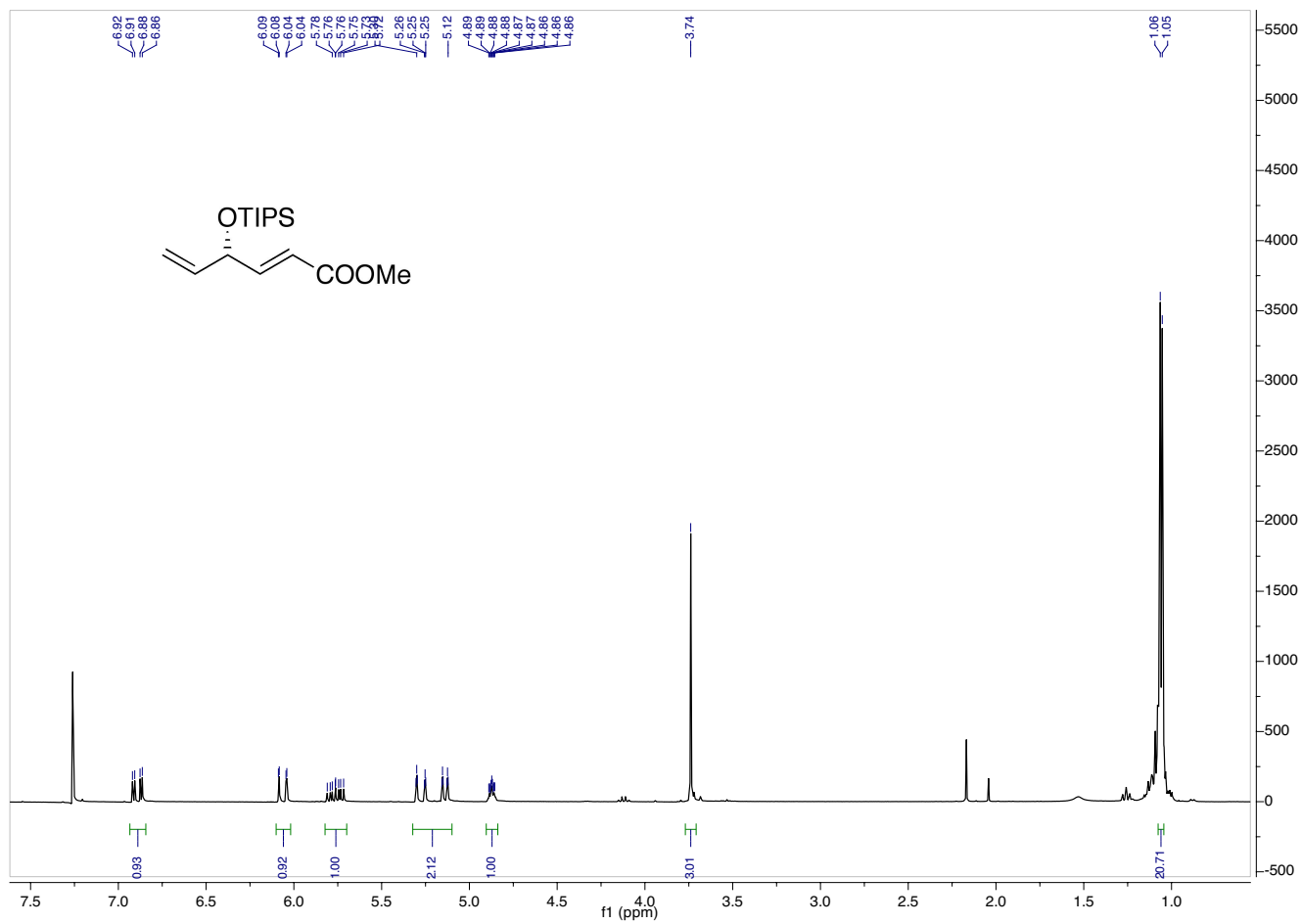
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2	28,14	n.a.	13,285	10,742	1,82	n.a.	BMB*
<b>Total:</b>			623,462	589,667	100,00	0,000	

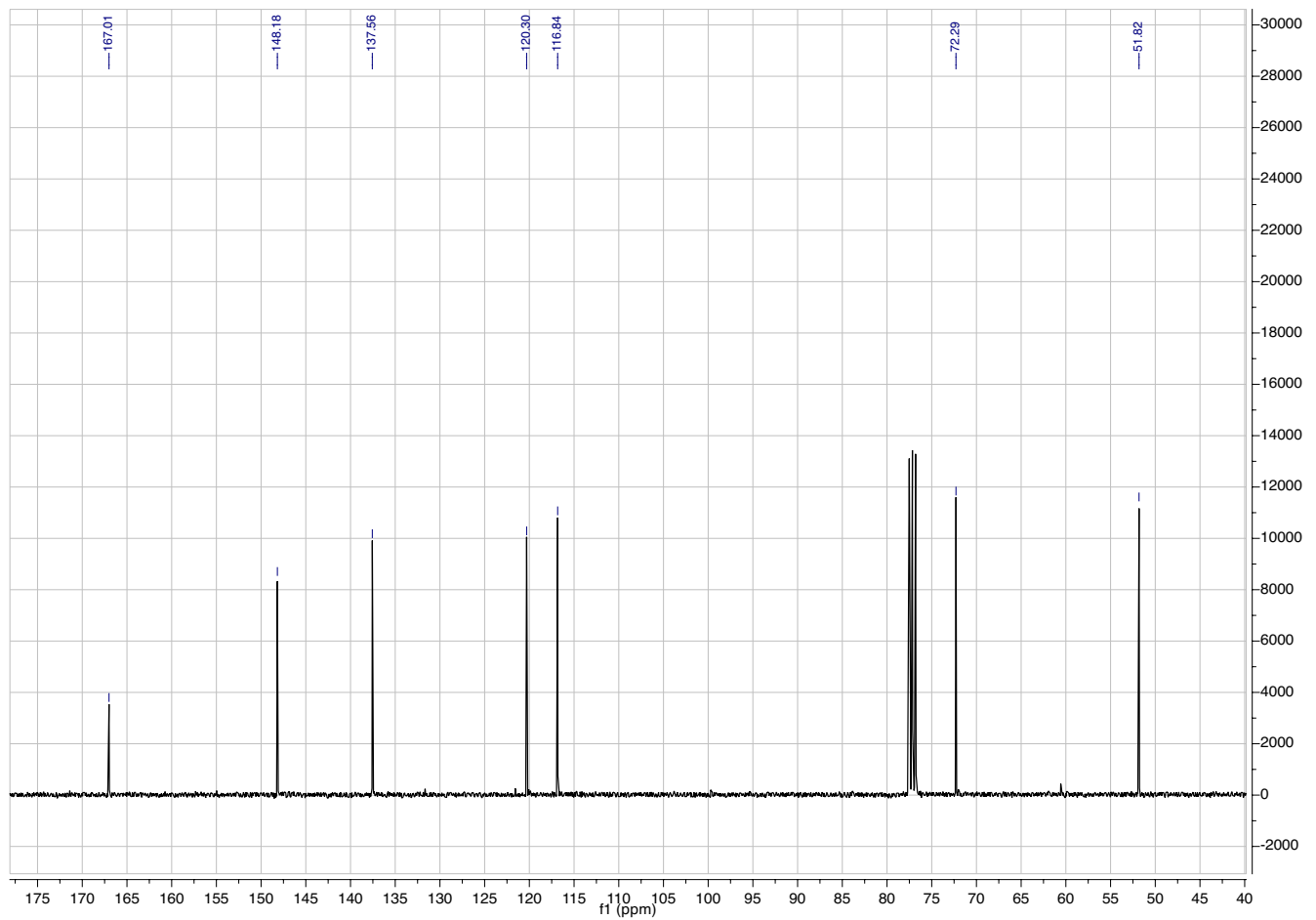
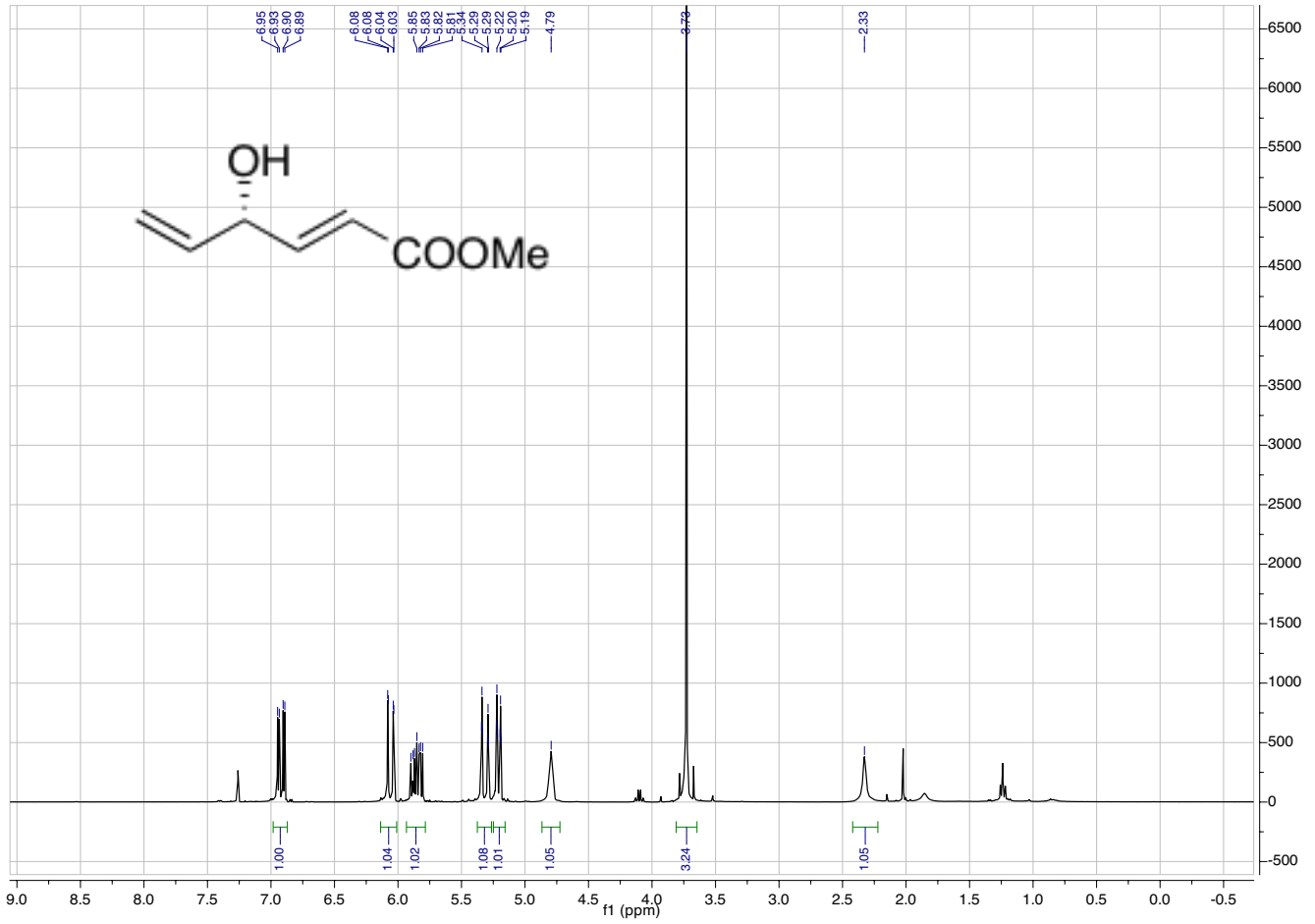


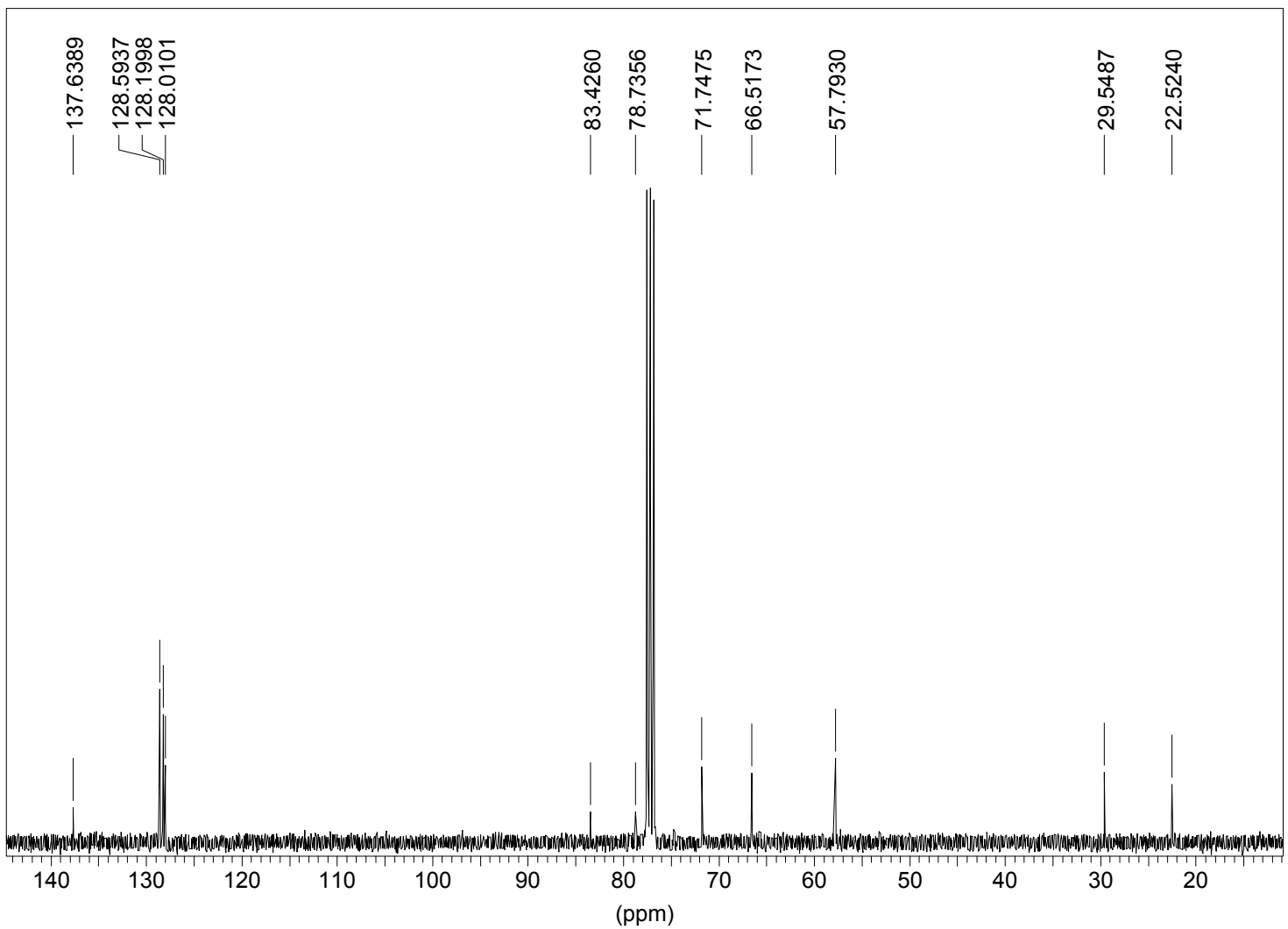
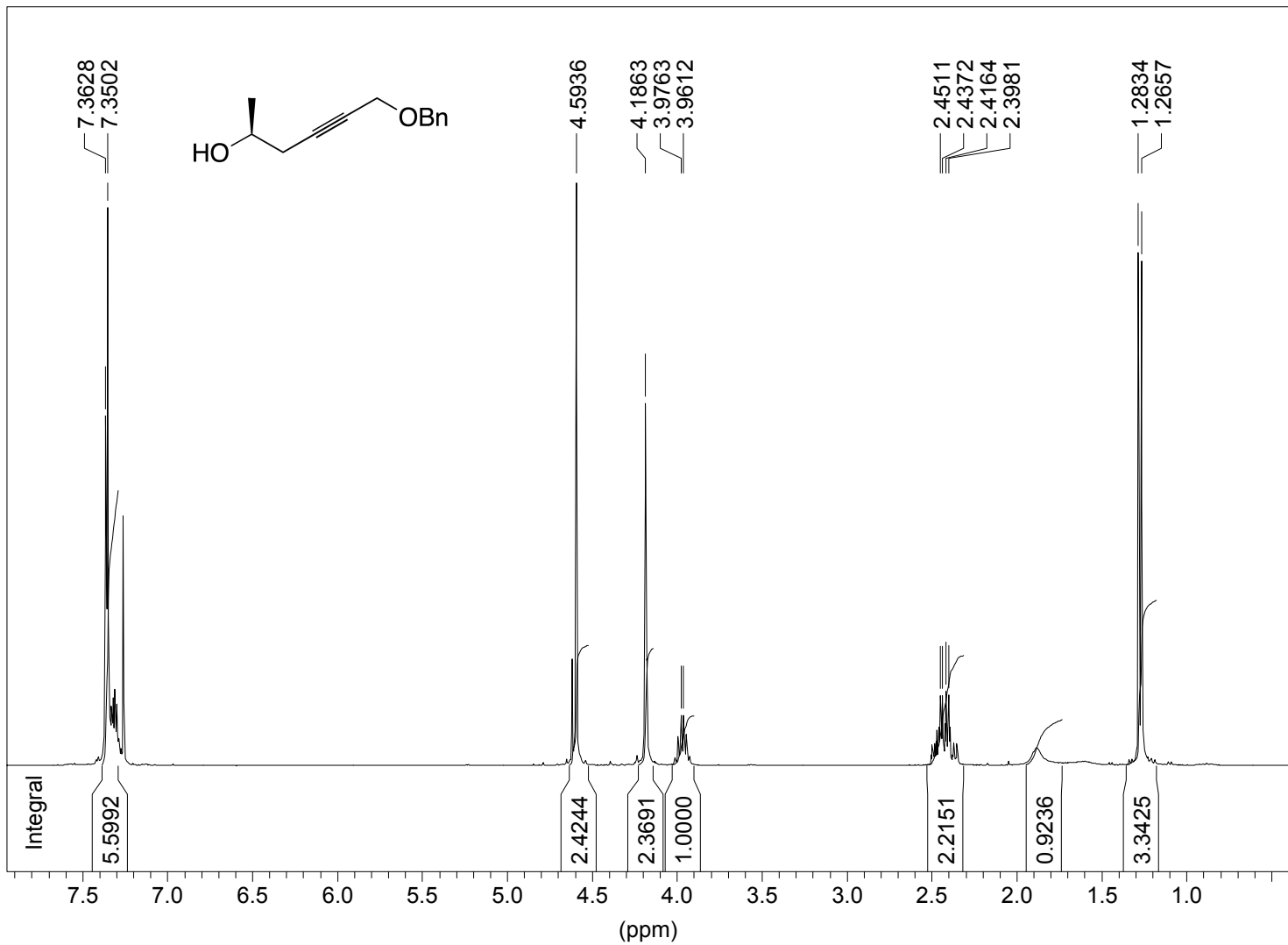


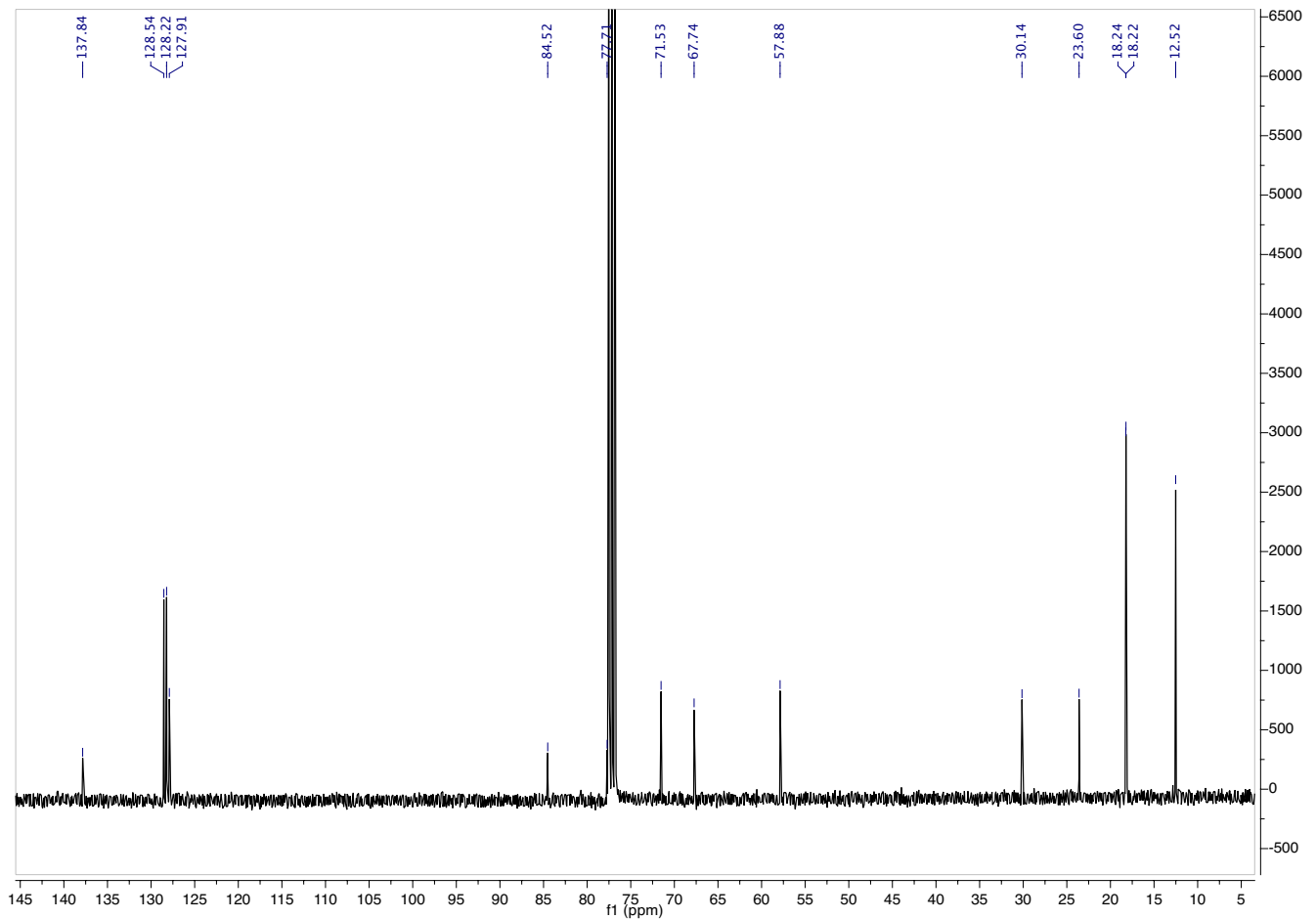
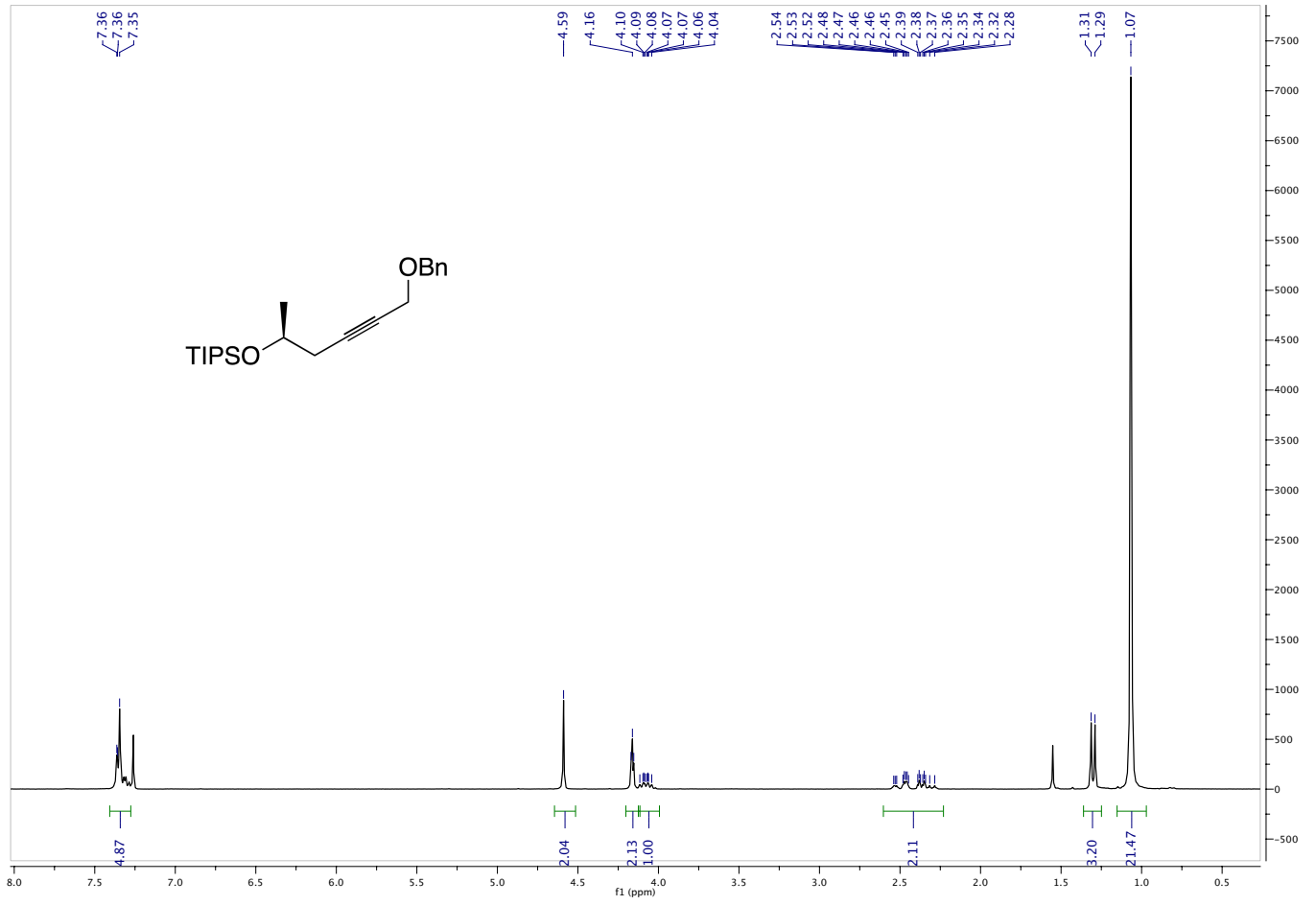


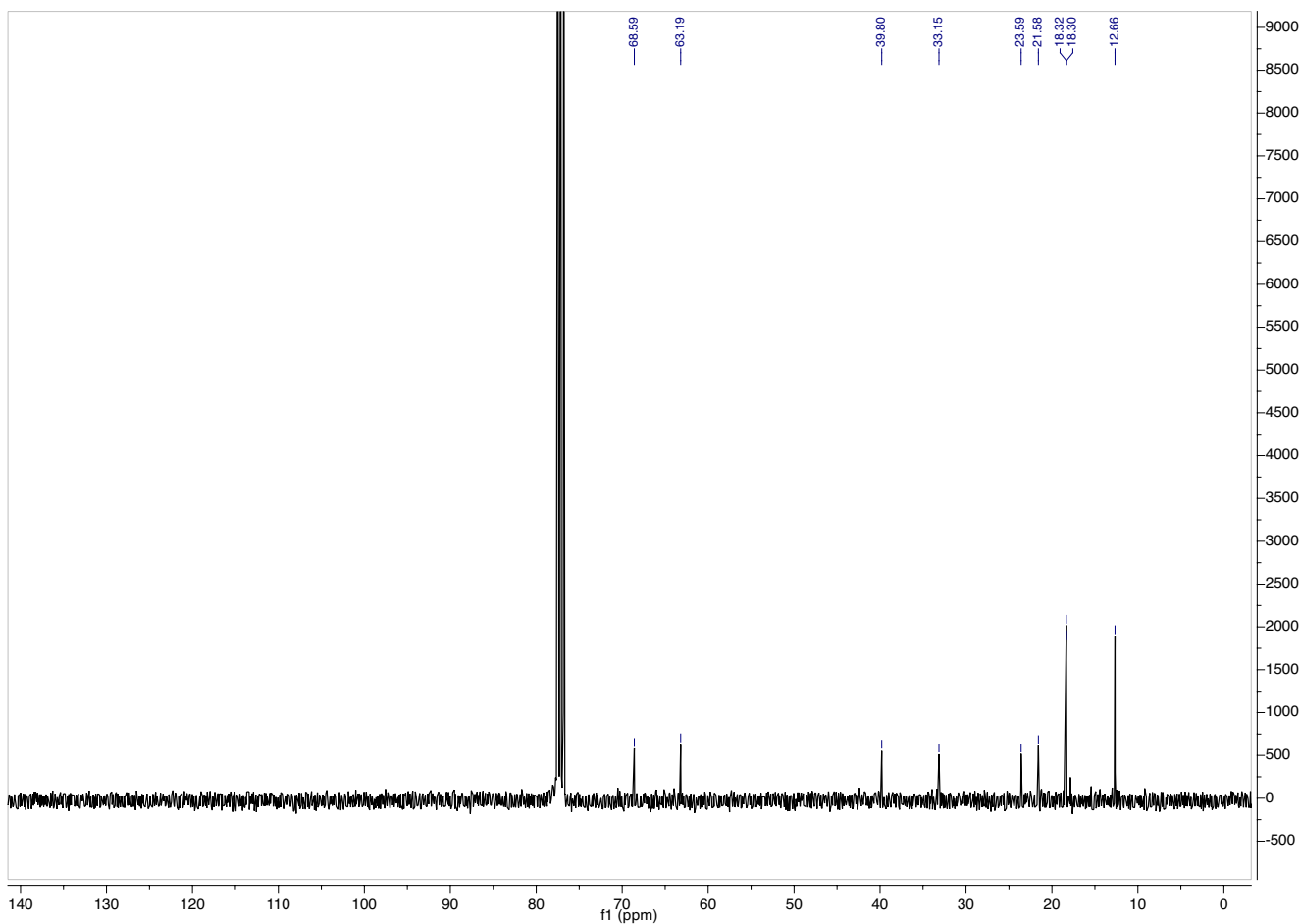
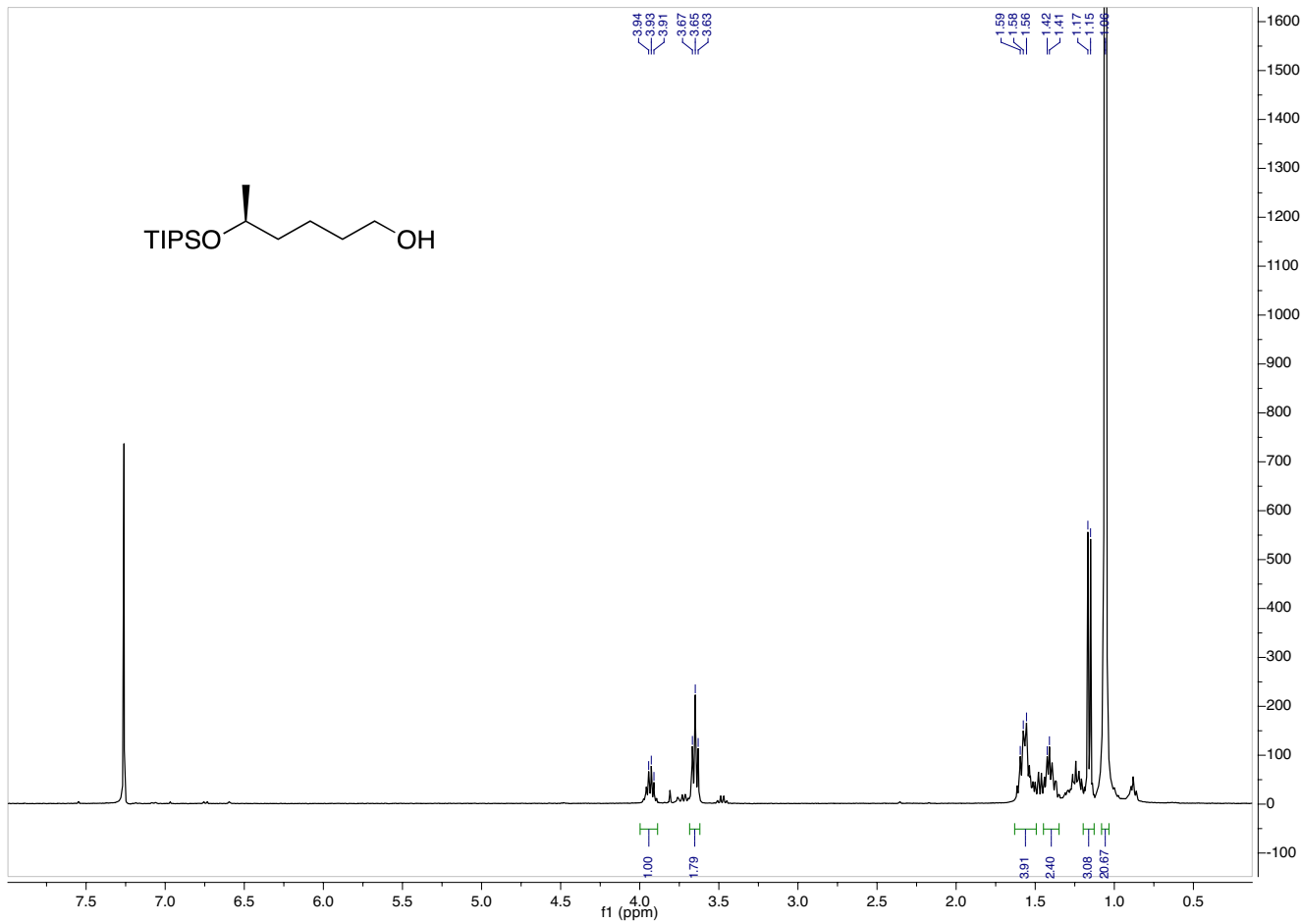


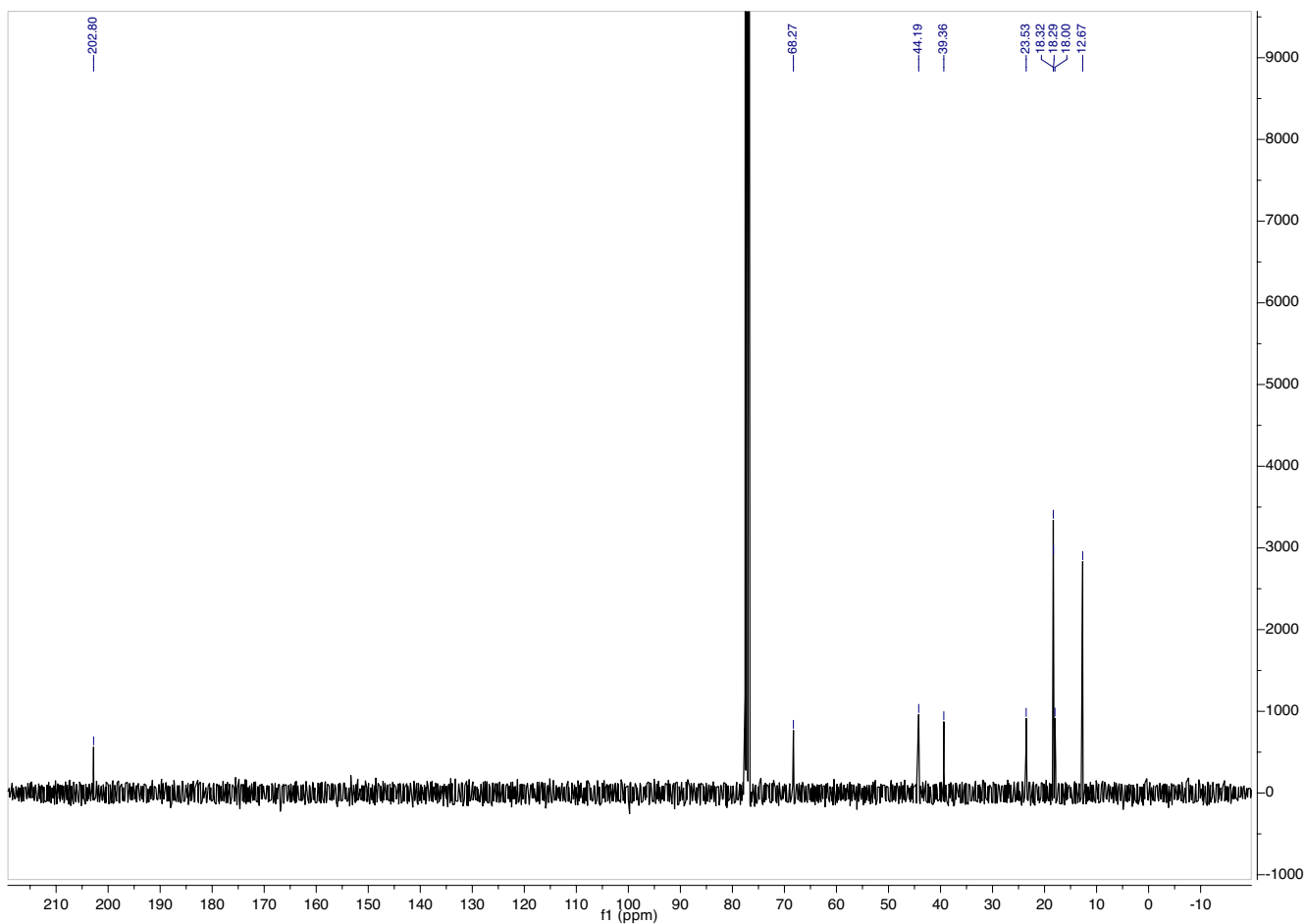
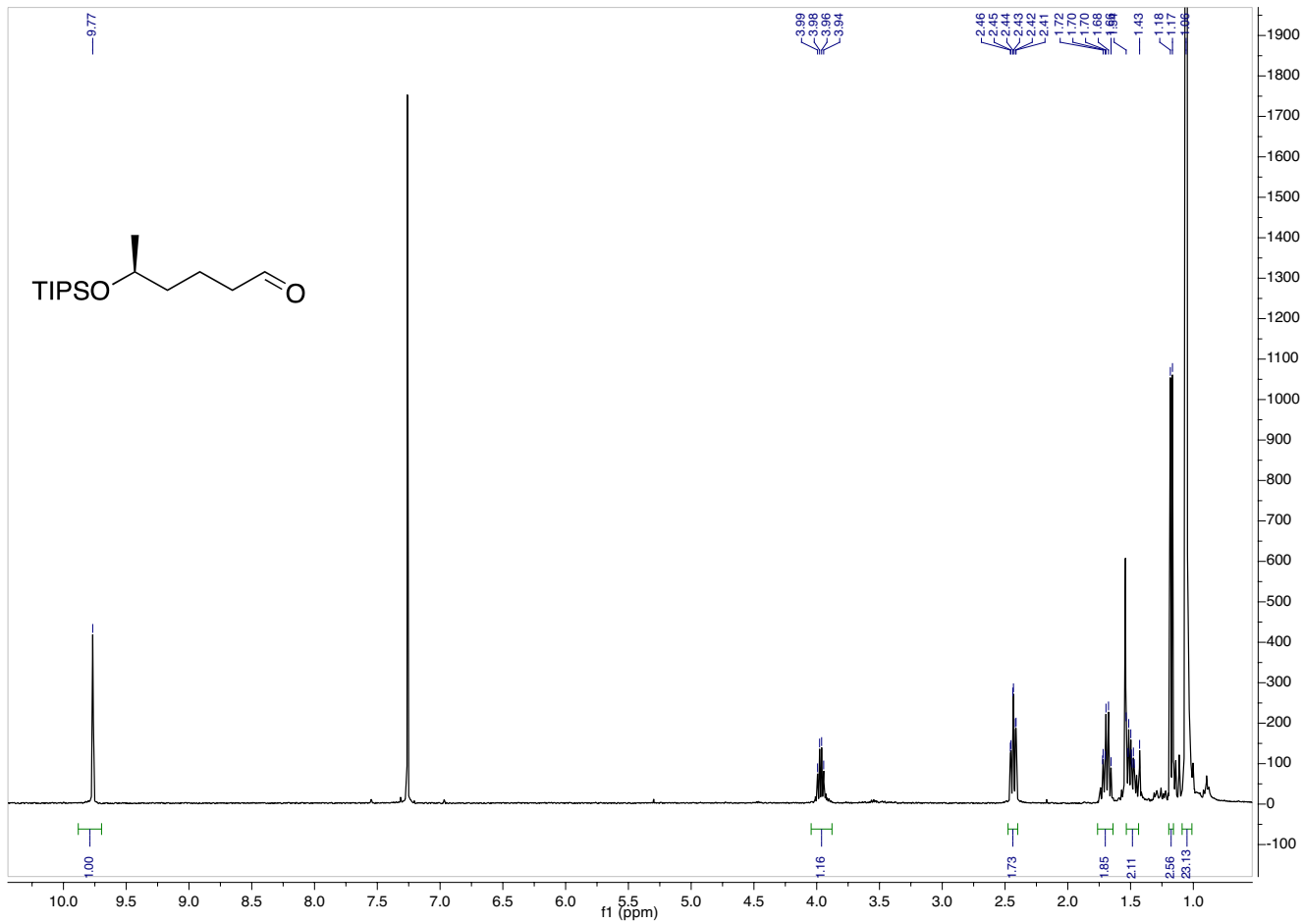


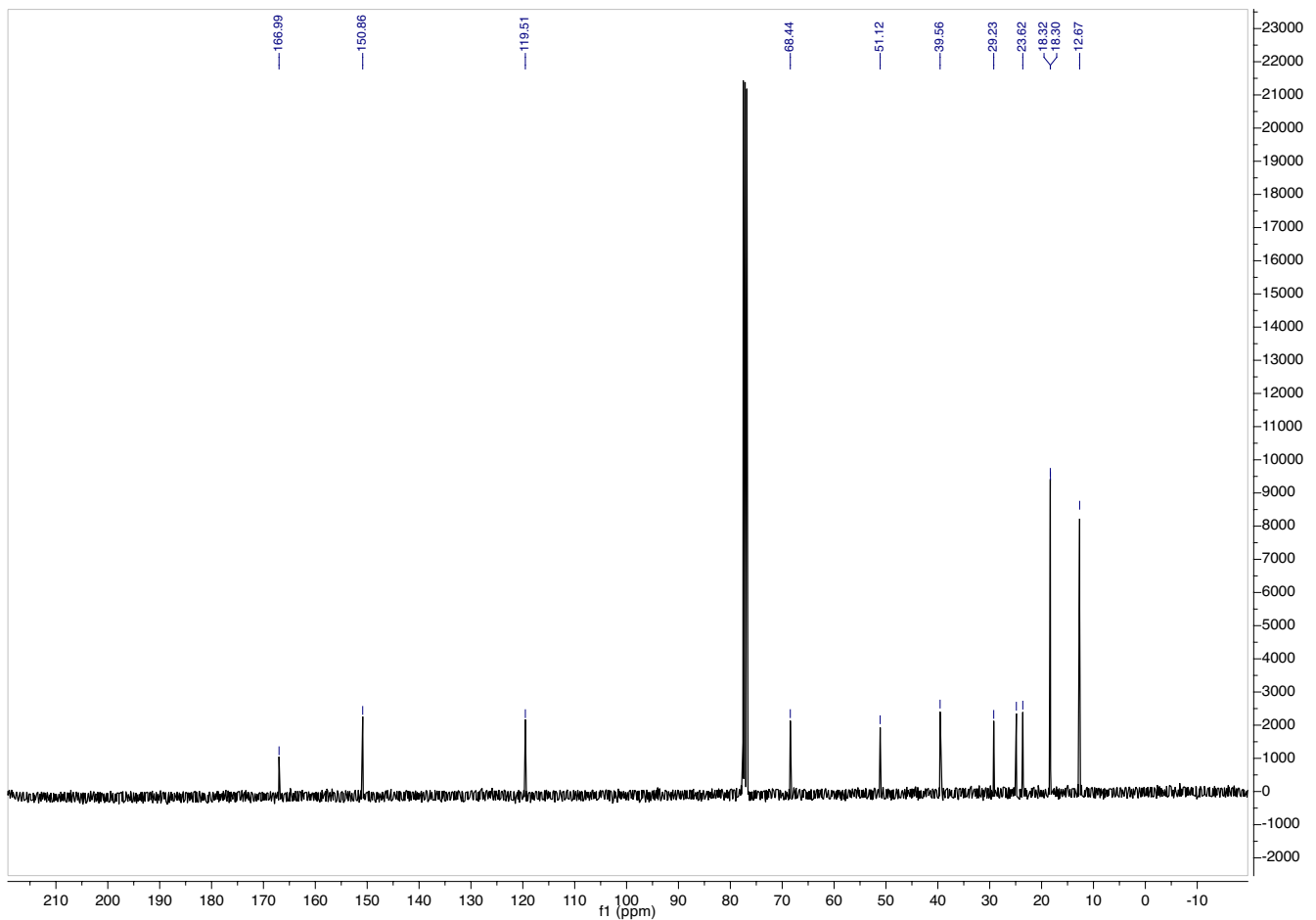
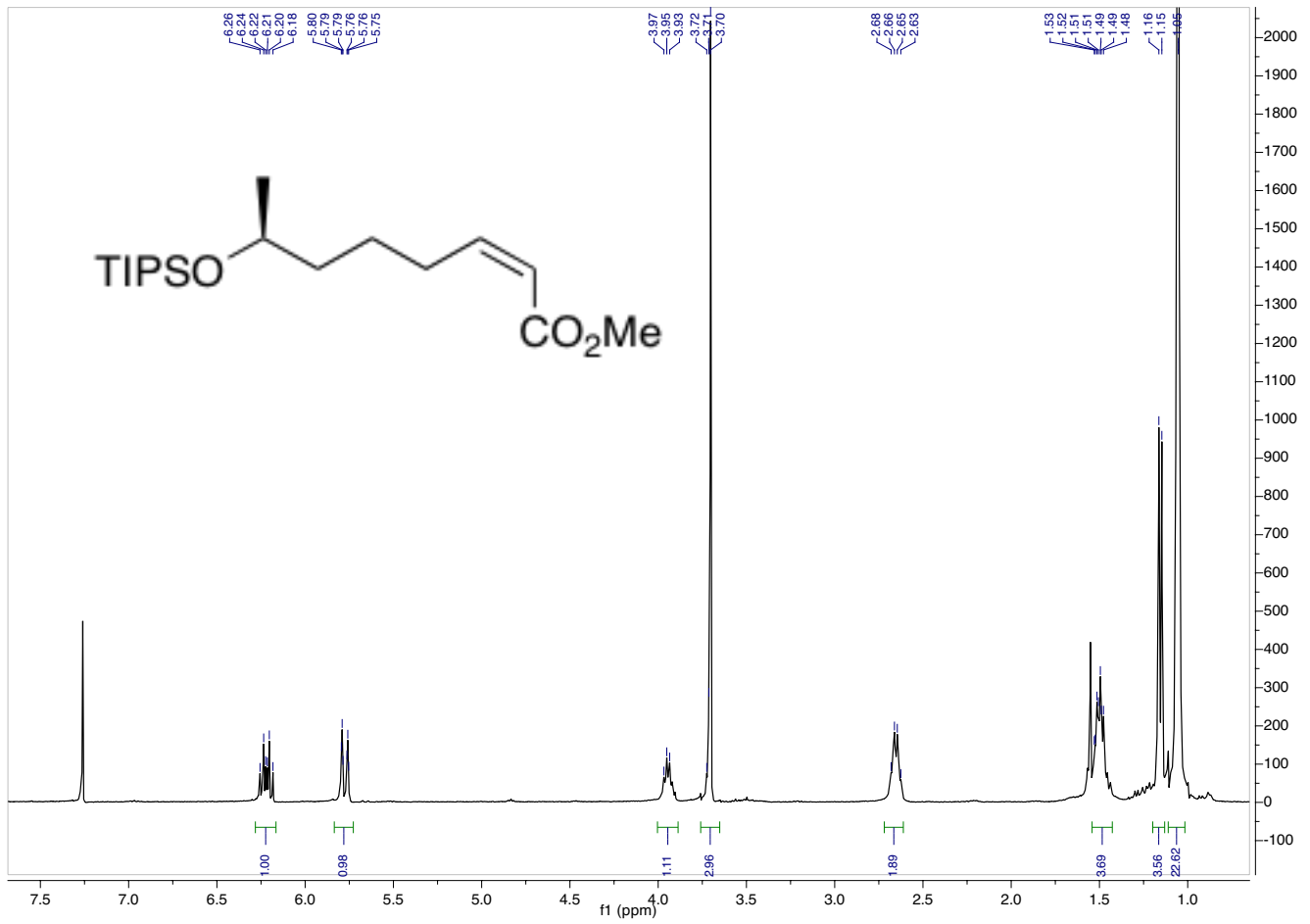


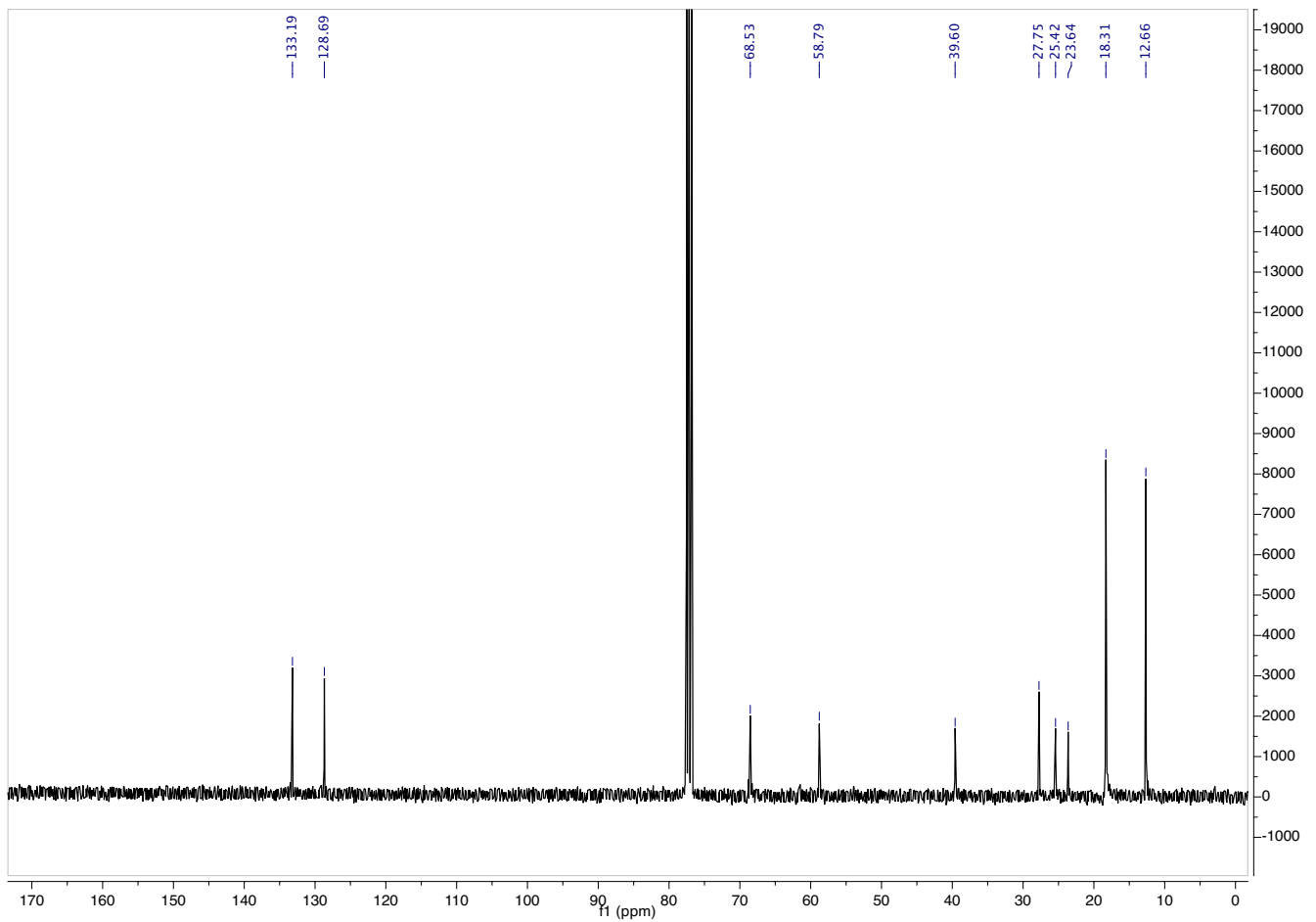
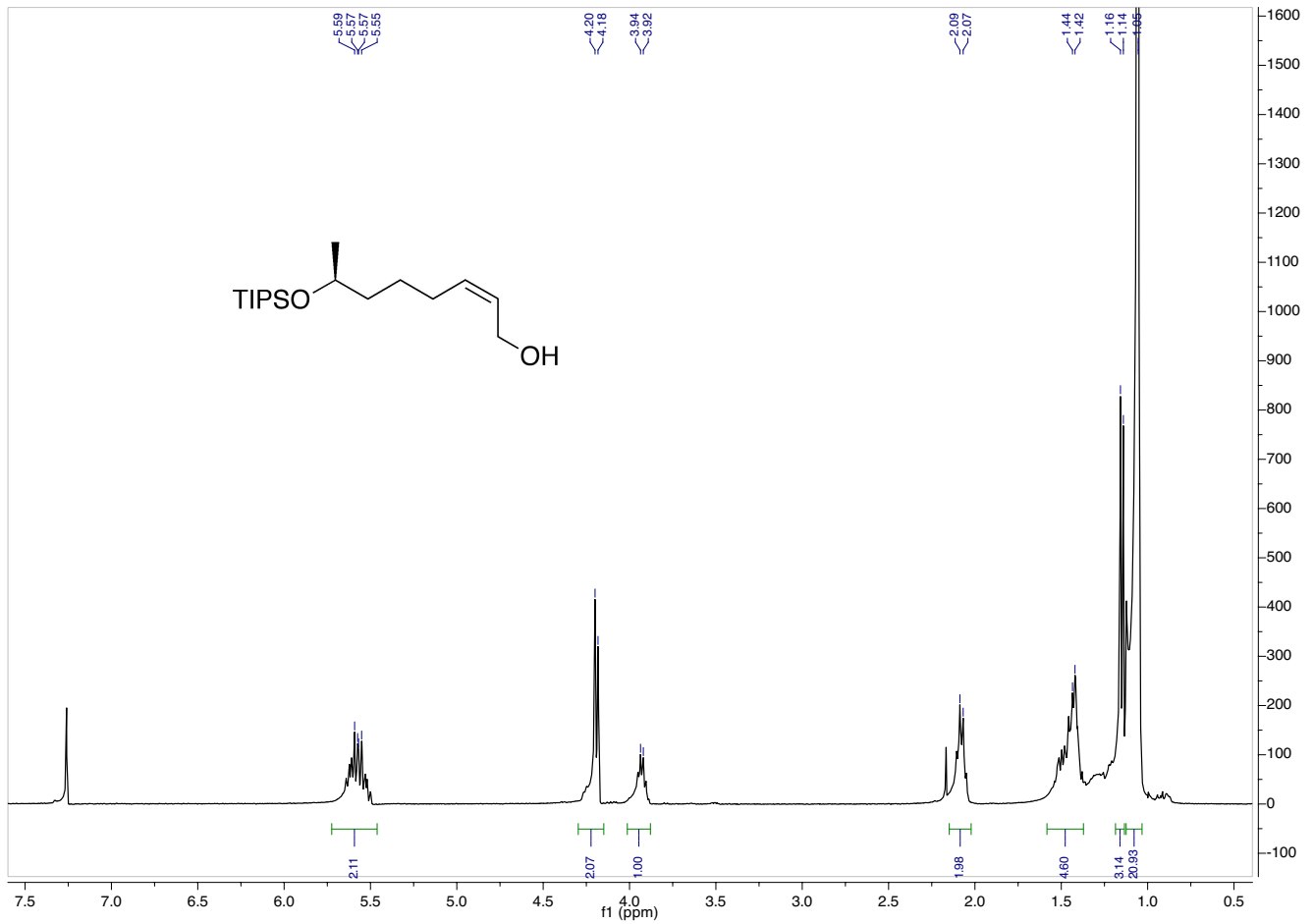




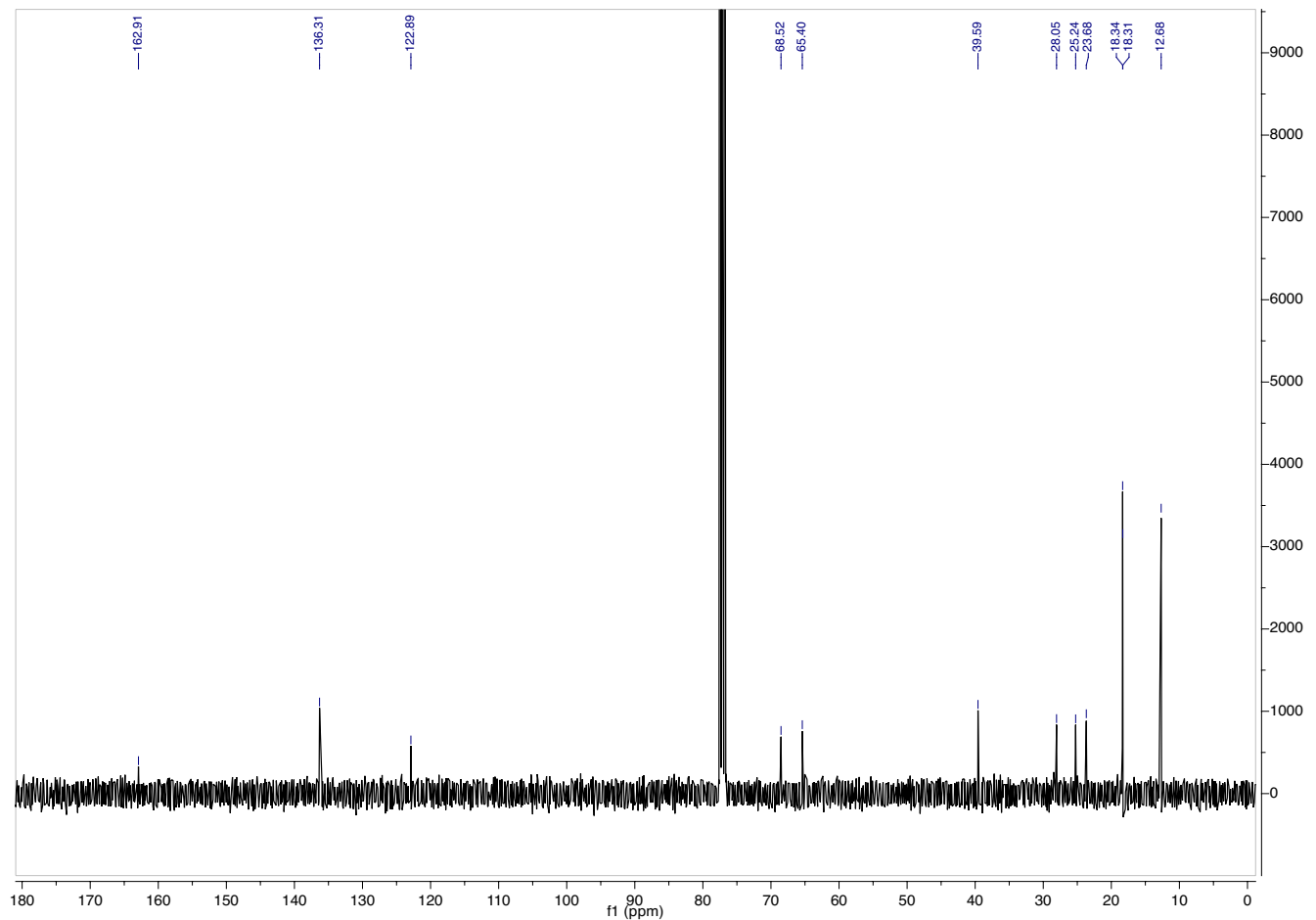
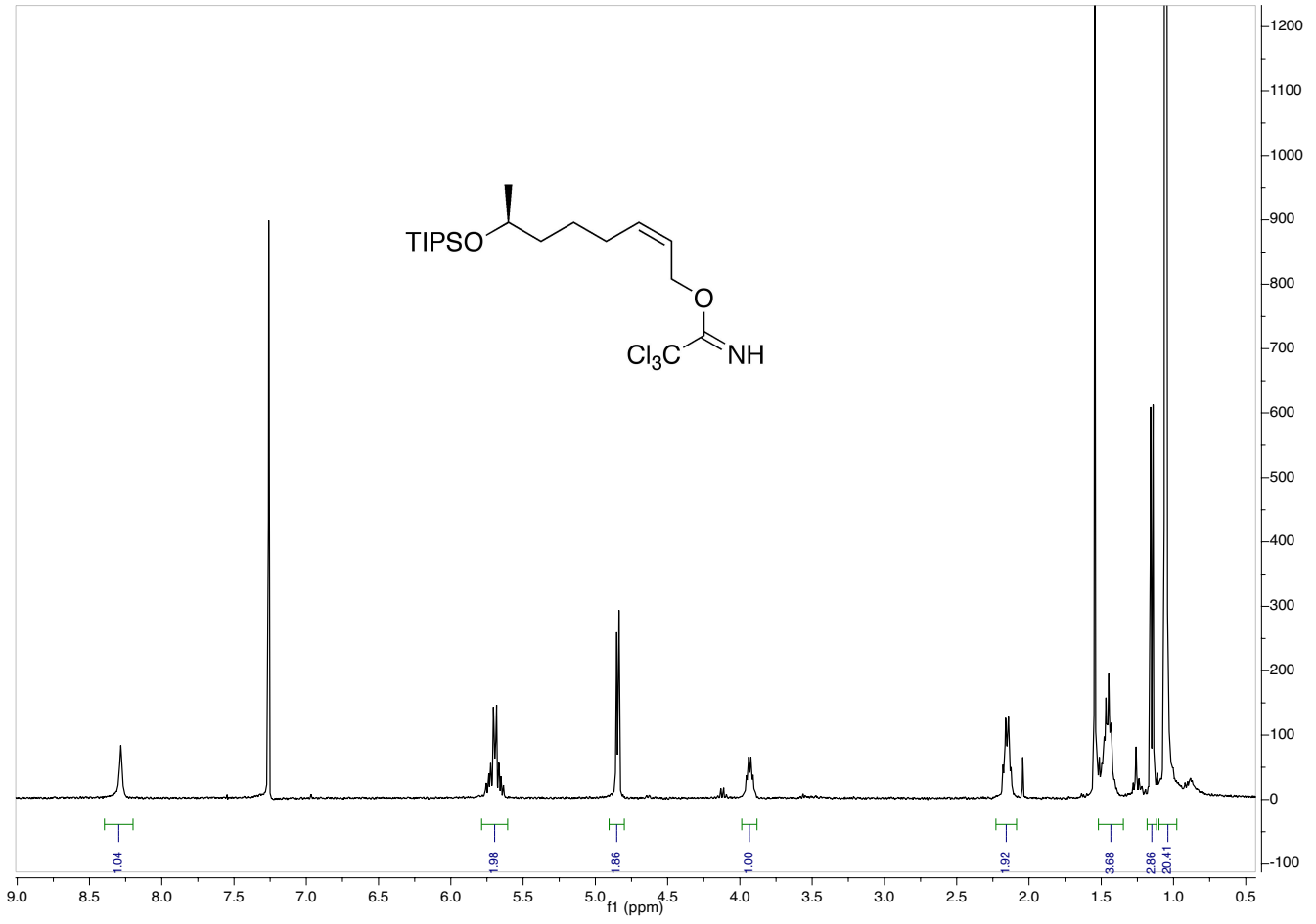


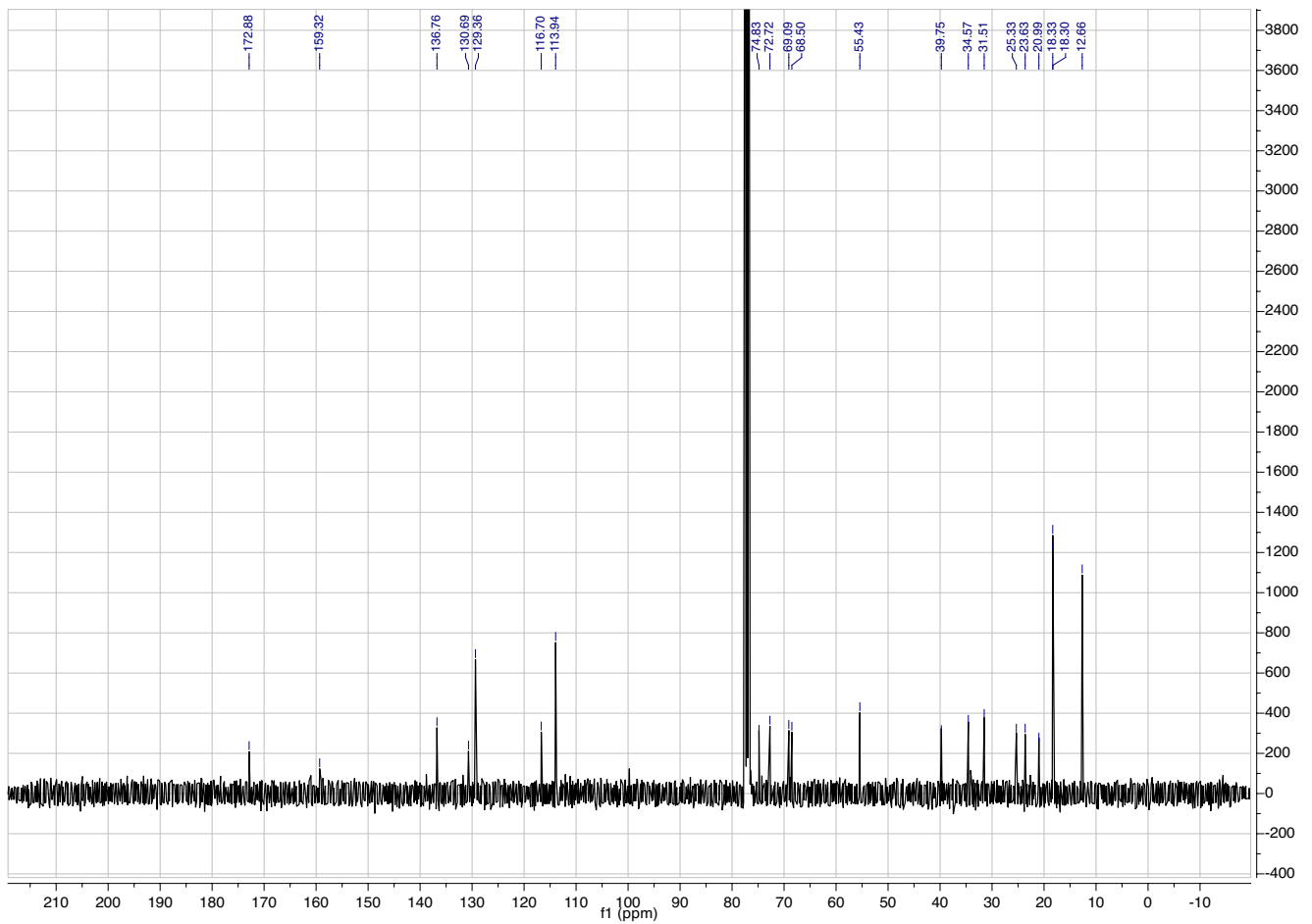
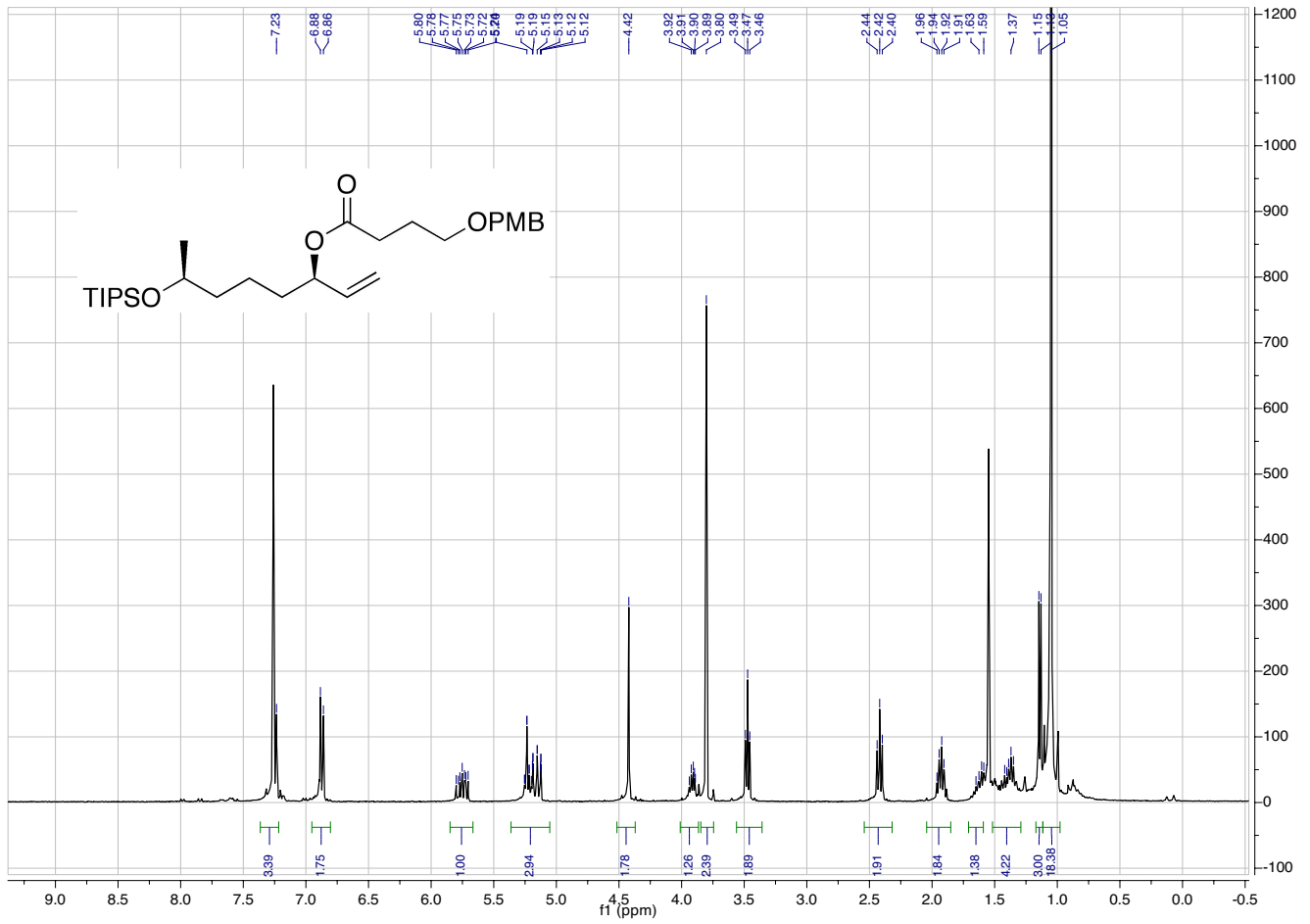


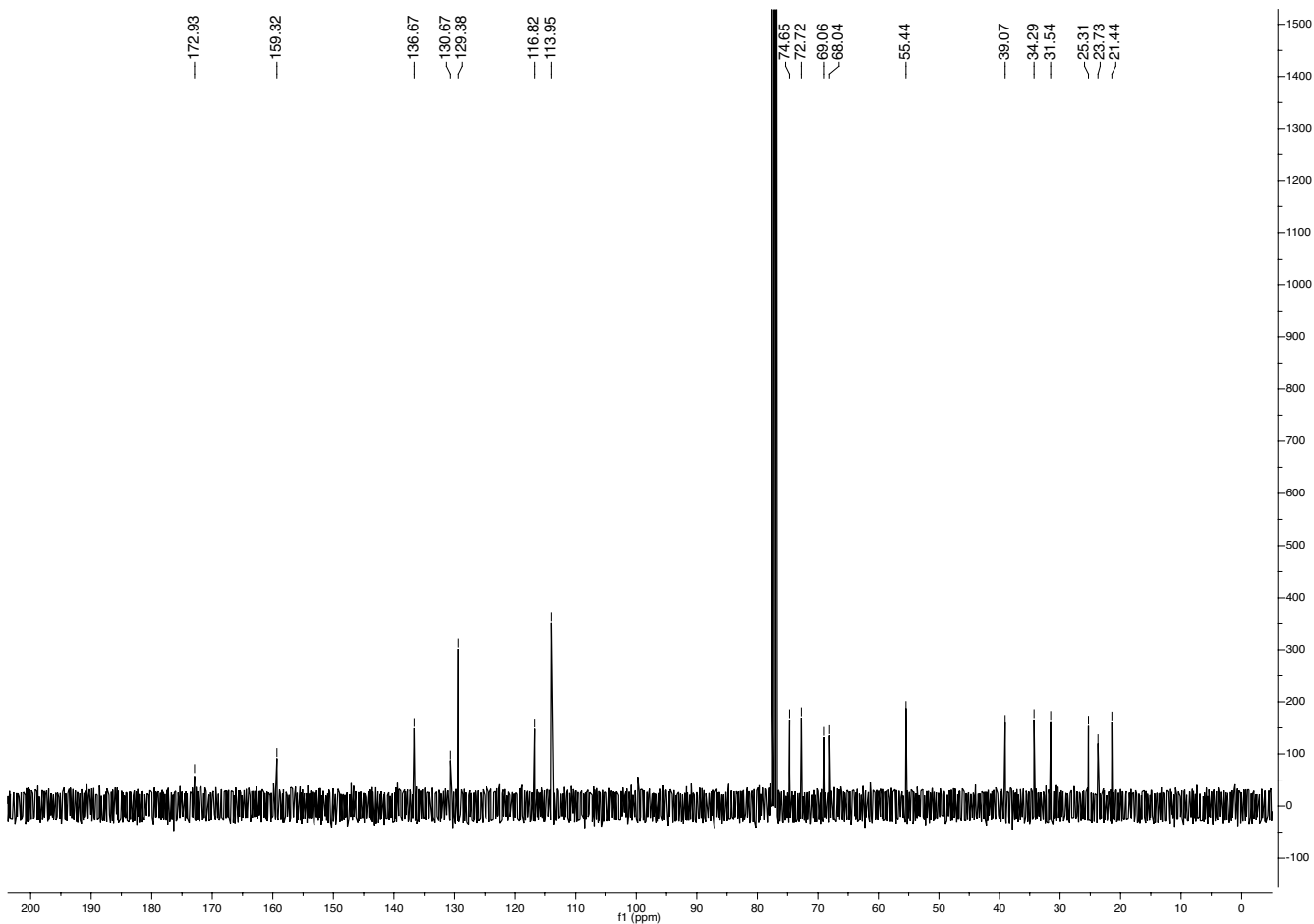
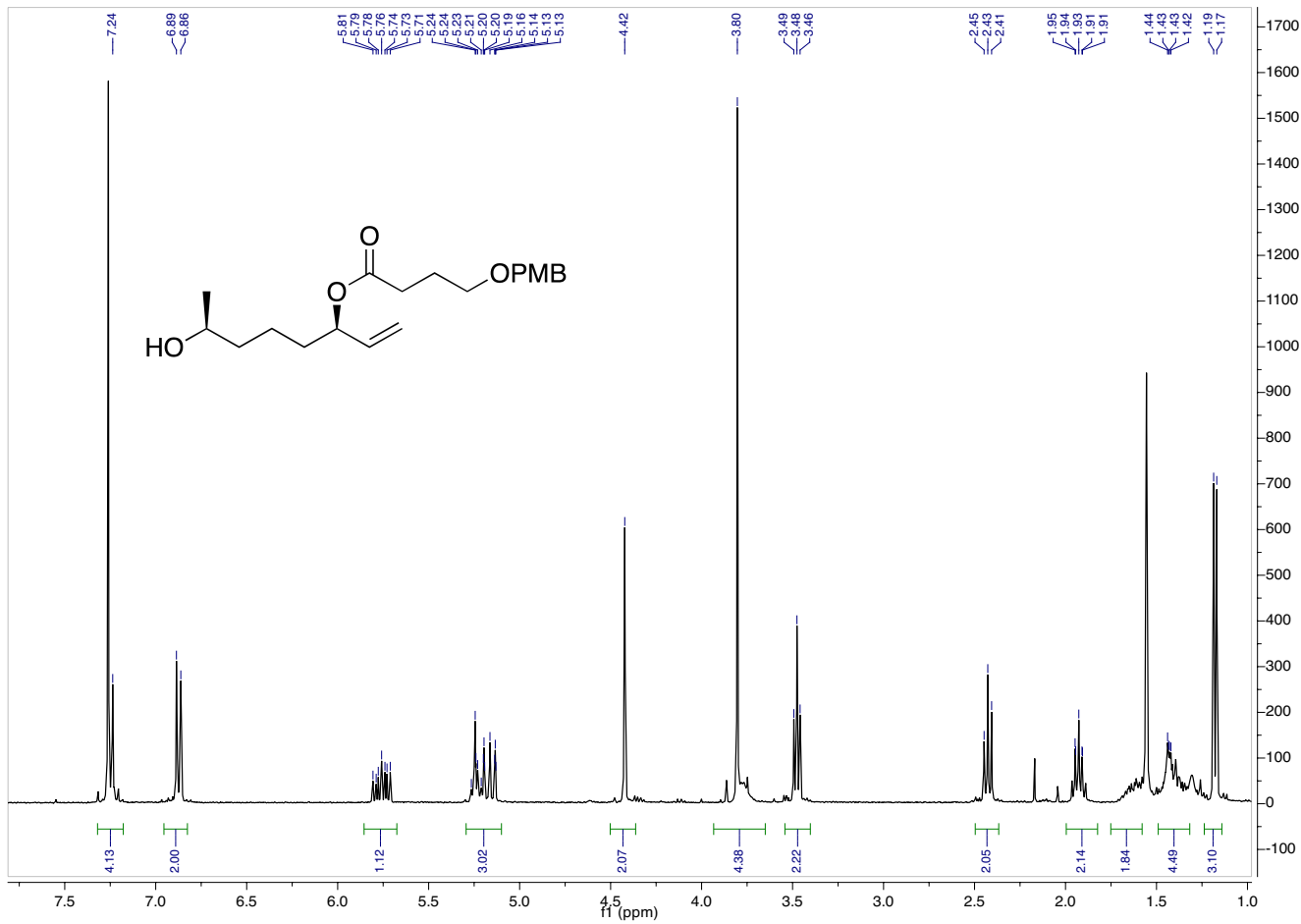


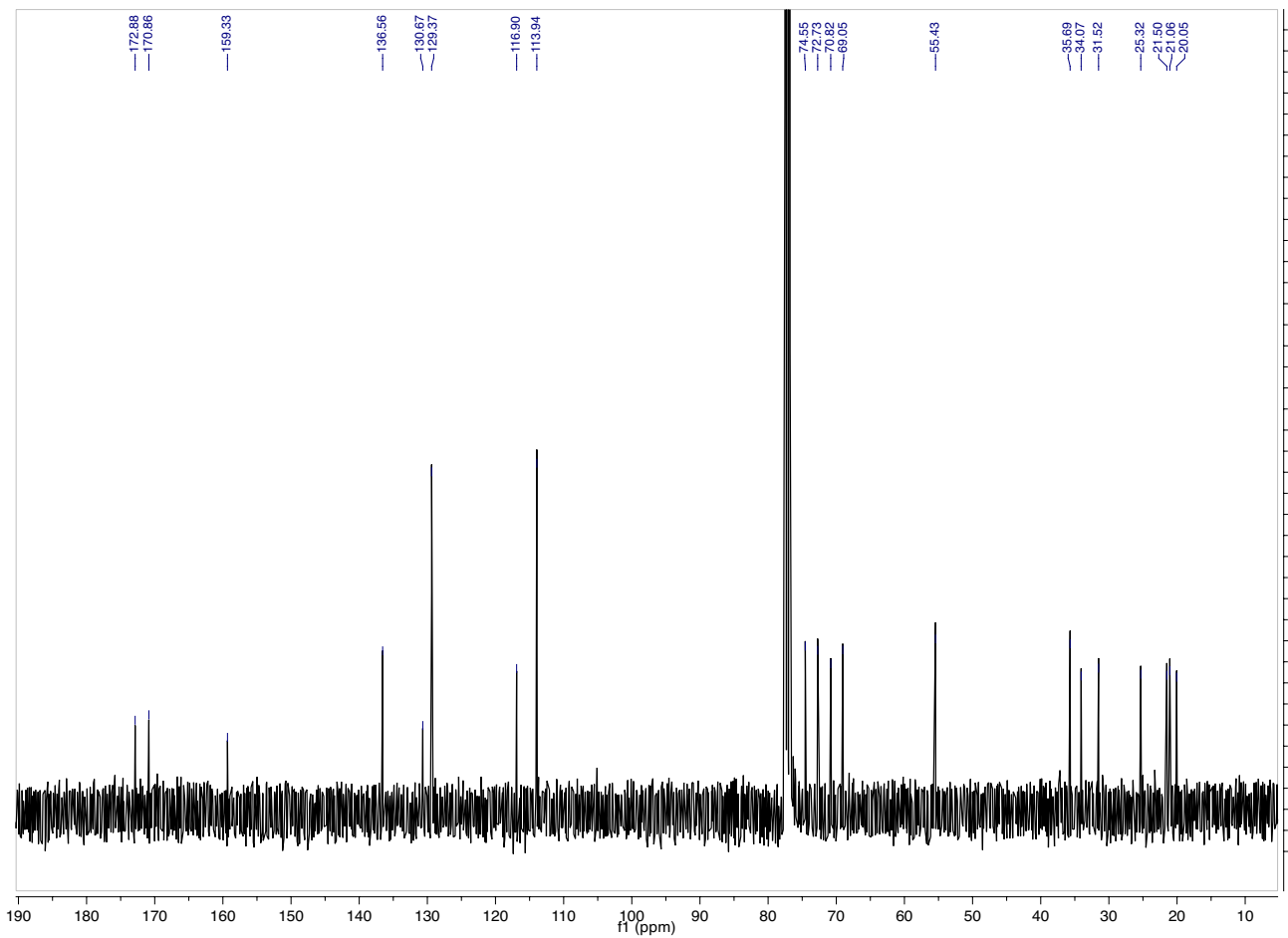
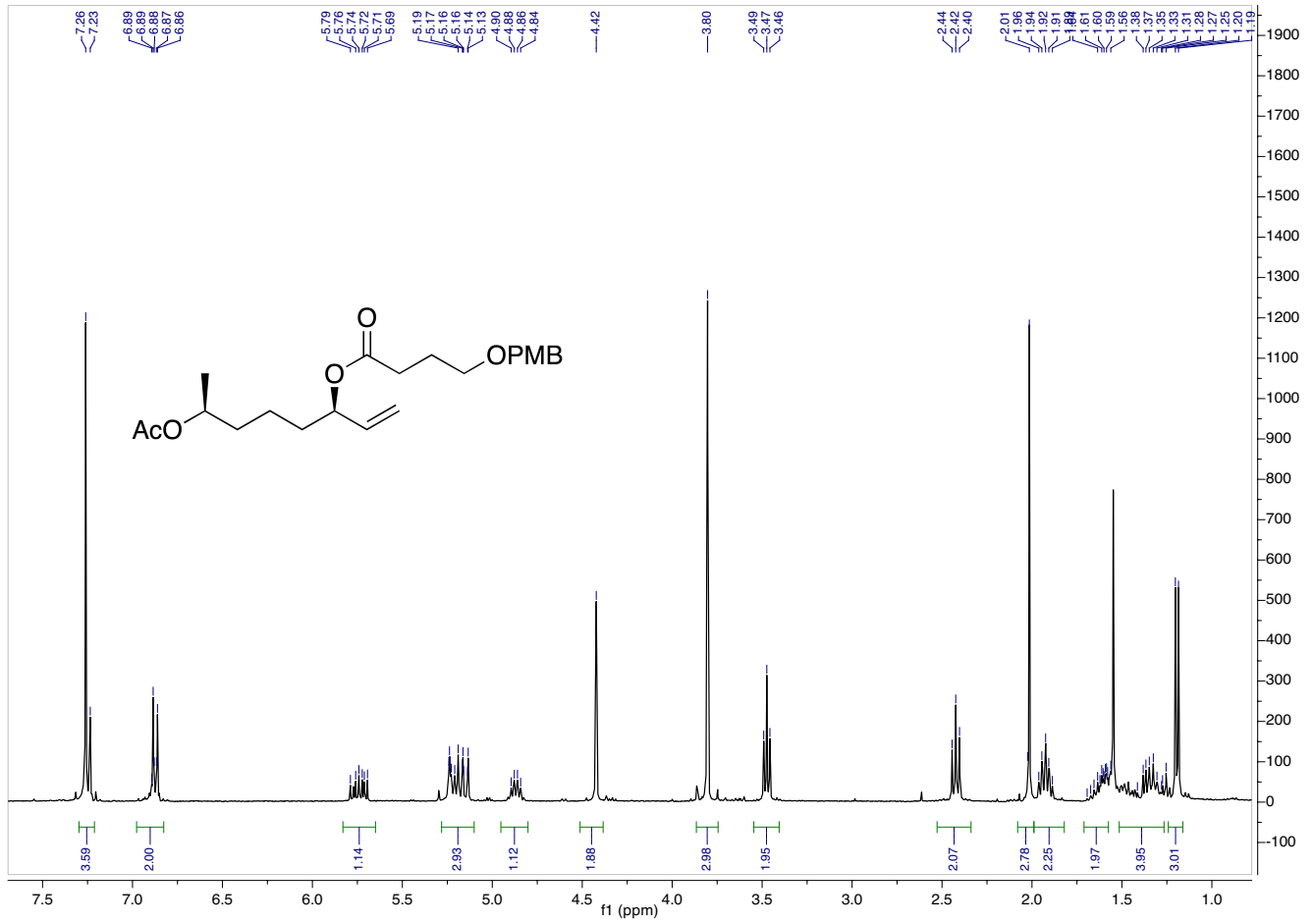


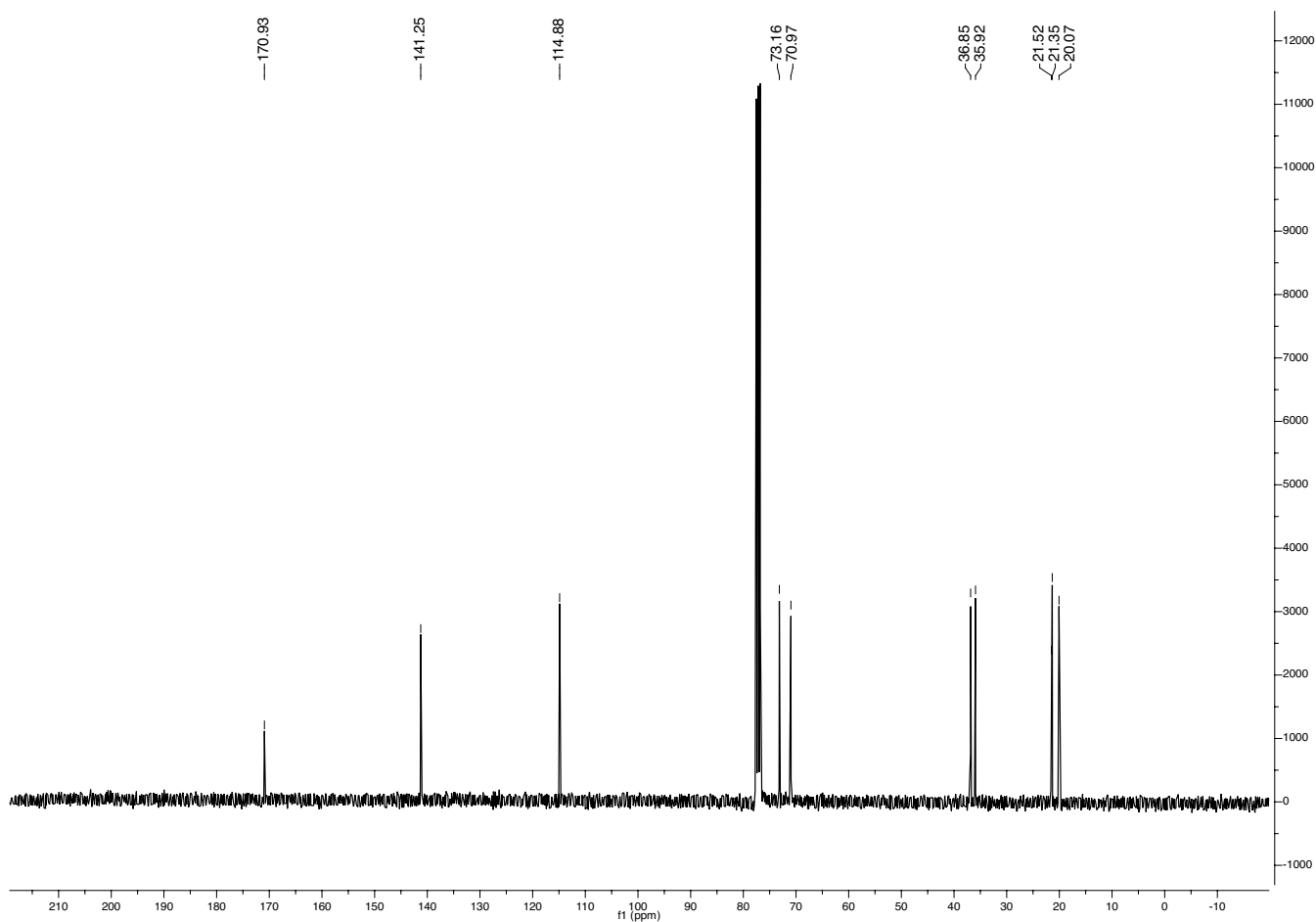
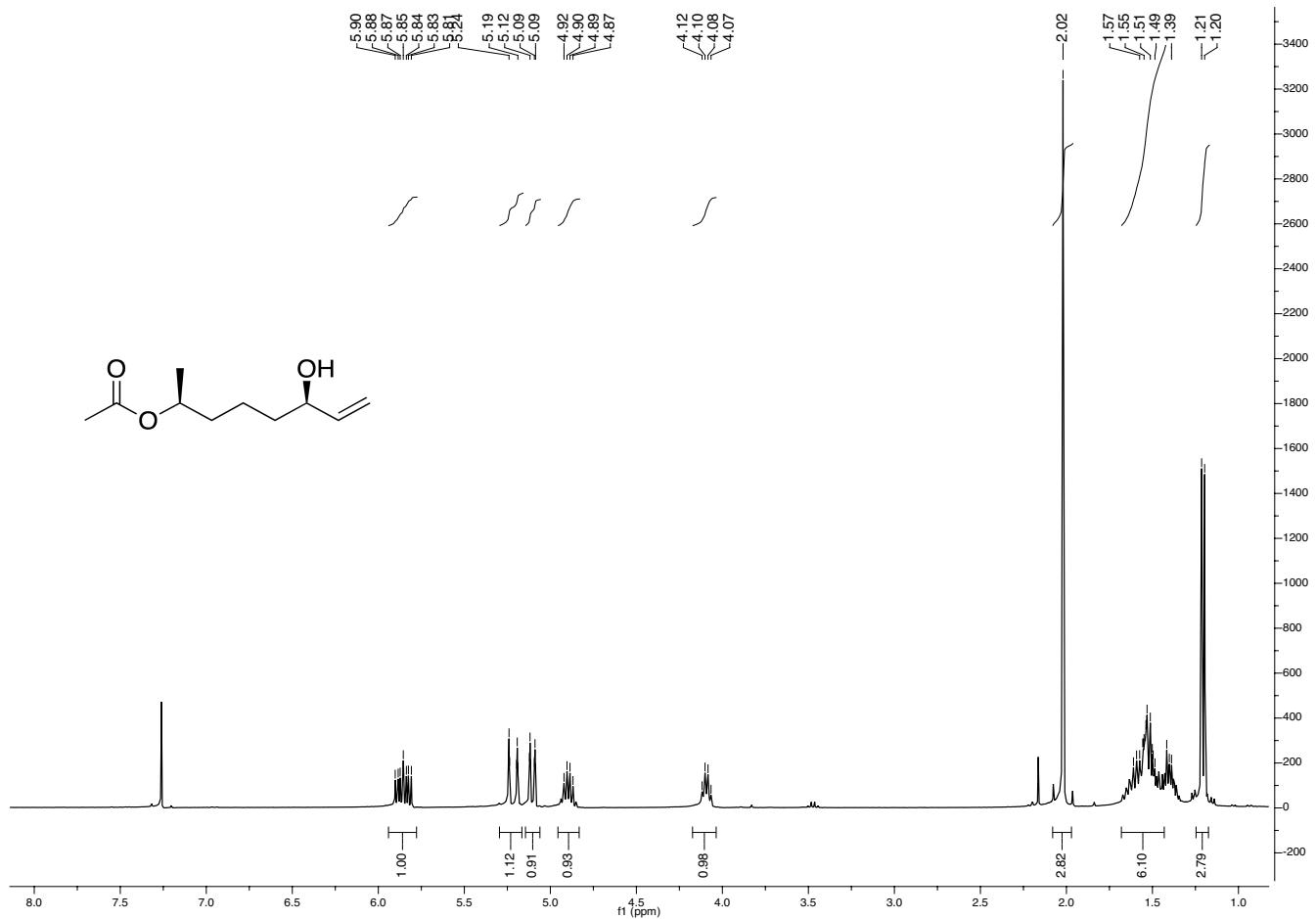


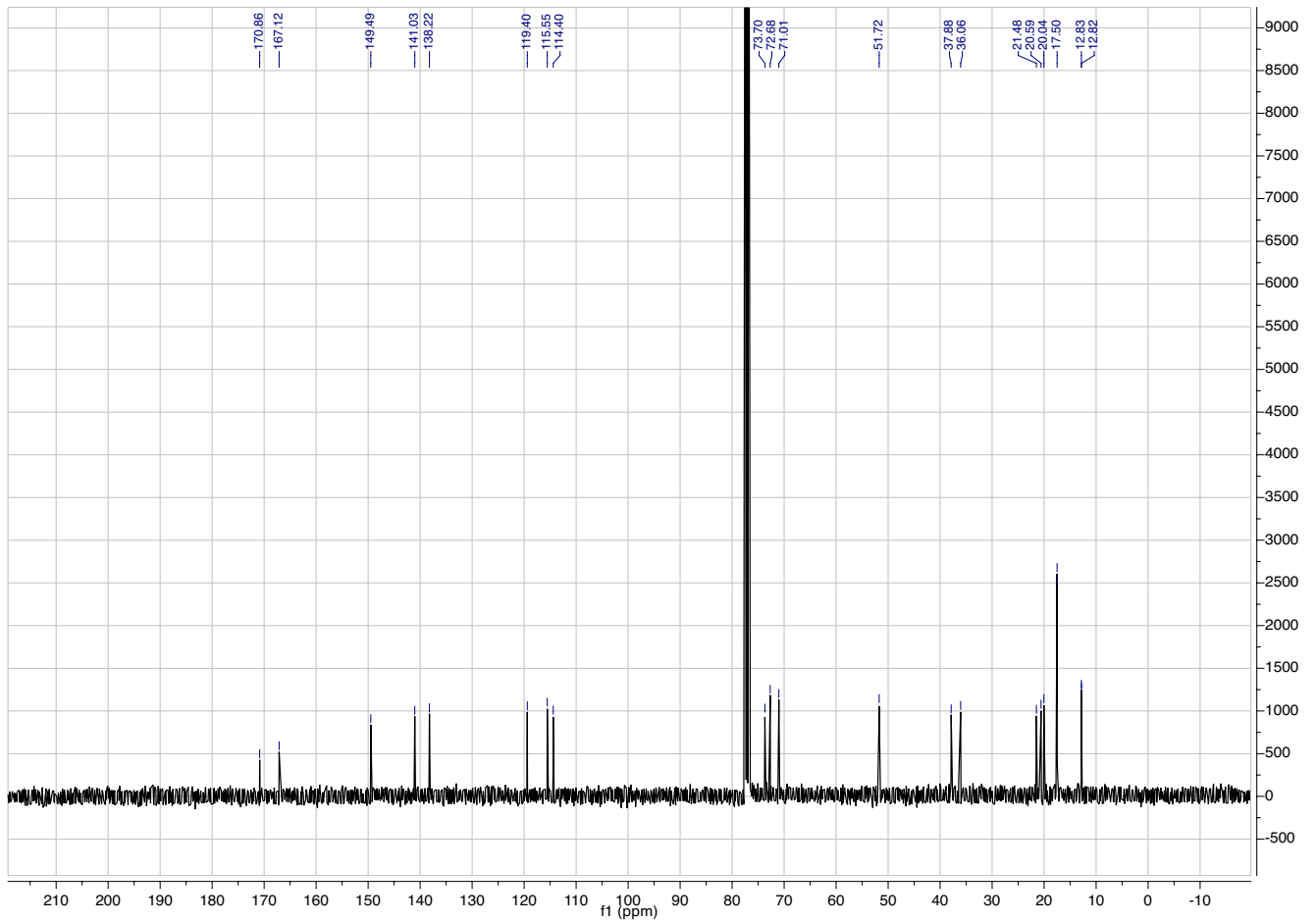
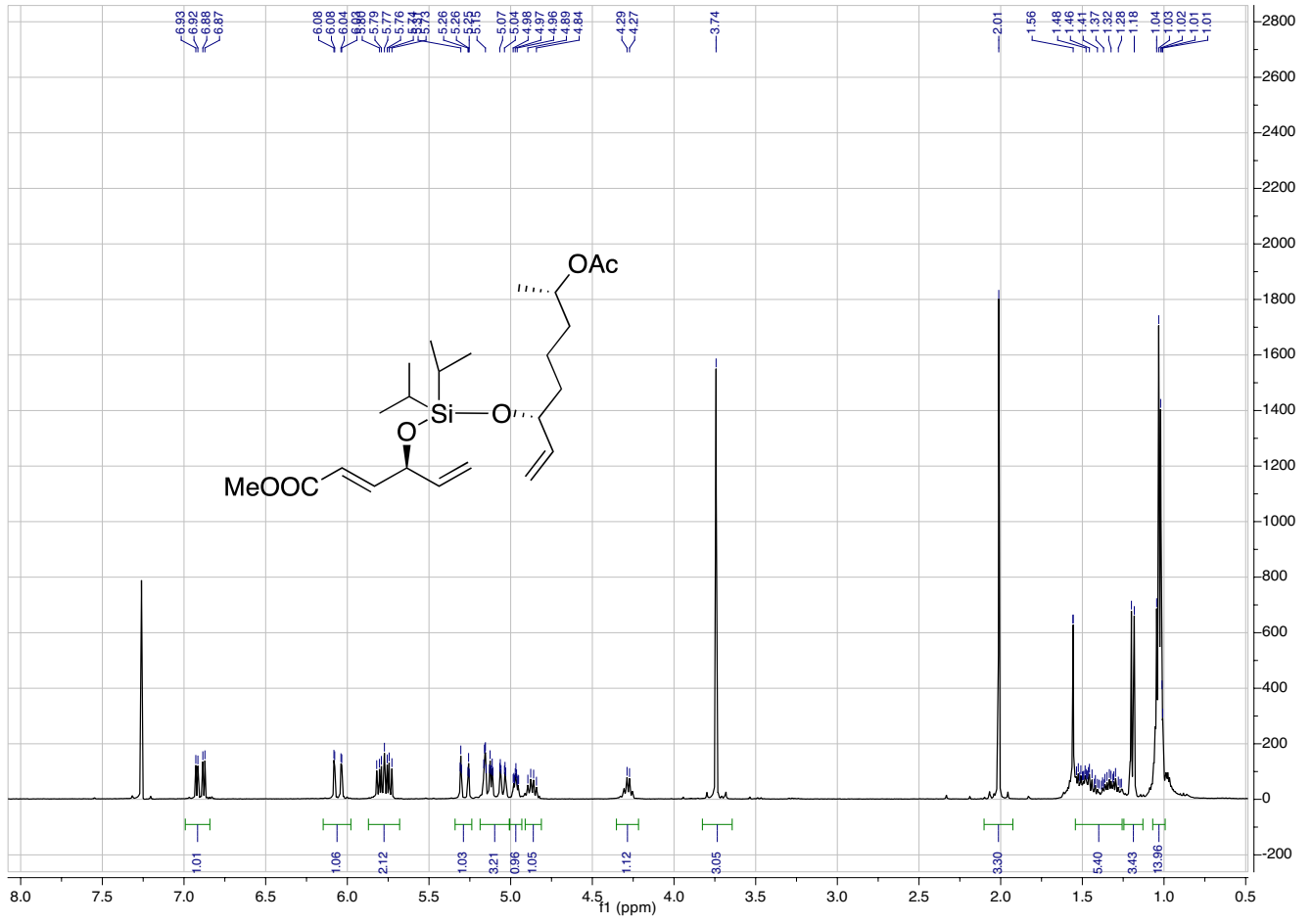


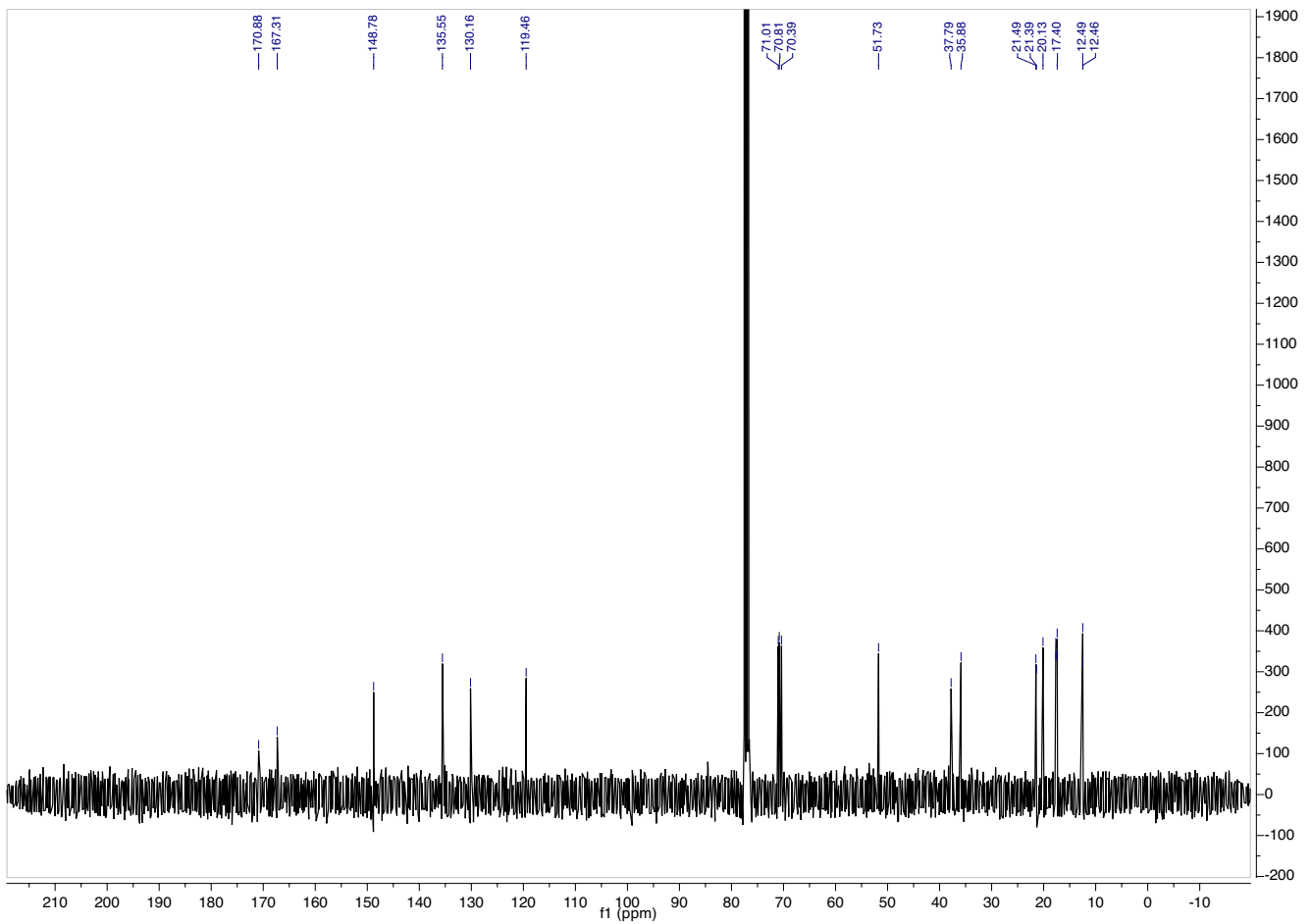
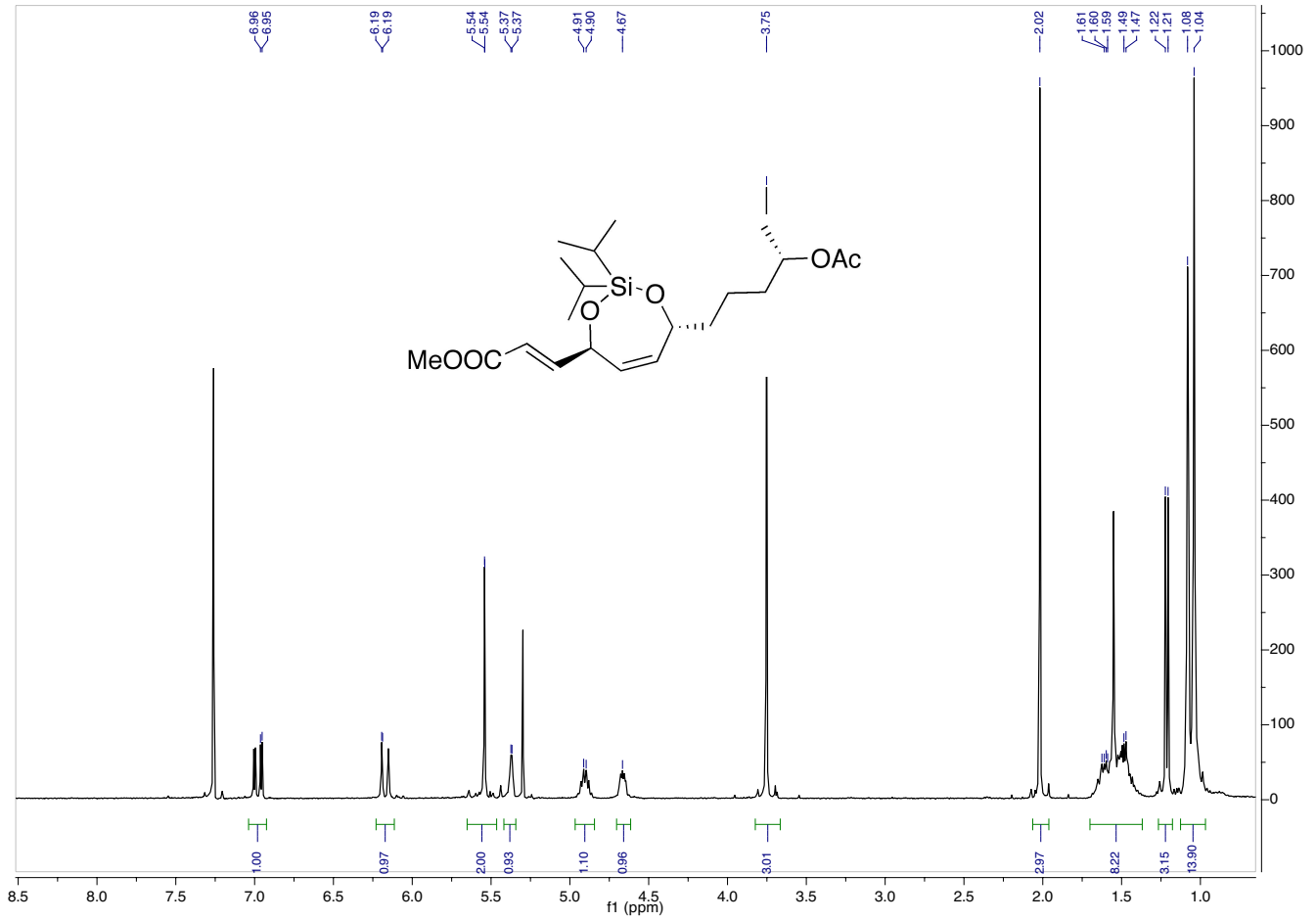


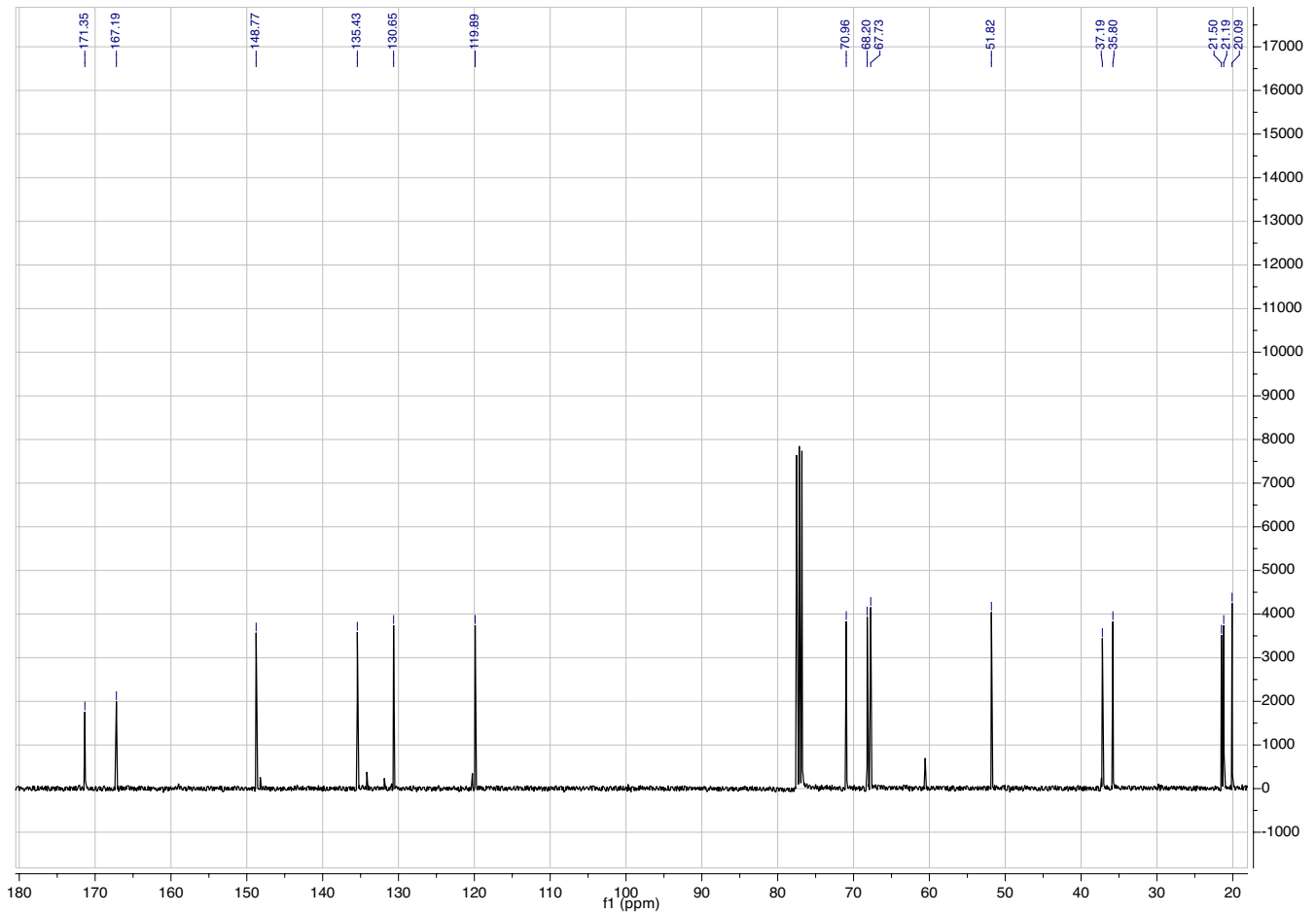
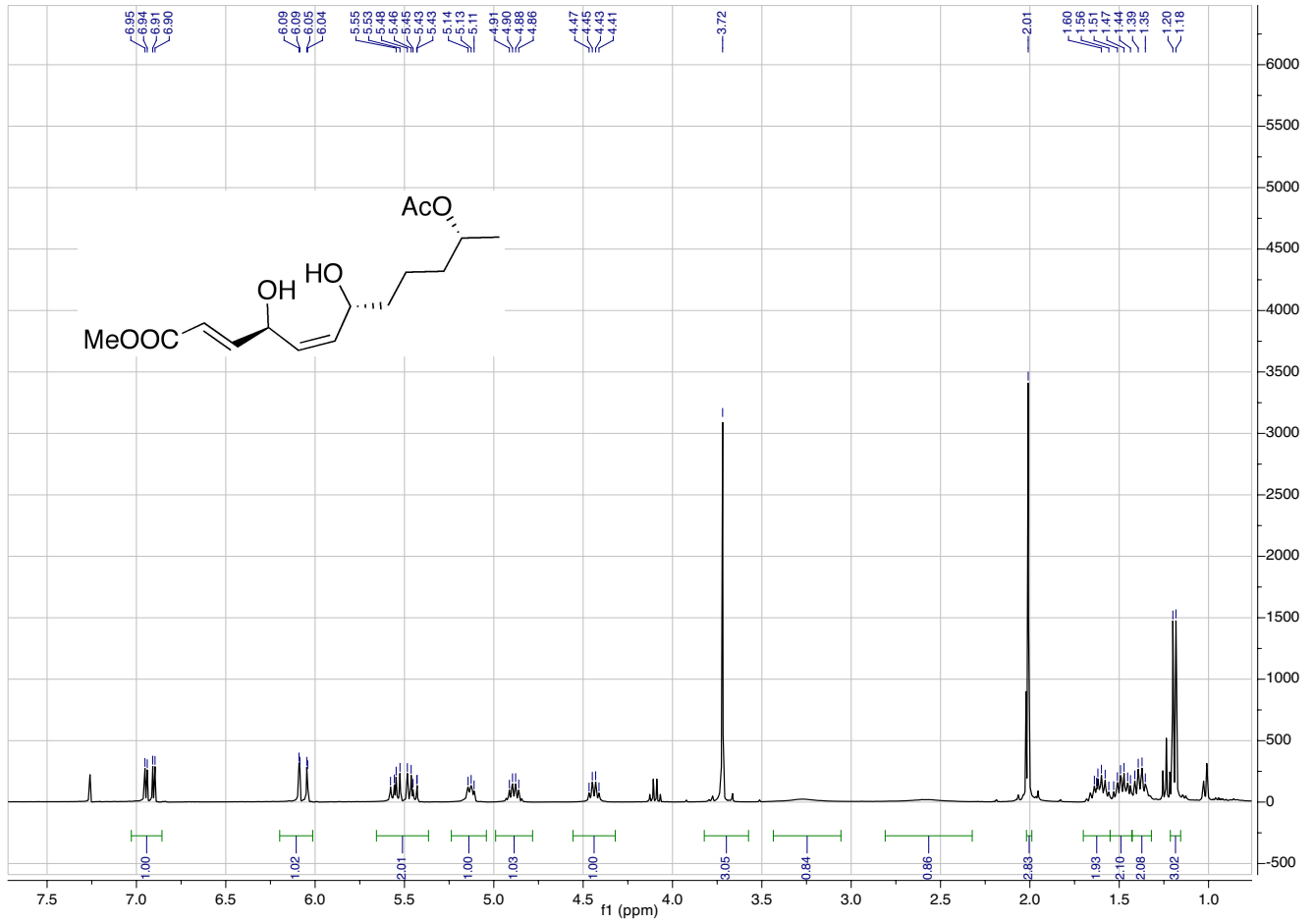




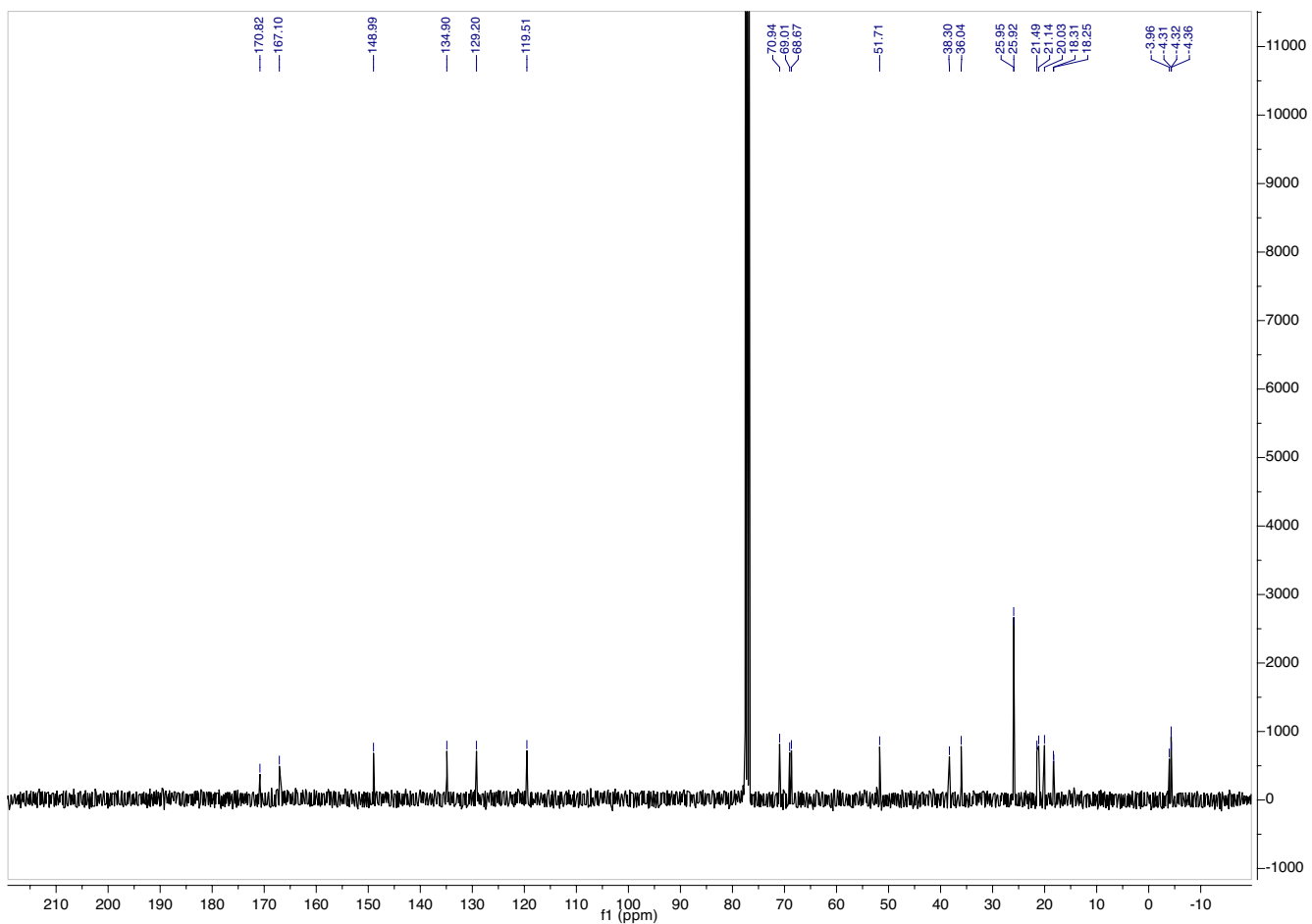
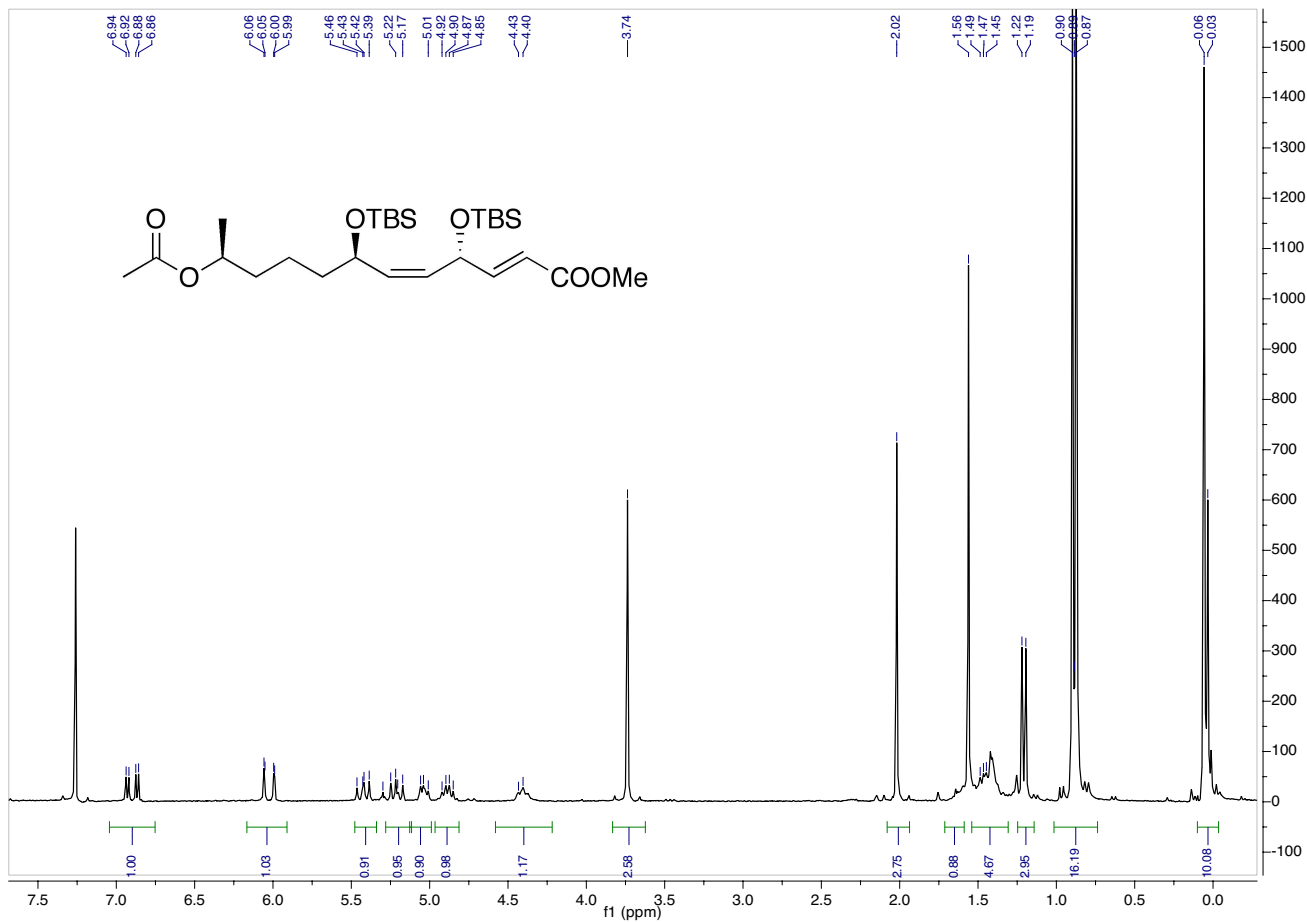


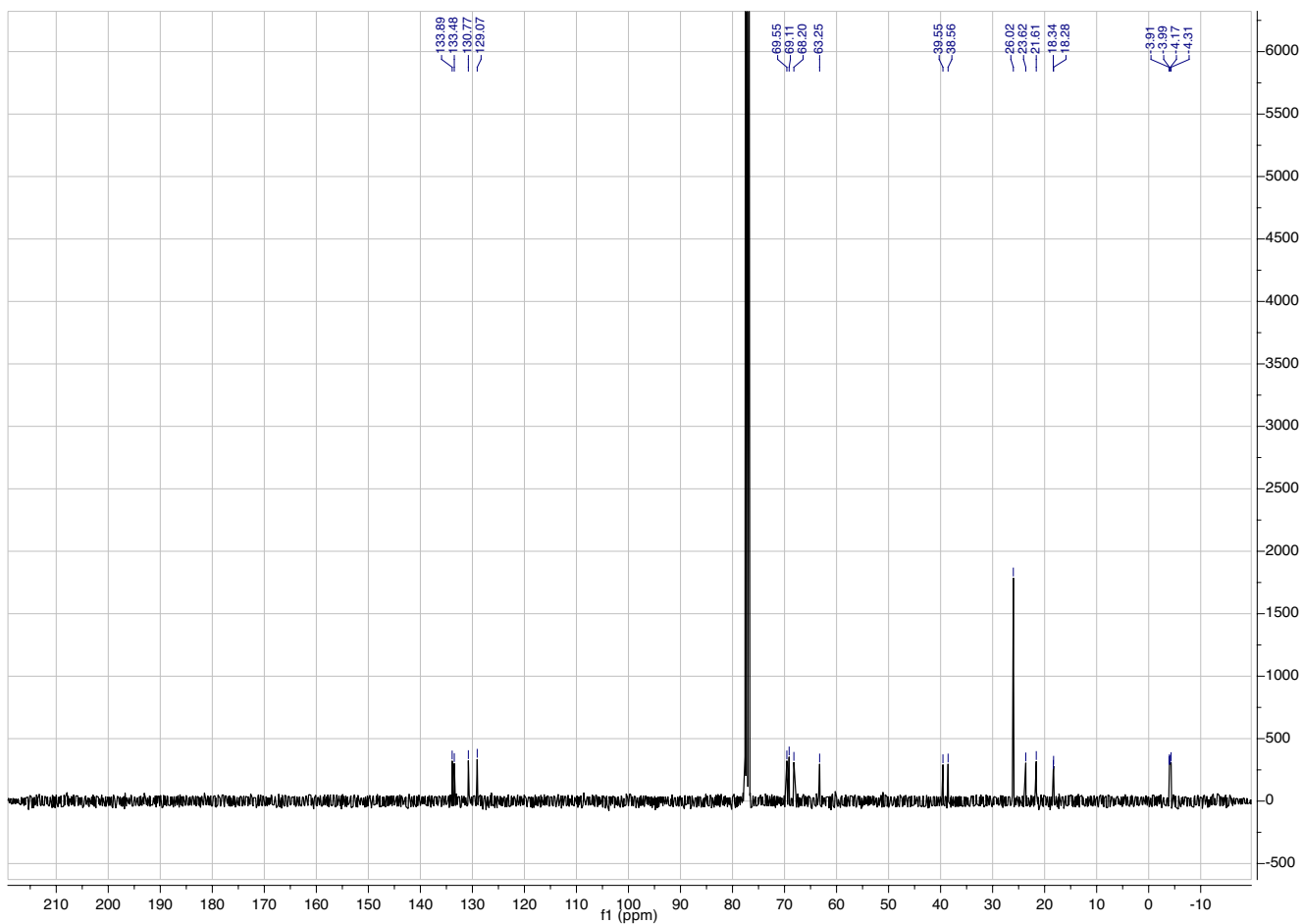
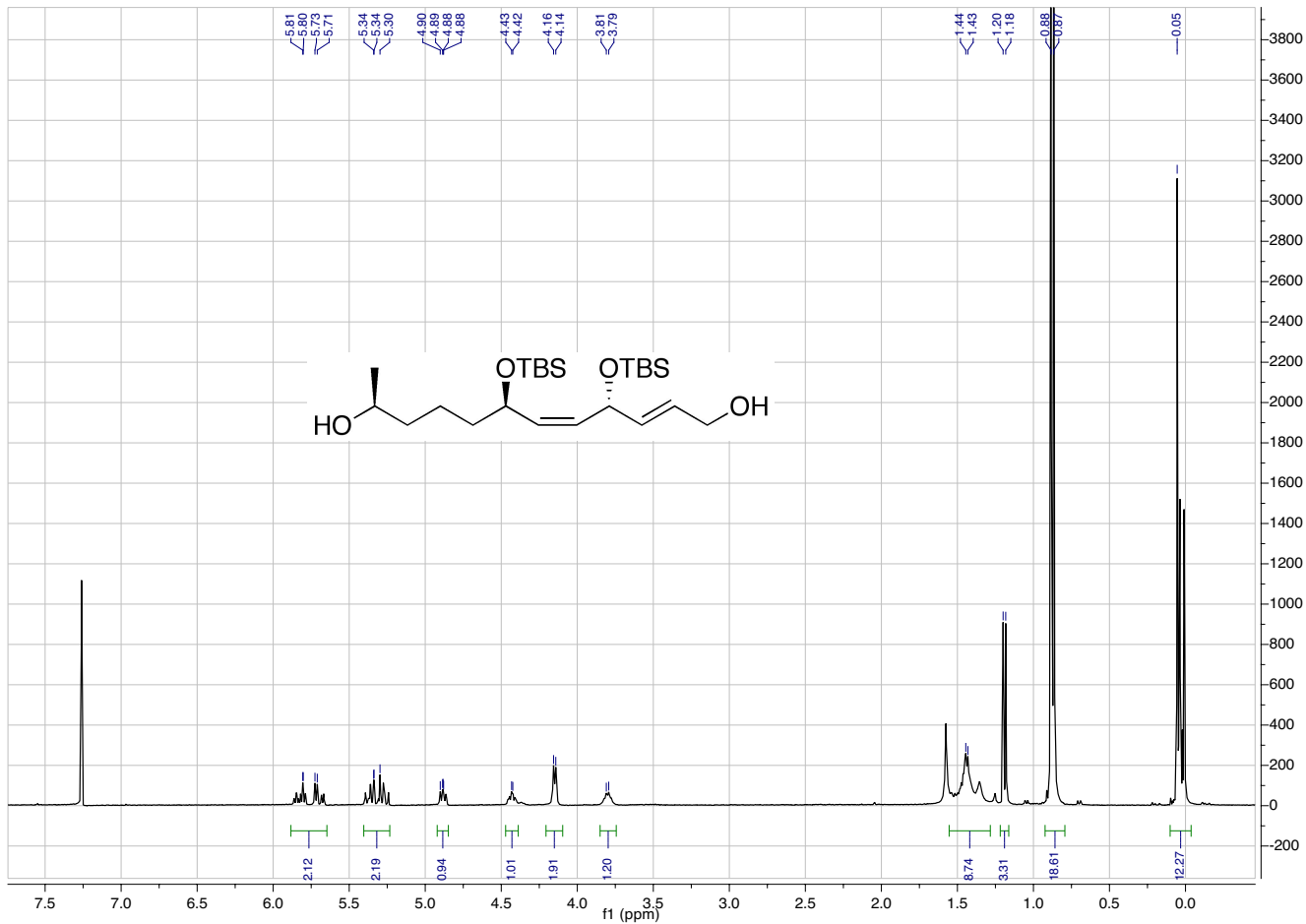


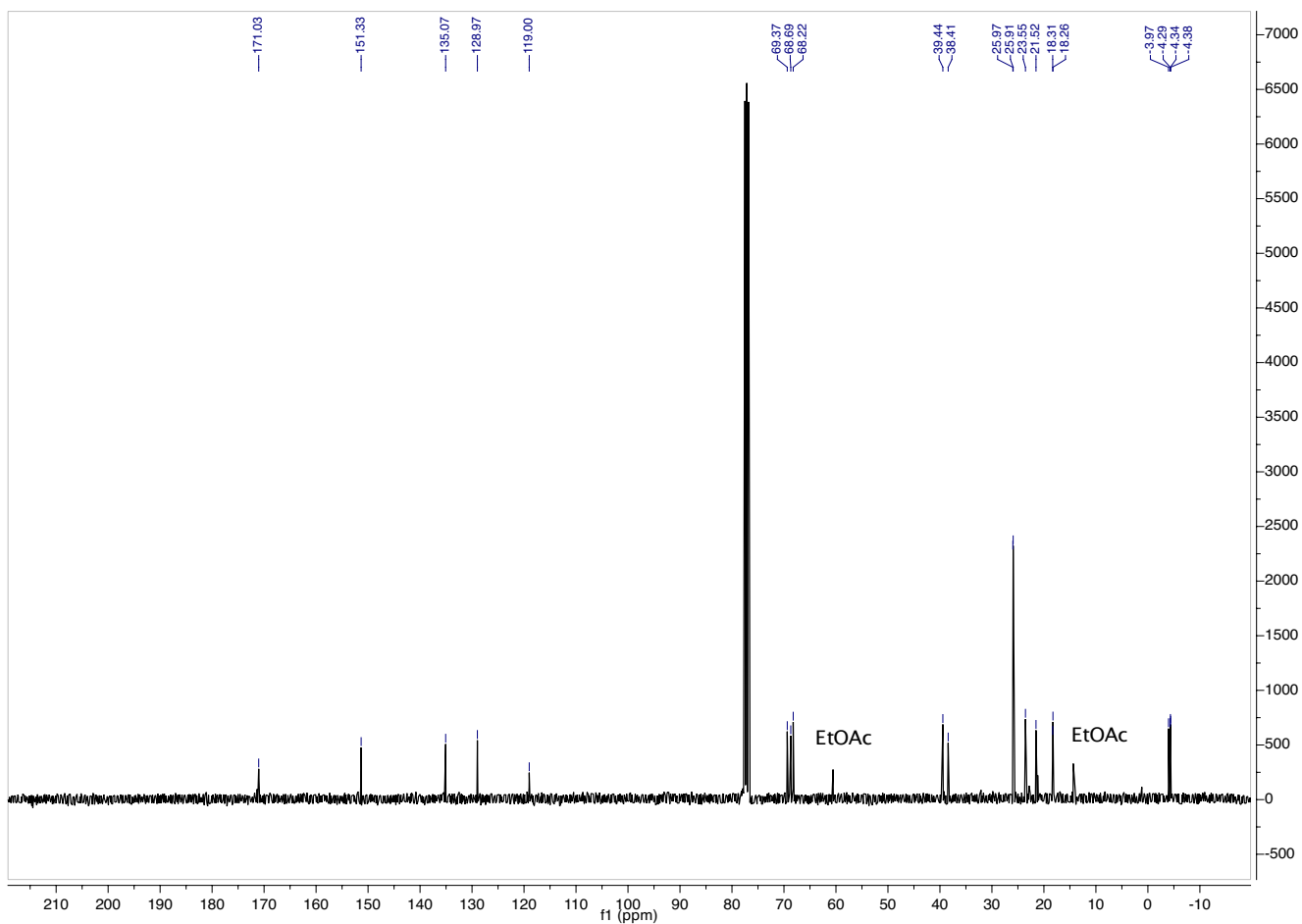
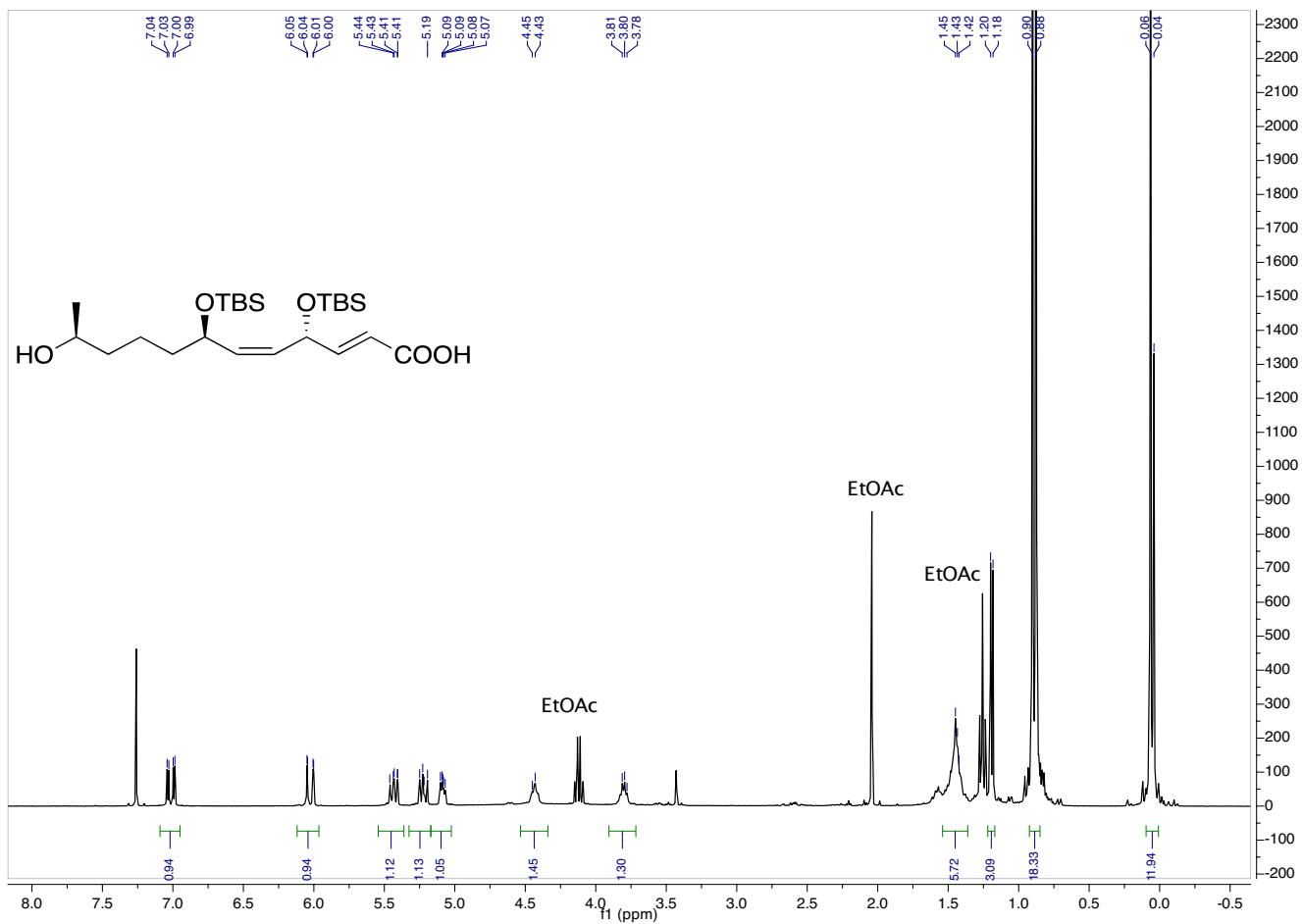


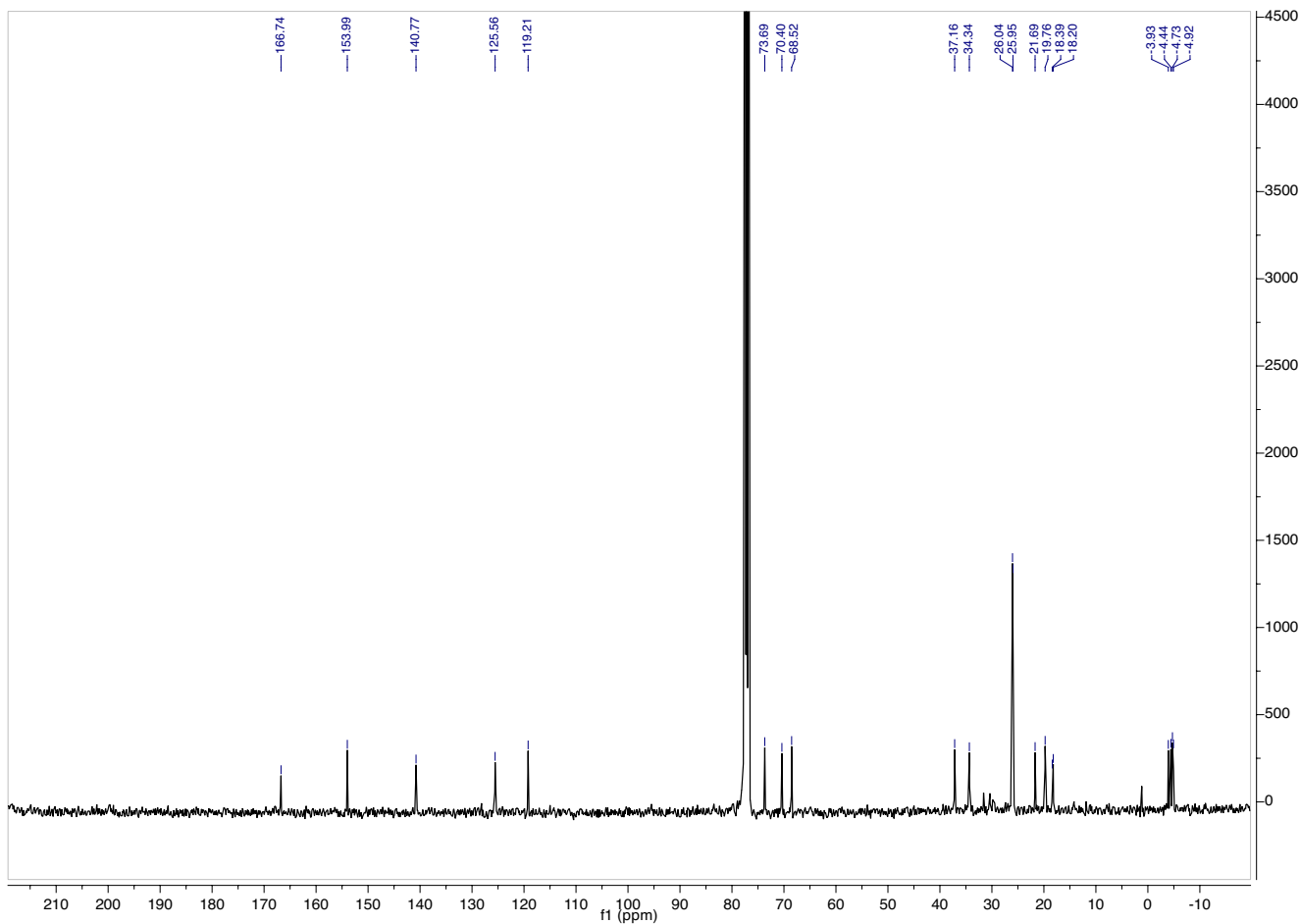
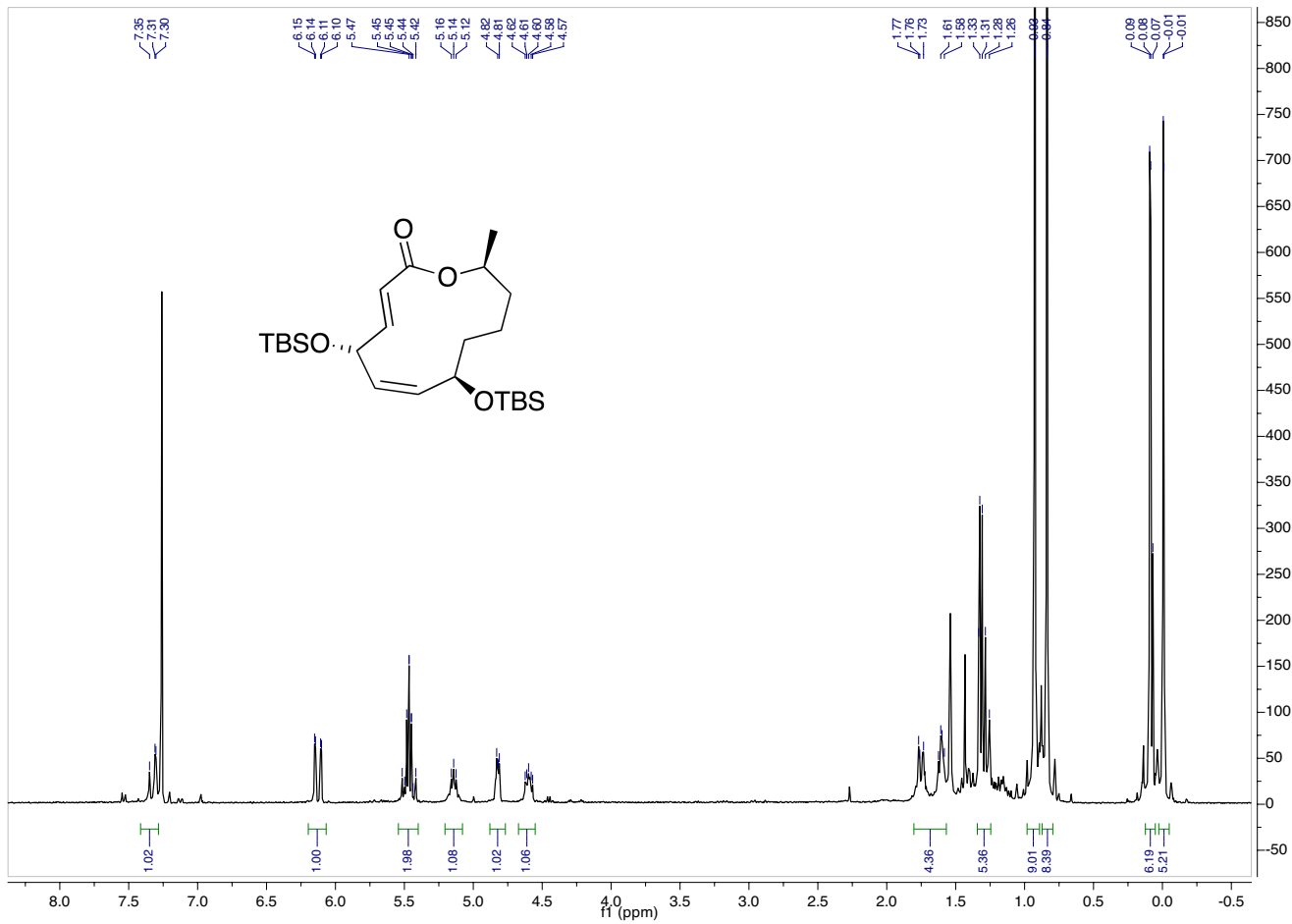


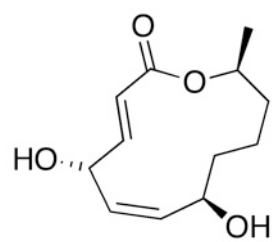




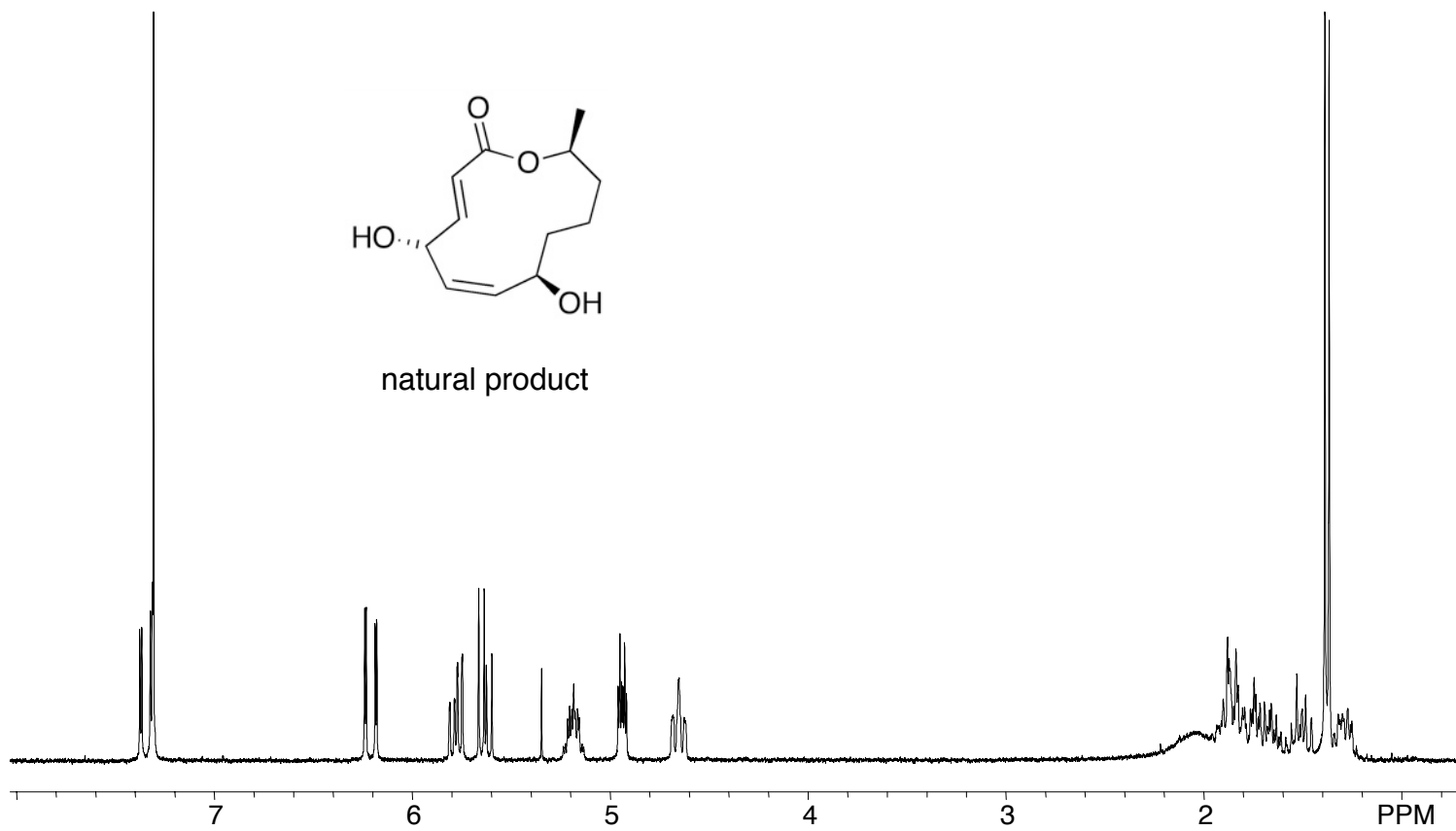




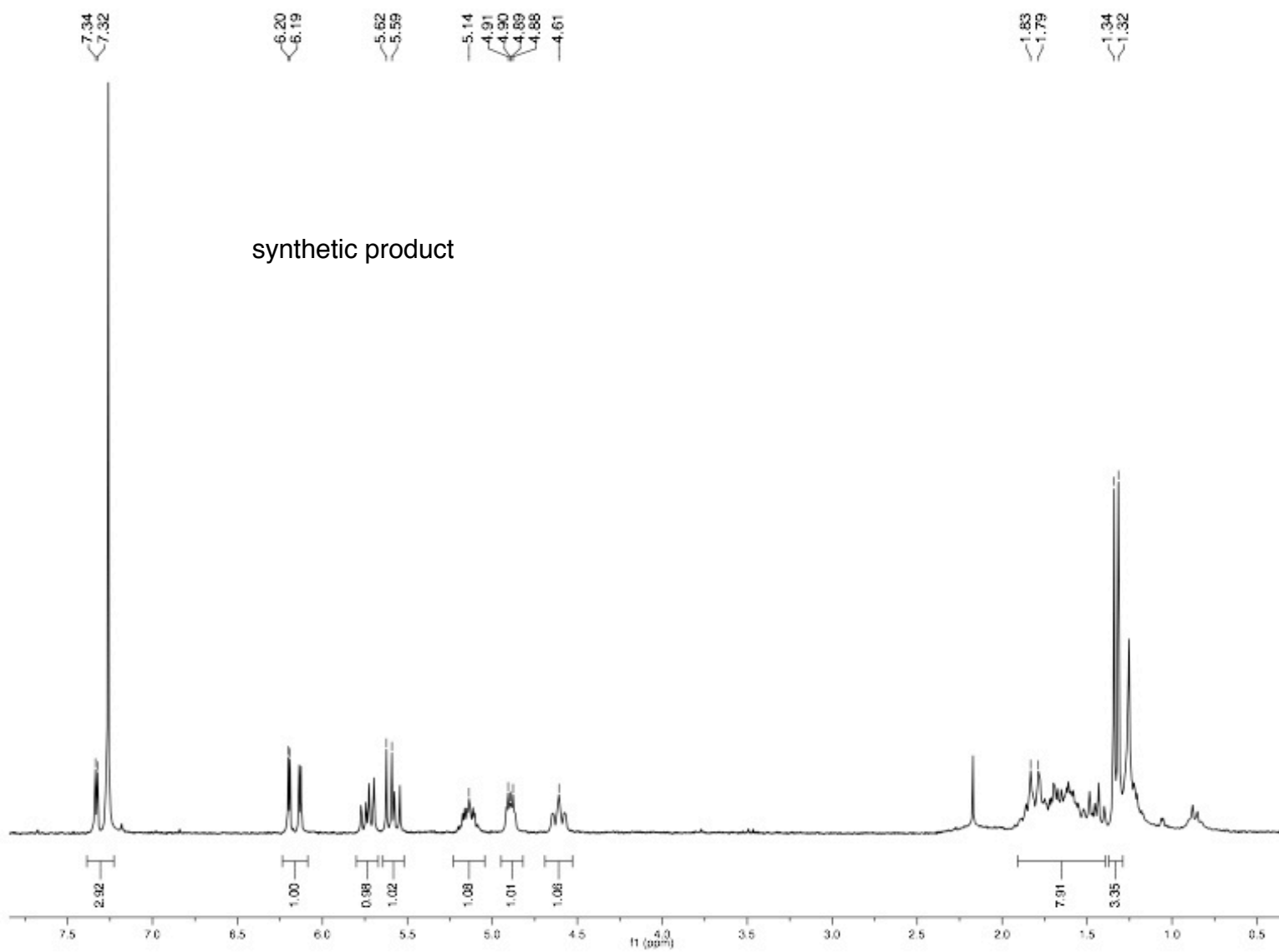


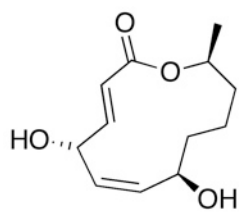


natural product



synthetic product





natural product

