

## **Enantioselective Synthesis of 15-Deoxy- $\Delta^{12,14}$ -Prostaglandin J<sub>2</sub>**

Jiaming Li<sup>†</sup>, Brian M. Stoltz<sup>\*,‡</sup> and Robert H Grubbs<sup>\*,†</sup>

<sup>†</sup> The Arnold and Mabel Beckman Laboratory of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, United States

<sup>‡</sup> The Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, 1200 East California Boulevard, MC 101-20, Pasadena, California 91125, United States

**Supporting Information:**

**Table of Contents:**

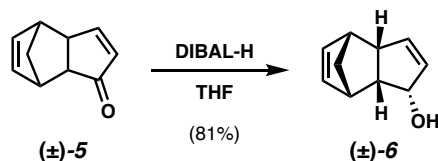
I.	Materials and Methods.....	S3
II.	Experimental Procedures and Characterization Data .....	S4
III.	References.....	S17
IV.	<sup>1</sup> H and <sup>13</sup> C NMR Spectral Data .....	S18

## I. Materials and Methods

Unless noted in the specific procedure, reactions were performed in flame-dried glassware under argon atmosphere. All metathesis reactions were carried out under air-free conditions in dry glassware in a Vacuum Atmospheres Glovebox filled with N<sub>2</sub>. General solvents were purified by passing through solvent purification columns. Commercially available substrates were used as received. All solvents and substrates were sparged with Ar before bringing into the glovebox and filtered over basic alumina (Brockmann I) prior to use. Reaction progress was monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F<sub>254</sub> precoated plates (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silicycle SiliaFlash P60 Academic Silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing Chiralcel OD-H and OJ-H columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 254 nm. Analytical SFC was performed with a Mettler SFC supercritical CO<sub>2</sub> analytical chromatography system utilizing Chiralcel OD-H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 210 nm. GC conversion data was obtained using an HP-5 capillary column with an Agilent 6850 FID gas chromatograph. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Varian Inova 500 spectrometer (500 MHz and 126 MHz, respectively), a Bruker AV III HD spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe (400 MHz and 101 MHz, respectively), or a Varian Mercury 300 spectrometer (300 MHz and 75 MHz, respectively) and are reported in terms of chemical shift relative to residual CHCl<sub>3</sub> (δ 7.26 and δ 77.16 ppm, respectively). Data for <sup>1</sup>H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Abbreviations are used as follows: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = complex multiplet. Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer using neat samples on ATR diamond, and are reported in frequency of absorption (cm<sup>-1</sup>). High-resolution mass spectra HRMS were acquired from the Caltech Mass Spectral Facility using fast-atom bombardment (FAB+), electrospray ionization (TOF ES+) or electron impact (EI+), and an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm pathlength cell at 589 nm.

## II. Experimental Procedures and Characterization Data

### 1. Preparation of (±)-6:

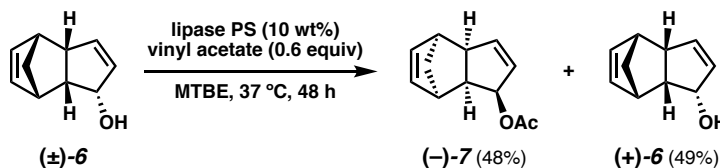


Racemic enone (±)-5 was obtained from photooxygenation of dicyclopentadiene catalyzed by tetraphenylporphyrin (TPP) according to Mihelich and Eickhoff's procedure.<sup>1</sup> In a 500 mL round bottom flask, (±)-5 (13.2 g, 8.9 mmol) was dissolved in anhydrous toluene (150 mL) under argon atmosphere. The solution was cooled to  $-78\text{ }^{\circ}\text{C}$ , and a solution of DIBAL-H (1.0 M solution in toluene, 13.4 mL, 13.4 mmol, 1.5 equiv) was added dropwisely. After 1.5 h, MeOH (50 mL) was added (dropwisely at beginning to avoid splashing). The reaction mixture was warmed to ambient temperature, poured into a saturated Na-K tartrate solution (150 mL), and the biphasic solution was stirred overnight. The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 200\text{ mL}$ ). The combined organic phases were dried with anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification by flash column chromatography on silica gel ( $\text{SiO}_2$ , 10:1 to 4:1 hexanes/EtOAc) afforded compound (±)-6 as a white solid (10.9 g, 81% yield).

**TLC (4:1 hexanes/EtOAc):**  $R_f = 0.3$  ( $\text{KMnO}_4$ ).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  6.15 (dd,  $J = 5.7, 2.6\text{ Hz}$ , 1H), 5.81 (dd,  $J = 5.7, 3.2\text{ Hz}$ , 1H), 5.59 (s, 2H), 4.67 (t,  $J = 9.0\text{ Hz}$ , 1H), 3.29 (dd,  $J = 7.6, 4.1\text{ Hz}$ , 1H), 2.99 – 2.87 (m, 3H), 1.51 (ddt,  $J = 46.0, 8.0, 1.6\text{ Hz}$ , 2H), 1.23 (d,  $J = 9.6\text{ Hz}$ , 1H)

### 2. Enzymatic kinetic resolution:



In a 250 mL round bottom flask, (±)-6 (4.8 g, 32.4 mmol) was dissolved in MTBE (100 mL, 0.33 M), and vinyl acetate (1.78 mL, 19.4 mmol, 0.6 equiv) was added via syringe. Lipase PS (10% on celite, 480 mg, 10 wt%) was added to the flask. The flask was sealed with a septum and kept under argon atmosphere, and placed in  $37\text{ }^{\circ}\text{C}$  oil bath. After 48 h, the reaction mixture was filtered through celite and concentrated. Column chromatography ( $\text{SiO}_2$ , 10:1 to 4:1 hexanes/EtOAc) afforded white solids (-)-7 (2.93 g, 48% yield) and (+)-6 (2.36 g, 49% yield).

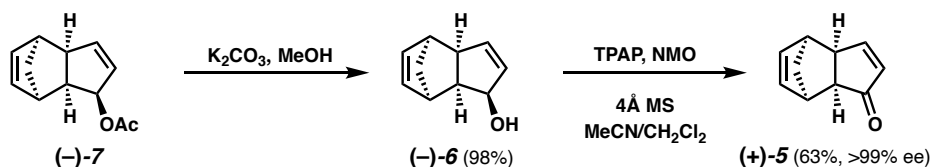
(-)-7

**TLC (10:1 hexanes/EtOAc):**  $R_f$  = 0.68 (KMnO<sub>4</sub>).**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  5.98 (dd,  $J$  = 5.7, 2.9 Hz, 1H), 5.76 (dd,  $J$  = 5.6, 3.1 Hz, 1H), 5.70 (dt,  $J$  = 5.8, 2.0 Hz, 1H), 5.55 (dt,  $J$  = 5.8, 1.9 Hz, 1H), 5.44 (dq,  $J$  = 9.0, 1.7 Hz, 1H), 3.28 (ddt,  $J$  = 7.6, 3.5, 1.7 Hz, 1H), 3.08 (ddd,  $J$  = 8.9, 7.7, 4.1 Hz, 1H), 2.89 (ddp,  $J$  = 4.3, 2.9, 1.3 Hz, 1H), 2.76 (s, 1H), 2.07 (s, 3H), 1.46 (ddt,  $J$  = 39.3, 8.2, 1.7 Hz, 2H).

(+) -6

**TLC (10:1 hexanes/EtOAc):**  $R_f$  = 0.28 (KMnO<sub>4</sub>).**<sup>1</sup>H NMR spectrum data matches ( $\pm$ )-6.** **$[\alpha]_D^{23}$ :** +117.9° ( $c$  = 1.0, CHCl<sub>3</sub>).

### 3. Preparation of enone (+)-5:



To a stirred solution of (-)-7 (2.8 g, 14.7 mmol) in MeOH (50 mL) was added K<sub>2</sub>CO<sub>3</sub> (2.03 g, 14.7 mmol, 1 equiv). The solution was stirred for 12 h and was concentrated, then dissolved in water (30 mL) and extracted by Et<sub>2</sub>O (30 mL). Column chromatography (SiO<sub>2</sub>, 4:1 hexanes/EtOAc) afforded (-)-6 as a white solid (2.04 g, 98%). Spectrum data matches ( $\pm$ )-6.

 **$[\alpha]_D^{23}$ :** -138.1° ( $c$  = 1.0, CHCl<sub>3</sub>).

A 100 mL round bottom flask containing 4 Å molecular sieves (9.0 g) was flame-dried under vacuum. (-)-6 (2.01 g, 13.6 mmol) and NMO (3.19 g, 27.2 mmol, 2 equiv) were added and dissolved in MeCN (3 mL) and CH<sub>2</sub>Cl<sub>2</sub> (27 mL). TPAP (150 mg, 0.42 mmol, 0.03 equiv) was then added and the reaction was stirred under argon for 1 hour, and the reaction progress was monitored by GC. The reaction mixture was filtered over celite and concentrated. Column chromatography (SiO<sub>2</sub>, 4:1 hexanes/EtOAc) afforded (+)-5 as a white solid (1.24 g, 63%). NMR spectrum data matches ( $\pm$ )-5.

**TLC (4:1 hexanes/EtOAc):**  $R_f$  = 0.35 (UV).**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  7.38 (dd,  $J$  = 5.7, 2.6 Hz, 1H), 5.95 (ddd,  $J$  = 7.8, 5.6, 2.3 Hz, 2H), 5.78 (dd,  $J$  = 5.7, 3.0 Hz, 1H), 3.42 (dddd,  $J$  = 5.6, 4.2, 2.6, 1.6 Hz, 1H), 3.22 (dt,  $J$  = 4.1, 1.8 Hz, 1H), 2.97 (ddt,  $J$  = 4.2, 2.7, 1.4 Hz, 1H), 2.80 (t,  $J$  = 5.1 Hz, 1H), 1.68 (dd,  $J$  = 54.4, 8.4 Hz, 2H).**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):**  $\delta$  210.9, 164.7, 137.1, 132.7, 52.9, 50.4, 48.4, 45.1, 44.2.

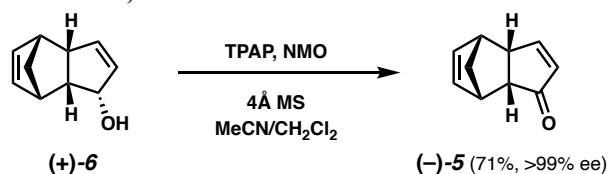
**FTIR (ATR):** 2990, 2972, 1683, 1576, 1347, 1333, 1294, 1251, 1224, 1194, 1178, 1120, 1091, 1018, 959, 853, 817, 784, 739, 721, 652  $\text{cm}^{-1}$ .

**HRMS (FAB+, m/z):** calc'd for  $\text{C}_{10}\text{H}_{11}\text{O}$   $[\text{M}+\text{H}]^+$  147.0810, found: 147.0809.

$[\alpha]_D^{23}$ : +136.6° (c = 1.0,  $\text{CHCl}_3$ ).

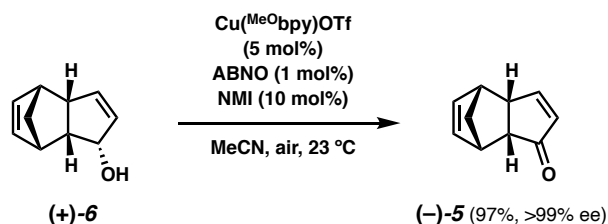
#### 4. Preparation of enone (-)-5:

##### A. Oxidation with TPAP, NMO



A 100 mL round bottom flask containing 4Å molecular sieves (9.0 g) was flame-dried under vacuum. (+)-6 (2.00 g, 13.5 mmol) and NMO (3.16 g, 27 mmol, 2 equiv) were added and dissolved in MeCN (3 mL) and  $\text{CH}_2\text{Cl}_2$  (27 mL). TPAP (142 mg, 0.41 mmol, 0.03 equiv) was then added and the reaction was stirred under argon for 1 hour, and the reaction progress was monitored by GC. The reaction mixture was filtered over celite and concentrated. Column chromatography ( $\text{SiO}_2$ , 4:1 hexanes/EtOAc) afforded (-)-5 as a white solid (1.41 g, 71%).

##### B. Oxidation using Stahl's conditions:



An oven-dried, 200 mL round-bottomed flask was charged with alcohol (+)-6 (2.01 g, 13.6 mmol, 1.0 equiv) and anhydrous MeCN (100 mL). The solution was vigorously stirred (>700 rpm) open to air while being treated with  $\text{MeObpy}$  (147 mg, 0.68 mmol, 0.05 equiv),  $\text{Cu}(\text{MeCN})_4\text{OTf}$  (256 mg, 0.68 mmol, 0.05 equiv), ABNO (0.04 M in MeCN, 3.4 mL, 135.6  $\mu\text{mol}$ , 0.01 equiv), and then NMI (110  $\mu\text{L}$ , 1.36 mmol, 0.10 equiv) via microsyringe. The resulting brick-red reaction mixture was vigorously stirred and exposed to air at ambient temperature until the reaction mixture turned blue-green in an hour, at which point TLC analysis indicated the complete consumption of starting material. The reaction mixture was diluted with  $\text{Et}_2\text{O}$  (50 mL), and filtered through Celite, washing with 50% EtOAc/hexanes. The filtrate was concentrated *in vacuo* and the crude residue was directly purified by flash chromatography ( $\text{SiO}_2$ , 4:1 hexanes/EtOAc) to afford (-)-5 (1.92 g, 97% yield) as a white solid.

**TLC (4:1 hexanes/EtOAc):**  $R_f = 0.35$  (UV).

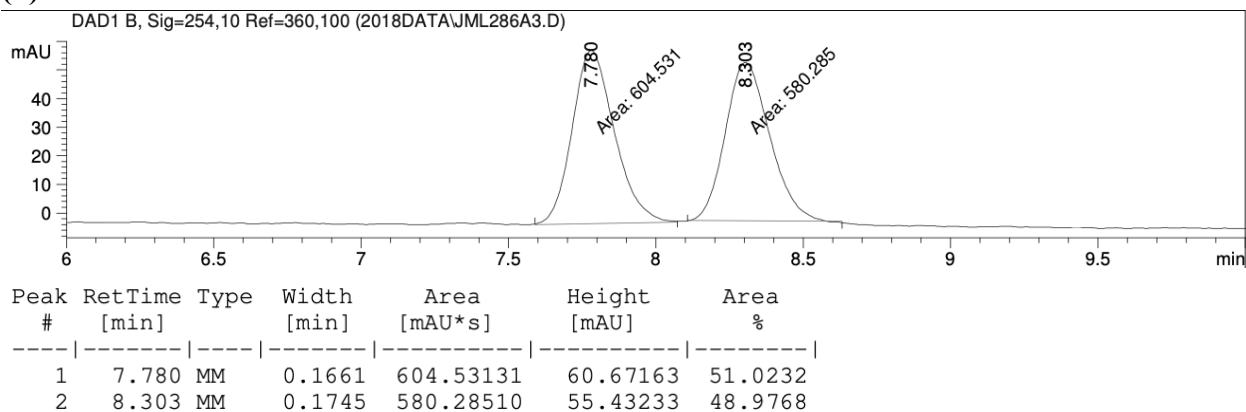
$^1\text{H}$  NMR spectrum data matches (+)-5.

$[\alpha]_D^{23}$ :  $-121.9^\circ$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

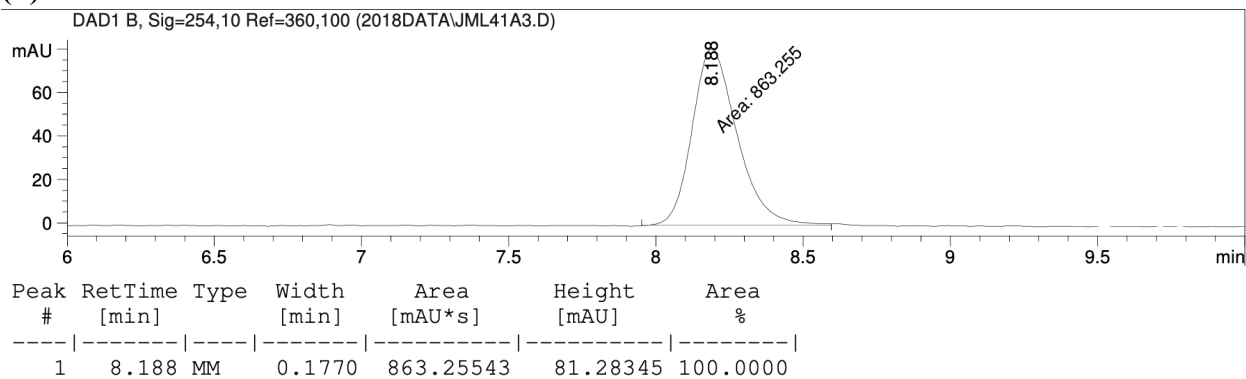
HPLC Conditions:

5% IPA, 1.0 mL/min, Chiralcel OJ-H column,  $\lambda = 254$  nm,  $t_R$  (min) = 7.78, 8.30

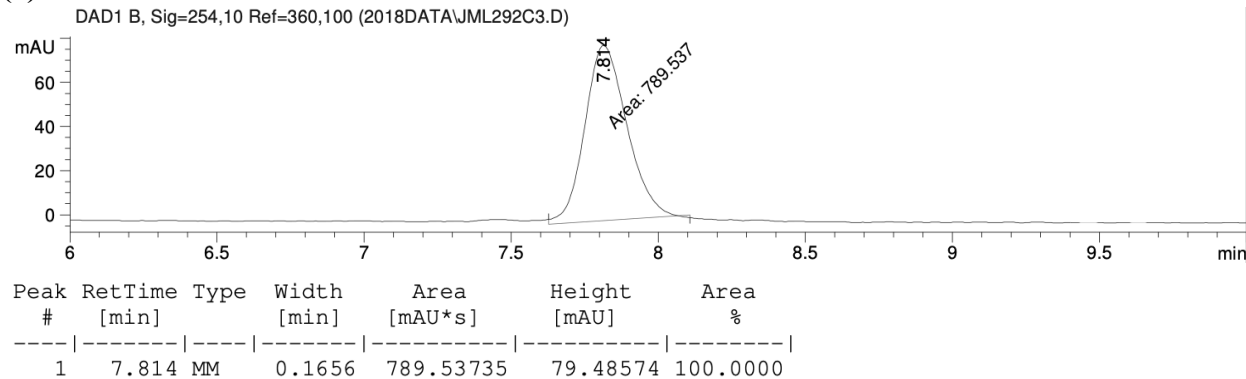
**(±)-5:**



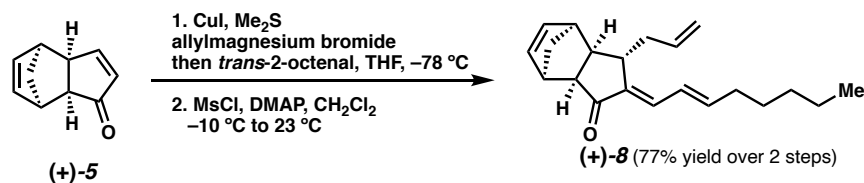
**(+)-5:**



**(-)-5:**

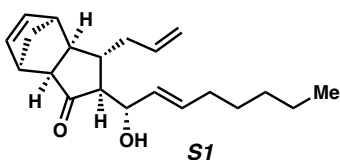


## 5. Preparation of (+)- and (-)-8:



A 250 mL flask was charged with CuI (2.56 g, 13.44 mmol, 1.2 equiv) and flame-dried under vacuum. After cooling to room temperature, anhydrous THF (100 mL) and Me<sub>2</sub>S (5 mL) were added, and the solution was vigorously stirred for 5 minutes at room temperature until a yellow homogeneous solution was formed. At -78 °C, allylmagnesium bromide (12.3 mL, 1.0 M solution in THF, 12.3 mmol, 1.1 equiv) was added slowly. The reaction mixture was stirred at -78 °C for 1 hour and a solution of (+)-5 (1.637 g, 11.2 mmol, 1.0 equiv) in THF (5 mL) was added slowly. After 30 minutes stirring at the same temperature, a solution of *trans*-2-octenal (2.826 g, 22.4 mmol, 2.0 equiv) in THF (3 mL) was added slowly. The reaction was stirred for additional 1 hour at -78 °C, and a solution of saturated NH<sub>4</sub>Cl and NH<sub>3</sub>•H<sub>2</sub>O (100 mL, 9:1 NH<sub>4</sub>Cl/NH<sub>3</sub>•H<sub>2</sub>O) was added. The biphasic solution was warmed to room temperature and was vigorously stirred until a homogeneous dark blue solution was formed in the aqueous phase. The phases were separated and the organic phase was washed with 20 mL saturated NH<sub>4</sub>Cl solution. The combined aqueous phase was extracted with Et<sub>2</sub>O (3 × 100 mL). The combined organic phase was dried with anhydrous magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by flash chromatography (SiO<sub>2</sub>, hexanes/EtOAc 15:1) to give a mixture of diastereomers of the aldol products (3.6 g).

A portion of the reaction mixture was taken out and the major diastereomer was isolated as follow:



**TLC (4:1 hexanes/EtOAc):** R<sub>f</sub> = 0.33 (*p*-anisaldehyde).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):** δ 6.18 (dd, *J* = 5.7, 2.9 Hz, 1H), 6.10 (dd, *J* = 5.8, 3.0 Hz, 1H), 5.80 (dddd, *J* = 15.7, 11.0, 8.1, 6.1 Hz, 1H), 5.63 (dt, *J* = 15.3, 6.7 Hz, 1H), 5.30 (ddt, *J* = 15.3, 8.0, 1.6 Hz, 1H), 5.13 – 5.06 (m, 2H), 4.18 (d, *J* = 1.9 Hz, 1H), 4.04 (td, *J* = 8.2, 1.9 Hz, 1H), 3.19 (ddt, *J* = 4.5, 3.0, 1.4 Hz, 1H), 3.09 (ddd, *J* = 10.2, 4.7, 2.4 Hz, 1H), 2.98 (tt, *J* = 2.9, 1.6 Hz, 1H), 2.64 (ddd, *J* = 9.9, 5.6, 4.1 Hz, 1H), 2.40 (dddd, *J* = 13.3, 5.5, 3.8, 1.7 Hz, 1H), 2.12 – 1.97 (m, 4H), 1.57 (dt, *J* = 8.4, 1.8 Hz, 1H), 1.51 – 1.42 (m, 2H), 1.41 – 1.22 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H).

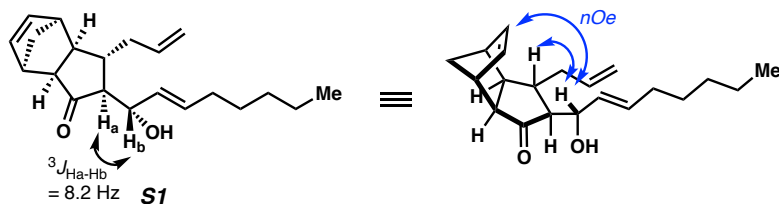
**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):** δ 136.3, 135.8, 134.0, 129.8, 117.2, 73.1, 61.8, 56.6, 52.5, 47.2, 45.9, 45.5, 40.9, 40.4, 32.3, 31.6, 28.8, 22.6, 14.1. (The carbonyl peak was not observed below 219 ppm)



**FTIR (ATR):** 3465, 3073, 2957, 2925, 2857, 1709, 1640, 1600, 1439, 1413, 1338, 1249, 1224, 1090, 973, 911, 836, 733  $\text{cm}^{-1}$ .

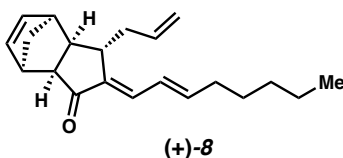
**HRMS (FAB+, m/z):** calc'd for  $\text{C}_{21}\text{H}_{29}\text{O}_2$   $[\text{M}+\text{H}-\text{H}_2]^+$  313.2168, found: 313.2158.

$[\alpha]_D^{23}$ : +28.1° (c = 1.0,  $\text{CHCl}_3$ ).



Kobayashi et al. establishes that for compounds **S1** (*anti*-aldols)  $^3J_{\text{Ha-Hb}}$  is in the range of 8.4 to 9.7 Hz, while for the corresponding *syn*-aldols  $^3J_{\text{Ha-Hb}}$  is around 3 Hz.<sup>2</sup> The stereochemistry of  $\text{H}_b$  was also confirmed by nOe analysis of **S1**.

Without further separation, the crude aldol product was dissolved in  $\text{CH}_2\text{Cl}_2$  (200 mL) and cooled to 0 °C. DMAP (20.5 g, 168 mmol, 15.0 equiv) and  $\text{MsCl}$  (2.6 mL, 33.6 mmol, 3.0 equiv) were added sequentially. The reaction mixture was slowly warmed to room temperature and was stirred for 16 h before washed with 1 M  $\text{HCl}$  (100 mL). The aqueous phase was extracted with  $\text{EtOAc}$  (3  $\times$  100 mL). The combined organic phase was dried with anhydrous magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by flash chromatography (hexanes/ $\text{EtOAc}$  20:1) to give (+)-**8** (2.55 g, 77% yield over 2 steps) as a yellow liquid.



**TLC (10:1 hexanes/ $\text{EtOAc}$ ):**  $R_f = 0.48$  (UV).

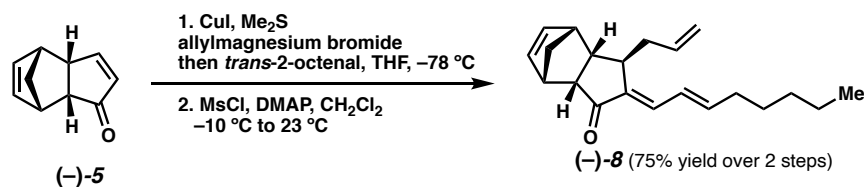
**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  6.70 (dd,  $J = 10.7, 2.1$  Hz, 1H), 6.20 – 6.04 (m, 2H), 5.97 (qd,  $J = 5.6, 2.7$  Hz, 2H), 5.79 (ddt,  $J = 17.1, 10.2, 6.9$  Hz, 1H), 5.14 – 5.05 (m, 2H), 3.24 (tq,  $J = 2.8, 1.4$  Hz, 1H), 3.01 (dp,  $J = 4.4, 1.4$  Hz, 1H), 2.97 (dd,  $J = 8.6, 4.8$  Hz, 1H), 2.64 – 2.56 (m, 2H), 2.35 – 2.26 (m, 1H), 2.22 – 2.07 (m, 3H), 1.49 – 1.37 (m, 4H), 1.35 – 1.23 (m, 4H), 0.89 (t,  $J = 6.8$  Hz, 3H).

**$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):**  $\delta$  209.8, 146.8, 141.1, 136.1, 136.0, 133.5, 132.7, 126.3, 117.1, 54.0, 51.5, 47.4, 47.2, 43.7, 41.2, 40.3, 33.5, 31.4, 28.5, 22.5, 14.0.

**FTIR (ATR):** 3062, 2957, 2928, 2858, 1701, 1625, 1600, 1438, 1341, 1293, 1202, 1178, 1122, 973, 912, 727, 698  $\text{cm}^{-1}$ .

**HRMS (FAB+, m/z):** calc'd for  $\text{C}_{21}\text{H}_{29}\text{O}$   $[\text{M}+\text{H}]^+$  297.2218, found: 297.2214.

$[\alpha]_D^{23}$ : +150.4° (c = 1.0,  $\text{CHCl}_3$ ).



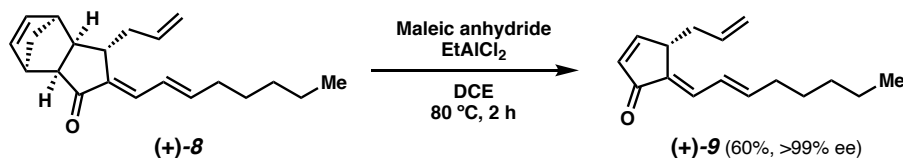
A 250 mL flask was charged with CuI (571 mg, 3 mmol, 1.2 equiv) and flame-dried under vacuum. After cooling to room temperature, anhydrous THF (25 mL) and Me<sub>2</sub>S (1 mL) were added, and the solution was vigorously stirred for 5 minutes at room temperature until a yellow homogeneous solution was formed. At -78 °C, allylmagnesium bromide (2.75 mL, 1.0 M solution in THF, 2.75 mmol, 1.1 equiv) was added slowly. The reaction mixture was stirred at -78 °C for 1 hour and a solution of (-)-**5** (365 mg, 2.5 mmol, 1.0 equiv) in THF (2 mL) was added slowly. After 30 minutes stirring at the same temperature, a solution of *trans*-2-octenal (631 mg, 5.0 mmol, 2.0 equiv) in THF (1 mL) was added slowly. The reaction was stirred for additional 1 hour at -78 °C, and a solution of saturated NH<sub>4</sub>Cl and NH<sub>3</sub>•H<sub>2</sub>O (25 mL, 9:1 NH<sub>4</sub>Cl/NH<sub>3</sub>•H<sub>2</sub>O) was added. The biphasic solution was warmed to room temperature and was vigorously stirred until a homogeneous dark blue solution was formed in the aqueous phase. The phases were separated and the organic phase was washed with 10 mL saturated NH<sub>4</sub>Cl solution. The combined aqueous phase was extracted with Et<sub>2</sub>O (3 × 30 mL). The combined organic phase was dried with anhydrous magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by flash chromatography (SiO<sub>2</sub>, hexanes/EtOAc 15:1) to give a mixture of diastereomers of the aldol products (790 mg).

Without further separation, the crude aldol product was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (40 mL) and cooled to 0 °C. DMAP (4.58 g, 37.5 mmol, 15.0 equiv) and MsCl (0.58 mL, 7.5 mmol, 3.0 equiv) were added sequentially. The reaction mixture was slowly warmed to room temperature and was stirred for 16 h before washed with 1 M HCl (40 mL). The aqueous phase was extracted with EtOAc (3 × 40 mL). The combined organic phase was dried with anhydrous magnesium sulfate, and was concentrated *in vacuo*. The residue was purified by flash chromatography (hexanes/EtOAc 20:1) to give (-)-**8** (559 mg, 75% yield over 2 steps) as a yellow liquid.

Characterization data matches (+)-**8**.

[ $\alpha$ ]<sub>D</sub><sup>23</sup>: -193.4° (c = 1.0, CHCl<sub>3</sub>).

## 6. Preparation of (+)- and (-)-**9**:



In a 100 mL round bottom flask, (+)-**8** (1.64 g, 5.54 mmol, 1.0 equiv) was dissolved in DCE (50 mL). Maleic anhydride (5.4 g, 55.4 mmol, 10.0 equiv) and EtAlCl<sub>2</sub> (6.0 mL, 1.0 M solution in hexanes, 6.0 mmol, 1.1 equiv) were added sequentially. A reflux condenser was attached and the reaction mixture was warmed to reflux under argon. After 2 hours, the reaction mixture was cooled down, concentrated and directly loaded on silica gel. Purification by flash chromatography (hexanes/EtOAc 15:1) afforded (+)-**9** (760 mg, 60% yield, >99% ee by chiral HPLC analysis) as a colorless liquid.

Spectral data (<sup>1</sup>H NMR, <sup>13</sup>C NMR, HRMS, IR) matched with the published data.<sup>3</sup>

**TLC (4:1 hexanes/EtOAc):** R<sub>f</sub> = 0.56 (UV).

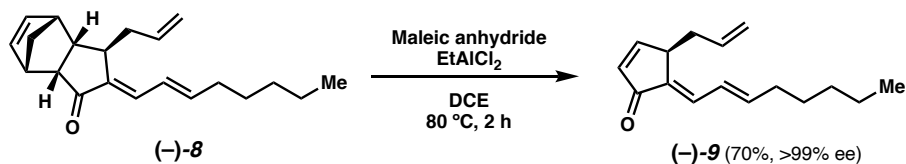
**<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):** δ 7.50 (ddd, *J* = 6.0, 2.6, 1.0 Hz, 1H), 6.95 (dt, *J* = 10.7, 1.2 Hz, 1H), 6.35 (dd, *J* = 6.0, 1.8 Hz, 1H), 6.33 – 6.15 (m, 2H), 5.81 – 5.64 (m, 1H), 5.11 – 5.01 (m, 2H), 3.60 (ddq, *J* = 8.5, 4.1, 1.9 Hz, 1H), 2.73 – 2.58 (m, 1H), 2.24 (dddd, *J* = 13.4, 9.7, 6.8, 1.5 Hz, 3H), 1.54 – 1.37 (m, 2H), 1.38 – 1.22 (m, 4H), 0.96 – 0.84 (t, *J* = 6.9 Hz, 3H).

**<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):** δ 197.5, 160.6, 147.1, 135.4, 134.9, 134.3, 131.8, 125.7, 117.8, 43.2, 37.4, 33.6, 31.5, 28.6, 22.6, 14.1.

**FTIR (ATR):** 2956, 2926, 2856, 1692, 1631, 1580, 1440, 1338, 1280, 1207, 1102, 977, 915, 871, 839, 801, 753, 730, 666 cm<sup>-1</sup>.

**HRMS (FAB+, *m/z*):** calc'd for C<sub>16</sub>H<sub>21</sub>O [M+H-H<sub>2</sub>]<sup>+</sup> 229.1586, found: 229.1581.

[α]<sub>D</sub><sup>23</sup>: +150.4° (c = 1.0, CHCl<sub>3</sub>).



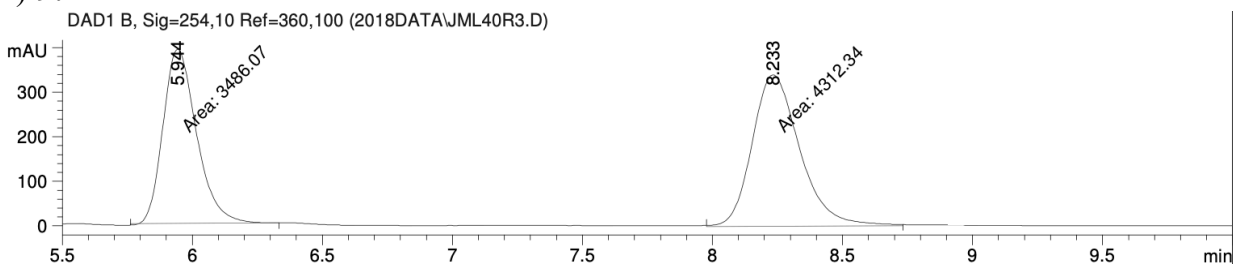
In a 50 mL round bottom flask, (-)-**8** (667 mg, 2.25 mmol, 1.0 equiv) was dissolved in DCE (20 mL). Maleic anhydride (2.2 g, 22.5 mmol, 10.0 equiv) and EtAlCl<sub>2</sub> (2.5 mL, 1.0 M solution in hexanes, 2.5 mmol, 1.1 equiv) were added sequentially. A reflux condenser was attached and the reaction mixture was warmed to reflux under argon. After 2 hours, the reaction mixture was cooled down, concentrated and directly loaded on silica gel. Purification by flash chromatography (hexanes/EtOAc 15:1) afforded (-)-**9** (361 mg, 70% yield, >99% ee by chiral HPLC analysis) as a colorless liquid.

Characterization data matches (+)-**9**.

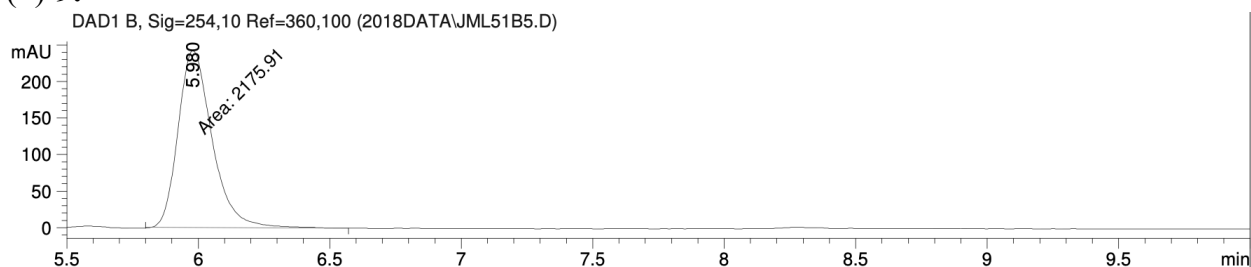
[α]<sub>D</sub><sup>23</sup>: -122.9° (c = 1.0, CHCl<sub>3</sub>).

HPLC Conditions:

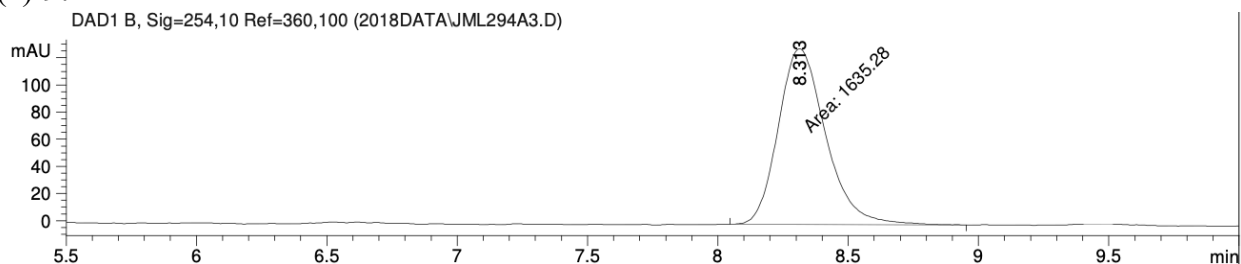
5% IPA, 1.0 mL/min, Chiralcel OD-H column, λ = 254 nm, t<sub>R</sub> (min) = 5.94, 8.23

**(±)-9:**

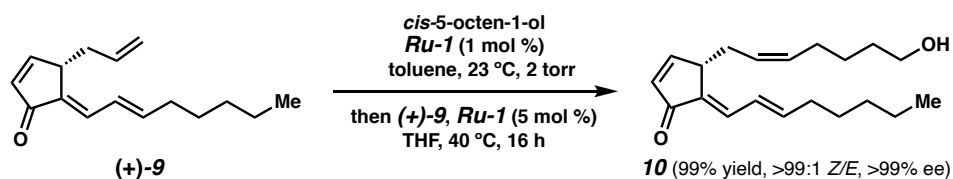
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.944	MM	0.1483	3486.06592	391.88913	44.7023
2	8.233	MM	0.2116	4312.34229	339.61151	55.2977

**(+)-9:**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.980	MM	0.1496	2175.91162	242.38094	100.0000

**(-)-9:**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.313	MM	0.2104	1635.28137	129.50676	100.0000

**7. Preparation of 10:****A. One-pot homodimerization/stereoretentive metathesis method:**

In a nitrogen-filled glovebox, *cis*-5-octen-1-ol (205 mg, 1.6 mmol, 8.0 equiv) was dissolved in toluene (2 mL) in a 50 mL Schlenk flask and a solution of catalyst **Ru-1** (13.5 mg, 16  $\mu$ mol, 1 mol%) in THF (0.8 mL) was added. The Schlenk flask was sealed and brought out of the glovebox, and then connected to high vacuum. The valve was gradually opened (*Caution: open slowly and stir well to avoid splashing*). After 15 minutes stirring, the flask was refilled with argon and sealed, and was brought back into the glovebox. The residue was diluted with THF (0.5 mL), and an aliquot was taken for GC analysis (conversion of the homodimerization step was >98% by GC analysis). A solution of (+)-**9** (46 mg, 0.2 mmol, 1.0 equiv) in THF (0.5 mL) was added into the Schlenk flask and an additional portion of catalyst **Ru-1** (8.5 mg, 10  $\mu$ mol, 5 mol%) solution in THF (0.5 mL) was added. The Schlenk flask was sealed and brought out of glovebox. The reaction was stirred for 16 h at 40 °C before being quenched with a few drops of ethyl vinyl ether. The solvent was removed under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc 2:1) to give **10** (60 mg, 99%, >99:1 *Z/E*, >99% ee by chiral HPLC analysis).

Spectral data ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, HRMS, IR) matched with the published data.<sup>3</sup>

**TLC (4:1 hexanes/EtOAc):**  $R_f$  = 0.2 (UV).

**$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.48 (ddd,  $J$  = 6.0, 2.6, 1.0 Hz, 1H), 6.95 (dt,  $J$  = 11.0, 1.3 Hz, 1H), 6.34 – 6.19 (m, 3H), 5.52 – 5.44 (m, 1H), 5.38 – 5.30 (m, 1H), 3.63 (t,  $J$  = 6.5 Hz, 2H), 3.60 – 3.55 (m, 1H), 2.60 (dddd,  $J$  = 14.0, 6.2, 4.3, 1.4 Hz, 1H), 2.30 (dtd,  $J$  = 14.4, 8.6, 1.2 Hz, 1H), 2.25 – 2.17 (m, 2H), 2.01 (qd,  $J$  = 7.3, 1.4 Hz, 2H), 1.59 – 1.49 (m, 3H), 1.48 – 1.37 (m, 4H), 1.34 – 1.29 (m, 4H), 0.89 (t,  $J$  = 7.0 Hz, 3H).

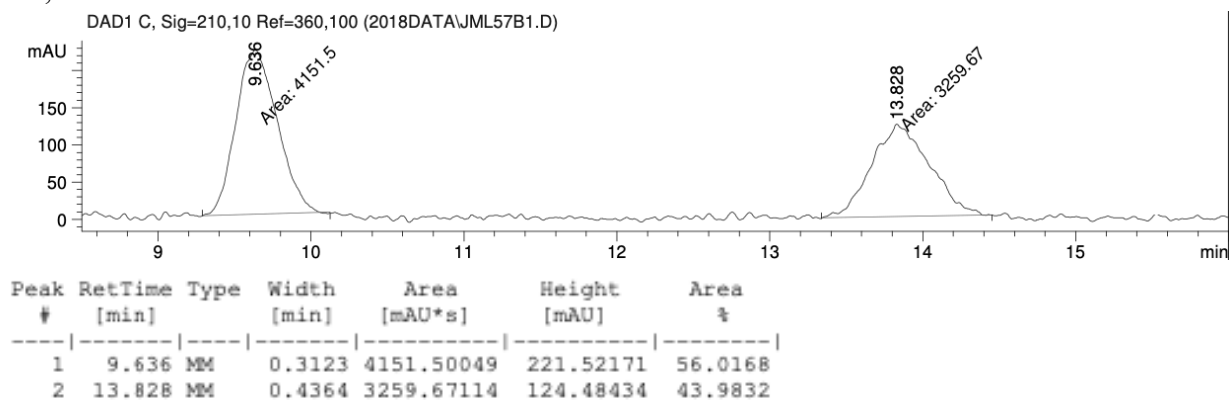
**$^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ ):**  $\delta$  197.6, 160.9, 147.0, 135.4, 135.3, 132.6, 131.8, 125.8, 125.3, 62.9, 43.7, 33.6, 32.5, 31.5, 30.9, 28.6, 27.2, 25.8, 22.6, 14.2.

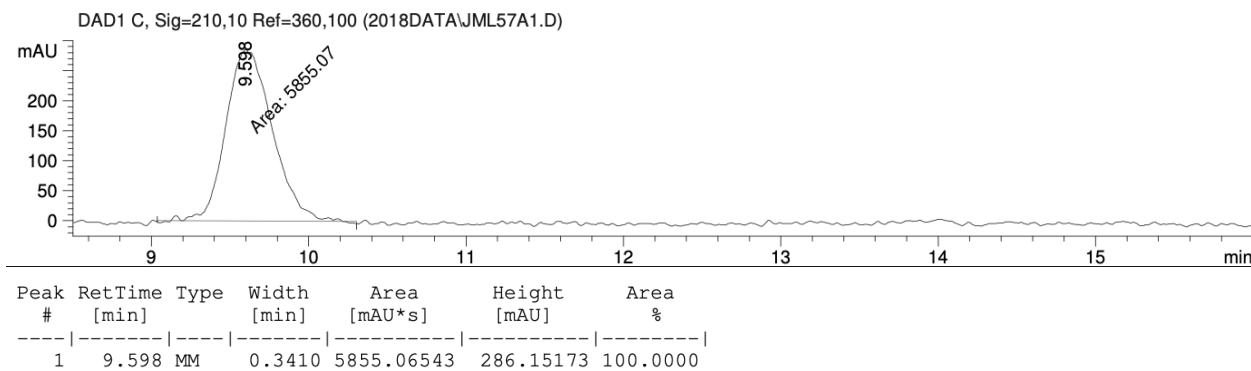
**FTIR (ATR):** 3445, 2960, 2930, 2862, 1690, 1629, 1580, 1447, 1264, 1207, 1054, 979, 732  $\text{cm}^{-1}$ .

**HRMS (TOF, ES+,  $m/z$ ):** calc'd for  $\text{C}_{20}\text{H}_{31}\text{O}_2$  [ $\text{M}+\text{H}$ ] $^+$  303.2319, found: 303.2320.

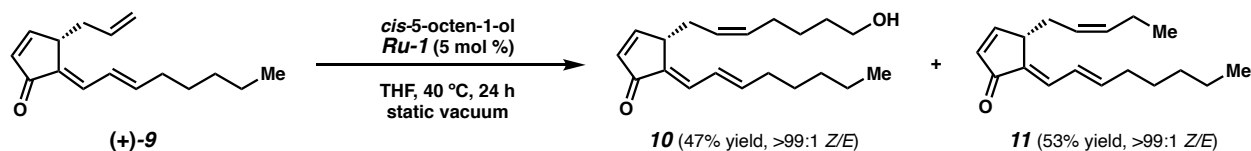
**$[\alpha]_D^{23}$ :** +142.6° ( $c$  = 0.5,  $\text{CHCl}_3$ ).

HPLC Conditions: 10% IPA, 1.0 mL/min, Chiralcel OD-H column,  $\lambda$  = 210 nm,  $t_R$  (min): major = 9.64, minor = 13.83

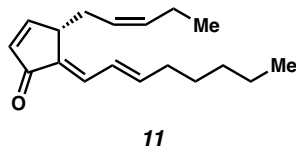




### B. Stereoretentive cross-metathesis method:



In a nitrogen-filled glovebox, (+)-**9** (49 mg, 0.21 mmol, 1.0 equiv) and *cis*-5-octen-1-ol (205 mg, 1.6 mmol, 7.6 equiv) were dissolved in THF (0.5 mL) in a 1-dram vial, and the solution was transferred to a 50 mL Schlenk flask. A solution of catalyst **Ru-1** (8.5 mg, 10  $\mu\text{mol}$ , 5 mol%) in THF (0.5 mL) was added. The Schlenk flask was sealed and brought out of the glovebox, and freeze-pump-thaw for one time to keep it under static vacuum. The reaction was stirred for 16 h at 40  $^\circ\text{C}$  before being quenched with a few drops of ethyl vinyl ether. The solvent was removed under reduced pressure. The residue was purified by flash chromatography (hexanes/EtOAc 10:1 to 2:1) to give **10** (30 mg, 47%, >99:1 Z/E) and **11** (29 mg, 53%, >99:1 Z/E) as two major products.



**TLC (4:1 hexanes/EtOAc):**  $R_f$  = 0.6 (UV).

**$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.48 (ddd,  $J$  = 5.9, 2.6, 1.0 Hz, 1H), 6.95 (dt,  $J$  = 11.2, 1.2 Hz, 1H), 6.39 – 6.17 (m, 3H), 5.53 – 5.43 (m, 1H), 5.34 – 5.24 (m, 1H), 3.56 (ddq,  $J$  = 8.6, 4.1, 2.0 Hz, 1H), 2.70 – 2.47 (m, 1H), 2.34 – 2.17 (m, 3H), 1.99 (pd,  $J$  = 7.5, 1.6 Hz, 2H), 1.46 (p,  $J$  = 7.3 Hz, 2H), 1.31 (tt,  $J$  = 5.6, 2.8 Hz, 4H), 0.93 (t,  $J$  = 7.6 Hz, 3H), 0.89 (t,  $J$  = 6.9 Hz, 3H).

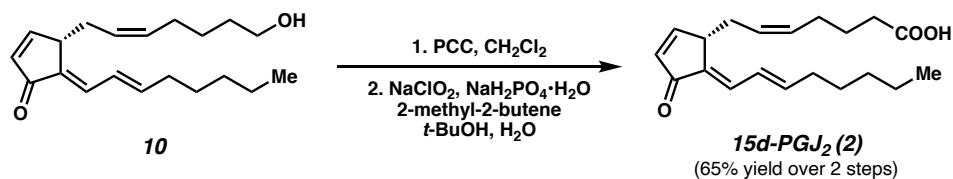
**$^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ ):**  $\delta$  197.6, 160.9, 146.8, 135.4, 134.6, 131.7, 125.8, 124.3, 43.8, 33.6, 31.5, 30.8, 28.6, 22.6, 20.8, 14.3, 14.1.

**FTIR (ATR):** 2959, 2927, 2856, 2360, 1693, 1632, 1579, 1459, 1376, 1337, 1294, 1203, 1100, 1069, 1020, 976, 923, 867, 834, 805, 728, 668  $\text{cm}^{-1}$ .

**HRMS (ESI,  $m/z$ ):** calc'd for  $\text{C}_{18}\text{H}_{27}\text{O}$  [ $\text{M}+\text{H}$ ] $^+$  259.2056, found: 259.2207.

**$[\alpha]_D^{23}$ :** +210.8 $^\circ$  ( $c$  = 1.0,  $\text{CHCl}_3$ ).

### 8. Preparation of 15-deoxy- $\Delta^{12,14}$ -prostaglandin J<sub>2</sub> (2):



Pyridinium chlorochromate (129 mg, 0.6 mmol, 3.0 equiv) was added to a solution of **10** (60 mg, 0.2 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at room temperature. The reaction progress was monitored by TLC. The reaction mixture was diluted with Et<sub>2</sub>O (2 mL) after stirring for 1 h. The resulting solution was filtered through a short pad of celite, concentrated, and subjected to the next step without further purification.

The residue was dissolved in *t*-BuOH (3 mL) at room temperature, 2-methyl-2-butene (210  $\mu$ L, 2.0 mmol, 10 equiv), a solution of NaH<sub>2</sub>PO<sub>4</sub>·H<sub>2</sub>O (41.4 mg, 0.3 mmol, 1.5 equiv) in H<sub>2</sub>O (0.72 mL), and a solution of NaClO<sub>2</sub> (80 %, 33.6 mg, 0.3 mmol, 1.5 equiv) in H<sub>2</sub>O (0.72 mL) were added sequentially. After stirring at room temperature for 30 minutes, the reaction mixture was diluted with a solution of NaH<sub>2</sub>PO<sub>4</sub>·H<sub>2</sub>O (648 mg) in H<sub>2</sub>O (12 mL) and was extracted with EtOAc (5  $\times$  10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (SiO<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>/MeOH 20:1) afforded pure compound **2** (41.0 mg, 65% yield over 2 steps) as a colorless oil.

Spectral data (<sup>1</sup>H NMR, <sup>13</sup>C NMR, HRMS, IR) matched with the published data.<sup>3</sup>

**TLC (100% EtOAc):** R<sub>f</sub> = 0.70 (UV).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  7.47 (dd, *J* = 6.0, 2.5 Hz, 1H), 6.95 (d, *J* = 11.0 Hz, 1H), 6.38 – 6.19 (m, 3H), 5.50 – 5.33 (m, 2H), 3.62 – 3.55 (m, 1H), 2.63 – 2.55 (m, 1H), 2.38 – 2.26 (m, 3H), 2.23 (q, *J* = 7.1 Hz, 2H), 2.05 (q, *J* = 7.3 Hz, 2H), 1.68 (p, *J* = 7.4 Hz, 2H), 1.46 (p, *J* = 7.1 Hz, 2H), 1.37 – 1.25 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H).

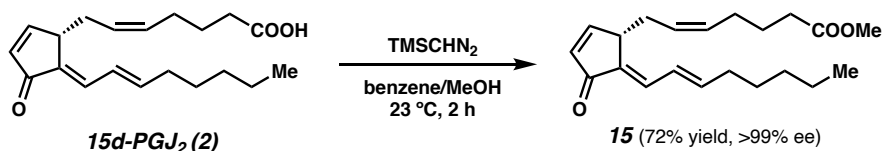
**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):**  $\delta$  197.6, 177.9, 160.8, 147.2, 135.5, 135.1, 131.9, 131.5, 126.2, 125.8, 43.6, 33.6, 33.2, 31.6, 30.8, 28.6, 26.7, 24.6, 22.6, 14.2.

**FTIR (ATR):** 2960, 2928, 2850, 1708, 1692, 1629, 1456, 1265, 1207, 978, 734, 703 cm<sup>-1</sup>.

**HRMS (TOF, ES+, *m/z*):** calc'd for C<sub>20</sub>H<sub>29</sub>O<sub>3</sub> [M+H]<sup>+</sup> 317.2111, found: 317.2127.

**[ $\alpha$ ]<sub>D</sub><sup>23</sup>:** +154.4° (*c* = 1.0, CHCl<sub>3</sub>).

### 9. Preparation of 15-deoxy- $\Delta^{12,14}$ -prostaglandin J<sub>2</sub> methyl ester (15):



In a 1-dram vial, 15d-PGJ<sub>2</sub> (**2**) (8.0 mg, 25  $\mu$ mol, 1.0 equiv) was dissolved in C<sub>6</sub>H<sub>6</sub>/MeOH (3:2, 0.75 mL) at 23 °C. A solution of trimethylsilyldiazomethane (20  $\mu$ L, 2.0 M in hexanes, 40  $\mu$ mol, 1.5 equiv) (yellow color persists). After stirring for 2 hours, the reaction mixture was concentrated under vacuum. The residue was purified by flash column chromatography (SiO<sub>2</sub>, hexanes/EtOAc, 4:1) to give **15** (6.0 mg, 72% yield, >99% ee) as a colorless oil.

**TLC (4:1 hexanes/EtOAc):** R<sub>f</sub> = 0.28 (UV).

**<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  7.47 (ddd,  $J$  = 6.0, 2.6, 1.0 Hz, 1H), 6.95 (dt,  $J$  = 11.0, 1.2 Hz, 1H), 6.37 – 6.17 (m, 3H), 5.50 – 5.31 (m, 2H), 3.66 (s, 3H), 3.57 (ddt,  $J$  = 8.7, 3.8, 2.0 Hz, 1H), 2.64 – 2.56 (m, 1H), 2.33 – 2.18 (m, 5H), 2.03 (q,  $J$  = 7.3 Hz, 2H), 1.66 (p,  $J$  = 7.5 Hz, 2H), 1.46 (p,  $J$  = 7.2 Hz, 2H), 1.31 (ddt,  $J$  = 9.3, 5.3, 3.6 Hz, 4H), 0.89 (t,  $J$  = 6.9 Hz, 3H).

**<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):**  $\delta$  197.5, 174.0, 160.8, 147.1, 135.5, 135.2, 131.8, 131.6, 126.1, 125.8, 51.7, 43.6, 33.6, 33.5, 31.6, 30.9, 28.6, 26.8, 24.8, 22.6, 14.1.

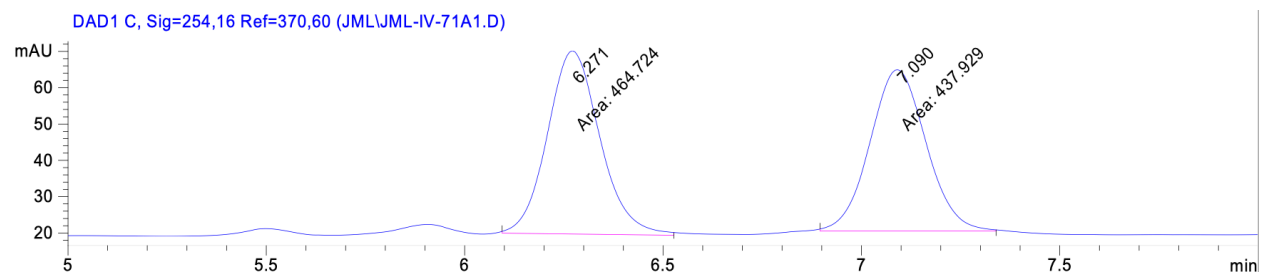
**FTIR (ATR):** 2953, 2927, 2856, 2360, 2342, 1736, 1694, 1632, 1579, 1436, 1364, 1205, 1090, 979, 836, 729, 668 cm<sup>-1</sup>.

**HRMS (ESI, m/z):** calc'd for C<sub>21</sub>H<sub>31</sub>O<sub>3</sub> [M+H]<sup>+</sup> 331.2268, found: 331.2720.

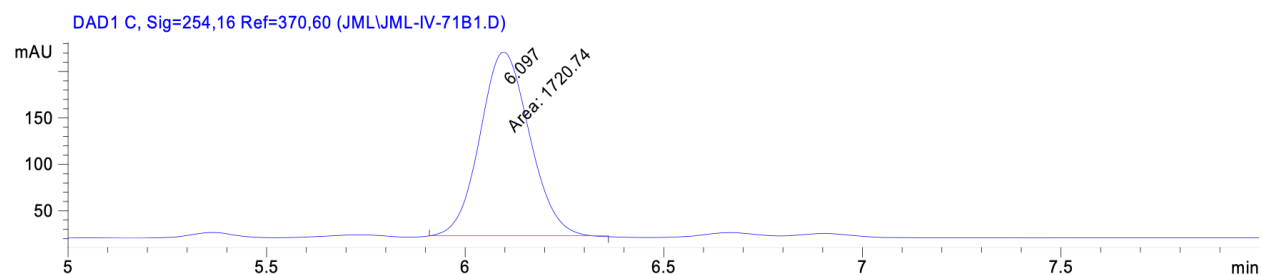
**$[\alpha]_D^{23}$ :** +72.1° (c = 0.2, CHCl<sub>3</sub>).

SFC Conditions:

10% IPA, 4.0 mL/min, Chiralcel OD-H column,  $\lambda$  = 254 nm, t<sub>R</sub> (min) = 6.27, 7.09



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.271	MM	0.1531	464.72391	50.58140	51.4842
2	7.090	MM	0.1639	437.92932	44.52127	48.5158

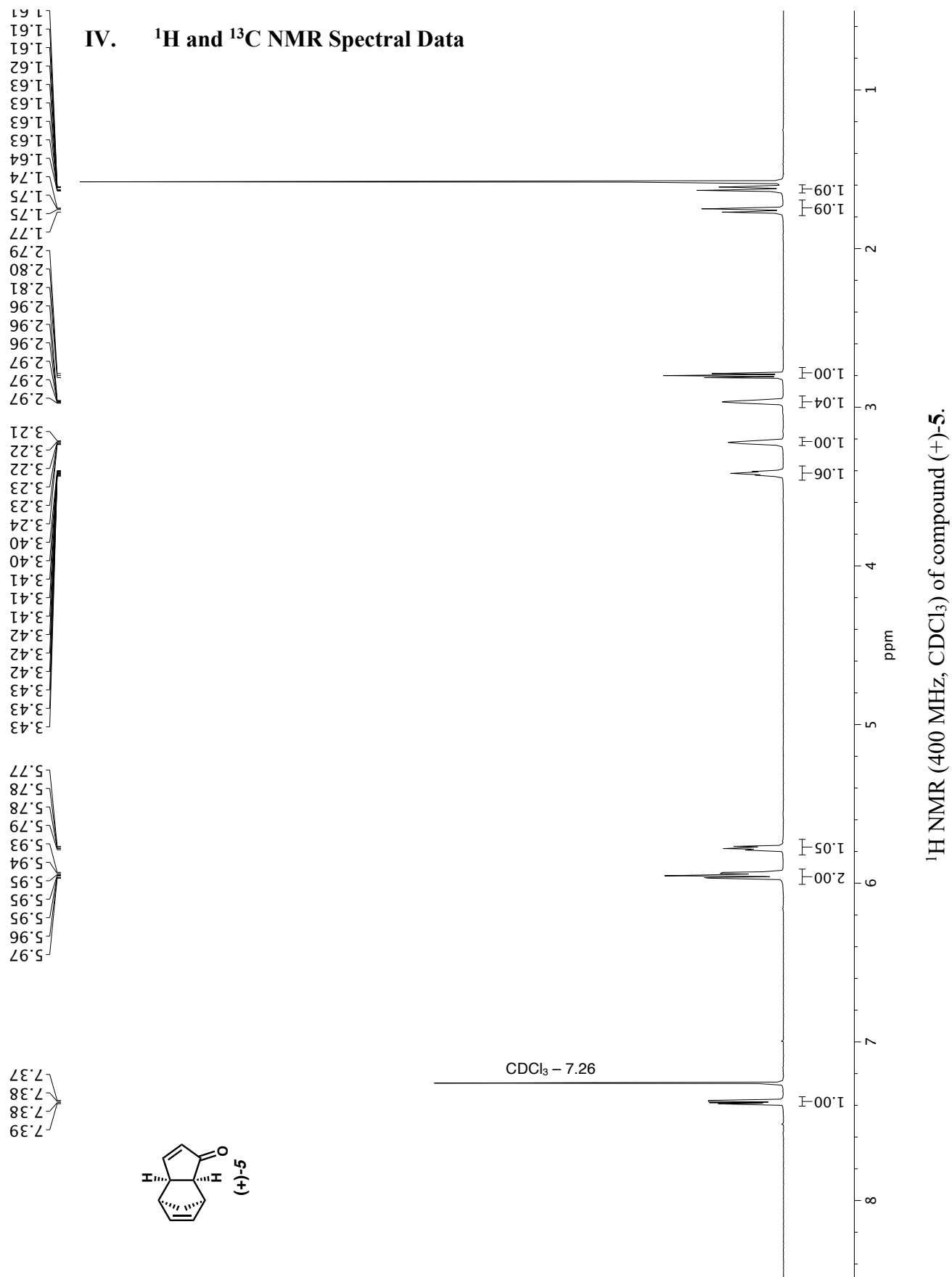


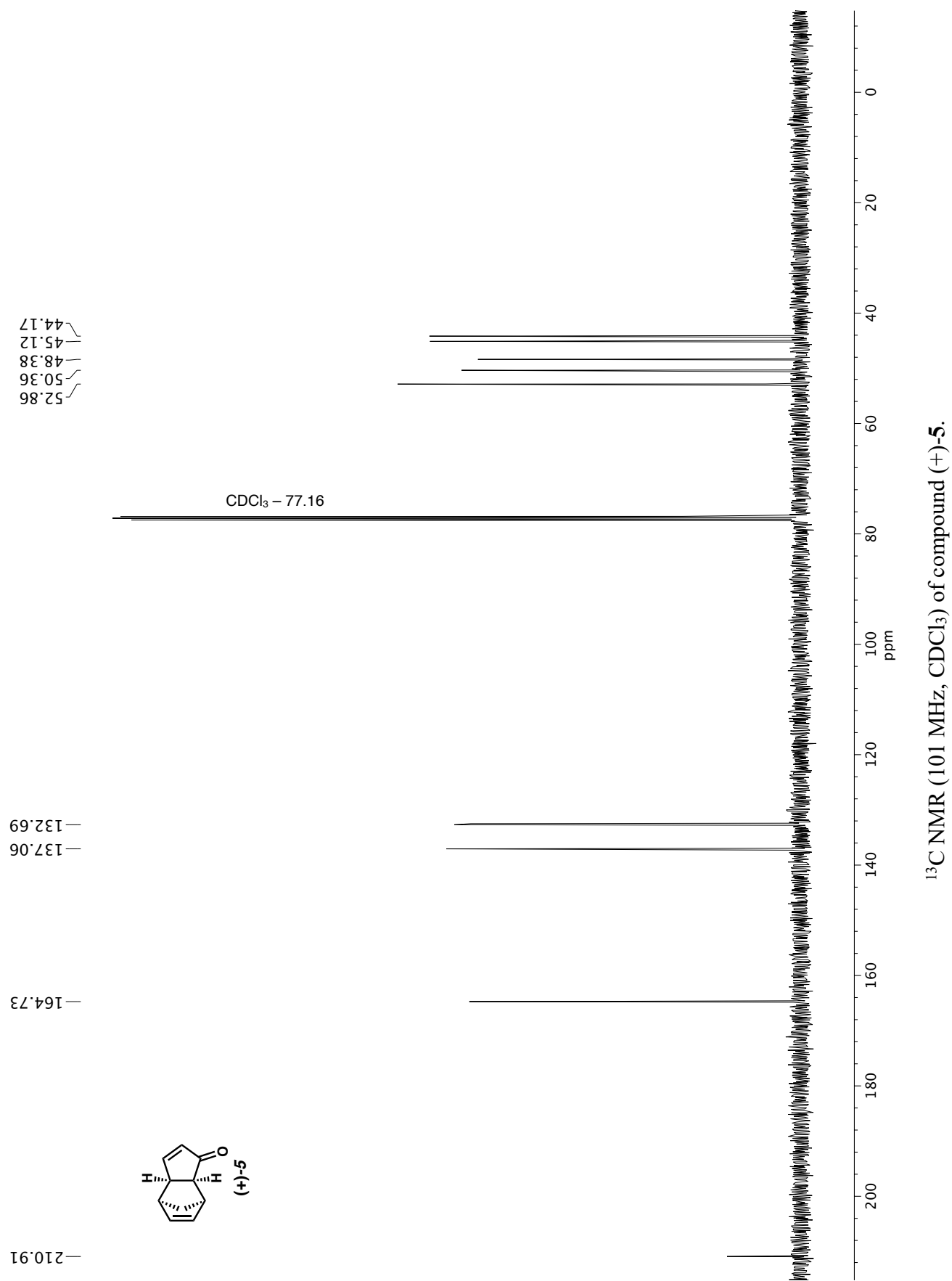
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.097	MM	0.1443	1720.74133	198.71785	100.0000

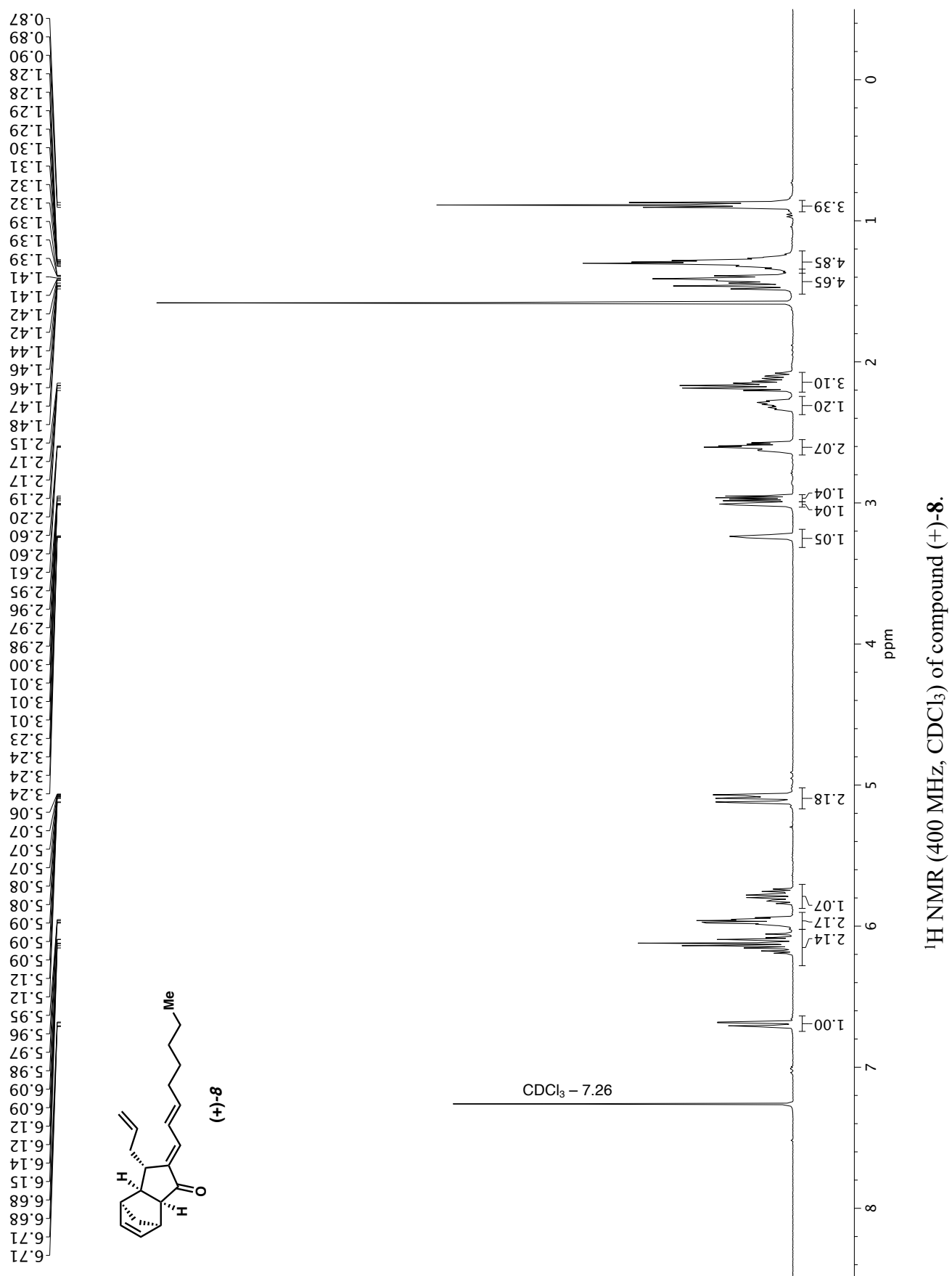


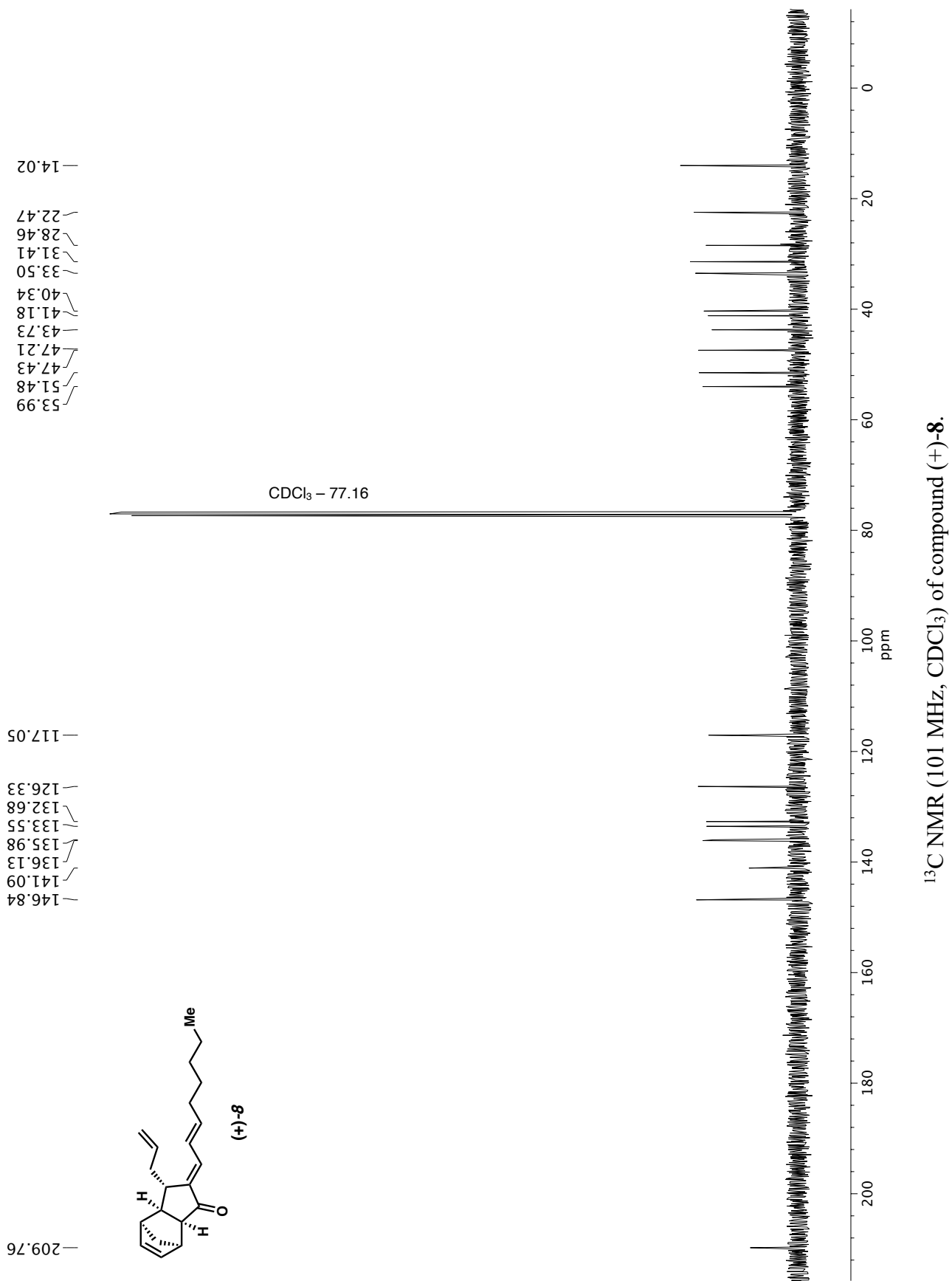
### III. References

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2. Kobayashi, Y.; Murugesu, M. G.; Nakano, M.; Takahisa, E.; Usmani, S. B.; Aina, T. *J. Org. Chem.* **2002**, *67*, 7110–7123.
3. Li, J.; Ahmed, T. S.; Xu, C.; Stoltz, B. M.; Grubbs, R. H. *J. Am. Chem. Soc.*, **2019**, *141*, 154–158.

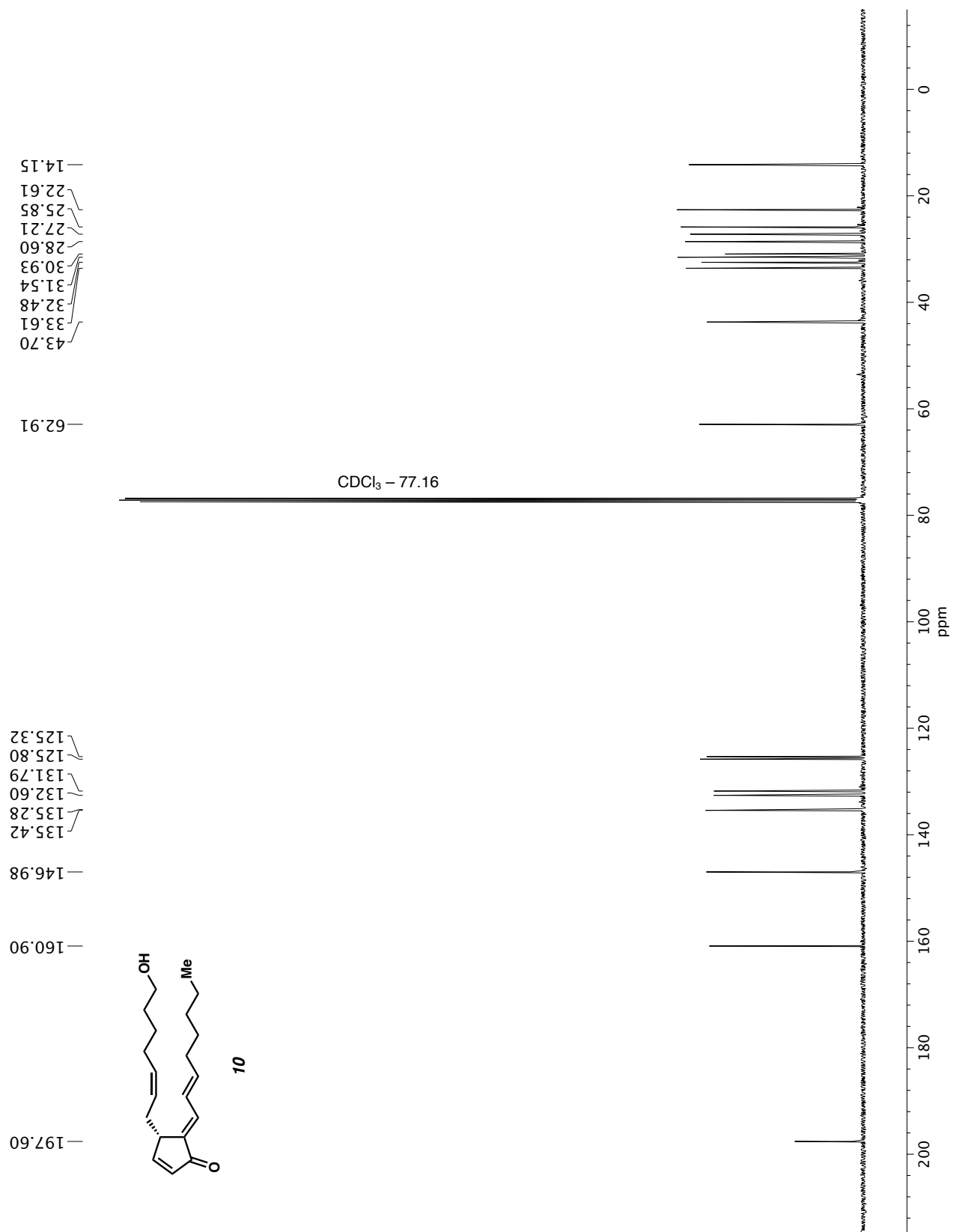


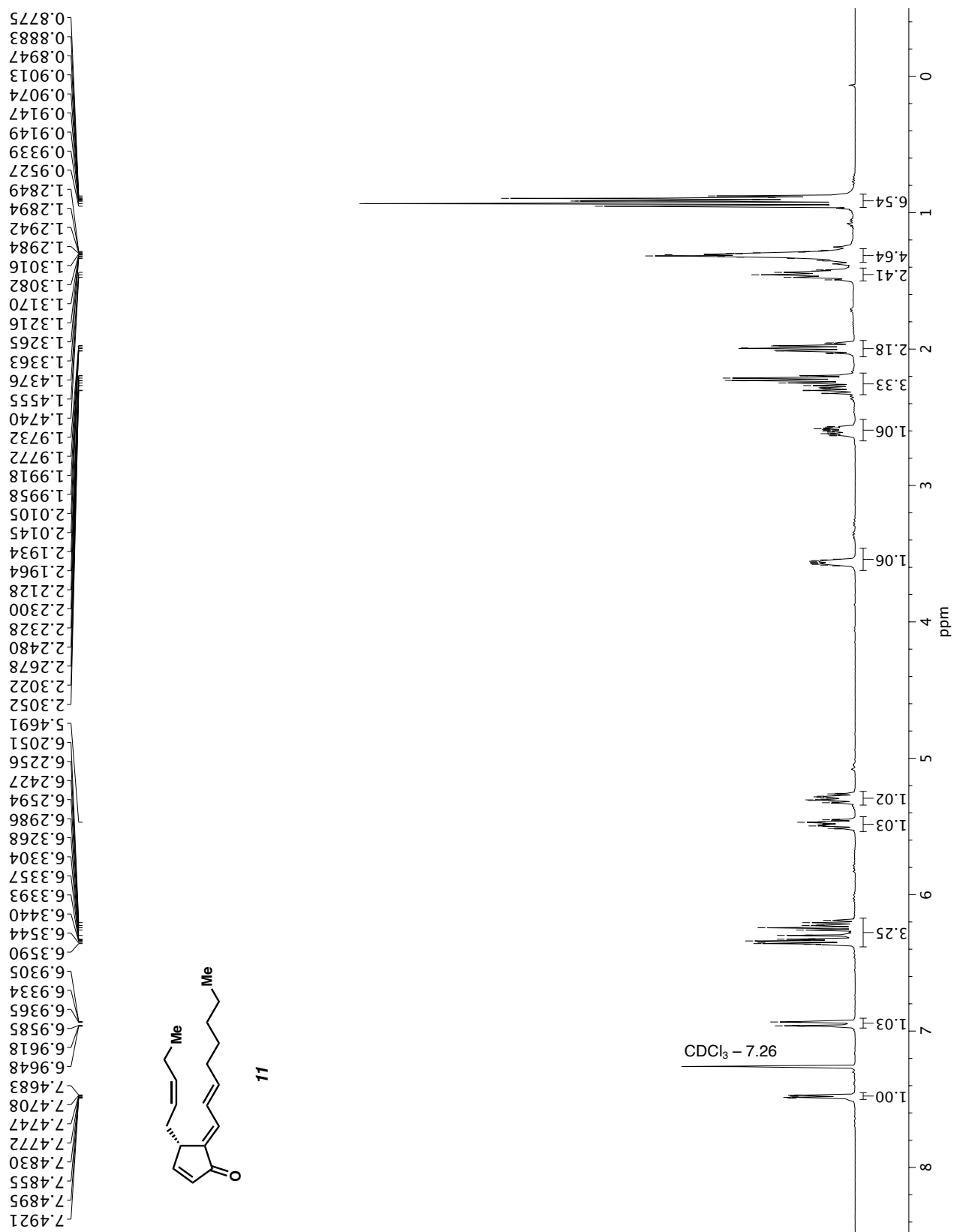




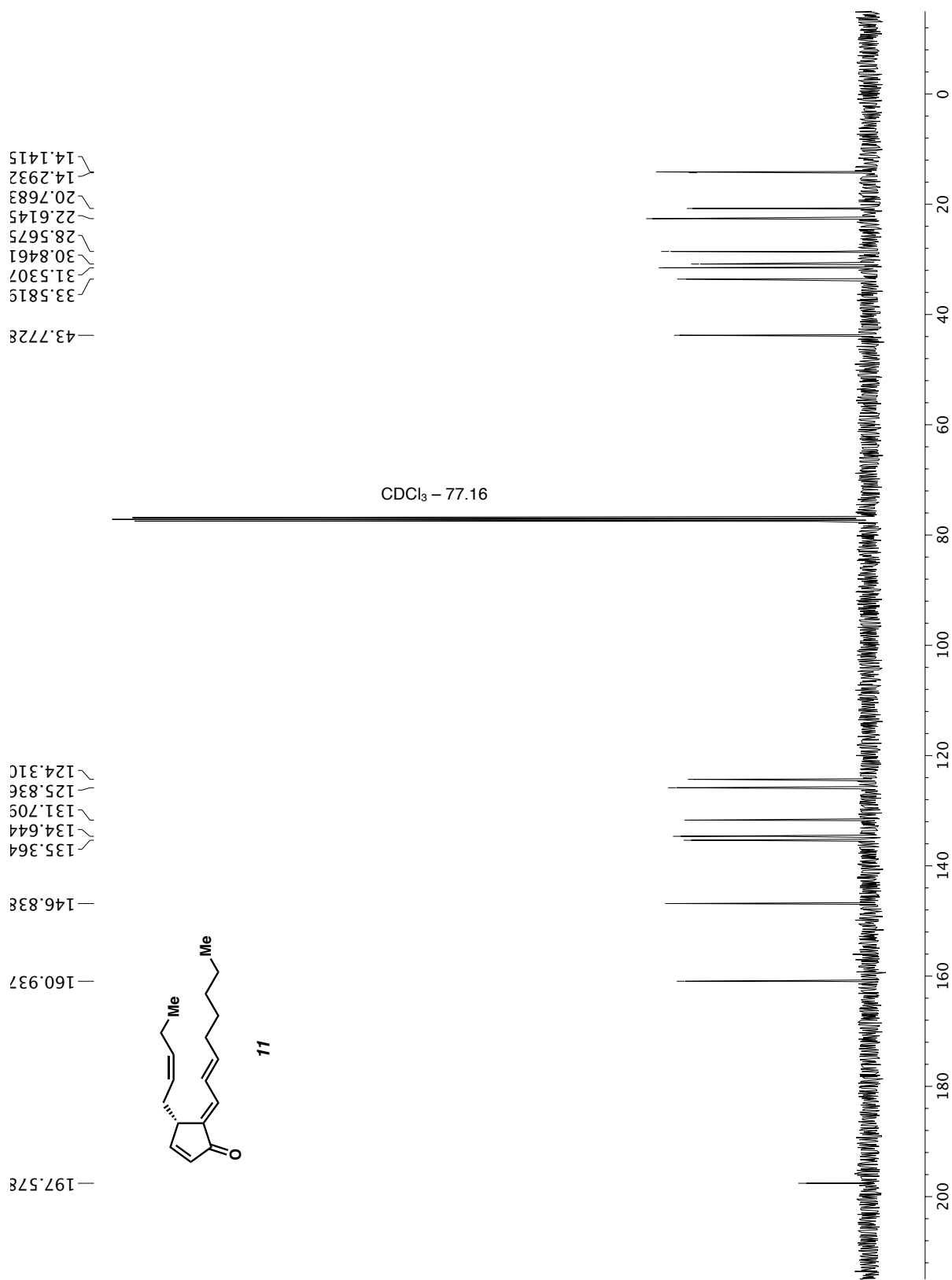


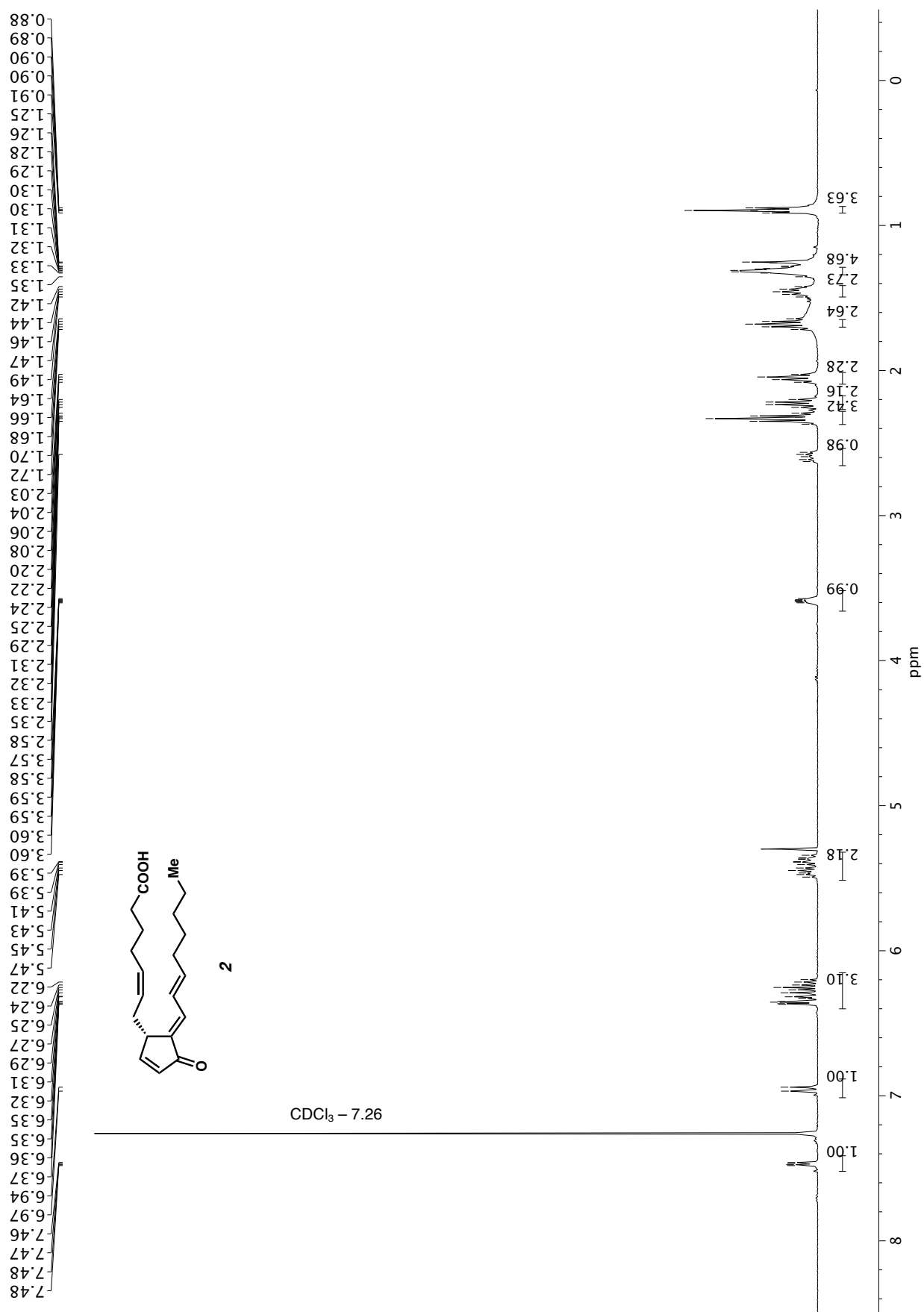


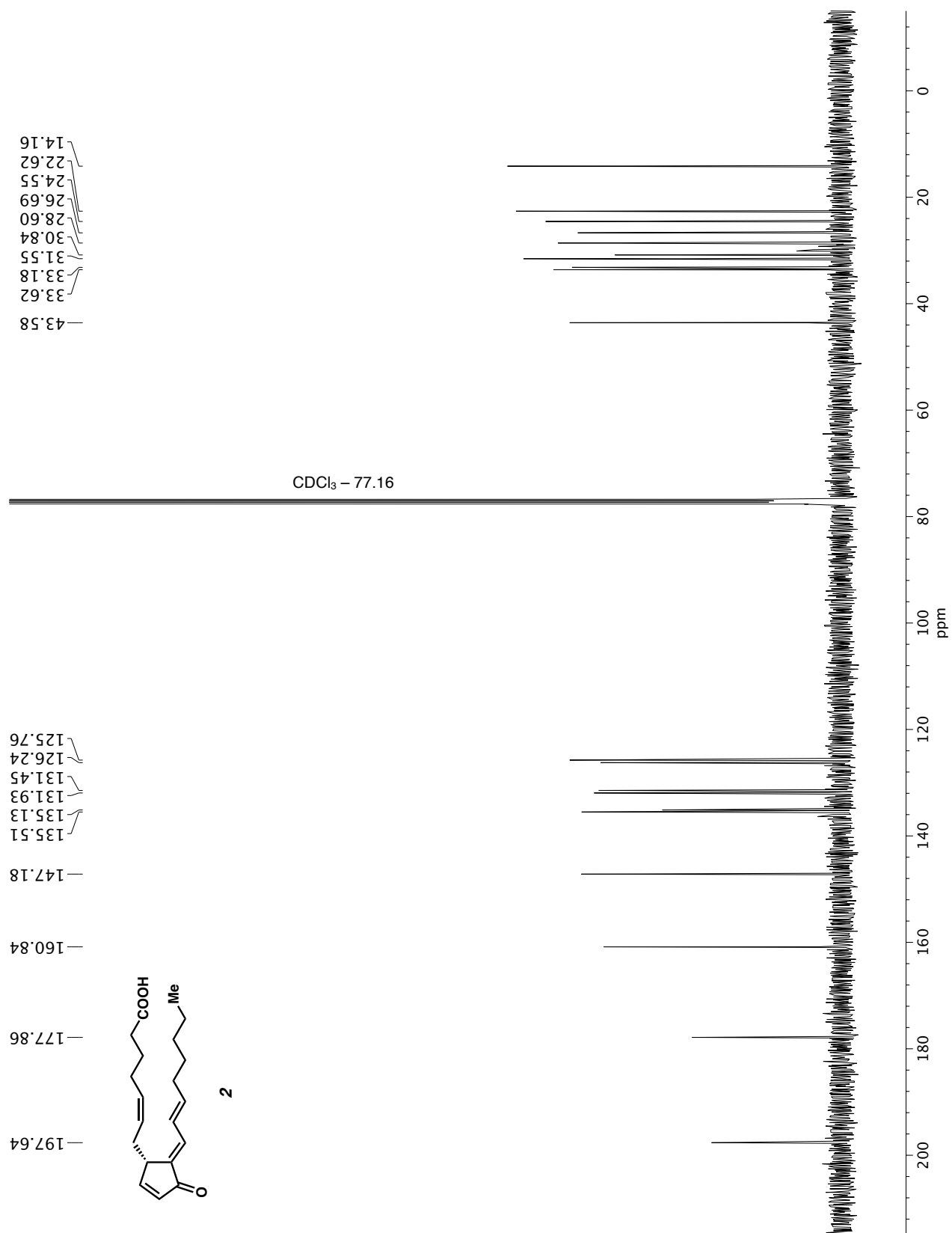


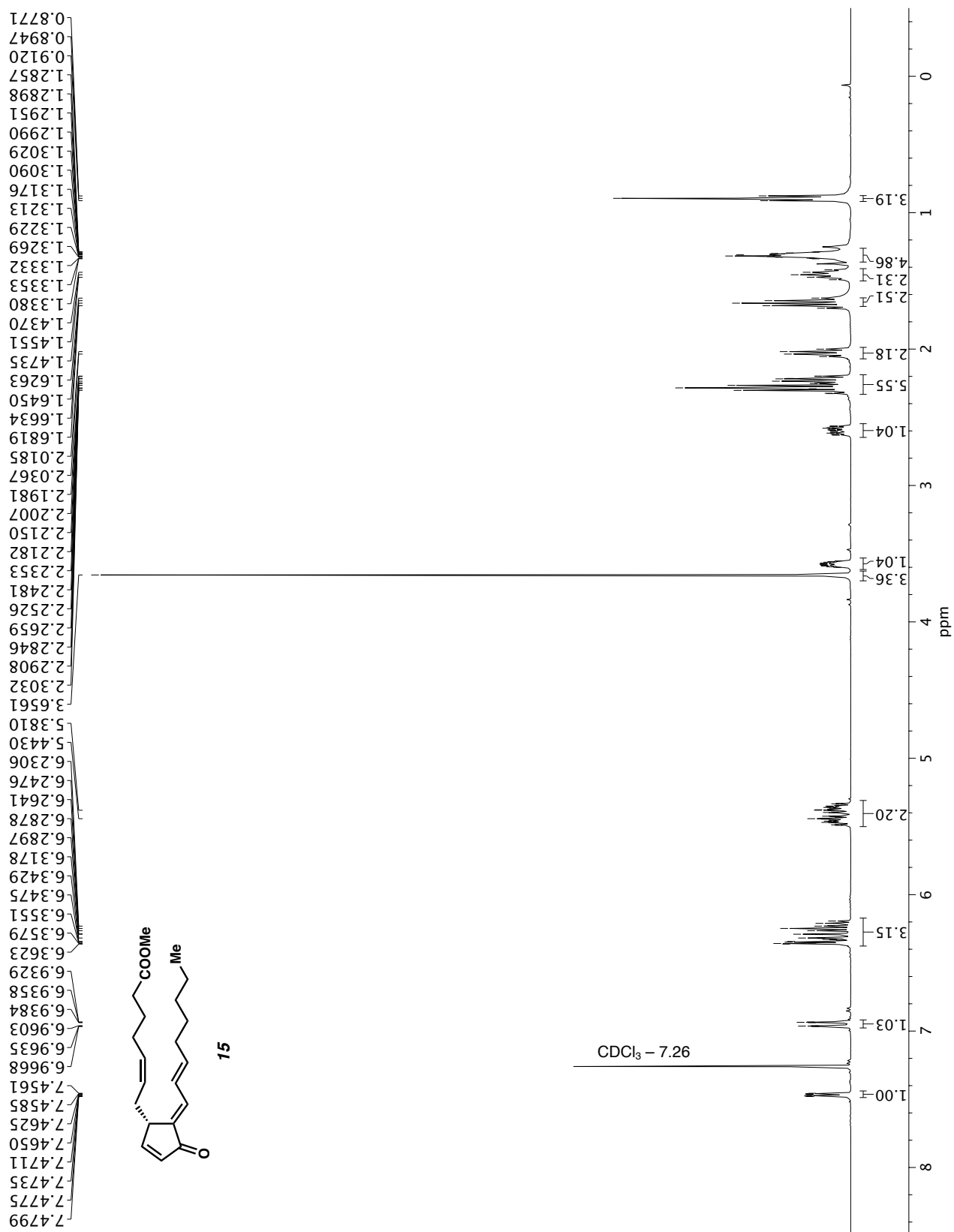


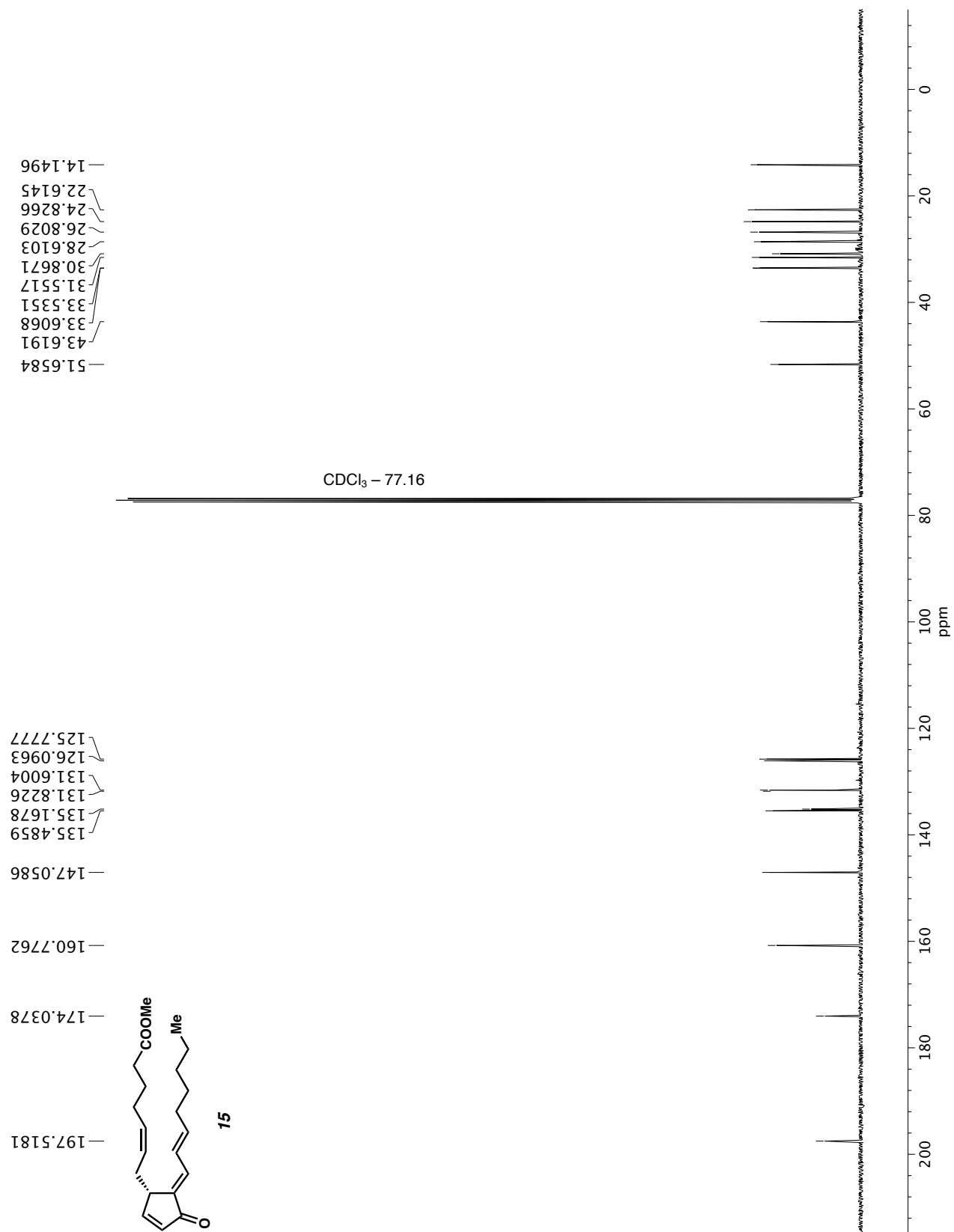


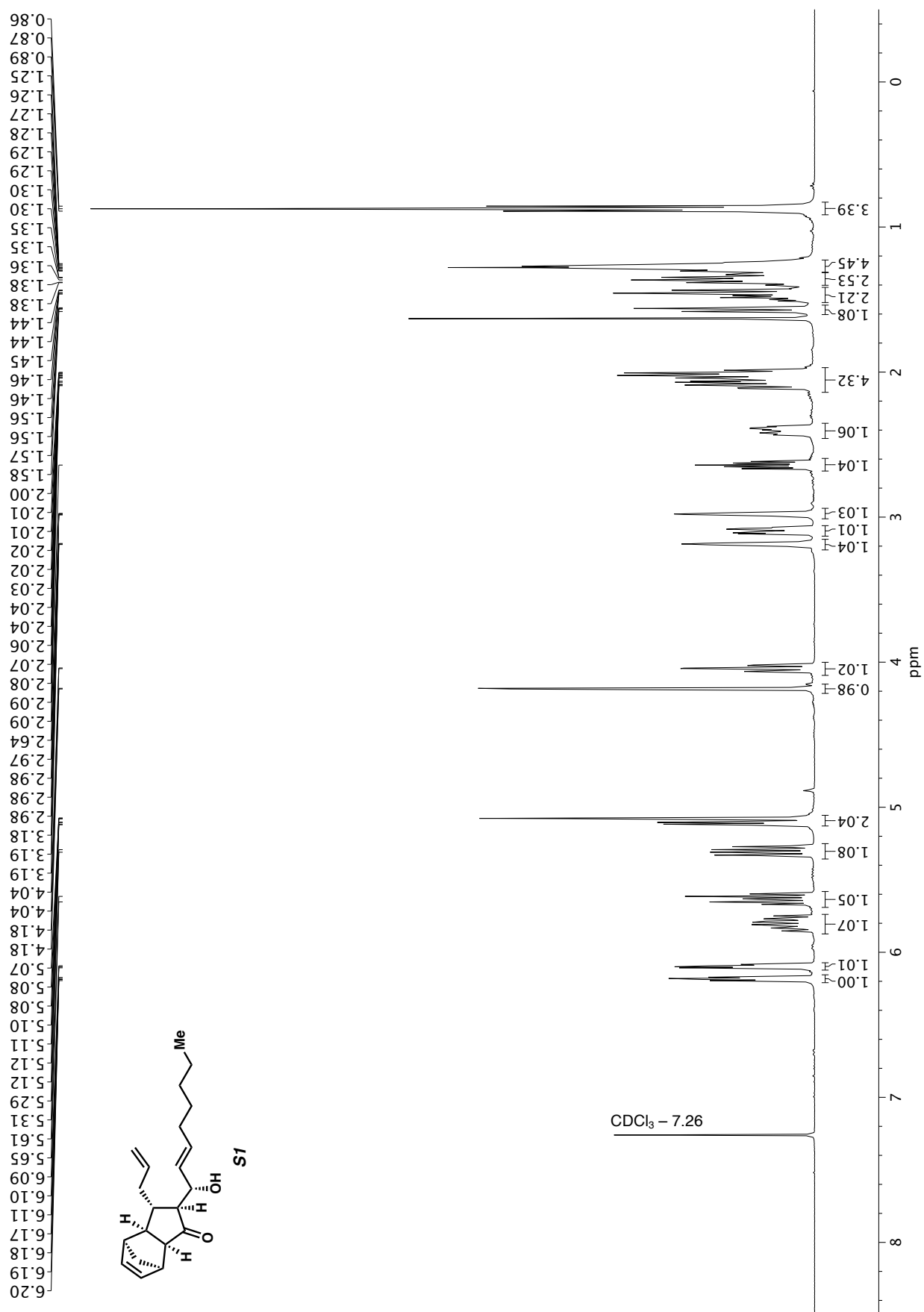


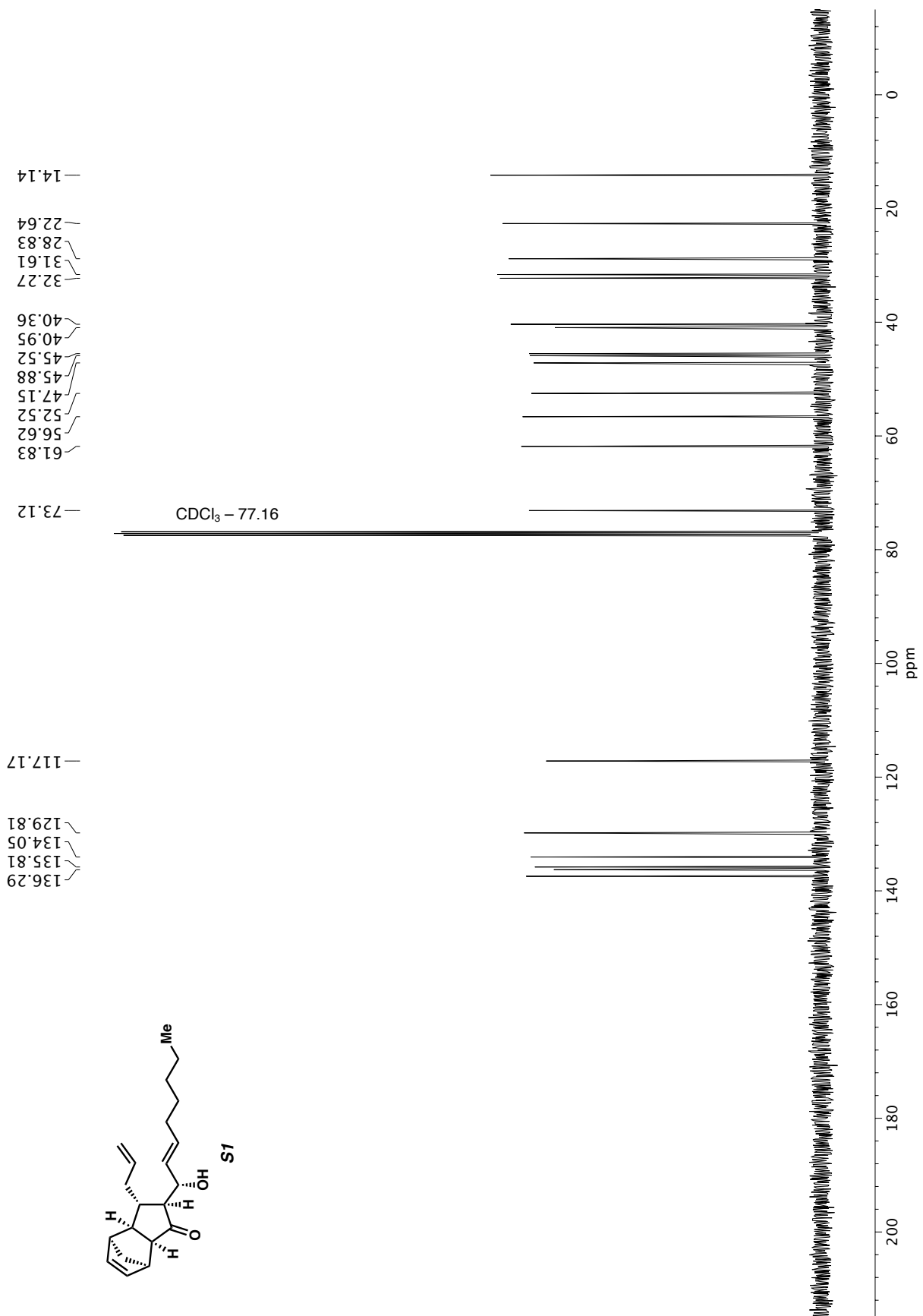


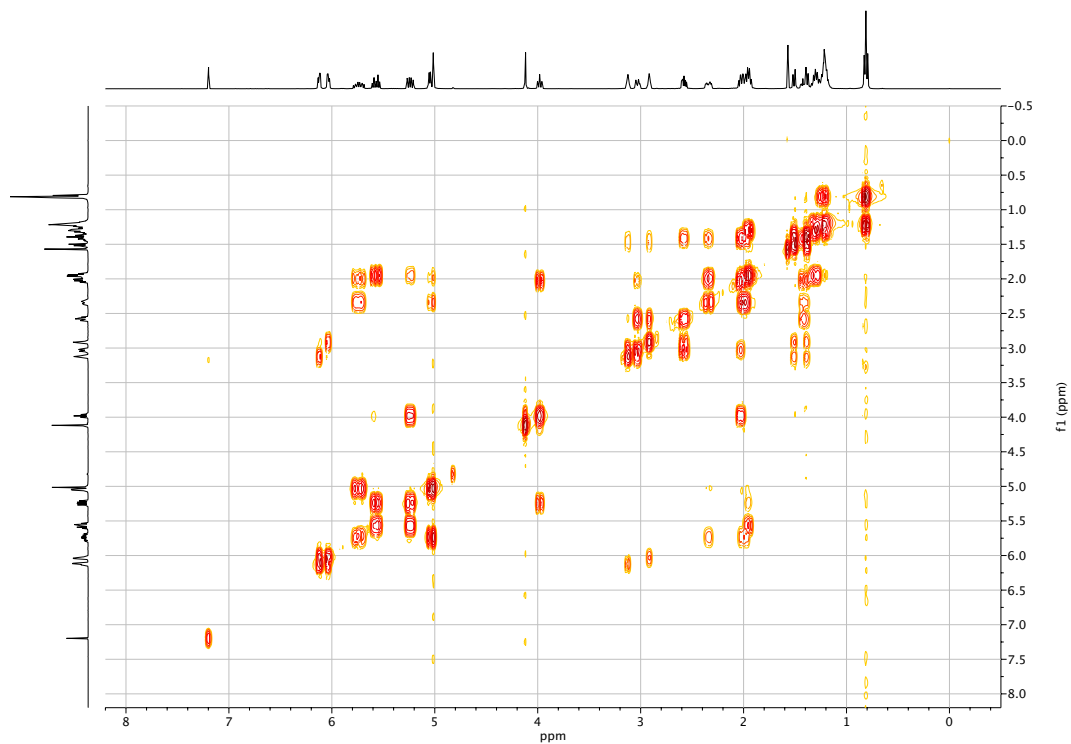




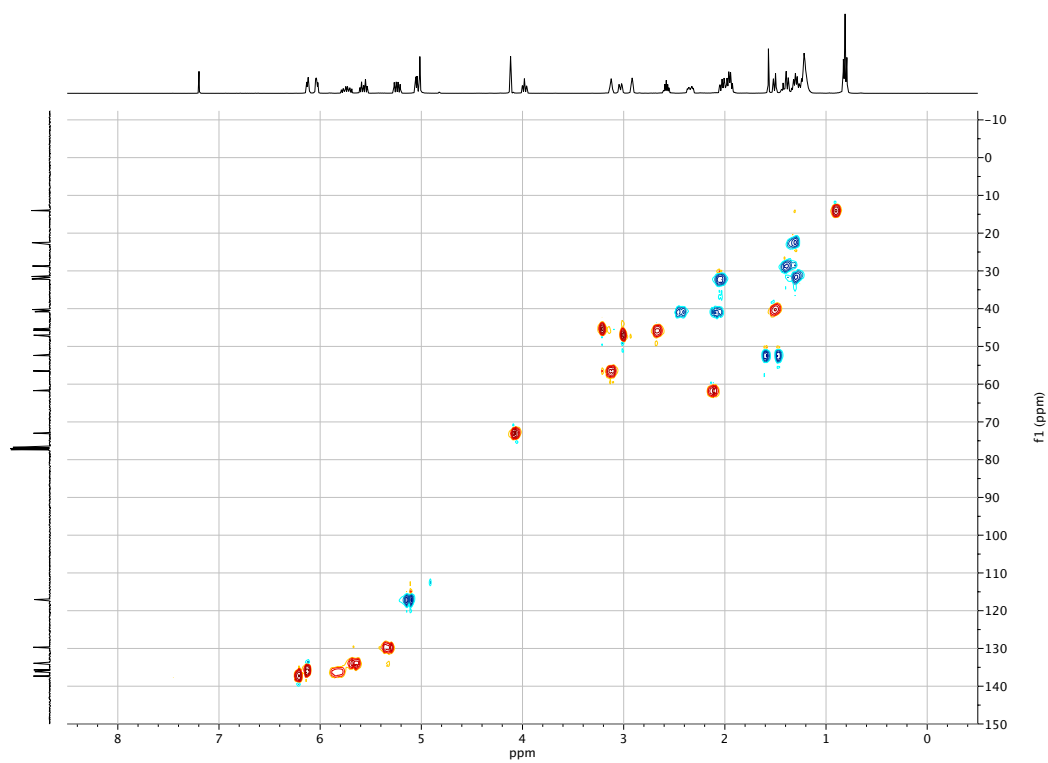






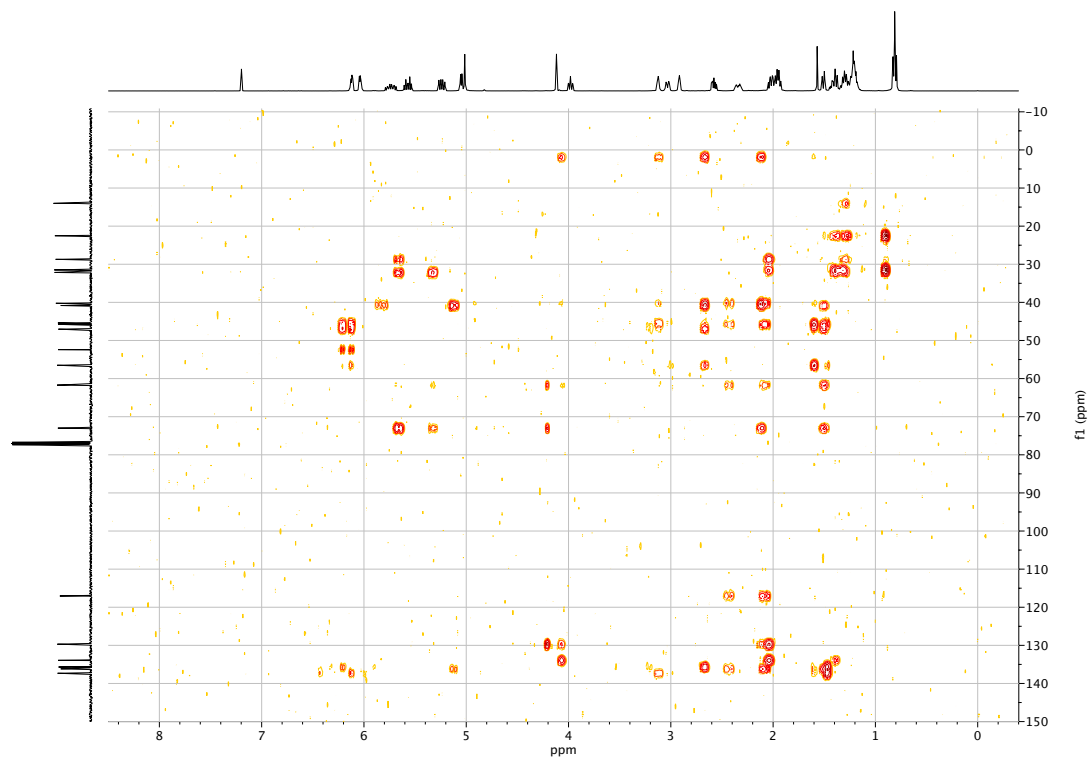


$^1\text{H}$ - $^1\text{H}$  COSY NMR (400 MHz,  $\text{CDCl}_3$ ) of compound S1.

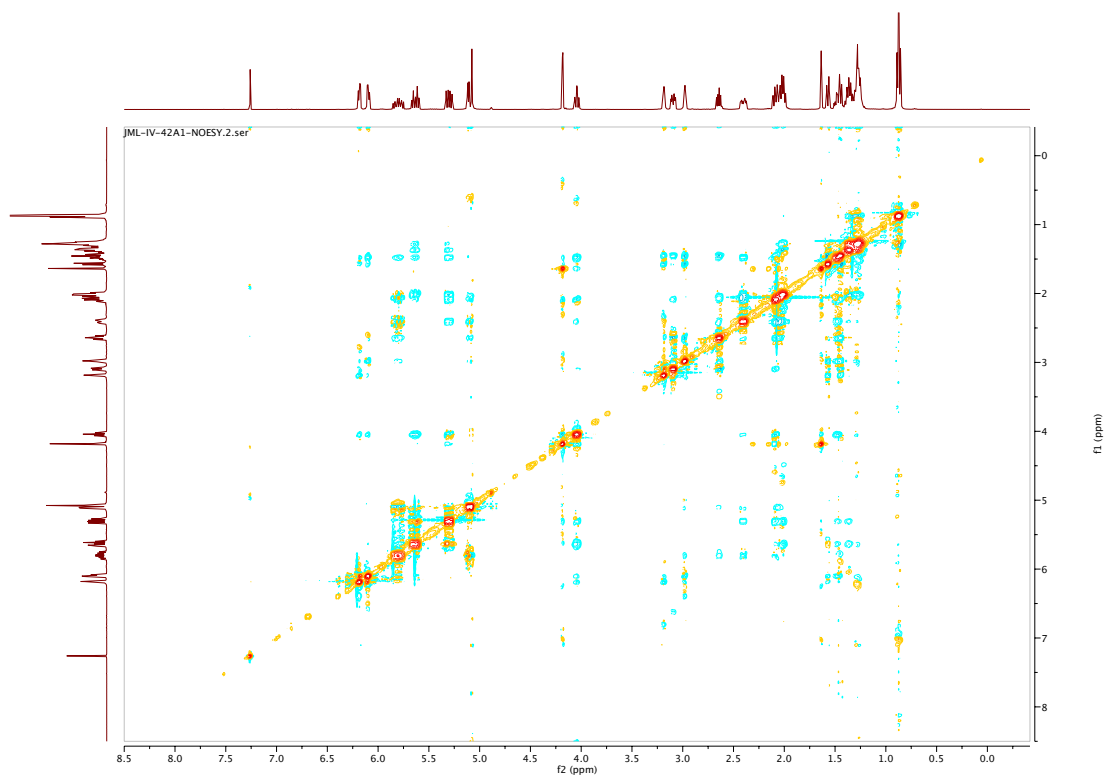


$^1\text{H}$ - $^{13}\text{C}$  HSQC NMR (400 MHz,  $\text{CDCl}_3$ ) of compound S1.





$^1\text{H}$ - $^{13}\text{C}$  HMBC NMR (400 MHz,  $\text{CDCl}_3$ ) of compound S1.



NOESY NMR (400 MHz,  $\text{CDCl}_3$ ) of compound S1.