

# Palladium-Catalyzed Long-Range Deconjugative Isomerization of Highly Substituted $\alpha,\beta$ -Unsaturated Carbonyl Compounds

Luqing Lin<sup>‡</sup>, Ciro Romano<sup>‡</sup>, Clément Mazet\*

<sup>‡</sup>These authors contributed equally

Department of Organic Chemistry, University of Geneva

Quai Ernest Ansermet 30, 1211 Geneva 4, Switzerland

e-mail: [clement.mazet@unige.ch](mailto:clement.mazet@unige.ch)

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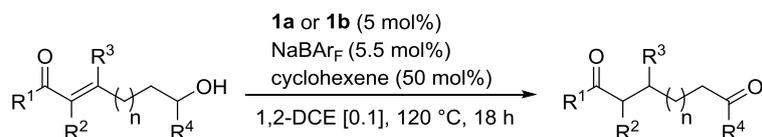
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## 1 General Methods

All reactions were carried out under an inert atmosphere of nitrogen using either two-manifold vacuum/inert gas lines or a *M. Braun* glove-box, unless otherwise noted. Solvents were dried over activated alumina columns and further degassed by three successive "freeze-pump-thaw" cycles if necessary. Commercial reagents were purchased from *Aldrich*, *Acros* or *Strem* and used without further purification, unless otherwise noted. Liquid reagents were transferred with stainless steel syringes or cannula. Thin layer chromatography (TLC) was performed on plates of silica precoated with 0.25 mm Kieselgel 60 F254. Flash chromatography was performed using silica gel 60 (230–400 mesh ASTM) from *Aldrich*. NaBAR<sub>F</sub> were prepared according to literature procedures<sup>1</sup>. NMR spectra were recorded on AMX-400 and AM-500 *Bruker Avance* spectrometers. <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H}-NMR chemical shifts are given in ppm relative to SiMe<sub>4</sub>, with the solvent resonance used as internal reference. <sup>31</sup>P{<sup>1</sup>H}-NMR chemical shifts are reported in ppm relative to H<sub>3</sub>PO<sub>4</sub>. Infrared spectra were obtained on a *Perkin-Elmer* 1650 FT-IR spectrometer using neat samples on a diamond ATR Golden Gate sampler. HPLC analyses were performed on a *Shimadzu* CTO-20AA using chiral column. Retention times (*t<sub>R</sub>*) are given in minutes. Chiral GC analyses were performed on an *Agilent* HP6850 gas chromatograph.

## 2 Experimental procedures

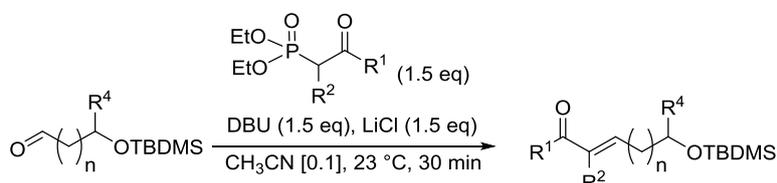
### 2.1 General procedure for deconjugative isomerization (GP1)



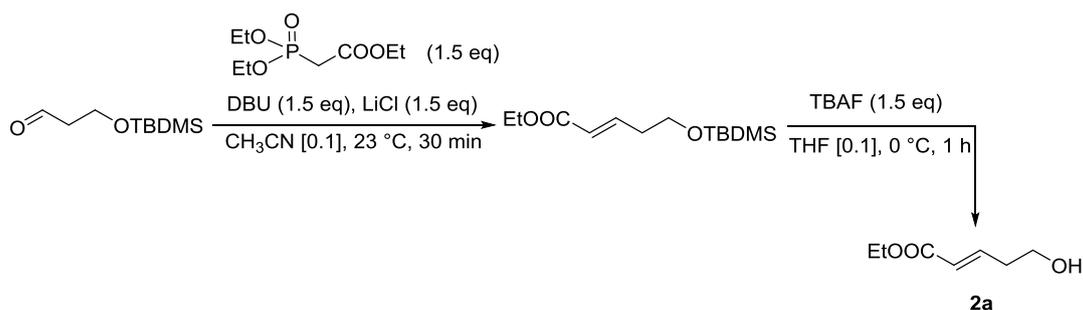
Inside the glovebox, a 5 mL Young valve Schlenk was charged with the appropriate palladium precatalyst **1a** or **1b** (0.0125 mmol) and NaBAR<sub>F</sub> (12.2 mg, 0.0138 mmol), dissolved in 1,2-dichloroethane (2.5 mL) and cyclohexene was added (13  $\mu$ L, 0.125 mmol). The reaction mixture was stirred for 5 minutes at room temperature. Next, the appropriate substrate (0.25 mmol) was added to the mixture, the Schlenk sealed and placed in an oil bath pre-heated at 120 °C. After 18 h, the conversion was assessed by <sup>1</sup>H-NMR analysis of the crude mixture using an internal standard, and the crude mixture was purified by flash chromatography on silica gel to afford the analytically pure dicarbonyl product.

### 2.2 Substrates synthesis

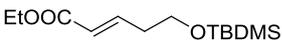
#### General procedure for Horner–Wadsworth–Emmons (HWE) reaction (GP2)



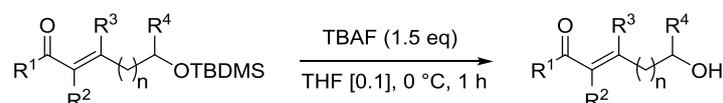
A round bottomed flask was charged with the appropriate phosphonate (1.5 eq), CH<sub>3</sub>CN (0.1 M) and LiCl (1.5 eq). To this, 1,8-Diaza-bicyclo[5.4.0]undec-7-ene (DBU) (1.5 eq) was added via syringe. The reaction mixture was stirred at room temperature for 15 minutes then cooled to 0 °C. The appropriate aldehyde (1 eq) in CH<sub>3</sub>CN (1 M) was added dropwise via cannula and the reaction mixture was monitored by TLC (reaction complete within 30 minutes) then quenched with cold water, extracted with diethyl ether (3 times), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*.



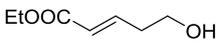
**Figure S1:** Synthesis of Ethyl (*E*)-5-hydroxypent-2-enoate (**2a**)

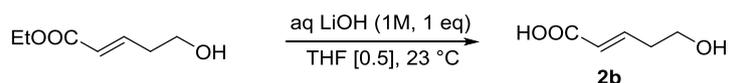
 **Ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)pent-2-enoate:** The reaction was run according to GP2 starting from 3-((*tert*-butyldimethylsilyl)oxy)propanal<sup>2</sup> (11.7 mmol). Flash chromatography (Pentane/Diethyl ether = 10:1) afforded the product as a colourless oil (2.9 g, 94% yield). All spectroscopic analyses were in agreement with those reported in the literature.<sup>3</sup>

**General procedure for *tert*-butyldimethylsilyl (TBDMS) deprotection with tetrabutylammonium fluoride (TBAF) (GP3)**



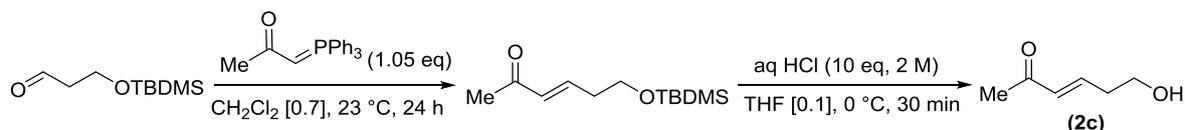
The appropriate protected alcohol (1 eq) was dissolved in THF (0.1 M) and TBAF (1.0 M in THF, 1.5 eq) was added slowly at 0 °C. After stirring for 1 h at 0 °C, the mixture was quenched with saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 times), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*.

 **Ethyl (*E*)-5-hydroxypent-2-enoate (**2a**):** The reaction was run according to GP3 starting from ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)pent-2-enoate (2.0 g, 7.8 mmol). Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) afforded **2a** in 68% yield (763 mg). All spectroscopic analyses were in agreement with those reported in the literature.<sup>4</sup>



**Figure S2:** Synthesis of (*E*)-5-hydroxypent-2-enoic acid (**2b**)

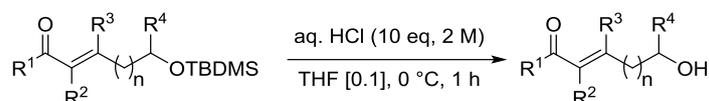
**(*E*)-5-hydroxypent-2-enoic acid (2b):** To a solution of ethyl (*E*)-5-hydroxypent-2-enoate (210 mg, 1.5 mmol) in THF (3 mL), an aqueous solution of LiOH (1 M, 1.5 mL) was added at 0 °C and stirred 16 h at room temperature. The reaction was quenched with an aqueous HCl solution (2 M, 2 mL), extracted with diethyl ether (3 x 5 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue was purified by flash chromatography on silica gel (EtOAc/Diethyl ether = 10:1) to give **2b** as colourless oil in 67% yield (120 mg). *R*<sub>f</sub> = 0.1 (Diethyl ether). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3259, 2949, 1691, 1653, 1411, 1041, 975. **<sup>1</sup>H NMR** (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  (ppm) 2.41 – 2.59 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.81 (t, <sup>3</sup>*J*<sub>HH</sub> = 6.3 Hz, 2H, CH<sub>2</sub>OH), 5.95 (dt, <sup>3</sup>*J*<sub>HH</sub> = 15.7 Hz, <sup>4</sup>*J*<sub>HH</sub> = 1.4 Hz, 1H, CH=CHCH<sub>2</sub>), 7.08 (dt, <sup>3</sup>*J*<sub>HH</sub> = 15.8, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 1H, CH=CHCH<sub>2</sub>). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  (ppm) 35.6 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.0 (CH<sub>2</sub>OH), 122.8 (CH=CHCH<sub>2</sub>), 148.1 (CH=CHCH<sub>3</sub>), 170.1 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 134.



**Figure S3:** Synthesis of (*E*)-6-((*tert*-butyldimethylsilyl)oxy)hex-3-en-2-one (**2c**)

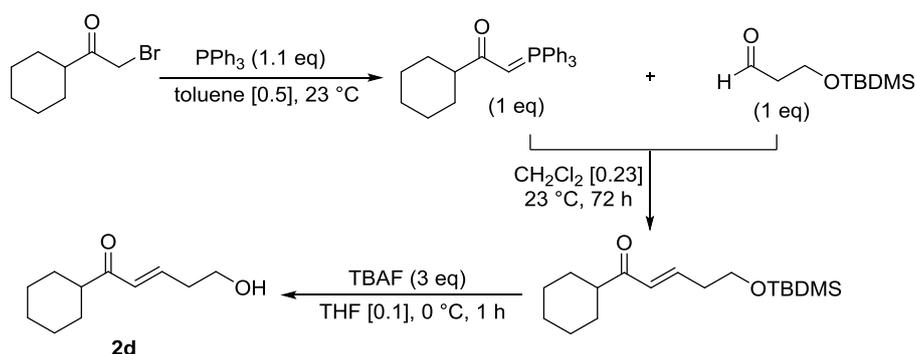
**(*E*)-6-((*tert*-butyldimethylsilyl)oxy)hex-3-en-2-one:** 3-((*tert*-butyldimethylsilyl)oxy)propanal (1.8 g, 9.6 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (14 mL) and 1-(triphenylphosphoranylidene)-2-propanone (3.35 g, 10 mmol, 1.05 eq) was added at 0 °C. The reaction mixture was stirred at room temperature for 24 h. Silica gel (5 g) was added and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (Pentane/Diethyl ether = 10:1) to afford the desired compound in 86% yield (2.0 g). All spectroscopic analyses were in agreement with those reported in the literature.<sup>5</sup>

### General procedure for *tert*-butyldimethylsilyl (TBDMS) deprotection with aqueous HCl (GP4)



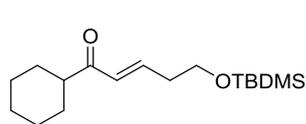
To a solution of the appropriate protected alcohol (1 eq) in THF (0.1 M), aqueous HCl (2 M, 10 eq) was added at 0 °C and stirred for 30 minutes then quenched with water, extracted with EtOAc (3 times), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*.

**(E)-6-hydroxyhex-3-en-2-one (2c):** The reaction was run according to GP4 starting from (*E*)-6-((*tert*-butyldimethylsilyl)oxy)hex-3-en-2-one (1.2 g, 5.2 mmol). The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:4) to give **2c** in 65% yield (430 mg). All spectroscopic analyses were in agreement with those reported in the literature.<sup>6</sup>



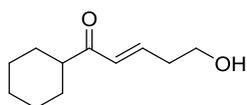
**Figure S4:** Synthesis of (*E*)-1-cyclohexyl-5-hydroxypent-2-en-1-one (**2d**)

**1-cyclohexyl-2-(triphenyl-λ<sup>5</sup>-phosphanylidene)ethan-1-one:** To a solution of 2-bromo-1-cyclohexylethan-1-one (6.8 g, 33 mmol) in toluene (30 mL), a second solution of triphenylphosphine (9.6 g, 36 mmol) in toluene (40 mL) was added slowly and stirred vigorously at room temperature. After 17 h, the solid obtained was filtered and redissolved in CH<sub>2</sub>Cl<sub>2</sub> (182 mL). An aqueous NaOH solution (2 N, 60 mL) was next added and the mixture stirred at room temperature. After 1 h, the organic phase was washed with water (2 × 90 mL) and concentrated to give the desired compound in 73% yield (9.4 g), which was used in the next step without further purification.



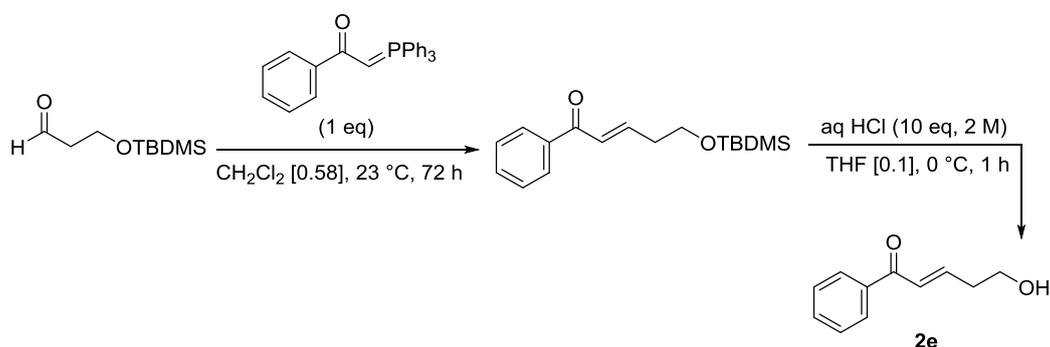
**(E)-5-((*tert*-butyldimethylsilyloxy)-1-cyclohexylpent-2-en-1-**

**one:** To a solution of 3-((*tert*-butyldimethylsilyloxy)propanal (4.4 g, 23 mmol) in  $\text{CH}_2\text{Cl}_2$  (100 mL), 1-1-cyclohexyl-2-(triphenyl- $\lambda^5$ -phosphanylidene)ethan-1-one (8.9 g, 23 mmol) was added at 0 °C. The reaction mixture was warmed to room temperature. After 72 h, silica gel (10 g) was added and the solvent was removed under reduced pressure. The solid deposit was charged on column of silica gel and flushed with Pentane/Diethyl ether = 20:1 to afford 5.4 g of an oil containing the desired enone<sup>7</sup> and the starting aldehyde in 6.7:1 ratio. This mixture was used for next step directly.



**(E)-1-cyclohexyl-5-hydroxypent-2-en-1-one (2d):** A part (1.6 g) of the

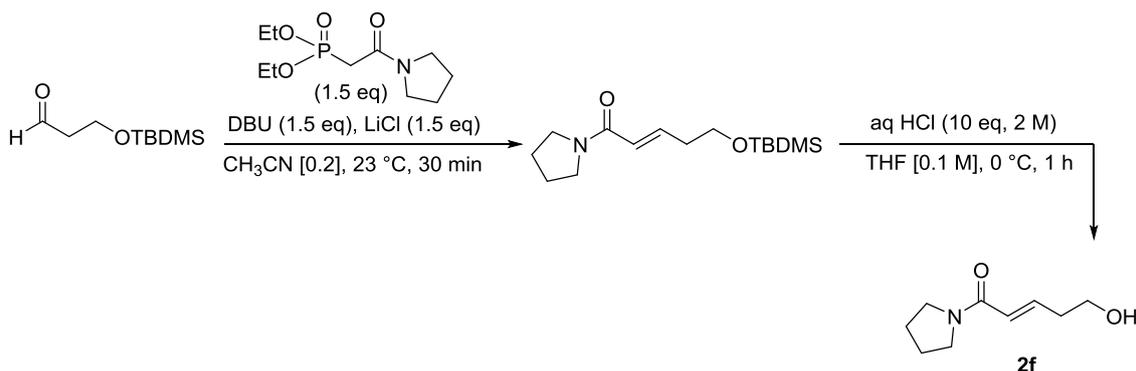
mixture obtained from the previous step was dissolved in THF (45 mL) and TBAF (1.0 M in THF, 6.8 mmol, 6.8 mL) was added slowly at 0 °C. After stirring for 1 h at 0 °C, the mixture was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (45 mL), extracted with diethyl ether (3 × 60 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. After purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1), the product was obtained in 72% yield (590 mg).  $R_f = 0.3$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3415, 2928, 2854, 1688, 1659, 1624, 1449, 1046$ . **<sup>1</sup>H NMR** (400 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 1.13 – 1.36 (m, 5H,  $\text{CH}_2\text{-Cy}$ ), 1.46 (t,  $^3J_{\text{HH}} = 5.5$  Hz, 1H, OH), 1.66 (m, 1H,  $\text{CH-Cy}$ ), 1.77 (m, 4H,  $\text{CH}_2\text{-Cy}$ ), 2.44 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.55 (m, 1H,  $\text{CH-Cy}$ ), 3.73 (m, 2H,  $\text{CH}_2\text{OH}$ ), 6.22 (dt,  $^3J_{\text{HH}} = 15.8$  Hz,  $^4J_{\text{HH}} = 1.5$  Hz, 1H,  $\text{CH=CHCOCy}$ ), 6.80 (dt,  $^3J_{\text{HH}} = 15.7$ ,  $^3J_{\text{HH}} = 7.1$  Hz, 1H,  $\text{CH=CHCOCy}$ ). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 26.1 ( $\text{CH}_2\text{-Cy}$ ), 26.3 ( $\text{CH}_2\text{-Cy}$ ), 29.1 ( $\text{CH}_2\text{-Cy}$ ), 36.1 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 48.9 ( $\text{CH-Cy}$ ), 61.4 ( $\text{CH}_2\text{OH}$ ), 130.9 ( $\text{CH=CHCOCy}$ ), 143.1 ( $\text{CH=CHCOCy}$ ), 203.1 ( $\text{C=O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 183$ ;  $[\text{M}+\text{NH}_4]^+ = 200$ .



**Figure S5:** Synthesis of (*E*)-5-hydroxy-1-phenylpent-2-en-1-one (**2e**)

**(E)-5-((tert-butyldimethylsilyl)oxy)-1-phenylpent-2-en-1-one:** The product was prepared in 72% yield (2.5 g) starting from 3-((tert-butyldimethylsilyl)oxy)propanal (2.2 g, 11.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) and 1-phenyl-2-(triphenyl-λ<sup>5</sup>-phosphanylidene)ethan-1-one<sup>8</sup> (3.62 g, 11.7 mmol) according to a procedure reported in the literature<sup>9</sup>.

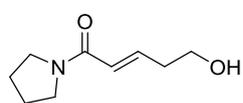
**(E)-5-hydroxy-1-phenylpent-2-en-1-one (2e):** To a solution of (E)-5-((tert-butyldimethylsilyl)oxy)-1-phenylpent-2-en-1-one (600 mg, 3.4 mmol) in THF (34 mL), aqueous HCl (2 M, 17 mL) was added and stirred for 30 minutes at 0 °C. The reaction was quenched with water (30 mL), extracted with diethyl ether (3 × 30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:4) to give **2e** in 90% yield (330 mg). The spectroscopic analyses were in agreement with those reported in the literature.<sup>10</sup>



**Figure S6:** Synthesis of (E)-5-hydroxy-1-(pyrrolidin-1-yl)pent-2-en-1-one (**2f**)

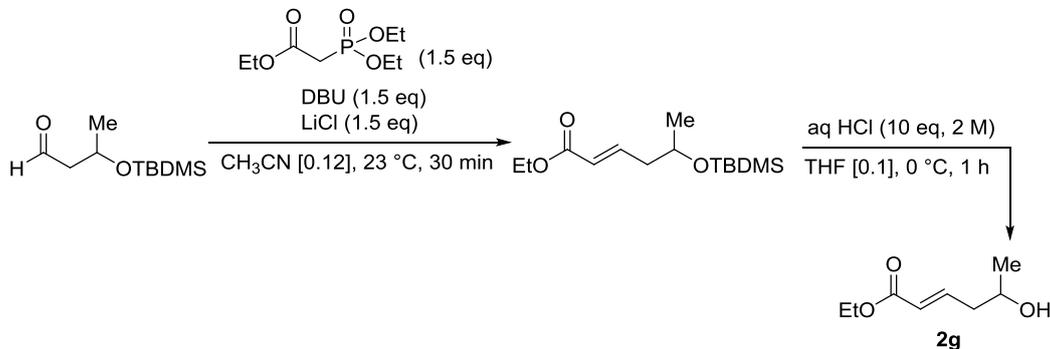
**(E)-5-((tert-butyldimethylsilyl)oxy)-1-(pyrrolidin-1-yl)pent-2-en-1-one:** The product was synthesized according to GP2 starting from the 3-((tert-butyldimethylsilyl)oxy)propanal (398 mg, 2.12 mmol) and diethyl 2-oxo-2-(pyrrolidin-1-yl)ethylphosphonate (791 mg, 3.18 mmol). Purification by flash chromatography (Pentane/EtOAc = 1:1) gave the product in 50% yield (370 mg) as light yellow oil. *R*<sub>f</sub> = 0.5 (Pentane/EtOAc = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2929, 2858, 1661, 1606, 1431, 833. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.80 – 1.98 (m, 4H, NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.41 (qd, <sup>3</sup>*J*<sub>HH</sub> = 6.9, 1.5 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.52 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.6 Hz, 4H, N(CH<sub>2</sub>)<sub>2</sub>), 3.71 (t, <sup>3</sup>*J*<sub>HH</sub> = 6.7 Hz, 2H, CH<sub>2</sub>OTBDMS), 6.16 (dt, <sup>3</sup>*J*<sub>HH</sub> = 15.1, <sup>3</sup>*J*<sub>HH</sub> = 1.5 Hz, 1H, CH=CHCH<sub>2</sub>), 6.88 (dt, <sup>3</sup>*J*<sub>HH</sub> = 14.7, <sup>4</sup>*J*<sub>HH</sub> = 7.1 Hz, 1H, CH=CHCH<sub>2</sub>). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -5.2 (CH<sub>3</sub>)<sub>2</sub>Si,

18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 24.5 (NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 36.1 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 46.0 (CH<sub>2</sub>NCH<sub>2</sub>), 46.6 (CH<sub>2</sub>NCH<sub>2</sub>), 62.0 (CH<sub>2</sub>OTBDMS), 123.5 (CH=CHCH<sub>2</sub>), 142.1 (CH=CHCH<sub>2</sub>), 164.8 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 284.

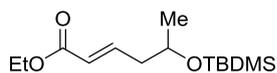


**(E)-5-hydroxy-1-(pyrrolidin-1-yl)pent-2-en-1-one (2f):** The product was prepared according to GP4 starting from the (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-1-(pyrrolidin-1-yl)pent-2-en-1-one (370 mg, 1.35

mmol). The residue was purified by flash chromatography (Pentane/EtOAc = 1:2) to give the product in 73% yield (160 mg) as a colourless oil.  $R_f$  = 0.1 (Pentane/EtOAc = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3398, 2950, 2875, 1658, 1590, 1440, 1045. **<sup>1</sup>H NMR** (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  (ppm) 1.80 – 1.89 (m, 2H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 1.91 – 2.00 (m, 2H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 2.04 (s, 1H, OH), 2.44 (dtd, <sup>3</sup>J<sub>HH</sub> = 7.6, 6.2 Hz, <sup>4</sup>J<sub>HH</sub> = 1.5 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.48 (m, 4H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 3.72 (t, *J* = 6.2 Hz, 2H, CH<sub>2</sub>OH), 6.23 (dt, <sup>3</sup>J<sub>HH</sub> = 15.2, <sup>4</sup>J<sub>HH</sub> = 1.5 Hz, 1H, CH=CHCH<sub>2</sub>), 6.82 (dt, <sup>3</sup>J<sub>HH</sub> = 14.8, 7.3 Hz, 1H, CH=CHCH<sub>2</sub>). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  (ppm) 24.3 (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 26.0 (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 35.8 (CH<sub>2</sub>CH<sub>2</sub>OH), 45.8 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 46.6 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 61.1 (CH<sub>2</sub>OH), 124.1 (CH=CHCH<sub>2</sub>), 141.6 (CH=CHCH<sub>2</sub>), 164.4 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 170.

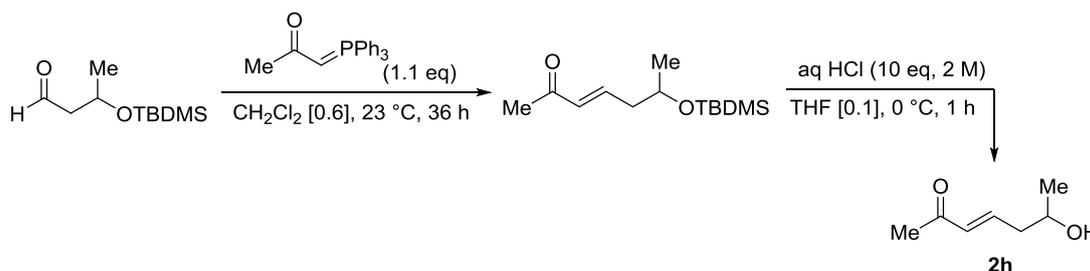


**Figure S7:** Synthesis of (*E*)-5-hydroxyhex-2-enoate (**2g**)



**Ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate:** The product was synthesized according to GP2 starting from 3-((*tert*-butyldimethylsilyl)oxy)butanal<sup>10</sup> (856 mg, 4.24 mmol) and triethyl phosphonate (1.4 g, 6.36 mmol). The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 5:1) to afford the desired product in 83% yield (960 mg) as a colourless oil. The spectroscopic analyses were in agreement with those reported in the literature.<sup>11</sup>

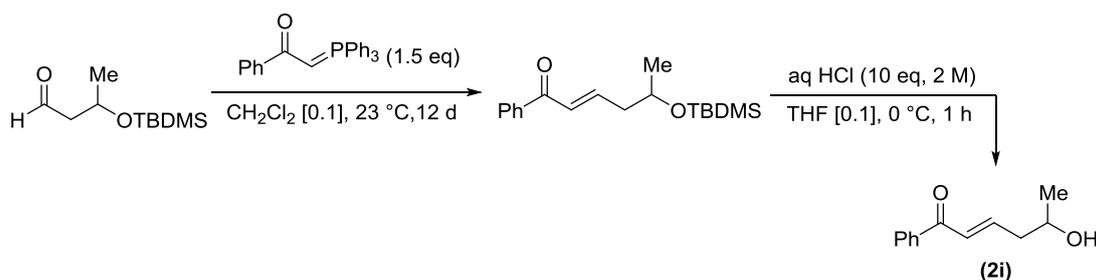
**Ethyl (*E*)-5-hydroxyhex-2-enoate (**2g**):** The product was prepared according to GP4 starting from ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (960 mg, 3.5 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:2) to give **2g** as a colorless oil in 77% yield (430 mg). The spectroscopic analyses were in agreement with those reported in the literature.<sup>12</sup>



**Figure S8:** Synthesis of (*E*)-6-hydroxyhept-3-en-2-one (**2h**)

**(*E*)-6-((*tert*-butyldimethylsilyl)oxy)hept-3-en-2-one:** To a solution of 3-((*tert*-butyldimethylsilyl)oxy)butanal (8 mmol) in  $\text{CH}_2\text{Cl}_2$  (14 mL) was added 1-(triphenylphosphoranylidene)-2-propanone (2.8 g, 8.8 mmol) at 0 °C. The reaction mixture was warmed to room temperature. After 36 h, silica gel was added (3 g) and the solvent was removed under reduced pressure. The solid deposit was charged on a column of silica gel and flushed with Pentane/Diethyl ether = 10:1 to afford 1.1 g of a mixture of the corresponding (*E*)- $\alpha,\beta$ -enone and starting aldehyde in 7:1 ratio. It was used in the next step directly.

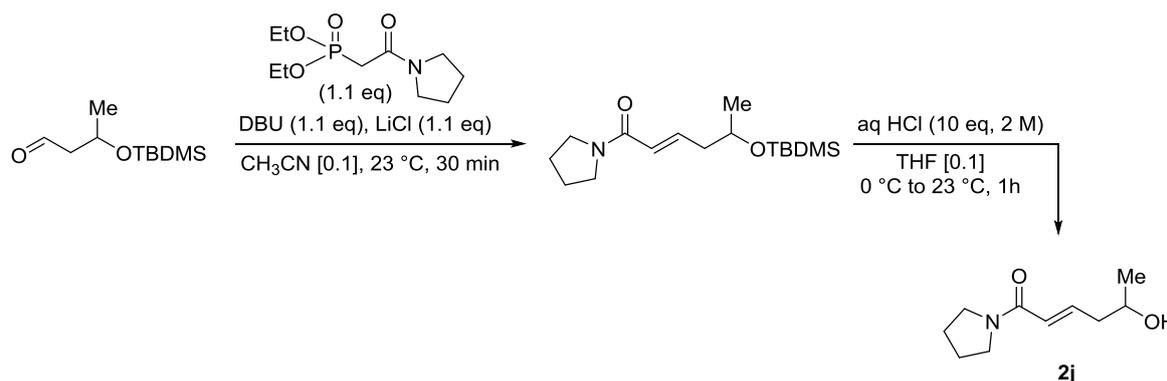
**(*E*)-6-hydroxyhept-3-en-2-one (**2h**):** The product was prepared according to GP4 starting from (*E*)-6-((*tert*-butyldimethylsilyl)oxy)hept-3-en-2-one (1.1 g, 4.0 mmol). The crude was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 2:1) to afford **2h** in 68% yield (350 mg) as a colourless oil. All spectroscopic analyses were in agreement with those reported in the literature.<sup>13</sup>



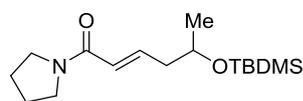
**Figure S9:** Synthesis of (*E*)-5-hydroxy-1-phenylhex-2-en-1-one (**2i**)

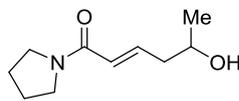
**(*E*)-5-((*tert*-butyldimethylsilyloxy)-1-phenylhex-2-en-1-one:** 1-phenyl-2-(triphenyl- $\lambda^5$ -phosphanylidene)ethan-1-one (1.91 g, 5.2 mmol) was added to a solution of 3-((*tert*-butyldimethylsilyloxy)butanal (700 mg, 3.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (35 mL) at 0 °C and warmed to room temperature. After 12 days, water (40 mL) was added and the organic phase was extracted with  $\text{CH}_2\text{Cl}_2$  (3  $\times$  30 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude mixture was passed through a pad of silica gel and concentrated to give an oil which was used in the next step without further purification.

**(*E*)-5-hydroxy-1-phenylhex-2-en-1-one (**2i**):** The mixture obtained in the previous step was engaged for TBDMS deprotection according to GP4. The crude mixture was purified by flash chromatography on silica gel (Pentane/EtOAc = 1:2) to afford **2i** in 71% yield (230 mg) as a colourless oil.  $R_f = 0.2$  (*n*-Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3416, 2970, 1666, 1617, 977$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 1.24 (d,  $^3J_{\text{HH}} = 6.3$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.58 – 1.65 (m, 1H,  $\text{CHOH}$ ), 2.40 – 2.54 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 4.00 (m, 1H,  $\text{CHOH}$ ), 6.89 – 7.14 (m, 2H,  $\text{CH}=\text{CH}$ ), 7.47 (m, 2H,  $\text{CH-Ar}$ ), 7.53 – 7.62 (m, 1H,  $\text{CH-Ar}$ ), 7.84 – 8.05 (m, 2H,  $\text{CH-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 23.1 ( $\text{CH}_3\text{CH}$ ), 42.3 ( $\text{CH}_2\text{CHOH}$ ), 66.7 ( $\text{CHOH}$ ), 128.1 ( $\text{PhCOCH}=\text{CH}$ ), 128.4 ( $\text{CH-Ar}$ ), 128.5 ( $\text{CH-Ar}$ ), 132.6 ( $\text{CH-Ar}$ ), 137.8 ( $\text{C}_{\text{quat}}$ ), 145.4 ( $\text{CH}=\text{CHCH}_2$ ), 190.1 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 191$ ;  $[\text{M}+\text{NH}_4]^+ = 208$ .

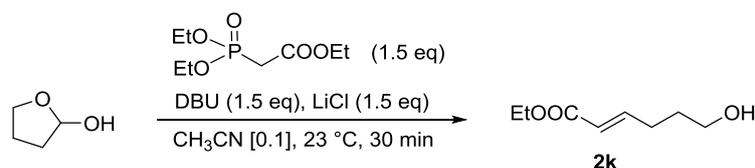


**Figure S10:** Synthesis of (*E*)-5-hydroxy-1-(pyrrolidin-1-yl)hex-2-en-1-one (**2j**)

 **(E)-5-((*tert*-butyldimethylsilyloxy)-1-(pyrrolidin-1-yl)hex-2-en-1-one:** The reaction was run according to GP2 starting from 3-((*tert*-butyldimethylsilyloxy)butanal (728 mg, 3.6 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:2) to afford the desired product in 77% yield (820 mg) as a colourless oil.  $R_f = 0.2$  (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2956, 2929, 1664, 1620, 1427, 835$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.05 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.15 (d,  $^3J_{\text{HH}} = 6.1$  Hz, 3H,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.74 – 2.01 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 2.19 – 2.46 (m, 2H,  $\text{CH}_2\text{CHOTBDMS}$ ), 3.52 (t,  $^3J_{\text{HH}} = 6.6$  Hz, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 3.92 (m, 1H,  $\text{CHOTBDMS}$ ), 6.12 (dt,  $^3J_{\text{HH}} = 15.1$ ,  $^4J_{\text{HH}} = 1.4$  Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ), 6.87 (dt,  $^3J_{\text{HH}} = 15.1$ , 7.6 Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -4.6 ( $(\text{CH}_3)_2\text{Si}$ ), -4.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 18.3 ( $(\text{CH}_3)_3\text{CSi}$ ), 23.8 ( $\text{CH}_3\text{CH}$ ), 24.4 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 43.0 ( $\text{CH}_2\text{CHOTBDMS}$ ), 46.0 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 46.6 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 67.9 ( $\text{CHOTBDMS}$ ), 123.8 ( $\text{CH}=\text{CHCH}_2$ ), 142.3 ( $\text{CH}=\text{CHCH}_2$ ), 164.8 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 299$ .

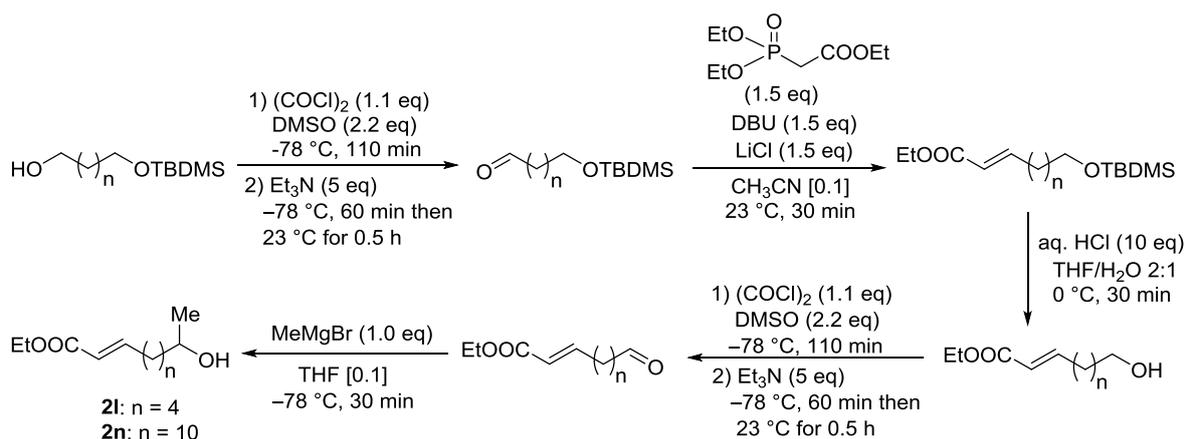
 **(E)-5-hydroxy-1-(pyrrolidin-1-yl)hex-2-en-1-one (**2j**):** The reaction was run according to GP4 starting from (*E*)-5-((*tert*-butyldimethylsilyloxy)-1-(pyrrolidin-1-yl)hex-2-en-1-one (480 mg, 1.6 mmol). The crude mixture was purified by flash chromatography on silica gel (EtOAc/MeOH = 10:1) to give **2j** in 55% yield (150 mg) as a light yellow oil.  $R_f = 0.2$  (EtOAc/MeOH = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3396, 2972, 2876, 1661, 1601, 1442, 1126, 980$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.10 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.54 (bs, 1H, OH), 1.67 – 1.89 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 2.17 – 2.32 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.34 (t,  $^3J_{\text{HH}} = 6.9$  Hz, 2H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 3.40 (t,  $^3J_{\text{HH}} = 6.8$  Hz, 3H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 3.76 – 3.91 (m, 1H,  $\text{CHOH}$ ), 6.10 (dt,  $^3J_{\text{HH}} = 15.1$ ,  $^4J_{\text{HH}} = 1.5$  Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ), 6.70 (dt,  $^3J_{\text{HH}} = 15.1$ , 7.5 Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 23.4 ( $\text{CH}_3\text{CH}$ ), 24.7 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 26.5 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 42.5

(CH<sub>2</sub>CHOH), 46.1 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 46.9 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 67.2 (CHOH), 125.0 (CH=CHCH<sub>2</sub>), 141.4 (CH=CHCH<sub>2</sub>), 164.7 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 184.



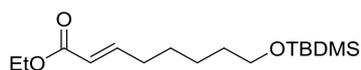
**Figure S11:** Synthesis of Ethyl (*E*)-6-hydroxyhex-2-enoate (**2k**)

**Ethyl (*E*)-6-hydroxyhex-2-enoate (**2k**):** The reaction was run according to GP2 starting from tetrahydrofuran-2-ol (15.6 mmol, 1.4 g). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:2) affording **2k** in 80% yield (1.9 g). All spectroscopic analyses were in agreement with those reported in the literature.<sup>14</sup>



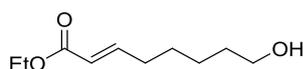
**Figure S12:** Synthesis of Ethyl (*E*)-8-hydroxynon-2-enoate (**2l**) and Ethyl (*E*)-14-hydroxypentadec-2-enoate (**2n**)

**General procedure for Swern oxidation (GP5):** To a solution of oxalyl chloride (1.1 eq) in CH<sub>2</sub>Cl<sub>2</sub> (0.3 M) at -78 °C, a solution of DMSO (2.2 eq) was added dropwise and stirred for 50 minutes at the same temperature. A solution of the appropriate alcohol (1.0 eq) in CH<sub>2</sub>Cl<sub>2</sub> (1.0 M) was slowly added and stirred at the same temperature for 60 minutes. Next, Et<sub>3</sub>N (5 eq) was added at -78 °C and stirred for 1 h, then warmed to room temperature and stirred for an additional 30 minutes. The reaction mixture was quenched with water, extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 times), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was filtered through a small pad of silica gel (Pentane/EtOAc = 10:1) to give the desired product which was used in the next step without any further purification.



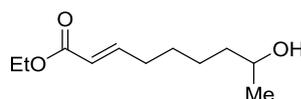
**Ethyl (E)-8-((tert-butyl dimethylsilyloxy)oct-2-enoate:** 6-  
(*tert*-Butyl dimethylsilyloxy)-1-hexanol<sup>15</sup> (6.5 mmol) was oxidized

to the corresponding aldehyde according to GP5. The following olefination was performed according to GP2. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) to give the desired product as a colourless oil in 81% yield (1.65 g) over 2 steps. All spectroscopic analyses were in agreement with those reported in the literature.<sup>16</sup>



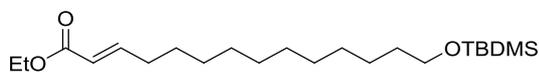
**Ethyl (E)-8-hydroxyoct-2-enoate:** The reaction was run according to GP4 starting from ethyl (E)-8-((tert-

butyl dimethylsilyloxy)oct-2-enoate (1.65 g, 5.5 mmol). The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 1:2) to give the free alcohol in 78% yield (800 mg) as a colourless oil. All spectroscopic analyses were in agreement with those reported in the literature.<sup>17</sup>



**Ethyl (E)-8-hydroxynon-2-enoate (2I):** Ethyl (E)-8-hydroxyoct-2-enoate (276 mg, 1.5 mmol) was oxidized according to GP5. A THF solution (10 mL) of the resulting aldehyde was cooled to  $-78^{\circ}\text{C}$

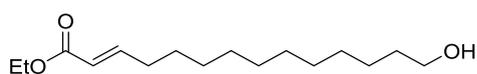
and a solution of MeMgBr (1.5 mmol) was added dropwise and stirred at the same temperature for 30 minutes. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution (10 mL), extracted with diethyl ether (3 x 10 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:2) to give **2I** in 40% yield (120 mg) over 2 steps. All spectroscopic analyses were in agreement with those reported in the literature.<sup>18</sup>



**Ethyl (E)-14-((tert-butyl dimethylsilyloxy)tetradec-2-enoate:** 12-

*tert*-Butyl dimethylsilyloxy dodecan-1-ol (2.8 mmol) was oxidized to the corresponding aldehyde<sup>19</sup> according to GP5. The following olefination was performed according to GP2. The crude mixture was purified by flash chromatography on silica gel to give the desired product as a colourless oil in 86% yield (920 mg) over 2 steps.  $R_f = 0.3$  (*n*-Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2927, 2855, 1723, 1097, 834, 775$ .  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.04 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.22 – 1.37 (m, 17H,  $\text{CH}_3\text{CH}_2\text{O}$ ;  $(\text{CH}_2)_7\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 1.41 – 1.52 (m, 4H,  $\text{CH}=\text{CHCH}_2\text{CH}_2$ ;  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 2.19 (qd,  $^3J_{\text{HH}} = 7.1$ ,  $^4J_{\text{HH}} = 1.5$  Hz, 2H,  $\text{CH}=\text{CHCH}_2$ ), 3.59 (t,  $^3J_{\text{HH}} = 6.6$

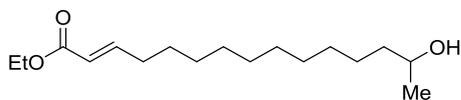
Hz, 2H,  $\text{CH}_2\text{OTBDMS}$ ), 4.18 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 5.81 (dt,  $^3J_{\text{HH}} = 15.6$ ,  $^4J_{\text{HH}} = 1.5$  Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ), 6.96 (dt,  $^3J_{\text{HH}} = 15.6$ , 6.9 Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.1 ( $(\text{CH}_3)_2\text{Si}$ ), 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.5 ( $\text{C}_{\text{quat}}$ ), 25.9 ( $\text{CH}_2$ ), 26.1 ( $(\text{CH}_3)_3\text{CSi}$ ), 28.2 ( $\text{CH}=\text{CHCH}_2\text{CH}_2$ ), 29.31 ( $\text{CH}_2$ ), 29.5 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 29.8 ( $\text{CH}_2$ ), 32.4 ( $\text{CH}=\text{CHCH}_2$ ), 33.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 60.3 ( $\text{CH}_3\text{CH}_2\text{OCO}$ ) 63.5 ( $\text{CH}_2\text{OTBDMS}$ ), 121.3 ( $\text{CH}=\text{CHCH}_2$ ), 149.7 ( $\text{CH}=\text{CHCH}_2$ ), 167.0 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 386$ .



**Ethyl (E)-14-hydroxytetradec-2-enoate:** The reaction was run according to GP4 starting from ethyl

(E)-14-((*tert*-butyldimethylsilyl)oxy)tetradec-2-enoate (920 mg, 2.4 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 2:1) to give the free alcohol in 99% yield (660 mg) as a colourless oil.  $R_f = 0.5$  (Pentane/Diethyl ether = 1:2).

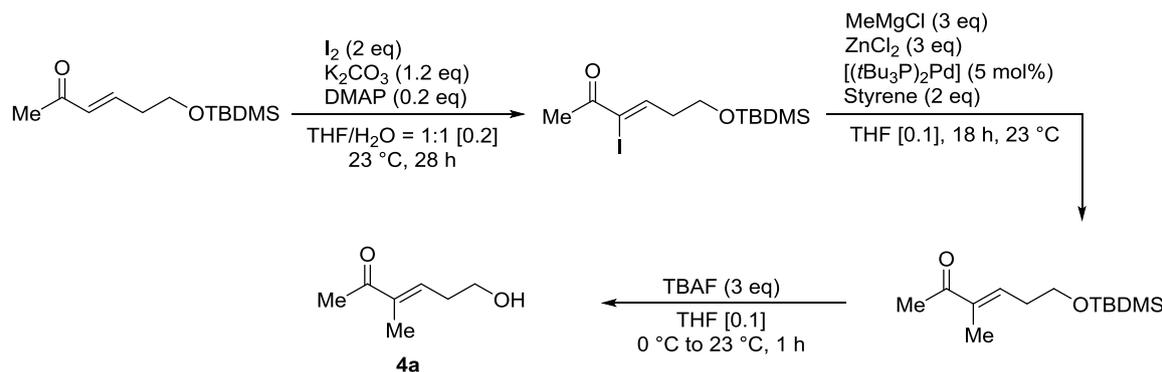
**IR (neat):**  $\nu(\text{cm}^{-1}) = 3419, 2925, 2854, 1720, 1266, 1179, 1042$ .  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.17 – 1.40 (m, 17H,  $(\text{CH}_2)_7\text{CH}_2\text{CH}_2\text{OH}$ ;  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.40 – 1.50 ( $\text{CH}=\text{CHCH}_2\text{CH}_2$ ), 1.50 – 1.66 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.16 – 2.22 (m, 2H,  $\text{CH}=\text{CHCH}_2$ ), 3.64 (t,  $^3J_{\text{HH}} = 6.6$  Hz, 2H,  $\text{CH}_2\text{OH}$ ), 4.18 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 5.81 (dt,  $^3J_{\text{HH}} = 15.6$ ,  $^4J_{\text{HH}} = 1.6$  Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ), 6.96 (dt,  $^3J_{\text{HH}} = 15.6$ , 6.9 Hz, 1H,  $\text{CH}=\text{CHCH}_2$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 25.9 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ ), 28.2 ( $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2$ ), 29.3 ( $\text{CH}_2$ ), 29.5 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 32.3 ( $\text{CH}=\text{CHCH}_2$ ), 33.0 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 60.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 63.3 ( $\text{CH}_2\text{OH}$ ), 121.4 ( $\text{CH}=\text{CHCH}_2$ ), 149.7 ( $\text{CH}=\text{CHCH}_2$ ), 167.0 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 271$ .



**Ethyl (E)-14-hydroxypentadec-2-enoate (2n):** The product was oxidized according to GP5 starting from ethyl (E)-14-hydroxytetradec-2-enoate (268 mg, 1.0

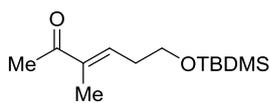
mmol). A THF solution (10 mL) of the resulting aldehyde was cooled to  $-78^\circ\text{C}$  and a solution of  $\text{MeMgBr}$  (1.0 mmol) was added dropwise. The mixture was stirred at the same temperature for 30 minutes then quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (10 mL), extracted with diethyl ether ( $3 \times 10$  mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (Pentane/Diethyl ether from 2:1 to 1:1) to give **2n** as a colourless oil in 45% yield (130 mg) over 2 steps.  $R_f = 0.5$  (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3473, 3436, 2925, 2854, 1720, 1180, 1042, 980$ .  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.19 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.24 – 1.50 (m, 22H,  $(\text{CH})_9\text{CHOH}$ ;  $\text{CH}_3\text{CH}_2\text{O}$ ;  $\text{OH}$ ), 2.16 – 2.22 (m, 2H,

CH=CHCH<sub>2</sub>), 3.75 – 3.83 (m, 1H, CHOH), 4.18 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.81 (dt, <sup>3</sup>J<sub>HH</sub> = 15.6, <sup>4</sup>J<sub>HH</sub> = 1.6 Hz, 1H, CH=CHCH<sub>2</sub>), 6.96 (dt, <sup>3</sup>J<sub>HH</sub> = 15.6, 6.9 Hz, 1H, CH=CHCH<sub>2</sub>). <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ (ppm) 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 23.7 (CH<sub>3</sub>CHOH), 25.9 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 28.2 (CH<sub>2</sub>CH<sub>2</sub>CH=CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.8 (CH<sub>2</sub>), 32.3 (CH=CHCH<sub>2</sub>), 39.5 (CH<sub>2</sub>CHOH), 60.3 (CH<sub>3</sub>CH<sub>2</sub>O), 68.3 (CHOH), 121.4 (CH=CHCH<sub>2</sub>), 149.6 (CH=CHCH<sub>2</sub>), 166.96 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 285.



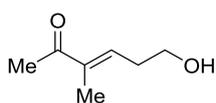
**Figure S13:** Synthesis of (*E*)-6-hydroxy-3-methylhex-3-en-2-one (**4a**)

**(Z)-6-((tert-butyldimethylsilyl)oxy)-3-iodohex-3-en-2-one:** To a solution of (*E*)-6-((tert-butyldimethylsilyl)oxy)hex-3-en-2-one<sup>5</sup> (5.9 g, 25.9 mmol) in THF/H<sub>2</sub>O 1:1 (130 mL) were sequentially added K<sub>2</sub>CO<sub>3</sub> (4.3 g, 1.2 mmol), I<sub>2</sub> (13.1 g, 51.8 mmol) and 4-dimethylaminopyridine (DMAP) (630 mg, 5.2 mmol). After 28 h, the reaction mixture was diluted with diethyl ether (300 mL) and washed with a saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (600 mL). The mixture was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered on a pad of silical gel and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 30:1) to afford the corresponding α-iodoenone in 44% yield (4.0 g). Note: the remaining starting material (25%, 1.5 g) could be recovered. **R<sub>f</sub>** = 0.3 (Pentane/Diethyl ether = 10:1). **IR (neat):** ν(cm<sup>-1</sup>) = 2953, 2929, 2857, 2130, 1681, 1092, 832, 774, 714. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ (ppm) 0.08 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.90 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>C), 2.51 (s, 3H, CH<sub>3</sub>CO), 2.64 (td, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 6.5 Hz, 2H, CH<sub>2</sub>), 3.80 (t, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 2H, CH<sub>2</sub>OTBDMS), 7.16 (t, <sup>3</sup>J<sub>HH</sub> = 6.5 Hz, 1H, CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>) δ (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 25.3 (CH<sub>3</sub>), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 41.6 (CH<sub>2</sub>CH<sub>2</sub>), 60.7 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 113.6 (C=CH), 150.9 (C=CH), 192.5 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 355.



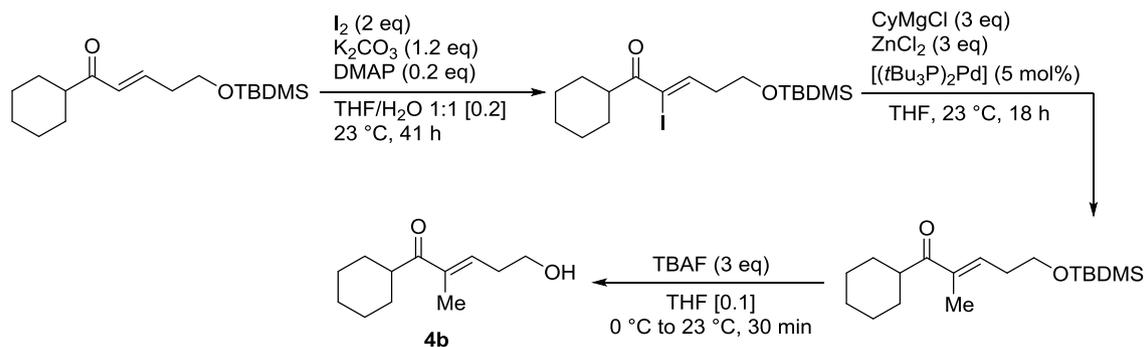
**(E)-6-((tert-butyl dimethylsilyl)oxy)-3-methylhex-3-en-2-one:** In a

Young valve Schlenk, the electrophilic alkylzinc reagent was prepared in situ by mixing MeMgCl (7.2 mL from 1.0 M in diethyl ether) and ZnCl<sub>2</sub> (7.2 mL from a 1.0 M in THF). A white precipitate formed rapidly. In a separate Schlenk, [(tBu<sub>3</sub>P)<sub>2</sub>Pd] (5 mol%) was dissolved in THF (60 mL) and (Z)-6-((tert-butyl dimethylsilyl)oxy)-3-iodohex-3-en-2-one (2.12 g, 6.0 mmol) was added. The latter solution was transferred by cannula to the suspension of the alkylzinc reagent and stirred at room temperature. After 18 h, the mixture was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (10 mL), extracted with diethyl ether (3 × 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) to afford the desired cross-coupling product in 52% yield (760 mg) as a colourless oil. *R*<sub>f</sub> = 0.25 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2954, 2930, 1670, 1253, 1096, 937, 833, 775. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.06 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.89 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.78 (q, <sup>4</sup>J<sub>HH</sub> = 1.0 Hz, 3H, CH<sub>3</sub>), 2.31 (s, 3H, CH<sub>3</sub>CO), 2.37 – 2.70 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.74 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.65 – 6.73 (m, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 11.5 (CH<sub>3</sub>C=CH), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 25.6 (CH<sub>3</sub>C=O), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 32.9 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 61.8 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 139.0 (C=O), 140.4 (C=CH), 200.0 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 243.



**(E)-6-hydroxy-3-methylhex-3-en-2-one (4a):** The reaction was run

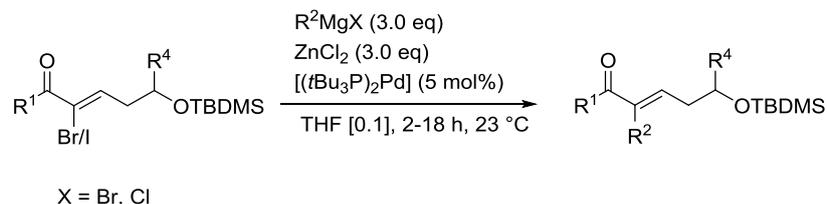
according to GP3 starting from (E)-6-((tert-butyl dimethylsilyl)oxy)-3-methylhex-3-en-2-one (760 mg, 3.1 mmol). The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 1:3) on silica gel to give **4a** in 51% yield (230 mg) as a colourless oil. *R*<sub>f</sub> = 0.1 (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3339, 2930, 2876, 1706, 1664, 1460, 1368, 1280, 1160. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.64 (s, 1H, OH), 1.80 (d, <sup>4</sup>J<sub>HH</sub> = 1.2 Hz, 3H, CH<sub>3</sub>C=CH), 2.32 (s, 3H, CH<sub>3</sub>CO), 2.46 – 2.61 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.80 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 6.68 (tq, <sup>3</sup>J<sub>HH</sub> = 7.2, <sup>4</sup>J<sub>HH</sub> = 1.3 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 11.6 (CH<sub>3</sub>C=CH), 25.7 (CH<sub>3</sub>CO), 32.6 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.6 (CH<sub>2</sub>CH<sub>2</sub>OH), 139.3 (C=CH), 139.7 (C=CH), 199.9 (C=O). **LRMS (IC)** found [M-OH]<sup>+</sup> = 111.



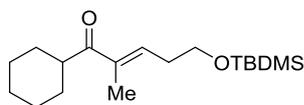
**Figure S14:** Synthesis of (*E*)-1-cyclohexyl-5-hydroxy-2-methylpent-2-en-1-one (**4b**)

**(Z)-5-((*tert*-butyldimethylsilyloxy)-1-cyclohexyl-2-iodopent-2-en-1-one:** To a solution of (*E*)-5-((*tert*-butyldimethylsilyloxy)-1-cyclohexylpent-2-en-1-one (2.4 g, 8.1 mmol) in THF/H<sub>2</sub>O 1:1 (40 mL) were sequentially added K<sub>2</sub>CO<sub>3</sub> (1.4 g, 1.0 mmol), I<sub>2</sub> (4.1 g, 16.2 mmol) and DMAP (196 mg, 1.6 mmol). After 41 h, the reaction mixture was diluted with diethyl ether (300 mL), washed with a saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (600 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered on a pad of silica gel and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel to afford the title compound in 47% yield (1.6 g) as a light yellow oil. Note: the remaining starting material (23%, 560 mg) could be recovered. **R<sub>f</sub>** = 0.5 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2930, 2856, 1678, 1450, 1253. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.08 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.91 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.18 – 1.52 (m, 5H, CH<sub>2</sub>-Cy), 1.66 – 1.90 (m, 5H, CH<sub>2</sub>-Cy), 2.63 (td, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 6.2 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.14 (tt, <sup>3</sup>J<sub>HH</sub> = 11.6, 3.1 Hz, 1H, CH-Cy), 3.80 (t, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 7.14 (t, <sup>3</sup>J<sub>HH</sub> = 6.5 Hz, 1H, CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) - 5.3 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.2 (CH<sub>3</sub>)<sub>3</sub>CSi), 25.8 (CH<sub>2</sub>-Cy), 30.0 (CH-Cy), 41.4 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 45.3 (CH<sub>2</sub>-Cy), 60.6 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 113.2 (C=CH<sub>i</sub>), 148.7 (C=CH), 198.2 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 423.

### Procedure for Negishi cross-coupling (GP6A)

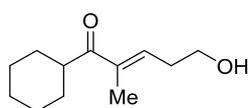


In a Young valve Schlenk, the electrophilic alkylzinc reagent was in situ prepared by mixing the appropriate Grignard (3.0 eq) and  $\text{ZnCl}_2$  (3.0 eq, 1.0 M in THF) for 10 to 30 minutes until a white precipitate formed. In a separate Schlenk,  $[(t\text{Bu}_3\text{P})_2\text{Pd}]$  (5 mol%) was dissolved in THF (0.1 M) and the appropriate bromo- or iodo-derivative (1 eq) was added. The latter solution was transferred by cannula to the suspension of the alkylzinc reagent and stirred at room temperature. After 2-18 h, the mixture was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution, extracted with diethyl ether (3 times), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*.



#### (E)-5-((tert-butyldimethylsilyl)oxy)-1-cyclohexyl-2-methylpent-

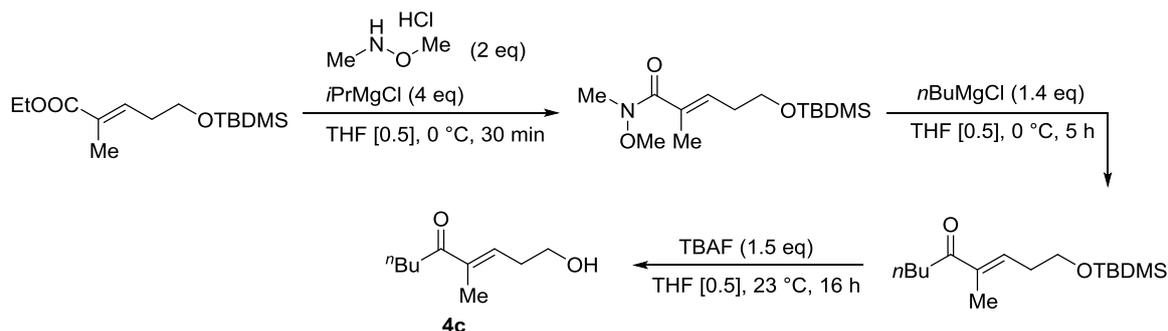
**2-en-1-one**: The reaction was performed according to GP6A starting from (*Z*)-5-((tert-butyldimethylsilyl)oxy)-1-cyclohexyl-2-iodopent-2-en-1-one (1.39 g, 3.2 mmol). After 2 h, the reaction was complete. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 20:1) to afford the desired product in 81% yield (800 mg).  $R_f = 0.5$  (Pentane/Diethyl ether = 10:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2929, 2856, 1664, 1253, 1099$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.07 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.90 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.20 – 1.83 (m, 10H,  $\text{CH}_2\text{-Cy}$ ), 1.77 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.46 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.02 (tt,  $^3J_{\text{HH}} = 11.4, 3.3$  Hz, 1H,  $\text{CH-Cy}$ ), 3.74 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.69 (t,  $^3J_{\text{HH}} = 7.0$ , 1H,  $\text{C}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 12.0 ( $(\text{CH}_3)_3\text{C}=\text{CH}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.1 ( $\text{CH}_2\text{-Cy}$ ), 30.0 ( $\text{CH-Cy}$ ), 32.7 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 44.4 ( $\text{CH}_2\text{-Cy}$ ), 61.8 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 137.4 ( $\text{C}=\text{CH}$ ), 138.4 ( $\text{C}=\text{CH}$ ), 205.7 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 311$ .



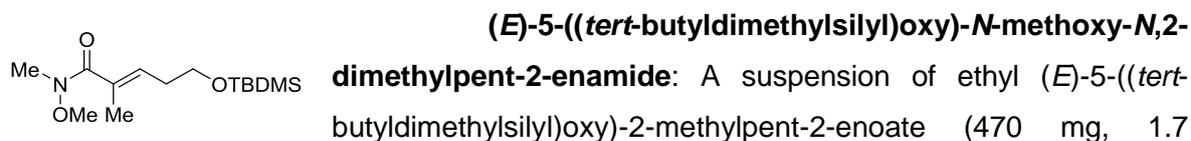
#### (E)-1-cyclohexyl-5-hydroxy-2-methylpent-2-en-1-one (**4b**):

The reaction was run according to GP3 starting from (*E*)-5-((tert-butyldimethylsilyl)oxy)-1-cyclohexyl-2-methylpent-2-en-1-one (775 mg, 2.5 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:3) to give **4b** in 74% yield (370 mg) as a colorless oil.  $R_f = 0.5$

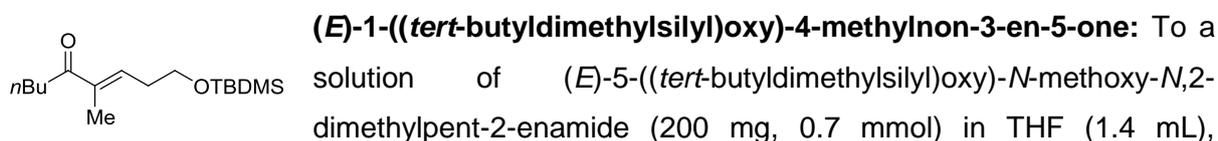
(Pentane/Diethyl ether = 1:2). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2929, 2856, 1664, 1253, 1099$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.16 – 1.46 (m, 6H,  $\text{CH}_2\text{-Cy}$ ;  $\text{OH}$ ), 1.65 – 1.85 (m, 5H,  $\text{CH}_2\text{-Cy}$ ), 1.80 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.53 (td,  $^3J_{\text{HH}} = 6.5, 5.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.02 (tt,  $^3J_{\text{HH}} = 11.4, 3.3$  Hz, 1H,  $\text{CH-Cy}$ ), 3.80 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 6.57 – 6.72 (m, 1H,  $\text{C}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 12.1 ( $\text{CH}_3\text{C}=\text{CH}$ ), 26.0 ( $\text{CH}_2\text{-Cy}$ ), 26.1 ( $\text{CH}_2\text{-Cy}$ ), 30.0 ( $\text{CH-Cy}$ ), 32.6 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 44.5 ( $\text{CH}_2\text{-Cy}$ ), 61.7 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 137.0 ( $\text{C}=\text{CH}$ ), 138.3 ( $\text{C}=\text{CH}$ ), 205.6 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 197$ .



**Figure S15:** Synthesis of (*E*)-1-hydroxy-4-methylnon-3-en-5-one (**4c**)

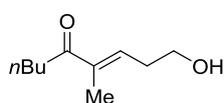


A suspension of ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-2-methylpent-2-enoate (470 mg, 1.7 mmol) and *N*,*O*-dimethoxyhydroxylamine hydrochloride (330 mg, 3.4 mmol) in THF (3 mL) was stirred for 10 minutes at  $-20$  °C. Isopropylmagnesium chloride (13.65 mmol, 4.55 mL, 3 M in THF) was added while maintaining the temperature below  $0$  °C. After 30 minutes at  $0$  °C, the reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (5 mL), extracted with EtOAc ( $2 \times 5$  mL), washed with brine (20 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The product was used in the next step without further purification.



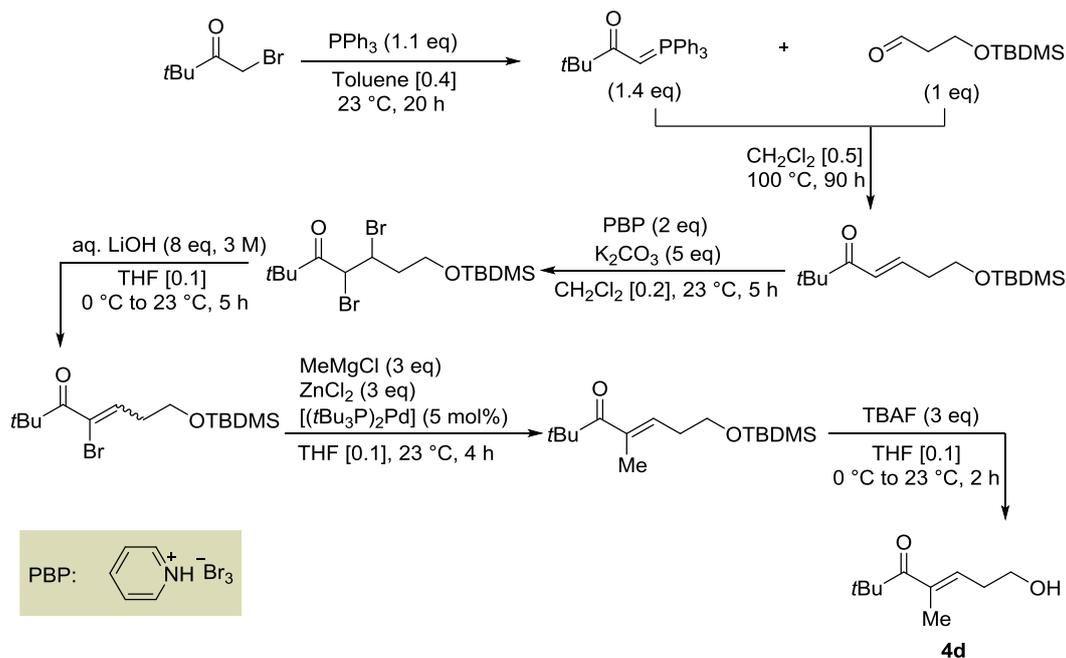
To a solution of (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-*N*-methoxy-*N*,2-dimethylpent-2-enamide (200 mg, 0.7 mmol) in THF (1.4 mL), *n*BuMgCl (1.7 M in THF/toluene, 0.16 mL) was slowly added at  $0$  °C and stirred for 5 h. The mixture was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (2 mL), extracted with diethyl ether ( $3 \times 10$  mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 50:1) to give the title compound as a colourless oil in 64% yield (127 mg) over 2 steps.  $R_f = 0.7$  (Pentane/Diethyl ether = 10:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2955, 2930, 1670, 1253, 1098, 833$ ,

775.  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.06 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 – 0.94 (m, 12H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ;  $(\text{CH}_3)_3\text{CSi}$ ), 1.29 – 1.37 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.53 – 1.62 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 1.78 (d,  $^4J_{\text{HH}} = 1.5$  Hz, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.41 – 2.52 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 2.59 – 2.72 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.74 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.59 – 6.78 (m, 1H,  $\text{C}=\text{CH}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 11.7 ( $\text{CH}_3\text{C}=\text{CH}$ ), 14.1 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 22.7 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.4 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 32.8 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 37.2 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 61.8 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 138.54 ( $\text{C}=\text{CH}$ ), 138.94 ( $\text{C}=\text{CH}$ ), 202.43 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 285$ .



**(E)-1-hydroxy-4-methylnon-3-en-5-one (4c):** The reaction was run according to GP3 starting from (*E*)-1-((*tert*-butyldimethylsilyl)oxy)-4-methyl non-3-en-5-one (160 mg, 0.56 mmol). Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:3) afforded **4c** in 57% yield (56 mg).

$R_f = 0.3$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2931, 1662, 1046, 755$ .  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.92 (t,  $^3J_{\text{HH}} = 7.3$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.33 (tq,  $^3J_{\text{HH}} = 14.6, 7.3$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.59 (tt,  $^3J_{\text{HH}} = 7.5$  Hz, 7.5 Hz, 2H,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.81 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.46 – 2.59 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 2.62 – 2.72 (m, 2H,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 3.80 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 6.56 – 6.76 (m, 1H,  $\text{C}=\text{CH}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 11.7 ( $\text{CH}_3\text{C}=\text{CH}$ ), 14.1 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 18.44 ( $(\text{CH}_3)_3\text{CSi}$ ), 22.7 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.4 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ), 32.8 ( $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ), 37.1 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 61.8 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 138.5 ( $\text{C}=\text{CH}$ ), 138.9 ( $\text{C}=\text{CH}$ ), 202.4 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 171$ ;  $[\text{M}+\text{NH}_4]^+ = 188$ .

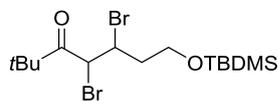


**Figure S16:** Synthesis of (*E*)-7-hydroxy-2,2,4-trimethylhept-4-en-3-one (**4d**)

**3,3-dimethyl-1-(triphenyl- $\lambda^5$ -phosphanylidene)butan-2-one:** To a toluene solution (60 mL) of 1-bromo-3,3-dimethylbutan-2-one (10 g, 56.2 mmol) was slowly added a solution of triphenylphosphine (16.2 g, 61.6 mmol) in toluene (80 mL). After 20 h at room temperature, the white solid obtained was filtered and redissolved in  $\text{CH}_2\text{Cl}_2$  (182 mL). To this solution was added an aqueous 2 N NaOH solution (60 mL) which was stirred for 1 h at room temperature. The reaction mixture was then washed with water and concentrated to afford the title compound in 87% yield (17.7 g).

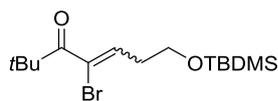
**(*E*)-7-((*tert*-butyldimethylsilyloxy)-2,2-dimethylhept-4-en-3-one:** To a stirred solution of 3-((*tert*-butyldimethylsilyloxy)propanal (6.4 g, 34 mmol) in THF (70 mL), 3,3-dimethyl-1-(triphenyl- $\lambda^5$ -phosphanylidene)butan-2-one (17.7 g, 49.1 mmol) was added in one portion and stirred for 90 h at 100 °C. After cooling to room temperature, 50 mL of pentane/diethyl ether (1:1, v/v) were added. The resulting white precipitate was filtered off and the remaining red solution was concentrated to give the crude product, which was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 20:1). The product was isolated in 33% yield (3.0 g) as colorless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2956, 2931, 1691, 1254, 1099, 834, 775$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.05 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.15 (s, 9H,  $(\text{CH}_3)_3\text{CC}=\text{O}$ ), 2.34 – 2.50 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.73 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.56 (dt,  $^3J_{\text{HH}} = 15.3$ ,  $^4J_{\text{HH}} = 1.5$  Hz, 1H,  $\text{COCH}=\text{CH}$ ), 6.92 (dt,  $^3J_{\text{HH}} = 15.2$ , 7.1 Hz, 1H,  $\text{COCH}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 18.4

((CH<sub>3</sub>)<sub>3</sub>CSi), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.3 ((CH<sub>3</sub>)<sub>3</sub>CC=O), 36.2 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 61.7 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 126.0 (COCH=CH), 144.2 (COCH=CH), 204.3 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 271.



**4,5-dibromo-7-((tert-butyldimethylsilyl)oxy)-2,2-dimethylheptan-**

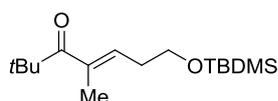
**3-one:** To a solution of (*E*)-6-((tert-butyldimethylsilyl)oxy)hex-3-en-2-one (750 mg, 2.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (14 mL), K<sub>2</sub>CO<sub>3</sub> (1.93 g, 14 mmol) and pyridinium tribromide (1.72 g, 5.4 mmol) were added in sequence. The mixture was stirred for 5 h at room temperature and then quenched with a saturated aqueous NaHCO<sub>3</sub> solution (30 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 40:1) to afford the dibrominated product in 71% yield (850 mg) as a yellow oil. **R<sub>f</sub>** = 0.3 (Pentane/Diethyl ether = 10:1). **IR (neat):** ν(cm<sup>-1</sup>) = 2956, 2931, 2859, 1714, 1472, 1255, 1100, 837. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ (ppm) 0.09 (d, *J* = 2.2 Hz, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.92 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.29 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CO), 1.98 – 2.04, 2.48 – 2.63 (m, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.74 – 3.99 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 4.65 (ddd, <sup>3</sup>*J*<sub>HH</sub> = 11.4, 9.3, 2.7 Hz, 1H, COCH(Br)CH(Br)), 4.98 (d, <sup>3</sup>*J*<sub>HH</sub> = 11.0 Hz, 1H, COCH(Br)CH(Br)). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>) δ (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 27.6 ((CH<sub>3</sub>)<sub>3</sub>CCO), 37.9 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 44.4 ((CH<sub>3</sub>)<sub>3</sub>CCO), 47.0 (COCH(Br)CH(Br)), 49.4 (COCH(Br)CH(Br)), 60.4 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 206.9 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 431.



**4-bromo-7-((tert-butyldimethylsilyl)oxy)-2,2-dimethylhept-4-en-3-**

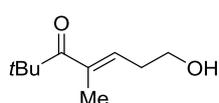
**one:** 4,5-dibromo-7-((tert-butyldimethylsilyl)oxy)-2,2-dimethylheptan-3-one was dissolved in THF (20 mL) and an aqueous LiOH solution (3 M, 5.25 mL) was added dropwise. The mixture was stirred for 5 h at room temperature and then poured into water (50 mL), extracted with diethyl ether (3 × 50 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 50:1) to give the (*E*)-isomer of the product in 58% yield (400 mg) and the (*Z*)-isomer in 32% yield (220 mg) as light yellow oils. (*E*)-isomer: **R<sub>f</sub>** = 0.4 (Pentane/Diethyl ether = 10:1). **IR (neat):** ν(cm<sup>-1</sup>) = 2958, 2859, 1692, 1101, 836. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ (ppm) 0.05 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.89 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.30 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CCO), 2.11 – 2.25 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.65 (t, <sup>3</sup>*J*<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.09 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.9 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>) δ (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.5 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 27.9 ((CH<sub>3</sub>)<sub>3</sub>CCO), 34.8 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 44.0 ((CH<sub>3</sub>)<sub>3</sub>CCO), 62.0 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 115.8 (C=CH), 132.3

(C=CH), 207.4 (C=O). **LRMS (IC)** found  $[M+H]^+ = 350$ . (*Z*)-isomer:  $R_f = 0.35$  (Pentane/Diethyl ether = 10:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2956, 2931, 2859, 1685, 1255, 1097, 837$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.06 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.31 (s, 9H,  $(\text{CH}_3)_3\text{CCO}$ ), 2.46 – 2.64 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.75 (t,  $^3J_{\text{HH}} = 6.2$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.67 (t,  $^3J_{\text{HH}} = 6.6$  Hz, 1H, C=CH).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 28.1 ( $(\text{CH}_3)_3\text{CCO}$ ), 35.6 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 44.2 ( $(\text{CH}_3)_3\text{CCO}$ ), 61.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 123.5 (C=CH), 136.6 (C=CH), 202.8 (C=O). **LRMS (IC)** found  $[M+H]^+ = 350$ .



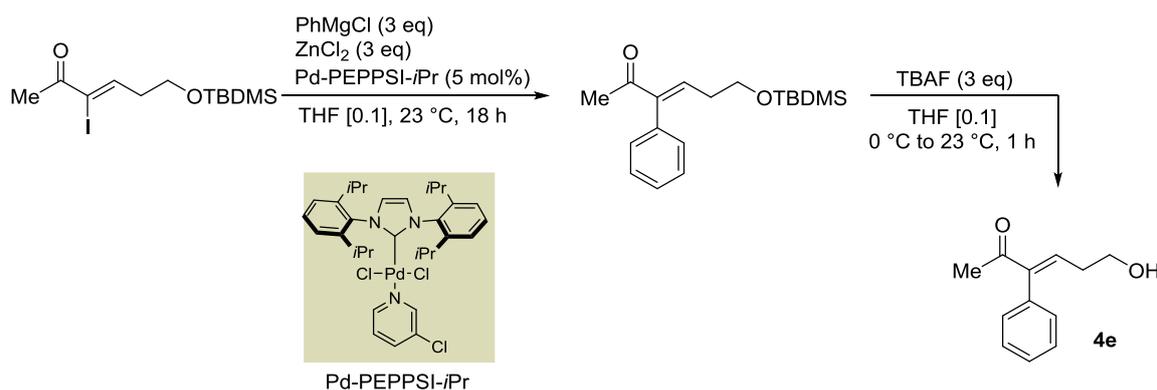
**(E)-7-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethylhept-4-en-3-**

**one**: The reaction was run according to GP6A starting from (*Z*)-4-bromo-7-((tert-butyldimethylsilyl)oxy)-2,2-dimethylhept-4-en-3-one (310 mg, 0.89 mmol). After 4 h, the reaction was complete and purification by flash chromatography on silica gel (Pentane/Diethyl ether = 20:1) afforded the product in 93% yield (235 mg) as a light yellow oil.  $R_f = 0.6$  (Pentane/Diethyl ether = 10:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2956, 2931, 2859, 1688, 1468, 1254, 1099, 836$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.06 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.24 (s, 9H,  $(\text{CH}_3)_3\text{CCO}$ ), 1.80 (q,  $^4J_{\text{HH}} = 1.1$  Hz, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.31 – 2.46 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.70 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBS}$ ), 6.11 (tq,  $^3J_{\text{HH}} = 7.1$ ,  $^4J_{\text{HH}} = 1.4$  Hz, 1H, C=CH).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 14.5 ( $\text{CH}_3\text{C}=\text{CH}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 28.4 ( $(\text{CH}_3)_3\text{CCO}$ ), 32.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 44.0 ( $(\text{CH}_3)_3\text{CCO}$ ), 62.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 132.3 (C=CH), 137.3 (C=CH), 211.5 (C=O). **LRMS (IC)** found  $[M+H]^+ = 285$ .

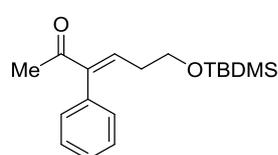


**(E)-7-hydroxy-2,2,4-trimethylhept-4-en-3-one (4d)**: The reaction was

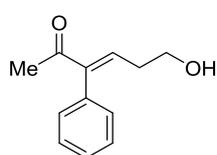
run according to GP3 starting from (*E*)-7-((tert-butyldimethylsilyl)oxy)-2,2,4-trimethylhept-4-en-3-one (225 mg, 0.79 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) to give **4d** in 84% yield (113 mg).  $R_f = 0.2$  (Pentane/Diethyl ether = 2:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 3412, 2960, 2874, 1658, 1462, 1367, 1048, 998$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.23 (s, 9H,  $(\text{CH}_3)_3\text{CCO}$ ), 1.78 – 1.90 (m, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.31 – 2.46 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.74 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 5.92 – 6.05 (m, 1H, C=CH).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.7 ( $\text{CH}_3\text{C}=\text{CH}$ ), 28.2 ( $(\text{CH}_3)_3\text{CCO}$ ), 31.7 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 44.1 ( $(\text{CH}_3)_3\text{CCO}$ ), 61.9 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 130.4 (C=CH), 138.7 (C=CH), 212.0 (C=O). **LRMS (IC)** found  $[M+H]^+ = 171$ .



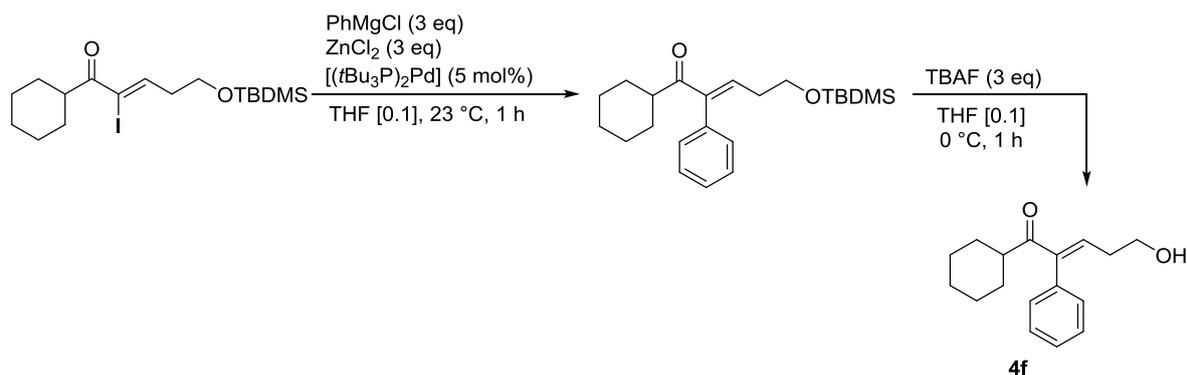
**Figure S17:** Synthesis of (*E*)-6-hydroxy-3-phenylhex-3-en-2-one (**4e**)



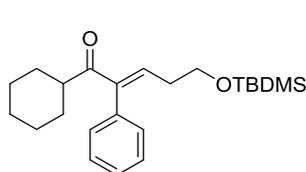
**(*E*)-6-((*tert*-butyldimethylsilyl)oxy)-3-phenylhex-3-en-2-one:** The reaction was run according to modified GP6A starting from (*Z*)-6-((*tert*-butyldimethylsilyl)oxy)-3-iodohex-3-en-2-one (860 mg, 2.4 mmol) and using [1,3-Bis(2,6-Diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride (Pd-PEPPSI-*i*Pr, 81.5 mg, 5 mol%) as precatalyst. The crude was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 50:1) to give the title compound in 60% yield (440 mg).  $R_f = 0.2$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2954, 2929, 2858, 1674, 1253, 1092, 834$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.03 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 2.25 – 2.36 (m, 3H,  $\text{CH}_3\text{CO}$ ; 2H  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.68 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.95 (t,  $^3J_{\text{HH}} = 7.4$  Hz, 1H, C=CH), 7.05 – 7.18 (m, 2H, CH-Ar), 7.30 – 7.44 (m, 3H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.4 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 33.5 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 62.0 ( $\text{CH}_3\text{CO}$ ), 127.6 (CH-Ar), 128.4 (CH-Ar), 129.7 (CH-Ar), 136.0 (C=CH), 141.3 (C=CH), 144.7 (C-Ar), 198.8 (C=O). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 306$ .



**(*E*)-6-hydroxy-3-phenylhex-3-en-2-one (**4e**):** The reaction was run according to GP3 starting from (*E*)-6-((*tert*-butyldimethylsilyl)oxy)-3-phenylhex-3-en-2-one (440 mg, 1.2 mmol). Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:3) afforded **4e** in 52% yield (142 mg) as a colorless oil.  $R_f = 0.1$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3428, 2924, 1665, 1353, 1050, 765, 699$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 2.29 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.35 (dt,  $^3J_{\text{HH}} = 7.5, 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.73 (t,  $J = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 6.94 (t,  $^3J_{\text{HH}} = 7.4$  Hz, 1H, C=CH), 7.06 – 7.17 (m, 2H, CH-Ar), 7.31 – 7.45 (m, 3H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 27.6 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 33.2 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 61.7 ( $\text{CH}_3\text{CO}$ ), 127.8 (CH-Ar), 128.5 (CH-Ar), 129.6 (CH-Ar), 135.9 (C=CH), 140.0 (C=CH), 145.1 (C-Ar), 198.8 (C=O). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 208$ .



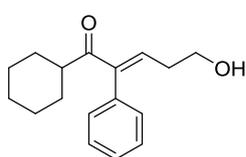
**Figure S18:** Synthesis of (*E*)-1-cyclohexyl-5-hydroxy-2-phenylpent-2-en-1-one (**4f**)



**(*E*)-5-((*tert*-butyldimethylsilyloxy)-1-cyclohexyl-2-phenylpent-**

**2-en-1-one:** The reaction was run according to GP6A starting from (*Z*)-5-((*tert*-butyldimethylsilyloxy)-1-cyclohexyl-2-iodopent-2-en-1-one (569 mg, 1.3 mmol). The reaction was complete after 1

h. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 20:1) to give the title compound in 69% (330 mg) as a colourless oil.  $R_f$  = 0.6 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2930, 2856, 1673, 1253, 1098, 836.  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.03 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.16 – 1.25 (m, 3H,  $\text{CH}_2\text{-Cy}$ ), 1.32 – 1.44 (m, 2H,  $\text{CH}_2\text{-Cy}$ ), 1.59 – 1.69 (m, 1H,  $\text{CH}_2\text{-Cy}$ ), 1.69 – 1.83 (m, 4H,  $\text{CH}_2\text{-Cy}$ ), 2.30 (dt,  $^3J_{\text{HH}}$  = 7.4, 6.3 Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 2.84 (tt,  $^3J_{\text{HH}}$  = 11.6, 3.2 Hz, 1H,  $\text{CH-Cy}$ ), 3.68 (t,  $^3J_{\text{HH}}$  = 6.3 Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.84 (t,  $^3J_{\text{HH}}$  = 7.4 Hz, 1H, C=CH), 7.08 – 7.19 (m, 2H,  $\text{CH-Ar}$ ), 7.27 – 7.41 (m, 3H,  $\text{CH-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -5.22 ( $(\text{CH}_3)_2\text{Si}$ ), 18.5 ( $(\text{CH}_3)_3\text{CSi}$ ), 25.9 ( $\text{CH}_2\text{-Cy}$ ), 26.0 ( $\text{CH}_2\text{-Cy}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 29.4 ( $\text{CH}_2\text{-Cy}$ ), 33.3 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 45.9 ( $\text{CH-Cy}$ ), 62.1 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 127.5 ( $\text{CH-Ar}$ ), 128.3 ( $\text{CH-Ar}$ ), 129.7 ( $\text{CH-Ar}$ ), 136.3 ( $\text{C-Ar}$ ), 139.2 ( $\text{C=CH}$ ), 143.6 ( $\text{C=CH}$ ), 204.9 ( $\text{C=O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 373$ .

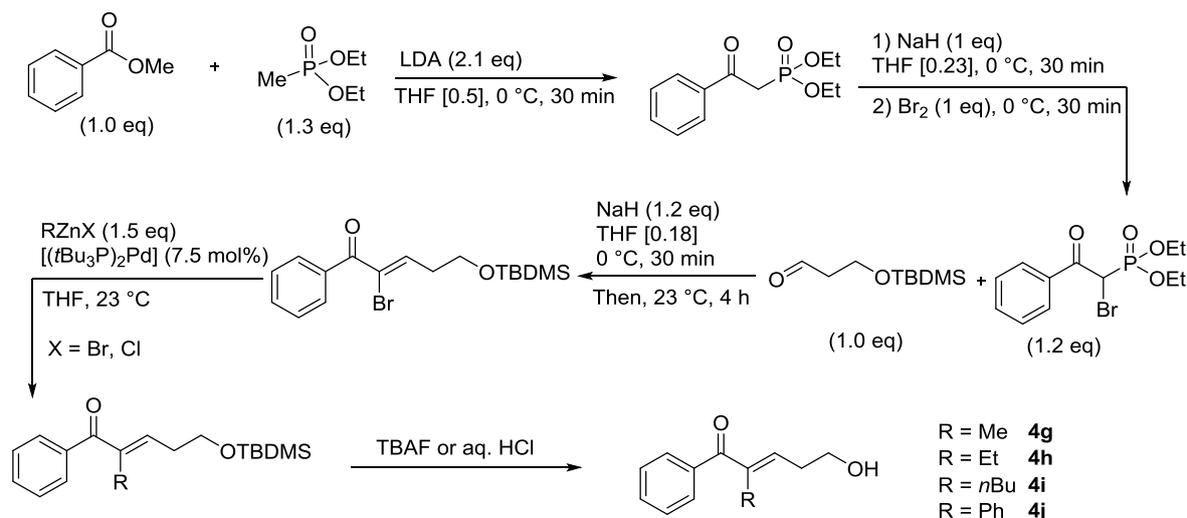


**(*E*)-1-cyclohexyl-5-hydroxy-2-phenylpent-2-en-1-one (**4f**):** (*E*)-5-

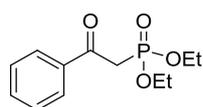
((*tert*-butyldimethylsilyloxy)-1-cyclohexyl-2-phenylpent-2-en-1-one (330 mg, 0.89 mmol) was dissolved in THF (8.9 mL) and TBAF (1.0 M in THF, 2.7 mmol, 2.7 mL) was added slowly at 0 °C. After stirring at

room temperature for 1 h, the mixture was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (5 mL), extracted with diethyl ether (3 x 20 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) afforded **4f** in 65% yield (150 mg) as a light yellow oil.  $R_f$  = 0.5 (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3428, 2929, 2855, 1668, 1448, 1052, 704.  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.10 – 1.25 (m, 3H,  $\text{CH}_2\text{-Cy}$ ), 1.30 – 1.44 (m, 3H,  $\text{CH}_2\text{-Cy}$ ; OH), 1.60 –

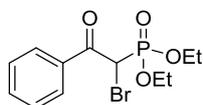
1.67 (m, 1H, CH<sub>2</sub>-Cy), 1.69 – 1.82 (m, 4H, CH<sub>2</sub>-Cy), 2.30 – 2.41 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 2.80 (tt, <sup>3</sup>J<sub>HH</sub> = 8.2, 4.0 Hz, 1H, CH-Cy), 3.72 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.81 (t, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, 1H, C=CH), 7.05 – 7.18 (m, 2H, CH-Ar), 7.31 – 7.45 (m, 3H, CH-Ar). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>) δ (ppm) 25.8 (CH<sub>2</sub>-Cy), 26.0 (CH<sub>2</sub>-Cy), 29.3 (CH<sub>2</sub>-Cy), 33.2 (CH<sub>2</sub>CH<sub>2</sub>OH), 46.1 (CH-Cy), 61.8 (CH<sub>2</sub>CH<sub>2</sub>OH), 127.6 (CH-Ar), 128.5 (CH-Ar), 129.6 (CH-Ar), 136.2 (C-Ar), 138.0 (C=CH), 144.4 (C=CH), 205.0 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 259; [M+NH<sub>4</sub>]<sup>+</sup> = 276.



**Figure S19:** Synthesis of  $\alpha,\beta$ -unsaturated ketones **4g-j**

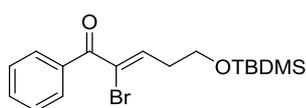


**Diethyl (2-oxo-2-phenylethyl)phosphonate:** In a 2-neck round bottomed flask, lithium diisopropylamide (LDA) was prepared by dropwise addition of *n*BuLi (52.22 mmol, 32.6 mL from a 1.6 M sol. in hexane) to a solution of diisopropylamine (52.22 mmol, 5.28 g) in THF (16 mL) at  $-78$  °C. In a separate 3-neck flask, methyl benzoate (23.68 mmol, 3.22 g) and methyl diethylphosphonate (30.79 mmol, 4.68 g) were dissolved in THF (37.5 mL) and cooled to 0 °C. After 30 minutes, LDA (49.73 mmol) was added dropwise to the latter solution and stirred for 30 minutes at 0 °C. The reaction was quenched with saturated aqueous NH<sub>4</sub>Cl solution (40 mL), extracted with diethyl ether (3 × 75 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Flash chromatography on silica gel (Diethyl ether) afforded the  $\beta$ -ketophosphonate in 96% yield (5.93 g) as a pale yellow oil. All spectroscopic analyses were in agreement with those reported in the literature.<sup>20</sup>



**Diethyl (1-bromo-2-oxo-2-phenylethyl)phosphonate:** To a solution of the  $\beta$ -ketophosphonate (19 mmol, 4.87 g) in THF (83 mL) at 0 °C, NaH (19

mmol, 456 mg) was added in three portions and stirred for 30 minutes. Next, Br<sub>2</sub> (19 mmol, 3.04 g) was carefully added at 0 °C and stirred at the same temperature for 30 minutes. The reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 × 100 mL), washed with a saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The product was purified by recrystallization in diethyl ether, affording the brominated product in 60% yield (3.85 g) as a white solid. **MP**: 33–35°C. **R<sub>f</sub>** = 0.5 (Diethyl ether). **IR (neat)**:  $\nu(\text{cm}^{-1})$  = 2996, 2937, 1689, 1594, 1579, 1475, 1447, 1392, 1369, 1328, 1269, 1247, 1200, 1147, 1105, 1017, 981, 961, 846, 818, 802, 759, 740, 715, 691, 652, 623. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 1.32 (dt, <sup>3</sup>J<sub>HH</sub> = 6.9 Hz, <sup>4</sup>J<sub>PH</sub> = 22.5 Hz, 6H, CH<sub>3</sub>CH<sub>2</sub>O), 4.20–4.33 (m, 4H, CH<sub>3</sub>CH<sub>2</sub>O), 5.34 (d, <sup>2</sup>J<sub>PH</sub> = 13.9 Hz, 1H, CHP), 7.47 – 7.51 (m, 2H, CH<sub>m</sub>-Ar), 7.60 – 7.63 (m, 1H, CH<sub>p</sub>-Ar), 8.00 – 8.02 (m, 2H, CH<sub>o</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) 16.4 (m, OCH<sub>2</sub>CH<sub>3</sub>), 38.6 (d, <sup>1</sup>J<sub>PC</sub> = 146.1 Hz, CHP), 64.7 (t, <sup>2</sup>J<sub>PC</sub> = 7.6 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 128.9 (CH<sub>m</sub>-Ar), 129.5 (CH<sub>o</sub>-Ar), 134.3 (CH<sub>p</sub>-Ar), 134.7 (C-Ar), 189.8 (C=O). **<sup>31</sup>P{<sup>1</sup>H, <sup>13</sup>C}-NMR** (CDCl<sub>3</sub>, 162 MHz):  $\delta$  (ppm) 13.4. **LRMS (IC)** found [M+H]<sup>+</sup> = 336, [M] = 335.

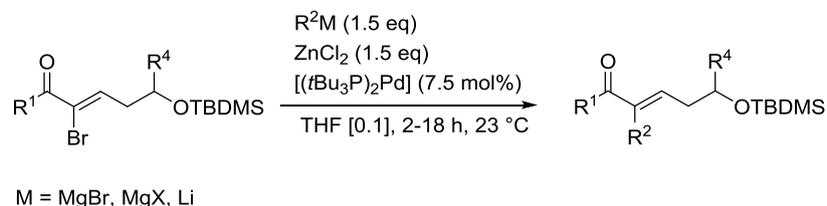


**(Z)-2-bromo-5-((tert-butylidimethylsilyloxy)-1-phenylpent-2-en-**

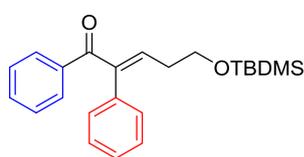
**1-one**: In a 3-neck-round-bottom flask equipped with a dropping funnel, the diethyl (1-bromo-2-oxo-2-phenylethyl)phosphonate (6.0 mmol, 2.01 g) was dissolved in THF (24 mL) and cooled to 0 °C. NaH (6.0 mmol, 144 mg) was added in two portions and stirred for 30 minutes at the same temperature. 3-((tert-butylidimethylsilyloxy)propanal (5.0 mmol, 0.94 g) in THF (10 mL) was added dropwise and stirred for 4 h at room temperature. The reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 × 40 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Column chromatography on silica gel (from Pentane to Pentane/Diethyl ether = 99:1) afforded the (Z)-isomer of the product in 28% yield (514 mg) as a pale yellow oil, the (E)-isomer in 13% yield (243 mg) and a mixture of the two isomers in 8% yield (136 mg, *E/Z* 1:3.8). (Z)-isomer: **R<sub>f</sub>** = 0.6 (Pentane/Diethyl ether = 9:1). **IR (neat)**:  $\nu(\text{cm}^{-1})$  = 2954, 2928, 2857, 1668, 1617, 1599, 1580, 1469, 1447, 1385, 1361, 1254, 1212, 1179, 1094, 1025, 1006, 938, 834, 775, 704, 649, 570. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 0.02 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.87 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 2.25 (dt, <sup>3</sup>J<sub>HH</sub> = 7.9, 6.3 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.64 (t, <sup>3</sup>J<sub>HH</sub> = 6.3 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.50 (t, <sup>3</sup>J<sub>HH</sub> = 7.9 Hz, 1H, C=CH), 7.59 – 7.62 (m, 1H, CH<sub>p</sub>-Ar), 7.47 – 7.50 (m, 2H, CH<sub>m</sub>-Ar), 7.97 – 7.98 (m, 2H, CH<sub>o</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.5 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 34.6 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 61.8 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 116.4 (C=CH), 128.9 (CH<sub>m</sub>-Ar), 130.1 (CH<sub>o</sub>-

Ar), 134.2 (CH<sub>p</sub>-Ar), 134.6 (C-Ar), 135.9 (C=CH), 191.2 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 370, [M] = 369.

### Procedure for Negishi cross-coupling (GP6B)



In a Young valve Schlenk, the electrophilic alkylzinc reagent was prepared by mixing the appropriate Grignard or alkyllithium reagent (1.5 eq) and ZnCl<sub>2</sub> (1.5 eq, 1.0 M in THF). A white precipitate formed rapidly. In separate Schlenk, [(tBu<sub>3</sub>P)<sub>2</sub>Pd] (7.55 mol%) was dissolved in THF (0.1 M) and the appropriate bromo-derivative (1 eq) was added. The latter solution was transferred by cannula to the suspension of the alkylzinc reagent and stirred at room temperature. After 2-18 h, the mixture was quenched with saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 times), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*.

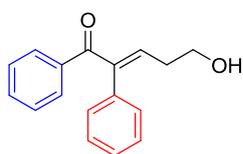


### **(E)-5-((tert-butyldimethylsilyloxy)-1,2-diphenylpent-2-en-1-**

**one:** The reaction was run according to GP6B starting from (*Z*)-2-bromo-5-((tert-butyldimethylsilyloxy)-1-phenylpent-2-en-1-one (2.0 g, 5.44 mmol, *E/Z* 1:2.7). The reaction was complete after 4 h.

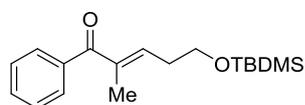
Purification by column chromatography on silica gel (from Pentane to Pentane/Diethyl ether = 98:2) afforded the (*E*)-isomer of the product in 19% yield (381 mg) as a pale green oil and a mixture of isomers in 29% yield (578 mg, *E/Z* 2.6:1) as a pale yellow oil. (*E*)-isomer: **R<sub>f</sub>** = 0.5 (Pentane/Diethyl ether = 9:1). **IR (neat):** ν(cm<sup>-1</sup>) = 3060, 2954, 2928, 2856, 1657, 1598, 1579, 1495, 1468, 1446, 1386, 1361, 1315, 1252, 1218, 1176, 1093, 1026, 1007, 944, 834, 810, 775, 761, 722, 697, 660, 626, 610. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 0.02 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.87 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 2.48 (q, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.72 (t, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.52 (t, <sup>3</sup>J<sub>HH</sub> = 7.4 Hz, 1H, C=CH), 7.30 – 7.32 (m, 2H, CH<sub>m</sub>-Ar), 7.30 – 7.33 (m, 1H, CH<sub>p</sub>-Ar), 7.36 – 7.39 (m, 2H, CH<sub>m</sub>-Ar), 7.40 – 7.43 (m, 2H, CH<sub>o</sub>-Ar), 7.49 – 7.53 (m, 1H, CH<sub>p</sub>-Ar), 7.80 – 7.82 (m, 2H, CH<sub>o</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz): δ (ppm) -5.3 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 33.2 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 62.1 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 127.7 (CH<sub>m</sub>-Ar), 128.2 (CH<sub>o</sub>-Ar), 128.3 (CH<sub>m</sub>-Ar), 129.7 (CH<sub>p</sub>-Ar),

129.9 (CH<sub>o</sub>-Ar), 132.1 (CH<sub>p</sub>-Ar), 136.0 (C-Ar), 138.4 (C=CH), 141.8 (C=CH), 143.0 (C-Ar), 197.4 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 368.



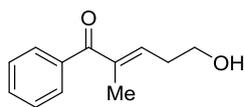
**(E)-5-hydroxy-1,2-diphenylpent-2-en-1-one (4j):** The reaction was run according to GP3 starting from (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-1,2-diphenylpent-2-en-1-one (0.56 mmol, 206 mg). Purification by column chromatography on silica gel (Pentane/Diethyl ether from 7:3 to 65:35)

afforded **4j** in 38% yield (53 mg) as yellow oil. (*E*)-isomer: **R<sub>f</sub>** = 0.3 (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3432, 3058, 2922, 2854, 1648, 1596, 1578, 1494, 1446, 1377, 1315, 1267, 1217, 1176, 1045, 1023, 920, 799, 724, 698. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 1.61 (OH), 2.44 (q, 2H, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, CH<sub>2</sub>CH<sub>2</sub>OH), 3.74 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 6.49 (t, <sup>3</sup>J<sub>HH</sub> = 7.4 Hz, 1H, C=CH), 7.28 – 7.30 (m, 2H, CH<sub>o</sub>-Ar), 7.30 – 7.33 (m, 1H, CH<sub>p</sub>-Ar), 7.36 – 7.39 (m, 2H, CH<sub>m</sub>-Ar), 7.40 – 7.43 (m, 2H, CH<sub>m</sub>-Ar), 7.49 – 7.53 (m, 1H, CH<sub>p</sub>-Ar), 7.79 – 7.81 (m, 2H, CH<sub>o</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) 33.1 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.9 (CH<sub>2</sub>CH<sub>2</sub>OH), 127.8 (CH<sub>p</sub>-Ar), 128.4 (CH<sub>m</sub>-Ar), 128.5 (CH<sub>m</sub>-Ar), 129.6 (CH<sub>o</sub>-Ar), 129.9 (CH<sub>o</sub>-Ar), 132.3 (CH<sub>p</sub>-Ar), 135.9 (C-Ar), 138.2 (C=CH), 140.1 (C=CH), 143.8 (C-Ar), 197.2 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 253.

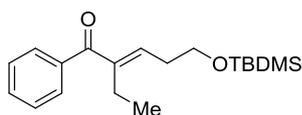


**(E)-5-((*tert*-butyldimethylsilyl)oxy)-2-methyl-1-phenylpent-2-en-1-one:** The reaction was run according to GP6B starting from (*Z*)-2-bromo-5-((*tert*-butyldimethylsilyl)oxy)-1-phenylpent-2-en-1-one (1.4

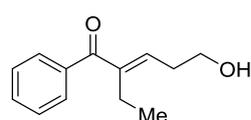
mmol). After purification by flash chromatography on silica gel (Pentane/Diethyl ether = 95:5) the product was obtained in 80% yield (342 mg) as a yellow oil. (*E*)-isomer: **R<sub>f</sub>** = 0.5 (Pentane/Diethyl ether = 9:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2954, 2930, 2891, 2858, 1647, 1598, 1577, 1469, 1446, 1384, 1360, 1321, 1283, 1252, 1217, 1162, 1096, 1048, 1006, 939, 834, 810, 775, 701, 662, 637. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 0.01 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.85 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.98 (s, 3H, CH<sub>3</sub>C=CH), 2.50 (q, <sup>3</sup>J<sub>HH</sub> = 7.2 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.70 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.33-6.36 (m, 1H, C=CH), 7.38 – 7.41 (m, 2H, CH<sub>m</sub>-Ar), 7.47 – 7.51 (m, 1H, CH<sub>p</sub>-Ar), 7.62 – 7.64 (m, 2H, CH<sub>o</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) -5.3 ((CH<sub>3</sub>)<sub>2</sub>Si), 12.8 (CH<sub>3</sub>C=CH), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 32.8 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 61.7 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 128.2 (CH<sub>m</sub>-Ar), 129.4 (CH<sub>o</sub>-Ar), 131.5 (CH<sub>p</sub>-Ar), 137.8 (C=CH), 138.8 (C-Ar), 143.6 (C=CH), 199.1 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 306.



**(E)-5-hydroxy-2-methyl-1-phenylpent-2-en-1-one (4g):** The product was synthesized according to GP3 starting from (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-2-methyl-1-phenylpent-2-en-1-one (1.12 mmol, 340 mg). Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) afforded **4g** in 71% yield (152 mg) as a yellow oil. (*E*)-isomer:  $R_f = 0.4$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3409, 3059, 2926, 2880, 1633, 1597, 1576, 1446, 1385, 1359, 1320, 1281, 1200, 1179, 1158, 1041, 940, 901, 785, 703, 637$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 1.54 (bs, *OH*), 2.00 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.57 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.75 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 6.31 (m, 1H,  $\text{C}=\text{CH}$ ), 7.40 – 7.43 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.63 – 7.65 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 7.49 – 7.52 (m, 1H,  $\text{CH}_p\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) 13.0 ( $\text{CH}_3\text{C}=\text{CH}$ ), 32.6 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 61.5 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 141.9 ( $\text{C}=\text{CH}$ ), 128.2 ( $\text{CH}_m\text{-Ar}$ ), 129.5 ( $\text{CH}_o\text{-Ar}$ ), 131.7 ( $\text{CH}_p\text{-Ar}$ ), 138.5 ( $\text{C-Ar}$  or  $\text{C}=\text{CH}$ ), 138.6 ( $\text{C-Ar}$  or  $\text{C}=\text{CH}$ ), 198.9 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 191$ .

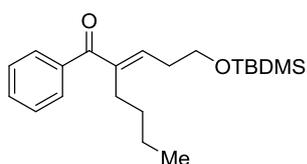


**(E)-5-((*tert*-butyldimethylsilyl)oxy)-2-ethyl-1-phenylpent-2-en-1-one:** The reaction was run according to GP6B starting from (*Z*)-2-bromo-5-((*tert*-butyldimethylsilyl)oxy)-1-phenylpent-2-en-1-one (1.95 mmol). After purification by flash chromatography on silica gel (Pentane/Diethyl ether = 9:1) the product was obtained in 80% yield (472 mg) as colourless oil. (*E*)-isomer:  $R_f = 0.1$  ( $\text{CH}_2\text{Cl}_2/\text{Acetone} = 1:1$ ). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2956, 2930, 2858, 1649, 1598, 1578, 1463, 1447, 1385, 1362, 1289, 1251, 1217, 1162, 1094, 1053, 1025, 1006, 988, 942, 832, 775, 724, 701, 662$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.02 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.86 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.06 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 3H,  $\text{CH}_2\text{CH}_3$ ), 2.48-2.53 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ; 2H,  $\text{CH}_2\text{CH}_3$ ), 3.70 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 6.22 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 1H,  $\text{C}=\text{CH}$ ), 7.39 – 7.42 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.48 – 7.51 (m, 1H,  $\text{CH}_p\text{-Ar}$ ), 7.64 – 7.66 (m, 2H,  $\text{CH}_o\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) -5.3 ( $(\text{CH}_3)_2\text{Si}$ ), 13.7 ( $\text{CH}_2\text{CH}_3$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 20.4 ( $\text{CH}_2\text{CH}_3$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 32.4 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 62.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 128.2 ( $\text{CH}_m\text{-Ar}$ ), 129.5 ( $\text{CH}_o\text{-Ar}$ ), 131.6 ( $\text{CH}_p\text{-Ar}$ ), 139.1 ( $\text{C-Ar}$ ), 142.1 ( $\text{C}=\text{CH}$ ), 143.9 ( $\text{C}=\text{CH}$ ), 199.0 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 320$ .



**(E)-2-ethyl-5-hydroxy-1-phenylpent-2-en-1-one (4h):** The reaction was run according to GP4 starting from (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-2-ethyl-1-phenylpent-2-en-1-one (1.39 mmol). The reaction was complete after 1.5 h. The crude mixture was purified on a small pad of silica gel (Pentane/Diethyl ether = 6:4) to afford **4h** in 52% yield (158 mg) as pale yellow oil. (*E*)-isomer:  $R_f = 0.2$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3420, 2966, 2870$ ,

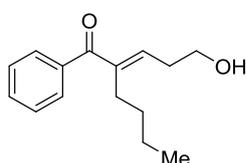
1635, 1596, 1577, 1446, 1380, 1313, 1288, 1253, 1046, 906, 860, 703. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 1.06 (td, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, <sup>5</sup>J<sub>HH</sub> = 0.9 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>), 1.58 (bs, OH). 2.52 (q, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>), 2.57 (q, <sup>3</sup>J<sub>HH</sub> = 7.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.74 (td, <sup>3</sup>J<sub>HH</sub> = 6.5 Hz, <sup>3</sup>J<sub>HH</sub> = 1.7 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 6.18 (t, <sup>3</sup>J<sub>HH</sub> = 7.3 Hz, 1H, C=CH), 7.40 – 7.43 (m, 2H, CH<sub>m</sub>-Ar), 7.65 – 7.67 (m, 2H, CH<sub>o</sub>-Ar), 7.49 – 7.52 (m, 1H, CH<sub>p</sub>-Ar). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) 13.7 (CH<sub>3</sub>CH<sub>2</sub>), 20.5 (CH<sub>3</sub>CH<sub>2</sub>), 32.2 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.8 (CH<sub>2</sub>CH<sub>2</sub>OH), 128.2 (CH<sub>m</sub>-Ar), 129.5 (CH<sub>o</sub>-Ar), 131.8 (CH<sub>p</sub>-Ar), 138.9 (C-Ar), 140.3 (C=CH), 144.7 (C=CH), 198.9 (C=O). LRMS (IC) found [M+H]<sup>+</sup> = 205.



**(E)-2-(3-((tert-butyldimethylsilyloxy)propylidene)-1-**

**phenylhexan-1-one:** The reaction was run according to GP6B starting from (Z)-2-bromo-5-((tert-butyldimethylsilyloxy)-1-phenylpent-2-en-1-one (2.08 mmol). After purification by flash chromatography on silica gel (Pentane/Diethyl ether 98:2) the product was obtained in 50%

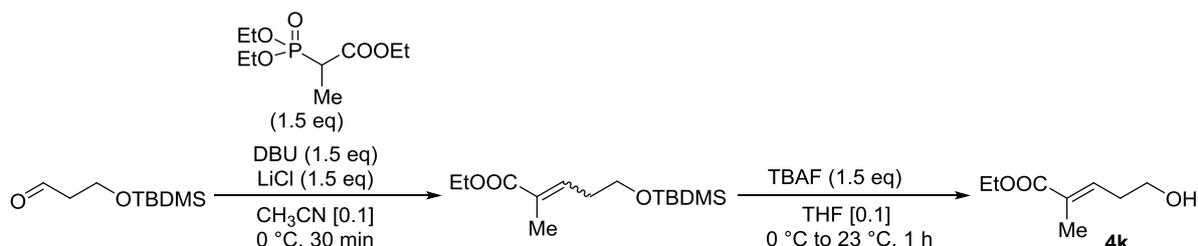
yield (360 mg) as colourless oil. (E)-isomer: R<sub>f</sub> = 0.5 (Pentane/Diethyl ether = 9:1). IR (neat): ν(cm<sup>-1</sup>) = 2993, 2929, 2854, 1650, 1597, 1578, 1463, 1446, 1387, 1275, 1253, 1094, 941, 834, 775, 701. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 0.02 (s, 9H(CH<sub>3</sub>)<sub>3</sub>CSi), 0.86 (s, 6H(CH<sub>3</sub>)<sub>2</sub>Si), 0.92 (t, 3H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.35-1.45 (m, 4H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.47-2.53 (m, 4H CH<sub>2</sub>CH<sub>2</sub>OTBDMS, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 3.69 (t, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 6.22 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 1H, C=CH), 7.38 – 7.42 (m, 2H, CH<sub>m</sub>-Ar), 7.48 – 7.51 (m, 1H, CH<sub>p</sub>-Ar), 7.65 – 7.67 (m, 2H, CH<sub>o</sub>-Ar). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) -5.3 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.1 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 23.0 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.8 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 31.3 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 32.6 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 62.0 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 128.2 (CH<sub>m</sub>-Ar), 129.6 (CH<sub>o</sub>-Ar), 131.6 (CH<sub>p</sub>-Ar), 139.1 (C-Ar), 142.2 (C=CH), 142.7 (C=CH), 199.0 (C=O). LRMS (IC) found [M+H]<sup>+</sup> = 348.



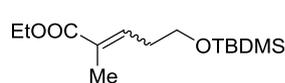
**(E)-2-(3-hydroxypropylidene)-1-phenylhexan-1-one:** The reaction was run according to GP4 starting from (E)-2-(3-((tert-butyldimethylsilyloxy)propylidene)-1-phenylhexan-1-one (0.72 mmol).

The reaction was complete after 1.5 h. Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 6:4) afforded **4i** in 73% yield (133 mg) as a pale yellow oil. (E)-isomer: R<sub>f</sub> = 0.2 (Pentane/Diethyl ether = 1:1). IR (neat): ν(cm<sup>-1</sup>) = 3420, 2968, 2867, 1636, 1596, 1580, 1444, 1387, 1311, 1285, 1250, 1038, 905, 869, 701. <sup>1</sup>H-NMR (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 0.92 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.35 – 1.39 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.41 – 1.46 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.57 (bs, OH), 2.50 – 2.53 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.58 (q, <sup>3</sup>J<sub>HH</sub> = 6.7 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.74 (t, <sup>3</sup>J<sub>HH</sub> = 7.3 Hz, 2H,

CH<sub>2</sub>CH<sub>2</sub>OH), 6.19 (t, <sup>3</sup>J<sub>HH</sub> = 7.3 Hz, 1H, C=CH), 7.40 – 7.43 (m, 2H, CH<sub>m</sub>-Ar), 7.50 – 7.53 (m, 1H, CH<sub>p</sub>-Ar), 7.66 – 7.68 (m, 2H, CH<sub>o</sub>-Ar). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) 14.1 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 23.0 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 27.0 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 31.3 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 32.3 (CH<sub>2</sub>CH<sub>2</sub>O), 61.8 (CH<sub>2</sub>CH<sub>2</sub>OH), 128.3 (CH<sub>m</sub>-Ar), 129.6 (CH<sub>o</sub>-Ar), 131.8 (CH<sub>p</sub>-Ar), 138.8 (C-Ar), 140.3 (C=CH), 143.6 (C=CH), 198.9 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 233.

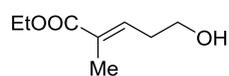


**Figure S20:** Synthesis of Ethyl (*E*)-5-hydroxy-2-methylpent-2-enoate (**4k**)



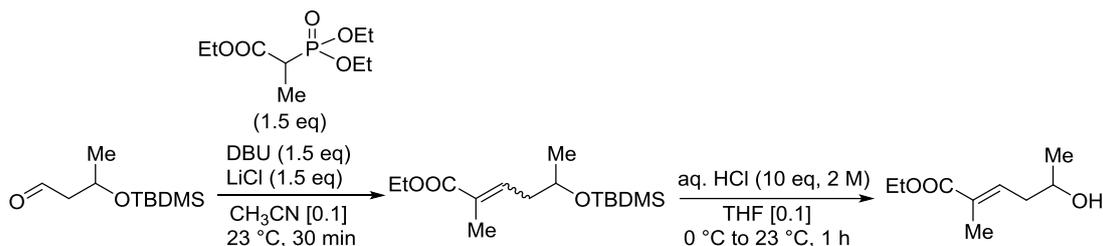
**Ethyl (*E*)-5-((*tert*-butyldimethylsilyloxy)-2-methylpent-2-enoate:**

The reaction was run according to GP2 starting from 3-((*tert*-butyldimethylsilyloxy)propanal (865 mg, 4.6 mmol). Purification by flash chromatography on silica gel (Pentane/EtOAc = 9:1) afforded the product in 84% yield (1g, *E/Z* = 11:1) as a colorless oil, which was used for the next step without further purification.

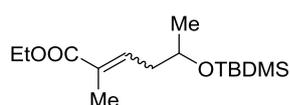


**Ethyl (*E*)-5-hydroxy-2-methylpent-2-enoate (**4k**):**

The product was synthesized according to GP3 starting from 5-((*tert*-butyldimethylsilyloxy)-2-methylpent-2-enoate (1.0 g, *E/Z* = 11:1, 3.8 mmol). Purification by column chromatography on silica gel (Pentane/Diethyl ether from 4:1 to 2:1) afforded **4k** in 73% yield (440 mg) as a colorless oil. All spectroscopic analyses were in agreement with those reported in the literature.<sup>21</sup>

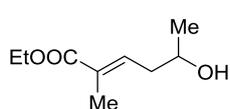


**Figure S21:** Synthesis of Ethyl (*E*)-5-hydroxy-2-methylhex-2-enoate (**4i**)



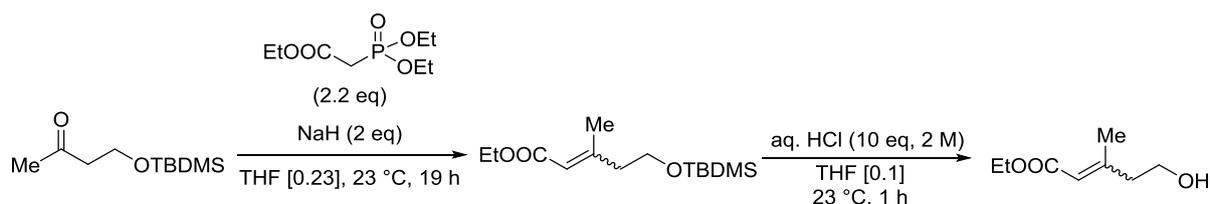
**Ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-2-methylhex-2-enoate:**

The reaction was run according to GP2 starting from 3-((*tert*-butyldimethylsilyl)oxy)butanal (500 mg, 2.5 mmol). Purification by flash chromatography (Pentane/Diethyl ether = 20:1) afforded the desired product in 89% yield (600 mg, *E/Z* = 8:1) as a colourless oil. (*E*)-isomer:  $R_f$  = 0.2 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3675, 2977, 2903, 1397, 1251, 1229, 1062, 894.  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.05 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.17 (d,  $^3J_{\text{HH}}$  = 6.1 Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.29 (t,  $^3J_{\text{HH}}$  = 7.1 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.83 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.23 – 2.41 (m, 2H,  $\text{CH}_2\text{CHOTBDMS}$ ), 3.85 – 3.99 (m, 1H,  $\text{CH}_2\text{CHOTBDMS}$ ), 4.18 (q,  $^3J_{\text{HH}}$  = 7.1 Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.80 (tq,  $^3J_{\text{HH}}$  = 7.5,  $^4J_{\text{HH}}$  = 1.4 Hz, 1H,  $\text{C}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -4.7 ( $(\text{CH}_3)_2\text{Si}$ ), -4.4 ( $(\text{CH}_3)_2\text{Si}$ ), 12.7 ( $\text{CH}_3\text{C}=\text{CH}$ ), 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.2 ( $\text{C}=\text{CH}$ ), 24.1 ( $\text{CH}_3\text{CH}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 39.1 ( $\text{CH}_2\text{CHOTBDMS}$ ), 60.5 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 68.0 ( $\text{CH}_2\text{CHOTBDMS}$ ), 129.0 ( $\text{C}=\text{CH}$ ), 139.1 ( $\text{C}=\text{CH}$ ), 168.3 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 287$ .



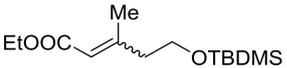
**Ethyl (*E*)-5-hydroxy-2-methylhex-2-enoate (**4i**):** The product was synthesized according to GP3 starting from ethyl (*E*)-5-((*tert*-butyldimethylsilyl)oxy)-2-methylhex-2-enoate (600 mg, 2.2 mmol). The

crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 1:1) to give **4i** in 74% yield (280 mg) as a colorless oil.  $R_f$  = 0.4 (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3424, 2973, 1702, 1368, 1282, 1252, 1085.  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.25 (d,  $^3J_{\text{HH}}$  = 6.2 Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.29 (t,  $^3J_{\text{HH}}$  = 7.1 Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.86 (s, 3H,  $\text{CH}_3\text{C}=\text{CH}$ ), 2.28 – 2.47 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.85 – 4.06 (m, 1H,  $\text{CH}_2\text{CHOH}$ ), 4.19 (q,  $^3J_{\text{HH}}$  = 7.1 Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.80 (tq,  $^3J_{\text{HH}}$  = 7.6,  $^4J_{\text{HH}}$  = 1.5 Hz, 1H,  $\text{C}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 12.81 ( $\text{CH}_3\text{C}=\text{CH}$ ), 14.42 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.43 ( $\text{CH}_3\text{CHOH}$ ), 38.54 ( $\text{CH}_2\text{CHOH}$ ), 60.71 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.43 ( $\text{CH}_2\text{CHOH}$ ), 130.27 ( $\text{C}=\text{CH}$ ), 137.75 ( $\text{C}=\text{CH}$ ), 168.12 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 190$ .



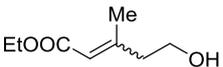
**Figure S22:** Synthesis of Ethyl (*E*)-5-hydroxyhex-2-enoate (**4m**)

**Ethyl (*E*)-5-((*tert*-butyldimethylsilyloxy)-3-methylhex-2-enoate:**

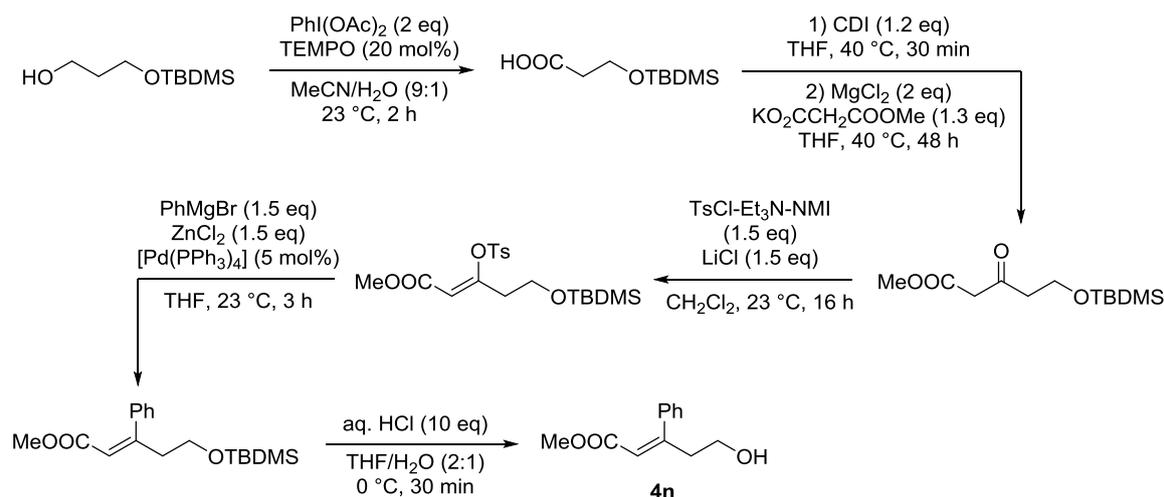


NaH (226 mg, 9.44 mmol) was dissolved in 15 mL of THF and triethyl phosphonacetate (2.0 mL, 10.4 mmol) was added dropwise at 0 °C. After 30 minutes, 4-((*tert*-butyldimethylsilyloxy)butan-2-one (0.95 g, 4.72 mmol) in THF (5 mL) was added at 0 °C and next stirred at room temperature. After 19 h, the reaction was quenched with water (80 mL), extracted with EtOAc (3 × 15 mL), washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. Purification by flash chromatography on silica gel (Pentane/Diethyl ether = 20:1) afforded the product in 30% yield (370 mg, *E/Z* = 3:1) as a colourless oil. (*E*)-isomer: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.27 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 2.18 (d, <sup>3</sup>J<sub>HH</sub> = 1.3 Hz, 3H, CH<sub>3</sub>C=CH), 2.34 (td, <sup>3</sup>J<sub>HH</sub> = 6.7, 1.1 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.74 (t, <sup>3</sup>J<sub>HH</sub> = 6.7 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 4.15 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.68 (q, <sup>3</sup>J<sub>HH</sub> = 1.3 Hz, 1H, CH=C). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>22</sup>

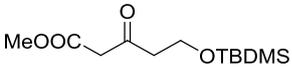
**Ethyl (*E*)-5-hydroxyhex-2-enoate (**4m**):**



To a solution of ethyl (*E*)-5-((*tert*-butyldimethylsilyloxy)hex-2-enoate (370 mg, 1.45 mmol) in THF (15 mL), aqueous HCl (2 M, 7.3 mL) was added at 0 °C and the mixture was stirred at room temperature for 1 h. The reaction was quenched with water (10 mL), extracted with EtOAc (3 × 30 mL) and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 1:2) to give **4m** in 83% yield (190 mg, *E/Z* = 10:1) as a colourless oil. (*E*)-isomer: *R*<sub>f</sub> = 0.2 (Pentane/Diethyl ether = 1:2). IR (neat): ν(cm<sup>-1</sup>) = 3404, 2981, 1706, 1646, 1220, 1144, 1038. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 1.30 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>OH), 2.22 (d, <sup>3</sup>J<sub>HH</sub> = 1.3 Hz, 3H, CH<sub>3</sub>C=CH), 2.43 (td, <sup>3</sup>J<sub>HH</sub> = 6.4, 1.1 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OH), 3.82 (t, <sup>3</sup>J<sub>HH</sub> = 6.3 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>OH), 4.18 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.76 (q, <sup>3</sup>J<sub>HH</sub> = 1.3 Hz, 1H, CH=C). <sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>) δ (ppm) 14.3 (CH<sub>3</sub>CH<sub>2</sub>O), 18.7 (CH<sub>3</sub>C=CH), 43.7 (CH<sub>2</sub>CH<sub>2</sub>OH), 59.7 (CH<sub>2</sub>CH<sub>2</sub>OH), 60.2 (CH<sub>3</sub>CH<sub>2</sub>O), 117.8 (CH=C), 155.8 (C=O), 166.4 (CH=C). LRMS (IC) found [M+Na]<sup>+</sup> = 171.

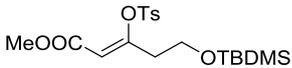


**Figure S23:** Synthesis of (*Z*)-4-hydroxy-2-phenylbut-1-en-1-yl acetate (**4n**)


**4-((tert-butyldimethylsilyl)oxy)-2-oxobutyl acetate**

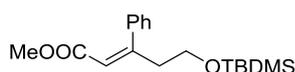
**3-((tert-butyldimethylsilyl)oxy)propanoic acid**

3-((tert-butyldimethylsilyl)oxy)propanoic acid was prepared using a known protocol reported in the literature.<sup>23</sup> In a Schlenk tube, MgCl<sub>2</sub> (15.76 mmol, 1.5 g) and potassium monomethyl malonate (20.49 mmol, 3.2 g) were suspended in THF (23 mL) and heated at 65 °C for 3 h. After the above reaction had proceeded for 2 h, in a second Schlenk, 3-((tert-butyldimethylsilyl)oxy)propanoic acid (3.2 g, 15.76 mmol) was dissolved in THF (16 mL) and carbonyldiimidazole (CDI) (3.07 g, 18.91 mmol) was added in five portions. The reaction was stirred at room temperature until CO<sub>2</sub> releasing ceased (ca. 30 minutes). This homogeneous solution was heated at 40 °C for additional 30 minutes. The magnesium malonate suspension was cooled to 30 °C and the other solution was added dropwise by a syringe. A white precipitate formed rapidly during this addition so vigorous stirring was necessary to avoid clamping. The resulting suspension was stirred at 40 °C for 48 h then cooled to 0 °C and quenched with a saturated aqueous NH<sub>4</sub>Cl solution (15 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic phases were sequentially washed with water (100 mL), a saturated aqueous NaHCO<sub>3</sub> solution (100 mL), brine (100 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*.<sup>24</sup> The product was used in the next step without further purification.


**(Z)-4-((tert-butyldimethylsilyl)oxy)-2-(tosyloxy)but-1-en-1-yl acetate**

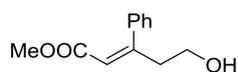
In a 2-neck-round-bottom flask, the crude β-ketoester (ca. 5 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (25 mL) and Et<sub>3</sub>N (7.5 mmol, 1 mL), NMI (7.5 mmol, 0.6 mL) and LiCl (7.5 mmol, 543 mg) were added sequentially. After 10 minutes at room temperature, TsCl (7.5 mmol, 1.43 g) was added at 0 °C. The reaction was stirred at room

temperature for 16 h and then quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL) and extracted with  $\text{Et}_2\text{O}$  (3 x 30 mL). The organic phases were combined, dried over  $\text{Na}_2\text{SO}_4$  and evaporated.<sup>25</sup> The resulting crude material was purified by flash chromatography on silica gel ( $\text{Et}_2\text{O}/\text{Acetone} = 10:1$ ) to afford the desired product as a pale yellow oil in 54% yield (1.12 g) over 3 steps.  $R_F = 0.4$  ( $\text{Et}_2\text{O}/\text{Acetone} = 10:1$ ).  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.01 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.85 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 2.45 (s, 3H,  $\text{CH}_3\text{Ar}$ ), 2.59 (t, 2H,  $^3J_{\text{HH}} = 6.4$  Hz,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.56 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.77 (t, 2H,  $^3J_{\text{HH}} = 6.1$  Hz,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 5.61 (m, 1H,  $\text{CH}=\text{C}$ ), 7.34 – 7.36 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.88 – 7.90 (m, 2H,  $\text{CH}_o\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) -5.4 ( $(\text{CH}_3)_2\text{Si}$ ), 18.3 ( $(\text{CH}_3)_3\text{CSi}$ ), 21.8 ( $\text{CH}_3\text{-Ar}$ ), 25.9 ( $(\text{CH}_3)_3\text{CSi}$ ), 38.8 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 51.5 ( $\text{CH}_3\text{O}$ ), 59.4 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 111.8 ( $\text{CH}=\text{C}$ ), 128.6 ( $\text{CH}_o\text{-Ar}$ ), 129.8 ( $\text{CH}_m\text{-Ar}$ ), 133.5 ( $\text{C}_{\text{ipso}}\text{-Ar}$ ), 145.5 ( $\text{C}_p\text{-Ar}$ ), 157.2 ( $\text{CH}=\text{C}$ ), 163.4 ( $\text{C}=\text{O}$ ). **LRMS (IC)** = found  $[\text{M}+\text{H}]^+ = 416$ . **IR (neat)**:  $\nu$  ( $\text{cm}^{-1}$ ) = 2952, 2930, 2858, 1733, 1673, 1598, 1461, 1435, 1377, 1317, 1289, 1255, 1218, 1171, 1132, 1091, 1063, 1017, 970, 928, 873, 834, 813, 775, 709, 687, 629, 590.



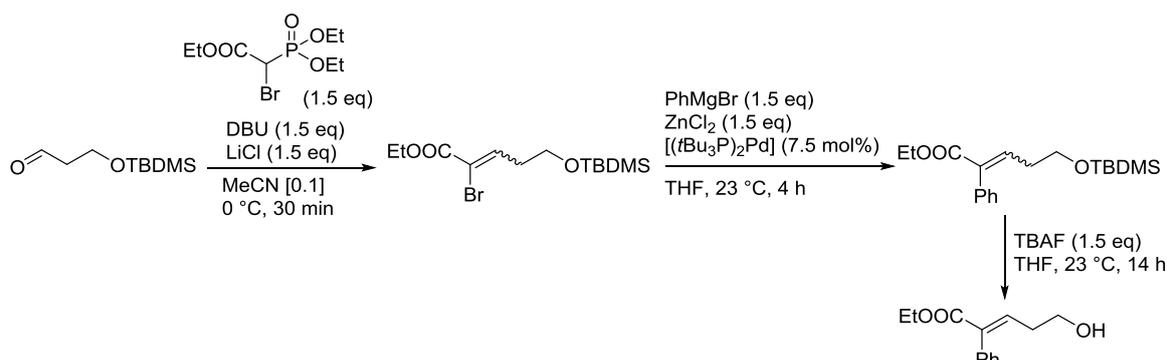
**(Z)-4-((tert-butyldimethylsilyloxy)-2-phenylbut-1-en-1-yl**

**acetate**: In a Schlenk, the electrophilic alkylzinc reagent was prepared in situ by diluting  $\text{PhMgBr}$  (3.6 mmol, 1.2 mL from a 3 M solution in  $\text{Et}_2\text{O}$ ) with THF (2.4 mL) and adding  $\text{ZnCl}_2$  (3.6 mL from a 1 M solution in THF) while stirring for 30 minutes. Inside the glovebox, a Young valve Schlenk was charged with  $[\text{Pd}(\text{PPh}_3)_4]$  (0.12 mmol, 139 mg). THF (17 mL) and (Z)-4-((tert-butyldimethylsilyloxy)-2-(tosyloxy)but-1-en-1-yl acetate (2.4 mmol, 995 mg) were added outside the glovebox. The latter solution was transferred by cannula to the alkylzinc suspension and stirred at room temperature for 3 h then quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution and extracted with  $\text{Et}_2\text{O}$  (3 x 20 mL). The organic phases were combined, dried over  $\text{Na}_2\text{SO}_4$  and evaporated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel ( $\text{Et}_2\text{O}/\text{Acetone} = 99:1$ ) to afford the desired product in 59% yield (433 mg) as a colourless oil.  $R_F = 0.4$  ( $\text{Et}_2\text{O}/\text{Acetone} = 95:5$ ).  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.00 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.87 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 2.65 (td, 2H,  $^3J_{\text{HH}} = 6.6$  Hz,  $^4J_{\text{HH}} = 1.1$  Hz,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.55 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.63 (t, 2H,  $^3J_{\text{HH}} = 6.6$  Hz,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 5.93 (m, 1H,  $\text{CH}=\text{C}$ ), 7.16 – 7.18 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 7.29 – 7.36 (m, 2H,  $\text{CH}_m\text{-Ar}$ ; 1H,  $\text{CH}_p\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) -5.3 ( $(\text{CH}_3)_2\text{Si}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 43.7 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 51.2 ( $\text{CH}_3\text{O}$ ), 60.7 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 118.5 ( $\text{CH}=\text{C}$ ), 127.3 ( $\text{CH}_o\text{-Ar}$ ), 127.9 ( $\text{CH}_p\text{-Ar}$ ), 128.0 ( $\text{CH}_m\text{-Ar}$ ), 139.7 ( $\text{C-Ar}$ ), 156.9 ( $\text{CH}=\text{C}$ ), 166.4 ( $\text{C}=\text{O}$ ). **LRMS (IC)** = found  $[\text{M}+\text{Na}]^+ = 344$ . **IR (neat)**:  $\nu$  ( $\text{cm}^{-1}$ ) = 2952, 2932, 2894, 1730, 1642, 1494, 1468, 1434, 1384, 1369, 1255, 1226, 1163, 1102, 1052, 1006, 932, 835, 775, 698, 665.



**(Z)-4-hydroxy-2-phenylbut-1-en-1-yl acetate (4n):** The product was synthesized according to GP4 starting from (Z)-4-((*tert*-butyldimethylsilyl)oxy)-2-phenylbut-1-en-1-yl acetate (1.25 mmol, 401

mg). The desired product was obtained in 69% yield (177 mg) as a pale yellow oil after flash chromatography on silica gel (Et<sub>2</sub>O/Acetone = 8:2).  $R_f = 0.2$  (Et<sub>2</sub>O/Acetone = 8:2). **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 1.34 (bt, 1H,  $^3J_{HH} = 5.5$  Hz, OH), 2.72 (td, 2H,  $^3J_{HH} = 6.3$  Hz,  $^4J_{HH} = 1.1$  Hz, CH<sub>2</sub>CH<sub>2</sub>OH), 3.55 (s, 3H, CH<sub>3</sub>O), 3.68 (q, 2H,  $^3J_{HH} = 6.1$  Hz, CH<sub>2</sub>CH<sub>2</sub>OH), 5.99 (bt, 1H,  $^4J_{HH} = 1.1$  Hz, CH=C), 7.18 – 7.20 (m, 2H, CH<sub>o</sub>-Ar), 7.31 – 7.39 (m, 2H, CH<sub>m</sub>-Ar; 1H, CH<sub>p</sub>-Ar). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) = 43.4 (CH<sub>2</sub>CH<sub>2</sub>OH), 51.3 (CH<sub>3</sub>O), 60.2 (CH<sub>2</sub>CH<sub>2</sub>OH), 119.0 (CH=C), 127.3 (CH<sub>o</sub>-Ar), 128.1 (CH<sub>p</sub>-Ar), 128.2 (CH<sub>m</sub>-Ar), 139.3 (C-Ar), 156.3 (CH=C), 166.1 (C=O). **LRMS (IC)** = found [M+NH<sub>4</sub>]<sup>+</sup> = 224. **IR (neat):**  $\nu$  (cm<sup>-1</sup>) = 3410, 2950, 2919, 2853, 1710, 1640, 1493, 1435, 1377, 1283, 1228, 1163, 1039, 918, 844, 773, 699.

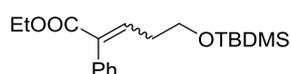


**Figure S24:** Synthesis of Ethyl (*E*)-5-hydroxy-2-phenylpent-2-enoate (**4o**)

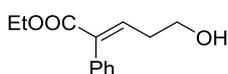


**Ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)pent-2-enoate:**

The compound was prepared according to GP2 starting from the 3-((*tert*-butyldimethylsilyl)oxy)propanal (20.89 mmol, 3.93 g). The product was obtained in 75% yield (4.93 g, *E/Z* = 1:4) after purification by flash chromatography on silica gel (Pentane/Diethyl ether 9:1). (*Z*)-isomer:  $R_f = 0.7$  (Pentane/Diethyl ether 9:1). **IR (neat):**  $\nu$  (cm<sup>-1</sup>) = 2931, 2858, 1723, 1628, 1468, 1367, 1254, 1094, 1044, 970, 937, 834, 775, 747, 663. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 0.06 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.89 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.32 (t,  $^3J_{HH} = 7.1$  Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 2.55 (q,  $^3J_{HH} = 6.4$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.75 (t,  $^3J_{HH} = 6.4$  Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 4.27 (q,  $^3J_{HH} = 7.1$  Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 7.38 (t,  $^3J_{HH} = 6.9$  Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.3 (CH<sub>3</sub>CH<sub>2</sub>O), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 35.9 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 60.8 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 62.5 (CH<sub>3</sub>CH<sub>2</sub>O), 117.6 (C=CH), 143.4 (C=CH), 162.6 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 338.

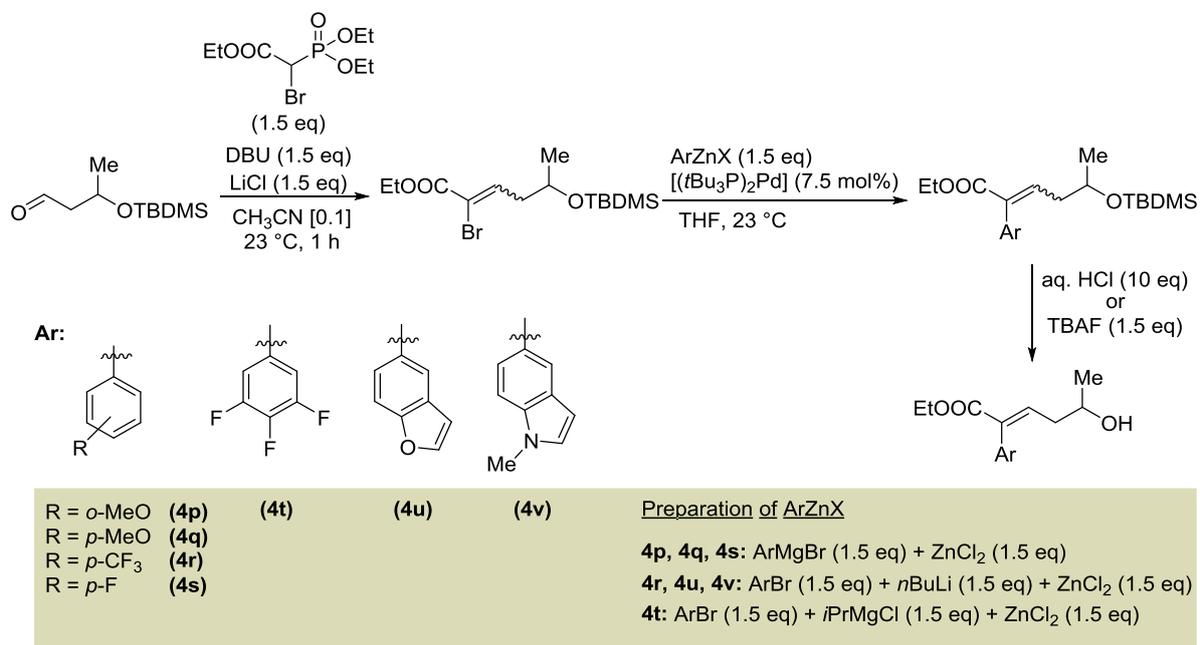

**Ethyl 5-((*tert*-butyldimethylsilyloxy)-2-phenylpent-2-enoate:**

The reaction was run according to GP6B starting from ethyl 2-bromo-5-((*tert*-butyldimethylsilyloxy)pent-2-enoate (14.6 mmol, 4.93 g). The reaction was complete after 4 h. Purification by column chromatography on silica gel (from Pentane to Pentane/Diethyl ether 98:2) afforded the (*Z*)-product in 3.5 % yield (165 mg), the (*E*)-product in 3.5 % yield (165 mg) and the mixture of the two isomers in 77% yield (3.75 g, *E/Z* = 4:1). (*Z*)-isomer:  $R_f$  = 0.6 (Pentane/Diethyl ether 9:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2930, 2858, 1718, 1467, 1371, 1254, 1193, 1092, 1029, 970, 938, 835, 775, 696, 661.  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.07 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.90 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.31 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.67 (q,  $^3J_{\text{HH}} = 6.6$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.77 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 4.29 (q, 2H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.26 (t, 1H,  $^3J_{\text{HH}} = 7.4$  Hz,  $\text{C}=\text{CH}$ ), 7.29 (m, 1H,  $\text{CH}_p\text{-Ar}$ ), 7.32 (m, 4H,  $\text{CH}_o\text{-Ar}$ ;  $\text{CH}_m\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) = -4.7 ( $(\text{CH}_3)_2\text{Si}$ ), 14.4 ( $\text{CH}_3\text{CH}_3\text{O}$ ), 18.5 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.1 ( $(\text{CH}_3)_3\text{CSi}$ ), 33.8 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 60.9 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 62.5 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 127.3 ( $\text{CH}_o\text{-Ar}$ ), 127.7 ( $\text{CH}_p\text{-Ar}$ ), 128.4 ( $\text{CH}_m\text{-Ar}$ ), 136.1 ( $\text{C}=\text{CH}$ ), 136.4 ( $\text{C}=\text{CH}$ ), 138.0 ( $\text{C-Ar}$ ), 168.3 ( $\text{C}=\text{O}$ ). **LRMS (IC)** = found  $[\text{M}+\text{H}]^+ = 335$ . (*E*)-isomer:  $R_f$  = 0.6 (Pentane/Diethyl ether 9:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2930, 2858, 1714, 1636, 1467, 1366, 1247, 1213, 1182, 1093, 1046, 939, 833, 774, 701, 662.  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.03 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.26 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.32 (q,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.68 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 4.21 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.10 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 1H,  $\text{C}=\text{CH}$ ), 7.20 (m, 1H,  $\text{CH}_p\text{-Ar}$ ), 7.36 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 7.31 (m, 2H,  $\text{CH}_m\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) = -5.2 ( $(\text{CH}_3)_2\text{Si}$ ), 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.5 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 33.3 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 60.9 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 62.0 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 127.5 ( $\text{CH}_p\text{-Ar}$ ), 128.1 ( $\text{CH}_o\text{-Ar}$ ), 129.9 ( $\text{CH}_m\text{-Ar}$ ), 135.4 ( $\text{C}=\text{CH}$ ), 135.5 ( $\text{C-Ar}$ ), 141.6 ( $\text{C}=\text{CH}$ ), 167.2 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 335$ .


**Ethyl (*E*)-5-hydroxy-2-phenylpent-2-enoate (4n):**

The reaction was run according to GP3 starting from ethyl 5-((*tert*-butyldimethylsilyloxy)-2-phenylpent-2-enoate (11.21 mmol, 3.75 g). Purification by column chromatography on silica gel (Pentane/Diethyl ether from 7:3 to 1:1) afforded **4n** in 67% yield (1.31 g) as an orange oil (Note: the *Z*-isomer cyclizes in this condition and was removed during purification).  $R_f$  = 0.2 (Pentane/Diethyl ether 1:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3426, 2966, 1707, 1636, 1495, 1444, 1368, 1240, 1183, 1095, 1043, 909, 865, 774, 702.  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 1.26 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.66 (bs, 1H,  $\text{OH}$ ), 2.37 (m, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.71 (t,  $^3J_{\text{HH}} = 6.4$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 4.21 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.09 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 1H,  $\text{C}=\text{CH}$ ), 7.19 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 7.36 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.32 (m, 1H,  $\text{CH}_p\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**

(CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 33.1 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.1 (CH<sub>2</sub>CH<sub>2</sub>OH), 61.7 (CH<sub>3</sub>CH<sub>2</sub>O), 127.7 (CH<sub>p</sub>-Ar), 128.2 (CH<sub>m</sub>-Ar), 129.8 (CH<sub>o</sub>-Ar), 135.3 (C-Ar), 136.3 (C=CH), 140.7 (C=CH), 167.2 (C=O). **LRMS (IC)** = found [M+H]<sup>+</sup> = 221.

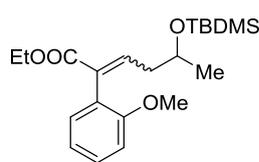


**Figure S25:** Synthesis of  $\alpha,\beta$ -unsaturated esters **4p-v**

**Ethyl 2-bromo-2-(diethoxyphosphoryl)acetate:** To a solution of triethyl phosphonacetate (44.6 mmol, 10 g) in THF (190 mL), NaH (53.5 mmol, 1.28 g) was added portionwise at 0 °C. After 30 minutes, Br<sub>2</sub> (53.5 mmol, 8.55 g) was carefully added and stirred for an additional 30 minutes. Conversion was monitored by <sup>1</sup>H-NMR (~ 89%) before quenching with a saturated aqueous NH<sub>4</sub>Cl solution (100 mL) and extracting with diethyl ether (3 x 100 mL). The organic phases were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and the volatiles removed *in vacuo*. Purification by flash chromatography on a small pad of silica gel (Pentane/EtOAc = 4:6) afforded ethyl 2-bromo-2-(diethoxyphosphoryl)acetate<sup>26</sup> in 89% yield (12.03 g) as a colourless oil.

**Ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate:** The reaction was performed according to GP2 using 3-((*tert*-butyldimethylsilyl)oxy)butanal (1.7, 8.4 mmol). Purification by flash chromatography (Pentane/Diethyl ether = 20:1) afforded ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate in 82% yield (2.38 g, *E/Z* = 2.8:1) as a light yellow oil. **R<sub>F</sub>** = 0.6 (Pentane/Et<sub>2</sub>O = 9:1). **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) Major Isomer: 0.05 (m,

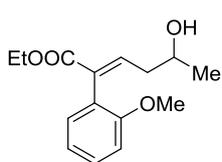
6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.89, (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.20 (d, 3H,  $^3J_{\text{HH}} = 6.1$  Hz,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.32 (t, 3H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.46 (m, 2H,  $\text{CH}_2\text{CHOTBDMS}$ ), 4.00 (h, 1H,  $^3J_{\text{HH}} = 6.1$  Hz,  $\text{CH}_3\text{CHOTBDMS}$ ), 4.28 (q, 2H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.39 (t, 1H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{C}=\text{CH}$ ). Minor Isomer: 0.05 (m, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88, (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.16 (d, 3H,  $^3J_{\text{HH}} = 6.1$  Hz,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.34 (t, 3H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.63 (m, 2H,  $\text{CH}_2\text{CHOTBDMS}$ ), 3.94 (3, 1H,  $\text{CH}_2\text{CHOTBDMS}$ ), 4.27 (q, 2H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.77 (t, 1H,  $^3J_{\text{HH}} = 7.7$  Hz,  $\text{C}=\text{CH}$ ).  $^{13}\text{C}\{^1\text{H}\}$ -NMR ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) Major Isomer: -4.4 ( $(\text{CH}_3)_2\text{Si}$ ), 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.2 ( $(\text{CH}_3)_3\text{CSi}$ ), 24.2 ( $\text{CH}_3\text{CHOTBDMS}$ ), 25.9 ( $(\text{CH}_3)_3\text{CSi}$ ), 42.3 ( $\text{CH}_2\text{CHOTBDMS}$ ), 62.5 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.1 ( $\text{CH}_2\text{CHOTBDMS}$ ), 117.5 ( $\text{C}=\text{CH}$ ), 143.5 ( $\text{C}=\text{CH}$ ), 162.5 ( $\text{C}=\text{O}$ ). Minor Isomer: -3.9 ( $(\text{CH}_3)_2\text{Si}$ ), 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.2 ( $(\text{CH}_3)_3\text{CSi}$ ), 24.0 ( $\text{CH}_3\text{COTBDMS}$ ), 25.9 ( $(\text{CH}_3)_3\text{CSi}$ ), 41.2 ( $\text{CH}_2\text{CHOTBDMS}$ ), 62.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.7 ( $\text{CH}_2\text{CHOTBDMS}$ ), 112.1 ( $\text{C}=\text{CH}$ ), 145.8 ( $\text{C}=\text{CH}$ ), 163.1 ( $\text{C}=\text{O}$ ). LRMS (IC) = found  $[\text{M}+\text{H}]^+ = 324$ . IR (neat):  $\nu$  ( $\text{cm}^{-1}$ ) = 2956, 2931, 2890, 2858, 1726, 1628, 1466, 1446, 1370, 1254, 1213, 1129, 1090, 1040, 998, 903, 833, 806, 774, 745, 662.



**Ethyl 5-((tert-butyldimethylsilyl)oxy)-2-(2-methoxyphenyl)hex-2-enoate**

The reaction was run according to GP6B starting from ethyl 2-bromo-5-((tert-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol,  $E/Z = 2.8:1$ ). The reaction was complete after 4 h and the crude mixture was

purified by flash chromatography (Pentane/Diethyl ether = 30:1) to give the title compound in 86% yield (450 mg,  $E/Z = 3:1$ ) as a colourless oil. The product was engaged in the next step without further purification.

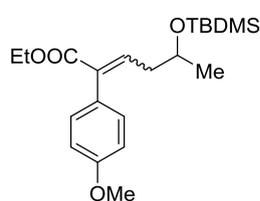


**Ethyl (E)-5-hydroxy-2-(2-methoxyphenyl)hex-2-enoate (4p)**

To a solution of ethyl 5-((tert-butyldimethylsilyl)oxy)-2-(2-methoxyphenyl)hex-2-enoate (430 mg, 1.07 mmol) in THF (11 mL), aqueous HCl (2 M, 5 mL) was added at 0 °C and stirred for 24 h at room temperature. The reaction

was quenched with water (30 mL), extracted with diethyl ether (3 x 30 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was treated with HCl in diethyl ether (1 M, 11 mL) and stirred for 4 h. The volatiles were removed under *vacuo* and the crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 5:1). Compound **4p** was obtained in 56% yield (180 mg) as a colourless oil.  $R_f = 0.2$  (Pentane/Diethyl ether = 1:2). IR (neat):  $\nu$  ( $\text{cm}^{-1}$ ) = 2971, 1710, 1248, 1047, 756.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.17 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.23 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.14 – 2.29 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.77 (s, 3H,  $\text{CH}_3\text{OAr}$ ), 3.88 – 3.98 (m, 1H,  $\text{CHOH}$ ), 4.12 – 4.27 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.88 – 7.01 (m, 2H,  $\text{CH-Ar}$ ), 7.04 – 7.13 (m, 1H,

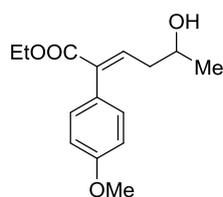
C=CH; 1H, *CH*-Ar), 7.29 – 7.36 (m, 1H, *CH*-Ar).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}$ ), 23.4 ( $\text{CH}_3\text{CHOH}$ ), 39.4 ( $\text{CH}_2\text{CHOH}$ ), 55.7 ( $\text{CH}_3\text{OAr}$ ), 60.8 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.2 ( $\text{CHOH}$ ), 111.0 (*CH*-Ar), 120.6 (*CH*-Ar), 124.6 (*C*-Ar), 129.4 (*CH*-Ar), 131.1 (*CH*-Ar), 133.5 (*C*=CH), 140.6 (*CH*-Ar), 157.1 ( $\text{COMe}$ ), 167.1 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 282$ .



**Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(4-methoxyphenyl)hex-2-**

**enoate**: : The reaction was run according to GP6B starting from ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol, *E/Z* = 2.8:1). The reaction was complete after 4 h and the crude mixture was filtered through a pad of silica gel and used in the next step without

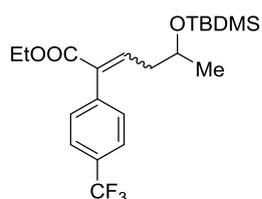
further purification.



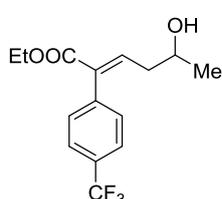
**Ethyl (*E*)-5-hydroxy-2-(4-methoxyphenyl)hex-2-enoate (4q):** To a

solution of ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(4-methoxyphenyl)hex-2-enoate (1.4 mmol) in THF (14 mL), aqueous HCl (2 M, 7 mL) was added at 0 °C and stirred at room temperature for 24 h. The reaction was quenched with water (40 mL), extracted with diethyl ether (3 × 40 mL),

dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. Purification by column chromatography on silica gel (Pentane/Diethyl ether from 5:1 to 1:2) gave **4q** in 59% yield (220 mg, *E/Z* = 4.5:1). The mixture was treated with HCl in diethyl ether (1 M, 11 mL) for 1 h at room temperature. After evaporation of the volatiles, the crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 5:1) to give **4q** in 73% yield (160 mg, *E/Z* >50:1) as a colourless oil.  $R_f = 0.2$  (Pentane/Diethyl ether = 1:2). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 3461, 2972, 1710, 1609, 1513, 1247, 1176, 1035, 835$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.18 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.27 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.37 – 1.44 (m, 1H, OH), 2.20 – 2.39 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.83 (s, 3H,  $\text{CH}_3\text{OAr}$ ), 3.90 – 4.03 (m, 1H,  $\text{CHOH}$ ), 4.21 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.85 – 6.95 (m, 2H, *CH*-Ar), 7.07 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 1H, *C*=CH), 7.10 – 7.13 (m, 2H, *CH*-Ar).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.5 ( $\text{CH}_3\text{CHOH}$ ), 39.2 ( $\text{CH}_2\text{CHOH}$ ), 55.4 ( $\text{CH}_3\text{OAr}$ ), 61.0 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.5 ( $\text{CHOH}$ ), 113.6 (*CH*-Ar), 127.5 (*C*=CH), 131.1 (*CH*-Ar), 135.8 (*C*-Ar), 140.1 (*C*=CH), 159.0 ( $\text{COCH}_3$ ), 167.4 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 282$ .

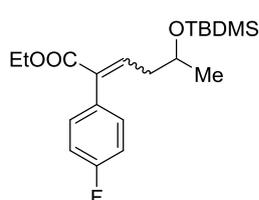
**Ethyl****5-((*tert*-butyldimethylsilyloxy)-2-(4-****(trifluoromethyl)phenyl)hex-2-enoate:**

To a solution of 1-bromo-4-(trifluoromethyl)benzene (337 mg, 1.5 mmol) in anhydrous THF (2 mL) at  $-78\text{ }^{\circ}\text{C}$ , *n*-butyl lithium (1.5 mmol, 1.6 M in hexane) was added dropwise. The reaction mixture was stirred at  $-78\text{ }^{\circ}\text{C}$  for 1 h before a solution of  $\text{ZnCl}_2$  (1.5 mmol) in THF (1.0 M) was added dropwise at the same temperature. The resulting homogeneous solution was stirred at room temperature for 1 h. Ethyl 2-bromo-5-((*tert*-butyldimethylsilyloxy)hex-2-enoate (350 mg, 1.0 mmol) and  $[(t\text{Bu}_3\text{P})_2\text{Pd}]$  (36 mg, 0.05 mmol) were dissolved in THF (4 mL) and then transferred to the alkylzinc solution by syringe. The mixture was stirred at room temperature for 17 h, quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution, extracted with diethyl ether ( $3 \times 5\text{ mL}$ ), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 40:1) to give predominantly the (*E*)-isomer of the product in 48% yield (200 mg).  $R_f = 0.4$  (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2957, 1717, 1325, 1128, 837$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.04 (d,  $^3J_{\text{HH}} = 2.4\text{ Hz}$ , 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.11 (d,  $^3J_{\text{HH}} = 6.0\text{ Hz}$ , 3H,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.27 (t,  $^3J_{\text{HH}} = 7.1\text{ Hz}$ , 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.12 – 2.31 (m, 2H,  $\text{CH}_2\text{CHOTBDMS}$ ), 3.91 (tdd,  $^3J_{\text{HH}} = 7.2$ ,  $^3J_{\text{HH}} = 6.1$ , 4.9 Hz, 1H,  $\text{CH}_2\text{CHOTBDMS}$ ), 4.22 (q,  $^3J_{\text{HH}} = 7.1\text{ Hz}$ , 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.19 (t,  $^3J_{\text{HH}} = 7.7\text{ Hz}$ , 1H, C=CH), 7.32 (d,  $^3J_{\text{HH}} = 8.0\text{ Hz}$ , 2H, CH-Ar), 7.62 (d,  $^3J_{\text{HH}} = 8.0\text{ Hz}$ , 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -4.7 ( $(\text{CH}_3)_2\text{Si}$ ), -4.4 ( $(\text{CH}_3)_2\text{Si}$ ), 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 18.2 ( $(\text{CH}_3)_3\text{CSi}$ ), 24.2 ( $\text{CH}_3\text{CHOTBDMS}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 39.6 ( $\text{CH}_2\text{CHOTBDMS}$ ), 61.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 68.0 ( $\text{CH}_2\text{CHOTBDMS}$ ), 124.4 (q,  $^1J_{\text{CF}} = 273.71\text{ Hz}$ ,  $\text{CF}_3$ ), 125.0 (q,  $^3J_{\text{CF}} = 3.8\text{ Hz}$ , CH-Ar), 129.1 (q,  $^2J_{\text{CF}} = 32.5$ ,  $\text{CCF}_3$ ), 130.4 (CH-Ar), 134.0 (C=CH), 139.3 (C-Ar), 143.2 (C=CH), 166.5 (C=O). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 417$ .

**Ethyl (*E*)-5-hydroxy-2-(4-(trifluoromethyl)phenyl)hex-2-enoate (4r):**

To a solution of ethyl 5-((*tert*-butyldimethylsilyloxy)-2-(4-(trifluoromethyl)phenyl)hex-2-enoate (200 mg, 0.48 mmol) in THF (5.5 mL), aqueous HCl (2 M, 2.5 mL) was added at  $0\text{ }^{\circ}\text{C}$  and stirred for 4 h at room temperature. The reaction was quenched with water (15 mL), extracted with diethyl ether ( $3 \times 15\text{ mL}$ ), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 5:1) to give **4r** in 69% yield (100 mg) as a colourless oil.  $R_f = 0.4$  (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3425, 2975, 1707, 1323, 1250, 1163, 1065, 847$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.19 (d,  $^3J_{\text{HH}} = 6.2\text{ Hz}$ , 3H,  $\text{CH}_3\text{CHOH}$ ), 1.27 (t,  $^3J_{\text{HH}} = 7.1\text{ Hz}$ , 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.39 (d,  $^3J_{\text{HH}} = 4.5\text{ Hz}$ , 1H, OH), 2.24 (ddd,  $^3J_{\text{HH}} = 7.4, 6.2$

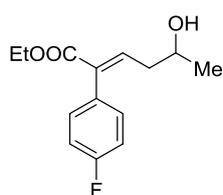
Hz,  $^2J_{\text{HH}} = 1.3$  Hz, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.97 (qd,  $^3J_{\text{HH}} = 6.2, 4.4$  Hz, 1H,  $\text{CH}_2\text{CHOH}$ ), 4.22 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.19 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 1H,  $\text{C}=\text{CH}$ ), 7.29 – 7.36 (m, 2H,  $\text{CH-Ar}$ ), 7.63 (dt,  $^3J_{\text{HH}} = 7.6, ^5J_{\text{HH}} = 1.0$  Hz, 2H,  $\text{CH-Ar}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.6 ( $\text{CH}_3\text{CHOH}$ ), 39.1 ( $\text{CH}_2\text{CHOH}$ ), 61.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.3 ( $\text{CH}_2\text{CHOH}$ ), 124.3 (q,  $^1J_{\text{CF}} = 272.9$  Hz,  $\text{CF}_3$ ), 125.1 (q,  $^3J_{\text{CF}} = 3.8$  Hz,  $\text{CH-Ar}$ ), 129.6 (q,  $^2J_{\text{CF}} = 32.5$ ,  $\text{CCF}_3$ ), 130.3 ( $\text{CH-Ar}$ ), 135.0 ( $\text{C}=\text{CH}$ ), 139.1 ( $\text{C-Ar}$ ), 141.9 ( $\text{C}=\text{CH}$ ), 166.5 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 303$ .



**Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(4-fluorophenyl)hex-2-enoate**

The reaction was run according to GP6B starting from ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol, *E/Z* = 2.8:1). The reaction was complete after 4 h and the crude mixture was filtered through a pad of silica gel and then used for the next step

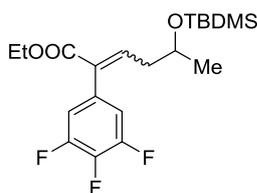
without any further purification.



**Ethyl (*E*)-2-(4-fluorophenyl)-5-hydroxyhex-2-enoate (4s)**

The product was prepared according to GP4 starting from ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(4-fluorophenyl)hex-2-enoate (1.4 mmol). The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) to give (*E*)-4s in 48% yield (170 mg).  $R_f =$

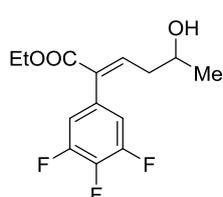
0.3 (Pentane/Diethyl ether = 1:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 3441, 2974, 1711, 1511, 1251, 1221, 1043, 841$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.19 (d,  $^3J_{\text{HH}} = 6.1$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.27 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.40 (d,  $^3J_{\text{HH}} = 4.6$  Hz, 1H,  $\text{OH}$ ), 2.17 – 2.34 (m, 2H,  $\text{CH}_2\text{CHOH}$ ), 3.84 – 4.07 (m, 1H,  $\text{CH}_2\text{CHOH}$ ), 4.21 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.99 – 7.23 (m, 1H,  $\text{C}=\text{CH}$ ; 4H,  $\text{CH-Ar}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.4 ( $\text{CH}_3\text{CHO}$ ), 39.0 ( $\text{CH}_2\text{CHOH}$ ), 61.0 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.3 ( $\text{CH}_2\text{CHOH}$ ), 115.0 (d,  $^2J_{\text{CF}} = 22.2$  Hz,  $\text{CH-Ar}$ ), 131.0 (d,  $^4J_{\text{CF}} = 4.0$  Hz,  $\text{C-Ar}$ ), 131.4 (d,  $^3J_{\text{CF}} = 8.0$  Hz,  $\text{CH-Ar}$ ), 135.1 ( $\text{C}=\text{CH}$ ), 140.8 ( $\text{C}=\text{CH}$ ), 162.2 (d,  $^1J_{\text{CF}} = 45.4$  Hz,  $\text{CF}$ ), 166.8 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 253$ .



**Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(3,4,5-trifluorophenyl)hex-2-enoate**

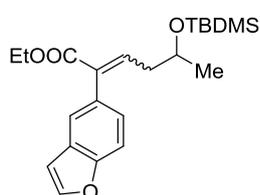
To a solution of the 5-bromo-1,2,3-trifluorobenzene (2.1 mmol) in anhydrous THF (2 mL) at 0 °C, isopropyl magnesium chloride (2.3 mmol, 2.0 M in THF) was added dropwise and stirred at 0 °C for 1 h. Subsequently, a THF solution of  $\text{ZnCl}_2$  (2.3 mmol, 1.0 M) was added dropwise

at 0 °C and the resulting mixture was stirred at room temperature for 1 h. Ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol, *E/Z* = 2.8:1) and [(*t*Bu<sub>3</sub>P)<sub>2</sub>Pd] (53.6 mg) in THF (4 mL) were added slowly by syringe and the resulting mixture was stirred at room temperature. After 4 h, the reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 × 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was filtered through a pad of silica gel and engaged in the next step without further purification.



**Ethyl (*E*)-5-hydroxy-2-(3,4,5-trifluorophenyl)hex-2-enoate (4t):** To a solution of ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(3,4,5-trifluorophenyl)hex-2-enoate (1.4 mmol) in THF (14 mL), aqueous HCl (2 M, 7 mL) was added at 0 °C and stirred at room temperature for 24 h.

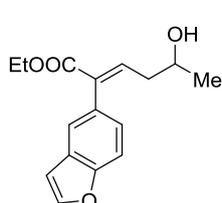
The reaction was quenched with water (40 mL), extracted with diethyl ether (3 × 40 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) to give **4t** in 47% yield (190 mg). *R<sub>f</sub>* = 0.2 (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3399, 2980, 1712, 1531, 1254, 1042, 668. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.21 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.2 Hz, 3H, CH<sub>3</sub>CHOH), 1.28 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.40 (d, <sup>3</sup>*J*<sub>HH</sub> = 4.6 Hz, 1H, OH), 2.19 – 2.32 (m, 2H, CH<sub>2</sub>CHOH), 3.90 – 4.07 (m, 1H, CH<sub>2</sub>CHOH), 4.22 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.78 – 6.92 (m, 2H, CH-Ar), 7.17 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.6 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.3 (CH<sub>3</sub>CH<sub>2</sub>O), 23.7 (CH<sub>3</sub>CHOH), 39.0 (CH<sub>2</sub>CHOH), 61.5 (CH<sub>3</sub>CH<sub>2</sub>O), 67.1 (CH<sub>2</sub>CHOH), 113.6 – 116.4 (m, CH-Ar), 131.2 (td, <sup>3</sup>*J*<sub>CF</sub> = 8.3, <sup>4</sup>*J*<sub>CF</sub> = 5.1 Hz, C-Ar), 133.5 (C=CH), 139.4 (dt, <sup>1</sup>*J*<sub>CF</sub> = 252.1, <sup>2</sup>*J*<sub>CF</sub> = 15.3 Hz, CF<sub>*p*</sub>-Ar), 142.6 (C=CH), 150.9 (ddd, <sup>1</sup>*J*<sub>CF</sub> = 250.1, <sup>2</sup>*J*<sub>CF</sub> = 10.0, <sup>3</sup>*J*<sub>CF</sub> = 4.2 Hz, CF<sub>*m*</sub>-Ar), 166.0 (C=O). **LRMS (IC)** found [M+NH<sub>4</sub>]<sup>+</sup> = 306.



**Ethyl 2-(benzofuran-5-yl)-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate:** To a solution of the 5-bromo-benzofuran (414 mg, 2.1 mmol) in anhydrous THF (2 mL) at –78 °C, *n*-butyl lithium (2.2 mmol, 1.0 M in hexane) was added dropwise and stirred for 1 h. A THF solution of ZnCl<sub>2</sub> (2.1 mmol, 1.0 M) was added dropwise at the same temperature

and the resulting homogeneous solution was stirred at room temperature for 1 h. Ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol, *E/Z* = 2.8:1) and [(*t*Bu<sub>3</sub>P)<sub>2</sub>Pd] (54 mg) in THF (4 mL) were added slowly by syringe. The resulting mixture was stirred at room temperature. After 4 h, the reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl

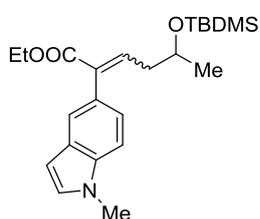
solution, extracted with diethyl ether (3 × 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The crude mixture was purified by flash chromatography to give the desired product in 64% yield (350 mg, *E/Z* = 2.5:1) which was used in the next step directly.



**Ethyl (E)-2-(benzofuran-5-yl)-5-hydroxyhex-2-enoate (4u):** Ethyl 2-(benzofuran-5-yl)-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (350 mg, 0.9 mmol, *E/Z* = 2.5 :1) was dissolved in THF (4.3 mL) and TBAF (1.0 M in THF, 2.7 mmol) was added slowly at 0 °C. The mixture was warmed to room temperature. After 2 h, the reaction was quenched with a saturated

aqueous NH<sub>4</sub>Cl solution (5 mL), extracted with diethyl ether (3 × 20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) to give **4u** in 36% yield (90 mg).

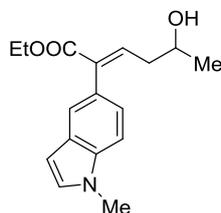
**R<sub>f</sub>** = 0.3 (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3435, 2974, 1702, 1245, 1109, 1030, 911, 770, 730. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.13 (d, <sup>3</sup>J<sub>HH</sub> = 6.2 Hz, 3H, CH<sub>3</sub>CHOH), 1.25 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 2.24 (dd, <sup>3</sup>J<sub>HH</sub> = 7.5, 6.2 Hz, 2H, CH<sub>2</sub>CHOH), 3.84 – 3.98 (m, 1H, CH<sub>2</sub>CHOH), 4.19 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.80 (dd, <sup>3</sup>J<sub>HH</sub> = 2.2, <sup>5</sup>J<sub>HH</sub> = 1.0 Hz, 1H, CH-Het), 7.10 (dd, <sup>3</sup>J<sub>HH</sub> = 8.5, <sup>4</sup>J<sub>HH</sub> = 1.7 Hz, 1H, CH-Het), 7.13 (t, <sup>3</sup>J<sub>HH</sub> = 7.6 Hz, 1H, C=CH), 7.41 (dd, <sup>4</sup>J<sub>HH</sub> = 1.7 Hz, <sup>5</sup>J<sub>HH</sub> = 0.7 Hz, 1H, CH-Het), 7.49 (ddd, <sup>3</sup>J<sub>HH</sub> = 8.4, <sup>5</sup>J<sub>HH</sub> = 0.7, <sup>5</sup>J<sub>HH</sub> = 1.0 Hz, 1H, CH-Het), 7.67 (d, <sup>3</sup>J<sub>HH</sub> = 2.2 Hz, 1H, CH-Het). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 23.6 (CH<sub>3</sub>CHOH), 39.5 (CH<sub>2</sub>CHOH), 61.2 (CH<sub>3</sub>CH<sub>2</sub>O), 67.6 (CH<sub>2</sub>CHOH), 107.0 (CH-Het), 111.1 (CH-Het), 122.8 (CH-Het), 126.6 (CH-Het), 127.6 (C-Het), 130.5 (C=CH), 136.3 (C-Het), 141.1 (C=CH), 145.9 (CH-Het), 154.6 (C-Het), 167.4 (C=O). **LRMS (IC)** found [M+NH<sub>4</sub>]<sup>+</sup> = 292.



**Ethyl 5-((*tert*-butyldimethylsilyl)oxy)-2-(1-methyl-1H-indol-5-yl)hex-2-enoate:** To a solution of the 5-bromo-*N*-Methyl indole (437

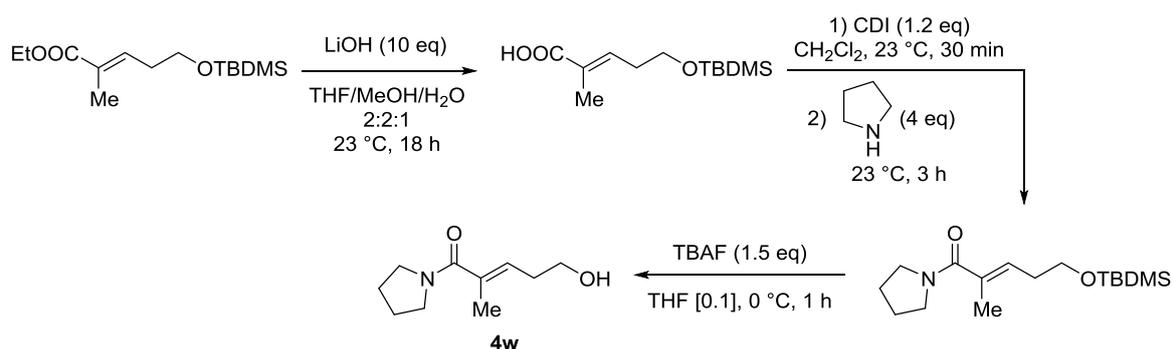
mg, 2.1 mmol) in anhydrous THF (2 mL) at –78 °C, *n*-butyl lithium (2.2 mmol, 1.0 M in hexane) was added dropwise. After 1 h at –78 °C, a THF solution of ZnCl<sub>2</sub> (2.1 mmol, 1.0 M) was added dropwise at the same temperature. The resulting homogeneous solution was stirred at room temperature for 1 h before ethyl 2-bromo-5-((*tert*-butyldimethylsilyl)oxy)hex-2-enoate (1.4 mmol, *E/Z* = 2.8:1) and [(*t*Bu<sub>3</sub>P)<sub>2</sub>Pd] (54 mg, 0.105 mmol) in THF (4 mL) were added slowly by syringe. The resulting mixture was stirred at room temperature for 4 h. The reaction was then quenched with a saturated aqueous NH<sub>4</sub>Cl solution, extracted with diethyl ether (3 × 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. The crude mixture was purified by flash

chromatography on silica gel (Pentane/Diethyl ether = 10:1) to give the desired product in 52% yield (440 mg, *E/Z* = 5:1). This mixture was used in the next step directly.

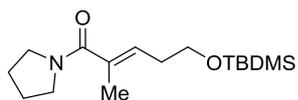


**Ethyl (E)-5-hydroxy-2-(1-methyl-1H-indol-5-yl)hex-2-enoate (4v):**

Ethyl 5-((*tert*-butyldimethylsilyloxy)-2-(1-methyl-1H-indol-5-yl)hex-2-enoate (330 mg, 0.81 mmol, *E/Z* = 5:1) was dissolved in THF (8.1 mL) and TBAF (1.0 M in THF, 2.4 mmol) was added slowly at 0 °C. The mixture was warmed to room temperature. After 2 h, the reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (5 mL), extracted with diethyl ether (3 × 20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) to give **4v** in 65% yield (152 mg) as a yellow oil. *R*<sub>f</sub> = 0.2 (Pentane/Diethyl ether = 1:2). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3437, 2971, 1705, 1246, 1042, 728. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.13 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.2 Hz, 3H, CH<sub>3</sub>CHOH), 1.25 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.42 (m, 1H, OH), 2.26 (dd, <sup>3</sup>*J*<sub>HH</sub> = 7.5, 6.2 Hz, 2H, CH<sub>2</sub>CHOH), 3.80 (s, 3H, CH<sub>3</sub>N), 3.88 – 3.97 (m, 1H, CH<sub>2</sub>CHOH), 4.19 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.46 (dd, <sup>3</sup>*J*<sub>HH</sub> = 3.1, <sup>5</sup>*J*<sub>HH</sub> = 0.9 Hz, 1H, CH-Het), 7.01 (dd, <sup>3</sup>*J*<sub>HH</sub> = 8.4, <sup>4</sup>*J*<sub>HH</sub> = 1.6 Hz, 1H, CH-Het), 7.06 – 7.18 (m, 1H, CH-Het; 1H, C=CH), 7.33 (ddd, <sup>3</sup>*J*<sub>HH</sub> = 8.4, <sup>5</sup>*J*<sub>HH</sub> = 0.8 Hz, <sup>5</sup>*J*<sub>HH</sub> = 0.9 Hz, 1H, CH-Het), 7.38 (dd, <sup>4</sup>*J*<sub>HH</sub> = 1.7, <sup>5</sup>*J*<sub>HH</sub> = 0.8 Hz, 1H, CH-Het). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.0 (CH<sub>3</sub>CH<sub>2</sub>O), 23.1 (CH<sub>3</sub>CH), 32.7 (CH<sub>3</sub>N), 39.0 (CH<sub>2</sub>CHOH), 60.6 (CH<sub>3</sub>CH<sub>2</sub>O), 67.2 (CH<sub>2</sub>CHOH), 100.7 (CH-Het), 108.6 (CH-Het), 121.7 (CH-Het), 123.2 (CH-Het), 126.2 (C-Het), 128.0 (C-Het), 129.2 (CH-Het), 135.9 (C-N), 136.7 (C=CH), 139.7 (C=CH), 167.4 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 288.

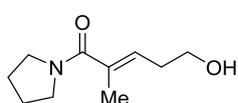


**Figure S26:** Synthesis of (*E*)-5-hydroxy-2-methyl-1-(pyrrolidin-1-yl)pent-2-en-1-one (**4w**)



**(E)-5-((tert-butyldimethylsilyloxy)-2-methyl-1-(pyrrolidin-1-yl)pent-2-en-1-one:** Ethyl (E)-5-((tert-butyldimethylsilyloxy)-2-methylpent-2-enoate (7.34 mmol) was dissolved in a solution of

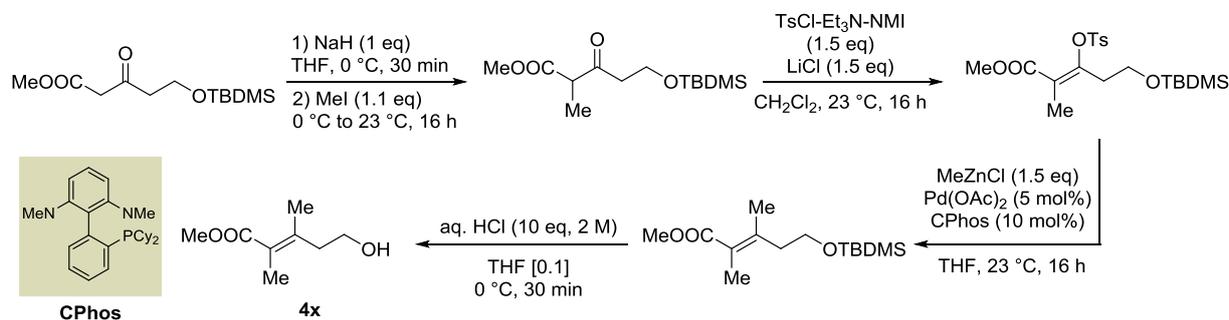
THF, MeOH, H<sub>2</sub>O (2:2:1, 183 mL) and LiOH (73.4 mmol, 1.76 g) was added and stirred at room temperature. After 16 h, the reaction was quenched with AcOH (pH adjusted to 5-6) and extracted with diethyl ether (3 × 100 mL) then the organic phases were combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. The residue was redissolved in CH<sub>2</sub>Cl<sub>2</sub> (32 mL) and 1,1'-carbonyldiimidazole (CDI) (8.4 mmol, 1.36 g) was added and stirred at room temperature for 30 minutes. Pyrrolidine (28 mmol, 2.3 mL) was added in one portion and stirred for 3 h at room temperature. The reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (30 mL), extracted with EtOAc (3 × 30 mL) then the organic phases combined, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated. The crude oil was purified by flash chromatography on silica gel (Diethyl ether) to afford (E)-5-((tert-butyldimethylsilyloxy)-2-methyl-1-(pyrrolidin-1-yl)pent-2-en-1-one as yellow oil in 51% yield (1.11 g) over two steps. **R<sub>f</sub>** = 0.4 (Diethyl ether). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2953, 2930, 2859, 1618, 1462, 1436, 1378, 1253, 1224, 1198, 1160, 1093, 1006, 936, 834, 775, 740, 664, 599, 568. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.87 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.84 (s, 3H, CH<sub>3</sub>C=CH), 1.84 – 1.86 (bm, 4H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 2.32 (q, 2H, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 3.42 – 3.44 (bm, 2H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 3.46 – 3.48 (bm, 2H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 3.65 (t, 2H, <sup>3</sup>J<sub>HH</sub> = 6.7 Hz, CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 5.66 (m, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -5.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.1 (CH<sub>3</sub>C=CH), 18.4 ((CH<sub>3</sub>)<sub>3</sub>CSi), 24.6 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.3 (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 31.6 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 45.5 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 49.0 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 62.2 (CH<sub>2</sub>CH<sub>2</sub>OTBDMS), 128.4 (C=CH), 134.4 (C=CH), 172.0 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 299.



**(E)-5-hydroxy-2-methyl-1-(pyrrolidin-1-yl)pent-2-en-1-one (4w):** The product was prepared according to GP3 starting from (E)-5-((tert-butyldimethylsilyloxy)-2-methyl-1-(pyrrolidin-1-yl)pent-2-en-1-one (3.74

mmol, 1.11 g). After column chromatography on silica gel (Diethyl ether then Acetone) the product **4w** was obtained in 32% yield (213 mg) as a pale yellow oil. **R<sub>f</sub>** = 0.2 (CH<sub>2</sub>Cl<sub>2</sub>/Acetone = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3376, 2952, 2928, 2876, 1657, 1590, 1436, 1378, 1341, 1252, 1227, 1186, 1159, 1051, 895, 870, 744, 653, 602, 576. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.68 (bs, 1H, OH), 1.86 – 1.92 (bm, 4H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 3H, CH<sub>3</sub>C=CH), 2.39 (q, 2H, <sup>3</sup>J<sub>HH</sub> = 6.7 Hz, CH<sub>2</sub>CH<sub>2</sub>OH), 3.42 – 3.45 (bm, 4H, (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 3.71 (t, 2H, <sup>3</sup>J<sub>HH</sub> = 6.4 Hz, CH<sub>2</sub>CH<sub>2</sub>OH), 5.69 (m, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.2 (CH<sub>3</sub>C=CH), 24.6 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 26.3 (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N, 31.4 (CH<sub>2</sub>CH<sub>2</sub>OH), 45.8 (CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N,

48.9 ( $\text{CH}_2\text{CH}_2\text{N}$ ), 61.9 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 127.8 ( $\text{C}=\text{CH}$ ), 135.5 ( $\text{C}=\text{CH}$ ), 171.9 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 184$ ,  $[\text{M}+\text{Na}]^+ = 206$ .

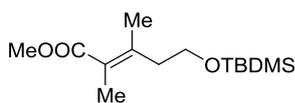


**Figure S27:** Synthesis of Methyl (*E*)-5-hydroxy-2,3-dimethylpent-2-enoate (**4x**)

**Methyl 5-((*tert*-butyldimethylsilyloxy)-2-methyl-3-oxopentanoate:** In a round bottom flask, the crude  $\beta$ -ketoester (15.76 mmol) was dissolved in THF (79 mL) and cooled to 0 °C. After the addition of NaH (15.76 mmol, 378 mg), the mixture was stirred 30 minutes at 0 °C. Next, methyl iodide (17.34 mmol, 1.1 mL) was added at 0 °C and the reaction stirred for 16 h at room temperature. The reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL), extracted with diethyl ether (3  $\times$  80 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The residual oil was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 95:5) to afford methyl 5-((*tert*-butyldimethylsilyloxy)-2-methyl-3-oxopentanoate in 50% yield (2.16 g) over 2 steps as a colourless oil.  $R_f = 0.4$  (Pentane/Diethyl ether). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2954, 2932, 2858, 1748, 1718, 1653, 1618, 1461, 1436, 1388, 1331, 1253, 1203, 1090, 1005, 921, 831, 776, 732, 663$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.05 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.87 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.34 (d,  $^3J_{\text{HH}} = 7.2$  Hz, 2H,  $\text{CH}_3\text{CH}$ ), 2.74 (td,  $^3J_{\text{HH}} = 6.2$ ,  $^2J_{\text{HH}} = 2.0$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.59 (q,  $^3J_{\text{HH}} = 7.2$  Hz, 1H,  $\text{CH}_3\text{CH}$ ), 3.73 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.89 (t,  $^3J_{\text{HH}} = 6.3$  Hz, 1H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ).  **$^{13}\text{C}\{^1\text{H}\}$ -NMR** ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) -5.4 ( $(\text{CH}_3)_2\text{Si}$ ), 12.6 ( $\text{CH}_3\text{CH}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 44.4 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 52.5 ( $\text{CH}_3\text{O}$ ), 53.4 ( $\text{CH}_3\text{CH}$ ), 58.8 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 171.0 ( $\text{CH}_3\text{O}_2\text{C}$ ), 204.9 ( $\text{CHC}(\text{O})$ ). **LRMS (IC)** found  $[\text{M}+\text{HCOOH}]^+ = 320$ .

**Methyl (Z)-5-((*tert*-butyldimethylsilyloxy)-2-methyl-3-tosyloxy)pent-2-enoate:** In a round-bottom flask, methyl 5-((*tert*-butyldimethylsilyloxy)-2-methyl-3-oxopentanoate (6.15 mmol, 1.69 g) was dissolved in  $\text{CH}_2\text{Cl}_2$  (31 mL). Next,  $\text{Et}_3\text{N}$  (9.23 mmol, 1.3 mL), NMI (9.23 mmol, 0.7 mL), LiCl (30.75 mmol, 1.3 g) and TsCl (9.23 mmol, 1.76 g) were added sequentially at 0 °C

and the reaction was stirred at room temperature for 16 h. The reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL), extracted with diethyl ether (3 x 30 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*.<sup>25</sup> The residual oil was purified by flash chromatography on silica gel (Pentane/Diethyl ether 9:1) to afford (*Z*)-tosylate in 59% yield (1.47 g) as a pale yellow oil. (*Z*)-isomer:  $R_f = 0.5$  (Pentane/Diethyl ether 8:2). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2930, 2861, 1725, 1375, 1258, 1193, 1086, 1019, 776, 733, 666, 548$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) -0.01 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.83 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ). 1.91 (m, 3H,  $\text{CH}_3\text{C}=\text{C}$ ), 2.45 (s, 3H,  $\text{CH}_3\text{Ar}$ ), 2.59 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.57 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.72 (t,  $^3J_{\text{HH}} = 6.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 7.33 – 7.35 (d,  $^3J_{\text{HH}} = 8.2$  Hz, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.80 – 7.82 (d,  $^3J_{\text{HH}} = 8.2$  Hz, 2H,  $\text{CH}_o\text{-Ar}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) -5.4 ( $(\text{CH}_3)_2\text{Si}$ ), 15.4 ( $\text{CH}_3\text{C}=\text{C}$ ), 18.3 ( $(\text{CH}_3)_3\text{CSi}$ ), 21.8 ( $\text{CH}_3\text{Ar}$ ), 25.9 ( $(\text{CH}_3)_3\text{CSi}$ ), 35.5 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 52.0 ( $\text{CH}_3\text{O}$ ), 59.7 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 122.0 ( $\text{CH}_3\text{C}=\text{C}$ ), 128.2 ( $\text{CH}_o\text{-Ar}$ ), 129.9 ( $\text{CH}_m\text{-Ar}$ ), 134.1 ( $\text{C}_{\text{ipso}}\text{-Ar}$ ), 148.7 ( $\text{CH}_3\text{C}=\text{C}$ ), 145.3 ( $\text{C}_p\text{-Ar}$ ), 167.1 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 430$ .

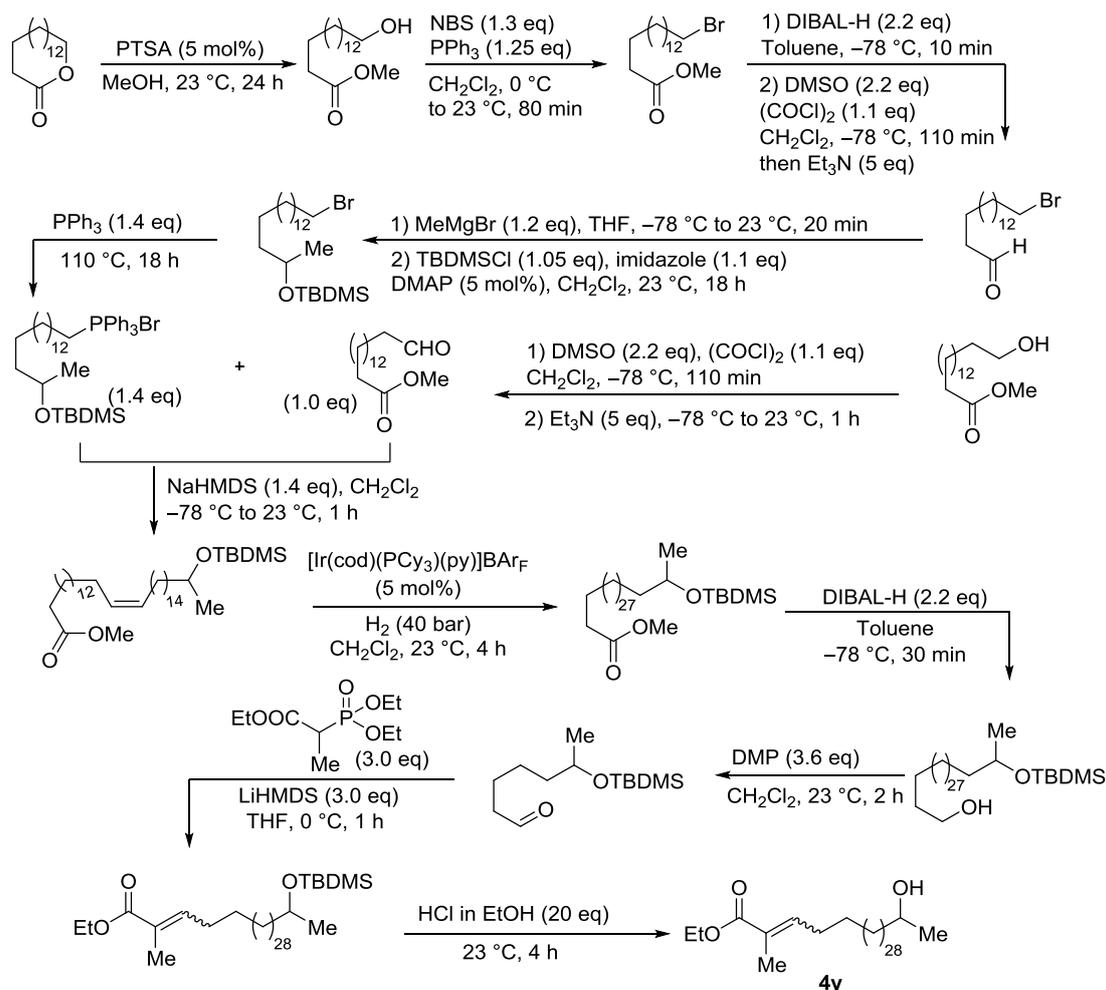


**Methyl (E)-5-((tert-butyldimethylsilyloxy)-2,3-dimethylpent-2-**

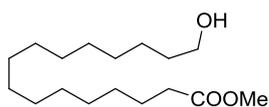
**enoate:** In a Schlenk, the electrophilic zinc reagent was prepared in situ by diluting  $\text{MeMgBr}$  (4.91 mmol, 1.6 mL, 3 M in diethyl ether) in

THF (3.3 mL) and adding 4.9 mL of a solution of  $\text{ZnCl}_2$  (1 M in THF). The resulting suspension was stirred 30 minutes before the addition of *CPhos* (0.327 mmol, 143 mg) along with a solution of  $\text{Pd}(\text{OAc})_2$  (0.164 mmol, 37 mg) in THF (2 mL). In another Schlenk tube, methyl (*Z*)-5-((tert-butyldimethylsilyloxy)-2-methyl-3-(tosyloxy)pent-2-enoate (3.27 mmol) was dissolved in THF (25 mL) and added to the alkylzinc suspension by cannula then stirred at room temperature. After 16 h, the reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (10 mL), extracted with diethyl ether (3 x 30 mL) and dried over  $\text{Na}_2\text{SO}_4$ .<sup>27</sup> The crude oil was purified by flash chromatography (Pentane/Diethyl ether 98:2) to afford the (*E*)-product in 85% yield (758 mg) as a colourless oil. (*E*)-isomer:  $R_f = 0.8$  (Pentane/Diethyl ether = 8:2). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2953, 2931, 2895, 2859, 1718, 1636, 1465, 1434, 1382, 1283, 1254, 1209, 1089, 1006, 911, 833, 774, 663$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) = 0.04 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.87 (s, 3H,  $\text{CH}_3\text{C}=\text{C}$ ), 1.98 (m, 3H,  $\text{C}=\text{CCH}_3$ ), 2.39 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.68 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 3.71 (s, 3H,  $\text{CH}_3\text{O}$ ).  **$^{13}\text{C}\{^1\text{H}\}\text{-NMR}$**  ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) = -5.3 ( $(\text{CH}_3)_2\text{Si}$ ), 15.7 ( $\text{CH}_3\text{C}=\text{C}$ ), 18.4 ( $(\text{CH}_3)_3\text{CSi}$ ), 21.7 ( $\text{C}=\text{CCH}_3$ ), 26.0 ( $(\text{CH}_3)_3\text{CSi}$ ), 39.6 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 51.4 ( $\text{CH}_3\text{O}$ ), 61.1 ( $\text{CH}_2\text{CH}_2\text{OTBDMS}$ ), 124.3 ( $\text{CH}_3\text{C}=\text{C}$ ), 143.4 ( $\text{C}=\text{CCH}_3$ ), 170.3 ( $\text{C}=\text{O}$ ). **LRMS (IC) (IS)** = found  $[\text{M}+\text{H}]^+ = 273$ .

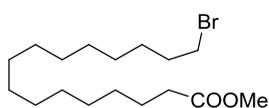
**Methyl (*E*)-5-hydroxy-2,3-dimethylpent-2-enoate (**4x**):** The reaction was run according to GP4 starting from methyl (*E*)-((tert-butylidimethylsilyloxy)-2,3-dimethylpent-2-enoate (2.78 mmol). After purification by flash chromatography on silica gel (Pentane/Diethyl ether 1:1), **4x** was obtained in 95% yield (420 mg) as a colourless oil. (*E*)-isomer:  $R_f = 0.3$  (Pentane/Diethyl ether 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3413, 2941, 1706, 1633, 1435, 1377, 1283, 1210, 1099, 1037, 991, 873, 773, 532$ .  **$^1\text{H-NMR}$**  ( $\text{C}_6\text{D}_6$ , 500 MHz):  $\delta$  (ppm) 1.41 (bs, 1H, OH), 1.81 (m, 2H,  $\text{CH}_3\text{C}=\text{C}$ ), 1.90 (q,  $^3J_{\text{HH}} = 1.5$  Hz, 2H,  $\text{C}=\text{CCH}_3$ ), 2.36 (t,  $^3J_{\text{HH}} = 6.8$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ), 3.63 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.65 (bt,  $^3J_{\text{HH}} = 5.9$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{OH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$ -NMR** ( $\text{C}_6\text{D}_6$ , 126 MHz):  $\delta$  (ppm) = 15.7 ( $\text{CH}_3\text{C}=\text{C}$ ), 21.4 ( $\text{C}=\text{CCH}_3$ ), 39.4 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 50.9 ( $\text{CH}_3\text{O}$ ), 60.3 ( $\text{CH}_2\text{CH}_2\text{OH}$ ), 124.9 ( $\text{CH}_3\text{C}=\text{C}$ ), 143.5 ( $\text{C}=\text{CCH}_3$ ), 169.5 ( $\text{C}=\text{O}$ ). **GC-MS** found  $[\text{M}] = 158$  (1%);  $[\text{M}] - \text{H}_2\text{O} = 140$  (38%),  $[\text{M}] - \text{CH}_3\text{OH} = 128$  (59%);  $[\text{M}] - \text{CH}_2\text{CH}_2\text{OH} = 110$  (15%);  $[\text{M}] - 3\text{CH}_3, -\text{OH} = 96$  (87%),  $[\text{M}] - \text{CH}_3\text{O}, -2\text{CH}_3, -\text{OH} = 79$  (52%);  $[\text{M}] - \text{CH}_3\text{OOC}, -\text{CH}_3, -\text{OH} = 67$  (100%);  $[\text{M}] - \text{CH}_3\text{OOC}, -2\text{CH}_3, -\text{OH} = 53$  (62%).



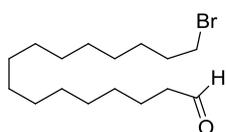
**Figure S28:** Synthesis of Ethyl 34-hydroxy-2-methylpentatriacont-2-enoate (**4y**)



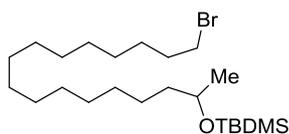
**Methyl 16-Hydroxyhexadecanoate:** This compound was prepared from the corresponding lactone according to the literature<sup>28</sup> and used without further purification.



**Methyl 16-bromohexadecanoate:** Triphenylphosphine (6.5 g, 25 mmol) was added to a stirred solution of methyl 16-hydroxyhexadecanoate (5.72 g, 20 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 mL) before NaHCO<sub>3</sub> (0.14 g) was added. The mixture was cooled to 0 °C and *N*-bromosuccinimide (NBS) (4.34 g, 26 mmol) was added in three portions over 20 minutes. After 1 h at room temperature Tlc analysis revealed complete disappearance of the starting material. A saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (120 mL) was added and the organic layer was separated. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 30 mL) and the combined organic layers were washed with water (100 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) to give the title compound as a white solid in 93% yield (6.5 g). All spectroscopic analyses were in agreement with those reported in the literature.<sup>29</sup>

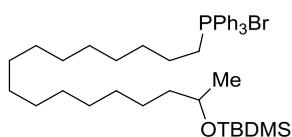


**16-bromohexadecanal:** To a solution of methyl 16-bromohexadecanoate (3.2 g, 10 mmol) in toluene (50 mL) at -78°C, diisobutylaluminium hydride (DIBAL-H) (21 mL, 1 M in THF) was added dropwise and stirred for 10 minutes at this temperature before warming up to 0 °C and stirring for an additional 30 minutes. The reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (2 mL) at 0° C and diluted with diethyl ether (100 mL). Stirring was continued for an additional 3 h. The mixture was extracted with diethyl ether (2 × 30 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The crude mixture was used for the following Swern oxidation (according to GP5). After purification by flash chromatography on silica gel (Pentane/Diethyl ether = 60:1) the product was obtained in 77% yield (2.4 g) over two steps. **R<sub>f</sub>** = 0.7 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2917, 2849, 1701, 1470, 1209, 719. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.17 – 1.38 (m, 20H, (CH<sub>2</sub>)<sub>10</sub>), 1.39 – 1.51 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 1.58 – 1.72 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 1.79 – 1.96 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 2.42 (td, <sup>3</sup>J<sub>HH</sub> = 7.4, 1.9 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 3.41 (t, <sup>3</sup>J<sub>HH</sub> = 6.9 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 9.76 (t, <sup>3</sup>J<sub>HH</sub> = 1.9 Hz, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 22.2 (CH<sub>2</sub>CH<sub>2</sub>CHO), 28.3 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 28.9 (CH<sub>2</sub>), 29.3 (CH<sub>2</sub>), 29.5 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.8 (CH<sub>2</sub>), 33.0 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 34.2 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Br), 44.1 (CH<sub>2</sub>CHO), 203.1 (CHO). **LRMS (IC)** found [M+NH<sub>4</sub>]<sup>+</sup> = 336.



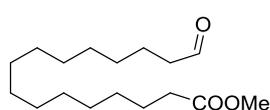
**((17-bromoheptadecan-2-yl)oxy)(tert-butyl)dimethylsilane:** To a

solution of 16-bromohexadecanal (1.7 g, 5.3 mmol) in THF (75 mL), MeMgBr (2.65 mL, 7.95 mmol, 3 M in THF) was added dropwise at  $-78\text{ }^{\circ}\text{C}$ . The mixture was warmed up to room temperature and stirred for 20 minutes then it was quenched with aqueous HCl (1 N, 8 mL) at  $0\text{ }^{\circ}\text{C}$  and stirred for 30 minutes. The mixture was dried over anhydrous  $\text{Na}_2\text{SO}_4$  then filtrated through a pad of silica gel and flushed with diethyl ether (50 mL). The volatiles were evaporated in vacuo to give 1.7 g of crude product, which was redissolved in  $\text{CH}_2\text{Cl}_2$  (40 mL) at  $0\text{ }^{\circ}\text{C}$ . Imidazole (0.42 g, 5.5 mmol) and DMAP (70 mg, 4 mol%) were added and stirred for 10 minutes. TBDMSCI (791 mg, 4.72 mmol) was added and stirred overnight at room temperature then quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  solution and extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 40 mL). The combined organic phases were dried over  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 40:1) to give the product in 88% yield (2.1 g) over two steps.  $R_f = 0.9$  (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2926, 2855, 2349, 1464, 1373, 1253, 1061, 835, 774, 526$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.04 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.11 (d,  $^3J_{\text{HH}} = 6.0\text{ Hz}$ , 3H,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.23 – 1.46 (m, 26H,  $(\text{CH}_2)_{13}$ ), 1.94 – 1.78 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Br}$ ), 3.41 (t,  $^3J_{\text{HH}} = 6.9\text{ Hz}$ , 2H,  $\text{CH}_2\text{CH}_2\text{Br}$ ), 3.66 – 3.85 (m, 1H,  $\text{CH}_3\text{CHOTBDMS}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -4.5 ( $(\text{CH}_3)_2\text{Si}$ ), -4.2 ( $(\text{CH}_3)_2\text{Si}$ ), 18.3 ( $(\text{CH}_3)_3\text{CSi}$ ), 24.0 ( $\text{CH}_3\text{CHOTBDMS}$ ), 26.0 ( $\text{CH}_2$ ), 26.1 ( $(\text{CH}_3)_3\text{CSi}$ ), 28.3 ( $\text{CH}_2$ ), 28.9 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 29.8 ( $\text{CH}_2$ ), 29.8 ( $\text{CH}_2$ ), 29.8 ( $\text{CH}_2$ ), 29.8 ( $\text{CH}_2$ ), 33.0 ( $\text{CH}_2\text{CH}_2\text{Br}$ ), 34.2 ( $\text{CH}_2\text{CH}_2\text{Br}$ ), 39.9 ( $\text{CH}_2\text{CHOTBDMS}$ ), 68.8 ( $\text{CH}_2\text{CHOTBDMS}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 468$ .

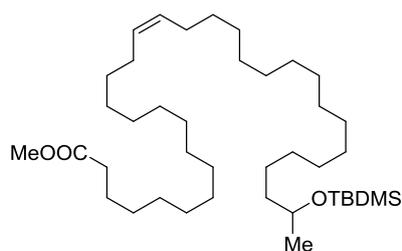


**Bromo(16-((tert-butyl dimethylsilyl)oxy)heptadecyl)triphenyl-15-**

**phosphane:** In a round-bottom flask, triphenylphosphine (1.68 g, 6.44 mmol) and ((17-bromoheptadecan-2-yl)oxy)(tert-butyl)dimethylsilane (2.1 g, 4.6 mmol) were added. The reaction mixture was heated at  $110\text{ }^{\circ}\text{C}$  and monitored by  $^1\text{H NMR}$  until the starting material was consumed completely (ca. 24 h). The resulting oil was engaged in the next step without further purification.

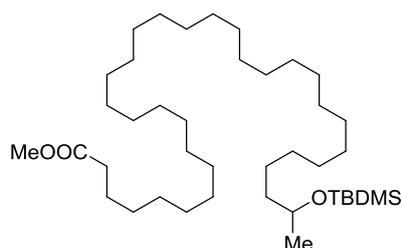


**Methyl 16-oxohexadecanoate:** This compound was prepared according to a literature procedure,<sup>29</sup> starting from methyl 16-hydroxyhexadecanoate (1.43 g, 5 mmol). The crude mixture was filtered through silica gel affording the product in 91% yield (1.3 g). All spectroscopic analyses were in agreement with those reported in the literature.<sup>30</sup>



**Methyl (Z)-32-((tert-butyl dimethylsilyl)oxy)trtriacont-16-enoate:**

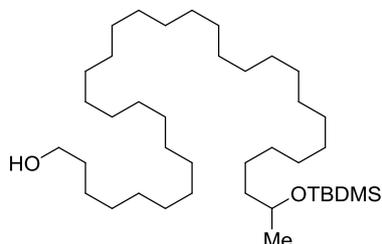
Bromo-(16-((tert-butyl dimethylsilyl)oxy)heptadecyl)triphenyl-15-phosphane (3.5 mmol) was dissolved in  $\text{CH}_2\text{Cl}_2$  (20 mL) and sodium hexamethyldisilazide (NaHMDS, 1.75 mL from a 2 M sol. in THF) was added at 0 °C and stirred for 15 minutes. Methyl 16-oxohexadecanoate in  $\text{CH}_2\text{Cl}_2$  (10 mL) was added dropwise at -78 °C and stirred at room temperature for 1 h. The reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (10 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (2 x 20 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo*. The crude mixture was purified by flash chromatography (Pentane/Diethyl ether = 30:1) to give the title product as a colourless oil in 36% yield (570 mg).  $R_f = 0.6$  (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2925, 2854, 1744, 1463, 1372, 835, 774$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.04 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.11 (d,  $^3J_{\text{HH}} = 6.0$  Hz, 3H,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.16 – 1.49 (m, 50H,  $25 \times \text{CH}_2$ ), 1.56 – 1.68 (m, 2H,  $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 1.90 – 2.08 (m, 4H,  $\text{CH}_2\text{CH}=\text{CHCH}_2$ ), 2.30 (td,  $^3J_{\text{HH}} = 7.6$ ,  $^2J_{\text{HH}} = 1.1$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 3.66 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.72 – 3.83 (m, 1H,  $\text{CH}_2\text{CHOTBDMS}$ ), 5.34 (td,  $^3J_{\text{HH}} = 4.5, 2.4$  Hz, 2H,  $\text{CH}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) -4.5 ( $(\text{CH}_3)_2\text{Si}$ ), -4.2 ( $(\text{CH}_3)_2\text{Si}$ ), 18.3 ( $(\text{CH}_3)_3\text{CSi}$ ), 24.0 ( $\text{CH}_3\text{CHOTBDMS}$ ), 25.1 ( $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 26.0 ( $\text{CH}_2$ ), 26.1 ( $(\text{CH}_3)_3\text{CSi}$ ), 27.4 ( $\text{CH}_2\text{CH}=\text{CHCH}_2$ ), 29.3 – 29.9 ( $23 \times \text{CH}_2$ ), 34.3 ( $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 39.9 ( $\text{CH}_2\text{CHOTBDMS}$ ), 51.6 ( $\text{CH}_3\text{O}$ ), 68.8 ( $\text{CH}_2\text{CHOTBDMS}$ ), 130.0 ( $\text{CH}=\text{CH}$ ), 174.5 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 655$ .



**Methyl 32-((tert-butyl dimethylsilyl)oxy)trtriacontanoate:**

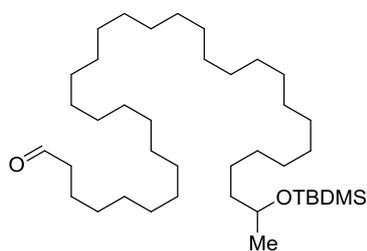
Methyl (Z)-32-((tert-butyl dimethylsilyl)oxy)trtriacont-16-enoate (570 mg.) and  $[\text{Ir}(\text{cod})(\text{PCy}_3)(\text{py})]$   $\text{BAR}_\text{F}$  (46 mg, 5 mol%) were dissolved in  $\text{CH}_2\text{Cl}_2$  (5 mL) in a 7 mL vial. The mixture was put into autoclave and filled with  $\text{H}_2$  under 40 bar pressure. After 4 h stirring, the autoclave was carefully opened to release  $\text{H}_2$  and the mixture was diluted with  $\text{CH}_2\text{Cl}_2$  (10 mL), quenched with water (15 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 10 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo* to give the desired product in 92% yield (458 mg) as a white wax.  $R_f = 0.6$  (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2918, 2850, 1743, 1462, 1372, 732$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.04 (s, 6H,  $(\text{CH}_3)_2\text{Si}$ ), 0.88 (s, 9H,  $(\text{CH}_3)_3\text{CSi}$ ), 1.11 (d,  $^3J_{\text{HH}} = 6.1$  Hz, 3H,  $\text{CH}_3\text{CHOTBDMS}$ ), 1.23 – 1.41 (m, 56H,  $(\text{CH}_2)_{28}$ ), 1.62 (t,  $^3J_{\text{HH}} = 7.3$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 2.30 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{COOMe}$ ), 3.66 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.70 – 3.81 (m, 1H,  $\text{CH}_2\text{CHOTBDMS}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR**

(101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -4.5 ((CH<sub>3</sub>)<sub>2</sub>Si), -4.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 24.0 (CH<sub>3</sub>CHOTBDMS), 25.1 (CH<sub>2</sub>CH<sub>2</sub>COOMe), 26.0 (CH<sub>2</sub>), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 29.3 – 29.8 (27  $\times$  CH<sub>2</sub>), 34.3 (CH<sub>2</sub>CH<sub>2</sub>COOMe), 40.0 (CH<sub>2</sub>CHOTBDMS), 51.6 (CH<sub>3</sub>O), 68.8 (CH<sub>2</sub>CHOTBDMS), 174.5 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 640.



**32-((tert-butyl dimethylsilyloxy)trtriacontan-1-ol:** To a solution of methyl 32-((tert-butyl dimethylsilyloxy)trtriacontanoate (458 mg, 0.72 mmol) in toluene (2.5 mL) at -78 °C, DIBAL-H (1.6 mL, 1 M in THF) was added dropwise and stirred for 10 minutes. The mixture was warmed to 0 °C and stirred for 30 minutes, then

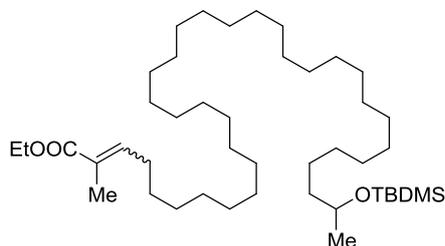
quenched with saturated aqueous NH<sub>4</sub>Cl solution (0.5 mL) at the same temperature. The mixture was diluted with diethyl ether (10 mL), stirred for 3 h and then dried by adding anhydrous Na<sub>2</sub>SO<sub>4</sub>. After 1 h, Na<sub>2</sub>SO<sub>4</sub> was removed by filtration, washed with diethyl ether (3  $\times$  10 mL) and the organic phase concentrated *in vacuo* to give the title compound in 93% yield (410 mg). It was used for next step without further purification.



**32-((tert-butyl dimethylsilyloxy)trtriacontanal:** To a solution of Dess–Martin periodinane (DMP, 0.57 mmol, 240 mg) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL), 32-((tert-butyl dimethylsilyloxy)trtriacontan-1-ol (0.47 mmol, 288 mg) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added dropwise at 0 °C. After 40 minutes at room temperature, another portion of DMP (0.57

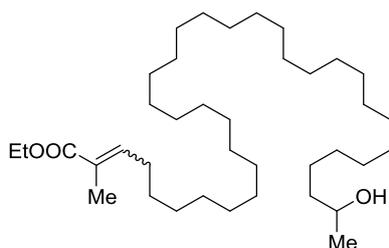
mmol, 240 mg) was added and stirred 40 minutes. This sequence was repeated one more time. The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and a solution of K<sub>2</sub>CO<sub>3</sub> (1.5 g) in water (10 mL) was added. The biphasic system was stirred for 20 minutes. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2  $\times$  3 mL) and the combined organic phases were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) to afford the title compound in 70% yield (200 mg) as a colourless oil. **R<sub>f</sub>** = 0.8 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu$ (cm<sup>-1</sup>) = 2917, 2850, 1725, 1463, 1353, 1135, 835. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.11 (d, <sup>3</sup>J<sub>HH</sub> = 6.0 Hz, 3H, CH<sub>3</sub>CHOTBDMS), 1.18 – 1.43 (m, 56H, (CH<sub>2</sub>)<sub>28</sub>), 1.58 – 1.70 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.42 (td, <sup>3</sup>J<sub>HH</sub> = 7.4, 1.9 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 3.69 – 3.83 (m, 1H, CH<sub>3</sub>CHOTBDMS), 9.76 (t, <sup>3</sup>J<sub>HH</sub> = 1.9 Hz, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -4.5 ((CH<sub>3</sub>)<sub>2</sub>Si), -4.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 22.2 (CH<sub>2</sub>CH<sub>2</sub>CHO), 24.0 (CH<sub>3</sub>CHOTBDMS), 26.0 (CH<sub>2</sub>), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 29.3 (CH<sub>2</sub>), 29.5

(CH<sub>2</sub>), 29.6 (CH<sub>2</sub>), 29.7 (CH<sub>2</sub>), 29.8 – 29.9 (CH<sub>2</sub> × 22), 39.9 (CH<sub>2</sub>CHOTBDMS), 44.1 (CH<sub>2</sub>CH<sub>2</sub>CHO), 68.8 (CH<sub>2</sub>CHOTBDMS), 203.1 (CHO). **LRMS (IC)** found [M+H]<sup>+</sup> = 610.



**Ethyl 34-((tert-butylidimethylsilyl)oxy)-2-methylpentatriacont-2-enoate:**

Lithium hexamethyldisilazide (LiHMDS, 1 mmol, 1 mL, 1.0 M in THF) was added dropwise to a solution of triethylphosphopropionate (236 mg, 0.99 mmol) in THF (3 mL) at 0 °C. After 15 minutes, 32-((tert-butylidimethylsilyl)oxy)trtriacontanal (200 mg, 0.33 mmol) in THF (2 mL) was added dropwise. After 1 h, the reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (0.5 mL), washed with water (15 mL), extracted with diethyl ether (3 × 10 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and then concentrated *in vacuo*. The residue was purified by flash chromatography (Hexane/Diethyl ether = 10:1) to afford the title compound in 87% yield (200 mg, *E/Z* = 2.3:1) as a colourless wax. **R<sub>f</sub>** = 0.6 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2919, 2850, 1717, 1650, 1469, 1371, 1254, 835. (*E*)-isomer: **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.11 (d, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CHOTBDMS), 1.24 – 1.41 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O; 56H, (CH<sub>2</sub>)<sub>28</sub>), 1.41 – 1.47 (m, 2H, CH<sub>2</sub>), 1.80 – 1.84 (m, 3H, CH<sub>3</sub>C=CH), 2.12 – 2.20 (m, 2H, C=CHCH<sub>2</sub>), 3.69 – 3.84 (m, 1H, CH<sub>3</sub>CHOTBDMS), 4.19 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.76 (tq, <sup>3</sup>J<sub>HH</sub> = 7.5, <sup>4</sup>J<sub>HH</sub> = 1.4 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -4.5 ((CH<sub>3</sub>)<sub>2</sub>Si), -4.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 12.5 (CH<sub>3</sub>C=CH), 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 18.3 ((CH<sub>3</sub>)<sub>3</sub>C=CH), 24.0 (CH<sub>3</sub>CHOTBDMS), 26.0 (CH<sub>2</sub>), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 28.7 – 29.9 (28 × CH<sub>2</sub>), 39.9 (CH<sub>2</sub>CHOTBDMS), 60.5 (CH<sub>3</sub>CH<sub>2</sub>O), 68.8 (CH<sub>3</sub>CHOTBDMS), 127.8 (C=CH), 142.6 (C=CH), 168.51 (C=O). (*Z*)-isomer: **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.11 (d, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CHOTBDMS), 1.24 – 1.41 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O; 56H, (CH<sub>2</sub>)<sub>28</sub>), 1.41 – 1.47 (m, 2H, CH<sub>2</sub>), 1.88 – 1.91 (m, 3H, CH<sub>3</sub>C=CH), 2.39 – 2.50 (m, 2H, C=CHCH<sub>2</sub>), 3.69 – 3.84 (m, 1H, CH<sub>3</sub>CHOTBDMS), 4.19 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.92 (tq, <sup>3</sup>J<sub>HH</sub> = 7.6, <sup>4</sup>J<sub>HH</sub> = 1.6 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -4.5 ((CH<sub>3</sub>)<sub>2</sub>Si), -4.2 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 20.8 (CH<sub>3</sub>C=CH), 24.0 (CH<sub>3</sub>CHOTBDMS), 26.0 (CH<sub>2</sub>), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 28.7 – 29.8 (28 × CH<sub>2</sub>), 39.9 (CH<sub>2</sub>CHOTBDMS), 60.1 (CH<sub>3</sub>CH<sub>2</sub>O), 68.8 (CH<sub>3</sub>CHOTBDMS), 128.6 (C=CH), 143.3 (C=CH), 168.51 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 694.



**Ethyl 34-hydroxy-2-methylpentatriacont-2-enoate (4y):**

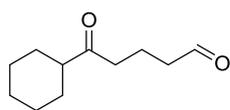
Ethyl 34-((*tert*-butyldimethylsilyl)oxy)-2-methylpentatriacont-2-enoate (270 mg, 0.39 mmol) was added to a solution of HCl in ethanol (1.25 M, 6.24 mL, 7.8 mmol) at room temperature. After stirring for 3 h, the reaction was diluted with water (15 mL), extracted with diethyl ether (3 × 30 mL),

dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 2:1) to afford **4y** in 75% yield (170 mg, *E/Z* = 2.9:1) as white wax. *R<sub>f</sub>* = 0.3 (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 2916, 2849, 1710, 1648, 1462, 1370, 728. (*E*)-isomer: **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.19 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CHOH), 1.24 – 1.49 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O; 58H, (CH<sub>2</sub>)<sub>29</sub>; 1H, OH), 1.79 – 1.85 (m, 3H, CH<sub>3</sub>C=CH), 2.10 – 2.22 (m, 2H, C=CHCH<sub>2</sub>), 3.74 – 3.85 (m, 1H, CH<sub>3</sub>CHOH), 4.19 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.76 (tq, <sup>3</sup>*J*<sub>HH</sub> = 7.5, <sup>4</sup>*J*<sub>HH</sub> = 1.4 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 12.5 (CH<sub>3</sub>C=CH), 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 23.6 (CH<sub>3</sub>CHOH), 25.9 (CH<sub>2</sub>), 28.7 – 29.8 (28 × CH<sub>2</sub>), 39.5 (CH<sub>2</sub>CHOH), 60.5 (CH<sub>3</sub>CH<sub>2</sub>O), 68.4 (CH<sub>2</sub>CHOH), 127.8 (C=CH), 142.6 (C=CH), 168.5 (C=O). (*Z*)-isomer: **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.19 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CHOH), 1.24 – 1.49 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O; 58H, (CH<sub>2</sub>)<sub>29</sub>; 1H, OH), 1.79 – 1.85 (m, 2H), 1.87 – 1.92 (m, 3H, CH<sub>3</sub>C=CH), 2.37 – 2.50 (m, 2H, C=CHCH<sub>2</sub>), 3.74 – 3.85 (m, 1H, CH<sub>3</sub>CHOH), 4.19 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.92 (tq, <sup>3</sup>*J*<sub>HH</sub> = 7.6, <sup>4</sup>*J*<sub>HH</sub> = 1.6 Hz, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 20.8 (CH<sub>3</sub>C=CH), 23.6 (CH<sub>3</sub>CHOH), 25.9 (CH<sub>2</sub>), 28.7 – 29.9 (28 × CH<sub>2</sub>), 39.5 (CH<sub>2</sub>CHOH), 60.2 (CH<sub>3</sub>CH<sub>2</sub>O), 68.4 (CH<sub>3</sub>CHOH), 127.1 (C=CH), 143.3 (C=CH), 168.50 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 580.

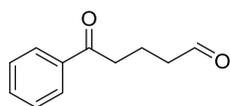
### 2.3 Characterization of isomerization products

**Ethyl 5-oxopentanoate (3a):** 19 mg, 53% yield. Colourless oil, **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.25 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 3H), 1.86 – 2.03 (m, 2H), 2.36 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.2 Hz, 2H), 2.53 (td, <sup>3</sup>*J*<sub>HH</sub> = 7.2, 1.3 Hz, 2H), 4.13 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H), 9.77 (t, <sup>3</sup>*J*<sub>HH</sub> = 1.4 Hz, 1H). The other spectroscopic analyses were in agreement with those reported in the literature.<sup>31</sup>

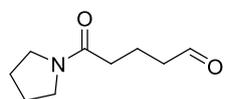
**5-oxohexanal (3c):** 13 mg, 46% yield. Colourless oil, **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.82 – 1.97 (m, 2H), 2.14 (s, 3H), 2.40 – 2.59 (m, 4H), 9.76 (t, <sup>3</sup>*J*<sub>HH</sub> = 1.4 Hz, 1H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>32</sup>



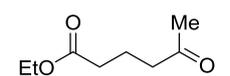
**5-cyclohexyl-5-oxopentanal (3d):** 28 mg, 61% yield. Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.17 – 1.36 (m, 5H), 1.63 – 1.71 (m, 1H), 1.74 – 1.83 (m, 4H), 1.90 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H), 2.22 – 2.38 (m, 1H), 2.43 – 2.57 (m, 4H), 9.75 (t,  $^3J_{\text{HH}} = 1.5$  Hz, 1H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>32</sup>



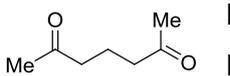
**5-oxo-5-phenylpentanal (3e):** 33 mg, 75% yield. Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 2.01 – 2.13 (m, 2H), 2.60 (td,  $^3J_{\text{HH}} = 7.1$ , 1.3 Hz, 2H), 3.05 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 2H), 7.40 – 7.51 (m, 2H), 7.51 – 7.64 (m, 1H), 7.83 – 8.10 (m, 2H), 9.82 (t,  $^3J_{\text{HH}} = 1.3$  Hz, 1H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>32</sup>



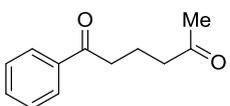
**5-oxo-5-(pyrrolidin-1-yl)pentanal (3f):** 21 mg, 50% yield. Colourless oil.  $R_f = 0.1$  (Diethyl ether/EtOAc = 1:2). IR (neat):  $\nu(\text{cm}^{-1}) = 2953, 2875, 1719, 1631, 1433$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 1.79 – 1.88 (m, 2H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 1.88 – 1.98 (m, 2H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.27 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.50 (td,  $^3J_{\text{HH}} = 7.1$ ,  $^3J_{\text{HH}} = 1.5$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO}$ ), 3.28 – 3.50 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 9.74 (t,  $^3J_{\text{HH}} = 1.5$  Hz, 1H, CHO).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 17.7 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 24.8 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 26.5 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 33.7 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO}$ ), 43.7 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CHO}$ ), 45.9 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 46.8 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 170.6 (C=O), 202.6 (CHO). LRMS (IC) found  $[\text{M}+\text{H}]^+ = 170$



**Ethyl 5-oxohexanoate (3g):** 30 mg, 94% yield. Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.25 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H), 1.84 – 1.96 (m, 2H), 2.14 (s, 3H), 2.32 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 2H), 2.50 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 2H), 4.12 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>33</sup>

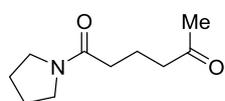


**Heptane-2,6-dione (3h):** 19 mg, 59% yield. Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.83 (p,  $^3J_{\text{HH}} = 7.1$  Hz, 2H), 2.13 (s, 6H), 2.47 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 4H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>34</sup>

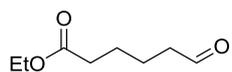


**1-phenylhexane-1,5-dione (3i):** 44 mg, 94% yield. Colourless oil.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.94 – 2.08 (m, 2H), 2.16 (s, 3H), 2.58 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 2H), 3.02 (t,  $^3J_{\text{HH}} = 7.0$  Hz, 2H), 7.46 (dd,  $^3J_{\text{HH}} = 8.4, 6.9$

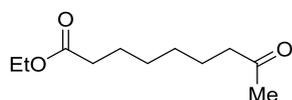
Hz, 2H), 7.53 – 7.65 (m, 1H), 7.91 – 8.03 (m, 2H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>35</sup>



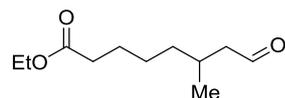
**1-(pyrrolidin-1-yl)hexane-1,5-dione (3j):** 44 mg, 96% yield. Colorless oil.  $R_f = 0.5$  (MeOH/ EtOAc = 1:10). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2962, 2950, 2874, 1710, 1630, 1433, 1354, 1278, 1125$ .  **$^1\text{H NMR}$**  (500 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 1.73 – 1.85 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 1.86 – 1.96 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 2.08 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.22 (t,  $^3J_{\text{HH}} = 7.3$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 2.49 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 3.29 – 3.42 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (126 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 19.3 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 24.8 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 26.5 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 30.0 ( $\text{CH}_3\text{CO}$ ), 33.9 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 43.2 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 45.9 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 46.8 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 171.0 ( $\text{C}=\text{O}$ ), 208.8 ( $\text{COCH}_3$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 184$ .



**Ethyl 6-oxohexanoate (3k):** 44 mg, 56% yield. Colourless oil.  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.25 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H), 1.60 – 1.73 (m, 4H), 2.24 – 2.55 (m, 4H), 4.13 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H), 9.77 (q,  $^3J_{\text{HH}} = 1.9$  Hz, 1H). All other spectroscopic analyses were in agreement with those reported in the literature.<sup>36</sup>

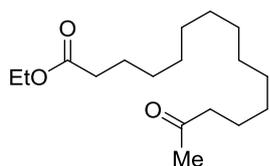


**Ethyl 8-oxononanoate (3l):** 42 mg, 84% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2936, 2860, 1732, 1176, 1034$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.25 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.28 – 1.36 (m, 4H,  $(\text{CH}_2)_2\text{CH}_2\text{CH}_2(\text{CH}_2)_2\text{COCH}_3$ ), 1.52 – 1.69 (m, 4H,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_2\text{CH}_2\text{CH}_2\text{COCH}_3$ ), 2.13 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.28 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 2H,  $\text{CH}_2(\text{CH}_2)_5\text{CO}$ ), 2.42 (t,  $^3J_{\text{HH}} = 7.4$  Hz, 2H,  $(\text{CH}_2)_5\text{CH}_2\text{CO}$ ), 4.12 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.7 ( $(\text{CH}_2)_4\text{CH}_2\text{CH}_2\text{CO}$ ), 24.9 ( $\text{CH}_2(\text{CH}_2)_5$ ), 28.9 ( $(\text{CH}_2)_5\text{CH}_2\text{CO}$ ), 29.0 ( $(\text{CH}_2)_2\text{CH}_2(\text{CH}_2)_3\text{CO}$ ), 30.0 ( $\text{CH}_3\text{CO}$ ), 34.4 ( $(\text{CH}_2)_5\text{CH}_2\text{CO}$ ), 43.8 ( $\text{CH}_2(\text{CH}_2)_5\text{CO}$ ), 60.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 173.9 ( $\text{COOEt}$ ), 209.3 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}-\text{H}]^+ = 199$ .



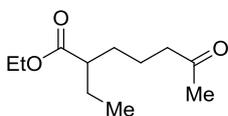
**Ethyl 6-methyl-8-oxooctanoate (3m):** 36 mg, 72% yield. Colourless oil.  $R_f = 0.6$  (Pentane/Diethyl ether = 3:2). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2933, 2718, 1727, 1462, 1374, 1239, 1168, 1104, 1033, 858, 738$ .  **$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 0.96 (d, 3H,  $^3J_{\text{HH}} = 6.7$  Hz,  $\text{CHCH}_3$ ), 1.22 – 1.41 (m, 4H,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_2$ ), 1.25 (t, 3H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.58 – 1.64 (m, 2H,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_2$ ), 2.05 (dh, 1H,  $^3J_{\text{HH}} = 13.9, 6.9$  Hz,  $\text{CHCH}_3$ ), 2.20 – 2.26 (ddd, 1H,  $^3J_{\text{HH}} = 16.1, 7.8, ^2J_{\text{HH}} = 2.5$  Hz,  $\text{CH}_2\text{CHO}$ ), 2.29 (t, 2H,  $^3J_{\text{HH}} = 7.5$  Hz,  $\text{CH}_2\text{CH}_2(\text{CH}_2)_2$ ), 2.36 – 2.40

(ddd, 1H,  $^3J_{\text{HH}} = 16.1, 5.7, ^2J_{\text{HH}} = 1.9$  Hz,  $\text{CH}_2\text{CHO}$ ), 4.12 (q, 2H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 9.75 (bd, 1H,  $^3J_{\text{HH}} = 2.2$  Hz,  $\text{CHO}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 20.0 ( $\text{CHCH}_3$ ), 25.1 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 26.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 28.1 ( $\text{CHCH}_3$ ), 34.4 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 36.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$ ), 51.1 ( $\text{CH}_2\text{CHO}$ ), 60.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 173.8 ( $\text{C}=\text{O}$ ), 203.0 ( $\text{CHO}$ ). LRMS (IC) found  $[\text{M}+\text{H}]^+ = 201$ .



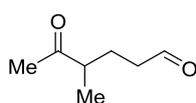
**Ethyl 14-oxopentadecanoate (3n):** 60 mg, 85% yield. Colourless solid. **Mp:** 37°C. **R<sub>f</sub>** = 0.5 (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2987, 2920, 1731, 1465, 1172, 1030$ .  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.24 – 1.30 (m, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ; 16H,  $\text{COCH}_2(\text{CH}_2)_8$ ),

1.55 – 1.67 (m, 2H,  $\text{COCH}_2\text{CH}_2$ ; 2H,  $\text{EtOCOCH}_2\text{CH}_2$ ), 2.13 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.28 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 2H,  $\text{EtOCOCH}_2$ ), 2.41 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 2H,  $\text{CH}_3\text{COCH}_2$ ), 4.12 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 24.0 ( $\text{CH}_3\text{COCH}_2\text{CH}_2$ ), 25.1 ( $\text{EtOCOCH}_2\text{CH}_2$ ), 29.3 ( $\text{CH}_2$ ), 29.3 ( $\text{CH}_2$ ), 29.4 ( $\text{CH}_2$ ), 29.5 ( $\text{CH}_2$ ), 29.6 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 30.0 ( $\text{CH}_3\text{CO}$ ), 34.6 ( $\text{CH}_3\text{COCH}_2$ ), 44.0 ( $\text{EtOOCCH}_2$ ), 60.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 174.1 ( $\text{EtOCO}$ ), 209.6 ( $\text{COCH}_3$ ). LRMS (IC) found  $[\text{M}+\text{H}]^+ = 285$ ;  $[\text{M}+\text{NH}_4]^+ = 302$ .



**Ethyl 2-ethyl-6-oxoheptanoate (3p):** 18 mg, 73% yield. Colourless oil. **R<sub>f</sub>** = 0.6 (Pentane/Diethyl ether 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2962, 2942, 2878, 1730, 1721, 1459, 1411, 1367, 1264, 1226, 1180, 1153, 1094,$

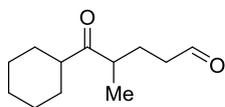
1028, 958, 859, 776, 752, 726, 595.  **$^1\text{H}$ -NMR** ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.88 (t,  $^3J_{\text{HH}} = 7.4$  Hz, 3H,  $\text{CHCH}_2\text{CH}_3$ ), 1.25 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.42 – 1.64 (m, 62H,  $\text{CHCH}_2\text{CH}_3$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 2.12 (s, 3H,  $\text{COCH}_3$ ), 2.25 (m, 1H,  $\text{CHCH}_2\text{CH}_3$ ), 2.42 (bt, 2H,  $^3J_{\text{HH}} = 6.9$  Hz,  $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 4.13 (qd, 2H,  $^3J_{\text{HH}} = 7.1$  Hz, 1.3 Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$ -NMR ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) 11.9 ( $\text{CHCH}_2\text{CH}_3$ ), 14.5 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 21.8 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 25.6 ( $\text{CHCH}_2\text{CH}_3$ ), 30.0 ( $\text{COCH}_3$ ), 31.5 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 43.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}$ ), 47.2 ( $\text{CHCH}_2\text{CH}_3$ ), 60.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 176.2 ( $\text{EtO}_2\text{C}$ ), 208.8 ( $\text{COCH}_3$ ). LRMS (IC) found  $[\text{M}+\text{H}]^+ = 201$ .



**4-methyl-5-oxohexanal (5a):** 19 mg, 60% yield. Colourless oil. **R<sub>f</sub>** = 0.1 (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2930, 1709, 1459, 1359, 1169$ .  **$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.13 (d,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,

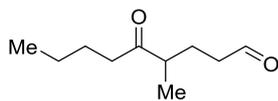
$\text{CH}_3\text{CH}$ ), 1.63 – 1.76 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ) 1.92 – 2.07 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.16 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.39 – 2.51 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.51 – 2.66 (m, 1H,  $\text{CH}_3\text{CH}$ ), 9.76 (t,  $^3J_{\text{HH}} = 1.4$  Hz, 1H,  $\text{CHO}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 16.6 ( $\text{CH}_3\text{CH}$ ), 24.6 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ),

28.4 (CH<sub>3</sub>CO), 41.5 (CH<sub>2</sub>CHO), 46.2 (CH<sub>3</sub>CH), 201.8 (CHO), 211.8 (CH<sub>3</sub>CO). **LRMS (IC)** found [M-OH]<sup>+</sup> = 111.



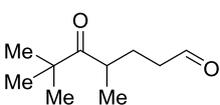
**5-cyclohexyl-4-methyl-5-oxopentanal (5b):** 32 mg, 65% yield.

Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3409, 2928, 2854, 1722, 1703, 1449, 992$ . **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.08 (d,  $^3J_{\text{HH}} = 7.0$  Hz, 3H, CH<sub>3</sub>CH), 1.14 – 1.44 (m, 5H, CH<sub>2</sub>-Cy), 1.59 – 1.84 (m, 4H, CH<sub>2</sub>-Cy), 1.59 – 1.66 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 1.92 – 2.01 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.30 – 2.51 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO; 1H, CH-Cy), 2.66 – 2.86 (m, 1H, CH<sub>3</sub>CH), 9.74 (t,  $^3J_{\text{HH}} = 1.5$  Hz, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 17.1 (CH<sub>3</sub>CH), 24.9 (CH<sub>2</sub>CH<sub>2</sub>CHO), 25.7 (CH<sub>2</sub>-Cy), 25.9 (CH<sub>2</sub>-Cy), 28.4 (CH<sub>2</sub>-Cy), 28.8 (CH<sub>2</sub>-Cy), 41.7 (CH<sub>2</sub>CH<sub>2</sub>CHO), 43.50 (CH<sub>3</sub>CH), 49.9 (CH-Cy), 202.0 (CHO), 216.9 (CyCO). **LRMS (IC)** found [M+H]<sup>+</sup> = 197.



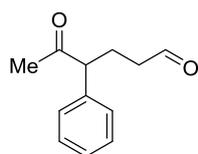
**4-methyl-5-oxononanal (5c):** 24 mg, 57% yield. Colourless oil.  $R_f =$

0.1 (Pentane/Diethyl ether = 10:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3488, 2958, 2930, 1709, 1459, 1127, 731$ . **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.90 (t,  $^3J_{\text{HH}} = 7.3$  Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.10 (d,  $^3J_{\text{HH}} = 7.0$  Hz, 3H, CH<sub>3</sub>CH), 1.25 – 1.34 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.46 – 1.59 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.60 – 1.76 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 1.87 – 2.07 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.31 – 2.53 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CO), 2.57 (td,  $^3J_{\text{HH}} = 7.3, 6.1$  Hz, 1H, CH<sub>3</sub>CH), 9.75 (t,  $^3J_{\text{HH}} = 1.4$  Hz, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.0 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 16.8 (CH<sub>3</sub>CH), 22.5 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 24.8 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 25.9 (CH<sub>2</sub>CH<sub>2</sub>CHO), 41.1 (CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 41.6 (CH<sub>2</sub>CH<sub>2</sub>CHO), 45.3 (CH<sub>3</sub>CH), 201.9 (CHO), 214.1 (COCH<sub>3</sub>). **LRMS (IC)** found [M+H]<sup>+</sup> = 171; [M+NH<sub>4</sub>]<sup>+</sup> = 188.

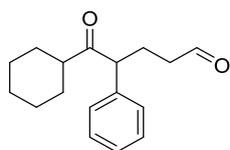


**(4,6,6-trimethyl-5-oxoheptanal (5d):** 27 mg, 64% yield. Colourless oil.

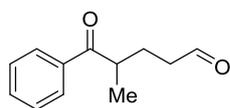
$R_f = 0.2$  (Pentane/Diethyl ether = 4:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2969, 2874, 2338, 1724, 1702, 1478, 1368, 1055$ . **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.06 (d,  $^3J_{\text{HH}} = 6.8$  Hz, 3H, CH<sub>3</sub>CH), 1.15 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CCO), 1.61 – 1.78 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 1.86 – 2.01 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.39 (td,  $^3J_{\text{HH}} = 7.4$  Hz, 1.5 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.94 – 3.24 (m, 1H, CH<sub>3</sub>CH), 9.74 (t,  $^3J_{\text{HH}} = 1.5$  Hz, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 18.41 (CH<sub>3</sub>CH), 26.10 ((CH<sub>3</sub>)<sub>3</sub>C), 26.15 (CH<sub>2</sub>CH<sub>2</sub>CHO), 38.48 (CH<sub>3</sub>CH), 41.54 (CH<sub>2</sub>CH<sub>2</sub>CHO), 44.67 ((CH<sub>3</sub>)<sub>3</sub>C), 201.79 (CHO), 219.02 ((CH<sub>3</sub>)<sub>3</sub>CC=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 171.



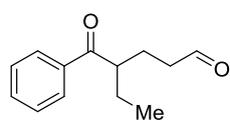
**5-oxo-4-phenylhexanal (5e):** 20 mg, 63% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2926, 1709, 1356, 1158, 700$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.97 – 2.42 (m, 4H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.05 (s, 3H,  $\text{CH}_3\text{CO}$ ), 3.61 – 3.77 (m, 1H, CH), 7.14 – 7.20 (m, 2H, CH-Ar), 7.27 – 7.39 (m, 3H, CH-Ar), 9.69 (t,  $^3J_{\text{HH}} = 1.2$  Hz, 1H, CHO).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 24.3 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 29.2 ( $\text{CH}_3\text{CO}$ ), 41.5 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 58.4 (CH), 127.8 (CH-Ar), 128.4 (CH-Ar), 129.3 (CH-Ar), 138.2 (C-Ar), 201.9 (CHO), 207.75 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 208$ .



**5-cyclohexyl-5-oxo-4-phenylpentanal (5f):** 18 mg, 28% yield. Colourless oil.  $R_f = 0.5$  (Pentane/diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2969, 2874, 2338, 1724, 1702, 1478, 1368, 1055$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.03 – 1.86 (m, 10H,  $\text{CH}_2\text{-Cy}$ ), 1.91 – 2.41 (m, 5H,  $\text{CH}_2\text{CHO}$ ;  $\text{CH}_2\text{CH}_2\text{CHO}$ ; CH-Cy), 3.74 – 3.92 (m, 1H, CH), 7.13 – 7.22 (m, 2H, CH-Ar), 7.26 – 7.36 (m, 3H, CH-Ar), 9.69 (t,  $^3J_{\text{HH}} = 1.3$  Hz, 1H, CHO).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 25.2 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 25.3 ( $\text{CH}_2\text{-Cy}$ ), 25.9 ( $\text{CH}_2\text{-Cy}$ ), 26.0 ( $\text{CH}_2\text{-Cy}$ ), 28.2 ( $\text{CH}_2\text{-Cy}$ ), 29.4 ( $\text{CH}_2\text{-Cy}$ ), 41.7 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 50.1 (CH-Cy), 55.9 (CH-Ar), 127.6 (CH-Ar), 128.6 (CH-Ar), 129.1 (CH-Ar), 138.2 (C-Ar), 202.0 (CHO), 212.9 ( $\text{COCH}_3$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 259$ .

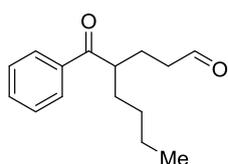


**4-methyl-5-oxo-5-phenylpentanal (5g):** 35 mg, 73% yield. Orange oil.  $R_f = 0.6$  Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2971, 2934, 2827, 2725, 1721, 1678, 1569, 1579, 1448, 1411, 1374, 1375, 1279, 1227, 1180, 1100, 1078, 1001, 971, 933, 905, 793, 702, 655$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 1.22 (d,  $^3J_{\text{HH}} = 7.0$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.77 – 1.84 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.11 – 2.18 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.41 – 2.57 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 3.55 (h,  $^3J_{\text{HH}} = 7.0$  Hz, 1H,  $\text{CH}_3\text{CH}$ ), 7.46 – 7.49 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 7.55 – 7.58 (m, 1H,  $\text{CH}_p\text{-Ar}$ ), 7.95 – 7.96 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 9.76 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ).  **$^{13}\text{C}\{^1\text{H}\}$ -NMR** ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) 17.8 ( $\text{CH}_3\text{CH}$ ), 25.5 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 39.7 ( $\text{CH}_3\text{CH}$ ), 41.6 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 128.4 ( $\text{CH}_o\text{-Ar}$ ), 128.9 ( $\text{CH}_m\text{-Ar}$ ), 133.3 ( $\text{CH}_p\text{-Ar}$ ), 136.4 (C-Ar), 202.0 (CHO), 203.1 ( $\text{COCH}_3$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 191$ .



**4-benzoylhexanal (5h):** 21 mg, 41% yield. Yellow oil.  $R_f = 0.6$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2964, 2723, 1751, 1676, 1596, 1577, 1447, 1382, 1219, 1001, 886, 785, 699, 535$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) 0.90 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 3H,  $\text{CH}_2\text{CH}_3$ ), 1.52 – 1.61 (m, 1H,  $\text{CH}_2\text{CH}_3$ ), 1.76 – 1.83 (m, 1H,  $\text{CH}_2\text{CH}_3$ ), 1.84 – 1.92 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.06-2.14 (m,

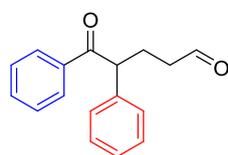
1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.35 – 2.41 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.47 – 2.53 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 3.43 – 3.48 (m, 1H, ArCOCH), 7.46 – 7.49 (m, 2H, CH<sub>m</sub>-Ar), 7.56 – 7.59 (m, 1H, CH<sub>p</sub>-Ar), 7.96 – 7.94 (m, 2H, CH<sub>o</sub>-Ar), 9.74 (bm, 1H, CHO). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) 11.7 (CH<sub>2</sub>CH<sub>3</sub>), 23.5 (CH<sub>2</sub>CH<sub>2</sub>CHO), 25.7 (CH<sub>2</sub>CH<sub>3</sub>), 41.6 (CH<sub>2</sub>CH<sub>2</sub>CHO), 46.4 (ArCOCH), 128.4 (CH<sub>o</sub>-Ar), 128.9 (CH<sub>m</sub>-Ar), 133.3 (CH<sub>p</sub>-Ar), 137.3 (C-Ar), 202.0 (CHO), 203.7 (ArCO). **LRMS (IC)** found [M+Na]<sup>+</sup> = 225.



**4-benzoyloctanal (5i):** 36 mg, 62% yield. Yellow oil. R<sub>f</sub> = 0.5

(Pentane/Diethyl ether = 7:3). **IR (neat):** ν(cm<sup>-1</sup>) = 2928, 2857, 2718, 1723, 1677, 1594, 1577, 1447, 1376, 1229, 1003, 934, 703. **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 0.84 (m, 3H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.25-1.28 (m,

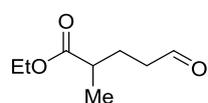
4H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.49 – 1.76 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 1.89 – 2.08 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.34 – 2.41 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 2.46 – 2.53 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHO), 3.47 – 3.53 (m, 1H, ArCOCH), 7.46 – 7.49 (m, 2H, CH<sub>m</sub>-Ar), 7.56 – 7.59 (m, 1H, CH<sub>p</sub>-Ar), 7.93 – 7.95 (m, 2H, CH<sub>o</sub>-Ar), 9.73 (m, 1H, CHO). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) 14.0 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 22.6 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 23.7 (CH<sub>2</sub>CH<sub>2</sub>CHO), 29.5 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 32.4 (CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 41.7 (CH<sub>2</sub>CH<sub>2</sub>CHO), 45.0 (ArCOCH), 128.0 (CH<sub>p</sub>-Ar), 128.9 (CH<sub>m</sub>-Ar), 133.3 (CH<sub>p</sub>-Ar), 137.3 (C-Ar), 202.0 (CHO), 203.8 (ArCO). **LRMS (IC)** found [M+H]<sup>+</sup> = 233.



**5-oxo-4,5-diphenylpentanal (5j):** 19 mg, 36% yield. Orange oil. R<sub>f</sub> = 0.5

(Pentane/Diethyl ether = 1:1). **IR (neat):** ν(cm<sup>-1</sup>) = 3061, 3028, 2929, 2827, 2725, 1721, 1678, 1597, 1580, 1492, 1448, 1390, 1353, 1257, 1231, 1205, 1176, 1100, 1072, 1002, 964, 934, 847, 754, 696, 617. **<sup>1</sup>H-**

**NMR** (CDCl<sub>3</sub>, 500 MHz): δ (ppm) 2.12-2.19 (m, 1H, CHCH<sub>2</sub>CH<sub>2</sub>CHO), 2.38 – 2.46 (m, 1H, CHCH<sub>2</sub>CH<sub>2</sub>CHO), 2.43 (m, 2H, CHCH<sub>2</sub>CH<sub>2</sub>CHO), 4.60 – 4.63 (m, 1H, CHCH<sub>2</sub>CH<sub>2</sub>CHO), 7.19 – 7.21 (m, 1H, CH<sub>p</sub>-Ar), 7.24 – 7.26 (m, 2H, CH<sub>o</sub>-Ar), 7.27 – 7.30 (m, 2H, CH<sub>m</sub>-Ar), 7.35 – 7.38 (m, 2H, CH<sub>m</sub>-Ar), 7.45 – 7.48 (m, 1H, CH<sub>p</sub>-Ar), 7.92 – 7.94 (m, 2H, CH<sub>o</sub>-Ar), 9.71 (s, 1H, CHCH<sub>2</sub>CH<sub>2</sub>CHO). <sup>13</sup>C{<sup>1</sup>H}-NMR (CDCl<sub>3</sub>, 126 MHz): δ (ppm) 26.1 (CHCH<sub>2</sub>CH<sub>2</sub>CHO), 41.6 (CHCH<sub>2</sub>CH<sub>2</sub>CHO), 52.4 (CHCH<sub>2</sub>CH<sub>2</sub>CHO), 127.5 (CH<sub>p</sub>-Ar), 128.3 (CH<sub>o</sub>-Ar), 128.7 (CH<sub>m</sub>-Ar), 128.9 (CH<sub>o</sub>-Ar), 129.2 (CH<sub>m</sub>-Ar), 133.2 (CH<sub>p</sub>-Ar), 136.2 (C-Ar), 138.7 (C-Ar), 199.3 (ArCO), 202.3 (CHO). **LRMS (IC)** found [M+H]<sup>+</sup> = 253.

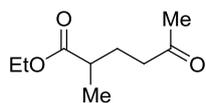


**Ethyl 2-methyl-5-oxopentanoate (5k):** 21 mg, 53% yield. Colourless oil.

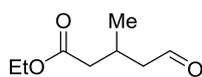
R<sub>f</sub> = 0.2 (Pentane/Diethyl ether = 2:1). **IR (neat):** ν(cm<sup>-1</sup>) = 2978, 2936, 1732, 1460, 1376, 1171, 1027. **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ (ppm) 1.18

(d, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 3H, CH<sub>3</sub>CH), 1.26 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.72 – 1.88 (m, 1H,

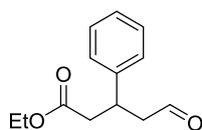
$\text{CH}_2\text{CH}_2\text{CHO}$ ), 1.89 – 2.03 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.38 – 2.57 (m, 1H,  $\text{CH}_3\text{CH}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 4.13 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 9.77 (s, 1H, CHO).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 17.3 ( $\text{CH}_3\text{CH}$ ), 25.9 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 38.9 ( $\text{CH}_3\text{CH}$ ), 41.7 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 60.6 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 176.0 (COOEt), 201.7 (CHO). **LRMS (IC)** found  $[\text{M}-\text{H}]^+ = 141$ .



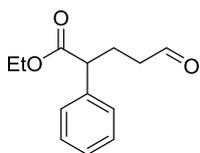
**Ethyl 2-methyl-5-oxohexanoate (5l)**: 39 mg, 91% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2978, 2940, 1719, 1462, 1369, 1161, 1026$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.16 (d,  $^3J_{\text{HH}} = 7.0$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.25 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.70 – 1.96 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.13 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.32 – 2.55 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 1H,  $\text{CH}_3\text{CH}$ ), 4.12 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 17.3 ( $\text{CH}_3\text{CH}$ ), 27.5 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 38.9 ( $\text{CH}_3\text{CH}$ ), 41.2 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 60.5 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 176.3 (EtOOC), 208.2 (COCH<sub>3</sub>). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 173$ .



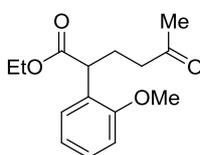
**Ethyl 3-methyl-5-oxopentanoate (5m)**: 22 mg, 56% yield. Colourless oil.  $R_f = 0.2$  (*n*-Pentane/Diethyl ether = 10:1). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2952, 1874, 1719, 1631, 1433$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.03 (d,  $^3J_{\text{HH}} = 6.6$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.26 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.20 – 2.65 (m, 5H,  $\text{CH}_2\text{CHCH}_2$ ), 4.13 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 9.75 (t,  $^3J_{\text{HH}} = 1.8$  Hz, 1H, CHO).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 20.3 ( $\text{CH}_3\text{CH}$ ), 25.4 ( $\text{CH}_3\text{CH}$ ), 41.1 (EtOOCCH<sub>2</sub>), 50.3 ( $\text{CH}_2\text{CHO}$ ), 60.6 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 172.4 (EtOOC), 201.7 (CHO). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 159$ .



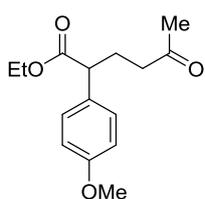
**Ethyl 5-oxo-3-phenylpentanoate (5n)**: 21 mg, 40% yield. Colourless oil.  $R_f = 0.3$  (Diethyl ether/Acetone = 8:2). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2957, 2924, 2857, 1726, 1672, 1605, 1495, 1453, 1437, 1367, 1318, 1258, 1195, 1160, 1083, 1012, 848, 764, 700, 569$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) 2.61 – 2.71 (m, 2H,  $\text{CH}_2\text{CHAr}$ ), 2.75 – 2.85 (m, 2H,  $\text{CH}_2\text{CHO}$ ), 3.58 (s, 3H,  $\text{CH}_3\text{O}$ ), 3.71 (p, 1H,  $^3J_{\text{HH}} = 7.4$  Hz,  $\text{CH}_2\text{CHPh}$ ), 7.21 – 7.24 (m, 2H,  $\text{CH}_o\text{-Ar}$ ; 1H,  $\text{CH}_p\text{-Ar}$ ), 7.29 – 7.33 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 9.64 (t, 1H,  $^3J_{\text{HH}} = 1.7$  Hz, CHO).  $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )  $\delta$  (ppm) = 36.5 ( $\text{CH}_2\text{CHAr}$ ), 41.0 ( $\text{CH}_2\text{CHAr}$ ), 49.8 ( $\text{CH}_2\text{CHO}$ ), 51.9 ( $\text{CH}_3\text{O}$ ), 127.3 ( $\text{CH}_p\text{-Ar}$ ), 127.7 ( $\text{CH}_o\text{-Ar}$ ), 129.1 ( $\text{CH}_m\text{-Ar}$ ), 143.2 (C-Ar), 172.2 (EtOOC), 201.0 (CHO). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 207$ ;  $[\text{M}+\text{Na}]^+ = 229$ .



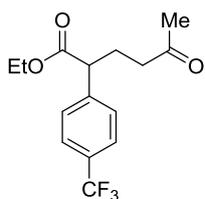
**Ethyl 5-oxo-2-phenylpentanoate (5o):** 12 mg, 45% yield. Clear oil.  $R_f = 0.5$  (Pentane/Diethyl ether = 6:4). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2981, 2726, 1724, 1602, 1494, 1453, 1370, 1257, 1216, 1159, 1096, 1070, 1025, 853, 768, 734, 699$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) = 1.20 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.12 – 2.36 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.40 – 2.43 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 3.58 (t,  $^3J_{\text{HH}} = 7.5$  Hz, 1H, ArCH), 4.06 – 4.18 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.20 – 7.28 (m, 2H,  $\text{CH}_o\text{-Ar}$ ), 7.26 (m, 1H,  $\text{CH}_p\text{-Ar}$ ), 7.31 – 7.34 (m, 2H,  $\text{CH}_m\text{-Ar}$ ), 9.71 (m, 1H, CHO).  **$^{13}\text{C}\{^1\text{H}\}$ -NMR** ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) 14.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 25.8 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 41.6 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 50.6 (ArCH), 61.0 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 127.6 ( $\text{CH}_p\text{-Ar}$ ), 128.0 ( $\text{CH}_o\text{-Ar}$ ), 128.9 ( $\text{CH}_m\text{-Ar}$ ), 138.4 (C-Ar), 173.5 (EtOOC), 201.4 (CHO). **LRMS (IC)** = found  $[\text{M}+\text{H}]^+ = 221$ .



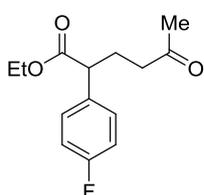
**Ethyl 2-(2-methoxyphenyl)-5-oxohexanoate (5p):** 55 mg, 83% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2959, 1722, 1494, 1245, 1156, 1028, 756, 535$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.19 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.08 (s, 3H,  $\text{CH}_3\text{CO}$ ), 1.92 – 2.06 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CO}$ ), 2.23 – 2.49 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CO}$ ), 3.81 (s, 3H,  $\text{CH}_3\text{OAr}$ ), 3.97 (t,  $^3J_{\text{HH}} = 7.3$  Hz, 1H, ArCH), 4.12 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.83 – 6.89 (m, 1H, CH-Ar), 6.90 – 6.97 (m, 1H, CH-Ar), 7.17 – 7.26 (m, 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 26.2 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.0 ( $\text{CH}_3\text{CO}$ ), 41.4 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 43.7 (ArCH), 55.6 ( $\text{CH}_3\text{OAr}$ ), 60.7 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 110.8 (CH-Ar), 120.9 (CH-Ar), 127.6 (C-Ar), 128.4 (CH-Ar), 128.6 (CH-Ar), 157.0 (COMe), 174.1 (EtOOC), 208.4 (CHO). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 256$ .



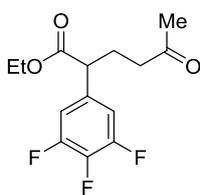
**Ethyl 2-(4-methoxyphenyl)-5-oxohexanoate: (5q):** 64 mg, 97% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2954, 1722, 1512, 1248, 1176, 1156, 1032$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.19 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.08 (s, 3H,  $\text{CH}_3\text{CO}$ ), 1.98 – 2.06 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.21 – 2.33 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.34 – 2.41 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.50 (t,  $^3J_{\text{HH}} = 7.7$  Hz, 1H, ArCH), 3.79 (s, 3H,  $\text{CH}_3\text{OAr}$ ), 3.99 – 4.26 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.80 – 6.88 (m, 2H, CH-Ar), 7.15 – 7.22 (m, 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.3 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 41.2 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 49.8 (ArCH), 55.4 ( $\text{CH}_3\text{OAr}$ ), 60.9 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 114.2 (CH-Ar), 129.1 (CH-Ar), 130.7 (C-Ar), 159.0 (COMe), 173.9 (EtOOC), 208.0 (CHO). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 282$ .



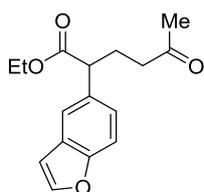
**Ethyl 5-oxo-2-(4-(trifluoromethyl)phenyl)hexanoate (5r):** 56 mg, 74% yield. Colourless oil.  $R_f = 0.4$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2940, 1728, 1326, 1164, 1069$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.21 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.10 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.00 – 2.10 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ) 2.26 – 2.44 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ;  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.65 (t,  $^3J_{\text{HH}} = 7.7$  Hz, 1H, ArCH), 4.05 – 4.22 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 7.41 (d,  $^3J_{\text{HH}} = 8.1$  Hz, 2H, CH-Ar), 7.58 (d,  $^3J_{\text{HH}} = 8.1$  Hz, 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.2 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 40.9 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 50.4 (ArCH), 61.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 124.2 (q,  $^1J_{\text{CF}} = 273.0$  Hz,  $\text{CF}_3$ ), 125.8 (q,  $^3J_{\text{CF}} = 3.8$  Hz, CH-Ar), 128.5 (CH-Ar), 129.9 (q,  $^2J_{\text{CF}} = 32.5$ ,  $\text{CCF}_3$ ), 142.7 (C-Ar), 173.0 (EtOOC), 207.6 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 320$ .



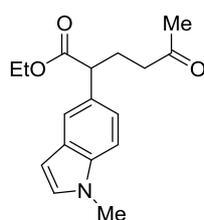
**Ethyl 2-(4-fluorophenyl)-5-oxohexanoate (5s):** 58 mg, 92% yield. Colourless oil.  $R_f = 0.4$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2980, 1726, 1604, 1510, 1224, 1157, 840$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.20 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.09 (s, 3H,  $\text{CH}_3\text{CO}$ ), 1.98 – 2.08 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.23 – 2.34 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.34 – 2.43 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.56 (t,  $^3J_{\text{HH}} = 7.6$  Hz, 1H, ArCH), 4.04 – 4.20 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.97 – 7.05 (m, 2H, CH-Ar), 7.22 – 7.28 (m, 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.4 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 41.1 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 49.9 (ArCH), 61.1 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 115.7 (d,  $^2J_{\text{CF}} = 21.2$  Hz, CH-Ar), 129.6 (d,  $^3J_{\text{CF}} = 8.1$  Hz, CH-Ar), 134.4 (d,  $^4J_{\text{CF}} = 3.2$  Hz, C-Ar), 161.3 (d,  $^1J_{\text{CF}} = 45.4$  Hz, C-F), 173.6 (EtOOC), 207.8 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 253$ .



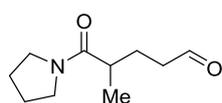
**Ethyl 5-oxo-2-(3,4,5-trifluorophenyl)hexanoate (5t):** 43 mg, 60% yield. Colourless oil.  $R_f = 0.2$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2981, 1725, 1620, 1530, 1451, 1361, 1160, 1041, 866$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.22 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.12 (s, 3H,  $\text{CH}_3\text{CO}$ ), 1.93 – 2.05 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.19 – 2.33 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.40 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.52 (t,  $^3J_{\text{HH}} = 7.8$  Hz, 1H, ArCH), 4.03 – 4.24 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.85 – 7.06 (m, 2H, CH-Ar).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.23 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.16 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.17 ( $\text{CH}_3\text{CO}$ ), 40.71 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 49.76 (ArCH), 61.49 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 112.20 – 112.41 (m, CH-Ar), 134.92 (td,  $^3J_{\text{HH}} = 7.5, 4.9$  Hz, C-Ar), 139.24 (dt,  $^1J_{\text{CF}} = 251.6, ^2J_{\text{CF}} = 15.1$  Hz,  $\text{CF}_p\text{-Ar}$ ), 151.34 (ddd,  $^1J_{\text{CF}} = 250.4, ^2J_{\text{CF}} = 9.8, ^3J_{\text{CF}} = 4.0$  Hz,  $\text{CF}_m\text{-Ar}$ ), 172.57 (EtOOC), 207.32 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 289$ .



**Ethyl 2-(benzofuran-5-yl)-5-oxohexanoate (5u):** 49 mg, 72% yield. Colourless oil.  $R_f = 0.3$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2980, 1723, 1468, 1158, 1030, 745$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.18 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.04 (s, 3H,  $\text{CH}_3\text{CO}$ ), 1.98 – 2.15 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.22 – 2.47 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.64 (dd,  $^3J_{\text{HH}} = 8.2, 7.1$  Hz, 1H, ArCH), 3.96 – 4.20 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.77 (dd,  $^3J_{\text{HH}} = 2.2, ^5J_{\text{HH}} = 1.0$  Hz, 1H, CH-Het), 7.21 (dd,  $^3J_{\text{HH}} = 8.6, ^4J_{\text{HH}} = 1.9$  Hz, 1H, CH-Het), 7.45 (dt,  $^3J_{\text{HH}} = 8.6, ^5J_{\text{HH}} = 0.8$  Hz, 1H, CH-Het), 7.52 (d,  $^4J_{\text{HH}} = 1.8$  Hz, 1H, CH-Het), 7.65 (d,  $^3J_{\text{HH}} = 2.2$  Hz, 1H, CH-Het).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.9 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 41.3 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 50.7 (ArCH), 61.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 106.9 (CH-Het), 111.7 (CH-Het), 120.9 (CH-Het), 124.7 (CH-Het), 128.2 (C-Het), 133.8 (C-Het), 146.0 (CH-Het), 154.7 (C-Het), 174.1 (EtOOC), 207.9 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{NH}_4]^+ = 292$ .

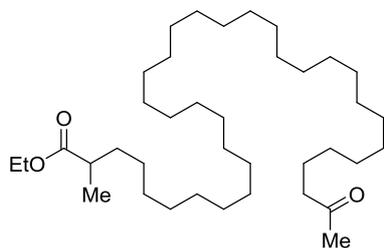


**Ethyl 2-(1-methyl-1H-indol-5-yl)-5-oxohexanoate (5v):** 44 mg, 61% yield. Colourless oil.  $R_f = 0.45$  (Pentane/Diethyl ether = 2:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2945, 1722, 1492, 1156, 725$ .  **$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.18 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 2.03 (s, 3H,  $\text{CH}_3\text{CO}$ ), 2.00 – 2.13 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 2.21 – 2.47 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CO}$ ), 3.60 (dd,  $^3J_{\text{HH}} = 8.4, 6.6$  Hz, 1H, ArCH), 3.77 (s, 3H, NCH<sub>3</sub>), 3.94 – 4.23 (m, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.42 (dd,  $^3J_{\text{HH}} = 3.2, ^5J_{\text{HH}} = 0.9$  Hz, 1H, CH-Het), 7.07 (d,  $^3J_{\text{HH}} = 3.1$  Hz, 1H, CH-Het), 7.12 (dd,  $^3J_{\text{HH}} = 8.5, ^4J_{\text{HH}} = 1.8$  Hz, 1H, CH-Het), 7.29 (dt,  $^3J_{\text{HH}} = 8.5, ^5J_{\text{HH}} = 0.8$  Hz, 1H, CH-Het), 7.47 (d,  $^4J_{\text{HH}} = 1.7$  Hz, 1H, CH-Het).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (101 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.3 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 27.9 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 30.1 ( $\text{CH}_3\text{CO}$ ), 33.2 ( $\text{CH}_3\text{N}$ ), 41.4 ( $\text{CH}_2\text{CH}_2\text{CO}$ ), 50.9 (ArCH), 61.0 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 101.1 (CH-Het), 109.8 (CH-Het), 120.3 (CH-Het), 121.7 (CH-Het), 129.1 (C-Het), 129.8 (CH-Het), 129.9 (C-Het), 136.5 (C-Het), 174.5 (EtOOC), 208.1 ( $\text{CH}_3\text{CO}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 288$ .

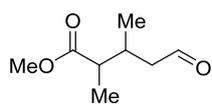


**4-methyl-5-oxo-5-(pyrrolidin-1-yl)pentanal (5w):** 20 mg, 44% yield. Yellow oil.  $R_f = 0.1$  (Diethyl ether = 6:4). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2952, 2924, 2856, 1724, 1633, 1459, 1440, 1374, 1341, 1254, 1227, 1190, 1170, 1116, 860$ .  **$^1\text{H-NMR}$**  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) = 1.11 (d,  $^3J_{\text{HH}} = 6.8$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.65-1.74 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 1.80-1.86 (m, 2H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 1.90-1.97 (m, 2H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 1.97-2.04 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.35-2.52 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CHO}$ ), 2.54-2.63 (m, 1H,  $\text{CH}_3\text{CH}$ ), 3.38-3.49 (m, 4H,  $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 9.72 (m, 1H, CHO).  **$^{13}\text{C}\{^1\text{H}\}$ -NMR** ( $\text{CDCl}_3$ , 126 MHz):  $\delta$  (ppm) 17.5 ( $\text{CH}_3\text{CH}$ ), 24.4 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ), 26.1 ( $\text{CH}_2\text{CH}_2\text{CHO}$ ), 26.3 ( $(\text{CH}_2\text{CH}_2)_2\text{N}$ ),

37.1 (CHCH<sub>3</sub>), 41.8 (CH<sub>2</sub>CH<sub>2</sub>CHO), 45.9 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 46.6 ((CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>N), 174.2 (NC=O), 202.5 (HC=O). **LRMS (IC)** = found [M+H]<sup>+</sup> = 184, [M+Na]<sup>+</sup> = 206.



**Ethyl 2-methyl-34-oxopentatriacontanoate (5y):** 42 mg, 72% yield. Colourless wax.  $R_f = 0.3$  (Pentane/Diethyl ether = 6:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2916, 2849, 1710, 1648, 1462, 1370, 728$ . **<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.13 (d, <sup>3</sup>J<sub>HH</sub> = 7.0 Hz, 3H, CH<sub>3</sub>CH), 1.22 – 1.29 (m, 3H, CH<sub>3</sub>CH<sub>2</sub>O; 56H, (CH<sub>2</sub>)<sub>28</sub>), 1.35 – 1.42 (m, 2H, CH<sub>2</sub>CHCOOEt; 2H, CH<sub>2</sub>CH<sub>2</sub>CO), 1.54 – 1.70 (m, 2H, CH<sub>2</sub>CHCOOEt; 2H, CH<sub>2</sub>CH<sub>2</sub>CO), 2.13 (s, 3H, CH<sub>3</sub>CO), 2.32 – 2.47 (m, 1H, CHCOOEt; 2H, CH<sub>2</sub>COCH<sub>3</sub>), 4.12 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O). **<sup>13</sup>C{<sup>1</sup>H} NMR** (101 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 17.2 (CH<sub>3</sub>CH), 24.0 (CH<sub>2</sub>CH<sub>2</sub>CO), 27.4 – 29.9 ((CH<sub>2</sub>)<sub>28</sub>), 30.0 (CH<sub>3</sub>CO), 34.0 (CH<sub>2</sub>CH<sub>2</sub>COOEt), 39.7 (CH<sub>3</sub>CH), 44.0 (CH<sub>2</sub>CO), 60.2 (CH<sub>3</sub>CH<sub>2</sub>O), 177.1 (EtOOC), 209.5 (CH<sub>3</sub>CO). **LRMS (IC)** found [M+H]<sup>+</sup> = 580.

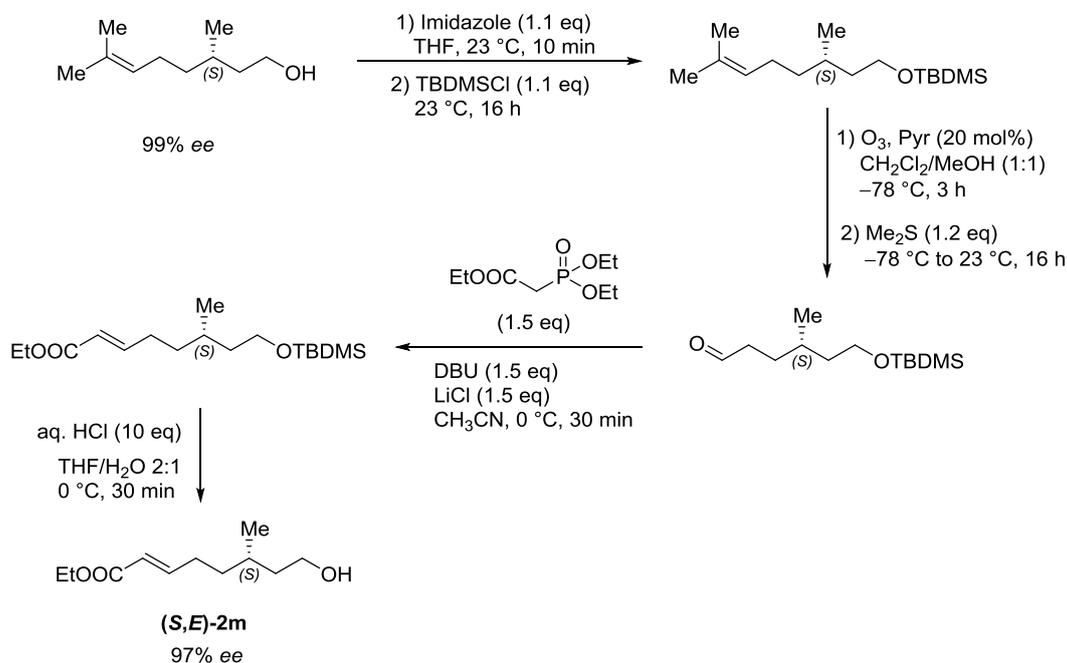


**Methyl 2,3-dimethyl-5-oxopentanoate (5x)** (dr = 50:50): 16 mg, 40% yield. Colourless oil.  $R_f = 0.6$  (Pentane/Diethyl ether = 6:4). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2949, 2886, 2724, 1725, 1637, 1457, 1436, 1381, 1257, 1197, 1167, 1094, 1035, 972, 839, 776$ . **<sup>1</sup>H-NMR** (C<sub>6</sub>D<sub>6</sub>, 500 MHz):  $\delta$  (ppm) = 0.68 (d, <sup>3</sup>J<sub>HH</sub> = 6.8 Hz, 3H, CH(CH<sub>3</sub>)CH<sub>2</sub>), 0.86 (d, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, C(O)CH<sub>3</sub>), 1.71 – 1.78 (m, 1H, CH(CH<sub>3</sub>)CH<sub>2</sub>), 1.91 – 1.96 (m, 1H, CH(CH<sub>3</sub>)CH<sub>2</sub>), 2.12 – 2.20 (m, 1H, C(O)CH), 2.22 – 2.31 (m, 1H, CH(CH<sub>3</sub>)CH<sub>2</sub>), 3.28 – 3.29 (s, 3H, CH<sub>3</sub>O), 9.25 – 9.27 (m, 1H, CHO). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (C<sub>6</sub>D<sub>6</sub>, 126 MHz):  $\delta$  (ppm) 13.1, 13.8 (C(O)CHCH<sub>3</sub>), 16.7, 17.4 (CH(CH<sub>3</sub>)CH<sub>2</sub>). 36.7 (CH(CH<sub>3</sub>)CH<sub>2</sub>), 43.9 (C(O)CHCH<sub>3</sub>), 48.5, 47.9 (CH(CH<sub>3</sub>)CH<sub>2</sub>), 50.9, 51.0 (CH<sub>3</sub>O), 175.0, 175.2 (CH<sub>3</sub>OOC), 199.9, 200.0 (CHO). **LRMS (IC)** = found [M+Na]<sup>+</sup> = 181, [M+MeOH+H]<sup>+</sup> = 191.

## 2.4 Mechanistic studies

### 2.4.1 Evidence for de-coordinative process

#### 2.4.1.1 Synthesis of 2m



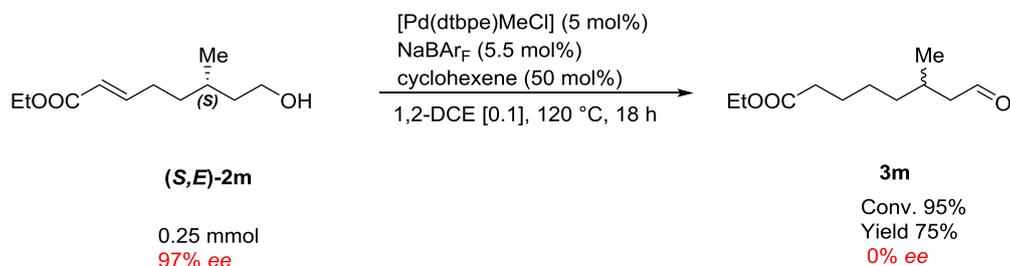
**Figure S29:** Synthesis of Ethyl (S,E)-8-hydroxy-6-methyloct-2-enoate (2m)

**Ethyl (S,E)-8-((tert-butyldimethylsilyl)oxy)-6-methyloct-2-enoate:** (S)-citronellol was protected with TBDMSCl in quantitative yield according to a procedure reported in the literature.<sup>37</sup> Subsequent ozonolysis was performed following a known protocol<sup>38</sup> and the resulting aldehyde was used in the next step without further purification. . The olefination step was run according to GP2 starting from 6-((tert-butyldimethylsilyl)oxy)-4-methylhexanal (2.17 mmol, 530 mg). The residual oil was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 95:5) to afford ethyl (S,E)-8-((tert-butyldimethylsilyl)oxy)-6-methyloct-2-enoate in 86% yield (588 mg) as a colourless oil.  $R_f = 0.75$  (Pentane/Diethyl ether = 9:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 2955, 2930, 2858, 1722, 1655, 1464, 1389, 1366, 1306, 1255, 1197, 1169, 1093, 1047, 983, 939, 896, 833, 774, 722, 663$ .  $[\alpha]_D^{23} = -5.14$  (c 0.25, CH<sub>2</sub>Cl<sub>2</sub>). **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 0.04 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.87 – 0.90 (m, 3H, CH<sub>3</sub>CH; 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.28 (s, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.27-1.36 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH; 1H, CHCH<sub>2</sub>CH<sub>2</sub>), 1.44 – 1.50 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH), 1.51 – 1.61 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH; 1H, CHCH<sub>2</sub>CH), 2.17 – 2.26 (m, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>2</sub>CH<sub>2</sub>CH), 4.18 (t, <sup>3</sup>J<sub>HH</sub> = 6.8 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.79 – 5.83 (m, 1H, CH=CH), 6.96 (dt, <sup>3</sup>J<sub>HH</sub> = 15.5, 6.9 Hz, 1H, CH<sub>2</sub>CH=CH). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) -5.1 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 18.5 ((CH<sub>3</sub>)<sub>3</sub>CSi), 19.6 (CH<sub>3</sub>CH), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 29.2 (CH<sub>2</sub>CH<sub>2</sub>CH), 29.9

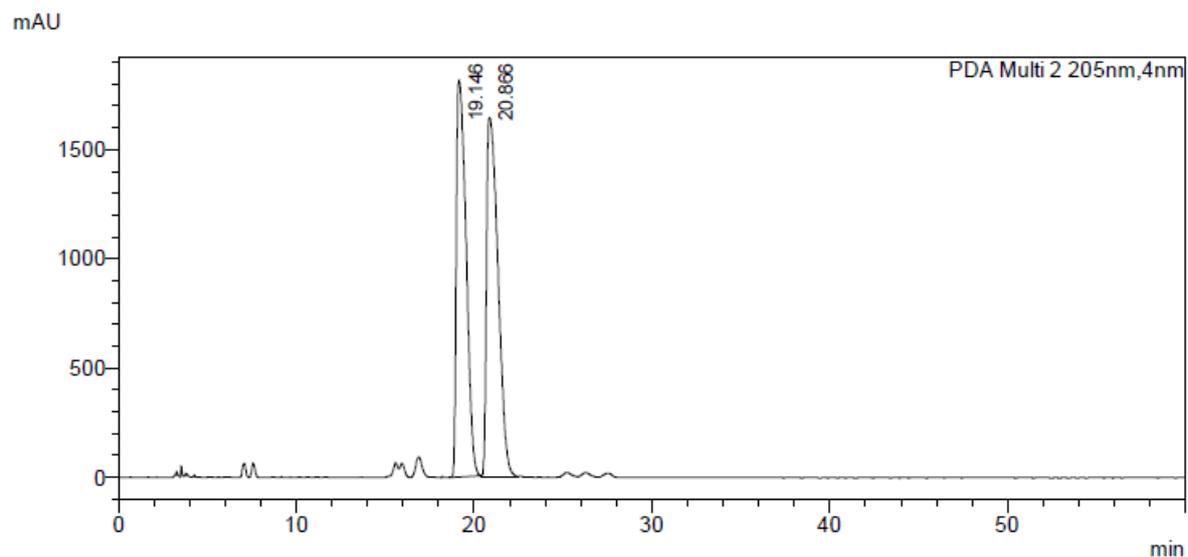
(CH<sub>2</sub>CH<sub>2</sub>CH), 35.4 (CH<sub>2</sub>CH<sub>2</sub>CH), 39.8 (CHCH<sub>2</sub>CH<sub>2</sub>), 60.3 (CH<sub>3</sub>CH<sub>2</sub>O), 61.3 (CHCH<sub>2</sub>CH<sub>2</sub>), 121.3 (CH=CH), 149.6 (CH=CH), 166.9 (C=O). **LRMS (IC)** found [M+Na]<sup>+</sup> = 337.

**Ethyl (S,E)-8-hydroxy-6-methyloct-2-enoate (2m):** The reaction was performed according to GP4. After purification by flash chromatography on silica gel (Pentane/Diethyl ether = 6:4) **(S,E)-2m** was obtained in 99% yield (352 mg) as a colourless oil. **R<sub>f</sub>** = 0.3 (Pentane/Diethyl ether = 6:4). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3409, 2925, 1713, 1653, 1457, 1369, 1268, 1175, 1121, 1046, 984, 918, 849, 732, 647. **[ $\alpha$ ]<sup>23</sup><sub>D</sub>** = -7.91 (c 0.25, CH<sub>2</sub>Cl<sub>2</sub>). **<sup>1</sup>H-NMR** (CDCl<sub>3</sub>, 500 MHz):  $\delta$  (ppm) 0.90 (d, 3H, <sup>3</sup>J<sub>HH</sub> = 6.6 Hz, CH<sub>3</sub>CH), 1.22 – 1.34 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH), 1.27 (s, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.37 – 1.43 (m, 1H, CHCH<sub>2</sub>CH<sub>2</sub>OH), 1.45 – 1.52 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH; 1H, OH), 1.57 – 1.64 (m, 1H, CHCH<sub>2</sub>CH; 1H, CHCH<sub>2</sub>CH<sub>2</sub>), 2.14 – 2.29 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH), 3.63 – 3.72 (m, 2H, CHCH<sub>2</sub>CH<sub>2</sub>OH), 4.17 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.81 (dt, <sup>3</sup>J<sub>HH</sub> = 15.6 Hz, <sup>4</sup>J<sub>HH</sub> = 1.6 Hz, 1H, CH=CH), 6.95 (m, <sup>3</sup>J<sub>HH</sub> = 15.6 Hz, 6.9 Hz, 1H, CH=CH). **<sup>13</sup>C{<sup>1</sup>H}-NMR** (CDCl<sub>3</sub>, 126 MHz):  $\delta$  (ppm) 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 19.4 (CH<sub>3</sub>CH), 29.8 (CH<sub>2</sub>CH<sub>2</sub>CH), 29.2 (CH<sub>2</sub>CH<sub>2</sub>CH), 35.4 (CH<sub>2</sub>CH<sub>2</sub>CH), 39.8 (CHCH<sub>2</sub>CH<sub>2</sub>), 60.3 (CH<sub>3</sub>CH<sub>2</sub>O), 61.0 (CHCH<sub>2</sub>CH<sub>2</sub>), 121.4 (CH=CHCH<sub>2</sub>), 149.4 (CH=CHCH<sub>2</sub>), 166.9 (C=O). **LRMS (IC)** found [M+H]<sup>+</sup> = 201.

#### 2.4.1.2 Isomerization of 2m

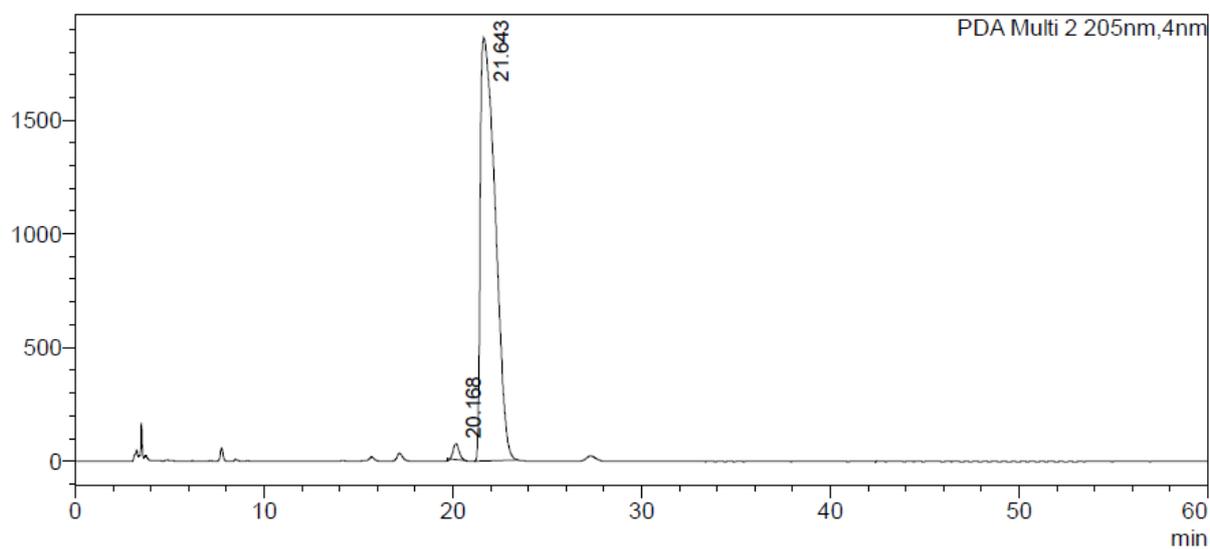


The reaction was performed according to GP1. The enantiomeric excess (ee) of **2m** (**Figure S30**) was measured by HPLC (column OJ-H, Hexane/*i*PrOH 98:2, 1 mL/min,  $\lambda$  205 nm) and those of **3m** (**Figure S31**) by GC (column HYDRODEX  $\gamma$ -DiMOM, method 100 °C for 120 minutes then 100 – 170 °C in 70 minutes).

**<Peak Table>**

PDA Ch2 205nm

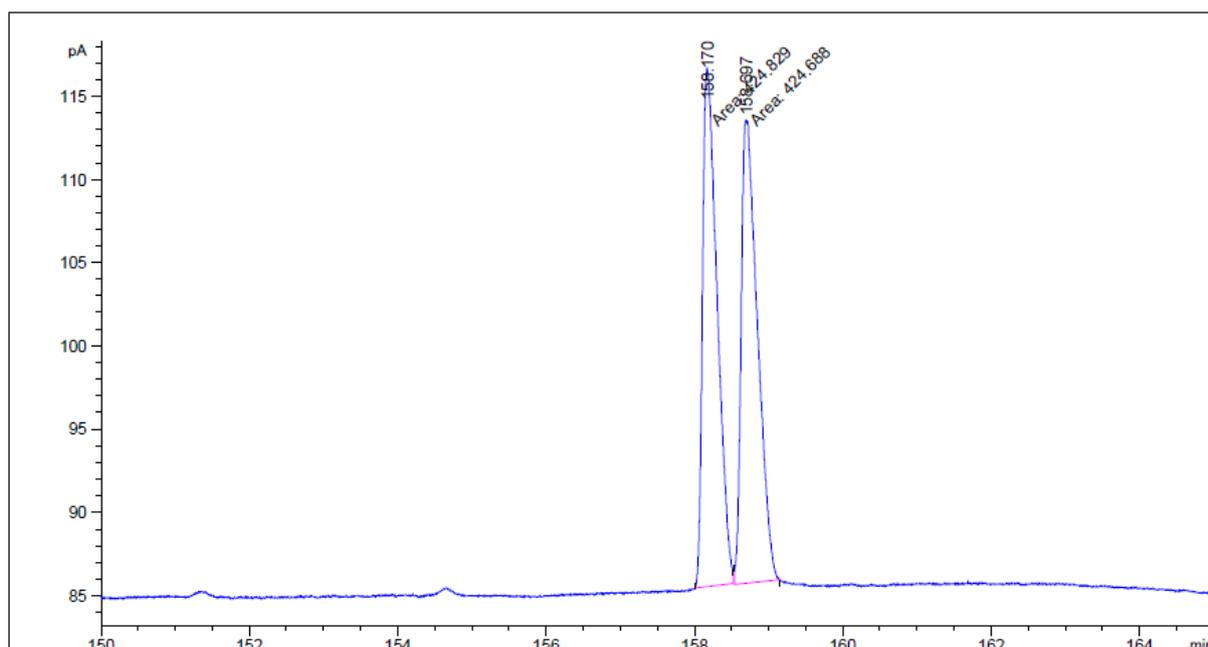
Peak#	Ret. Time	Area%
1	19.146	48.467
2	20.866	51.533
Total		100.000



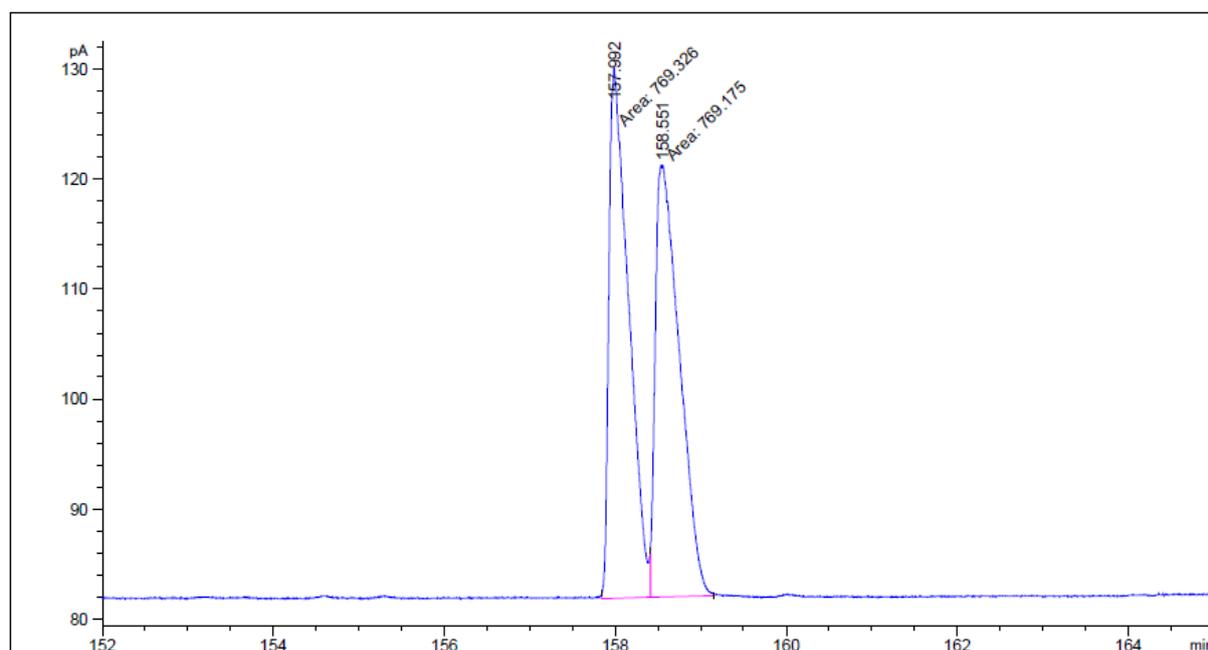
PDA Ch2 205nm

Peak#	Ret. Time	Area%
1	20.168	1.488
2	21.643	98.512
Total		100.000

**Figure S30:** HPLC traces of racemic **2m** (top) and enantio-enriched **2m** (bottom)



Peak #	RetTime [min]	Area %
1	158.170	50.00831
2	158.697	49.99169

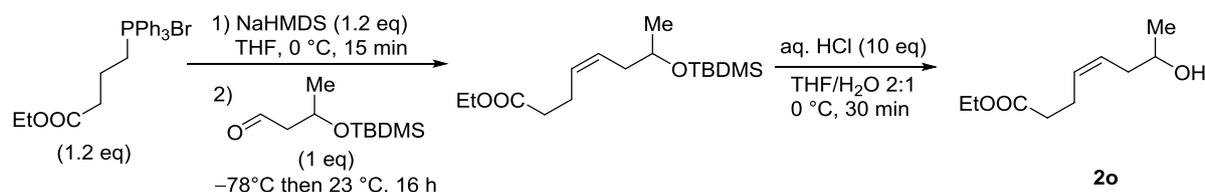


Peak #	RetTime [min]	Area %
1	157.992	50.00491
2	158.551	49.99509

**Figure S31:** GC traces of **3m**, starting from racemic **2m** (top) and enantio-enriched **2m** (bottom)

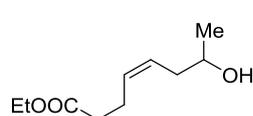
## 2.4.2 Assessment of the bidirectional nature of the process

### 2.4.2.1 Synthesis of 2o



**Figure S32:** Synthesis of Ethyl (*Z*)-7-hydroxyoct-4-enoate (**2o**)

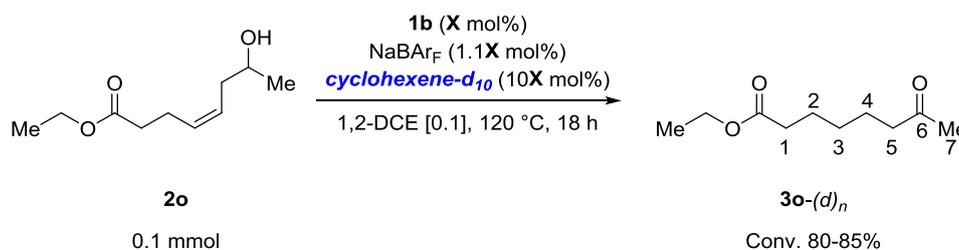
**Ethyl (*Z*)-7-((tert-butyldimethylsilyl)oxy)oct-4-enoate:** Ethyl 4-(bromotriphenyl-15-phosphanyl)butanoate was prepared from ethyl 4-bromobutanoate according to a known procedure reported in the literature.<sup>39</sup> In a 3-neck flask, equipped with a dropping funnel, ethyl 4-(bromotriphenyl-15-phosphanyl)butanoate (4.56 mmol, 2 g) was dissolved in THF (18 mL) and cooled to 0 °C before the dropwise addition of NaHMDS (4.56 mmol, 2.3 mL from a 2 M solution in THF). After 15 minutes, this solution was cooled to -78 °C and 3-((tert-butyldimethylsilyl)oxy)butanal (3.8 mmol, 769 mg) in THF (15 mL) added dropwise. After 16 h at room temperature, the reaction was quenched with water, extracted with diethyl ether (3 × 30 mL), the organic phases combined, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent evaporated. The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 98:2) to afford ethyl (*Z*)-7-((tert-butyldimethylsilyl)oxy)oct-4-enoate in 58% yield (661 mg) as a pale yellow oil. *R<sub>f</sub>* = 0.6 (Pentane/Diethyl ether = 9:1). **IR (neat)**  $\nu(\text{cm}^{-1})$  = 2957, 2931, 2858, 1736, 1463, 1373, 1252, 1161, 1131, 1087, 1049, 1004, 832, 809, 774, 725, 662. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 0.04 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.05 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.12 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CH), 1.25 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 2.13 – 2.25 (m, 2H, CH<sub>2</sub>CH), 2.32 – 2.39 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH=CH; 2H, CH<sub>2</sub>CH<sub>2</sub>CH=CH), 3.82 (h, <sup>3</sup>*J*<sub>HH</sub> = 6.1 Hz, 1H, CH<sub>2</sub>CH), 4.11 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 5.39 – 5.48 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH=CH; 1H, CH<sub>2</sub>CH<sub>2</sub>CH=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) -4.4 ((CH<sub>3</sub>)<sub>2</sub>Si), -4.5 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.2 (CH<sub>3</sub>CH<sub>2</sub>O), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 23.1 (CH<sub>2</sub>CH<sub>2</sub>CH=CH), 23.7 (CH<sub>3</sub>CH), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 34.5 (CH<sub>2</sub>CH<sub>2</sub>CH=CH), 37.6 (CH<sub>2</sub>CH), 60.5 (CH<sub>3</sub>CH<sub>2</sub>O), 68.7 (CH<sub>2</sub>CH), 127.9 (CH<sub>2</sub>CH<sub>2</sub>CH=CH), 129.1 (CH<sub>2</sub>CH<sub>2</sub>CH=CH), 173.3 (C=O). **LRMS (IC)** found [M+Na]<sup>+</sup> = 319.



**Ethyl (*Z*)-7-hydroxyoct-4-enoate (**2o**):** The reaction was performed according to GP4 starting from ethyl (*Z*)-7-((tert-butyldimethylsilyl)oxy)oct-4-enoate (2.20 mmol, 661 mg). After

purification by flash chromatography on silica gel (Pentane/Diethyl ether = 7:3) **2o** was obtained in 78% yield (314 mg) as a pale yellow oil.  $R_f = 0.2$  (*n*-Pentane/Diethyl ether = 6:4).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 1.22 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CH}$ ), 1.25 (t,  $^3J_{\text{HH}} = 7.1$ , 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.59 (bs, 1H, OH), 2.18 – 2.23 (m, 1H,  $\text{CH}_2\text{CH}$ ), 2.26 – 2.31 (m, 1H,  $\text{CH}_2\text{CH}$ ), 2.34 – 2.45 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ), 3.81 – 3.87 (m, 1H,  $\text{CH}_2\text{CH}$ ), 4.13 (t, 2H,  $^3J_{\text{HH}} = 7.1$  Hz,  $\text{CH}_3\text{CH}_2\text{O}$ ), 5.45 – 5.54 (m, 1H,  $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ; 1H,  $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ).  $^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 23.0 ( $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ), 23.1 ( $\text{CH}_3\text{CH}$ ), 34.2 ( $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ), 37.2 ( $\text{CH}_2\text{CH}$ ), 60.6 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 67.7 ( $\text{CH}_2\text{CH}$ ), 127.1 ( $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ), 131.0 ( $\text{CH}_2\text{CH}_2\text{CH}=\text{CH}$ ), 173.4 (C=O). LRMS (IC) found  $[\text{M}+\text{H}]^+ = 187$ . IR (neat):  $\nu(\text{cm}^{-1}) = 3417, 2971, 2932, 1732, 1451, 1422, 1373, 1378, 1258, 1163, 1120, 1163, 1120, 1077, 1041, 941, 885, 720$ .

#### 2.4.2.2 Isotopic labelling experiments



Inside the glovebox, a 5 mL Young valve Schlenk was charged with precatalyst **1b** (**X** mmol),  $\text{NaBAR}_\text{F}$  (1.1**X** mmol) and 1,2-dichloroethane (1 mL). After 5 minutes at room temperature, cyclohexene-  $d_{10}$  (10**X** mmol, 98% in deuterium) was added and the mixture stirred for 5 minutes at room temperature. Substrate **2o** (0.1 mmol) was added, the Schlenk sealed and immersed in an oil bath pre-heated at 120 °C. After 18 h, the reaction mixture was cooled to room temperature, the solvent was removed *in vacuo* and 1,1,2,2-tetrachloroethane (0.05 mmol) was added as internal standard. The conversion was assessed by  $^1\text{H-NMR}$  while the extent of deuterium incorporation was established by comparison of the  $^1\text{H-NMR}$  spectra of **3o** and **3o-(d)<sub>n</sub>** at different catalyst loadings (**Figure S34-S36**).

The  $^2\text{H-NMR}$  spectra of the crude reaction mixtures at different catalyst loadings are shown below (**Figure S37-S39**) to qualitatively support the effective deuterium incorporation in **3o-(d)<sub>n</sub>**.

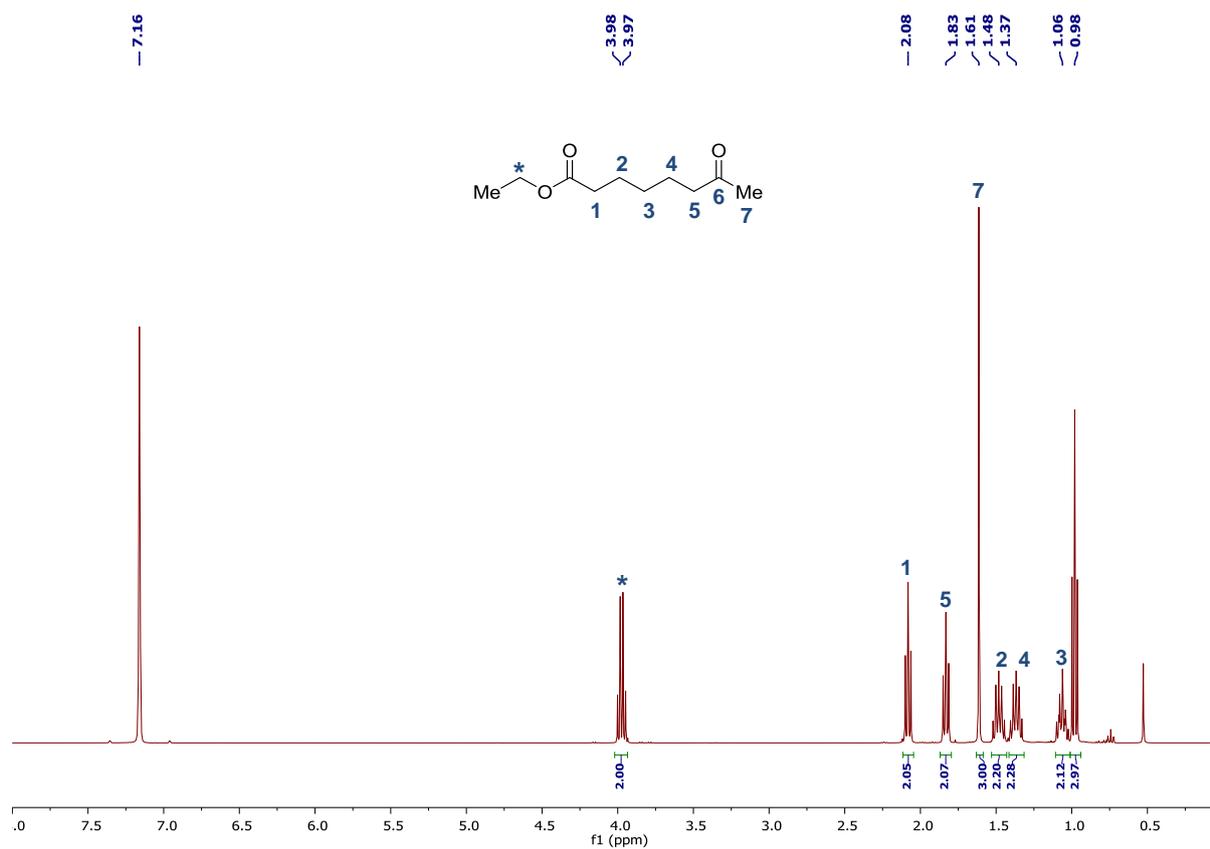


Figure S33:  $^1\text{H-NMR}$  in  $\text{C}_6\text{D}_6$  of **3o**

<b>1b (mol%)</b>	<b>pos. 1</b>	<b>pos. 2</b>	<b>pos. 3</b>	<b>pos. 4</b>	<b>pos. 5</b>	<b>pos. 7</b>
<b>10</b>	2.0%	3.0%	3.3%	0.9%	3.6%	0.7%
<b>20</b>	2.5%	1.6%	2.9%	2.2%	3.6%	0.7%
<b>40</b>	2.0%	2.1%	5.0%	n.d. <sup>a</sup>	4.4%	0.6%

<sup>a</sup> Integration higher than in **3o** because of an overlap with signals from the catalyst

**Table 1:** Extent of deuterium incorporation at various catalyst loadings

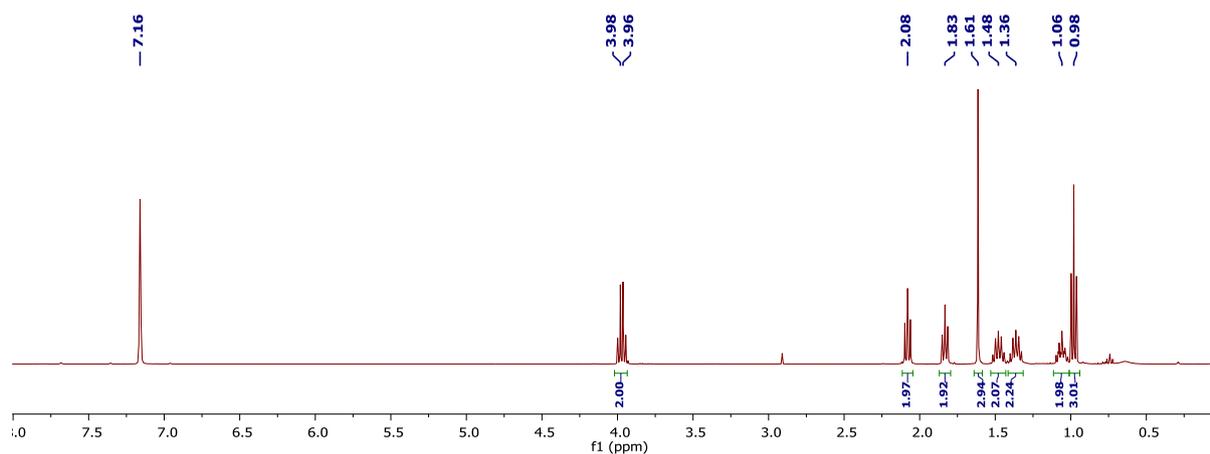


Figure S34:  $^1\text{H-NMR}$  in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 10 mol% of **1b**

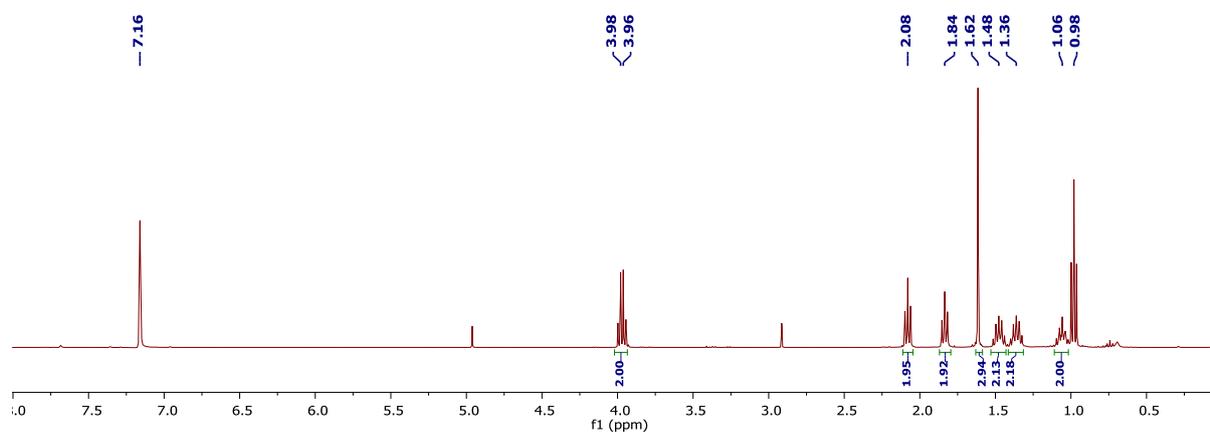


Figure S35:  $^1\text{H-NMR}$  in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 20 mol% of **1b**

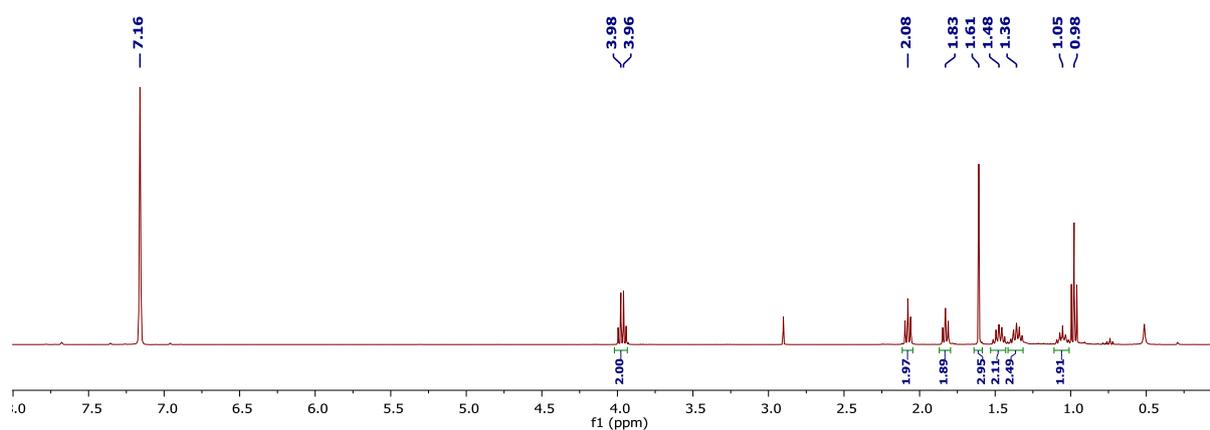
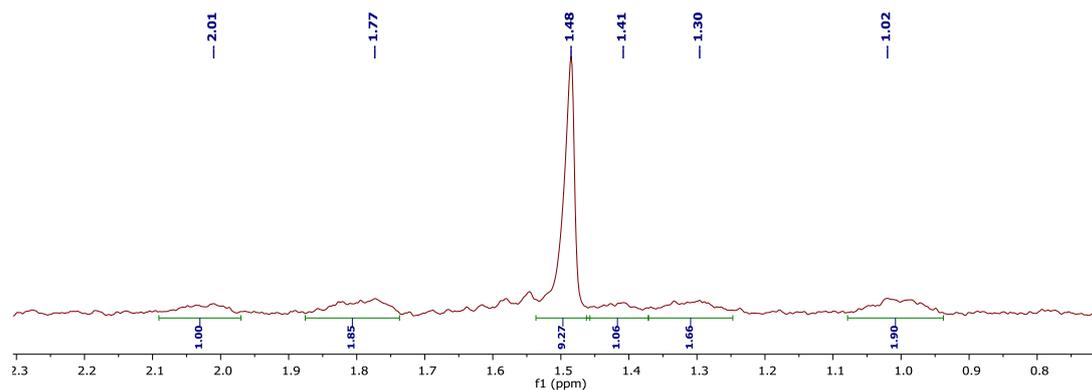
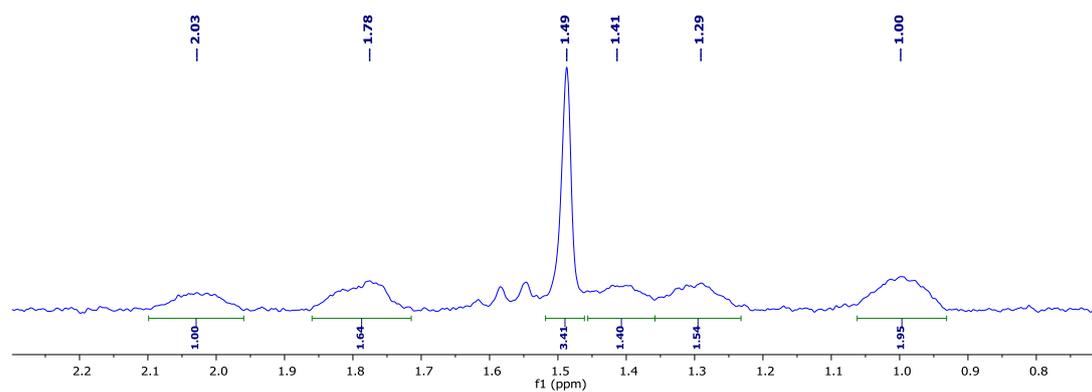


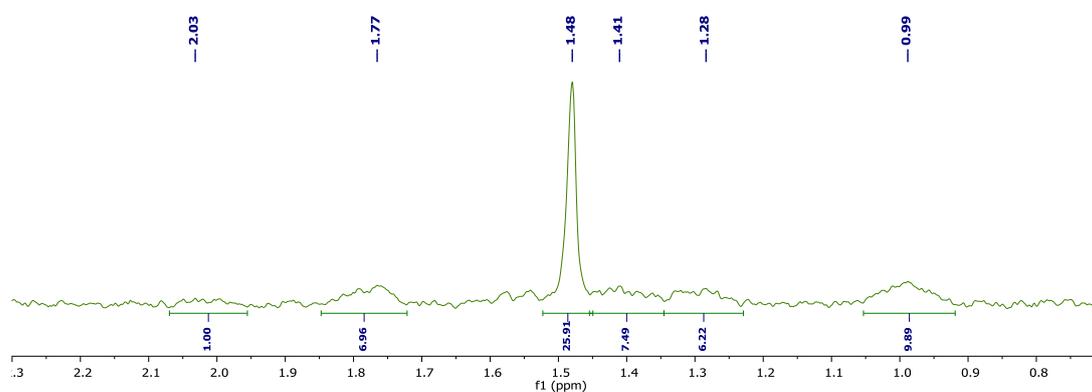
Figure S36:  $^1\text{H-NMR}$  in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 40 mol% of **1b**



**Figure S37:** Expansion of  $^2\text{H}$ -NMR in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 10 mol% of **1b**



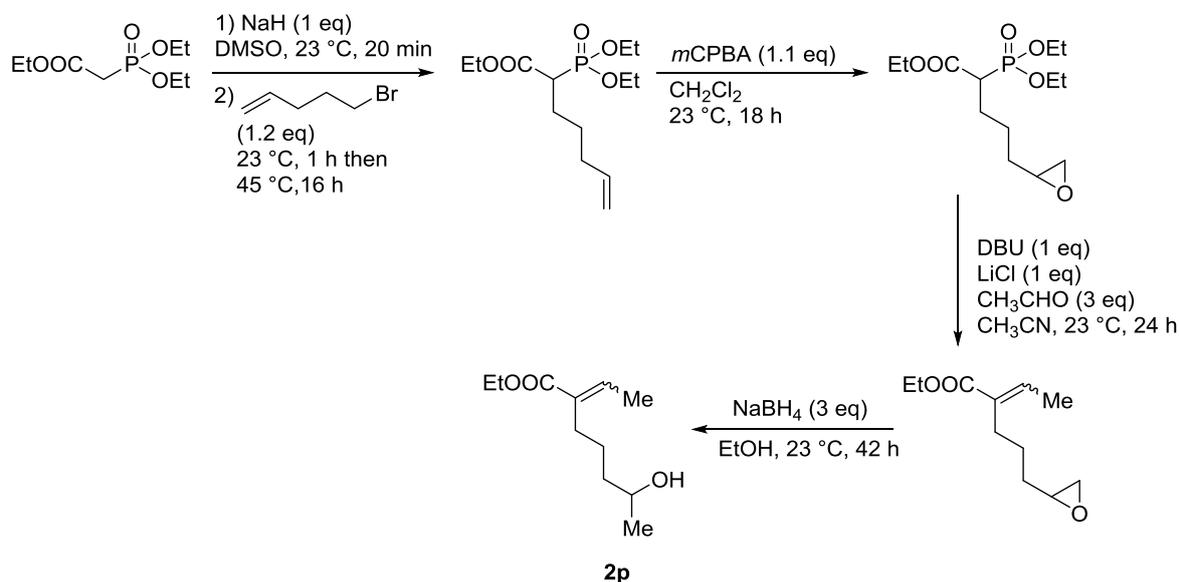
**Figure S38:** Expansion of  $^2\text{H}$ -NMR in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 20 mol% of **1b**



**Figure S39:** Expansion of  $^2\text{H}$ -NMR in  $\text{C}_6\text{D}_6$  of the crude reaction mixture using 40 mol% of **1b**

## 2.4.3 Assessment of site-selectivity of [Pd-H] insertion

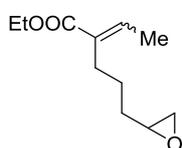
### 2.4.3.1 Synthesis of 2p



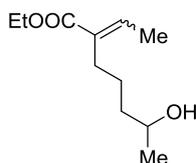
**Figure S40:** Synthesis of Ethyl 2-ethylidene-6-hydroxyheptanoate (**2p**)

**1-(diethoxyphosphoryl)-4-(oxiran-2-yl)butyl propionate:** The  $\alpha$ -alkylation of triethyl phosphonacetate was performed according to a known procedure<sup>40</sup> affording ethyl 2-(diethoxyphosphoryl)hept-6-enoate in 71% yield. In a round-bottom flask the  $\alpha$ -alkylated phosphonacetate (5 mmol, 1.46 g) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (12.5 mL) and cooled to 0 °C. Next, *m*CPBA (70% wt purity, 5.5 mmol, 1.36 g) was added in two portions. After 18 h at room temperature, all starting material had been consumed (TLC monitoring) and water (10 mL) was added. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 15 mL), washed with 5% aqueous NaOH, a saturated aqueous NaHCO<sub>3</sub> solution, water and brine. The organic phases were combined, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent removed *in vacuo*. The residue was purified by flash chromatography on silica gel (Diethyl ether) to afford the epoxide as a pale yellow oil in 72% (1.1 g).  $R_f = 0.2$  (Diethyl ether = 6:4). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 1.29 (td, <sup>3</sup>J<sub>HH</sub> = 7.1, 1.0 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.33 (td, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, <sup>4</sup>J<sub>PH</sub> = 3.9 Hz, 6H, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>P), 1.43 – 1.62 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>; 2H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.84 – 1.94 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 1.99 – 2.09 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 2.45 – 2.47 (m, 1H, CH(O)CH<sub>2</sub>), 2.73 – 2.75 (m, 1H, CH(O)CH<sub>2</sub>), 2.87 – 2.90 (m, 1H, CH(O)CH<sub>2</sub>), 2.91 – 2.98 (m, 1H, CHP), 4.11 – 4.18 (m, 4H, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>P), 4.19 – 4.27 (m, 2H, CH<sub>3</sub>CH<sub>2</sub>O). <sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) 14.3 (CH<sub>3</sub>CH<sub>2</sub>O), 16.5 (dd, <sup>3</sup>J<sub>CP</sub> = 6.0, 3.9 Hz, (CH<sub>3</sub>CH<sub>2</sub>O)<sub>2</sub>P), 25.0 (dd, <sup>3</sup>J<sub>CP</sub> = 15.3, 5.9 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 26.9 (m, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 32.2 (d, <sup>4</sup>J<sub>CP</sub> = 10.3 Hz, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>), 45.9 (d, <sup>1</sup>J<sub>CP</sub> = 131.3 Hz, CHP), 47.2 (d, <sup>6</sup>J<sub>CP</sub> = 14.4 Hz, CH(O)CH<sub>2</sub>), 52.0 (d, <sup>5</sup>J<sub>CP</sub> = 3.2 Hz, CH(O)CH<sub>2</sub>), 61.6 (CH<sub>3</sub>CH<sub>2</sub>O),

62.9 (dd,  $^2J_{CP} = 10.7, 6.6$  Hz,  $(\text{CH}_3\text{CH}_2\text{O})_2\text{P}$ ), 169.3 (dd,  $^2J_{CP} = 4.9, 1.0$  Hz,  $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 309$ ,  $[\text{M}+\text{Na}]^+ = 331$ . **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2983, 2935, 2870, 1731, 1446, 1392, 1369, 1332, 1250, 1209, 1158, 1097, 1019, 958, 845, 789, 760, 645$ .



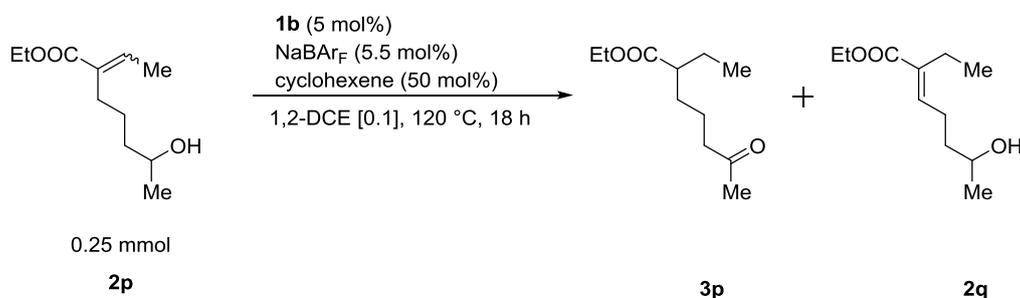
**Ethyl 2-ethylidene-5-(oxiran-2-yl)pentanoate:** In a 2-neck round bottom flask, 1-(diethoxyphosphoryl)-4-(oxiran-2-yl)butyl propionate (3.4 mmol, 1.05 g) was dissolved in  $\text{CH}_3\text{CN}$  (23 mL) and  $\text{LiCl}$  (3.4 mmol, 144 mg) was added at room temperature. After 5 minutes,  $\text{DBU}$  (3.4 mmol, 0.5 mL) was added and the mixture stirred for 5 more minutes. The reaction was cooled to  $0^\circ\text{C}$  and acetaldehyde (10.2 mmol, 0.57 mL) in  $\text{CH}_3\text{CN}$  (10 mL) was slowly added stirred at room temperature. After 24 h, the reaction was quenched with a saturated aqueous  $\text{NH}_4\text{Cl}$  solution (20 mL) and extracted with diethyl ether (3 x 20 mL). The organic phases were combined and dried over  $\text{Na}_2\text{SO}_4$  and the solvent removed *in vacuo*. The residual oil was purified by flash chromatography on silica gel (Pentane/Diethyl ether 7:3) to afford ethyl 2-ethylidene-5-(oxiran-2-yl)pentanoate as a yellow oil in 31% yield (213 mg, *E/Z* 3.3:1).  $R_f = 0.3$  (Diethyl ether). **IR (neat)**:  $\nu(\text{cm}^{-1}) = 2977, 2934, 2861, 1706, 1648, 1451, 1384, 1370, 1285, 1255, 1184, 1134, 1106, 1044, 951, 918, 832, 786, 750, 581$ .  **$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) Major Isomer: 1.28 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.50 – 1.59 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.79 (d,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3$ ), 2.34 – 2.37 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 2.46 – 2.47 (dd,  $^3J_{\text{HH}} = 5.0, 2.7$  Hz, 1H,  $\text{CH}(\text{O})\text{CH}_2$ ), 2.73 – 2.74 (m, 1H  $\text{CH}(\text{O})\text{CH}_2$ ), 2.88 – 2.93 (m, 1H,  $\text{CH}(\text{O})\text{CH}_2$ ), 4.17 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.86 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 1H,  $\text{C}=\text{CH}$ ). Minor Isomer: 1.30 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.50 – 1.59 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.95 (m, 3H,  $\text{CH}_3$ ), 2.27 – 2.30 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 2.44-2.46 (m, 1H,  $\text{CH}(\text{O})\text{CH}_2$ ), 2.73-2.74 (m, 1H,  $\text{CH}(\text{O})\text{CH}_2$ ), 2.88-2.93 (m, 1H,  $\text{CH}(\text{O})\text{CH}_2$ ), 4.21 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 5.98 (m, 1H,  $\text{C}=\text{CH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) Major Isomer: 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 14.4 ( $\text{CH}_3\text{CH}=\text{C}$ ), 25.5 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 26.2 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 32.3 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 47.2 ( $\text{CH}(\text{O})\text{CH}_2$ ), 52.3 ( $\text{CH}(\text{O})\text{CH}_2$ ), 60.5 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 133.1 ( $\text{C}=\text{CH}$ ), 137.6 ( $\text{C}=\text{CH}$ ), 167.9 ( $\text{C}=\text{O}$ ). Minor Isomer: 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 14.4 ( $\text{CH}_3\text{CH}=\text{C}$ ), 25.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 32.0 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 34.4 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 47.2 ( $\text{CH}(\text{O})\text{CH}_2$ ), 52.3 ( $\text{CH}(\text{O})\text{CH}_2$ ), 60.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 132.7 ( $\text{C}=\text{CH}$ ), 136.6 ( $\text{C}=\text{CH}$ ), 168.2 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{K}]^+ = 237$ .



**Ethyl 2-ethylidene-6-hydroxyheptanoate (2p):** In a round-bottom flask, ethyl 2-ethylidene-5-(oxiran-2-yl)pentanoate (0.77 mmol, 153 mg) was dissolved in abs. EtOH (15 mL) and  $\text{NaBH}_4$  (2.31 mmol, 88 mg) was added in a single portion. After stirring for 42 h at room temperature, the solvent was removed *in vacuo* and the crude mixture was purified by flash chromatography on silica

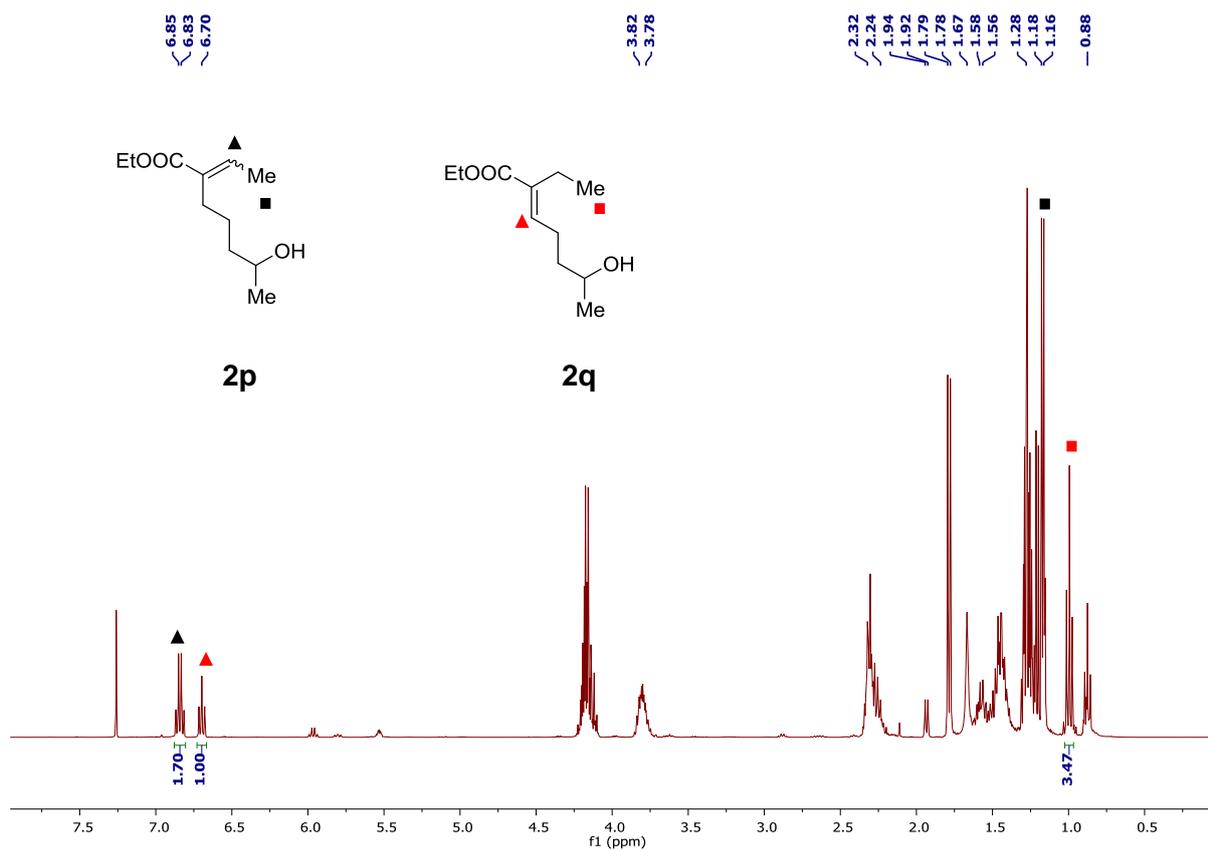
gel (Pentane/Diethyl ether 7:3) to afford **2p** in 79% yield (122 mg, *E/Z* 3.2:1) as a pale yellow oil.  $R_f = 0.5$  (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1}) = 3442, 2965, 2932, 2864, 1707, 1648, 1449, 1391, 1381, 1329, 1283, 1258, 1180, 1135, 1095, 1041, 941, 856, 749, 666$ .  **$^1\text{H NMR}$**  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) Major Isomer: 1.19 (d,  $^3J_{\text{HH}} = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ), 1.29 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 1.38 – 1.67 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 1H, *OH*), 1.80 (d,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{C}=\text{CHCH}_3$ ), 2.23 – 2.35 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 3.77 – 3.85 (m, 1H, *CHOH*), 4.19 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 6.86 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 1H,  $\text{C}=\text{CH}$ ). Minor Isomer: 1.31 (t,  $^3J_{\text{HH}} = 7.1$  Hz, 3H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 4.22 (q,  $^3J_{\text{HH}} = 7.1$  Hz, 2H,  $\text{CH}_3\text{CH}_2\text{O}$ ), 5.98 (m, 1H,  $\text{C}=\text{CH}$ ), 1.95 (m, 3H,  $\text{C}=\text{CHCH}_3$ ), 2.23 – 2.35 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 1.38 – 1.67 (m, 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 2H,  $\text{CH}_2\text{CH}_2\text{CH}_2$ ; 1H, *OH*), 3.77 – 3.85 (m, 1H, *CHOH*), 1.16 (d,  $J = 6.2$  Hz, 3H,  $\text{CH}_3\text{CHOH}$ ).  **$^{13}\text{C}\{^1\text{H}\}$  NMR** (126 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) Major Isomer: 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 14.4 ( $\text{C}=\text{CHCH}_3$ ), 23.6 ( $\text{CH}_3\text{CHOH}$ ), 25.3 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 26.2 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 38.9 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 60.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 68.0 (*CHOH*), 133.4 ( $\text{C}=\text{CH}$ ), 137.4 ( $\text{C}=\text{CH}$ ), 168.0 ( $\text{C}=\text{O}$ ). Minor Isomer: 14.4 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 15.8 ( $\text{C}=\text{CHCH}_3$ ), 23.6 ( $\text{CH}_3\text{CHOH}$ ), 25.4 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 34.6 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 38.8 ( $\text{CH}_2\text{CH}_2\text{CH}_2$ ), 60.2 ( $\text{CH}_3\text{CH}_2\text{O}$ ), 68.0 (*CHOH*), 133.0 ( $\text{C}=\text{CH}$ ), 136.3 ( $\text{C}=\text{CH}$ ), 168.4 ( $\text{C}=\text{O}$ ). **LRMS (IC)** found  $[\text{M}+\text{H}]^+ = 201$ ,  $[\text{M}+\text{Na}]^+ = 223$

#### 2.4.3.2 Isomerization of **2p**



The reaction was performed according to GP1. After 18 h, conversion into **3p** was 39% (34% yield) and consumption was 69%.

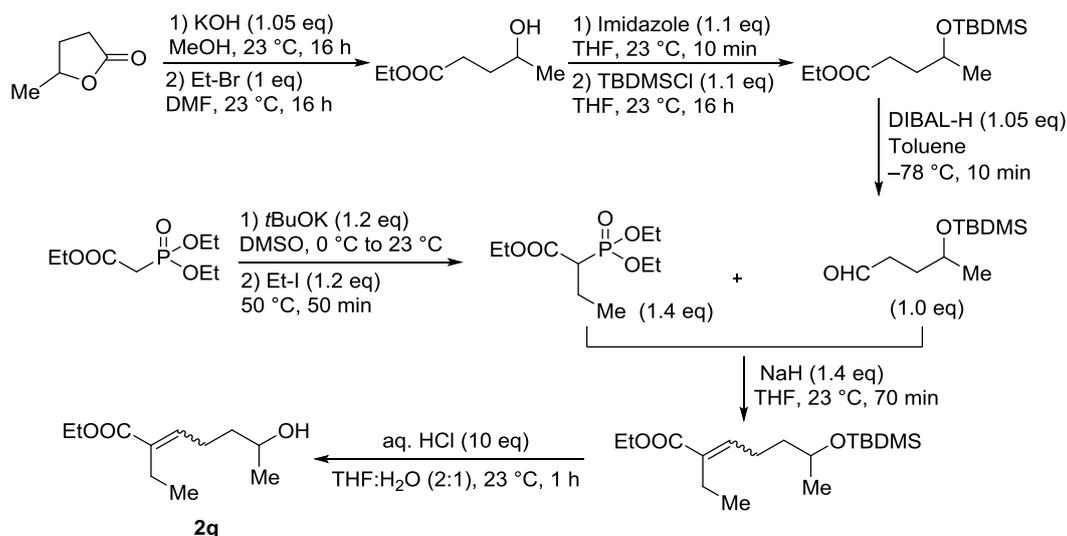
Note: No formation of **2q** was detected when the starting material was subjected to the same reaction conditions in absence of the palladium precatalyst.



**Figure S41:**  $^1\text{H-NMR}$  spectrum of the fraction containing **2p/2q**

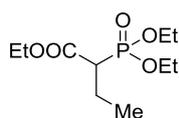
To confirm the identity of the second product present in this reaction mixture, spiking experiments were performed using **2q** prepared by an independent synthesis (see below).

## 2.4.3.3 Independent synthesis of 2q



**Figure S42:** Synthesis of Ethyl 2-ethyl-6-hydroxyhept-2-enoate (**2q**)

**4-((*tert*-butyldimethylsilyl)oxy)pentanal:** In a 2-neck round bottom flask,  $\gamma$ -valerolactone (10 mmol, 1 g) was dissolved in MeOH (50 mL) and KOH (10.5 mmol, 589 mg) was added at room temperature. After 16 h, the solvent was evaporated and the residual material redissolved in DMF (50 mL). To this solution was added dropwise ethylbromide (10 mmol, 1.09 g) at room temperature. After 16 h, the reaction was quenched with water and extracted with diethyl ether (3  $\times$  50 mL). The organic phases were combined, dried over Na<sub>2</sub>SO<sub>4</sub> and the solvent evaporated to afford a clear oil that was used in the next step without further purification.<sup>41</sup> The crude oil was dissolved in THF (26 mL), imidazole (8.6 mmol, 584 mg) was added and the solution stirred at room temperature for 10 minutes before the addition of TBDMSCl (8.6 mmol, 1.30 g) in a single portion. The reaction was stirred for 16 h at room temperature and then quenched with a saturated aqueous NaHCO<sub>3</sub> solution (20 mL), extracted with diethyl ether (3  $\times$  30 mL) and washed with brine. The organic phases were combined, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The clear oil obtained was dissolved in toluene (30 mL) and cooled to -78 °C before the dropwise addition of DIBAL-H (1.9 mL from a 1 M solution in hexane). After 10 minutes, the reaction was quenched at 0 °C with a saturated aqueous NH<sub>4</sub>Cl solution and extracted with diethyl ether (3  $\times$  30 mL). The organic phases were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. The residual material was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) affording 4-((*tert*-butyldimethylsilyl)oxy)pentanal as a colourless oil in 36% yield (140 mg) over 4 steps.

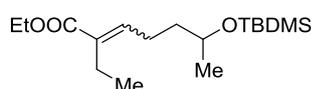


**Ethyl 2-(diethoxyphosphoryl)butanoate:** In a 2-neck round bottom flask,

triethyl phosphonacetate (10 mmol, 2.24 g) was dissolved in DMSO (6.7 mL)

and cooled to 0 °C. Next, *t*BuOK (12 mmol, 1.34 g) was added and the

resulting suspension was stirred at room temperature until complete consumption of the base. Ethyliodide (12 mmol, 1.87 g) was added dropwise and stirred for 50 minutes at 50 °C.<sup>42</sup> The reaction was quenched with a saturated aqueous NH<sub>4</sub>Cl solution and extracted with diethyl ether (3 x 10 mL). The organic phases were combined, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated. After flash chromatography on silica gel (Diethyl ether) the product was obtained in 73% yield (1.85 g) as a colourless oil.



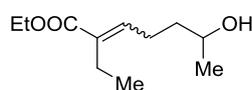
**Ethyl 6-((tert-butyldimethylsilyloxy)-2-ethylhept-2-enoate:** In

a 2-necked flask, ethyl 2-(diethoxyphosphoryl)butanoate (0.975 mmol, 246 mg) was dissolved in THF (5 mL) before the addition of

NaH (0.975 mmol, 23 mg) in one portion. After 10 minutes at room temperature, 4-((tert-butyldimethylsilyloxy)pentanal (0.65 mmol) in THF (1 mL) was added dropwise and stirred for 1 h. The reaction was quenched with water (5 mL), extracted with diethyl ether (3 x 10 mL), the organic phases combined, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. After flash chromatography on silica gel (Pentane/Diethyl ether = 10:1) the product was obtained in 67% yield (137 mg, *E/Z* = 1.7:1) as a colourless oil. *R*<sub>f</sub> = 0.7 (Pentane/Diethyl ether = 10:1).

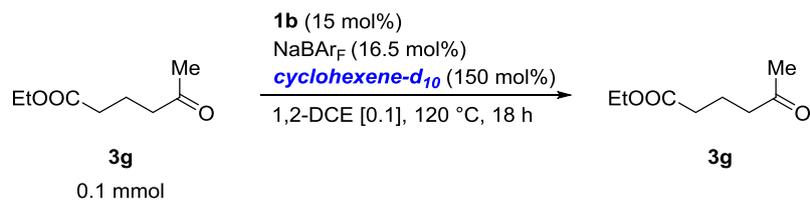
**IR (neat):**  $\nu(\text{cm}^{-1})$  = 2963, 2936, 2886, 2857, 1713, 1461, 1446, 1374, 1285, 1252, 1201, 1140, 1087, 1037, 996, 836, 804, 774, 613. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) Major Isomer: 0.05 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.06 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.89 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.00 (t, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, 3H, CCH<sub>2</sub>CH<sub>3</sub>), 1.15 (d, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, 3H, CH<sub>3</sub>CHOH), 1.29 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.51 – 1.57 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 2.10 – 2.20 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 2.24 – 2.29 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 2.31 (q, <sup>3</sup>J<sub>HH</sub> = 7.5 Hz, 2H, CCH<sub>2</sub>CH<sub>3</sub>), 3.84 (h, <sup>3</sup>J<sub>HH</sub> = 5.5 Hz, 1H, CH<sub>2</sub>CH<sub>2</sub>CH), 4.19 (q, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.72 (t, <sup>3</sup>J<sub>HH</sub> = 7.6 Hz, 1H, C=CH), 26.3 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), Minor Isomer: 0.04 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.05 (s, 3H, (CH<sub>3</sub>)<sub>2</sub>Si), 0.88 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 1.02 (t, 3H, CCH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J<sub>HH</sub> = 7.4 Hz), 1.13 (d, <sup>3</sup>J<sub>HH</sub> = 6.6 Hz, 3H, CH<sub>3</sub>CHOH), 1.30 (t, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.51 – 1.57 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 2.24 – 2.29 (m, 2H, CCH<sub>2</sub>CH<sub>3</sub>), 2.35 – 2.48 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 3.80 (h, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, 1H, CH<sub>2</sub>CH<sub>2</sub>CH), 4.20 (q, 2H, CH<sub>3</sub>CH<sub>2</sub>O, <sup>3</sup>J<sub>HH</sub> = 7.1 Hz), 5.81 – 5.85 (m, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) Major Isomer: -4.2, -4.6 ((CH<sub>3</sub>)<sub>2</sub>Si), 14.1 (CCH<sub>2</sub>CH<sub>3</sub>), 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 20.2 (CCH<sub>2</sub>CH<sub>3</sub>), 23.8 (CH<sub>3</sub>CHOH), 24.8 (CH<sub>2</sub>CH<sub>2</sub>CHO), 26.0 ((CH<sub>3</sub>)<sub>3</sub>CSi), 38.9 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 60.4 (CH<sub>3</sub>CH<sub>2</sub>O), 68.2 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 134.2 (C=CH), 141.9 (C=CH), 168.1 (C=O). Minor Isomer: -4.3, -4.6 ((CH<sub>3</sub>)<sub>2</sub>Si), 13.8 (CCH<sub>2</sub>CH<sub>3</sub>), 14.5 (CH<sub>3</sub>CH<sub>2</sub>O), 18.3 ((CH<sub>3</sub>)<sub>3</sub>CSi), 23.9 (CH<sub>3</sub>CHOH), 26.1 ((CH<sub>3</sub>)<sub>3</sub>CSi), 26.1 (CH<sub>2</sub>CH<sub>2</sub>CHOH),

27.7 (CCH<sub>2</sub>CH<sub>3</sub>), 39.6 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 60.2 (CH<sub>3</sub>CH<sub>2</sub>O), 68.4 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 133.9 (C=CH), 140.1 (C=CH), 168.5 (C=O). **LRMS (IC)** found [M+Na]<sup>+</sup> = 338.



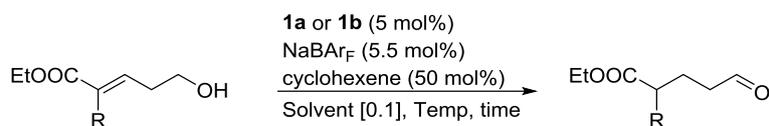
**Ethyl 2-ethyl-6-hydroxyhept-2-enoate (2q):** In a round-bottomed flask ethyl 6-((tert-butyldimethylsilyl)oxy)-2-ethylhept-2-enoate (0.41 mmol) was dissolved in THF/H<sub>2</sub>O 2:1 (4 mL) and cooled to 0 °C before the dropwise addition of aqueous HCl (0.7 mL from a 6 M solution). After 1 h at room temperature, the reaction was diluted with water and extracted with diethyl ether (3 × 5 mL) then the organic phases were combined, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated *in vacuo*. Flash chromatography on silica gel (Pentane/Diethyl ether = 1:1) afforded the desired product in 80% yield (66 mg, *E/Z* = 1.7:1) as a colourless oil. *R<sub>f</sub>* = 0.2 (Pentane/Diethyl ether = 1:1). **IR (neat):**  $\nu(\text{cm}^{-1})$  = 3418, 2969, 2933, 1704, 1464, 1458, 1374, 1291, 1240, 1193, 1140, 1098, 1036, 943, 847, 765. **<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) Major Isomer: 1.01 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.5 Hz, 3H, CCH<sub>2</sub>CH<sub>3</sub>), 1.22 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.2 Hz, 3H, CH<sub>3</sub>CHOH), 1.29 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.54 – 1.61 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 1.72, (bs, 1H, OH), 2.24 – 2.35 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH; 2H, CCH<sub>2</sub>CH<sub>3</sub>), 3.83 (h, <sup>3</sup>*J*<sub>HH</sub> = 6.3 Hz, 1H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 4.19 (q, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 2H, CH<sub>3</sub>CH<sub>2</sub>O), 6.71 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.6 Hz, 1H, C=CH), Minor Isomer: 1.03 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.4 Hz, 3H, CCH<sub>2</sub>CH<sub>3</sub>), 1.19 (d, <sup>3</sup>*J*<sub>HH</sub> = 6.2 Hz, 3H, CH<sub>3</sub>CHOH), 1.31 (t, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz, 3H, CH<sub>3</sub>CH<sub>2</sub>O), 1.54 – 1.61 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 1.72, (bs, 1H, OH), 2.24 – 2.35 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>CHOH; 2H, CCH<sub>2</sub>CH<sub>3</sub>), 3.75 – 3.80 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>CHOH), 4.22 (q, 2H, CH<sub>3</sub>CH<sub>2</sub>O, <sup>3</sup>*J*<sub>HH</sub> = 7.1 Hz), 5.80 – 5.83 (m, 1H, C=CH). **<sup>13</sup>C{<sup>1</sup>H} NMR** (126 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm) Major Isomer: 13.8 (CCH<sub>2</sub>CH<sub>3</sub>), 14.1 (CCH<sub>2</sub>CH<sub>3</sub>), 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 20.2 (CCH<sub>2</sub>CH<sub>3</sub>), 23.2 (CH<sub>3</sub>CHOH), 23.8 (CH<sub>3</sub>CHOH), 24.8 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 38.4 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 60.5 (CH<sub>3</sub>CH<sub>2</sub>O), 67.7 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 134.6 (C=CH), 141.2 (C=CH), 168.0 (C=O). Minor Isomer: 14.4 (CH<sub>3</sub>CH<sub>2</sub>O), 26.6 (CCH<sub>2</sub>CH<sub>3</sub>), 27.7 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 38.4 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 60.6 (CH<sub>3</sub>CH<sub>2</sub>O), 66.5 (CH<sub>2</sub>CH<sub>2</sub>CHOH), 134.9 (C=CH), 139.5 (C=CH), 168.9 (C=O). **LRMS (IC)** found [M+Na]<sup>+</sup> = 224.

#### 2.4.4 Control experiment using **3g**



Inside the glovebox, a 5 mL Young valve Schlenk was charged with the precatalyst **1b** (0.015 mmol, 7.1 mg), NaBAR<sub>F</sub> (0.0165 mmol, 14.6 mg) and 1,2-dichloroethane (1 mL). After stirring at room temperature for 5 minutes, cyclohexene-*d*<sub>10</sub> (0.15 mmol, 15 μL) was added and the mixture stirred for 5 minutes. Next, substrate **3g** (0.1 mmol, 15.8 mg) was added to the mixture and the sealed Schlenk was placed in an oil bath pre-heated at 120 °C. After 18 h, deuterium incorporation was assessed by <sup>2</sup>H-NMR using 1,1,2,2-tetrachloroethane (0.05 mmol) as internal standard. No deuterium incorporation was detectable.

## 2.5 Optimization of the deconjugative isomerization under microwave (MW) irradiation



Inside the glovebox, a 5 mL microwave reaction vial was charged with **1a** or **1b** (0.0125 mmol), NaBAR<sub>F</sub> (12.2 mg, 0.0138 mmol) and the solvent (2.5 mL). After 5 minutes, cyclohexene (0.125 mmol, 13 μL) was added and the reaction mixture stirred for 5 minutes. Next, the appropriate substrate (0.25 mmol) was added. The sealed reaction vial was placed in a microwave oven and stirred at the desired temperature for the appropriate time. The mixture was then cooled to room temperature and the solvent removed *in vacuo*.

Entry	Cat.	R	Solvent	MW	Temp (°C)	Time (h)	Yield (%)
1	<b>1a</b>	Me	1,2-DCE	Yes	160	2	28
2	<b>1a</b>	Me	Toluene	Yes	160	2	50
3	<b>1a</b>	Me	DMF	Yes	160	2	0
4	<b>1a</b>	Ph	1,2-DCE	No	120	18	45
5	<b>1a</b>	Ph	1,2-DCE	Yes	120	4	45
6	<b>1a</b>	Ph	1,2-DCE	Yes	140	2	49
7	<b>1a</b>	Ph	1,2-DCE	Yes	140	4	55
8	<b>1a</b>	Ph	1,2-DCE	Yes	160	2	56
9	<b>1a</b>	Ph	1,2-DCE	Yes	160	4	47
10	<b>1b</b>	Ph	1,2-DCE	Yes	140	2	50

**Table 2:** Reaction optimization under microwave irradiation

## 2.5.1 Chiral ligand screening

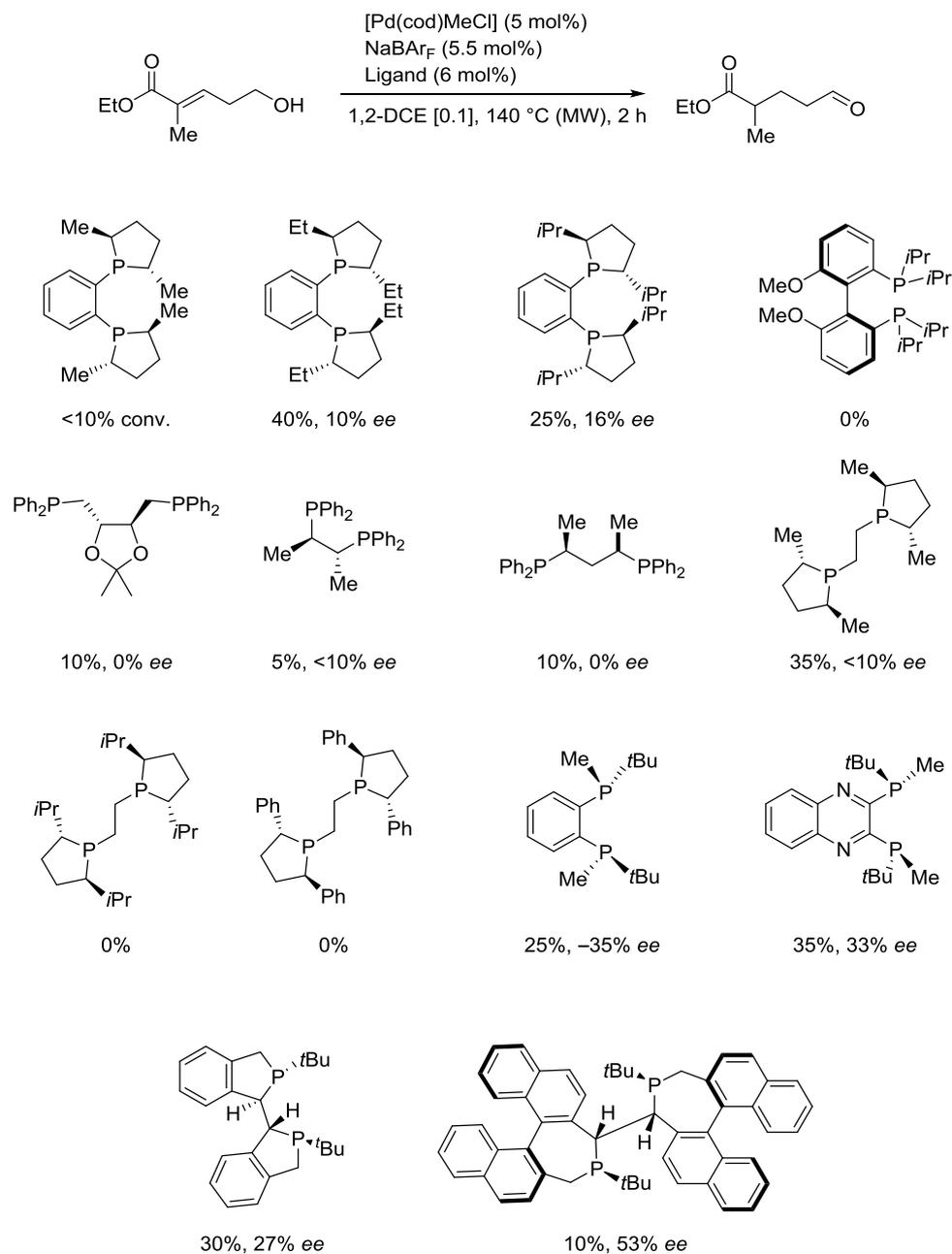
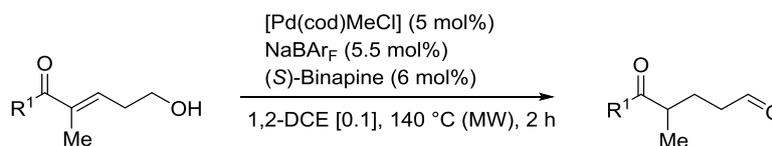
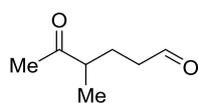


Figure S43: Ligand screening

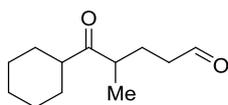
## 2.6 General procedure for enantioselective deconjugative isomerization



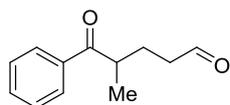
Inside the glovebox, a 5 mL microwave reaction vial was charged with [Pd(cod)MeCl] (3.4 mg, 0.0125 mmol), (S)-Binapine (11 mg, 0.015 mmol) and 1,2-dichloroethane (2.5 mL). The mixture was stirred for 5 minutes at room temperature then NaBAR<sub>F</sub> (12.2 mg, 0.0138 mmol) was added and the reaction mixture stirred 5 minutes. The appropriate substrate (0.25 mmol) was added and the sealed reaction vial was placed in a microwave oven. After 2 h at 140 °C, the mixture was cooled to room temperature and the solvent removed *in vacuo*. The crude mixture was purified by flash chromatography on silica gel to afford the analytically pure dicarbonyl product.



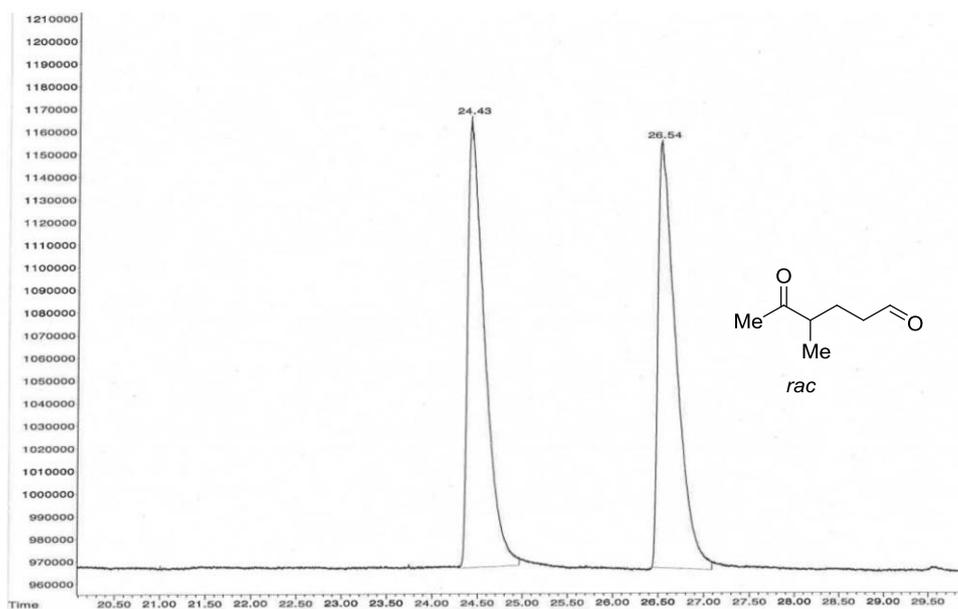
**4-methyl-5-oxohexanal (5a):** The residue was purified by flash chromatography on silica gel (Pentane/EtOAc = 40:1) affording **5a** in 50% yield (16 mg, 73% ee) as a colourless oil. The enantiomeric excess was determined by GC analysis: column HYDRODEX TBDM, method: 60 °C to 170 °C in 110 minutes then 170 °C for 30 minutes,  $t_R = 24.4$  and 26.5 min (**Figure S44**). Carrier gas: H<sub>2</sub> (60cm/s).  $[\alpha]_D^{23} = +0.71$  (c = 0.2, EtOH).



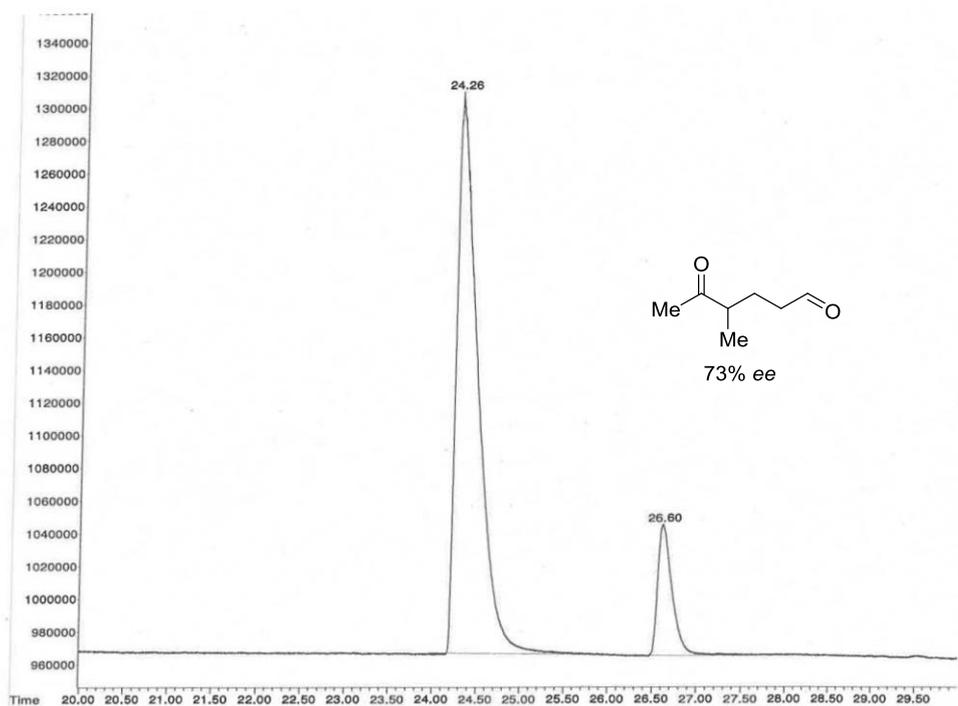
**5-cyclohexyl-4-methyl-5-oxopentanal (5b):** The residue was purified by flash chromatography on silica gel (Pentane/EtOAc = 40:1) affording **5b** in 57% yield (28 mg, 75% ee) as colourless oil. The enantiomeric excess was determined by GC analysis: column HYDRODEX  $\gamma$ -DiMOM, method: 60 °C to 170 °C in 110 minutes then 170 °C for 20 minutes,  $t_R = 96.1$  and 96.5 min (**Figure S45**). Carrier gas: H<sub>2</sub> (60cm/s).  $[\alpha]_D^{23} = -7.5$  (c = 0.5, EtOH).



**4-methyl-5-oxo-5-phenylpentanal (5g):** The residue was purified by flash chromatography on silica gel (Pentane/Diethyl ether = 7:3) affording **5g** in 99% yield (47 mg, 88% ee) as yellow oil. The enantiomeric excess was determined by HPLC analysis: AD-H column, Hexane/*i*PrOH 98:2, flow 1 mL/min,  $\lambda = 288$  nm,  $t_R = 11.6$  and 12.7 min (**Figure S46**).  $[\alpha]_D^{23} = -30.9$  (c = 0.25, CH<sub>2</sub>Cl<sub>2</sub>).

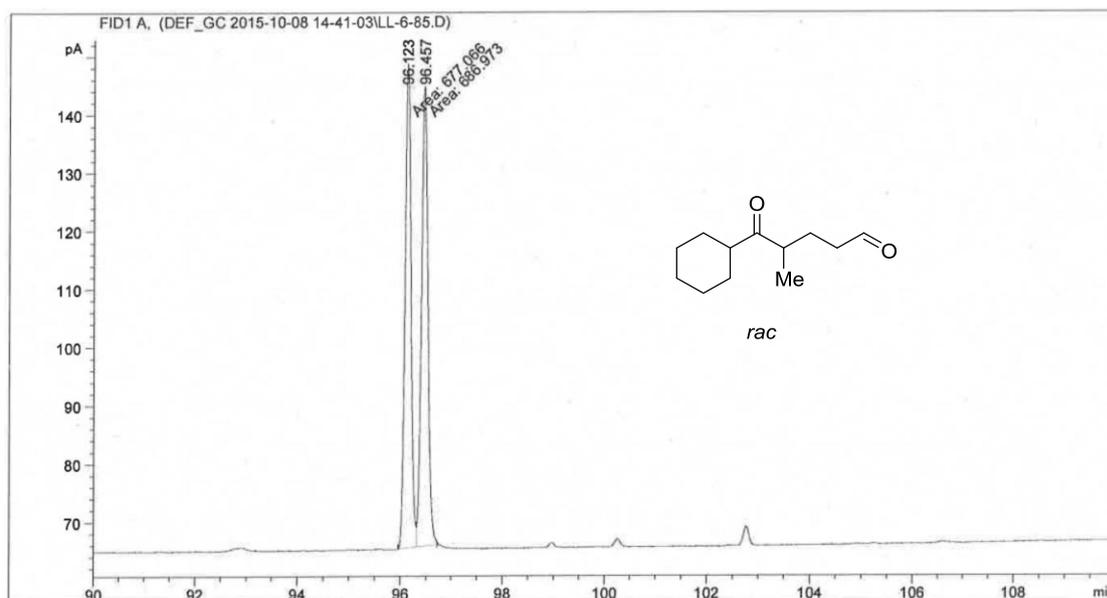


peak #	R.T. min	Start min	End min	PK TY	peak height	peak area	peak % max.	% of total
1	24.427	24.289	24.965	M	199747	25859894	99.79%	49.948%
2	26.539	26.413	27.089	M	189186	25914120	100.00%	50.052%

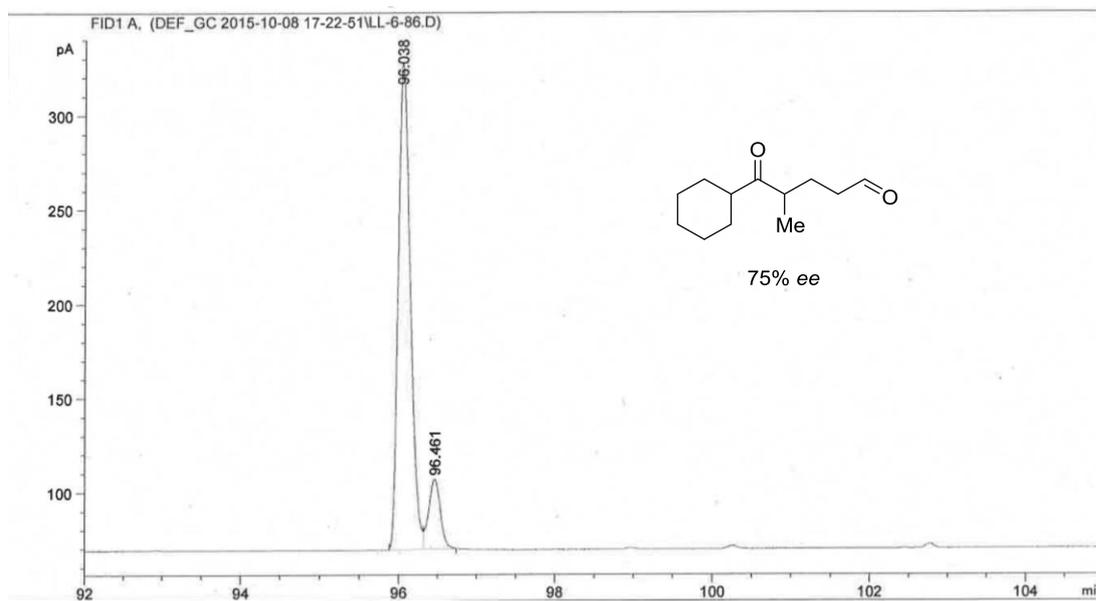


peak #	R.T. min	Start min	End min	PK TY	peak height	peak area	peak % max.	% of total
1	24.259	23.976	25.703	M	343483	57826235	100.00%	86.330%
2	26.602	26.294	27.540	M	80433	9156302	15.83%	13.670%

**Figure S44:** GC traces of racemic **5a** (top) and enantio-enriched **5a** (bottom)

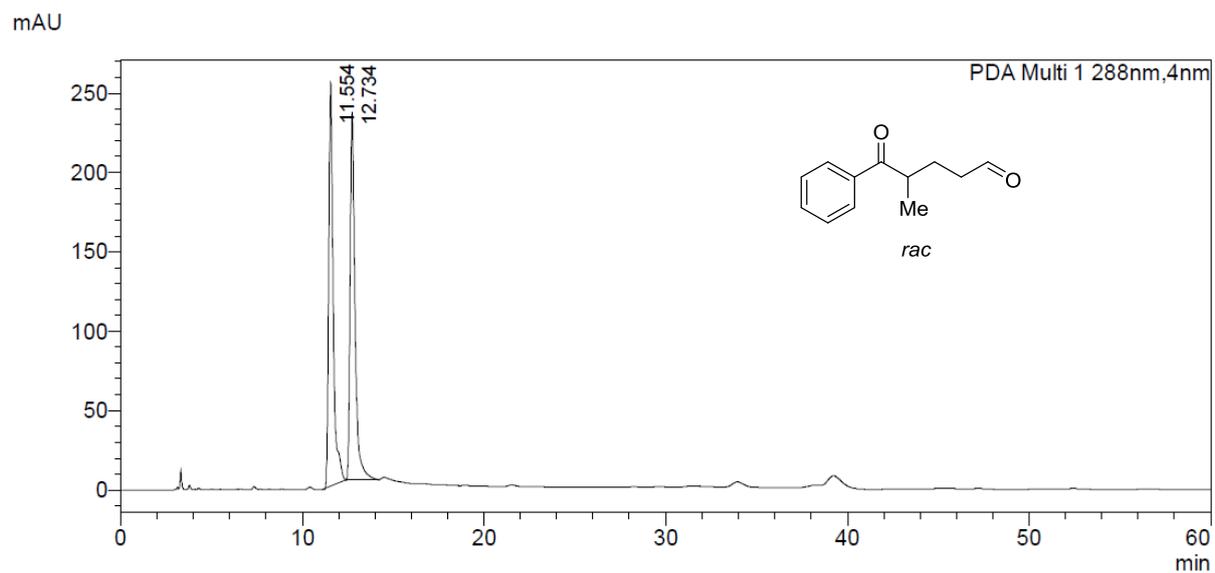


Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	96.123	MF	0.1355	677.06616	83.30847	49.63684
2	96.457	FM	0.1449	686.97339	79.02203	50.36316



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	96.038	BV	0.1364	2750.84058	257.92410	87.60887
2	96.461	VB	0.1265	389.07056	37.04260	12.39113

**Figure S45:** GC traces of racemic **5b** (top) and enantio-enriched **5b** (bottom)



PDA Ch1 288nm

Peak#	Ret. Time	Area%
1	11.554	50.059
2	12.734	49.941
Total		100.000

mAU

PDA Multi 1 288nm,4nm

11.448  
12.643

Me  
88% ee

0 25 50 75 100

0 10 20 30 40 50 min

PDA Ch1 288nm

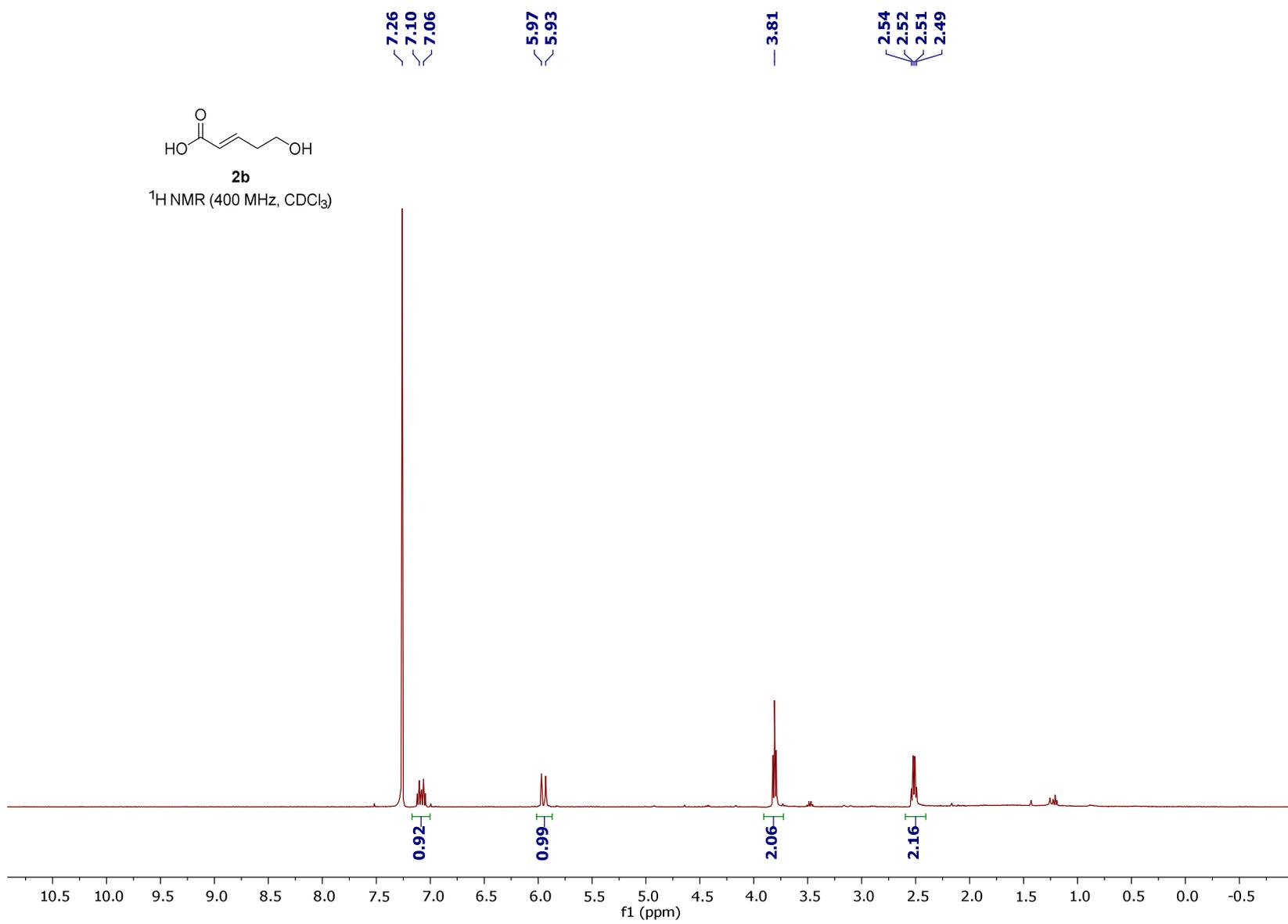
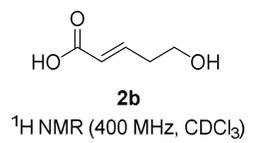
Peak#	Ret. Time	Area%
1	11.448	93.655
2	12.643	6.345
Total		100.000

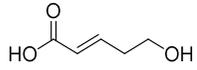
**Figure S46:** HPLC traces of racemic **5g** (top) and enantioenriched **5g** (bottom)

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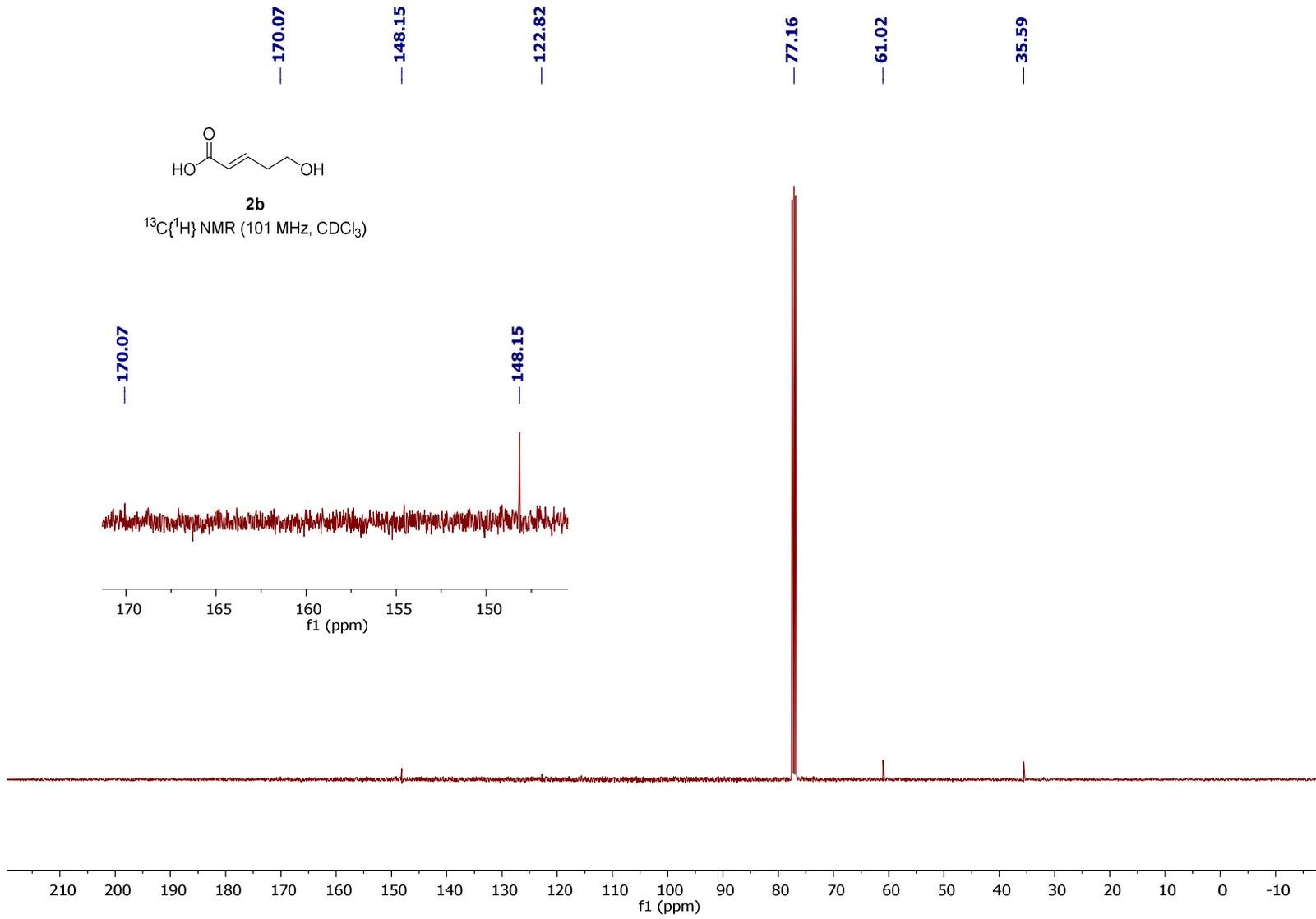
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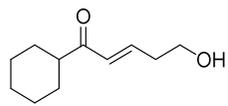




**2b**

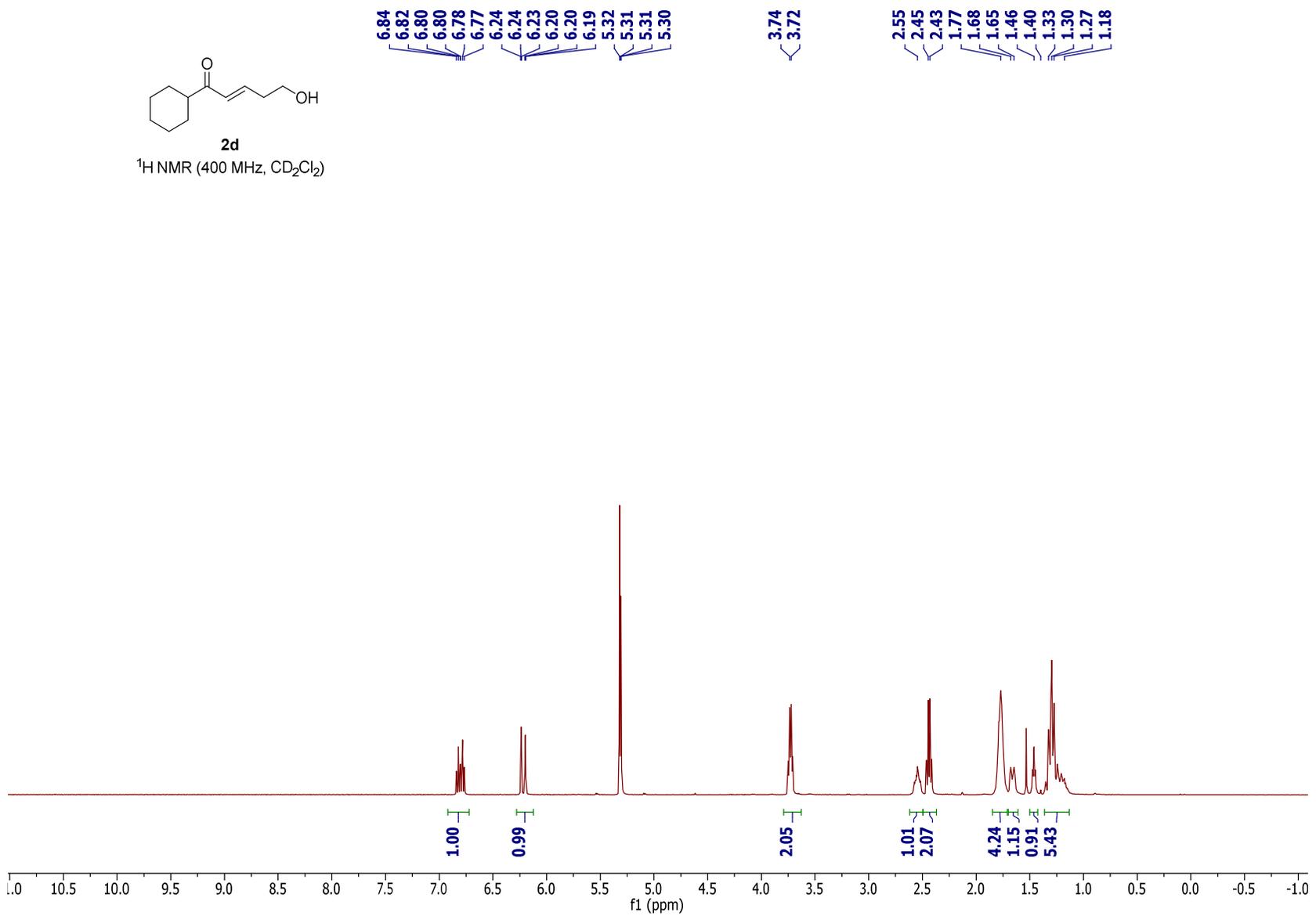
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





**2d**

<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)



— 203.09

— 143.11

— 130.94

— 61.42

— 53.84

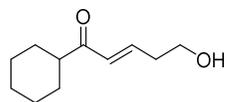
— 48.88

— 36.12

— 29.09

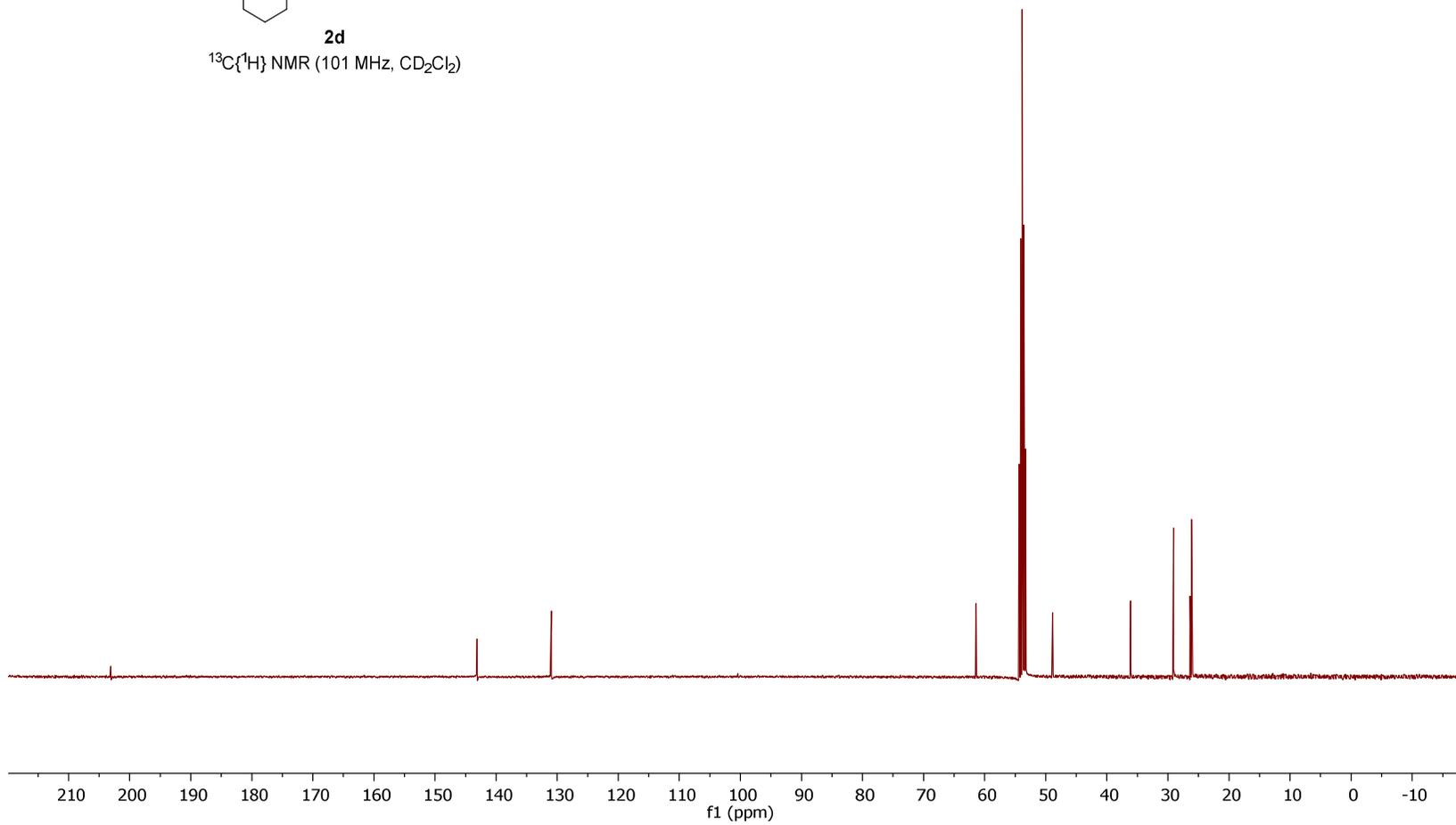
— 26.35

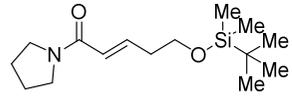
— 26.14



**2d**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )





<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

7.26  
6.91  
6.90  
6.88  
6.86  
6.84  
6.18  
6.18  
6.15  
6.14  
6.14

3.73  
3.71  
3.70  
3.51

2.42  
2.41

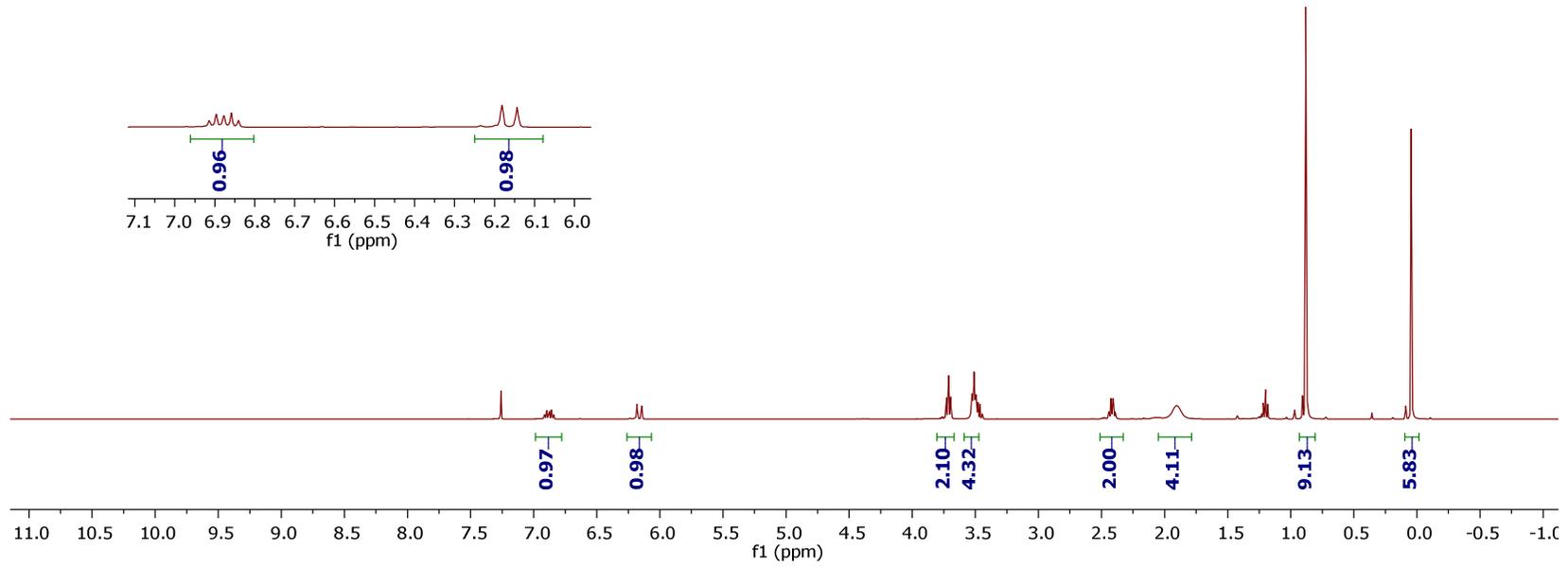
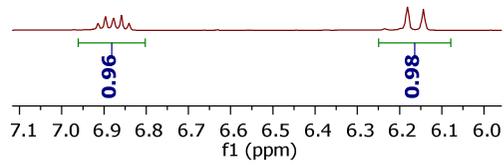
1.90

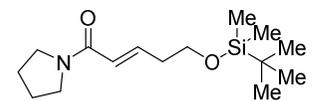
0.97  
0.88

0.04

6.91  
6.90  
6.86  
6.84

6.18  
6.14





$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 164.83

— 142.12

— 123.51

— 77.16

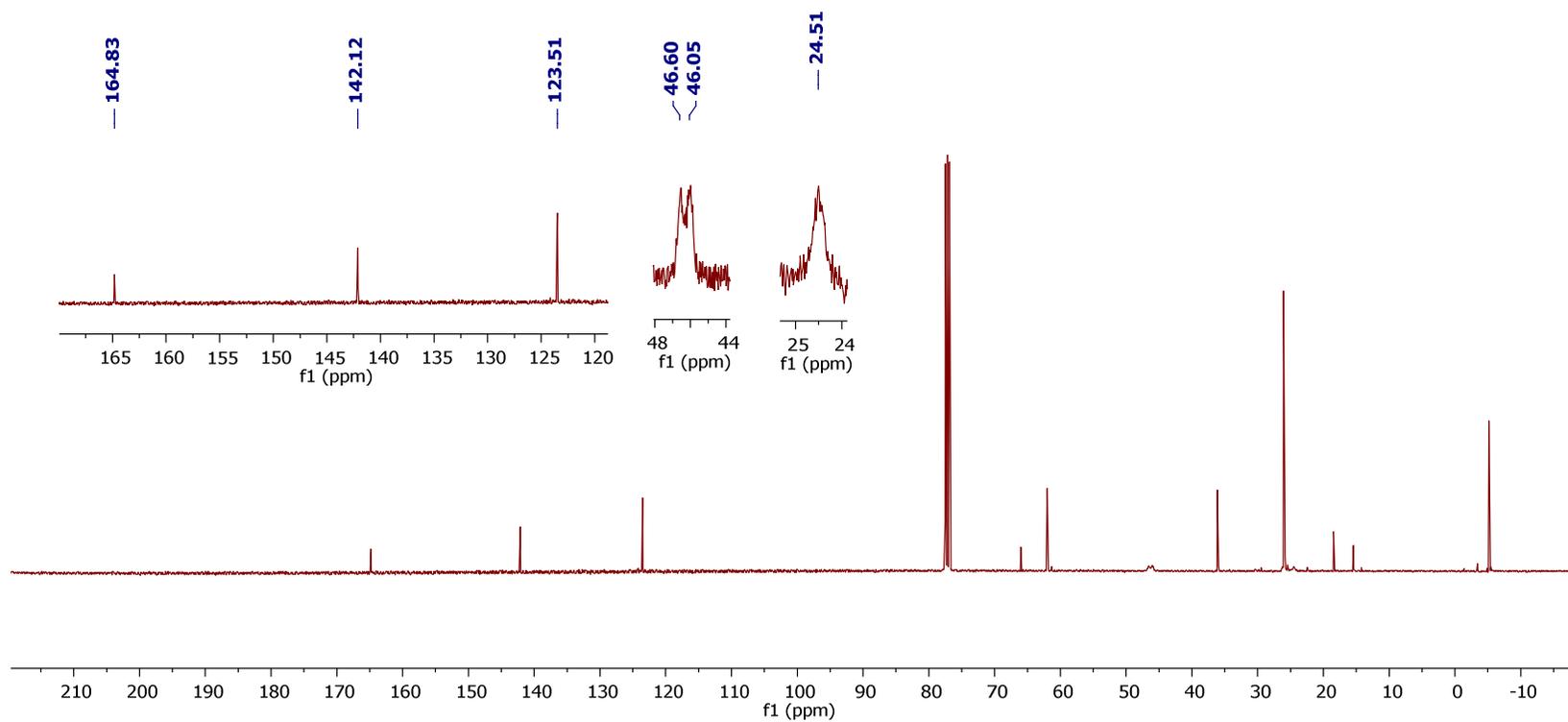
— 62.00

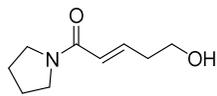
46.60  
46.05

— 36.11

26.05  
24.51  
18.44

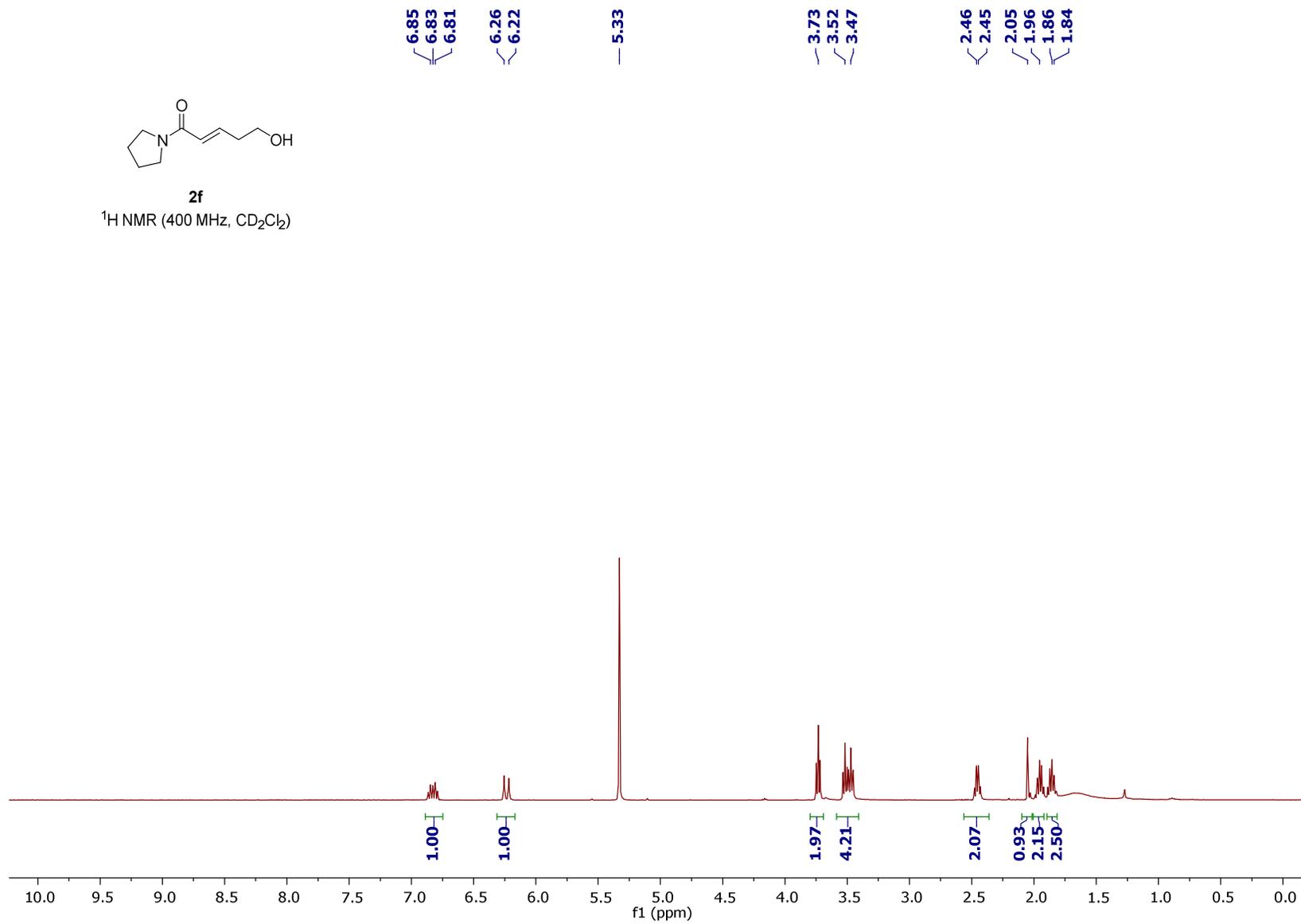
— -5.16

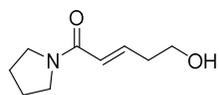




**2f**

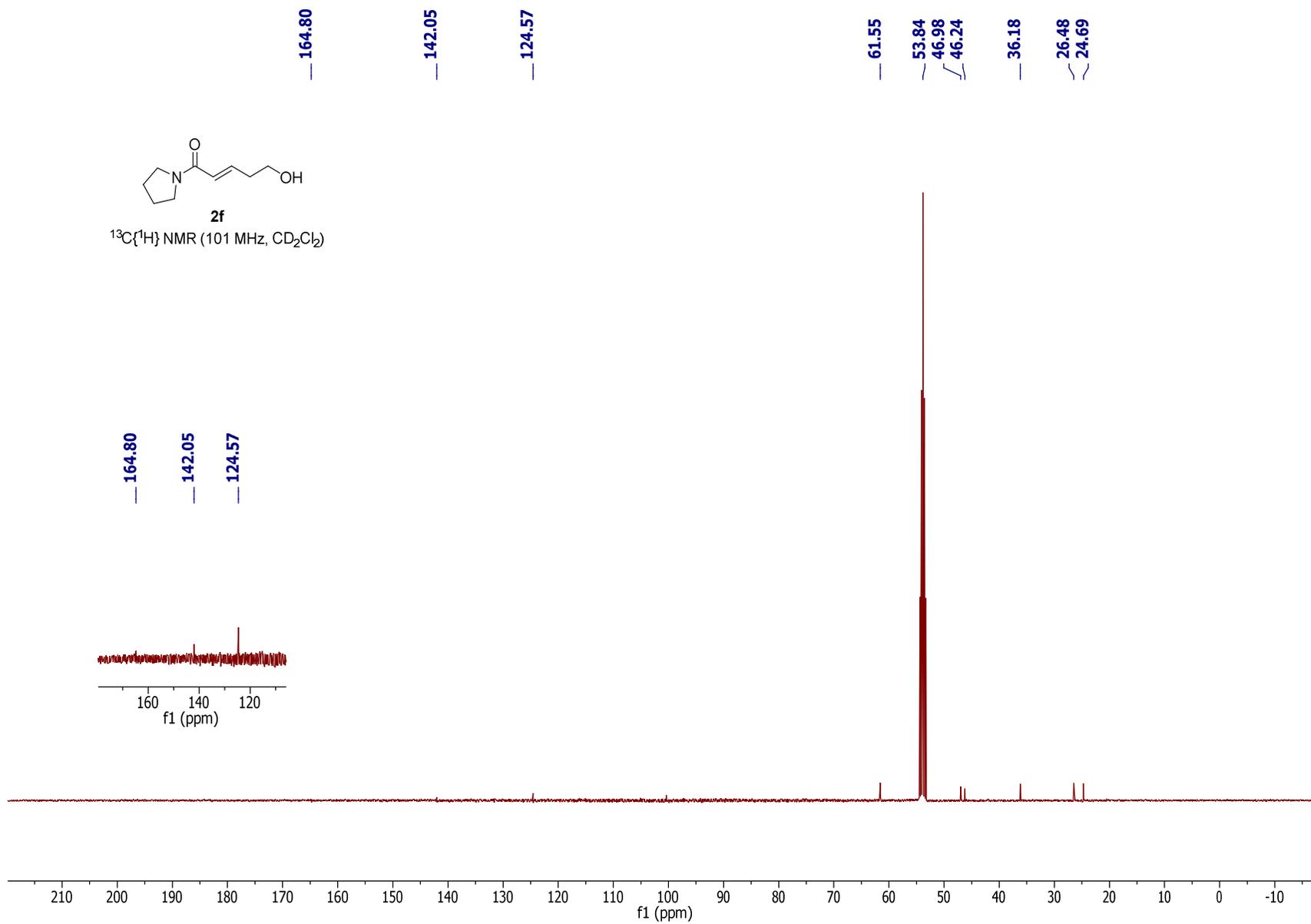
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)

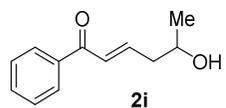




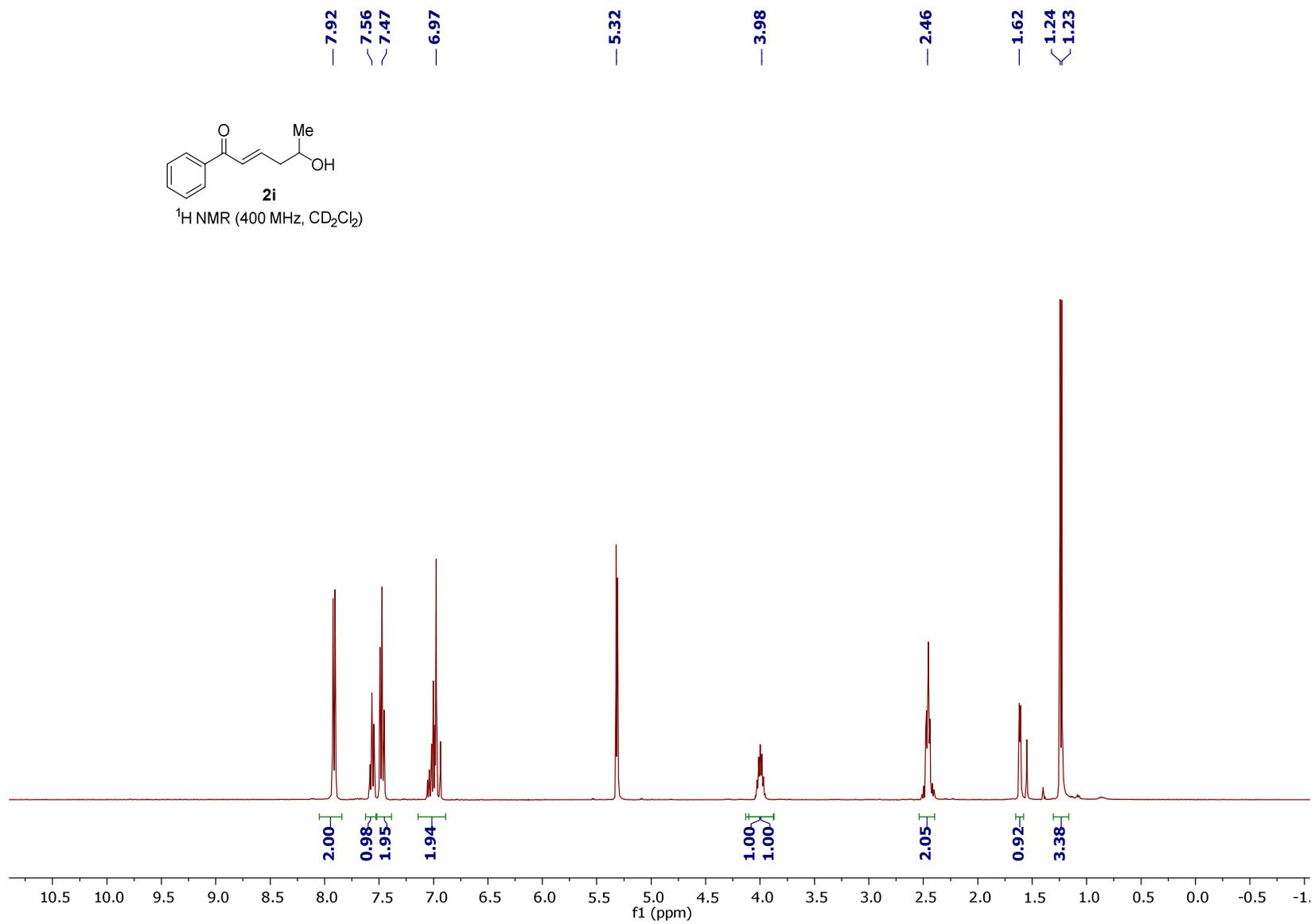
**2f**

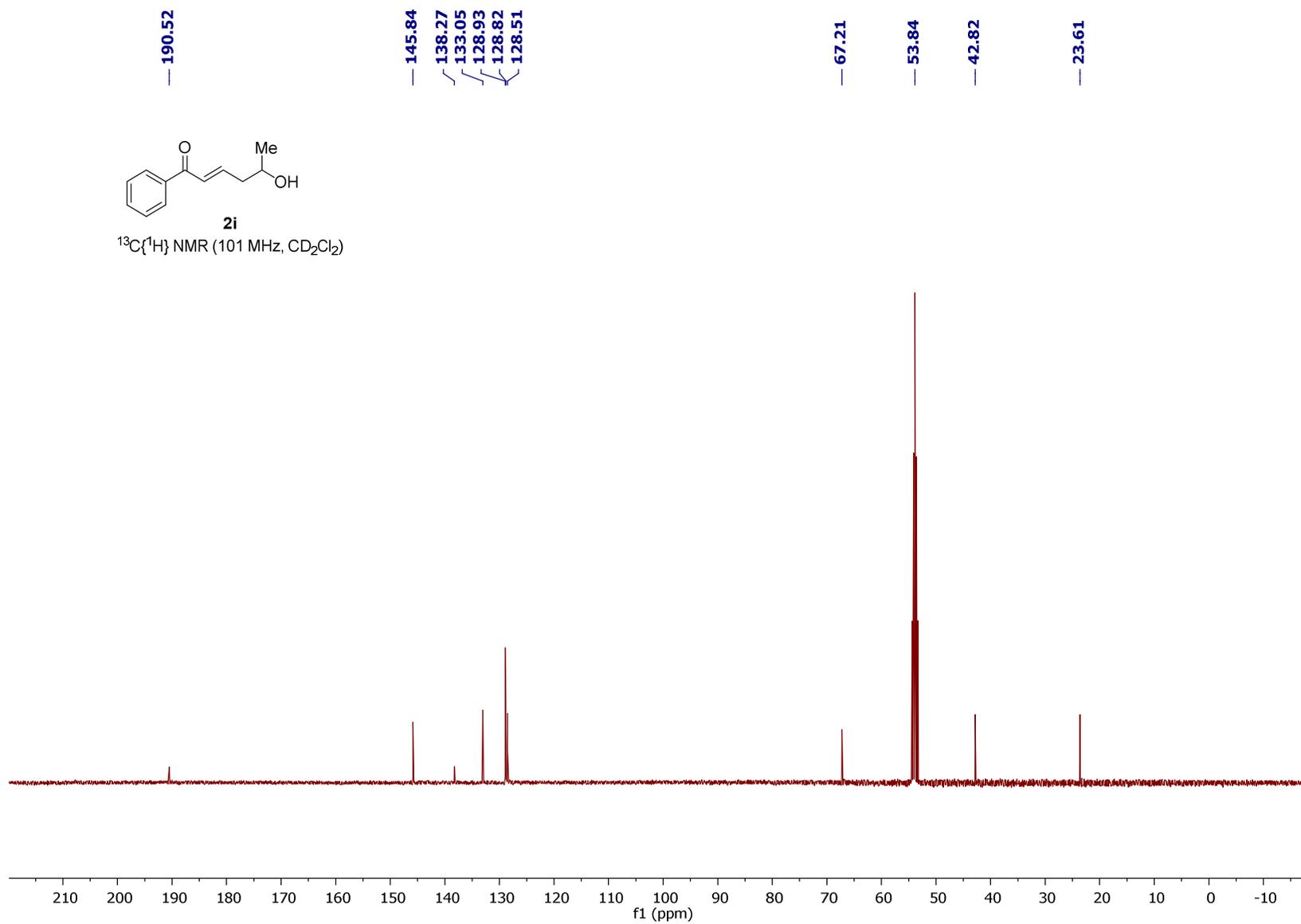
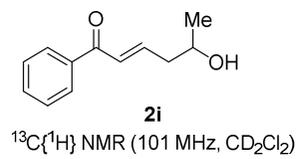
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )

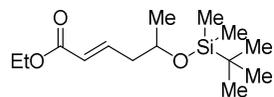




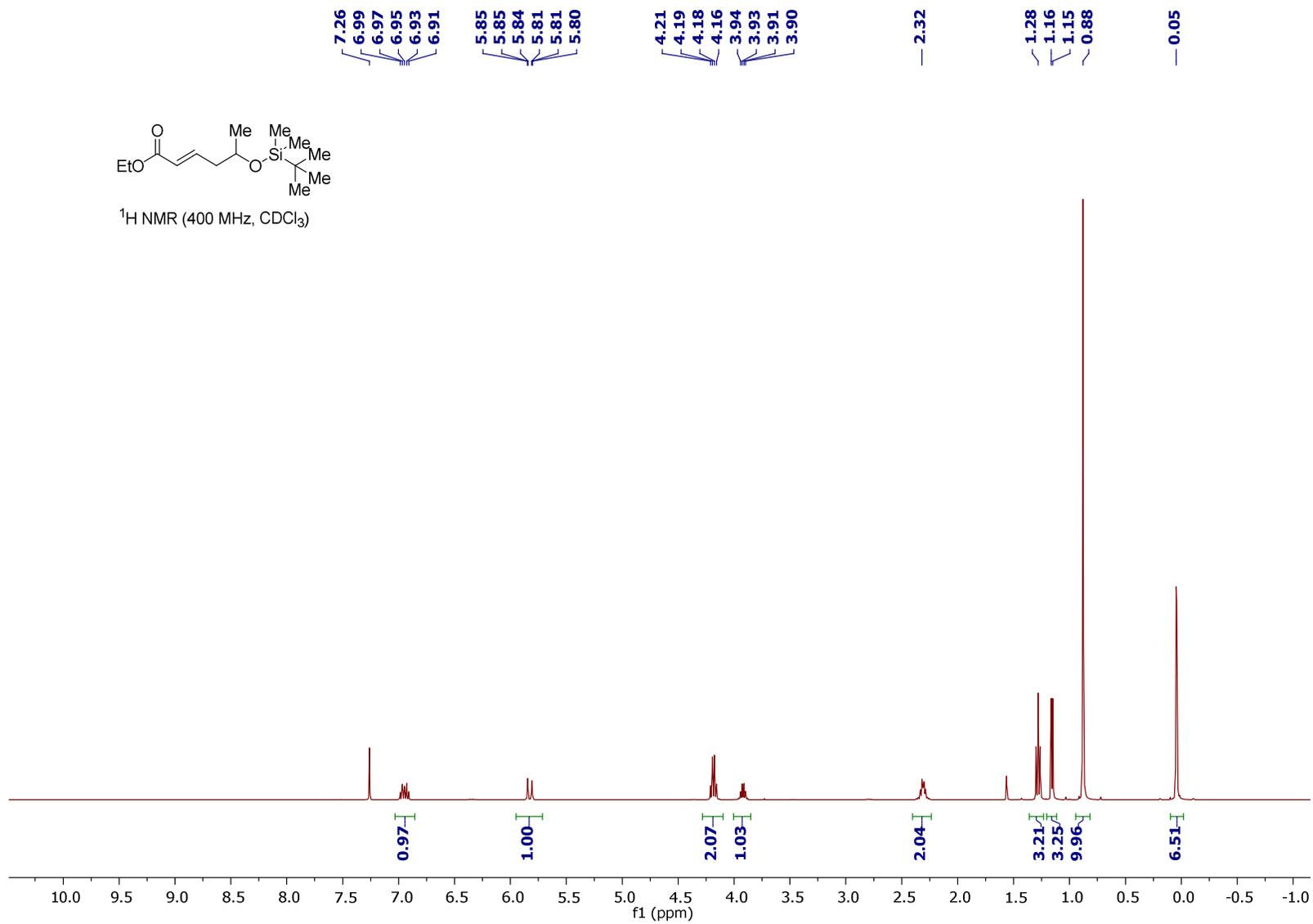
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)

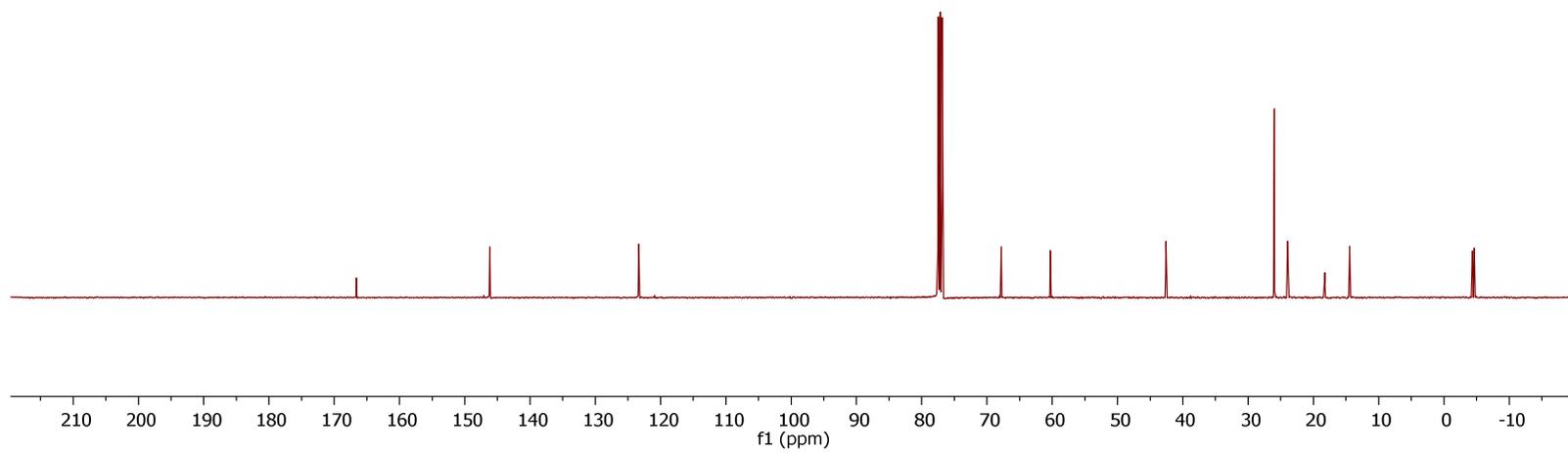
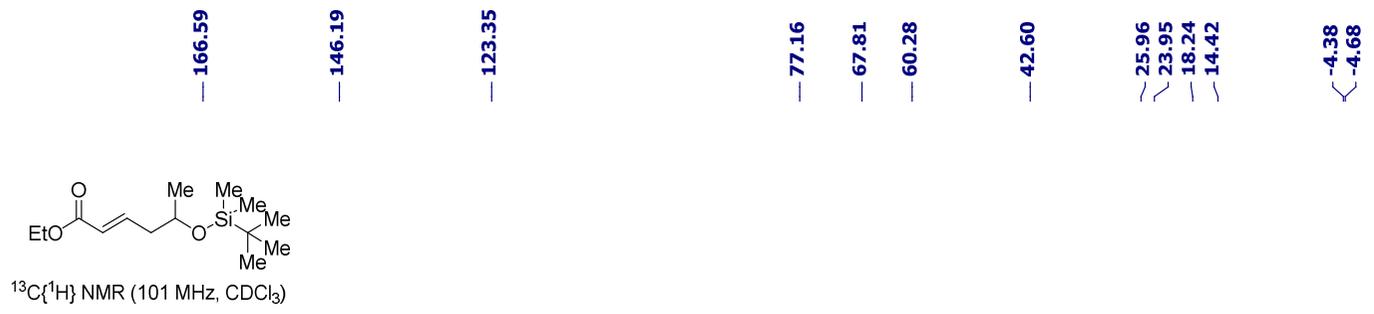


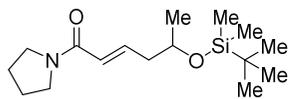




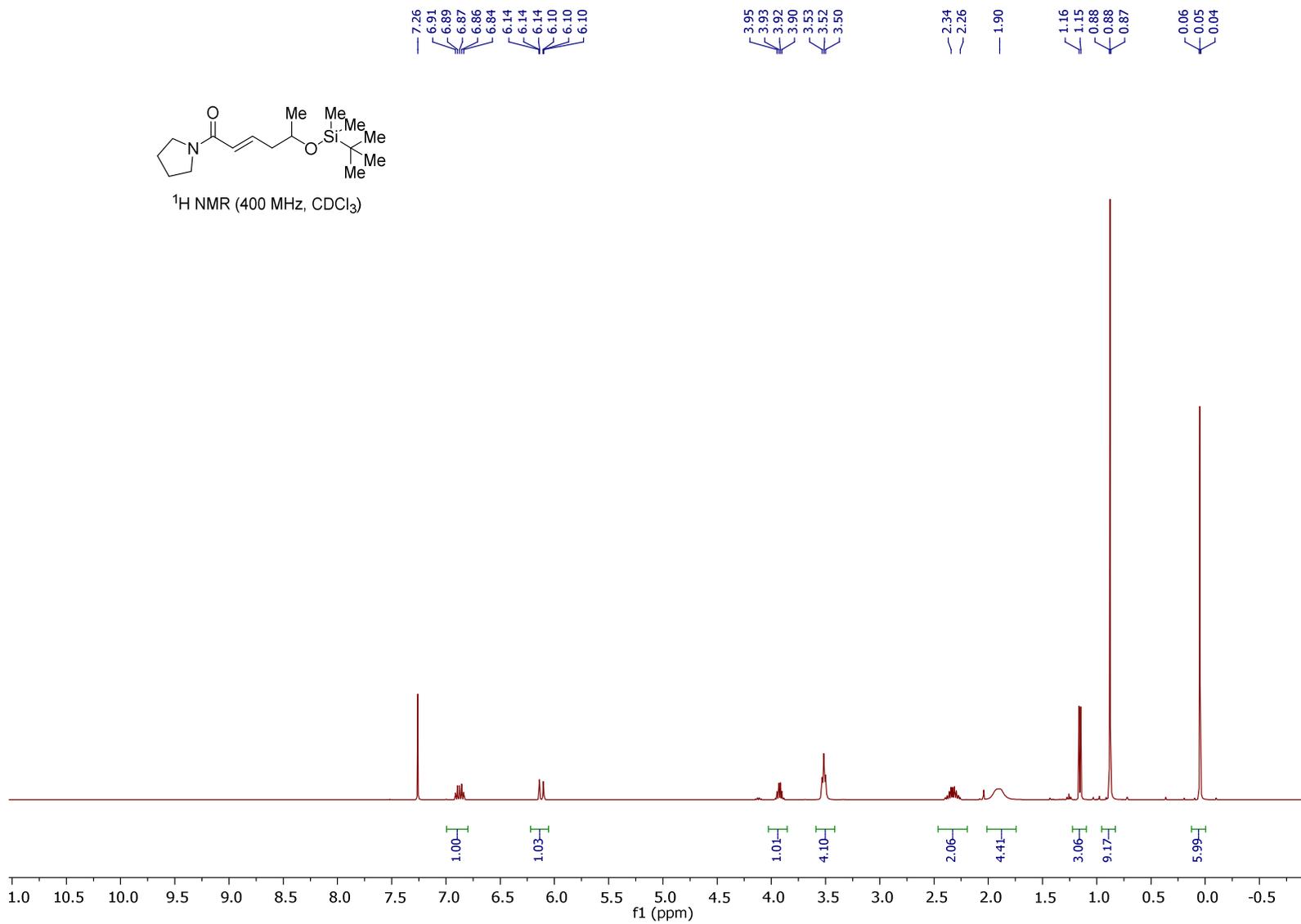
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

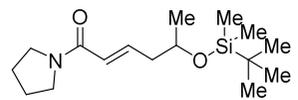




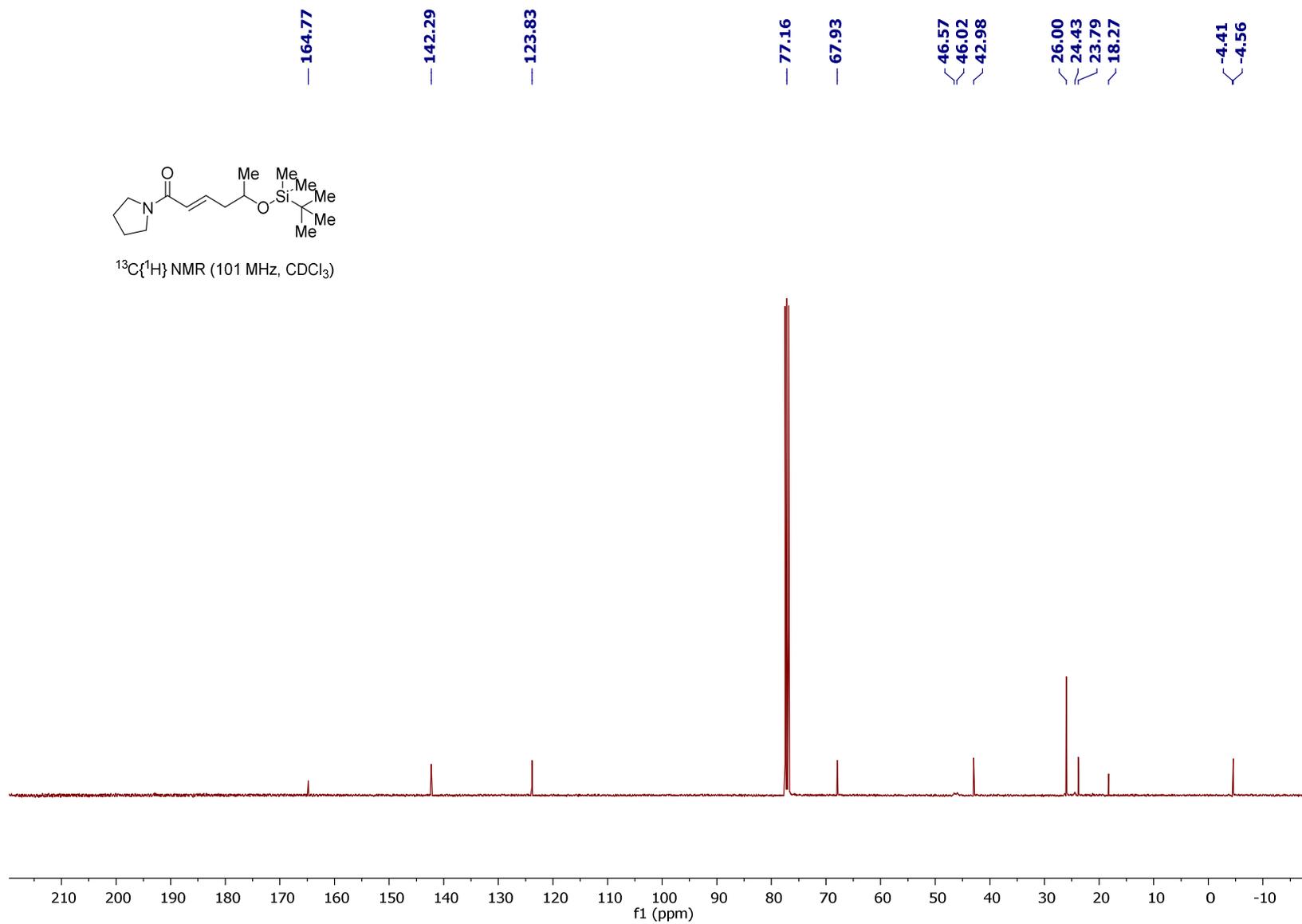


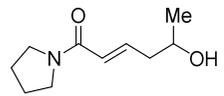
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )





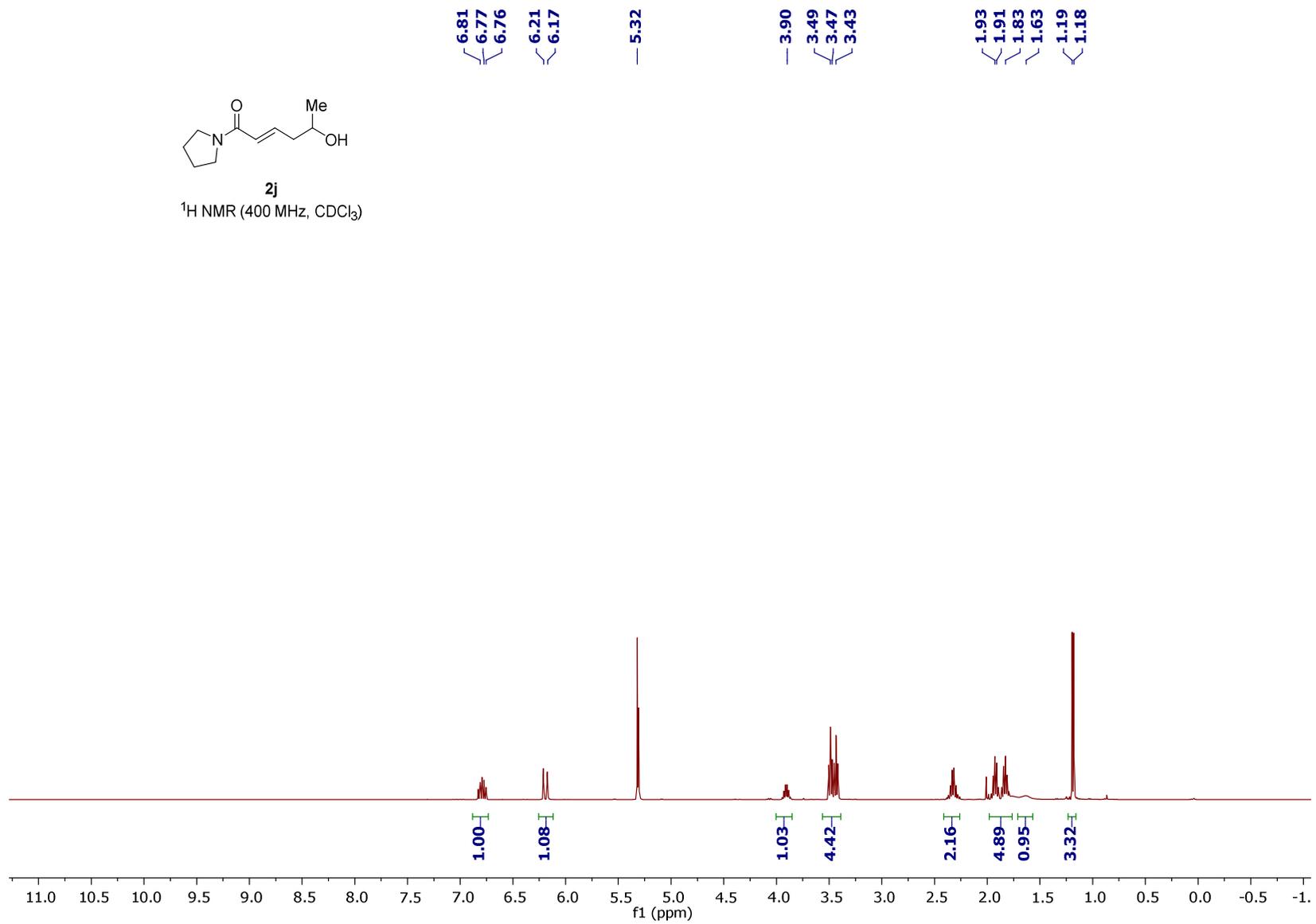
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

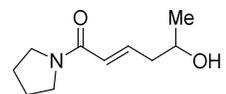




**2j**

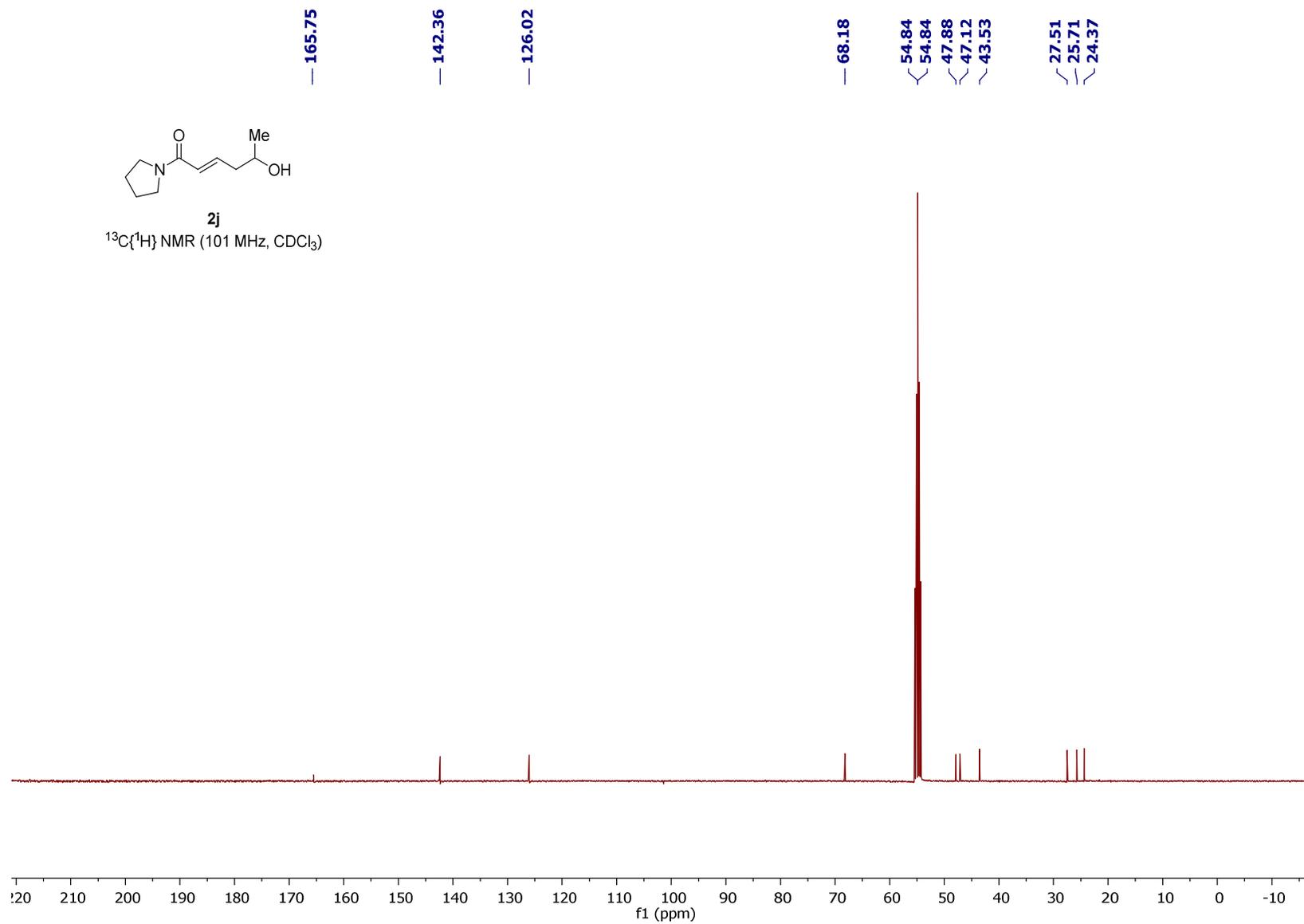
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

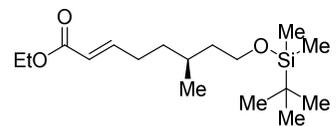




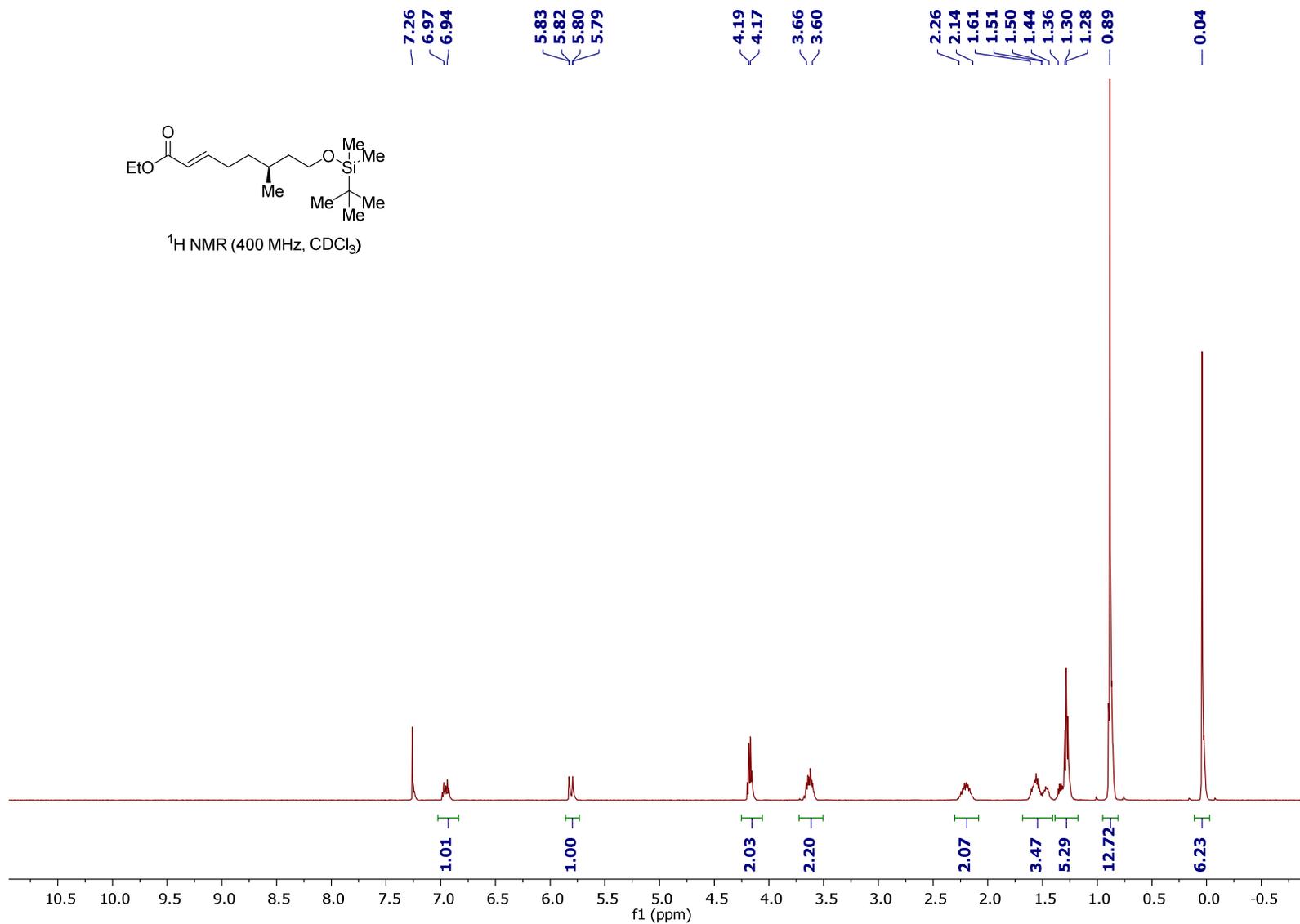
**2j**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

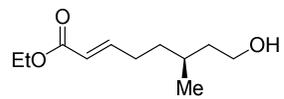




<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

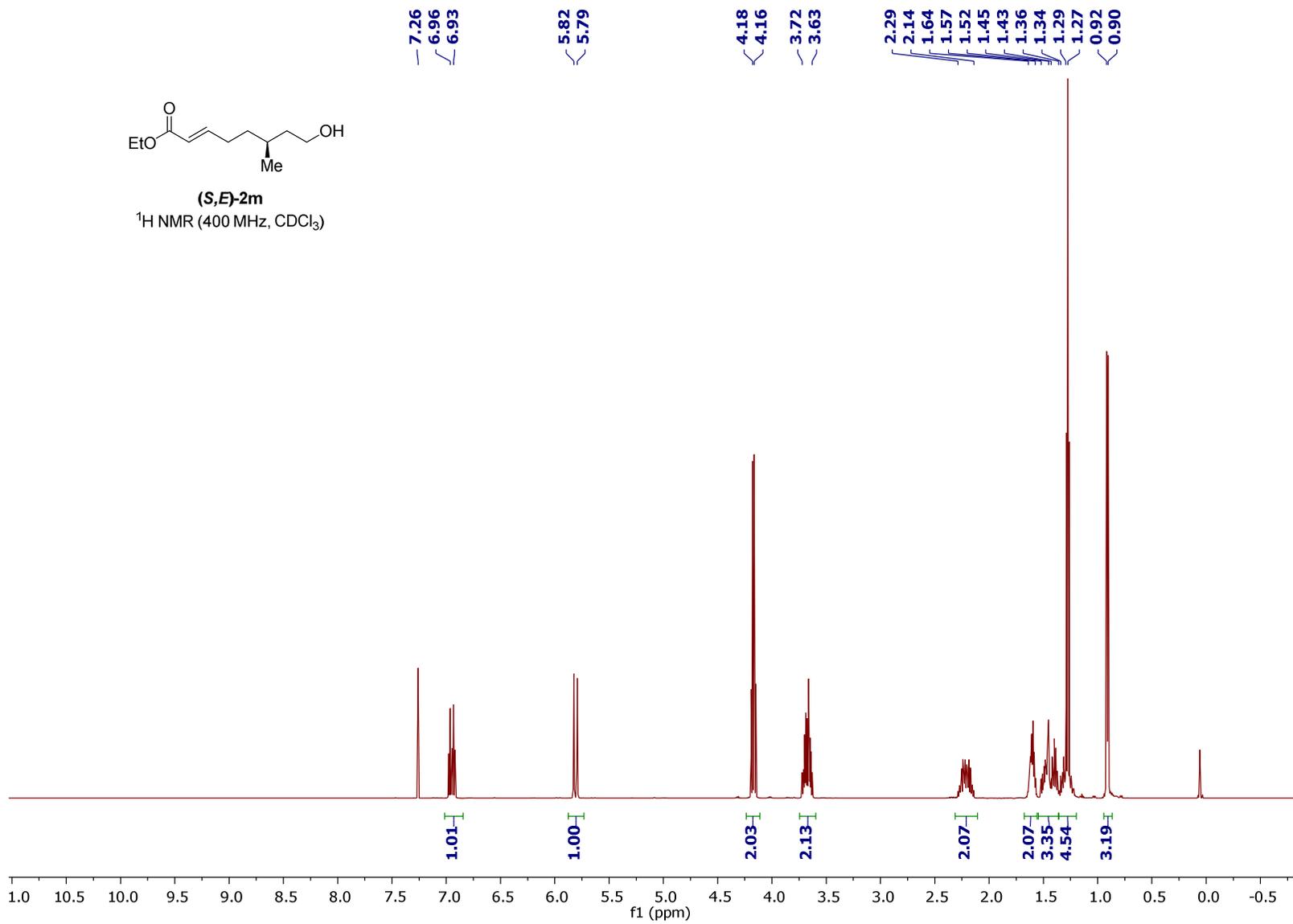


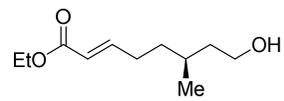




**(S,E)-2m**

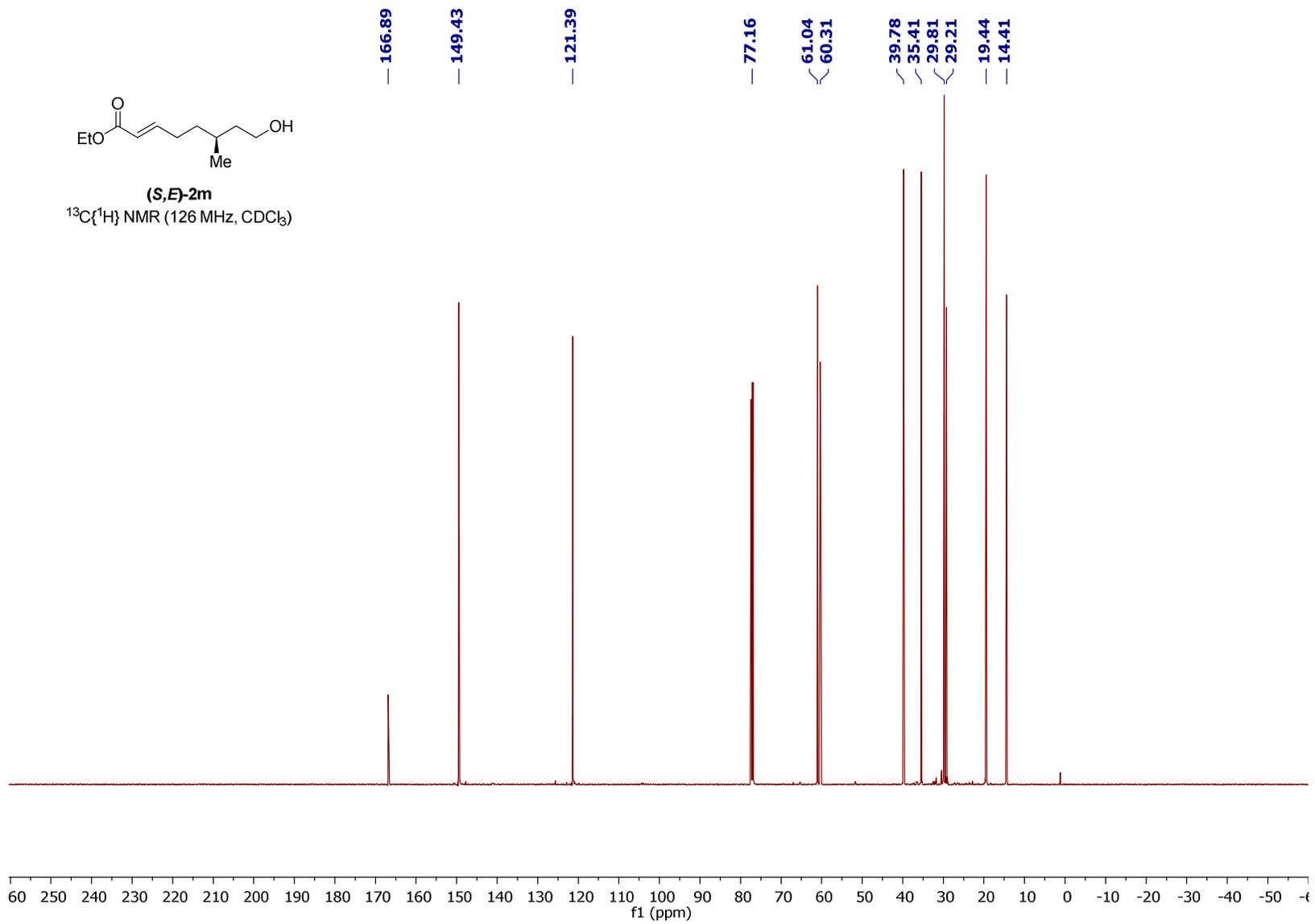
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

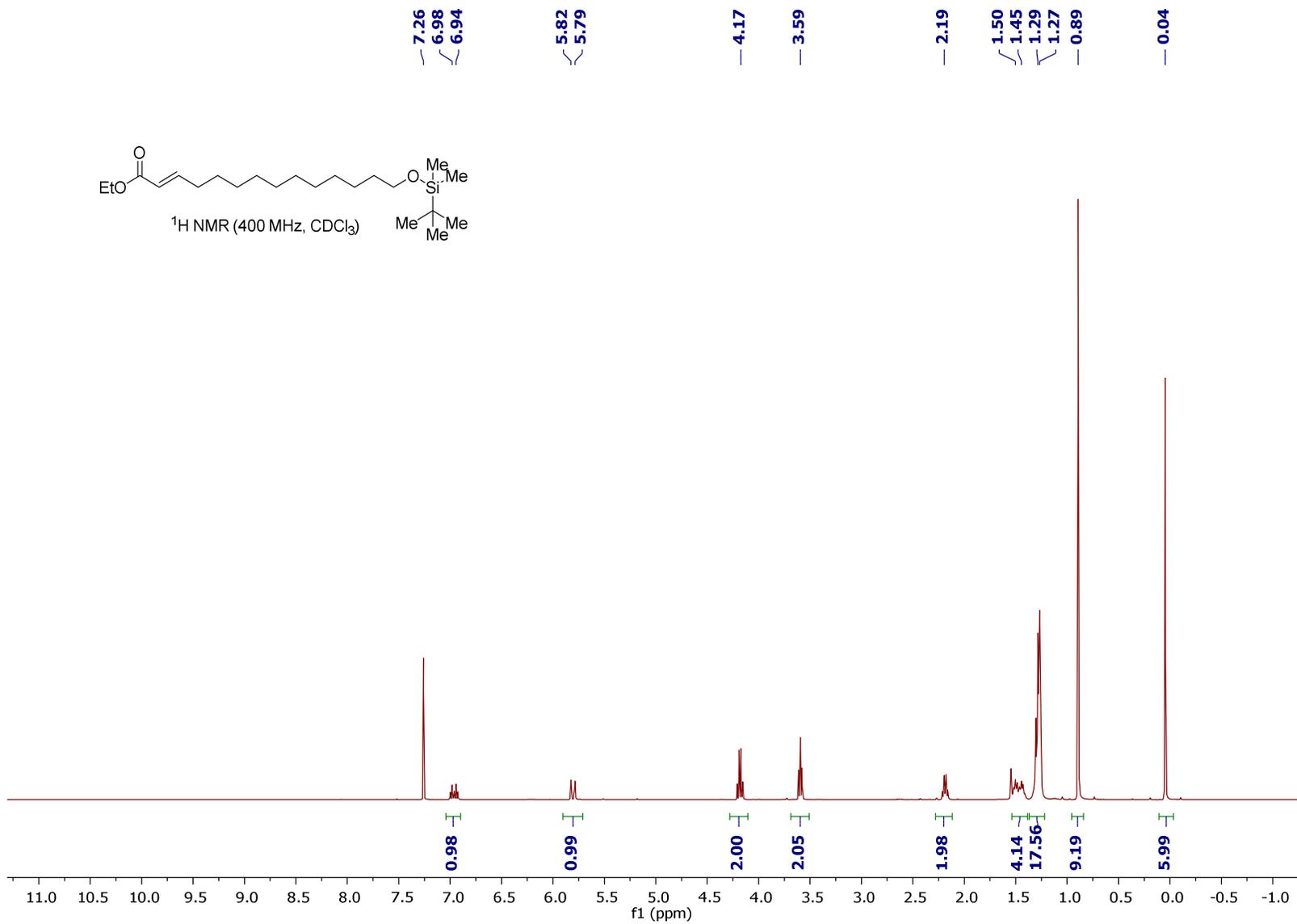
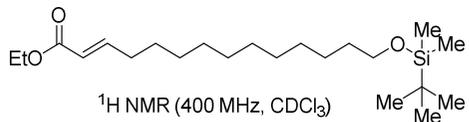


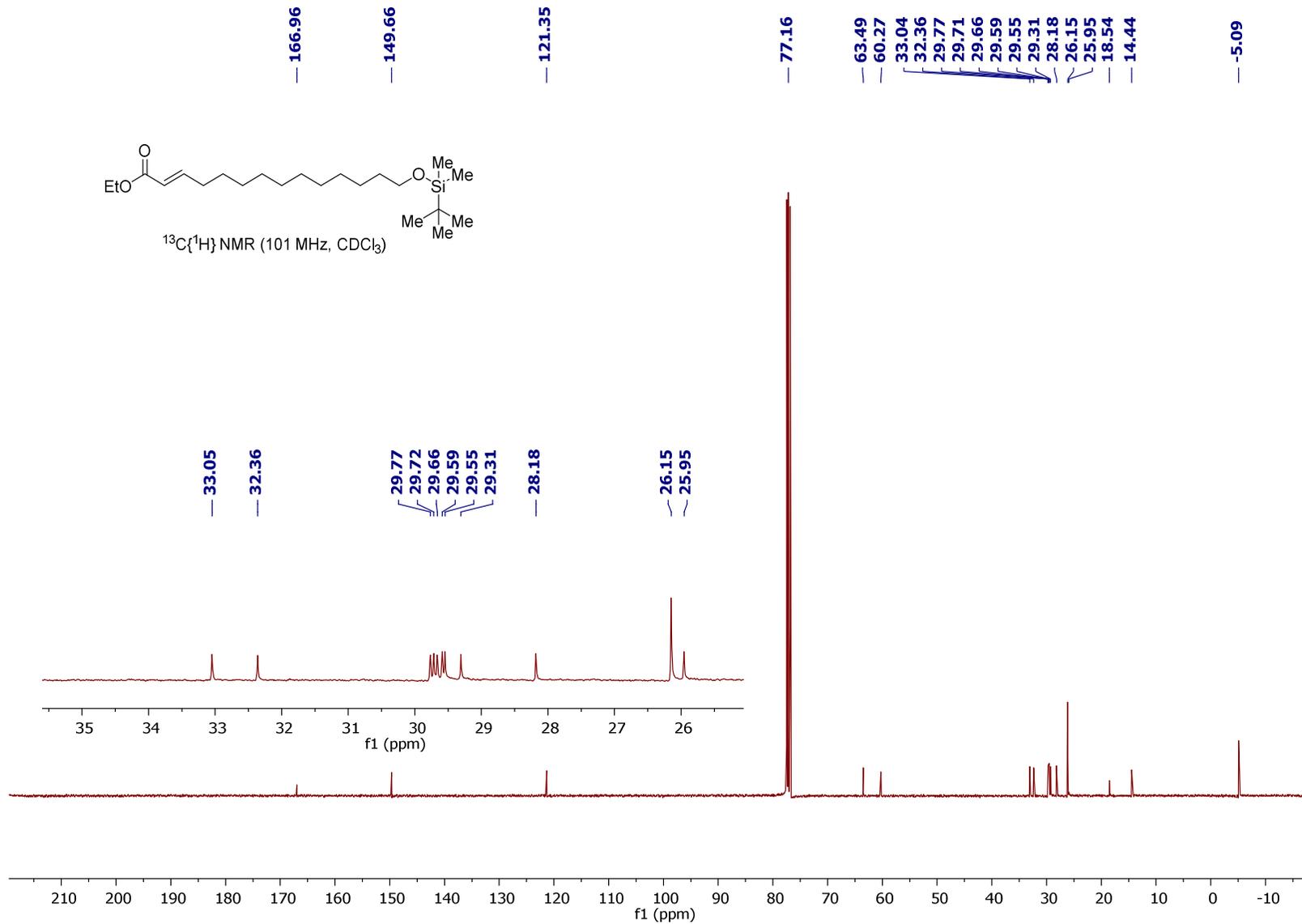
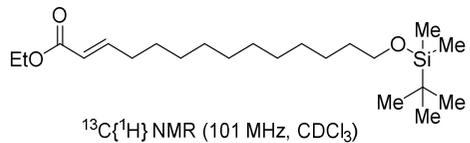


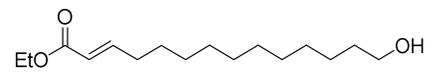
**(S,E)-2m**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

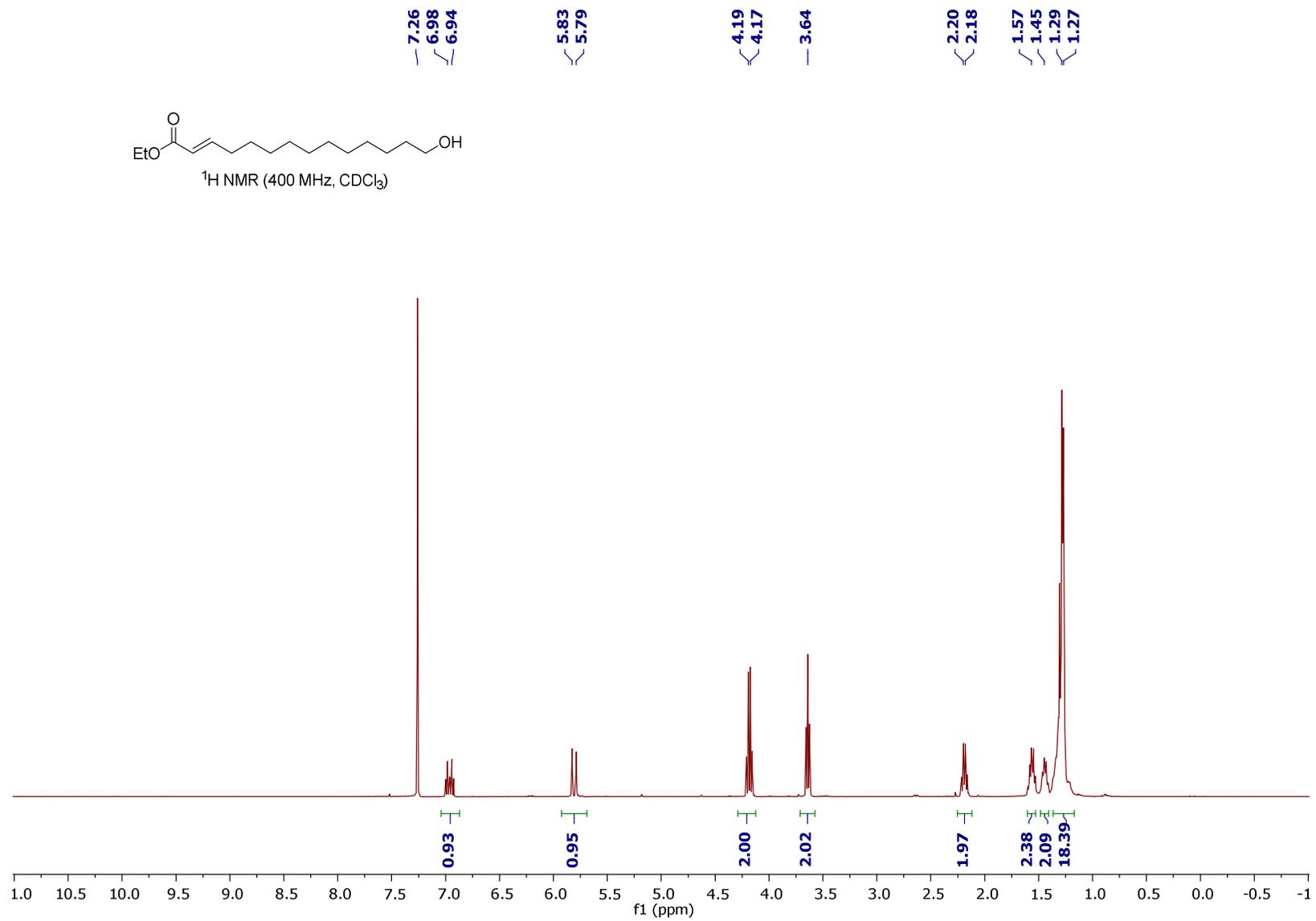


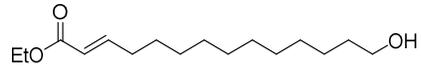




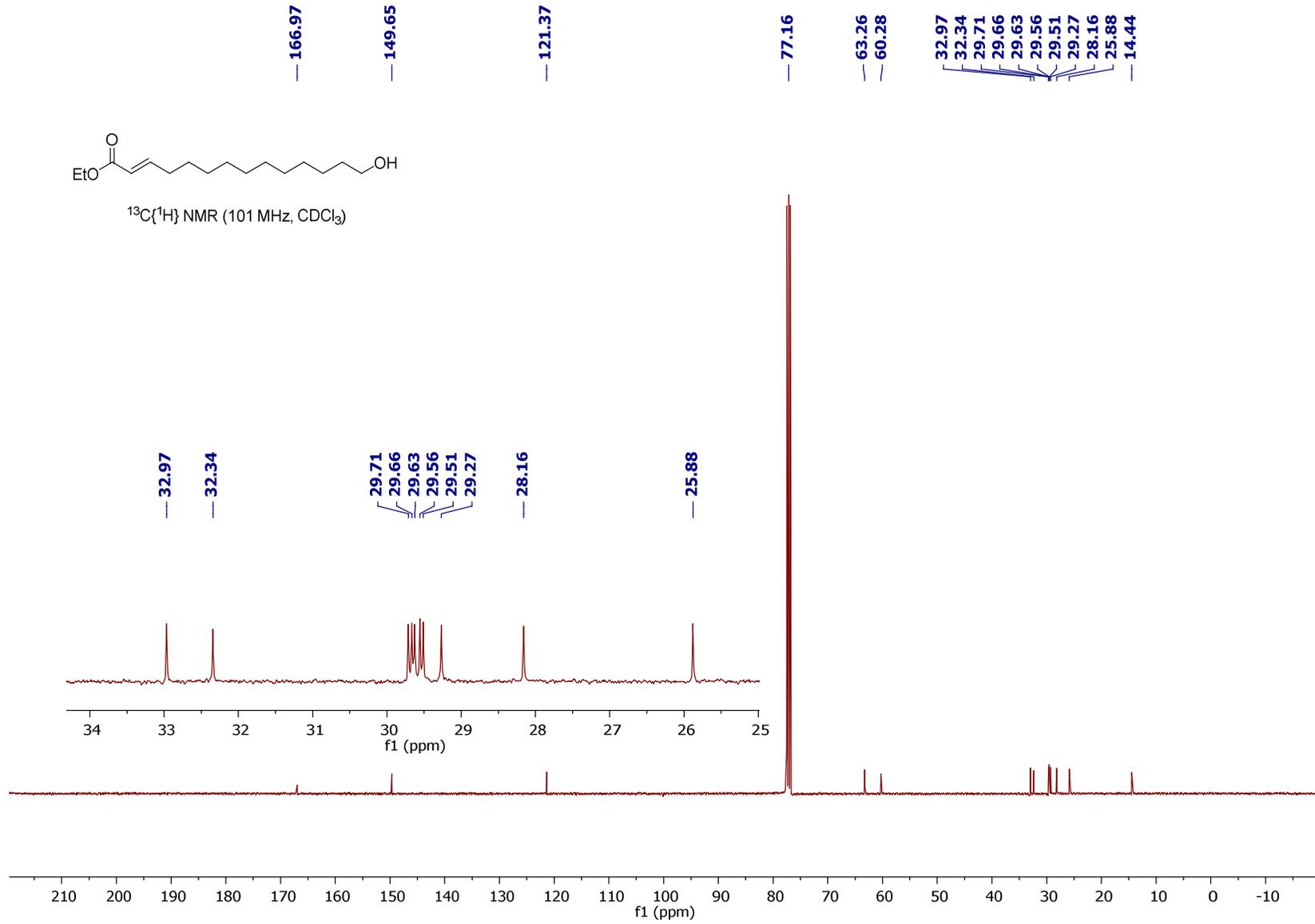


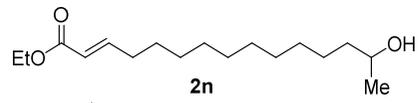
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



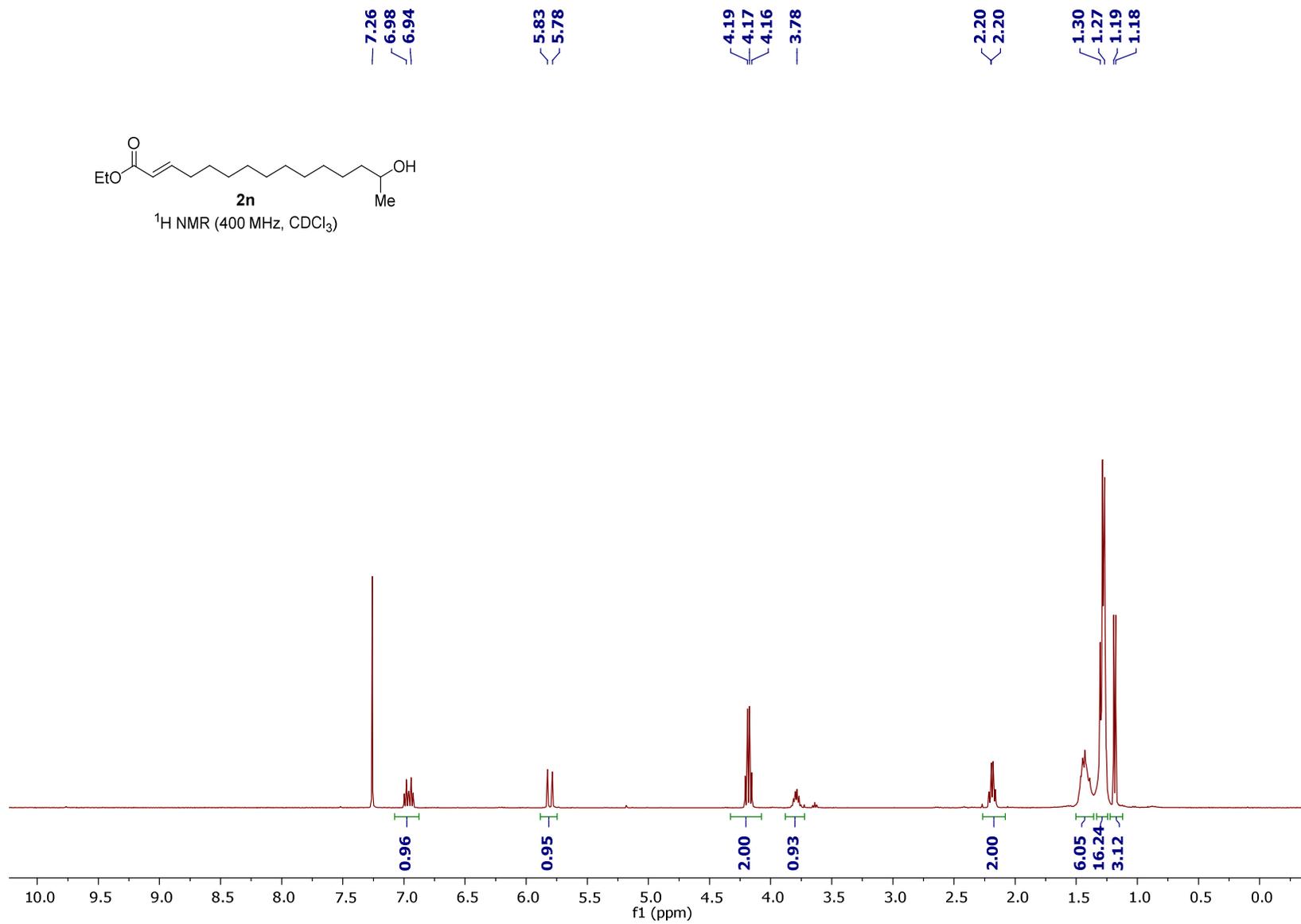


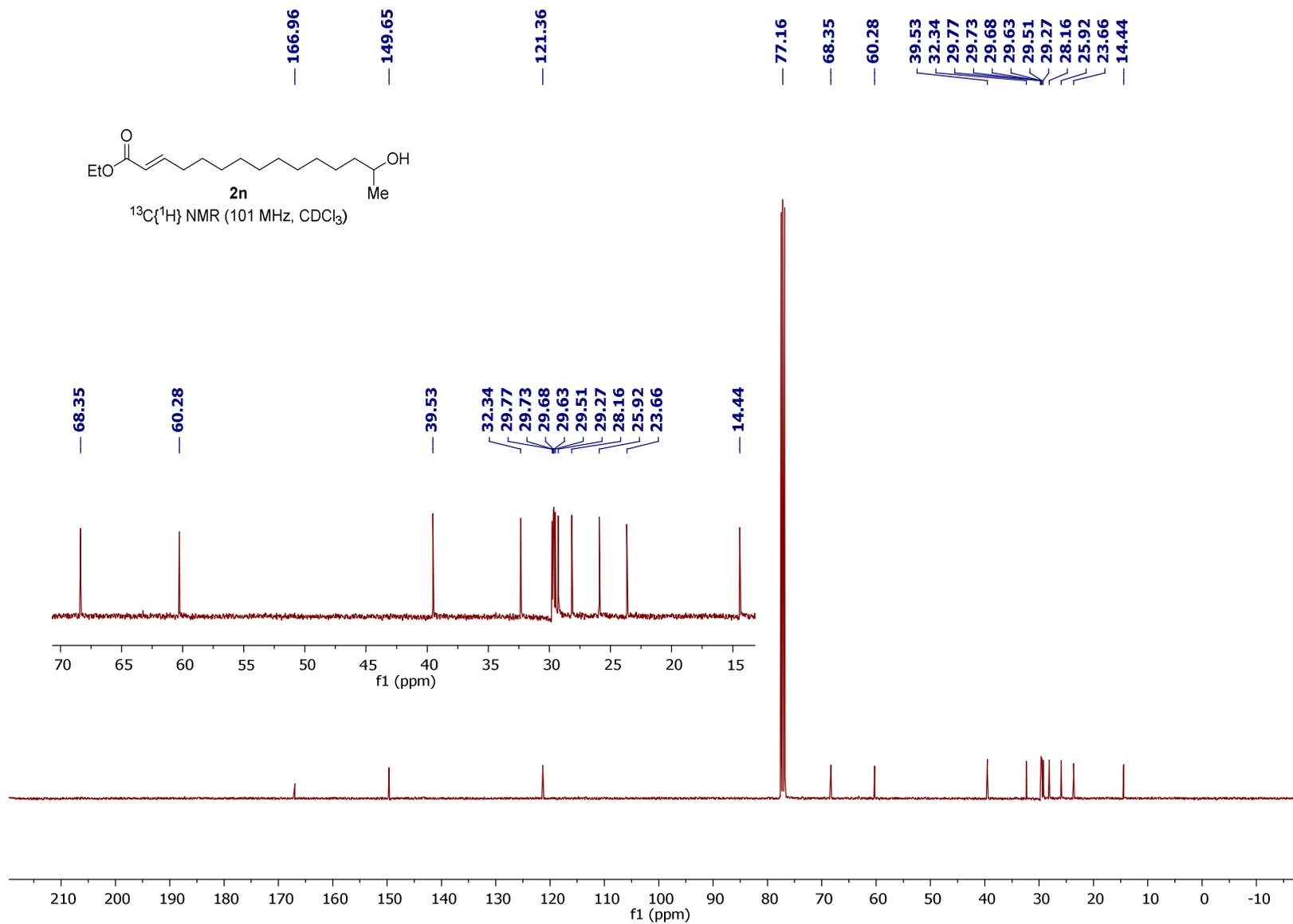
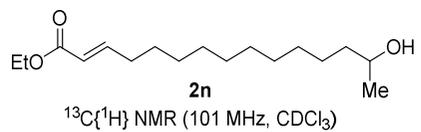
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

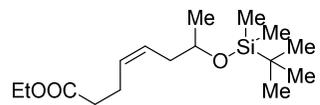




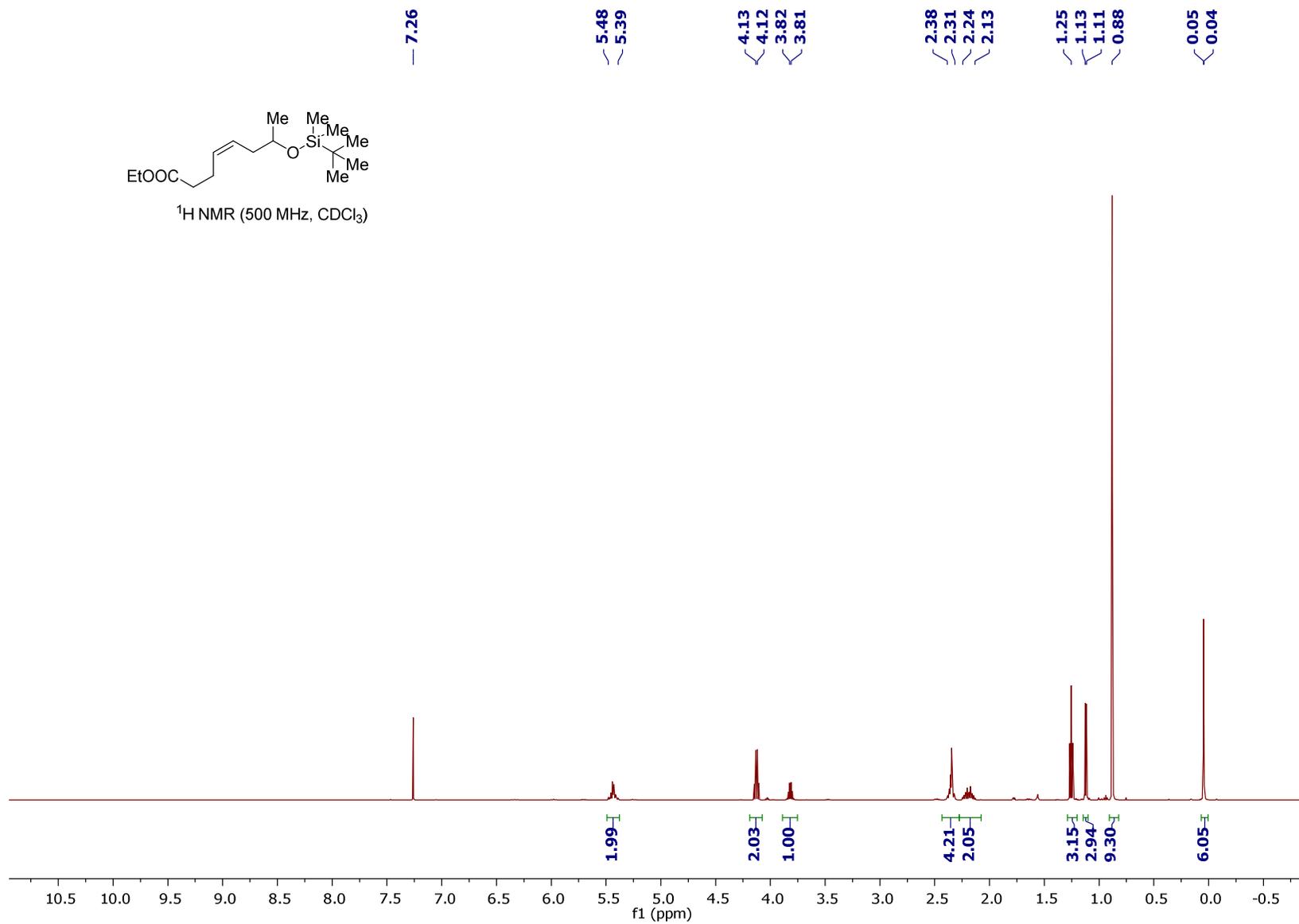
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

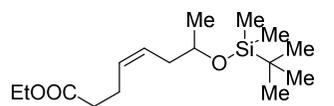




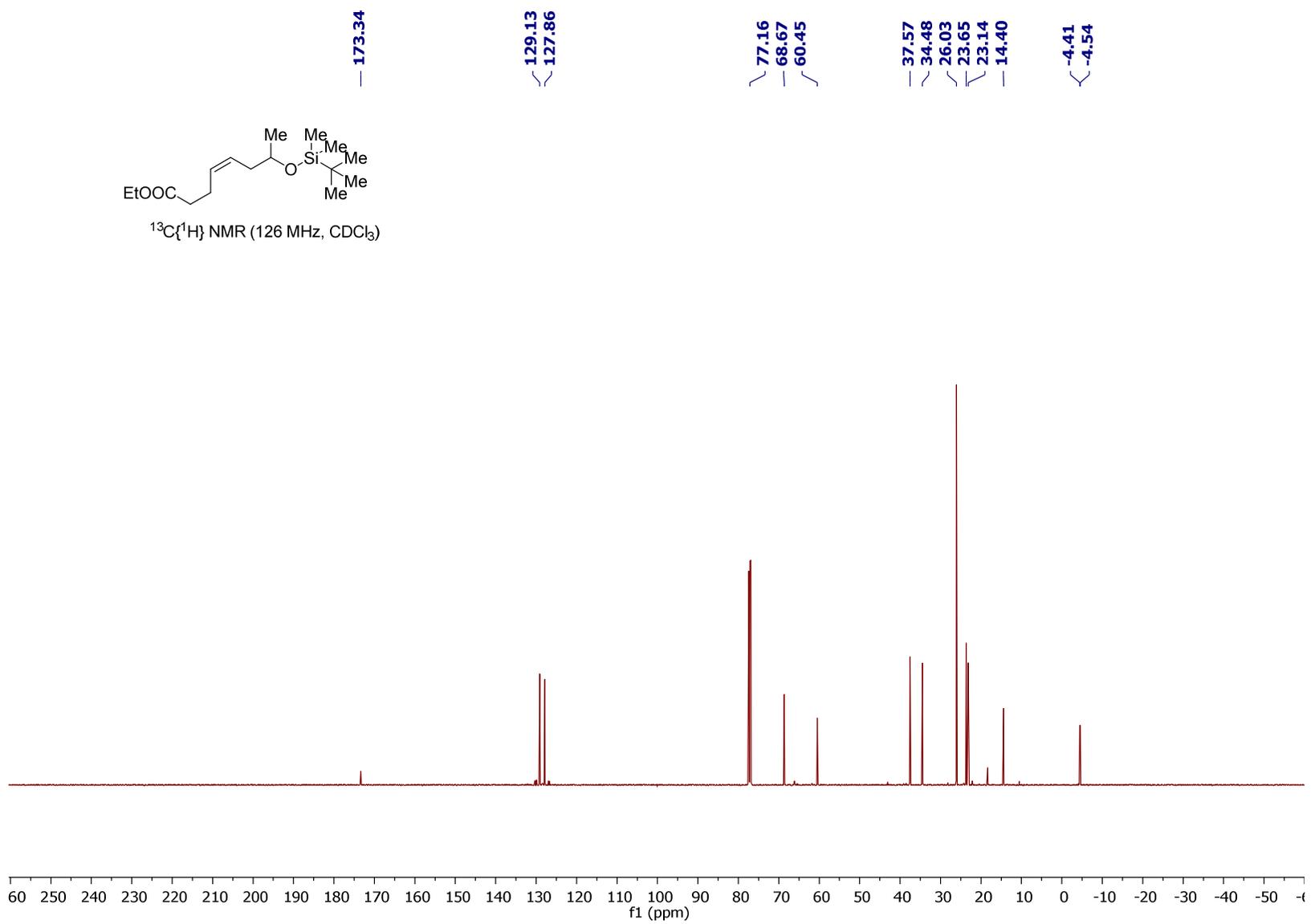


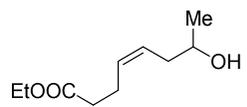
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





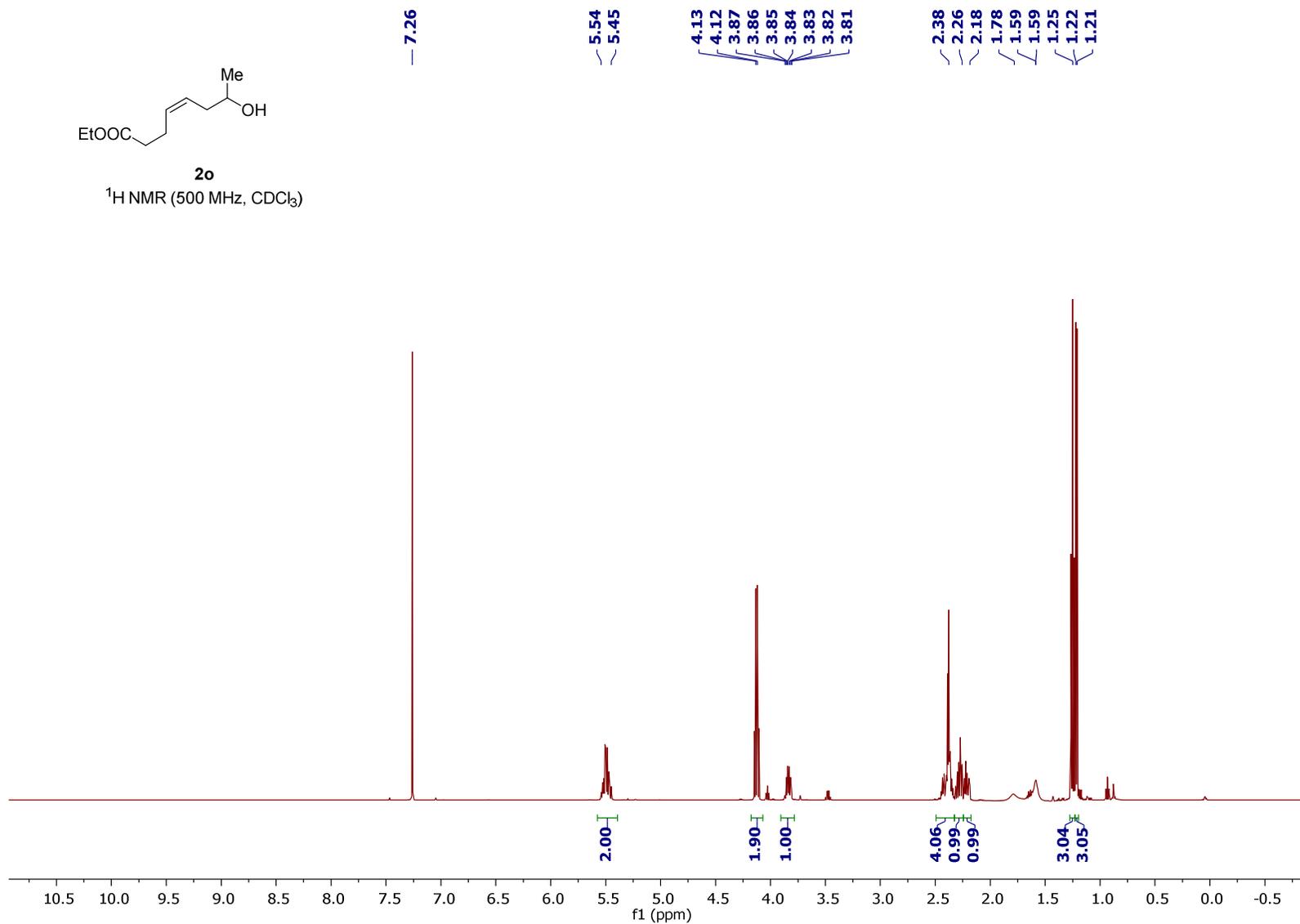
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

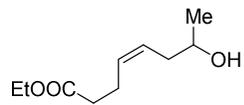




**2o**

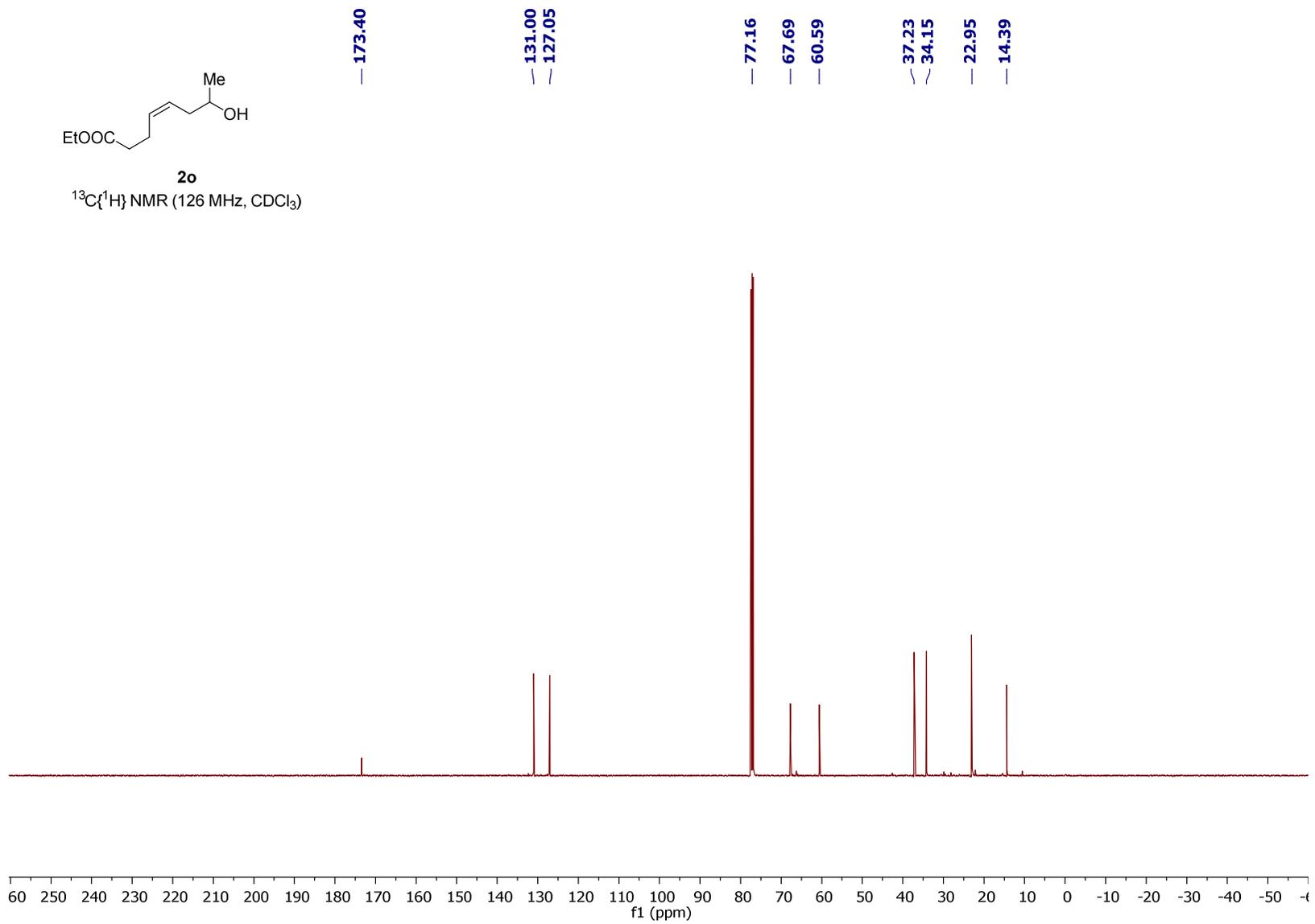
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

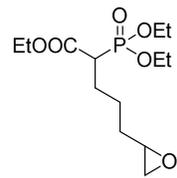




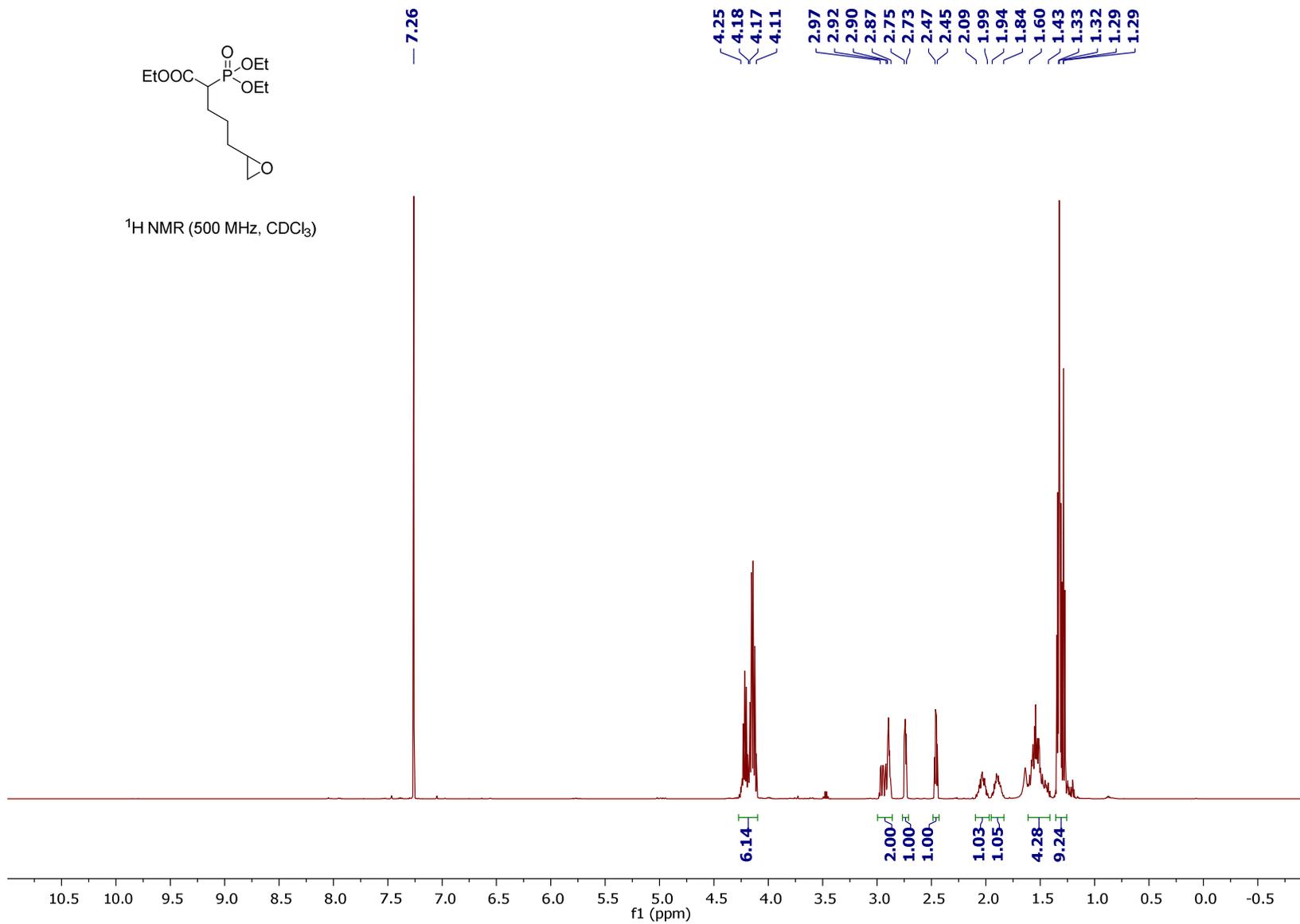
**2o**

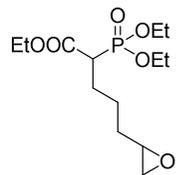
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )



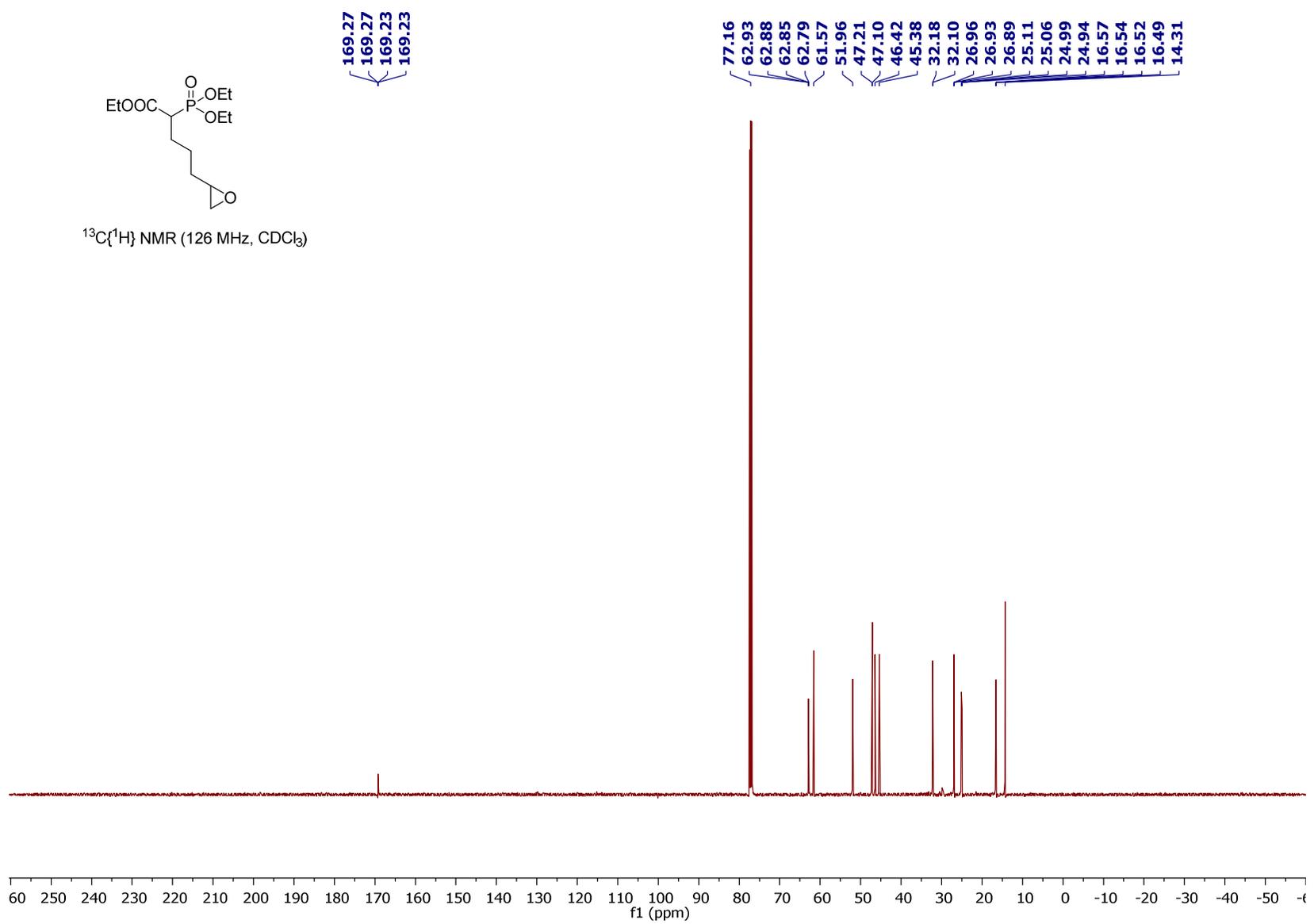


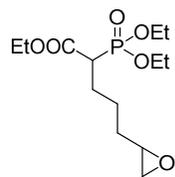
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





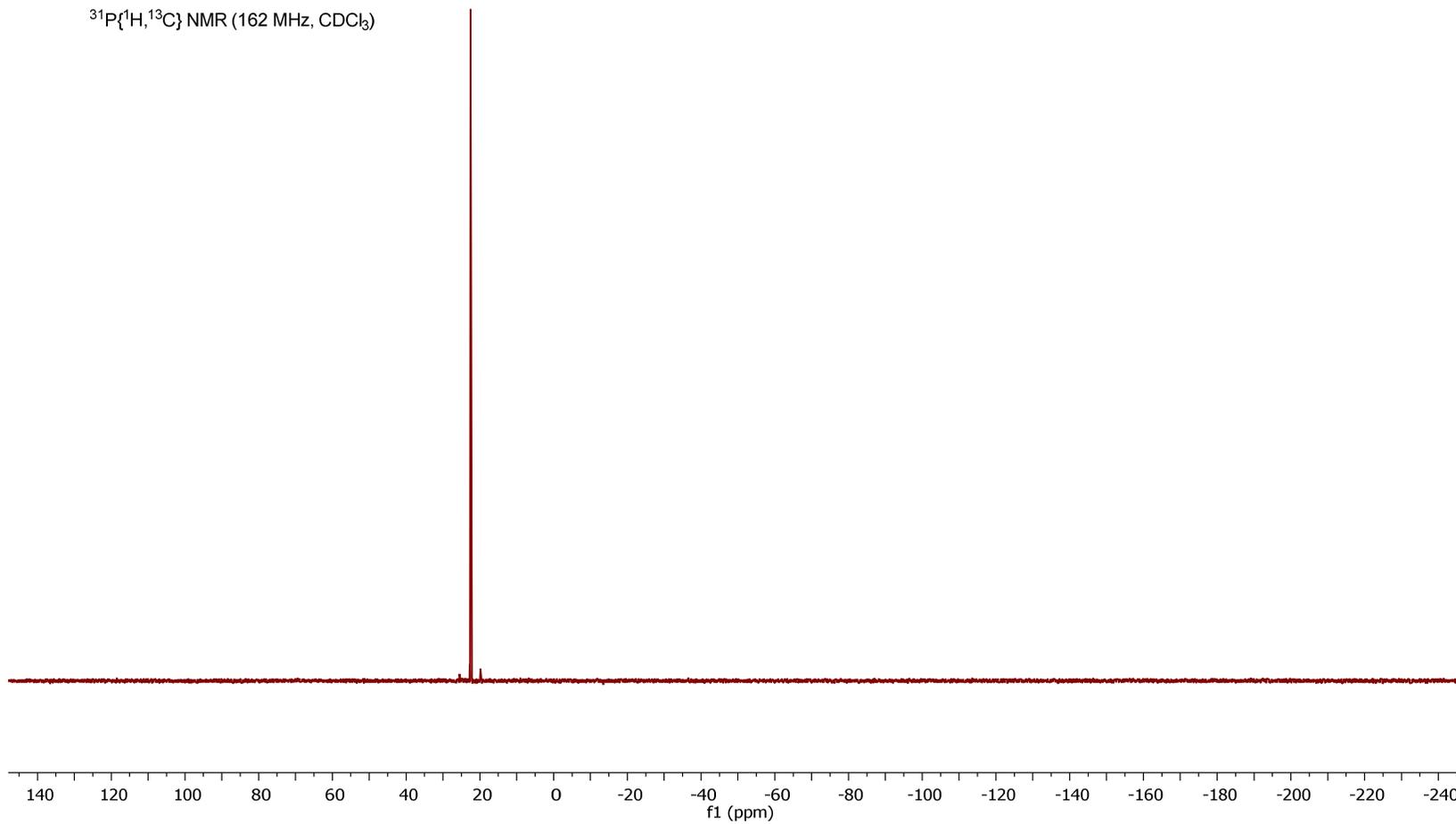
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

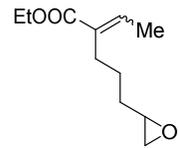




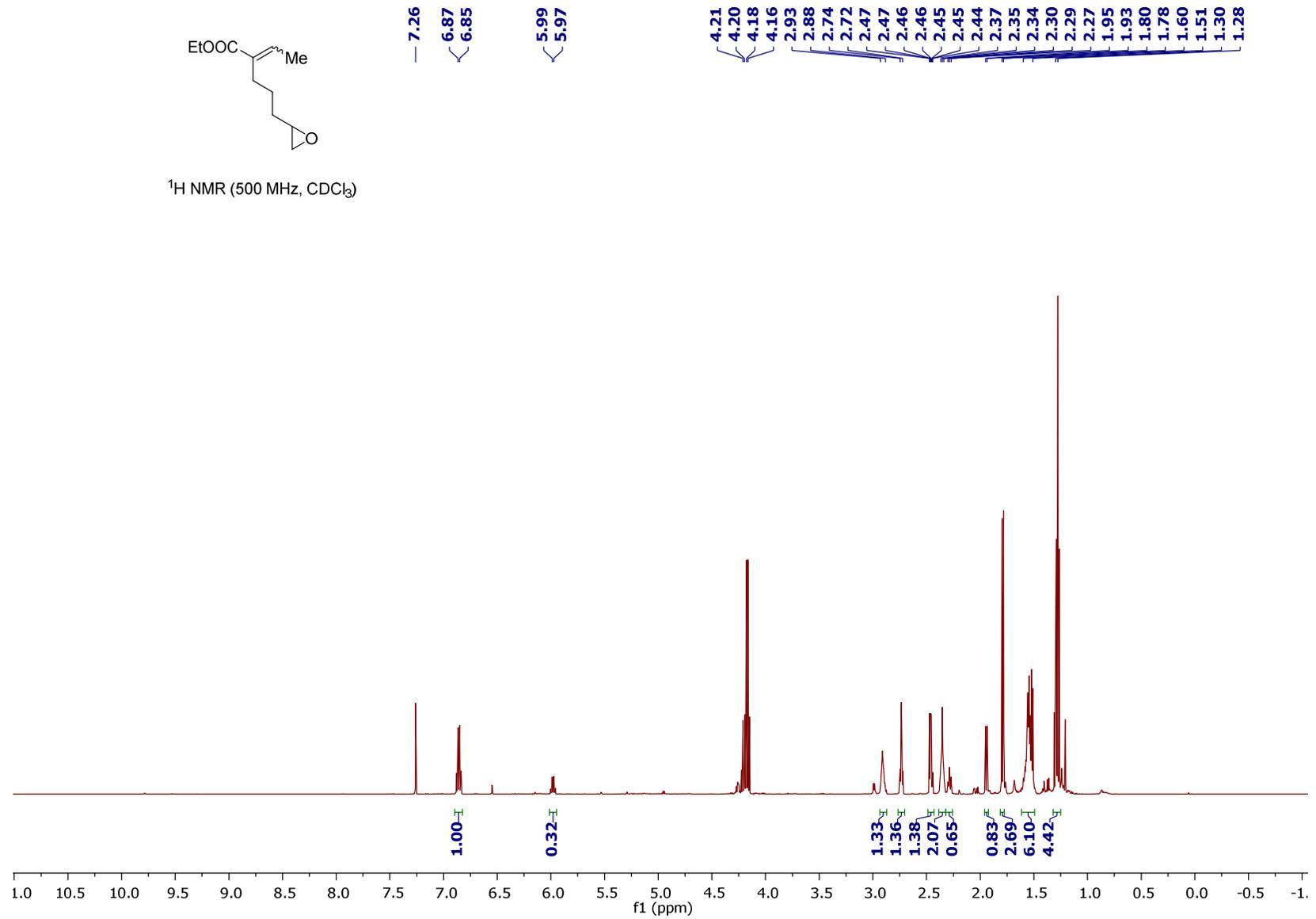
— 22.51

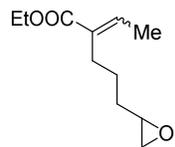
$^{31}\text{P}\{^1\text{H},^{13}\text{C}\}$  NMR (162 MHz,  $\text{CDCl}_3$ )





<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



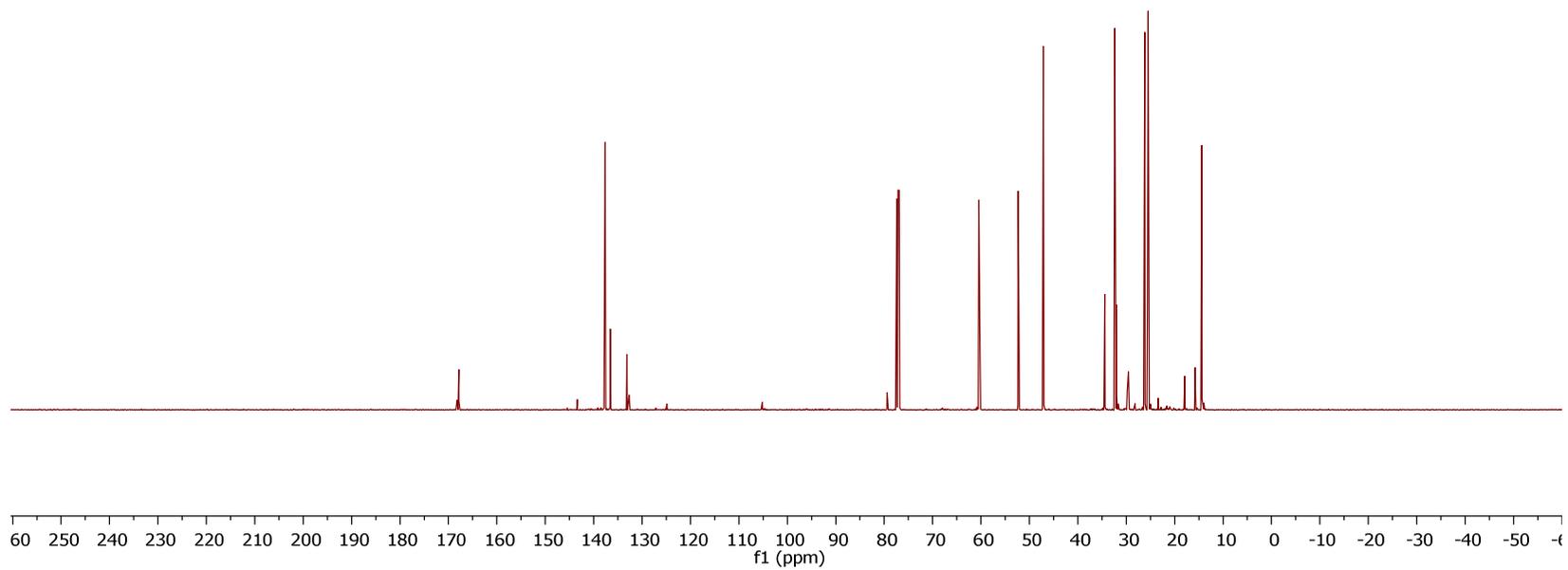


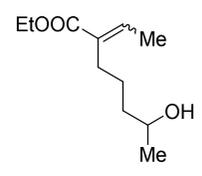
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

168.19  
167.86

137.63  
136.58  
133.12  
132.71

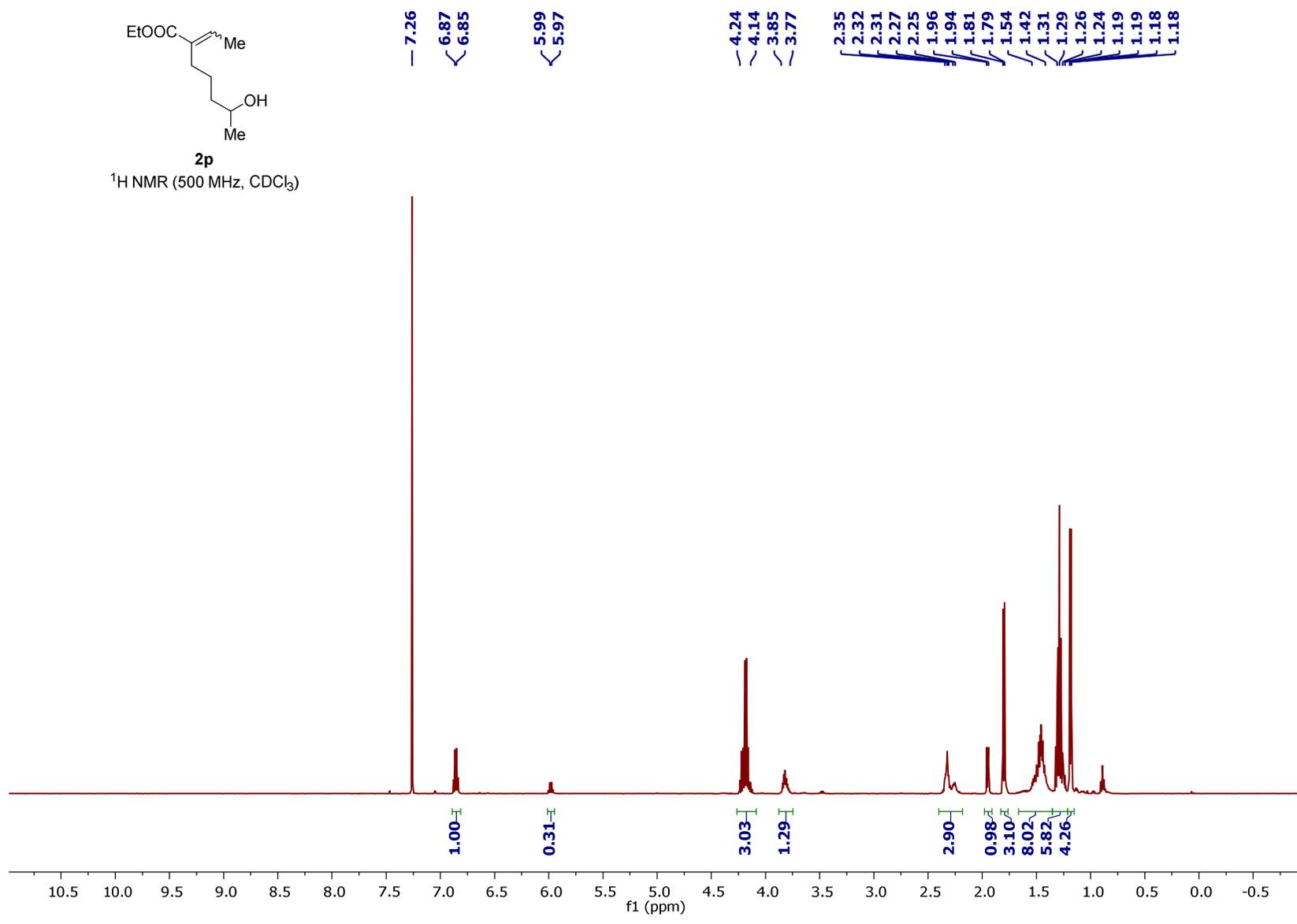
77.16  
60.47  
60.19  
52.29  
52.28  
47.17  
47.15  
34.42  
32.34  
32.03  
26.20  
25.61  
25.46  
14.39

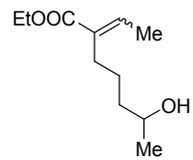




2p

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





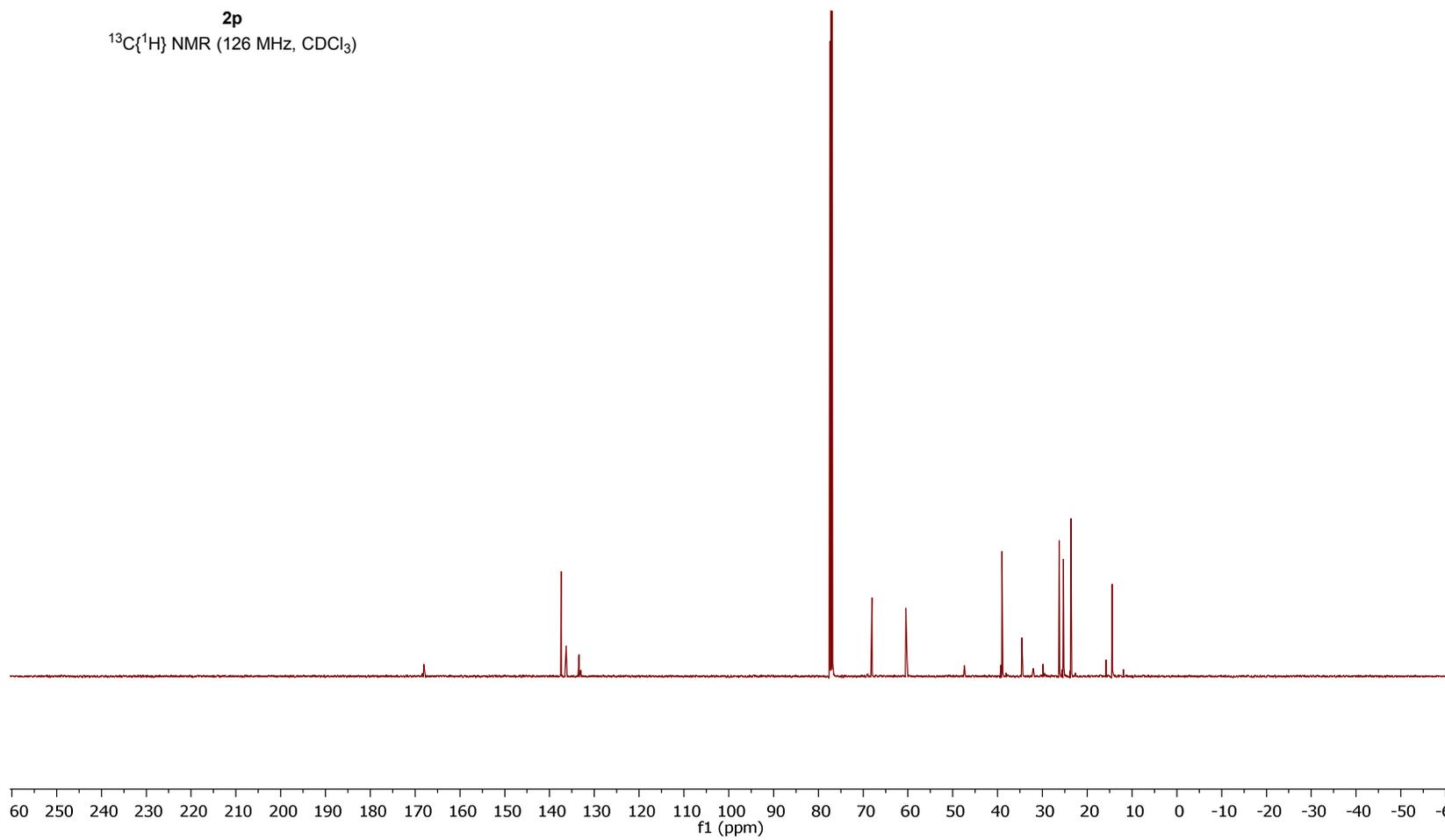
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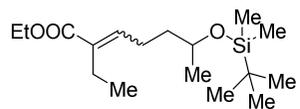
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

168.37  
168.03

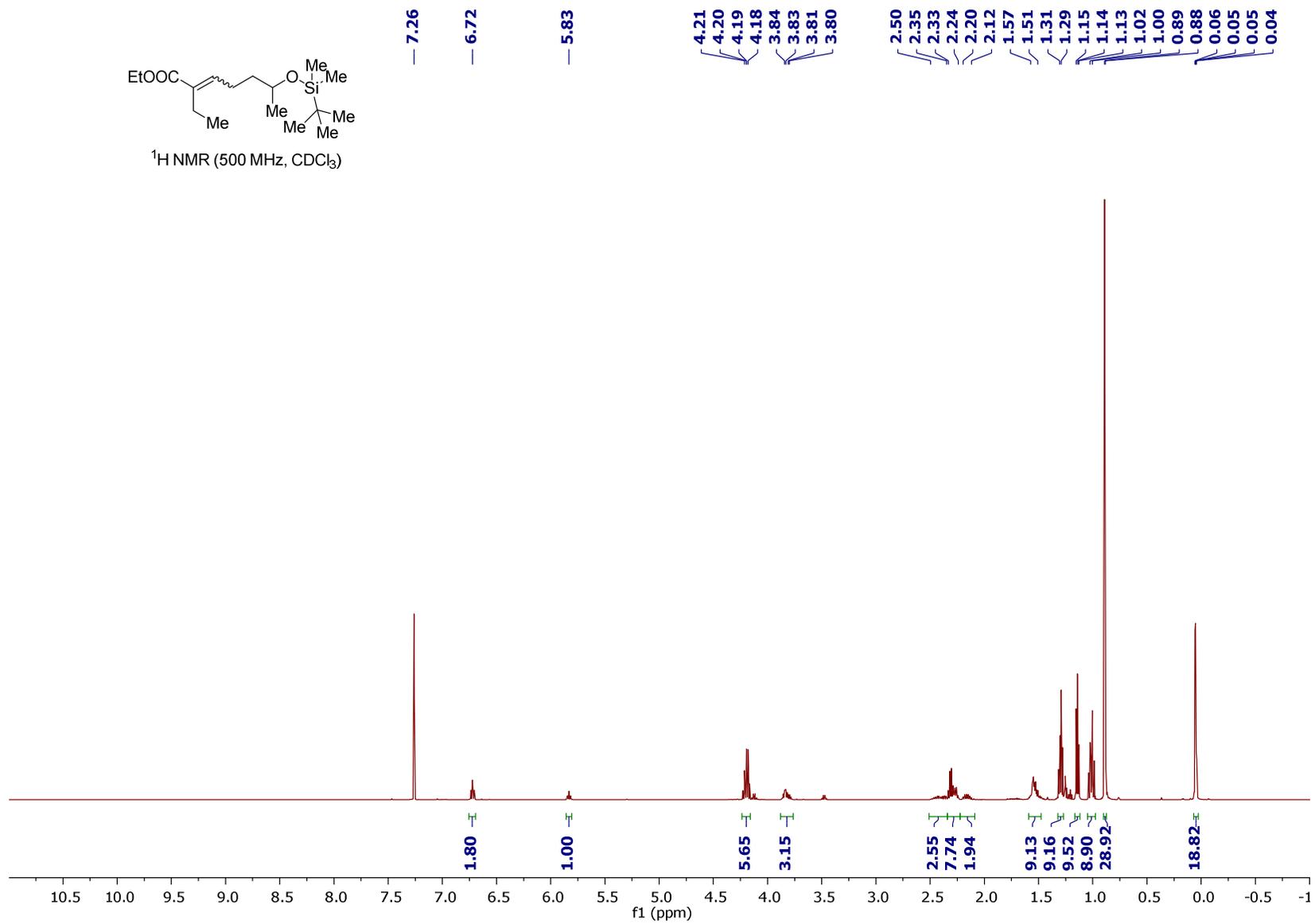
137.42  
136.27  
133.42  
133.04

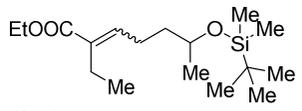
77.16  
68.04  
68.02  
60.49  
60.21  
47.42  
39.29  
38.84  
34.60  
29.86  
26.23  
25.43  
25.30  
23.62  
15.83  
14.44  
11.94



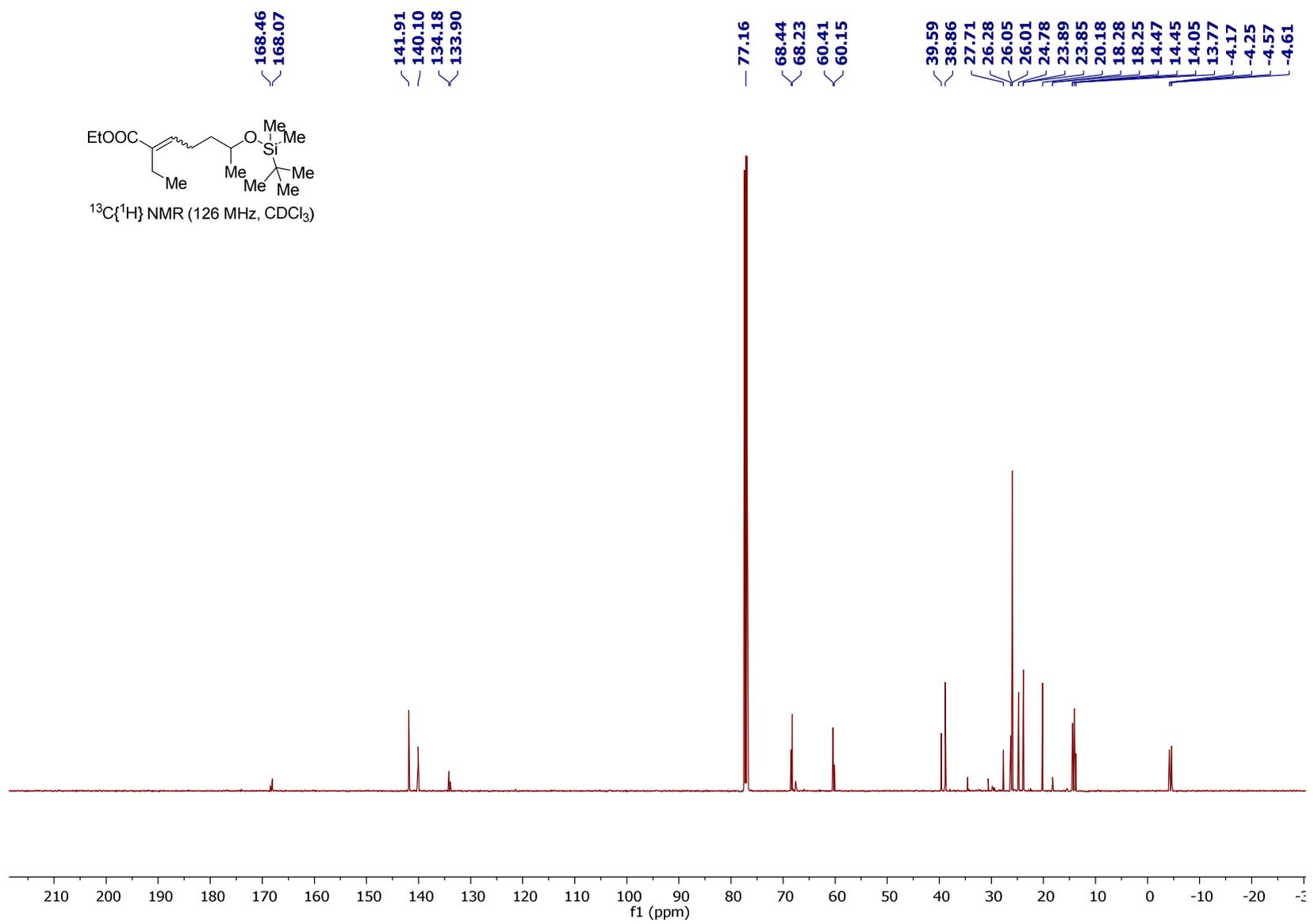


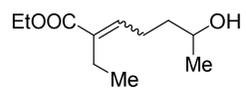
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





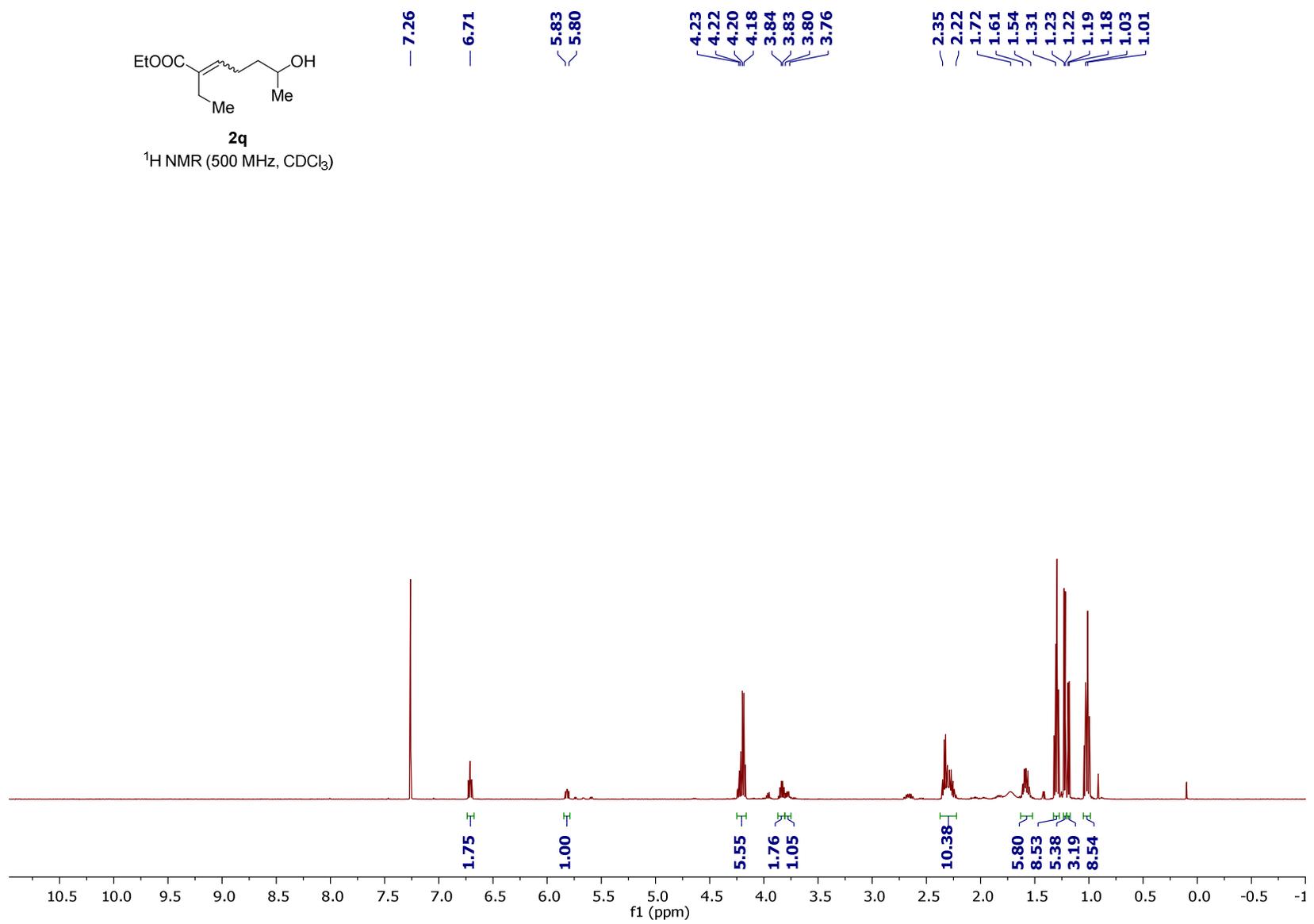
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

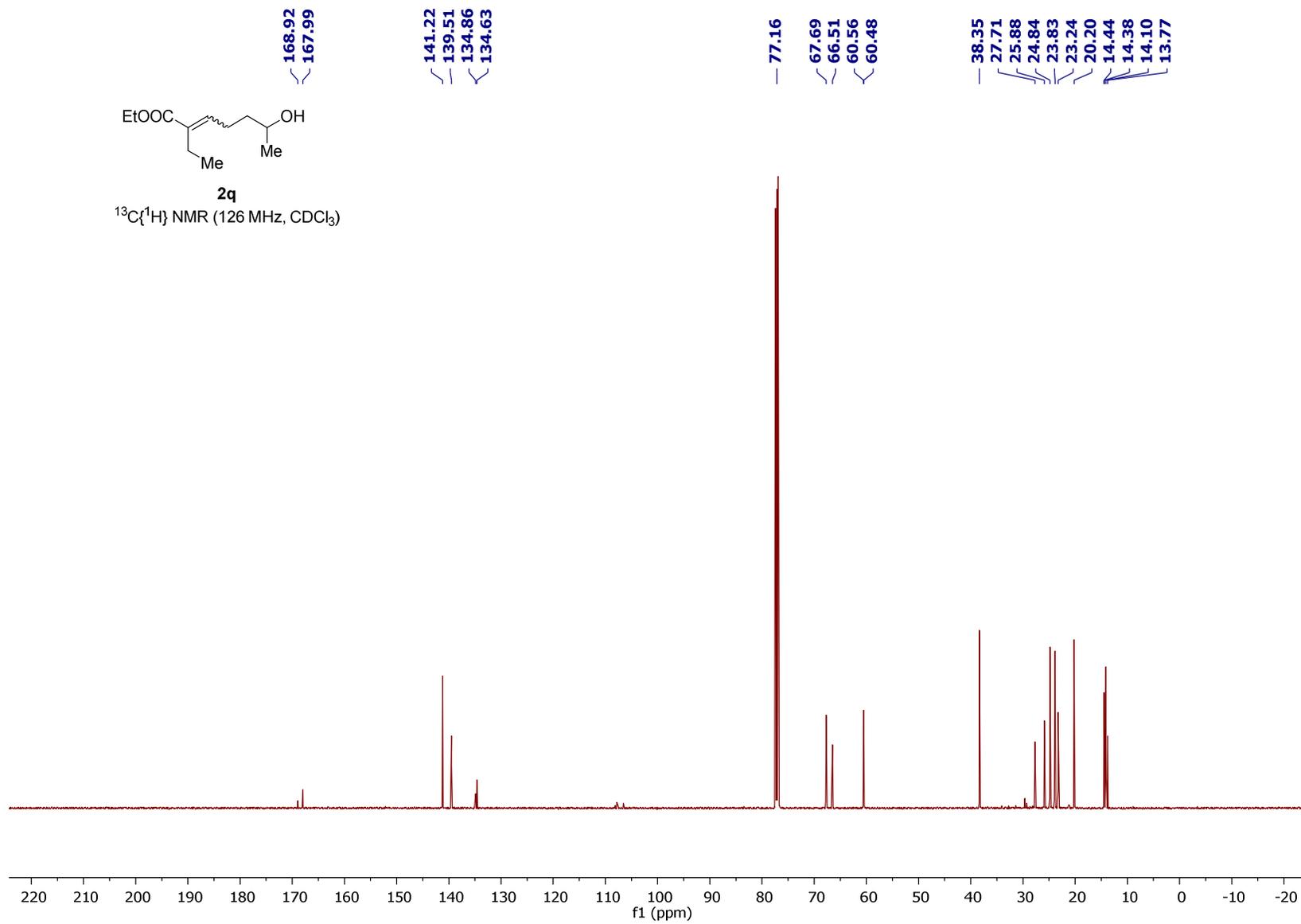
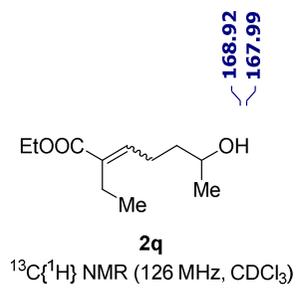


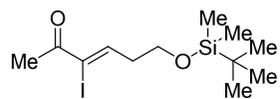


**2q**

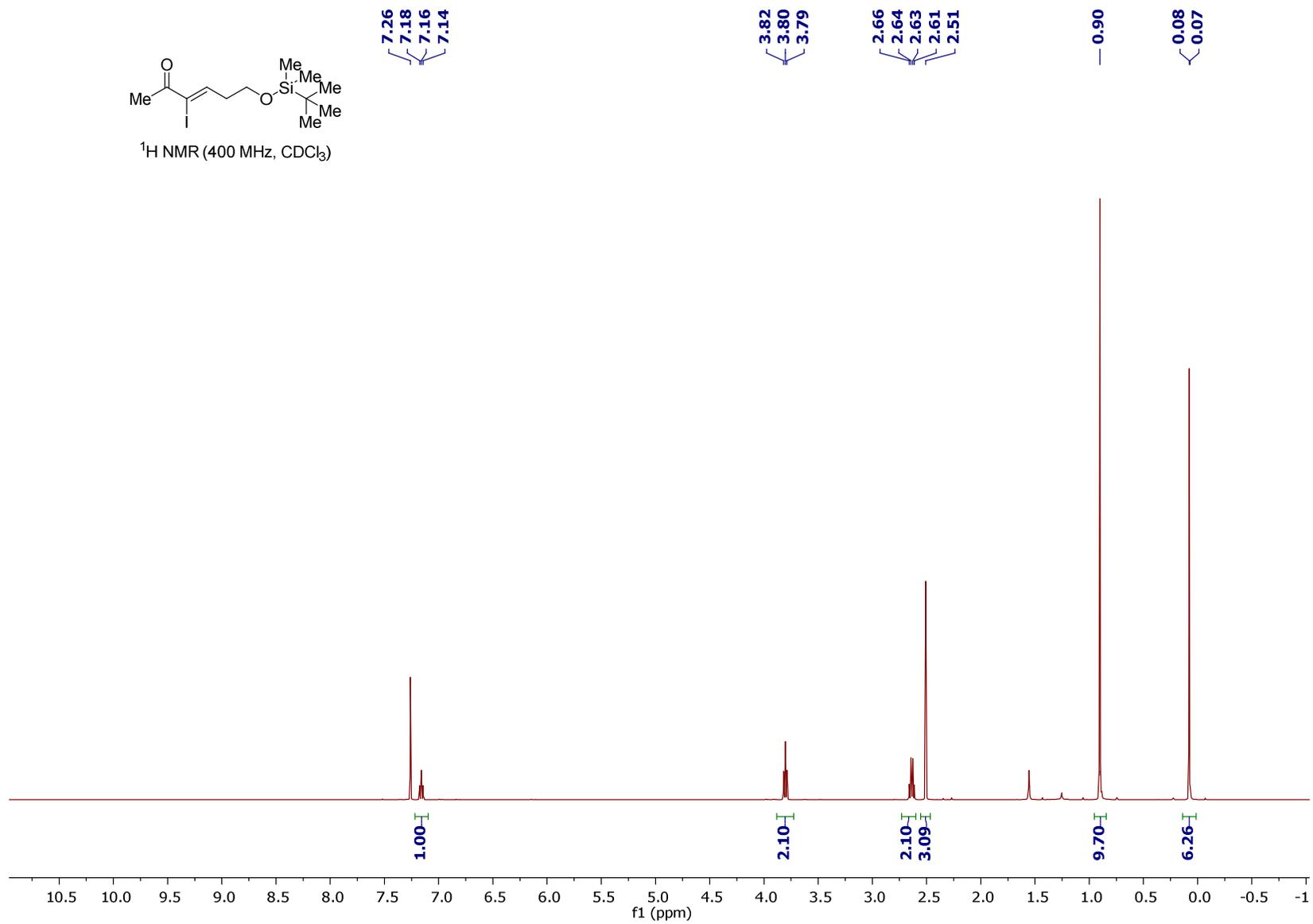
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

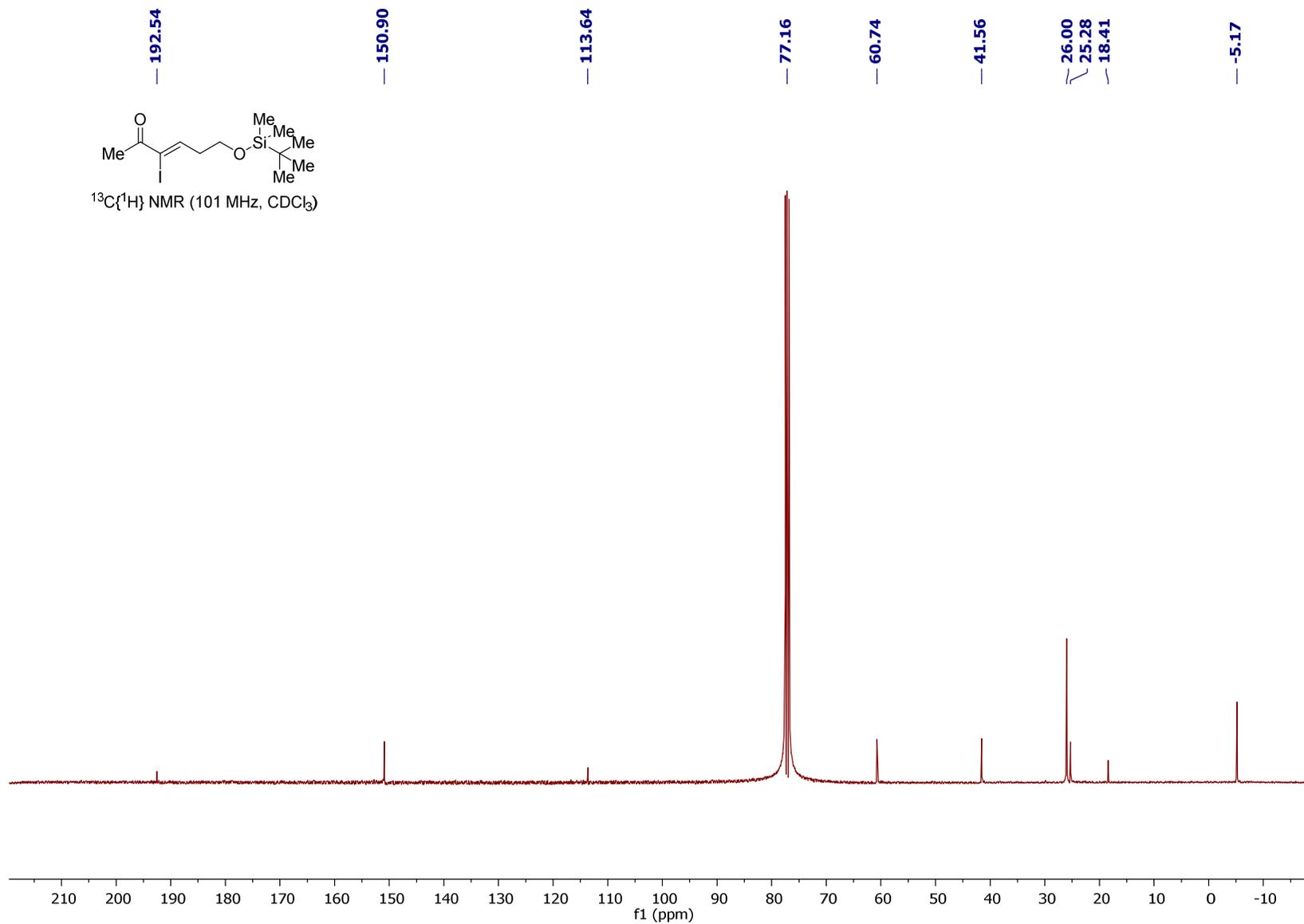
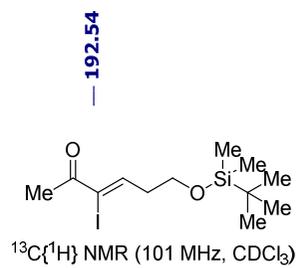


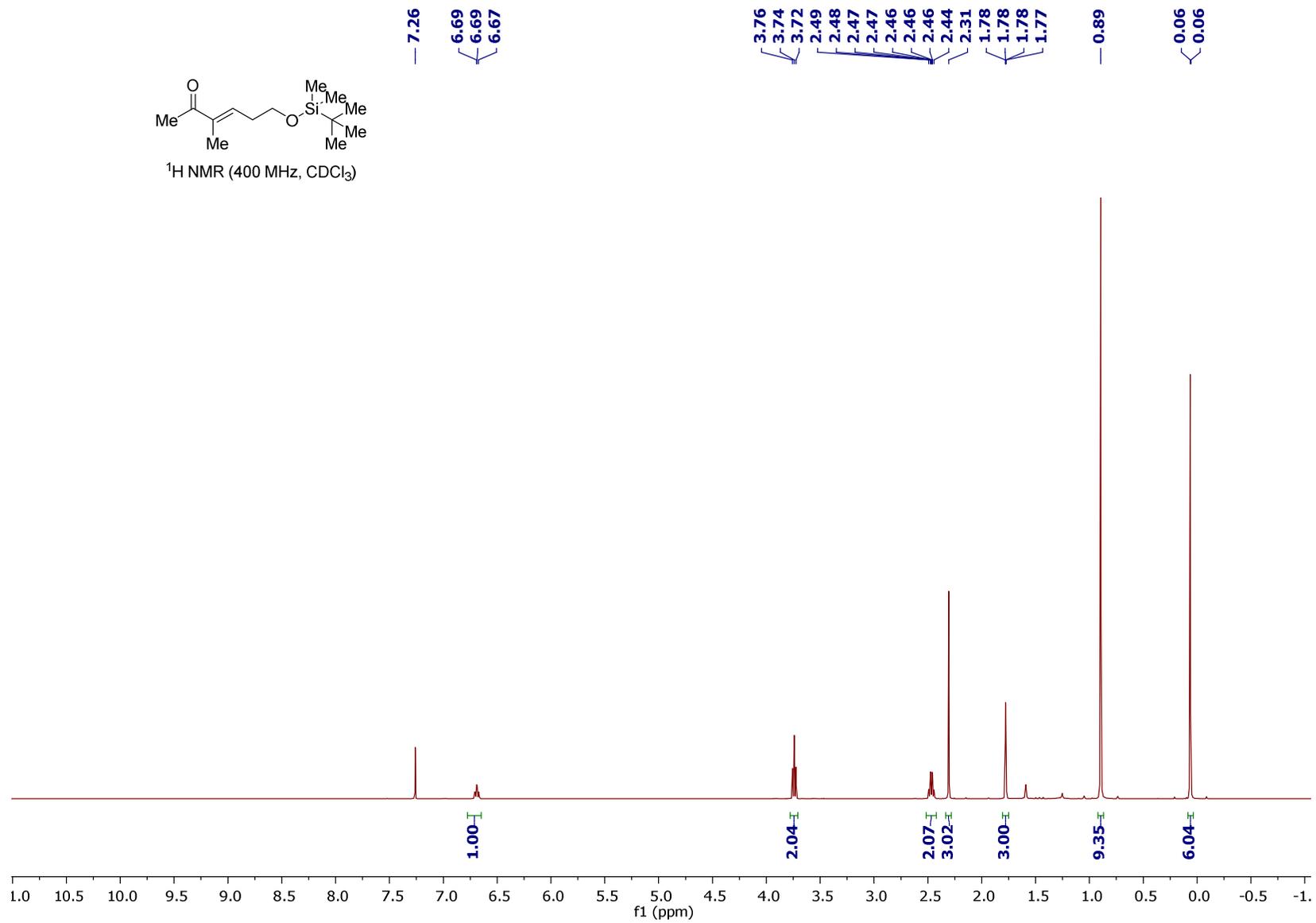
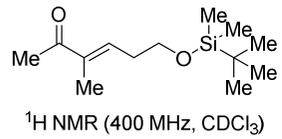


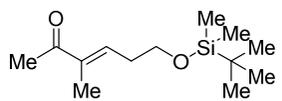


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

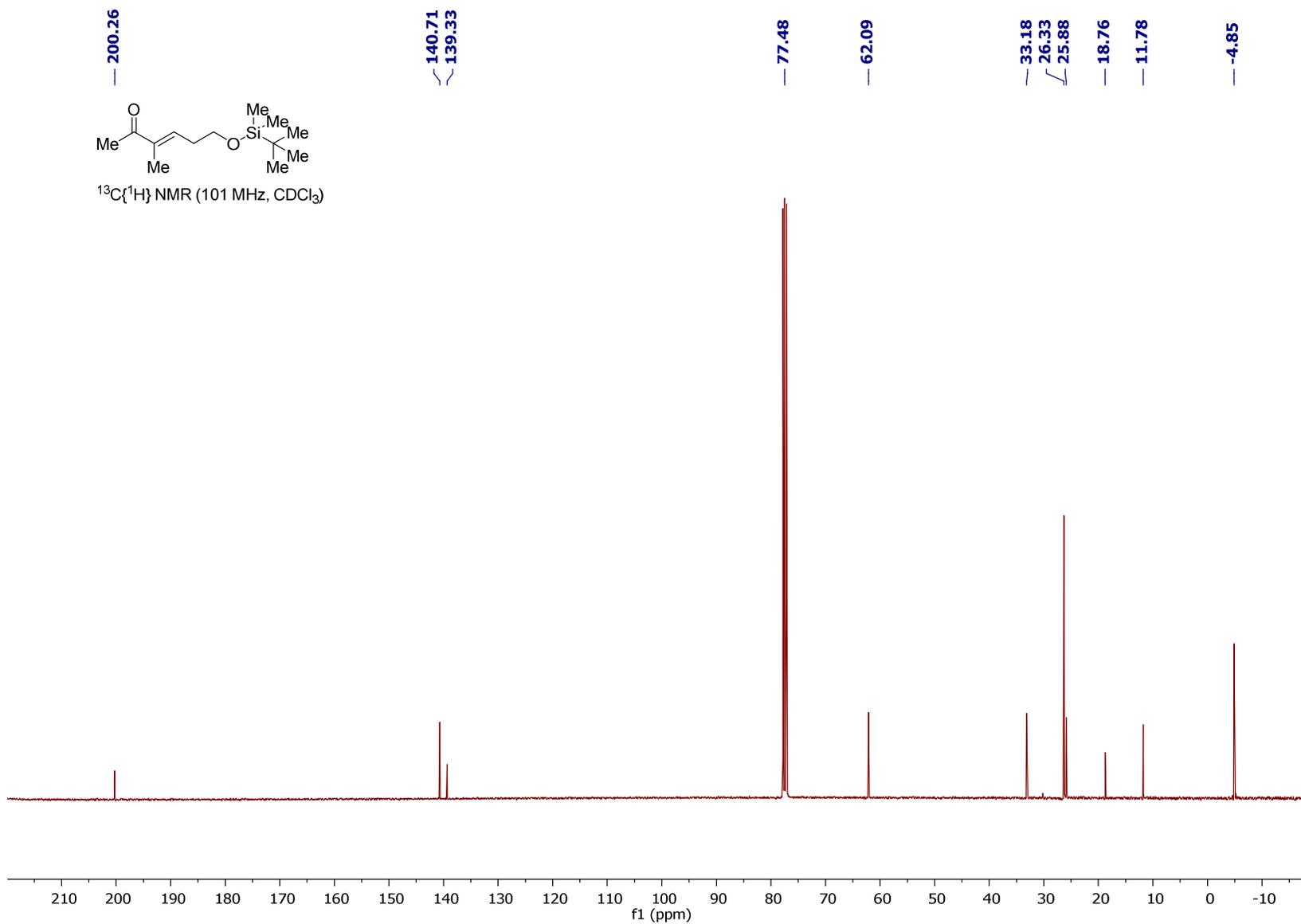


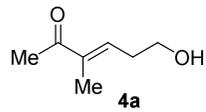






$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



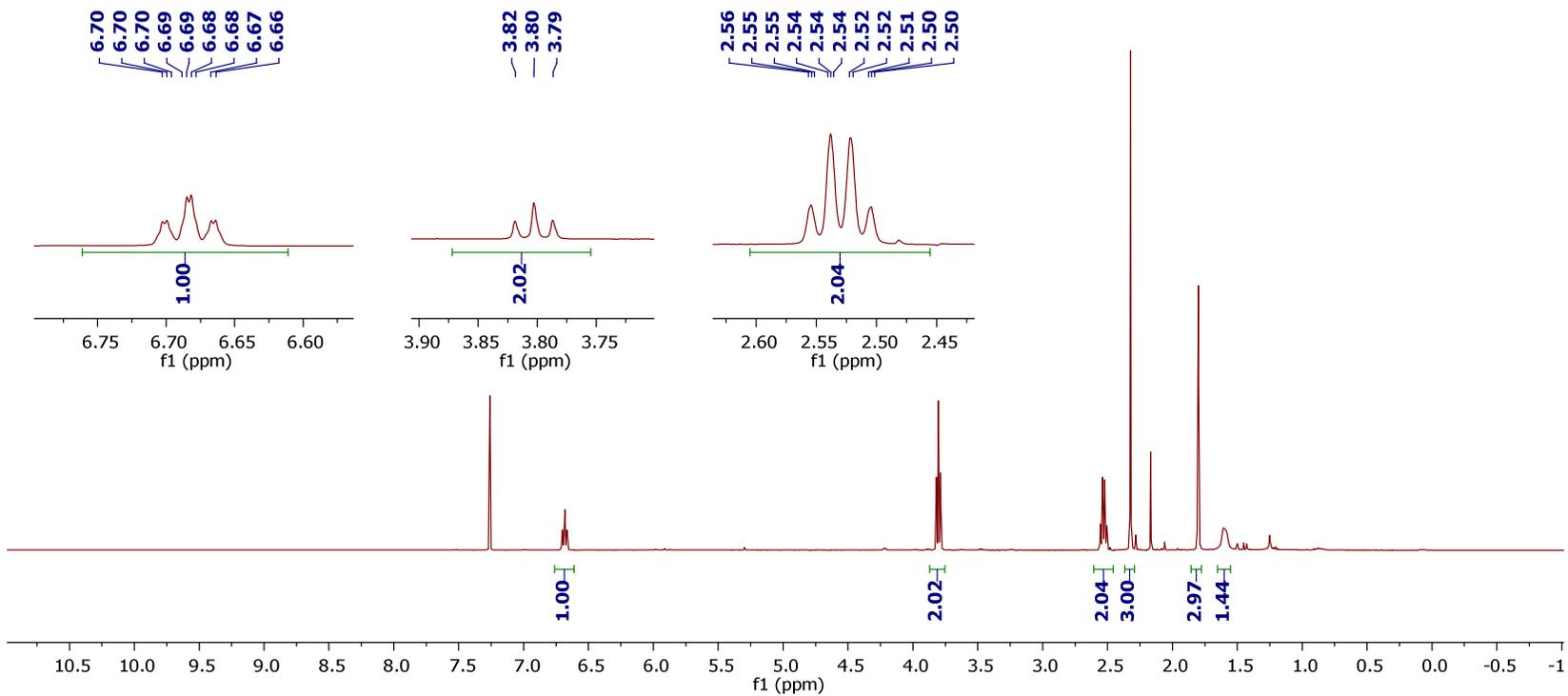


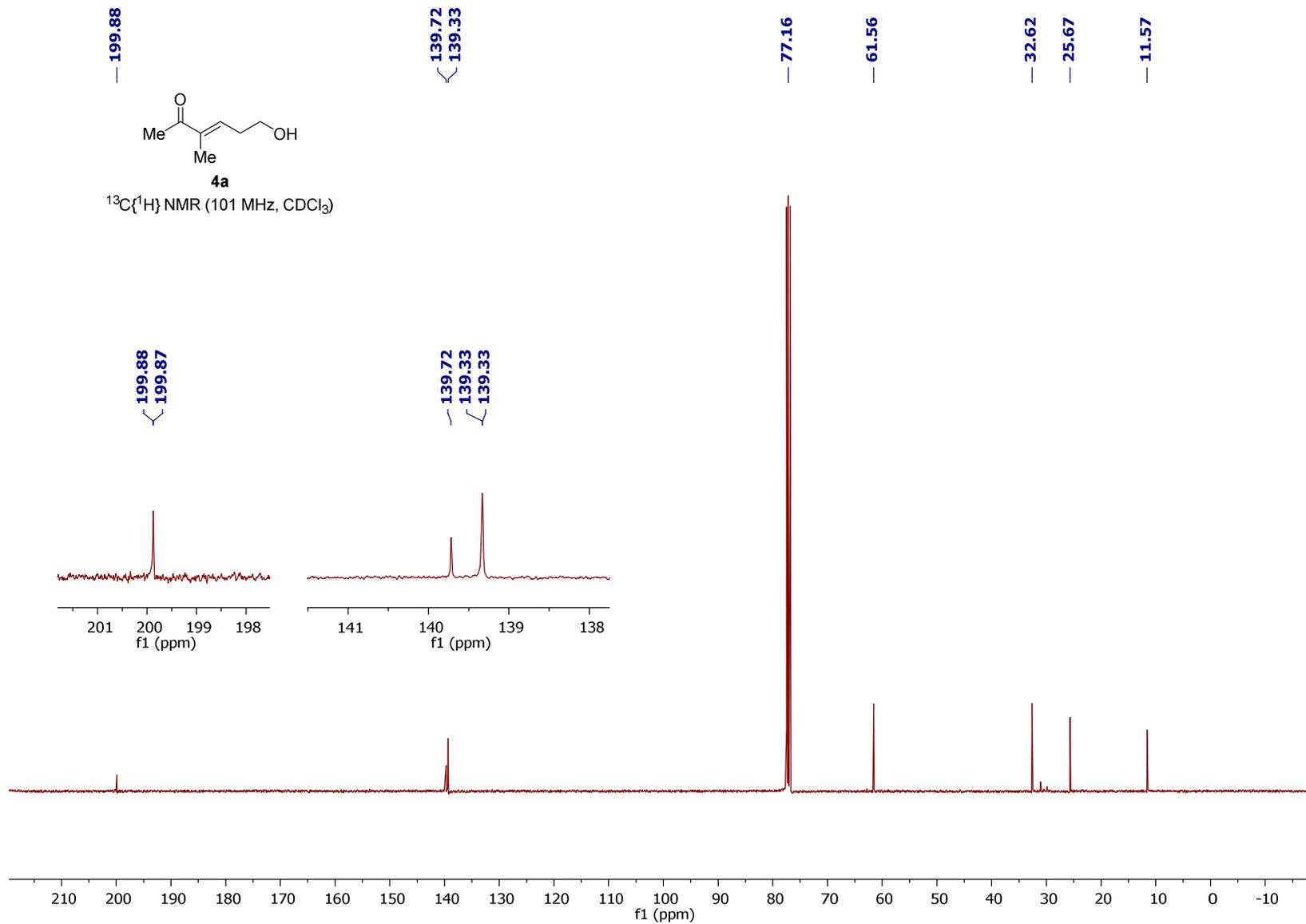
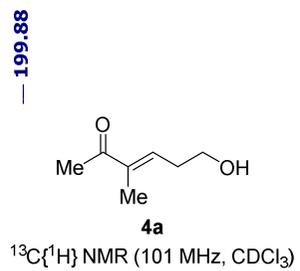
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

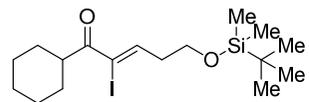
7.26  
6.70  
6.70  
6.70  
6.69  
6.69  
6.68  
6.68  
6.67  
6.66

3.82  
3.80  
3.79

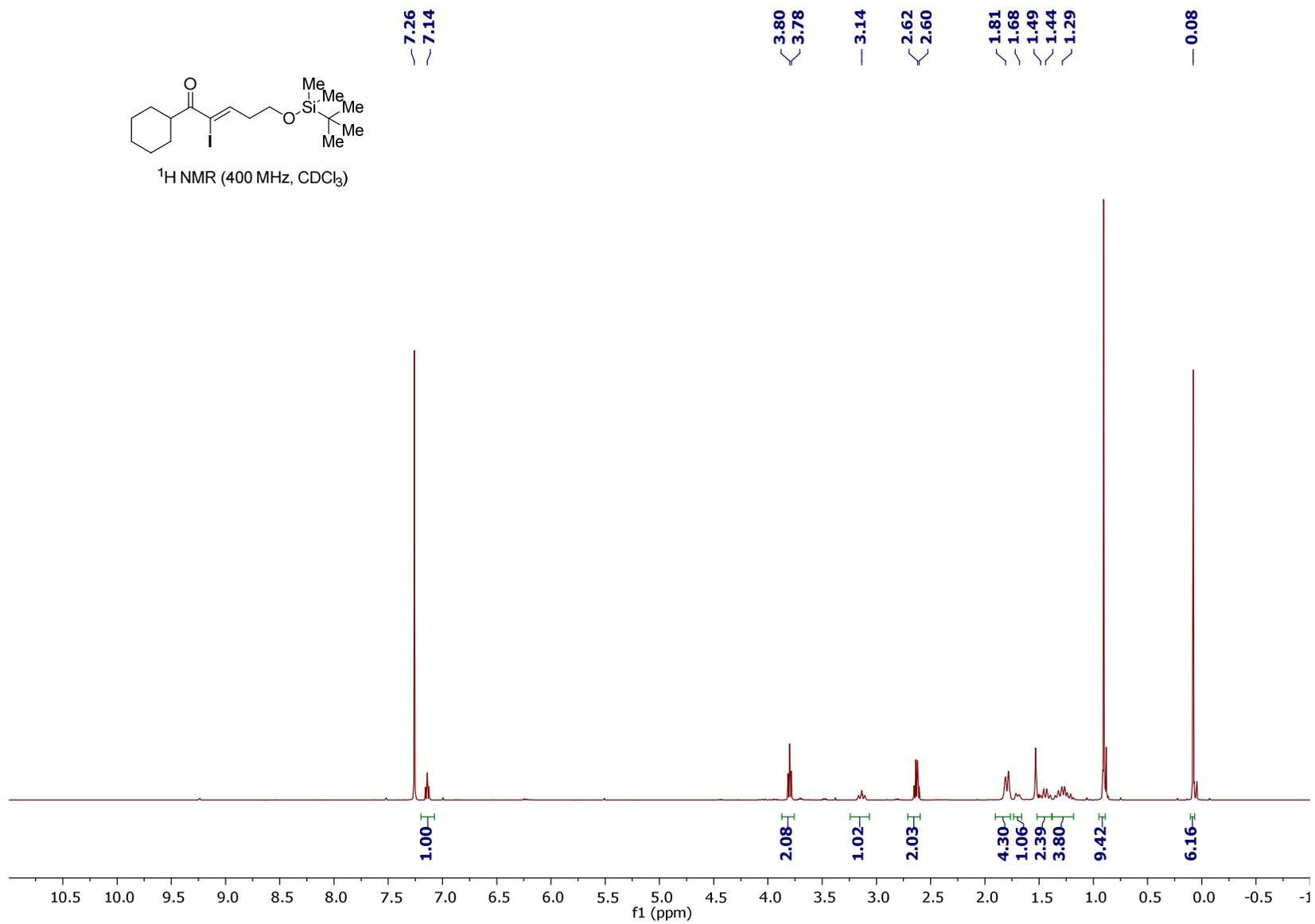
2.54  
2.52  
2.32  
2.28  
2.17  
2.06  
1.80  
1.61

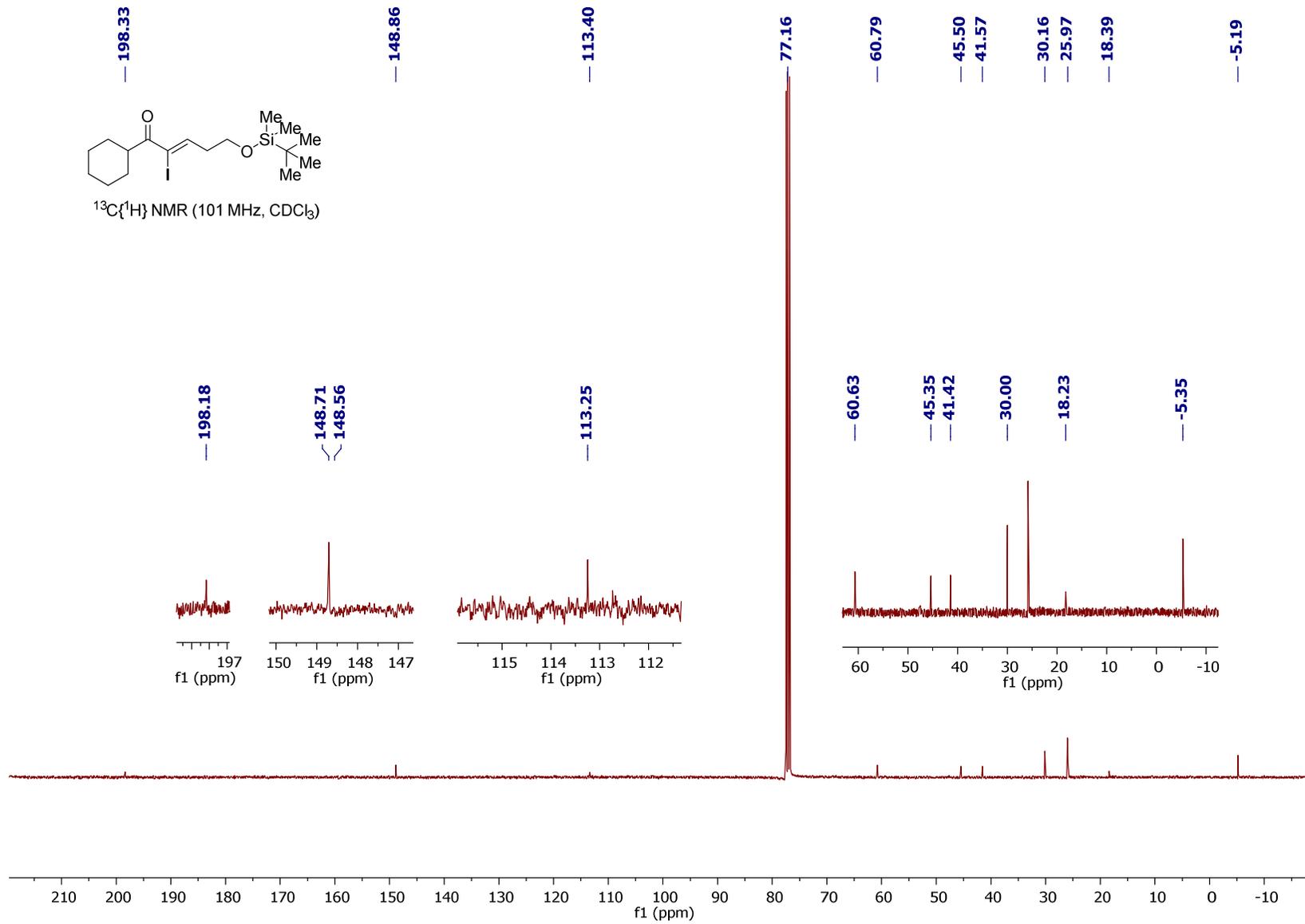
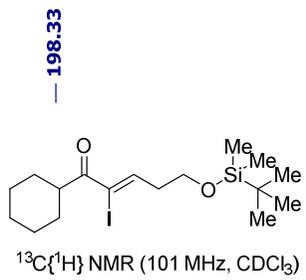


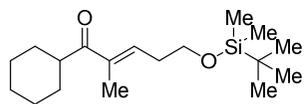




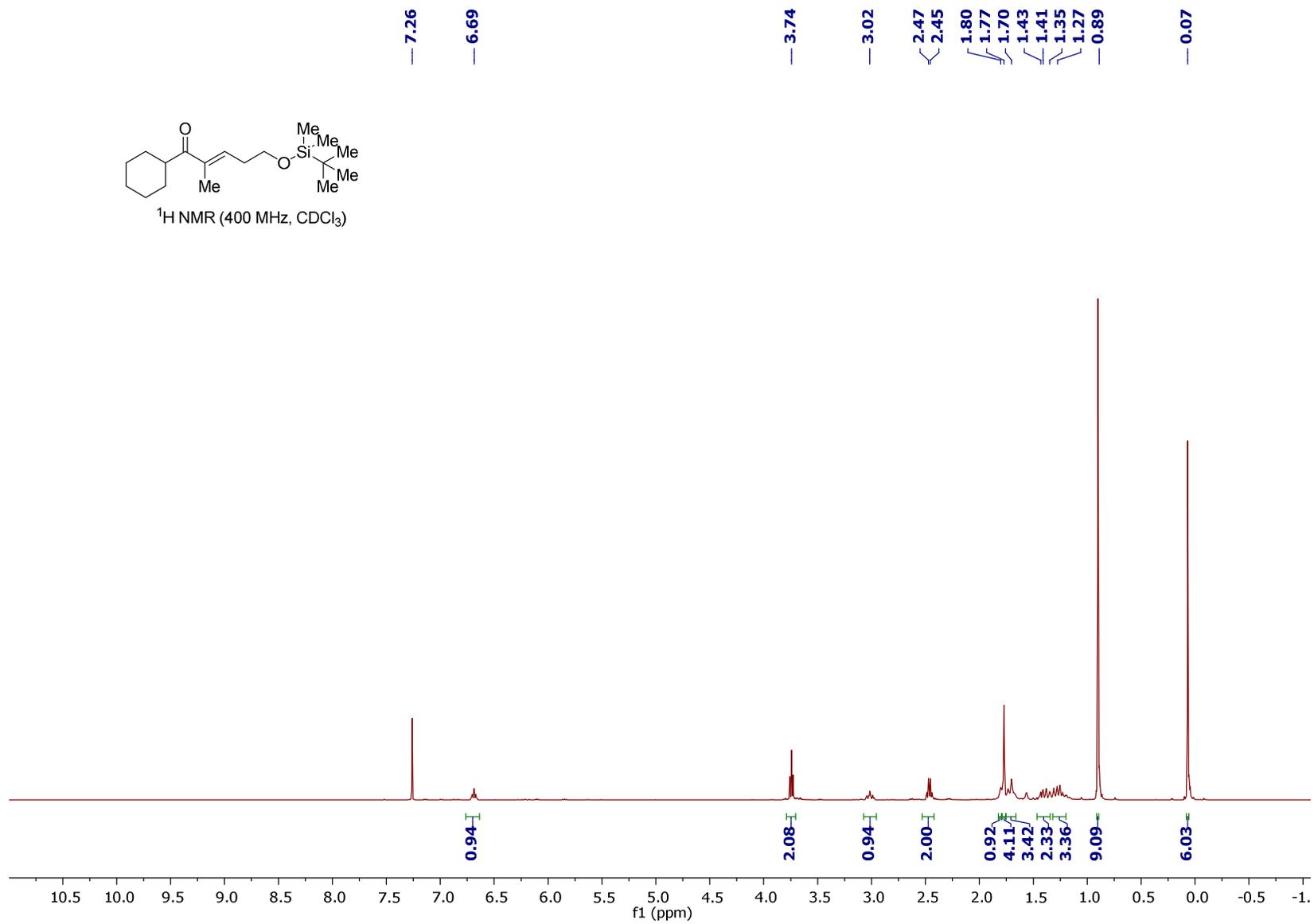
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)







<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



— 205.66

— 159.45

138.37  
137.37

— 77.16

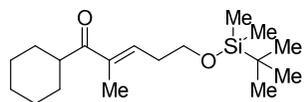
— 61.81

— 44.46

32.74  
30.05  
26.10  
26.02

— 18.43  
— 11.96

— -5.18



$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 205.66

— 137.37

26.10  
26.02  
25.82

— 61.81

— 44.46

32.74  
30.05  
26.10  
26.02

— 18.43  
— 11.96

— -5.18

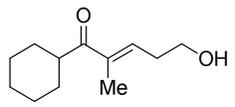
207 206 205 204  
f1 (ppm)

139 138 137 136  
f1 (ppm)

27 26 25  
f1 (ppm)

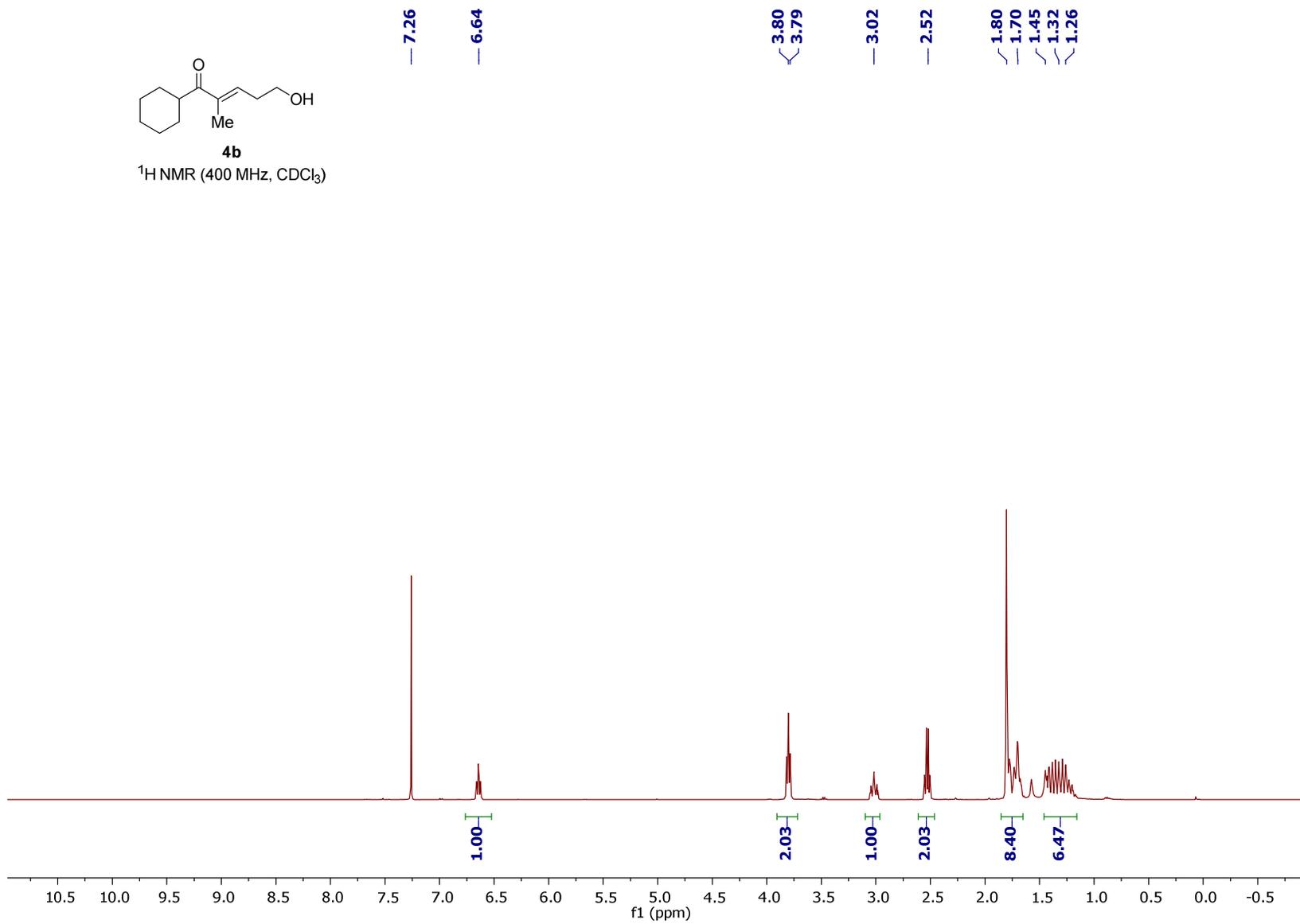
60 50 40 30 20 10 0  
f1 (ppm)

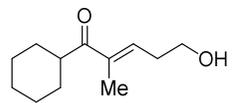
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10  
f1 (ppm)



**4b**

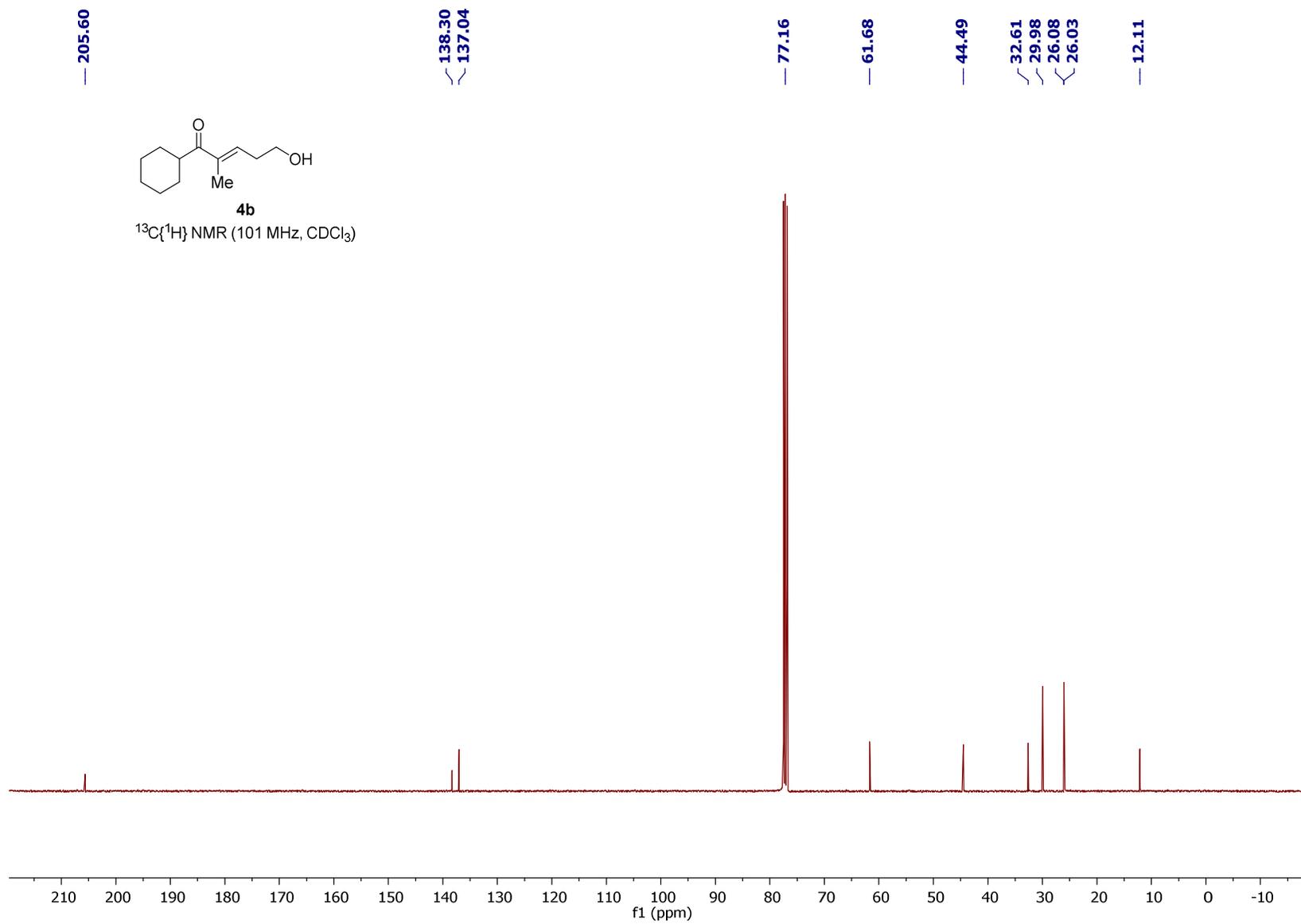
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

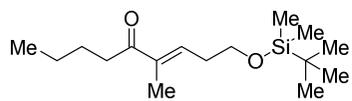




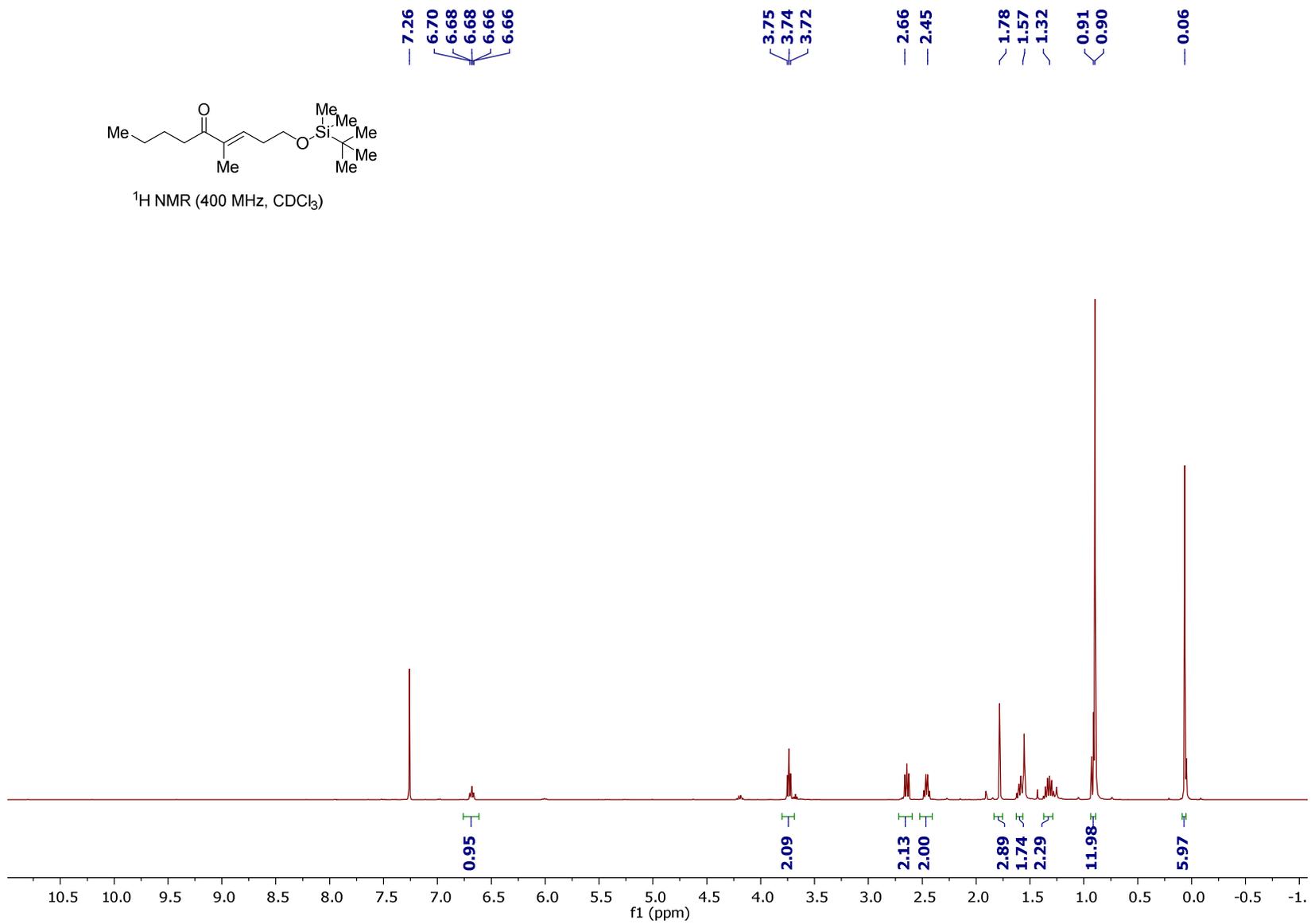
**4b**

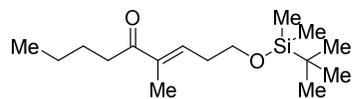
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



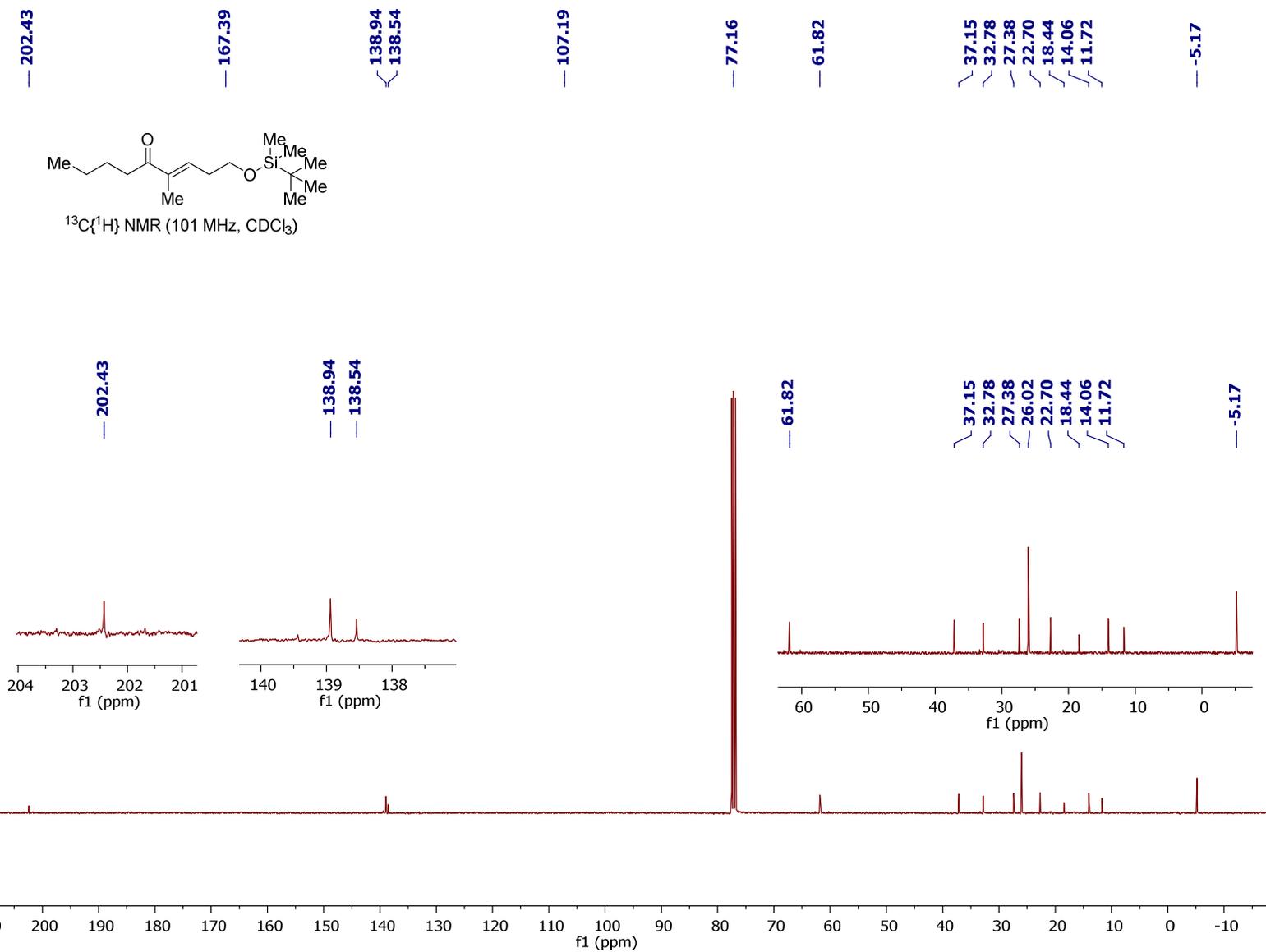


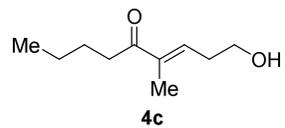
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



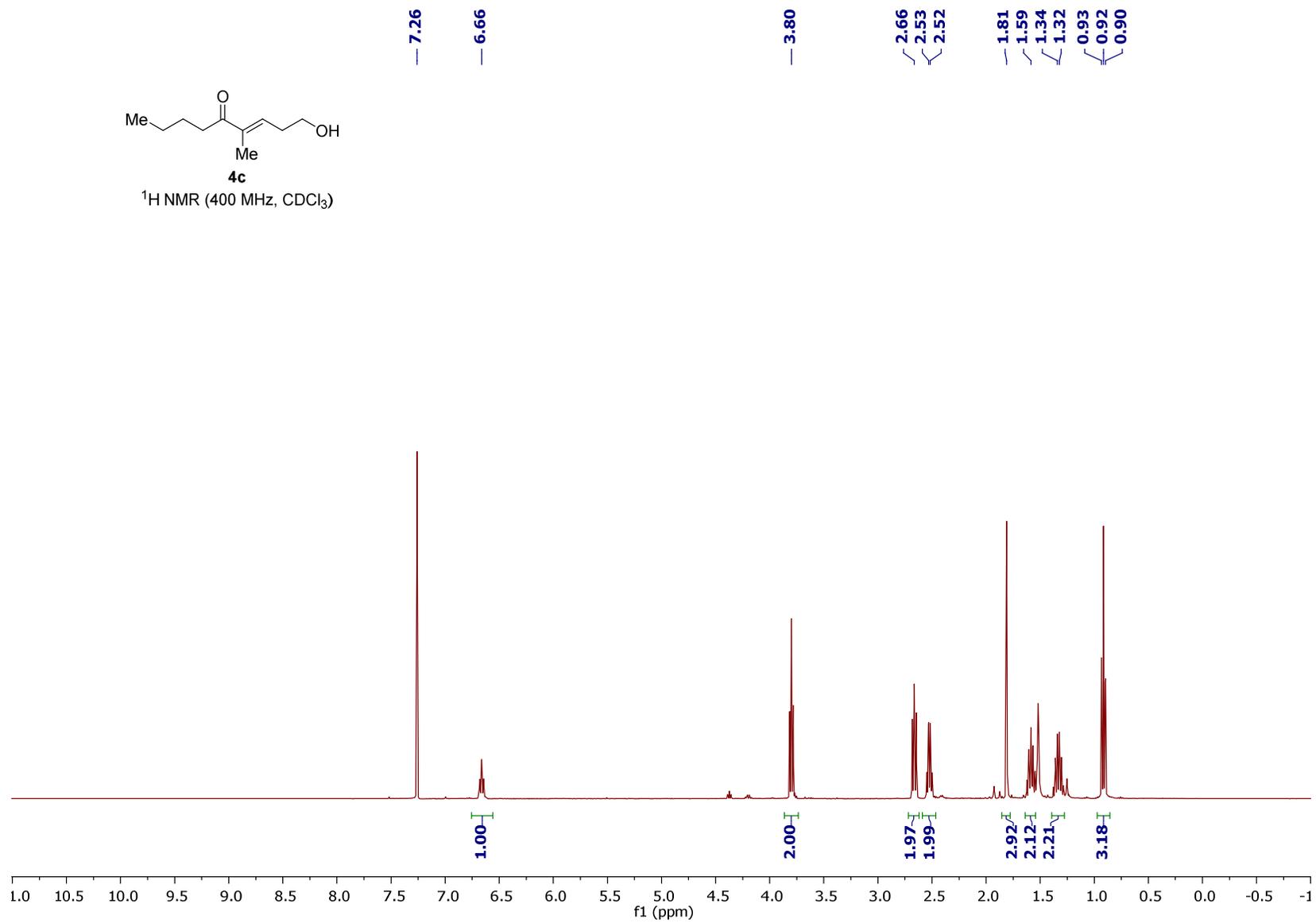


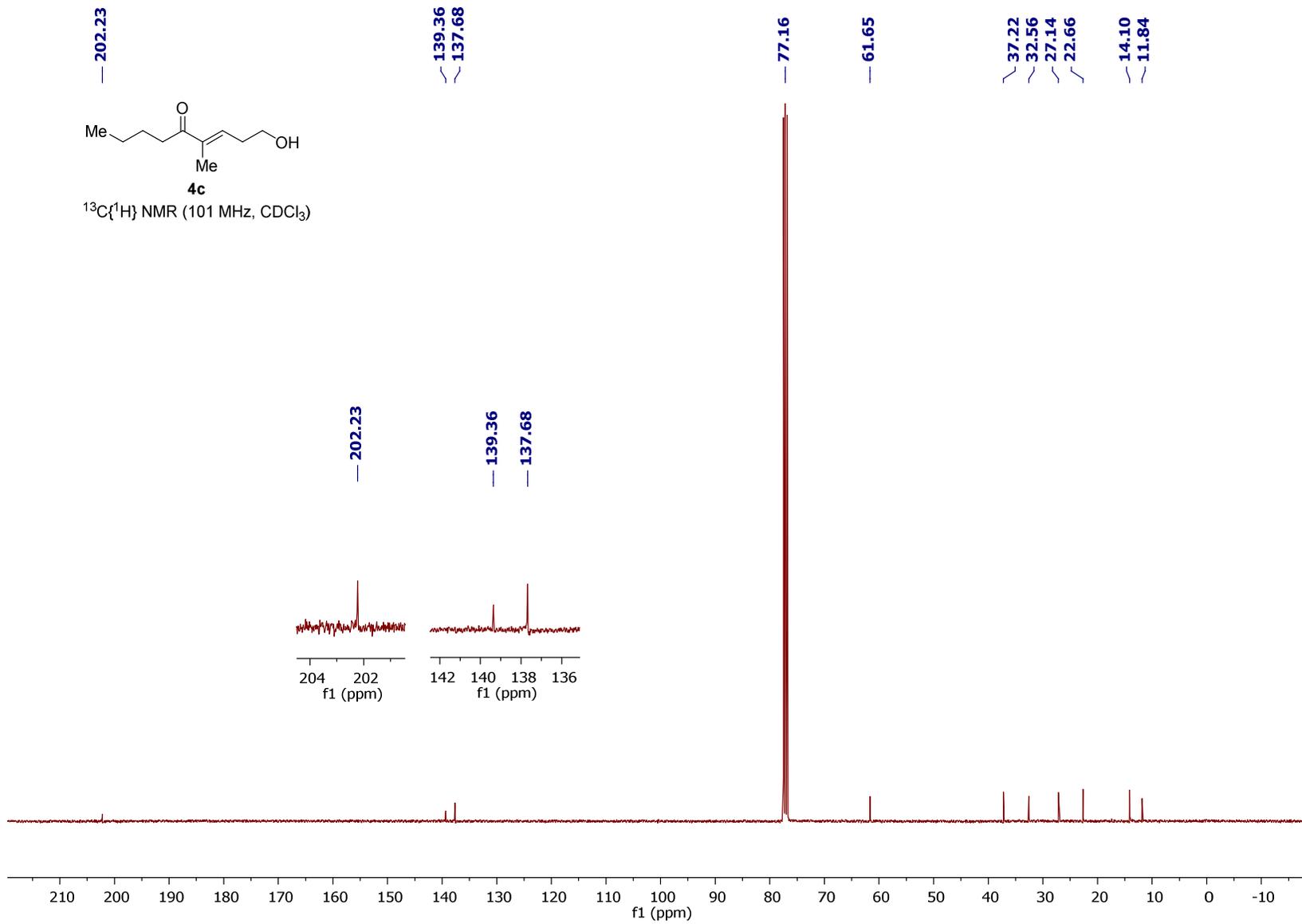
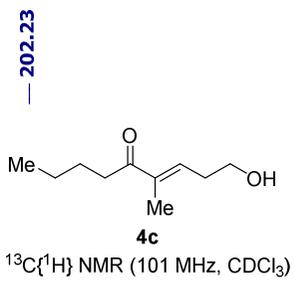
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

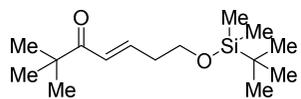




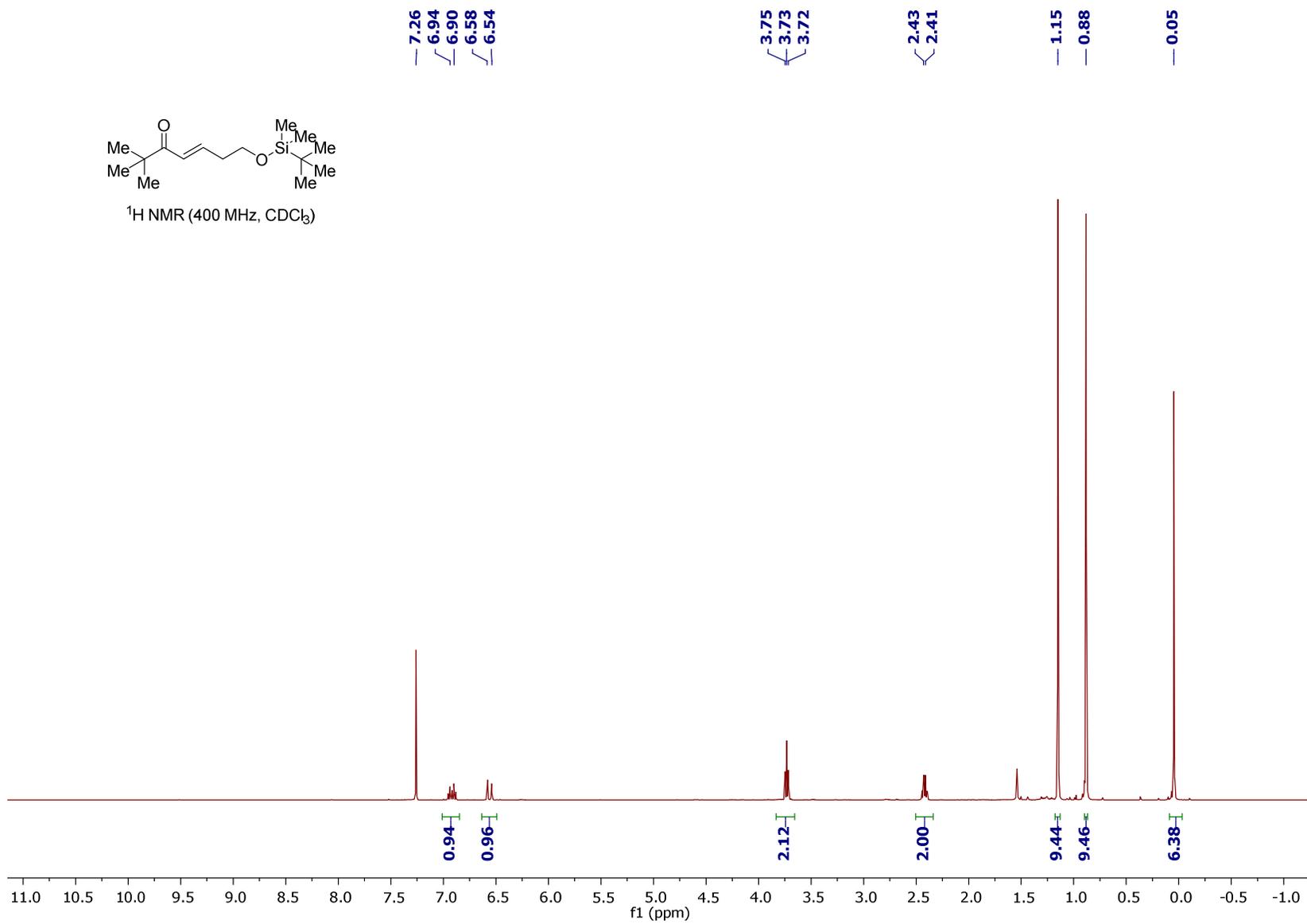
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)







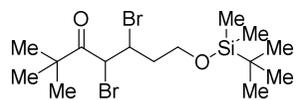
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)







— 206.87



$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 77.16

— 60.43

~ 49.44

~ 47.02

~ 44.39

~ 37.85

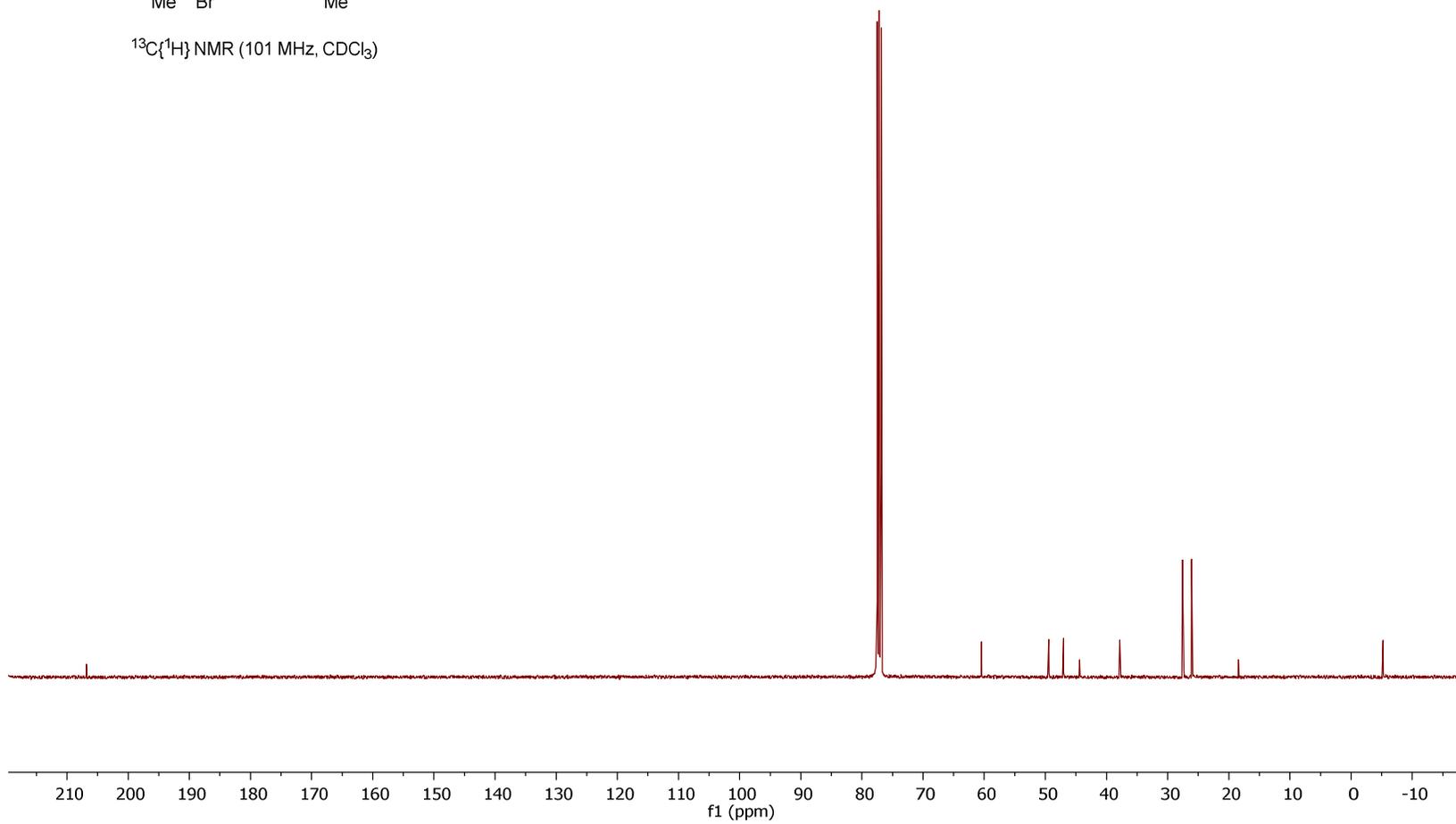
~ 27.58

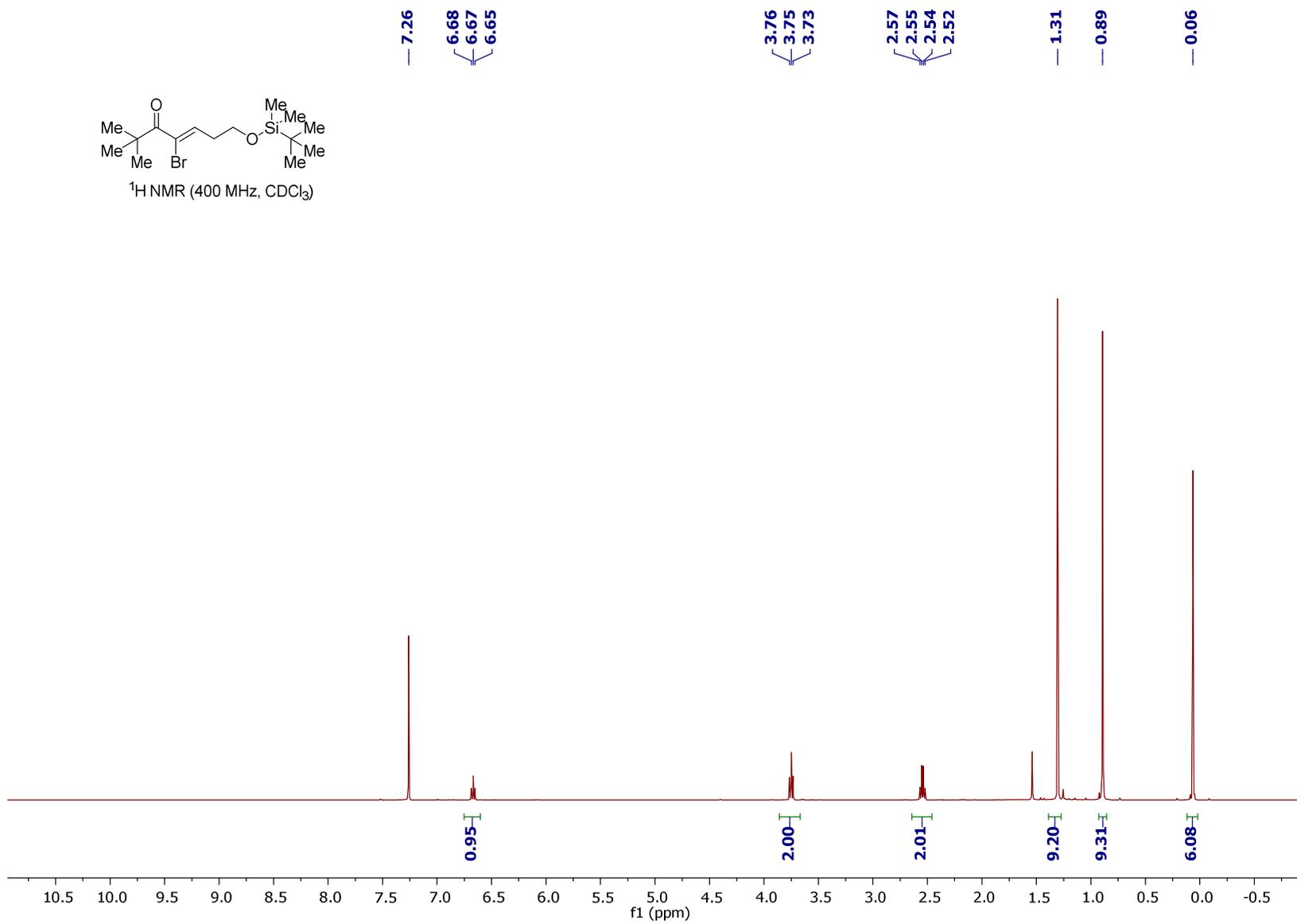
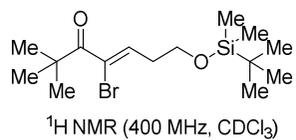
~ 26.08

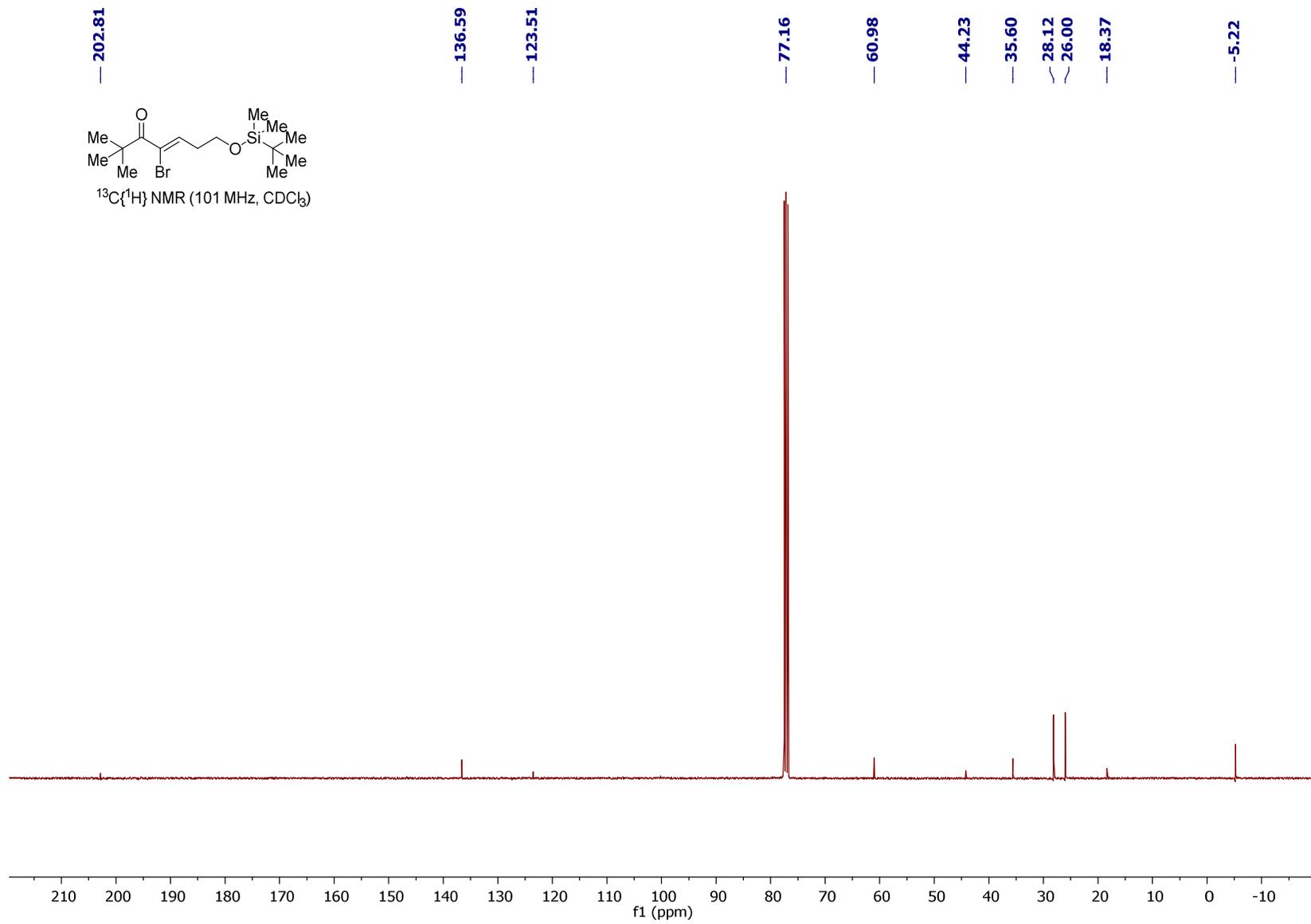
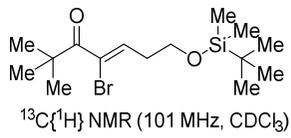
— 18.43

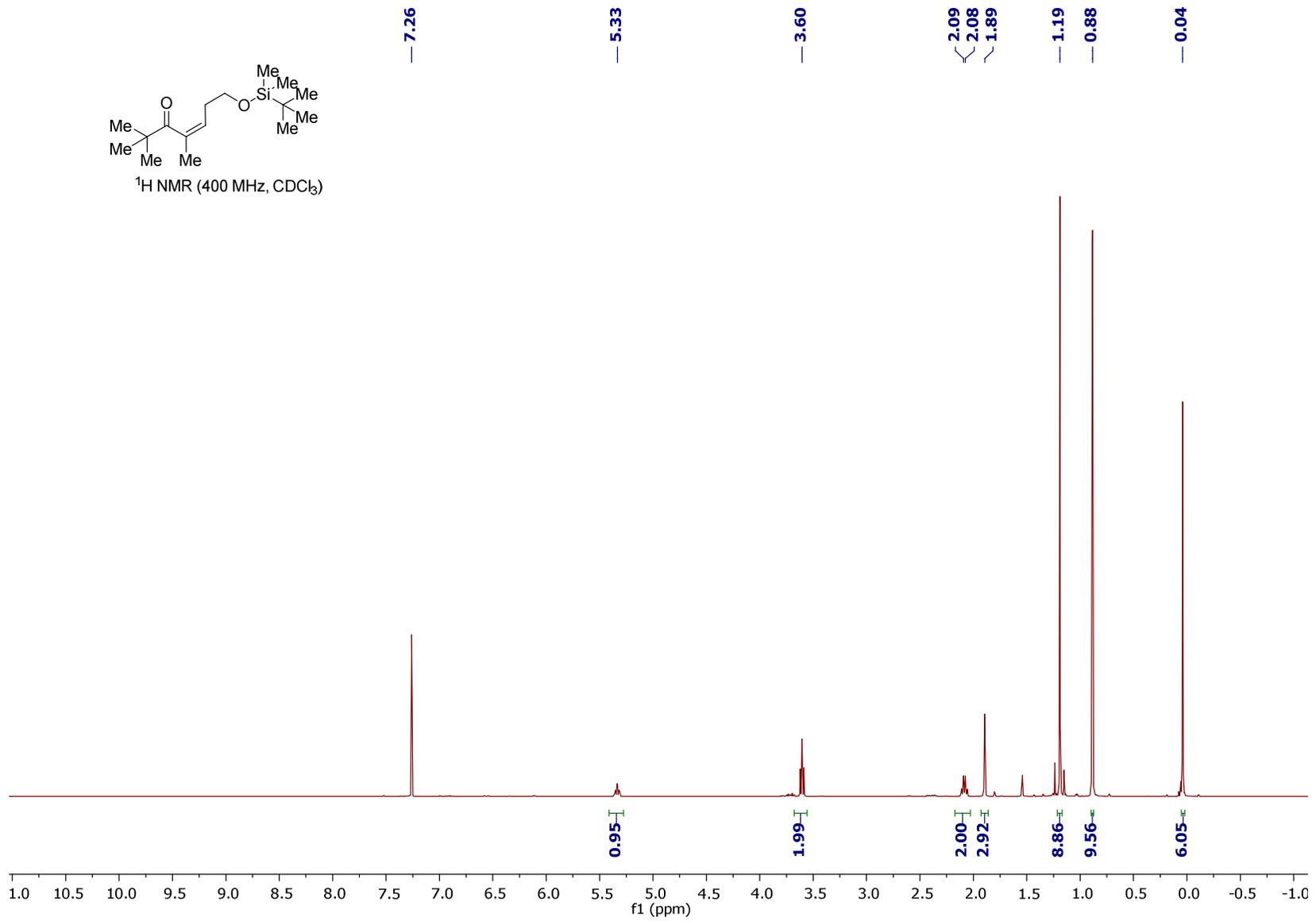
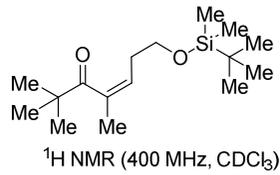
~ -5.17

~ -5.21









— 217.24

— 139.53

— 125.40

— 77.16

— 62.86

— 43.80

— 33.84

— 28.36

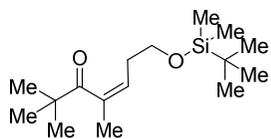
— 27.34

— 26.10

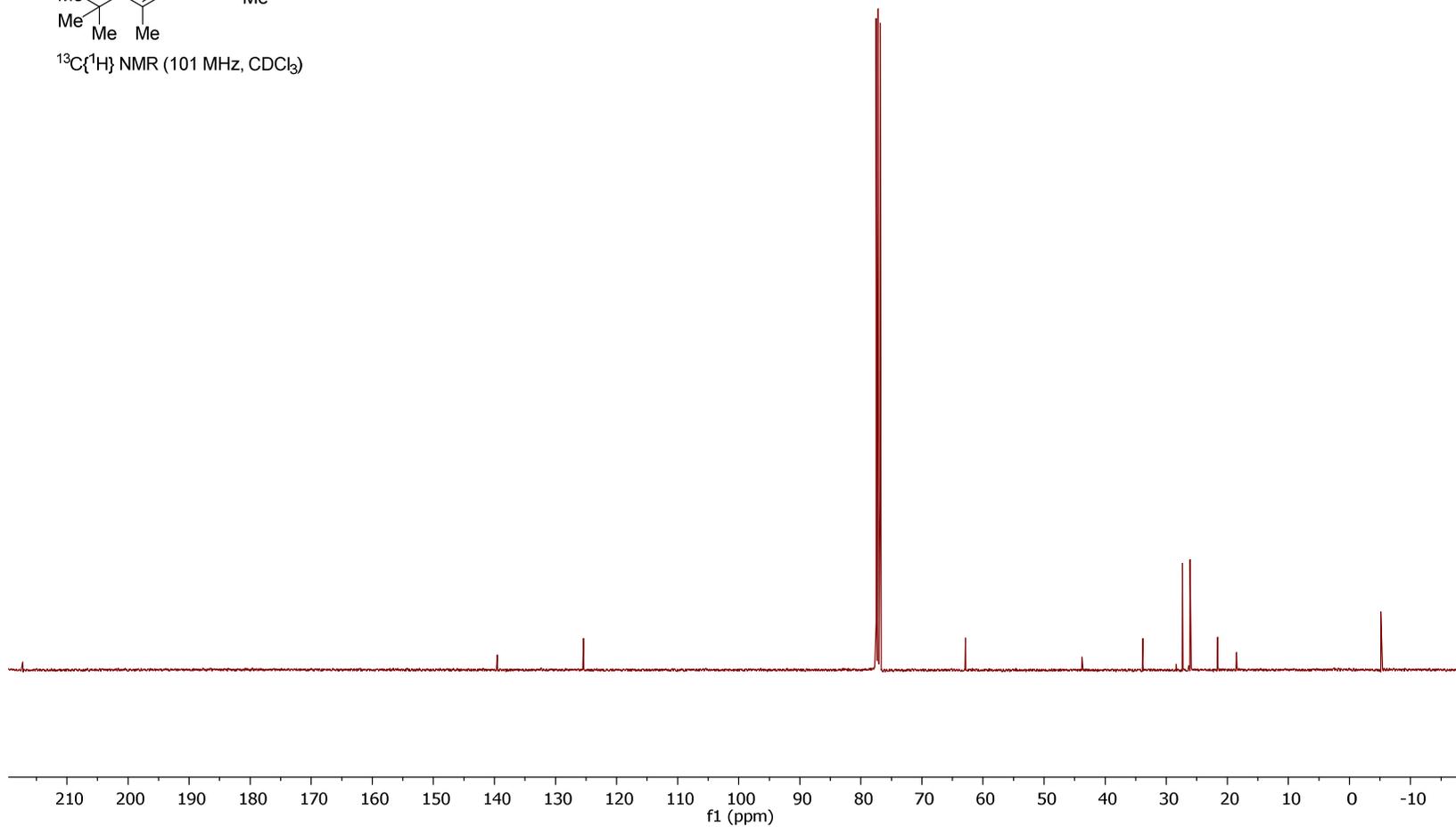
— 21.55

— 18.51

— -5.14

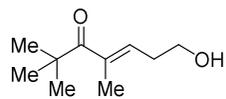


<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)



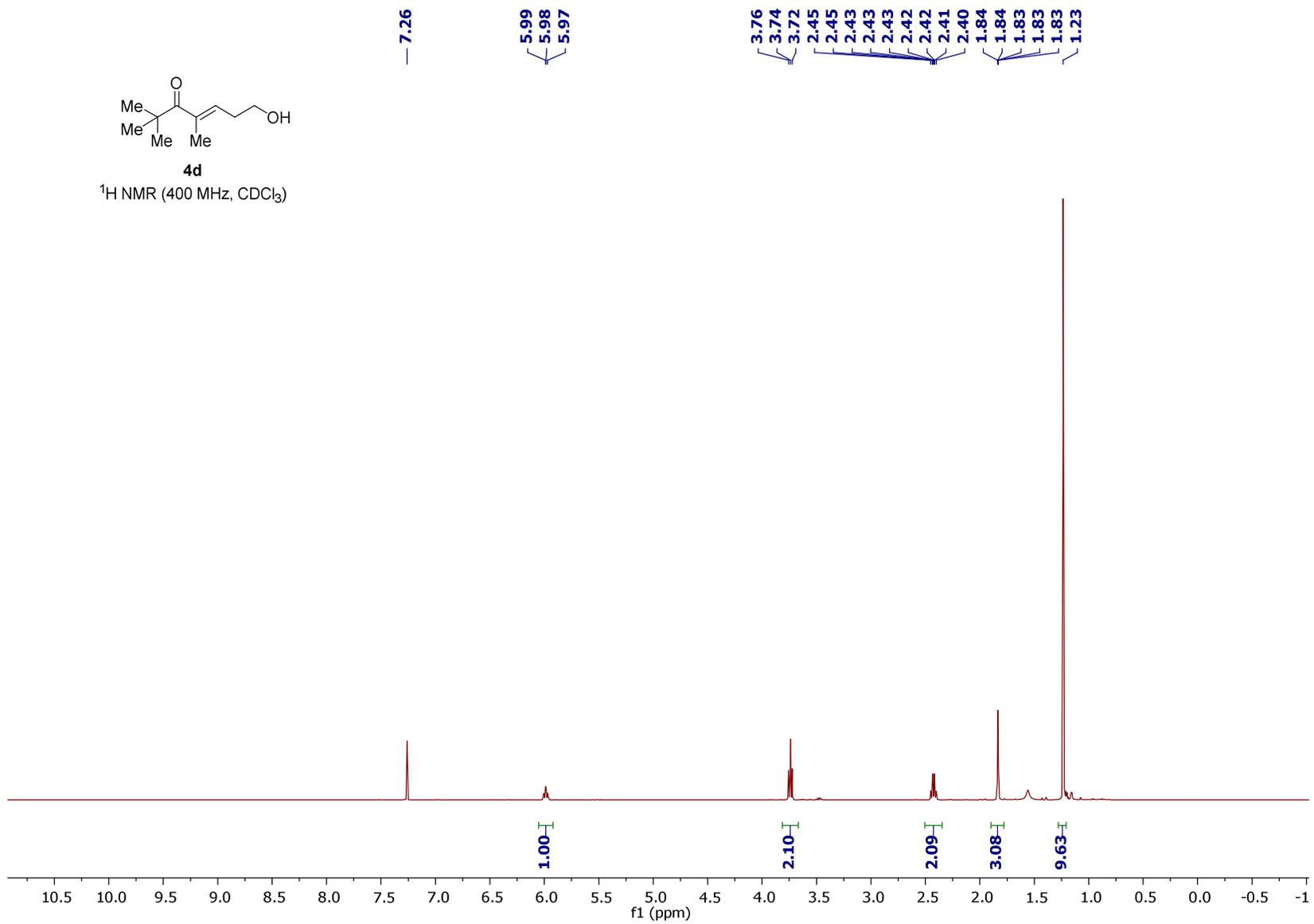






**4d**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



— 212.02

— 138.73

— 130.38

— 77.16

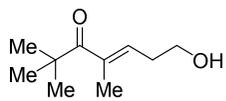
— 61.86

— 44.09

— 31.73

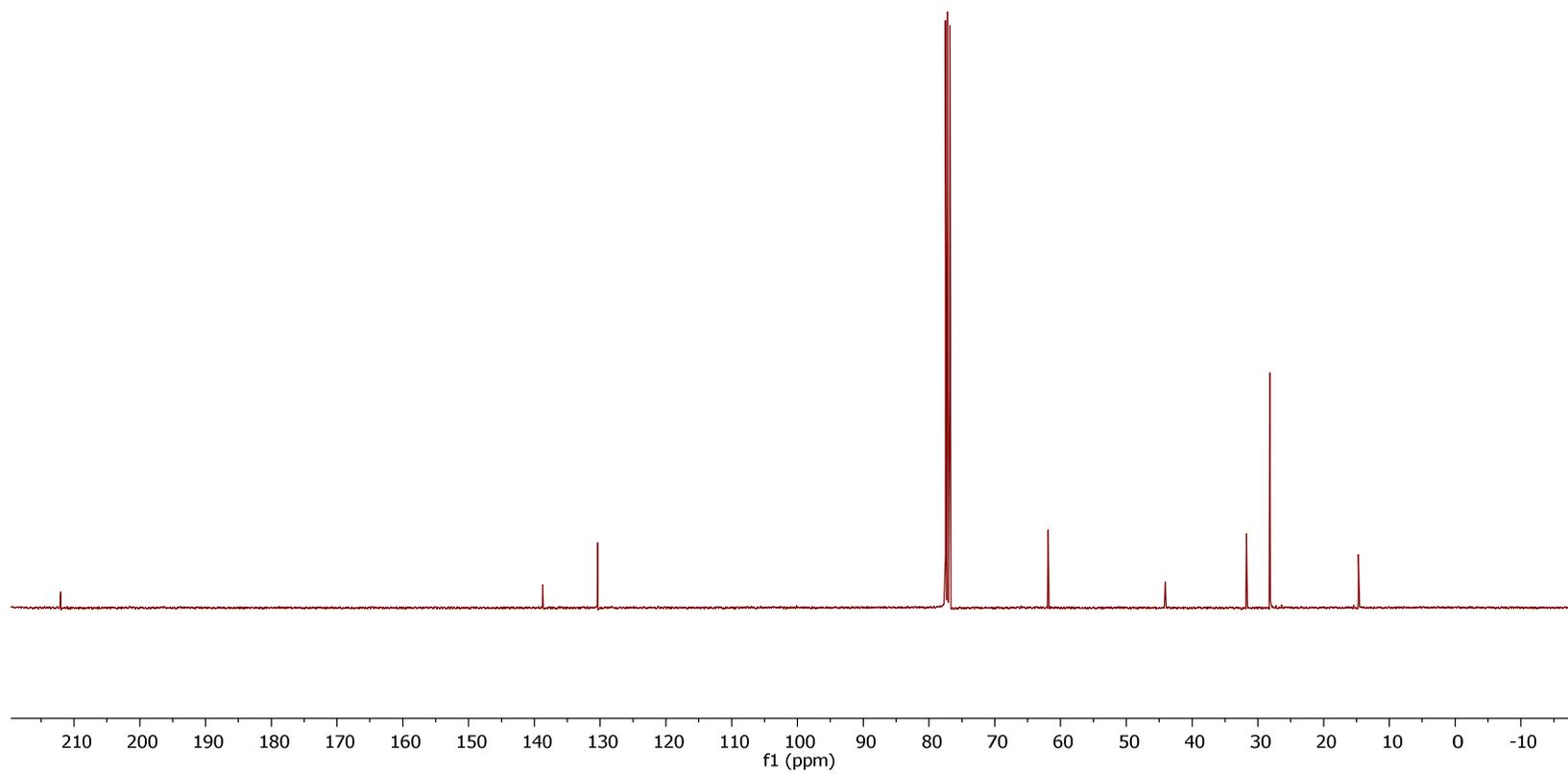
— 28.17

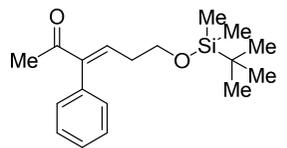
— 14.71



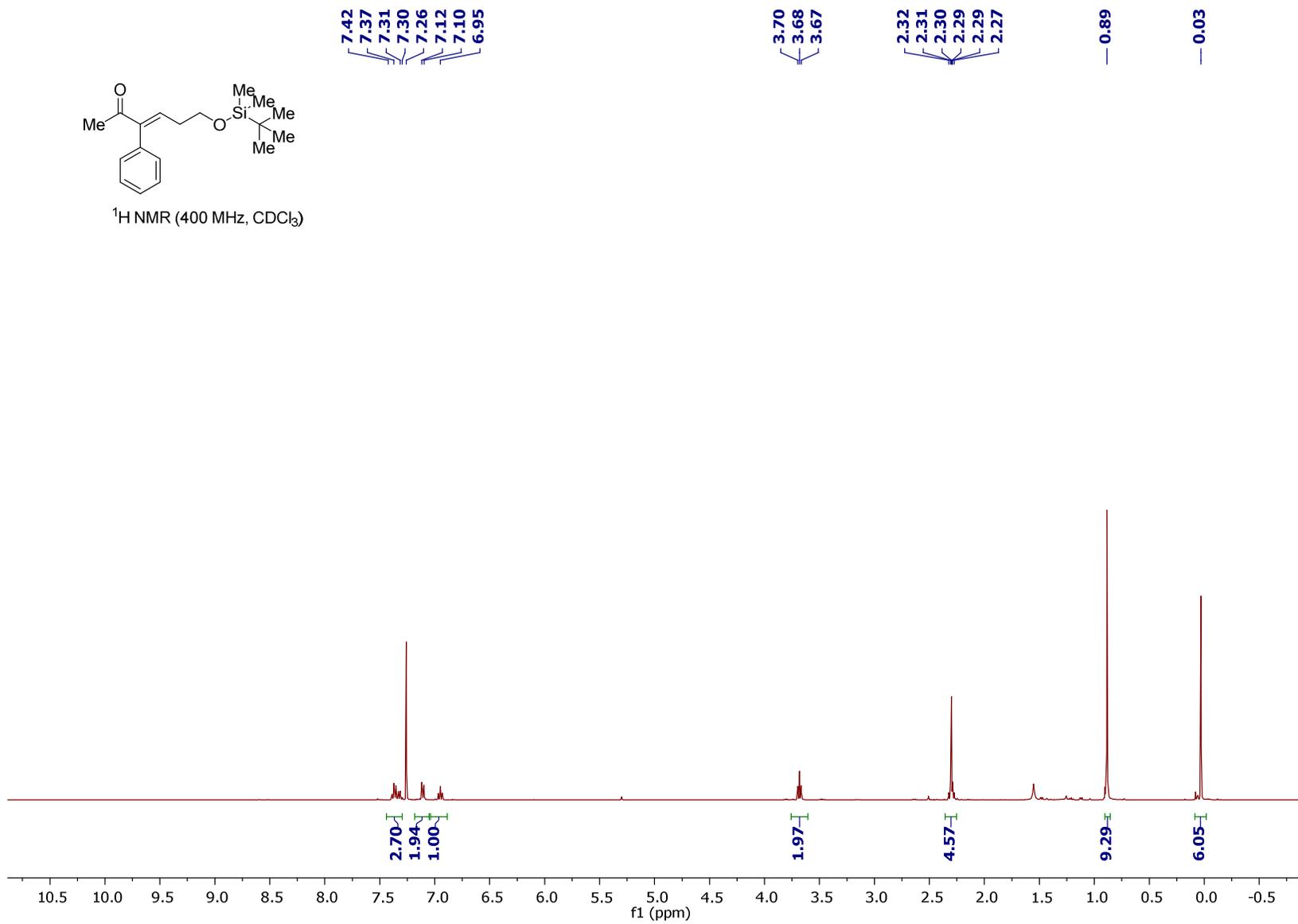
**4d**

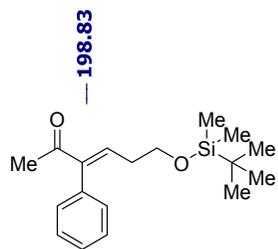
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



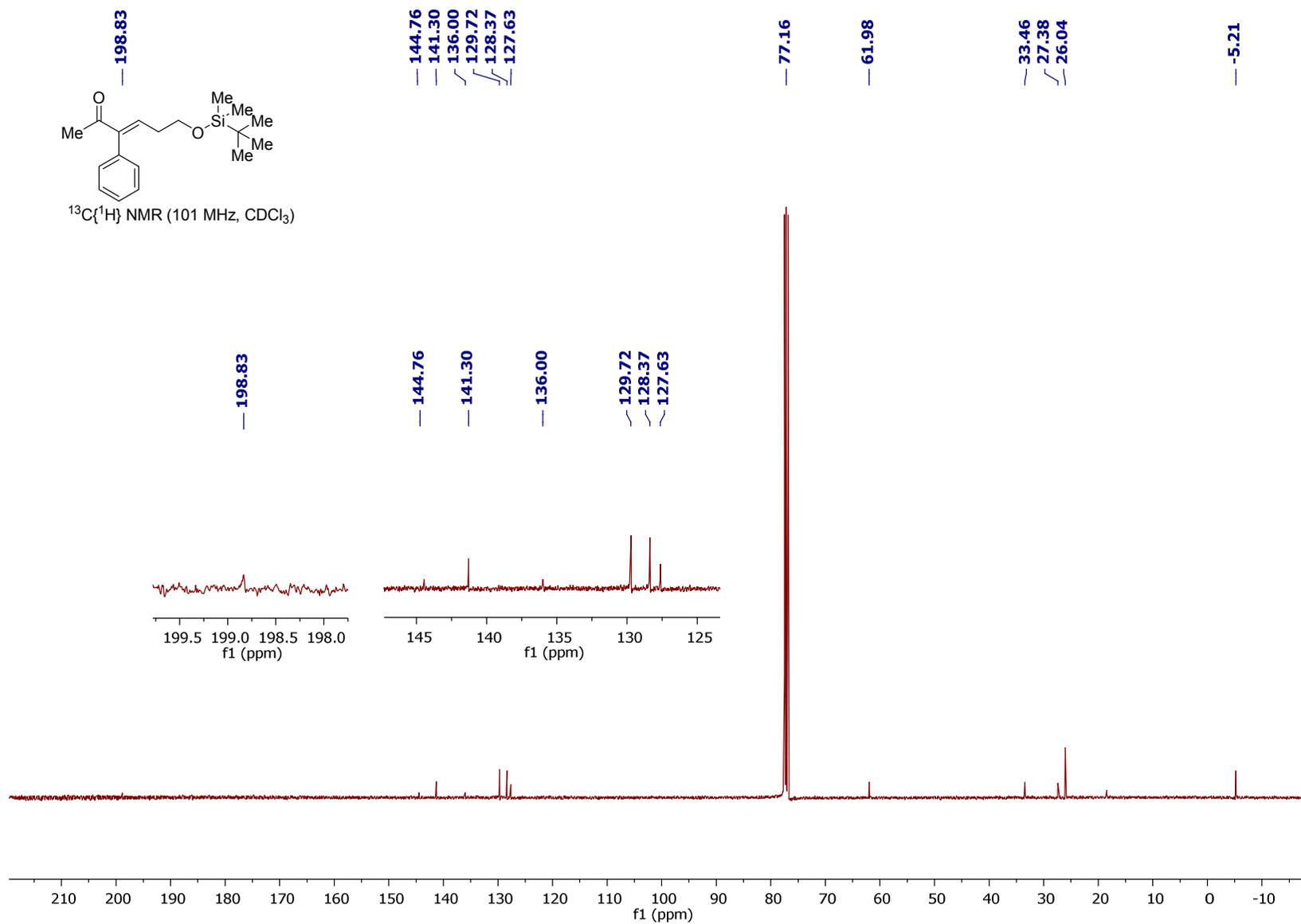


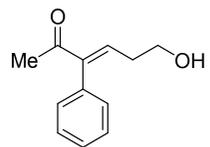
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)





$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





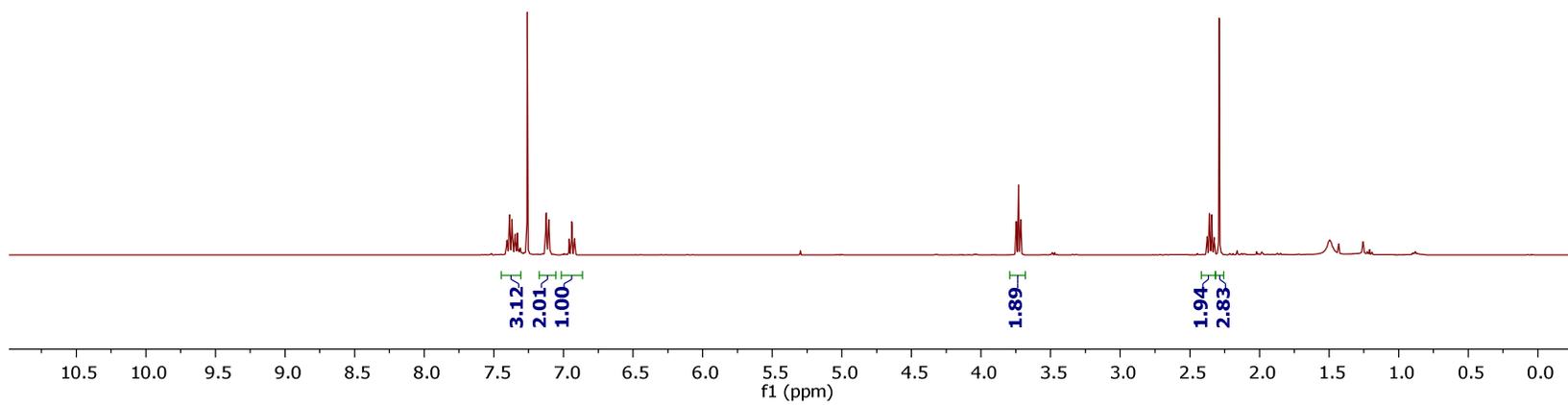
**4e**

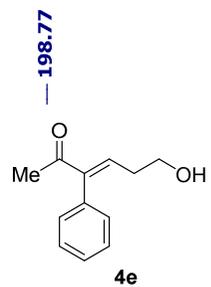
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

7.39  
7.37  
7.35  
7.26  
7.12  
7.11  
6.94

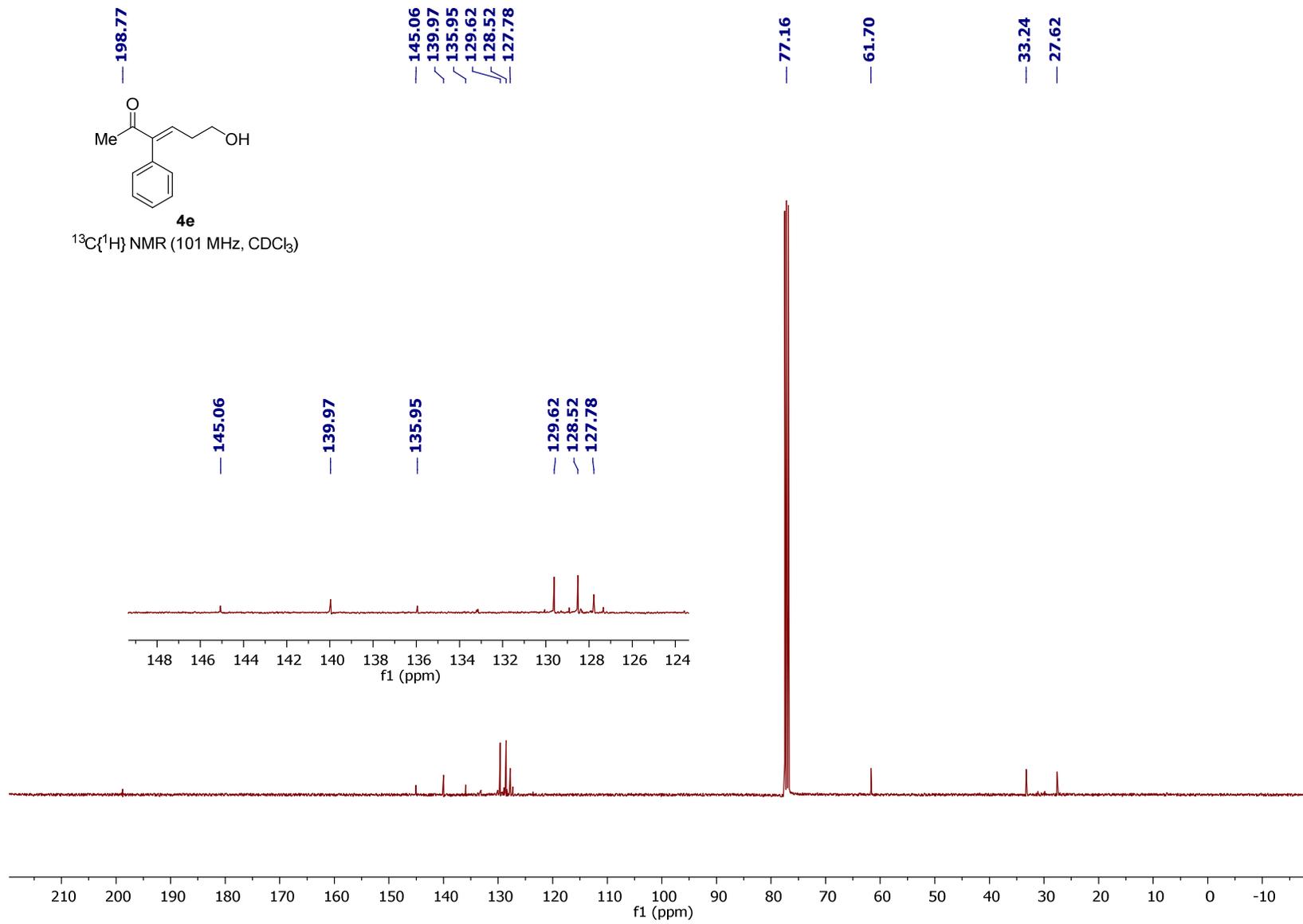
3.75  
3.73  
3.72

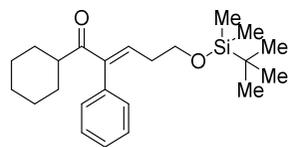
2.36  
2.34  
2.29



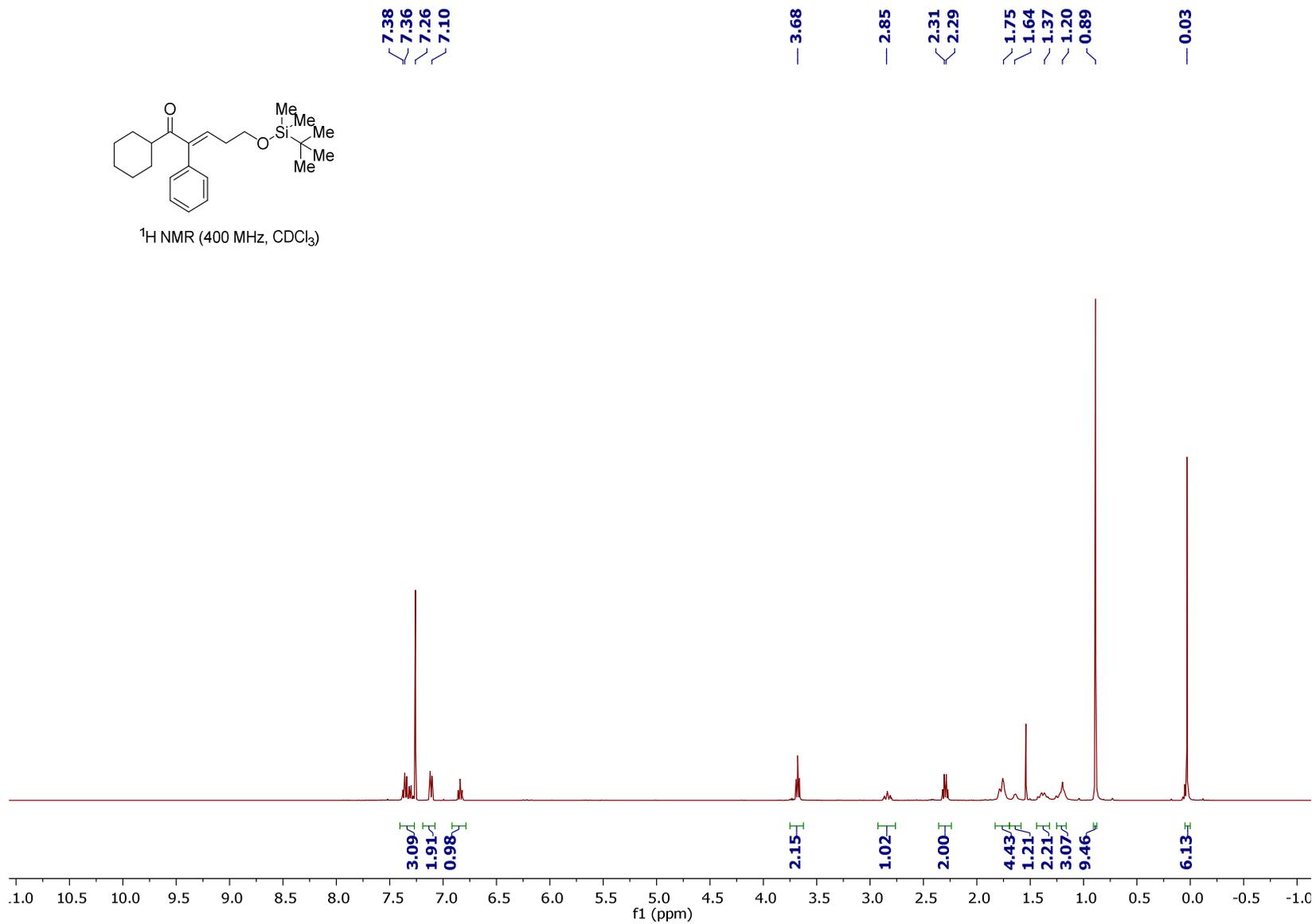


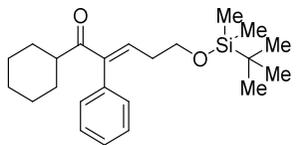
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



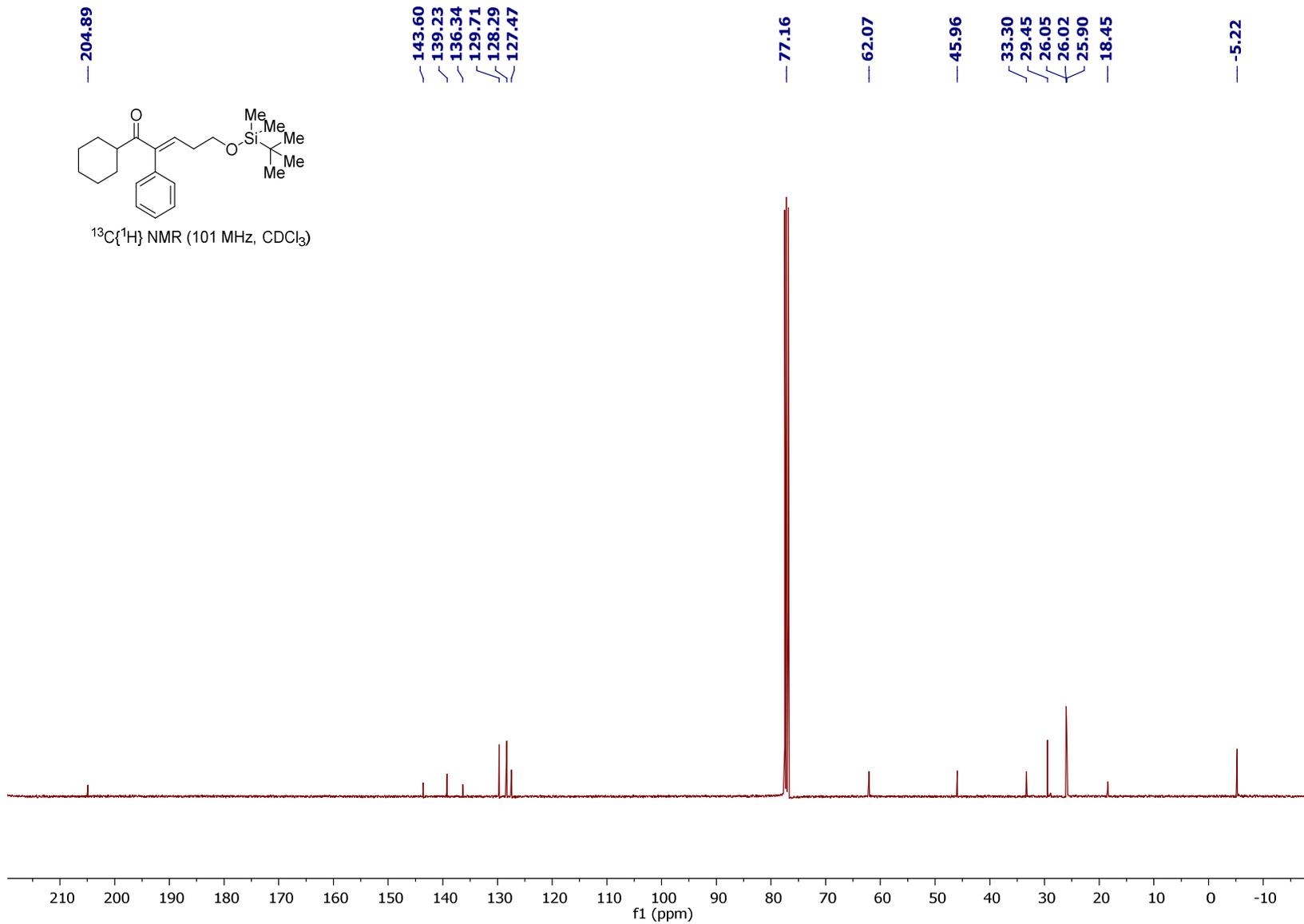


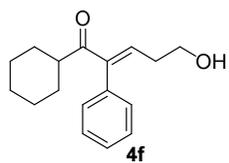
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



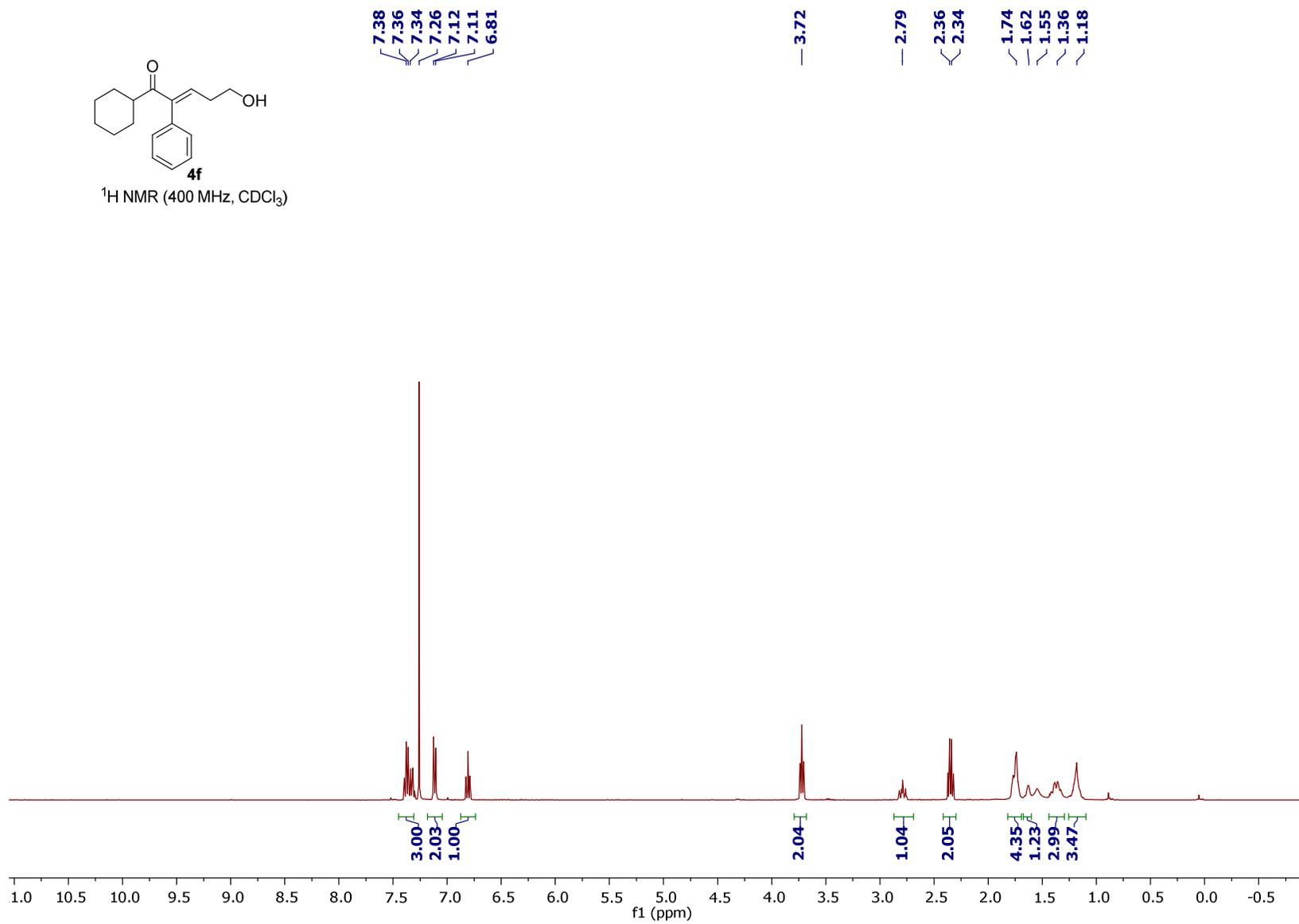


$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



— 204.95

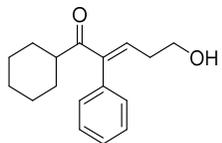
— 144.40  
— 137.98  
— 136.23  
— 129.59  
— 128.45  
— 127.64

— 77.16

— 61.78

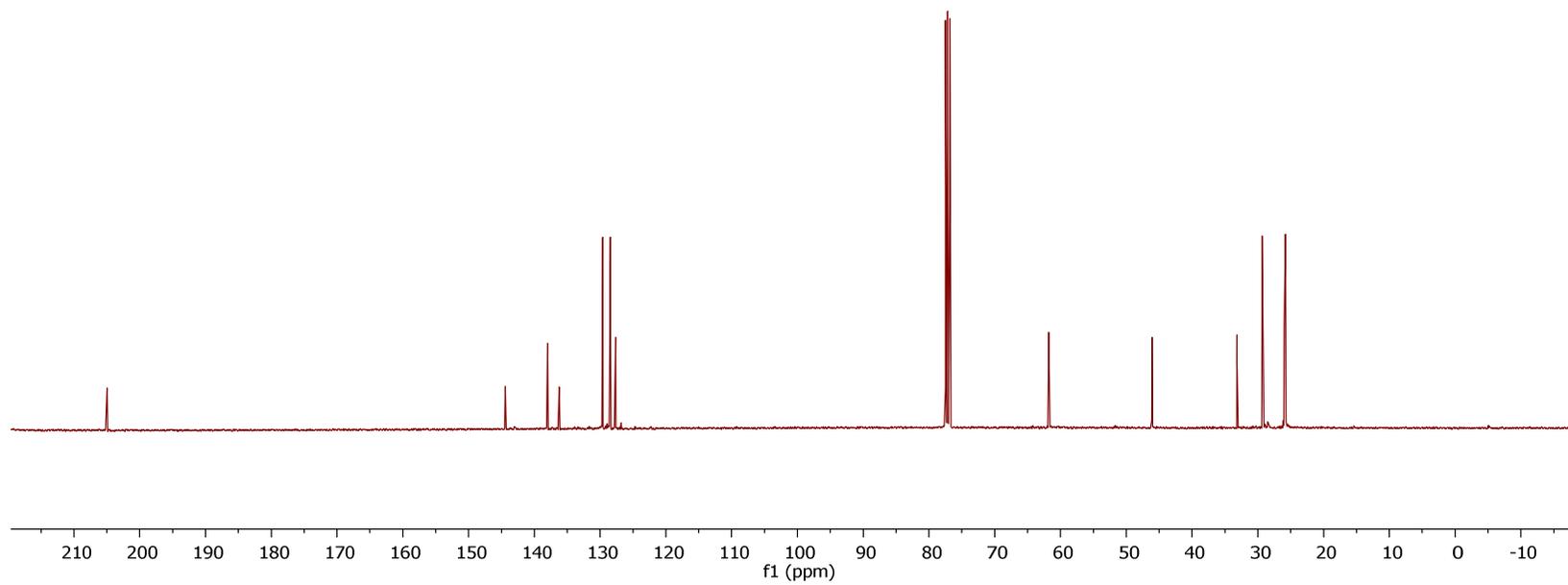
— 46.09

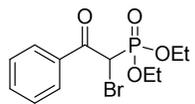
— 33.16  
— 29.32  
— 25.97  
— 25.81



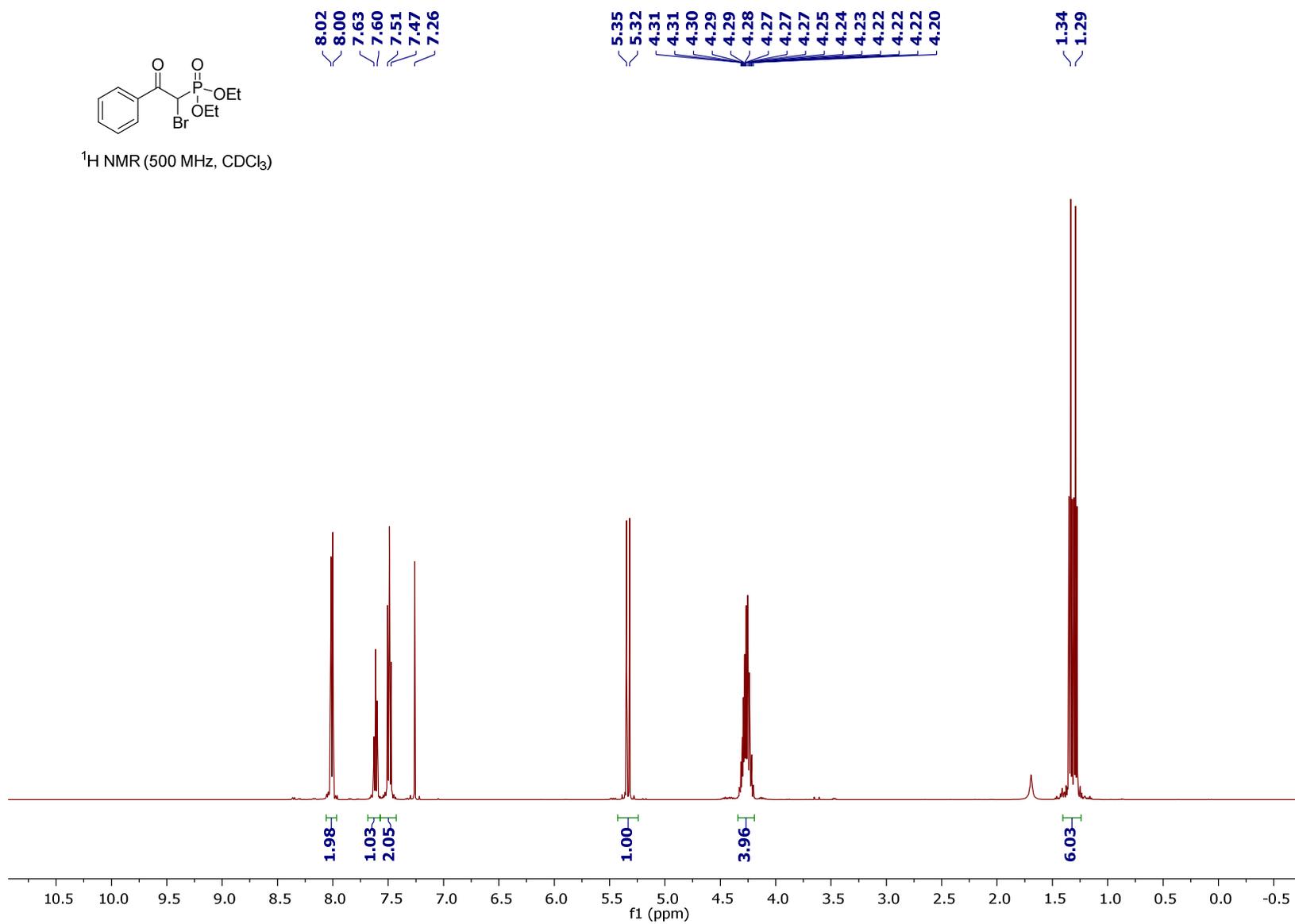
**4f**

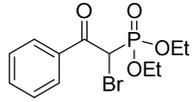
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



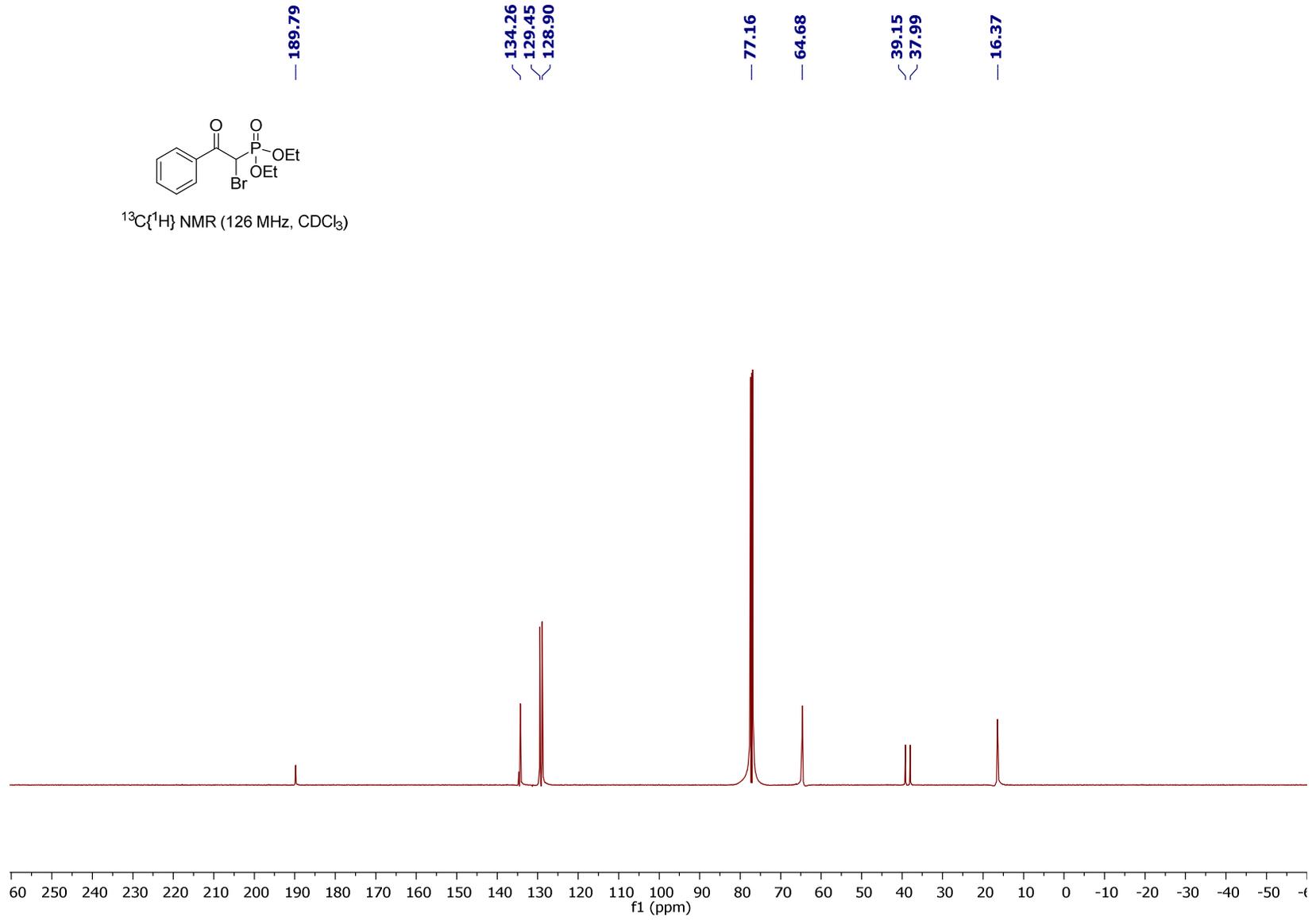


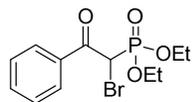
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )





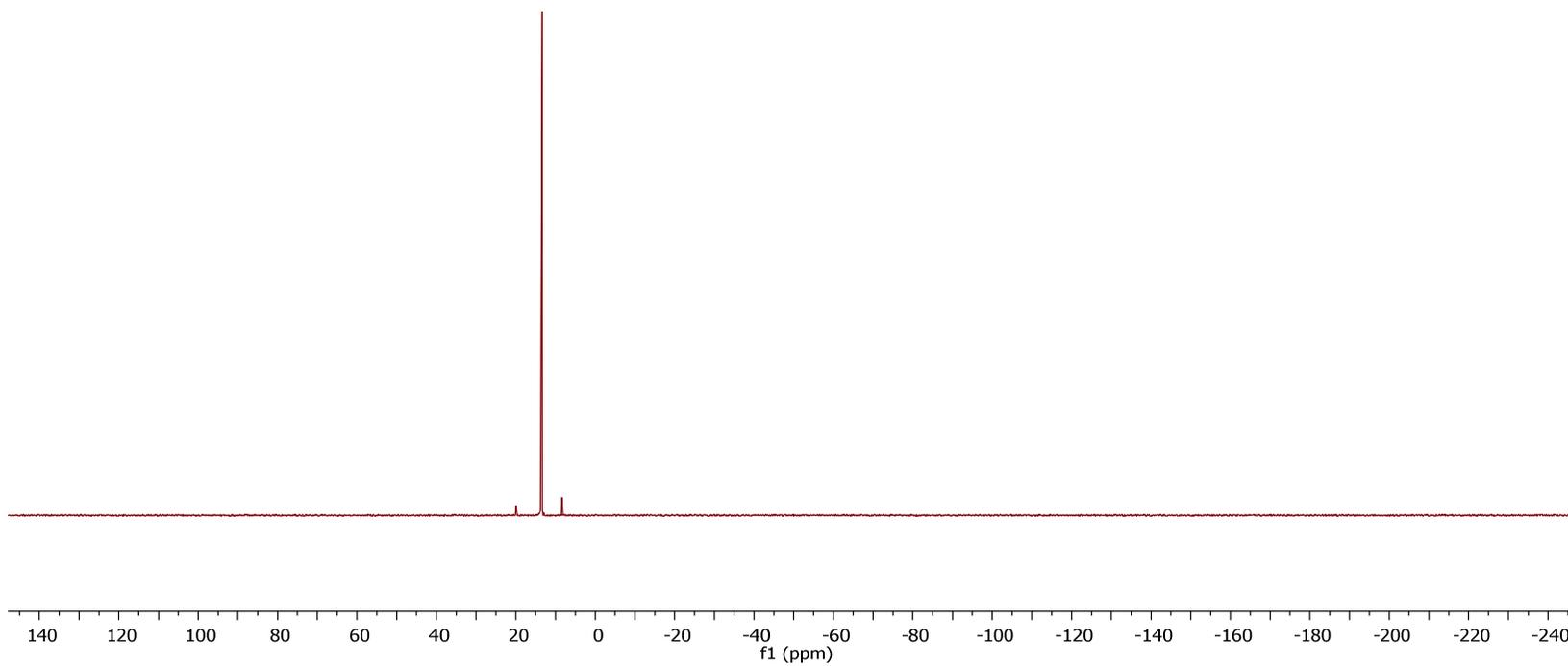
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

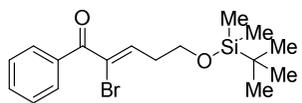




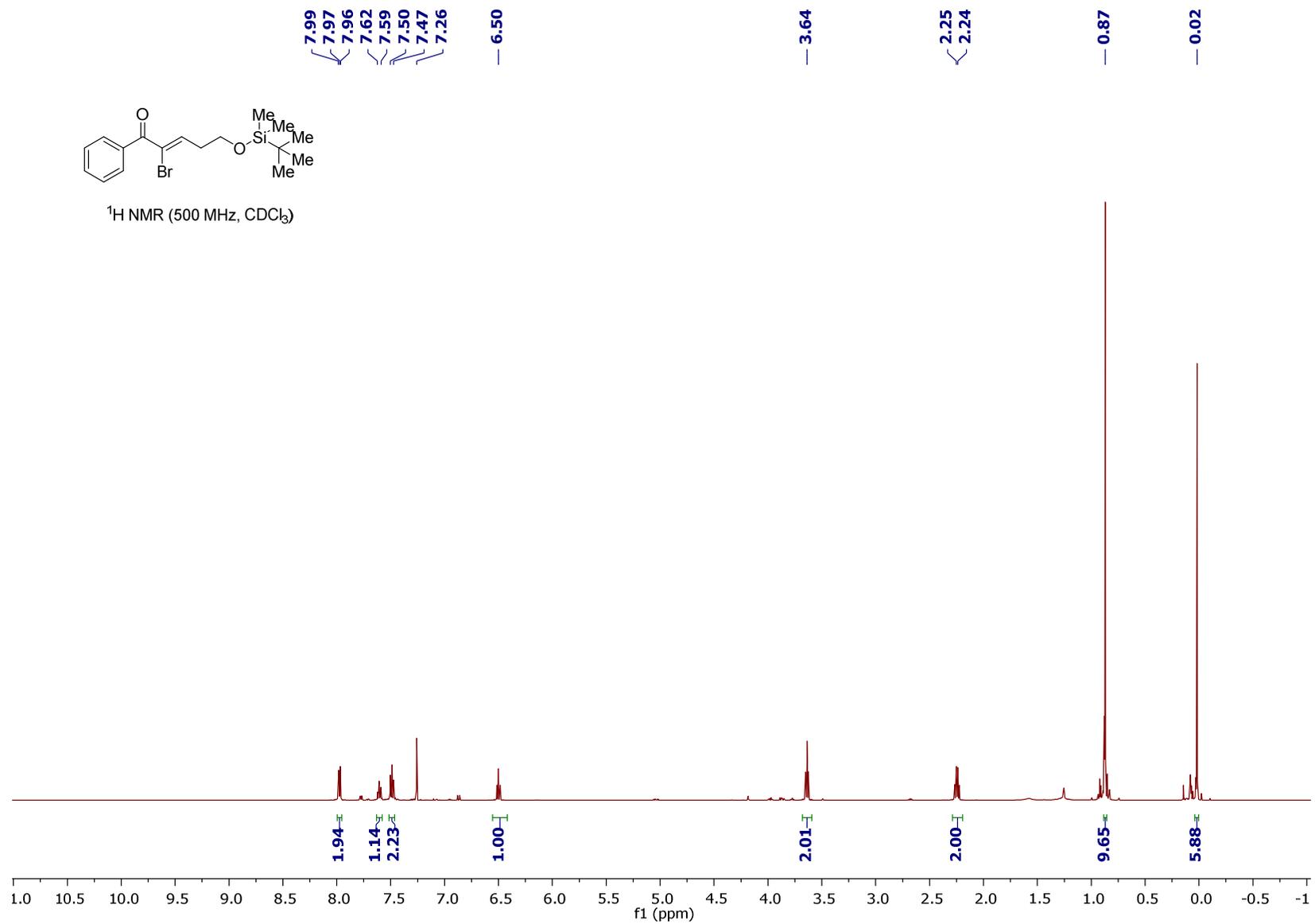
$^{31}\text{P}\{^1\text{H},^{13}\text{C}\}$  NMR (162 MHz,  $\text{CDCl}_3$ )

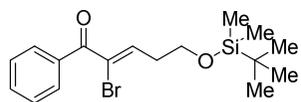
— 13.37



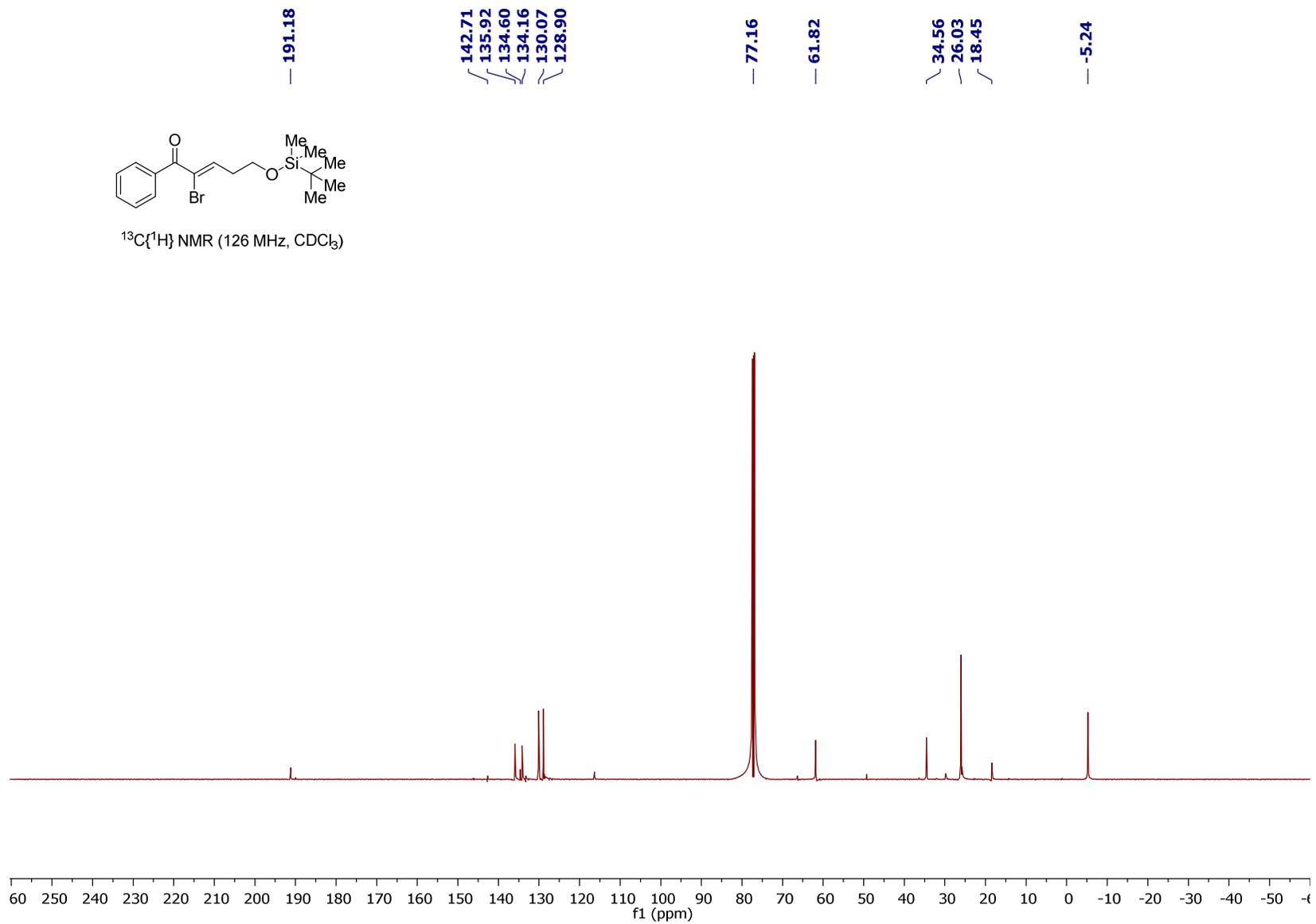


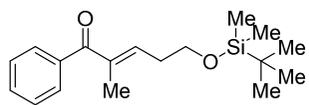
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



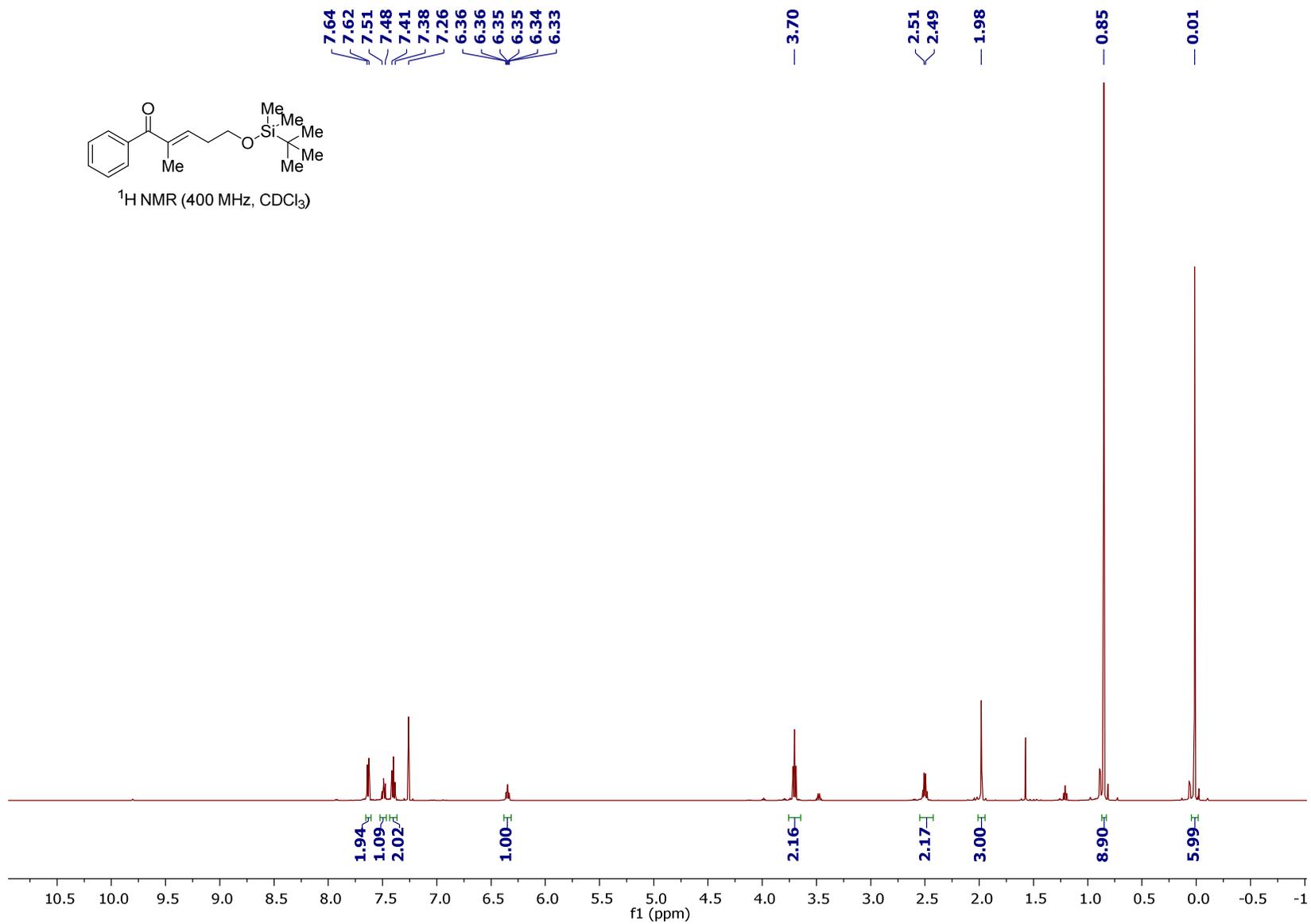


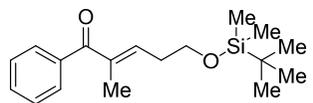
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )





<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)





$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

— 199.09

143.55  
138.80  
137.82  
131.45  
129.44  
128.15

— 77.16

— 61.72

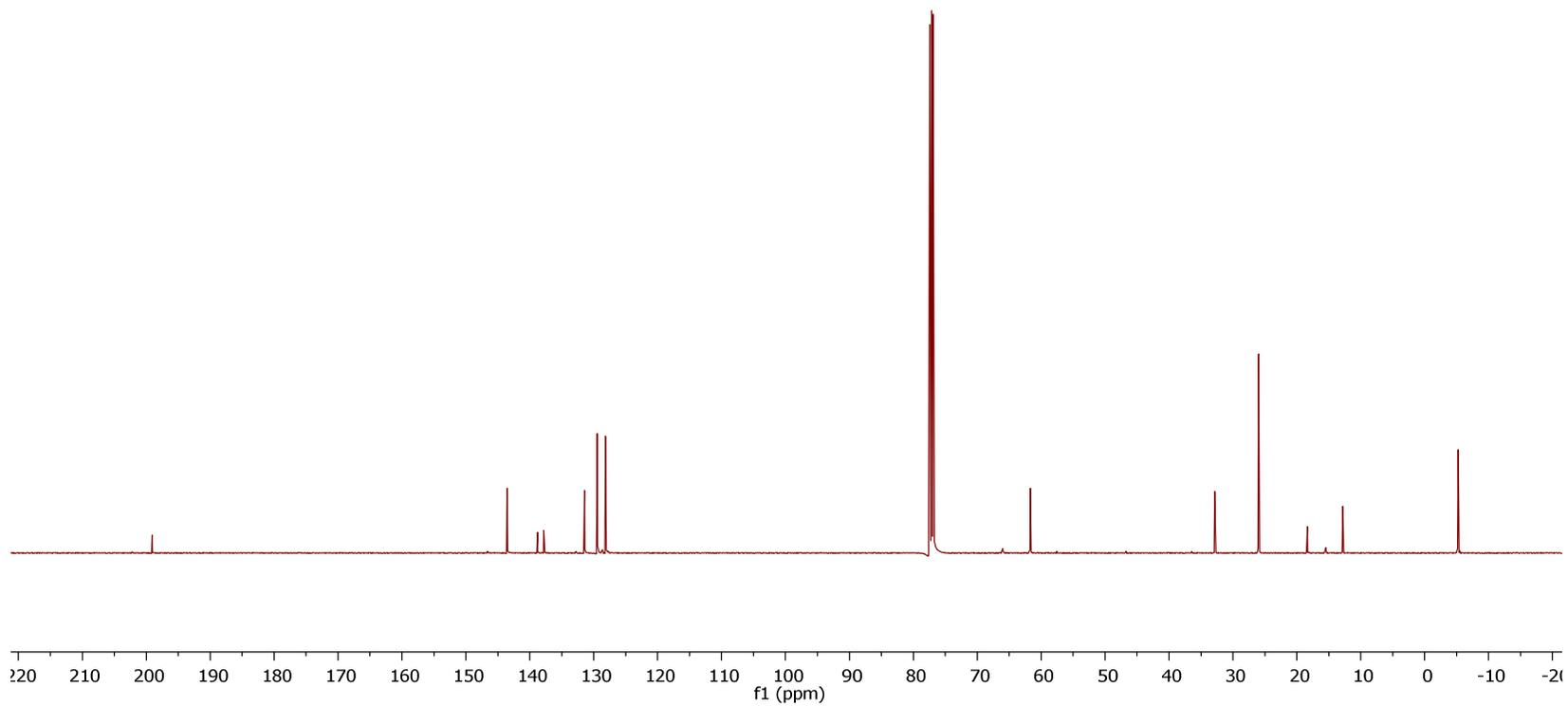
— 32.84

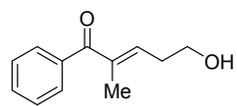
— 25.98

— 18.36

— 12.81

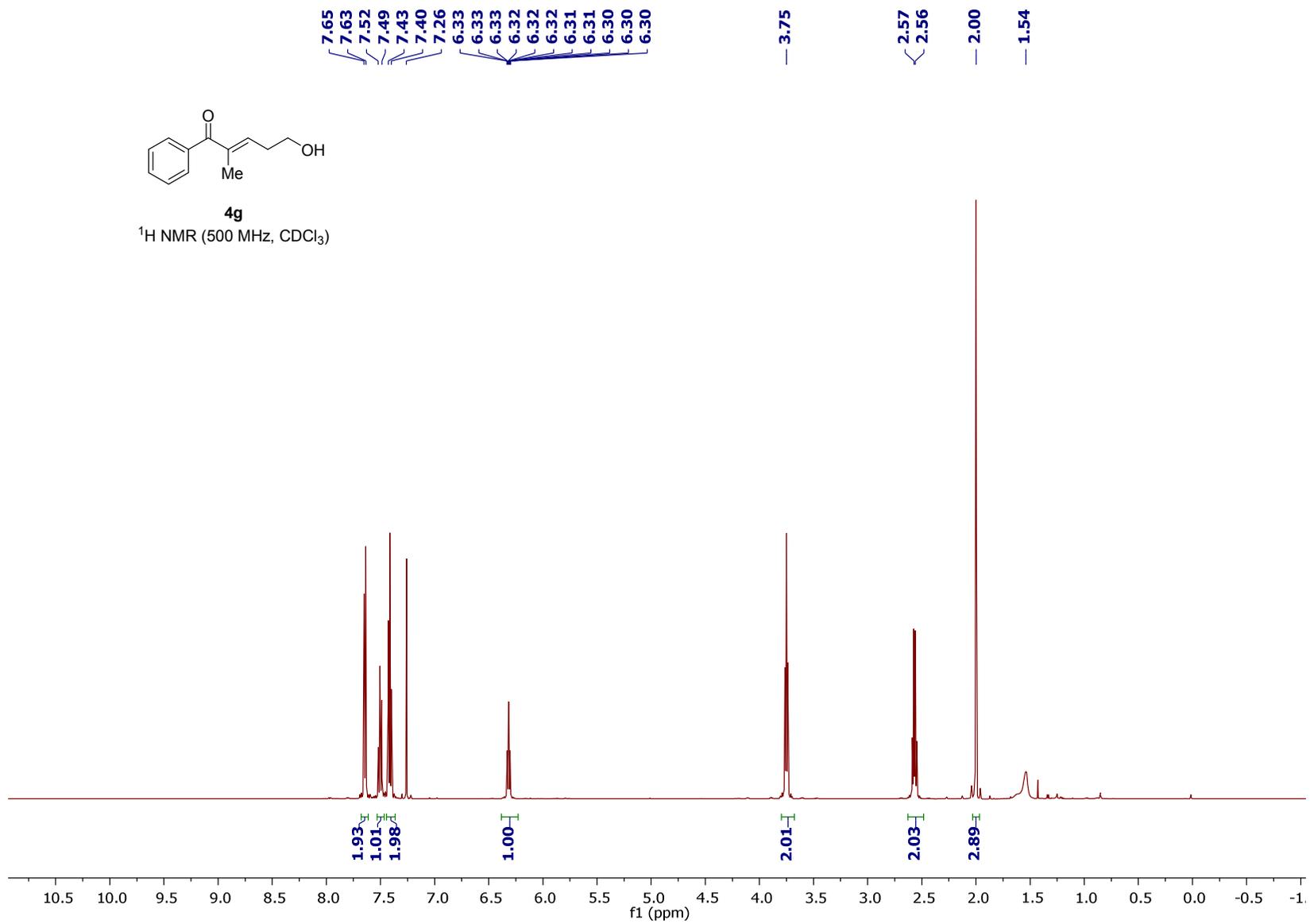
— -5.25

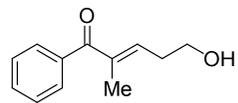




**4g**

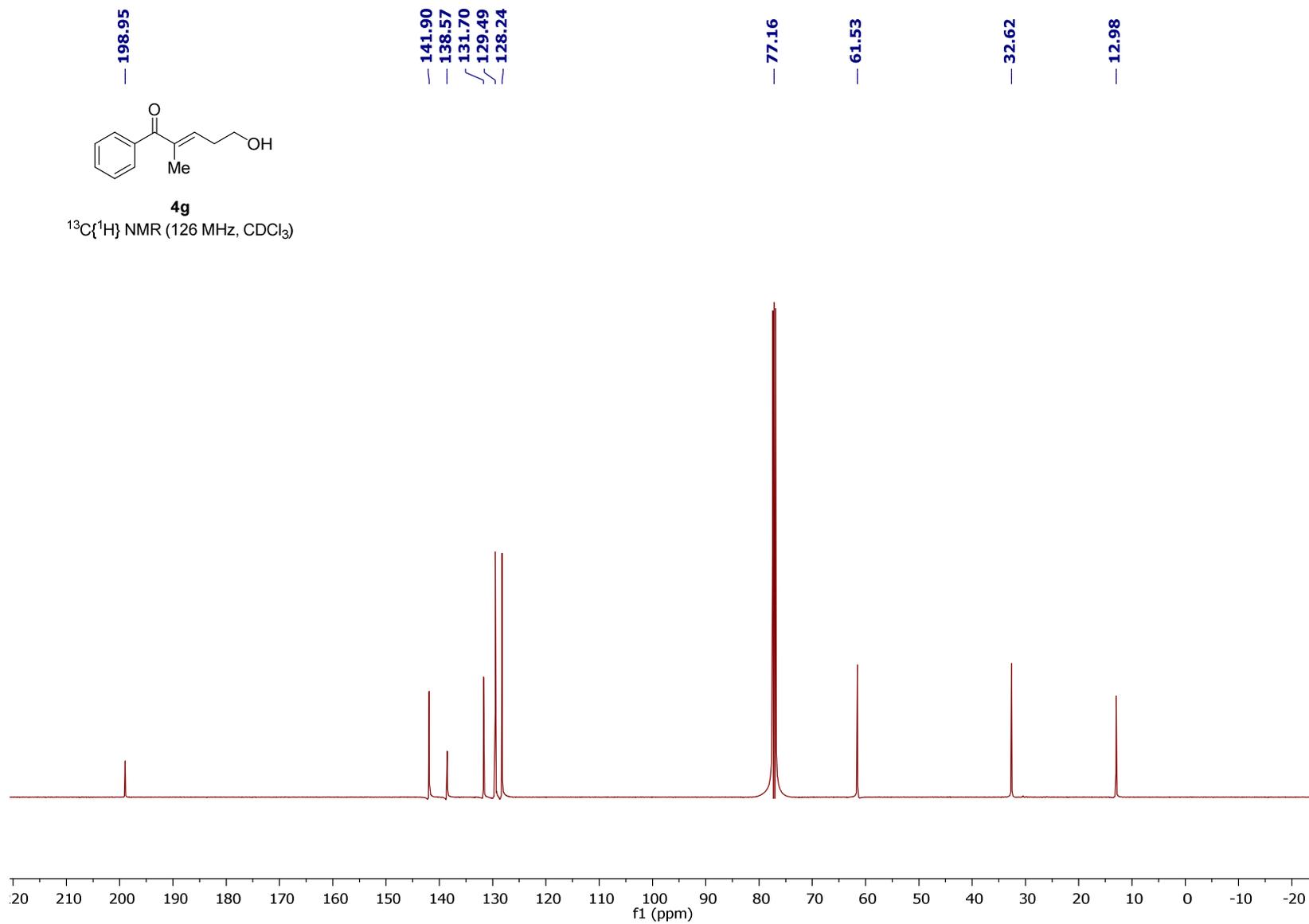
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

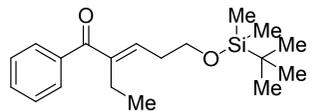




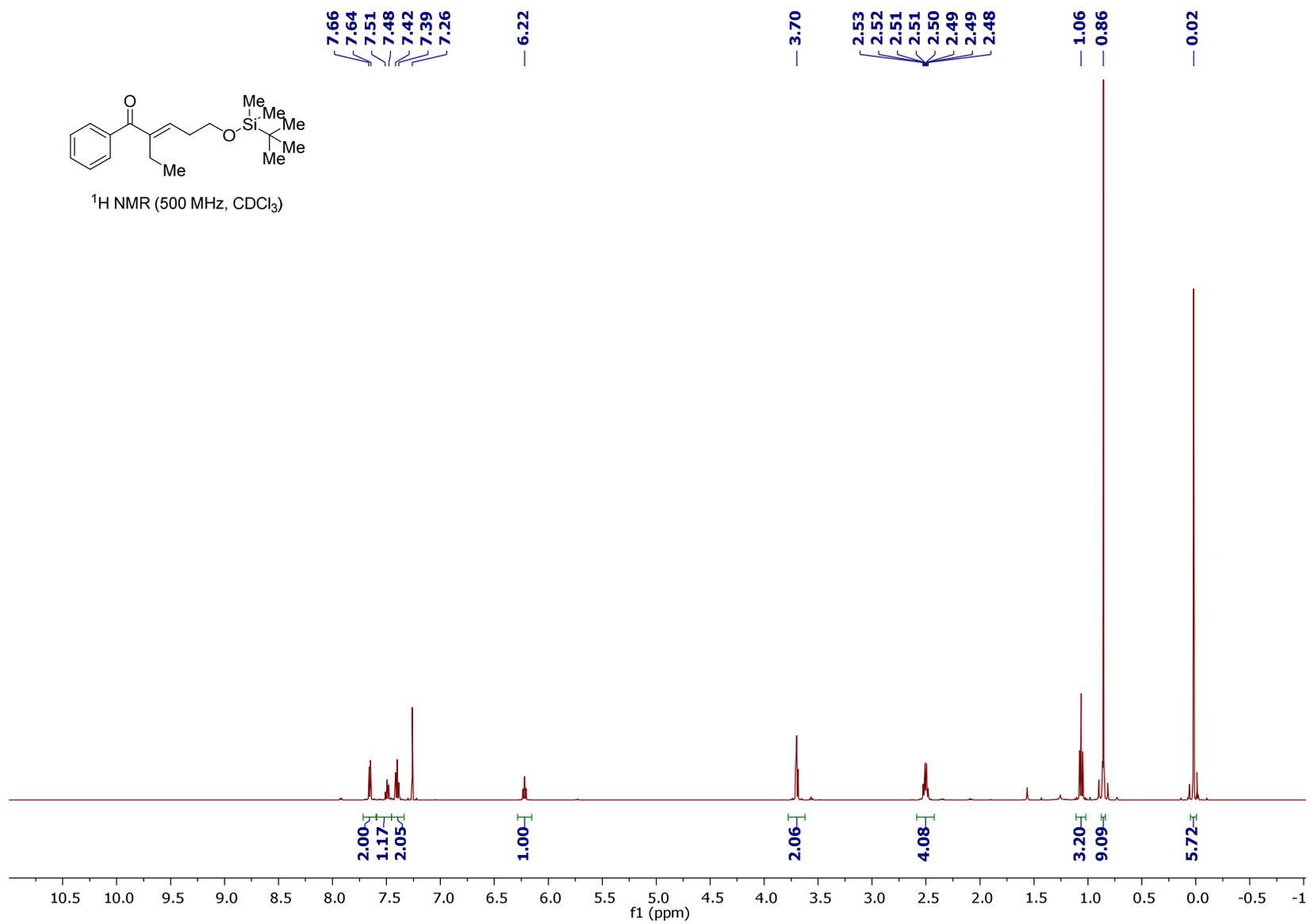
**4g**

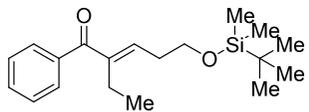
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )



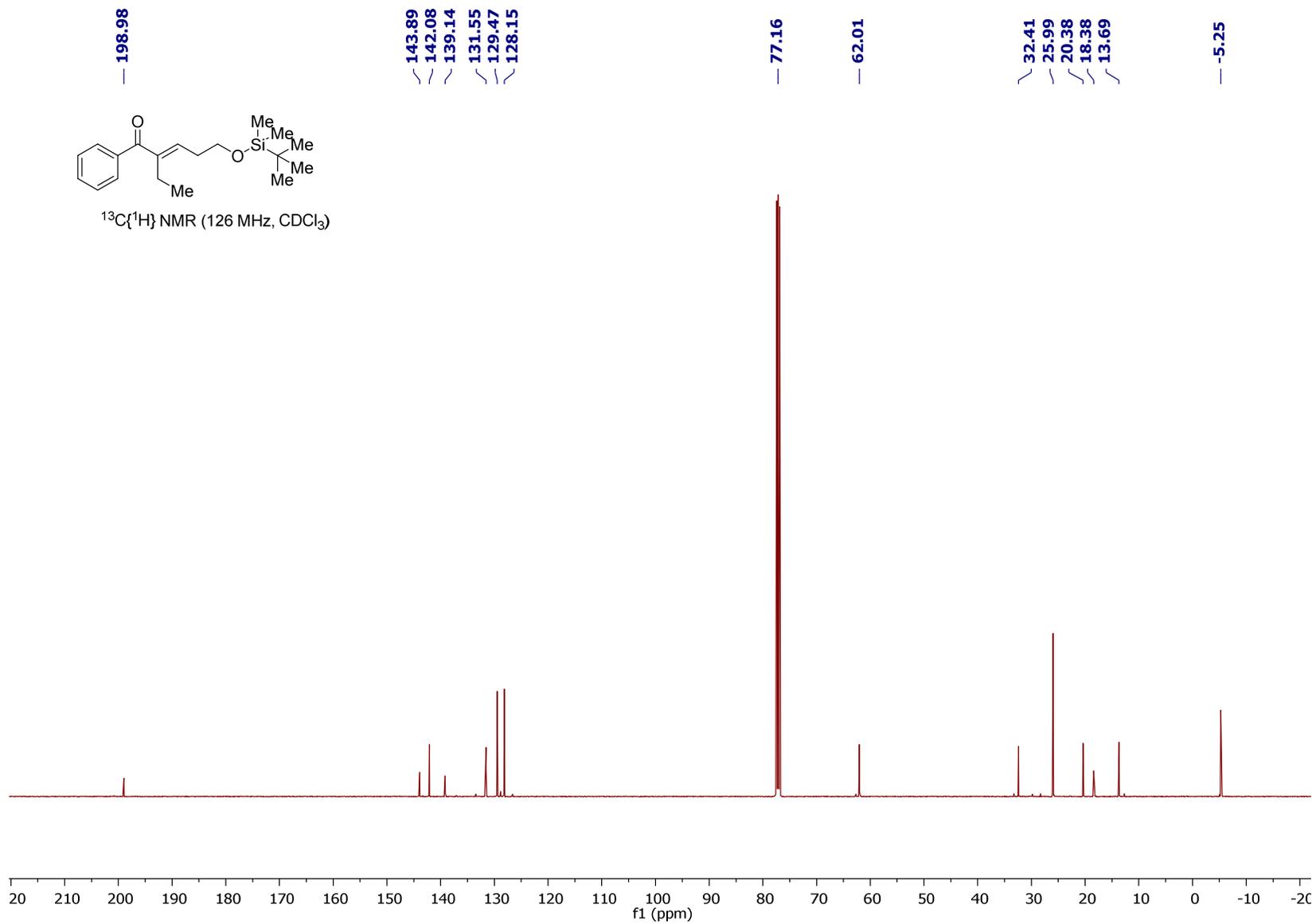


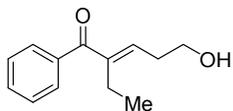
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )





**4h**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

7.67  
7.65  
7.52  
7.49  
7.43  
7.40  
7.26

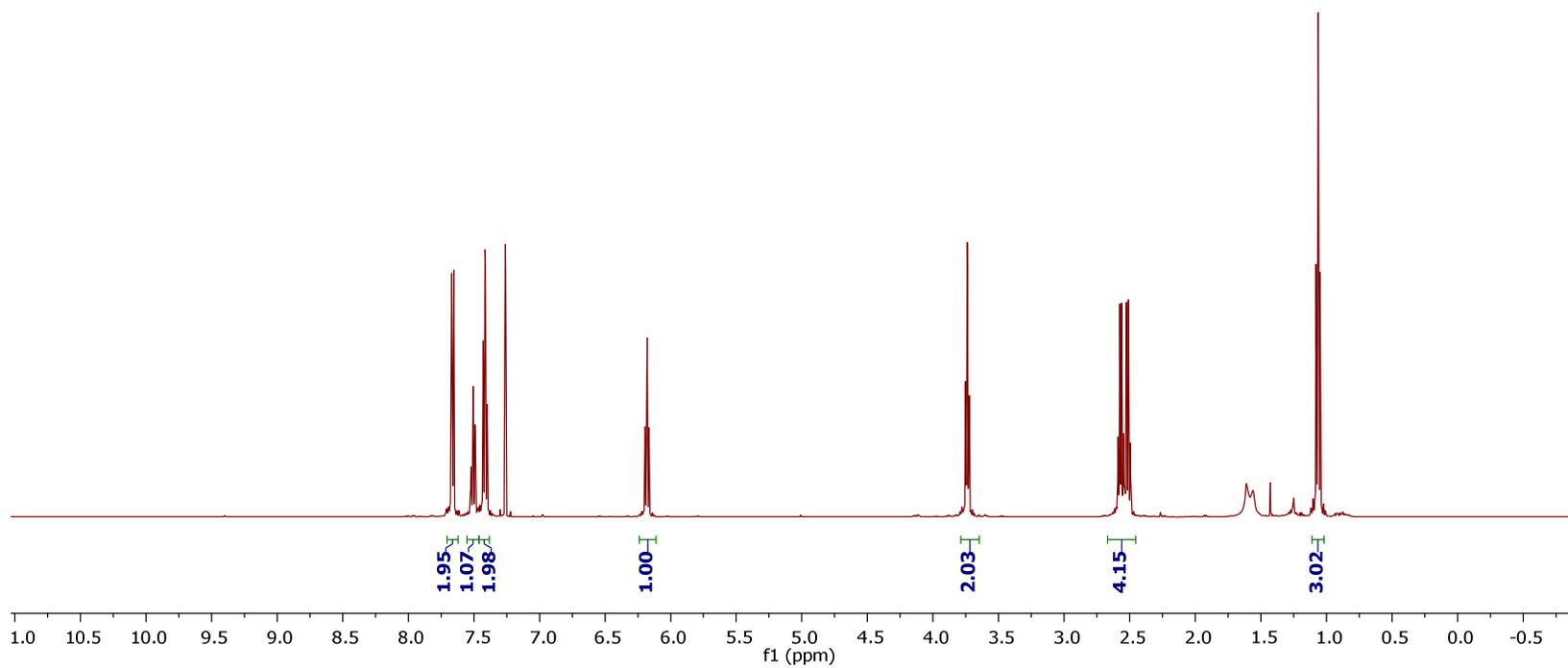
— 6.18

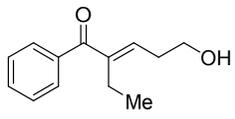
— 3.74

2.58  
2.56  
2.53  
2.51

1.61  
1.56

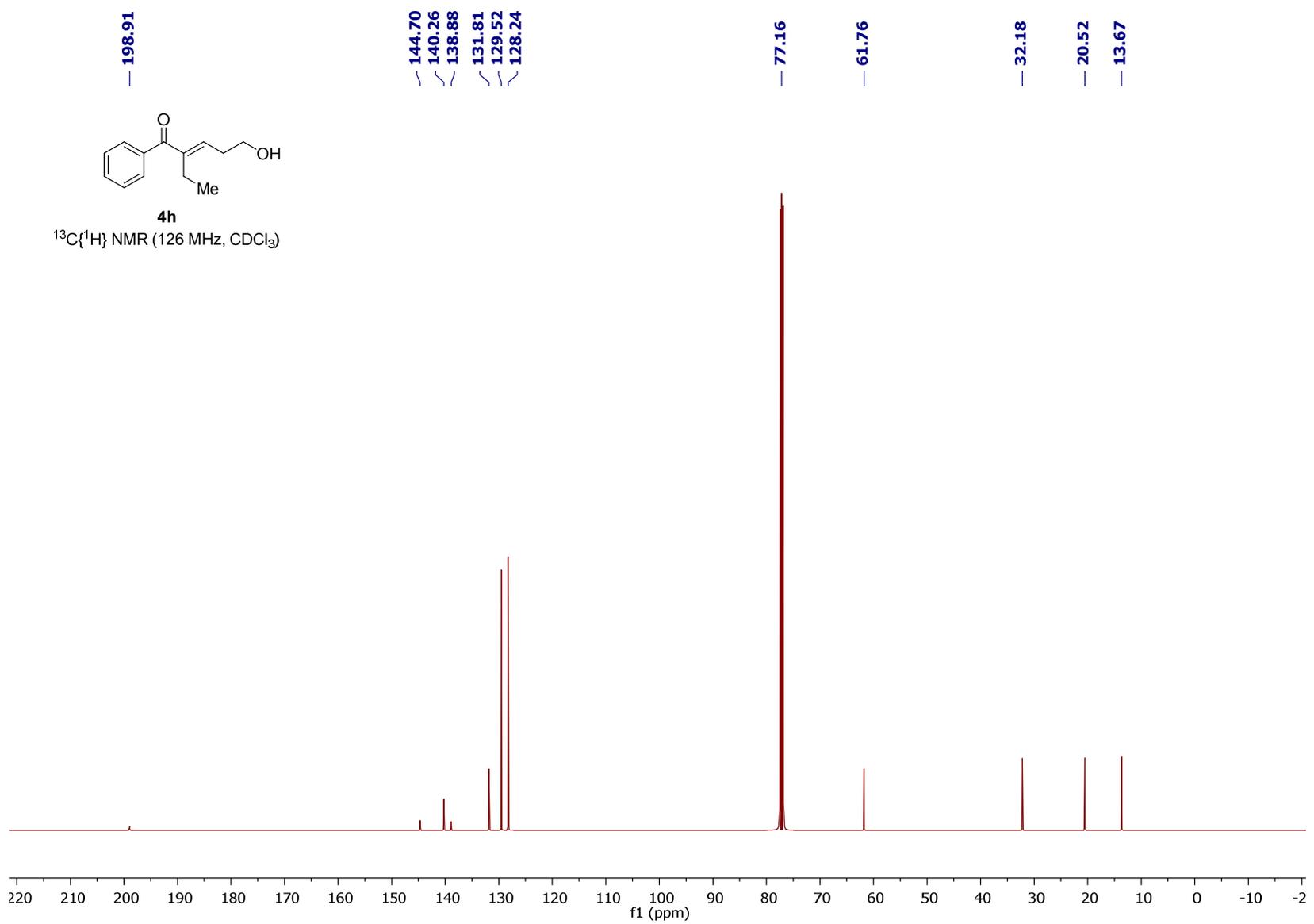
— 1.06

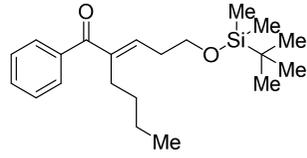




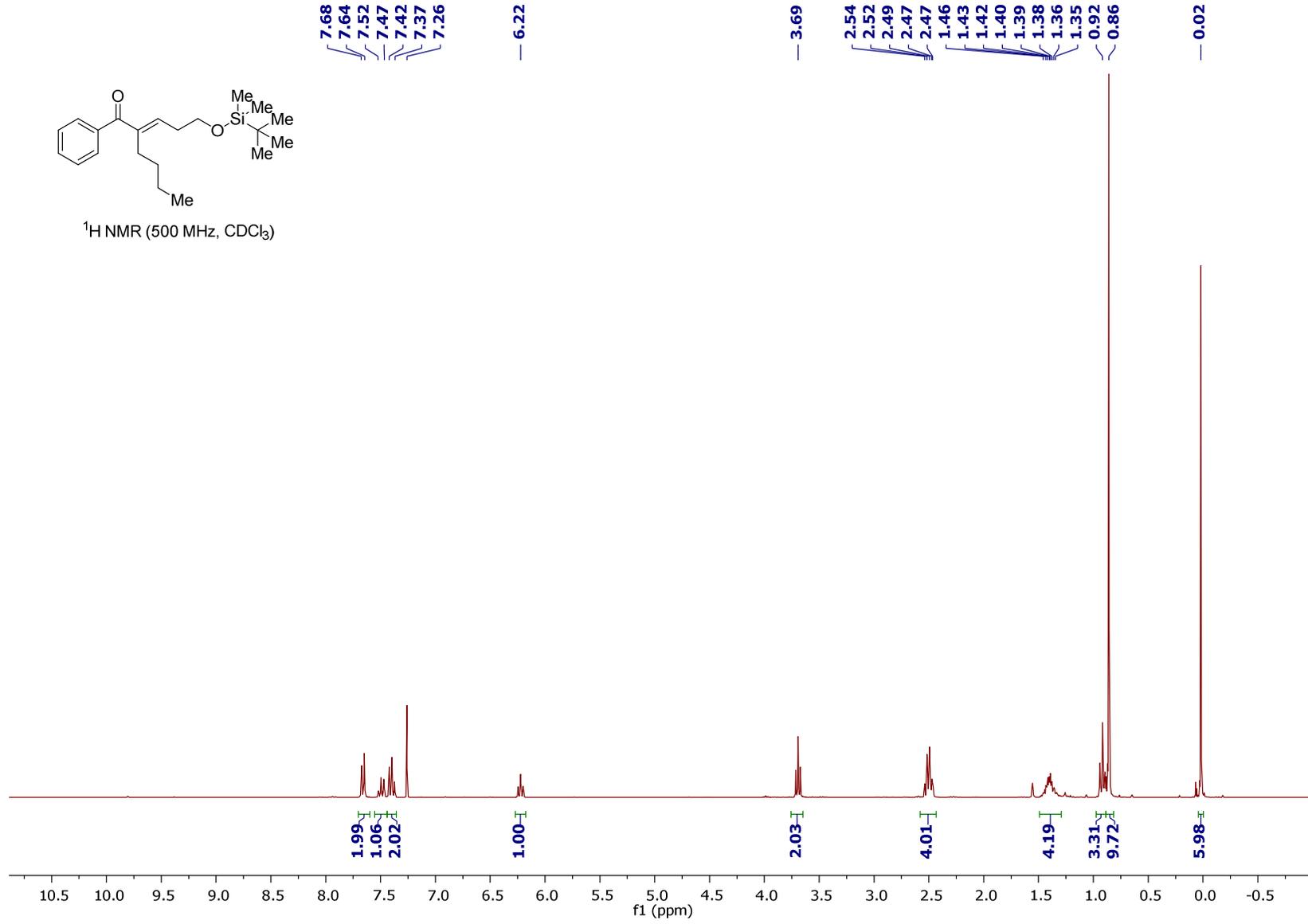
**4h**

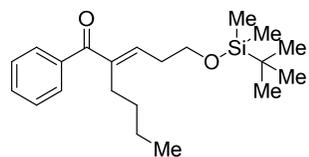
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )



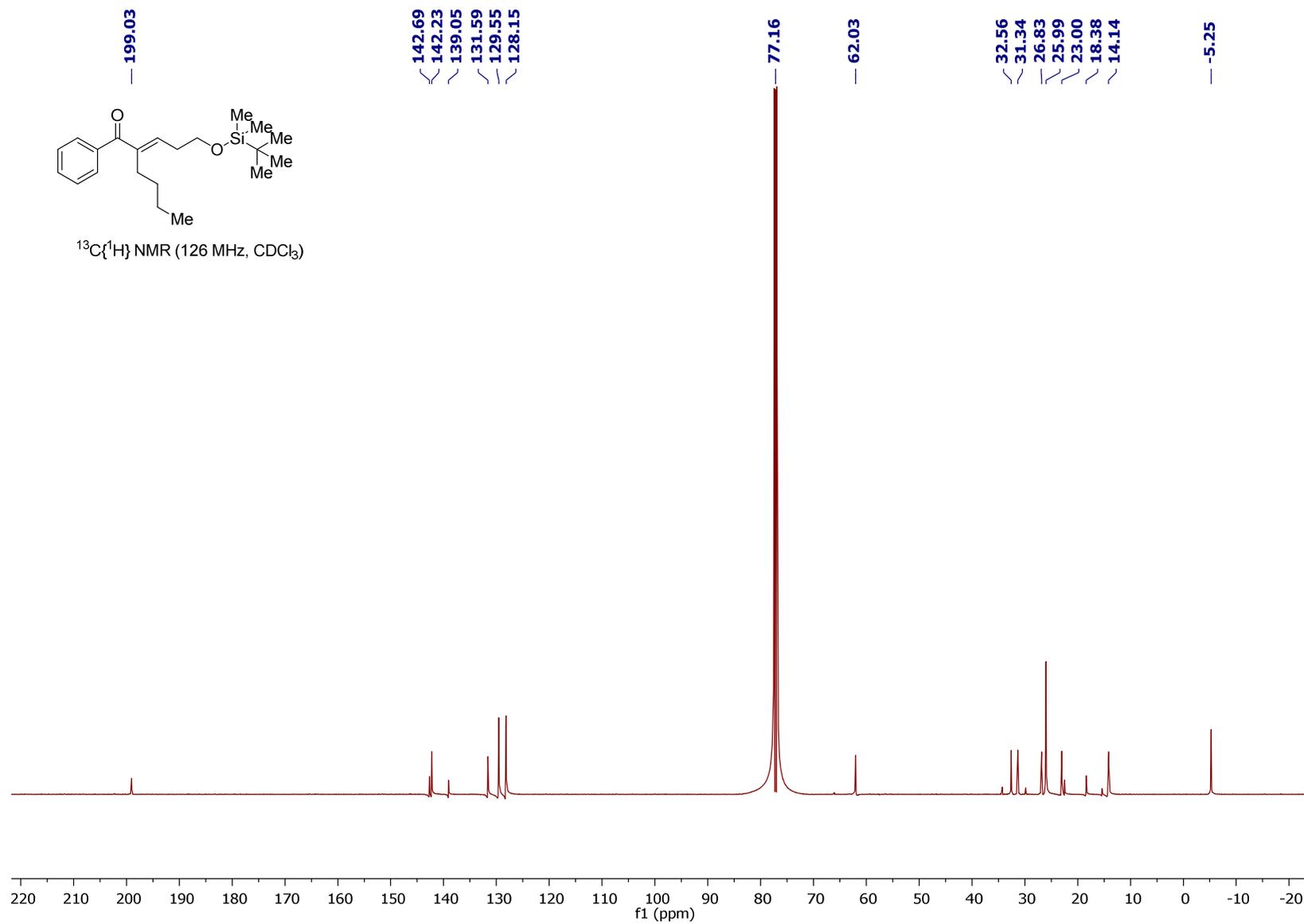


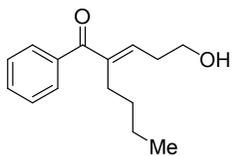
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )





**4i**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

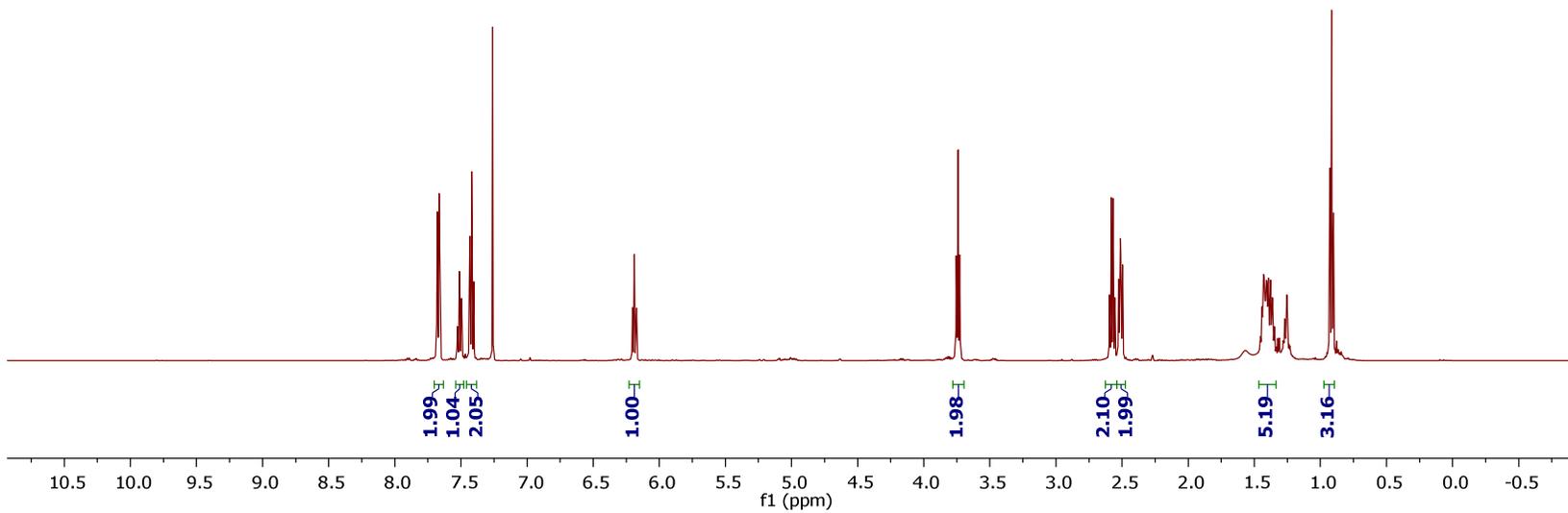
7.68  
7.66  
7.53  
7.50  
7.43  
7.40  
7.26

6.20  
6.19  
6.17

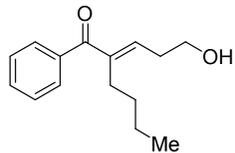
3.75  
3.74  
3.73

2.59  
2.58  
2.57  
2.55  
2.53  
2.50

1.45  
1.35  
0.95  
0.94  
0.93  
0.92  
0.90



— 198.89



**4i**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

143.57  
140.34  
138.82  
131.85  
129.60  
128.26

— 77.16

— 61.81

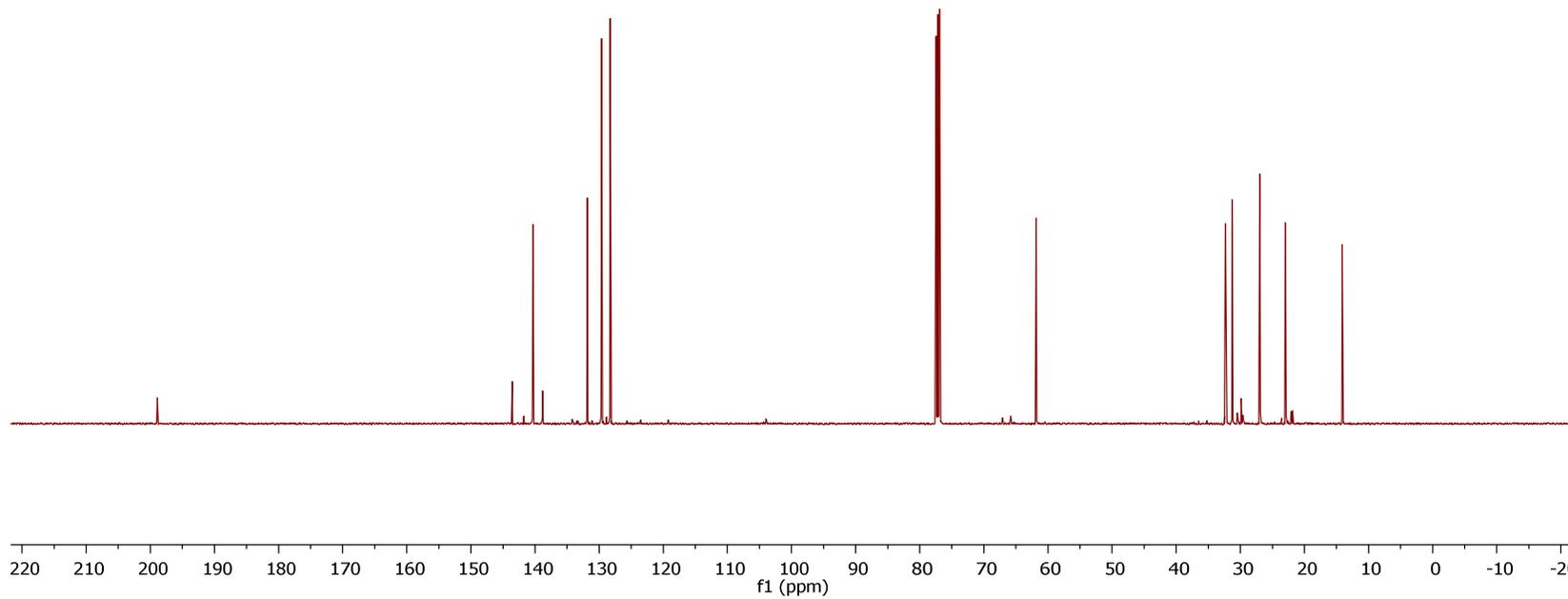
32.33

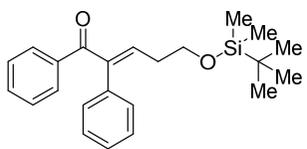
31.31

26.98

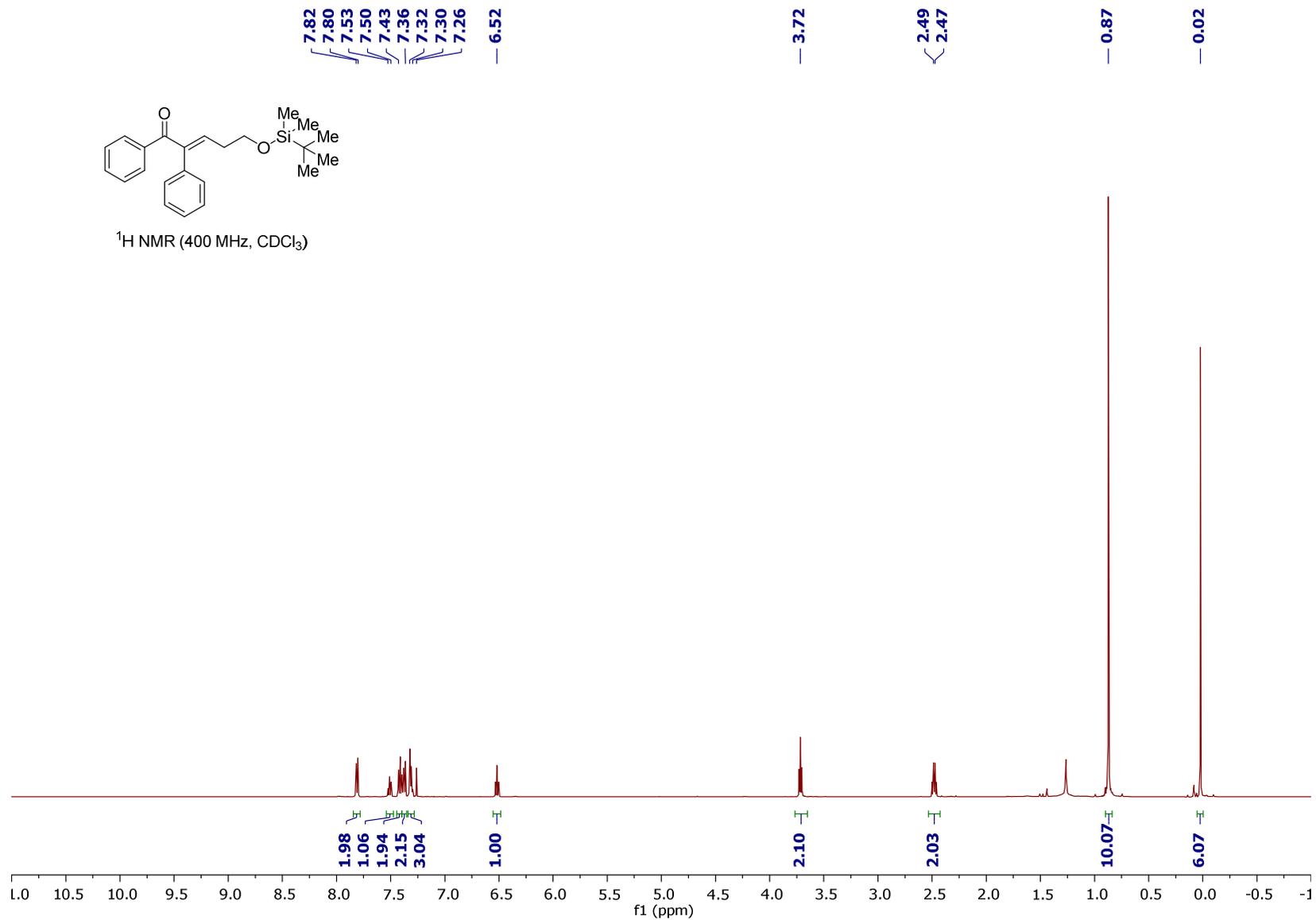
22.99

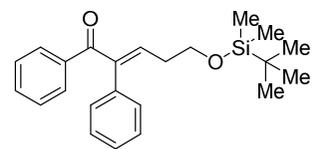
— 14.12



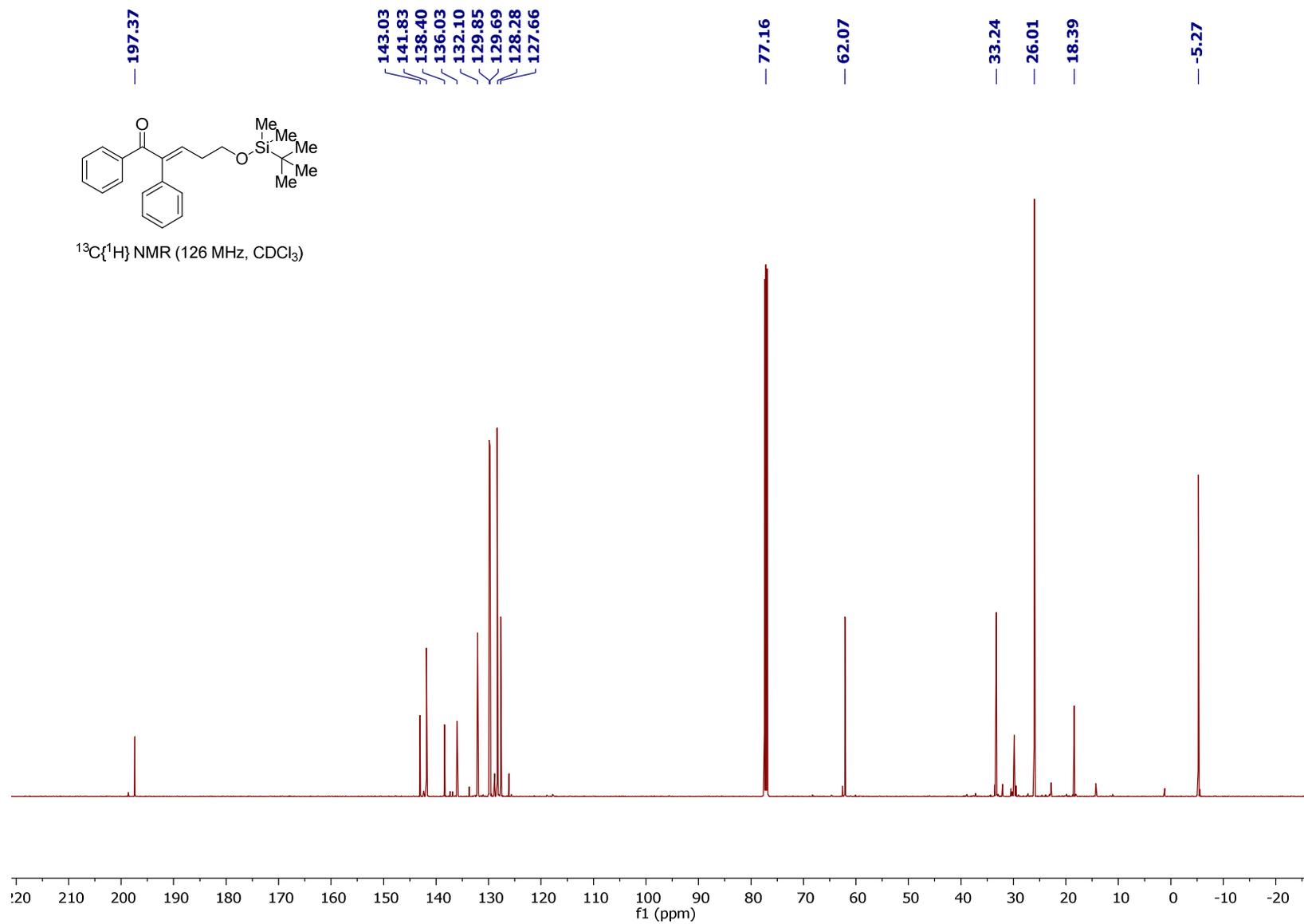


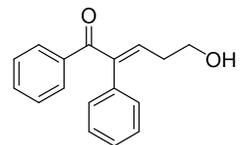
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)





$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )





**4j**

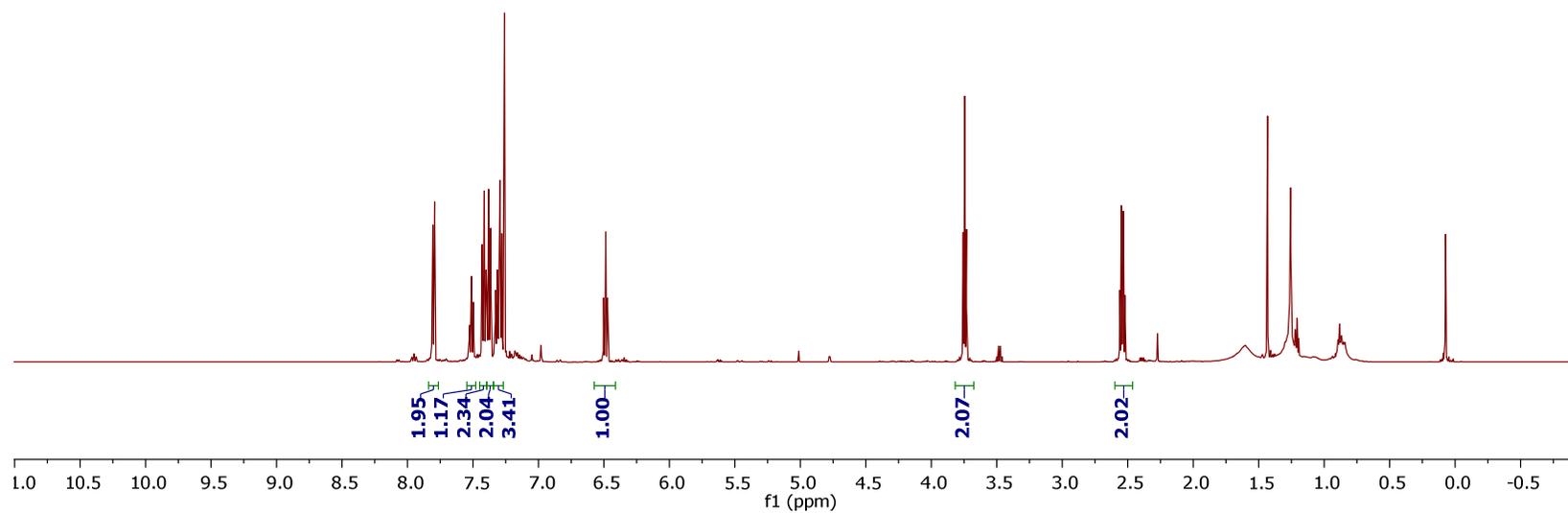
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

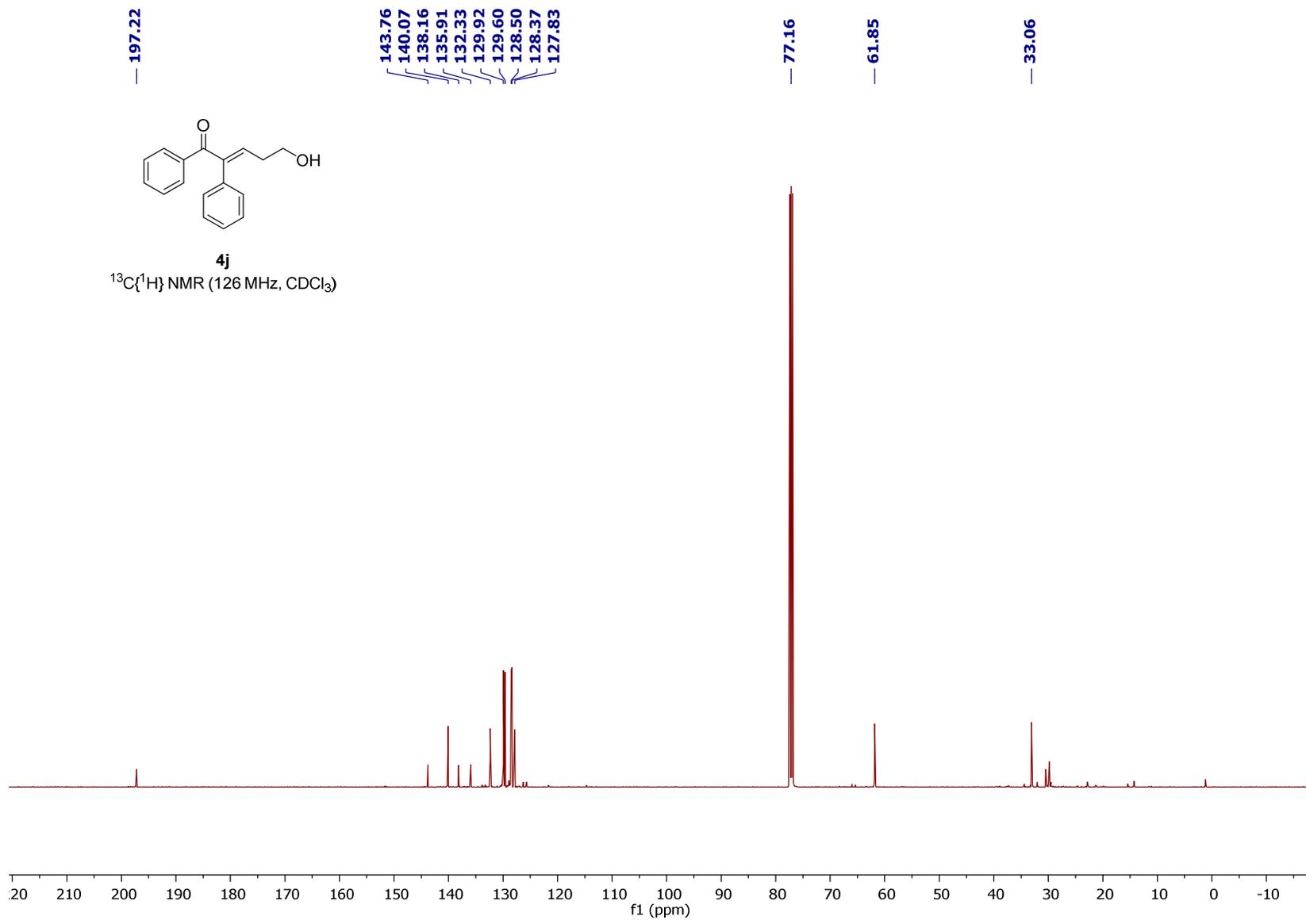
7.81  
7.79  
7.53  
7.49  
7.43  
7.40  
7.39  
7.37  
7.33  
7.28  
7.26  
— 6.49

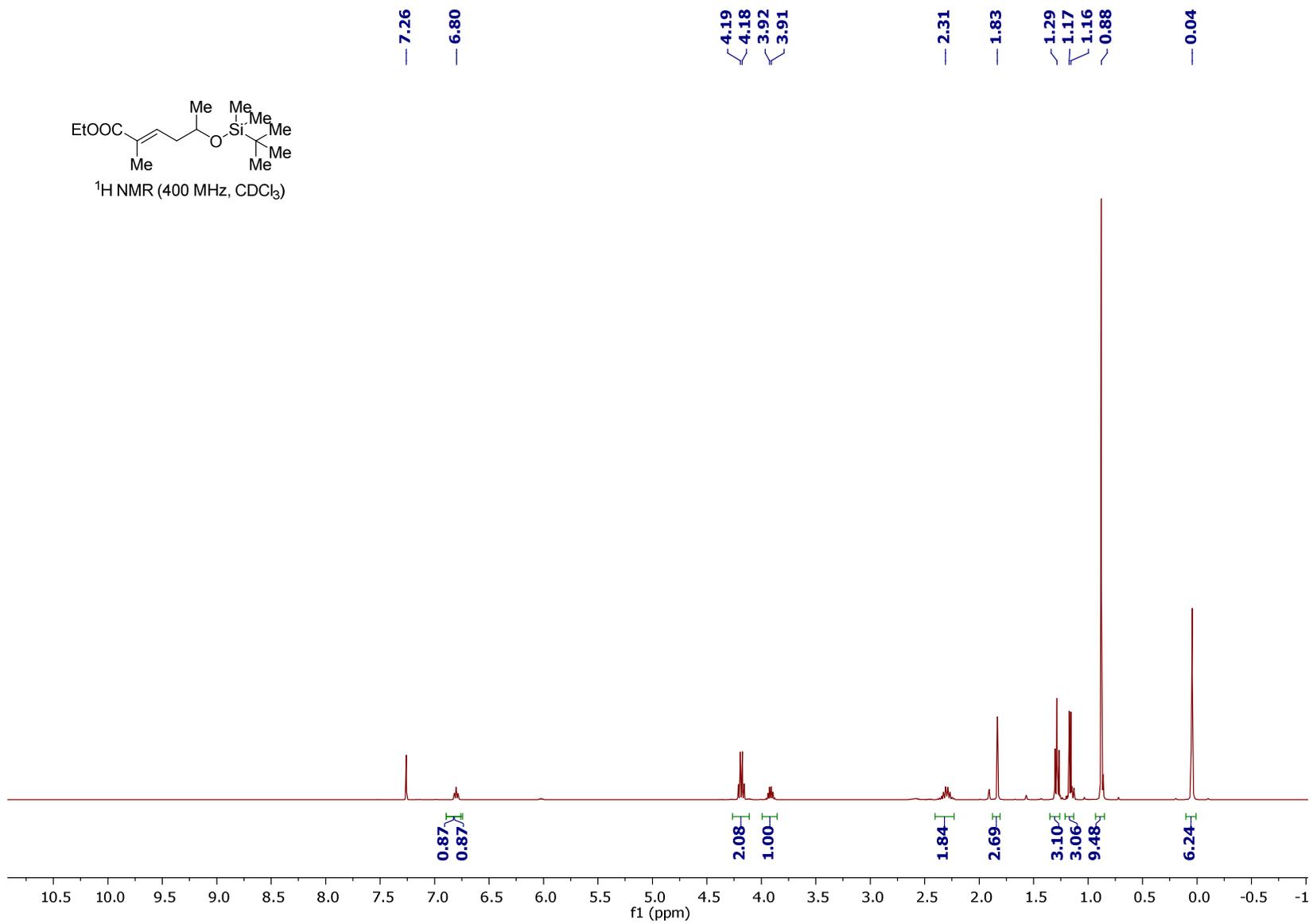
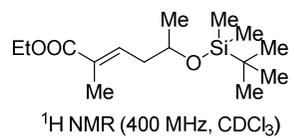
— 3.74

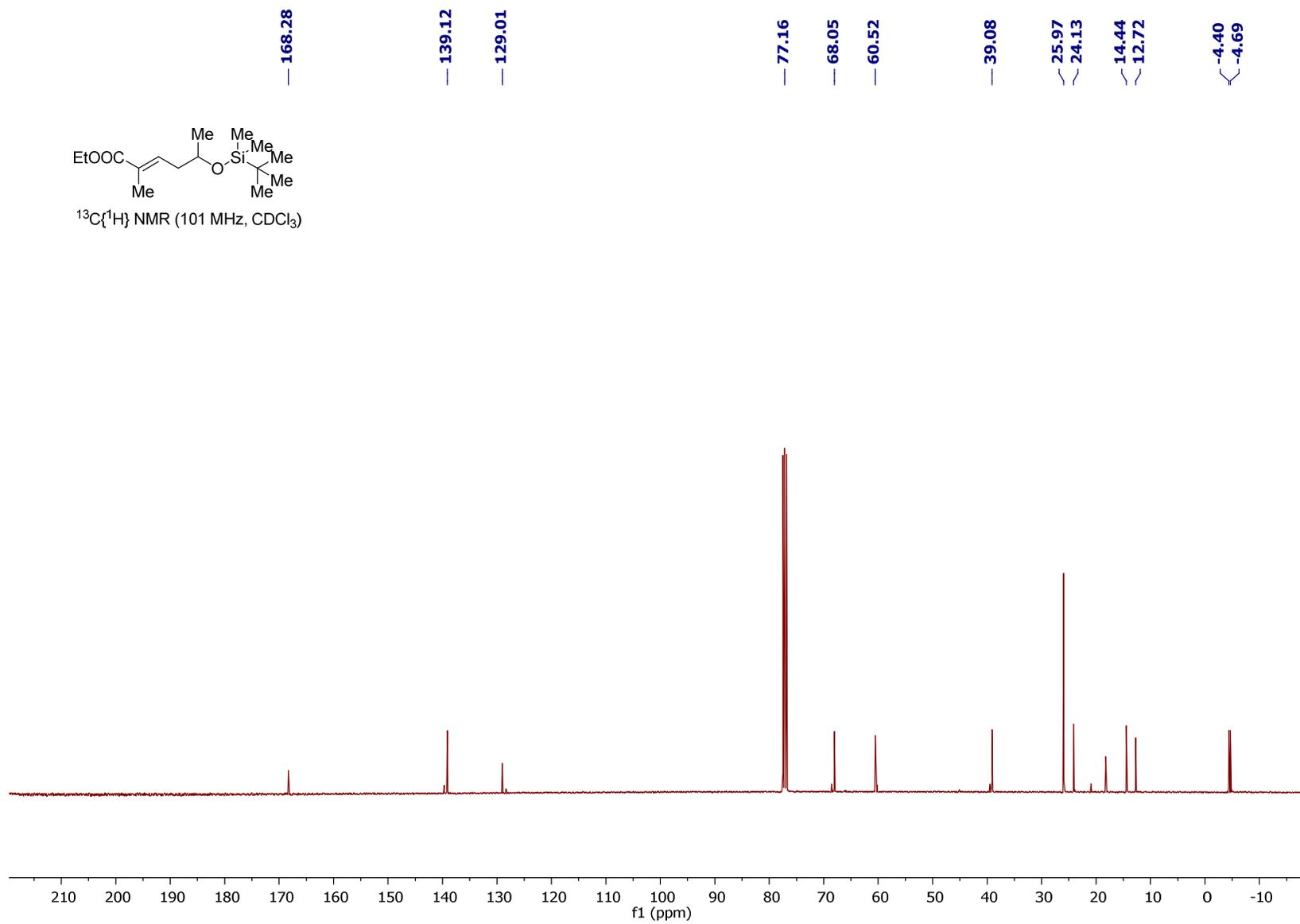
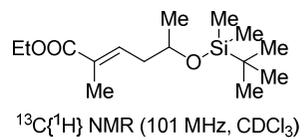
2.55  
2.53

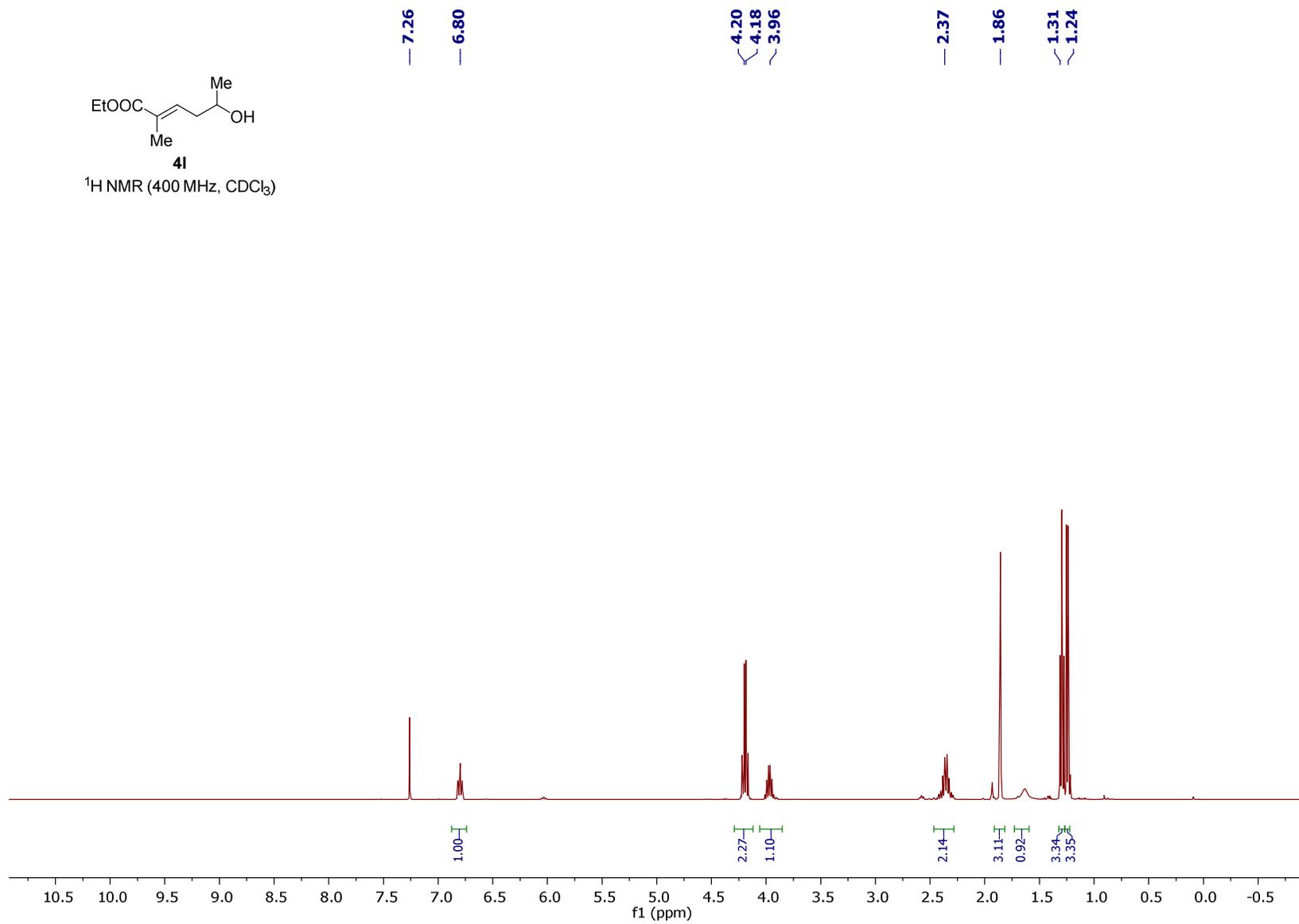
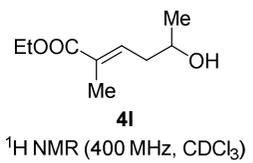
— 1.60

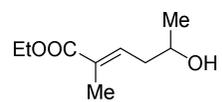






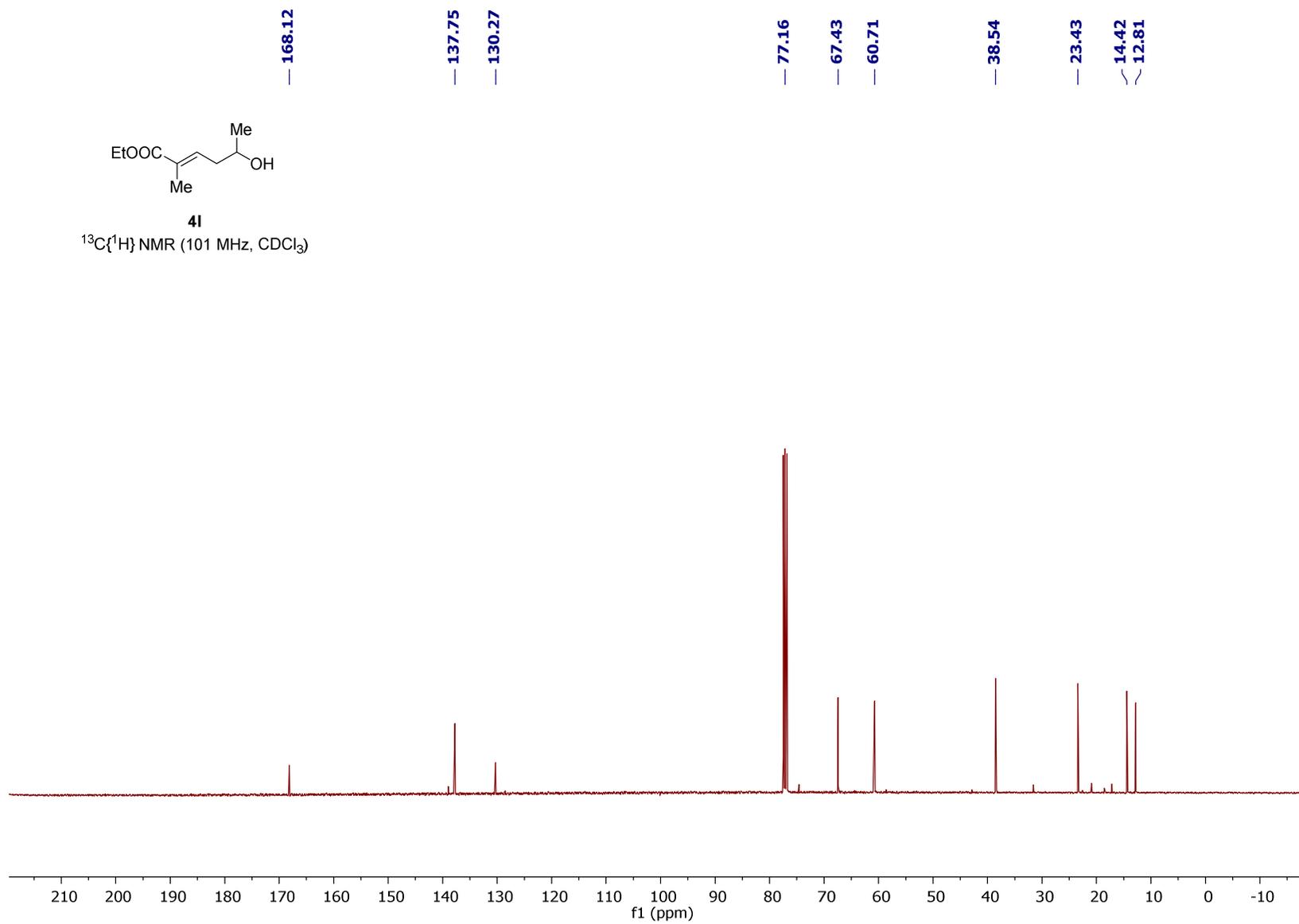


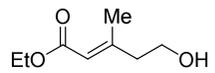




**41**

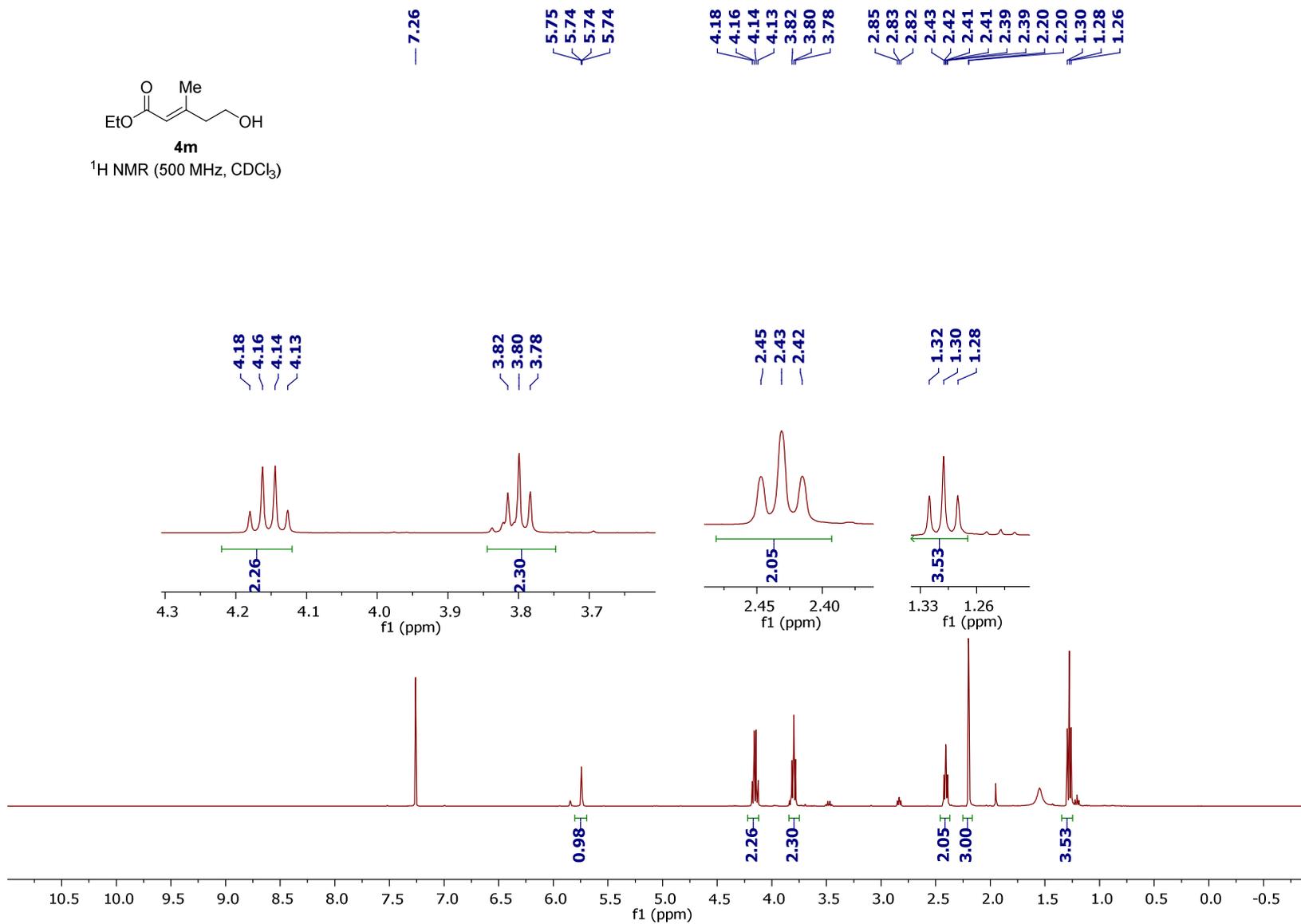
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

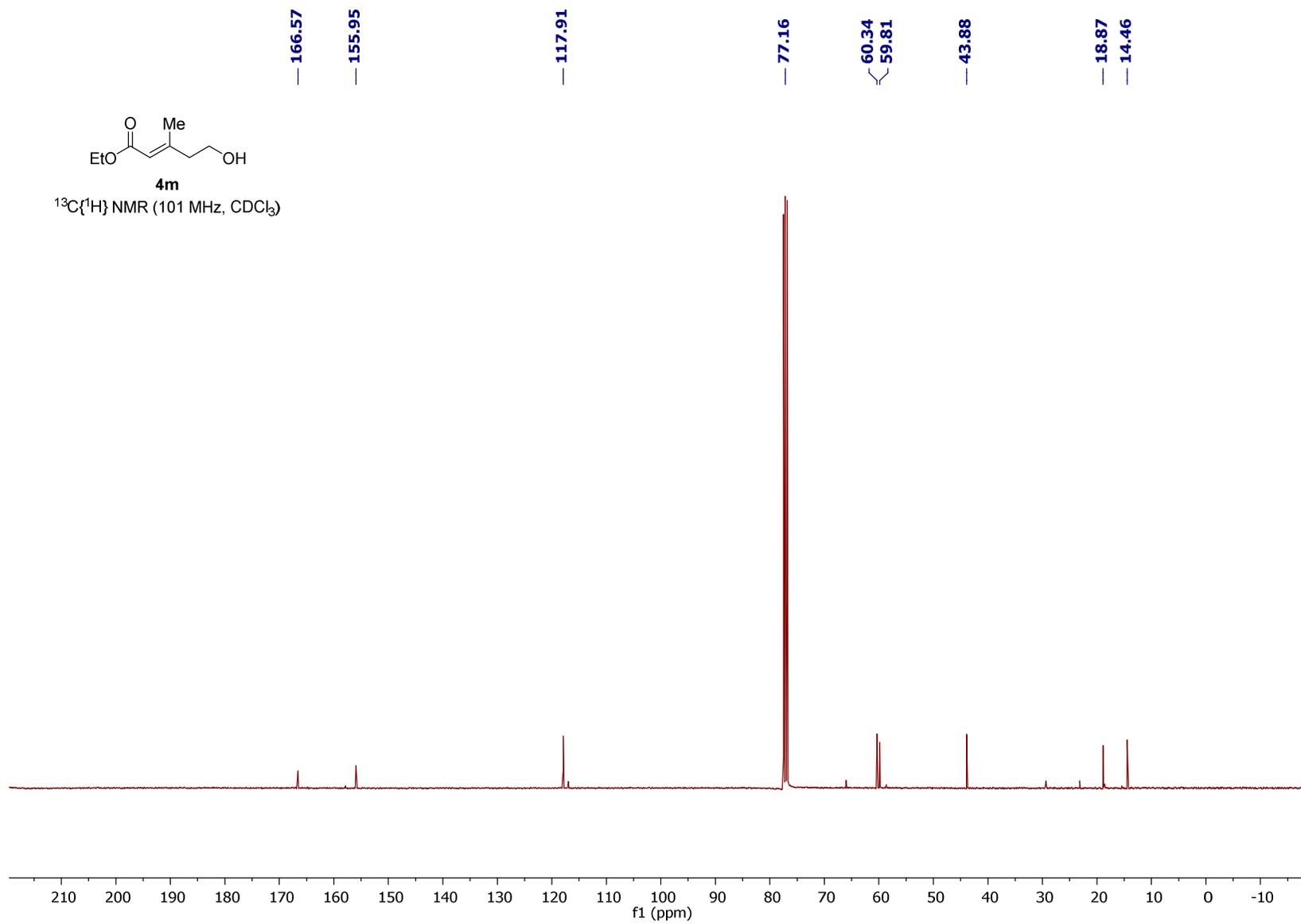
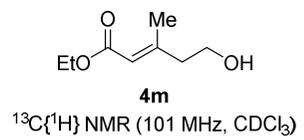


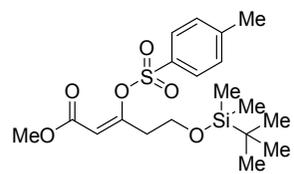


**4m**

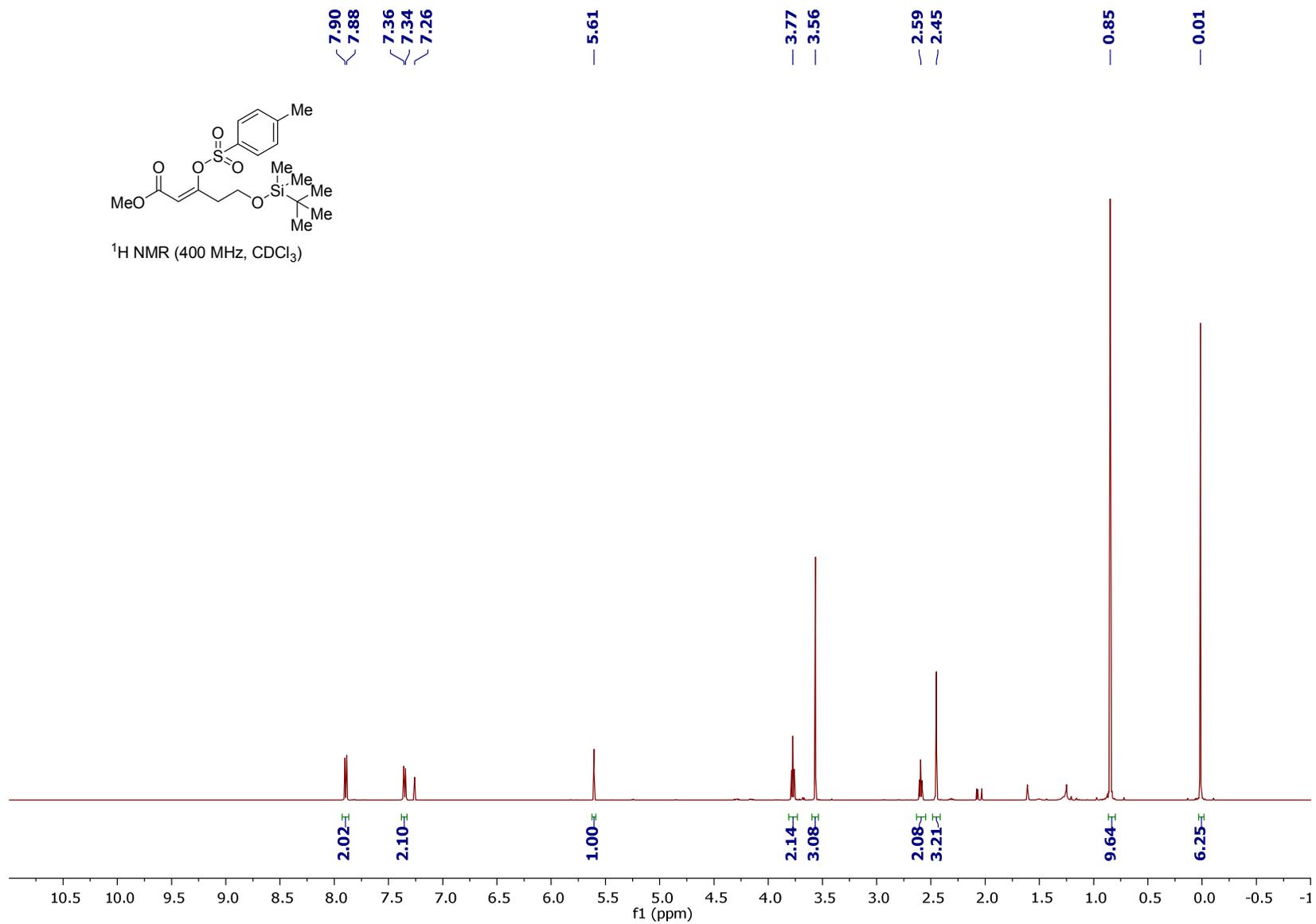
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

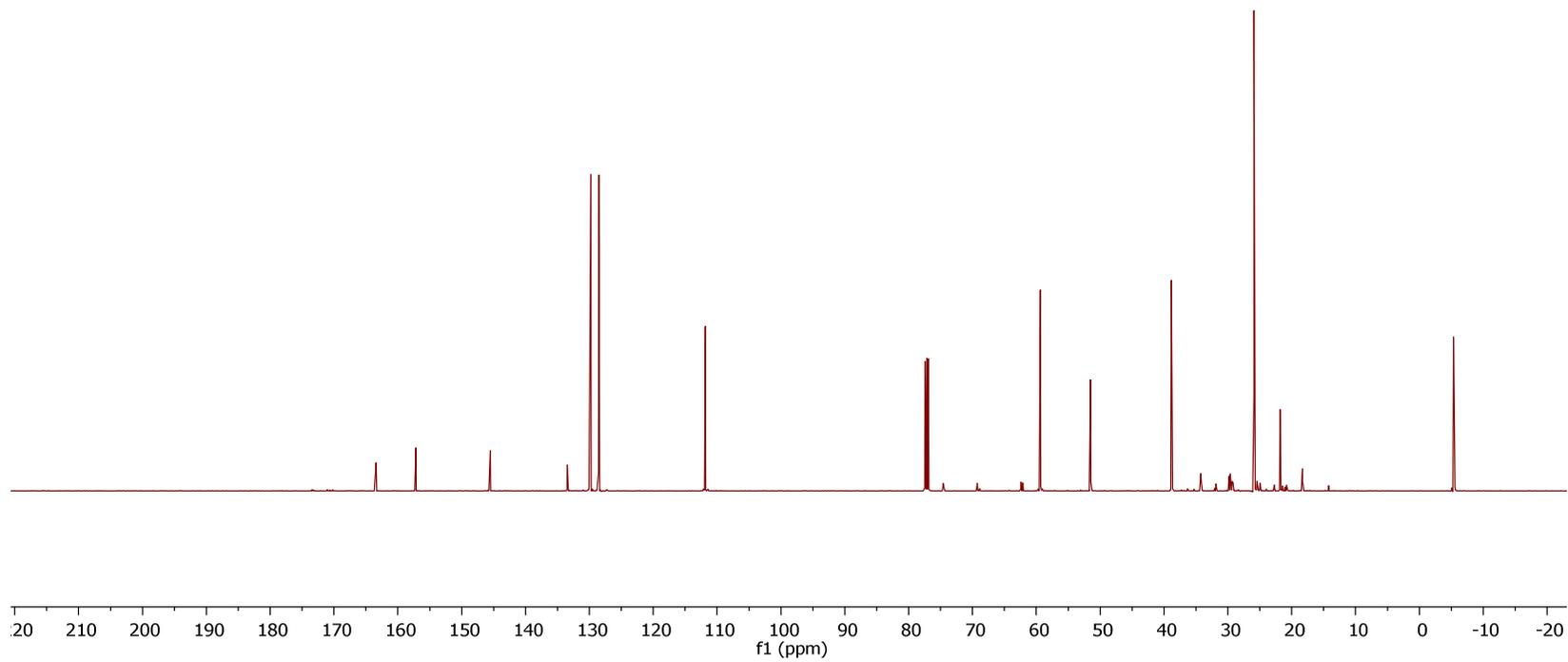
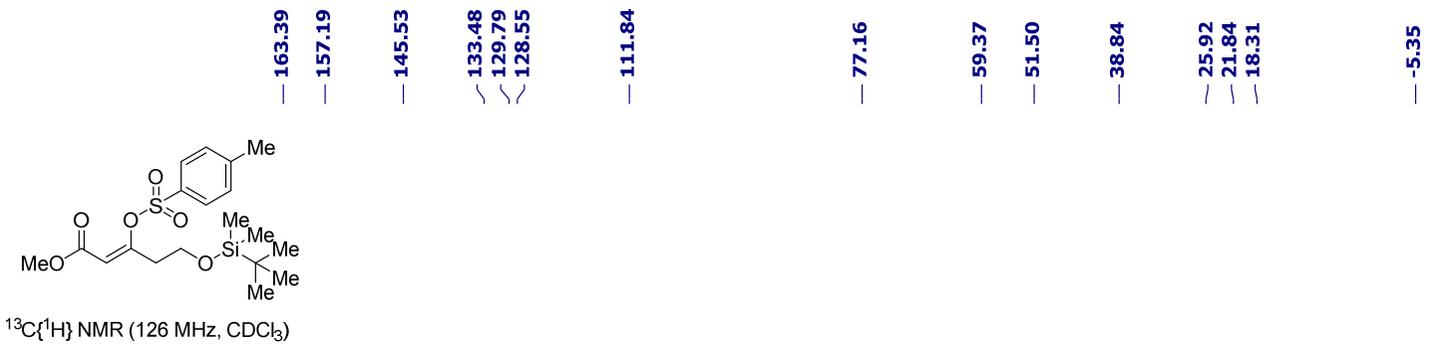


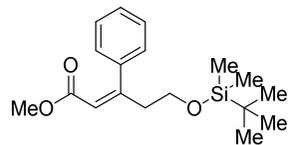




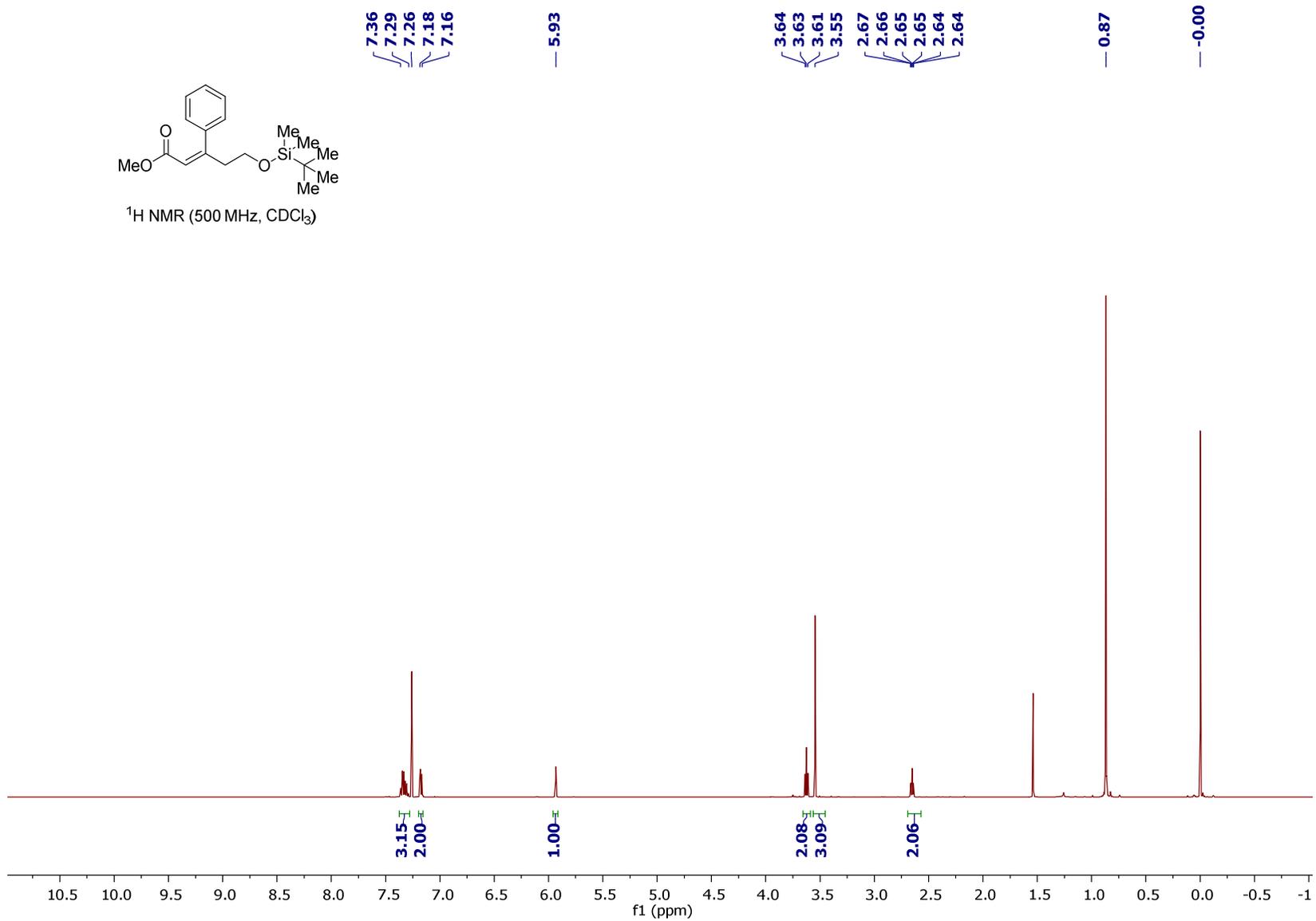
$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )

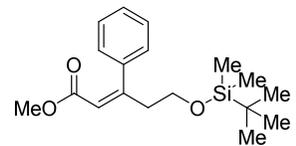




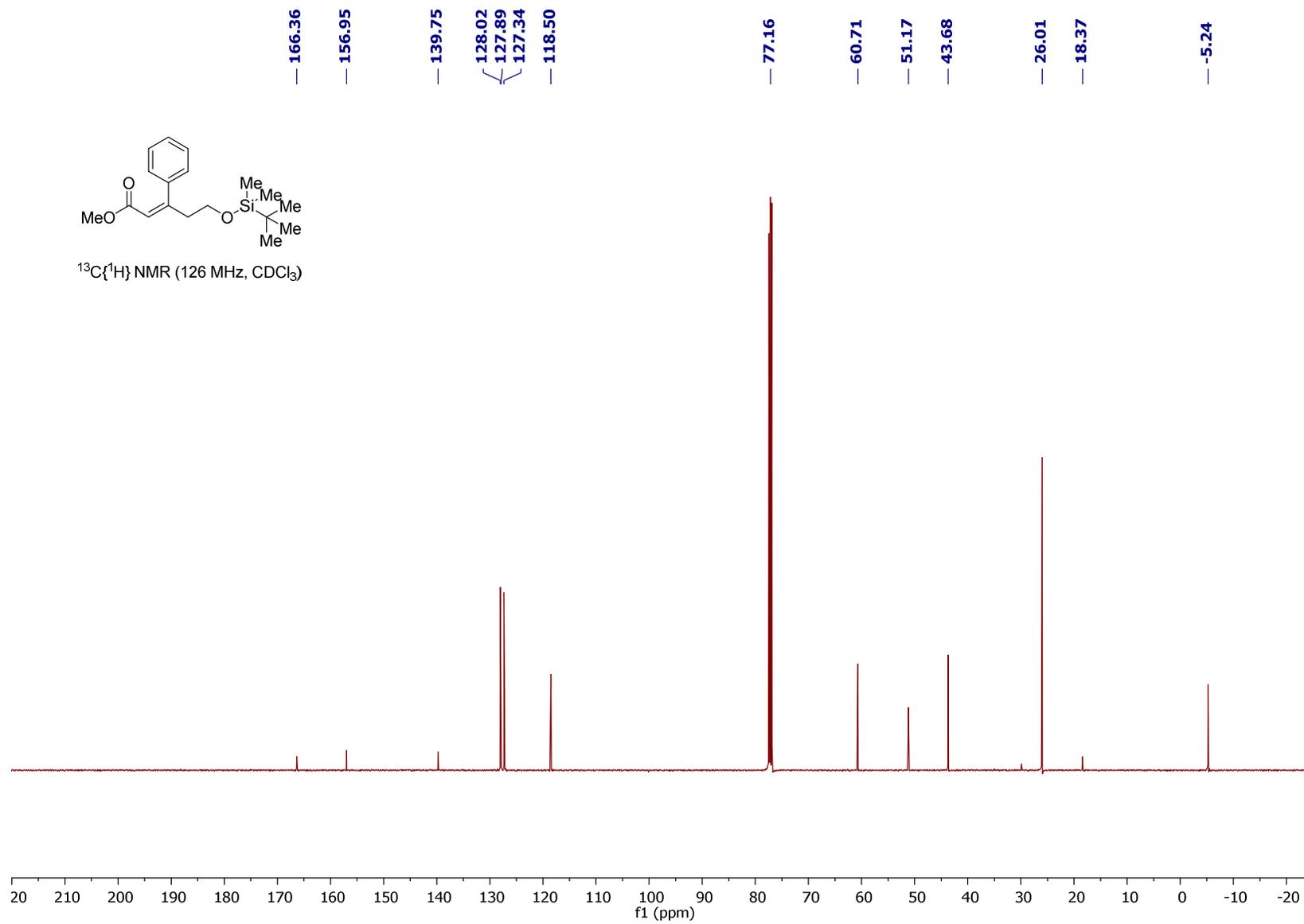


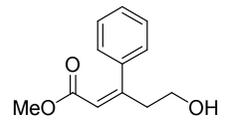
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





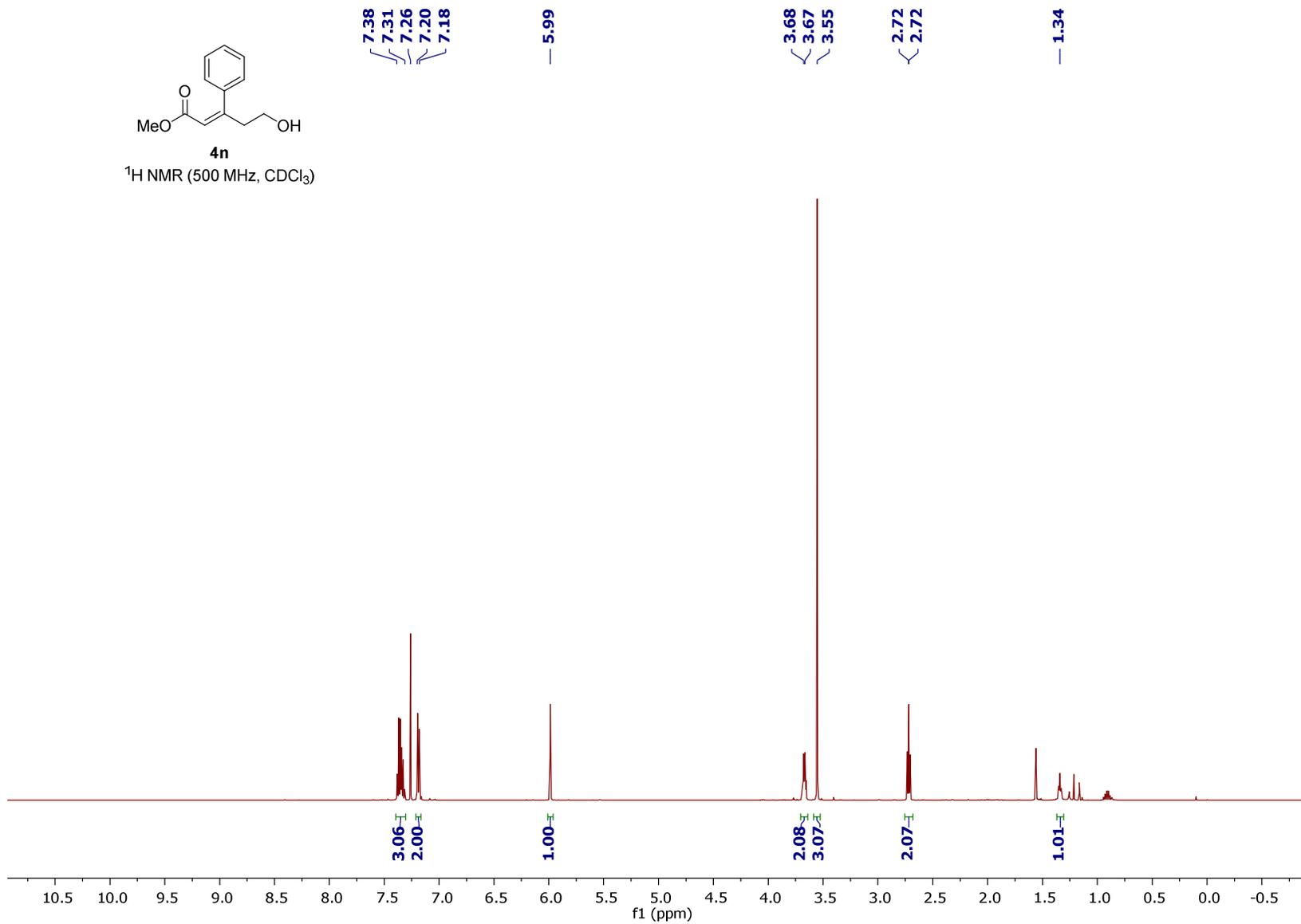
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

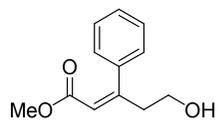




**4n**

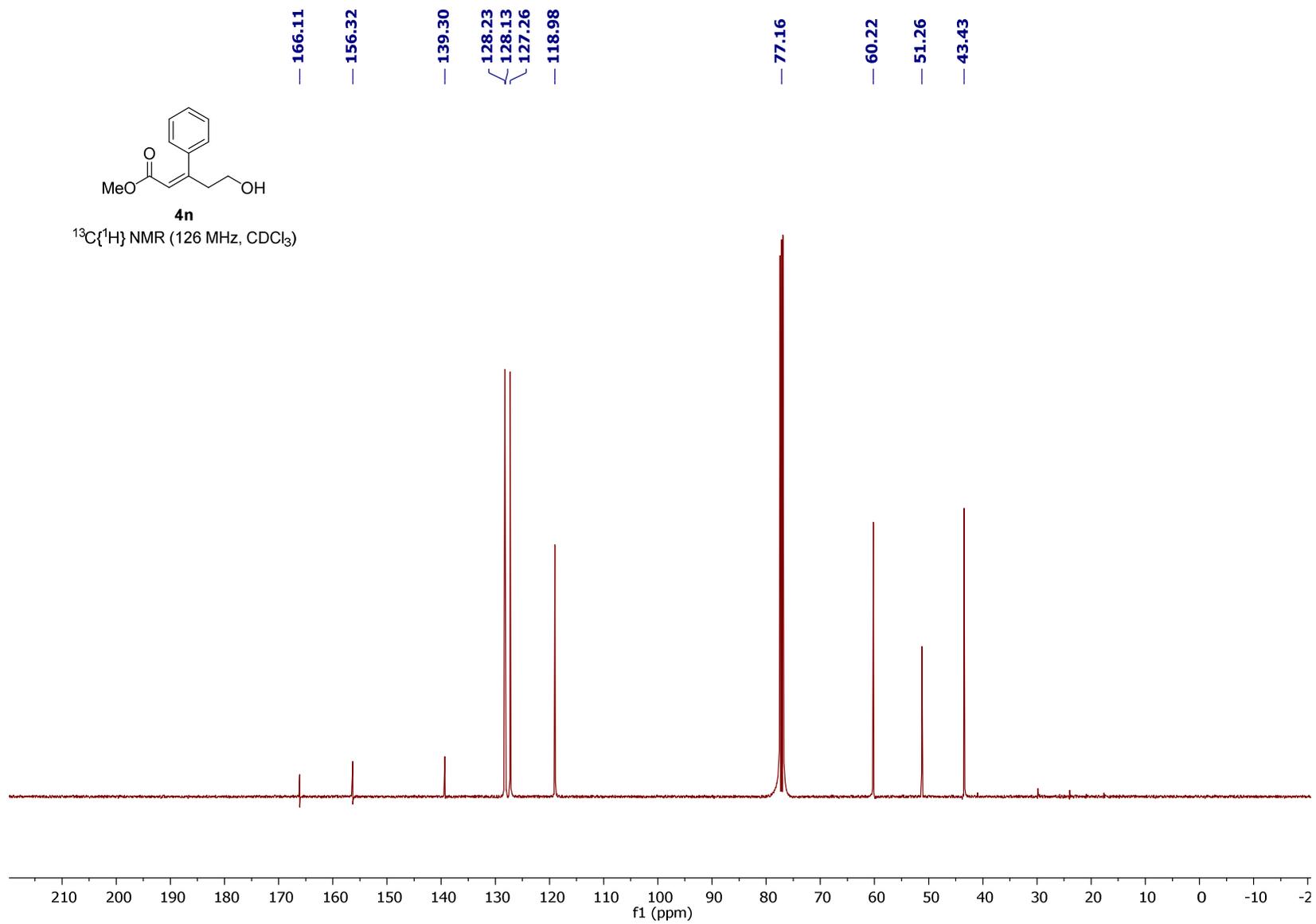
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



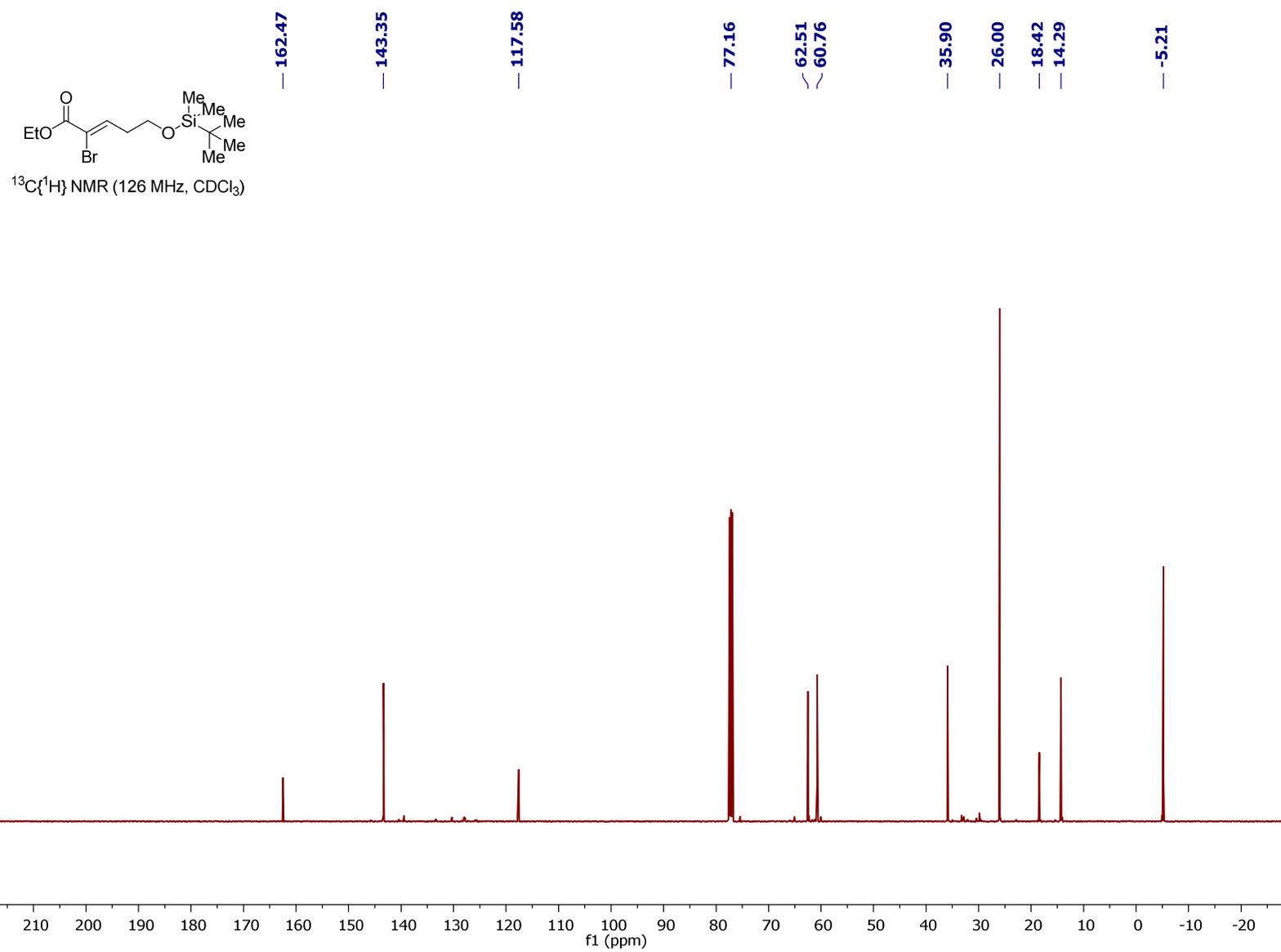


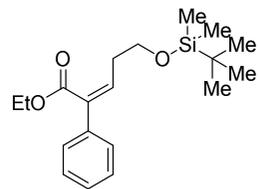
**4n**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

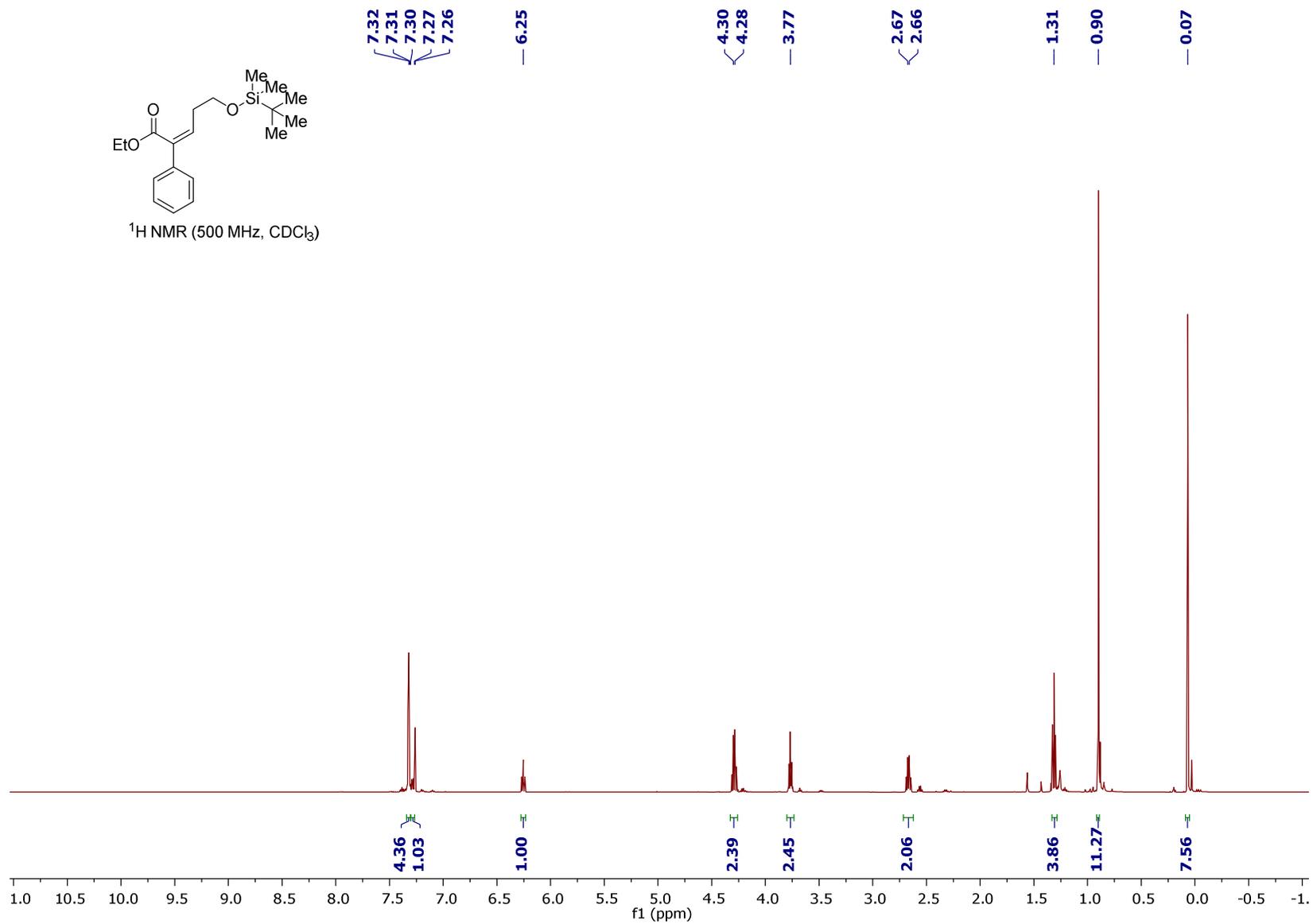




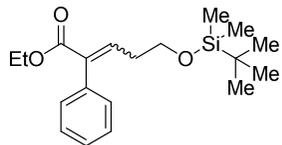




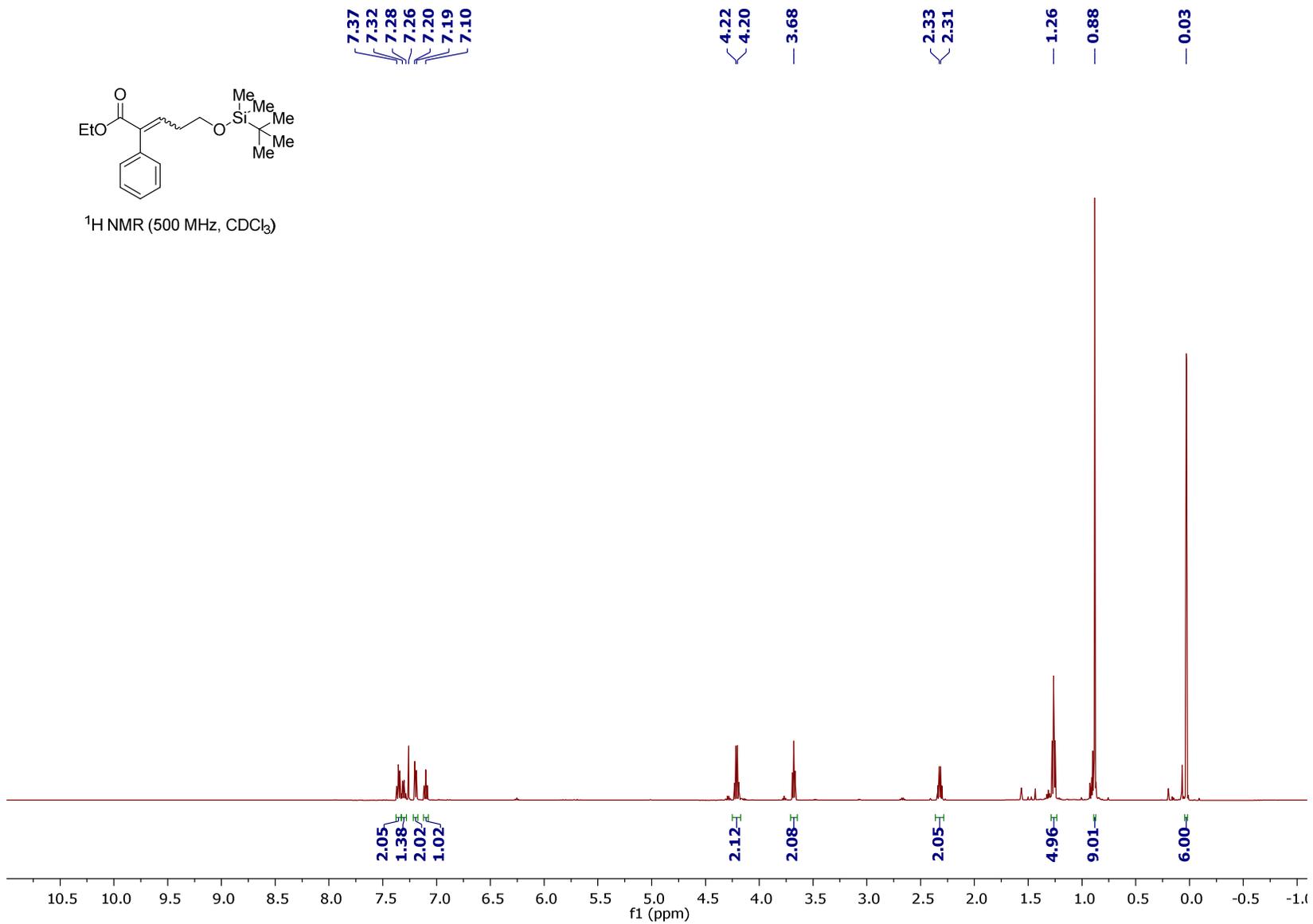
$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )

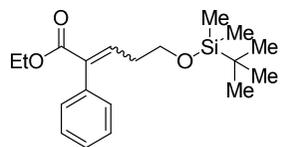




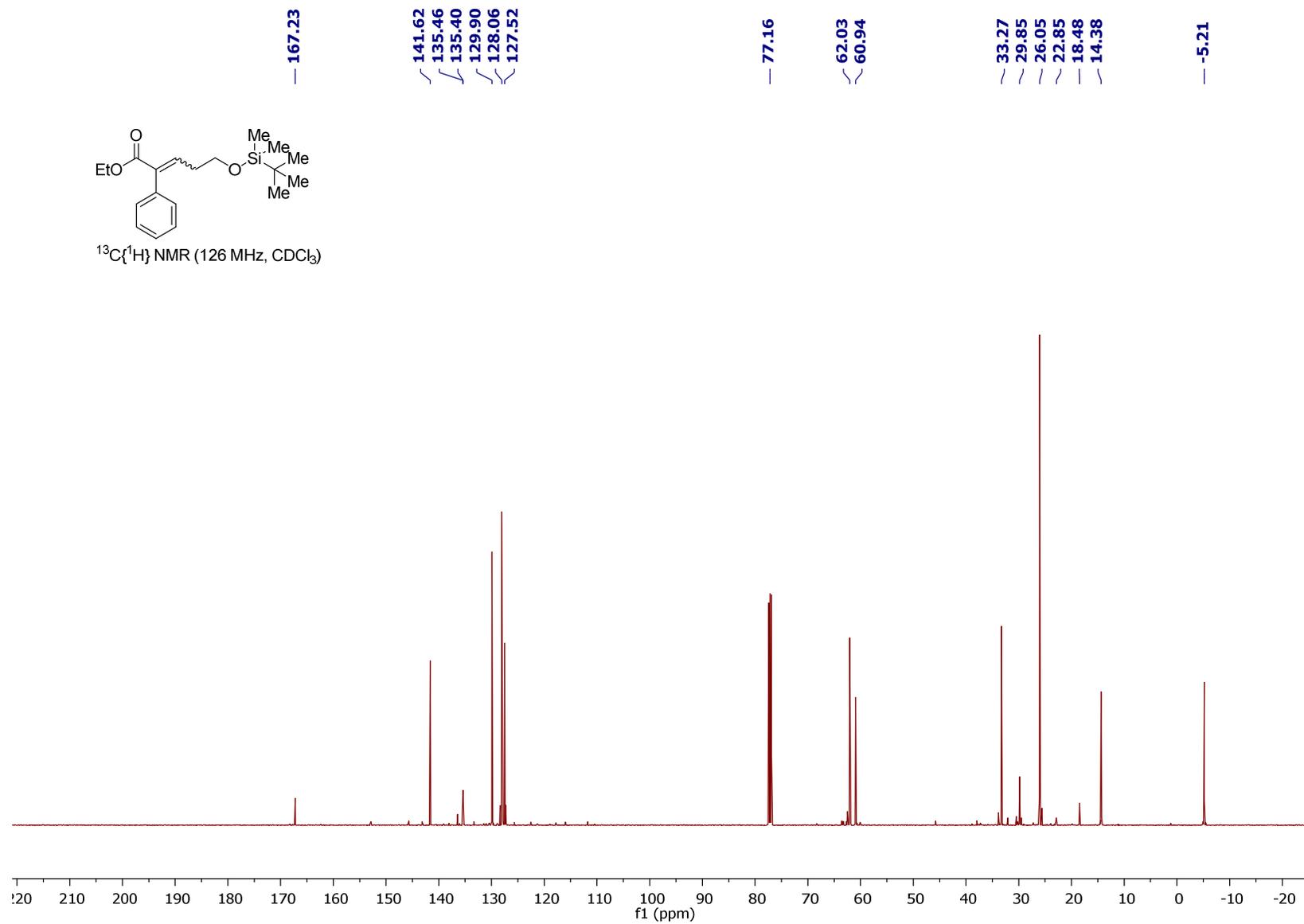


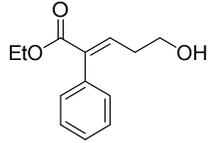
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





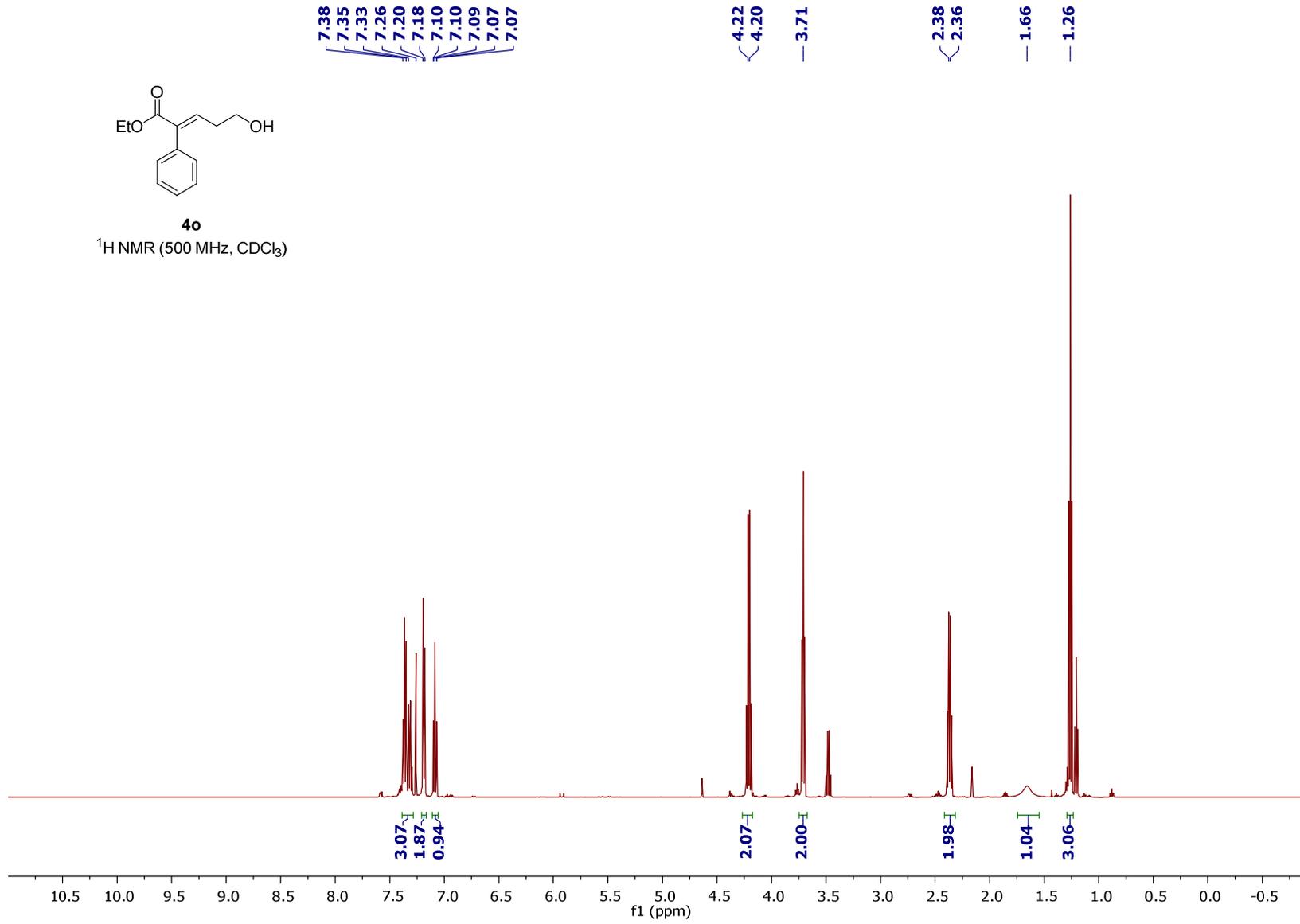
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

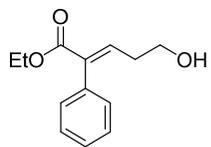




**4o**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





**4o**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

— 167.15

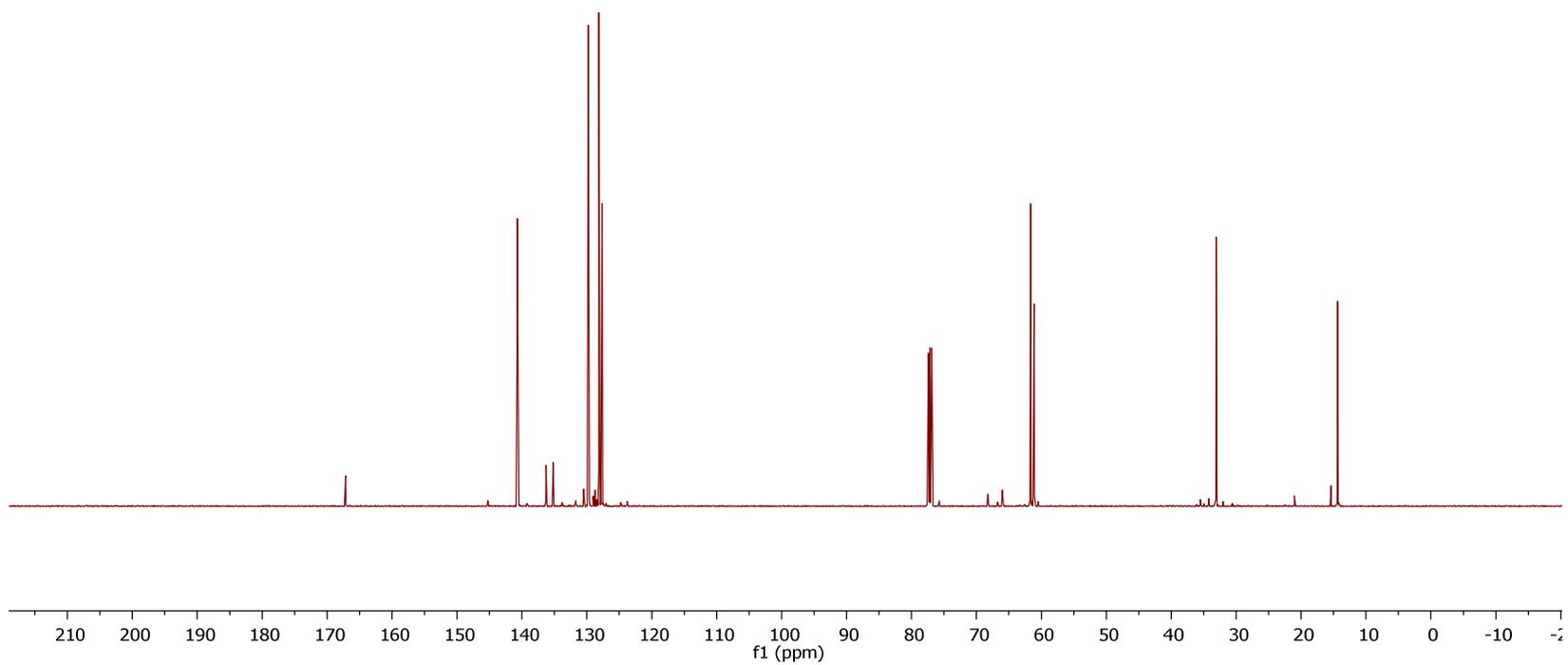
140.71  
136.29  
135.21  
129.81  
128.15  
127.65

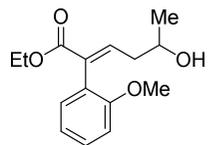
— 77.16

61.68  
61.10

— 33.09

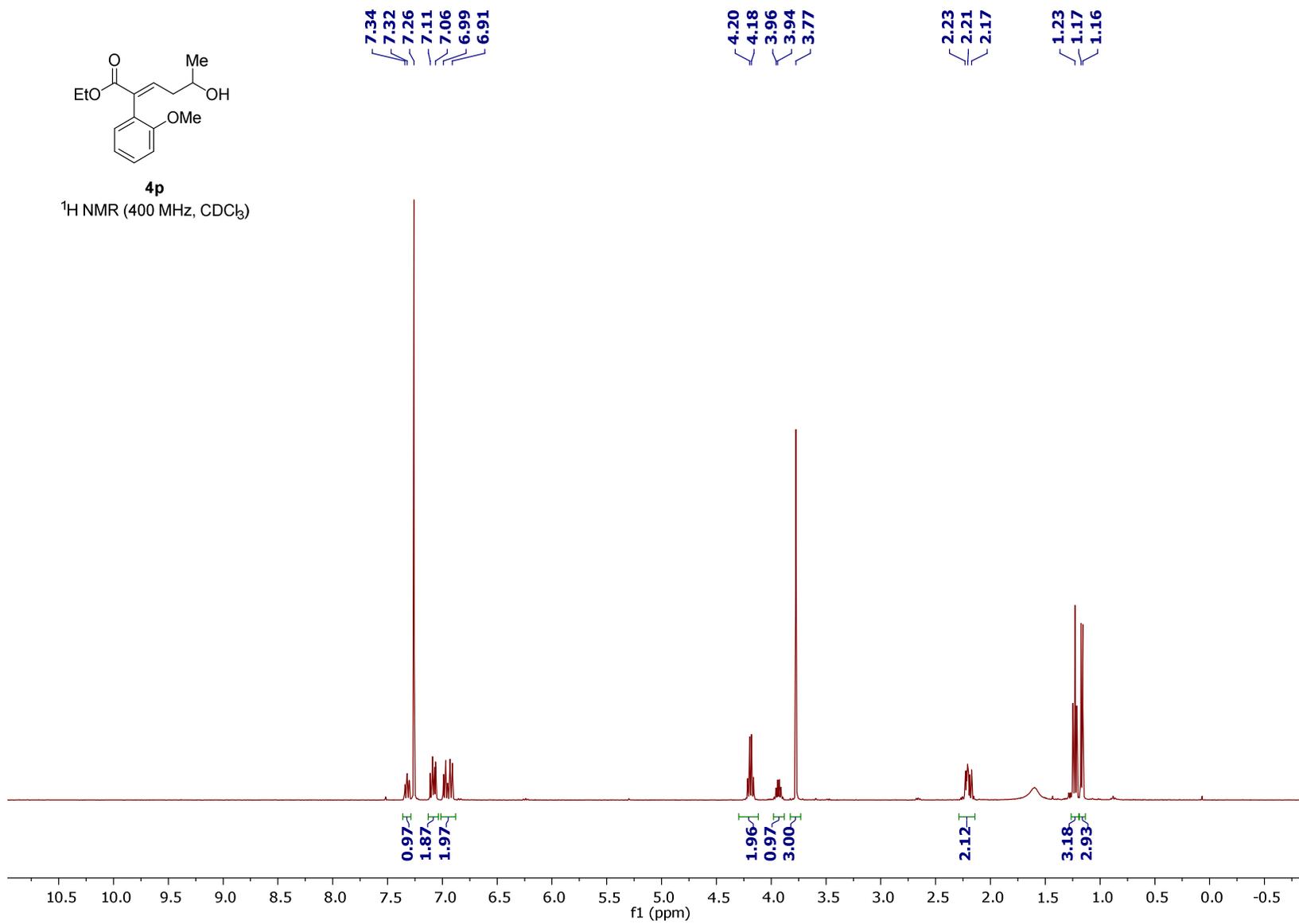
— 14.37

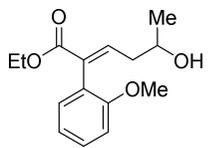




**4p**

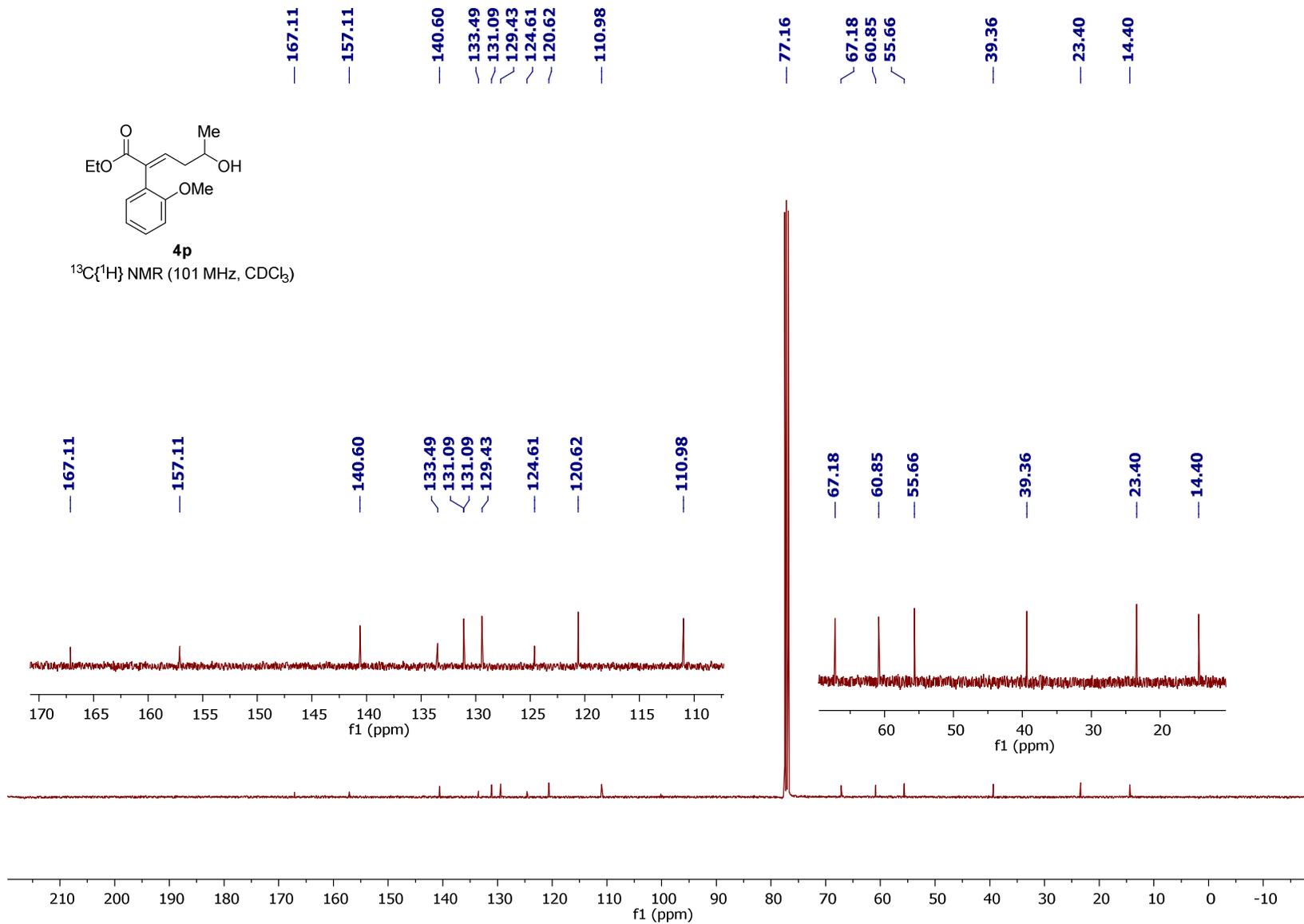
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

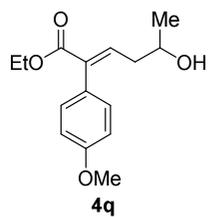




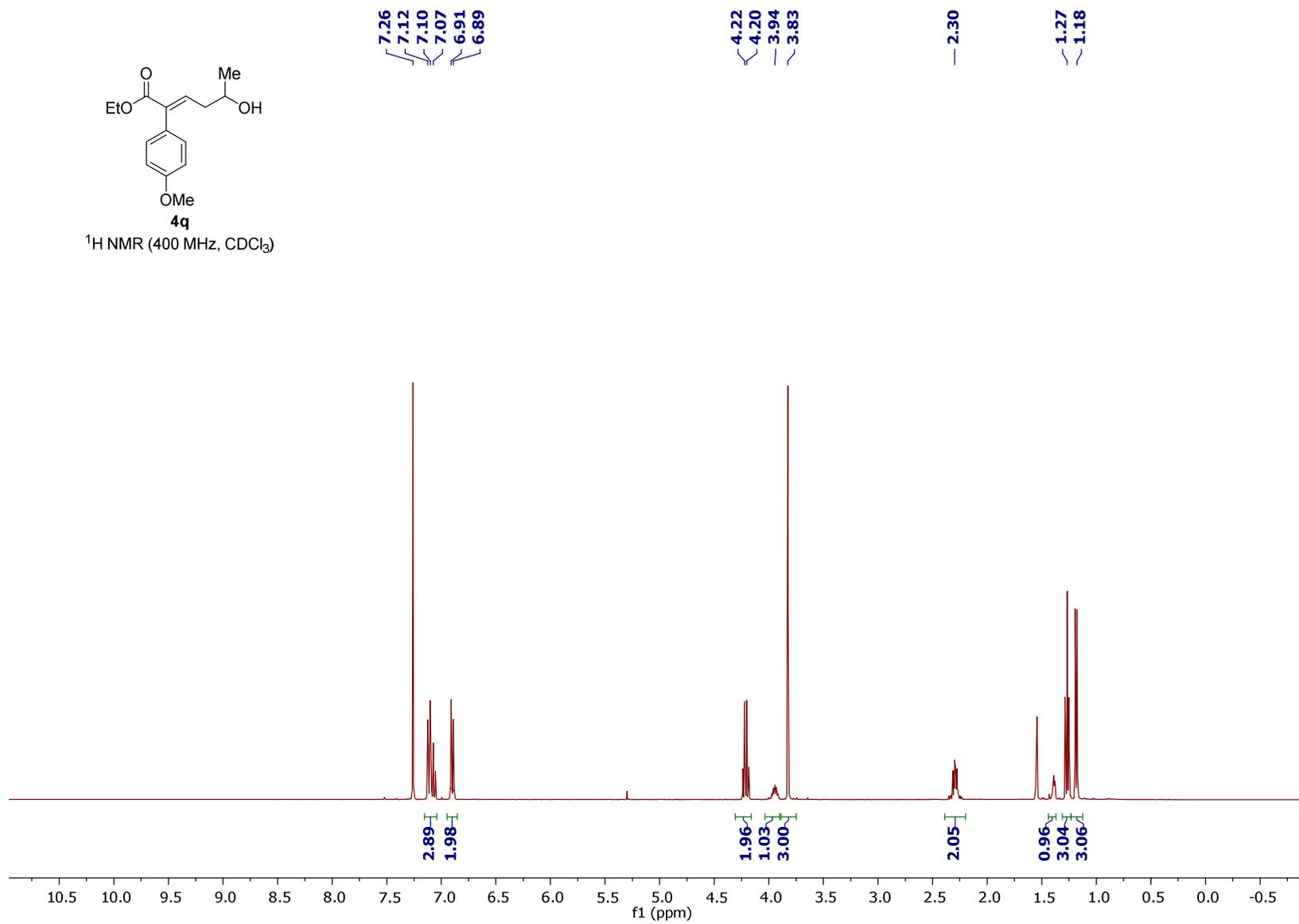
4p

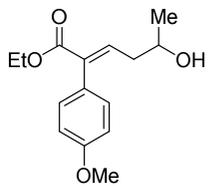
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





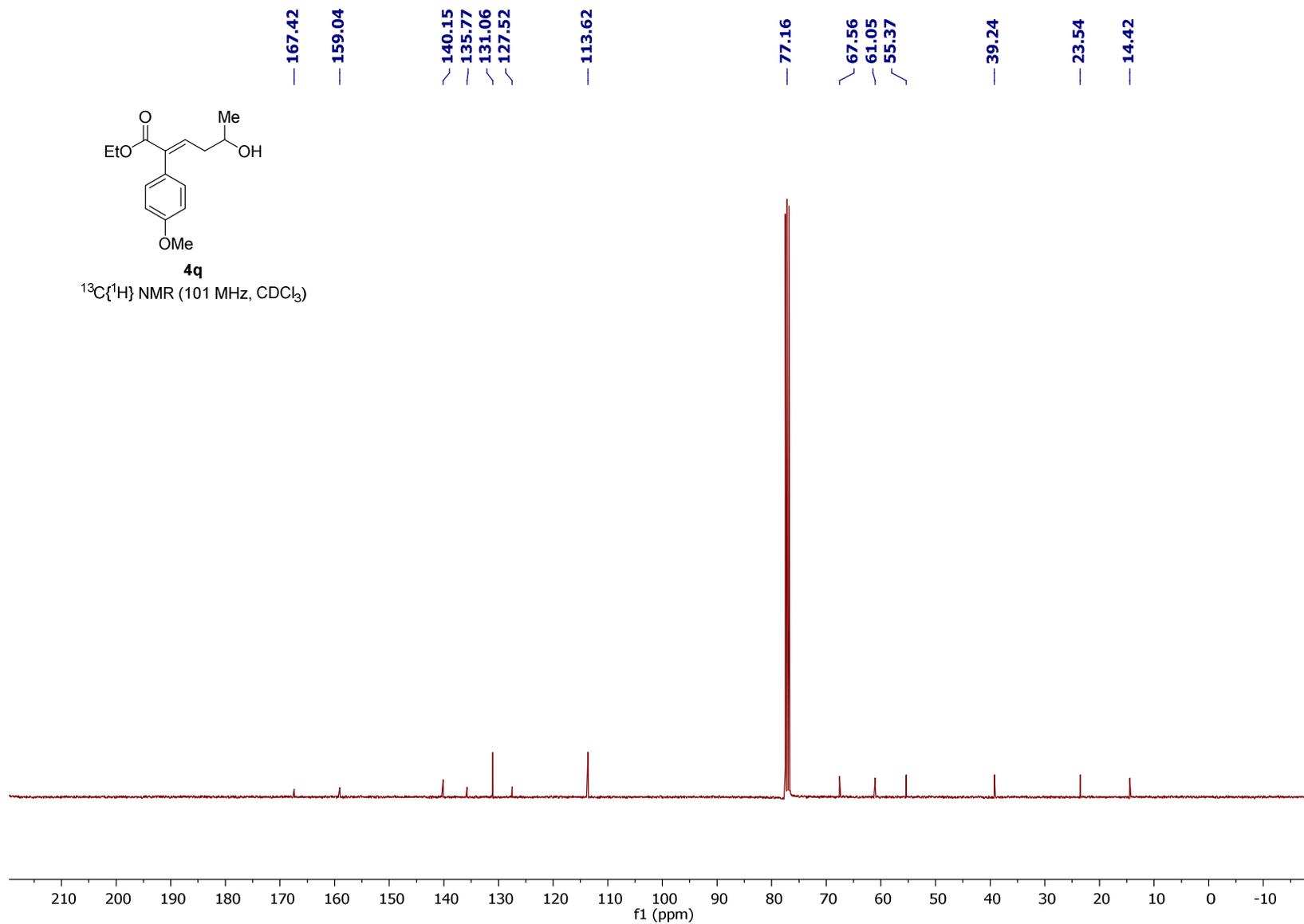
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

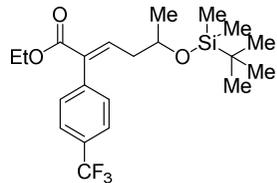




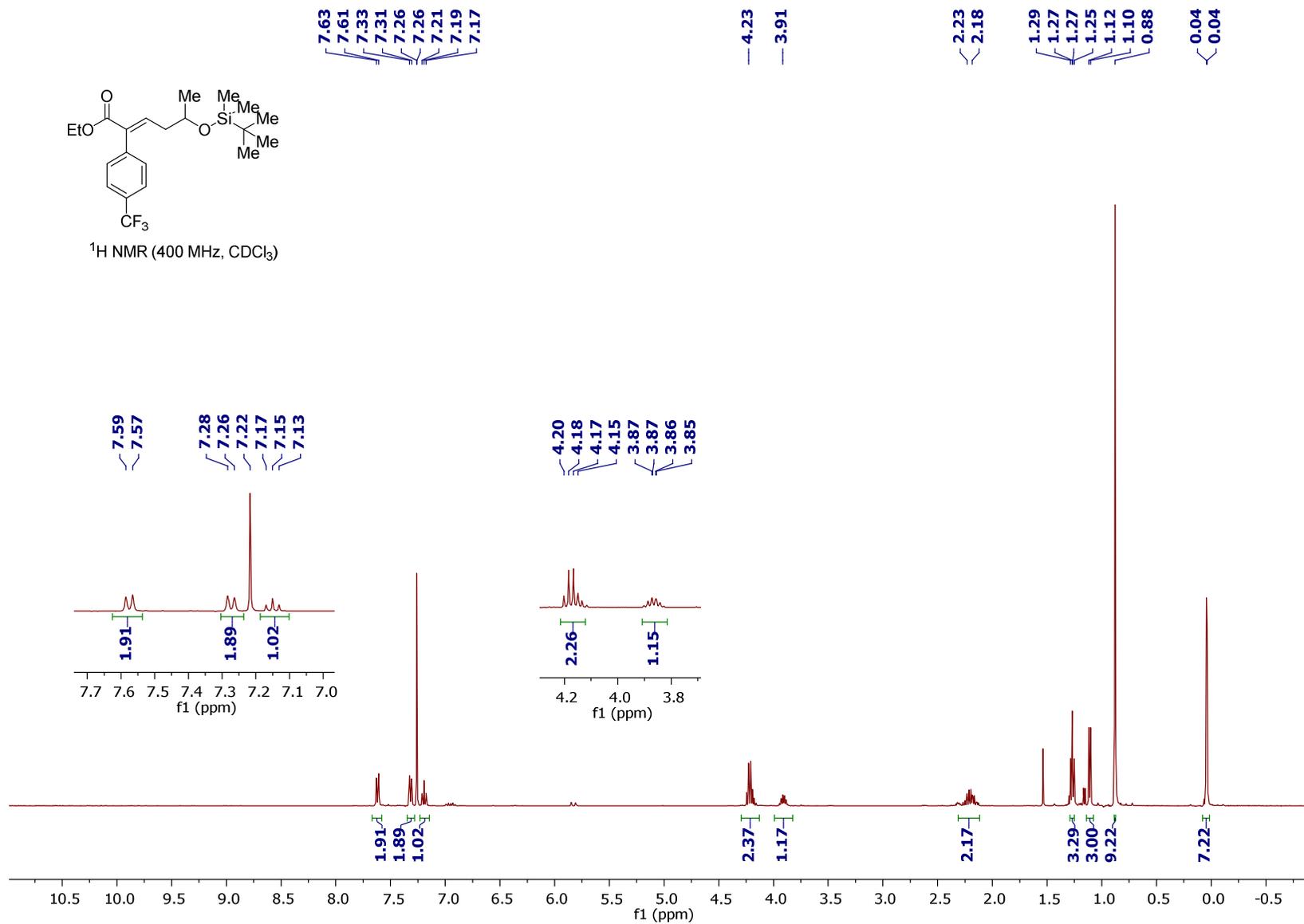
**4q**

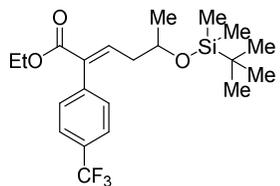
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



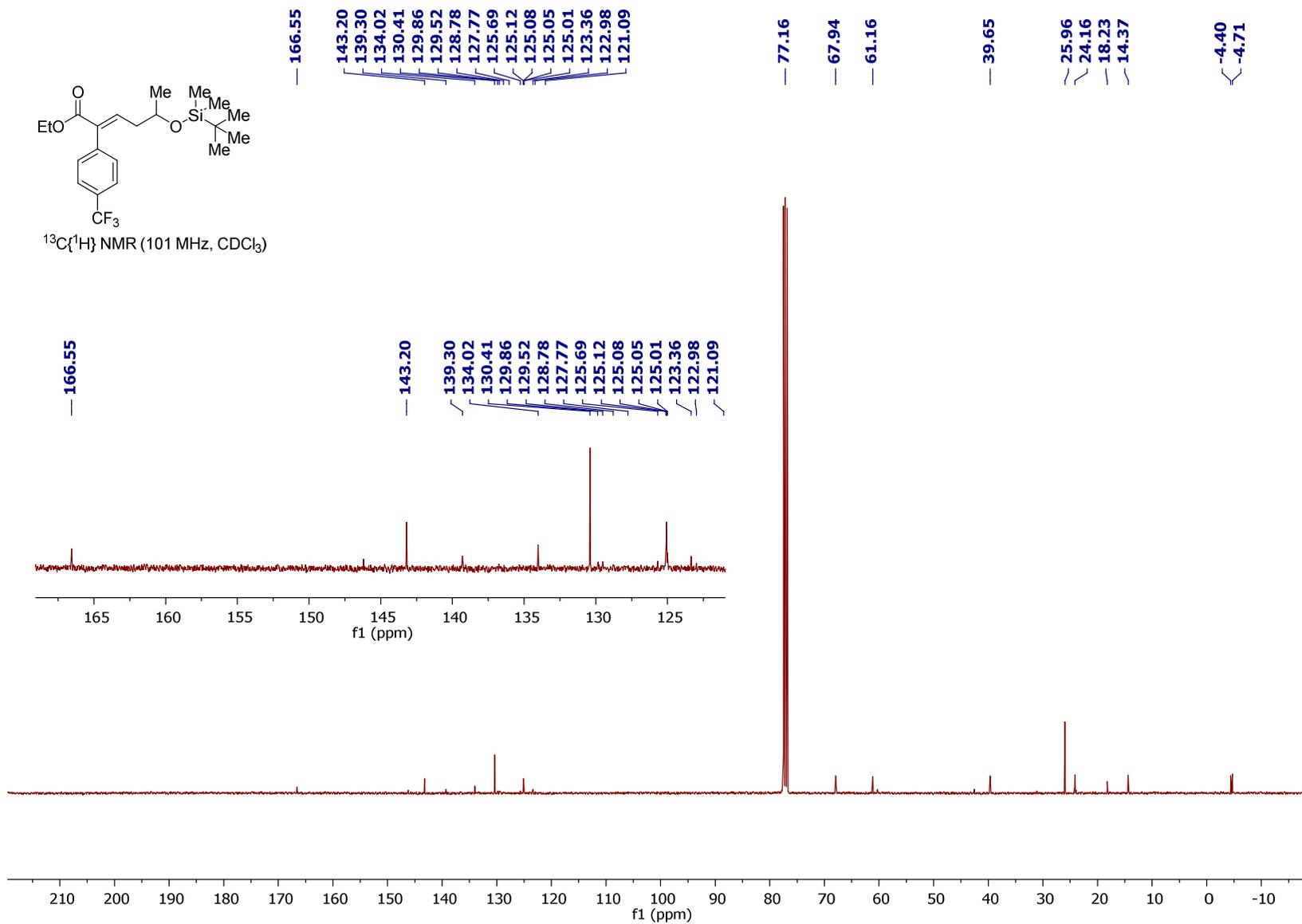


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

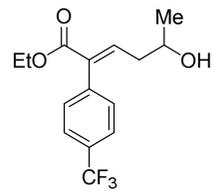




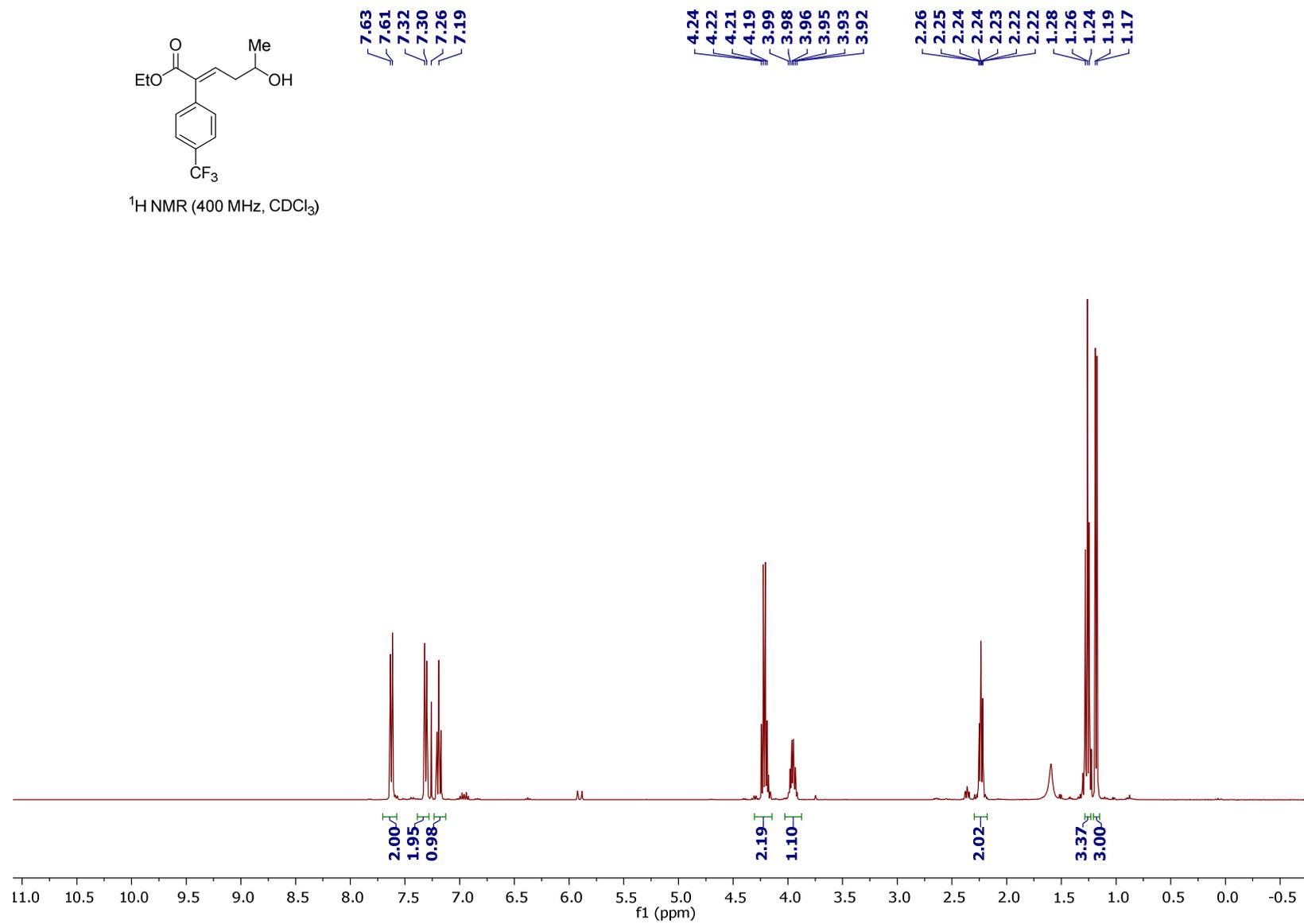
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

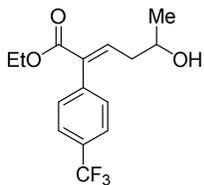






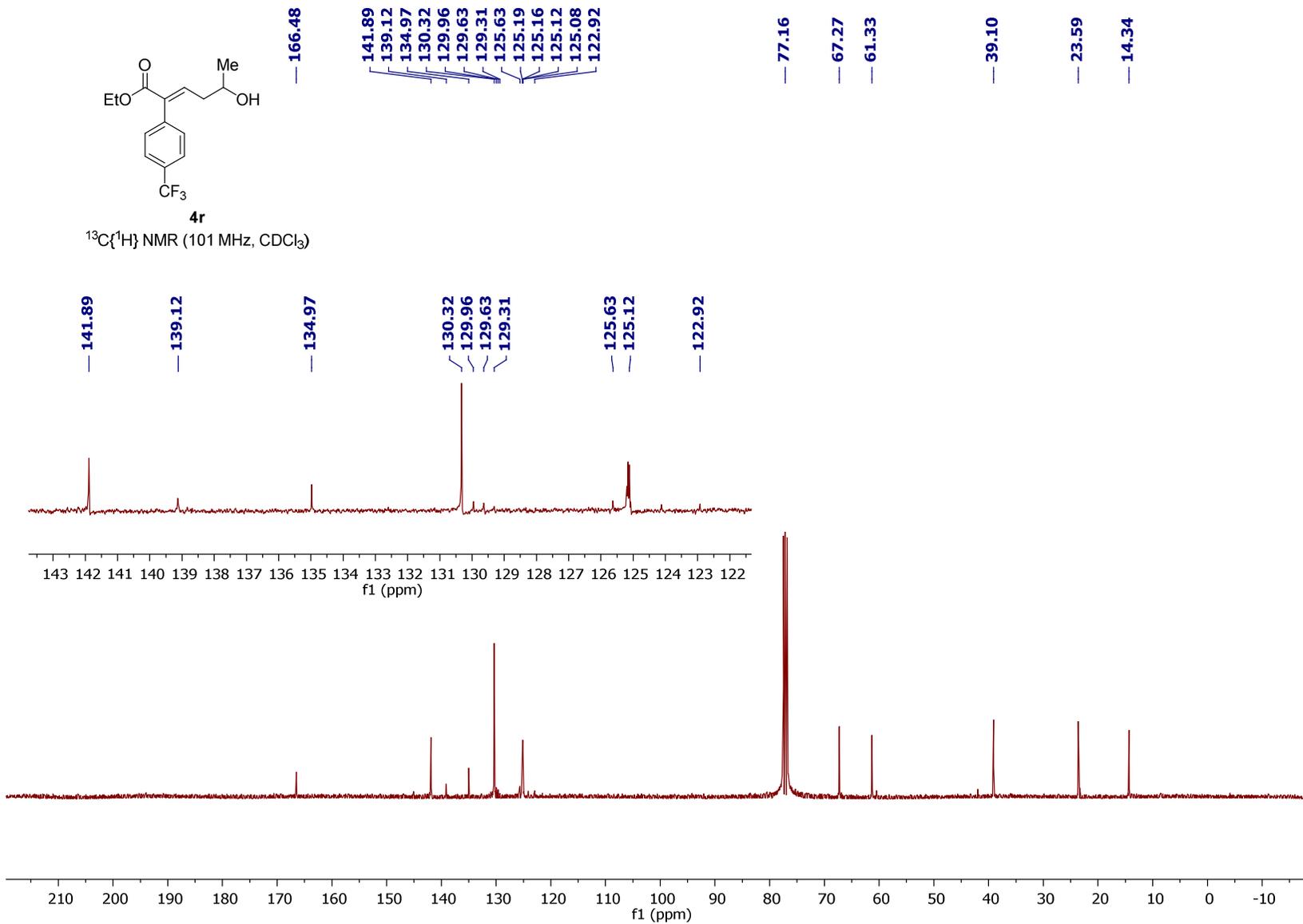
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )

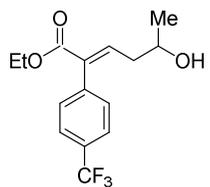




**4r**

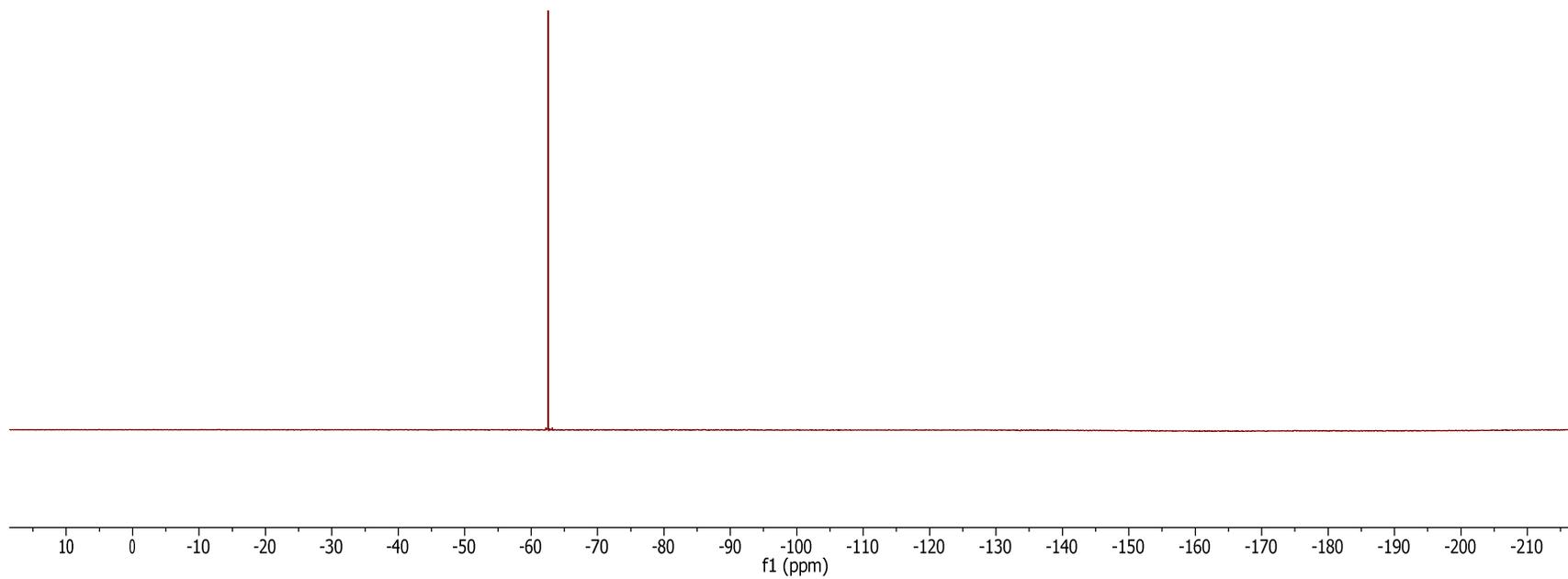
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

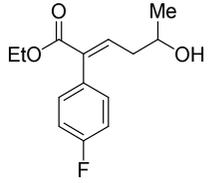




**4r**

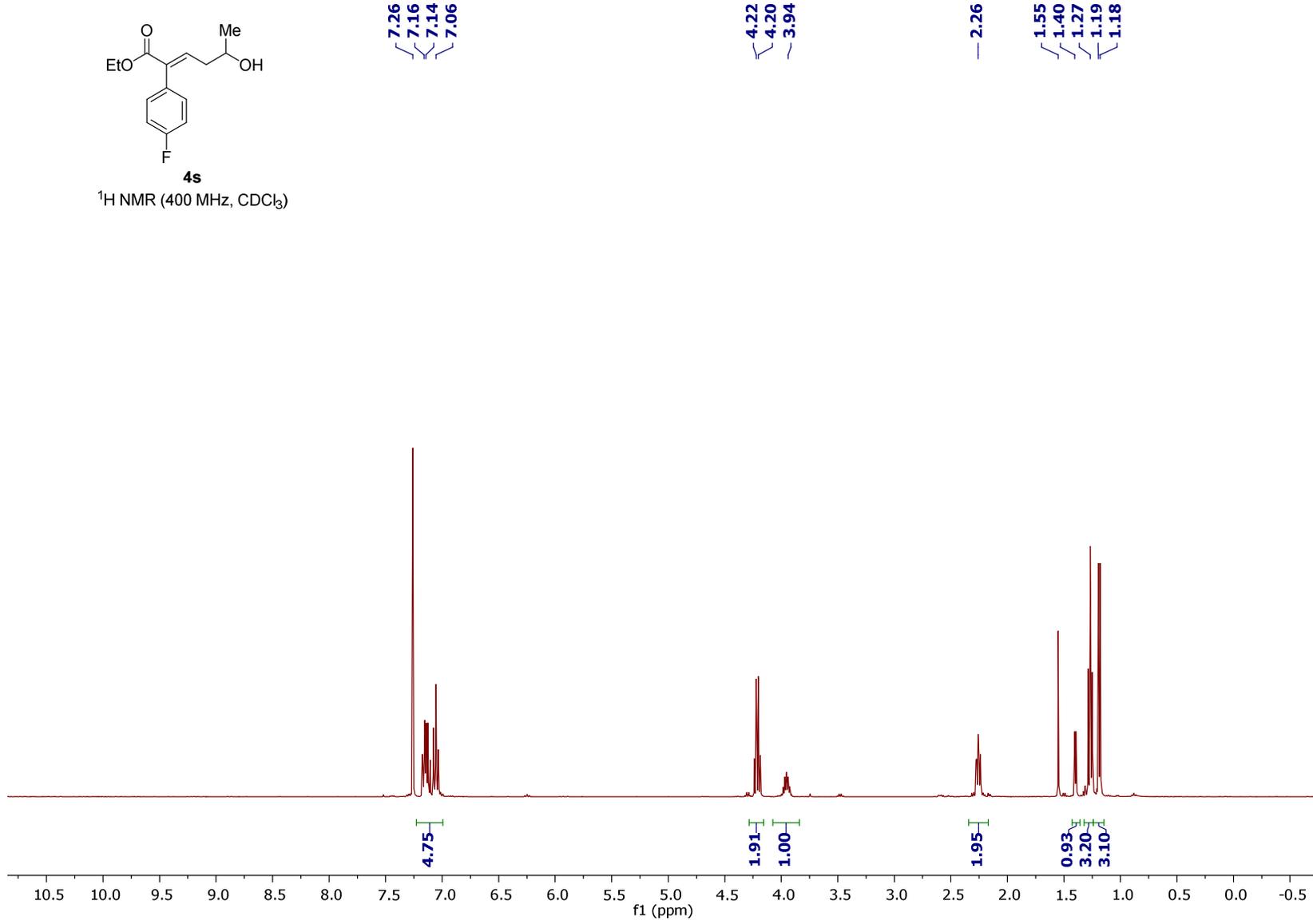
$^{19}\text{F}\{^1\text{H}, ^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )

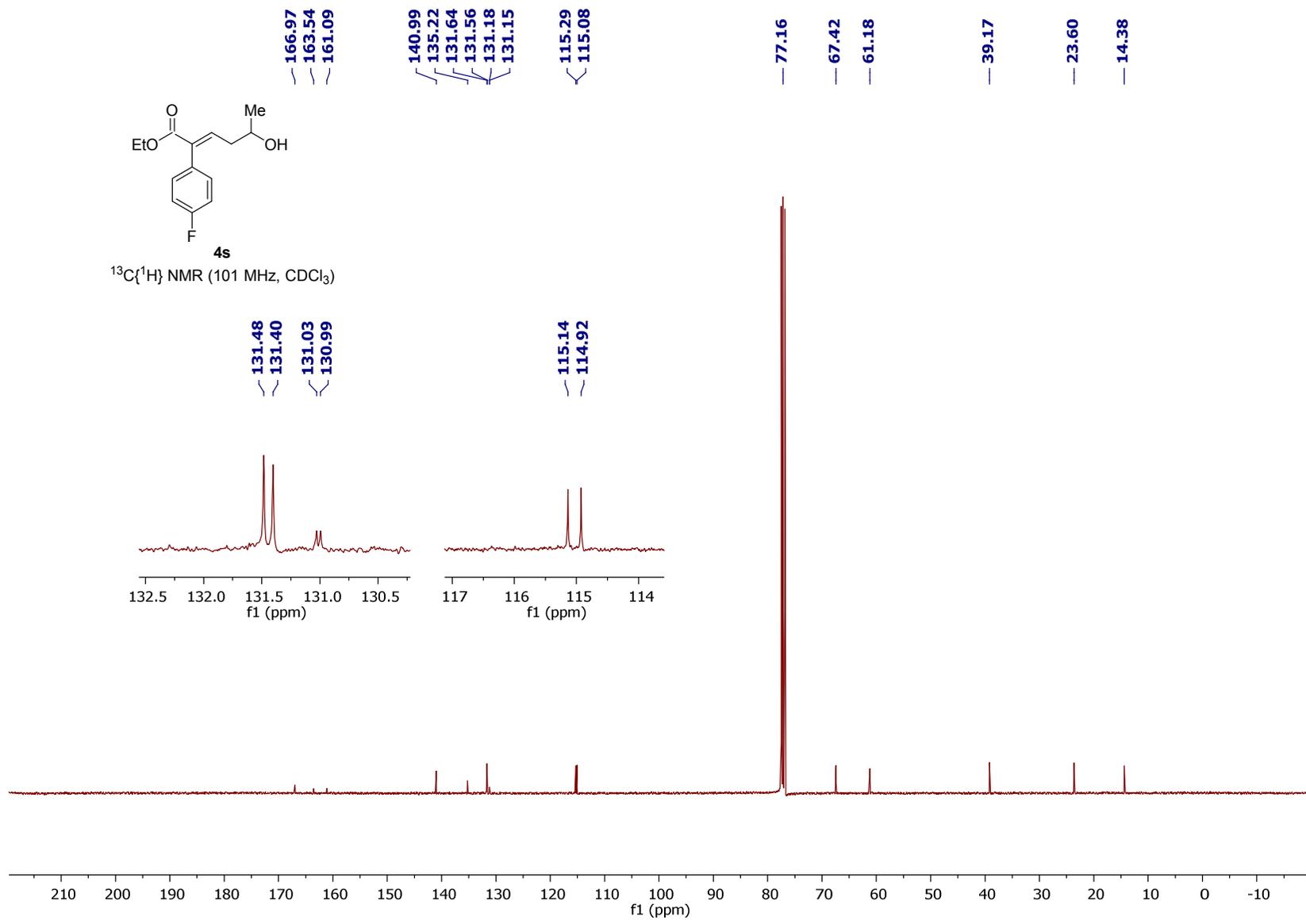


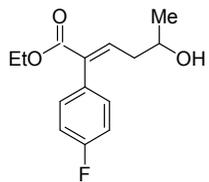


**4s**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

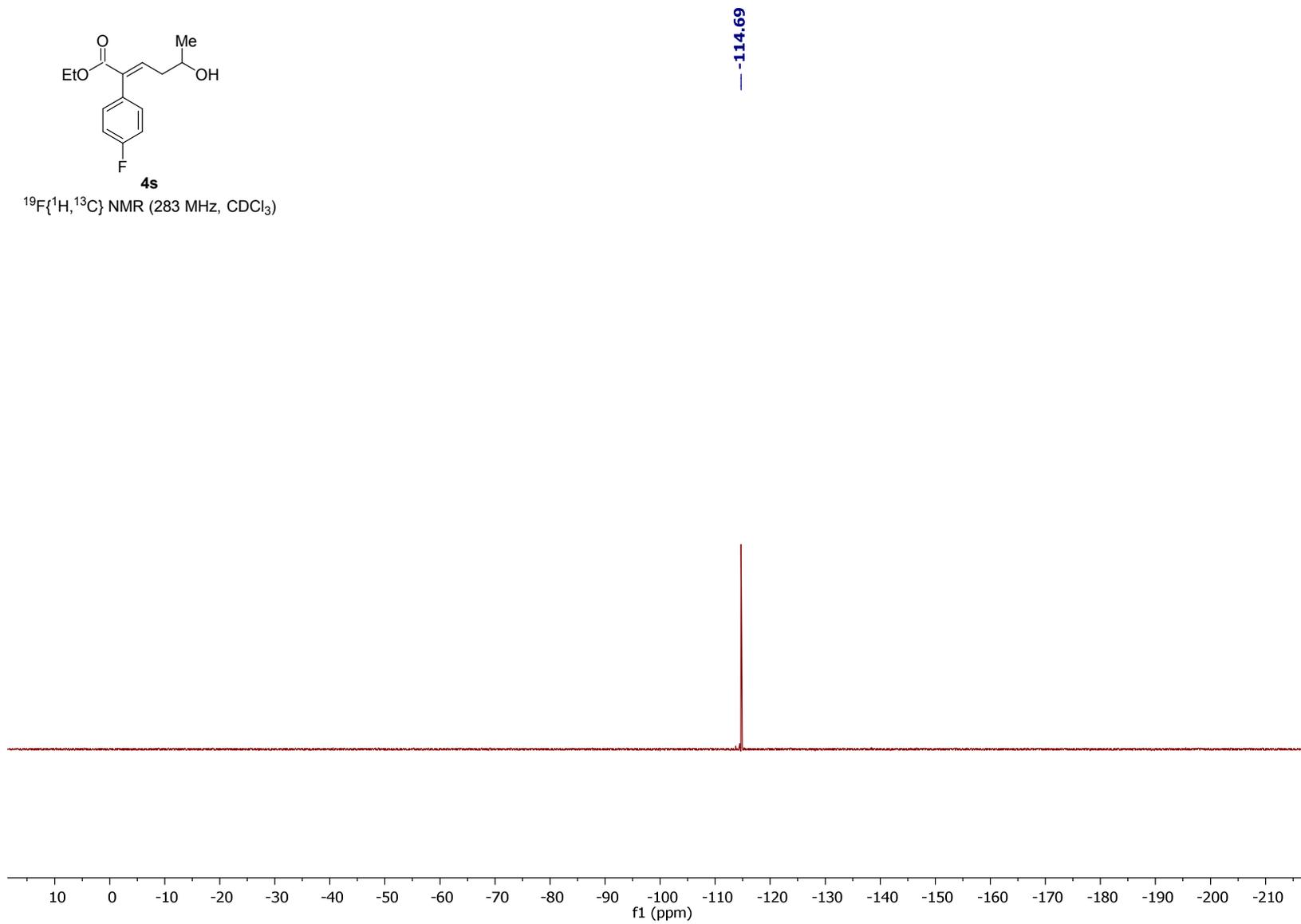


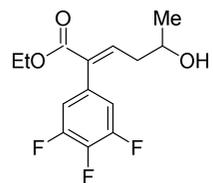




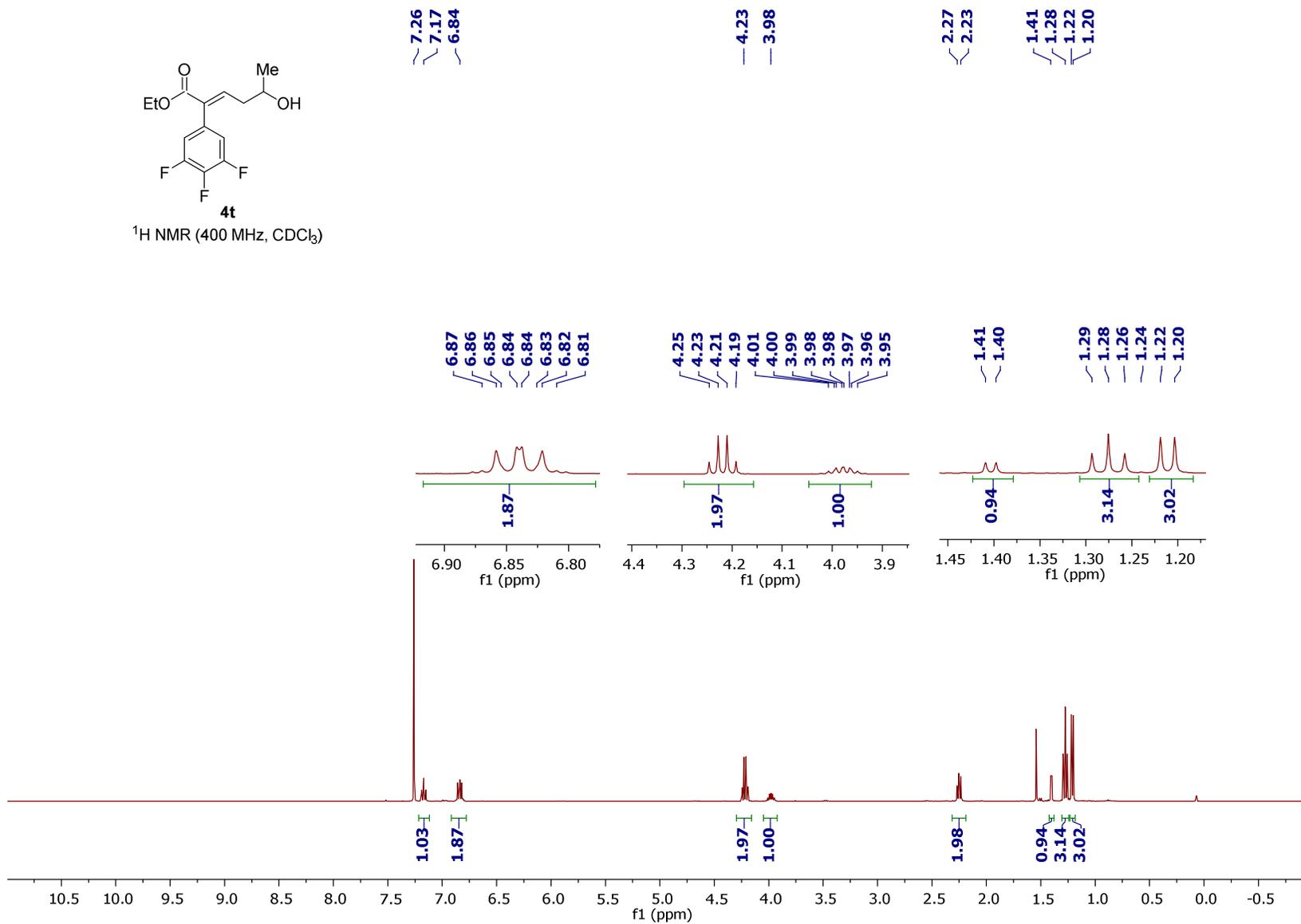
**4s**

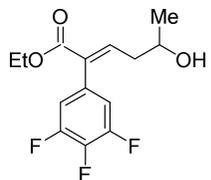
$^{19}\text{F}\{^1\text{H},^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )





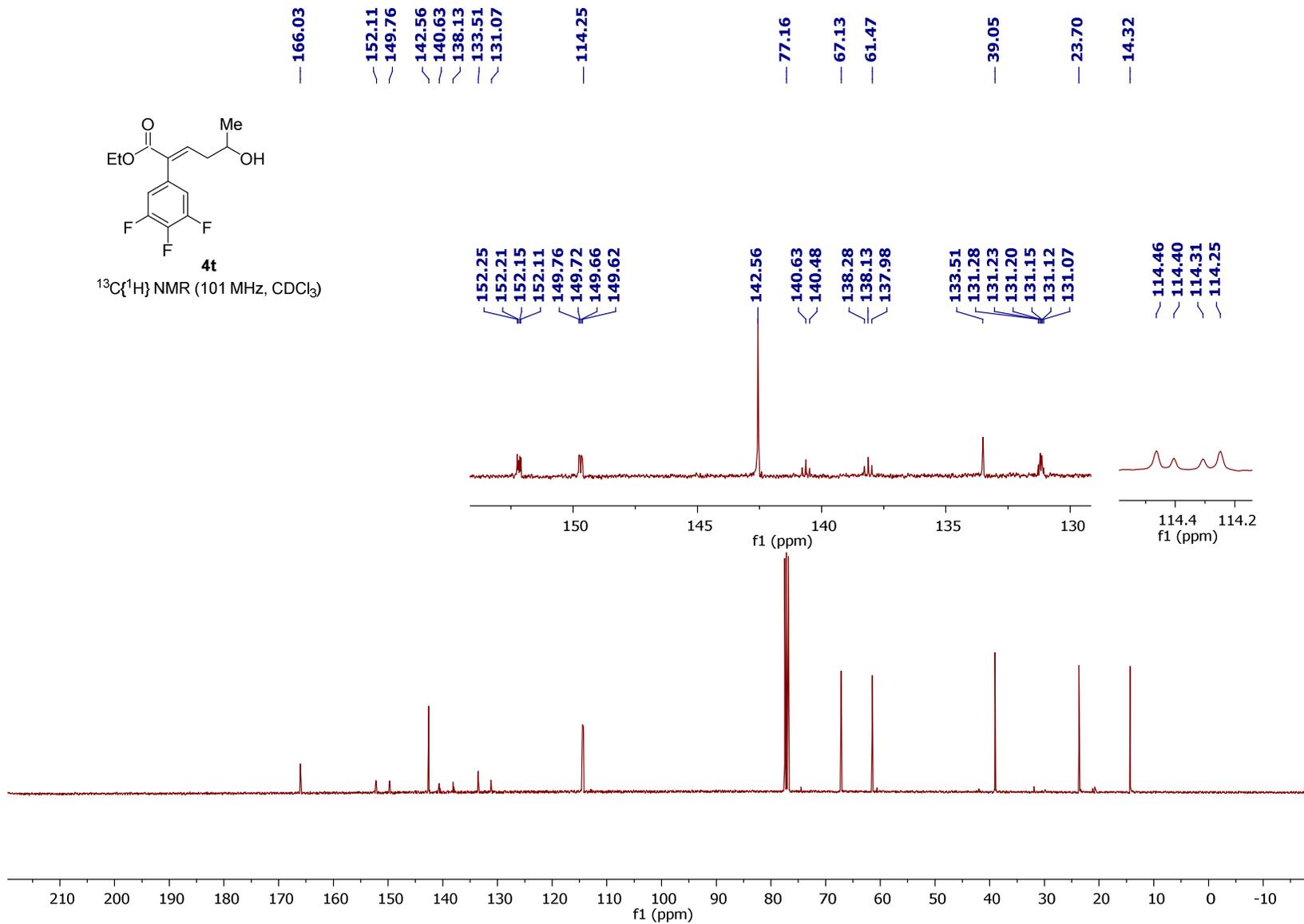
**4t**  
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

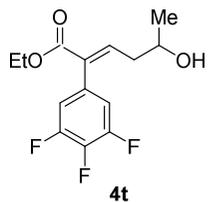




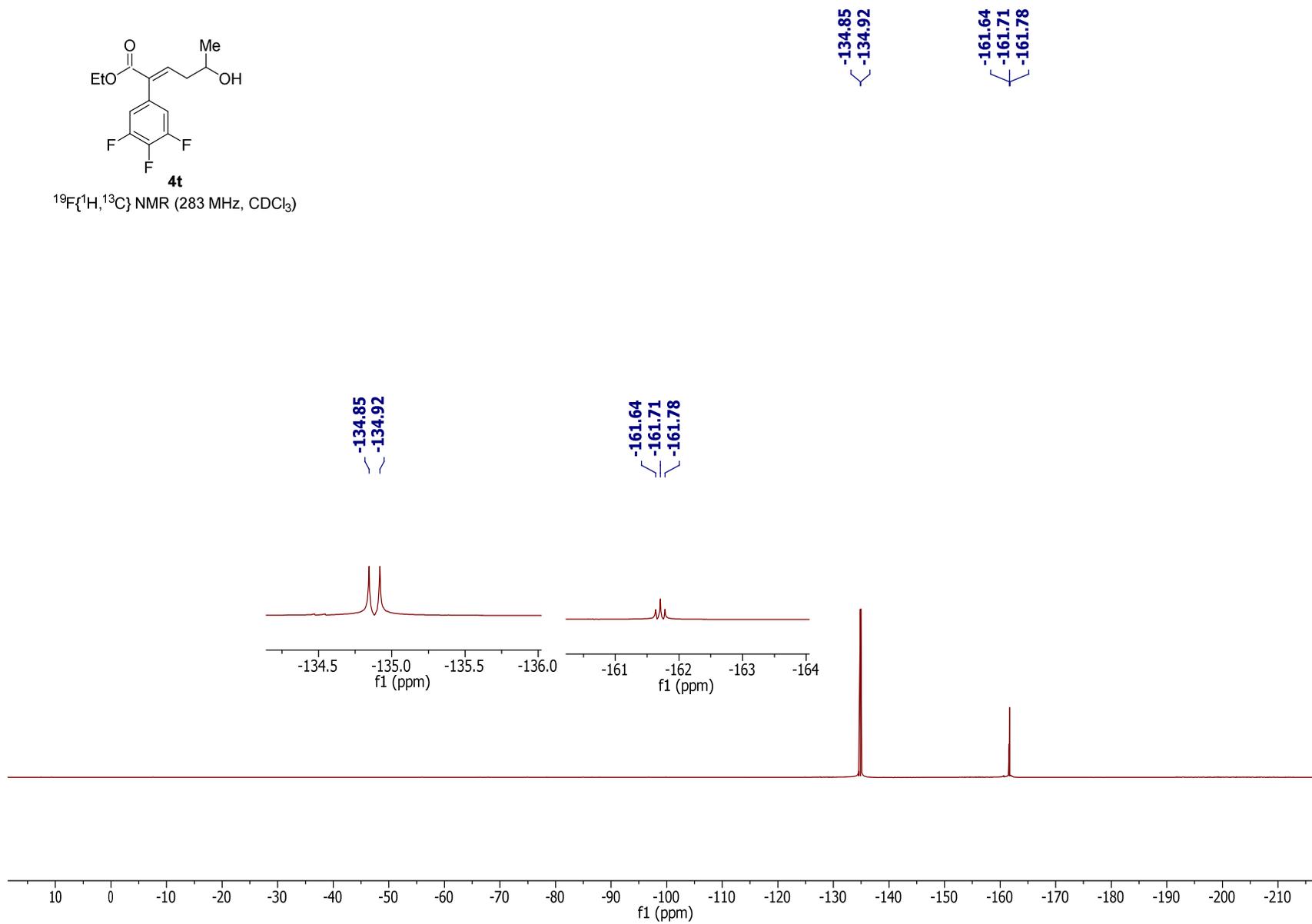
4t

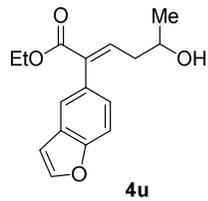
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



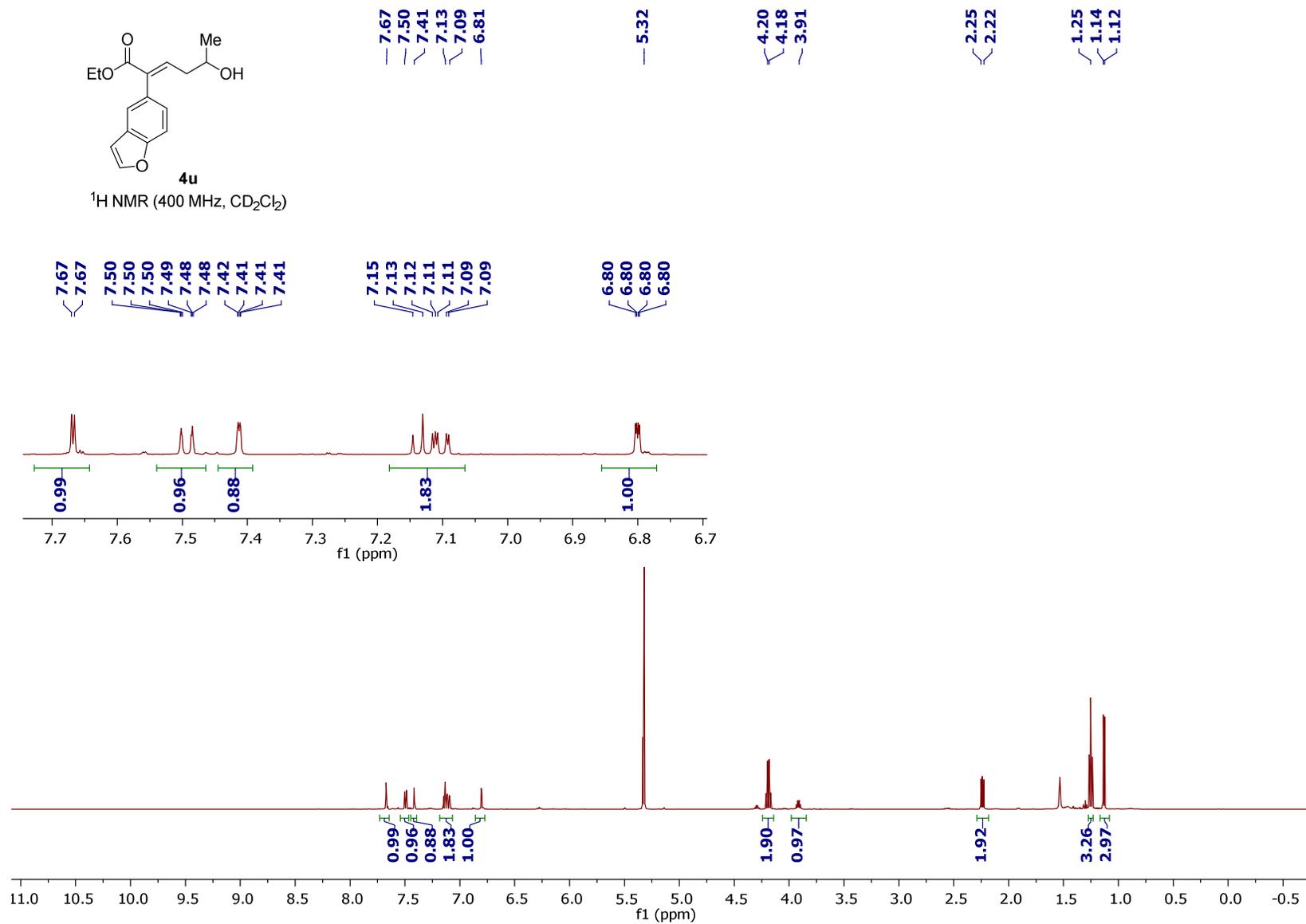


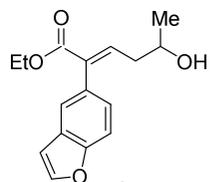
$^{19}\text{F}\{^1\text{H},^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )





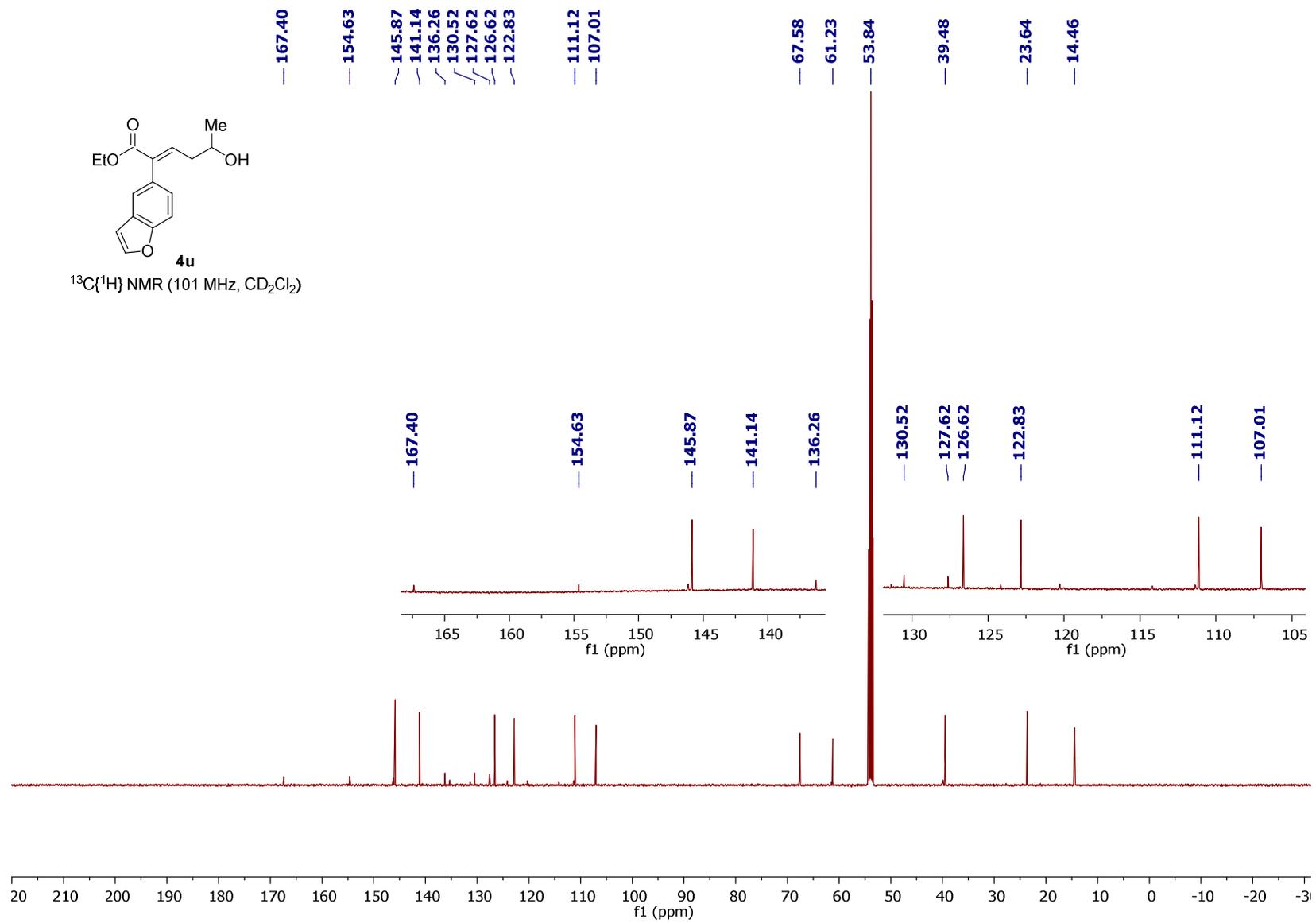
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)

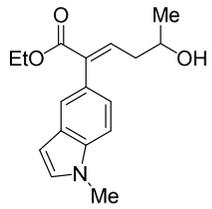




**4u**

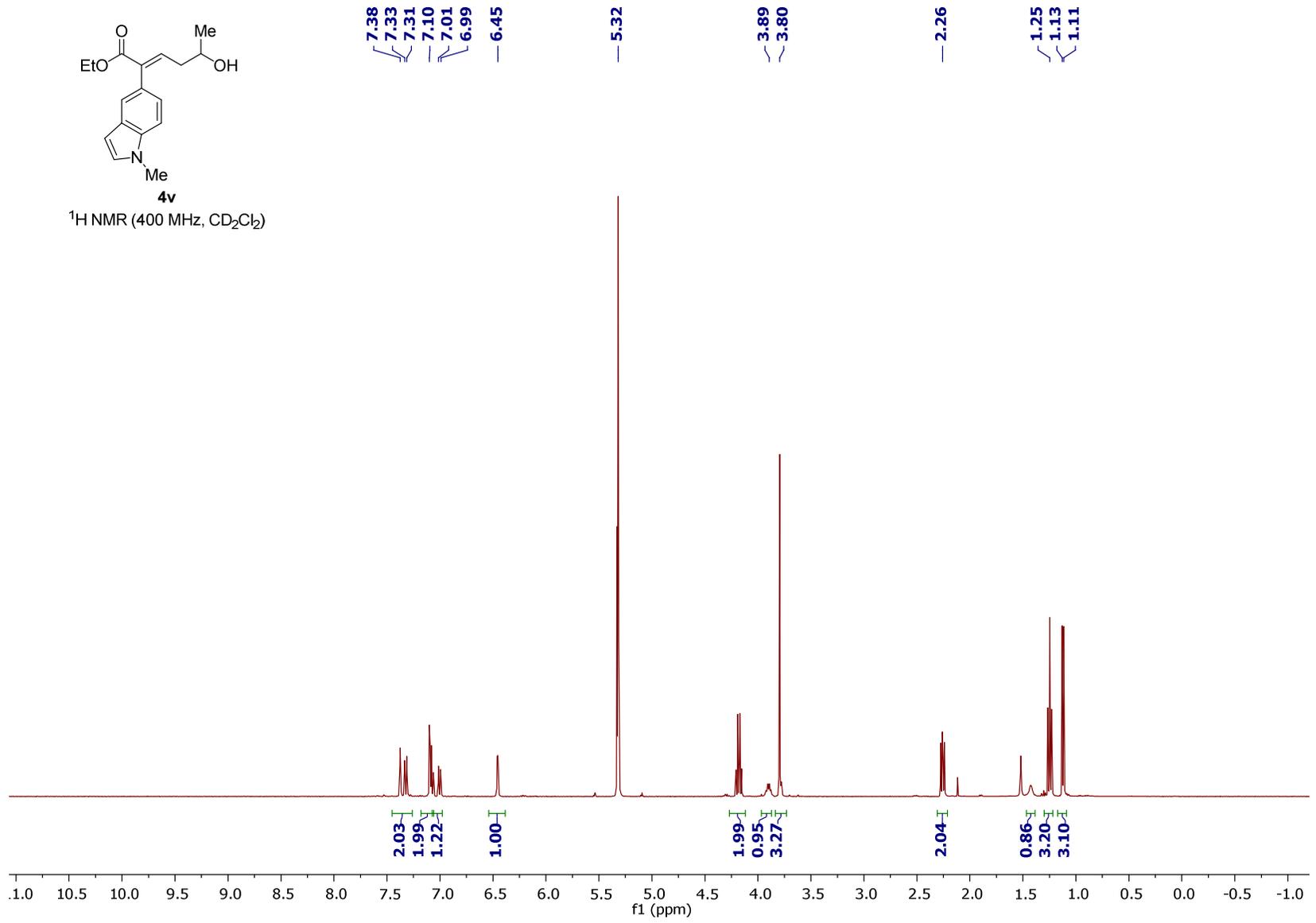
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )

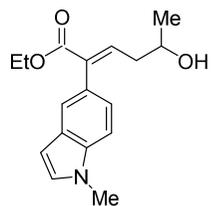




**4v**

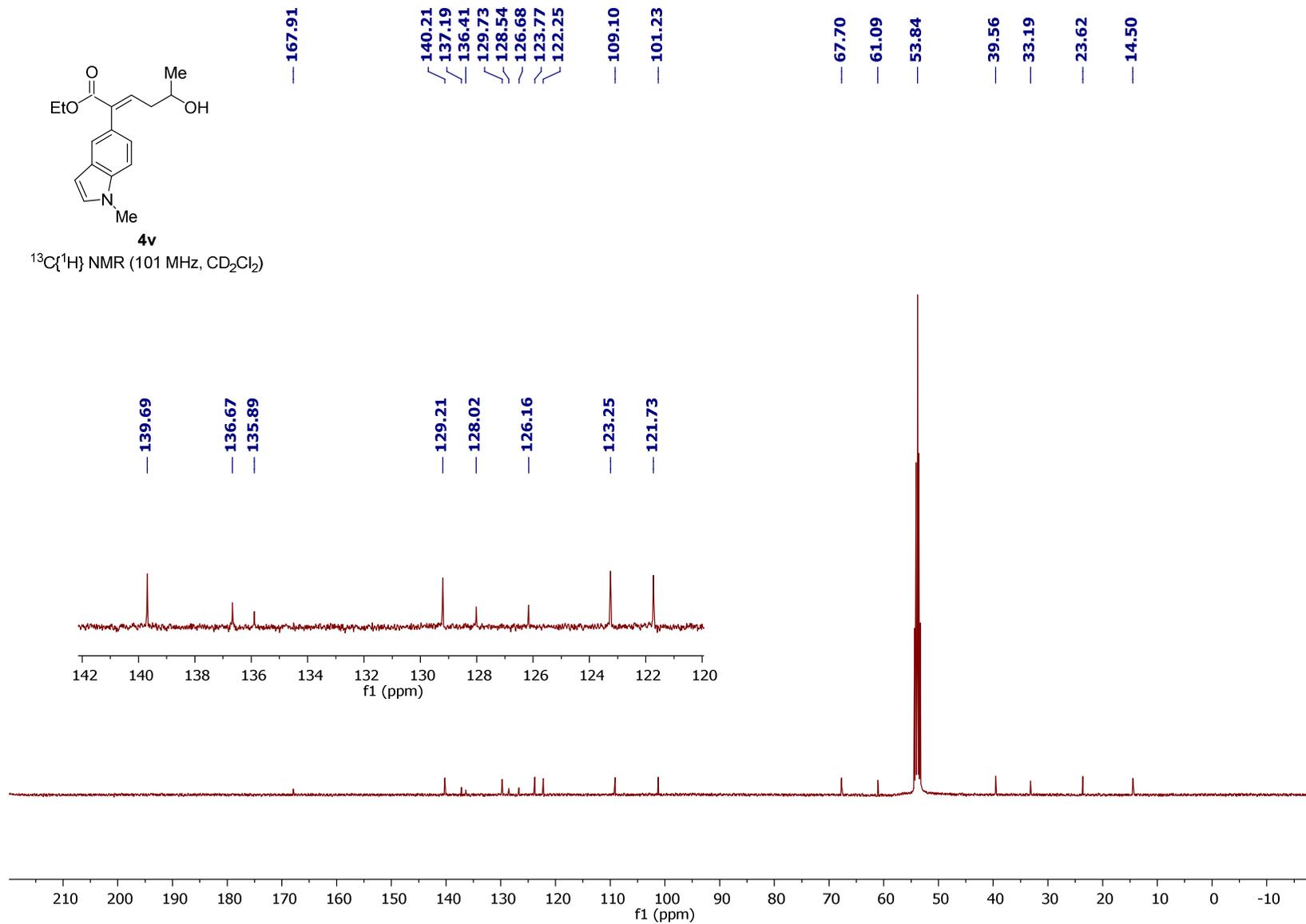
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)

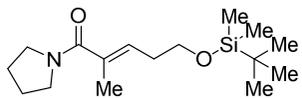




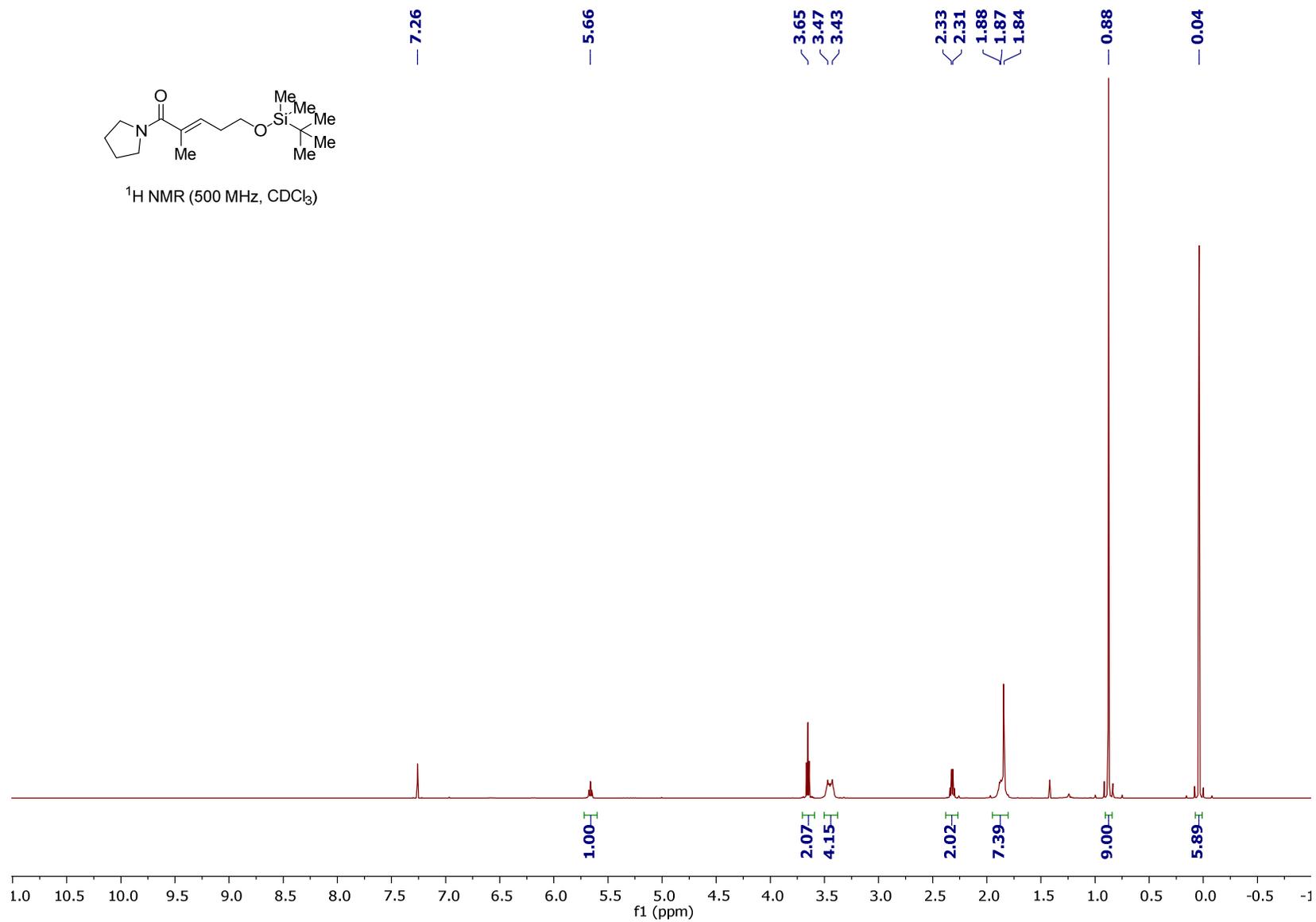
**4v**

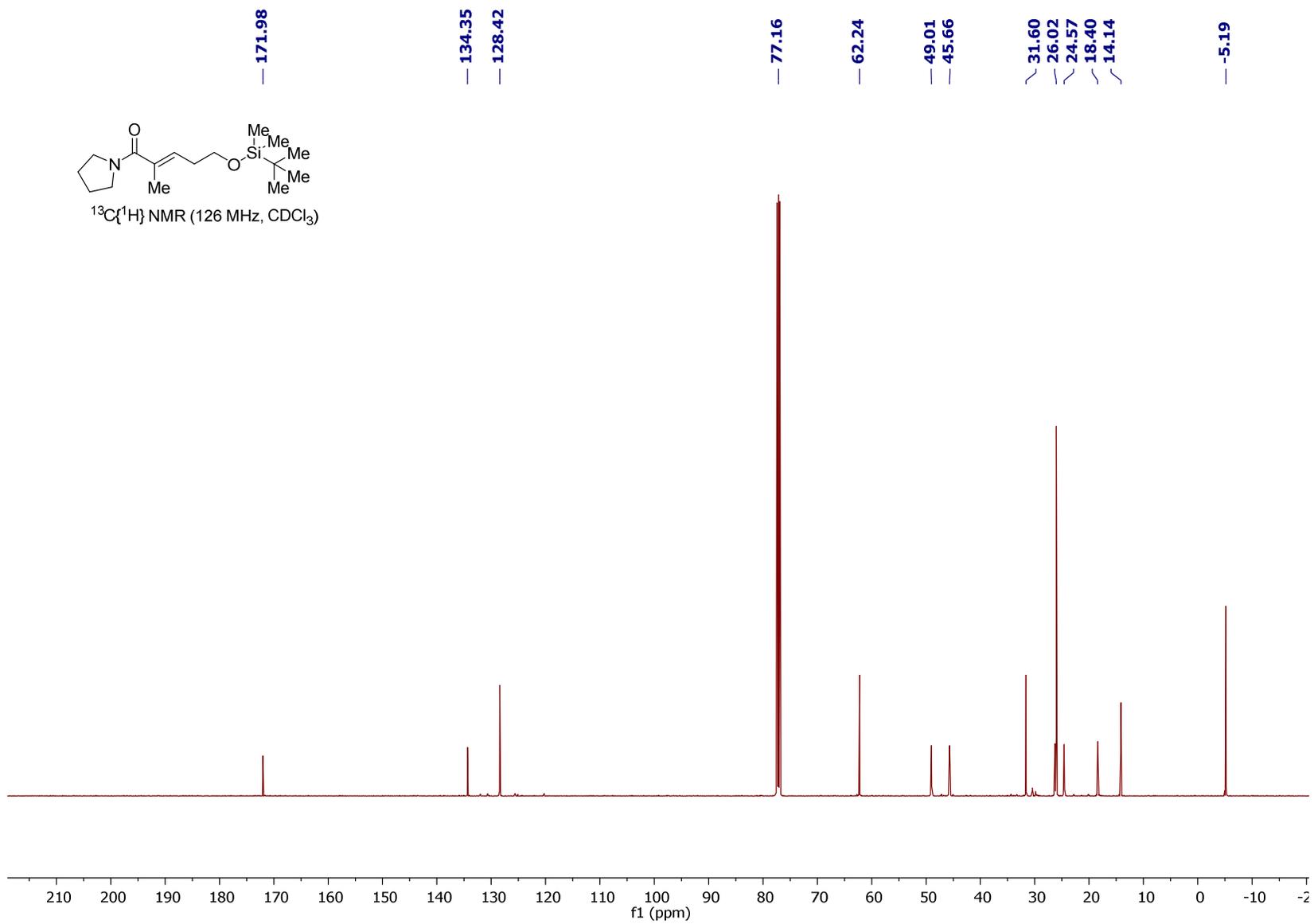
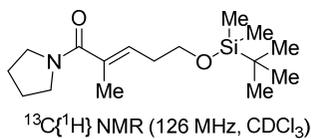
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )

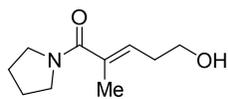




$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )

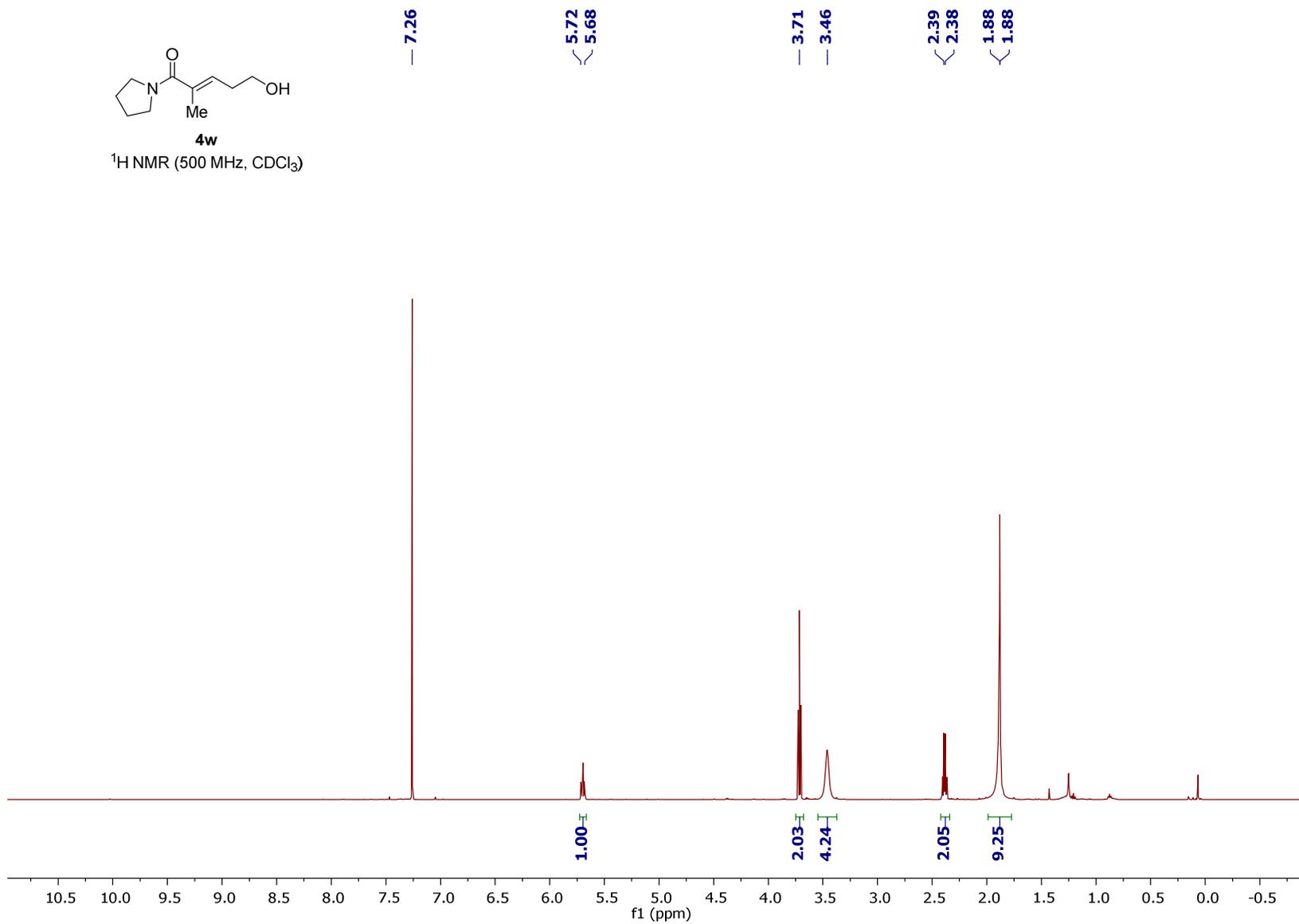


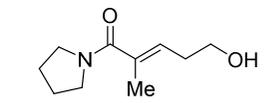




**4w**

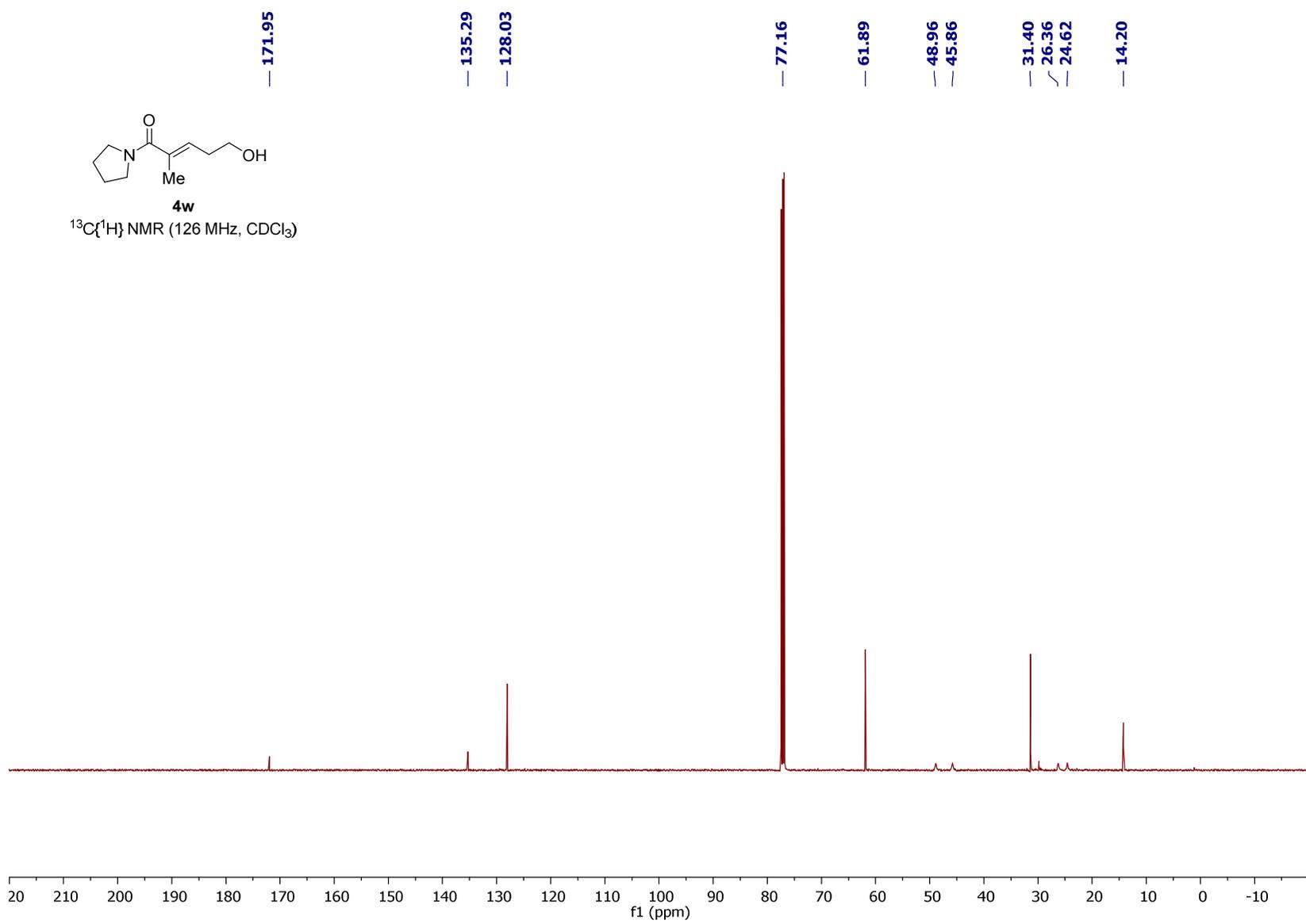
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

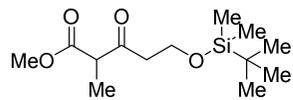




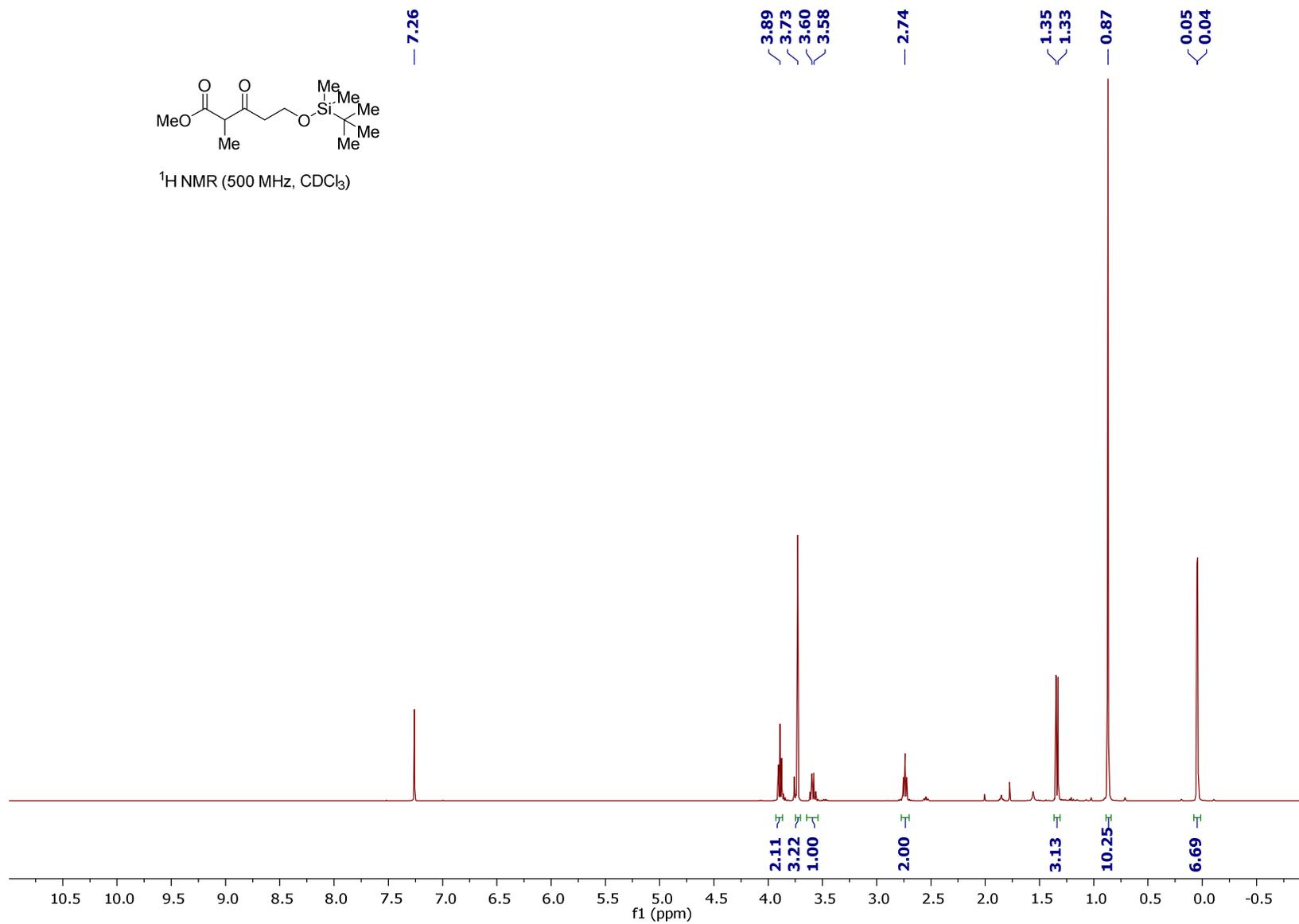
**4w**

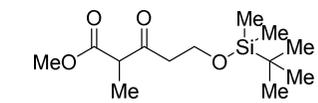
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )



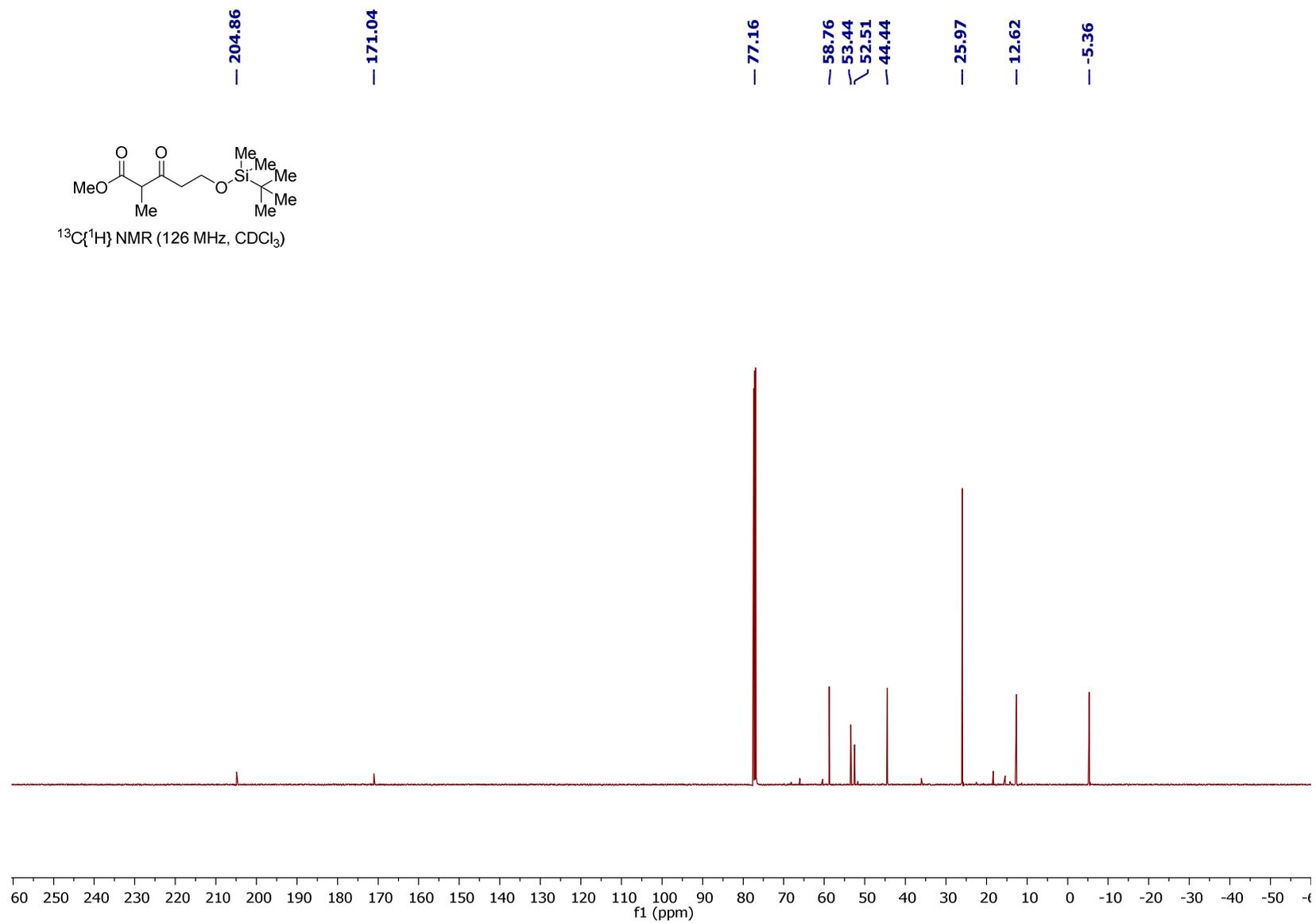


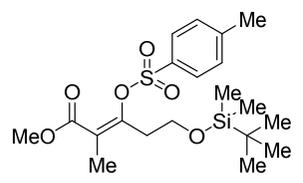
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



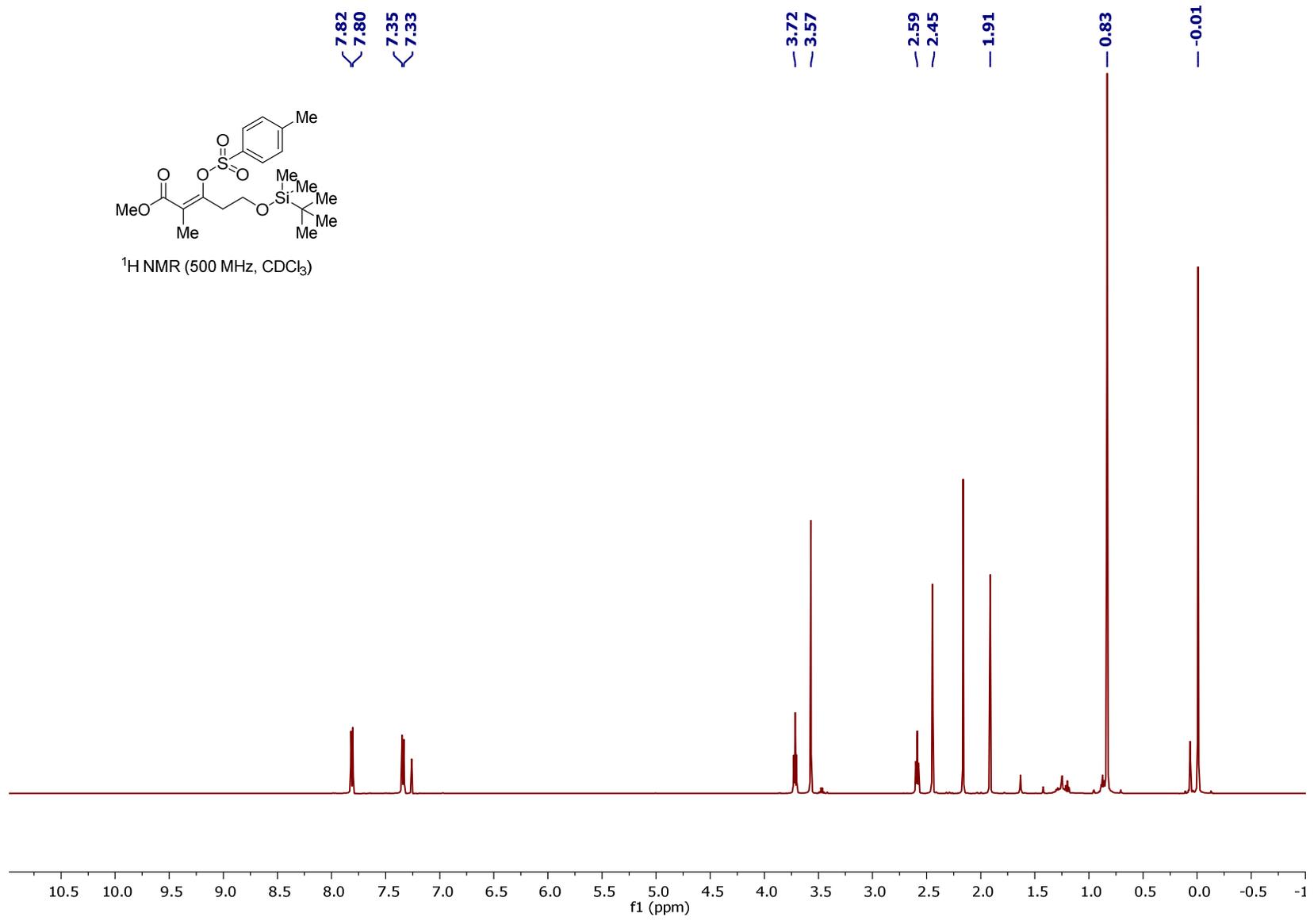


$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )





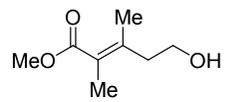
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)





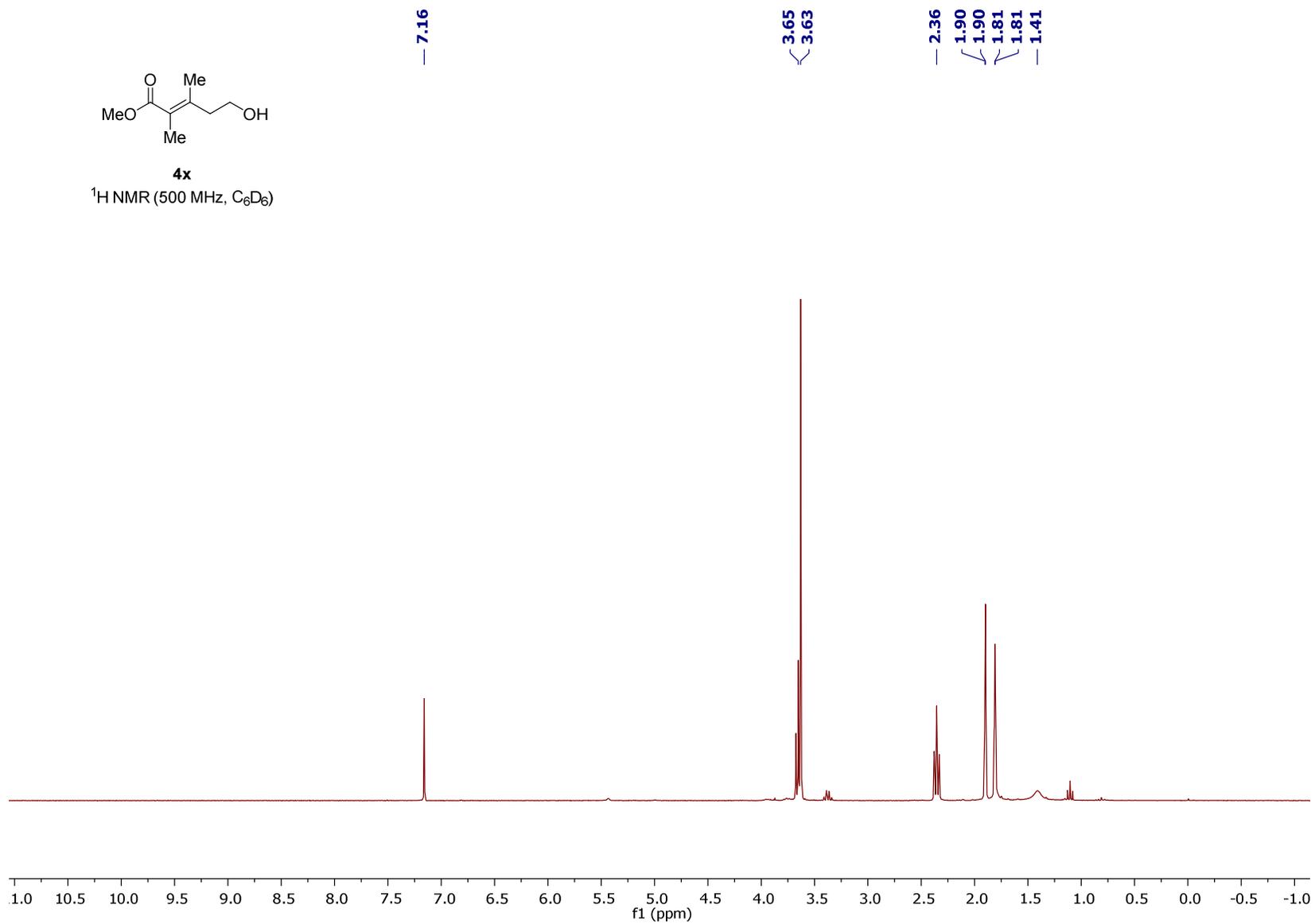


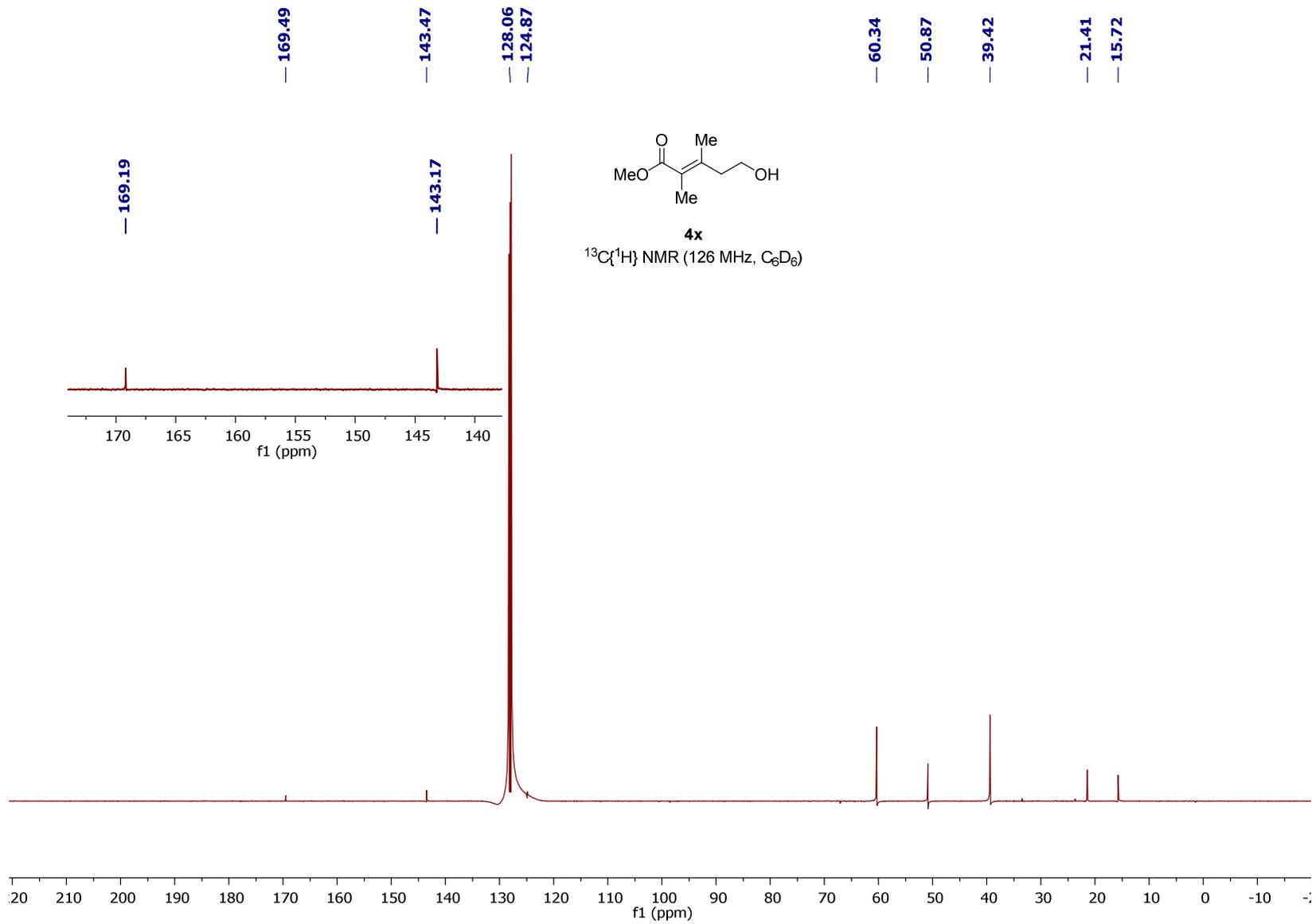


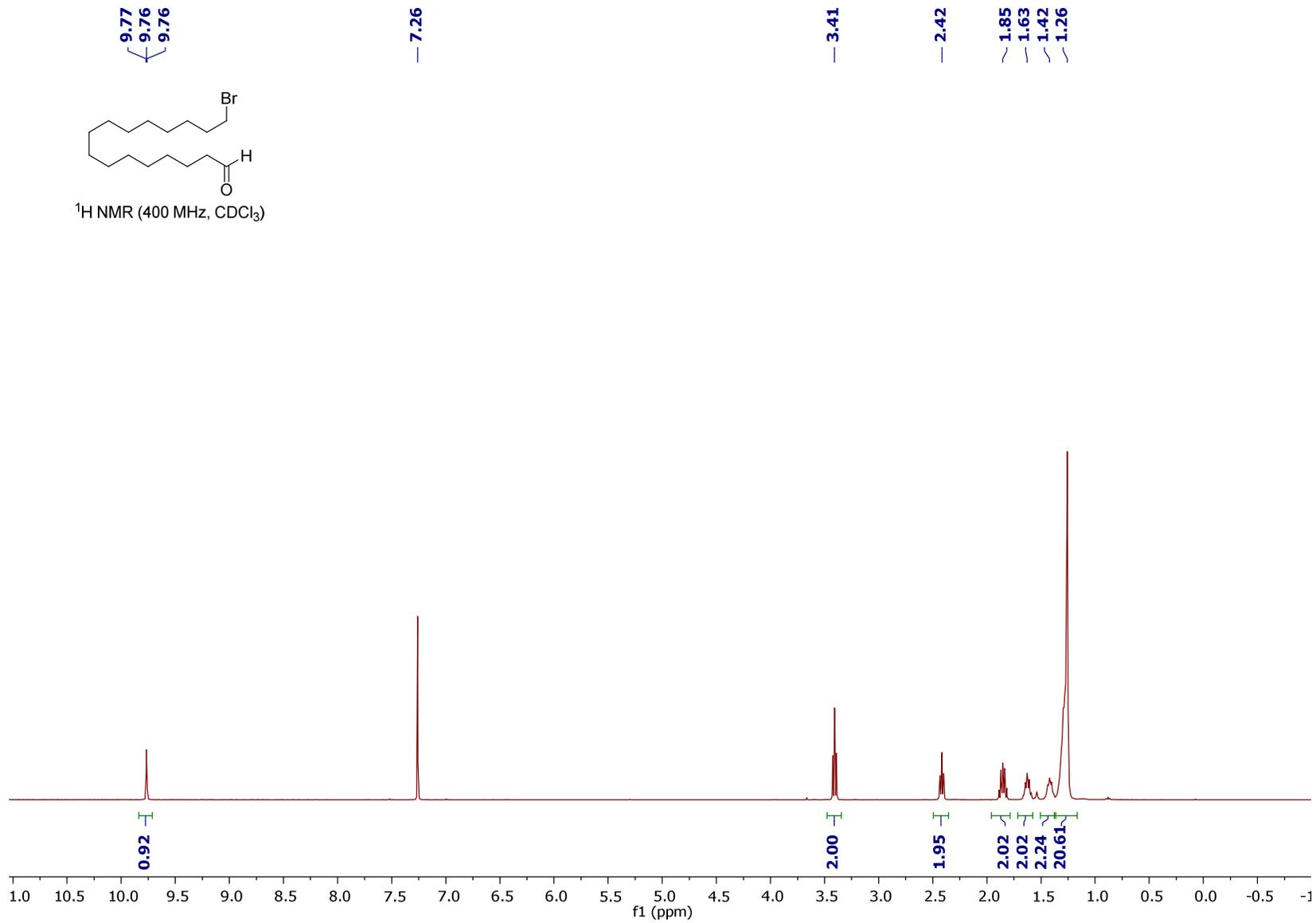
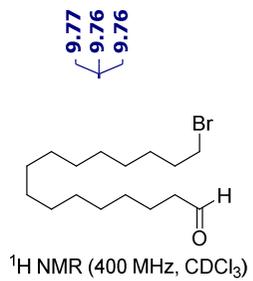


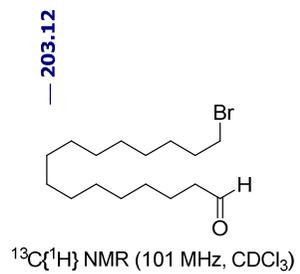
**4x**

<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>)



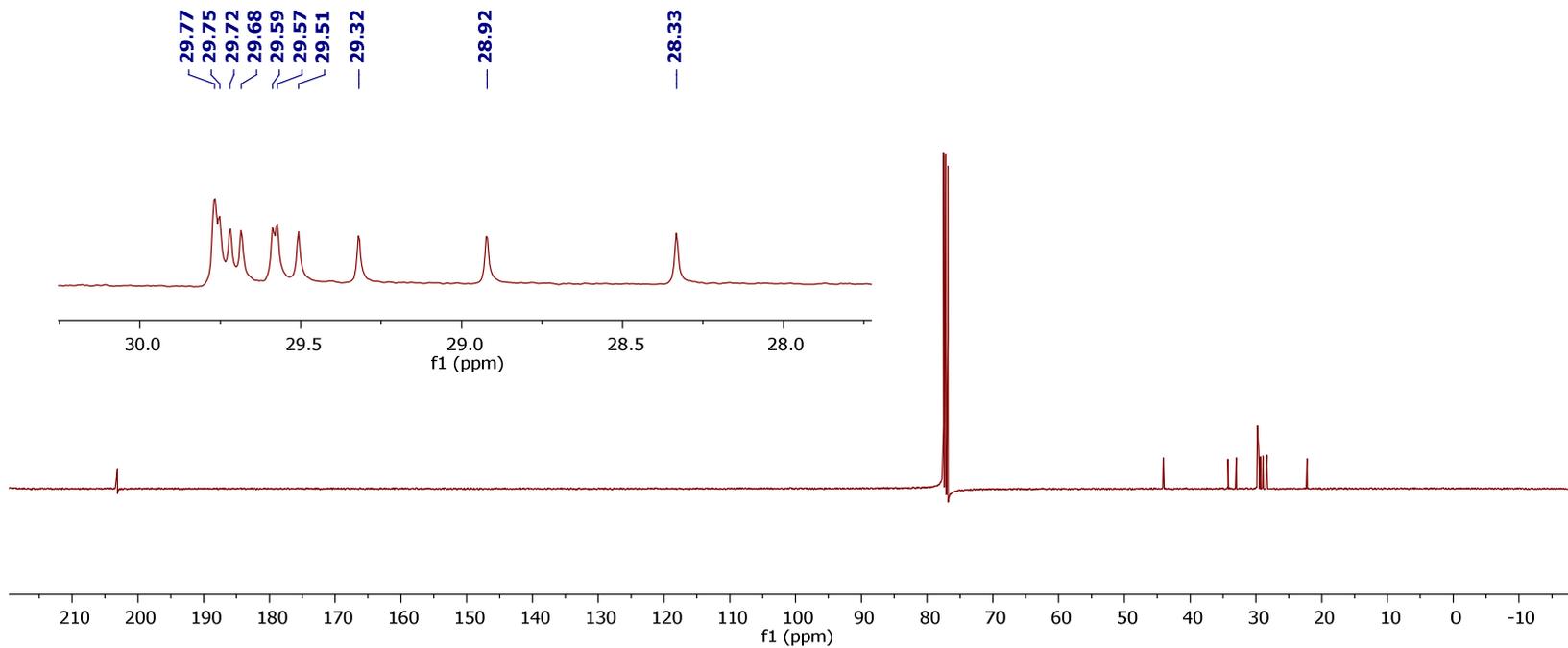


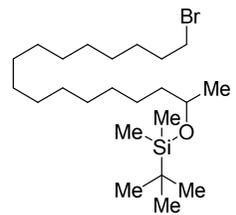




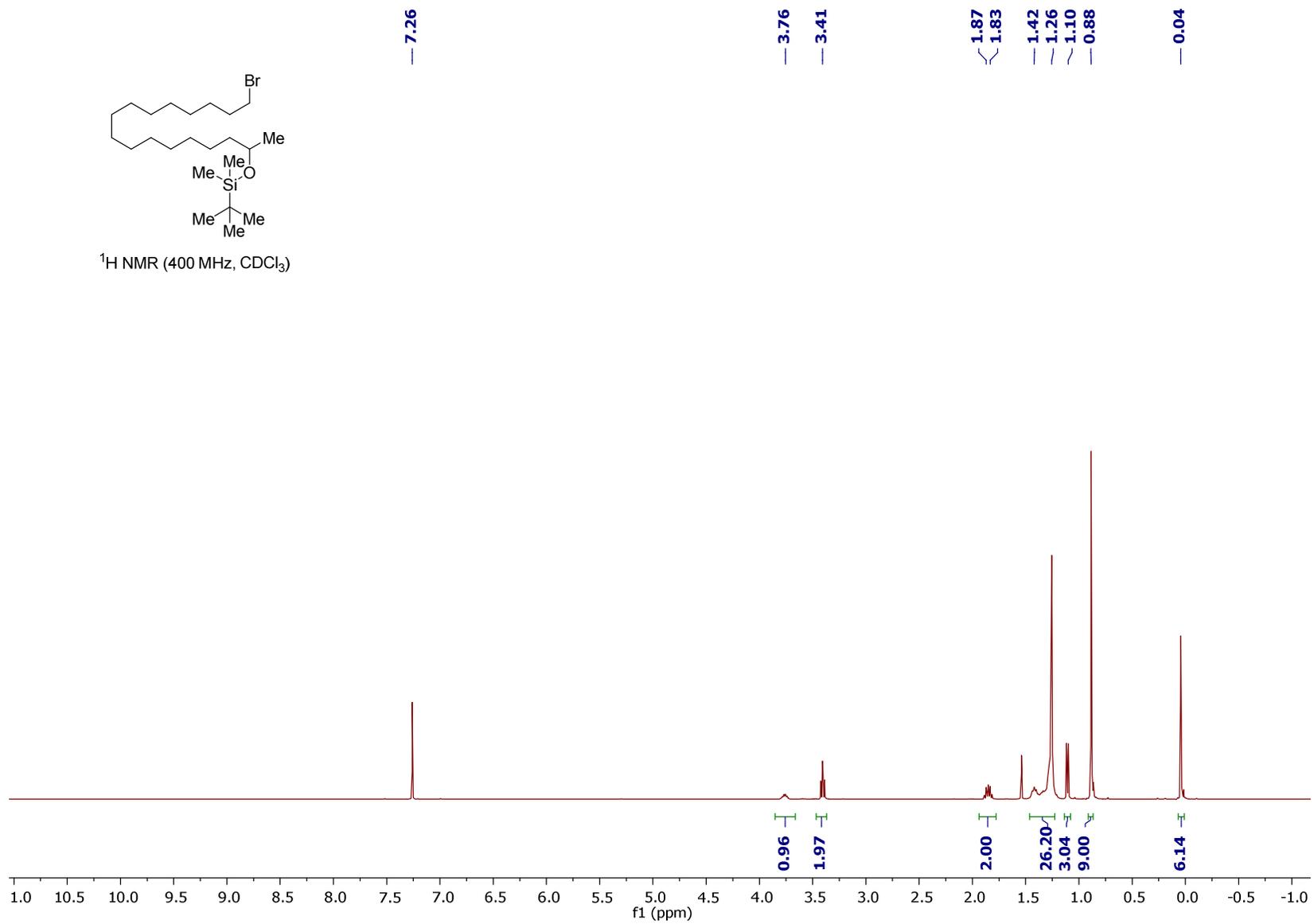
**77.16**

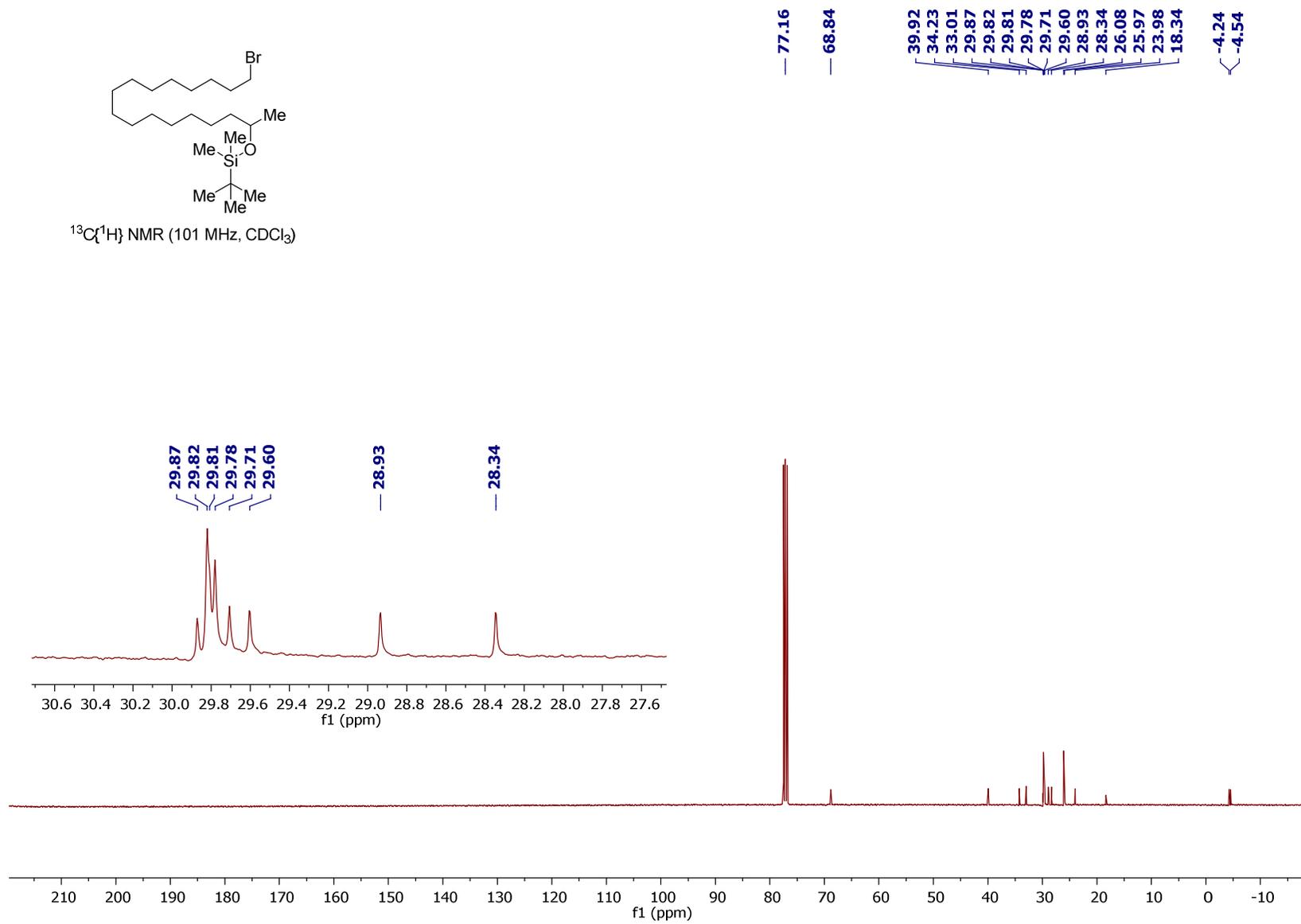
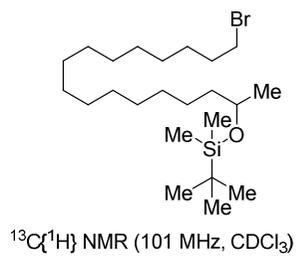
**44.08**  
**34.23**  
**32.99**  
**29.77**  
**29.75**  
**29.72**  
**29.68**  
**29.59**  
**29.57**  
**29.51**  
**29.32**  
**28.92**  
**28.33**  
**22.24**

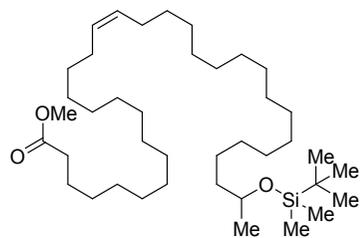




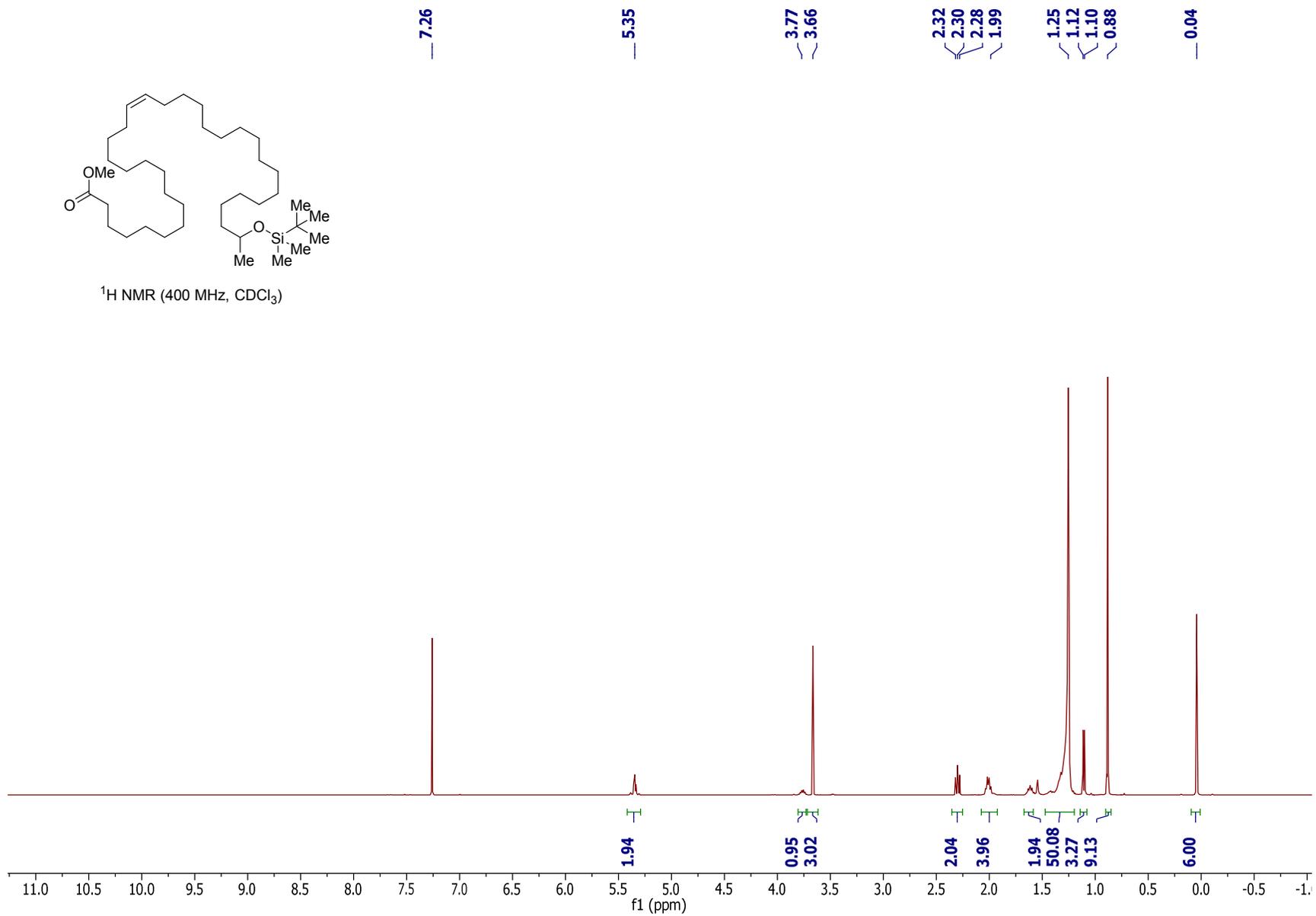
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

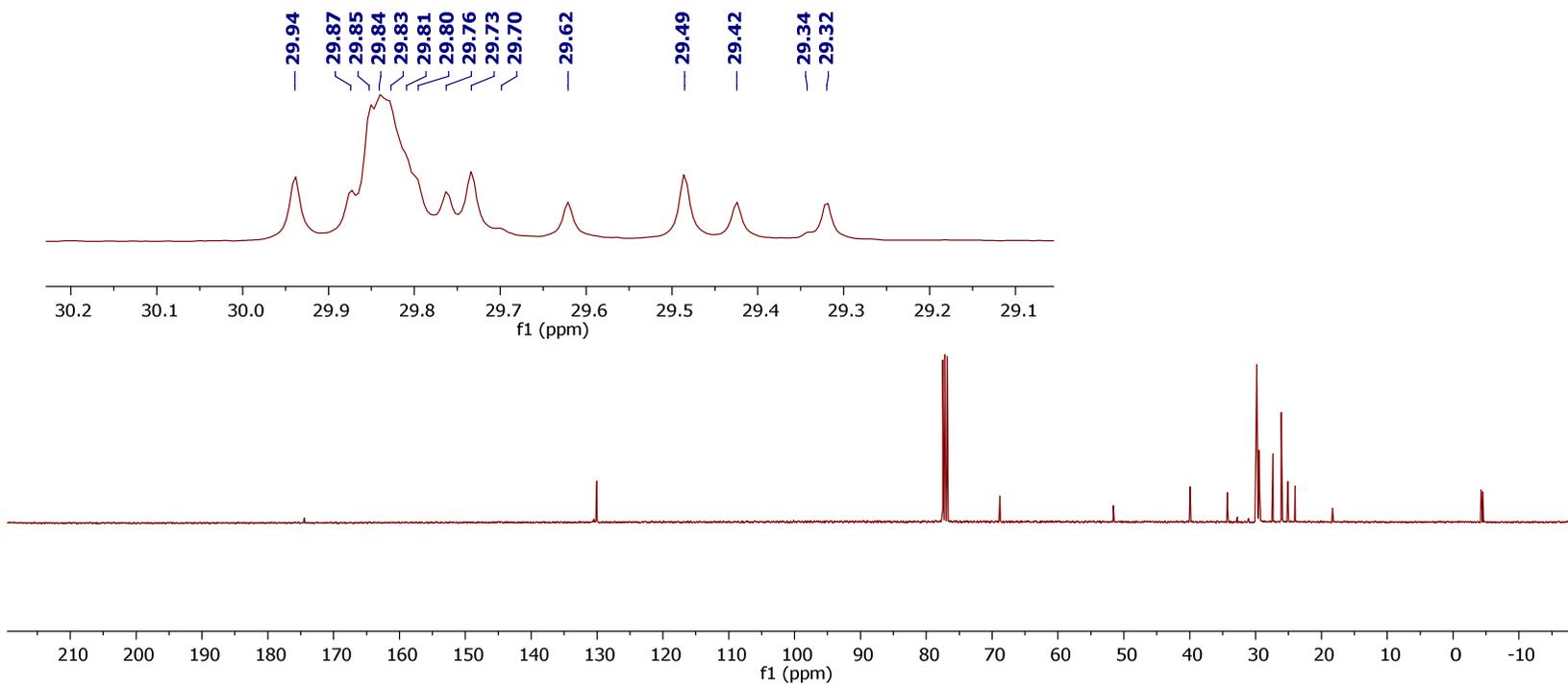
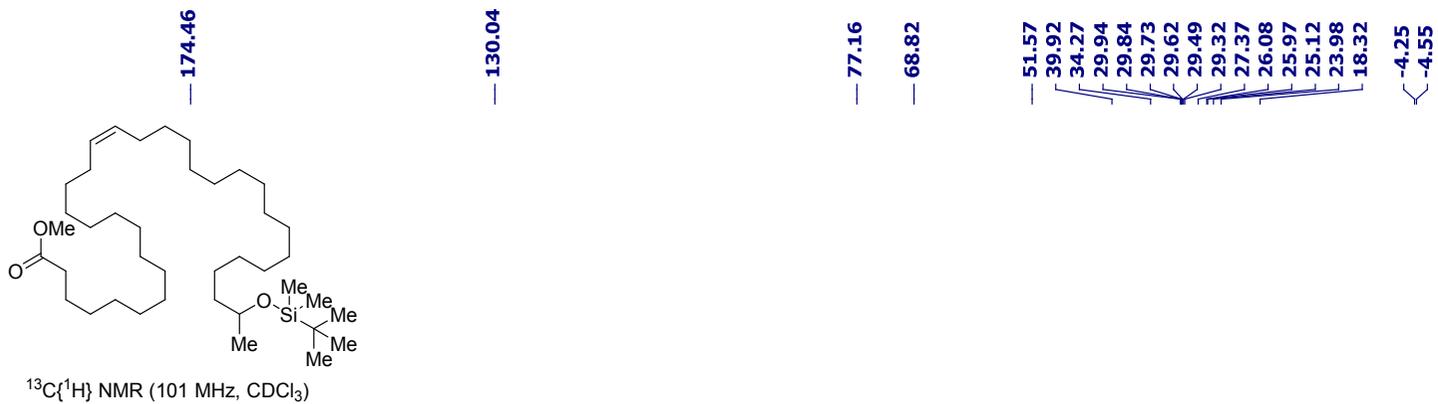


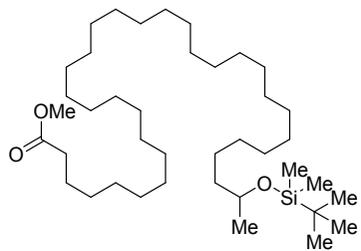




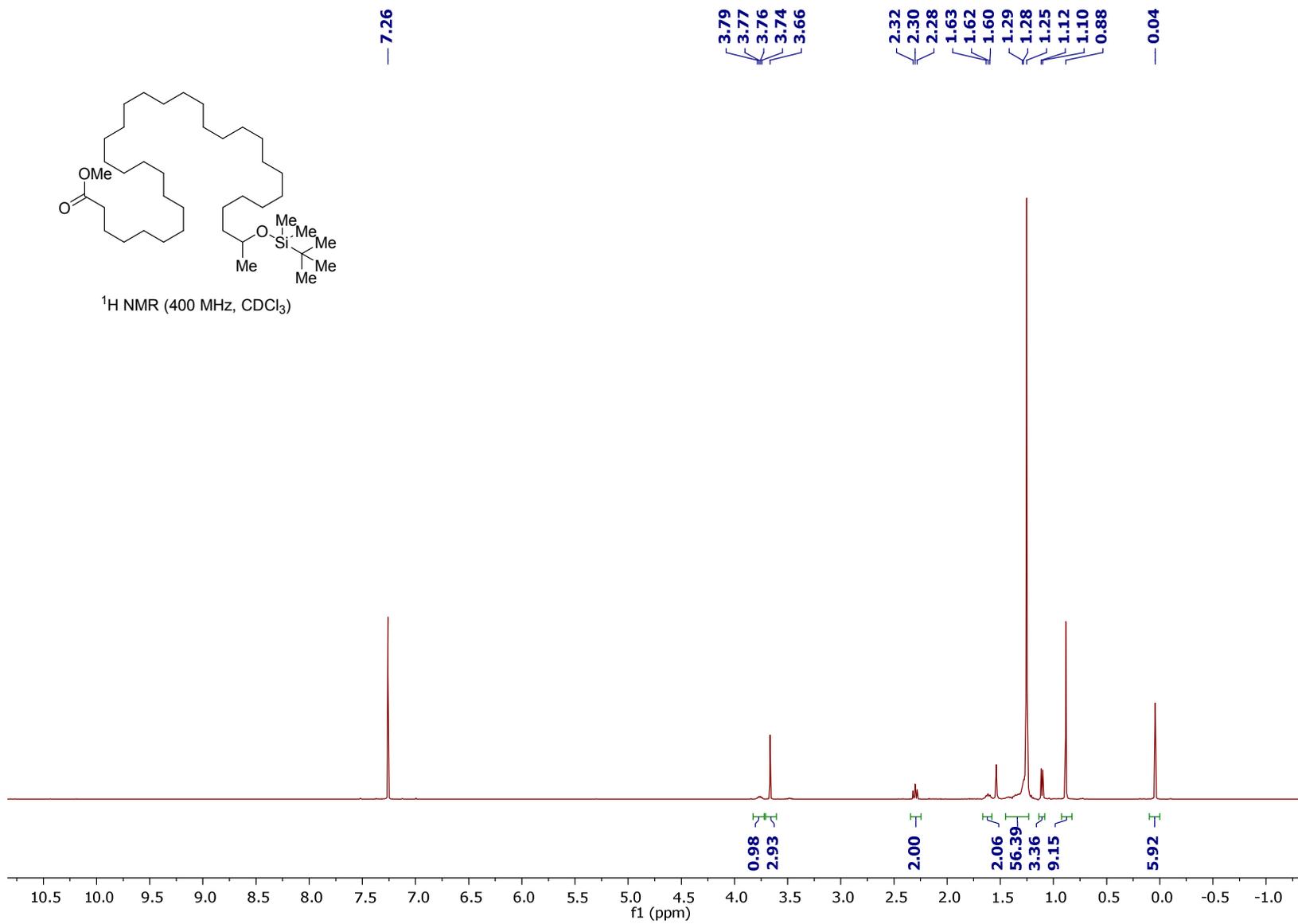
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

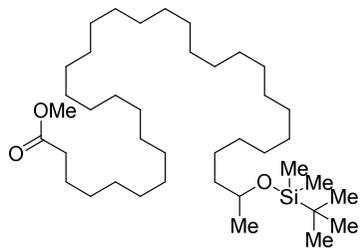




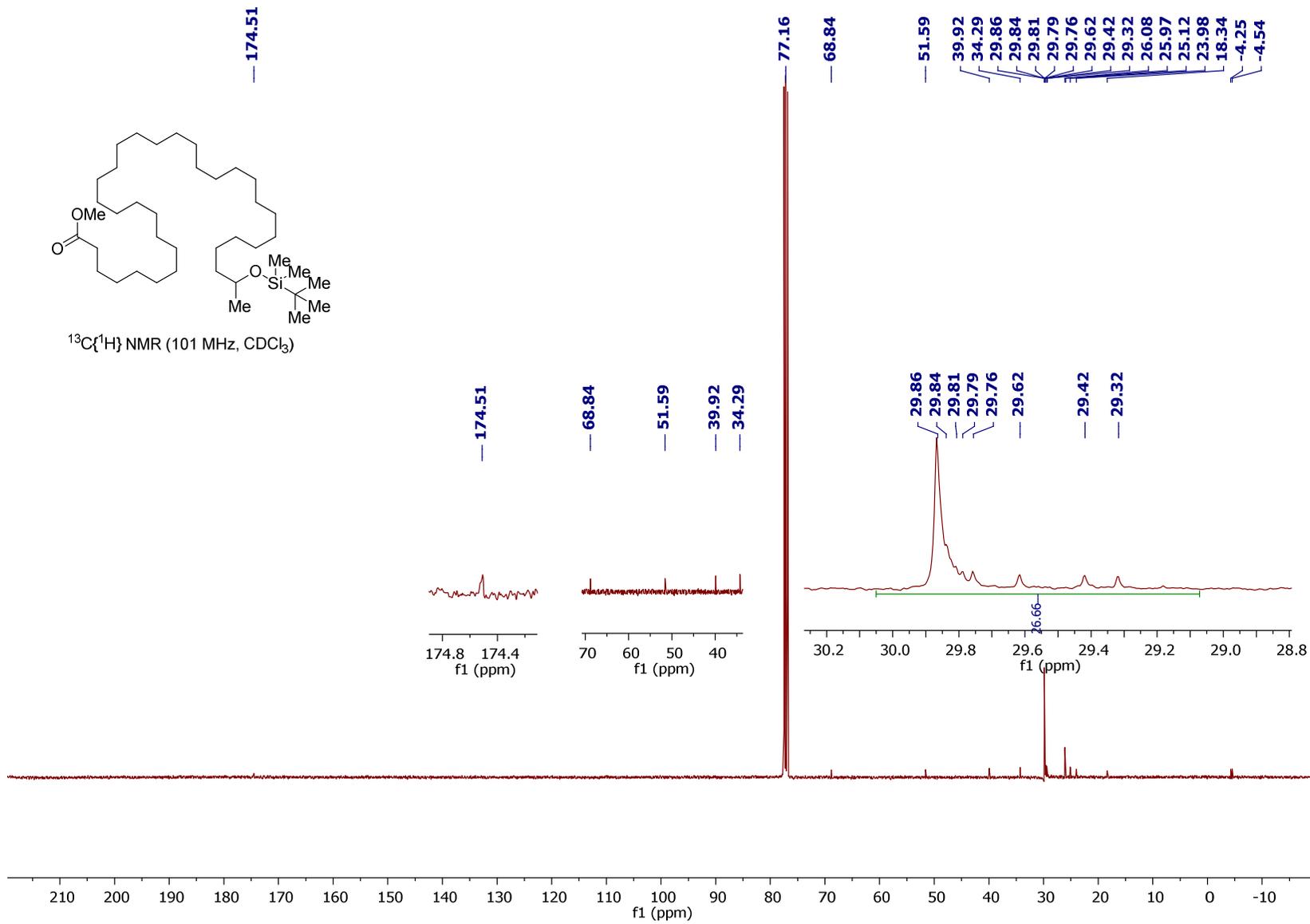


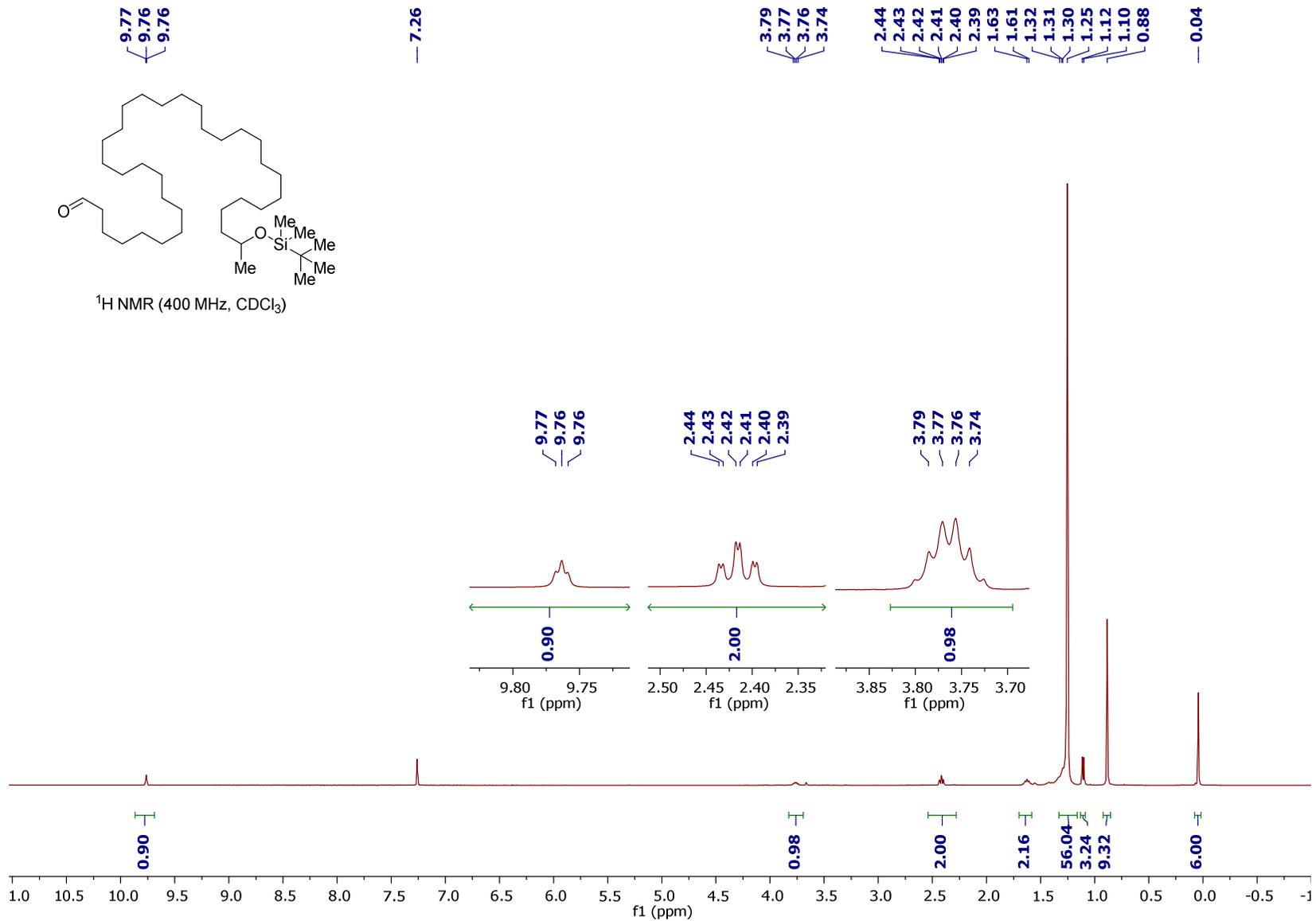
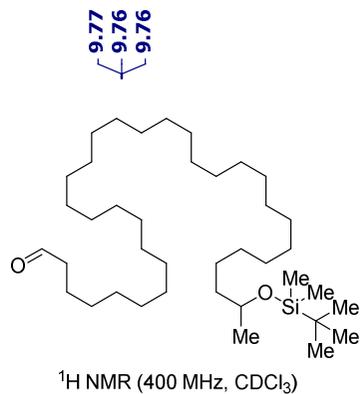
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

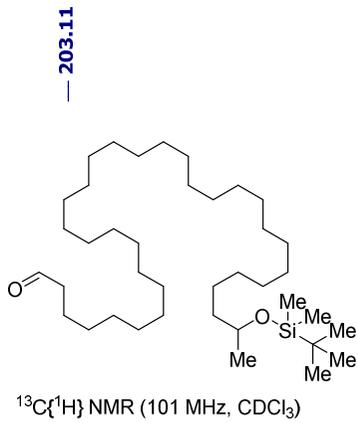




<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)

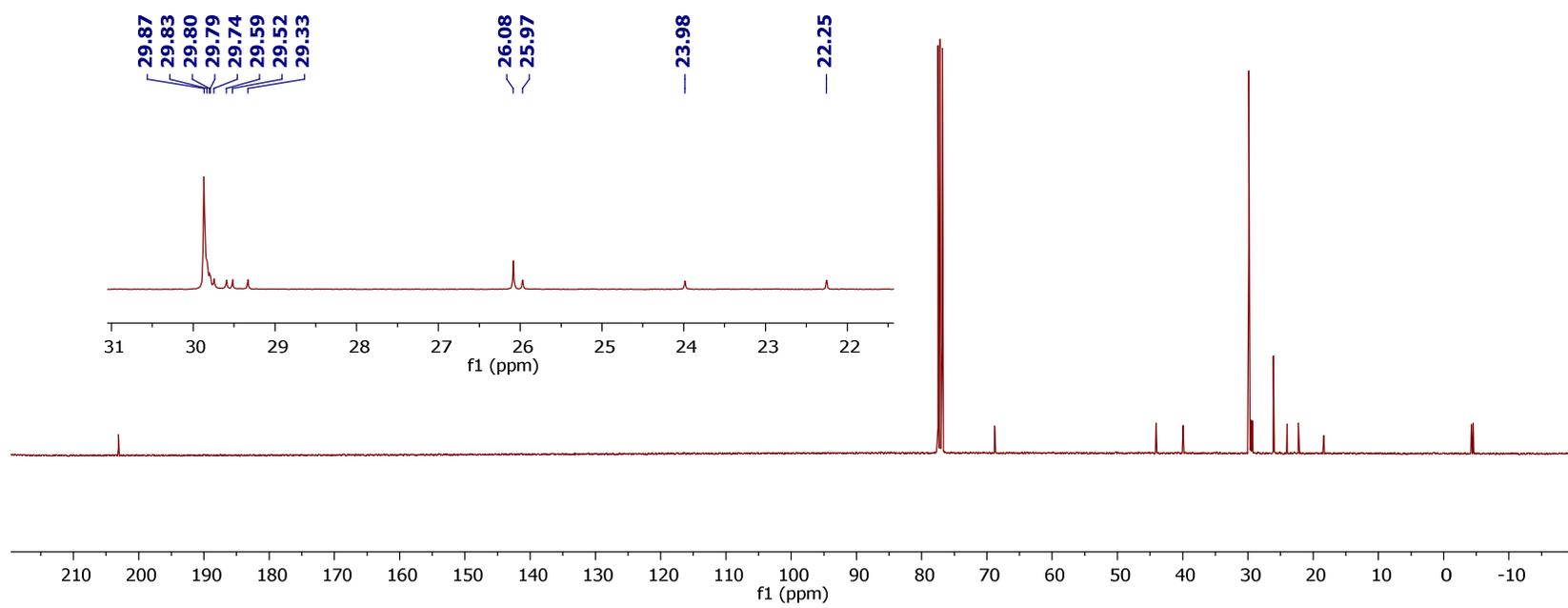


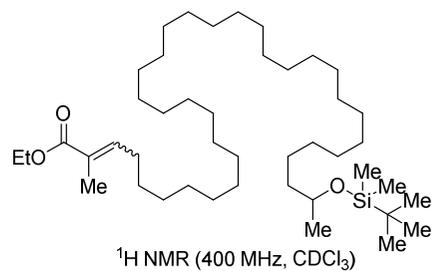




— 77.16 — 68.84

— 44.08 — 39.92 — 29.87 — 29.83 — 29.80 — 29.79 — 29.74 — 29.59 — 29.52 — 29.33 — 26.08 — 23.98 — 22.25 — 18.34 — 4.24 — 4.54





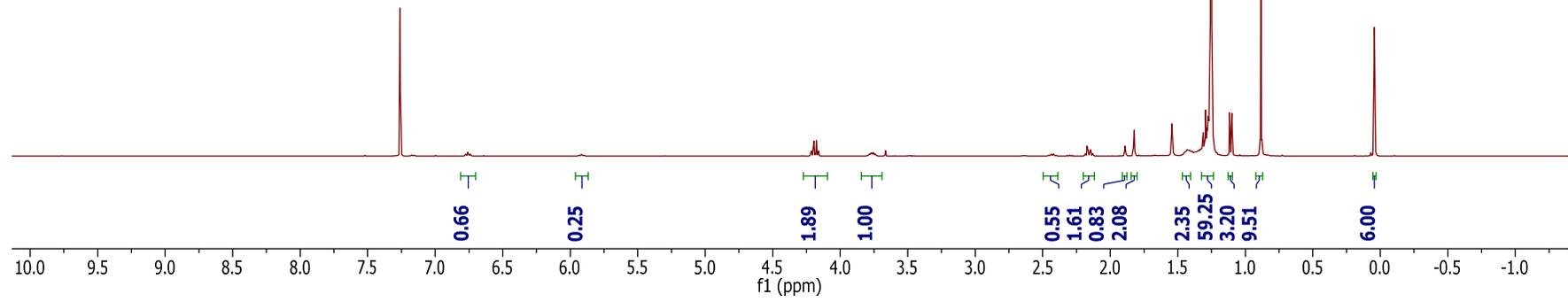
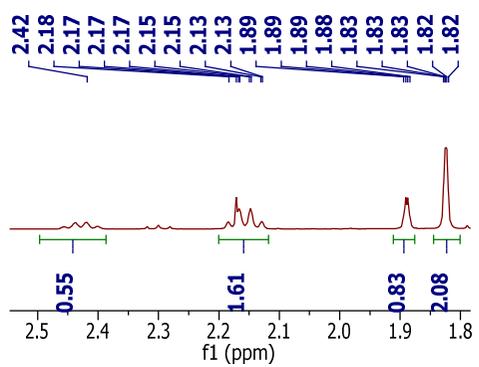
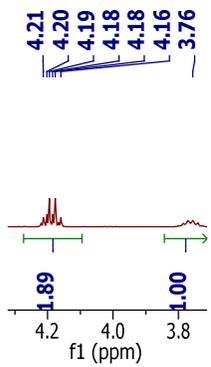
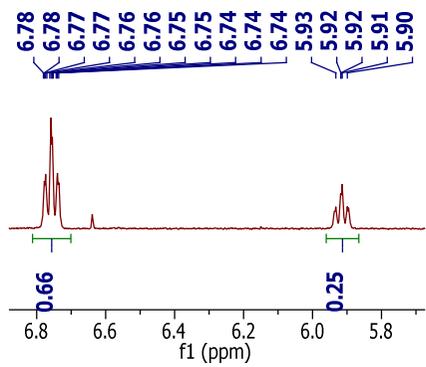
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7.00  
6.78

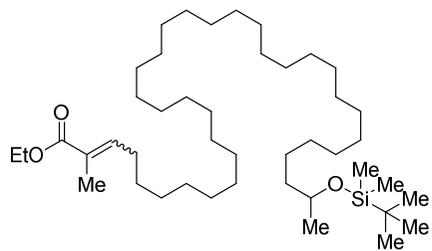
5.92  
5.92

4.19  
3.77

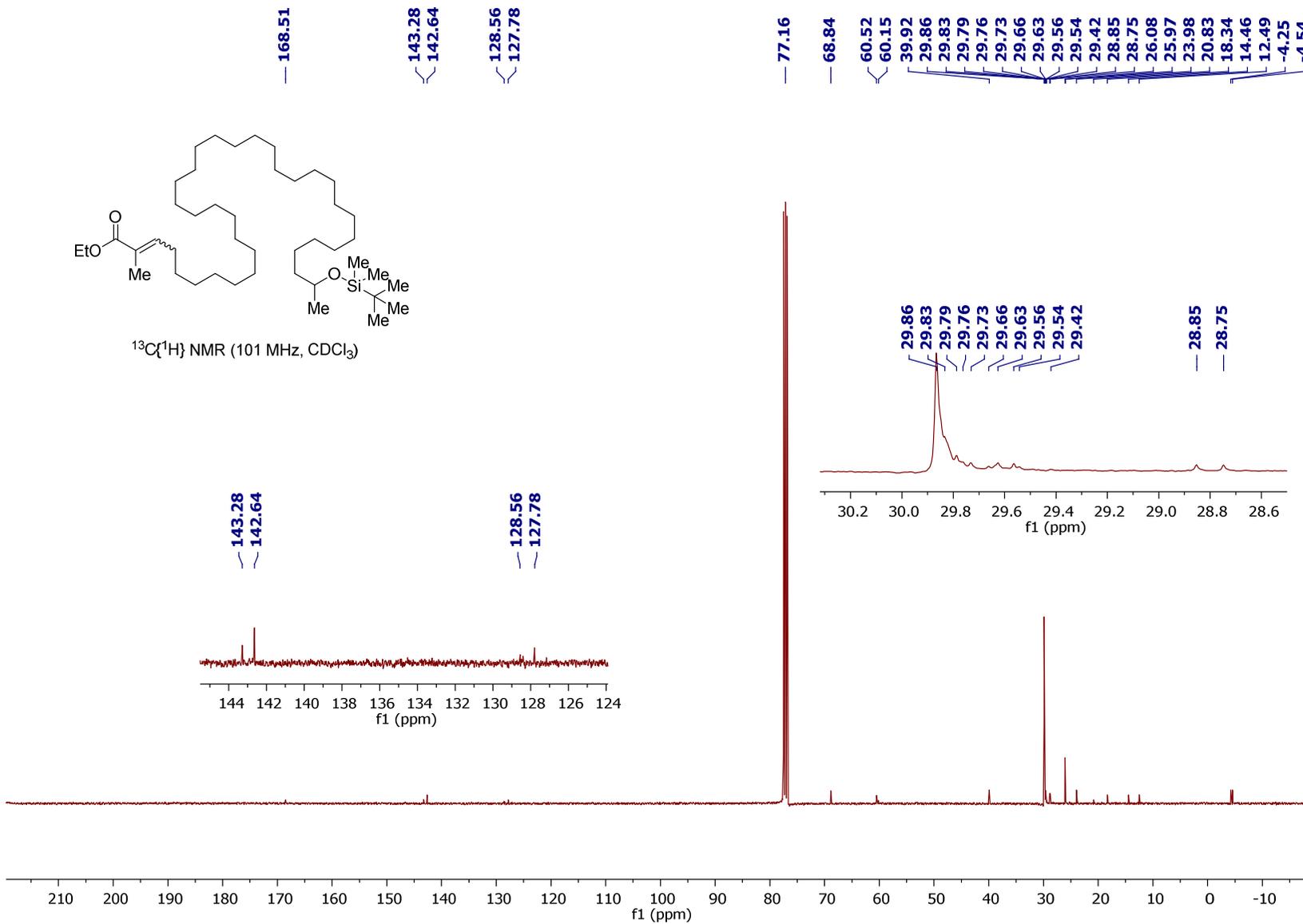
2.17  
1.89  
1.83  
1.54  
1.25  
1.12  
0.88

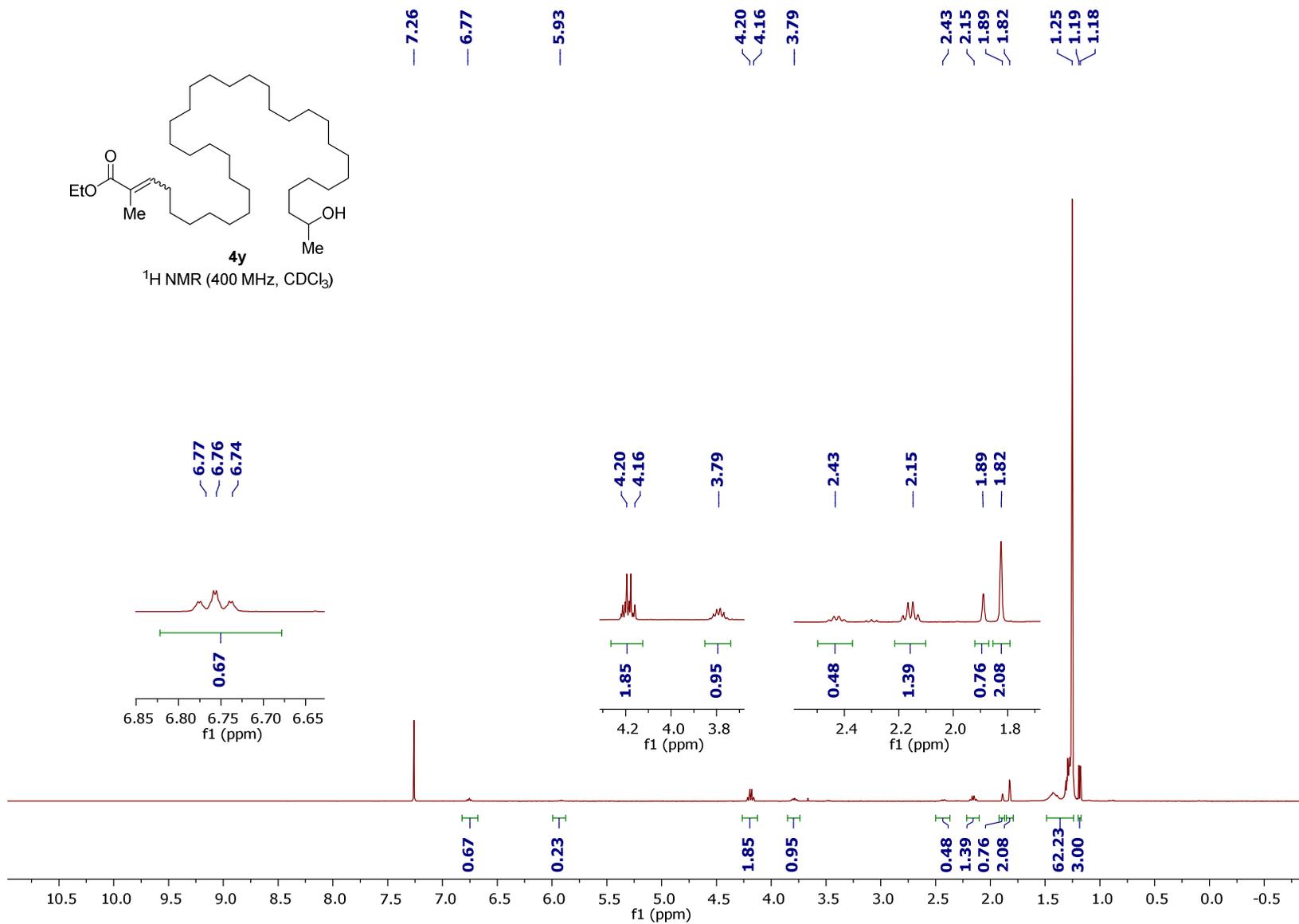
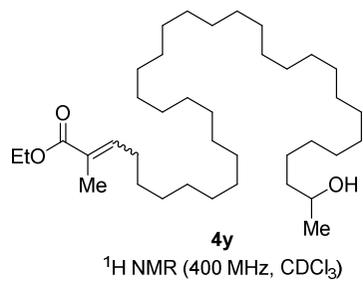
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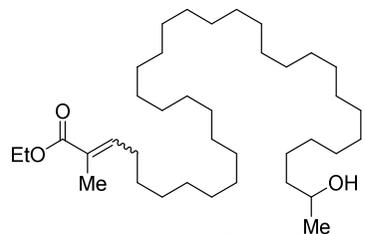




$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

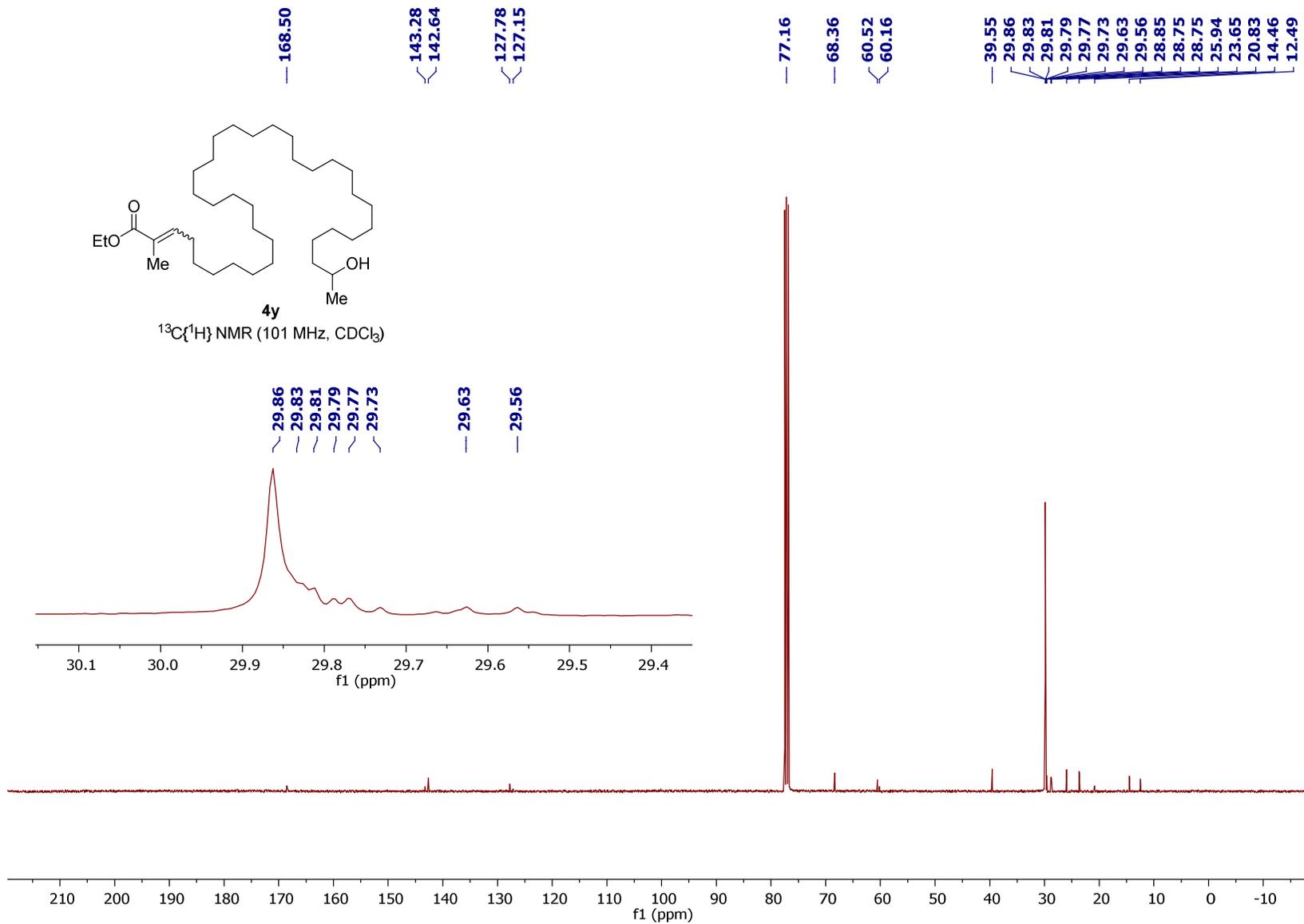




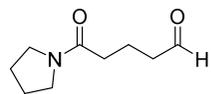


**4y**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



9.73  
9.73  
9.72



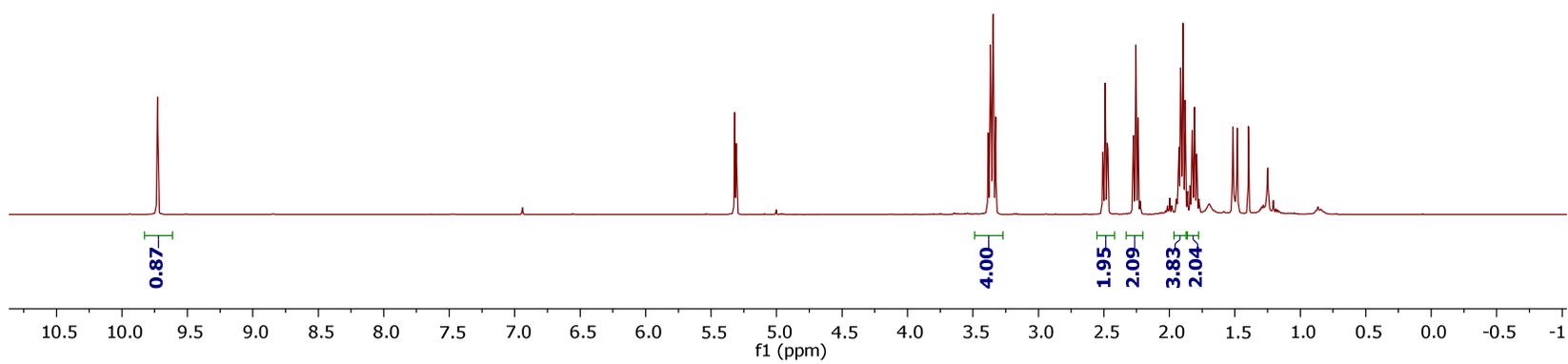
**3f**

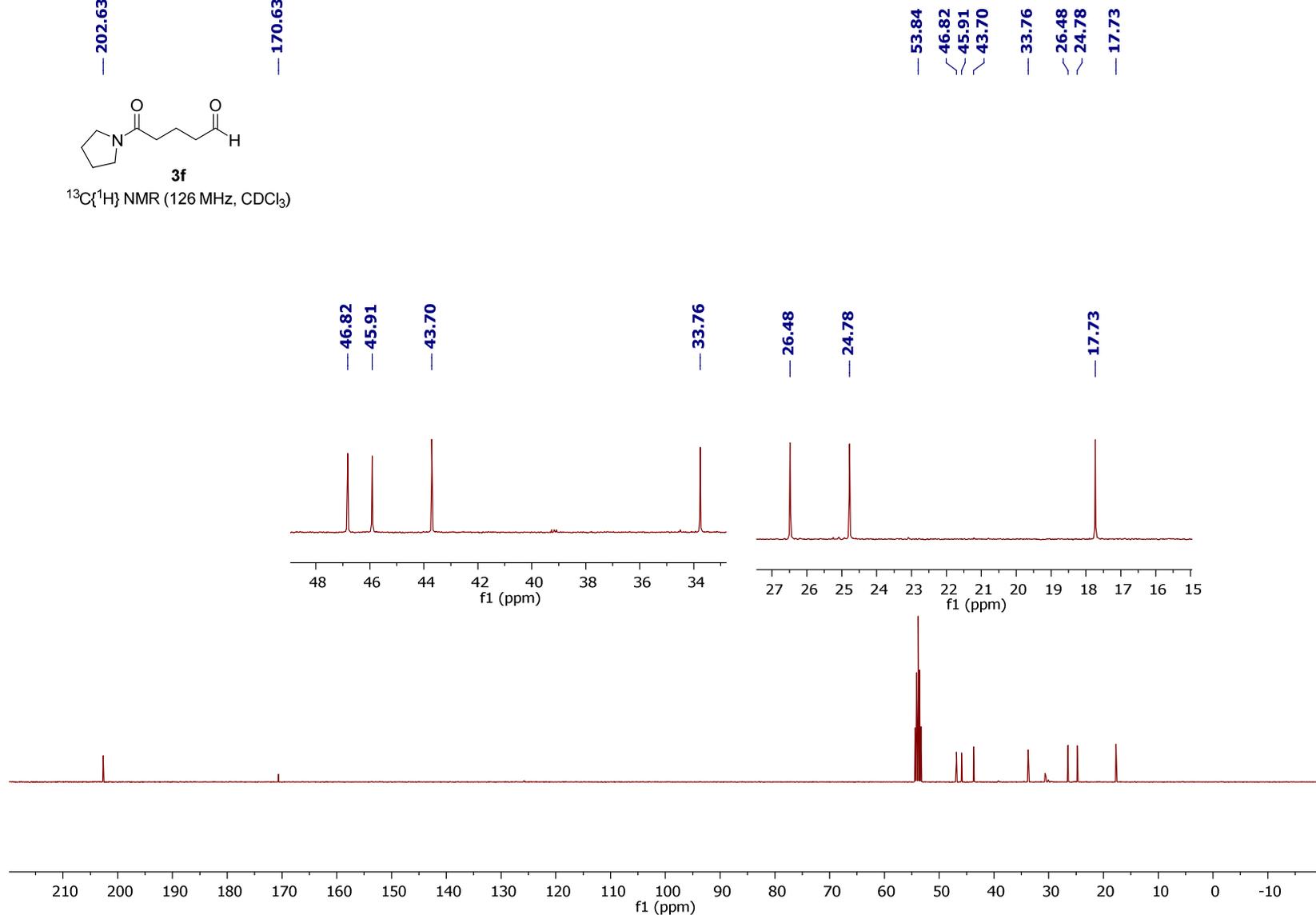
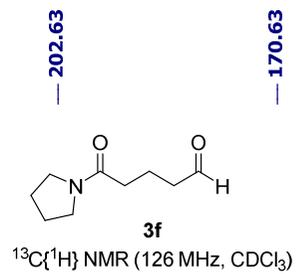
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

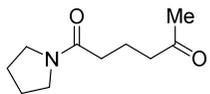
5.32

3.34

2.49  
2.26  
1.91  
1.81

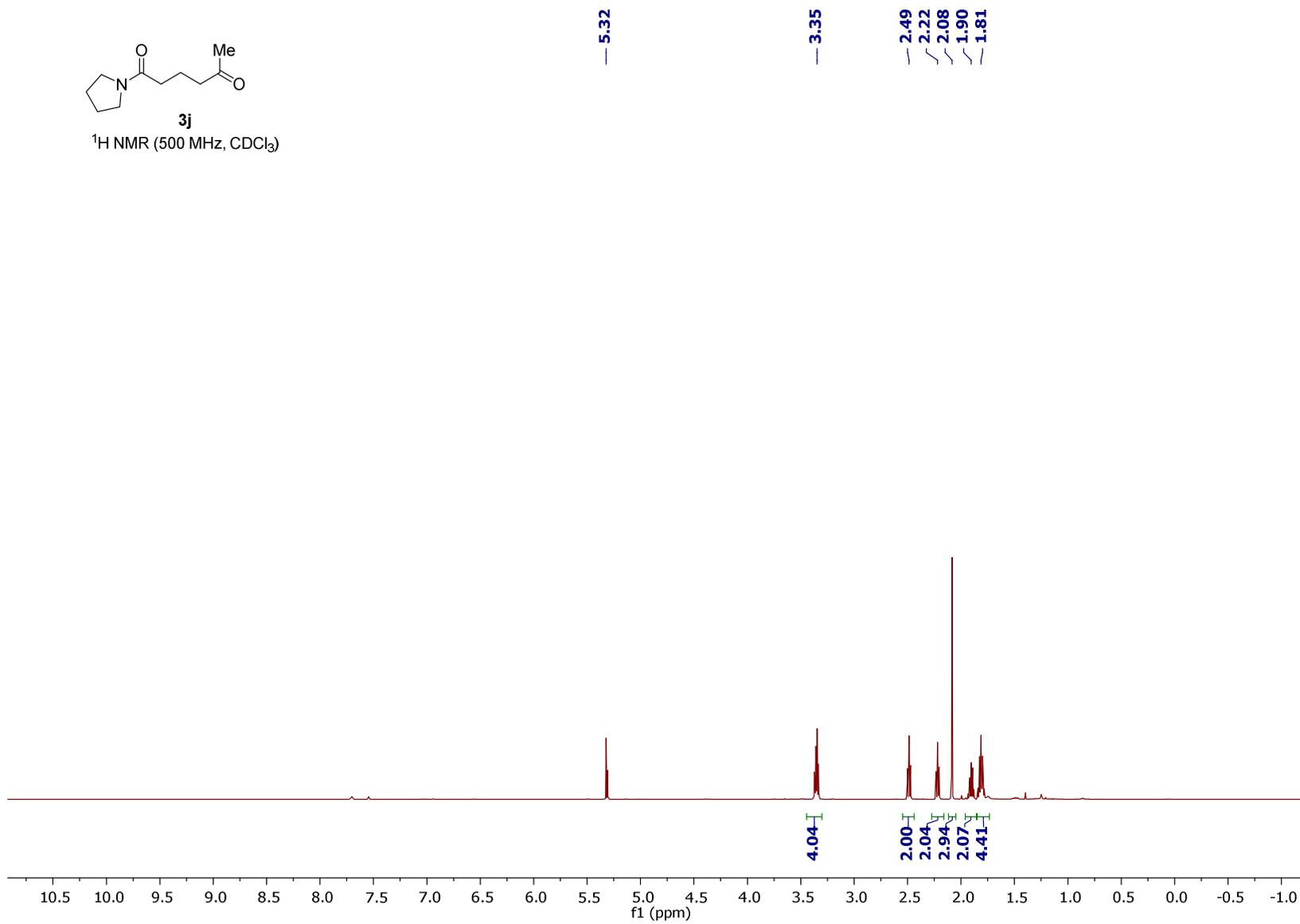






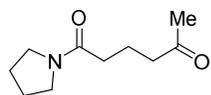
**3j**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



— 208.81

— 170.98



**3j**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

— 53.84

— 46.85

— 45.89

— 43.14

— 33.87

— 30.04

— 26.48

— 24.78

— 19.28

— 208.81

— 170.98

— 46.85

— 45.89

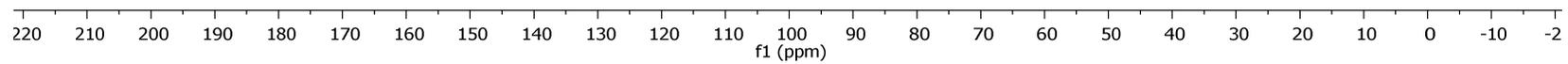
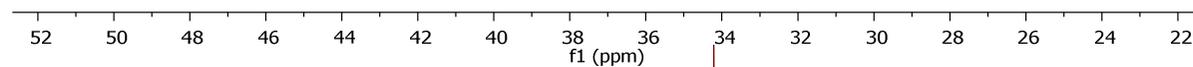
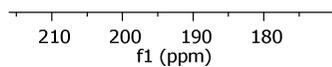
— 43.14

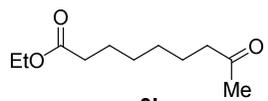
— 33.87

— 30.04

— 26.48

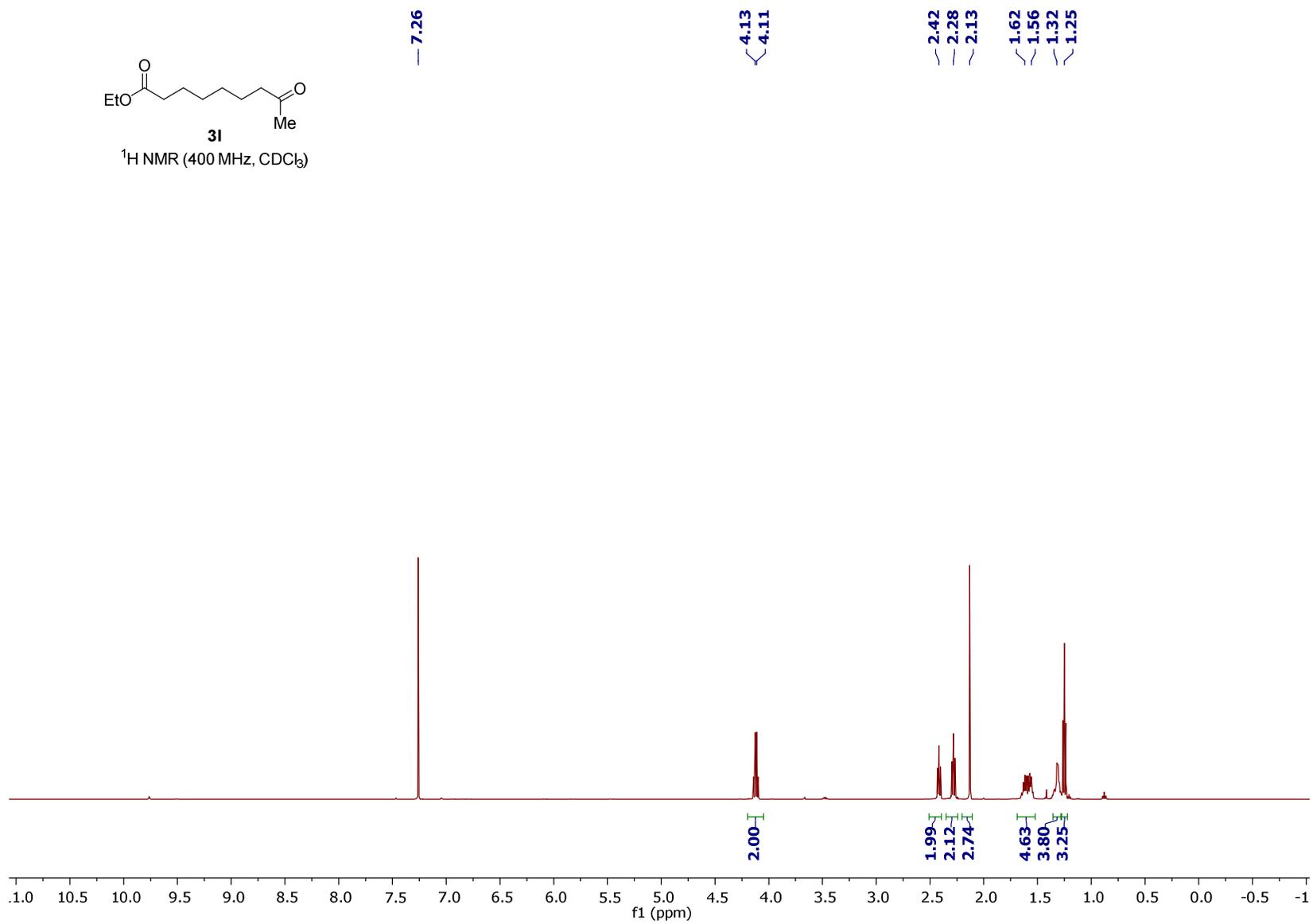
— 24.78

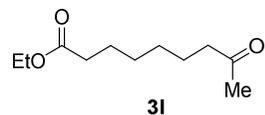




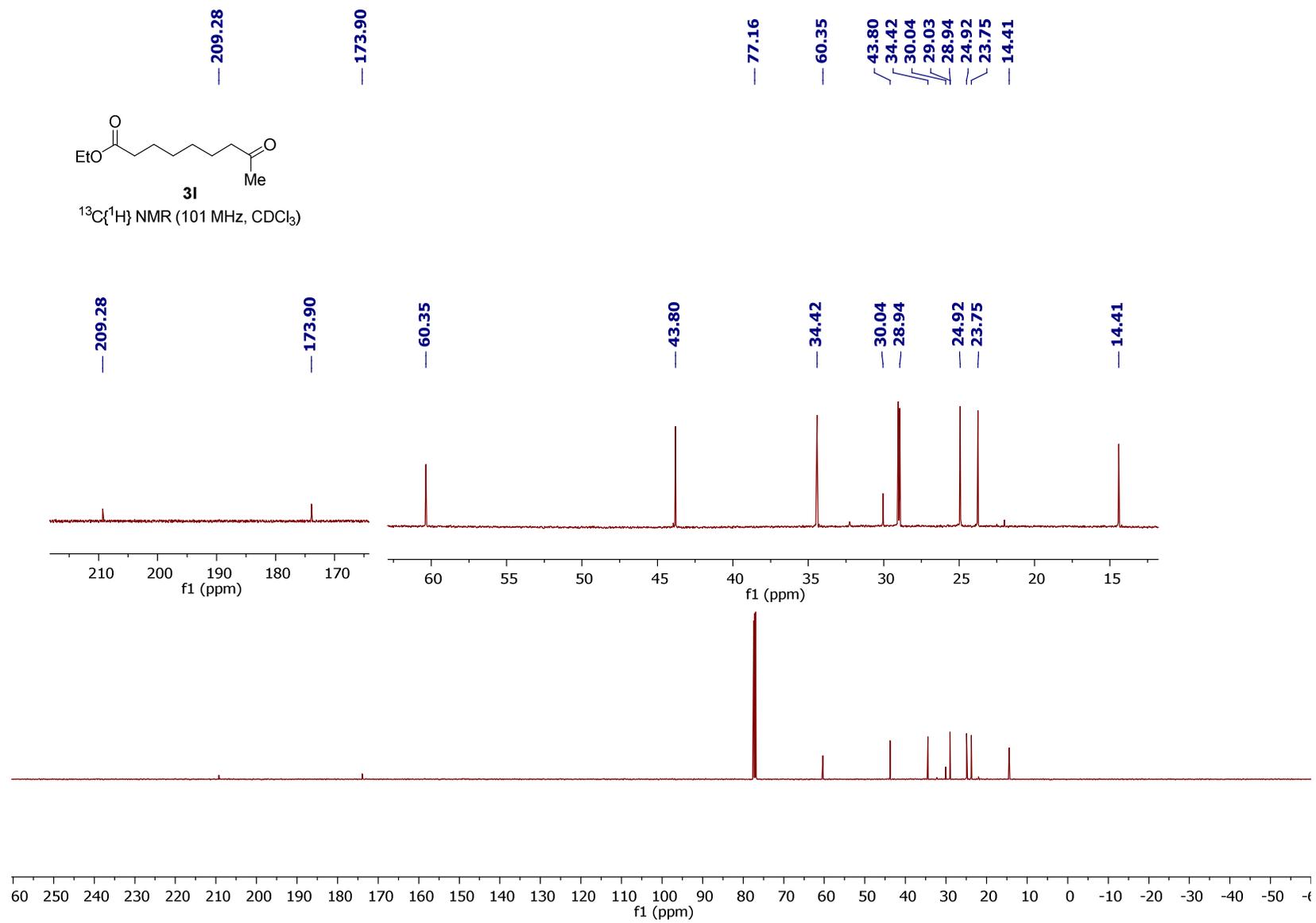
**3I**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

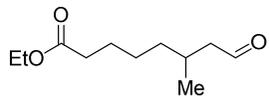




$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

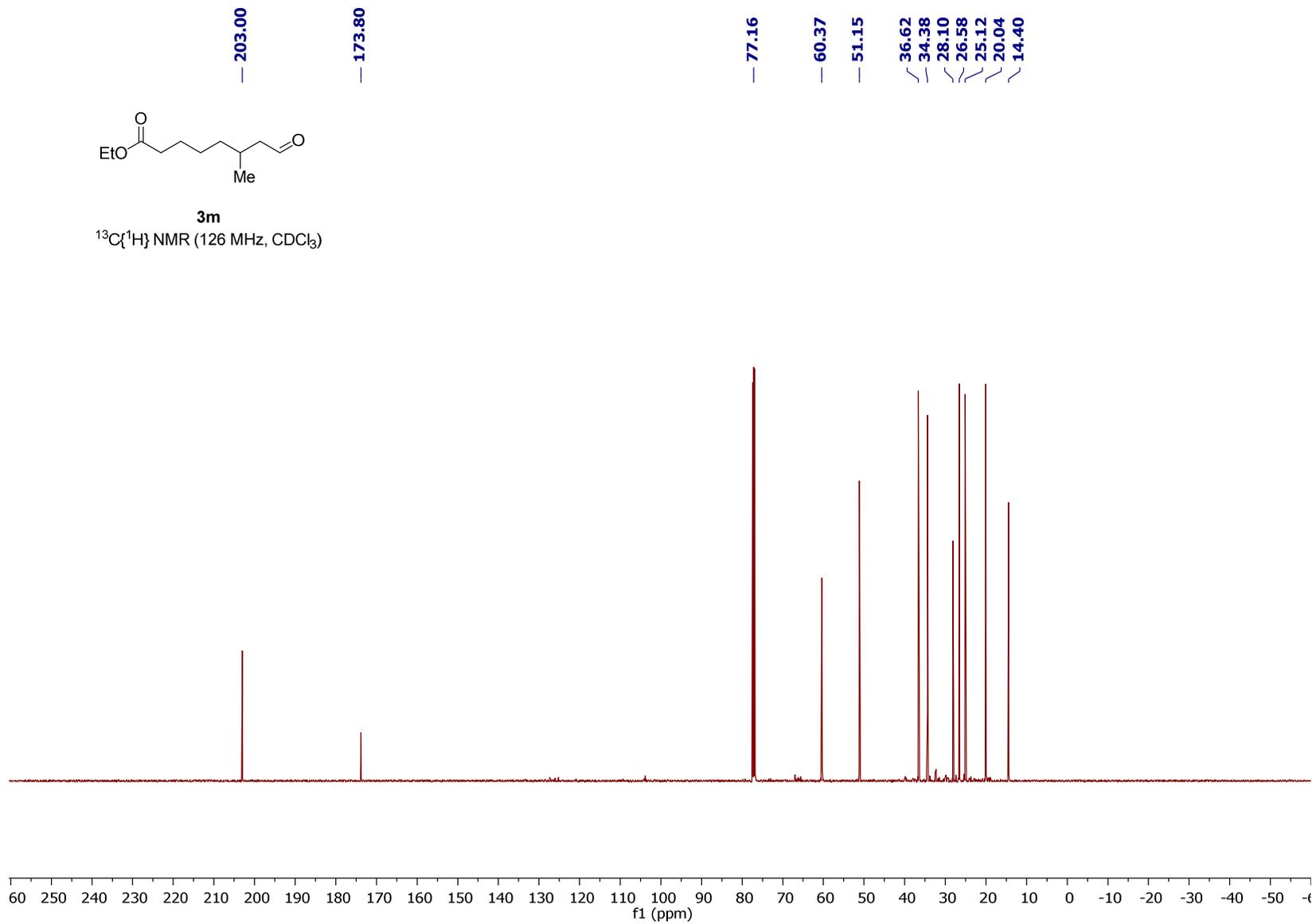


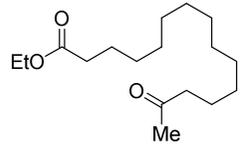




**3m**

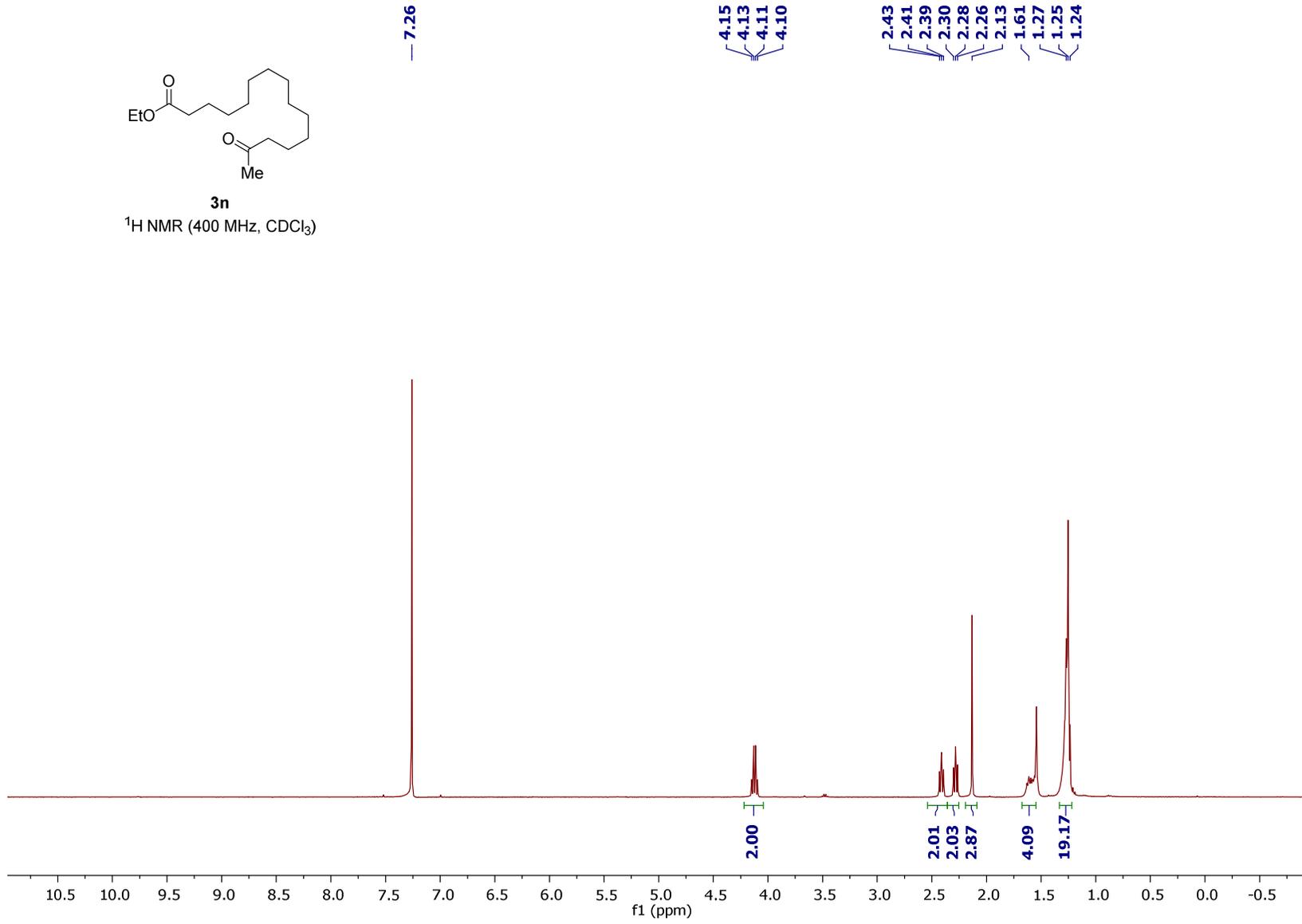
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

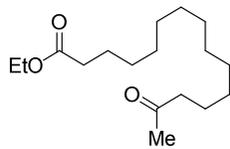




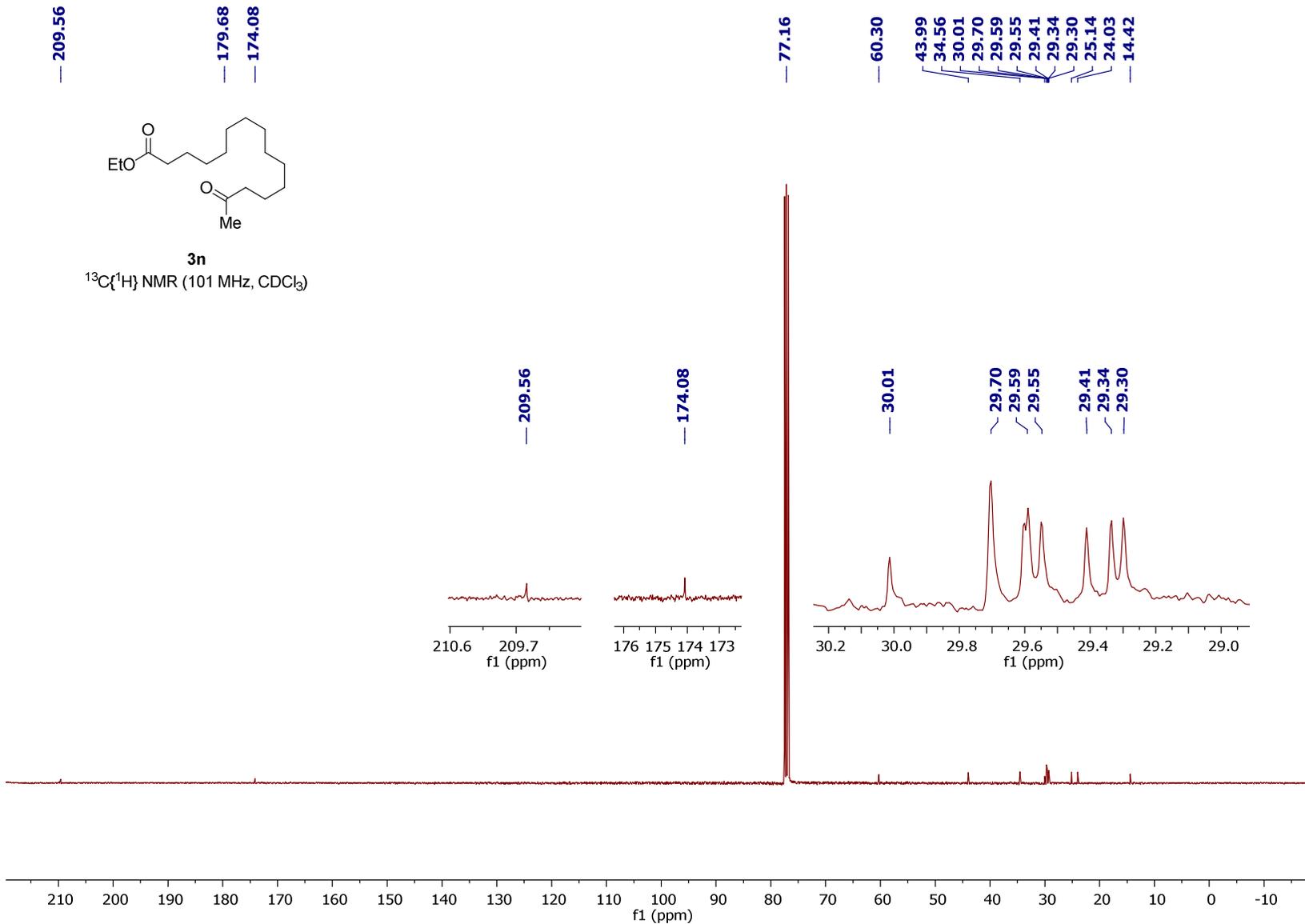
**3n**

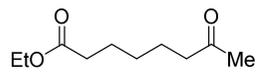
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)





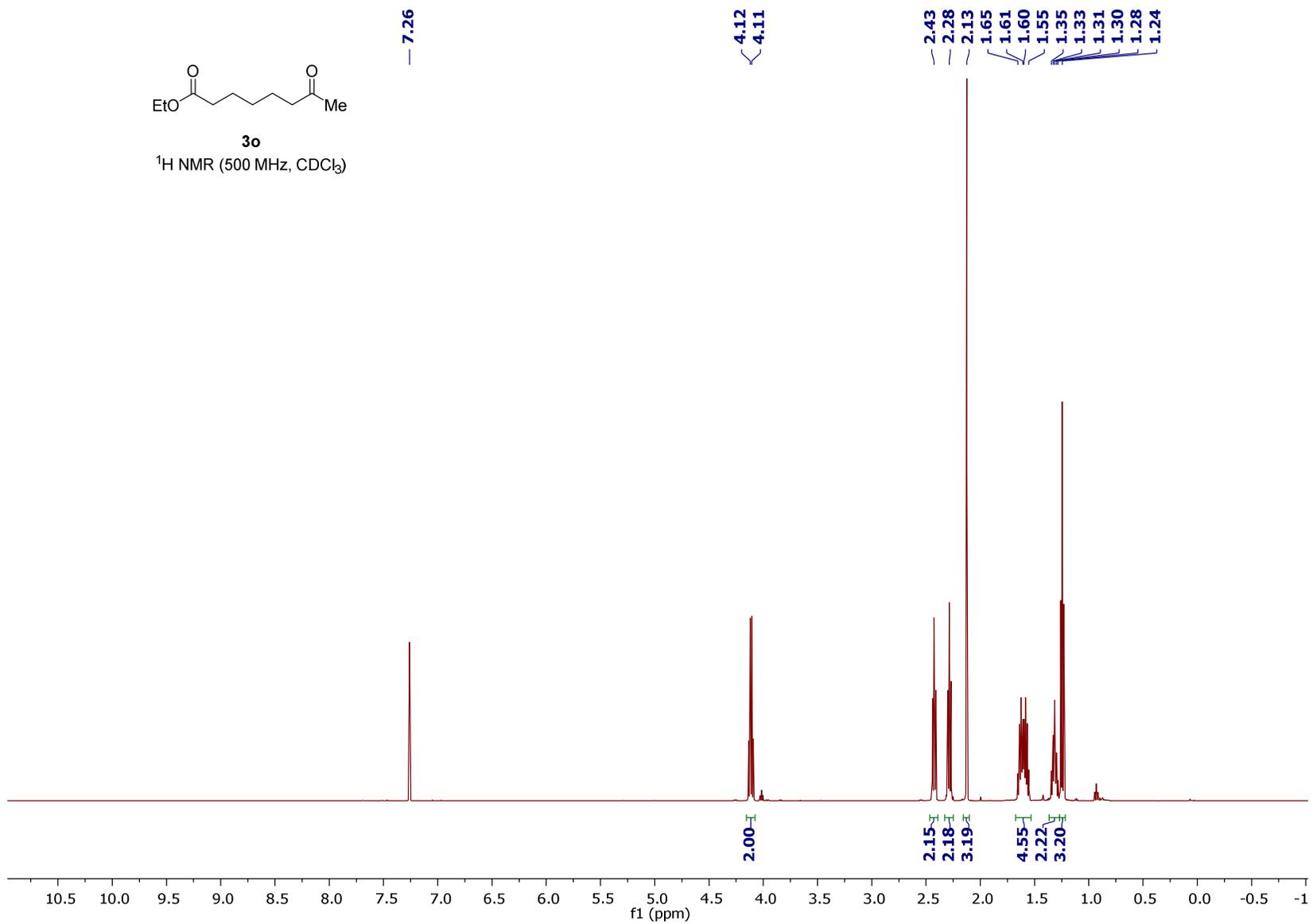
**3n**  
 $^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

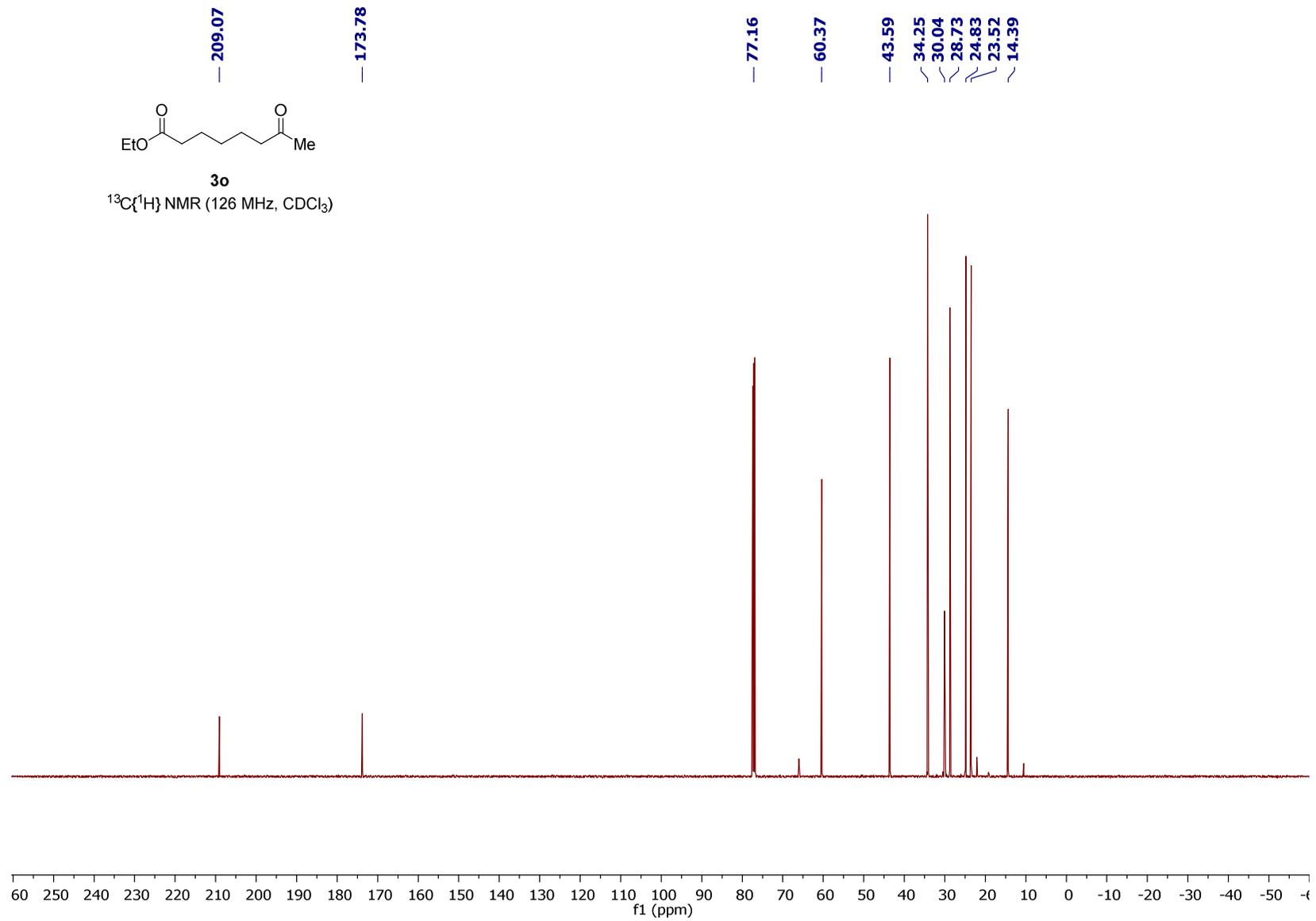
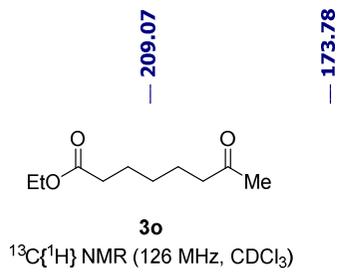


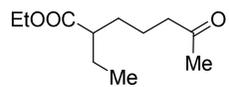


**3o**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

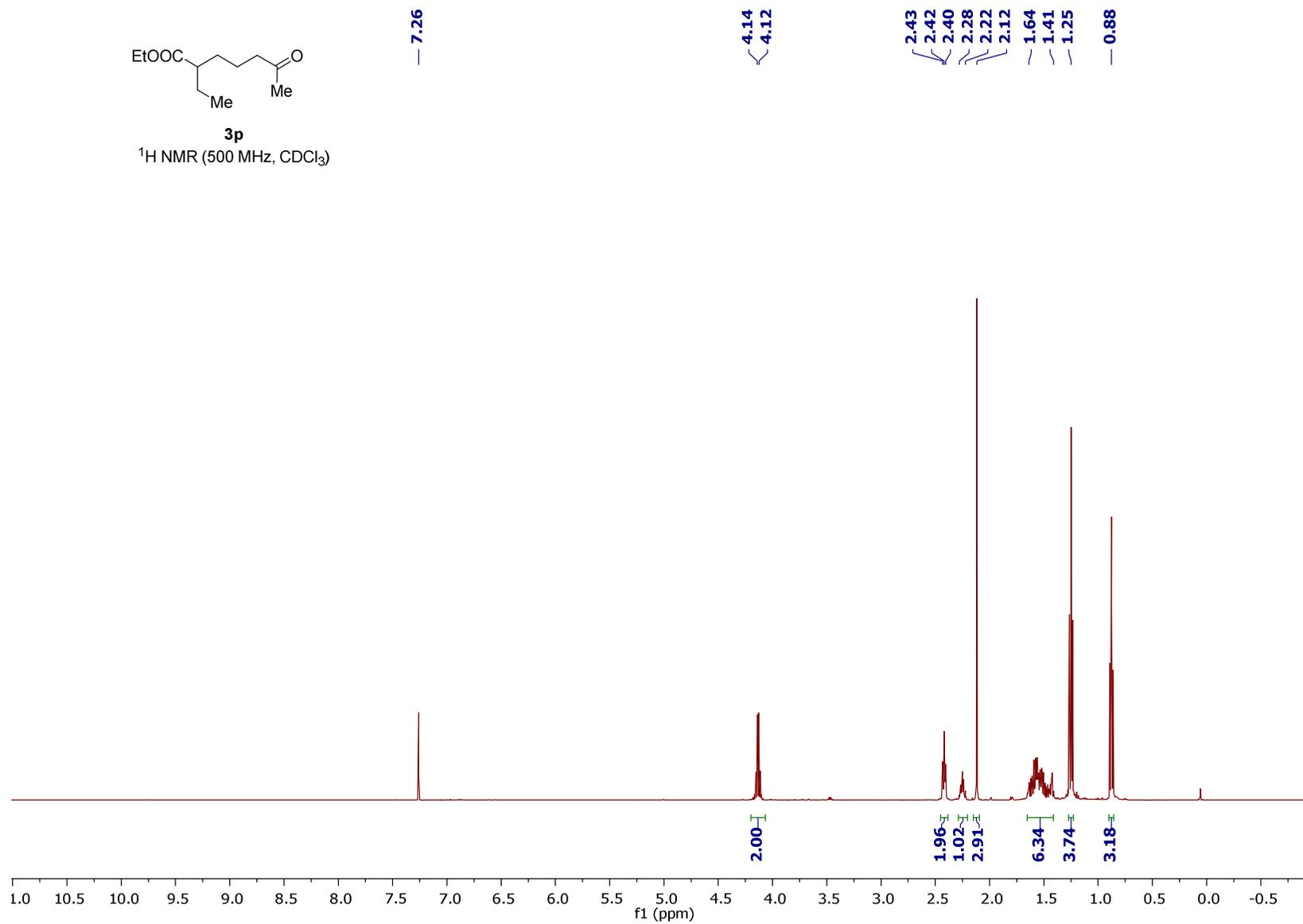


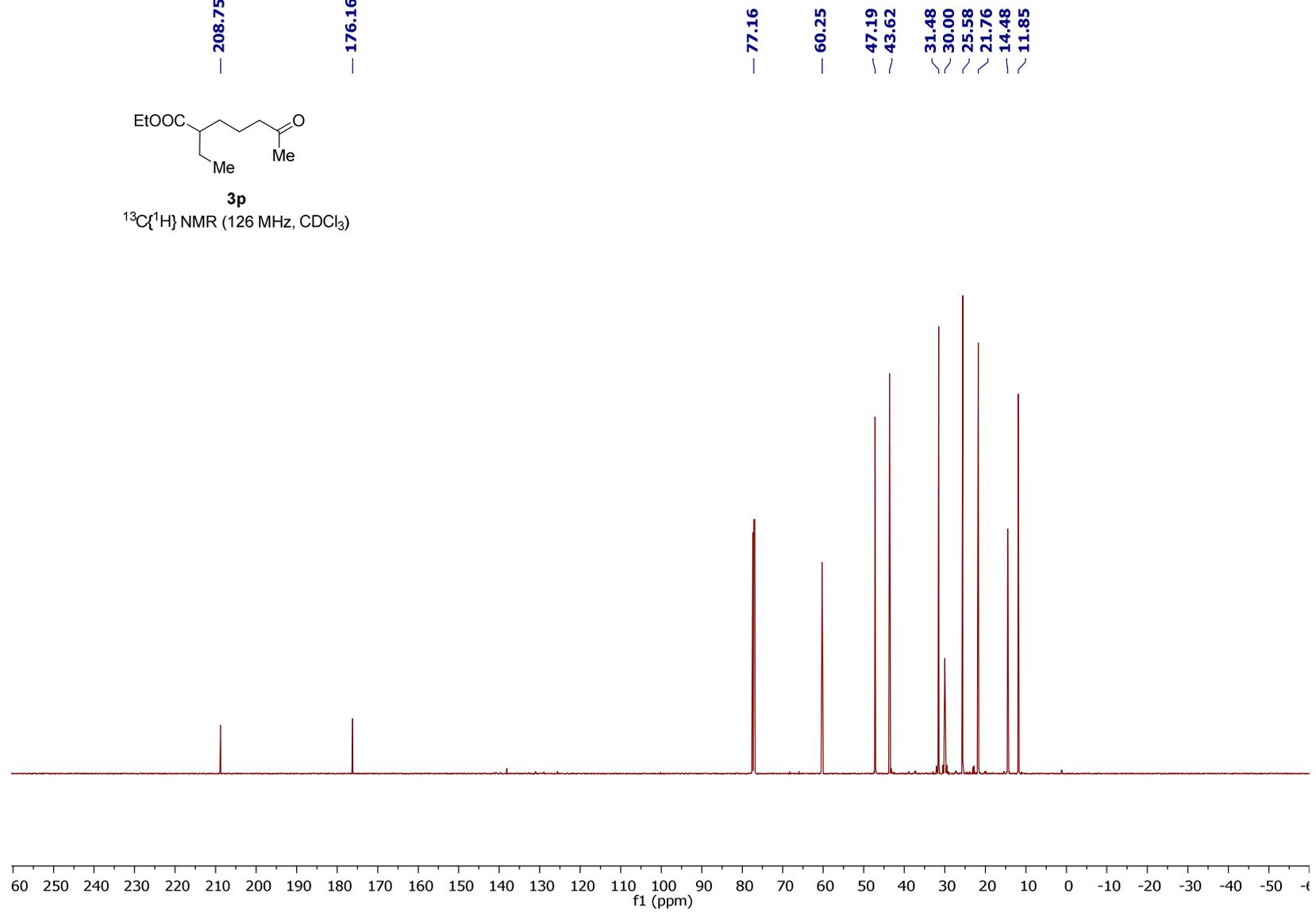
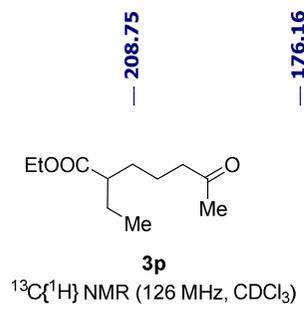


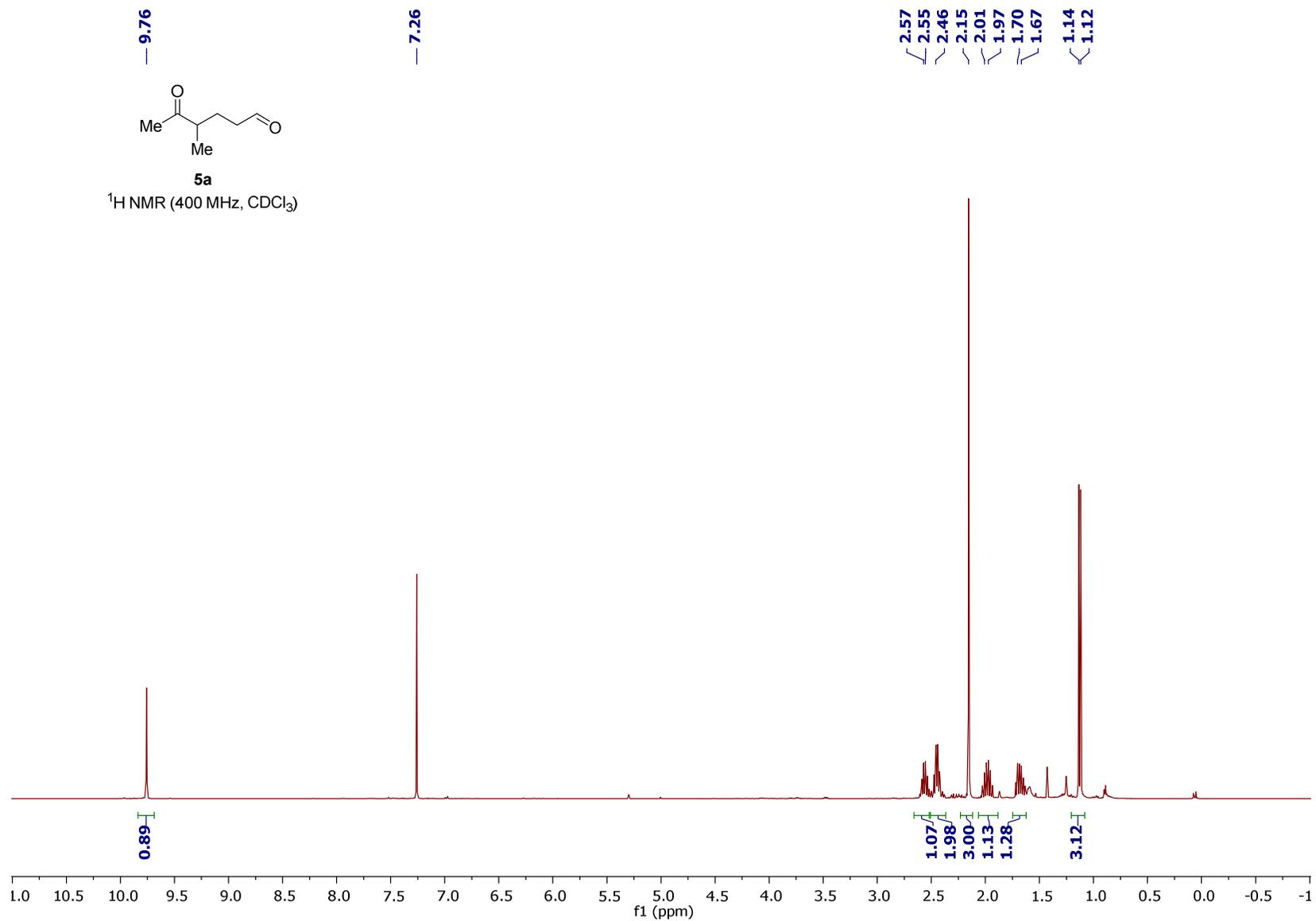
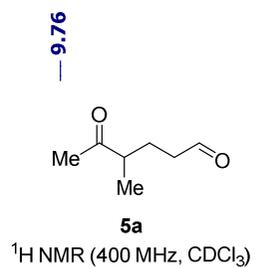


**3p**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)







— 211.83

— 201.79

— 77.16

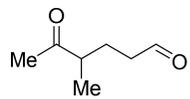
— 46.17

— 41.54

— 28.39

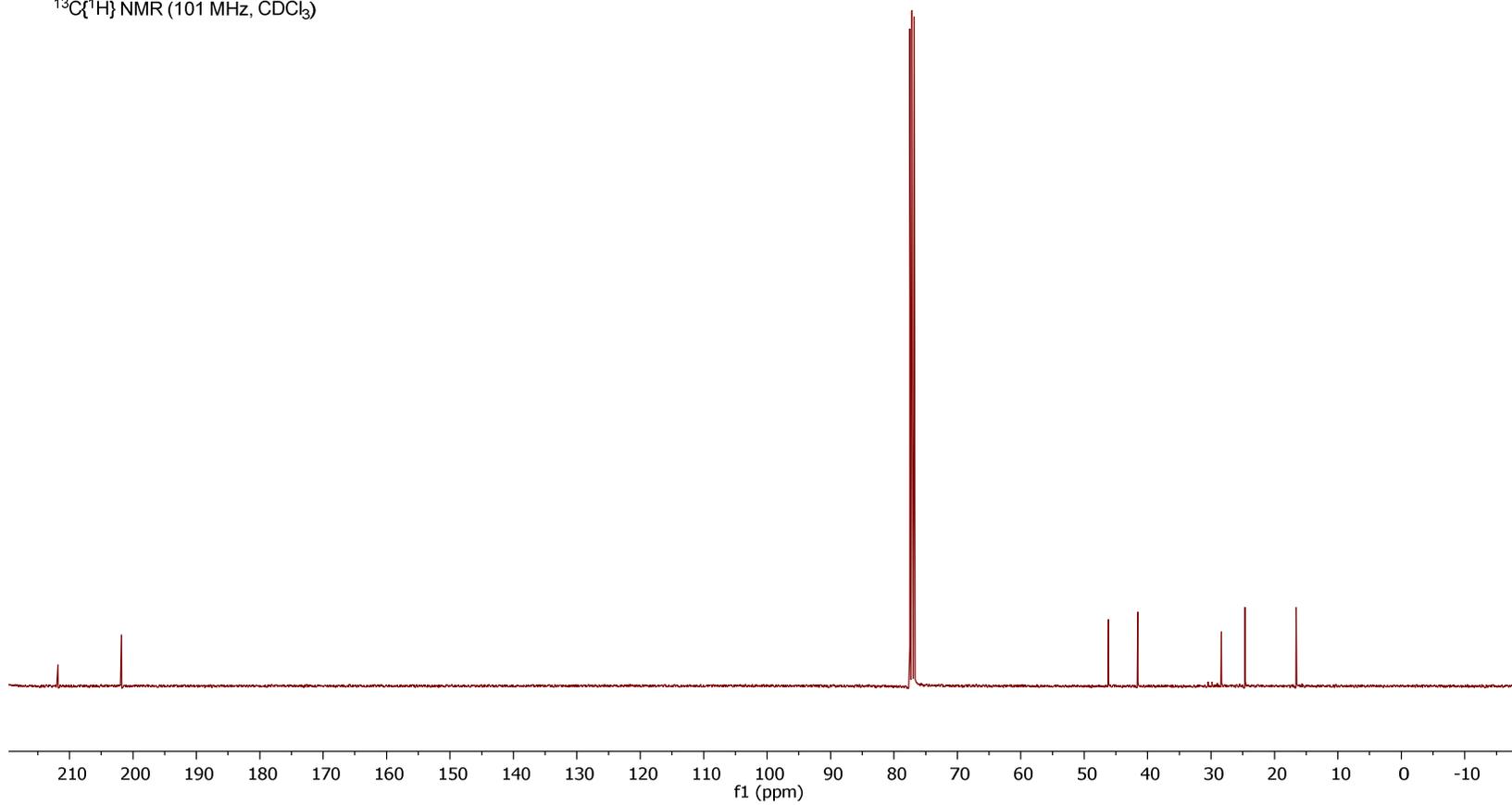
— 24.63

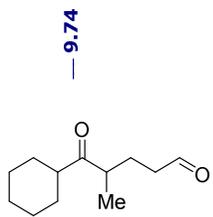
— 16.58



**5a**

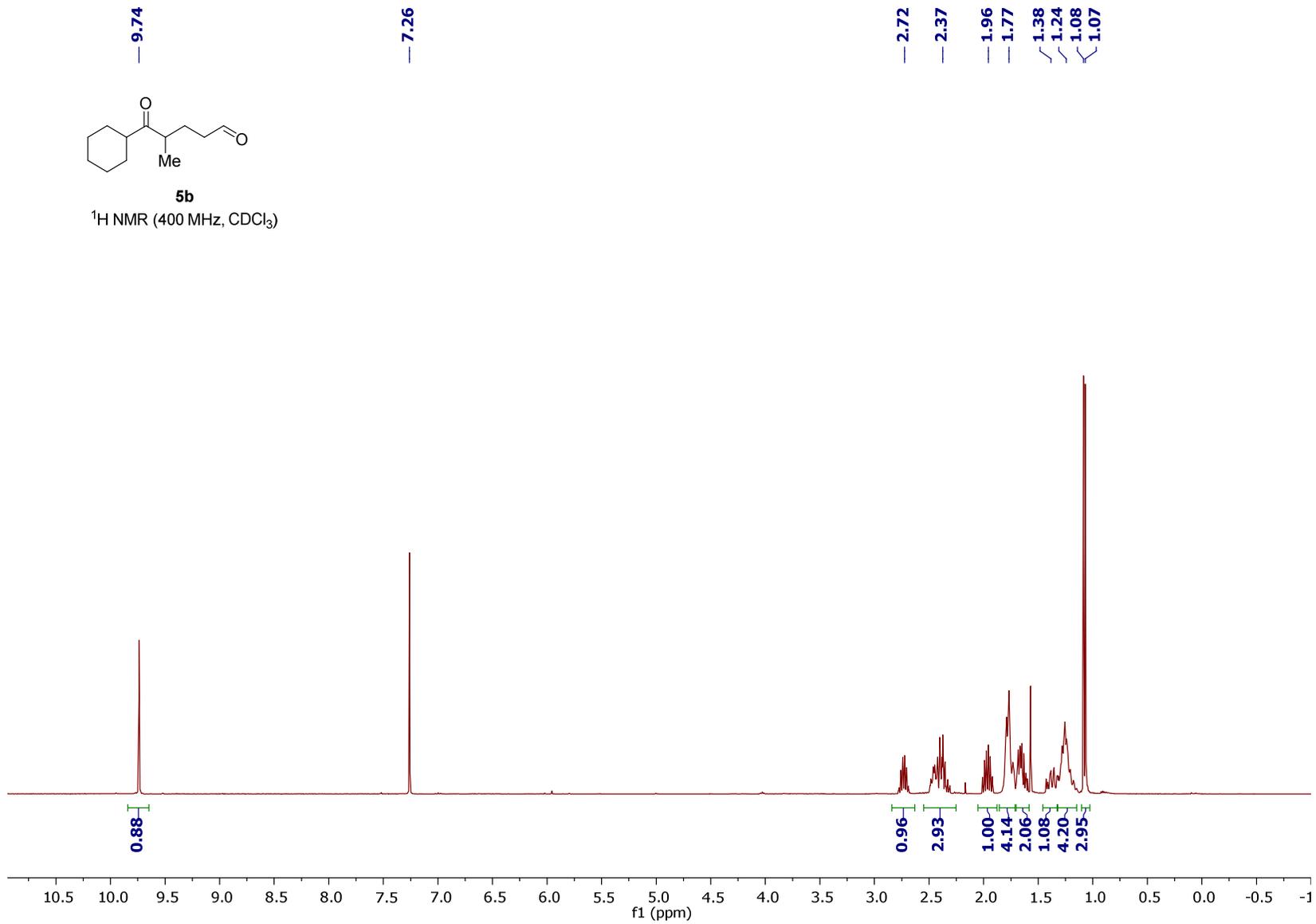
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





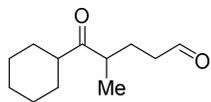
**5b**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



— 216.93

— 202.01



**5b**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 77.16

49.88

43.50

41.75

28.76

28.44

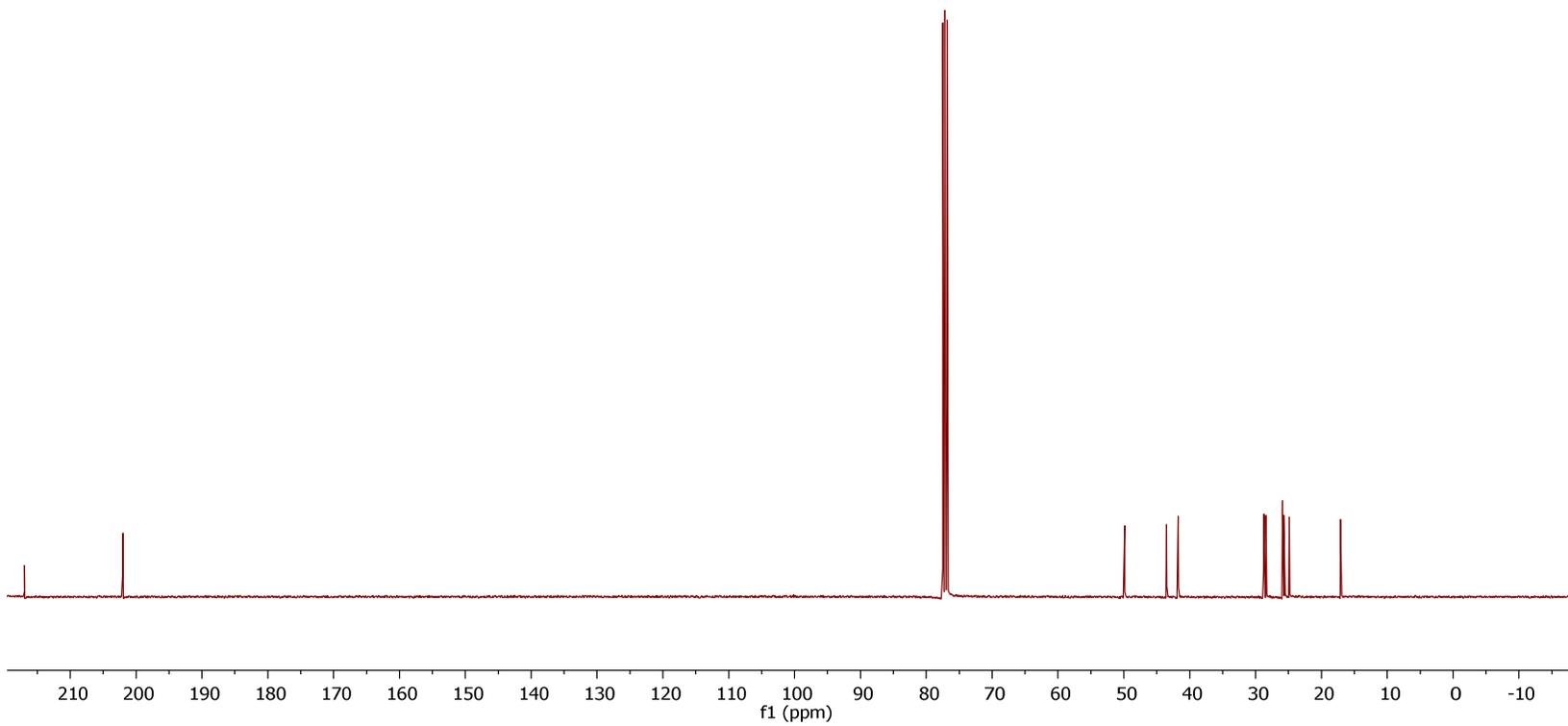
25.95

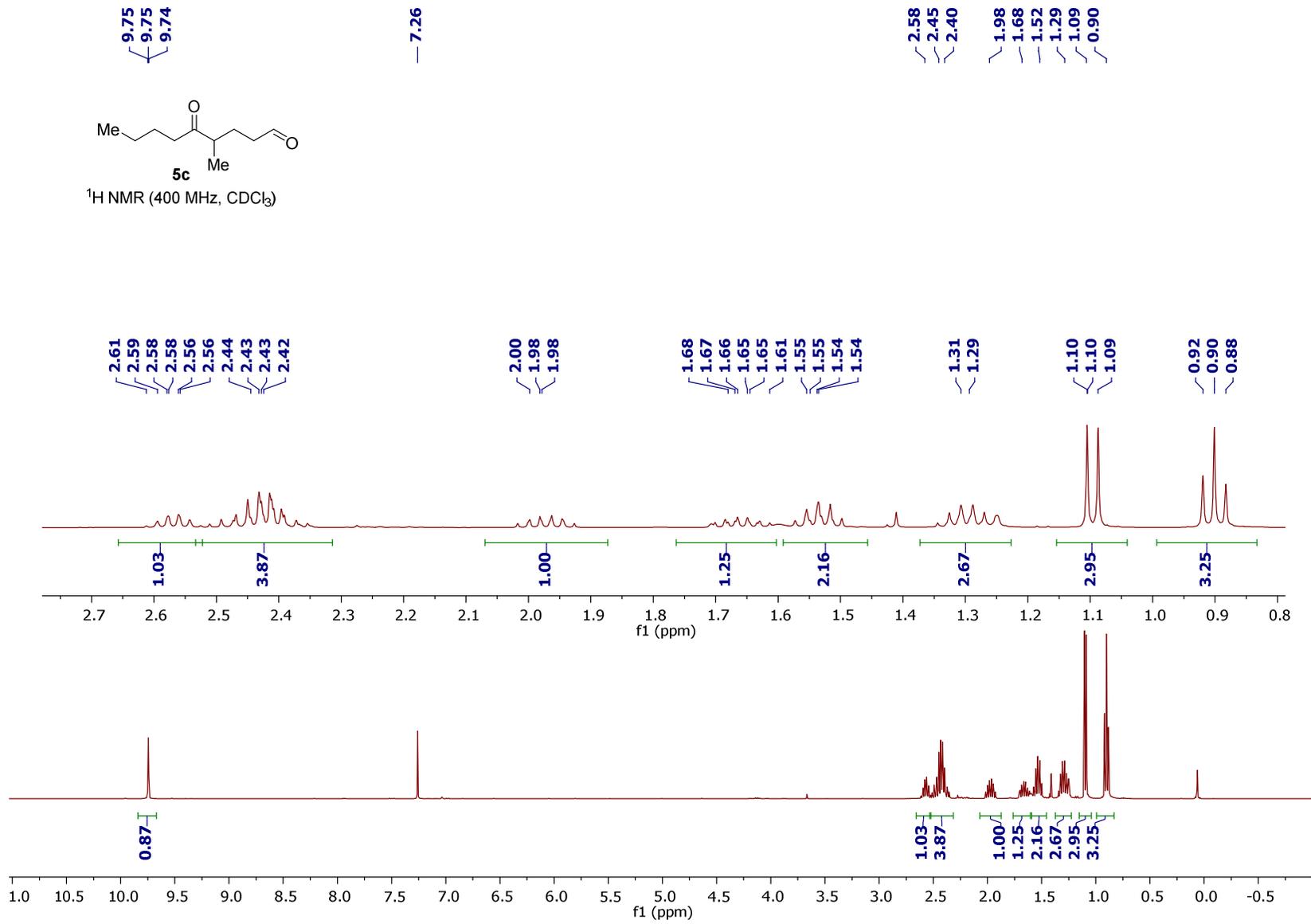
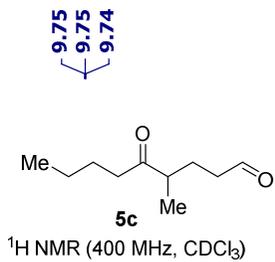
25.92

25.69

24.90

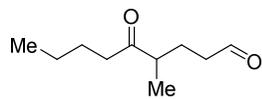
— 17.10





— 214.12

— 201.90



**5c**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 77.16

— 45.30

— 41.61

— 41.14

— 25.92

— 24.78

— 22.53

— 16.76

— 14.02

— 45.30

— 41.61

— 41.14

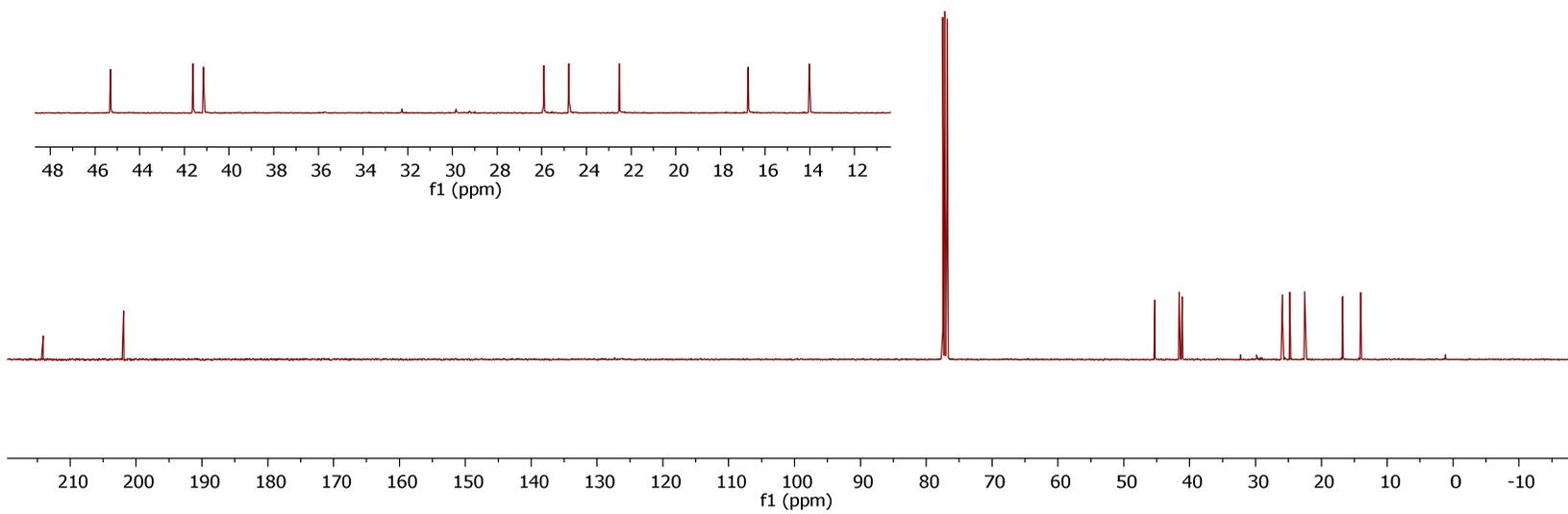
— 25.92

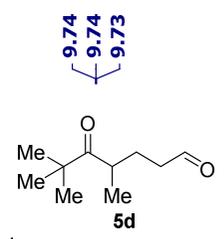
— 24.78

— 22.53

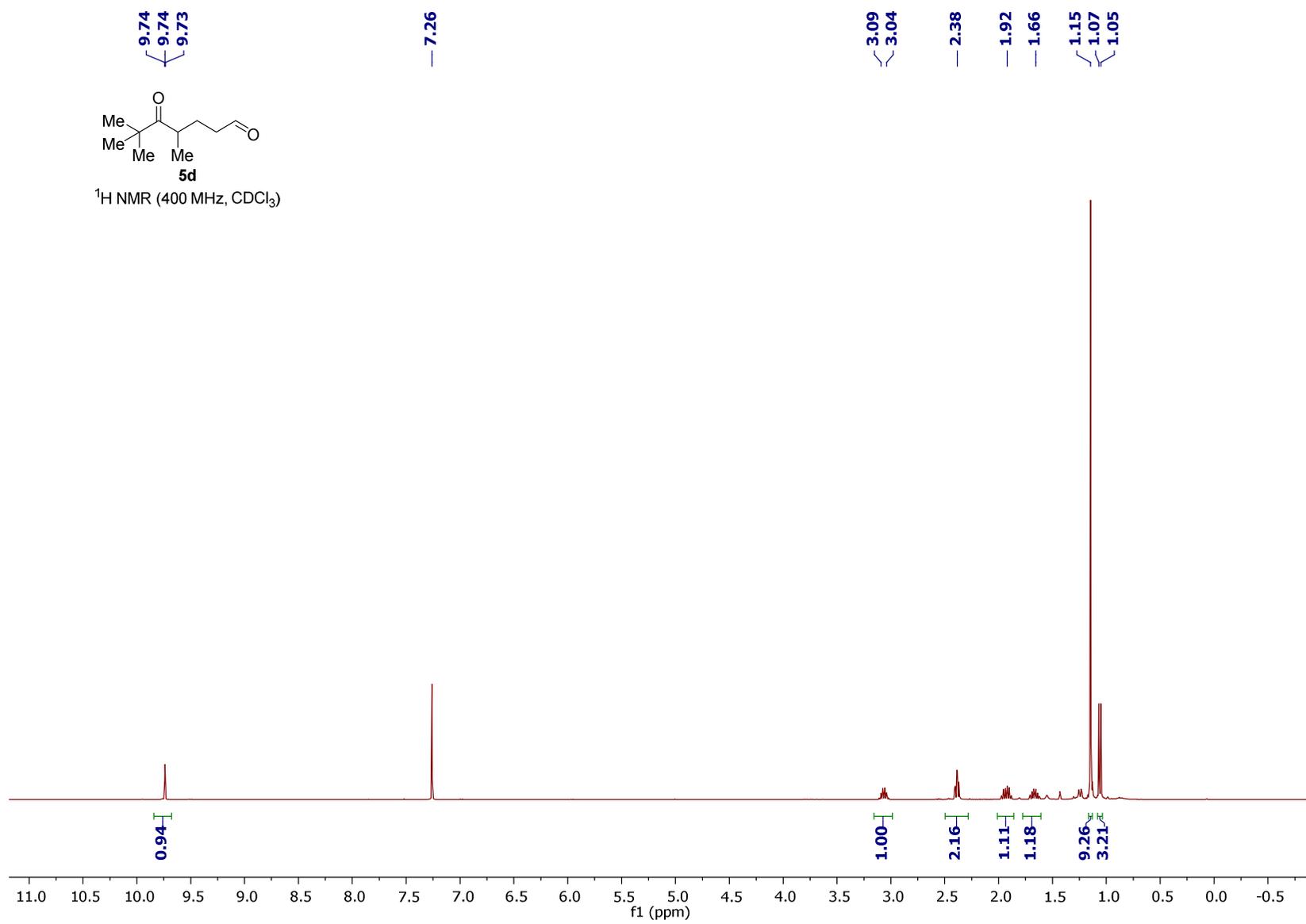
— 16.76

— 14.02

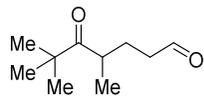




<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



201.94



5d

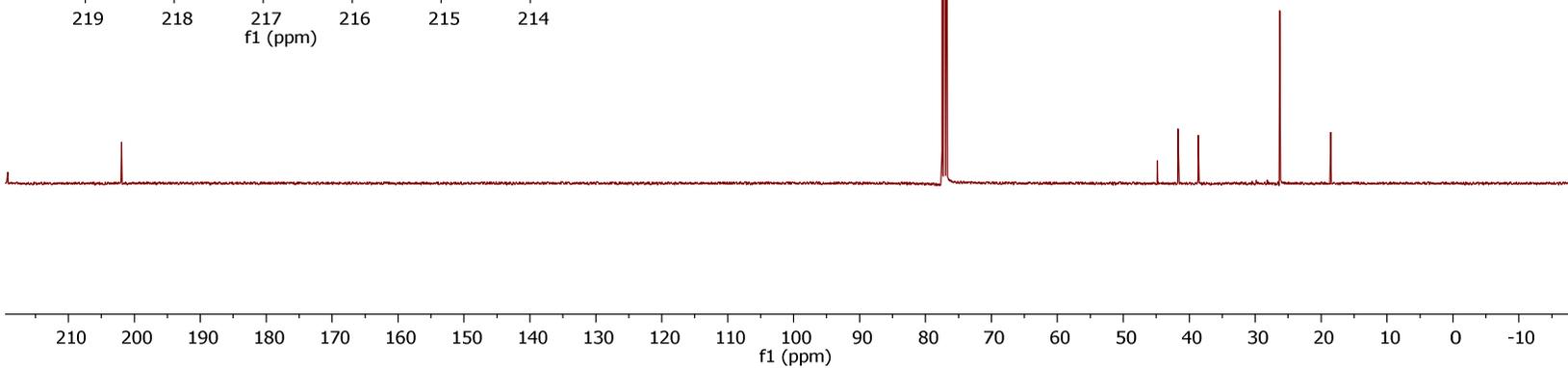
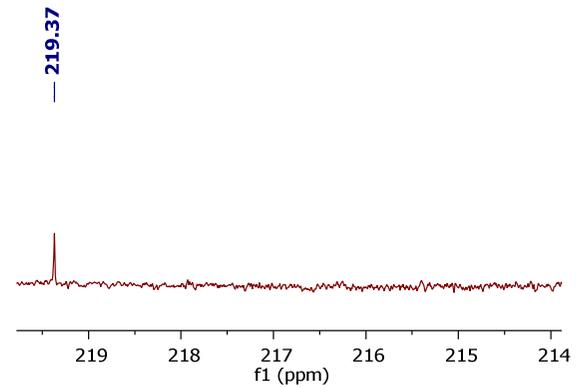
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

77.16

44.82  
41.70  
38.64

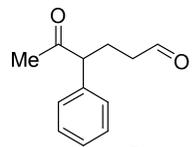
26.30  
26.26  
18.56

219.37





— 207.75  
— 201.89



**5e**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

— 138.16  
— 129.33  
— 128.44  
— 127.82

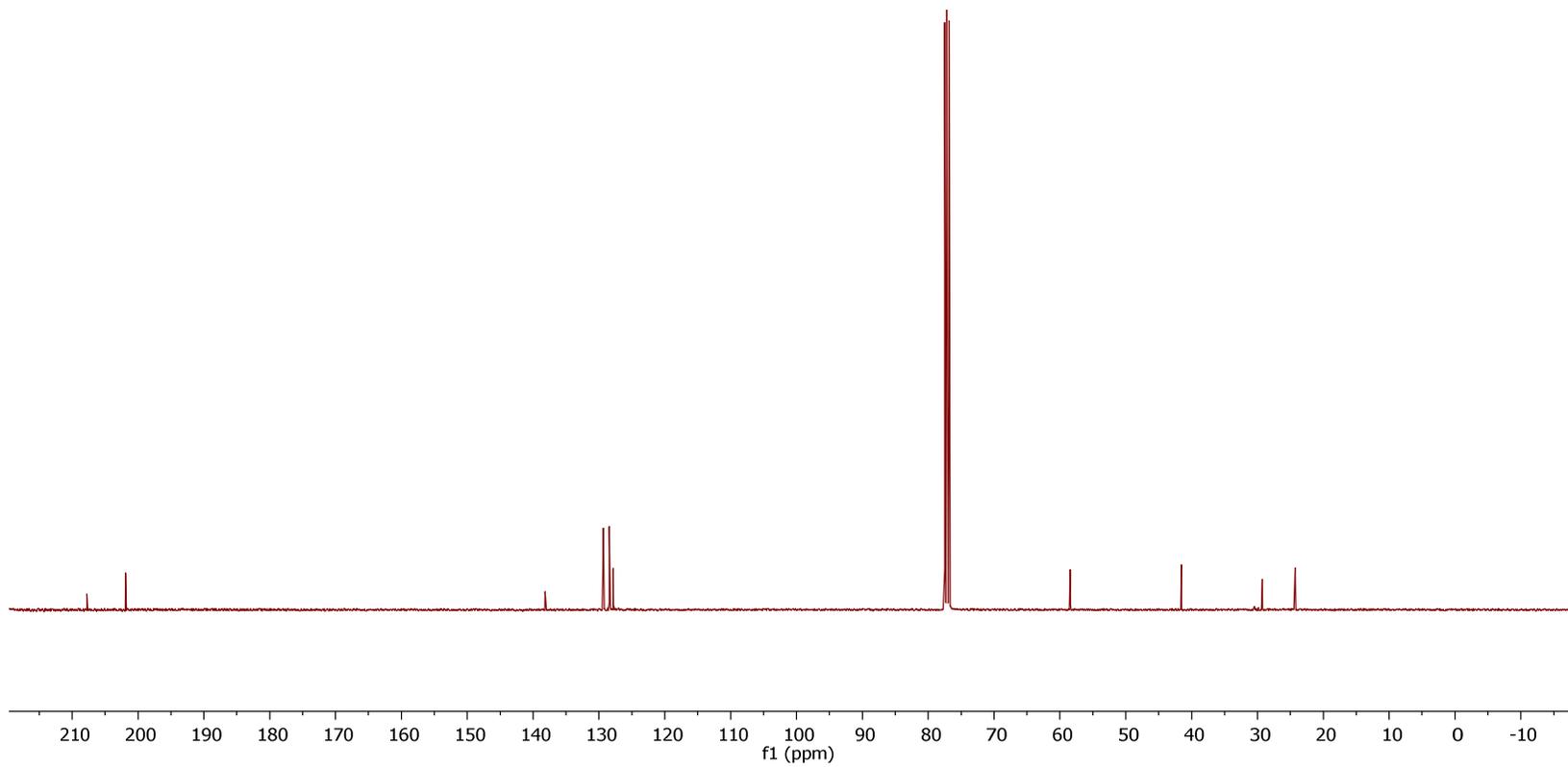
— 77.16

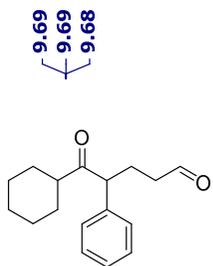
— 58.43

— 41.55

— 29.25

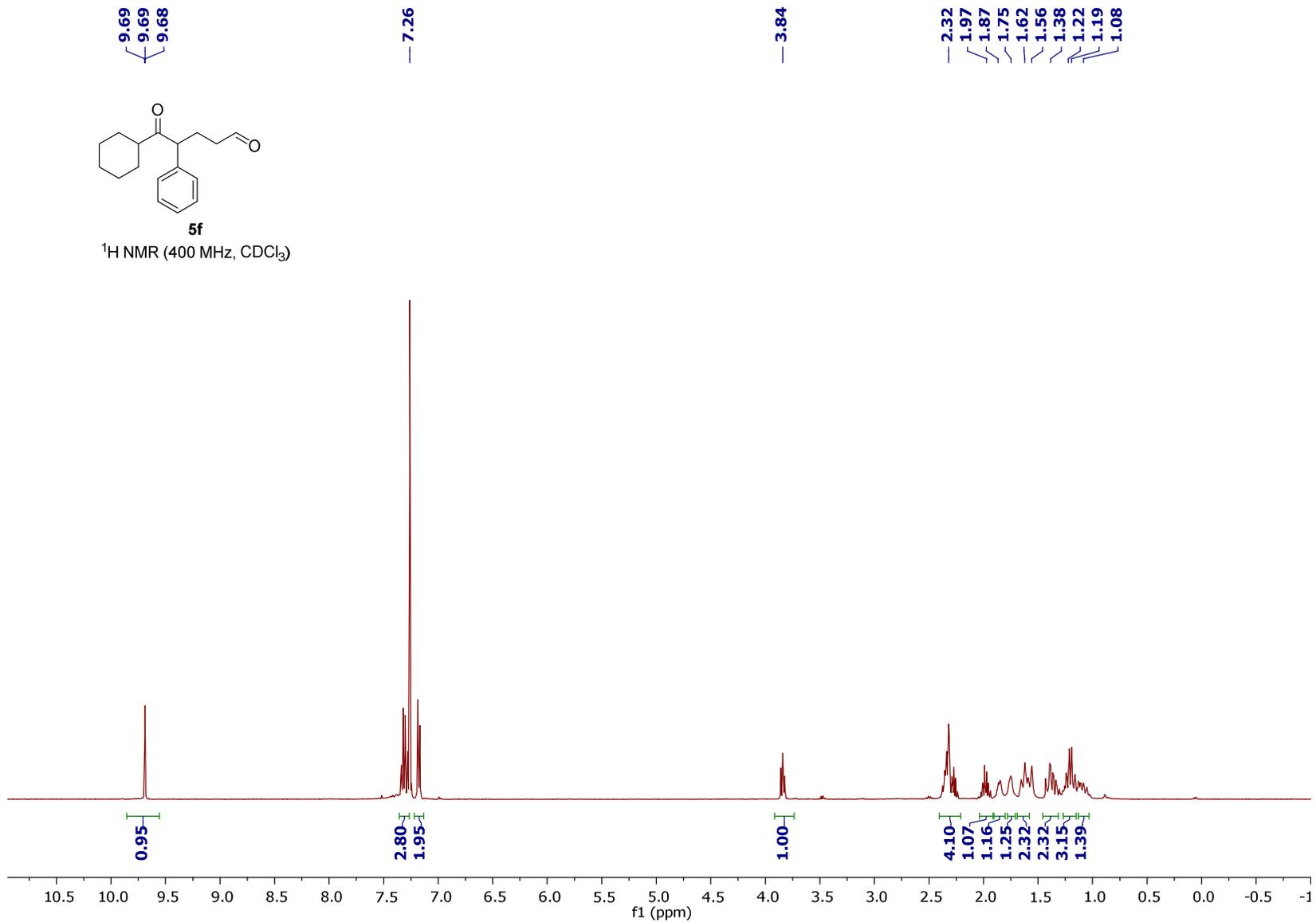
— 24.29





**5f**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



— 212.87

— 201.99

— 138.18

129.15

128.57

127.62

— 77.16

— 55.87

— 50.13

— 41.76

29.37

28.25

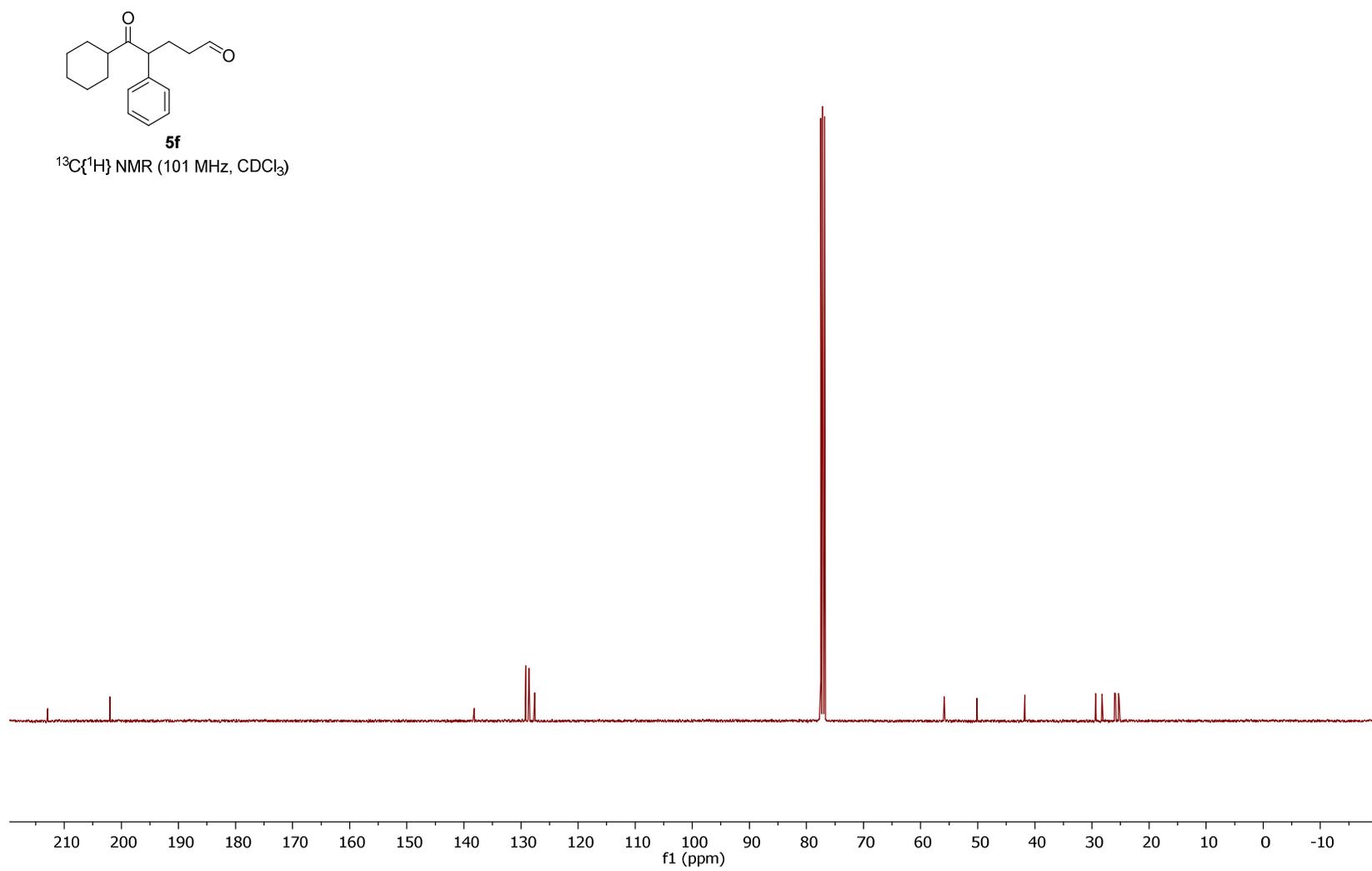
26.03

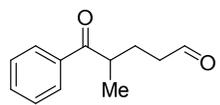
25.86

25.32

**5f**

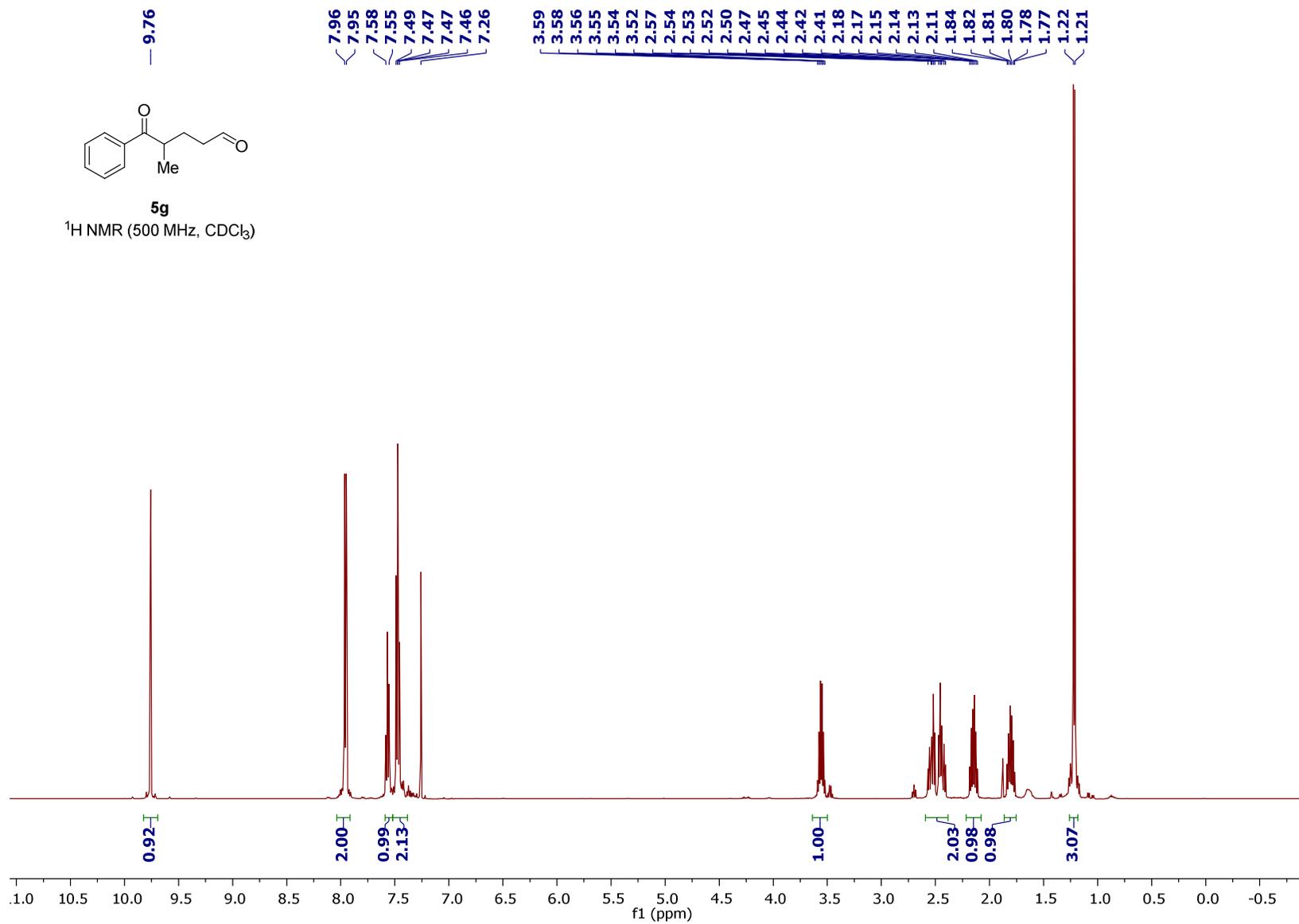
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



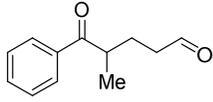


**5g**

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)



203.59  
201.97



**5g**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

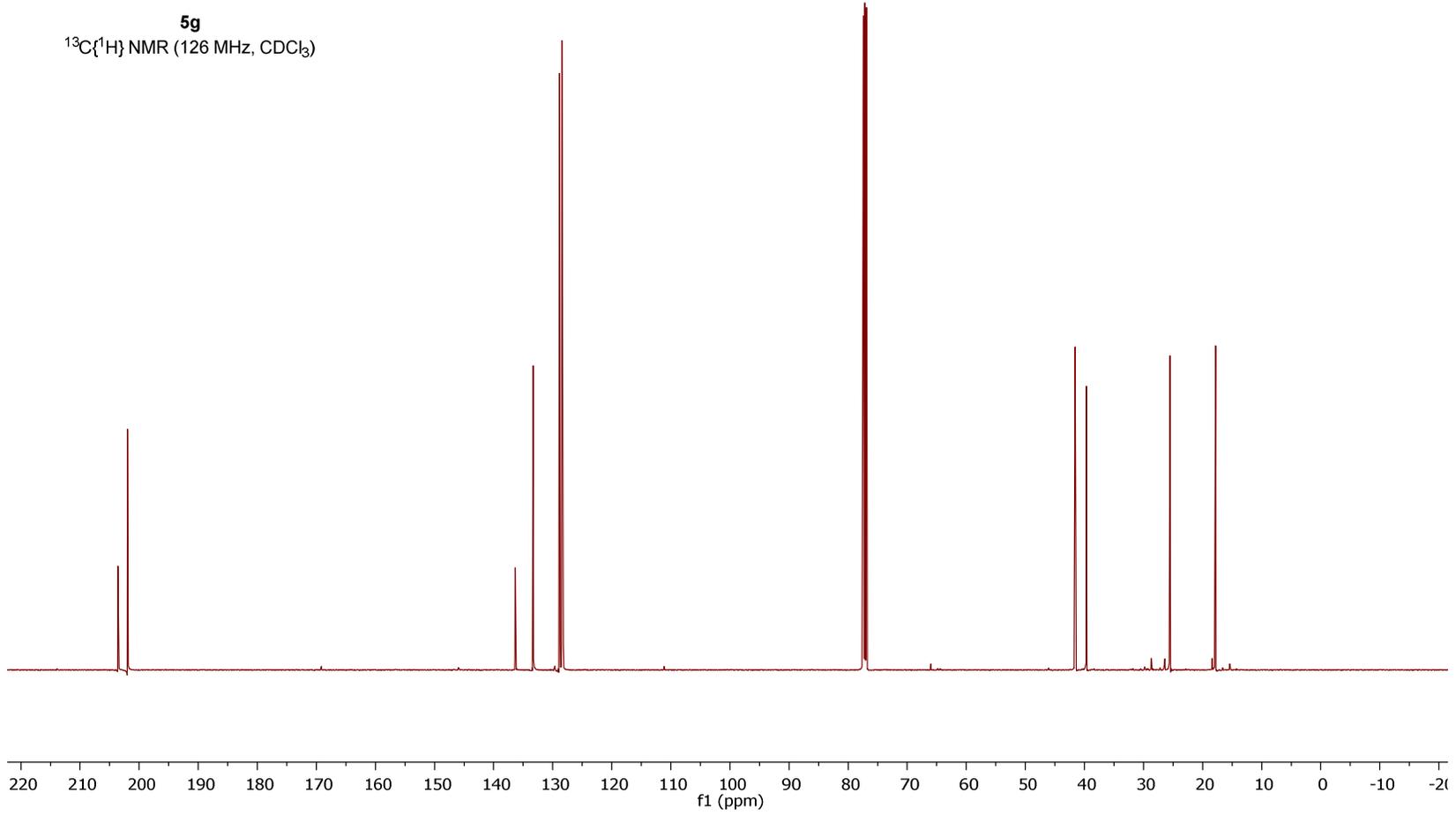
136.36  
133.29  
128.87  
128.44

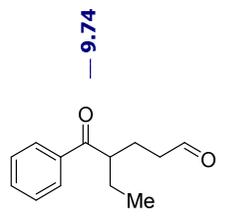
77.16

41.58  
39.67

25.51

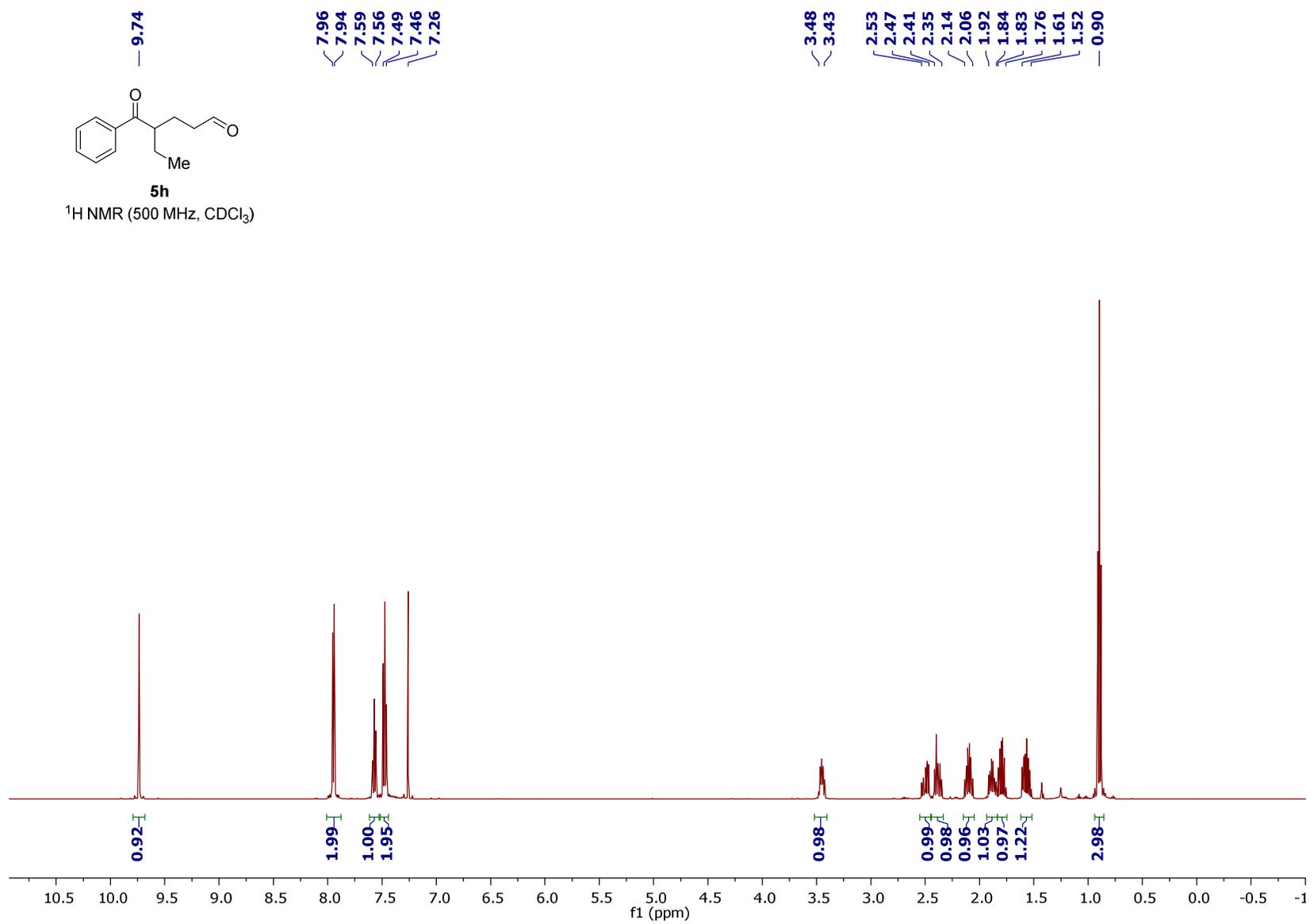
17.81

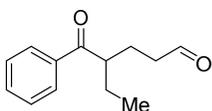




**5h**

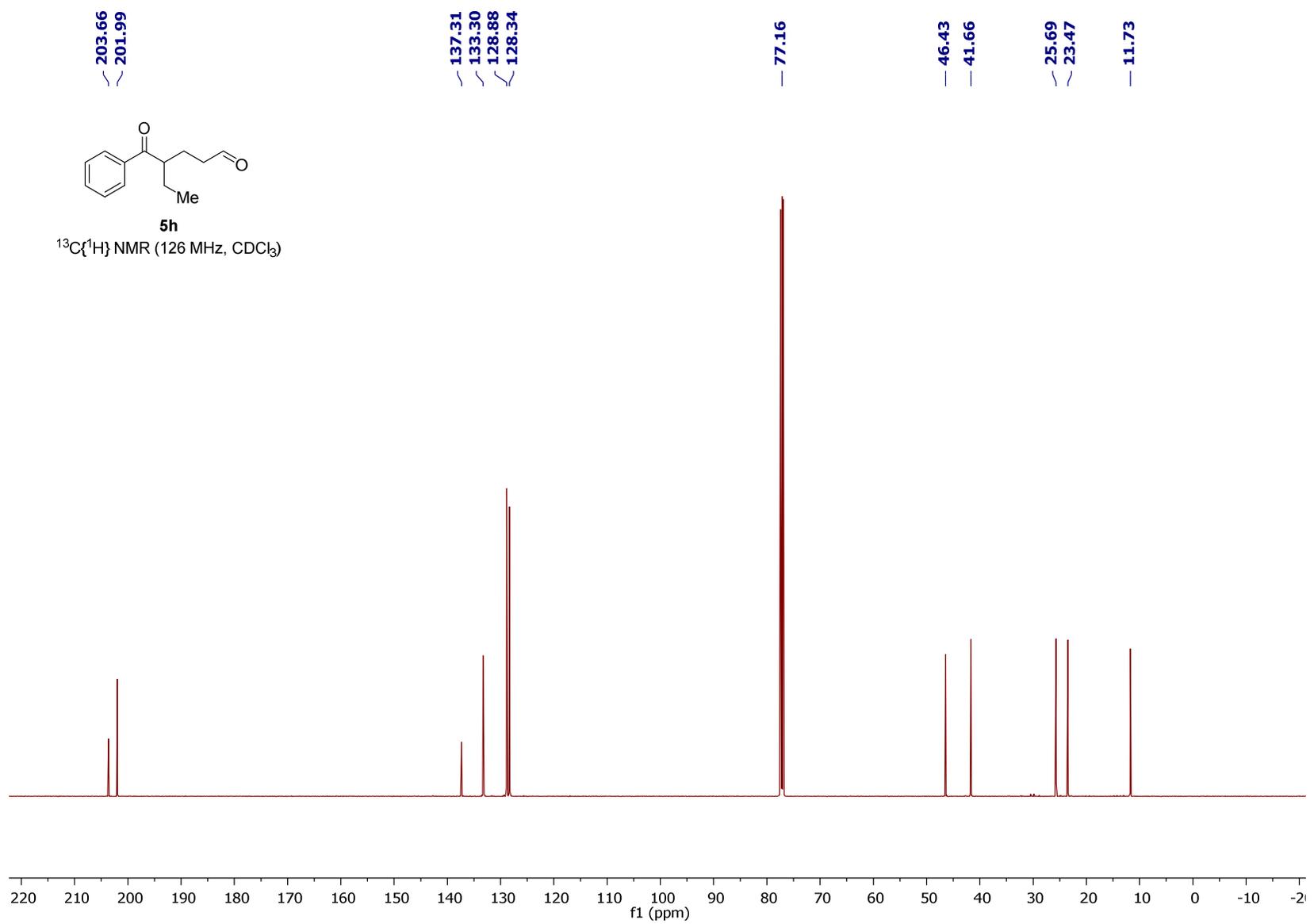
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

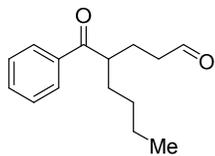




**5h**

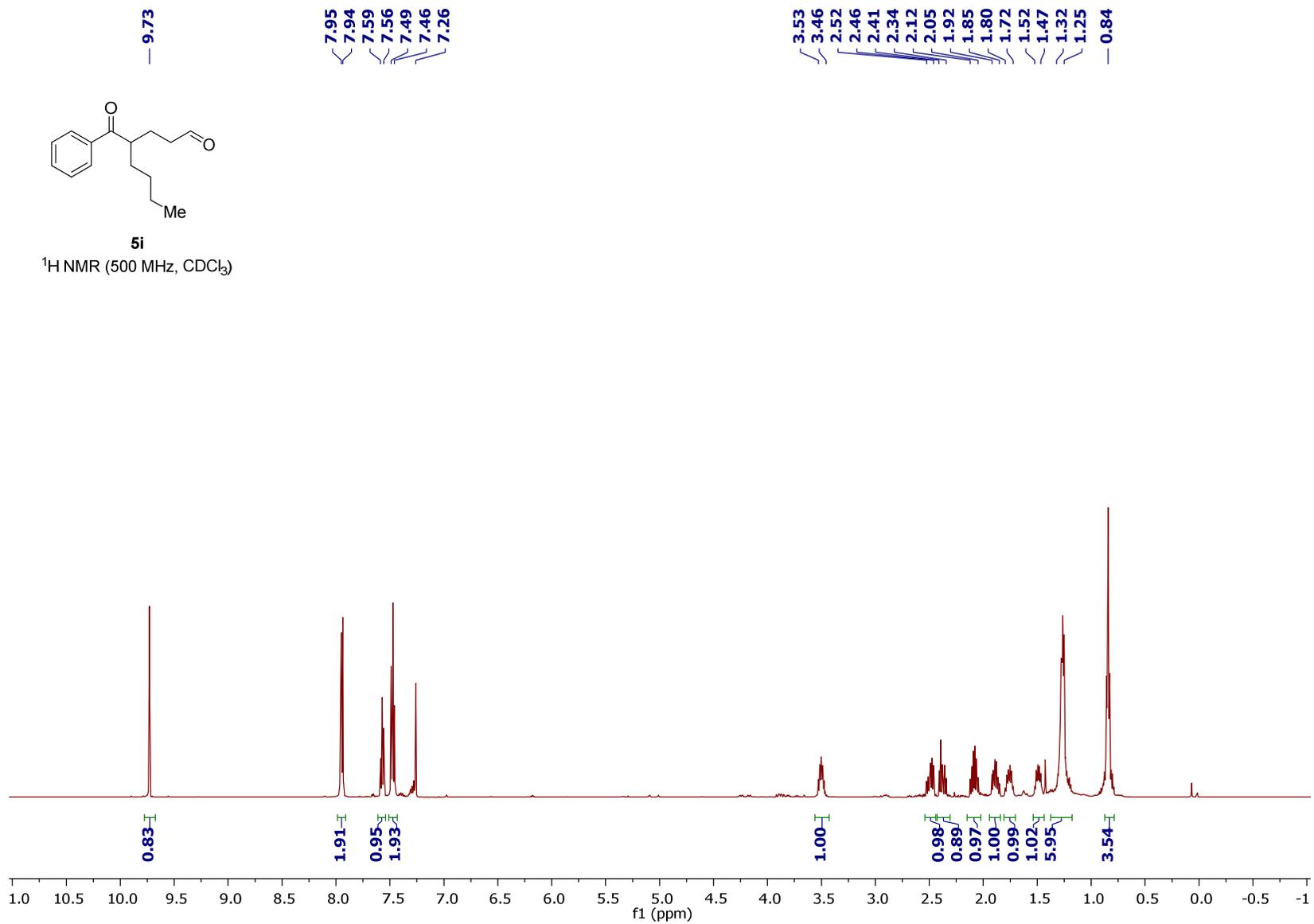
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

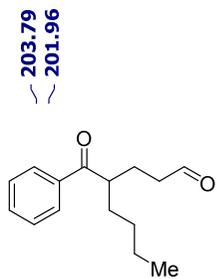




**5i**

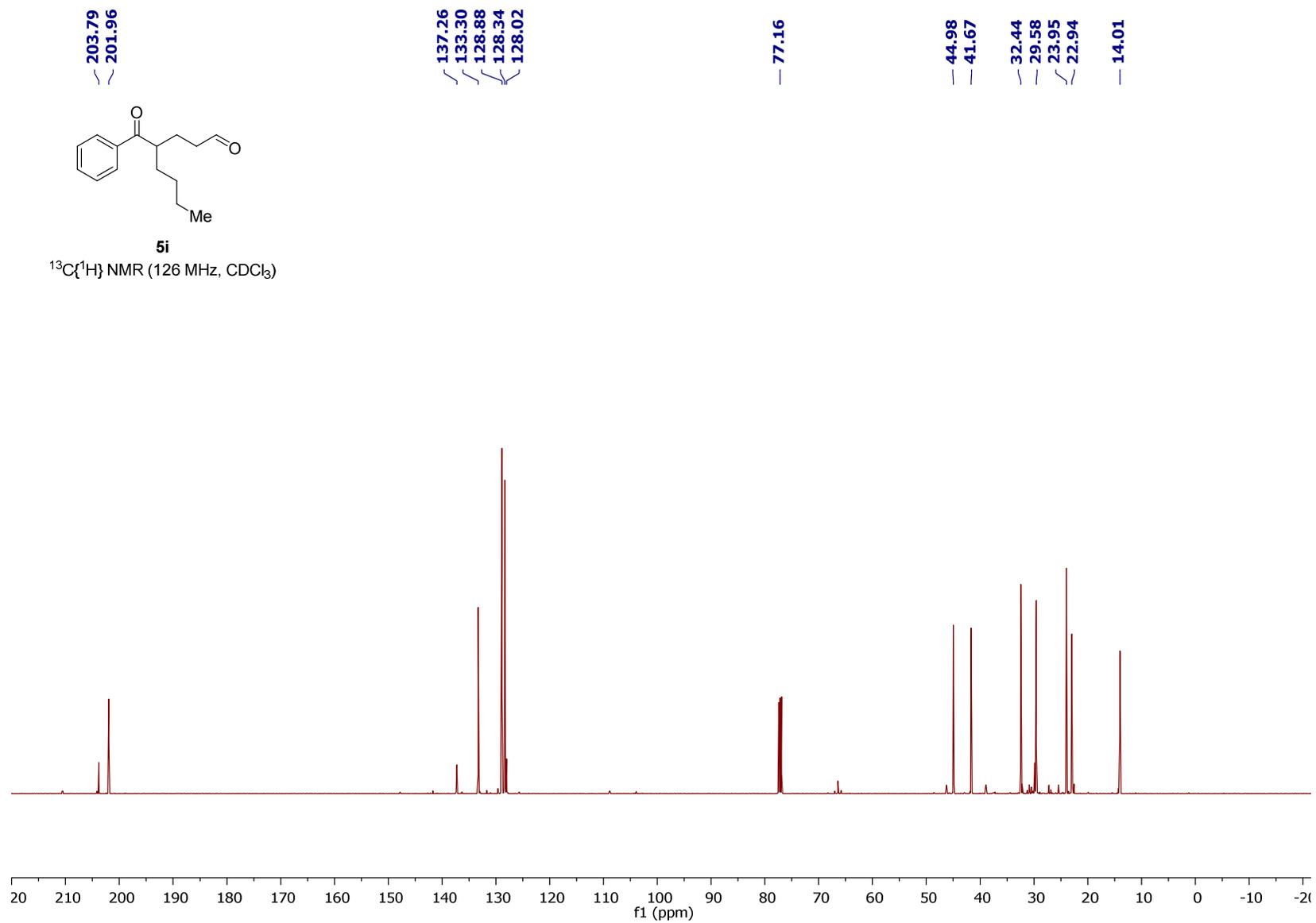
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

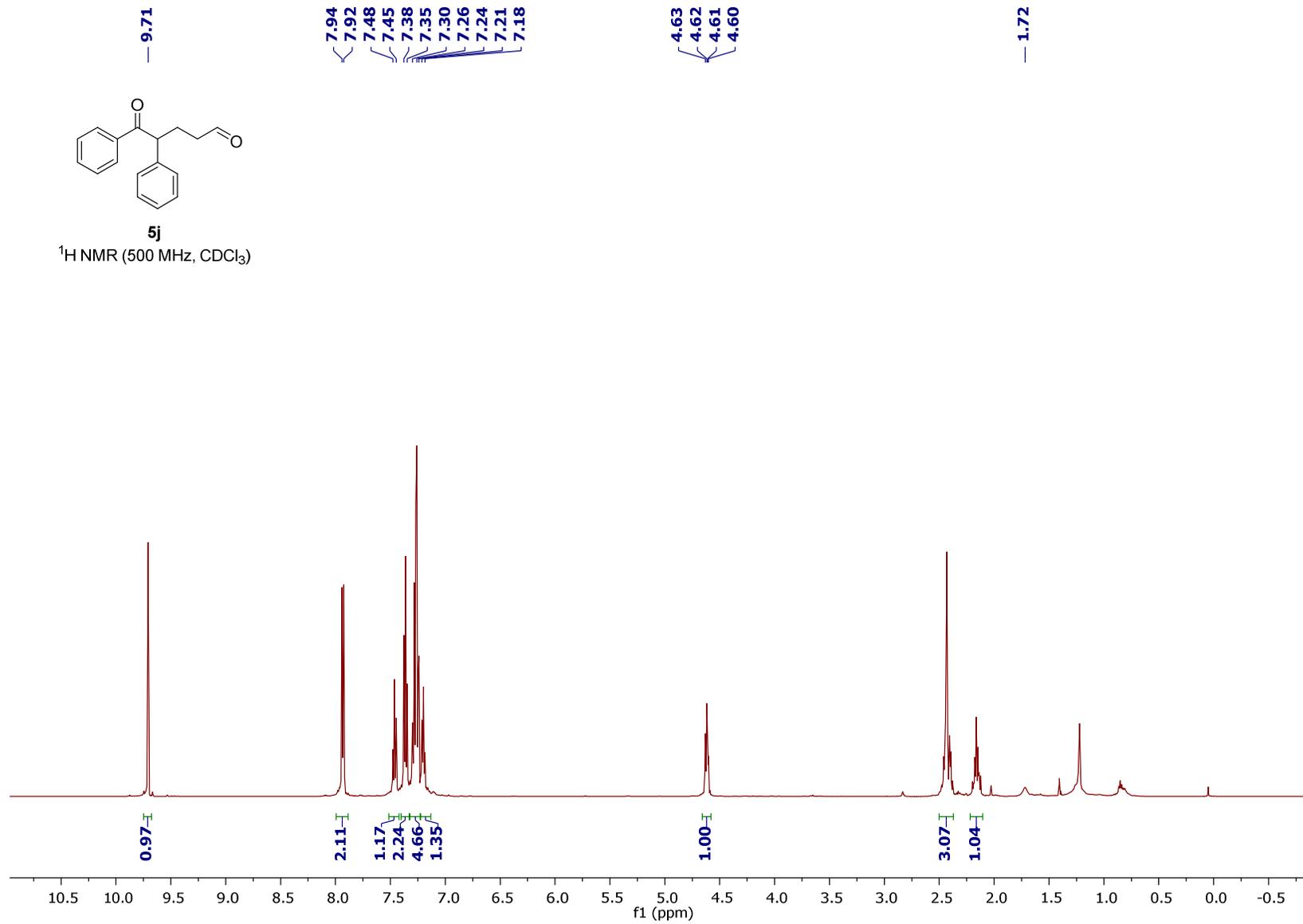
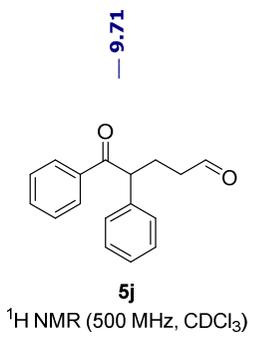


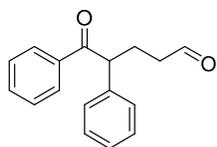


**5i**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

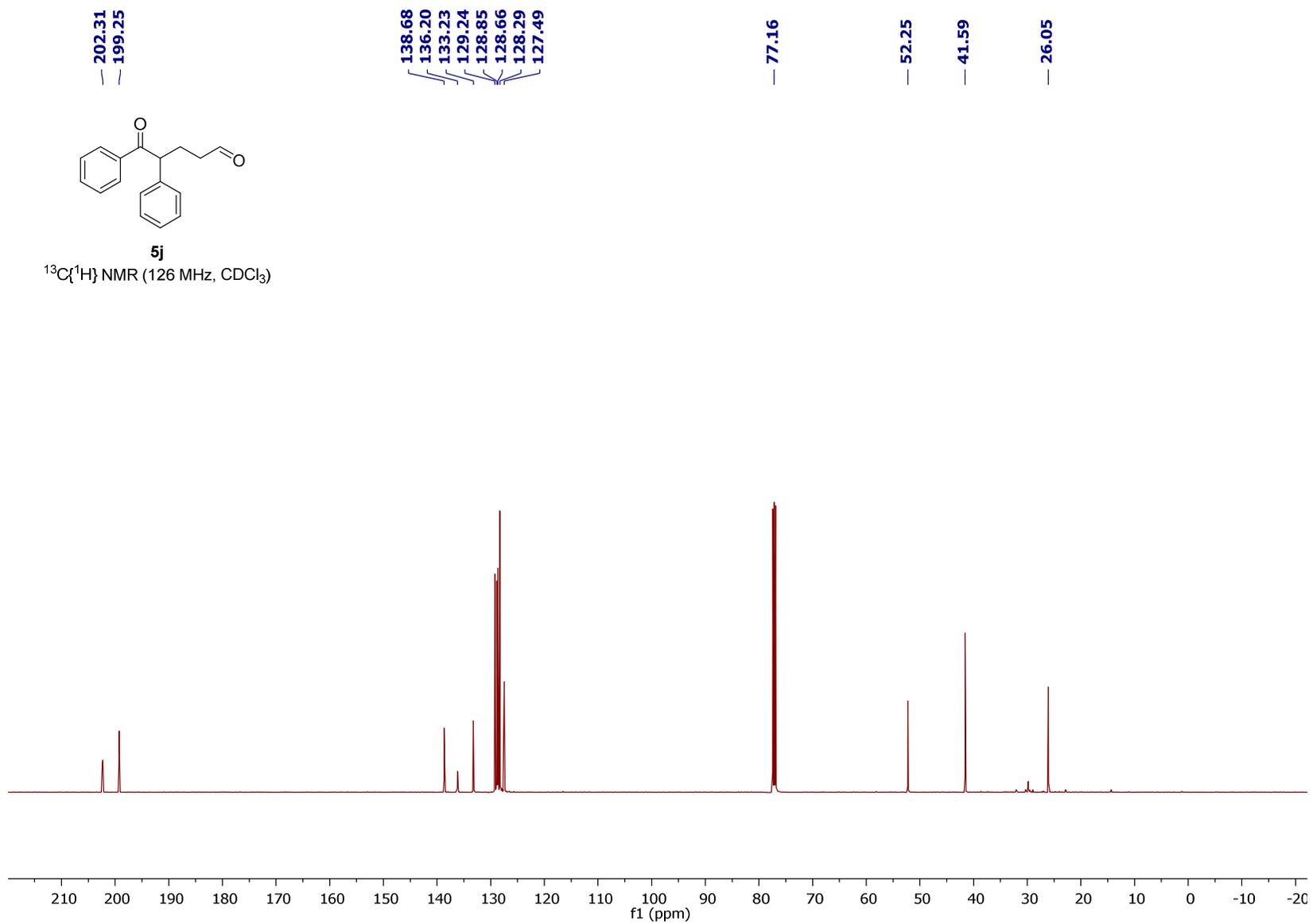


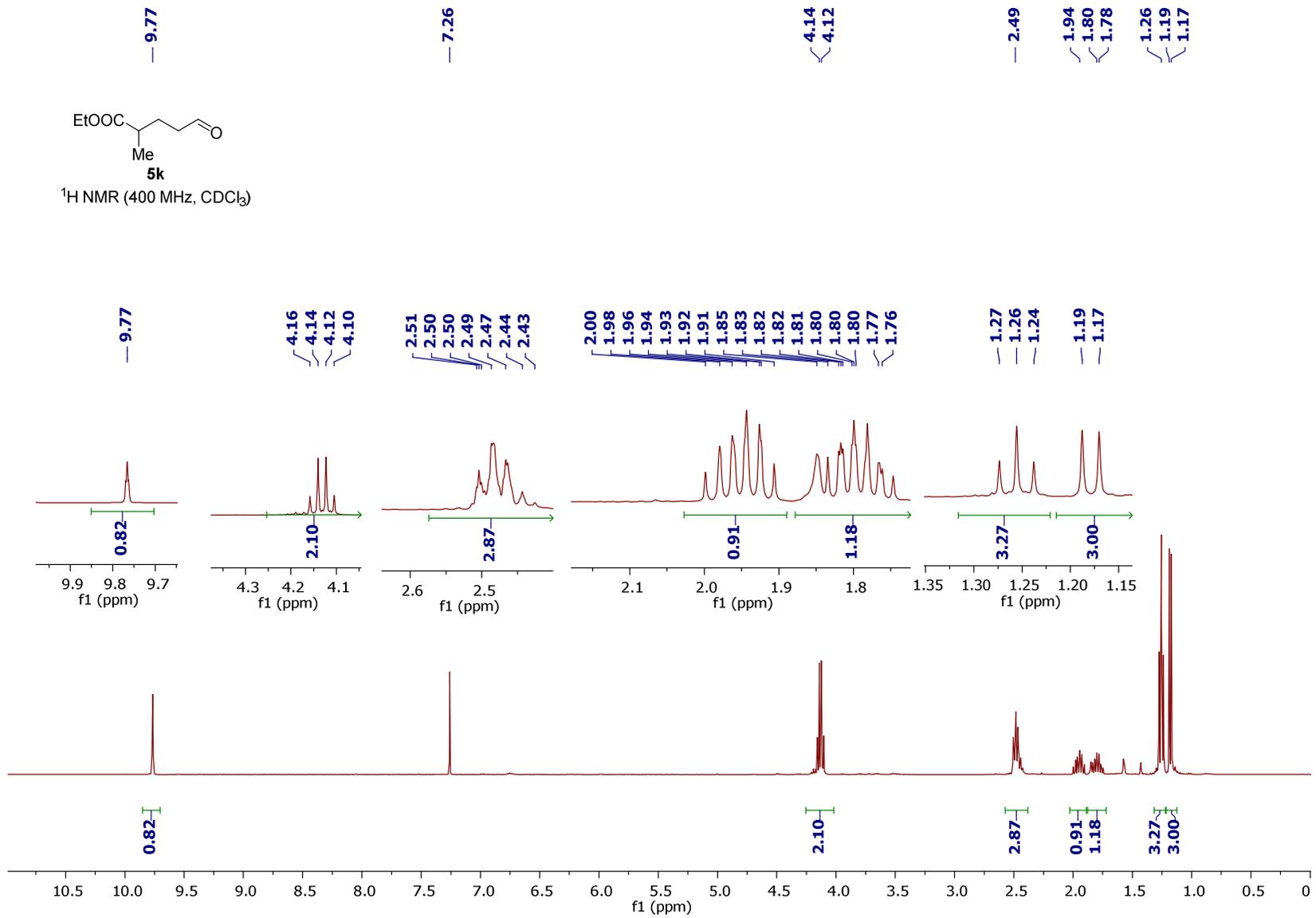
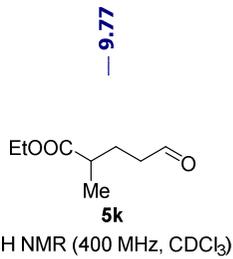


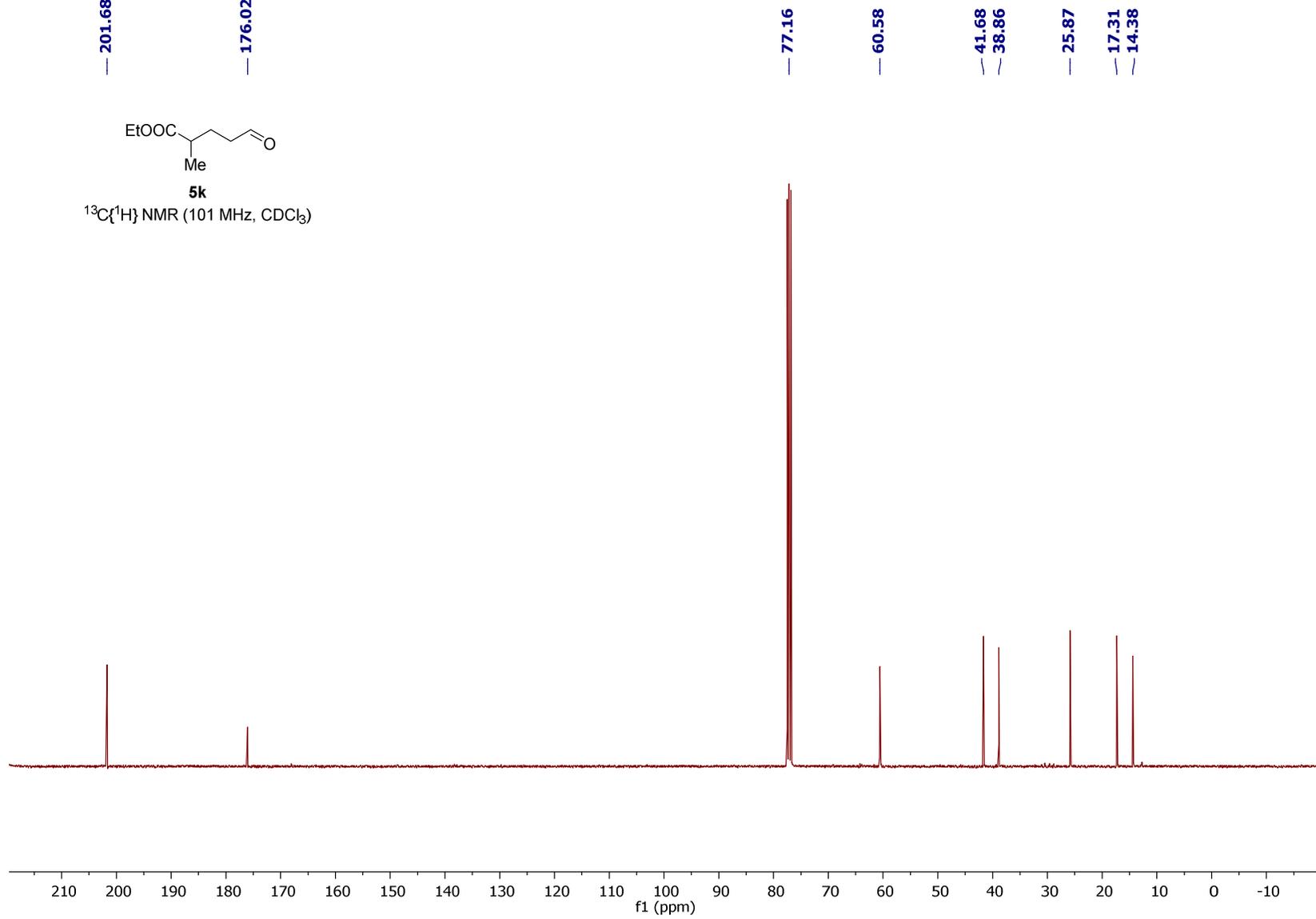
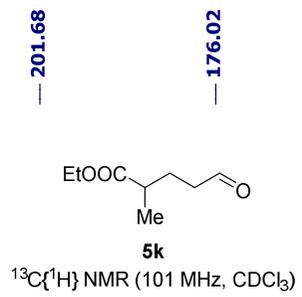


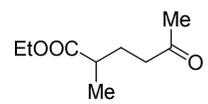
**5j**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )



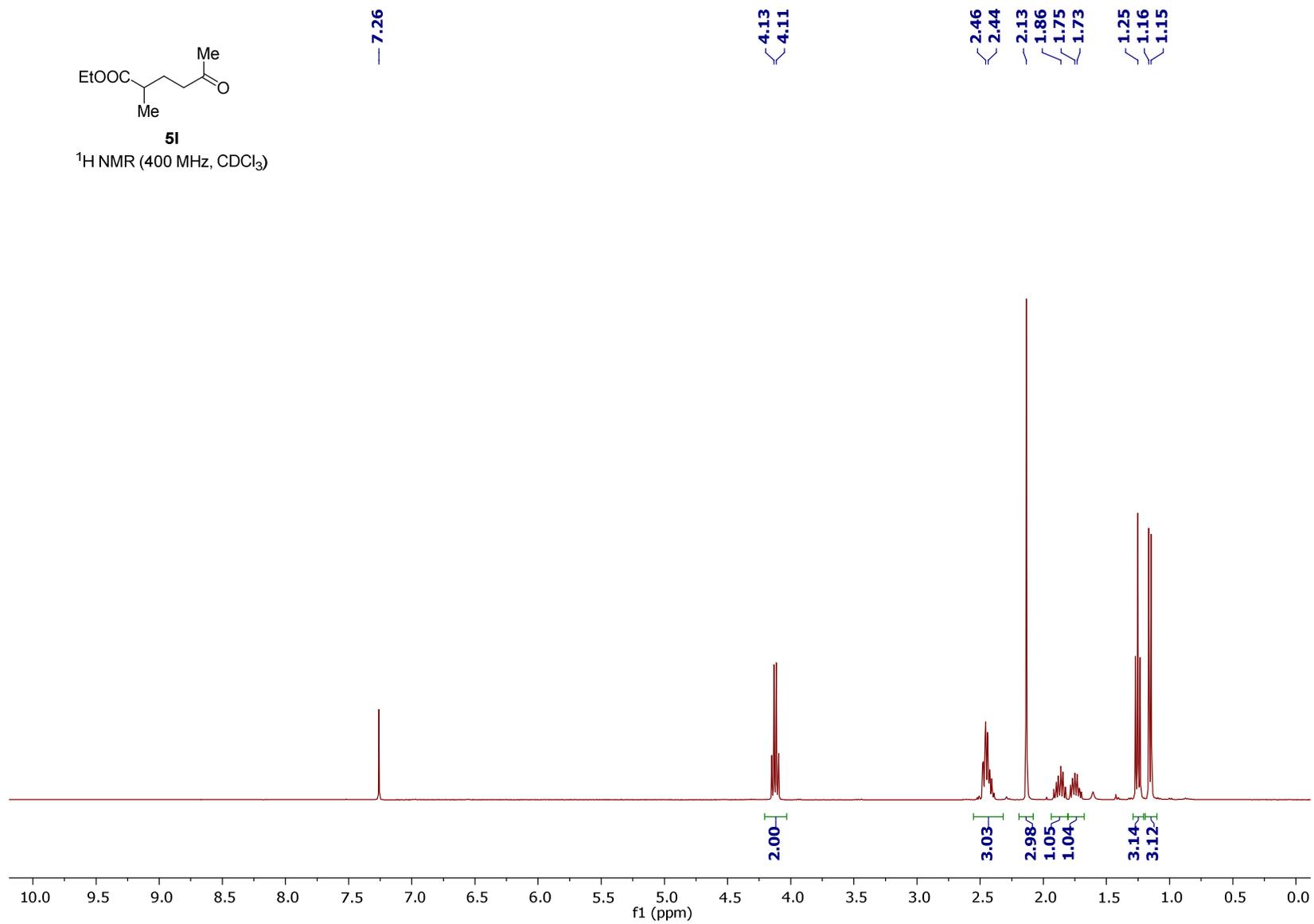




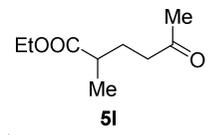


**51**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

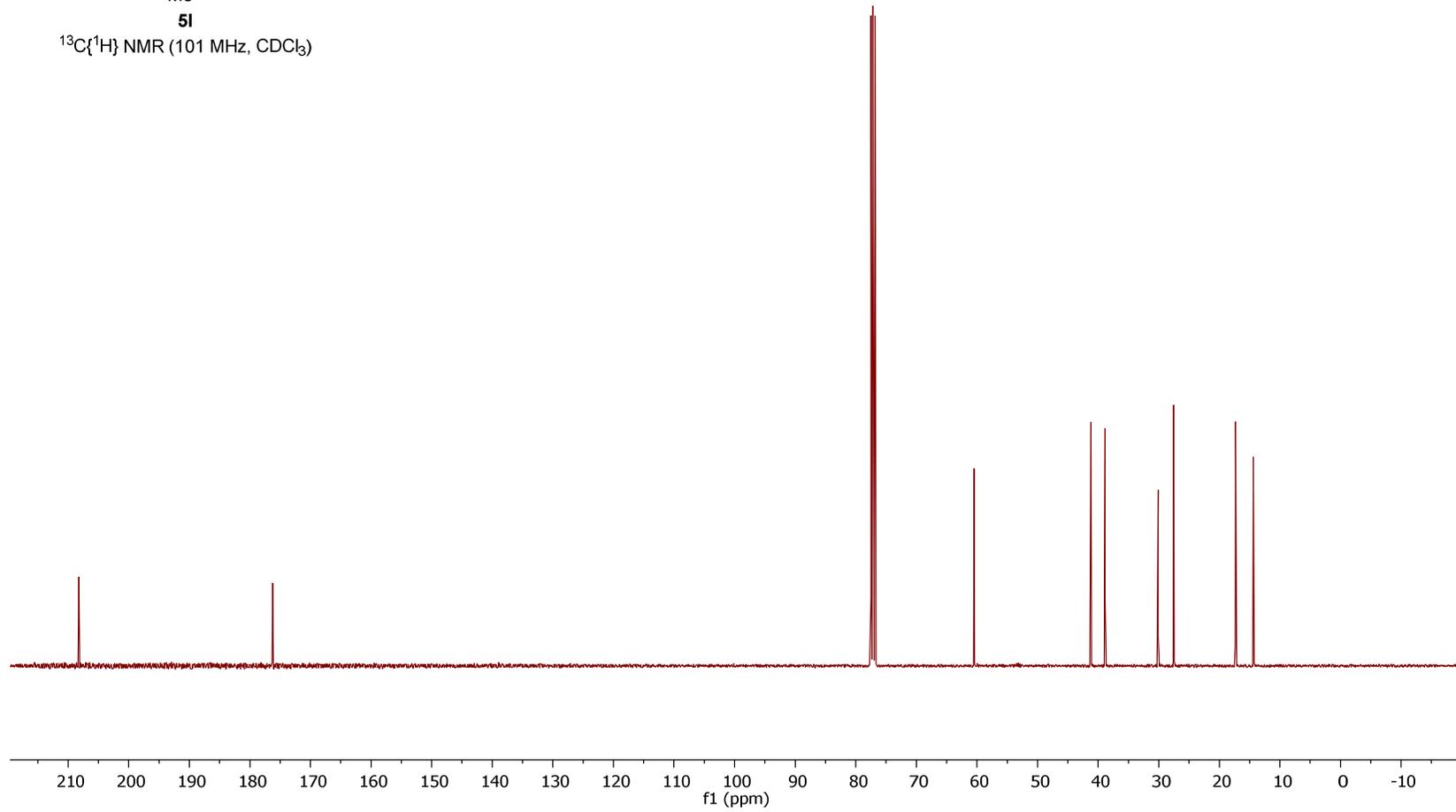


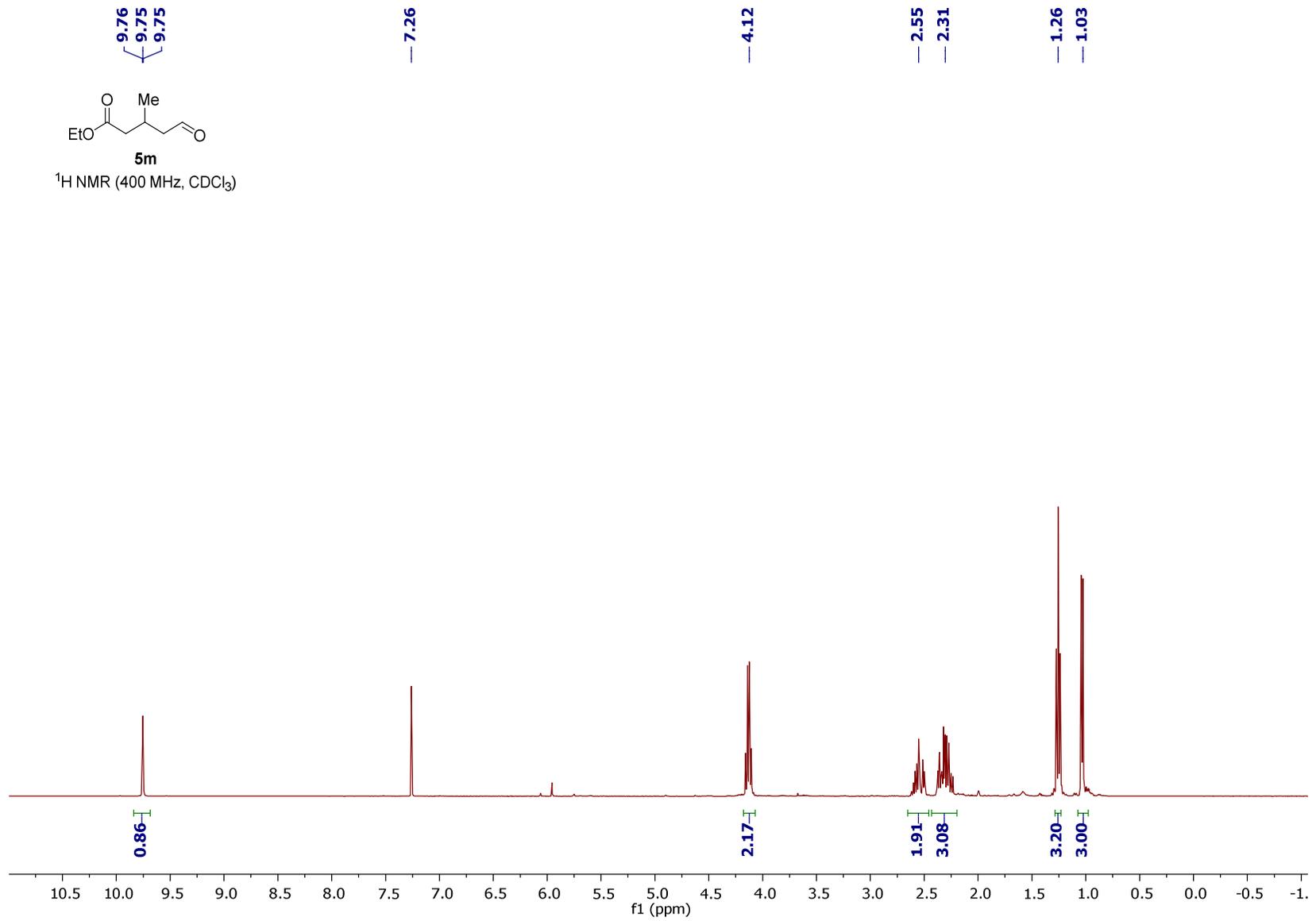
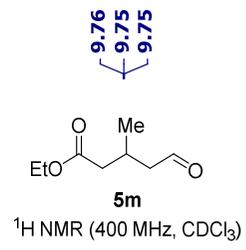
— 208.21 —  
— 176.27 —

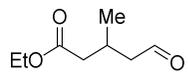


<sup>13</sup>C{<sup>1</sup>H} NMR (101 MHz, CDCl<sub>3</sub>)

— 77.16 —  
— 60.46 —  
— 41.20 —  
— 38.88 —  
— 30.10 —  
— 27.51 —  
— 17.33 —  
— 14.39 —

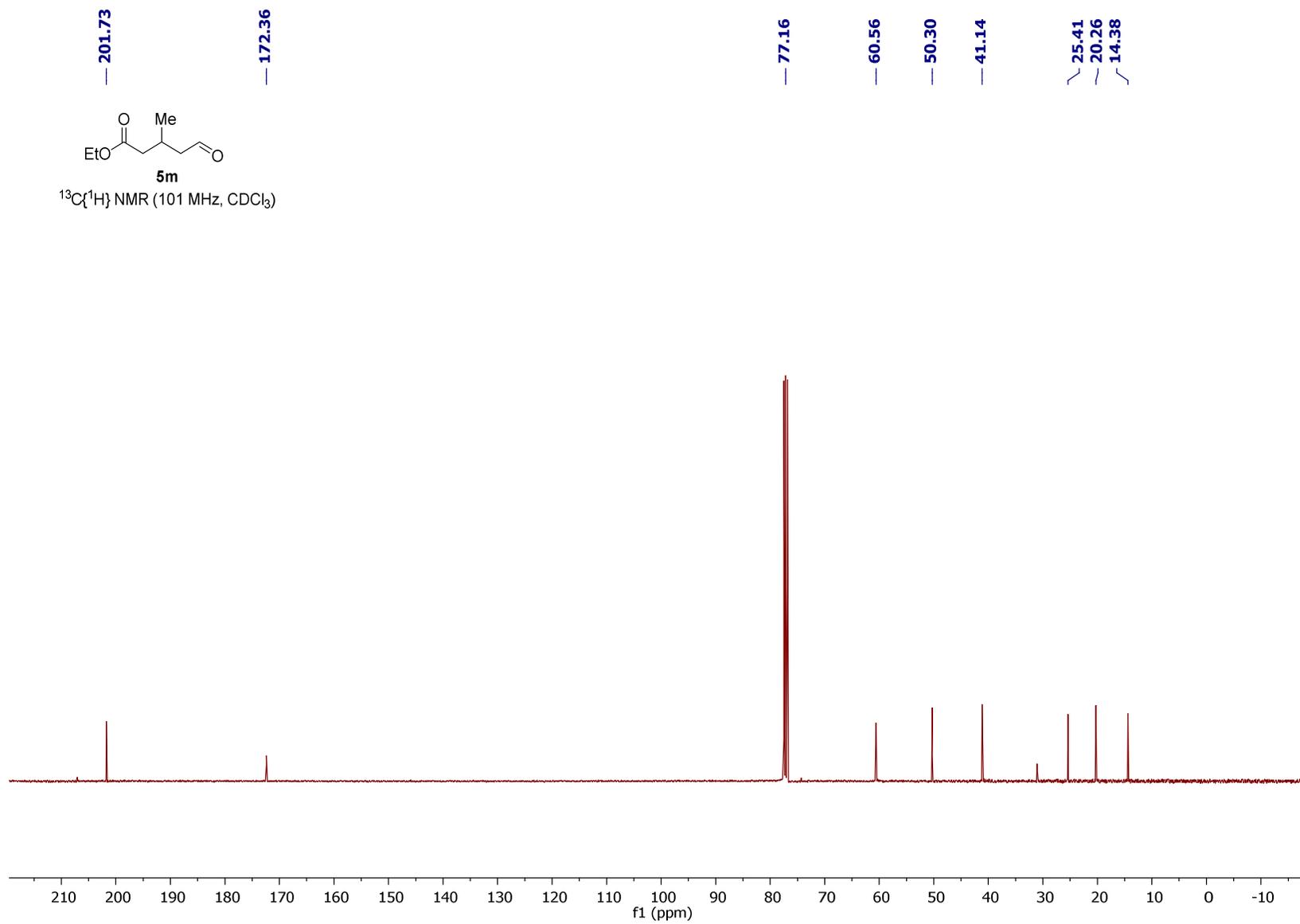


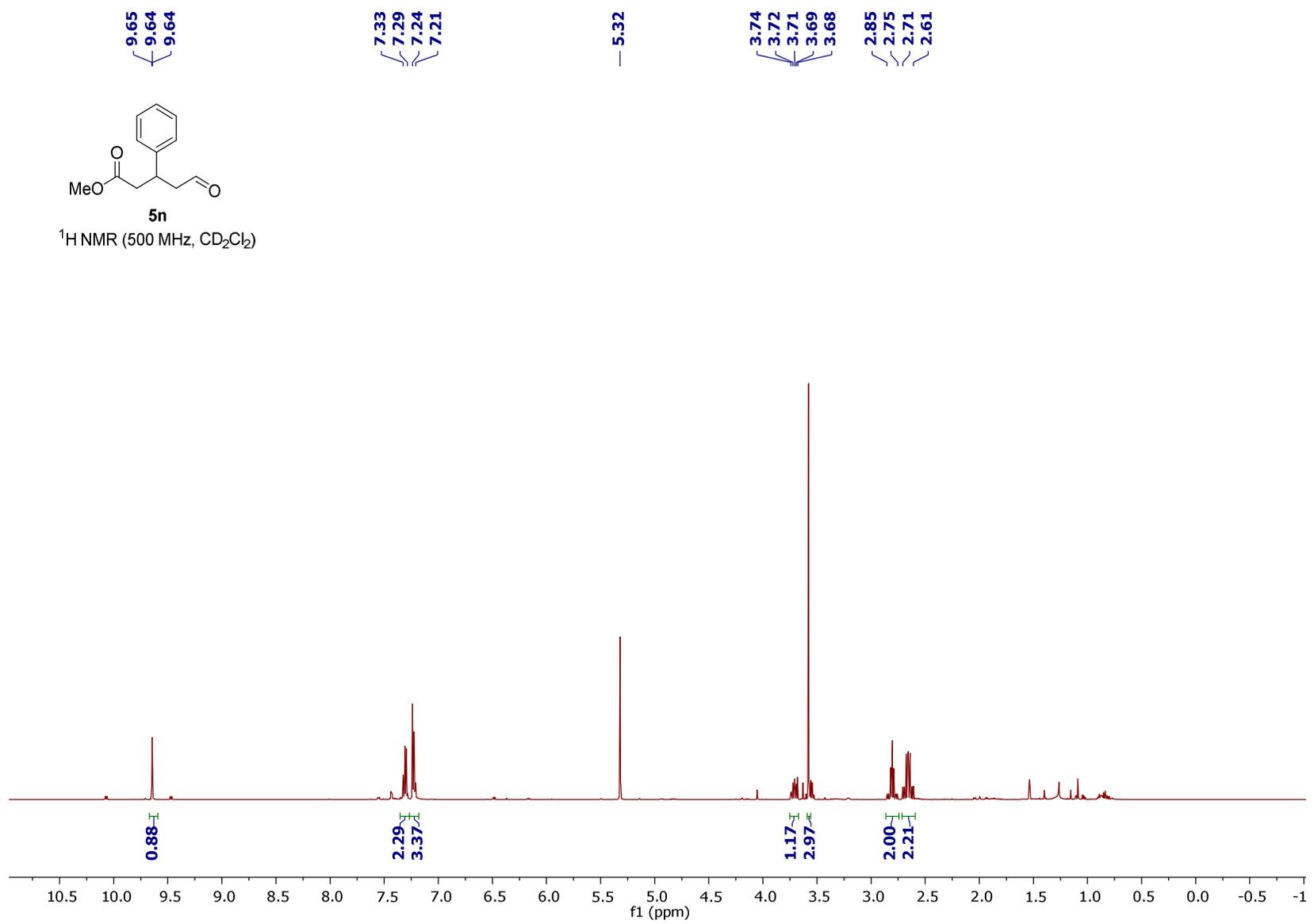
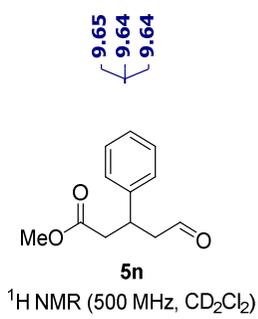


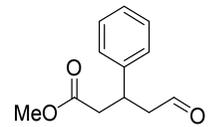


5m

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )







**5n**

$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CD}_2\text{Cl}_2$ )

— 201.03

— 172.23

— 143.17

129.06

127.69

127.33

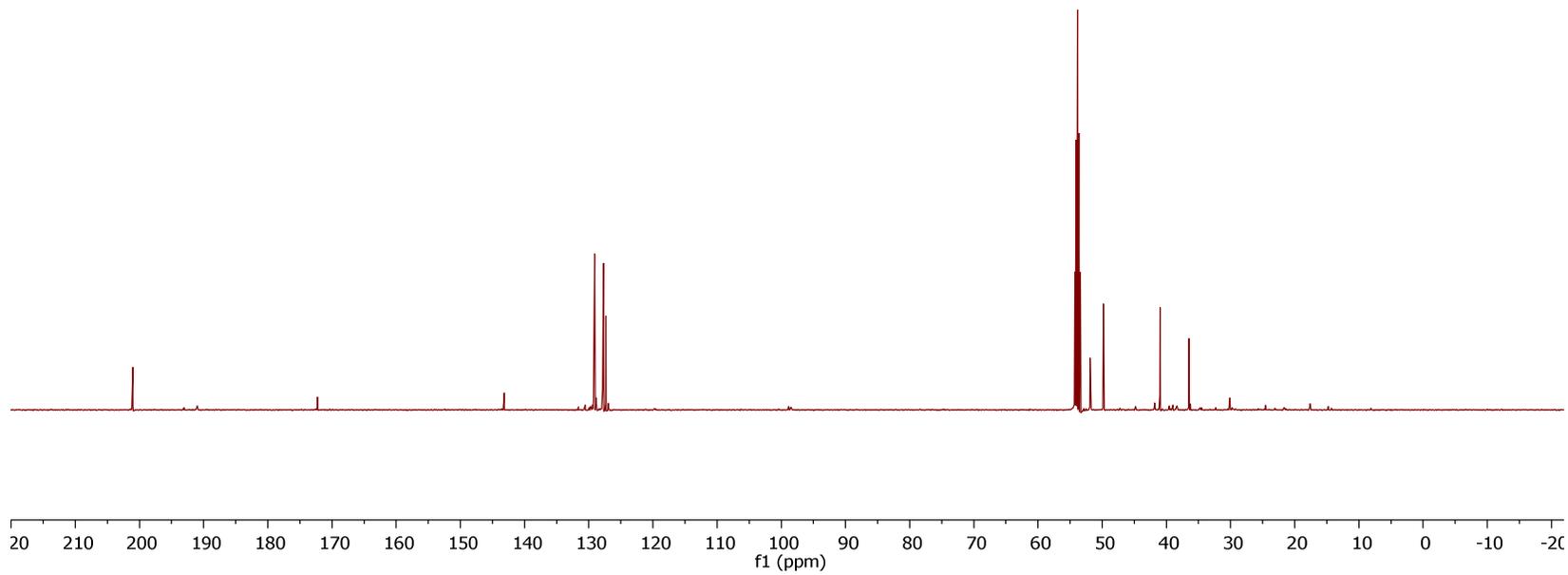
53.84

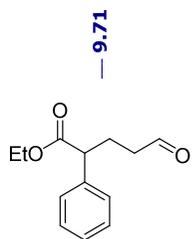
51.87

49.79

40.99

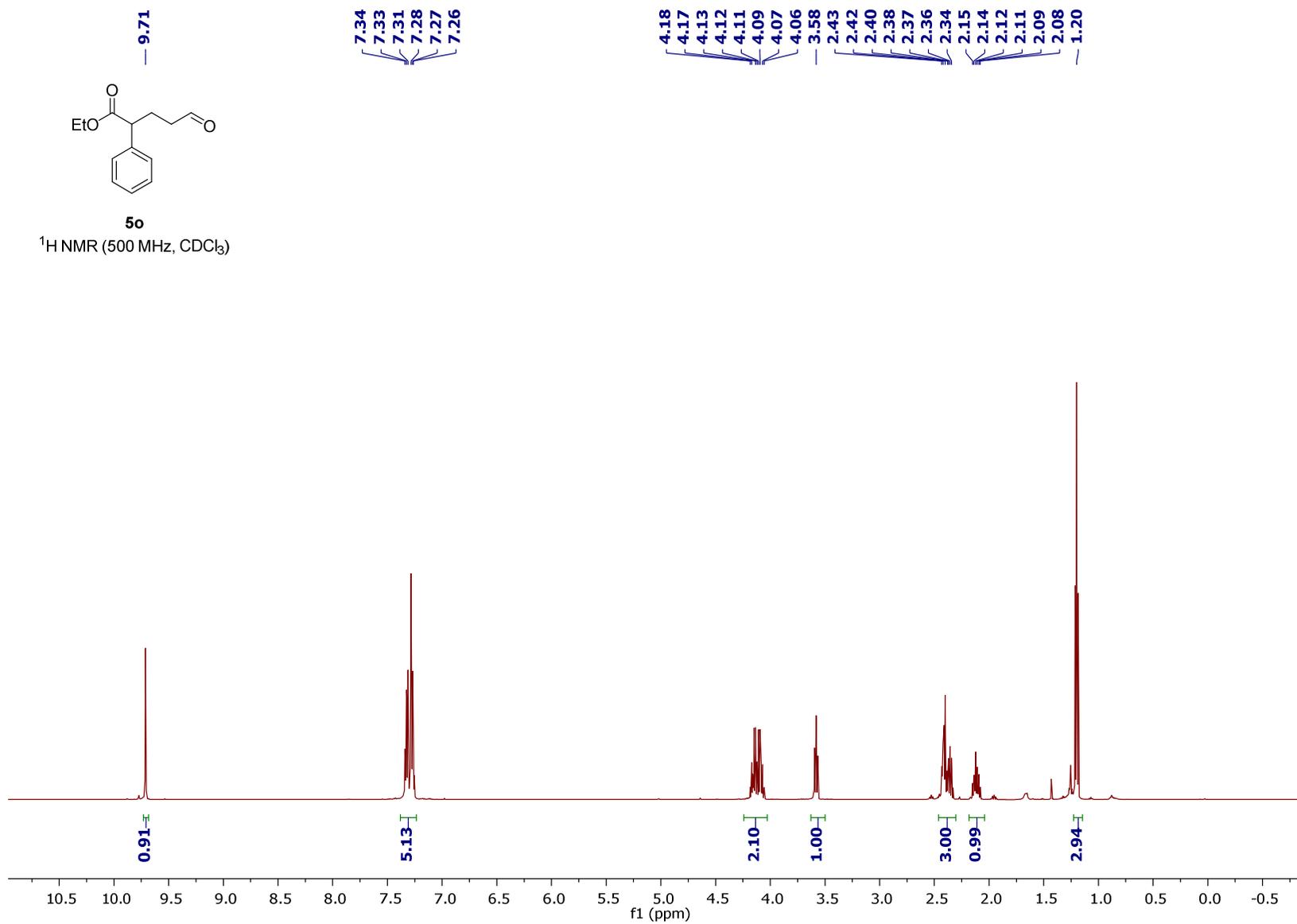
36.50

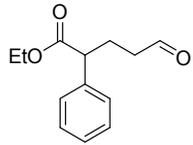




**5o**

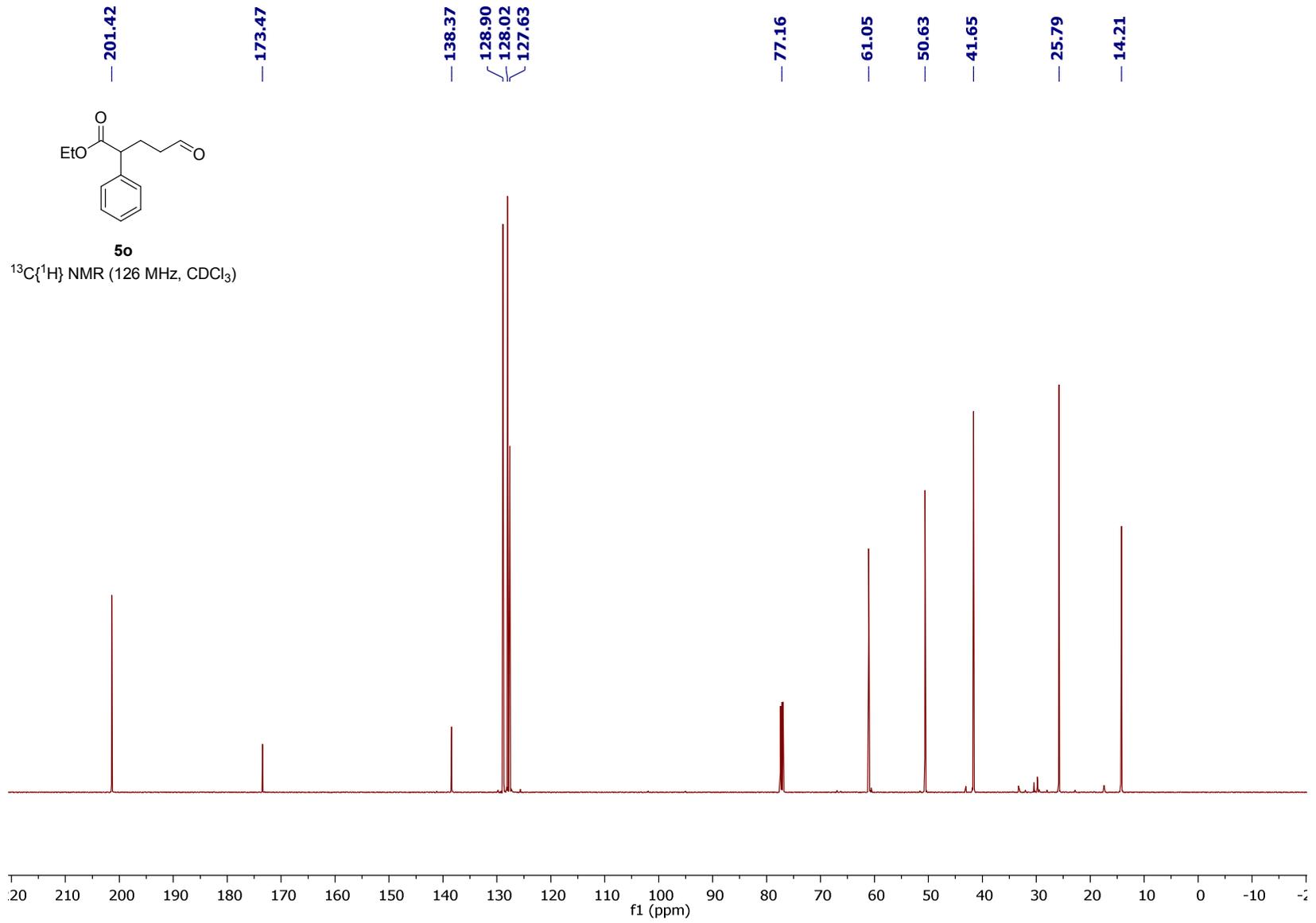
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)

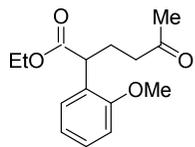




**5o**

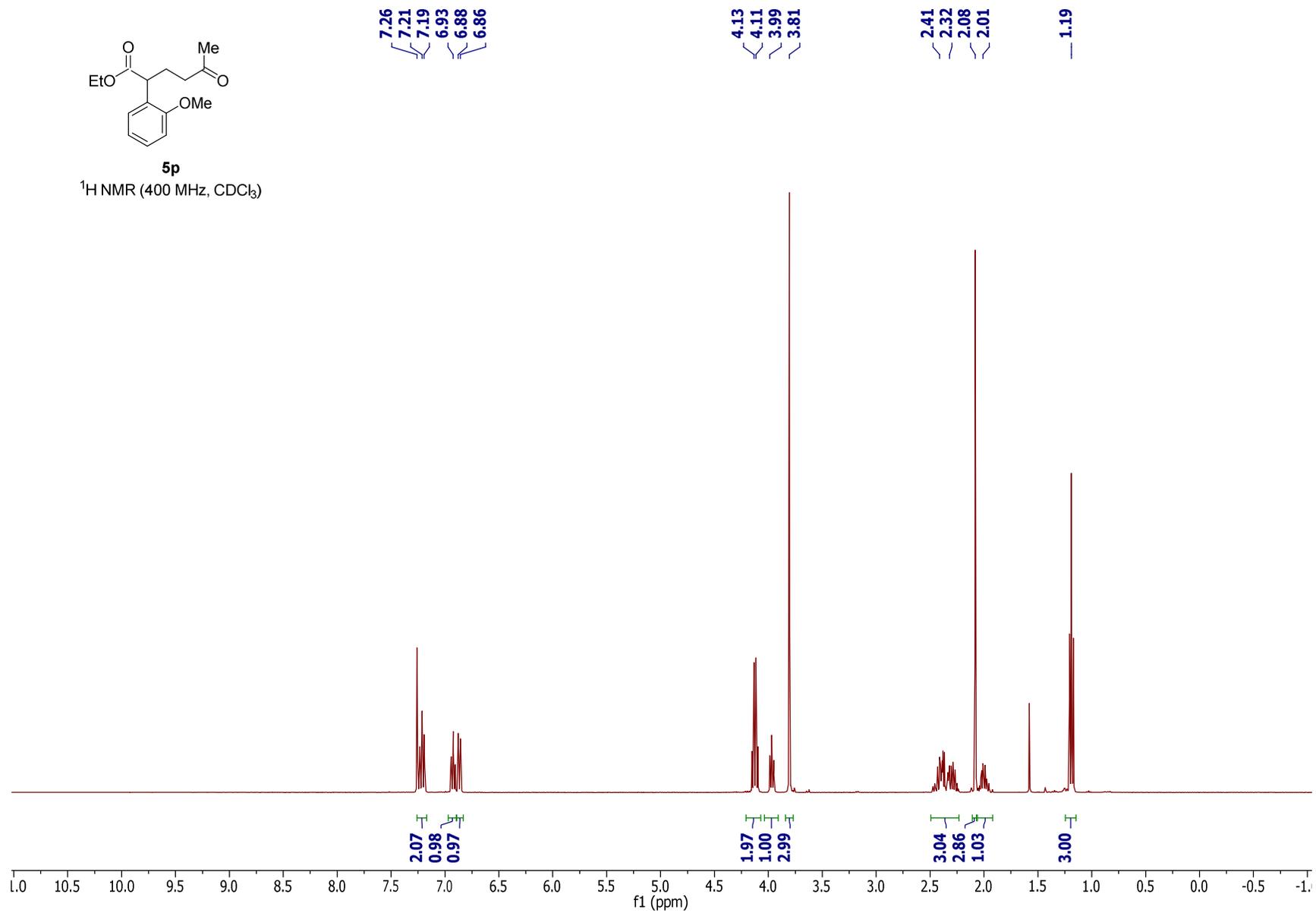
$^{13}\text{C}\{^1\text{H}\}$  NMR (126 MHz,  $\text{CDCl}_3$ )

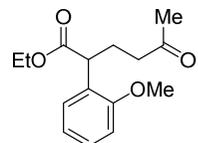




**5p**

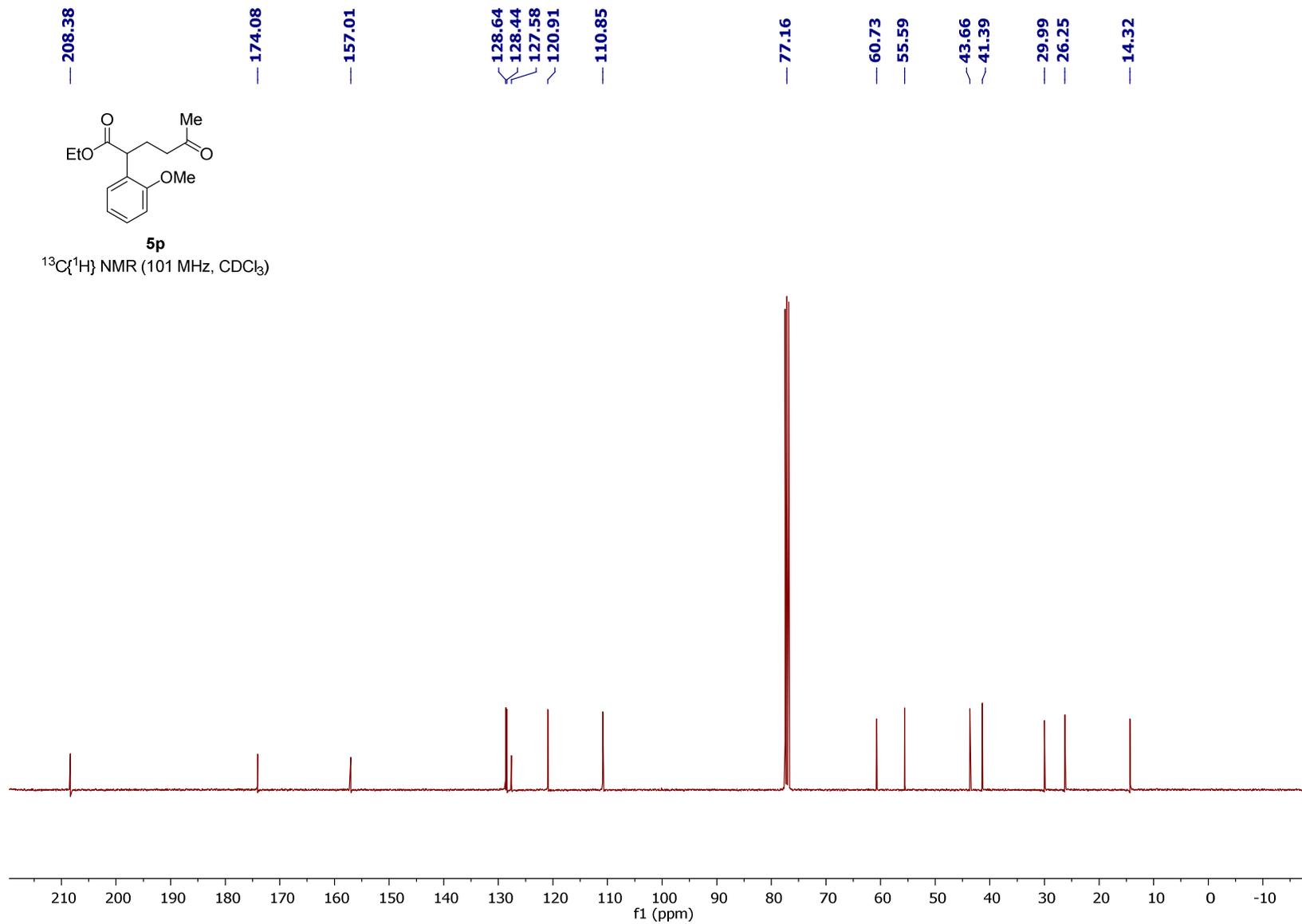
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

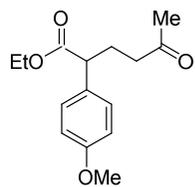




**5p**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )





**5q**

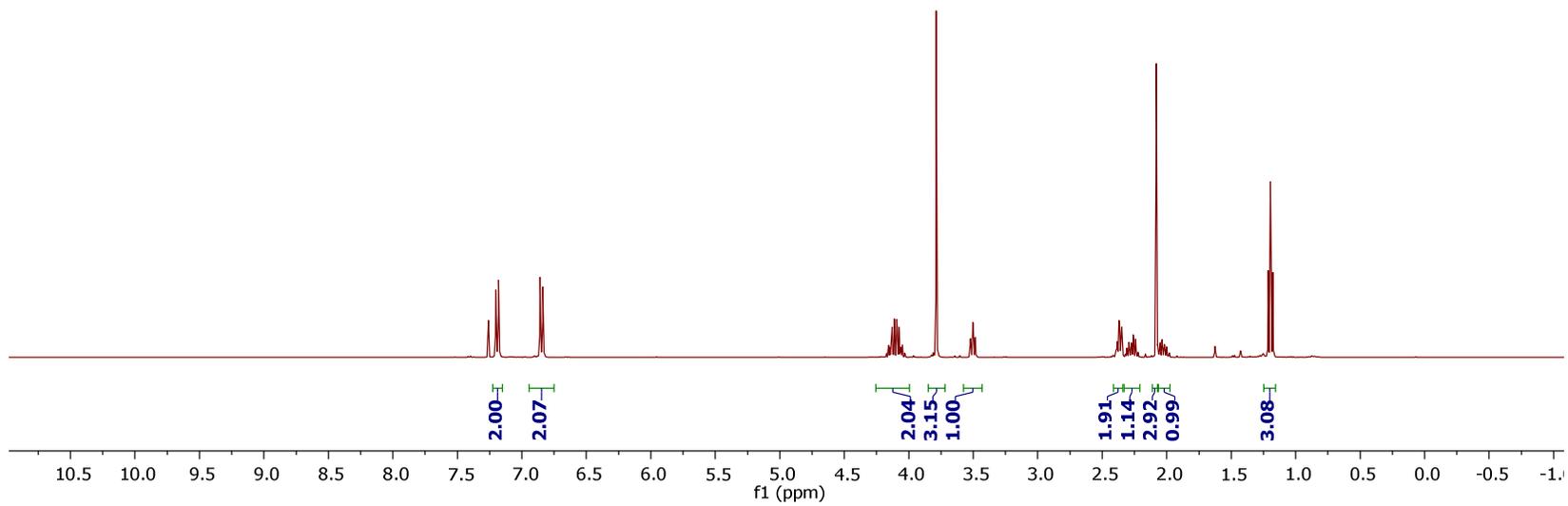
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

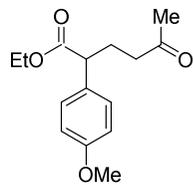
7.26  
7.20  
7.18  
6.86  
6.84

4.11  
3.79  
3.50

2.35  
2.26  
2.08  
2.04

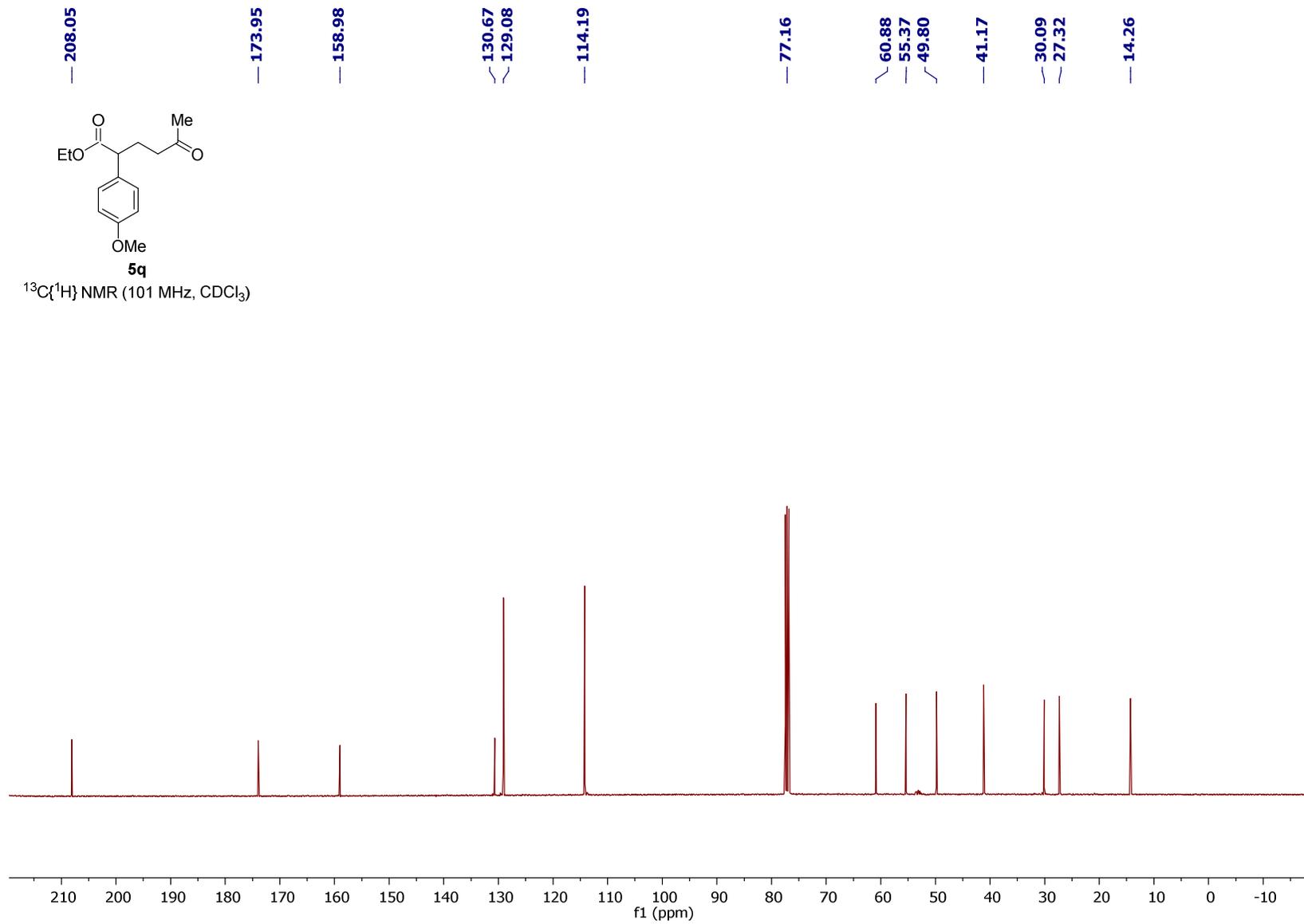
1.19

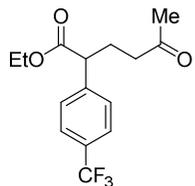




**5q**

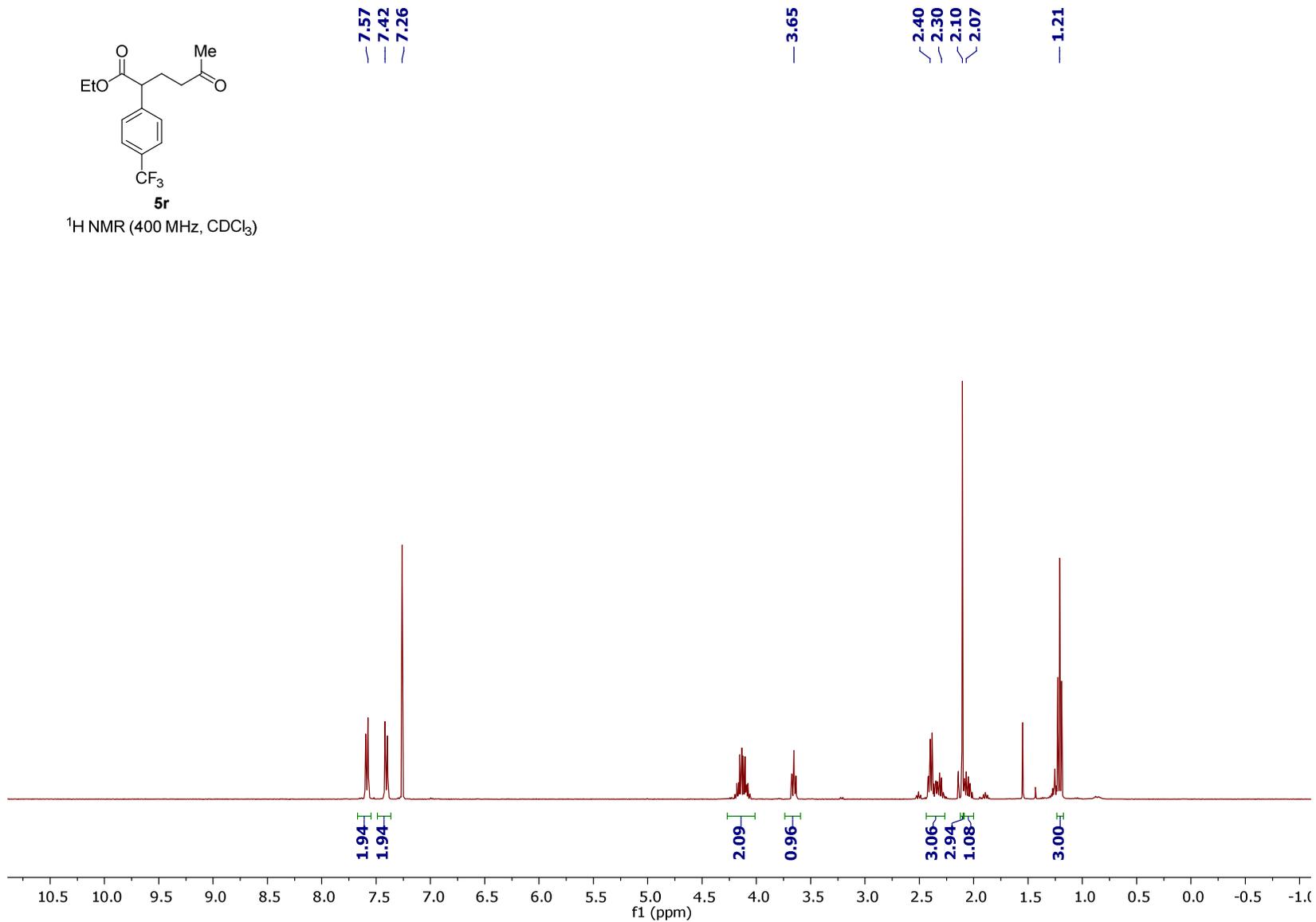
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

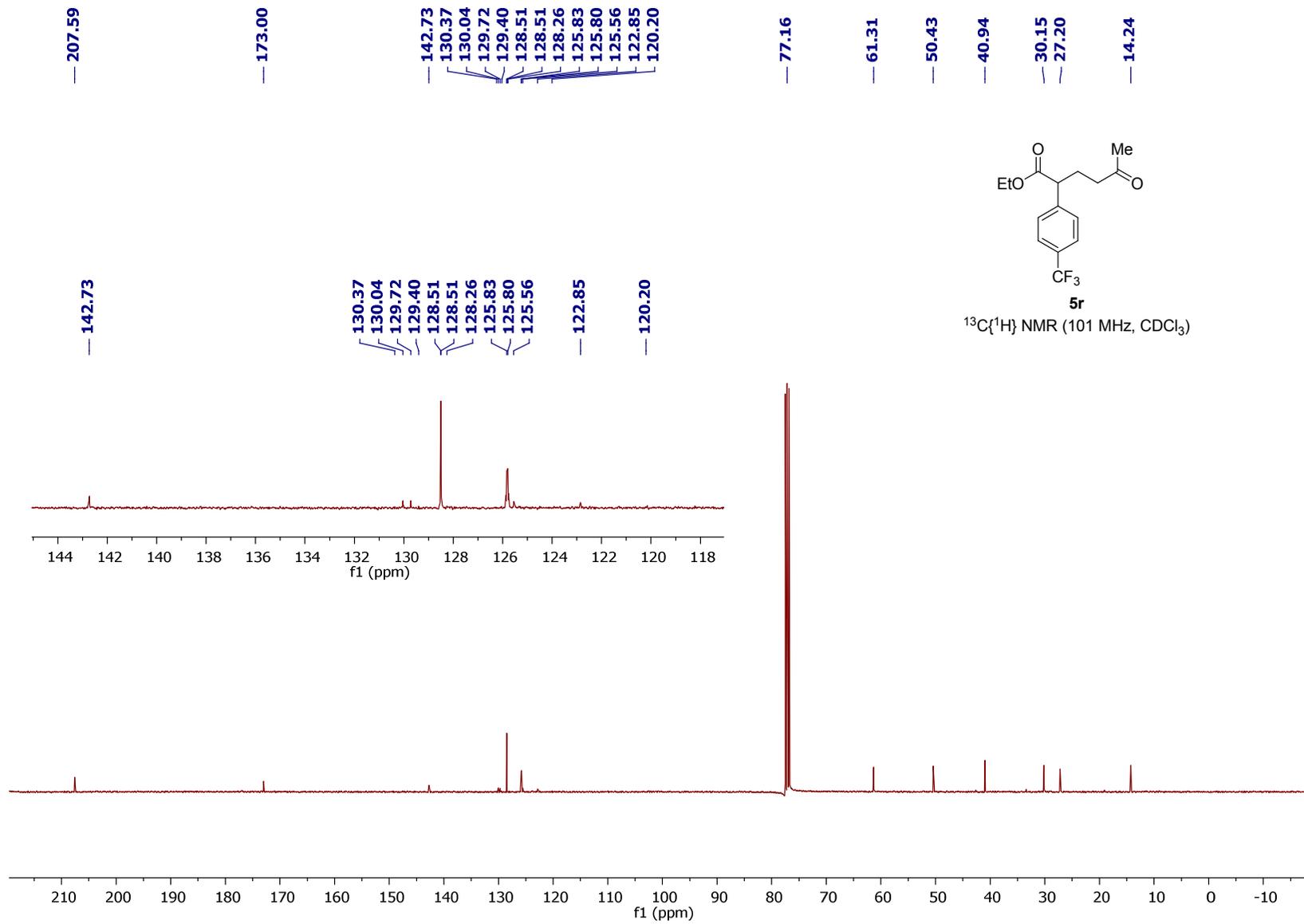


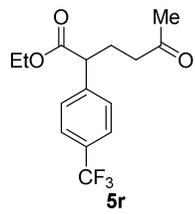


**5r**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

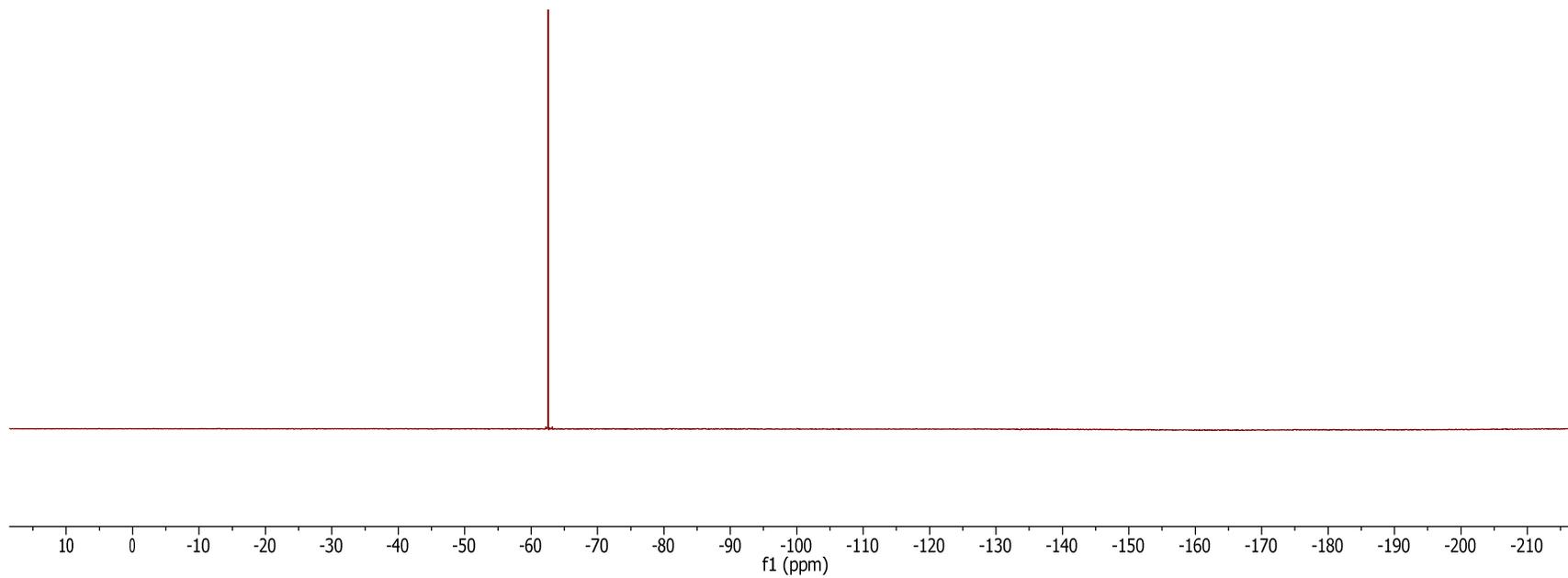


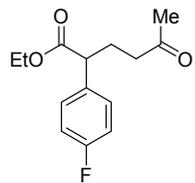




$^{19}\text{F}\{^1\text{H},^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )

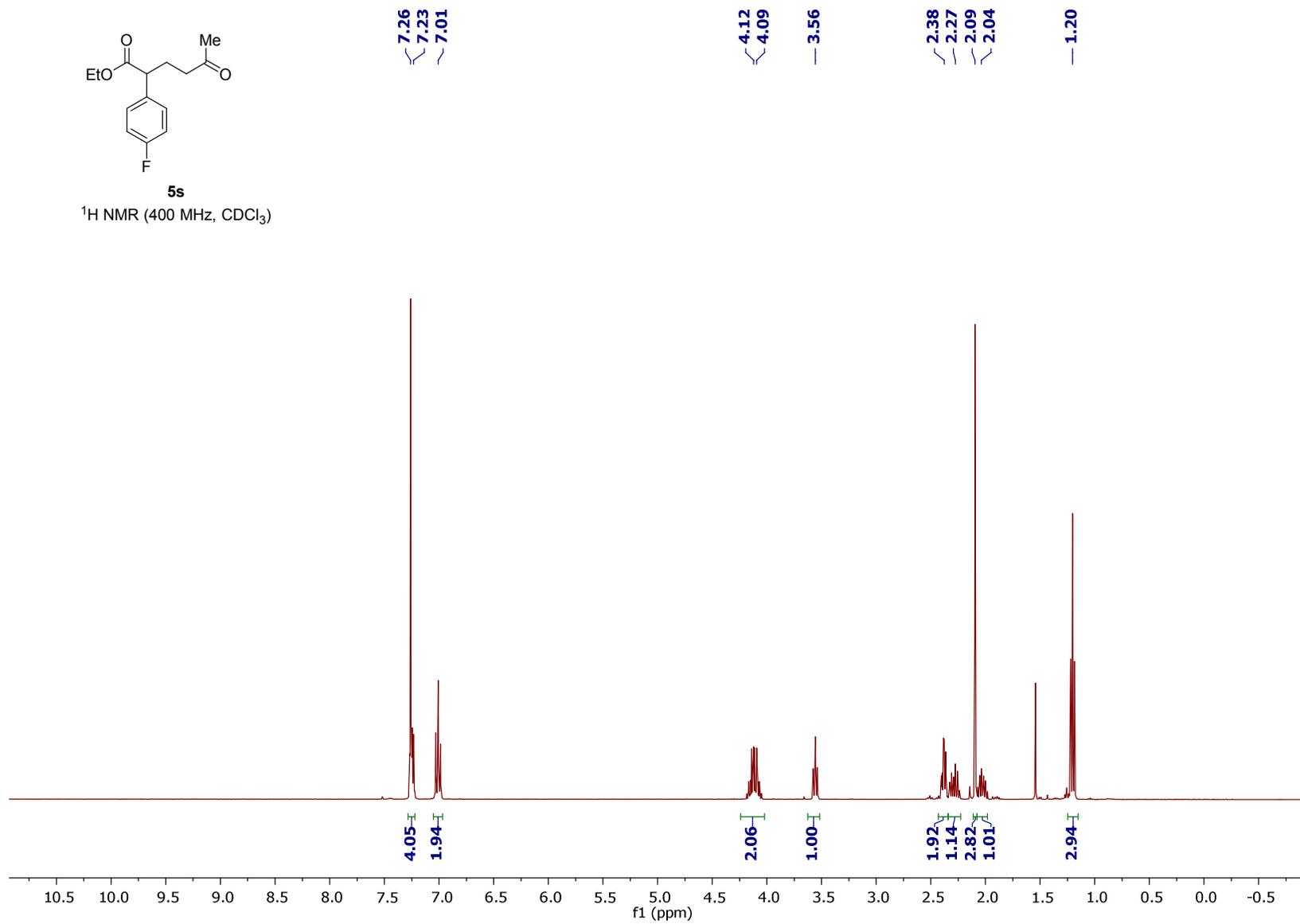
-62.59

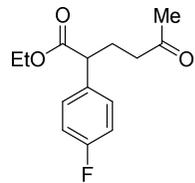




**5s**

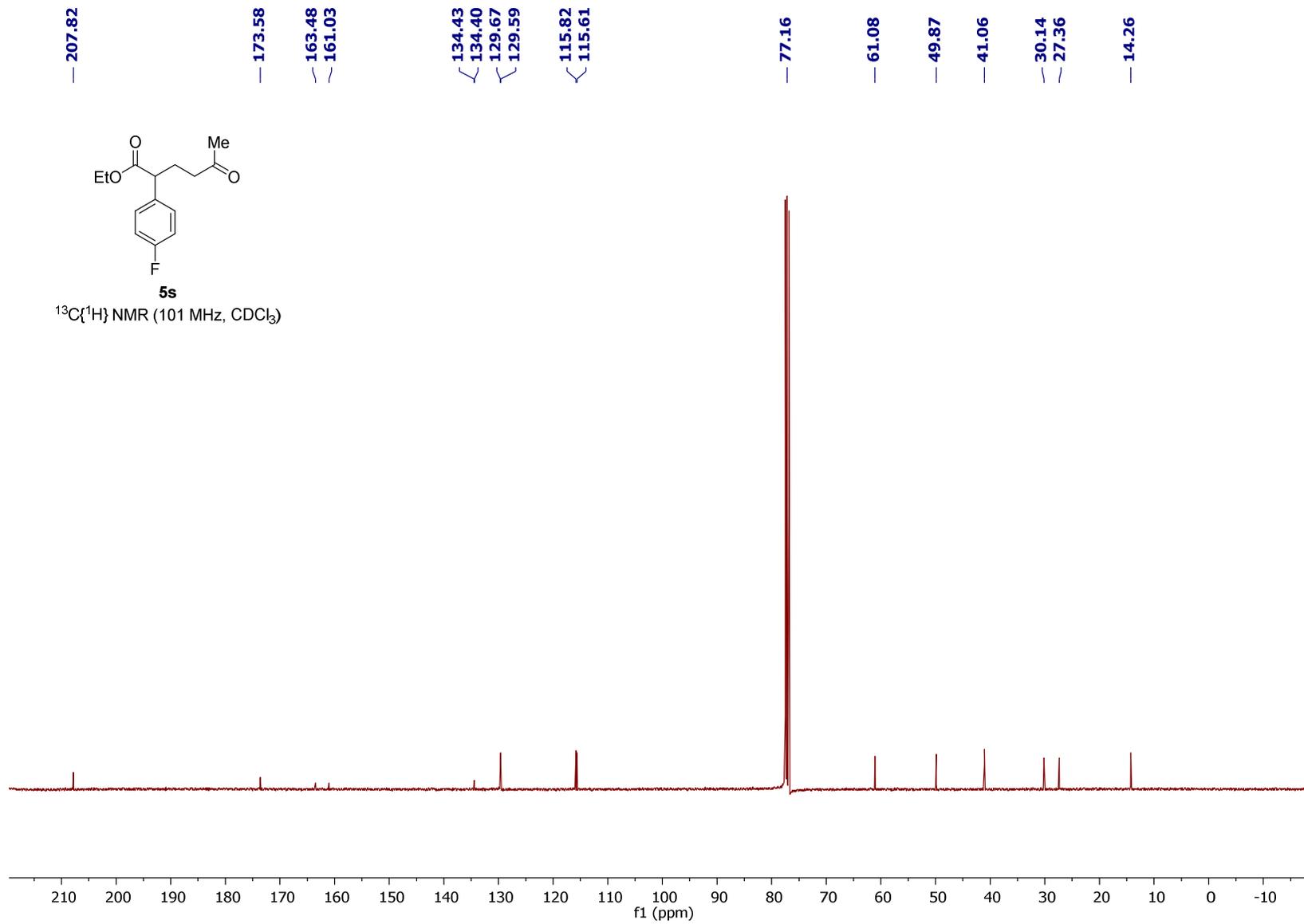
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

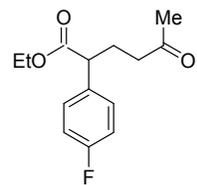




**5s**

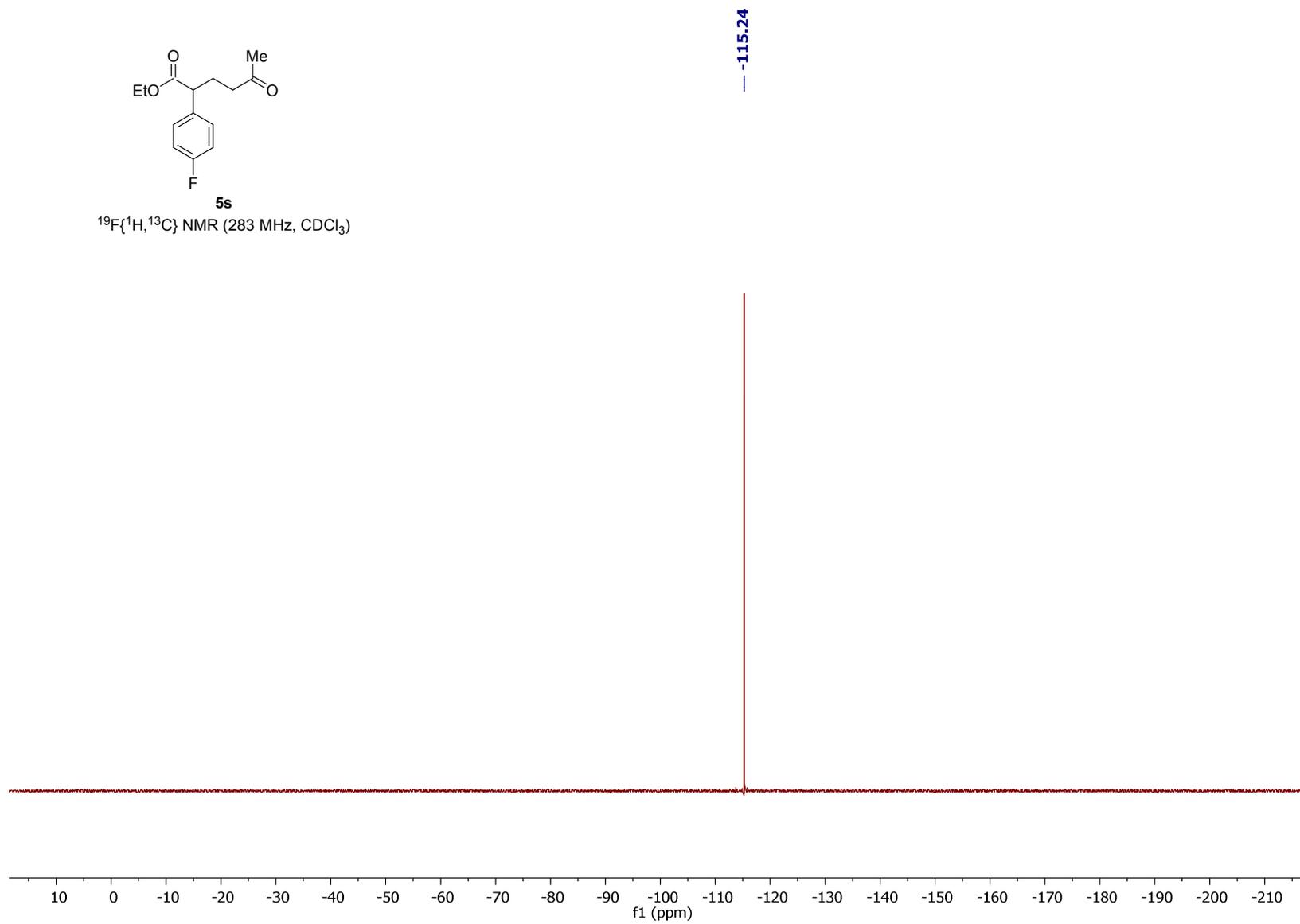
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )

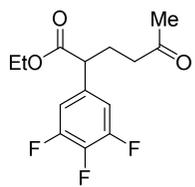




**5s**

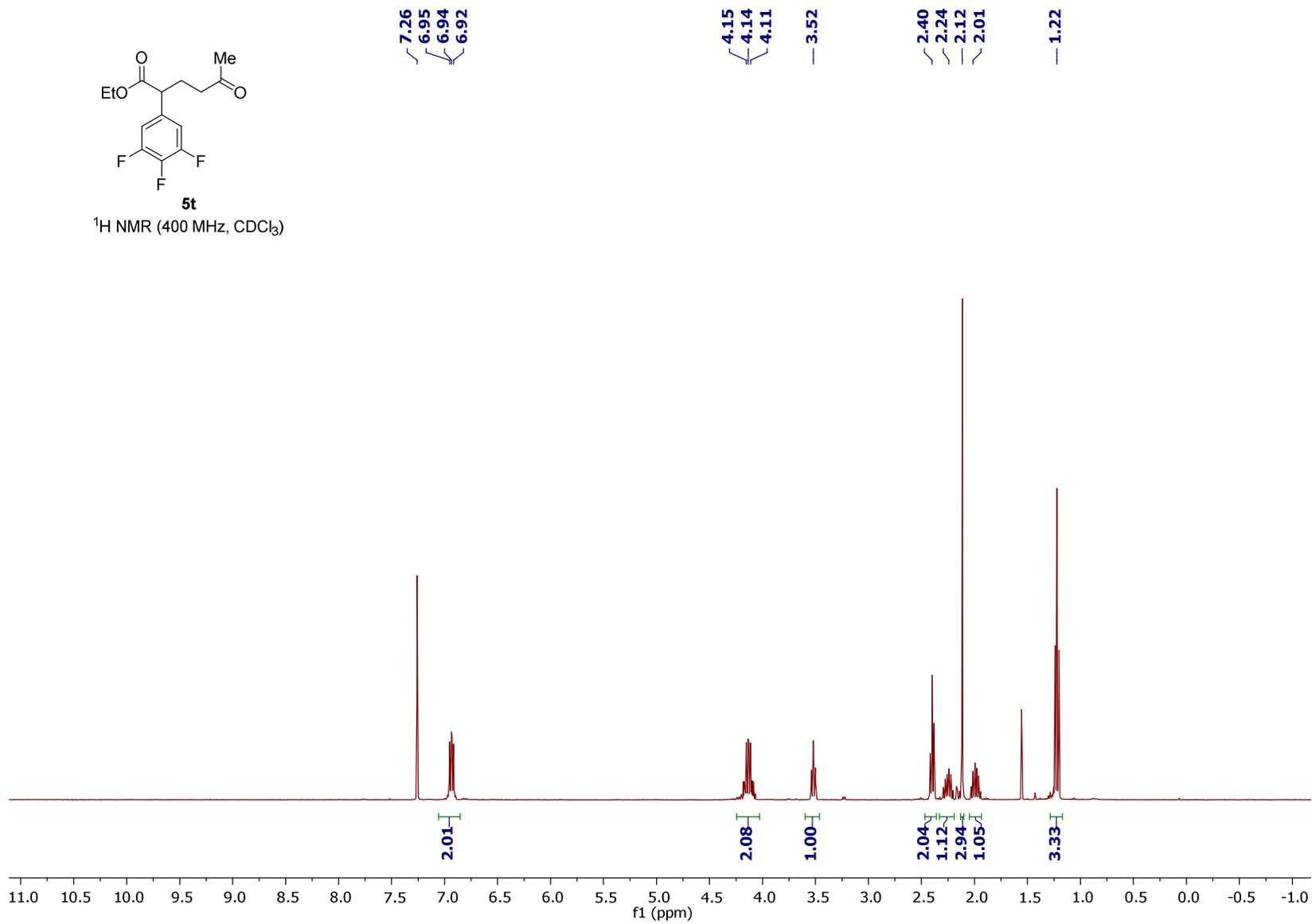
$^{19}\text{F}\{^1\text{H},^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )

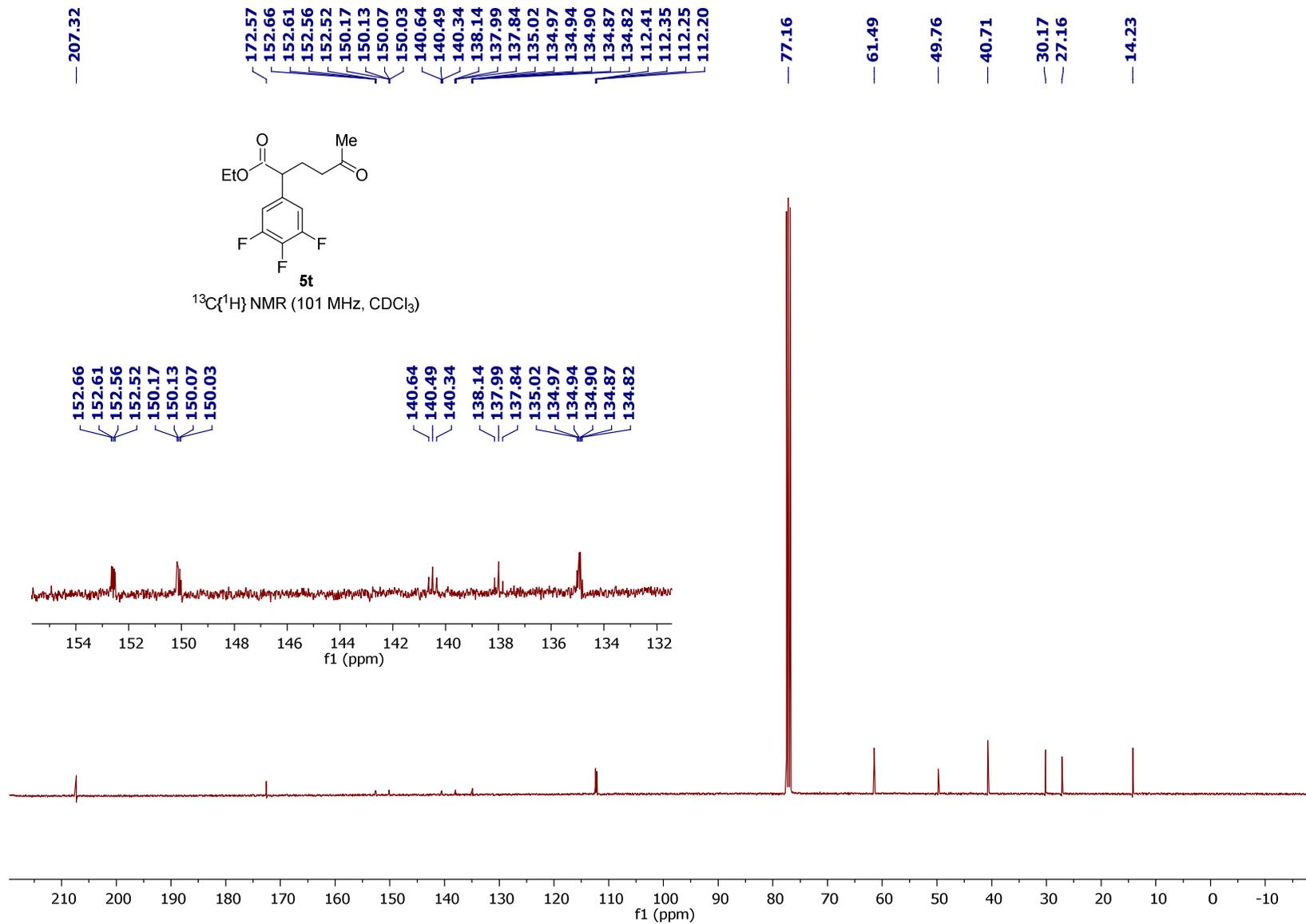


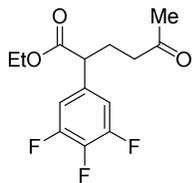


**5t**

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

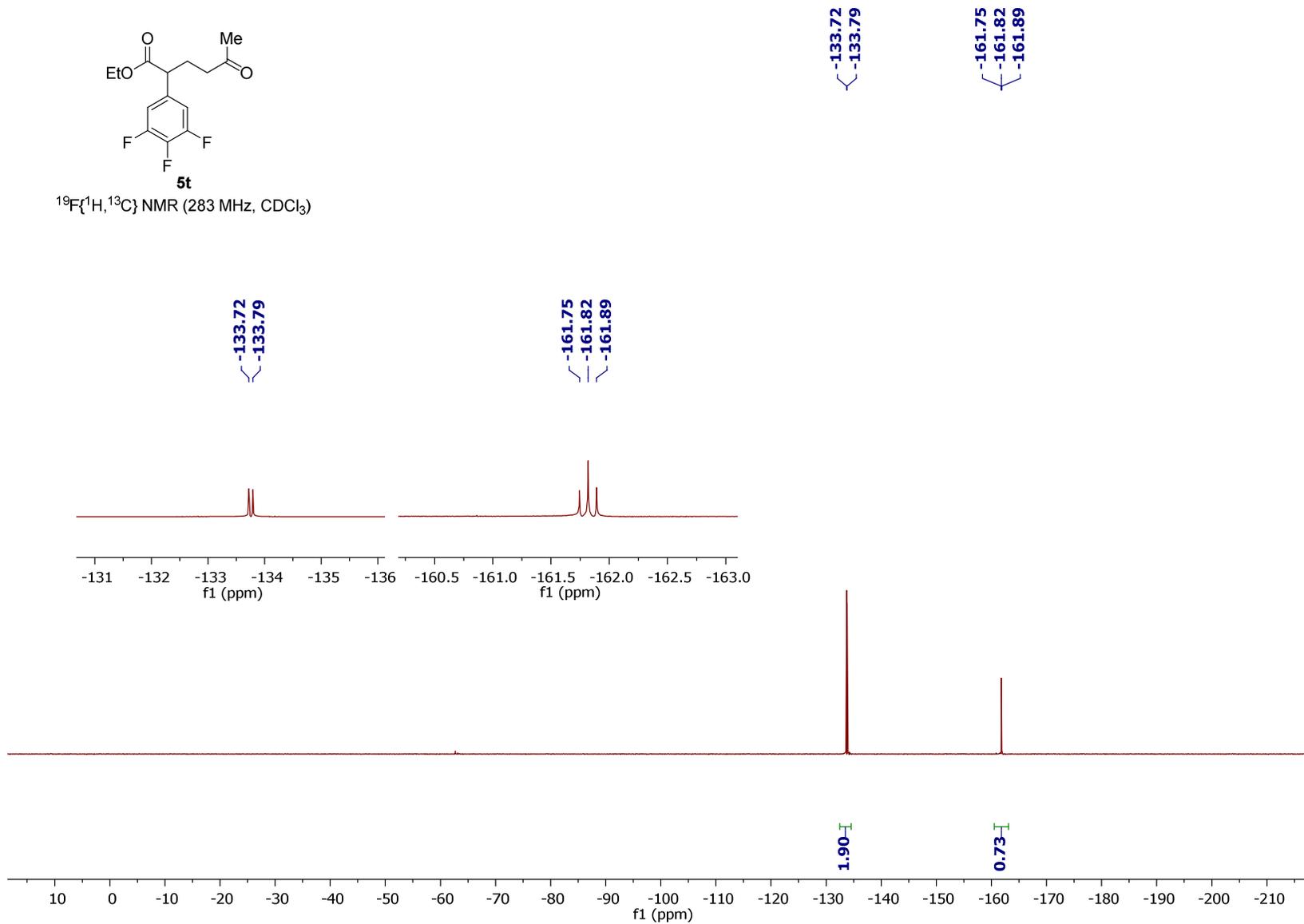


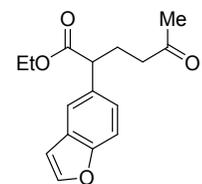




**5t**

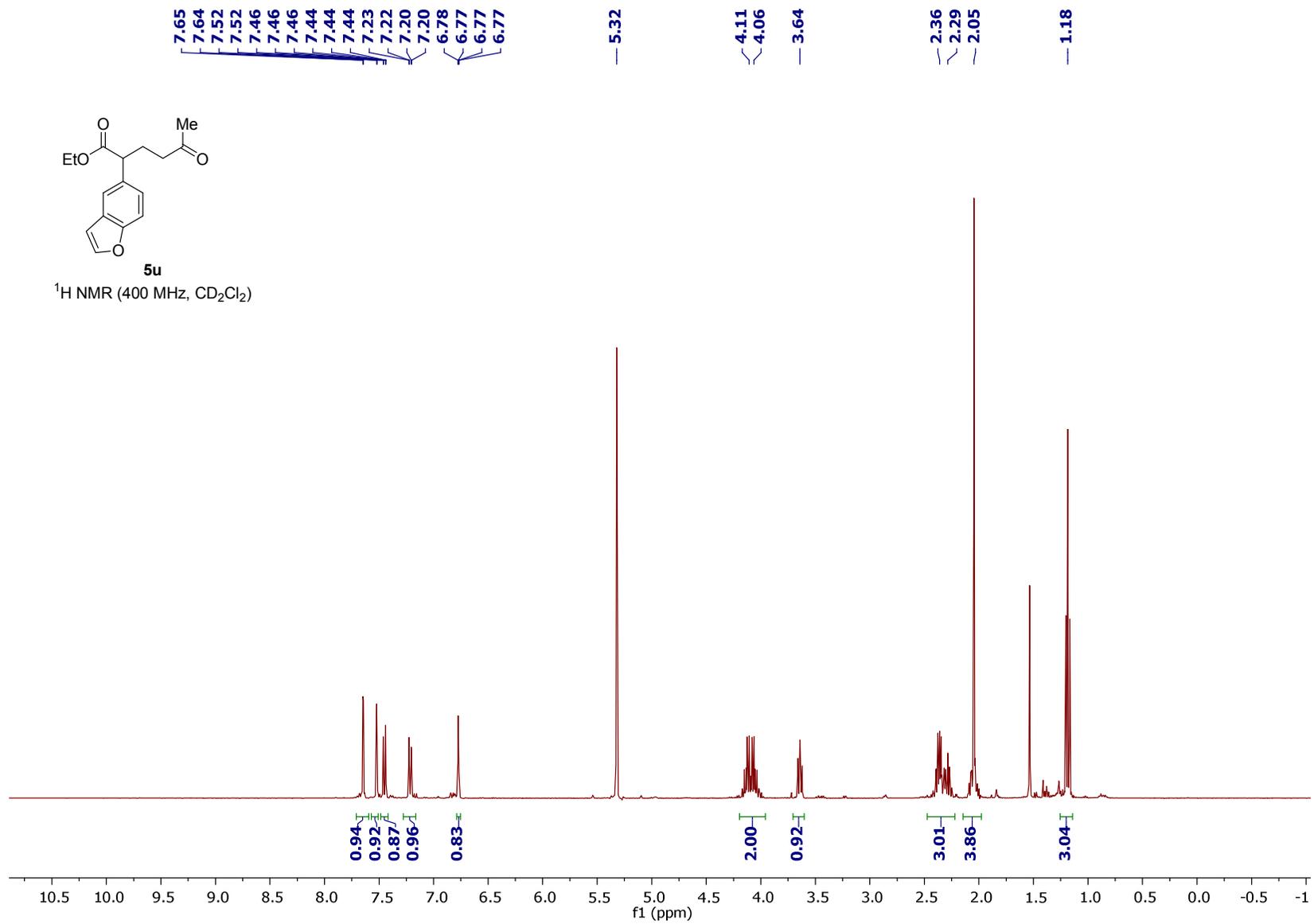
$^{19}\text{F}\{^1\text{H}, ^{13}\text{C}\}$  NMR (283 MHz,  $\text{CDCl}_3$ )





**5u**

<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)



— 207.93

— 174.10

— 154.66

— 146.02

— 133.84

— 128.15

— 124.68

— 120.87

— 111.68

— 106.92

— 61.17

— 53.84

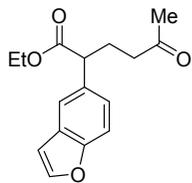
— 50.72

— 41.30

— 30.10

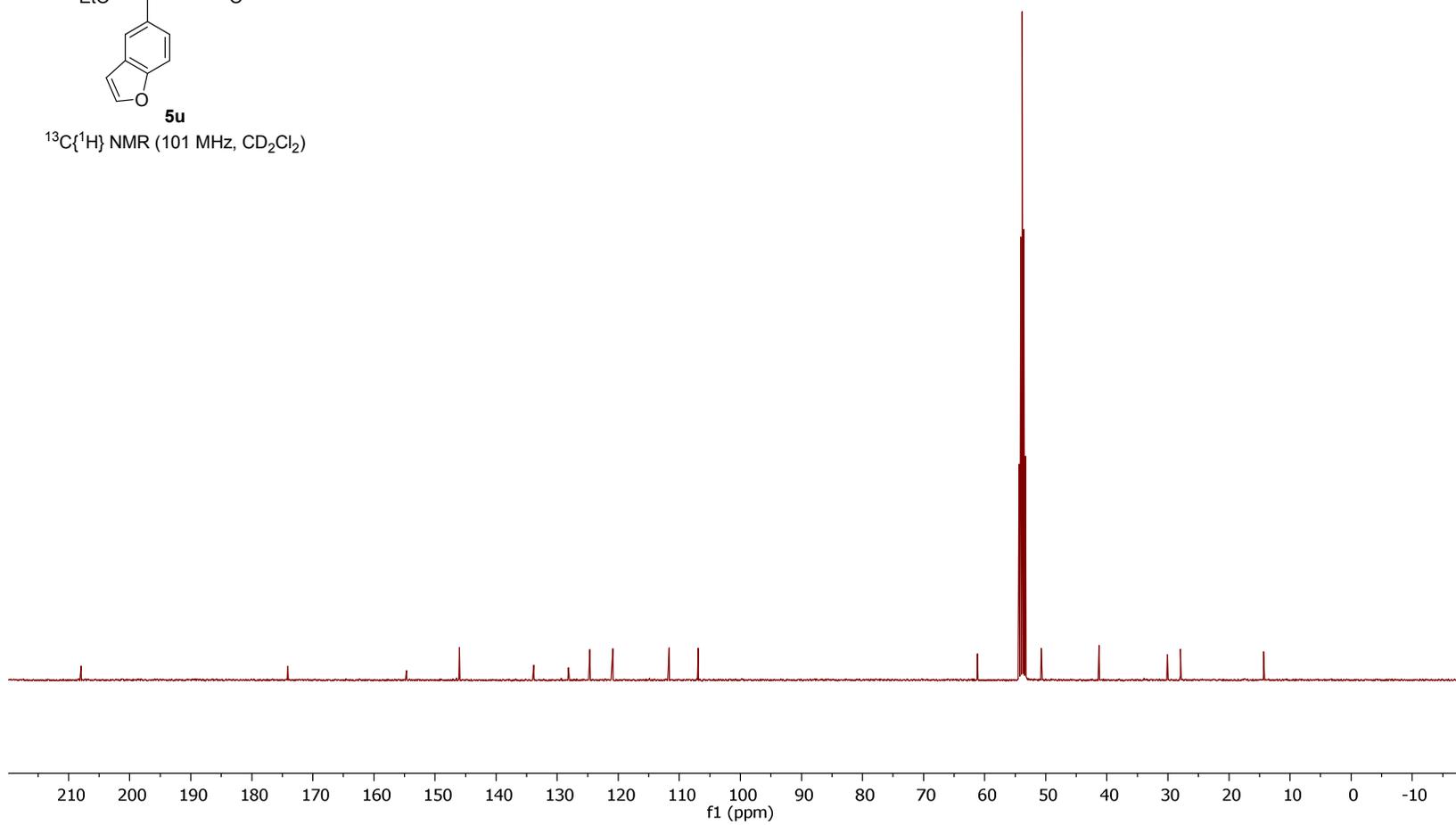
— 27.93

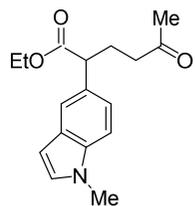
— 14.32



**5u**

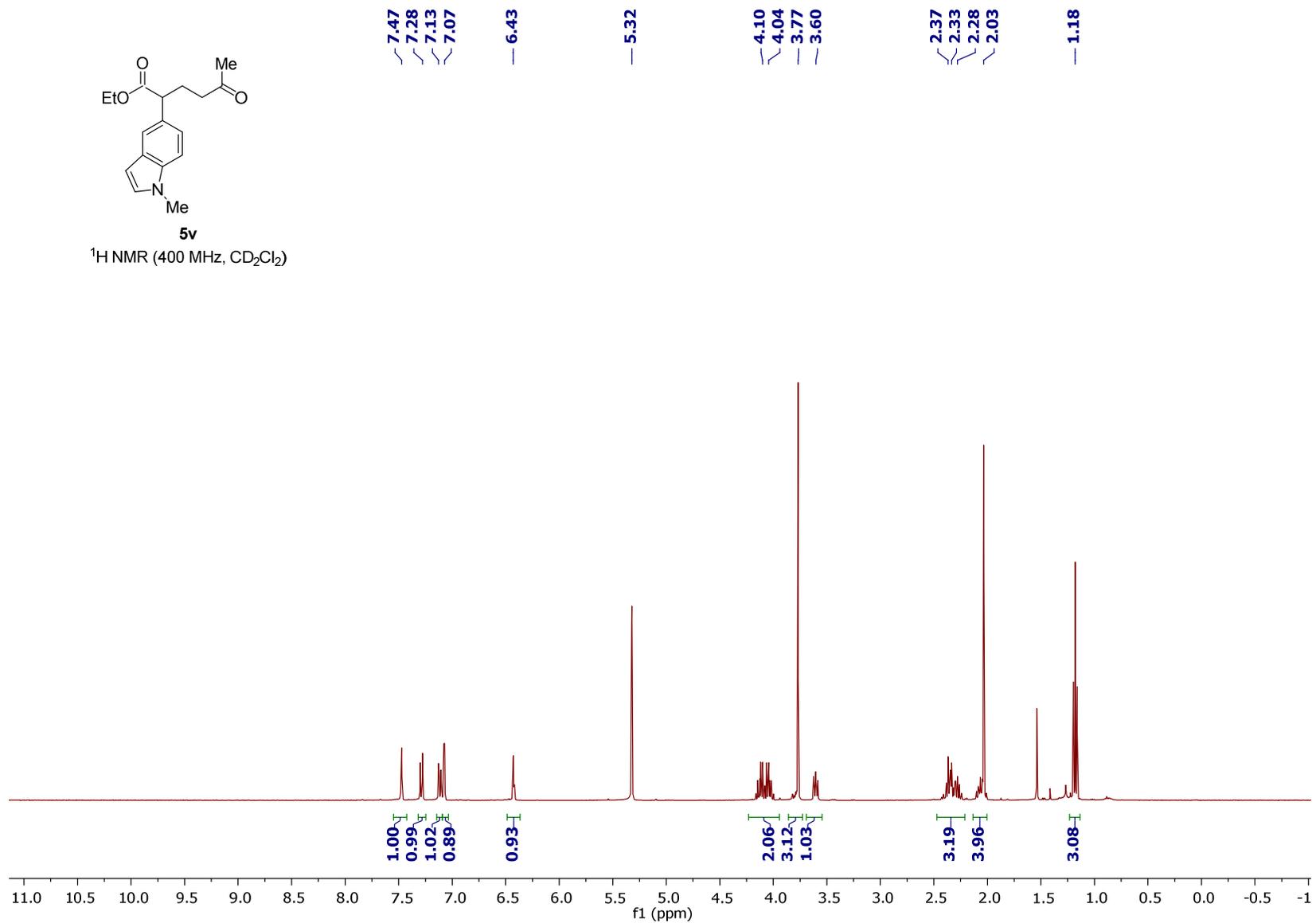
$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )

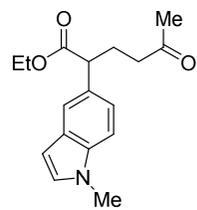




**5v**

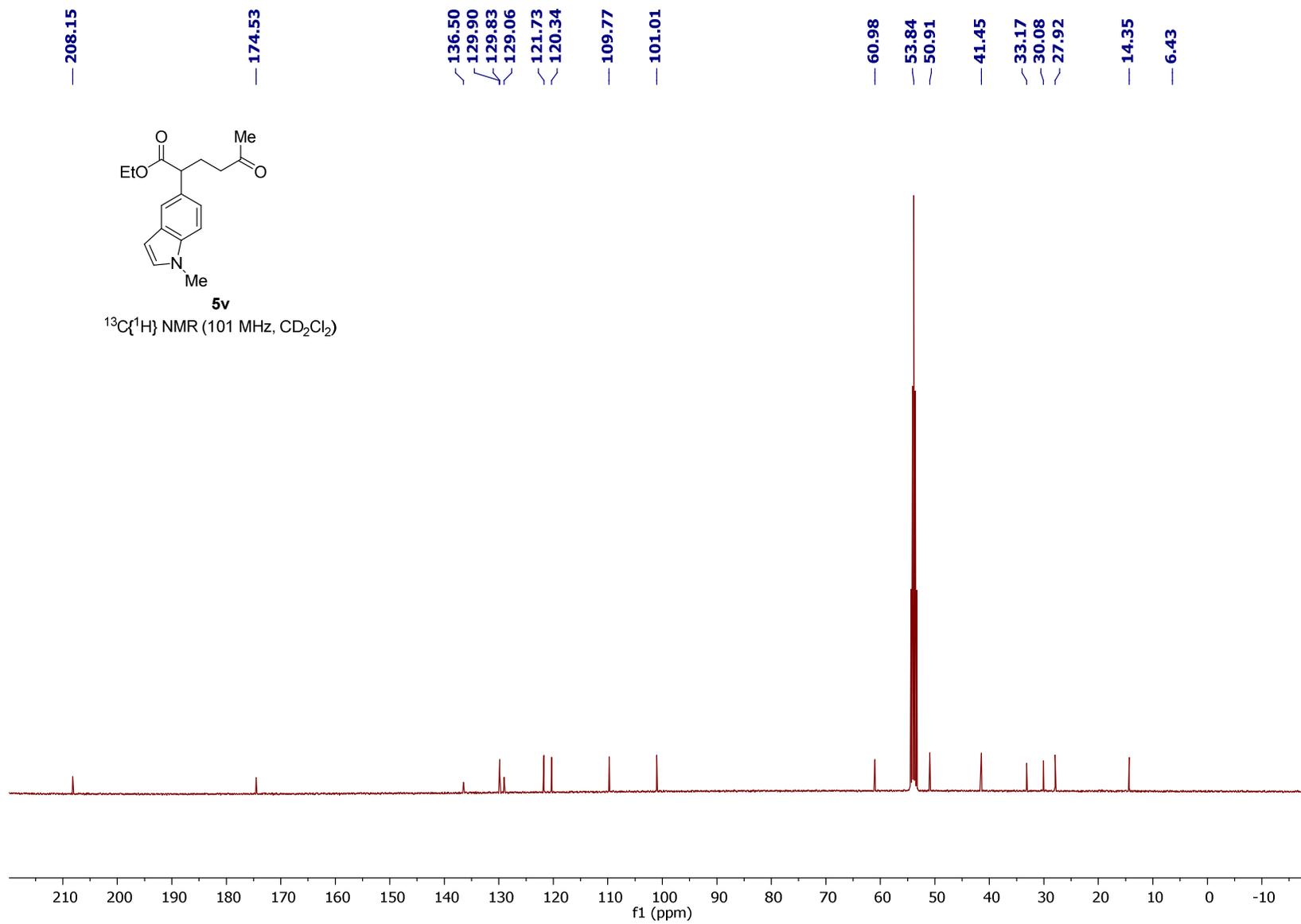
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)

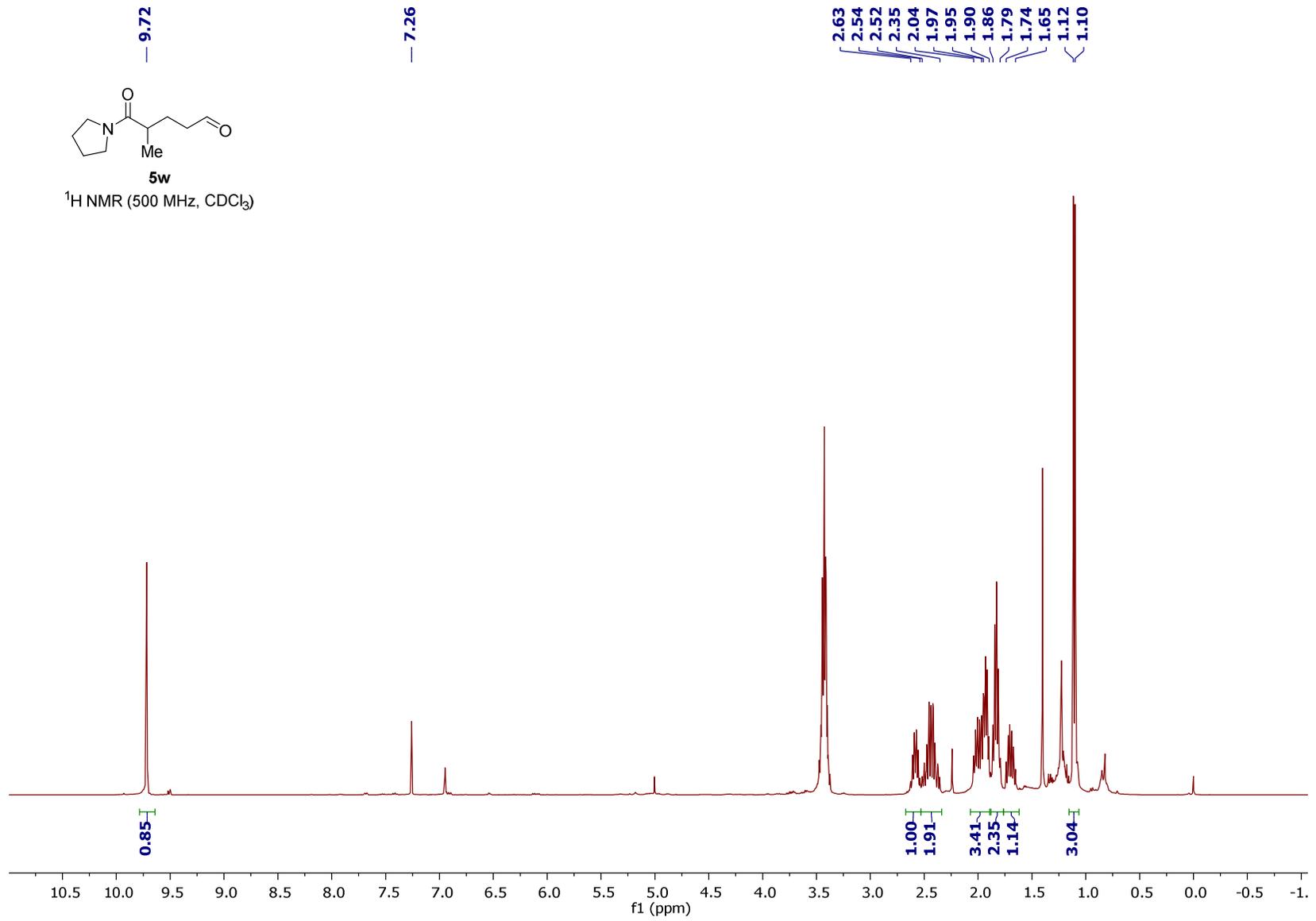
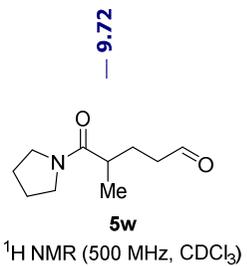


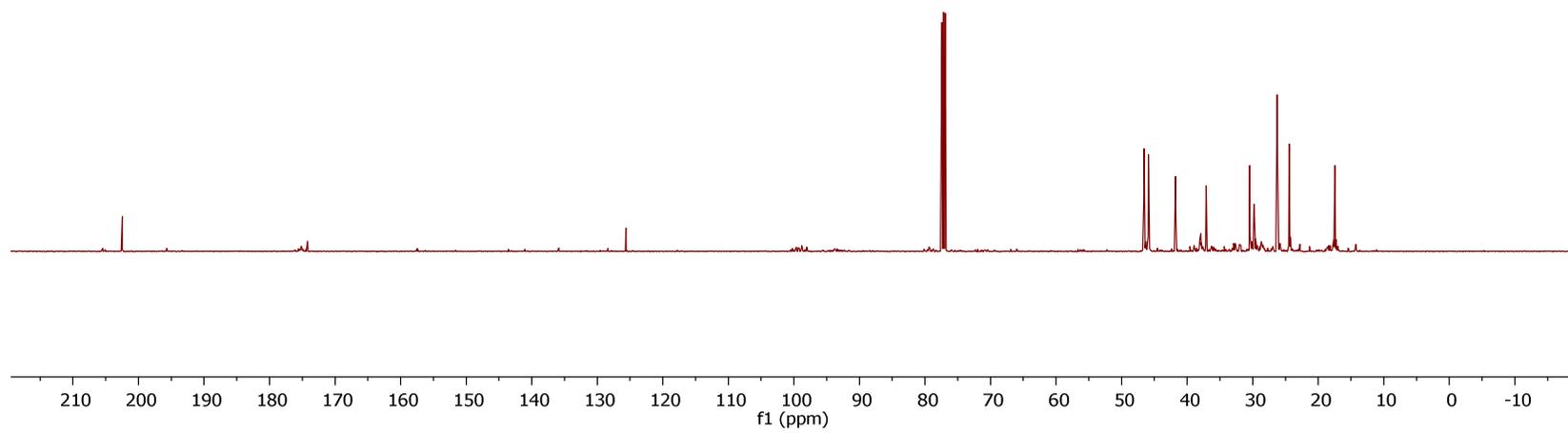


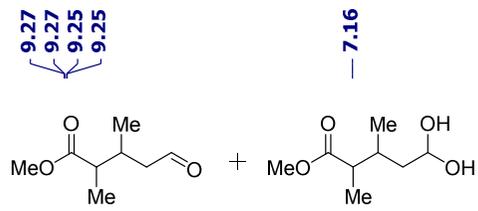
**5v**

$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CD}_2\text{Cl}_2$ )

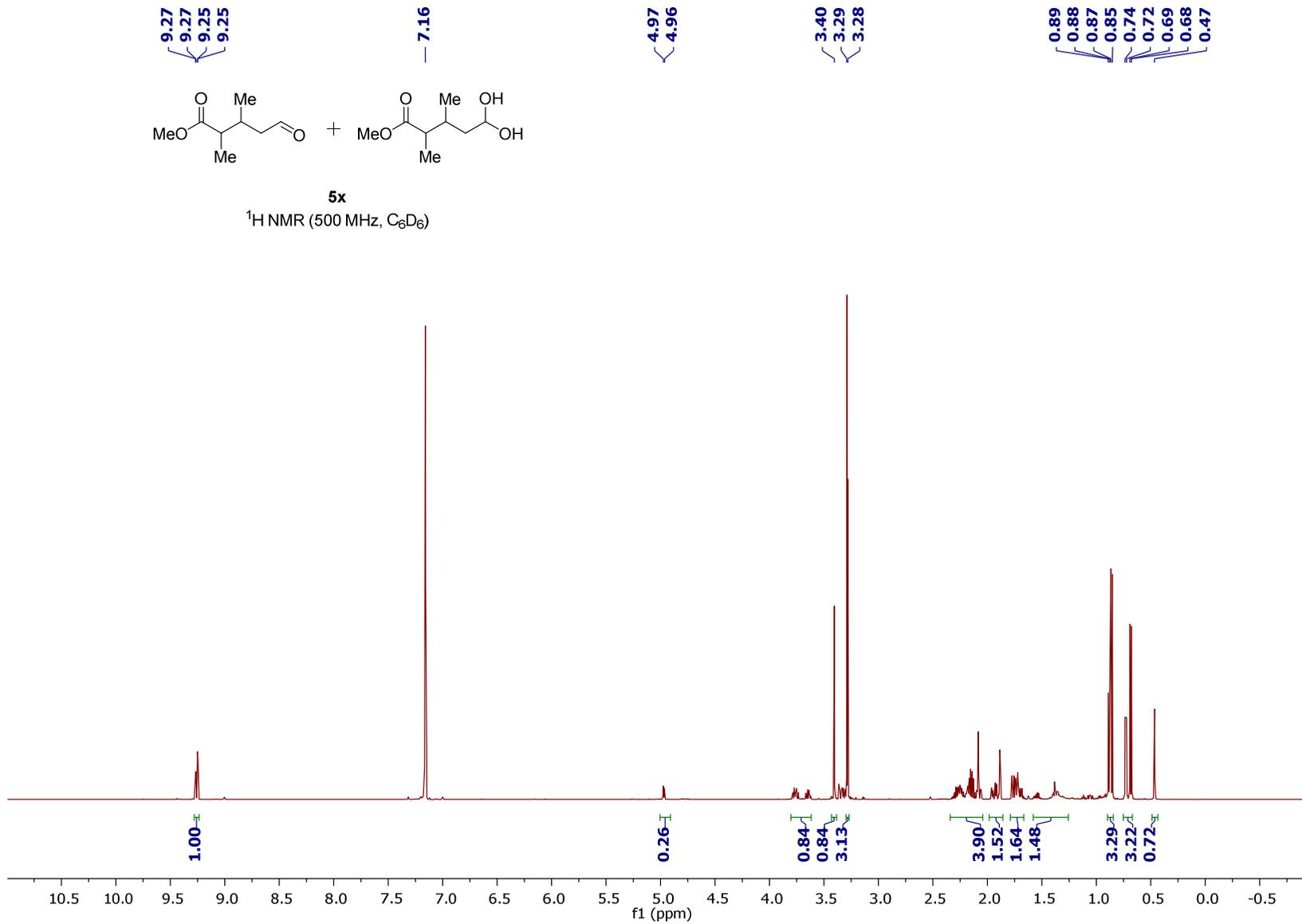


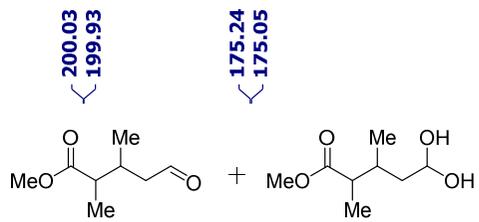




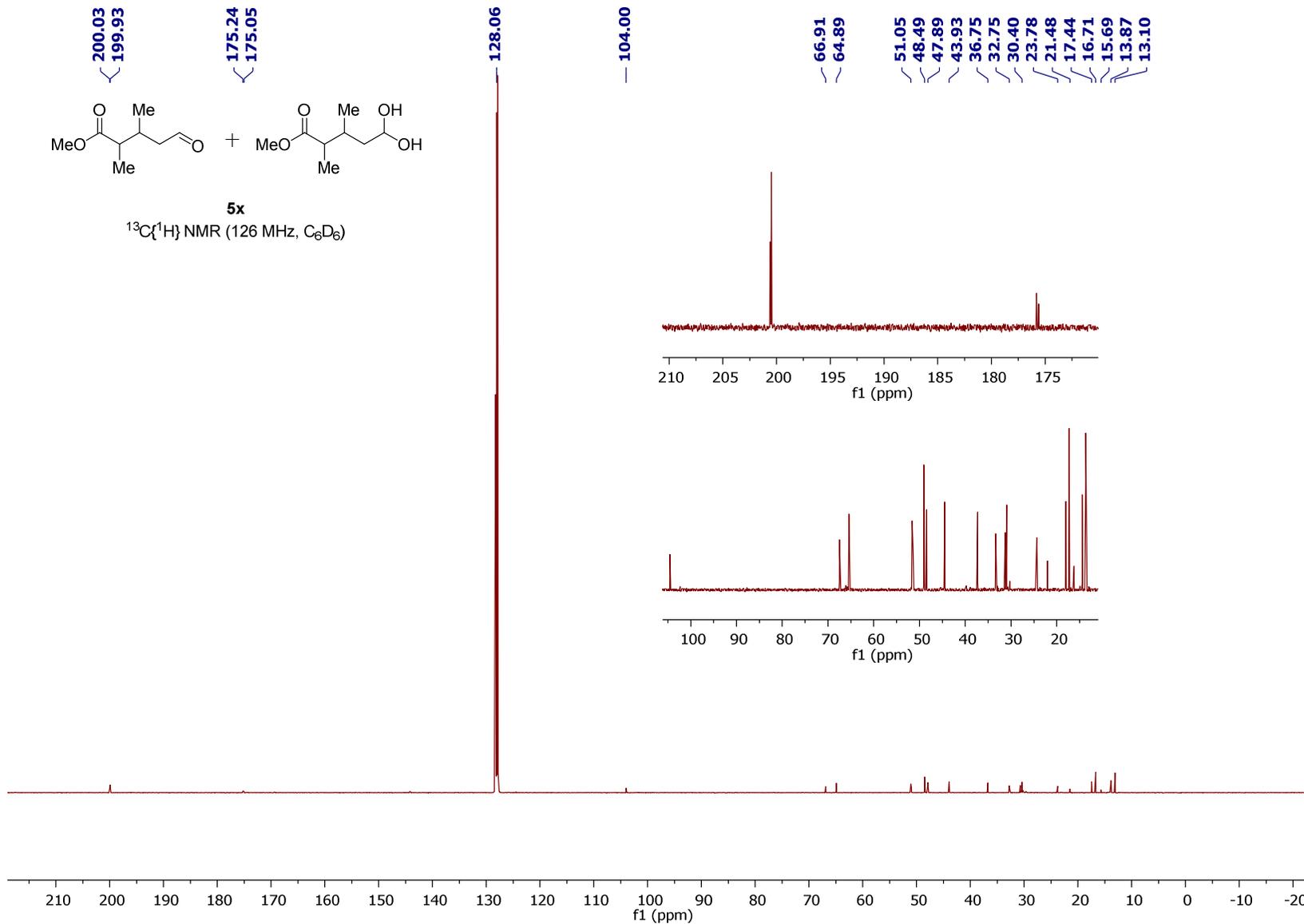


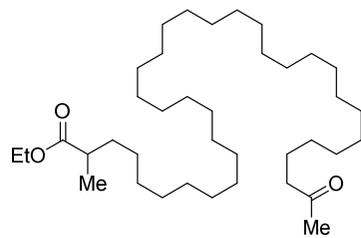
5x  
<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>)



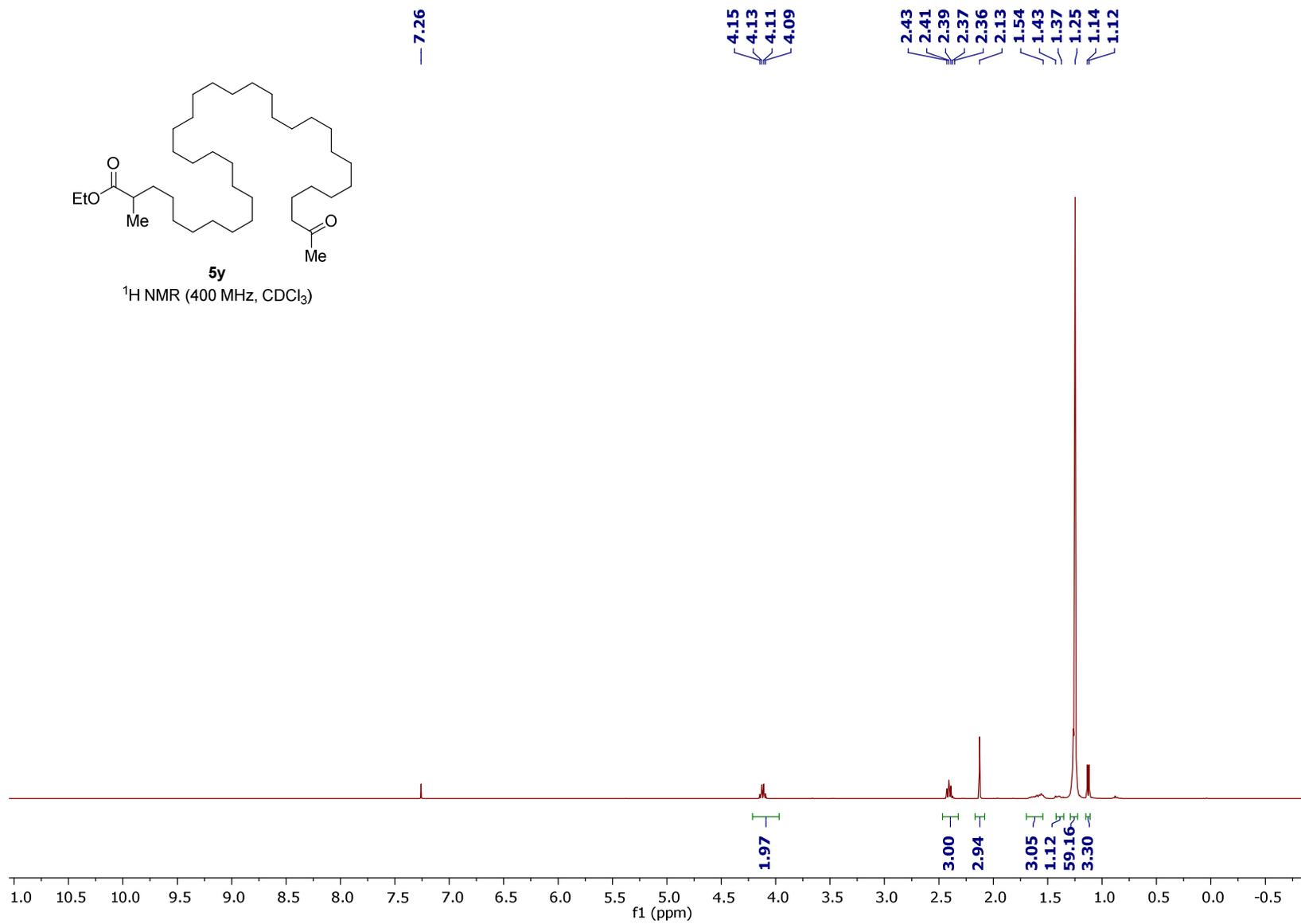


5x  
<sup>13</sup>C{<sup>1</sup>H} NMR (126 MHz, C<sub>6</sub>D<sub>6</sub>)



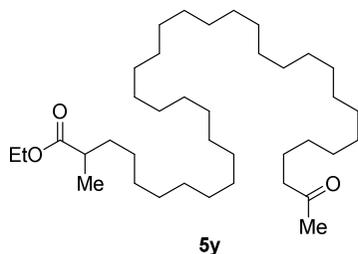


<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)

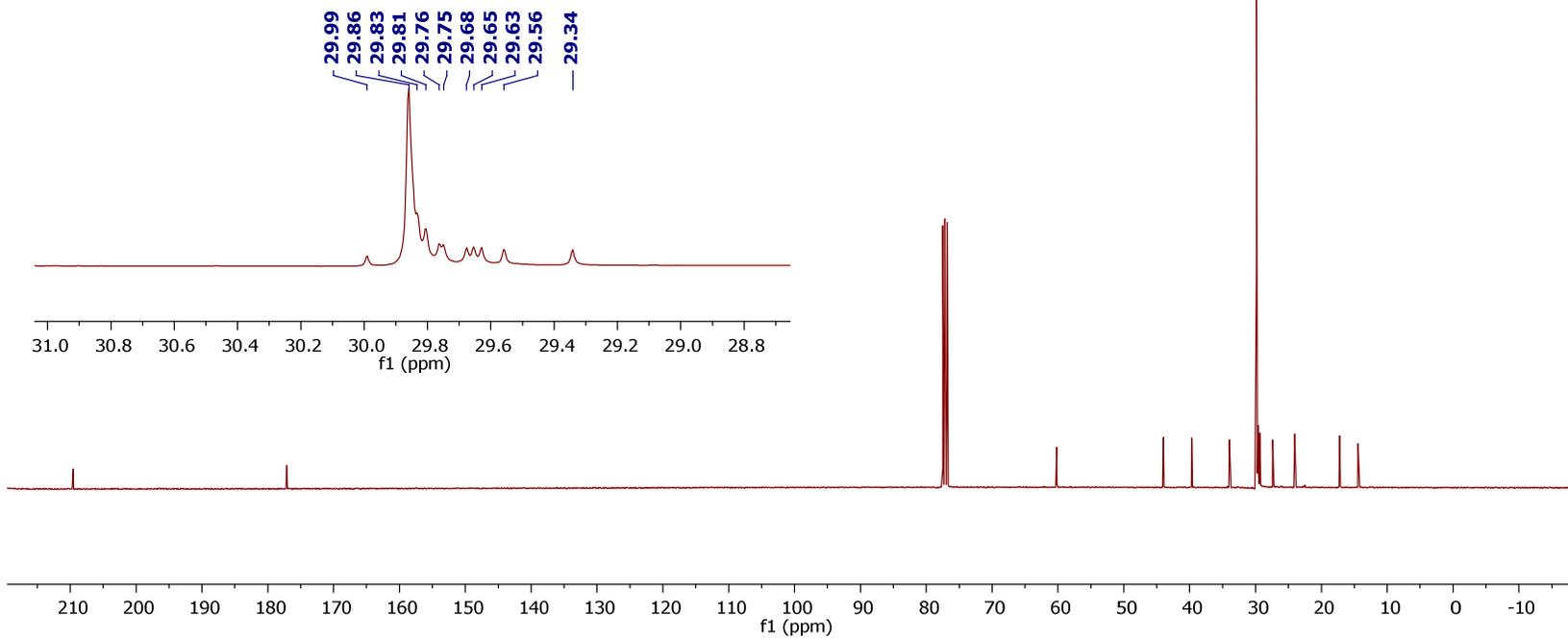


— 209.52

— 177.12



$^{13}\text{C}\{^1\text{H}\}$  NMR (101 MHz,  $\text{CDCl}_3$ )



— 77.16