

## Supporting Information

### Organocatalytic Enantioselective Mannich and Retro-Mannich Reactions and Combinations of These Reactions to Afford Tetrasubstituted $\alpha$ -Amino Acid Derivatives

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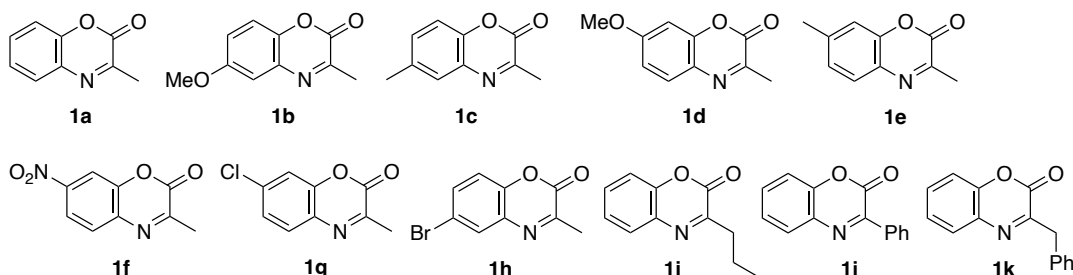
#### 1. General

For thin layer chromatography (TLC), Merck silica gel 60 F254 aluminum sheets were used, and the compounds were visualized by irradiation with UV light. Flash column chromatography was performed using Merck silica gel 60 (230-400 mesh). For preparative TLC, TLC plates Miles Scientific Uniplate silica gel GF UV254, 1000 micron, were used.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Avance 500 or a Bruker Avance 400. Proton chemical shifts are reported in ppm downfield from tetramethylsilane ( $\delta$  0.00 ppm) or relative to the residual proton signal of the deuterated solvent in  $\text{CDCl}_3$  ( $\delta$  7.26 ppm) or in  $(\text{CD}_3)_2\text{SO}$  ( $\delta$  2.50 ppm). Carbon chemical shifts were internally referenced to the deuterated solvent signal in  $\text{CDCl}_3$  ( $\delta$  77.0 ppm) or in  $(\text{CD}_3)_2\text{SO}$  ( $\delta$  40.0 ppm). High-resolution mass spectra were recorded on a Thermo Scientific LTQ Orbitrap ESI ion trap mass spectrometer or a Bruker Times TOF ESI mass spectrometer. Enantiomer ratios were determined by chiral-phase HPLC analyses using a Hitachi instrument. Optical rotations were measured on a Jasco P2200 polarimeter.

## 2. Synthesis of 1

Imines **1a-i** were synthesized from 2-aminophenols and  $\alpha$ -ketoester derivatives by the reported procedures<sup>1-3</sup> under slightly modified conditions.

Compound characterization data of imines **1a**,<sup>2,4,5,6</sup> **1c**,<sup>4</sup> **1e**,<sup>4</sup> **1g**,<sup>4</sup> **1h**,<sup>7</sup> **1i**,<sup>8</sup> **1j**,<sup>5,6</sup> and **1k**<sup>4</sup> have been reported.



### General procedure for the synthesis of imines **1a-c** and **1e**

Imines **1a**,<sup>2,4,5,6</sup> **1b**, **1c**,<sup>4</sup> and **1e**<sup>4</sup> were synthesized by the reported procedures<sup>1,2,3</sup> under slightly modified conditions. To a solution of corresponding 2-aminophenol (5.0 mmol, 1.0 equiv) in 2-PrOH (5.0 mL), ethyl pyruvate (5.0 mmol, 1.0 equiv) was added, and the mixture was stirred at room temperature (25 °C) for 18 to 24 h (monitored by TLC analysis). The mixture was concentrated under reduced pressure and purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give imine **1**.

### Compound **1b**

Yellow solid (618 mg, 65%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.21 (d,  $J$  = 9.0 Hz, 1H), 7.18 (d,  $J$  = 3.0 Hz, 1H), 7.05 (dd,  $J$  = 9.0 Hz, 3.0 Hz, 1H), 3.86 (s, 3H), 2.57 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  156.9, 155.5, 153.5, 140.7, 131.5, 118.4, 117.0, 110.7, 55.9, 21.4. HRMS (ESI):  $m/z$  calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>N [M+H]<sup>+</sup> 192.0655, found 192.0692.

### Synthesis of **1d**

Imine **1d**<sup>9</sup> was synthesized by the reported method<sup>9</sup> under slightly modified conditions. To a solution of 2-hydroxy-4-methoxyaniline hydrochloride (878 mg, 5.0 mmol, 1.0 equiv) in EtOH (7.5 mL), K<sub>2</sub>CO<sub>3</sub> (691 mg, 5.0 mmol, 1.0 equiv) was added, and the mixture was stirred at room temperature (25 °C) for 30 min. To the mixture, ethyl pyruvate (1.11 mL, 10 mmol, 2.0 equiv) was added followed by acetic acid (1.83 mL, 32 mmol), and the mixture was stirred at the same temperature for 18 h (monitored by TLC analysis). The mixture was concentrated under reduced pressure and purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give **1d** (413 mg, 43%) as a yellow solid.

### Compound **1d**<sup>9</sup>

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.60 (d,  $J$  = 9.0 Hz, 1H), 6.90 (dd,  $J$  = 9.0 Hz, 2.5 Hz, 1H), 6.76 (d,  $J$  = 2.5 Hz, 1H), 3.88 (s, 3H), 2.52 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  161.4, 153.6, 151.3, 148.0, 129.4, 125.7, 112.9, 100.4, 55.9, 21.0. HRMS (ESI):  $m/z$  calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>N [M+H]<sup>+</sup> 192.0655 found 192.0642.

### General procedure for the synthesis of **1f-i**

Imines **1f**, **1g**,<sup>4</sup> **1h**,<sup>7</sup> and **1i**<sup>8</sup> were synthesized by the reported method for the synthesis of **1a**.<sup>2,8</sup>

Under N<sub>2</sub>, to a mixture of corresponding 2-aminophenol (10 mmol, 1.0 equiv) and 4 Å molecular sieve (2 g) in toluene (100 mL), ethyl pyruvate (10 mmol, 1.0 equiv) was added at room temperature, and the mixture was stirred under reflux at 110 °C (oil bath) for 18-24 h (monitored by TLC analysis). After being cooled to room temperature, the mixture was filtered. The filtrate was concentrated under reduced pressure and purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give **1**.

### Compound 1f

Yellow solid (1.39 g, 67%). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 8.22 (dd, *J* = 9.0 Hz, 2.5 Hz, 1H), 8.16 (d, *J* = 2.5 Hz, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 2.65 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 159.0, 151.7, 147.9, 146.4, 134.9, 129.6, 120.3, 112.5, 21.8. HRMS (ESI): *m/z* calcd for C<sub>9</sub>H<sub>7</sub>O<sub>4</sub>N<sub>2</sub> [M+H]<sup>+</sup> 207.0400 found 207.0384.

### Synthesis of 1j

Imine **1j**<sup>5,6</sup> was synthesized by the reported method.<sup>10</sup> To a solution of 2-aminophenol (546 mg, 5.0 mmol, 1.0 equiv) in water (30 mL), benzoylformic acid (1.12 g, 7.5 mmol, 1.5 equiv) was added at room temperature, and the mixture was stirred under reflux at 110 °C (oil bath) for 12 h (monitored by TLC analysis). After being cooled to room temperature, the mixture was quenched with saturated NaHCO<sub>3</sub> solution (50 mL) and extracted with EtOAc (5 x 30 mL). Organic layers were combined, washed with brine (80 mL), dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give **1j** (549 mg, 49%) as a colorless solid.

### Synthesis of 1k

Imine **1k**<sup>4</sup> was synthesized by the reported method<sup>4</sup> under slightly modified conditions.<sup>4</sup> To a solution of 2-aminophenol (546 mg, 5.0 mmol, 1.0 equiv) and ethyl phenylpropionate (826 μL, 5.0 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL), triphenylphosphine (1.31 g, 5.0 mmol, 1.0 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added dropwise at 0 °C over 10 min, and the mixture was stirred at room temperature (25 °C) for 16 h (monitored by TLC analysis). The mixture was concentrated under reduced pressure and purified by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>) to give **1k** (599 mg, 51%) as a pale brown solid.

## 3. Evaluations of Catalysts and Conditions (Table 1)

### General procedure for the evaluations of catalysts and conditions for the reaction of 1a and 2a to afford 3a (Table 1, entries 1-11)

The reaction was performed in a glass vial with a cap. An inert atmosphere (nitrogen or argon) was not used. To a solution of imine **1a** (1.0 mmol, 1.0 equiv) and acetone (**2a**) (370 μL, 5.0 mmol, 5.0 equiv) in solvent (1.0 mL), catalyst (indicated in the Table) was added, and the mixture was stirred at room temperature (25 °C) for 48 h. The reaction was monitored by TLC analysis. At 48 h, a portion (5 μL) of the mixture was taken out, diluted with CDCl<sub>3</sub>, and analyzed by <sup>1</sup>H NMR to determine the yield of **3a** based on the ratio between **1a** and **3a**. At the same time, a portion (12 μL) of the mixture was taken out, and to this portion, EtOAc (300 μL) and aqueous saturated NH<sub>4</sub>Cl solution (300 μL) were added. This was extracted with EtOAc. Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by preparative TLC plate (*n*-hexane/EtOAc = 75:25) to give **3a**, which was used to determine the er by chiral-phase HPLC analysis.

## General procedure for the evaluations of catalysts and conditions for the reaction of **1a** and **2a** to afford **3a** (Table 1, entries 1 and 12-15)

The reaction was performed in a glass vial with a cap. An inert atmosphere (nitrogen or argon) was not used. To a mixture of (*S*)-proline (indicated in the Table) in DMSO (1.0 mL), acetone (**2a**) (370  $\mu$ L, 5.0 mmol, 5.0 equiv) was added, and the mixture was stirred at room temperature (25  $^{\circ}$ C) for approximately 1 min. After checking the mixture was a solution or a suspension, imine **1a** (1.0 mmol, 1.0 equiv) was added, and the mixture was stirred at the same temperature for 48 h. The reaction was monitored by TLC analysis. At 48 h, a portion (5  $\mu$ L) of the mixture was taken out, diluted with  $\text{CDCl}_3$ , and analyzed by  $^1\text{H}$  NMR to determine the yield of **3a** based on the ratio between **1a** and **3a**. At the same time, a portion (12  $\mu$ L) of the mixture was taken out, and to this portion, EtOAc (300  $\mu$ L) and aqueous saturated  $\text{NH}_4\text{Cl}$  solution (300  $\mu$ L) were added. This was extracted with EtOAc. Organic layers were combined, washed with brine, dried over  $\text{MgSO}_4$ , filtered, concentrated under reduced pressure, and purified by preparative TLC plate (*n*-hexane/EtOAc = 75:25) to give **3a**, which was used to determine the er by chiral-phase HPLC analysis.

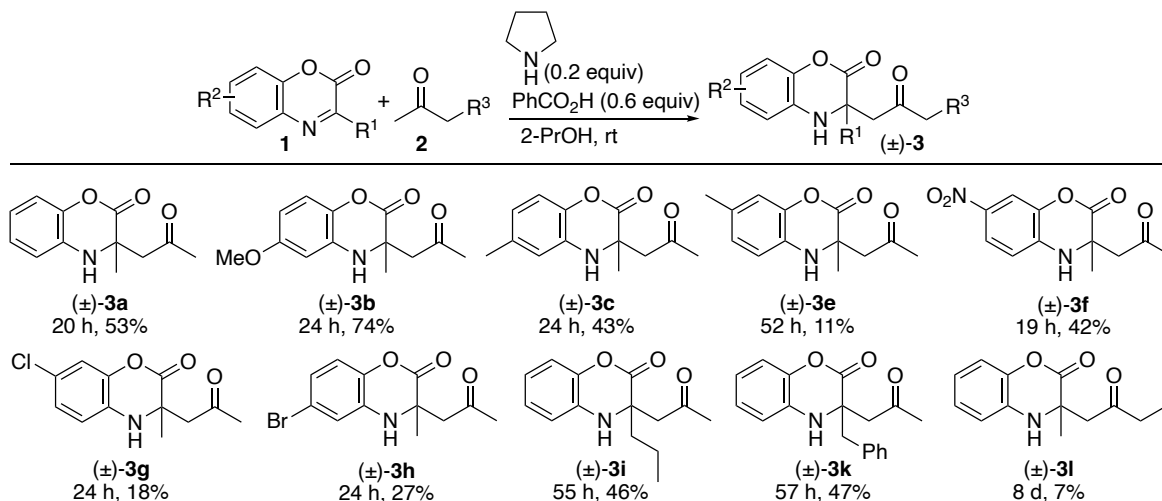
For entry 1, the experiments by both procedures were performed, and the same results were obtained.

For entry 13, (*S*)-proline (0.3 equiv) was not fully dissolved before addition of the imine and during the reaction. For entries 1, 12, 14, and 15, (*S*)-proline was fully dissolved before the addition of the imine.

## 4. Mannich Reactions to Afford **3** (Scheme 2)

### 4.1. Synthesis of Racemic Standards of ( $\pm$ )-**3**: Mannich Reactions to Afford ( $\pm$ )-**3**

#### Synthesis of racemic standards of **3**



For each case, total reaction time and isolated yield are shown.

### General procedure for the synthesis of racemic standards of **3**

The reaction was performed in glass vial with a cap. An inert atmosphere (nitrogen or argon) was not used. To a solution of pyrrolidine (0.2 mmol, 0.2 equiv) and benzoic acid (0.6 mmol, 0.6 equiv) in 2-PrOH (1.0 mL), ketone **2** (10 mmol, 10 equiv) was added followed by imine **1** (1.0 mmol, 1.0 equiv), and the mixture was stirred at room temperature (25  $^{\circ}$ C) for 4 h. To the mixture, ketone **2** (10 mmol, 10 equiv) was added,

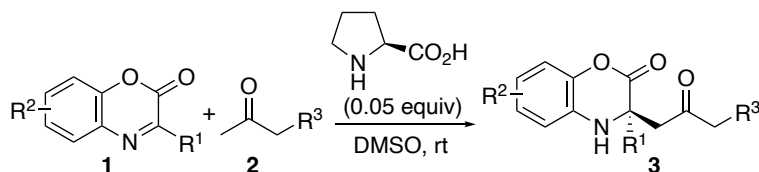
and the mixture was stirred at the same temperature (monitored by TLC analysis). The mixture was concentrated under reduced pressure and dissolved in EtOAc (20 mL). Aqueous saturated NaHCO<sub>3</sub> solution (20 mL) was added, and the mixture was extracted with EtOAc. Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give (±)-**3**.

Compounds (±)-**3d** and (±)-**3j** were synthesized by the reactions of corresponding **1** and **2** using (±)-proline (0.05 equiv) as the catalyst in DMSO.

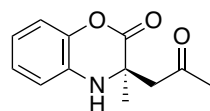
## 4.2 Enantioselective Mannich Reactions to Afford **3** (Scheme 2)

### General procedure for the (*S*)-proline-catalyzed Mannich reactions of **1** and **2** to afford **3** (Scheme 2)

The reaction was performed in glass vial with a cap. An inert atmosphere (nitrogen or argon) was not used. To a solution of (*S*)-proline (0.05 mmol, 0.05 equiv) in DMSO (1.0 mL), ketone **2** (5.0 mmol, 5.0 equiv) was added followed by imine **1** (1.0 mmol, 1.0 equiv), and the mixture was stirred at room temperature (25 °C) (monitored by TLC analysis). The mixture was diluted with EtOAc (20 mL), and aqueous saturated NH<sub>4</sub>Cl solution (20 mL) was added. The mixture was extracted with EtOAc. Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3**.

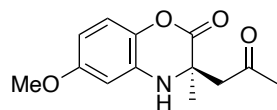


### Compound **3a**



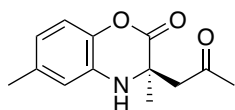
General procedure, 96 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 188 mg (86 %, er 97:3), pale yellow oil.  $[\alpha]_{\text{D}}^{25} +50.2$  (*c* = 1.0, MeOH, er 97:3). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.02-6.97 (m, 2H), 6.84 (td, *J* = 8.0 Hz, 1.5 Hz, 1H), 6.78 (dd, *J* = 8.0 Hz, 1.5 Hz, 1H), 5.08 (s, 1H), 3.13 (d, *J* = 18.0 Hz, 1H), 3.01 (d, *J* = 18.0 Hz, 1H), 2.21 (s, 3H), 1.48 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 207.2, 167.9, 140.7, 131.4, 125.21, 120.3, 116.4, 115.9, 56.0, 47.9, 31.5, 21.7. HRMS (ESI): *m/z* calcd for C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>N [M+H]<sup>+</sup> 220.0968, found 220.0973. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min, λ = 220 nm): *t<sub>R</sub>* (major enantiomer) = 17.6 min, *t<sub>R</sub>* (minor enantiomer) = 25.4 min.

### Compound **3b**



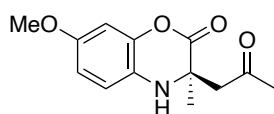
General procedure, 96 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 219 mg (88 %, er 97:3), brown gum.  $[\alpha]_{\text{D}}^{25} +47.2$  (*c* = 1.0, MeOH, er 97:3). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 6.91 (d, *J* = 9.0 Hz, 1H), 6.37 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 6.31 (d, *J* = 3.0 Hz, 1H), 5.09 (s, 1H), 3.76 (s, 3H), 3.13 (d, *J* = 18.0 Hz, 1H), 3.00 (d, *J* = 18.0 Hz, 1H), 2.21 (s, 3H), 1.48 (s, 3H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 207.3, 167.9, 157.1, 134.9, 132.2, 116.9, 105.3, 101.3, 55.9, 55.6, 47.8, 31.5, 21.7. HRMS (ESI): *m/z* calcd for C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>N [M+H]<sup>+</sup> 250.1095, found 250.1095. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min, λ = 220 nm): *t<sub>R</sub>* (major enantiomer) = 26.2 min, *t<sub>R</sub>* (minor enantiomer) = 50.0 min.

### Compound 3c



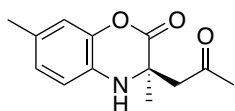
General procedure, 96 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 205 mg (88 %, er 97:3), colorless solid.  $[\alpha]_D^{25} +52.2$  ( $c = 1.0$ , MeOH, er 97:3).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.87 (d,  $J = 8.0$  Hz, 1H), 6.64 (d,  $J = 8.0$  Hz, 1H), 6.59 (s, 1H), 5.00 (s, 1H), 3.11 (d,  $J = 18.0$  Hz, 1H), 3.00 (d,  $J = 18.0$  Hz, 1H), 2.27 (s, 3H), 2.21 (s, 3H), 1.47 (s, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.3, 168.0, 138.7, 135.1, 131.1, 120.8, 116.3, 116.0, 56.0, 47.8, 31.5, 21.6, 20.9. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{16}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  234.1117, found 234.1117. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (major enantiomer) = 14.7 min,  $t_R$  (minor enantiomer) = 19.1 min.

### Compound 3d



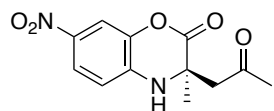
General procedure, 72 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 31 mg (12 %, er 91:9), yellow oil.  $[\alpha]_D^{25} +42.4$  ( $c = 1.0$ , MeOH, er 91:9).  $^1\text{H NMR}$  (500 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  6.67 (d,  $J = 8.5$  Hz, 1H), 6.64 (d,  $J = 3.0$  Hz, 1H), 6.58 (dd,  $J = 8.5$  Hz, 3.0 Hz, 1H), 5.79 (s, 1H), 3.67 (s, 3H), 3.04 (d,  $J = 17.0$  Hz, 1H), 2.85 (d,  $J = 17.0$  Hz, 1H), 2.07 (s, 3H), 1.31 (s, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $(\text{CD}_3)_2\text{SO}$ ):  $\delta$  205.6, 168.8, 152.9, 140.8, 126.2, 116.0, 111.2, 102.7, 56.1, 55.6, 50.8, 31.3, 24.6. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{16}\text{O}_4\text{N}$   $[\text{M}+\text{H}]^+$  250.1095, found 250.1040. HPLC (Daicel Chiralpak IA-3, *n*-hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (minor enantiomer) = 18.1 min,  $t_R$  (major enantiomer) = 20.4 min.

### Compound 3e



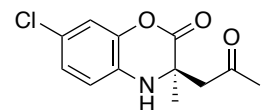
General procedure, 96 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 85 mg (36 %, er 97:3), colorless solid.  $[\alpha]_D^{25} +56.8$  ( $c = 1.0$ , MeOH, er 97:3).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.81 (s, 1H), 6.80 (d,  $J = 8.5$  Hz, 1H), 6.68 (d,  $J = 8.5$  Hz, 1H), 4.94 (s, 1H), 3.09 (d,  $J = 18.0$  Hz, 1H), 3.01 (d,  $J = 18.0$  Hz, 1H), 2.27 (s, 3H), 2.20 (s, 3H), 1.45 (s, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.2, 168.1, 140.8, 130.3, 128.7, 125.7, 116.7, 116.0, 56.1, 47.8, 31.4, 21.6, 20.6. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{16}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  234.1118, found 234.1118. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (major enantiomer) = 14.6 min,  $t_R$  (minor enantiomer) = 22.8 min.

### Compound 3f



General procedure, 4 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 74 mg (28 %, er 50:50), yellow solid.  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.96 (dd,  $J = 8.5$  Hz, 2.0 Hz, 1H), 7.92 (d,  $J = 2.0$  Hz, 1H), 6.78 (d,  $J = 8.5$  Hz, 1H), 5.78 (s, 1H), 3.24 (d,  $J = 18.5$  Hz, 1H), 3.05 (d,  $J = 18.5$  Hz, 1H), 2.25 (s, 3H), 1.55 (s, 3H).  $^{13}\text{C NMR}$  (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.0, 165.8, 140.1, 138.6, 137.4, 121.9, 114.1, 113.0, 56.0, 48.5, 31.3, 23.0. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{12}\text{H}_{13}\text{O}_5\text{N}_2$   $[\text{M}+\text{H}]^+$  265.0809, found 265.0809. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 70:30, flow rate = 0.5 mL/min,  $\lambda = 220$  nm):  $t_R = 27.1$  min, 29.5 min.

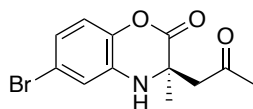
### Compound 3g



General procedure, 28 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 72 mg (28 %, er 97:3), orange gum.  $[\alpha]_D^{25} +22.6$  ( $c = 1.0$ , MeOH, er 97:3).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.01 (d,  $J = 2.5$  Hz, 1H), 6.97 (dd,  $J = 8.5$

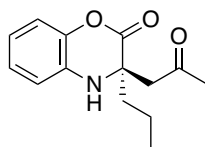
Hz, 2.5 Hz, 1H), 6.71 (d,  $J = 8.5$  Hz, 1H), 5.12 (s, 1H), 3.13 (d,  $J = 18.0$  Hz, 1H), 3.00 (d,  $J = 18.0$  Hz, 1H), 2.22 (s, 3H), 1.47 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.2, 167.1, 140.9, 130.1, 125.2, 124.8, 116.7, 116.6, 55.9, 47.8, 31.4, 21.7. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{12}\text{H}_{13}\text{O}_3\text{NCl}$   $[\text{M}+\text{H}]^+$  254.0578, found 254.0554. HPLC (Daicel Chiralpak IA-3,  $n$ -hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (minor enantiomer) = 16.0 min,  $t_R$  (major enantiomer) = 18.9 min.

### Compound 3h



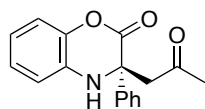
General procedure, 96 h, flash column chromatography ( $n$ -hexane/EtOAc = 90:10 and 80:20), 189 mg (64 %, er 96:4), pale orange solid.  $[\alpha]_{\text{D}}^{25} +33.5$  ( $c = 1.0$ , MeOH, er 96:4).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.94 (dd,  $J = 8.5$  Hz, 2.5 Hz, 1H), 6.92 (d,  $J = 2.5$  Hz, 1H), 6.86 (d,  $J = 8.5$  Hz, 1H), 5.18 (s, 1H), 3.14 (d,  $J = 18.5$  Hz, 1H), 2.99 (d,  $J = 18.5$  Hz, 1H), 2.22 (s, 3H), 1.48 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.1, 167.1, 139.6, 132.8, 122.9, 118.4, 117.8, 117.6, 55.8, 47.9, 31.4, 21.8. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{12}\text{H}_{13}\text{O}_3\text{NBr}$   $[\text{M}+\text{H}]^+$  298.0073, found 298.0035. HPLC (Daicel Chiralpak AS-3,  $n$ -hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (major enantiomer) = 25.9 min,  $t_R$  (minor enantiomer) = 52.4 min.

### Compound 3i



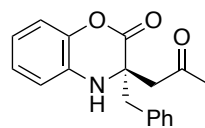
General procedure, 14 days, flash column chromatography ( $n$ -hexane/EtOAc = 90:10 and 80:20), 170 mg (69 %, er 97:3), pale orange solid.  $[\alpha]_{\text{D}}^{25} +55.4$  ( $c = 1.0$ , MeOH, er 97:3).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  6.97 (t,  $J = 7.5$  Hz, 1H), 6.96 (d,  $J = 7.5$  Hz, 1H), 6.80 (t,  $J = 7.5$  Hz, 1H), 6.73 (d,  $J = 7.5$  Hz, 1H), 3.12 (d,  $J = 18.5$  Hz, 1H), 3.02 (d,  $J = 18.5$  Hz, 1H), 2.20 (s, 3H), 1.87-1.72 (m, 2H), 1.45-1.21 (m, 2H), 0.85 (t,  $J = 7.5$  Hz, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.0, 167.2, 140.4, 131.3, 125.2, 119.8, 116.3, 115.4, 59.5, 47.3, 38.2, 31.3, 17.7, 14.0. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{14}\text{H}_{18}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  248.1281, found 248.1295. HPLC (Daicel Chiralpak AS-3,  $n$ -hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (major enantiomer) = 13.2 min,  $t_R$  (minor enantiomer) = 21.1 min.

### Compound 3j



General procedure, 15 days, flash column chromatography ( $n$ -hexane/EtOAc = 90:10 and 80:20), 61 mg (22 %, er 99:1), colorless solid.  $[\alpha]_{\text{D}}^{25} +102.0$  ( $c = 1.0$ , MeOH, er 99:1).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.38 (d,  $J = 7.5$  Hz, 1H), 7.31-7.24 (m, 2H), 7.21 (t,  $J = 7.5$  Hz, 1H), 7.02 (t,  $J = 7.5$  Hz, 1H), 6.98 (d,  $J = 7.5$  Hz, 1H), 6.84 (d,  $J = 7.5$  Hz, 1H), 6.77 (t,  $J = 7.5$  Hz, 1H), 3.68 (d,  $J = 17.5$  Hz, 1H), 3.28 (d,  $J = 17.5$  Hz, 1H), 2.06 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.4, 165.7, 140.9, 137.2, 131.5, 128.7, 128.3, 126.0, 125.2, 120.5, 116.5, 116.1, 61.7, 50.9, 31.8. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  282.1180, found 282.1180. HPLC (Daicel Chiralpak AS-3,  $n$ -hexane/2-PrOH = 80:20, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_R$  (major enantiomer) = 9.6 min,  $t_R$  (minor enantiomer) = 24.7 min.

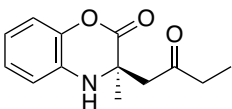
### Compound 3k



General procedure, 15 days, flash column chromatography ( $n$ -hexane/EtOAc = 90:10 and 80:20), 134 mg (45 %, er 98:2), pale orange solid.  $[\alpha]_{\text{D}}^{25} +42.5$  ( $c = 1.0$ , MeOH, er 98:2).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.30-7.22 (m, 3H), 7.07-7.03 (m, 2H), 7.01 (td,  $J = 7.8$  Hz, 1.5 Hz, 1H), 6.98 (dd,  $J = 7.8$  Hz, 1.5 Hz, 1H), 6.82 (td,  $J = 7.8$  Hz,

1.5 Hz, 1H), 6.76 (dd,  $J = 7.8$  Hz, 1.5 Hz, 1H), 3.10 (d,  $J = 14.0$  Hz, 1H), 3.07 (d,  $J = 18.0$  Hz, 1H), 3.04 (d,  $J = 14.0$  Hz, 1H), 2.93 (d,  $J = 18.0$  Hz, 1H), 2.18 (s, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  206.5, 167.0, 140.6, 134.3, 130.9, 130.2, 128.6, 127.5, 125.3, 120.1, 116.5, 115.7, 59.8, 47.3, 41.1, 31.1. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{18}\text{H}_{18}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  296.1281, found 296.1296. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_{\text{R}}$  (major enantiomer) = 15.1 min,  $t_{\text{R}}$  (minor enantiomer) = 39.5 min.

### Compound 3l



General procedure, 12 days, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 38 mg (16 %, er 97:3), pale brown solid.  $[\alpha]_{\text{D}}^{25} +53.9$  ( $c = 1.0$ , MeOH, er 97:3).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.02-6.97 (m, 2H), 6.84 (ddd,  $J = 7.8$  Hz, 7.3 Hz, 1.5 Hz, 1H), 6.78 (dd,  $J = 7.8$  Hz, 1.5 Hz, 1H), 5.15 (s, 1H), 3.11 (d,  $J = 18.0$  Hz, 1H), 2.96 (dd,  $J = 18.0$  Hz, 0.5 Hz, 1H), 2.55-2.41 (m, 2 Hz), 1.47 (d,  $J = 0.5$  Hz, 3H), 1.07 (t,  $J = 7.5$  Hz, 3H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  210.2, 167.9, 140.7, 131.4, 125.2, 120.2, 116.3, 115.9, 56.1, 46.5, 37.4, 21.7, 7.4. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{13}\text{H}_{16}\text{O}_3\text{N}$   $[\text{M}+\text{H}]^+$  234.1123, found 234.1123. HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda = 220$  nm):  $t_{\text{R}}$  (major enantiomer) = 10.8 min,  $t_{\text{R}}$  (minor enantiomer) = 13.0 min.

## 5. Analyses of the Reactions at Various Time Points (Scheme 3)

### Analysis of the (*S*)-proline-catalyzed Mannich Reaction at various time points (Scheme 3a)

The reaction of **1a** and **2a** in the presence of (*S*)-proline was performed using the general procedure described in section 4.2. At the indicated time, a portion (5  $\mu\text{L}$ ) of the mixture was taken out, diluted with  $\text{CDCl}_3$ , and analyzed by  $^1\text{H}$  NMR to determine the yield of **3a** based on the ratio between **1a** and **3a**. At the same time, a portion (12  $\mu\text{L}$ ) of the mixture was taken out, and to this portion, EtOAc and aqueous saturated  $\text{NH}_4\text{Cl}$  solution were added. This was extracted with EtOAc. Organic layers were combined, washed with brine, dried over  $\text{MgSO}_4$ , filtered, concentrated under reduced pressure, and purified by preparative TLC (*n*-hexane/EtOAc = 75:25) to give **3a**, which was used to determine the er by chiral-phase HPLC analysis.

### Analysis of the retro-Mannich reactions of ( $\pm$ )-**3a** in the presence of (*S*)-proline at various time points (Scheme 3b)

Top: To a solution of ( $\pm$ )-**3a** (1.0 mmol, 1.0 equiv) in DMSO (1.0 mL), (*S*)-proline (0.05 mmol, 0.05 equiv) was added, and the mixture was stirred at room temperature (25  $^\circ\text{C}$ ). Bottom: To a solution of ( $\pm$ )-**3a** (0.5 mmol, 1.0 equiv) in DMSO (5.0 mL), (*S*)-proline (0.15 mmol, 0.3 equiv) was added, and the mixture was stirred at 40  $^\circ\text{C}$ . At the indicated time, the ratio between **3a** and **1a** and the er of **3a** were analyzed by  $^1\text{H}$  NMR and HPLC, respectively, as described in the analysis for the reaction of Scheme 3a.

### Analysis of the retro-Mannich reactions of (*S*)- and (*R*)-**3a** in the presence of (*S*)-proline at various time points (Scheme 3c)

To a solution of (*R*)-**3a** ( $R:S = 95:5$ ) or (*S*)-**3a** ( $R:S = 2:98$ ) (0.5 mmol, 1.0 equiv) in DMSO (5.0 mL), (*S*)-proline (0.15 mmol, 0.3 equiv) was added, and the mixture was stirred at 40  $^\circ\text{C}$ . At the indicated time, the ratio between **3a** and **1a** and the er of **3a** were analyzed by  $^1\text{H}$  NMR and HPLC, respectively, as described in the analysis for the reaction of Scheme 3a.

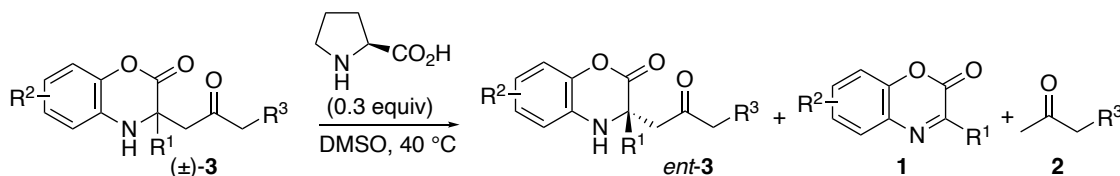


## 6. Kinetic Resolutions of ( $\pm$ )-**3** via Retro-Mannich Reactions (Scheme 4)

### General procedure for the (*S*)-proline-catalyzed kinetic resolutions of ( $\pm$ )-**3** via retro-Mannich reactions (Scheme 4)

Before the reaction for the isolation of the product, a test reaction to observe the consumption of **3** (i.e., to determine the suitable/possible reaction time for the kinetic resolution). Test reaction: To a solution of ( $\pm$ )-**3** (0.5 mmol, 1.0 equiv) in DMSO (5.0 mL), (*S*)-proline (0.15 mmol, 0.3 equiv) was added, and the mixture was stirred at 40 °C (heating block) (monitored by TLC analysis). Several times during the reaction, a portion (5  $\mu$ L) of the mixture was taken out, diluted with CDCl<sub>3</sub>, and analyzed by <sup>1</sup>H NMR to determine the conversion based on the ratio between **3** and **1**. The reaction time suitable for isolation of the product of the kinetic resolution was determined as the time that reached to 50% consumption (decomposition) of **3** or the time that the consumption (decomposition) of **3** was slowed or ceased (even the consumption (decomposition) was far less than 50%).

Kinetic resolution reaction to isolate the product: To a solution of ( $\pm$ )-**3** (0.5 mmol, 1.0 equiv) in DMSO (5.0 mL), (*S*)-proline (0.15 mmol, 0.3 equiv) was added, and the mixture was stirred at 40 °C (heating block) (monitored by TLC analysis). After the reaction time determined by the test reaction, the mixture was diluted with EtOAc (20 mL), and aqueous saturated NH<sub>4</sub>Cl solution (20 mL) was added. The mixture was extracted with EtOAc. Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3**.



### Compound *ent*-**3a**

General procedure (kinetic resolution), 48 h (consumption of **3a** estimated by the test reaction: 50%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 49 mg (45 %, er 92:8), pale yellow oil. [ $\alpha$ ]<sub>D</sub><sup>25</sup> -45.0 (c = 1.0, MeOH, er 92:8). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm): *t*<sub>R</sub> (minor enantiomer) = 17.7 min, *t*<sub>R</sub> (major enantiomer) = 24.3 min.

### Compound **3a**

General procedure (kinetic resolution) but using (*R*)-proline instead of (*S*)-proline, 48 h, flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 46 mg (42%, er 93:7), pale yellow oil. [ $\alpha$ ]<sub>D</sub><sup>25</sup> +46.6 (c = 1.0, MeOH, er 93:7). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm): *t*<sub>R</sub> (major enantiomer) = 16.3 min, *t*<sub>R</sub> (minor enantiomer) = 23.2 min.

### Compound *ent*-**3b**

General procedure (kinetic resolution), 72 h (consumption of **3b** estimated by the test reaction: 47%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 48 mg (39 %, er 87:13), brown gum. [ $\alpha$ ]<sub>D</sub><sup>25</sup> -36.8 (c = 1.0, MeOH, er 87:13). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm): *t*<sub>R</sub> (minor enantiomer) = 26.5 min, *t*<sub>R</sub> (major enantiomer) = 47.0 min.

### Compound *ent-3c*

General procedure (kinetic resolution), 48 h (consumption of **3c** estimated by the test reaction: 51%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 52 mg (45 %, er 91:9), colorless solid.  $[\alpha]_{\text{D}}^{25} -47.2$  (*c* = 1.0, MeOH, er 91:9). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (minor enantiomer) = 14.8 min,  $t_{\text{R}}$  (major enantiomer) = 18.8 min.

### Compound *ent-3d*

General procedure (kinetic resolution), 24 h (consumption of **3d** estimated by the test reaction: 70%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 30 mg (24 %, er 94:6), brown oil.  $[\alpha]_{\text{D}}^{25} -54.5$  (*c* = 1.0, MeOH, er 94:6). HPLC (Daicel Chiralpak IA-3, *n*-hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (major enantiomer) = 17.5 min,  $t_{\text{R}}$  (minor enantiomer) = 20.7 min.

### Compound *ent-3e*

General procedure (kinetic resolution), 24 h (consumption of **3e** estimated by the test reaction: 50%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 38 mg (33 %, er 93:7), yellow oil.  $[\alpha]_{\text{D}}^{25} -40.2$  (*c* = 1.0, MeOH, er 93:7). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (minor enantiomer) = 14.7 min,  $t_{\text{R}}$  (major enantiomer) = 21.8 min.

### Compound *ent-3g*

General procedure (kinetic resolution), 72 h (consumption of **3g** estimated by the test reaction: 20%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 64 mg (51 %, er 79:21), orange solid. HPLC (Daicel Chiralpak IA-3, *n*-hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (major enantiomer) = 15.5 min,  $t_{\text{R}}$  (minor enantiomer) = 19.2 min.

### Compound *ent-3h*

General procedure (kinetic resolution), 96 h (consumption of **3h** estimated by the test reaction: 22%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 95 mg (64 %, er 72:28), pale orange solid.  $[\alpha]_{\text{D}}^{25} -9.8$  (*c* = 1.0, MeOH, er 72:28). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (minor enantiomer) = 26.0 min,  $t_{\text{R}}$  (major enantiomer) = 50.1 min.

### Compound *ent-3i*

General procedure (kinetic resolution), 96 h (consumption of **3i** estimated by the test reaction: 47%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 52 mg (42 %, er 95:5), pale orange solid.  $[\alpha]_{\text{D}}^{25} -54.4$  (*c* = 1.0, MeOH, er 95:5). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (minor enantiomer) = 13.4 min,  $t_{\text{R}}$  (major enantiomer) = 19.9 min.

### Compound *ent-3j*

General procedure (kinetic resolution), 168 h (consumption of **3j** estimated by the test reaction: 42%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 63 mg (45 %, er 93:7), yellow oil.  $[\alpha]_{\text{D}}^{25} -91.5$  (*c* = 1.0, MeOH, er 93:7). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 80:20, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_{\text{R}}$  (minor enantiomer) = 9.6 min,  $t_{\text{R}}$  (major enantiomer) = 24.3 min.

### Compound *ent*-3k

General procedure (kinetic resolution), 168 h (consumption of **3k** estimated by the test reaction: 15%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 71 mg (48 %, er 89:11), pale orange solid.  $[\alpha]_D^{25} -39.9$  (*c* = 1.0, MeOH, er 89:11). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_R$  (minor enantiomer) = 15.1 min,  $t_R$  (major enantiomer) = 38.3 min.

### Compound *ent*-3l

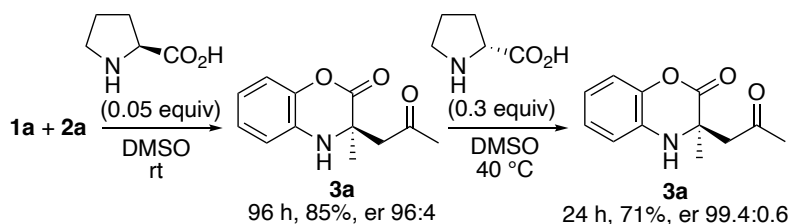
General procedure (kinetic resolution), 10 days (consumption of **3l** estimated by the test reaction: 20%), flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20), 75 mg (64 %, er 62:38), pale brown solid.  $[\alpha]_D^{25} -11.6$  (*c* = 1.0, MeOH, er 62:38). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_R$  (minor enantiomer) = 10.9 min,  $t_R$  (major enantiomer) = 12.8 min.

## 7. Combination of the Mannich Reaction and the Retro-Mannich Reaction to Afford **3** (Scheme 5)

### Formation of **3a** with er >99:1: Procedure for the combination of the (*S*)-proline-catalyzed Mannich reaction and (*R*)-proline-catalyzed retro-Mannich reaction (Scheme 5)

To a solution of (*S*)-proline (5.8 mg, 0.05 mmol, 0.05 equiv) in DMSO (1.0 mL), acetone (**2a**) (370  $\mu$ L, 5.0 mmol, 5.0 equiv) was added followed by imine **1a** (161 mg, 1.0 mmol, 1.0 equiv), and the mixture was stirred at room temperature (25 °C) for 96 h (monitored by TLC analysis). The mixture was diluted with EtOAc (20 mL), and aqueous saturated NH<sub>4</sub>Cl solution (20 mL) was added. The mixture was extracted with EtOAc (4 times). Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3a** (187 mg, 85%, er 96:4).

The obtained **3a** (er 96:4, 187 mg, 0.85 mmol, 1.0 equiv) was dissolved in DMSO (8.5 mL), and (*R*)-proline (30 mg, 0.26 mmol, 0.3 equiv) was added at room temperature (25 °C). The mixture was stirred at 40 °C (heating block) for 24 h (monitored by TLC analysis). After being cooled to room temperature, the mixture was diluted with EtOAc (40 mL), and aqueous saturated NH<sub>4</sub>Cl solution (100 mL) was added. The mixture was extracted with EtOAc (4 times). Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3a** (156 mg, 71%, er 99.4:0.6). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min,  $\lambda$  = 220 nm):  $t_R$  (major enantiomer) = 17.6 min,  $t_R$  (minor enantiomer) = 25.8 min.



### Formation of **3b** with er >99:1 (Scheme 5)

Compound **3b** (synthesized by (*S*)-proline-catalyzed Mannich reaction, er 97:3, 50.0 mg, 0.2 mmol, 1.0 equiv) was dissolved in DMSO (2.0 mL), and (*R*)-proline (6.9 mg, 0.06 mmol, 0.3 equiv) was added at room

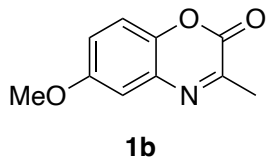
temperature (25 °C). The mixture was stirred at 40 °C (heating block) for 18 h (monitored by TLC analysis). After being cooled to room temperature, the mixture was diluted with EtOA (40 mL), and aqueous saturated NH<sub>4</sub>Cl solution (100 mL) was added. The mixture was extracted with EtOAc (4 times). Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3b** (38 mg, 76%, er >99:1). HPLC (Daicel Chiralpak AS-3, *n*-hexane/2-PrOH = 90:10, flow rate = 1.0 mL/min, λ = 220 nm): *t<sub>R</sub>* (major enantiomer) = 26.3 min, *t<sub>R</sub>* (minor enantiomer) = 51.2 min.

#### Formation of **3d** with er >99:1 (Scheme 5)

Compound **3d** (synthesized by (*S*)-proline-catalyzed Mannich reaction, er 91:9, 50.0 mg, 0.2 mmol, 1.0 equiv) was dissolved in DMSO (2.0 mL), and (*R*)-proline (6.9 mg, 0.06 mmol, 0.3 equiv) was added at room temperature (25 °C). The mixture was stirred at 40 °C (heating block) for 22 h (monitored by TLC analysis). After being cooled to room temperature, the mixture was diluted with EtOA (40 mL), and aqueous saturated NH<sub>4</sub>Cl solution (100 mL) was added. The mixture was extracted with EtOAc (4 times). Organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, concentrated under reduced pressure, and purified by flash column chromatography (*n*-hexane/EtOAc = 90:10 and 80:20) to give **3d** (31 mg, 62%, er >99:1). HPLC (Daicel Chiralpak IA-3, *n*-hexane/2-PrOH = 95:5, flow rate = 1.0 mL/min, λ = 220 nm): *t<sub>R</sub>* (minor enantiomer) = 18.5 min, *t<sub>R</sub>* (major enantiomer) = 20.1 min.

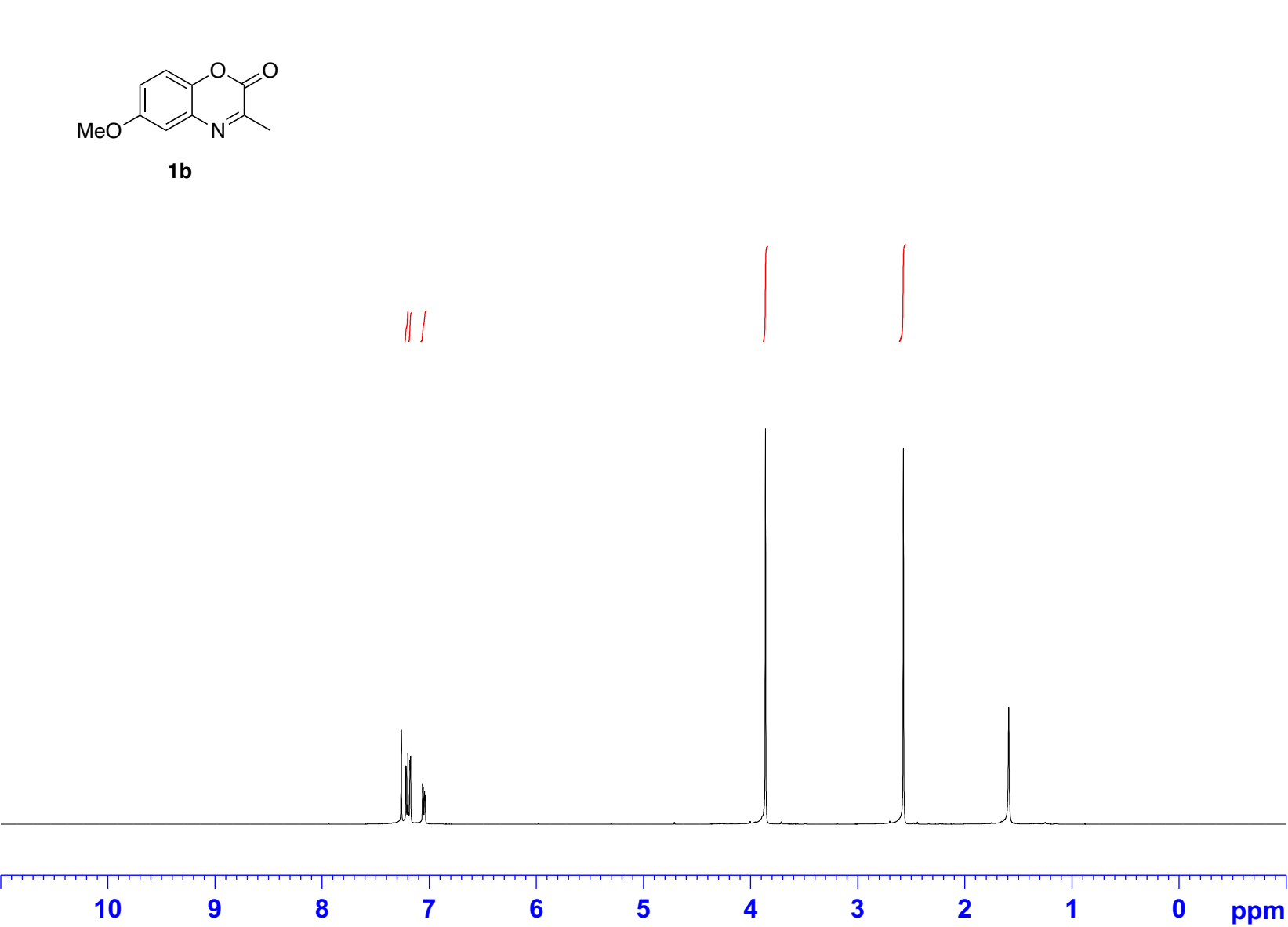
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7.260  
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 7.198  
 7.178  
 7.173  
 7.061  
 7.055  
 7.043  
 7.037

— 3.859  
 — 2.571  
 — 1.588

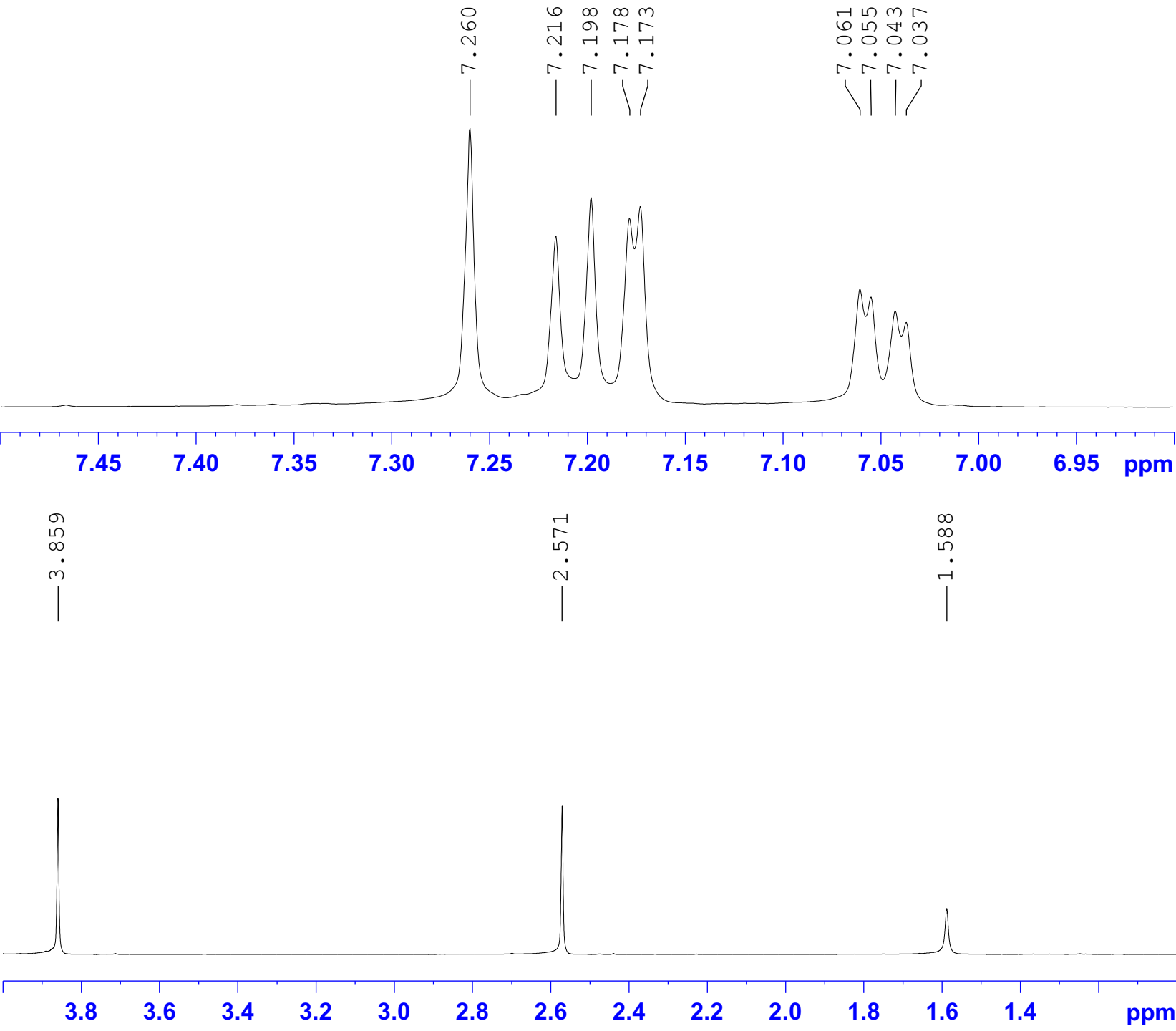


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 1.00  
 1.05

3.24

3.30

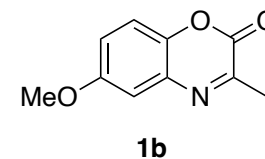
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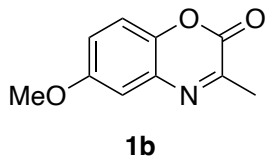


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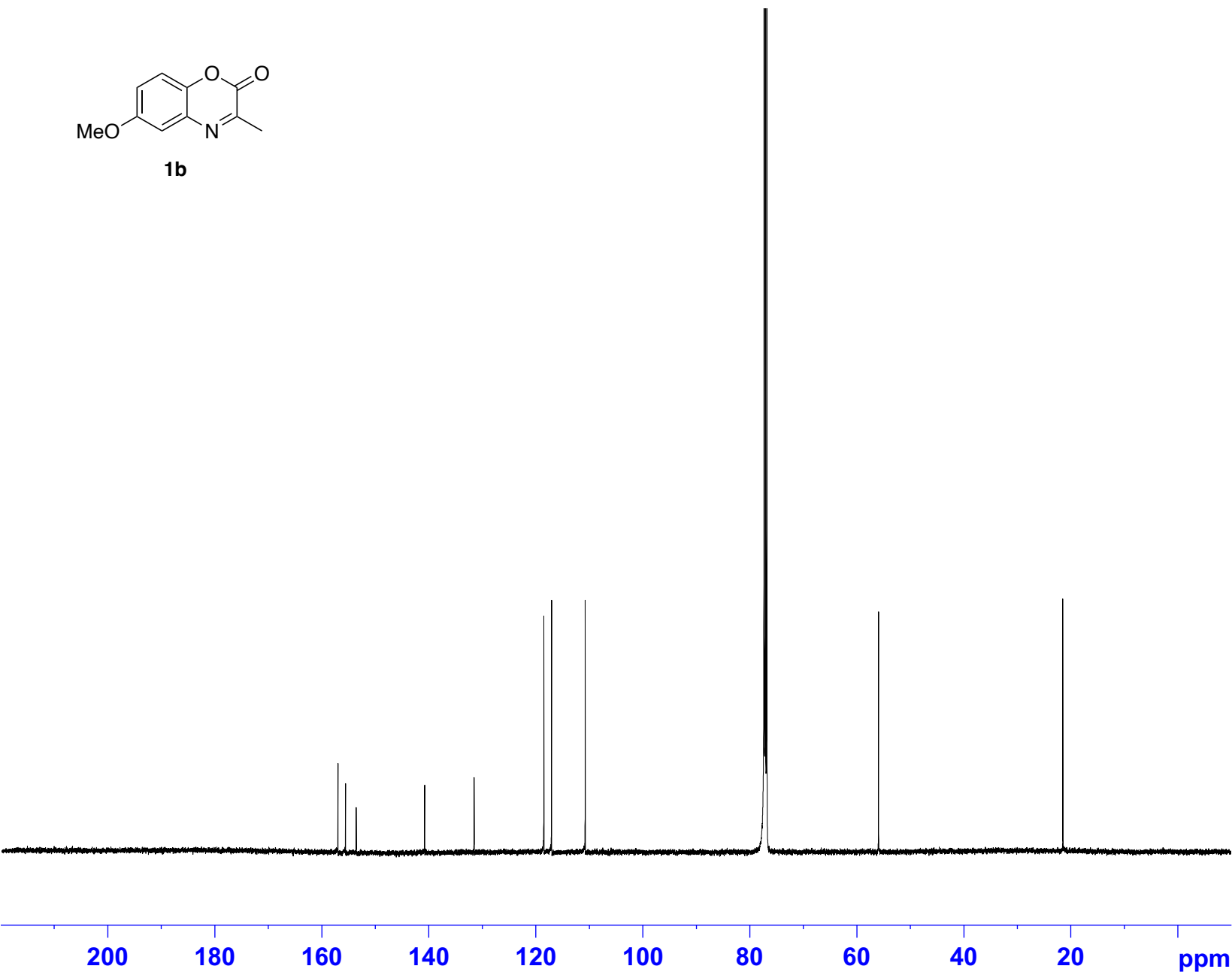
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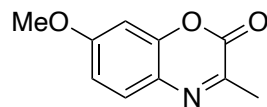
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21.41



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RG 101  
DW 16.600 usec  
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TE 298.2 K  
D1 2.00000000 sec  
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NUC1 13C  
P0 3.00 usec  
P1 9.00 usec  
PLW1 39.00000000 W  
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NUC2 1H  
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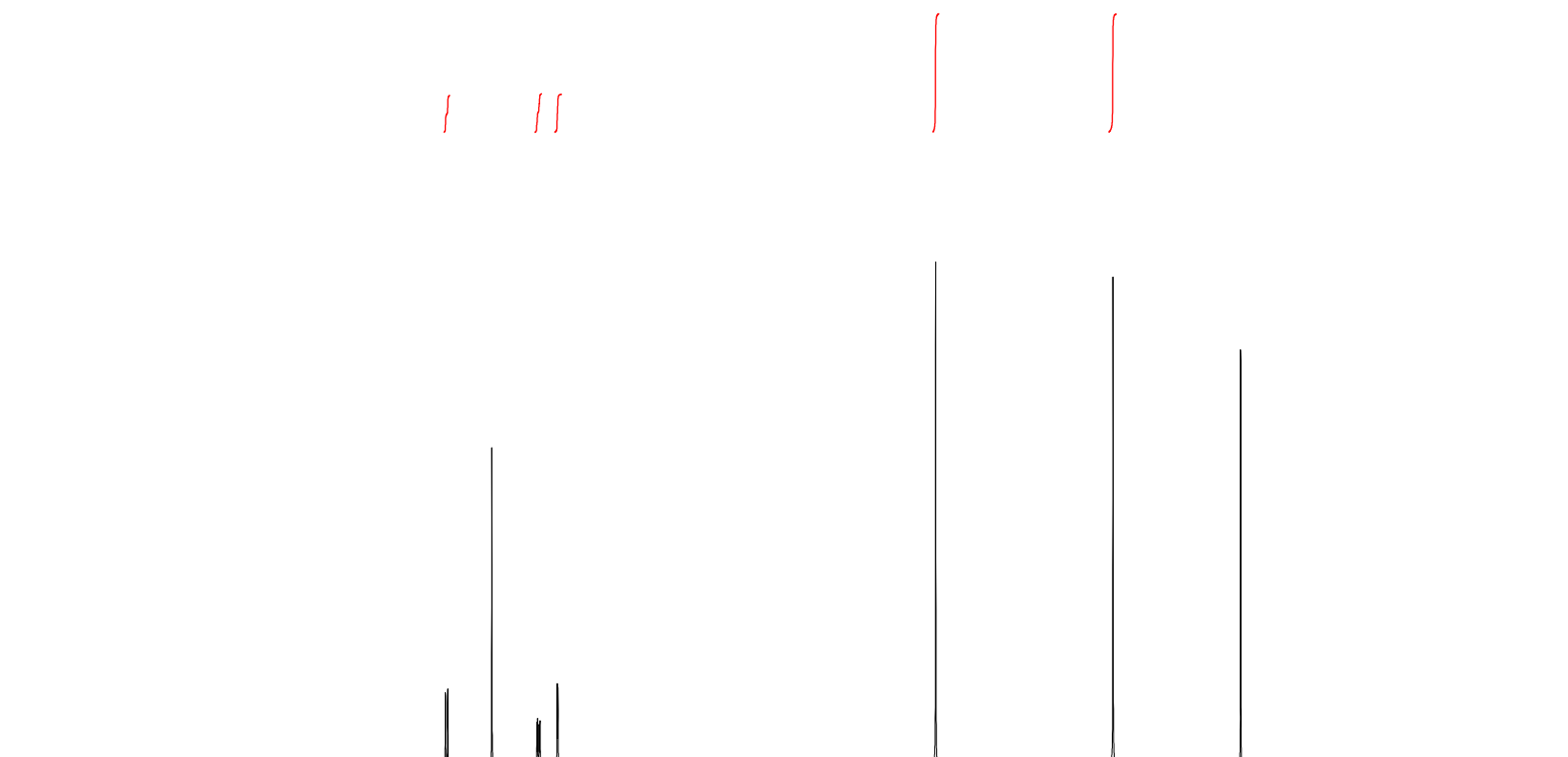
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6.915  
6.910  
6.898  
6.892  
6.761  
6.756

3.876

2.524

1.551



10 9 8 7 6 5 4 3 2 1 0 ppm

1.00

1.04

1.03

3.21

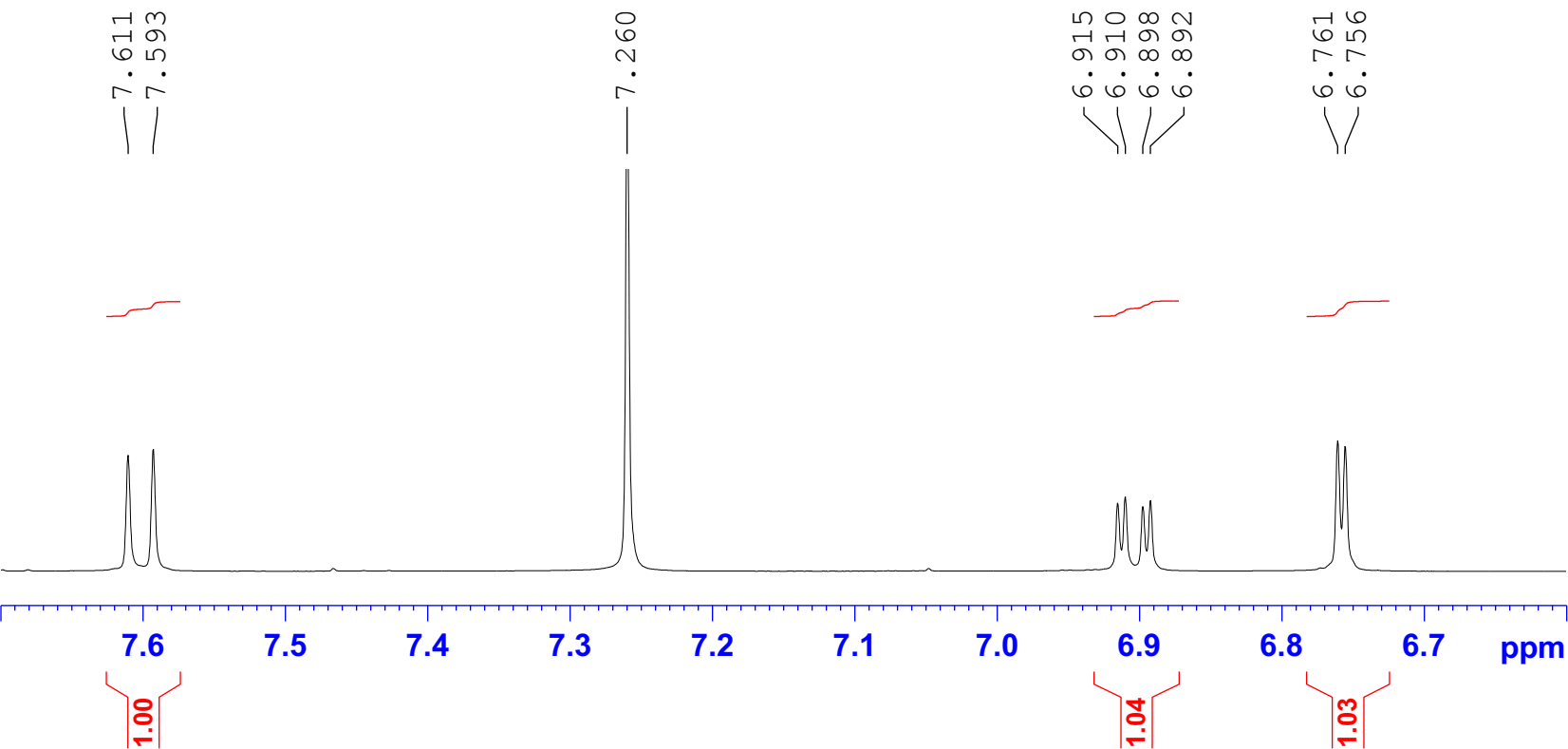
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AQ 3.2767999 sec  
RG 101  
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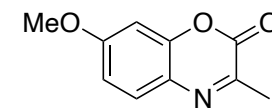




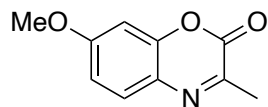
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 SOLVENT CDCl3  
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 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
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 DE 54.20 usec  
 TE 298.2 K  
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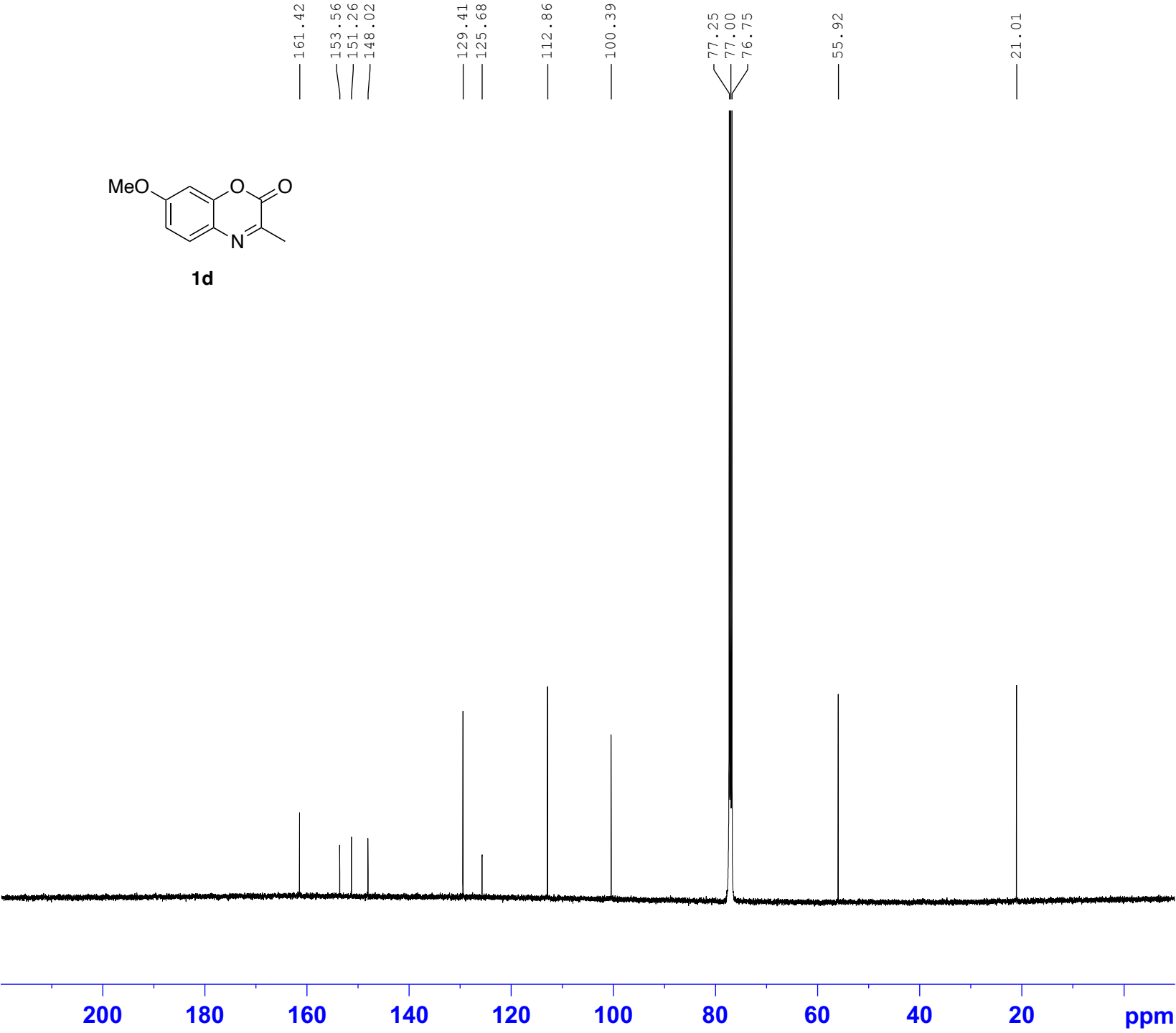
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**1d**



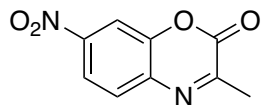
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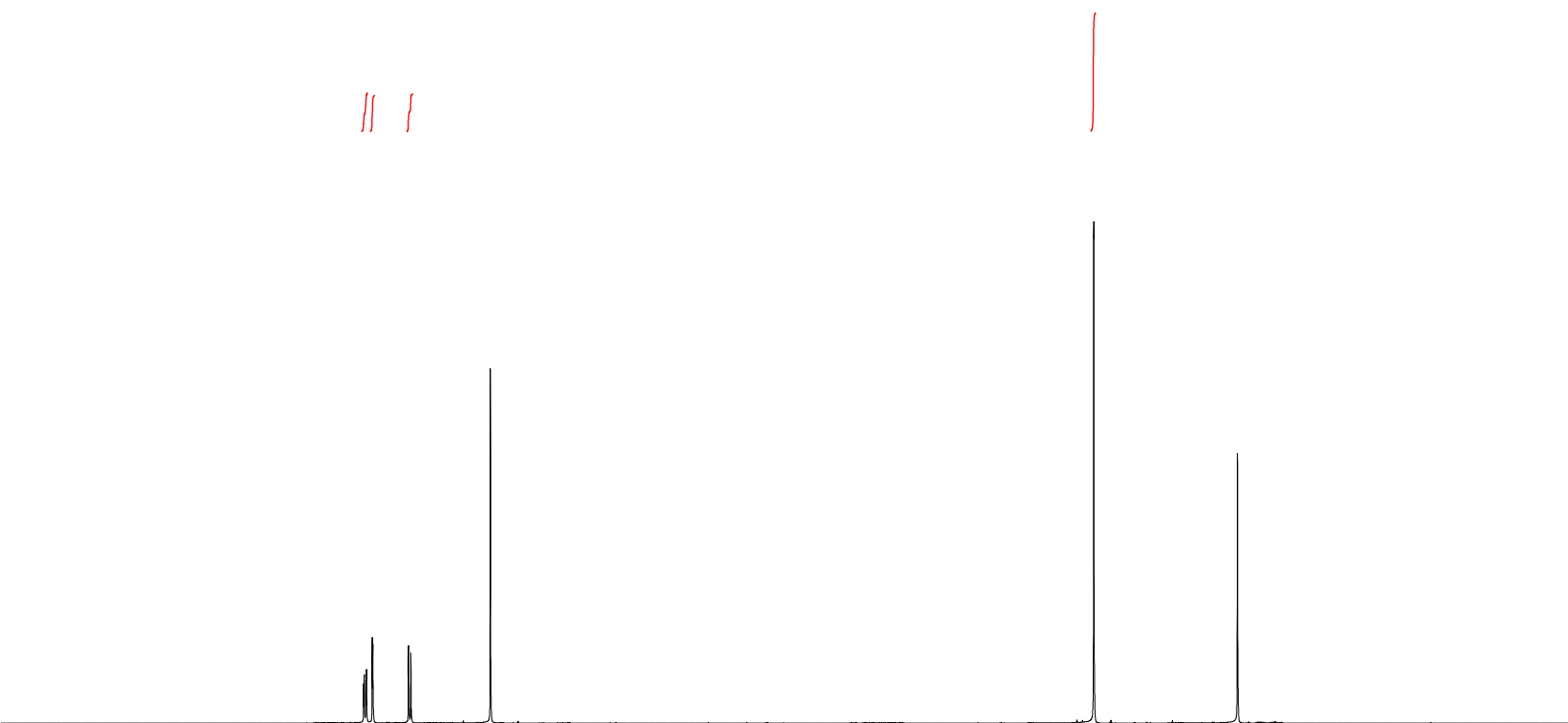


1f

8.229  
8.224  
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8.206  
8.162  
8.157  
7.884  
7.867  
7.260

2.646

1.547



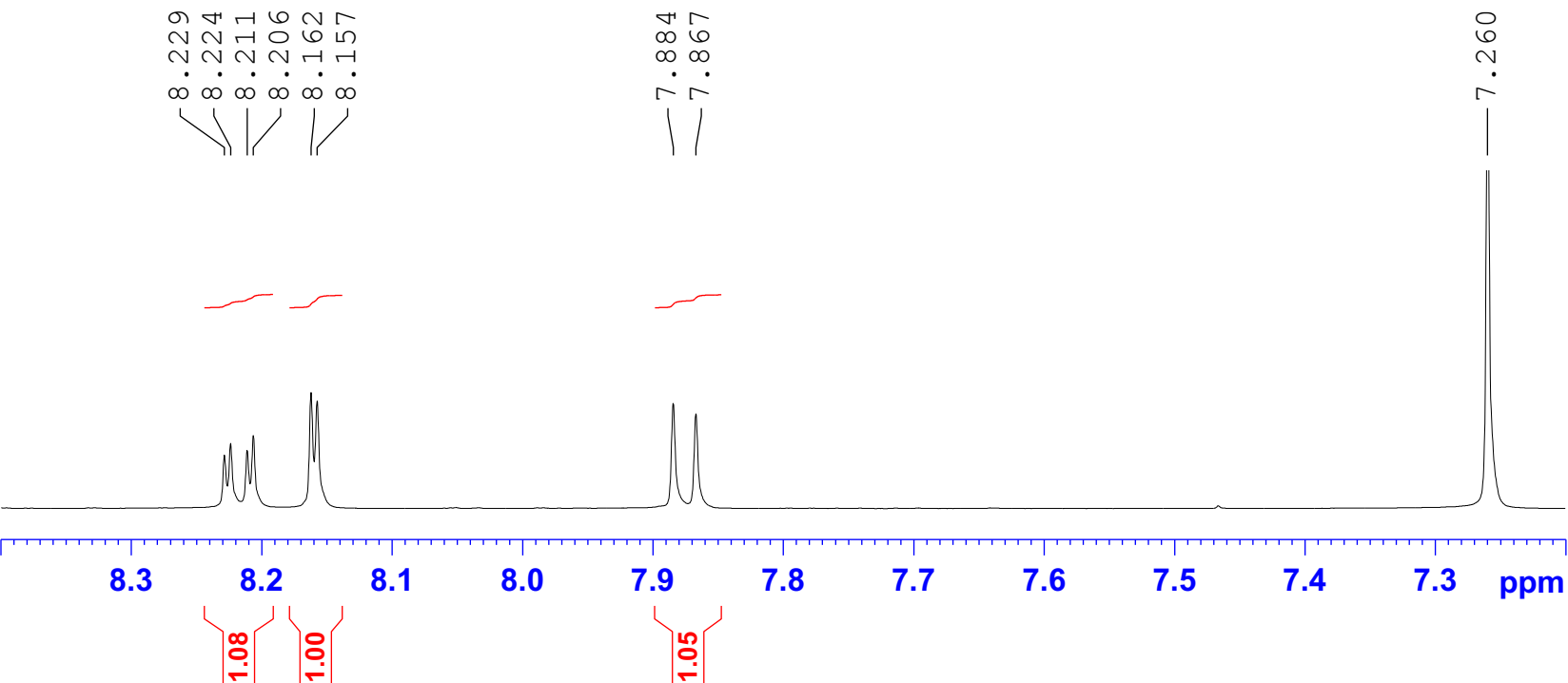
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1.05

3.29

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 TE 298.1 K  
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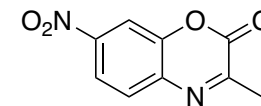
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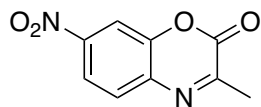
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 DE 54.20 usec  
 TE 298.1 K  
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 P1 12.00 usec  
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**1f**

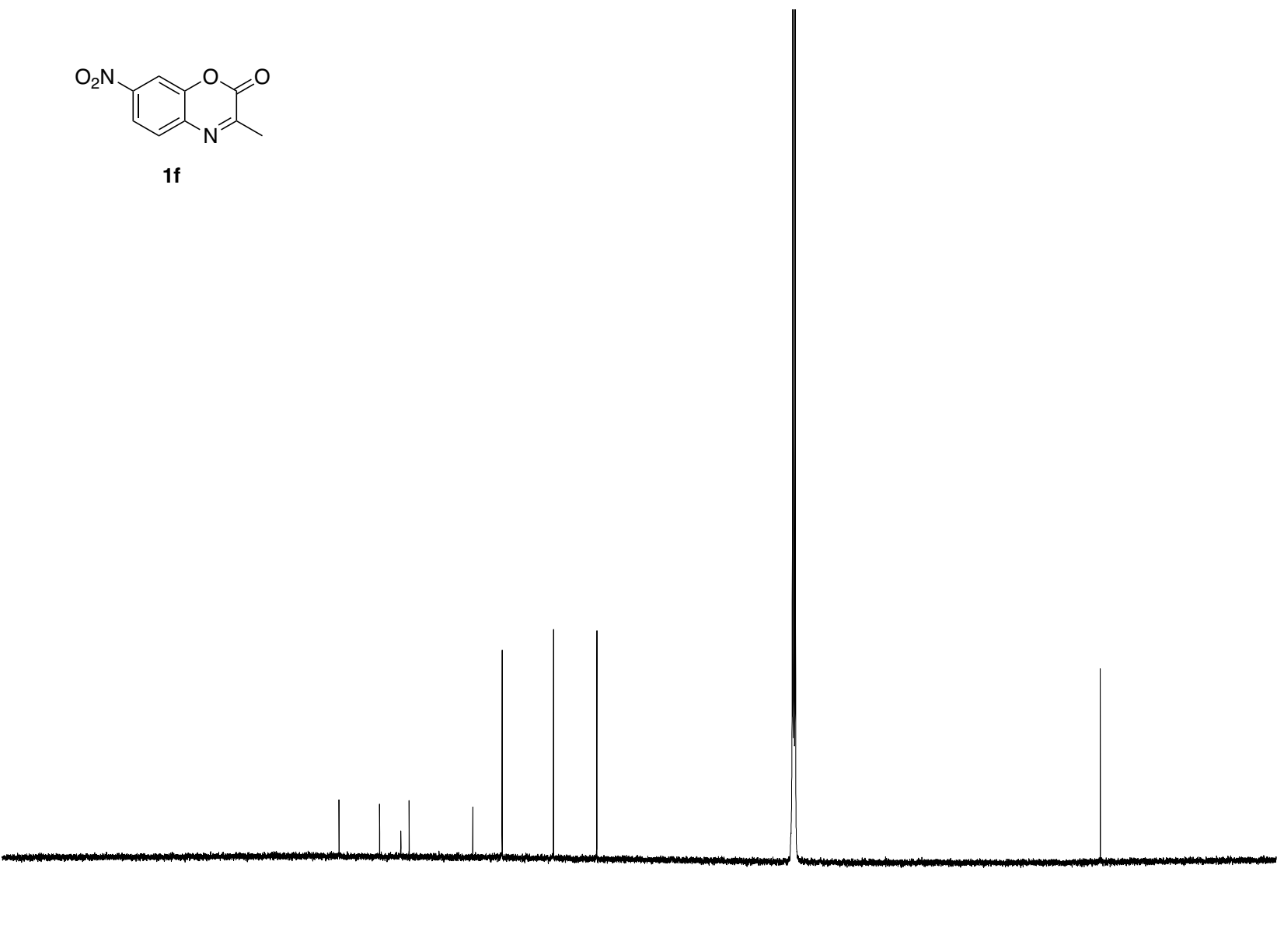


**1f**

— 159.01  
 — 151.71  
 — 147.88  
 — 146.38  
 — 134.89  
 — 129.59  
 — 120.34  
 — 112.54

77.25  
 77.00  
 76.75

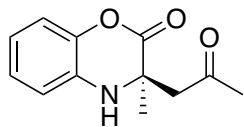
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 RG 101  
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 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
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 SFO2 500.1320005 MHz  
 NUC2 1H  
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**3a**

7.260  
7.016  
7.013  
7.005  
7.002  
7.000  
6.998  
6.989  
6.986  
6.985  
6.860  
6.857  
6.845  
6.844  
6.842  
6.829  
6.826  
6.787  
6.784  
6.771  
6.768  
5.082

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3.116  
3.030  
2.994  
2.211  
1.572  
1.477

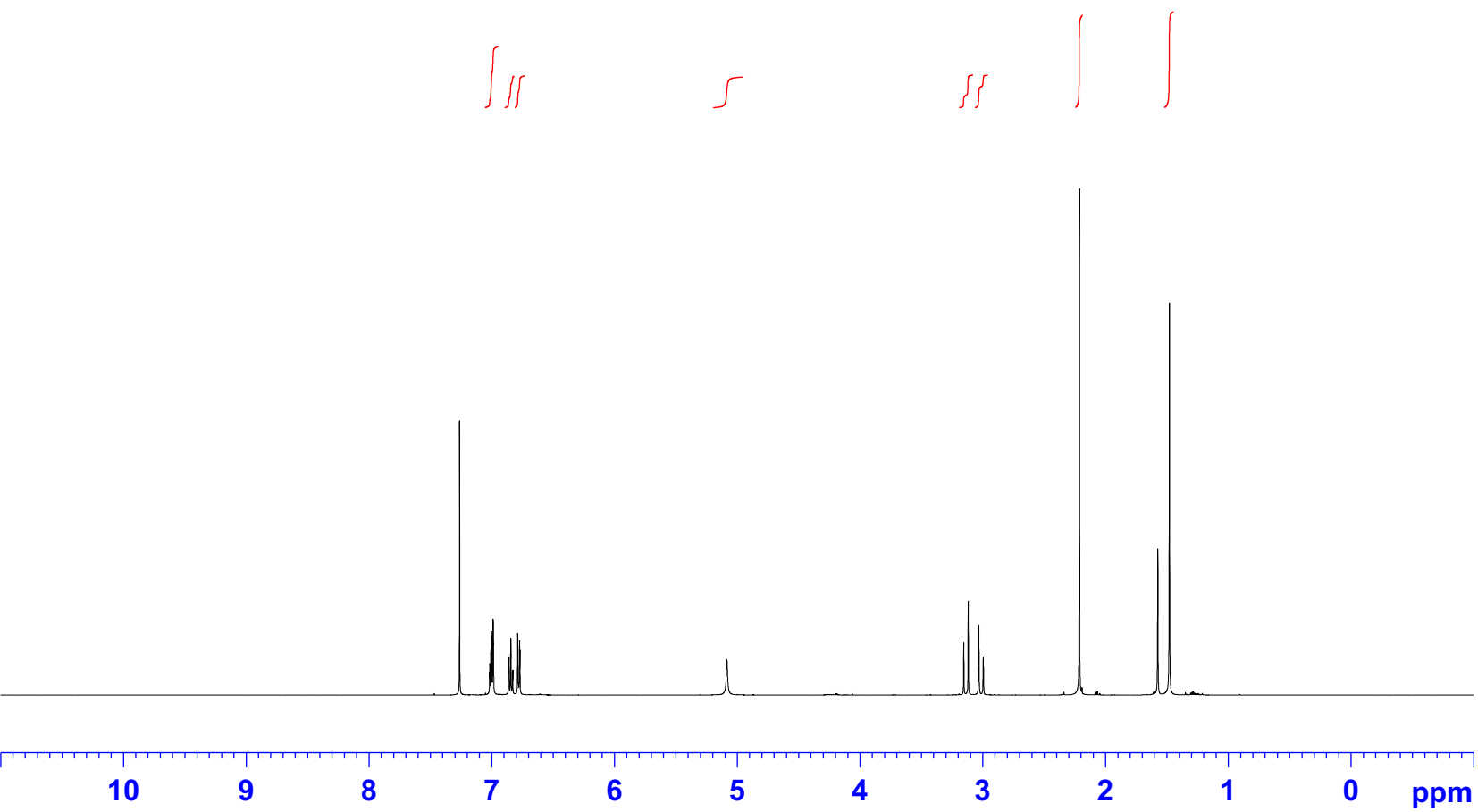
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RG 101  
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NUC1 1H  
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P1 12.30 usec  
PLW1 8.00000000 W

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1.04  
1.04  
1.01  
1.07  
1.07  
3.04  
3.15

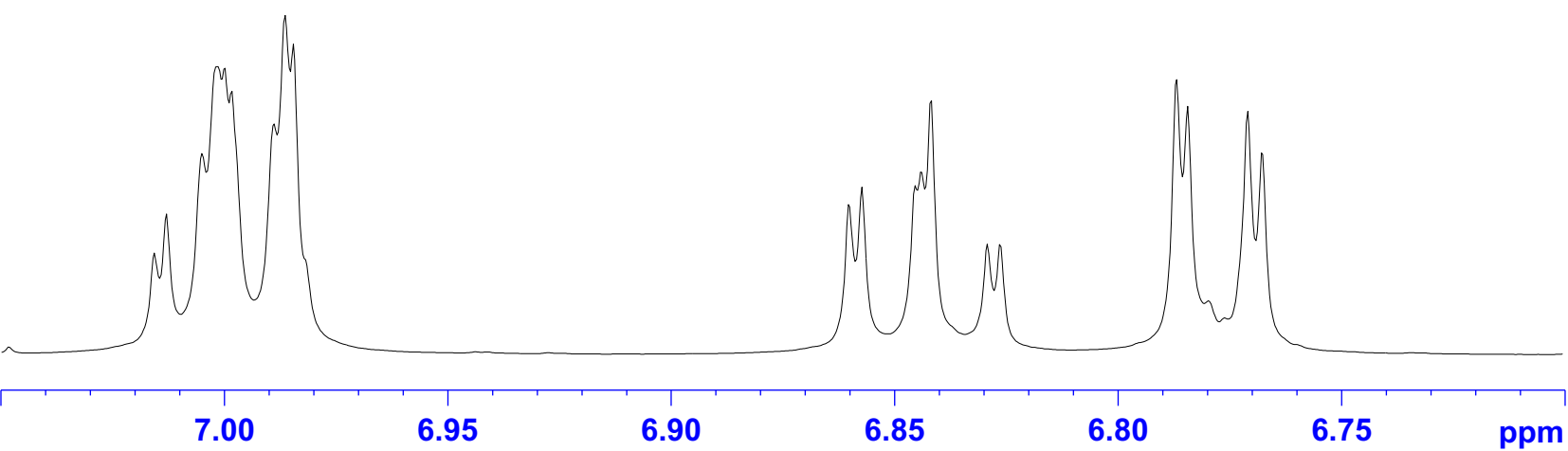
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6.860  
6.857  
6.845  
6.844  
6.842  
6.829  
6.826

6.787  
6.784  
6.771  
6.768

Current Data Parameters  
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EXPNO 10  
PROCNO 1

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SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.15 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
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P0 4.10 usec  
P1 12.30 usec  
PLW1 8.00000000 W



7.00 6.95 6.90 6.85 6.80 6.75 ppm

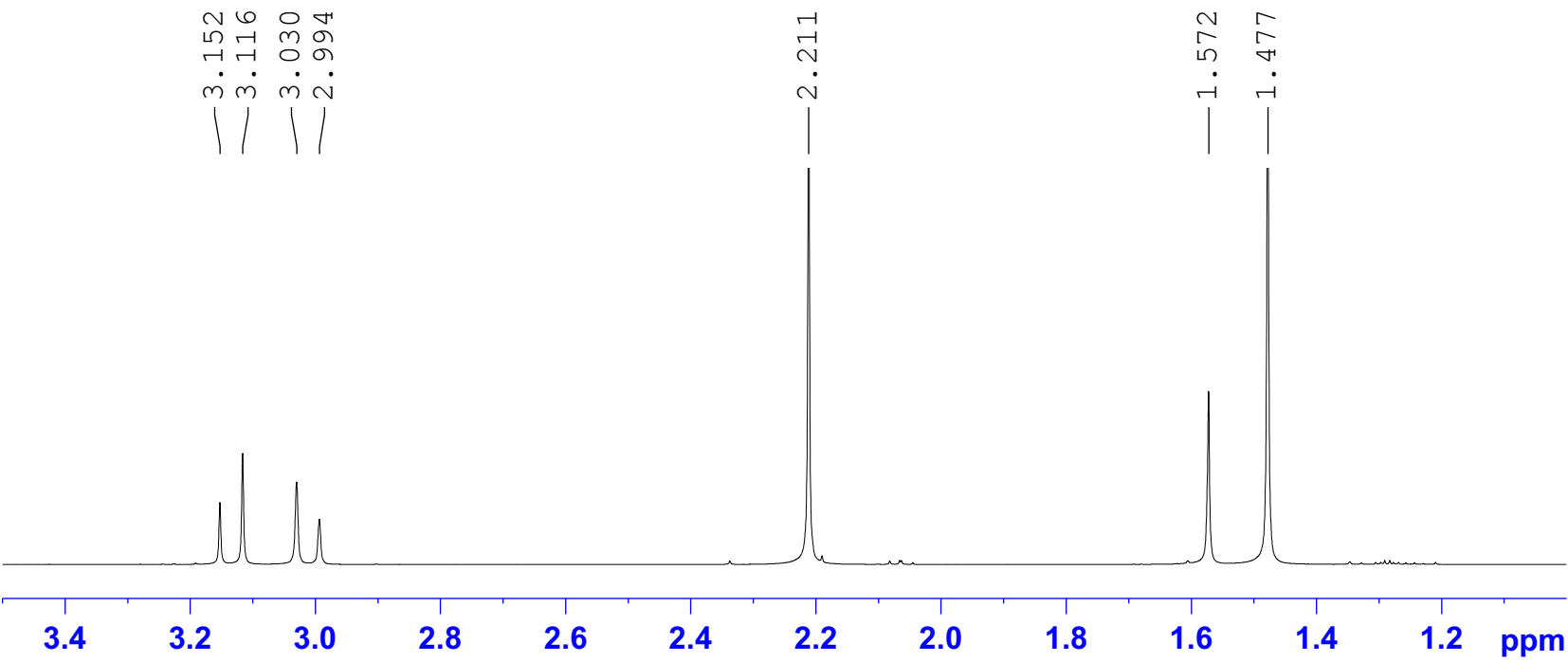
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3.030  
2.994

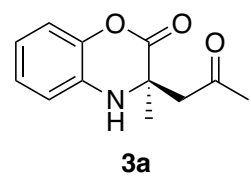
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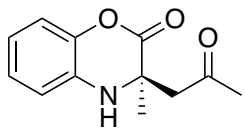
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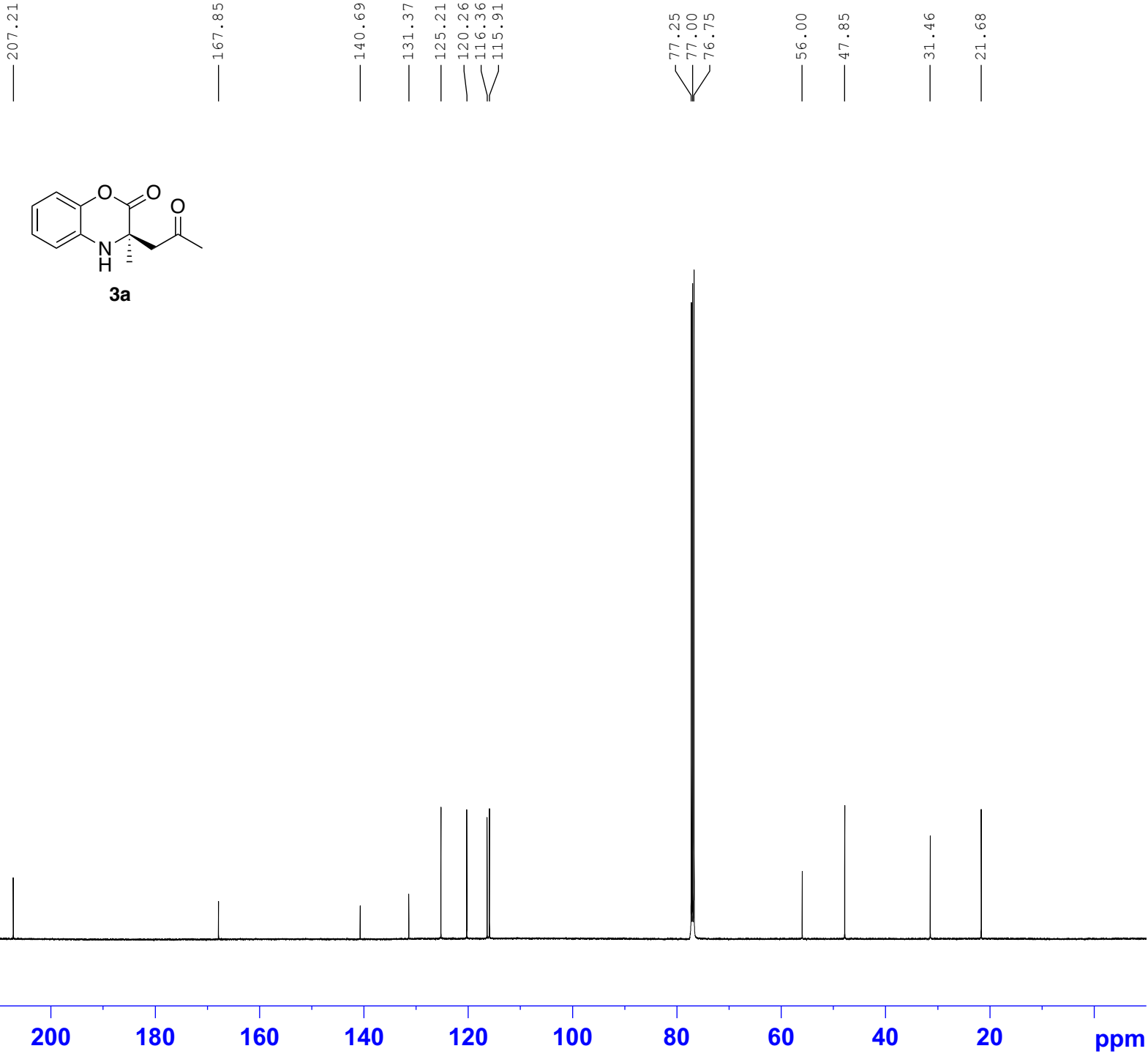


3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 ppm





**3a**

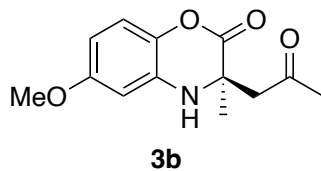


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 NS 392  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
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 P0 3.33 usec  
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 PLW1 28.94899940 W  
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 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577930 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

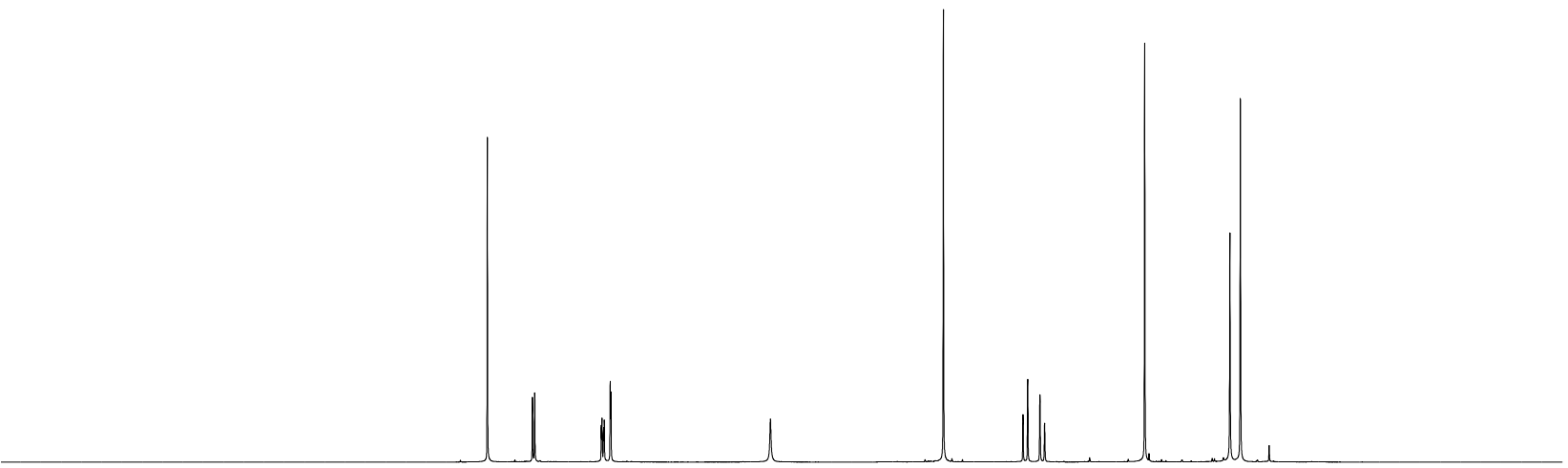




7.260  
 6.914  
 6.896  
 6.385  
 6.379  
 6.367  
 6.361  
 6.316  
 6.311  
 — 5.086  
 — 3.757  
 3.145  
 3.109  
 3.015  
 2.979  
 — 2.211  
 1.556  
 1.475

Integration values for the peaks in the spectrum:

1.00  
 1.04  
 1.00  
 1.01  
 3.16  
 1.08  
 1.06  
 3.17  
 3.15

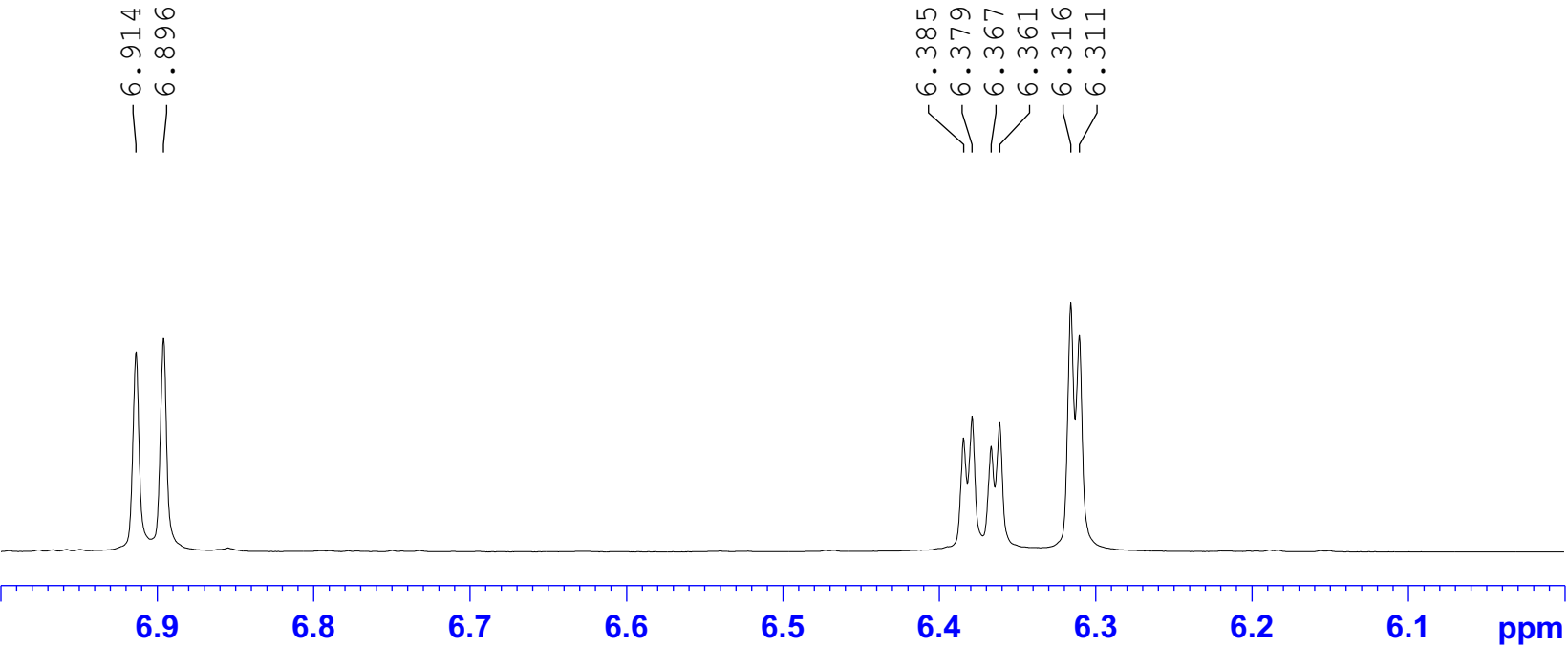


10 9 8 7 6 5 4 3 2 1 0 ppm

Current Data Parameters  
 NAME KLC-PhD223A\_P2\_spectrum collect  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230708  
 Time\_ 0.36 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (   
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

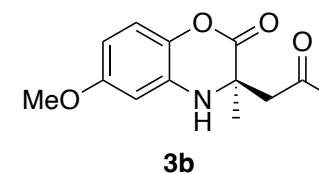
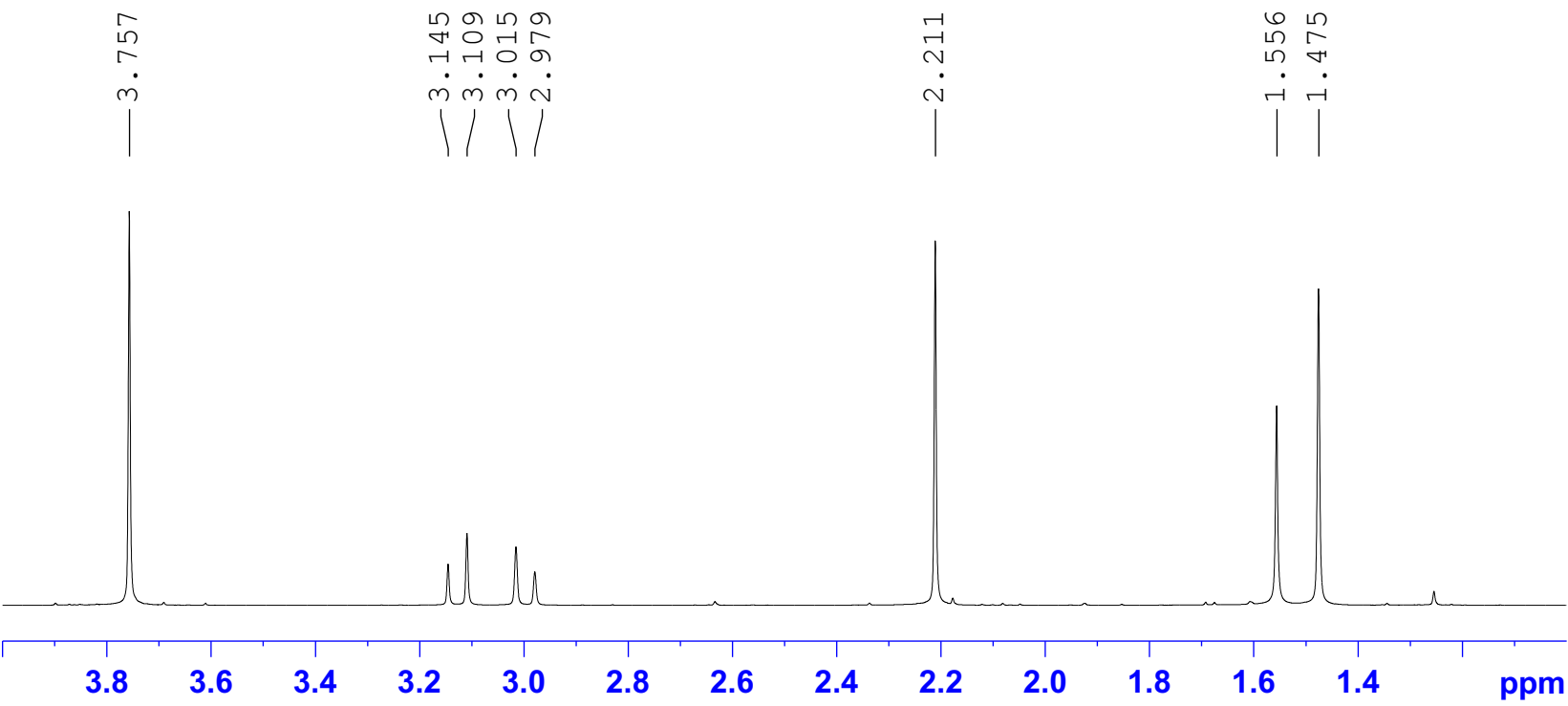
F2 - Processing parameters  
 SI 65536  
 SF 500.1300125 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

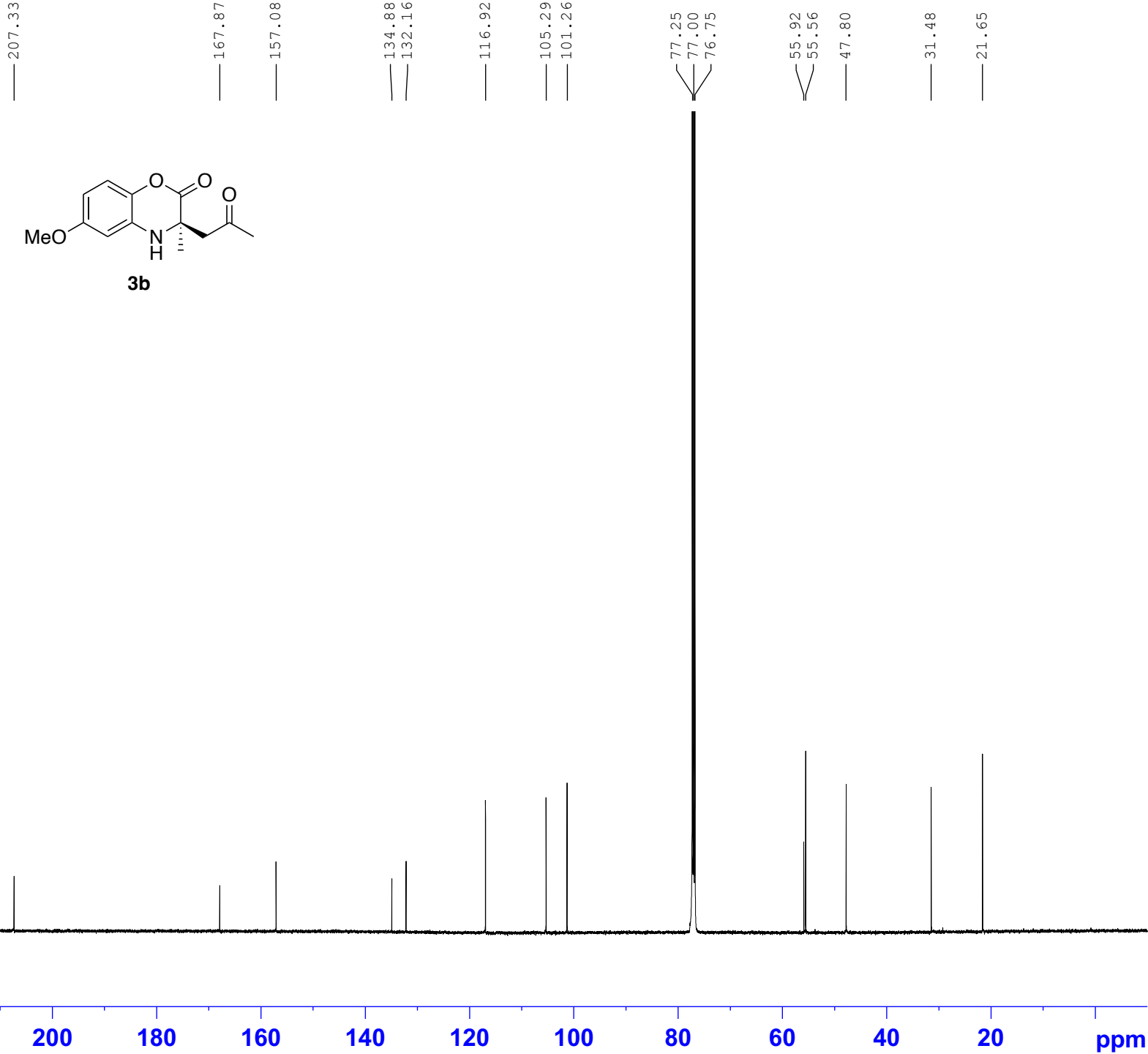
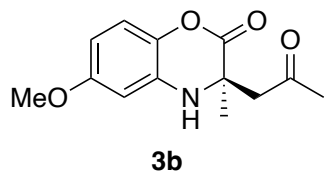


Current Data Parameters  
 NAME KLC-PhD223A\_P2\_spectrum collect  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230708  
 Time\_ 0.36 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (zg30)  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.0000000 sec  
 TD0 1  
 SFO1 500.1300883 MHz  
 NUC1 1H  
 PO 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300125 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00





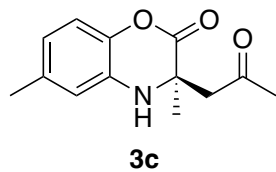
Current Data Parameters  
 NAME KLC-PhD223A\_P2\_spectrum collect  
 EXPNO 12  
 PROCNO 1

F2 - Acquisition Parameters

Date 20230708  
 Time 4.00 h  
 INSTRUM Avance  
 PROBHD Z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.2 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters

SI 32768  
 SF 125.7577919 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

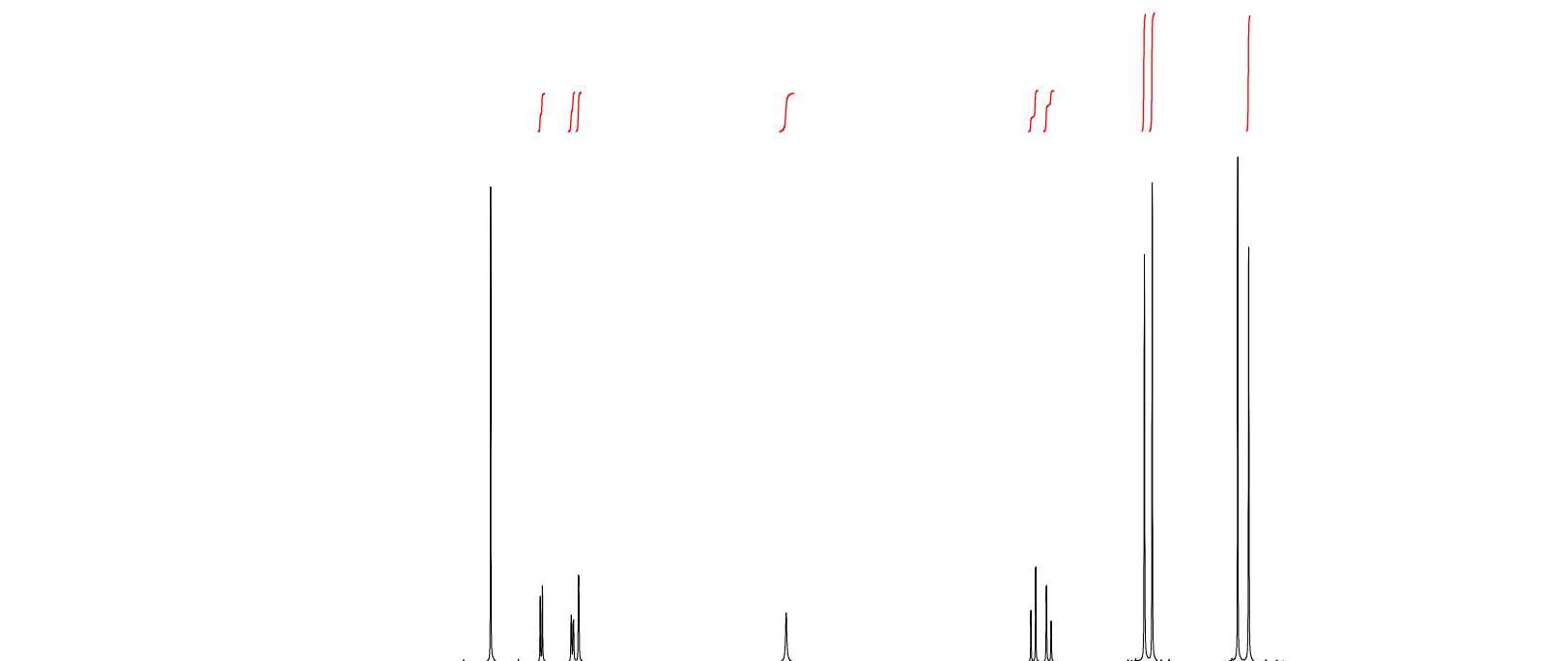


7.260  
6.881  
6.865  
6.643  
6.627  
6.589

— 5.002

3.132  
3.096  
3.014  
2.978  
2.265  
2.205

1.552  
1.469



10 9 8 7 6 5 4 3 2 1 0 ppm

1.00  
1.03  
1.03

1.00

1.08  
1.07

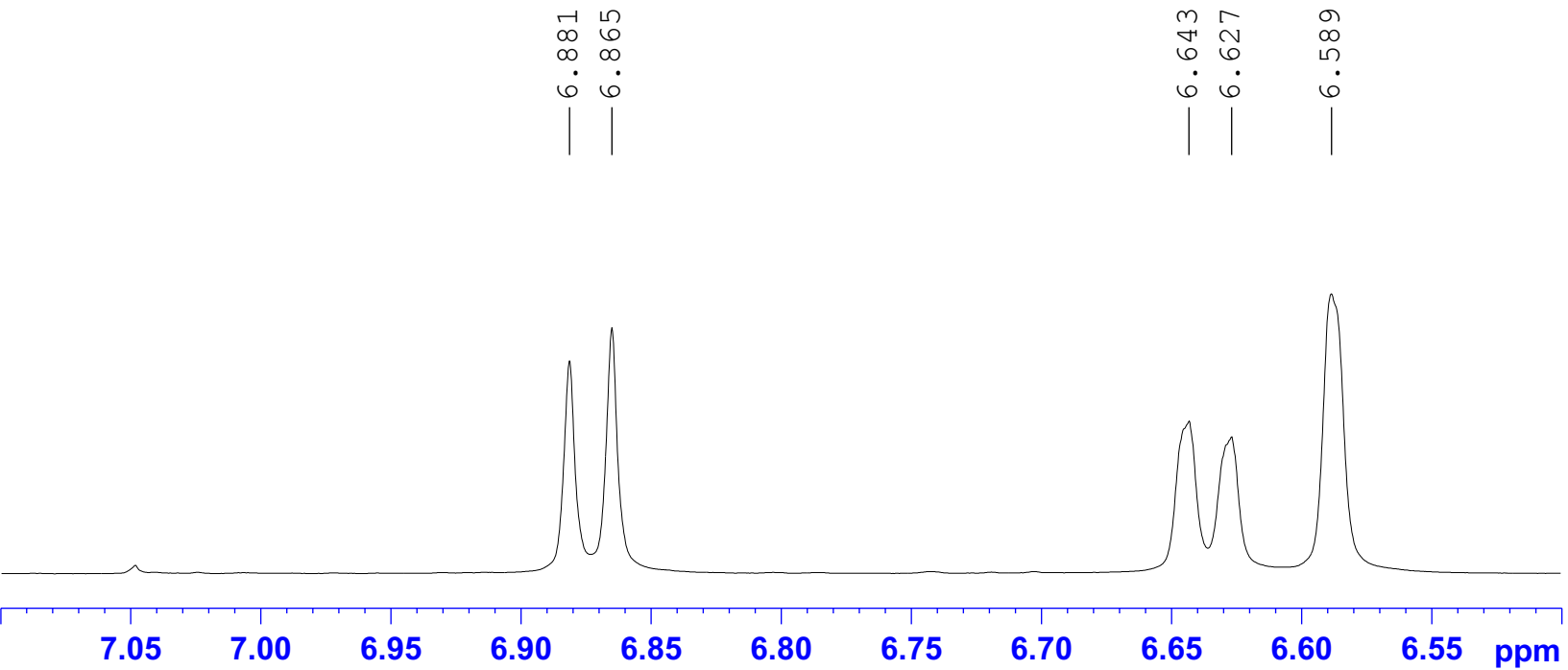
3.06  
3.08

3.02

Current Data Parameters  
NAME KLC-PhD224\_P2  
EXPNO 10  
PROCNO 1

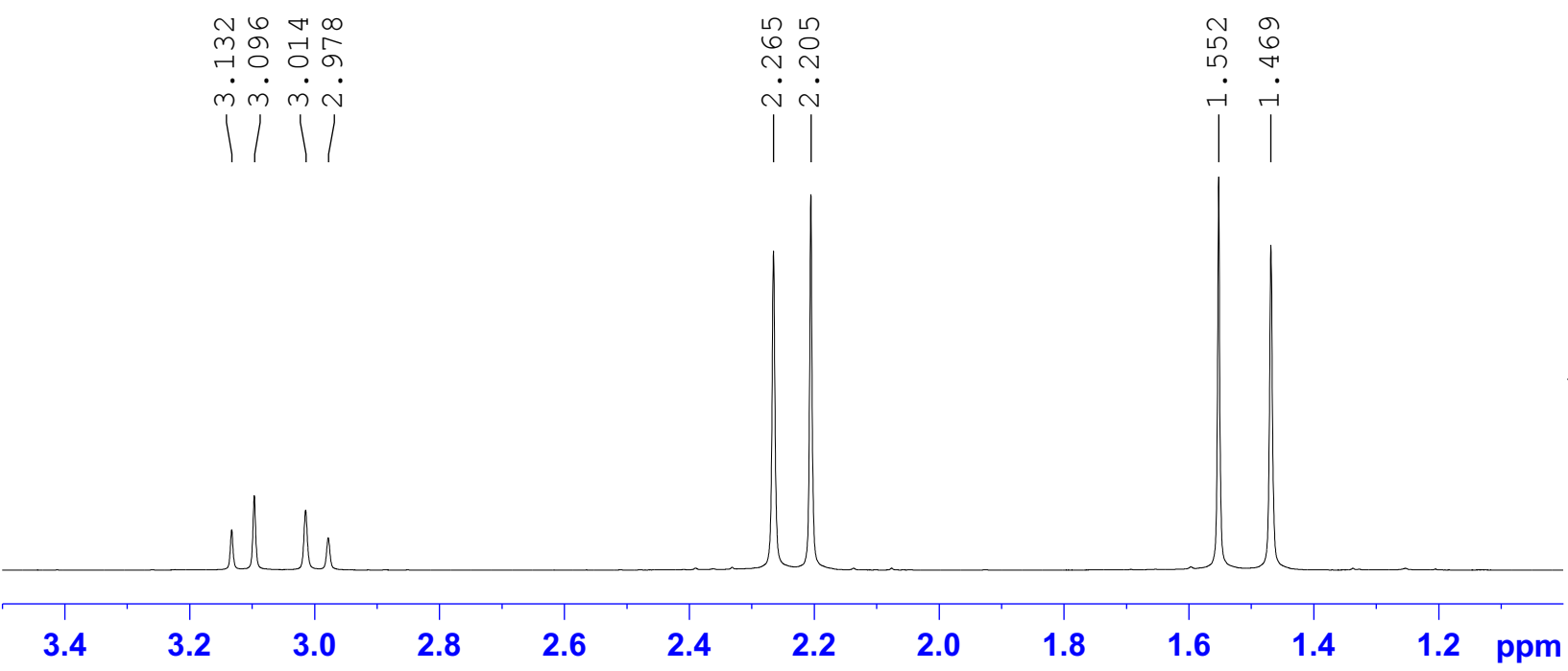
F2 - Acquisition Parameters  
Date\_ 20230310  
Time 17.40 h  
INSTRUM Avance  
PROBHD z167889\_0002 (   
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300126 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

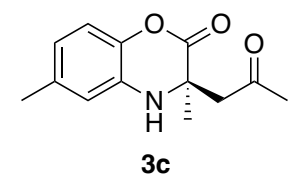


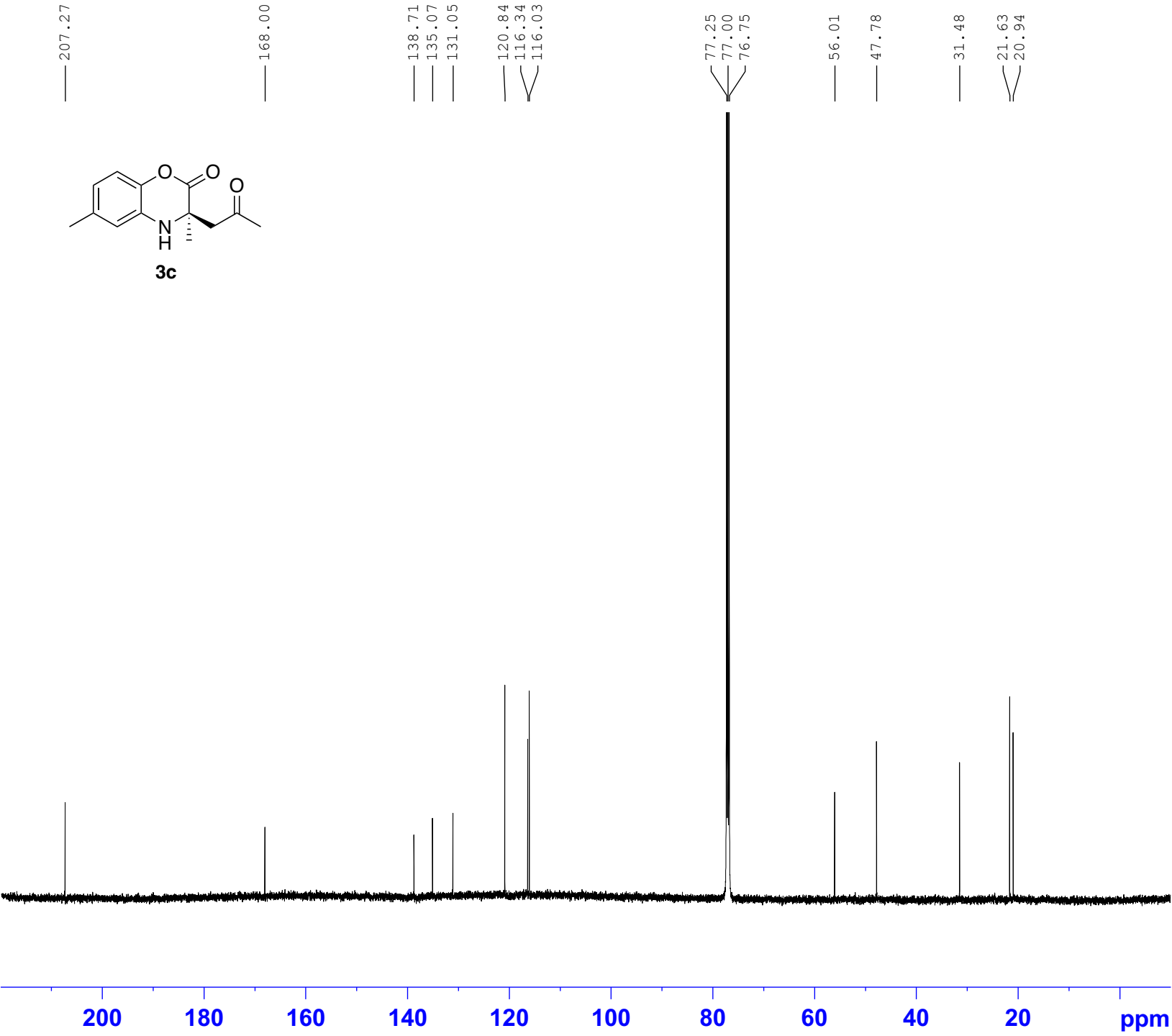
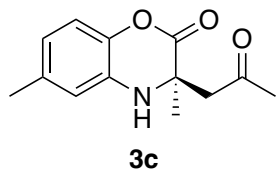
Current Data Parameters  
 NAME KLC-PhD224\_P2  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230310  
 Time 17.40 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W



F2 - Processing parameters  
 SI 65536  
 SF 500.1300126 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

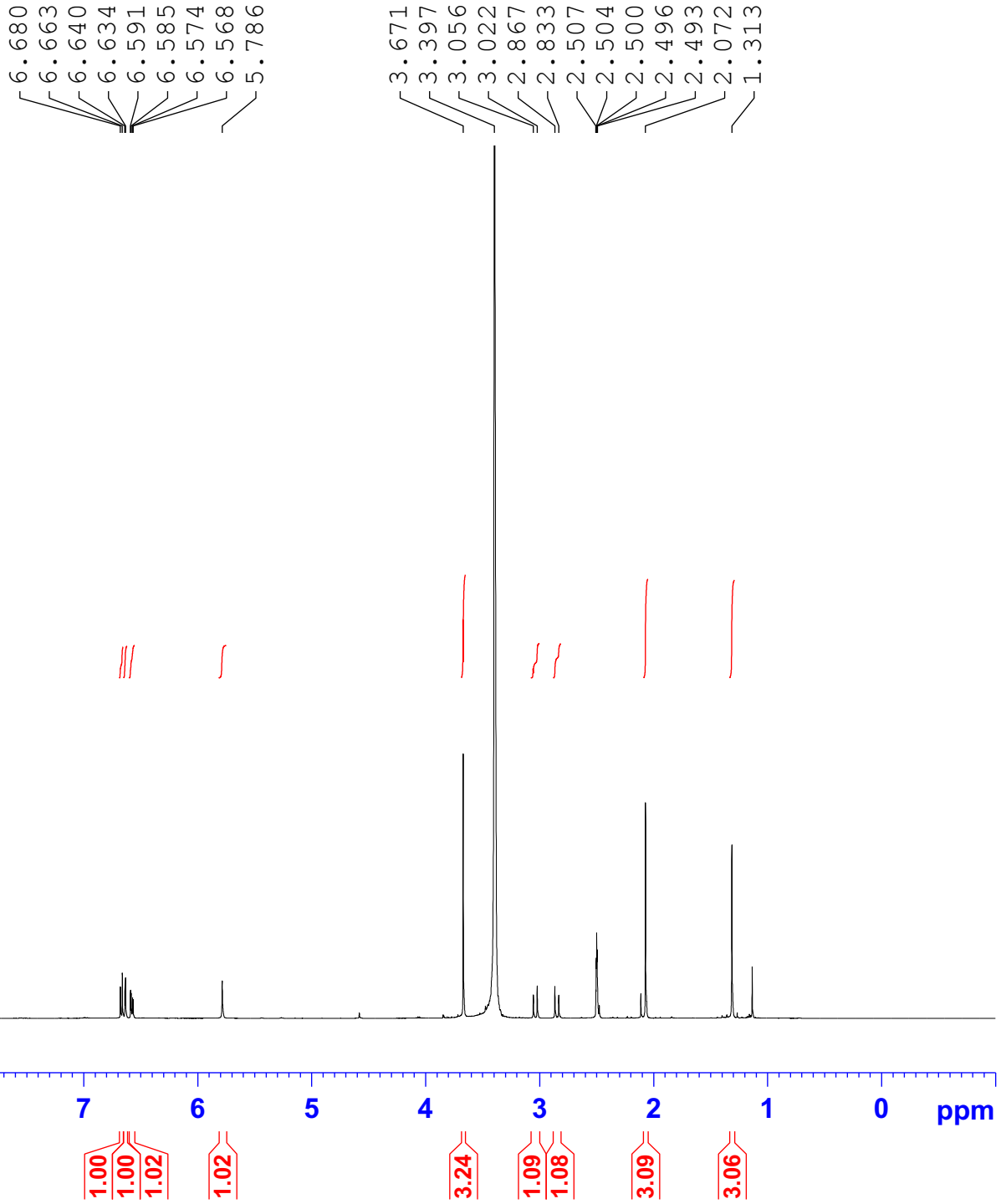
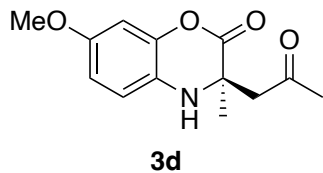




Current Data Parameters  
 NAME KLC-PhD224\_P2  
 EXPNO 12  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230310  
 Time\_ 18.39 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 465  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.2 K  
 D1 2.0000000 sec  
 D11 0.0300000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

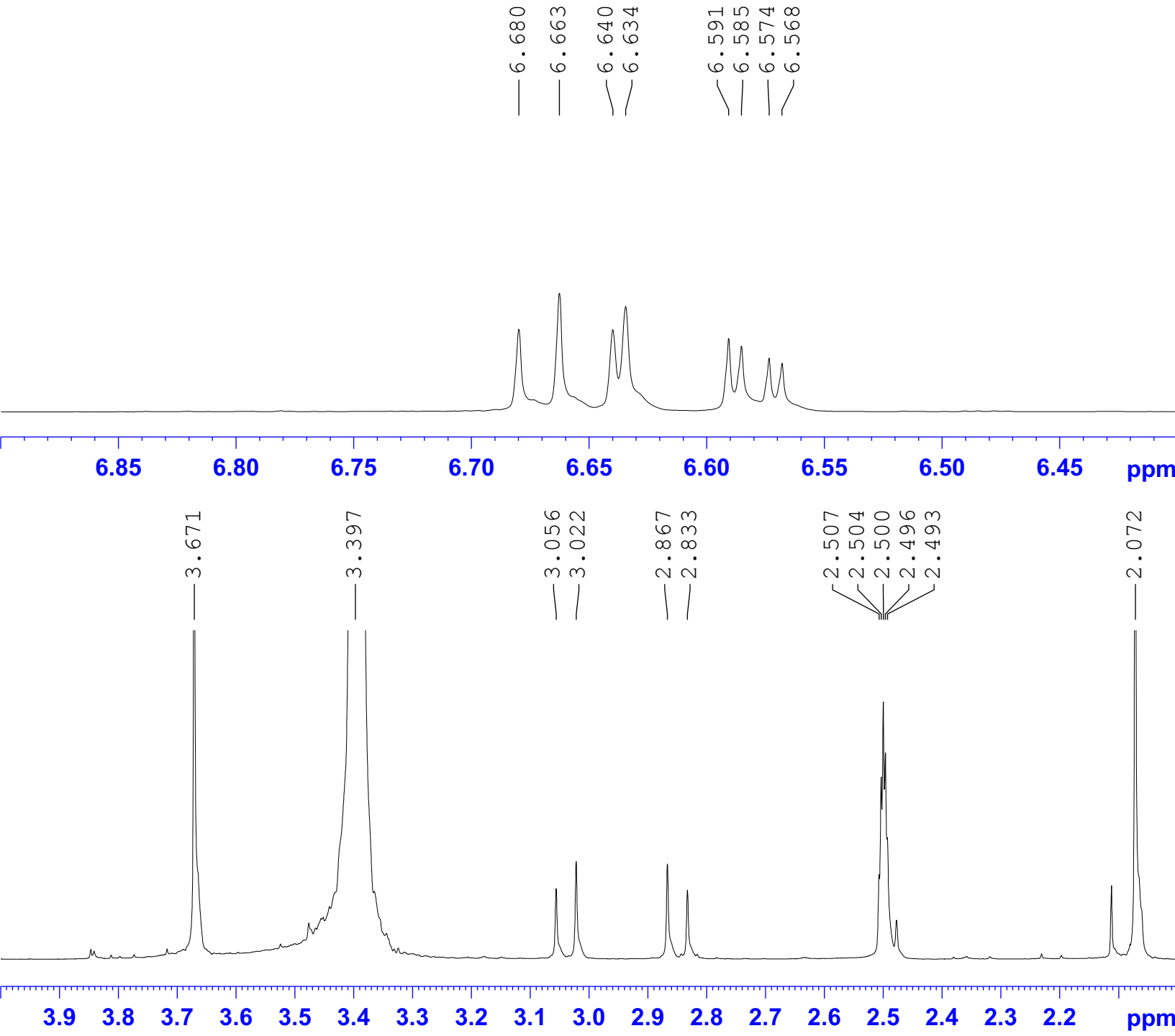
F2 - Processing parameters  
 SI 32768  
 SF 125.7577920 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



Current Data Parameters  
 NAME KLC-PhD460\_P2  
 EXPNO 11  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230721  
 Time\_ 23.32 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (   
 PULPROG zg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 71.8  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

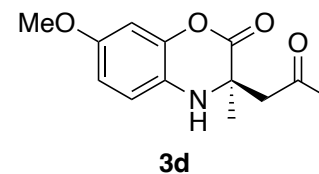
F2 - Processing parameters  
 SI 65536  
 SF 500.1300046 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00



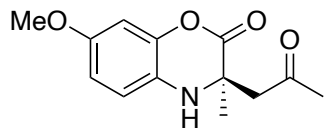
Current Data Parameters  
 NAME KLC-PhD460\_P2  
 EXPNO 11  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230721  
 Time\_ 23.32 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT DMSO  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 71.8  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.0302000 W

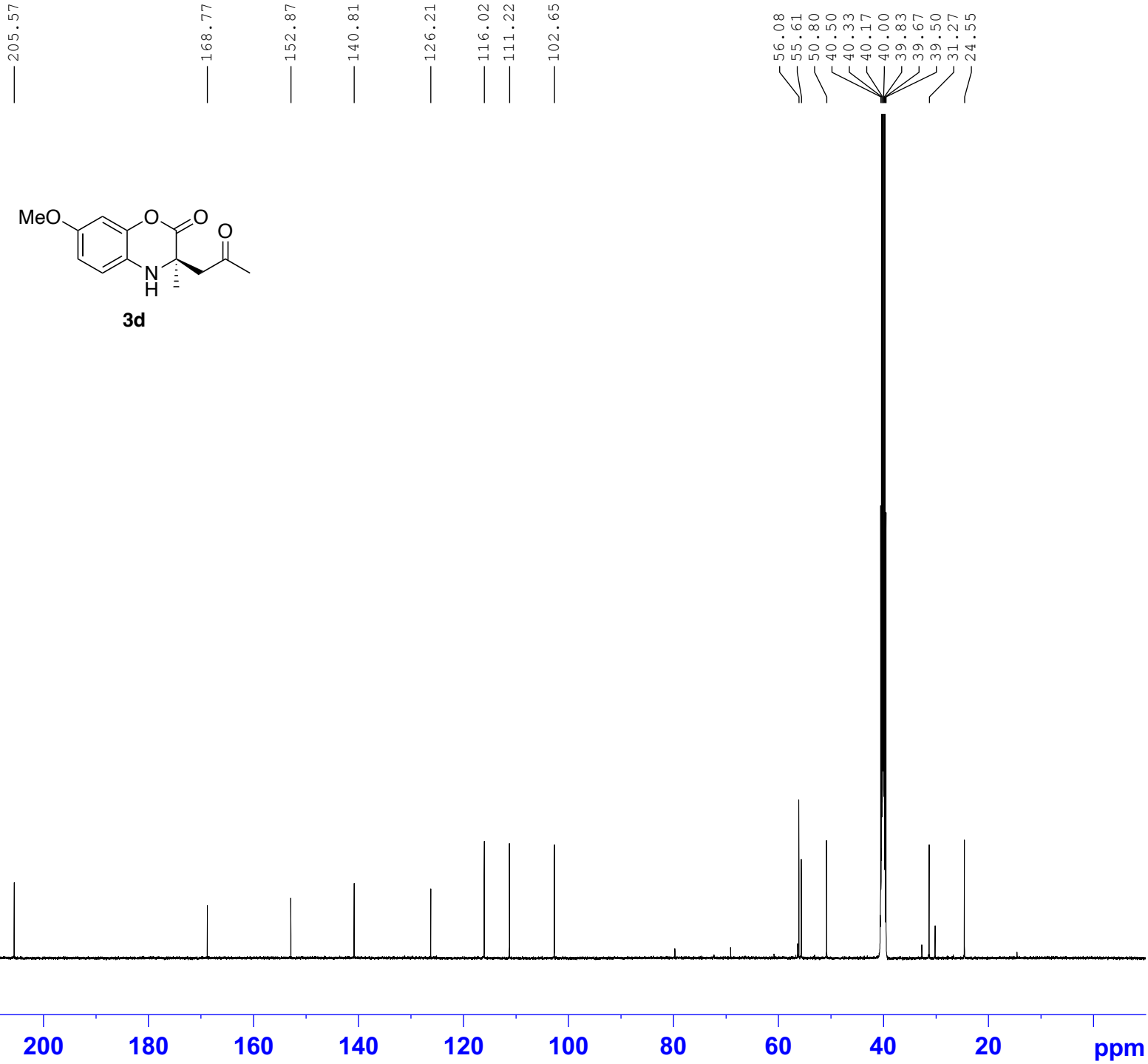
F2 - Processing parameters  
 SI 65536  
 SF 500.1300046 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00







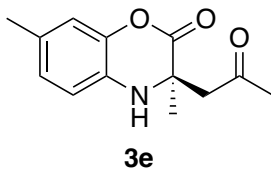
**3d**



Current Data Parameters  
 NAME KLC-PhD460\_P2  
 EXPNO 12  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230722  
 Time\_ 0.05 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT DMSO  
 NS 603  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.2 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577775 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

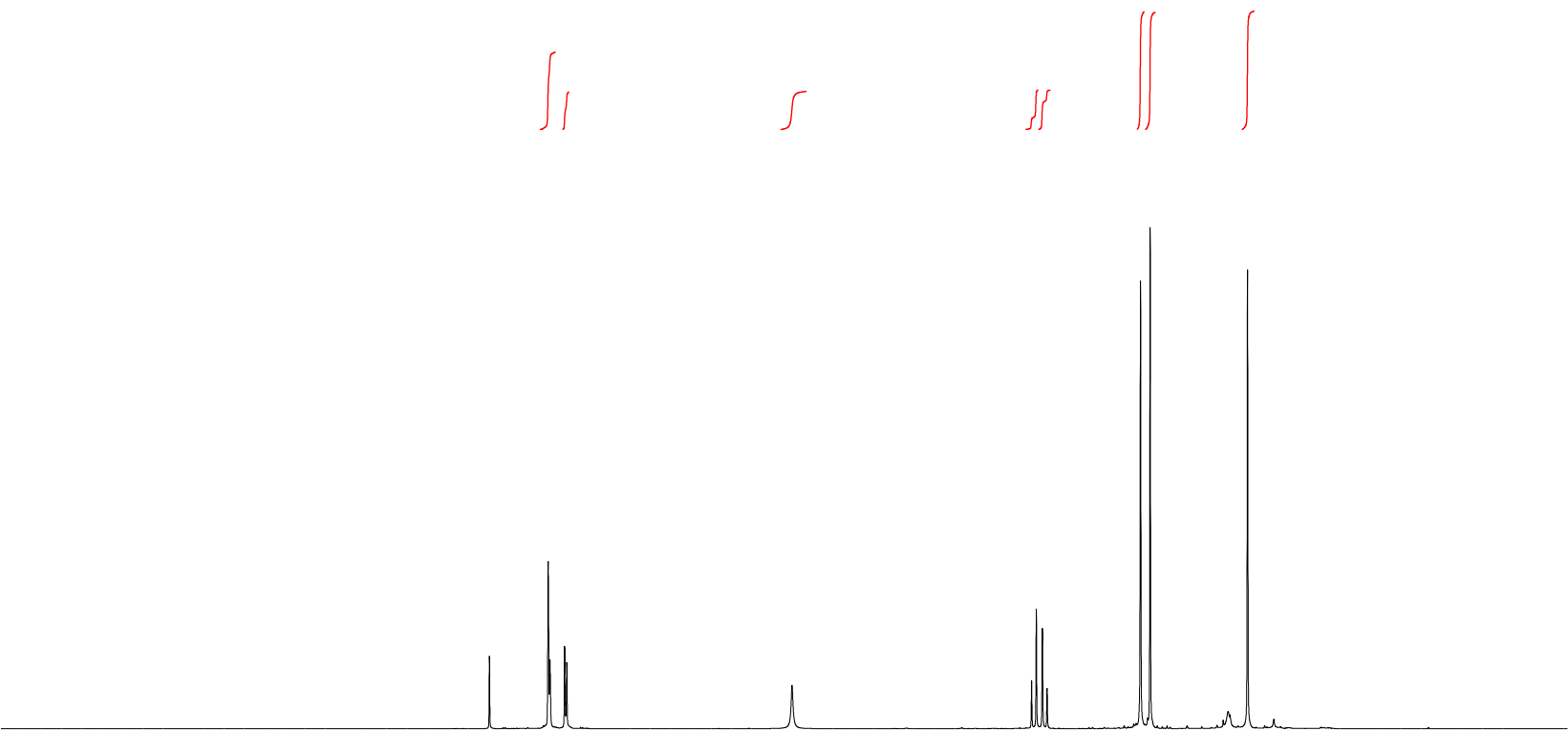


7.260  
6.810  
6.796  
6.684  
6.667

4.941

3.106  
3.070  
3.024  
2.988  
2.272  
2.198

1.452



2.05  
1.00

1.01

1.05  
1.04

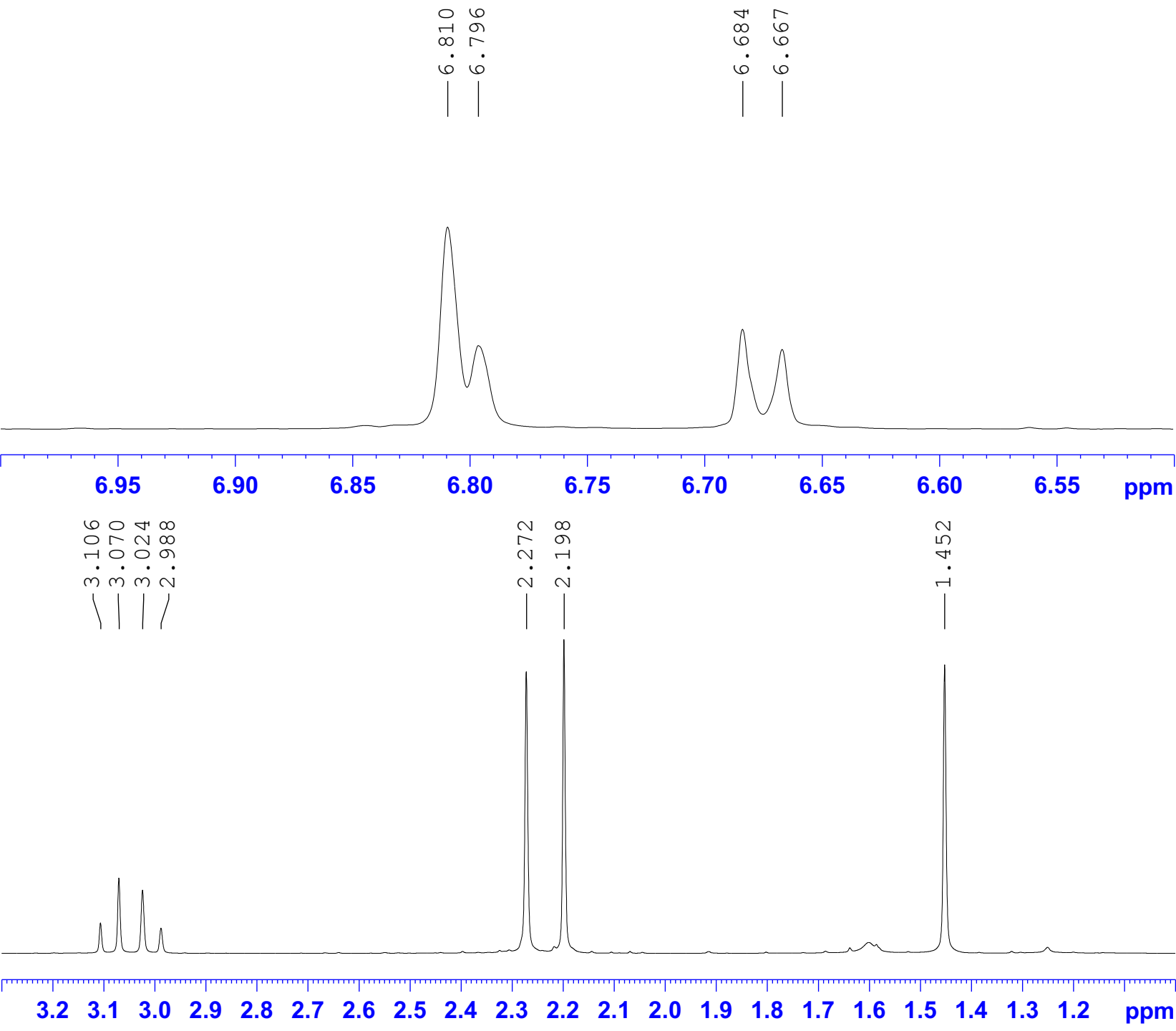
3.12  
3.10

3.13

Current Data Parameters  
NAME KLC-PhD225\_P2  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20230310  
Time\_ 18.45 h  
INSTRUM Avance  
PROBHD z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.2 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

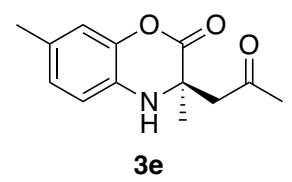
F2 - Processing parameters  
SI 65536  
SF 500.1300126 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

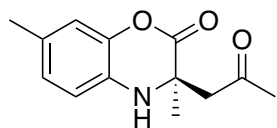


Current Data Parameters  
 NAME KLC-PhD225\_P2  
 EXPNO 10  
 PROCNO 1

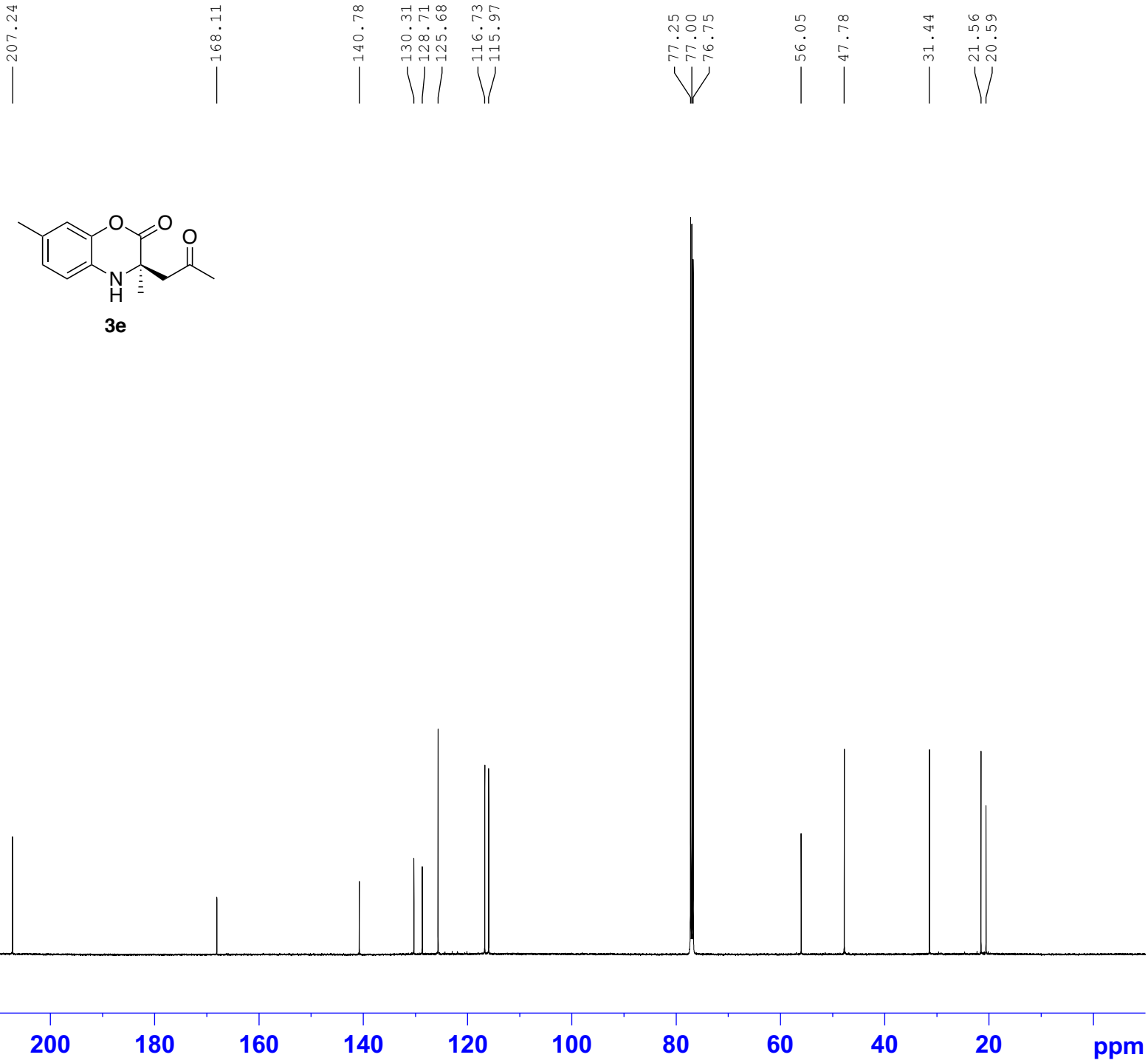
F2 - Acquisition Parameters  
 Date 20230310  
 Time 18.45 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.2 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300126 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00





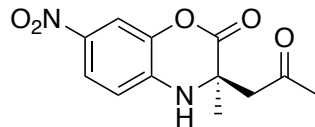
**3e**



Current Data Parameters  
 NAME KLC-PhD225\_P2  
 EXPNO 11  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230310  
 Time\_ 19.12 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDC13  
 NS 502  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577935 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



**3f**

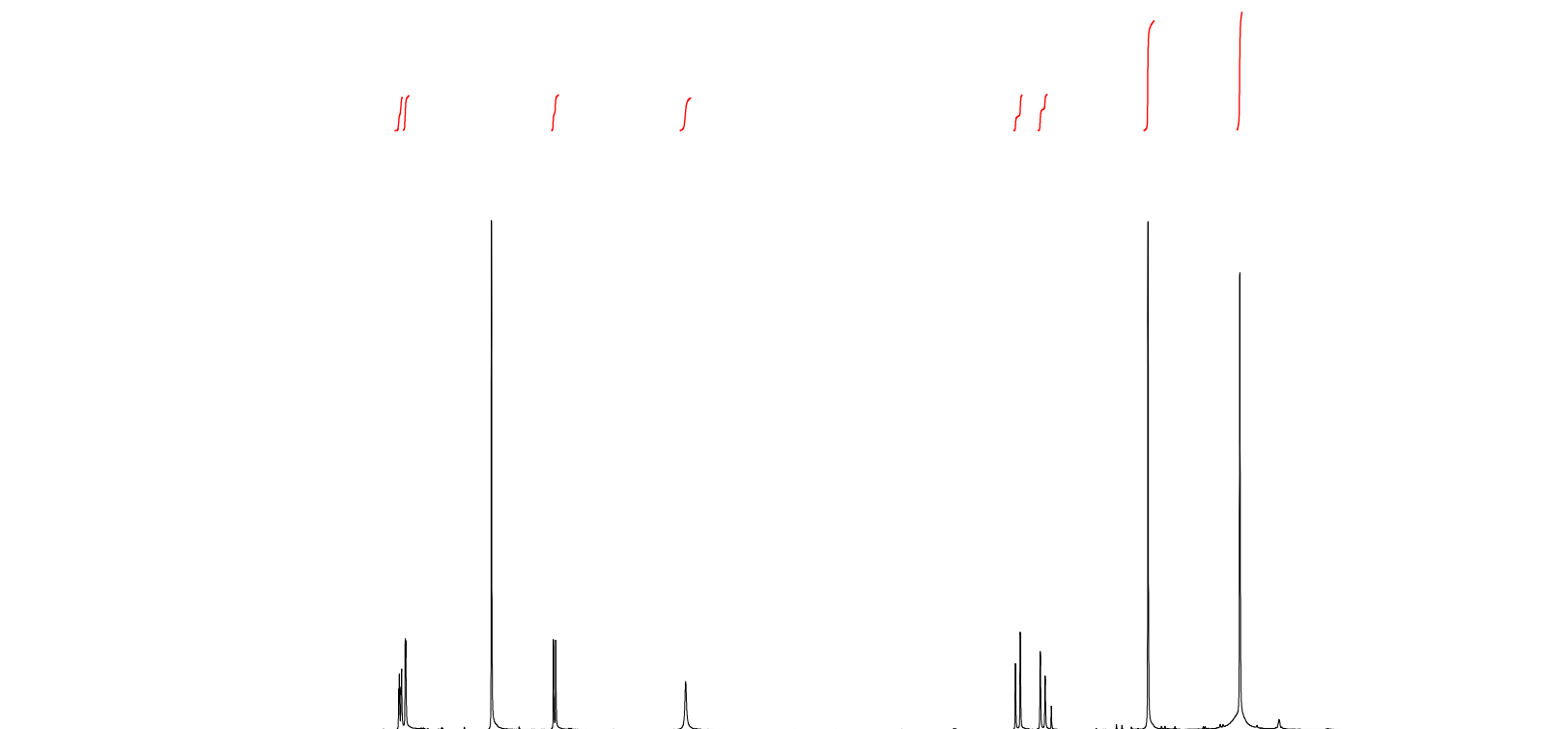
7.967  
7.962  
7.949  
7.945  
7.917  
7.913  
7.260  
6.787  
6.770

— 5.778

3.263  
3.226  
3.073  
3.036

— 2.251

— 1.551



10 9 8 7 6 5 4 3 2 1 0 ppm

1.00  
1.05

1.06

0.97

1.06  
1.08

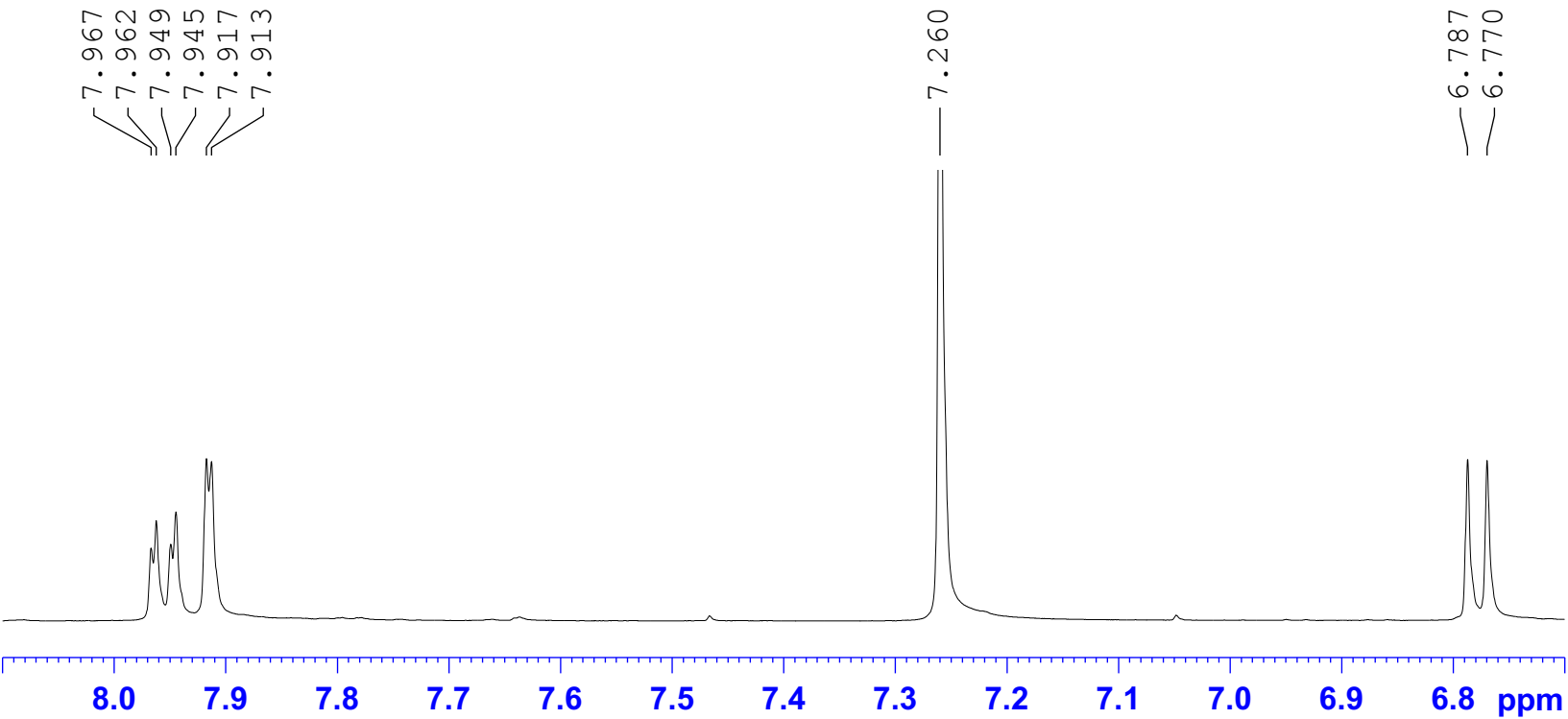
3.25

3.54

Current Data Parameters  
NAME KLC-PhD281\_P4  
EXPNO 20  
PROCNO 1

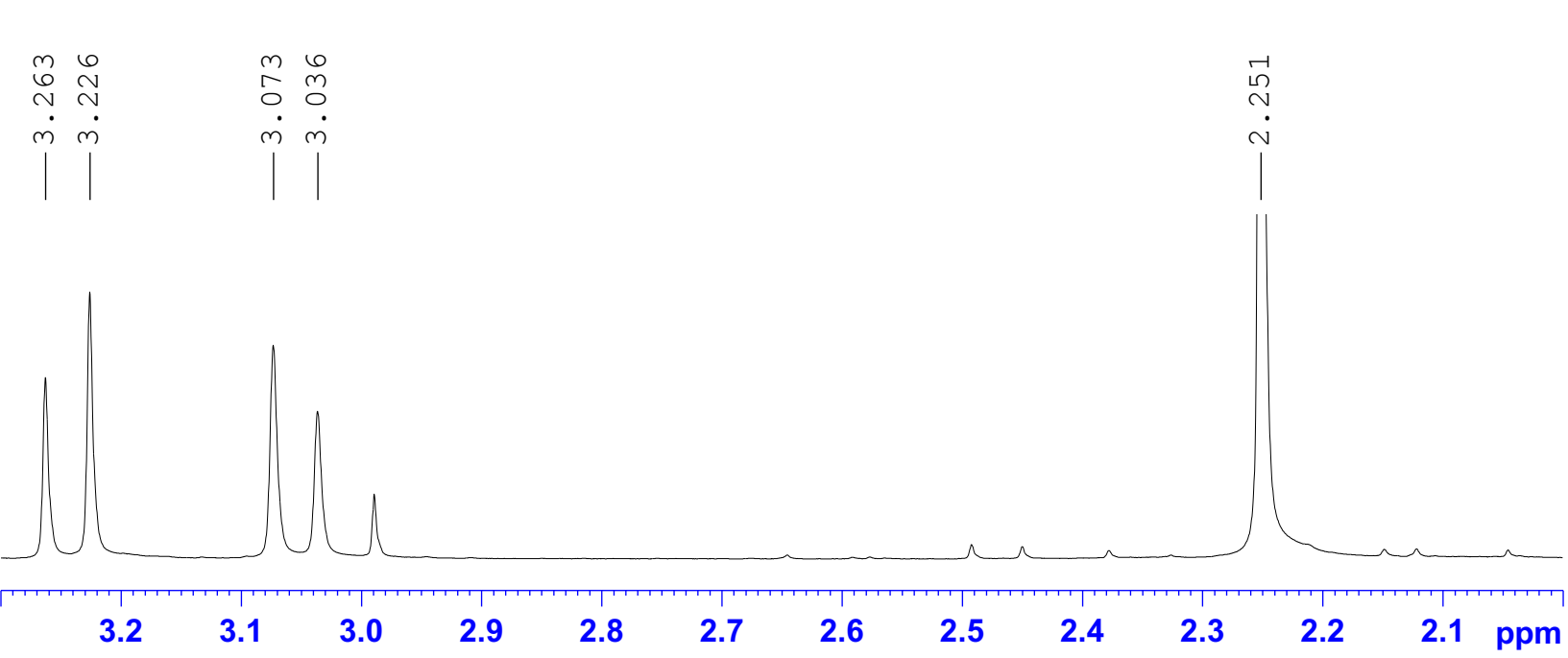
F2 - Acquisition Parameters  
Date\_ 20230316  
Time\_ 2.06 h  
INSTRUM Avance  
PROBHD z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.2 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300123 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

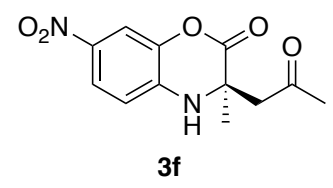


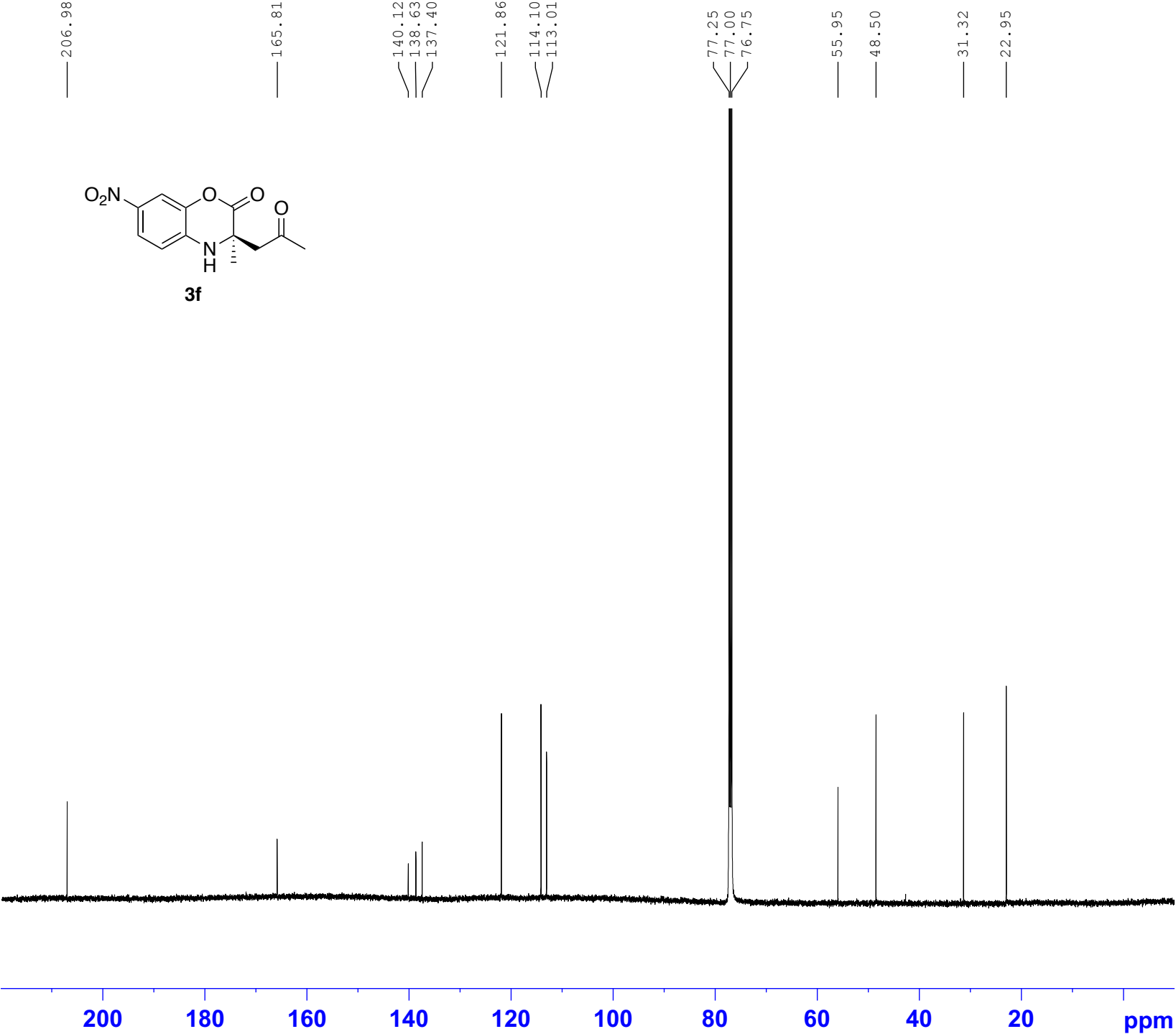
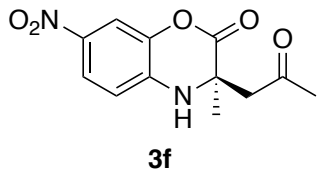
Current Data Parameters  
 NAME KLC-PhD281\_P4  
 EXPNO 20  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230316  
 Time\_ 2.06 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.2 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W



F2 - Processing parameters  
 SI 65536  
 SF 500.1300123 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

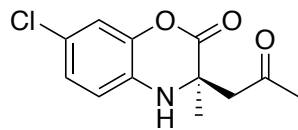




Current Data Parameters  
 NAME KLC-PhD281\_P4  
 EXPNO 21  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230316  
 Time\_ 4.20 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.0000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577916 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



**3g**

7.260  
7.009  
7.005  
6.983  
6.978  
6.966  
6.961  
6.716  
6.699

5.121

3.147  
3.111  
3.015  
2.979

2.216

1.572  
1.466

Current Data Parameters  
NAME KLC-PhD458\_P2  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters

Date 20230712  
Time 22.21 h  
INSTRUM Avance  
PROBHD Z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDC13  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

F2 - Processing parameters

SI 65536  
SF 500.1300000 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

10 9 8 7 6 5 4 3 2 1 0 ppm

1.00  
1.07  
1.03

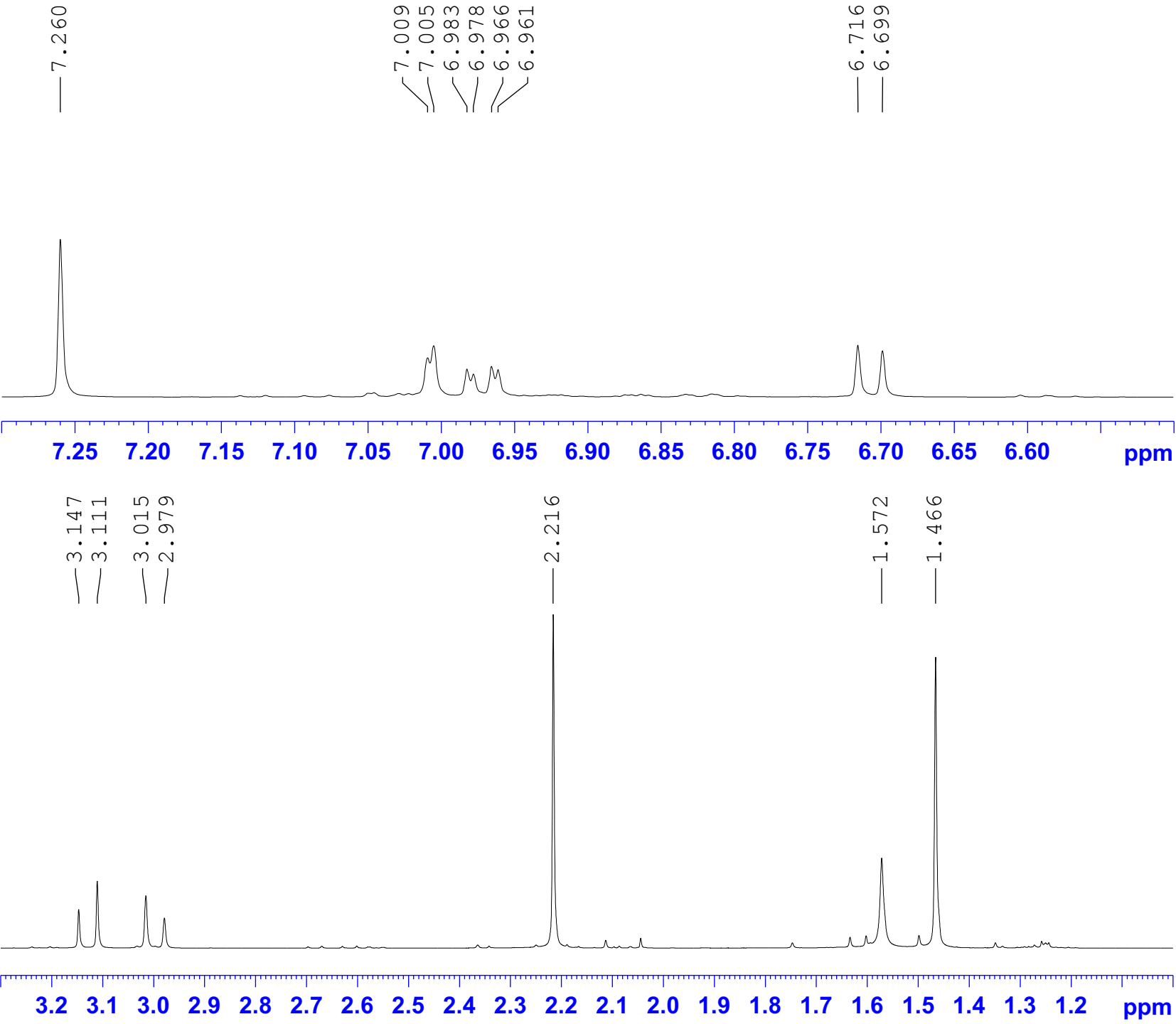
1.02

1.08  
1.09

3.12

3.31

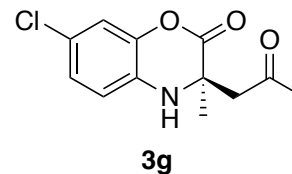


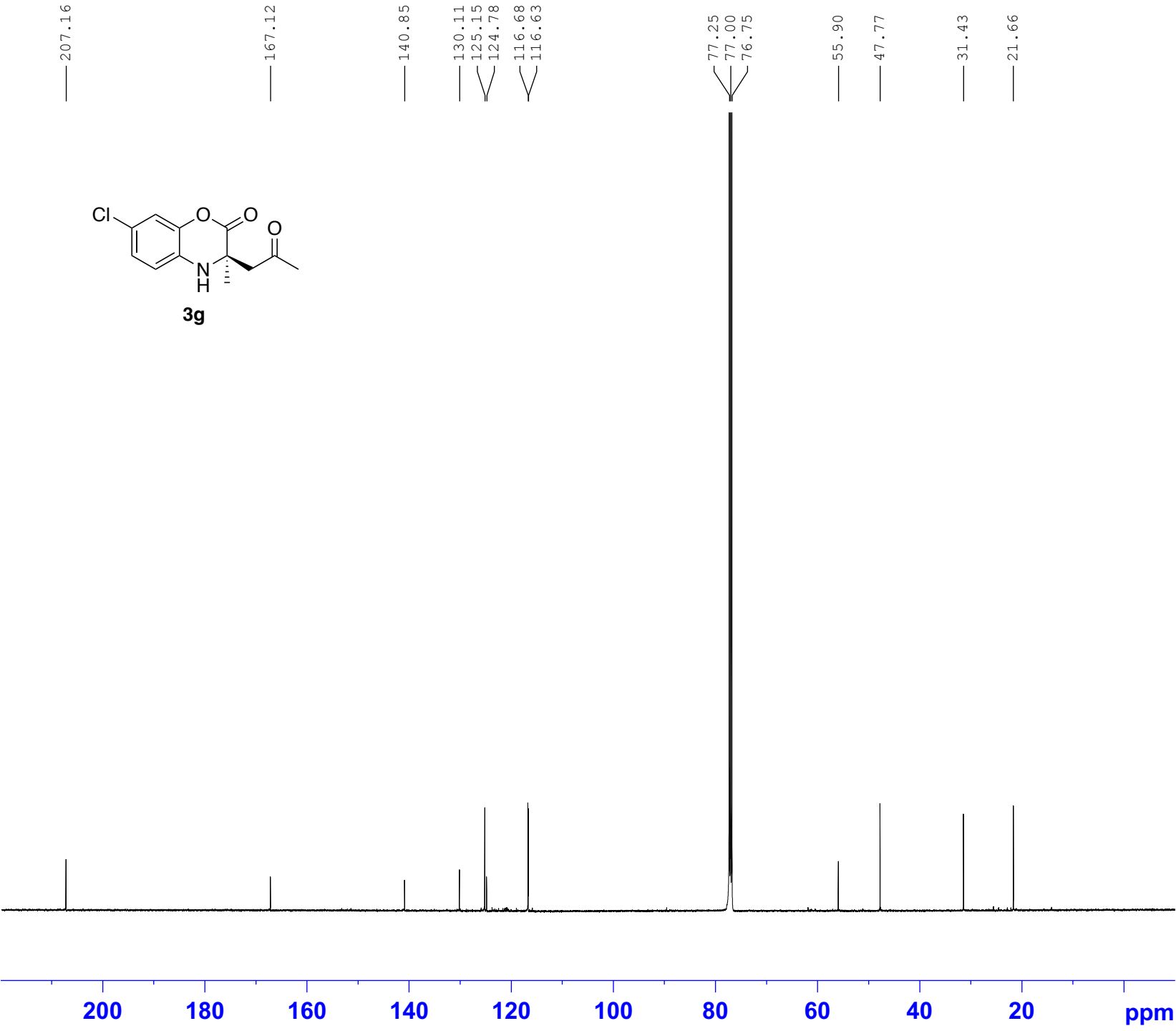
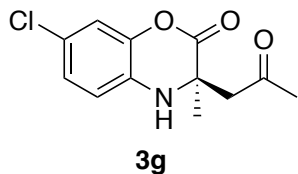


Current Data Parameters  
 NAME KLC-PhD458\_P2  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230712  
 Time\_ 22.21 h  
 INSTRUM Avance  
 PROBHD Z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.0000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.0302000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300126 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

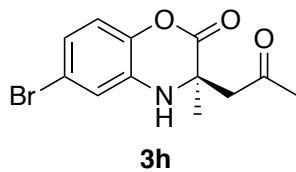




Current Data Parameters  
 NAME KLC-PhD458\_P2  
 EXPNO 11  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230712  
 Time\_ 23.17 h  
 INSTRUM Avance  
 PROBHD Z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577923 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



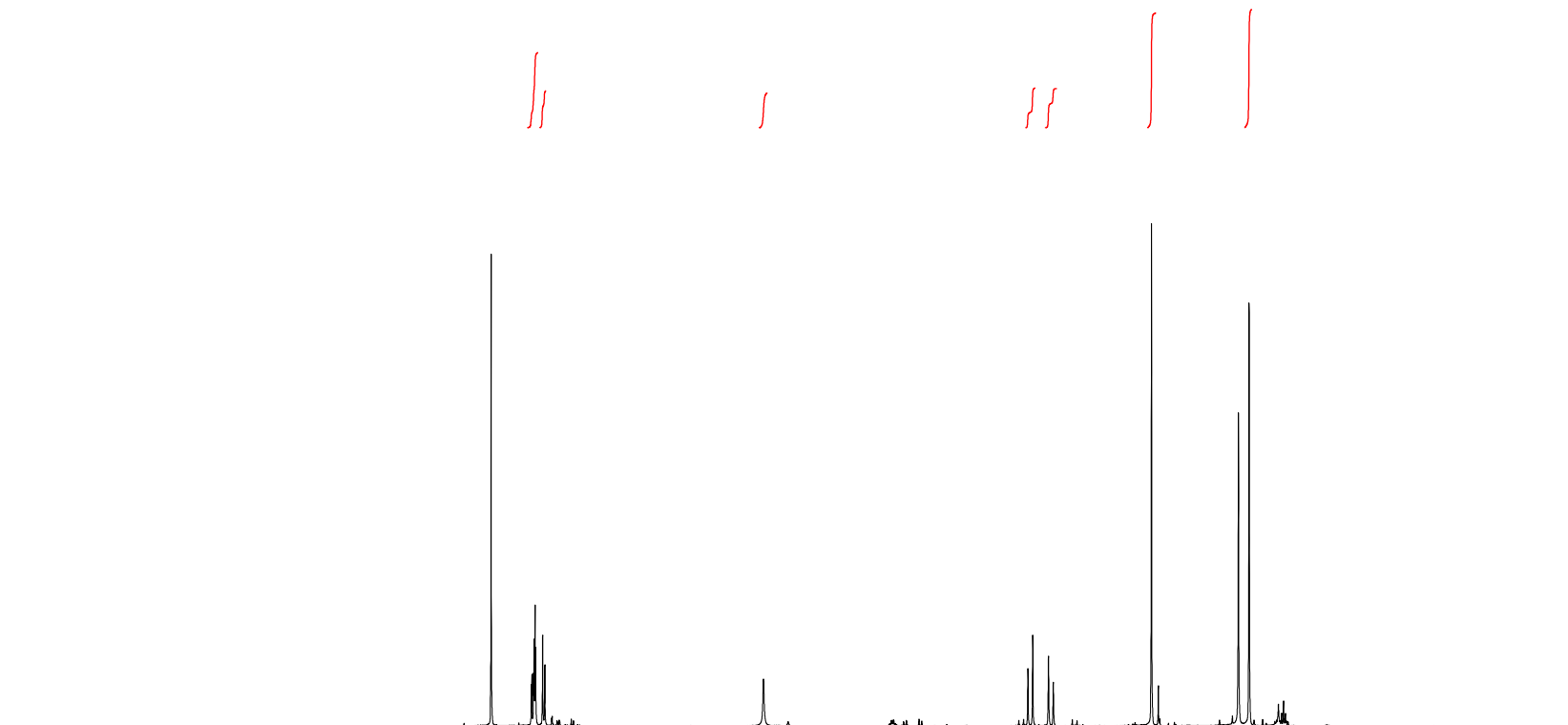
7.260  
6.954  
6.949  
6.937  
6.933  
6.925  
6.920  
6.867  
6.850

5.181

3.163  
3.126  
3.006  
2.969

2.220

1.556  
1.475



10 9 8 7 6 5 4 3 2 1 0 ppm

2.02  
1.00

0.95

1.07  
1.06

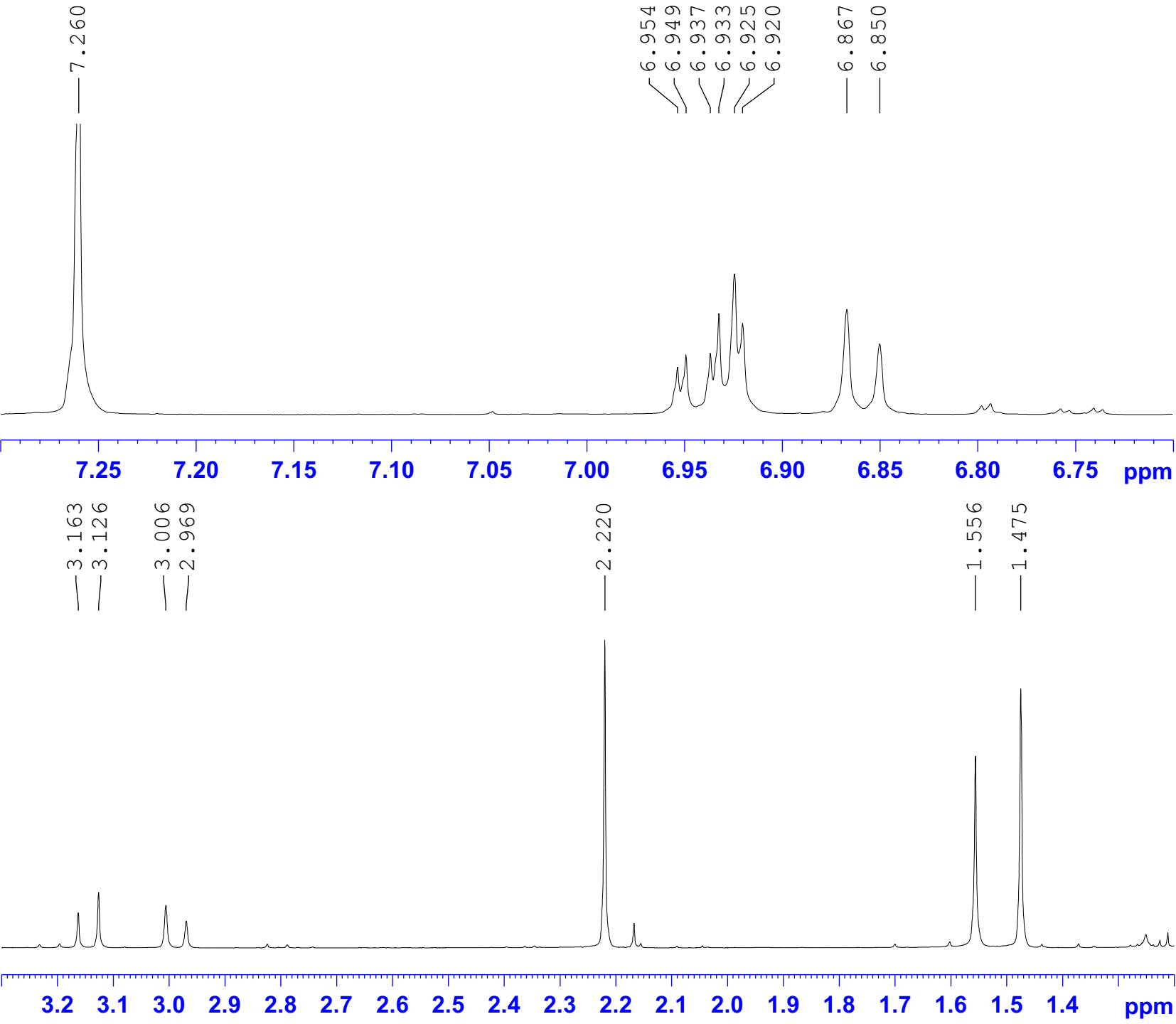
3.08

3.18

Current Data Parameters  
NAME KLC-PhD454\_P2  
EXPNO 32  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20230708  
Time\_ 23.13 h  
INSTRUM Avance  
PROBHD z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

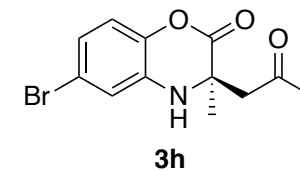
F2 - Processing parameters  
SI 65536  
SF 500.1300123 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

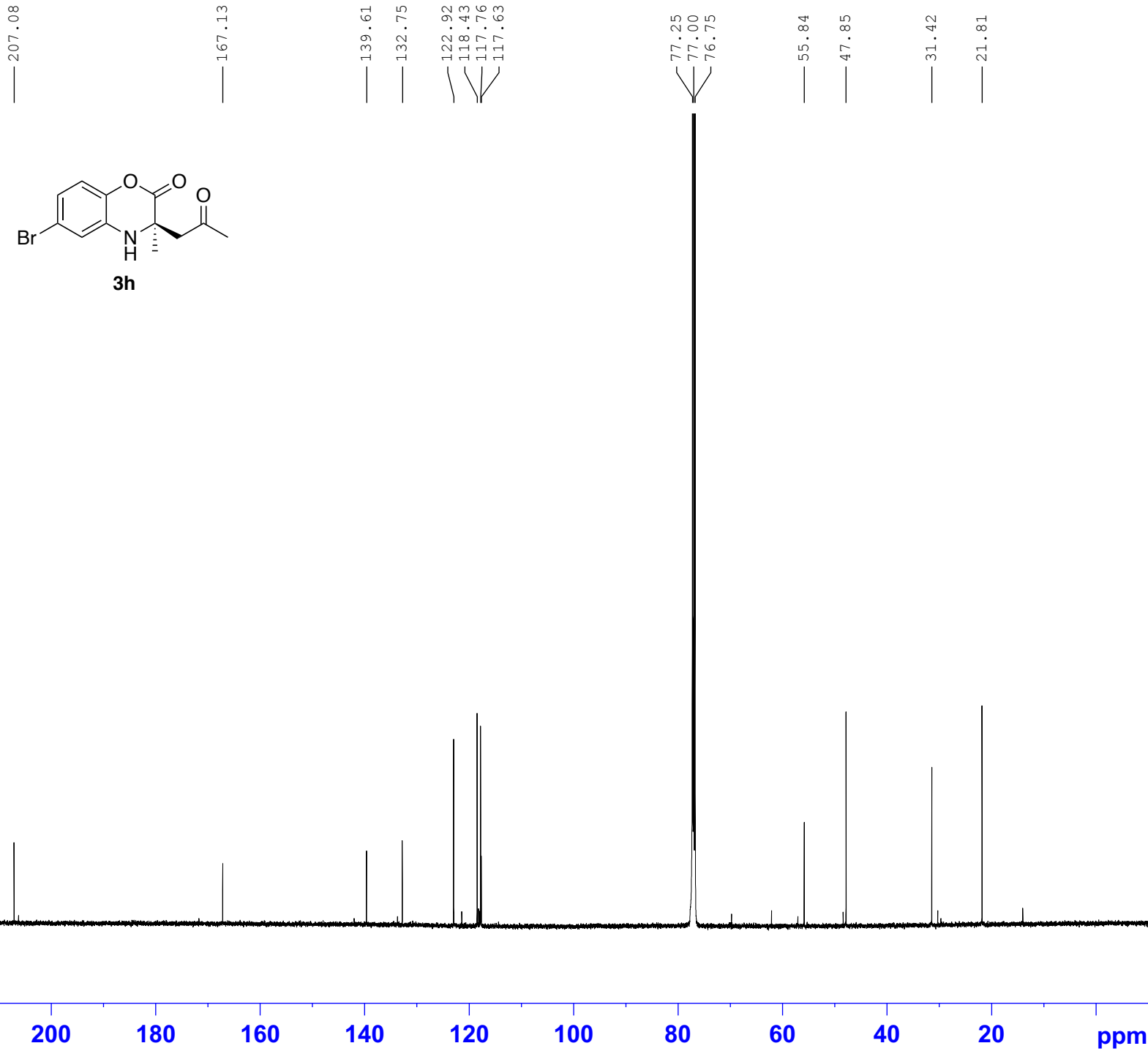
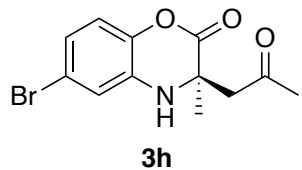


Current Data Parameters  
 NAME KLC-PhD454\_P2  
 EXPNO 32  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230708  
 Time\_ 23.13 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDC13  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300123 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

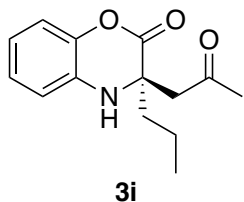




Current Data Parameters  
 NAME KLC-PhD454\_P2  
 EXPNO 33  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230709  
 Time\_ 0.07 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577920 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

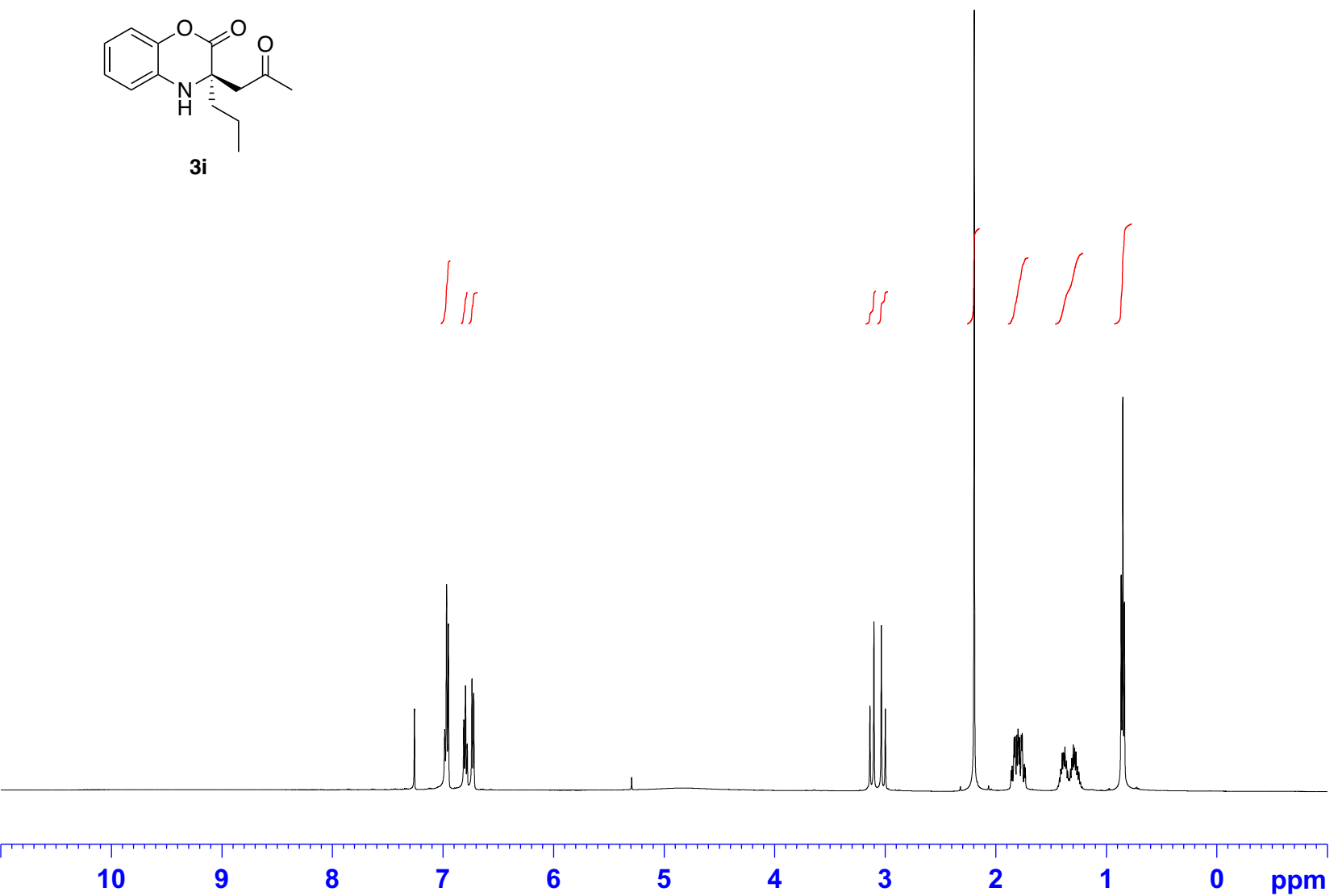


7.260  
6.986  
6.970  
6.953  
6.813  
6.798  
6.782  
6.739  
6.724  
3.140  
3.103  
3.036  
3.000  
2.196  
1.863  
1.852  
1.835  
1.825  
1.811  
1.800  
1.796  
1.785  
1.771  
1.762  
1.743  
1.734  
1.426  
1.415  
1.400  
1.389  
1.376  
1.361  
1.351  
1.337  
1.326

Current Data Parameters  
NAME KLC-PhD093\_P4-1  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20220328  
Time\_ 13.17 h  
INSTRUM Avance  
PROBHD Z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDC13  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 7.81300020 W

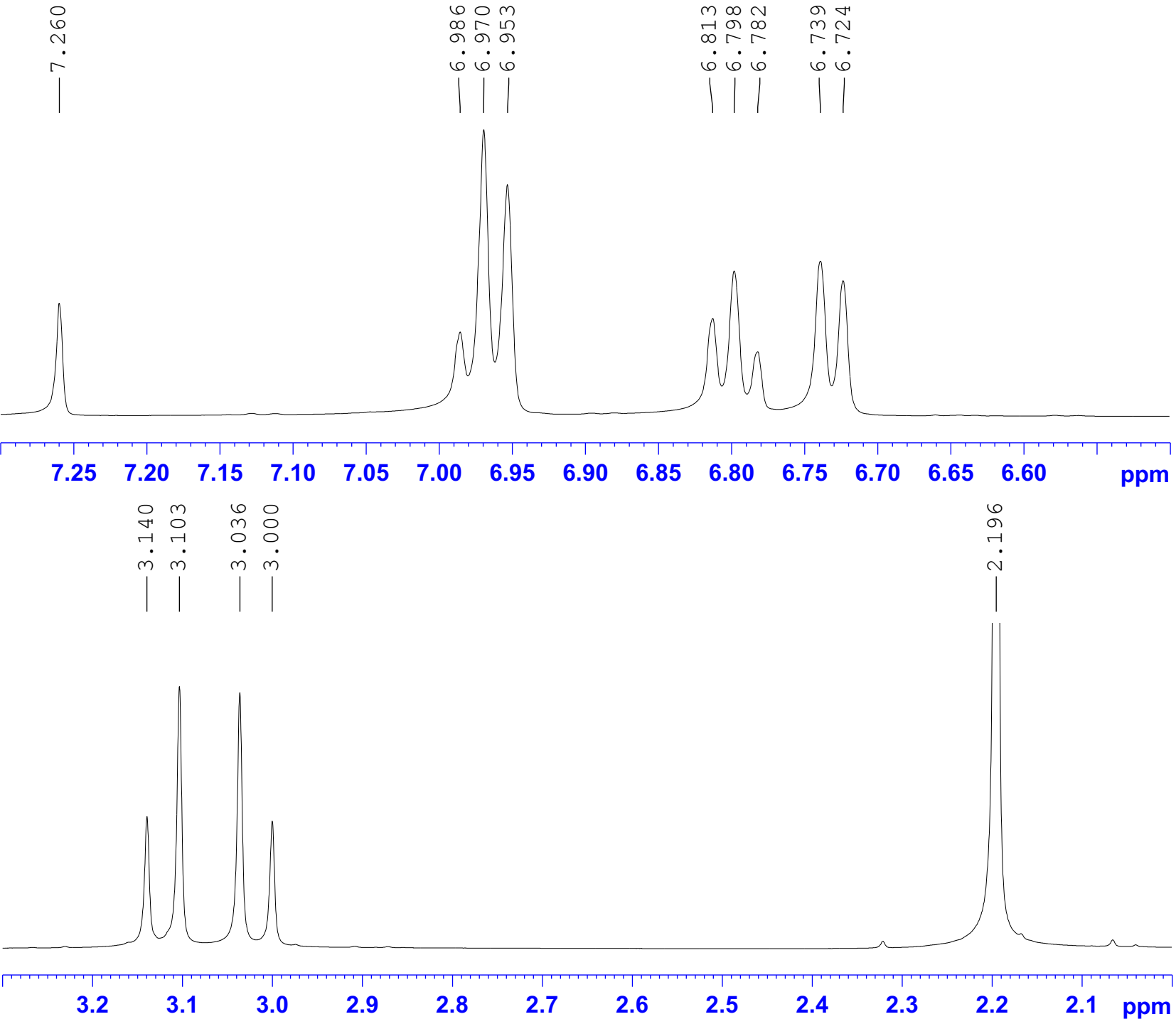
F2 - Processing parameters  
SI 65536  
SF 500.1300124 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00



2.03  
1.03  
1.01

1.06  
1.04

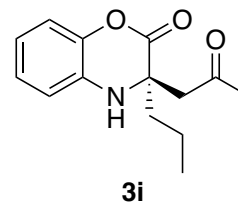
3.07  
2.13  
2.27  
3.22

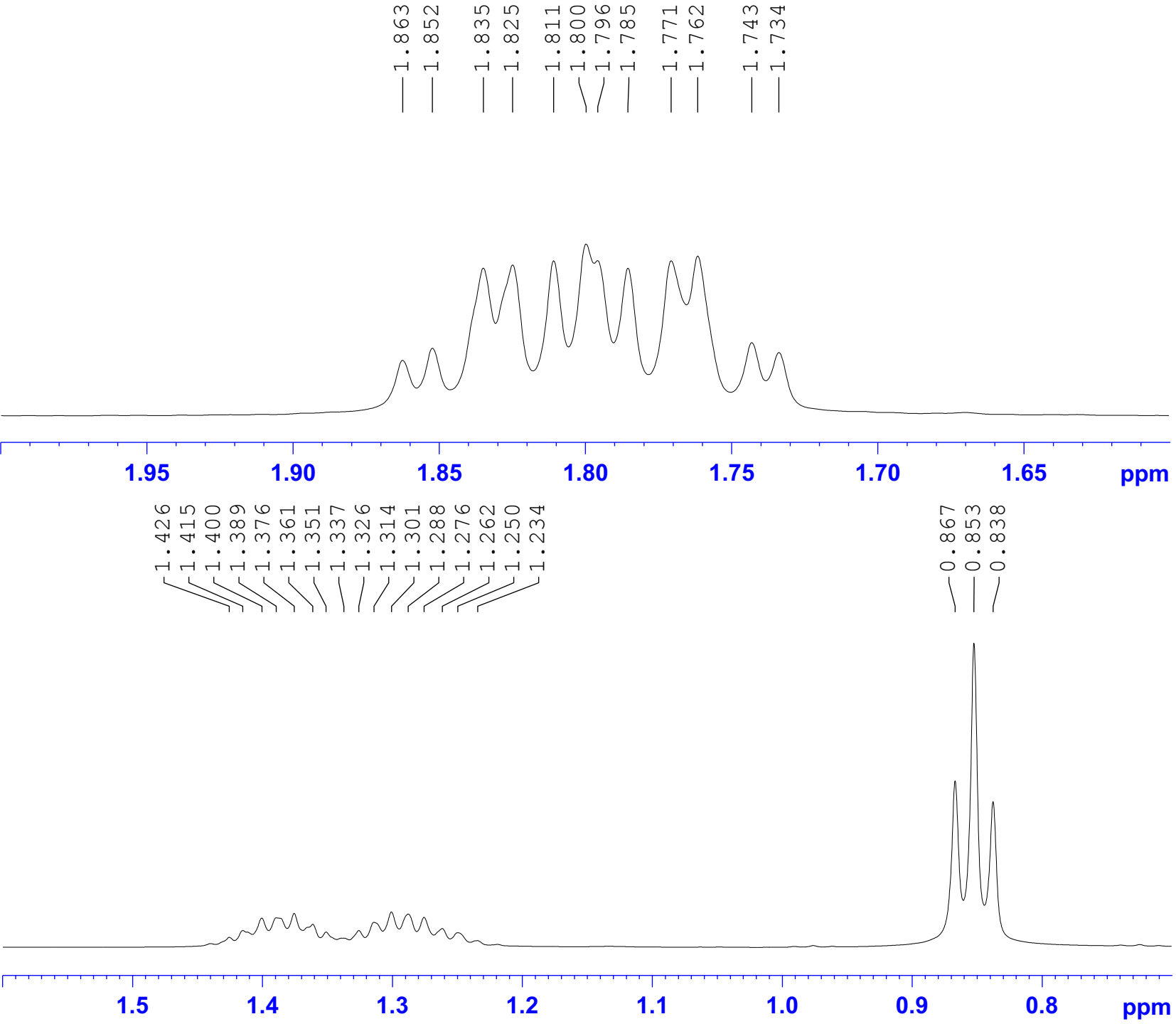


Current Data Parameters  
 NAME KLC-Phd093\_P4-1  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20220328  
 Time\_ 13.17 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 7.81300020 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300124 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00

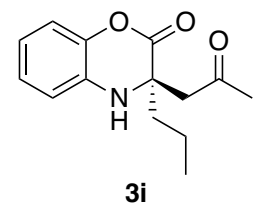




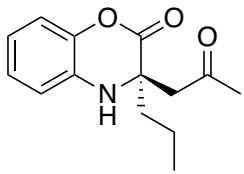
Current Data Parameters  
 NAME KLC-PhD093\_P4-1  
 EXPNO 10  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20220328  
 Time\_ 13.17 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 7.81300020 W

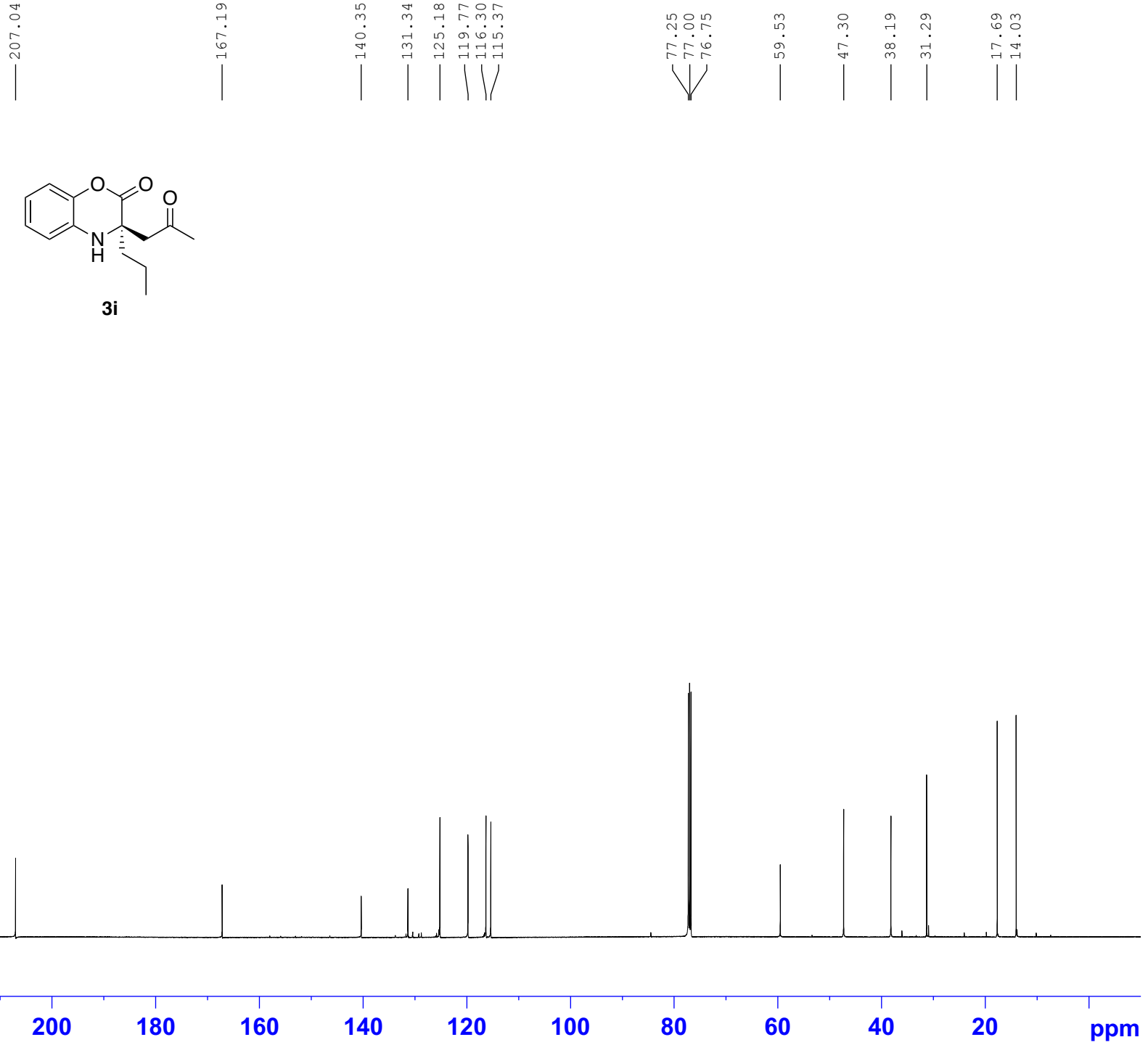
F2 - Processing parameters  
 SI 65536  
 SF 500.1300124 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00







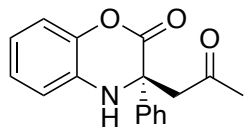
**3i**



Current Data Parameters  
 NAME KLC-Phd093\_P4-1  
 EXPNO 21  
 PROCNO 1

F2 - Acquisition Parameters  
 Date 20220328  
 Time 22.58 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDC13  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.0000000 sec  
 D11 0.0300000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.18899918 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 7.81300020 W  
 PLW12 0.17579000 W  
 PLW13 0.08842200 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577933 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

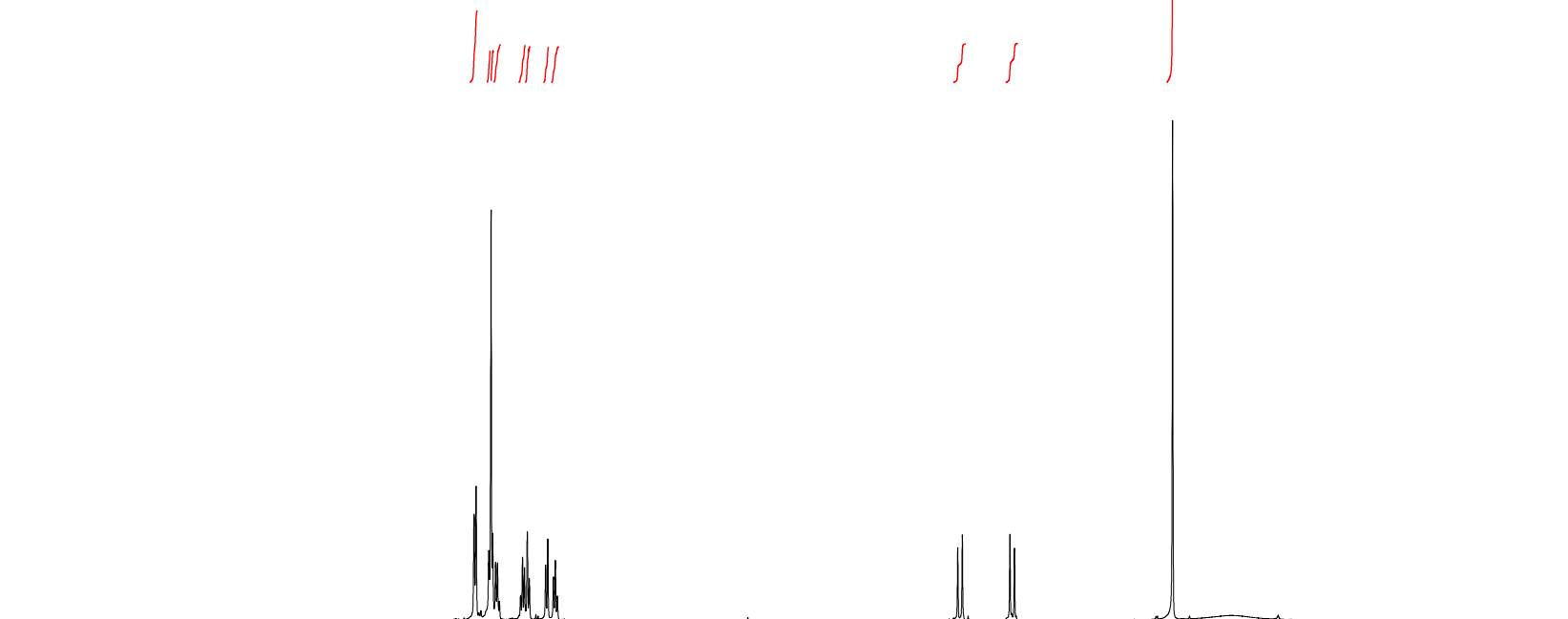


**3j**

7.390  
7.375  
7.278  
7.260  
7.248  
7.226  
7.211  
7.197  
7.035  
7.020  
7.005  
6.983  
6.969  
6.843  
6.827  
6.784  
6.769  
6.755

3.698  
3.663  
3.299  
3.264

2.057



10 9 8 7 6 5 4 3 2 1 0 ppm

2.02  
1.20  
0.92  
1.06  
1.06  
1.01  
1.00  
1.00

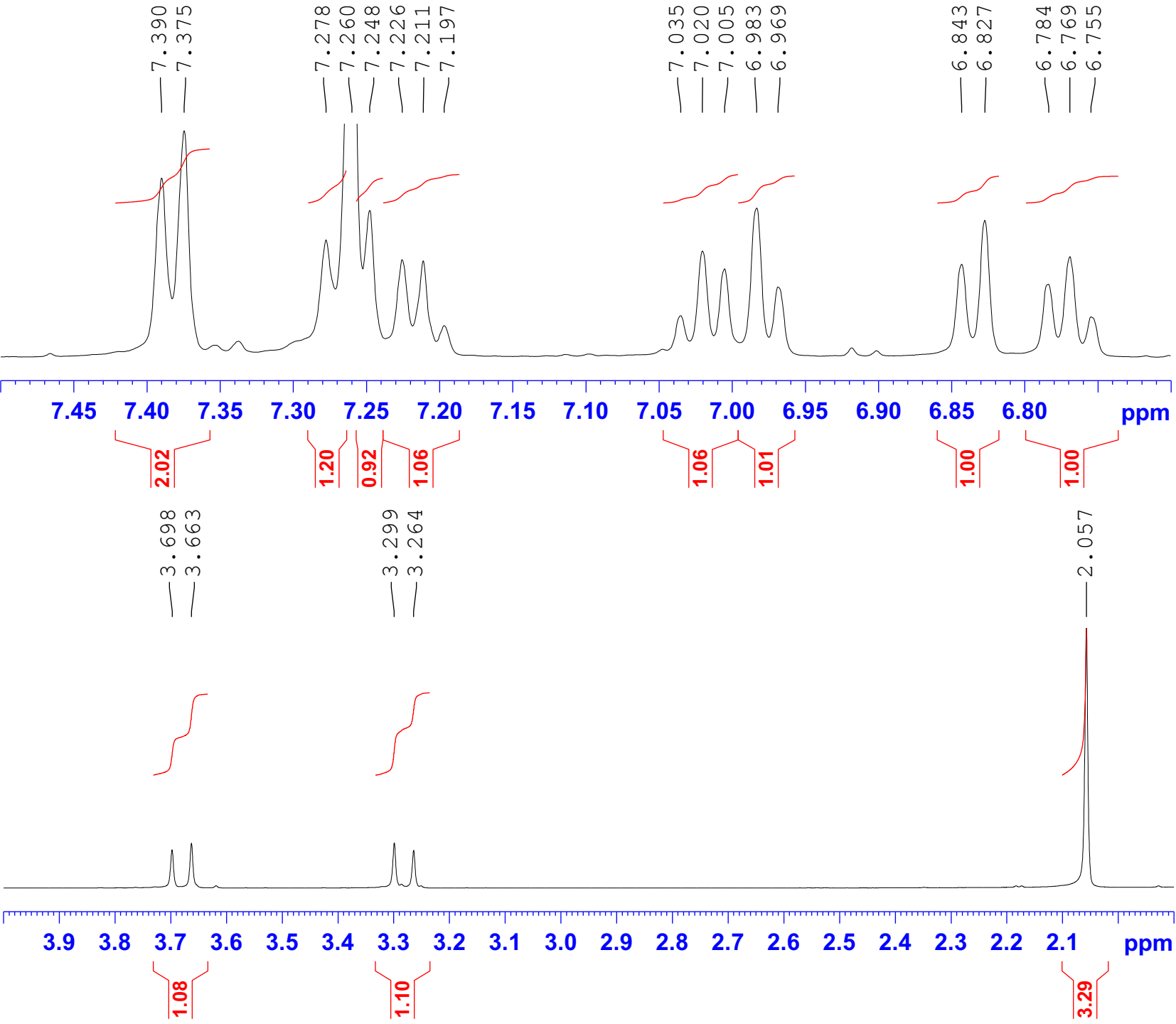
1.08  
1.10

3.29

Current Data Parameters  
NAME KLC-Phd099\_P2  
EXPNO 10  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20220408  
Time\_ 6.08 h  
INSTRUM Avance  
PROBHD Z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDC13  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.25 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 3.90 usec  
P1 11.70 usec  
PLW1 8.00000000 W

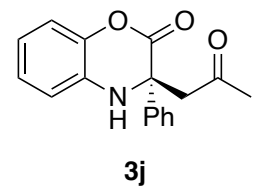
F2 - Processing parameters  
SI 65536  
SF 500.1300128 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

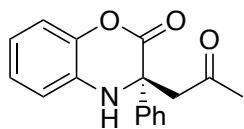


Current Data Parameters  
 NAME KLC-PhD099\_P2  
 EXPNO 10  
 PROCNO 1

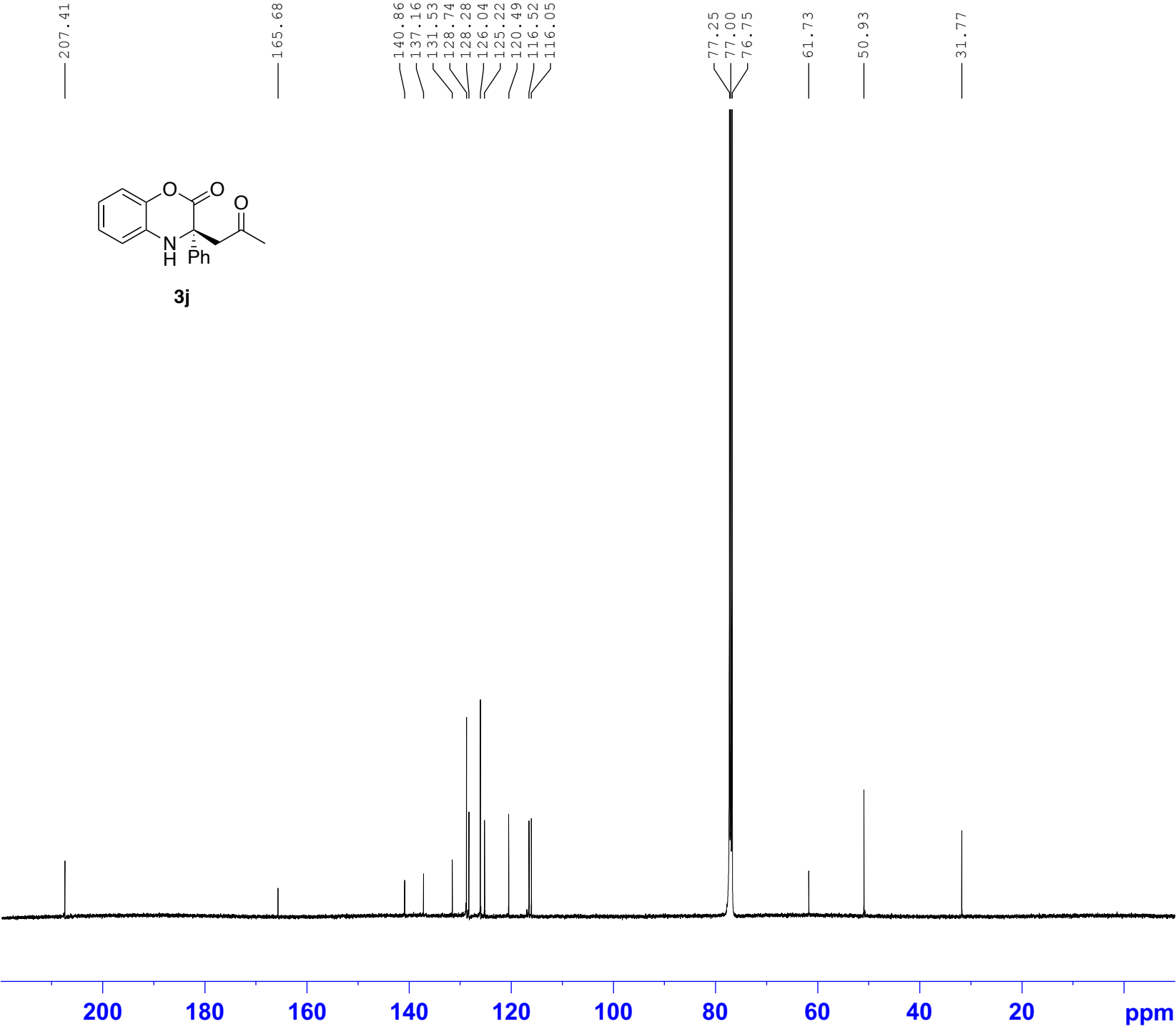
F2 - Acquisition Parameters  
 Date\_ 20220408  
 Time\_ 6.08 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (   
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.25 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 3.90 usec  
 P1 11.70 usec  
 PLW1 8.00000000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300128 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00





**3j**

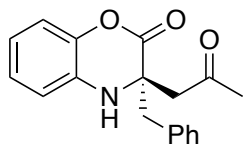


Current Data Parameters  
 NAME KLC-PhD099\_P2  
 EXPNO 11  
 PROCNO 1

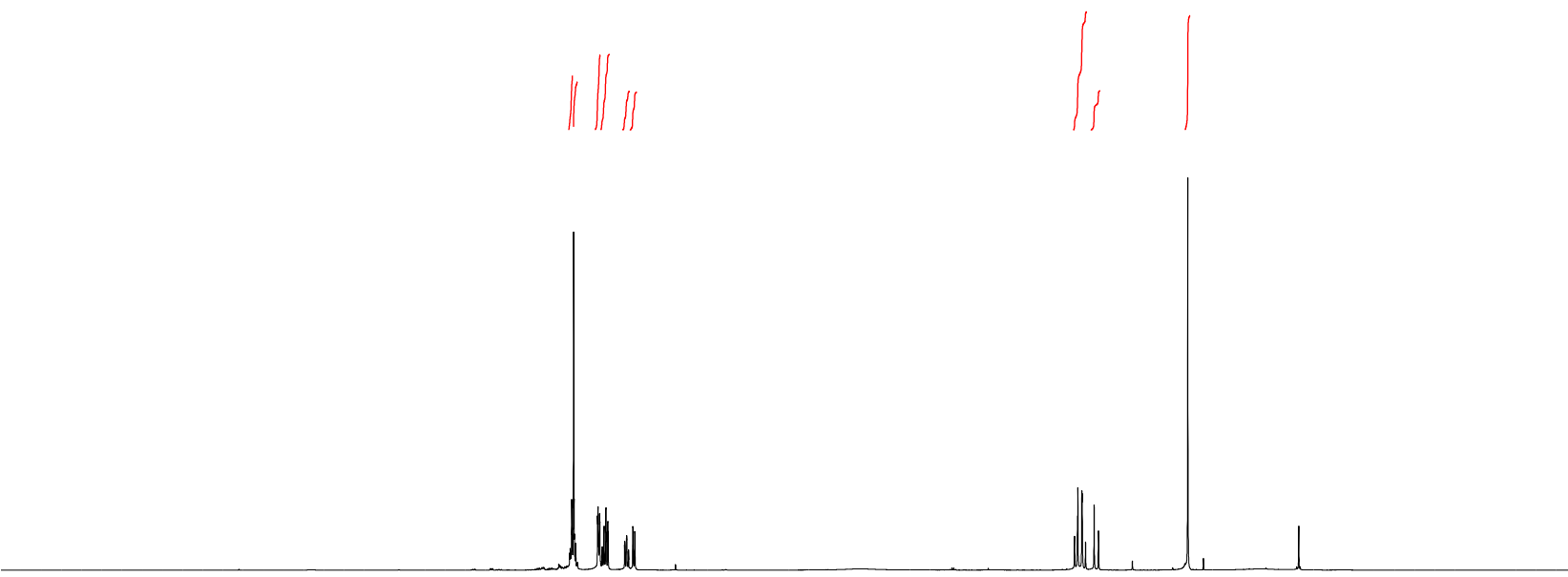
F2 - Acquisition Parameters  
 Date\_ 20220408  
 Time\_ 7.03 h  
 INSTRUM Avance  
 PROBHD Z167889\_0002 (  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDC13  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.2 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.00 usec  
 P1 9.00 usec  
 PLW1 39.00000000 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.00000000 W  
 PLW12 0.17111000 W  
 PLW13 0.08606800 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577934 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

7.294  
7.289  
7.276  
7.273  
7.265  
7.260  
7.257  
7.253  
7.244  
7.243  
7.062  
7.058  
7.046  
7.043  
7.026  
7.023  
7.011  
7.008  
6.993  
6.991  
6.978  
6.975  
6.839  
6.836  
6.823  
6.821  
6.808  
6.805  
6.771  
6.768  
6.755  
6.752  
3.113  
3.089  
3.086  
3.053  
3.050  
3.022  
2.951  
2.915  
2.175



**3k**



1.67  
1.29  
2.00  
2.00  
1.04  
1.00

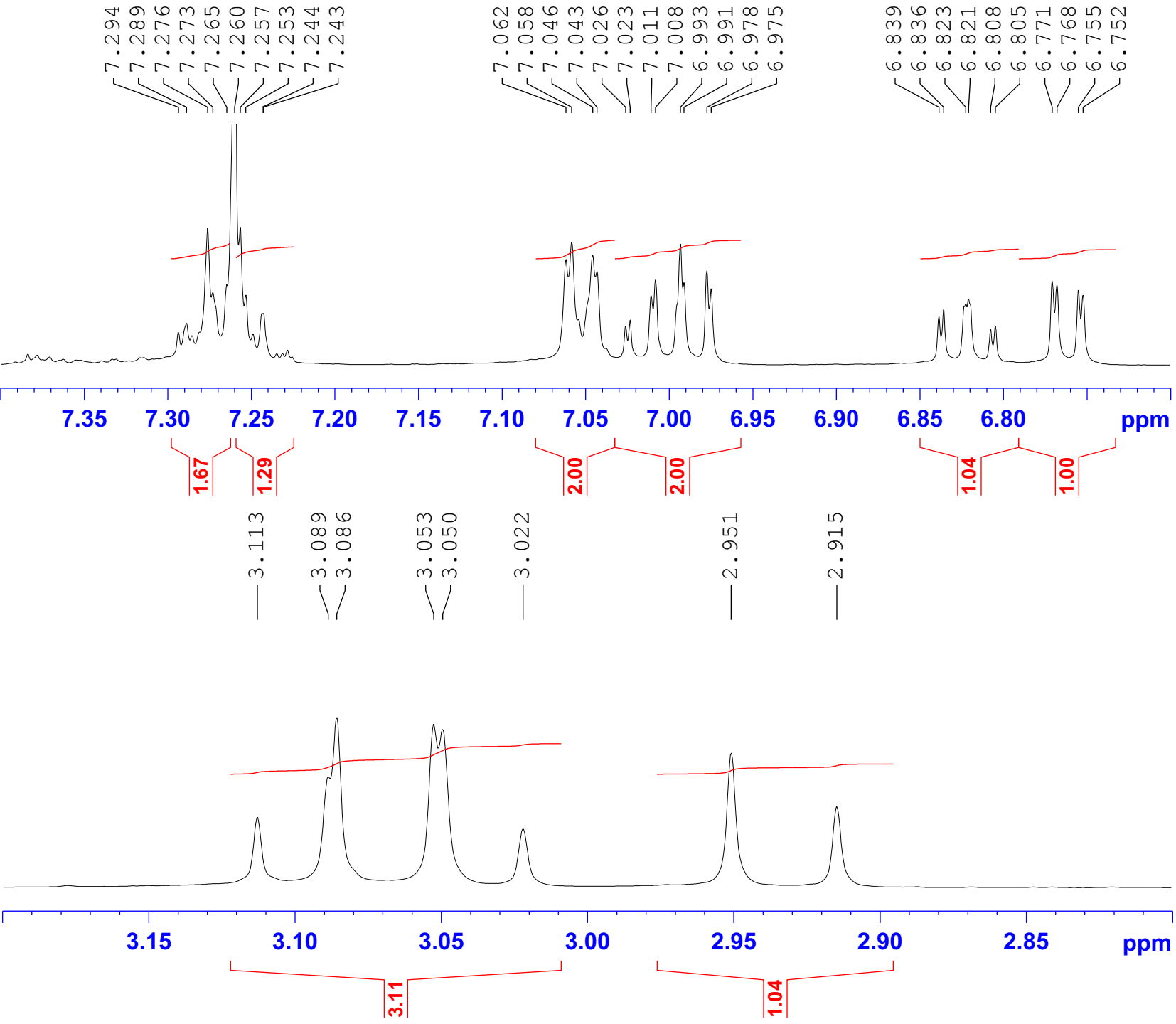
3.11  
1.04  
3.02

Current Data Parameters  
NAME KLC-PhD274\_P4  
EXPNO 11  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20230315  
Time\_ 23.17 h  
INSTRUM Avance  
PROBHD Z167889\_0002 (  
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.20 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.00 usec  
P1 12.00 usec  
PLW1 8.03020000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300129 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

11 10 9 8 7 6 5 4 3 2 1 0 ppm



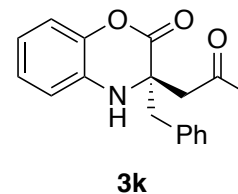
Current Data Parameters  
 NAME KLC-PhD274\_P4  
 EXPNO 11  
 PROCNO 1

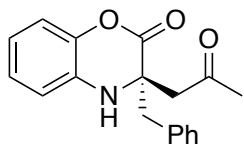
F2 - Acquisition Parameters

Date\_ 20230315  
 Time\_ 23.17 h  
 INSTRUM Avance  
 PROBHD Z167889\_0002 (  
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.20 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.00 usec  
 P1 12.00 usec  
 PLW1 8.03020000 W

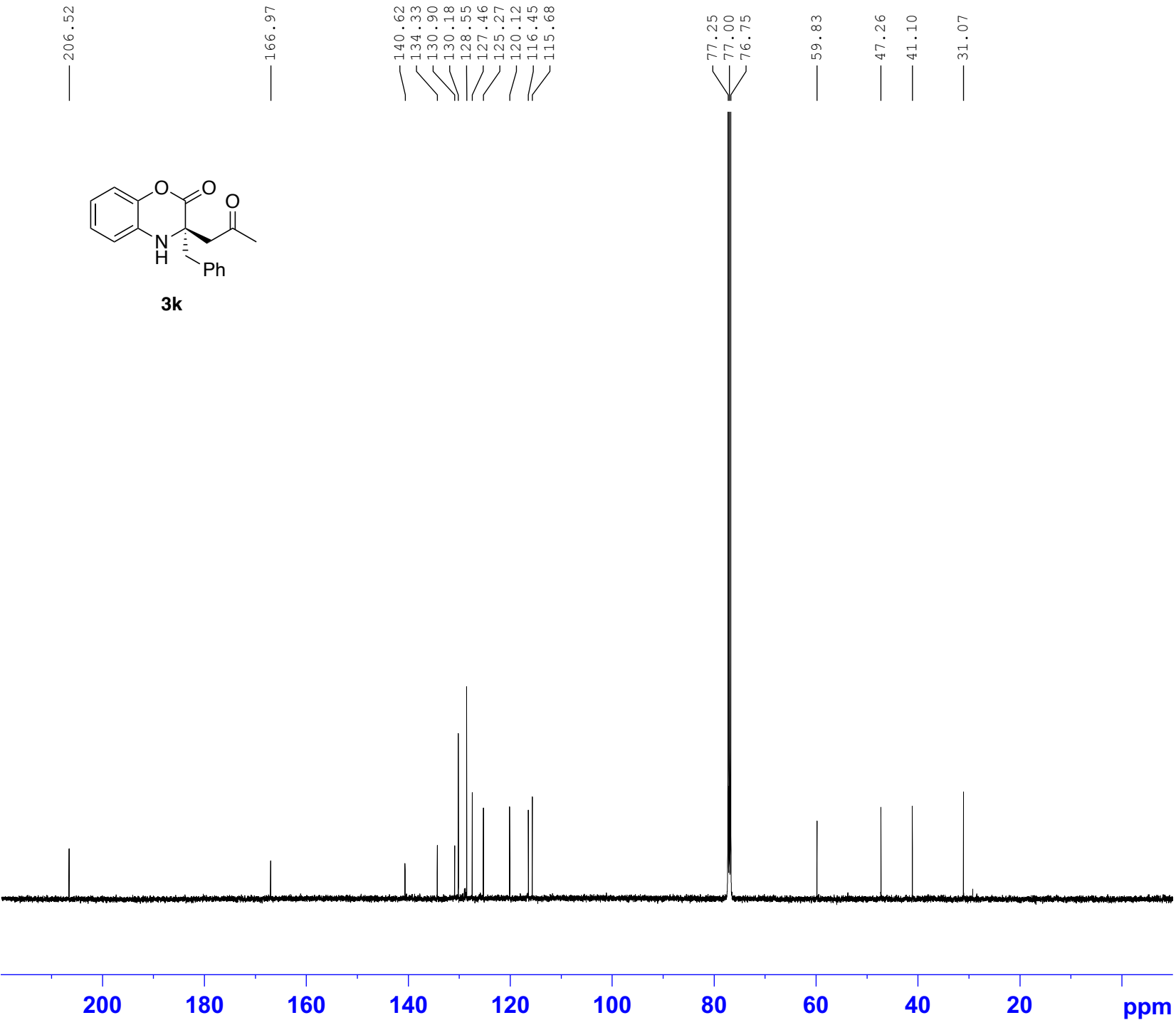
F2 - Processing parameters

SI 65536  
 SF 500.1300129 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00





**3k**

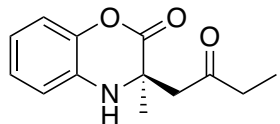


Current Data Parameters  
 NAME KLC-PhD274\_P4  
 EXPNO 13  
 PROCNO 1

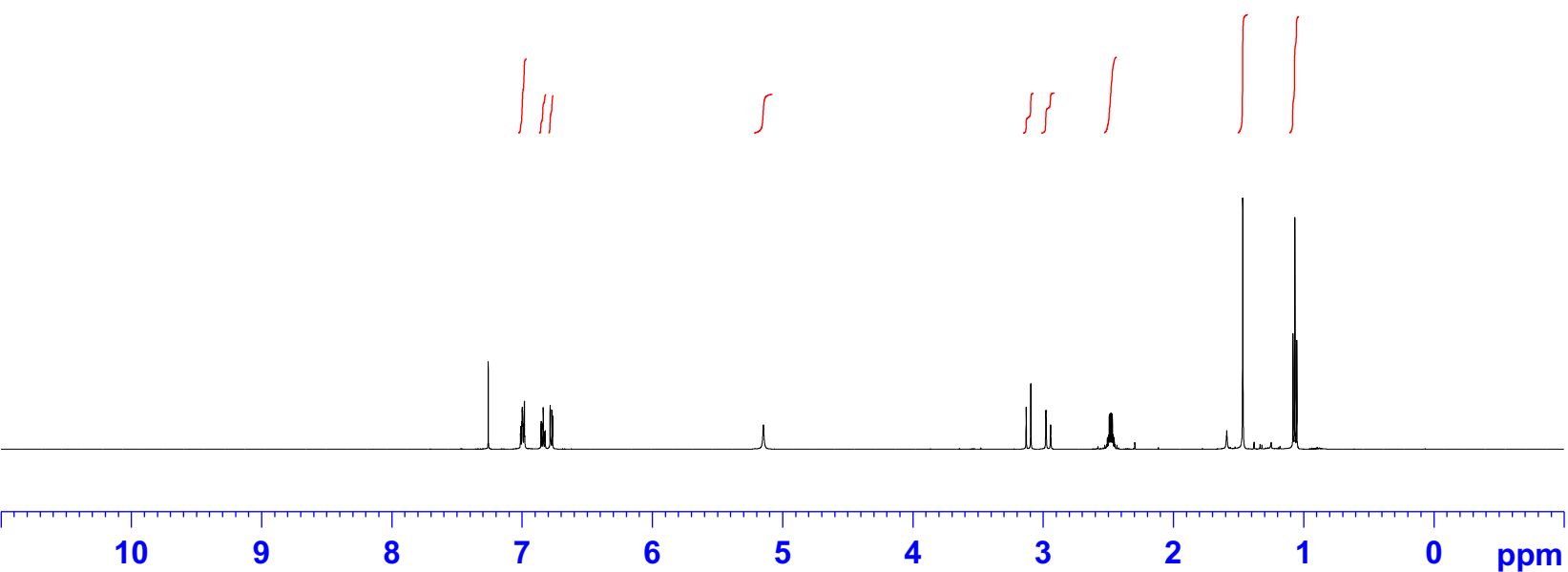
F2 - Acquisition Parameters  
 Date\_ 20230315  
 Time\_ 23.49 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 ( )  
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 86  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 3.33 usec  
 P1 10.00 usec  
 PLW1 28.94899940 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.03020000 W  
 PLW12 0.18068001 W  
 PLW13 0.09088100 W

F2 - Processing parameters  
 SI 32768  
 SF 125.7577924 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40

7.260  
7.013  
7.010  
7.002  
6.998  
6.997  
6.995  
6.986  
6.983  
6.982  
6.979  
6.855  
6.853  
6.841  
6.839  
6.837  
6.825  
6.822  
6.785  
6.782  
6.769  
6.766  
5.147  
3.130  
3.094  
2.978  
2.977  
2.942  
2.941  
2.506  
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2.491  
2.483  
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2.454  
1.467  
1.466  
1.081  
1.066  
1.051



**3I**

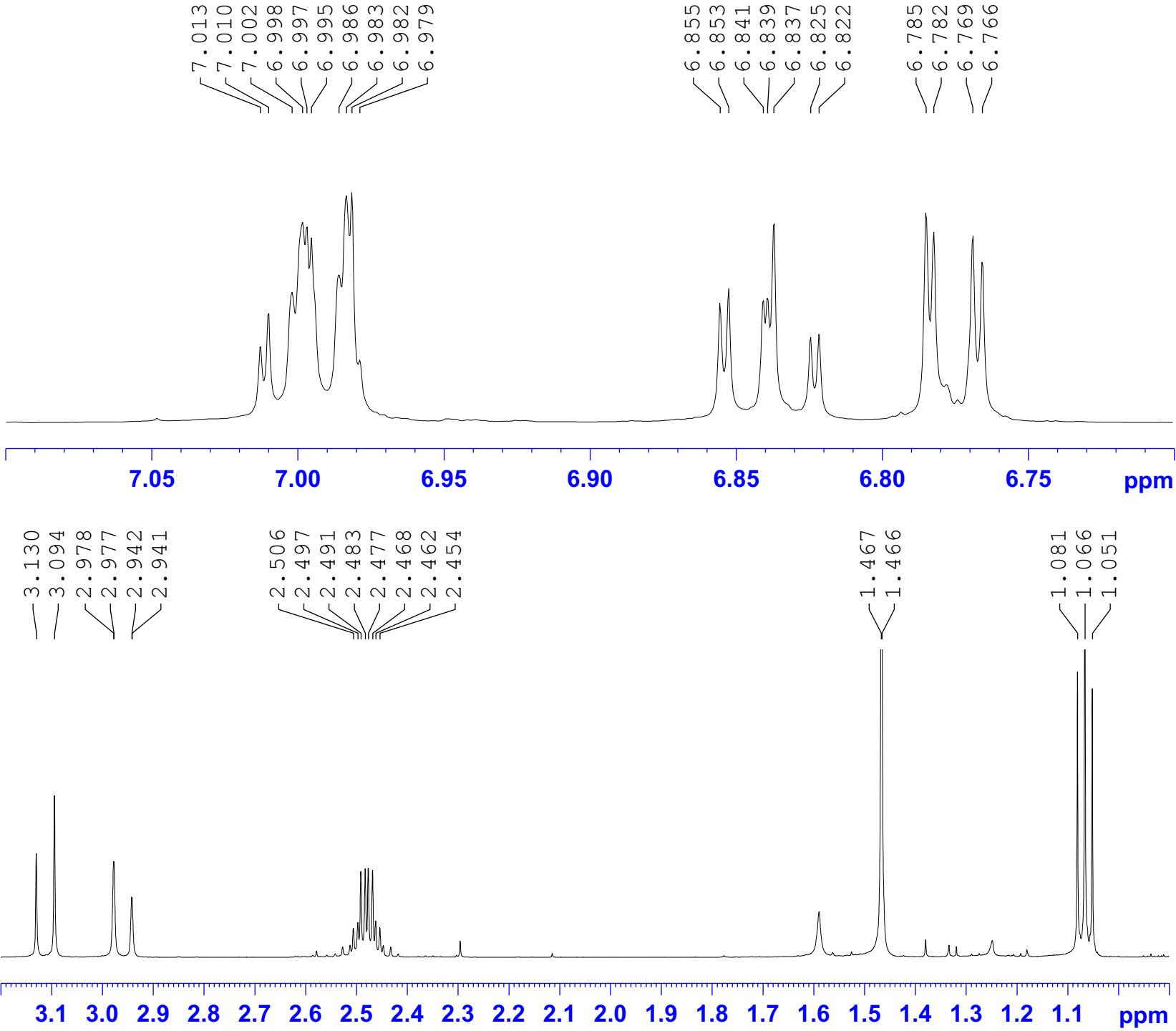


Current Data Parameters  
NAME KLC-Phd254\_P2  
EXPNO 11  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20230218  
Time\_ 22.08 h  
INSTRUM Avance  
PROBHD Z167889\_0002 (   
PULPROG zg30  
TD 65536  
SOLVENT CDCl3  
NS 16  
DS 2  
SWH 10000.000 Hz  
FIDRES 0.305176 Hz  
AQ 3.2767999 sec  
RG 101  
DW 50.000 usec  
DE 54.15 usec  
TE 298.1 K  
D1 1.00000000 sec  
TD0 1  
SFO1 500.1330883 MHz  
NUC1 1H  
P0 4.10 usec  
P1 12.30 usec  
PLW1 8.00000000 W

F2 - Processing parameters  
SI 65536  
SF 500.1300125 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

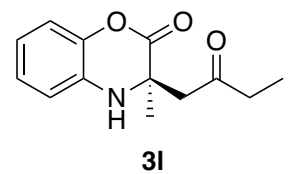




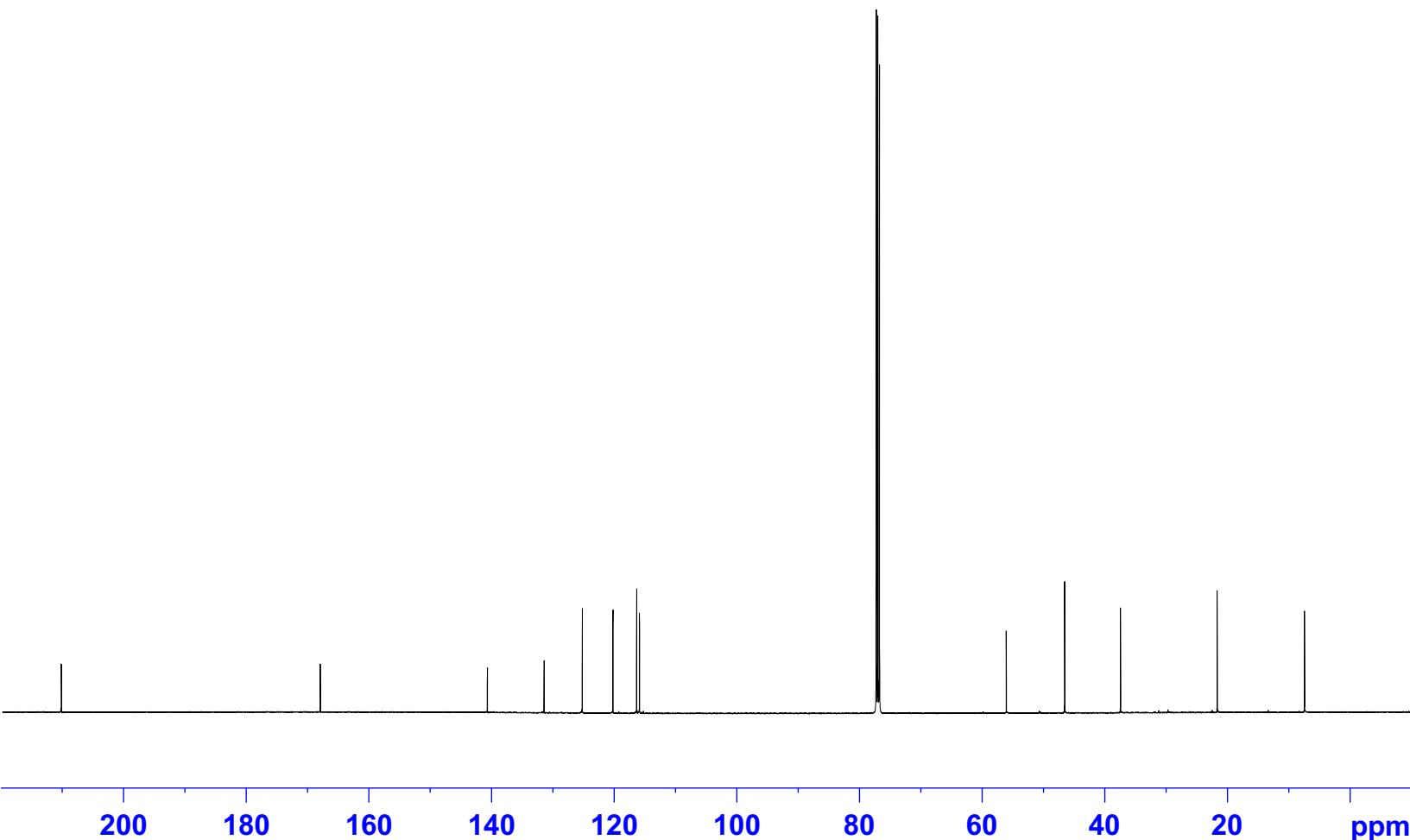
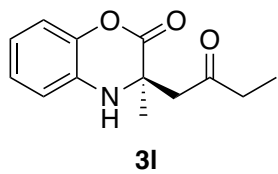
Current Data Parameters  
 NAME KLC-PhD254\_P2  
 EXPNO 11  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230218  
 Time\_ 22.08 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (   
 PULPROG zg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 16  
 DS 2  
 SWH 10000.000 Hz  
 FIDRES 0.305176 Hz  
 AQ 3.2767999 sec  
 RG 101  
 DW 50.000 usec  
 DE 54.15 usec  
 TE 298.1 K  
 D1 1.00000000 sec  
 TD0 1  
 SFO1 500.1330883 MHz  
 NUC1 1H  
 P0 4.10 usec  
 P1 12.30 usec  
 PLW1 8.00000000 W

F2 - Processing parameters  
 SI 65536  
 SF 500.1300125 MHz  
 WDW EM  
 SSB 0  
 LB 0.30 Hz  
 GB 0  
 PC 1.00



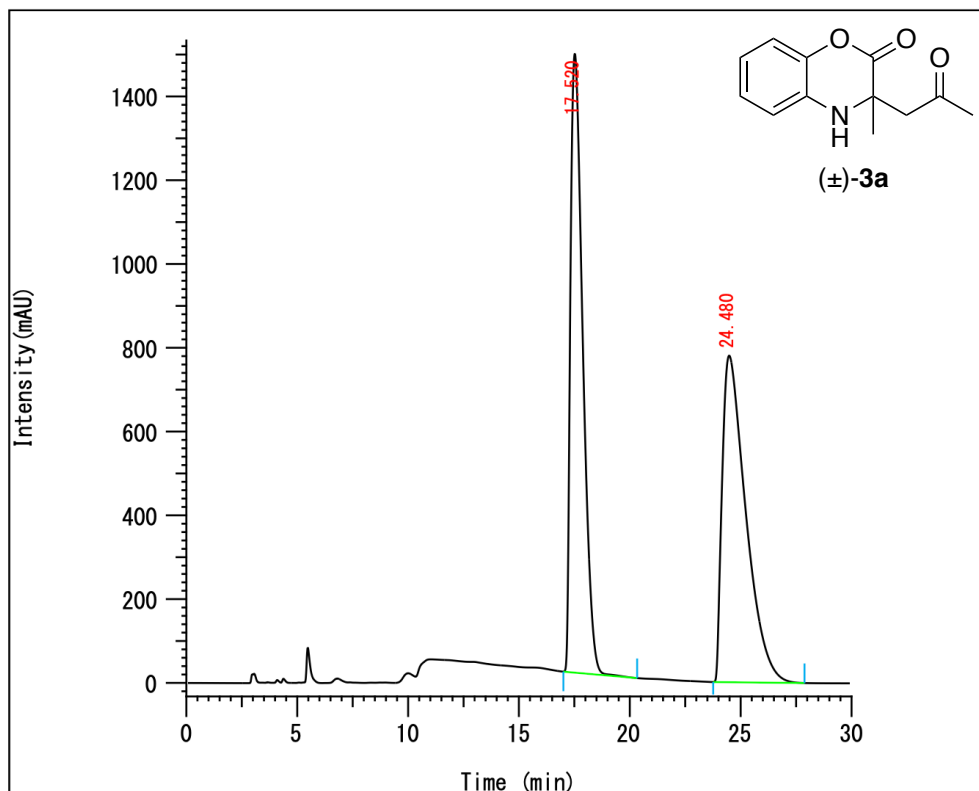
— 210.15 — 167.93 — 140.69 — 131.43 — 125.21 — 120.21 — 116.34 — 115.87 — 77.25 — 77.00 — 76.75 — 56.05 — 46.54 — 37.43 — 21.67 — 7.43



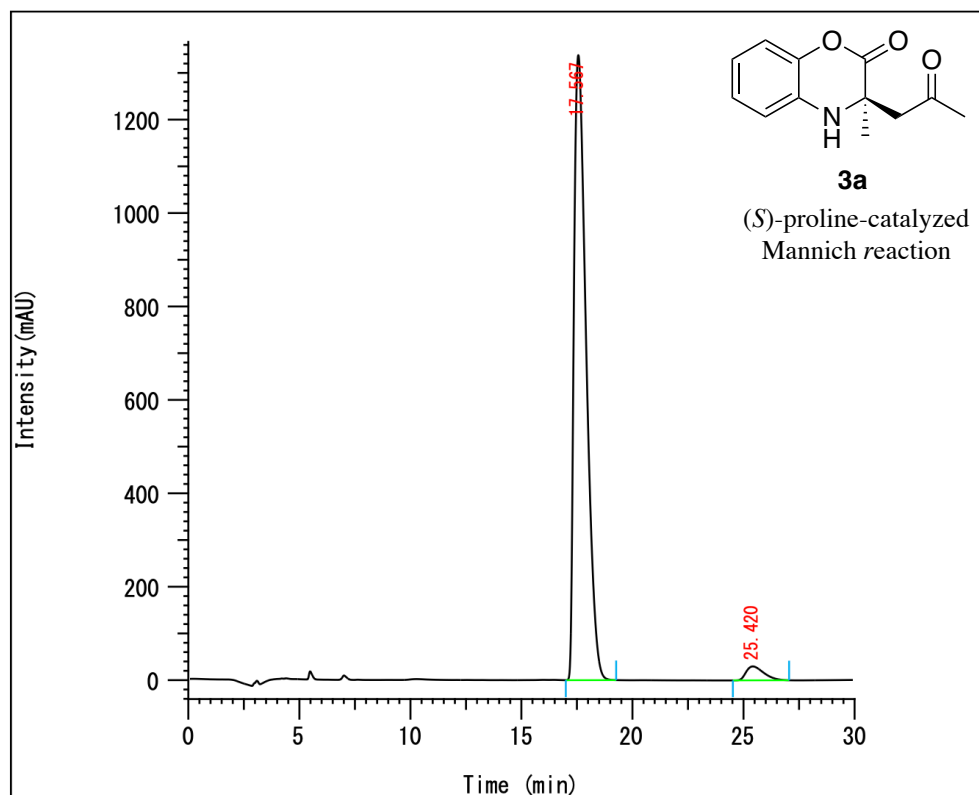
Current Data Parameters  
 NAME KLC-PhD254\_P2  
 EXPNO 12  
 PROCNO 1

F2 - Acquisition Parameters  
 Date\_ 20230218  
 Time\_ 23.04 h  
 INSTRUM Avance  
 PROBHD z167889\_0002 (   
 PULPROG zgpg30  
 TD 65536  
 SOLVENT CDCl3  
 NS 1024  
 DS 4  
 SWH 30120.482 Hz  
 FIDRES 0.919204 Hz  
 AQ 1.0878977 sec  
 RG 101  
 DW 16.600 usec  
 DE 33.20 usec  
 TE 298.1 K  
 D1 2.00000000 sec  
 D11 0.03000000 sec  
 TD0 1  
 SFO1 125.7703643 MHz  
 NUC1 13C  
 P0 2.87 usec  
 P1 8.60 usec  
 PLW1 39.00000000 W  
 SFO2 500.1320005 MHz  
 NUC2 1H  
 CPDPRG[2] waltz65  
 PCPD2 80.00 usec  
 PLW2 8.00000000 W  
 PLW12 0.18911000 W  
 PLW13 0.09512200 W

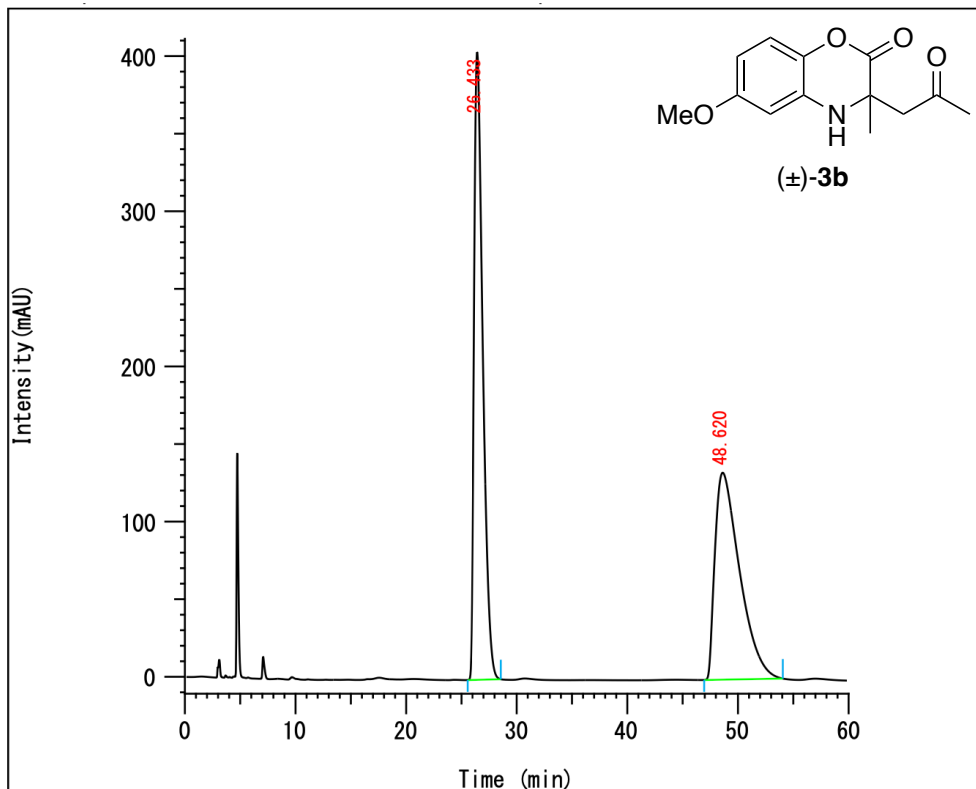
F2 - Processing parameters  
 SI 32768  
 SF 125.7577944 MHz  
 WDW EM  
 SSB 0  
 LB 1.00 Hz  
 GB 0  
 PC 1.40



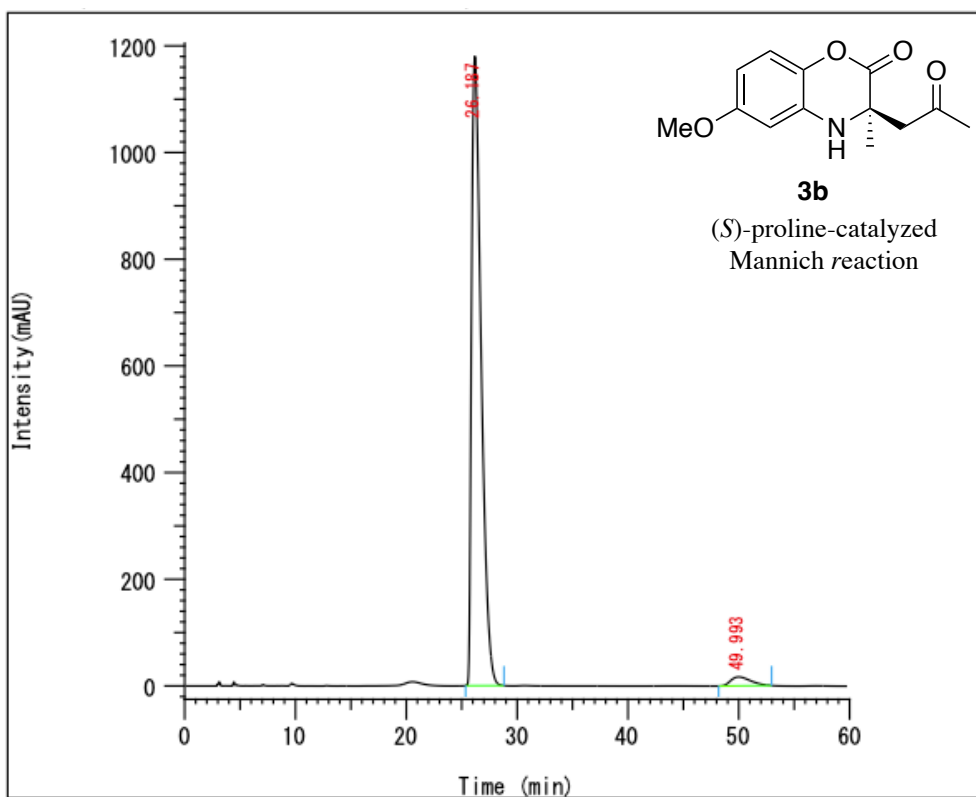
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.520	57232992	49.739	1477762
2	Peak 2	24.480	57834731	50.261	779842
			115067722	100.000	2257604



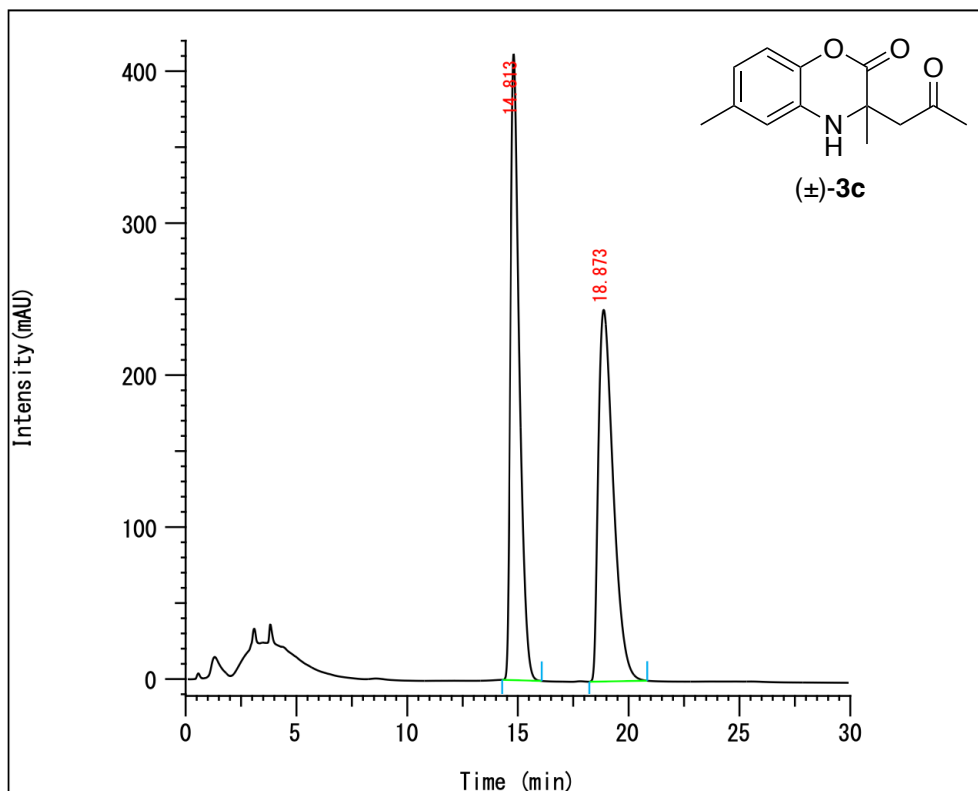
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.567	50999139	96.856	1338267
2	Peak 2	25.420	1655411	3.144	29932
			52654550	100.000	1368199



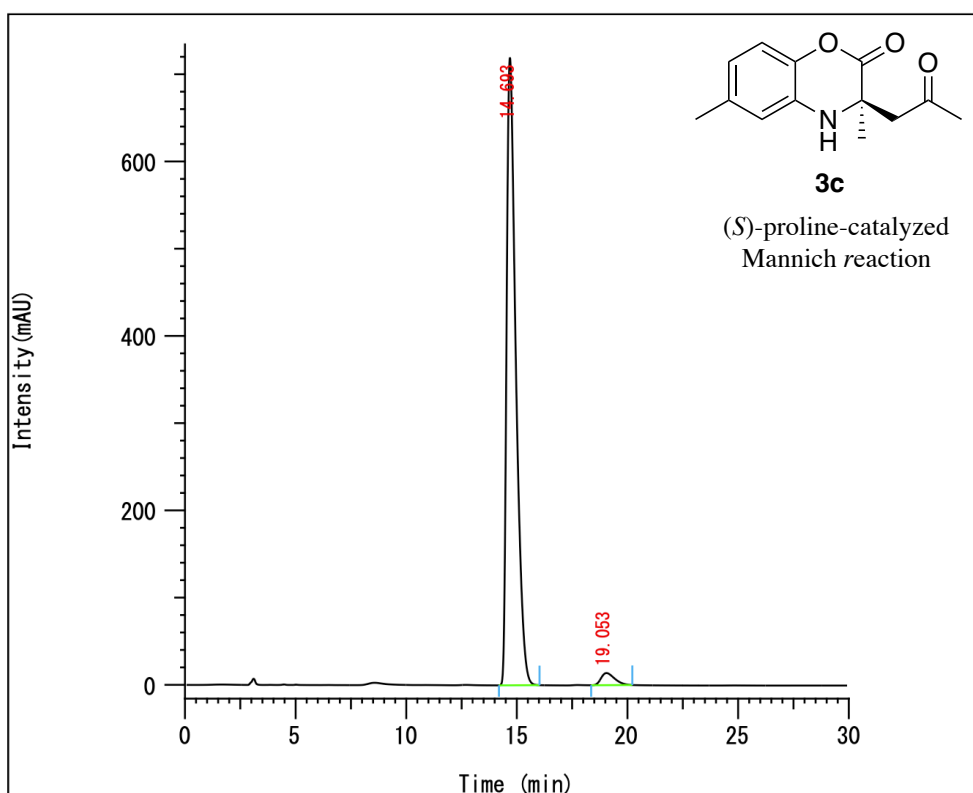
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	26.433	22217138	51.836	404661
2	Peak 2	48.620	20643218	48.164	133403
			42860356	100.000	538064



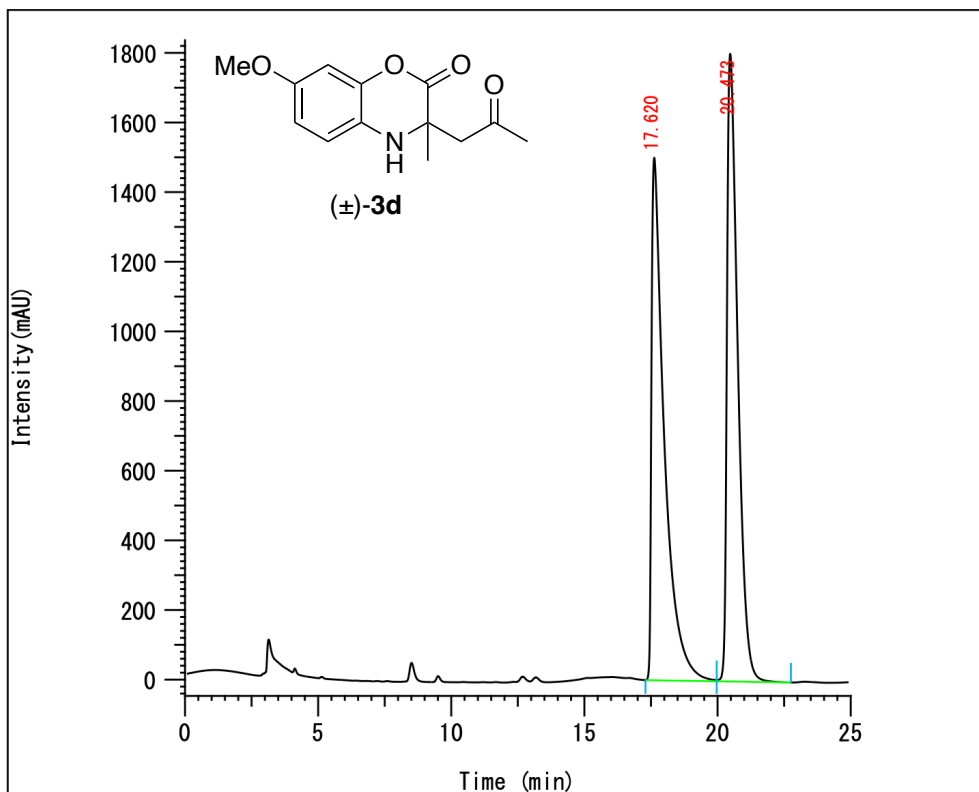
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	26.187	70858281	97.119	1180036
2	Peak 2	49.993	2101640	2.881	16725
			72959922	100.000	1196761



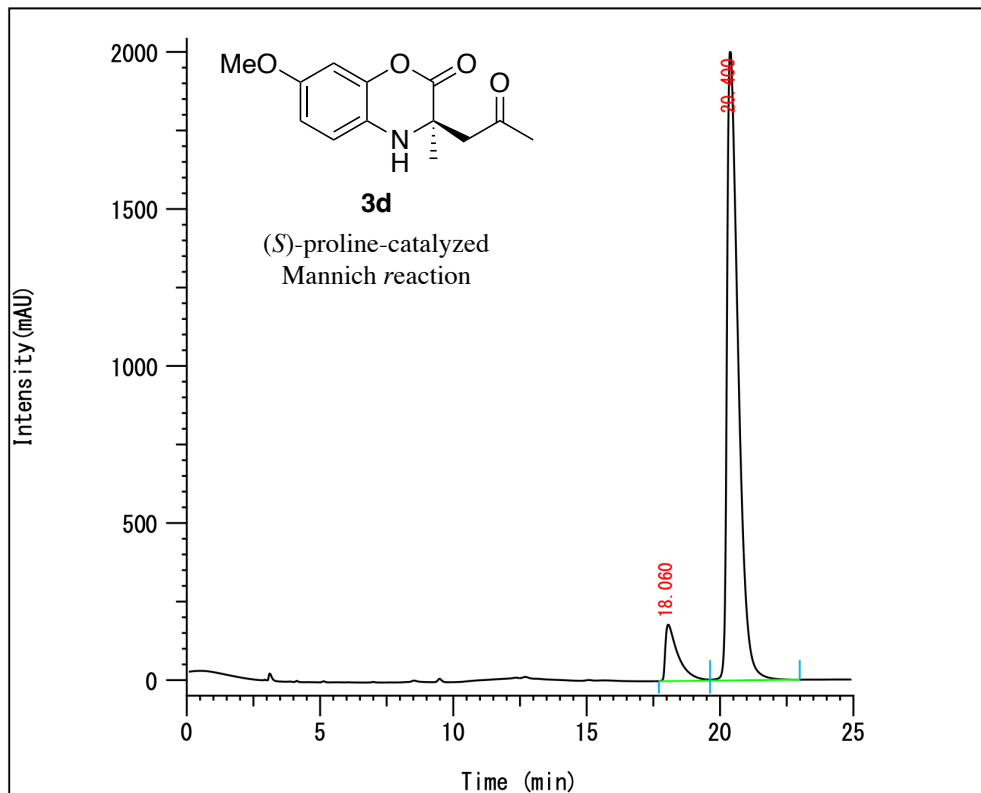
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	14.813	11616225	50.289	412145
2	Peak 2	18.873	11482601	49.711	244628
			23098826	100.000	656772



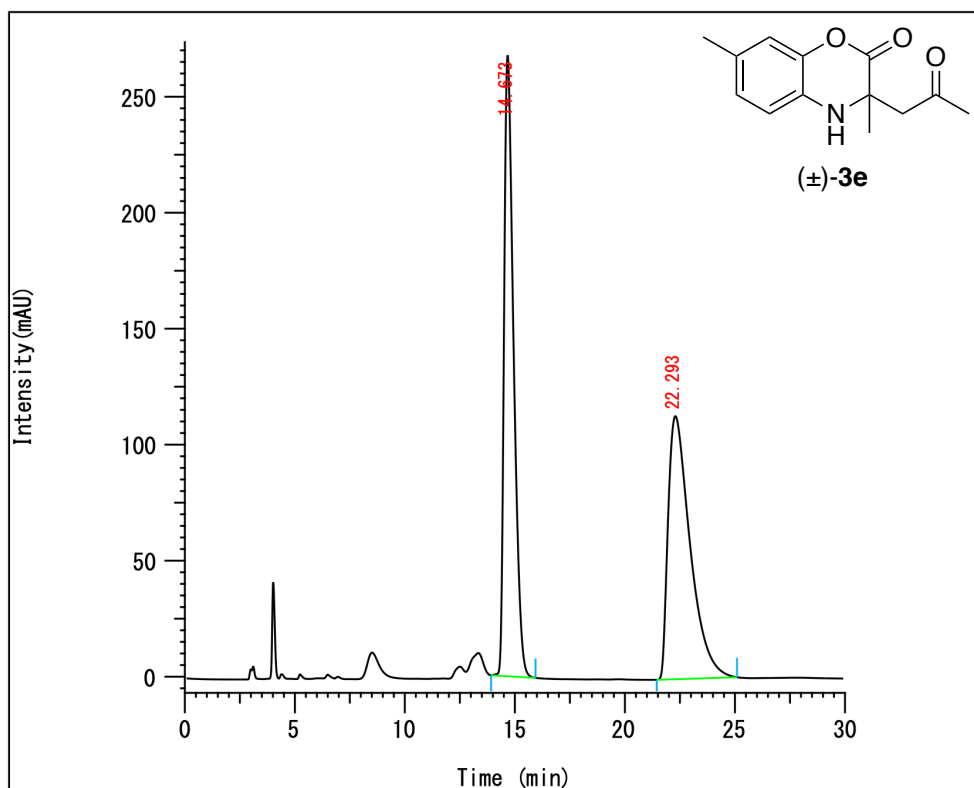
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	14.693	20812365	97.233	719732
2	Peak 2	19.053	592170	2.767	13891
			21404535	100.000	733623



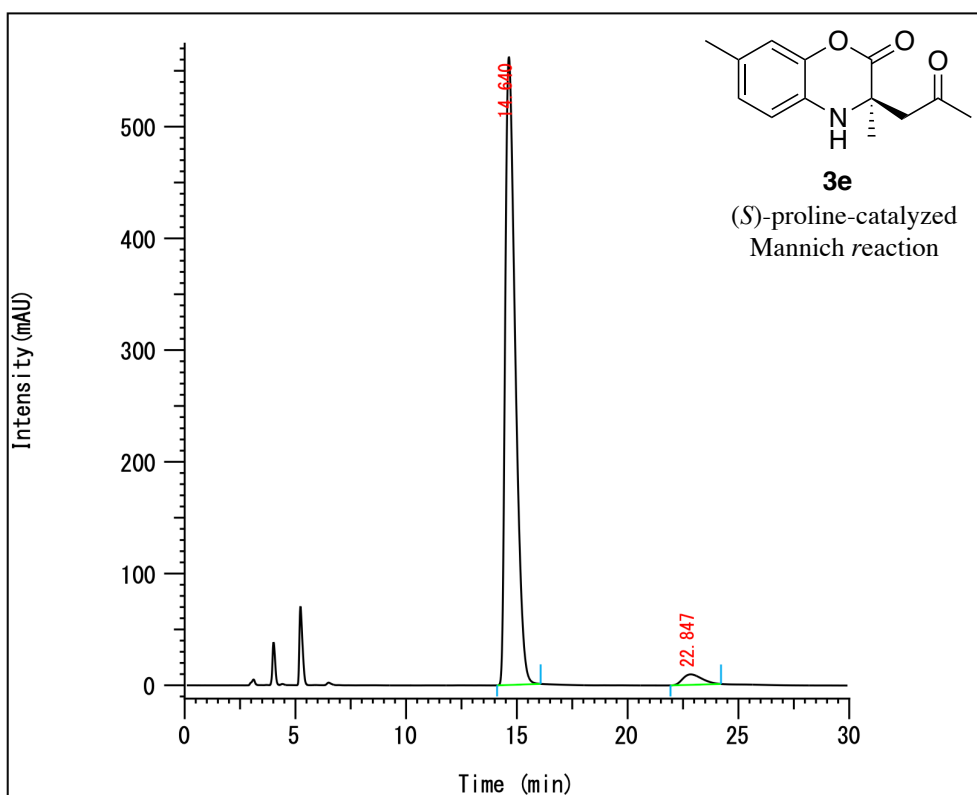
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.620	50260175	49.723	1500978
2	Peak 2	20.473	50820720	50.277	1803889
			101080895	100.000	3304867



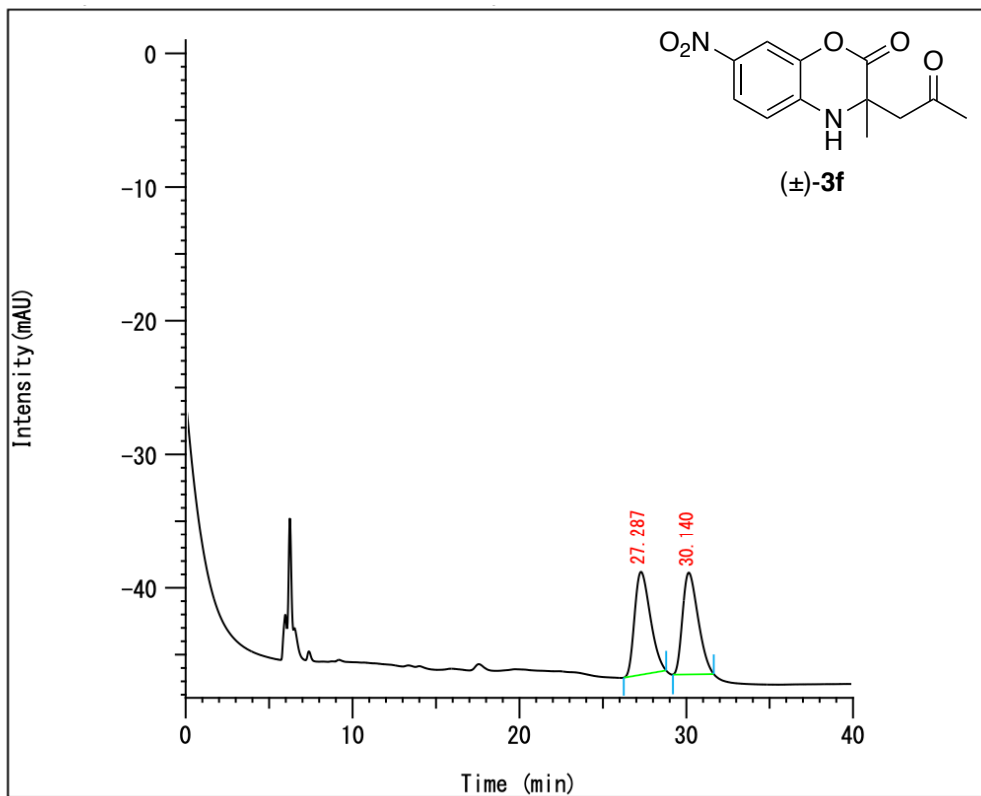
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	18.060	5957167	9.256	179977
2	Peak 2	20.400	58402631	90.744	2000953
			64359798	100.000	2180930



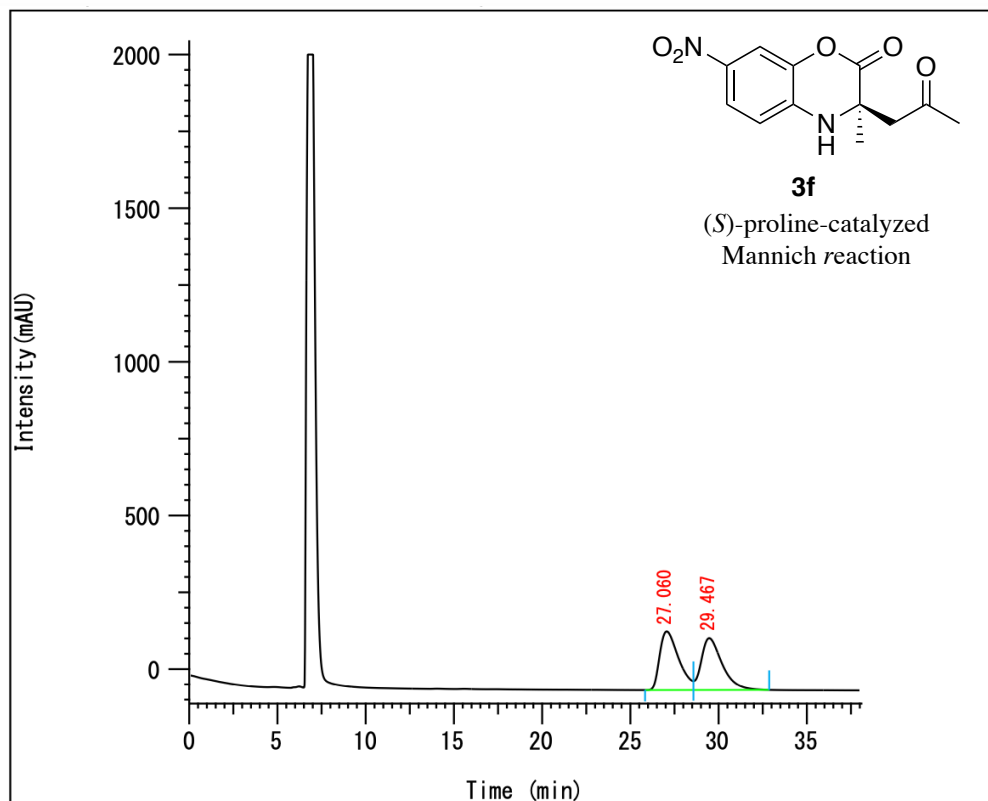
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	14.673	8048185	50.511	267742
2	Peak 2	22.293	7885349	49.489	113387
			15933534	100.000	381129



No.	Compounds	RT	Area	Area%	Height
1	Peak 1	14.640	17700731	96.910	562245
2	Peak 2	22.847	564394	3.090	9365
			18265125	100.000	571609

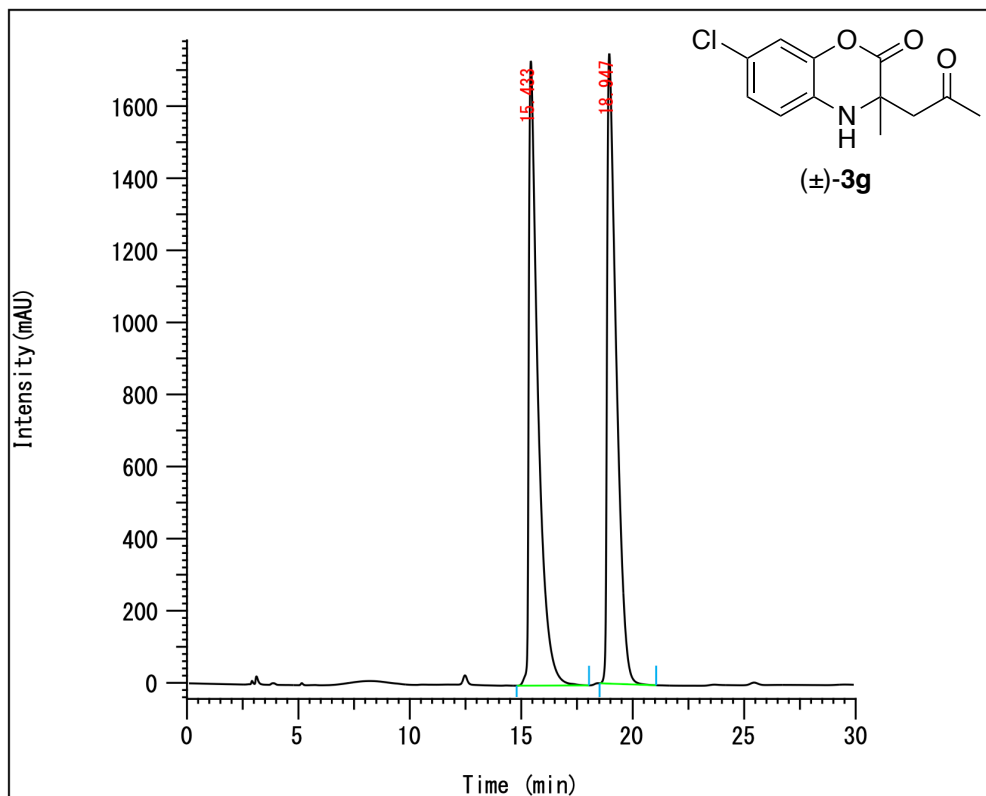


No.	Compounds	RT	Area	Area%	Height
1	Peak 1	27.287	503504	50.569	7699
2	Peak 2	30.140	492170	49.431	7617
			995674	100.000	15316

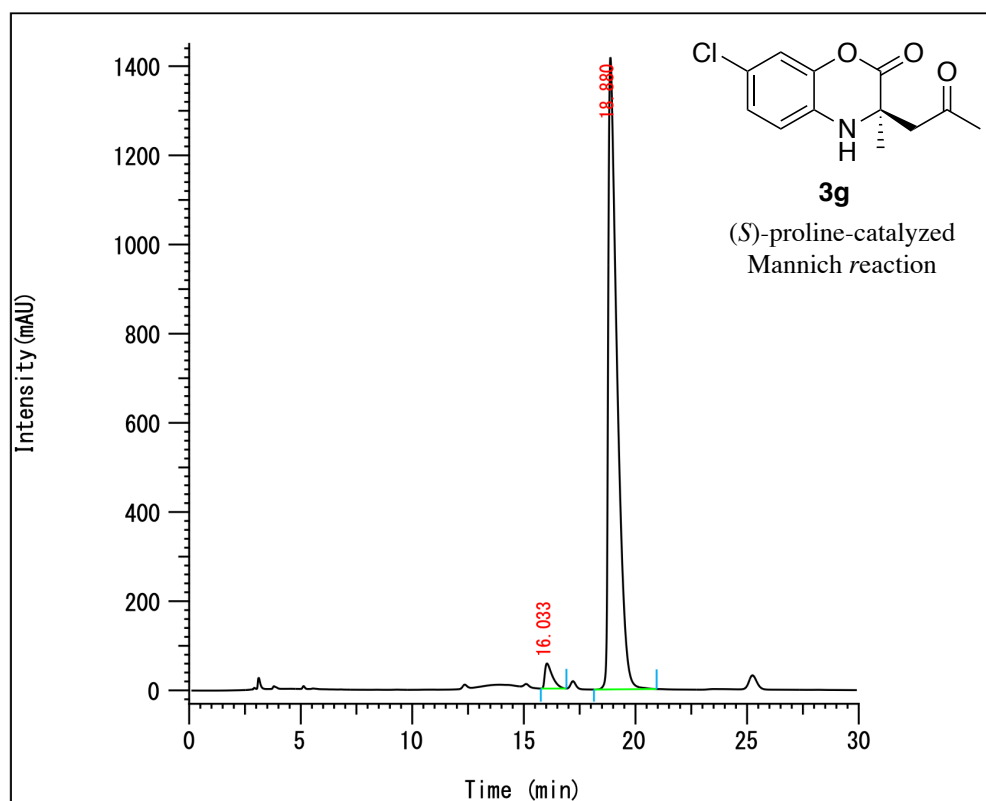


No.	Compounds	RT	Area	Area%	Height
1	Peak 1	27.060	14356783	50.548	191641
2	Peak 2	29.467	14045345	49.452	169485
			28402128	100.000	361126

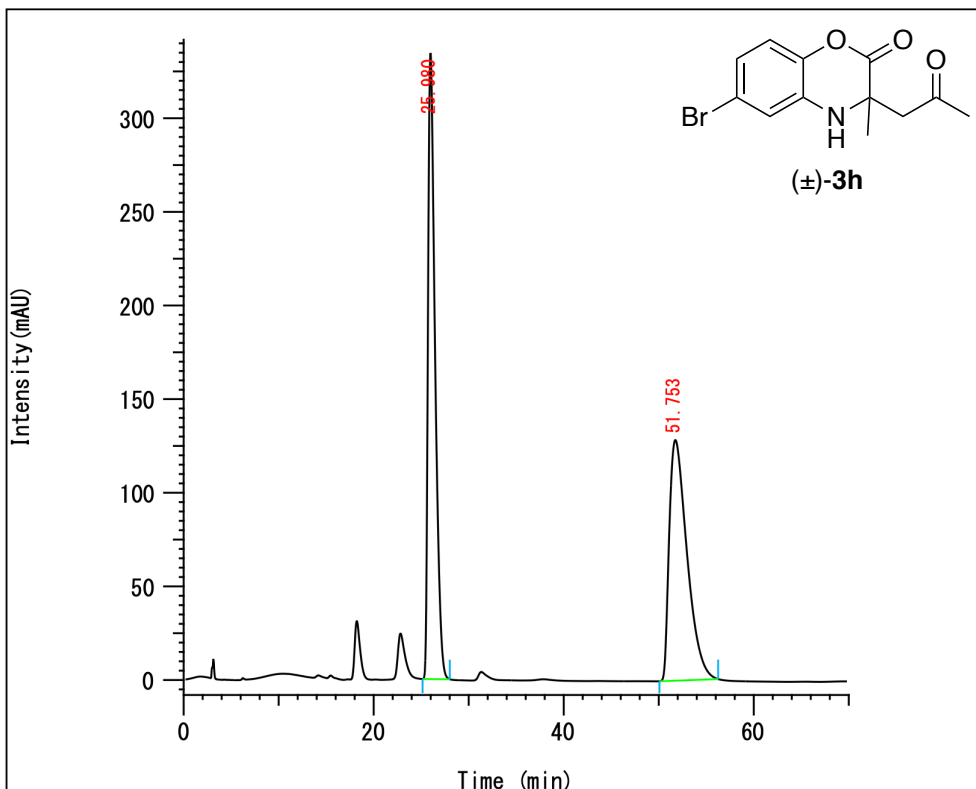




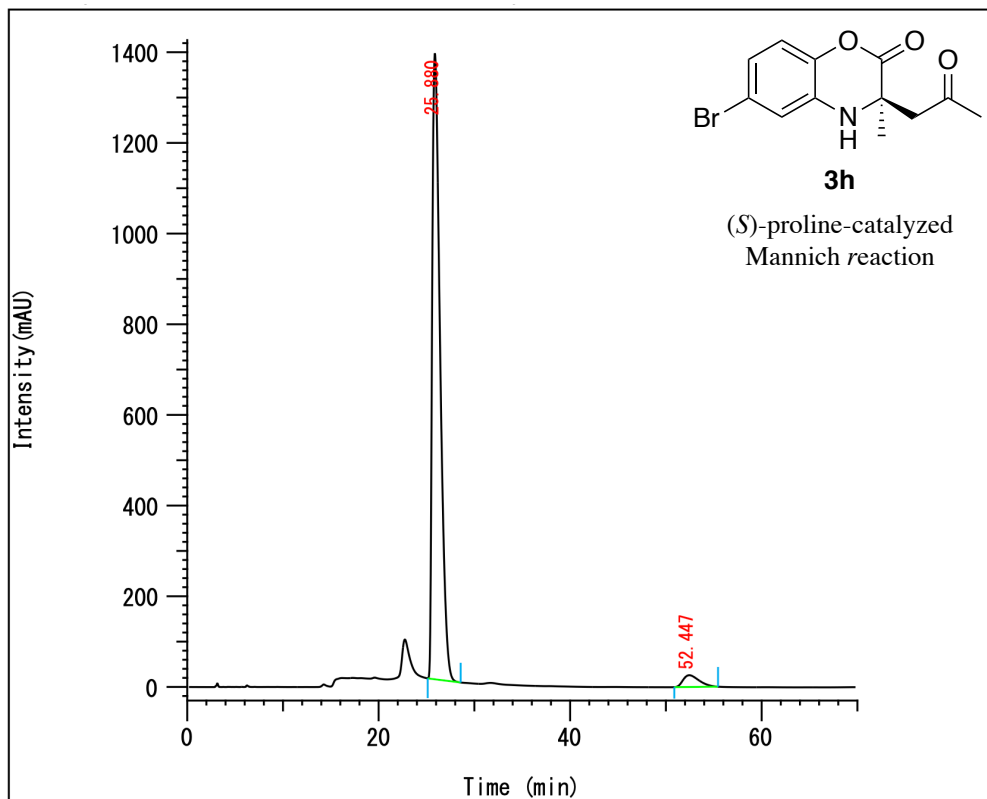
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	15.433	49335373	49.609	1733578
2	Peak 2	18.947	50113821	50.391	1748104
			99449194	100.000	3481682



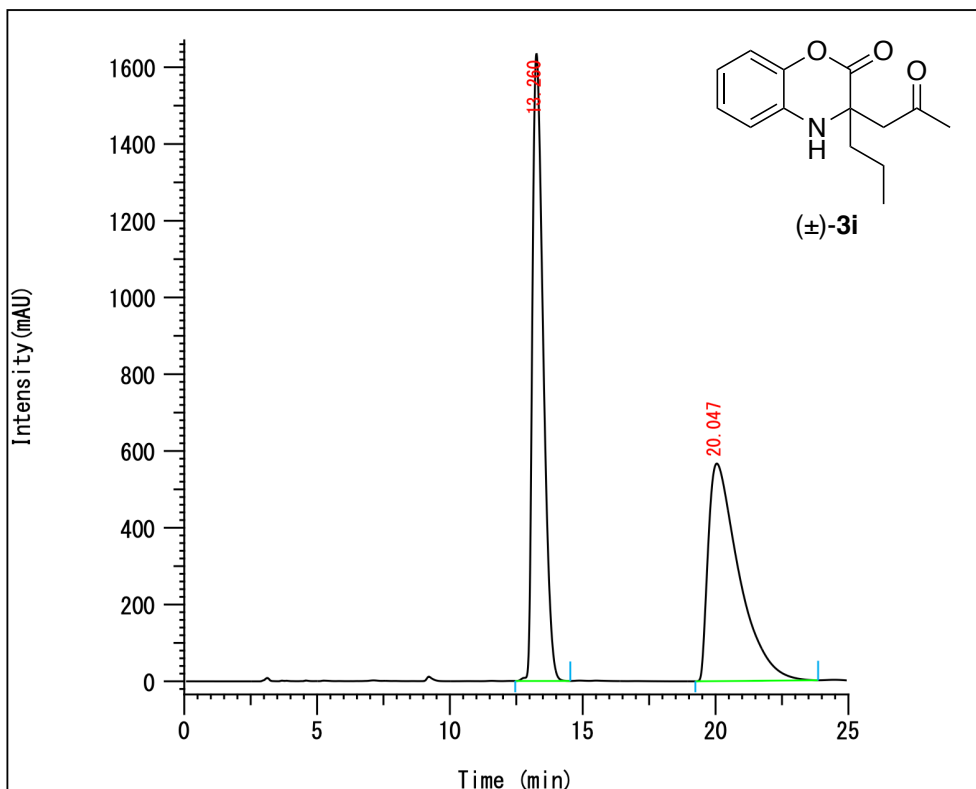
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	16.033	1317317	3.273	56320
2	Peak 2	18.880	38931485	96.727	1418123
			40248802	100.000	1474443



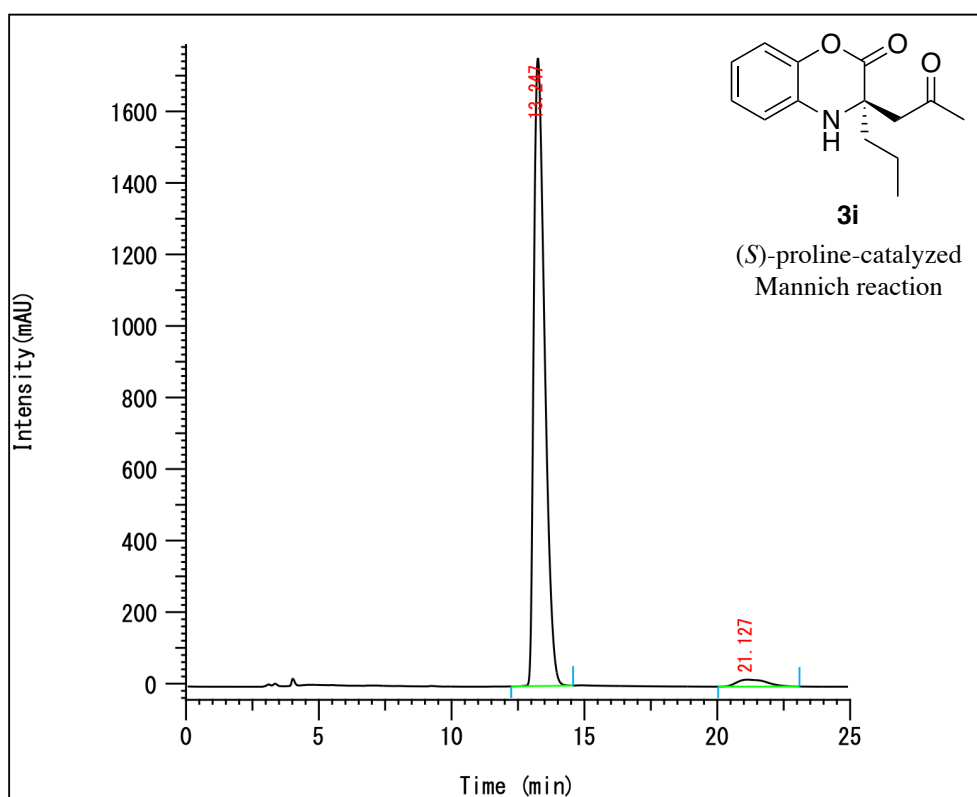
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	25.980	17257183	50.789	334435
2	Peak 2	51.753	16721132	49.211	128543
			33978315	100.000	462978



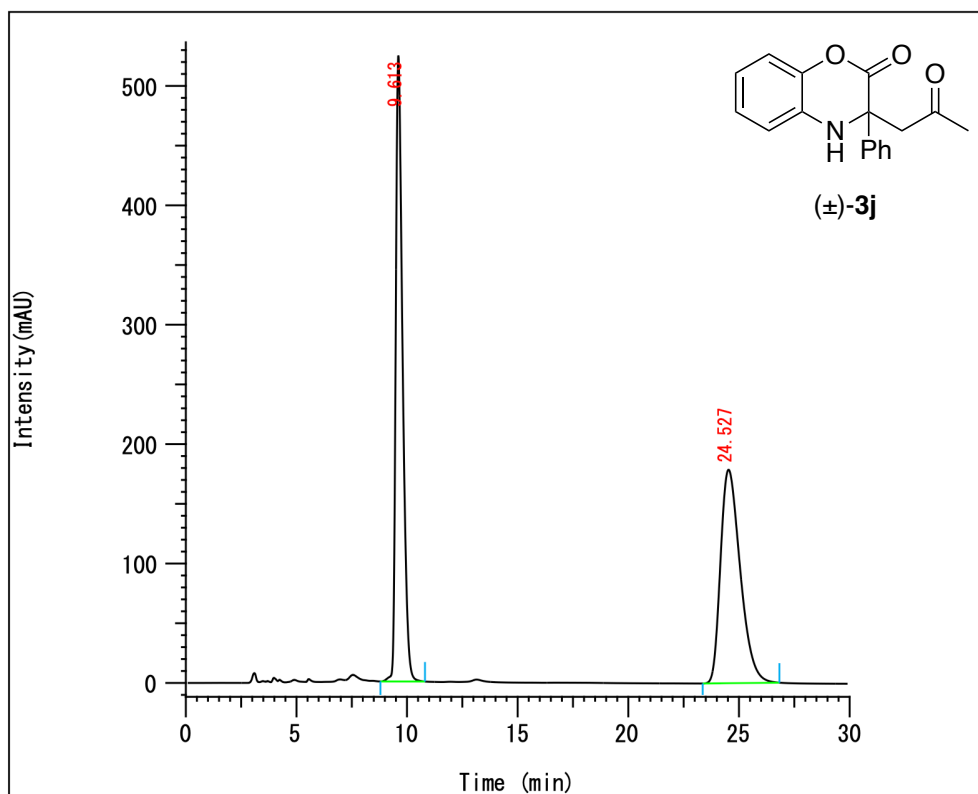
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	25.880	79081345	96.315	1380667
2	Peak 2	52.447	3025372	3.685	25995
			82106717	100.000	1406662



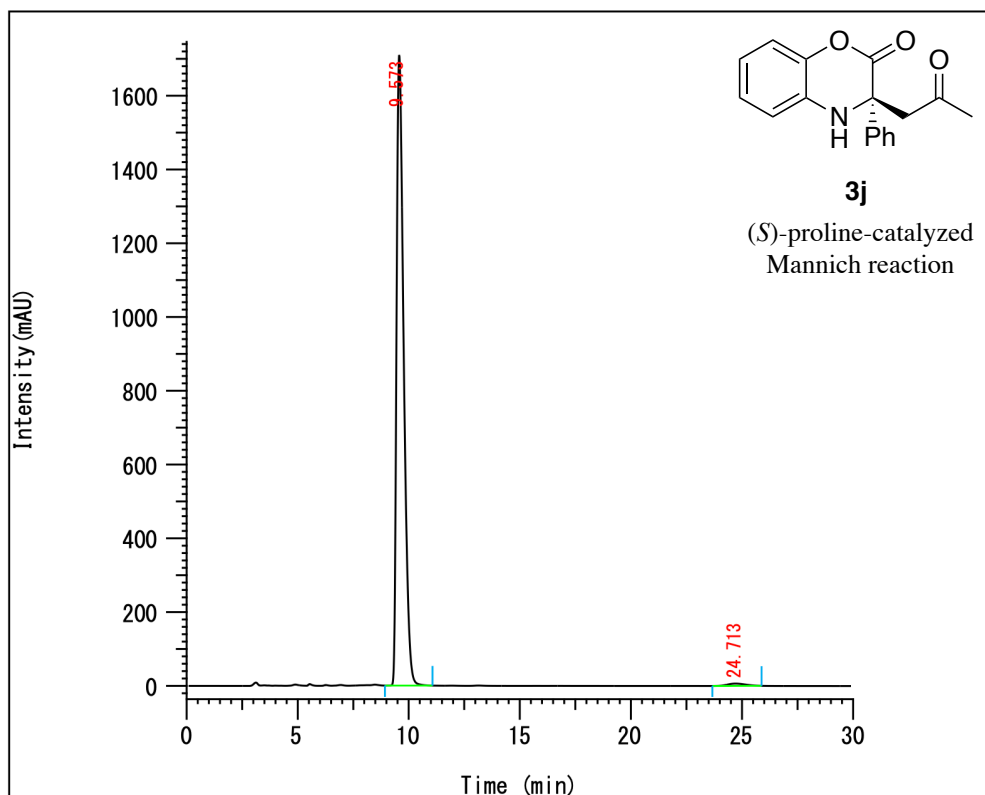
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	13.260	46209920	50.364	1635005
2	Peak 2	20.047	45541060	49.636	566921
			91750980	100.000	2201925



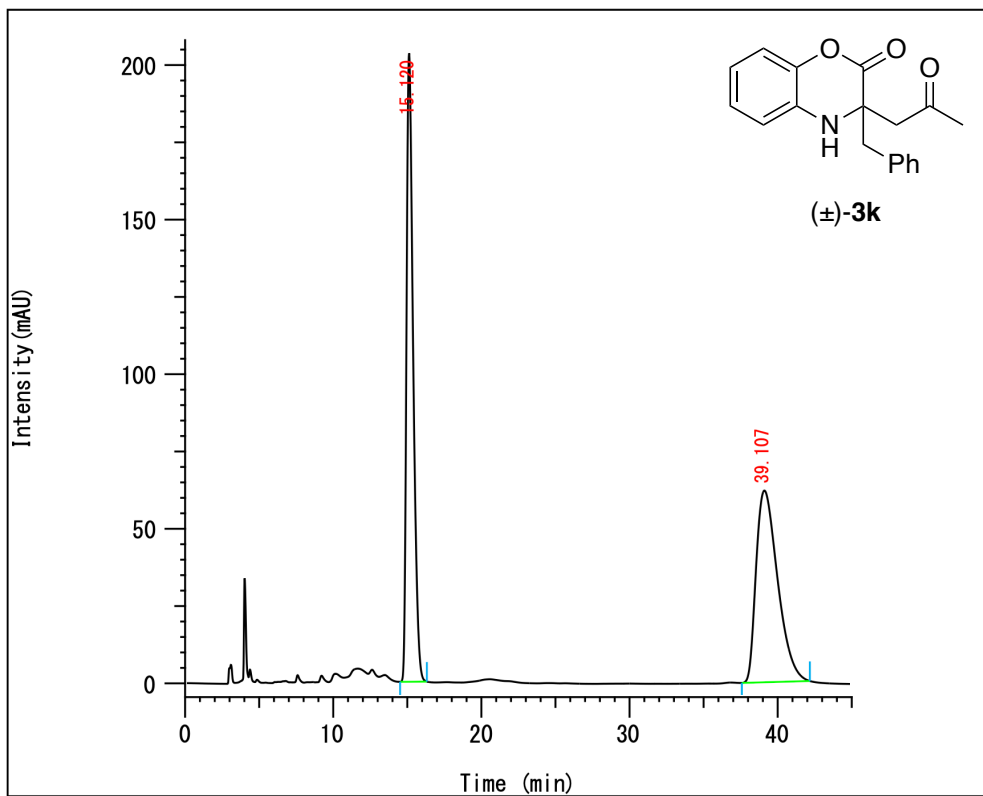
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	13.247	49833779	97.002	1755905
2	Peak 2	21.127	1539966	2.998	19444
			51373746	100.000	1775349



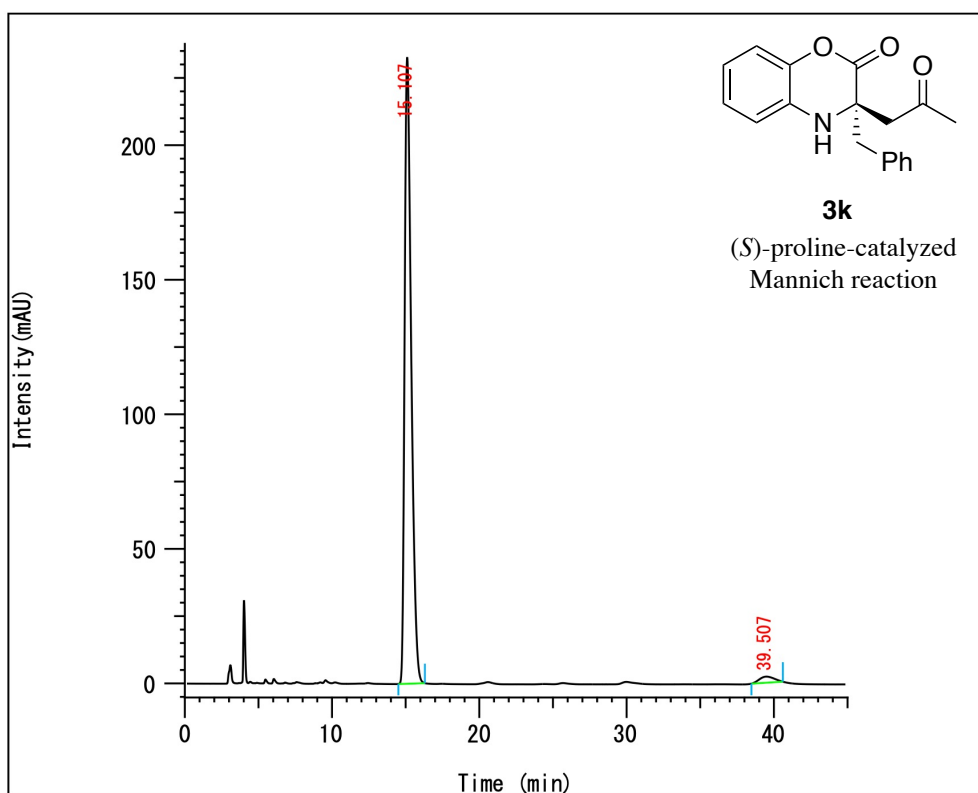
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	9.613	11298335	50.525	524326
2	Peak 2	24.527	11063707	49.475	178824
			22362042	100.000	703151



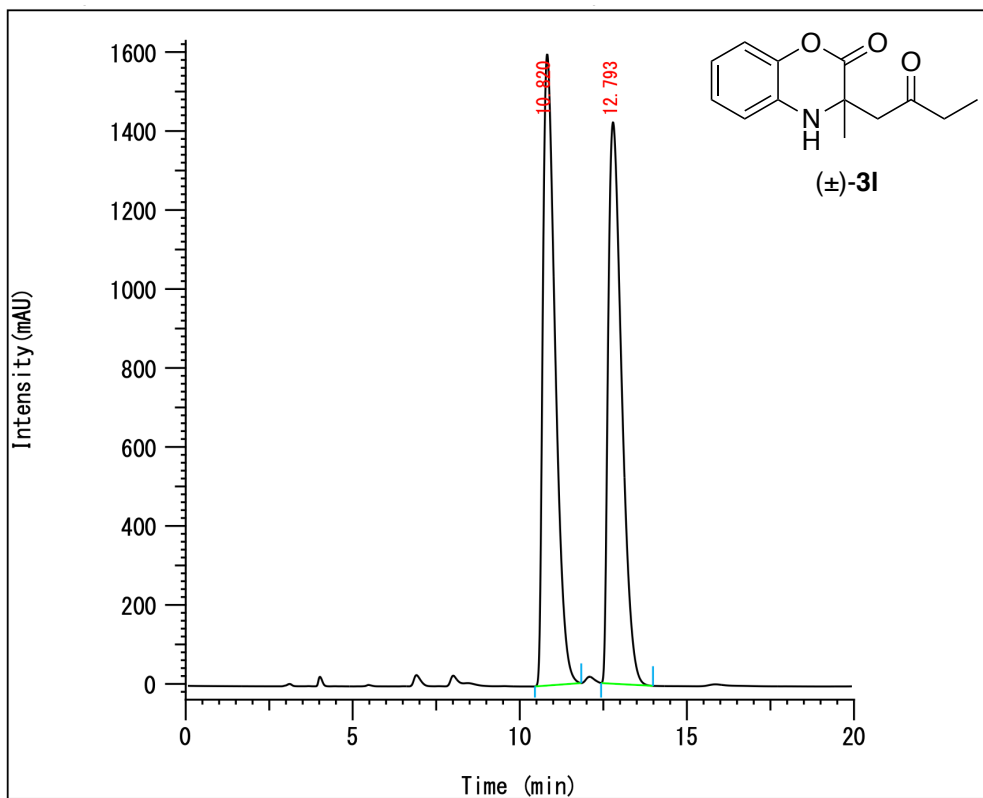
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	9.573	38161121	99.085	1709469
2	Peak 2	24.713	352331	0.915	6249
			38513452	100.000	1715718



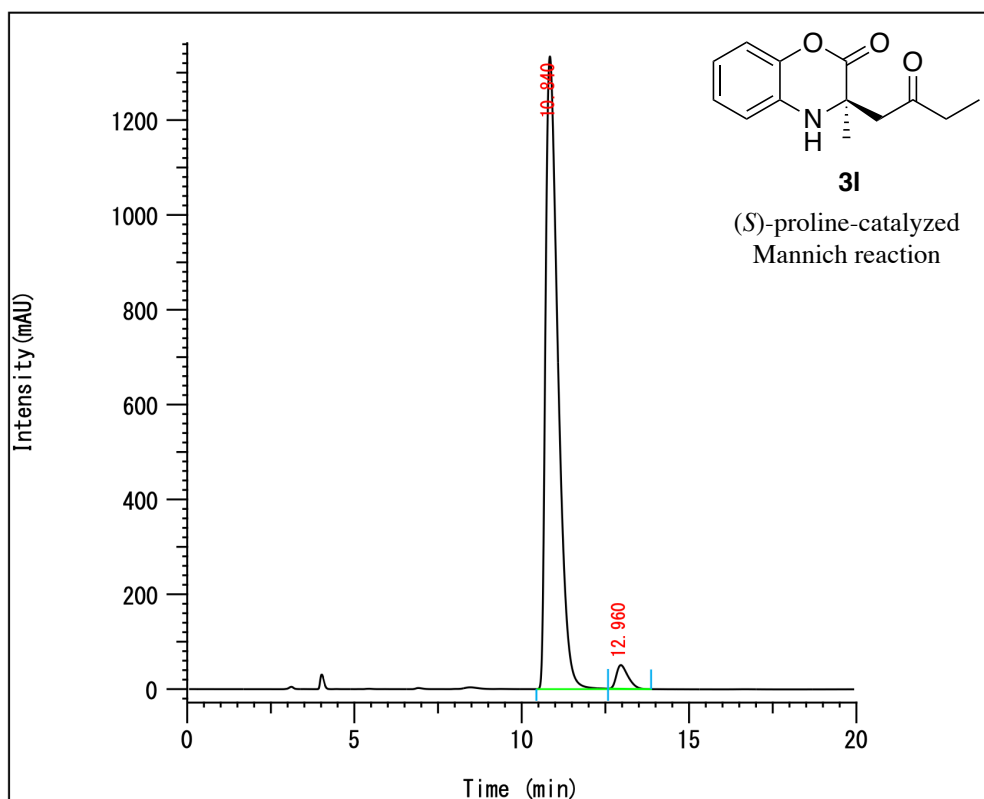
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	15.120	6308373	50.182	203283
2	Peak 2	39.107	6262709	49.818	62023
			12571083	100.000	265306



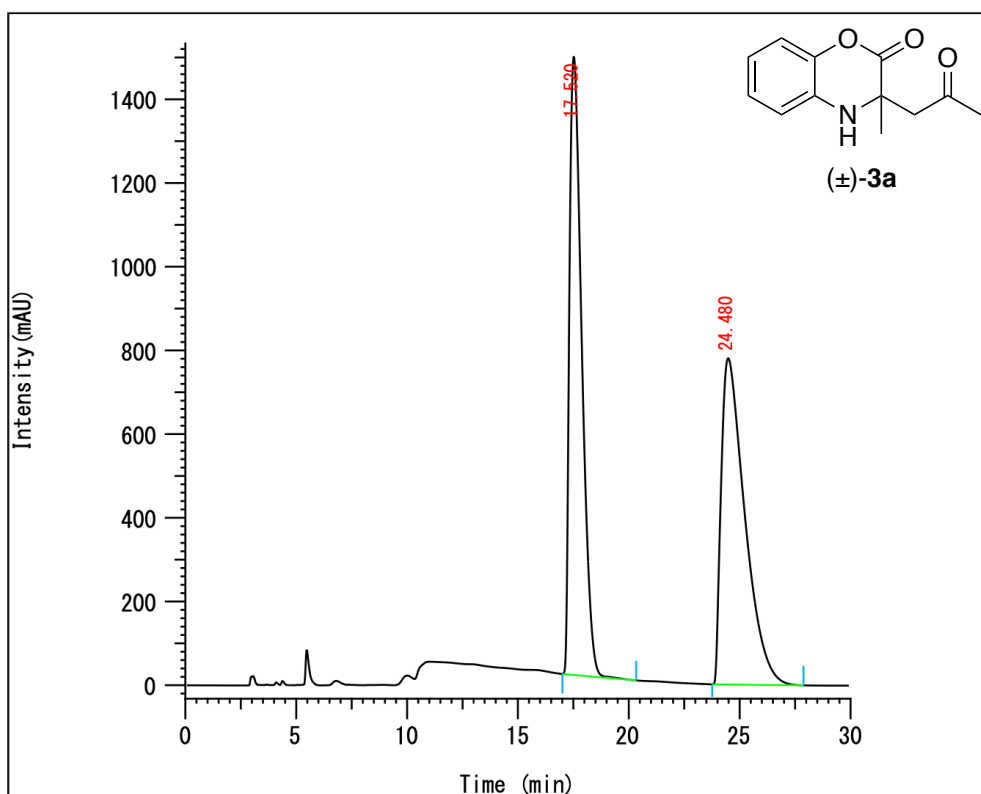
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	15.107	7248626	97.858	232908
2	Peak 2	39.507	158656	2.142	2270
			7407282	100.000	235178



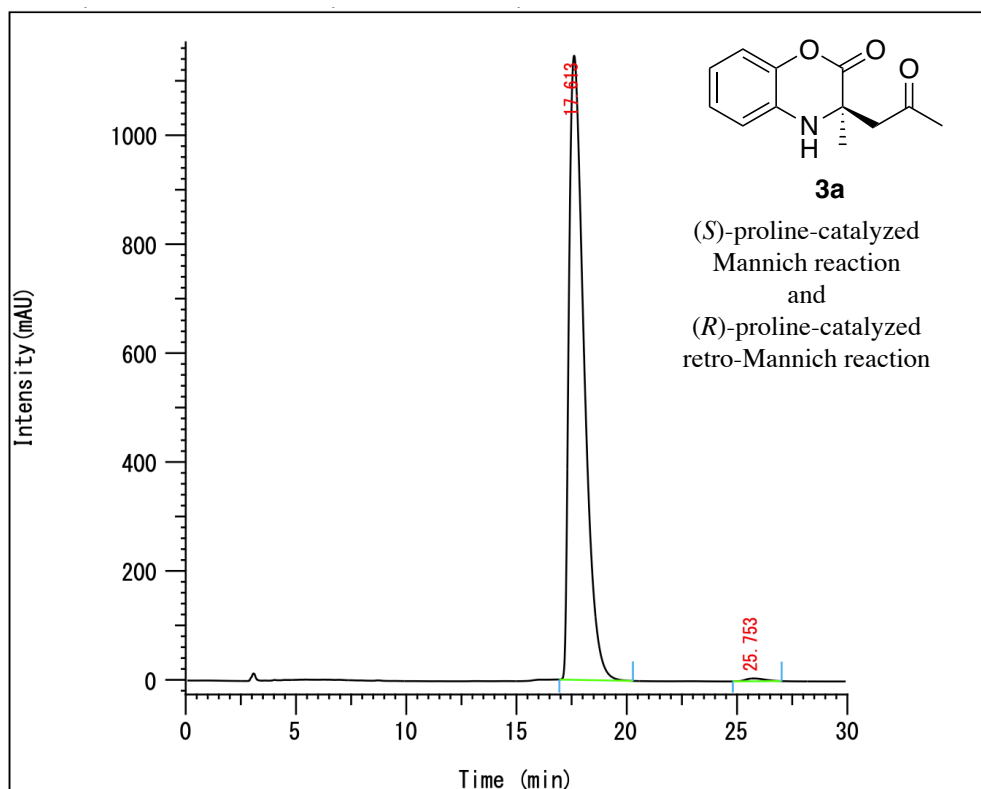
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	10.820	41187805	50.659	1599175
2	Peak 2	12.793	40116086	49.341	1421906
			81303891	100.000	3021081



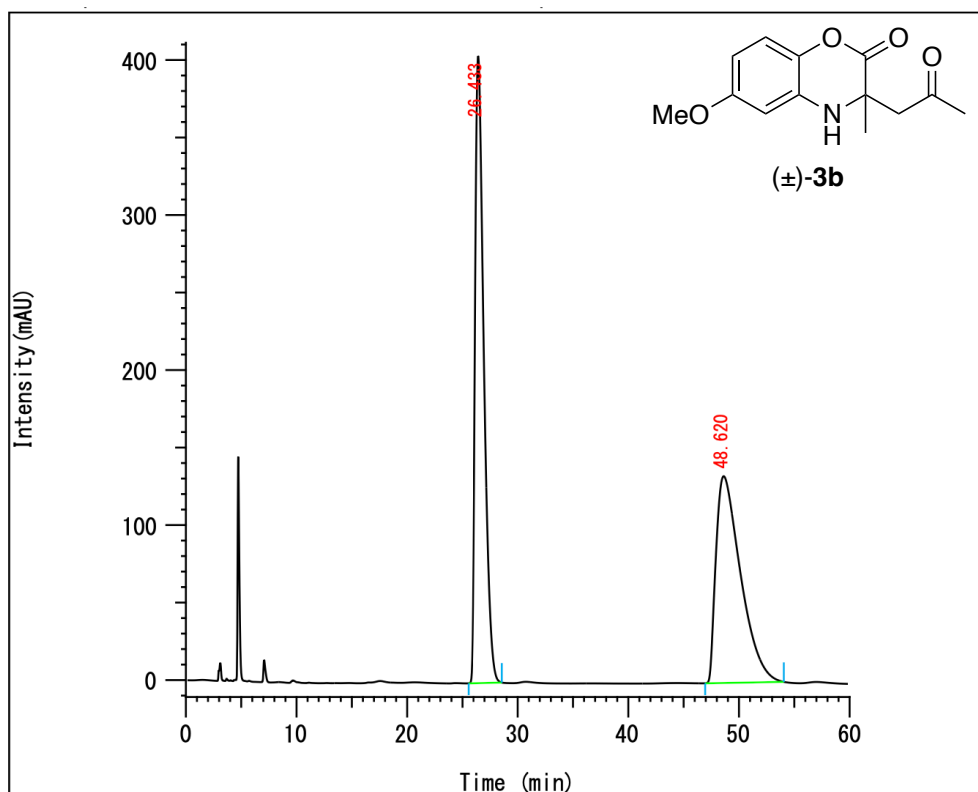
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	10.840	34385251	96.602	1334368
2	Peak 2	12.960	1209417	3.398	49998
			35594668	100.000	1384366



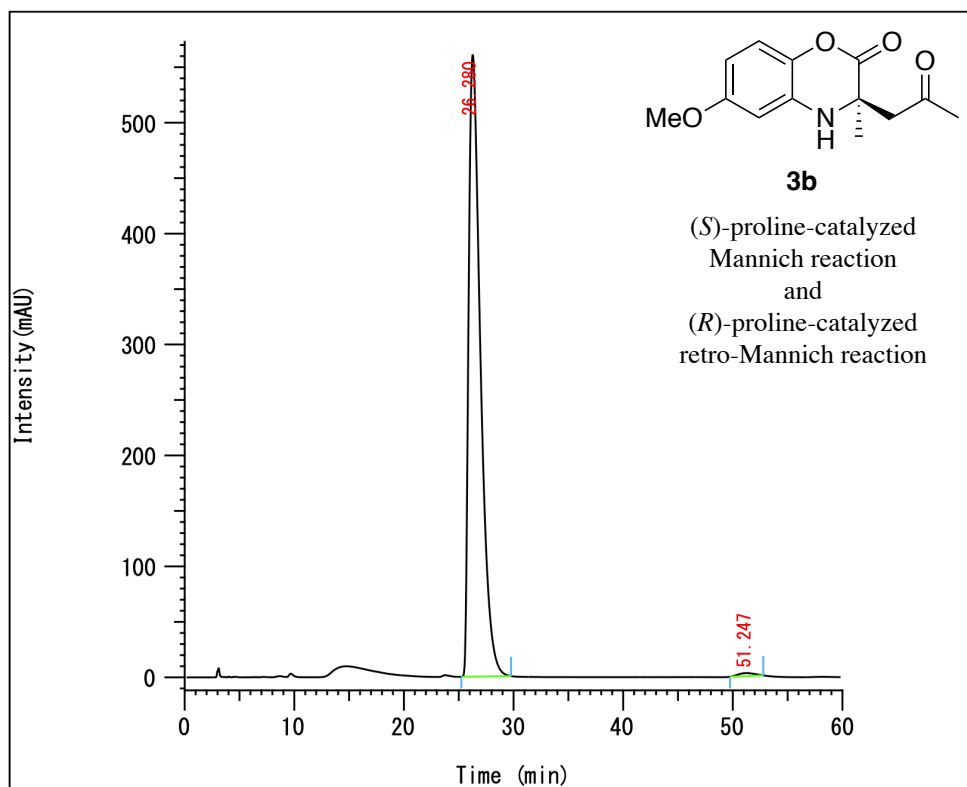
No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.520	57232992	49.739	1477762
2	Peak 2	24.480	57834731	50.261	779842
			115067722	100.000	2257604



No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.613	54293824	99.433	1146699
2	Peak 2	25.753	309805	0.567	5224
			54603628	100.000	1151923

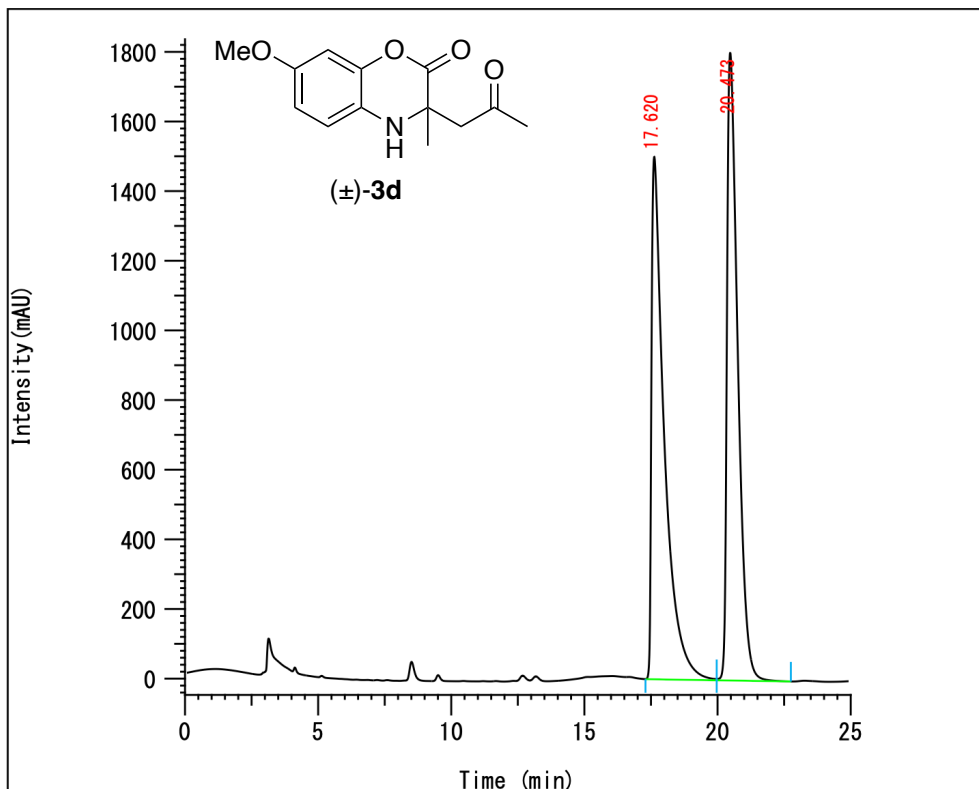


No.	Compounds	RT	Area	Area%	Height
1	Peak 1	26.433	22217138	51.836	404661
2	Peak 2	48.620	20643218	48.164	133403
			42860356	100.000	538064

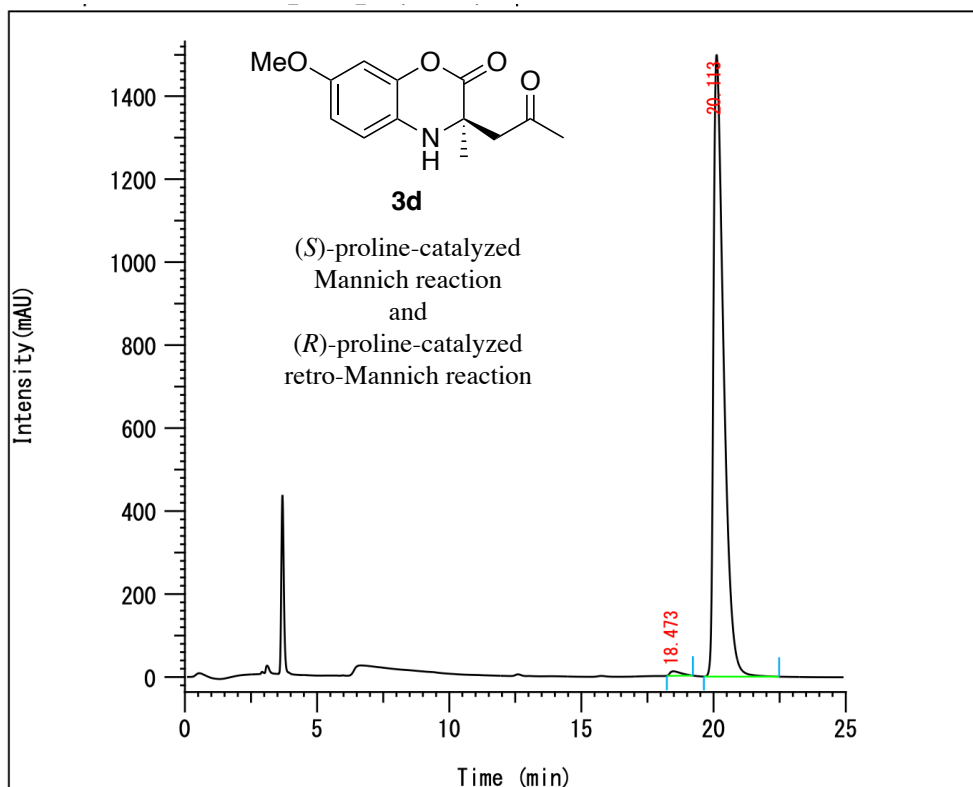


No.	Compounds	RT	Area	Area%	Height
1	Peak 1	26.280	42021621	99.332	560554
2	Peak 2	51.247	282750	0.668	2716
			42304371	100.000	563269





No.	Compounds	RT	Area	Area%	Height
1	Peak 1	17.620	50260175	49.723	1500978
2	Peak 2	20.473	50820720	50.277	1803889
			101080895	100.000	3304867



No.	Compounds	RT	Area	Area%	Height
1	Peak 1	18.473	320806	0.797	10963
2	Peak 2	20.113	39920847	99.203	1499699
			40241654	100.000	1510662