An Efficient Method for retro-Claisen-type C-C Bond Cleavage of Diketones with Tropylium Catalyst

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Supporting Information

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General Methods

Reactions, unless otherwise stated, were conducted under a positive pressure of argon in oven-dried glassware. Water for the hydration reactions was deionized water. Commercially available solvents and reagents were used as purchased unless otherwise noted. Analytical thin layer chromatography was performed using aluminium plates precoated with silica gel 60 F_{254} (0.2 mm). Flash chromatography employed 230-400 mesh silica gel. Solvents used for chromatography are quoted as volume/volume ratios.

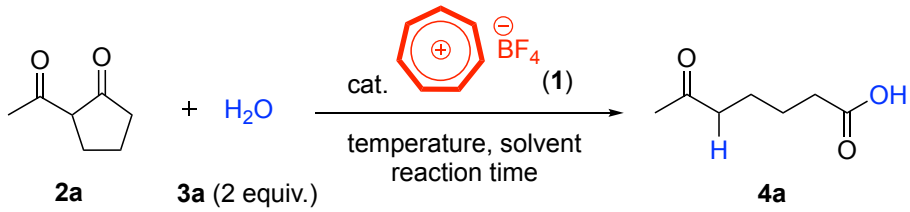
NMR spectroscopy was performed at 298 K using an Avance III HD 400 (400.1 MHz, ^{1}H; 100.6 MHz, ^{13}C, 376.5 MHz, ^{19}F) or an Avance III 300 (300 MHz, ^{1}H; 75 MHz, ^{13}C; 282.5 MHz, ^{19}F). Data is expressed in parts per million (ppm) downfield shift from tetramethylsilane with residual solvent as an internal reference (δ 7.26 ppm for chloroform, 5.27 ppm for dichloromethane) and is reported as position (δ in ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (J in Hz) and integration (number of protons). ^{13}C NMR spectra were recorded at 298 K with complete proton decoupling. Data is expressed in parts per million (ppm) downfield shift relative to the internal reference (δ 77.2 ppm for the central peak of deuterated chloroform).

Infrared spectra were obtained on a ThermoNicolet Avatar 370 FT-IR spectrometer and are reported in wavenumbers (cm^{-1}). HRMS were performed at the Bioanalytical Mass Spectrometry Facility within the Mark Wainwright Analytical Centre at the University of New South Wales on an Orbitrap LTQ XL (Thermo Fisher Scientific, San Jose, CA, USA) ion trap mass spectrometer.

Flow reactions were conducted on a Vapourtec R-Series flow reactor.

General Procedure for Optimization Studies

Table S1. Optimization of tropylium-promoted hydrolysis reaction of substrate **2a**[a]



2a **3a** (2 equiv.) **4a**

Entry	mol% cat.	solvent	T (°C)	time[b]	Yield[c]
1	10	no solvent	rt	48	18%
2	10	no solvent	60	24	52%
3	10	no solvent	80	24	96%
4	**10**	**no solvent**	**100**	**16**	**99%**
5	5	no solvent	100	16	62%
6	2.5	no solvent	100	16	56%
7	1	no solvent	100	16	38%
8	no cat.	no solvent	100	16	traces
9[d]	10	water as solvent	100	16	80%
10	10	MeCN	reflux	16	45%
11	10	toluene	reflux	16	46%
12	10	DCE	reflux	16	70%
13	10	TFE	reflux	12	99%
14	**10**	**TFE**	**rt**	**24**	**98%**
15	10	water as solvent	rt	48	21%
16	10	MeCN	rt	48	62%
17	10	toluene	rt	48	37%
18	10	DCE	rt	48	64%
19[e]	10% HBF_4	no solvent	100	24	67%
20[e]	10% TfOH	no solvent	100	24	78%
21[e]	10% HBF_4	TFE	rt	48	59%
22[e]	10% TfOH	TFE	rt	48	76%

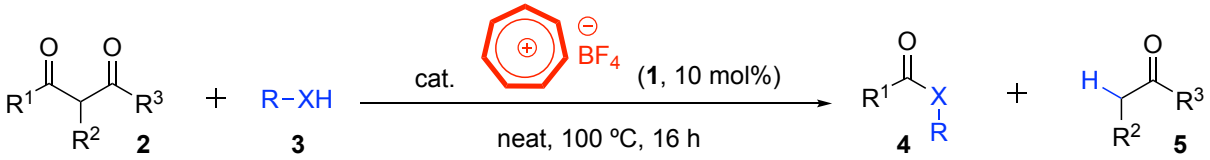
[a] Conditions: diketone **2a** (1 mmol), water (**3a**, 2 mmol) and cat. **1** (0.1 mmol) in the indicated solvent (0.6 mL) under N_2 atmosphere. [b] Reaction time (hour) until no further or total consumption of substrate **2a**. [c] Yield of the isolated product. [d] 0.5 mL water was used. [e] 10 mol% of a Brønsted acid catalyst was used instead of tropylium catalyst **1**.

A mixture of 2-acetylcyclopentanone (**2a**, 1 mmol), water (**3a**, 2 mmol) and a corresponding amount tropylium tetrafluoroborate catalyst **1** was charged into a 4 mL reaction vial and the reaction mixture was topped up with 0.6 mL of the indicated solvent. The reaction was stirred

at the indicated temperature for the indicated reaction time. The reaction was monitored by TLC or ^{1}H NMR. The reaction mixture was subsequently concentrated under reduced pressure. The product was isolated by column chromatography (silica-gel, ethyl acetate: hexane = 1:9) to obtain 6-oxoheptanoic acid **4a** as a yellowish solid.

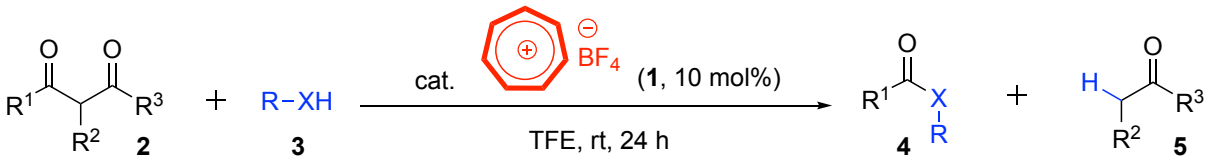
General Procedures for the Tropylium-Promoted retro-Claisen Reactions

Procedure A



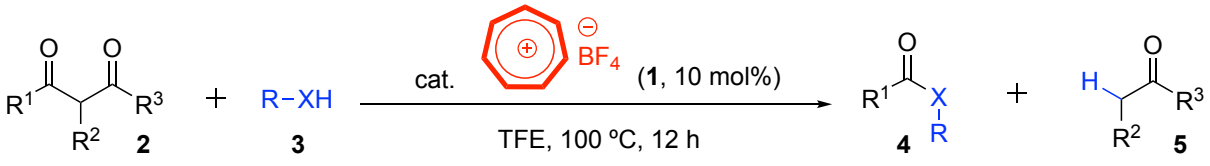
A mixture of 1,3-diketone **2** (1 mmol, 1 equiv), nucleophile **3** (water, alcohol, amine or thiol, 2 mmol, 2 equiv) and tropylium tetrafluoroborate catalyst **1** (0.1 mmol, 10 mol%) was charged into a 4 mL reaction vial and the reaction mixture was stirred at 100 °C for 16 h under solvent free and closed-vessel conditions. The reaction was monitored by TLC or ^{1}H NMR. The reaction mixture was subsequently concentrated under reduced pressure. The product was isolated by column chromatography (silica-gel, ethyl acetate: hexane = 1:9) to obtain product **4**.

Procedure B



A mixture of 1,3-diketone **2** (1 mmol, 1 equiv), nucleophile **3** (water, alcohol, amine or thiol, 2 mmol, 2 equiv) and tropylium tetrafluoroborate catalyst **1** (0.1 mmol, 10 mol%) was charged into a 4 mL reaction vial containing 2,2,2-trifluoroethanol (0.6 mL) and the reaction mixture was stirred at room temperature for 24 h. The reaction was monitored by TLC or ^{1}H NMR. The reaction mixture was subsequently concentrated under reduced pressure. The product was isolated by column chromatography (silica-gel, ethyl acetate: hexane = 1:9) to obtain product **4**.

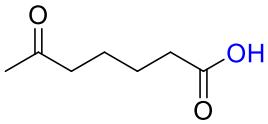
Procedure C



A mixture of 1,3-diketone **2** (1 mmol, 1 equiv), nucleophile **3** (water, alcohol, amine or thiol, 2 mmol, 2 equiv) and tropylium tetrafluoroborate catalyst **1** (0.1 mmol, 10 mol%) was charged into a 4 mL reaction vial containing 2,2,2-trifluoroethanol (0.6 mL) and the reaction mixture was stirred at 100 °C for 12 h under closed-vessel conditions. The reaction was monitored by TLC or ^{1}H NMR. The reaction mixture was subsequently concentrated under reduced pressure. The product was isolated by column chromatography (silica-gel, ethyl acetate: hexane = 1:9) to obtain product **4**.

Characterization Data of Products

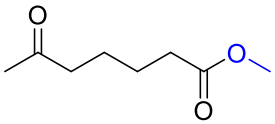
6-Oxoheptanoic acid[1] **(**compound number **4a):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and water to give the title compound as a yellowish solid (100 mg, 99% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (t, J =6.7 Hz, 2H), 2.36 (t, J =7.0 Hz, 2H), 2.14 (s, 3H), 1.66-1.59 (m, 4H), ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.8, 179.6, 43.3, 33.9, 30.0, 24.2, 23.2 ppm.

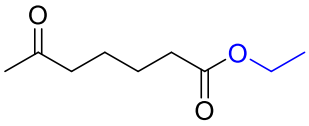
Methyl 6-oxo-heptanoate[2] **(**compound number **4b):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and methanol to give the title compound as a yellowish liquid (130 mg, 97% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.44 (t, J = 6.8 Hz, 2H), 2.31 (t, J = 7.1 Hz, 2H), 2.12 (s, 3H), 1.62-1.57 (m, 4H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.8, 174.0, 51.7, 43.4, 33.9, 30.0, 24.5, 23.3 ppm.

Ethyl 6-oxo-heptanoate[3] **(**compound number **4c):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and ethanol to give the title compound as a yellow oil (160 mg, 94% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (q, J = 7.1 Hz, 2H), 2.43 (t, J = 6.9 Hz, 2H), 2.29 (t, J = 7.1 Hz, 2H), 2.12 (s, 3H), 1.62-1.54 (m, 4H), 1.23 (t, J = 7.1 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.0, 173.6, 60.5, 43.4, 34.1, 29.9, 24.5, 23.3, 14.3 ppm.

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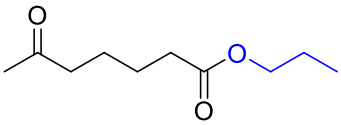
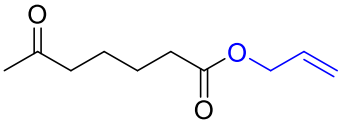
[1] V. Mandadapu, F. Wu, A. I. Day, *Org. Lett.,* **2014**, *16*, 1275-1277.
[2] M. A. Valencia, G. Achonduh, H. Alper, *J. Org. Chem.,* **2015**, *80*, 6419-6424.
[3] X. J. Baringo, J. Clark, M. J. Gutmann, D. J. Procter, *Angew. Chem. Int. Ed.,* **2016**, *55*, 12499-12502.

***n*-Propyl 6-oxoheptanoate**[4] **(**compound number **4d):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and *n*-propanol to give the title compound as a pale-yellow oil (156 mg, 84% yield).



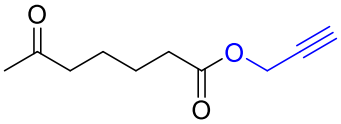
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.01 (t, J = 6.7 Hz, 2H), 2.44 (t, J = 6.7, 6.9 Hz, 2H), 2.31 (t, J = 7.2, 6.9 Hz, 2H), 2.13 (s, 3H), 1.67-1.58 (m, 6H), 0.92 (t, J = 7.5 Hz, 3H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 173.2, 66.2, 43.4, 34.2, 30.0, 24.5, 23.3, 22.0, 10.1 ppm.

Allyl 6-oxoheptanoate[1] **(**compound number **4e):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and allyl alcohol to give the title compound as a yellowish liquid (180 mg, 97% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94-5.85 (m, 1H), 5.32-5.20 (m, 2H,), 4.56 (dt, J = 1.4, 1.3 Hz, 2H), 2.44 (t, J = 6.7 Hz, 2H), 2.33 (t, J = 7.0 Hz, 2H) 2.12 (s, 3H), 1.63-1.57 (m, 4H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 173.2, 132.3, 118.4, 65.2, 43.4, 34.0, 29.9, 24.5, 23.3, ppm.

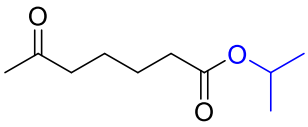
Prop-2-ynyl 6-oxoheptanoate[1] **(**compound number **4f):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and propargyl alcohol to give the title compound as a yellowish oil (135 mg, 74% yield).



[4] L. He, M. Kanamori, C. A. Horiuchi, *J. Chem. Research*., **1999**, *2*, 122-123.

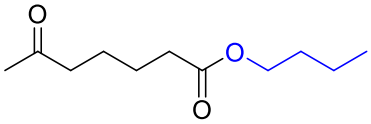
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (d, J=2.5 Hz, 2H), 2.45 (t, J = 7.0 Hz, 2H), 2.37 (t, J = 7.0 Hz, 2H), 2.13 (s, 3H), 1.68-1.56 (m, 4H) ppm (C_{alkyne}-H signal not observed);
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 172.7, 77.8, 74.9, 52.0, 43.3, 33.9, 30.0, 24.4, 23.2 ppm.

Isopropyl 6-oxoheptanoate[1] **(**compound number **4g):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and isopropanol to give the title compound as a yellowish oil (131 mg, 70% yield).



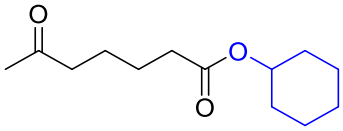
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.97-4.88 (m, 1H), 2.39 (t, J = 6.4, 6.6 Hz, 2H), 2.21 (p, J = 4.2, 2.7, 2.9, 3.7 Hz, 2H), 2.08 (s, 3H), 1.54 (p, J = 3.5 Hz, 4H), 1.16 (d, J = 6.3 Hz, 6H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 173.1, 67.6, 43.4, 34.5, 29.9, 24.5, 23.3, 21.9 ppm.

***n*-Butyl 6-oxoheptanoate**[1] **(**compound number **4h):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and *n*-butyl alcohol to give the title compound as a yellowish liquid (185 mg, 92% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.05 (t, J = 6.6 Hz, 2H), 2.43 (t, J = 6.9 Hz, 2H), 2.45 (t, J = 6.9 Hz, 2H), 2.12 (s, 3H), 1.62-1.55 (m, 6H), 1.40-1.31 (m, 2H), 0.91 (t, J = 7.8 Hz, 3H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 173.7, 64.4, 43.4, 34.2, 30.8, 29.9, 24.5, 23.3, 19.2, 13.8 ppm.

Cyclohexyl 6-oxoheptanoate (compound number **4i):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and cyclohexanol to give the title compound as a yellowish oil (152 mg, 67% yield).



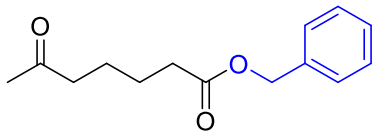
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77-4.70 (m, 1H), 2.44 (t, J = 6.7 Hz, 2H), 2.28 (t, J = 7 Hz, 2H), 2.12 (s, 3H), 1.83 (q, J = 5.8 Hz, 2H), 4.13 (q, J = 5.8 Hz, 2H), 1.60 (p, J = 3.5 Hz, 4H), 1.43-1.22 (m, 6H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 172.9, 72.7, 43.4, 34.6, 31.8, 30.1, 25.5, 24.7, 23.9, 23.3 ppm;

IR (KBr) 2933, 2858, 1715, 1450, 1358 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{13}H_{22}O_3Na$ 249.1461; Found 249.1461.

Benzyl 6-oxoheptanoate (compound number **4j):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and benzyl alcohol to give the title compound as a yellow oil (131 mg, 70% yield).



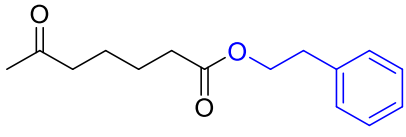
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 5.11 (s, 2H), 2.43 (t, J = 7.0 Hz, 2H), 2.37 (t, J = 7.0 Hz, 2H), 2.12 (s, 3H), 1.68-1.57 (m, 4H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 173.4, 136.1, 128.7 (two coincident resonances), 128.4, 66.4, 43.4, 34.1, 30.0, 24.5, 23.3 ppm;

IR (KBr) 2947, 1731, 1713, 1603, 1529, 1453 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{18}O_3$+Na 257.1148; Found 257.1147.

6-Oxo-heptanoic acid phenethyl ester[5] **(**compound number **4k):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and 2-phenylethanol to give the title compound as a colorless oil (176 mg, 71% yield).

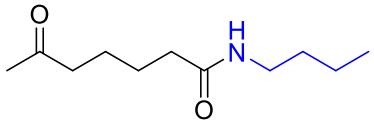


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.20 (m, 5H), 4.28 (t, J = 7.0 Hz, 2H), 2.93 (t, J = 7.0 Hz, 2H), 2.41 (t, J = 6.7 Hz, 2H), 2.29 (t, J = 6.7 Hz, 2H), 2.12 (s, 3H), 1.61-1.54 (m, 4H) ppm;

[5]C. B. Rao, D. C. Rao, D. C. Babu, Y. Venkateswarlu, *Eur. J. Org. Chem.,* **2010**, *15*, 2855-2859.

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 173.5, 137.9, 129.0, 128.6, 126.7, 64.5, 43.4, 35.2, 34.1, 30.0, 24.5, 23.3 ppm.

***N*-butyl-6-oxoheptanamide (**compound number **4l):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and *n*-butyl amine to give the title compound as a white solid (165 mg, 83% yield).



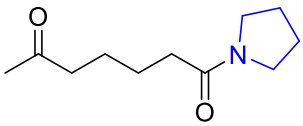
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (s, 1H), 3.25 (q, J = 7.0 Hz, 2H), 2.46 (t, J = 6.7 Hz, 2H), 2.16 (t, J = 6.7 Hz, 2H), 2.13 (s, 3H), 1.61 (p, J = 3.6 Hz, 4H), 1.48 (p, J = 7.0 Hz, 2H), 1.39-1.29 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 172.6, 43.4, 39.4, 36.6, 31.9, 30.1, 25.2, 23.3, 20.2, 13.9 ppm;

IR (KBr) 3292, 3084, 2930, 2867, 1710, 1639, 1544, 1437 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{11}H_{21}NO_2Na$ 222.1465; Found 222.1465.

1-(Pyrrolidin-1-yl) heptane-1,6-dione (compound number **4m):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and pyrrolidine to give the title compound as a yellowish oil (170 mg, 86% yield).



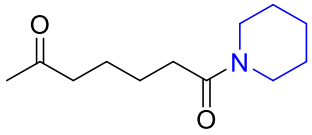
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43 (s, 4H), 2.46 (t, J = 6.6 Hz, 2H), 2.28 (t, J = 6.6 Hz, 2H), 2.13 (s, 3H), 1.93 (d, J = 26.0 Hz, 4H), 1.66-1.59 (m, 4H), ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 171.4, 46.7, 45.8, 43.7, 34.6, 30.0, 26.2, 24.5, 23.7, 22.6 ppm;

IR (KBr) 2947, 2872, 1708, 1619, 1436 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{11}H_{19}NO_2Na$ 220.1308; Found 220.1309.

1-(Piperidin-1-yl) heptane-1,6-dione (compound number **4n):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and piperidine to give the title compound as a yellow oil (179 mg, 85% yield).



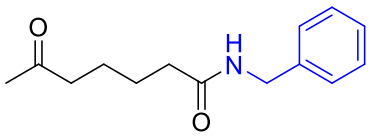
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.51 (d, 4H), 2.45 (t, J = 6.9 Hz, 2H), 2.31 (t, J = 7.2 Hz, 2H), 2.12 (s, 3H), 1.65-1.52 (m, 10H), ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 170.9, 46.7, 43.5, 33.0, 29.9, 25.6, 24.8, 24.6, 23.6 ppm;

IR (KBr) 2934, 2858, 1704, 1609, 1445 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{12}H_{21}NO_2Na$ 234.1465; Found 234.1465.

***N*-benzyl-6-oxoheptanamide (**compound number **4o):** Prepared using the general procedure A from (2-acetylcyclopentanone **2a**) and benzylamine to give the title compound as a yellow oil (178 mg, 76% yield).



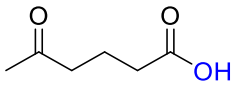
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 5.91 (s, 1H), 4.34 (d, J = 5.8 Hz, 2H), 2.45 (t, J = 6.9 Hz, 2H), 2.21 (t, J = 6.9 Hz, 2H), 2.12 (s, 3H), 1.68-1.56 (m, 4H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 172.6, 138.5, 128.8, 127.9, 127.5, 43.7, 43.4, 36.4, 30.0, 25.1, 23.33 ppm;

IR (KBr) 2932, 1705, 1639, 1542, 1452, 1424 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{19}NO_2Na$ 256.1308; Found 256.1306.

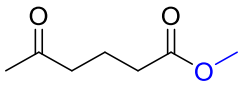
5-Oxohexanoic acid[6] **(**compound number **4p):** Prepared using the general procedure A from (1,3-cyclohexanedione) and water to give the title compound as a colourless oil (116 mg, 90% yield).



[6] D. A. Chaudhari, R. A. Fernandes, *J. Org. Chem*., **2016**, *81*, 2113-2121.

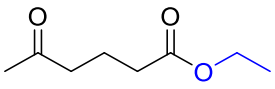
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (t, J = 7.2 Hz, 2H), 2.39 (t, J = 7.2 Hz, 2H), 2.15 (s, 3H), 1.90 (p, J = 7.2, 7.1 Hz, 2H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 178.5, 42.4, 32.9, 30.1, 18.7 ppm.

Methyl 5-oxohexanoate[7] **(**compound number **4q):** Prepared using the general procedure A from (1,3-cyclohexanedione) and methanol to give the title compound as a colourless oil (130 mg, 88% yield)



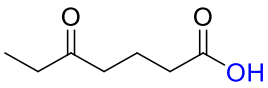
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.64 (s, 3H), 2.48 (t, J = 7.2 Hz, 2H), 2.32 (t, J = 7.2 Hz, 2H), 2.11 (s, 3H), 1.86 (p, J = 7.2, 7.3 Hz, 2H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 173.7, 51.7, 42.5, 33.1, 30.0, 18.9 ppm.

Ethyl 5-oxohexanoate[8] **(**compound number **4r):** Prepared using the general procedure A from (1,3-cyclohexanedione) and ethanol to give the title compound as a colourless oil (121 mg, 76% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (q, J = 7.2, 7.0 Hz, 2H), 2.49 (t, J = 7.2 Hz, 2H), 2.31 (t, J = 7.2 Hz, 2H), 2.13 (s, 3H), 1.88 (p, J = 7.2 Hz, 2H), 1.24 (t, J = 7.0 Hz, 3H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2, 173.3, 60.5, 42.6, 33.4, 30.1, 19.0, 14.4 ppm.

5-Oxohexanoic acid[9] **(**compound number **4s):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and water to give the title compound as a white solid (108 mg, 75% yield).

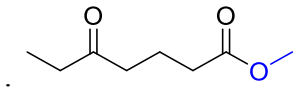


^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (t, J = 7.2 Hz, 2H), 2.45-2.37 (m, 4H), 1.91 (p, J = 7.2, Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H) ppm;

[7] K. Miyamoto, Y. Sei. K. Yamaguchi, M. Ochiai, *J. Am. Chem. Soc*., **2009**, *131*, 1382-1383.
[8] L. Lin, C. Romano, C. Mazet, *J. Am. Chem. Soc*., **2016**, *138*, 10344-10350.
[9] Y. Xu, M. C. Young, G. Dong, *J. Am. Chem. Soc.,* **2017**, *139*, 5716-5719.

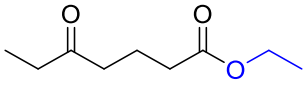
^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 179.5, 41.0, 36.1, 33.1, 18.7, 7.9 ppm.

Methyl 5-oxoheptanoate[10] (compound number **4t):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and methanol to give the title compound as a colourless oil (123 mg, 78% yield).



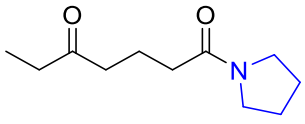
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.49-2.32 (m, 6H), 1.89 (p, J = 7.2 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 173.8, 51.7, 41.2, 36.0, 33.2, 19.1, 7.9 ppm.

Ethyl 5-oxoheptanoate[11] (compound number **4u):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and ethanol to give the title compound as a colourless oil (122 mg, 72% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 4.13 (q, J = 7.1 Hz, 2H), 2.48-2.38 (m, 4H), 2.31 (t, J = 7.2 Hz, 2H), 1.88 (p, J = 7.1, 7.3 Hz, 2H), 1.24 (t, J = 7.2, 6.9 Hz, 3H), 1.05 (t, J = 7.3 Hz, 3H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 173.3, 60.5, 41.2, 36.0, 33.5, 19.1, 14.3, 7.9 ppm.

1-(Pyrrolidin-1-yl) heptane-1,5-dione[12] (compound number **4w):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and pyrrolidine to give the title compound as a yellowish oil (138 mg, 70% yield).



[10] M. S. Chen, M.C. White, *Science*, **2010**, *327*, 566-571.
[11] T. Fischera, J. Pietruszkaa, *Adv. Synth. Catal.,* **2012**, *354*, 2521-2530.

[12] D. A. Oare, M. A. Henderson, M. A. Sanner, C. H. Heathcock, *J. Org. Chem*., **1990**, *55*, 132-157.

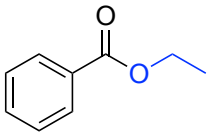
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.43 (dt, J = 6.8 Hz, 4H), 2.52 (t, J = 7.0 Hz, 2H), 2.42 (q, J = 7.3 Hz, 2H), 2.27 (t, J = 7.2 Hz, 2H), 1.96-177 (m, 6H), 1.03 (t, J = 7.3 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 211.7, 171.1, 46.7, 45.7, 41.6, 35.9, 33.8, 26.2, 24.5, 19.1, 7.9 ppm;

IR (KBr) 2969, 2874, 1707, 1620, 1438 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{11}H_{19}NO_2Na$ 220.1308; Found 220.1307.

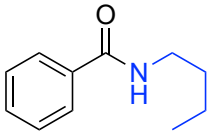
Ethyl benzoate[13] (compound number **4y1**): Prepared according to the general procedure A from (1,3-diphenylpropane-1,3-dione) and ethanol to give the title compound as a colorless oil (80 mg, 53% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2H), 7.56-7.51 (m, 1H), 7.45-7.40 (m, 2H), 4.38 (q, J = 8.0 Hz, 2H), 1.39 (t, J = 8.0 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 132.9, 130.7, 129.6, 128.4, 61.0, 14.4 ppm.

***N*-Butylbenzamide**[14] (compound **4y2**): Prepared according to the general procedure A from (1,3-diphenylpropane-1,3-dione) and *n*-butylamine to give the title compound as a white solid (79 mg, 45% yield).

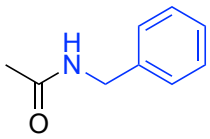


^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (m, 2H), 7.46 (m, 1H), 7.41 (m, 2H), 6.18 (bs, 1H), 3.45 (q, J = 4.0 Hz, 2H), 1.60 (m, 2H), 1.40 (m, 2H), 0.96 (t, J = 8.0 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 135.0, 131.5, 128.7, 127.0, 40.0, 31.9, 20.3, 14.0 ppm.

[13] Jagadeesh, R. V.; Junge, H.; Pohl, M.-M.; Radnik, J.; Brueckner, A.; Beller, M. *J. Am. Chem. Soc.* **2013**, *135*, 10776.
[14] Wang, N.; Zou, X.; Ma, J.; Li, F. *Chem. Commun.* **2014**, *50*, 8303.

***N*-Benzylacetamide**[15] (compound **4z**): Prepared according to the general procedure A from acetoacetone and benzylamine to yield a white solid (80 mg, 54% yield).



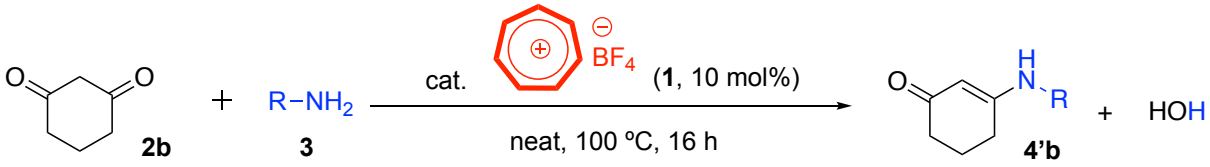
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.25 (m, 5H), 6.52 (bs, 1H), 4.36 (d, J = 4.0 Hz, 2H), 1.96 (s, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 136.1, 128.7 (two coincident resonances), 128.4, 66.5, 21.1 ppm.

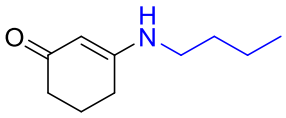
[15] Rao, S. N.; Mohan, D. C.; Adimurthy, S. *Org. Lett.* **2013**, *15*, 1496.

Enamine Formation with 1,3-Cyclohexanediones as Reaction Substrates

Reactions between 1,3-cyclohexanedione (substrate **2b**) and 2-methyl-1,3-cyclohexanedione (substrate **2c**) and amines did not lead to the C-C bond cleavage but form the enamine condensation products **4'b** and **4c'** instead. This difference in reactivity between amines and alcohol substrates (see *retro*-Claisen products **4p**-**4r** above) could be attributed to the relative stability of these conjugated enamine products under the reaction conditions.



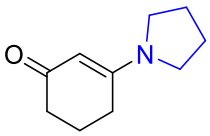
3-(*n*-Butylamino)cyclohex-2-enone[16] **(**compound number **4'b1):** Prepared using the general procedure A from (1,3-cyclohexanedione) and *n*-butyl amine to give the title compound as a yellow oil (136 mg, 81% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (s, 1H), 4.43 (s, 1H), 3.09 (q, J = 7.0, 5.5 Hz, 2H), 2.31 (t, J = 6.5 Hz, 4H), 1.96 (p, J = 6.2 Hz, 2H), 1.60-1.53 (m, 2H), 1.41-1.32 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 97.1, 42.8, 36.5, 30.7, 22.1, 20.3, 13.8 ppm.

3-(Pyrrolidin-1-yl)cyclohex-2-enone[17] **(**compound number **4'b2):** Prepared using the general procedure A from (1,3-cyclohexanedione) and pyrrolidine to give the title compound as a yellow oil (104 mg, 63% yield).

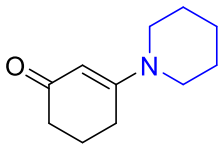


^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (s, 1H), 3.45 (t, J = 5.3 Hz, 2H), 3.22 (t, J = 5.5 Hz, 2H), 2.44 (t, J = 6.2 Hz, 2H), 2.28 (t, J = 6.3 Hz, 2H), 1.99-1.95 (m, 6H) ppm;

[16] D. Bhattacherjee, V. Thakur, A. K. Shil, P. Das, *Adv. Synth. Catal.*, **2017**, *359*, 2202-2208.
[17] J. Zhang, Q. Jiang, D. Yang, X. Zhao, Y. Dong, R. Liu, *Chem. Sci.*, **2015**, *6*, 4674-4680.

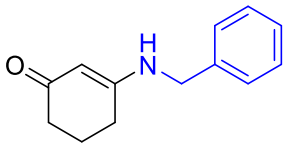
^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 90.6, 49.7, 49.4, 27.8, 25.0, 24.6, 20.6 ppm.

3-(Piperidin-1-yl)cyclohex-2-enone[18] (compound number **4'b3):** Prepared using the general procedure A from (1,3-cyclohexanedione) and piperidine to give the title compound as a yellow oil (135 mg, 75% yield).

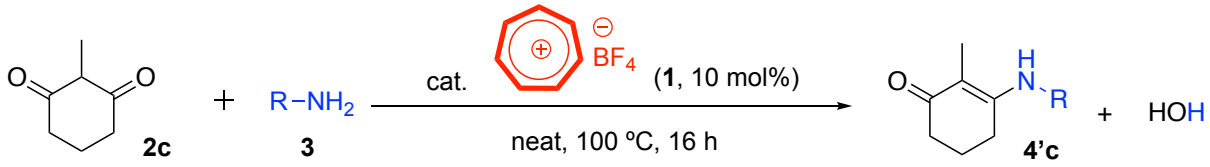


^{1}H NMR (400 MHz, $CDCl_3$) δ 5.29 (s, 1H), 3.33 (t, J = 5.3 Hz, 4H), 2.40 (t, J = 6.2 Hz, 2H), 2.28 (t, J = 6.0, 6.8 Hz, 2H), 1.98 (p, J = 6.2, 6.4 Hz, 2H), 1.68-1.56 (m, 6H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 194.7, 99.5, 47.7, 35.6, 27.2, 25.6, 24.5, 22.4 ppm.

3- (Benzylamino)cyclohex-2-enone[9] (compound number **4'b4):** Prepared using the general procedure A from (1,3-cyclohexanedione) and benzylamine to give the title compound as a yellow oil (152 mg, 73% yield).



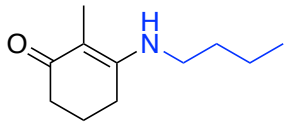
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.17 (m, 5H), 5.91 (s, 1H), 5.05 (s, 1H), 4.14 (d, J = 5.3 Hz, 2H), 2.33 (t, J = 6.2 Hz, 2H), 2.18 (t, J = 6.3 Hz, 2H), 1.86 (q, J = 6.5, 6.2 Hz, 2H) ppm;
^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 165.2, 136.9, 128.8, 128.6, 127.7, 96.9, 47.1, 36.3, 29.5, 21.9 ppm.



2c **3** **4'c**

[18] K. C. Kreß, T. Fischer, J. Stumpe, W. Frey, M. Raith, O. Beiraghi, S. H. Eichhorn, S. T. ger, S. Laschat, *ChemPlusChem,* **2014**, *79*, 223-232.

3-(butylamino)-2-methylcyclohex-2-en-1-one (compound number **4c'1):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and *n*-butyl amine to give the title compound as a white solid (169 mg, 93% yield).



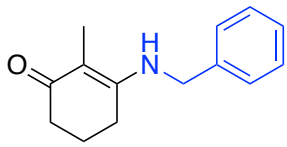
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42 (s, 1H), 3.26 (q, J = 7.0, 6.0 Hz, 2H), 2.44 (t, J = 6.2, Hz, 2H), 2.31 (t, J = 6.4, 6.7 Hz, 2H), 1.93 (p, J = 6.5 Hz, 2H), 1.69 (s, 3H), 1.61-153 (m, 4H), 1.44-1.35 (m, 2H), 0.96 (t, J = 7.3, Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.5, 161.5, 104.4, 43.1, 36.2, 32.9, 25.4, 21.4, 20.1, 13.9, 7.6 ppm;

IR (KBr) 2935, 2868, 1731, 1612, 1418 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{11}H_{19}NONa$ 204.1359; Found 204.1357.

3-(benzylamino)-2-methylcyclohex-2-en-1-one (compound number **4c'2):** Prepared using the general procedure A from (2-methyl-1,3-cyclohexanedione) and benzylamine to give the title compound as a (150 mg, 70% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 5.91 (s, 1H), 4.43 (d, J = 5.7 Hz, 2H), 2.45 (t, J = 7.0 Hz, 2H), 2.21(t, J = 7.0 Hz, 2H), 2.12 (s, 3H), 1.68-1.56 (m, 4H) ppm;

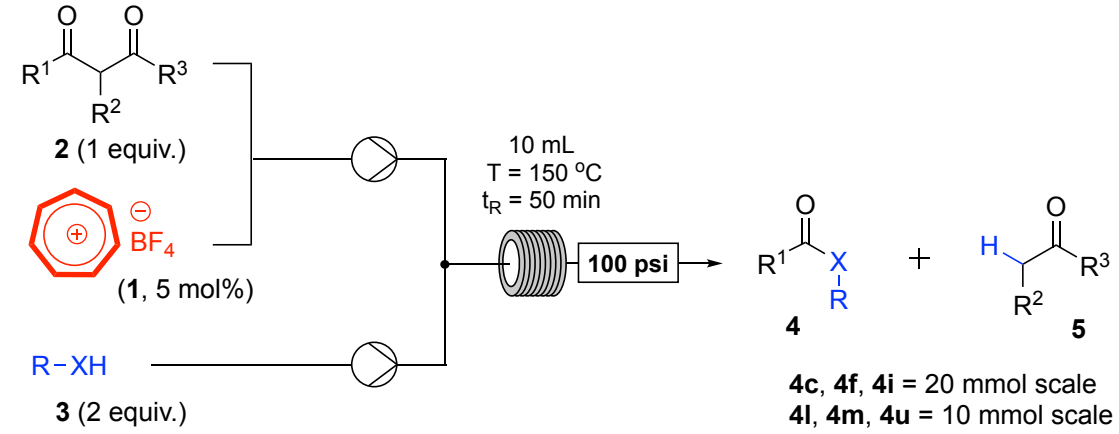
^{13}C NMR (100 MHz, $CDCl_3$) δ 2.8.9, 172.6, 138.5, 128.7, 127.9, 127.5, 43.7, 43.4, 36.4, 30.0, 25.5, 23.3 ppm;

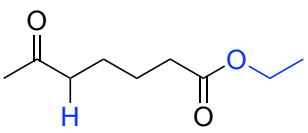
IR (KBr) 3061, 2938, 2861, 1708, 1655, 1530, 1449, 1403 cm^{-1};

HRMS (ESI+) m/z: $[M+H]^+$ Calcd. for $C_{14}H_{18}NO$ 216.1383; Found 216.1381.

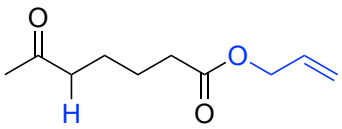
General Procedure for the *retro*-Claisen Reactions in Continuous Flow

Flow reactions were conducted on a Vapourtec R-Series flow reactor.

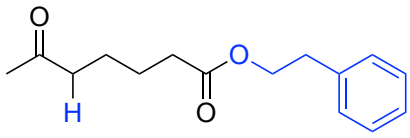




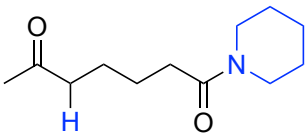
4c (93%, 3.20 g)



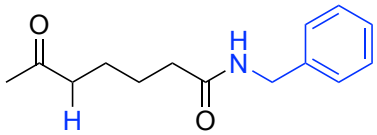
4f (91%, 3.35 g)



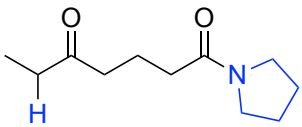
4i (84%, 4.16 g)



4l (84%, 1.76 g)



4m (81%, 1.89 g)



4u (78%, 1.54 g)

Optimization of catalyst loading for flow chemistry: The *retro*-Claisen ethanolysis reactions of substrate **2a** to form **4c** with 10, 5 and 2.5 mol% tropylium tetrafluoroborate in flow indicated that 5 mol% catalyst loading is optimal for the reaction.

Catalyst loading	Yield of **4c**	
10 mol%	97%	
5 mol%	95% (at 1 mmol scale)	93% (at 20 mmol scale)
2.5 mol%	88%	

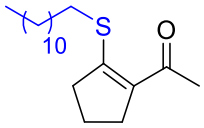
Reaction conditions:

A solution of diketone **2** (1.0 equiv) and tropylium tetrafluoroborate **1** (0.05 equiv, 5 mol%) in TFE (0.5 M, solution #1) and a solution of nucleophile **3** (2.0 equiv) in TFE (1 M, solution #2) were prepared as stock solutions. The flow system was fitted with a high temperature 10

mL tube reactor and a (8 + 8 = 16) bar back-pressure regulator and the entire reactor was flushed with TFE. The solution of reagents was injected at flow rates corresponding to the residence time of 30 minutes (pump #1 for solution #1: 0.33 mL/min, pump #2: 0.33 mL/min). The resulting reaction mixture was collected and concentrated under reduced pressure before being worked up in similar fashion to batch reactions.

Dehydrative Thiolation of 1,3-Diketones with Thiols

1-(2-(Dodecylthio)cyclopent-1-en-1-yl)ethan-1-one (compound number **8a):** Prepared using the general procedure A from (2-acetylcyclopentanone) and 1-dodecanethiol to give the title compound as a yellow oil (216 mg, 69% yield).



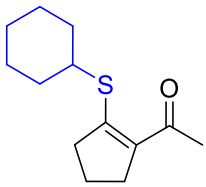
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81(t, J = 7.4 Hz, 4H), 2.72 (t, J = 7.6, 7.2 Hz, 2H), 2.20 (s, 3H), 1.97 (p, J = 7.5 Hz, 2H), 1.61 (p, J = 7.2, 7.6 Hz, 2H), 1.41-1.24 (m, 20H), 0.87 (t, J = 7.0, 6.5 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 157.1, 131.9, 37.4, 33.9, 32.0, 31.9, 29.9, 29.8, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.0, 22.8, 22.6, 14.2 ppm;

IR (KBr) 2921, 2851, 1645, 1525, 1461, 1425 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{19}H_{34}OSNa$ 333.2223, Found 333.2220.

1-(2-(Cyclohexylthio)cyclopent-1-en-1-yl)ethan-1-one (compound number **8b):** Prepared using the general procedure A from (2-acetylcyclopentanone) and cyclohexyl thiol to give the title compound as a yellowish liquid (183 mg, 82% yield).



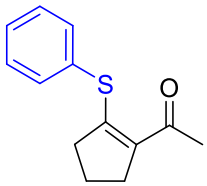
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (tt, J = 3.4, 3.6, 3.9 Hz, 1H), 2.86 (t, J = 7.6, 7.4 Hz, 2H), 2.71 (t, J = 7.5, 7.2 Hz, 2H), 2.22 (s, 3H), 1.96 (t, J = 7.4 Hz, 4H), 1.80 (dt, J = 3.7 Hz, 2H), 1.70-1.50 (t, J = 4.3 Hz, 2H), 1.47-1.18 (s, 4H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.7, 155.9, 132.3, 44.3, 37.3, 34.7, 33.8, 29.7, 26.2, 25.5, 22.7 ppm;

IR (KBr) 2925, 2849, 1698, 1642, 1522, 1429 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{13}H_{20}OSNa$ 247.1127, Found 247.1129.

1-(2-(Phenylthio)cyclopent-1-en-1-yl)ethan-1-one (compound number **8c):** Prepared using the general procedure A from (2-acetylcyclopentanone) and thiophenol to give the title compound as a yellow oil (155 mg, 71% yield).



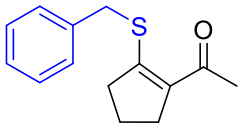
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.51 (m, 2H), 7.39-7.31 (m, 3H), 2.78-2.73 (m, 2H), 2.50-2.25 (tt, J = 1.9 Hz, 2H), 2.25 (s, 3H), 1.83 (p, J =7.4 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.9, 156.5, 135.2, 132.1, 131.7, 129.3, 129.0, 38.7, 34.2, 29.3, 22.4 ppm;

IR (KBr) 2947, 2845, 1647, 1530 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{13}H_{14}OSNa$ 241.0663, Found 241.0658.

1-(2-(Benzylthio)cyclopent-1-en-1-yl)ethan-1-one (compound number **8d):** Prepared using the general procedure A from (2-acetylcyclopentanone) and benzyl mercaptan to give the title compound as a brown liquid (200 mg, 86% yield).



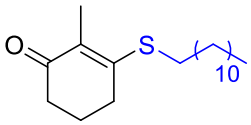
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.24 (m, 5H), 4.08 (s, 2H), 2.84 (tt, J = 1.7 Hz, 2H), 2.73 (tt, J = 1.7, 1.9, 1.8 Hz, 2H), 2.21 (s, 3H), 1.97 (p, J = 7.7, 7.4, 7.5 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 156.4, 137.1, 132.0, 128.8, 128.7, 127.3, 37.5, 36.6, 33.6, 29.3, 22.5 ppm;

IR (KBr) 2920, 2916, 2850, 1629, 1564, 1457, cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{16}OSNa$ 255.0820, Found 255.0813.

3-(Dodecylthio)-2-methylcyclohex-2-en-1-one (compound number **8e):** Prepared using the general procedure A from (2-methylcyclohexane-1,3-dione) and 1-dodecanethiol to give the title compound as a white solid (186 mg, 60% yield).



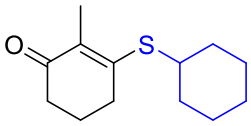
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84 (t, J = 7.4 Hz, 2H), 2.61 (td, J = 1.6 Hz, 2H), 2.39 (t, J = 6.1, 7.1 Hz, 2H), 2.01(p, J = 6.4, 6.2, 6.3 Hz, 2H), 1.84 (t, J = 1.6 Hz, 3H), 1.63 (p, J = 7.0, 7.5, 7.6 Hz, 2H), 1.43-1.26 (m, 18H), 0.87 (t, J = 6.7, 7.0 Hz, 3H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 194.7, 158.3, 129.6, 36.9, 31.9, 30.8, 29.9, 30.0, 29.7, 29.6, 29.5, 29.4, 29.2, 29.0, 28.8, 22.8, 22.7, 14.2, 11.9 ppm;

IR (KBr) 2916, 2850, 1629, 1564, 1457 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{19}H_{34}OSNa$ 333.2223, Found 333.2221.

3-(Cyclohexylthio)-2-methylcyclohex-2-en-1-one (compound number **8f):** Prepared using the general procedure A from (2-methylcyclohexane-1,3-dione) and cyclohexyl thiol to give the title compound as a yellow oil (175 mg, 78% yield).



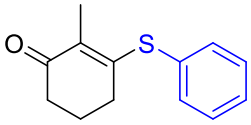
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17-3.10 (m, 1H), 2.16 (td, J = 1.6, 1.5, 1.6 Hz, 2H), 2.35 (t, J = 6.1, 7.1 Hz, 2H), 1.99-188 (m, 4H), 1.80 (t, J = 1.6 Hz, 3H), 1.78-1.73 (m, 2H), 1.61-1.17 (m, 6H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 157.8, 130.3, 43.3, 37.1, 34.4, 29.3, 26.0, 25.4, 22.9, 12.1 ppm;

IR (KBr) 2927, 2851, 1712, 1686, 1566, 1446 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{13}H_{20}OSNa$ 247.1127, Found 247.1126.

2-Methyl-3-(phenylthio)cyclohex-2-en-1-one (compound number **8g):** Prepared using the general procedure A from (2-methylcyclohexane-1,3-dione) and thiophenol to give the title compound as a yellowish solid (175 mg, 80% yield).



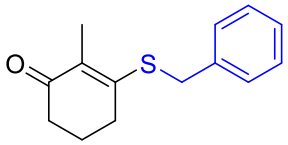
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.41-7.35 (m, 3H), 2.36 (t, J = 6.2, 7.0 Hz, 2H), 2.19-214 (m, 2H), 1.95 (t, J = 1.7 Hz, 3H), 1.90-1.70 (p, J = 6.3, 6.7, 6.2, 6.0 Hz, 2H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 157.8, 135.5, 130.2, 130.1, 129.5, 129.4, 37.2, 30.4, 22.8, 12.3 ppm;

IR (KBr) 3281, 3054, 2940, 1756, 1650, 1574, 1474, 1437 cm^{-1};

HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{13}H_{14}OSNa$ 241.0663, Found 241.0657.

3-(Benzylthio)-2-methylcyclohex-2-en-1-one (compound number **8h):** Prepared using the general procedure A from (2-methylcyclohexane-1,3-dione) and benzyl mercaptan to give the title compound as a yellow oil (179 mg, 72% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.10 (s, 2H), 2.60 (td, J = 1.4, 1.2 Hz, 2H), 2.37 (t, J = 6.3, 7.0 Hz, 2H), 1.98 (p, J = 6.3, 6.4, 6.2 Hz, 2H) 1.85 (s, 3H) ppm;

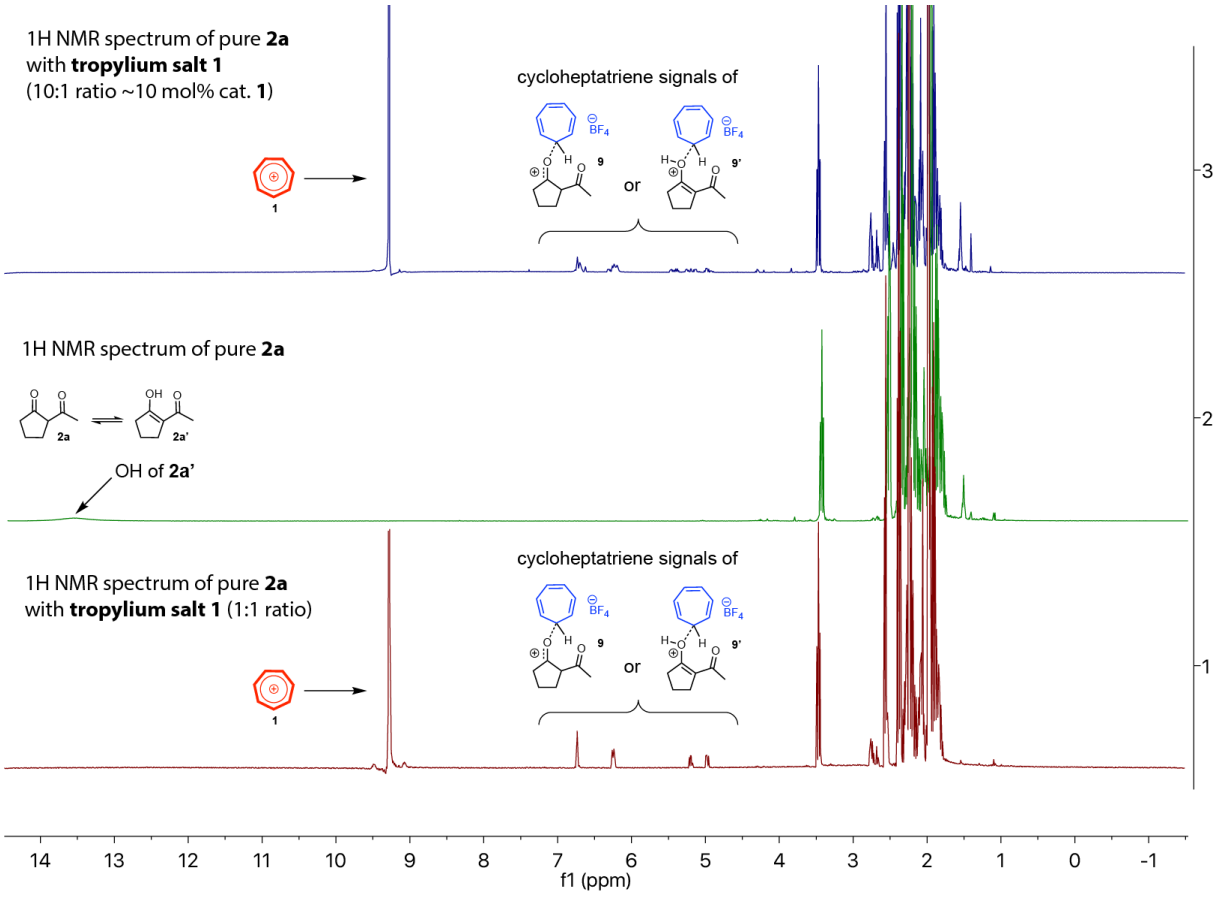
^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 157.5, 136.4, 130.0, 128.9, 128.8, 127.7, 36.9, 35.6, 29.5, 22.7, 12.0 ppm;

IR (KBr) 2939, 1640, 1569, 1493, 1424 cm^{-1};

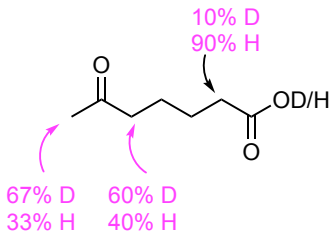
HRMS (ESI+) m/z: $[M+Na]^+$ Calcd. for $C_{14}H_{16}OSNa$ 255.0820, Found 255.0816.

Mechanistic NMR Studies

^{1}H NMR studies of mixtures of substrate **2a** (2-acetylcyclopentanone) and tropylium tetrafluoroborate (**1**) in 1:1 ratio or 10:1 ratio (equal to the typical catalyst loading of 10 mol% of **1** in retro-Claisen reactions) both showed clear evidence of the coordination of tropylium ion to **2a**.



Deuterated 6-oxoheptanoic acid (compound number **4aD):** Prepared using the general procedure A from (2-acetylcyclopentanone) and deuterium oxide to give the title compound as a colorless oil (128 mg, ~88% yield, accurate yield cannot be determined).

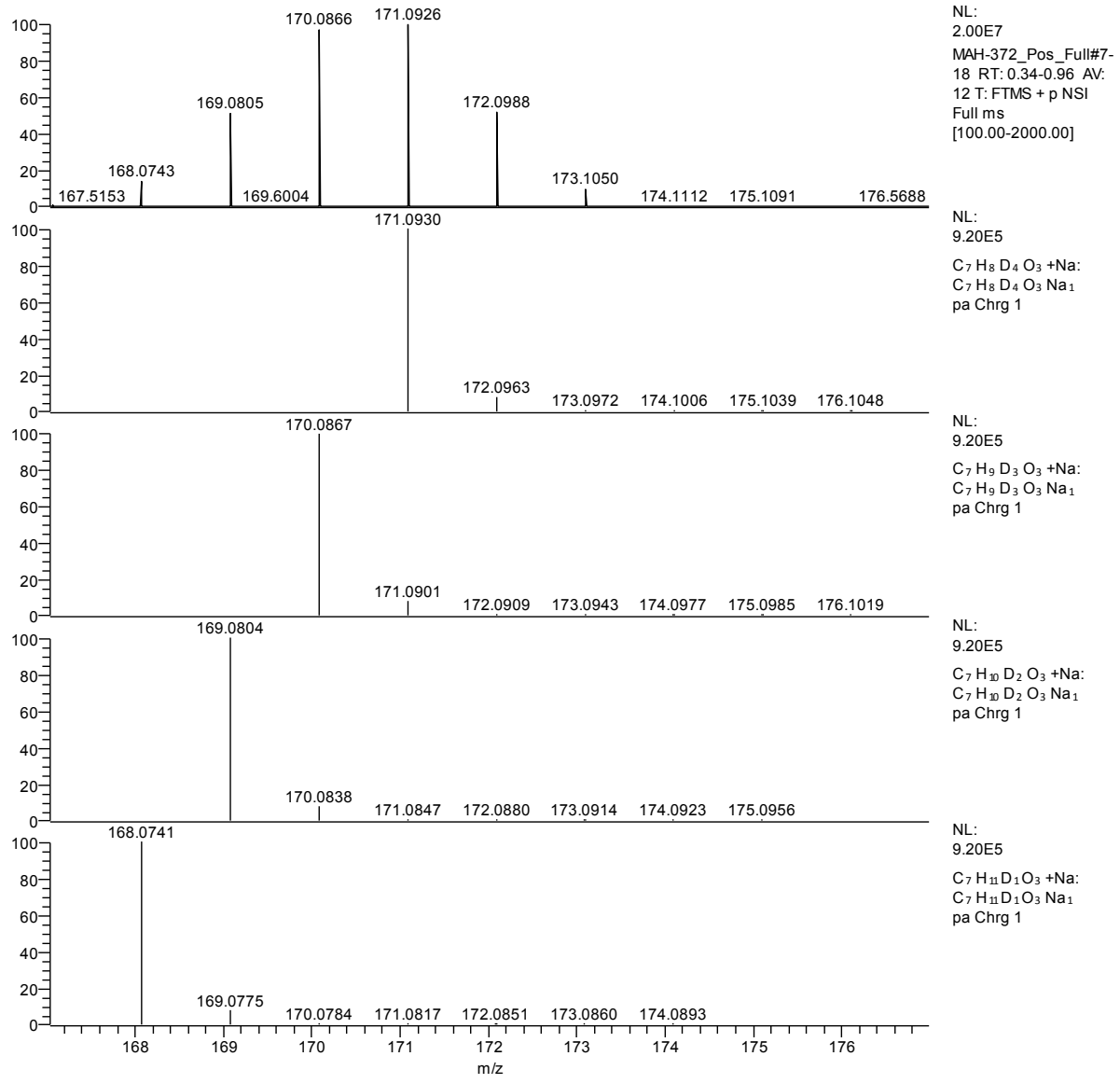


^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47-2.33 (m, 2.6H), 2.13-2.09 (m, 1H), 1.67-1.60 (m, 4H) ppm;

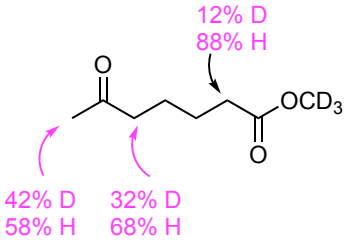
^{13}C NMR (100 MHz, $CDCl_3$) δ 209.1, 179.6, 43.3, 43.1, 42.9, 42.7, 42.5, 42.3, 42.2, 33.9, 33.8, 33.7, 33.6, 33.4, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 24.1, 24.1, 24.0, 23.1, 23.0, 22.1 ppm

IR (KBr) 2937, 2870, 1699, 1456, 1407 cm^{-1};

HRMS (ESI+) m/z: See spectrum below.



Deuterated d_3-ethyl 6-oxoheptanoate (compound number **4bD):** Prepared using the general procedure A from (2-acetylcyclopentanone) and deuterated methanol to give the title compound as a colorless oil (122 mg, ~74% yield, accurate yield cannot be determined).

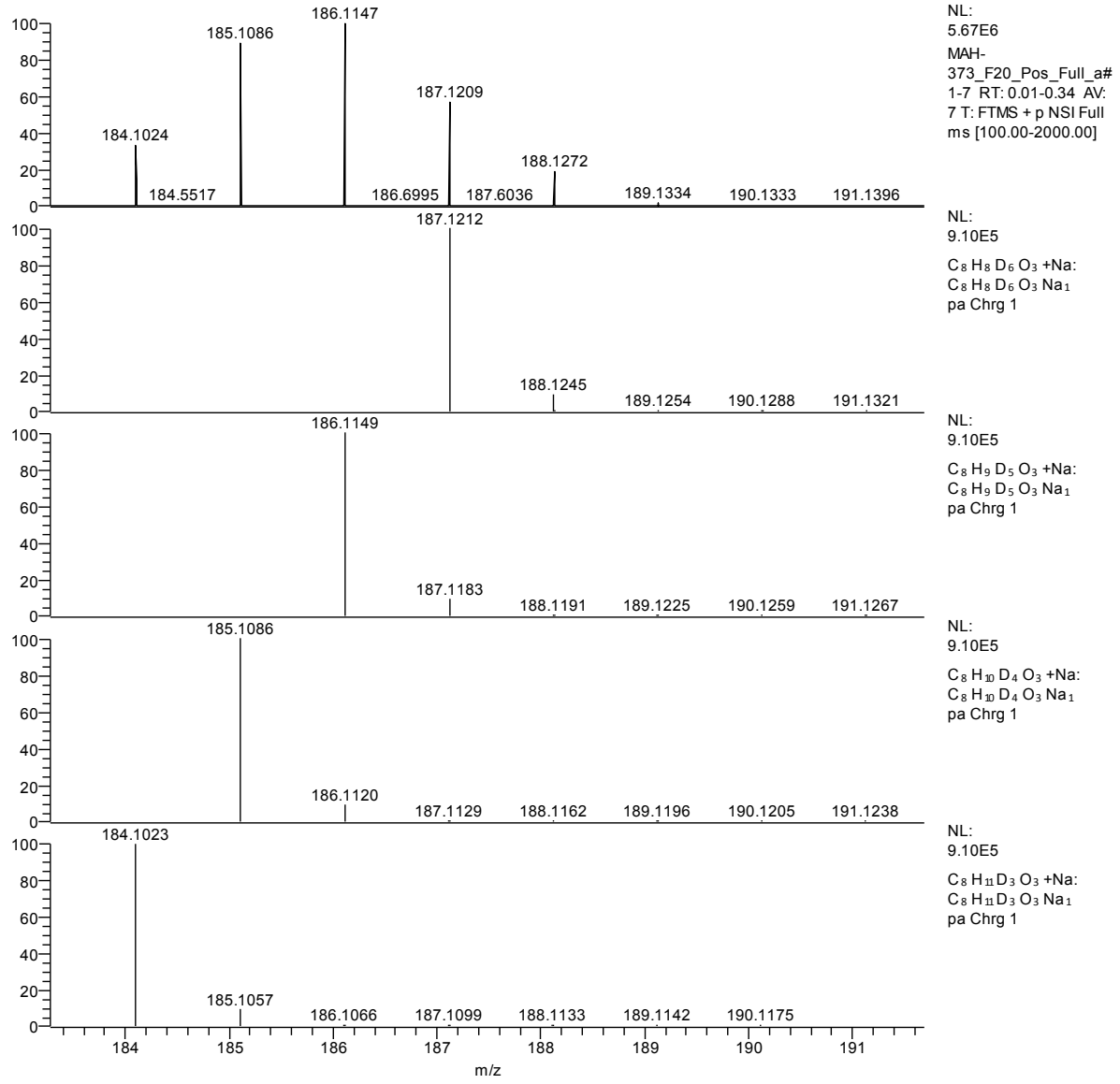


^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50-2.30 (m, 3.1H), 2.13-2.09 (m, 1.8H), 1.62-1.58 (m, 4H) ppm;

^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 208.6, 208.5, 208.5, 173.9, 51.3, 51.0, 50.8, 50.6, 50.4, 43.3, 43.1, 42.1, 42.7, 42.5, 42.4, 33.9, 33.8, 33.7, 33.5, 33.3, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 29.2, 29.0 ppm

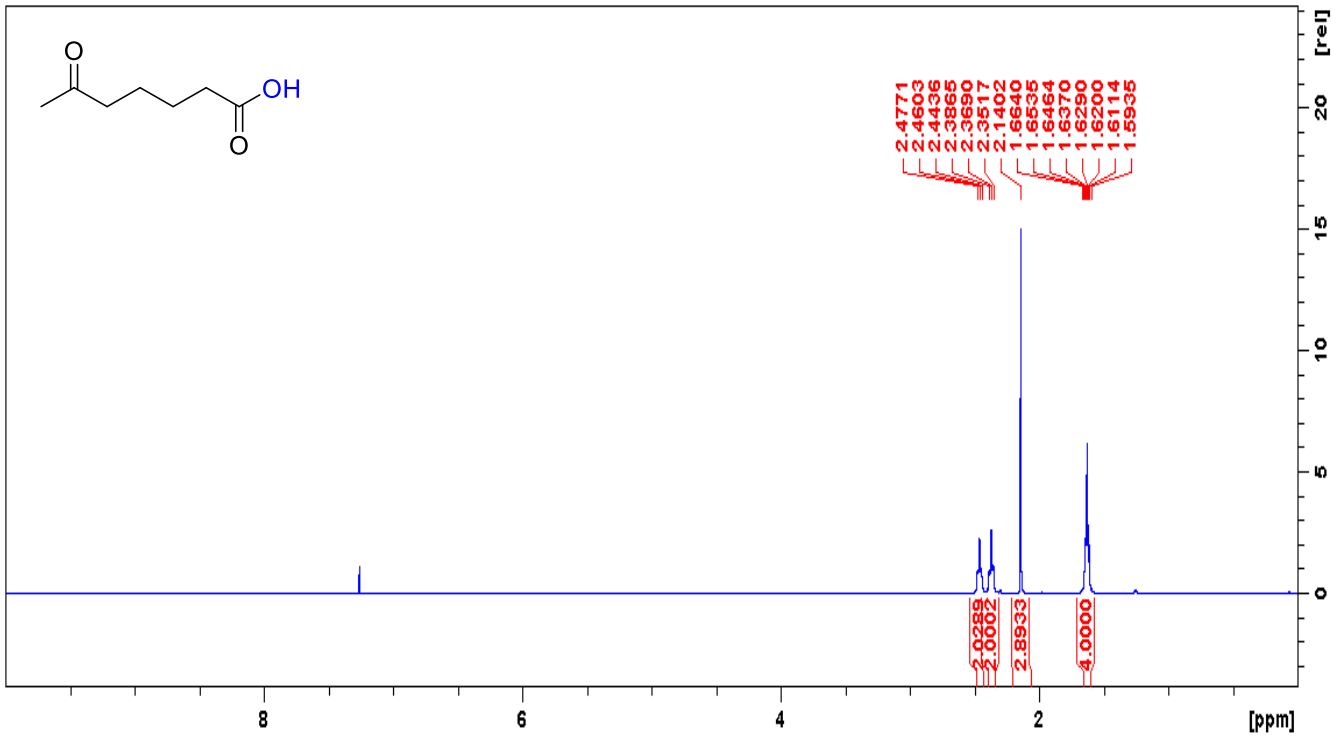
IR (KBr) 2924, 2864, 1731.7, 1664, 1510, 1444, 1426 cm^{-1};

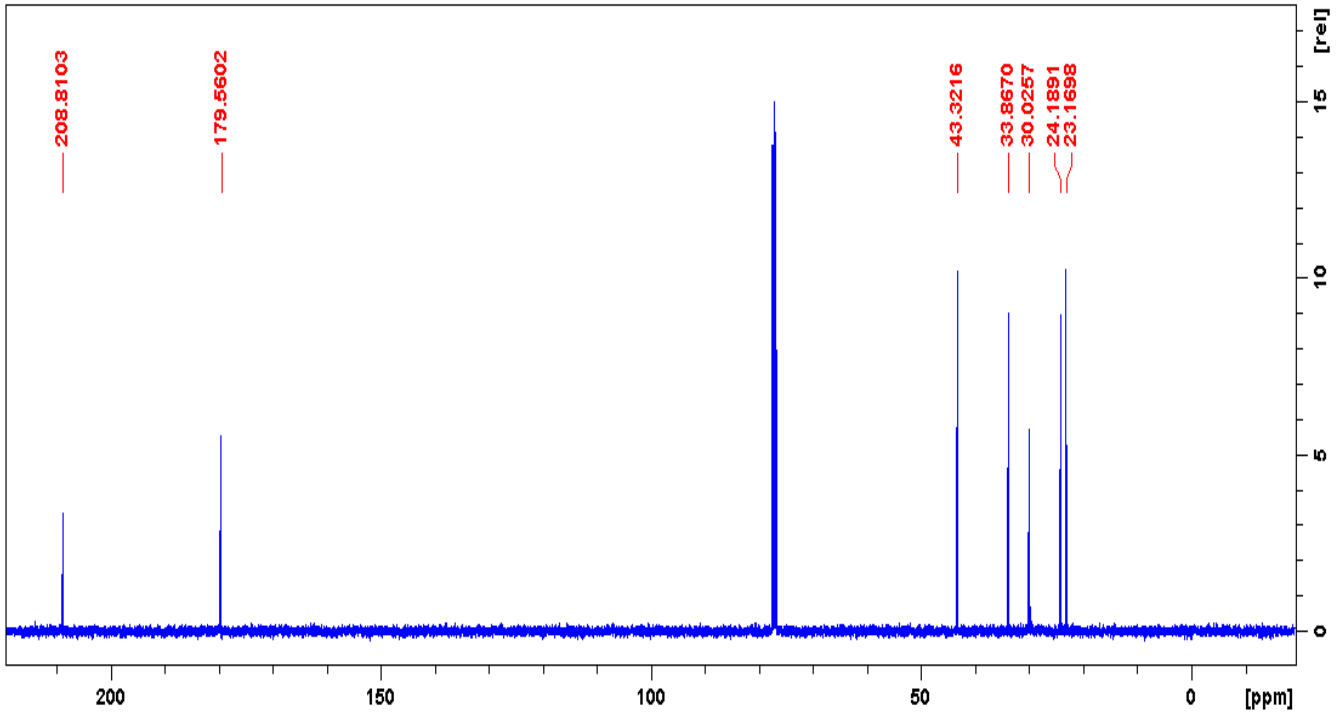
HRMS (ESI+) m/z: See spectrum below.



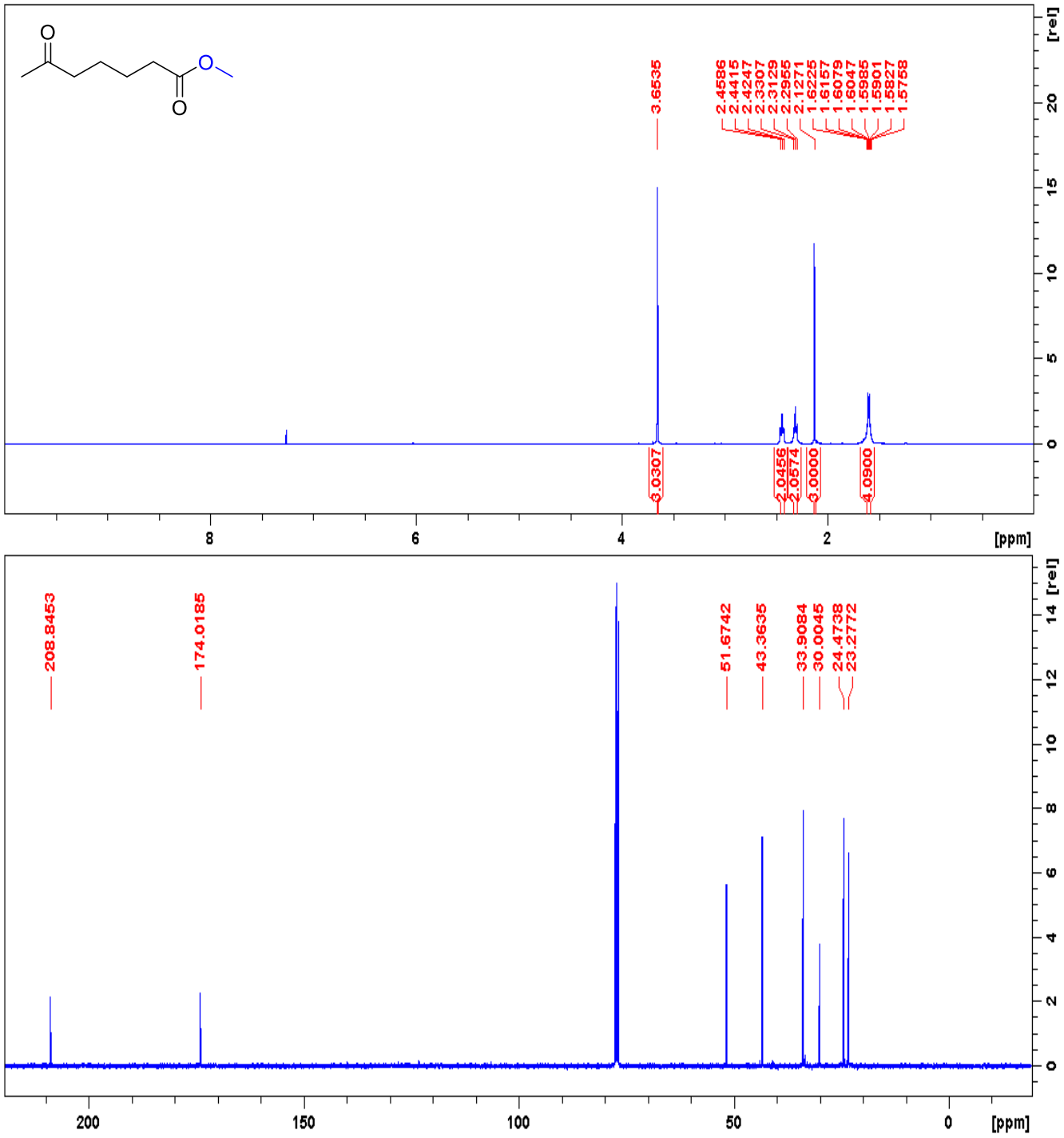
NMR Spectra

6-Oxoheptanoic acid **(4a)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

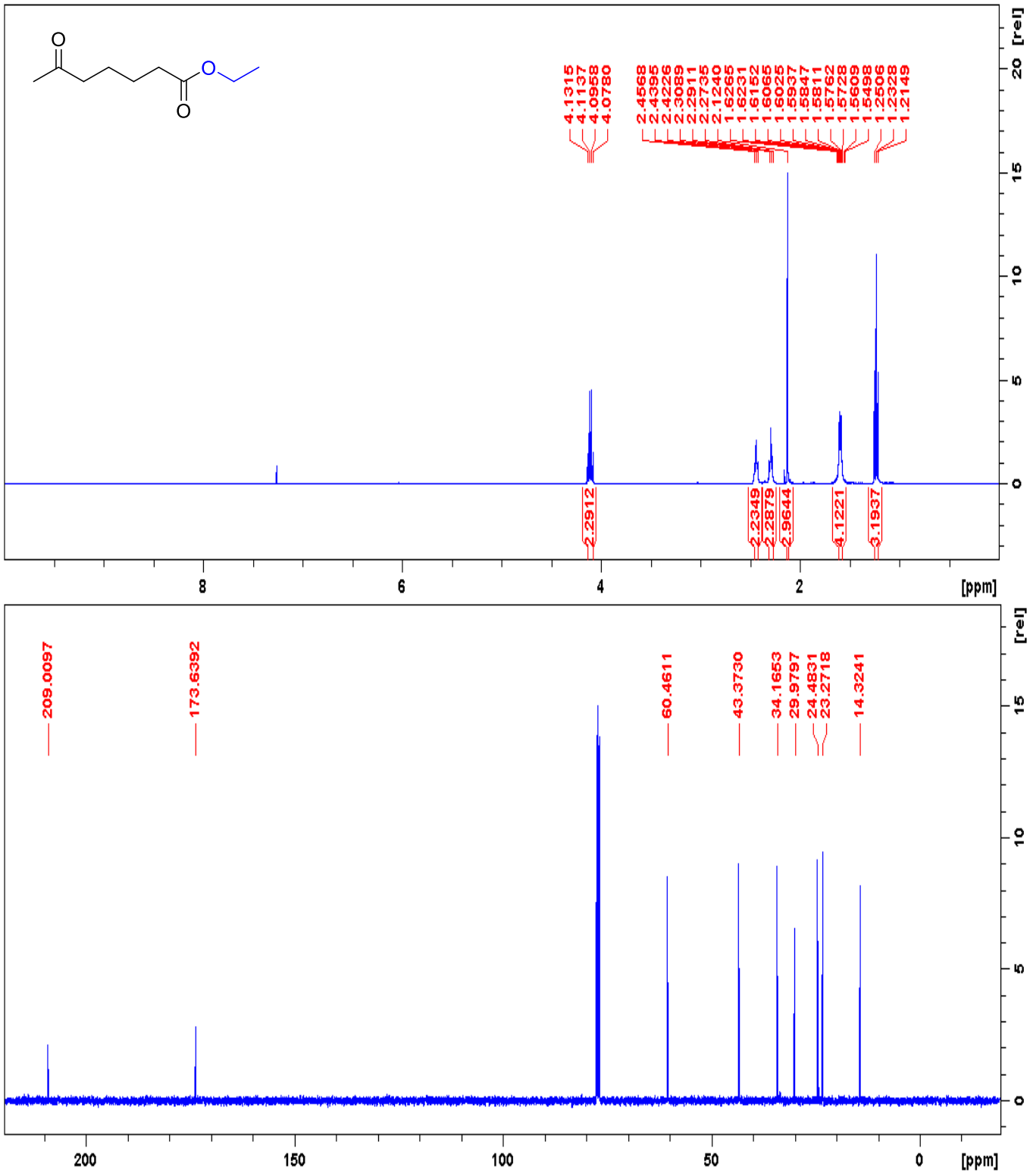




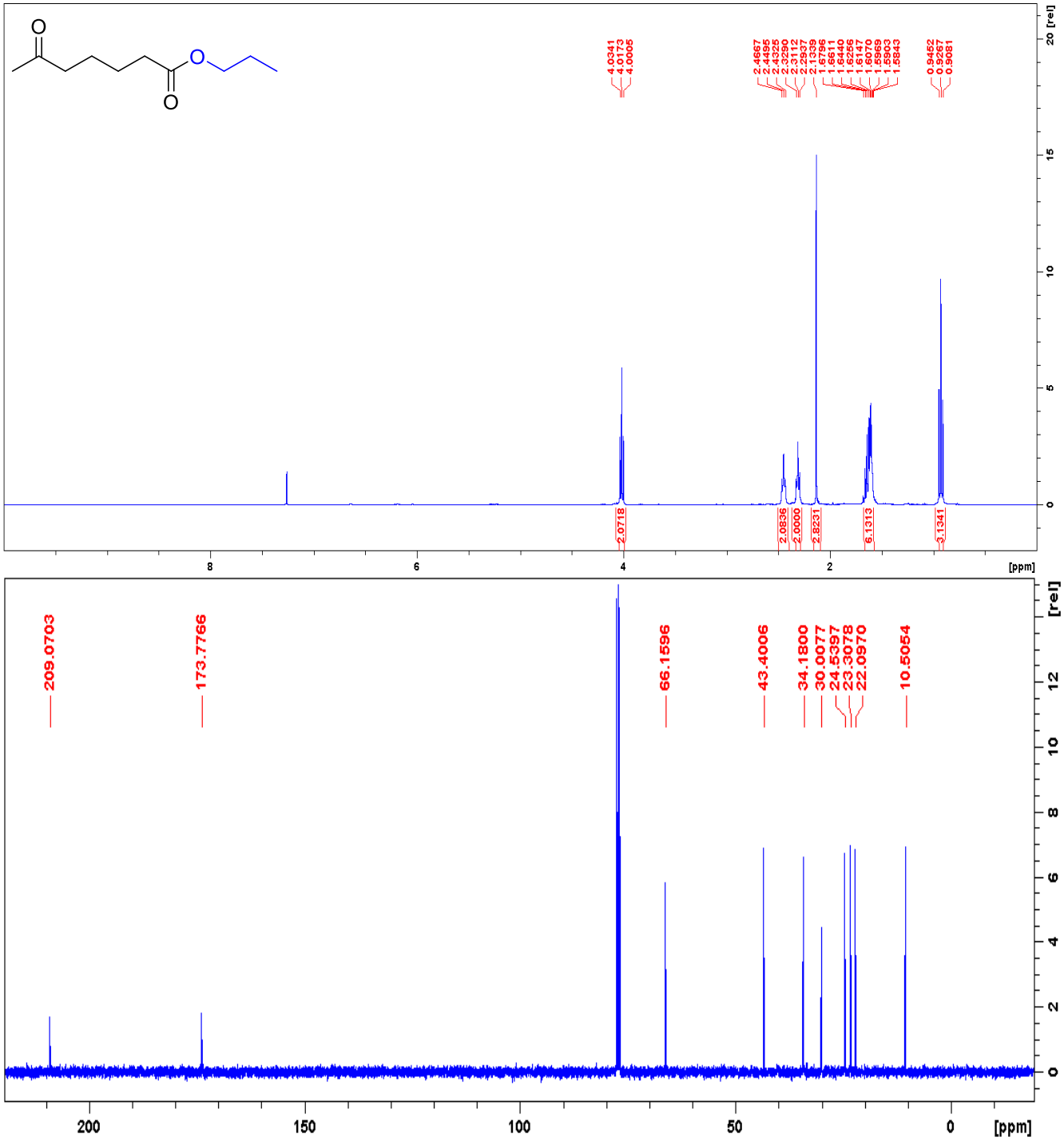
Methyl 6-oxo-heptanoato **(4b)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



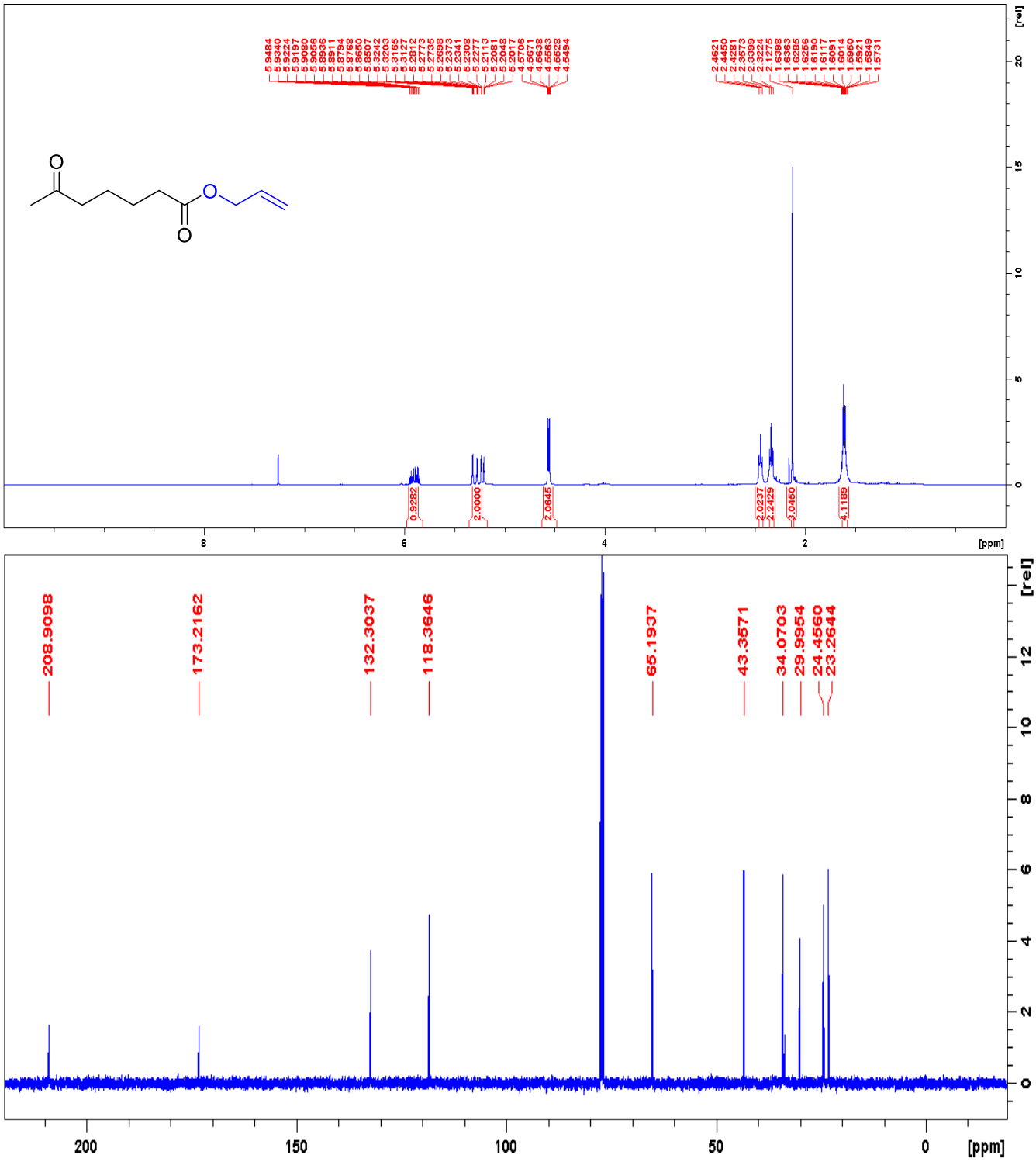
Ethyl 6-oxo-heptanoate **(4c)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



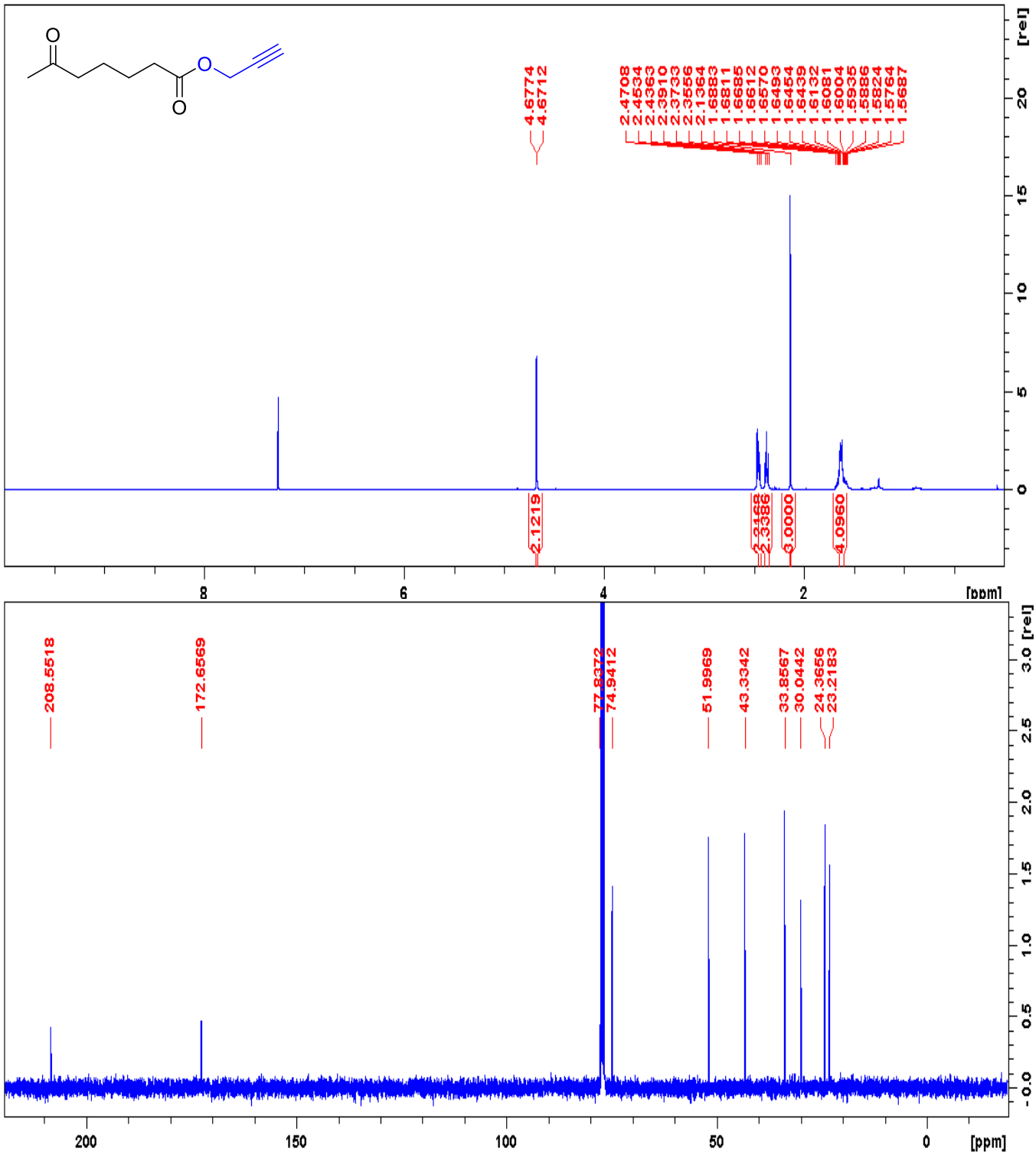
Propyl 6-oxoheptanoate **(4d)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



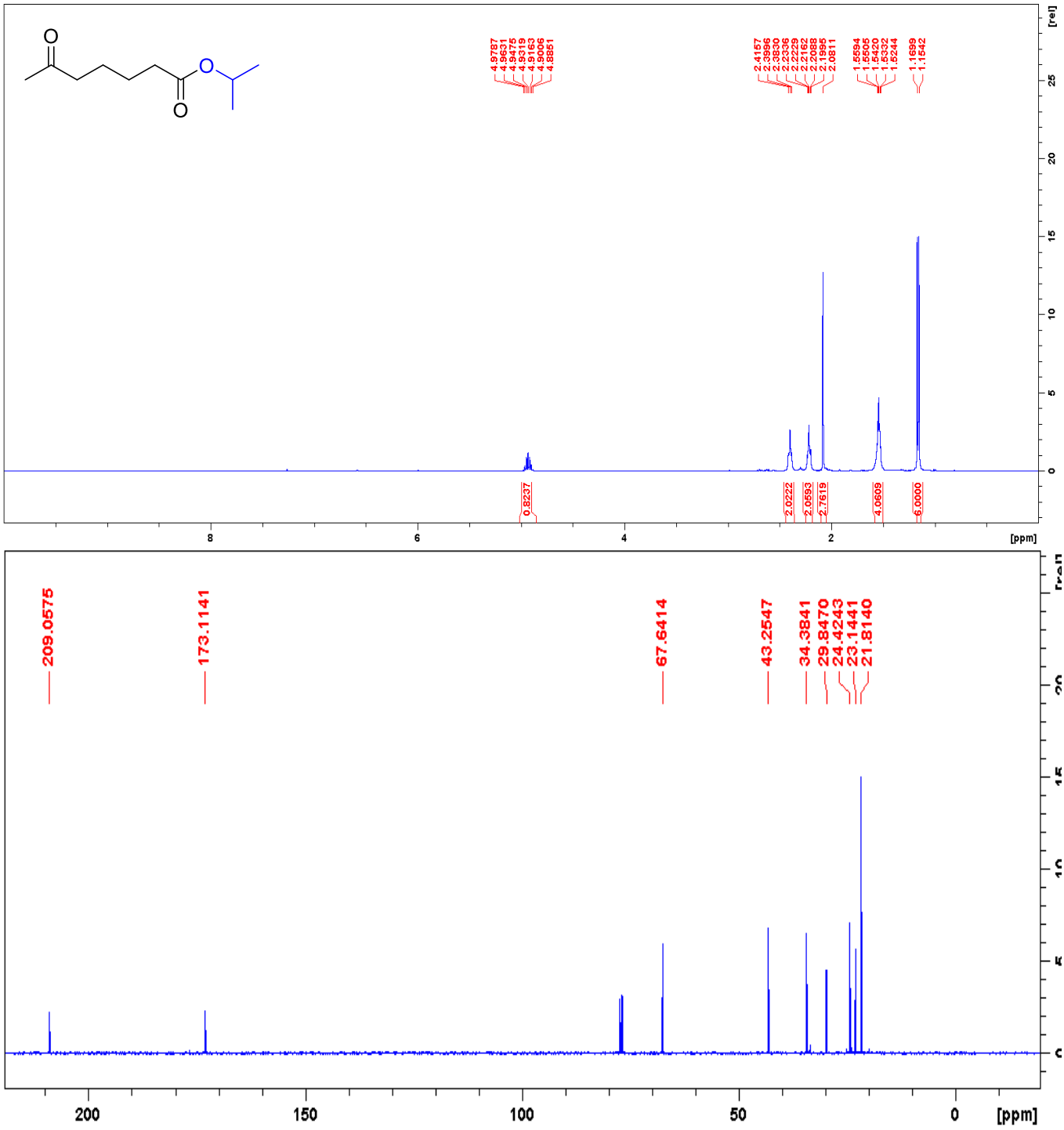
Allyl 6-oxoheptanoate **(4e)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



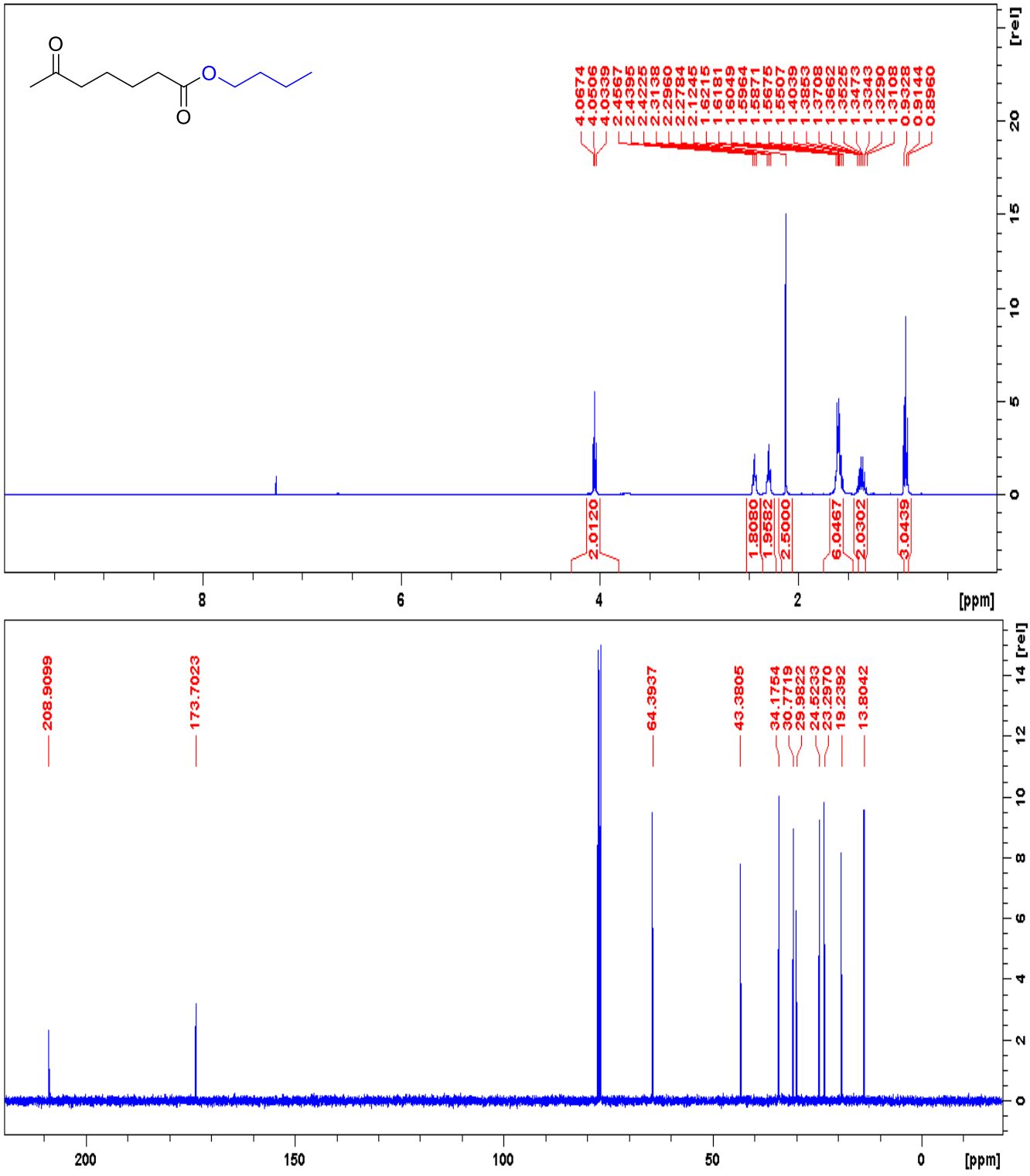
Prop-2-ynyl 6-oxoheptanoate **(4f)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



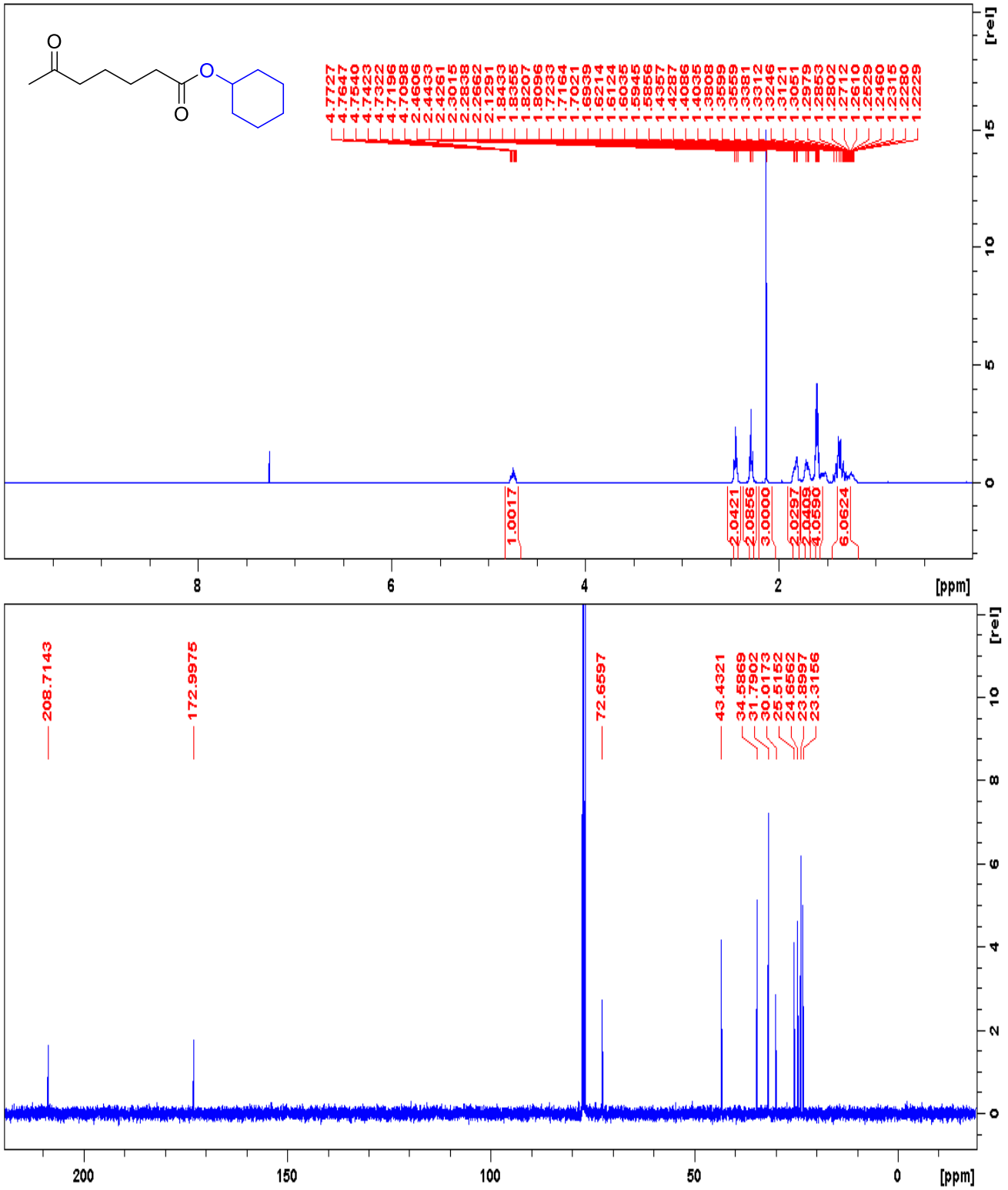
Isopropyl 6-oxoheptanoate **(4g)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



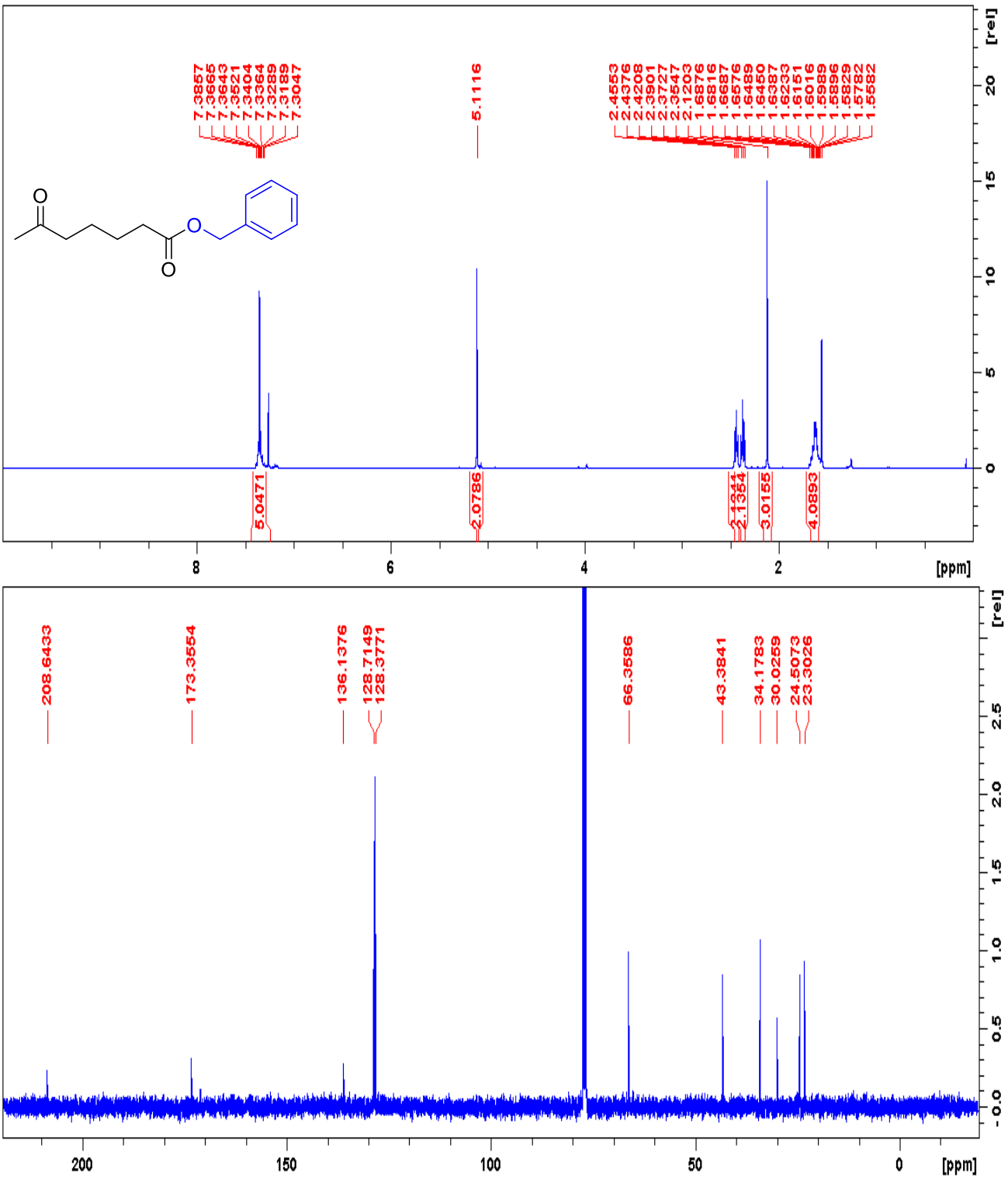
Butyl 6-oxoheptanoate **(4h)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



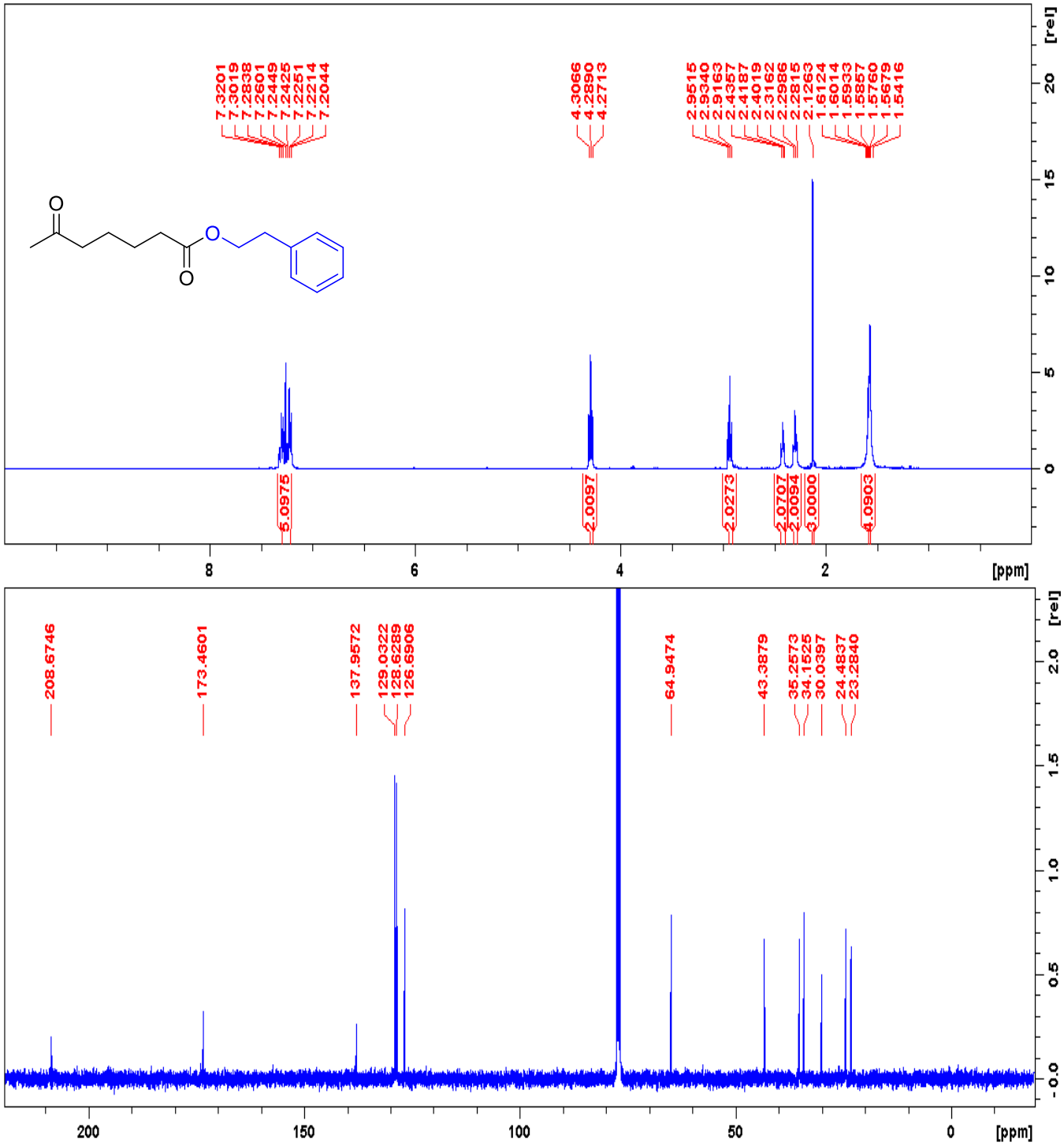
Cyclohexyl 6-oxoheptanoate **(4i)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



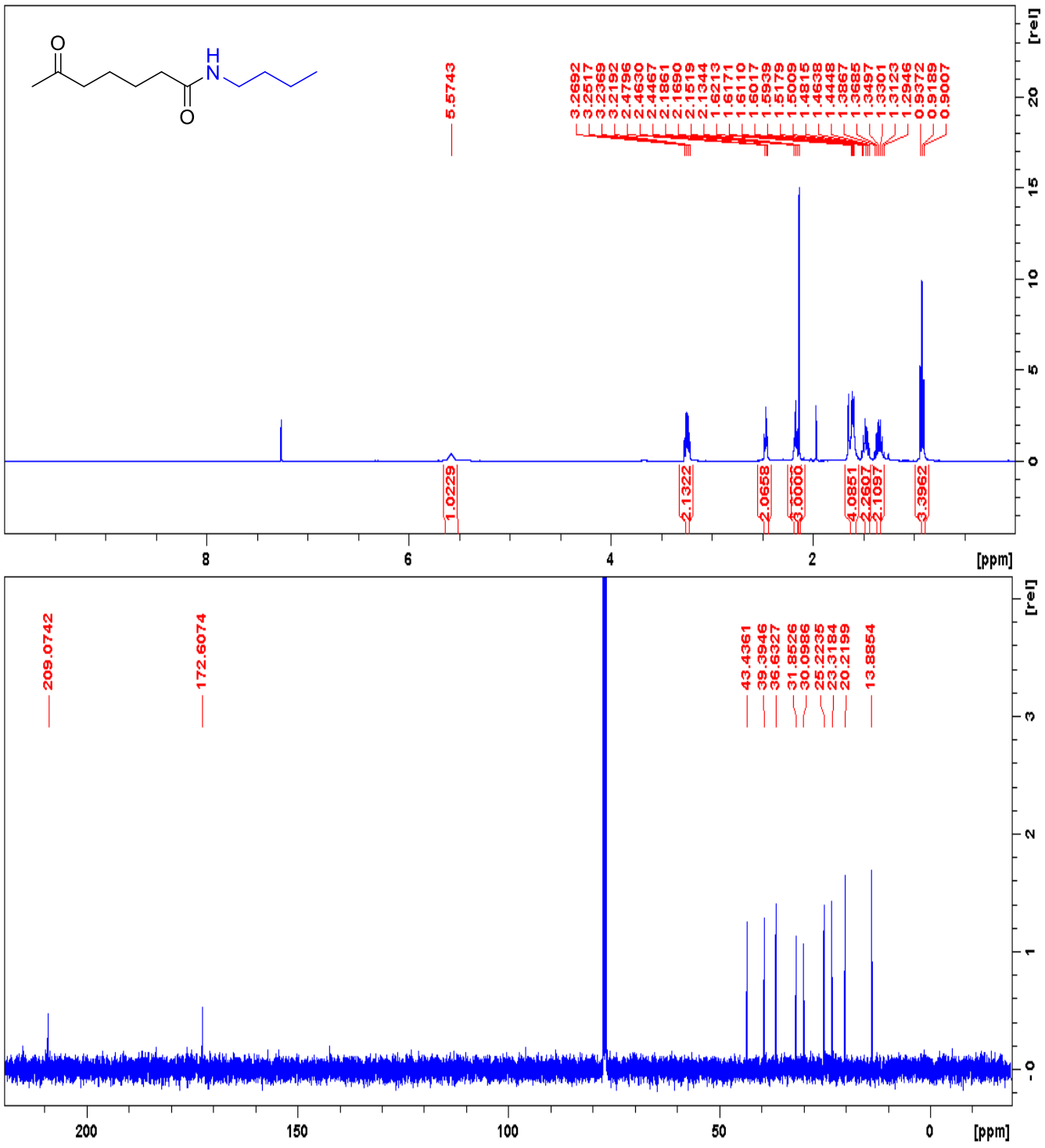
Benzyl 6-oxoheptanoate **(4j)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



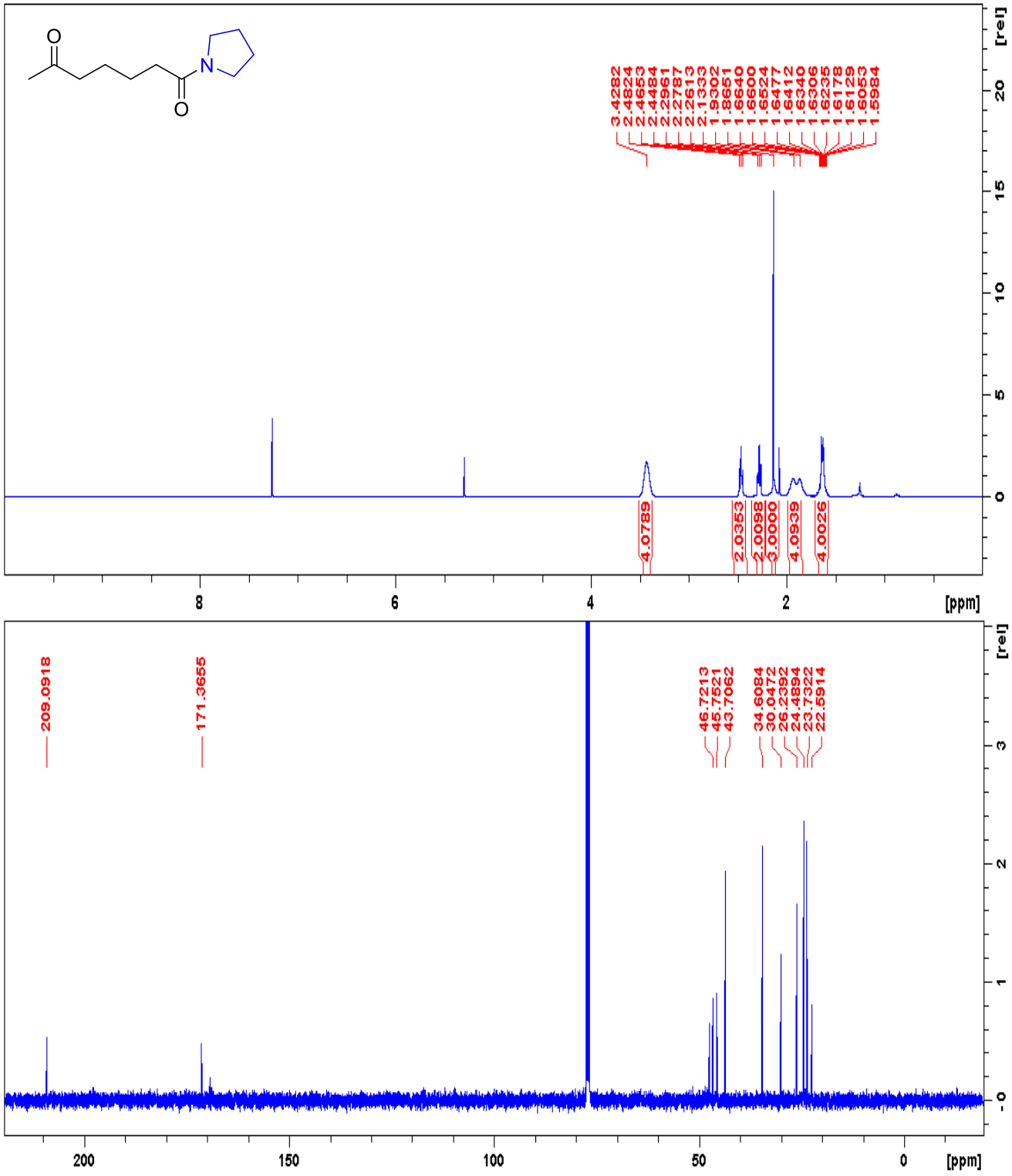
6-Oxo-heptanoic acid phenethyl ester **(4k)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



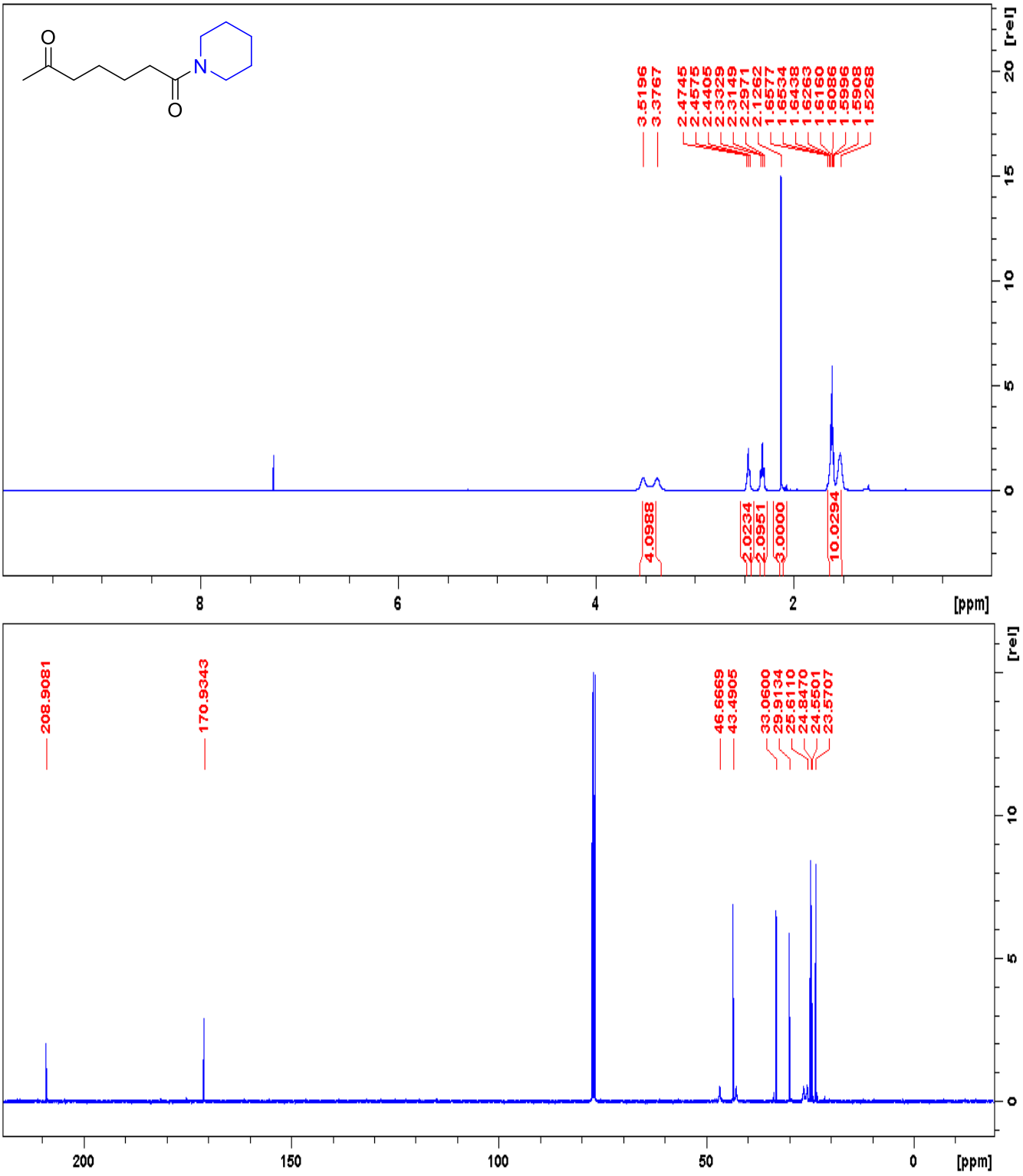
N-butyl-6-oxoheptanamide **(4l)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



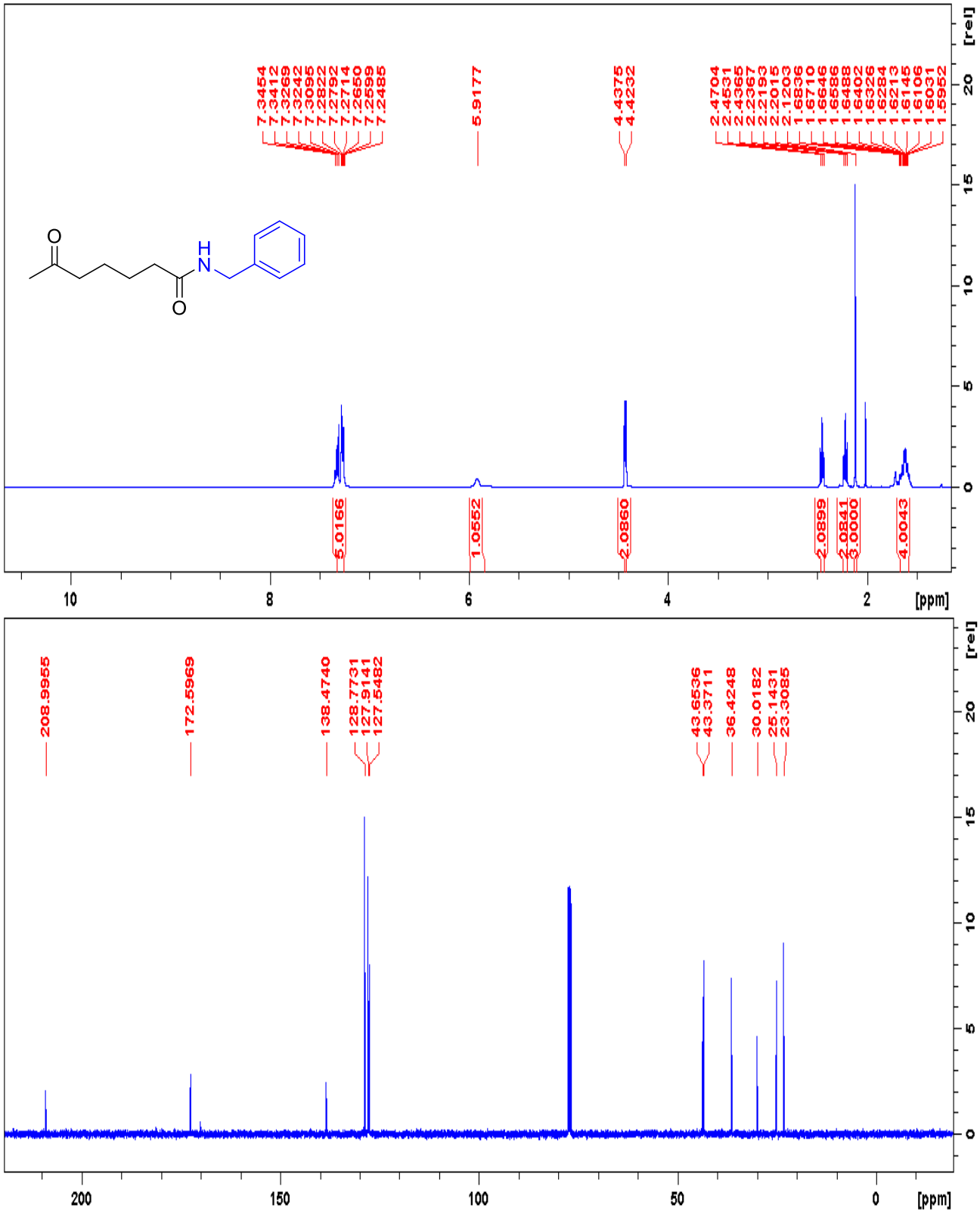
1-(Pyrrolidin-1-yl) heptane-1,6-dion **(4m)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



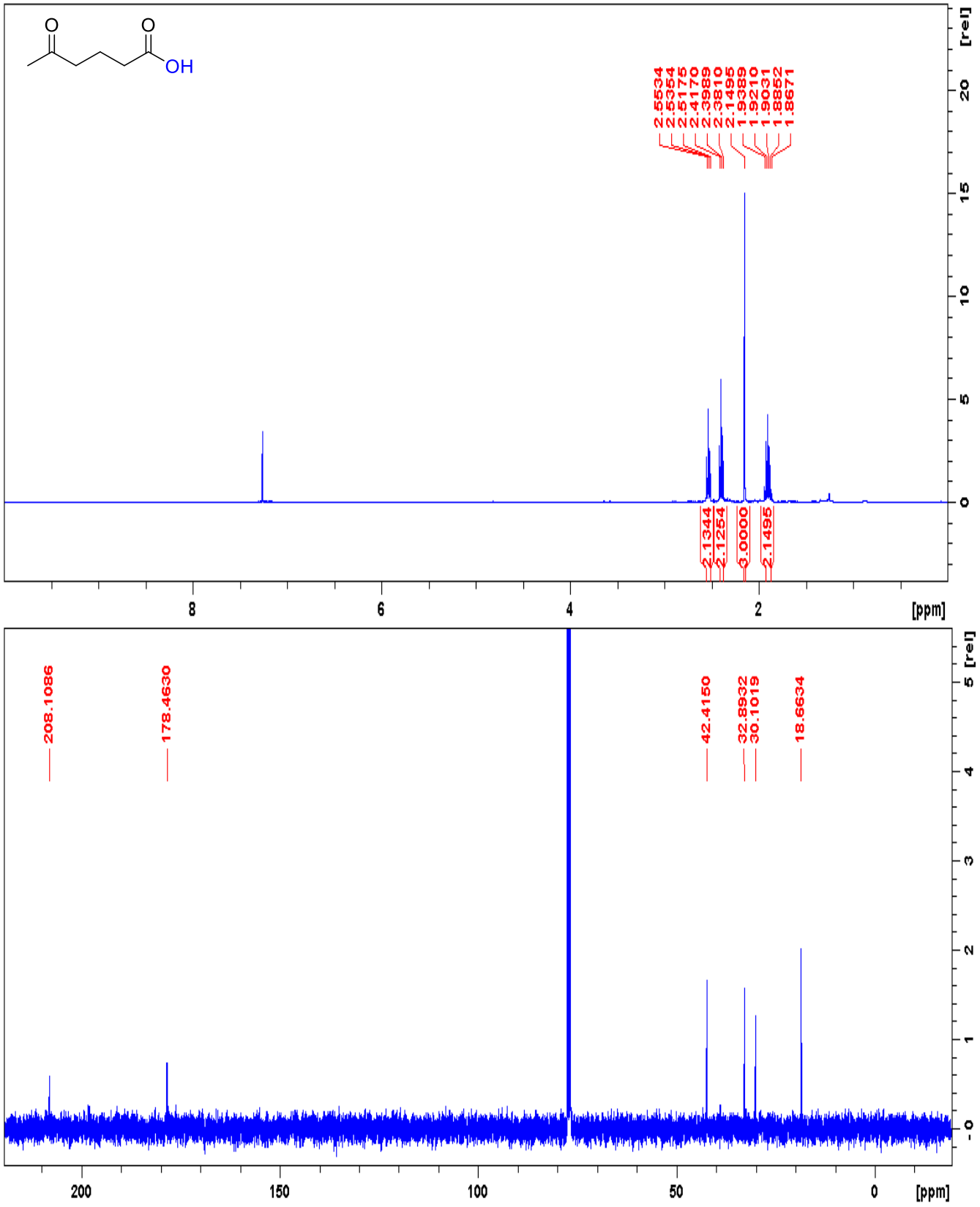
1-(Piperidin-1-yl) heptane-1,6-dione **(4n)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



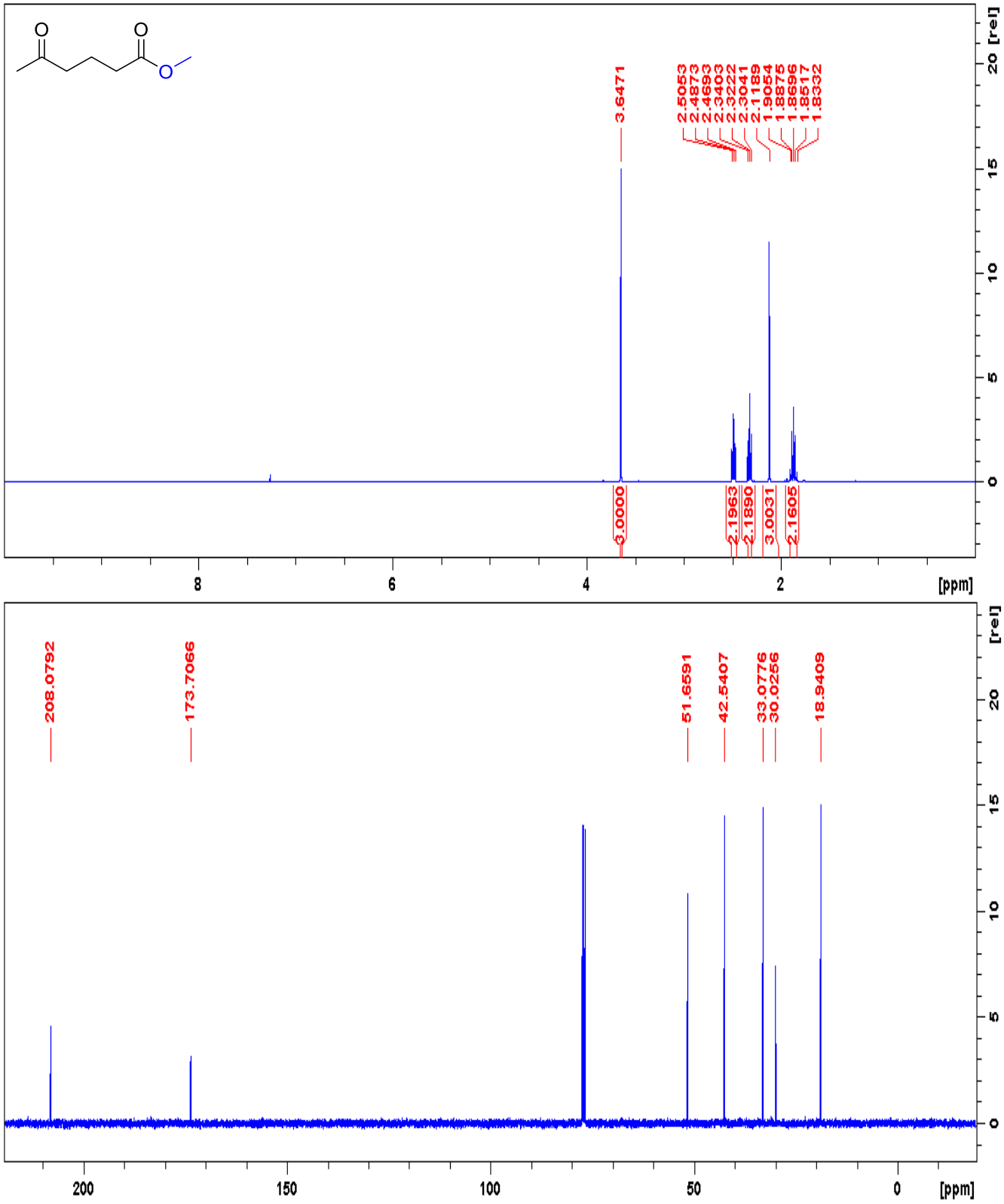
N-benzyl-6-oxoheptanamide **(4o)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



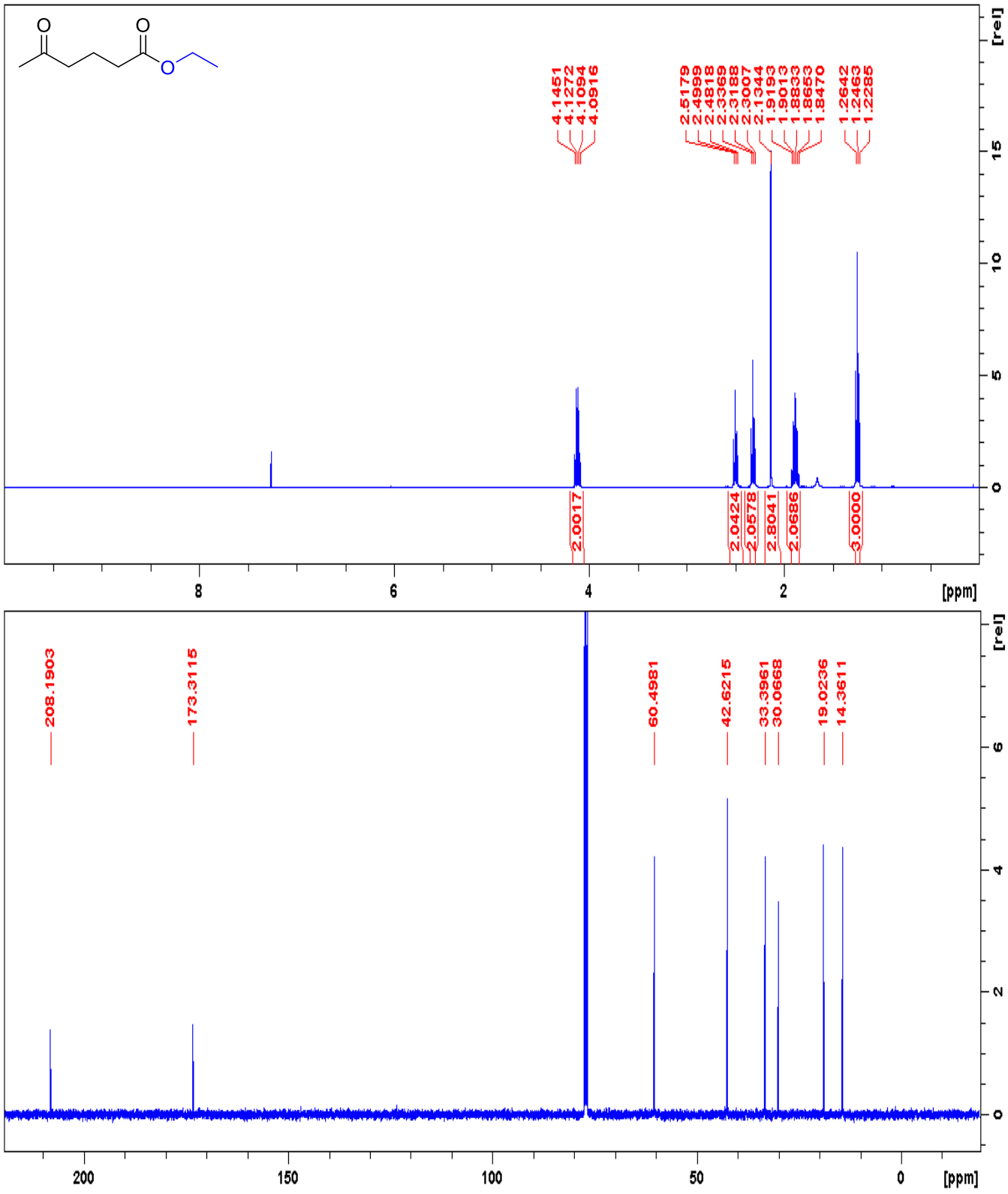
5-Oxohexanoic acid **(4p)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



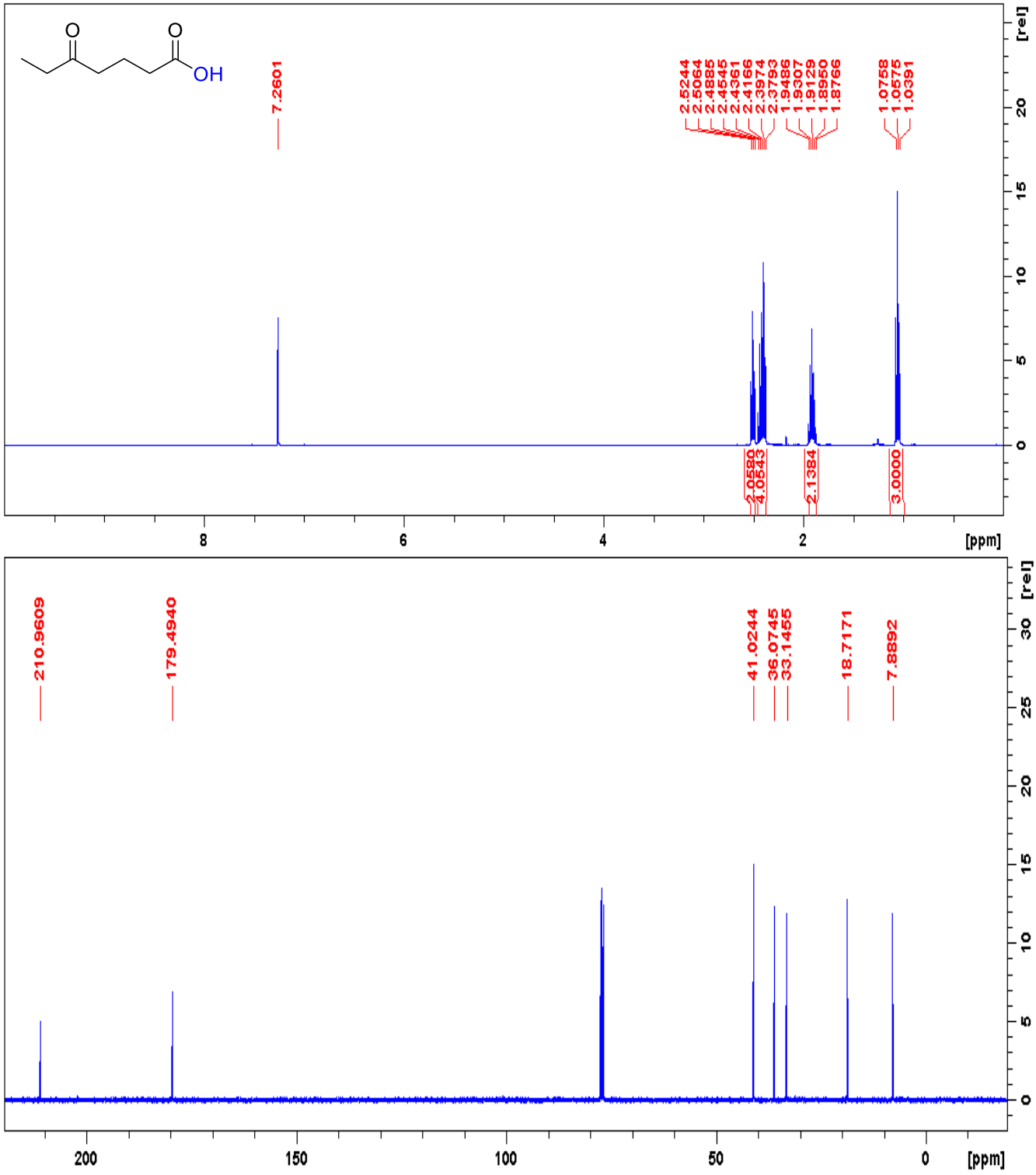
Methyl 5-oxohexanoate **(4q)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



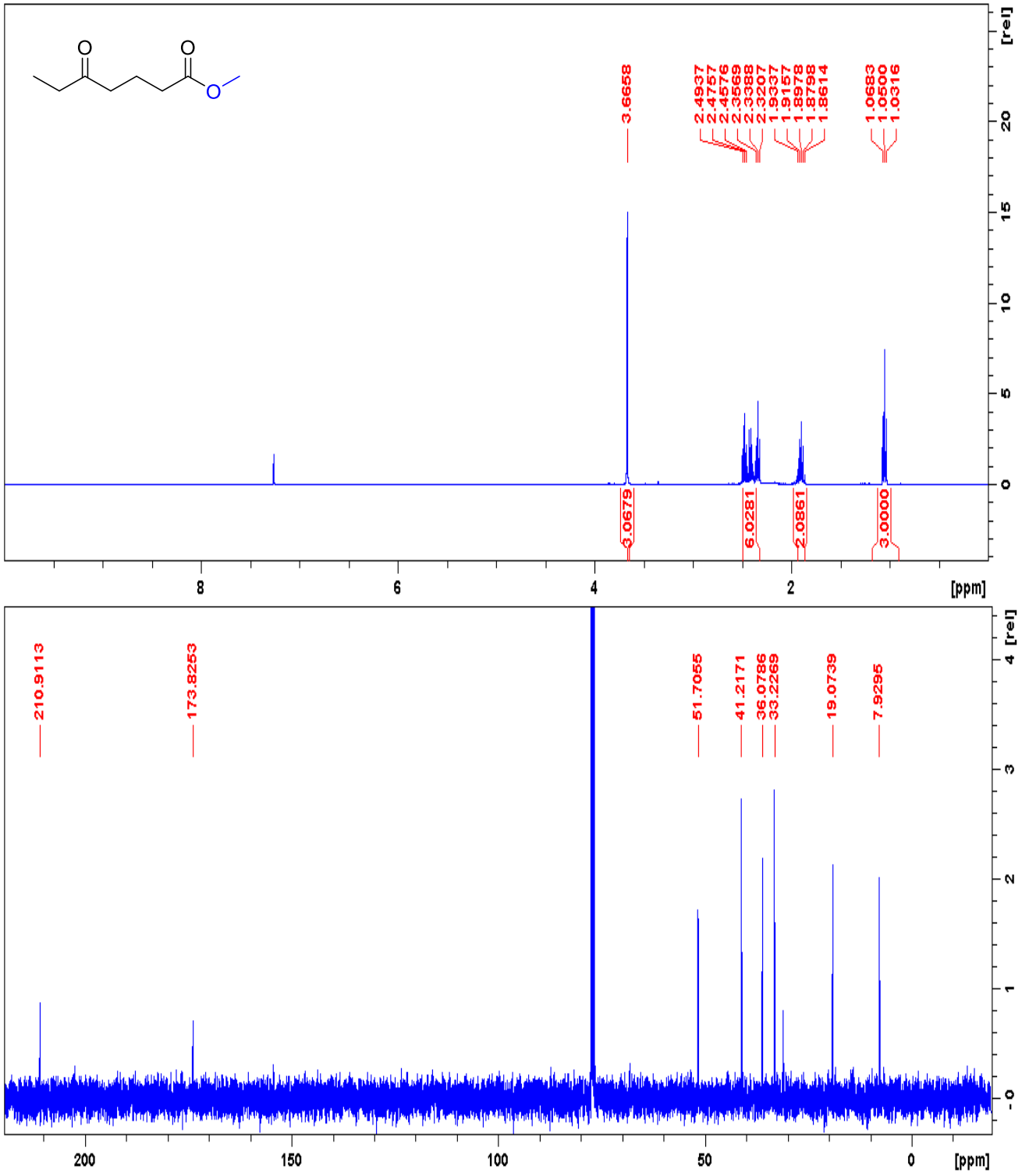
Ethyl 5-oxohexanoate **(4r)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



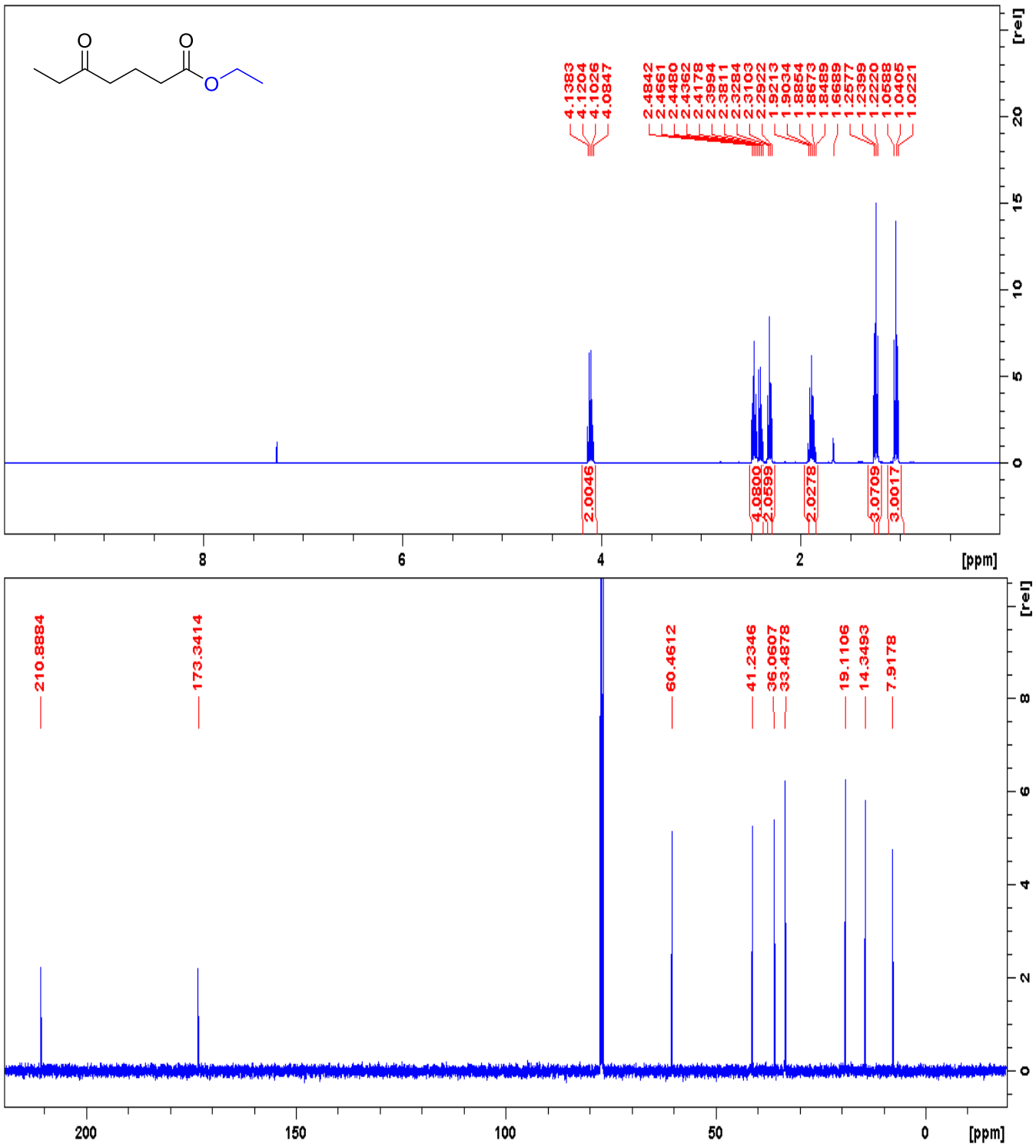
5-Oxohexanoic acid **(4s)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



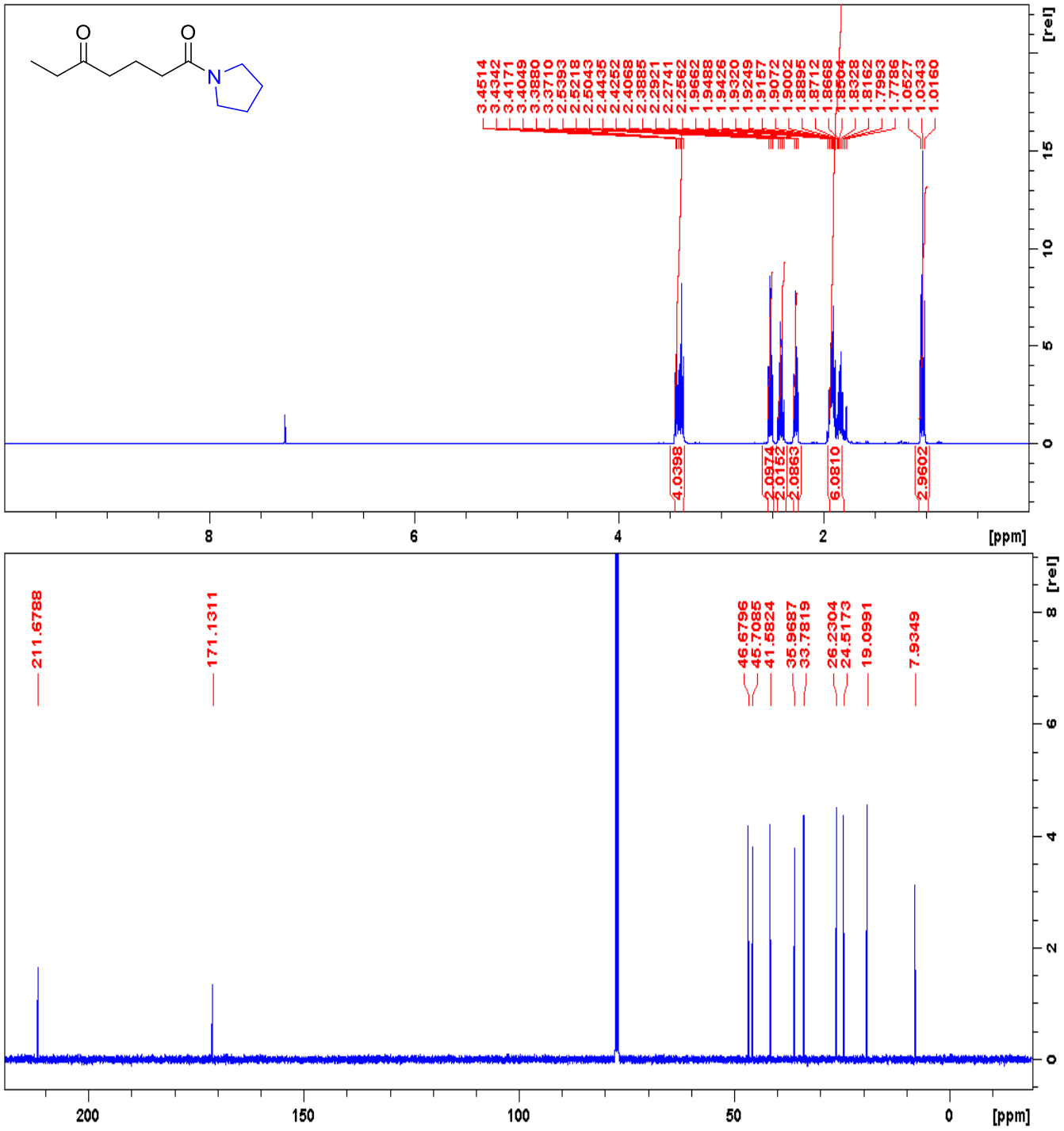
Methyl 5-oxoheptanoate **(4t)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



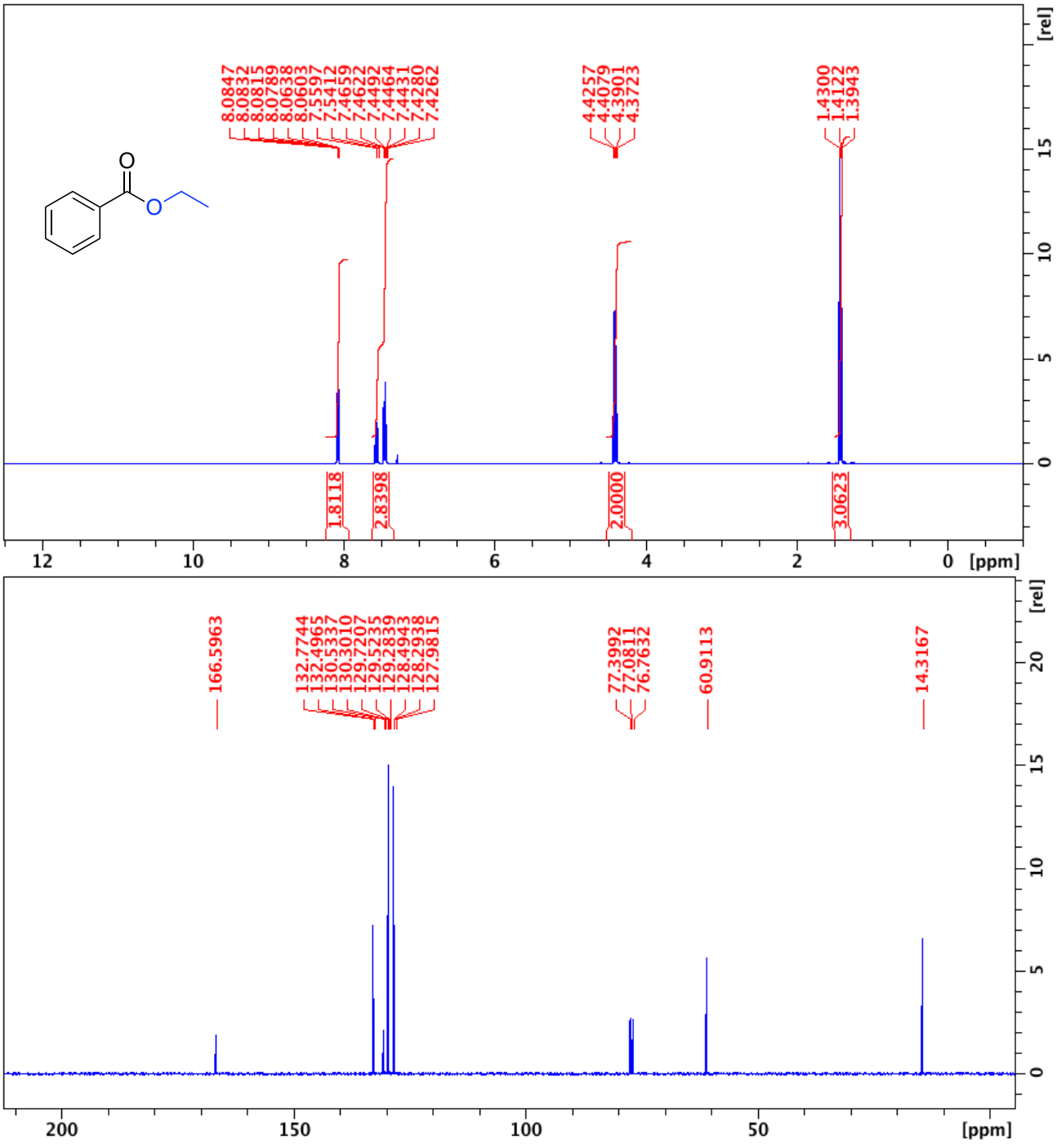
Ethyl 5-oxoheptanoate **(4u)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



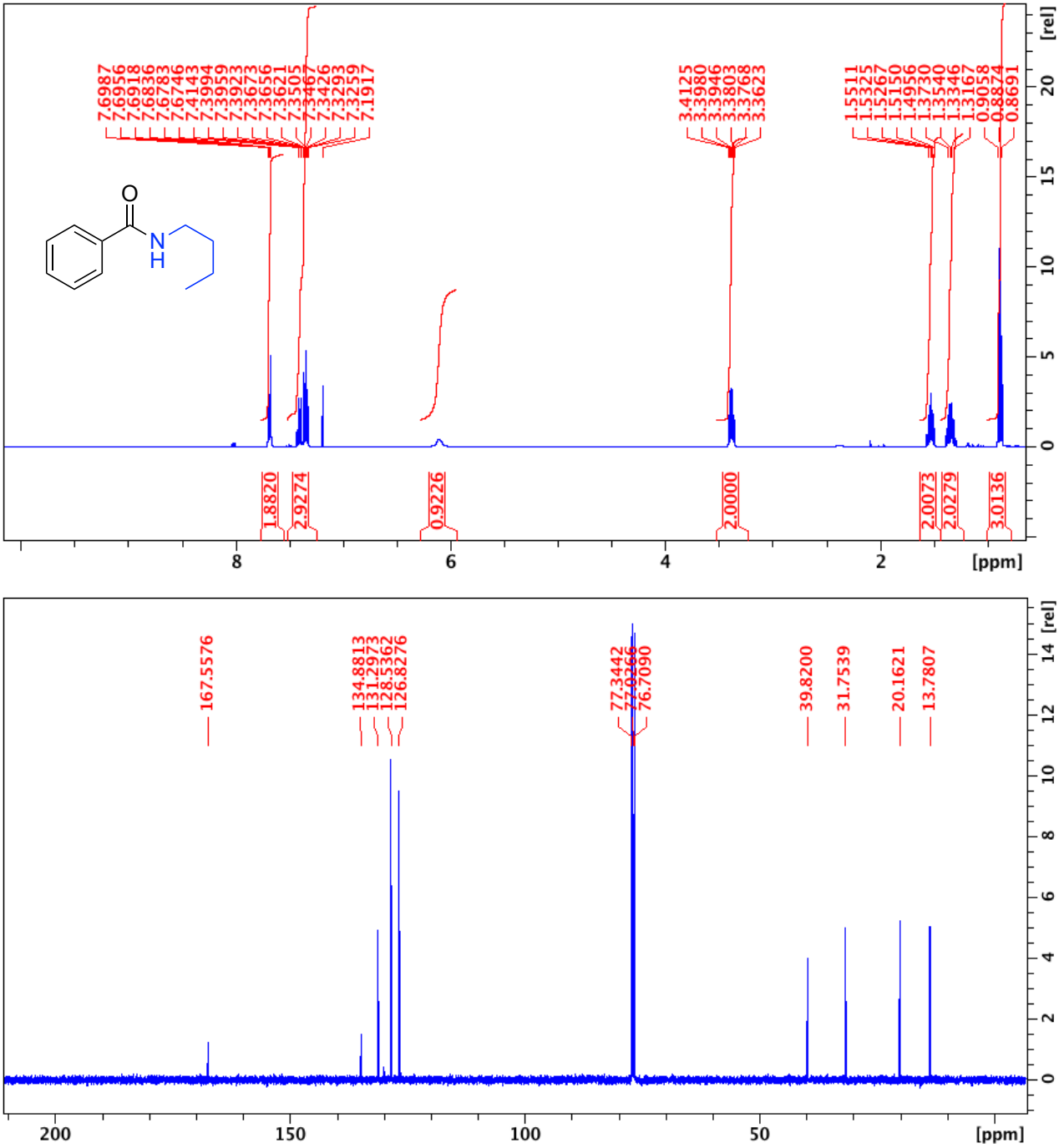
1-Pyrrolidin heptane-1,5-dione **(4w)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



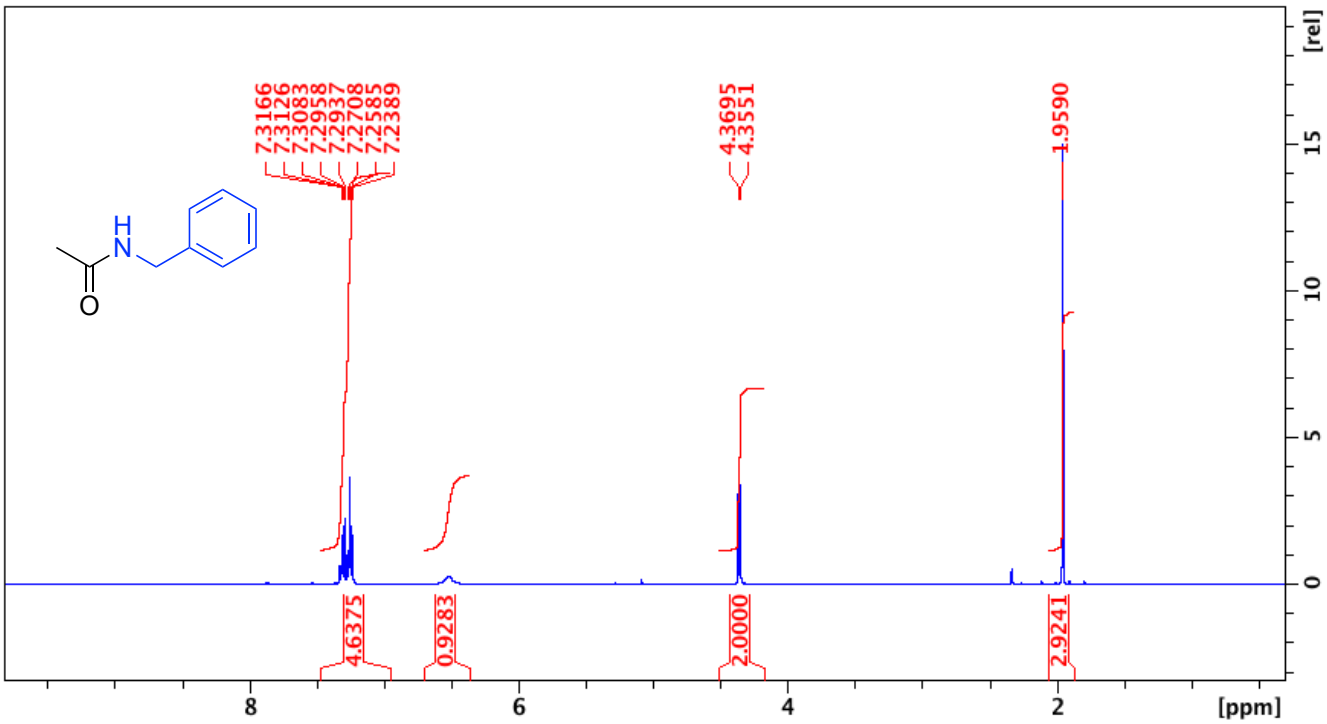
Ethyl benzoate (**4y1**); **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

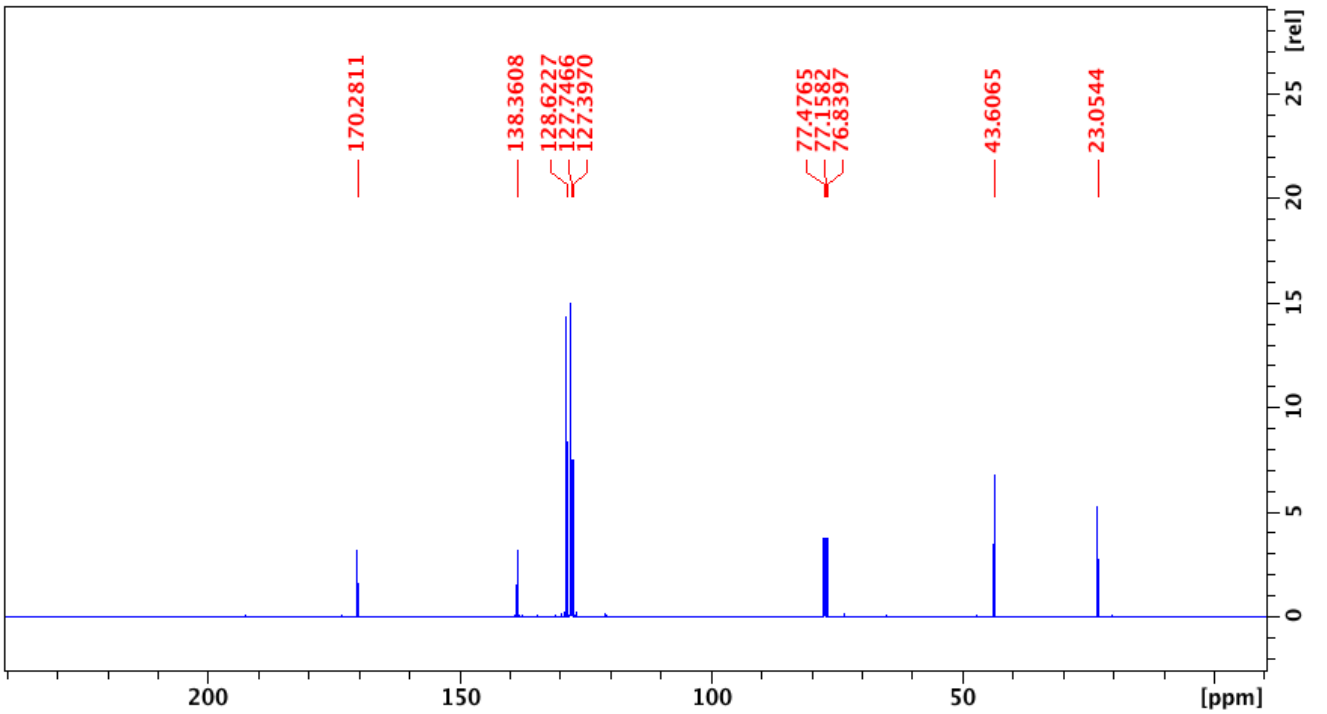


N-Butylbenzamide (**4y2**); **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

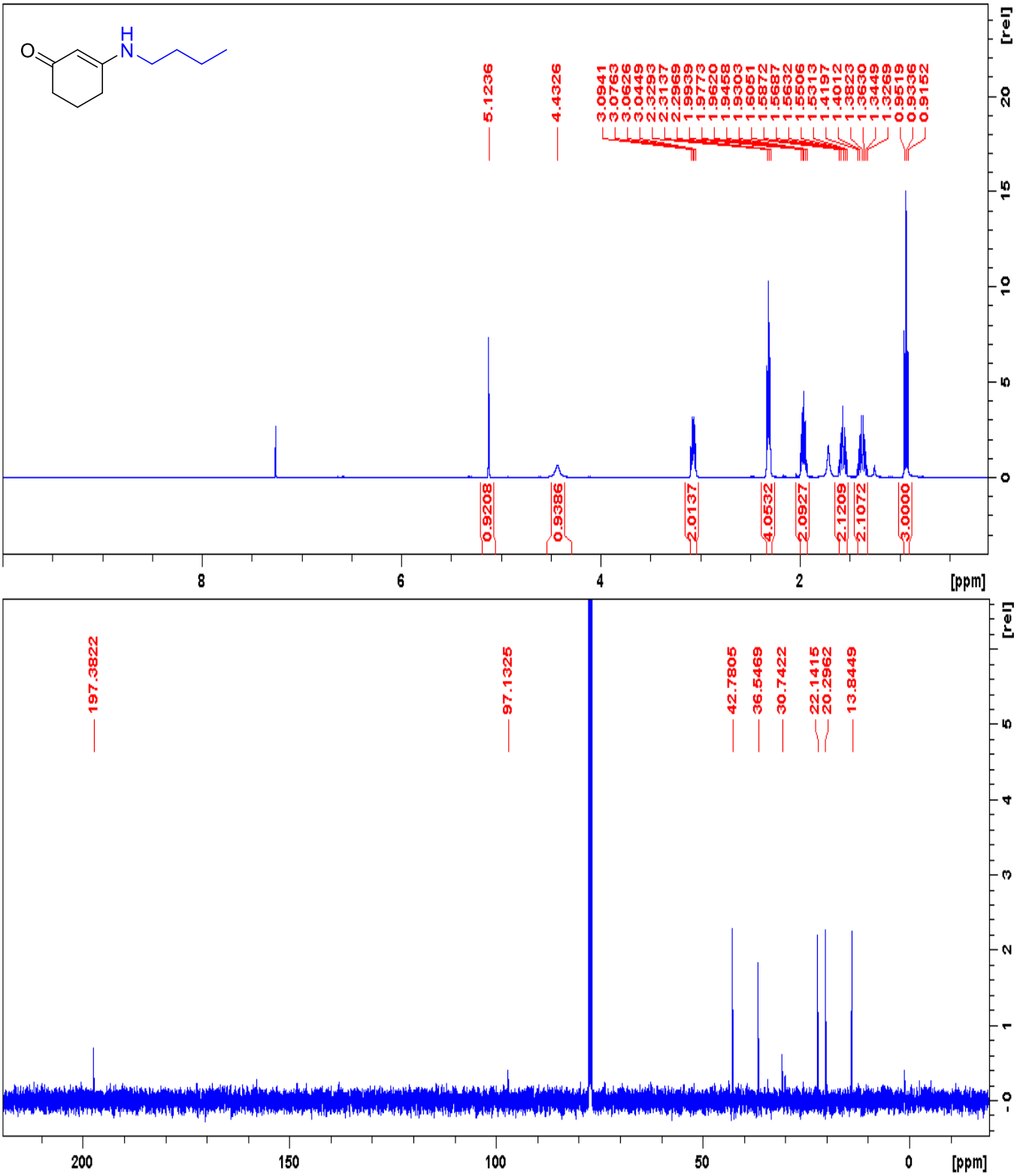


N-Benzylacetamide (**4z**); **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

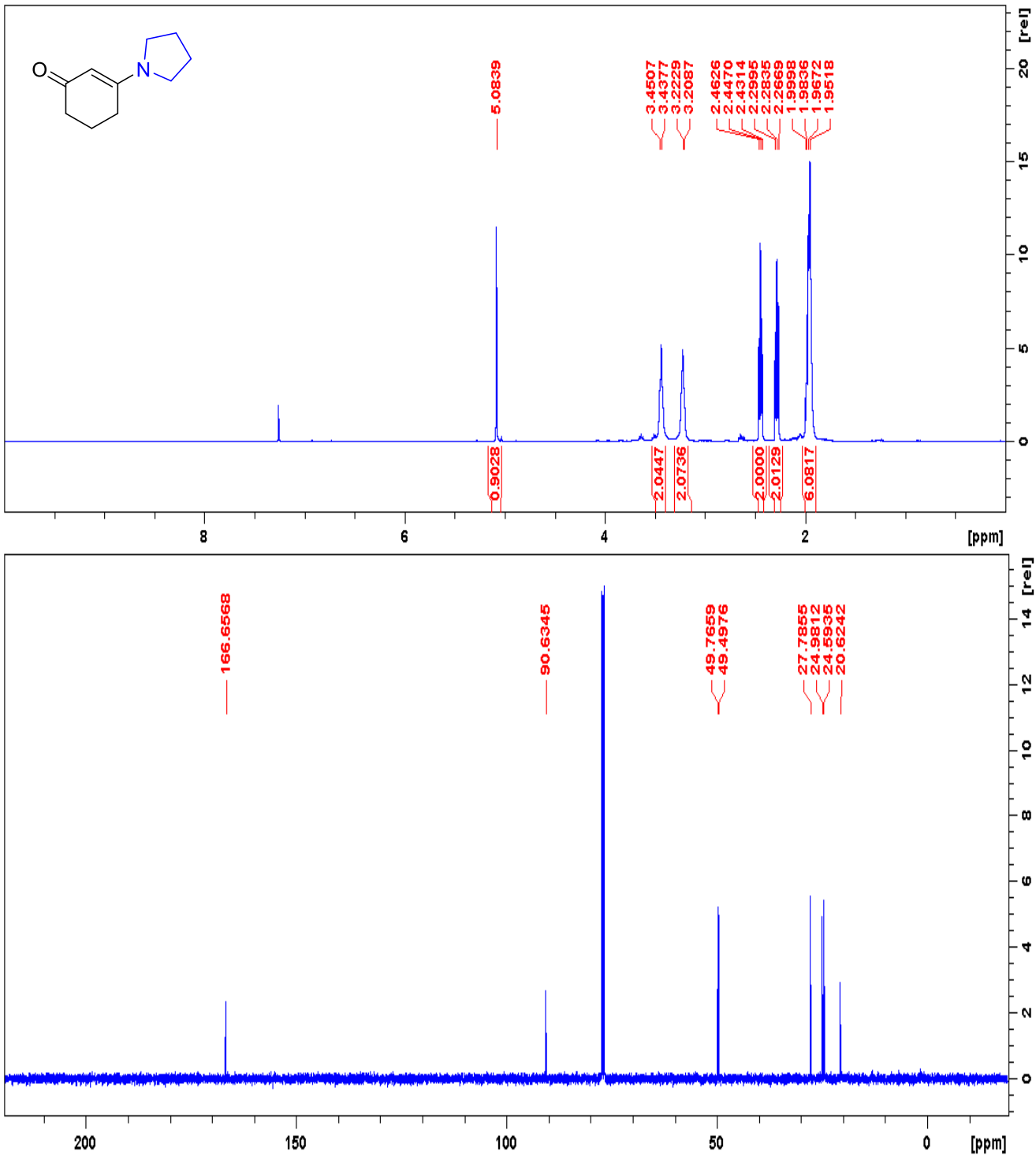




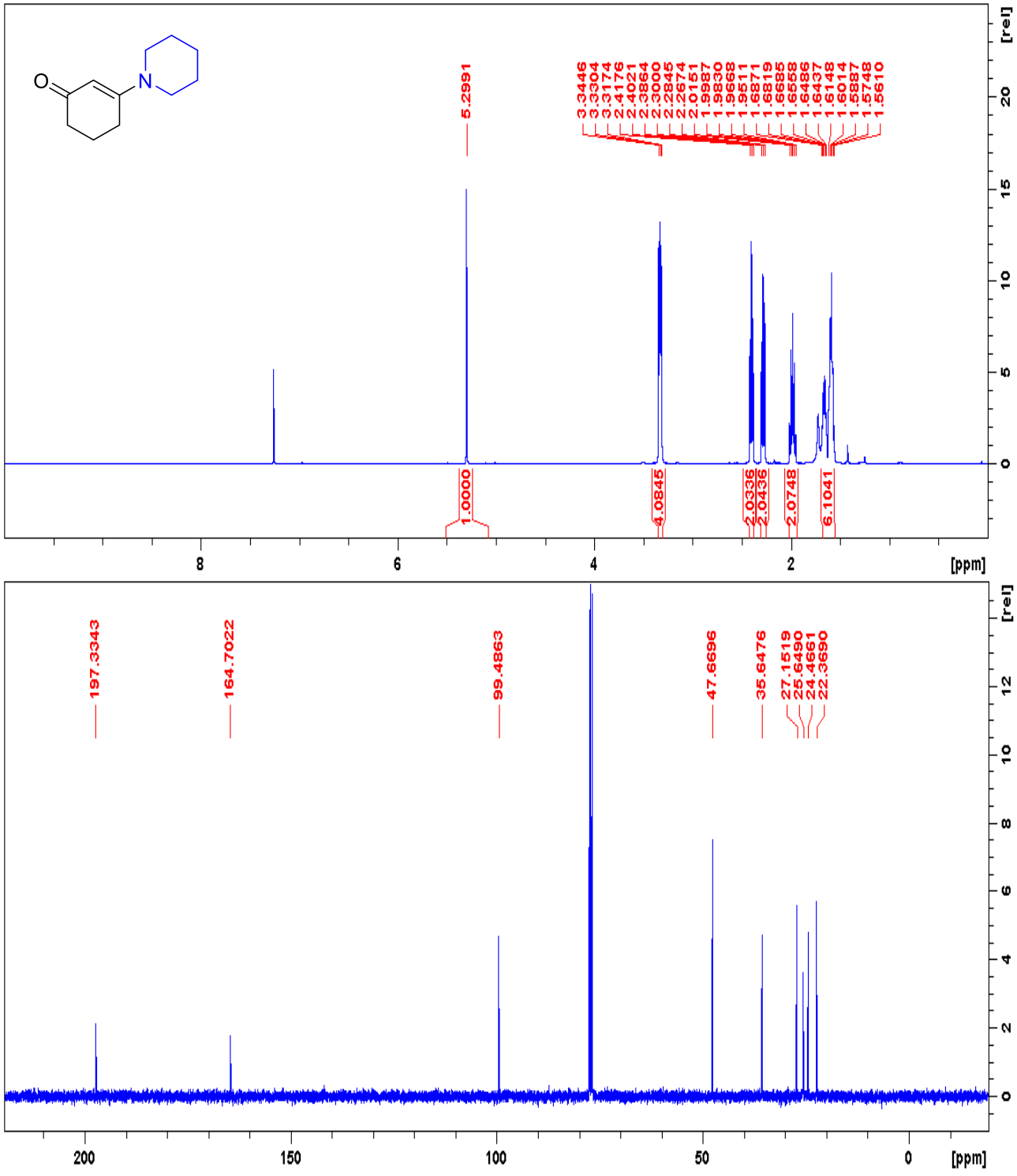
3-(Butylamino)cyclohex-2-enone **(4'b1)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



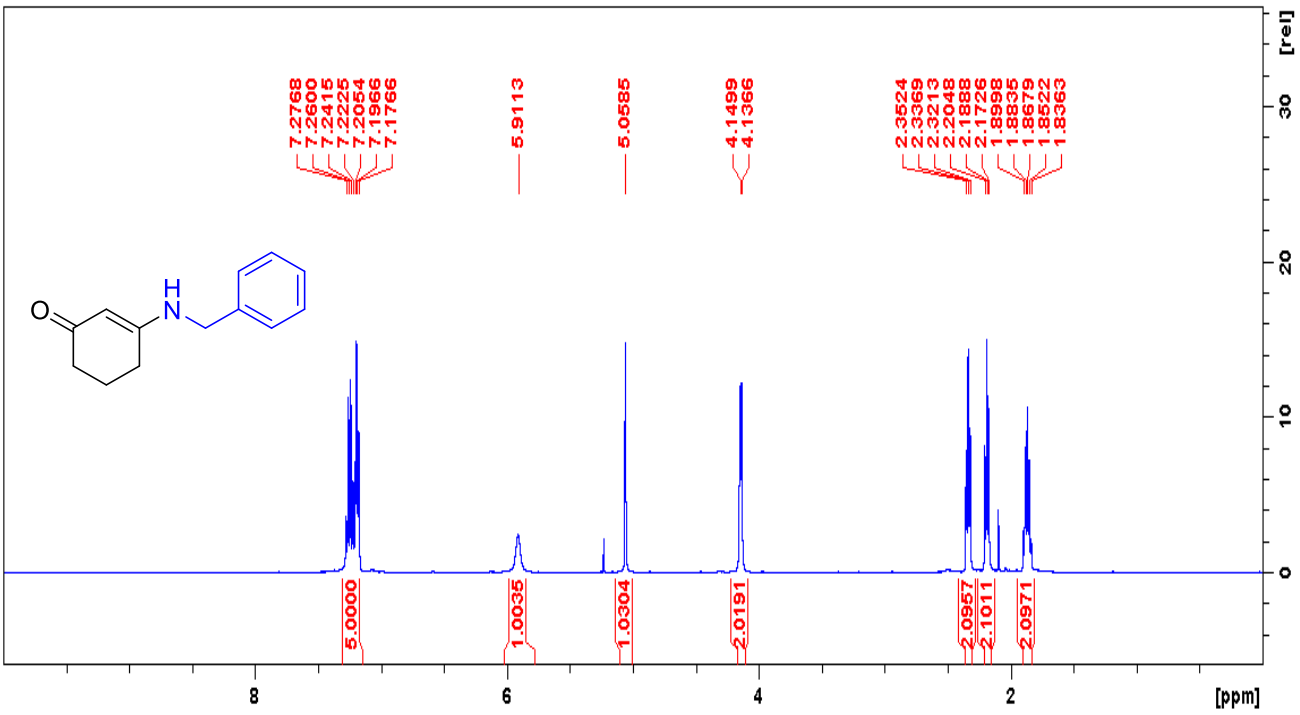
2-(Pyrrolidin-1-yl) cyclohexane-1,3-dione **(4'b2)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

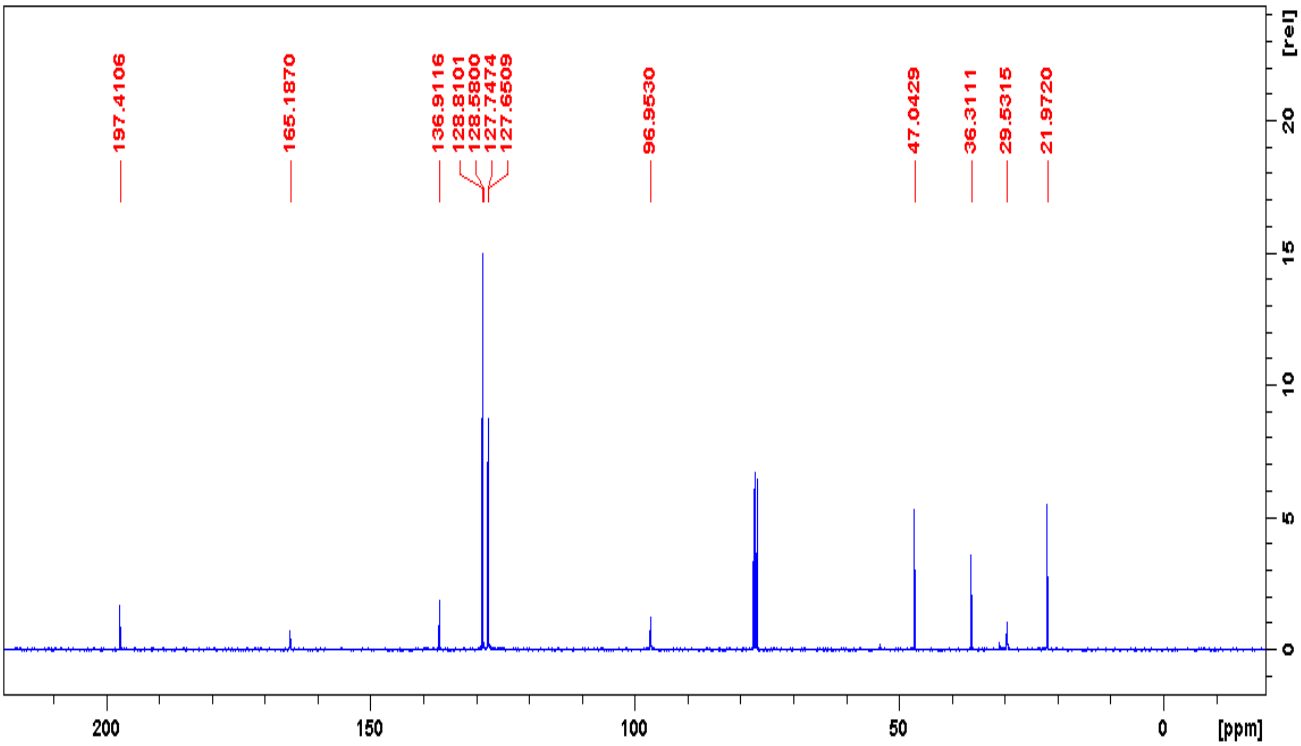


1-(Piperidin-1-yl) hexane-1,5-dione **(4'b3)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

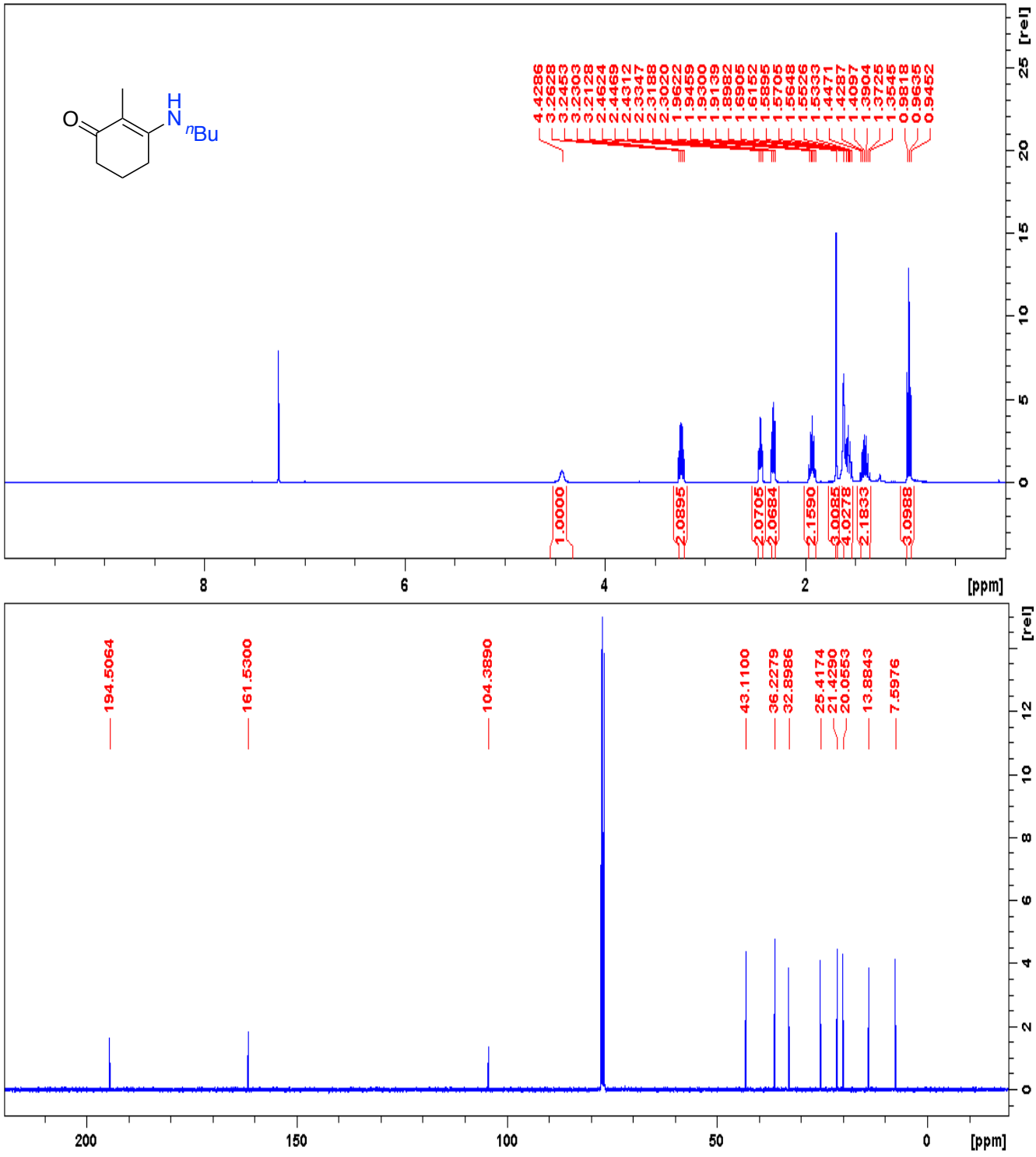


N-benzyl-5-oxohexanamide **(4'b4)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

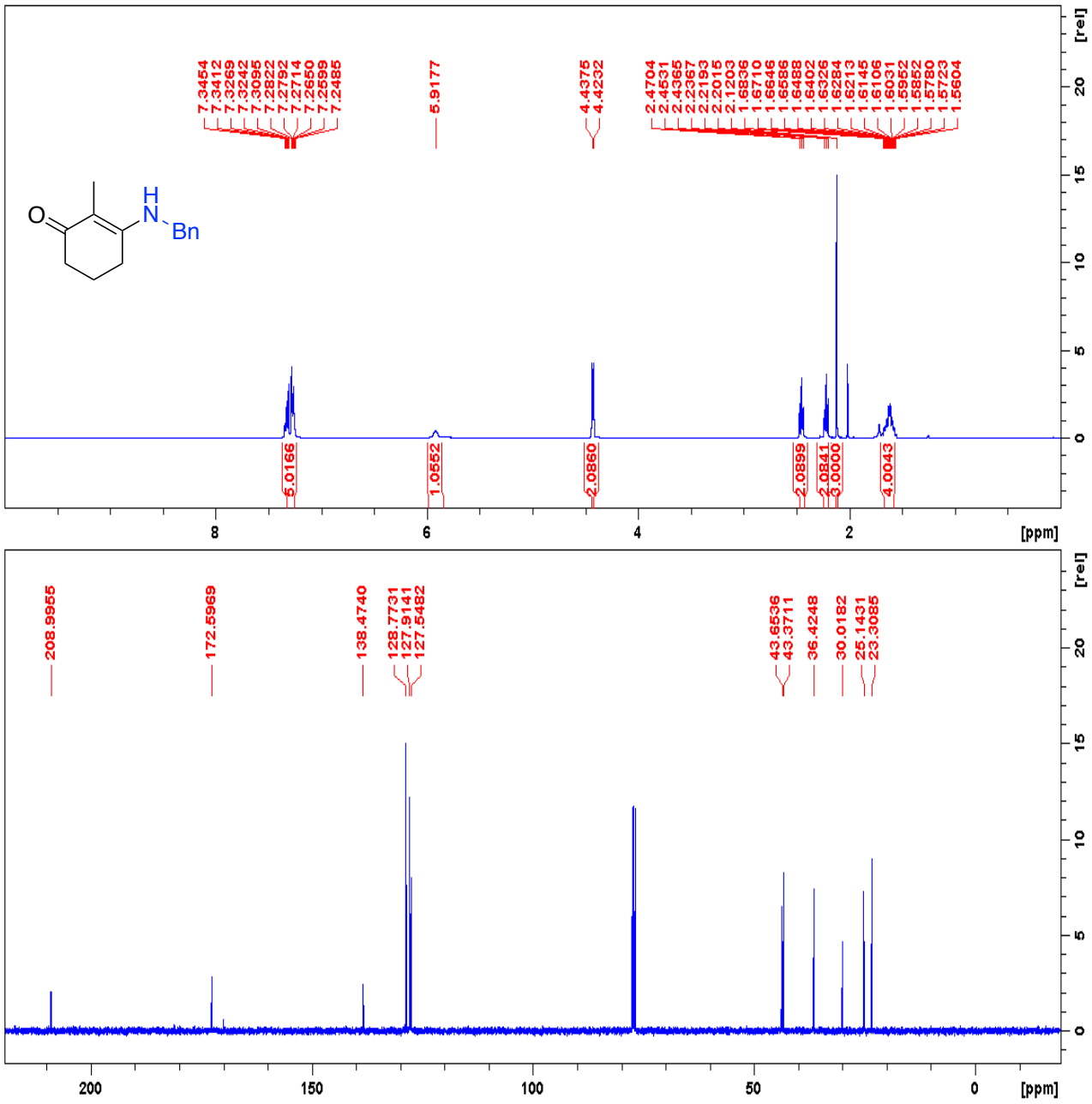




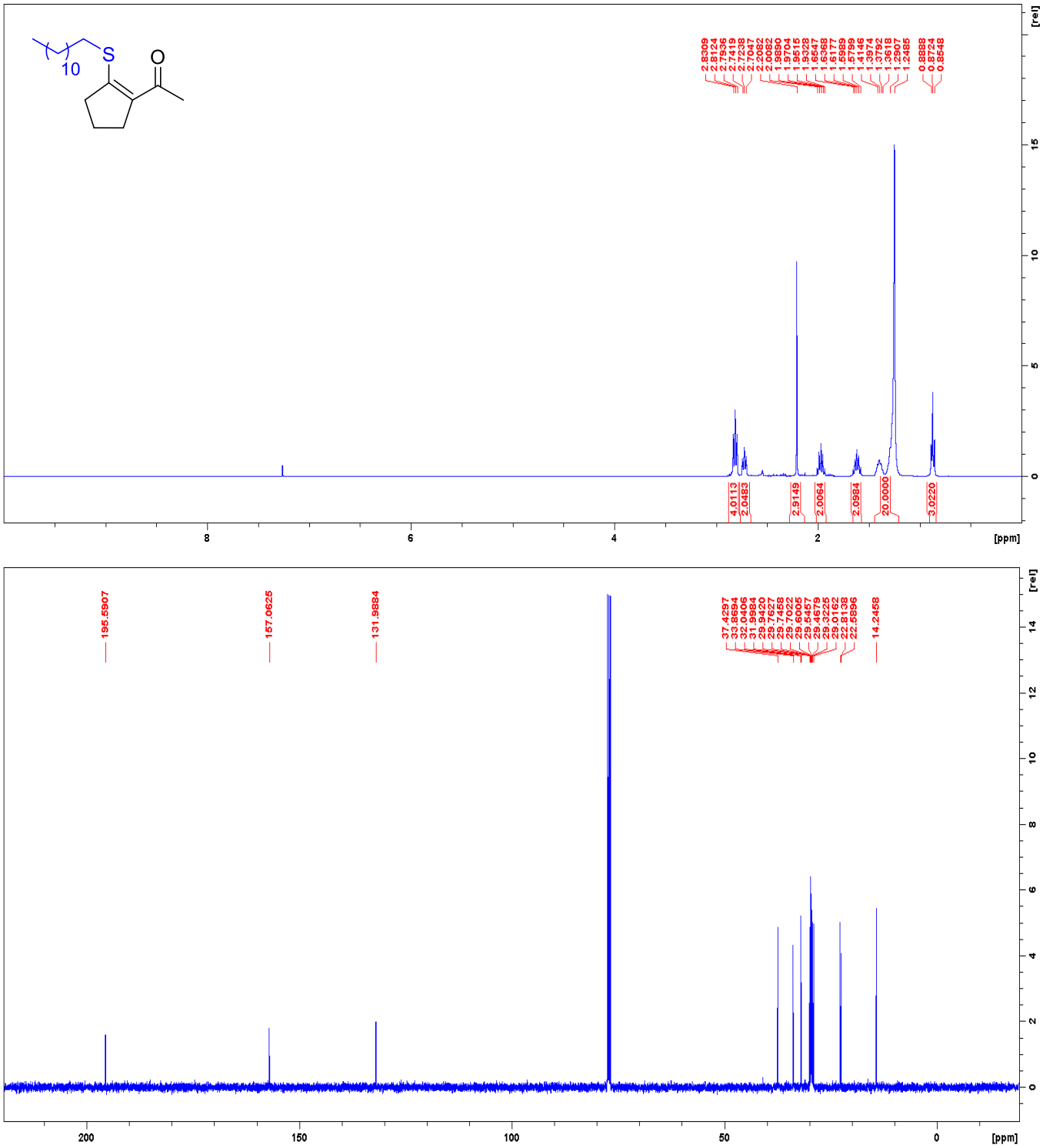
3-(butylamino)-2-methylcyclohex-2-en-1-one **(4c'1)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



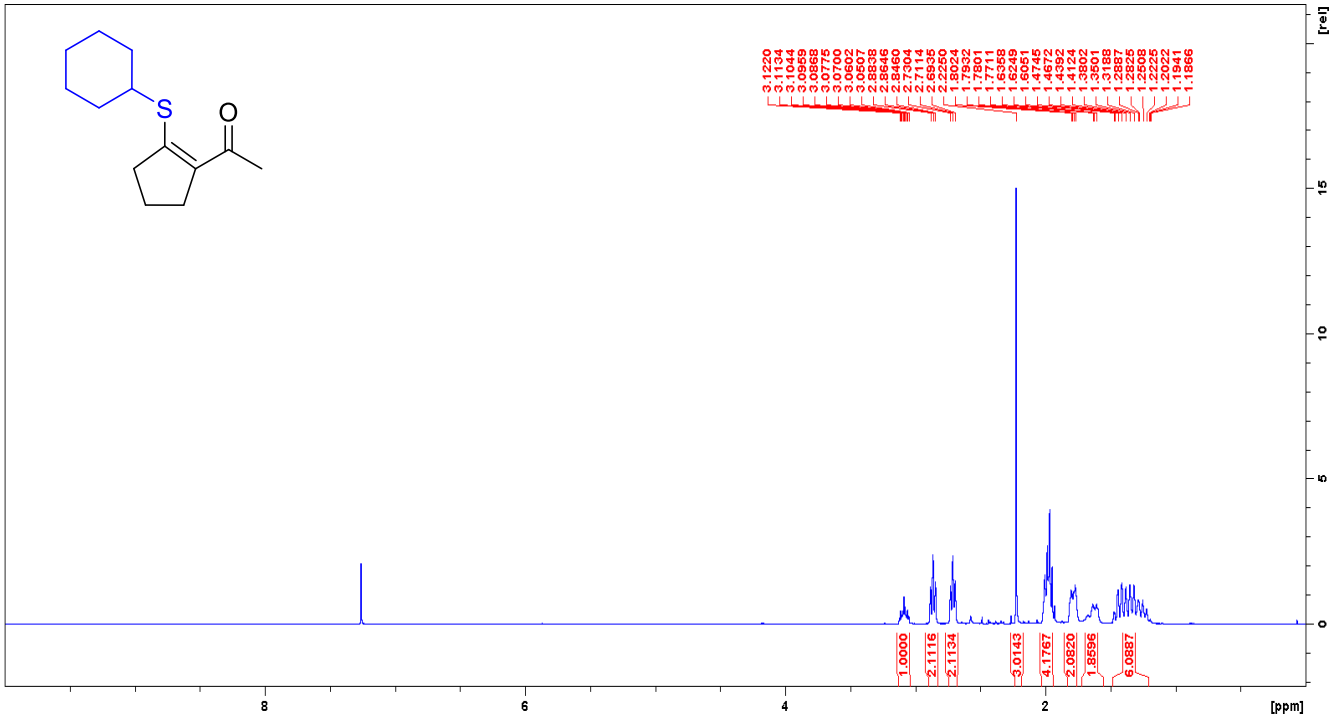
3-(benzylamino)-2-methylcyclohex-2-en-1-one **(4c'2)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

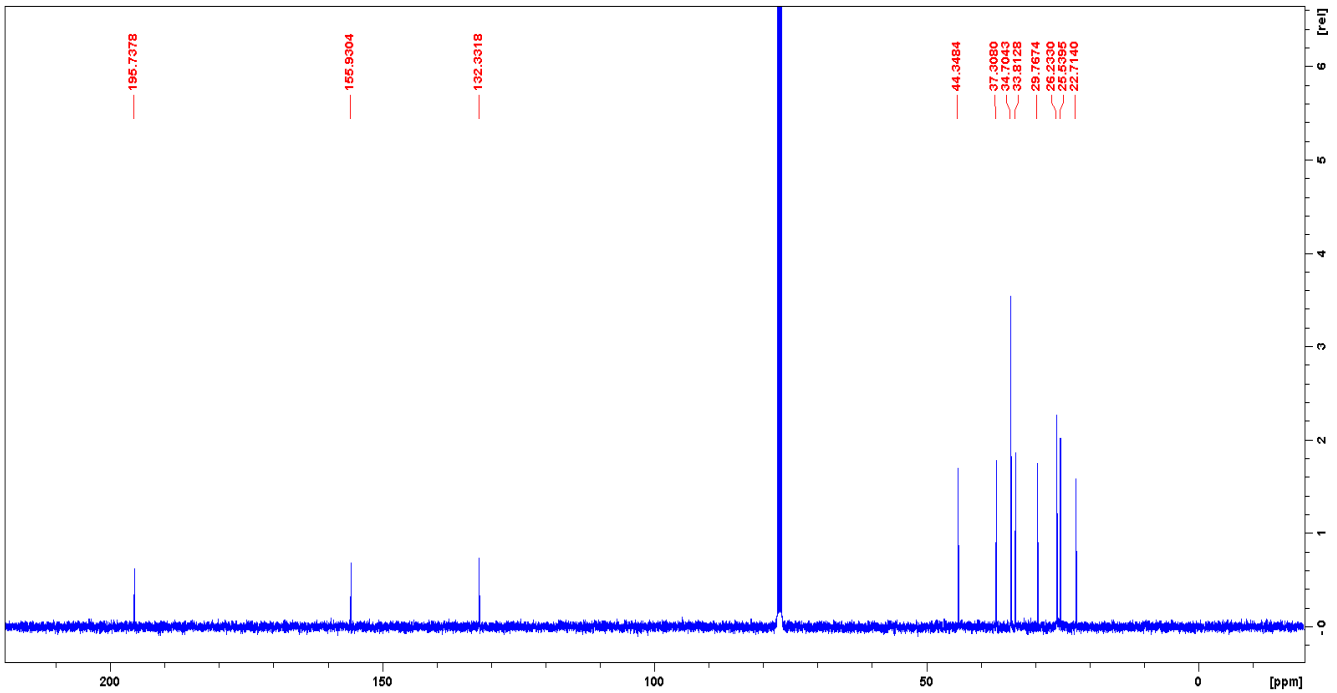


1-(2-(Dodecylthio)cyclopent-1-en-1-yl)ethan-1-one **(8a)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

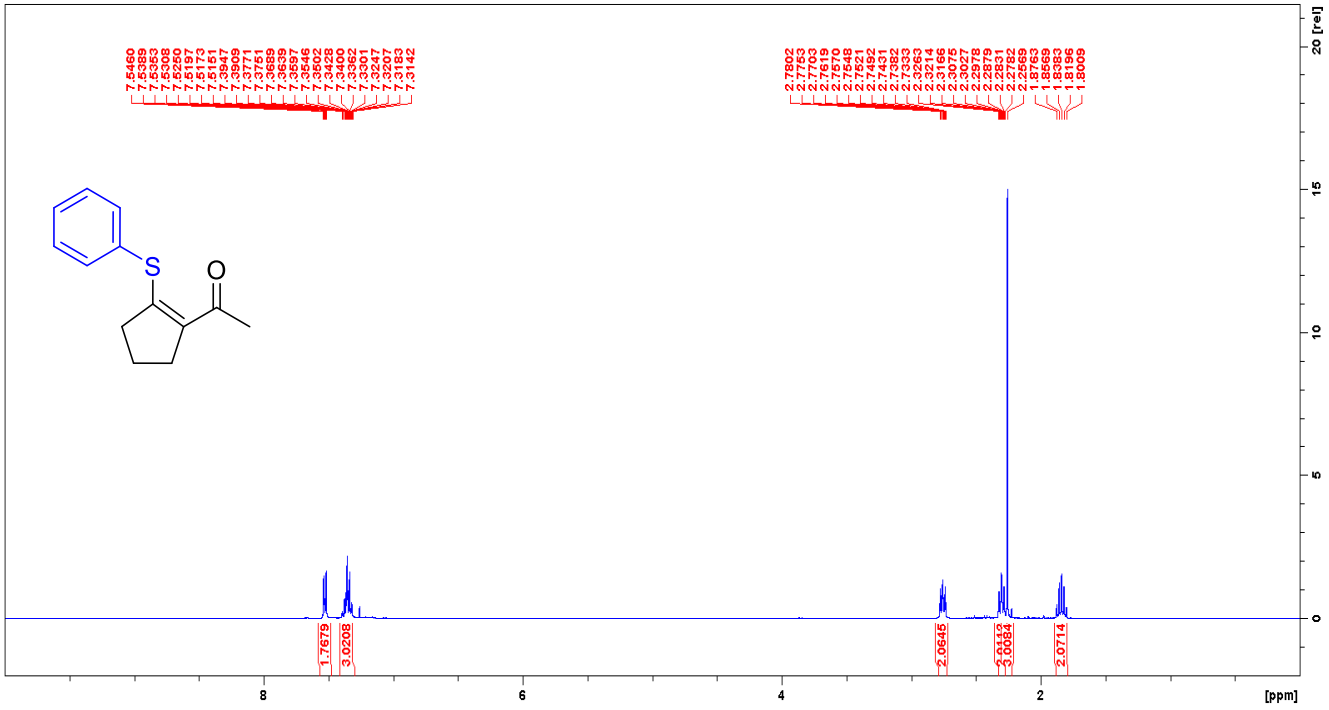


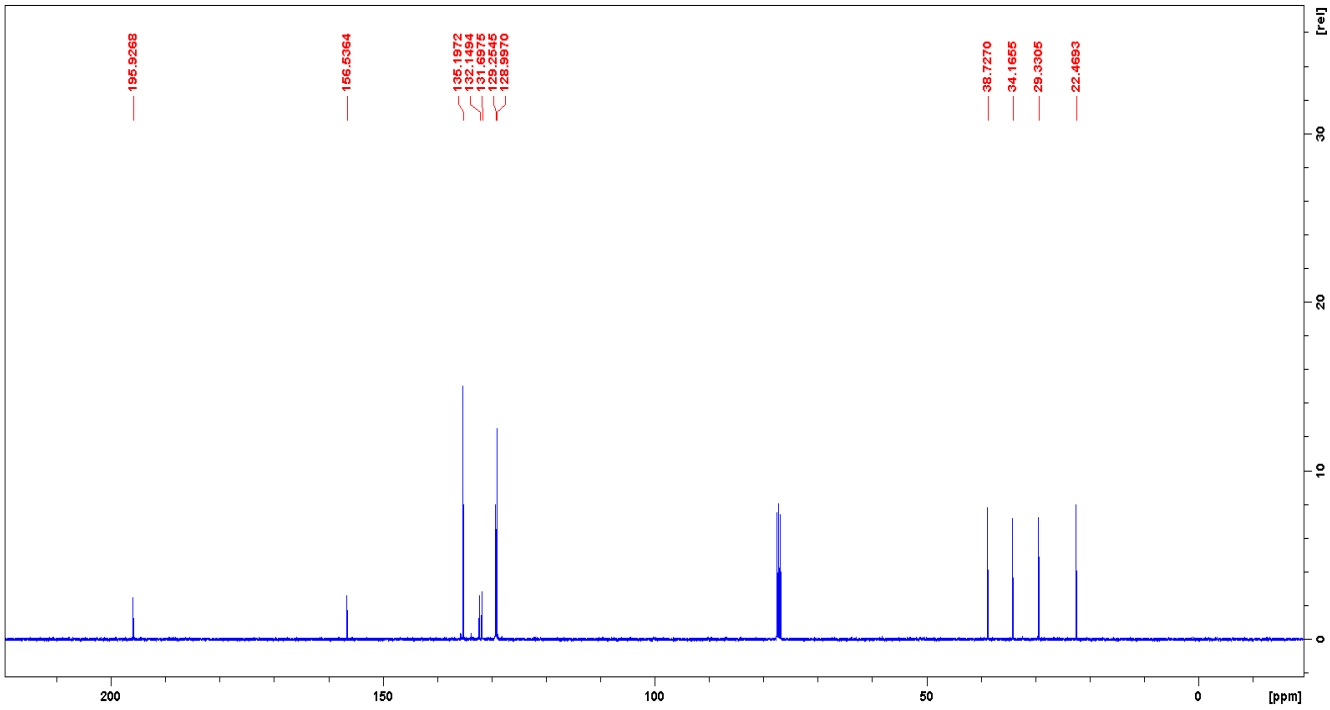
1-(2-(Cyclohexylthio)cyclopent-1-en-1-yl)ethan-1-one **(8b)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



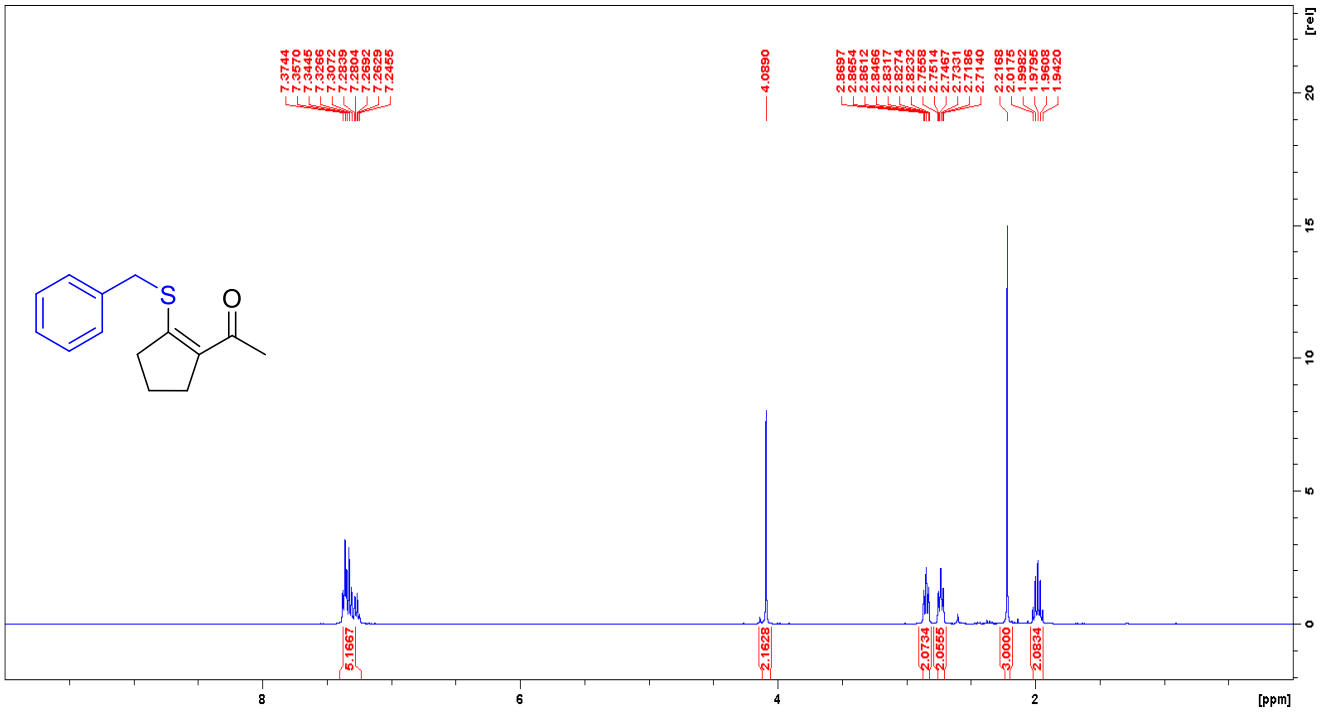


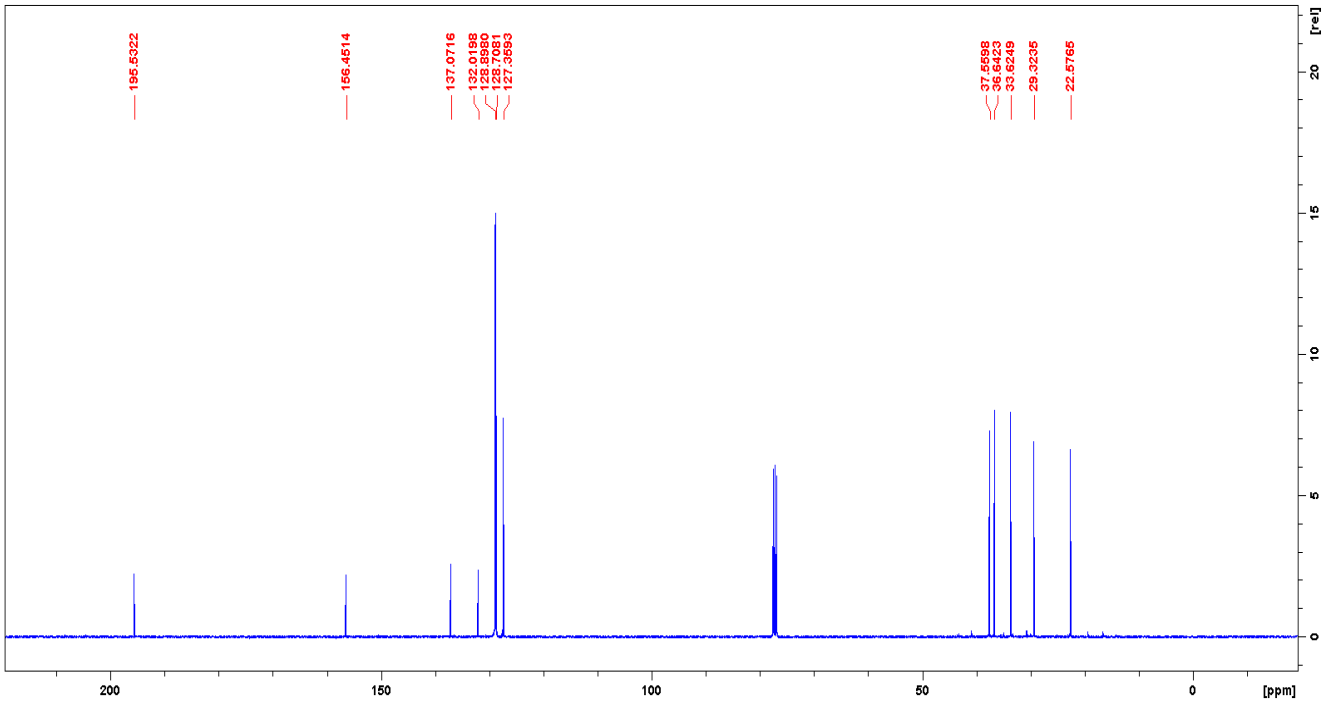
1-(2-(Phenylthio)cyclopent-1-en-1-yl)ethan-1-one **(8c)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



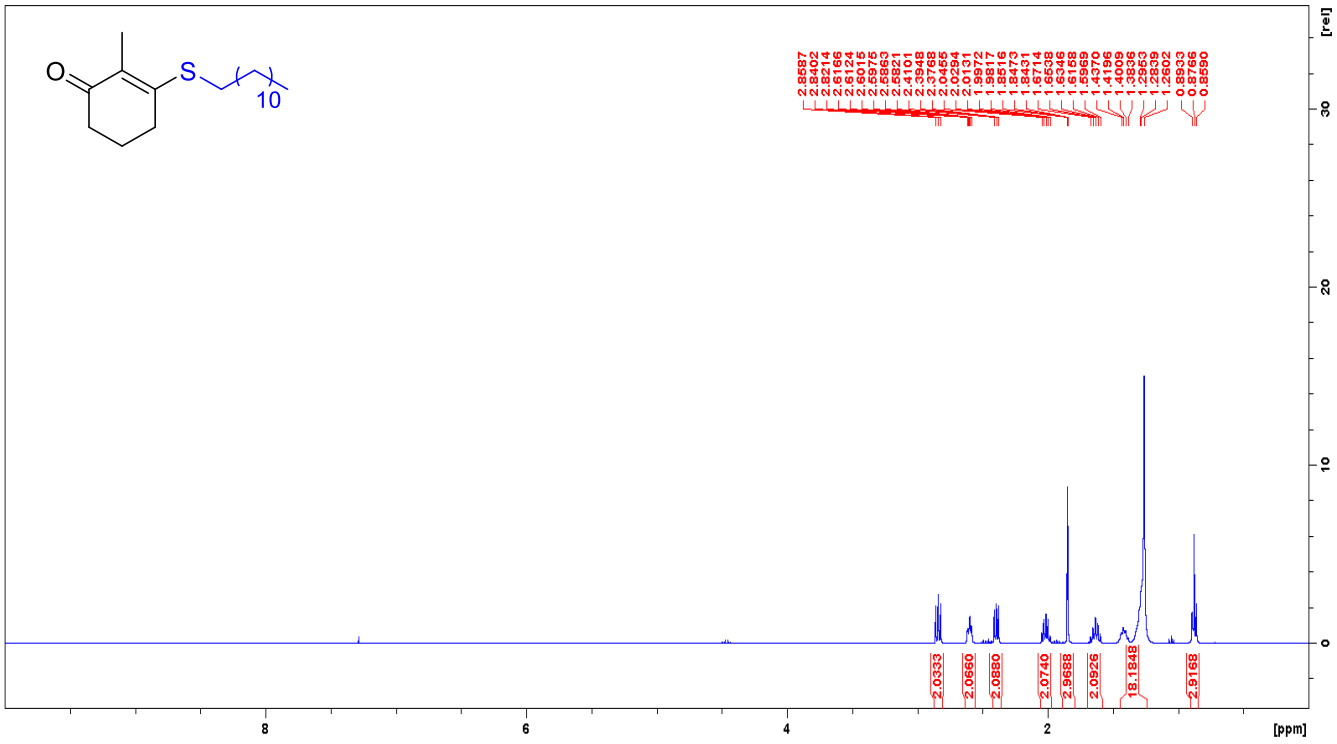


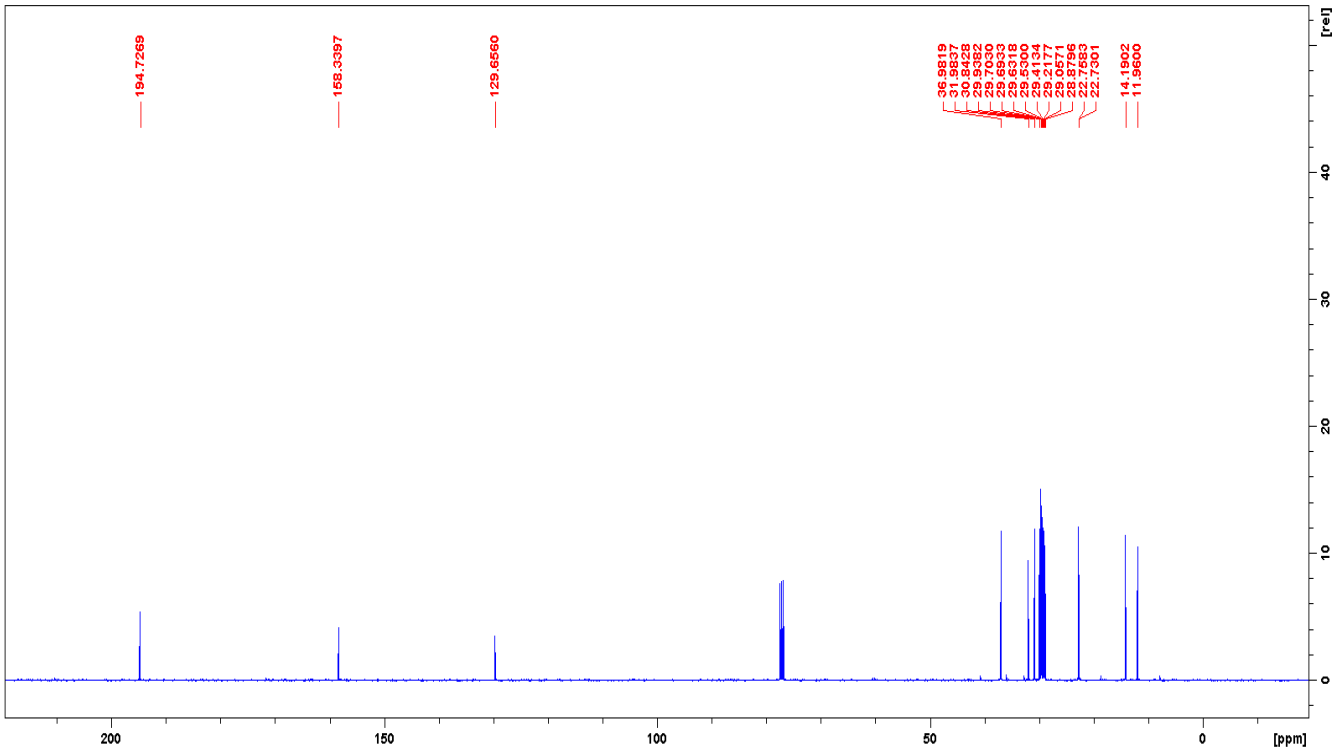
1-(2-(Benzylthio)cyclopent-1-en-1-yl)ethan-1-one **(8d)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



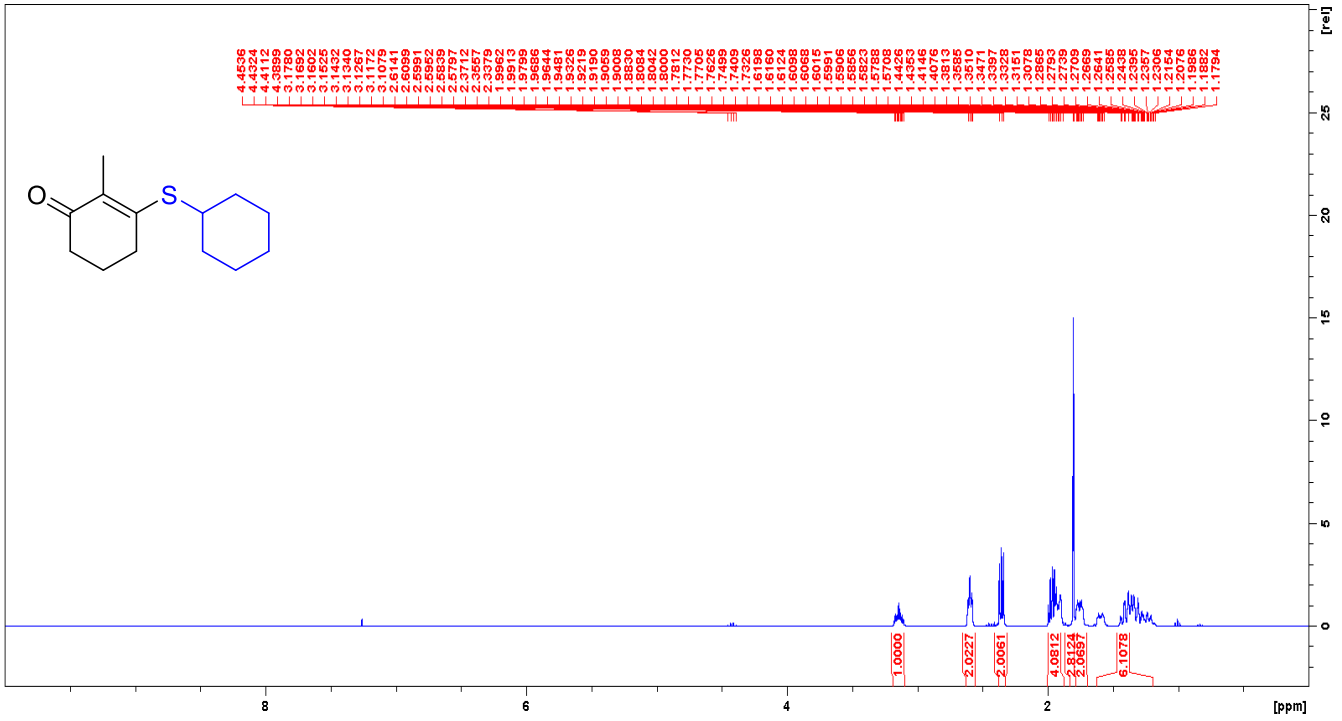


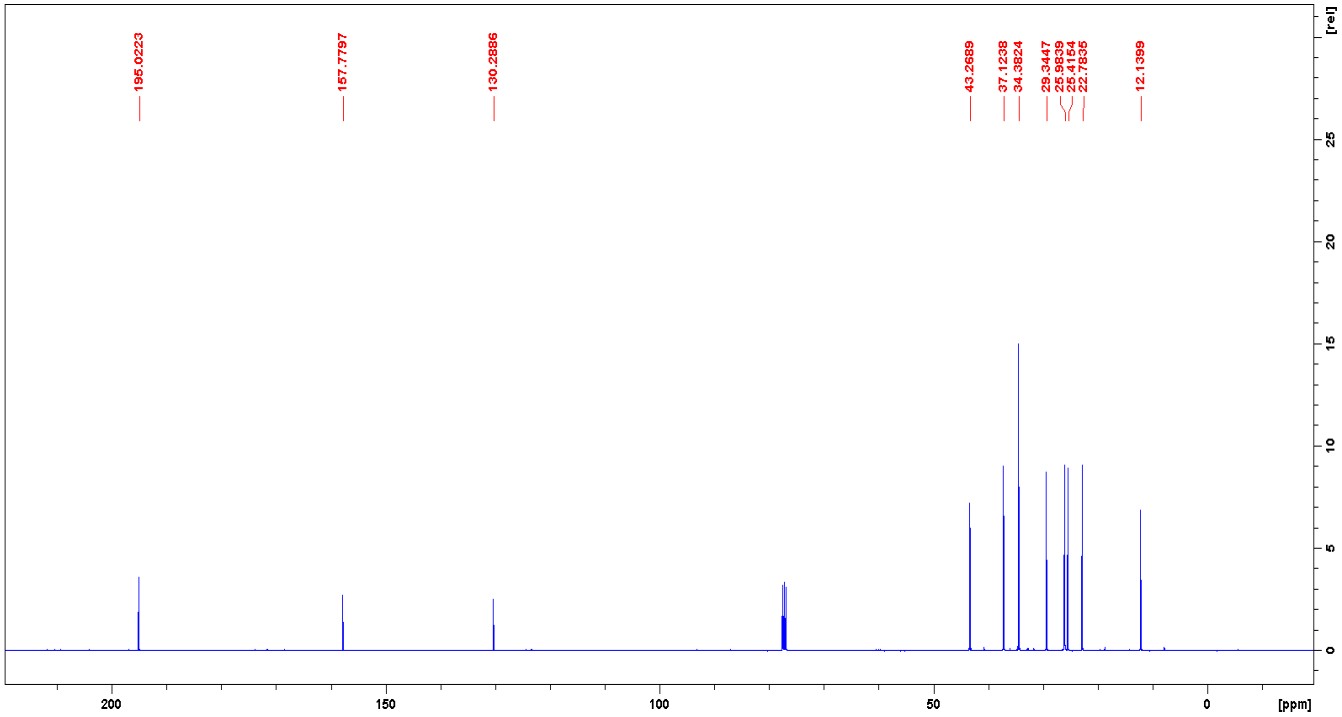
3-(Dodecylthio)-2-methylcyclohex-2-en-1-one **(8e)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



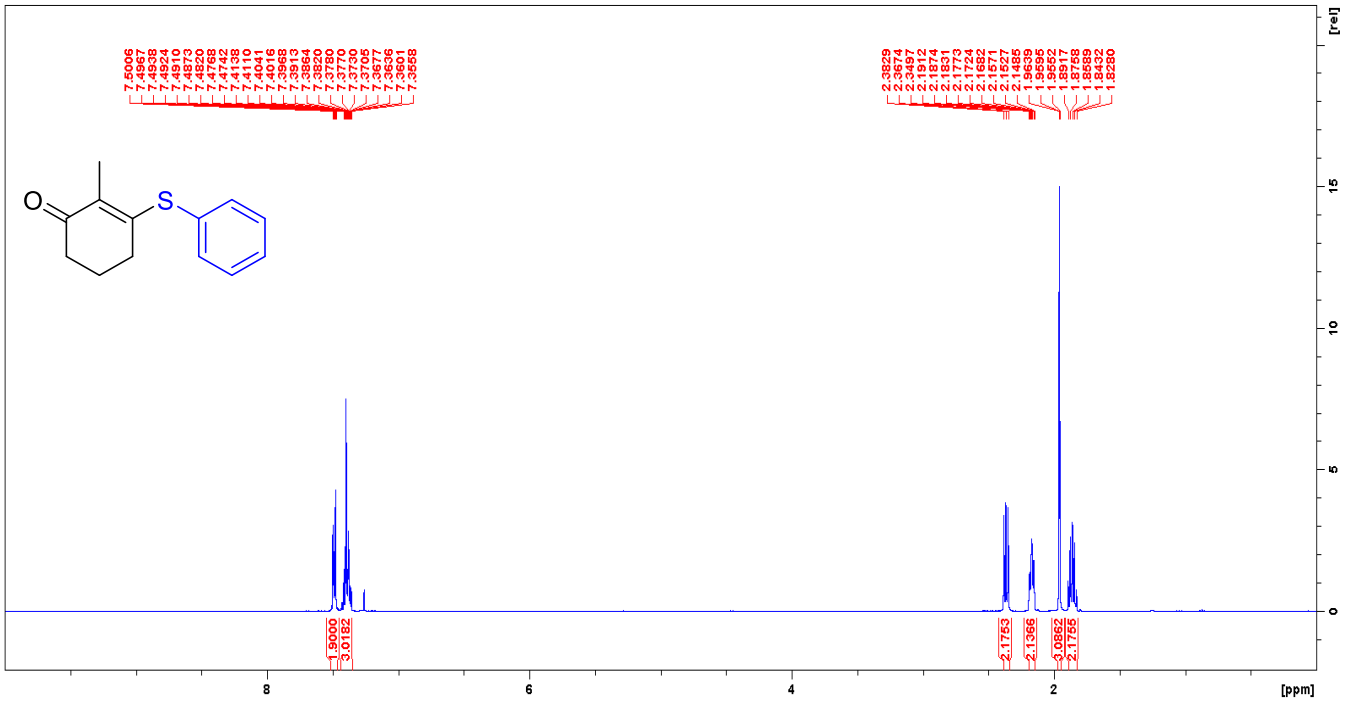


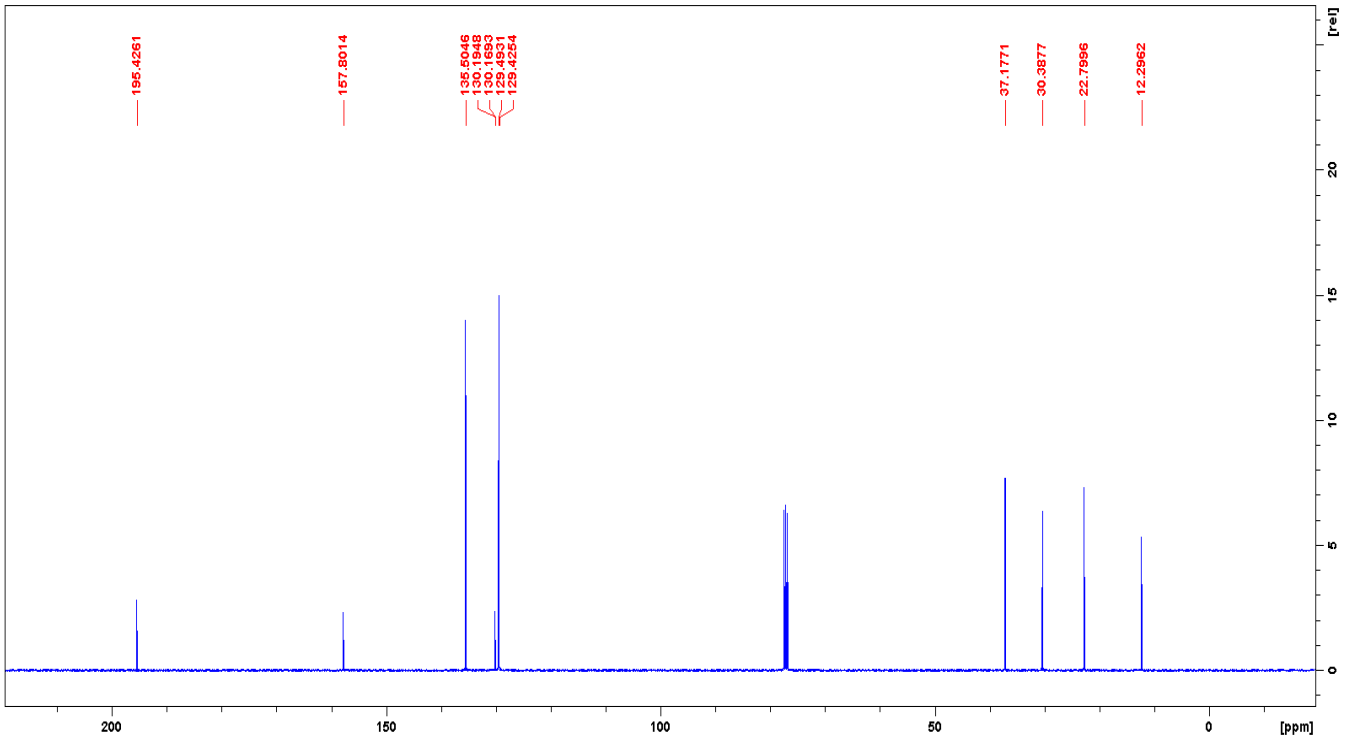
3-(Cyclohexylthio)-2-methylcyclohex-2-en-1-one **(8f)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



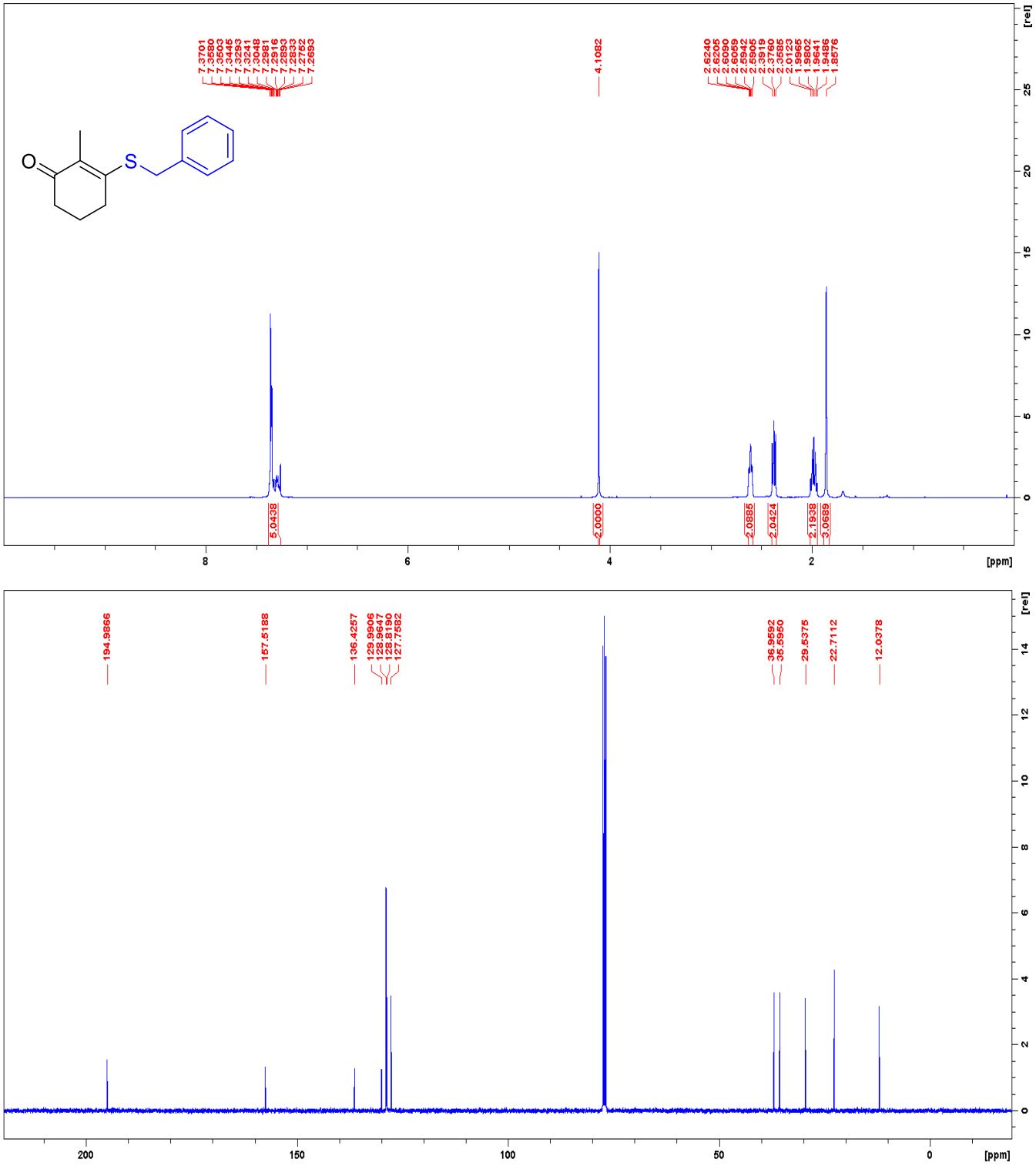


2-Methyl-3-(phenylthio)cyclohex-2-en-1-one **(8g)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).

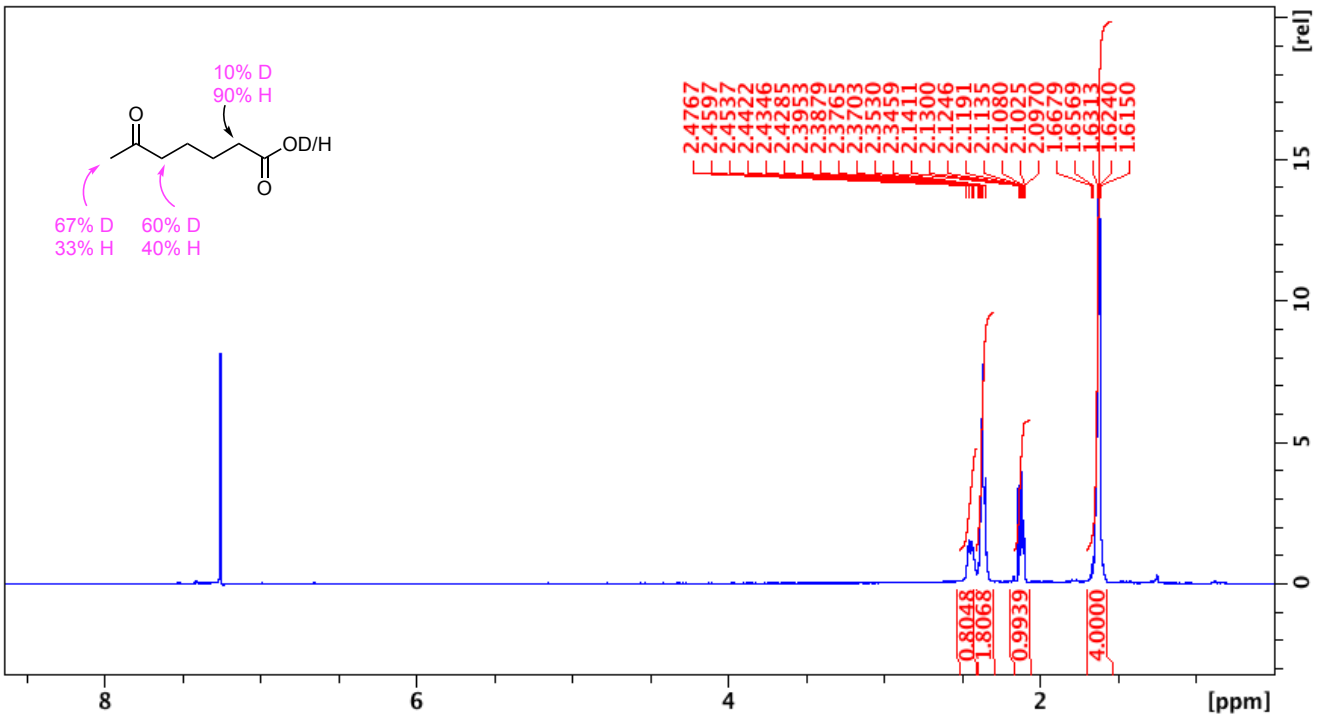


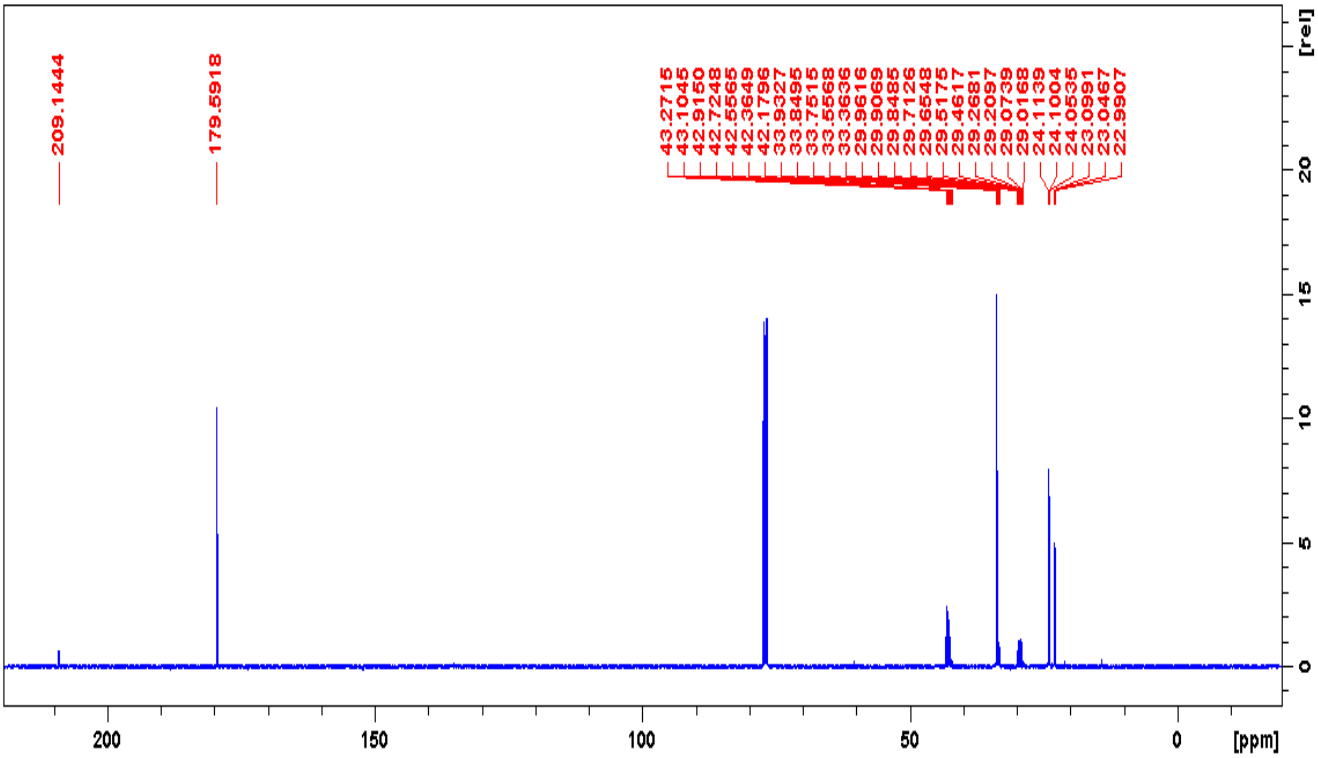


3-(Benzylthio)-2-methylcyclohex-2-en-1-one **(8h)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).



6-Oxoheptanoic-5,7,7,7-d_4 acid-d **(4aD)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).





Methyl-d_3 6-oxoheptanoate-5,7,7,7-d_4 **(4bD)**; **^{1}H NMR** (400 MHz, $CDCl_3$), **^{13}C NMR** (100 MHz, $CDCl_3$).