

## “Hydroacylation Avoided: NHC-Catalysed, Completely Chemoselective Crossed-Acyloin Reactions”

AUTHORS: Christopher A. Rose<sup>#</sup>, Sivaji Gundala<sup>†</sup>, Claire-Louise Fagan<sup>†</sup>, Johannes F. Franz<sup>#</sup>, Stephen J. Connon<sup>†</sup>, Kirsten Zeitler<sup>#</sup>

<sup>†</sup>Centre for Synthesis and Chemical Biology, Department of Chemistry,  
University of Dublin, Trinity College, Dublin 2, Ireland  
E-mail: [connons@tcd.ie](mailto:connons@tcd.ie). Fax: 00353-1-6712826 and

<sup>#</sup>Institut für Organische Chemie, Universität Regensburg,  
Universitätsstrasse 31, D-93053 Regensburg, Germany  
E-mail: [kirsten.zeitler@chemie.uni-regensburg.de](mailto:kirsten.zeitler@chemie.uni-regensburg.de). Fax: 0049-941-943 4121

## Supporting Information

### Table of Contents

1. General Methods	S2
2. General Procedures	S3
3. Data of Catalyst Screening	S5
4. Experimental Data for Cross Coupled Products	S6
4.1 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling of Aliphatic Aldehydes with Ethyl Pyruvate	S6–S10
4.2 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling of Aromatic Aldehydes with Ethyl Pyruvate	S10–S13
4.3 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling with Various $\alpha$ -Ketoesters	S13
4.4 Experimental Data for Decarboxylation Experiments	S17
4.5 Experimental Data for Catalyst <b>78</b>	S19
5. HPLC Chromatograms - Cross Coupled Product	S20
6. $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra of Products	S22–S90

## 1 General Methods

Unless otherwise noted, all commercially available compounds were used as provided without further purification.

NMR spectra were recorded on 300 MHz (300.13 MHz), 400 MHz (400.13 MHz) or 600 MHz (600.13 MHz) spectrometers using the solvent peak as internal reference ( $\text{CDCl}_3$ :  $\delta$  H 7.26;  $\delta$  C 77.0 and  $\text{DMSO-d}_6$ :  $\delta$  H 2.51;  $\delta$  C 39.5). Multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet); coupling constants ( $J$ ) are in Hertz (Hz). Mass spectra (MS ESI) were recorded using a Finnigan MAT 95 or Varian MAT 311A. All reactions were monitored by thin-layer chromatography using Merck silica gel plates 60 F<sub>254</sub>; visualization was accomplished with UV light and/or staining with appropriate stains ( $\text{KMnO}_4$ , anisaldehyde, vaniline, ninhydrin or phosphomolybdic acid). Standard flash chromatography procedures were followed (particle size 40–63  $\mu\text{m}$ ). Infrared spectra were obtained using neat samples on spectrometers equipped with a universal ATR (attenuated total reflectance) sampling accessory. Optical rotation measurements are quoted in units of  $10^{-1}$  deg  $\text{cm}^2 \text{ g}^{-1}$ . Analytical CSP-HPLC was performed using a Daicel CHIRALCEL OJ-H (4.6 mm x 25 cm) column.

Tetrahydrofuran was distilled from sodium/benzophenone. All reactions were carried out under a protective atmosphere of dry nitrogen or argon using oven-dried glassware unless otherwise stated.

Liquid aldehydes and  $\alpha$ -ketoesters were distilled over EDTA prior to use. Solid aldehydes were washed acid-free with 10% aq.  $\text{K}_2\text{CO}_3$ -solution prior to use.

For the cross coupling experiments,  $\text{K}_2\text{CO}_3$  was finely ground prior to use.

Triazolium pre-catalyst **22** was synthesized according to the procedure described by Rovis et al.<sup>1</sup> and catalysts **76**, **77** and **78** were prepared as described earlier.<sup>2</sup>

Aldehydes **23-28**, **32** and **45-52** are commercially available. Aldehyde **29**,<sup>3</sup> **30**,<sup>4</sup> **31**,<sup>5</sup> and **32**,<sup>6</sup> were prepared according to known protocols. Ketoesters **13**, **61**, **62** and **65** are commercially available. Ketoester **63**,<sup>7</sup> **64**,<sup>8</sup> and **74**,<sup>9</sup> and **79**,<sup>10</sup> were prepared according to known literature procedures.

<sup>1</sup> a) M. S. Kerr, J. Read de Alaniz, T. Rovis, *J. Org. Chem.* **2005**, *70*, 5725; b) H. U. Vora, S. P. Lathrop, N. T. Reynolds, M. S. Kerr, J. Read de Alaniz, T. Rovis, *Org. Synth.* **2010**, *87*, 350.

<sup>2</sup> a) L. Baragwanath, C. A. Rose, K. Zeitler, S. J. Connon, S. J., *J. Org. Chem.* **2009**, *74*, 9214; b) S. E. O'Toole, C. A. Rose, S. Gundala, K. Zeitler, S. J. Connon, *J. Org. Chem.* **2011**, *76*, 347

<sup>3</sup> C. Gennari, P. G. Cozzi, *J. Org. Chem.* **1988**, *53*, 4015-4021.

<sup>4</sup> Y. Ikeda, J. Ukai, N. Ikeda, H. Yamamoto, *Tetrahedron* **1987**, *43*, 731-741.

<sup>5</sup> Y.-X. Wang, L.-N. Zhang, G. M. Rubanyi, WO 2010025043 **2010**.

<sup>6</sup> R. M. de Figueiredo, R. Fröhlich, M. Christmann, *Angew. Chem. Int. Ed.* **2008**, *47*, 1450-1453.

<sup>7</sup> K. Nakamura, K. Inoue, K. Ushio, S. Oka, A. Ohno, *J. Org. Chem.* **1988**, *53*, 2589-2593.

<sup>8</sup> M. Rambaud, M. Bakasse, G. Duguay, J. Villieras, *Synthesis* **1988**, 564-566.

<sup>9</sup> J. M. Domagala, *Tetrahedron Lett.* **1980**, *21*, 4997-5000.

<sup>10</sup> S. Hu, D C. Neckers, *J. Org. Chem.* **1996**, *61*, 6407-6415.

## 2 General Procedures

### **General Procedure 1 (for the Cross coupling of Aliphatic Aldehydes and Ethyl Pyruvate)**

A flame dried screw-capped Schlenk tube equipped with a magnetic stirring bar was charged with  $\text{K}_2\text{CO}_3$  (7mg, 0.05 mmol, 10 mol%) and evacuated. The solid was then heated to 650 °C for 30 seconds and subsequently cooled to ambient temperature under  $\text{N}_2$ . After this procedure has been repeated once triazolium precatalyst (9 mg, 0.025 mmol, 5 mol%) was added.<sup>11</sup> The solids were additionally dried for 1h under high vacuum at ambient temperature. Dry THF (0.45 mL) was added and the resulting mixture was stirred for 10 min at ambient temperature. To the orange suspension was added ethyl pyruvate (55  $\mu\text{L}$ , 0.5 mmol, 1 equiv.) followed by the aliphatic aldehyde (0.5 mmol, 1 equiv.). The Schlenk tube was sealed with a cap and the reaction mixture was stirred for 20h at 40 °C under  $\text{N}_2$ .<sup>12</sup> After 20h the solvent was evaporated. The resulting mixture was subjected to column chromatography yielding the corresponding  $\alpha$ -hydroxy- $\beta$ -ketoester.

### **General Procedure 2 (for the Cross coupling of Aromatic Aldehydes and Ethyl Pyruvate)**

A flame dried screw-capped Schlenk tube equipped with a magnetic stirring bar was charged with  $\text{K}_2\text{CO}_3$  (14 mg, 0.1 mmol, 20 mol%) and evacuated. The solid was then heated to 650 °C for 30 seconds and subsequently cooled to ambient temperature under  $\text{N}_2$ . After this procedure has been repeated once triazolium precatalyst (18 mg, 0.05 mmol, 10 mol%) was added. The solids were dried for an additional 1h under high vacuum at ambient temperature. Dry  $\text{CHCl}_3$  (0.45 mL) was added and the resulting mixture was stirred for 10 min at ambient temperature. To the orange suspension was added ethyl pyruvate (66  $\mu\text{L}$ , 0.6 mmol, 1.2 equiv.)<sup>13</sup> followed by the aromatic aldehyde (0.5 mmol, 1 equiv.). The Schlenk tube was sealed with a cap and the reaction mixture was stirred at 40 °C under  $\text{N}_2$ . After 20h the solvent was evaporated. The resulting mixture was subjected to column chromatography yielding the corresponding  $\alpha$ -hydroxy- $\beta$ -ketoester.

### **General Procedure 2A (for the Cross coupling of Aromatic Aldehydes and Aromatic Pyruvates)**

General procedure 2 was followed as described above. However, the following changes appeared to be favourable: The aryl pyruvate was used in higher excess (1.5 mmol, 3 equiv.); to the mixture of catalyst, base and pyruvate was finally added the aromatic aldehyde (0.5 mmol, 1 equiv.). The Schlenk tube was sealed with a cap and the reaction mixture was stirred at 45 °C (favourable to the standard 40 °C) under  $\text{N}_2$ .

<sup>11</sup> For quantitative NMR experiments *trans*-stilbene (23 mg, 0.125 mmol, 25 mol%) is additionally added at this stage.

<sup>12</sup> For quantification of products, residual starting material etc. via NMR spectroscopy, an aliquot of the reaction mixture was transferred into a NMR tube by dipping in a pasteur pipet (without cap) several times.

<sup>13</sup> In some cases 1.7 equiv. have been used (see notes for the corresponding compounds).

### **General Procedure 3 (for the Cross Coupling of Octanal and Various $\alpha$ -Ketoesters)**

A flame dried screw-capped Schlenk tube equipped with a magnetic stirring bar was charged with  $K_2CO_3$  (7 mg, 0.05 mmol, 10 mol%) and evacuated. The solid was then heated to 650 °C for 30 seconds and subsequently cooled to ambient temperature under  $N_2$ . After this procedure has been repeated once triazolium precatalyst (9 mg, 0.025 mmol, 5 mol%) was added. The solids were dried for a further 1h under high vacuum at ambient temperature. Dry THF (0.45 mL) was added and the resulting mixture was stirred for 10 min at ambient temperature. To the orange suspension was added  $\alpha$ -ketoester (0.5 mmol, 1 equiv.) followed by octanal (77  $\mu$ L, 0.5 mmol, 1 equiv.). The Schlenk tube was sealed with a cap and the reaction mixture was stirred at 40 °C under  $N_2$ . After 20h the solvent was evaporated. The resulting mixture was subjected to column chromatography yielding the corresponding  $\alpha$ -hydroxy- $\beta$ -ketoester.

### **General Procedure 4 (for Large Scale Cross Coupling)**

A flame dried 50 mL Schlenk flask equipped with a magnetic stirring bar and a reflux condenser was charged with  $K_2CO_3$  (206 mg, 1.5 mmol, 10 mol%) and evacuated. The solid was then heated to 650 °C for 30 seconds and subsequently cooled to ambient temperature under  $N_2$ . After this procedure has been repeated once triazolium precatalyst (271 mg, 0.75 mmol, 5 mol%) was added. The solids were additionally dried for 1h under high vacuum at ambient temperature. Dry THF (14 mL) was added and the resulting mixture was stirred for 10 min at ambient temperature. To the orange suspension was added ethyl pyruvate (1.65 mL, 15 mmol, 1 equiv.) followed by the aldehyde (e. g. hydrocinnamaldehyde (1.96 mL, 15 mmol, 1 equiv.)). The reaction mixture was stirred for 20h at 40 °C under  $N_2$ . After 20h the reaction mixture was diluted with 50 mL dichloromethane and extracted with 20 mL  $H_2O$ . The aqueous layer was back-extracted with dichloromethane (3 x 20 mL). The combined organic layers were washed with brine, dried over anhydrous  $Na_2SO_4$  and concentrated. The resulting brown oil was subjected to column chromatography (silica gel).

### **General Procedure 5 (for Acetylation)**

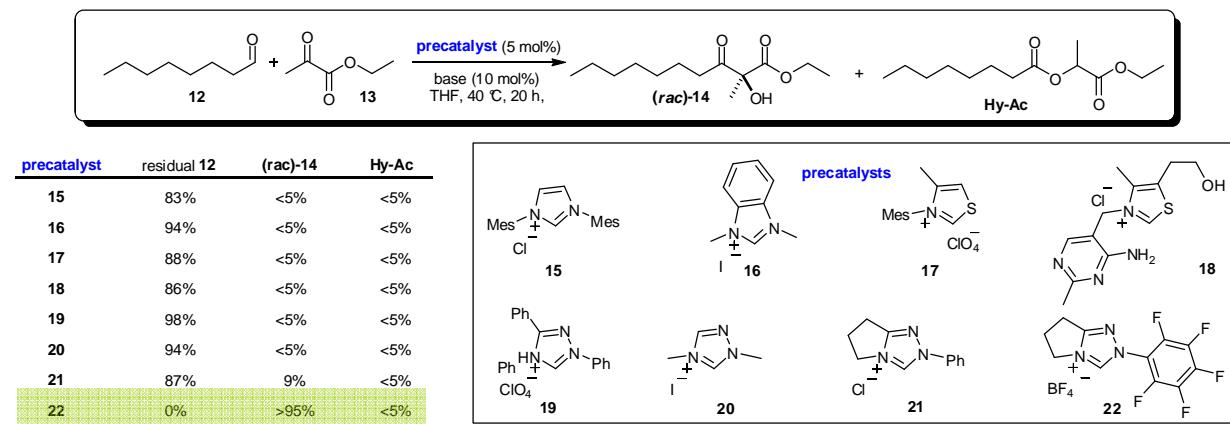
An oven-dried 10 mL round bottomed flask, equipped with a magnetic stirrer, was charged with the selected  $\alpha$ -hydroxy- $\beta$ -ketoester (1.0 mmol), DMAP (12.5 mg, 0.10 mmol, 10 mol%) and the reaction put under an atmosphere of Argon.  $CH_2Cl_2$  (2.00 mL) was injected *via* syringe to give a solution followed by the addition of  $NEt_3$  (2.5 mmol, 2.5 equiv.) and  $Ac_2O$  (2.0 mmol, 2.0 equiv.). The reaction was

stirred for 16 h; the resulting mixture was worked-up by the initial careful addition of water, followed by Na<sub>2</sub>CO<sub>3</sub> until CO<sub>2</sub> evolution ceased and the aqueous layer remained basic. The product was extracted with CH<sub>2</sub>Cl<sub>2</sub> dried over anhydrous MgSO<sub>4</sub> and concentrated *in vacuo*. The remaining residue was purified by column chromatography.

### General Procedure 6 (for the Debenzyloxycarbonylation of Cross Coupled $\alpha$ -Hydroxy- $\beta$ -Ketoester)

To a 25 mL round bottomed flask, equipped with a magnetic stirring bar, was added the acetylated  $\alpha$ -hydroxy- $\beta$ -ketoester (0.5 mmol), 10% Pd/C (20 wt%) and EtOAc (0.05 M solution) together with 4 Å molecular sieves. The flask was evacuated and then purged with N<sub>2</sub>. This cycle was performed twice and finally the flask was evacuated and backfilled with hydrogen. The reaction was then stirred vigorously at ambient temperature under an atmosphere of hydrogen (hydrogen generator), overnight. After reaching full conversion the reaction mixture was filtered through celite® and concentrated *in vacuo*. The crude product was purified by column chromatography.

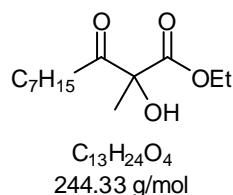
## 3 Catalyst Screening



## 4 Experimental Data for Cross Coupled Products

### 4.1 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling of Aliphatic Aldehydes with Ethyl Pyruvate

#### Ethyl-2-hydroxy-2-methyl-3-oxodecanoate (14)

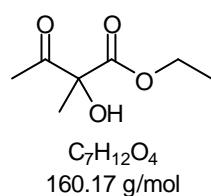


according to the **general procedure 1**: yield after column chromatography (silica gel, 20%  $Et_2O/n$ -pentane): 112 mg (92 %), colourless oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.32.

$^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  4.28 – 4.18 (m, 3H), 2.70 – 2.44 (m, 2H), 1.65 – 1.52 (m, 5H), 1.31 – 1.20 (m, 11H), 0.90 – 0.82 (m, 3H).

$^{13}C$  NMR (75.5 MHz,  $CDCl_3$ ):  $\delta$  207.2, 171.5, 80.9, 62.5, 36.4, 31.6, 29.0 (2C), 23.5, 22.6, 21.8, 14.1, 14.0. HRMS (EI;  $C_{13}H_{24}O_4$ ): calcd.: 244.1675, found: 244.1674. IR:  $\tilde{\nu}$  = 3493, 2929, 2859, 1721, 1465, 1373, 1257, 1014, 632, 540  $cm^{-1}$ .

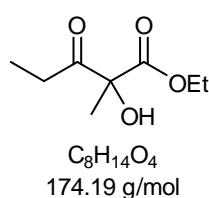
#### Ethyl 2-hydroxy-2-methyl-3-oxobutanoate (34, Table 2, entry 1)



according to the **general procedure 1**: (using 2 equiv. of the aliphatic aldehyde instead of 1 equiv.): yield according to quantitative  $^1H$  NMR (internal standard: *trans*-Stilbene): 92%

$^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  4.27 – 4.19 (m, 2H), 4.18 (br s, 1H), 2.25 (s, 3H), 1.57 (s, 3H), 1.27 (t,  $J$  = 7.14 Hz, 3H).  $^{13}C$  NMR (75.5 MHz,  $CDCl_3$ ):  $\delta$  204.9, 171.3, 81.0, 62.6, 24.2, 21.8, 14.0.<sup>14</sup>

#### Ethyl 2-hydroxy-2-methyl-3-oxopentanoate (35, Table 2, entry 2)



according to the **general procedure 1**: yield after column chromatography (silica gel, hexanes/ $Et_2O$  4/1): 162 mg (93 %),<sup>15</sup> colourless oil.  $R_f$  (hexanes/ $Et_2O$  4/1) 0.28.

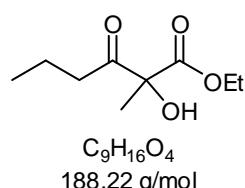
<sup>14</sup> Experimental data in accordance to previously reported literature values: X. Baucherel, E. Levoirier, J. Uziel, S. Juge, *Tetrahedron Lett.* **2000**, *41*; 1385.

<sup>15</sup> The reaction was performed using the double amount of the described size of the general procedure.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 4.26–4.20 (m, 3H), 2.72–2.65 (m, 1H), 2.58–2.54 (m, 1H), 1.58 (s, 3H), 1.28 (t, *J* = 7.5 Hz, 3H) 1.08 (t *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 207.6, 171.3, 80.6, 62.3, 29.6, 21.7, 13.8, 7.5. HRMS (ESI; C<sub>8</sub>H<sub>14</sub>O<sub>4</sub> + Na): calcd.: 197.0790, found: 197.0792.

IR :  $\tilde{\nu}$  = 3477, 2984, 2941, 1717, 1449, 1373, 1258, 1016, 807, 676 cm<sup>-1</sup>.

### Ethyl 2-hydroxy-2-methyl-3-oxohexanoate (36, table 2, entry 3)

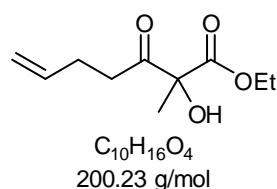


according to the **general procedure 1**: yield after column chromatography (silica gel, hexanes/Et<sub>2</sub>O 4/1): 177 mg (94 %),<sup>15</sup> colourless oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 4/1) 0.28.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 4.25–4.20 (m, 3H), 2.65–2.42 (m, 2H), 1.66–1.58 (m, 2H), 1.56 (s, 3H), 1.27 (t, *J* = 7.4 Hz, 3H) 0.89 (t, *J* = 7.8 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 206.8, 171.3, 80.7, 62.3, 38.0, 21.5, 16.8, 13.8, 13.3. HRMS (ESI; C<sub>9</sub>H<sub>16</sub>O<sub>4</sub> + Na): calcd. 211.0946, found: 211.0950.

IR :  $\tilde{\nu}$  = 3481, 2970, 2878, 1716, 1449, 1371, 1253, 1017, 825, 672 cm<sup>-1</sup>.

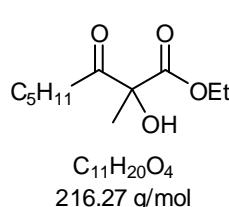
### Ethyl 2-hydroxy-2-methyl-3-oxohept-6-enoate (37, Table 2, entry 4)



according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 87 mg (87 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.27.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 5.84 – 5.68 (m, 1H), 5.08 – 4.93 (m, 2H), 4.23 (q, *J* = 7.14 Hz, 2H), 4.16 (s, 1H), 2.84 – 2.54 (m, 2H), 2.39–2.29 (m, 2H), 1.57 (s, 3H), 1.27 (t, *J* = 7.14 Hz, 3H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 206.3, 171.5, 136.5, 115.6, 80.9, 62.6, 35.7, 27.4, 21.8, 14.0. HRMS (EI; C<sub>10</sub>H<sub>16</sub>O<sub>4</sub>) calcd.: 200.1049, found: 200.1041. IR :  $\tilde{\nu}$  = 3481, 2984, 1721, 1642, 1447, 1260, 1014, 916, 632, 538 cm<sup>-1</sup>.

### Ethyl 2-hydroxy-2-methyl-3-oxooctanoate (38, Table 2, entry 5)

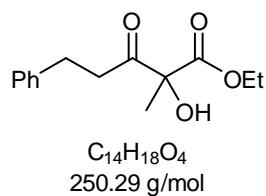


according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 98 mg (91 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.30.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.27 – 4.18 (m, 3H), 2.70 – 2.44 (m, 2H),

1.63 – 1.53 (m, 5H), 1.35 – 1.19 (m, 7H), 0.87 (t,  $J = 7.00$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.2, 171.5, 80.9, 62.5, 36.3, 31.2, 23.2, 22.4, 21.8, 14.0, 13.9. HRMS (EI;  $\text{C}_{11}\text{H}_{20}\text{O}_4$ ): calcd.: 216.1362, found: 216.1362. IR :  $\tilde{\nu} = 3480, 2960, 2873, 1720, 1449, 1374, 1260, 1019, 802, 632, 538 \text{ cm}^{-1}$ .

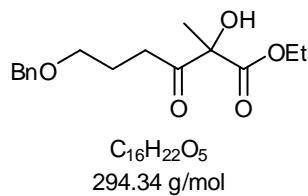
**Ethyl 2-hydroxy-2-methyl-3-oxo-5-phenylpentanoate (39, Table 2, entry 6)**



$\text{C}_{14}\text{H}_{18}\text{O}_4$   
250.29 g/mol

according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 119 mg (95 %), almost colourless oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.22.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.32 – 7.13 (m, 5H), 4.20 – 4.09 (m, 3H), 3.08–2.78 (m, 4H), 1.54 (s, 3H), 1.22 (t,  $J = 7.14$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  206.2, 171.4, 140.5, 128.6, 128.4, 126.3, 81.0, 62.7, 38.3, 29.5, 21.7, 14.0. HRMS (EI;  $\text{C}_{14}\text{H}_{18}\text{O}_4$ ): calcd.: 250.1205, found: 250.1208. IR :  $\tilde{\nu} = 3480, 2986, 1720, 1454, 1259, 1160, 701, 632, 538 \text{ cm}^{-1}$ .

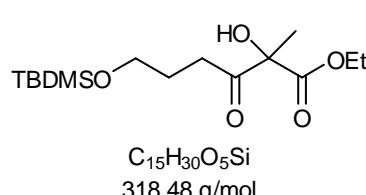
**Ethyl 6-(benzyloxy)-2-hydroxy-2-methyl-3-oxohexanoate (40, Table 2, entry 7)**



$\text{C}_{16}\text{H}_{22}\text{O}_5$   
294.34 g/mol

according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 7/1): 129 mg (88 %), colourless oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.22.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39 – 7.24 (m, 5H), 4.47 (s, 2H), 4.27 – 4.16 (m, 3H), 3.47 (t,  $J = 6.04$  Hz, 2H), 2.85 – 2.60 (m, 2H), 1.98 – 1.85 (m, 2H), 1.57 (s, 3H), 1.26 (t,  $J = 7.14$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.0, 171.5, 138.3, 128.4, 127.6 (2C), 80.9, 72.9, 68.9, 62.6, 33.2, 23.8, 21.9, 14.0. HRMS (EI;  $\text{C}_{16}\text{H}_{22}\text{O}_5$ ): calcd.: 294.1467, found: 294.1459. IR :  $\tilde{\nu} = 3455, 2870, 1721, 1454, 1367, 1260, 1113, 1026, 741, 632, 537 \text{ cm}^{-1}$ .

**Ethyl 6-(*tert*-butyldimethylsilyloxy)-2-hydroxy-2-methyl-3-oxohexanoate (41, Table 2, entry 8)**

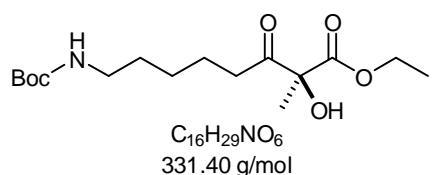


$\text{C}_{15}\text{H}_{30}\text{O}_5\text{Si}$   
318.48 g/mol

according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 121 mg (76 %), colourless oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.35.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.25 – 4.16 (m, 3H), 3.58 (t, J = 6.04 Hz, 2H), 2.77 – 2.54 (m, 2H), 1.85 – 1.68 (m, 2H), 1.55 (s, 3H), 1.25 (t, J = 7.14 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 6H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 207.2, 171.5, 80.9, 62.5, 61.8, 32.8, 26.7, 25.9, 21.9, 18.3, 14.0, -5.4. HRMS (ESI; C<sub>15</sub>H<sub>31</sub>O<sub>5</sub>Si): calcd.: 319.1941, found: 319.1941. IR:  $\tilde{\nu}$  = 2937, 2858, 1722, 1473, 1259, 1101, 1201, 835, 632, 539 cm<sup>-1</sup>.

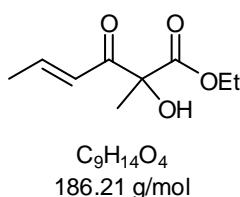
**Ethyl 8-(tert-butoxycarbonylamino)-2-hydroxy-2-methyl-3-oxooctanoate (42, Table 2, entry 9)**



according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 5/2): 127 mg (77 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/2) 0.27.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.52 (s, 1H), 4.23 (q, J = 7.1 Hz, 2H), 4.18 (s, 1H), 3.15 – 3.01 (m, 2H), 2.72 – 2.59 (m, 1H), 2.58 – 2.45 (m, 1H), 1.66 – 1.57 (m, 2H), 1.56 (s, 3H), 1.50 – 1.39 (m, 11H), 1.32 – 1.24 (m, 5H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 207.0, 171.5, 155.9, 80.8, 79.1, 62.6, 40.3\*, 36.2, 29.8, 28.4\*, 26.1, 23.1, 21.8, 14.0. HRMS (ESI; C<sub>16</sub>H<sub>29</sub>NO<sub>6</sub>Na): calcd.: 354.1887, found: 354.1892. IR:  $\tilde{\nu}$  = 3950, 2983, 2937, 2865, 1702, 1517, 1455, 1392, 1366, 1250, 1166, 1015, 911, 861 cm<sup>-1</sup>.

**(E)-Ethyl 2-hydroxy-2-methyl-3-oxohex-4-enoate (43, Table 2, entry 10)**



according to the **general procedure 1**: yield after column chromatography (Silica gel, hexanes/ Et<sub>2</sub>O 4/1): 90 mg (48 %),<sup>16</sup> colourless oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 4/1) 0.32.

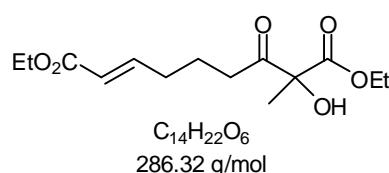
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.19 (m, 1H), 6.53 (m, 1H), 4.37 (s, 1H), 4.25 (q, J = 7.0 Hz, 2H), 1.97 (d, J = 7.0 Hz, 3H), 1.62 (s, 3H), 1.29 (t, J = 7.0 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 194.3, 171.0, 147.0, 123.4, 79.6, 62.0, 21.6, 18.3, 13.5. HRMS (ESI; C<sub>9</sub>H<sub>14</sub>O<sub>4</sub> + Na): calcd.: 209.0799, found: 209.0790.

IR:  $\tilde{\nu}$  = 3471, 2938, 1736, 1444, 1375, 1252, 1014, 844, 669 cm<sup>-1</sup>.

<sup>16</sup> The reaction was performed using the double amount of the described size of the general procedure.

\* Signals of the rotamer of the Boc group: 39.5 resp. 28.0 ppm.

**(E)-Diethyl- 8-hydroxy-8-methyl-7-oxonon-2-enedioate (44, Table 2, entry 11)**

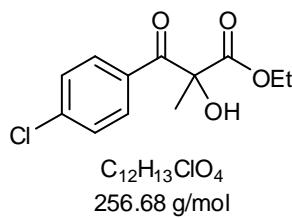


according to the **general procedure 1**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 129 mg (90 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.16.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 6.95 – 6.83 (m, 1H), 5.85 – 5.76 (m, 1H), 4.28 – 4.11 (m, 5H), 2.70 (td, J = 18.20 Hz, 7.27 Hz, 1H), 2.53 (td, J = 18.20 Hz, 7.07 Hz, 1H), 2.25 – 2.14 (m, 2H), 1.83 – 1.71 (m, 2H), 1.56 (s, 3H), 1.27 (t, J = 7.13 Hz, 6H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 206.5, 171.5, 166.5, 147.6, 122.2, 80.8, 62.7, 60.3, 35.5, 31.1, 21.9, 21.8, 14.3, 14.0. HRMS (EI; C<sub>14</sub>H<sub>22</sub>O<sub>6</sub>): calcd: 286.1416, found: 286.1411. IR:  $\tilde{\nu}$  = 2962, 1722, 1653, 1259, 1090, 1016, 795, 632, 537 cm<sup>-1</sup>.

## 4.2 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling of Aromatic Aldehydes with Ethyl Pyruvate

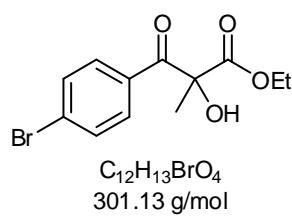
**Ethyl 3-(4-chlorophenyl)-2-hydroxy-2-methyl-3-oxopropanoate (53, Table 3, entry 2)**



according to the **general procedure 2**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 10/1): 107 mg (83 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.24.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.98 – 7.91 (m, 2H), 7.45 – 7.39 (m, 2H), 4.29 (s, 1H), 4.23 (q, J = 7.14 Hz, 2H), 1.72 (s, 3H), 1.17 (t, J = 7.14 Hz, 3H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 194.6, 172.5, 140.2, 131.6, 131.0, 129.0, 79.6, 62.8, 23.5, 13.9. HRMS (EI; C<sub>12</sub>H<sub>13</sub>O<sub>4</sub><sup>35</sup>Cl): calcd.: 256.0502, found: 256.0507. IR:  $\tilde{\nu}$  = 3450, 3104, 2995, 1721, 1686, 1587, 1487, 1453, 1403, 1271, 1228, 1158, 1113, 1090, 1013, 991, 940, 844, 776, 739, 715, 683, 566, 530 cm<sup>-1</sup>.

**Ethyl 3-(4-bromophenyl)-2-hydroxy-2-methyl-3-oxopropanoate (54, Table 3, entry 3)**



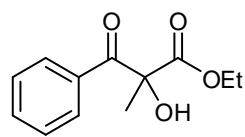
according to the **general procedure 2**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 8/1): 115 mg (76 %), almost colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.26.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.89 – 7.83 (m, 2H), 7.61 – 7.55 (m, 2H), 4.31 – 4.28 (m, 1H), 4.27 – 4.18 (br q, J = 6.95 Hz, 2H), 1.71 (s, 3H),

1.17 (t,  $J = 7.14$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  194.8, 172.4, 132.1, 132.0, 131.0, 129.0, 79.6, 62.8, 23.5, 13.9. HRMS (EI;  $\text{C}_{12}\text{H}_{13}\text{O}_4^{79}\text{Br}$ ): calcd.: 299.9997, found: 299.9997.

IR :  $\tilde{\nu} = 3452, 3101, 2992, 1721, 1686, 1581, 1475, 1452, 1399, 1268, 1227, 1160, 1113, 1070, 1010, 990, 940, 843, 774, 732, 679, 524 \text{ cm}^{-1}$ .

### Ethyl 2-hydroxy-2-methyl-3-oxo-3-phenylpropanoate (55, Table 3, entry 4)

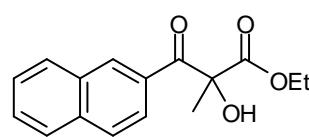


$\text{C}_{12}\text{H}_{14}\text{O}_4$   
222.24 g/mol

according to the **general procedure 2**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 8/1): 96 mg (86 %), pale yellow oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.21.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.00 – 7.95 (m, 2H), 7.61 – 7.54 (m, 1H), 7.49 – 7.41 (m, 2H), 4.46 (s, 1H), 4.22 (q,  $J = 7.14$  Hz, 2H), 1.73 (s, 3H), 1.15 (t,  $J = 7.14$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  196.0, 172.3, 133.7, 133.1, 129.5, 128.6, 79.5, 62.5, 23.5, 13.8. HRMS (EI;  $\text{C}_{12}\text{H}_{14}\text{O}_4$ ): calcd.: 222.0892, found: 222.0892. IR :  $\tilde{\nu} = 3469, 2988, 1742, 1695, 1450, 1374, 1271, 1233, 1150, 632, 539 \text{ cm}^{-1}$ .

### Ethyl 2-hydroxy-2-methyl-3-(naphthalen-2-yl)-3-oxopropanoate (56, Table 3, entry 5)

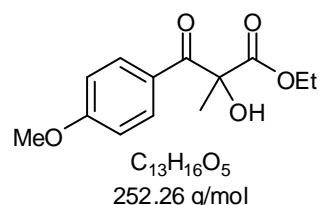


$\text{C}_{16}\text{H}_{16}\text{O}_4$   
272.30 g/mol

according to the **general procedure 2**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 7/1): 115 mg (84 %), pale yellow oil.  $R_f$  (petroleum ether/ethylacetate 5/1) 0.21.

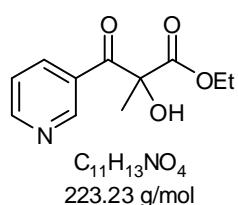
$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.57 (s, 1H), 8.04 – 7.84 (m, 4H), 7.66 – 7.52 (m, 2H), 4.55 (s, 1H), 4.24 (q,  $J = 7.14$  Hz, 2H), 1.82 (s, 3H), 1.15 (t,  $J = 7.14$  Hz, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  195.9, 172.5, 135.7, 132.3, 131.6, 130.4, 129.9, 129.1, 128.5, 127.7, 127.0, 124.8, 79.7, 62.6, 23.8, 13.9. HRMS (EI;  $\text{C}_{16}\text{H}_{16}\text{O}_4$ ): calcd.: 272.1049, found: 272.1049. IR :  $\tilde{\nu} = 3474, 3058, 2985, 1739, 1687, 1627, 1370, 1280, 1251, 1148, 1116, 1014, 632, 539 \text{ cm}^{-1}$ .

**Ethyl 2-hydroxy-3-(4-methoxyphenyl)-2-methyl-3-oxopropanoate (57, Table 3, entry 6)**



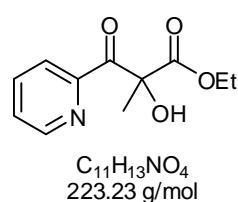
according to the **general procedure 2** (note: reaction time 48h): yield after column chromatography (silica gel, petroleum ether/ethylacetate 7/1): 117 mg (93 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.17. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 8.03 – 7.96 (m, 2H), 6.96 – 6.89 (m, 2H), 4.61 (s, 1H), 4.21 (q, *J* = 7.14 Hz, 2H), 3.87 (s, 3H), 1.73 (s, 3H), 1.16 (t, *J* = 7.14 Hz, 3H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 194.4, 172.4, 164.0, 132.1, 125.6, 113.9, 79.2, 62.4, 55.6, 23.8, 13.9. HRMS (EI; C<sub>15</sub>H<sub>16</sub>O<sub>5</sub>): calcd.: 252.0998, found: 252.1003. IR :  $\tilde{\nu}$  = 2983, 1738, 1682, 1602, 1513, 1263, 1152, 1030, 632, 540 cm<sup>-1</sup>.

**Ethyl 2-hydroxy-2-methyl-3-oxo-3-(pyridin-3-yl)propanoate (58, Table 3, entry 7)**



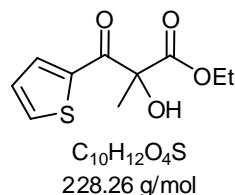
according to the **general procedure 2**, except using 97.2 μL (0.85 mmol, 1.7 eq.) of **13**: yield after column chromatography (silica gel, hexanes/Et<sub>2</sub>O 1/1): 101 mg (91%), orange oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 1/1) 0.36. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 9.23 (s, 1H), 8.80 (app. s, 1H), 8.32 (d, *J* = 8.2 Hz, 1H), 7.39 (dd, *J* = 8.2 Hz, *J* = 4.8 Hz, 1H), 4.81 (broad s, 1H), 4.27 (q, *J* = 7.0 Hz, 2H), 1.76 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 194.3, 171.9, 152.8, 150.1, 136.6, 129.1, 123.0, 79.5, 62.4, 22.9, 13.4. HRMS (EI; C<sub>11</sub>H<sub>13</sub>NO<sub>4</sub> + H): calcd.: 224.0923, found: 224.0930. IR :  $\tilde{\nu}$  = 3092, 2986, 2939, 1698, 1587, 1420, 1370, 1267, 1232, 1160, 1107, 1028, 1014, 983, 859, 701 cm<sup>-1</sup>.

**Ethyl 2-hydroxy-2-methyl-3-oxo-3-(pyridin-2-yl)propanoate (59, Table 3, entry 8)**



according to the **general procedure 2**, except using 97.2 μL (0.85 mmol, 1.7 eq.) of **13**: yield after column chromatography (silica gel, hexanes/Et<sub>2</sub>O 9/1): 102 mg (92%), yellow oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 9/1) 0.18. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.61 (d, *J* = 4.6 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.98-7.89 (m, 1H), 7.56-7.49 (m, 1H), 5.31 (broad s, 1H), 4.17 (app. q, 2H), 1.70 (s, 3H), 1.10 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 193.5, 172.1, 150.6, 147.7, 137.4, 127.2, 123.2, 78.6, 61.1, 20.6, 13.4. HRMS (ESI; C<sub>11</sub>H<sub>13</sub>NO<sub>4</sub> + Na): calcd.: 246.0742, found: 246.0741. IR :  $\tilde{\nu}$  = 3462, 2985, 1752, 1710, 1570, 1585, 1441, 1301, 1275, 1237, 1133, 1095, 941, 705, 684.

**Ethyl 2-hydroxy-2-methyl-3-oxo-3-(thiophen-2-yl)propanoate (60, Table 3, entry 9)**

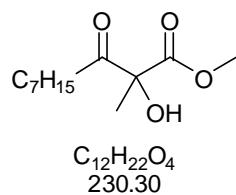


C<sub>10</sub>H<sub>12</sub>O<sub>4</sub>S  
228.26 g/mol

according to the **general procedure 2**, except using 97.2 µL (0.85 mmol, 1.7 eq.) of **13**: yield after column chromatography (silica gel, hexanes/Et<sub>2</sub>O 1/1): 98 mg (86%), yellow oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 1/1) 0.24. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.91 (d, J = 4.1 Hz, 1H), 7.70 (d, J = 4.9 Hz 1H), 7.12 (app. t, 1H), 4.50 (s, 1H), 4.21 (q, J = 7.2 Hz, 2H) 1.75 (s, 3H), 1.18 (t, J = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 188.5, 171.7, 138.3, 134.8, 134.1, 127.8, 79.5, 62.24, 23.2, 13.4. HRMS (neg. ESI; C<sub>10</sub>H<sub>11</sub>O<sub>4</sub>S - H): calcd.: 227.0378, found: 227.0386. IR:  $\tilde{\nu}$  = 3463, 2985, 1732, 1655, 1514, 1445, 1371, 1268, 1123, 911, 847, 681, 664.

### 4.3 Experimental Data for $\alpha$ -Hydroxy- $\beta$ -Ketoesters from Cross-Coupling with Various $\alpha$ -Ketoesters

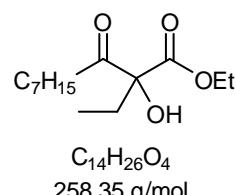
**Methyl 2-hydroxy-2-methyl-3-oxodecanoate (66, Table 4, entry 1)**



C<sub>12</sub>H<sub>22</sub>O<sub>4</sub>  
230.30

according to the **general procedure 3**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 20/1): 103 mg (90 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 5/1) 0.30. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.22 (s, 1H), 3.78 (s, 3H), 2.70 – 2.46 (m, 2H), 1.63 – 1.53 (m, 5H), 1.30 – 1.21 (m, 8H), 0.90 – 0.83 (m, 3H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>): δ 207.2, 171.9, 81.0, 53.3, 36.3, 31.6, 29.0, 29.0, 23.5, 22.6, 22.0, 14.1. HRMS (EI; C<sub>12</sub>H<sub>22</sub>O<sub>4</sub>): calcd. C<sub>12</sub>H<sub>22</sub>O<sub>4</sub>: 230.1518, found: 230.1516. IR:  $\tilde{\nu}$  = 3480, 2930, 2857, 1722, 1456, 1262, 1157, 632, 537 cm<sup>-1</sup>.

**Ethyl 2-ethyl-2-hydroxy-3-oxodecanoate (67, Table 4, entry 2)**

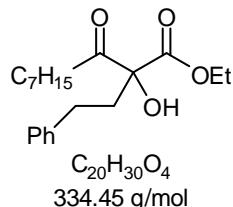


C<sub>14</sub>H<sub>26</sub>O<sub>4</sub>  
258.35 g/mol

according to the **general procedure 3**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 30/1): 116 mg (90 %), colourless oil. R<sub>f</sub> (petroleum ether/ethylacetate 10/1) 0.27. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.31 – 4.17 (m, 2H), 4.16 s, 1H), 2.73 – 2.60 (m, 1H), 2.55 – 2.41 (m, 1H), 2.19 – 2.03 (m, 1H), 2.00 – 1.86 (m, 1H), 1.62

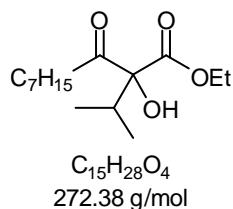
– 1.49 (m, 2H), 1.31 – 1.20 (m, 11H), 0.90 – 0.81 (m, 6H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.3, 171.1, 84.4, 62.5, 36.8, 31.6, 29.0 (2C), 28.3, 23.6, 23.5, 22.6, 14.1, 7.4. HRMS (EI;  $\text{C}_{14}\text{H}_{26}\text{O}_4$ ): calcd.: 258.1838, found: 258.1831. IR:  $\tilde{\nu} = 3492, 2959, 2931, 2858, 1717, 1462, 1259, 1017, 804, 632, 537, 500 \text{ cm}^{-1}$ .

### Ethyl 2-hydroxy-3-oxo-2-phenethyldecanoate (68, Table 4, entry 3)



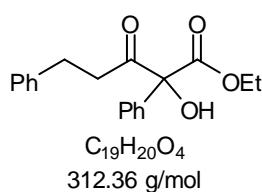
according to the **general procedure 3**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 50/1): 117 mg (70 %), colourless oil.  $R_f$  (petroleum ether/ethylacetate 10/1) 0.24.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.33 – 7.13 (m, 5H), 4.29 (s, 1H), 4.21 (q,  $J = 7.14 \text{ Hz}$ , 2H), 2.78 – 2.36 (m, 5H), 2.26 – 2.13 (m, 1H), 1.62 – 1.50 (m, 2H), 1.33 – 1.20 (m, 11H), 0.91 – 0.84 (m, 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  207.0, 171.0, 141.0, 128.5, 128.5, 126.2, 83.8, 62.7, 37.1, 36.8, 31.6, 29.6, 29.0 (2C), 23.5, 22.6, 14.1. HRMS (EI;  $\text{C}_{20}\text{H}_{30}\text{O}_4$ ): calcd.: 334.2144, found: 334.2147. IR:  $\tilde{\nu} = 3485, 2930, 2857, 1716, 1497, 1455, 1368, 1247, 1190, 1126, 1095, 1074, 1019, 748, 699, 503 \text{ cm}^{-1}$ .

### Ethyl 2-hydroxy-2-isopropyl-3-oxodecanoate (69, Table 4, entry 4)



according to the **general procedure 3**: yield after column chromatography (silica gel, petroleum ether/ethylacetate 50/1): 54 mg (40 %), colourless oil.  $R_f$  (petroleum ether/ethylacetate 10/1) 0.35.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.33 – 4.16 (m, 2H), 4.10 (s, 1H), 2.82 – 2.64 (m, 2H), 2.54 (td,  $J = 18.20 \text{ Hz}$ , 7.48 Hz, 1H), 1.64 – 1.47 (m, 2H), 1.35 – 1.18 (m, 11H), 0.95 – 0.83 (m, 6H), 0.77 (d,  $J = 6.86 \text{ Hz}$ , 3H).  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  208.0, 171.1, 87.7, 62.5, 37.2, 33.8, 31.7, 29.0 (2C), 23.5, 22.6, 16.8, 16.1, 14.1, 14.1. HRMS (EI;  $\text{C}_{15}\text{H}_{28}\text{O}_4$ ): calcd.: 272.1986, found: 272.1987. IR:  $\tilde{\nu} = 2962, 2930, 1716, 1251, 1037, 632, 544 \text{ cm}^{-1}$ .

### Ethyl 2-hydroxy-3-oxo-2,5-diphenylpentanoate (70, Table 4, entry 5)

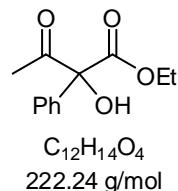


according to the **general procedure 2**: yield after column chromatography (silica gel, hexanes/ $\text{Et}_2\text{O}$  4/1): 250 mg (80 %),<sup>17</sup> colourless oil.  $R_f$  (hexanes/ $\text{Et}_2\text{O}$  4/1) 0.28.

<sup>17</sup> The reaction was performed using the double amount of the described size of the general procedure.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.53–7.51 (m, 2H), 7.40–7.37 (m, 3H), 7.27–7.16 (m, 3H), 7.09 (app d, 2H), 4.72 (s, 1H), 4.38–4.24 (m, 2H), 3.02–2.82 (m, 4H), 1.32 (t, *J* = 7.4 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 204.8, 170.2, 140.4, 135.8, 128.3, 128.2, 128.1, 126.2, 126.0, 84.2, 63.0, 38.9, 29.7, 13.8. 28.0. HRMS (ESI; C<sub>19</sub>H<sub>20</sub>O<sub>4</sub> + Na): calcd.: 335.1257, found: 335.1257. IR:  $\tilde{\nu}$  = 3479, 2981, 1714, 1603, 1496, 1453, 1255, 1059, 859, 698 cm<sup>-1</sup>.

### Ethyl 2-hydroxy-3-oxo-2-phenylbutanoate (71, Table 4, entry 6)



according to the **general procedure 2**: yield after column chromatography (SiO<sub>2</sub>, hexanes /Et<sub>2</sub>O 4/1): 183 mg (82 %),<sup>17</sup> colourless oil.

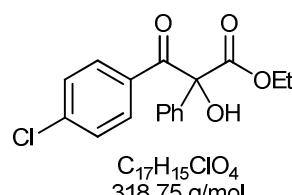
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.58–7.56 (m, 2H), 7.46–7.42 (m, 3H),

4.78 (s, 1H), 4.40–4.28 (m, 2H), 2.24 (s, 3H), 1.34 (t, *J* = 7.4 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 203.5, 170.2, 136.1, 128.7, 128.4, 126.3,

84.5, 63.0, 25.0, 13.9. HRMS (ESI; C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> + Na): calcd.: 245.0790, found: 245.0786. IR:  $\tilde{\nu}$  = 3456, 2981, 1771, 1449, 1354, 1249, 1072, 857, 656 cm<sup>-1</sup>.

### Ethyl 3-(4-chlorophenyl)-2-hydroxy-3-oxo-2-phenylpropanoate (72, Table 4, entry 7)



according to the **general procedure 2A**: yield after column chromatography (hexanes/Et<sub>2</sub>O 4/1): 204 mg (64 %), yellowish oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 4/1) 0.21.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.85 (d, *J* = 7.52 Hz, 2H), 7.56 (m, 2H),

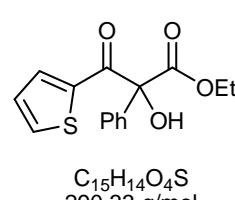
7.55 – 7.39 (m, 3H), 7.30 (m, 2H), 4.84 (s, 1H), 4.44 – 4.38 (m, 1H),

4.30–4.24 (m, 1H), 1.29 (t, *J* = 7.0 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 193.4, 171.1, 139.1, 136.4,

131.7, 131.1, 128.2, 128.1, 128.0, 127.9, 125.8, 83.7, 63.2, 13.4. HRMS (ESI; C<sub>17</sub>H<sub>15</sub>ClO<sub>4</sub> + Na): calcd.: 341.0557, found: 341.0559

IR:  $\tilde{\nu}$  = 3461, 2929, 1725, 1683, 1569, 1449, 1244, 1176, 1112, 1012, 965, 698 cm<sup>-1</sup>.

### Ethyl 2-hydroxy-3-oxo-2-phenyl-3-(thiophen-2-yl)propanoate (73, Table 4, entry 8)



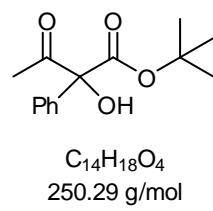
according to the **general procedure 2A**: yield after column chromatography (silica gel, hexanes/Et<sub>2</sub>O 4/1): 192 mg (66 %), yellowish oil. R<sub>f</sub> (hexanes/Et<sub>2</sub>O 4/1) 0.24.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.67 – 7.65 (m, 3H), 7.61–7.60 (m, 1H), 7.40–

7.37 (m, 3H), 7.01 (t,  $J = 4.2$  Hz, 1H), 4.84 (s, 1H), 4.46–4.38 (m, 1H), 4.32–4.24 (m, 1H), 1.31 (t,  $J = 7.0$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  188.0, 170.7, 138.7, 136.2, 135.5, 134.3, 128.1, 127.8, 127.5, 126.2, 83.7, 63.1, 13.4. HRMS (ESI;  $\text{C}_{15}\text{H}_{14}\text{O}_4\text{S} + \text{Na}$ ): calcd.: 313.0518, found: 313.0511.

IR:  $\tilde{\nu} = 3433, 1713, 1650, 1452, 1408, 1352, 1294, 1251, 1177, 1028, 860, 754, 734, 704 \text{ cm}^{-1}$ .

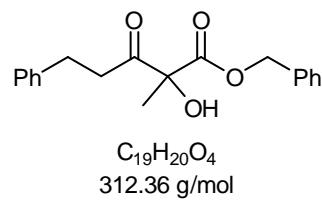
### **tert-Butyl-2-hydroxy-3-oxo-2-phenylbutanoate (75)**



according to the **general procedure 1** (at 20 °C, 40 h, using chiral catalyst **77** and 3 equiv. of volatile  $\text{CH}_3\text{CHO}$ ): yield after column chromatography ( $\text{SiO}_2$ , hexanes/  $\text{Et}_2\text{O}$  4/1): 73 mg (58 %), colourless solid, m. p. 41–43 °C.  $R_f$  (hexanes/ $\text{Et}_2\text{O}$  4/1) 0.34.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.58 (m, 2H), 7.39 (m, 3H), 4.65 (s, 1H), 2.22 (s, 3H), 1.53 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  203.2, 169.0, 136.0, 128.0, 127.8, 126.0, 84.0, 83.9, 21.2, 24.3. HRMS (ESI;  $\text{C}_{14}\text{H}_{18}\text{O}_4 + \text{Na}$ ): calcd.: 273.1096, found: 273.1032. IR :  $\tilde{\nu} = 3447, 2979, 2933, 1721, 1449, 1369, 1257, 1074, 839, 661 \text{ cm}^{-1}$ .  $[\alpha]_D^{20} = +73.63$  ( $c$  0.33 in acetone, 73% ee).<sup>18</sup>

### **Benzyl 2-hydroxy-2-methyl-3-oxo-5-phenylpentanoate (80)**

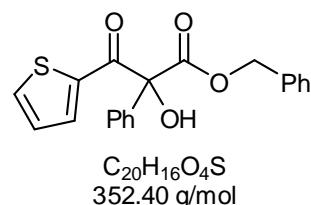


according to the **general procedure 1**: yield after column chromatography ( $\text{SiO}_2$ , hexanes/  $\text{Et}_2\text{O}$  4/1): 275 mg (88 %),<sup>17</sup> white solid, m. p. 38–41 °C.  $R_f$  (hexanes/ $\text{Et}_2\text{O}$  4/1) 0.27.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.39–7.37 (m, 3H), 7.34–7.31 (m, 2H), 7.30–7.26 (m, 2H), 7.23–7.19 (m, 1H), 7.12–7.10 (m, 2H), 5.16 (d,  $J = 3.5$  Hz, 2H), 4.20 (s, 1H), 2.97–2.75 (m, 4H), 1.59 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  205.5, 170.6, 139.9, 134.3, 128.3 (2C), 128.0 (2C), 127.9, 125.8, 80.6, 67.6, 37.8, 29.0, 21.2. HRMS (ESI;  $\text{C}_{19}\text{H}_{20}\text{O}_4 + \text{Na}$ ): calcd. 335.1259, found: 335.1269. IR :  $\tilde{\nu} = 3466, 3028, 2981, 1714, 1453, 1365, 1259, 1061, 745, 696 \text{ cm}^{-1}$ .

<sup>18</sup> See HPLC chromatograms on page 20.

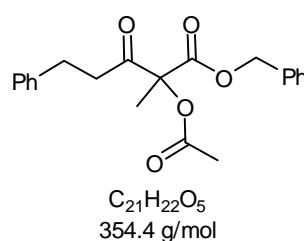
**Phenyl 2-hydroxy-3-oxo-2-phenyl-3-(thiophen-2-yl)propanoate (84, Scheme 5)**



according to the **general procedure 2**, except using THF as solvent and 240.0 mg (1.0 mmol, 2 eq.) of **83**: yield after column chromatography (silica gel, hexanes/EtOAc 4/1): 148 mg (84%), yellow oil.  $R_f$  (hexanes/EtOAc 4/1) 0.24.  
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.66-7.62 (m, 3H), 7.60 (d,  $J = 4.8$  Hz, 1H), 7.41-7.36 (m, 3H), 7.35-7.31 (m, 3H), 7.27-7.23 (m, 2H), 6.99 (t,  $J = 4.2$  Hz, 1H), 5.37 (d,  $J = 12.5$  Hz, 1H), 5.27 (d,  $J = 12.5$  Hz, 1H), 4.83 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  188.2, 171.1, 139.1, 137.6, 136.1, 134.8, 134.7, 128.7, 128.5, 128.4, 128.3, 128.0, 127.8, 126.7, 84.4, 68.7. HRMS (ESI;  $\text{C}_{20}\text{H}_{16}\text{O}_4\text{S} + \text{Na}$ ): calcd.: 375.0667, found: 375.0669. IR:  $\tilde{\nu} = 3463, 3065, 3033, 1728, 1655, 1497, 1450, 1408, 1353, 1244, 1187, 1062, 1029, 906, 727, 695 \text{ cm}^{-1}$ .

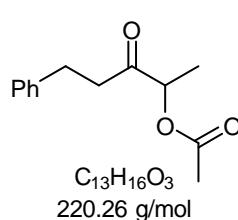
#### 4.4 Experimental Data for Decarboxylation Experiments

**Benzyl 2-acetoxy-2-methyl-3-oxo-5-phenylpentanoate (81)**



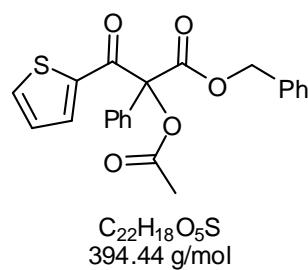
according to the **general procedure 5**: yield after column chromatography ( $\text{SiO}_2$ , hexanes/  $\text{Et}_2\text{O}$  4/1): 340 mg (96 %), colourless oil.  $R_f$  (hexanes/ $\text{Et}_2\text{O}$  4/1) 0.39.  
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.36-7.21 (m, 7H), 7.20-7.14 (m, 3H), 5.17 (s, 2H), 3.00-2.88 (m, 4H), 2.15 (s, 3H), 1.71 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  201.9, 169.1, 167.0, 140.2, 134.5, 128.2, 128.1, 128.0, 127.9, 127.8, 125.7, 85.0, 67.4, 39.3, 29.1, 20.4, 19.5. HRMS (ESI,  $\text{C}_{21}\text{H}_{22}\text{O}_5 + \text{Na}$ ): calcd.: 377.1368, found: 377.1365. IR:  $\tilde{\nu} = 2942, 1714, 1497, 1370, 1116, 1056, 747, 696 \text{ cm}^{-1}$ .

**3-Oxo-5-phenylpentan-2-yl acetate (82)**



according to the **general procedure 6**: yield after column chromatography ( $\text{SiO}_2$ , hexanes/  $\text{Et}_2\text{O}$  4/1): 190 mg (96 %), colourless oil.  $R_f$  (hexanes/ $\text{Et}_2\text{O}$  4/1) 0.32.  
 $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.30-7.29 (m, 2H), 7.22-7.20 (m, 3H), 5.1 (q,  $J = 7.2$  Hz, 1H), 2.93-2.74 (m, 4H), 2.14 (s, 3H), 1.35 (d,  $J = 7.2$  Hz, 3H).  
 $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  206.4, 169.9, 140.3, 128.1, 127.9, 125.8, 74.2, 39.5, 28.7, 20.3, 15.5. HRMS (EI,  $\text{C}_{13}\text{H}_{16}\text{O}_3$ ): calcd.: 220.1099, found: 220.1089. IR:  $\tilde{\nu} = 2942, 1714, 1497, 1370, 1116, 1056, 747, 696 \text{ cm}^{-1}$ .

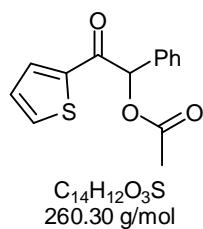
**Benzyl 2-acetoxy-3-oxo-2-phenyl-3-(thiophen-2-yl)propanoate (85, Scheme 6)**



according to the **general procedure 5**: yield after column chromatography (silica gel, 100%  $CH_2Cl_2$ ): 189 mg (96%), yellow oil.  $R_f$  (100%  $CH_2Cl_2$ ) 0.35.

$^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.63-7.59 (m, 2H), 7.57-7.53 (m, 2H), 7.47-7.37 (m, 3H), 7.34-7.28 (m, 3H), 7.26-7.21 (m, 2H), 7.96 (dd,  $J = 4.9$  Hz,  $J = 4.0$  Hz, 1H), 5.28 (d,  $J = 12.5$  Hz, 1H), 5.23 (d,  $J = 12.5$  Hz, 1H), 2.28 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  183.0, 169.0, 165.4, 139.1, 134.6, 133.6, 133.1, 128.7, 128.2, 128.0, 127.7, 127.3, 127.2, 126.0, 86.9, 67.7, 52.9, 20.6. HRMS (EI;  $C_{22}H_{18}O_5S + H$ ): calcd.: 395.0953, found: 395.0952. IR:  $\tilde{\nu} = 3065, 3034, 1744, 1674, 1497, 1449, 1409, 1369, 1243, 1226, 1064, 1036, 1002, 995, 908, 724, 695\text{ cm}^{-1}$ .

**2-Oxo-1-phenyl-2-(thiophen-2-yl)ethyl acetate (86, Scheme 6)**

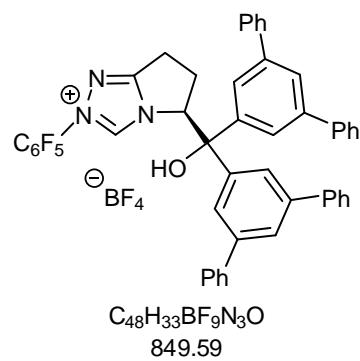


according to the **general procedure 6**: yield after column chromatography (silica gel, 100%  $CH_2Cl_2$ ): 122 mg (94%), yellow oil.  $R_f$  (100%  $CH_2Cl_2$ ): 0.29.

$^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  7.78 (dd,  $J = 4.0$  Hz,  $J = 1.1$  Hz, 1H), 7.65 (dd,  $J = 4.9$  Hz,  $J = 1.1$  Hz, 1H), 7.58-7.51 (m, 2H), 7.44-7.37 (m, 3H), 7.10 (dd,  $J = 4.9$  Hz,  $J = 4.0$  Hz, 1H), 6.68 (s, 1H), 2.24 (s, 3H).  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  186.1, 169.9, 140.2, 134.0, 133.4, 132.8, 129.0, 128.7, 128.1, 127.8, 77.8, 20.4. HRMS (ESI;  $C_{14}H_{12}O_3S+Na$ ): calcd.: 283.0405, found: 283.0411. IR:  $\tilde{\nu} = 3065, 3034, 1747, 1675, 1514, 1497, 1450, 1409, 1369, 1353, 1243, 1226, 1064, 1037, 1002, 908, 725, 695\text{ cm}^{-1}$ .

#### 4.5 Experimental Data for Catalyst 78

**(5S)-[Bis-(3,5-diphenyl-phenyl)-hydroxy-methyl]-2-pentafluorophenyl-6,7-dihydro-5*H*pyrrolo[2,1-*c*][1,2,4]triazol-2-i um tetrafluoroborate (78)**



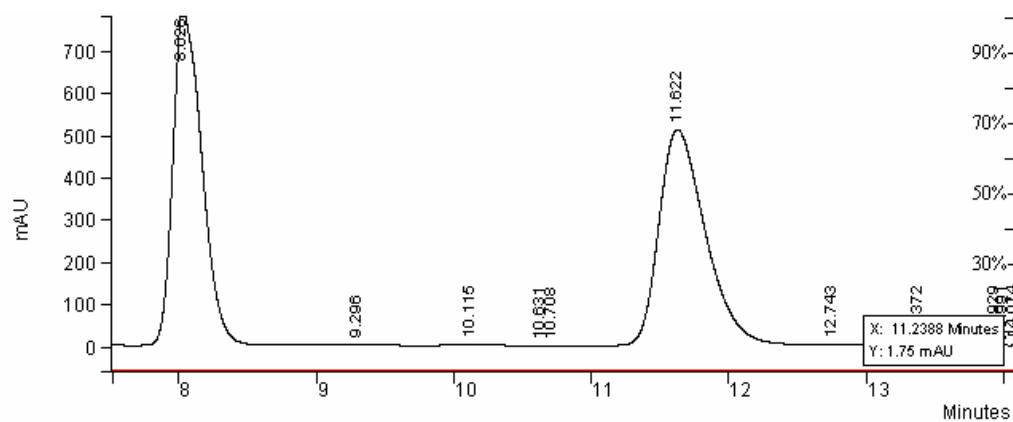
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 11.28 (s, 1H), 7.93 (s, 1H), 7.83 (s, 1H), 7.74–7.63 (m, 4H), 7.61–7.40 (m, 8H), 7.39–7.34 (m, 5H), 7.30–7.28 (m, 7H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.50 (s, 1H), 3.27 – 3.05 (m, 2H), 2.89– 2.72 (m, 2H). HRMS (ESI; C<sub>48</sub>H<sub>33</sub>F<sub>5</sub>N<sub>3</sub>O<sup>+</sup>): calcd.: 762.2544 , found: 762.2549

## 5 HPLC Chromatograms - Crossed Acyloin Products

HPLC Chromatograms of crossed acyloin **75**

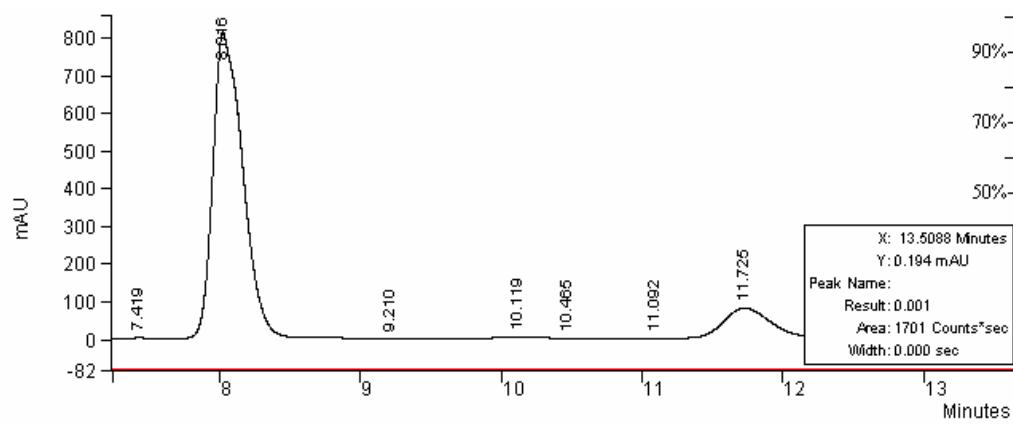
Chiralpak OJ-H (4.6 mm x 25 cm), solvent hexane/IPA: 90/10, flow rate 1.0 mL min<sup>-1</sup>, RT, UV detection  $\lambda = 254$  nm.

Resolved HPLC chromatogram for acyloin **75** – racemate



Peak No	Result	Ret. Time (min)	Area (counts)
1	44.9788	8.026	117317160
2	45.4291	11.622	121099888

Resolved HPLC chromatogram for enantioenriched acyloin **75**.(using catalyst **77**).

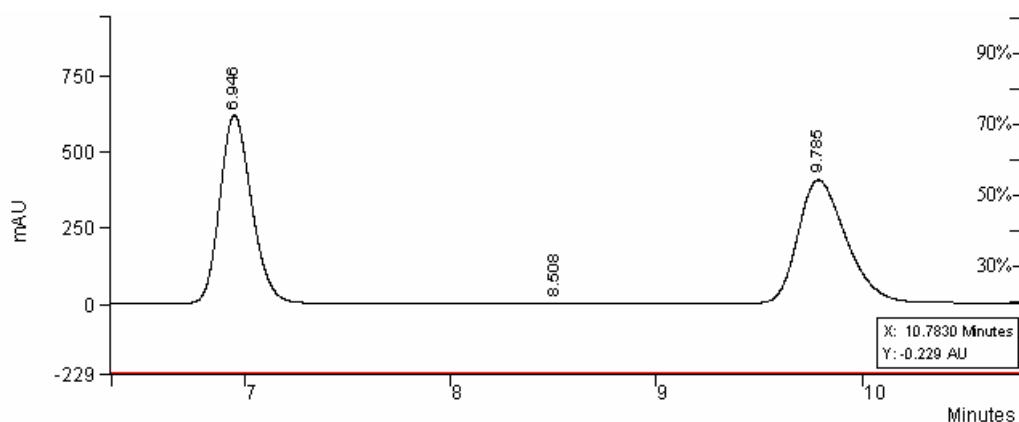


Peak No	Result	Ret. Time (min)	Area (counts)
1	82.6950	8.646	119587688
2	12.8176	11.725	19201968

Retention times ca. 8.6 min (major enantiomer) and 11.7 min (minor enantiomer): 73 % ee

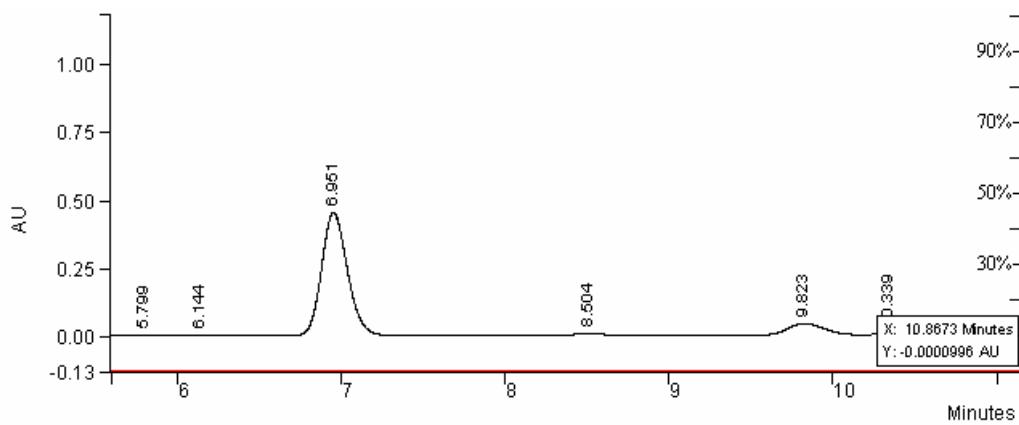
HPLC Chromatograms of crossed acyloin **75**.

Chiralpak OJ-H (4.6 mm x 25 cm), solvent hexane/IPA: 90/10, flow rate 1 mL min<sup>-1</sup>, RT, UV detection  $\lambda = 254$  nm.



Peak No	Result	Ret. Time (min)	Area (counts)
1	46.7385	6.946	117317160
2	46.9409	9.785	121099888

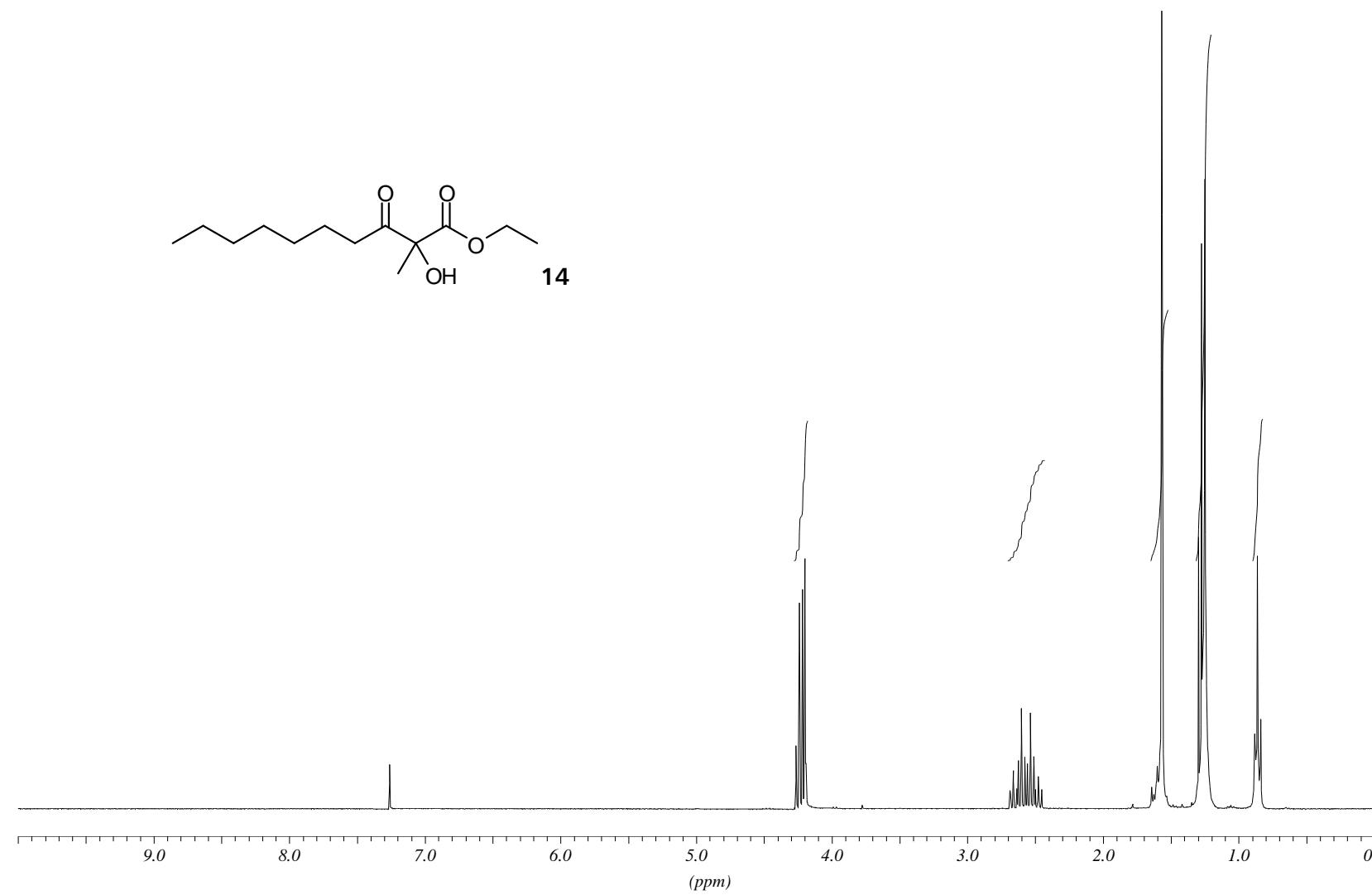
Resolved HPLC chromatogram for enantioenriched acyloin **75**.(using catalyst **78**).

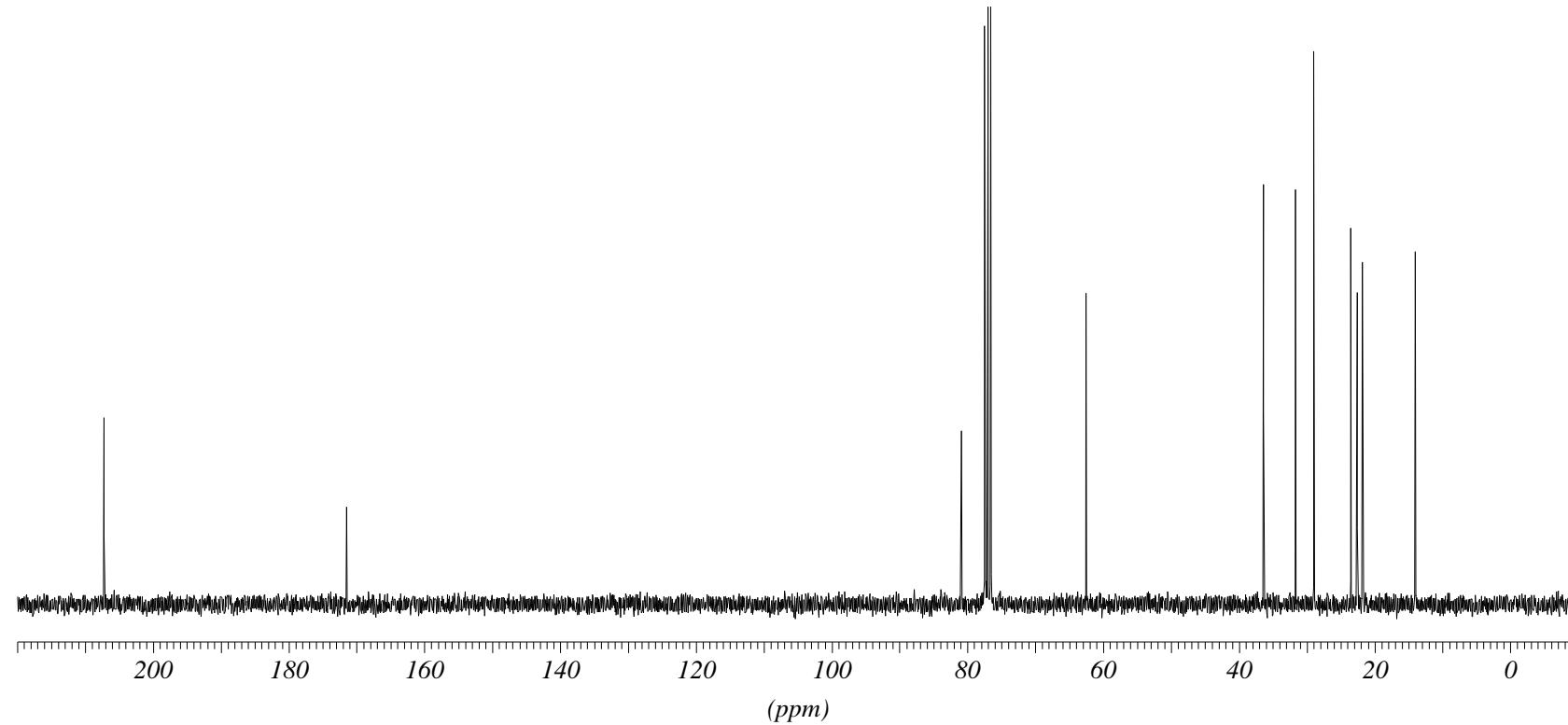
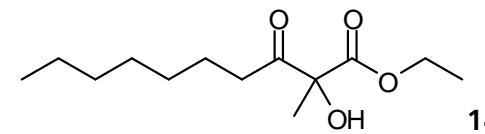


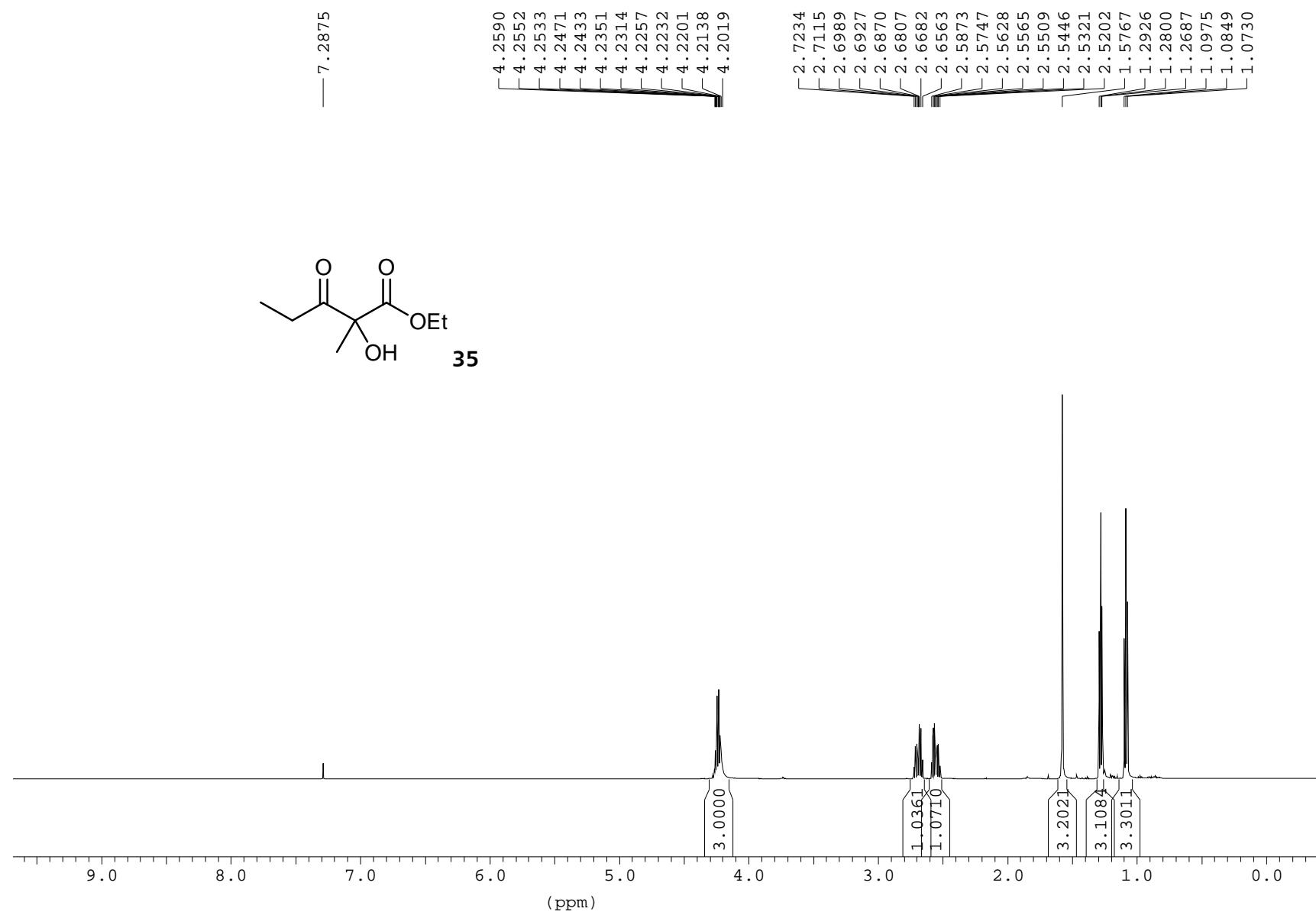
Peak No	Result	Ret. Time (min)	Area (counts)
1	81.8321	6.951	49626952
2	11.0326	9.823	7134865

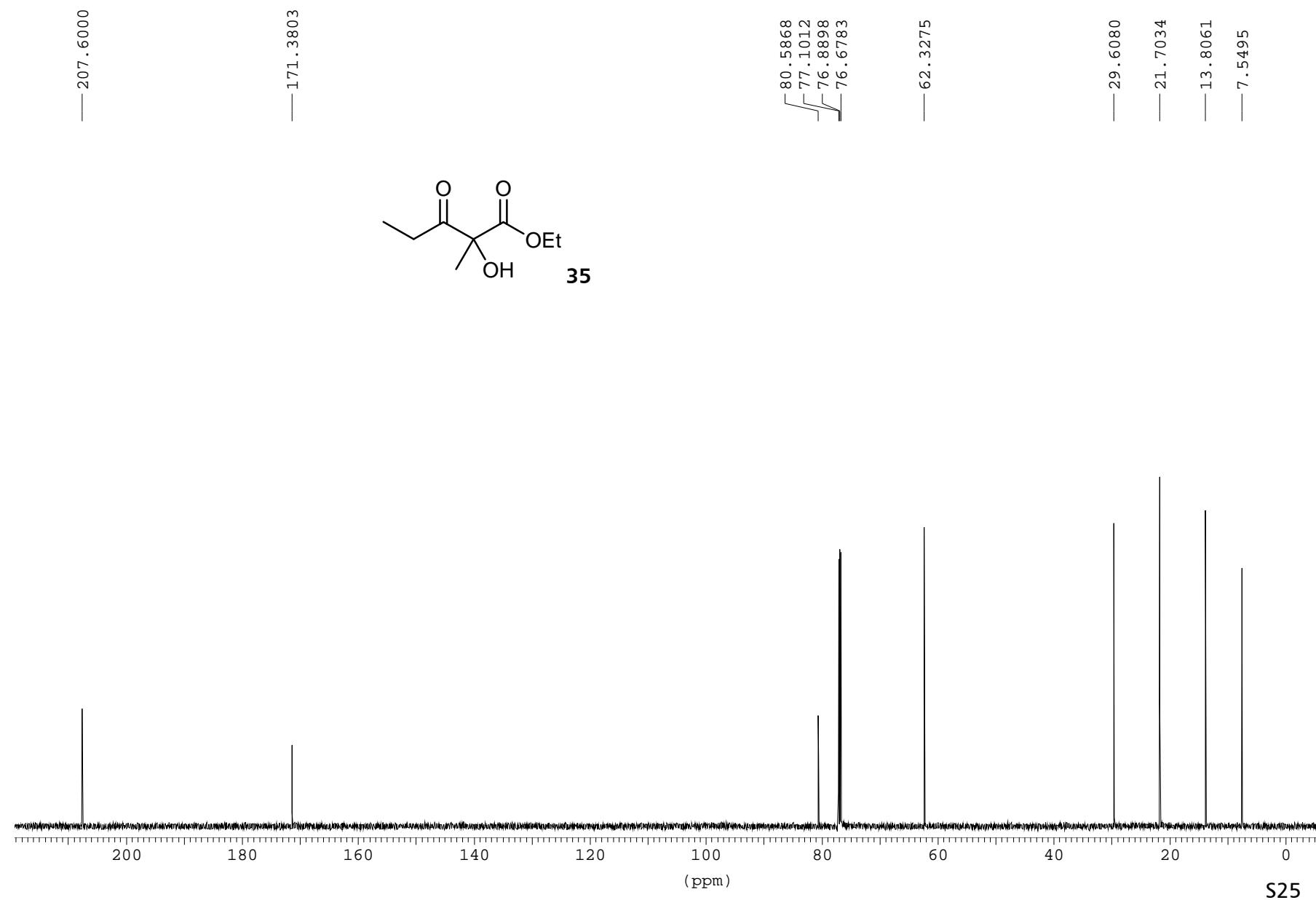
Retention times ca. 7.0 min (major enantiomer) and 9.8 min (minor enantiomer): 76 % ee

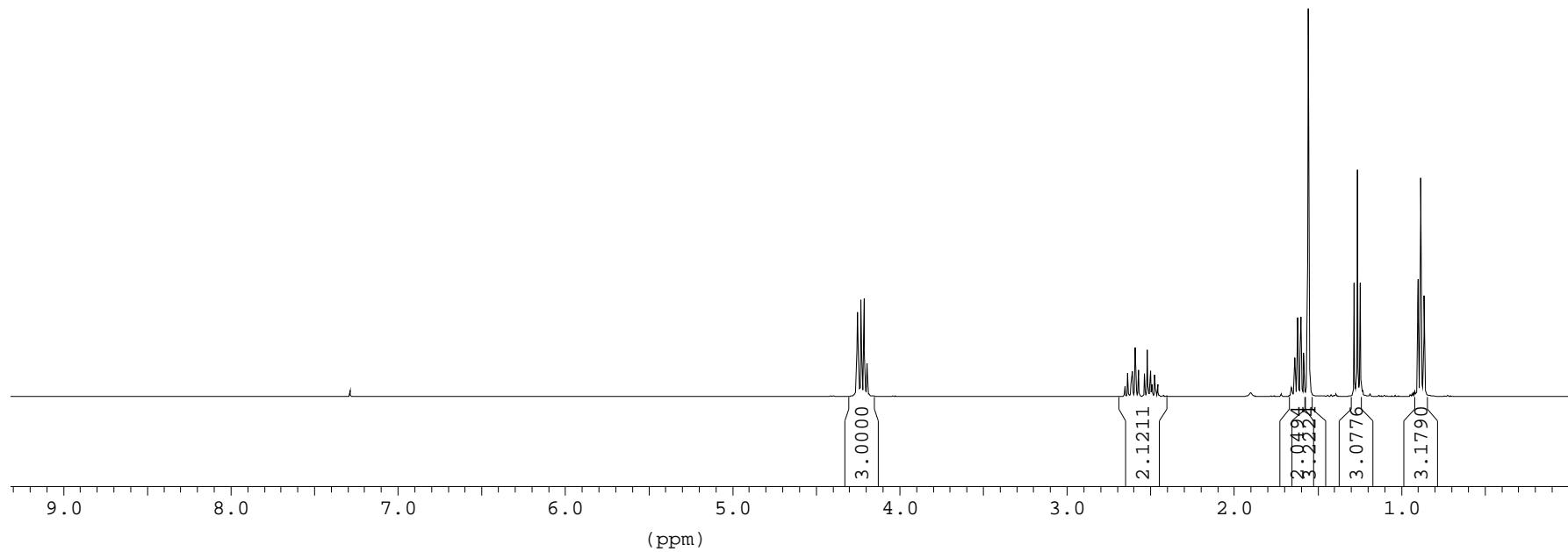
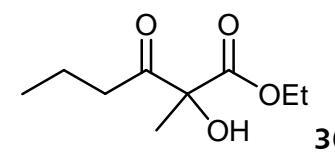
## 6 $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra of Products

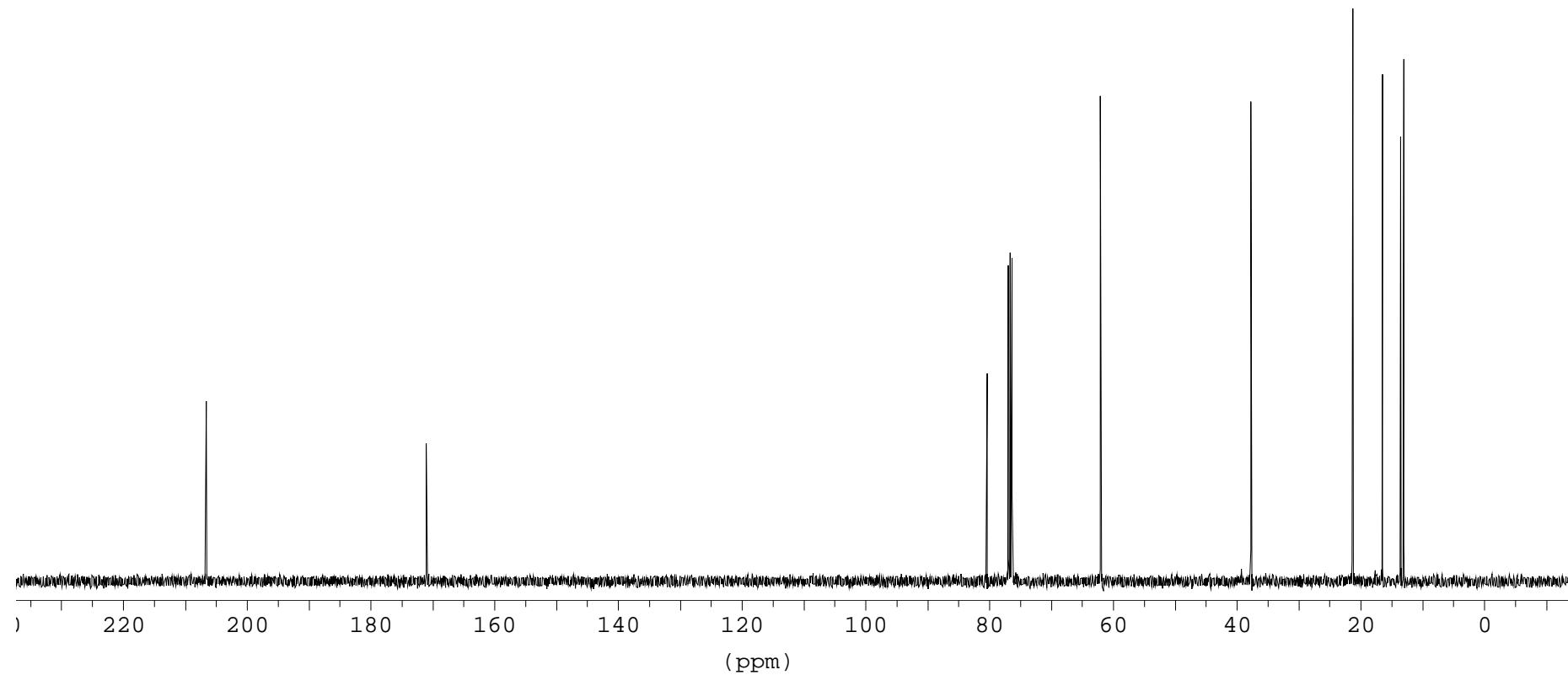
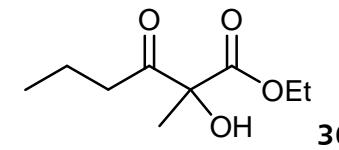


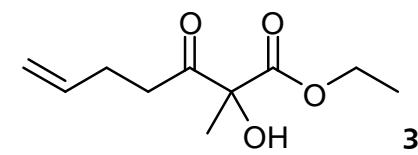




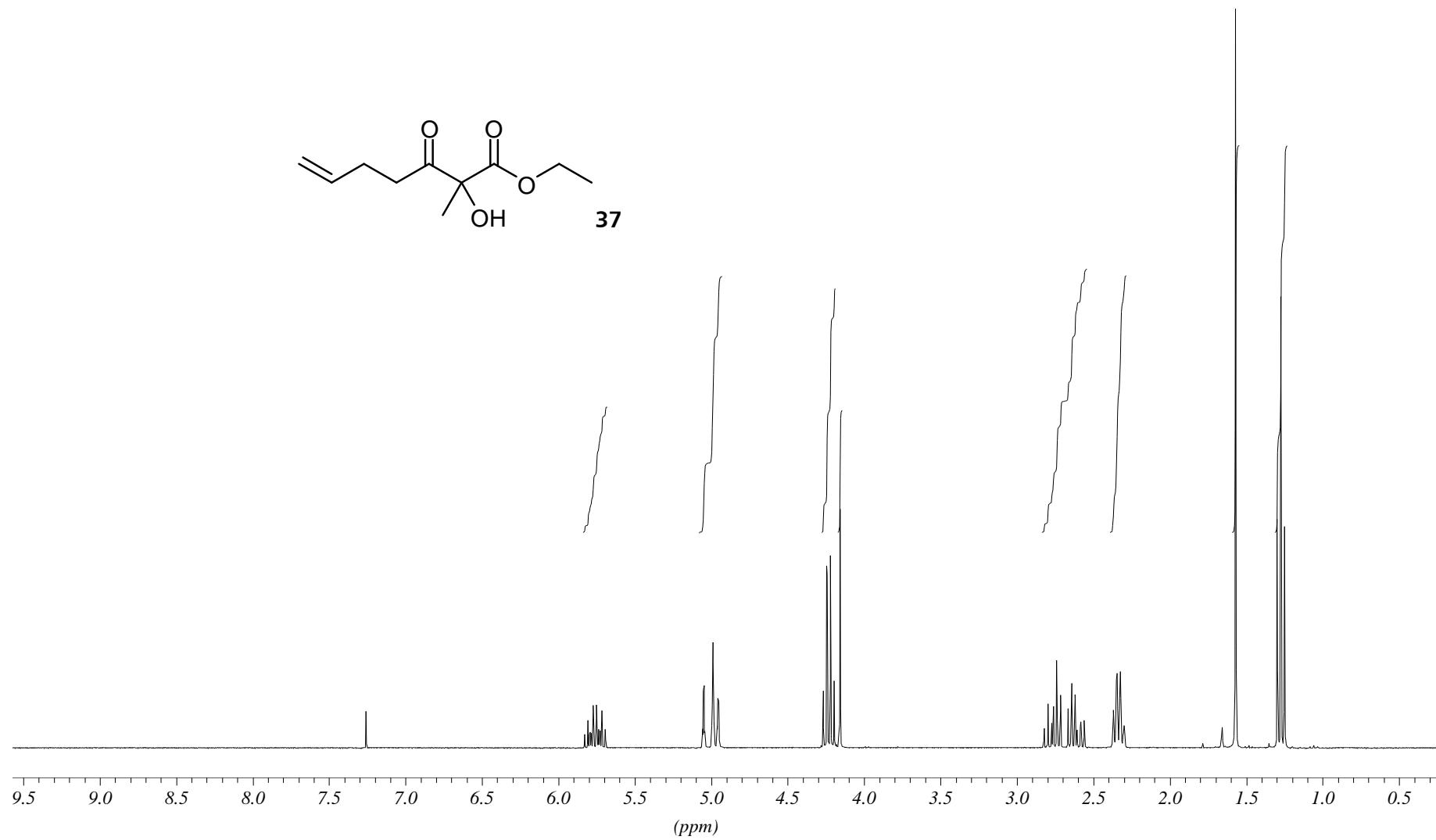


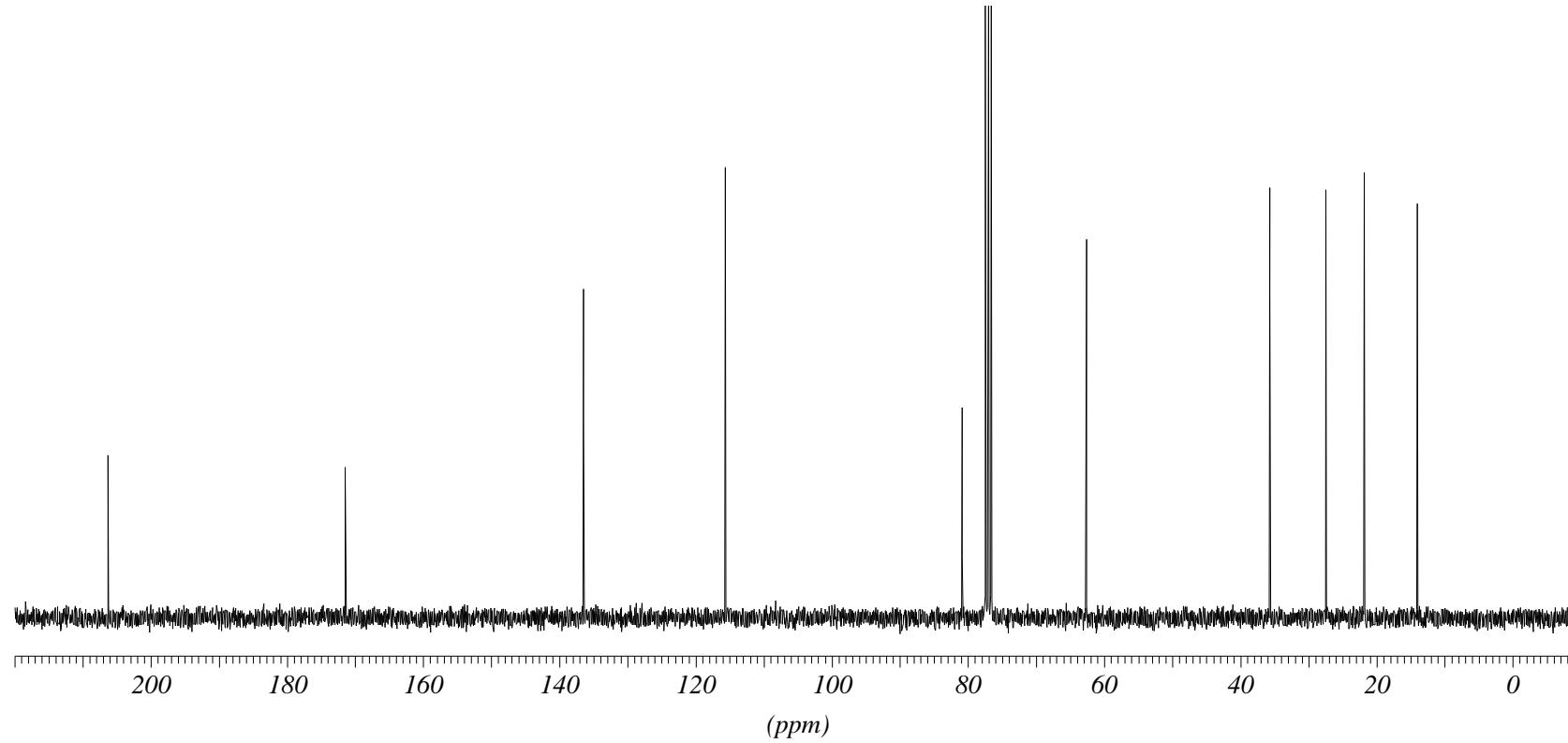
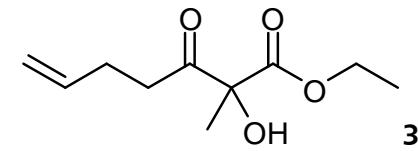


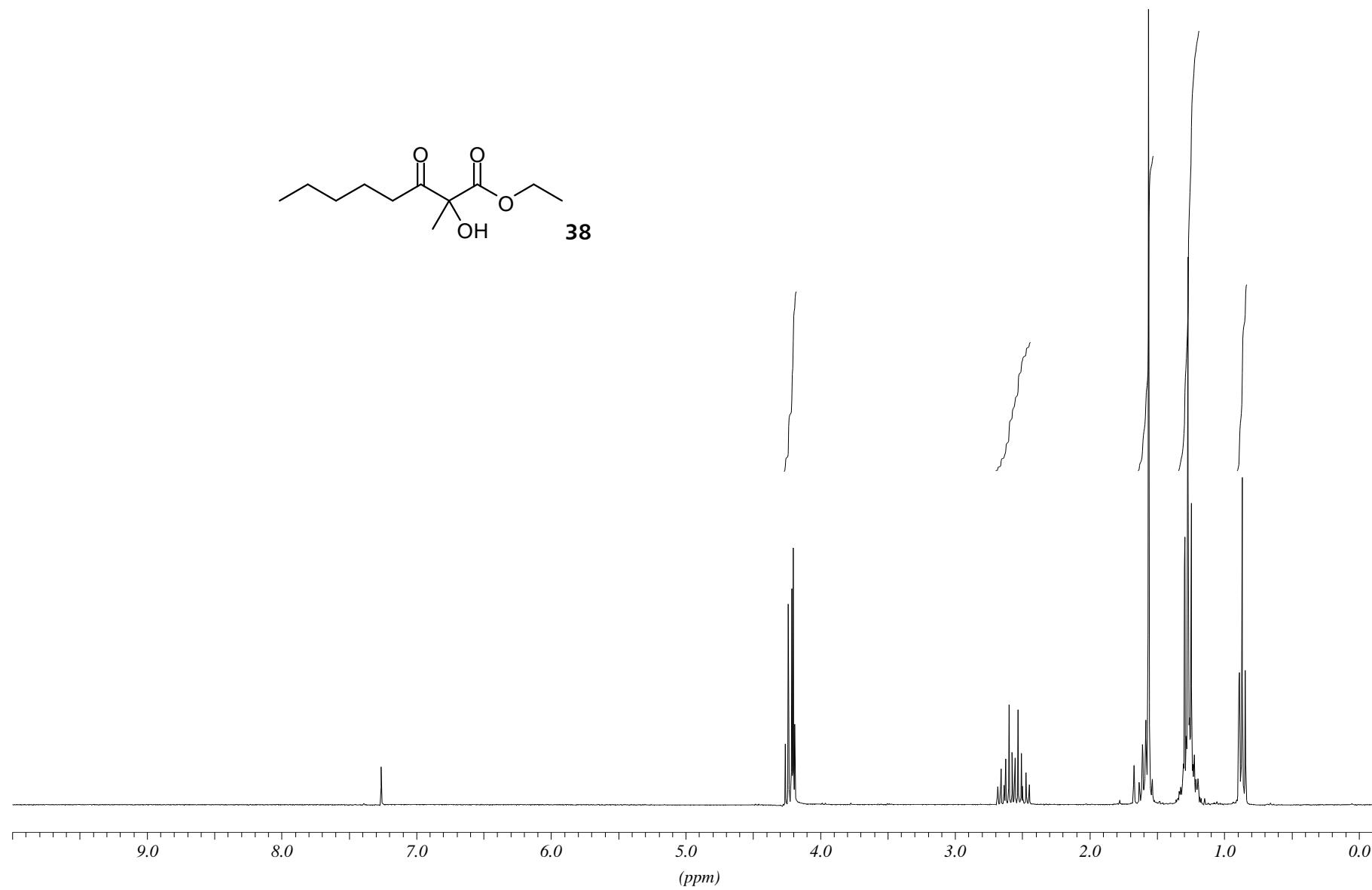
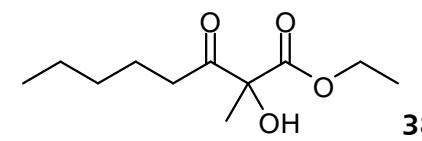


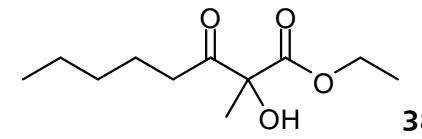


37

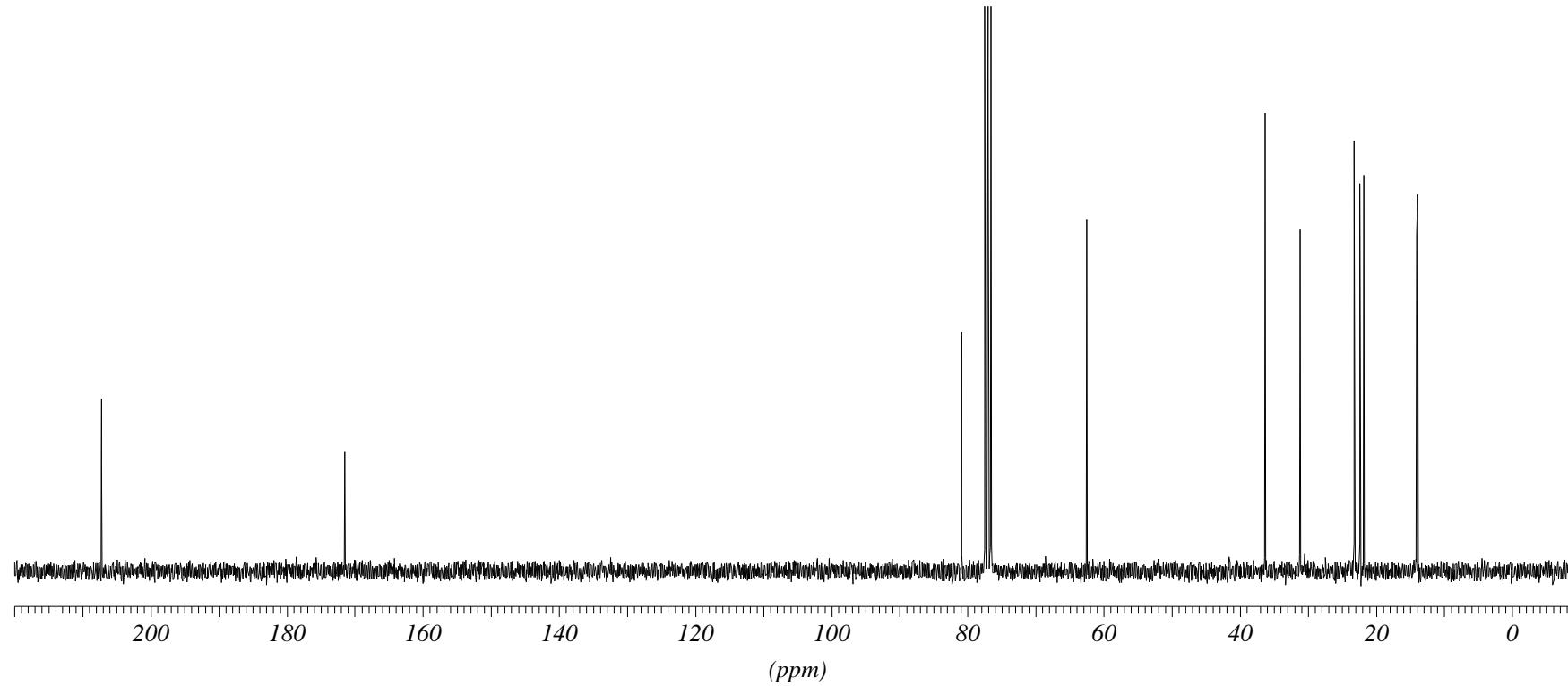


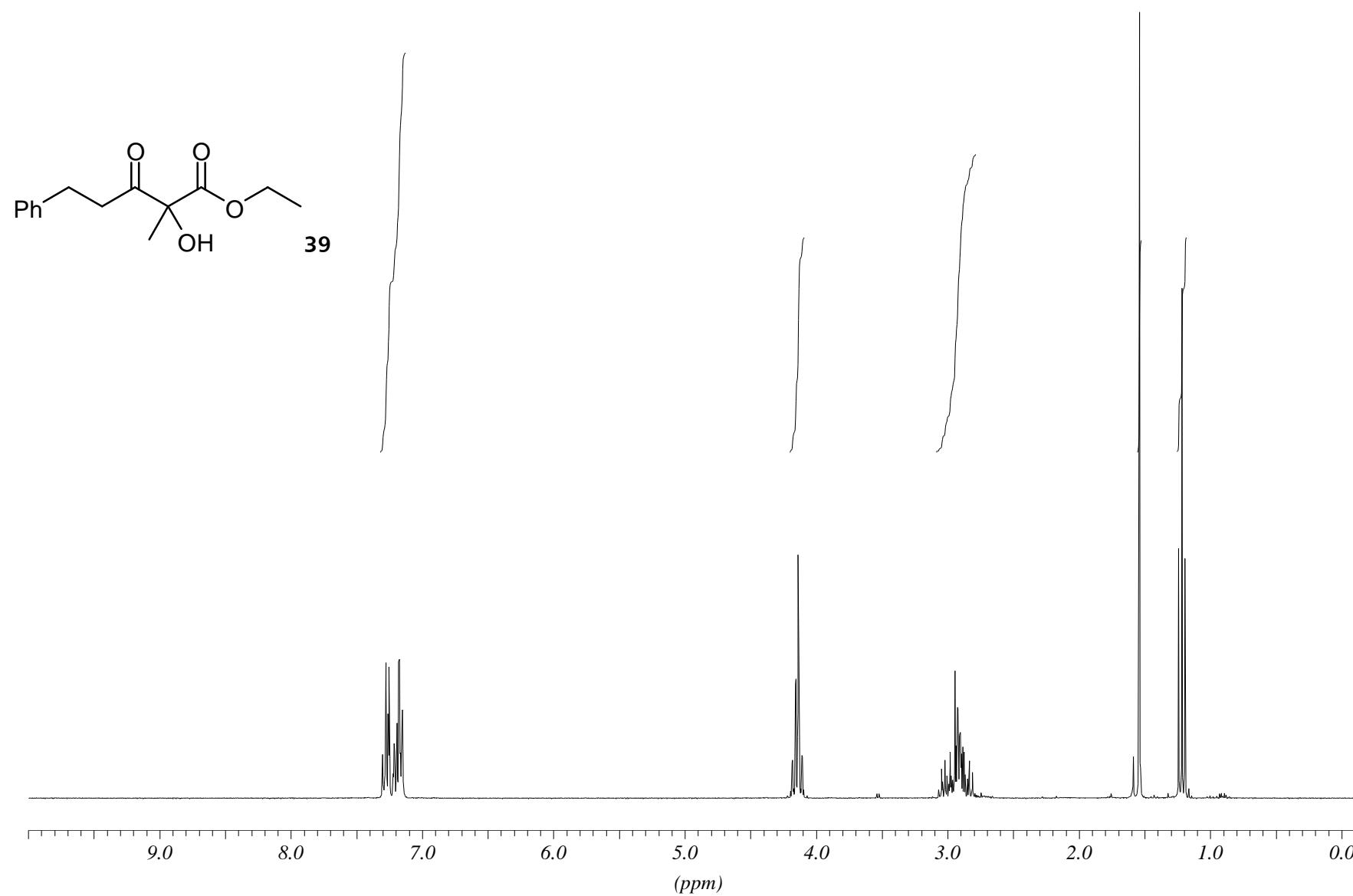


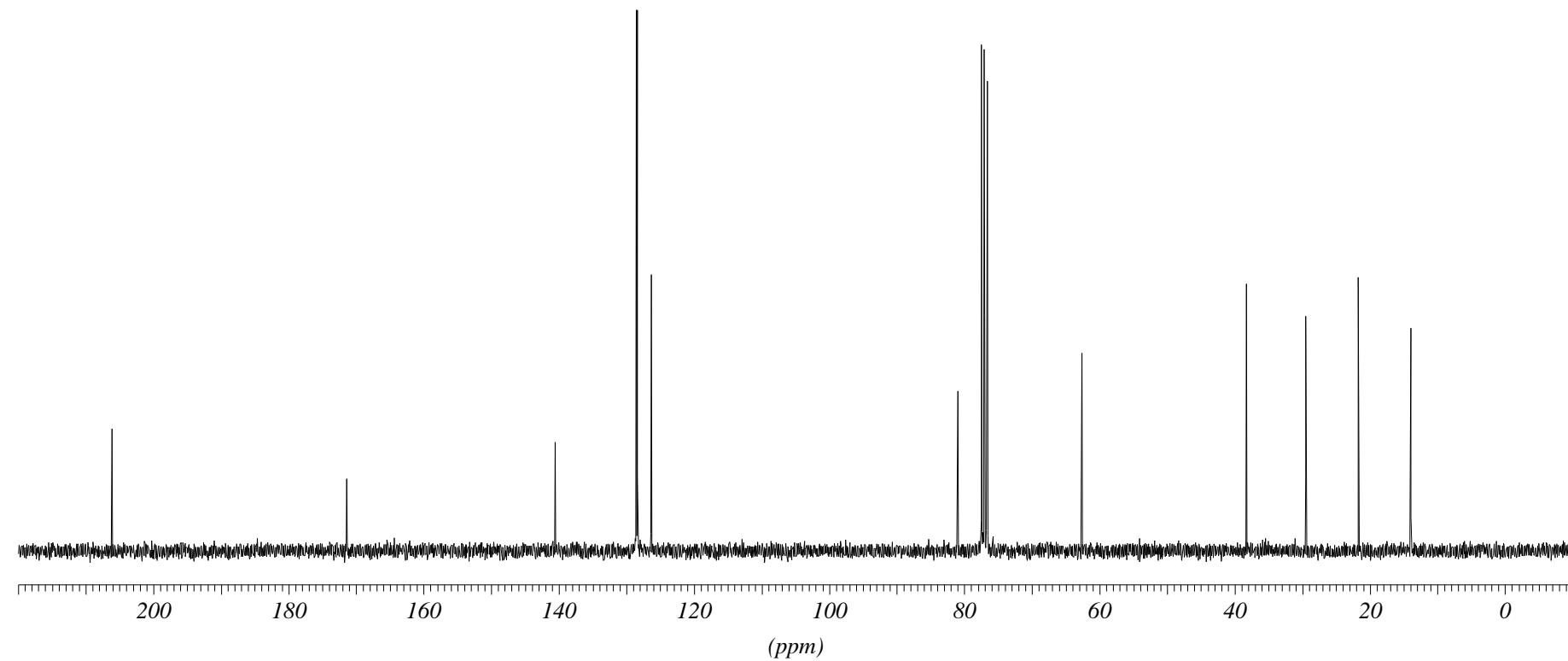
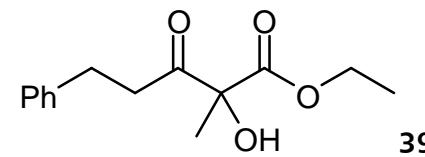


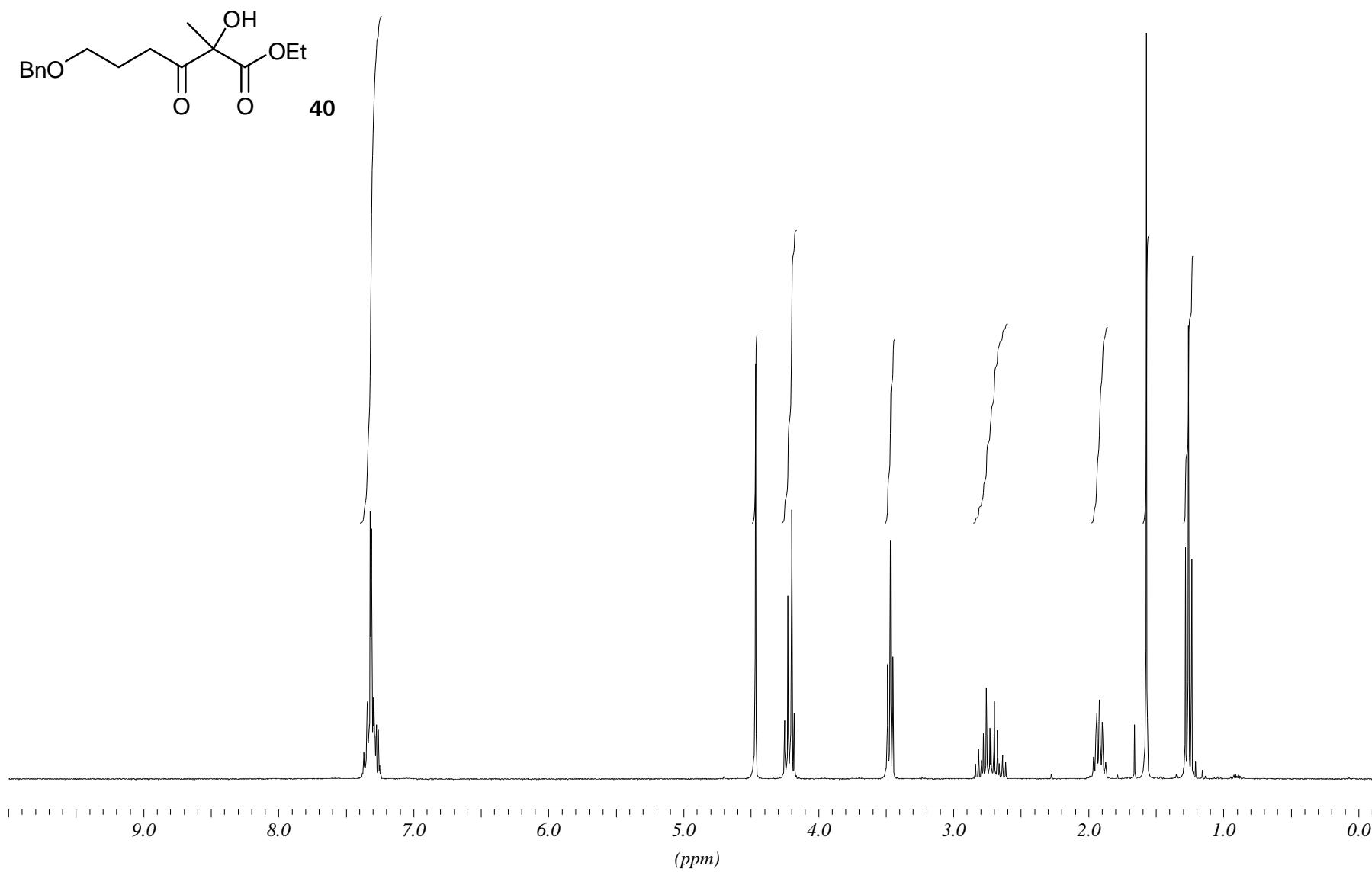


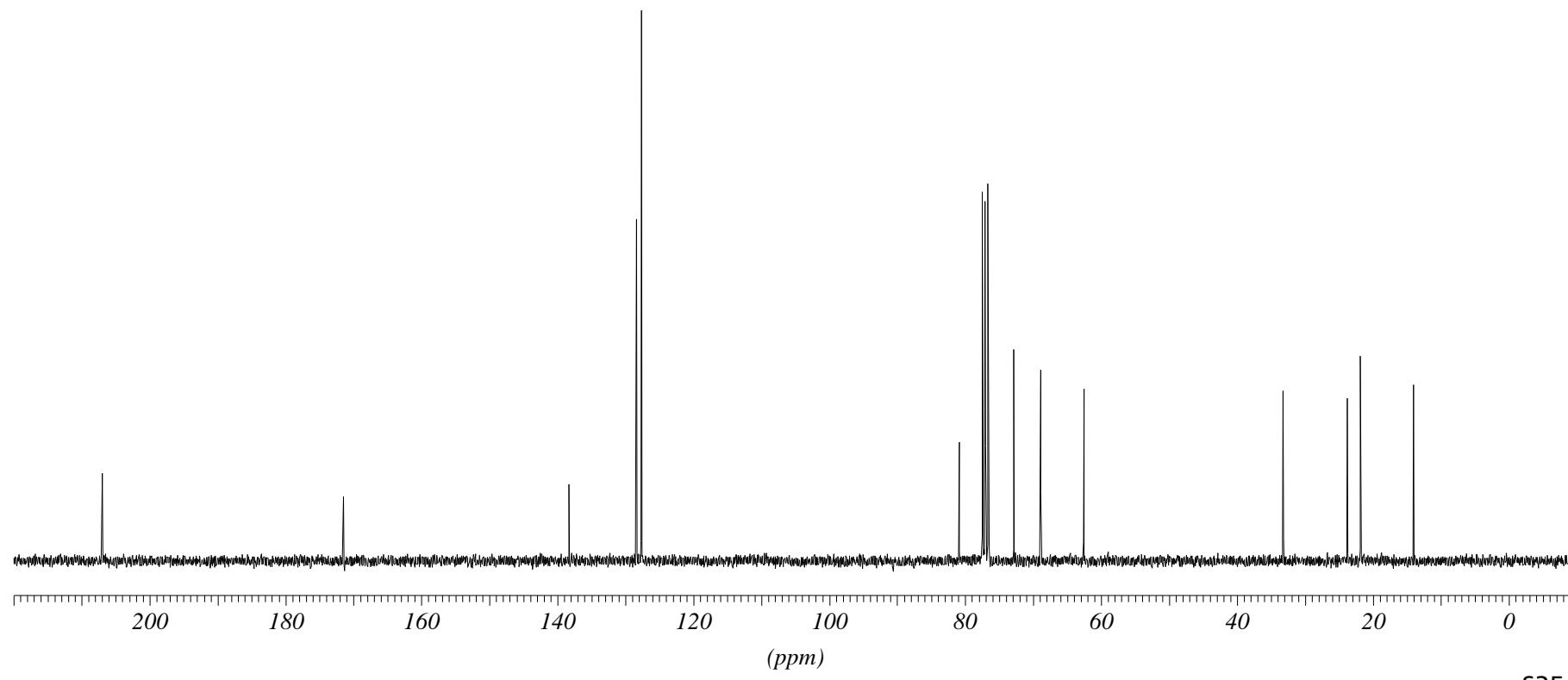
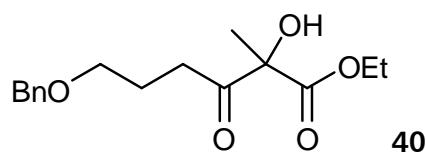
38

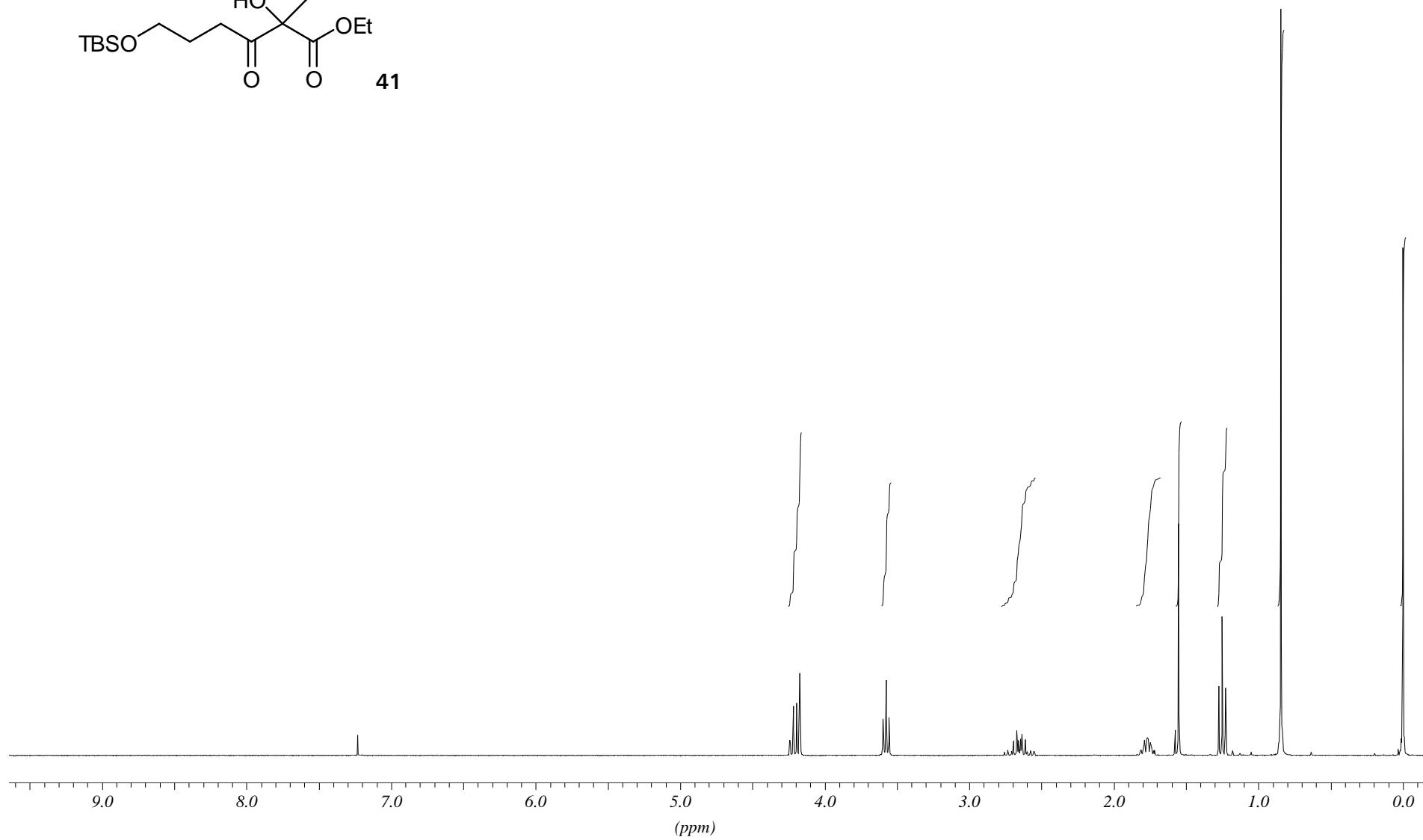
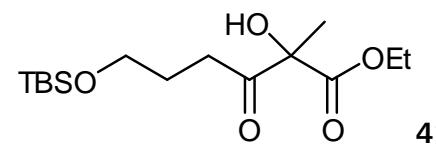


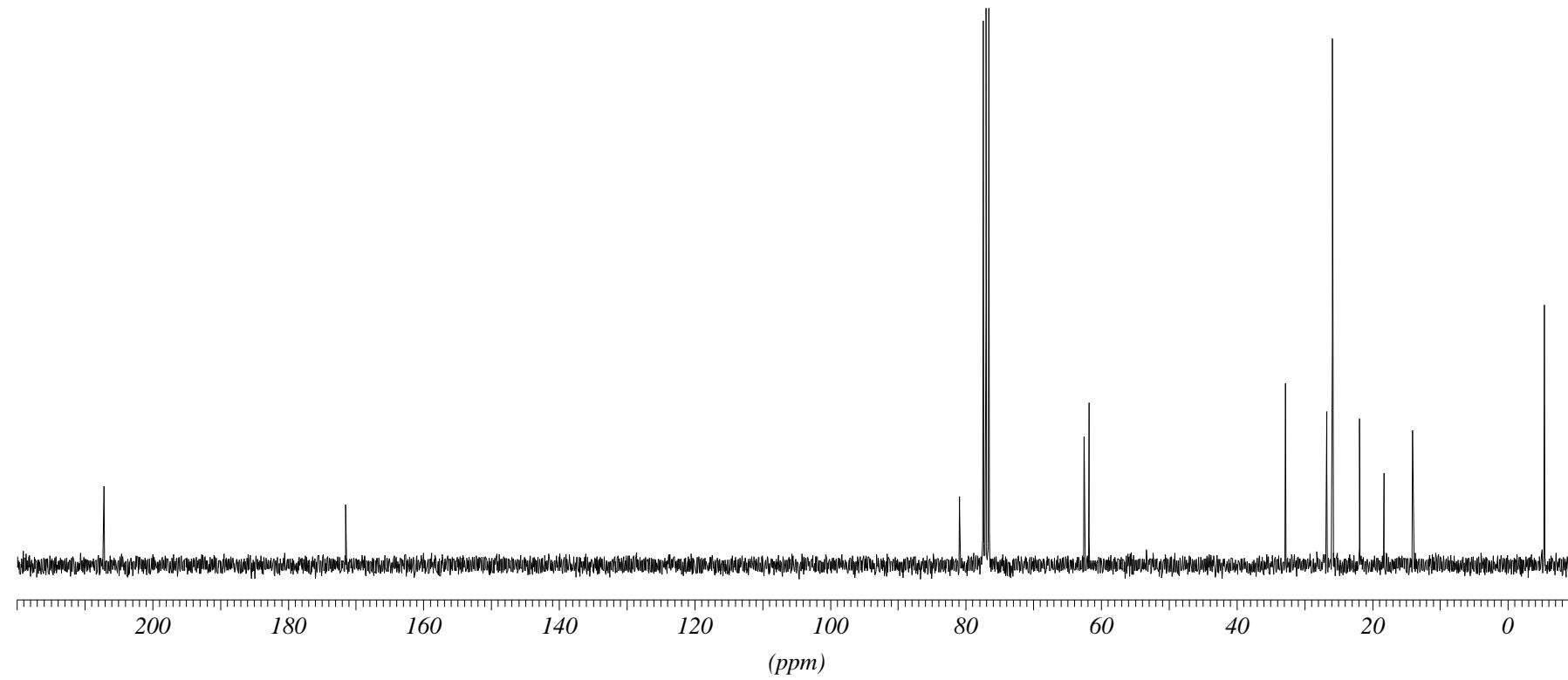
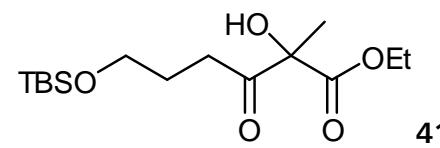


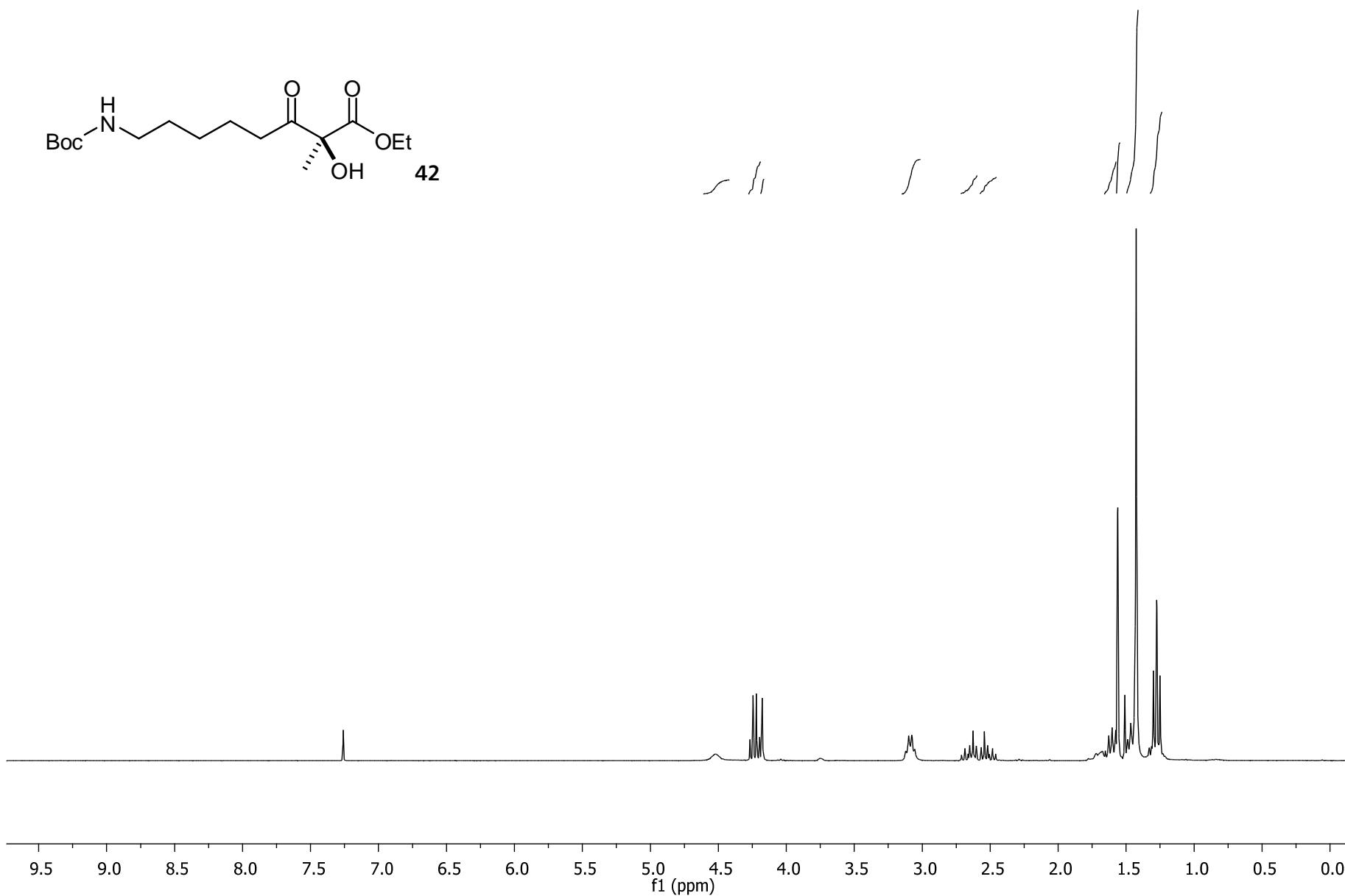


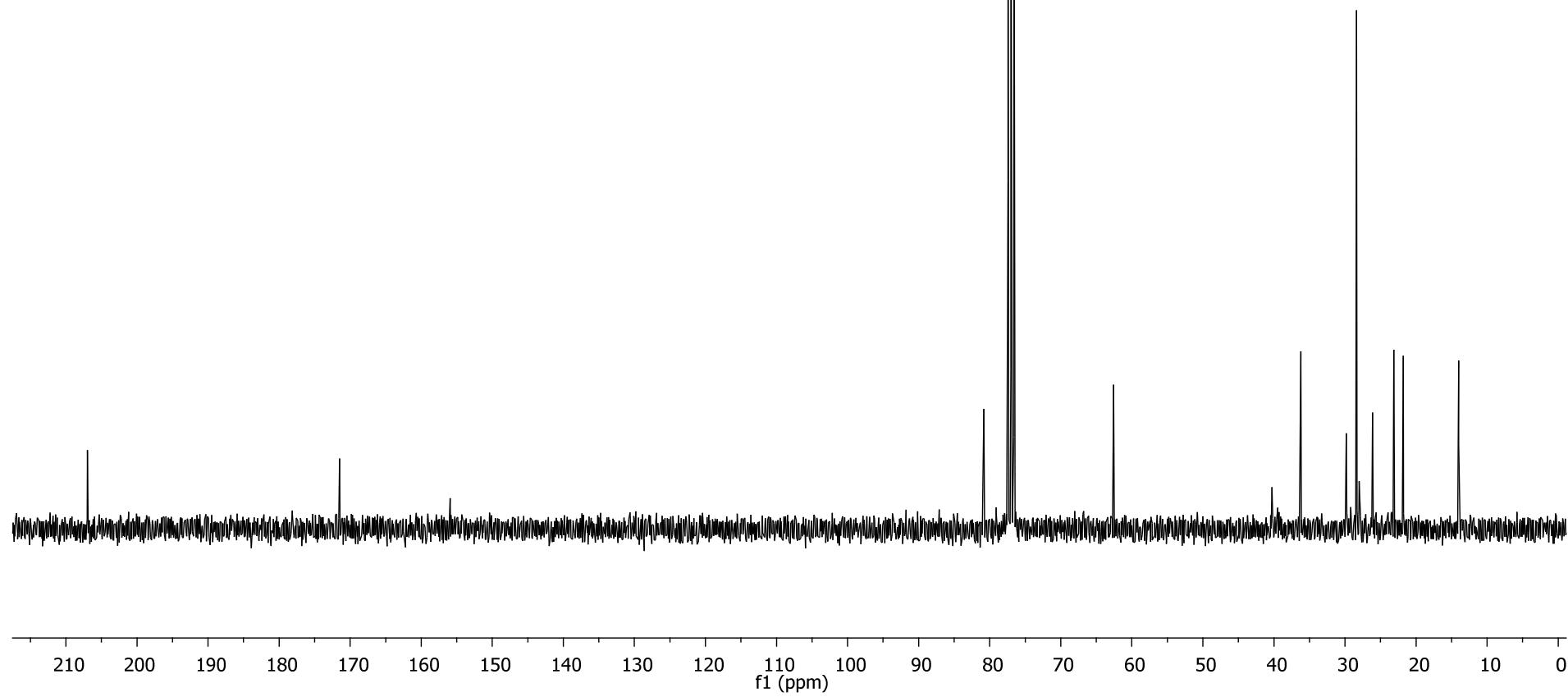
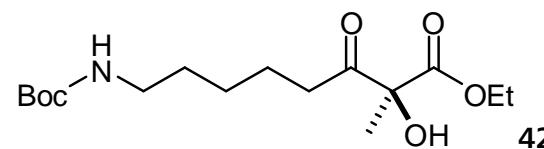


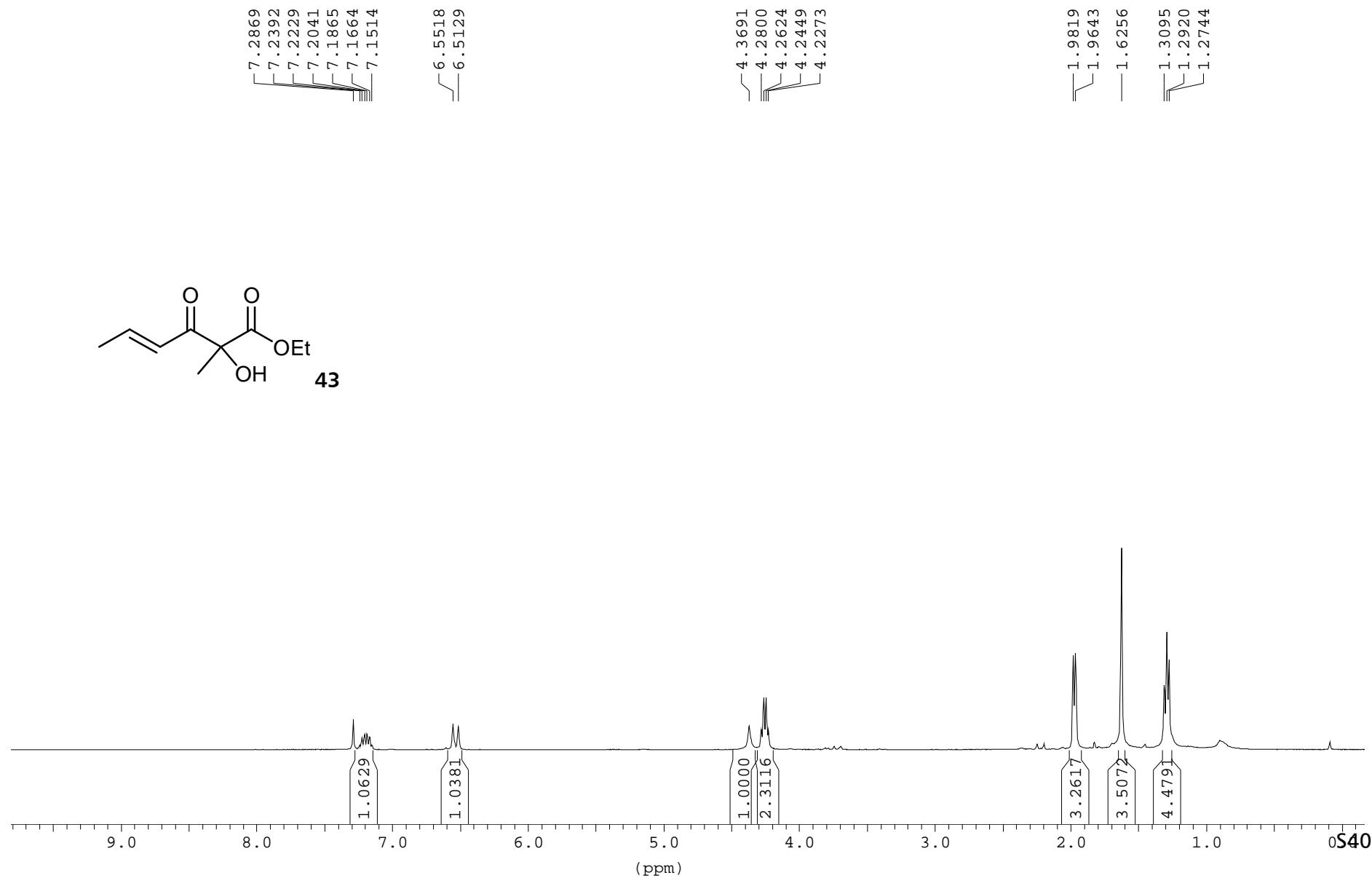


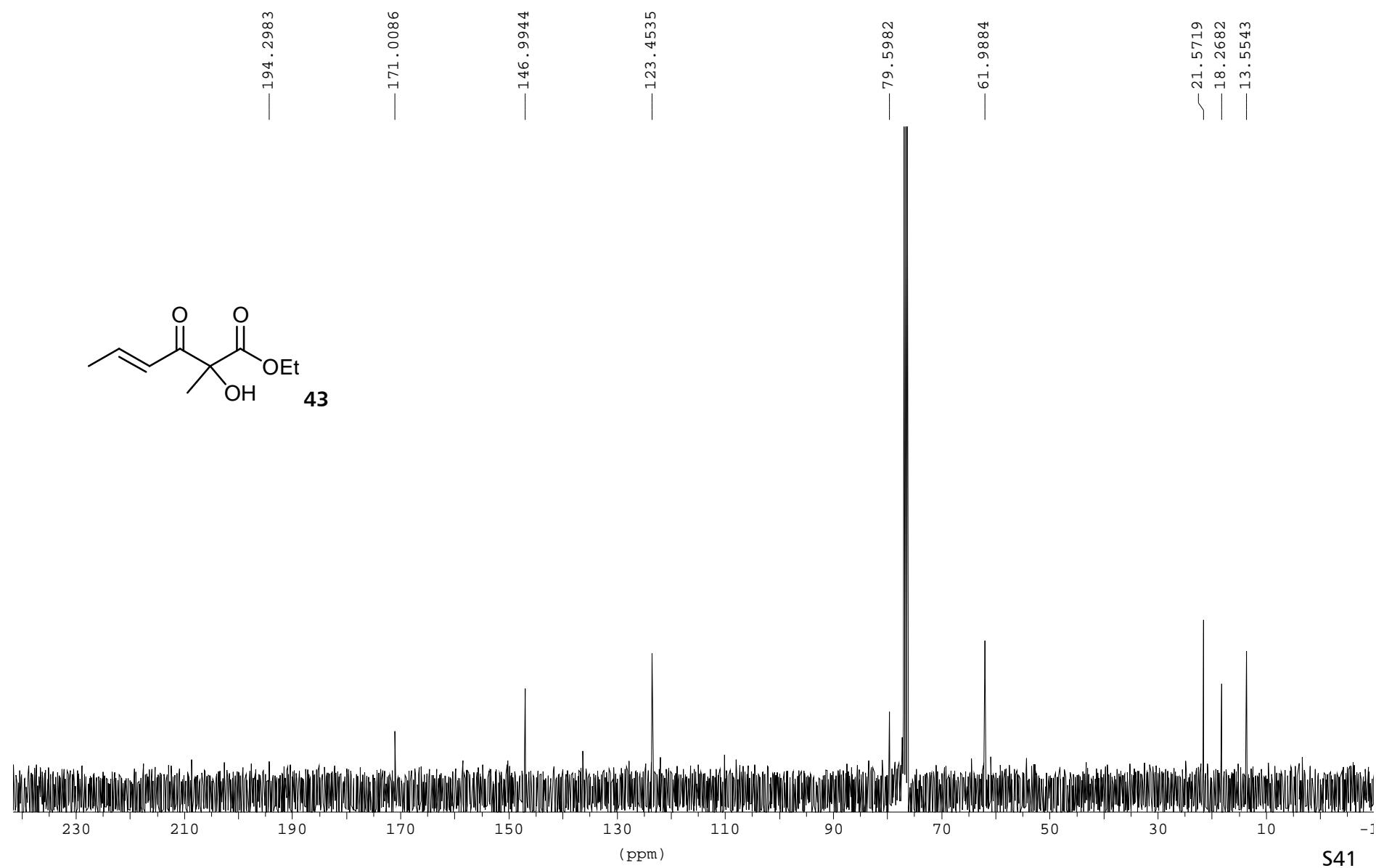


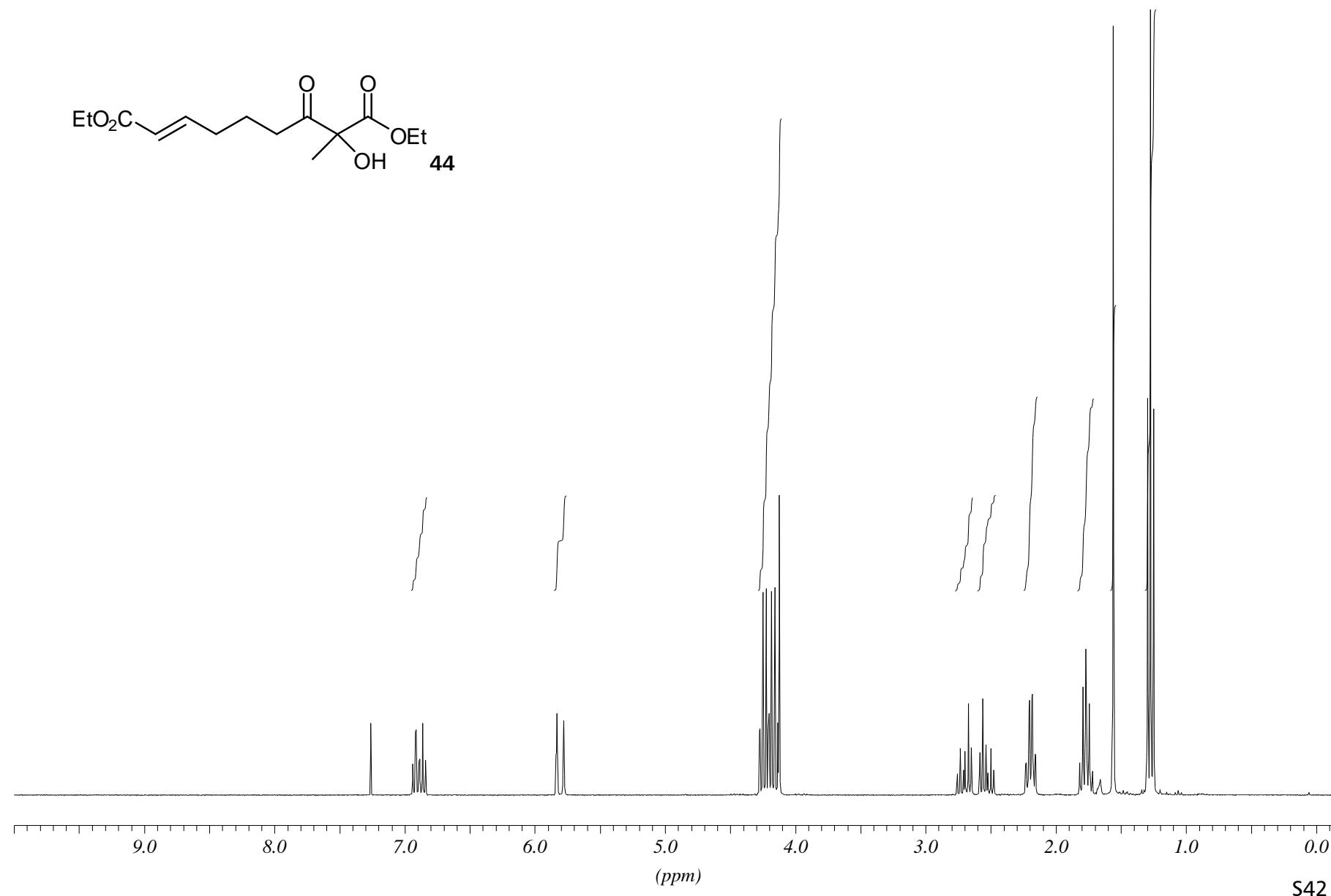


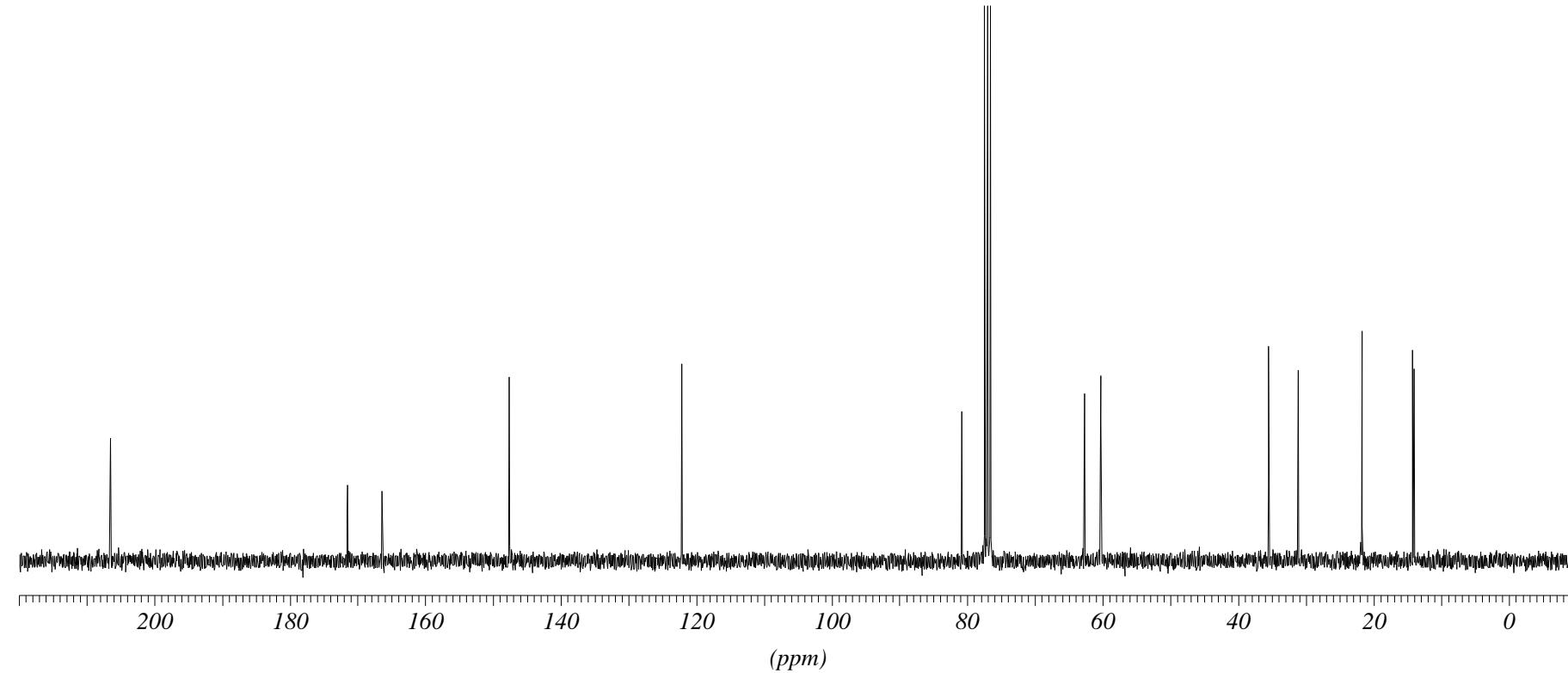
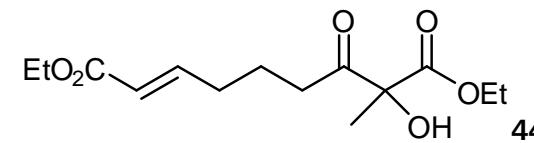


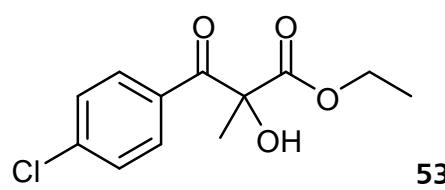




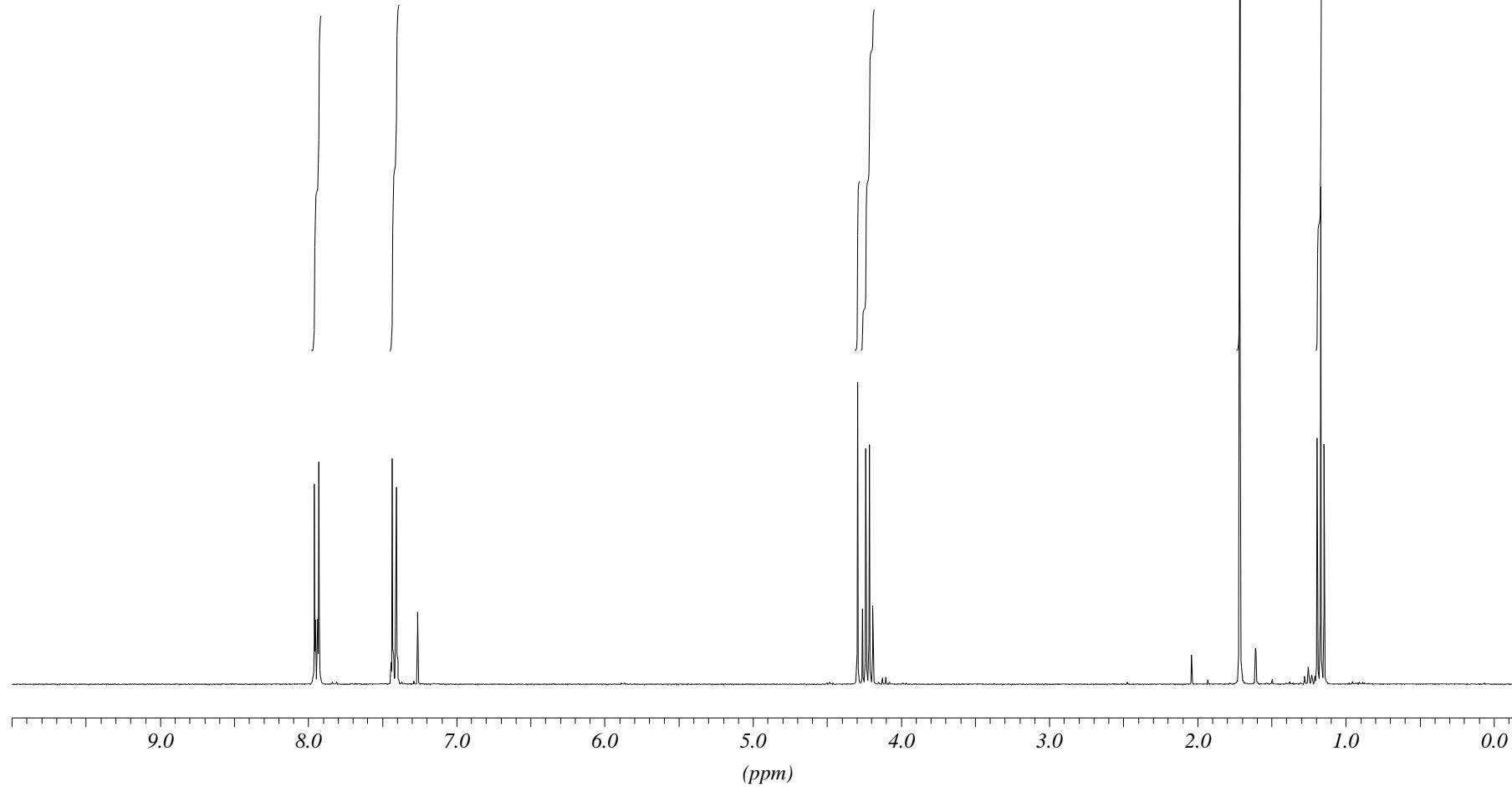




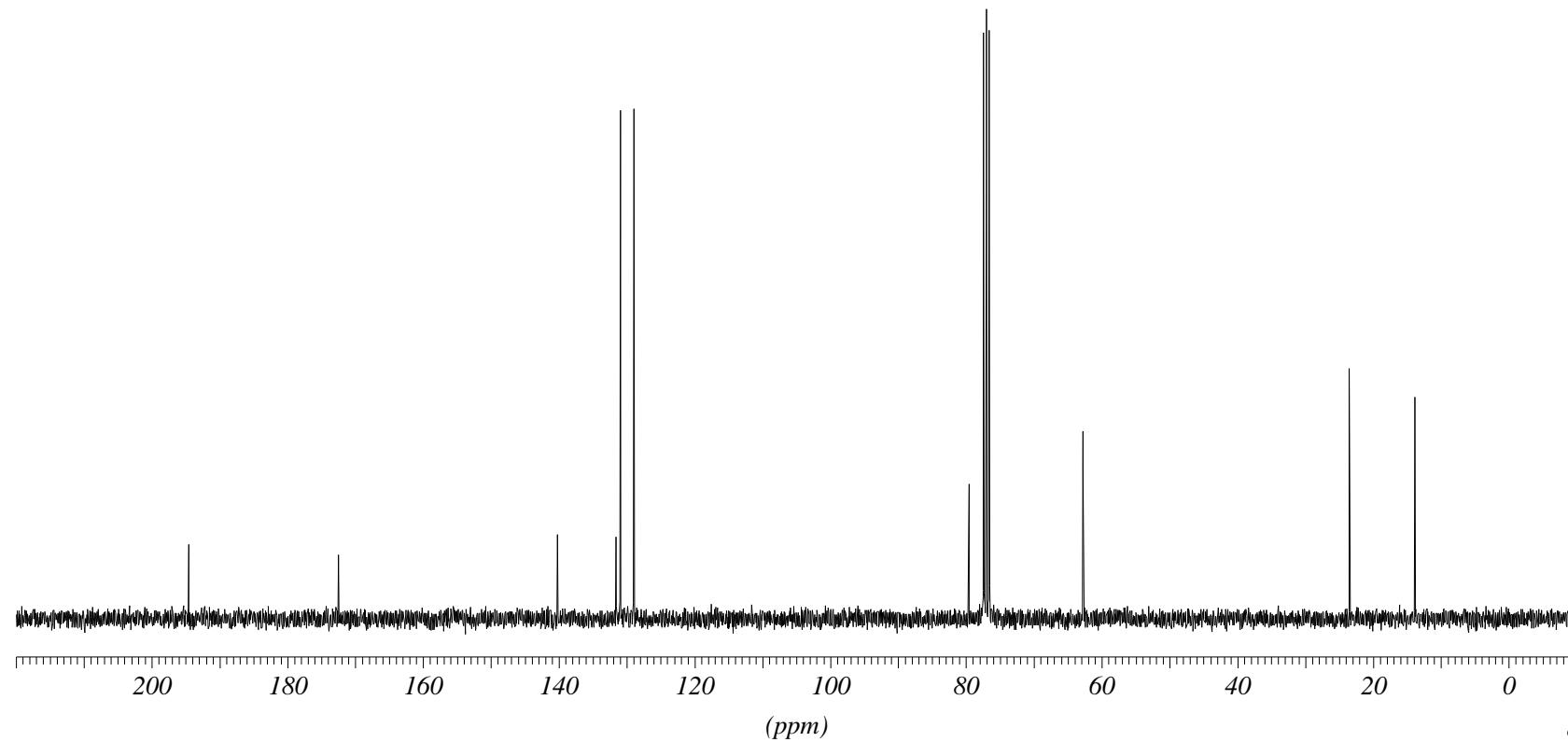
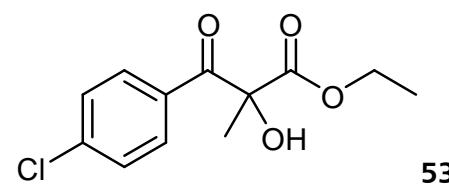


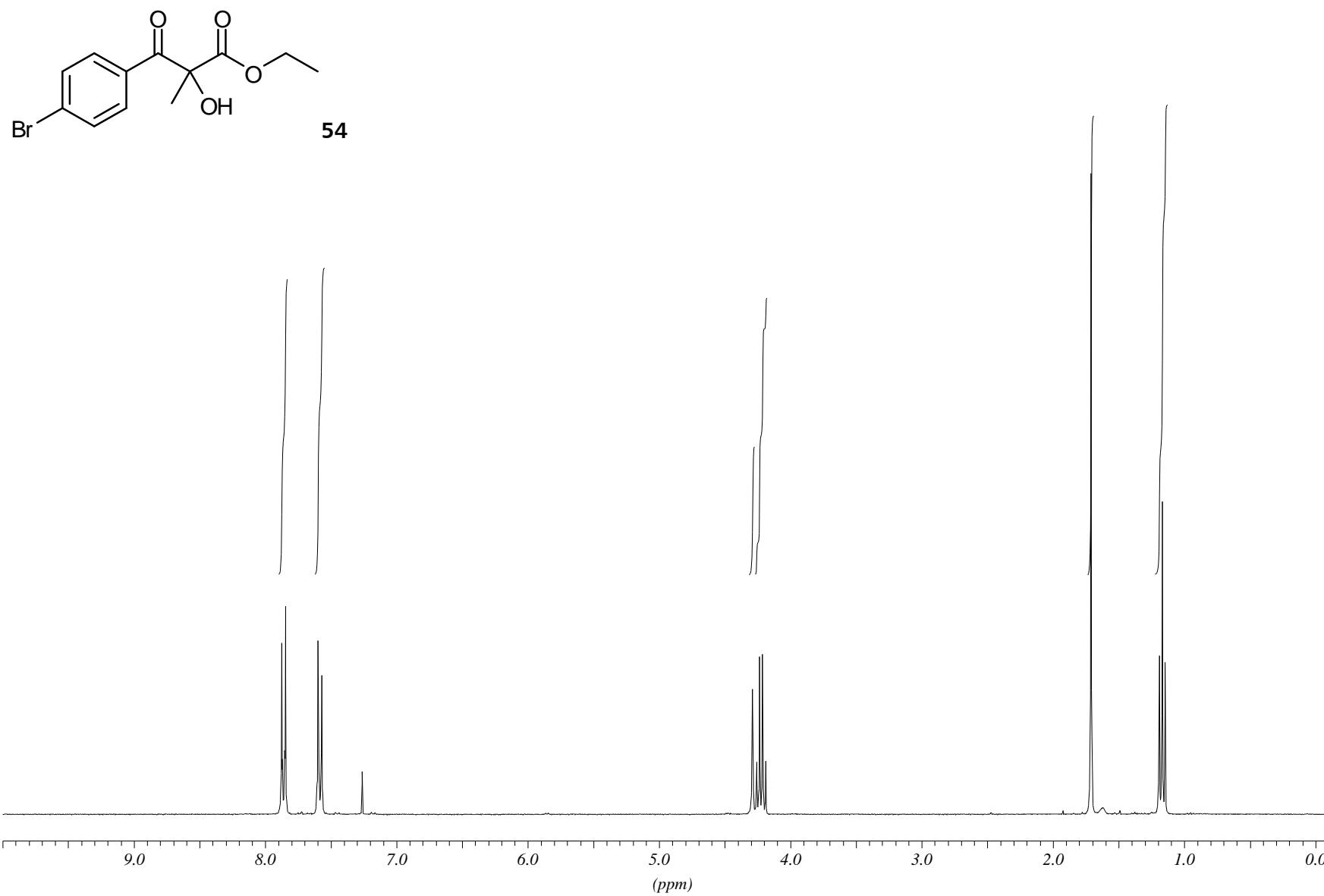


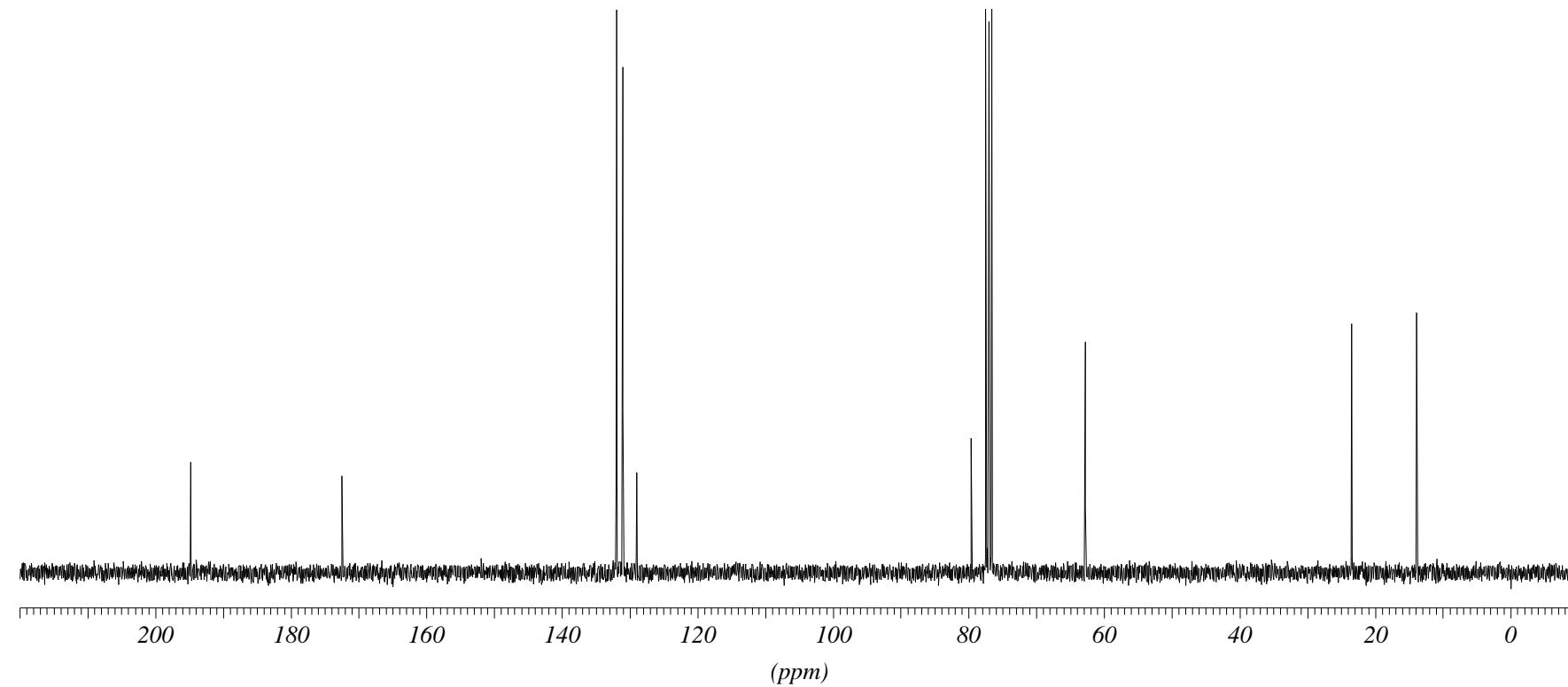
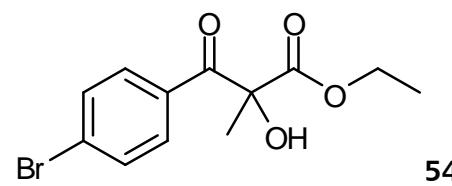
53

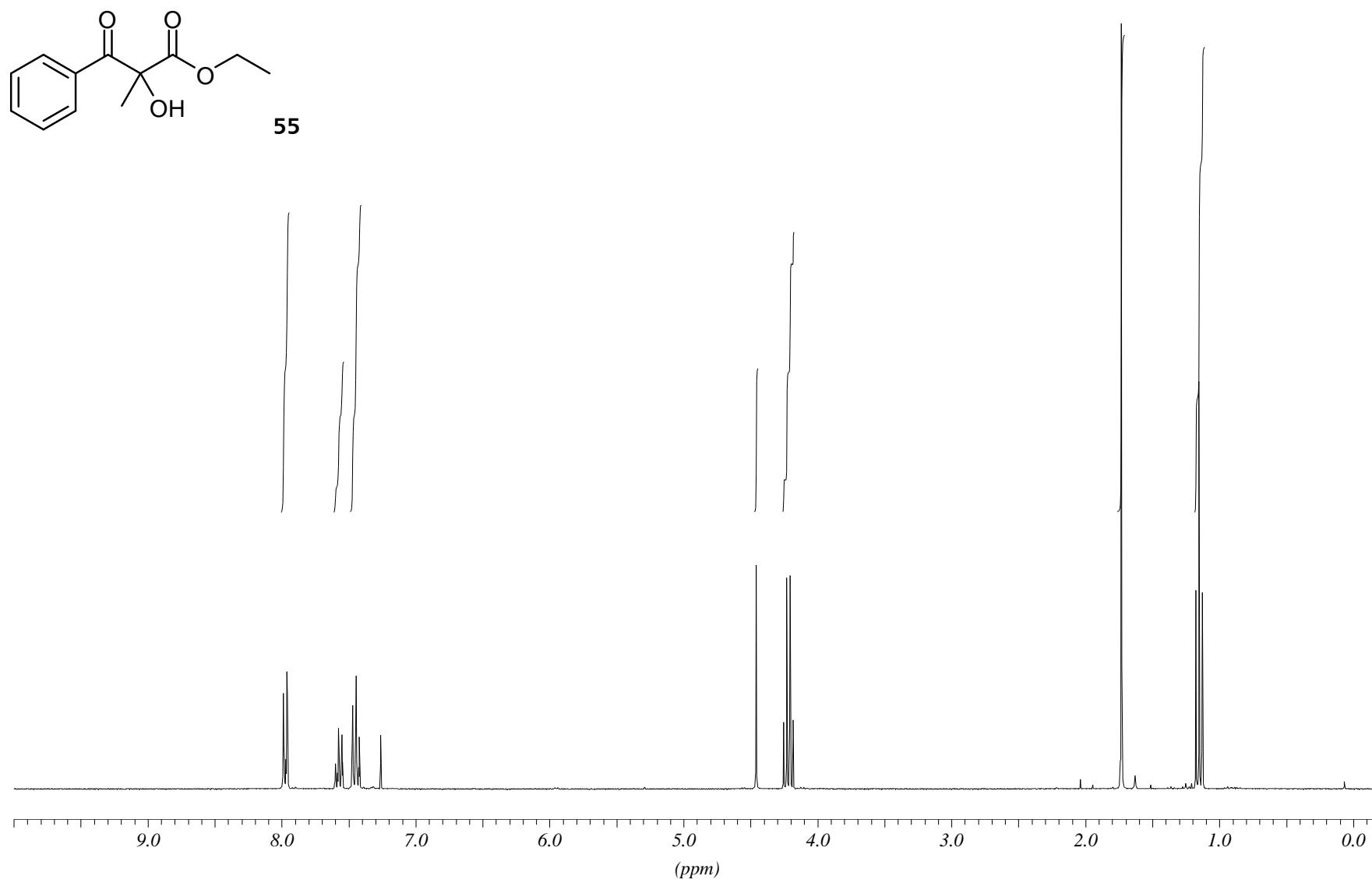


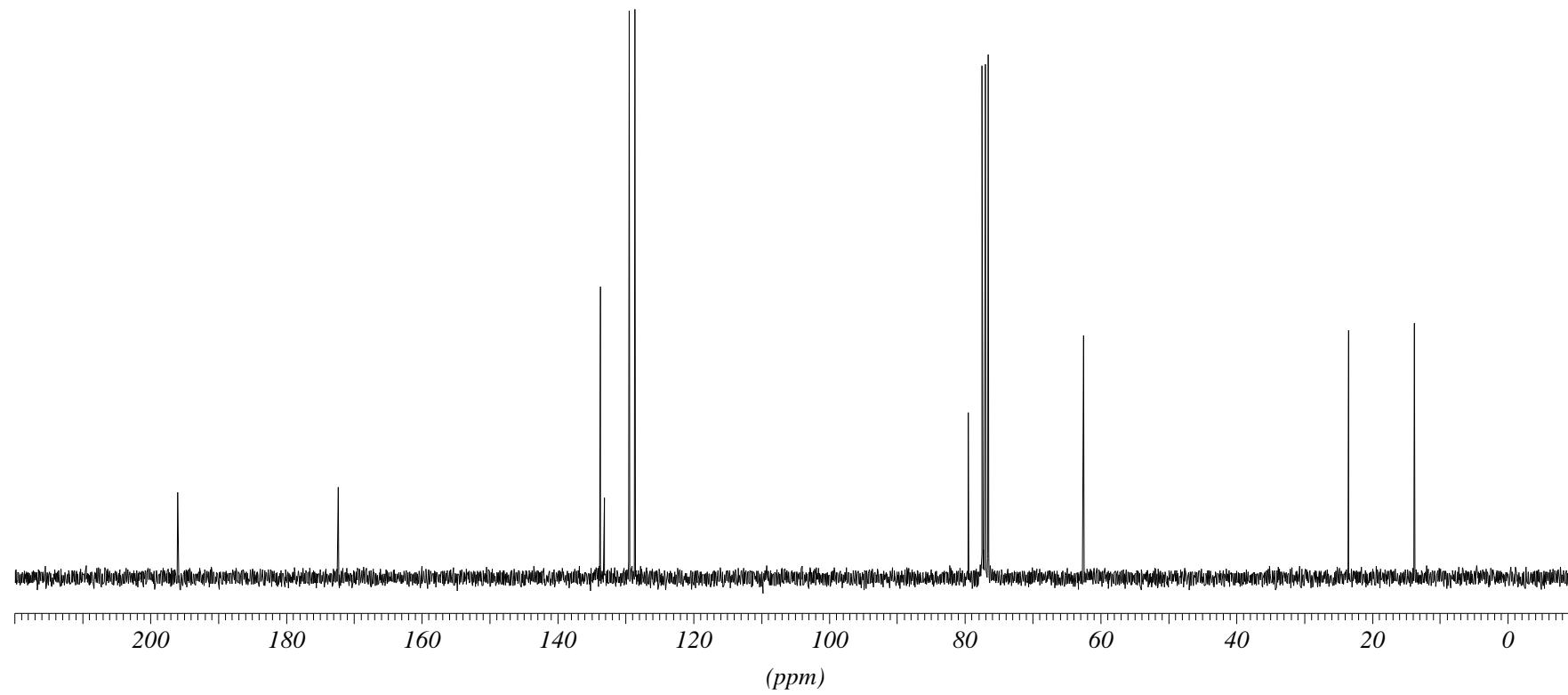
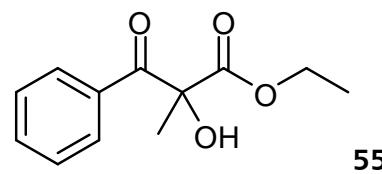
S44

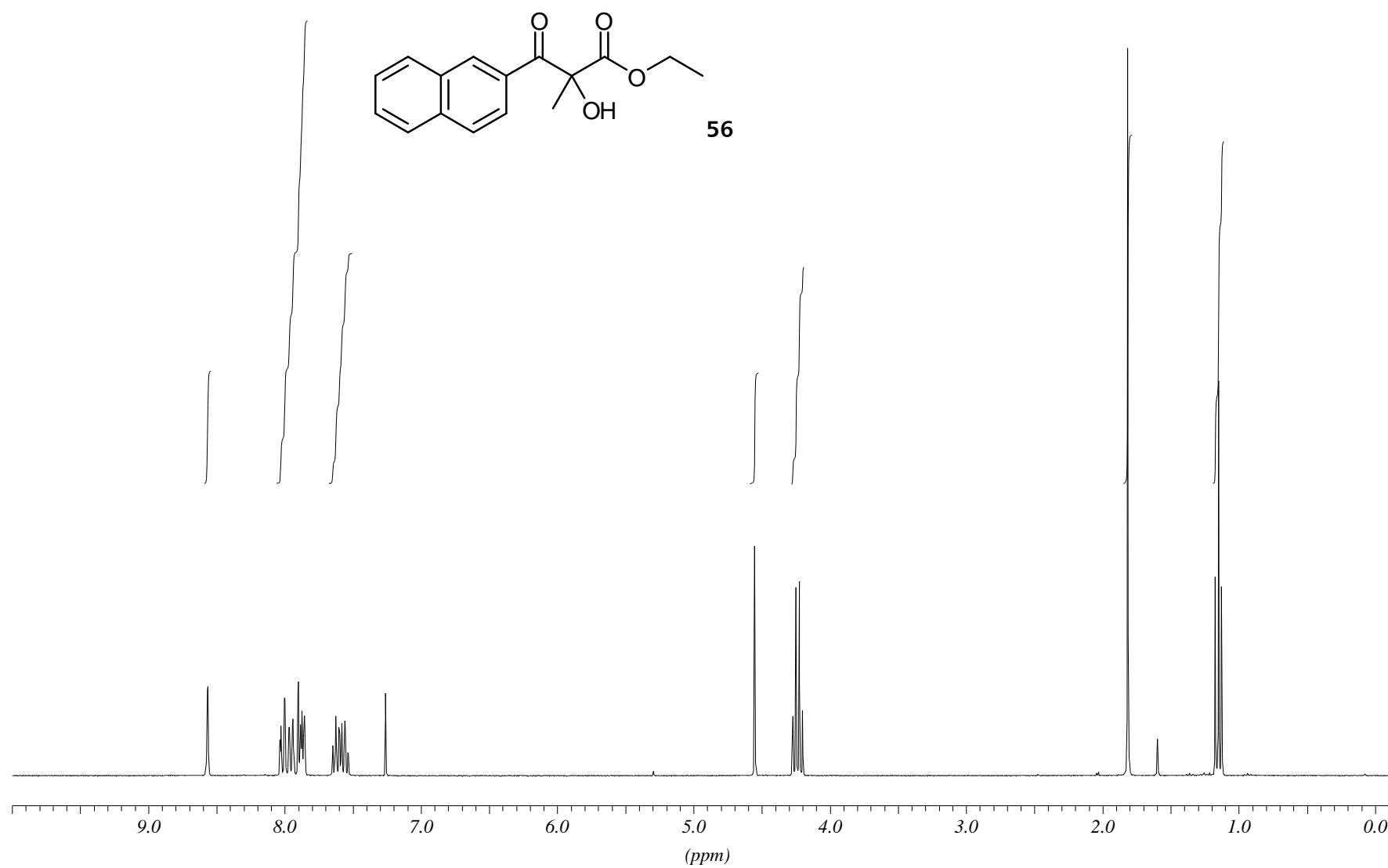


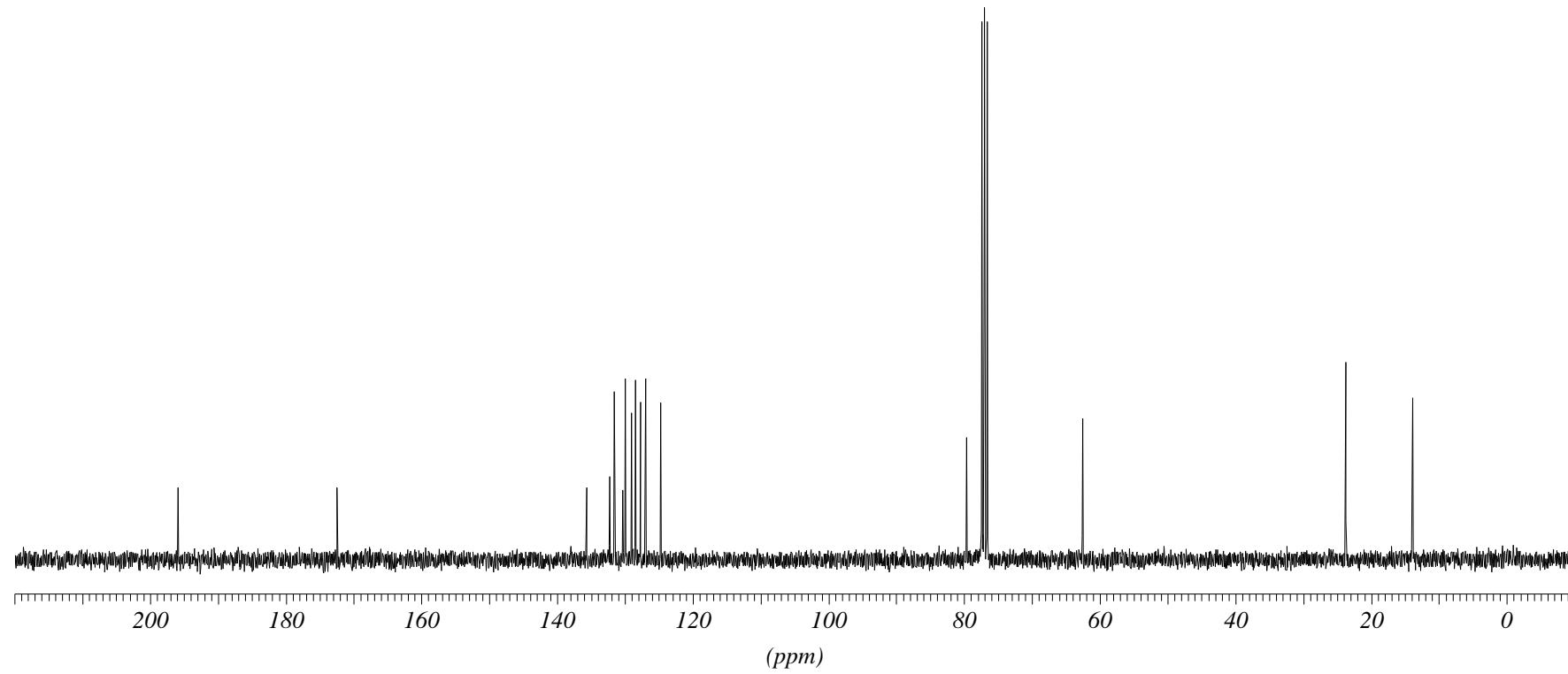
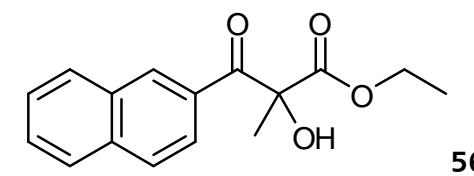


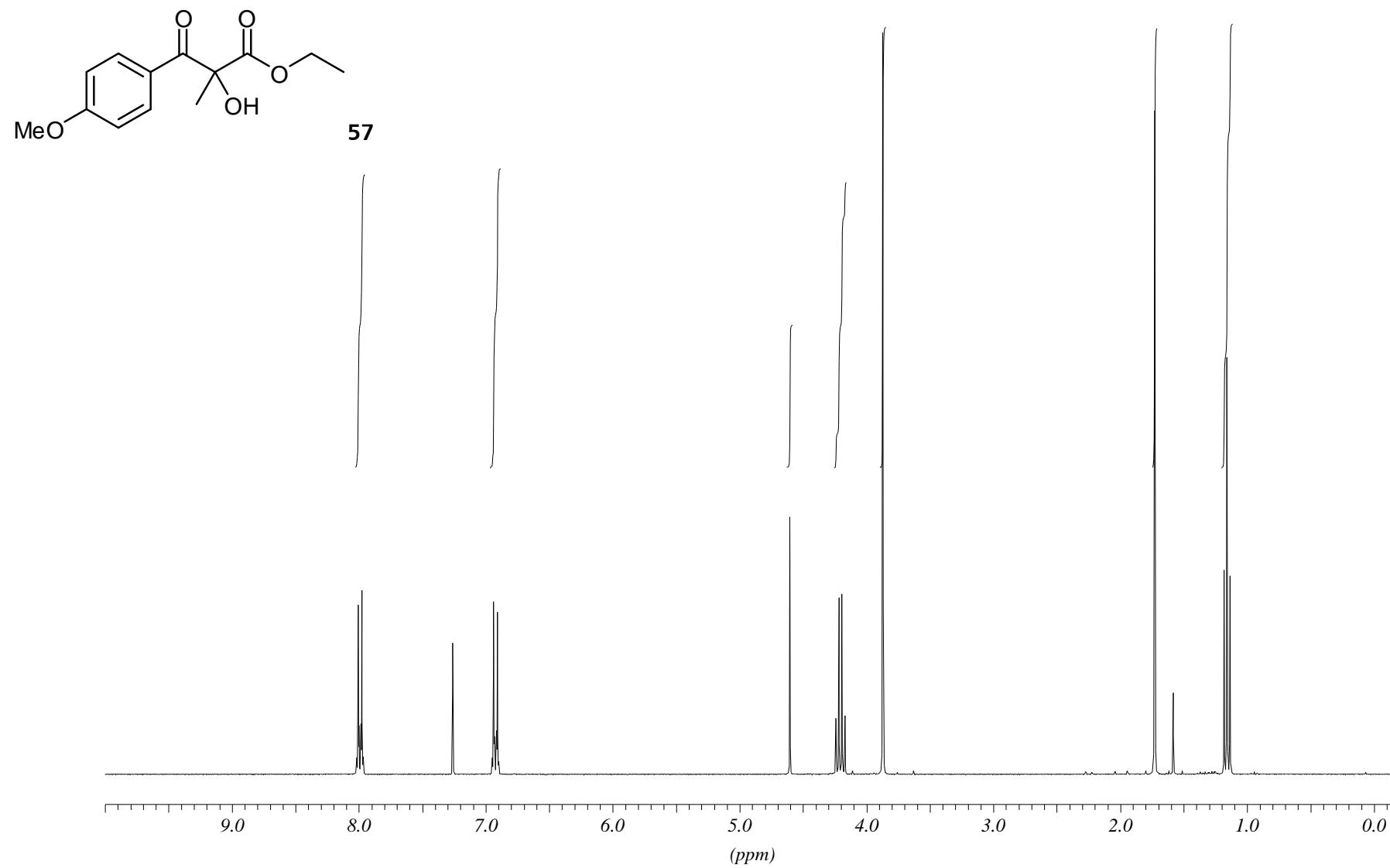


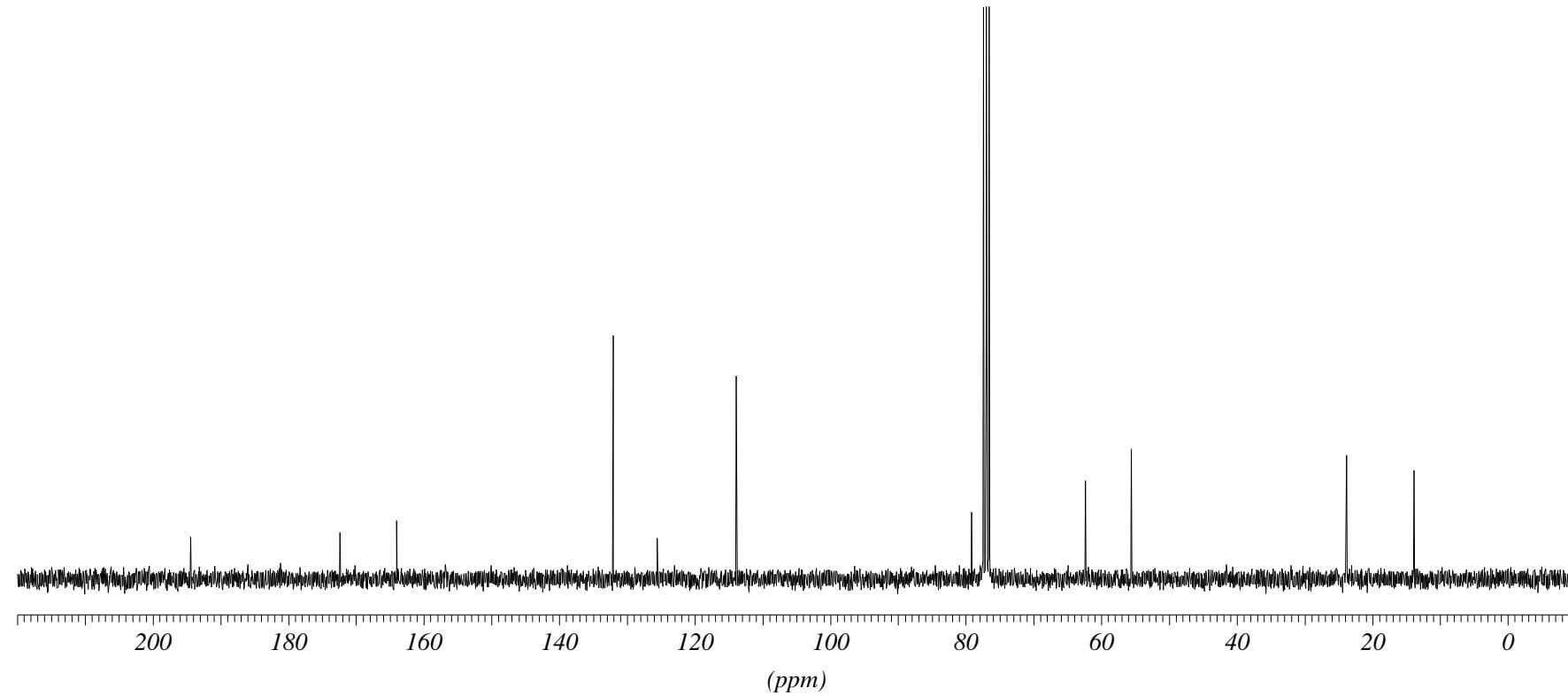
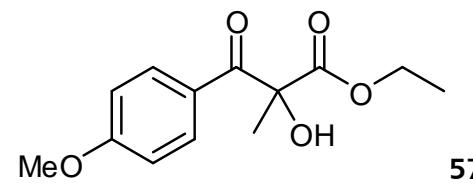


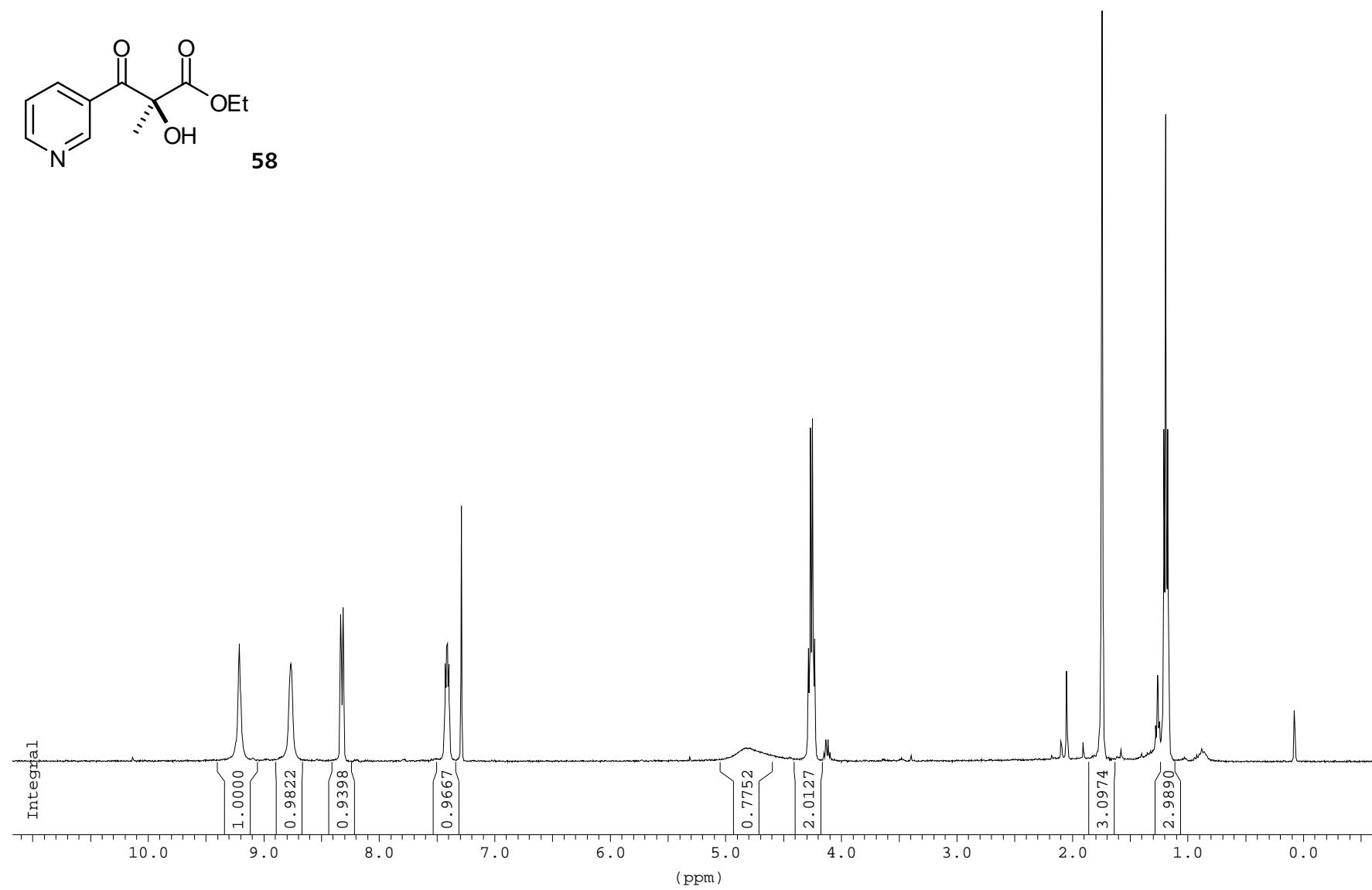


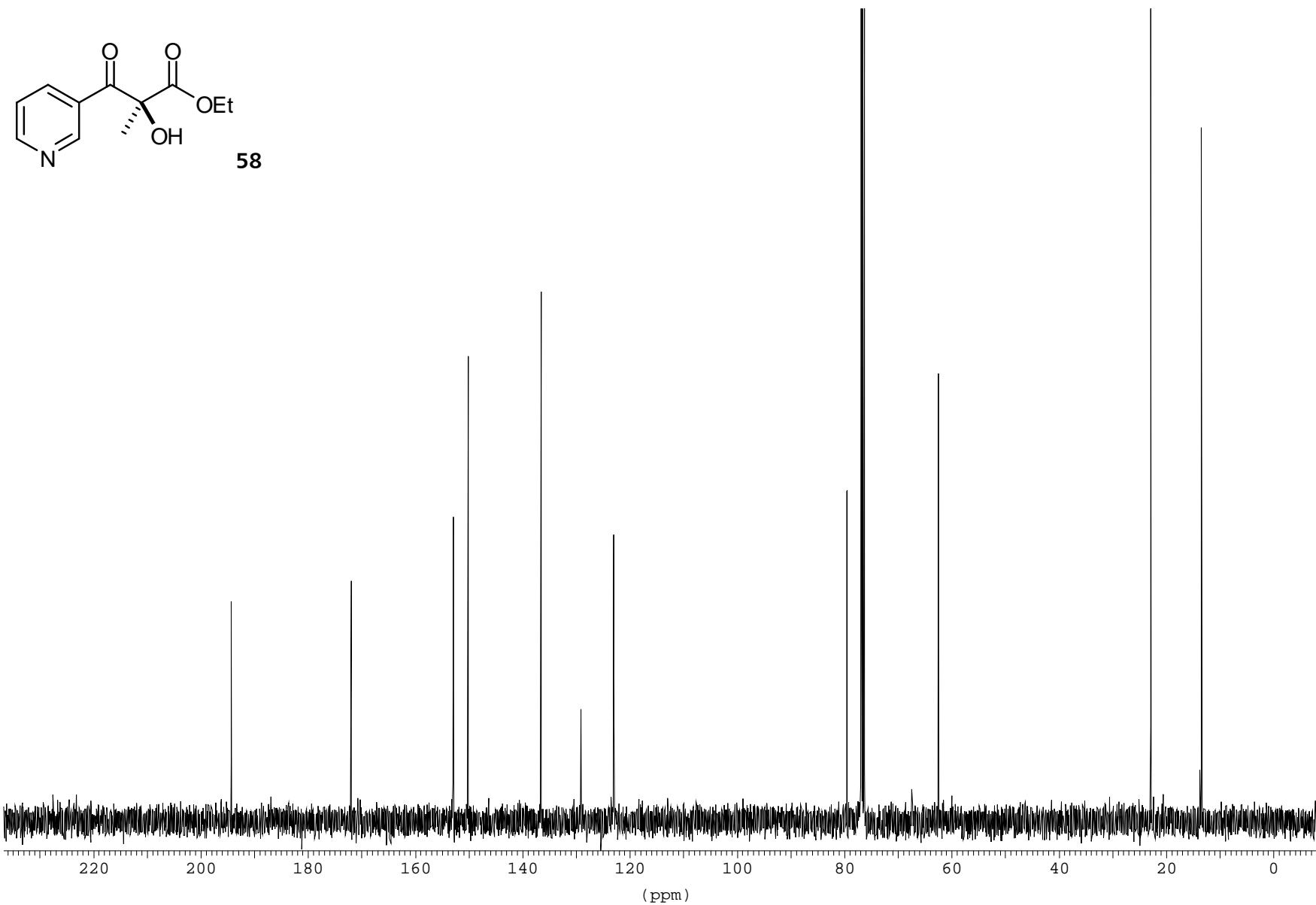


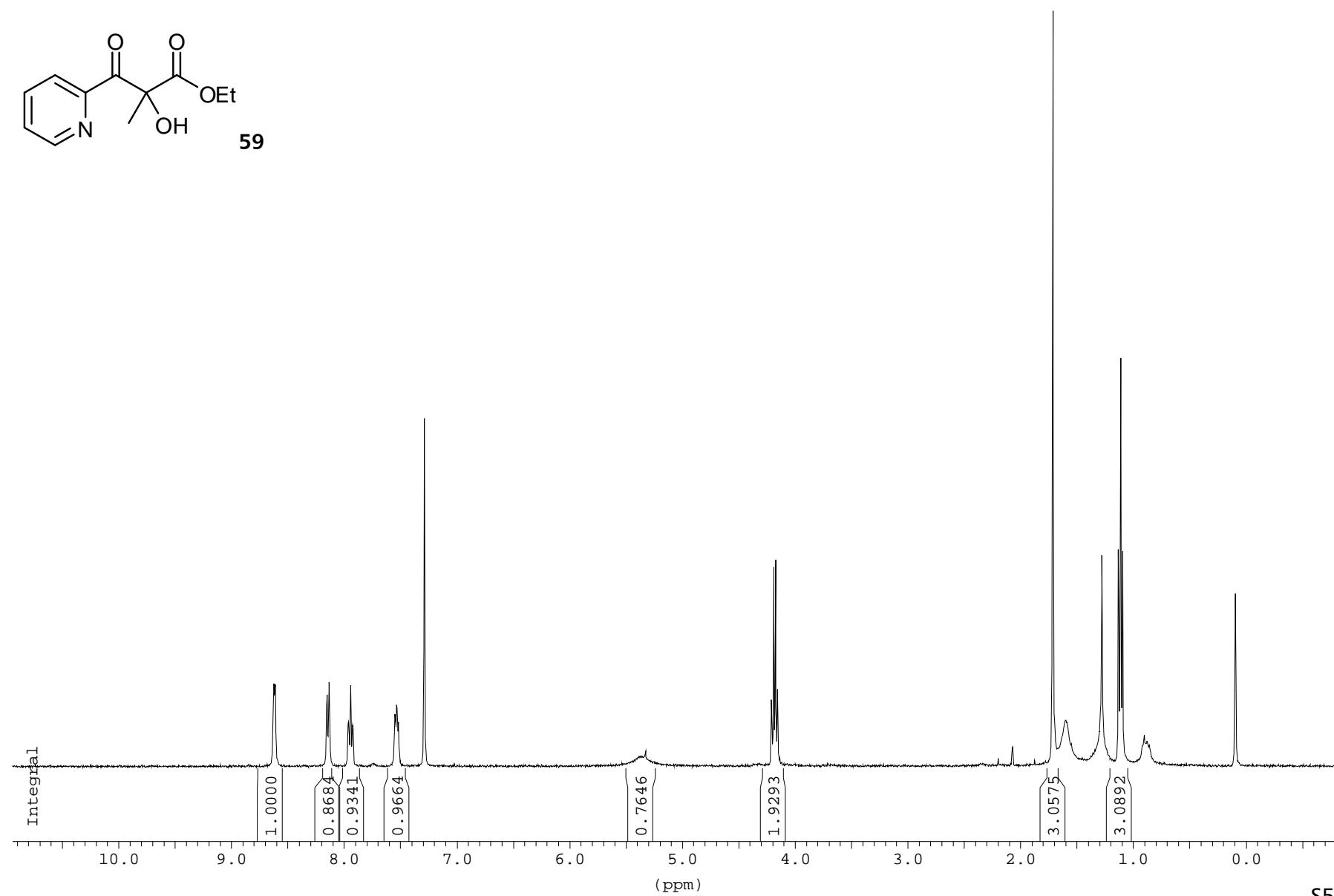


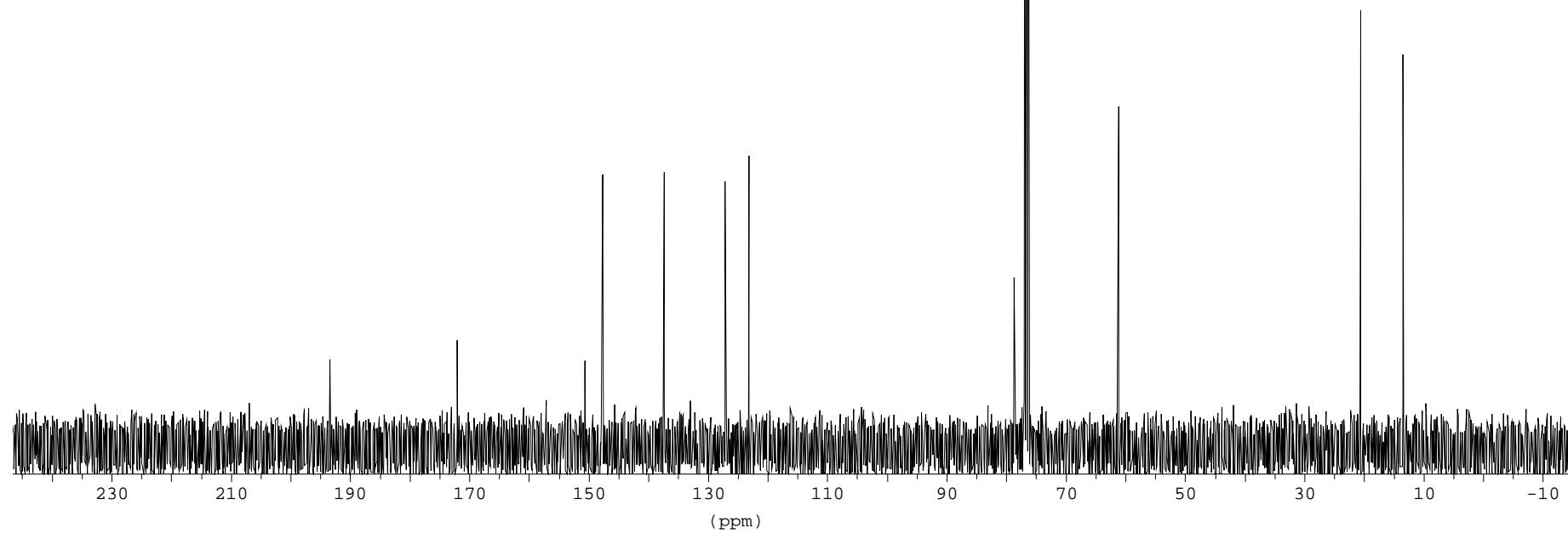
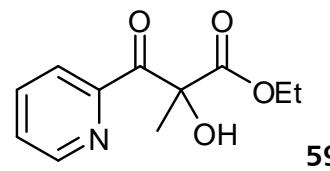


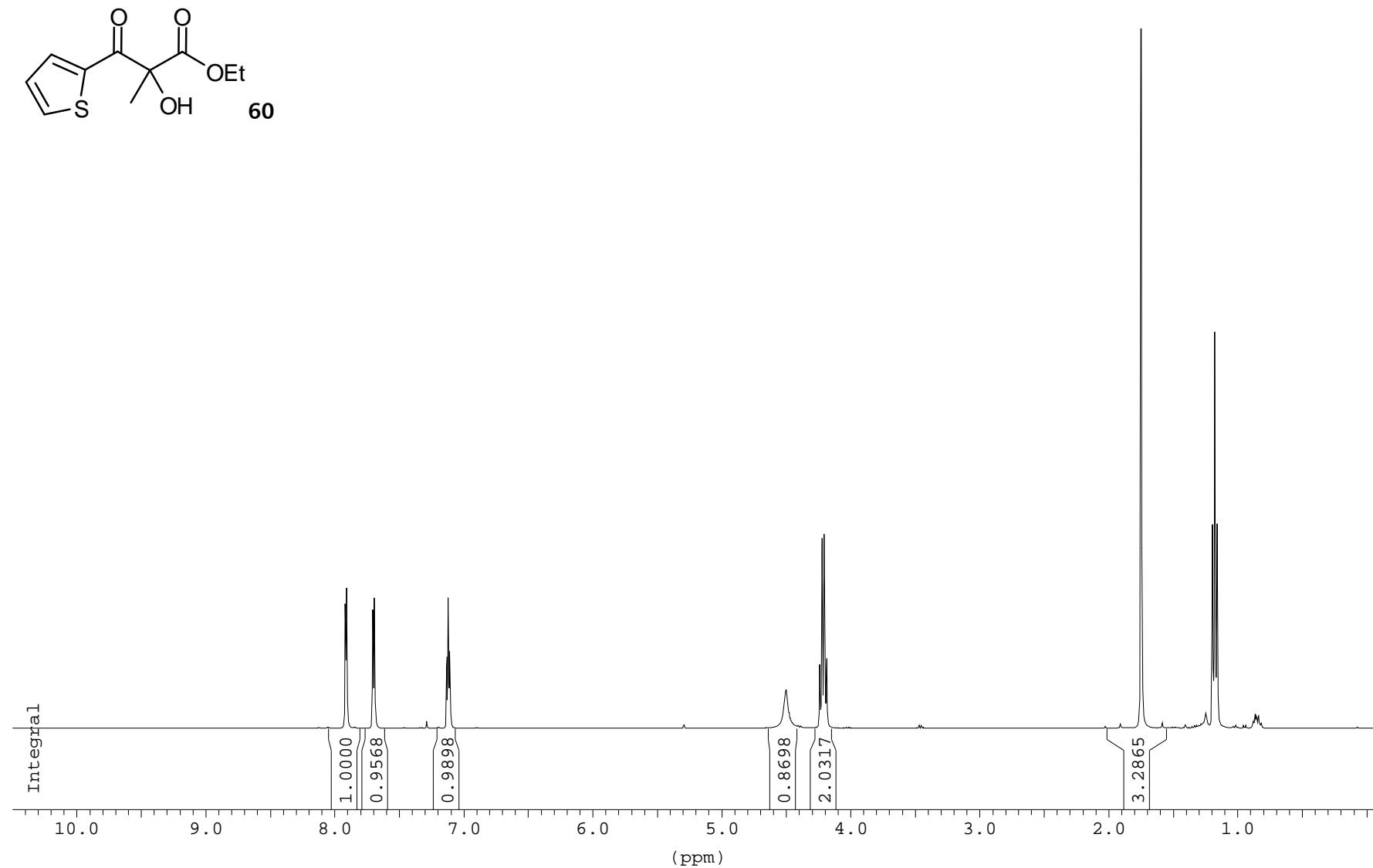


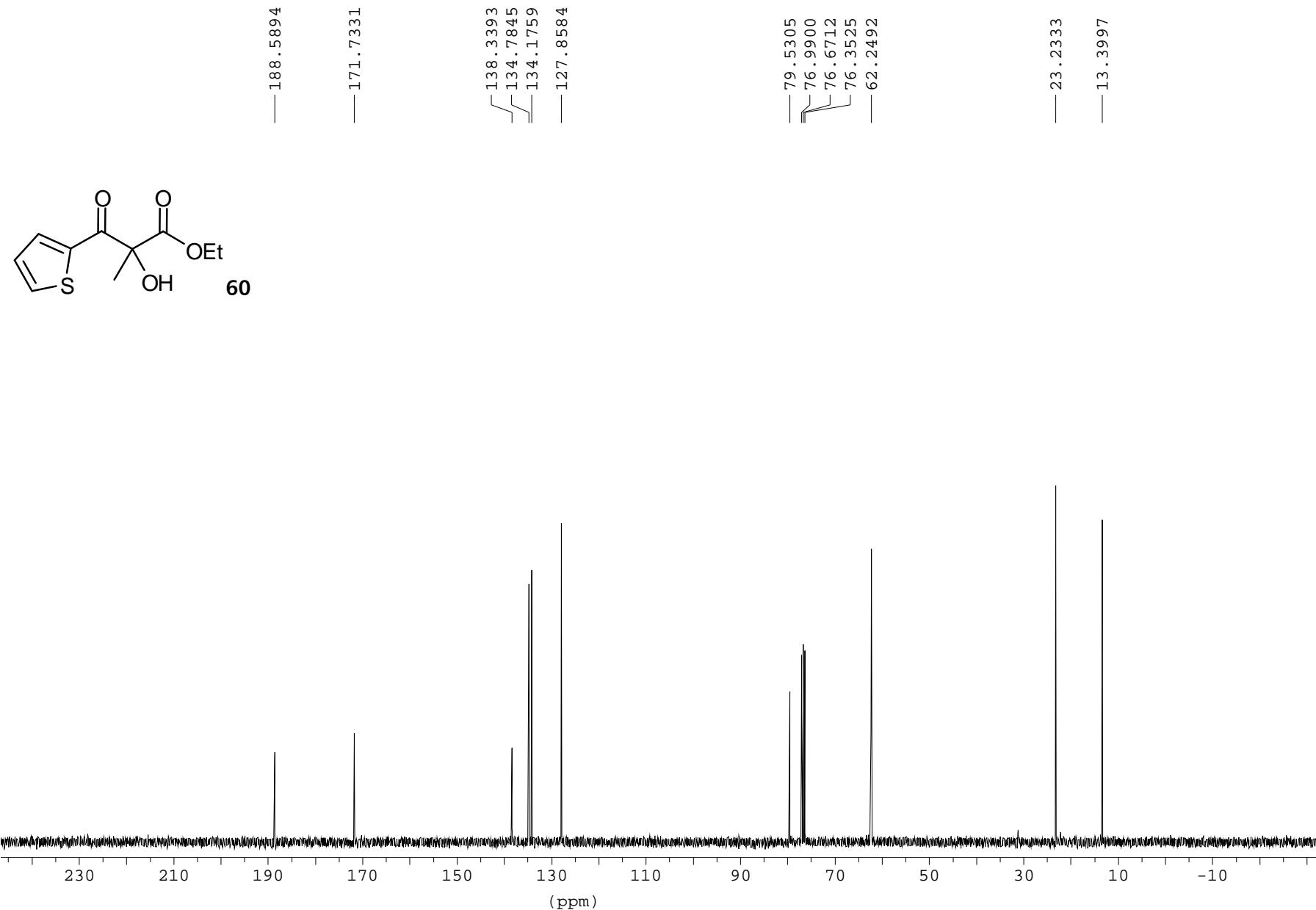


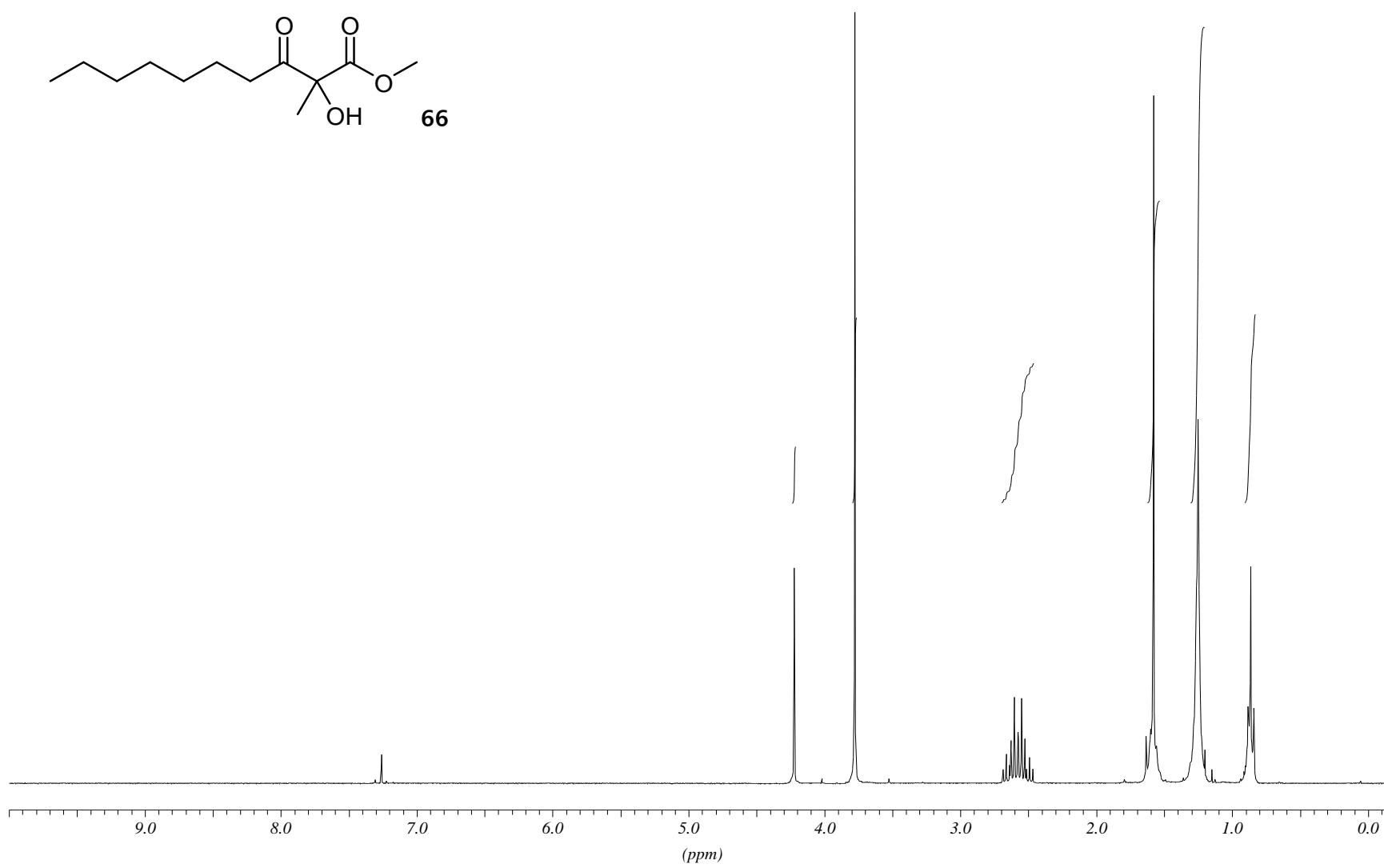


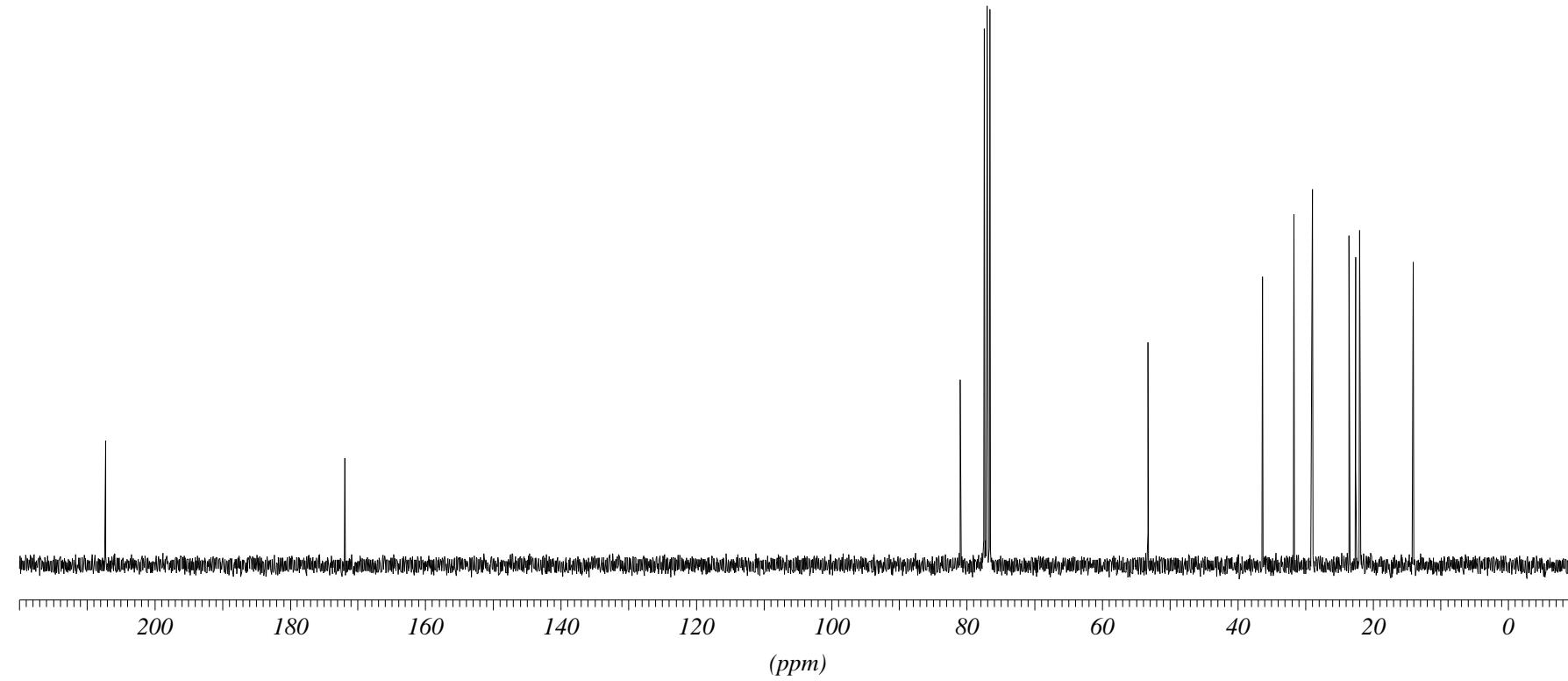
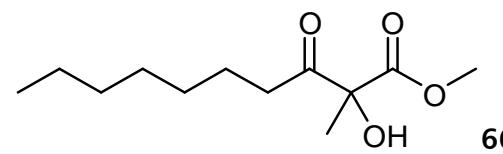


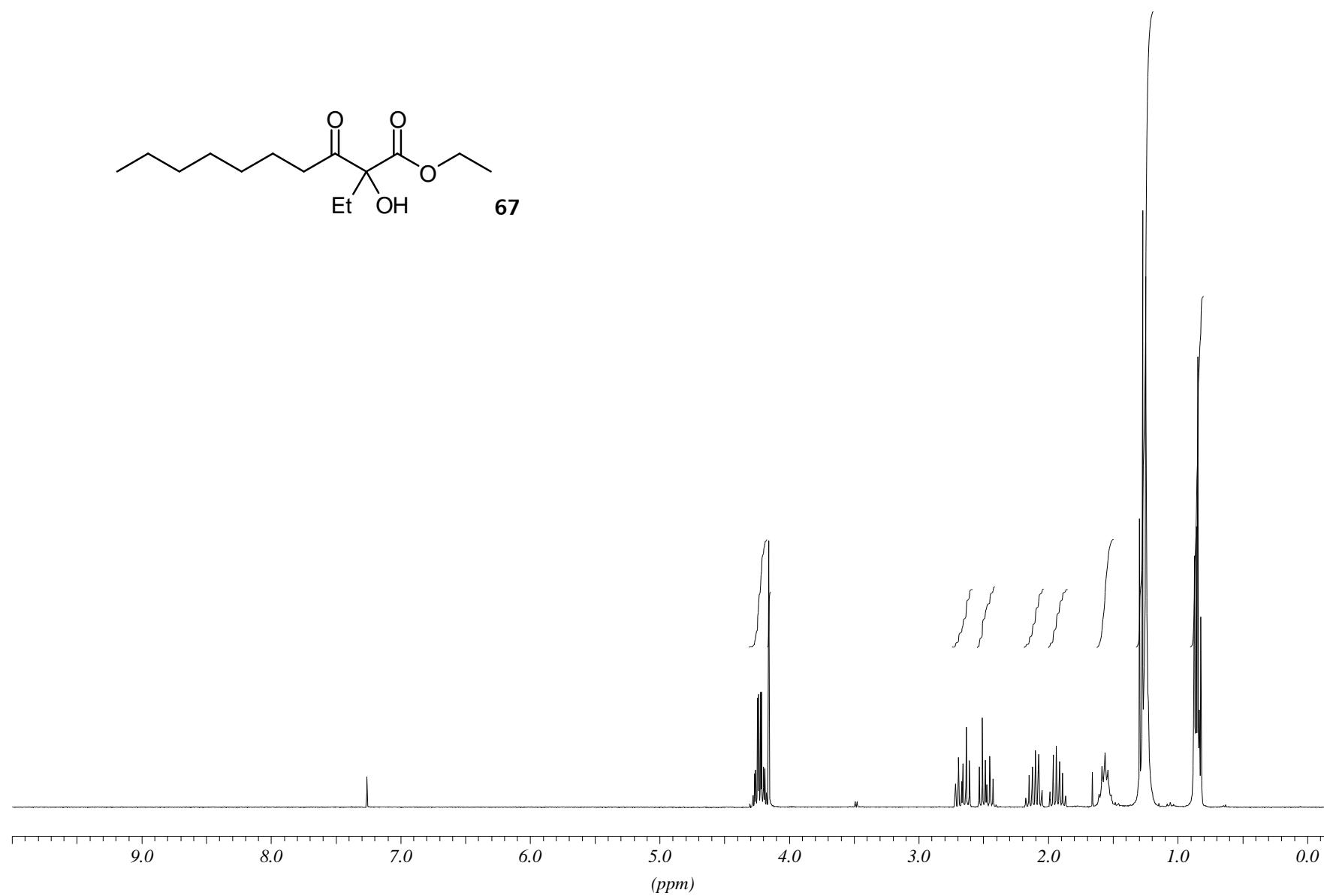


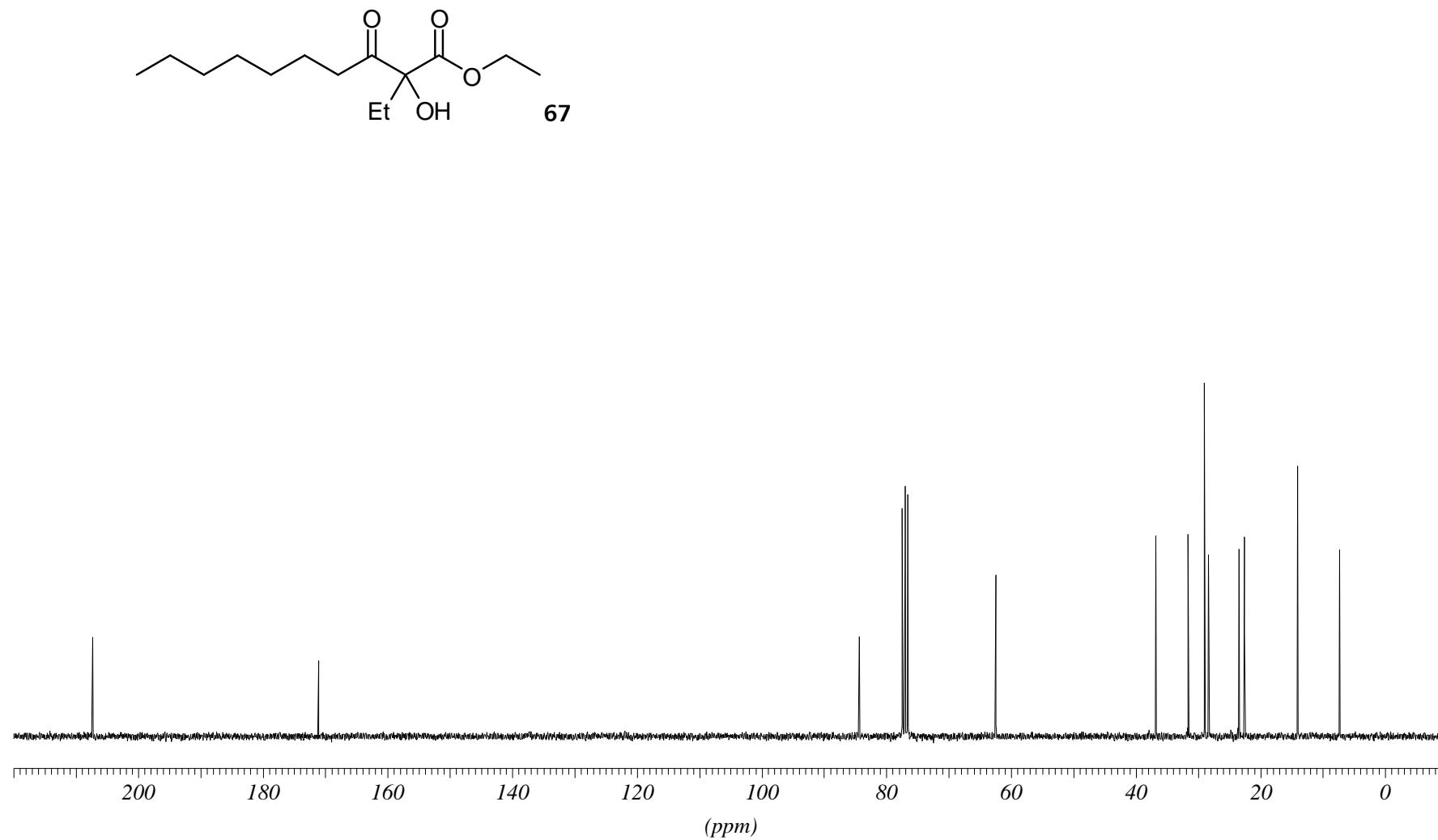


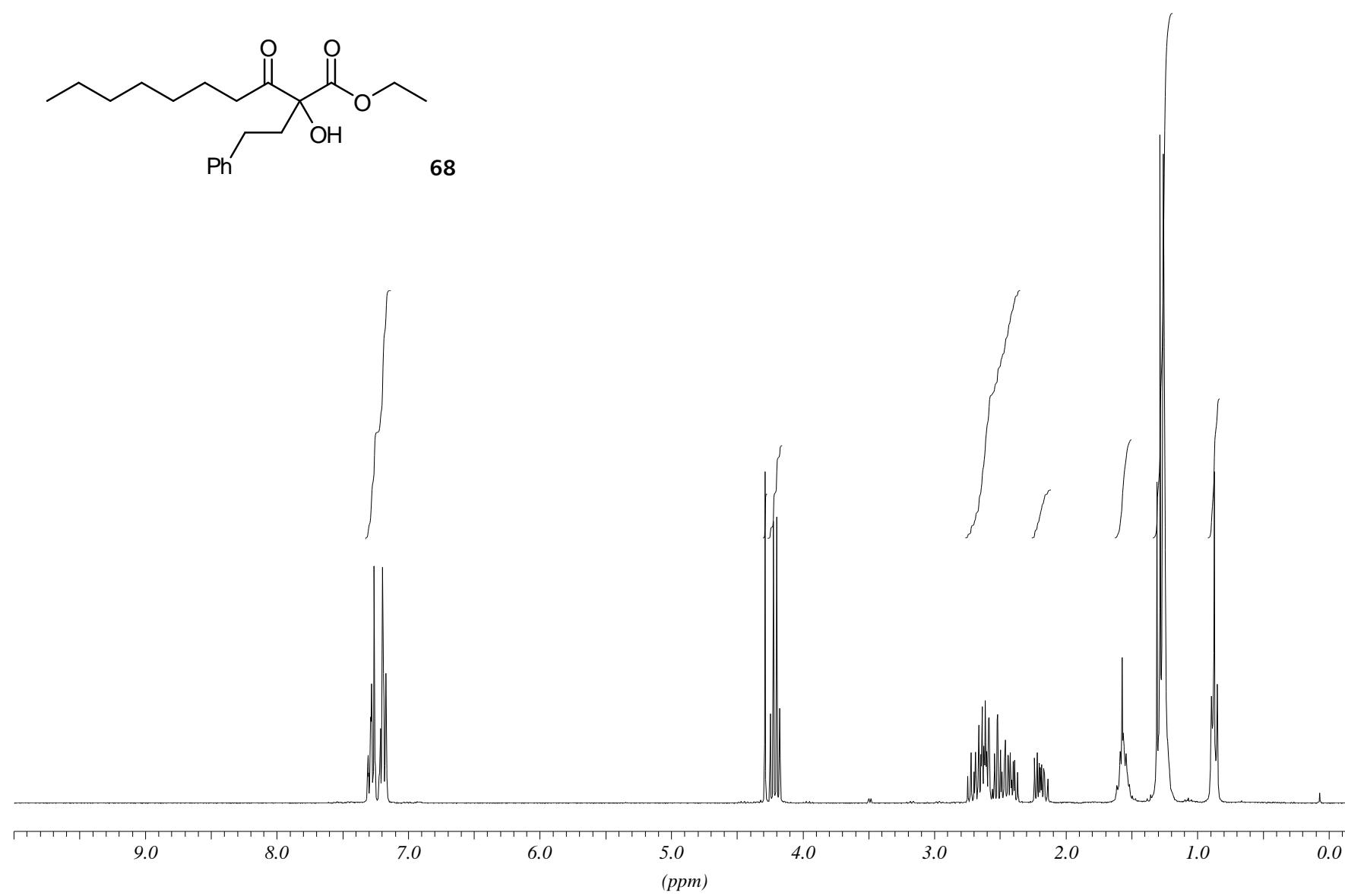


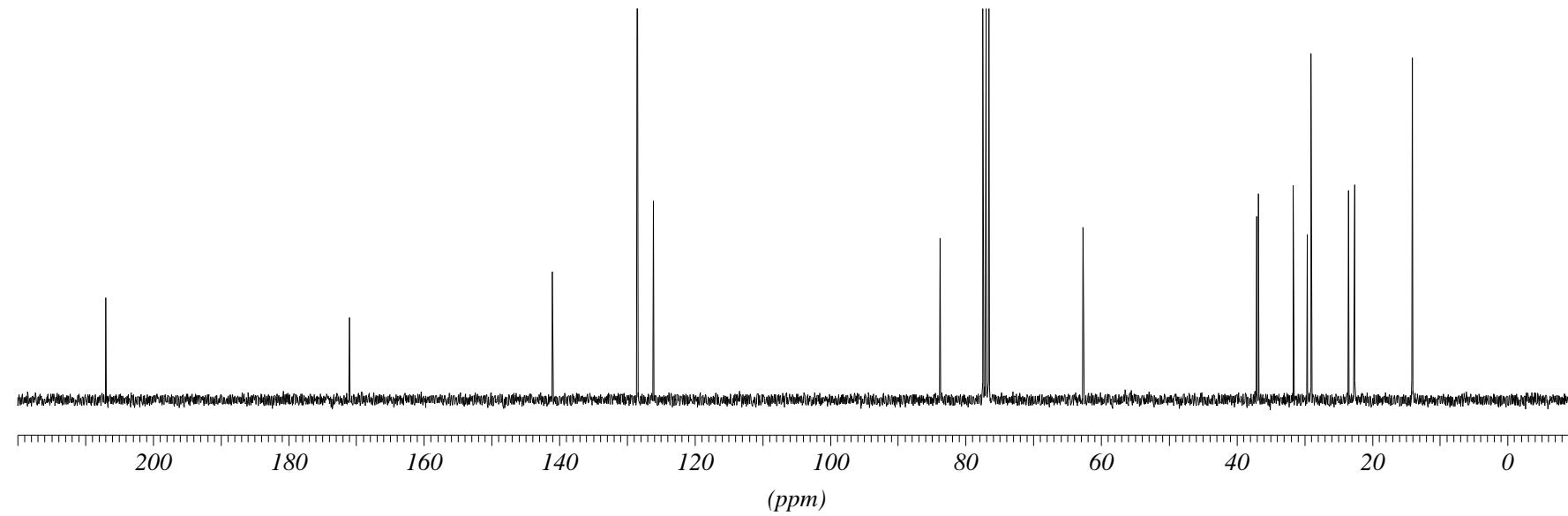
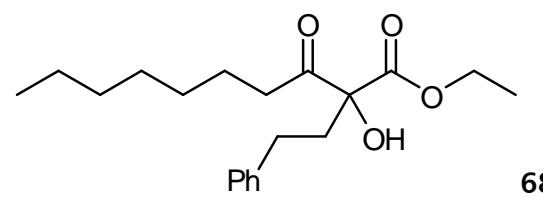


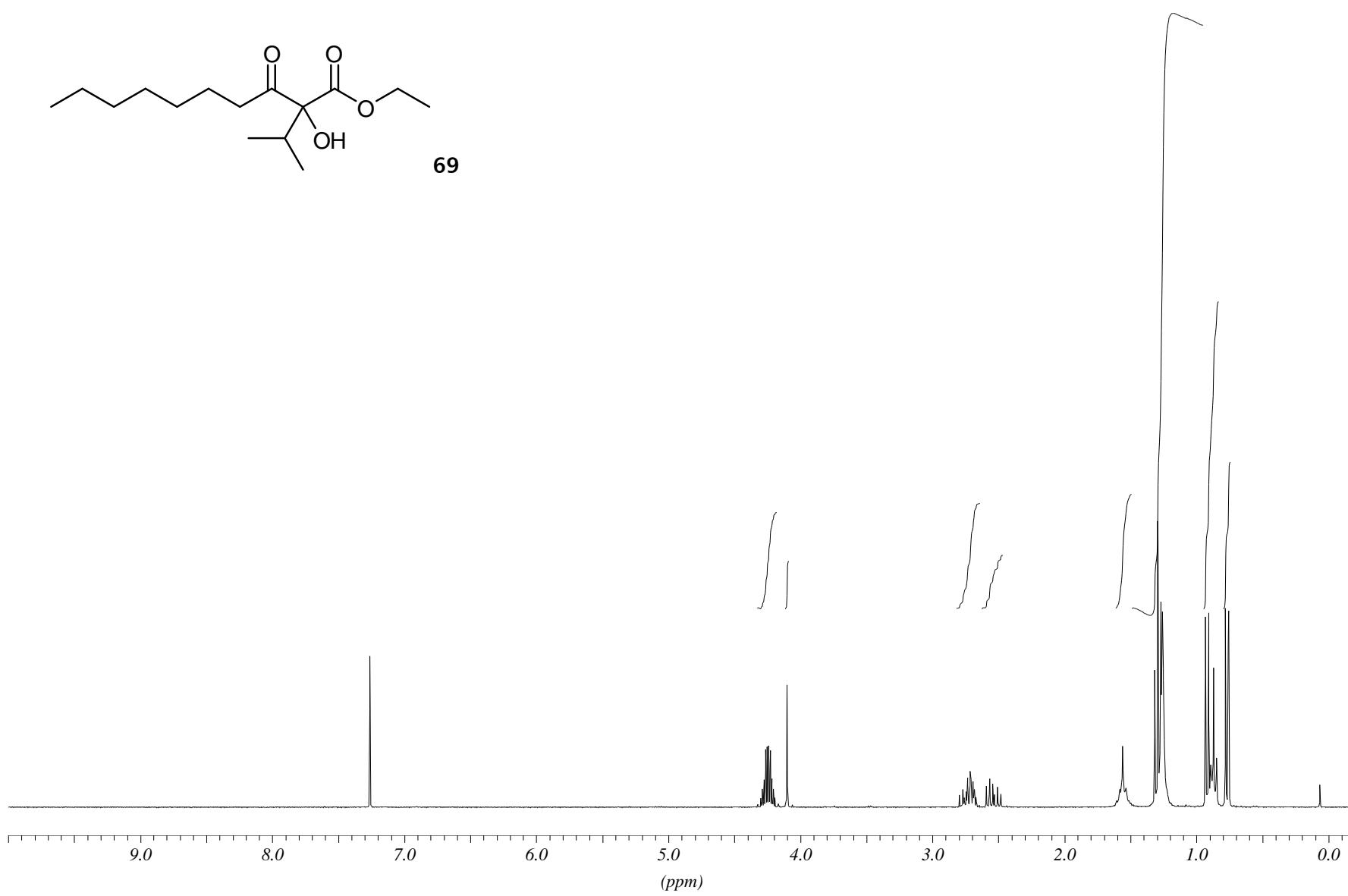


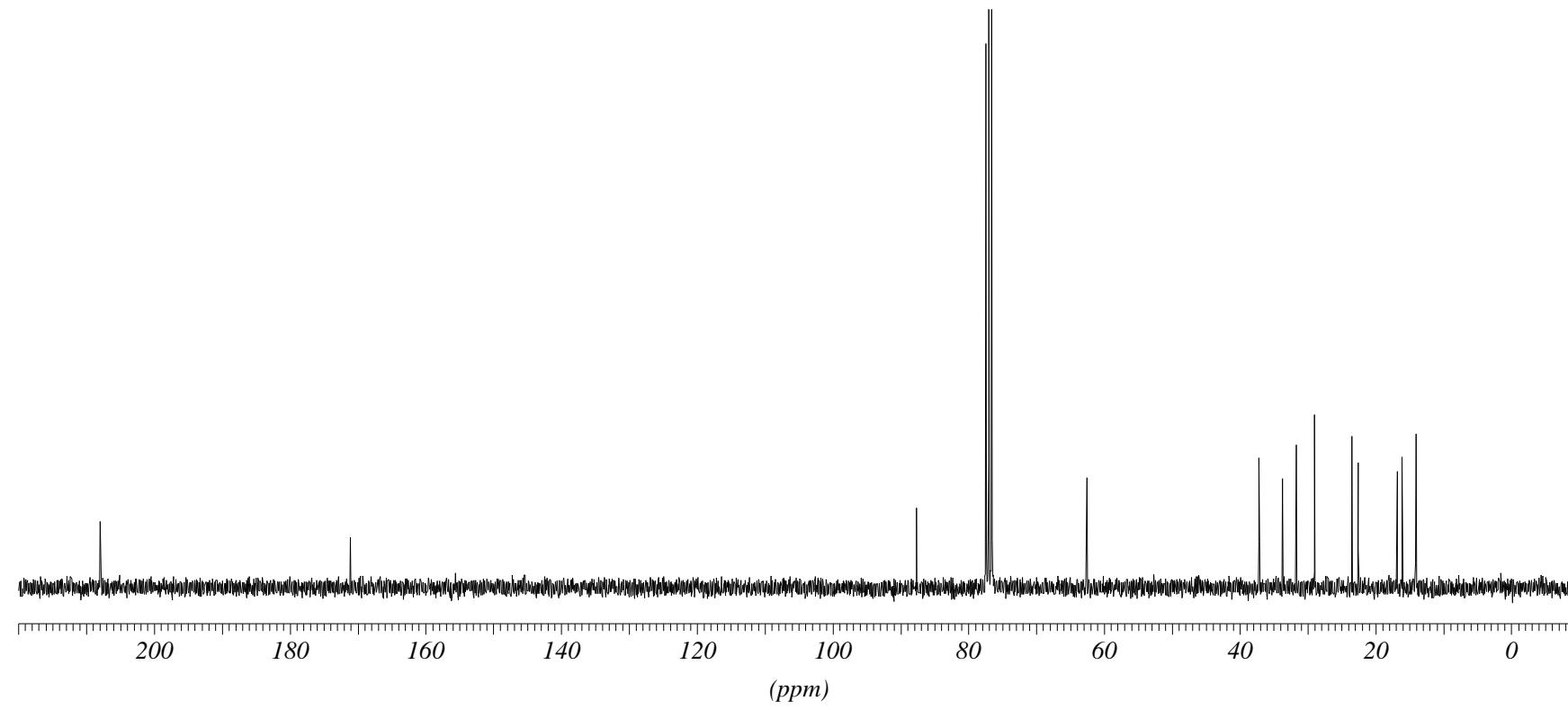
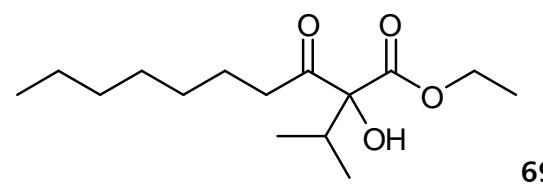


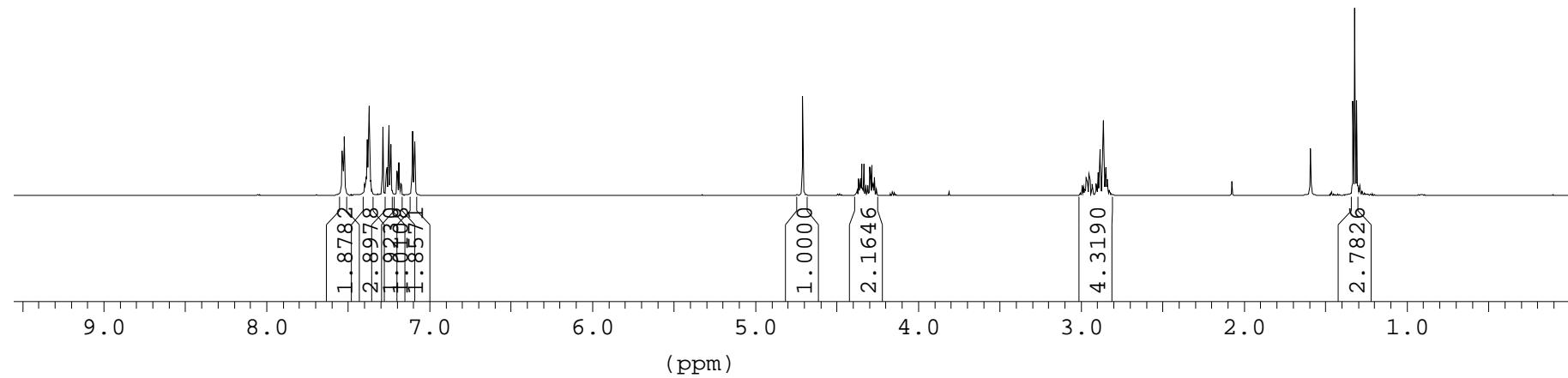
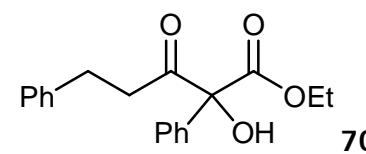


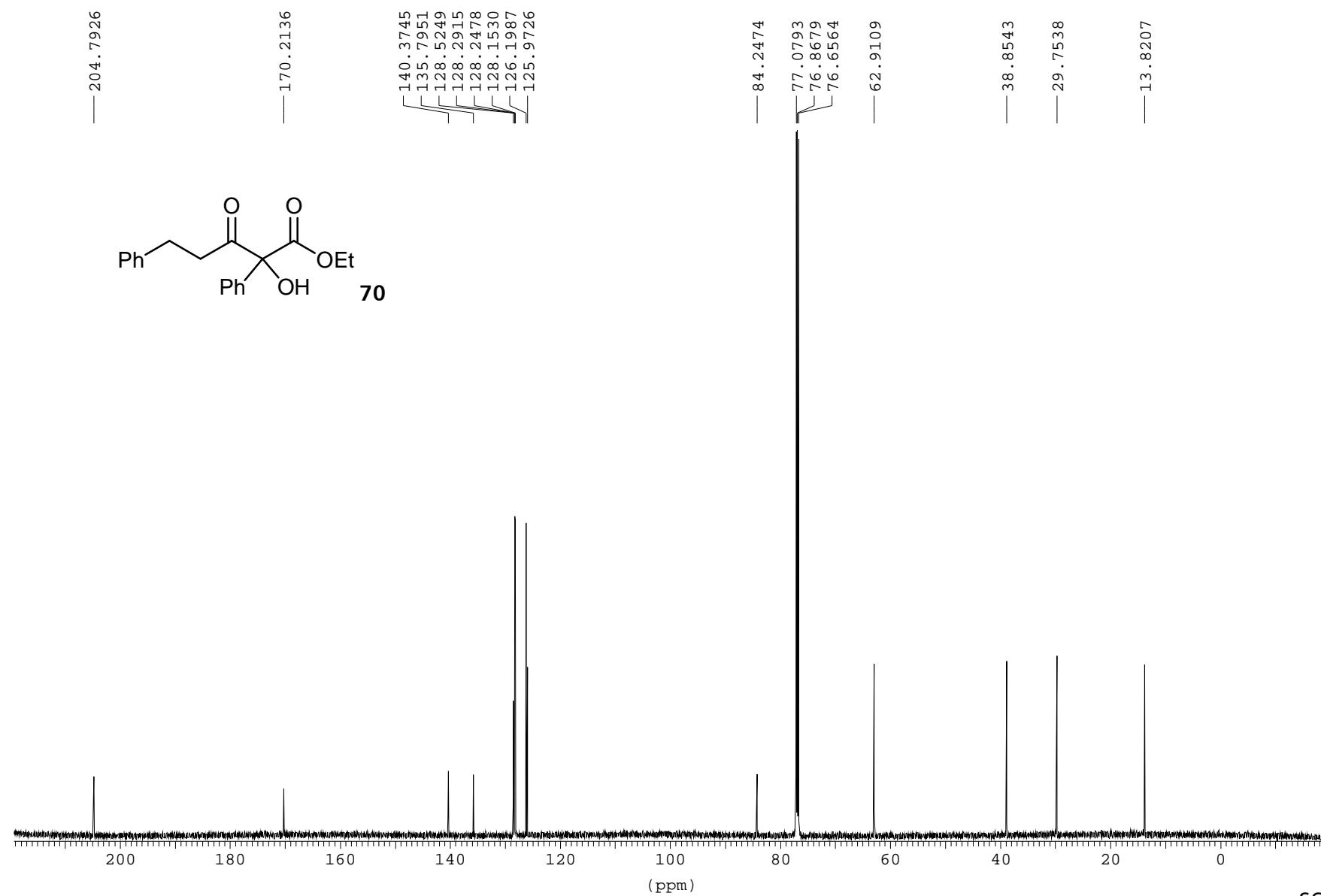


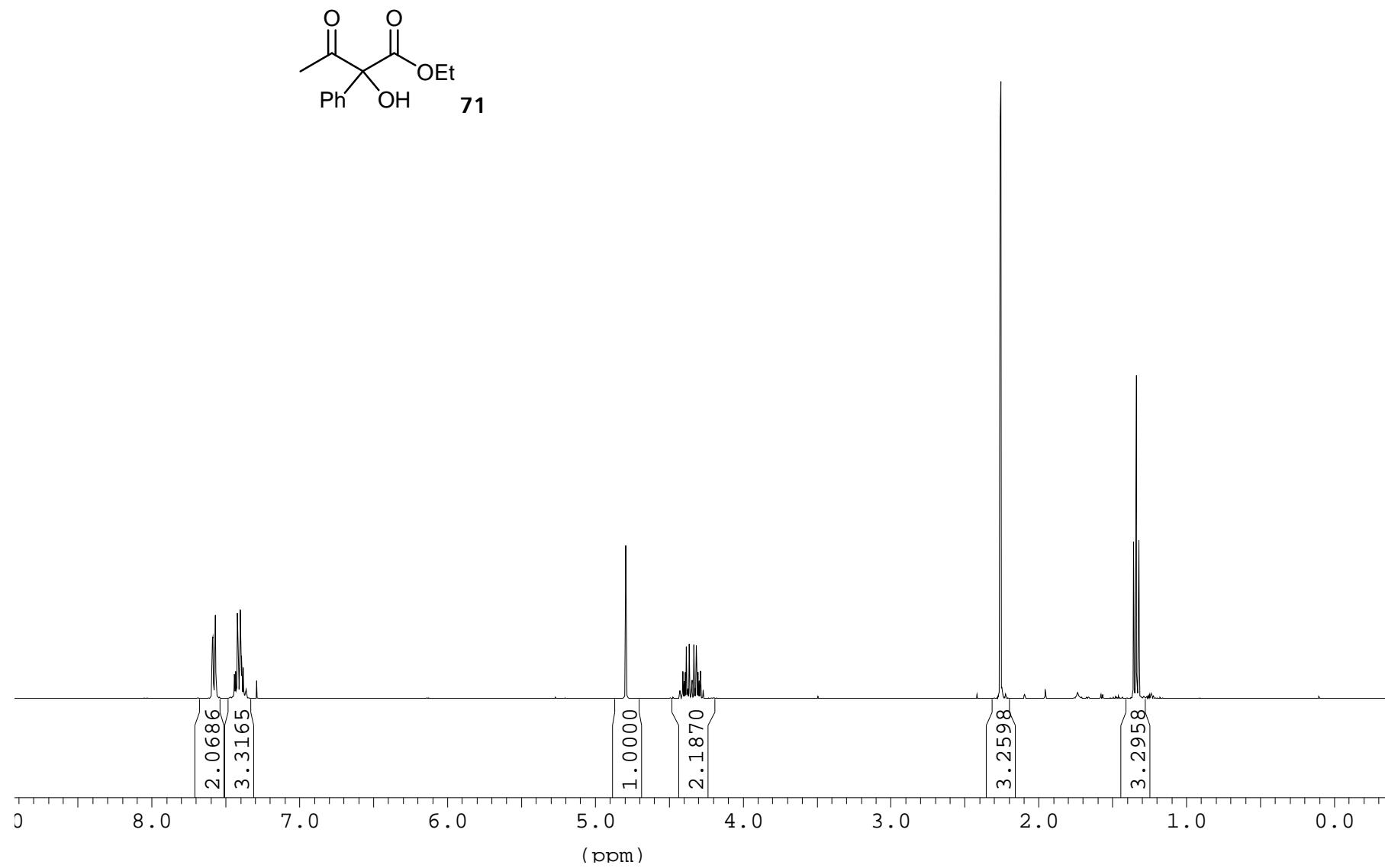


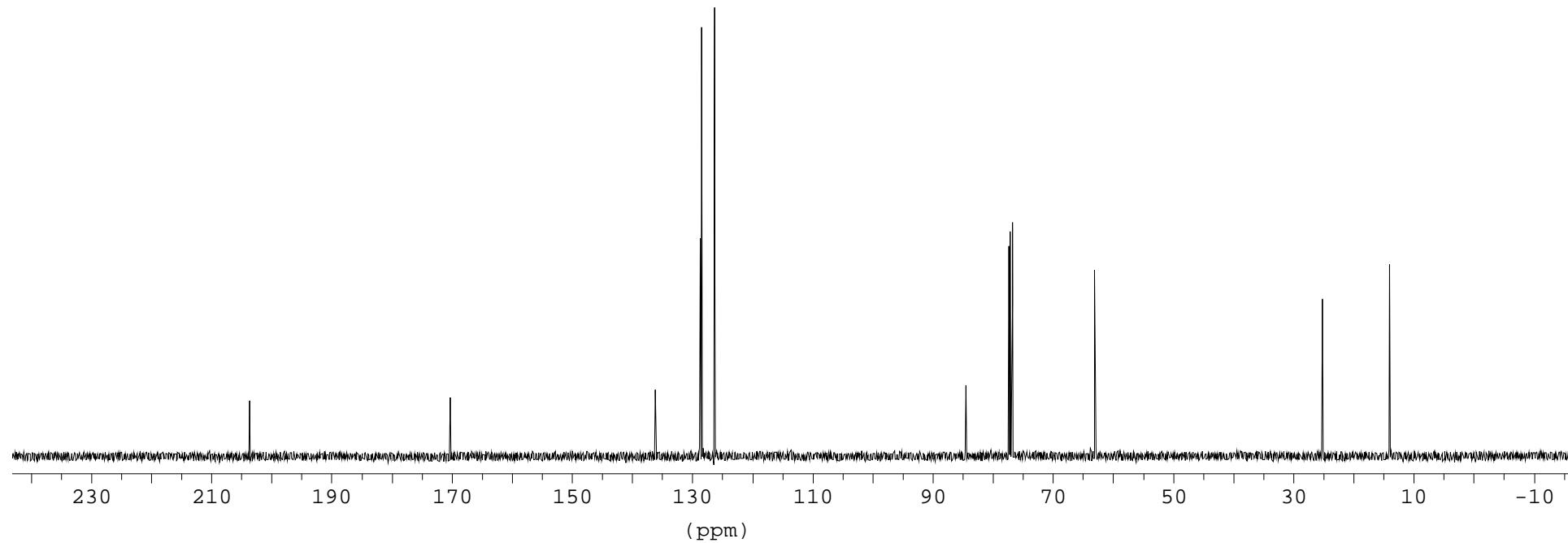
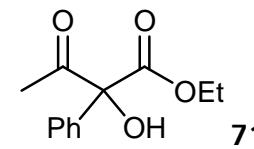


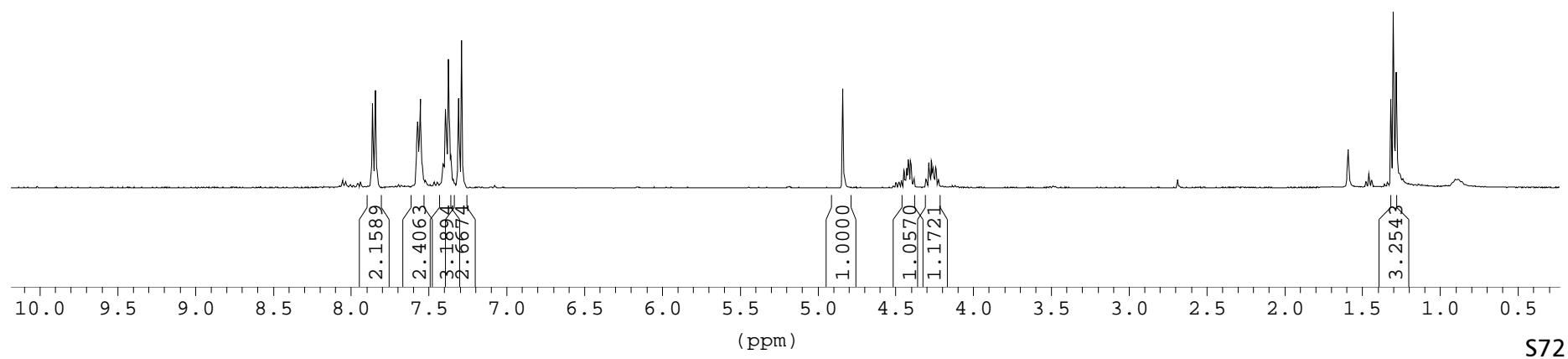
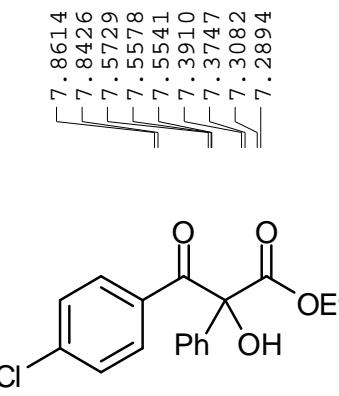




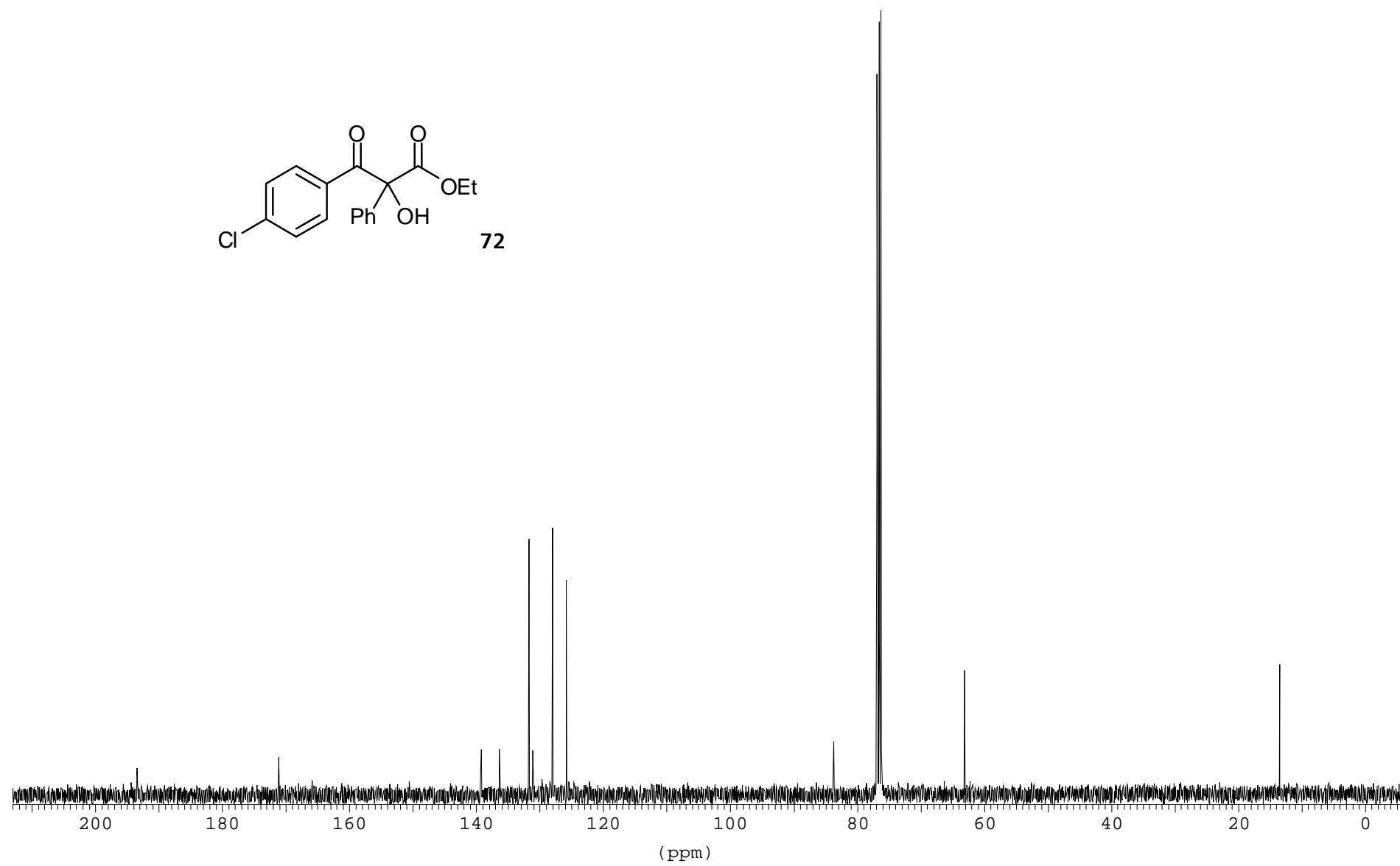
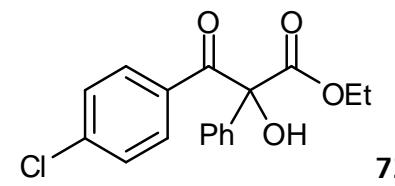


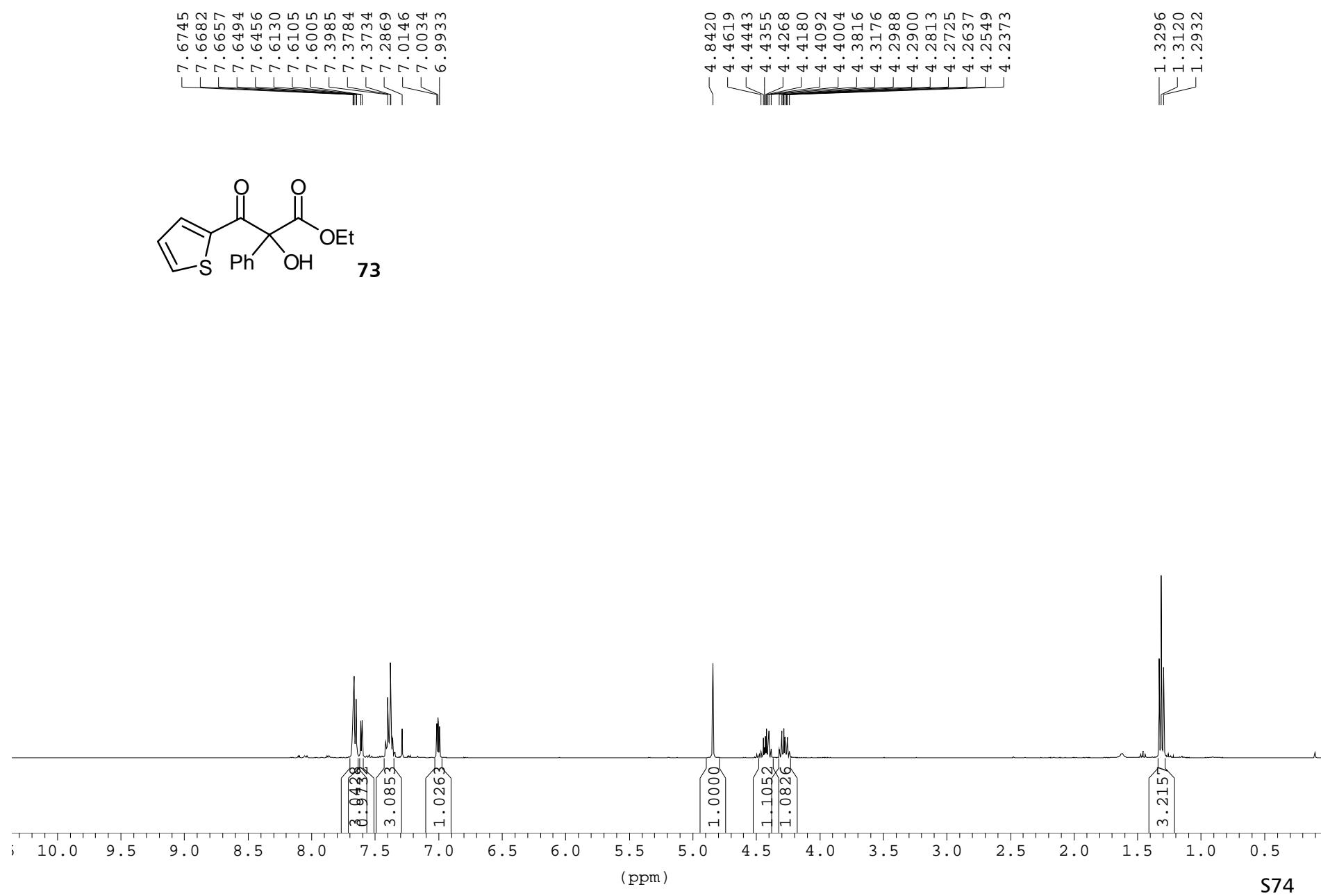


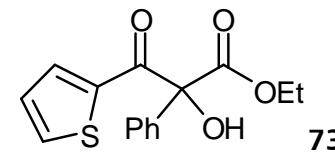




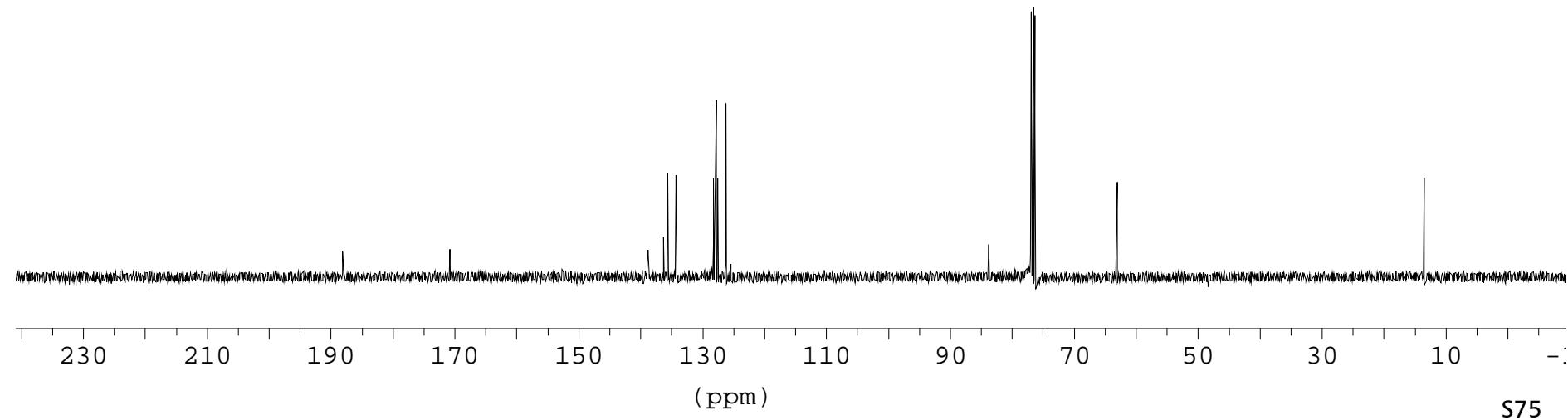
S72



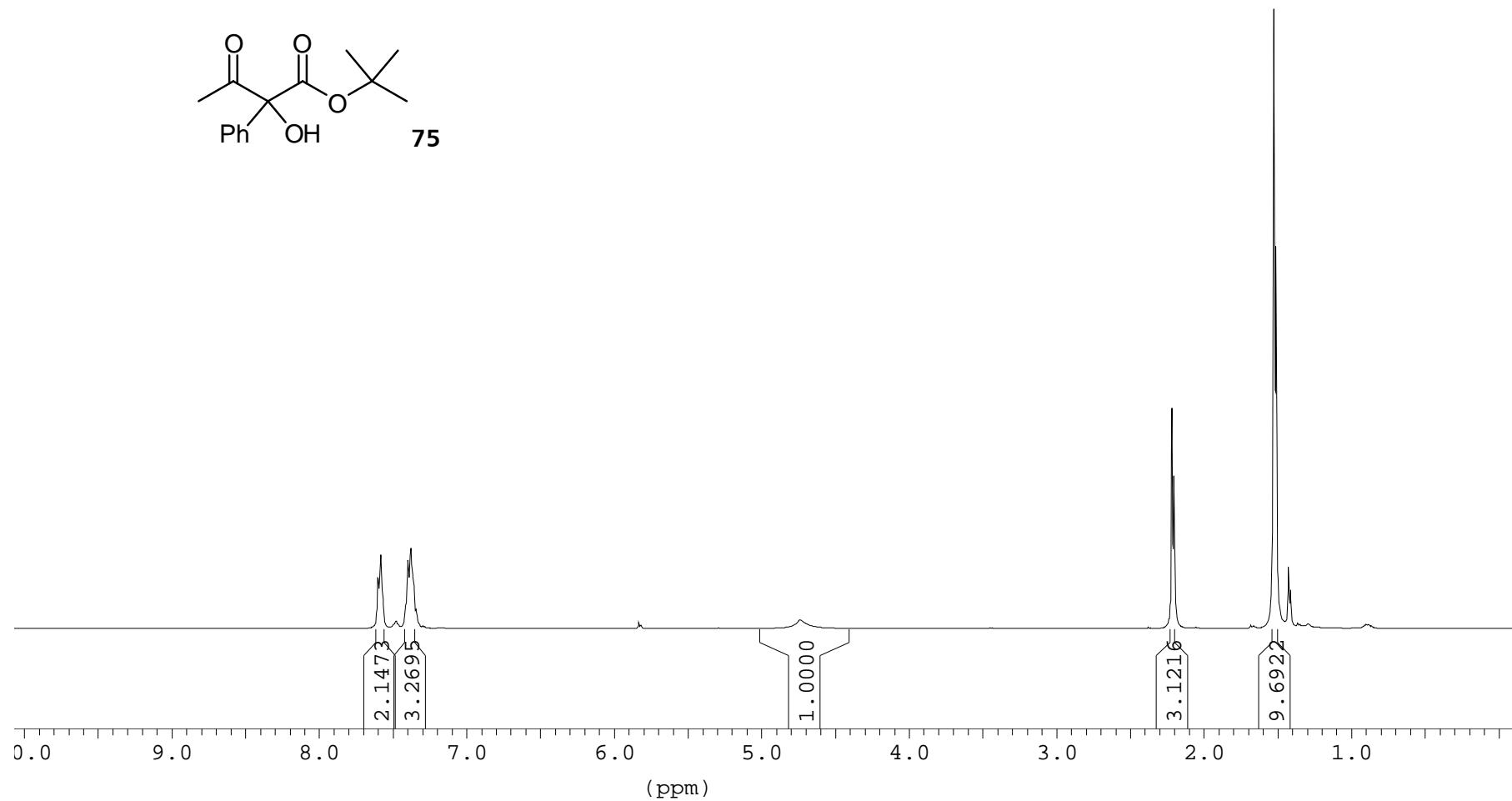


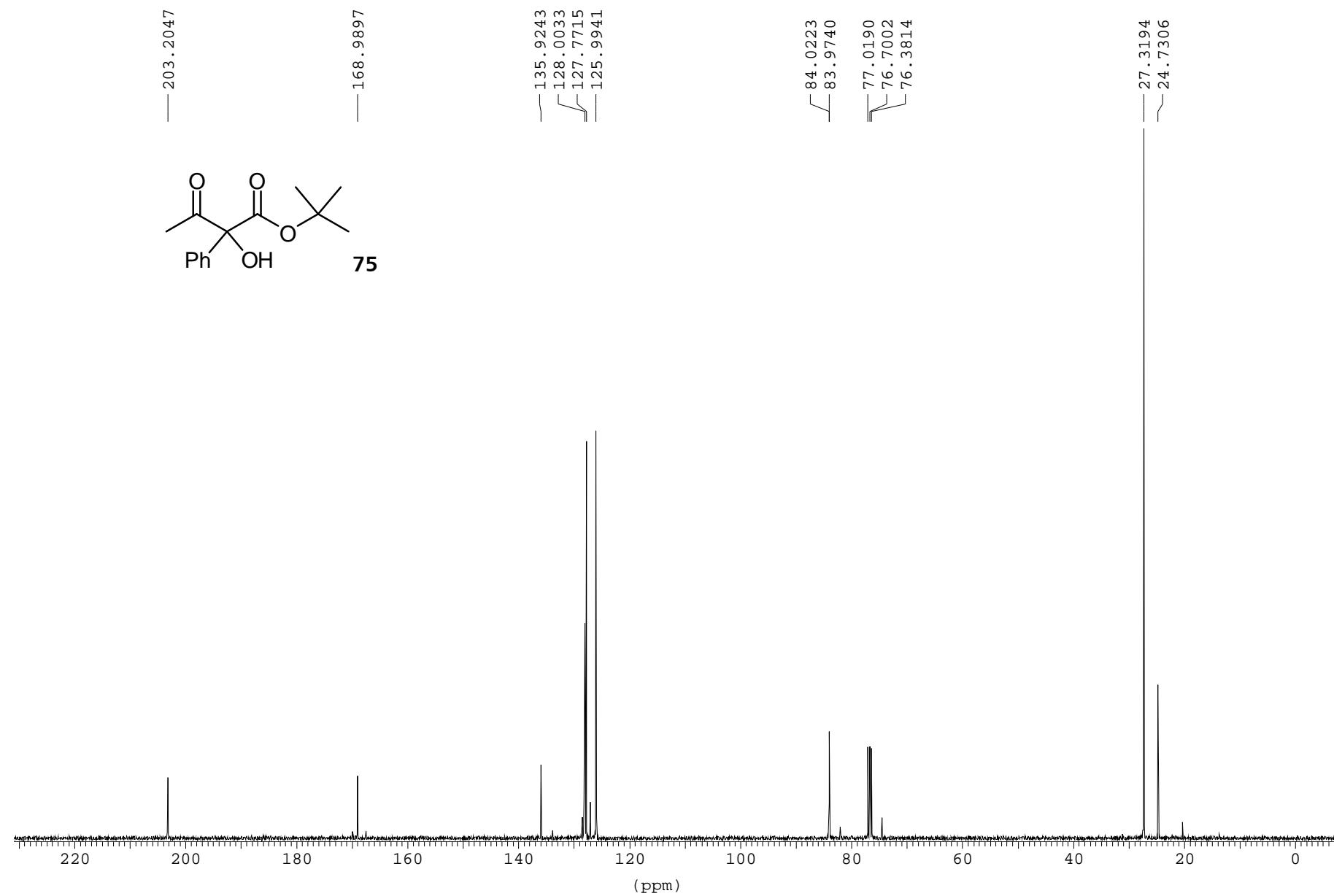


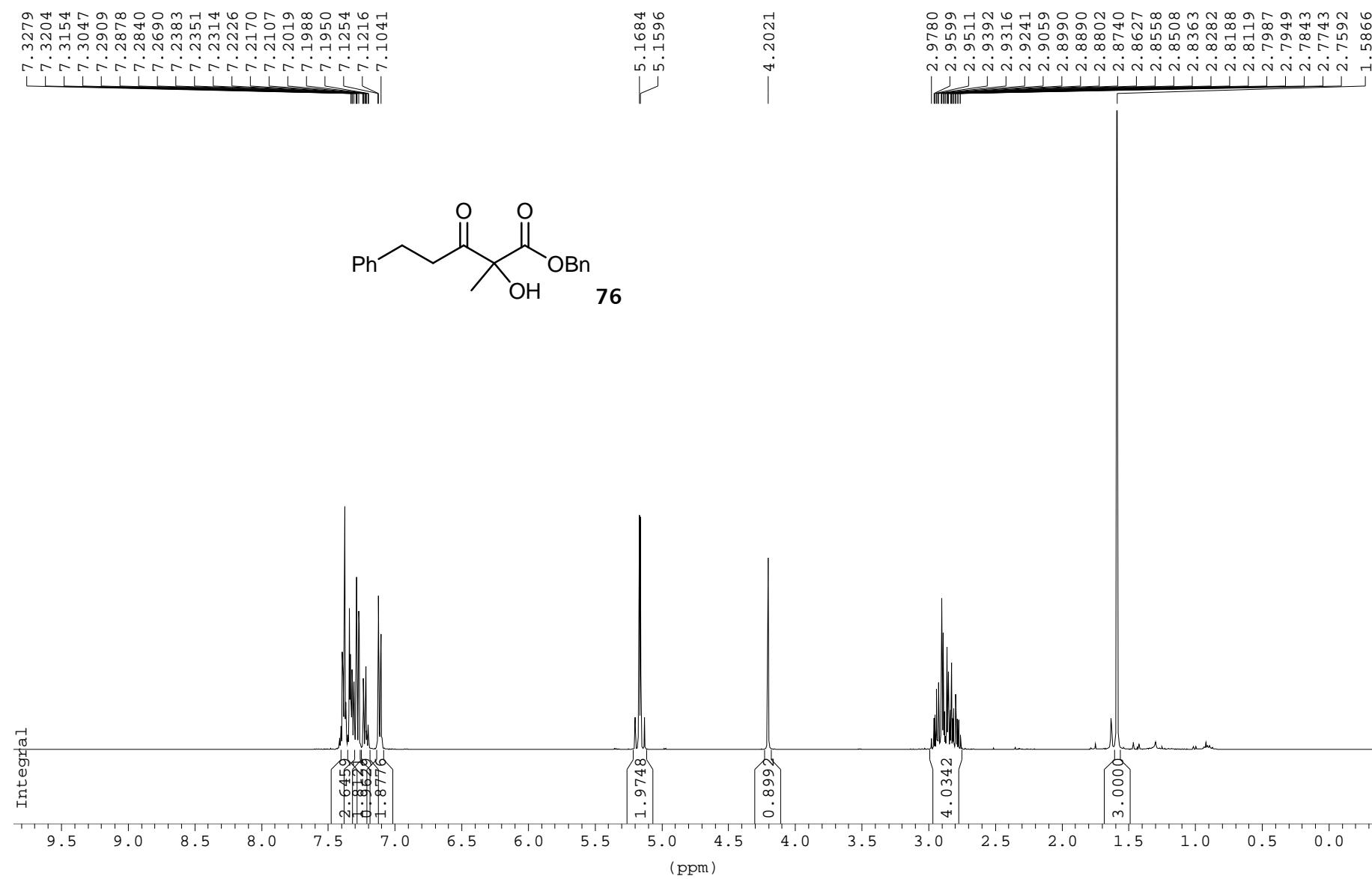
73

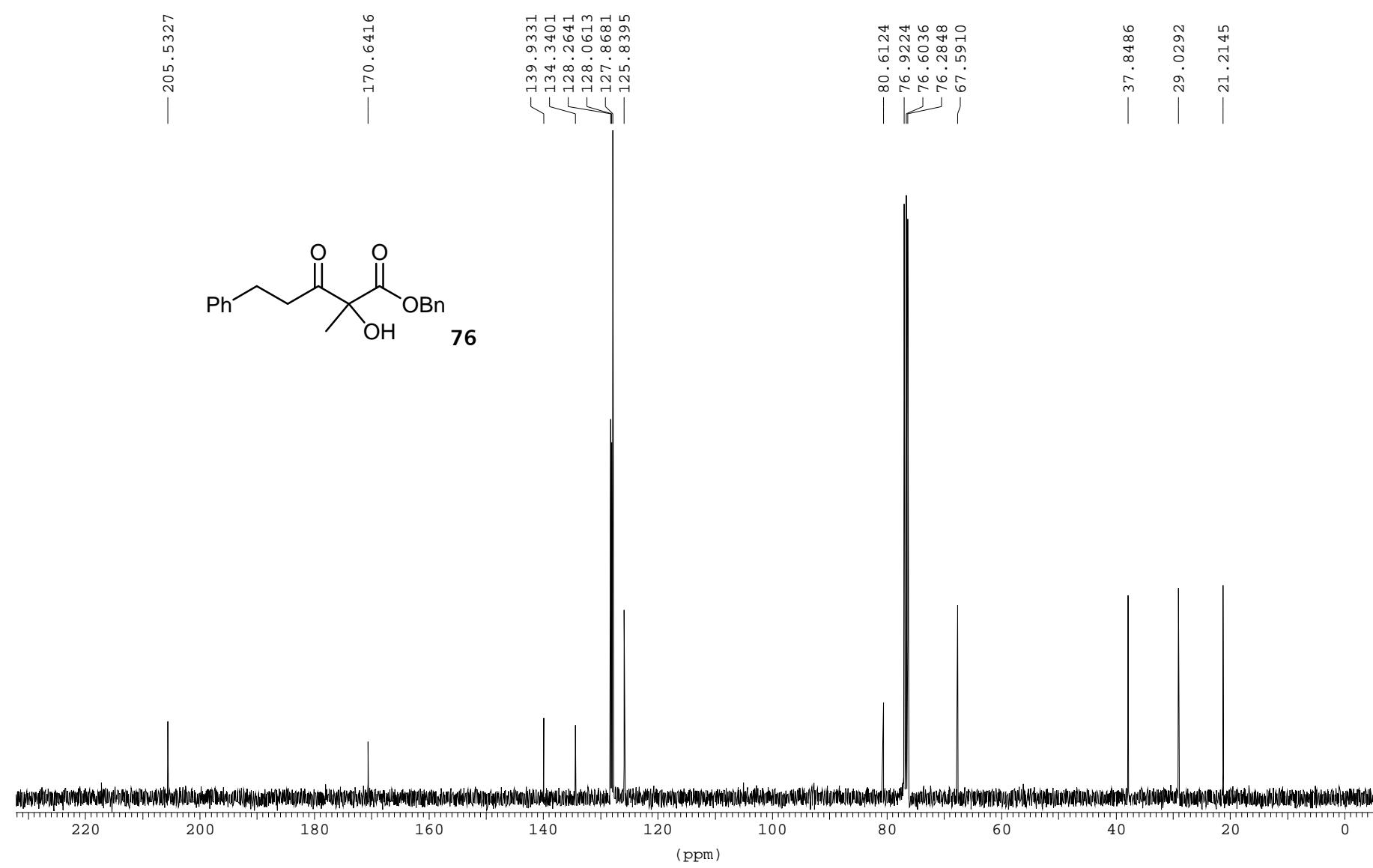


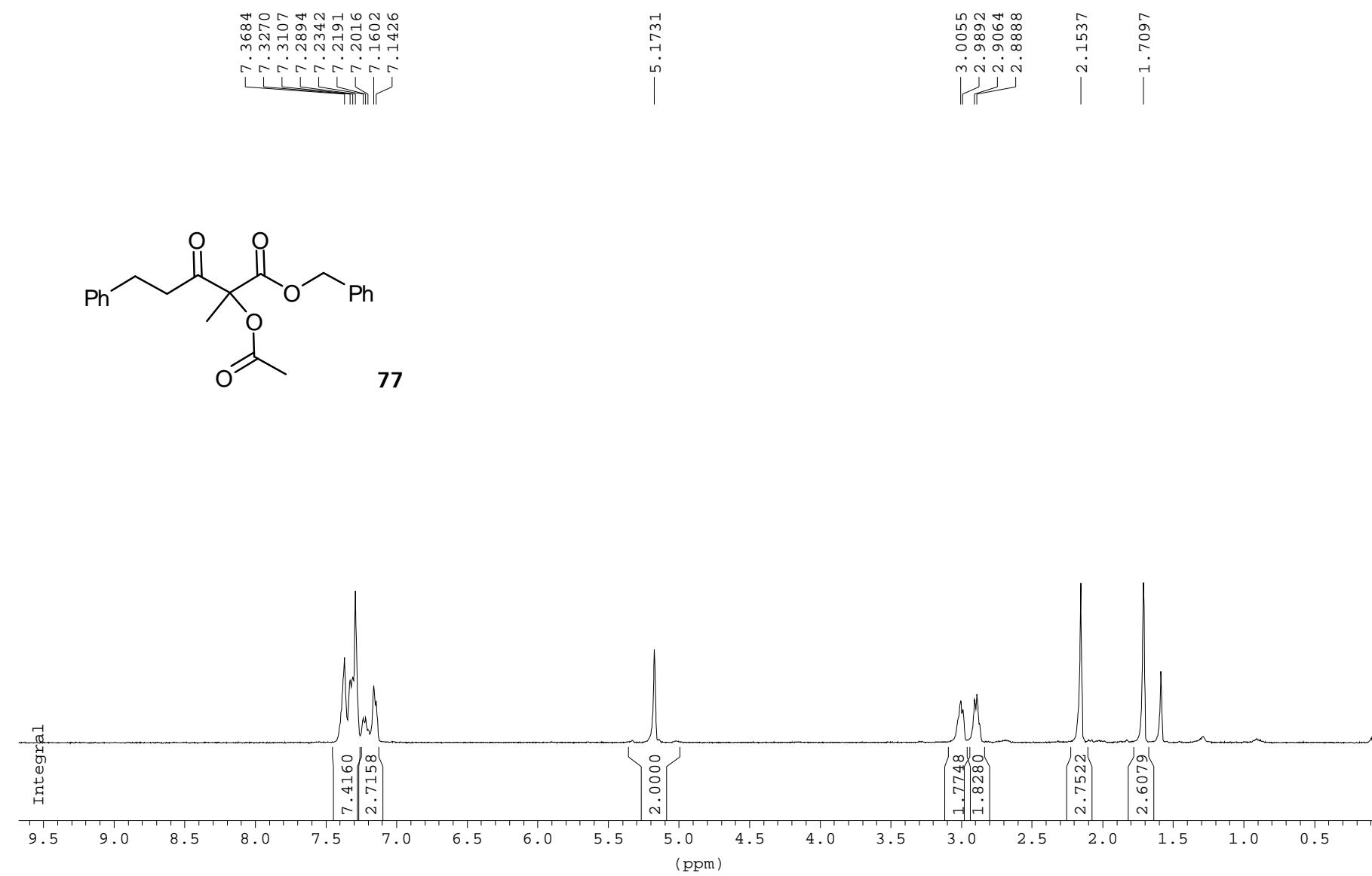
S75

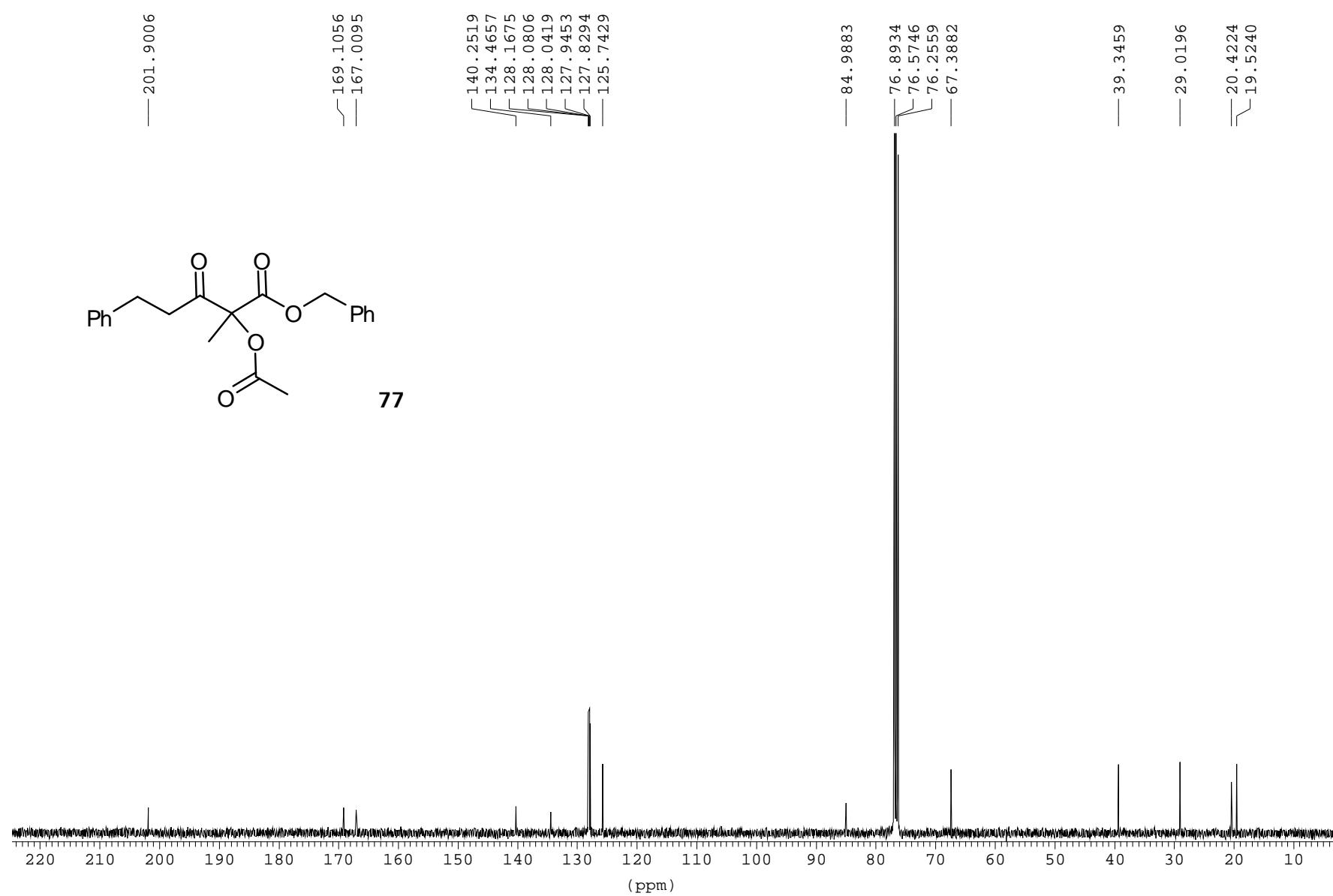


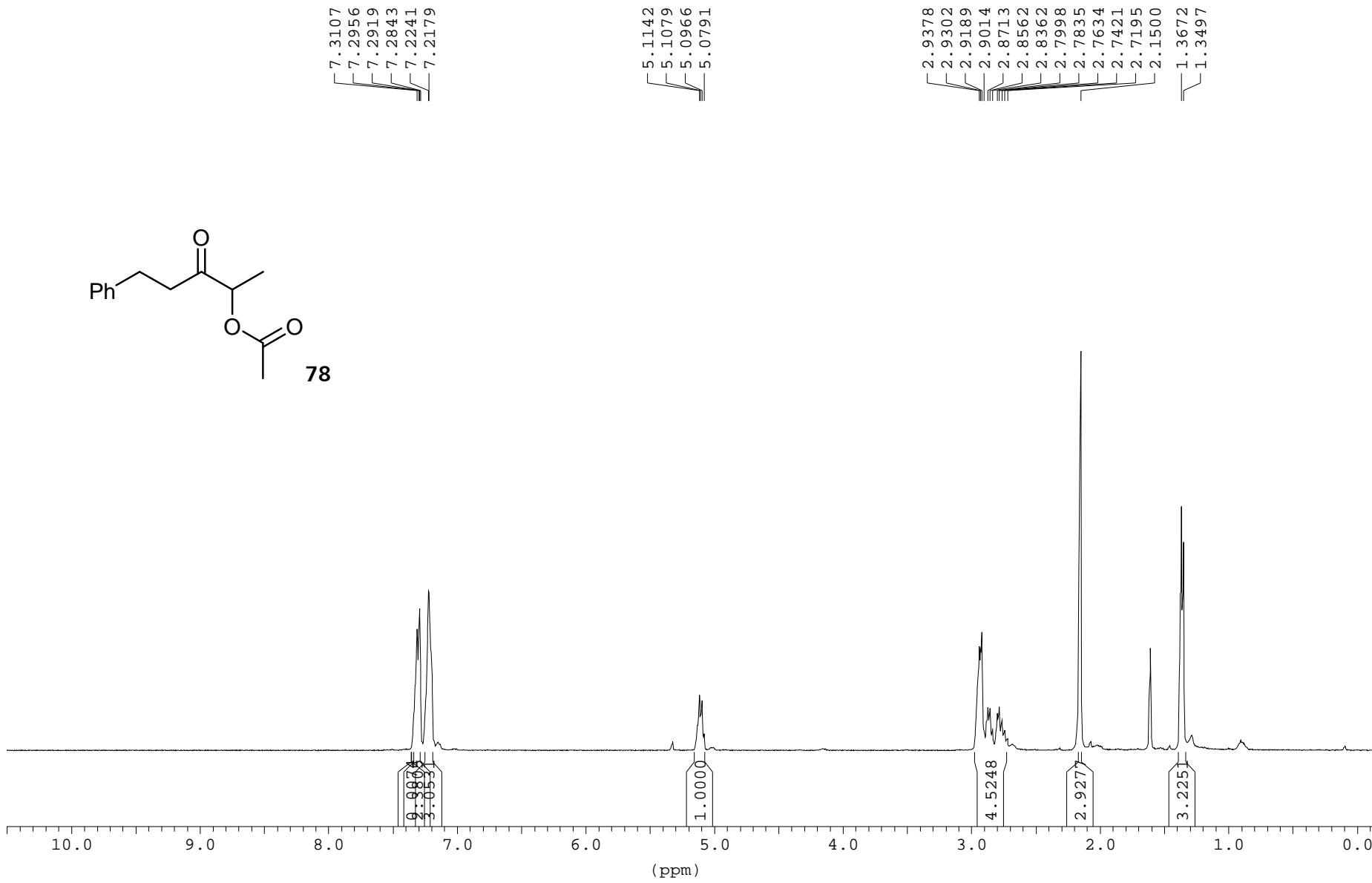


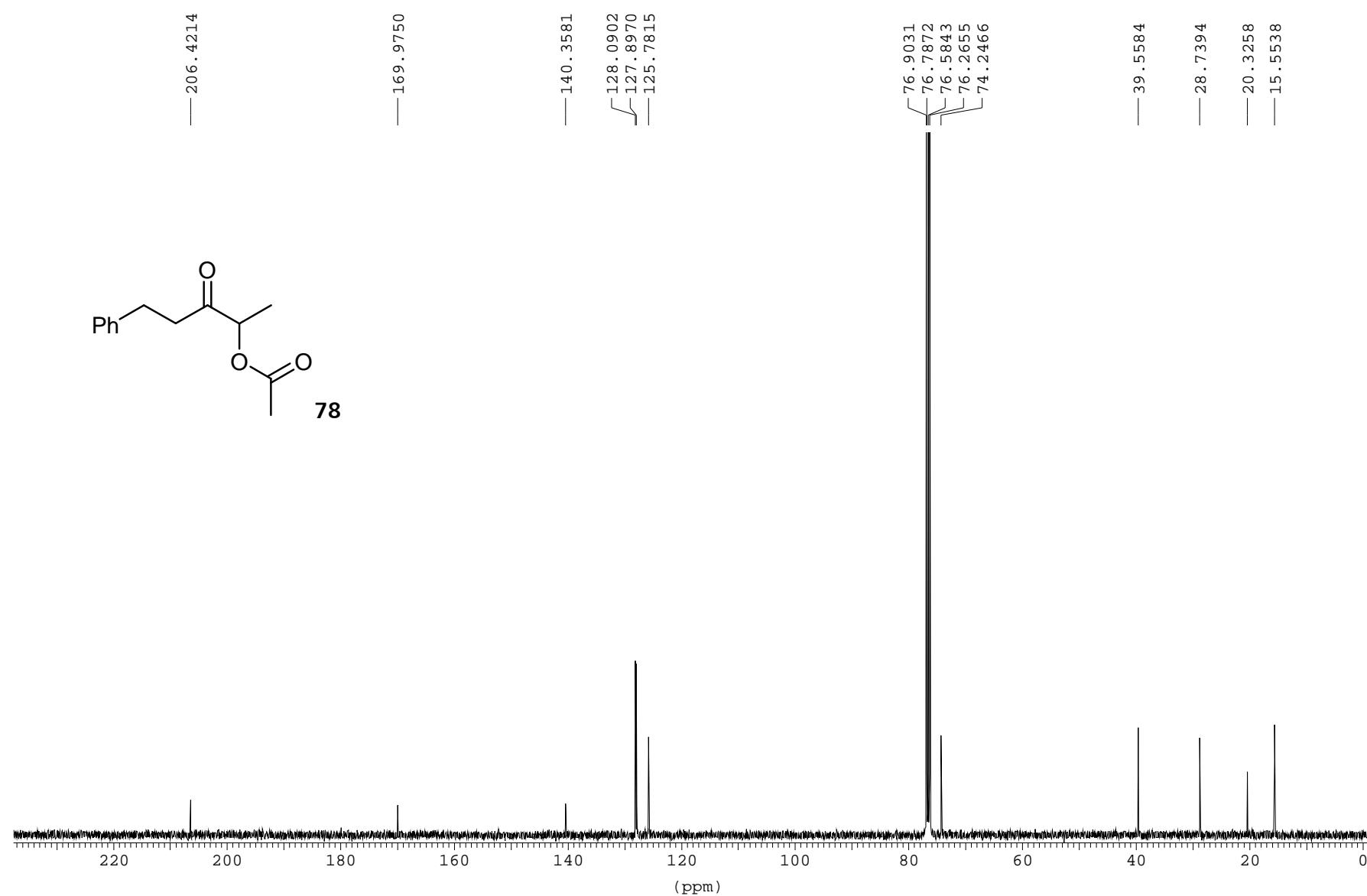


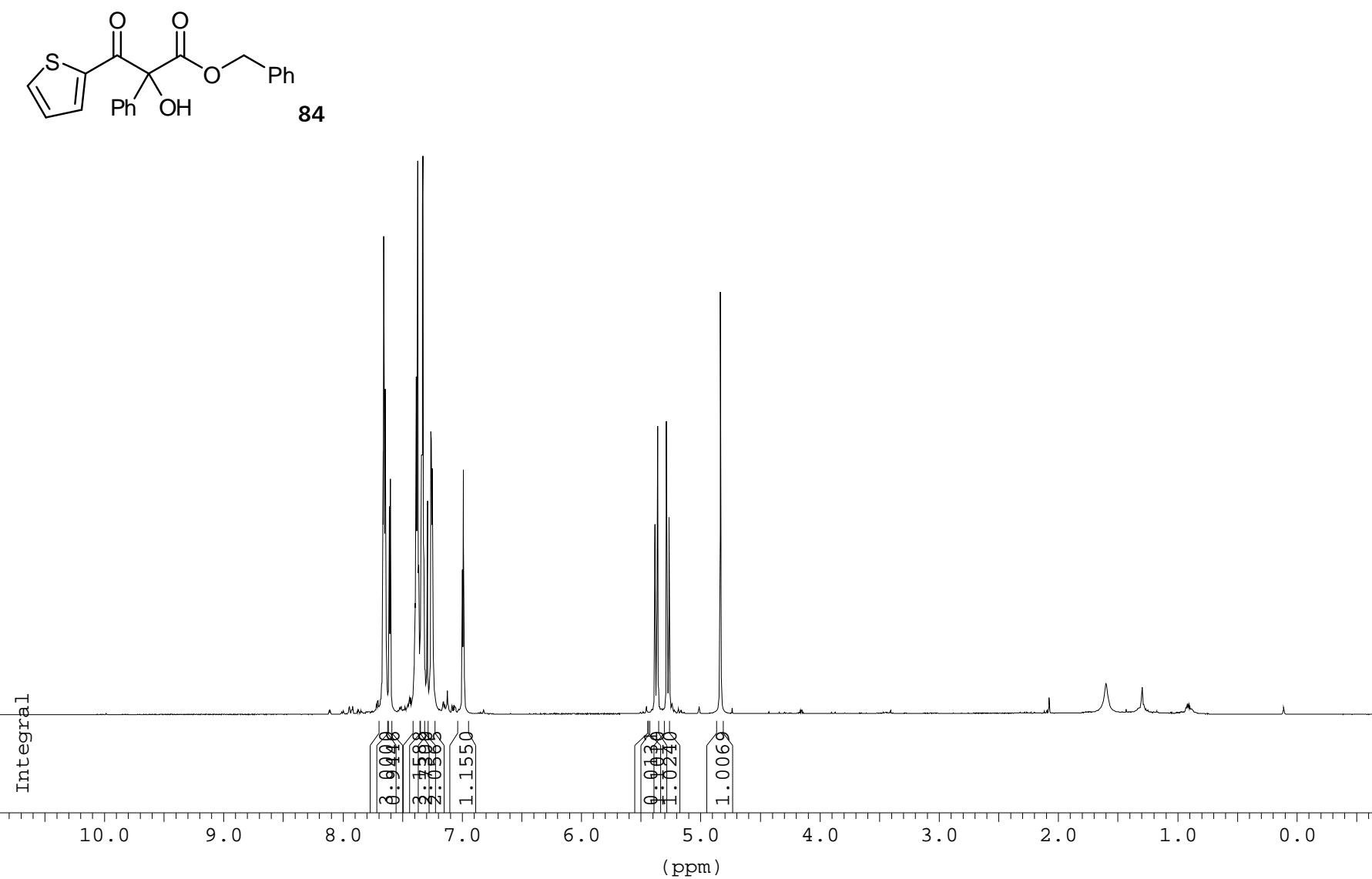


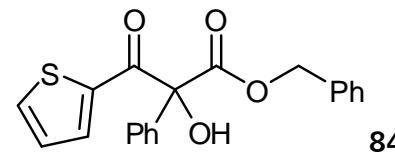




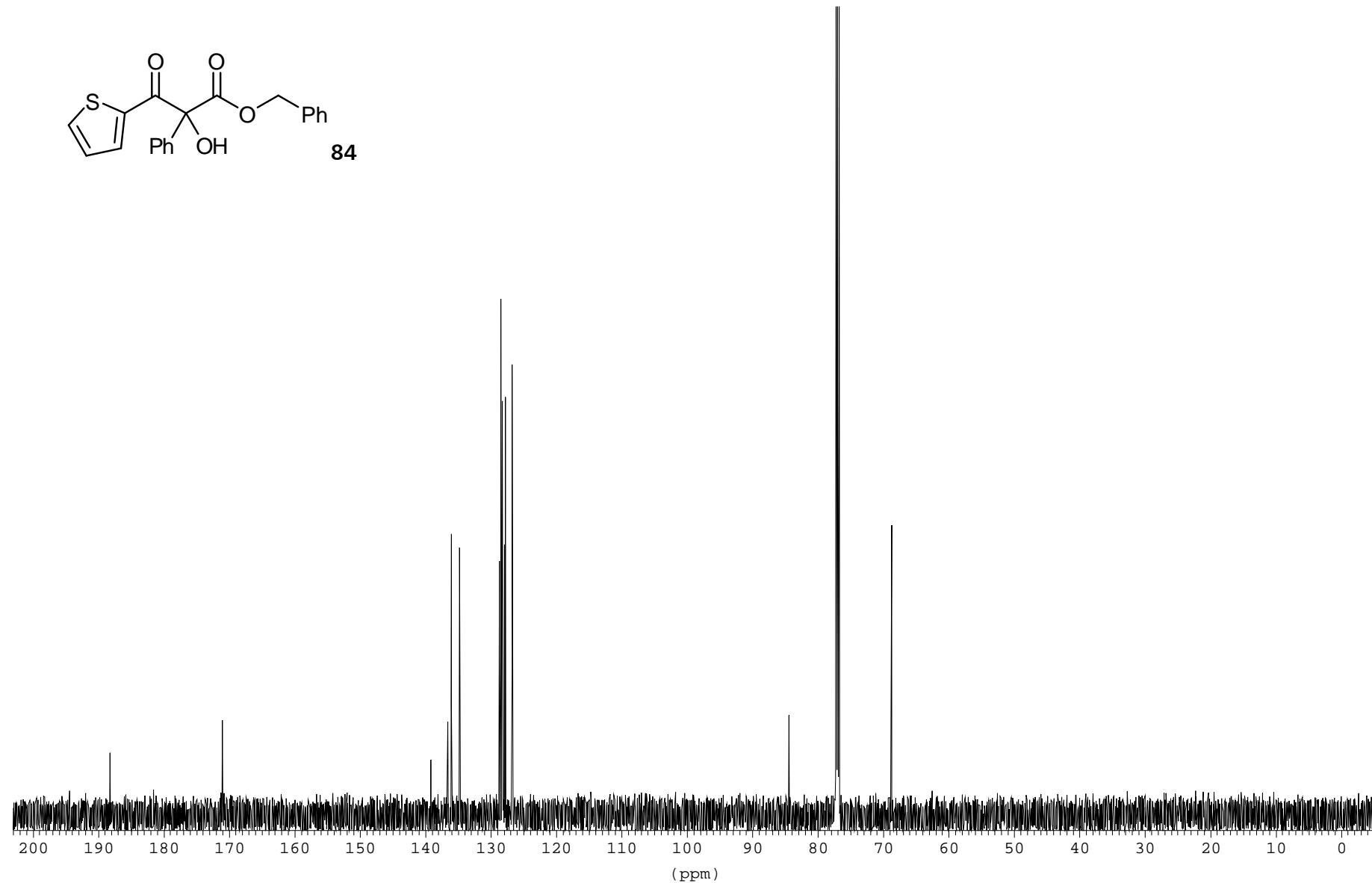




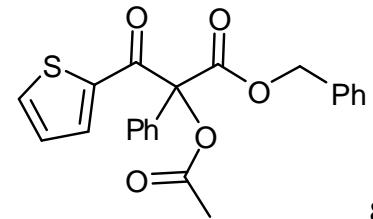




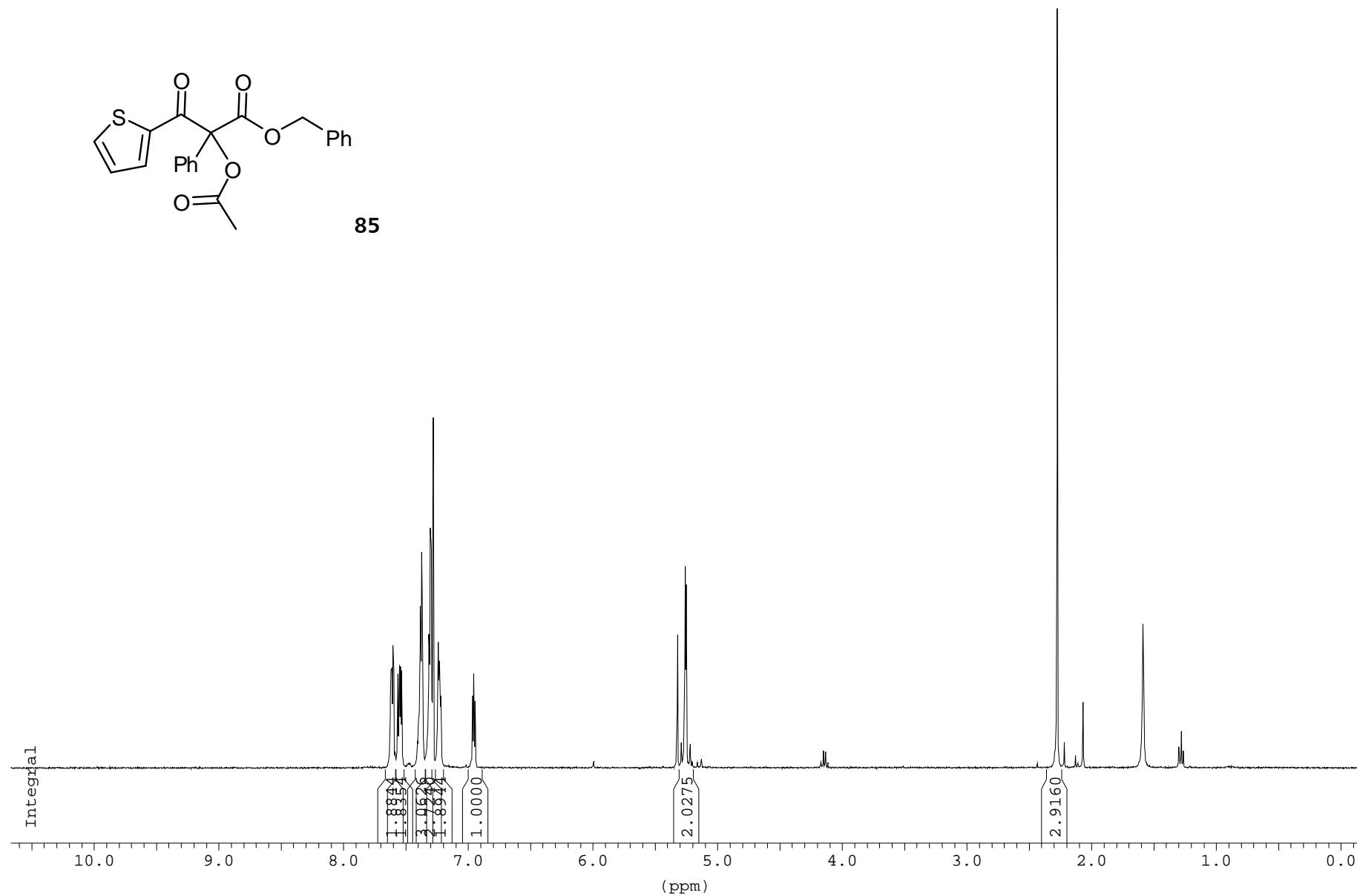
84



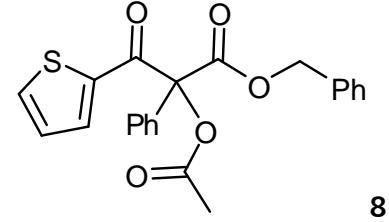
S85



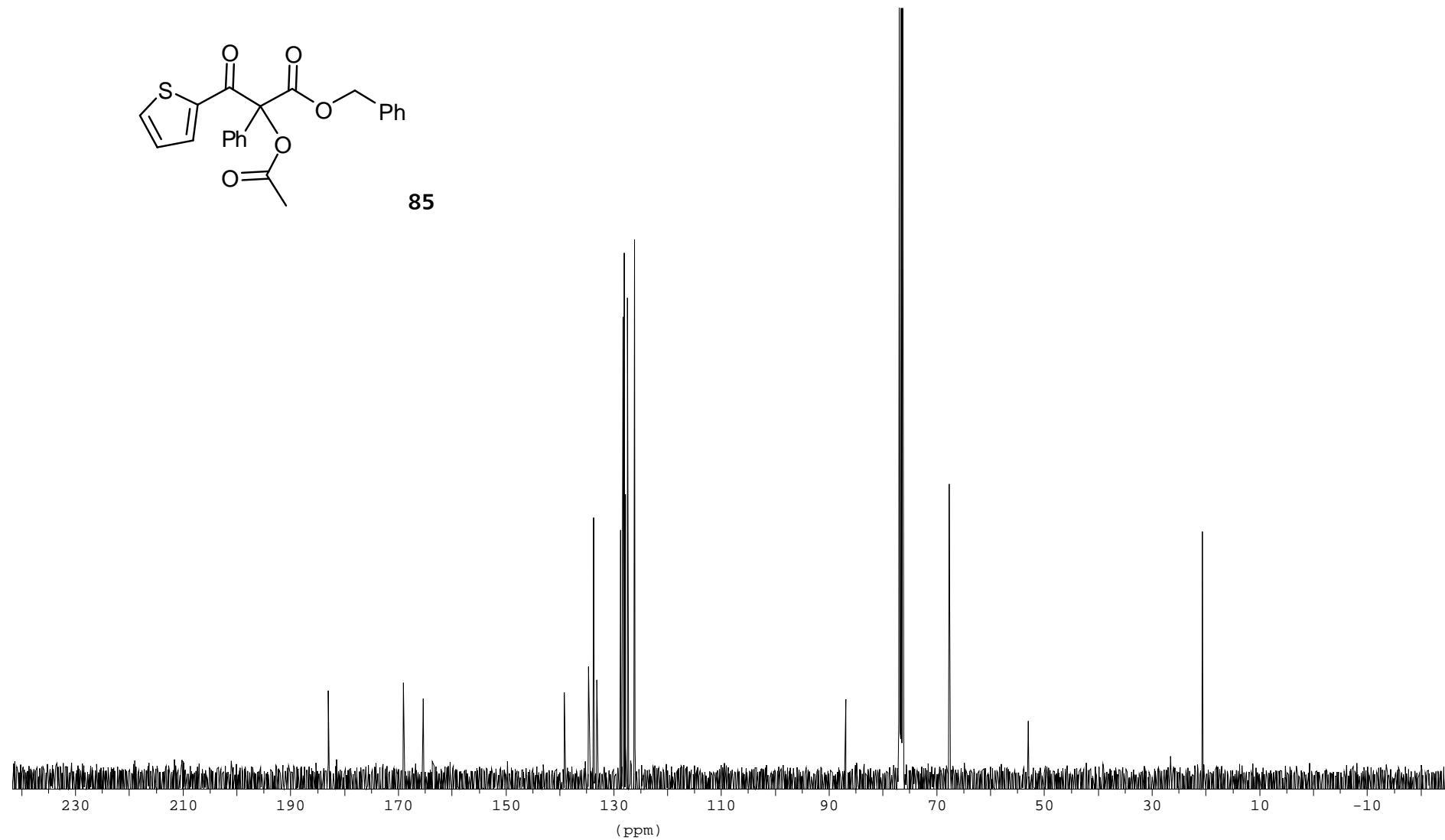
85

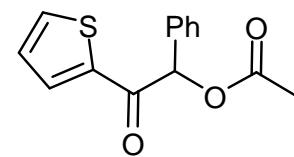


S86



85





86

