*Supporting Information*

# Ru-Catalyzed Hydrogenation of 3,5-Diketo Amides: Simultaneous Control of Chemo- and Enantioselectivity

Wanfang Li[†], Weizheng Fan[†], Xin Ma[†], Xiaoming Tao[†], Xiaoming Li[†], Xiaomin Xie[†], and Zhaoguo Zhang[†§]*

*[†]School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, China, [§]State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, 345 Lingling Road, Shanghai 200032, China*

*zhaoguo@sjtu.edu.cn*

**Table of Contents**



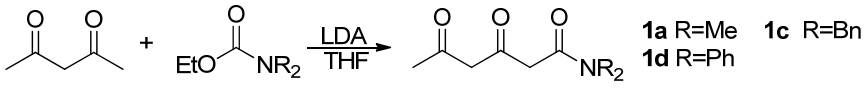
## General and Materials

**General:** All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques unless otherwise noted. $^{1}$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra were obtained on a 400 MHz NMR spectrometer. The chemical shifts for $^{1}$H NMR were recorded in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. The chemical shifts for $^{13}$C NMR were recorded in ppm downfield using the central peak of $CDCl_3$ (77.00 ppm) as the internal standard. Coupling constants (*J*) are reported in Hz and refer to apparent peak multiplications. Flash column chromatography was performed on silica gel (300-400 mesh).

**Materials:** Commercially available reagents were used throughout without further purification other than those detailed below. The solvents used in catalyst preparation and hydrogenation reactions were pretreated by the following procedures: THF was distilled over sodium benzopheneone ketyl under nitrogen. $CH_2Cl_2$ was distilled over calcium hydride. EtOH was distilled over magnesium under nitrogen.

**`1. Preparation of 1a-h**

***Method 1:*** [1]

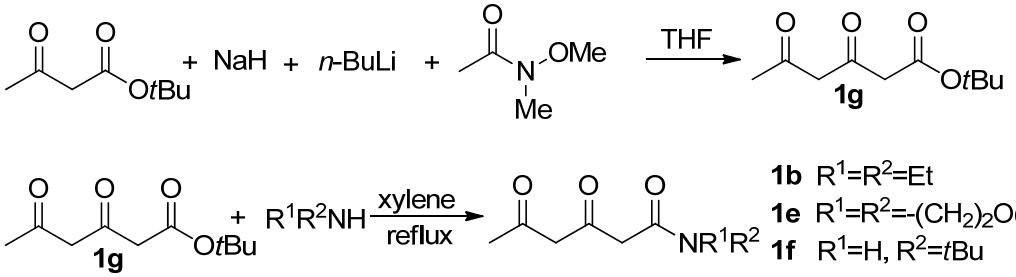



***N, N*-dimethyl-3, 5-dioxohexanamide (1a):** 2, 4-Pentadione (9.0 g, 89.9 mmol) was added dropwise to a solution of LDA (180 mmol) (prepared from 19.1 g of $^{i}Pr_2NH$ and 75 mL of 2.4 M *n*-BuLi in hexane) in 150 mL of THF at -78 °C during half an hour. Then warmed to -5 °C, ethyl dimethylcarbamate (9.5 g, 58.5 mmol) was added dropwise. The mixture was stirred overnight and the solvent was evaporated. The residue was dissolved in 50 mL water and washed with 20 mL $Et_2O$ to remove the unreacted 2, 4-pentadione. The water phase was acidified with cold 10% HCl to pH=3 and extracted with $CHCl_3$, washed with brine and dried over $Na_2SO_4$. Flash column chromatography (PE/EA=3/1) to give **1a** (11.5 g, 83% yield).

**1c** and **1d** were prepared similarly with corresponding carbamates. Ethyl dibenzylcarbamate[2] was prepared according to the literature. Ethyl diphenylcarbamate was prepared by the following modified procedure: [3]


To a solution of diphenylamine (12.0 g, 70.9 mmol) in 150 mL of THF at room temperature was added NaH (60% dispersion in mineral oil, 3.4 g, 85.1 mmol) and then ethyl chloroformate (9.6 g, 88.6 mmol). The reaction mixture was refluxed overnight and quenched with cold 10% HCl to pH=3. The aqueous phase was extracted with EtOAc and the combined organic phased was dried over $Na_2SO_4$. The solvent was removed in vacuum to give the desired product as yellow oil which was used directly for the following step. $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.40-7.15 (m, 10H), 4.29-4.20 (q, *J*=7.1 Hz 2H), 1.30- 1.20 (t, *J*=7.1 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 154.7, 142.6, 128.8, 126.9, 125.9, 61.9, 14.4.

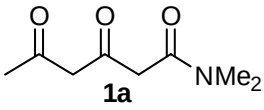
***Method 2:***




***tert*-Butyl 3,5-dioxohexanoate (1g)[4]:** tert-Butyl acetoacetate (20 g, 126.4 mmol) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 5.6 g, 139.1 mmol) in 200 mL of anhydrous THF at 0 °C. The mixture was stirred for an additional 10 min. The clear solution was cooled to -10 °C, and *n*-BuLi (58 mL, 2.4 M in hexane) was added dropwise. After stirring for an additional 30 min at this temperature, *N*-methoxy-*N*-methylacetamide (14.4 g, 139.1 mmol) was added dropwise at -40 °C. Then the mixture was warmed to room temperature within 2 h and quenched with 10% aqueous HCl to pH=3-4. The solvent was rotoevaporated for the sake of better extraction. The residue and aqueous phase was combined and extracted with EtOAc three times, washed with aqueous $NaHCO_3$, brine and

dried over $Na_2SO_4$. Flash column chromatography (PE/EA=15/1) to give (24.1 g, 95% yield) as colorless liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.60 (s, 0.73H), 3.74-3.71 (m, 0.26H), 3.47-3.44 (m, 1H), 3.24 (s, 2H), 2.25 (s, 1H), 2.07 (s, 2H), 1.47 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.0, 187.5, 166.6, 100.3, 81.7, 57.1, 50.6, 46.1, 27.8, 24.2.

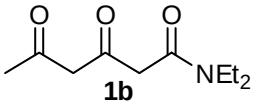
**1b**, **1e** and **1f** were prepared by amminolysis of the *tert*-butyl 5-dioxohexanoate[5] with the corresponding amines with good yields (85-90%).



**1a**

***N*, *N*-dimethyl-3, 5-dioxohexanamide**[1]

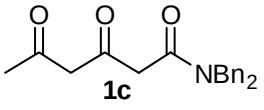
Light yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 15.16 (s, 1H), 15.04 (s, 1H), 5.64 (s, 0.72H), 5.21 (s, 0.07H), 3.76 (s, 0.35H), 3.62 (s, 0.35H), 3.42 (s, 1.72H), 2.99 (t, *J* = 18.8 Hz, 6H), 2.27 (s, 0.23H), 2.23 (s, 0.22H), 2.05 (s, 2.5H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 202.4, 198.4, 189.5, 188.7, 169.7, 166.6, 99.9, 88.7, 56.8, 50.6, 48.8, 44.9, 37.6, 37.4, 35.2, 34.9, 30.5, 23.7.



**1b**

***N*, *N*-diethyl-3, 5-dioxohexanamide**

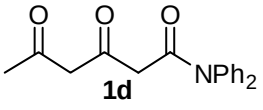
Light yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.67 (s, 0.51H), 5.16 (s, 0.18H), 3.79 (s, 0.28H), 3.58 (s, 0.30H), 3.38 (s, 1.78H), 3.44-3.22 (m, 4H), 2.26 (d, *J* = 10.6 Hz, 1H), 2.05 (s, 2H), 1.22-1.09 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.8, 189.7, 188.8, 170.5, 169. 9, 165.8, 165.5, 100.0, 88.9, 56.9, 50.8, 48.6, 44.8, 42.4, 41.8, 40.0, 30.5, 29.4, 23.8, 13.9, 13.8, 12.9, 12.6. HRMS Calculated for $C_{10}H_{17}NO_3$ (M+H): 200.1287, found: 200.1264.



**1c**

***N*, *N*-dibenzyl-3, 5-dioxohexanamide**

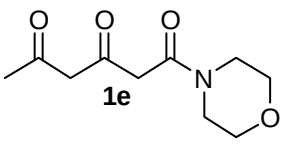
Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.41-7.12 (m, 10H), 5.65 (s, 0.7H), 5.30-5.27 (m, 0.19H), 4.63 (s, 2H), 4.49 (s, 2H), 3.78 (s, 0.29H), 3.71 (s, 0.30H), 3.51 (s, 1.59H), 3.24 (s, 0.25H), 2.24 (d, *J* = 2.0 Hz, 0.77H), 2.05 (s, 2.23H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 202.8, 202.2, 198.4, 189.4, 188.8, 172.0, 170.9, 167.5, 167.2, 136.6, 135.8, 128.8, 128.4, 128.0, 127.9, 127.6, 127.3, 126.4, 126.2, 100.2, 89.0, 57.1, 50.8, 50.4, 49.6, 48.8, 48.2, 48.1, 47.7, 45.0, 30.6, 29.5, 23.8. HRMS Calculated for $C_{20}H_{21}NO_3$ (M+Na): 346.1419, found: 346.1423.



**1d**

**3, 5-dioxo-*N*, *N*-diphenylhexanamide**

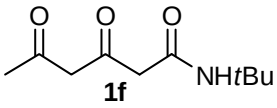
Pale yellow solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.48-7.13 (m, 10H), 5.57 (s, 0.58H), 4.96 (s, 0.18H), 3.73 (s, 0.35H), 3.55 (s, 0.37H), 3.37 (s, 1.35H), 3.16 (s, 0.40H), 2.23 (s, 0.49H), 2.21 (s, 0.46H)，2.03 (s, 1.89H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.3, 189.1, 188.8, 171.3, 170.5, 166.8, 142.1, 141.6, 129.7, 129.0, 128.7, 128.4, 128.3, 128.1, 126.2, 120.5, 117.4, 100.4, 92.0, 57.3, 50.5, 50.0, 45.9, 30.6, 29.6, 23.9. HRMS Calculated for $C_{18}H_{17}NO_3$ (M+Na): 318.1106, found: 318.1104.



**1e**

**1-morpholinohexane-1, 3, 5-trione**

Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 0.66H), 3.68-3.63 (m, 6H), 3.52-3.50(m, 2H), 3.41 (s, 2.25H), 2.26(s, 0.77H), 2.04 (s, 2.22H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 202.2, 198.1, 189.4, 188.4, 165.0, 164.7, 99.8, 88.0, 66.2, 66.12, 56.7, 50.4, 48.6, 46.4, 46.2, 44.7, 41.9, 41.7, 30.4, 23.4. HRMS Calculated for $C_{10}H_{15}NO_4$ (M+Na): 236.0899, found: 236.0893.



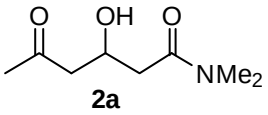

**1f**

***N*-(tert-butyl)-3, 5-dioxohexanamide**

Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 5.61 (s, 0.61H), 3.74 (s, 0.18H), 3.37 (s, 0.18H), 3.32 (s, 0.35H), 3.17 (s, 1.44H), 2.25 (s, 1H), 2.07 (s, 2H), 1.34 (d, $J$ = 1.4 Hz, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.2, 189.4, 165.2, 100.6, 57.1, 51.4, 51.1, 47.4, 28.3, 23.8. HRMS Calculated for $C_{10}H_{17}NO_3$ (M+Na): 222.1106, found: 222.1081.

## 2. Preparation of 2a-g

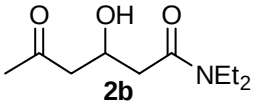
**Typical procedure for asymmetric hydrogenation reactions**[6]: To a 20 mL Schlenk tube were added $[Ru(benzene)Cl_2]_2$ (6.2 mg, 12.5 μmol) and (*S*)-SunPhos (18.3 mg, 27.5 μmol). The tube was vacuumed and purged with nitrogen three times before addition of freshly distilled and freeze-and-thaw degassed EtOH/$CH_2Cl_2$ (1 mL/1 mL). The resulting mixture was heated at 50 °C for 1 h and then cooled to room temperature. The solvent was then removed under vacuum to give the catalyst as a brownish yellow solid. The catalyst was dissolved in degassed THF (10 mL) and then the solution was equally divided into five vials which contained 1 mmol of substrates. To each vial 3 mL more of THF was added. Then the vials were taken into an autoclave. The autoclave was purged three times with $H_2$ and the required pressure of $H_2$ was set. Then the autoclave was stirred under specified reaction conditions. After being cooled to ambient temperature and careful release of the hydrogen, the autoclave was opened and the solvent was evaporated. The enantiomeric excess was determined by HPLC (derivation by 4-nitrobenzoyl chloride if needed) after passing the samples through a short pad of silica gel eluted with petroleum ether and ethyl acetate.




**2a**

**3-hydroxy-*N*, *N*-dimethyl-5-oxohexanamide.**

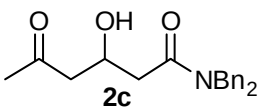
Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 4.43 (dd, $J$ = 3.6, 2.4 Hz, 1H), 4.42-4.39 (m, 1H), 2.98 (s, 3H), 2.94 (s, 3H), 2.77-2.66 (m, 2H), 2.60-2.33 (m, 2H), 2.19 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.9, 171.6, 64.5, 49.4, 38.5, 36.9, 34.9, 30.6. HPLC (Chiralcel AD-H column, hexane/$^i$PrOH 89/11, 0.75 mL min$^{-1}$, 220 nm): $t_1$ = 23.1 min, $t_2$ =27.6 min. HRMS Calculated for $C_8H_{15}NO_3$ (M+Na): 196.0950, found: 196.0957. $[\alpha]^{25}_D$ = 40.4 (c 0.41, $CH_2Cl_2$).




**2b**

**3-hydroxy-*N*, *N*-diethyl-5-oxohexanamide.**

Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.67 (s, 0.51H), 5.16 (s, 0.18H), 3.79 (s, 0.28H), 3.58 (s, 0.30H), 3.38 (s, 1.78H), 3.44-3.22 (m, 4H), 2.26 (d, $J$ = 10.6 Hz, 1H), 2.05 (s, 2H), 1.22-1.09 (m, 6H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.8, 189.7, 188.8, 170.5, 169.9, 165.8, 165.5, 100.0, 88.9, 56.9, 50.8, 48.6, 44.8, 42.4, 41.8, 40.0, 30.5, 29.4, 23.8, 13.9, 13.9, 12.9, 12.6. HPLC (Chiralcel IA-3 column, hexane/$^i$PrOH/EtOH 90/5/5, 0.7 mL min$^{-1}$, 220 nm): $t_1$ = 26.3 min, $t_2$ =28.5 min. HRMS Calculated for $C_{10}H_{19}NO_3$ (M+H): 224.1263, found: 224.1259. $[\alpha]^{25}_D$ = 40.9 (c 0.49, $CH_2Cl_2$).

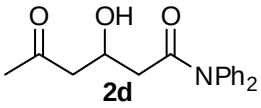



**2c**

***N*, *N*-dibenzyl-3-hydroxy-5-oxohexanamide**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47-7.03 (m, 10H), 4.60 (q, $J$ = 15.0 Hz, 2H), 4.51-4.56 (m, 1H), 4.44 (s, 2H), 4.36 (d, $J$ = 3.3 Hz, 1H),

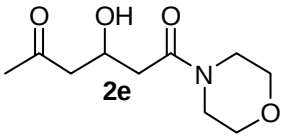
2.78-2.48 (m, 4H), 2.18 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.4, 172.0, 136.4, 135.5, 128.5, 128.2, 127.6, 127.2, 127.0, 126.0, 64.5, 49.4, 49.2, 47.6, 38.5, 30.2. HPLC (Chiralcel OJ-H column, hexane/$^{i}$PrOH 88/12, 0.8 mL min$^{-1}$, 220 nm): $t_1$ = 35.6 min, $t_2$ =38.8 min. HRMS Calculated for $C_{20}H_{23}NO_3$ (M+Na): 348.1576, found: 348.1574. $[\alpha]^{25}_D$ = 14.1 (c 0.51, $CH_2Cl_2$).



**2d**

**3-hydroxy-5-oxo-*N*, *N*-diphenylhexanamide**

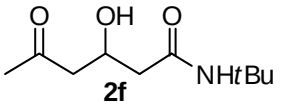
Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.50-7.10 (m, 10H), 4.54-4.43 (m, 1H), 4.12 (d, *J* = 3.4 Hz, 1H), 2.70-2.55 (m, 2H), 2.51-2.38 (m, 2H), 2.15 (d, *J* = 2.0 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.7, 171.8, 141. 9, 129.7, 128.8, 128.4, 128.0, 126.2, 64.8, 49.3, 40.8, 30.5. HPLC (Chiralcel AD-H column, hexane/$^{i}$PrOH 87/13, 0.8 mL min$^{-1}$, 254 nm): $t_1$ = 38.9 min, $t_2$ =42.3 min. HRMS Calculated for $C_{18}H_{19}NO_3$ (M+Na): 320.1263, found: 320.1255. $[\alpha]^{25}_D$ = -4.7 (c 0.90, $CH_2Cl_2$).



**2e**

**3-hydroxy-1-morpholinohexane-1, 5-dione**

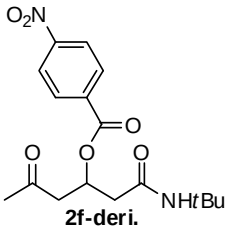
Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 4.45 (s, 1H), 4.14 (s, 1H), 3.70-3.64 (m, 4H), 3.64-3.58 (m, 2H), 3.50-3.41 (m, 2H), 2.71 (dd, *J* = 12.6, 6.3 Hz, 2H), 2.56-2.20 (m, 2H), 2.20 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.9, 170.09, 66.4, 66.2, 64.4, 49.3, 45.6, 41.5, 38.4, 30.6. HPLC (Chiralcel AS-H column, hexane/$^{i}$PrOH 84/16, 0.9 mL min$^{-1}$, 220 nm): $t_1$ = 32.7 min, $t_2$ =45.4 min. HRMS Calculated for $C_{10}H_{17}NO_4$ (M+Na): 238.1055, found: 238.1050. $[\alpha]^{25}_D$ = 35.6 (c 0.56, $CH_2Cl_2$).



**2f**

***N*-(tert-butyl)-3-hydroxy-5-oxohexanamide**

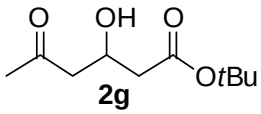
Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.84 (s, 1H), 4.39-4.33 (m, 1H), 4.15 (s, 1H), 2.65 (t, *J* = 6.5 Hz, 2H), 2.27 (dd, *J* = 8.6, 5.9 Hz, 2H), 2.18 (s, 3H), 1.34 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 208.3, 170.7, 64.8, 50.8, 49.4, 42.5, 30.4, 28.4. HRMS Calculated for $C_{10}H_{19}NO_3$ (M+H): 202.1443, found: 202.1433.



**2f-deri.**

**1-(tert-butylamino)-1, 5-dioxohexan-3-yl 4-nitrobenzoate**

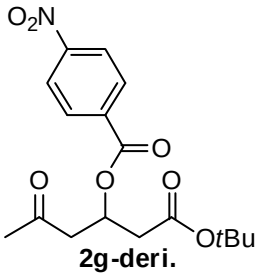
White solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.0 Hz, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 5.76-5.68 (m, 1H), 5.49 (s, 1H), 3.08 (qd, *J* = 17.3, 6.2 Hz, 2H), 2.61 (d, *J* = 6.1 Hz, 2H), 2.20 (s, 3H), 1.29 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 205.2, 167.9, 163.7, 150.4, 135.2, 130.6, 123.4, 69.2, 51.2, 46.5, 40.9, 30.3, 28.5. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 88/12, 0.8 mL min$^{-1}$, 254 nm): $t_1$ = 22.7 min, $t_2$ =31.4 min. HRMS Calculated for $C_{17}H_{22}N_2O_6$ (M+Na): 373.1376, found: 373.1374.



**2g**

**tert-butyl 3-hydroxy-5-oxohexanoate**

Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 4.47 – 4.35 (m, 1H), 3.48 (s, 1H), 2.65 (dd, *J* = 8.3, 6.2 Hz, 2H), 2.42 (d, *J* = 6.4 Hz, 2H), 2.19 (s, 3H), 1.44 (d, *J* = 5.2 Hz, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 208.1, 171.0, 80.9, 64.2, 49.1, 41.6, 30.5, 27.8. HRMS Calculated for $C_{10}H_{18}O_4$ (M+Na): 225.1103, found: 225.1126.



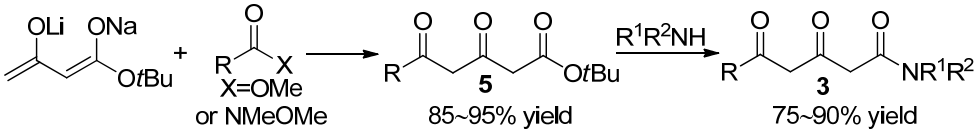

**1-(tert-butoxy)-1,5-dioxohexan-3-yl 4-nitrobenzoate**

$^1$H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.0 Hz, 2H), 8.15 (d, *J* = 9.0 Hz, 2H), 5.80 – 5.72 (m, 1H), 2.99 (qd, *J* = 17.1, 6.4 Hz, 2H), 2.75 (qd, *J* = 15.7, 6.2 Hz, 2H), 2.21 (s, 3H), 1.40 (s, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 204.5, 168.67, 163.3, 150.2, 135.1, 130.4, 123.2, 80.9, 68.3, 46.4, 39.4, 30.1, 27.6. HPLC (Chiralcel IA-3 column, hexane/$^i$PrOH 93/7, 0.7mL min$^{-1}$, 254 nm): $t_1$ =27.7 min, $t_2$=36.2 min. HRMS Calculated for $C_{17}H_{21}NO_7$ (M+Na): 374.1198, found: 374.1216.

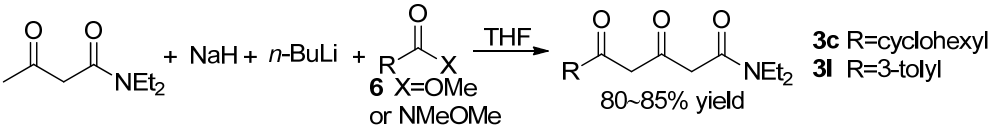
### 3. Preparation of 3a-t

**3a-t** were prepared by the following route **A** or **B:**

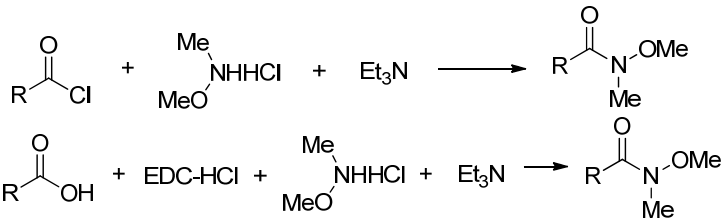
***Route A:***



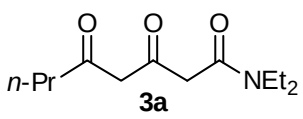

***Route B:***




The Weinreb amides were prepared from the corresponding acid or acid chlorides with the standard methods in the literature. [7]



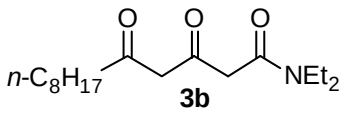

*Note*: Route **A**[8] have the occasional purification problem as the starting material *tert*-butyl acetoacetate were difficult to be separated from several β, δ-diketo esters **5,** which were obtained by the similar procedure for **1h** on page S2. The one-step route **B** [9] is relatively convenient except that the poor solubility of the sodium enolate of the *N*, *N*-diethyl-3-oxobutanamide in THF at low temperature (0 °C) made magnetic stirring problematic until *n*-BuLi was carefully added. Two equivalence of LDA can avoid the trouble. Both methyl esters and Weinreb amides can be used as the acylation reagents, the latter were preferred as they usually gave better yields.




***N, N*-diethyl-3, 5-dioxooctanamide**

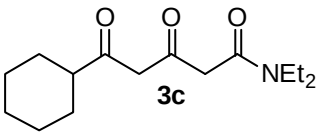
Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 0.62H), 3.76 (s, 0.36H), 3.58 (s, 0.36H),3.39(s, 1.8H) 3.43-3.22(m, 4H), 2.58-2.20 (m, 2H), 1.66-1.59 (m, 2H), 1.23-1.06 (m, 6H), 0.92 (dt, *J* = 10.2, 7.4 Hz,

3H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 204.3, 198.6, 191.4, 189.8, 169.9, 165.6, 99.1, 88.6, 55.9, 49.7, 48.5, 45.0, 44.8, 43.8, 42.2, 41.6, 39.8, 38.9, 18.6, 16.3, 13.7, 13.1, 13.0, 12.3. HRMS Calculated for $C_{12}H_{21}NO_3$ (M+H): 228.1600, found: 228.1588.



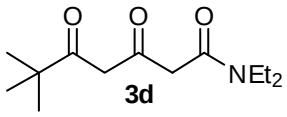

***N*, *N*-diethyl-3, 5-dioxotridecanamide**

Yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.66 (s, 0.59H), 5.15 (s, 0.09H), 3.76 (s, 0.35H), 3.59 (s, 0.35H), 3.39-2.42(m, 1.44H), 3.42-3.27(m. 4H), 2.52 (dd, *J* = 19.9, 12.5 Hz, 0.52H), 2.30-2.22 (m, 1.29H), 1.57 (dd, *J* = 15.1, 7.5 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 9H), 1.21-1.08 (m, 6H), 0.95-0.79 (m, 3H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 204.5, 198.6, 191.8, 189.7, 170.4, 170.0, 165.6, 165.4, 99.1, 88.6, 55.9, 49.8, 48.5, 44.8, 43.2, 42.2, 42.1, 41.6, 39.8, 37.1, 31.4, 28.8, 28.7, 28.7, 25.3, 23.1, 22.9, 22.2, 13.7, 13.6, 12.8, 12.4. HRMS Calculated for $C_{17}H_{31}NO_3$ (M+H): 298.2382, found: 298.2379.



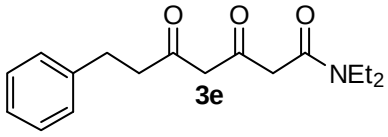

**5-cyclohexyl-*N*, *N*-diethyl-3, 5-dioxopentanamide**

Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 1H), 5.14 (s, 1H), 3.81 (s, 0.28H), 3.59 (s, 0.27H), 3.40 (s, 1.79H), 3.40-3.23 (m, 4H), 2.12-2.19 (m, 1H), 1.93-1.56 (m, 6H), 1.42-1.20 (m, 4H), 1.19-1.09 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 207.7, 199.2, 194.9, 190.6, 170.3, 165.8, 97.4, 88.8, 54.1, 51.1, 48.7, 47.7, 45.4, 45.2, 42.4, 39.9, 29.2, 28.0, 27.7, 25.4, 25.4, 25.2, 25.1, 13.9, 12.5. HRMS Calculated for $C_{15}H_{25}NO_3$ (M+H): 268.1913, found: 268.1917.



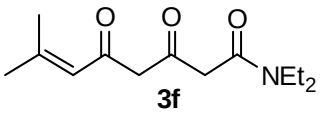

***N*, *N*-diethyl-6, 6-dimethyl-3, 5-dioxoheptanamide**

Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.75 (s, 0.59H), 3.88 (s, 0.25H), 3.60 (s, 0.24H), 3.42 (s, 1.53H), 3.42-3.25 (m, 4H), 1.24-1.06 (m, 6H), 1.17-1.14 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.2, 190.5, 165.7, 95.2, 88.9, 50.6, 48.7, 45.1, 42.3, 39.8, 38.2, 26.8, 25.7, 25.6, 13.8, 12.5, 12.4. HRMS Calculated for $C_{13}H_{23}NO_3$ (M+H): 242.1756, found: 242.1750.



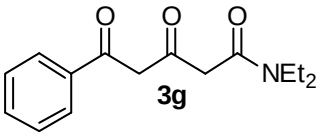

***N*, *N*-diethyl-3, 5-dioxo-7-phenylheptanamide**

Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.34-7.08 (m, 5H), 5.65 (s, 0.55H), 5.11 (s, 0.13H), 3.76 (s, 0.35H), 3.38 (s, 1.79H), 3.41– 3.23 (m, 4H), 2.96-2.84 (m, 2H), 2.62-2.58 (m, 1.43H), 2.28 (s, 0.31H), 1.20-1.08 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 203.9, 203.3, 198.5, 190.8, 189.3, 169.7, 165.5, 140.0, 128.0, 127.8, 125.8, 125.7, 99.5, 88.8, 56.1, 49.9, 48.4, 44.5, 43.4, 42.2, 39.8, 38.8, 31.1, 29.0, 28.9, 13.8, 12.4. HRMS Calculated for $C_{17}H_{23}NO_3$ (M+Na): 312.1576, found: 312.1577.



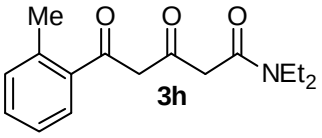

***N*, *N*-diethyl-7-methyl-3, 5-dioxooct-6-enamide**

Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.64 (d, *J* = 1.2 Hz, 1H), 5.57 (s, 1H), 3.76 (s, 1H), 3.61 (s, 1H), 3.42-3.40 (m, 2H), 3.40-3.25(m, 4H), 2.17 (s, 3H), 1.91 (s, 3H), 1.15 (dt, *J* = 14.2, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.3, 181.2, 165.8, 153.9, 122.9, 122.3, 120.4, 100.3, 88.6, 57.5, 51.0, 48.6, 45.5, 42.3, 39.8, 27.9, 27.3, 20.6, 13.8, 12.4. HRMS Calculated for $C_{13}H_{21}NO_3$ (M+H): 240.1600, found: 240.1579.



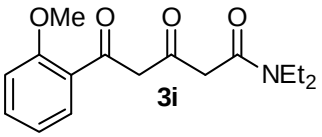

***N, N*-diethyl-3, 5-dioxo-5-phenylpentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.03-7.83 (m, 2H), 7.61-7.39 (m, 3H), 6.37 (s, 1H), 4.34 (s, 1H), 3.68 (s, 1H), 3.54 (s, 1H), 3.46-3.26 (m, 4H), 2.28 (s, 1H), 1.24-1.08 (m, 6H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.9, 181.5, 165.9, 133.9, 132.4, 128.6, 128.5, 128.4, 126.9, 96.4, 52.9, 49.8, 48.8, 46.0, 42.6, 42.5, 40.2, 40.1, 14.1, 12.8. HRMS Calculated for $C_{15}H_{19}NO_3$ (M+Na): 284.1263, found: 284.1239.



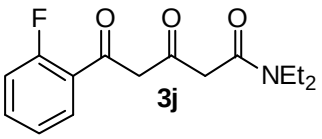

***N, N*-diethyl-3, 5-dioxo-5-(o-tolyl)pentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.54-7.45 (m, 1H), 7.34 (d, *J* = 6.5 Hz, 1H), 7.31-7.17 (m, 2H), 6.03 (s, 0.78H), 4.30 (s, 0.18H), 3.68 (s, 0.19H), 3.52 (s, 1.93H), 3.49-3.29 (m, 4H), 2.50 (s, 3H), 1.18 (dt, *J* = 22.8, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.7, 196.7, 190.6, 185.3, 170.3, 165.1, 136.3, 134.1, 131.3, 130.6, 130.1, 129.0, 127.7, 125.1, 125.0, 100.0, 88.5, 54.5, 48.1, 47.6, 44.6, 41.9, 41.8, 41.2, 39.5, 39.3, 20.7, 20.0, 13.4, 12.1. HRMS Calculated for $C_{16}H_{21}NO_3$ (M+H): 276.1600, found: 276.1584.



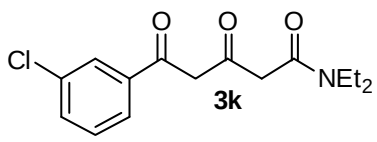

***N, N*-diethyl-5-(2-methoxyphenyl)-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.78-7.89 (m, 1H), 7.55-7.37 (m, 1H), 7.07-6.89 (m, 2H), 6.62 (s, 0.79H), 4.26 (s, 0.38H), 3.89 (d, *J* = 5.0 Hz, 3H), 3.66 (s, 0.35H), 3.52 (s, 1.60H), 3.44-3.27 (m, 4H), 1.16 (dt, *J* = 16.1, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.8, 194.0, 192.0, 178.7, 165.4, 157.9, 134.0, 132.6, 129.7, 129.2, 122.0, 119.9, 119.8, 111.1, 111.0, 101.0, 88.2, 57.0, 54.8, 49.7, 48.4, 45.2, 42.0, 41.9, 39.5, 39.3, 13.4, 12.1.HRMS Calculated for $C_{16}H_{21}NO_4$ (M+H): 192.1549, found: 192.1555.



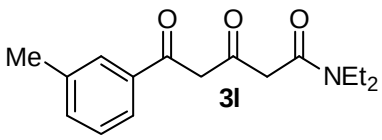

***N, N*-diethyl-5-(2-fluorophenyl)-3,5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.96-7.87 (m, 1H), 7.56-7.41 (m, 1H), 7.27-7.19 (m, 1H), 7.11 (m, 1H), 6.43 (s, 1H), 4.3o (s, 0.20H), 3.68-3.66 (m, 0.19H), 3.54 (s, 1.70H), 3.38 (dd, *J* = 21.3, 7.1 Hz, 4H), 1.22-1.13 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 192.7, 177.2, 165.8, 162.3, 159.8, 135.4, 135.3, 133.6, 133.5, 130.6, 129.9, 124.4, 124.4, 122.4, 122.3, 116.8, 116.6, 116.3, 101.3, 101.1, 56.7, 49.4, 45.9, 42.7, 40.2, 14.2, 12.7. HRMS Calculated for $C_{15}H_{18}NO_3F$ (M+H): 280.1349, found: 280.1342.



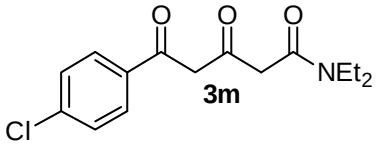

**5-(3-chlorophenyl)-*N, N*-diethyl-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.85 (t, *J* = 1.9 Hz, 1H), 7.74 (ddd, *J* = 7.8, 1.6, 1.1 Hz, 1H), 7.47 (dd, *J* = 2.1, 1.1 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 6.34 (s, 1H), 3.81 (s, 1H), 3.66 (s, 1H), 3.54 (s, 2H), 3.40 (dd, *J* = 17.0, 7.2 Hz, 4H), 1.18 (dt, *J* = 19.2, 7.1 Hz, 6H). $^{13}$C NMR (100MHz, $CDCl_3$) δ 198.6, 191.9, 179.0, 165.2, 135.2, 134.0, 131.6, 129.5, 129.3, 126.2, 124.4, 96.5, 88.8, 52.4, 48.0, 45.0, 42.1, 39.7, 13.6, 12.3. HRMS Calculated for $C_{15}H_{18}NO_3Cl$ (M+H): 296.1053, found: 296.1054.



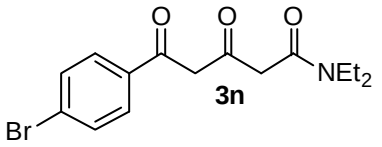

***N, N*-diethyl-3, 5-dioxo-5-(m-tolyl)pentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.70-7.66 (m, 2H), 7.44-7.28 (m, 2H), 6.35 (s, 0.79H), 4.33 (s, 0.22H), 3.68 (s, 0.21H), 3.53 (s, 1.68H), 3.48-3.26 (m, 4H), 2.40 (s, 3H), 1.29-1.03 (m, 6H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.5, 191.8, 181.7, 165.9, 138.2, 134.4, 133.8, 133.2, 128.8, 128.5, 128.4, 127.4, 125.7, 124.1, 96.3, 89.0, 52.9, 48.8, 46.0, 42.6, 42.5, 40.2, 21.2, 14.1, 14.0, 12.7. HRMS Calculated for $C_{16}H_{21}NO_3$ (M+H): 276.1600, found: 276.1588.



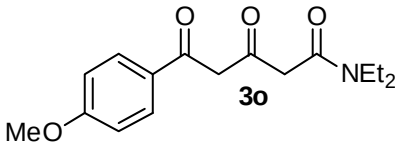

**5-(4-chlorophenyl)-*N, N*-diethyl-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.02-7.69 (m, 2H), 7.52-7.30 (m, 2H), 6.34 (s, 0.77H), 4.32 (s, 0.1H), (s, 0.1H), 3.51 (s, 1.67H), 3.45-3.35 (m, 4H), 1.22-1.11 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.8, 180.0, 165.6, 138.3, 132.2, 129.7, 128.7, 128.6, 128.1, 96.3, 2.8, 48.4, 45.5, 42.4, 40.1, 14.0, 12.6. HRMS Calculated for HRMS Calculated for $C_{15}H_{18}NO_3Cl$ (M+H): 296.1053, found: 296.1050.



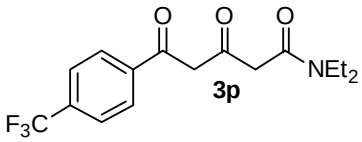

**5-(4-bromophenyl)-*N, N*-diethyl-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.90-7.69 (m, 2H), 7.64-7.51 (m, 2H), 6.33 (s, 0.79H), 4.31 (s, 0.16H), 3.64 (s, 0.15H), 3.52 (s, 1.76H), 3.43-3.34 (m, 4H), 1.17 (dt, $J$ = 20.0, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.8, 191.8, 179.7, 170.0, 165.4, 132.4, 131.4, 131.3, 129.6, 129.6, 128.0, 126.7, 96.18, 88.7, 52.5, 48.1, 45.2, 42.2, 42.1, 39.8, 39.7, 13.7, 12.4. HRMS Calculated for $C_{15}H_{18}NO_3Br$ (M+Na): 362.0368, found: 362.0355.



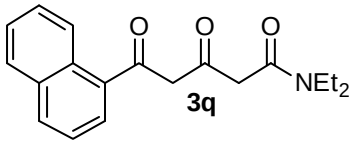

***N, N*-diethyl-5-(4-methoxyphenyl)-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.03-7.83 (m, 2H), 6.97-6.87 (m, 2H), 6.29 (s, 0.73H), 5.20 (s, 0.08H), 4.28 (s, 0.35H), 3.86 (s, 2.82H), 3.79-3.77 (m, 0.17H), 3.67 (s, 0.36H), 3.50 (s, 1.53H), 3.44-3.36 (m, 4H), 1.27-1.06 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.1, 192.4, 189.5, 181.9, 170.7, 165.6, 162.7, 130.4, 130.3, 128.6, 125.9, 113.4, 95.1, 88.5, 54.8, 52.3, 48.2, 44.7, 42.1, 42.0, 39.7, 39.6, 13.6, 12.3. HRMS Calculated for $C_{16}H_{21}NO_4$ (M+H): 292.1525, found: 292.1540.




***N,N*-diethyl-3,5-dioxo-5-(4-(trifluoromethyl)phenyl)pentanemide**

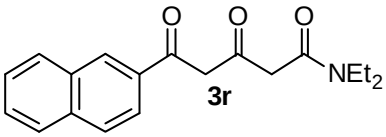
Yellow solid. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, $J$ = 8.2 Hz, 2H), 7.69 (d, $J$ = 8.3 Hz, 2H), 6.41 (s, 0.82H), 4.38 (s, 0.11H), 3.65 (s, 0.11H), 3.56 (s, 1.70H), 3.45-3.35 (m, 4H), 1.18 (dt, $J$ = 21.5, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 193.3, 178.8, 165.6, 137.2, 133.7, 133.3, 129.0, 128.9, 127.2, 125.5, 125.4, 124.9, 122.1, 97.3, 89.2, 53.2, 48.4, 46.1, 42.6, 40.3, 14.1, 12.7. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -63.61, -63.78. HRMS Calculated for $C_{16}H_{18}NO_4F_3$ (M+H): 330.1317, found: 330.1310.




***N, N*-diethyl-5-(naphthalen-1-yl)-3, 5-dioxopentanamide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.45 (dd, $J$ = 8.3, 1.0 Hz, 1H), 8.04-7.85 (m, 2H), 7.74 (dd, $J$ = 7.2, 1.2 Hz, 1H),

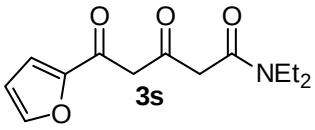
7.58-7.48 (m, 3H), 6.21 (s, 1H), 4.46 (s, 0.16H), 3.55 (s, 1.78H), 3.47-3.35 (m, 4H), 1.19 (dt, *J* = 28.2, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.4, 186.2, 165.7, 133.6, 133.5, 133.0, 131.7, 129.8, 128.3, 128.1, 127.2, 127.0, 126.3, 126.1, 125.5, 125.2, 124.5, 124.2, 101.46, 55.6, 48.8, 45.1, 42.5, 40.2, 14.0, 12.7. HRMS Calculated for $C_{19}H_{21}NO_3$ (M+H): 312.1600, found: 312.1584.



**3r**

***N, N*-diethyl-5-(naphthalen-2-yl)-3, 5-dioxopentanamide**

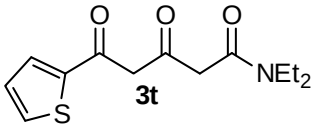
Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.09-7.79 (m, 4H), 7.64-7.48 (m, 2H), 6.52 (s, 0.89H), 3.97 (s, 0.1H), 3.72 (s, 0.2H), 3.58 (s, 1.77H), 3.37-3.49 (m, 4H), 1.26-1.12 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 199.3, 194.3, 191.8, 181.2, 165.9, 135.0, 132.4, 131.0, 130.7, 129.0, 128.4, 128.2, 128.1, 127.9, 127.5, 126.7, 126.5, 122.8, 96.6, 89.0, 52.9, 48.6, 45.8, 42.5, 42.4, 40.1, 40.0, 14.0, 12.7. HRMS Calculated for $C_{19}H_{21}NO_3$ (M+H): 312.1600, found: 312.1595.



**3s**

***N, N*-diethyl-5-(furan-2-yl)-3, 5-dioxopentanamide**

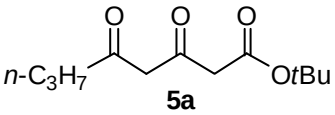
Pale yellow solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.62-7.56 (m, 1H), 7.33-7.14 (m, 1H), 6.56-6.53 (m, 1H), 6.23 (s, 0.57H), 5.24 (s, 0.1H), 4.17 (s, 0.34H), 3.68 (d, *J* = 6.7 Hz, 0.51H), 3.48 (s,1.39H), 3.47-3.25 (m, 4H), 1.10-1.22 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.4, 187.8, 174.2, 165.8, 149.5, 147.2, 145.0, 146.2, 118.9, 118.7, 115.9, 112.6, 112.4, 96.0, 52.6, 48.8, 45.6, 44.5, 42.6, 40.2, 40.1, 14.1, 14.0, 12.7. HRMS Calculated for $C_{13}H_{17}NO_4$ (M+Na): 274.1055, found: 274.1044.



**3t**

***N, N*-diethyl-3, 5-dioxo-5-(thiophen-2-yl)pentanamide**

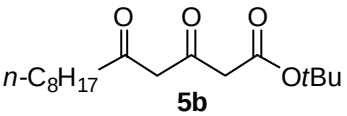
Brownish solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.87-7.58 (m, 2H), 7.15 (d, *J* = 4.1 Hz, 1H), 6.19 (s, 0.55H), 5.26 (s, 0.11H), 4.27 (s, 0.40H), 3.75 (s, 0.21H), 3.67 (s,0.41H), 3.48 (s, 1.29H), 3.46-3.19 (m, 4H), 1.22-1.11 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.2, 186.4, 185.1, 180.0, 169.9, 165.6, 165.4, 143.0, 140.2, 134.7, 134.3, 133.6, 133.2, 132.4, 130.3, 128.1, 128.0, 96.3, 88.8, 53.3, 49.3, 48.2, 46.3, 43.3, 42.3, 42.2, 41.7, 39.9, 39.8, 13.8, 13.7, 12.5. HRMS Calculated for $C_{13}H_{17}NO_3S$ (M+Na): 290.0827, found: 290.0825.



**5a**

***tert*-butyl 3, 5-dioxooctanoate**

Colorless liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.59 (s, 0.77H), 3.71 (s, 0.34H), 3.47 (s, 0.35H), 3.25 (s, 2H), 2.31- 2.24 (m, 2H), 1.64 (dd, *J* = 14.9, 7.5 Hz, 2H), 1.48-1.46 (m, 9H), 0.95 (dd, *J* = 13.6, 6.2 Hz, 3H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 192.8, 187.9, 166.7, 99.7, 81.8, 56.4, 50.6, 46.5, 39.6, 27.8, 19.0, 13.6. HRMS Calculated for $C_{12}H_{20}O_4$ (M+Na): 251.1259, found: 251.1242.

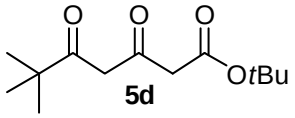


**5b**

***tert*-butyl 3, 5-dioxotridecanoate**

Light yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.58 (s, 0.68H), 3.70 (s, 0.26H), 3.46 (s, 0.28H), 3.24 (s, 1.45H), 2.54-2.47 (m, 0.36H), 2.33-2.24 (m, 1.56H), 1.59 (d, *J* = 7.6 Hz, 2H), 1.57-1.39 (m,

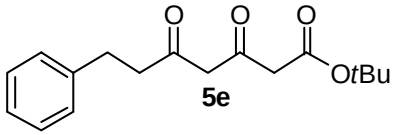
9H), 1.24-1.30 (m, 10H), 0.87 (t, $J$ = 6.9 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 204.8, 203.9, 197.3, 193.0, 187.7, 166.61, 99.5, 81.6, 56.3, 50.5, 46.3, 43.5, 37.7, 31.6, 29.1, 29.0, 28.9, 28.8, 28.1, 27.7, 25.5, 23.2, 22.5, 13.9. HRMS Calculated for $C_{17}H_{30}O_4$ (M+H): 299.2222, found: 299.2209.



**5d**

***tert*-butyl 6,6-dimethyl-3, 5-dioxoheptanoate**

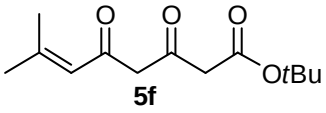
Colorless liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.66 (d, $J$ = 1.3 Hz, 1H), 5.50 (s, 1H), 3.70 (s, 0.21H), 3.48 (s, 0.22H), 3.26 (s, 1.87H), 2.19 (d, $J$ = 1.1 Hz, 3H), 1.92 (d, $J$ = 1.2 Hz, 3H), 1.47-1.45 (m, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.4, 182.3, 166.8, 154.4, 120.8, 100.9, 81.6, 58.0, 50.6, 46.9, 28.2, 27.8, 20.9. HRMS Calculated for $C_{13}H_{22}O_4$ (M+Na): 265.1416, found: 265.1426.



**5e**

***tert*-butyl 3, 5-dioxo-7-phenylheptanoate**

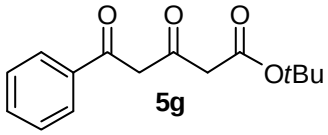
Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.33-7.14 (m, 5H), 5.57 (s, 0.69H), 3.70 (s, 0.28H), 3.43 (s, 0.28H), 3.35 (s, 0.34H), 3.23 (s, 1.44H), 2.97-2.83 (m, 2H), 2.62 (dd, $J$ = 8.7, 7.1 Hz, 2H), 1.49-1.43 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 192.2, 187.2, 166.6, 140.4, 128.4, 128.2, 126.2, 99.9, 81.8, 56.6, 51.4, 50.6, 46.2, 45.0, 39.6, 31.4, 29.3, 27.9. HRMS Calculated for $C_{17}H_{22}O_4$ (M+Na): 313.1428, found: 313.1416.



**5f**

***tert*-butyl 7-methyl-3, 5-dioxooct-6-enoate**

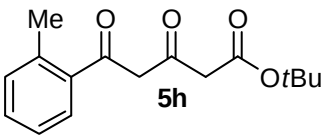
Yellow liquid. $^1$H NMR (400 MHz, $CDCl_3$) δ 5.66 (d, $J$ = 1.3 Hz, 1H), 5.50 (s, 1H), 3.70 (s, 0.21H), 3.48 (s, 0.22H), 3.26 (s, 1.87H), 2.19 (d, $J$ = 1.1 Hz, 3H), 1.92 (d, $J$ = 1.2 Hz, 3H), 1.47-1.45 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.4, 182.3, 166.8, 154.4, 120.8, 100.9, 81.6, 58.0, 50.6, 46.9, 28.2, 27.8, 20.9. HRMS Calculated for $C_{13}H_{20}O_4$ (M+Na): 263.1259, found: 263.1245.



**5g**

***tert*-butyl 3, 5-dioxo-5-phenylpentanoate**[10]

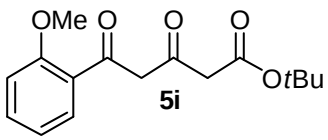
White solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.88 (ddd, $J$ = 7.0, 2.4, 1.0 Hz, 2H), 7.60-7.40 (m, 3H), 6.28 (s, 0.92H), 4.29-4.24 (m, 0.12H), 3.57-3.54 (m, 0.13H), 3.39 (s, 2.07H), 1.51-1.46 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.7, 182.3, 166.6, 134.0, 132.4, 128.6, 128.5, 128.4, 126.9, 96.5, 81.8, 52.9, 50.4, 47.0, 27.8.



**5h**

***tert*-butyl 3, 5-dioxo-5-(o-tolyl)pentanoate**

Thick oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, $J$ = 7.4 Hz, 1H), 7.34 (d, $J$ = 7.6 Hz, 1H), 7.25 (dd, $J$ = 7.0, 3.9 Hz, 2H), 5.95 (s, 1H), 3.36 (d, $J$ = 0.5 Hz, 2H), 2.50 (s, 3H), 1.48 (d, $J$ = 0.5 Hz, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.0, 186.9, 166.6, 137.1, 135.1, 132.2, 131.4, 130.8, 128.4, 125.7, 100.7, 81.9, 46.9, 27.9. HRMS Calculated for $C_{16}H_{20}O_4$ (M+Na): 299.1259, found: 299.1269.

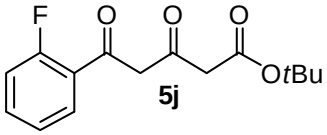


**5i**

***tert*-butyl 5-(2-methoxyphenyl)-3, 5-dioxopentanoate**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, $J$ = 7.8, 1.8 Hz, 1H), 7.49-7.45 (m, 1H), 7.00-6.95(m, 2H), 6.57 (s, 0.77H), 4.19 (s, 0.32H), 3.91 (s, 3H), 3.50 (s, 0.33H), 3.38 (s, 1.69H), 1.48 (s, 9H).

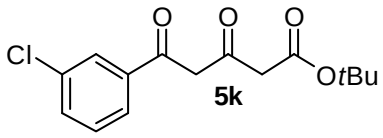
$^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.5, 180.1, 166.8, 158.4, 134.7, 133.2, 130.7, 130.1, 123.0, 120.8, 120.6, 111.6, 111.4, 101.5, 81.6, 57.7, 55.5, 55.4, 50.6, 47.4, 27.8. HRMS Calculated for $C_{16}H_{20}O_5$ (M+Na): 315.1208, found: 315.1217.



**5j**

***tert*-butyl 5-(2-fluorophenyl)-3, 5-dioxopentanoate**

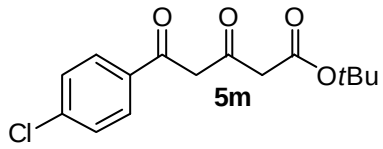
Light yellow solid.$^1$H NMR (400 MHz, $CDCl_3$) δ 7.93-7.97 (m, 1H), 7.45-7.51 (m, 1H), 7.26-7.22 (m, 1H), 7.10-7.15 (m, 1H), 6.40 (d, *J* = 0.9 Hz, 1H), 3.53 (s, 1H), 3.39 (s, 2H), 1.49 (s, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.9, 177.6, 166.4, 162.3, 159.7, 133.7, 133.6, 129.9, 124.4, 124.4, 116.5, 116.3, 101.3, 101.1, 81.9, 47.3, 27.8. HRMS Calculated for $C_{15}H_{17}FO_4$ (M+Na): 303.1009, found: 303.1009.



**5k**

***tert*-butyl 5-(3-chlorophenyl)-3, 5-dioxopentanoate**

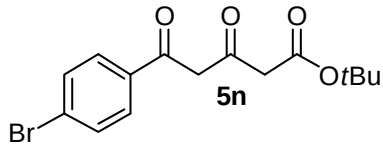
Thick oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.85 (t, *J* = 1.9 Hz, 1H), 7.78-7.71 (m, 1H), 7.50 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 6.25 (s, 1H), 3.56-3.53 (m, 0.15H), 3.40 (s, 2.14H), 1.49 (s, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 190.0, 180.8, 166.4, 135.9, 134.85, 132.2, 129.8, 127.0, 125.0, 96.9, 47.0, 27.8. HRMS Calculated for $C_{15}H_{17}ClO_4$ (M+Na): 319.0713, found: 319.0730.



**5m**

***tert*-butyl 5-(4-chlorophenyl)-3, 5-dioxopentanoate**

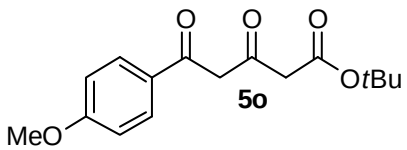
White solid upon cooling. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 6.25 (s, 1H), 3.38 (s, 2H), 1.49 (s, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.7, 181.4, 166.6, 138.7, 132.7, 129.9, 129.1, 128.9, 128.3, 96.6, 82.0, 47.0, 27.9. HRMS Calculated for $C_{15}H_{17}ClO_4$ (M+Na): 319.0713, found: 319.0700



**5n**

***tert*-butyl 5-(4-bromophenyl)-3, 5-dioxopentanoate**

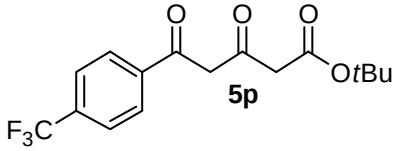
Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.8 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 6.25 (s, 1H), 3.38 (s, 1.89H), 3.36-3.35 (m, 0.36H), 1.48 (s, 9H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.4, 182.3, 166.8, 154.4, 120.8, 100.9, 81.6, 58.0, 50.6, 46.9, 28.2, 27.8, 20.9. HRMS Calculated for $C_{15}H_{17}BrO_4$(M+Na): 363.0208, found:363.0218.



**5o**

***tert*-butyl 5-(4-methoxyphenyl)-3, 5-dioxopentanoate**

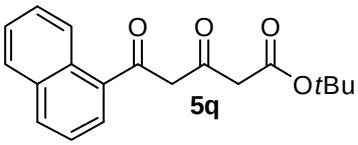
Thick oil, solidified upon cooling. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.17 (s, 1H), 4.15 (s, 0.24H), 3.78 (s, 3H), 3.50 (s, 0.22H), 3.34-3.27 (m, 1.65H), 1.44 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 187.53, 183.12, 166.75, 163.13, 130.75, 128.98, 126.60, 113.80, 95.60, 81.6155.21, 52.82, 50.32, 46.44, 27.77. HRMS Calculated for $C_{16}H_{20}O_5$ (M+Na): 315.1208, found: 315.1202.



**5p**

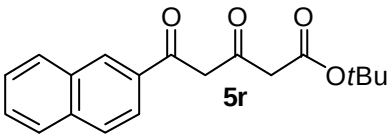
***tert*-butyl 3, 5-dioxo-5-(4-(trifluoromethyl)phenyl) pentano-ate**

White solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 2H), 6.32 (s, 1H), 4.31 (s, 0.1H), 3.55 (s, 0.1H), 3.42 (s, 1.8H), 1.49 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.1, 180.0, 166.5, 137.4, 128.9, 127.3, 125.6, 125.6, 124.9, 97.4, 82.2, 47.3, 27.9. HRMS Calculated for $C_{16}H_{17}F_3O_4$ (M+Na): 353.0977, found: 353.0974.



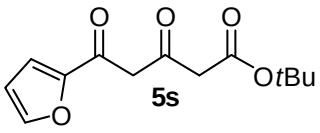

***tert*-butyl 5-(naphthalen-1-yl)-3,5-dioxopentanoate**

Thick oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.3 Hz, 1H), 8.00-7.80 (m, 2H), 7.74 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.59-7.44 (m, 3H), 6.15 (s, 0.95H), 4.39 (s, 0.13H), 3.61 (s, 0.12H), 3.40 (d, *J* = 2.7 Hz, 1.75H), 1.56-1.38 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 188.4, 187.0, 166.5, 133.6, 133.2, 131.8, 129.9, 128.4, 127.1, 126.2, 125.4, 124.6, 101.6, 81.9, 46.5, 27.8. HRMS Calculated for $C_{19}H_{20}O_4$ (M+Na): 355.1259, found: 355.1264.



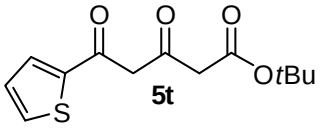

***tert*-butyl-(naphthalen-2-yl)-3, 5-dioxopentanoate**

Thick oil, solidified upon cooling. $^1$H NMR (400 MHz, $CDCl_3$) 8.40 (s, 1H), 7.95-7.72 (m, 4H), 7.60-7.40 (m, 2H), 6.40 (s, 1H), 3.41 (s, 2H), 1.49 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 189.6, 182.2, 166.7, 135.8, 132.5, 131.3, 129.2, 128.3, 128.2, 128.1, 127.6, 126.7, 122.8, 96.9, 81.9, 47.1, 27.9. HRMS Calculated for $C_{19}H_{20}O_4$ (M+Na): 355.1259, found: 355.1266.




***tert*-butyl 5-(furan-2-yl)-3,5-dioxopentanoate**

Light yellow solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.17 (dd, *J* = 3.6, 0.7 Hz, 1H), 6.55 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.18 (s, 1H), 4.11 (s, 1H), 3.54 (s, 1H), 3.33 (d, *J* = 1.0 Hz, 2H), 1.48 (s, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 185.6, 175.0, 166.6, 149.8, 147.1, 146.2, 118.6, 116.0, 112.7, 112.5, 96.2, 81.9, 52.8, 50.6, 45.8, 27.8. HRMS Calculated for $C_{13}H_{16}O_5$ (M+Na): 275.0895, found: 275.0898.

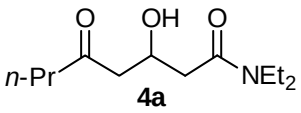



***tert*-butyl -dioxo-5-(thiophen-2-yl)pentanoate**

Thick brown yellow. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 3.8, 0.7 Hz, 1H), 7.61 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.13 (dd, *J* = 4.7, 4.1 Hz, 1H), 6.13 (s, 0.69H), 4.19 (s, 0.28H), 3.56 (s, 0.28H), 3.32 (s, 1.52H), 1.51-1.44 (m, 9H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 183.1, 180.9, 166.6, 140.7, 135.0, 133.6, 132.6, 130.5, 128.3, 128.2, 96.7, 81.9, 53.7, 50.3, 45.1, 27.8. HRMS Calculated for $C_{13}H_{16}O_4S$ (M+H): 291.0667, found: 291.0666.

**4. Preparation of 4a-t**

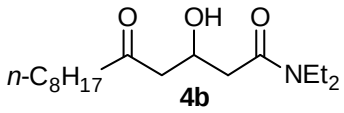
The same procedure as described on page **S3**. The ee of **4q** was determined upon its bromoacetate: To a stirred solution of **4q** (120 mg, 383 μmol ) in 2 mL anhydrous THF was added pyridine (48 mg, 612 μmol) and bromoacetyl bromide (116 mg, 574 μmol) at 0 °C. The solution was stirred at 0 °C for 3 h and then purified by flash column chromatography (PE/EA=5/1) to gave the desired product in quantitative yield.



**4a**

***N, N*-diethyl-3-hydroxy-5-oxooctanamide**

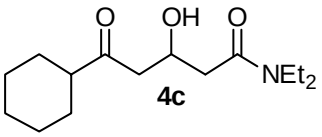
Yellow liquid. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.58 (d, *J* = 3.2 Hz, 1H), 4.50-4.36 (m, 1H), 3.32 (dq, *J* = 21.8, 7.1 Hz, 4H), 2.80-2.55 (m, 3H), 2.52-2.31 (m, 3H), 1.73-1.52 (m, 2H), 1.14 (dt, *J* = 19.9, 7.1 Hz, 6H), 0.91 (t, *J* = 7.4 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 209.6, 170.6, 64.5, 48.4, 45.0, 41.5, 39.6, 38.0, 16.5, 13.6, 13.2, 12.5. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 94/6, 0.65 mL min$^{-1}$, 220 nm): $t_1$ = 29.6 min, $t_2$ =32.2 min. HRMS Calculated for $C_{12}H_{23}NO_3$ (M+H): 230.1756, found: 230.1735. $[\alpha]^{25}_{D}$ = 31.4 (c 0.65, $CH_2Cl_2$).



**4b**

***N, N*-diethyl-3-hydroxy-5-oxotridecanamide**

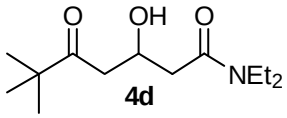
Yellow liduid. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.57 (d, *J* = 3.3 Hz, 1H), 4.41 (dd, *J* = 7.3, 4.1 Hz, 1H), 3.39-3.25 (m, 4H), 2.79-2.53 (m, 3H), 2.49-2.31 (m, 3H), 1.55 (d, *J* = 6.9 Hz, 2H), 1.34-1.18 (m, 10H), 1.20-1.06 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 209.7, 170.1, 64.2, 48.3, 43.1, 41.5, 39.6, 38.2, 31.3, 28.8, 28.6, 23.0, 22.1, 13.6, 12.5. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 90/10, 0.7 mL min$^{-1}$, 220 nm): $t_1$ = 24.8 min, $t_2$ =30.1 min. HRMS Calculated for $C_{17}H_{33}NO_3$ (M+H): 300.2539, found: 300.2556. $[\alpha]^{25}_{D}$ = 23.2 (c 0.71, $CH_2Cl_2$).



**4c**

**5-cyclohexyl-*N, N*-diethyl-3-hydroxy-5-oxopentanamide**

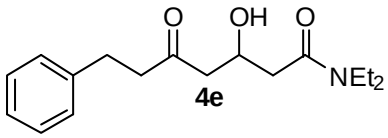
Yellow liquid.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.57 (d, *J* = 3.4 Hz, 1H), 4.46-4.35 (m, 1H), 3.42-3.23 (m, 4H), 2.84-2.63 (m, 2H), 2.61-2.34 (m, 2H), 2.40-2.30 (m, 1H), 1.92-1.60 (m, 6H), 1.40-1.20 (m, 4H), 1.20-1.05 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 212.3, 212.2, 170.4, 64.3, 50.4, 46.1, 41.3, 39.3, 37.8, 27.5, 25.1, 24.9, 13.4, 12.3. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 93/7, 0.6 mL min$^{-1}$, 220 nm): $t_1$ = 29.7 min, $t_2$ =32.3 min. HRMS Calculated for $C_{15}H_{27}NO_3$ (M+H): 270.2069, found: 270.2052. $[\alpha]^{25}_{D}$ = 22.6 (c 0.61, $CH_2Cl_2$).



**4d**

***N, N*-diethyl-3-hydroxy-6, 6-dimethyl-5-oxoheptanamide**

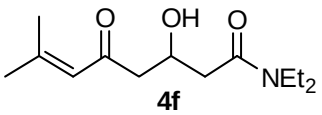
Yellow liquid. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.56 (s, 1H), 4.39 (s, 1H), 3.42-3.23 (m, 4H), 2.89-2.68 (m, 2H), 2.65-2.26 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.14-1.11 (m, 9H), 1.10 (t, *J* = 7.1 Hz, 4H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 214.7, 170.7, 64.7, 43.8, 42.4, 41.6, 39.6, 37.9, 25.7, 13.6, 12.5. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 93/7, 0.6 mL min$^{-1}$, 220 nm): $t_1$ = 21.7 min, $t_2$ =23.4 min. HRMS Calculated for $C_{13}H_{25}NO_3$ (M+H): 244.1913, found: 244.1892. $[\alpha]^{25}_{D}$ = 26.1 (c 0.55, $CH_2Cl_2$).



**4e**

***N, N*-diethyl-3-hydroxy-5-oxo-7-phenylheptanamide**

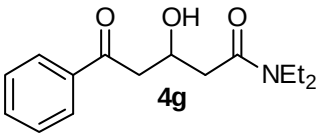
Yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.16-7.29 (m, 5H), 4.58 (d, *J* = 3.3 Hz, 1H), 4.40-4.45 (m, 1H), 3.31 (dq, *J* = 21.9, 7.1 Hz, 4H), 2.92-2.70 (m, 4H), 2.62-2.53 (m, 2H), 2.34 (dd, *J* = 16.1, 8.4 Hz, 2H), 1.19-1.10 (m, 6H). $^{13}$C NMR (100MHz, $CDCl_3$) δ 208.6, 170.7, 140.5, 128.0, 127.9, 125.6, 64.6, 48.7, 44.6, 41.6, 39.7, 38.0, 29.1, 22.0, 13.7, 12.6. HPLC (Chiralcel AD-H column, hexane/$^{i}$PrOH 88/12, 0.7 mL min$^{-1}$, 220 nm): $t_1$ = 18.7 min, $t_2$ =20.7 min. HRMS Calculated for $C_{17}H_{25}NO_3$ (M+Na): 314.1732, found: 314.1725. $[\alpha]^{25}_{D}$ = 23.6 (c 0.88, $CH_2Cl_2$).



**4f**

***N, N*-diethyl-3-hydroxy-7-methyl-5-oxooct-6-enamide**

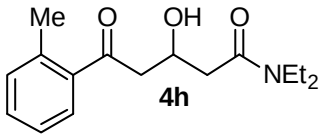
Yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 6.13-6.06 (m, 0.91H), 4.61 (s, 0.07H), 4.49-4.36 (m, 1H), 3.42-3.21 (m, 4H), 2.79-2.61 (m, 2H), 2.59-2.29 (m, 2H), 2.14 (d, *J* = 1.1 Hz, 2H), 1.88 (d, *J* = 1.2 Hz, 2H), 1.18-1.09(m, 6H), 0.90 (d, *J* = 6.6 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 210.0, 199.3, 171.1, 156.2, 123.8, 65.2, 64.8, 52.5, 50.0, 49.0, 41.9, 40.0, 38.3, 38.2, 27.6, 24.3, 22.4, 20.7, 13.9, 12.4. HPLC (Chiralcel AS-H column, hexane/$^{i}$PrOH 91/9, 0.65 mL min$^{-1}$, 254 nm): $t_1$ = 22.9 min, $t_2$ =25.6 min. HRMS Calculated for $C_{13}H_{23}NO_3$ (M+H): 242.1756, found: 242.1743. $[\alpha]^{25}_{D}$ = 30.6 (c 0.30, $CH_2Cl_2$).



**4g**

***N, N*-diethyl-3-hydroxy-5-oxo-5-phenylpentanamide**

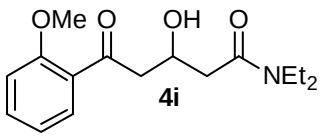
Thick oil.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.03-7.91 (m, 2H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.47 (dd, *J* = 10.7, 4.5 Hz, 2H), 4.72 (d, *J* = 3.5 Hz, 1H), 4.66-4.55 (m, 1H), 3.43-3.16 (m, 6H), 2.77-2.44 (m, 2H), 1.15 (dt, *J* = 18.0, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.7, 170.8, 136.5, 132.9, 128.2, 127.7, 65.0, 44.5, 41.6, 39.7, 38.2, 13.7, 12.6. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 22.2 min, $t_2$ =24.5 min. HRMS Calculated for $C_{15}H_{21}NO_3$ (M+Na): 286.1419, found: 286.1411. $[\alpha]^{25}_{D}$ = 36.4 (c 0.50, $CH_2Cl_2$).



**4h**

***N, N* -diethyl-3-hydroxy-5-oxo-5-(o-tolyl)pentanamide**

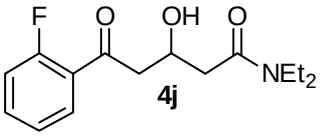
Thick oil.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.72-7.64 (m, 1H), 7.35 (td, *J* = 7.5, 1.3 Hz, 1H), 7.28-7.18 (m, 2H), 4.64 (s, 1H), 4.60-4.52 (m, 1H), 3.41-3.26 (m, 4H), 3.22-3.08 (m, 2H), 2.72-2.43 (m, 2H), 2.49 (s, 3H), 1.19-1.07 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.8, 137.7, 137.3, 131.6, 131.1, 128.4, 125.4, 65.2, 47.4, 41.7, 39.8, 38.2, 20.9, 13.7, 12.7. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 17.9 min, $t_2$ =20.1 min. HRMS Calculated for $C_{16}H_{23}NO_3$ (M+H): 278.1756, found: 278.1739. $[\alpha]^{25}_{D}$ = 19.5 (c 0.52, $CH_2Cl_2$).



**4i**

***N, N* -diethyl-3-hydroxy-5-(2-methoxyphenyl)-5-oxopentanamide**

Thick oil.$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.45 (ddd, *J* = 8.4, 7.3, 1.8 Hz, 1H), 7.02-6.92 (m, 2H), 4.68 (d, *J* = 3.0 Hz, 1H), 4.60-4.50 (m, 1H), 3.89 (s, 3H), 3.40-3.35 (m, 2H), 3.35-3.13 (m, 4H), 2.56 (m, 2H), 1.13 (dt, *J* = 21.4, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 200.2, 170.9, 158.2, 133.3, 129.7, 127.3, 120.0, 111.1, 64.8, 55.0, 49.7, 41.5, 39.6, 38.0, 13.6, 12.5. HPLC (Chiralcel AD-H column, hexane/$^{i}$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 33.0 min, $t_2$ =35.1 min. HRMS Calculated for $C_{16}H_{23}NO_4$ (M+Na): 316.1525, found: 316.1550. $[\alpha]^{25}_{D}$ = 57.2 (c 0.53, $CH_2Cl_2$).

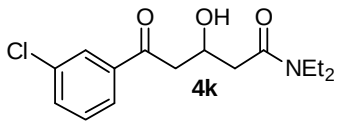


**4j**

***N, N* -diethyl-5-(2-fluorophenyl)-3-hydroxy-5-oxopentanamide**

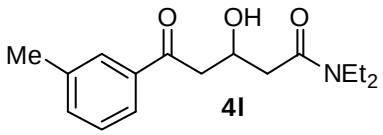
Thick oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.85 (td, *J* = 7.6, 1.9 Hz, 1H), 7.56-7.45 (m, 1H), 7.28-7.07 (m, 2H), 4.62 (s, 1H), 4.63-4.58 (m, 1H), 3.37 (q, *J* = 7.1 Hz, 2H), 328 ((q, *J* = 7.1 Hz, 2H), 3.28-3.15 (m, 2H), 2.43-2.71 (m, 2H), 1.14 (dt, *J* = 22.8, 7.2 Hz, 6H). $^{13}$C NMR (100MHz, $CDCl_3$) δ 196.8, 171.0, 162.9, 160.4, 134.6, 134.5, 130.3, 125.4, 125.3, 124.2, 124.2, 116.6, 116.4, 64.7, 49.6, 49.5, 41.8, 39.9, 38.2, 13.9, 12.8. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -109.93. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 90/10,

0.75 mL min$^{-1}$, 254 nm): $t_1$ = 24.1 min, $t_2$ =26.7 min. HRMS Calculated for $C_{15}H_{20}NO_3F$ (M+Na): 304.1325, found: 304.1314. $[\alpha]^{25}_D$ = 25.3 (c 0.57, $CH_2Cl_2$).



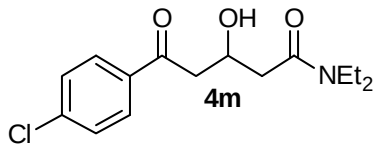

**5-(3-chlorophenyl)-*N, N* -diethyl-3-hydroxy-5-oxopentanamide**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 1.8 Hz, 1H), 7.85 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.57-7.51 (m, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 4.69 (d, = 3.5 Hz, 1H), 4.65-4.54 (m, 1H), 3.42-3.29 (m, 4H), 3.27-3.14 (m, 2H), 2.76-2.44 (m, 2H), 1.21-1.08 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 197.4, 170.7, 138.1, 134.5, 132.7, 129.6, 127.8, 126.0, 64.9, 44.7, 41.7, 39.8, 38.1, 13.8, 12.7. HPLC (Chiralcel OJ-H column, hexane/$^i$PrOH 92/8, 0.65 mL min$^{-1}$, 254 nm): $t_1$ = 16.4 min, $t_2$ =17.7 min. HRMS Calculated for $C_{15}H_{20}NO_3Cl$ (M+H): 298.1210, found: 298.1196. $[\alpha]^{25}_D$ = 21.1 (c 0.59, $CH_2Cl_2$).



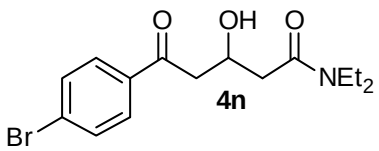

***N, N* -diethyl-3-hydroxy-5-oxo-5-(m-tolyl)pentanamide**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.77 (ddd, *J* = 7.1, 1.6, 0.6 Hz, 2H), 7.41-7.30 (m, 2H), 4.74 (d, *J* = 3.4 Hz, 1H), 4.60 (s, 1H), 3.46-3.20 (m, 4H), 3.34-3.16 (m, 2H), 2.77-2.43 (m, 2H), 2.40 (s, 3H), 1.14 (dt, *J* = 17.8, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.8, 170.8, 137.9, 136.5, 133. 7, 128.2, 128.1, 125.0, 65.0, 44.5, 41.6, 39.7, 38.1, 20.9, 13.7, 12.6. HPLC (Chiralcel AD-H column, hexane/$^i$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 20.1 min, $t_2$ =21.1 min. HRMS Calculated for $C_{16}H_{23}NO_3$ (M+H): 278.1756, found: 278.1768. $[\alpha]^{25}_D$ = 23.8 (c 0.57, $CH_2Cl_2$).



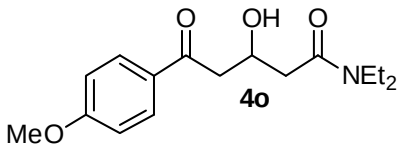

**5-(4-chlorophenyl)-*N, N* -diethyl- 3-hydroxy-5-oxopentan-amide**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.6 Hz, 2H), 4.69 (d, *J* = 3.6 Hz, 1H), 4.63-4.54 (m, 1H), 3.42-3.30 (m, 4H), 3.29-3.13 (m, 2H), 2.76-2.44 (m, 3H), 1.15 (dt, *J* = 19.0, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 197.4, 170.7, 139.2, 134.9, 129.3, 128.4, 64.9, 44.5, 41.6, 39.7, 38.1, 13.7, 12.6. HPLC (Chiralcel OJ-H column, hexane/$^i$PrOH 92/8, 0.65 mL min$^{-1}$, 254 nm): $t_1$ = 16.5 min, $t_2$ =18.2 min. HRMS Calculated for $C_{15}H_{20}NO_3Cl$ (M+Na): 320.1029, found: 320.1014. $[\alpha]^{25}_D$ = 14.5 (c 0.55, $CH_2Cl_2$).




**5-(4-bromophenyl)-*N, N*-diethyl-3-hydroxy-5-oxopentan-amide**

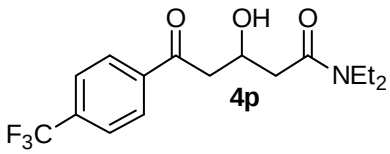
Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.7 Hz, 2H), 7.61 (d, *J* = 8.7 Hz, 2H), 4.70 (s, 1H), 4.59 (d, *J* = 4.3 Hz, 1H), 3.44-3.24 (m, 4H), 3.29-3.12 (m, 2H), 2.76-2.44(m, 2H), 1.28-1.08 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.1, 171.2, 135.6, 131.9, 129.7, 128.6, 128.5, 128.1, 65.3, 44.8, 42.0, 40.1, 38.3, 14.1, 13.0. HPLC (Chiralcel OB-H column, hexane/$^i$PrOH 90/10, 0.7 mL min$^{-1}$, 254 nm): $t_1$ = 23.2 min, $t_2$ =36.7 min. HRMS Calculated for $C_{15}H_{20}NO_3Br$ (M+Na): 364.0524, found: 364.0508. $[\alpha]^{25}_D$ = 12.5 (c 0.51, $CH_2Cl_2$).




***N, N* -diethyl-3-hydroxy-5-(4-methoxyphenyl)-5-oxopent-anamide**

Thick yellow oil. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 4.73 (d, *J* = 3.4 Hz, 1H),

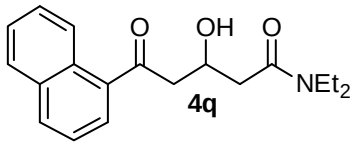
4.65-4.53 (m, 1H), 3.87 (s, 3H), 3.41-3.28 (m, 4H), 3.77-3.44 (m, 2H), 2.77-2.44 (m, 2H), 1.14 (dt, *J* = 17.1, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 197.2, 170.8, 163.2, 130.0, 129.6, 113.3, 65.1, 55.0, 44.1, 41.6, 39.7, 38.2, 13.7, 12.6. HPLC (Chiralcel IA-3 column, hexane/$^{i}$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 37.0 min, $t_2$ =41.2 min. HRMS Calculated for $C_{16}H_{23}NO_4$ (M+Na): 316.1525, found: 316.1520. $[\alpha]^{25}_{D}$ = 14.6 (c 0.75, $CH_2Cl_2$).



**4p**

***N, N* -diethyl-3-hydroxy-5-oxo-5-(4-(trifluoromethyl)phenyl)-pentanamide**

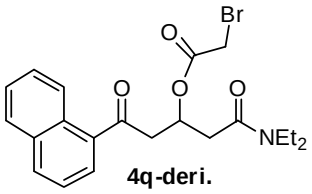
Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.8, 0.7 Hz, 2H), 7.78-7.63 (m, 2H), 4.70 (s, 1H), 4.64-4.56 (m, 1H), 3.42-3.29 (m, 4H), 3.28-3.14 (m, 2H), 2.75-2.45 (m, 2H), 1.14 (dt, *J* = 21.4, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 197.8, 170.7, 139.3, 134.3, 134.0, 133.7, 133.3, 128.2, 125.2, 125.2, 64.9, 44.9, 41.6, 39.8, 38.2, 13.6, 12.5. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -63.67. HPLC (Chiralcel OJ-H column, hexane/$^{i}$PrOH 94/6, 0.6 mL min$^{-1}$, 254 nm): $t_1$ = 19.6 min, $t_2$ =21.5 min. HRMS Calculated for $C_{16}H_{20}NO_4F_3$ (M+H): 332.1474, found: 332.1456. $[\alpha]^{25}_{D}$ = 12.1 (c 0.53, $CH_2Cl_2$).



**4q**

***N, N*-diethyl-3-hydroxy-5-(naphthalen-1-yl)-5-oxopentanamide**

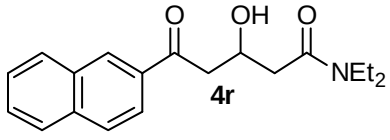
Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.68-8.61 (m, 1H), 8.03-7.86 (m, 3H), 7.64-7.48 (m, 3H), 4.71 (d, *J* = 3.5 Hz, 1H), 4.70-4.64 (m, 1H), 3.47-3.31 (m, 4H), 3.31-3.25 (m, 2H), 2.65 (ddd, *J* = 24.0, 16.0, 5.8 Hz, 2H), 1.15 (dt, *J* = 16.1, 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 202.8, 170.9, 135.3, 133.6, 132.6, 129.8, 128.2, 128.0, 127.7, 126.2, 125.5, 124.1, 65.5, 48.0, 41.7, 39.8, 38.2, 13.8, 12.8. HRMS Calculated for $C_{19}H_{23}NO_3$ (M+H):314.1756, found: 314.1762.



**4q-deri.**

**1-(diethylamino)-5-(naphthalen-1-yl)-1, 5-dioxopentan-3-yl 2-bromoacetate**

Thick brown oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.07-7.83 (m, 3H), 7.67-7.48 (m, 3H), 5.84-5.81 (m, 1H), 3.75 (d, *J* = 1.0 Hz, 2H), 3.73-3.48 (m, 2H), 3.37 (dd, *J* = 14.5, 7.4 Hz, 4H), 276-2.92 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 200.6, 167.9, 166.4, 134.9, 133.9, 133.1, 130.0, 128.4, 128.4, 128.0, 126.4, 125.6, 124.4, 70.6, 45.2, 42.1, 40.1, 36.7, 25.8, 14.3, 13.0. HPLC (Chiralcel AD-H column, hexane/$^{i}$PrOH 90/10, 0.75 mL min$^{-1}$, 254 nm): $t_1$ = 17.9 min, $t_2$ =20.1 min. HRMS Calculated for $C_{21}H_{24}NO_4Br$ (M+H): 434.0967, found: 434.0986.

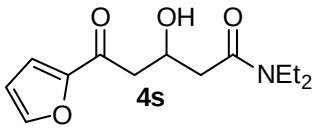


**4r**

***N, N*-diethyl-3-hydroxy-5-(naphthalen-2-yl)-5-oxopentana-mide**

Thick yellow oil. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.07-7.86 (m, 4H), 7.64-7.53 (m, 2H), 4.78 (d, *J* = 3.4 Hz, 1H), 4.67 (s, 1H), 3.43-3.25 (m, 4H), 3.55-3.38 (m, 2H), 2.83-2.50(m, 2H), 1.16 (dt, *J* = 17.5, 7.1 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 198.5, 170.8, 135.2, 133.8, 132.0, 129.7, 129.2, 128.2, 128.0, 127.3, 126.4, 123.3, 65.2, 44.6, 41.6, 39.7, 38.2, 13.7, 12.7. HPLC (Chiralcel AS-H column, hexane/$^{i}$PrOH

91/9, 0.7 mL $min^{-1}$, 254 nm): $t_1$ = 40.2 min, $t_2$ =45.5 min. HRMS Calculated for $C_{19}H_{23}NO_3$ (M+H): 314.1756, found: 314.1763. $[\alpha]^{25}_D$ = 7.1 (c 0.56, $CH_2Cl_2$).




***N, N*-diethyl-5-(furan-2-yl)-3-hydroxy-5-oxopentanamide**

Pale solid. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 1.6, 0.7 Hz, 1H), 7.26-7.22 (m, 1H), 6.54 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.71 (d, *J* = 3.6 Hz, 1H), 4.62-4.48 (m, 1H), 3.45-3.24 (m, 4H), 3.24-3.00 (m, 2H), 2.73-2.44 (m, 2H), 1.14 (dt, *J* = 17.7, 7.1 Hz, 6H).$^{13}$C NMR (100 MHz, $CDCl_3$) δ 187.0, 170.6, 152.1, 146.3, 117.5, 111.9, 64.8, 44.3, 41.5, 39.6, 38.0, 13.6, 12.5. HPLC (Chiralcel IA-3 column, hexane/$^i$PrOH 90/10, 0.7 mL $min^{-1}$, 254 nm): $t_1$ = 34.2 min, $t_2$ =43.7 min. HRMS Calculated for $C_{13}H_{19}NO_4$ (M+Na): 276.1212, found: 276.1203. $[\alpha]^{25}_D$ = 18.3 (c 0.53, $CH_2Cl_2$).

**Determination of the absolute configuration of 4s by X-ray crystallography:**

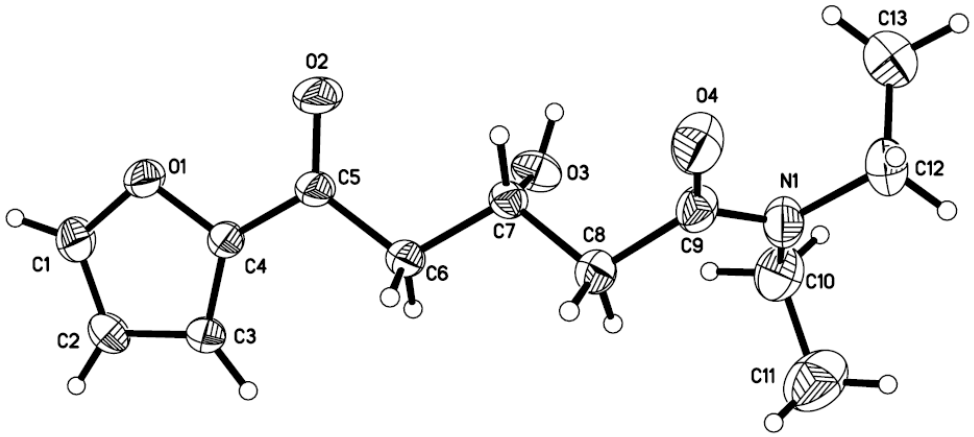


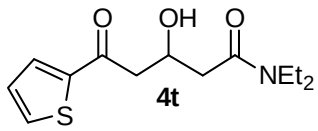

**Figure S1** The Structure of (*S*)-**4s**.

Single crystal of **4s** was obtained from hexane/$CH_2Cl_2$. The data was collected on a Bruker Smart 1000 CCD diffractometer with Cu-Kα radiation (λ = 1.54178 Å). The empirical absorption correction was applied by using the SADABS program (G. M. Sheldrick, SADABS, program for empirical absorption correction of area detector data; University of Göttingen, Göttingen, Germany, 1996). The structure was solved using direct method, and refined by full-matrix least-squares on $F^2$ (G. M. Sheldrick, SHELXTL97, program for crystal structure refinement, University of Göttingen, Germany, 1997) The related crystallographic data are listed in the **Table S1**:

**Table S1** Crystal Data and Structure Refinement for (*S*)-**4s**.

| | |
|---|---|
| Identification code | (*S*)-**4s** |
| Empirical Formula | $C_{13}H_{19}NO_4$ |
| Temperature (K) | 293(2) |
| Crystal system | Orthorhombic |
| Space group | $P2_12_12_1$ |
| Unit cell dimensions | a = 7.7341(4) Å α = 90°<br>b = 8.4900(5) Å β = 90°<br>c = 20.9282(11) Å γ = 90° |

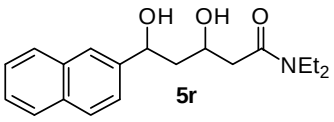
| | |
|---|---|
| Volume (Å$^3$), Z | 1374.20(13), 4 |
| Density (calculated) (mg/m$^3$) | 1.224 |
| Absorption coefficient (mm$^{-1}$) | 0.748 |
| F(000) | 544 |
| θ range for data collection (°) | 4.22 to 68.33 |
| Limiting indices | -6<=h<=9, -10<=k<=8, -25<=l<=25 |
| Reflections collected / unique | 2426 |
| Completeness to theta | 0.0268 |
| Data / restraints / parameters | 2426/0/163 |
| Goodness-of-fit on F$^2$ | 0.681 |
| Final R indices [I > 2sigma(I)] | R1=0.0415, wR2 = 0.1369 |
| R indices (all data) | R1=0.0420, wR2 = 0.1389 |
| Absolute structure parameter | 0.0(2) |
| Largest diff. peak and hole | 0.354 and -0.16 e.Å$^{-3}$ |



**4t**

***N, N*-diethyl-3-hydroxy-5-oxo-5-(thiophen-2-yl)pentanamide**

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.65 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.14 (dd, *J* = 4.9, 3.8 Hz, 1H), 4.75 (d, *J* = 3.7 Hz, 1H), 4.63-4.50 (m, 1H), 3.42-3.28 (m, 4H), 3.27-3.10 (m, 2H), 2.76-2.44 (m, 2H), 1.19-1.07 (m, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$) δ 191.2, 170.5, 143.8, 133.6, 132.3, 127.8, 65.0, 45.1, 41.5, 39.5, 38.0, 13.5, 12.5. HPLC (Chiralcel AD-H column, hexane/$^i$PrOH 89/11, 0.7 mL min$^{-1}$, 254 nm): $t_1$ = 27.7 min, $t_2$ =31.7 min. HRMS Calculated for $C_{13}H_{17}NO_3S$ (M+Na): 290.0827, found: 290.0825. $[\alpha]^{25}_D$ = 24.6 (c 0.56, $CH_2Cl_2$).



**5r**

***N,N*-diethyl-3,5-dihydroxy-5-(naphthalen-2-yl)pentanamide**

$^1$H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.71 (m, 4H), 7.59 – 7.35 (m, 3H), 5.21 – 5.11 (m, 2H), 4.44 (d, *J* = 17.6 Hz, 2H), 3.46 – 3.16 (m, 4H), 2.43 (qd, *J* = 16.4, 6.0 Hz, 2H), 2.06 – 1.79 (m, 2H), 1.22 – 1.10 (m, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 171.1, 141.8, 133.1, 132.6, 127.8, 127.8, 127.4, 125.8, 125.4, 124.2, 124.0, 74.0, 68.8, 44.8, 41.7, 40.0, 39.0, 25.1, 13.8, 12.8.

## 5. References

1 J. S. Hubbard and T. M. Harris, *J. Org. Chem.*, 1981, **46**, 2566.

2 H. T. Ravert, W. B. Mathews, J. L. Musachio and R. F. Dannals, *J. Labelled Compd. Radiopharm.*, 1995, **36**, 365.

3 P. Wipf and J. P. Maciejewski, *Org. Lett.*, 2008, **10**, 4383 Page *S14* of Supporting Information.

4 T. N. Yoshino, Fay; Danishefsky, Samuel J. , *J. Am. Chem. Soc.*, 2006, **128**, 14185.

5 J. Stewart Witzeman and W. Dell Nottingham, *J. Org. Chem.*, 1991, **56**, 1713.

6 W.-F. Li, X. Ma, W.-Z. Fan, X.-M. Tao, X.-M. Li, X.-M. Xie and Z.-G. Zhang, *Org. Lett.*, 2011, **13**, 3876.

7 (a) T. Persson and J. Nielsen, *Org. Lett.*, 2006, **8**, 3219; (b) K. Uehara, C. B. Wagner, T. Vogler, H.

Luftmann and A. Studer, *Angew. Chem. Int. Ed.*, 2010, **49**, 3073; (c) J. M. Kraus, C. L. M. J. Verlinde, M. Karimi, G. I. Lepesheva, M. H. Gelb and F. S. Buckner, *J. Med. Chem.*, 2009, **52**, 1639; (d) D. K. Friel, M. L. Snapper and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2008, **130**, 9942; (e) K.-H. Lee, C.-E. Park, K.-H. Min, Y.-J. Shin, C.-M. Chung, H.-H. Kim, H.-J. Yoon, K. Won, E.-J. Ryu, Y.-J. Shin, H.-S. Nam, J.-W. Cho and H.-Y. Lee, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 5567; (f) T. Hiyama, G. B. Reddy, T. Minami and T. Hanamoto, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 350.

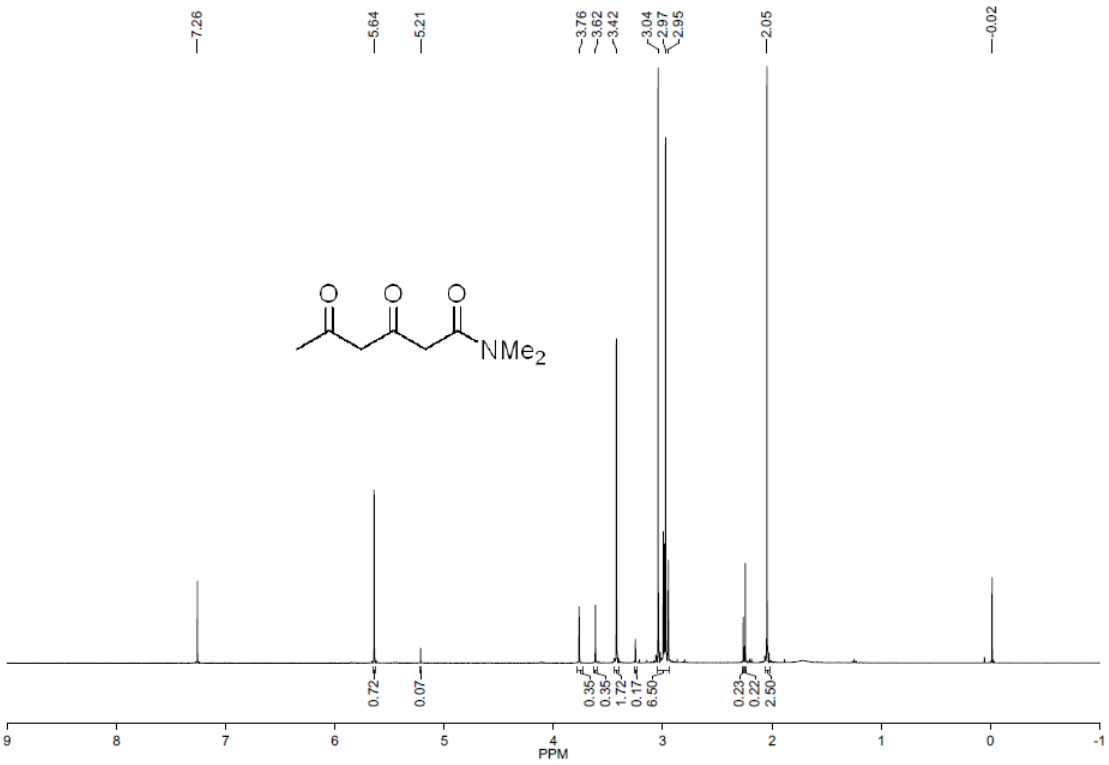
8 M. Wolberg, W. Hummel and M. Müller, *Chem.—Eur. J.*, 2001, **7**, 4562.

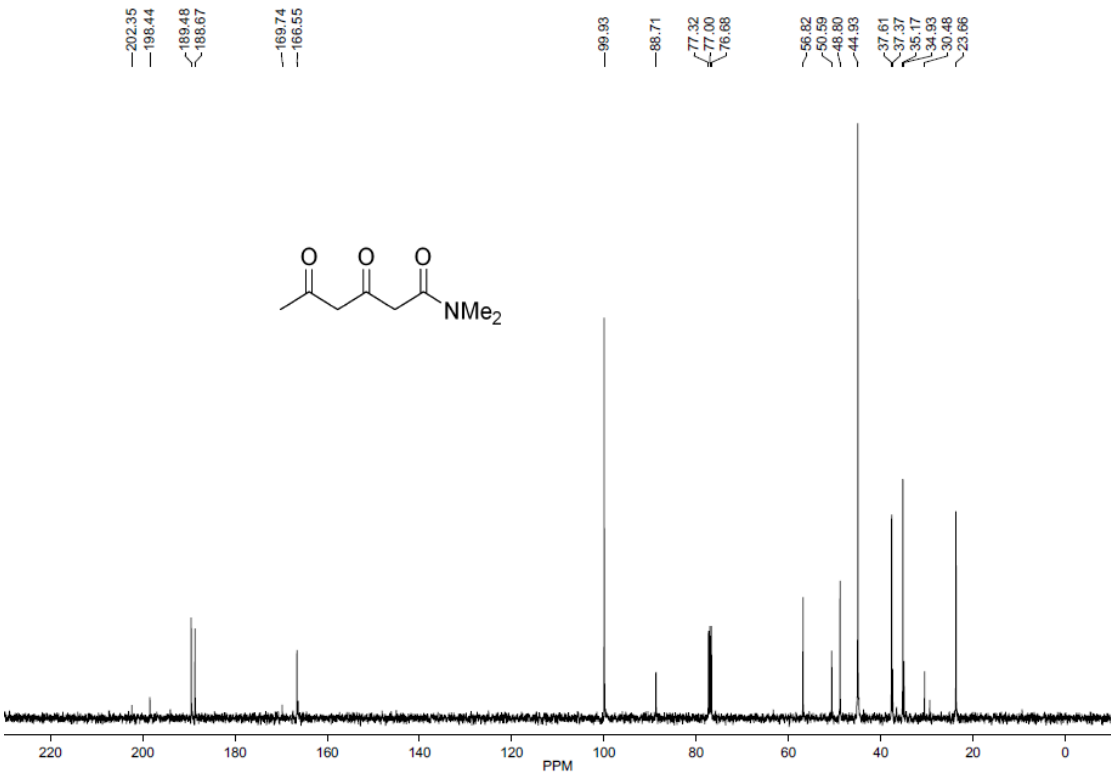
9 J. S. Hubbard and T. M. Harris, *Tetrahedron Lett.*, 1978, **47**, 4601.

10 B. Lygo, *Tetrahedron*, 1995, **51**, 12859.

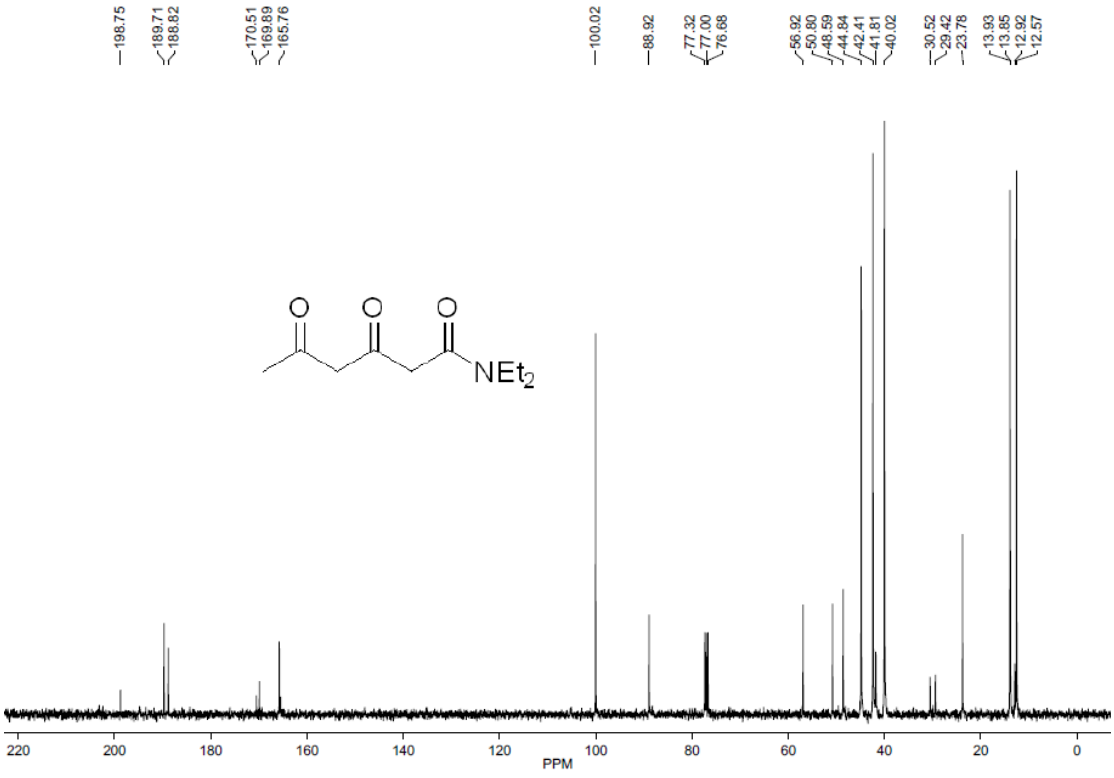
## 6. NMR Copies for 1-5

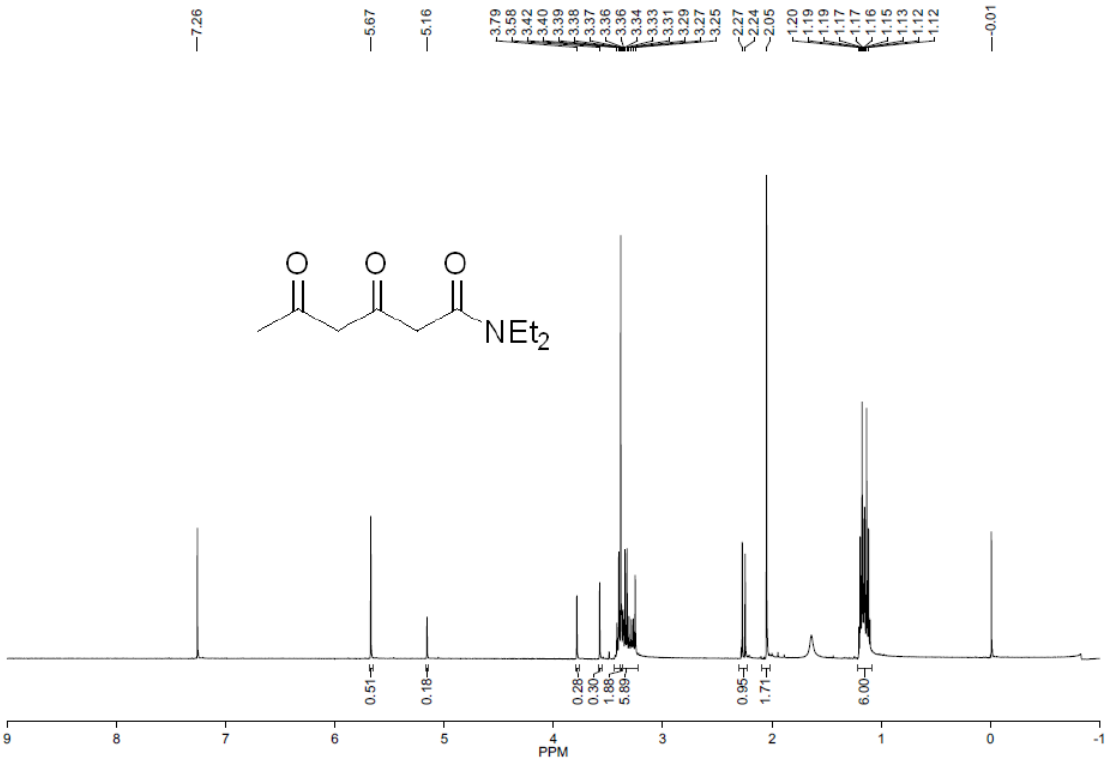
### (1a) *N, N*-dimethyl-3, 5-dioxohexanamide



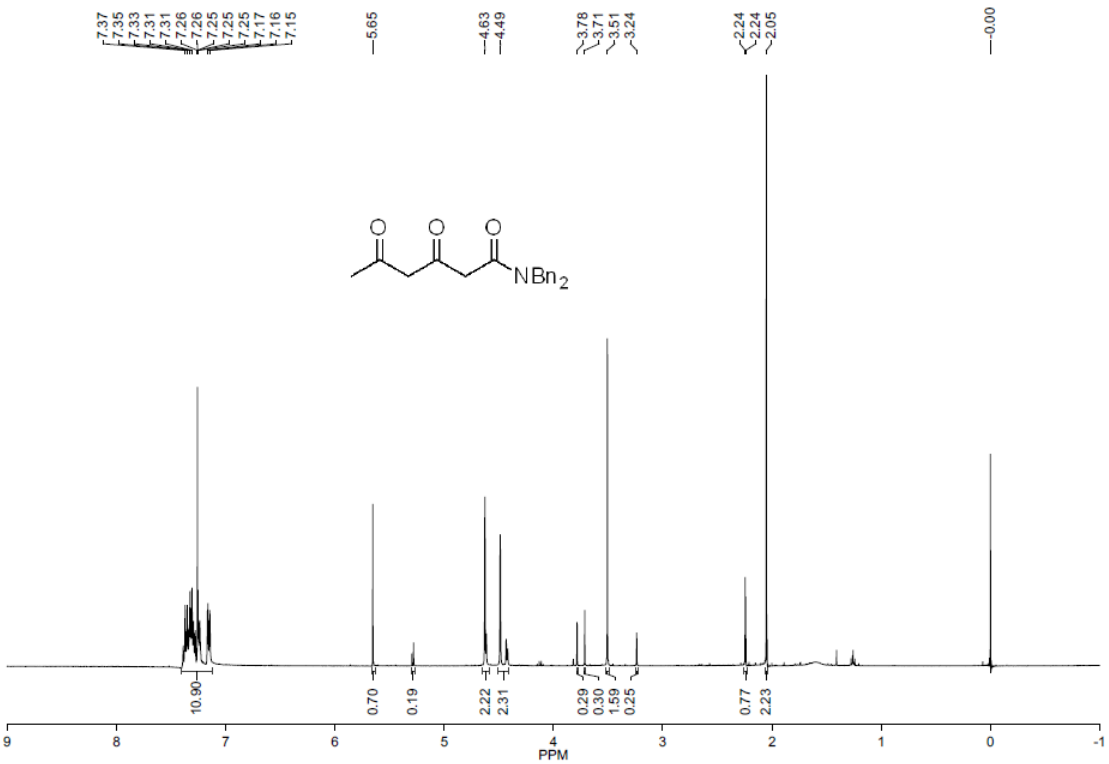


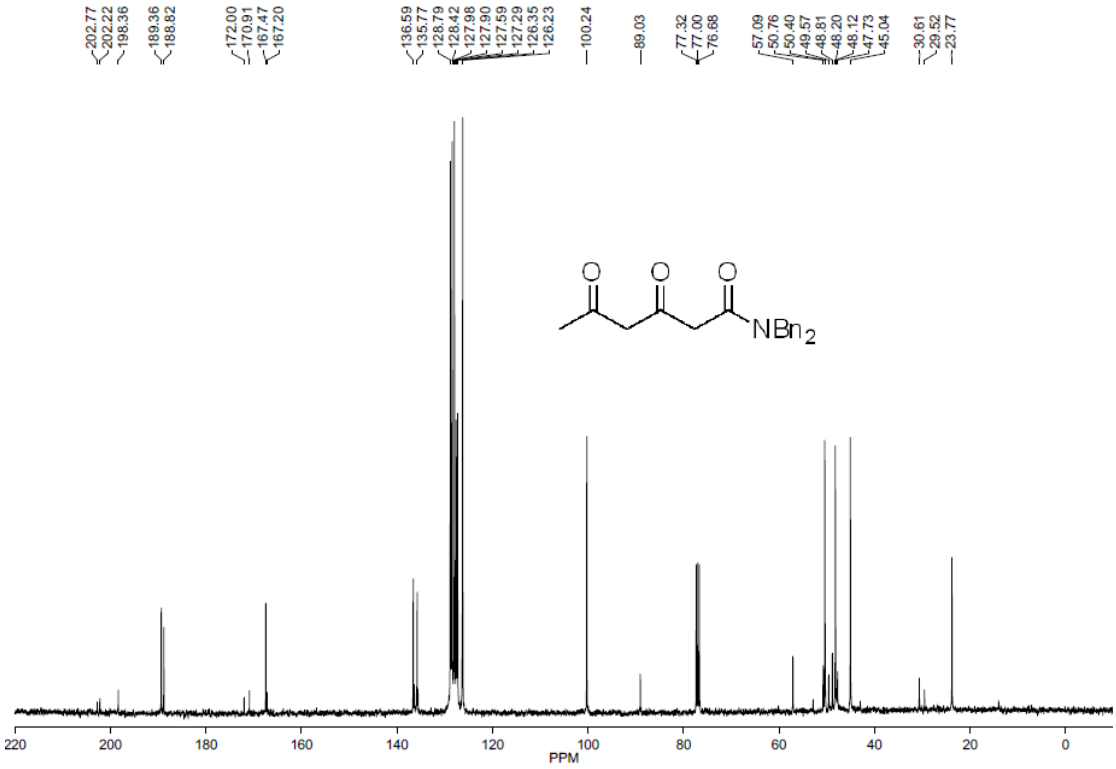

**(1b) *N*, *N*-diethyl-3, 5-dioxohexanamide**



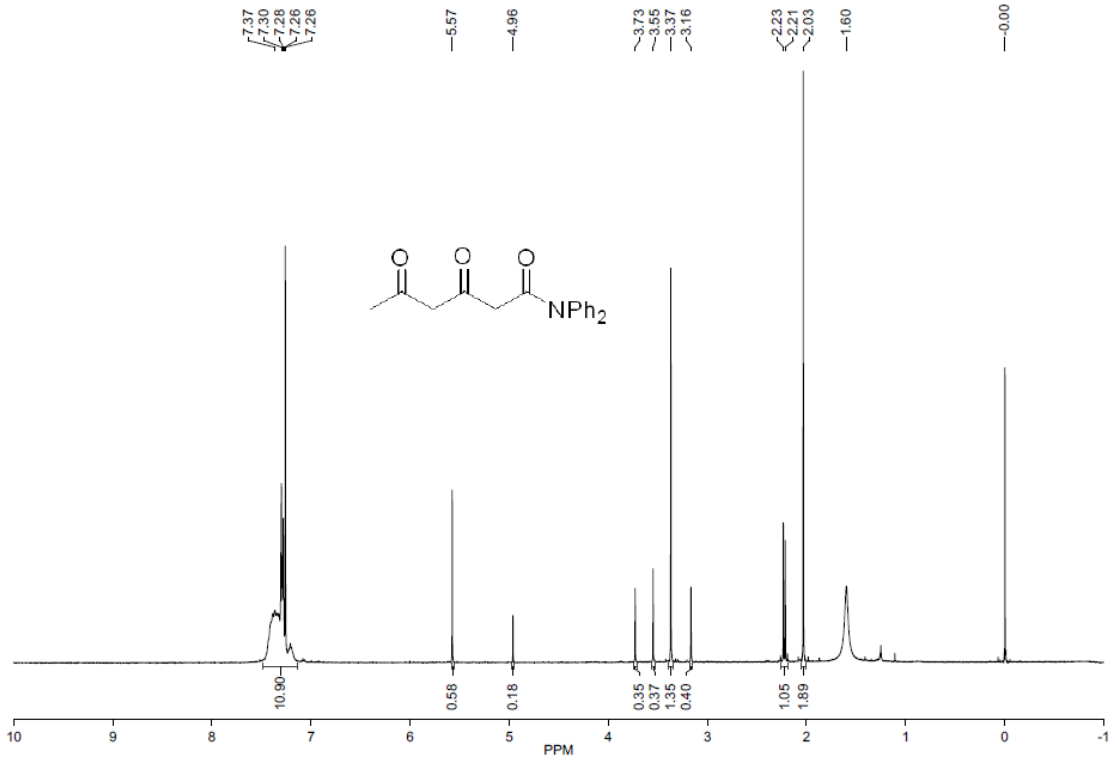


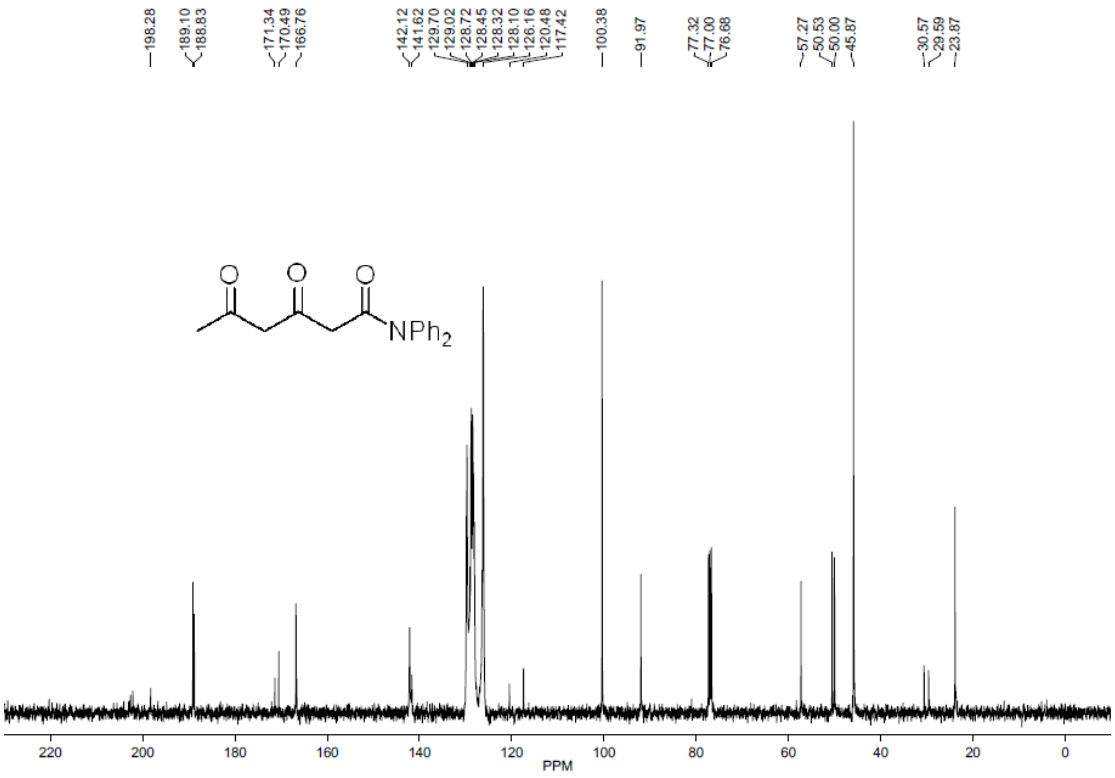

**(1c) *N, N*-dibenzyl-3, 5-dioxohexanamide**



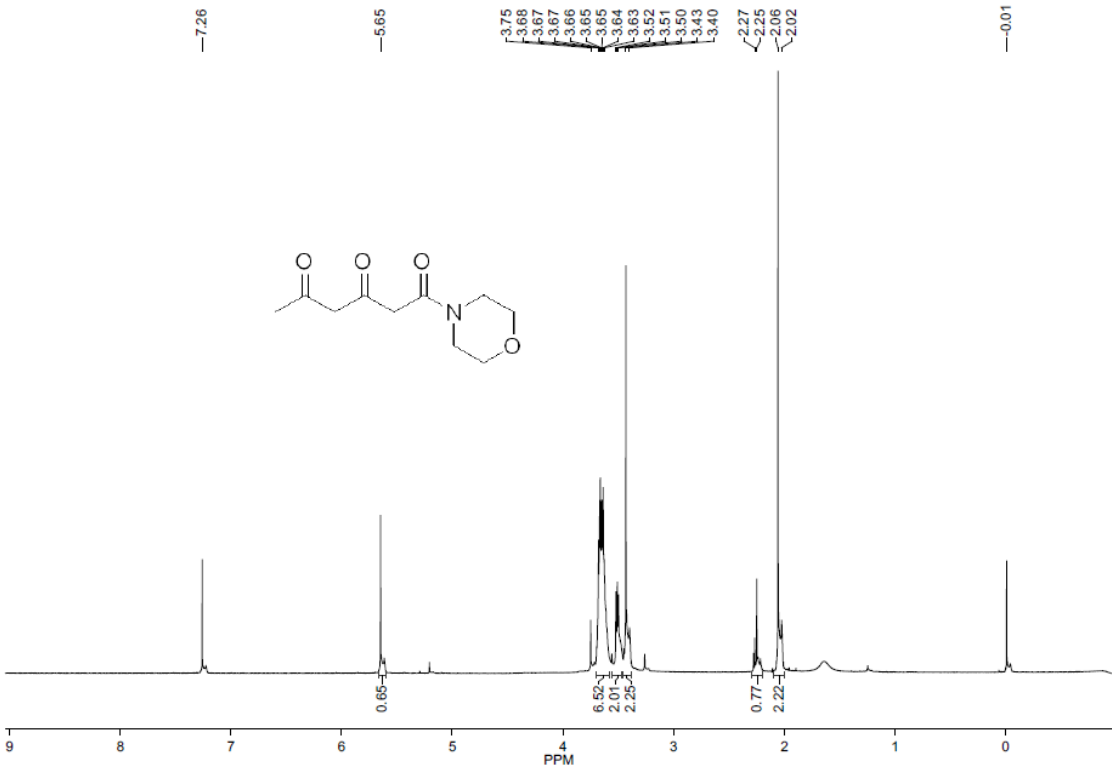


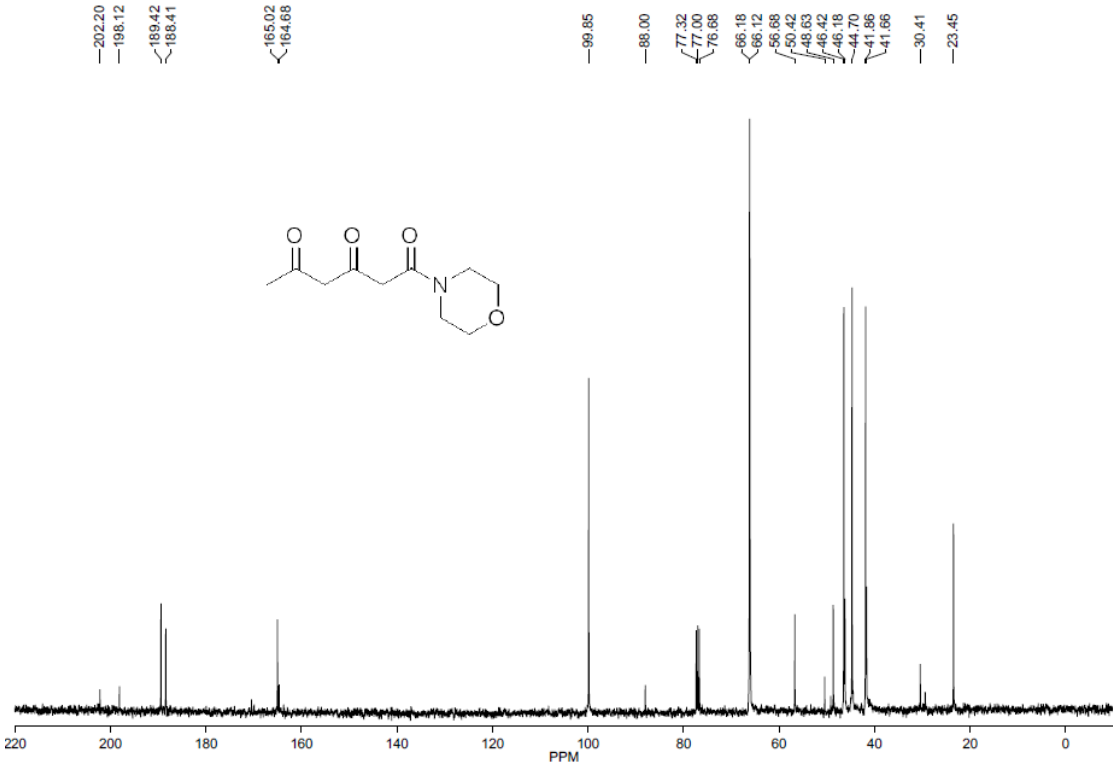

**(1d) 3, 5-dioxo-*N*, *N*-diphenylhexanamide**



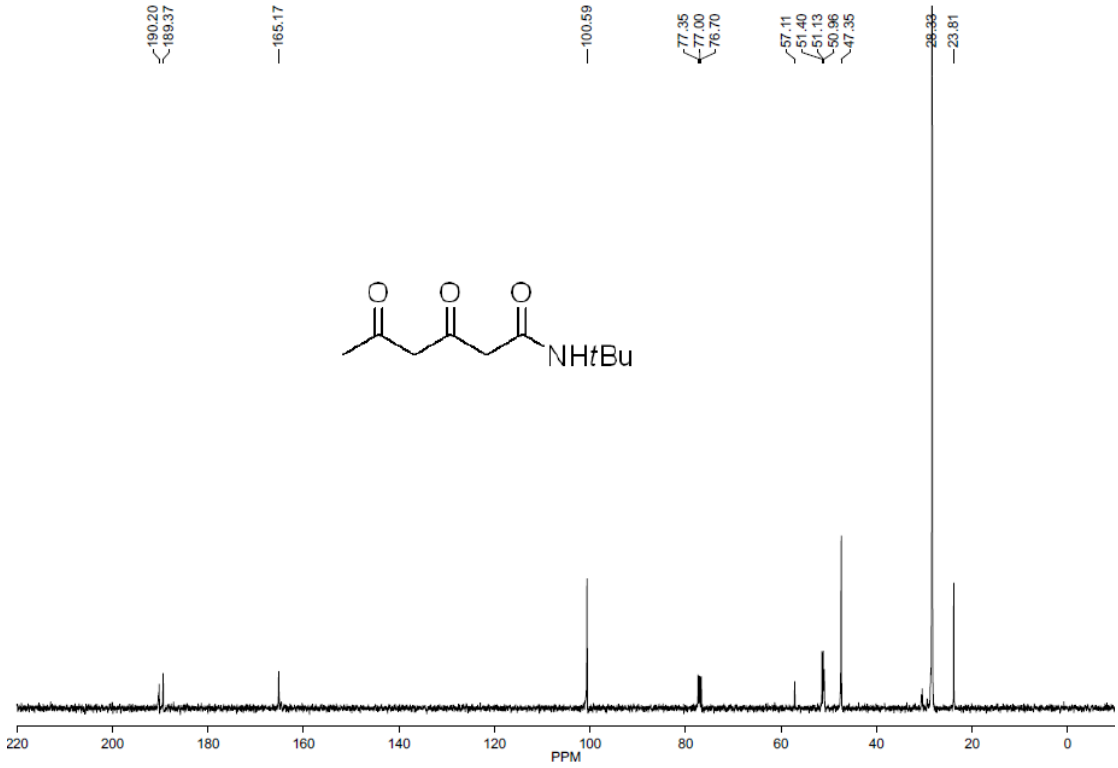



**(1e) 1-morpholinohexane-1, 3, 5-trione**

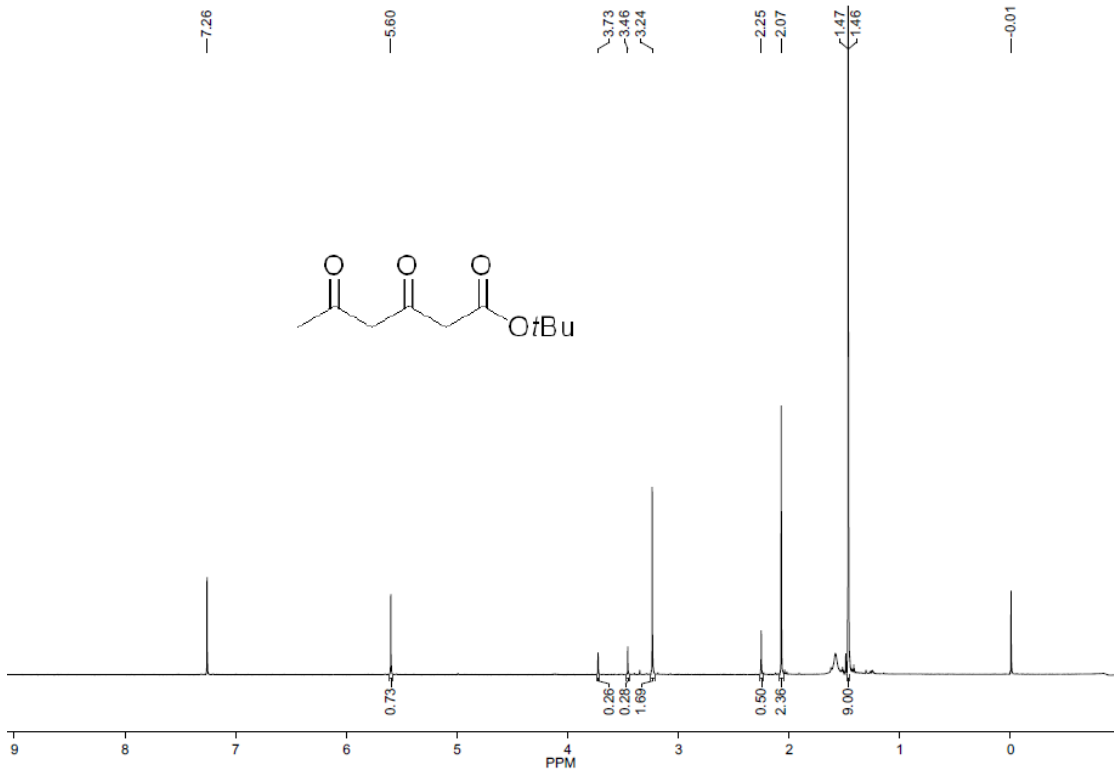


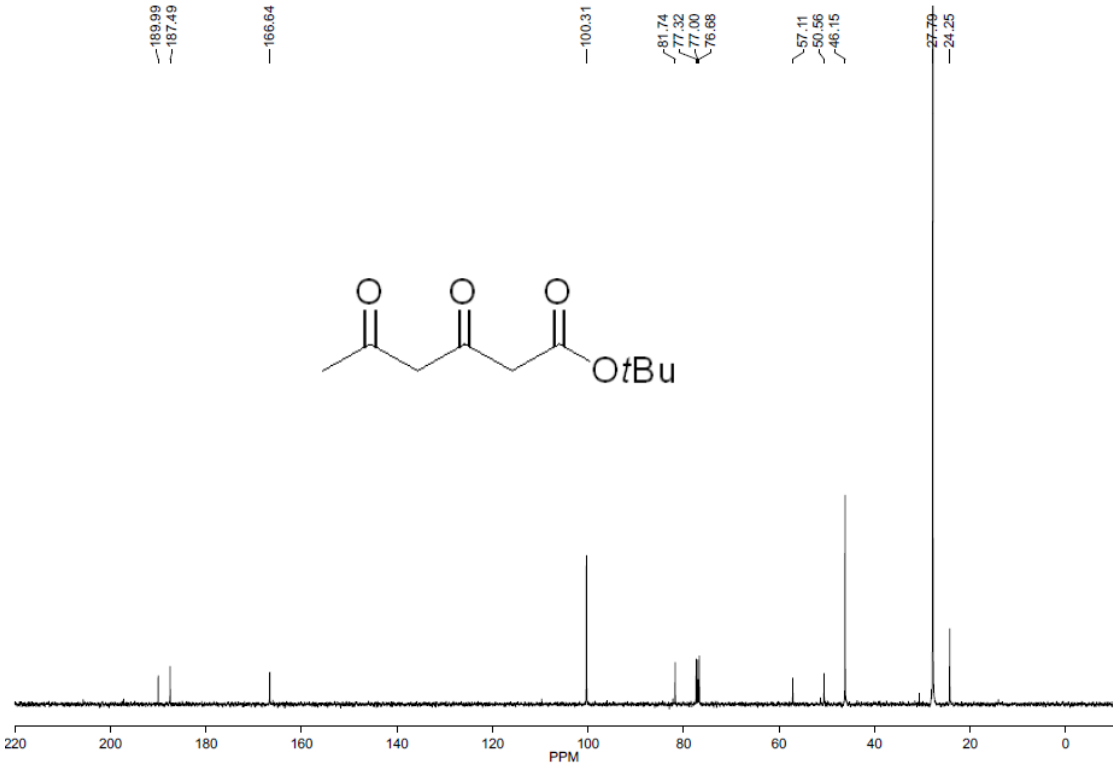



**(1f) *N*-(tert-butyl)-3, 5-dioxohexanamide**

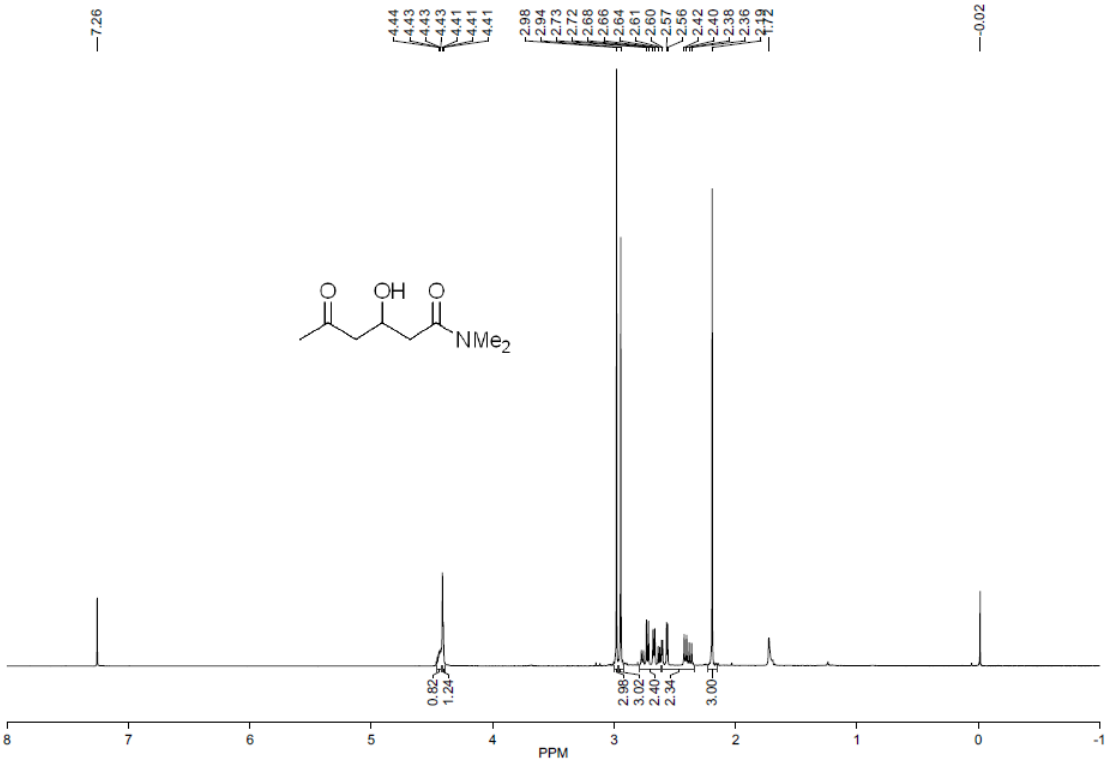


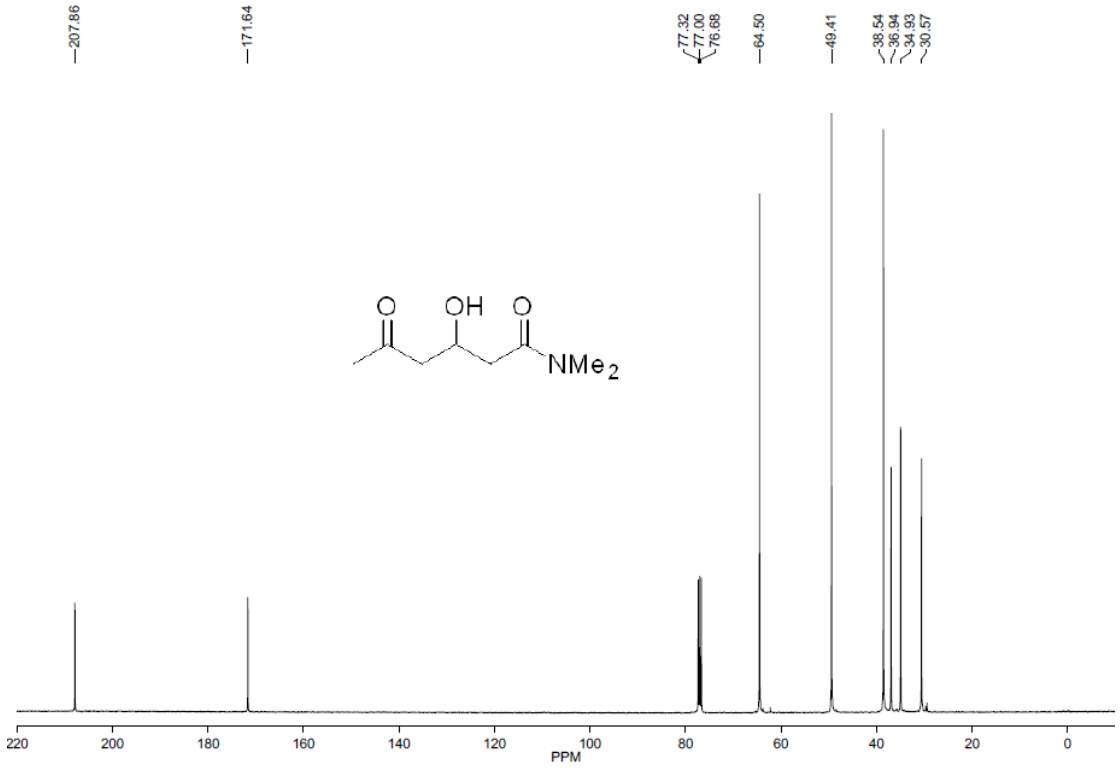

**(1g) tert-butyl 3, 5-dioxohexanoate**



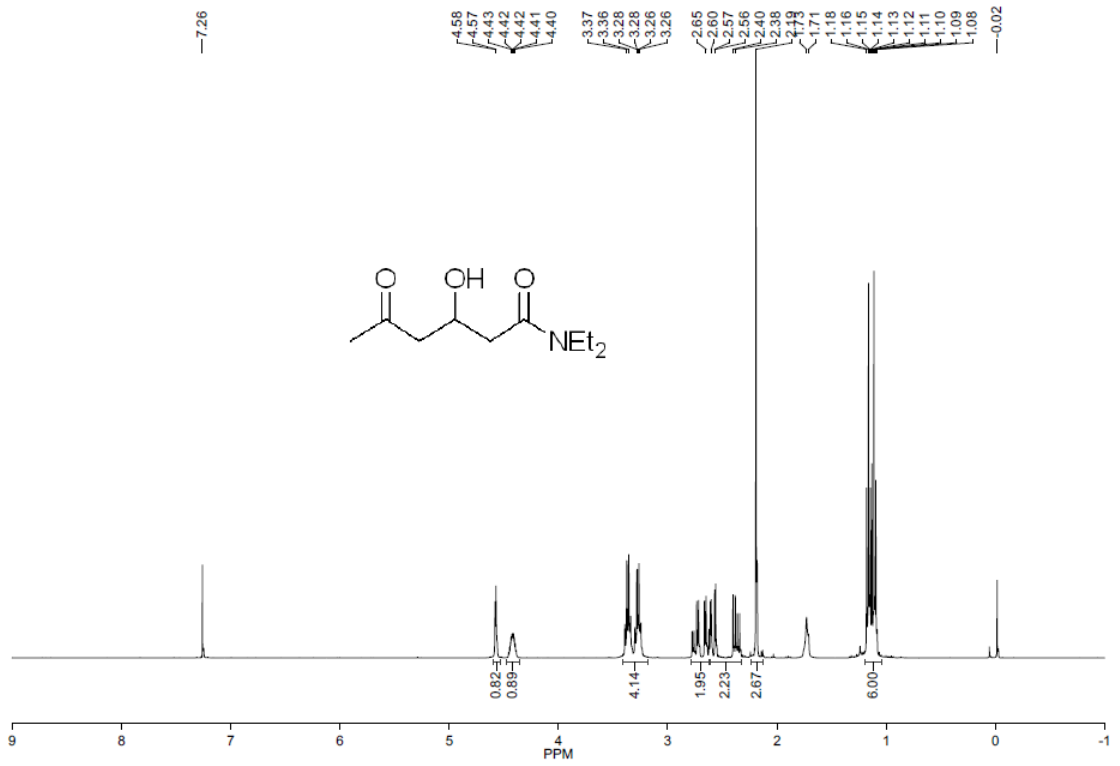


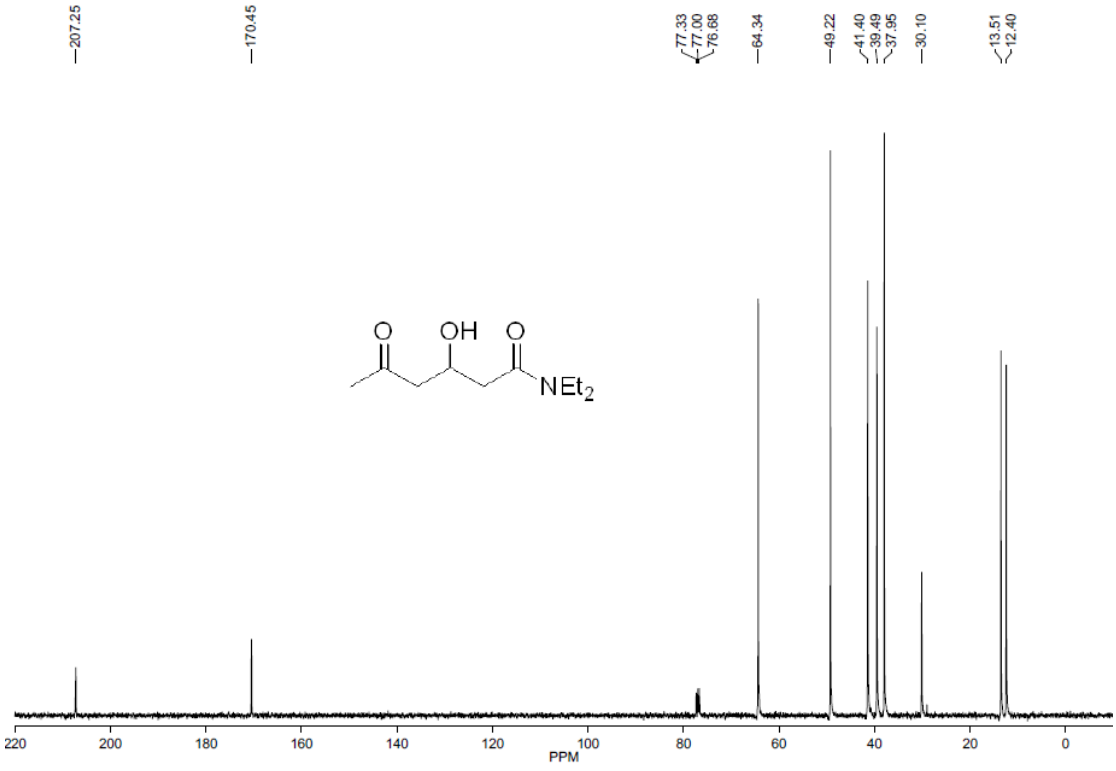

**(2a) 3-Hydroxy-*N*, *N*-dimethyl-5-oxohexanamide**



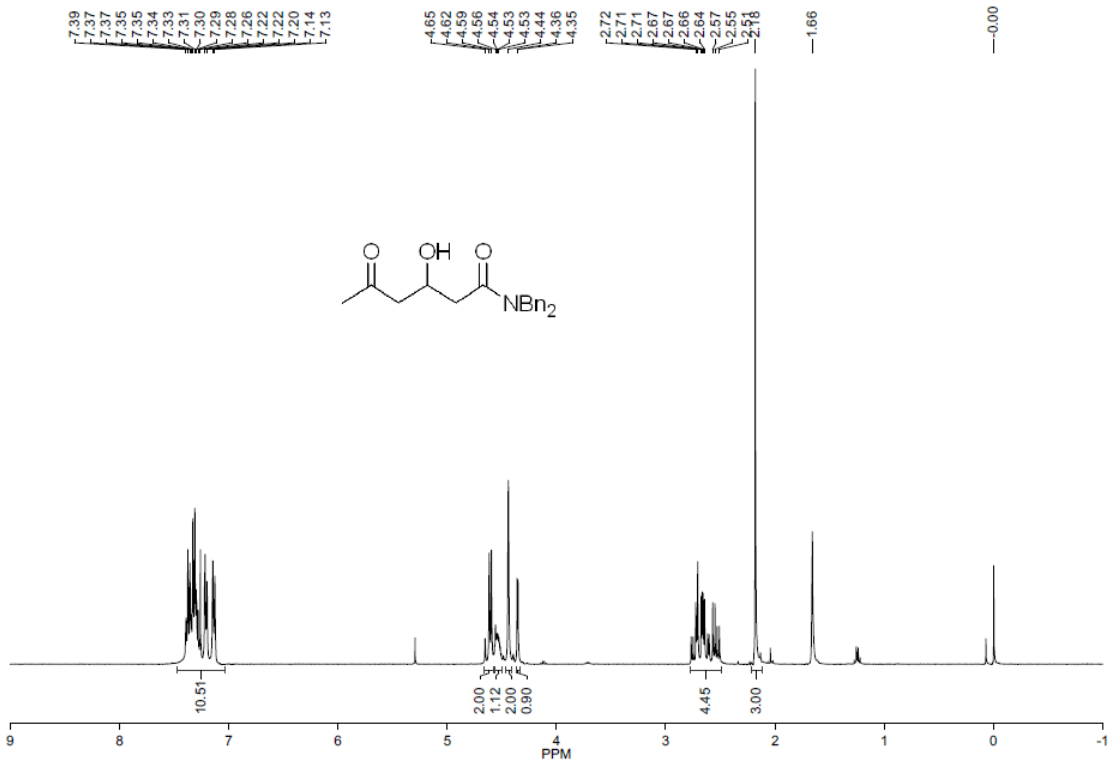


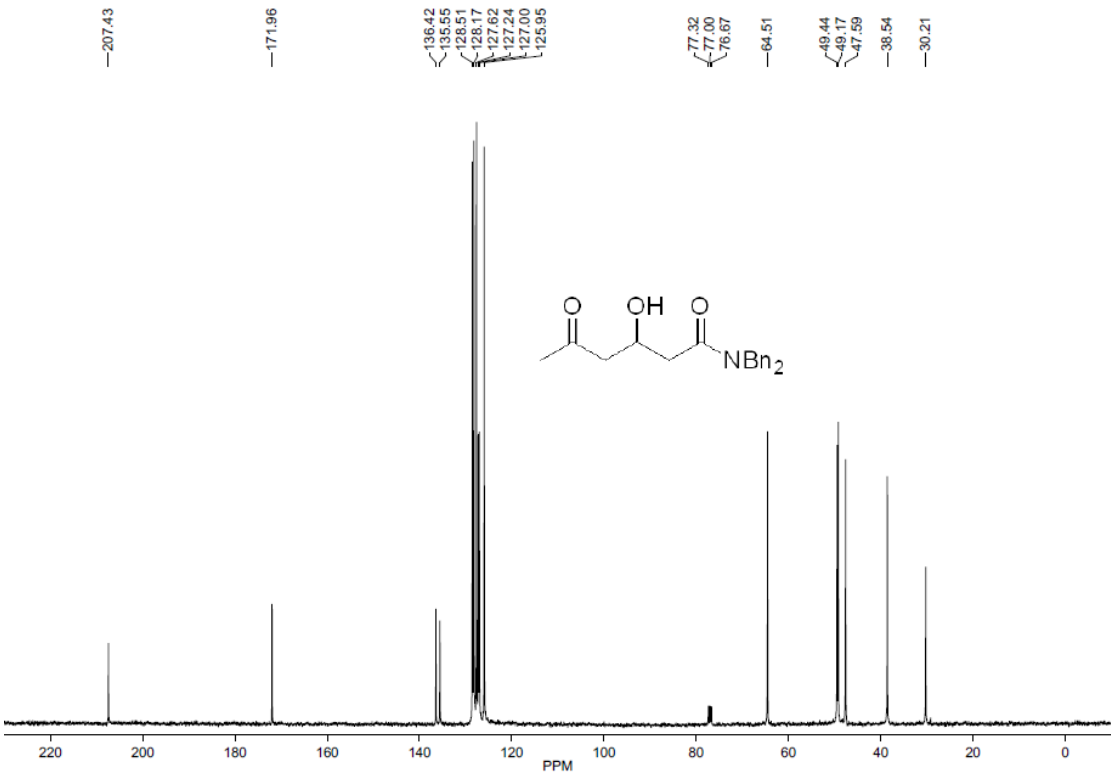

**(2b) 3-Hydroxy-*N*, *N*-diethyl-5-oxohexanamide**



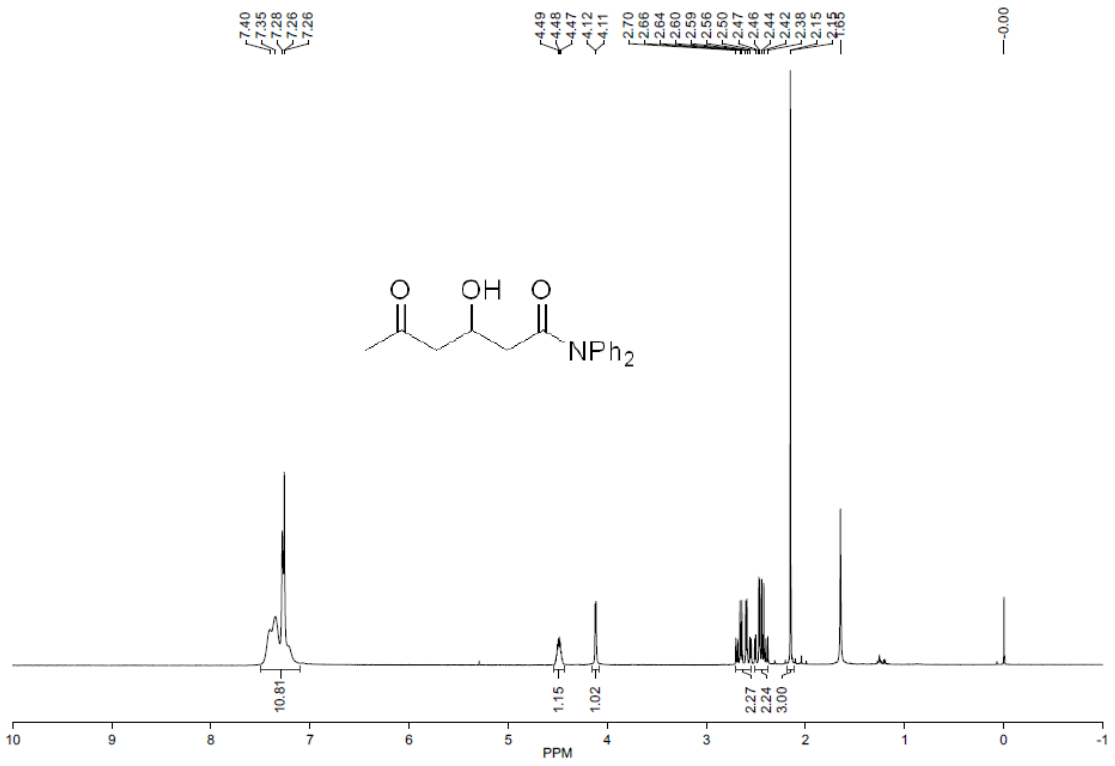


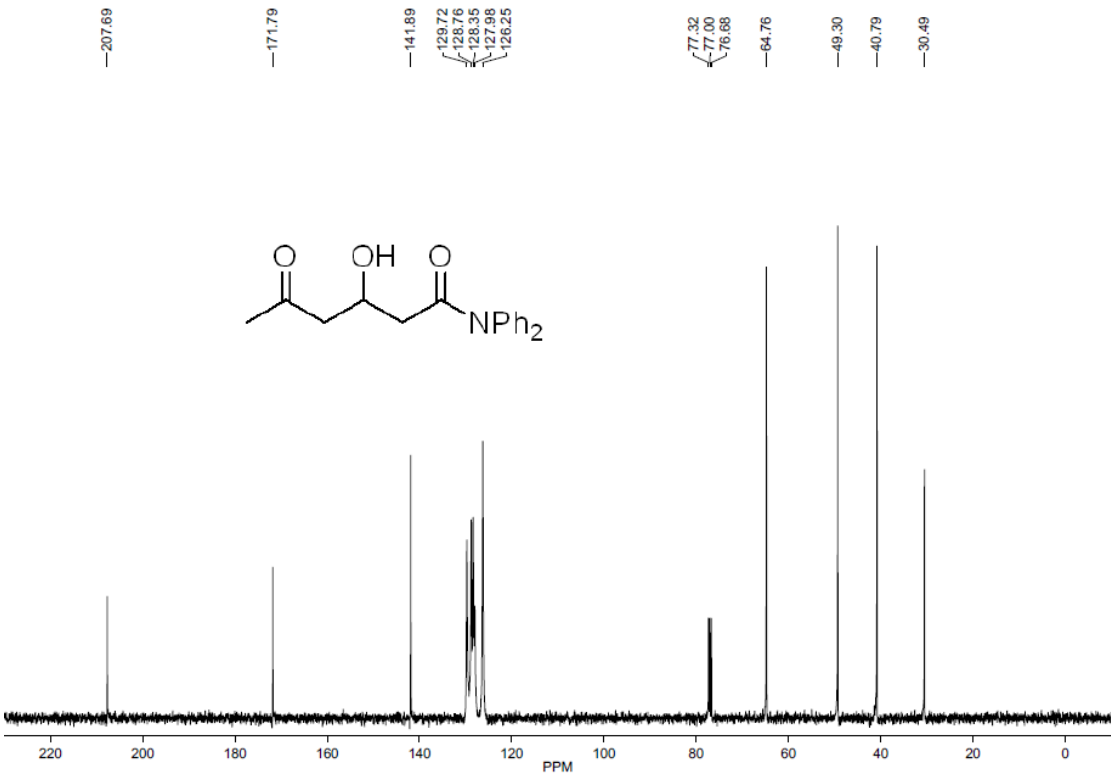

**(2c) *N*, *N*-dibenzyl-3-hydroxy-5-oxohexanamide**



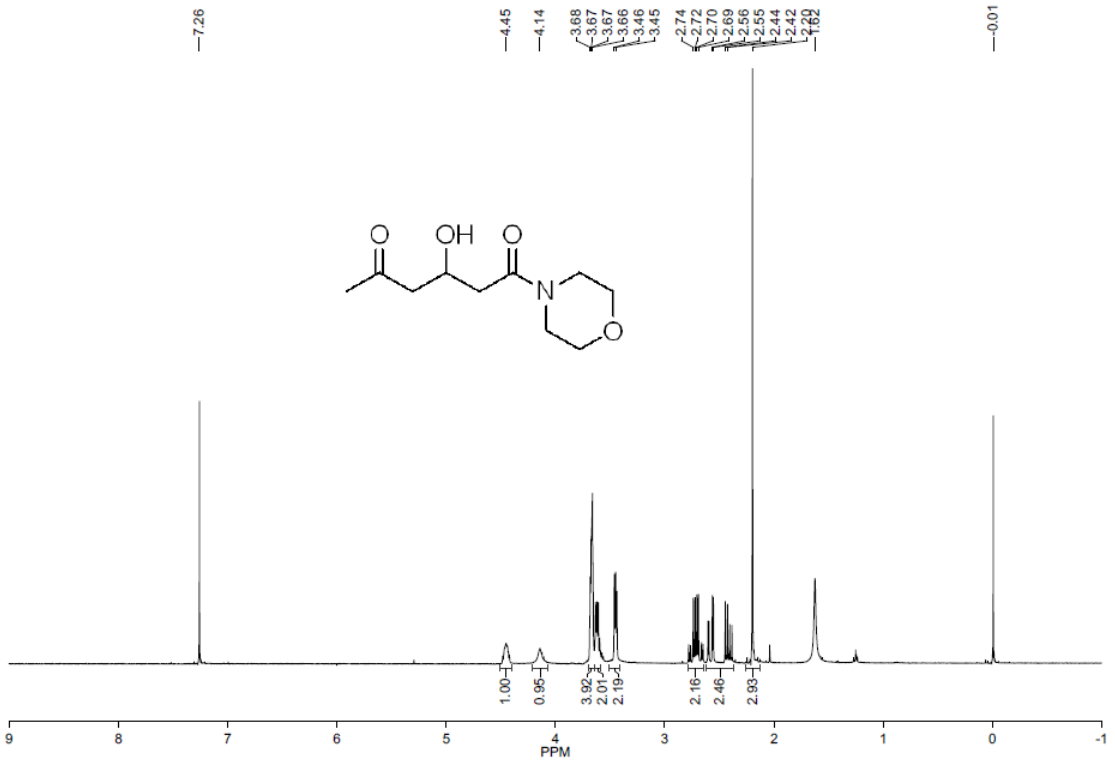


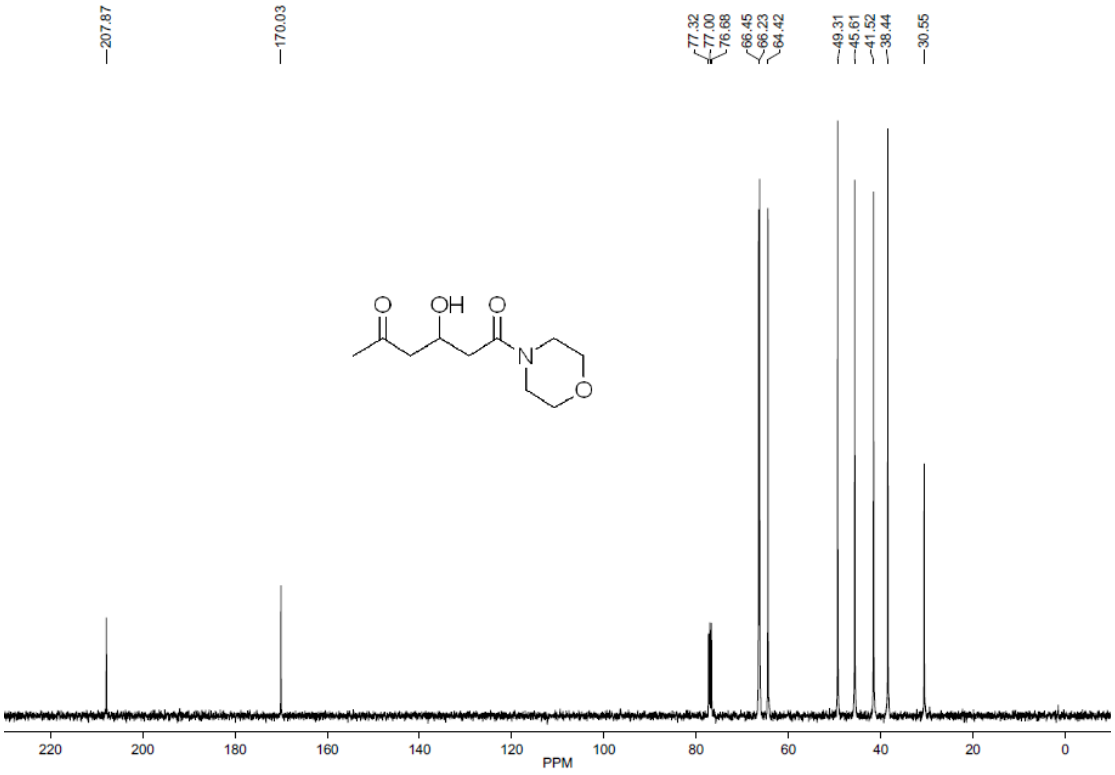

**(2d) 3-hydroxy-5-oxo-*N*, *N*-diphenylhexanamide**



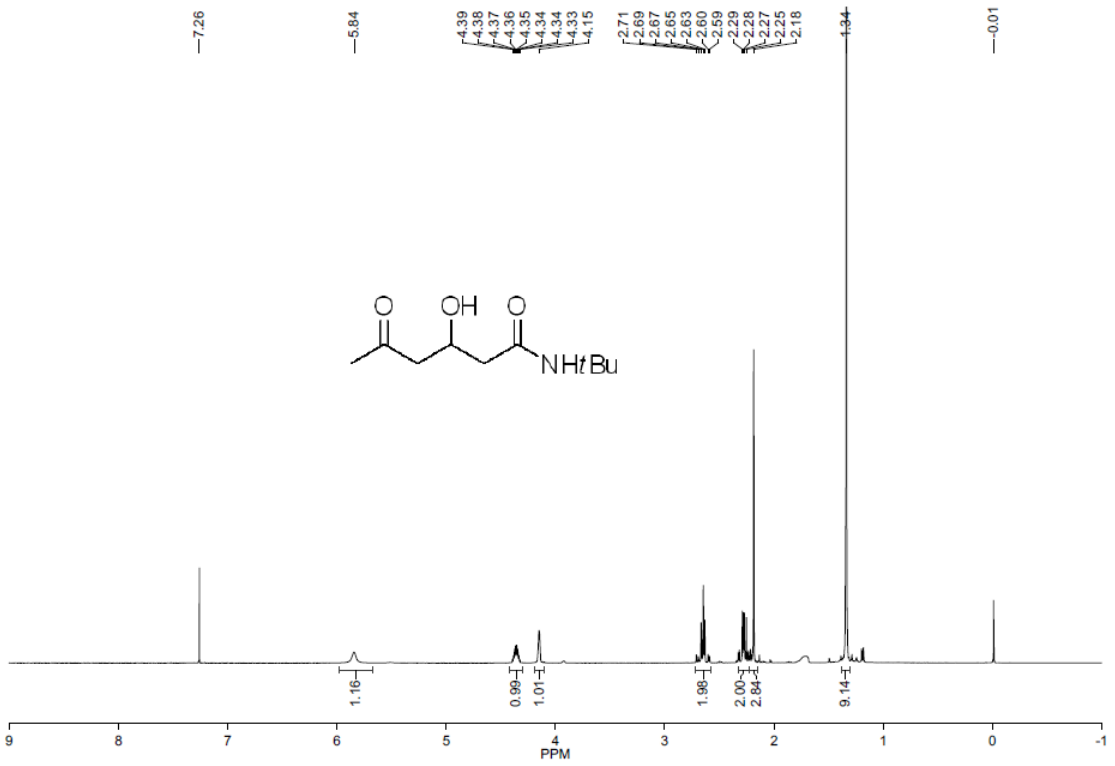


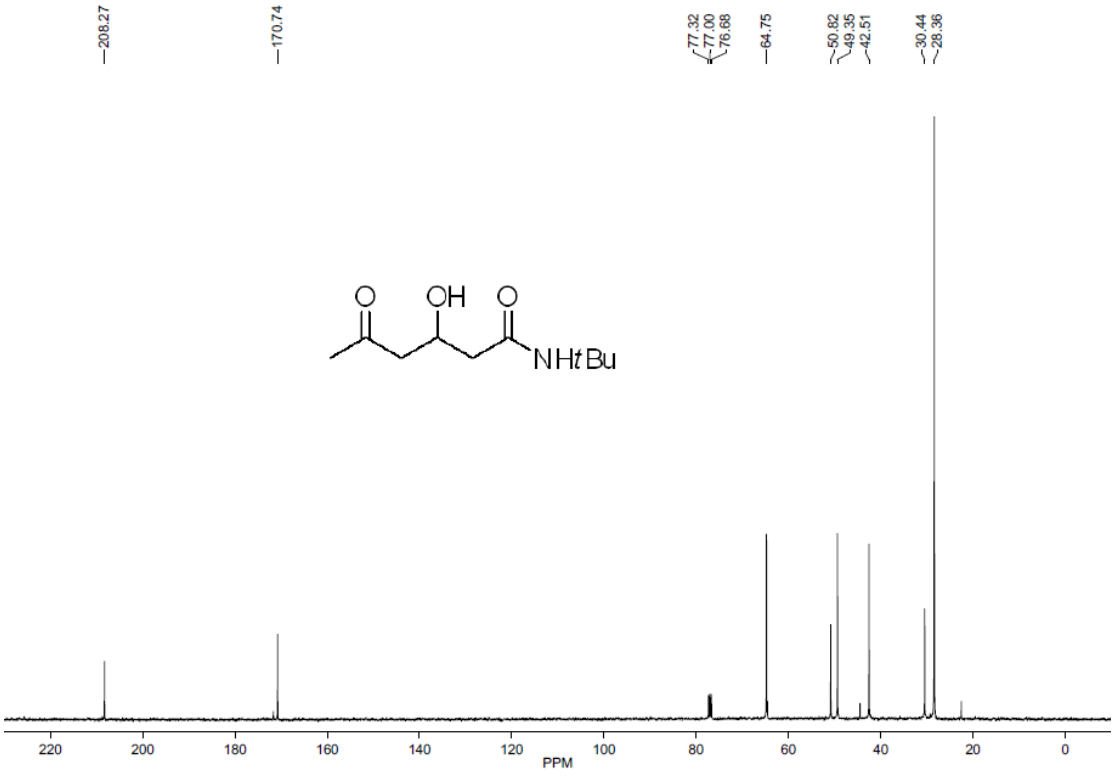

**(2e) 3-hydroxy-1-morpholinohexane-1, 5-dione**



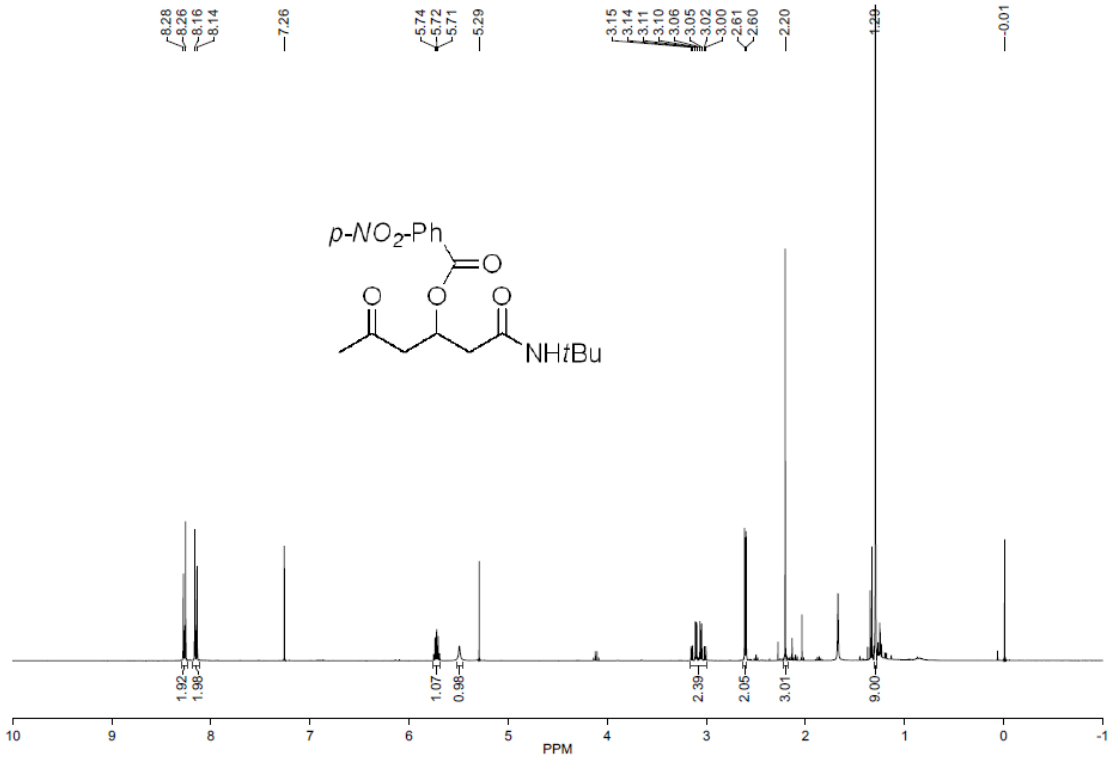


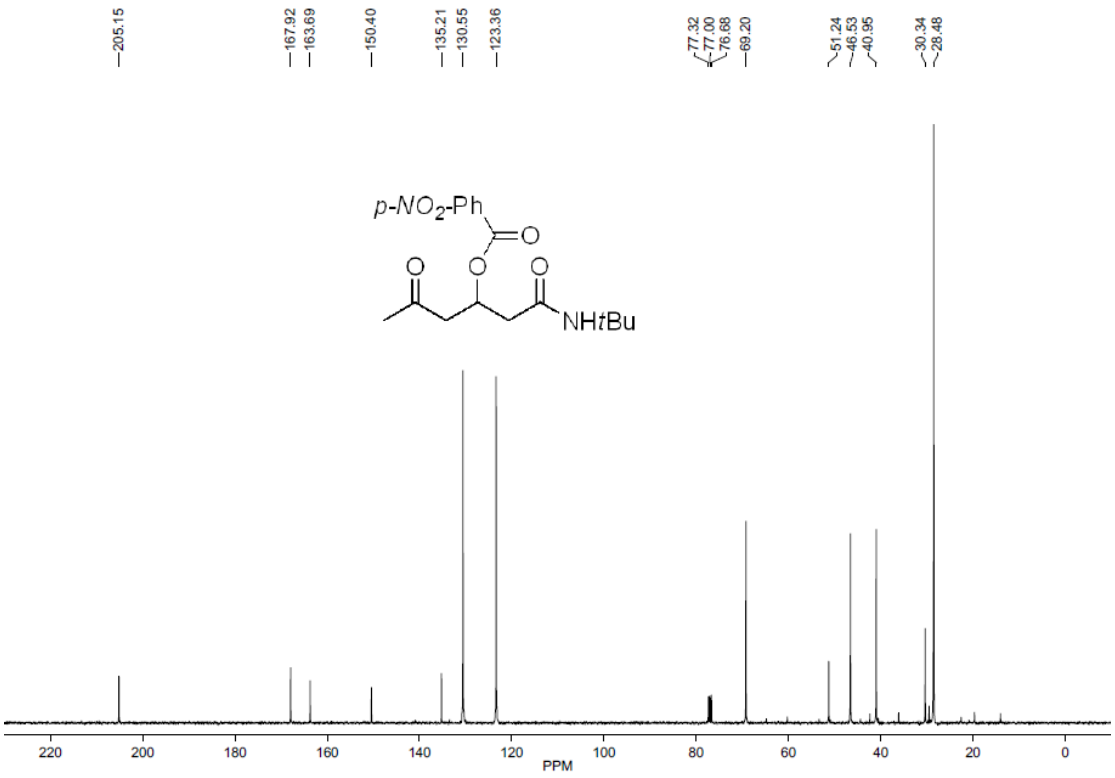

**(2f) *N*-(tert-butyl)-3-hydroxy-5-oxohexanamide**



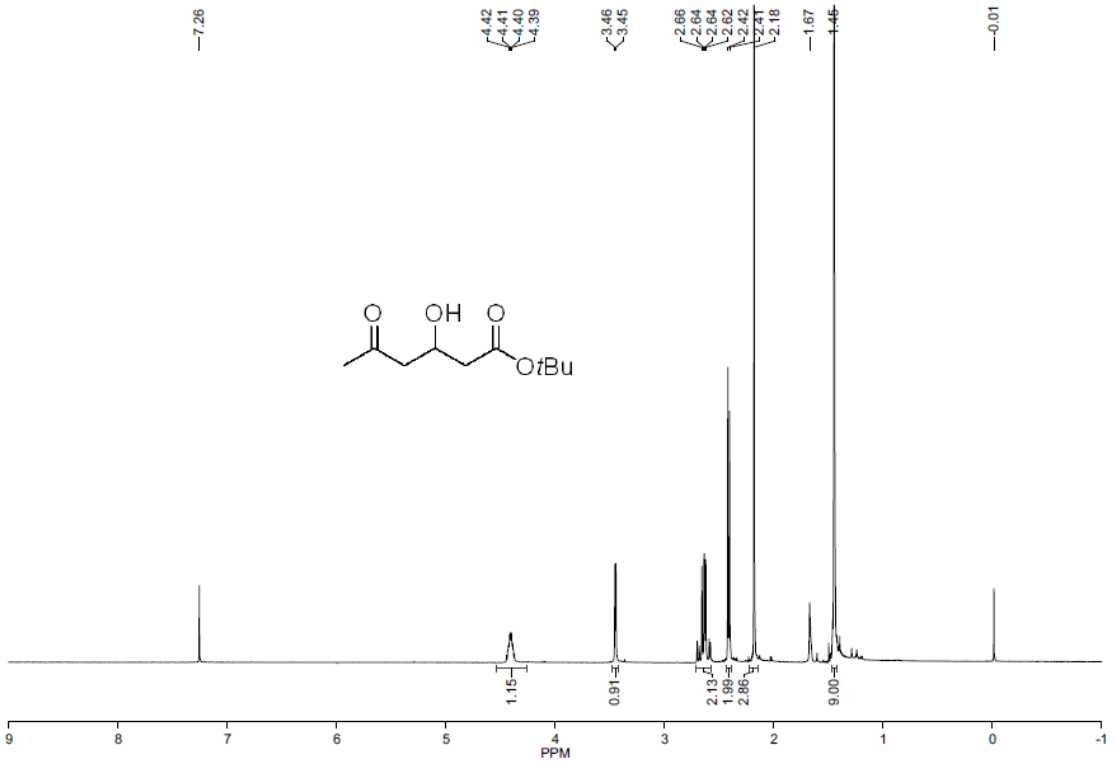


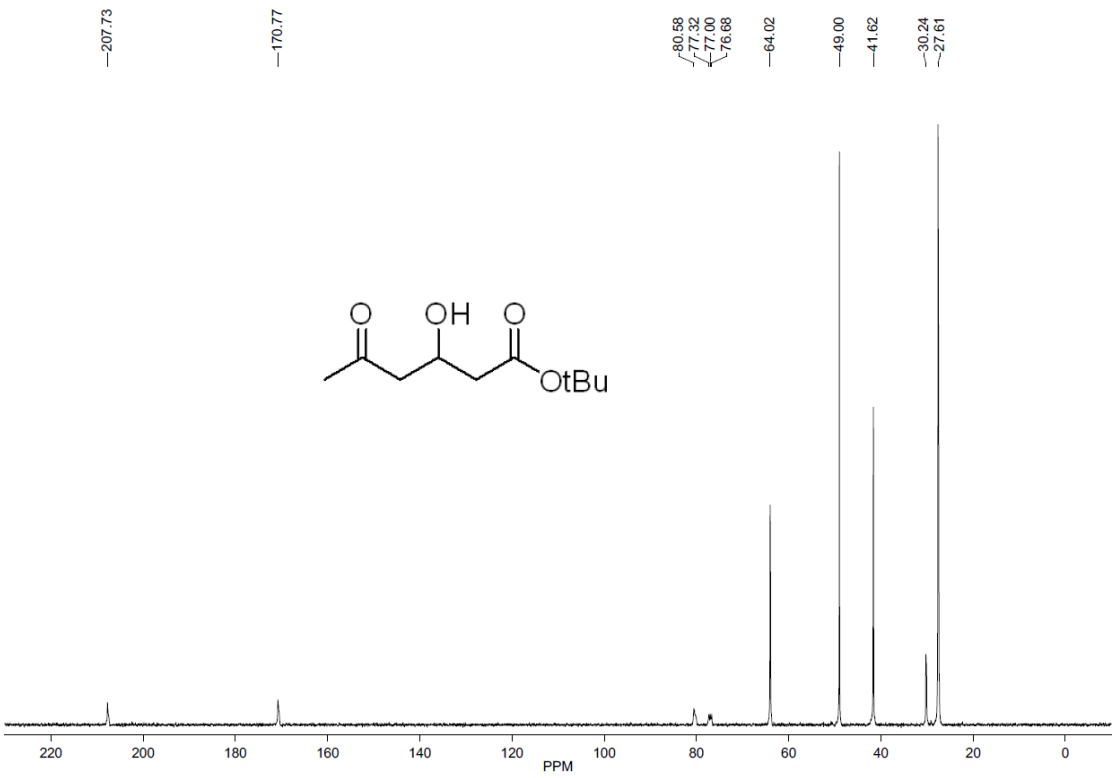

**2f-derivative: 1-(tert-butylamino)-1, 5-dioxohexan-3-yl 4-nitrobenzoate**



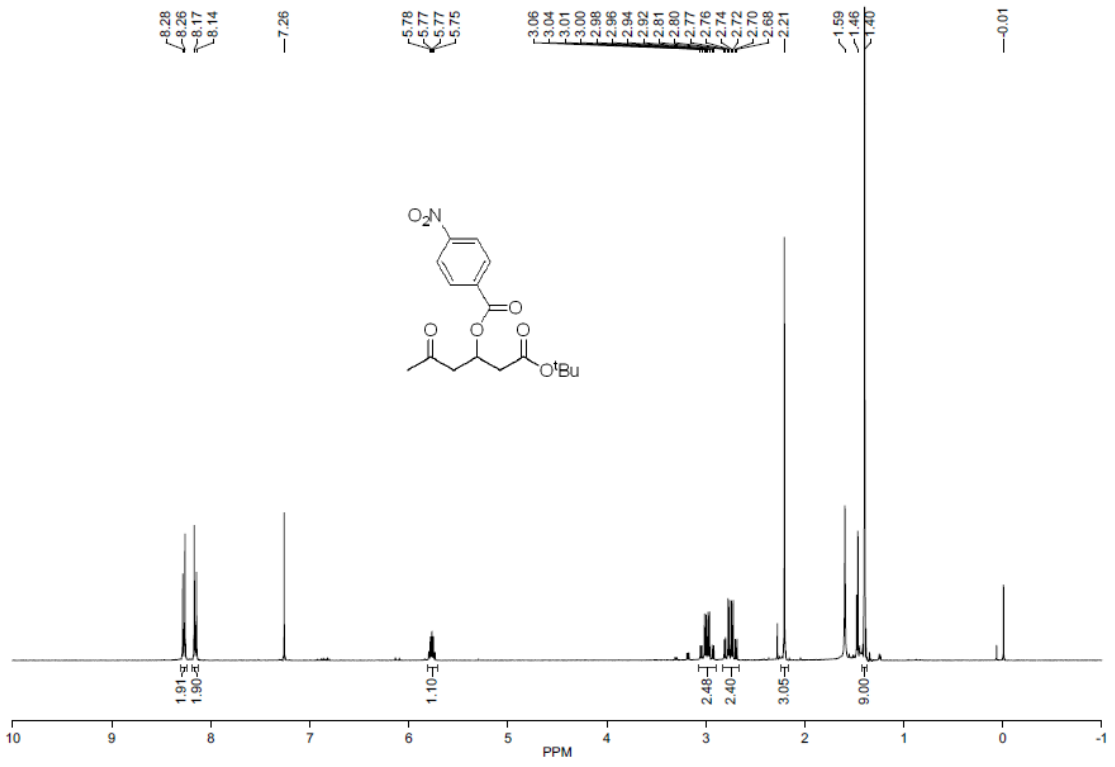


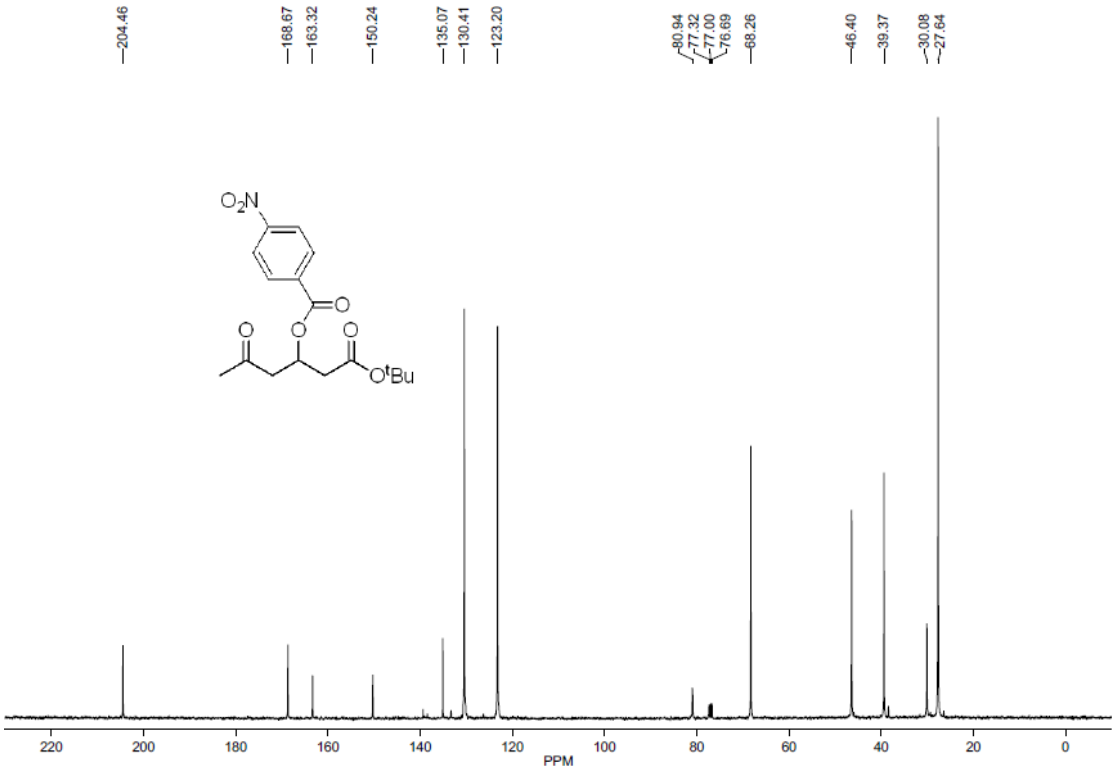

**(2g) tert-butyl 3-hydroxy-5-oxohexanoate**



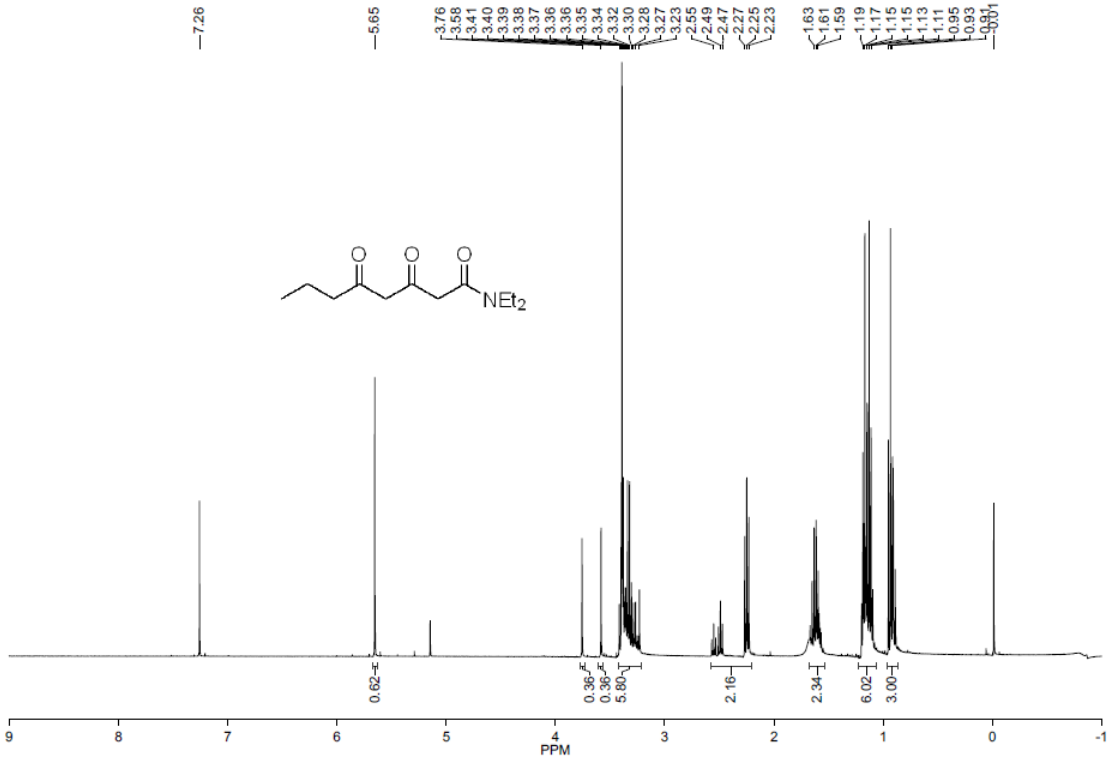


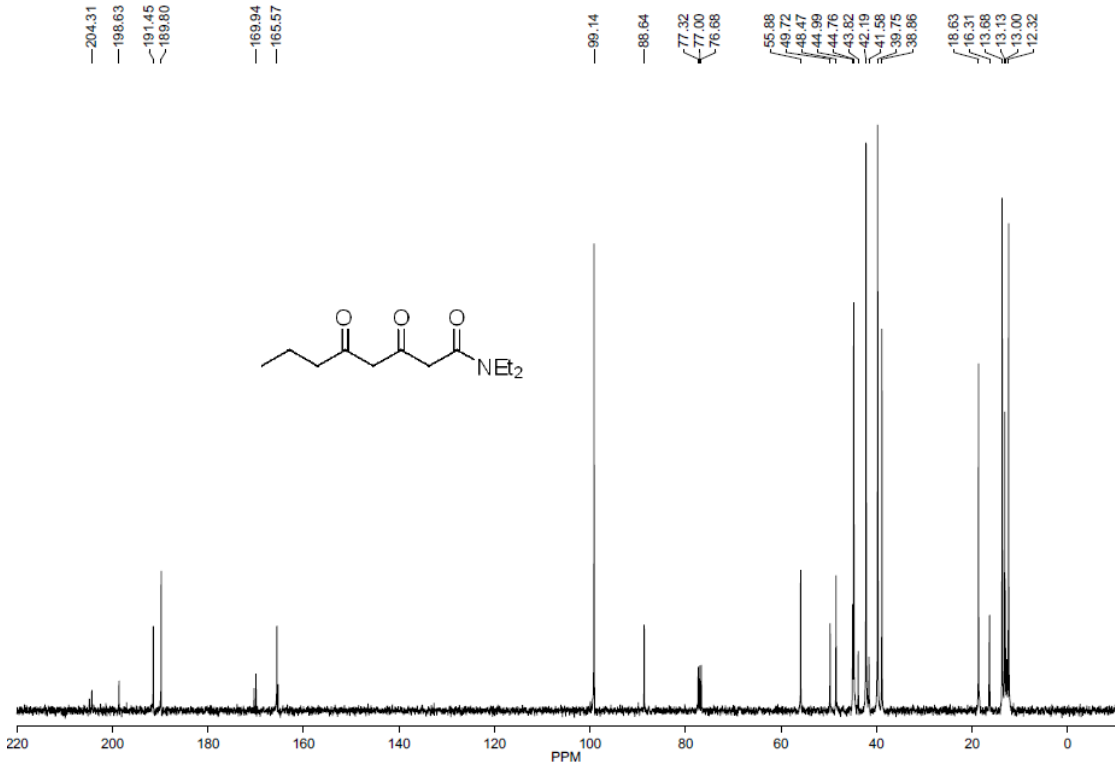

**2g-derivative: 1-(tert-butoxy)-1,5-dioxohexan-3-yl 4-nitrobenzoate**



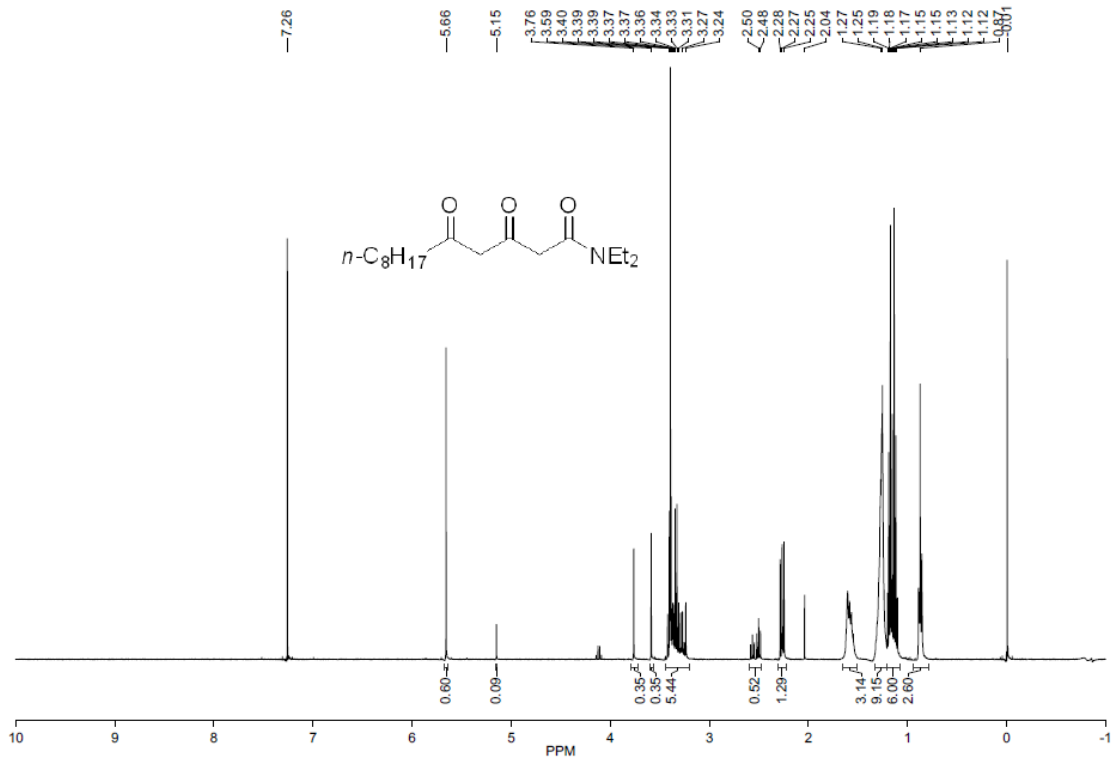


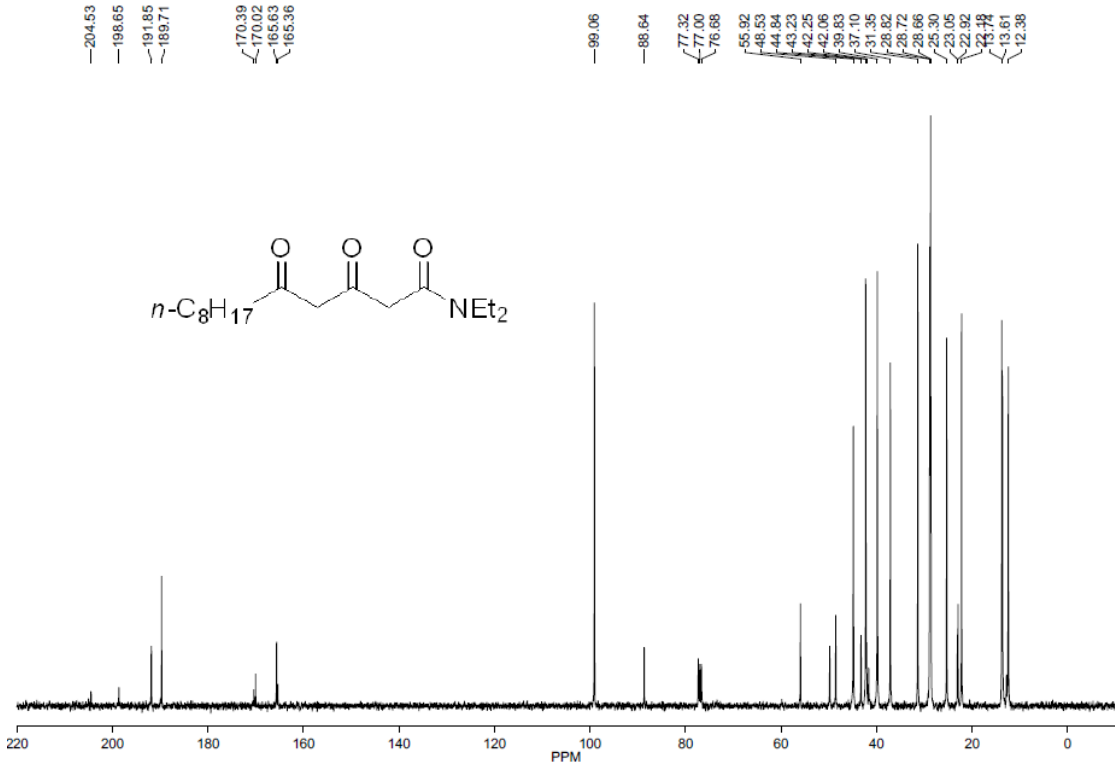

**(3a) *N*, *N*-diethyl-3, 5-dioxooctanamide**



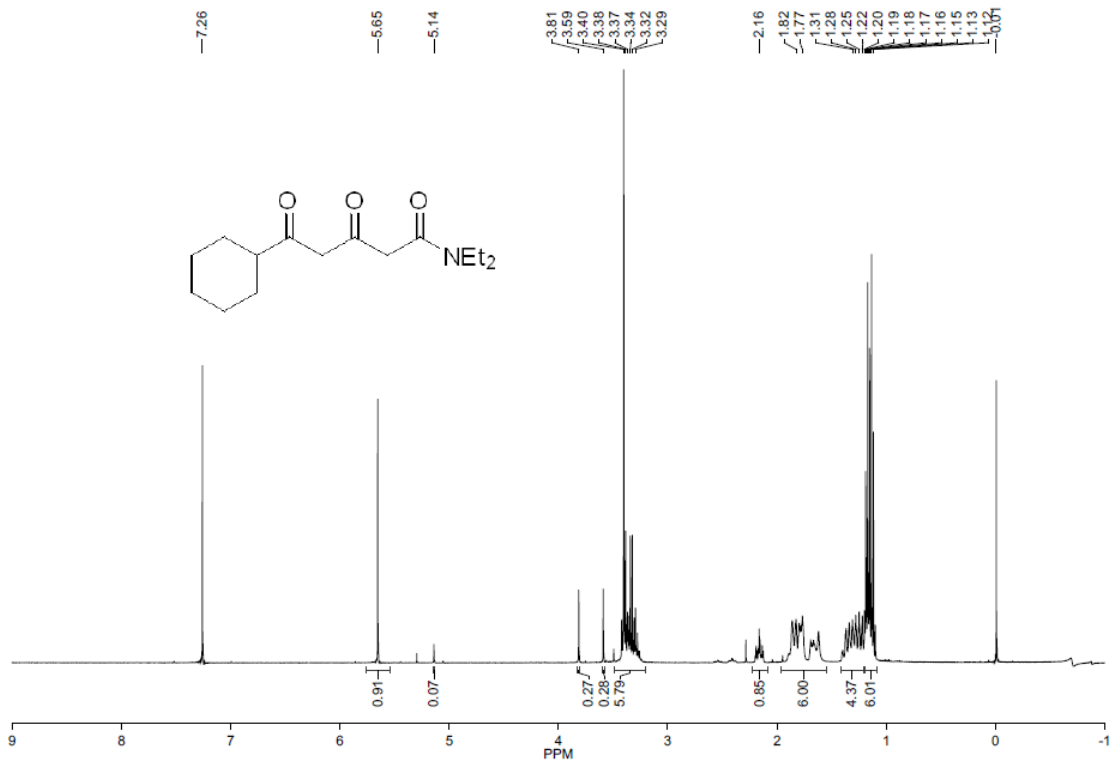


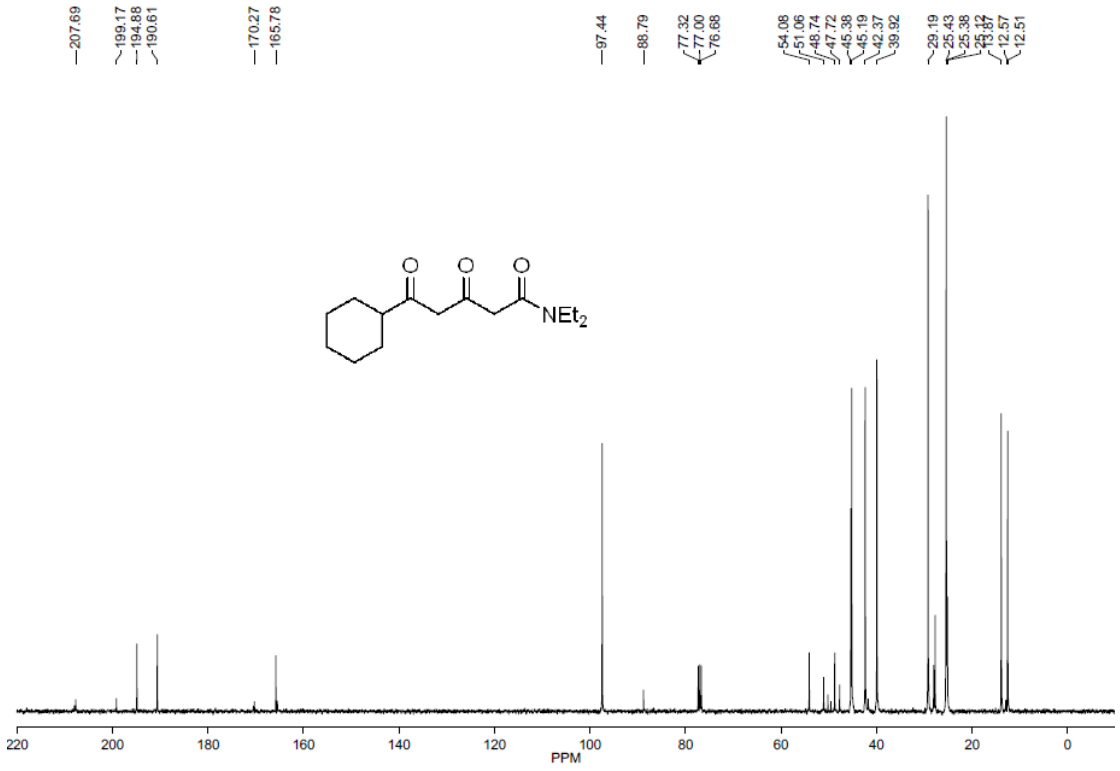

**(3b) *N*, *N*-diethyl-3, 5-dioxotridecanamide**



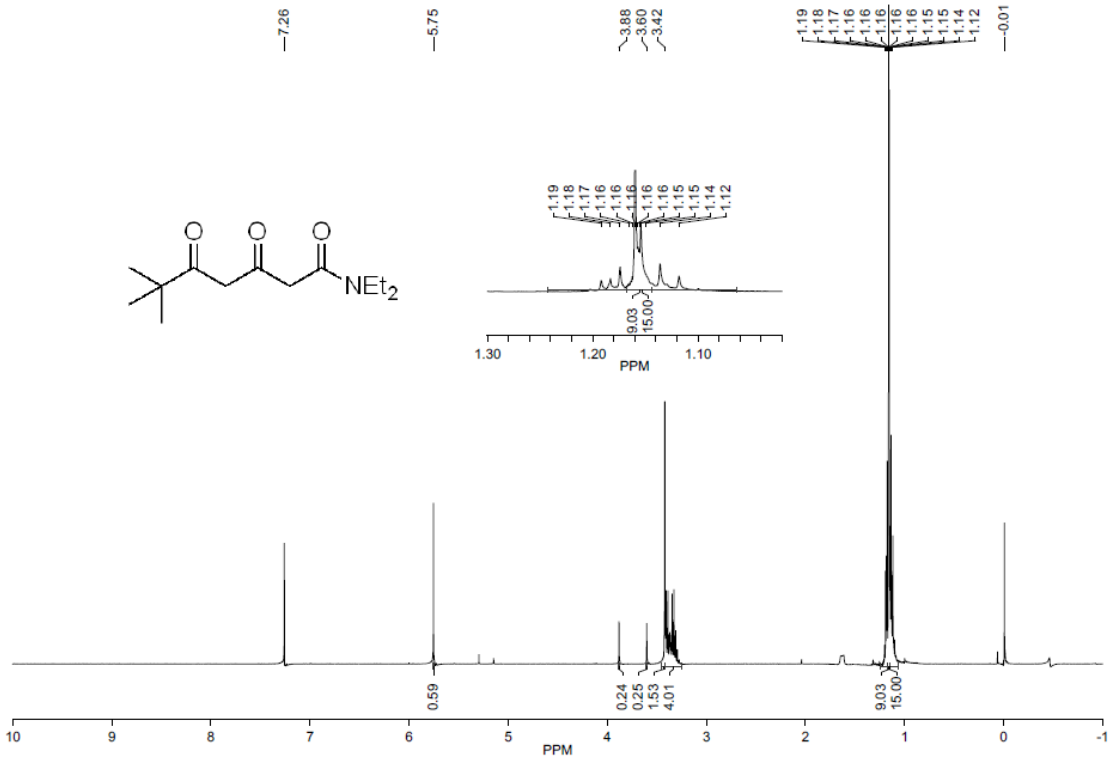


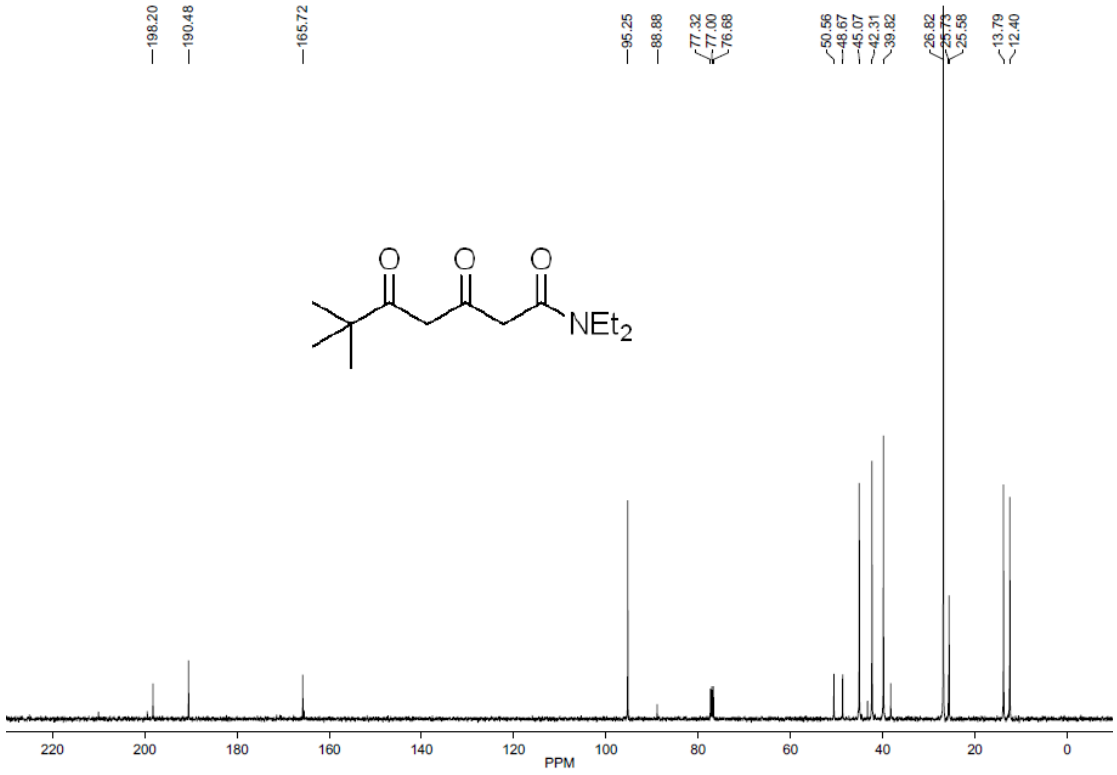

**(3c) 5-cyclohexyl-*N*, *N*-diethyl-3, 5-dioxopentanamide**



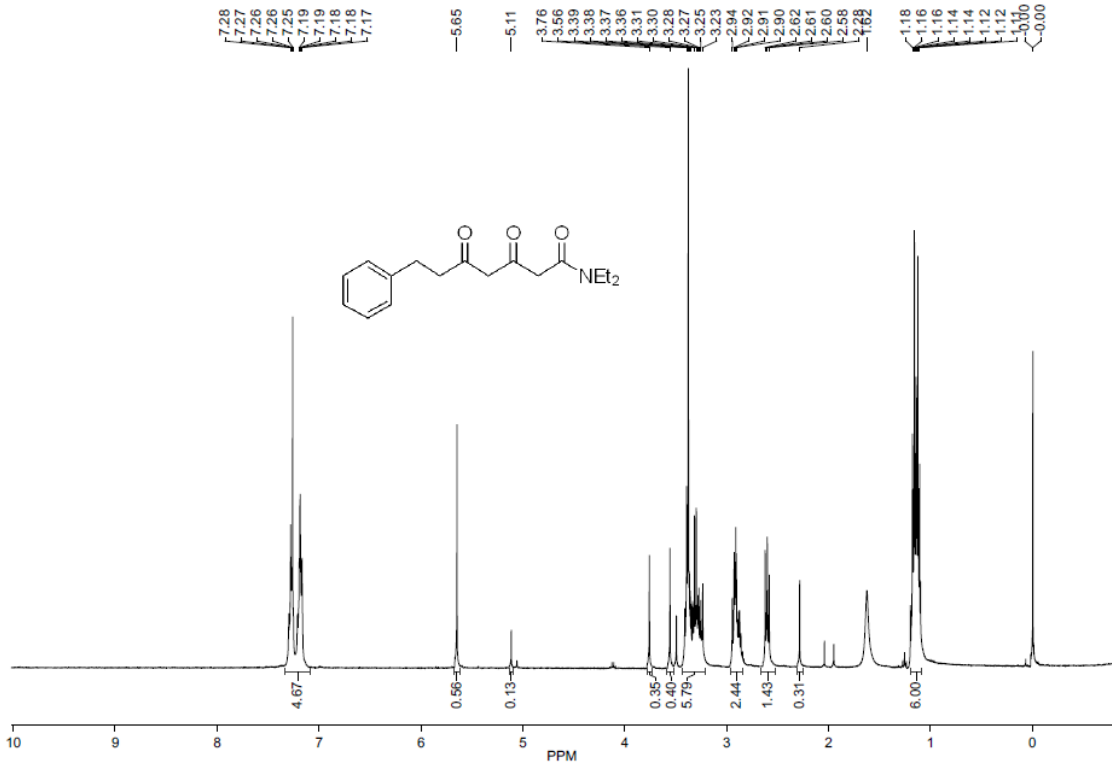


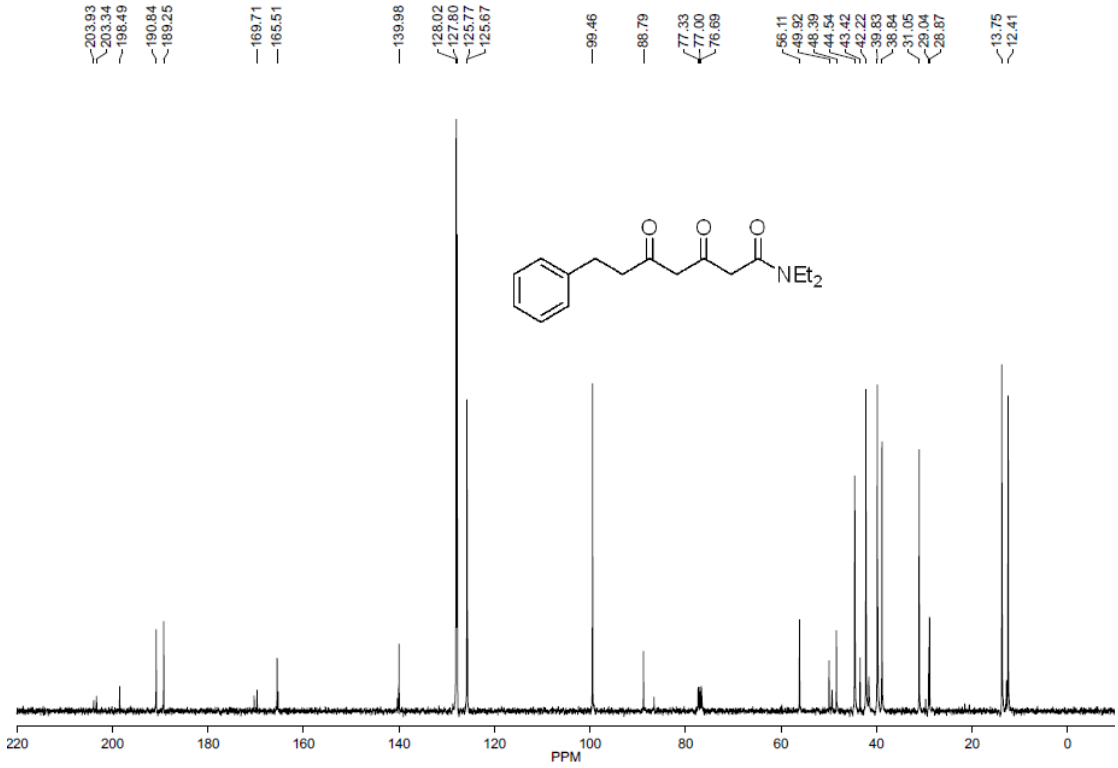

**(3d)** ***N, N*-diethyl-6, 6-dimethyl-3, 5-dioxoheptanamide**



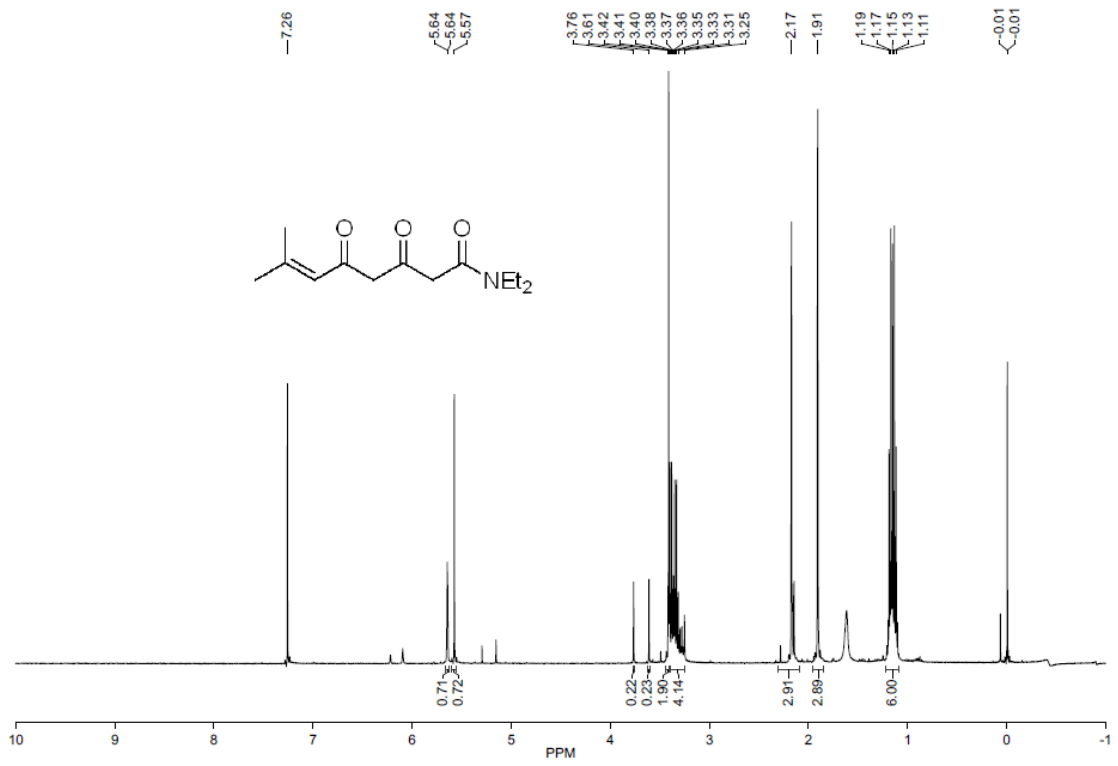


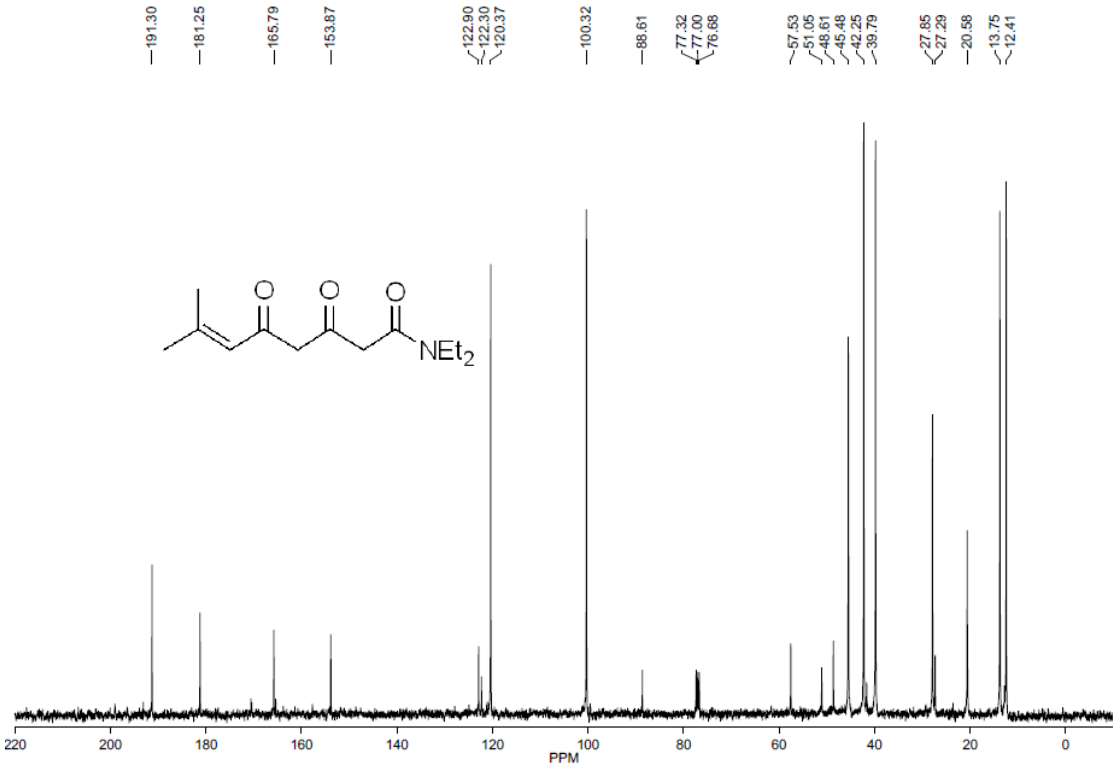

**(3e) *N*, *N*-diethyl-3, 5-dioxo-7-phenylheptanamide**



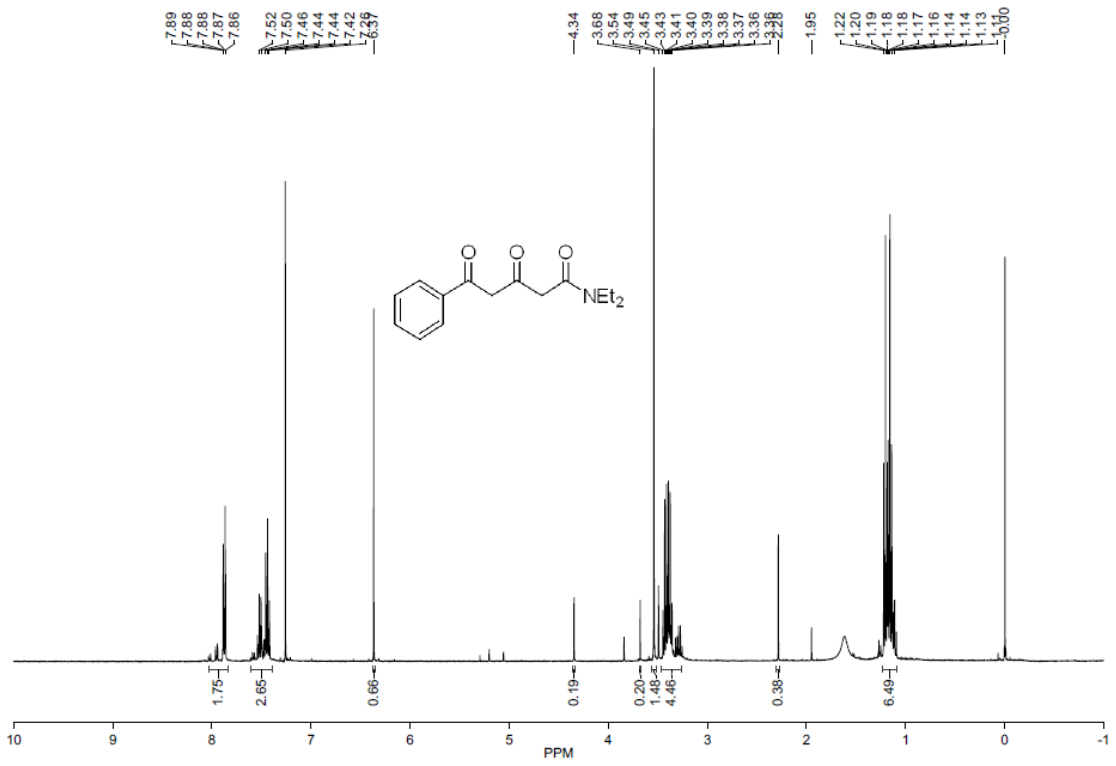


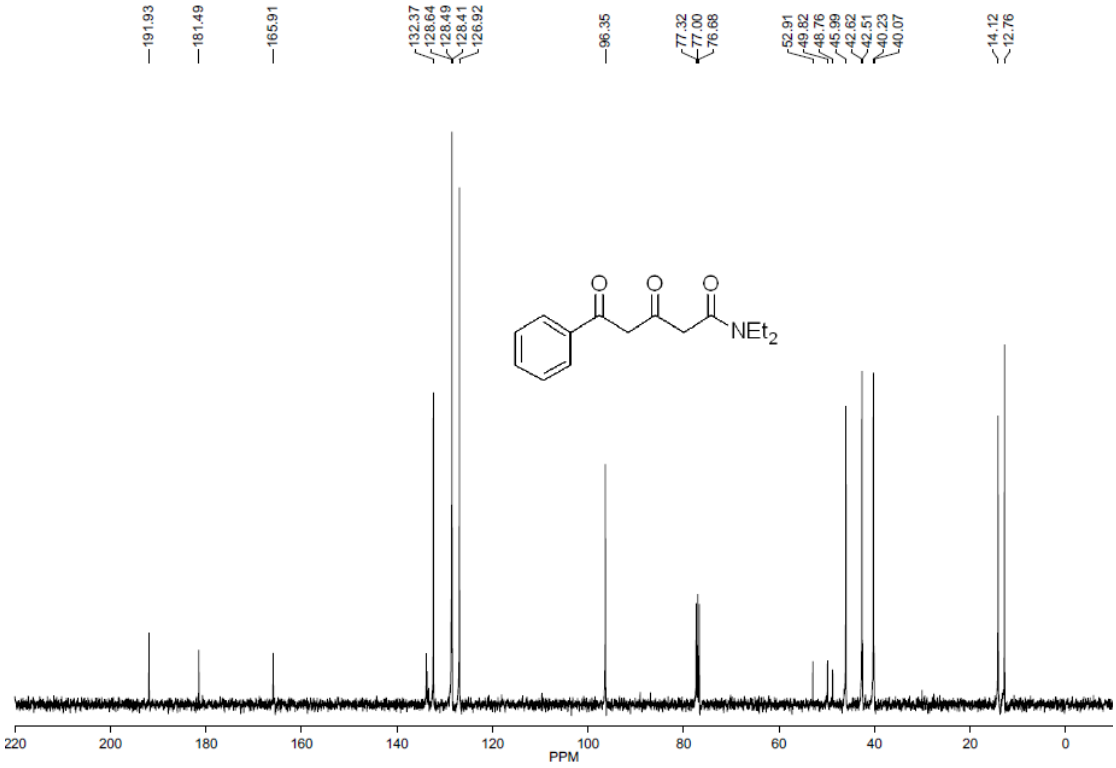

**(3f)** ***N*, *N*-diethyl-7-methyl-3, 5-dioxooct-6-enamide**



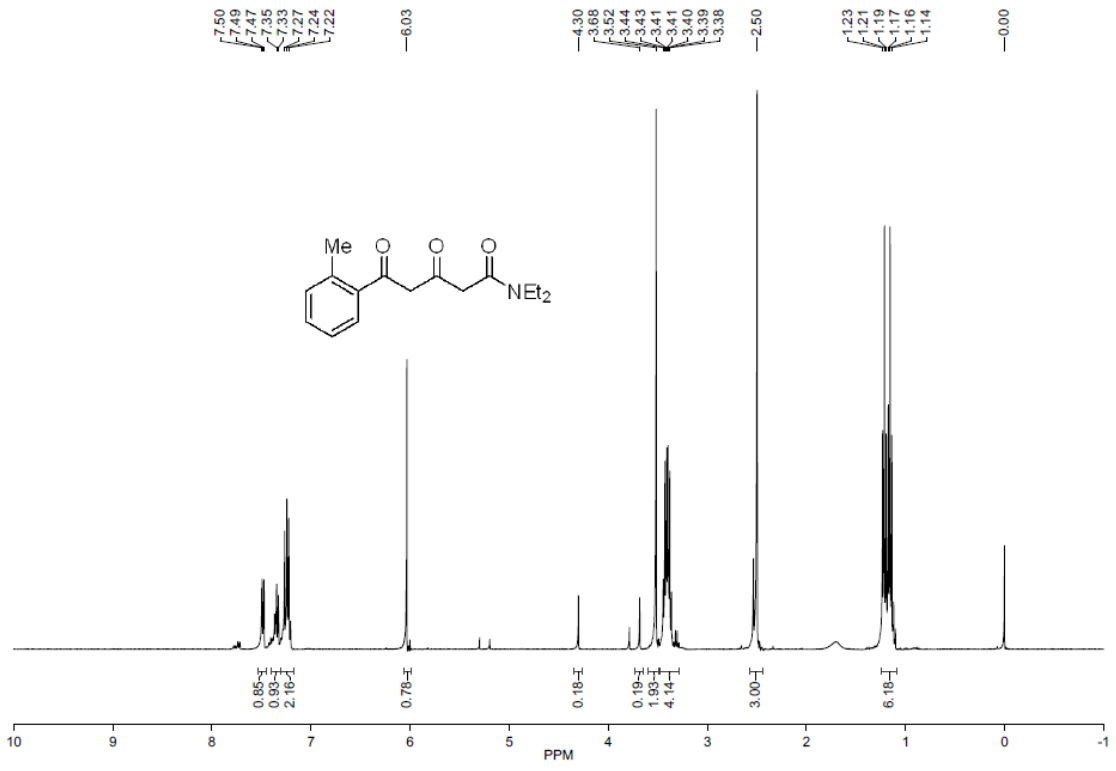


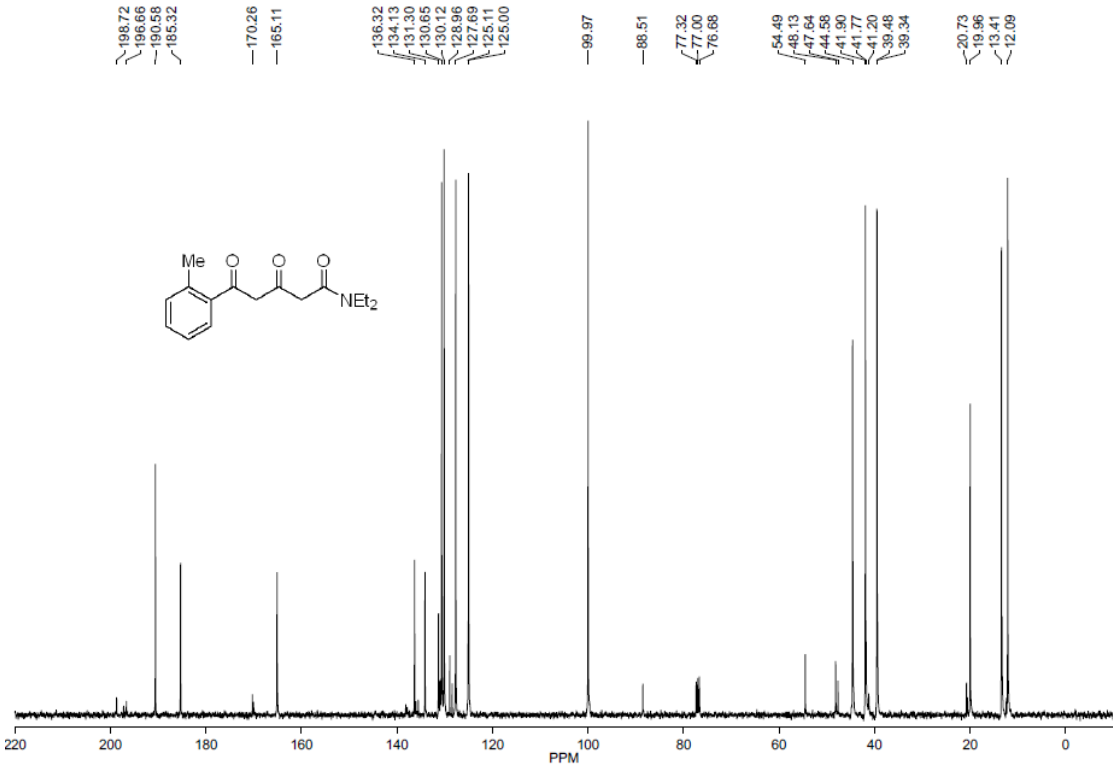

**(3g) *N*, *N*-diethyl-3, 5-dioxo-5-phenylpentanamide**



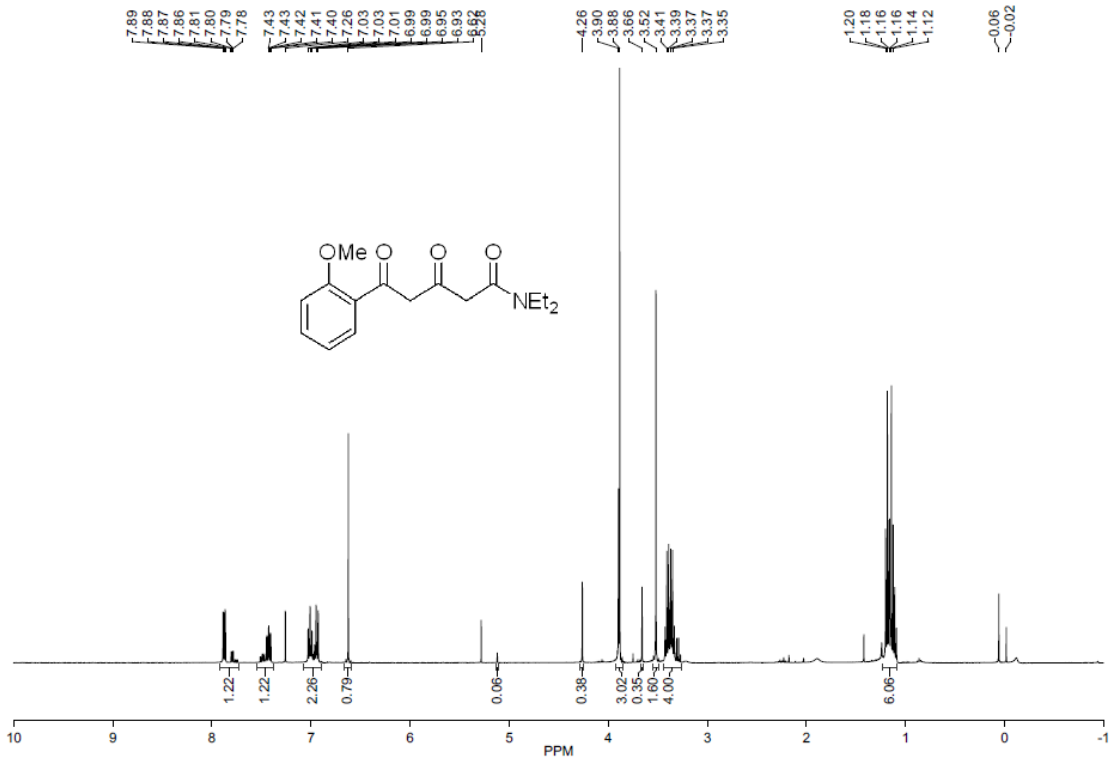


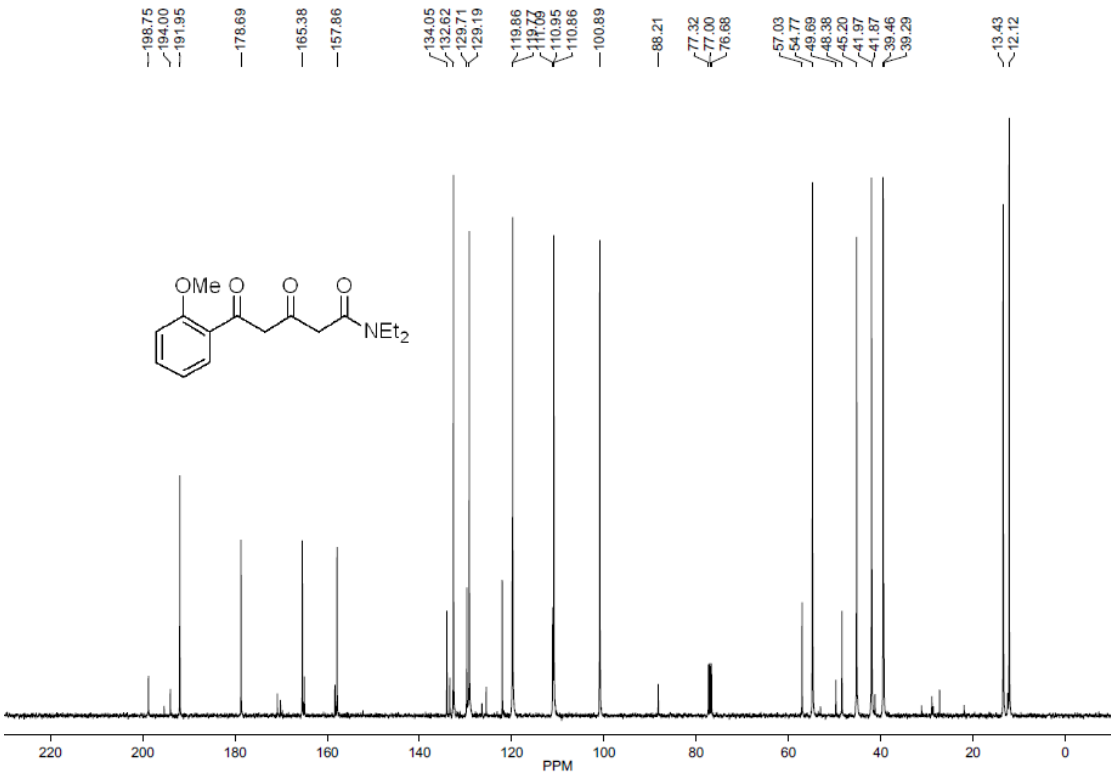

**(3h)** ***N, N*-diethyl-3, 5-dioxo-5-(o-tolyl)pentanamide**



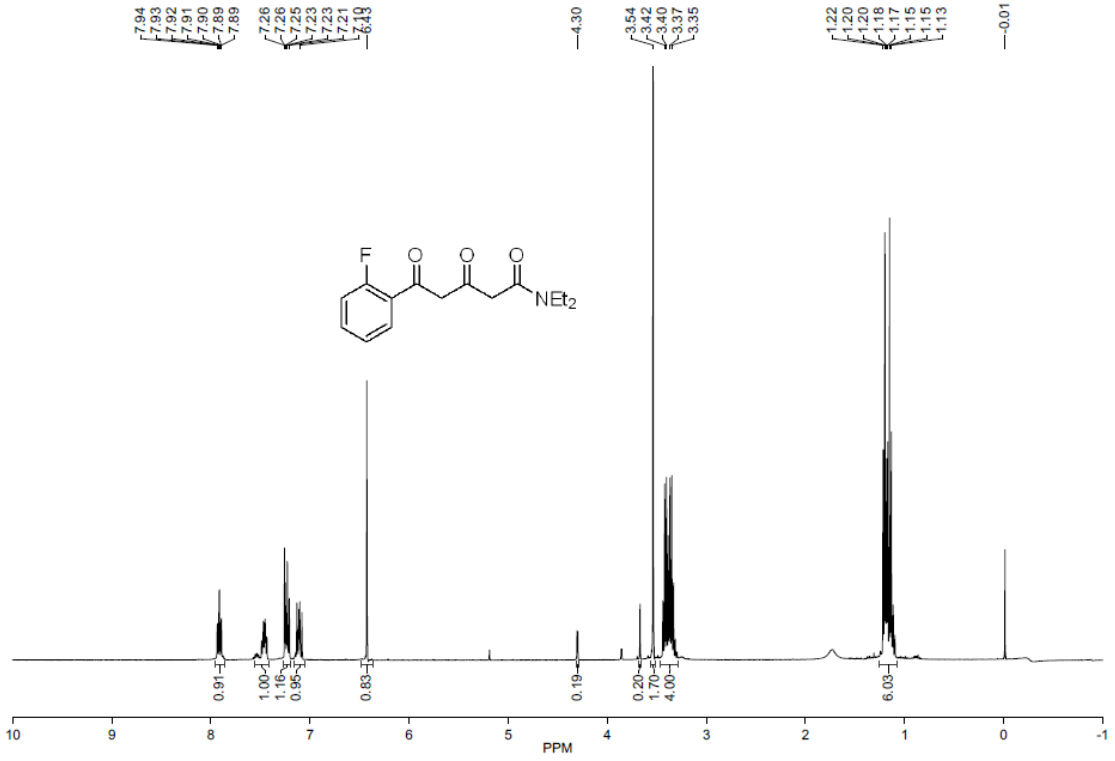


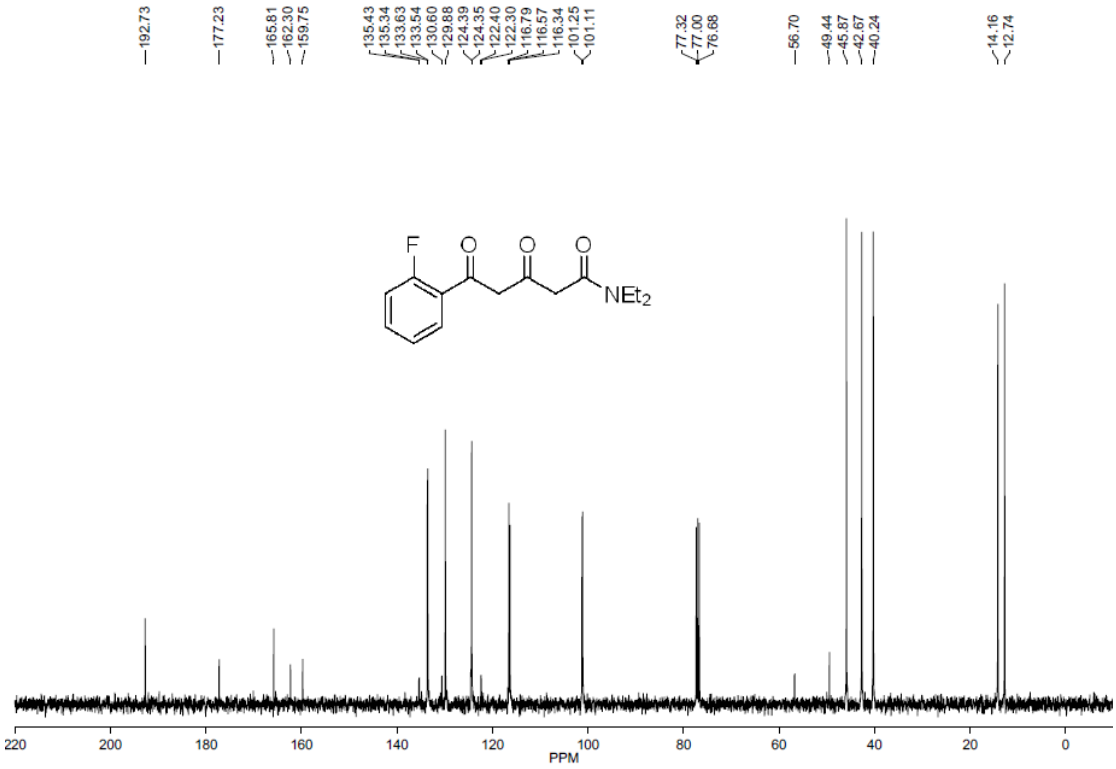

**(3i)** ***N, N*-diethyl-5-(2-methoxyphenyl)-3, 5-dioxopentanamide**



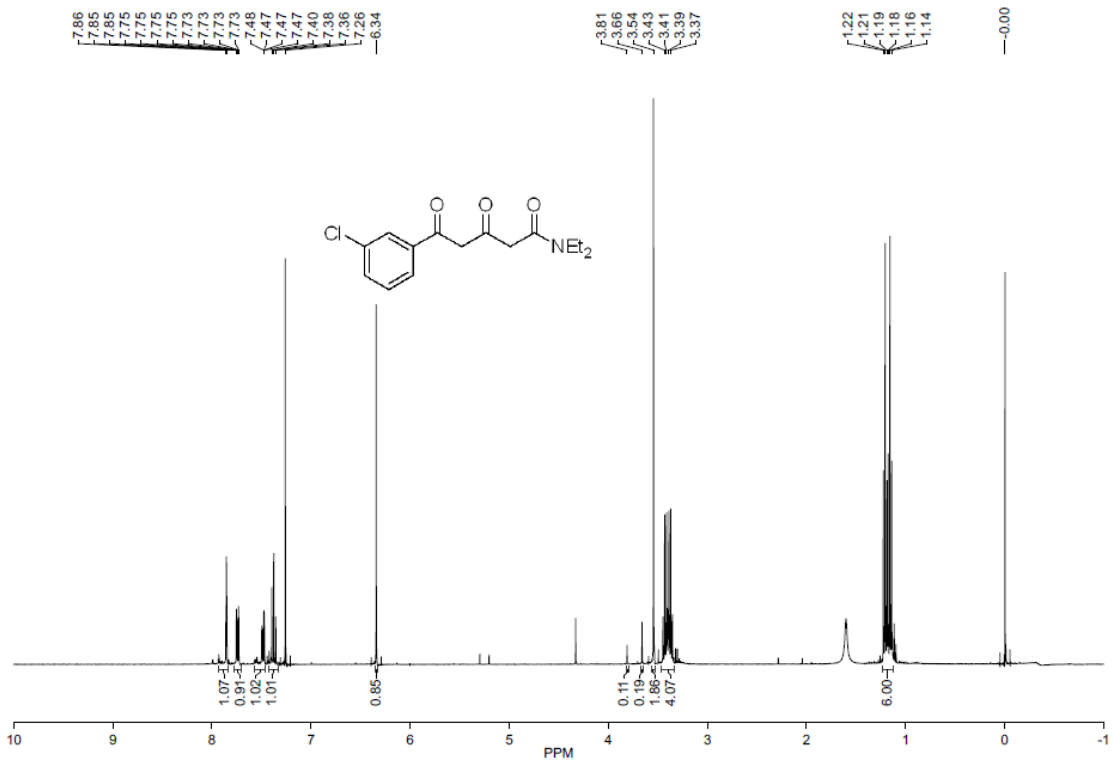


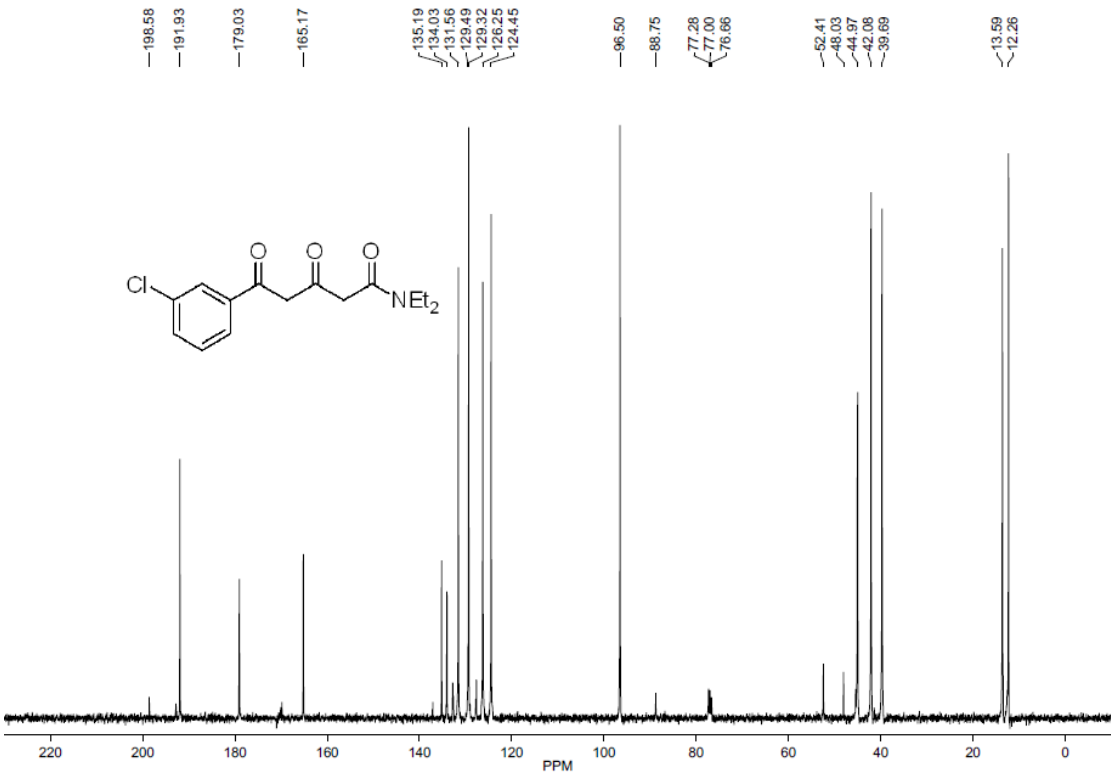

**(3j)** ***N, N*-diethyl-5-(2-fluorophenyl)-3, 5-dioxopentanamide**



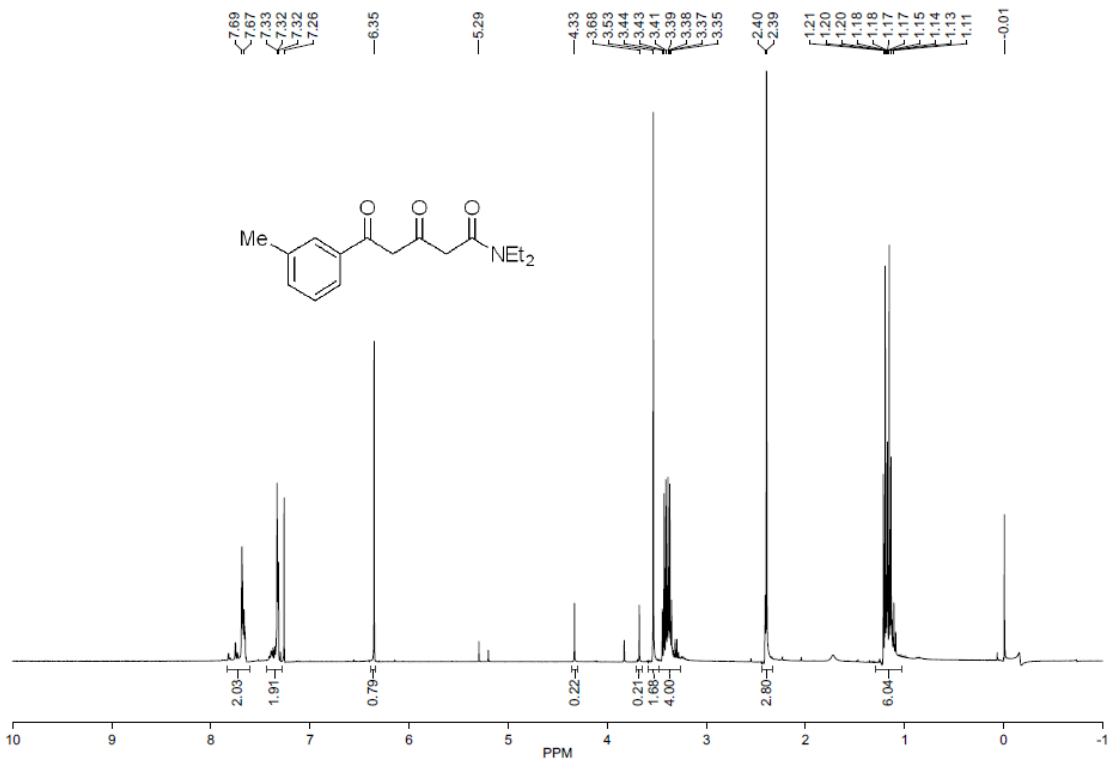


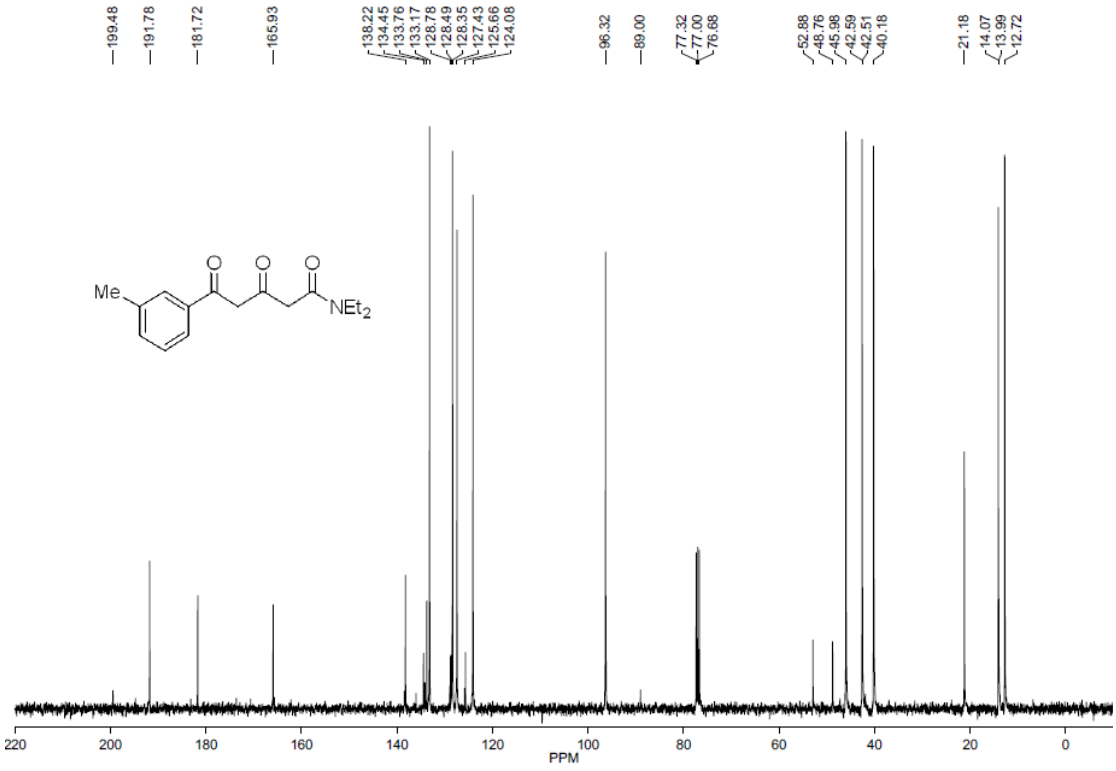

**(3k) 5-(3-chlorophenyl)-*N, N*-diethyl-3, 5-dioxopentanamide**



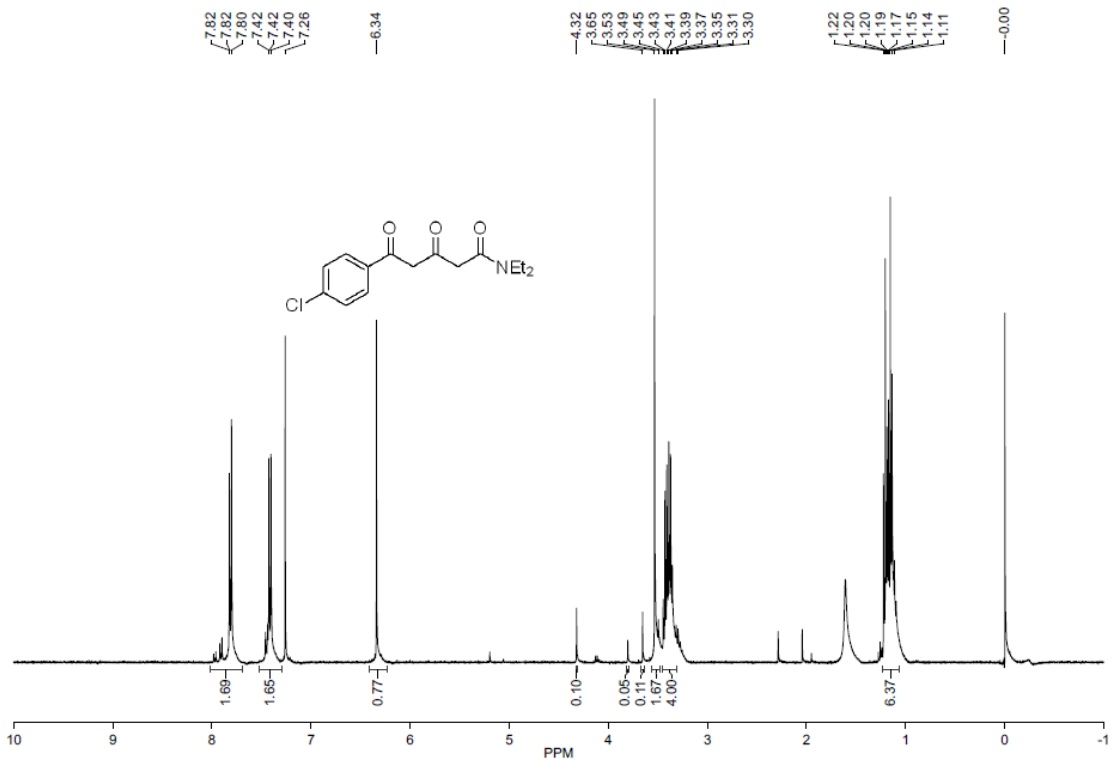


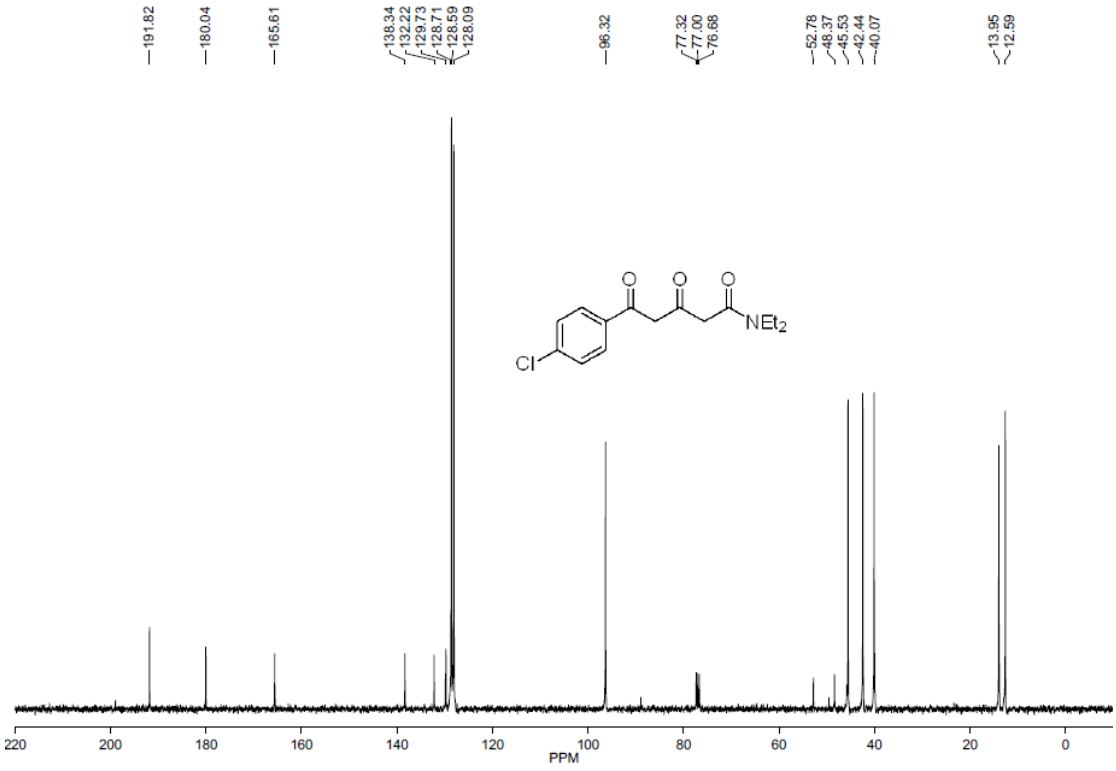

**(3l)** ***N, N*-diethyl-3, 5-dioxo-5-(m-tolyl)pentanamide**



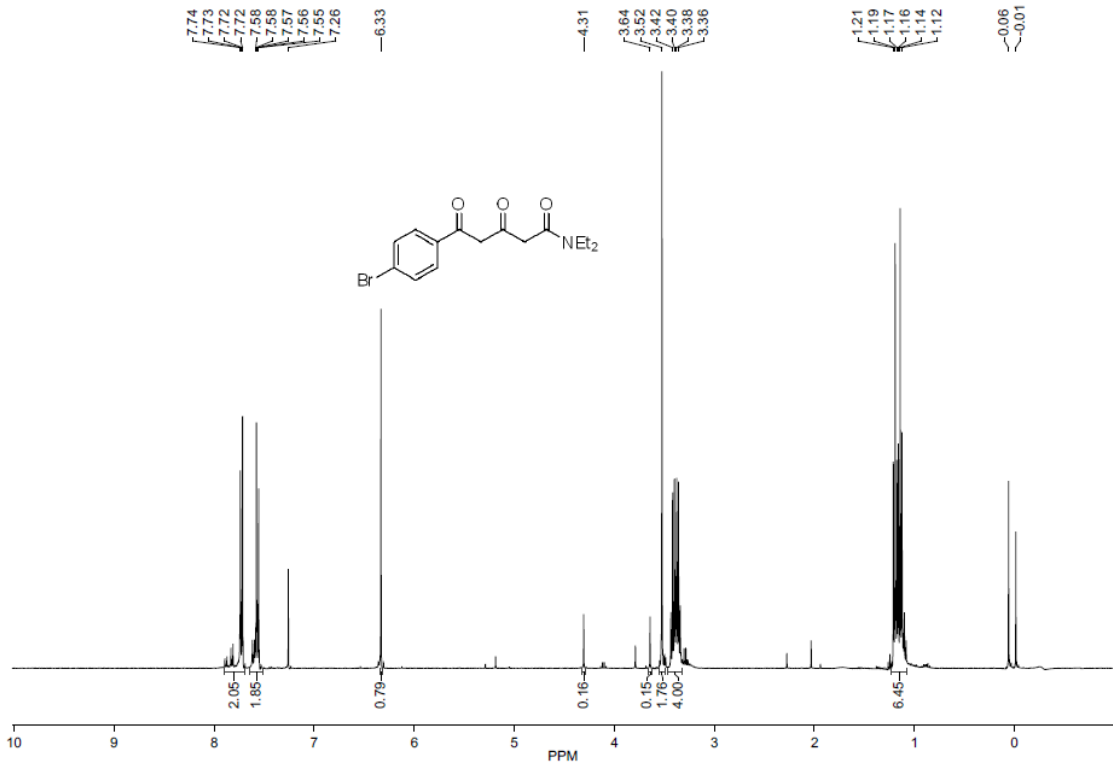


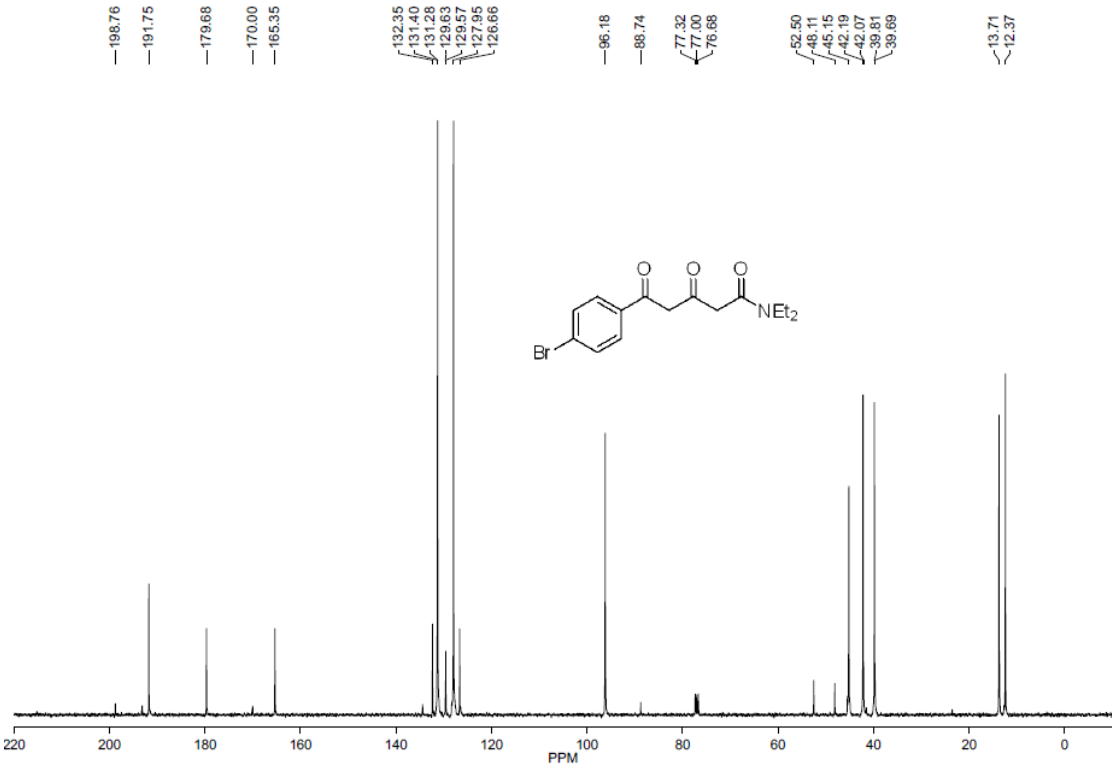

**(3m) 5-(4-chlorophenyl)-*N* ,*N*-diethyl-3, 5-dioxopentanamide**



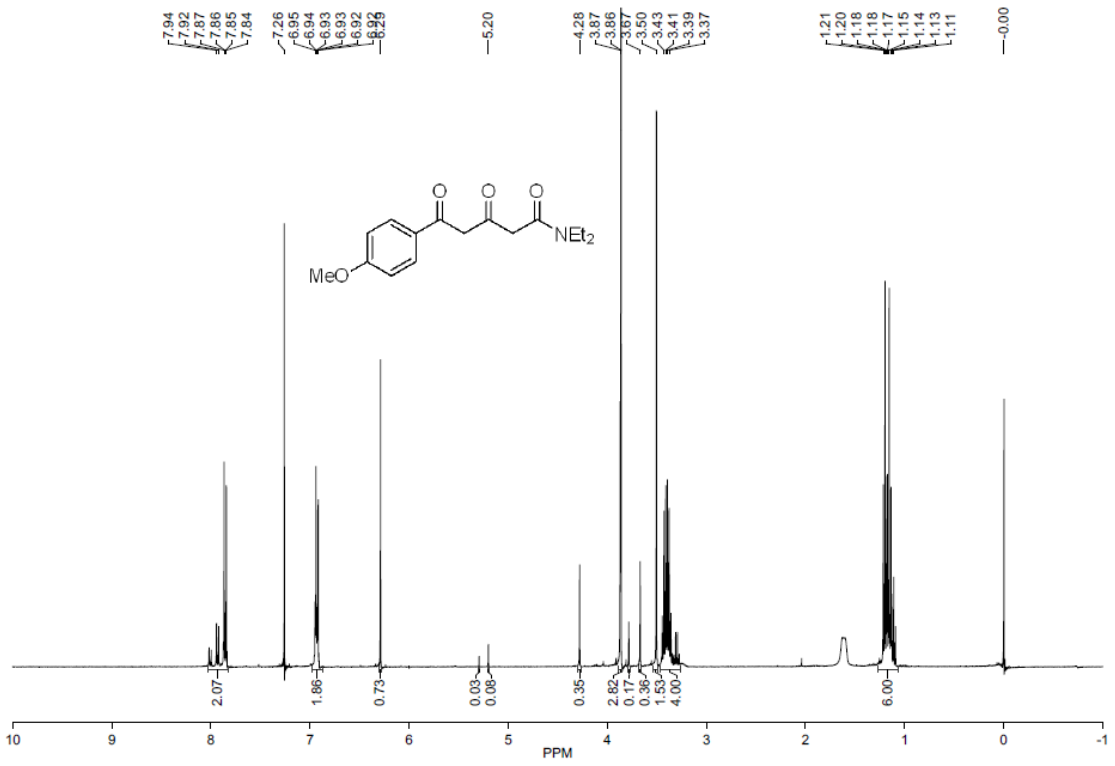


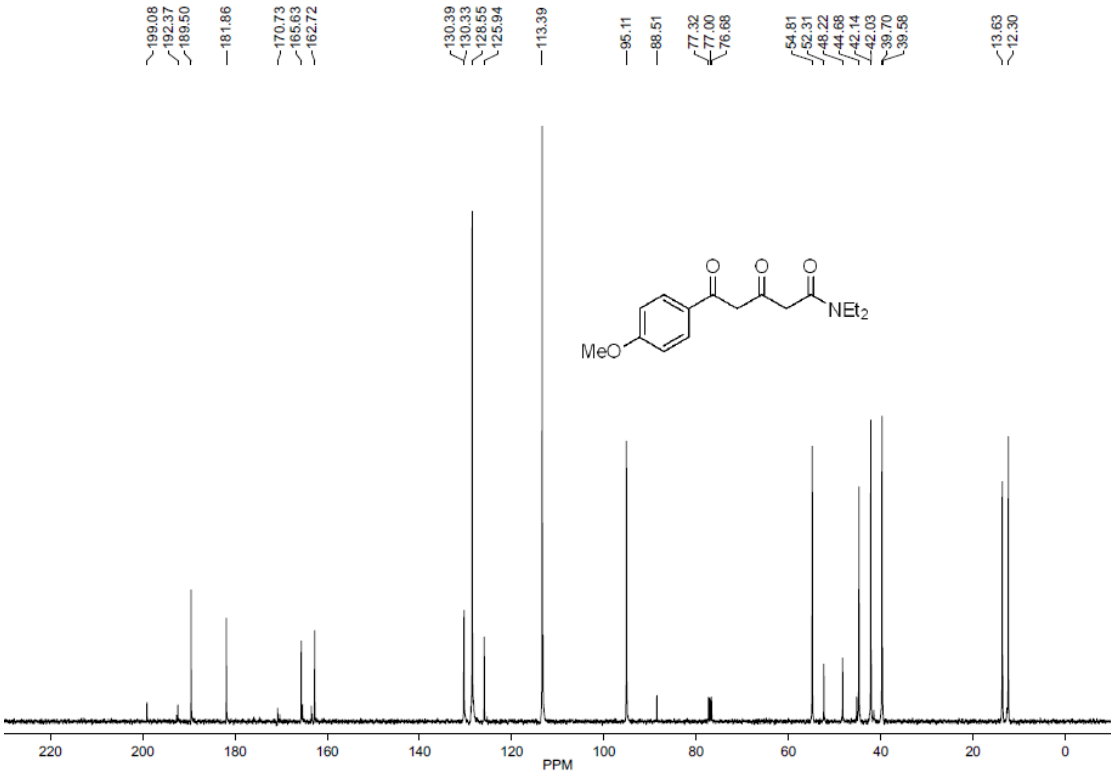

**(3n) 5-(4-bromophenyl)-*N*,*N*-diethyl-3, 5-dioxopentanamide**



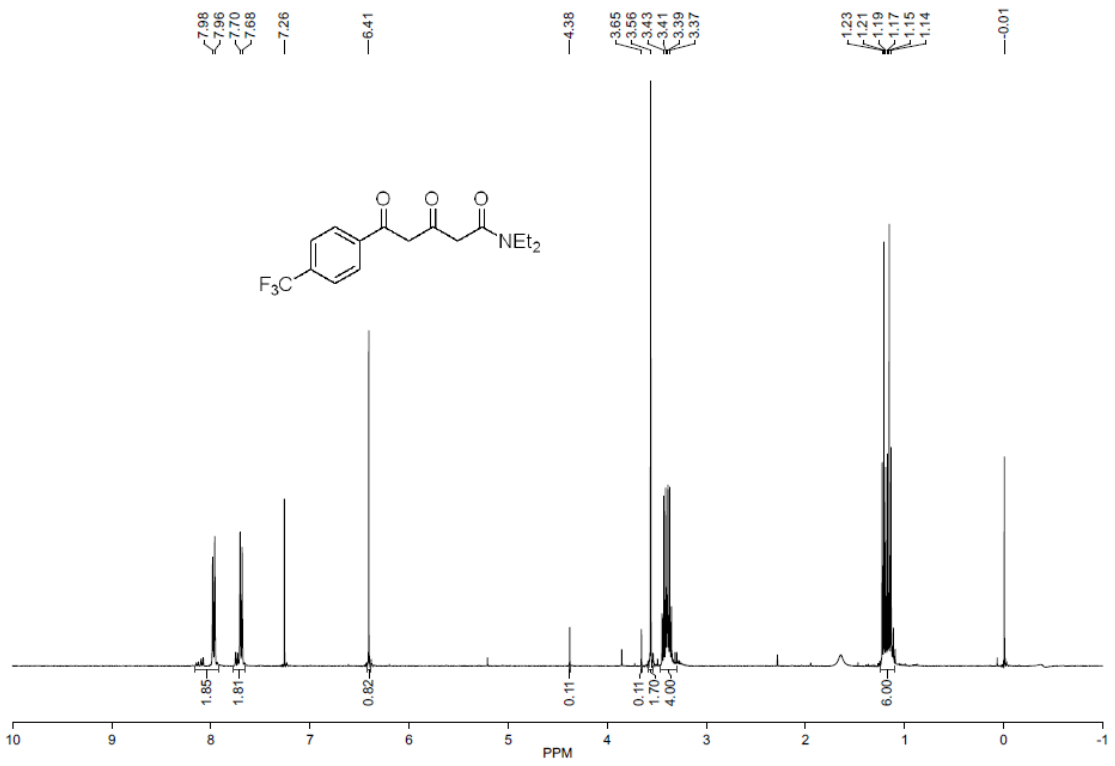


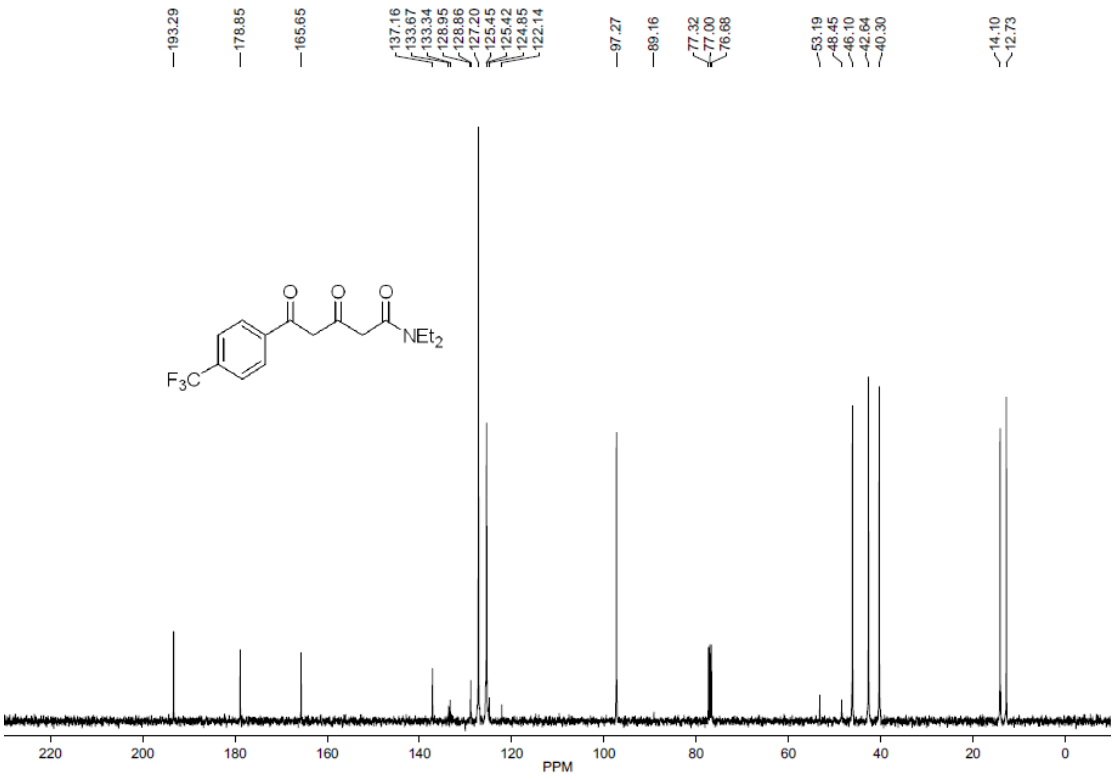

**(3o) *N*, *N*-diethyl-5-(4-methoxyphenyl)-3, 5-dioxopentanamide**



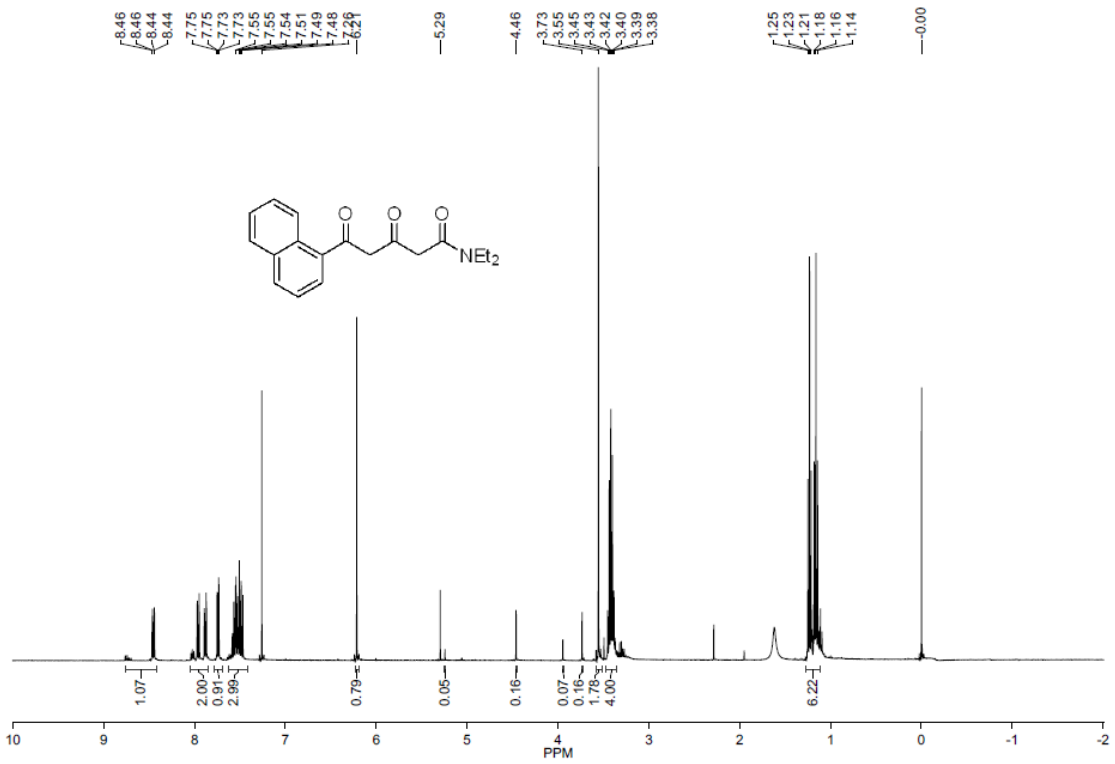


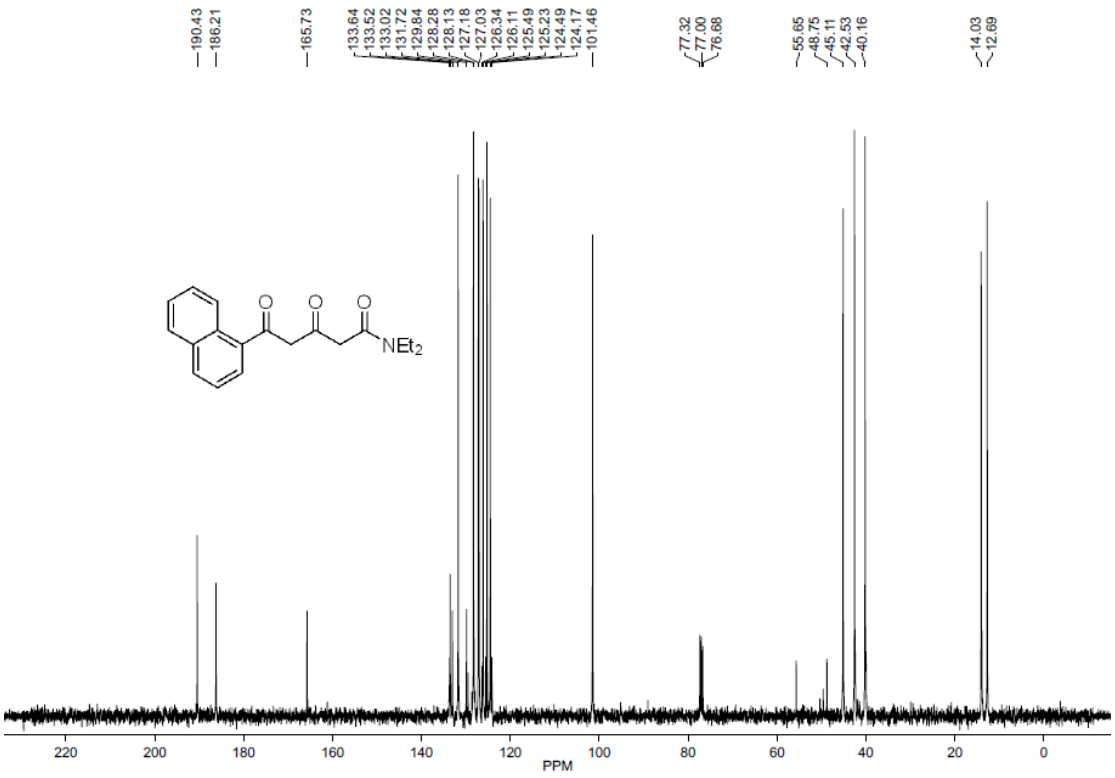

**(3p) *N, N*-diethyl-3, 5-dioxo-5-(4-(trifluoromethyl)phenyl)pentanamide**



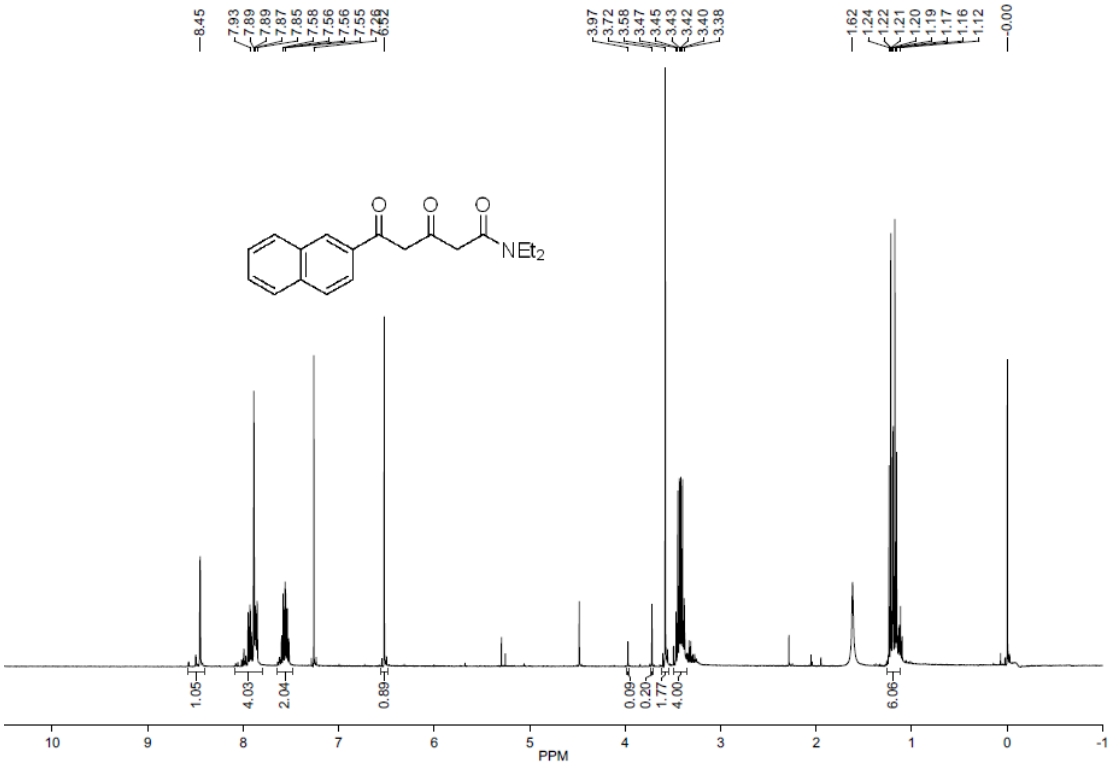


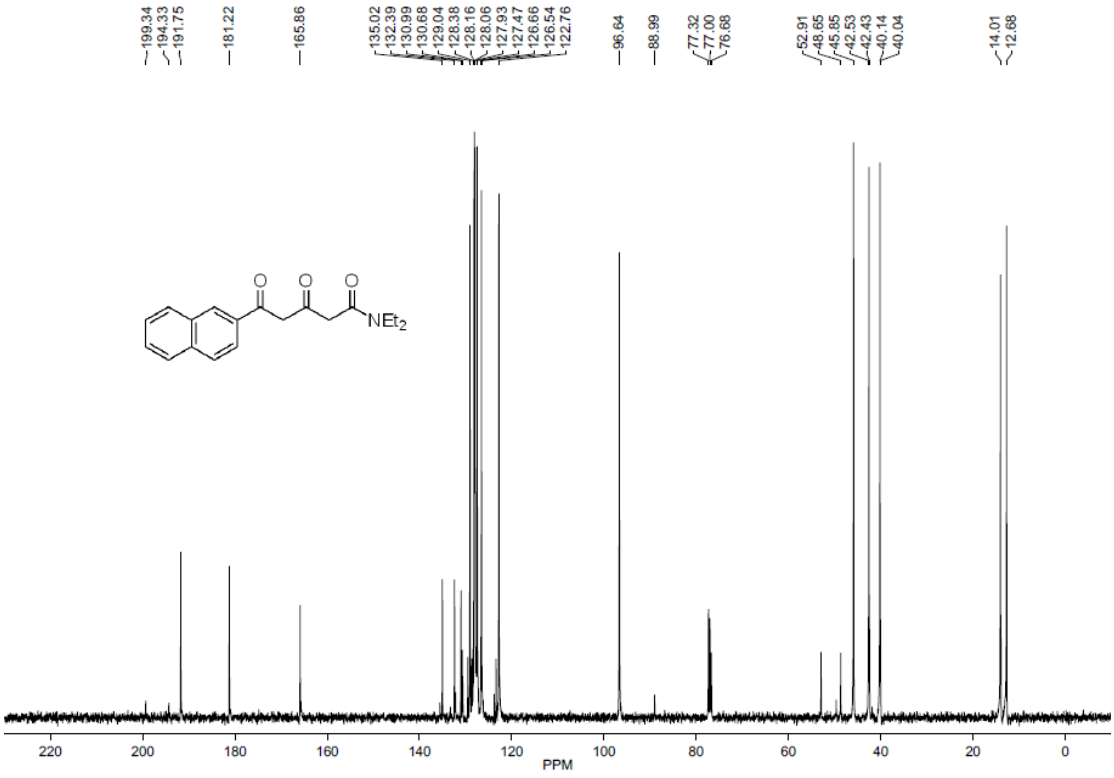

**(3q) *N, N*-diethyl-5-(naphthalen-1-yl)-3, 5-dioxopentanamide**



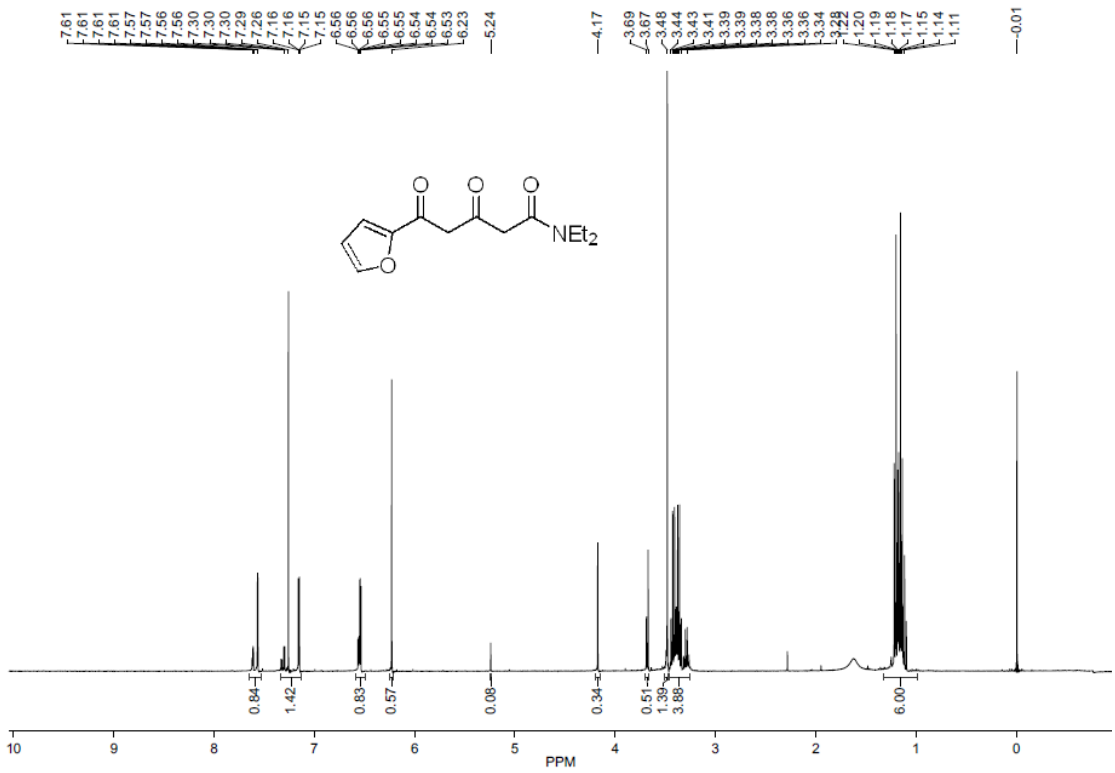


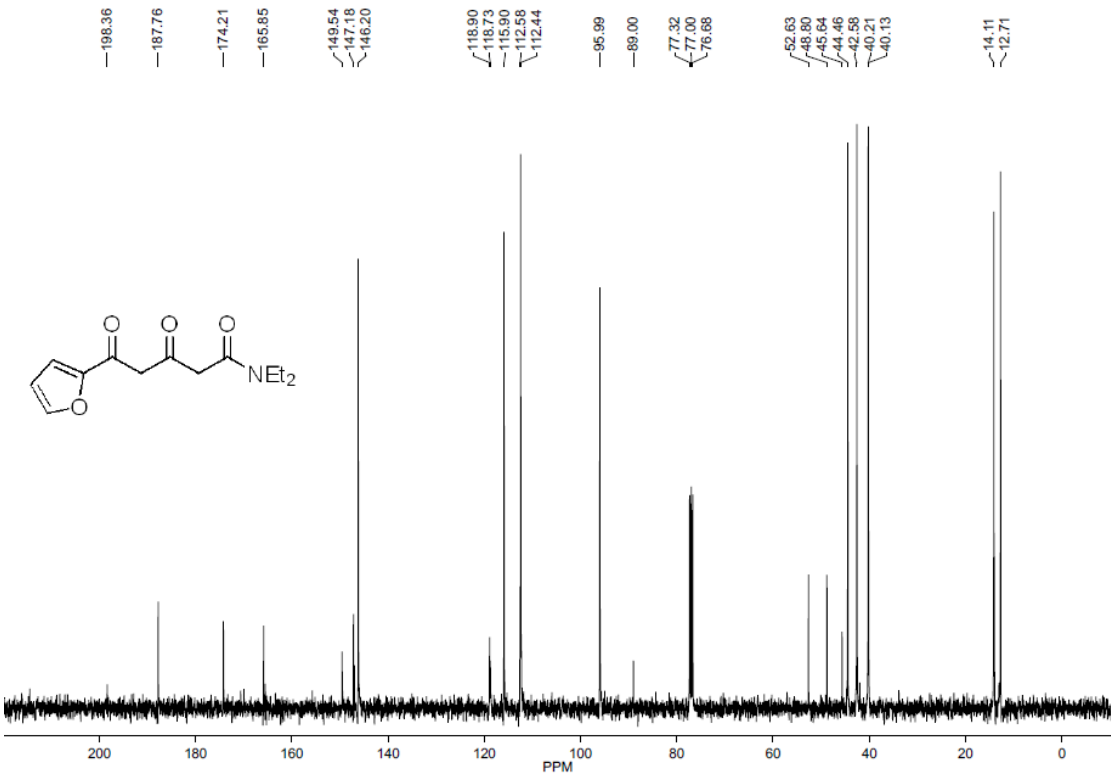

**(3r) *N*, *N*-diethyl-5-(naphthalen-2-yl)-3, 5-dioxopentanamide**



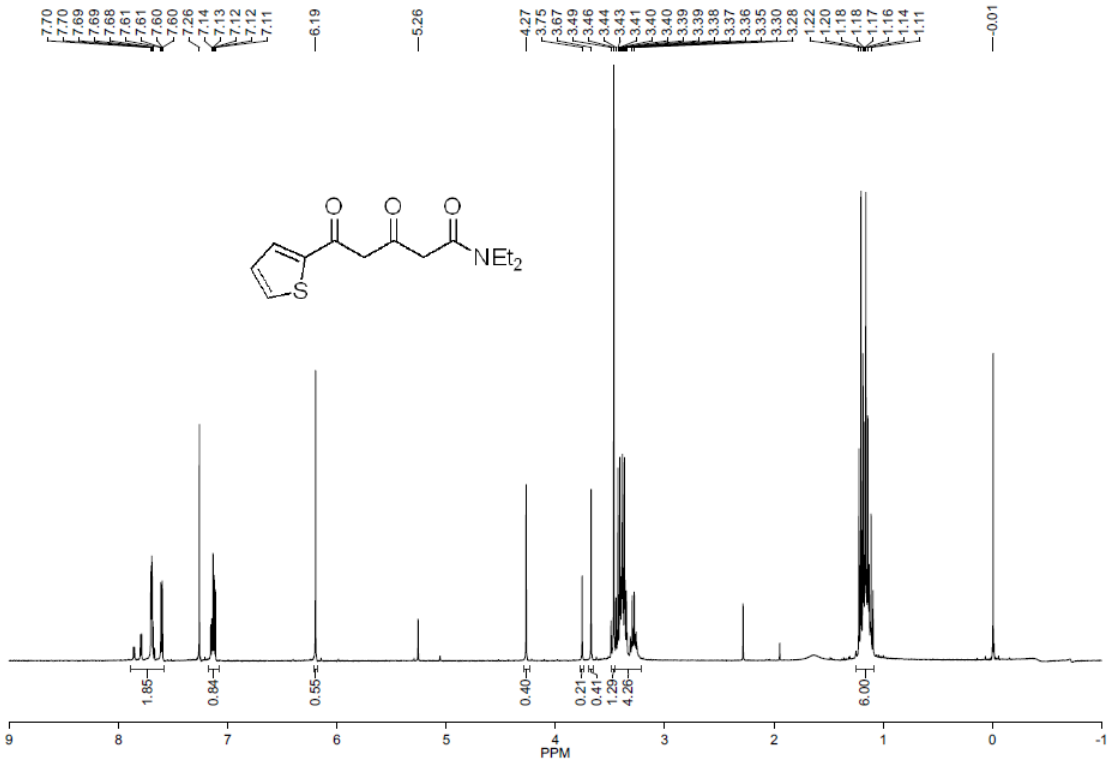


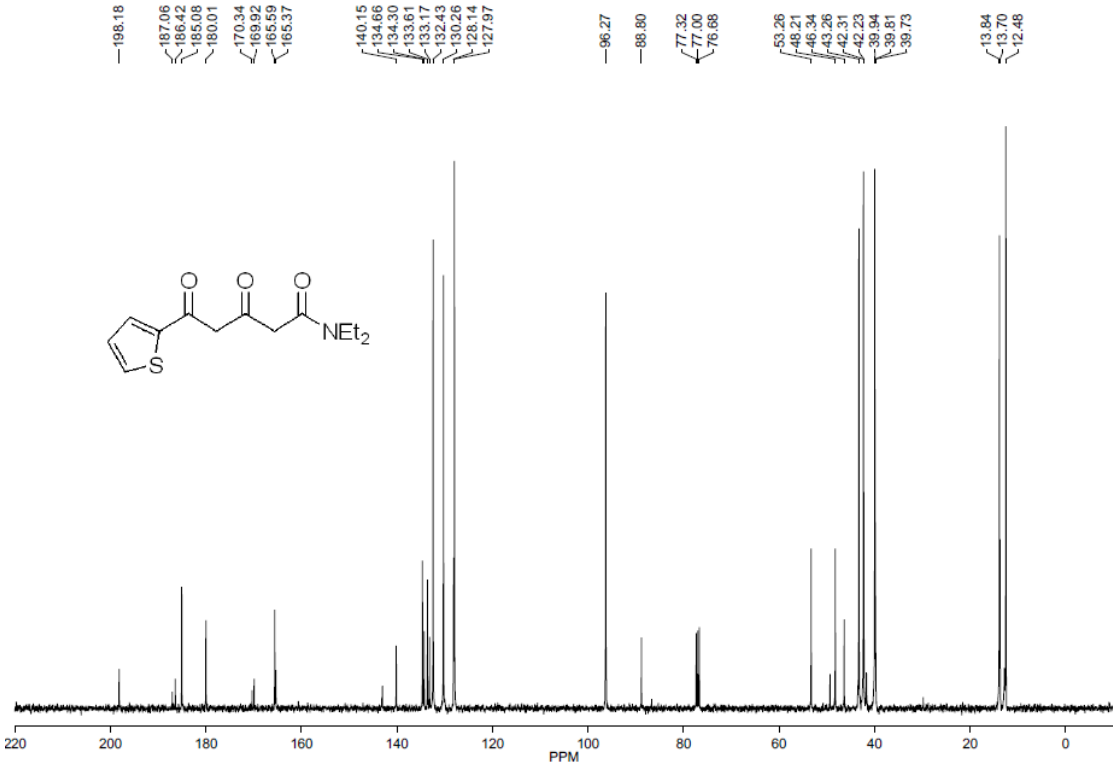

**(3s)** ***N, N*-diethyl-5-(furan-2-yl)-3, 5-dioxopentanamide**



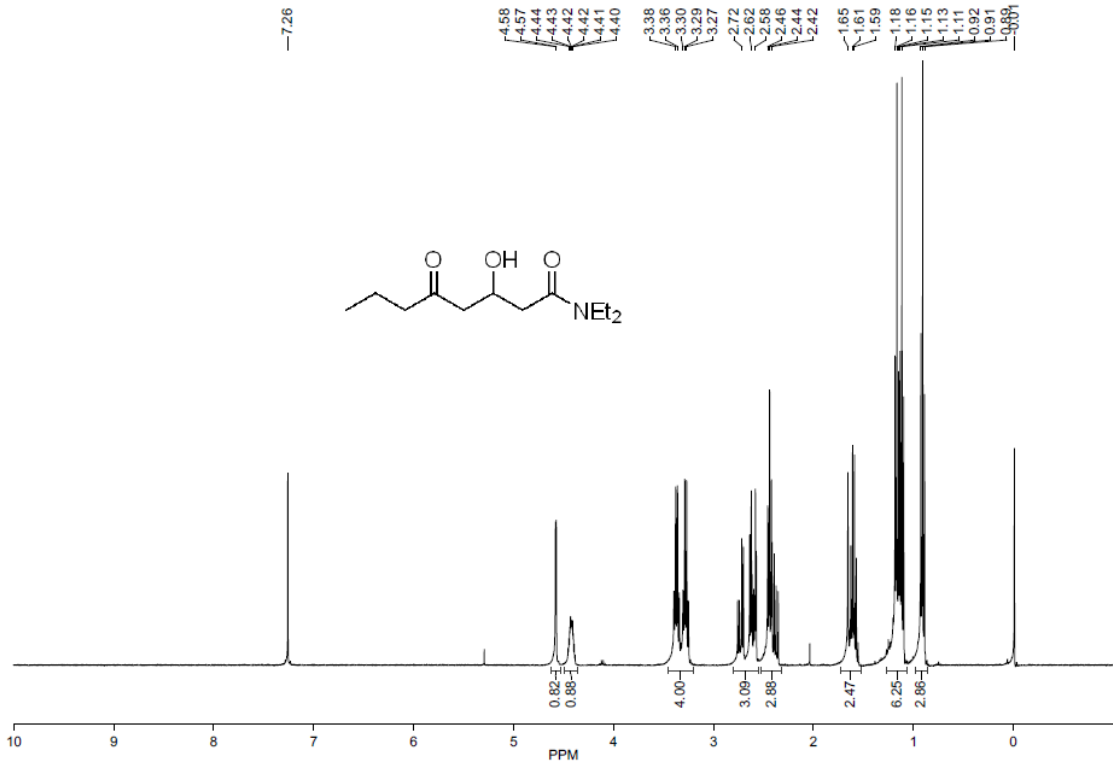


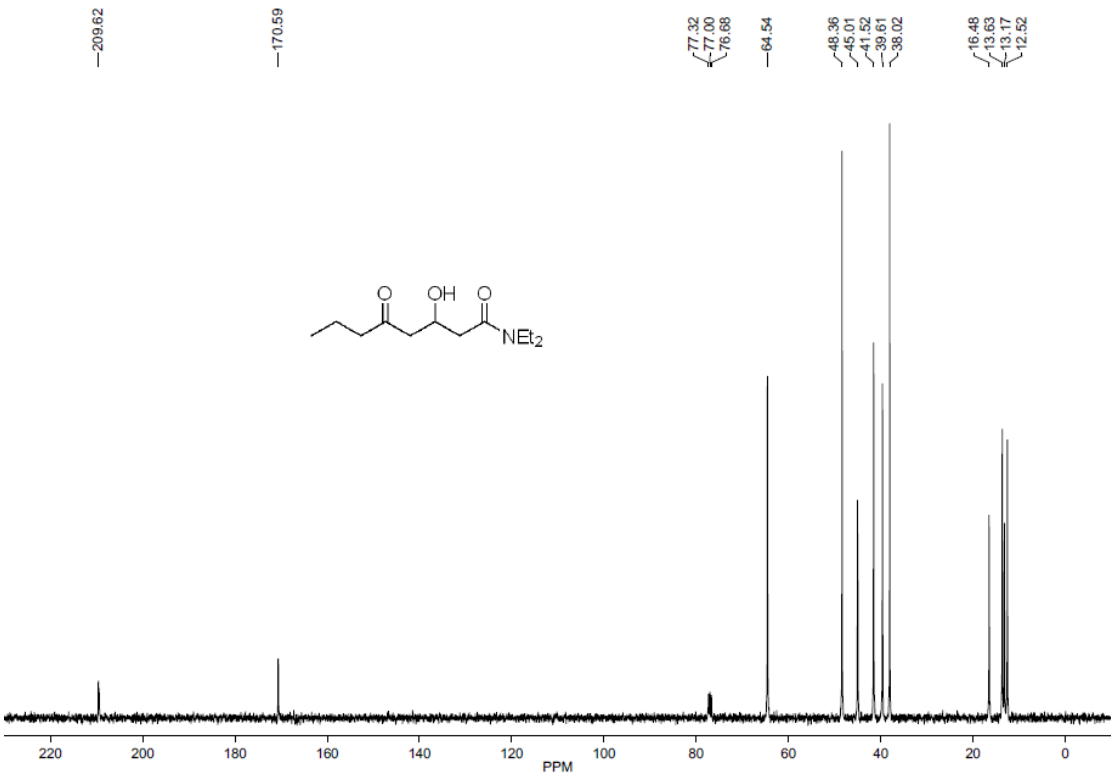

**(3t) *N, N*-diethyl-3, 5-dioxo-5-(thiophen-2-yl)pentanamide**



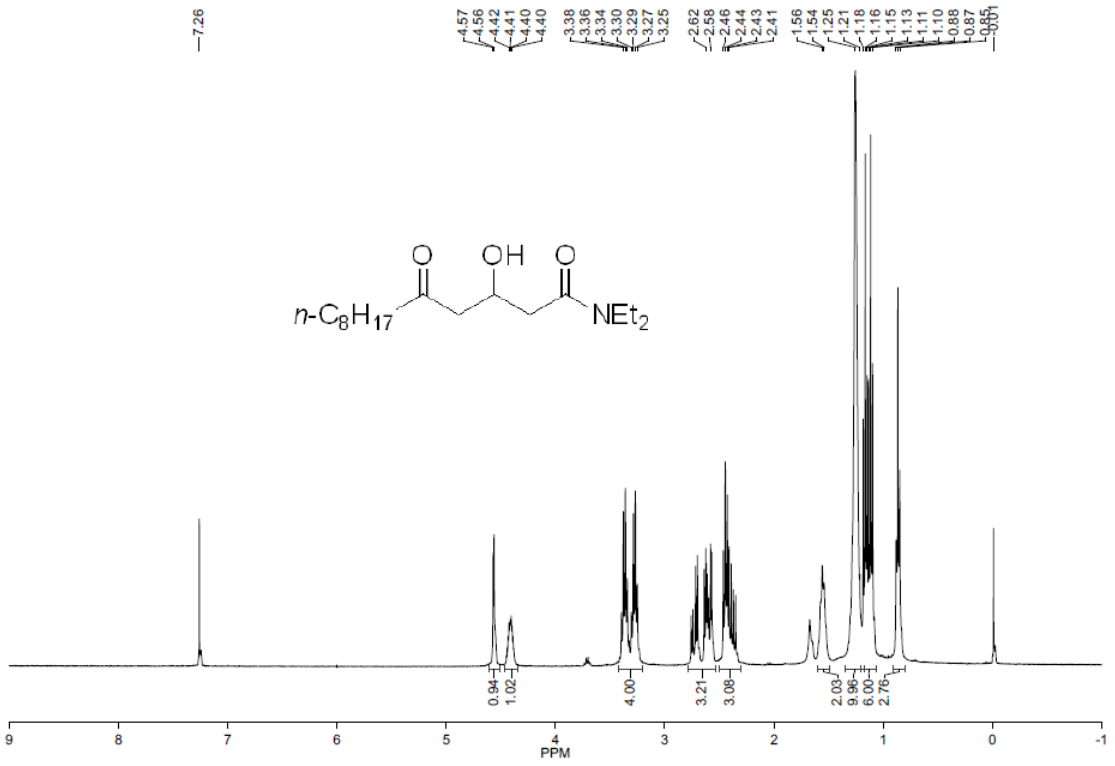


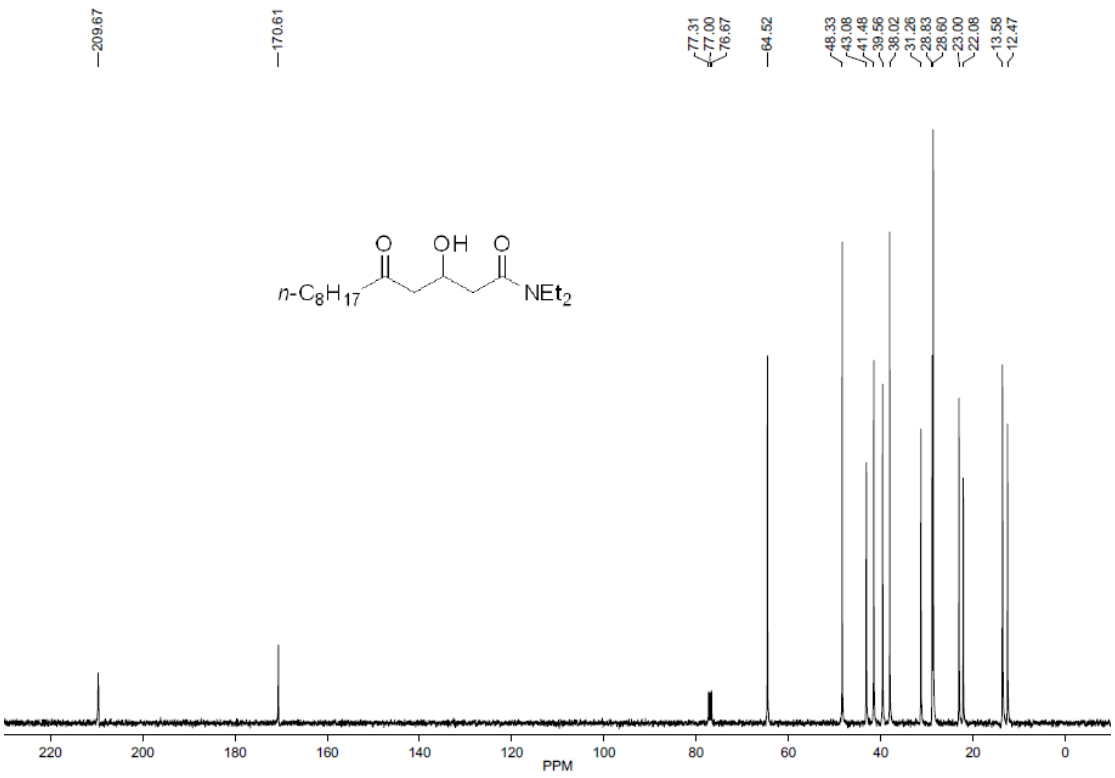

**(4a) *N*, *N*-diethyl-3-hydroxy-5-oxooctanamide**



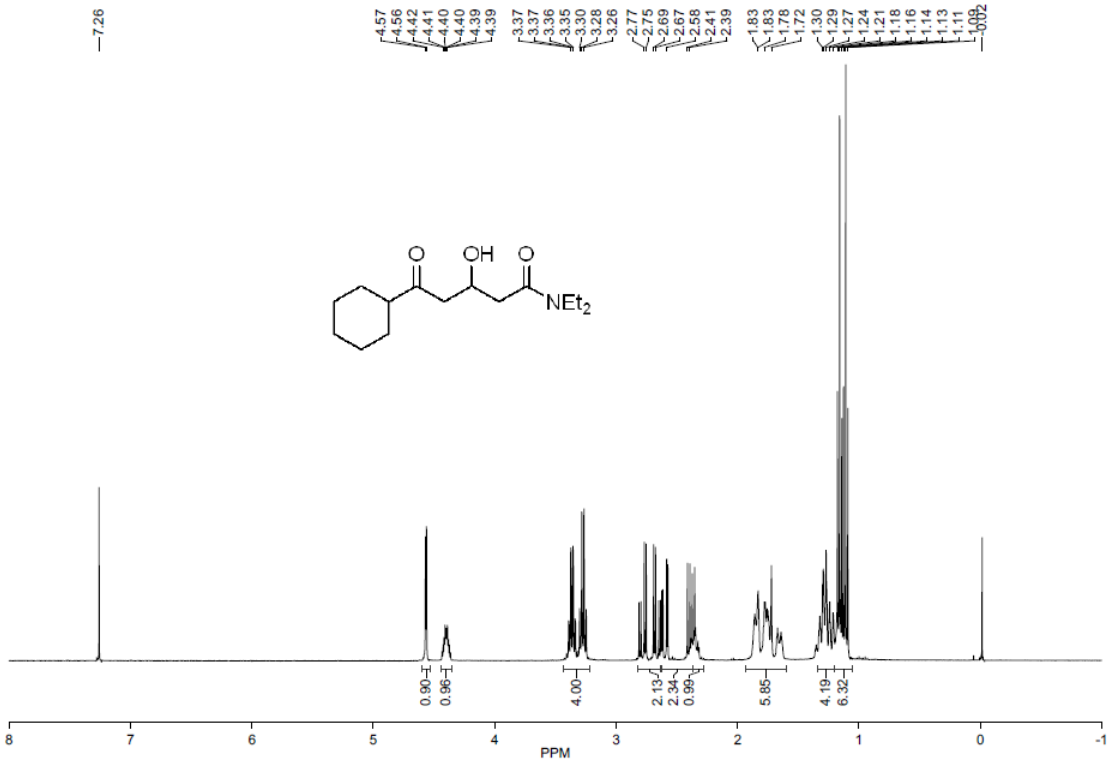


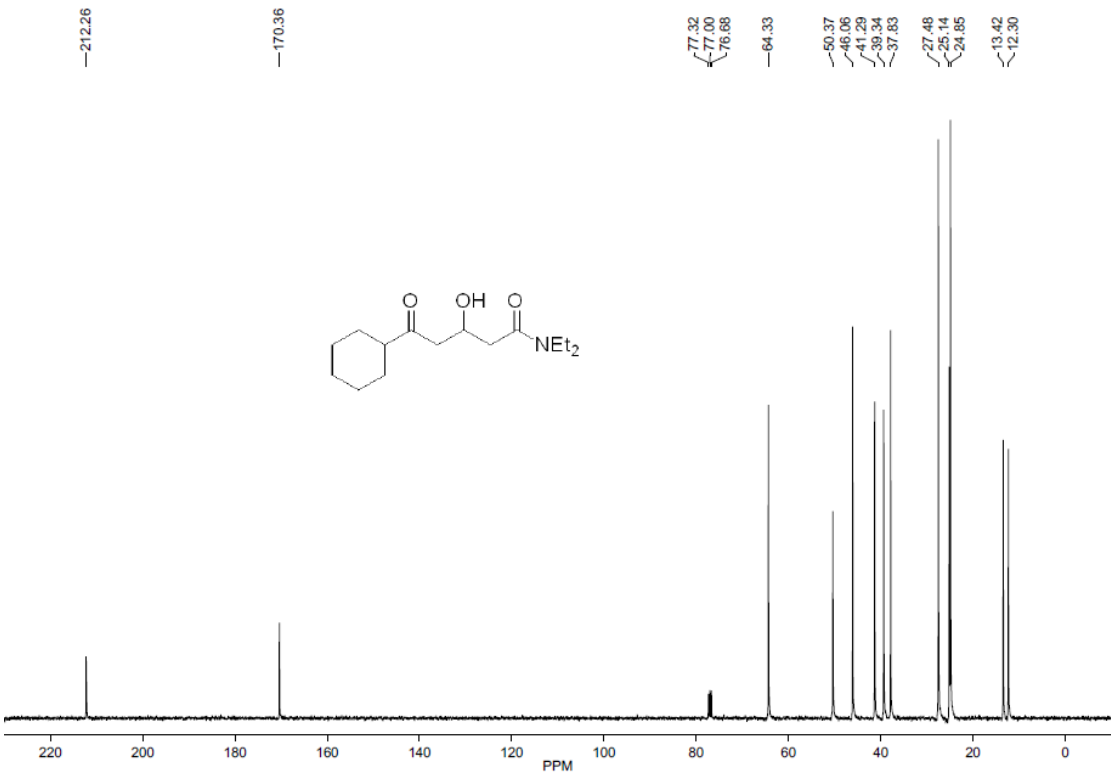

**(4b) *N, N*-diethyl-3-hydroxy-5-oxotridecanamide**



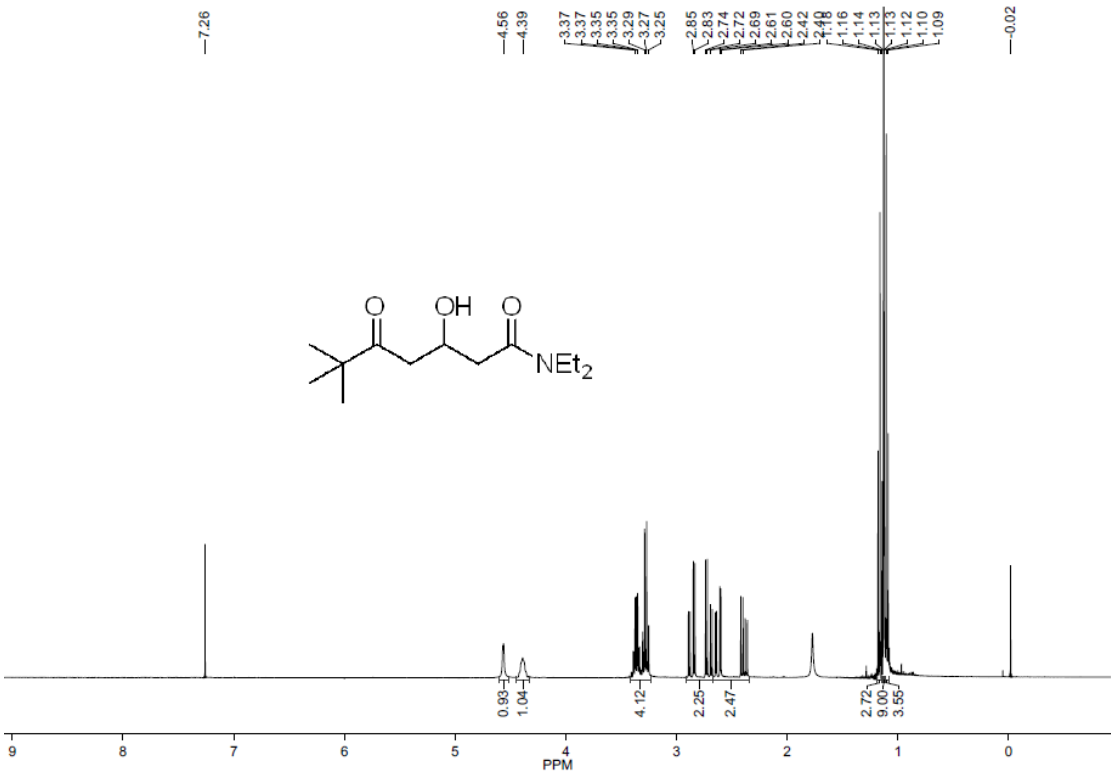


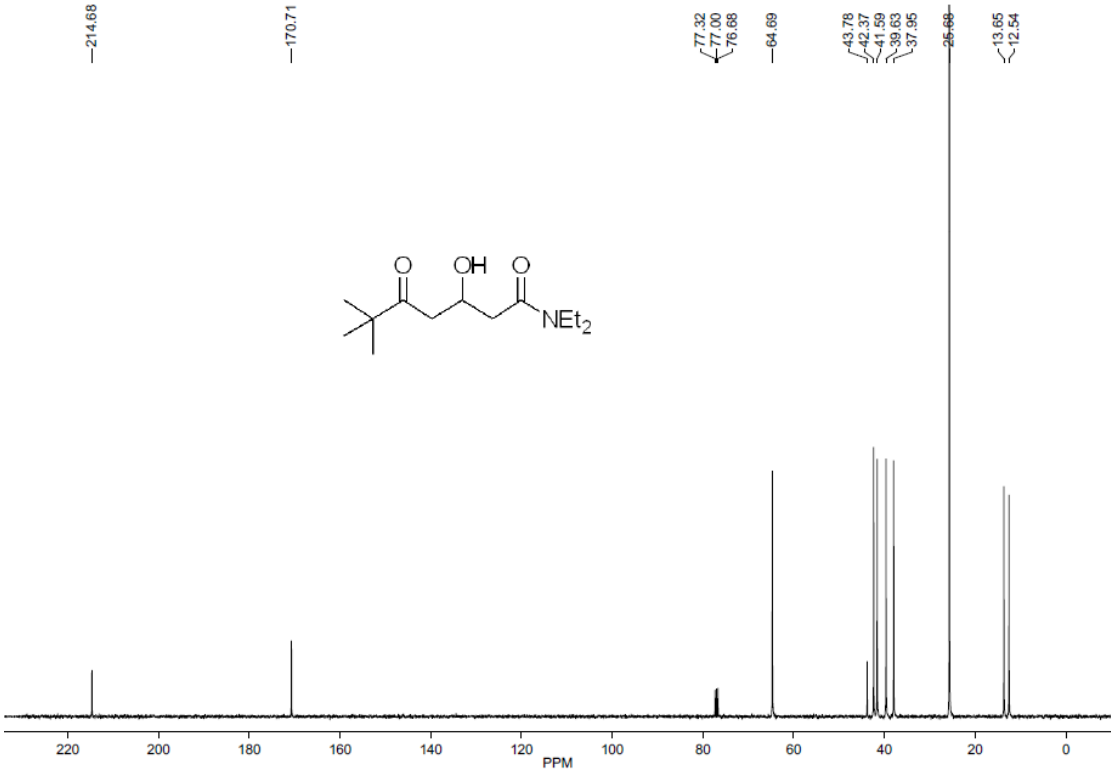

**(4c) 5-cyclohexyl-*N*, *N*-diethyl-3-hydroxy-5-oxopentanamide**



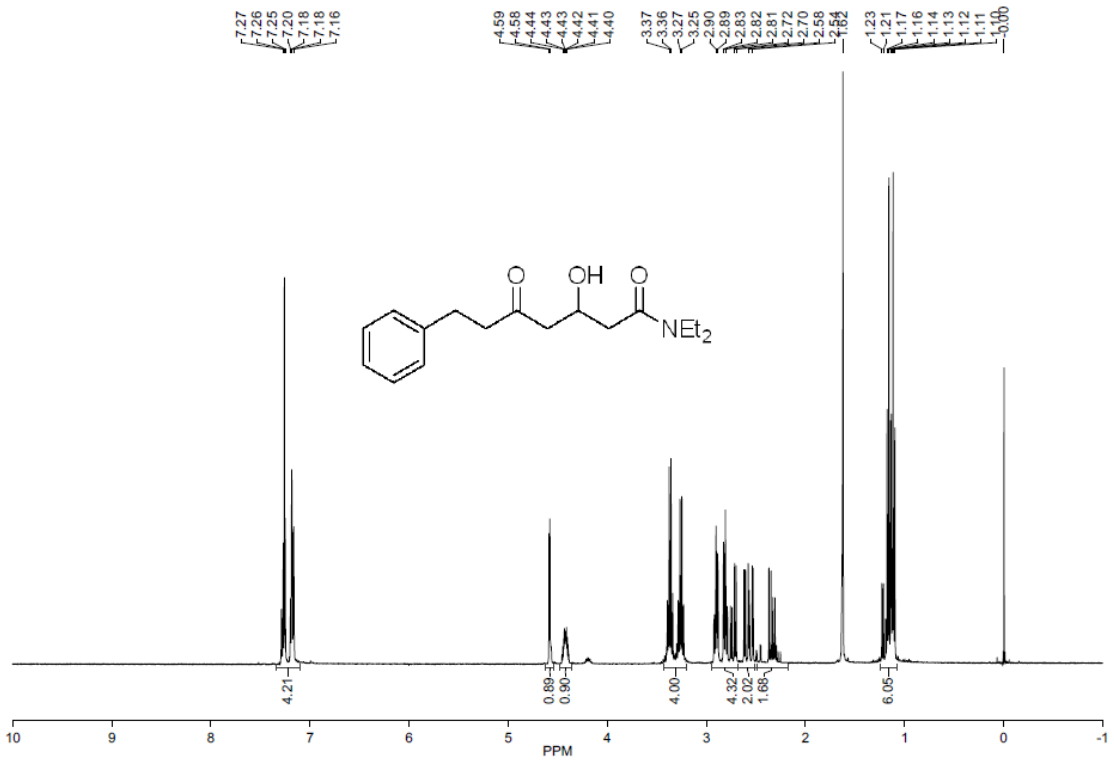


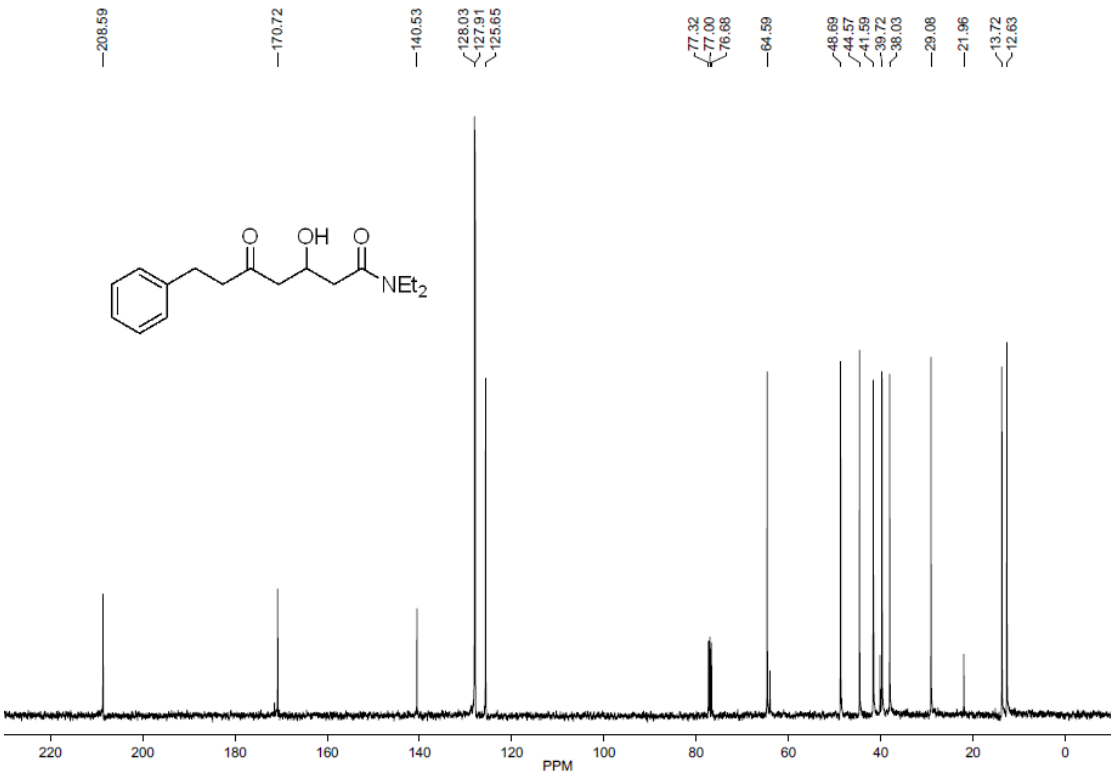

**(4d) *N, N*-diethyl-3-hydroxy-6, 6-dimethyl-5-oxoheptanamide**



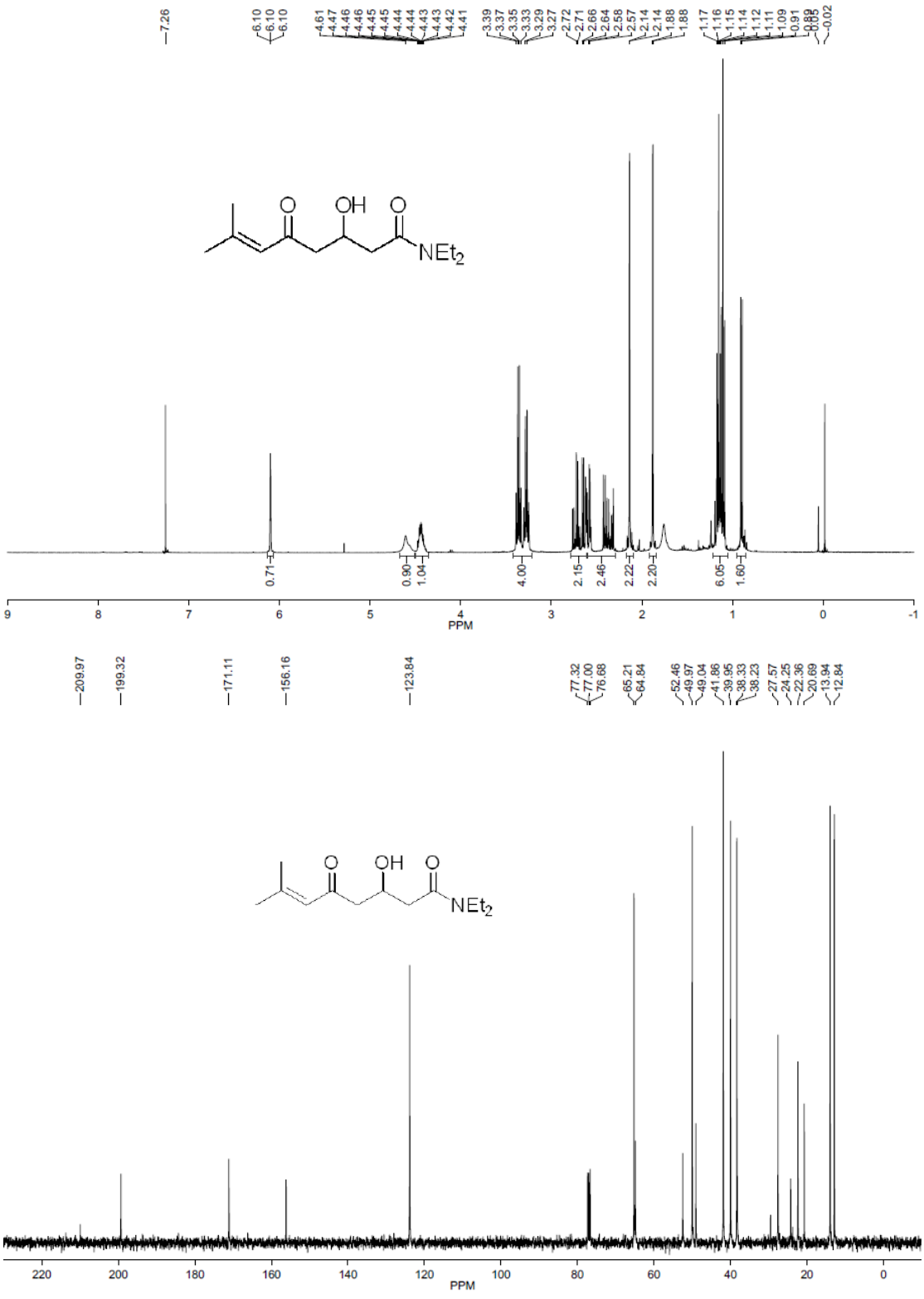



**(4e)** ***N, N*-diethyl-3-hydroxy-5-oxo-7-phenylheptanamide**

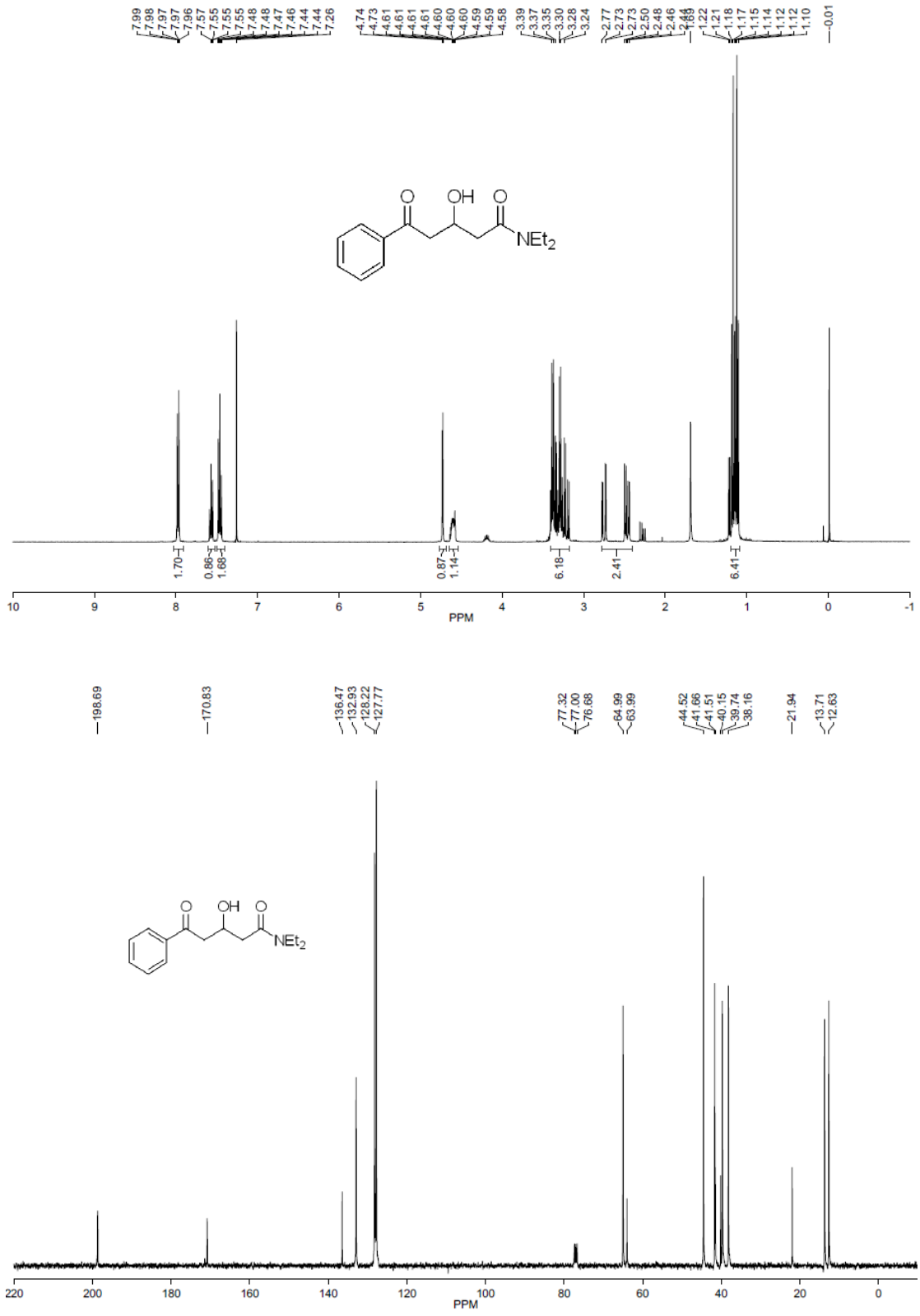




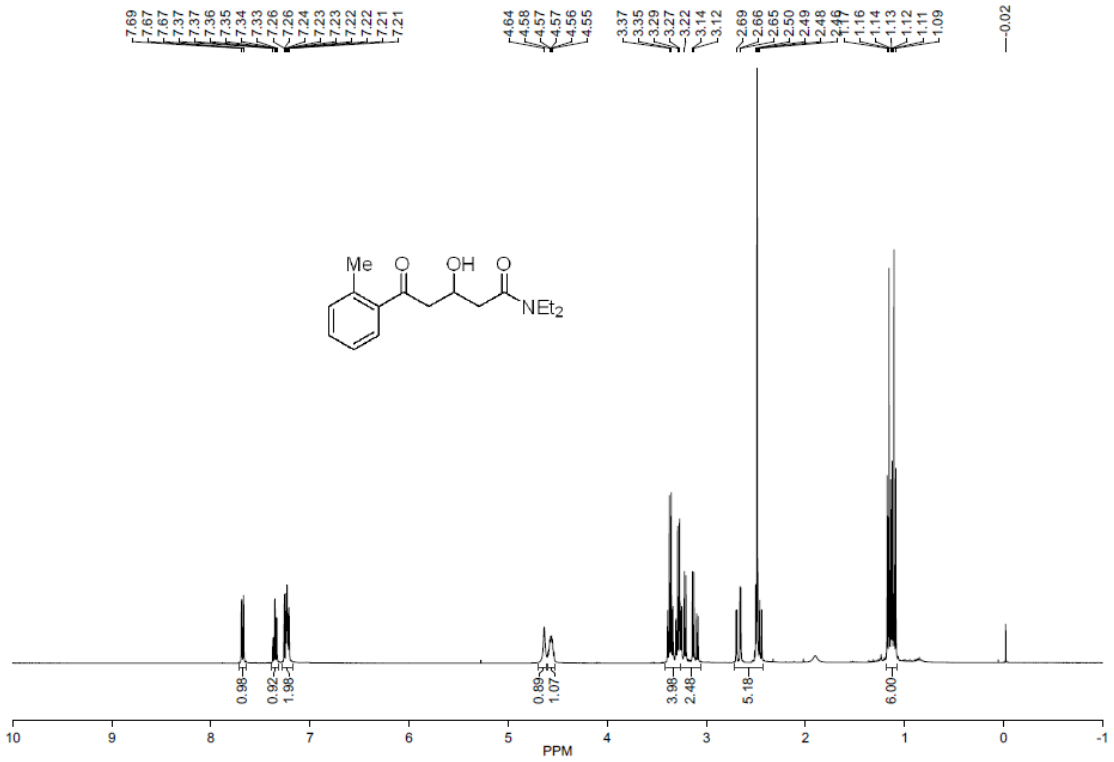

**(4f) *N, N*-diethyl-3-hydroxy-7-methyl-5-oxooct-6-enamide**

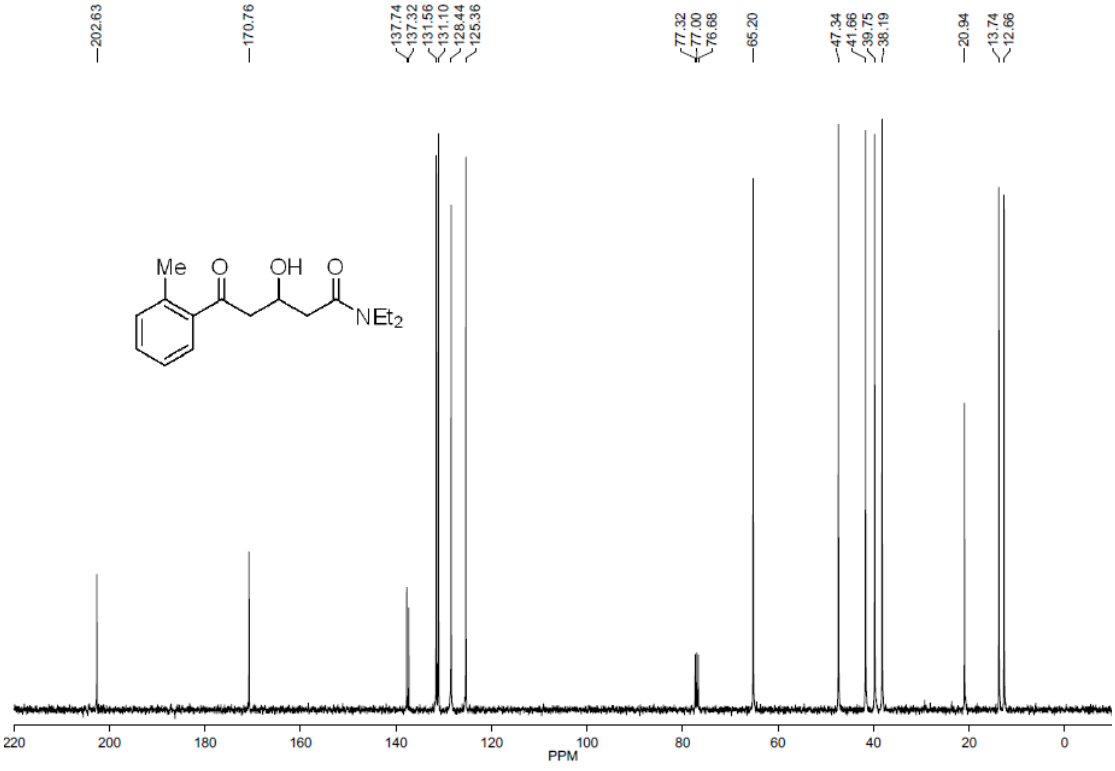



**(4g) *N*, *N*-diethyl-3-hydroxy-5-oxo-5-phenylpentanamide**

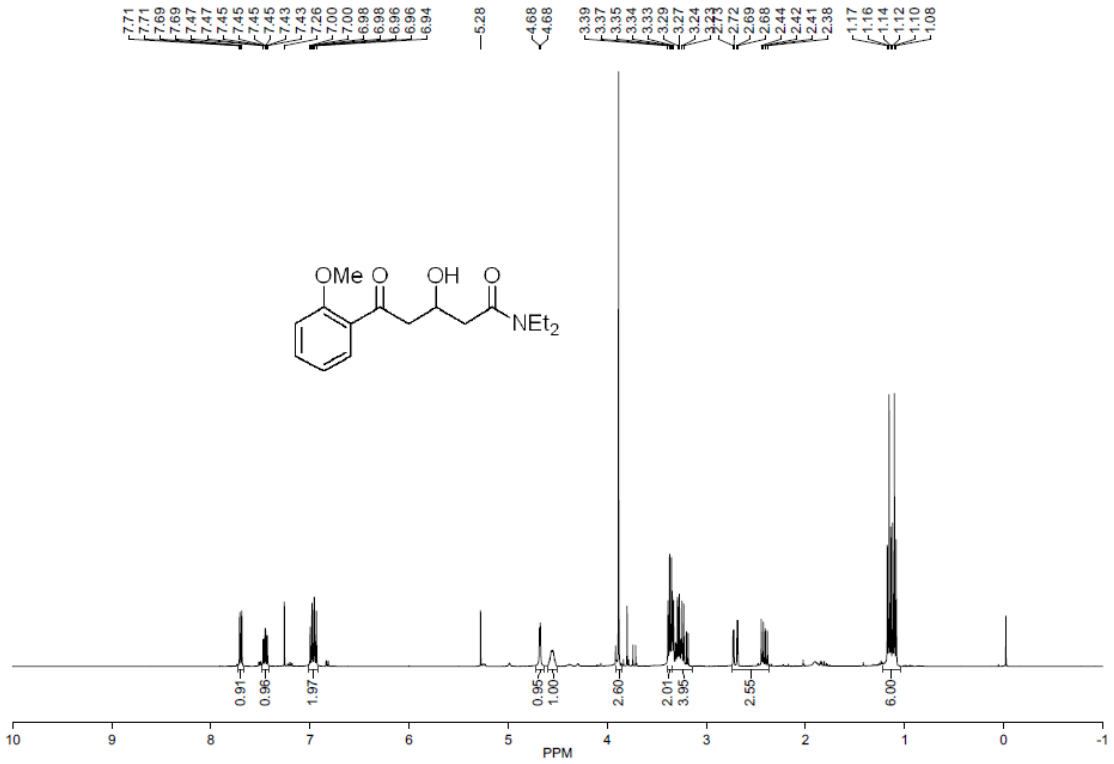


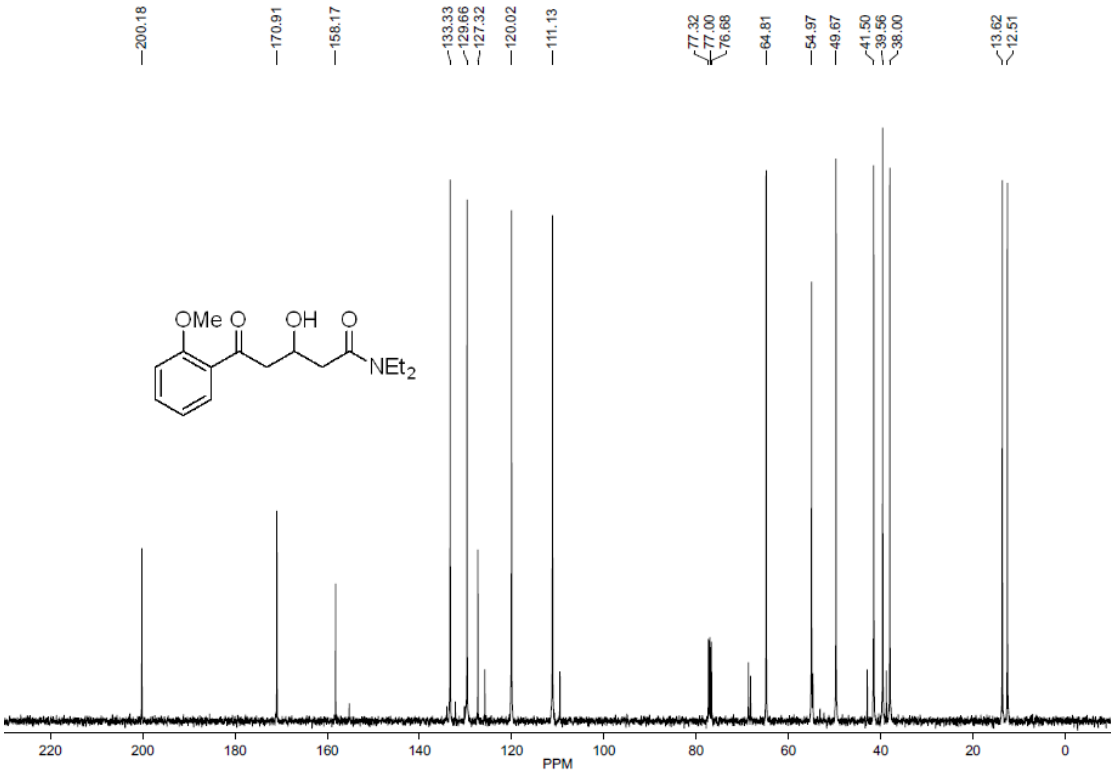

**(4h) *N, N*-diethyl-3, 5-dioxo-5-(o-tolyl)pentanamide**



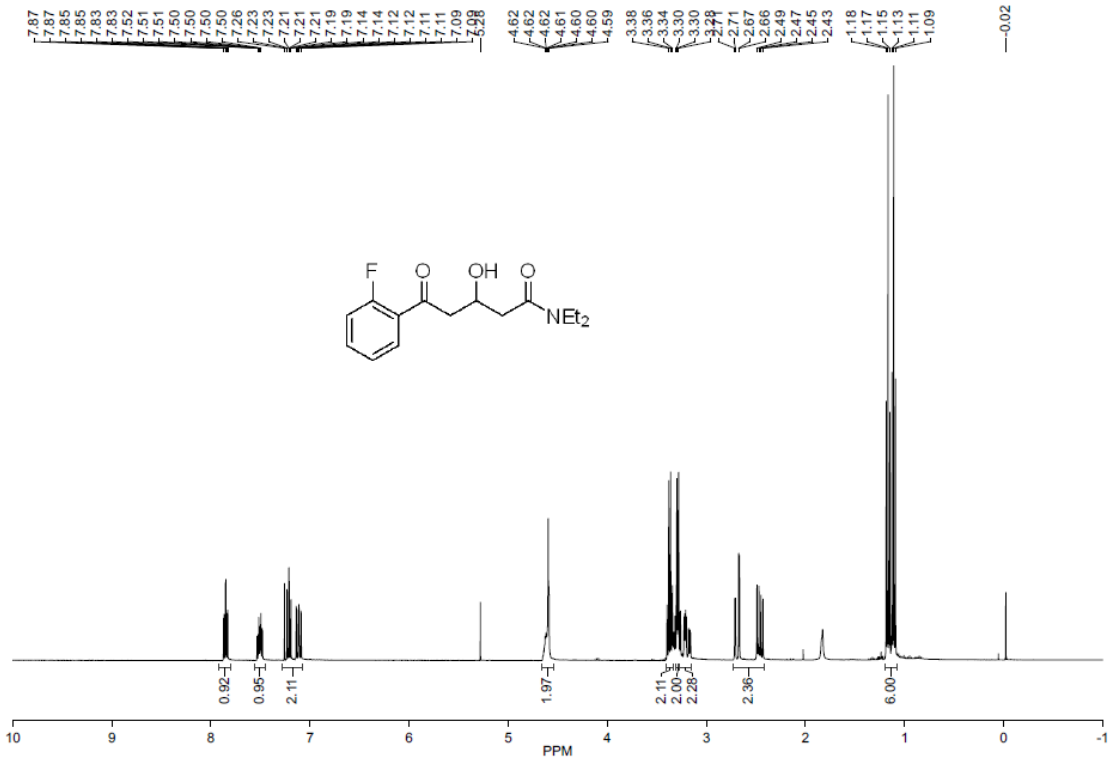



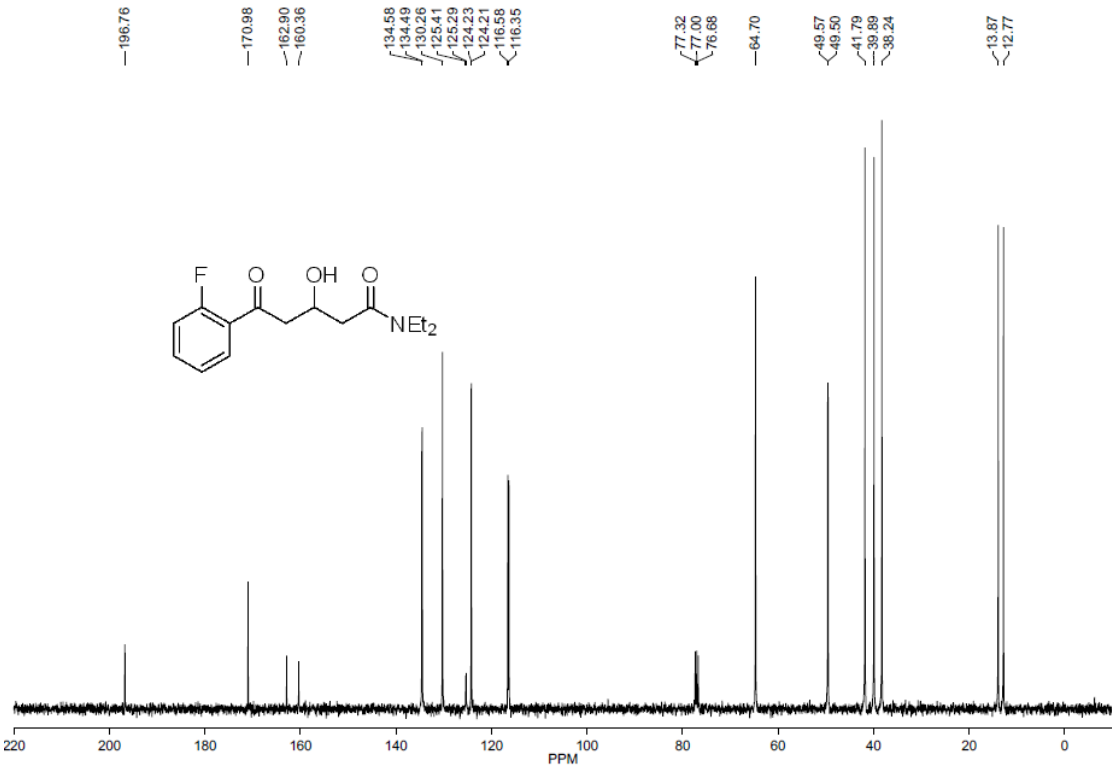

**(4i) *N, N*-diethyl-3-hydroxy-5-(2-methoxyphenyl)-5-oxopentanamide**



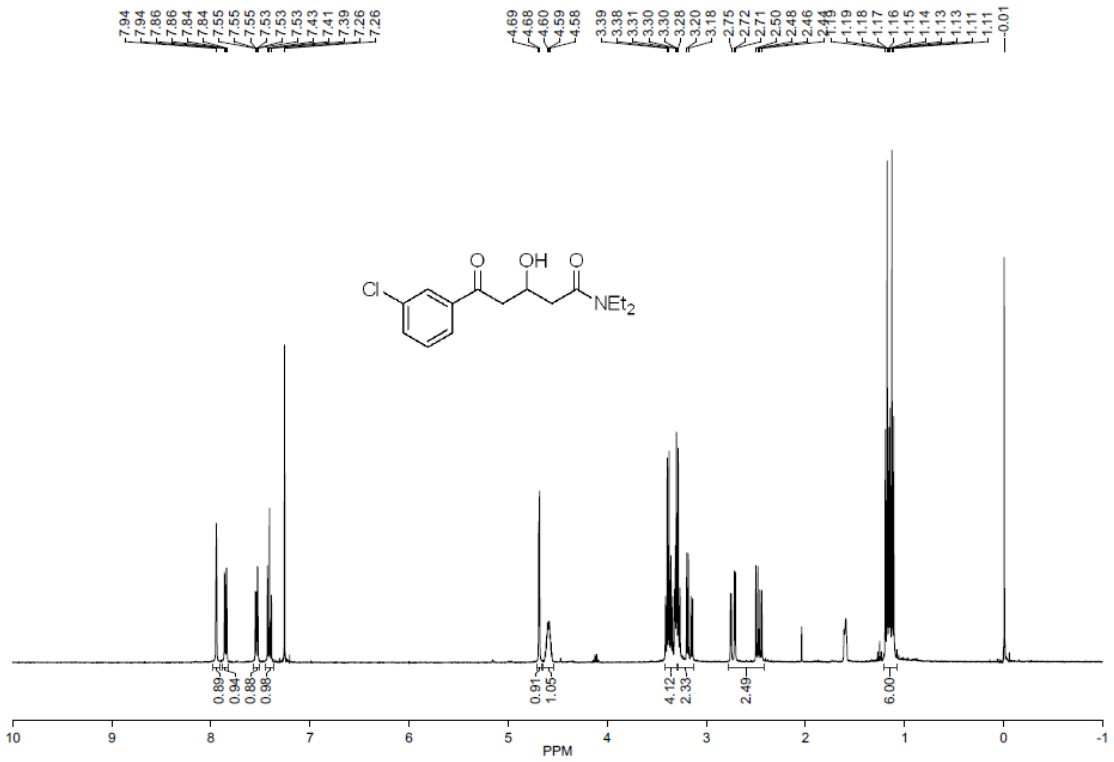



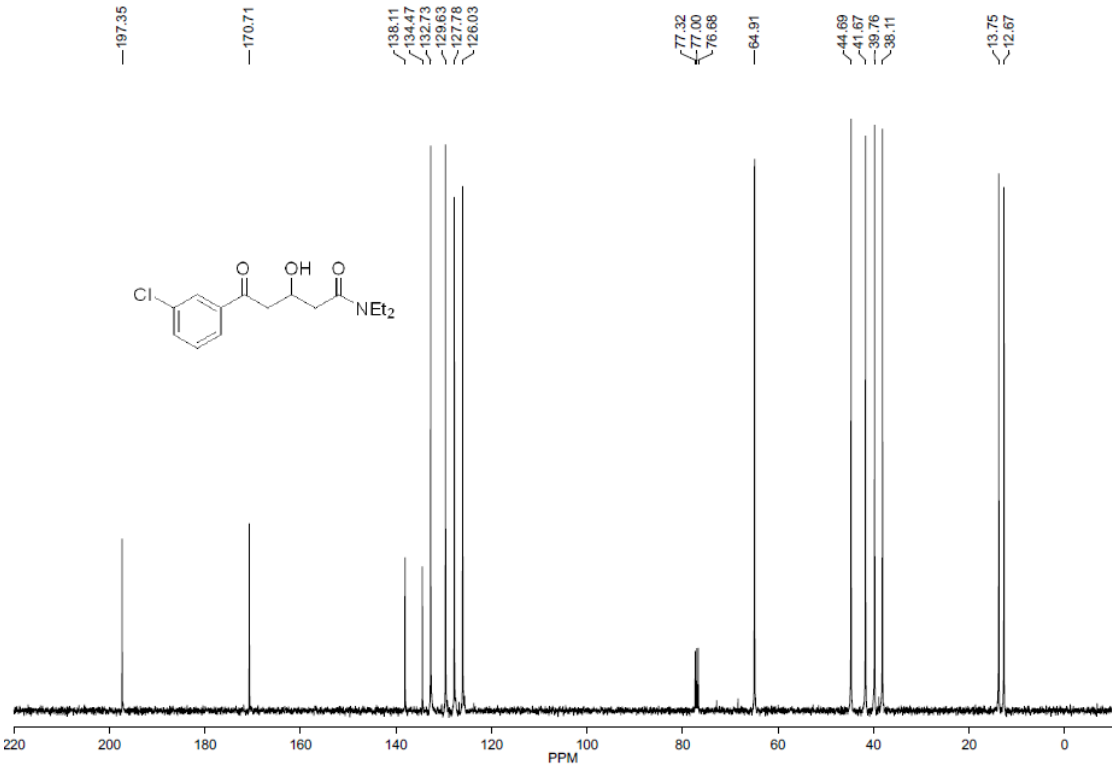

**(4j)** ***N, N*-diethyl-5-(2-fluorophenyl)-3-hydroxy-5-oxopentanamide**



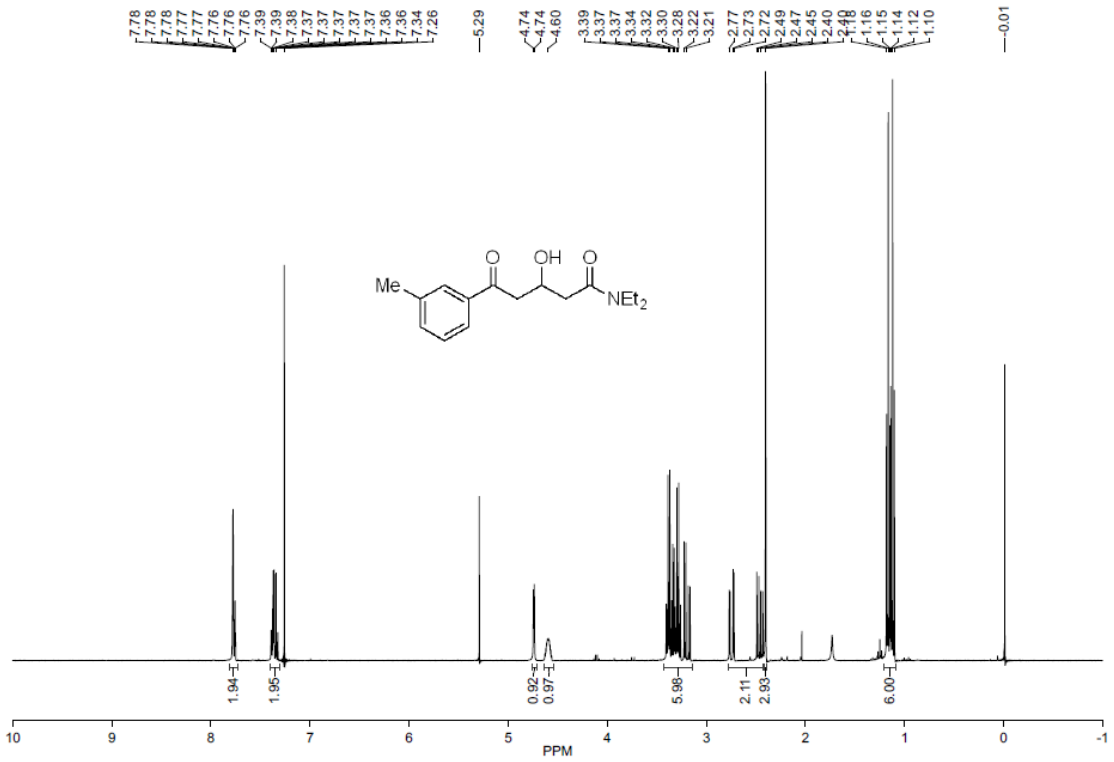



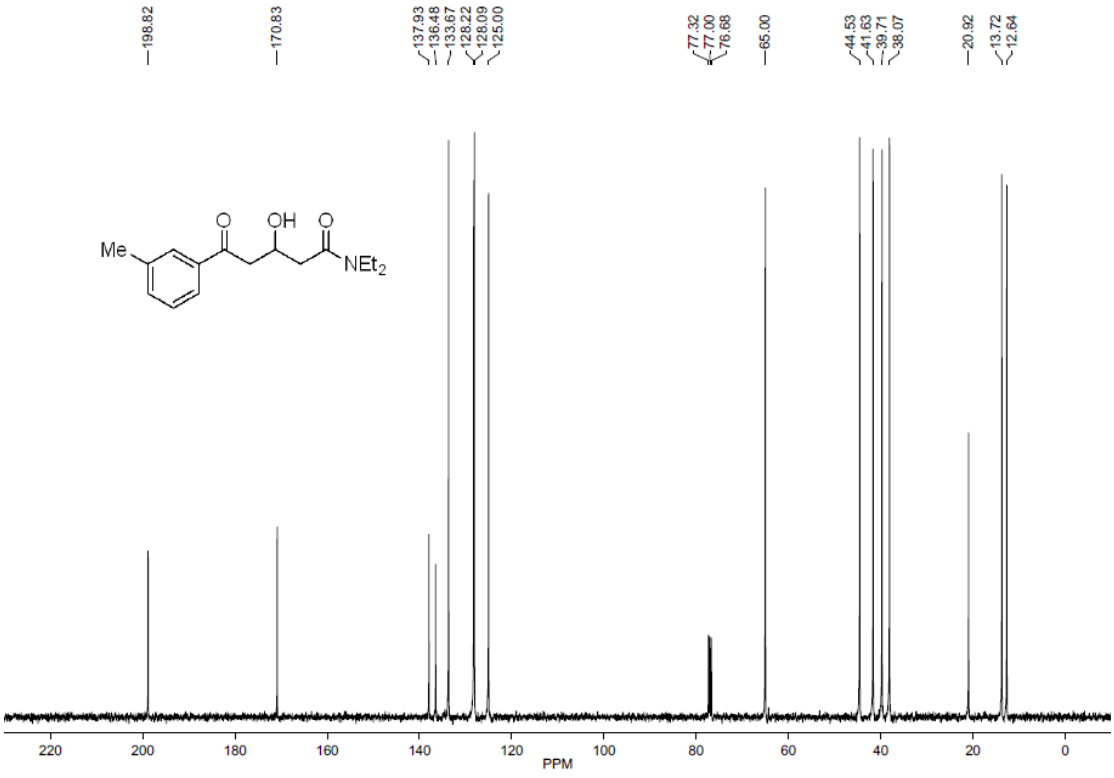

**(4k) 5-(3-chlorophenyl)-*N, N*-diethyl-3-hydroxy-5-oxopentanamide**



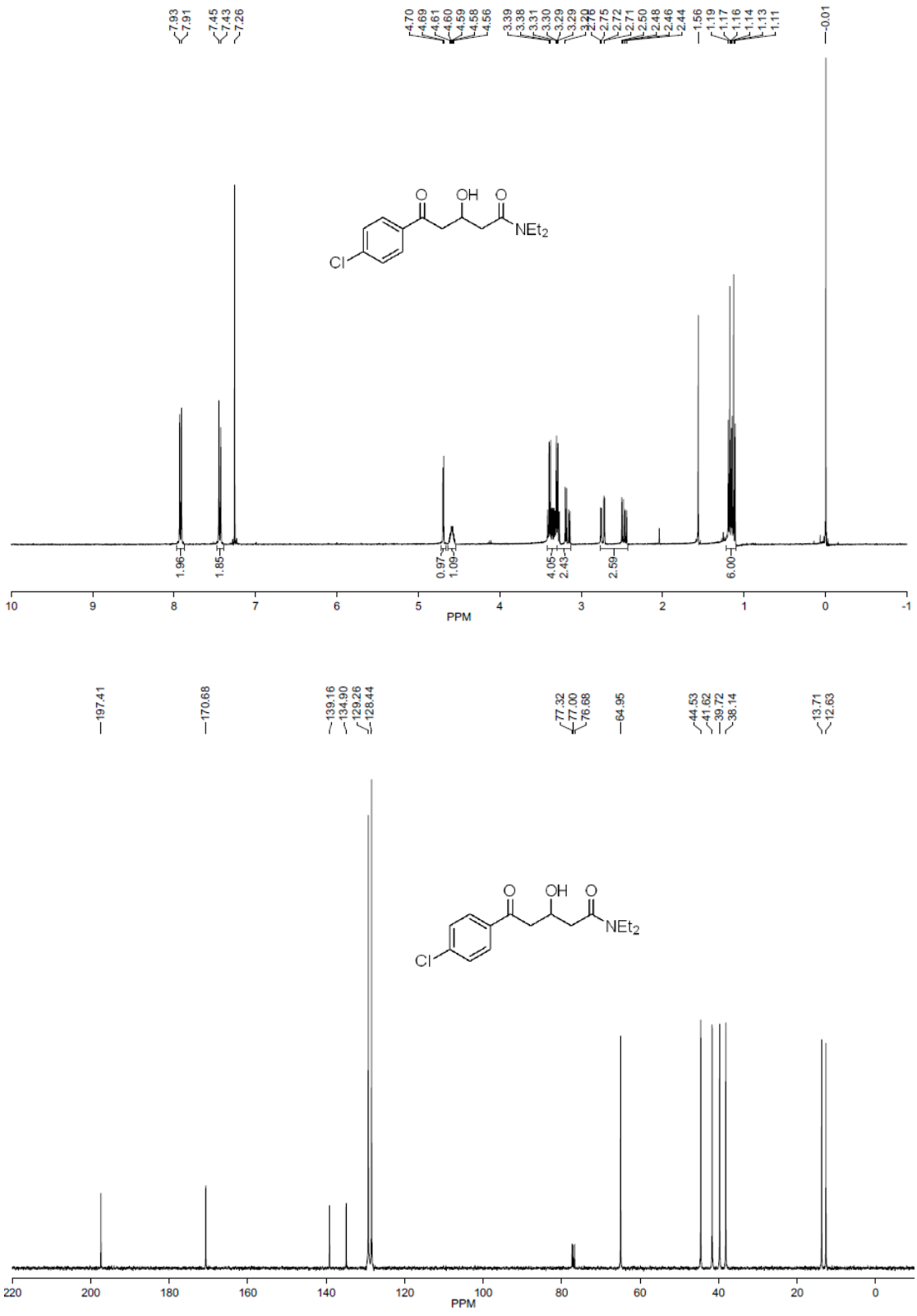




**(4l) *N, N*-diethyl-3-hydroxy-5-oxo-5-(m-tolyl)pentanamide**

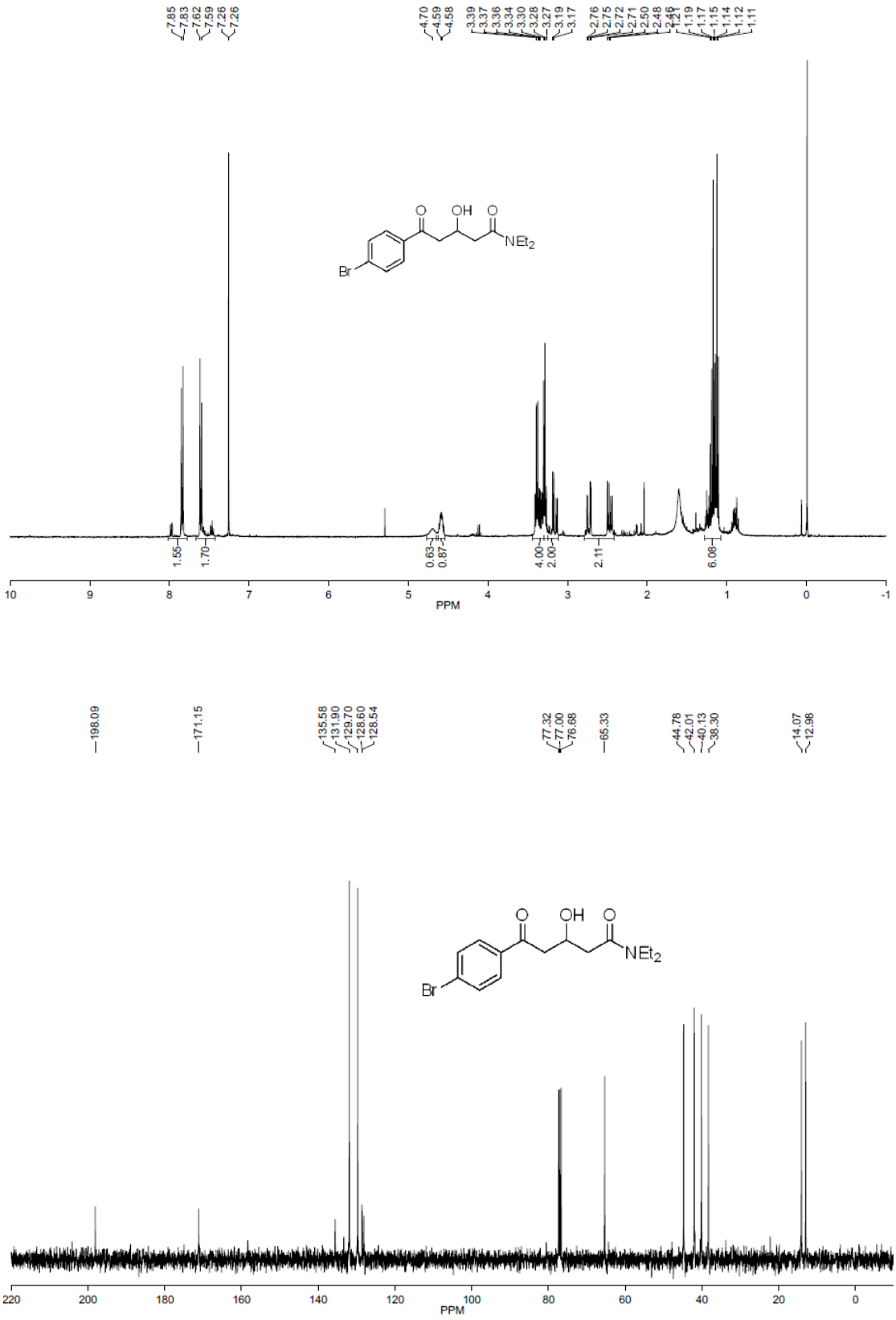


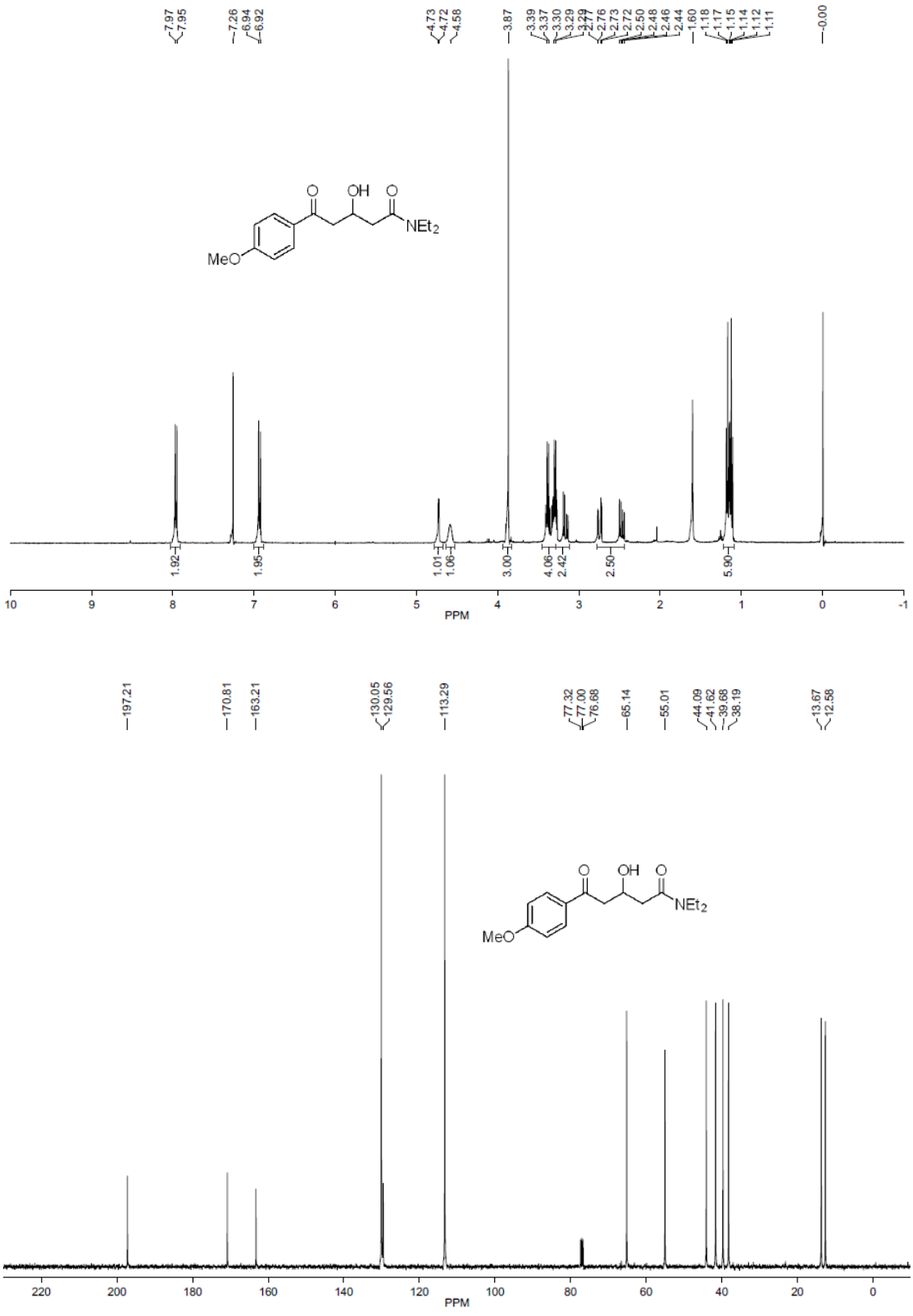

**(4m) 5-(4-chlorophenyl)-*N, N*-diethyl-3-hydroxy-5-oxopentanamide**



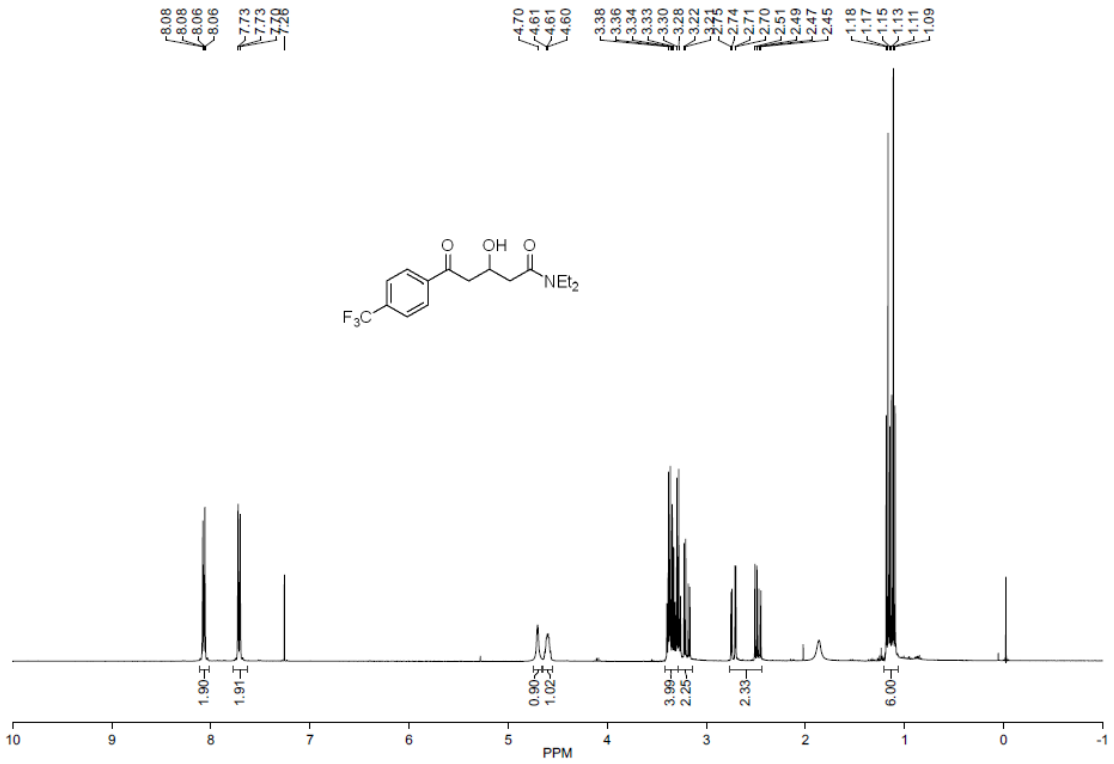

**(4n) 5-(4-bromophenyl)-*N, N*-diethyl-3-hydroxy-5-oxopentanamide**

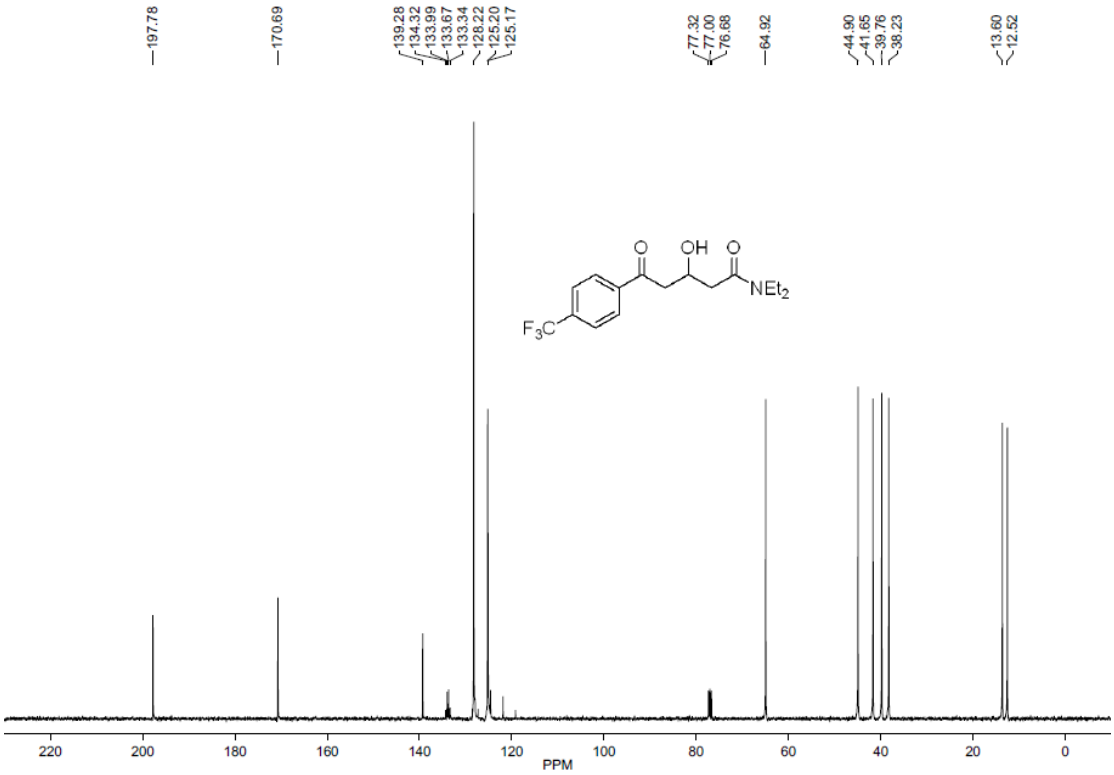



**(4o) *N, N*-diethyl-3-hydroxy-5-(4-methoxyphenyl)-5-oxopentanamide**

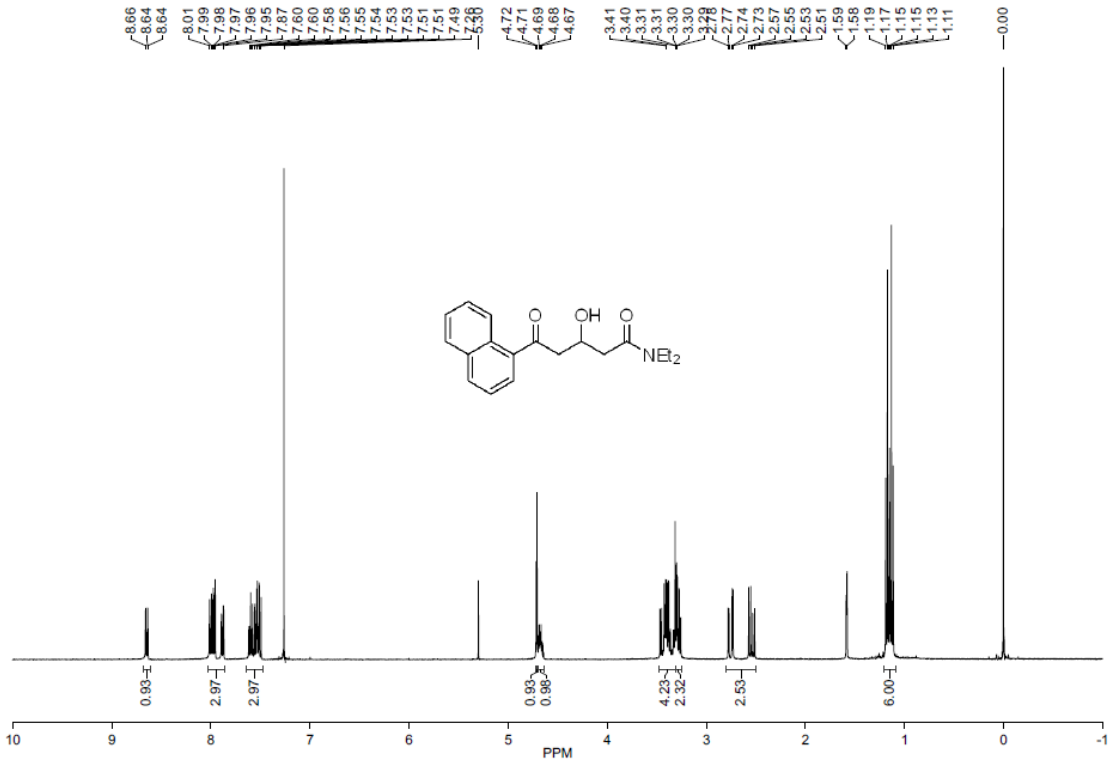


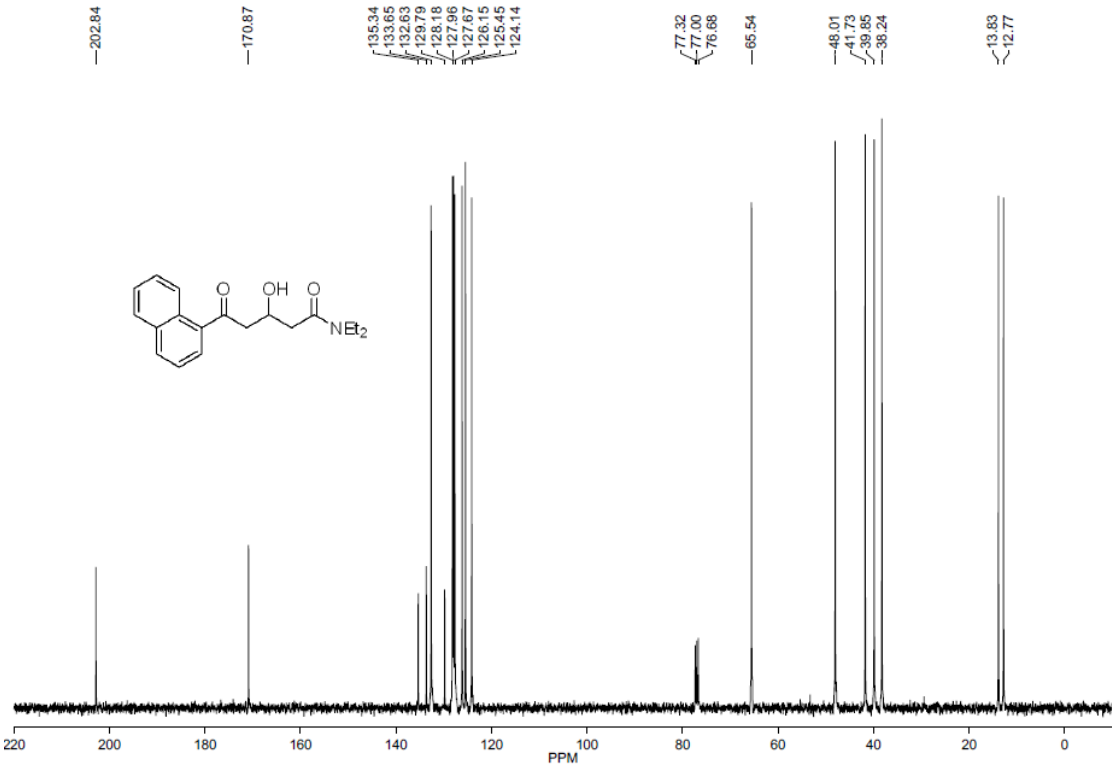

**(4p) *N*, *N*-diethyl-3-hydroxy-5-oxo-5-(4-(trifluoromethyl)phenyl)pentanamide**

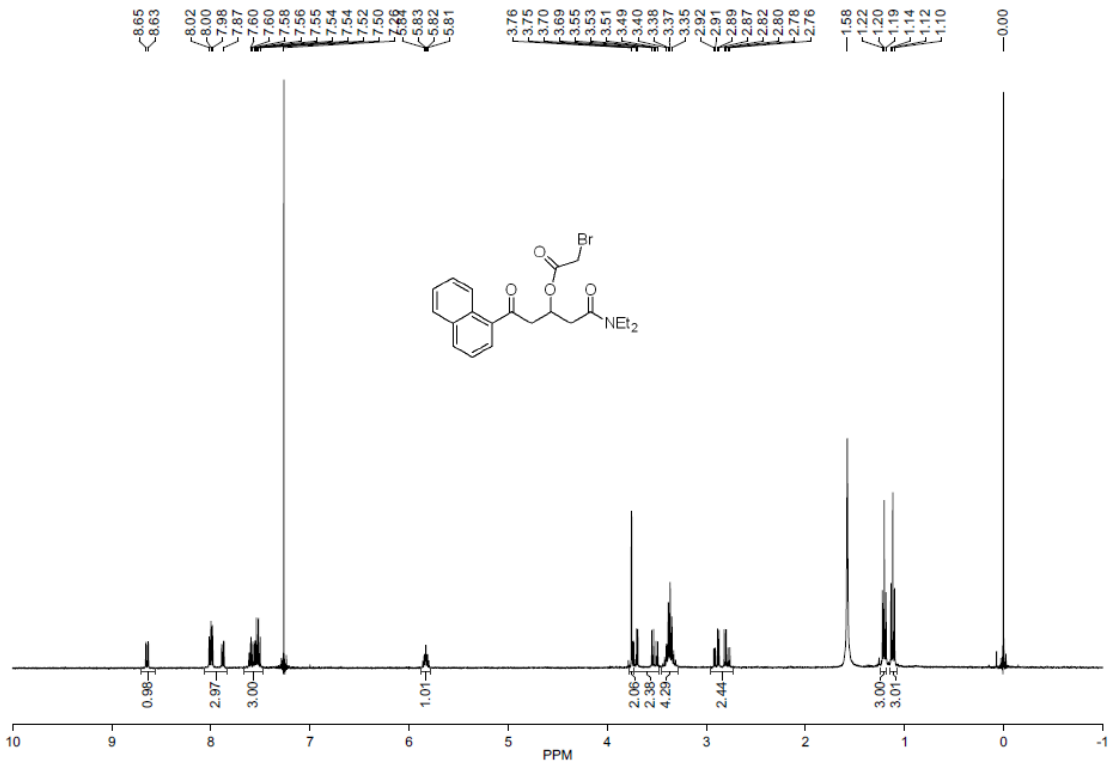


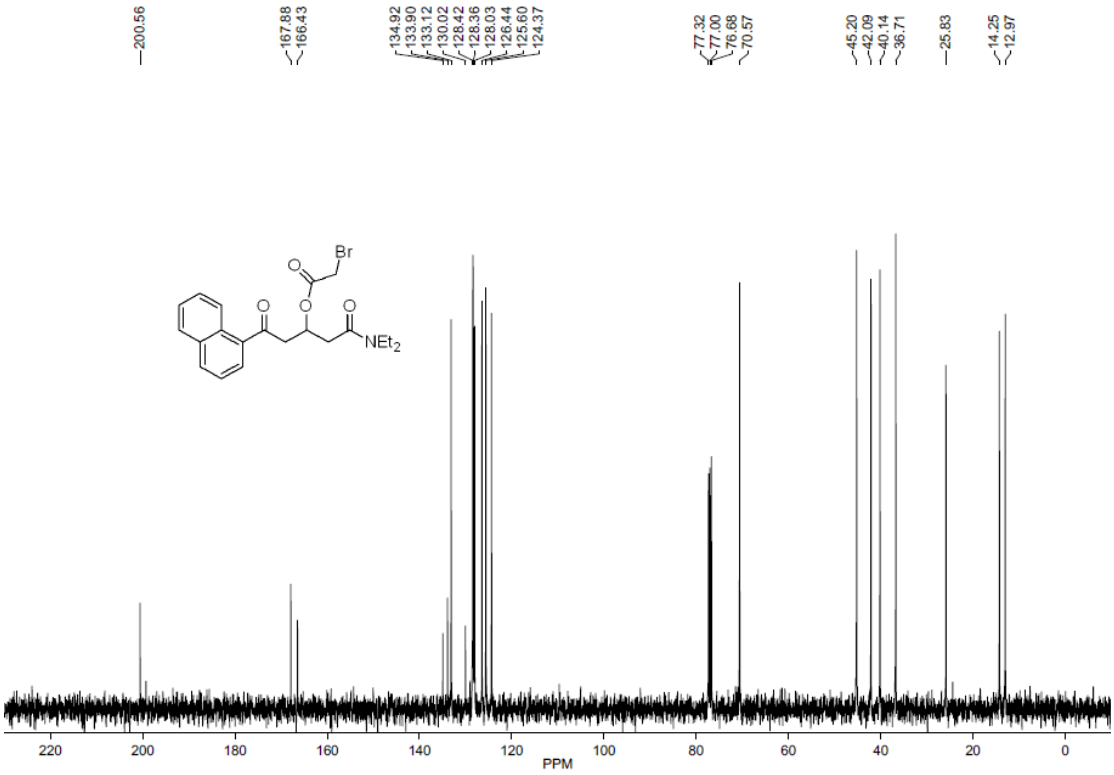




**(4q) *N, N*-diethyl-3-hydroxy-5-(naphthalen-1-yl)-5-oxopentanamide**

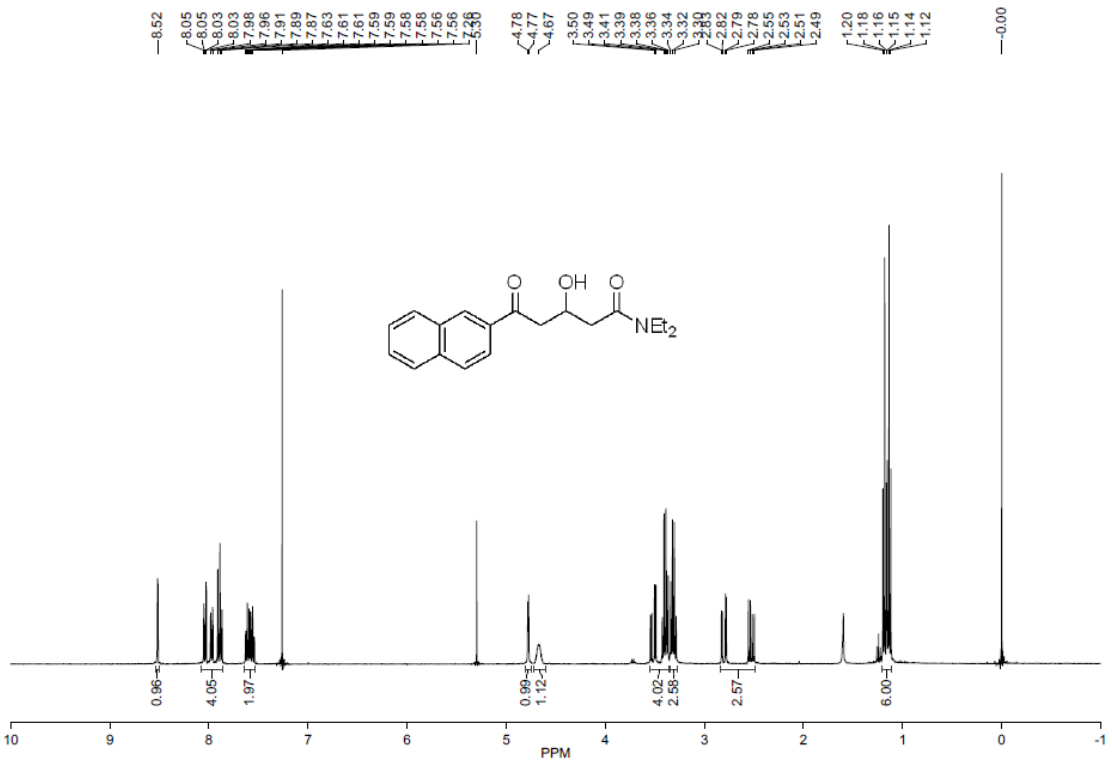

8.66
8.64
8.64
8.01
7.99
7.98
7.97
7.96
7.95
7.87
7.60
7.60
7.58
7.56
7.55
7.54
7.53
7.53
7.51
7.51
7.49
7.26
5.30
4.72
4.71
4.69
4.68
4.67
3.41
3.40
3.31
3.31
3.30
3.30
2.78
2.77
2.74
2.73
2.57
2.55
2.53
2.51
1.59
1.58
1.19
1.17
1.15
1.15
1.13
1.11
0.00
O
OH
O
NEt2
0.93
2.97
2.97
0.93
0.98
4.23
2.32
2.53
6.00
10
9
8
7
6
5
4
3
2
1
0
-1
PPM

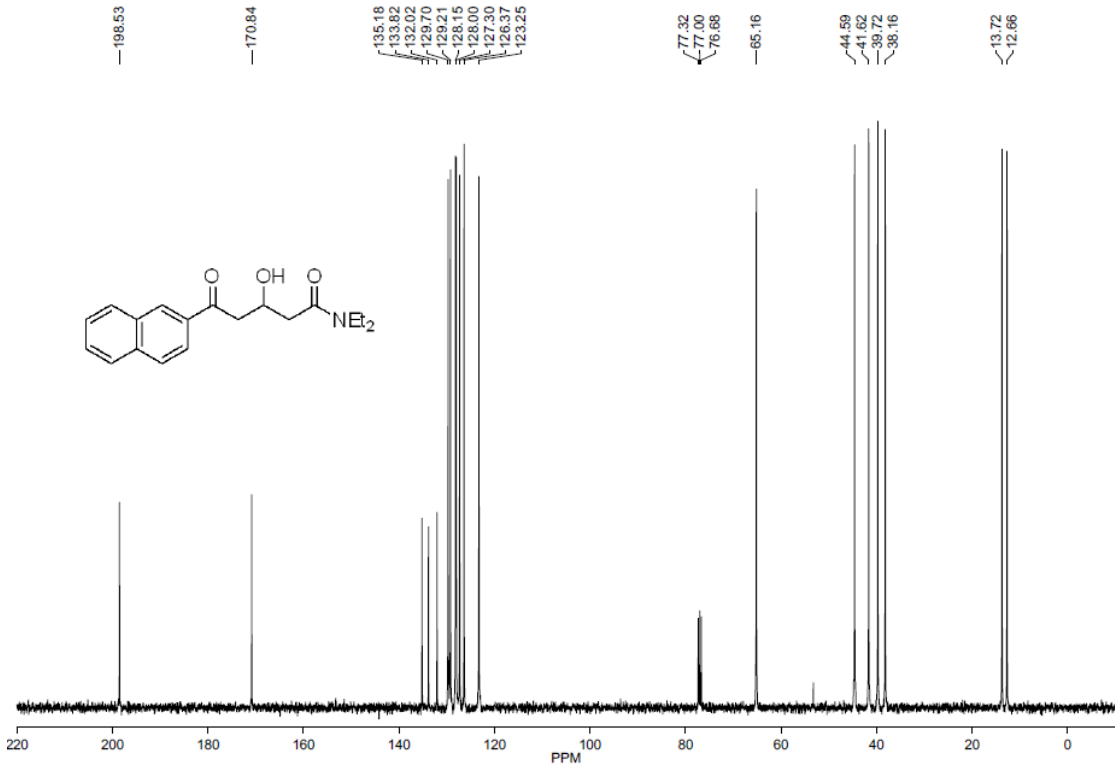

202.84
170.87
135.34
133.65
132.63
129.79
128.18
127.96
127.67
126.15
125.45
124.14
77.32
77.00
76.68
65.54
48.01
41.73
39.85
38.24
13.83
12.77
O
OH
O
NEt2
220
200
180
160
140
120
100
80
60
40
20
0
PPM


8.65
8.63
8.02
8.00
7.98
7.87
7.60
7.58
7.56
7.55
7.54
7.52
7.50
5.84
5.83
5.82
5.81
3.76
3.75
3.70
3.69
3.55
3.53
3.51
3.49
3.40
3.38
3.37
3.35
2.92
2.91
2.89
2.87
2.82
2.80
2.78
2.76
1.58
1.22
1.20
1.19
1.14
1.12
1.10
0.00
Br
O
O
O
O
NEt2
0.98
2.97
3.00
1.01
2.06
2.38
4.29
2.44
3.00
3.01
10
9
8
7
6
5
4
3
2
1
0
-1
PPM

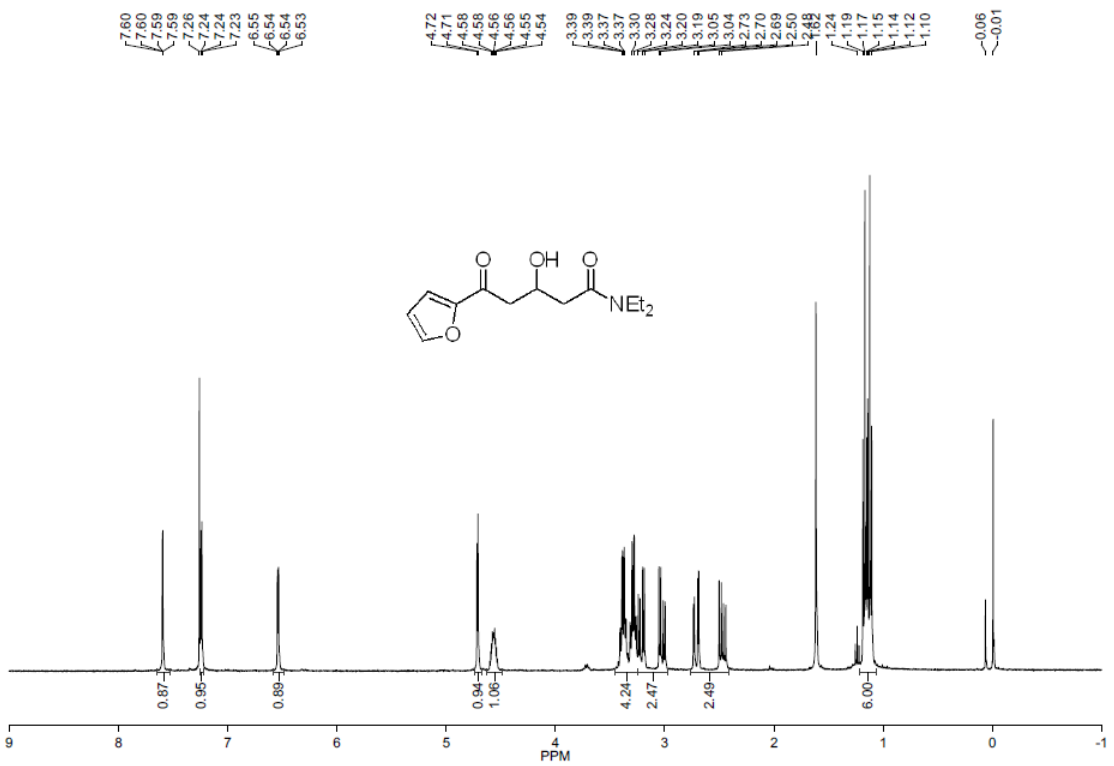

200.56
167.88
166.43
134.92
133.90
133.12
130.02
128.42
128.36
128.03
126.44
125.60
124.37
77.32
77.00
76.68
70.57
45.20
42.09
40.14
36.71
25.83
14.25
12.97
Br
O
O
O
O
NEt2
220
200
180
160
140
120
100
80
60
40
20
0
PPM

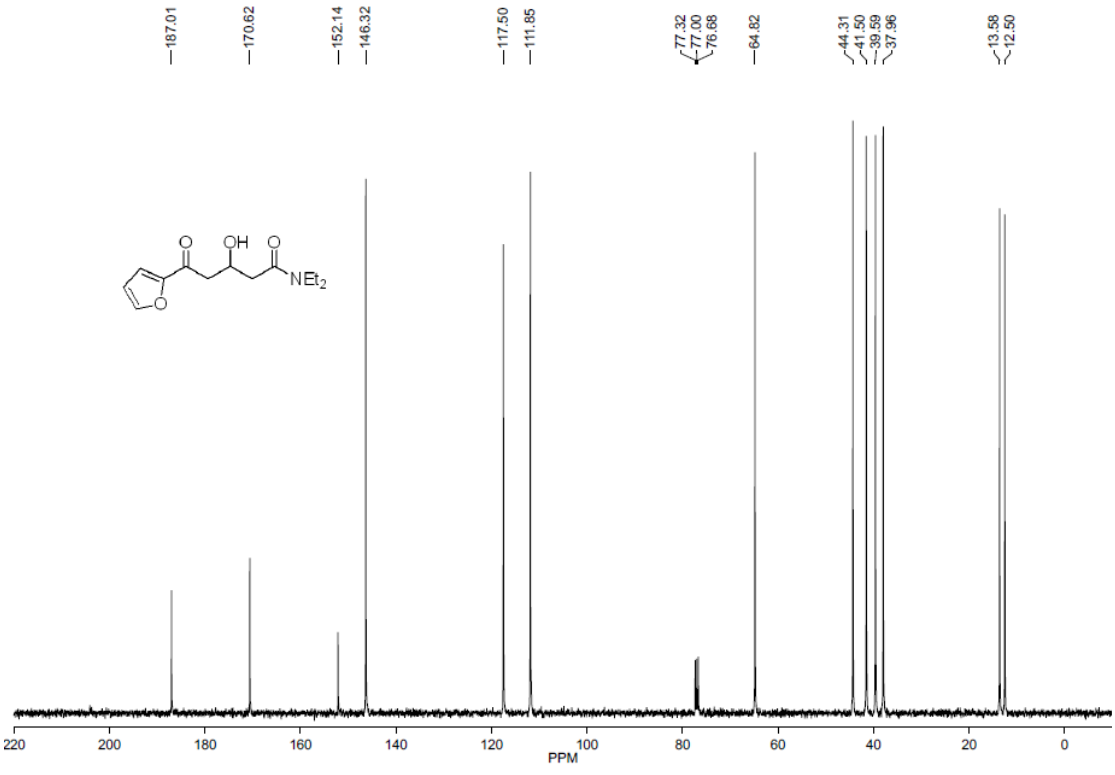
**(4r) *N, N*-diethyl-3-hydroxy-5-(naphthalen-2-yl)-5-oxopentanamide**



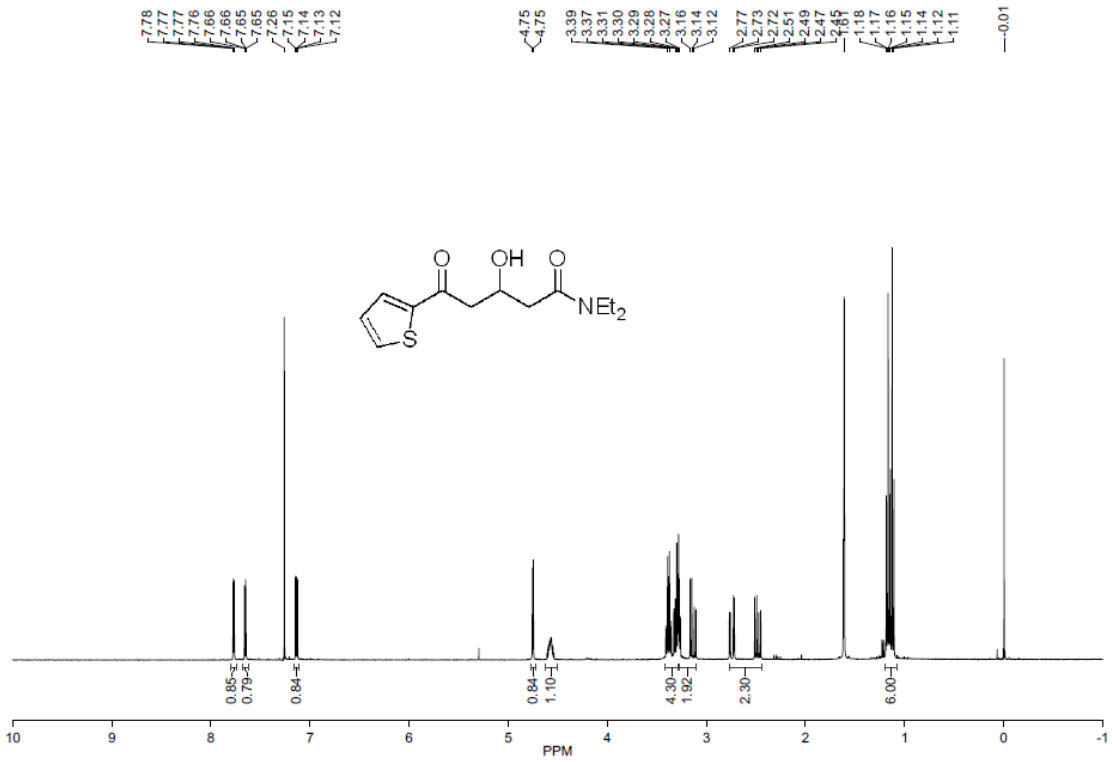



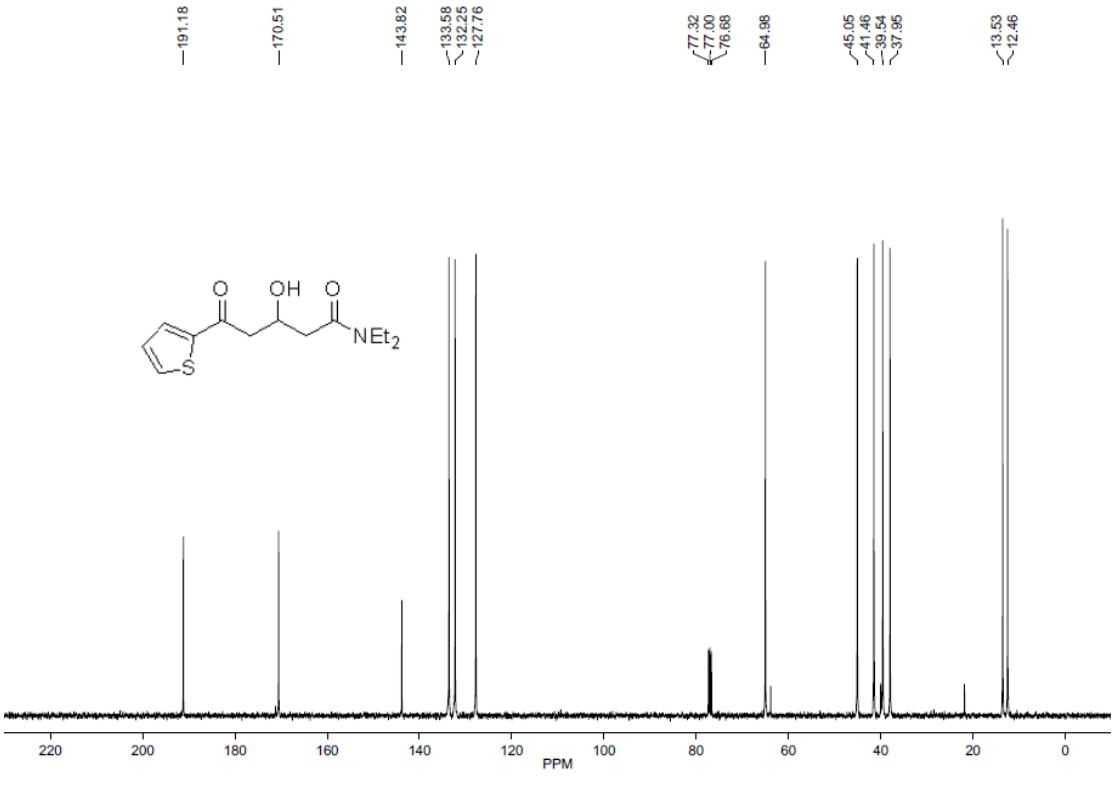
**(4s) *N, N*-diethyl-5-(furan-2-yl)-3-hydroxy-5-oxopentanamide**



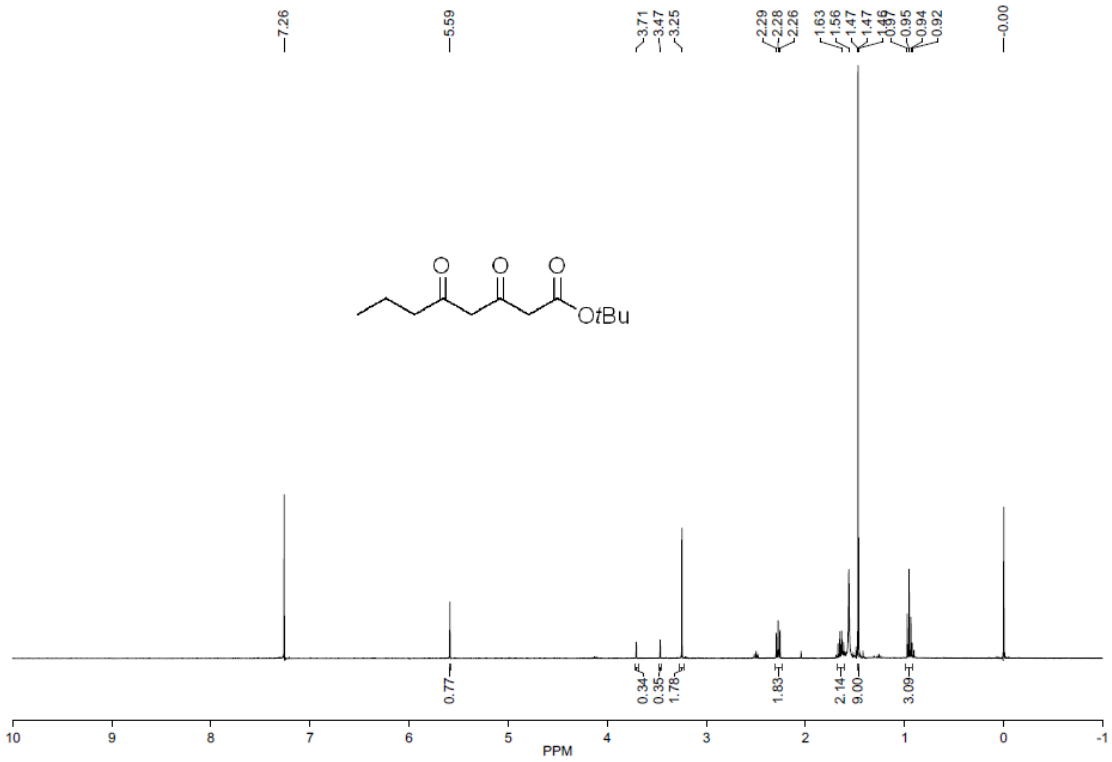



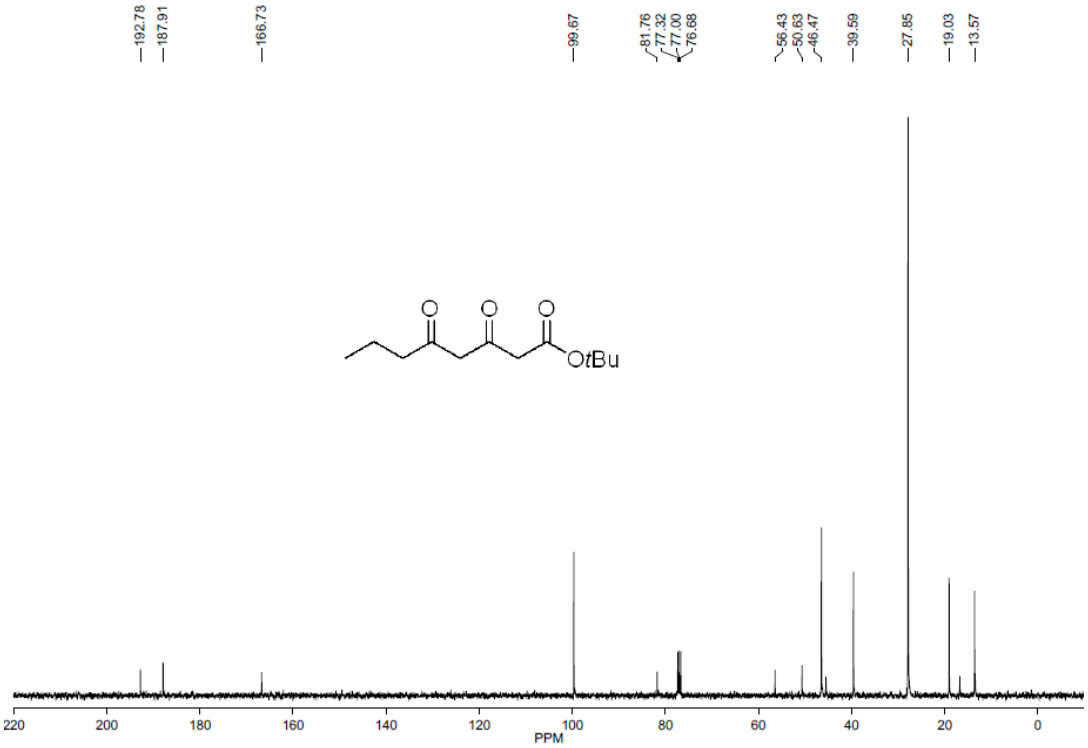
**(4t) *N, N*-diethyl-3-hydroxy-5-oxo-5-(thiophen-2-yl)pentanamide**



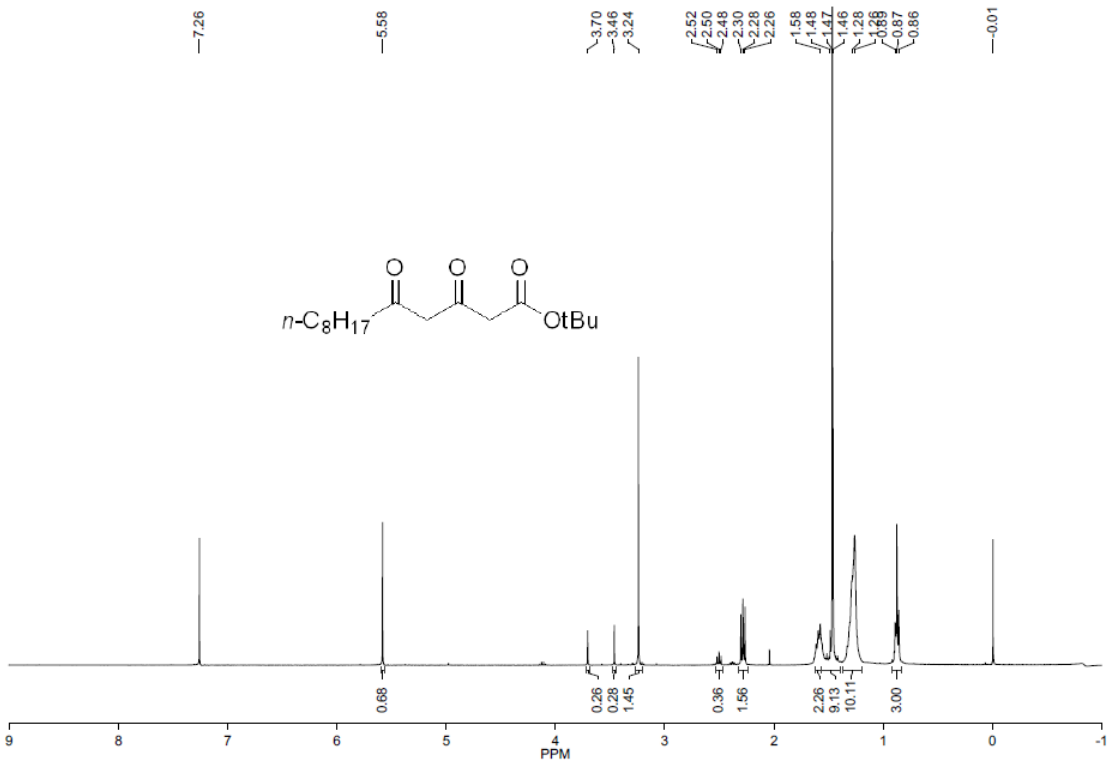



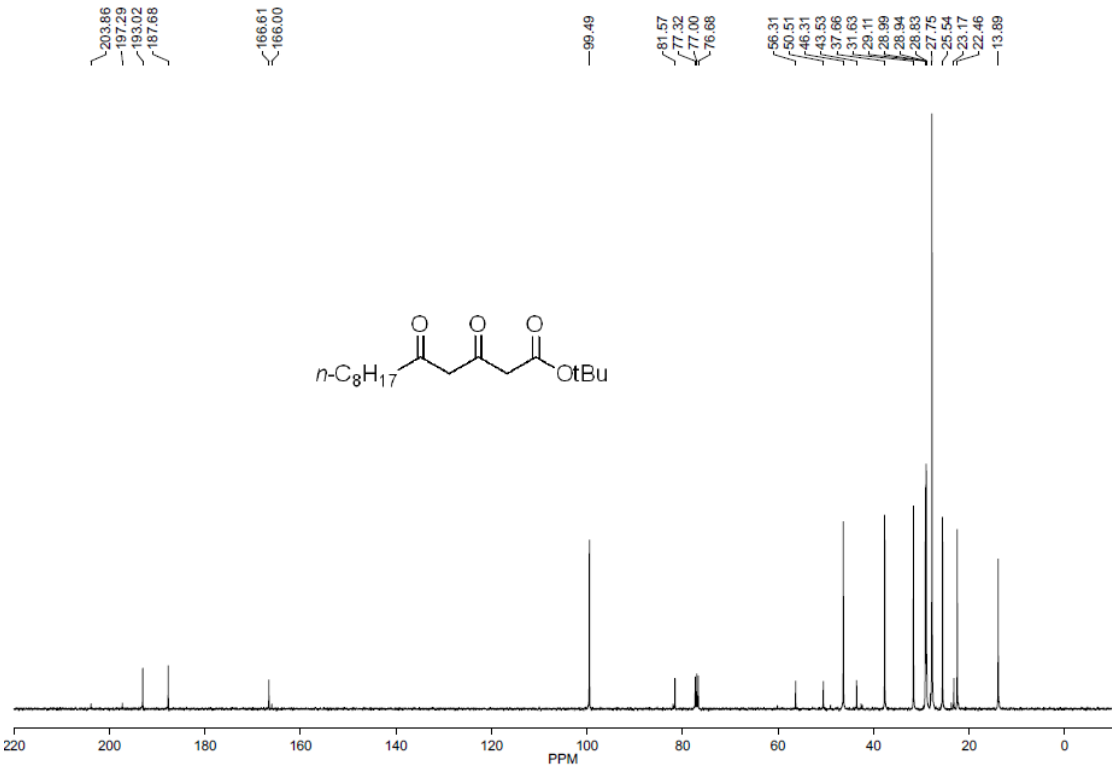
**(5a) tert-butyl 3, 5-dioxooctanoate**



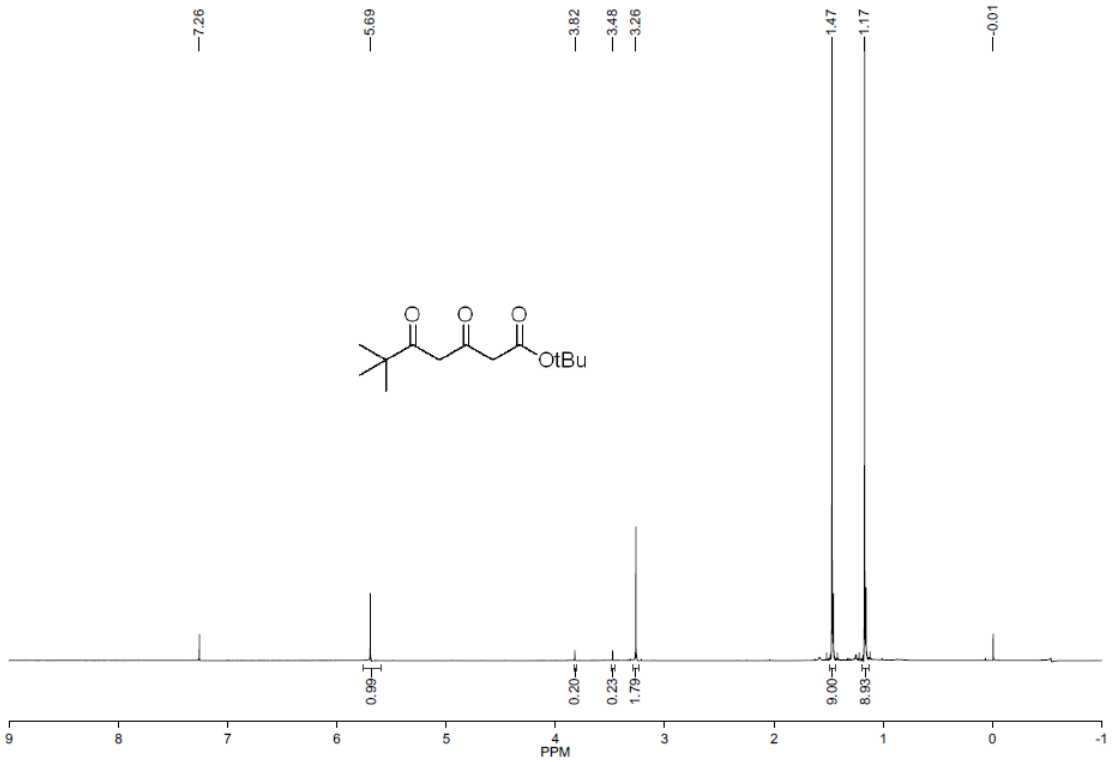



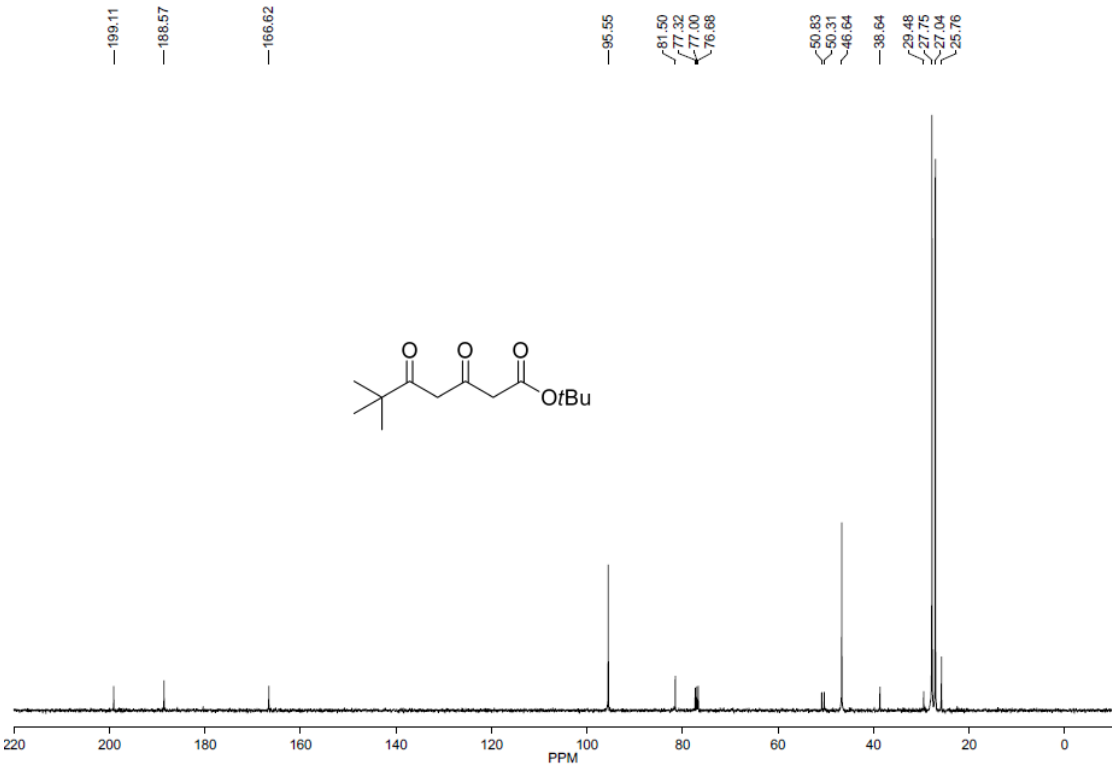
**(5b) tert-butyl 3, 5-dioxotridecanoate**



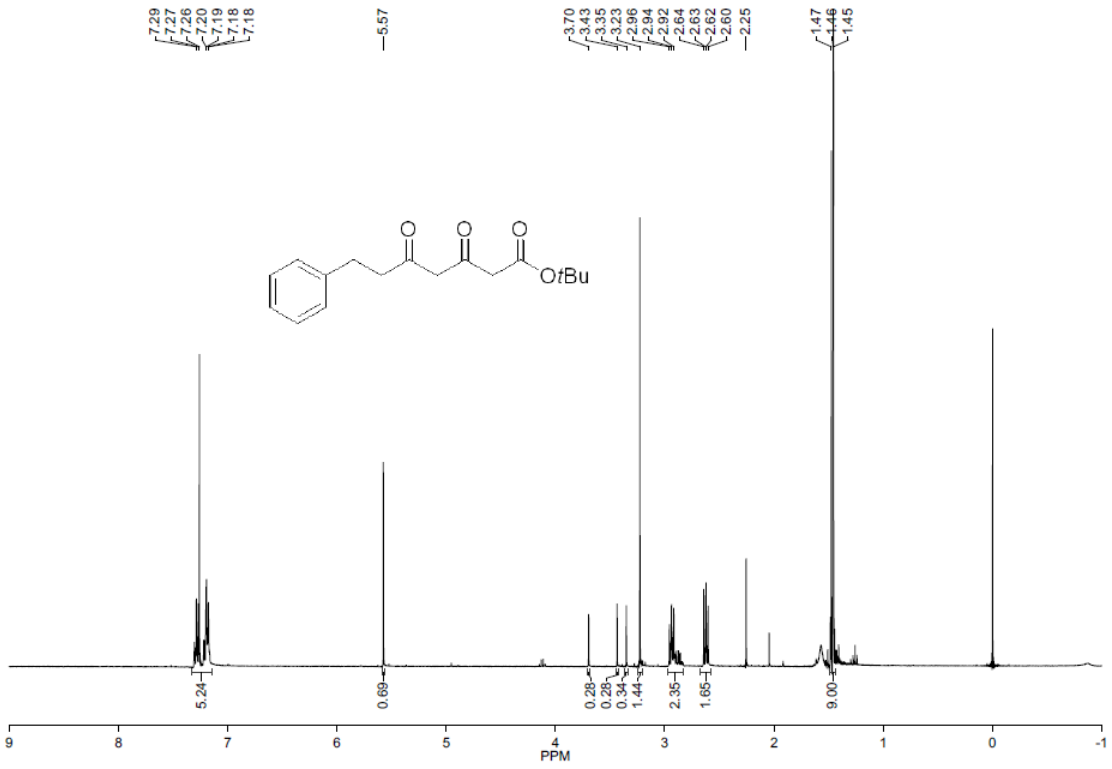



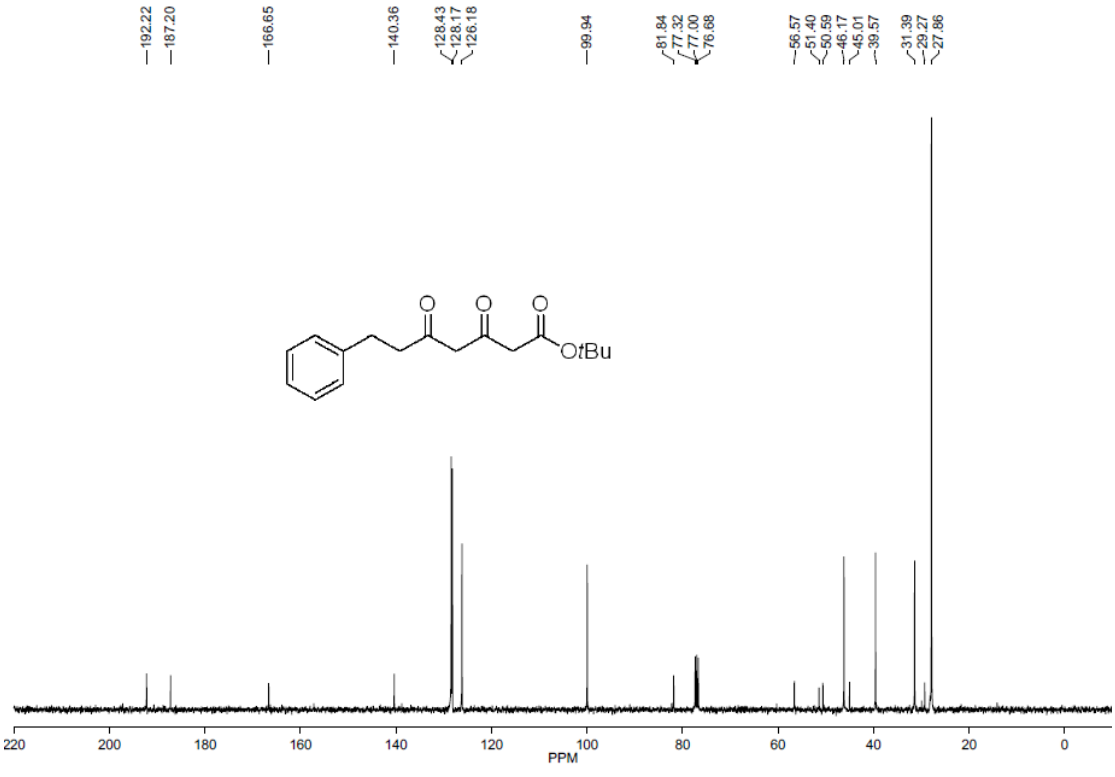
**(5d) tert-butyl 6, 6-dimethyl-3, 5-dioxoheptanoate**



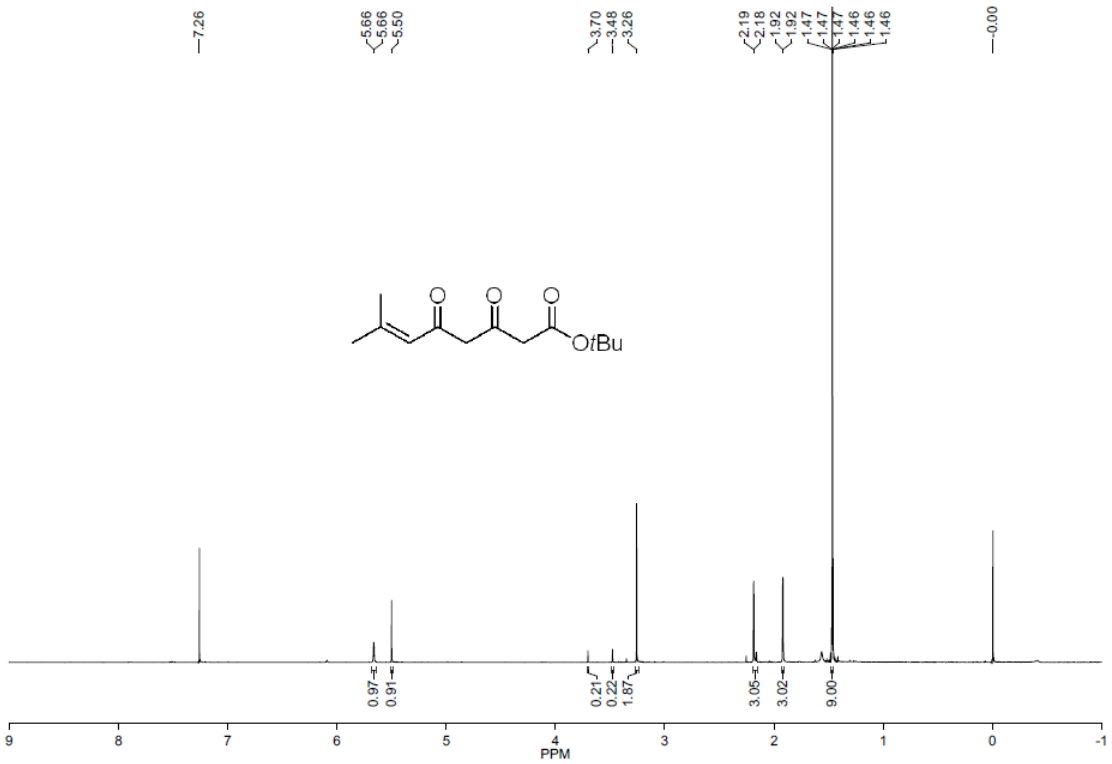



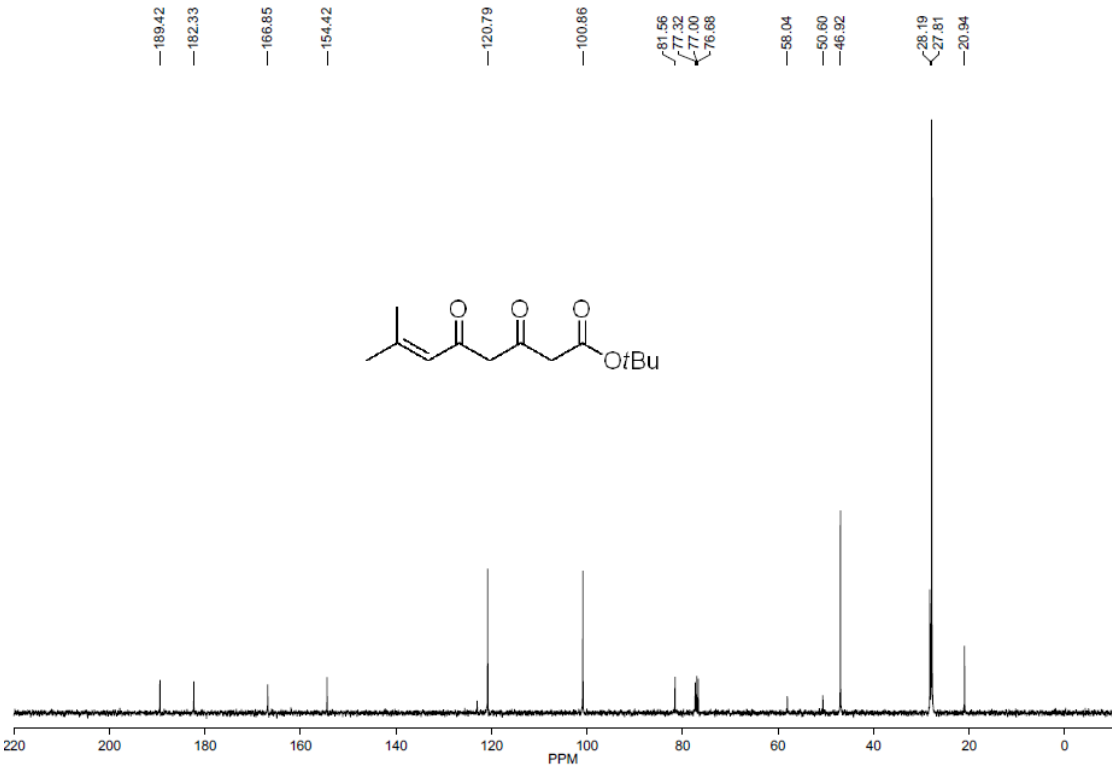
**(5e) tert-butyl 3, 5-dioxo-7-phenylheptanoate**



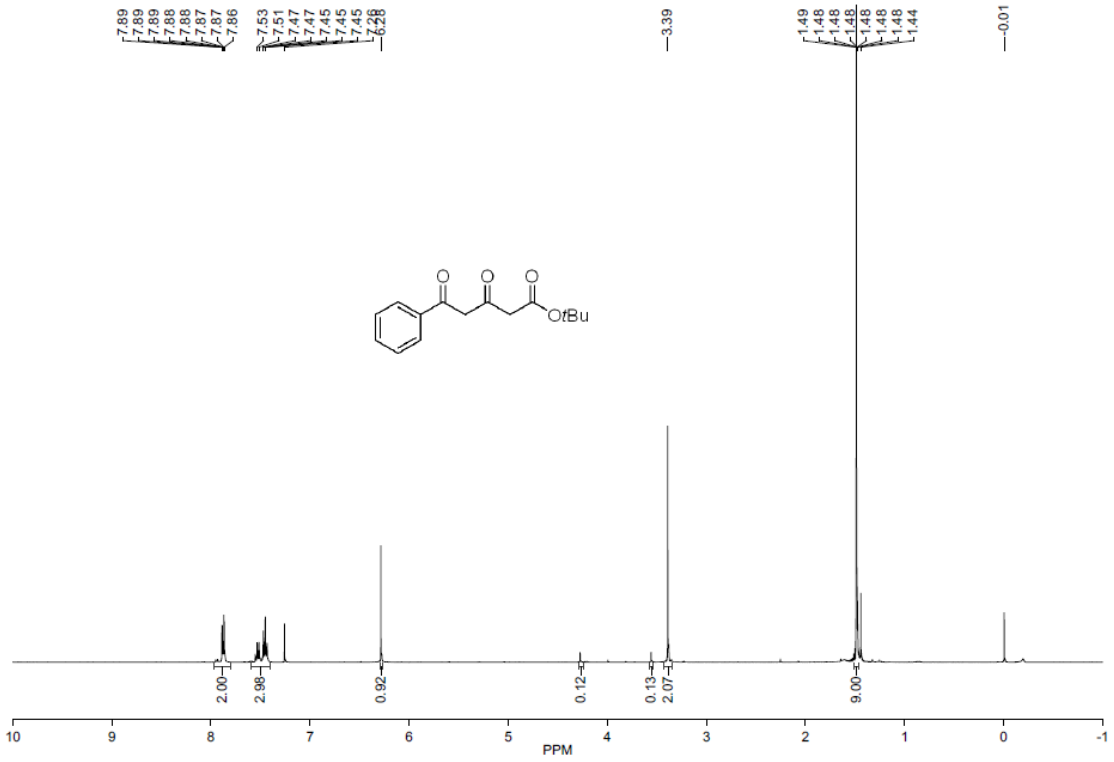



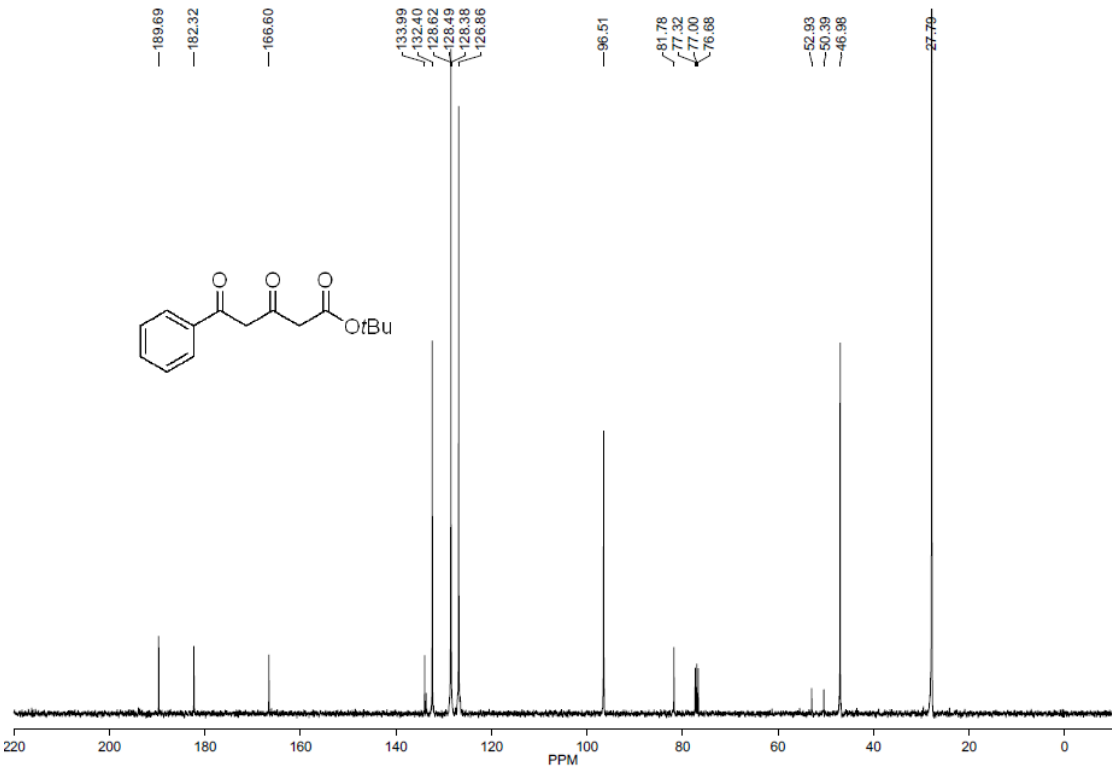
**(5f) tert-butyl 7-methyl-3, 5-dioxooct-6-enoate**



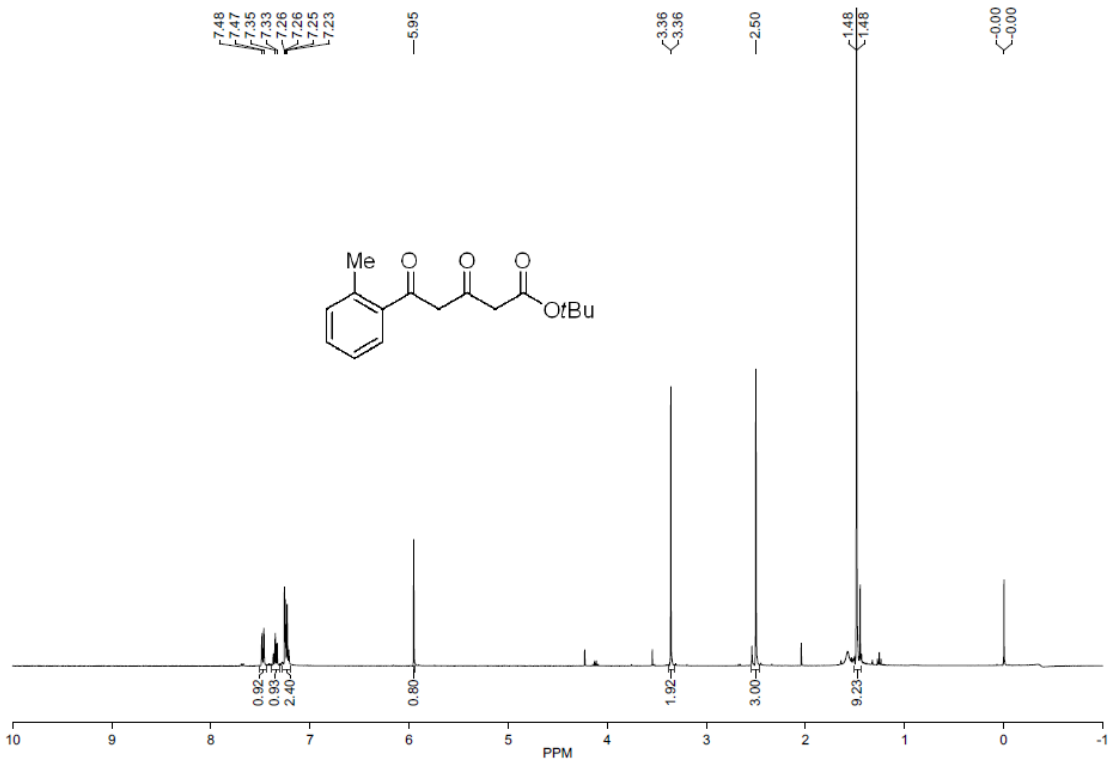



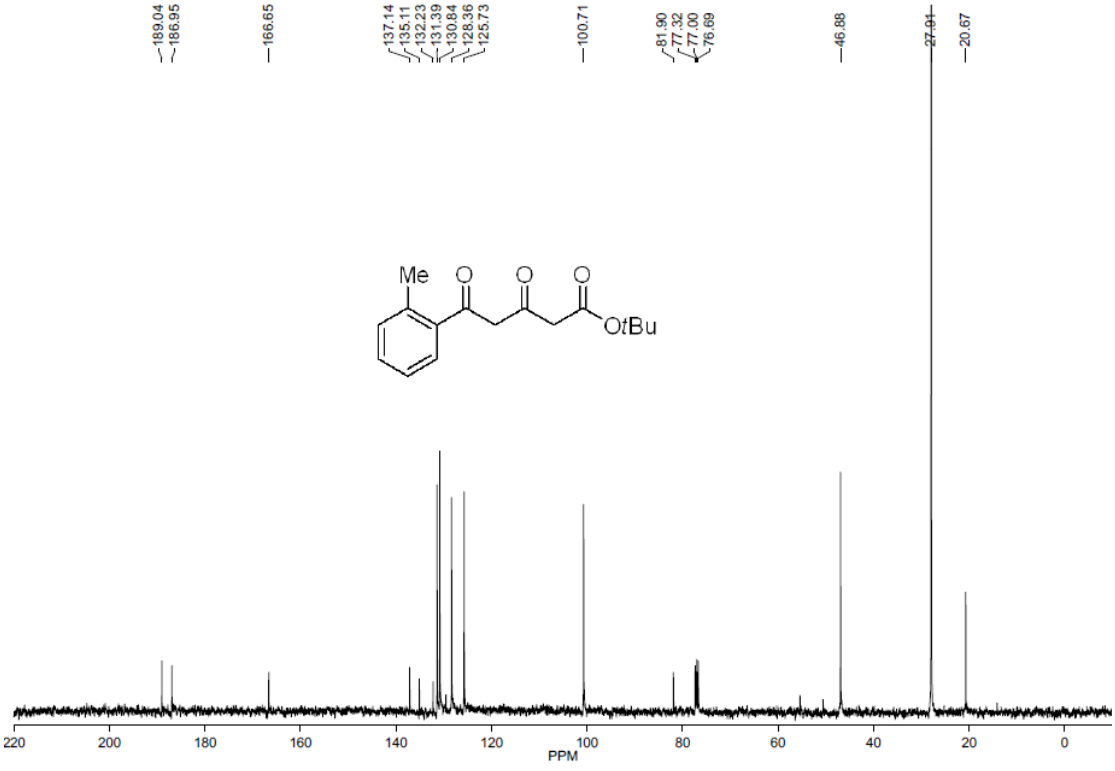
**(5g) tert-butyl 3, 5-dioxo-5-phenylpentanoate**



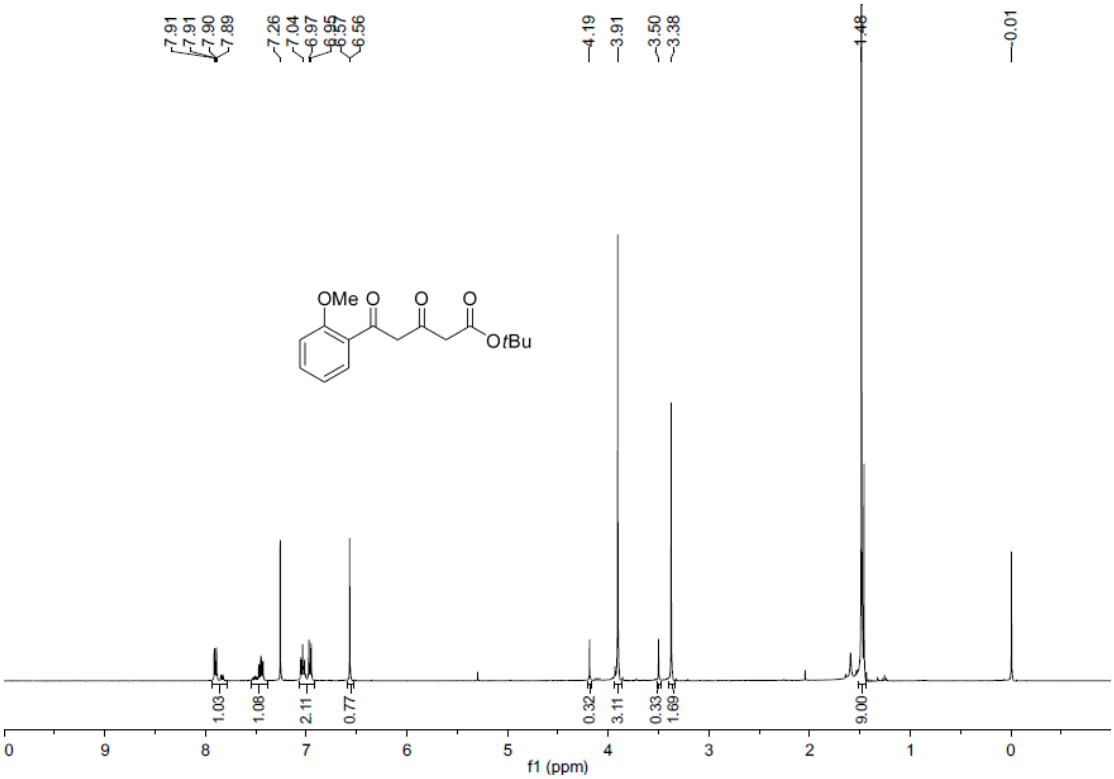



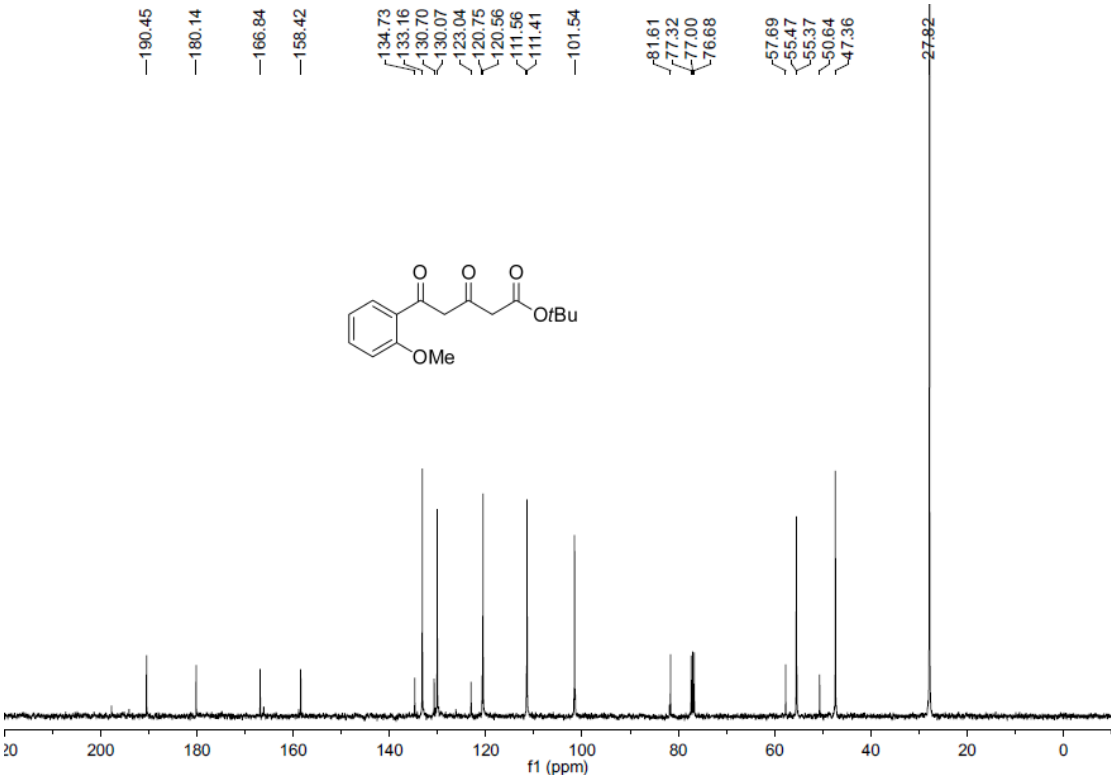
**(5h) tert-butyl 3, 5-dioxo-5-(o-tolyl)pentanoate**



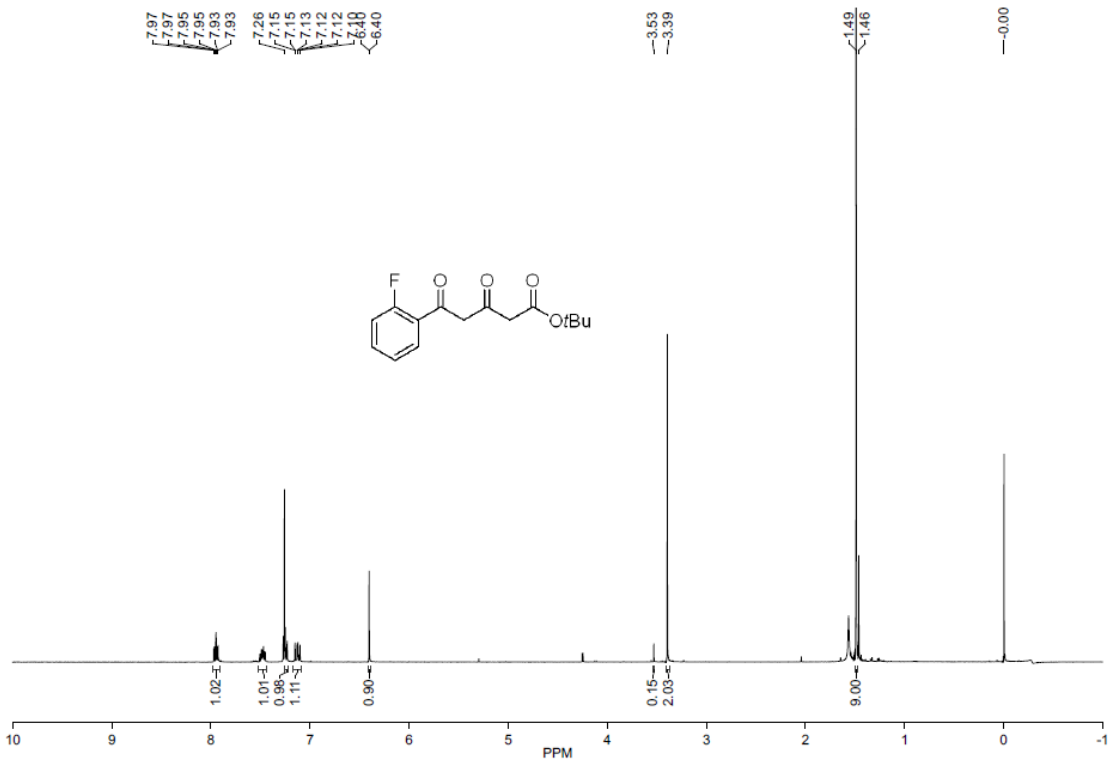



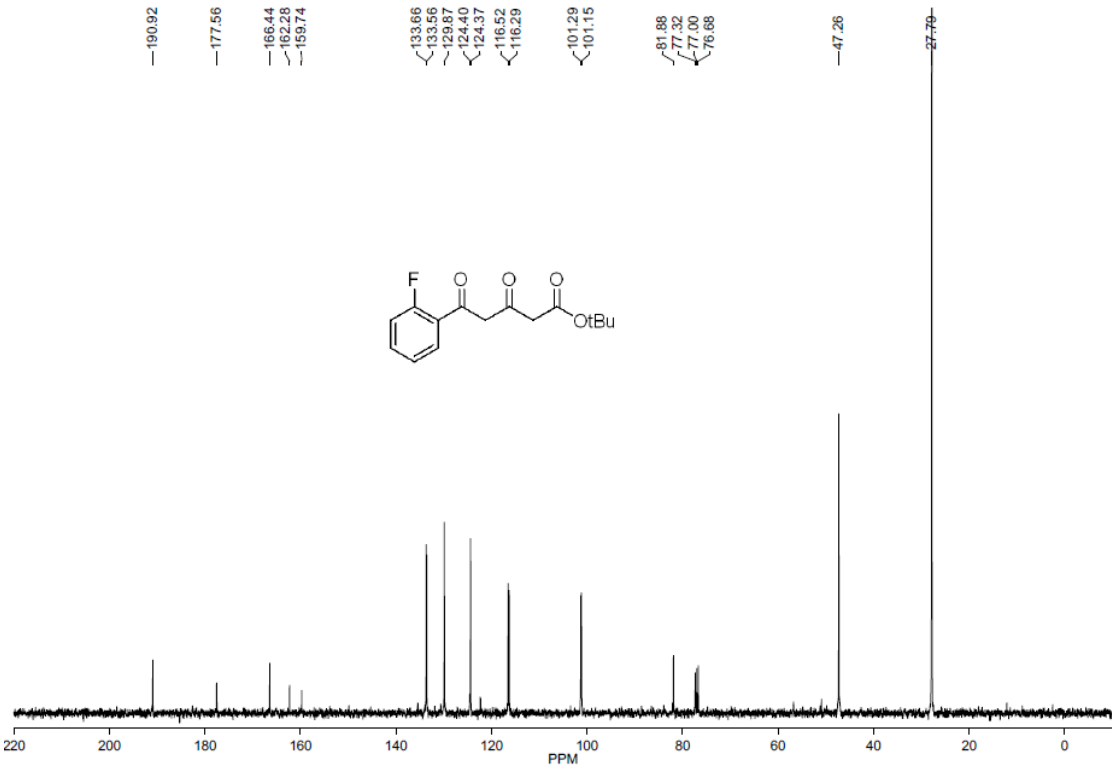
**(5i) tert-butyl 5-(2-methoxyphenyl)-3, 5-dioxopentanoate**



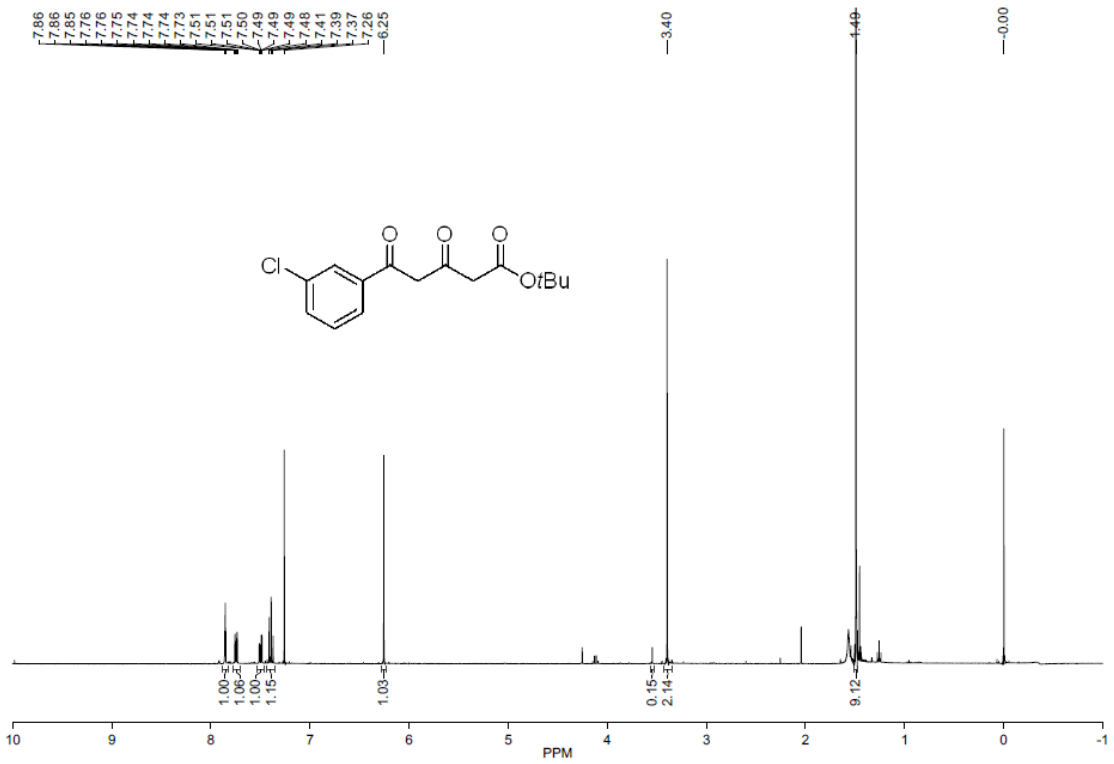



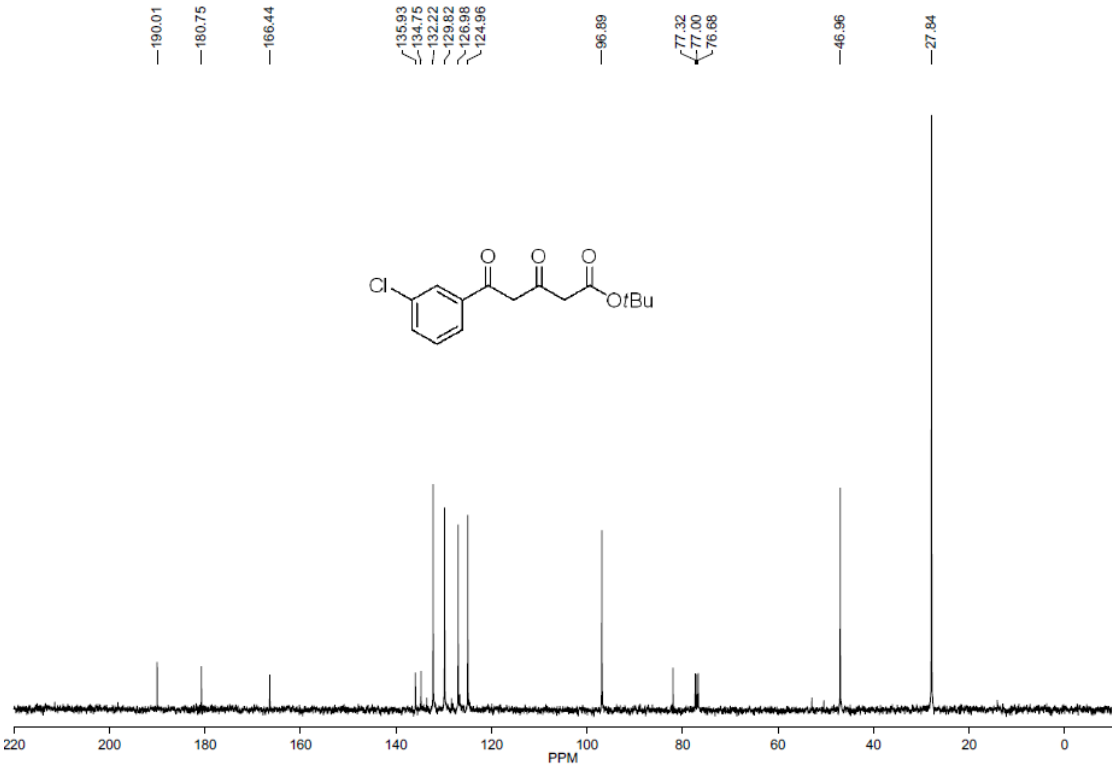
**(5j) tert-butyl 5-(2-fluorophenyl)-3, 5-dioxopentanoate**



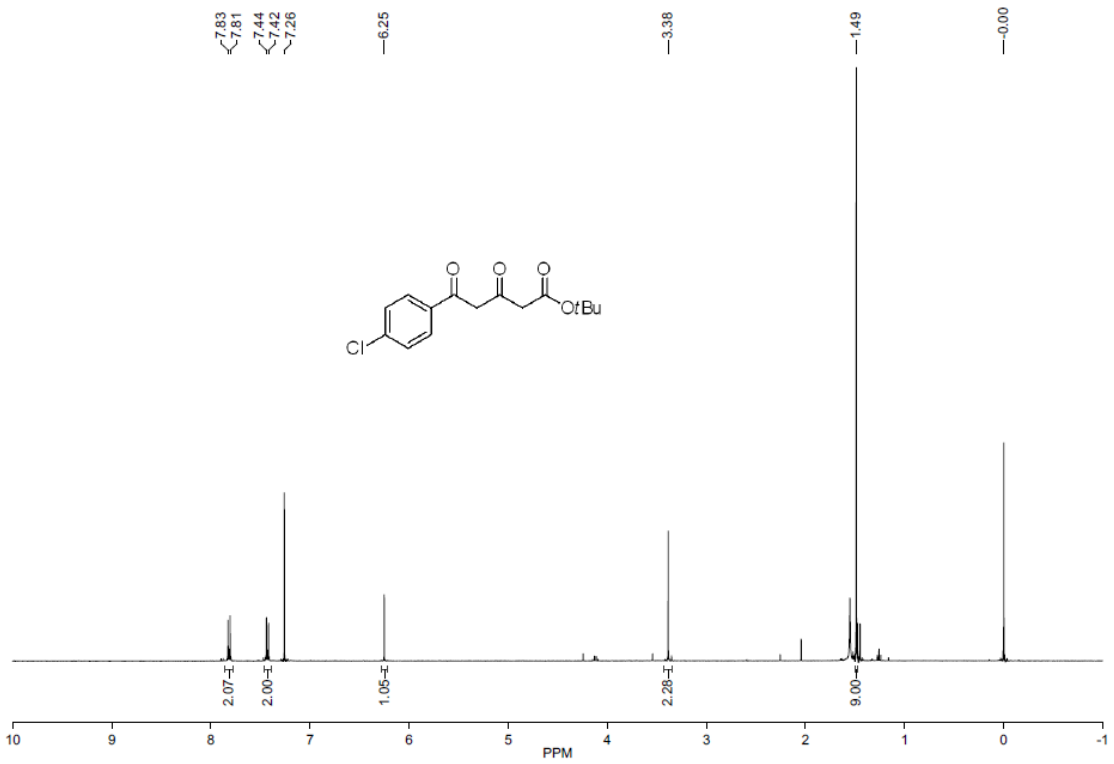



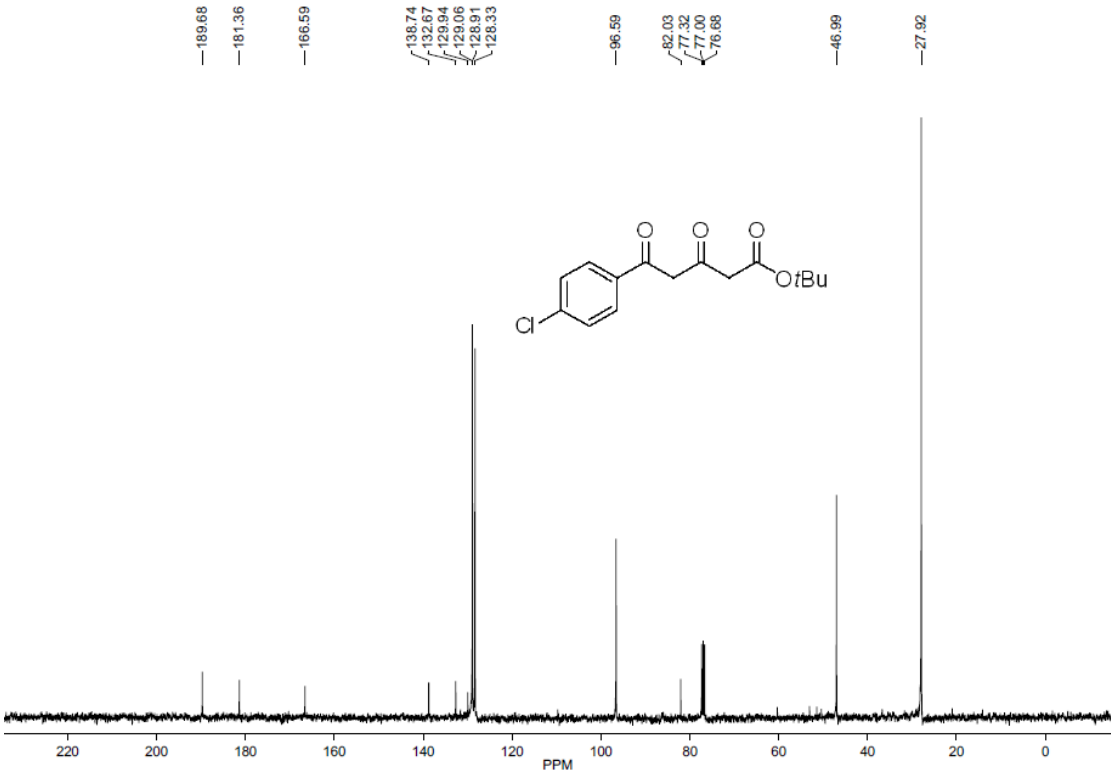
**(5k) tert-butyl 5-(3-chlorophenyl)-3, 5-dioxopentanoate**



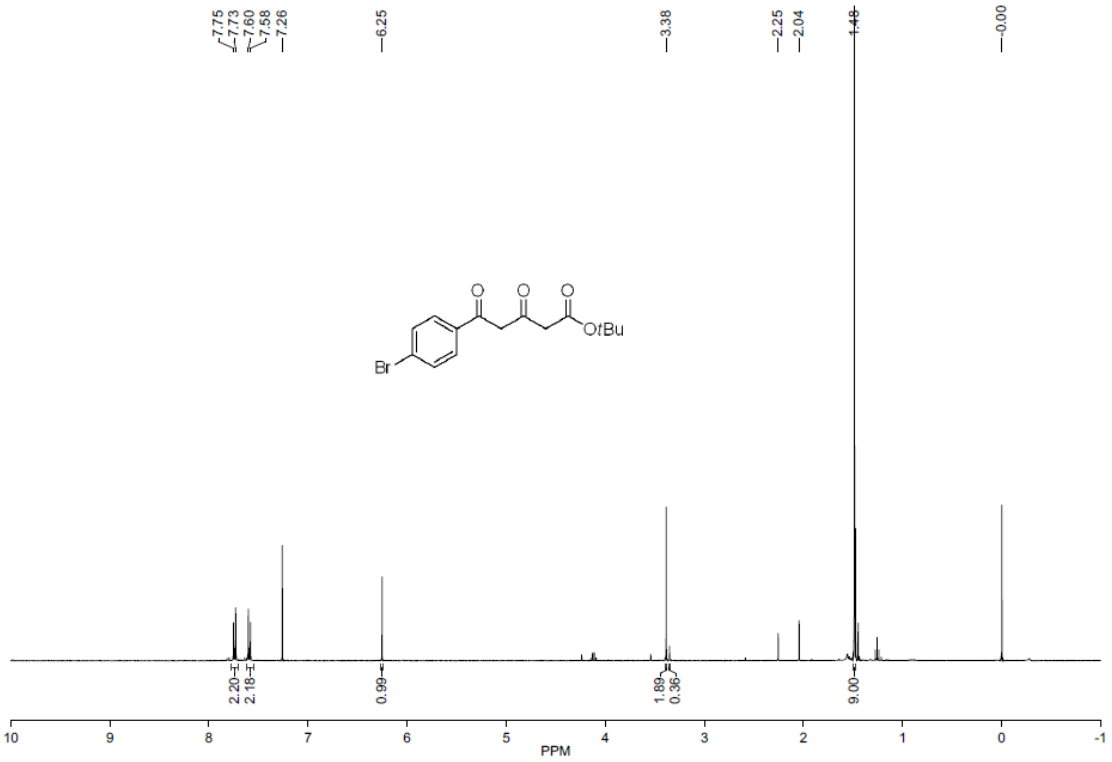



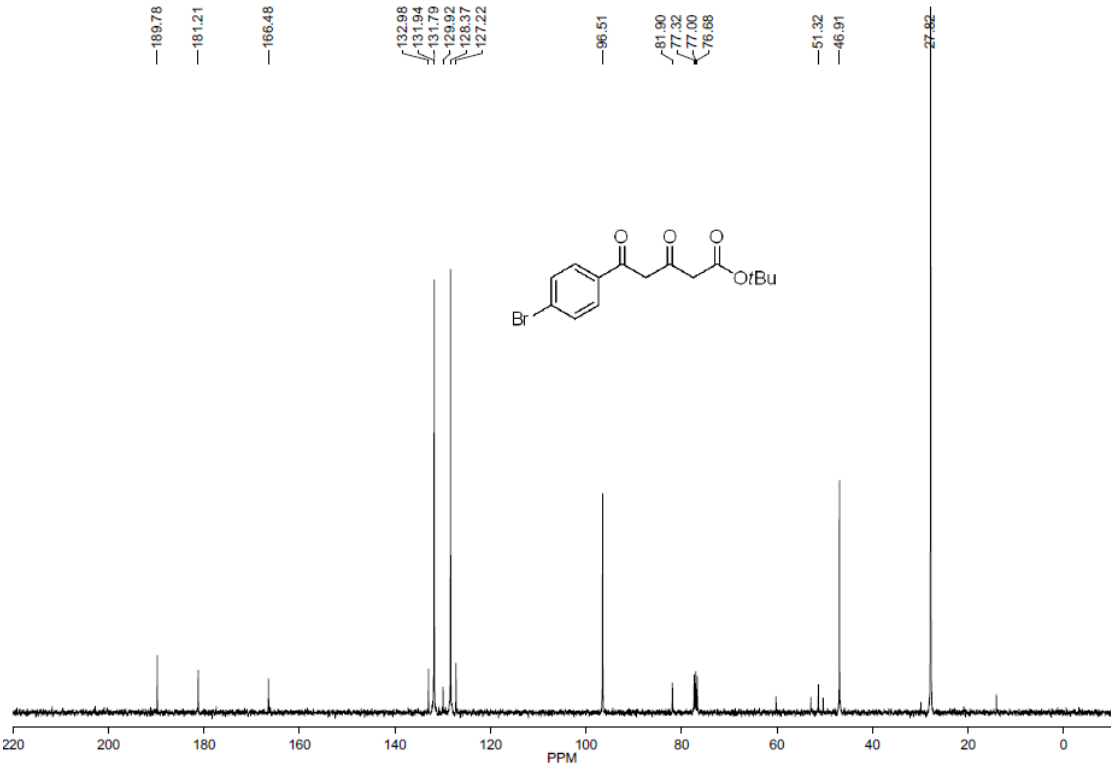
**(5m) tert-butyl 5-(4-chlorophenyl)-3, 5-dioxopentanoate**



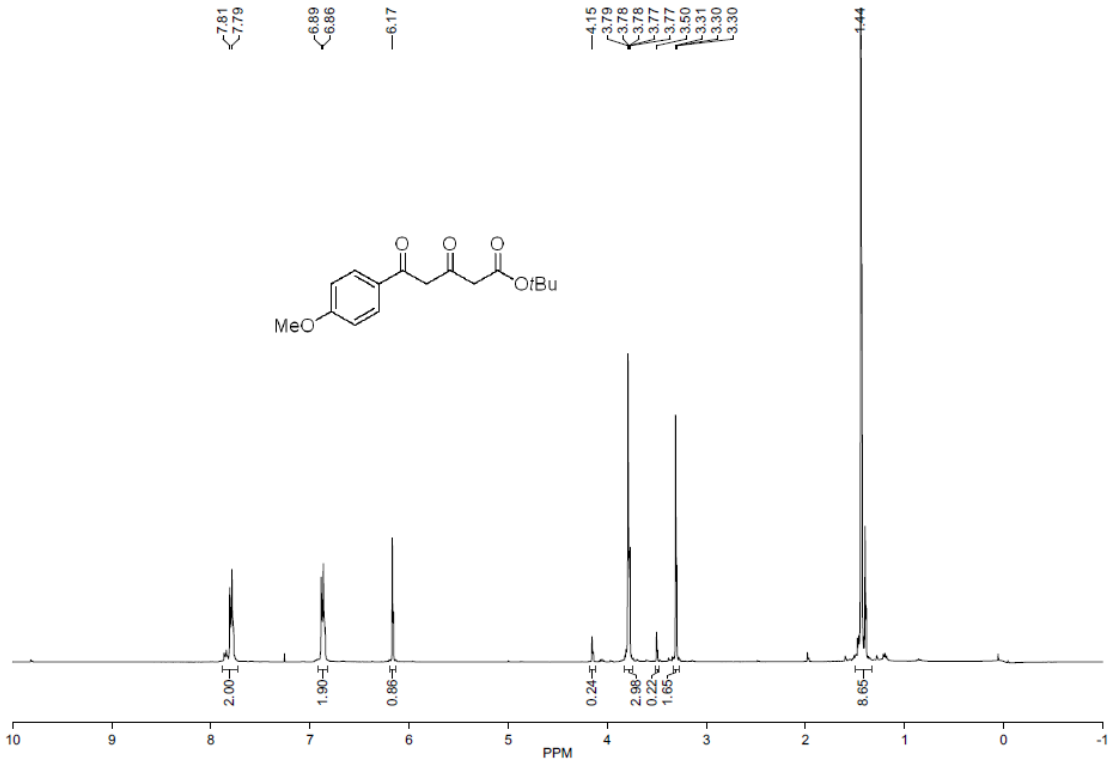



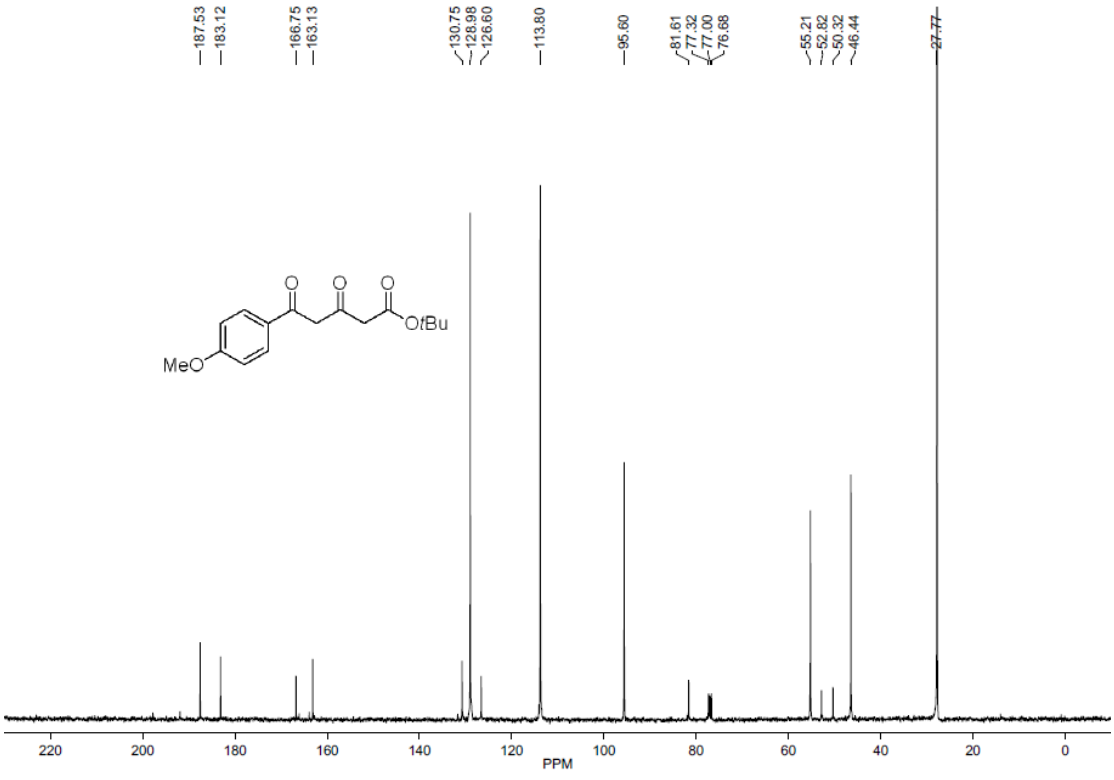
**(5n) tert-butyl 5-(4-bromophenyl)-3, 5-dioxopentanoate**



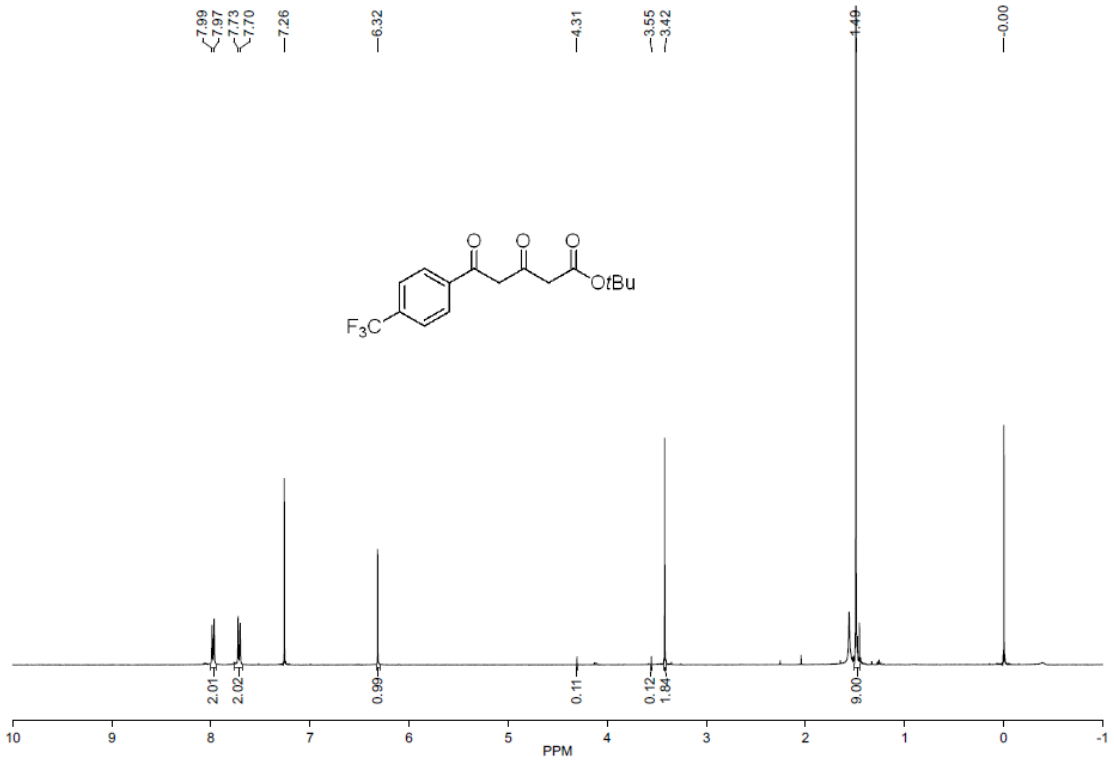



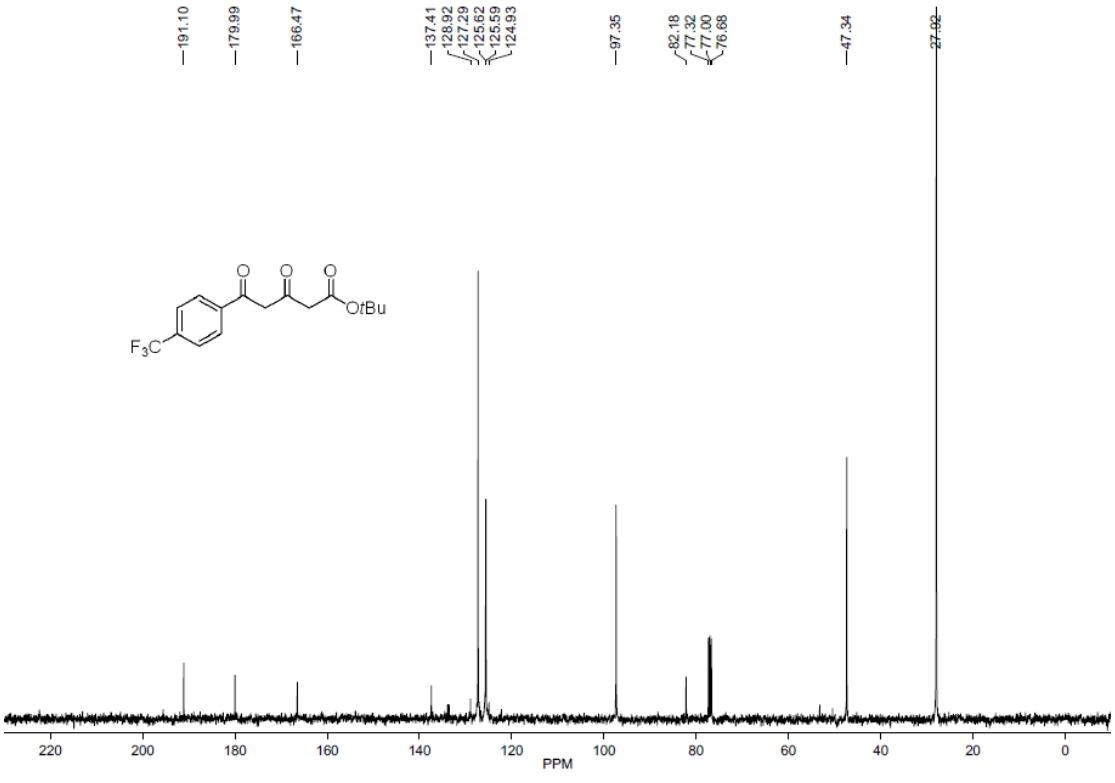
**(5o) tert-butyl 5-(4-methoxyphenyl)-3, 5-dioxopentanoate**



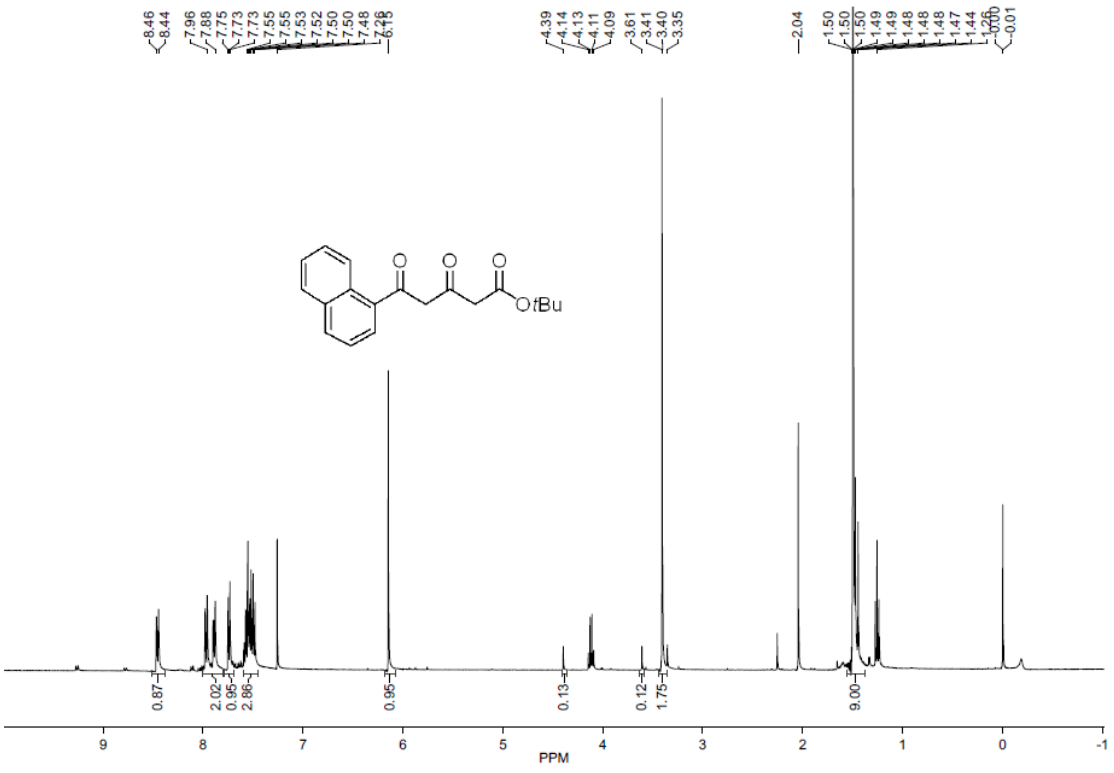



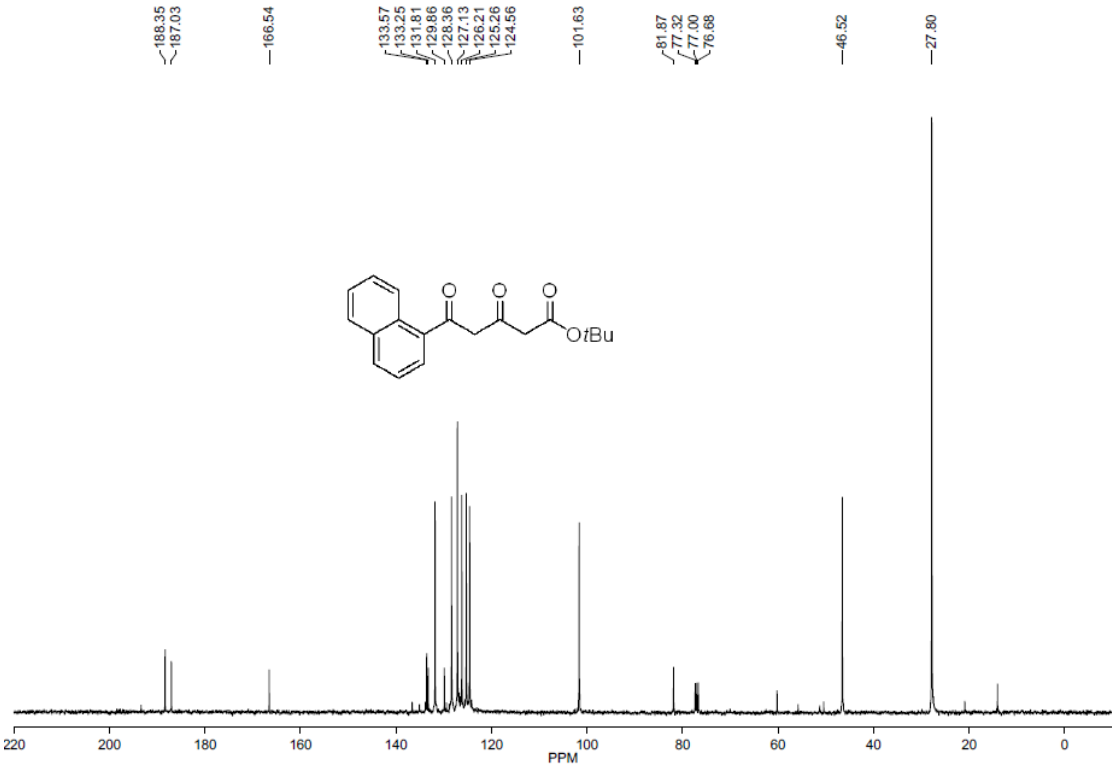
**(5p) tert-butyl 3, 5-dioxo-5-(4-(trifluoromethyl)phenyl) -pentanoate**



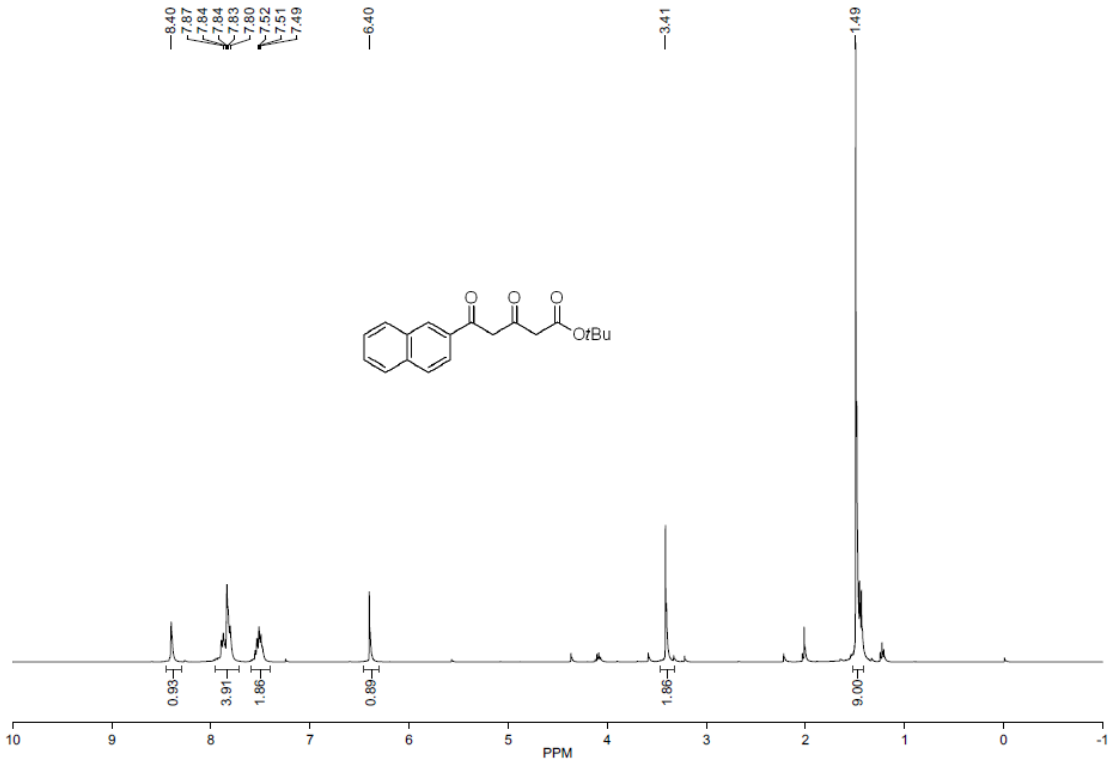



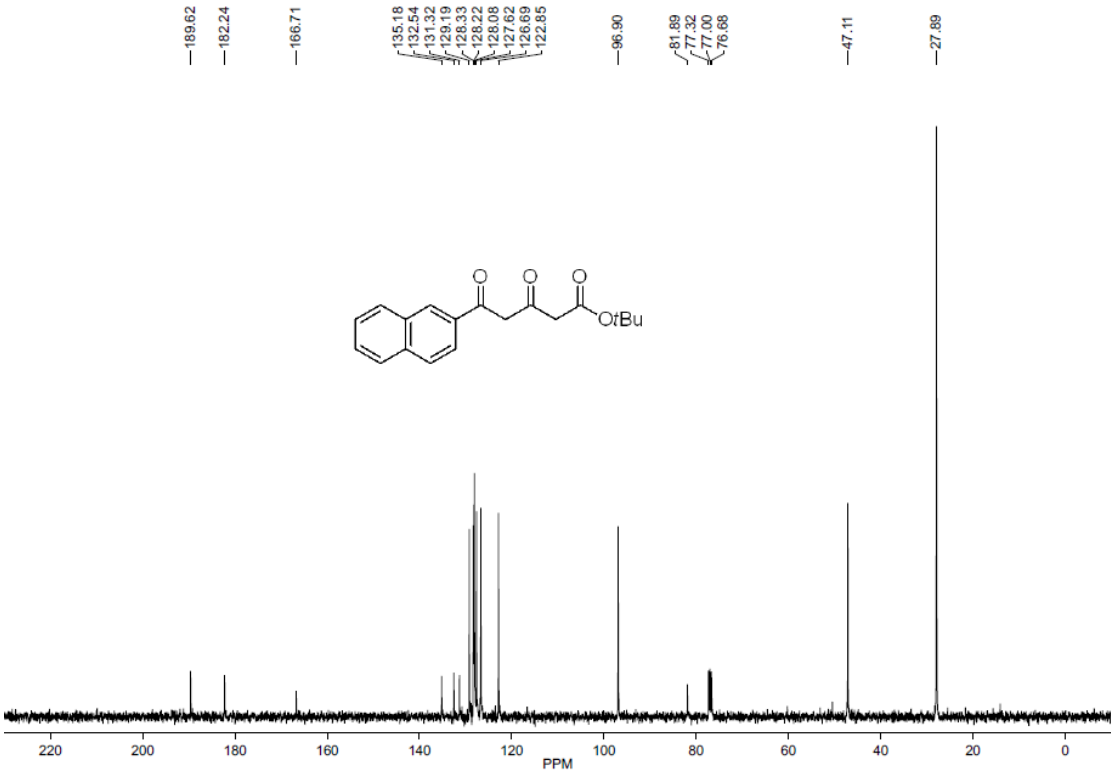
**(5q) tert-butyl 5-(naphthalen-1-yl)-3, 5-dioxopentanoate**



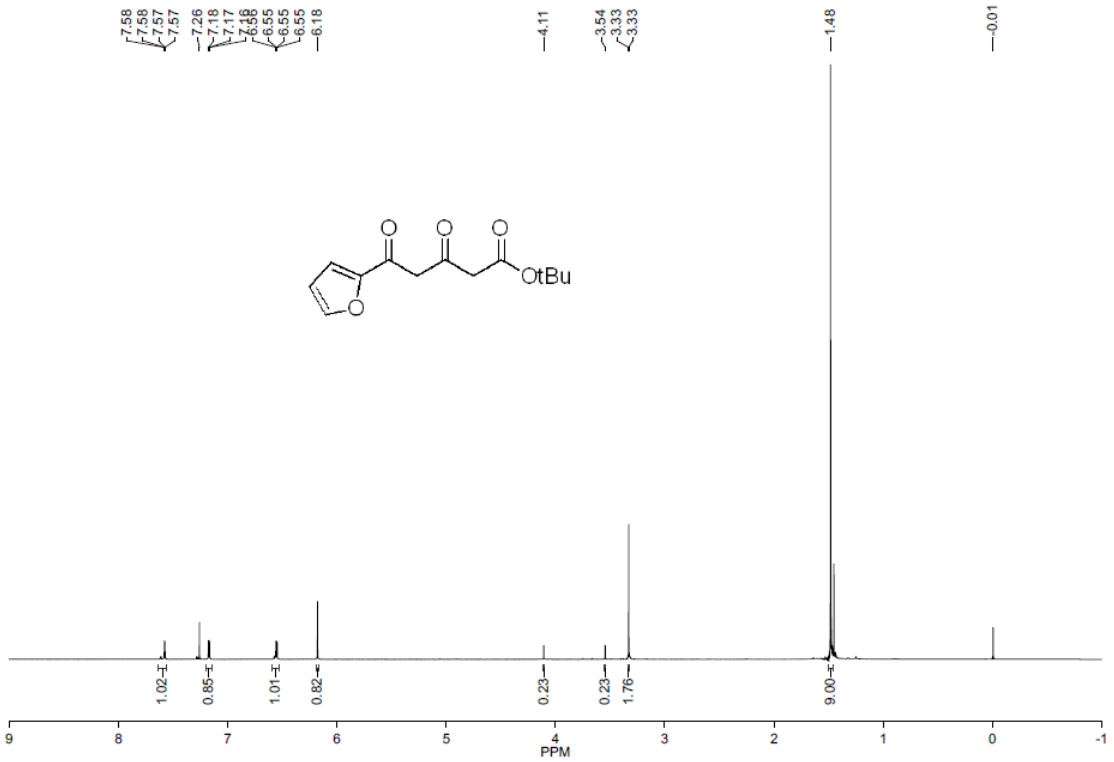



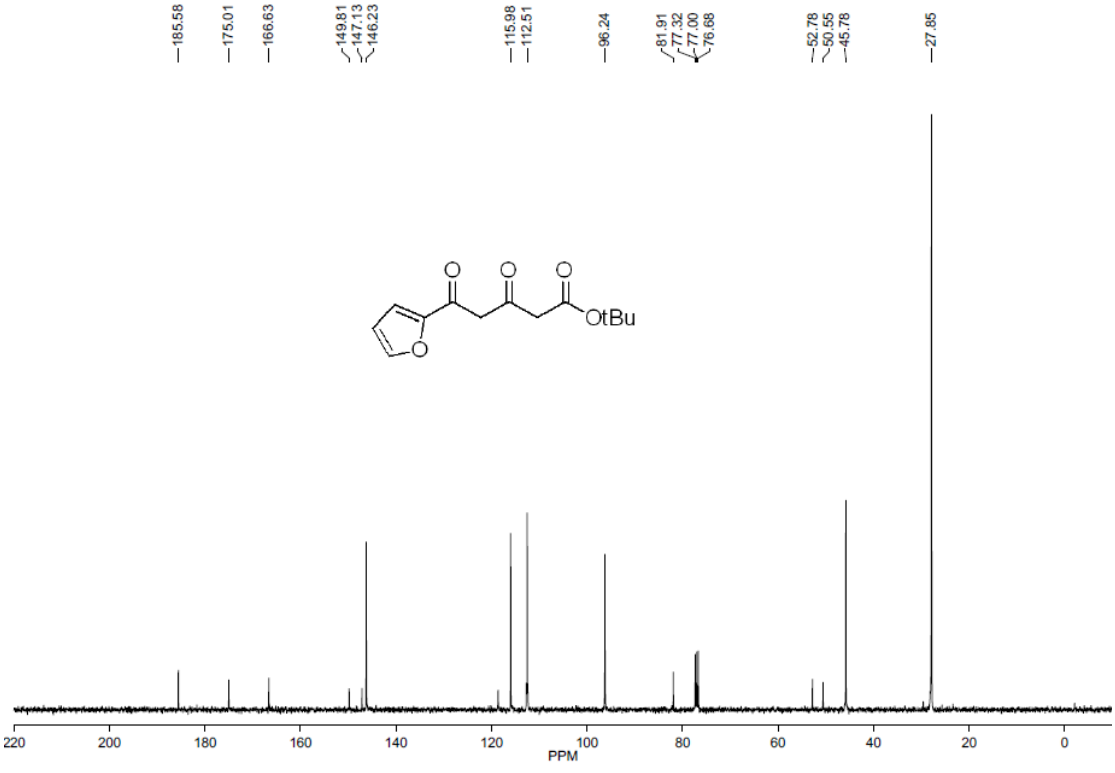
**(5r) tert-butyl 5-(naphthalen-2-yl)-3, 5-dioxopentanoate**



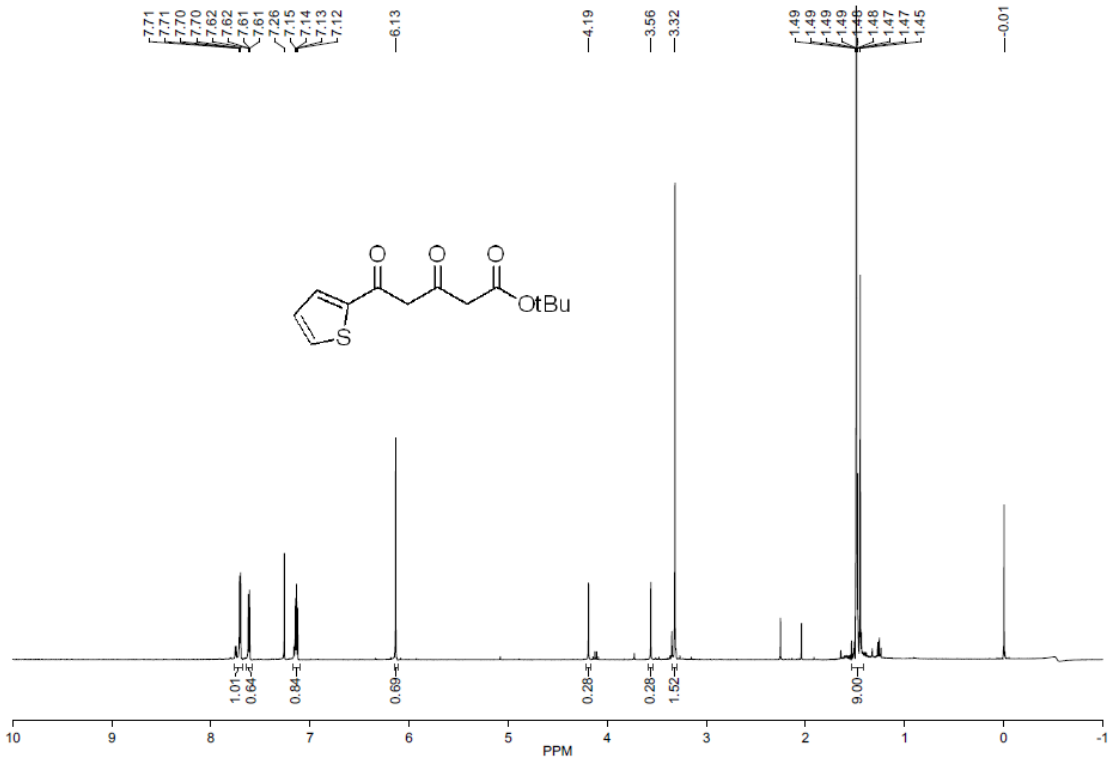



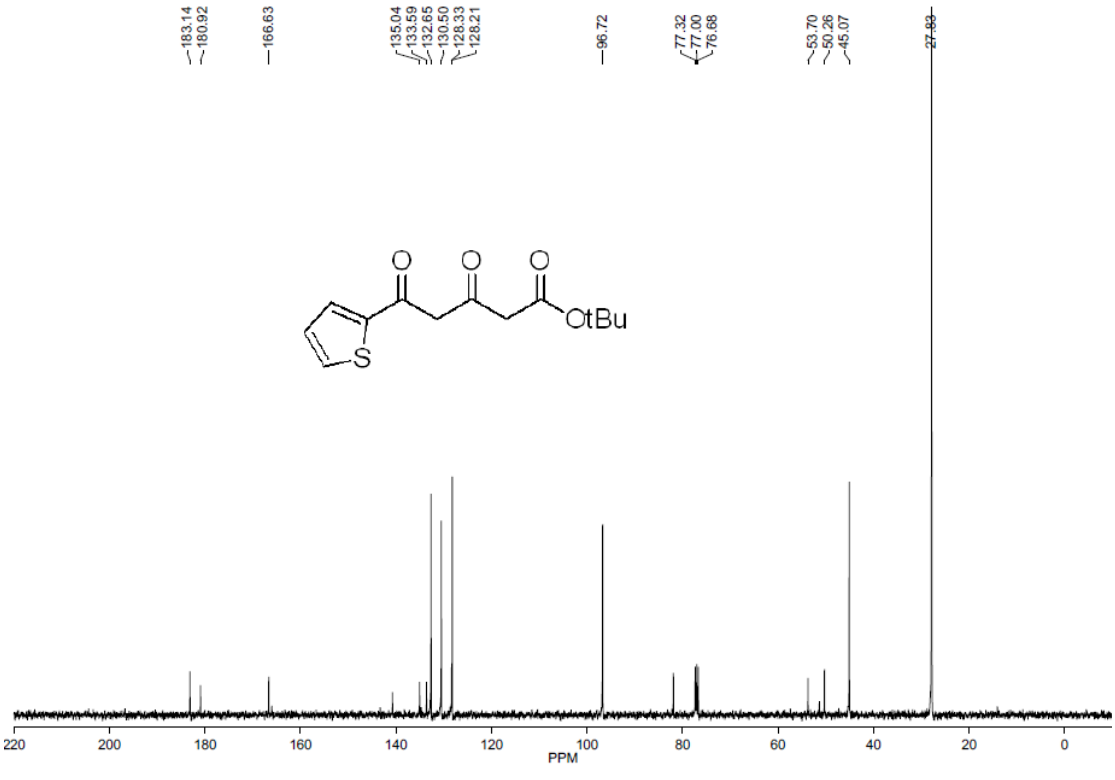
## (5s) tert-butyl 5-(furan-2-yl)-3, 5-dioxopentanoate



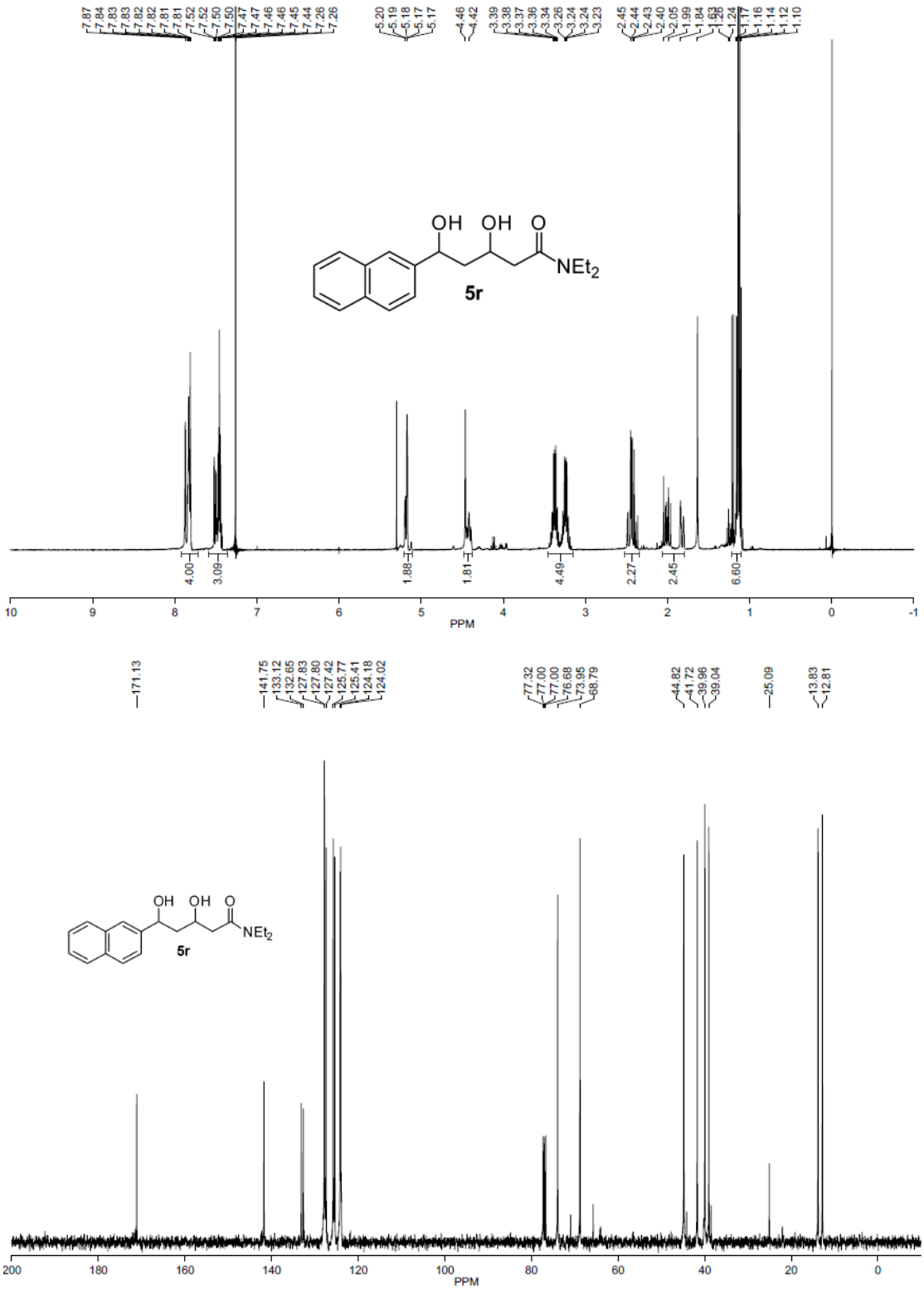



**(5t) tert-butyl -dioxo-5-(thiophen-2-yl)pentanoate**



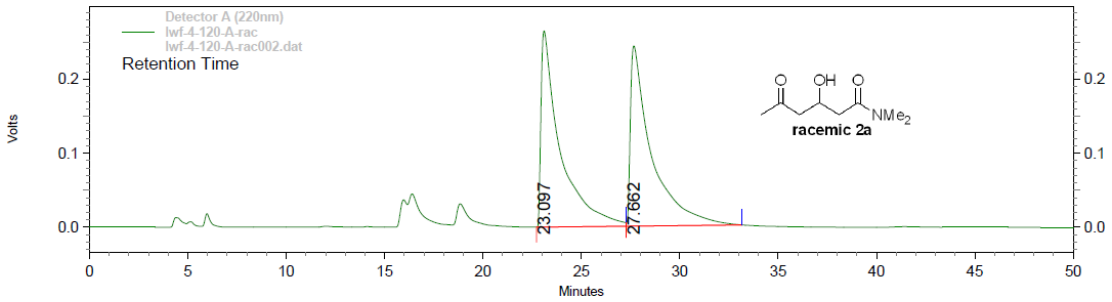




**5r in the maintext:** ***N,N*-diethyl-3,5-dihydroxy-5-(naphthalen-2-yl)pentanamide**

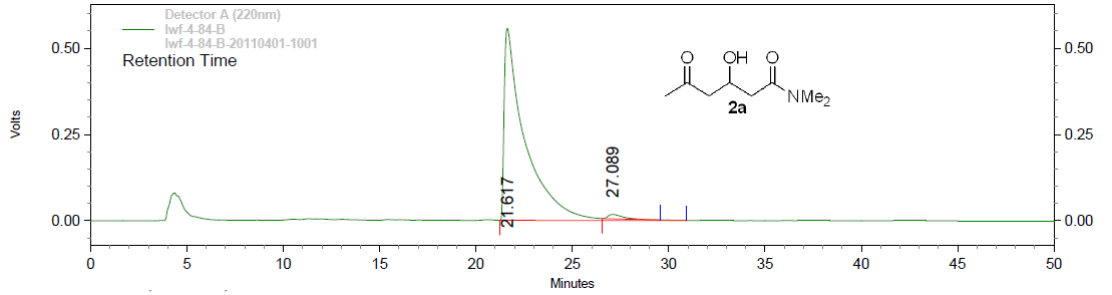



**7. HPLC diagrams for ee determination.**

**Table 1, entry 1**

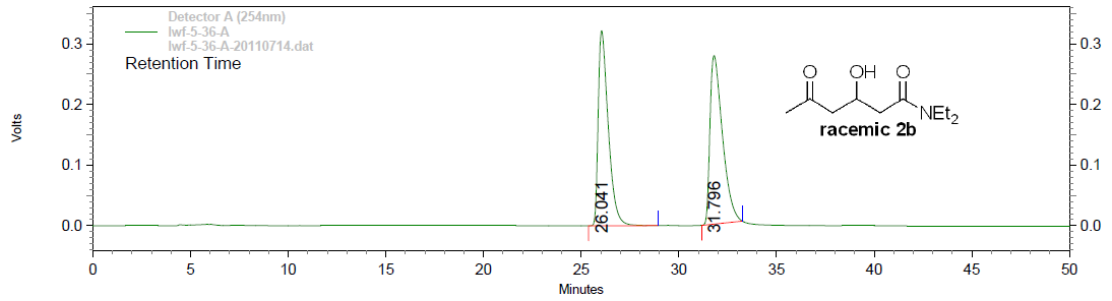



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 23.097 | 17936851 | 49.823 | 265216 | 52.125 |
| 2 | 27.662 | 18064276 | 50.177 | 243590 | 47.875 |

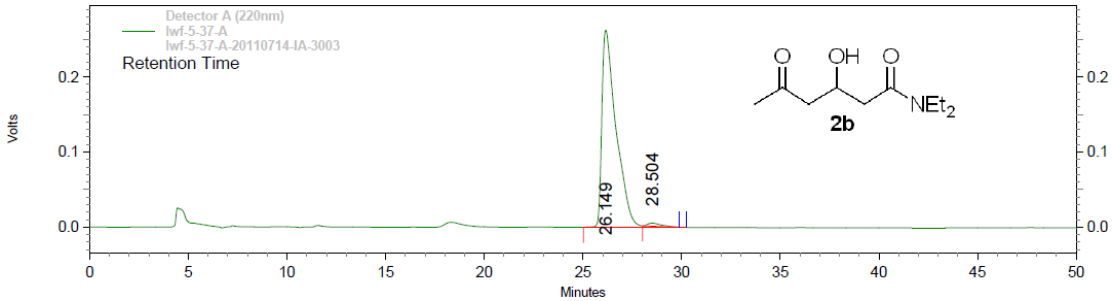



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 21.617 | 42260195 | 98.423 | 557262 | 97.779 |
| 2 | 27.089 | 677071 | 1.577 | 12660 | 2.221 |

**Table 1, entry 2**

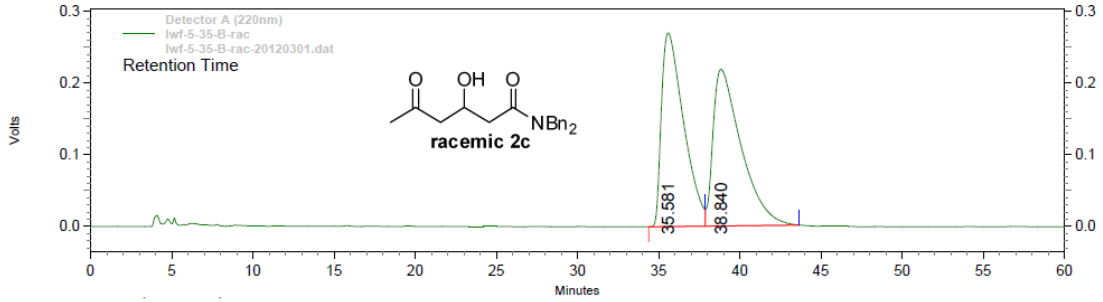



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 26.041 | 11522087 | 48.305 | 321812 | 53.646 |
| 2 | 31.796 | 12330762 | 51.695 | 278072 | 46.354 |

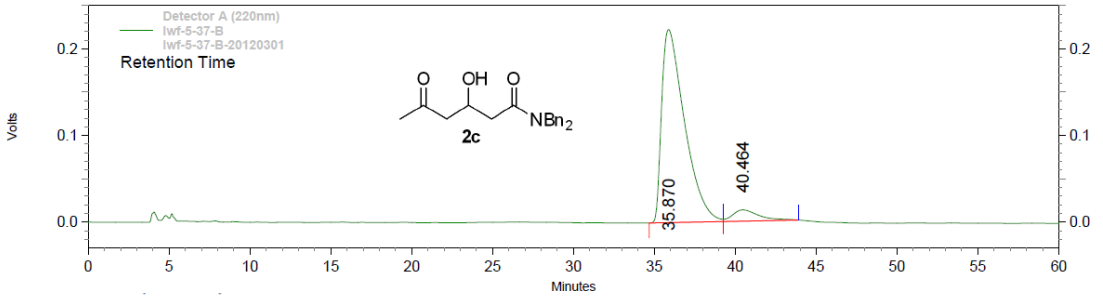


| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 26.149 | 13216768 | 98.575 | 262673 | 98.449 |
| 2 | 28.504 | 191123 | 1.425 | 4138 | 1.551 |

**Table 1, entry 3**

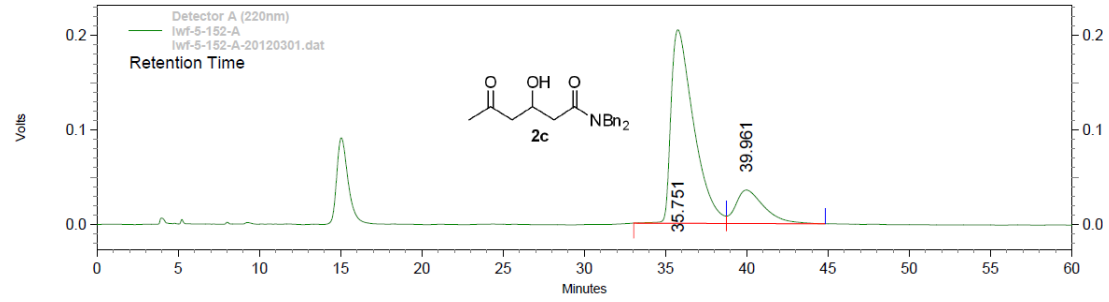



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 35.581 | 25616940 | 49.344 | 269931 | 55.257 |
| 2 | 38.840 | 26297779 | 50.656 | 218567 | 44.743 |



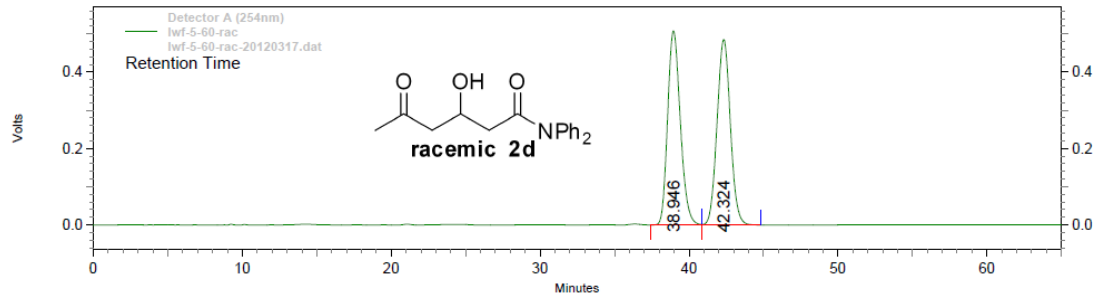

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 35.870 | 21898175 | 93.639 | 222803 | 94.471 |
| 2 | 40.464 | 1487661 | 6.361 | 13039 | 5.529 |

**Equation 2 ( ee in MeOH):**

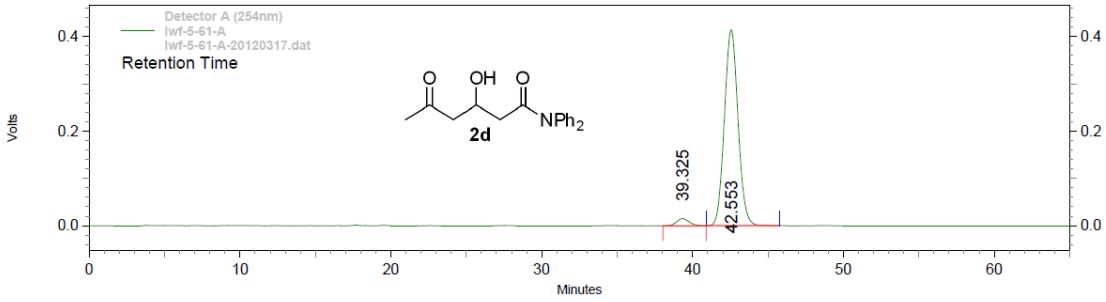



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 35.751 | 19924126 | 82.136 | 204927 | 85.250 |
| 2 | 39.961 | 4333282 | 17.864 | 35457 | 14.750 |

**Table 1, entry 4**

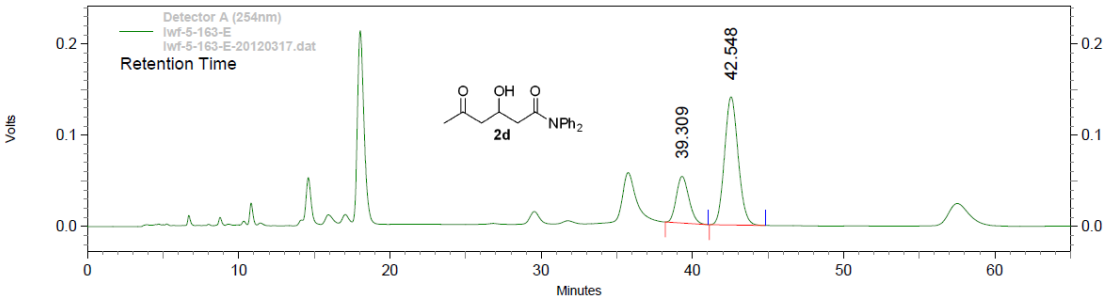



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 38.946 | 30083130 | 49.863 | 508015 | 51.131 |
| 2 | 42.324 | 30248479 | 50.137 | 485540 | 48.869 |



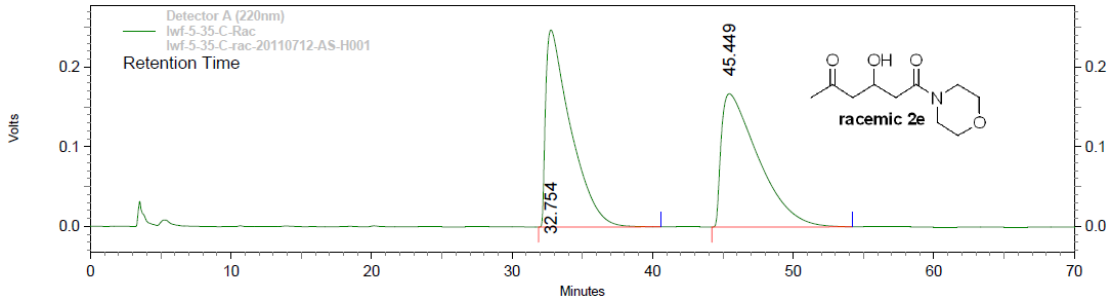

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 39.325 | 866711 | 3.223 | 14921 | 3.478 |
| 2 | 42.553 | 26021155 | 96.777 | 414081 | 96.522 |

**Equation 3 ( ee in MeOH)**

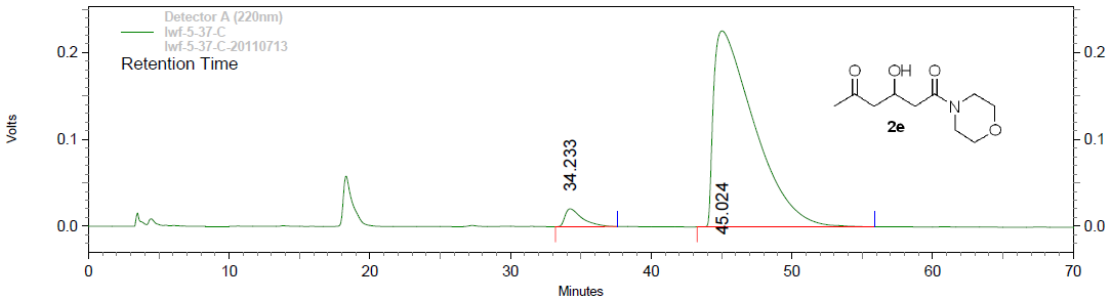



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 39.309 | 2955403 | 25.139 | 51153 | 26.697 |
| 2 | 42.548 | 8800673 | 74.861 | 140451 | 73.303 |

**Table 1, entry 5**

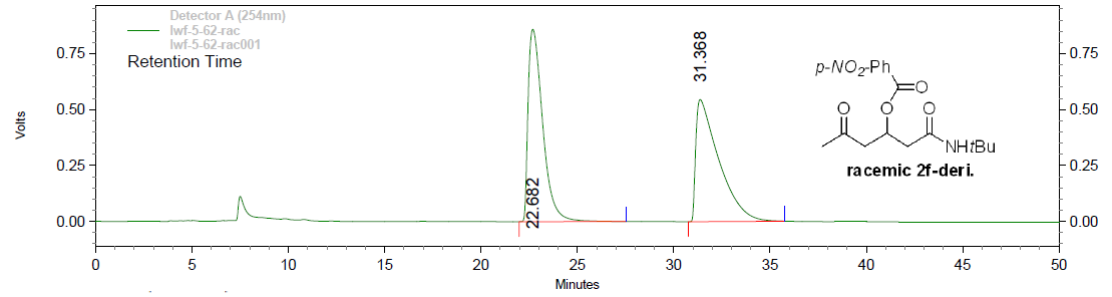



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 32.754 | 30548099 | 49.948 | 247245 | 59.657 |
| 2 | 45.449 | 30611128 | 50.052 | 167201 | 40.343 |

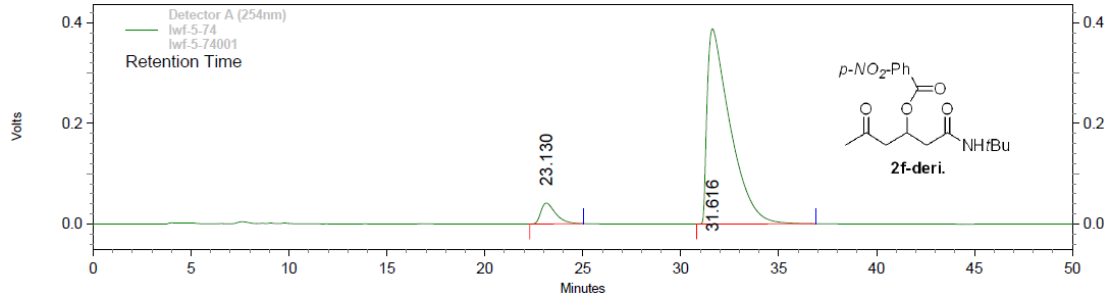



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 34.233 | 1760546 | 3.726 | 20649 | 8.377 |
| 2 | 45.024 | 45490975 | 96.274 | 225862 | 91.623 |

**Table 1 entry 6**

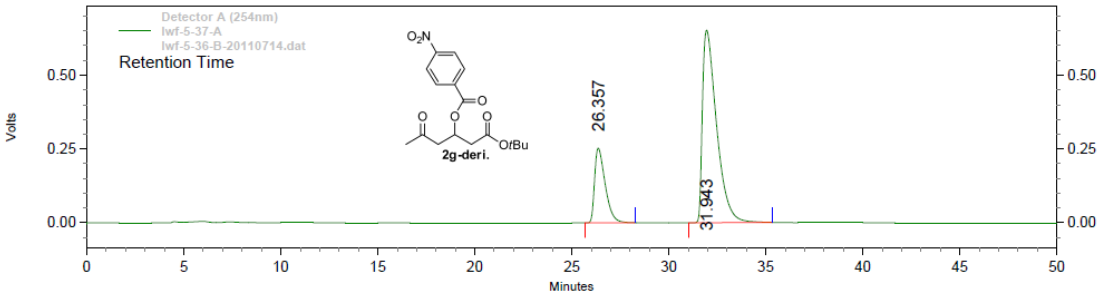



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 22.682 | 45287777 | 49.928 | 860055 | 61.157 |
| 2 | 31.368 | 45419161 | 50.072 | 546250 | 38.843 |



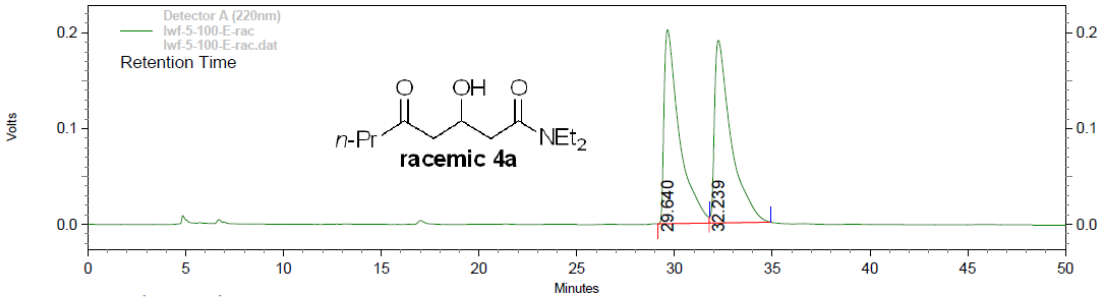
| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 23.130 | 2182428 | 6.427 | 41596 | 9.675 |
| 2 | 31.616 | 31773242 | 93.573 | 388330 | 90.325 |

**Table 1 entry 7**



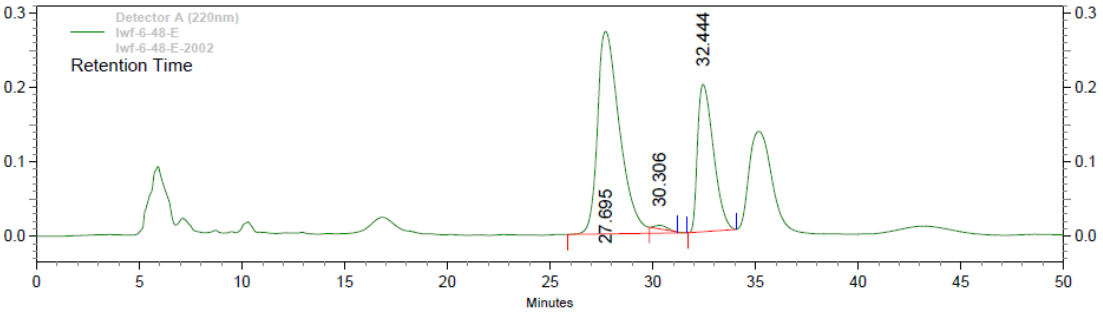

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 26.357 | 9549248 | 22.432 | 252825 | 27.923 |
| 2 | 31.943 | 33020829 | 77.568 | 652615 | 72.077 |

**Table 1, 1-7,**




| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 29.640 | 11085576 | 49.638 | 202726 | 51.507 |
| 2 | 32.239 | 11247360 | 50.362 | 190862 | 48.493 |

Table 2, entry 1:

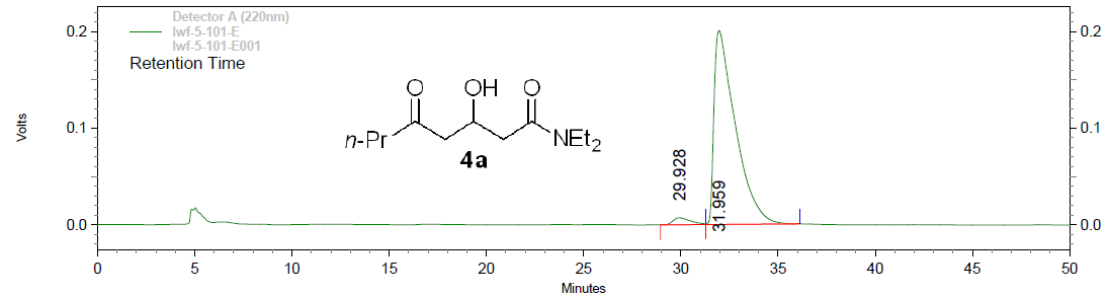



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 27.695 | 20843488 | 65.711 | 272542 | 57.319 |
| 2 | 30.306 | 202599 | 0.639 | 4747 | 0.998 |
| 3 | 32.444 | 10673741 | 33.650 | 198196 | 41.683 |

Note: The HPLC analysis of the reaction with 60% conversion of the **3a**. The ee was estimated based

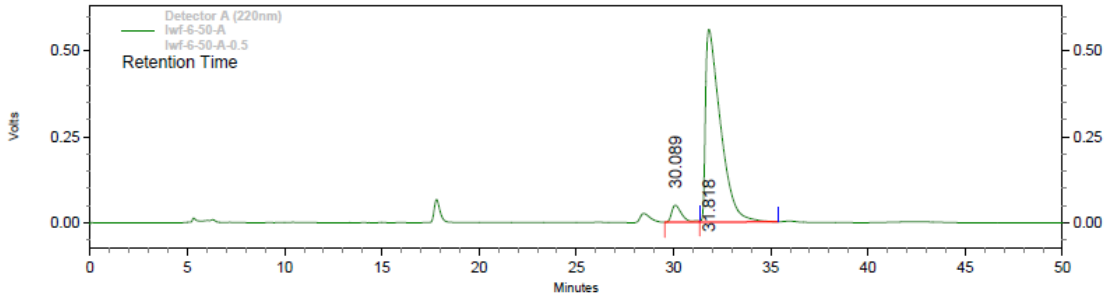
on the peak height: 198196/4747=41.7/1, thus the ee of **4a** was *ca*. 95.3%  (41.7-1)/(41.7+1)X100%

**Table 2, entry 2/ Table 3, entry 1**



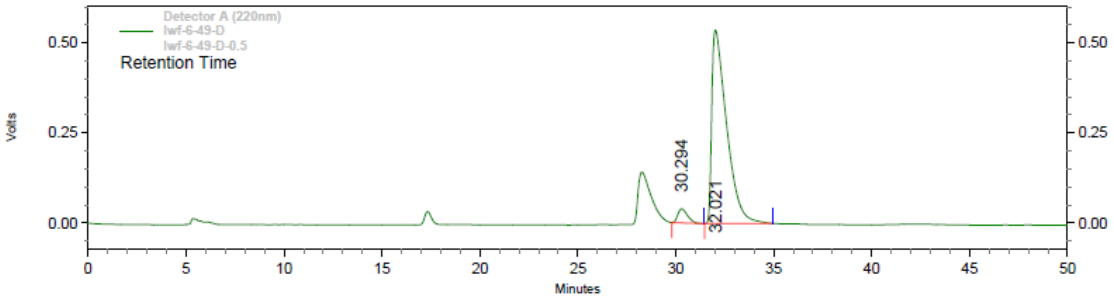

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 29.928 | 448895 | 2.841 | 7213 | 3.466 |
| 2 | 31.959 | 15352468 | 97.159 | 200893 | 96.534 |

**Table 2, entry 3**



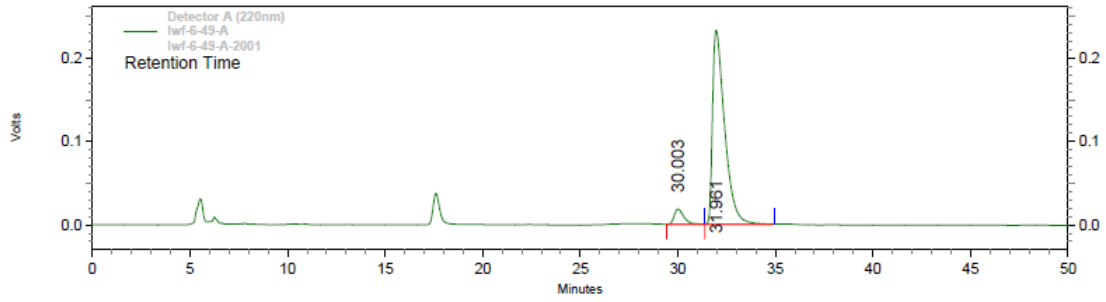

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 30.089 | 1801968 | 5.629 | 49762 | 8.139 |
| 2 | 31.818 | 30209697 | 94.371 | 561662 | 91.861 |

**Table 2, entry 4**



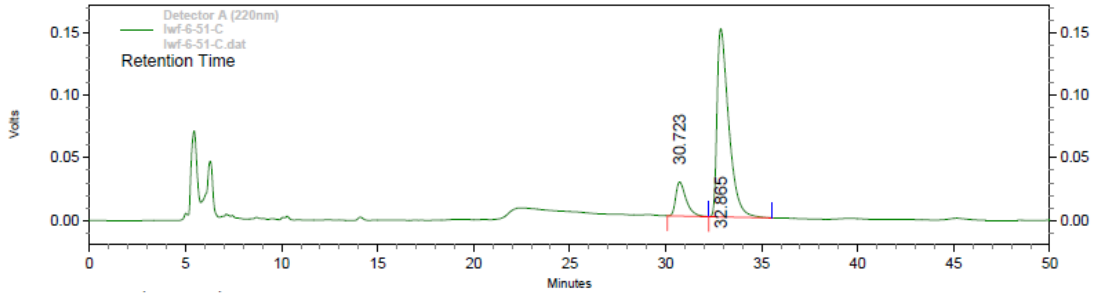

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 30.294 | 1340893 | 4.539 | 38871 | 6.749 |
| 2 | 32.021 | 28198398 | 95.461 | 537110 | 93.251 |

**Table 2, entry 5 ( with L2= (S)-BINAP )**



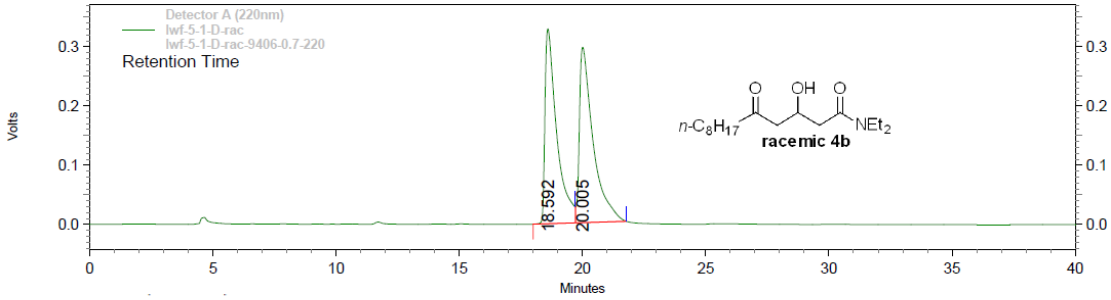

| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 30.003 | 629079 | 5.904 | 18256 | 7.268 |
| 2 | 31.961 | 10025595 | 94.096 | 232914 | 92.732 |

**Table 2, entry 6 ( L3= (S)-SegPhos)**

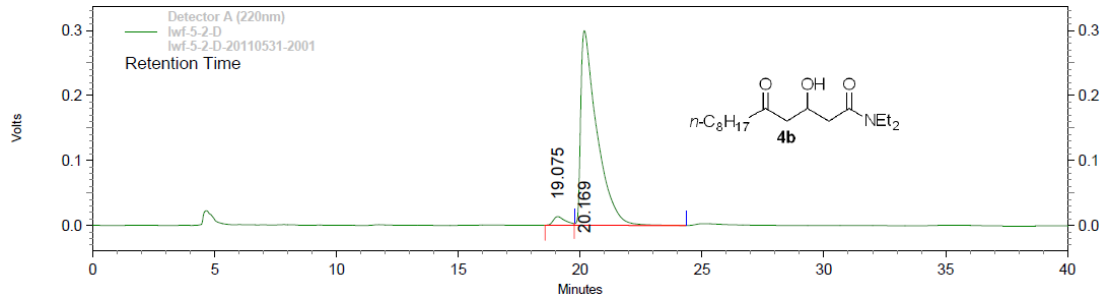



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 30.723 | 1023190 | 13.862 | 27238 | 15.339 |
| 2 | 32.865 | 6358102 | 86.138 | 150335 | 84.661 |

**Table 3, entry 2**

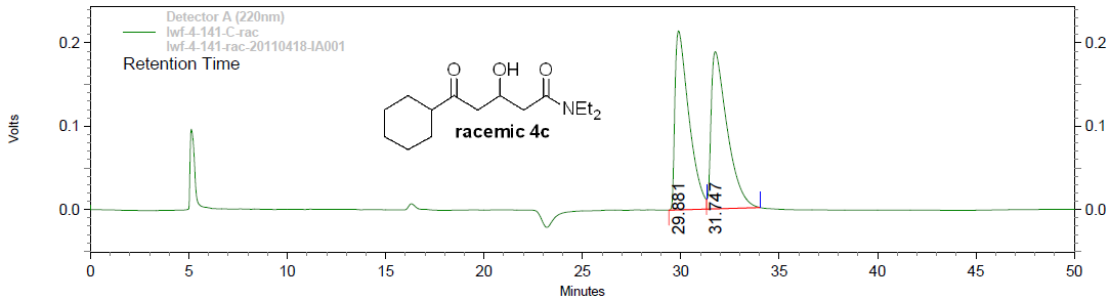



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 18.592 | 10874660 | 48.690 | 329210 | 52.648 |
| 2 | 20.005 | 11459779 | 51.310 | 296090 | 47.352 |

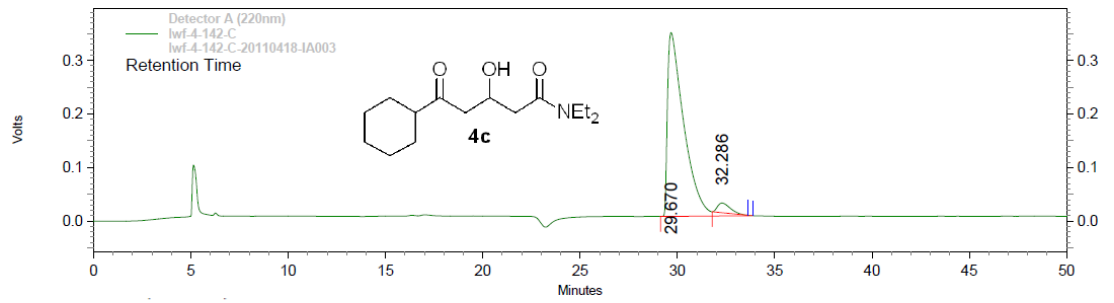


| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 19.075 | 461648 | 3.232 | 13337 | 4.263 |
| 2 | 20.169 | 13820329 | 96.768 | 299558 | 95.737 |

**Table 3 entry 3**

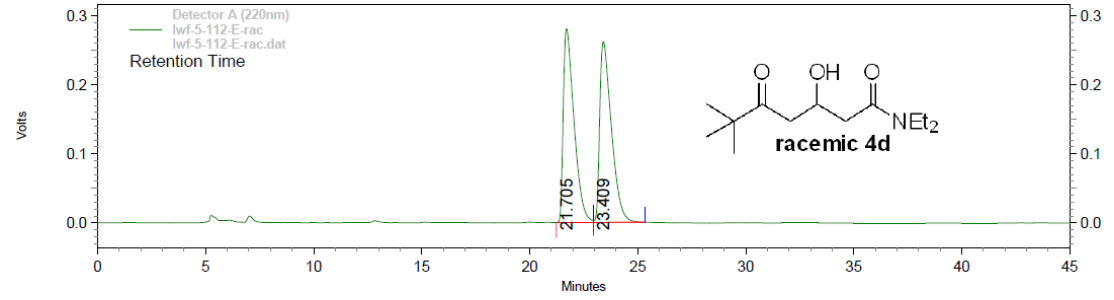



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 29.881 | 10607007 | 49.664 | 214660 | 53.245 |
| 2 | 31.747 | 10750479 | 50.336 | 188496 | 46.755 |

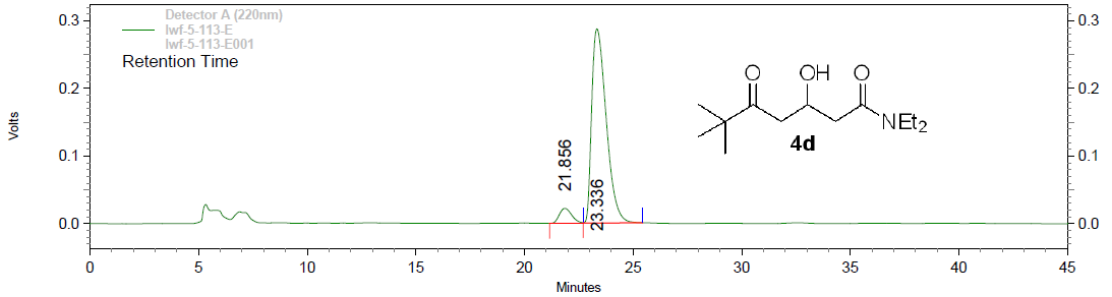



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 29.670 | 20339600 | 96.111 | 343174 | 94.993 |
| 2 | 32.286 | 823093 | 3.889 | 18088 | 5.007 |

**Table 3 entry 4**

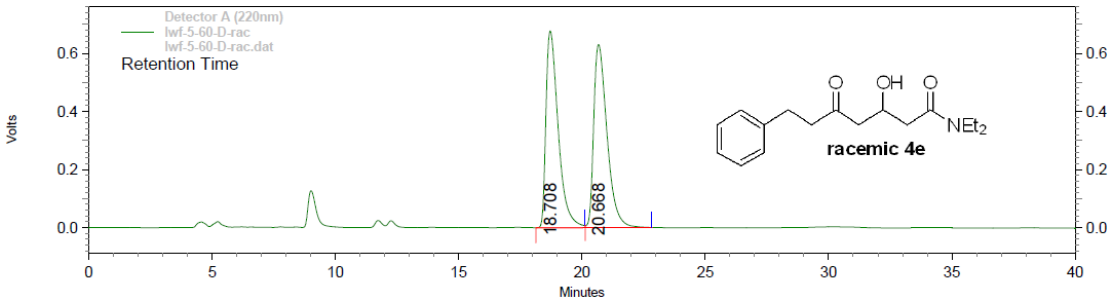


| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 21.705 | 9692100 | 49.473 | 281202 | 51.768 |
| 2 | 23.409 | 9898522 | 50.527 | 261997 | 48.232 |

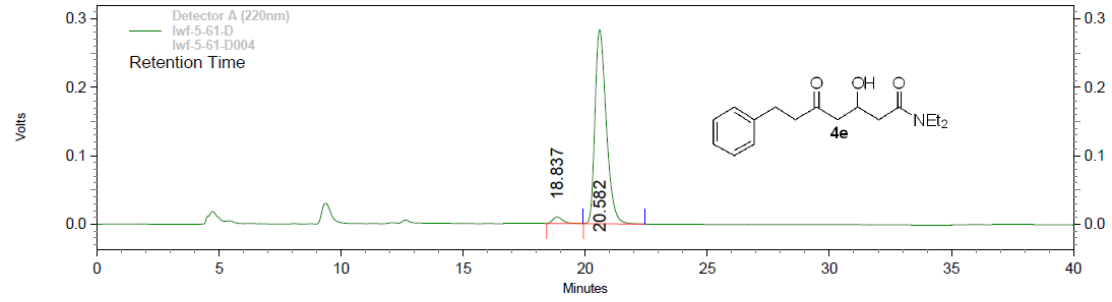



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 21.856 | 868027 | 6.117 | 22047 | 7.129 |
| 2 | 23.336 | 13322416 | 93.883 | 287210 | 92.871 |

**Table 3 entry 5**

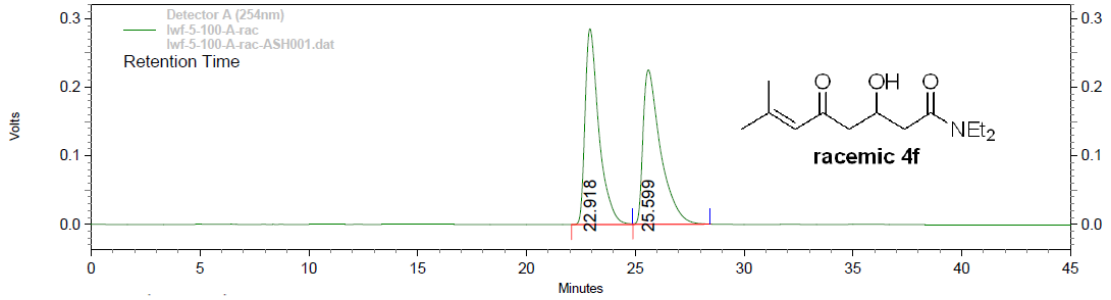



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 18.708 | 23355360 | 49.708 | 677936 | 51.799 |
| 2 | 20.668 | 23630076 | 50.292 | 630836 | 48.201 |

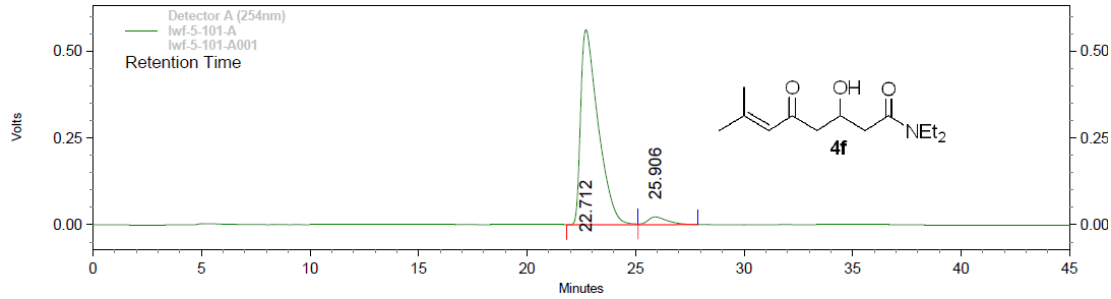



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 18.837 | 272620 | 2.910 | 9713 | 3.315 |
| 2 | 20.582 | 9095065 | 97.090 | 283313 | 96.685 |

**Table 3 entry 6**

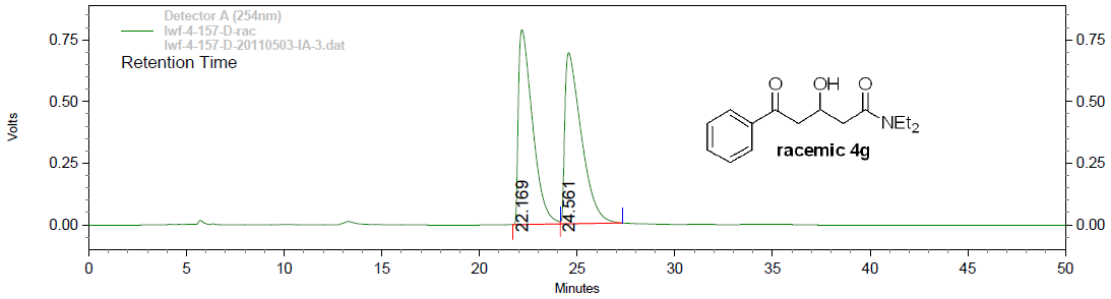



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 22.918 | 12626462 | 49.977 | 285497 | 55.890 |
| 2 | 25.599 | 12638025 | 50.023 | 225327 | 44.110 |

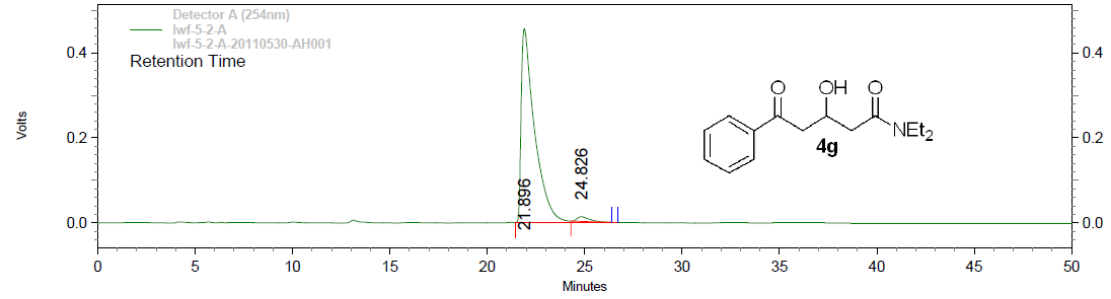



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 22.712 | 31478289 | 95.777 | 561636 | 96.170 |
| 2 | 25.906 | 1387944 | 4.223 | 22369 | 3.830 |

**Table 3 entry 7**

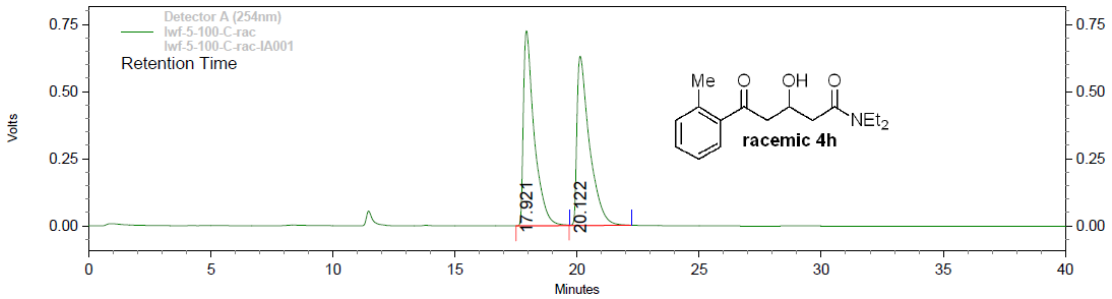



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 22.169 | 39693472 | 49.414 | 789391 | 53.227 |
| 2 | 24.561 | 40635106 | 50.586 | 693660 | 46.773 |



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 21.896 | 22037759 | 97.793 | 456374 | 97.592 |
| 2 | 24.826 | 497462 | 2.207 | 11260 | 2.408 |

**Table 3 entry 8**




| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 17.921 | 22290985 | 49.821 | 726293 | 53.530 |
| 2 | 20.122 | 22450788 | 50.179 | 630510 | 46.470 |

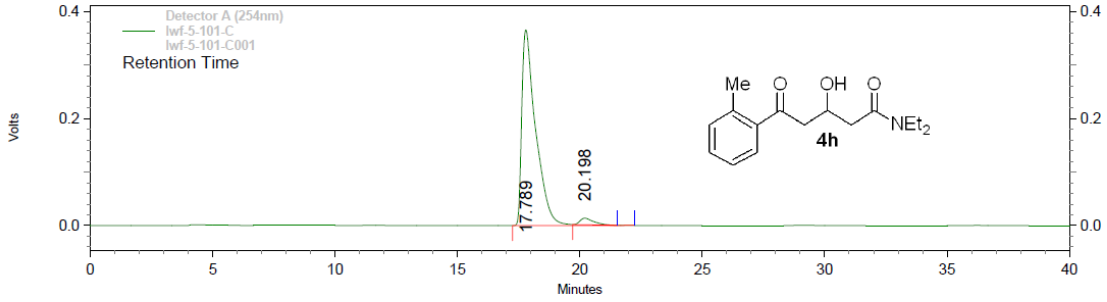
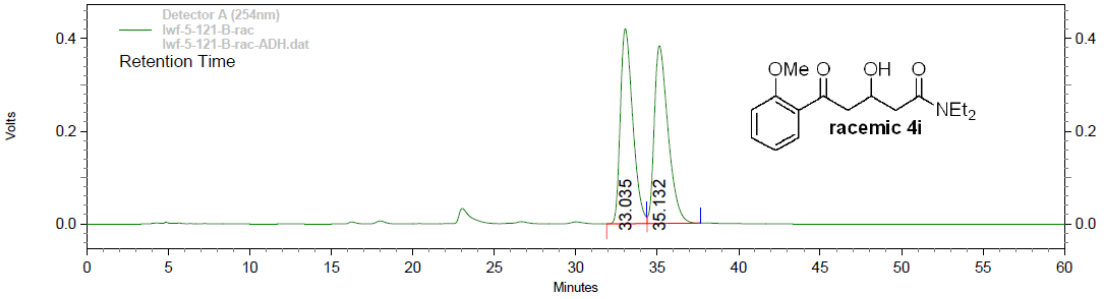
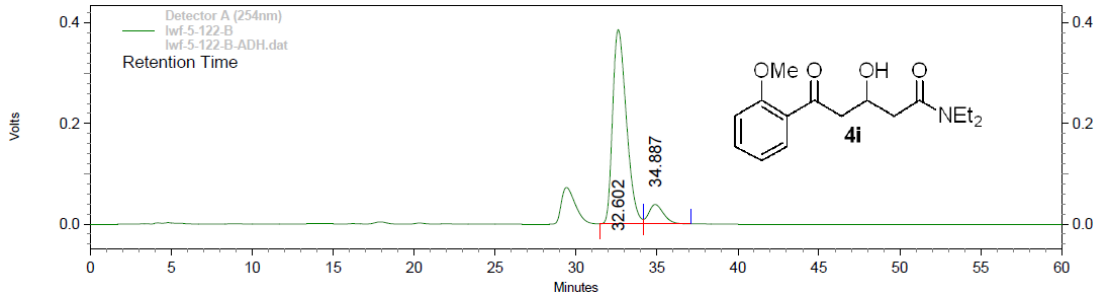



**Table 3 entry 9**

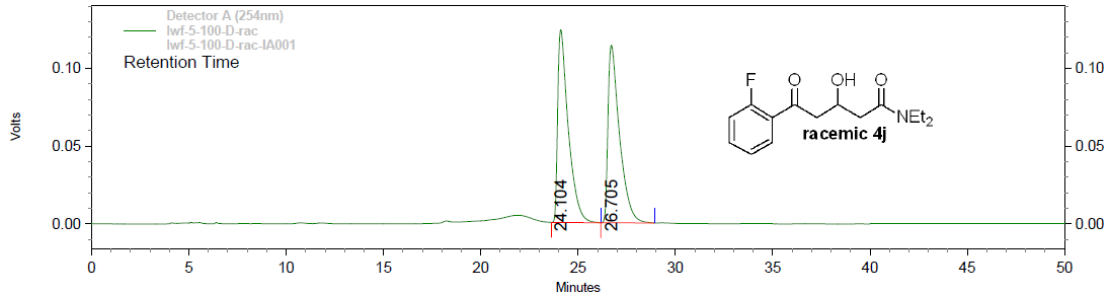



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 33.035 | 22281346 | 49.592 | 420762 | 52.322 |
| 2 | 35.132 | 22648001 | 50.408 | 383409 | 47.678 |

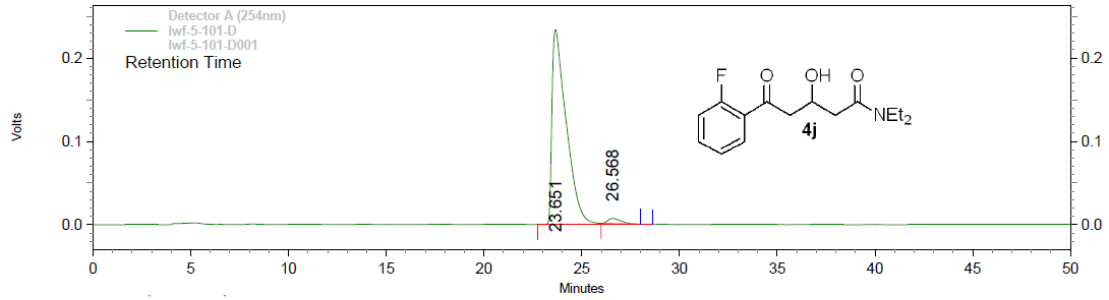



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 32.602 | 22857460 | 90.322 | 386200 | 90.912 |
| 2 | 34.887 | 2449285 | 9.678 | 38605 | 9.088 |

**Table 3 entry 10**

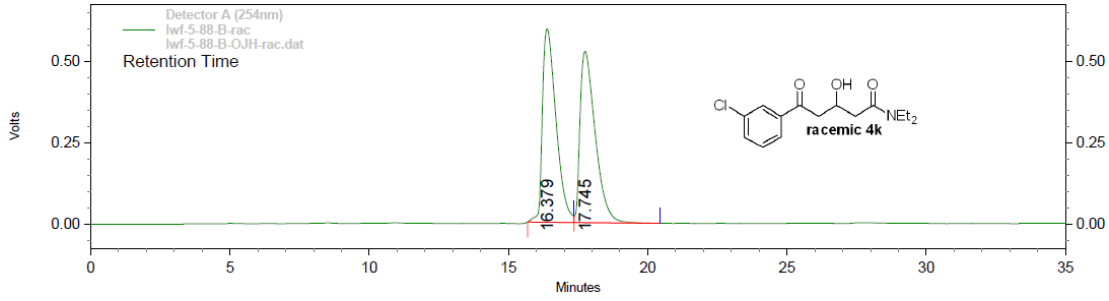



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 24.104 | 4691691 | 49.947 | 124032 | 52.063 |
| 2 | 26.705 | 4701592 | 50.053 | 114203 | 47.937 |

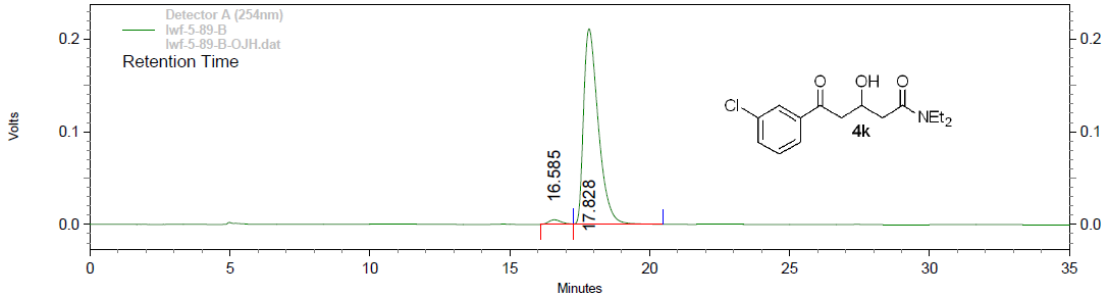



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 23.651 | 11949022 | 97.601 | 233737 | 97.358 |
| 2 | 26.568 | 293759 | 2.399 | 6342 | 2.642 |

**Table 3 entry 11**

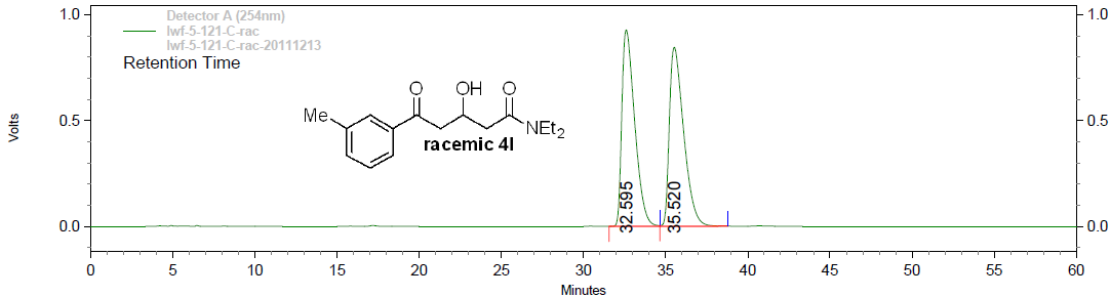


| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 16.379 | 20291223 | 50.392 | 595951 | 53.041 |
| 2 | 17.745 | 19975880 | 49.608 | 527618 | 46.959 |

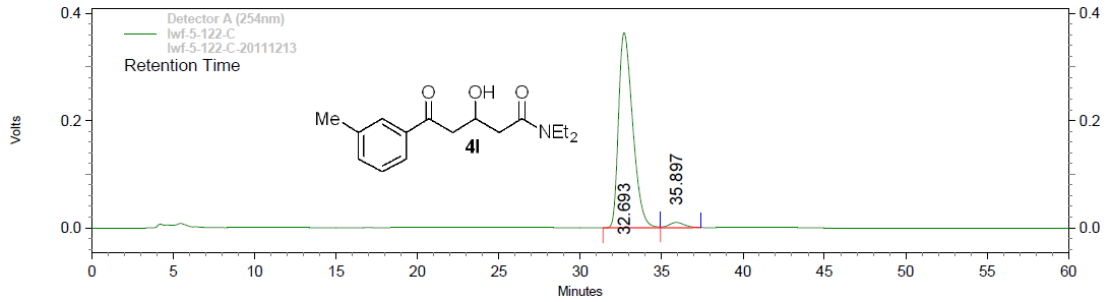



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 16.585 | 159688 | 2.024 | 5006 | 2.318 |
| 2 | 17.828 | 7730495 | 97.976 | 211018 | 97.682 |

**Table 3 entry 12**

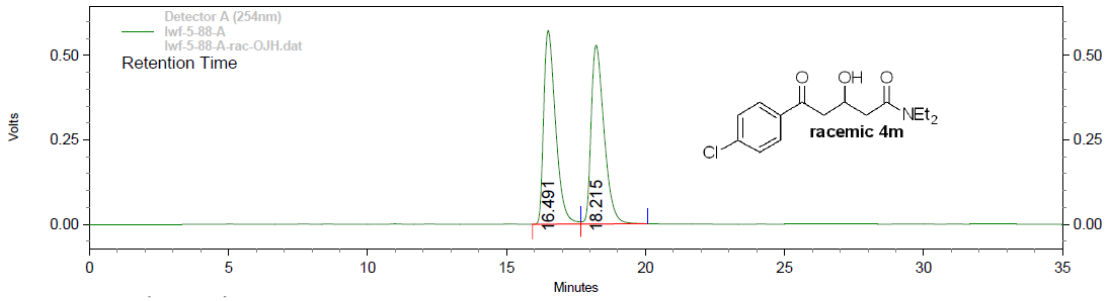



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 32.595 | 50503002 | 49.658 | 928039 | 52.328 |
| 2 | 35.520 | 51198144 | 50.342 | 845464 | 47.672 |

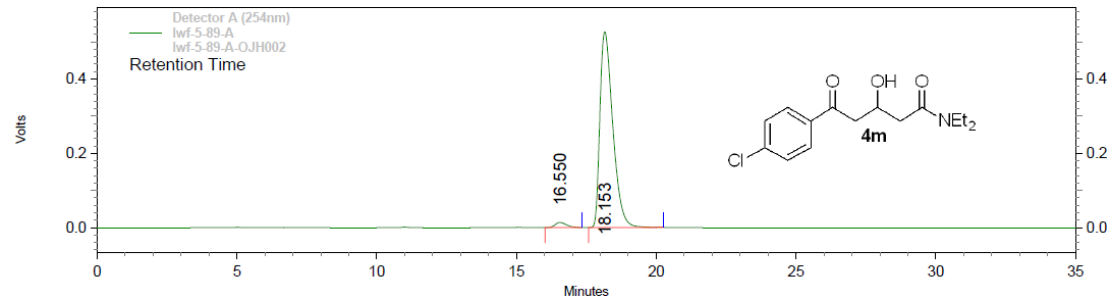



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 32.693 | 21969423 | 97.195 | 363616 | 97.395 |
| 2 | 35.897 | 633976 | 2.805 | 9727 | 2.605 |

**Table 3 entry 13**

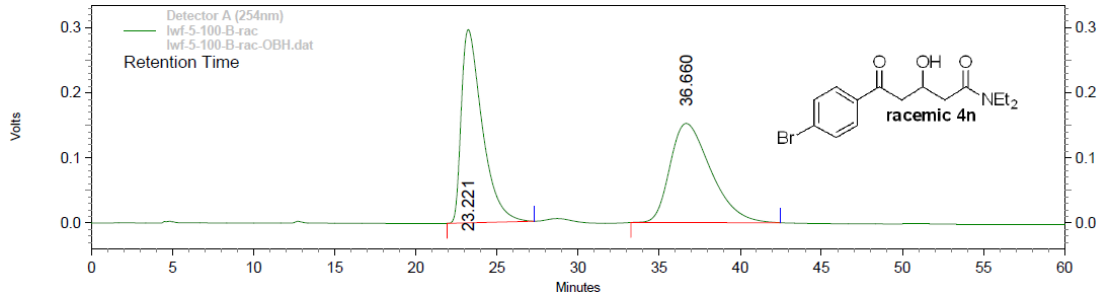



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 16.491 | 17129386 | 49.977 | 573828 | 51.999 |
| 2 | 18.215 | 17145203 | 50.023 | 529712 | 48.001 |

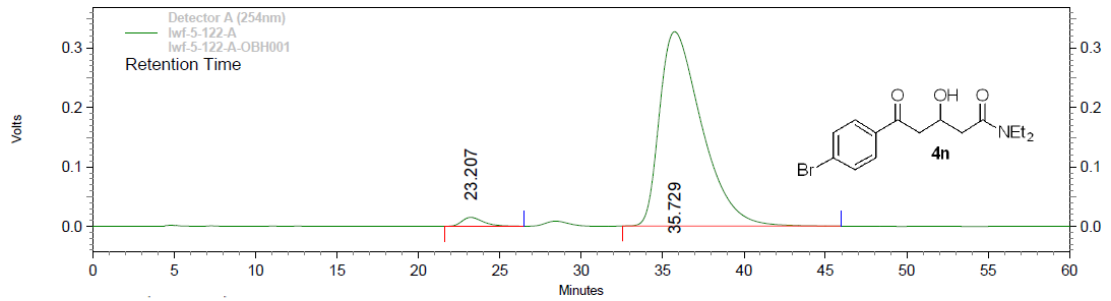



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 16.550 | 388882 | 2.254 | 13753 | 2.544 |
| 2 | 18.153 | 16863143 | 97.746 | 526771 | 97.456 |

**Table 3 entry 14**

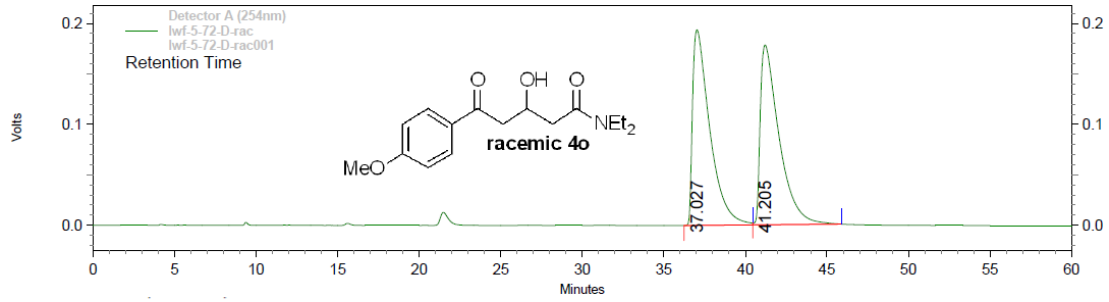



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 23.221 | 26663560 | 49.969 | 296998 | 66.090 |
| 2 | 36.660 | 26697173 | 50.031 | 152385 | 33.910 |

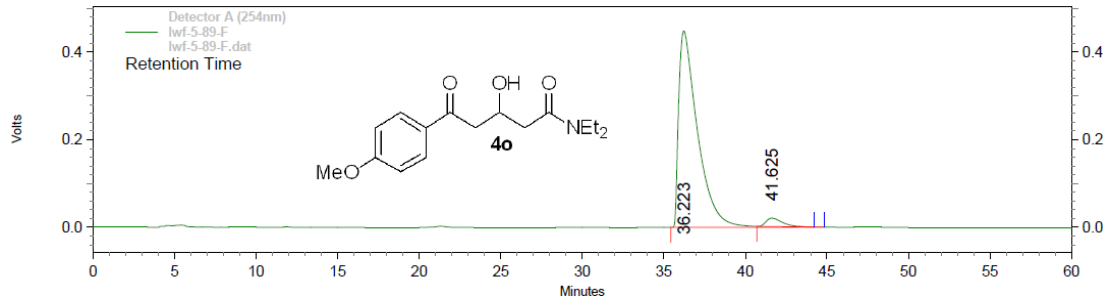



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 23.207 | 1374931 | 2.275 | 15043 | 4.395 |
| 2 | 35.729 | 59071582 | 97.725 | 327194 | 95.605 |

**Table 3 entry 15**

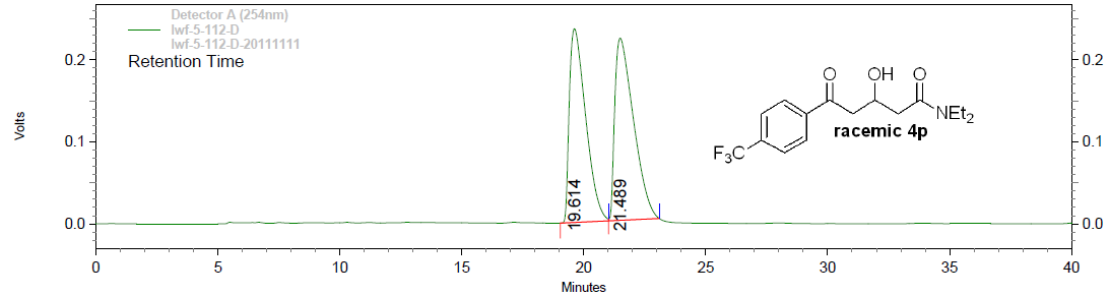



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 37.027 | 14259706 | 49.956 | 193929 | 52.106 |
| 2 | 41.205 | 14284672 | 50.044 | 178255 | 47.894 |

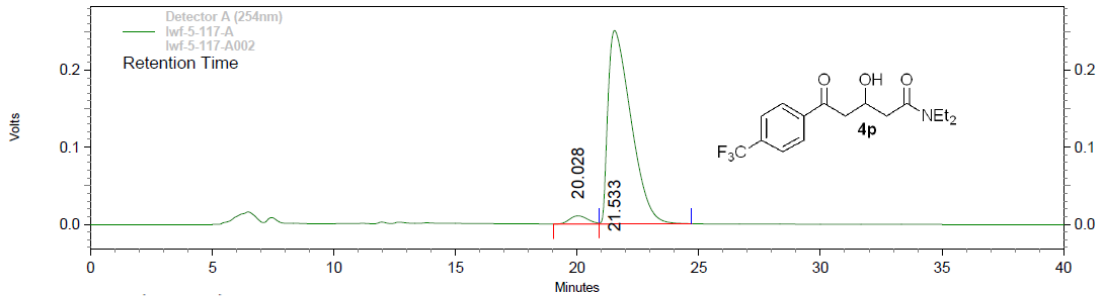



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 36.223 | 36054859 | 96.438 | 448404 | 95.886 |
| 2 | 41.625 | 1331795 | 3.562 | 19240 | 4.114 |

**Table 3 entry 16**

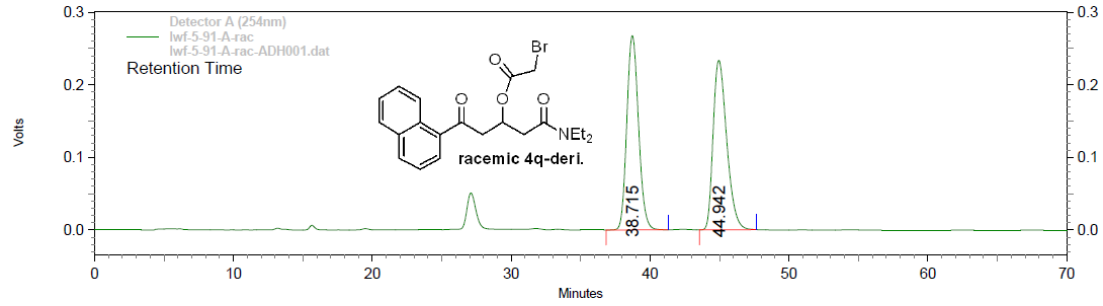



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 19.614 | 11026210 | 48.128 | 236378 | 51.537 |
| 2 | 21.489 | 11884132 | 51.872 | 222279 | 48.463 |

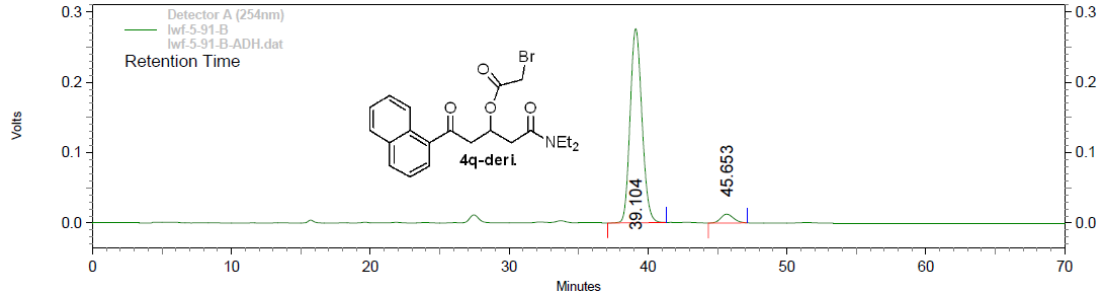



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 20.028 | 551194 | 3.231 | 10612 | 4.062 |
| 2 | 21.533 | 16506586 | 96.769 | 250661 | 95.938 |

**Table 3 entry 17**

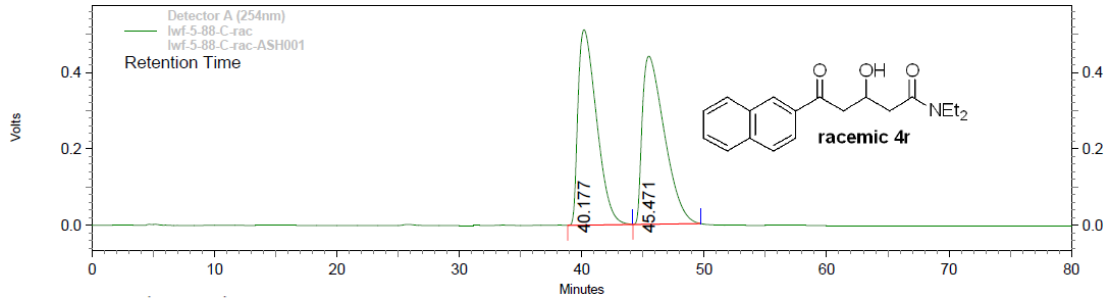



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 38.715 | 15702256 | 49.681 | 267508 | 53.401 |
| 2 | 44.942 | 15904158 | 50.319 | 233430 | 46.599 |

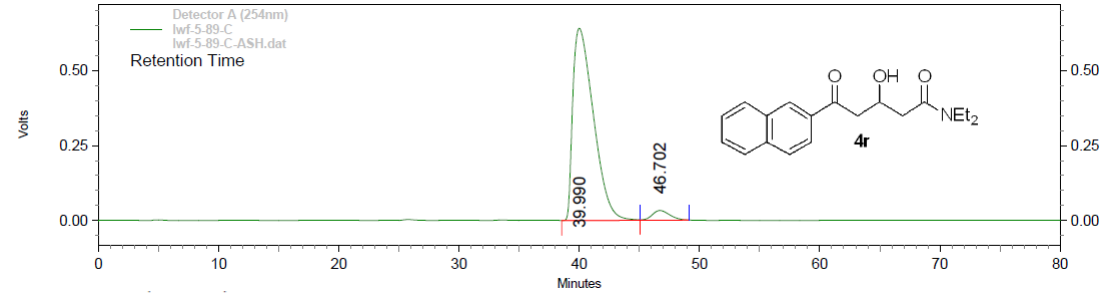



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 39.104 | 16311688 | 95.377 | 275844 | 95.677 |
| 2 | 45.653 | 790702 | 4.623 | 12464 | 4.323 |

**Table 3 entry 18**

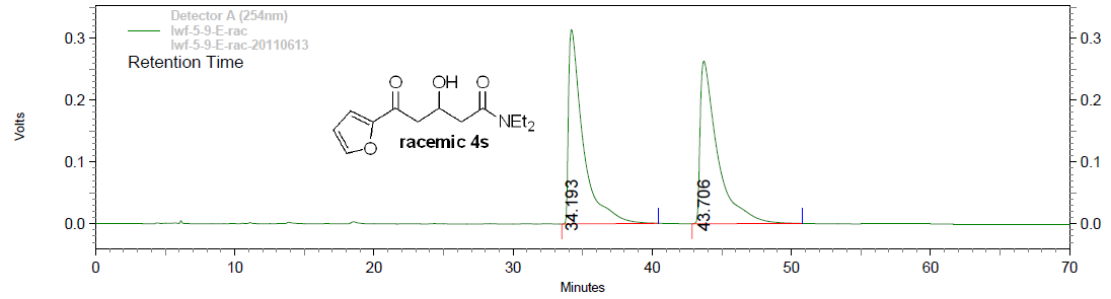



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 40.177 | 53937618 | 49.325 | 511249 | 53.745 |
| 2 | 45.471 | 55414304 | 50.675 | 440007 | 46.255 |

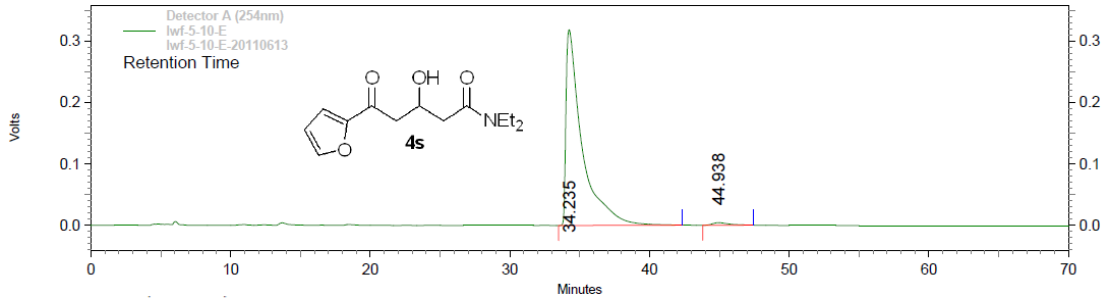



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 39.990 | 76570278 | 95.891 | 640295 | 95.199 |
| 2 | 46.702 | 3280898 | 4.109 | 32293 | 4.801 |

**Table 3, entry 19**

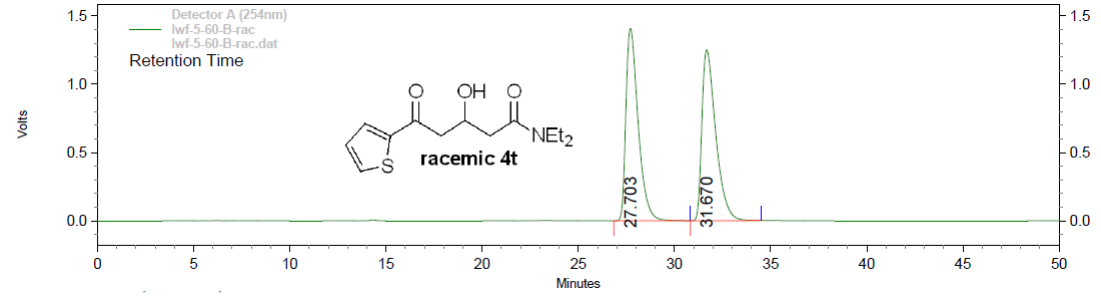



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 34.193 | 22889401 | 50.005 | 314317 | 54.440 |
| 2 | 43.706 | 22884700 | 49.995 | 263049 | 45.560 |

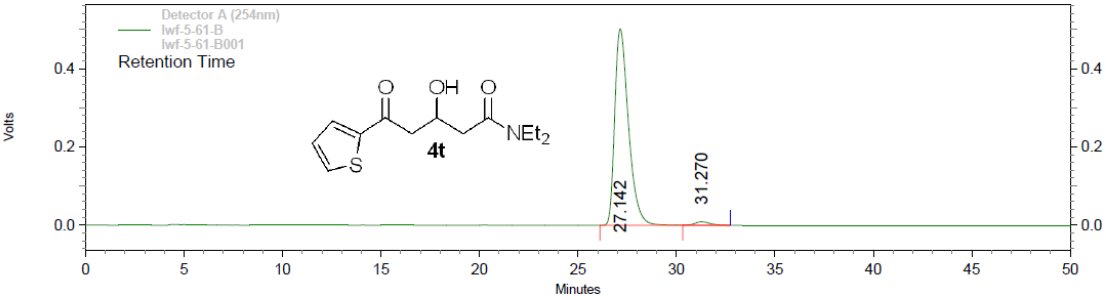



| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 34.235 | 25483810 | 98.694 | 318679 | 98.701 |
| 2 | 44.938 | 337283 | 1.306 | 4193 | 1.299 |

**Table 3 entry 20**




| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 27.703 | 62359041 | 49.913 | 1408911 | 52.996 |
| 2 | 31.670 | 62576646 | 50.087 | 1249635 | 47.004 |




| Pk # | Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|---|
| 1 | 27.142 | 24426621 | 98.194 | 502308 | 98.294 |
| 2 | 31.270 | 449346 | 1.806 | 8716 | 1.706 |