Electronic Supporting Information

sp^3C-H bond alkylation of ketones with alkenes via ruthenium(II) catalysed dehydrogenation of alcohols

Bin Li,[a,b] Christophe Darcel,[a] Pierre H. Dixneuf[a]

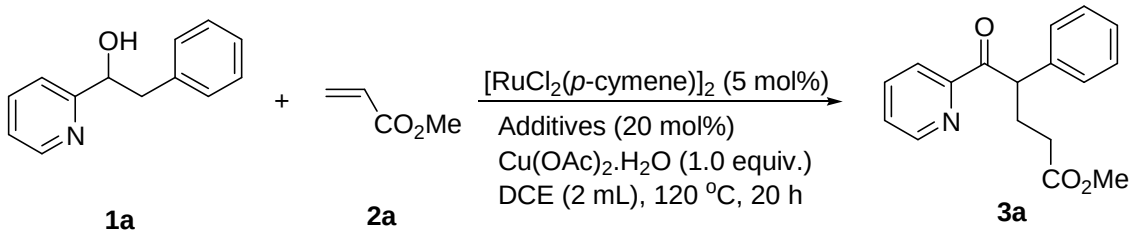
[a]*Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS-Université de Rennes 1, Team "Organometallics: Materials and Catalysis" Centre for Catalysis and Green Chemistry, Campus de Beaulieu, 35042 Rennes, France*

[b]*Present address: School of Chemical & Environmental Engineering, Wuyi University, Jiangmen 529020, Guangdong Province, P.R. China*

Table of Contents

1- ***Optimisation studies for the alkylation of 2-phenyl-1-pyridyl ethanol with ruthenium catalyst***

Table S1 *Optimisation study of additives for sp^3 C-H alkylation of 2-phenyl-1-pyridyl ethanol* **1a** *with methyl acrylate and $[RuCl_2(p\text{-cymene})]_2$ as the catalyst.*[a]

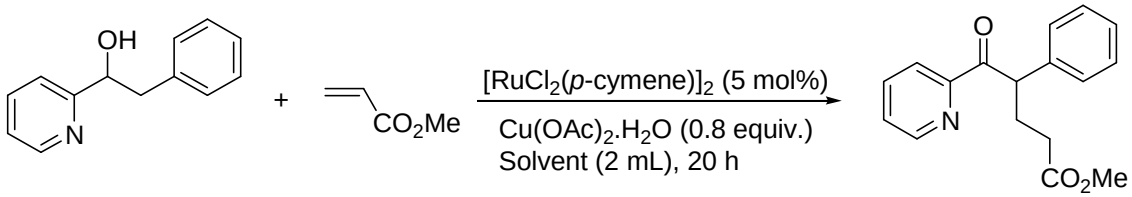


1a **2a** **3a**

Entry	Additive	Conv. (%)[b]
1	$AgSbF_6$	20
2	KOAc	36
3	$C_6H_5CO_2H$	52
4	BNPAH	7
5	KPF_6	15
6	KOPiv	50
7	$C_6H_5CO_2K$	57
8	---	53
9	$CF_3C_6H_5CO_2H$	34
10	$(CH_3)CC_6H_5CO_2H$	50
11	2,6-$(OMe)_2$-$C_6H_3CO_2H$	54
12[c]	----	---
13[d]	----	----

[a]2-Phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (4 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), additive (20 mol%), $Cu(OAc)_2.H_2O$ (1 equiv.), 1,2-dichloroethane (DCE) (2 mL), 120 °C, 20 h. [b]Determined by GC. [c]Without $Cu(OAc)_2.H_2O$. [d]Without Ru catalyst.

Table S2 *Optimisation study of solvents and amount of $Cu(OAc)_2.H_2O$ for sp^3 C-H alkylation of 2-phenyl-1-pyridyl ethanol* **1a** *with methyl acrylate* ***2a*** *with $[RuCl_2(p\text{-cymene})]_2$ as the catalyst.*[a]

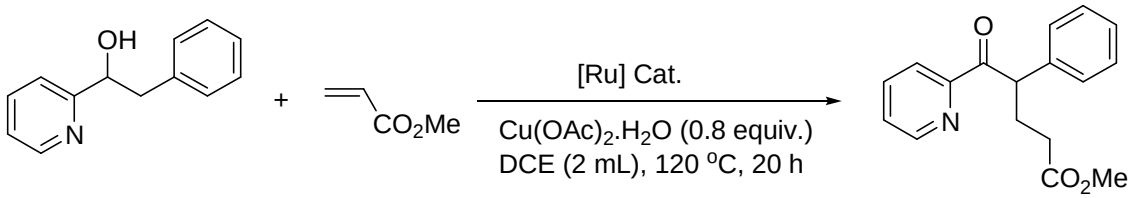


1a **2a** **3a**

Entry	Amount of **2a** (equiv.)	$Cu(OAc)_2.H_2O$ (equiv.)	Solvent	Temperature (^oC)	Conv. (%)[b]
1	2.0	0.2	DCE	120	18
2	2.0	0.5	DCE	120	47
3	2.0	0.8	DCE	120	53
4	2.0	1.0	DCE	120	56
5	2.0	1.2	DCE	120	29
6	2.0	0.8	toluene	140	57
7	2.0	0.8	DMF	140	13
8	2.0	0.8	xylene	140	7
9	2.0	0.8	CH_3CN	100	12
10	4.0	0.8	DCE	120	69(46)
11[c]	4.0	0.8	DCE	120	9
12	6.0	0.8	DCE	120	72
13[d]	4.0	0.8	DCE	120	75
14[e]	4.0	0.8	DCE	120	80(68)
15	4.0	0.8	toluene	150	74(54)

[a]2-phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (2-6 equiv.), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $Cu(OAc)_2.H_2O$ (0.2-1.2 equiv.), DCE (2 mL), 20 h. [b]Determined by GC, in parenthesis, isolated yields of purified alkylated product **3a**. [c]Under air. [d]7.5 mol% of $[RuCl_2(p\text{-cymene})]_2$. [e]Run in 0.5 mmol scale, 36 h.

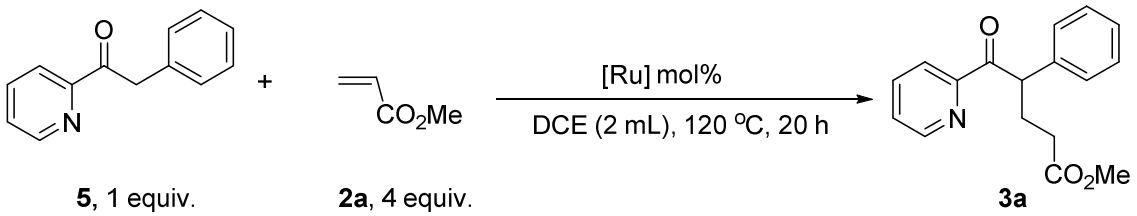
Table S3 *Optimisation study of ruthenium catalysts for the sp^3 C-H alkylation of 2-phenyl-1-pyridyl ethanol* **1a** *with methyl acrylate* ***2a***[a]



1a **2a** **3a**

Entry	Ru catalyst (mol%)	Conv.%[b]
1	$[RuCl_2(mesitylene)]_2$ (5)	56
2	$[RuCl_2(hmb)]_2$ (5)	14
3	$[RuCl_2(1,2,4,5\text{-tetramethylbenzene})]_2$ (5)	47
4	$[RuCl_2(p\text{-cymene})]_2$ (5)	69(46)
5	$[RuCl_2(p\text{-cymene})(PPh_3)]$ (10)	22
6	$[CpRuCl(PPh_3)_2]$ (10)	2
7	$[Ru(OAc)_2(p\text{-cymene})]$ (10)	60

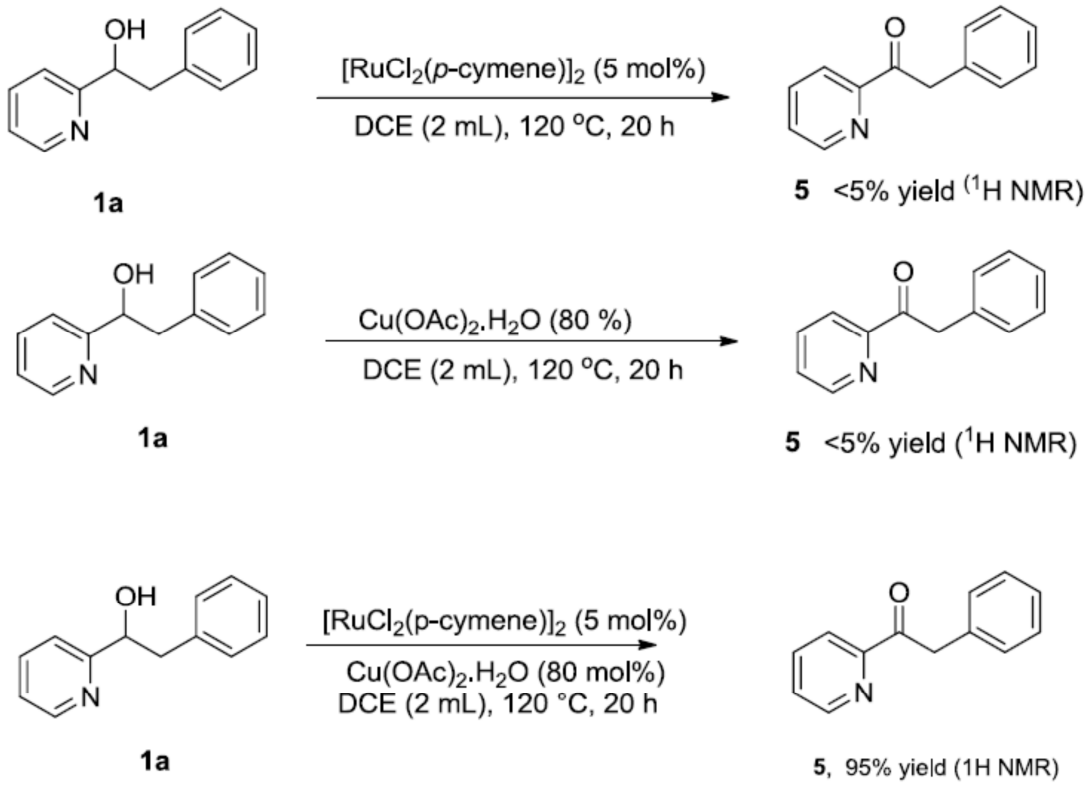
[a]2-phenyl-1-pyridyl ethanol (0.25 mmol), methyl acrylate (4 equiv.), [Ru], $Cu(OAc)_2.H_2O$ (0.8 equiv.), DCE (2 mL), 120 °C, 20 h. [b]Deterrmined by GC, in parenthesis, isolated yields of purified alkylated product **3a**. hmb = hexamethylbenzene.



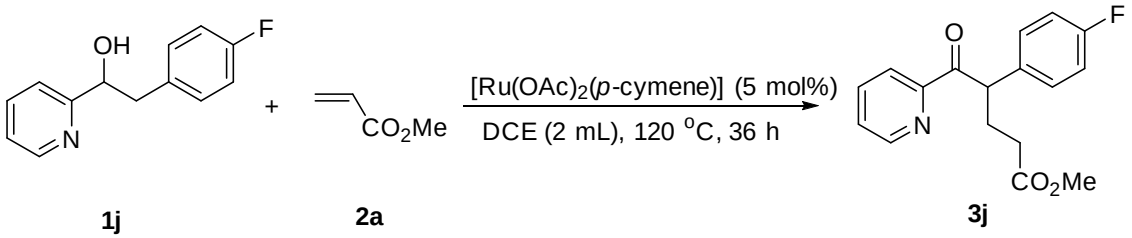
5, 1 equiv. **2a**, 4 equiv. **3a**

[Ru] (mol%)	$Cu(OAc)_2.H_2O$ (mol%)	GC-Yield (%)
$[RuCl_2(p\text{-cymene})]_2$ (10)	----	----
----	80	4
$[RuCl_2(p\text{-cymene})]_2$ (5)	80	10
$Ru(OAc)_2(p\text{-cymene})$ (10)	----	10

Scheme S1 Ru(II)-catalyzed sp^3 C-H alkylation of pyridyl ketone **5** with methyl acrylate **2a** in DCE



Scheme S2. Influence of $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2$ on the dehydrogenation of alcohol **1a** into ketone **5**.



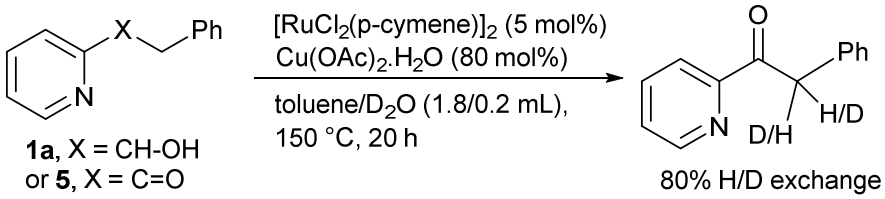
with $Cu(OAc)_2.H_2O$ (0.8 equiv.), conv > 98%, **3j** is the unique product obatined. without $Cu(OAc)_2.H_2O$ (0.8 equiv.), conv = 90%, a mixture of products is obtained, including **3j** (30%) and the ketone Pyr -CO-CH_2-C_9H_4-*p*F (10□%)

Scheme S3- Influence $Cu(OAc)_2.H_2O$ on sp^3 C-H alkylation of 2-phenyl-1-pyridyl ethanol **1a** with methyl acrylate **2a** catalysed by $[Ru(OAc)_2(p\text{-cymene})]$

Notably in the presence of either the ruthenium catalyst or the copper acetate, no reaction occurred.

The reaction of the ketone **5** with 4 equiv. of methyl acrylate **2a** in the presence of $Ru(OAc)_2$(*p*-cymene) (10 mol%) without addition of $Cu(OAc)_2$ gave the compound **3a** in only 10% GC-yield. The similar reaction in the presence of both 5 mol% of $[RuCl_2$(*p*-cymene)$]_2$ and 0.8 equiv. of $Cu(OAc)_2$ only led to 10% of **3a**. The presence of the alcohol functionality in **1a** appears to play a key role to generate an active catalyst able to perform the alkylation of **5** with **2a** without an additional base. (see also Scheme S1)

Starting from the alcohol **1a**, the enolate formation under the conditions described in Table 1, entry 12, but without addition of the alkene **2** was shown to occur by H/D exchange at the α-position as after 20 h of reaction, 80% of deuterium incorporation took place at the α C-H bonds of the ketone **5**. Similarly, starting from **5** under similar catalytic conditions, the same amount of deuterium incorporation was observed, indicating that the ketone **5** may be an intermediate in the sequential reaction. (Scheme S2)



Scheme S4. Deuterium incorporation studies.

The intermediate enolate formation is supported as both **1a** and **5** under the reaction conditions in the presence of D_2O led to 80% deuterium incorporation at the carbonyl a carbon of **5** (Scheme S4).

3- General remarks

All reagents were obtained from commercial sources and used as received. 1,2-Dichloroethane (DCE), was distilled under conventional methods (sodium, benzophenone), and stored under an argon atmosphere. Toluene was dried over Braun MB-SPS-800 solvent purification system, and stored under an argon atmosphere. Technical grade petroleum ether (40-60 °C bp.) and ethyl acetate were used for chromatography column.

^{1}H NMR spectra were recorded in $CDCl_3$ at ambient temperature on AVANCE I 300, AVANCE III 400 spectrometers at 300.1 MHz and 400.1 MHz, respectively, using the solvent as internal standard (7.26 ppm). ^{13}C NMR spectra were obtained at 75 or 100 MHz and referenced to the internal solvent signals (central peak is 77.2 ppm). Chemical shift (δ) and coupling constants (J) are given in ppm and in Hz, respectively. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, and br. for broad.

GC analyses were performed with GC-2014 (Shimadzu) 2010 equipped with a 30-m capillary column (Supelco, SPBTM-20, fused silica capillary column, 30 M×0.25 mm×0.25 mm film thickness), was used with N_2/air as vector gas. GCMS were measured by GCMS-QP2010S (Shimadzu) with GC-2010 equipped with a 30-m capillary column (Supelco, SLBTM-5ms, fused silica capillary column, 30 M×0.25 mm×0,25 mm film thickness), was used with helium as vector gas. The following GC conditions were used: initial temperature 100 °C for 2 minutes, then rate 10 °C/min until 250 °C and 250 °C for 20 minutes.

Melting points were performed on a LEICA VMHB Kofler system are uncorrected.

HRMS analyses were performed on a Thermo Fischer Scientic Q-Exactive apparatus in the CRMPO center, Rennes, France.

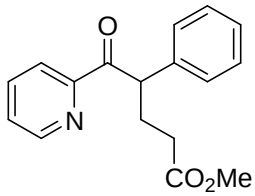
Pyridyl ethanol derivatives were synthesized by known method[1].

General procedure for $[RuCl_2(p\text{-cymene})]_2$ catalyzed alkylation of 2-phenyl-1-pyridyl ethanol derivatives with functional alkenes

$[RuCl_2(p\text{-cymene})]_2$ (0.025 mmol, 15.3 mg), functional alkene (2.0 mmol), 2-phenyl-1-pyridyl ethanol derivative (0.5 mmol), $Cu(OAc)_2.H_2O$ (0.4 mmol, 80 mg), and DCE (2 mL) were introduced in a Schlenck tube under argon, equipped with a magnetic stirring bar and was stirred at 120 ^{o}C for 36 h. When the reaction was completed, the conversion of the reaction was analyzed by gas chromatography. The solvent was then evaporated under vacuum and the desired product was purified by silica gel chromatography column (0.5 mol% Et_3N) and a mixture of petrol ether/ethyl acetate as the eluent.

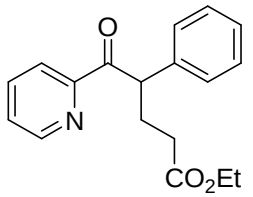
4- Characterization data of products

Methyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3a)



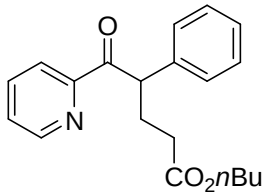
Light yellow oil, yield = 68%, 97 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66 (m, 1H), 8.02-8.00 (m, 1H), 7.77 (dt, 1H, *J* = 1.8 Hz, *J* = 7.5 Hz), 7.42-7.38 (m, 3H), 7.30-7.24 (m, 2H), 7.21-7.16 (m, 1H), 5.41 (dd, 1H, *J* = 7.8 Hz, *J* = 1.8 Hz), 3.65 (s, 3H), 2.51-2.43 (m, 1H), 2.36-2.23 (m, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 200.8, 173.8, 153.0, 149.0, 138.5, 136.9, 129.1, 128.8, 127.2, 127.1, 122.9, 51.7, 50.1, 32.2, 28.0. GC: t_R = 17.0 min. MS (EI): m/z: 283 (M^+, 20), 210 (50), 117 (100), 106 (40), 91 (25), 78 (80), 51 (20).

Ethyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3b)



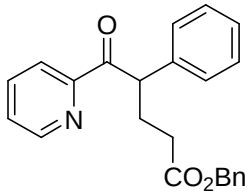
Light yellow oil, yield = 56%, 83 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66-8.64 (m, 1H), 8.00 (d, 1H, *J* = 7.8 Hz), 7.76 (dt, 1H, *J* = 1.5 Hz, *J* = 7.8 Hz), 7.41-7.37 (m, 3H), 7.29-7.16 (m, 3H), 5.43 (dd, 1H, *J* = 7.8 Hz, *J* = 2.7 Hz), 4.15-4.07 (q, 2H, *J* = 7.2 Hz), 2.51-2.43 (m, 1H), 2.32-2.23 (m, 3H), 1.23 (t, 3H, *J* = 6.9 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 200.9, 173.4, 153.0, 149.0, 138.6, 136.9, 129.1, 128.7, 127.2, 127.1, 122.8, 60.5, 50.1, 32.4, 28.1, 14.4. GC: t_R = 17.5 min. MS (EI): m/z: 297 (M^+, 30), 252 (20), 210 (60), 117 (100), 106 (40), 91 (25), 78 (80), 51 (15).

n-Butyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3c)



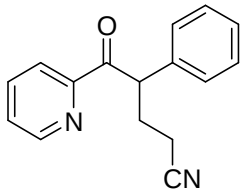
Light yellow oil, yield = 55%, 90 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.65-8.64 (m, 1H), 8.02-7.99 (m, 1H), 7.75 (dt, 1H, *J* = 1.5 Hz, *J* = 7.5 Hz), 7.41-7.36 (m, 3H), 7.29-7.16 (m, 3H), 5.43 (dd, 1H, *J* = 7.8 Hz, *J* = 2.4 Hz), 4.06 (t, 2H, *J* = 6.6 Hz), 2.51-2.43 (m, 1H), 2.35-2.22 (m, 3H), 1.63-1.54 (m, 2H), 1.42-1.32 (m, 2H), 0.92 (t, 3H, *J* = 7.2 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 200.8, 173.4, 153.0, 149.0, 138.5, 136.9, 129.1, 128.7, 127.2, 127.1, 122.8, 64.4, 50.0, 32.4, 30.8, 28.1, 19.3, 13.9. GC: t_R = 20.5 min. MS (EI): m/z: 325 (M^+, 25), 252 (20), 210 (75), 117 (100), 106 (50), 91 (25), 78 (98), 51 (20). HRMS (ESI): *m/z* calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$ 360.1594, found 360.1596.

Benzyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3d)



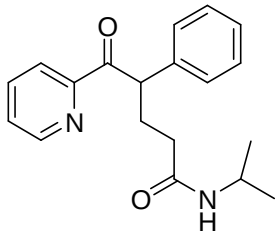
Light yellow solid, yield = 51%, 92 mg, M. p.: 53-55 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66-8.64 (m, 1H), 8.01 (d, 1H, *J* = 7.8 Hz), 7.75 (dt, 1H, *J* = 1.5 Hz, *J* = 7.8 Hz), 7.41-7.32 (m, 8H), 7.29-7.16 (m, 3H), 5.46 (t, 1H, *J* = 7.8 Hz), 5.12 (d, 2H, *J* = 1.5 Hz), 2.55-2.46 (m, 1H), 2.42-2.27 (m, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ =200.8, 173.1, 152.9, 149.0, 138.5, 136.9, 136.1, 129.1, 128.7, 128.6, 128.3, 128.2, 127.2, 127.1, 122.8, 66.3, 50.0, 32.4, 28.0. GC: t_R = 21.9 min. MS (EI): m/z: 359 (M^+, 10), 268 (20), 210 (15), 117 (5), 106 (30), 91 (100), 78 (40), 51 (10).

5-oxo-4-phenyl-5-(2'-pyridyl) pentanitrile (3e)



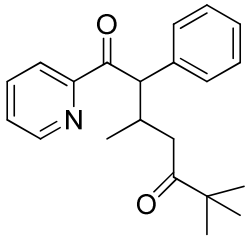
Light yellow solid, yield = 57%, 71 mg, M. p.: 64-66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67-8.65 (m, 1H), 8.02-8.00 (m, 1H), 7.77 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.43-7.39 (m, 3H), 7.33-7.19 (m, 3H), 5.56-5.51 (m, 1H), 2.53-2.23 (m, 4H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 199.9, 152.5, 149.1, 137.2, 137.0, 129.1, 129.0, 127.7, 127.4, 122.9, 119.5, 49.8, 28.3, 15.4. GC: t_R = 16.6 min. MS (EI): m/z: 250 (M^+, 5), 210 (35), 106 (50), 91 (10), 78 (100), 57 (20).

N'-isopropyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanamide (3f)



Light yellow solid, yield = 50%, 77 mg, M. p.: 137-139 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.67-8.64 (m, 1H), 8.01-7.98 (m, 1H), 7.77 (dt, 1H, *J* = 1.8 Hz, *J* = 7.5 Hz), 7.43-7.37 (m, 3H), 7.30-7.18 (m, 3H), 5.43 (t, 1H, *J* = 7.5 Hz), 5.36 (brs, 1H), 4.12-4.03 (m, 1H), 2.51-2.42 (m, 1H), 2.28-2.19 (m, 1H), 2.15-2.07 (m, 2H), 1.16-1.11 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 201.1, 171.5, 153.1, 149.0, 138.7, 137.0, 129.1, 128.7, 127.2, 127.1, 122.9, 50.2, 41.4, 34.9, 29.0, 23.0, 22.9. GC: t_R = 21.9 min. MS (EI): m/z: 310 (M^+, 10), 251 (40), 210 (50), 106 (45), 91 (50), 78 (100), 57 (20). HRMS (ESI): *m/z* calcd for $C_{21}H_{26}NO_2$ $[M + H]^+$ 324.1958, found 324.1961.

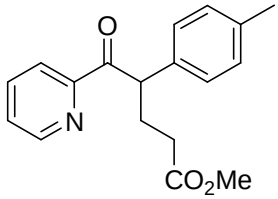
3,6,6-trimethyl-2-phenyl-1-(2'-pyridyl)hepta-1,5-dione (3h)



Light yellow oild, yield = 70%, 112 mg, M. p.: 87-89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): major stereoisomer: δ = 8.67 (s, 1H), 7.74 (t, 1H, *J* = 7.5 Hz), 7.45-7.13 (m, 6H), 5.42 (d, 1H, *J* = 10.8

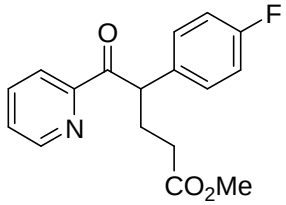
Hz), 3.16-3.00 (m, 1H), 2.55-2.20 (m, 2H), 1.00-0.97 (m, 7H); minor stereoisomer: δ = 8.67 (s, 1H), 7.99 (t, 1H, *J* = 8.1 Hz), 7.45-7.13 (m, 6H), 5.32 (d, 1H, *J* = 10.5 Hz), 3.16-3.00 (m, 1H), 2.55-2.20 (m, 2H), 1.08 (s, 3.8H), 0.76 (d, 1.2H, *J* = 6.9 Hz). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$): major stereoisomer: δ =215.13, 201.34, 153.42, 148.91, 137.87, 136.96, 129.70, 128.65, 127.15, 127.09, 122.69, 55.78, 44.32, 41.00, 32.23, 26.33, 19.03; minor stereoisomer: δ =214.73, 201.34, 153.40, 148.93, 137.81, 136.94, 129.72, 128.56, 127.15, 127.04, 122.72, 55.33, 44.36, 42.10, 31.87, 26.40, 17.92. GC: t_R = 18.8 min. MS (EI): m/z: 323 (M^+, 15), 248 (25), 224 (35), 198 (25), 106 (25), 91 (10), 78 (45), 57 (100).

Methyl 5-oxo-5-(2'-pyridyl)-4-(*p*-tolyl) pentanoate (3i)



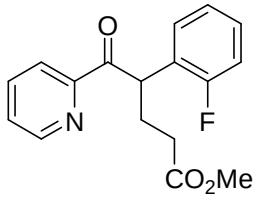
Light yellow oil, yield = 67%, 100 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66-8.63 (m, 1H), 8.01-7.98 (m, 1H), 7.74 (dt, 1H, *J* = 1.8 Hz, *J* = 7.5 Hz), 7.40-7.35 (m, 1H), 7.29-7.26 (m, 2H), 7.09-7.03 (m, 2H), 5.38 (t, 1H, *J* = 7.8 Hz), 3.64 (s, 3H), 2.49-2.41 (m, 1H), 2.35-2.21 (m, 6H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$): δ = 200.8, 173.8, 153.0, 149.0, 136.9, 136.8, 135.4, 129.5, 129.0, 127.0, 122.8, 51.6, 49.7, 32.1, 28.0, 21.1. GC: t_R = 18.5 min. MS (EI): m/z: 297 (M^+, 20), 224 (35), 131 (100), 106 (20), 91 (30), 78 (50), 51 (15).

Methyl 5-oxo-5-(2'-pyridyl)-4-(*p*-fluorophenyl) pentanoate (3j)



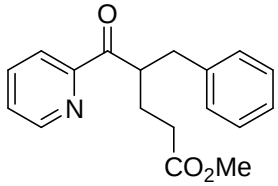
Light yellow oil, yield = 71%, 107 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.66-8.64 (m, 1H), 8.01 (d, 1H, *J* = 7.8 Hz), 7.78 (dt, 1H, *J* = 1.5 Hz, *J* = 7.5 Hz), 7.43-7.34 (m, 3H), 6.98-6.93 (m, 2H), 5.42 (t, 1H, *J* = 7.8 Hz), 3.64 (s, 3H), 2.49-2.40 (m, 1H), 2.34-2.18 (m, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$): δ = 200.6, 173.7, 162.1 (d, J_{CF} = 245.5 Hz), 152.8, 149.0, 137.0, 134.2 (d, J_{CF} = 3.8 Hz), 130.7 (d, J_{CF} = 8.0 Hz), 127.3, 122.9, 115.6 (d, J_{CF} = 21.2 Hz), 51.7, 49.2, 32.1, 28.1. ppm. GC: t_R = 16.8 min. MS (EI): m/z: 301 (M^+, 20), 228 (45), 135 (100), 106 (40), 78 (80), 51 (20).

Methyl 5-oxo-5-(2'-pyridyl)-4-(*o*-fluorophenyl) pentanoate (3k)



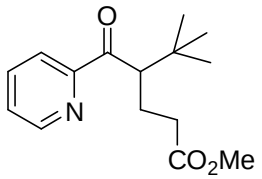
Light yellow oil, yield = 56%, 84 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.62-8.61 (m, 1H), 8.02 (d, 1H, *J* = 8.1 Hz), 7.77 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.41-7.37 (m, 1H), 7.30-7.24 (m, 1H), 7.18-7.14 (m, 1H), 7.07-6.99 (m, 2H), 5.65-5.60 (m, 1H), 3.65 (s, 3H), 2.52-2.45 (m, 1H), 2.41-2.30 (m, 2H), 2.27-2.17 (m, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$): δ = 200.3, 173.6, 161.0 (d, J_{CF} = 247.0 Hz), 152.8, 149.2, 136.9, 129.6 (d, J_{CF} = 3.9 Hz), 128.8 (d, J_{CF} = 8.2 Hz), 127.2, 126.0 (d, J_{CF} = 15.2 Hz), 124.4 (d, J_{CF} = 3.6 Hz) 122.7, 115.8 (d, J_{CF} = 22.5 Hz), 51.7, 43.3 (d, J_{CF} = 1.8 Hz), 32.0, 27.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -117.0 ppm. GC: t_R = 17.3 min. MS (EI): m/z: 301 (M^+, 15), 228 (35), 135 (60), 106 (50), 78 (100), 51 (20).

Methyl 4-benzyl-5-oxo-5-(2'-pyridyl) pentanoate (3l)



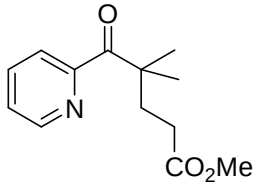
Light yellow oil, yield = 66%, 98 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69-8.67 (m, 1H), 8.02 (d, 1H, *J* = 7.8 Hz), 7.80 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.45-7.42 (m, 1H), 7.25-7.13 (m, 5H), 4.58-4.49 (m, 1H), 3.60 (s, 3H), 3.16 (dd, 1H, *J* = 6.6 Hz, *J* = 13.8 Hz), 2.74 (dd, 1H, *J* = 7.5 Hz, *J* = 13.8 Hz), 2.35-2.21 (m, 2H), 2.16-2.06 (m, 1H), 1.98-1.90 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ =203.9, 173.7, 153.2, 149.1, 139.6, 137.0, 129.2, 128.4, 127.2, 126.3, 122.4, 51.6, 45.5, 37.9, 31.9, 26.2. GC: t_R = 18.3 min. MS (EI): m/z: 297 (M^+, 5), 210 (20), 182 (25), 106 (30), 91 (45), 79 (100), 51 (10).

Methyl 4-*tert*-butyl-5-oxo-5-(2'-pyridyl) pentanoate (3m)



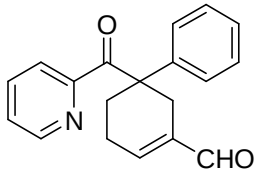
Light yellow oil, yield = 25%, 34 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.70-8.68 (m, 1H), 8.04 (d, 1H, *J* = 7.8 Hz), 7.83 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.48-7.43 (m, 1H), 4.33-4.28 (m, 1H), 3.61 (s, 3H), 2.19-2.09 (m, 3H), 2.06-1.97 (m, 1H), 0.96 (s, 9H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 206.4, 173.9, 155.2, 148.9, 137.1, 127.0, 121.8, 51.6, 50.8, 34.6, 33.0, 28.2, 23.9. GC: t_R = 13.4 min. MS (EI): m/z: 263 (M^+, 20), 248 (35), 190 (50), 134 (75), 106 (70), 78 (100), 55 (40).

Methyl 4-methyl-5-oxo-5-(2'-pyridyl) pentanoate (3n)



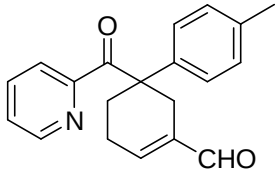
Light yellow oil, yield = 40%, 48 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64-8.61 (m, 1H), 7.91-7.88 (m, 1H), 7.80 (dt, 1H, *J* = 1.8 Hz, *J* = 7.5 Hz), 7.42-7.37 (m, 1H), 3.63 (s, 3H), 2.43-2.38 (m, 2H), 2.28-2.22 (m, 2H), 1.43 (s, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 205.9, 174.3, 154.8, 148.0, 136.9, 126.2, 123.7, 51.7, 47.3, 35.3, 30.2, 25.5. GC: t_R = 12.3 min. MS (EI): m/z: 235 (M^+, 2), 162 (15), 134 (30), 107 (20), 79 (100), 55 (15). HRMS (ESI): *m/z* calcd for $C_{13}H_{18}NO_3$ $[M + H]^+$ 236.1281, found 236.1280.

(1-phenyl-3-formyl lyllohex-3-en-1-yl) (2'-pyridyl)ketone (4a)



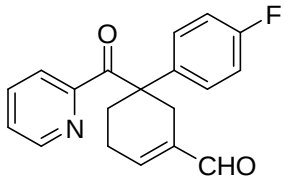
White solid, yield = 68%, 99 mg, M. p.: 116-118 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.54 (s, 1H), 8.41-8.38 (m, 1H), 7.86-7.83 (m, 1H), 7.67 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.28-7.14 (m, 6H), 6.83-6.80 (m, 1H), 3.37 (d, 1H, *J* = 17.7 Hz), 2.99 (d, 1H, *J* = 17.7 Hz), 2.82-2.74 (m, 1H), 2.41-2.30 (m, 2H), 2.18-2.05 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ =201.1, 193.7, 153.2, 150.7, 148.3, 141.8, 140.4, 136.5, 128.5, 126.6, 126.5, 126.1, 123.9, 53.1, 31.1, 30.3, 24.4. GC: t_R = 20.6 min. MS (EI): m/z: 291 (M^+, 15), 155 (20), 107 (30), 91 (75), 79 (100), 51 (20). HRMS (ESI): *m/z* calcd for $C_{19}H_{17}NO_2$ $[M + H]^+$ 292.1332, found 292.1332.

[1-(*p*-tolyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4b)



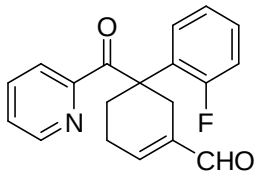
Light yellow oil, yield = 57%, 86 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.53 (s, 1H), 8.43-8.41 (m, 1H), 7.81 (d, 1H, *J* = 8.1 Hz), 7.66 (dt, 1H, *J* = 1.8 Hz, *J* = 7.8 Hz), 7.25-7.21 (m, 1H), 7.17 (d, 2H, *J* = 8.1 Hz), 7.06 (d, 2H, *J* = 8.4 Hz), 6.80-6.79 (m, 1H), 3.35 (d, 1H, *J* = 17.7 Hz), 2.99 (d, 1H, *J* = 17.7 Hz), 2.78-2.71 (m, 1H), 2.39-2.15 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ =201.2, 193.7, 153.4, 150.8, 148.3, 140.4, 138.5, 136.5, 136.2, 129.2, 126.5, 126.0, 123.9, 52.8, 31.1, 30.2, 24.4, 21.1. GC: t_R = 22.2 min. MS (EI): m/z: 305 (M^+, 15), 199 (30), 105 (80), 91 (15), 79 (100), 51 (20).

[1-(*p*-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4c)



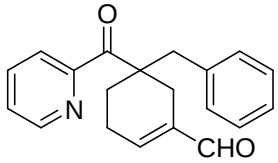
Light yellow oil, yield = 66%, 102 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.54 (s, 1H), 8.42-8.40 (m, 1H), 7.88 (d, 1H, *J* = 8.1 Hz), 7.70 (dt, 1H, *J* = 1.8 Hz, *J* = 7.5 Hz), 7.27-7.21 (m, 3H), 7.00-6.91 (m, 2H), 6.82-6.81 (m, 1H), 3.37 (d, 1H, *J* = 17.7 Hz), 2.98 (d, 1H, *J* = 17.7 Hz), 2.80-2.73 (m, 1H), 2.42-2.30 (m, 2H), 2.18-2.05 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 200.8, 193.7, 161.6 (d, J_{CF} = 245.3 Hz), 153.0, 150.6, 148.3, 140.2, 137.5 (d, J_{CF} = 3.2 Hz), 136.6, 128.3 (d, J_{CF} = 7.9 Hz), 126.3, 124.0, 115.3 (d, J_{CF} = 21.2 Hz), 52.6, 31.1, 30.4, 24.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -116.4 ppm. GC: t_R = 20.4 min. MS (EI): m/z: 309 (M^+, 10), 203 (10), 109 (75), 79 (100), 51 (20).

[1-(*o*-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4d)



Light yellow solid, yield = 58%, 90 mg, M. p.: 115-117 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.59 (s, 1H), 8.27 (d, 1H, *J* = 4.5 Hz), 7.98 (d, 1H, *J* = 7.8 Hz), 7.72 (dt, 1H, *J* = 1.5 Hz, *J* = 7.5 Hz), 7.32-7.21 (m, 2H), 7.14-7.04 (m, 2H), 6.89-6.76 (m, 2H), 3.51 (d, 1H, *J* = 18.0 Hz), 2.84-2.65 (m, 2H), 2.44-2.35 (m, 2H), 2.07-1.95 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 201.1, 193.6, 160.3 (d, J_{CF} = 245.4 Hz), 153.1 (d, J_{CF} = 1.5 Hz), 150.5, 147.8, 140.2, 136.6, 130.4 (d, J_{CF} = 12.6 Hz), 128.4 (d, J_{CF} = 3.7 Hz), 128.3 (d, J_{CF} = 7.4 Hz), 126.3, 124.0 (d, J_{CF} = 3.2 Hz), 123.6, 115.6 (d, J_{CF} = 22.6 Hz), 50.4 (d, J_{CF} = 1.7 Hz), 30.3, 28.7 (d, J_{CF} = 2.3 Hz), 24.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -114.3 ppm. GC: t_R = 20.4 min. MS (EI): m/z: 309 (M^+, 10), 203 (5), 109 (85), 79 (100), 51 (20). HRMS (ESI): *m/z* calcd for $C_{19}H_{17}NO2$ $[M + H]^+$ 310.1238, found 310.1238.

[1-benyl-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4e)

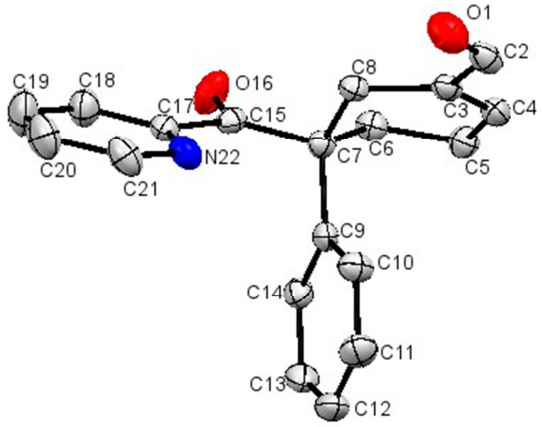


Colorless oil, yield = 37%, 60 mg. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.42 (s, 1H), 8.75-8.72 (m, 1H), 7.88-7.80 (m, 2H), 7.49-7.45 (m, 1H), 7.21-7.16 (m, 3H), 7.01-6.96 (m, 2H), 6.72-6.71 (m, 1H), 3.65-3.54 (m, 2H), 3.18 (d, 1H, *J* = 17.1 Hz), 2.84-2.78 (m, 1H), 2.51-2.28 (m, 3H), 1.87-1.77 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 203.1, 193.7, 154.6, 149.7, 148.1, 140.6, 137.4, 137.1, 130.3, 128.2, 126.6, 126.5, 124.0, 51.5, 43.8, 29.9, 29.6, 24.9. GC: t_R = 23.5 min. MS (EI): m/z: 305 (M^+, 5), 214 (10), 106 (20), 91 (50), 79 (100), 51 (15).

6- References

[1] F. Shibahara, R. Sugiura, E. Yamaguchi, A. Kitagawa, T. Murai *J. Org. Chem.*, **2009**, *74*, 3566.

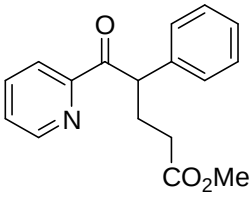
7- Table of crystallographic data for 4a.

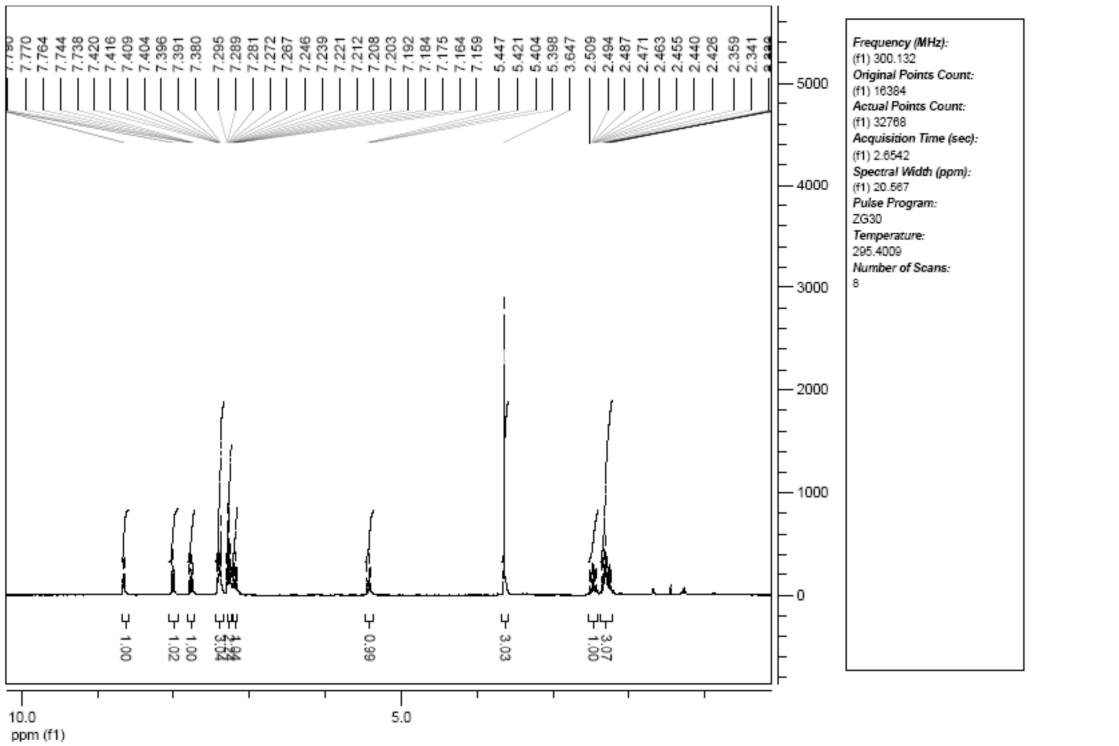


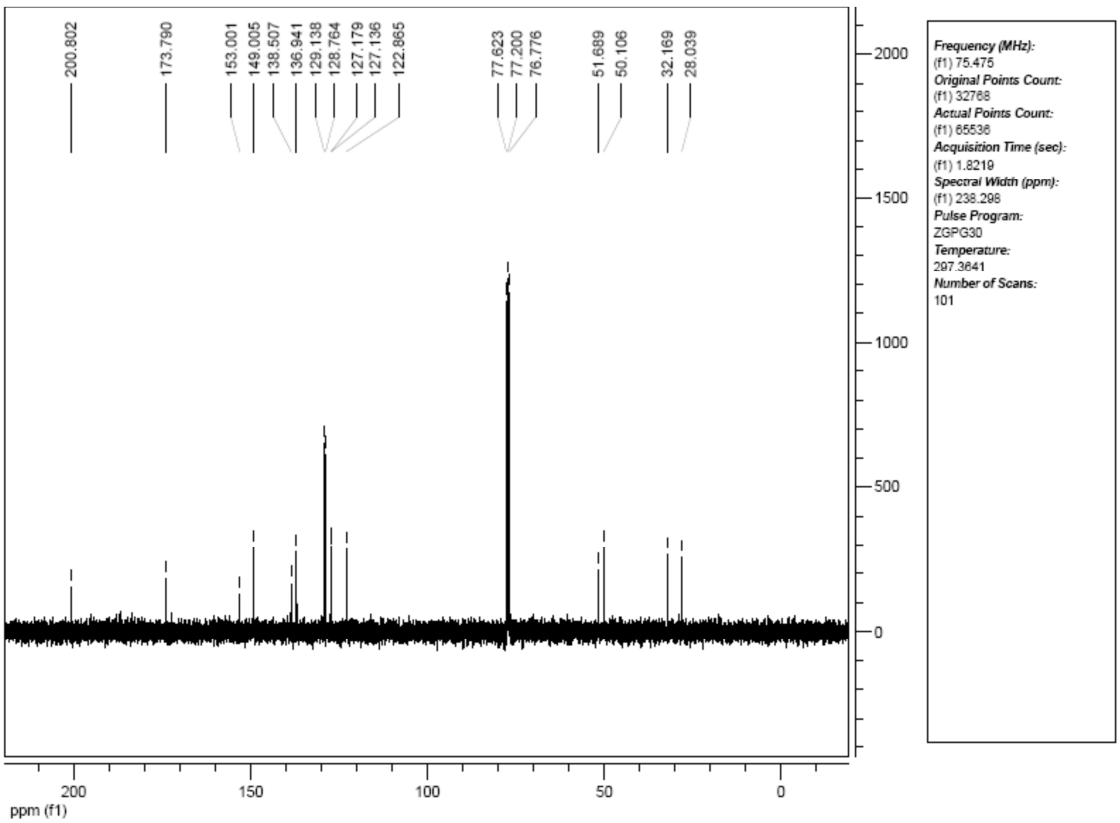
Complex	**4a**
Empirical formula	C19 H17 N O2
Formula weight	291.34
T (K)	150 (2)
λ(Å)	0.71073
Crystal system	Monoclinic
Color, habit	Colourless, prism
Crystal size (mm)	0.49 × 0.27 × 0.1
Space group	C 2/c
a (Å)	26.6705(16)
b (Å)	8.2605(4)
c (Å)	15.9671(9)
α (°)	90
β (°)	119.939(2)
γ (°)	90
V (Å^3)	3048.3(3)
Z	8
Absorption coefficient (mm^{-1})	0.082
θ range (°)	1.76-27.49
Index range	-34≤h≤33, -10≤k≤7, -20≤l≤18
Reflections collected	13311
Independent reflections (R_{int})	3466 (0.0429)
Data/restraints/parameters	3466/0/199
Goodness-of-fit on F^2	1.071
Final R indices [I>2σ(I)]	R_1=0.0503, wR_2=0.1343
R indices (all data)	R_1=0.0682, wR_2=0.1515
Largest diff. peak and hole (e. Å^3)	0.329 and -0.313

8- *[1]H and [13]C NMR Spectra of alkylated products*

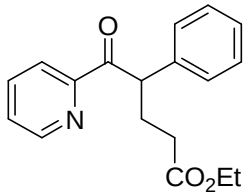
Methyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3a)

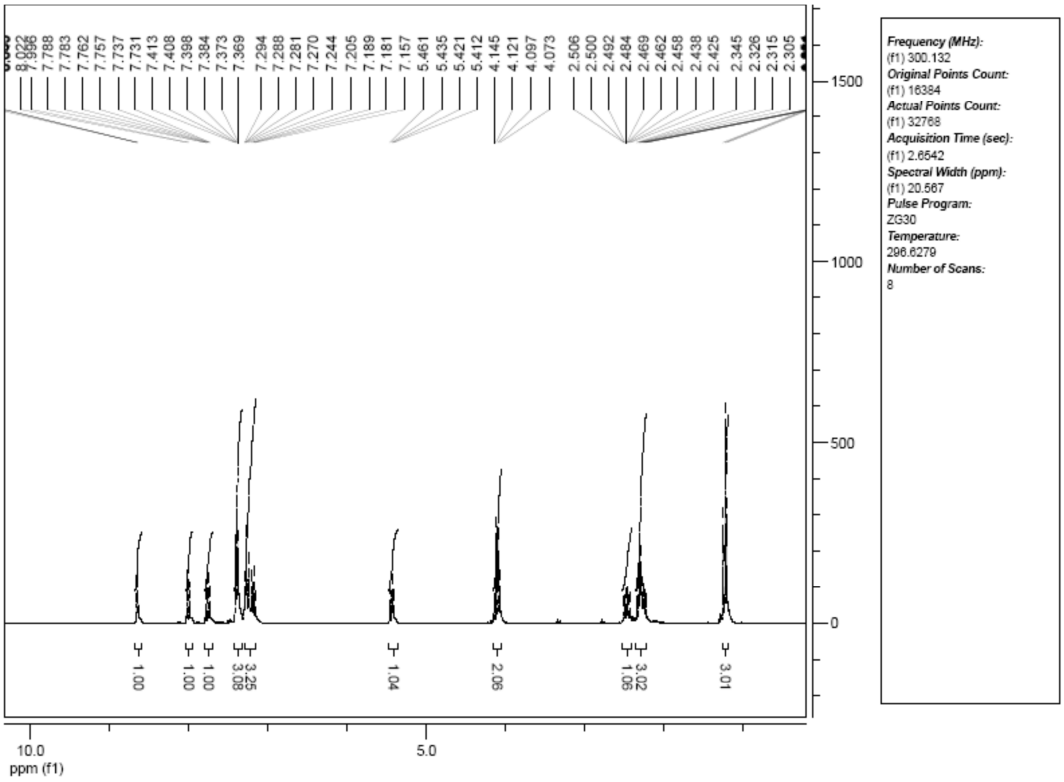


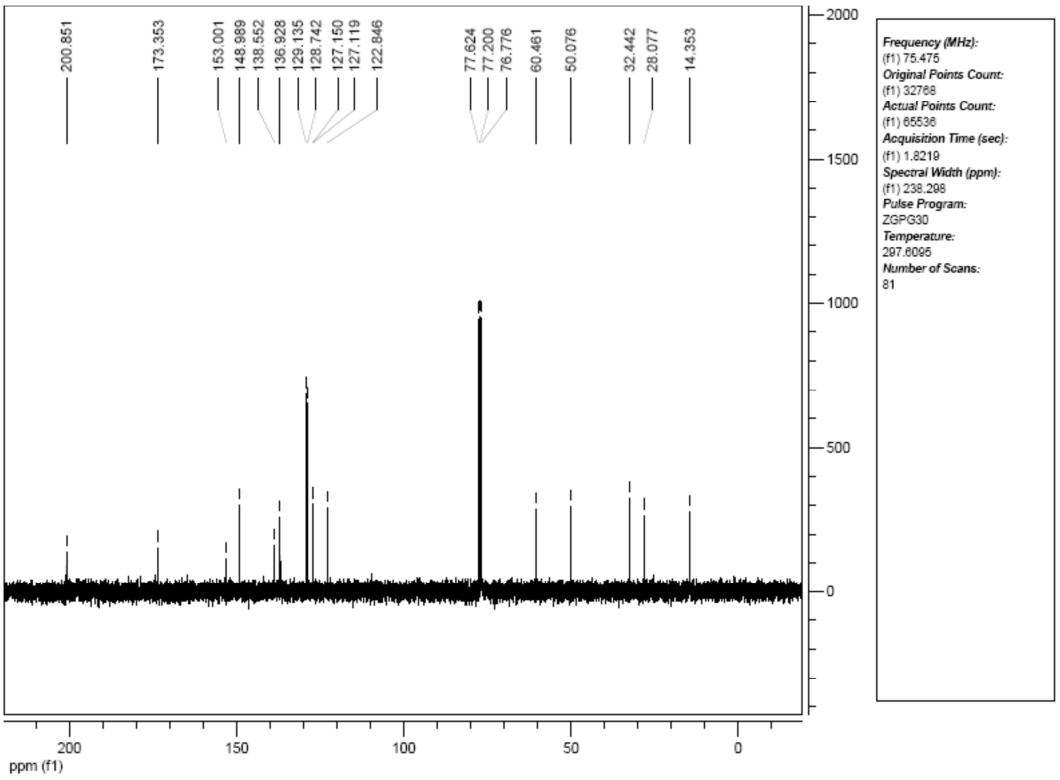




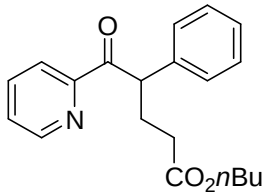
Ethyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3b)

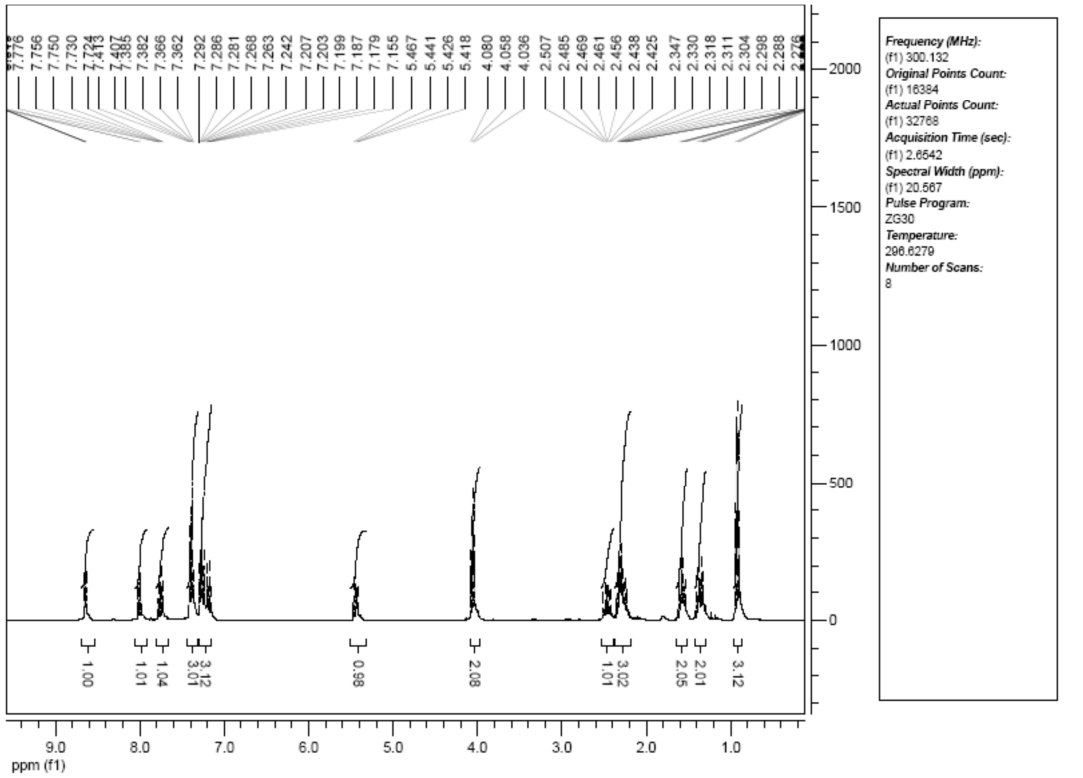


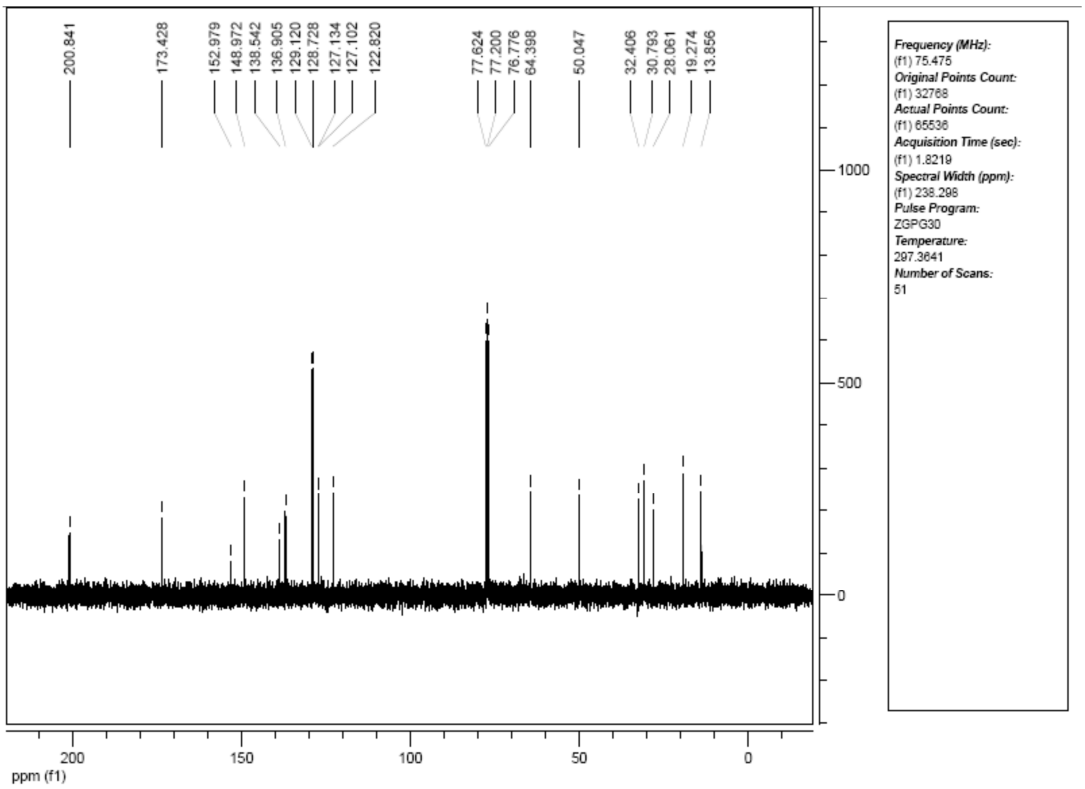




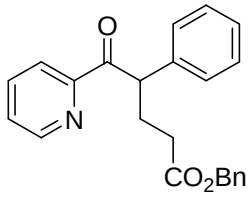
n-Butyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3c)

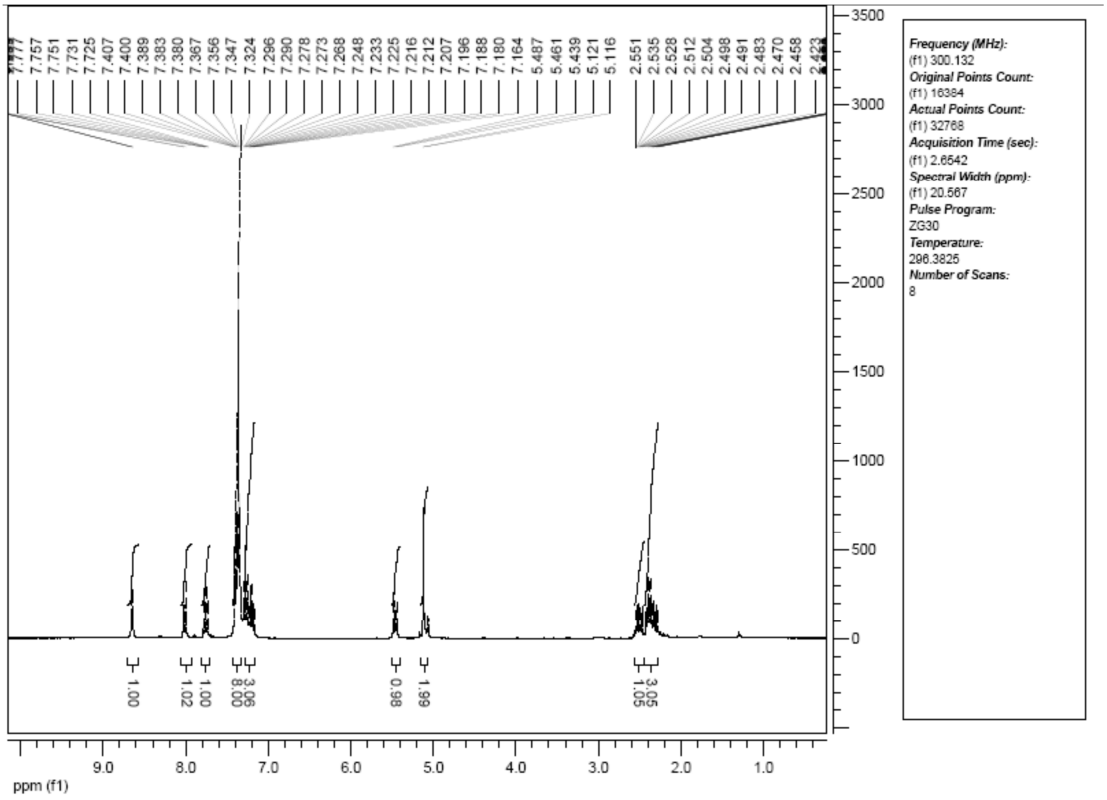


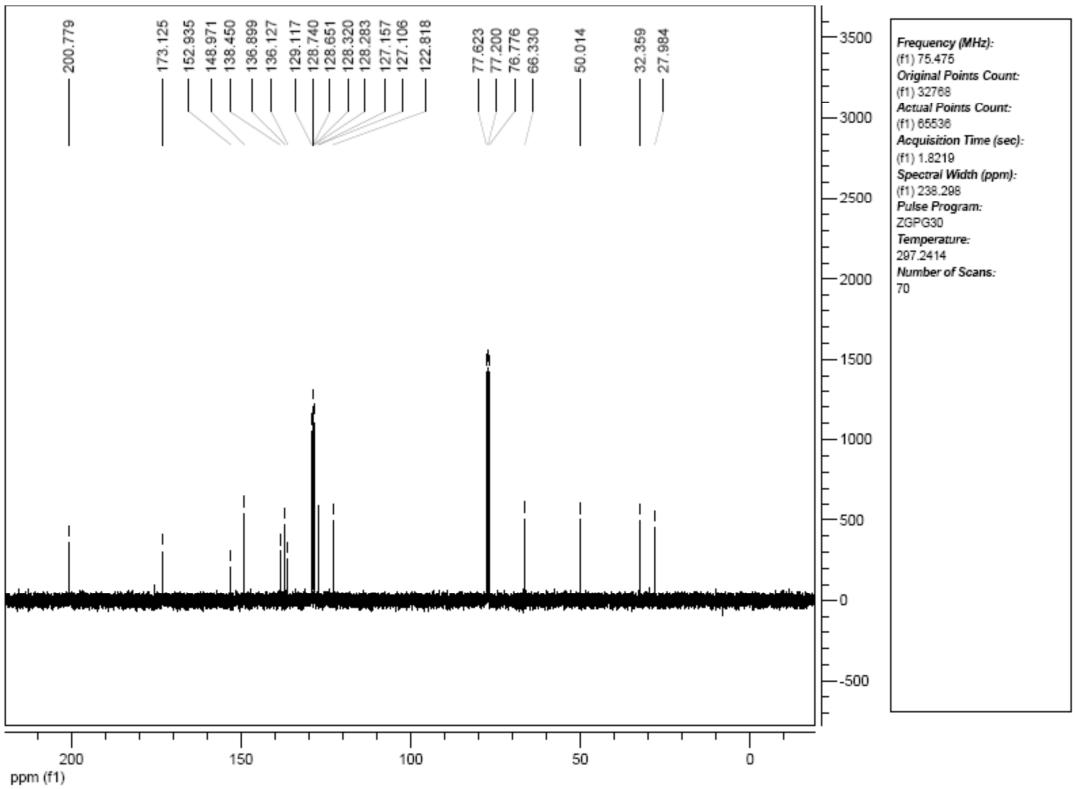




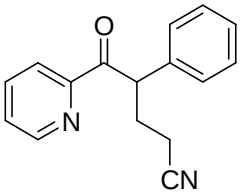
Benzyl 5-oxo-4-phenyl-5-(2'-pyridyl) pentanoate (3d)

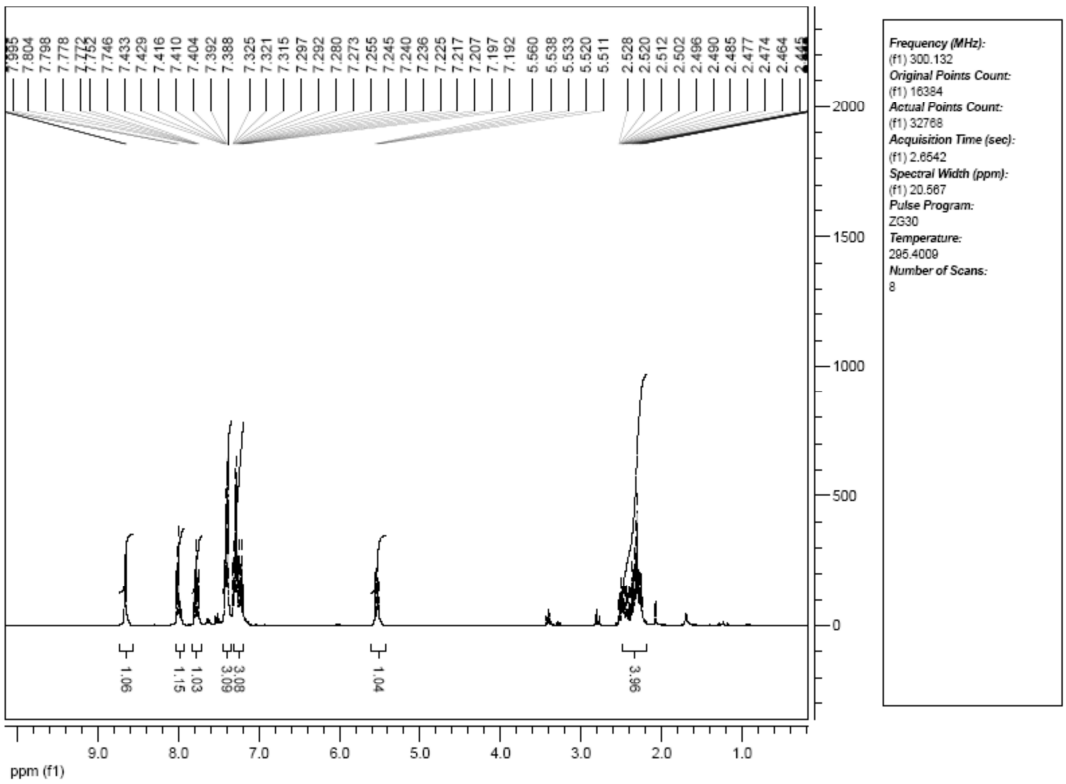


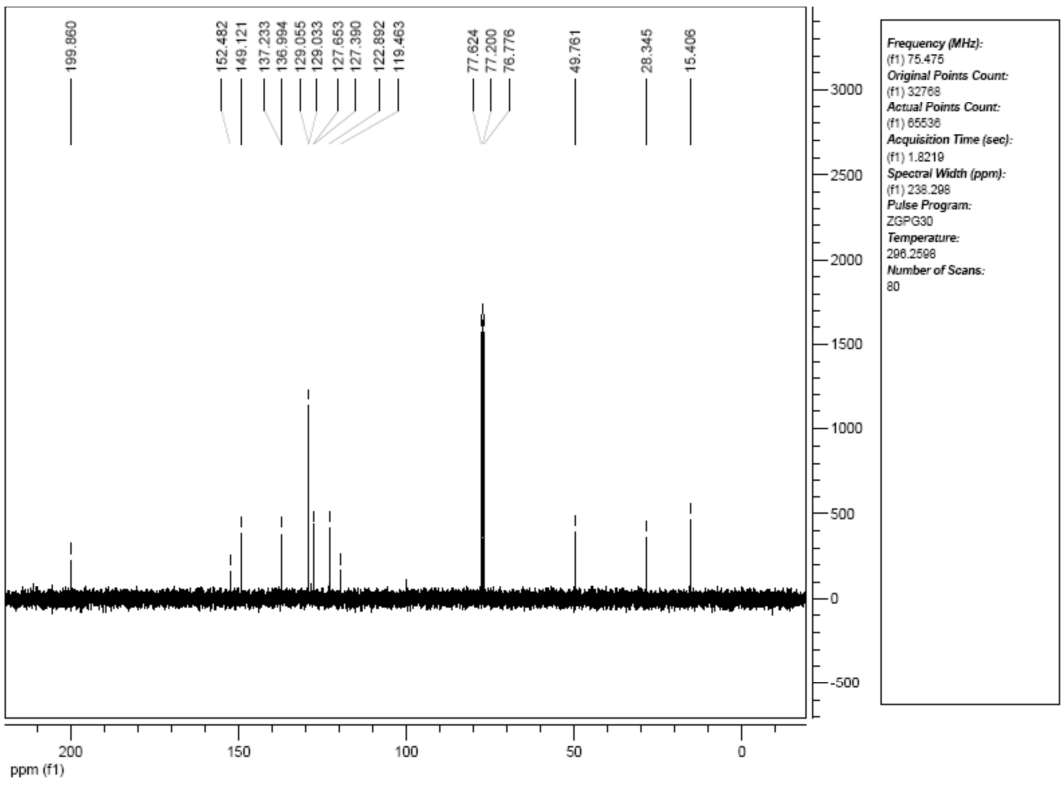




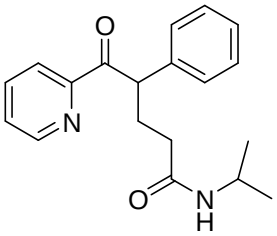
5-oxo-4-phenyl-5-(2'-pyridyl) pentanitrile (3e)

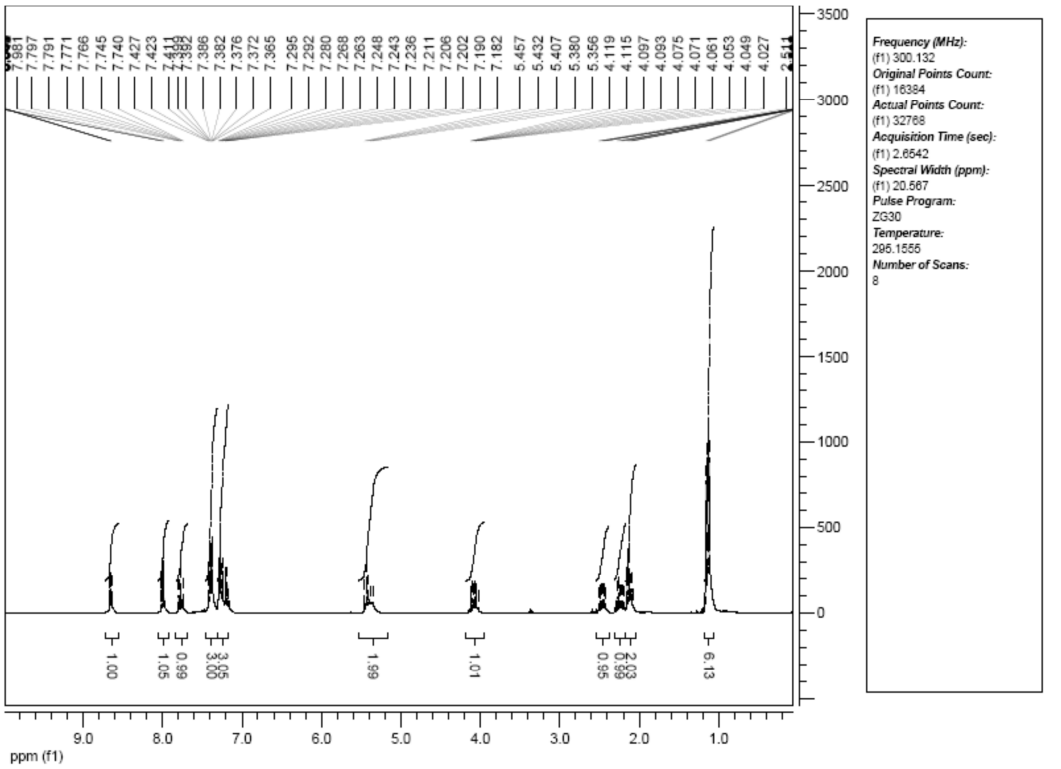


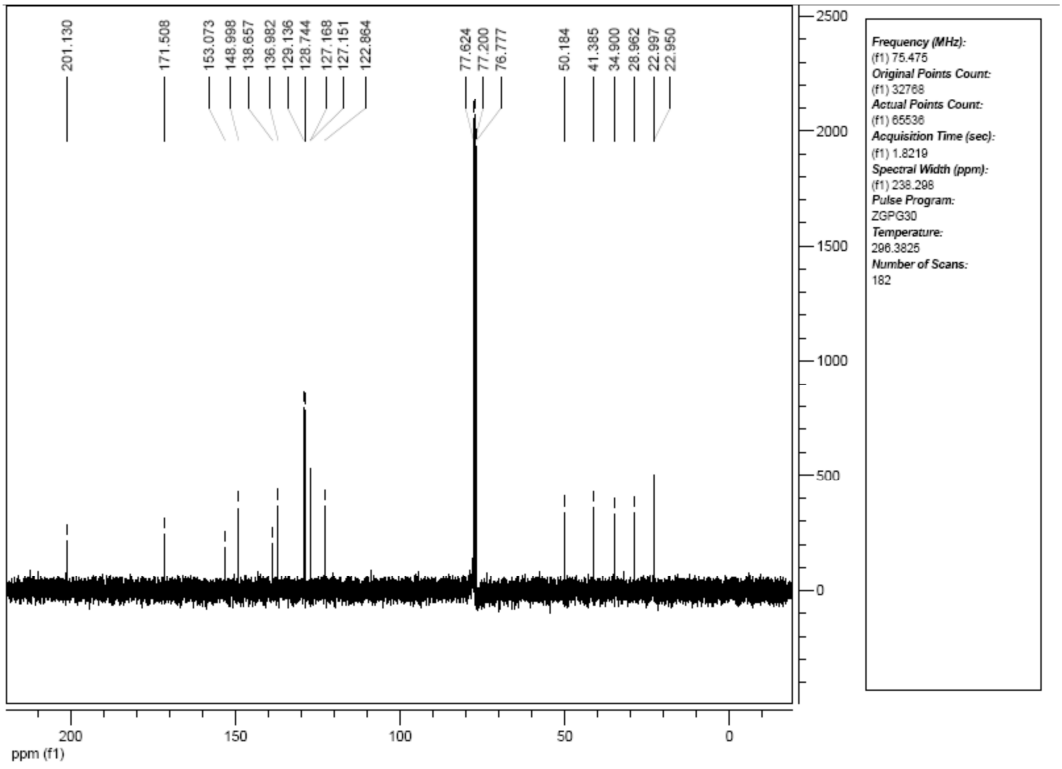




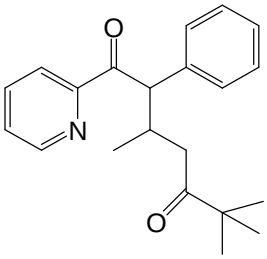
N’-isopropyl 5-oxo-4-phenyl-5-(2’-pyridyl) pentanamide (3f)

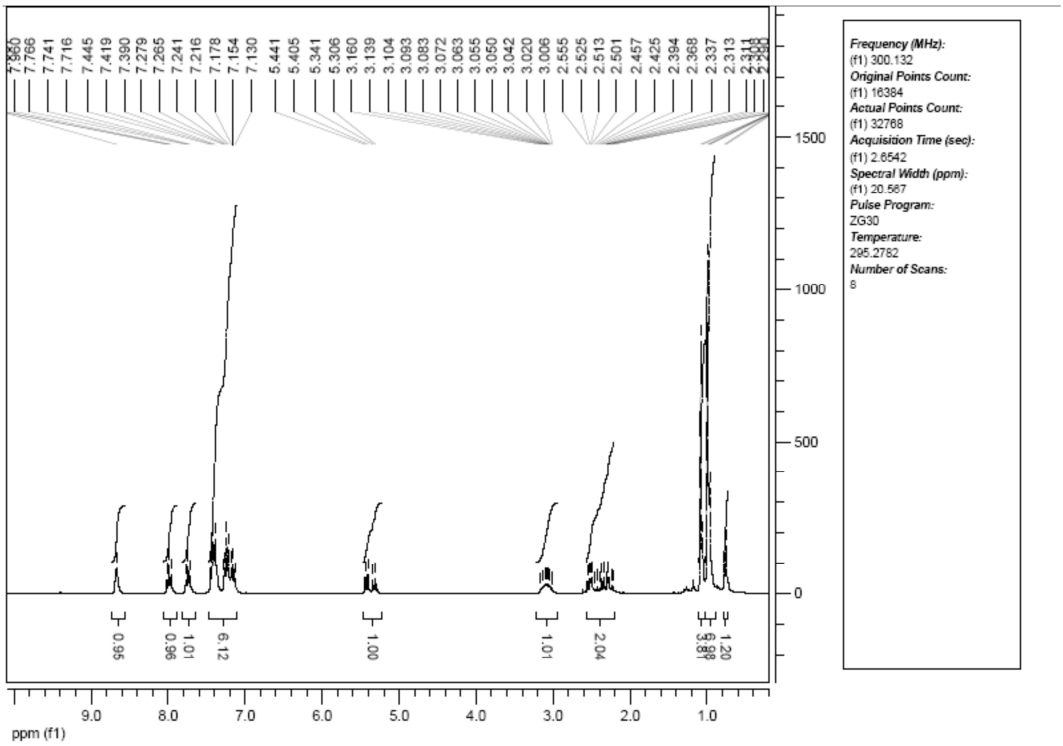


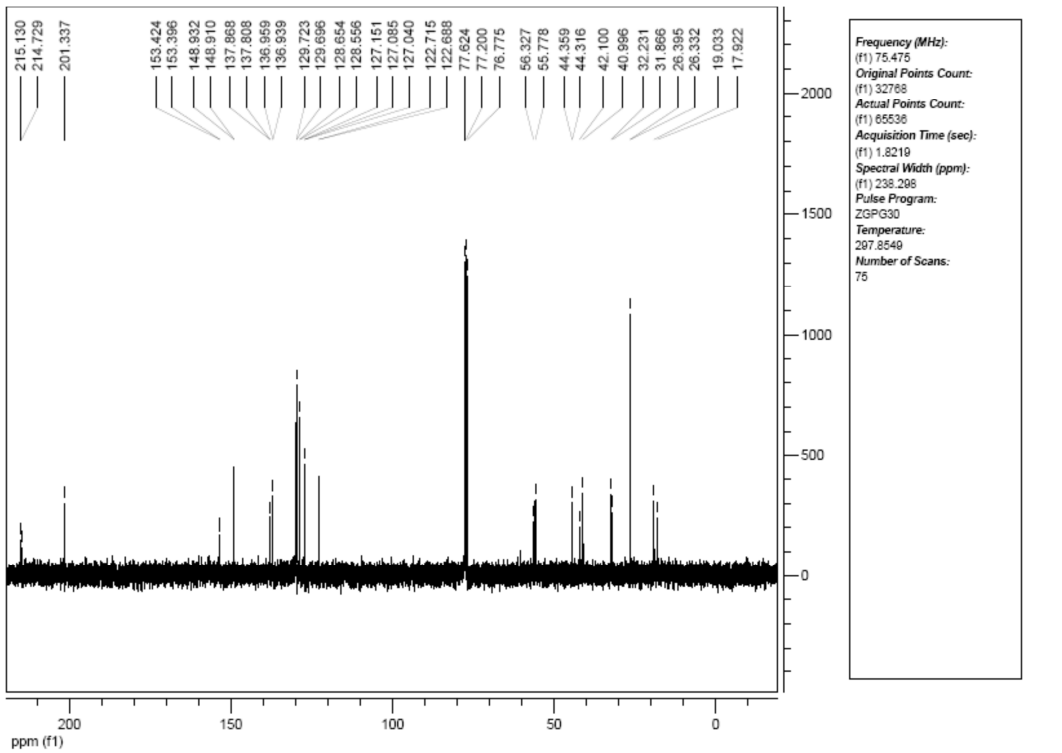




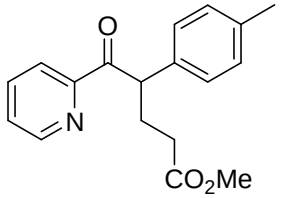
3,6,6-trimethyl-2-phenyl-1-(2'-pyridyl)hepta-1,5-dione (3h)

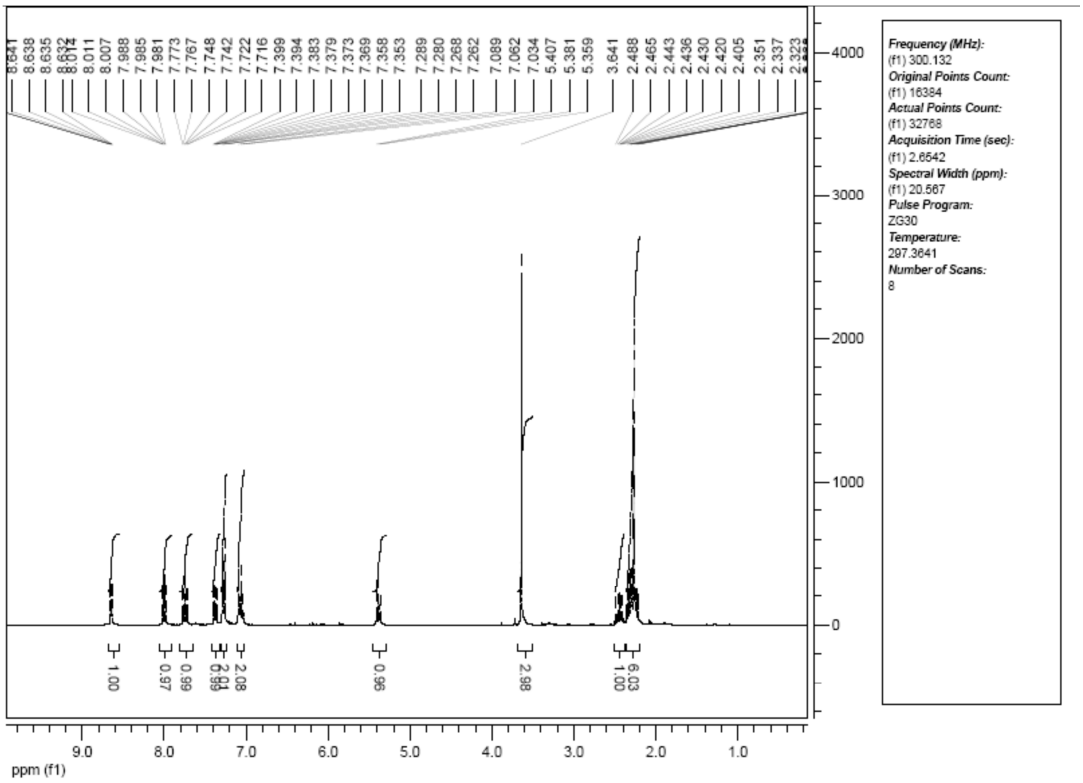


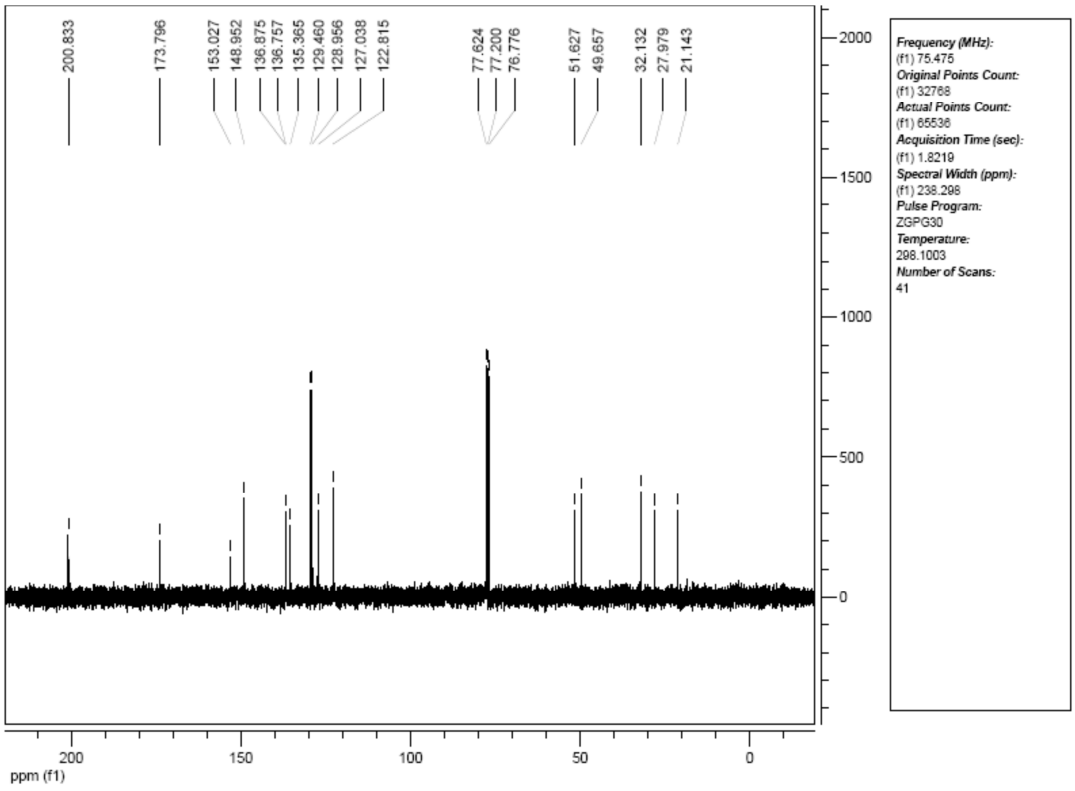




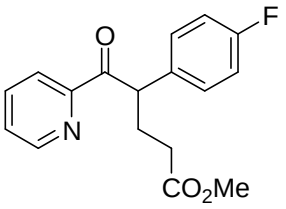
Methyl 5-oxo-5-(2'-pyridyl)-4-(*p*-tolyl) pentanoate (3i)

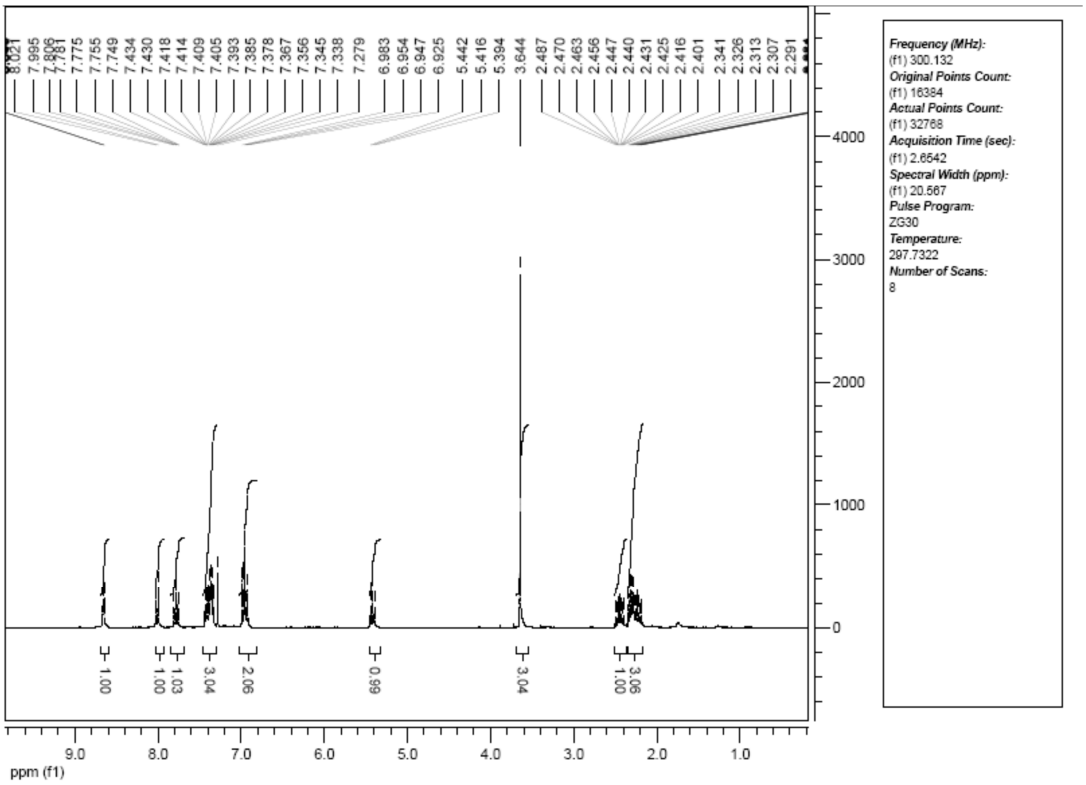


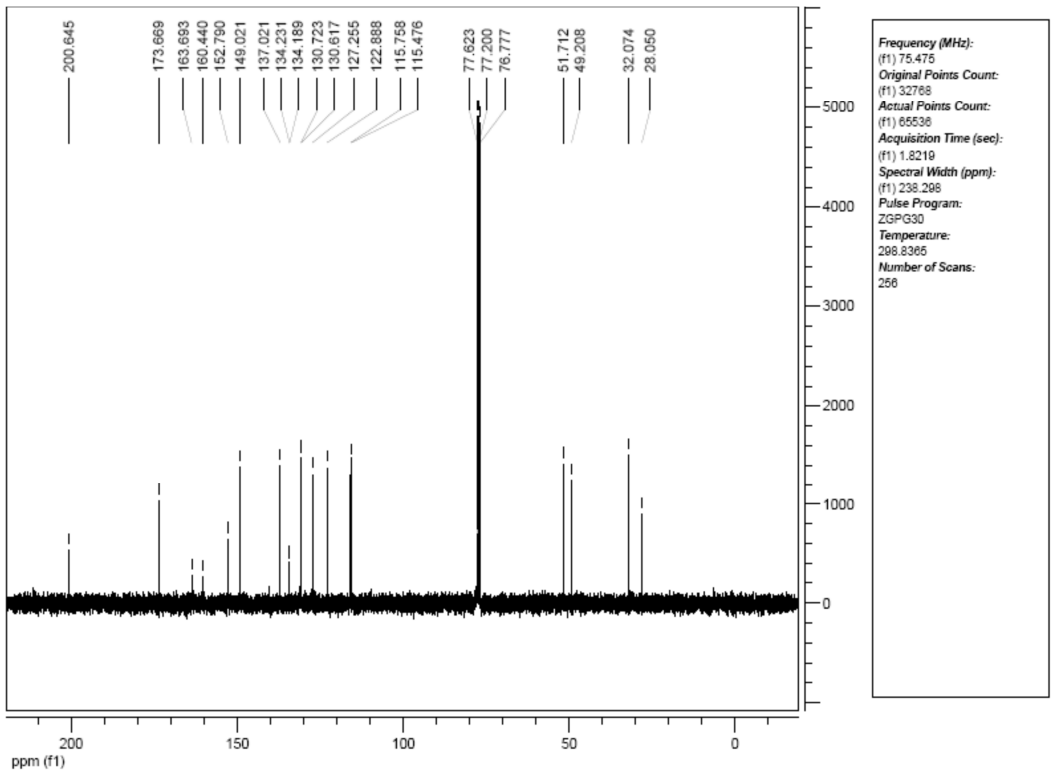




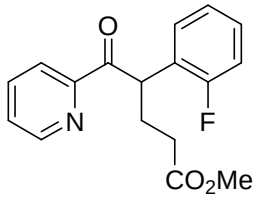
Methyl 5-oxo-5-(2'-pyridyl)-4-(*p*-fluorophenyl) pentanoate (3j)

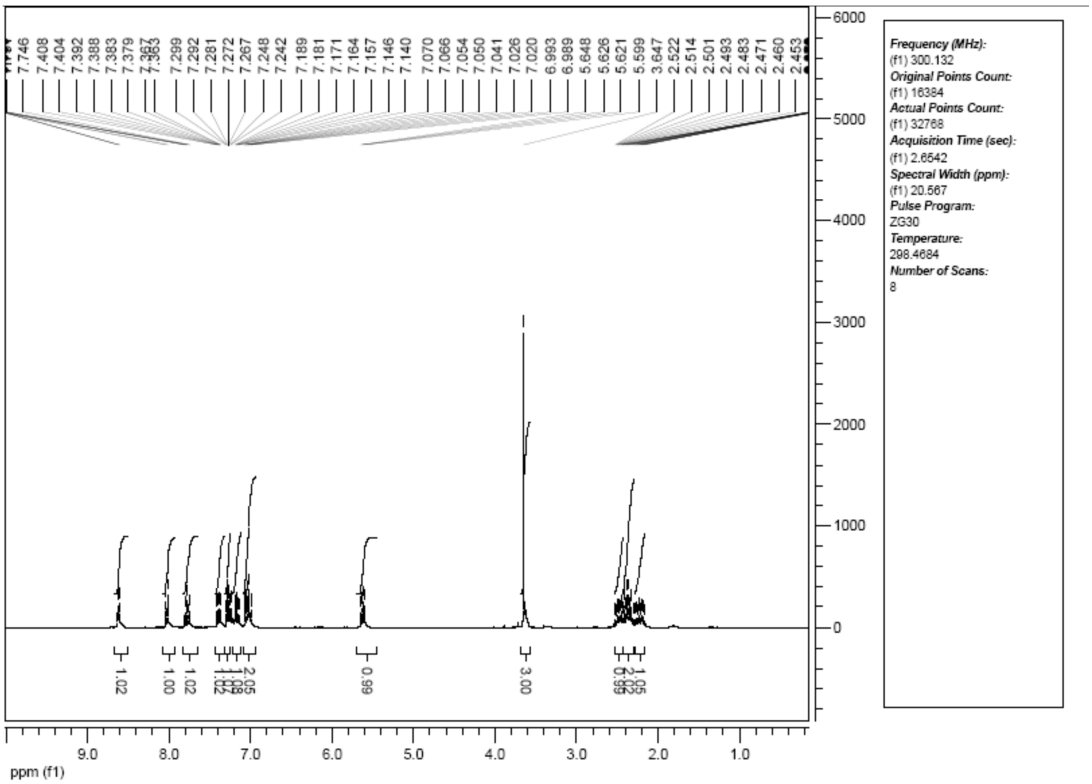


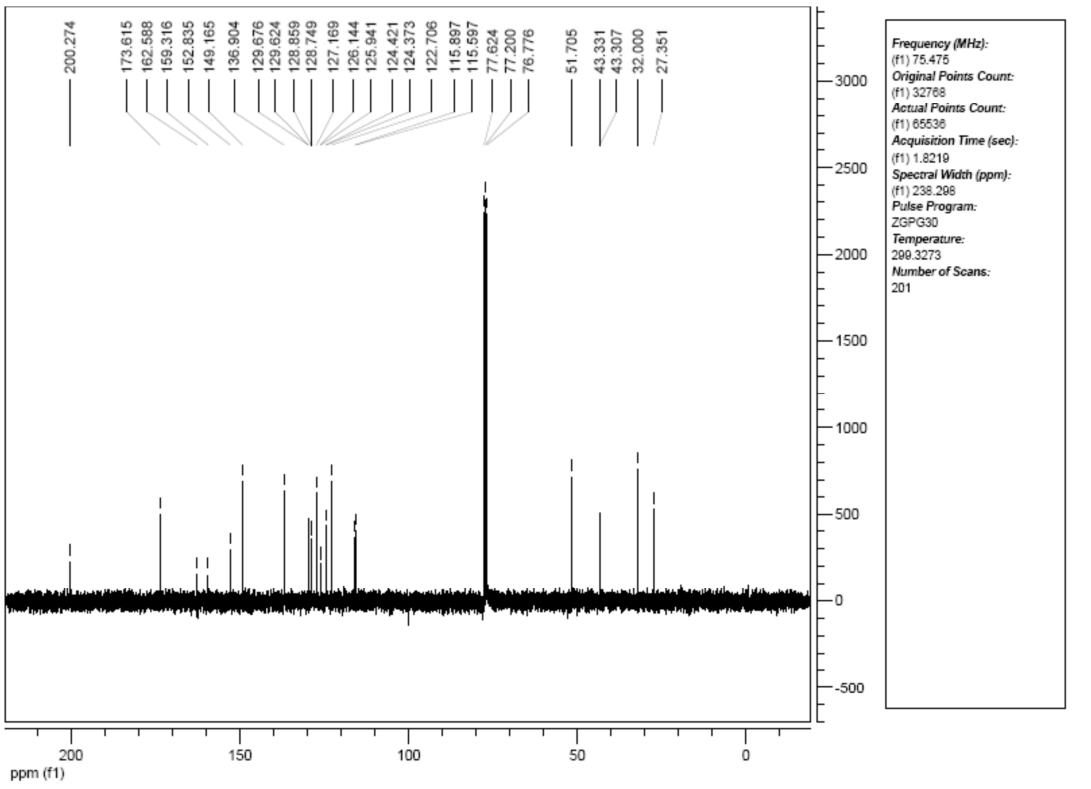




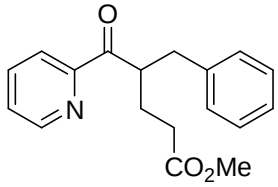
Methyl 5-oxo-5-(2'-pyridyl)-4-(*o*-fluorophenyl) pentanoate (3k)

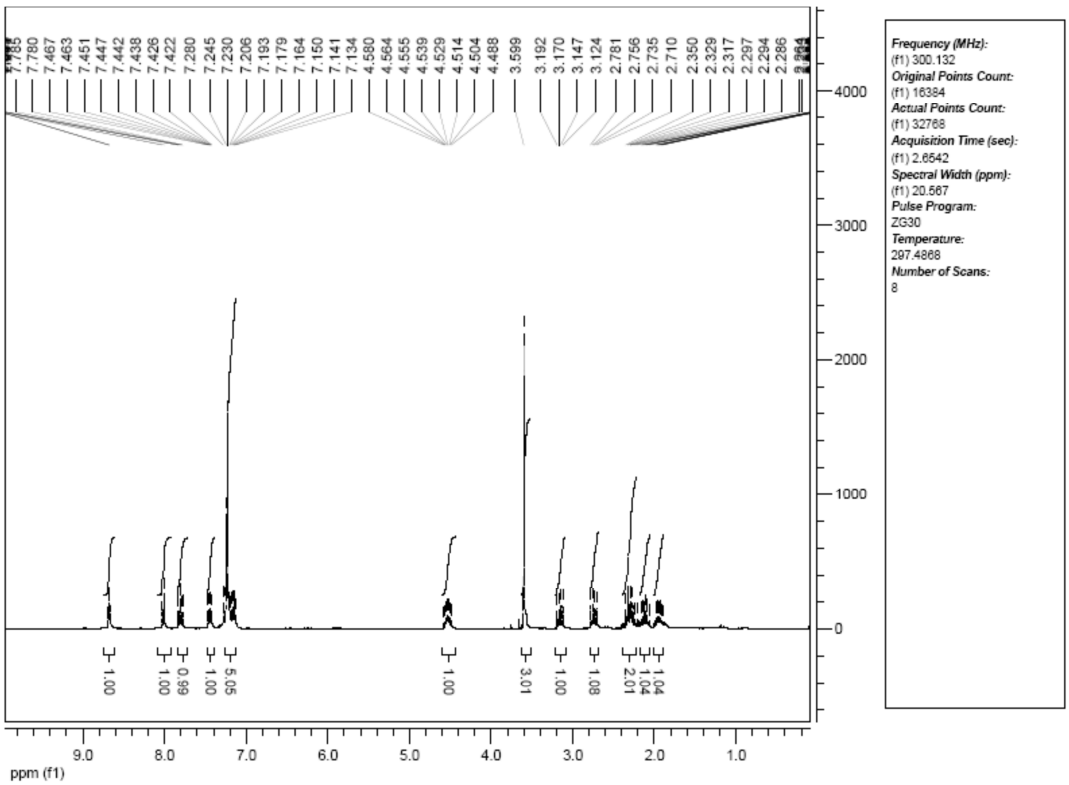


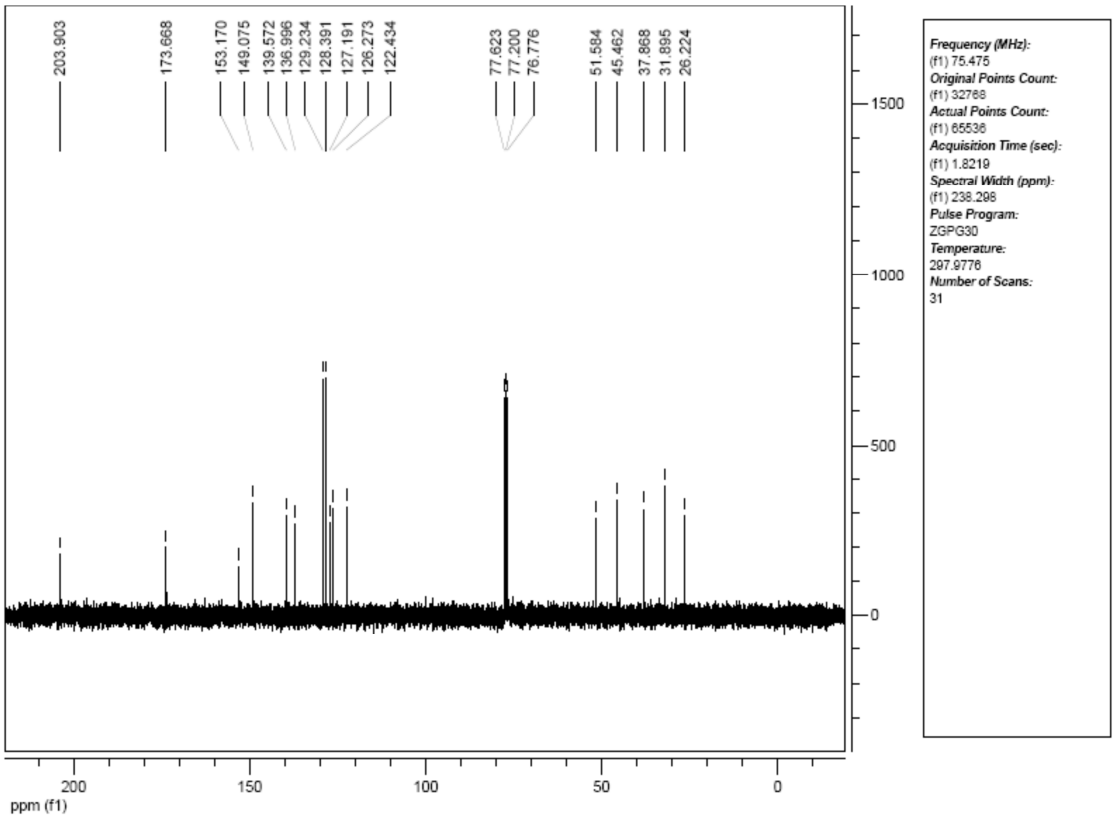




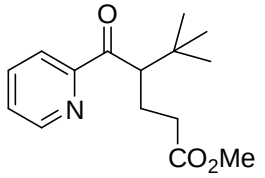
Methyl 4-benzyl-5-oxo-5-(2'-pyridyl) pentanoate (3l)

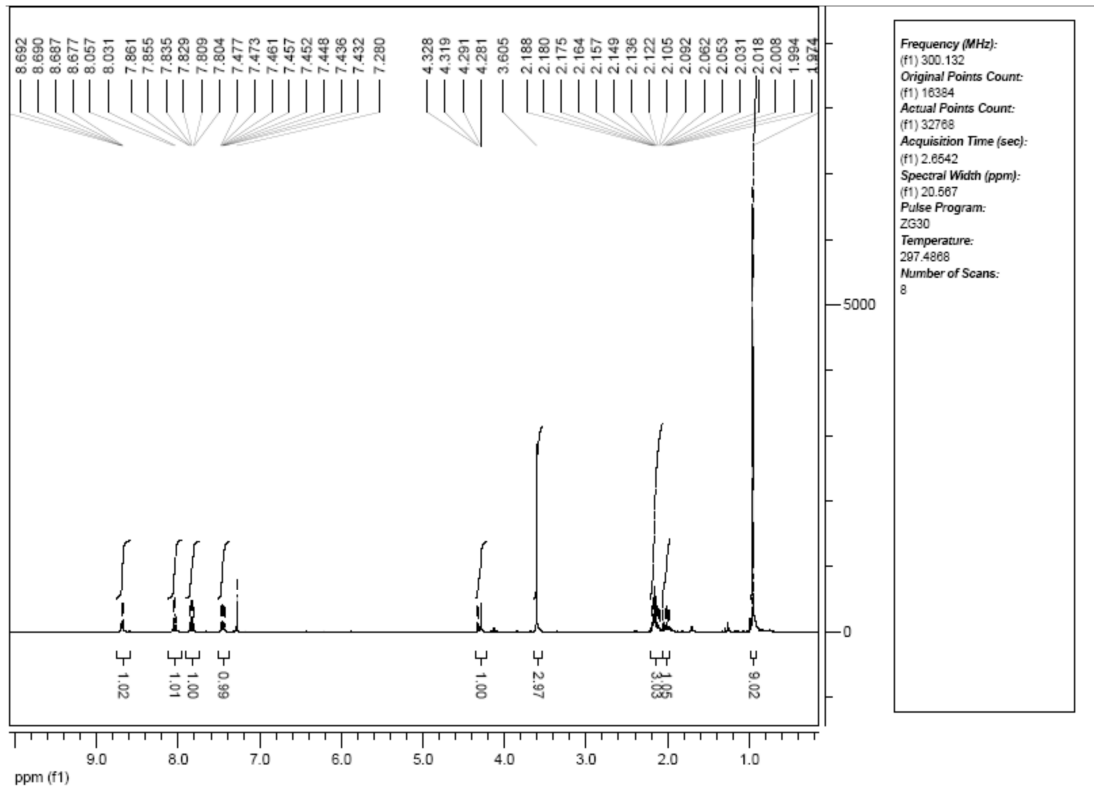


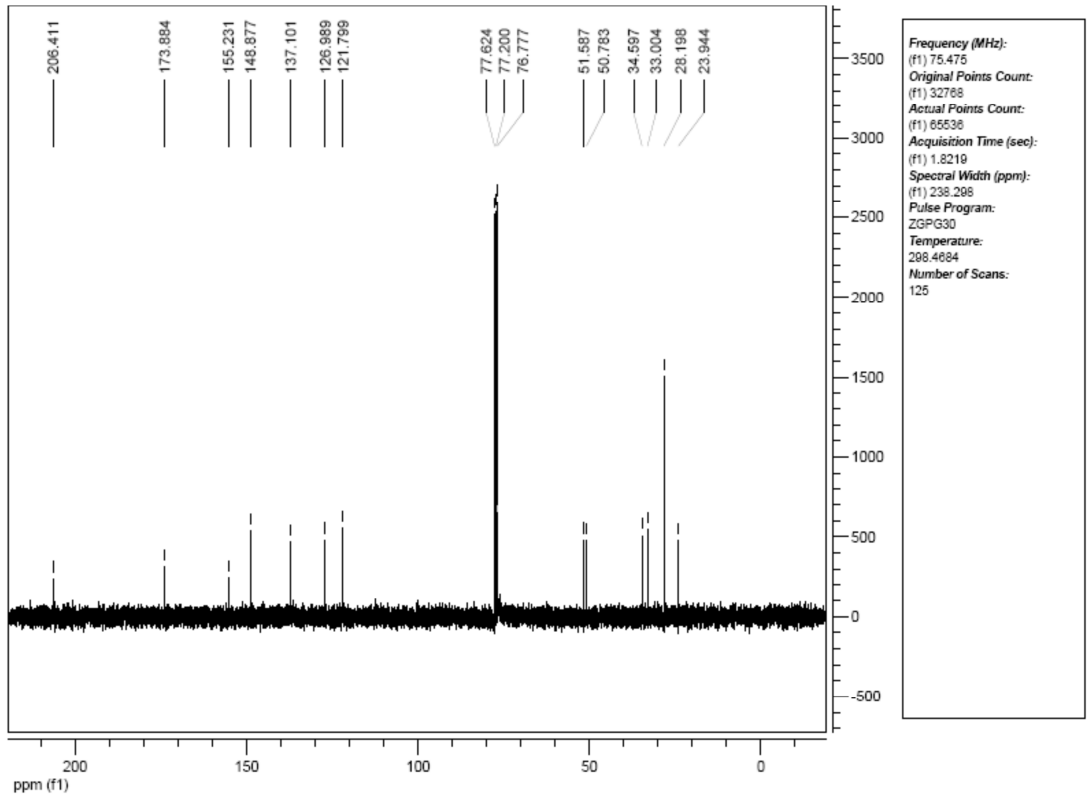




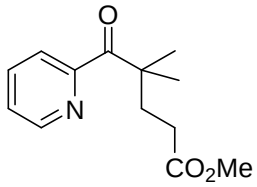
Methyl 4-*tert*-butyl-5-oxo-5-(2'-pyridyl) pentanoate (3m)

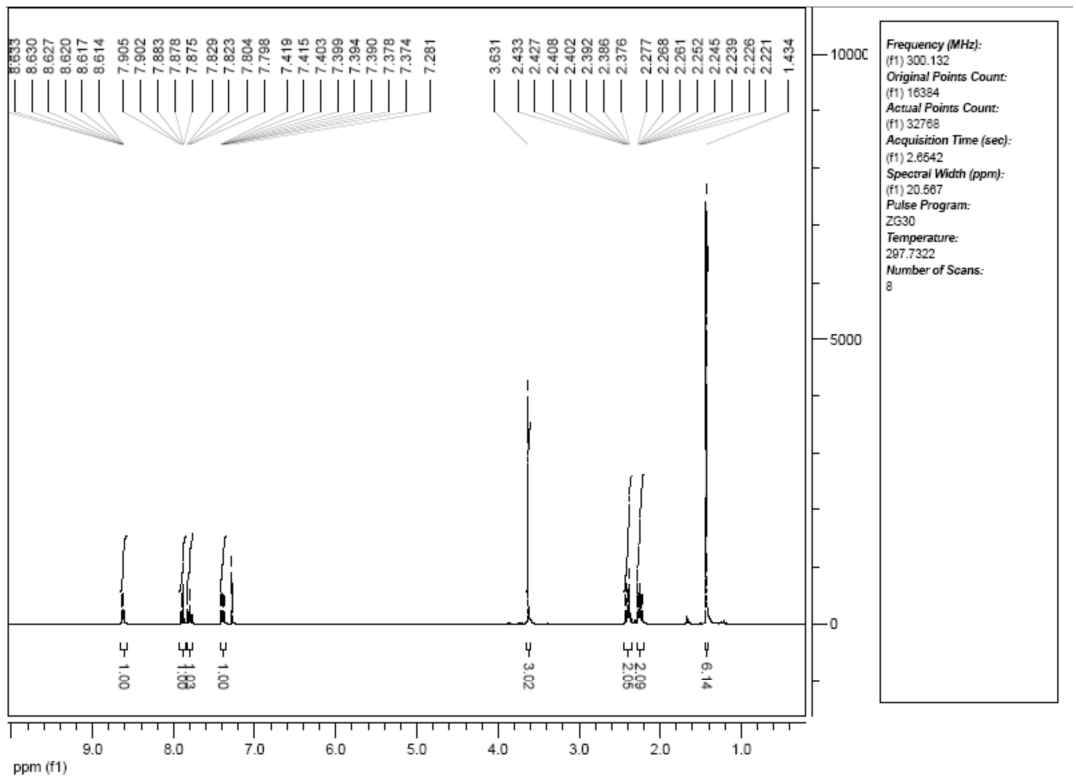


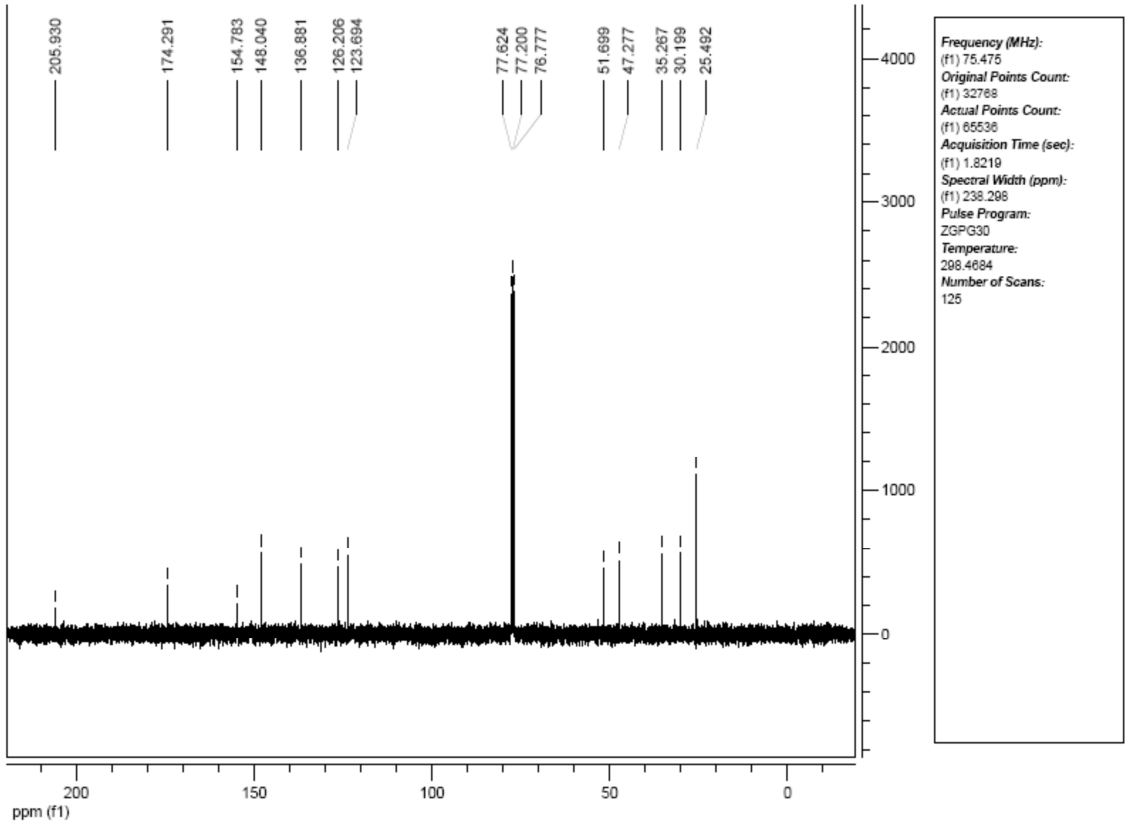




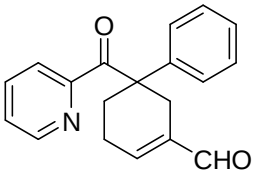
Methyl 4-methyl-5-oxo-5-(2'-pyridyl) pentanoate (3n)

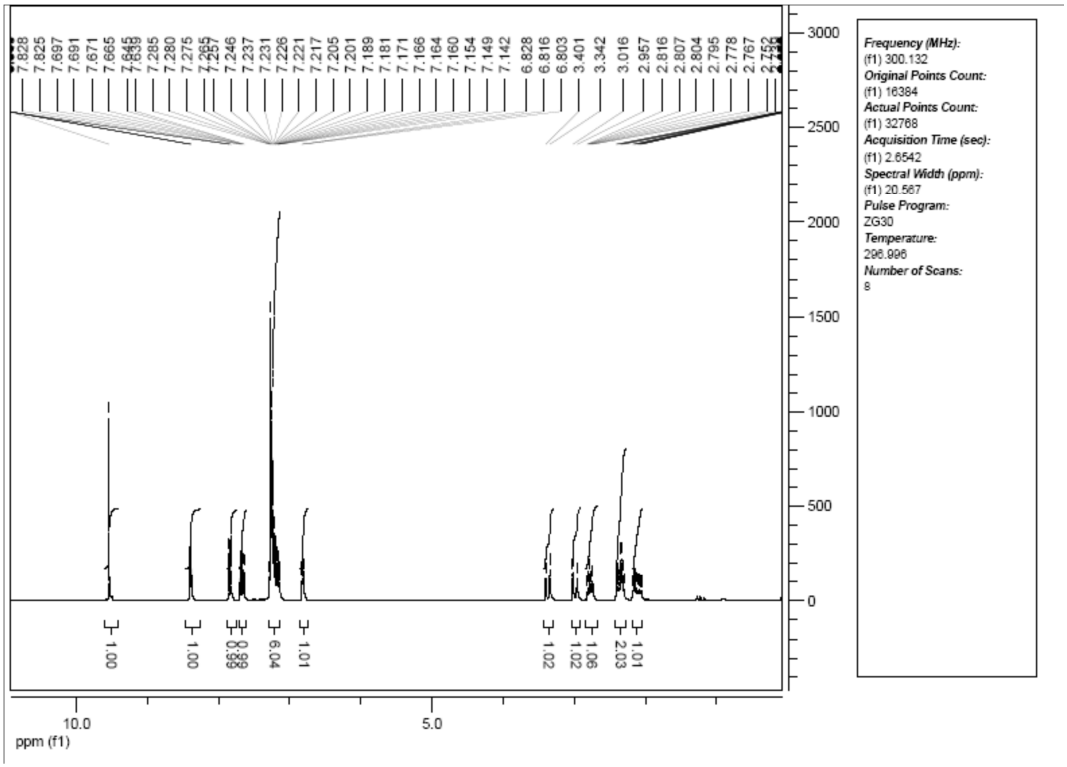


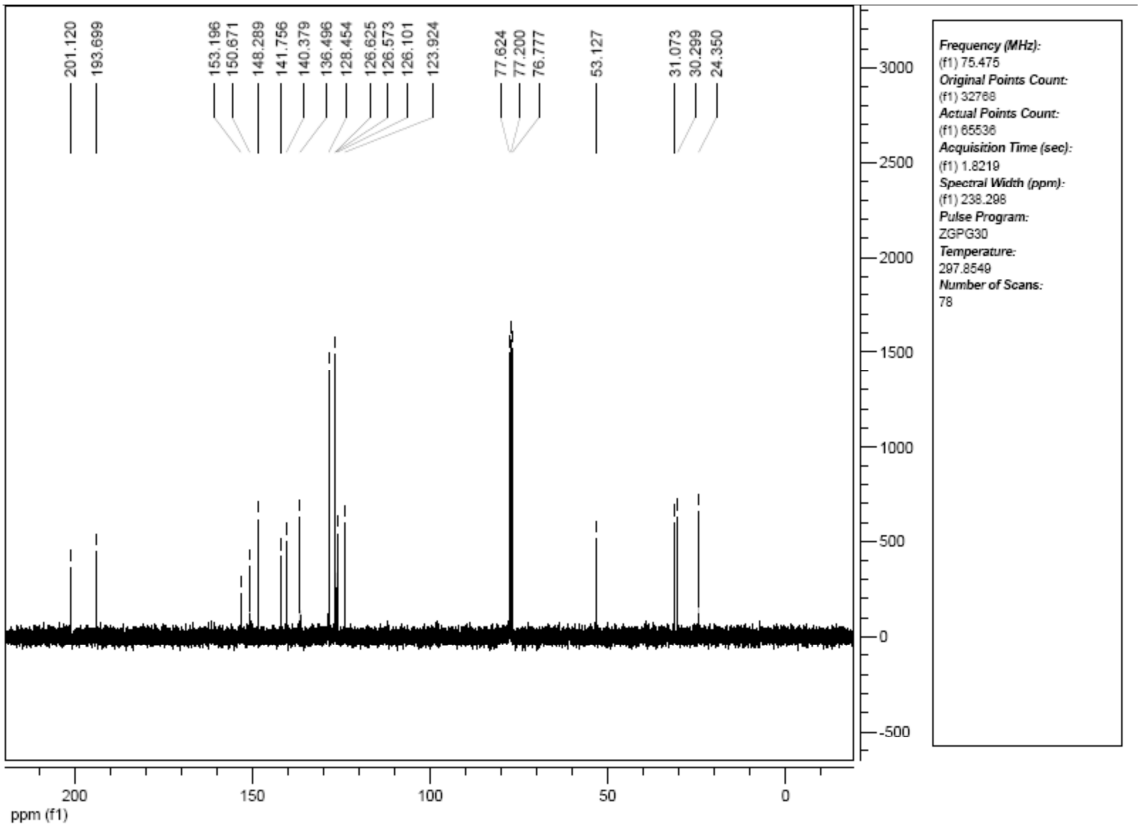




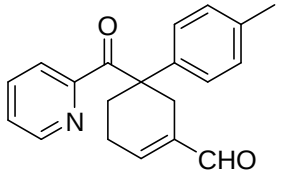
(1-phenyl-3-formyl lyllohex-3-en-1-yl) (2’-pyridyl)ketone (4a)

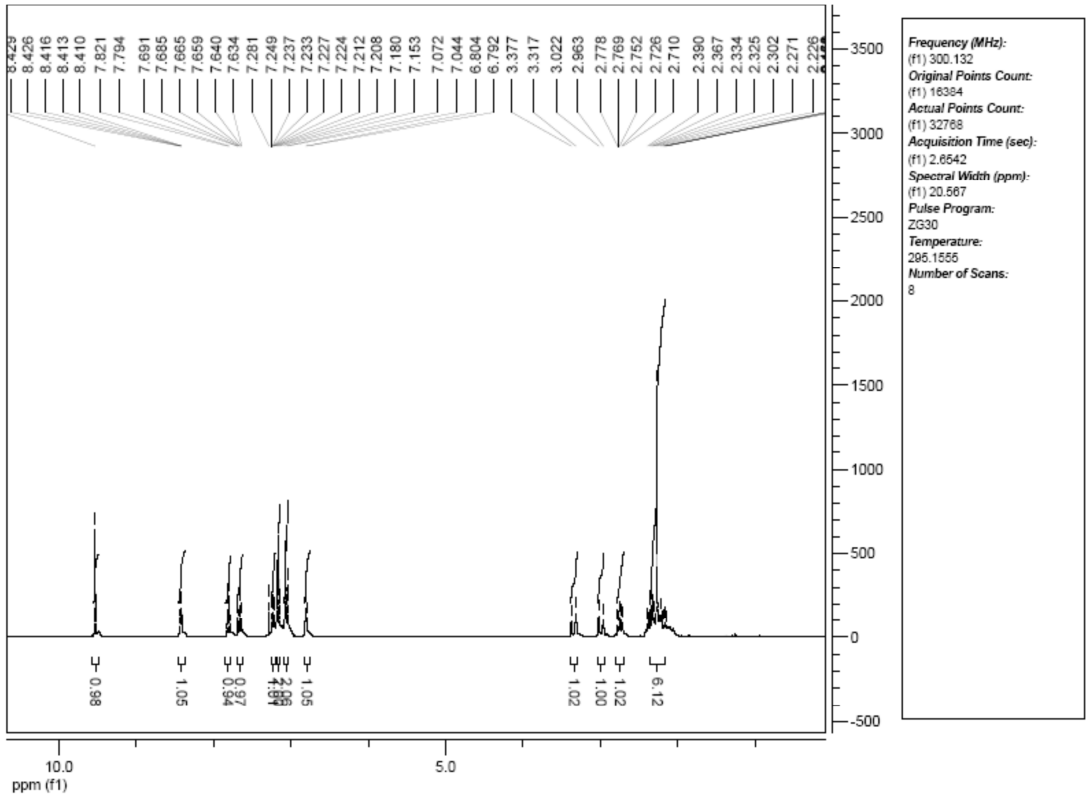


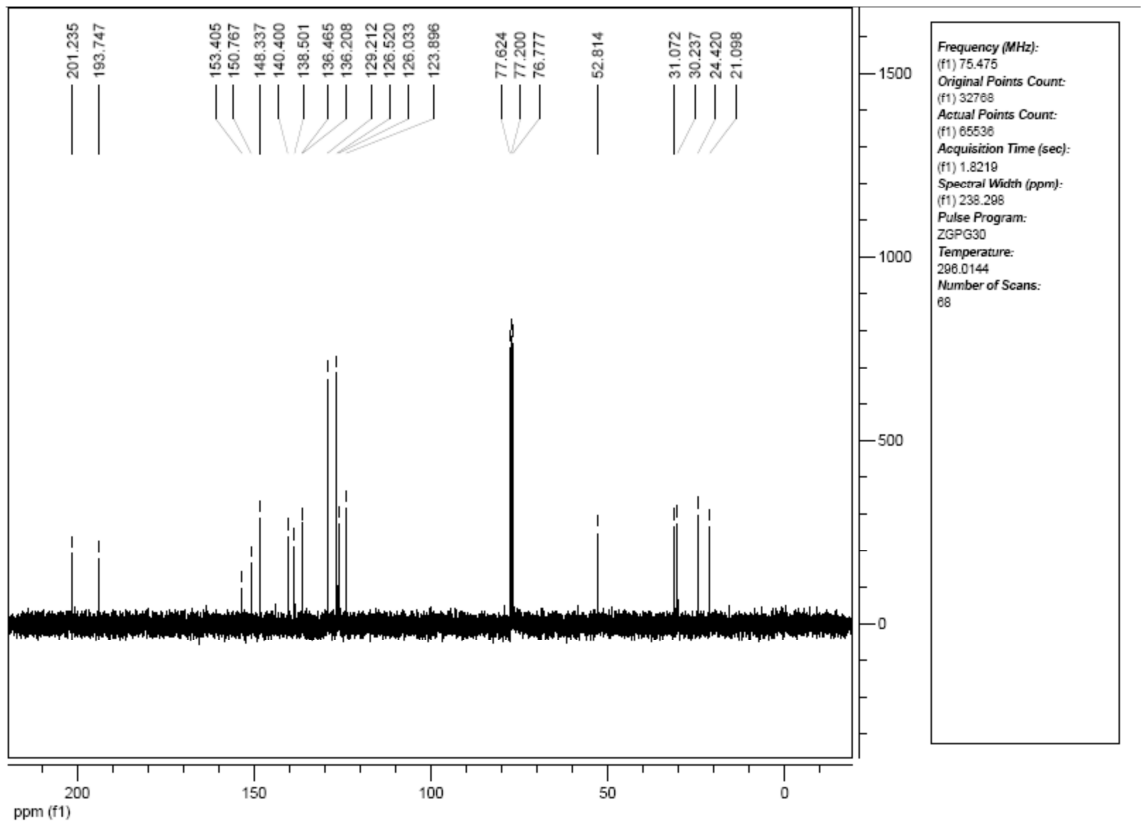




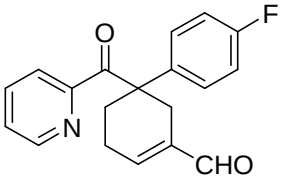
[1-(*p*-tolyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4b)

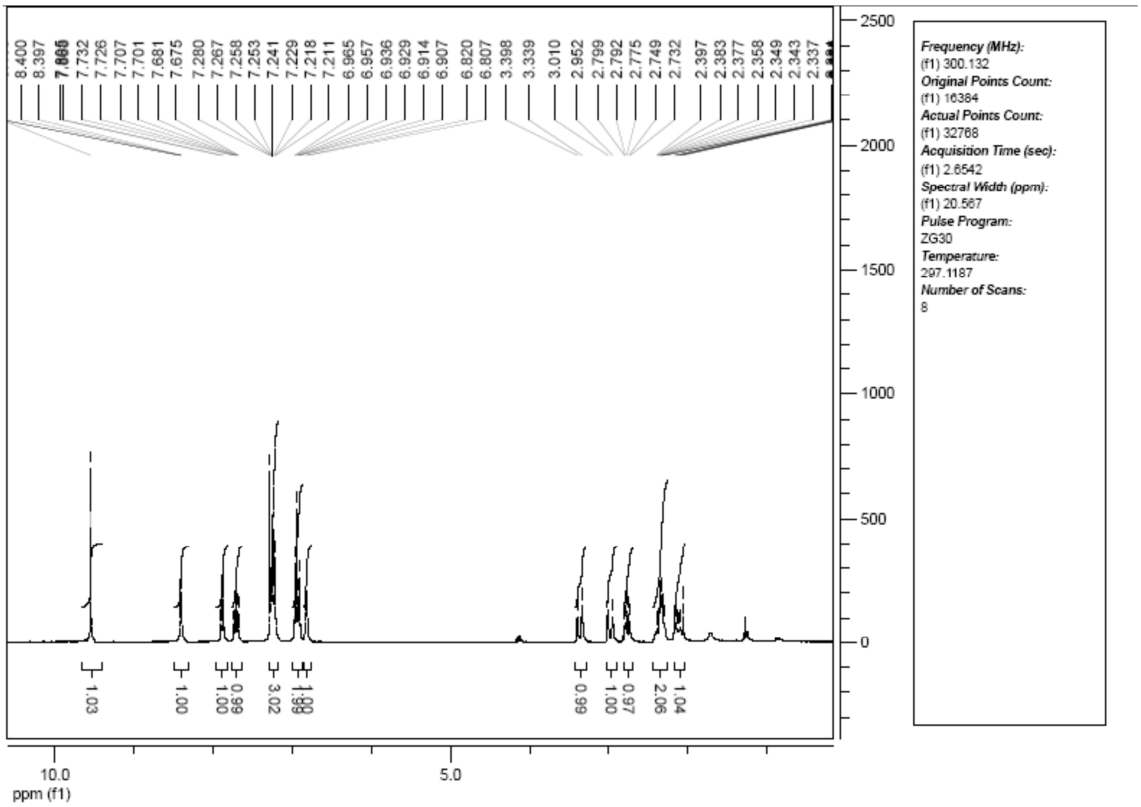


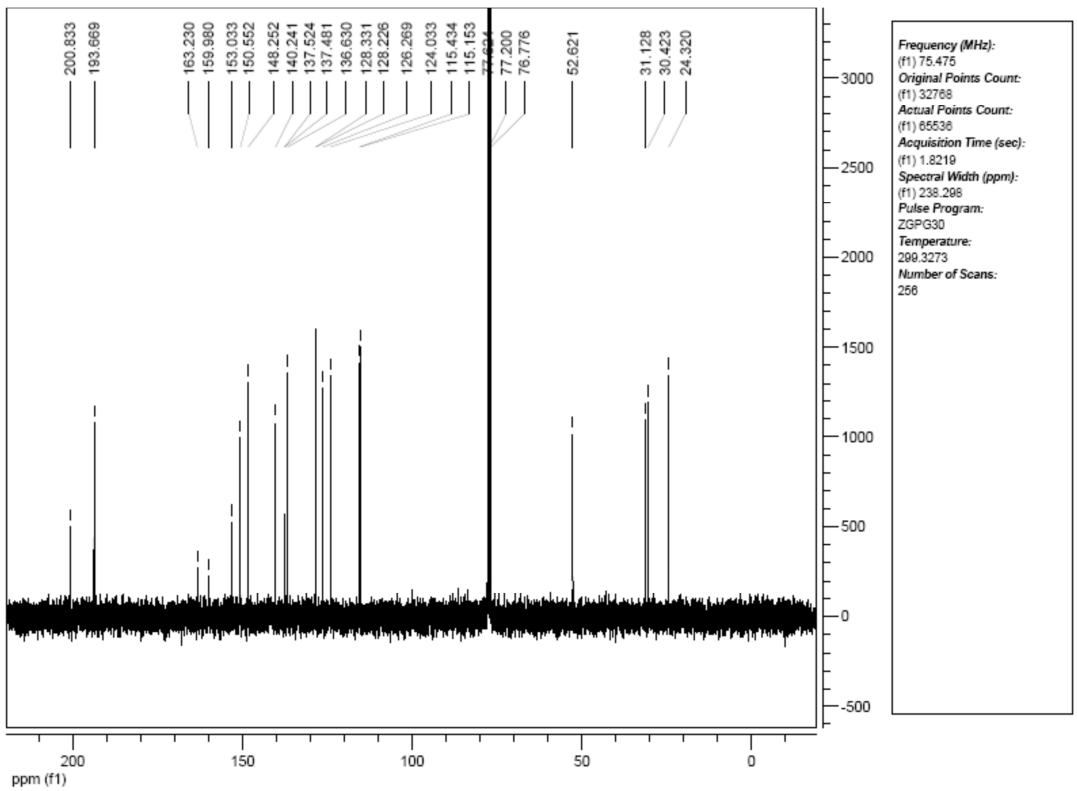




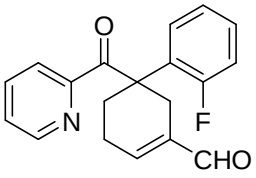
[1-(*p*-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4c)

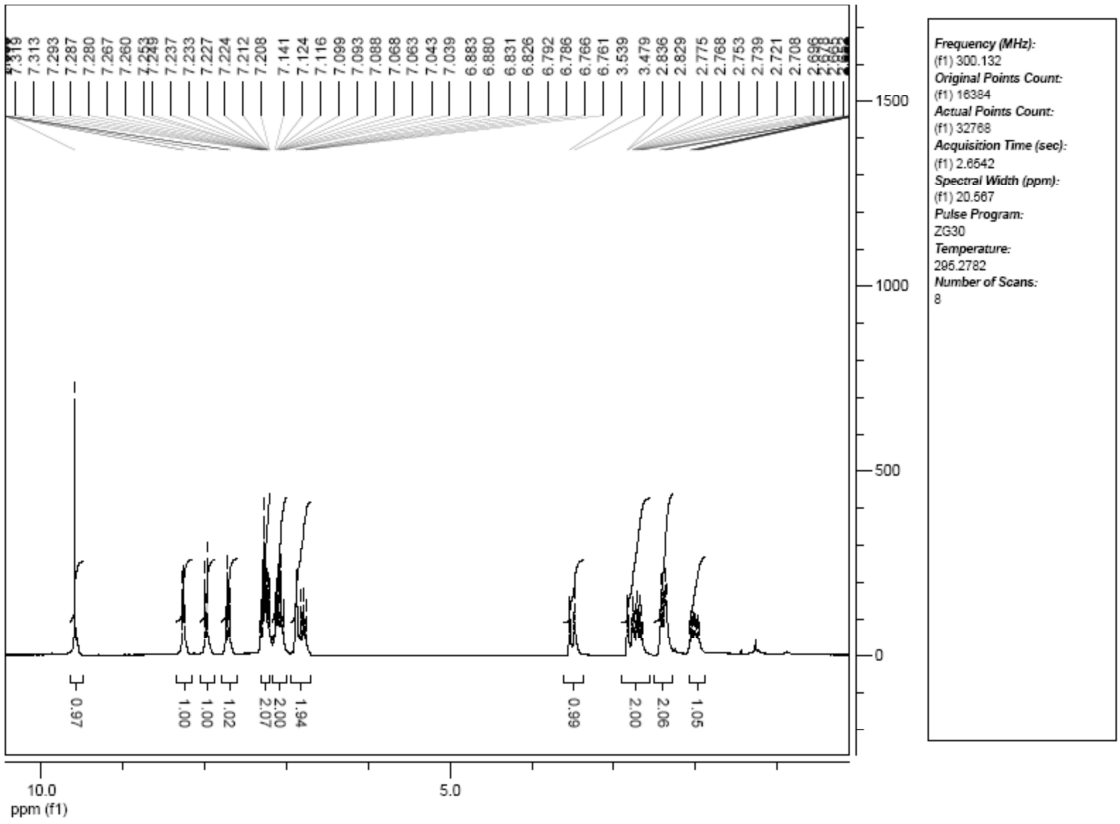


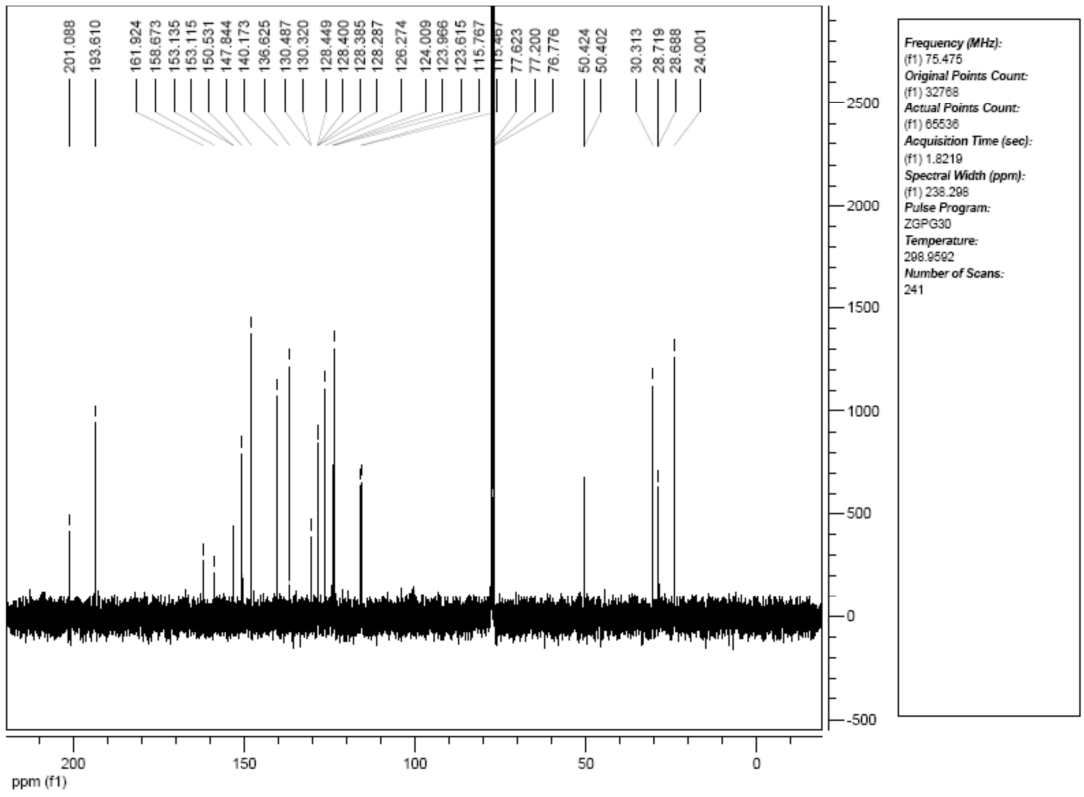




[1-(*o*-fluorophenyl)-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4d)







[1-benyl-3-formyl lyllohex-3-en-1-yl] (2'-pyridyl)ketone (4e)