Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Visible-light photoredox catalyzed hydroacylation of electron-deficient alkenes: carboxylic anhydride as acyl radical source

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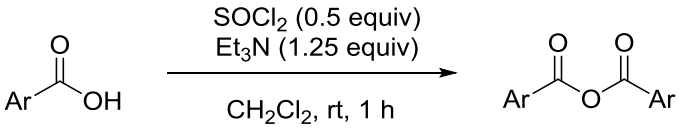
1. General Information

General Information. Proton nuclear magnetic resonance (^{1}H-NMR) spectra and carbon nuclear magnetic resonance (^{13}C-NMR) spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. ^{19}F-NMR spectra were recorded on a Bruker AV-400 spectrometer (376 MHz). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High resolution mass spectrometry (ESI) were carried out using a Waters Quatro Macro triple quadrupole mass spectrometer Mass spectra (EI) were measured on a Waters Micromass GCT spectrometer. Melting points were measured on a XT3A apparatus.

Starting Materials. Unless otherwise noted, all reactions were performed under nitrogen atmosphere in Schlenk tube, all chemicals were purchased from commercial sources and used as received. All other solvents, including those for NMR analysis, were used without further purification.

2. Synthesis of Substrates and Photocatalysts

Anhydrides： Benzoic anhydride is commercially available, other symmetric anhydrides were synthesized according to a modified literature procedure,[1] mixed anhydride **5a** was synthesized according to a literature procedure.[2]



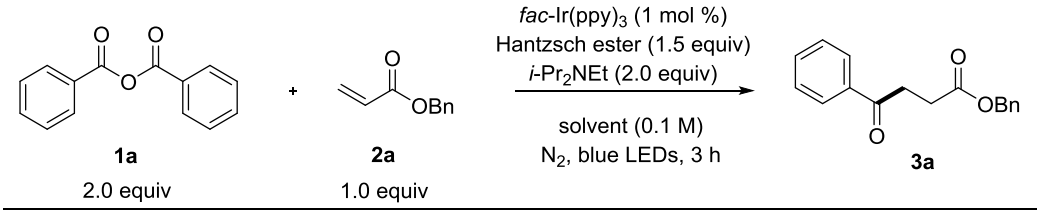
4-Methylbenzoic acid (20 mmol, 2.72g) and triethylamine (25 mmol, 2.53g) were suspended in CH_2Cl_2 (50 ml), and a CH_2Cl_2 solution (10 ml) of $SOCl_2$ (10mmol, 1.19g) was added dropwise, followed by stirring for 1 h at room temperature. The reaction solution was then diluted with CH_2Cl_2 and washed with sat. NH_4Cl. The organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure and the crude residue was purified by flash chromatography (CH_2Cl_2 as eluent) to yield 4-methylbenzoic anhydride (2.5g, 95% yield).

Michael acceptors: 2b, **2c**, **2f**, **2i**, **2j**, **2k**, **2l**, **2m** are commercially available, **2a**, **2d**, **2g** were synthesized according to a literature procedure[3], **2e** was synthesized according to a literature procedure[4], **2h** was synthesized according to a literature procedure[5], **2n**, **2o** were synthesized according to a literature procedure.[6]

Photocatalysts: All photocatalysts were syhthesized according to literature procetures, $Ru(bpy)_3Cl_2$[7], $Ir(ppy)_2(dtbbpy)PF_6$[8], $Ir[(dF(CF_3)ppy)_2(dtbbpy)]PF_6$[9], *fac*-$Ir(ppy)_3$[10].

3. Optimization Studies

3.1 Solvent Screening[a]

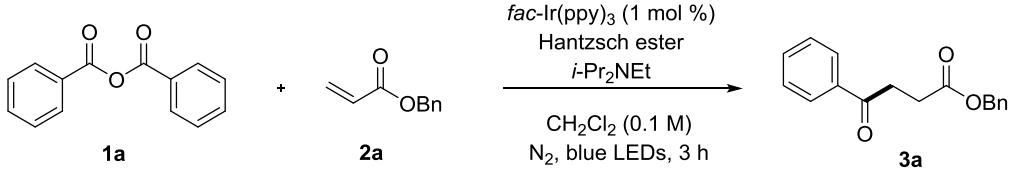


1a 2.0 equiv + **2a** 1.0 equiv → **3a**

entry	solvent	yield (%)[b]
1	DMA	46
2	CH_3CN	54
3	Acetone	50
4	**CH_2Cl_2**	**65**
5	DCE	63
6	THF	trace
7	DMSO	trace
8	CH_2Cl_2/H_2O=1mL/1mL	55
9[c]	CH_2Cl_2	61
10[d]	CH_2Cl_2	52
11[e]	CH_2Cl_2	63
12[f]	CH_2Cl_2	58

[a]Reactions performed on a 0.2 mmol scale. [b]Isolated yield. [c]The reaction was carried out using 32 W CFL as light source. [d]The reaction was carried out under air. [e]The reaction concentration was 0.05 M. [f]The reaction concentration was 0.2 M.

3.2 Study of the amount of Hantzsch ester and *i*-Pr_2NEt[a]

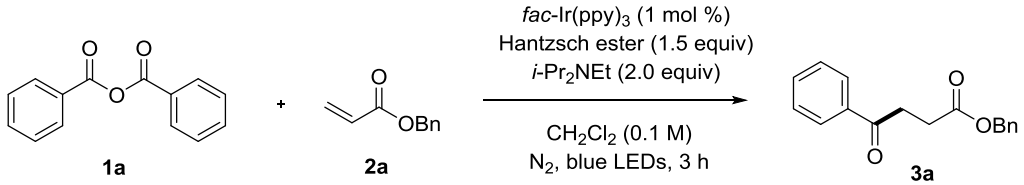


1a 2.0 equiv + **2a** 1.0 equiv → **3a**

entry	Hantzsch ester (equiv)	*i*-Pr_2NEt (equiv)	yield (%)[b]
1[c]	—	2.0	20
2[c]	2.0	—	0
3	1.1	2.0	60
4	**1.5**	**2.0**	**65**
5	2.0	2.0	58
6	3.0	2.0	42
7	1.5	1.0	54
8	1.5	1.5	62
9	**1.5**	**3.0**	**75**
10	1.5	5.0	69

[a]Reactions performed on a 0.2 mmol scale. [b]Isolated yield. [c]Reaction time 24 h.

3.3 Study of the ratio of substrates[a]

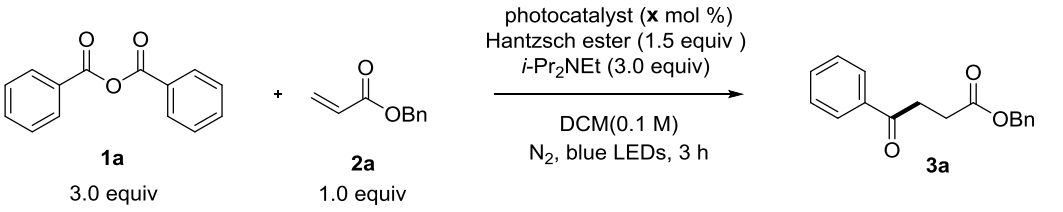


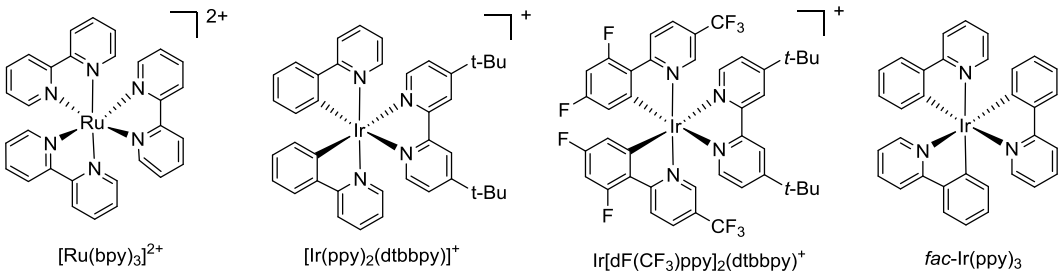
1a **x** equiv + **2a** **y** equiv → **3a**

entry	x	y	yield (%)[b]
1	2.0	1.0	65
2	3.0	1.0	78
3[c]	**3.0**	**1.0**	**80**
4	1.0	1.0	45
5	1.0	1.5	45
6	1.0	2.0	47

[a]Reactions performed on a 0.2 mmol scale. [b]Isolated yield. [c]3.0 equiv *i*-Pr_2NEt was added.

3.4 Catalyst Screening and loadings[a]



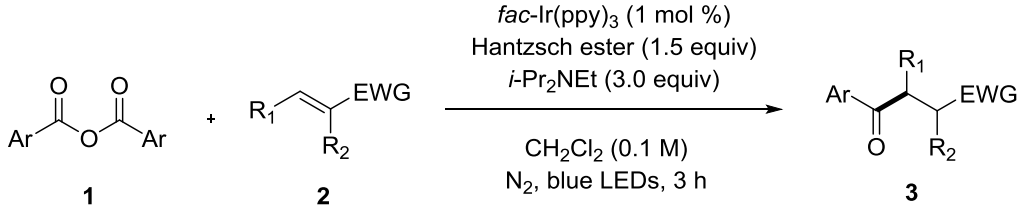


entry	x	photocatalyst	yield (%)[b]
1	1.0	$Ru(bpy)_3Cl_2$	0
2	1.0	$Ir(ppy)_2(dtbbpy)PF_6$	65
3	1.0	$Ir[(dF(CF_3)ppy)_2(dtbbpy)]PF_6$	47
4	**1.0**	***fac*-Ir(ppy)$_3$**	**80**
5	0.5	*fac*-$Ir(ppy)_3$	78
6	2.0	*fac*-$Ir(ppy)_3$	79
7	3.0	*fac*-$Ir(ppy)_3$	77
8	5.0	Riboflavin	0
9	5.0	Mes-$AcrClO_4$	0
10	5.0	Eosin Y	54
11	5.0	Rhodamine B	60

[a]Reactions on a 0.2 mmol scale. [b]Isolated yield. Mes-$AcrClO_4$ = 9-mesityl-10-methyl-acridinium perchlorate.

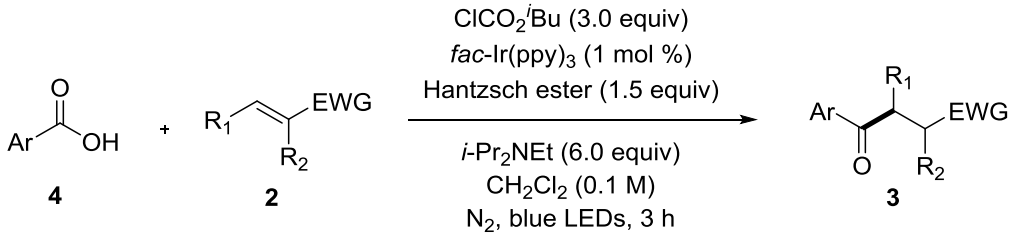
4. General Procedure and Characterization of Products

4.1 General Procedure A



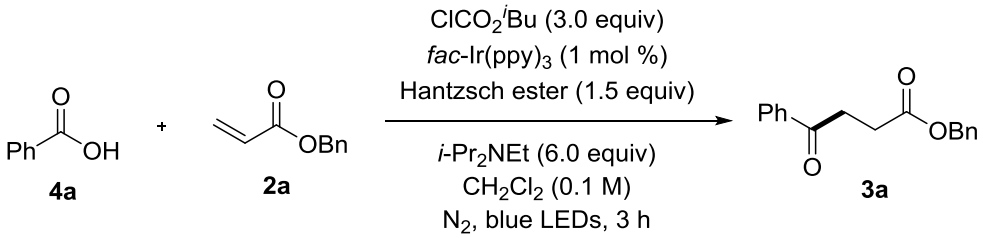
Symmetric carboxylic anhydride **1** (0.6 mmol, 3.0 equiv), Michael acceptor **2** (0.2 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (2 μmol, 1.3 mg, 0.01 equiv), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), *i*-Pr$_2$NEt (0.6 mmol, 77.5 mg, 3.0 equiv) and solvent CH_2Cl_2 (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_{max}= 453 nm) and stirred at room temperature until TLC showed consumption of starting material. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield corresponding addition products (**3**).

4.2 General Procedure B



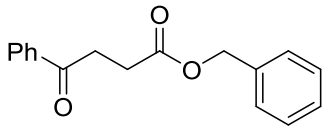
Carboxylic acid **4** (0.6 mmol, 3.0 equiv), Michael acceptor **2** (0.2 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (2 μmol, 1.3 mg, 0.01 equiv), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), *i*-Pr$_2$NEt (1.2 mmol, 155.1 mg, 6.0 equiv), isobutyl chloroformate (0.6 mmol, 3.0 equiv) and solvent CH_2Cl_2 (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_{max}= 453 nm) and stirred at room temperature until TLC showed consumption of starting material. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield corresponding addition products (**3**).

4.3 Gram-Scale Reaction

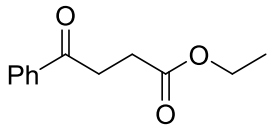


According to General Procedure B, benzoic acid **4a** (2.93 g, 24 mmol), benzyl acrylate **2a** (1.30 g, 8 mmol), *fac*-Ir(ppy)$_3$ (52.4 mg, 0.08 mmol), *i*-Pr$_2$NEt (6.2 g, 48 mmol), Hantzsch ester (3.04 g, 12 mmol), isobutyl chloroformate (3.28 g, 24 mmol) and solvent CH_2Cl_2 (80 mL) were added to a 200 mL transparent Schlenk flask charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction flask was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_{max}= 453 nm) and stirred at room temperature for 3 h. The reaction mixture was then concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (Petroleum Ether/CH_2Cl_2, 2:1) to yield desired product **3a** (1.64 g, 76%) as colorless oil.

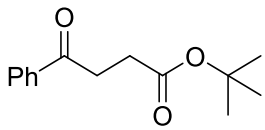
4.4 Characterization of Products



Benzyl 4-oxo-4-phenylbutanoate (3a). The product was obtained in 80% yield, 43.0 mg (78% yield, 41.9 mg from procedure B), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.38-7.29 (m, 5H), 5.15 (s, 2H), 3.33 (t, *J* = 6.6 Hz, 2H), 2.82 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 172.9, 136.6, 136.3 , 136.0, 133.3, 128.7, 128.6, 128.3, 128.3, 128.1, 66.6, 33.4, 28.4; HRMS (ESI) calcd for $C_{17}H_{17}O_3$ (M+H) 269.1178, found 269.1182.

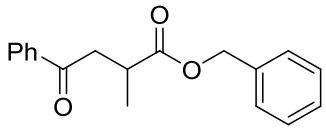


Ethyl 4-oxo-4-phenylbutanoate (3b). The product was obtained in 73% yield, 30.1 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.32 (t, *J* = 6.6 Hz, 2H), 2.76 (t, *J* = 6.6 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 173.0, 136.7, 133.3, 128.7, 128.1, 60.8, 33.5, 28.4, 14.3; HRMS (ESI) calcd for $C_{12}H_{15}O_3$ (M+H) 207.1021, found 207.1025.

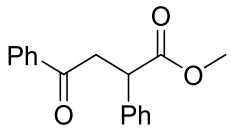


Tert-butyl 4-oxo-4-phenylbutanoate (3c). The product was obtained in 70% yield, 32.8

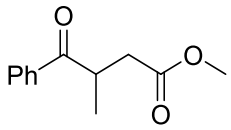
mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04-7.92 (m, 2H), 7.61-7.51 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 2H) , 3.26 (t, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.5, 172.3, 136.9, 133.2, 128.7, 128.1, 80.7, 33.6, 29.6, 28.2. HRMS (ESI) calcd for $C_{14}H_{19}O_3$ (M+H) 235.1334, found 235.1332.



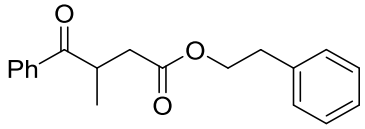
Benzyl 2-methyl-4-oxo-4-phenylbutanoate (3d). The product was obtained in 57% yield, 32.2 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.92 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.37-7.26 (m, 5H), 5.14 (q, *J* = 12.4 Hz, 2H), 3.50 (dd, *J* = 17.7, 7.9 Hz, 1H), 3.28-3.13 (m, 1H), 3.04 (dd, *J* = 17.7, 5.5 Hz, 1H), 1.30 (d, *J* = 7.2 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 175.9, 136.8, 136.2, 133.4, 128.7, 128.6, 128.2, 128.2, 128.2, 66.6, 42.0, 35.2, 17.4; HRMS (ESI) calcd for $C_{18}H_{19}O_3$ (M+H) 283.1334, found 283.1330.



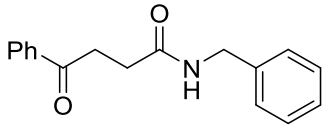
Methyl 4-oxo-2,4-diphenylbutanoate (3e). The product was obtained in 60% yield, 32.2 mg (58% yield, 31.1 mg from procedure B), white solid, mp 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.60-7.52 (m, 1H), 7.45 (dd, *J* = 10.8, 4.4 Hz, 2H), 7.38-7.26 (m, 5H), 4.30 (dd, *J* = 10.3, 4.1 Hz, 1H), 3.95 (dd, *J* = 18.0, 10.3 Hz, 1H), 3.69 (s, 3H), 3.27 (dd, *J* = 18.0, 4.1 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 174.0, 138.5, 136.5, 133.5, 129.1, 128.7, 128.2, 128.0, 127.7, 52.5, 46.5, 42.9; HRMS (ESI) calcd for $C_{17}H_{17}O_3$ (M+H) 269.1178, found 269.1175.



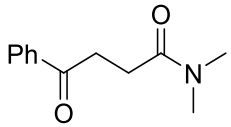
Methyl 4-oxo-2,4-diphenylbutanoate (3f). The product was obtained in 72% yield, 29.7 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 5.2, 3.4 Hz, 1H), 7.60-7.54 (m, 1H), 7.48 (dd, *J* = 10.4, 4.7 Hz, 1H), 4.06- 3.87 (m, 1H), 3.65 (s, 2H), 2.97 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.47 (dd, *J* = 16.8, 5.8 Hz, 1H), 1.23 (d, *J* = 7.2 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.9, 173.0, 136.0, 133.2, 128.8, 128.6, 51.9, 37.4, 18.0; HRMS (ESI) calcd for $C_{17}H_{17}O_3$ (M+H) 207.1021, found 207.1024.



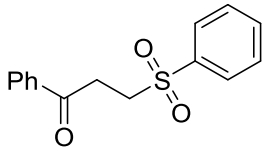
Phenethyl 3-methyl-4-oxo-4-phenylbutanoate (3g). The product was obtained in 68% yield, 40.3 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.28 (dd, *J* = 12.6, 5.1 Hz, 2H), 7.20 (dd, *J* = 17.2, 7.1 Hz, 3H), 4.27 (t, *J* = 7.1 Hz, 2H), 4.02-3.80 (m, 1H), 3.03-2.76 (m, 3H), 2.44 (dd, *J* = 16.8, 5.8 Hz, 1H), 1.20 (d, *J* = 7.2 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 172.4, 137.9, 136.0, 133.2, 129.0, 128.8, 128.6, 128.6, 126.7, 65.2, 37.6, 37.3, 35.2, 18.0; HRMS (ESI) calcd for $C_{17}H_{17}O_3$ (M+H) 297.1491, found 297.1493.



N-benzyl-4-oxo-4-phenylbutanamide (3h). The product was obtained in 49% yield, 26.2 mg(52% yield, 27.8 mg from procedure B), white solid, mp 111-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01-7.92 (m, 2H), 7.59-7.50 (m, 1H), 7.48-7.40 (m, 2H), 7.34-7.20 (m, 5H), 6.40 (s, 1H), 4.41 (d, *J* = 5.8 Hz, 1H), 3.35 (t, *J* = 6.6 Hz, 1H), 2.64 (t, *J* = 6.6 Hz, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.2, 172.1, 138.4, 136.6, 133.3, 128.7, 128.7, 128.2, 127.8, 127.4, 43.7, 34.1, 30.2; HRMS (ESI) calcd for $C_{17}H_{18}NO_2$ (M+H) 268.1338, found 268.1339.

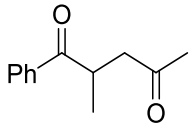


N,N-dimethyl-4-oxo-4-phenylbutanamide (3i). The product was obtained in 48% yield, 19.7 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05-7.99 (m, 2H), 7.59-7.52 (m, 1H), 7.49-7.43 (m, 2H), 3.35 (t, *J* = 6.6 Hz, 2H), 3.09 (s, 3H), 2.96 (s, 3H), 2.78 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.3, 171.8, 136.9, 133.0, 128.5, 128.1, 37.2, 35.6, 33.7, 27.3; HRMS (ESI) calcd for $C_{12}H_{16}NO_2$ (M+H) 206.1181, found 206.1185.

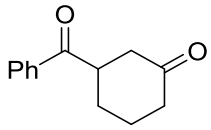


1-phenyl-3-(phenylsulfonyl)propan-1-one (3j). The product was obtained in 73% yield, 40.0 mg, white solid, mp 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 14.8, 7.4 Hz, 4H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.59 (dd, *J* = 9.6, 5.5 Hz, 3H), 7.48 (t, *J* = 7.7 Hz, 2H), 3.61-3.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 139.1, 135.9, 134.1, 133.9, 129.6,

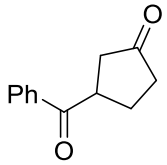
128.9, 128.2, 128.1, 51.1, 31.5; HRMS (ESI) calcd for $C_{15}H_{15}O_3S$ (M+H) 275.0742, found 275.0740.



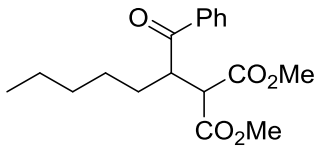
2-methyl-1-phenylpentane-1,4-dione (3k). The product was obtained in 40% yield, 15.2 mg(61% yield, 23.2 mg from procedure B), colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.61-7.52 (m, 1H), 7.51-7.42 (m, 2H), 3.97 (dqd, *J* = 14.4, 7.2, 5.1 Hz, 1H), 3.17 (dd, *J* = 18.0, 8.5 Hz, 1H), 2.55 (dd, *J* = 18.0, 5.0 Hz, 1H), 2.18 (s, 3H), 1.19 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.2, 203.4, 136.1, 133.1, 128.8, 128.6, 47.0, 36.3, 30.2, 17.9; HRMS (ESI) calcd for $C_{12}H_{15}O_2$ (M+H) 191.1072, found 191.1075.



3-benzoylcyclohexan-1-one (3l). The product was obtained in 67% yield, 27.1 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.89 (m, 2H), 7.60 (ddd, *J* = 8.6, 2.3, 1.1 Hz, 1H), 7.48 (dd, *J* = 10.6, 4.7 Hz, 2H), 3.84 (tt, *J* = 10.5, 4.2 Hz, 1H), 2.72 (dd, *J* = 14.6, 10.7 Hz, 1H), 2.53-2.37 (m, 3H), 2.11 (dd, *J* = 9.9, 4.8 Hz, 2H), 1.95-1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.4, 200.5, 135.4, 133.6, 129.0, 128.5, 45.2, 43.2, 41.1, 28.5, 24.9; HRMS (ESI) calcd for $C_{13}H_{15}O_2$ (M+H) 203.1072, found 203.1073.

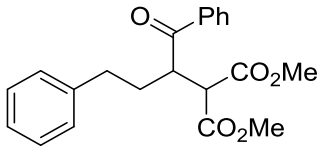


3-benzoylcyclopentan-1-one (3m). The product was obtained in 87% yield, 32.7 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.3 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 4.14 (p, *J* = 7.5 Hz, 1H), 2.72 (dd, *J* = 18.4, 7.9 Hz, 1H), 2.53-2.09 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.1, 200.4, 135.7, 133.7, 129.0, 128.6, 43.2, 41.1, 37.5, 27.1; HRMS (ESI) calcd for $C_{12}H_{13}O_2$ (M+H) 189.0916, found 189.0912.

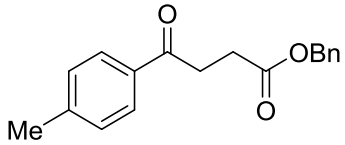


Dimethyl 2-(1-oxo-1-phenylheptan-2-yl)malonate (3n). The product was obtained in 66%

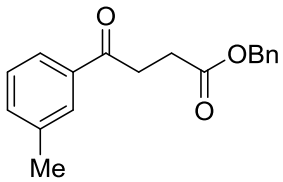
yield, 42.3 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 4.24 (dt, *J* = 11.5, 5.9 Hz, 1H), 4.09 (d, *J* = 10.9 Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 1.66–1.54 (m, 2H), 1.27-1.01 (m, 6H), 0.77 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9, 169.3, 169.0, 137.0, 133.3, 128.8, 128.6, 53.7, 52.8, 45.3, 31.9, 30.7, 25.6, 22.3, 13.9; HRMS (ESI) calcd for $C_{18}H_{25}O_5$ (M+H) 321.1702, found 321.1700.



Dimethyl 2-(1-oxo-1,4-diphenylbutan-2-yl)malonate (3o). The product was obtained in 68% yield, 48.2 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.61-7.55 (m, 1H), 7.46 (dd, *J* = 10.5, 4.8 Hz, 2H), 7.26-7.12 (m, 3H), 7.02-6.97 (m, 2H), 4.37-4.25 (m, 1H), 4.17 (d, *J* = 10.9 Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 2.54 (ddd, *J* = 13.8, 9.6, 7.1 Hz, 1H), 2.39 (ddd, *J* = 13.8, 9.9, 6.9 Hz, 1H), 2.02–1.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.6, 169.2, 168.9, 140.9, 136.8, 133.4, 128.8, 128.7, 128.5, 128.4, 126.2, 53.6, 52.9, 52.9, 44.9, 32.4, 32.3; HRMS (ESI) calcd for $C_{21}H_{23}O_5$ (M+H) 355.1545, found 355.1548.

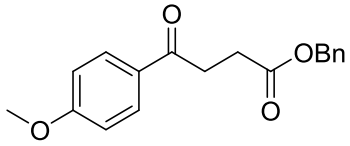


Benzyl 4-oxo-4-(p-tolyl)butanoate (3p). The product was obtained in 71% yield, 40.1 mg, white solid, mp 51-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.39-7.19 (m, 7H), 5.14 (s, 2H), 3.30 (t, *J* = 6.7 Hz, 2H), 2.81 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.7, 172.8, 144.0, 136.0, 134.1, 129.3, 128.6, 128.2, 128.2, 66.5, 33.3, 28.4, 21.7; HRMS (ESI) calcd for $C_{18}H_{19}O_3$ (M+H) 283.1334, found 283.1330.

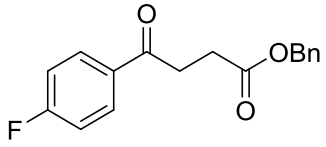


Benzyl 4-oxo-4-(m-tolyl)butanoate (3q). The product was obtained in 73% yield, 41.2 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.9 Hz, 2H), 7.42-7.28 (m, 7H), 5.14 (s, 2H), 3.31 (t, *J* = 6.6 Hz, 2H), 2.81 (t, *J* = 6.6 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 172.9, 138.5, 136.6, 136.0, 134.1, 128.7, 128.6, 128.6, 128.3,

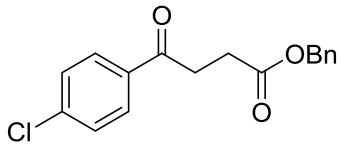
125.3, 66.6, 33.5, 28.4, 21.4; HRMS (ESI) calcd for $C_{18}H_{19}O_3$ (M+H) 283.1334, found 283.1332.



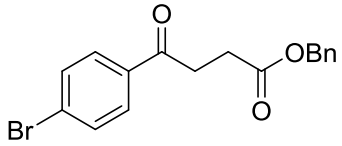
Benzyl 4-(4-methoxyphenyl)-4-oxobutanoate (3r). The product was obtained in 58% yield, 34.6 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02-7.89 (m, 2H), 7.35 (dd, *J* = 7.4, 4.2 Hz, 5H), 6.97-6.87 (m, 2H), 5.15 (s, 2H), 3.86 (s, 3H), 3.28 (t, *J* = 6.7 Hz, 2H), 2.81 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 173.0, 163.7, 136.1, 130.4, 129.8, 128.7, 128.3, 113.9, 66.6, 55.6, 33.1, 28.5; HRMS (ESI) calcd for $C_{18}H_{19}O_4$ (M+H) 299.1283, found 299.1285.



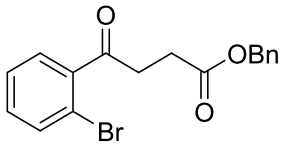
Benzyl 4-(4-fluorophenyl)-4-oxobutanoate (3s). The product was obtained in 70% yield, 40.1 mg, yellow solid, mp 57-58 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04-7.94 (m, 2H), 7.40-7.26 (m, 5H), 7.16-7.07 (m, 2H), 5.14 (s, 2H), 3.29 (t, *J* = 6.6 Hz, 2H), 2.82 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5, 172.8, 165.9 (d, *J* = 254.8 Hz), 136.0, 133.1 (d, *J* = 3.0 Hz), 130.8 (d, *J* = 9.3 Hz), 128.7, 128.3, 128.3, 115.8 (d, *J* = 21.9 Hz), 66.6, 33.3, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -105.0 (m, 1F); HRMS (ESI) calcd for $C_{17}H_{16}BrO_3$ (M+H) 286.1005, found 286.1001.



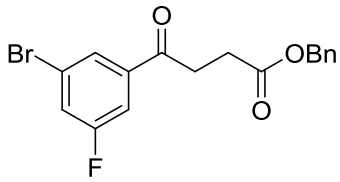
Benzyl 4-(4-chlorophenyl)-4-oxobutanoate (3t). The product was obtained in 73% yield, 44.2 mg, yellow solid, mp 77-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.39-7.26 (m, 5H), 5.14 (s, 2H), 3.28 (t, *J* = 6.6 Hz, 2H), 2.81 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.9, 172.7, 139.8, 135.9, 135.0, 129.6, 129.0, 128.7, 128.3, 128.3, 66.7, 33.4, 28.3; HRMS (ESI) calcd for $C_{17}H_{16}ClO_3$ (M+H) 303.0788, found 303.0787.



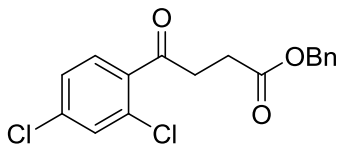
Benzyl 4-(4-bromophenyl)-4-oxobutanoate (3u). The product was obtained in 42% yield, 29.2 mg, yellow solid, mp 83-84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.80 (m, 2H), 7.63-7.57 (m, 2H), 7.39-7.27 (m, 5H), 5.14 (s, 2H), 3.28 (t, J = 6.6 Hz, 2H), 2.82 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 172.7, 135.9, 135.4, 132.1, 129.7, 128.7, 128.5, 128.4, 128.3, 66.7, 33.4, 28.3; HRMS (ESI) calcd for $C_{17}H_{16}BrO_3$ (M+H) 347.0283, found 347.0284.



Benzyl 4-(2-bromophenyl)-4-oxobutanoate (3v). The product was obtained in 48% yield, 33.3 mg, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J = 7.9, 1.1 Hz, 1H), 7.44 (dd, J = 7.6, 1.8 Hz, 1H), 7.39- 7.26 (m, 7H), 5.15 (s, 2H), 3.25 (t, J = 6.5 Hz, 2H), 2.83 (t, J = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9, 172.3, 141.3, 135.8, 133.7, 131.7, 128.7, 128.6, 128.3, 127.4, 118.6, 66.6, 37.4, 28.5; HRMS (ESI) calcd for $C_{17}H_{16}BrO_3$ (M+H) 347.0283, found 347.0281.

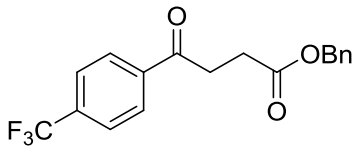


Benzyl 4-(3-bromo-5-fluorophenyl)-4-oxobutanoate (3w). The product was obtained in 72% yield, 52.6 mg, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (t, J = 1.6 Hz, 1H), 7.58 (ddd, J = 8.8, 2.4, 1.4 Hz, 1H), 7.44 (ddd, J = 7.7, 2.4, 1.7 Hz, 1H), 7.39-7.30 (m, 5H), 5.14 (s, 2H), 3.25 (t, J = 6.5 Hz, 2H), 2.82 (t, J = 6.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.5 (d, J = 2.1 Hz), 172.3, 162.6 (d, J = 252.9 Hz), 139.5 (d, J = 6.6 Hz), 135.7, 128.6, 128.3, 128.2, 127.2 (d, J = 3.3 Hz), 123.6 (d, J = 24.6 Hz), 123.2 (d, J = 8.9 Hz), 113.9 (d, J = 22.4 Hz), 66.7, 33.5, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$): δ -109.04 – -109.24 (m, 1F); HRMS (ESI) calcd for $C_{17}H_{15}BrFO_3$ (M+H) 365.0189, found 365.0186.

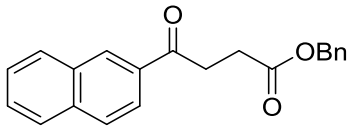


Benzyl 4-(2,4-dichlorophenyl)-4-oxobutanoate (3x). The product was obtained in 79% yield, 53.3 mg, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 1.9 Hz, 1H), 7.39-7.26 (m, 6H), 5.13 (s, 2H), 3.40-3.13 (m, 2H), 2.92-2.57 (m, 2H).;

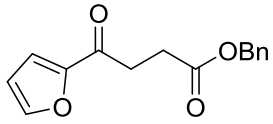
^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 172.4, 137.7, 137.1, 135.9, 132.2, 130.6, 130.6, 128.7, 128.4, 128.3, 127.5, 66.7, 37.7, 28.7; HRMS (ESI) calcd for $C_{17}H_{15}Cl_2O_3$ (M+H) 337.0398, found 337.0395.



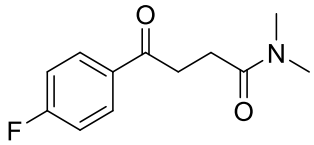
Benzyl 4-oxo-4-(4-(trifluoromethyl)phenyl)butanoate (3y). The product was obtained in 75% yield, 50.4 mg, white solid, mp 89-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.40-7.27 (m, 5H), 5.15 (s, 2H), 3.34 (t, *J* = 6.5 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 172.6, 139.3, 135.9, 134.7 (q, *J* = 32.7 Hz), 128.7, 128.5, 128.4, 128.4, 125.8(q, *J* = 3.7 Hz), 123.7 (d, *J* = 272.7 Hz), 66.8, 33.8, 28.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -63.1 (s, 3F); HRMS (ESI) calcd for $C_{17}H_{16}BrO_3$ (M+H) 337.1054, found 337.1052.



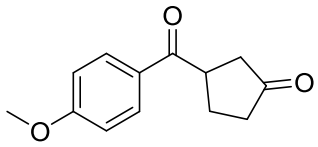
Benzyl 4-(naphthalen-2-yl)-4-oxobutanoate (3z). The product was obtained in 79% yield, 50.3 mg, white solid, mp 74-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (s, 1H), 8.02 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.90-7.82 (m, 2H), 7.56 (dddd, *J* = 19.8, 8.1, 6.9, 1.3 Hz, 2H), 7.41-7.26 (m, 5H), 5.16 (s, 2H), 3.45 (t, *J* = 6.7 Hz, 2H), 2.87 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 172.9, 136.0, 135.7, 134.0, 132.6, 129.8, 129.7, 128.6, 128.6, 128.5, 128.3, 127.8, 126.9, 123.8, 66.6, 33.5, 28.5; HRMS (ESI) calcd for $C_{21}H_{19}O_3$ (M+H) 319.1334, found 319.1330.



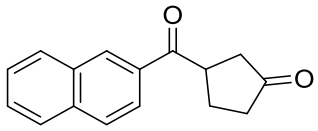
Benzyl 4-(furan-2-yl)-4-oxobutanoate (3ab). The product was obtained in 62% yield, 32.0 mg, white solid, mp 49-50 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (dd, *J* = 1.6, 0.6 Hz, 1H), 7.40-7.28 (m, 5H), 7.22 (dd, *J* = 3.6, 0.5 Hz, 1H), 6.53 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.14 (s, 2H), 3.19 (t, *J* = 6.7 Hz, 2H), 2.80 (t, *J* = 6.7 Hz, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 172.6, 152.5, 146.5, 136.0, 128.6, 128.3, 128.3, 117.2, 112.4, 66.6, 33.1, 27.9; HRMS (ESI) calcd for $C_{15}H_{15}O_4$ (M+H) 259.0970, found 259.0974.



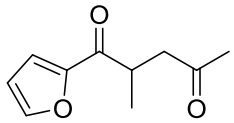
4-(4-fluorophenyl)-N,N-dimethyl-4-oxobutanamide (3ac). The product was obtained in 67% yield, 29.9 mg, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-7.98 (m, 2H), 7.13 (t, *J* = 8.6 Hz, 2H), 3.31 (t, *J* = 6.5 Hz, 2H), 3.10 (s, 3H), 2.96 (s, 3H), 2.78 (t, *J* = 6.5 Hz, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 171.6, 167.0, 164.4, 133.3 (d, *J* = 3.1 Hz), 130.8, 130.7, 115.7, 115.5, 37.1, 35.5, 33.5, 27.3; ^{19}F NMR (376 MHz, $CDCl_3$): δ -105.6 (m, 1F); HRMS (ESI) calcd for $C_{12}H_{15}FNO_2$ (M+H) 224.1087, found 224.1084.



3-(4-methoxybenzoyl)cyclopentan-1-one (3ad). The product was obtained in 62% yield, 27.1 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03-7.94 (m, 2H), 7.04-6.92 (m, 2H), 4.17-4.02 (m, 1H), 3.89 (s, 3H), 2.77-2.62 (m, 1H), 2.50-2.24 (m, 4H), 2.21-2.09 (m, 1H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 217.2, 198.7, 163.8, 130.8, 128.6, 114.0, 55.6, 42.7, 41.1, 37.4, 27.1; HRMS (ESI) calcd for $C_{13}H_{15}O_3$ (M+H) 219.1021, found 219.1024.

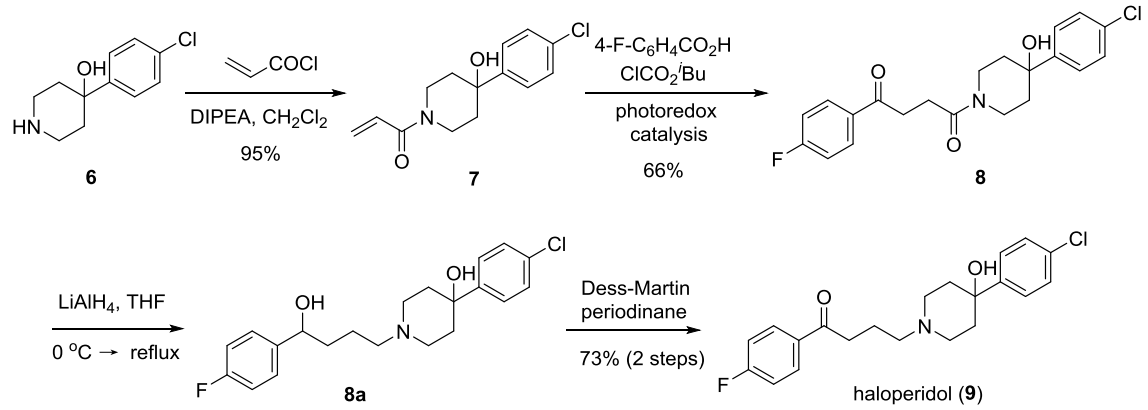


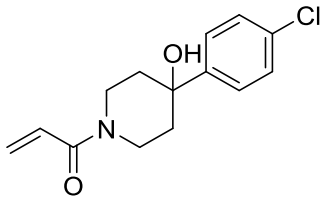
3-(2-naphthoyl)cyclopentan-1-one (3ae). The product was obtained in 53% yield, 25.3 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 1.7 Hz, 1H), 8.05 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.00-7.88 (m, 3H), 7.61 (dddd, *J* = 20.5, 8.1, 6.9, 1.3 Hz, 2H), 4.38-4.18 (m, 1H), 2.84-2.70 (m, 1H), 2.57-2.17 (m, 5H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 216.9, 200.2, 135.8, 132.9, 132.5, 130.2, 129.6, 128.8, 127.8, 127.0, 124.1, 43.1, 41.2, 37.4, 27.2; HRMS (ESI) calcd for $C_{16}H_{15}O_2$ (M+H) 239.1072, found 239.1070.



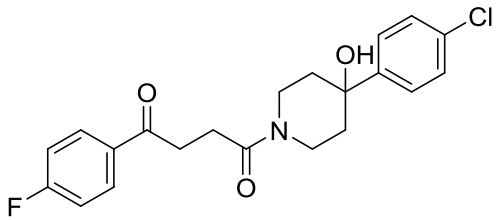
1-(furan-2-yl)-2-methylpentane-1,4-dione (3af). The product was obtained in 40% yield, 14.4 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.24 (dd, *J* = 3.5, 0.7 Hz, 1H), 6.54 (dd, *J* = 3.6, 1.7 Hz, 1H), 3.74 (ddd, *J* = 8.7, 7.1, 5.1 Hz, 1H), 3.12 (dd, *J* = 18.0, 8.7 Hz, 1H), 2.53 (dd, *J* = 18.1, 5.1 Hz, 1H), 2.16 (s, 3H), 1.21 (d, *J* = 7.2 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.8, 191.9, 151.9, 146.4, 117.6, 112.2, 46.3, 36.9, 30.0, 17.6; HRMS (ESI) calcd for $C_{10}H_{13}O_3$ (M+H) 181.0865, found 181.0867.

5. Synthetic Procedure and Characterization of Haloperidol

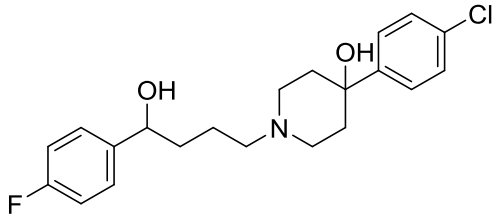




1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)prop-2-en-1-one (7): To a solution of **6** (1.60 g, 7.56 mmol) in CH_2Cl_2 (40 mL) was added DIPEA (1.08 g, 8.32 mmol) and cooled to 0 ℃, 0.61 mL acryloyl chloride (7.56 mmol) in CH_2Cl_2 (5 mL) was added drop-wise and then the mixture was stirred at room temperature. for 4 h. The reaction mixture was diluted with 40 mL CH_2Cl_2, and washed sequentially with 1 M HCl, saturated $NaHCO_3$ and brine, the organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH, 20:1) to give **7** (1.90 g, 95 %) as a white solid, mp 183-185 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.51 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.84 (dd, *J* = 16.7, 10.5 Hz, 1H), 6.12 (dd, *J* = 16.7, 2.5 Hz, 1H), 5.67 (dd, *J* = 10.5, 2.5 Hz, 1H), 5.29 (s, 1H), 4.42-4.36 (m, 1H), 3.96 (d, *J* = 13.5 Hz, 1H), 3.51-3.40 (m, 2H), 3.03 (td, *J* = 12.6, 2.7 Hz, 1H), 1.91-1.73 (m, 2H), 1.63 (d, *J* = 13.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.1, 148.2, 131.0, 128.6, 127.8, 126.8, 126.8, 69.9, 41.5, 38.4, 37.8, 37.4.; HRMS (ESI) calcd for $C_{14}H_{17}ClNO_2$ (M+H) 266.0948, found 266.0945.

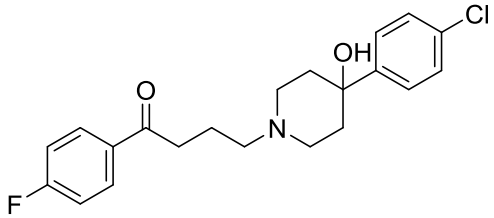


1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-4-(4-fluorophenyl)butane-1,4-dione (8): According to the General Procedure B, 4-F-C_6H_4COOH (2.52 g, 18 mmol), **7** (1.594 g, 6 mmol), *fac*-Ir(ppy)$_3$ (39.3 mg, 0.06 mmol), Hantzsch ester (2.28 g, 9 mmol), *i*-Pr_2NEt (4.65 g, 36 mmol), isobutyl chloroformate (2.46 g,18 mmol) and solvent CH_2Cl_2 (50 mL) were added to a 100 mL transparent Schlenk flask charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction flask was then placed in an irradiation apparatus (at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_{max}= 453 nm) and stirred at room temperature until TLC showed consumption of **7**. The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH, 30:1) to yield addition product **8** (1.55 g, 66%) as a white solid, mp 156 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14-8.01 (m, 2H), 7.56-7.48 (m, 2H), 7.43-7.28 (m, 4H), 5.27 (s, 1H), 4.42-4.17 (m, 1H), 3.97-3.77 (m, 1H), 3.46 (td, *J* = 13.0, 2.6 Hz, 1H), 3.34-3.11 (m, 2H), 2.95 (td, *J* = 12.7, 3.0 Hz, 1H), 2.82-2.70 (m, 2H), 1.96 (td, *J* = 12.8, 4.2 Hz, 1H), 1.81-1.52 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 197.7, 169.4, 166.1, 163.6, 148.4, 133.6 (d, *J* = 2.9 Hz), 131.0, 130.8, 130.7, 127.8, 126.8, 115.7, 115.5, 69.9, 41.2, 37.9, 37.6, 37.4, 33.1, 26.7. ^{19}F NMR (376 MHz, DMSO-d_6): δ -106.48 (dt, *J* = 9.5, 3.9 Hz); HRMS (ESI) calcd for $C_{21}H_{22}ClFNO_3$ (M+H) 390.1272, found 390.1275.



4-(4-chlorophenyl)-1-(4-(4-fluorophenyl)-4-hydroxybutyl)piperidin-4-ol (8a): A solution of **8** (1.6 g, 4.1 mmol) in anhydrous THF (40 mL) was added dropwise to a solution of $LiAlH_4$ (778 mg, 20.5 mmol) in anhydrous THF (20 mL) and the resulting mixture was heated at reflux for 8 h. The mixture was cooled to room temperature and water (800 μL), aq 4 M NaOH (800 μL) and water (2.4 mL) were added sequentially. The resulting colourless suspension was stirred at room temperature for 30 min and filtered, washing with CH_2Cl_2 (40 mL), and concentrated in vacuo to afford the crude **8a** (1.5 g) as a white

solid. This material was used in the next stage without further purification.[11] ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.50 (d, J = 8.6 Hz, 2H), 7.37 (dd, J = 8.4, 5.6 Hz, 4H), 7.14 (t, J = 8.9 Hz, 2H), 4.91 (s, 1H), 4.56 (t, J = 6.1 Hz, 1H), 2.71-2.57 (m, 2H), 2.33 (dt, J = 13.9, 6.7 Hz, 4H), 1.89 (td, J = 12.8, 4.3 Hz, 2H), 1.68-1.50 (m, 5H), 1.42 (dp, J = 14.5, 7.2, 6.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.1, 159.7, 149.1, 142.6 (d, J = 2.9 Hz), 130.7, 127.7, 127.6, 127.5, 126.8, 114.6, 114.4, 71.6, 69.5, 58.0, 49.1, 48.8, 37.8, 37.8, 37.7, 22.9. ^{19}F NMR (376 MHz, DMSO-d_6): δ -115.69 – -117.61 (m); HRMS (ESI) calcd for $C_{21}H_{26}ClFNO_2$ (M+H) 378.1636, found 378.1632.



Haloperidol (9): Crude **8a** (1.5 g, 3.97 mmol) from last step was dissolved in CH_2Cl_2 (40 mL) and Dess–Martin periodinane (3.4 g, 7.94 mmol, 2.0 equiv) were added. The reaction contents were stirred for 8 h at 25 ℃ at which point they were quenched with saturated $NaHCO_3$ (50 mL), the organic phase was washed with saturated $Na_2S_2O_3$ (50 mL) and dried with $MgSO_4$. The organic phase was then concentrated in vacuo and the crude residue was purified by flash chromatography on silica gel (EtOAc/MeOH/NH_3 H_2O, 95:5:1) to yield haloperidol **9** (1.09 g, 73 % for 2 steps).as a white solid. mp 142 ℃ ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11-8.04 (m, 2H), 7.40-7.30 (m, 6H), 4.85 (s, 1H), 2.98 (t, J = 6.8 Hz, 2H), 2.62-2.54 (m, 2H), 2.40-2.22 (m, 4H), 1.84 (p, J = 6.8 Hz, 2H), 1.67 (td, J = 12.7, 4.3 Hz, 2H), 1.46 (dd, J = 13.4, 2.4 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.2, 166.0, 163.5, 149.1, 133.9 (d, J = 2.8 Hz), 130.9, 130.8, 130.7, 127.6, 126.7, 115.6, 115.4, 69.4, 57.2, 48.8, 37.6, 35.6, 21.9. ^{19}F NMR (376 MHz, DMSO-d_6): δ -115.69 – -117.61 (m); HRMS (ESI) calcd for $C_{21}H_{26}ClFNO_2$ (M+H) 378.1636, found 378.1632.

6. Radical Trapping Experiments

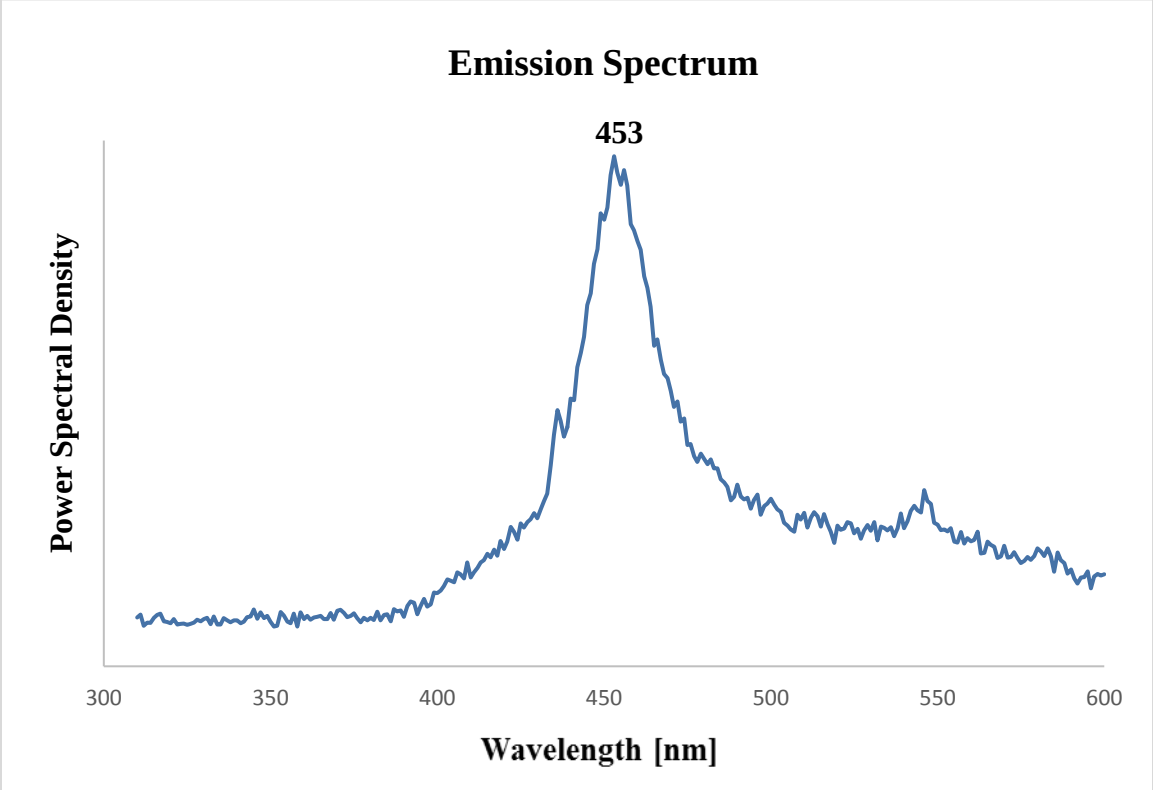
Benzoic anhydride **1a** (0.6 mmol, 3.0 equiv), Benzyl acrylate **2a** (0.2 mmol, 1.0 equiv), *fac*-Ir(ppy)$_3$ (2 μmol, 1.3 mg, 0.01 equiv), Hantzsch ester (0.3 mmol, 76 mg, 1.5 equiv), *i*-Pr_2NEt (0.6 mmol, 77.5 mg, 3.0 equiv), TEMPO (0.6 mmol, 3 equiv) and solvent CH_2Cl_2 (2 mL) were added to a 10 mL transparent Schlenk tube charged with a magnetic stir bar. The resulting solution was degassed and backfilled with nitrogen via the freeze-pump-thaw procedure for three cycles. The reaction tube was then placed in an irradiation apparatus

(at approximately 2 cm away from the light source) equipped with a 24 W blue light LED strip (λ_{max}= 453 nm) and stirred at room temperature for 24 h. After 24 h, The reaction mixture was concentrated under reduced pressure and the crude residue was purified by flash chromatography to yield 2,2,6,6-tetramethylpiperidin-1-yl benzoate **10** in 83% yield (based on benzoic anhydride).

2,2,6,6-tetramethylpiperidin-1-yl benzoate (10)

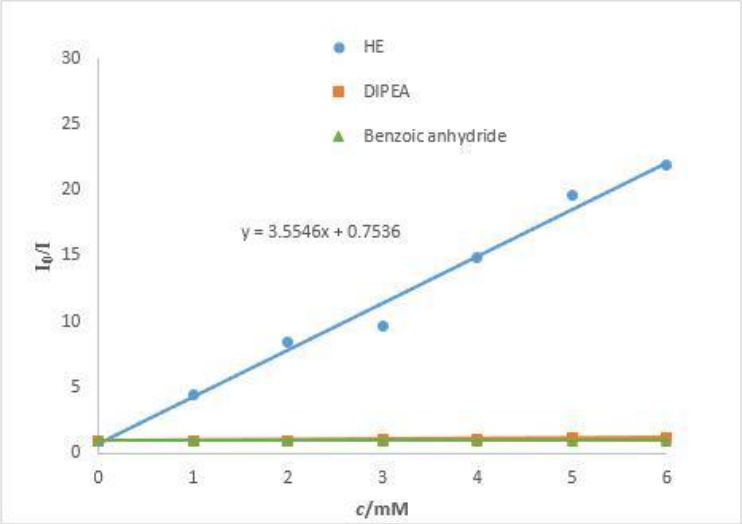
White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12-8.03 (m, 2H), 7.61-7.53 (m, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 1.84-1.65 (m, 3H), 1.65-1.51 (m, 2H), 1.51-1.40 (m, 1H), 1.28 (s, 6H), 1.12 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 132.9, 129.8, 129.7, 128.6, 60.5, 39.2, 32.1, 20.9, 17.2.

7. Emission Spectrum of the Light Source



8. Emission Quenching Experiments (Stern–Volmer Studies)

Emission intensities were recorded using a Varian Cary Eclipse Fluorescence Spectrophotometer equipped with a Xenon flash lamp. All *fac*-Ir(ppy)$_3$ solutions were excited at 320 nm and the emission intensity was collected at 518 nm. In a typical experiment, the dichloromethane solution of *fac*-Ir(ppy)$_3$ (0.1 mM) was added the appropriate amount of quencher in a screw-top quartz cuvette. After degassing with nitrogen for 10 min, the emission spectra of the samples were collected.



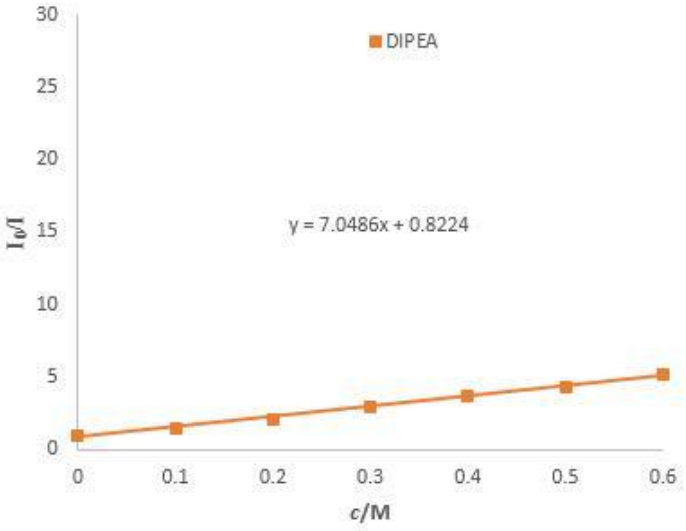
$I_0/I = 1 + K_q\tau_0[Q]$

$K_q\tau_0 = 3.5546 \times 10^3\ L \cdot mol^{-1}$

$\tau_0 = 1.9\ \mu s$

$K_q = 1.87 \times 10^9\ L \cdot mol^{-1} \cdot S^{-1}$

Scheme S1. *fac*-Ir(ppy)$_3$ Emission Quenching with different Components



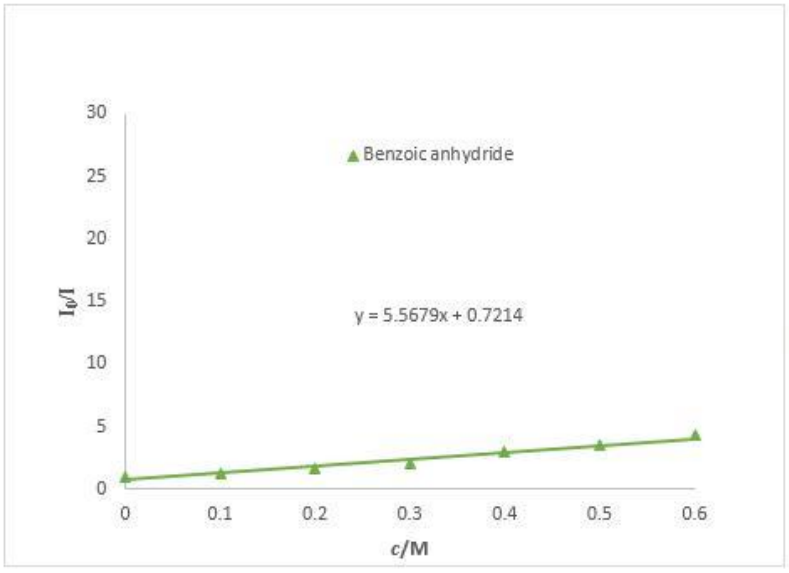
$I_0/I = 1 + K_q\tau_0[Q]$

$K_q\tau_0 = 7.0486\ L \cdot mol^{-1}$

$\tau_0 = 1.9\ \mu s$

$K_q = 3.71 \times 10^6\ L \cdot mol^{-1} \cdot S^{-1}$

Scheme S2. *fac*-Ir(ppy)$_3$ Emission Quenching with DIPEA



$I_0/I = 1 + K_q\tau_0[Q]$

$K_q\tau_0 = 5.5679\ L \cdot mol^{-1}$

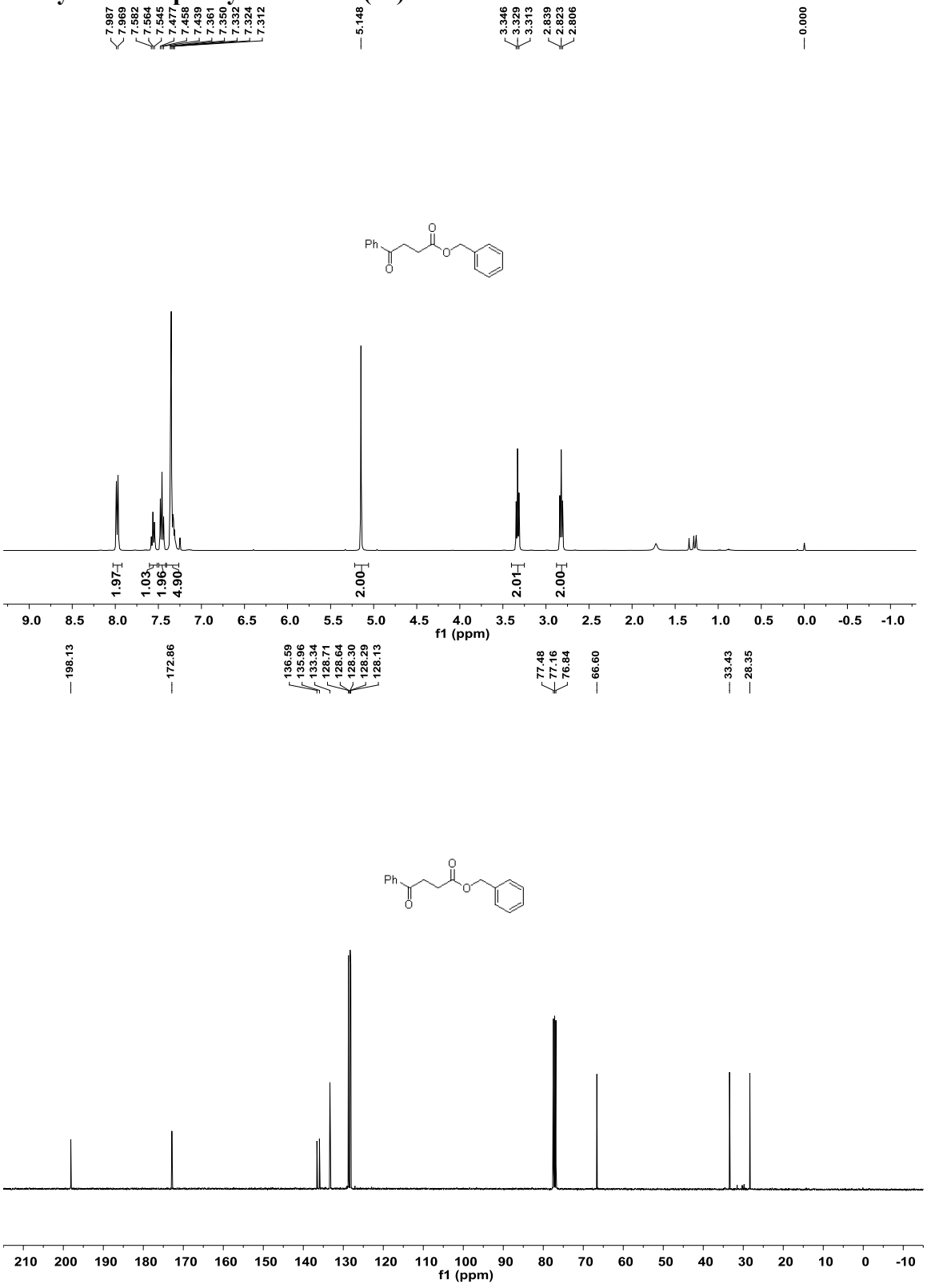
$\tau_0 = 1.9\ \mu s$

$K_q = 2.93 \times 10^6\ L \cdot mol^{-1} \cdot S^{-1}$

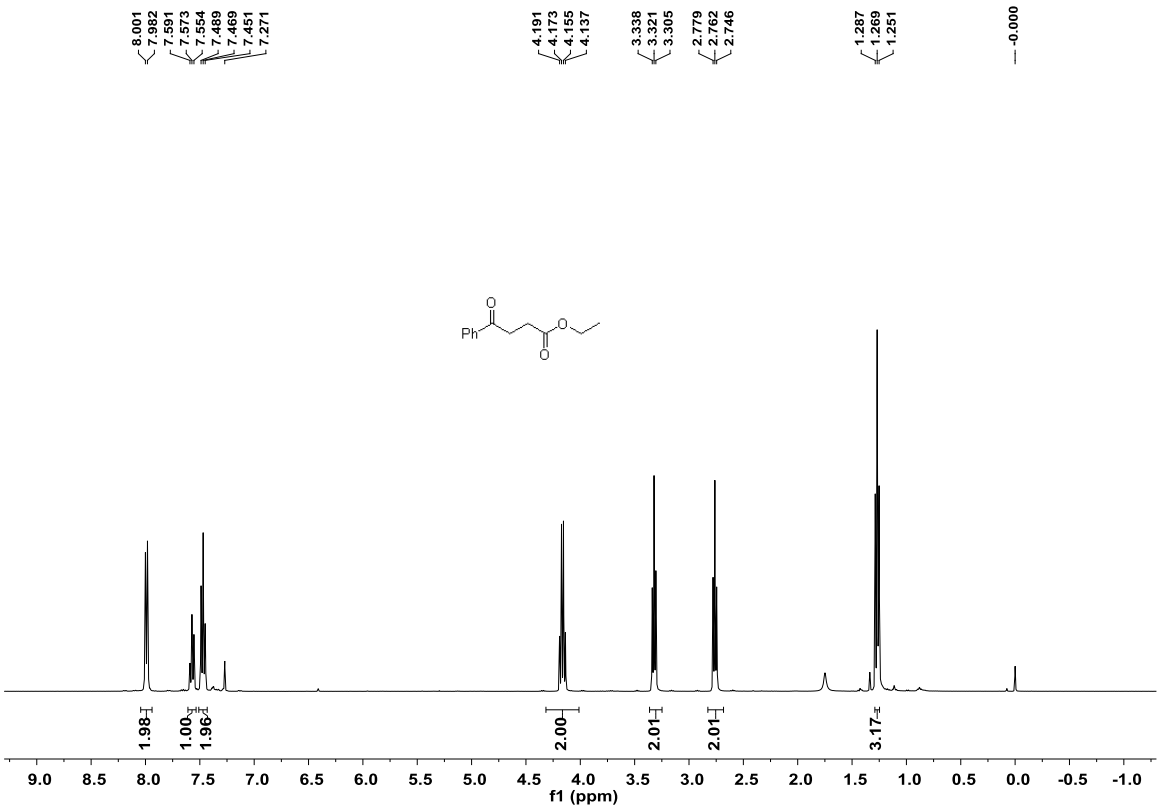
Scheme S3. *fac*-Ir(ppy)$_3$ Emission Quenching with Benzoic anhydride.

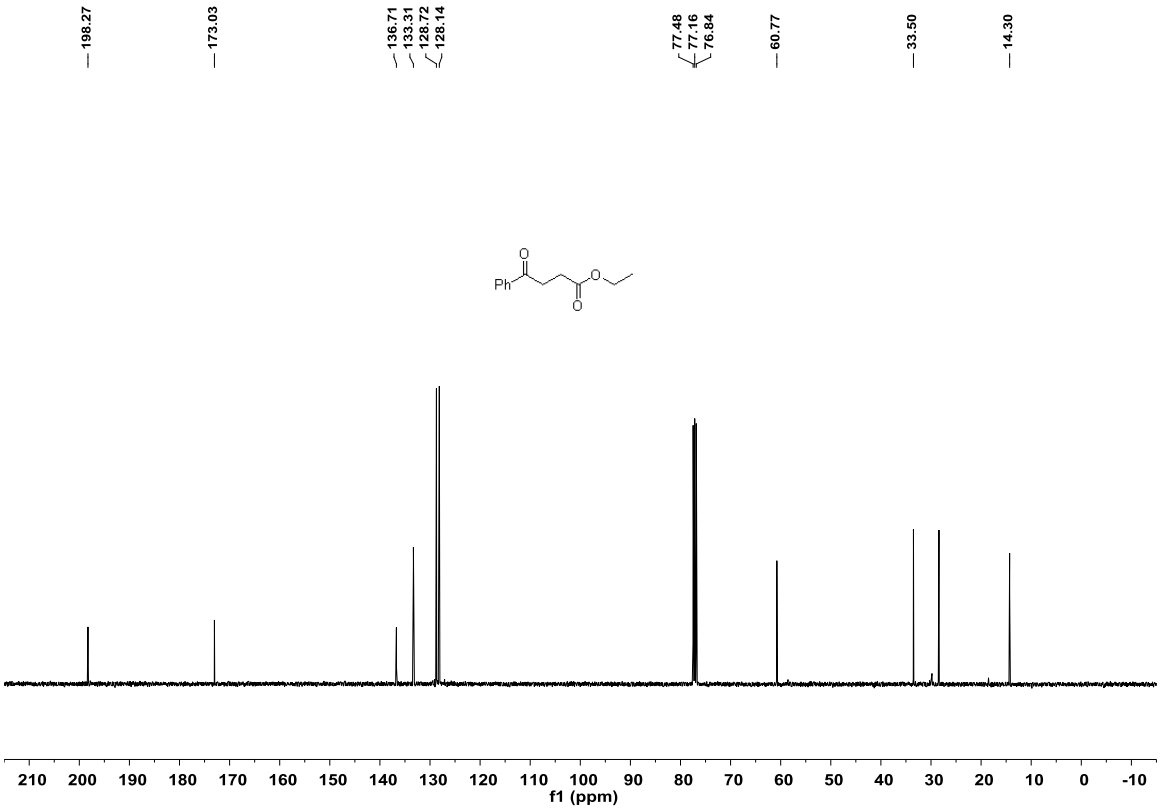
9. NMR Spectra of Products

Benzyl 4-oxo-4-phenylbutanoate (3a)

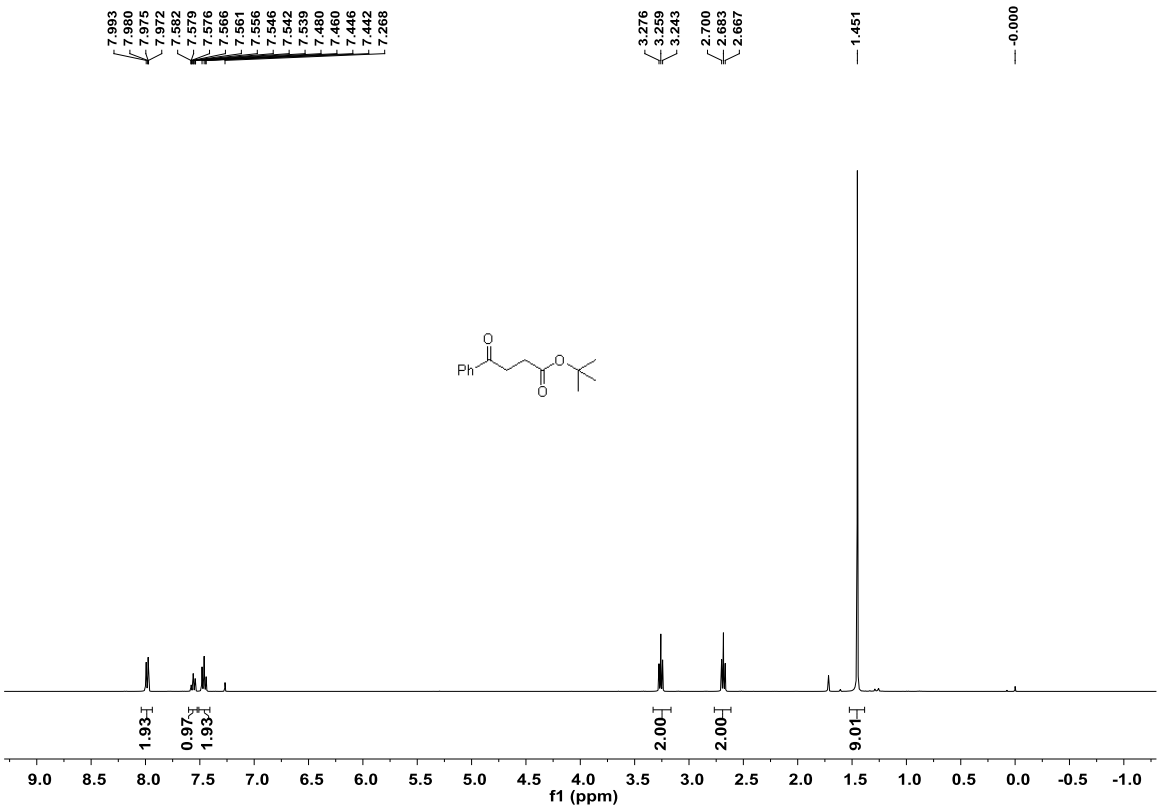


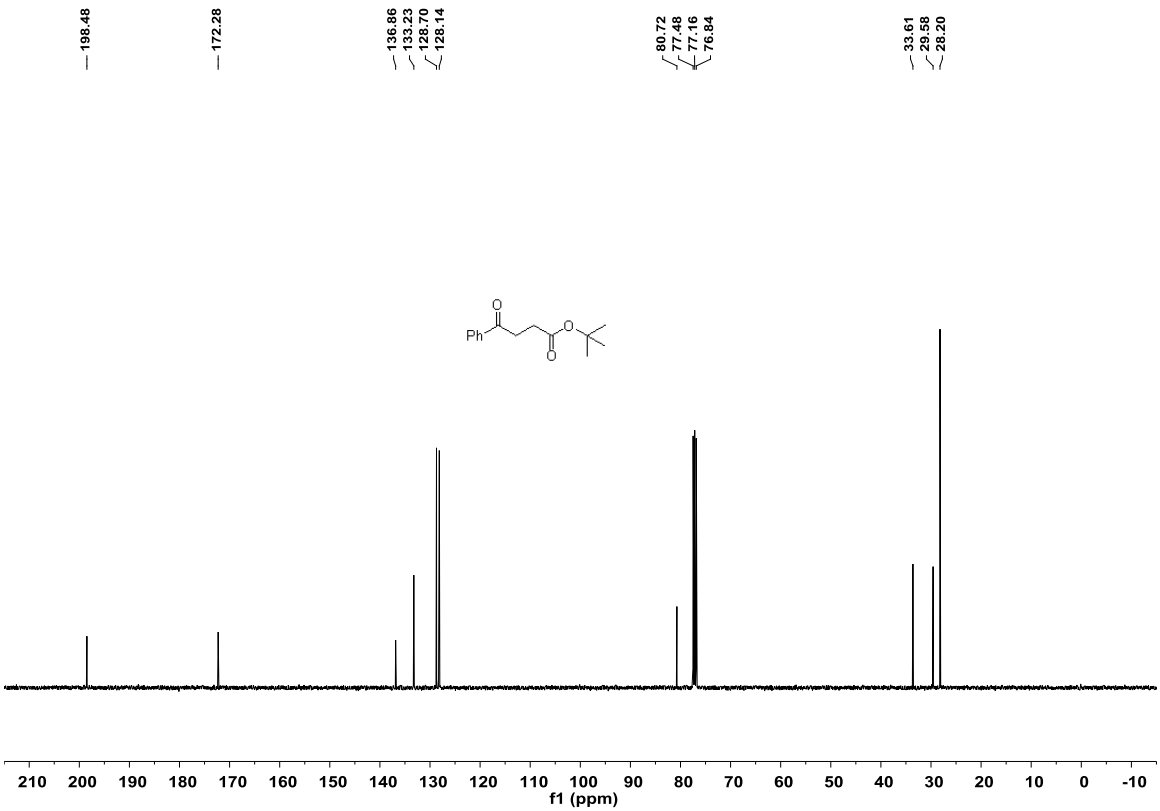
Ethyl 4-oxo-4-phenylbutanoate (3b)



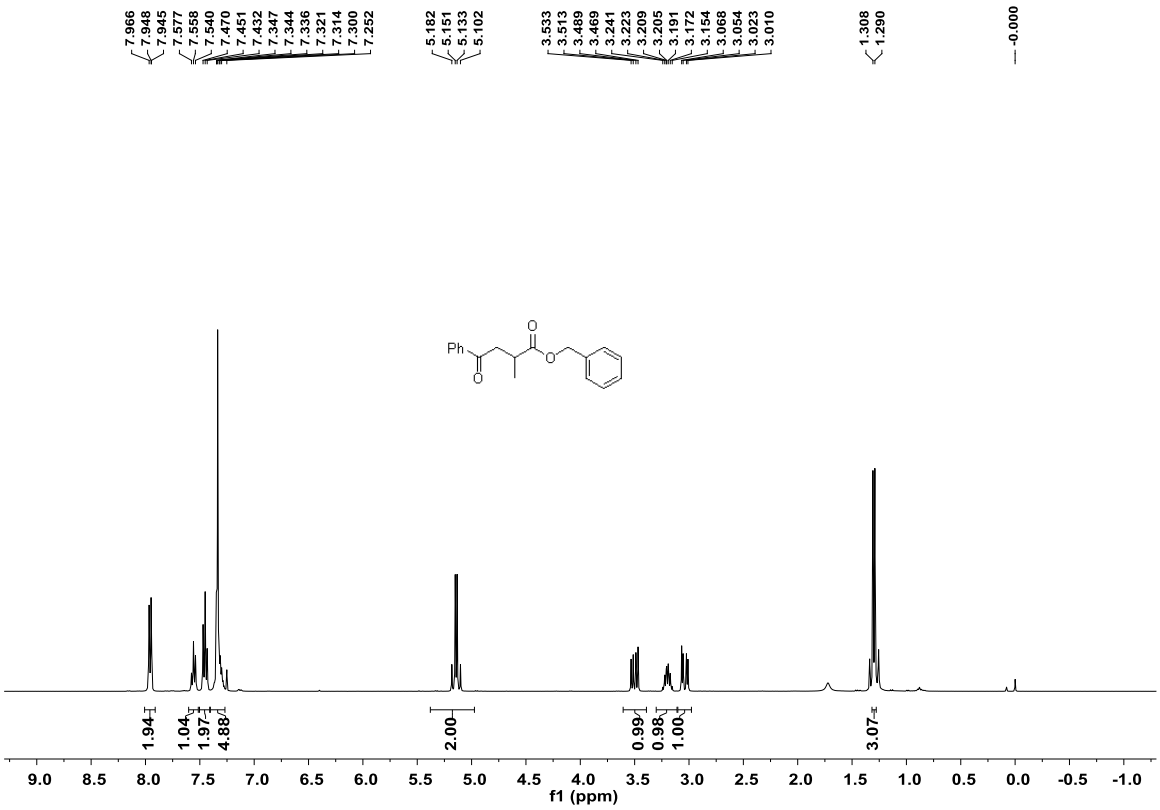


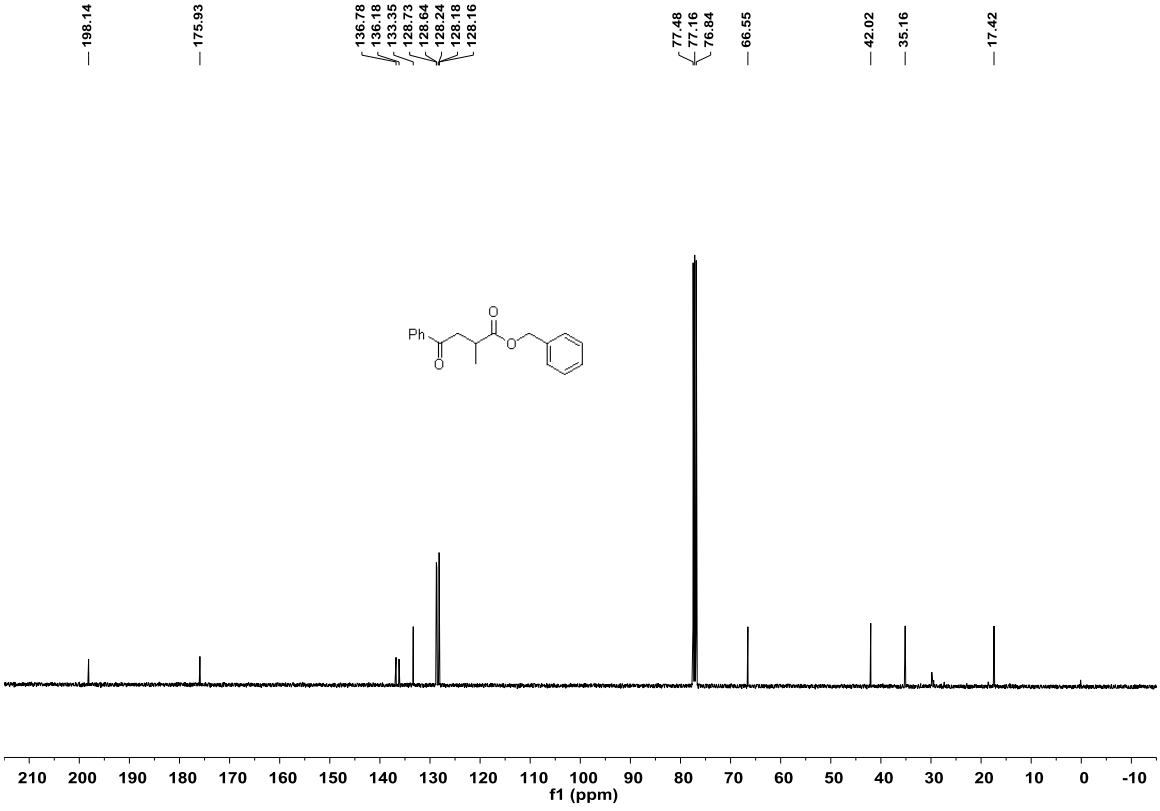
Tert-butyl 4-oxo-4-phenylbutanoate (3c)



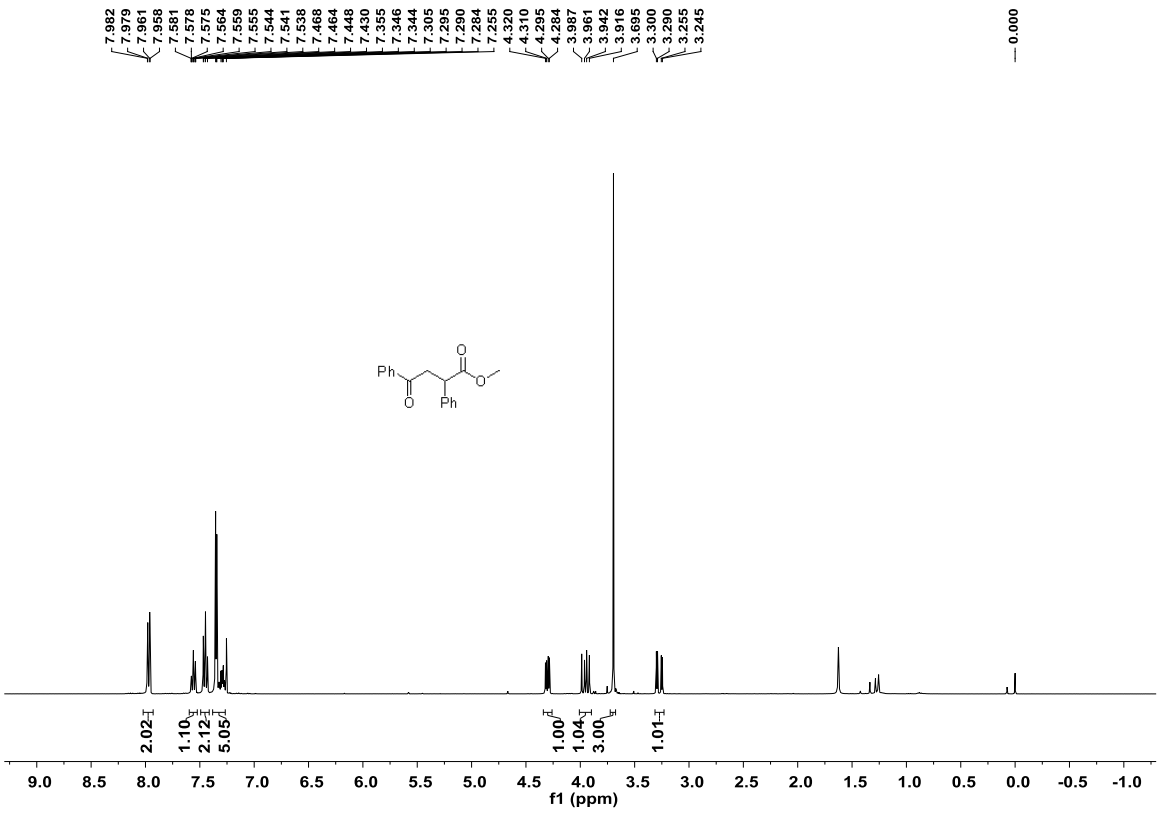


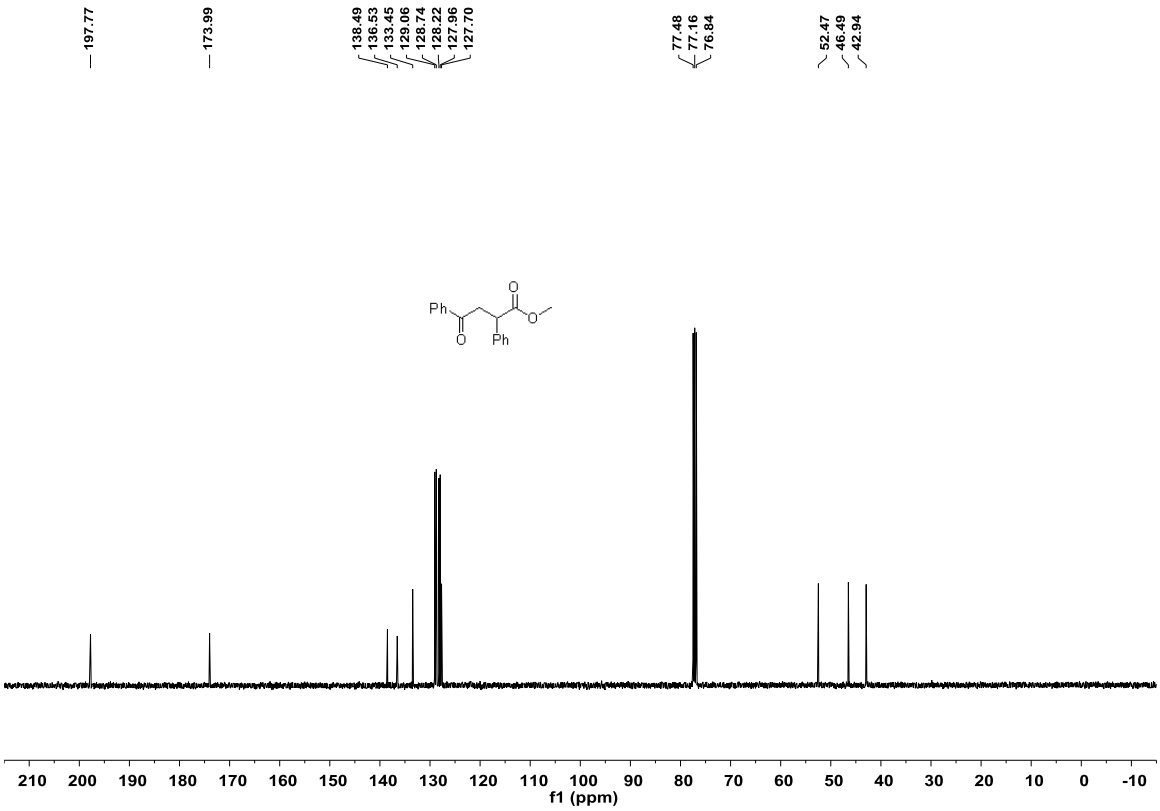
Benzyl 2-methyl-4-oxo-4-phenylbutanoate (3d)



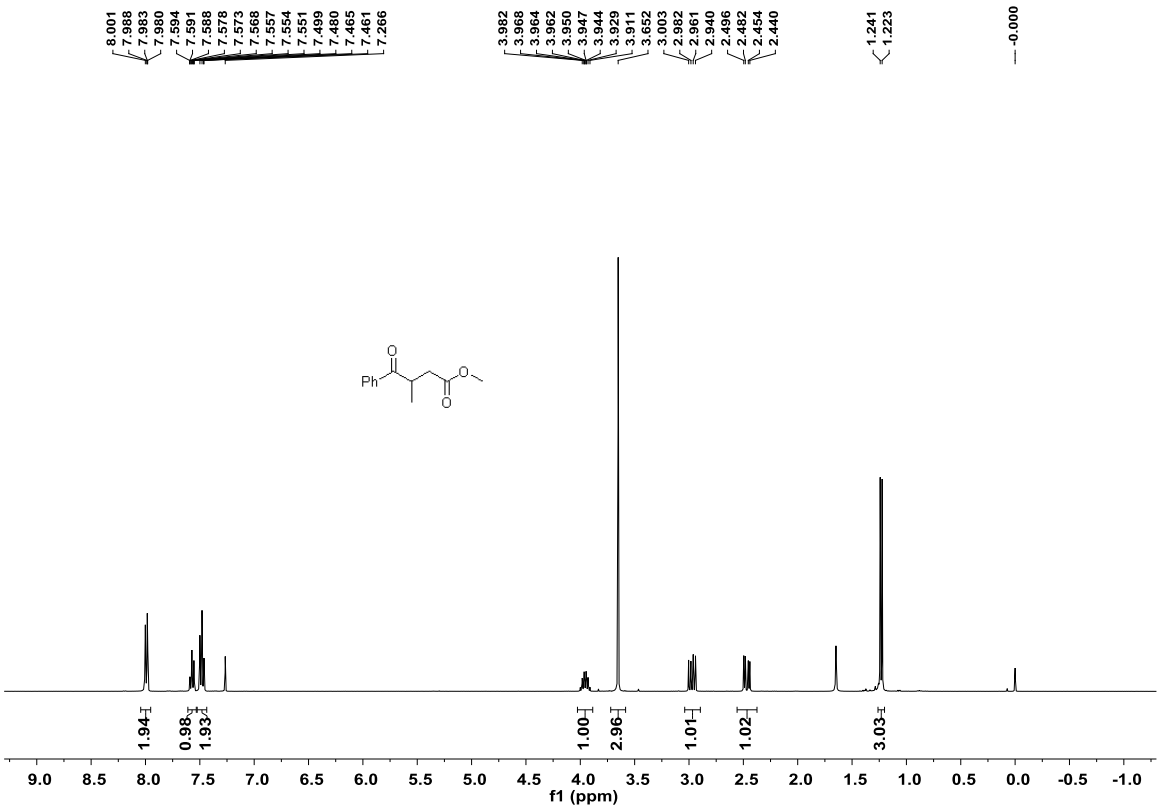


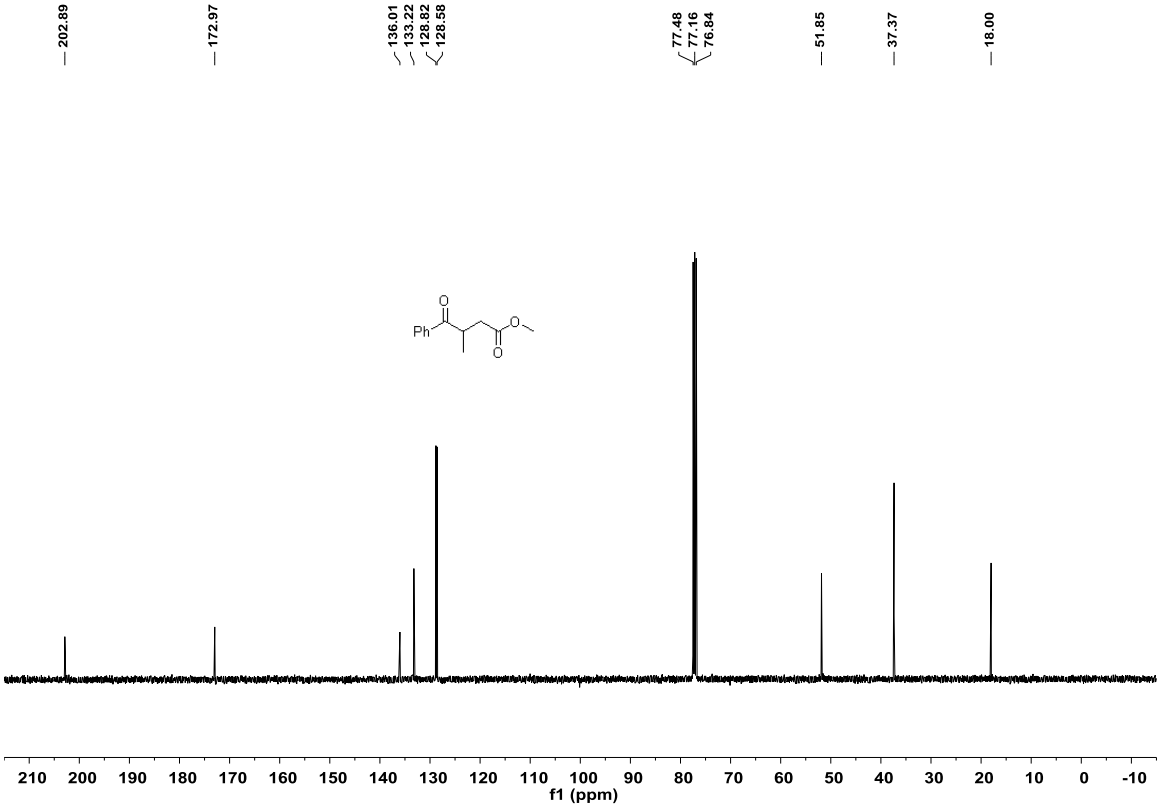
Methyl 4-oxo-2,4-diphenylbutanoate (3e)



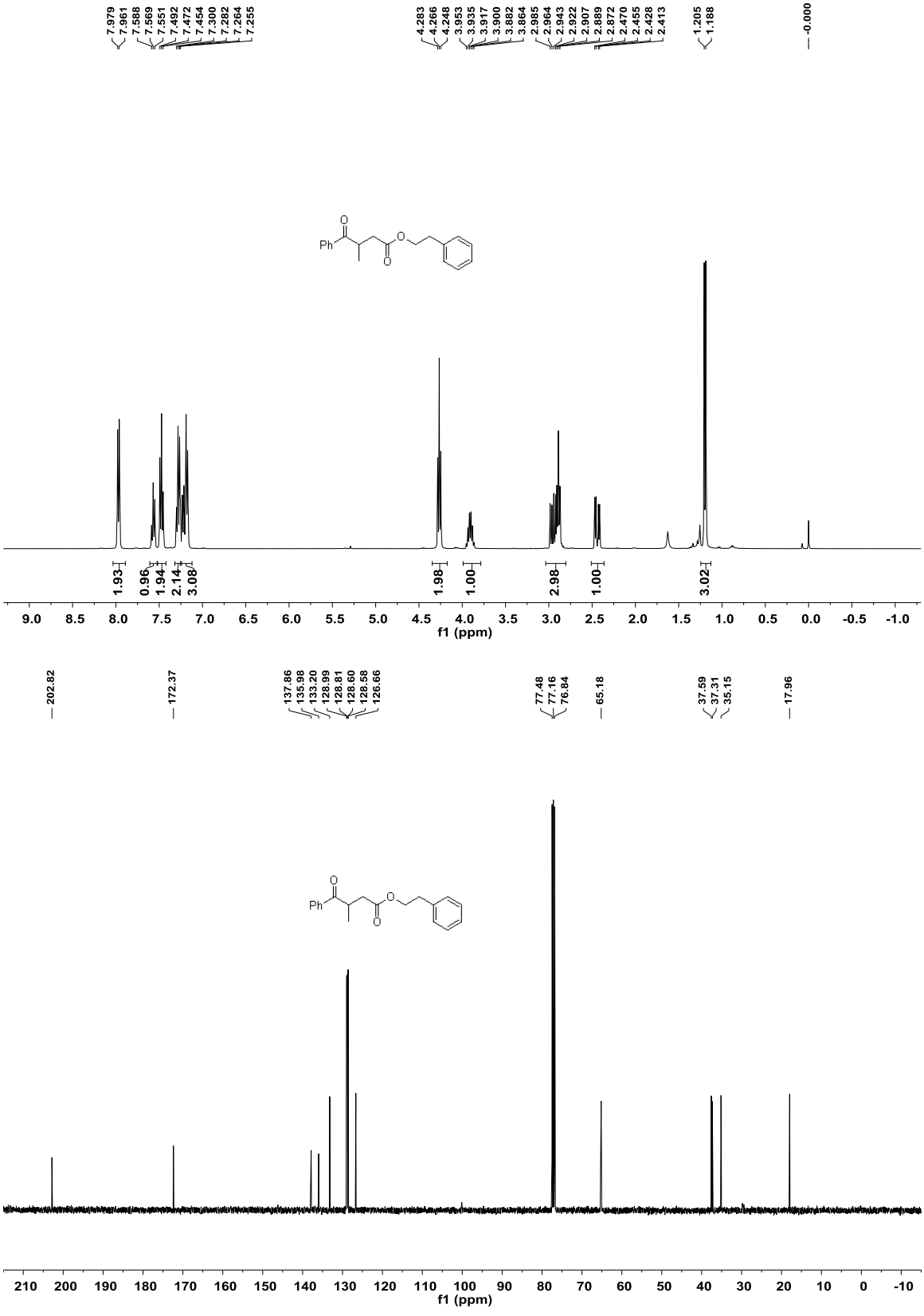


Methyl 4-oxo-2,4-diphenylbutanoate (3f)

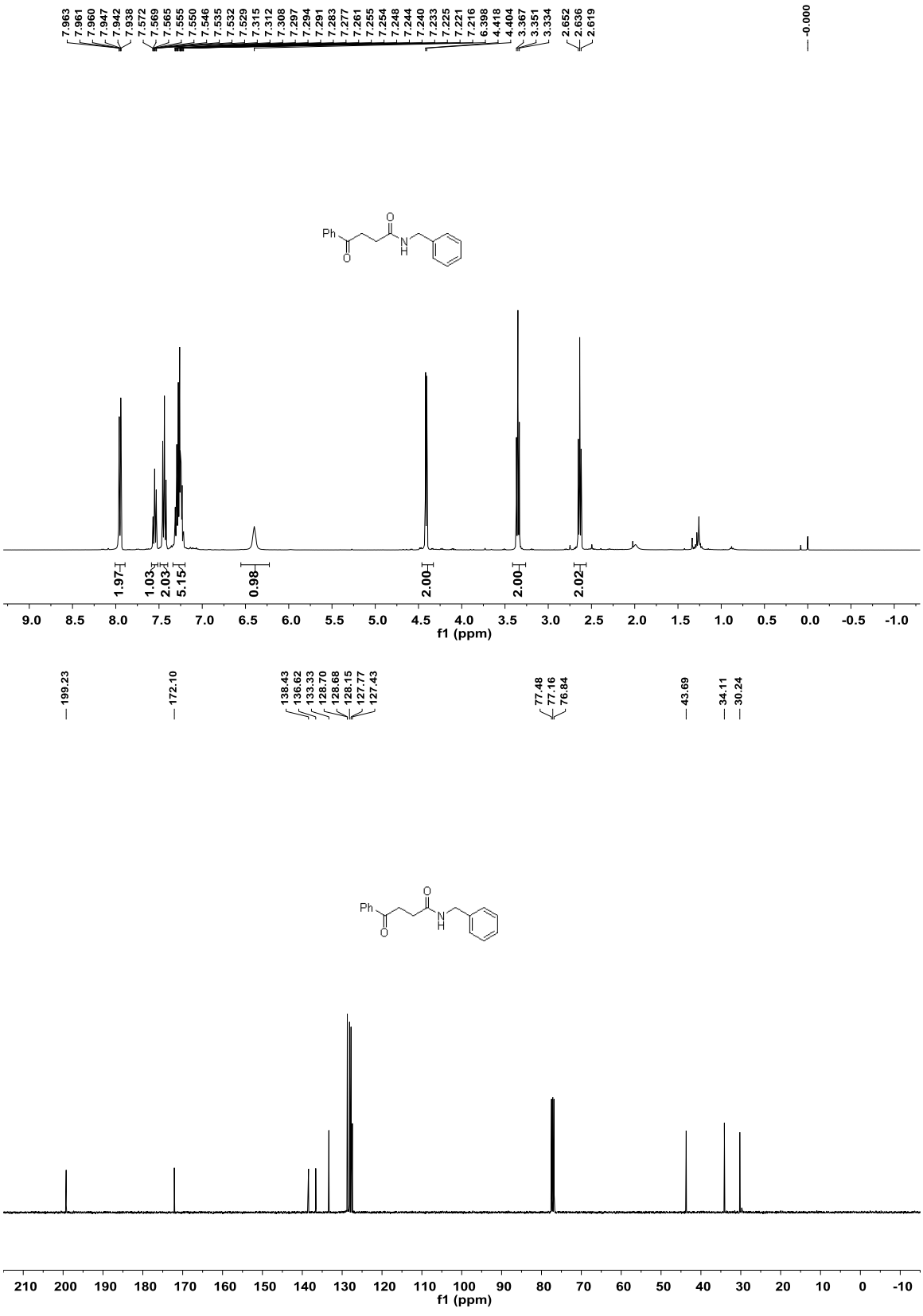




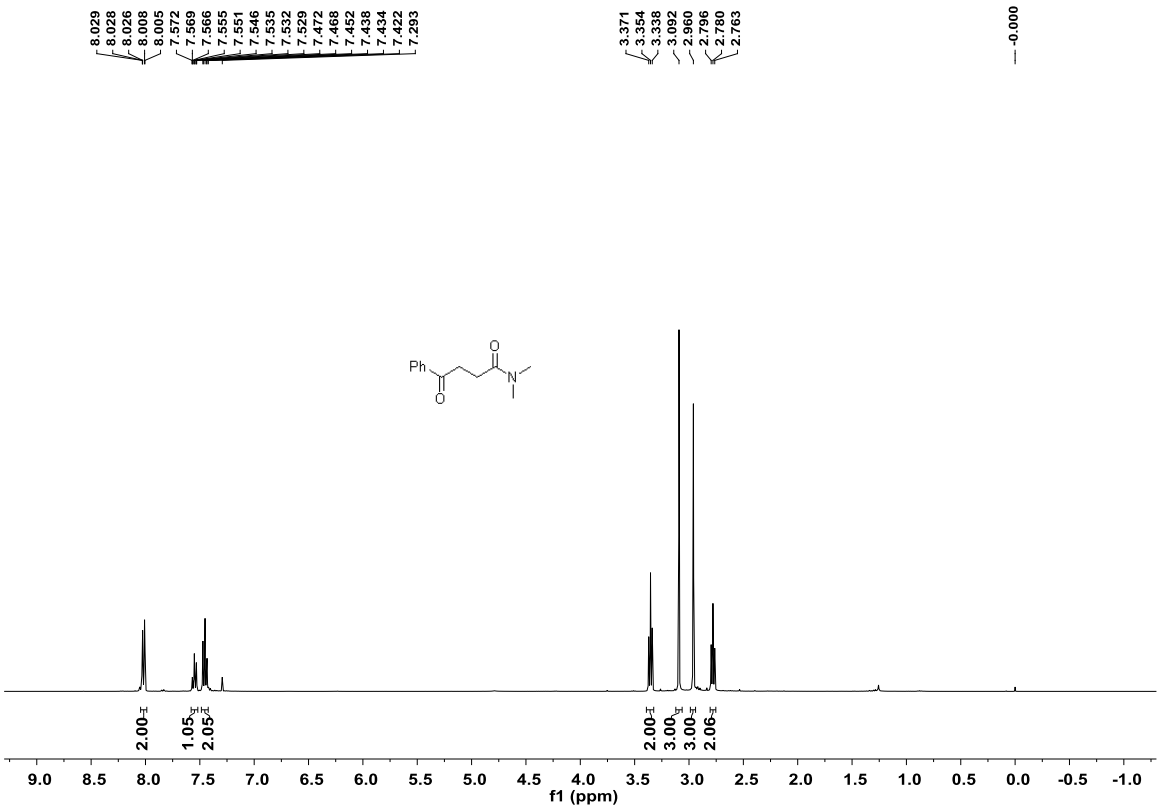
Phenethyl 3-methyl-4-oxo-4-phenylbutanoate (3g)

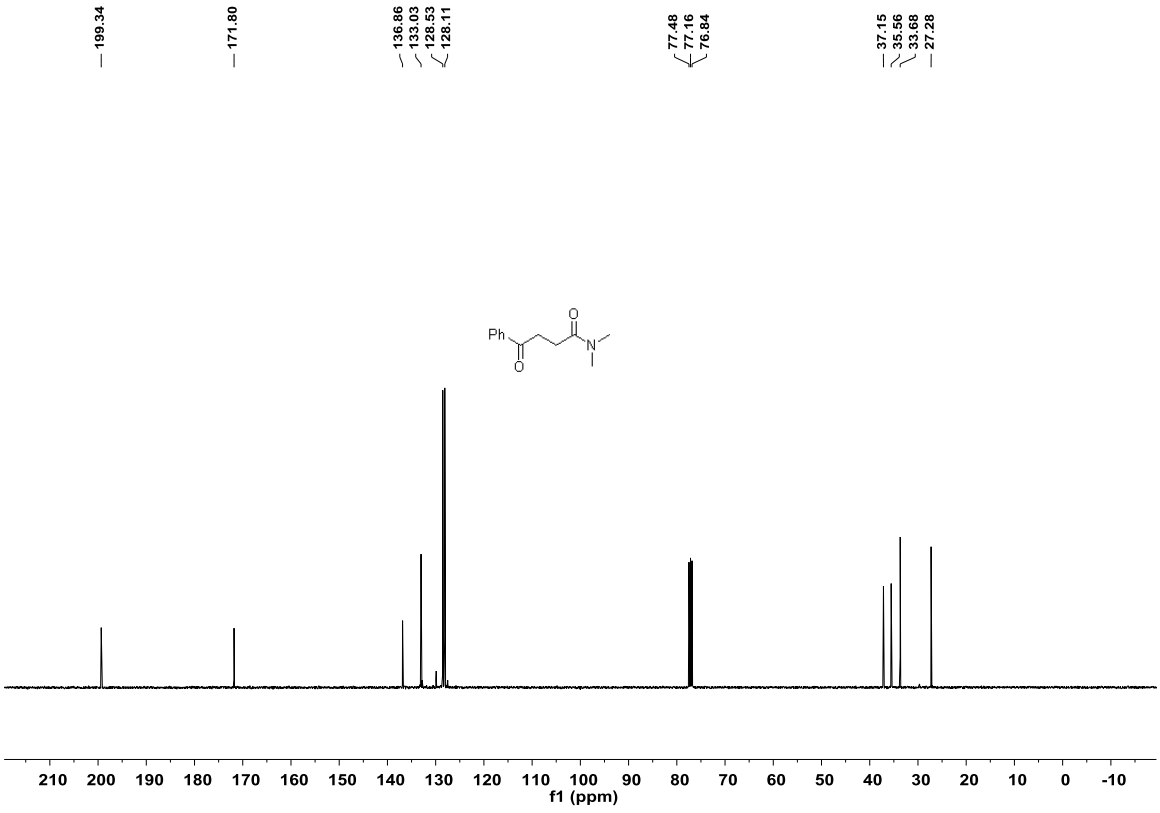


N-benzyl-4-oxo-4-phenylbutanamide (3h)

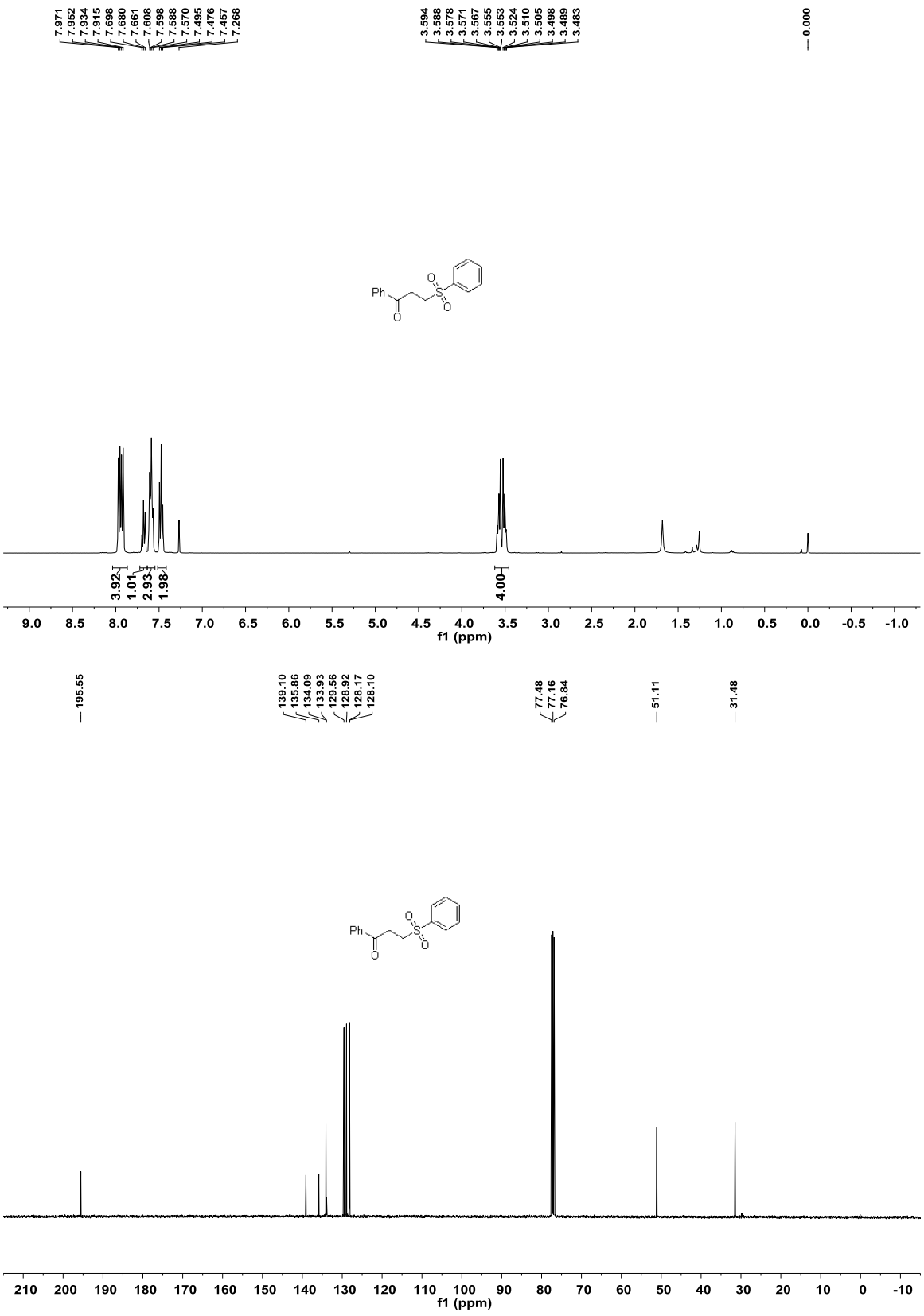


N,N-dimethyl-4-oxo-4-phenylbutanamide (3i)

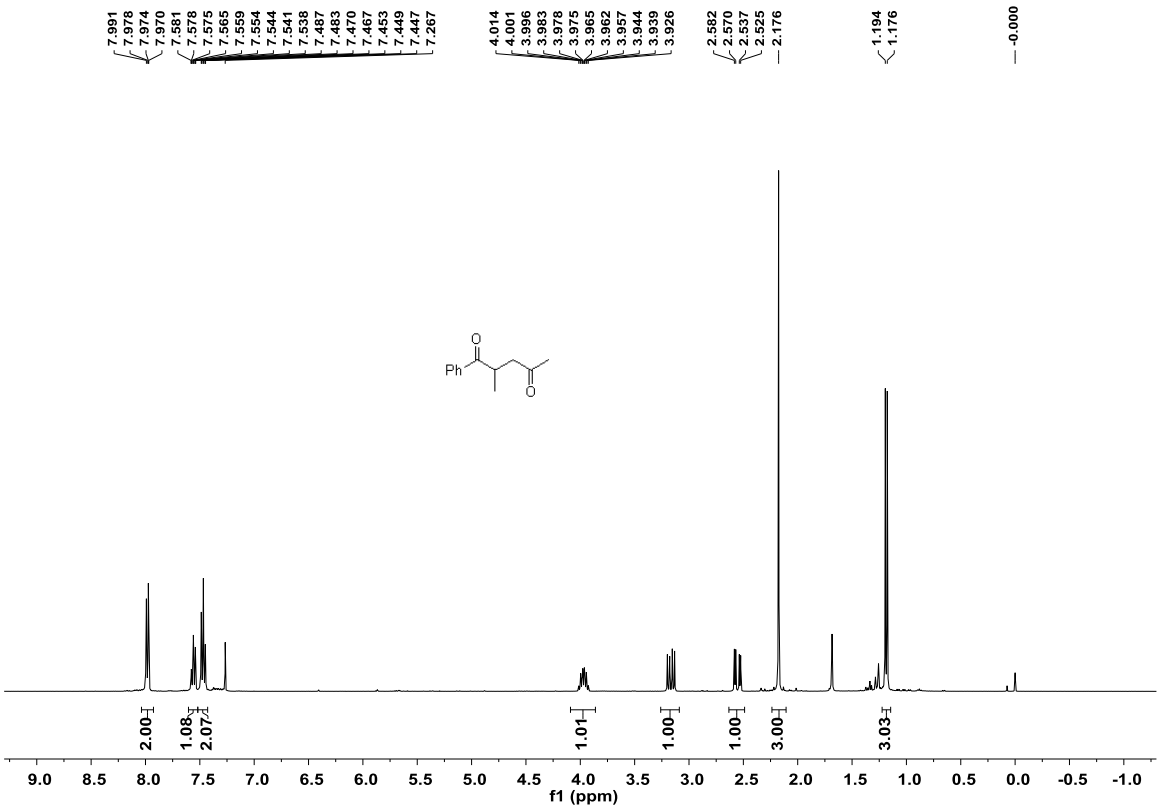


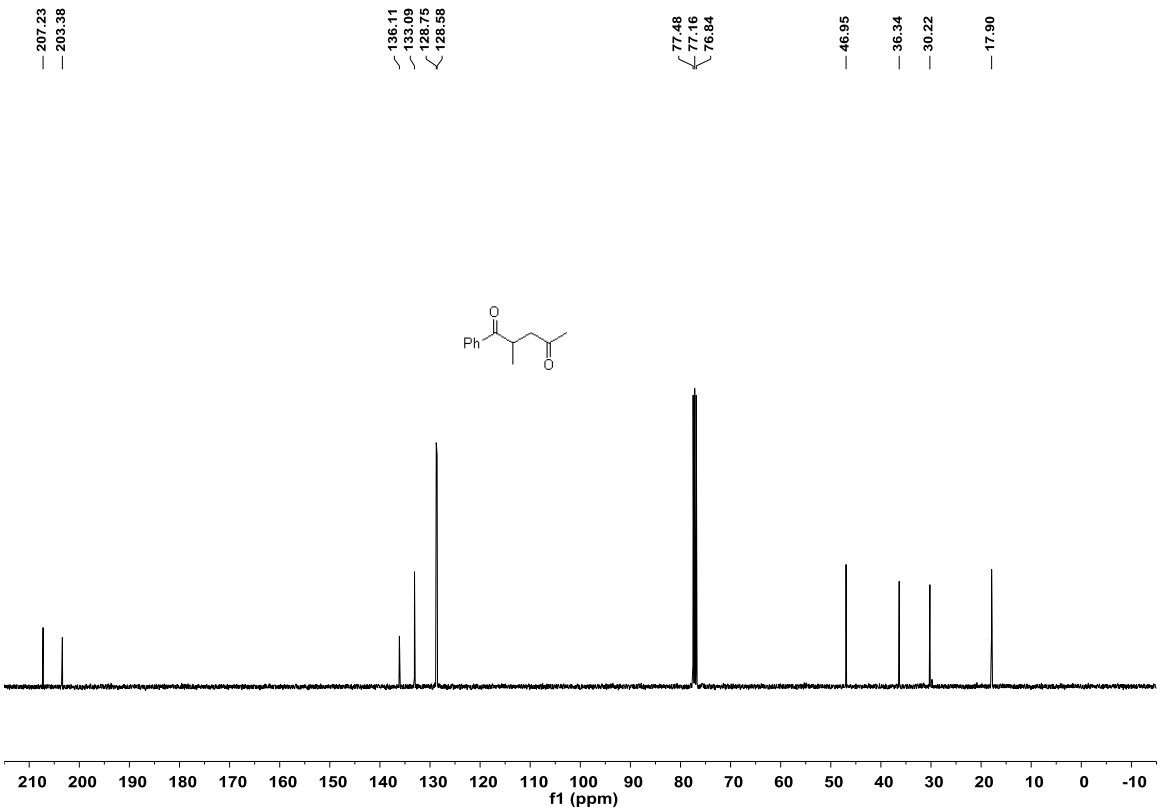


1-phenyl-3-(phenylsulfonyl)propan-1-one (3j)

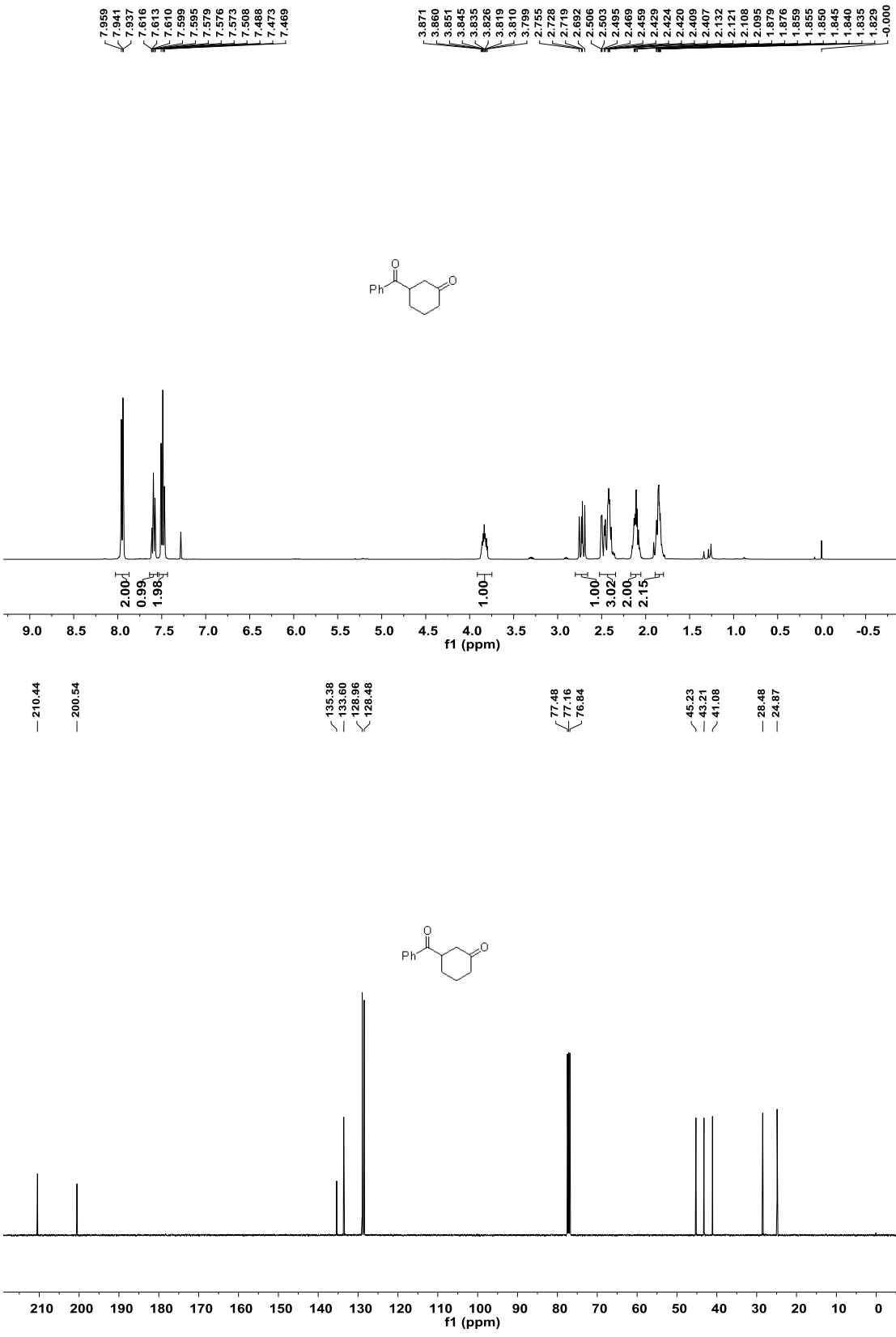


2-methyl-1-phenylpentane-1,4-dione (3k)

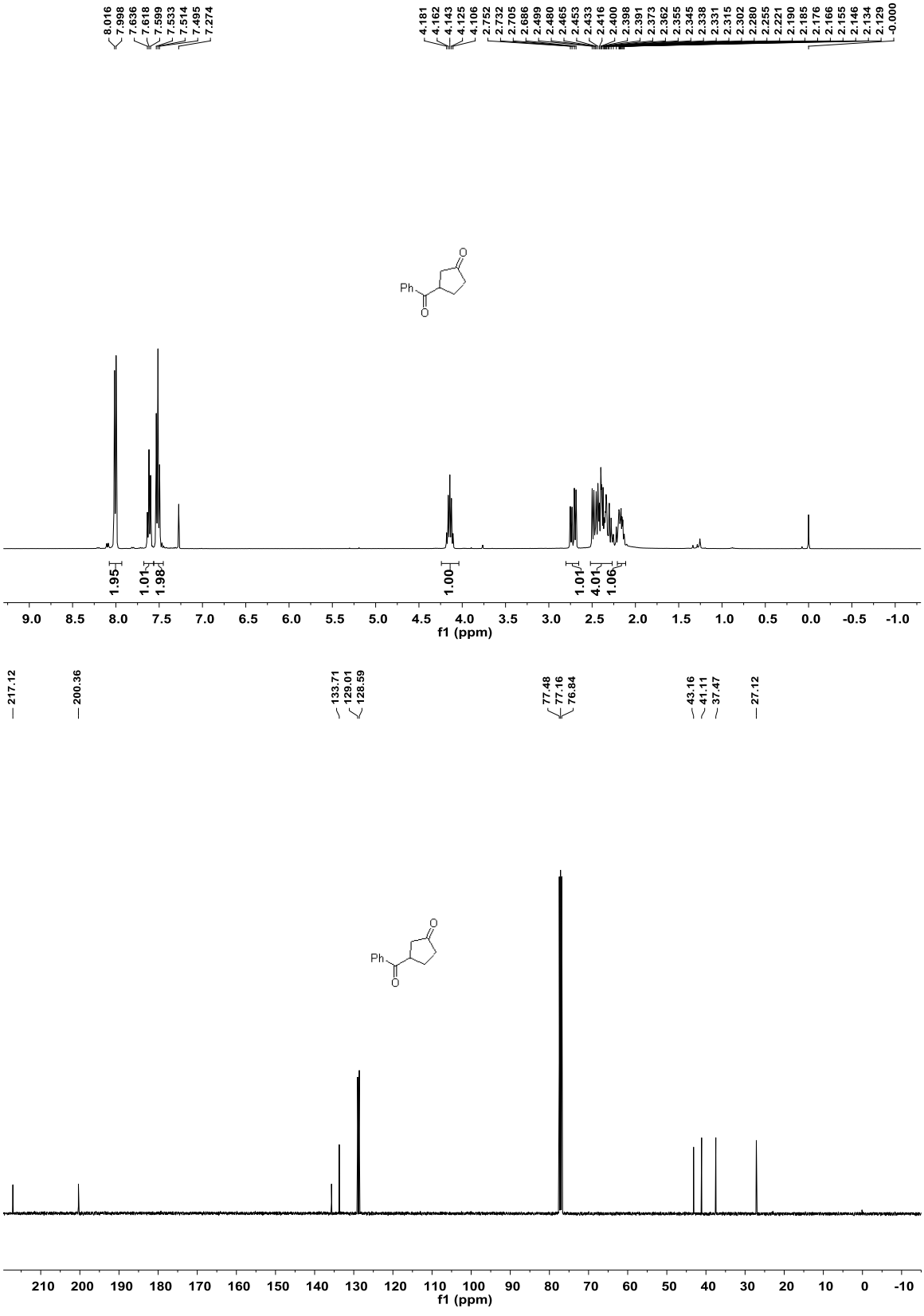




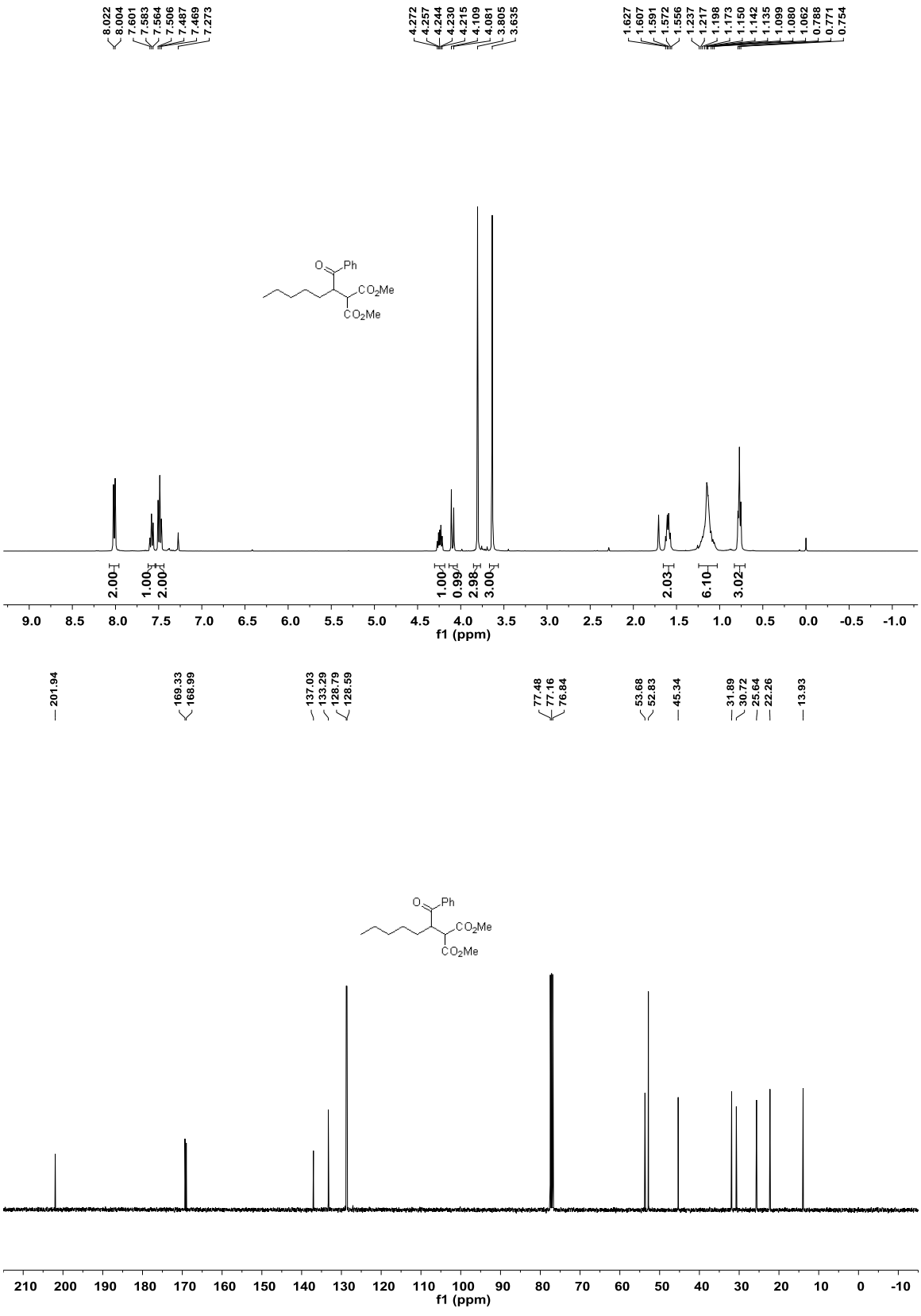
3-benzoylcyclohexan-1-one (3l)



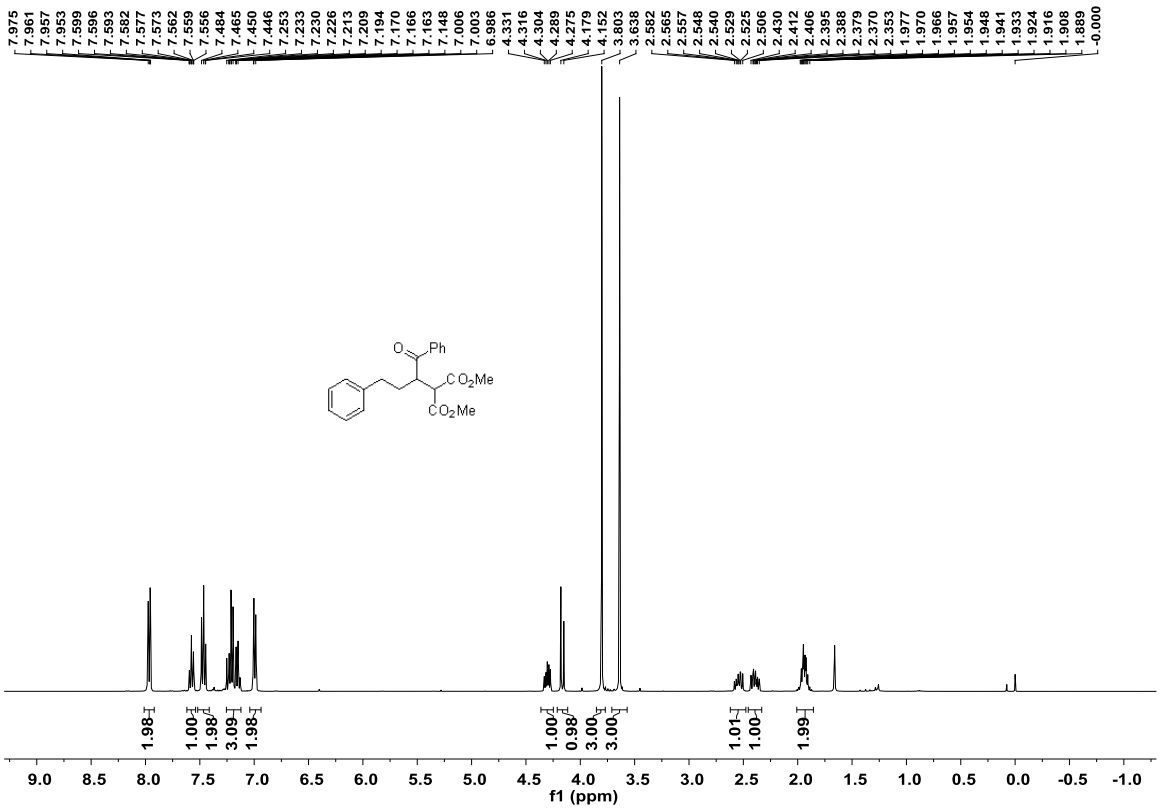
3-benzoylcyclopentan-1-one (3m)

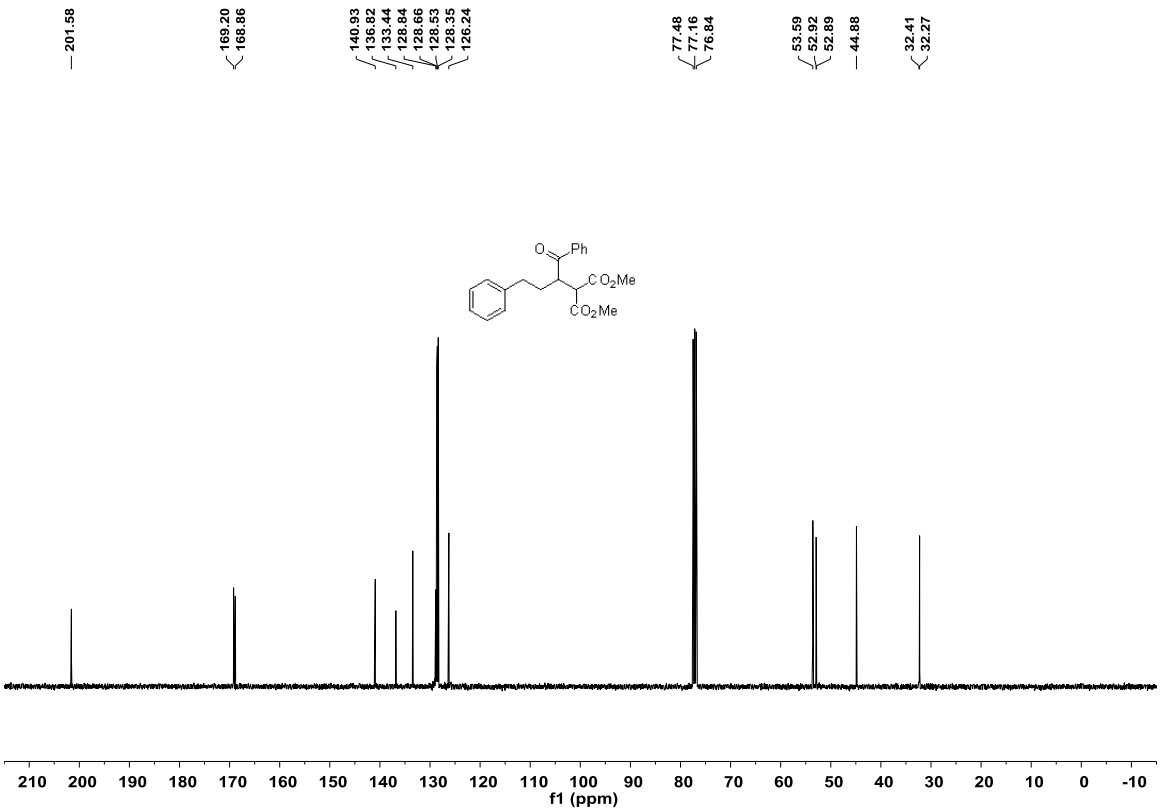


Dimethyl 2-(1-oxo-1-phenylheptan-2-yl)malonate (3n)

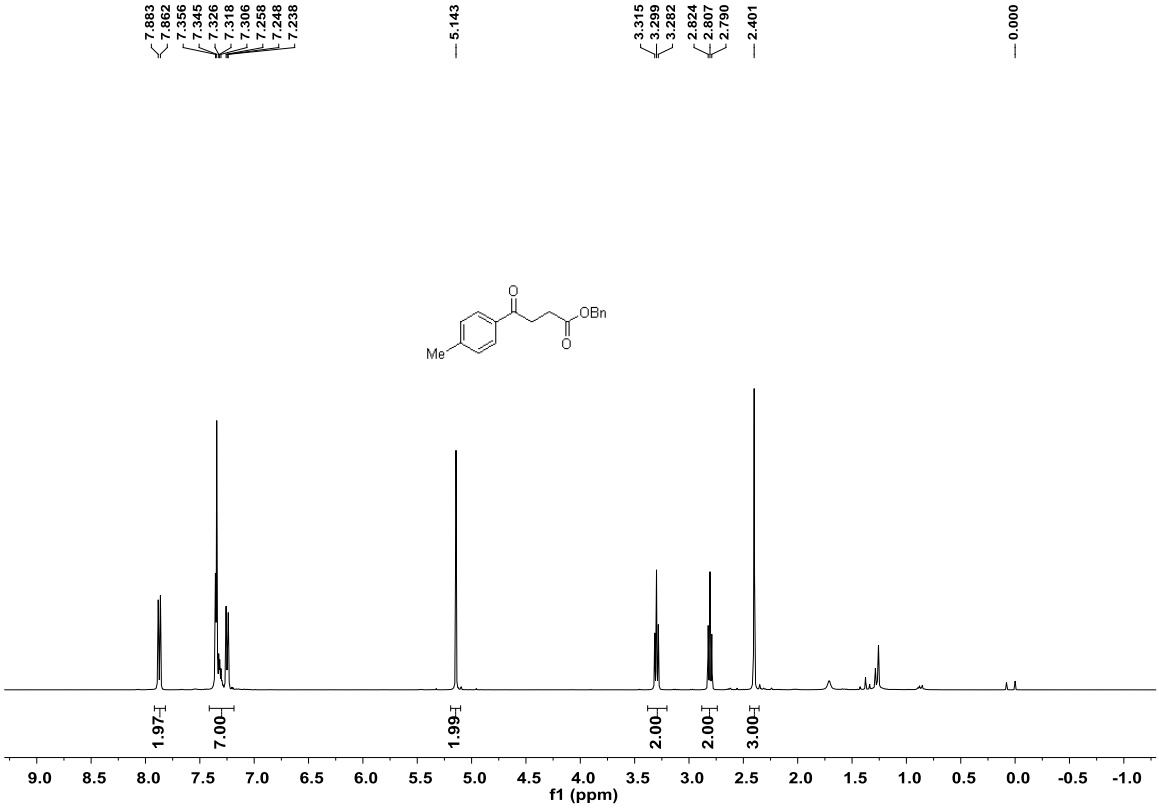


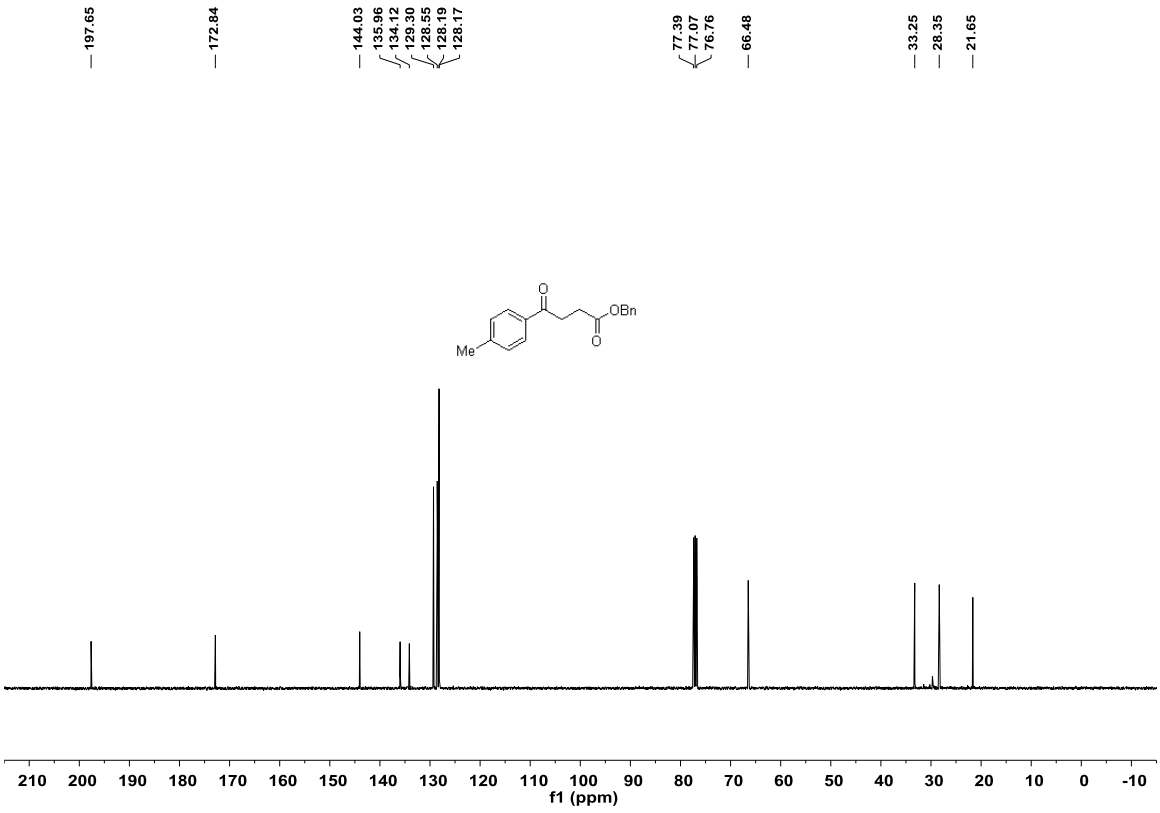
Dimethyl 2-(1-oxo-1,4-diphenylbutan-2-yl)malonate (3o)



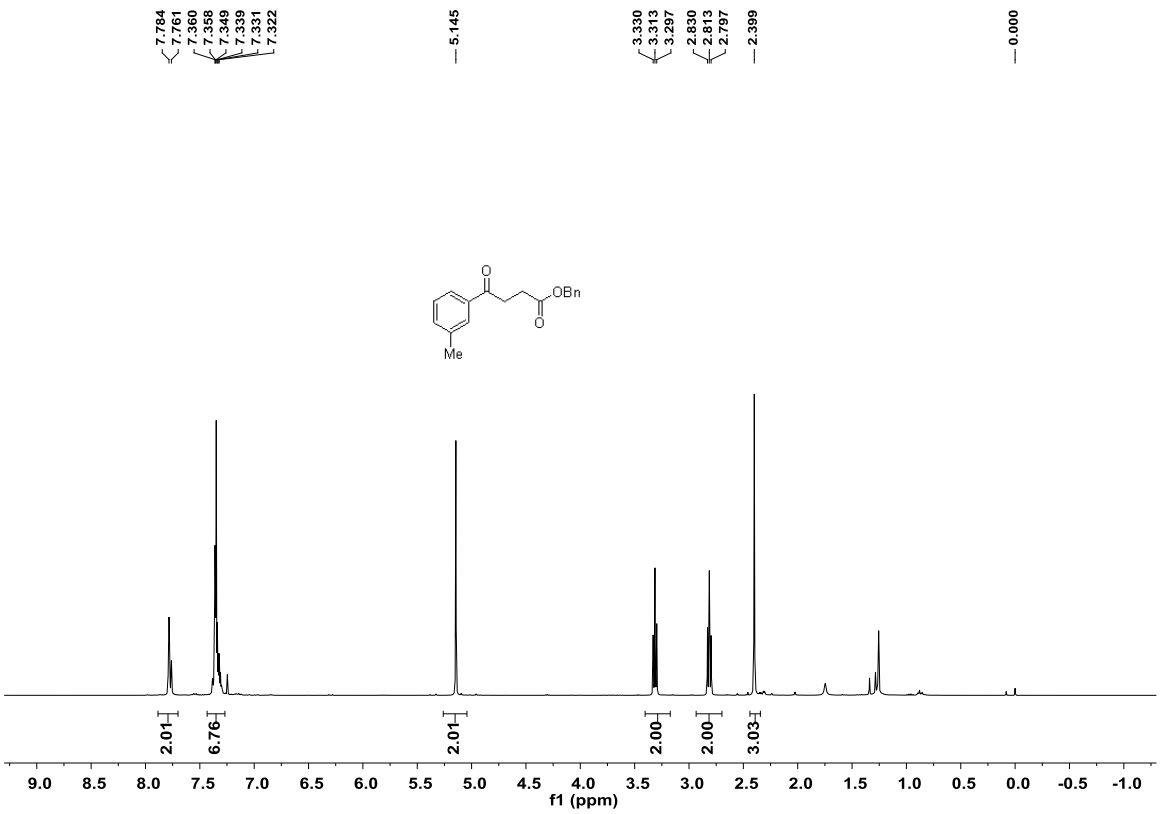


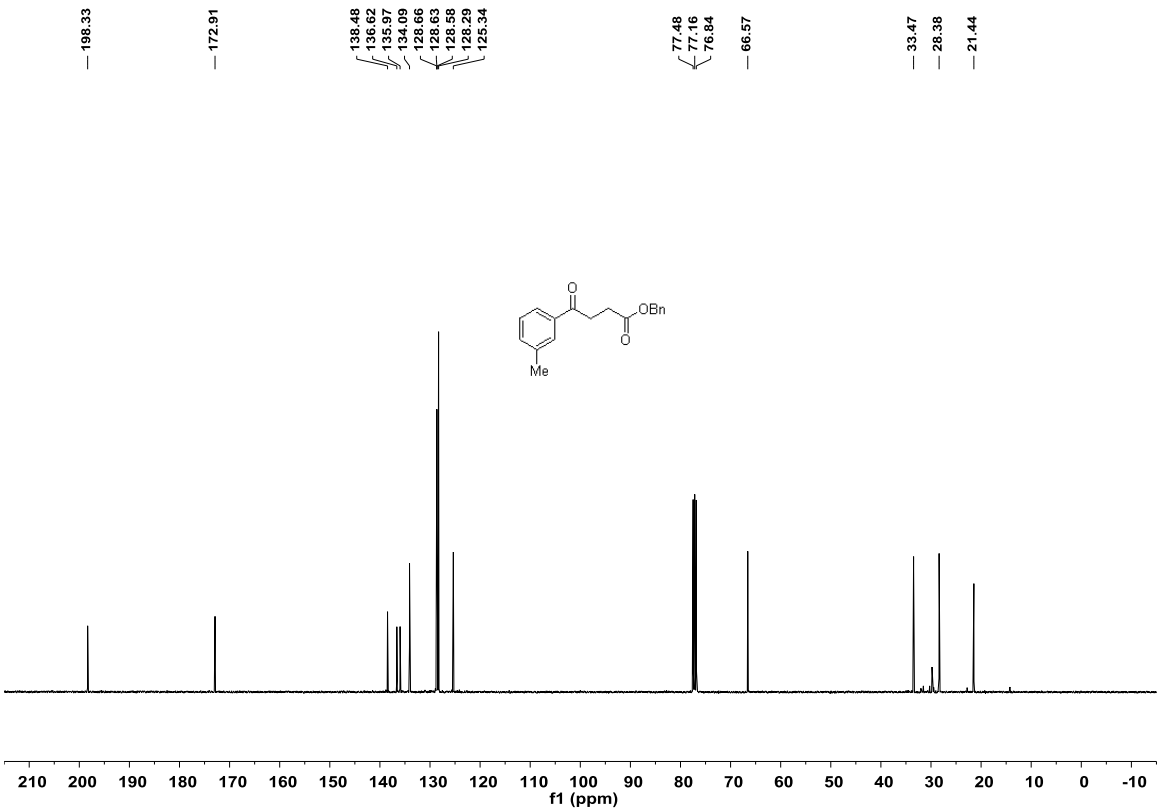
Benzyl 4-oxo-4-(p-tolyl)butanoate (3p)



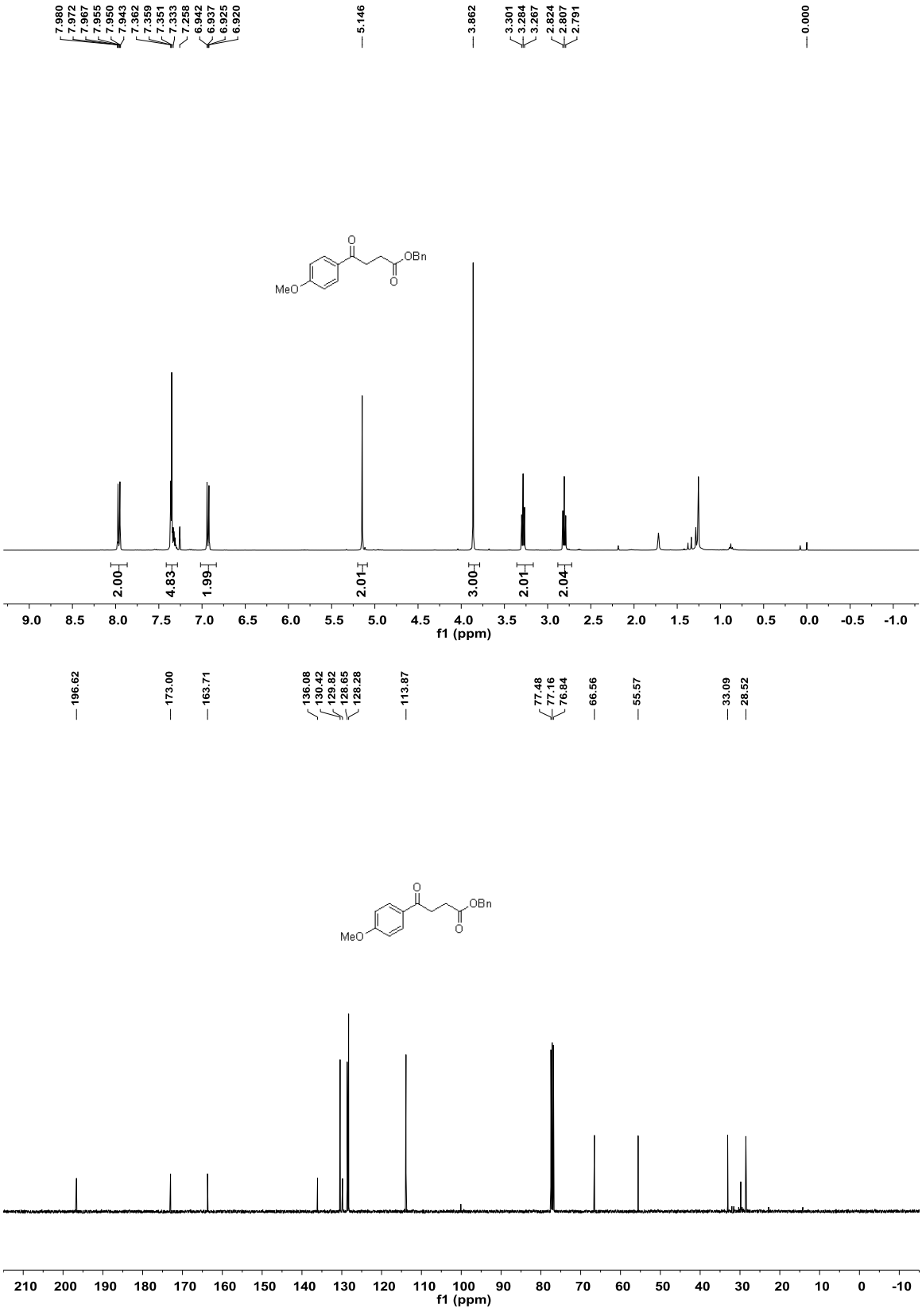


Benzyl 4-oxo-4-(m-tolyl)butanoate (3q)

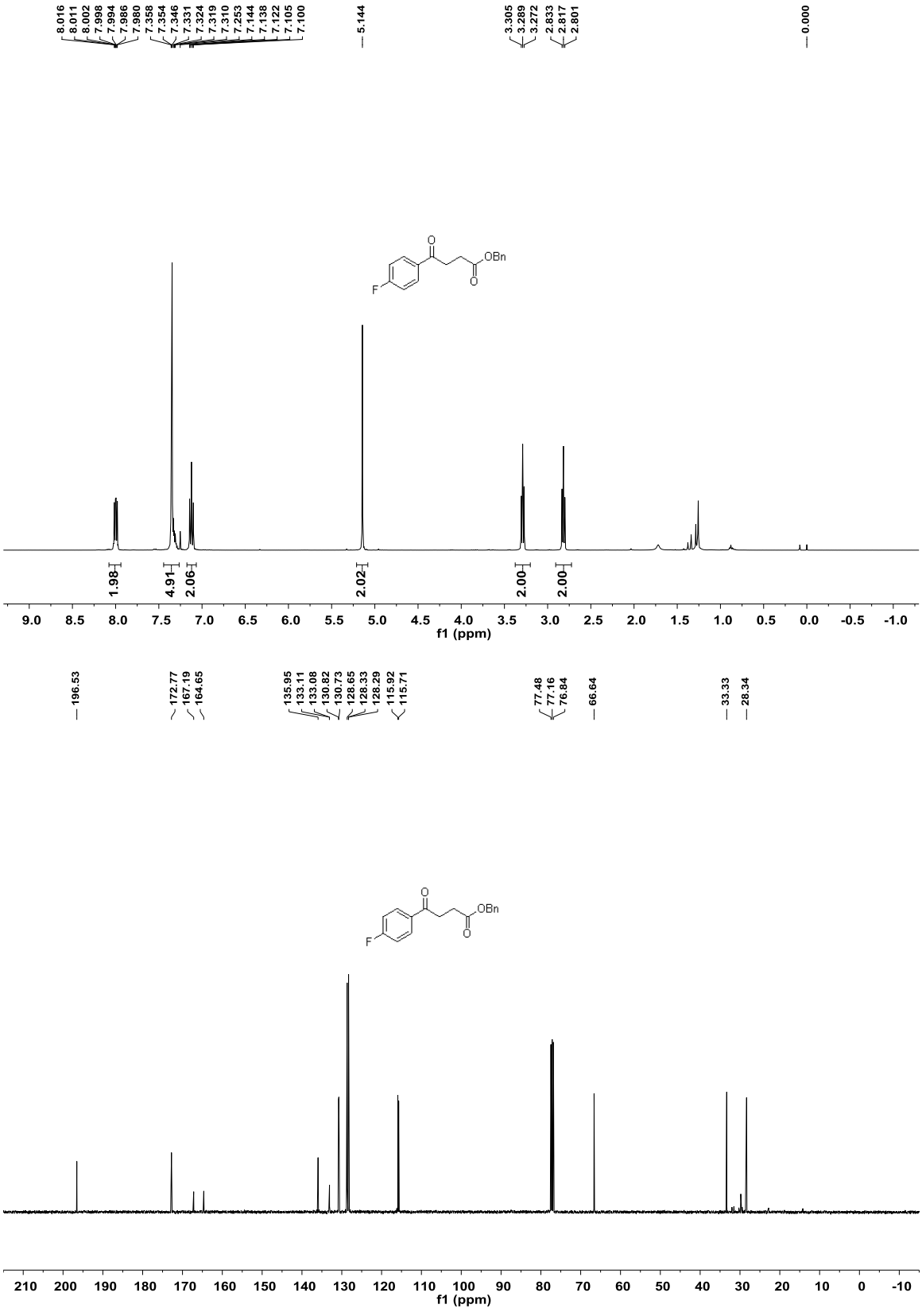


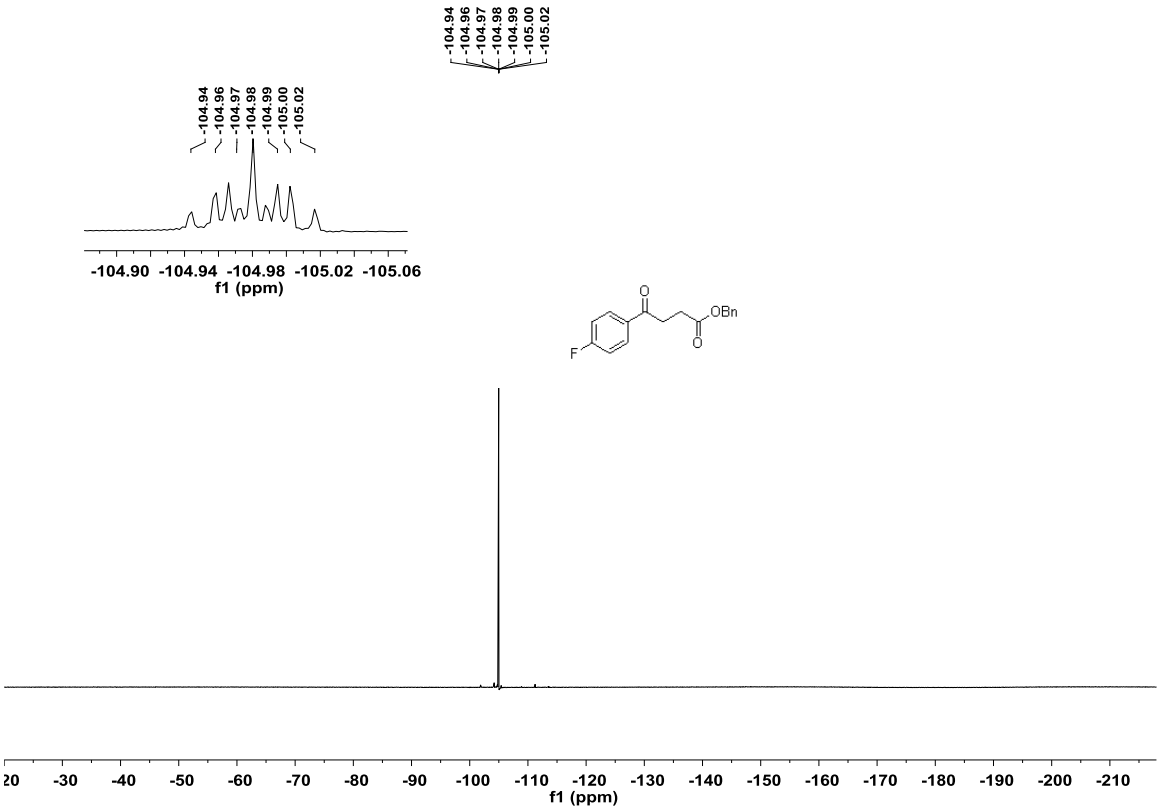


Benzyl 4-(4-methoxyphenyl)-4-oxobutanoate (3r)

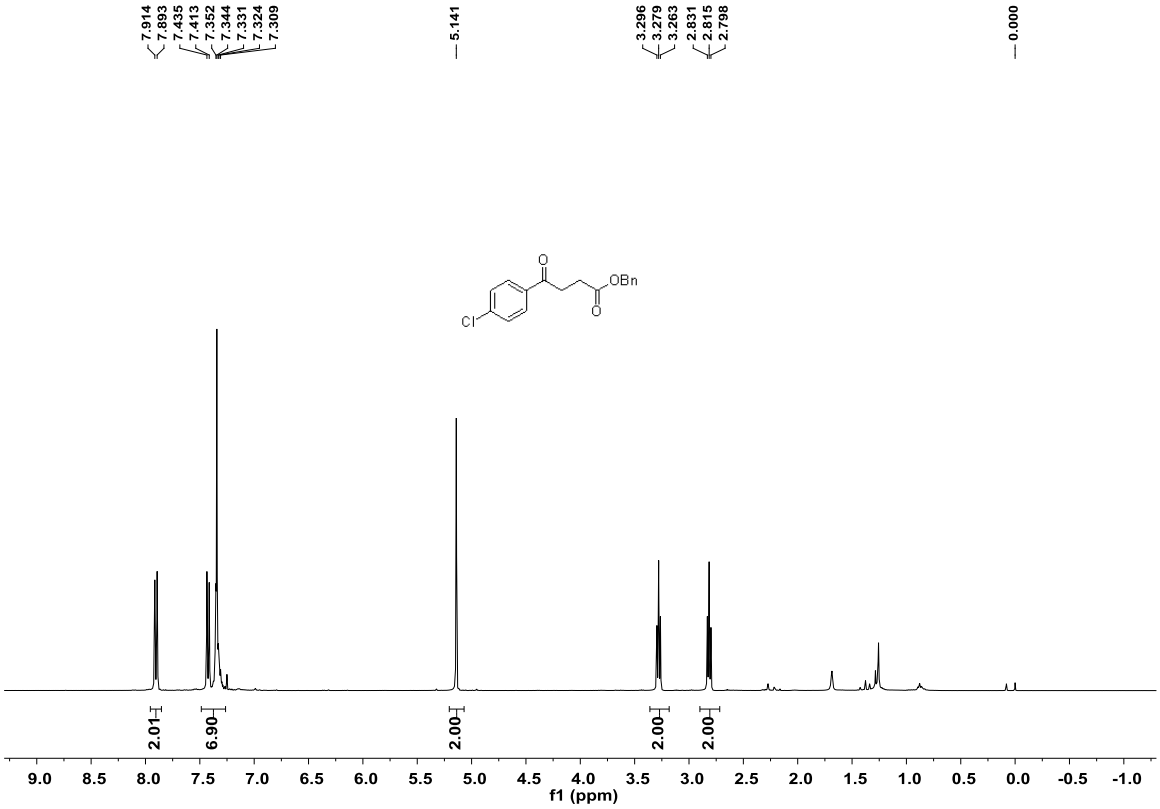


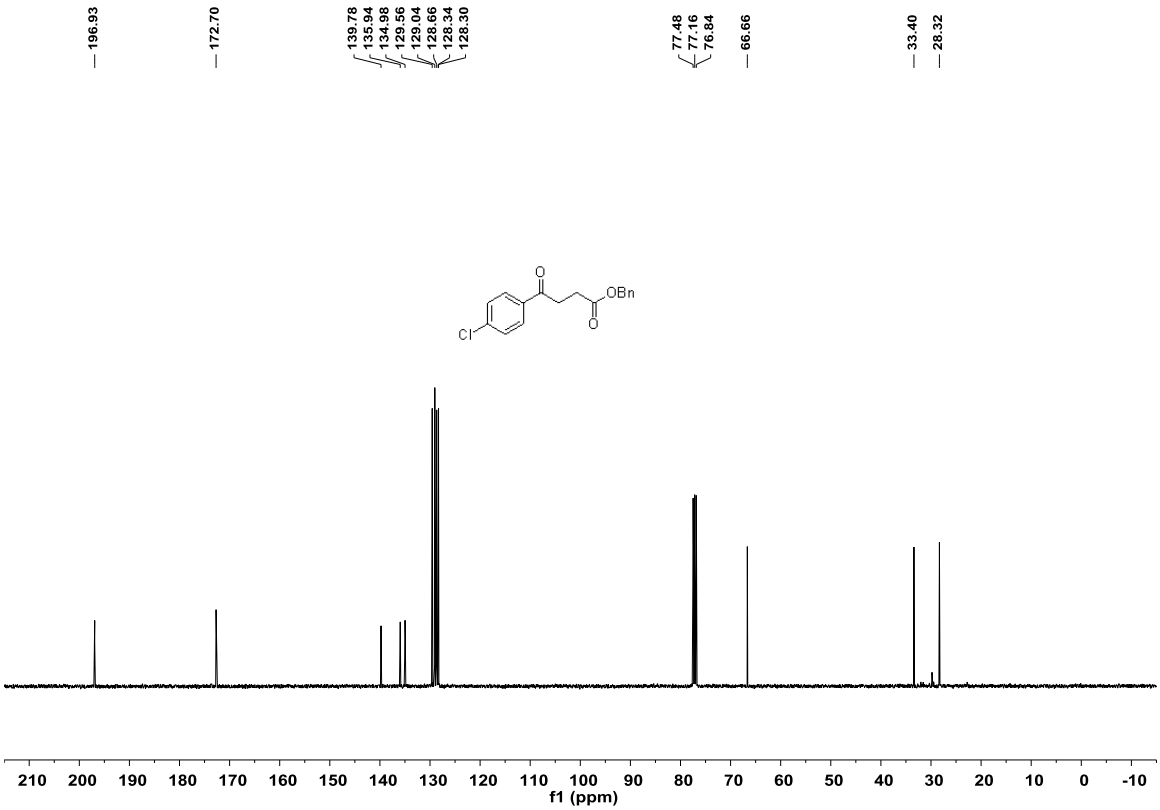
Benzyl 4-(4-chlorophenyl)-4-oxobutanoate (3s)



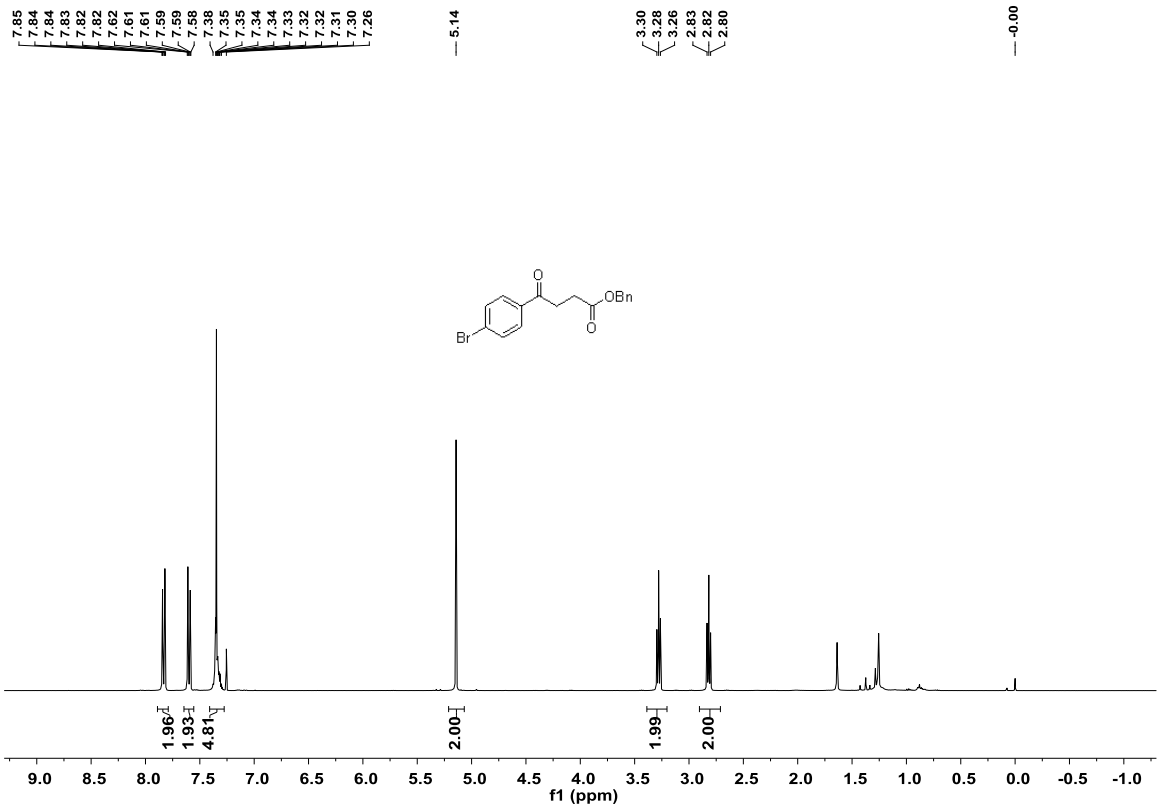


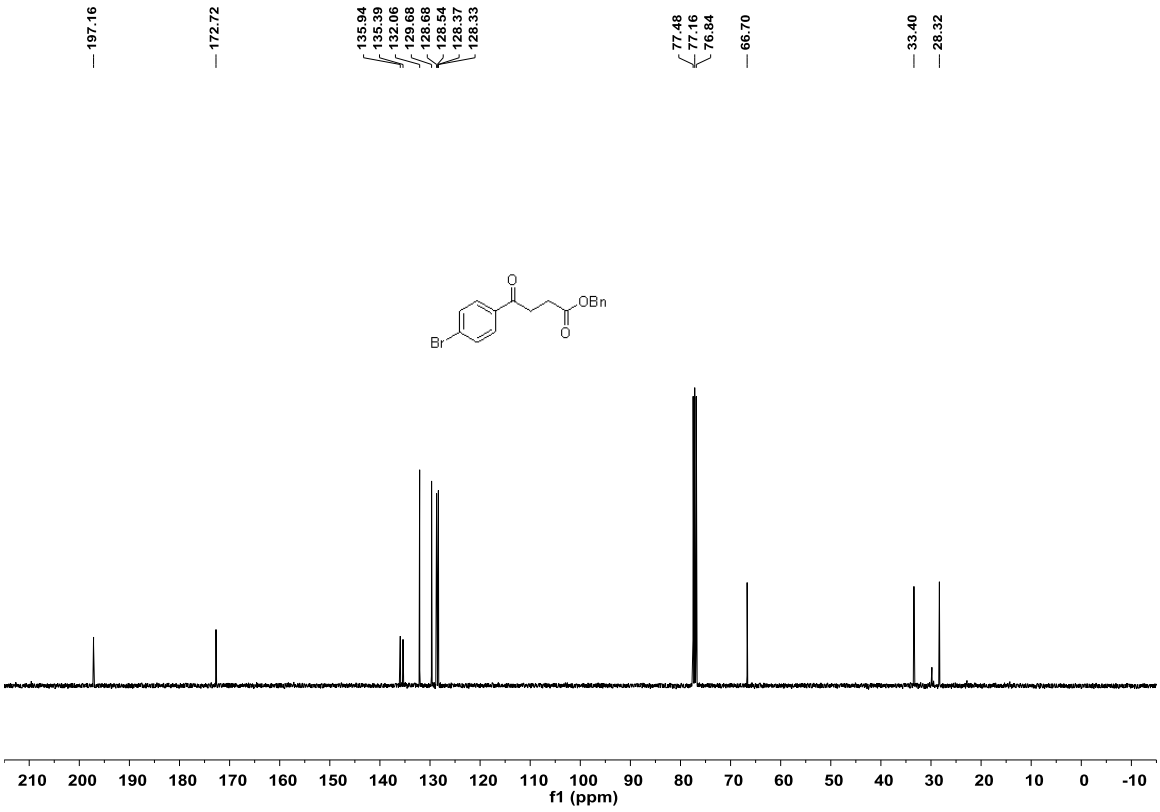
Benzyl 4-(4-fluorophenyl)-4-oxobutanoate (3t)



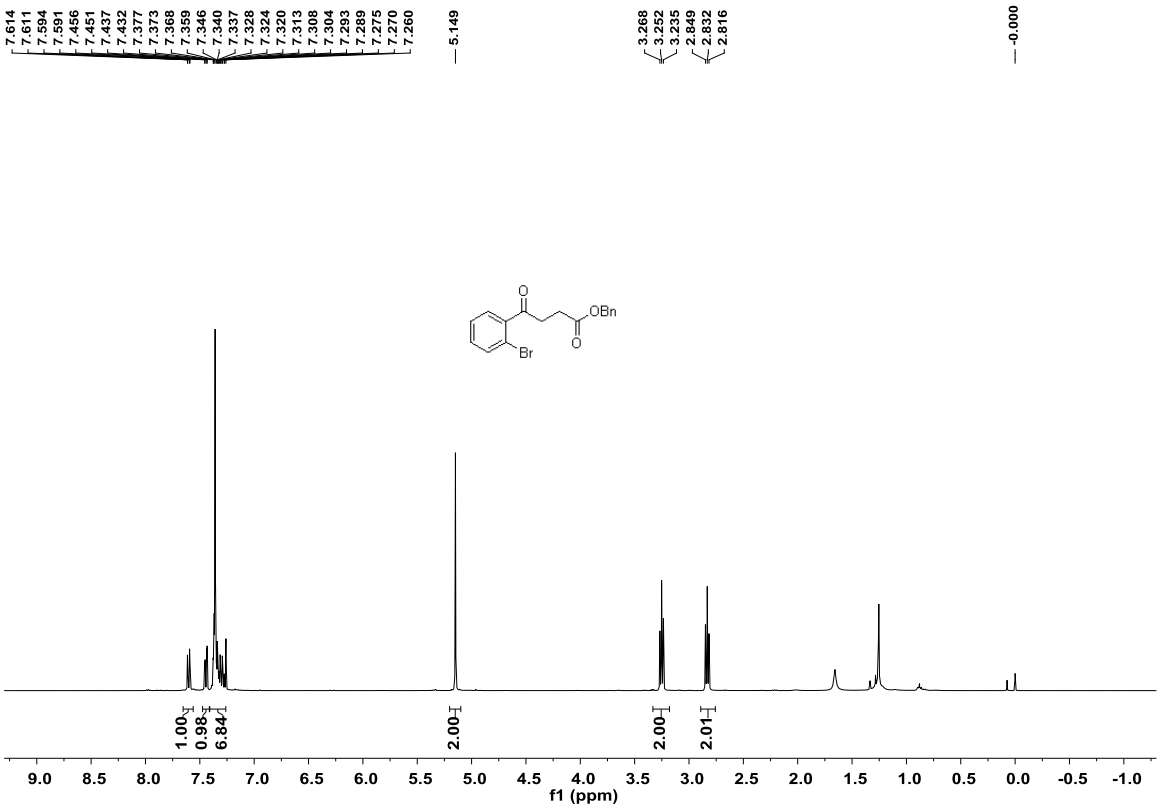


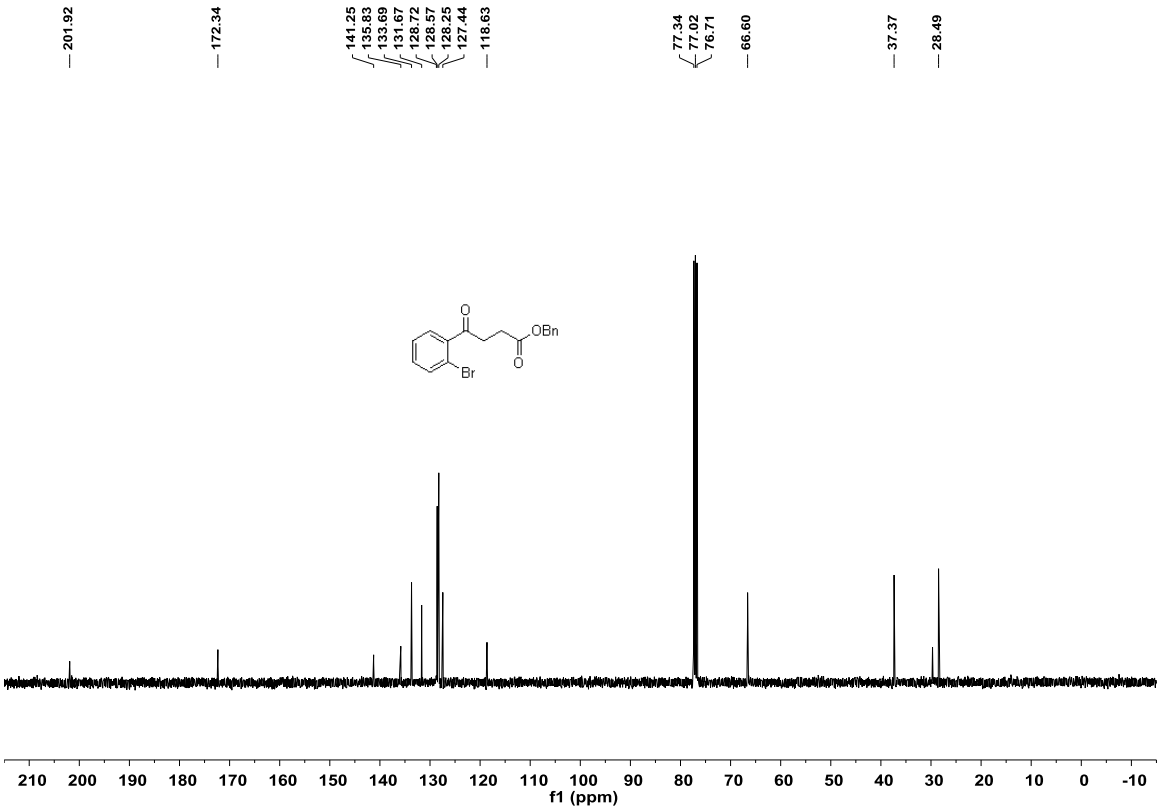
Benzyl 4-(4-bromophenyl)-4-oxobutanoate (3u)



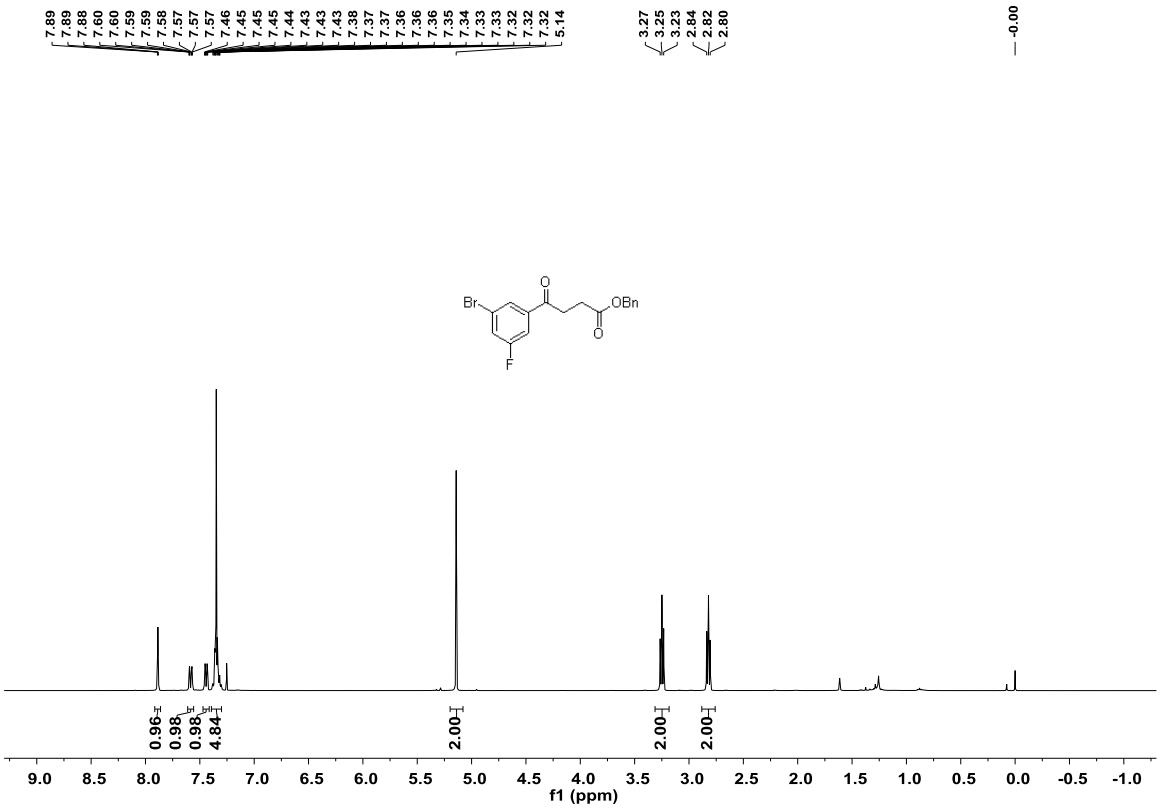


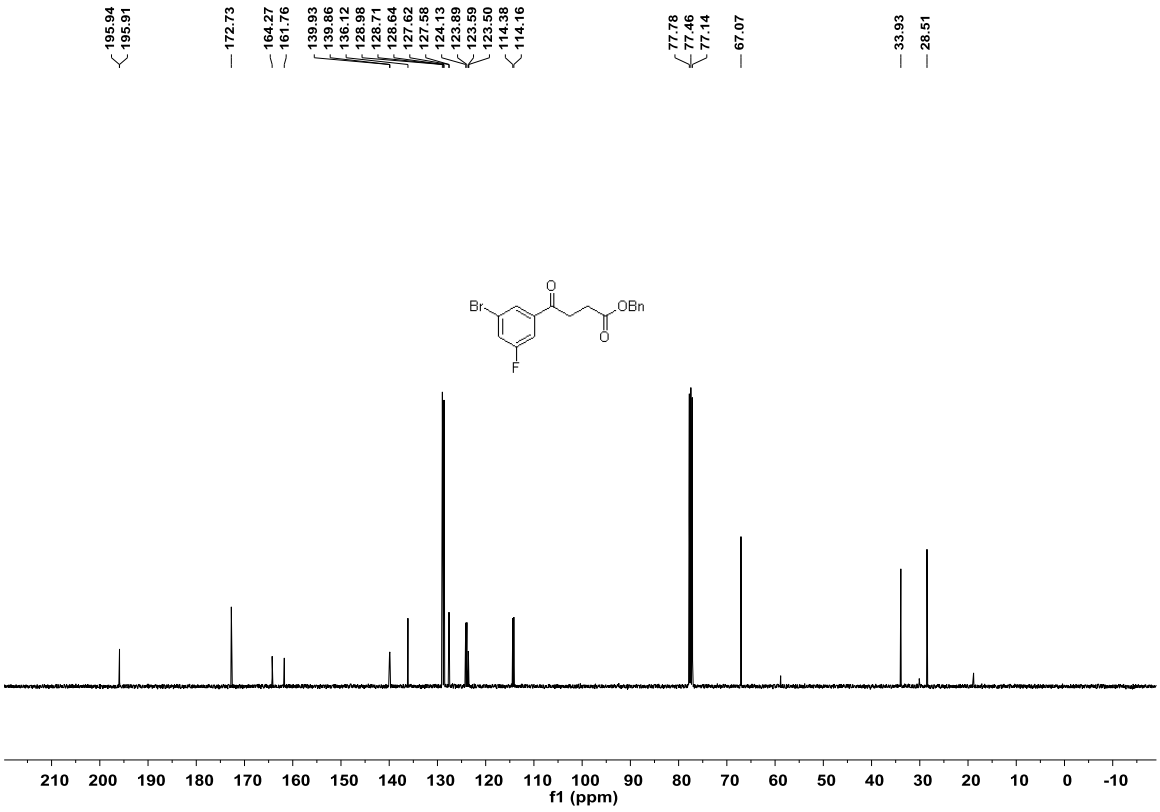
Benzyl 4-(2-bromophenyl)-4-oxobutanoate (3v)





Benzyl 4-(3-bromo-5-fluorophenyl)-4-oxobutanoate (3w)

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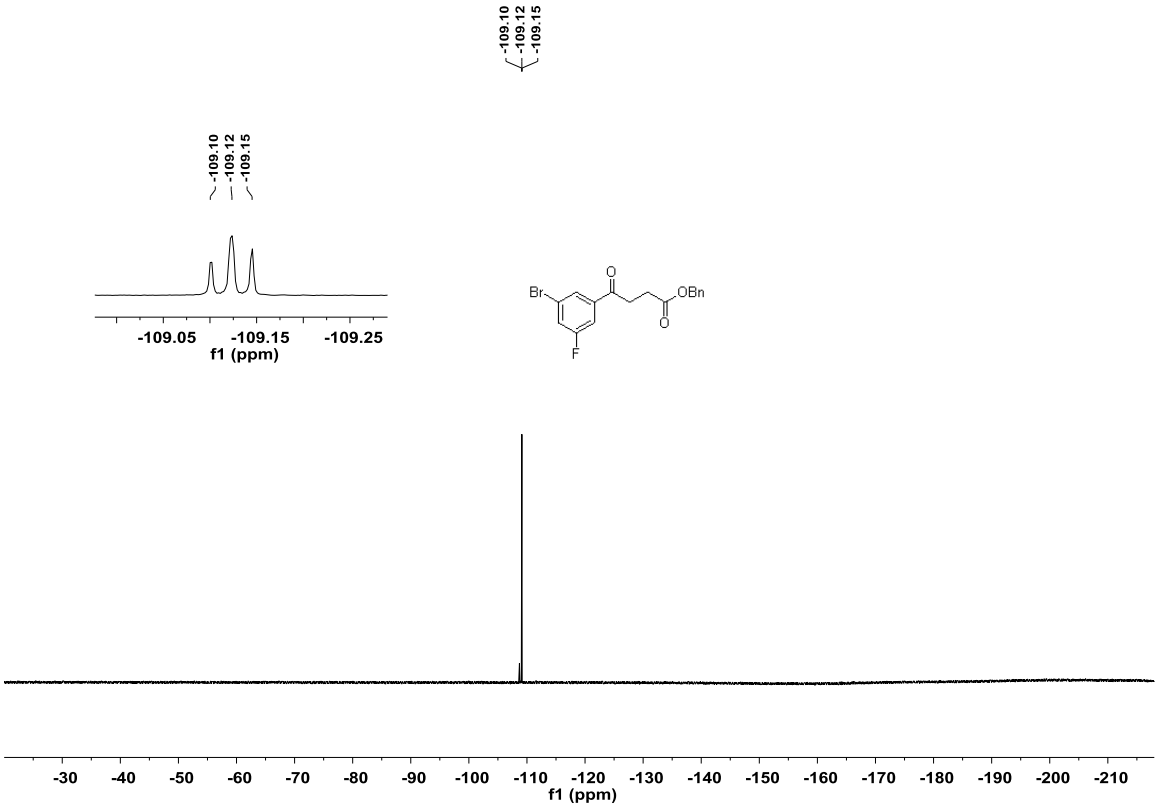
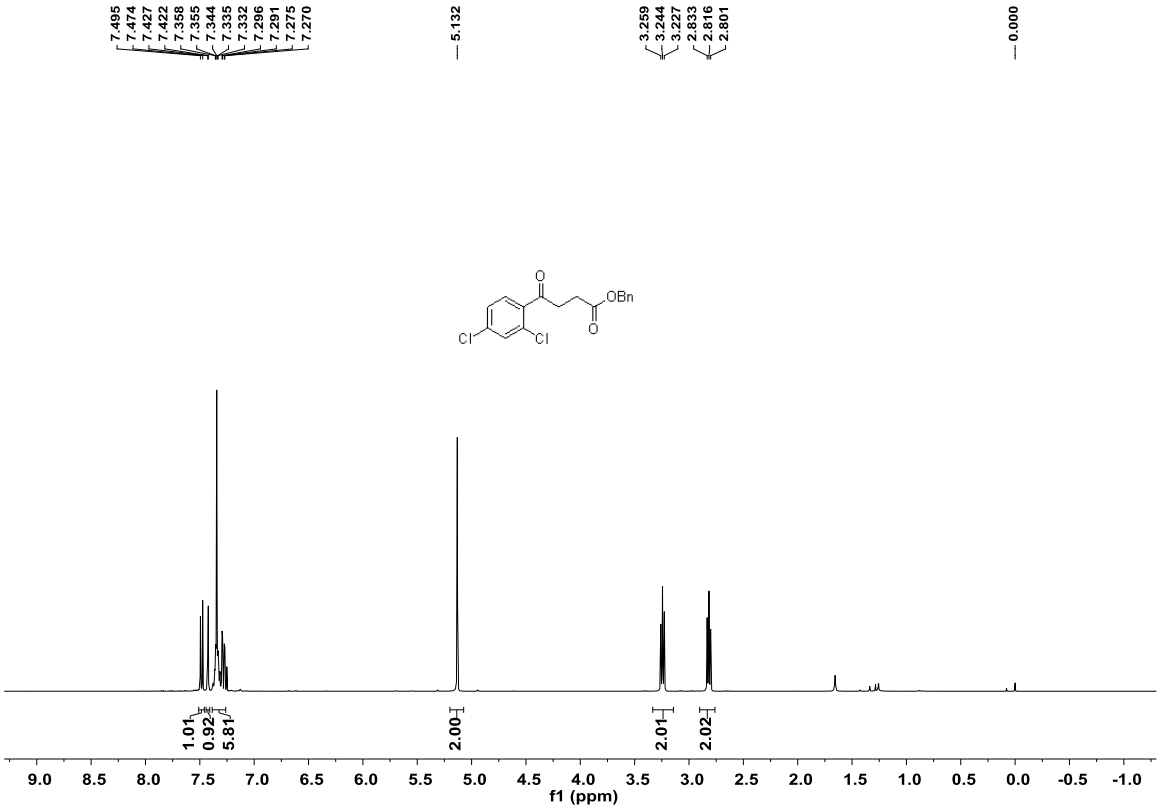
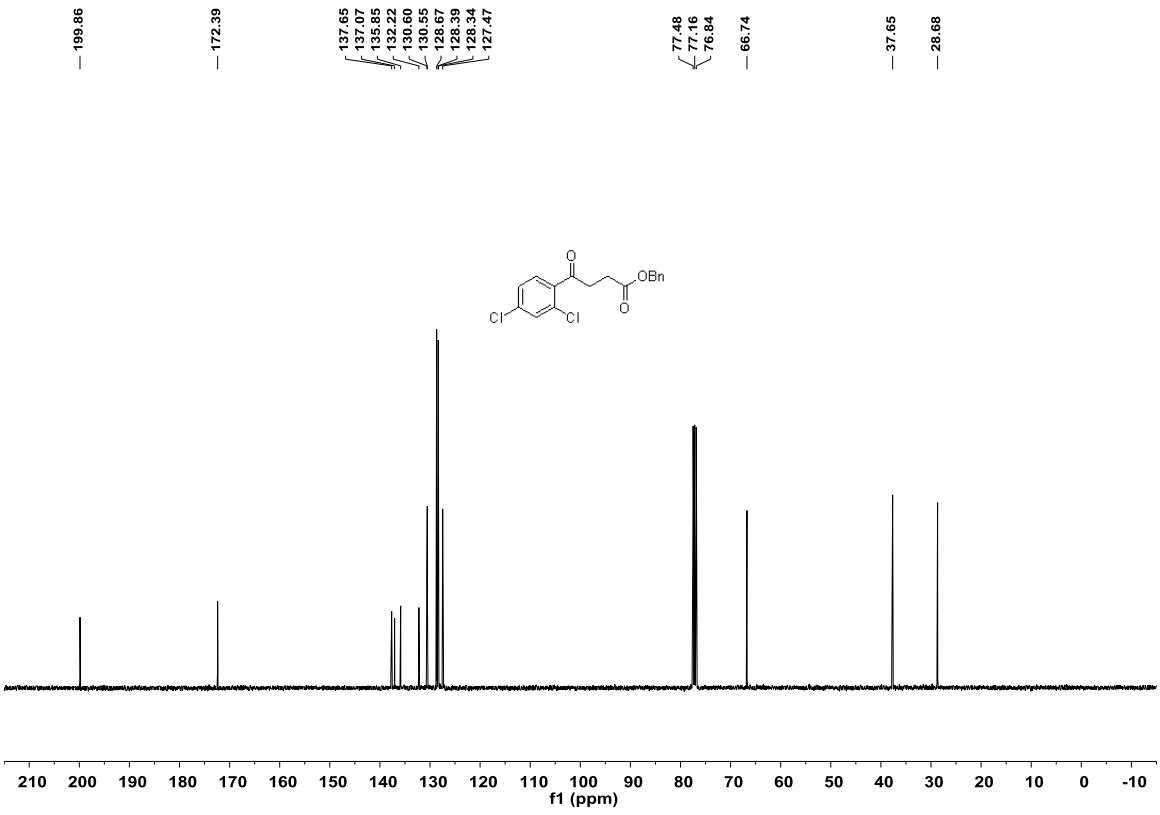
195.91
172.73
164.27
161.76
139.93
139.86
136.12
128.98
128.71
128.64
127.62
127.58
124.13
123.89
123.59
123.50
114.38
114.16
77.78
77.46
77.14
67.07
33.93
28.51
Br
O
OBn
O
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

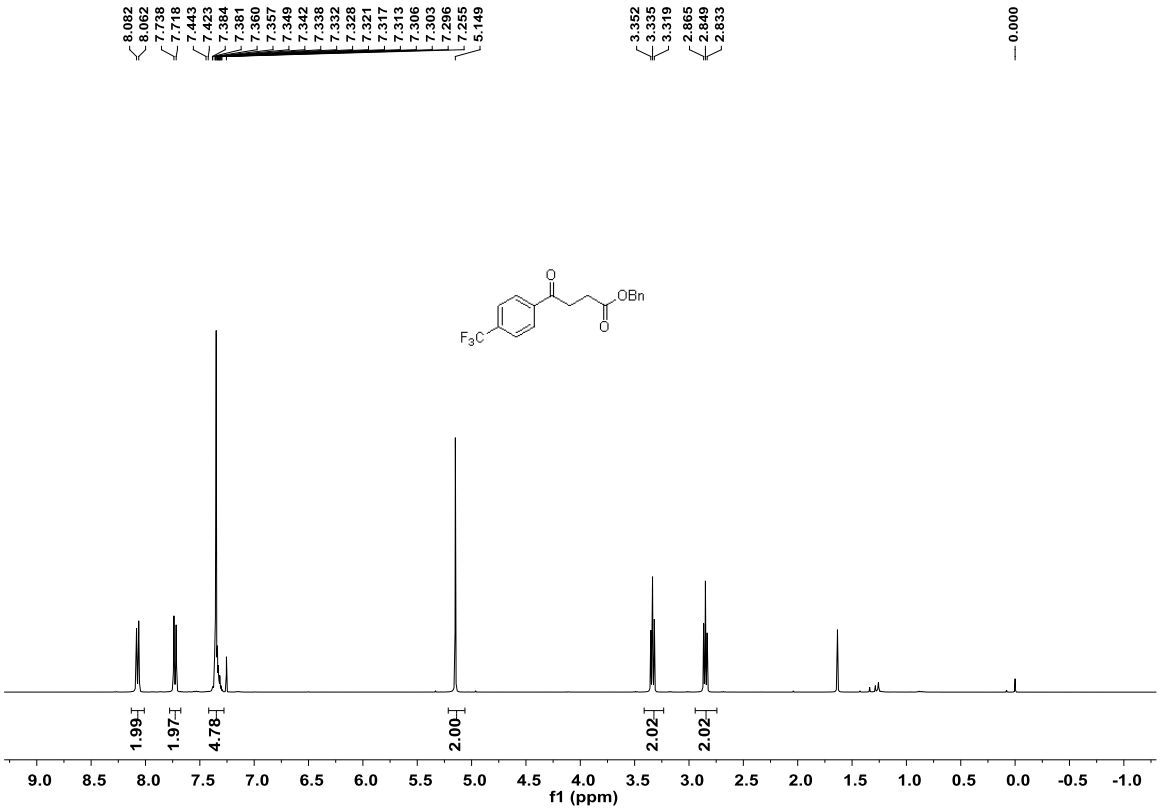

-109.10
-109.12
-109.15
-109.10
-109.12
-109.15
-109.05
-109.15
-109.25
f1 (ppm)
Br
O
OBn
O
F
-30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

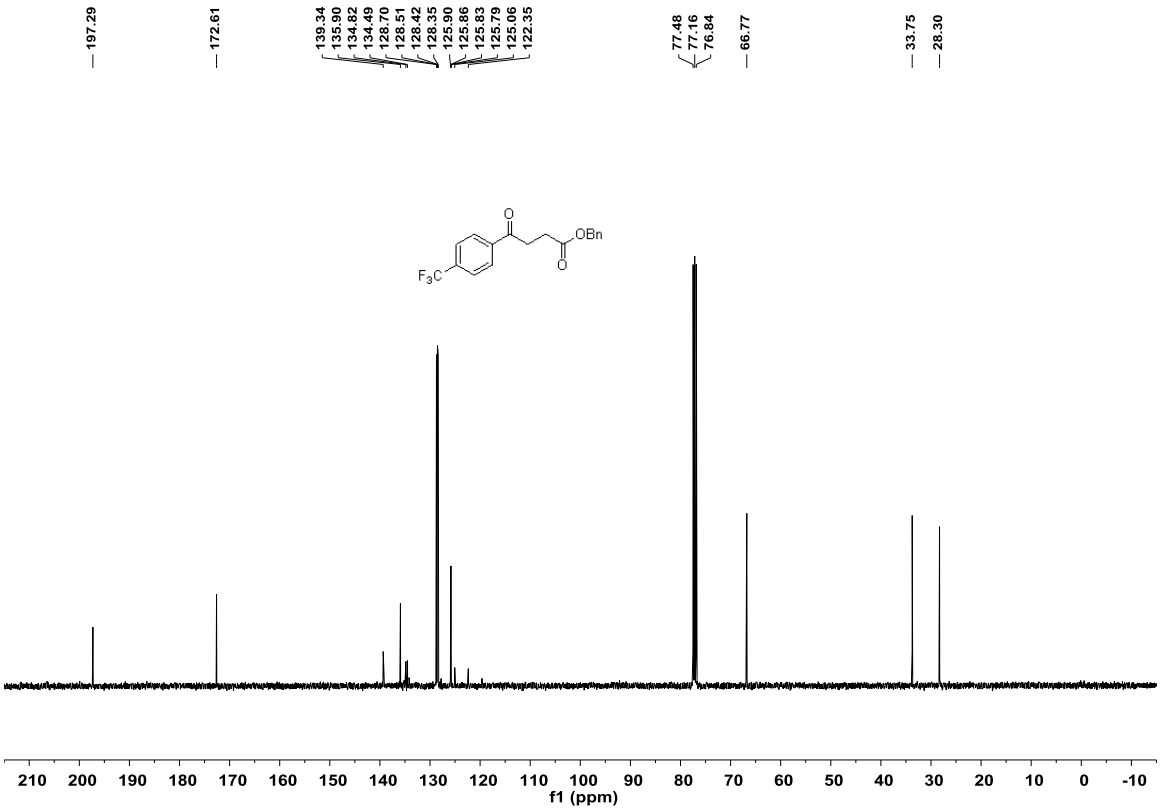
Benzyl 4-(2,4-dichlorophenyl)-4-oxobutanoate (3x)

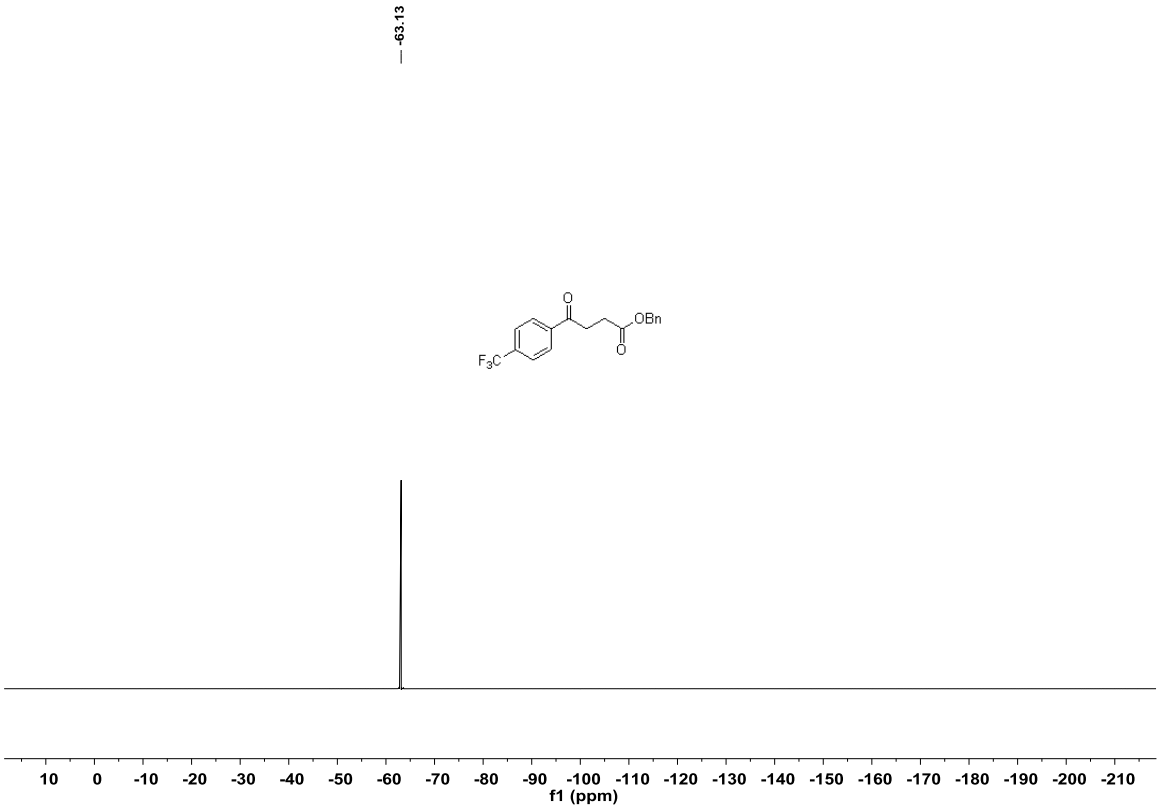




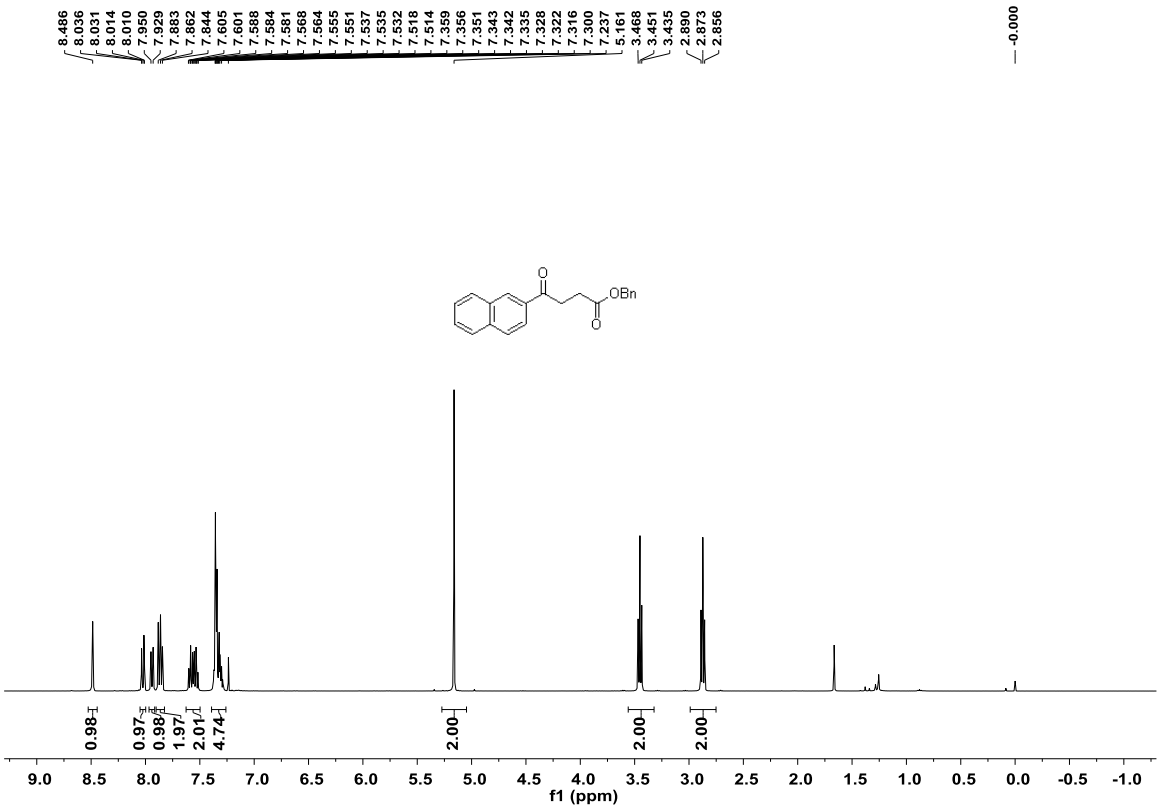
Benzyl 4-oxo-4-(4-(trifluoromethyl)phenyl)butanoate (3y)







Benzyl 4-(naphthalen-2-yl)-4-oxobutanoate (3z)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8.031
8.014
8.010
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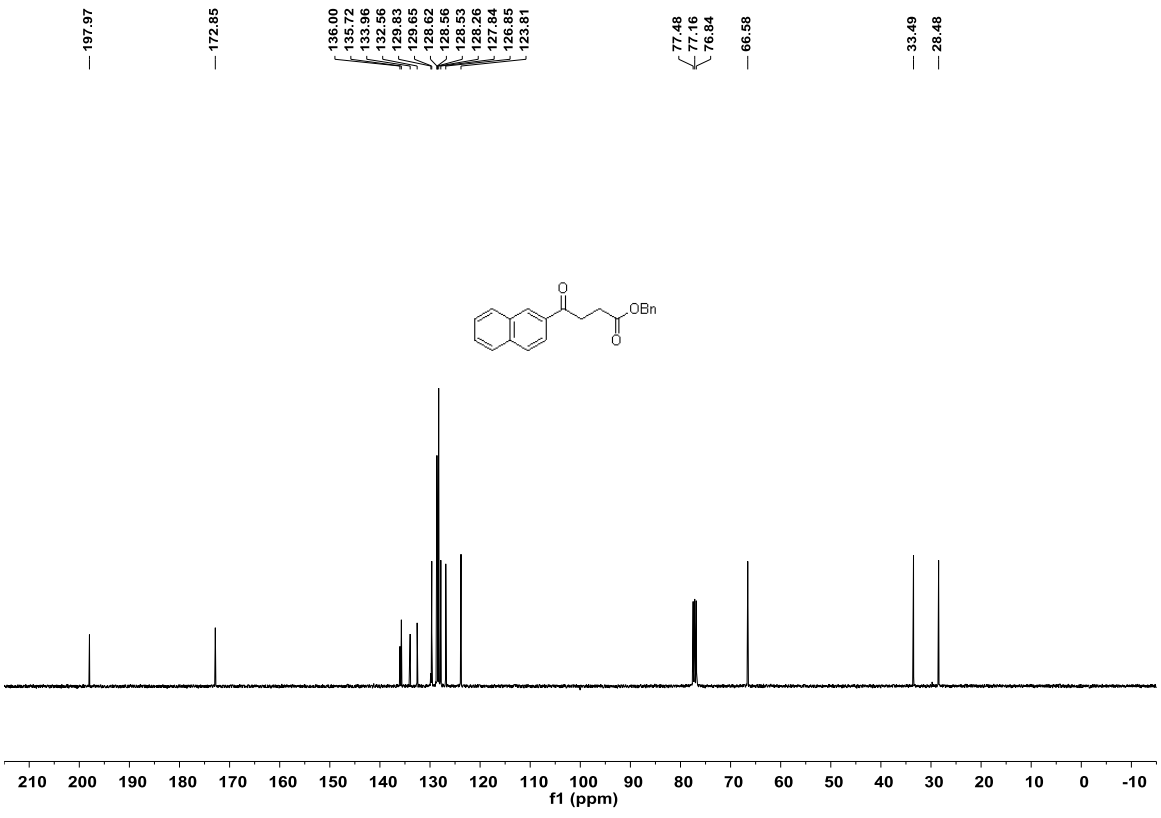
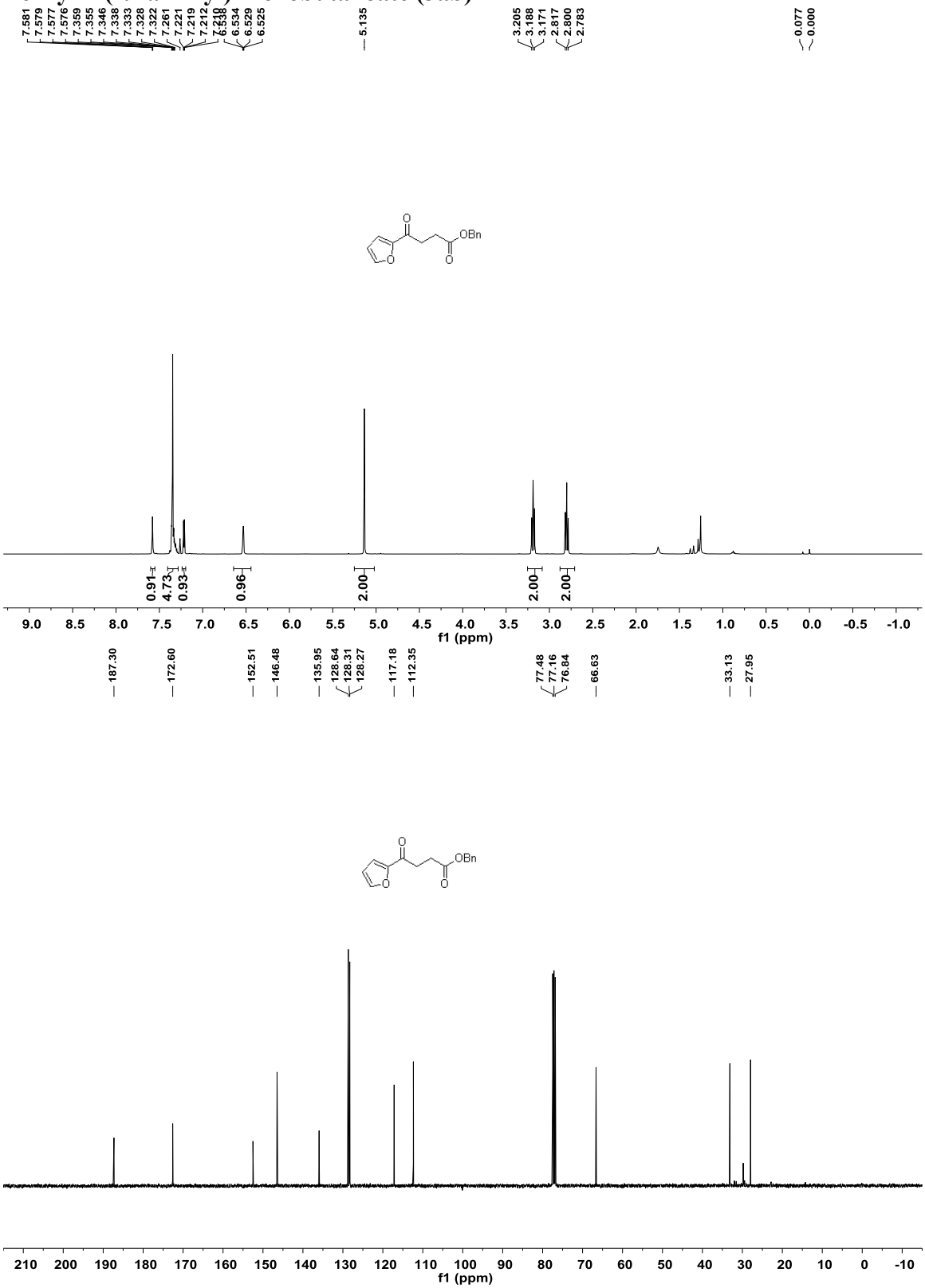
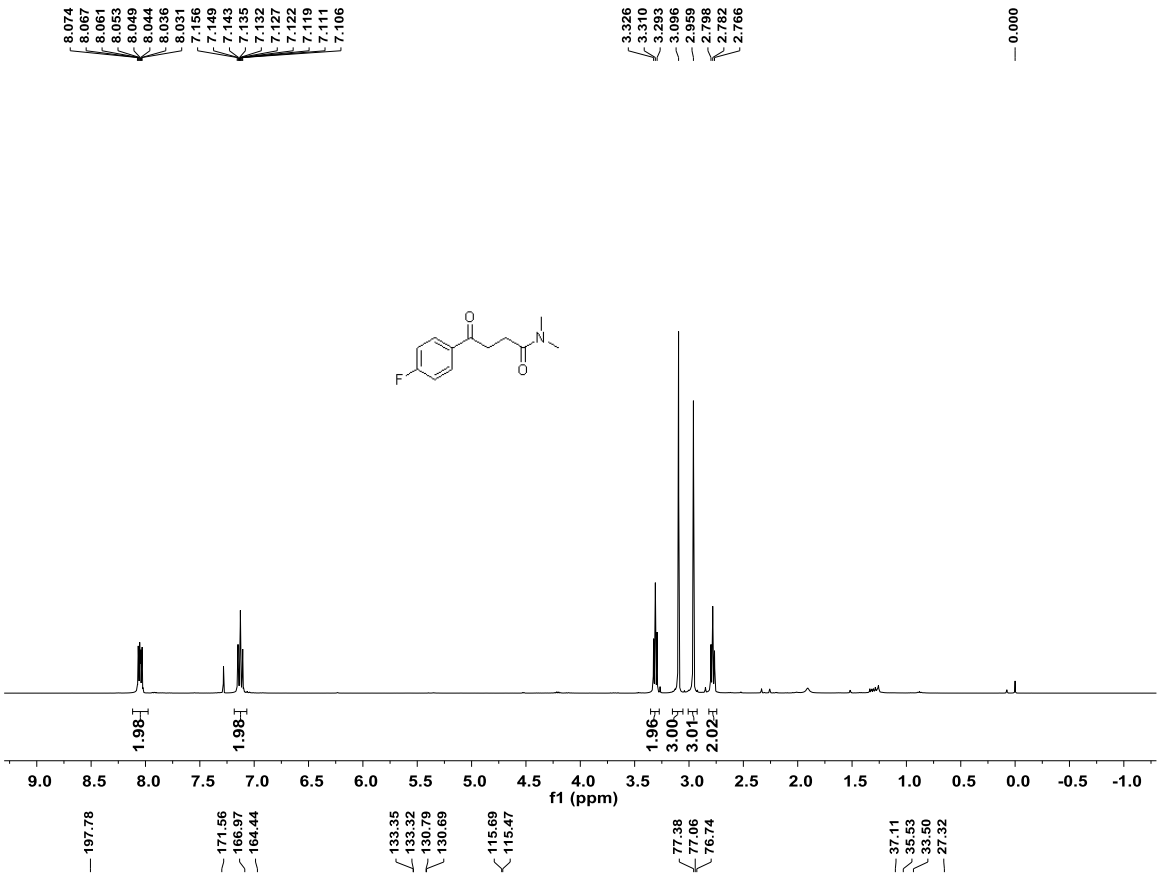
7.929
7.883
7.862
7.844
7.605
7.601
7.588
7.584
7.581
7.568
7.564
7.555
7.551
7.537
7.535
7.532
7.518
7.514
7.359
7.356
7.351
7.343
7.342
7.335
7.328
7.322
7.316
7.300
7.237
5.161
3.468
3.451
3.435
2.890
2.873
2.856
-0.000
OBn
0.98
0.97
0.98
1.97
2.01
4.74
2.00
2.00
2.00
f1 (ppm)


197.97
172.85
136.00
135.72
133.96
132.56
129.83
129.65
128.62
128.56
128.53
128.26
127.84
126.85
123.81
77.48
77.16
76.84
66.58
33.49
28.48
OBn
f1 (ppm)

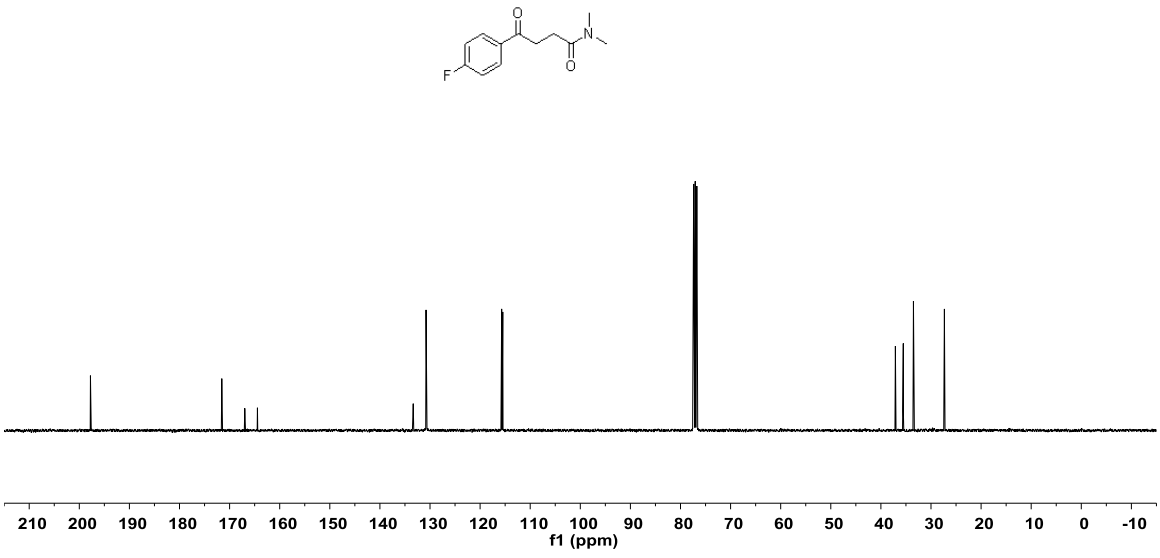
Benzyl 4-(furan-2-yl)-4-oxobutanoate (3ab)

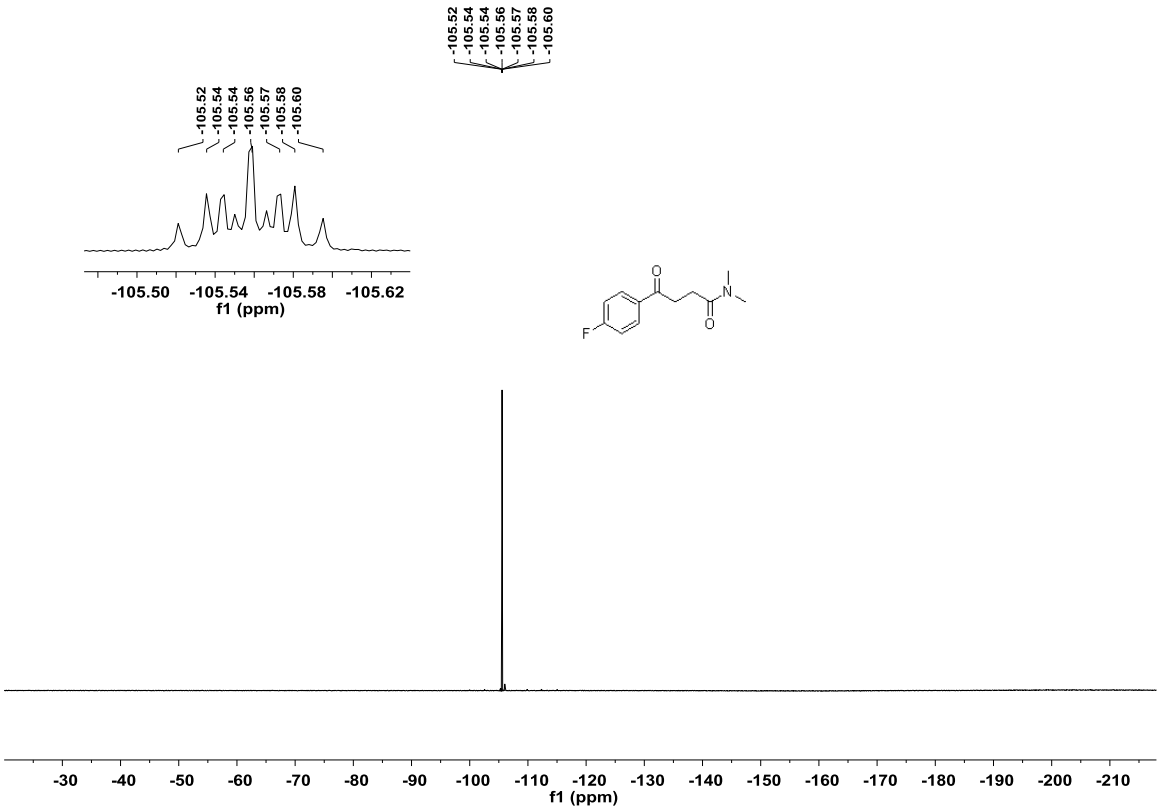


4-(4-fluorophenyl)-N,N-dimethyl-4-oxobutanamide (3ac)

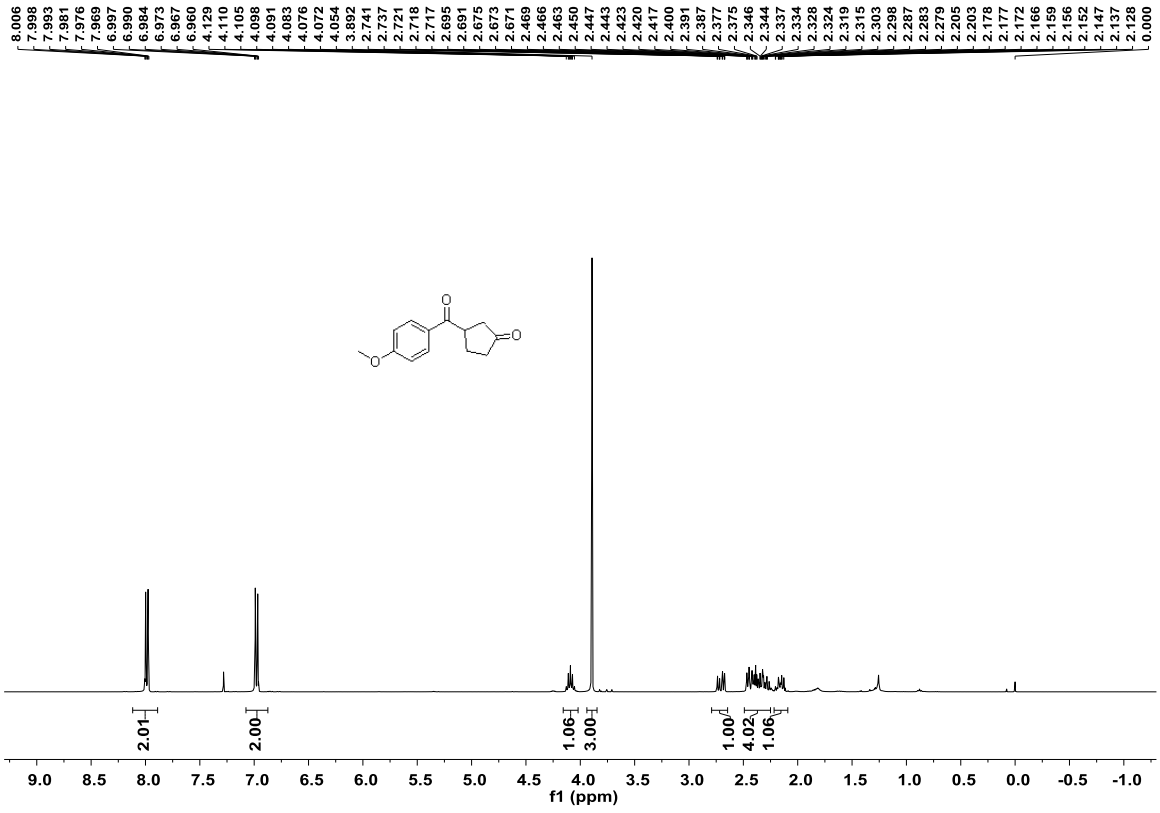

8.074
8.067
8.061
8.053
8.049
8.044
8.036
8.031
7.156
7.149
7.143
7.135
7.132
7.127
7.122
7.119
7.111
7.106
3.326
3.310
3.293
3.096
2.959
2.798
2.782
2.766
0.000
F
O
N
O
1.98
1.98
1.96
3.00
3.01
2.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

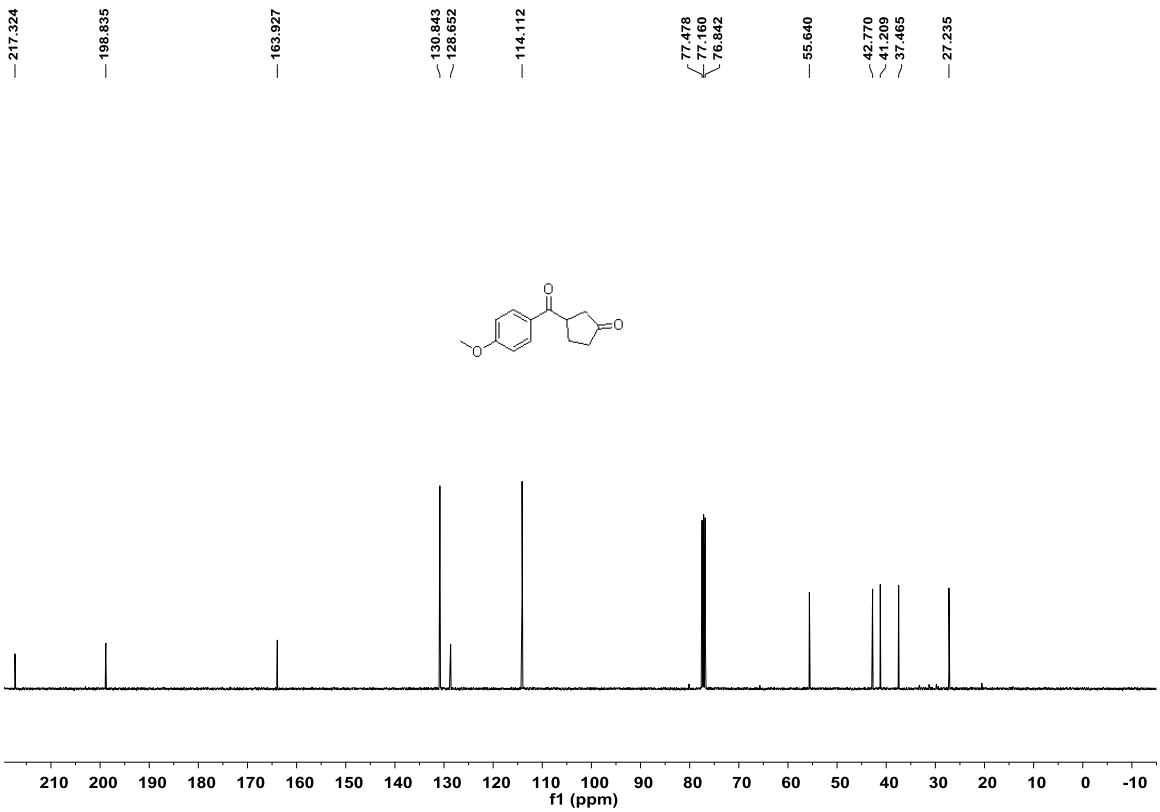
197.78
171.56
166.97
164.44
133.35
133.32
130.79
130.69
115.69
115.47
77.38
77.06
76.74
37.11
35.53
33.50
27.32


F
O
N
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

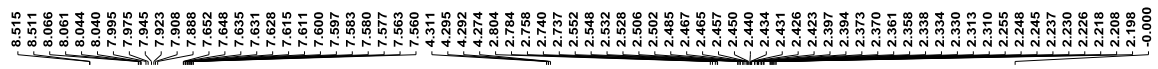


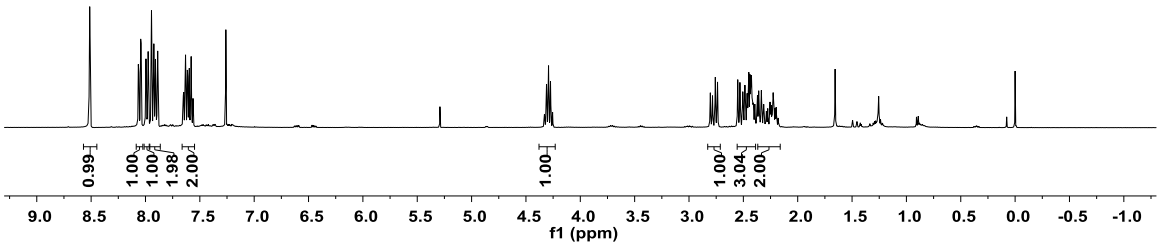
3-(4-methoxybenzoyl)cyclopentan-1-one (3ad)

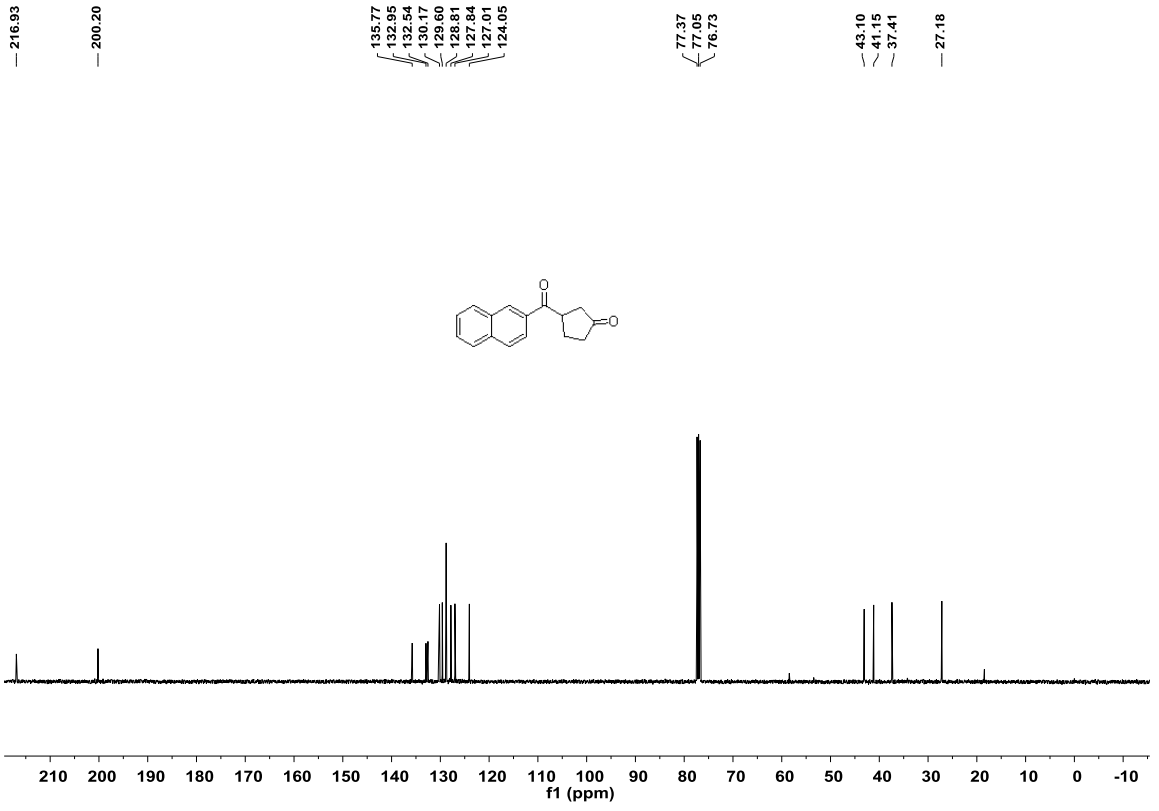




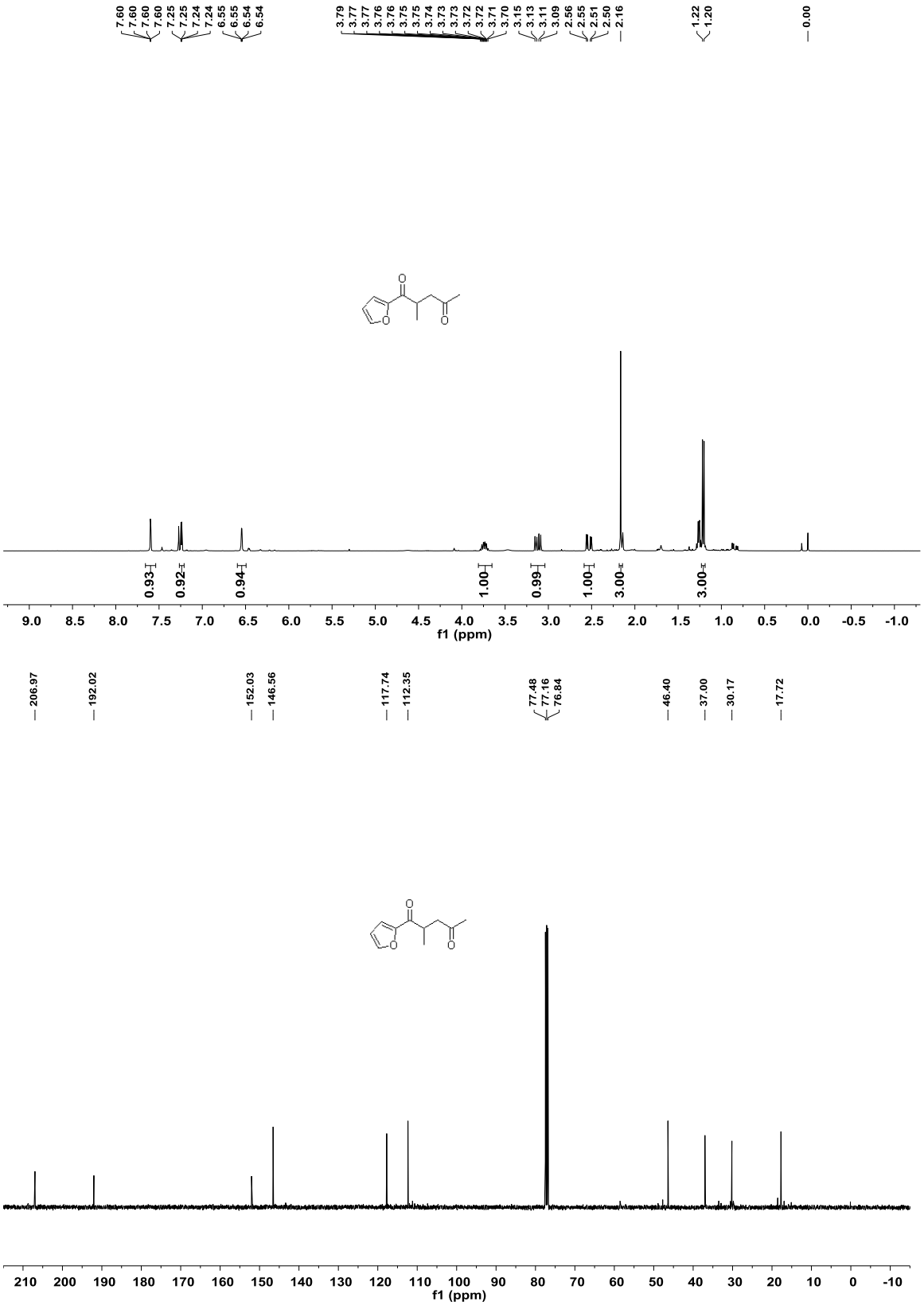
3-(2-naphthoyl)cyclopentan-1-one (3ae)



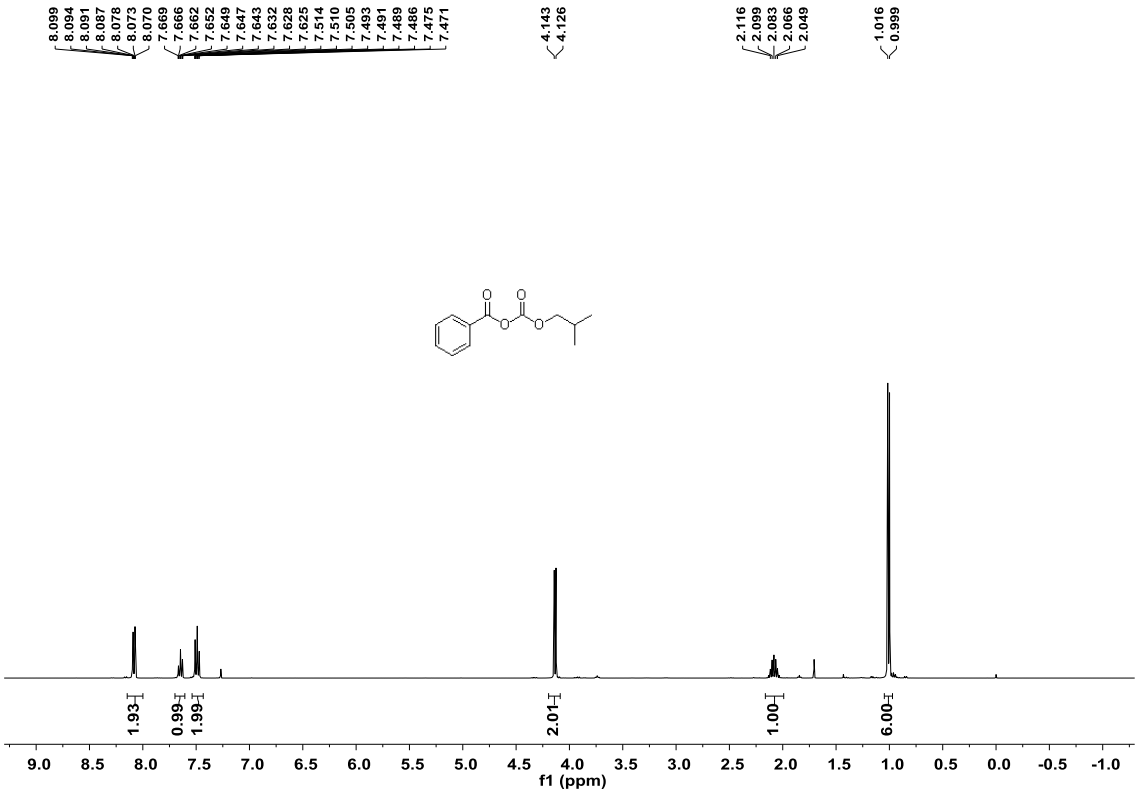




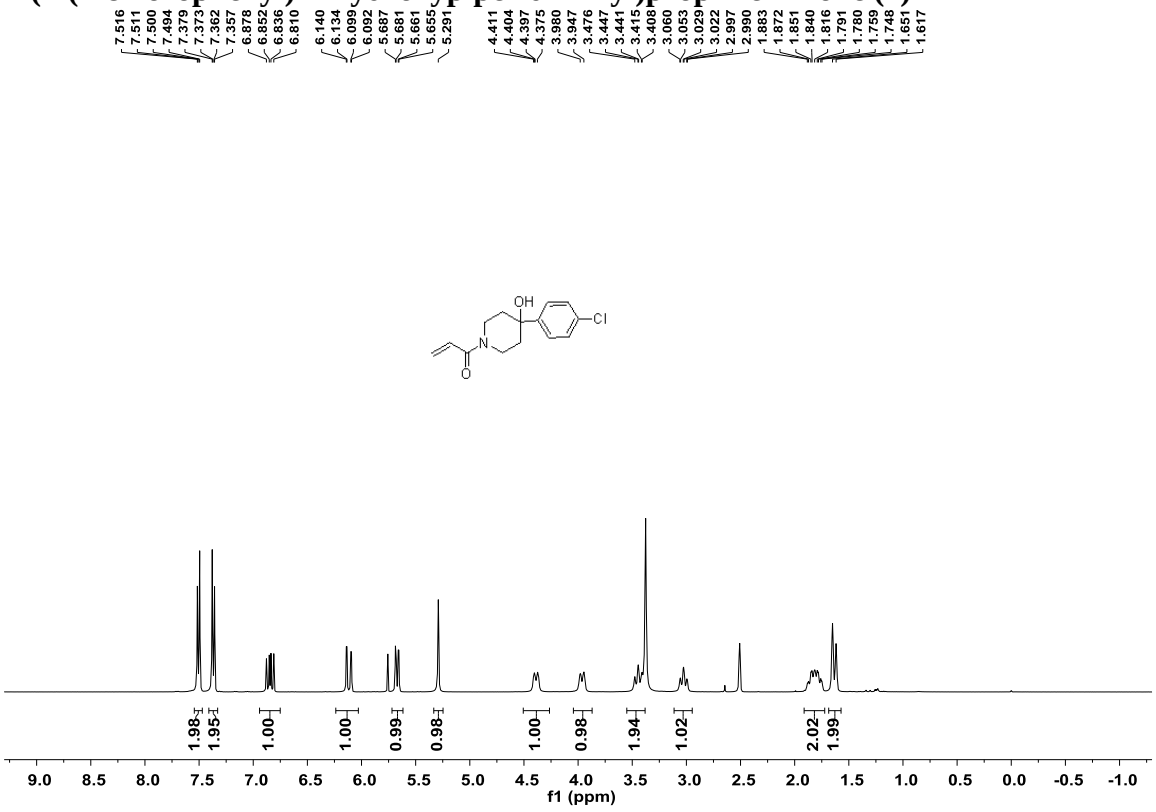
1-(furan-2-yl)-2-methylpentane-1,4-dione (3af)

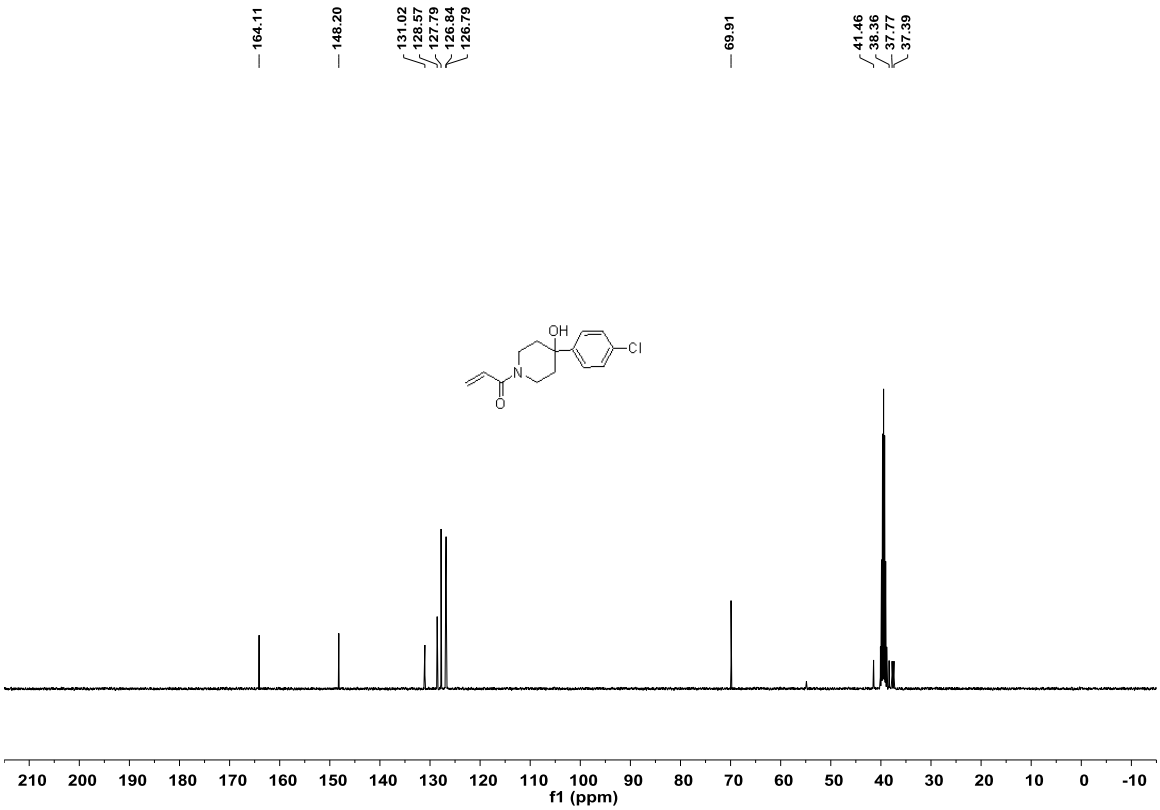


Benzoic (isobutyl carbonic) anhydride (5a)

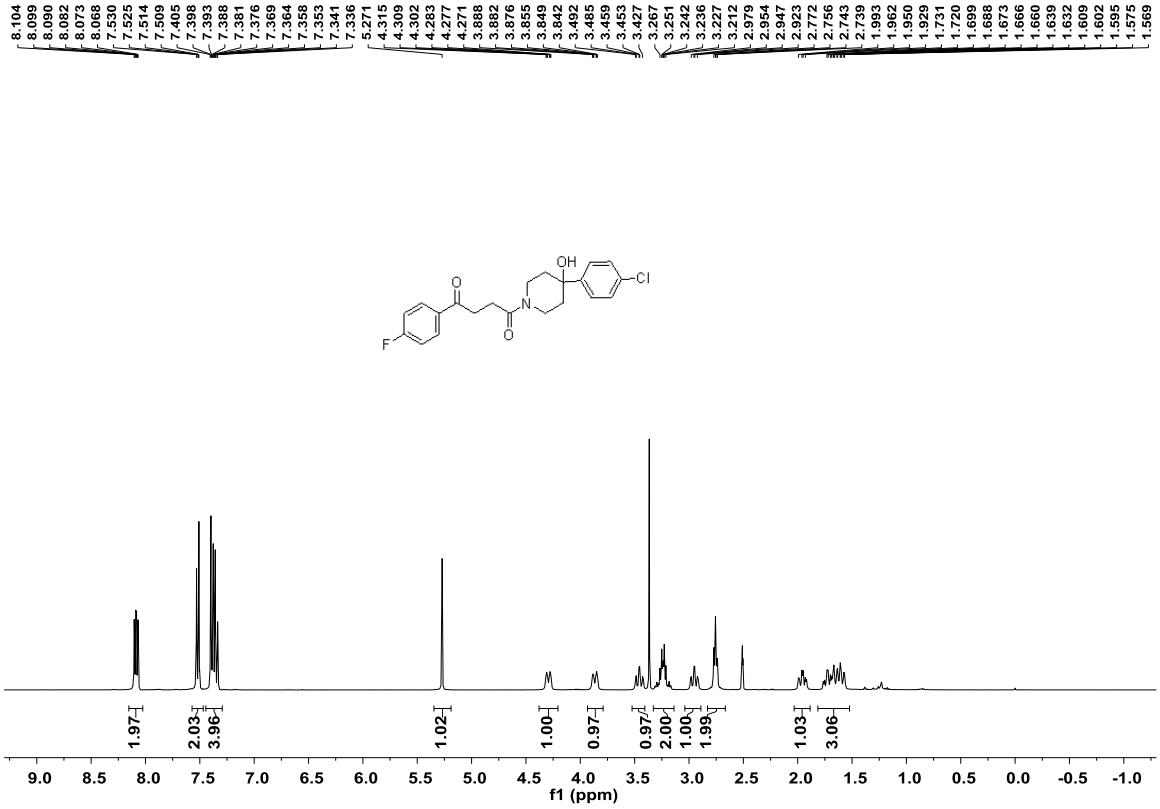


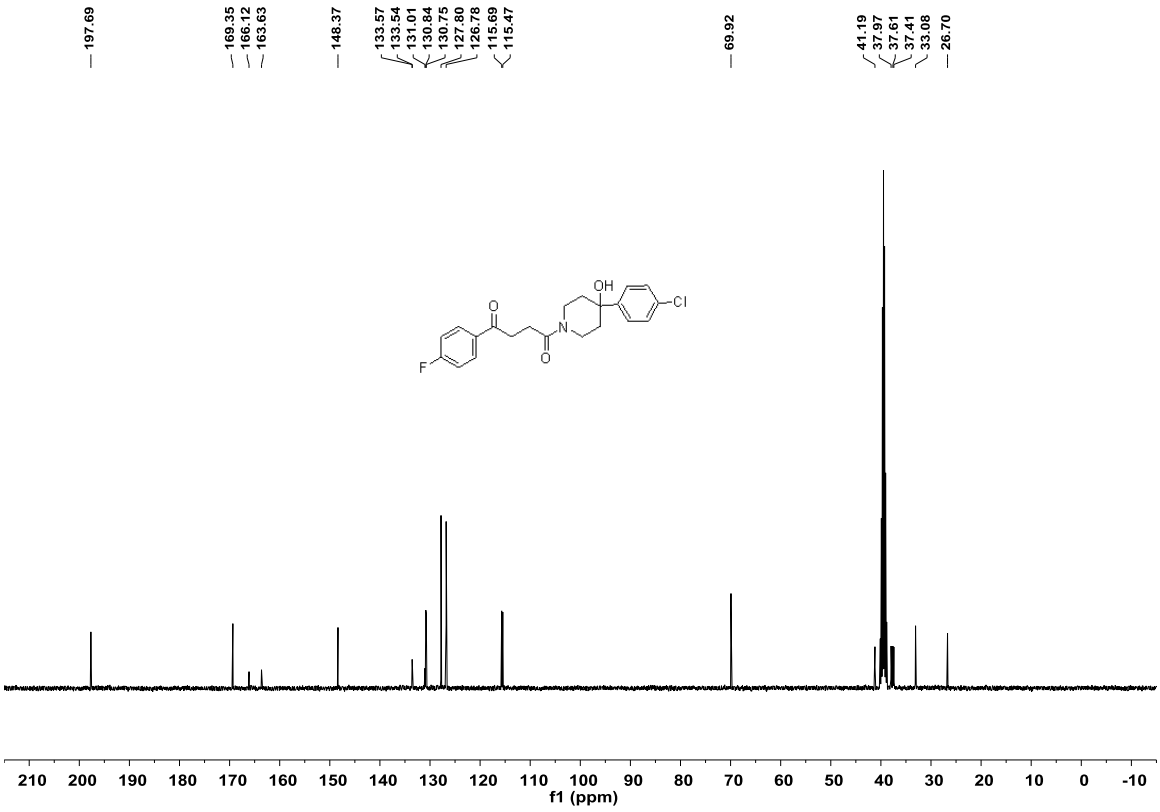
1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)prop-2-en-1-one (7)

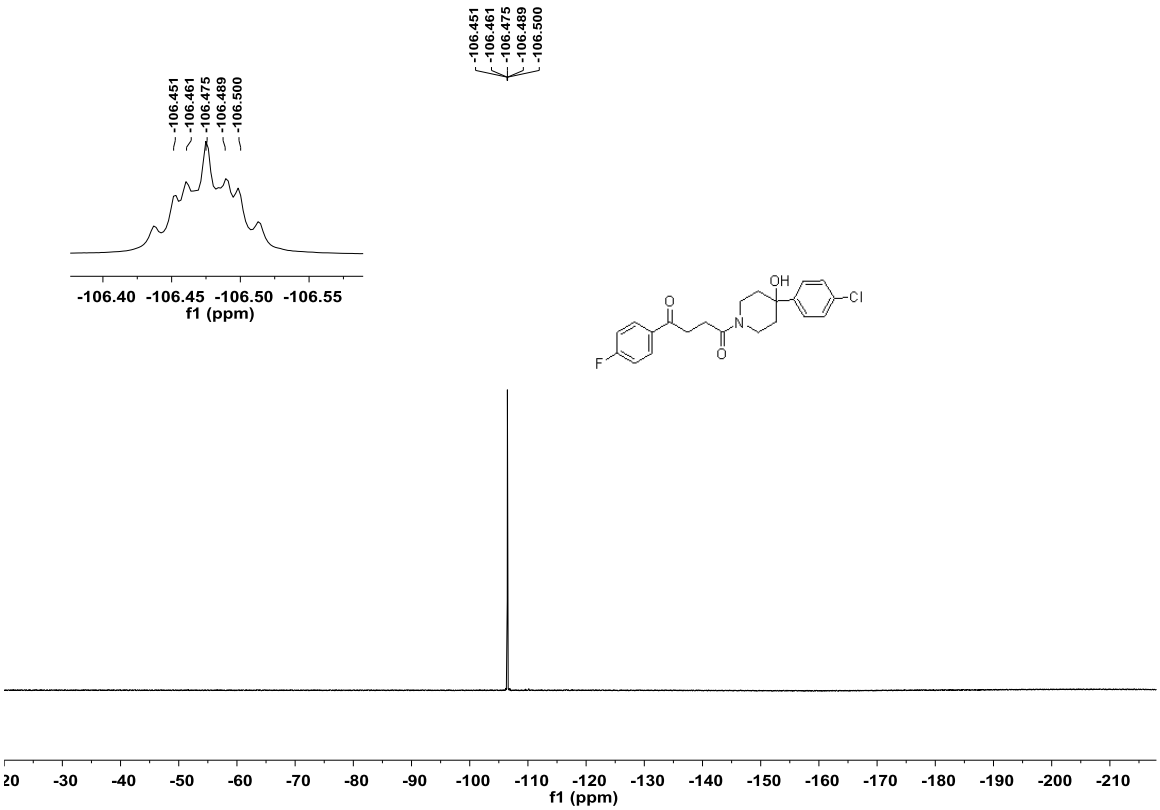




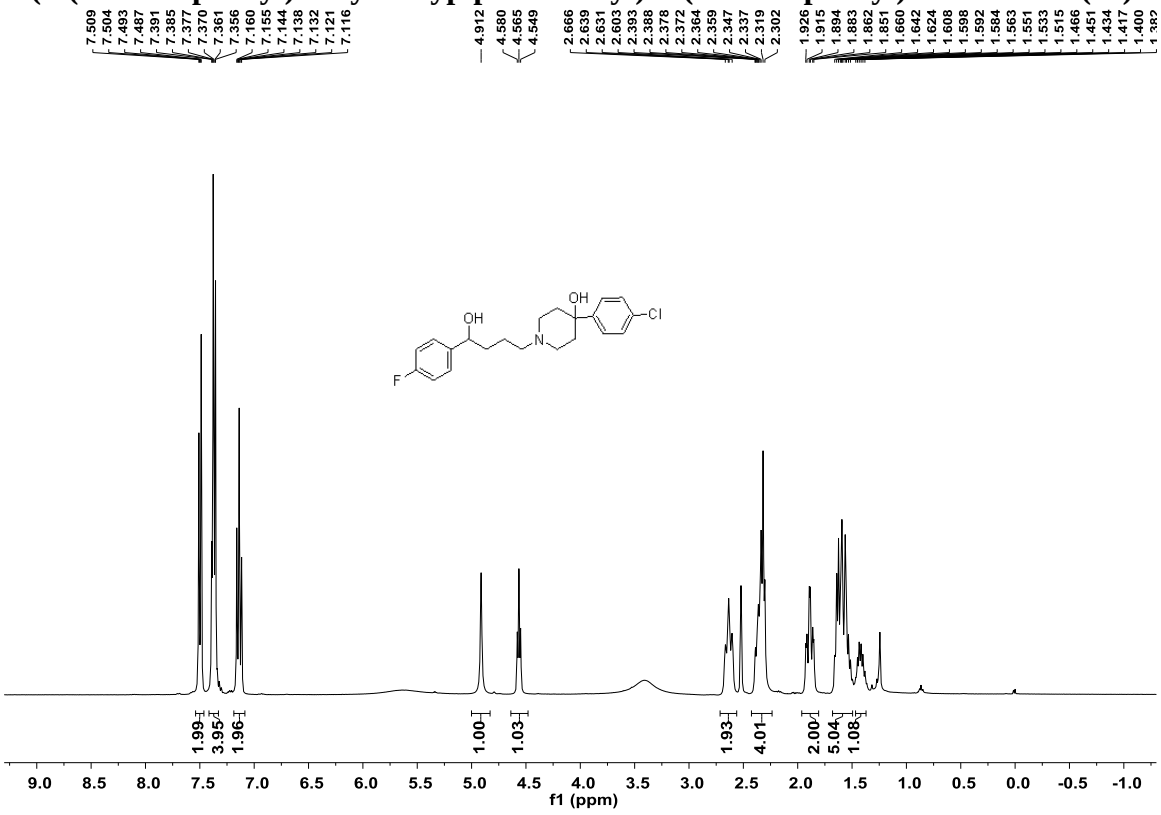
1-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-4-(4-fluorophenyl)butane-1,4-dione (8)

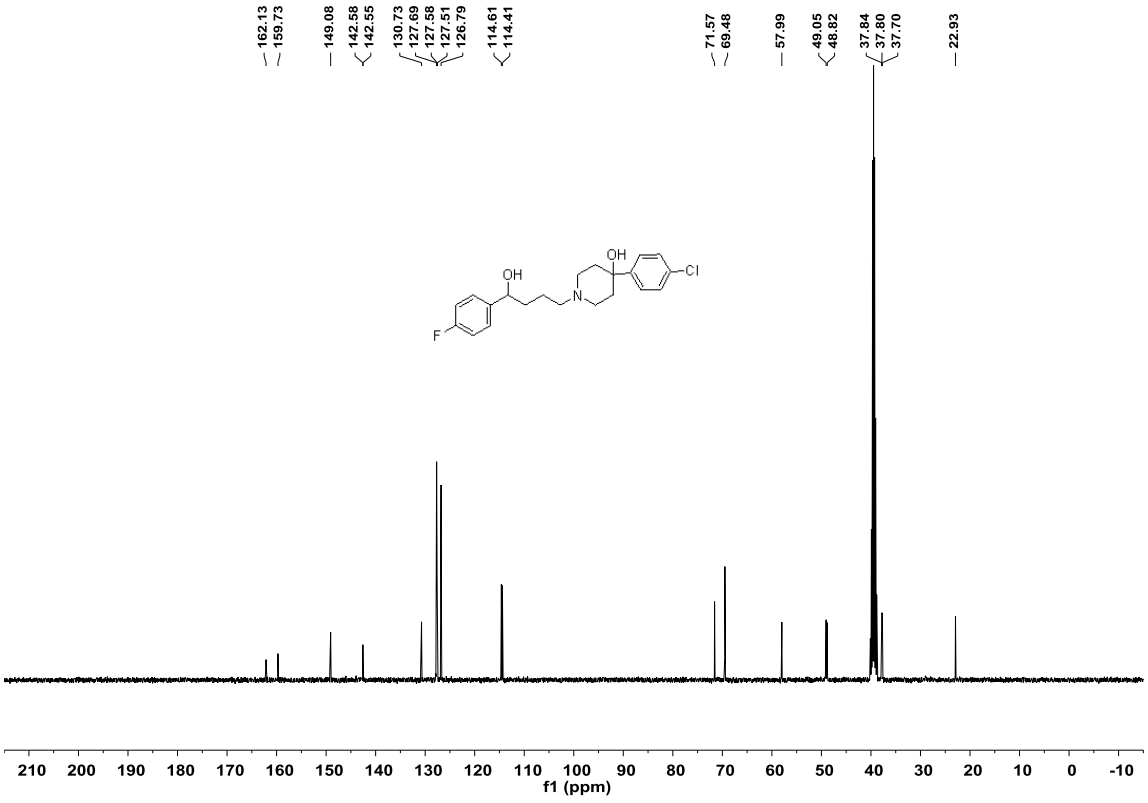


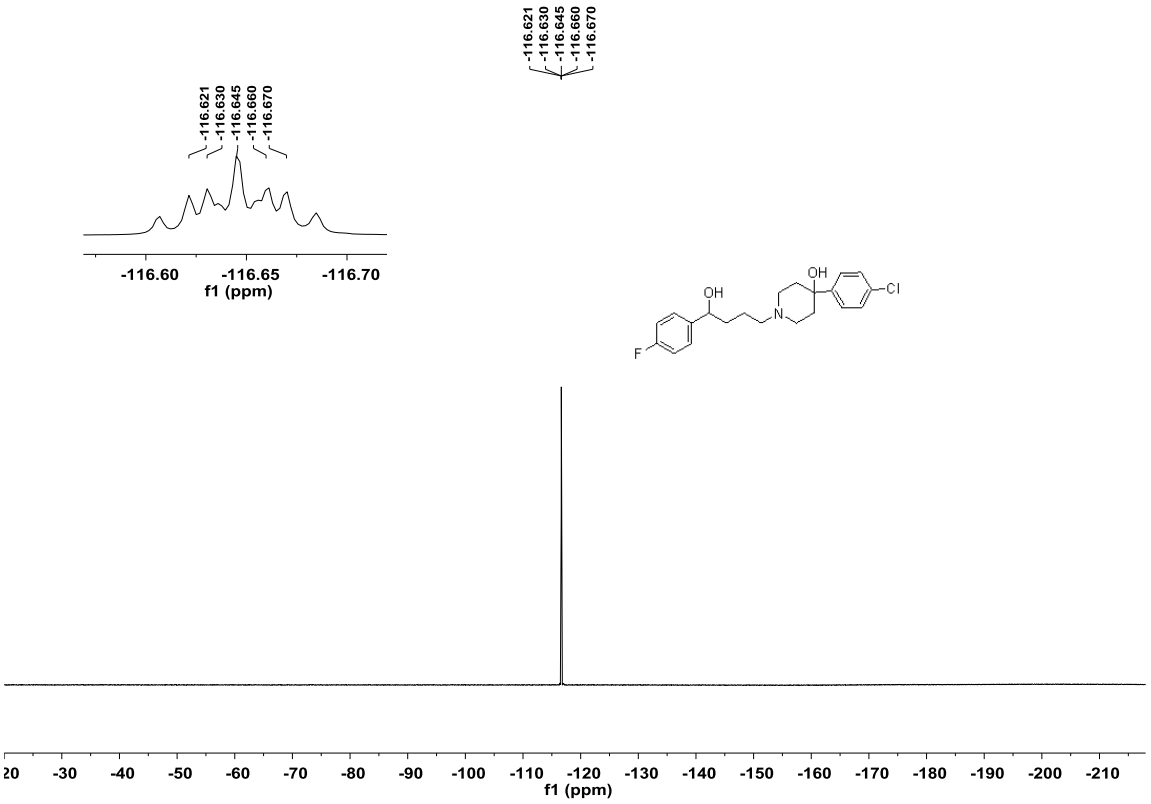

197.69
169.35
166.12
163.63
148.37
133.57
133.54
131.01
130.84
130.75
127.80
126.78
115.69
115.47
69.92
41.19
37.97
37.61
37.41
33.08
26.70
OH
Cl
O
N
O
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-106.451
-106.461
-106.475
-106.489
-106.500
-106.40 -106.45 -106.50 -106.55
f1 (ppm)
OH
Cl
O
N
O
F
20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

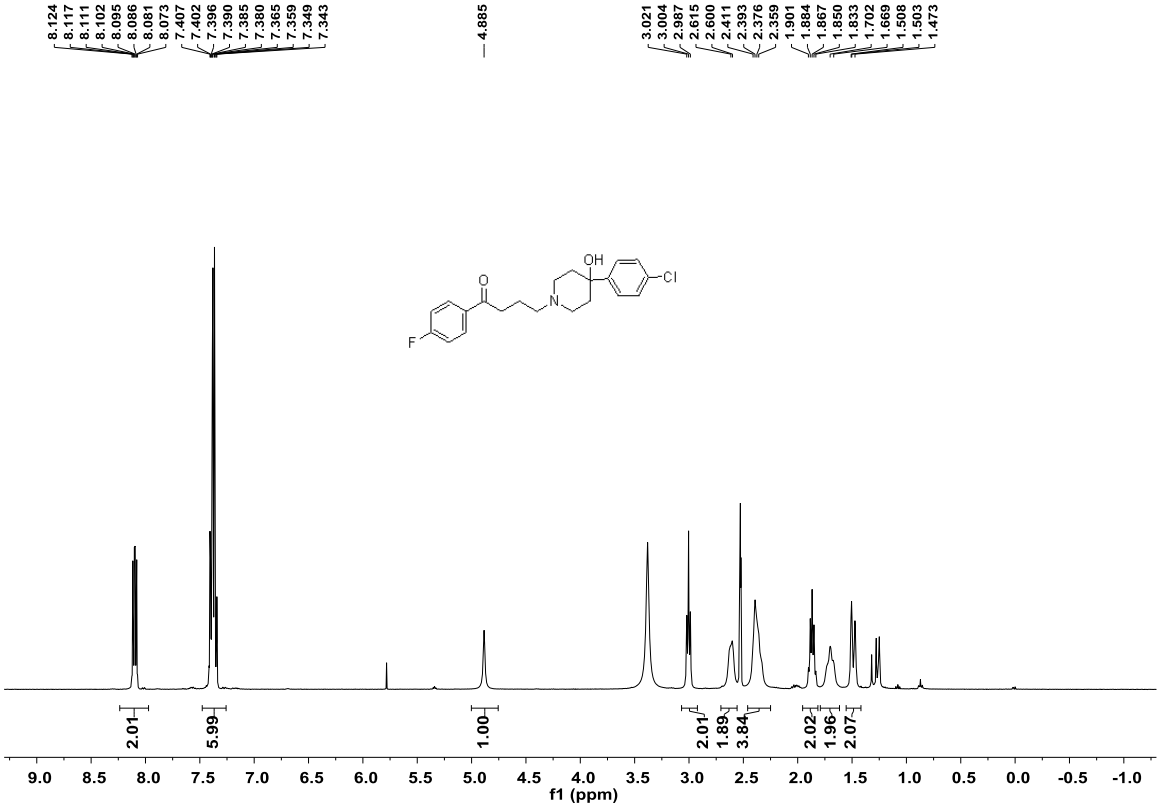
4-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-1-(4-fluorophenyl)butan-1-one (8a)

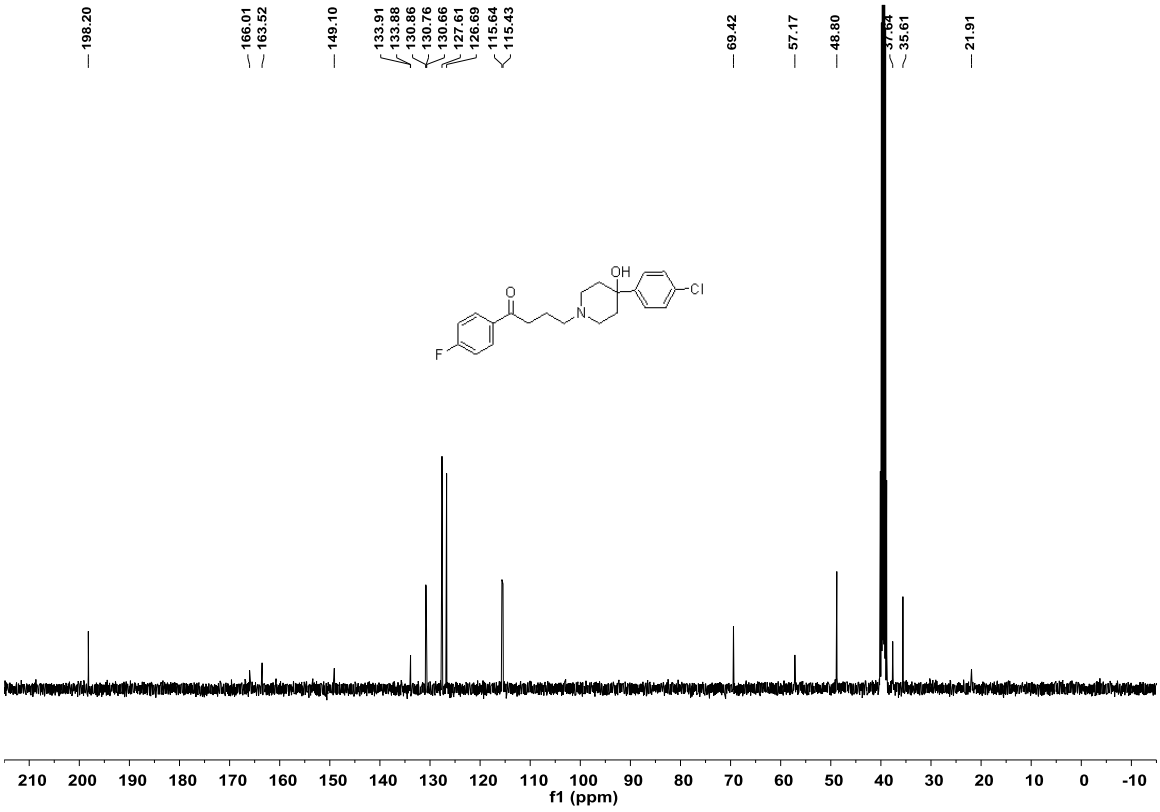


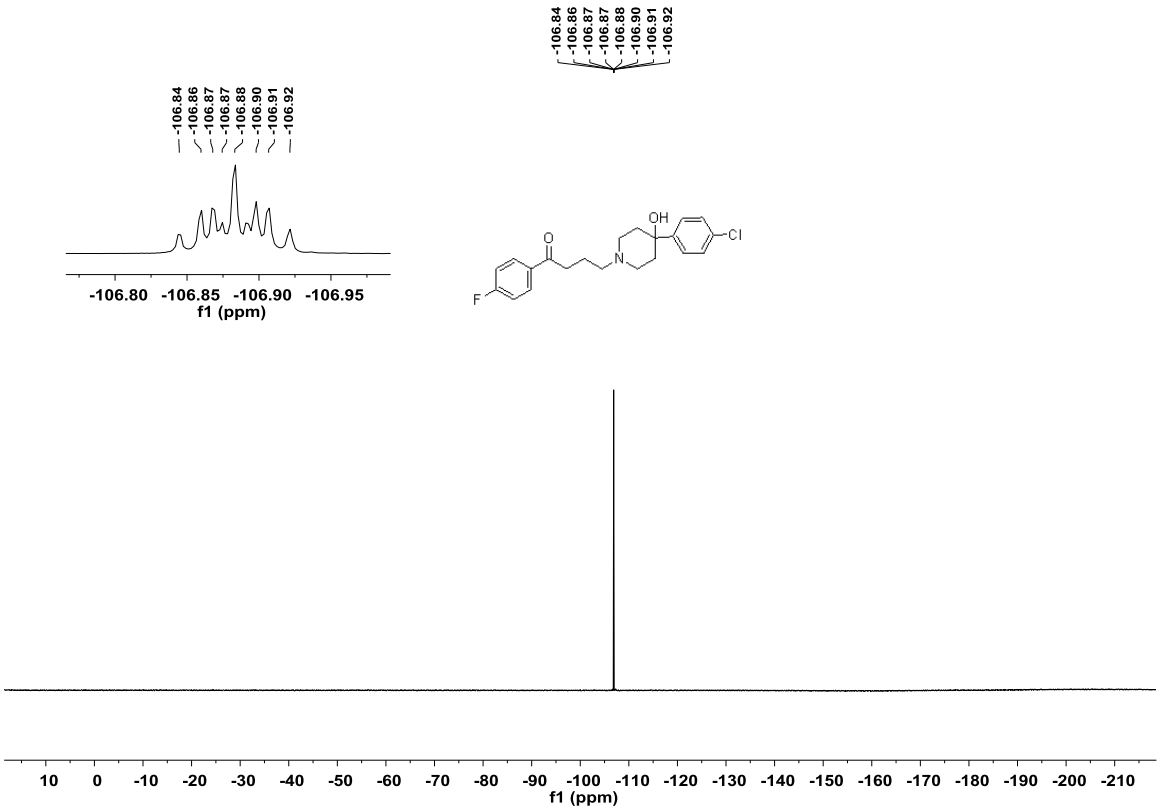




Haloperidol (9)




198.20
166.01
163.52
149.10
133.91
133.88
130.86
130.76
130.66
127.61
126.69
115.64
115.43
69.42
57.17
48.80
37.64
35.61
21.91
OH
Cl
O
N
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-106.84
-106.86
-106.87
-106.87
-106.88
-106.90
-106.91
-106.92
-106.80 -106.85 -106.90 -106.95
f1 (ppm)
OH
Cl
O
N
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

10. References

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