Supporting Information

The Copper-catalyzed Selective Monoalkylation of Active Methylene Compounds with Alkylsilyl Peroxides

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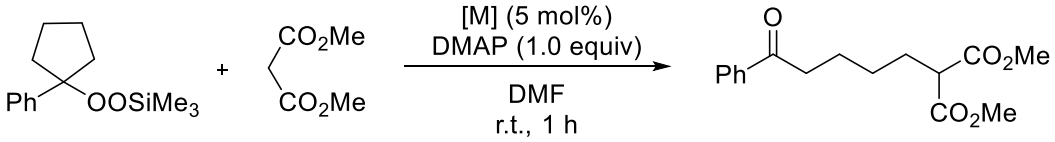
1. General information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE III 400 MHz spectrometer (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR) and Bruker AVANCE DPX-500MHz spectrometer (500 MHz for ^{1}H NMR, 125 MHz for ^{13}C NMR). Tetramethylsilane (TMS) was used as an internal standard (0 ppm) for the ^{1}H NMR spectra, and $CDCl_3$ was used as the internal standard (77.16 ppm) for the ^{13}C NMR spectra. High-resolution mass spectra (HRMS) were recorded on a ThermoFisher Q-Exactive Orbitrap spectrometer with an electrospray ionization (ESI) and an atmospheric-pressure chemical ionization (APCI). Infrared (IR) spectra were obtained on a Thermo-Filsher Nicolet 6700 spectrometer. All the reactions were performed under argon atmosphere. Reactions were monitored by thin-layer chromatography (TLC, silica gel HSGF 254, 0.2-0.3 mm). Reaction products were purified by column chromatography on silica gel (Qingdao Haiyang Chemical Co., Ltd., zcx-II, 300-400 mesh). Copper(I) iodide (98%, Aladdin Chemicals, Shanghai, China) was used as received. Commercially available reagents were used as received. Peroxides **2a**[1], **2b**[1], **2c**[1], **2d**[1], **2e**[1], **2f**[2] and **2g**[1] were prepared according to the previous literatures. Active methylene compound **1e** was prepared according to the literature[3].

2. Reaction optimization of the coupling reaction with active methylene compounds

Table S1. The effect of catalyst[a]

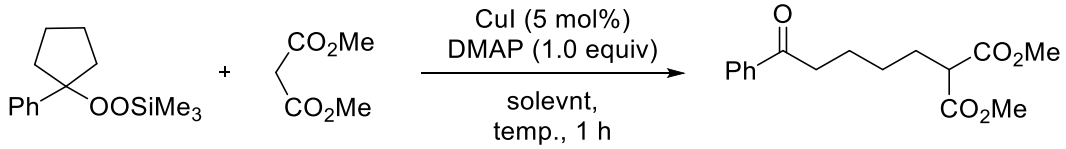


2a (1.4 equiv) **1a** **3a**

Entry	Catalyst	Yield[b] (%)
1	CuI	>99
2	CuBr	98
3	CuCl	99
4	CuOAc	99
5	$CuBr_2$	79
6	$Cu(OAc)_2$	60
7	$FeCl_2$	0
8	$FeCl_3$	0
9	$Pd(PPh_3)_4$	0
10	$Pd(OAc)_2$	0
11	$NiBr_2$	0
14[c]	CuI	63

[a]Reactions were carried out in the presence of **1a** (0.2 mmol), **2a** (0.28 mmol), DMAP (0.2 mmol) and catalyst (5 mol%) in dry DMF (2.0 mL) at room temperature for 1 h under argon atmosphere. [b]The yield of **3a** was determined by ^1H NMR spectroscopy using nitromethane (CH_3NO_2) as an internal standard. [c]1,10-Phen (5 mol%) was used instead of DMAP.

Table S2. The effect of solvents and temperature[a]

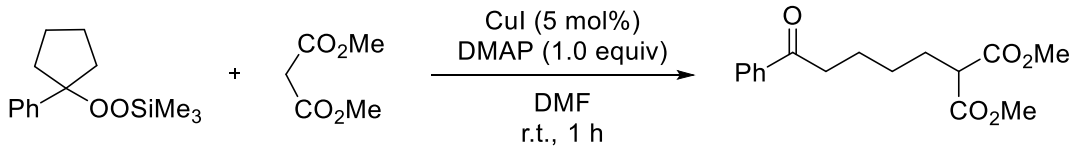


2a (1.4 equiv) **1a** **3a**

Entry	Solvent	Temp. (°C)	Yield[b] (%)
1	C_6H_6	r.t.	62
2	DCE	r.t.	20
3	THF	r.t.	74
4	AcOEt	r.t.	33
5	MeCN	r.t.	0
6	DMSO	r.t.	>99
7	DMF	r.t.	>99
8	DMF	50	>99
9[c]	DMF	25	> 99
10[d]	DMF	0	40

[a]Reactions were carried out in the presence of **1a** (0.2 mmol), **2a** (0.28 mmol), DMAP (0.2 mmol) and CuI (5 mol%) in solvent (2 mL) at 0~50 °C for 1 h under argon atmosphere. [b]The yield of **3a** was determined by ^{1}H NMR spectroscopy using CH_3NO_2 as an internal standard. [c]Constant temperature bath was used. [d]For 4 h.

Table S3. The effect of the ratio between alkylsilyl peroxide and active methylene compound[a]

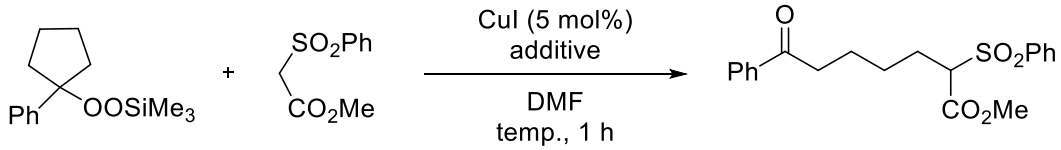


2a **1a** **3a**

Entry	**2a** (equiv)	**1a** (equiv)	Yield[b] (%)
1	1.4	1.0	> 99
2	1.2	1.0	76
3	1.0	1.0	80
4	1.0	1.2	79
5	1.0	1.5	88
6[c]	1.0	1.5	88

[a]Reactions of **1a** and **2a** (1.0 equiv = 0.2 mmol) were carried out in the presence of DMAP (0.2 mmol) and CuI (5 mol%) in DMF (2.0 mL) at room temperature for 1 h under argon atmosphere. [b]The yield of **3a** was determined by ^{1}H NMR spectroscopy using CH_3NO_2 as an internal standard. [c]DMAP (1.5 equiv).

Table S4. Optimization of the reaction of 2a with 1b

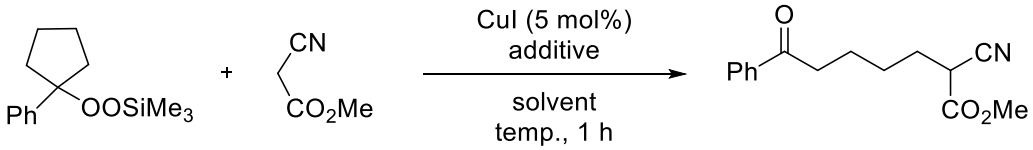


2a **1b** **3b**

Entry	Additive	DMF (mol/L)	Temp. (°C)	Yield[b] (%)
1	DMAP (1.0 equiv)	0.1	r.t.	93
2	DMAP (1.0 equiv)	0.1	50	78
3	DMAP (1.0 equiv)	0.1	80	63
4	DMAP (1.0 equiv)	0.2	r.t.	96
5	DMAP (1.0 equiv)	0.2	50	96
6	DMAP (1.5 equiv)	0.1	50	83
7	1,10-Phen (5 mol%)	0.1	50	78

[a]Reactions**1b** (0.2 mmol) and **2a** (0.28 mmol) were carried out in the presence of CuI (5 mol%) and additive in DMF at room temperature~80 °C for 1 h under argon atmosphere. [b]The yield of **3b** as determined by ^{1}H NMR spectroscopy using CH_3NO_2 as an internal standard.

Table S5. Optimization of the reaction of 2a with 1d



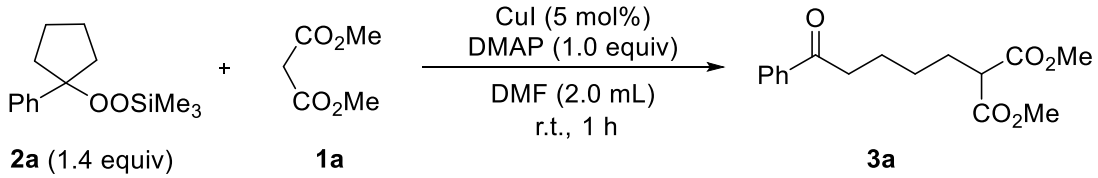
2a **1d** **3d**

Entry	Additive	Solvent (mol/L)	Temp. (°C)	Yield[b] (%)
1	DMAP (1.0 equiv)	DMF (0.2)	r.t.	36
2	DMAP (1.0 equiv)	DMF (0.2)	50	52
3	DMAP (1.0 equiv)	DMF (0.1)	r.t.	56
4	1,10-Phen (5 mol%)	DMF (0.1)	r.t.	46
5[c]	1,10-Phen (5 mol%)	DMF (0.1)	r.t.	25
6[c]	DMAP (1.0 equiv)	DMF (0.1)	50	44
7	DMAP (1.0 equiv)	THF (0.1)	r.t.	56
8	DMAP (1.0 equiv)	THF (0.1)	50	49
9	DMAP (1.0 equiv)	MeCN (0.1)	r.t.	40
10	DMAP (1.0 equiv)	MeCN (0.1)	50	24

[a]Reactions were carried out in the presence of **2e** (0.2 mmol) and **1a** (0.28 mmol), CuI (5 mol%) and additive in solvent for 1 h under argon atmosphere. [b]The yield of **3e** as determined by ^{1}H NMR spectroscopy using CH_3NO_2 as an internal standard. [c]**1a** (0.4 mmol, 2.0 equiv) was used.

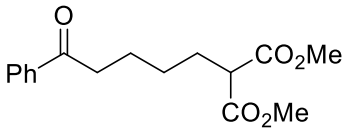
3. General procedure for the coupling reaction with active methylene compounds

I. Reaction of alkylsilyl peroxide 2a with dimethyl malonate 1a (table 1, entry 4)



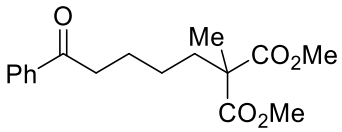
A solution of CuI (1.9 mg, 5 mol%), 4-dimethylaminopyridine (DMAP, 24.4 mg, 1.0 equiv), dimethyl malonate **1a** (26.4 mg, 0.2 mmol) in dry DMF (1.0 mL) was stirred for 10 min at room temperature under argon atmosphere. To the solution was added the solution of alkylsilyl peroxide **2a** (70.0 mg, 1.4 equiv) in dry DMF (1.0 mL) was added dropwise and the rection mixture was stirred for 1 h. The mixture was then diluted with ethyl acetate/hexane (volume ratio, 1:3) and washed with H_2O three times. The organic layer was filtrated thorough silica pad and the filtrate was concentrated under reduced pressure. The residue was analyzed by ^1H NMR for the determination of NMR yield using CH_3NO_2 as an internal standard. The crude product was purified by flash column chromatography on silica gel (eluted with AcOEt /hexane = 1:5) to afford **3a** in 99% yield.

Dimethyl 2-(5-oxo-5-phenylpentyl)malonate (3a)



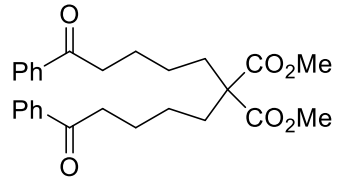
White solid, 99% isolated yield (58.4 mg, 0.20 mmol); ^1H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 7.0Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.46 (t, J =8.0 Hz, 2H), 3.74 (s, 6H), 3.39 (t, J = 7.5 Hz, 1H), 2.98 (t, J = 7.5 Hz, 2H), 1.99–1.94 (m, 2H), 1.81–1.75 (m, 2H), 1.45–1.39 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.9, 169.8, 136.9, 133.0, 128.6, 128.0, 52.5, 51.5, 38.1, 28.7, 27.0, 23.7; IR (KBr): 2950, 1754, 1442, 1165, 727, 693 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{20}NaO_5$: m/z 315.1208 $[M+Na]^+$, found: 315.1201 $[M+Na]^+$.

Dimethyl 2-methyl-2-(5-oxo-5-phenylpentyl)malonate (5)



White solid, 25% isolated yield (15.3 mg, 0.05 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.72 (s, 6H), 2.98 (t, J = 7.3 Hz, 2H), 1.94–1.91 (m, 2H), 1.78–1.73 (m, 2H), 1.42 (s, 3H), 1.34–1.30 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0, 172.8, 137.0, 133.0, 128.6, 128.0, 53.7, 52.5, 38.2, 35.5, 24.3, 24.1, 20.0; IR (KBr): 1727, 1465, 1368, 1220, 1166, 728, 687 cm^{-1};. HRMS (ESI): calcd. for $C_{17}H_{22}NaO_5$: m/z 329.1365 $[M+Na]^+$, found: m/z 329.1356.

Dimethyl 2,2-bis(5-oxo-5-phenylpentyl)malonate (6)



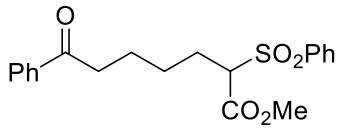
Colorless oil, 15% isolated yield (13.6 mg, 0.030 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.4 Hz ,4H), 7.55 (t, J = 7.4 Hz, 2H), 7.45 (t, J = 7.6 Hz, 4H), 3.70 (s, 6H), 2.97 (t, J = 7.6 Hz, 4H), 1.96–1.92 (m, 4H), 1.77–1.73 (m, 4H), 1.29–1.26 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 172.2, 137.0, 133.0, 128.6, 128.0, 57.6, 52.4, 38.1, 32.4, 24.3, 23.9; IR (KBr): 1732, 1682, 1448, 753, 691 cm^{-1}; HRMS (APCI): calcd. for $C_{27}H_{33}O_6$: m/z 453.2277 $[M+H]^+$, found: 453.2264 $[M+H]^+$.

II. Reaction of alkylsilyl peroxide 2 with active methylene compound 1 (table 2, table3, and scheme 2)

To a solution of CuI (1.9 mg, 5 mol%), DMAP (24.4 mg, 1.0 equiv), active methylene compound **1** (0.2 mmol) in dry DMF (0.5 mL) was added the solution of alkylsilyl peroxide **2** (1.4 equiv) in dry DMF (0.5 mL) at indicated temperature and the reaction mixture was stirred at the same temperature for 1 h. The reaction mixture was then diluted with ethyl acetate/hexane (volume ratio, 1:3) and washed with H_2O three times. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. The residue was analyzed by ^1H NMR for the determination of NMR yield using CH_3NO_2 as an internal standard. The crude product was purified by flash column chromatography on silica gel (eluted with AcOEt/hexane = 1:5) to obtain corresponding products.

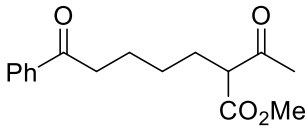
Unless otherwise noted, reactions in tables 2 and 3 were performed at room temperature and 50 °C, respectively.

Methyl 7-oxo-7-phenyl-2-(phenylsulfonyl)heptanoate (3b)



Yellow oil, 91% isolated yield (68.3 mg, 0.18 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.86–7.73 (m, 4H), 7.60 (t, J = 7.4 Hz, 1H), 7.51–7.45 (m, 3H), 7.36 (t, J = 7.6 Hz, 2H), 3.92–3.89 (m, 1H), 3.57 (s, 3H), 2.86 (t, J = 7.2 Hz, 2H), 2.00–1.92 (m, 2H), 1.71–1.60 (m, 2H), 1.35–1.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 166.4, 137.0, 136.8, 134.4, 133.1, 129.3, 129.1, 128.6, 128.0, 70.6, 53.0, 37.8, 26.6, 26.5, 23.4; IR (KBr): 1740, 1447, 1323, 757, 689 cm^{-1}; HRMS (ESI): calcd. for $C_{20}H_{22}NaO_5S$: m/z 397.1086 $[M+Na]^+$, found: 397.1078 $[M+Na]^+$.

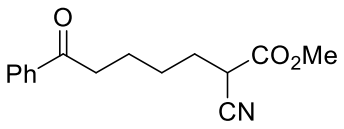
Methyl 2-acetyl-7-oxo-7-phenylheptanoate (3c)



Performed at 50 °C. White solid, 45% isolated yield. (25.2 mg, 0.091 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.2 Hz ,2H), 7.55 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.74 (s, 3H), 3.46 (t, J = 7.2 Hz, 1H), 2.98 (t, J = 7.2 Hz, 2H), 2.23 (s, 3H), 1.93–1.87 (m, 2H), 1.79–1.73 (m, 2H), 1.42–1.36 (m , 2H); ^{13}C NMR (100 MHz,

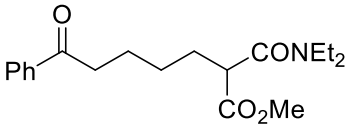
$CDCl_3$): δ 203.3, 199.9, 170.3, 136.9, 133.0, 128.6, 128.0, 59.4, 52.4, 38.1, 29.0, 28.0, 27.1, 23.8; IR (KBr): 1715, 1461, 1207, 731, 692 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{20}NaO_4$: m/z 299.1259 $[M+Na]^+$, found: 299.1251 $[M+Na]^+$.

Methyl 2-cyano-7-oxo-7-phenylheptanoate (3d)



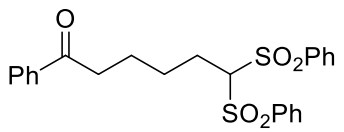
White solid, 48% isolated yield (24.8 mg, 0.10 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 3.82 (s, 3H), 3.55 (t, J = 8.0 Hz, 1H), 3.02 (t, J = 7.2 Hz, 2H), 2.05–1.99 (m, 2H), 1.84–1.78 (m, 2H), 1.65–1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 166.6, 136.8, 133.1, 128.7, 128.0, 116.4, 53.5, 37.9, 37.3, 29.7, 26.5, 23.2; IR (KBr): 2249, 1747, 1682, 1179, 751, 691 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{16}NO_3$: m/z 258.1130 $[M-H]^-$, found: 258.1134 $[M-H]^-$.

Methyl 2-(diethylcarbamoyl)-7-oxo-7-phenylheptanoate (3e)



Performed at 50 °C. Yellow oil, 63% isolated yield (40.0 mg, 0.13 mmol). ^1H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 3.71 (s, 3H), 3.55 (t, J = 7.2 Hz, 1H), 3.45–3.32 (m, 4H), 2.99 (t, J = 7.2, 2H), 2.02–1.97 (m, 2H), 1.81–1.75 (m, 2H), 1.44–1.37 (m, 2H), 1.20 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.2, 170.6, 167.8, 136.9, 133.0, 128.6, 128.0, 52.4, 48.7, 42.2, 40.7, 38.1, 29.3, 27.2, 24.0, 14.5, 12.8; IR (KBr): 1744, 1684, 1643, 1448, 1219, 755, 692 cm^{-1}; HRMS (ESI): calcd. for $C_{19}H_{27}NaNO_4$: m/z 356.1838 $[M+Na]^+$, found: 356.1829 $[M+Na]^+$.

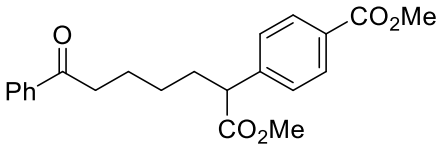
1-Phenyl-6,6-bis(phenylsulfonyl)hexan-1-one (3f)



Performed at 50 °C. Colorless oil, 63% isolated yield (57.5 mg, 0.13 mmol). ^1H NMR (500 MHz, $CDCl_3$): δ 7.96 (d, J = 7.5 Hz, 4H), 7.93 (d, J = 7.3 Hz, 2H), 7.68 (t, J = 7.5 Hz, 2H), 7.58–7.55 (m, 5H), 7.47 (t, J = 7.7 Hz, 2H), 4.49 (t, J = 5.6 Hz, 1H), 2.94–2.92

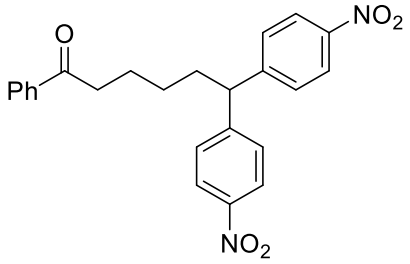
(m, 2H), 2.21–2.19 (m, 2H), 1.69–1.67 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 138.4, 137.9, 136.8, 134.9, 134.6, 133.2, 129.6, 129.4, 129.2, 128.9, 128.7, 128.0, 83.3, 37.6, 27.5, 25.5, 23.1; IR (KBr): 1682, 1330, 752, 688 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{24}NaO_5S_2$: m/z 479.0963 $[M+Na]^+$, found: 479.0956 $[M+Na]^+$.

Methyl 4-(1-methoxy-1,7-dioxo-7-phenylheptan-2-yl)benzoate (3g)



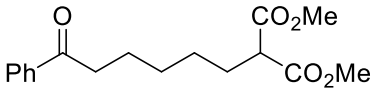
Yellow solid, 80% isolated yield (59.0 mg, 0.16 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 7.0 Hz ,2H), 7.55 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 3.90 (s, 3H), 3.66 (s, 3H), 3.63 (t, J = 7.7 Hz, 1H), 2.95–2.92 (m, 2H), 2.19–2.11(m, 1H), 1.88–1.80 (m, 1H), 1.78–1.72 (m, 2H), 1.38–1.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0, 173.8, 166.8, 144.2, 136.9, 133.0, 123.0, 129.2, 128.6, 128.1, 128.0, 52.2, 52.1, 51.4, 38.2, 33.2, 27.2, 23.8; IR (KBr): 1717, 1376, 1207, 1166, 867, 743, 725, 703, 690 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{24}NaO_5$: m/z 391.1521 $[M+Na]^+$, found: 391.1514 $[M+Na]^+$.

6,6-Bis(4-nitrophenyl)-1-phenylhexan-1-one (3h)



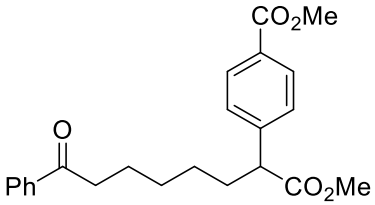
Performed at 50 °C. Colorless oil, 27% isolated yield (22.3 mg, 0.054 mmol); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.4 Hz, 4H), 7.91 (d, J = 7.9 Hz, 2H), 7.56 (t, J = 7.1 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.38 (d, J = 8.4 Hz, 4H), 4.16 (t, J = 7.8 Hz, 1H), 2.95 (t, J = 7.0 Hz, 2H), 2.20–2.14 (m, 2H), 1.85–1.78 (m, 2H), 1.39–1.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.8, 150.7, 146.9, 136.9, 133.2, 128.7, 128.6, 128.0, 124.1, 50.8, 38.1, 35.0, 29.7, 27.4, 23.8; IR (KBr): 1717, 1518, 1457, 856, 830, 746, 691 cm^{-1}; HRMS (ESI): calcd. for $C_{24}H_{21}N_2O_5$: m/z 417.1450 $[M-H]^-$, found: 417.1459 $[M-H]^-$.

Dimethyl 2-(6-oxo-6-phenylhexyl)malonate (7b)



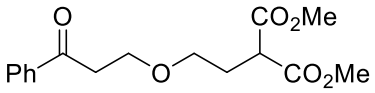
White solid, 62% isolated yield (37.9 mg, 0.12 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.0 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 3.74 (s, 6H), 3.37 (t, J = 7.5 Hz, 1H), 2.96 (t, J = 7.3 Hz, 2H), 1.95–1.90 (m, 2H), 1.78–1.72 (m, 2H), 1.44–1.35 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3, 169.9, 137.0, 133.0, 128.6, 128.0, 52.5, 51.6, 38.3, 28.9, 28.7, 27.2, 23.9; IR (KBr): 1470, 1373, 1193, 1159, 750, 729, 688 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{22}NaO_5$: m/z 329.1365 $[M+Na]^+$, found: 329.1355 $[M+Na]^+$.

Methyl 4-(1-methoxy-1,8-dioxo-8-phenyloctan-2-yl)benzoate (8b)



Performed at room temperature. Colorless oil, 56% isolated yield (42.8 mg, 0.11 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 7.2 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 3.90 (s, 3H), 3.66 (s, 3H), 3.61 (t, J = 8.0 Hz, 1H), 2.93 (t, J = 7.2 Hz, 2H), 2.15–2.06 (m, 1H), 1.84–1.76 (m, 1H), 1.73–1.67 (m, 2H), 1.42–1.36 (m, 2H), 1.34–1.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.4, 173.9, 167.0, 144.4, 137.1, 133.0, 132.8, 130.0, 129.2, 128.6, 128.0, 52.1, 51.6, 38.3, 33.2, 29.0, 27.3, 24.0; IR (KBr): 2926, 1724, 1611, 1448, 855, 747, 691 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{26}NaO_5$: m/z 405.1678 $[M+Na]^+$, found: 405.1671 $[M+Na]^+$.

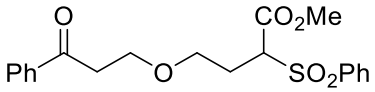
Dimethyl 2-(2-(3-oxo-3-phenylpropoxy)ethyl)malonate (7c)



Colorless oil, 55% isolated yield (33.9 mg, 0.11 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98–7.93 (m, 2H), 7.59–7.53 (m, 1H), 7.47 (t, J = 7.6 Hz, 2H), 3.83 (t, J = 6.4 Hz, 2H), 3.71 (s, 6H), 3.59–3.49 (m, 3H), 3.21 (t, J = 6.4 Hz, 2H), 2.19–2.15 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 169.8, 168.9, 137.0, 133.2, 128.6, 128.1, 68.2, 66.1, 52.5,

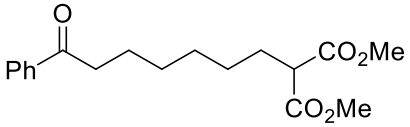
48.6, 38.7, 28.9; IR (KBr): 1735, 1448, 1259, 1157, 750, 692 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{20}NaO_6$: m/z 331.1158 $[M+Na]^+$, found: 331.1150 $[M+Na]^+$.

Methyl 4-(3-oxo-3-phenylpropoxy)-2-(phenylsulfonyl)butanoate (9c)



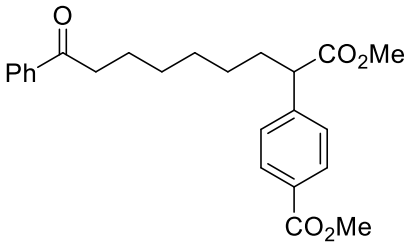
Yellow oil, 80% isolated yield (61.5 mg, 0.16 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.2 Hz, 2H), 7.86 (d, J = 7.2 Hz, 2H), 7.67 (t, J = 7.6 Hz, 1H), 7.55 (t, J = 8.0 Hz, 3H), 7.46 (t, J = 7.6 Hz, 2H), 4.17–4.14 (m, 1H), 3.82–3.75 (m, 2H), 3.61–3.56 (m, 4H), 3.49–3.43 (m, 1H), 3.21–3.12 (m, 2H), 2.36–2.30 (m, 1H), 2.25–2.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 166.2, 137.1, 136.9, 134.3, 133.3, 129.2, 129.1, 128.7, 128.1, 68.1, 67.5, 66.0, 52.9, 38.5, 27.0; IR (KBr): 2873, 1742, 1479, 1323, 1212, 758, 689 cm^{-1}; HRMS (ESI): calcd. for $C_{20}H_{22}NaO_6S$: m/z 413.1035 $[M+Na]^+$, found: 413.1025 $[M+Na]^+$.

Dimethyl 2-(7-oxo-7-phenylheptyl)malonate (7d)



Performed at room temperature. White solid, 92% isolated yield (59.0 mg, 0.18 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.0 Hz ,2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.73 (s, 6H), 3.36 (t, J = 7.2 Hz, 1H), 2.96 (t, J = 7.4 Hz, 2H), 1.93-1.88 (m, 2H), 1.75–1.71 (m, 2H), 1.38–1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.4, 169.9, 137.0, 132.9, 128.6, 128.0, 52.4, 51.7, 38.5, 29.0, 28.8, 27.2, 24.1; IR (KBr): 1750, 1731, 1466, 1161, 757, 722, 687 cm^{-1}; HRMS (ESI): calcd. for $C_{18}H_{24}NaO_5$: m/z 343.1521 $[M+Na]^+$, found: 343.1513 $[M+Na]^+$.

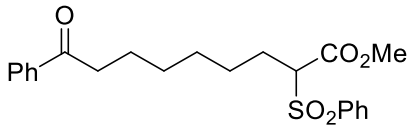
Methyl 4-(1-methoxy-1,9-dioxo-9-phenylnonan-2-yl)benzoate (8d)



Performed at room temperature. White solid, 75% isolated yield (59.4 mg, 0.15 mmol).

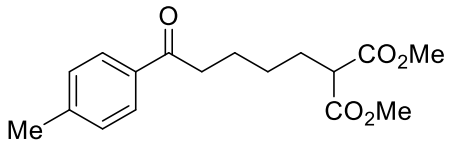
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 3.90 (s, 3H), 3.66 (s, 3H), 3.60 (t, J = 7.7 Hz, 1H), 2.94 (t, J = 7.4 Hz, 2H), 2.09 (m, 1H), 1.88–1.73 (m, 1H), 1.73–1.59 (m, 3H), 1.42–1.32 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.5, 173.9, 166.9, 144.3, 137.0, 132.9, 129.9, 129.2, 129.1, 128.6, 128.0, 128.0, 52.2, 52.1, 51.6, 38.5, 33.4, 29.2, 29.1, 27.4, 24.2; IR (KBr): 2851, 1717, 1466, 1203, 1166, 859, 757, 718, 691 cm^{-1}; HRMS (ESI): calcd. for $C_{24}H_{28}NaO_5$: m/z 419.1834 $[M+Na]^+$, found: 419.1828 $[M+Na]^+$.

Methyl 9-oxo-9-phenyl-2-(phenylsulfonyl)nonanoate (9d)



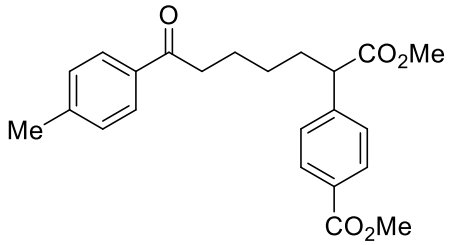
Yellow oil, 64% isolated yield (51.5 mg, 0.13 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.2 Hz, 2H), 7.87 (d, J = 7.2 Hz, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.61–7.54 (m, 3H), 7.46 (t, J = 7.6 Hz, 2H), 3.96–3.93 (m, 1H), 3.66 (s, 3H), 2.94 (t, J = 7.2 Hz, 2H), 2.11–1.83 (m, 2H), 1.76–1.58 (m, 2H), 1.38–1.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.3, 166.5, 137.1, 137.0, 134.3, 133.0, 129.3, 129.1, 128.6, 128.5, 128.0, 70.9, 52.9, 38.4, 28.9, 28.8, 26.8, 26.7, 24.0; IR(KBr): 2923, 1737, 1711, 1462, 1320, 1199, 741, 718, 618 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{26}NaO_5S$: m/z 425.1399 $[M+Na]^+$, found: 425.1392 $[M+Na]^+$.

Dimethyl 2-(5-oxo-5-(4-tolyl)pentyl)malonate (7e)



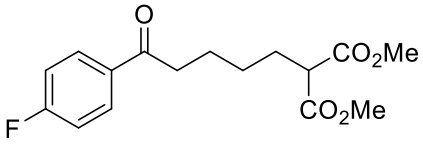
White solid, 77% isolated yield (47.1 mg, 0.15 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, J = 8.2 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 3.74 (s, 6H), 3.39 (t, J = 7.5 Hz, 1H), 2.95 (t, J = 7.3 Hz, 2H), 2.41 (s, 3H), 1.98–1.94 (m, 2H), 1.79–1.73 (m, 2H), 1.43–1.40 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.6, 169.8, 143.7, 134.5, 129.3, 128.1, 52.5, 51.5, 38.0, 28.7, 27.0, 23.8, 21.6; IR (KBr): 2955, 1751, 1733, 1461, 1163, 822 cm^{-1}; HRMS (ESI): calcd. for $C_{17}H_{22}NaO_5$: m/z 329.1365 $[M+Na]^+$, found: 329.1359 $[M+Na]^+$.

Methyl 4-(1-methoxy-1,7-dioxo-7-(4-tolyl)heptan-2-yl)benzoate (8e)



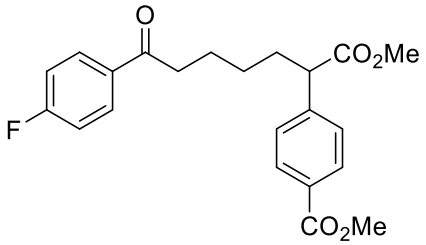
White solid, 73% isolated yield (55.8 mg, 0.15 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 3.91 (s, 3H), 3.66 (s, 3H), 3.63 (t, J = 7.7 Hz, 1H), 2.91 (t, J = 7.3 Hz, 2H), 2.40 (s, 3H), 2.17–2.12 (m, 1H), 1.87–1.79 (m, 1H), 1.76–1.71 (m, 2H), 1.36–1.31 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 173.8, 166.9, 144.2, 143.8, 133.4, 130.0, 129.3, 129.2, 128.1, 128.0, 52.2, 52.1, 51.4, 38.1, 33.3, 27.2, 23.9, 21.6; IR (KBr): 2895, 1717, 1466, 1179, 1168, 817 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{26}NaO_5$: m/z 405.1678 $[M+Na]^+$, found: 405.1670 $[M+Na]^+$.

Dimethyl 2-(5-(4-fluorophenyl)-5-oxopentyl)malonate (7f)



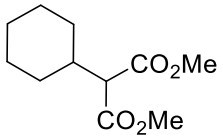
Colorless oil, 76% isolated yield (47.1 mg, 0.15 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00–7.96 (m, 2H), 7.12 (t, J = 8.6 Hz, 2H), 3.74 (s, 6H), 3.39 (t, J = 7.5 Hz, 1H), 2.95 (t, J = 7.2 Hz, 2H), 1.99–1.93 (m, 2H), 1.81–1.73 (m, 2H), 1.46–1.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 169.8, 165.7 (d, $J_{C\text{-}F}$ = 250.0 Hz), 133.5, 130.6 (d, $J_{C\text{-}F}$ = 9.3 Hz), 115.7 (d, $J_{C\text{-}F}$ = 21.8 Hz), 52.5, 51.5, 38.0, 28.6, 26.9, 23.6; IR (KBr): 2954, 1735, 1435, 1409, 1156, 838 cm^{-1}; HRMS (ESI): calcd. for $C_{16}H_{19}FNaO_5$, m/z 333.1114 $[M+Na]^+$, found: 333.1105 $[M+Na]^+$.

Methyl 4-(7-(4-fluorophenyl)-1-methoxy-1,7-dioxoheptan-2-yl)benzoate (8f)



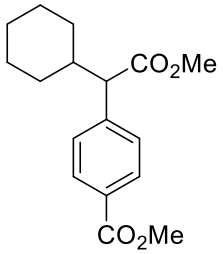
White solid, 50% isolated yield (38.6 mg, 0.10 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.11 (t, J = 8.3 Hz ,2H), 3.91 (s, 3H), 3.66 (s, 3H), 3.63 (t, J = 7.7 Hz, 1H), 2.91 (t, J = 7.3 Hz, 2H), 2.20–2.11 (m, 1H), 1.87–1.81 (m, 1H), 1.78–1.71 (m,3H), 1.36–1.32 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.3, 173.8, 166.8, 165.7 (d, $J_{C\text{-}F}$ = 252.9 Hz), 144.1, 133.3 (d, $J_{C\text{-}F}$ = 3.0 Hz), 130.6 (d, $J_{C\text{-}F}$ = 9.3 Hz), 130.0, 129.2, 128.0, 115.7 (d, $J_{C\text{-}F}$ = 21.8 Hz), 52.2, 52.1, 51.4, 38.1, 33.2, 27.1, 23.8; IR (KBr): 2952, 1735, 1717, 1464, 1410, 1157, 840 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{23}FNaO_5$: m/z 409.1427 $[M+Na]^+$, found: 409.1418 $[M+Na]^+$.

Dimethyl 2-cyclohexylmalonate (7g)[4]



Colorless oil, 52% isolated yield (22.3 mg, 0.10 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.73 (s, 6H), 3.19 (d, J = 9.2 Hz, 1H), 2.12–2.02 (m, 1H), 1.74–1.65 (m, 5H), 1.34–1.24 (m, 2H), 1.18–1.13 (m, 1H), 1.08–1.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.2, 58.1, 52.2, 38.0, 30.7, 26.0, 25.9.

Methyl 4-(1-cyclohexyl-2-methoxy-2-oxoethyl)benzoatev (8g)[5]

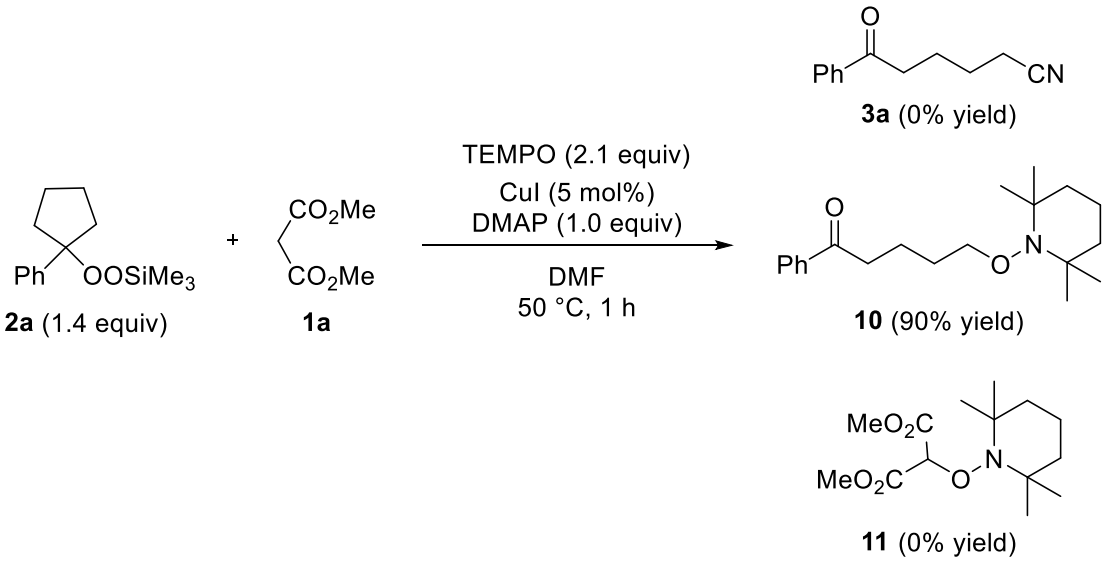


Performed at room temperature. Colorless oil, 55% isolated yield (31.9 mg, 0.11 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 3.90 (s, 1H), 3.65 (s, 3H), 3.30 (d, J = 10.6 Hz, 3H), 2.06–1.99 (m, 1H), 1.81–1.59 (m, 5H),

1.37–1.32 (m, 1H), 1.15–1.04 (m, 3H), 0.78–0.73 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.8, 166.9, 143.1, 129.7, 129.1, 128.7, 58.8, 52.1, 51.9, 41.2, 31.9, 30.4, 28.2, 25.9.

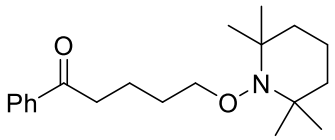
4. Control experiment

Radical trapping experiment (Scheme 4)



To a solution of CuI (1.9 mg, 5 mol%), DMAP (24.4 mg, 1.0 equiv), dimethyl malonate **1a** (26.4 mg, 0.2 mmol) and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) (65.6 mg, 2.1 equiv) in dry DMF (1.0 mL) was added a solution of alkylsilyl peroxide **2a** (70.0 mg, 1.4 equiv) in dry DMF (1.0 mL) slowly at 50 °C. After stirring at 50 °C for 1 h, the reaction mixture was diluted with the mixture of AcOEt/hexane (volume ratio, 1:3) and washed with H_2O three times. The organic layer was dried over Na_2SO_4, filtrated and concentrated under reduced pressure. The residue was analyzed by ^1H NMR for the determination of NMR yields of **3a**, **10** and **11** using CH_3NO_2 as an internal standard. The crude product was purified by flash column chromatography on silica gel (eluted with AcOEt/hexane = 1:5) to afford TEMPO adduct of **10**.

1-Phenyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-1-one (10)[6]



Colorless oil, 92% isolated yield (81.7 mg, 0.26 mmol). ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.2 Hz, 2H), 7.56 (t, 1H), 7.46 (t, J = 7.6 Hz, 2H), 3.79 (t, J = 6.4 Hz, 2H), 3.02 (t, J = 7.2 Hz, 2H), 1.86–1.83 (m, 2H), 1.65–1.61 (m, 2H), 1.44–1.42 (m, 2H), 1.15 (s, 6H), 1.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.4, 137.1, 132.9, 128.6, 128.1, 76.6, 59.7, 39.6, 38.7, 33.1, 28.5, 21.5, 20.2, 17.2.

5. References

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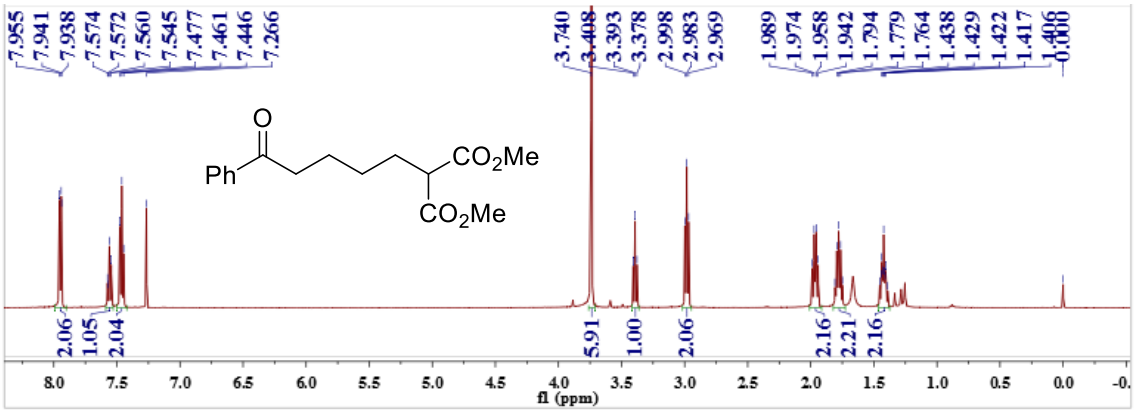
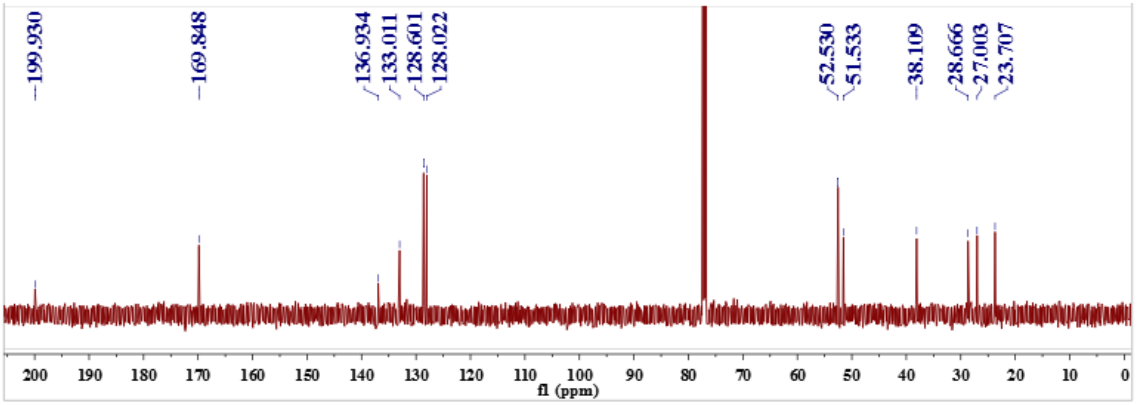
6. ^{1}H NMR and ^{13}C NMR Spectra

NMR Spectra of dimethyl 2-(5-oxo-5-phenylpentyl)malonate (3a)

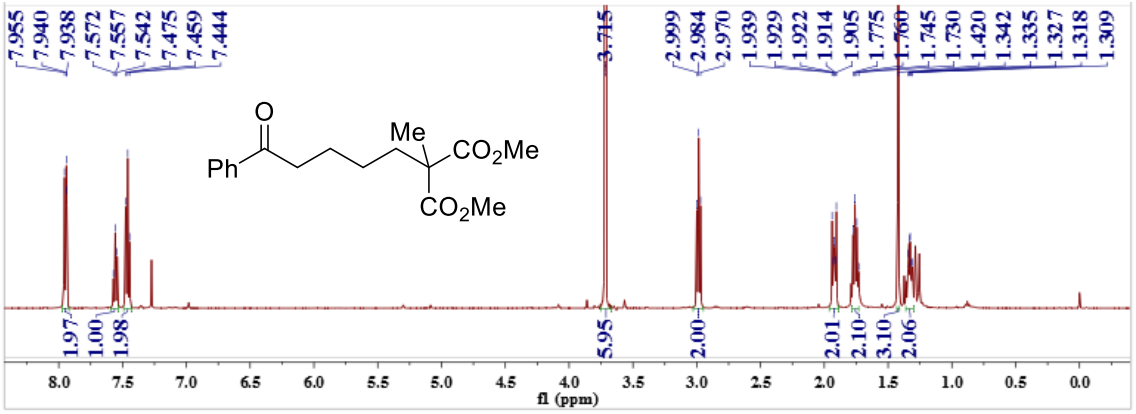


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3a**

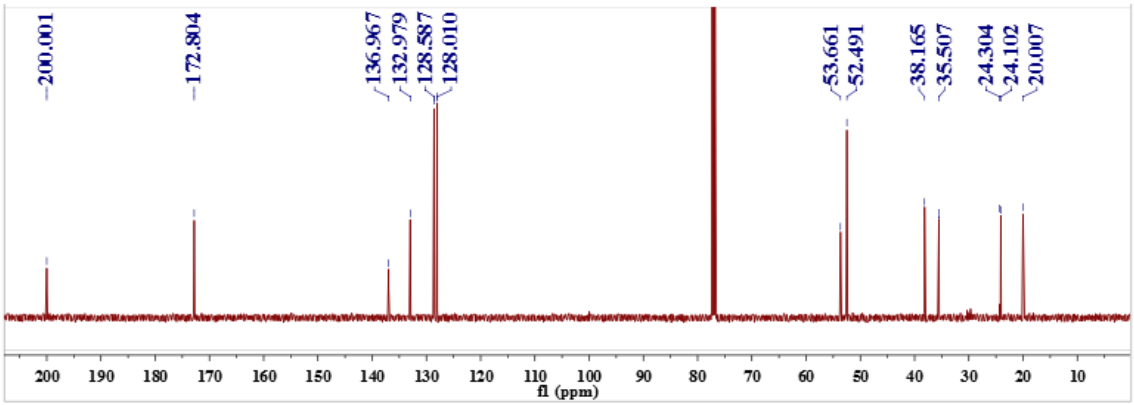


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3a**

NMR Spectra of dimethyl 2-methyl-2-(5-oxo-5-phenylpentyl)malonate (5)

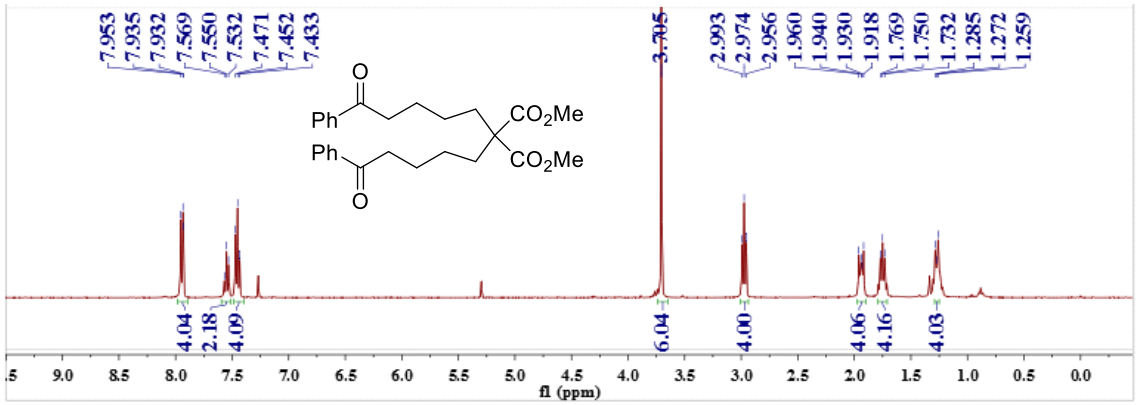


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **5**

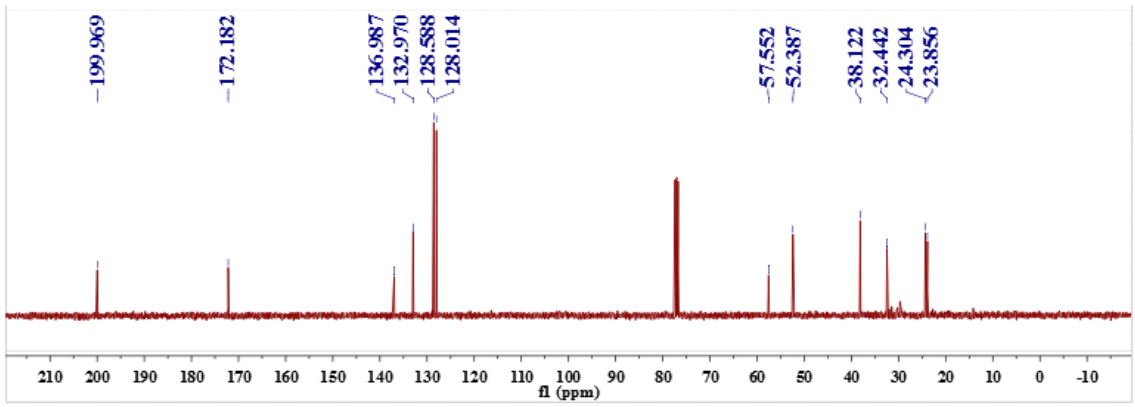


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **5**

NMR Spectra of dimethyl 2,2-bis(5-oxo-5-phenylpentyl)malonate (6)

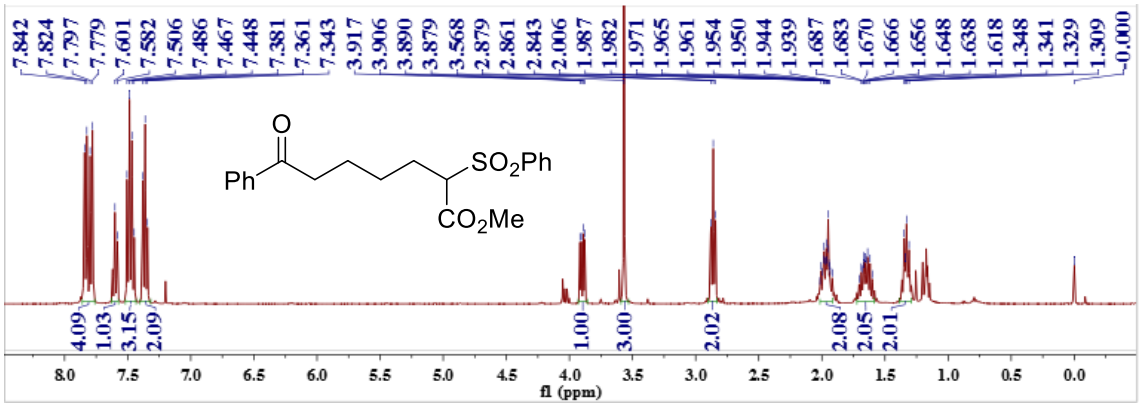


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **6**

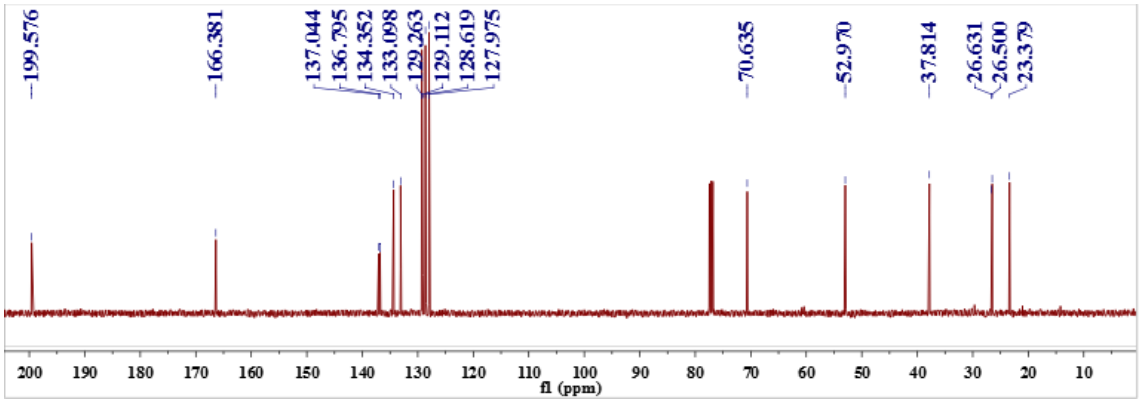


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **6**

NMR Spectra of methyl 7-oxo-7-phenyl-2-(phenylsulfonyl)heptanoate (3b)

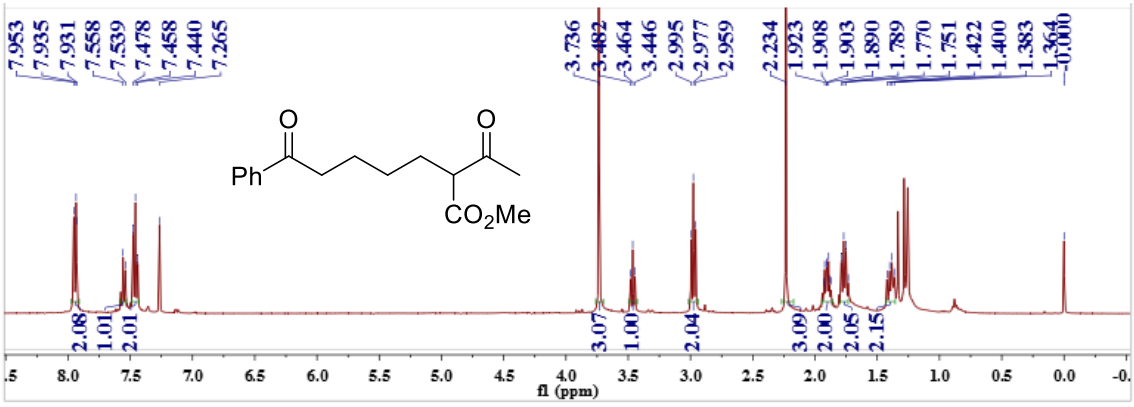


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3b**

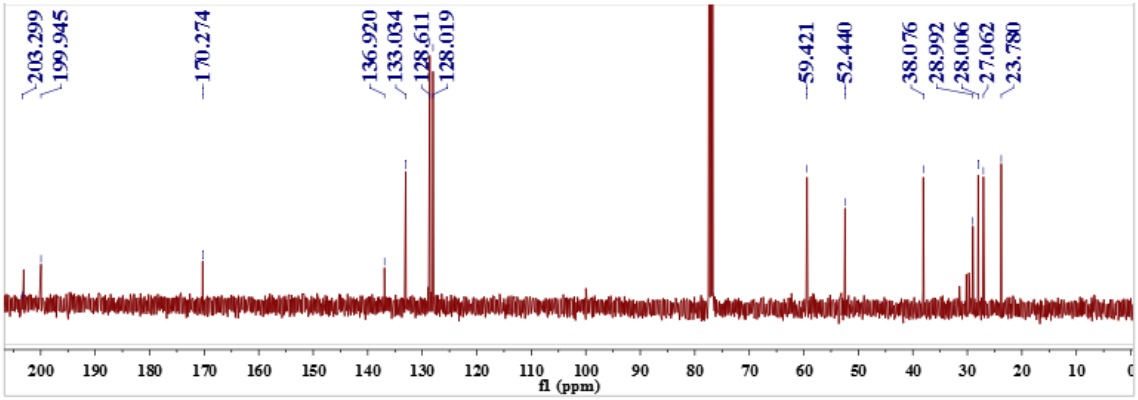


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3b**

NMR Spectra of methyl 2-acetyl-7-oxo-7-phenylheptanoate (3c)

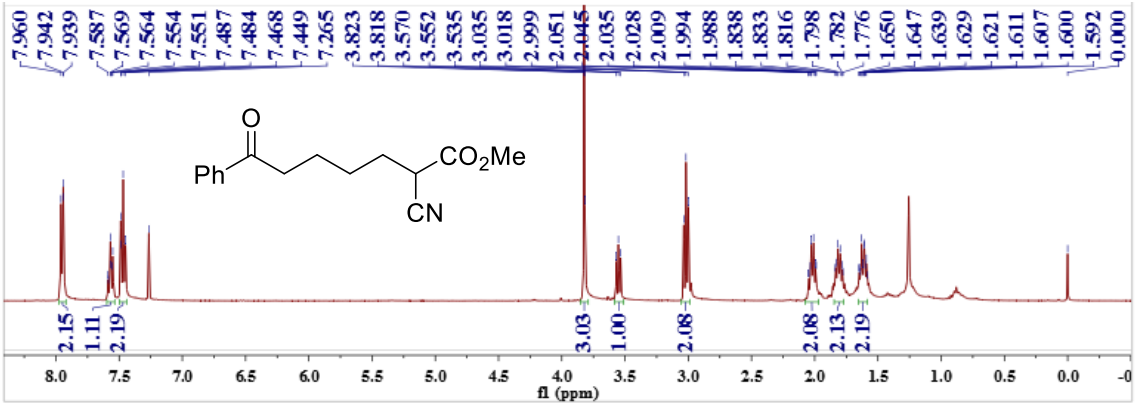


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3c**

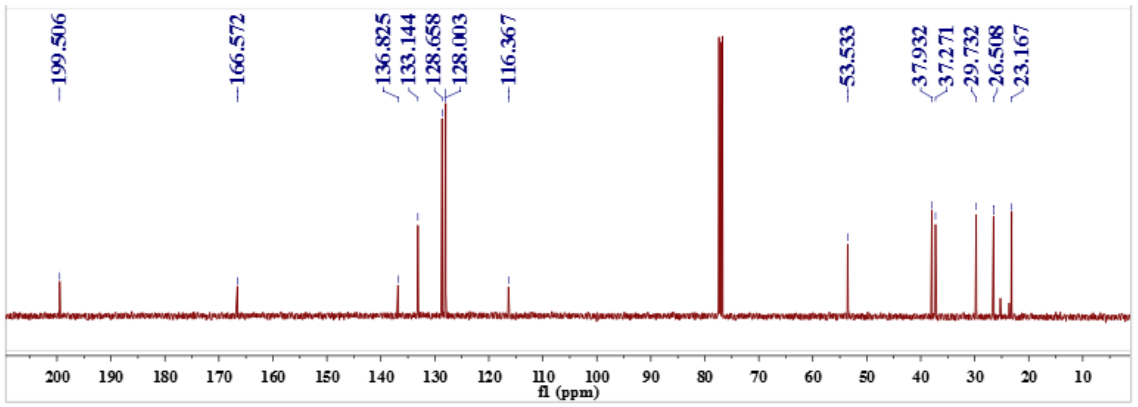


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3c**

NMR Spectra of methyl 2-cyano-7-oxo-7-phenylheptanoate (3d)

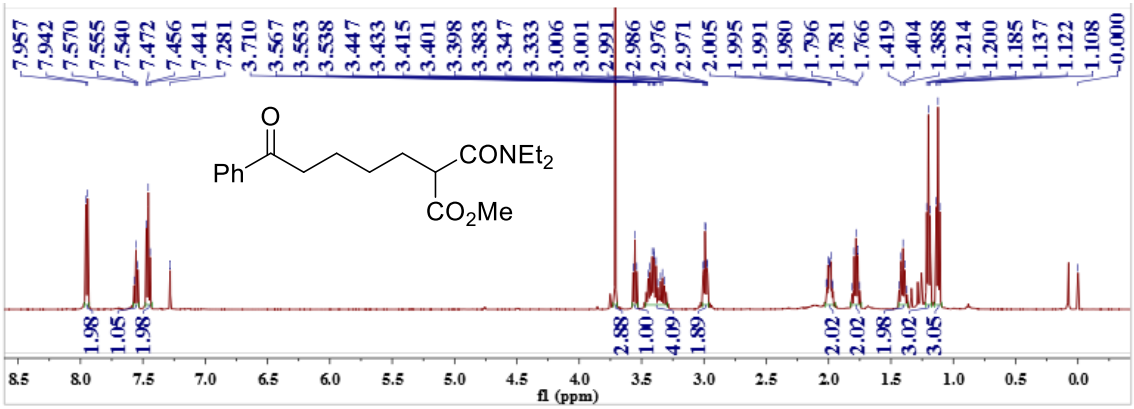


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3d**

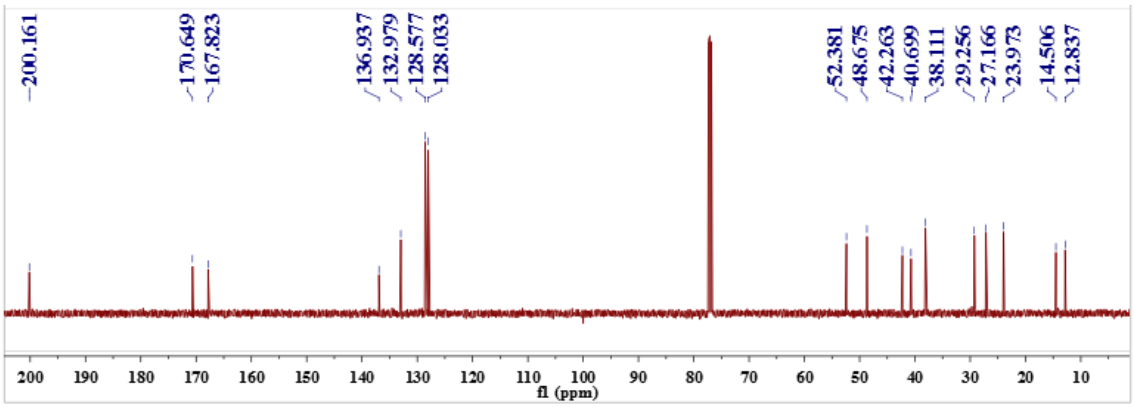


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3d**

NMR Spectra of methyl 2-(diethylcarbamoyl)-7-oxo-7-phenylheptanoate (3e)

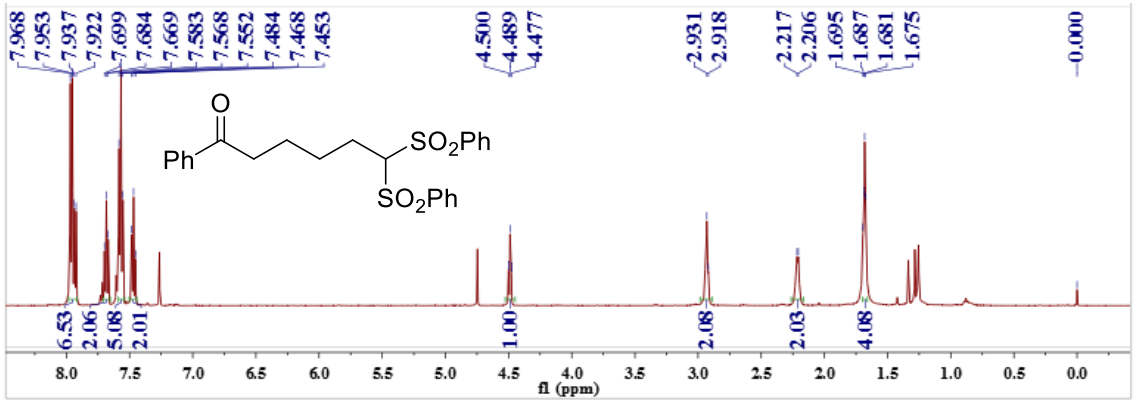


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3e**

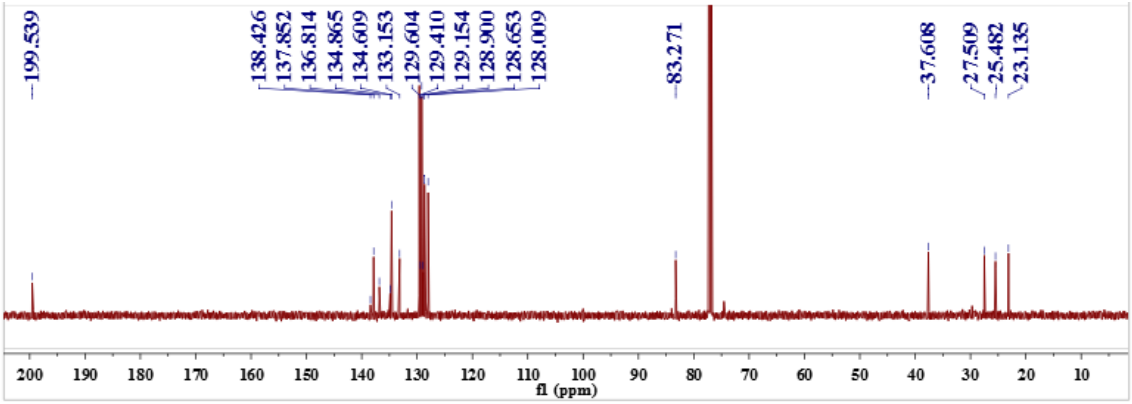


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3e**

NMR Spectra of 1-phenyl-6,6-bis(phenylsulfonyl)hexan-1-one (3f)

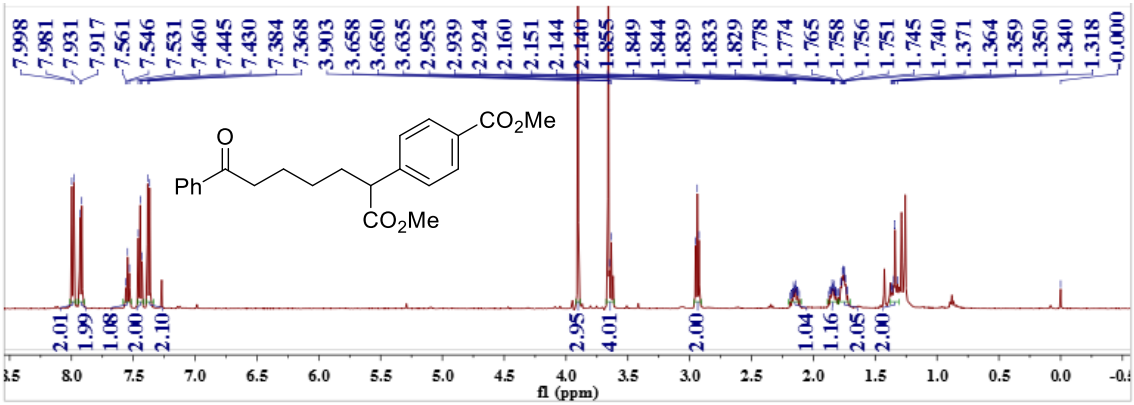


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3f**

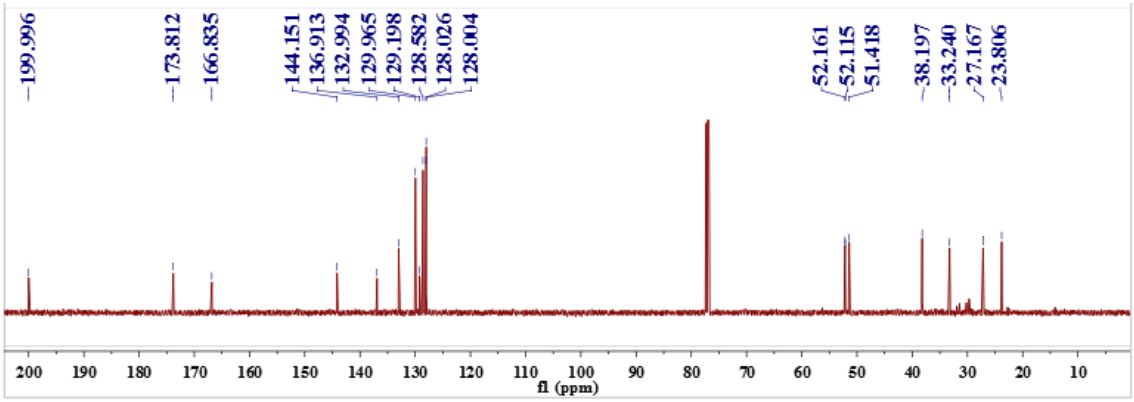


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3f**

NMR Spectra of methyl 4-(1-methoxy-1,7-dioxo-7-phenylheptan-2-yl)benzoate (3g)

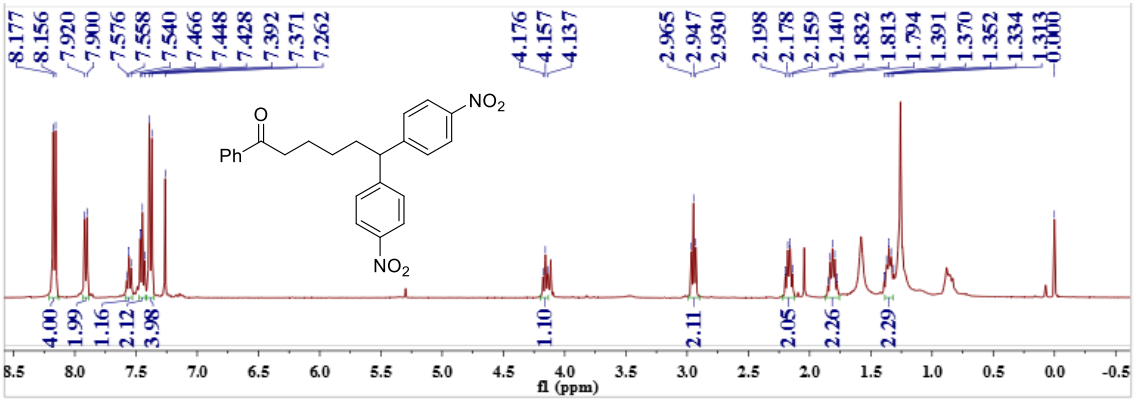


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **3g**

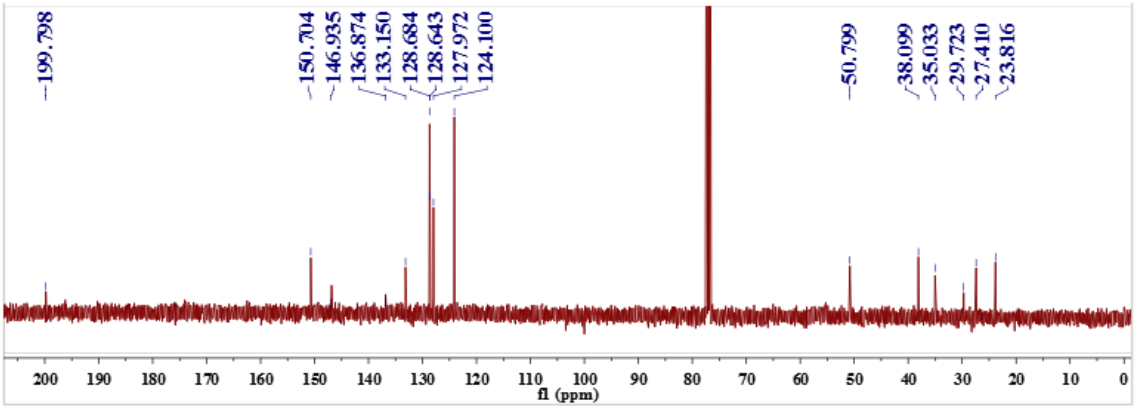


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **3g**

NMR Spectra of 6,6-bis(4-nitrophenyl)-1-phenylhexan-1-one (3h)

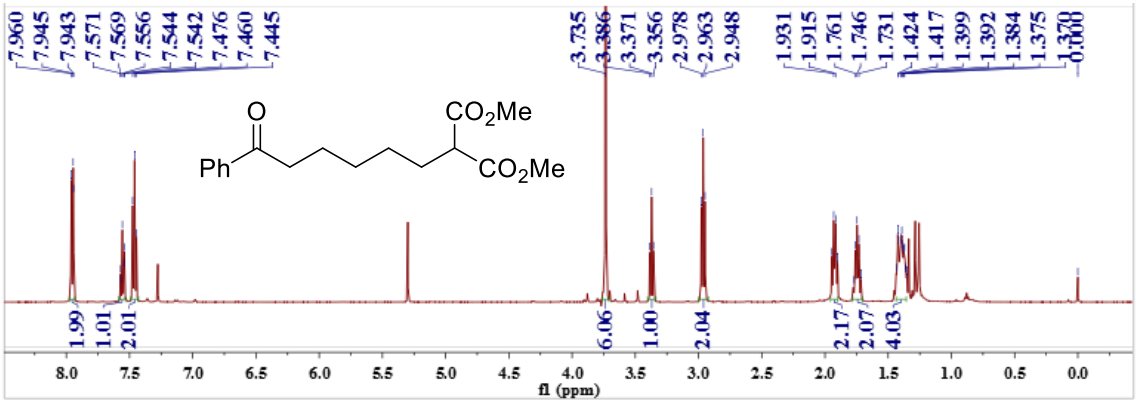


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **3h**

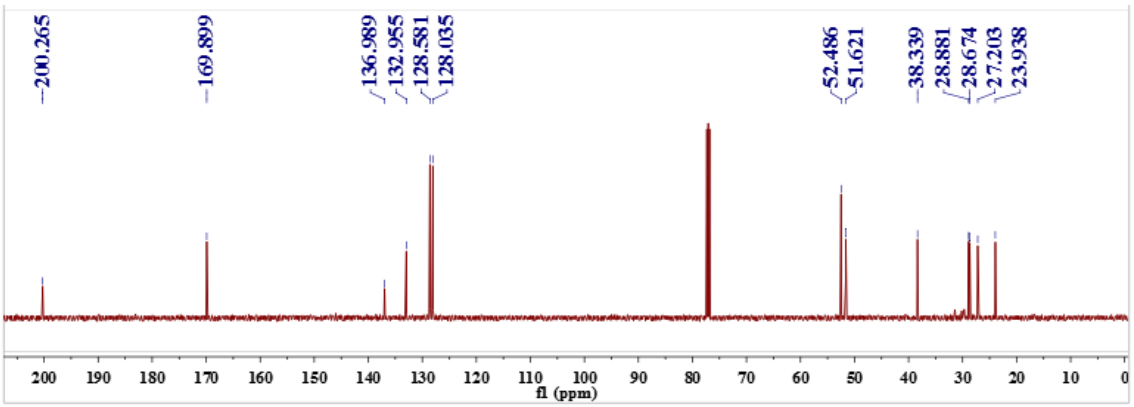


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **3h**

NMR Spectra of dimethyl 2-(6-oxo-6-phenylhexyl)malonate (7b)

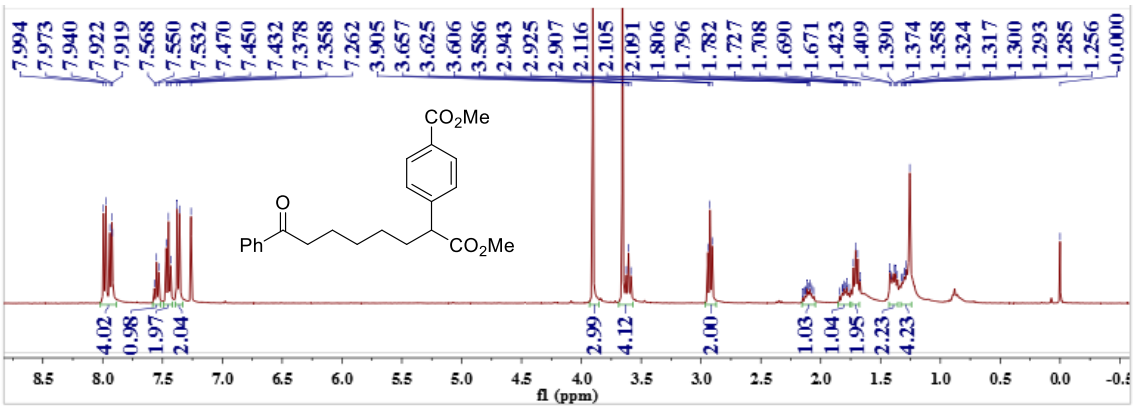


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **7b**

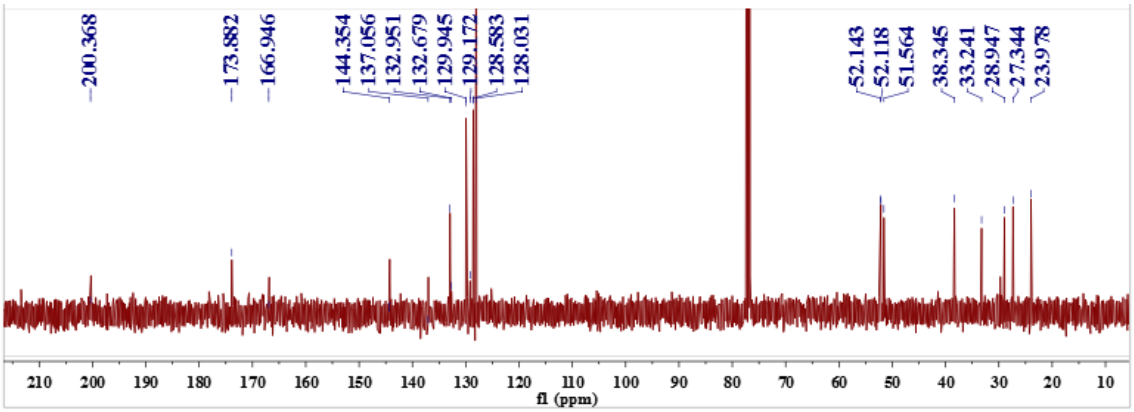


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **7b**

NMR Spectra of methyl 4-(1-methoxy-1,8-dioxo-8-phenyloctan-2-yl)benzoate (8b)

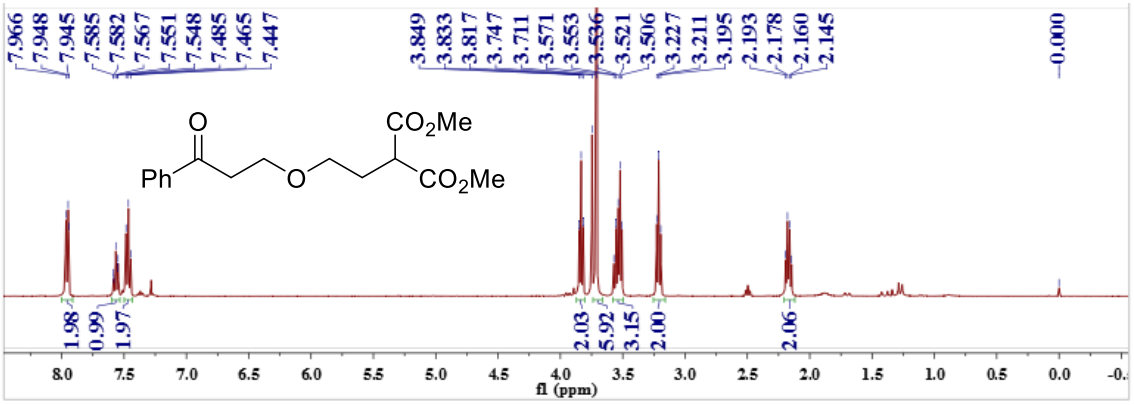


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **8b**

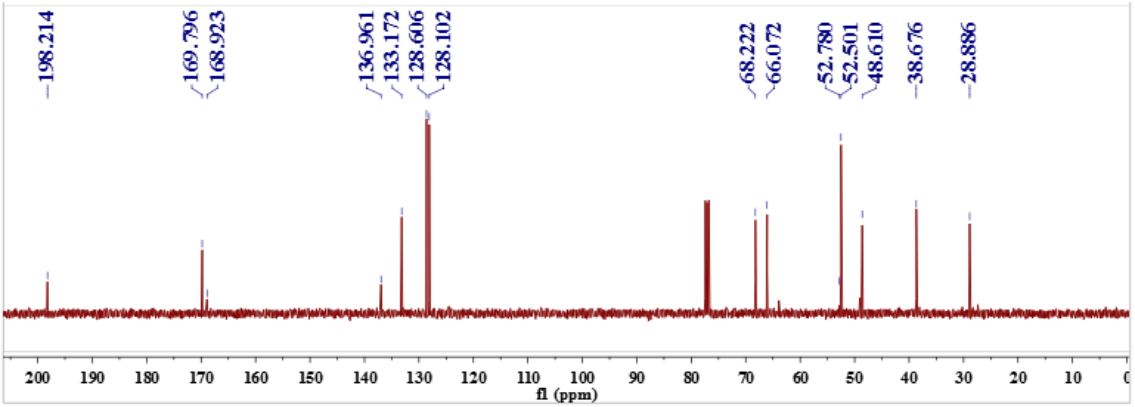


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **8b**

NMR Spectra of dimethyl 2-(2-(3-oxo-3-phenylpropoxy)ethyl)malonate (7c)

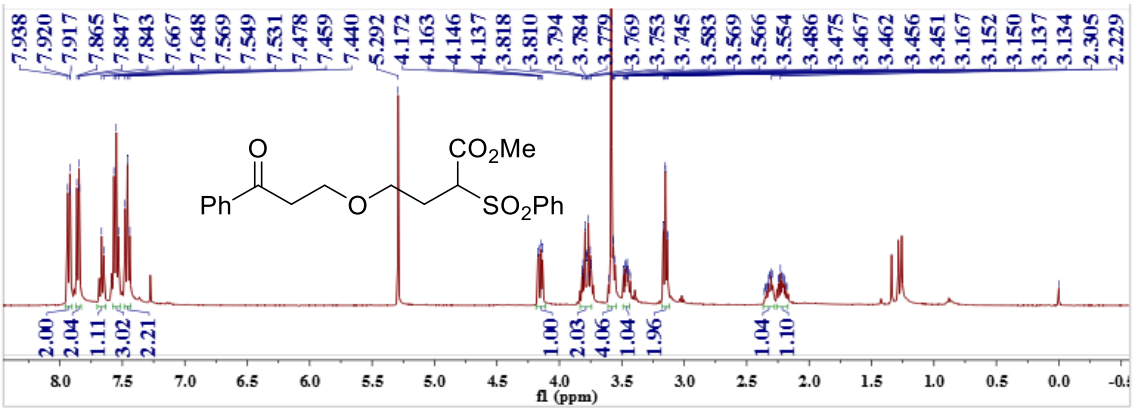


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **7c**

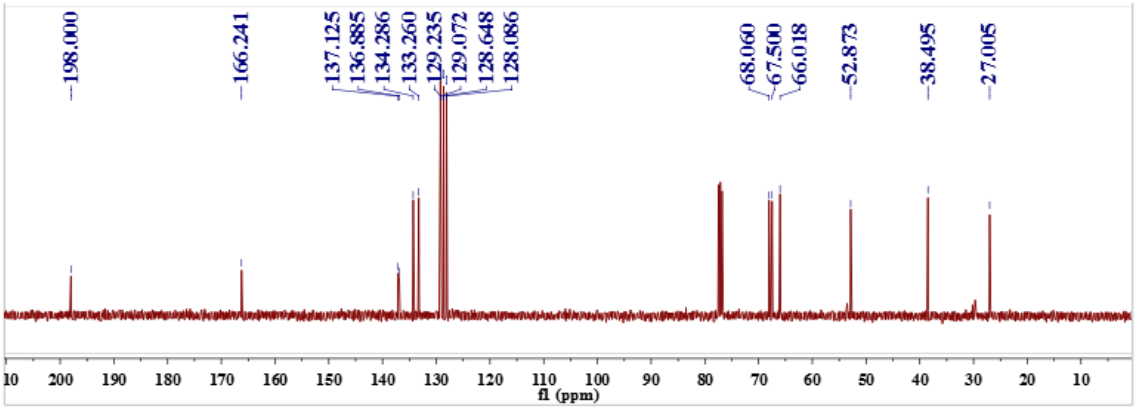


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **7c**

NMR Spectra of methyl 4-(3-oxo-3-phenylpropoxy)-2-(phenylsulfonyl)butanoate (9c)

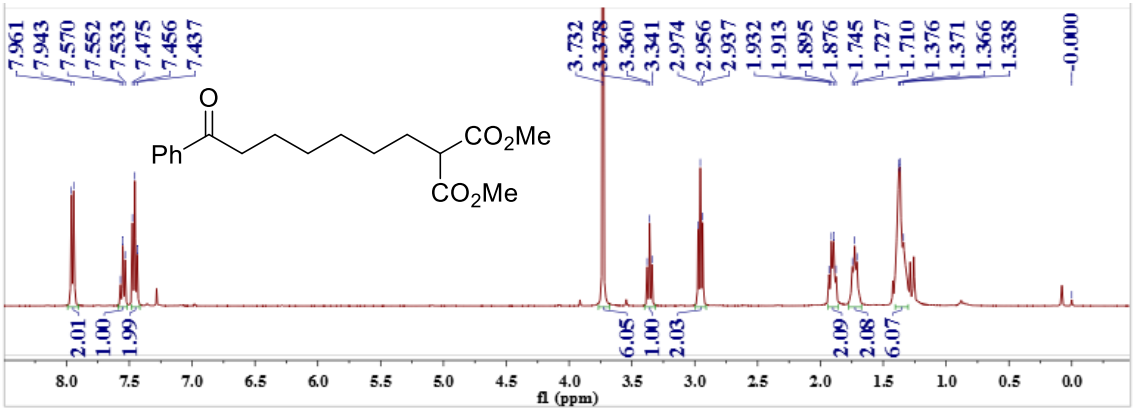


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **9c**

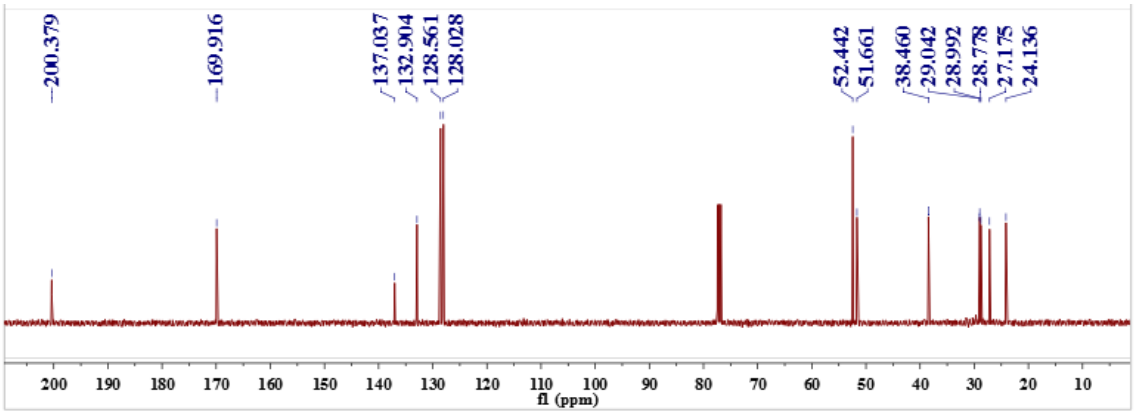


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **9c**

NMR Spectra of dimethyl 2-(7-oxo-7-phenylheptyl)malonate (7d)

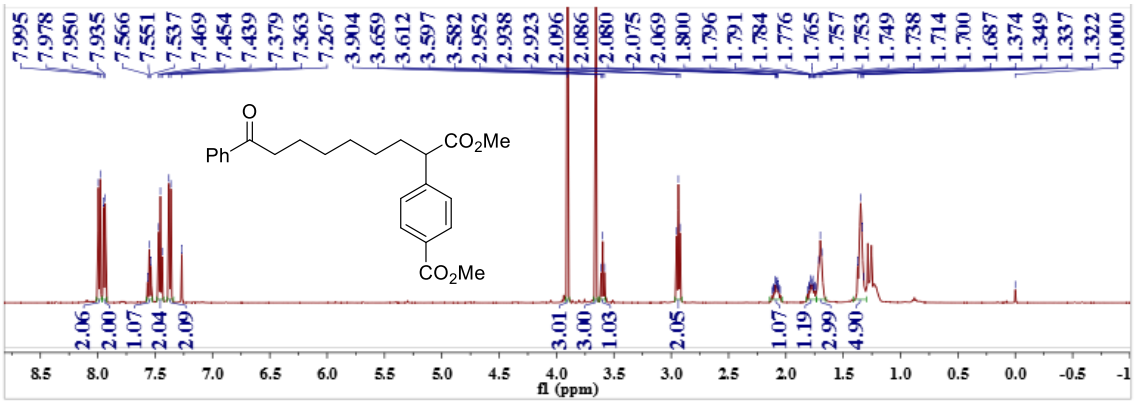


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **7d**

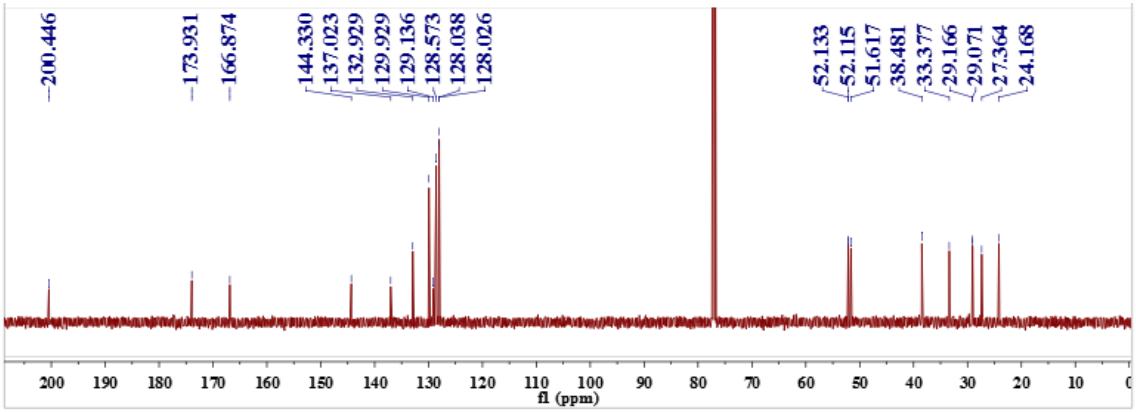


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **7d**

NMR Spectra of methyl 4-(1-methoxy-1,9-dioxo-9-phenylnonan-2-yl)benzoate (8d)

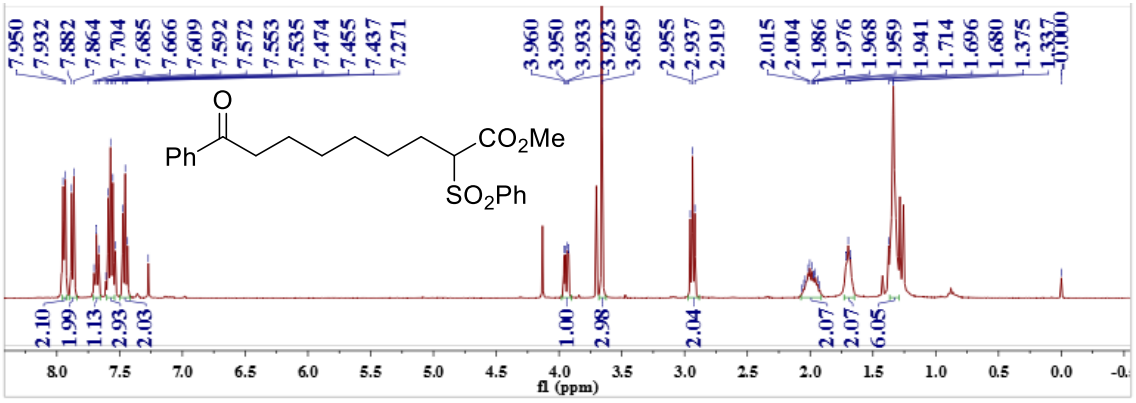


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **8d**

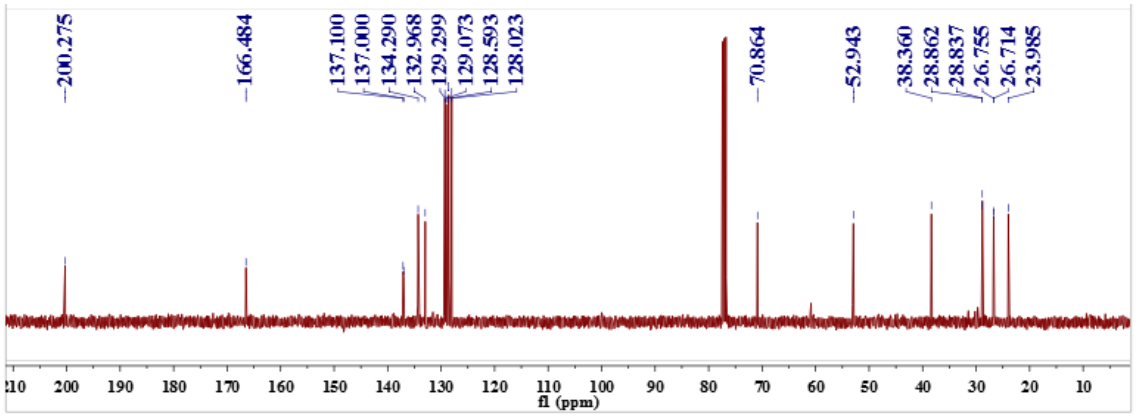


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **8d**

NMR Spectra of methyl 9-oxo-9-phenyl-2-(phenylsulfonyl)nonanoate (9d)

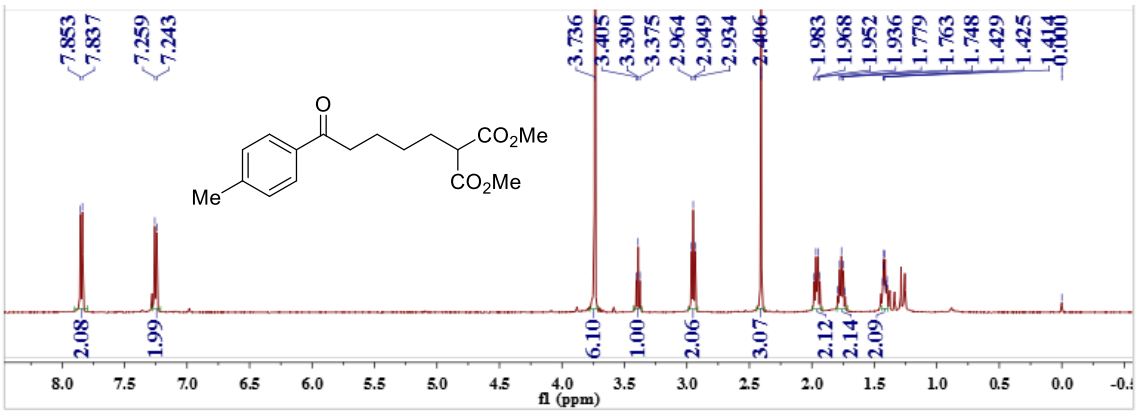


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **9d**

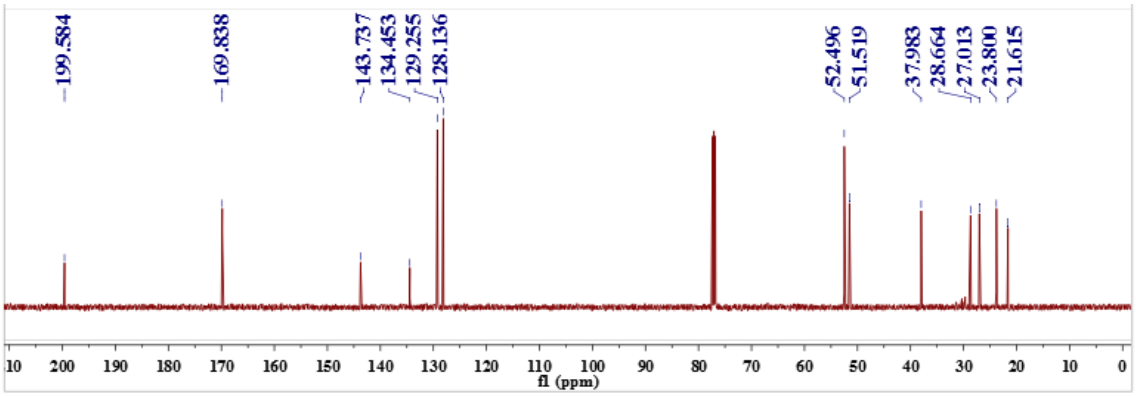


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **9d**

NMR Spectra of dimethyl 2-(5-oxo-5-(p-tolyl)pentyl)malonate (7e)

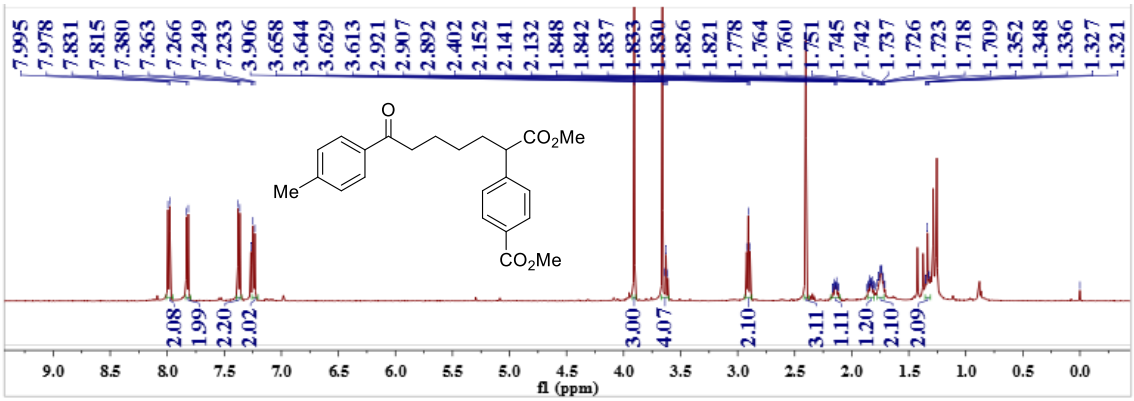


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **7e**

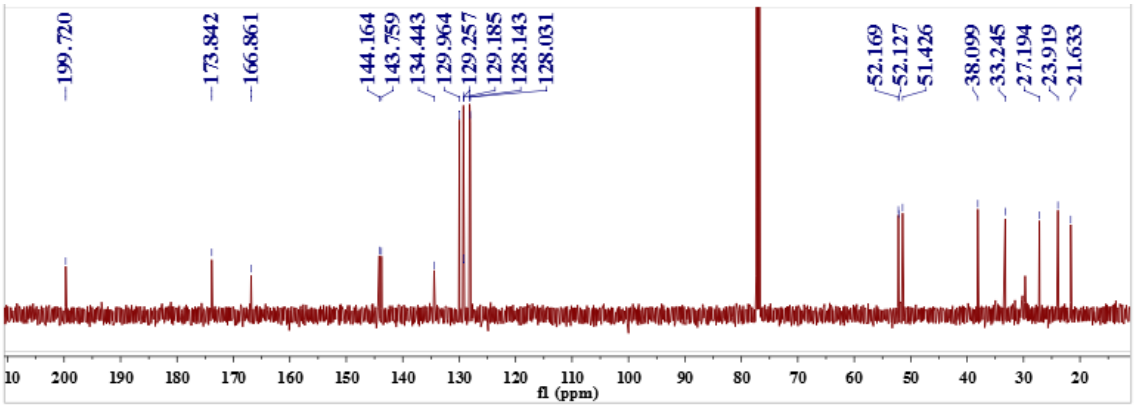


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **7e**

NMR Spectra of methyl 4-(1-methoxy-1,7-dioxo-7-(p-tolyl)heptan-2-yl)benzoate (8e)

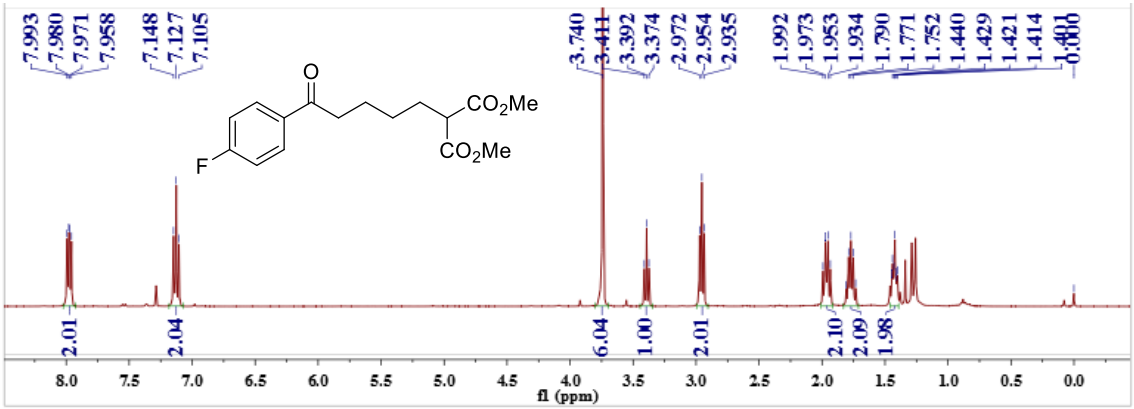


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **8e**

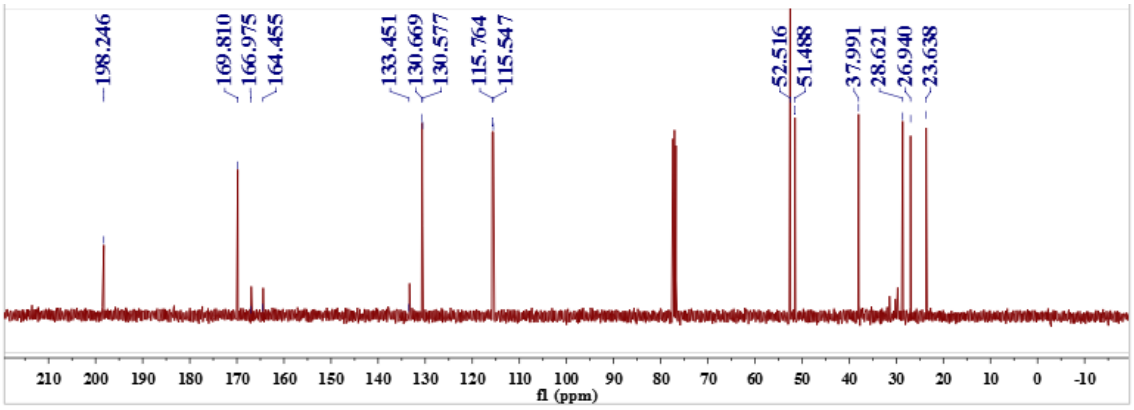


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **8e**

NMR Spectra of dimethyl 2-(5-(4-fluorophenyl)-5-oxopentyl)malonate (7f)

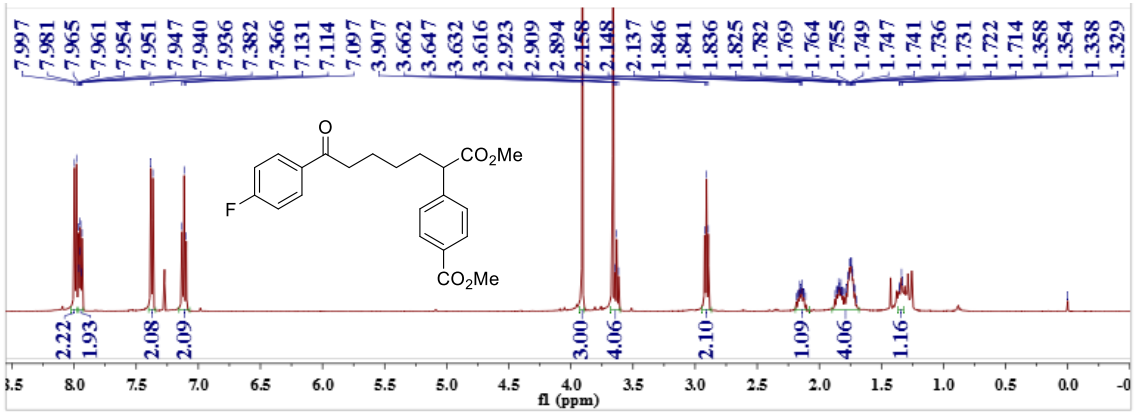


^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **7f**

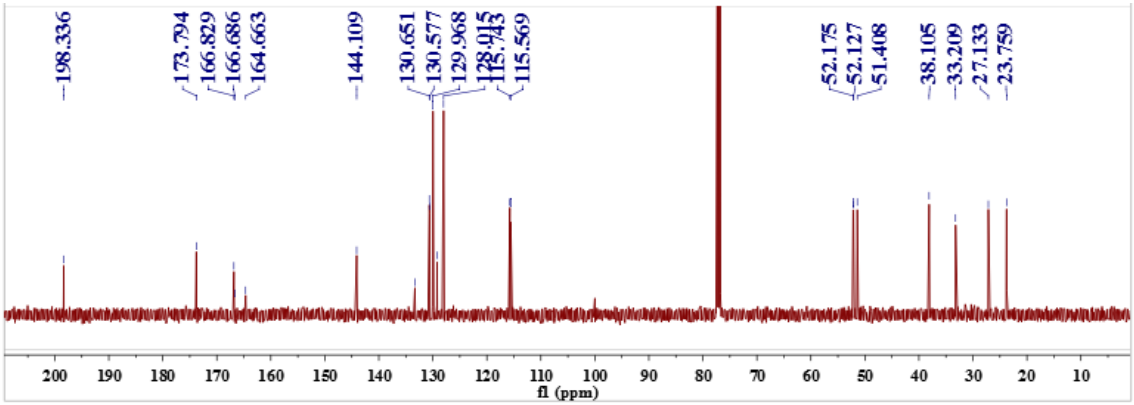


^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **7f**

NMR Spectra of methyl 4-(7-(4-fluorophenyl)-1-methoxy-1,7-dioxoheptan-2-yl) benzoate (8f)

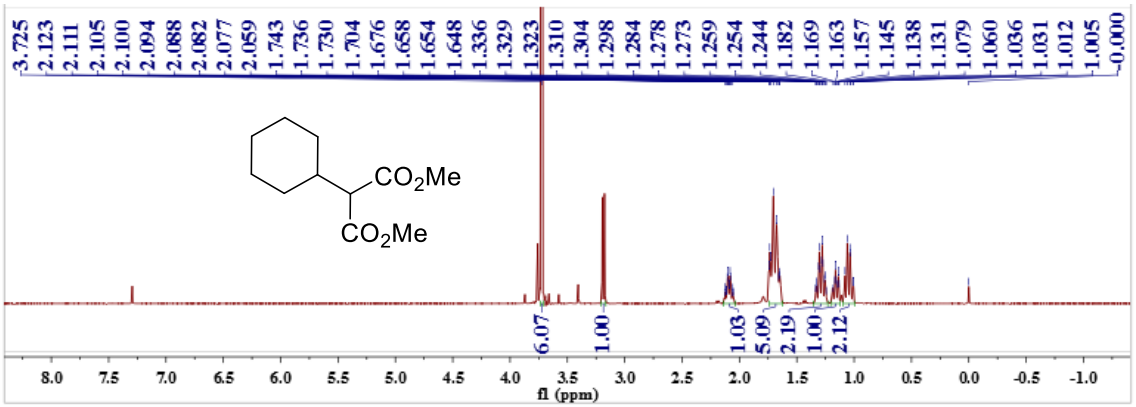


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **8f**

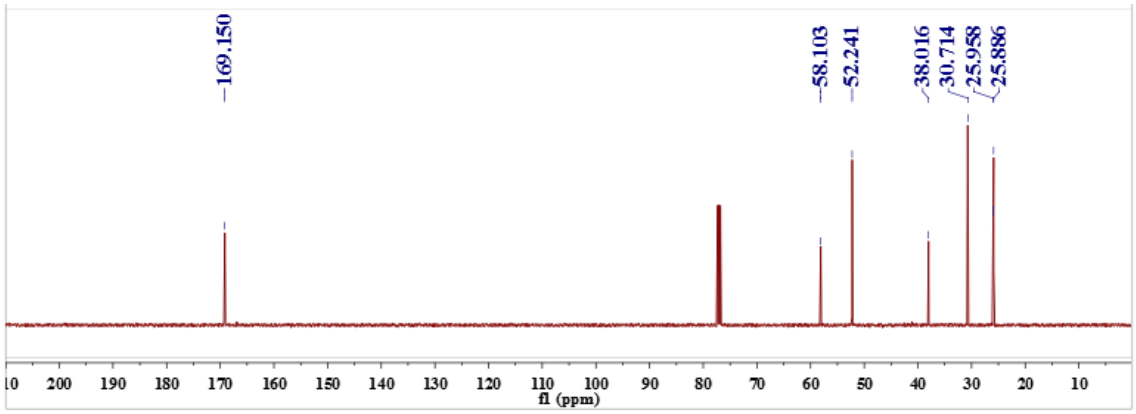


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **8f**

NMR Spectra of dimethyl 2-cyclohexylmalonate (7g)

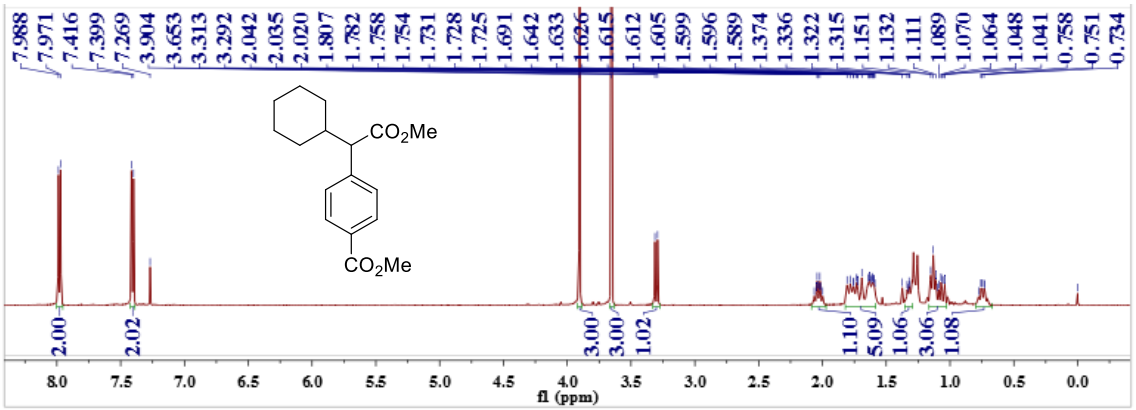


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **7g**

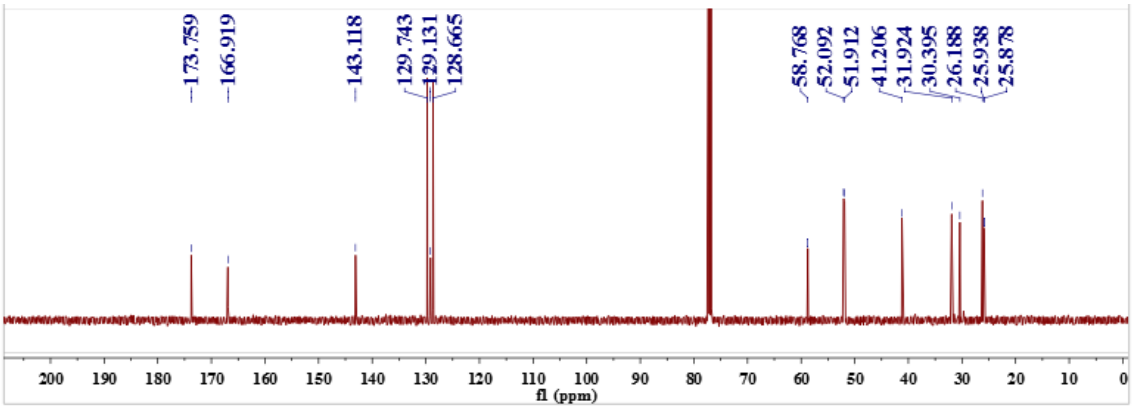


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **7g**

NMR Spectra of methyl 4-(1-cyclohexyl-2-methoxy-2-oxoethyl)benzoatev (8g)

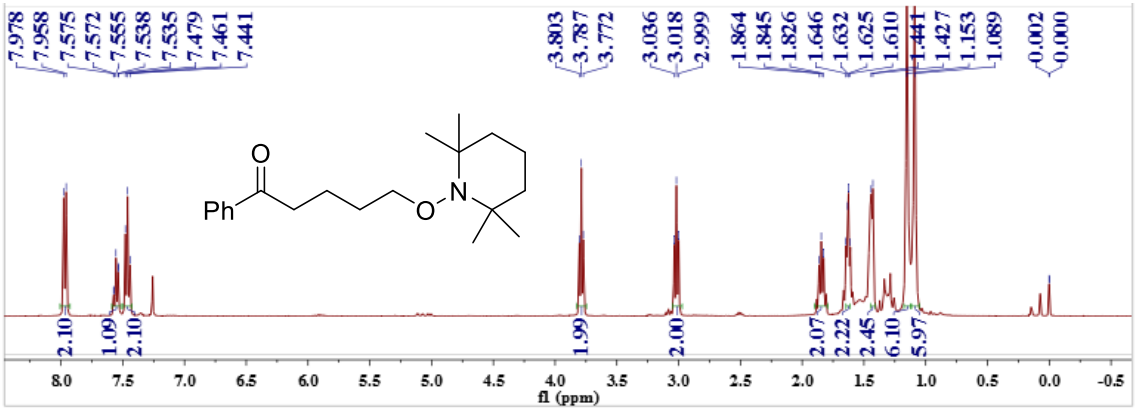


^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **8g**

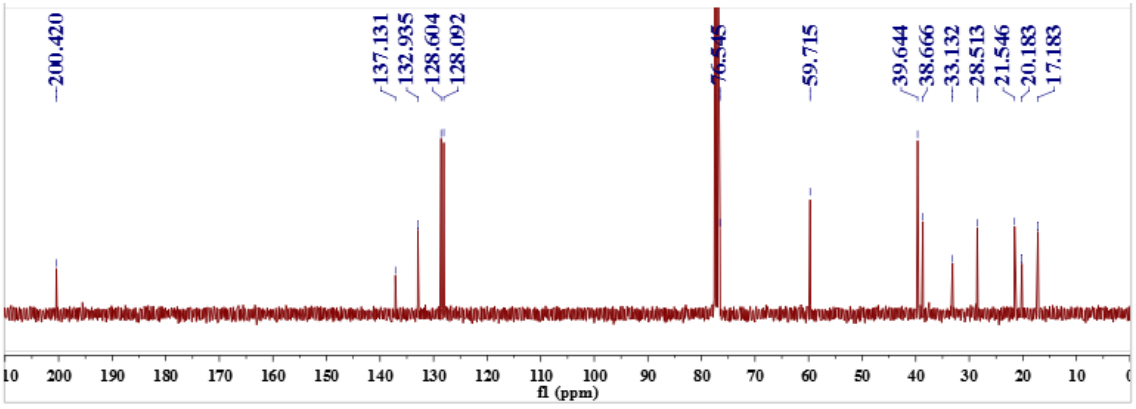


^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **8g**

NMR spectra of 1-phenyl-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pentan-1-one (10)



^{1}H NMR (400 MHz, $CDCl_3$) spectrum of **10**



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of **10**