Dual Transition Metal Electrocatalysis Enables Selective C(sp^3)–C(sp^3) Bond Cleavage and Arylation of Cyclic Alcohols

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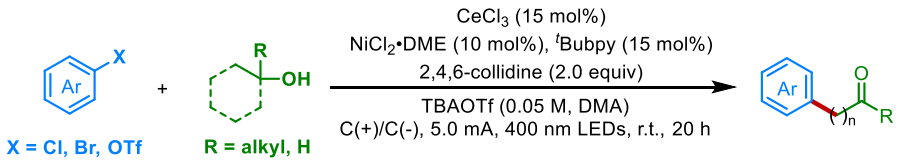
1. Materials and Methods

Unless stated otherwise, reactions were performed in oven-dried glassware under nitrogen atmosphere. *N*,*N*-dimethylacetamide (DMA) was purchased from commercial sources and was dried over 4 Å molecular sieves overnight prior to use. Reagents obtained from commercial sources were used as supplied unless stated otherwise. Thin layer chromatography (TLC) was performed on pre-coated plates Sorbent Technologies, silica gel 60 PF254 (0.25 mm). Flash chromatography was performed on silica gel 60 (240-400 mesh). ^{1}H NMR spectra were recorded on a Bruker Avance (300, 400 or 500 MHz) spectrometer using $CDCl_3$ as solvent and referenced relative to residual $CHCl_3$ (δ = 7.26 ppm). Chemical shifts are reported in ppm and coupling constants (J) in Hertz. ^{13}C NMR spectra were recorded on the same instruments (75 MHz, 101 MHz or 126 MHz) with total proton decoupling referenced relative to residual $CHCl_3$ (δ = 77.16 ppm). The following abbreviations were used to express the multiplicities: s = singlet; d= doublet; t = triplet; q = quartet; m = multiplet; br = broad. Infrared spectra were obtained on Thermo Fisher Nicolet 6700. High-resolution mass spectra were recorded on commercial instruments (APCI or ESI). Cyclic voltammetry spectra were recorded on Shanghai Chenhua CHI660E.

2. Experimental Procedures

2.1 General procedure for ring-opening arylation of cycloalkanols (Method A):



Stock solutions: All stock solutions were prepared using DMA as the solvent, which was degassed by sparging with nitrogen gas. Stoichiometries of reagents were given in regard to a reaction at 0.20 mmol scale.

Solution A: Stock solution of $CeCl_3$ (7.5 mg per milliliter, 15 mol% loading to a reaction at 0.2 mmol scale) was freshly prepared using DMA under nitrogen atmosphere.

Solution B: Stock solution of $NiCl_2$·DME (4.4 mg, 0.020 mmol, 10 mol%) and ^{t}Bubpy (8.0 mg per milliliter, 15 mol% loading to a reaction at 0.2 mmol scale) was freshly prepared using DMA under nitrogen atmosphere.

Reaction setup: An oven-dried two-neck tube was equipped with a stir bar, a rubber septum, a threaded Teflon cap fitted with two carbon felt ($4 \times 10 \times 15$ mm^3, connected to the electrical feedthrough via a 9.0 cm in length, 2.0 mm in diameter graphite rod). Under nitrogen atmosphere, TBAOTf (78.2 mg, 0.20 mmol, 1.0 eq.), cycloalkanol (0.60 mmol, 3.0 eq.), and aryl halide (0.20 mmol, 1.0 eq.) were added to this reaction vessel. After that, solution **A** (1.0 mL), solution **B** (1.0 mL) and 2.0 mL DMA were added via syringe. The reaction mixture was then sparged with nitrogen for 5 minutes and maintained under nitrogen atmosphere with a nitrogen balloon. Then, 2,4,6-collidine (48.4 mg, 0.40 mmol, 2.0 eq.) was added. The reaction was irradiated with LEDs (10 W, 400 nm) under the vessel and electrolysis was initiated at a constant current of 5.0 mA. After 20 hours at room temperature, the photolysis and electrolysis were terminated, the tube cap was removed and electrodes were rinsed with ethyl acetate, which was combined with the crude mixture. The organic layers were further washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel to give the pure product.

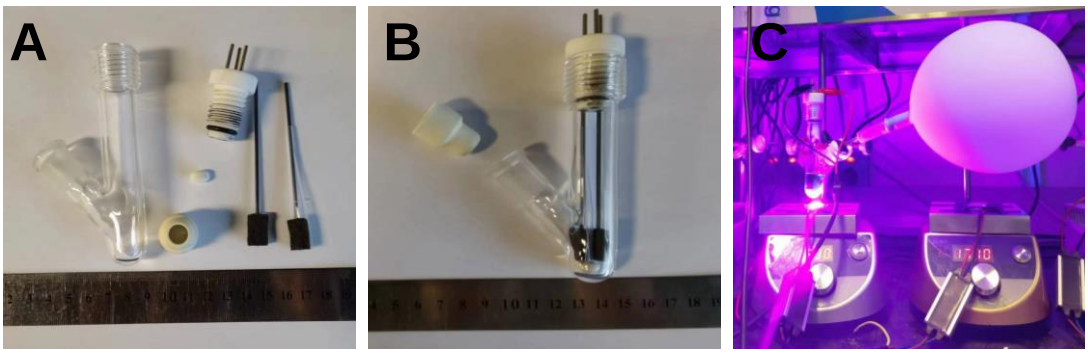
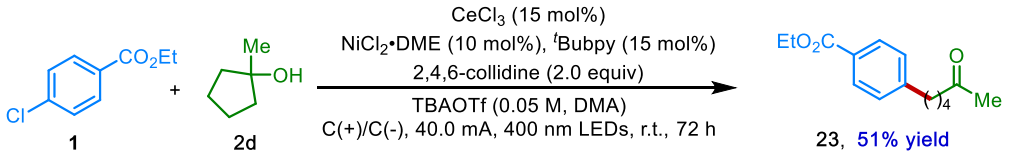


Figure S1. Components of the reaction setup (A). Assembled reaction vessel (B). Typical appearance during electrolysis and irradiation (C).

2.2 General procedure for arylation of cycloalkanol - Scale-up reaction (Method B):



Stock solutions: All stock solutions were prepared using DMA as the solvent, which was degassed by sparging with nitrogen gas. Stoichiometries of reagents were given in regard to a reaction at 5.0 mmol scale.

Solution C: Stock solution of $CeCl_3$ (184.5 mg, 15 mol% loading to a reaction at 5.0 mmol scale) was freshly prepared using 10 mL DMA under nitrogen atmosphere.

Solution D: Stock solution of $NiCl_2$ ĐME (109.5 mg, 10 mol%) and ^{t}Bubpy (201 mg, 15 mol% loading to a reaction at 5.0 mmol scale) was freshly prepared using 10 mL DMA under nitrogen atmosphere.

Reaction setup: An two-neck tube (5.0 cm in diameter, 13.0 cm in length) was equipped with a stir bar, a rubber septum, a threaded Teflon cap fitted with electrical feedthroughs, two carbon felt electrode, measuring 6 cm in length, 3 cm in width, and 4 mm in thickness. Under nitrogen atmosphere, TBAOTf (1.95 g, 5.0 mmol, 1.0 eq.), **2d** (1.5 g, 15.0 mmol, 3.0 eq.), and **1** (0.92 g, 5.0 mmol, 1.0 eq.) were added to this reaction vessel. After that, solution **C**, solution **D** and 60.0 mL DMA were added via syringe. The reaction mixture was then sparged with nitrogen and maintained under nitrogen atmosphere with a balloon. Then, 2,4,6-collidine (1.21 g, 10.0 mmol, 2.0 eq.) was added. The reaction was irradiated with two Kessil lamps (Model PR160L-390 nm, 100 W) and electrolysis was initiated at a constant current of 40.0 mA. After 3 days at room temperature, the photolysis and electrolysis were terminated, the tube cap was removed and electrodes were rinsed with EtOAc, which was combined with the crude mixture. The organic layers were further washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude material was purified by flash column chromatography on silica gel to give the pure product 632.4 mg **23**, with a yield of 51%.

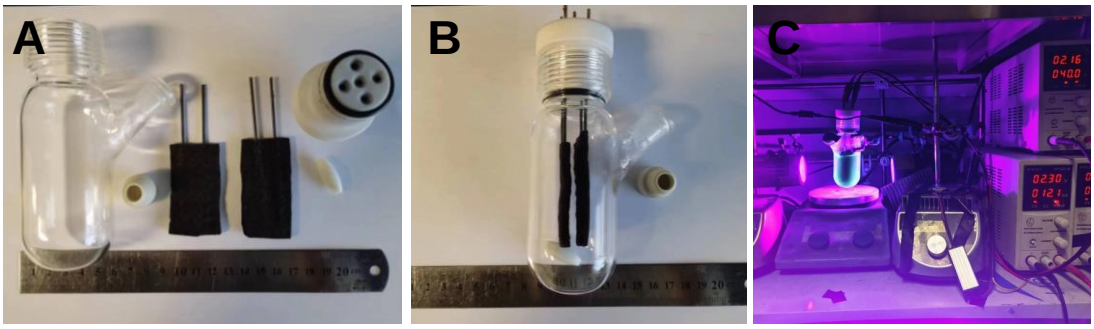
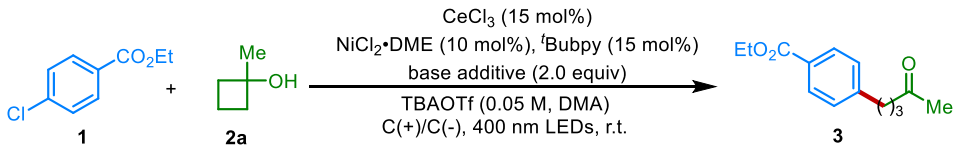


Figure S2. Components of the reaction setup (A and B). Typical appearance during electrolysis and irradiation (C).

3. Reaction Discovery and Optimization

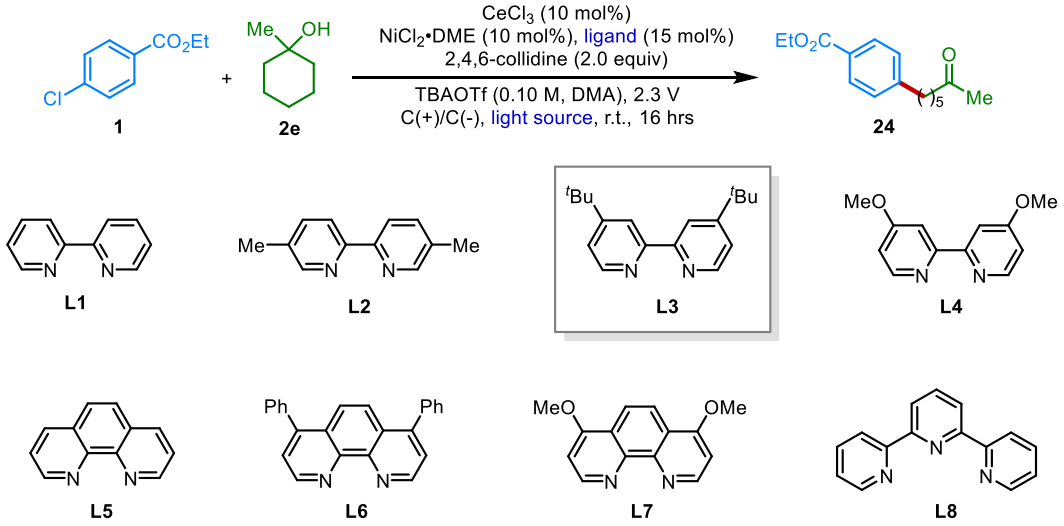
Table S1. Reaction optimizations and control experiments.



Entry	Electrolysis method	Base additive	Conversion (%)[a]	Yield (%)[a]
1[b]	E_{cell} = 2.3 V, 16 hrs	2,4,6-collidine	56	54
2	E_{cell} = 2.3 V, 16 hrs	2,4,6-collidine	>99	71
3	3 mA, 20 hrs	2,4,6-collidine	33	10
4	4 mA, 20 hrs	2,4,6-collidine	>99	44
5	5 mA, 20 hrs	2,4,6-collidine	>99	76
6	10 mA, 20 hrs	2,4,6-collidine	>99	71
7	5 mA, 20 hrs, in DMF	2,4,6-collidine	80	9
8	5 mA, 20 hrs, in DMSO	2,4,6-collidine	34	<5
9	5 mA, 20 hrs	no base additive	40	<5
10	5 mA, 20 hrs	Na_2CO_3	37	23
11	5 mA, 20 hrs	pyridine	33	10
12	5 mA, 20 hrs	2,6-lutidine	88	42
13[c]	5 mA, 20 hrs	2,4,6-collidine	48	n.d.
14[d]	5 mA, 20 hrs	2,4,6-collidine	28	n.d.
15[e]	5 mA, 20 hrs	2,4,6-collidine	60	n.d.
16[f]	0 mA, 20 hrs	2,4,6-collidine	10	n.d.

Reaction conditions: **1** (0.2 mmol, 1.0 equiv), **2a** (0.6 mmol, 3.0 equiv), DMA (4.0 mL), TBAOTf (0.2 mmol, 1.0 equiv), base additive (0.4 mmol, 2.0 equiv), carbon felt electrode (4*10*15 mm^3), under N_2, in an undivided cell. [a]Conversion of **1** and yields were determined by ^1H NMR using 1,1,2,2-tetrachloroethane as the internal standard. [b]$CeCl_3$ (10 mol%). [c]No $CeCl_3$. [d]No nickel catalyst. [e]No light. [f]No current.

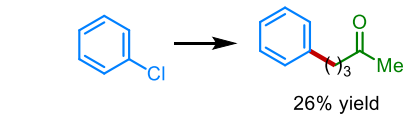
Table S2. Effects of ligands and light sources on the reaction.



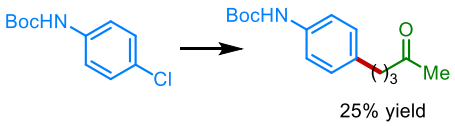
Entry	Light source	Ligand	Conversion (%)[a]	Yield (%)[a]
1	400 nm	**L1**	60	18
2	400 nm	**L2**	66	9
3	400 nm	**L3**	**83**	**43**
4	400 nm	**L4**	88	35
5	400 nm	**L5**	50	25
6	400 nm	**L6**	29	11
7	400 nm	**L7**	78	13
8	400 nm	**L8**	17	n.d.
9	440 nm	**L3**	57	27
10	460 nm	**L3**	56	30
11	490 nm	**L3**	54	3

Reaction conditions: **1** (0.2 mmol, 1.0 equiv), **2e** (0.3 mmol, 1.5 equiv), DMA (4.0 mL), TBAOTf (0.4 mmol, 2.0 equiv), 2,4,6-collidine (0.4 mmol, 2.0 equiv), carbon felt electrode (4*10*15 mm^3), under N_2, in an undivided cell. [a]Conversion of **1** and yields were determined by ^1H NMR using 1,1,2,2-tetrachloroethane as the internal standard.

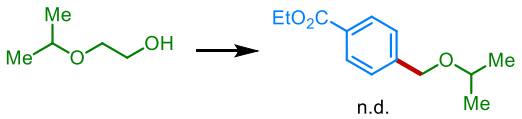
4. Suboptimal and unsuccessful substrates



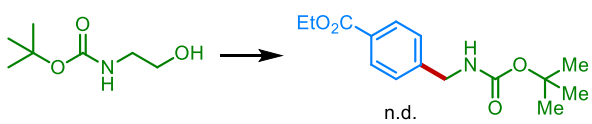
26% yield



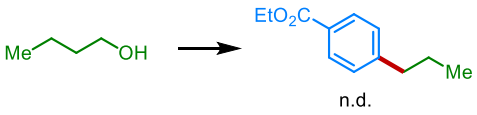
25% yield



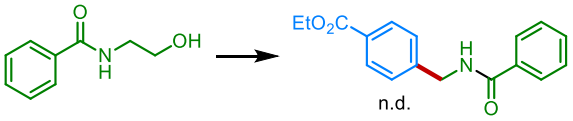
n.d.



n.d.



n.d.



n.d.

5. Mechanistic studies

5.1 Cyclic voltammetry studies

General information: Cyclic voltammetry (CV) studies were performed in a 10 mL glass vial fitted with a glassy carbon working electrode (3.0 mm in diameter), a $Ag/AgNO_3$ reference electrode, and a platinum wire counter electrode. The solution of interest was sparged with nitrogen for 3-5 minutes before data collection.

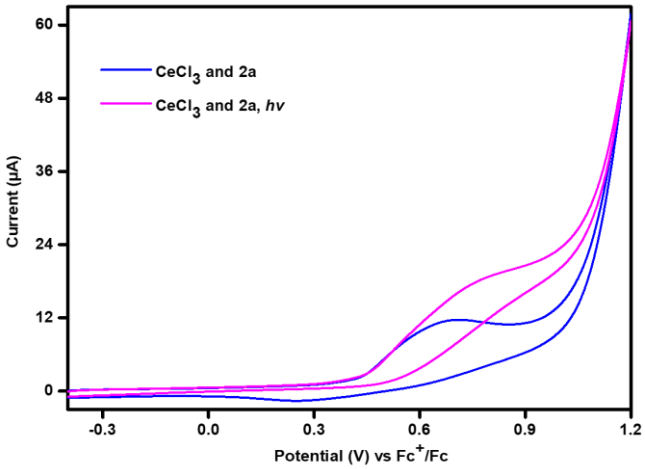
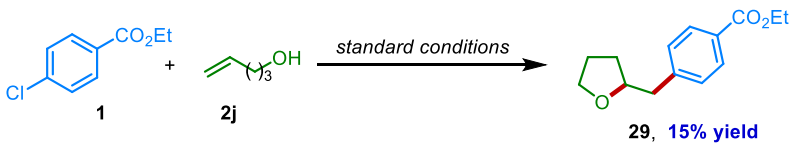


Figure S3. Cyclic voltammogram of $CeCl_3$ and **2a** in DMA and the mixture under irradiation of 400 nm LEDs. Conditions: DMSO (10 mL), TBAOTf (0.05 M), $CeCl_3$ (0.3 mM) and **2a** (0.3 mM); Scan rate: 20 mV/s.

5.2 Radical probe experiment



4-penten-1-ol **2j** was subjected to the standard conditions (**Method A**), and the cyclization/arylation product **29** was isolated in 15% yield, indicating the involvement of oxygen-centered radical intermediate in the reaction.

5.3 Voltage profile of the reaction

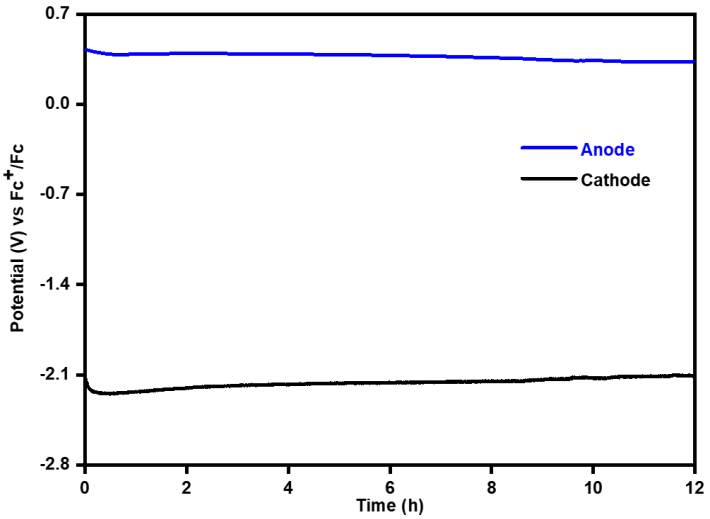
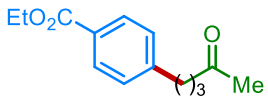


Figure S4. Electrode potentials throughout the reaction of **1** and **2a** under the optimal conditions.

6. Spectral data

ethyl 4-(4-oxopentyl)benzoate (**3**)



Synthesized following general method 37.0 mg isolated (79%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

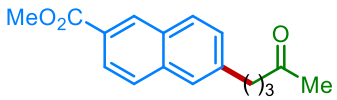
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.1 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.43 (t, *J* = 7.3 Hz, 2H), 2.11 (s, 3H), 1.92 (m, 2H), 1.38 (t, *J* = 7.1, 2.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.4, 166.6, 147.0, 129.7, 128.4, 128.4, 60.8, 42.6, 35.0, 30.0, 24.8, 14.4.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{14}H_{19}O_3$ 235.1329; Found 235.1325.

FT-IR (neat): 2935, 1713, 1276, 1106 cm^{-1}.

methyl 6-(4-oxopentyl)-2-naphthoate (**4**)[1]



Synthesized following general method 37.8 mg isolated (70%).

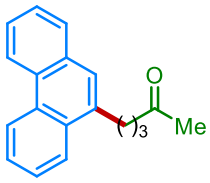
Colorless oil.

R_f = 0.2 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.04 (dt, *J* = 8.7, 1.7 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.64 (s, 1H), 7.39 (dd, *J* = 8.4, 1.7 Hz, 1H), 3.97 (d, *J* = 1.4 Hz, 3H), 2.81 (t, *J* = 7.6 Hz, 2H), 2.48 (t, *J* = 7.3 Hz, 2H), 2.13 (d, *J* = 1.4 Hz, 3H), 2.01 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 167.4, 142.1, 135.8, 131.2, 130.9, 129.5, 128.2, 127.7, 126.5, 125.5, 52.3, 42.8, 35.4, 30.1, 24.9.

5-(phenanthren-9-yl)pentan-2-one (**5**)[2]



Synthesized following general method 26.2 mg isolated (50%).

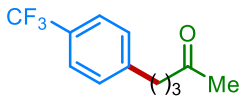
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78-8.71 (m, 1H), 8.71-8.63 (m, 1H), 8.20-8.10 (m, 1H), 7.88-7.79 (m, 1H), 7.71-7.55 (m, 5H), 3.13 (t, *J* = 7.6 Hz, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.13 (d, *J* = 9.8 Hz, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 135.9, 131.9, 131.3, 130.8, 129.9, 128.2, 126.8, 126.4, 126.4, 126.2, 124.6, 123.3, 122.6, 43.2, 32.7, 30.2, 24.1.

5-(4-(trifluoromethyl)phenyl)pentan-2-one (**6**)



Synthesized following general method 37.3 mg isolated (81%).

Colorless oil.

R_f = 0.4 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 2.67 (t, J = 7.7 Hz, 2H), 2.44 (t, J = 7.3 Hz, 2H), 2.13 (s, 3H), 1.91 (m, 2H).

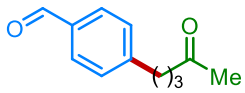
^{13}C NMR (101 MHz, $CDCl_3$) δ 124.5 (q, J = 271.7 Hz), 125.4 (q, J = 3.8 Hz), 128.5 (q, J = 32.3 Hz), 208.4 , 145.9 , 128.9 , 42.7, 35.0, 30.1, 25.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.35.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{14}OF_3$ 231.0991; Found 231.1012.

FT-IR (neat): 2936, 1714, 1327, 1163, 1120, 1067 cm^{-1}.

4-(4-oxopentyl)benzaldehyde (**7**)[3]



Synthesized following general method 18.2 mg isolated (48%).

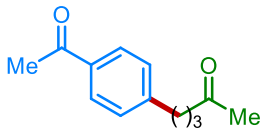
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.70 (t, *J* = 7.7 Hz, 2H), 2.46 (t, *J* = 7.3 Hz, 2H), 2.13 (s, 4H), 1.93 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.4, 192.1, 149.2, 134.8, 130.1, 129.3, 42.8, 35.4, 30.2, 24.9.

5-(4-acetylphenyl)pentan-2-one (**8**)[3]



Synthesized following general method 25.7 mg isolated (63%).

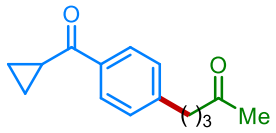
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 2.68 (t, *J* = 7.7 Hz, 2H), 2.59 (s, 3H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.13 (s, 3H), 1.93 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.4, 197.9, 147.5, 135.3, 128.8, 128.7, 42.7, 35.1, 30.1, 26.7, 24.9.

5-(4-(cyclopropanecarbonyl)phenyl)pentan-2-one (**9**)



Synthesized following general method 28.1 mg isolated (61%).

Colorless oil.

R_f = 0.2 (petroleum ether/EtOAc 10:1)

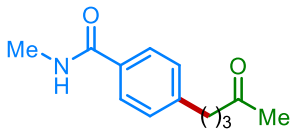
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 2.74-2.62 (m, 3H), 2.45 (t, J = 7.3 Hz, 2H), 2.13 (s, 3H), 1.93 (m, 2H), 1.23 (m, 2H), 1.03 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.5, 200.3, 147.1, 136.2, 128.7, 128.4, 42.8, 35.1, 30.1, 24.9, 17.1, 11.6.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{19}O_2$ 231.1380; Found 231.1378.

FT-IR (neat): 2925, 1711, 1665, 1382, 1229, 993, 836 cm^{-1}.

N-methyl-4-(4-oxopentyl)benzamide (**10**)



Synthesized following general method 19.7 mg isolated (45%).

Yellow solid.

R_f = 0.1 (petroleum ether/EtOAc 10:1)

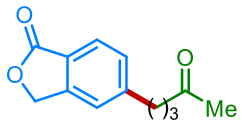
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.20 (s, 1H), 3.00 (d, *J* = 4.8 Hz, 3H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.11 (s, 3H), 1.90 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 168.2, 145.4, 132.6, 128.8, 127.1, 42.8, 34.9, 30.1, 26.9, 25.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{18}O_2N$ 220.1332; Found 220.1331.

FT-IR (neat): 3336, 2937, 1710, 1640, 1551, 1411, 1308, 1161 cm^{-1}.

5-(4-oxopentyl)isobenzofuran-1(3H)-one (**11**)[5]



Synthesized following general method 28.3 mg isolated (65%).

Colorless oil.

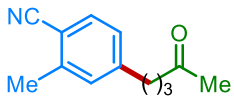
R_f = 0.4 (petroleum ether/EtOAc 5:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.29 (s, 1H), 5.27 (s, 2H), 2.73 (dd, *J* = 8.7, 6.8 Hz, 2H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.13 (s, 3H), 1.93 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.0, 147.2, 129.6, 125.7, 123.8, 121.8, 69.5, 42.5, 35.4, 30.0, 24.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{15}O_3$ 219.1016; Found 219.1016.

2-methyl-4-(4-oxopentyl)benzonitrile (**12**)



Synthesized following general method 22.5 mg isolated (56%).

White solid.

R_f = 0.2 (petroleum ether/EtOAc 10:1)

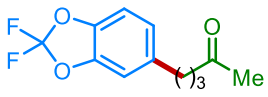
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.9 Hz, 1H), 7.12 (s, 1H), 7.06 (dd, *J* = 7.9, 1.6 Hz, 1H), 2.64-2.59 (m, 2H), 2.51 (s, 3H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.12 (s, 3H), 1.88-1.85 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.3, 147.2, 142.1, 132.7, 130.5, 126.5, 118.4, 110.4, 42.7, 35.2, 30.2, 24.8, 20.6.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{13}H_{16}ON$ 202.1226; Found 202.1225.

FT-IR (neat): 2921, 2851, 2220, 1711, 1413, 1361, 1159 cm^{-1}.

5-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)pentan-2-one (**13**)[4]



Synthesized following general method 29.5 mg isolated (61%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

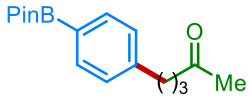
1H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, J = 8.1 Hz, 1H), 6.88 (d, J = 1.6 Hz, 1H), 6.85 (dd, J = 8.1, 1.7 Hz, 1H), 2.65-2.56 (m, 2H), 2.43 (t, J = 7.3 Hz, 2H), 2.13 (s, 3H),

1.87 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.3, 143.8, 142.0, 137.8, 131.6 (t, *J* = 254.4 Hz), 123.2, 109.6, 109.1, 42.5, 34.8, 30.0, 25.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -50.13.

5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)pentan-2-one (**14**)[5]



Synthesized following general method 24.2 mg isolated (42%).

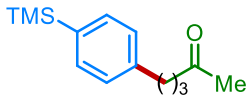
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.6 Hz, 2H), 7.18 (d, J = 7.6 Hz, 2H), 2.63 (t, J = 7.5 Hz, 2H), 2.41 (t, J = 7.4 Hz, 2H), 2.10 (s, 3H), 1.94-1.86 (m, 2H), 1.33 (s, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 145.1, 135.1, 128.1, 83.8, 42.8, 35.3, 30.1, 25.1, 25.0.

5-(4-(trimethylsilyl)phenyl)pentan-2-one (**15**)[5]



Synthesized following general method 28.1 mg isolated (60%).

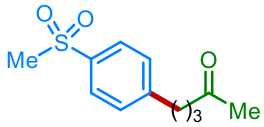
Colorless oil.

R_f = 0.4 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.13 (s, 3H), 1.92 (m, 2H), 0.26 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.9, 142.3, 137.8, 133.6, 128.1, 43.0, 35.1, 30.1, 25.2.

5-(4-(methylsulfonyl)phenyl)pentan-2-one (**16**)



Synthesized following general method 34.6 mg isolated (72%).

White solid.

R_f = 0.3 (petroleum ether/EtOAc 5:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 3.03 (s, 2H), 2.75-2.66 (m, 1H), 2.45 (t, *J* = 7.2 Hz, 1H), 2.13 (s, 2H), 1.92 (p, *J* = 7.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.2, 148.4, 138., 129.5, 127.7, 44.7, 42.6, 35.0, 30.2, 24.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{12}H_{17}O_3S$ 241.0893; Found 241.0891.

FT-IR (neat): 2927, 1710, 1303, 1149, 958, 762, 527 cm^{-1}.

5-(4-(morpholinosulfonyl)phenyl)pentan-2-one (**17**)

Synthesized following general method 48.5 mg isolated (78%).

White solid

R_f = 0.3 (petroleum ether/EtOAc 5:1)

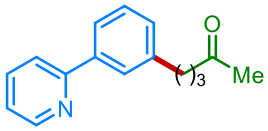
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.9 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 3.72 (t, *J* = 4.7 Hz, 4H), 2.97 (t, *J* = 4.7 Hz, 4H), 2.68 (t, *J* = 7.7 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 2.12 (s, 3H), 1.91 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.2, 147.7, 132.7, 129.2, 128.1, 66.2, 46.1, 42.6, 34.9, 30.1, 24.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{15}H_{22}O_4NS$ 312.1264; Found 312.1260.

FT-IR (neat): 2922, 2858, 1710, 1348, 1164, 1112, 944, 730, 570, 537 cm^{-1}.

5-(3-(pyridin-2-yl)phenyl)pentan-2-one (**18**)



Synthesized following general method 31.1 mg isolated (65%).

White solid.

R_f = 0.2 (petroleum ether/EtOAc 10:1)

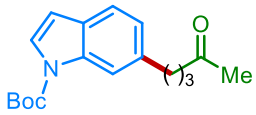
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78-8.60 (m, 1H), 7.82 (d, *J* = 1.9 Hz, 1H), 7.81-7.76 (m, 1H), 7.76-7.69 (m, 2H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.23-7.20 (m, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.11 (s, 3H), 1.98-1.92 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.8, 157.5, 149.6, 142.1, 139.5, 136.8, 129.1, 128.8, 127.1, 124.6, 122.1, 120.7, 42.9, 35.1, 30.0, 25.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{18}ON$ 240.1383; Found 240.1381.

FT-IR (neat): 2930, 1710, 1583, 1400, 1362, 1156, 773 cm^{-1}.

tert-butyl 6-(4-oxopentyl)-1H-indole-1-carboxylate (**19**)



Synthesized following general method 31.9 mg isolated (53%).

Yellow solid.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

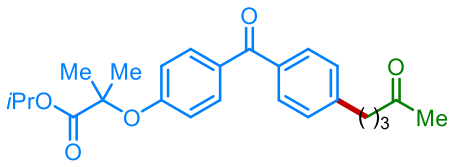
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.52 (d, *J* = 3.7 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 3.7 Hz, 1H), 2.75 (t, *J* = 7.5 Hz, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.11 (s, 3H), 1.97-2.01 (m, 2H), 1.67 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.0, 149.9, 138.1, 135.7, 128.8, 125.6, 123.6, 120.8, 115.1, 107.2, 83.6, 43.0, 35.6, 30.1, 28.3, 25.8.

HRMS (ESI) m/z: $[M+Na]^+$ Calcd. for $C_{18}H_{23}O_3NNa$ 324.1570; Found 324.1564.

FT-IR (neat): 2932, 1715, 1375, 1343, 1150 cm^{-1}.

isopropyl 2-methyl-2-(4-(4-(4-oxopentyl)benzoyl)phenoxy)propanoate (**20**)



Synthesized following general method 45.1 mg isolated (55%).

White solid.

R_f = 0.1 (petroleum ether/EtOAc 10:1)

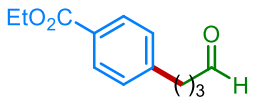
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 6.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.09 (hept, *J* = 6.4 Hz, 1H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.3 Hz, 2H), 2.14 (s, 3H), 1.95 (m, 2H), 1.66 (s, 6H), 1.21 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.6, 173.3, 146.4, 136.1, 132.1, 131.0, 130.2, 128.4, 117.3, 69.4, 42.8, 35.2, 30.2, 25.5, 25.0, 21.7.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{31}O_5$ 411.2166; Found 411.2155.

FT-IR (neat): 2923, 1722, 1651, 1600, 1281, 1249, 1148, 1102 cm^{-1}.

ethyl 4-(4-oxobutyl)benzoate (**21**)[6]



Synthesized following general method 19.4 mg isolated (44%).

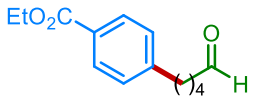
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.5 Hz, 1H), 8.00-7.94 (m, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.46 (td, *J* = 7.2, 1.5 Hz, 2H), 1.98 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.0, 166.7, 146.7, 129.9, 128.6, 128.5, 60.9, 43.1, 35.1, 23.4, 14.4.

ethyl 4-(5-oxopentyl)benzoate (**22**)[6]



Synthesized following general method 15.0 mg isolated (32%).

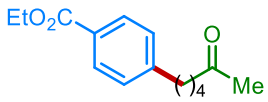
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.75 – 2.64 (m, 2H), 2.45 (d, *J* = 7.1 Hz, 2H), 1.67 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.2, 166.6, 147.3, 129.7, 128.4, 128.3, 60.8, 43.7, 35.7, 30.5, 21.6, 14.4.

ethyl 4-(5-oxohexyl)benzoate (**23**)[7]



Synthesized following general method 30.8 mg isolated (62%).

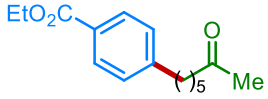
Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 6.4 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.67 (t, *J* = 7.1 Hz, 2H), 2.44 (t, *J* = 6.7 Hz, 2H), 2.12 (s, 3H), 1.62 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.9, 166.8, 147.7, 129.8, 128.5, 128.3, 60.9, 43.6, 35.9, 30.7, 30.0, 23.5, 14.5.

ethyl 4-(6-oxoheptyl)benzoate (**24**)



Synthesized following general method 26.2 mg isolated (50%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

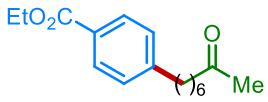
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.11 (s, 3H), 1.65-1.61 (m, 4H), 1.38-1.29 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.1, 166.8, 148.0, 129.7, 128.5, 128.2, 60.9, 43.7, 35.8, 31.0, 30.0, 28.8, 23.6, 14.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{23}O_3$ 263.1642; Found 263.1638.

FT-IR (neat): 2934, 2860, 1276, 1107, 1022, 763 cm^{-1}.

ethyl 4-(7-oxooctyl)benzoate (**25**)



Synthesized following general method 35.9 mg isolated (65%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

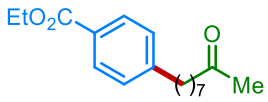
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.68-2.61 (m, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.11 (s, 3H), 1.65-1.52 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.34-1.28 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.2, 166.8, 148.2, 129.7, 128.5, 128.2, 6, 43.8, 36.0, 31.0, 30.0, 29.1, 23.8, 14.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{17}H_{25}O_3$ 277.1798; Found 277.1793.

FT-IR (neat): 2931, 2857, 1714, 1276, 1107, 762 cm^{-1}.

ethyl 4-(8-oxononyl)benzoate (**26**)



Synthesized following general method 41.2 mg isolated (71%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

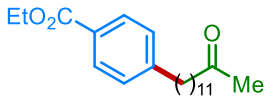
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.2 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.67-2.59 (m, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.12 (s, 3H), 1.61-1.55 (m, 4H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.34-1.25 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.2, 148.2, 129.6, 128.4, 128.0, 60.7, 43.7, 36.0, 31.0, 29.8, 29.2, 29.0, 29.0, 23.8, 14.4.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{18}H_{27}O_3$ 291.1955; Found 291.1948.

FT-IR (neat): 2930, 2856, 1715, 1276, 1107, 762 cm^{-1}.

ethyl 4-(12-oxotridecyl)benzoate (**27**)



Synthesized following general method 39.4 mg isolated (57%).

White solid.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

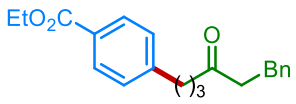
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.11 (s, 3H), 1.62-1.57 (m, 4H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.26 (d, *J* = 14.9 Hz, 14H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 148.5, 129.7, 128.5, 128.1, 60.8, 43.9, 36.1, 31.2, 29.9, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 24.0, 14.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{35}O_3$ 347.2581; Found 347.2578.

FT-IR (neat): 2927, 2855, 1716, 1275, 1107, 762 cm^{-1}.

ethyl 4-(4-oxo-6-phenylhexyl)benzoate (**28**)



Synthesized following general method 41.5 mg isolated (64%).

Colorless oil.

R_f = 0.3 (petroleum ether/EtOAc 10:1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 7.3 Hz, 2H), 7.22-7.08 (m, 5H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.69 (t, *J* = 7.6

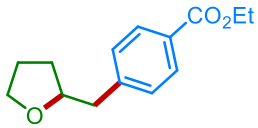
Hz, 2H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 1.93-1.90 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.6, 166.7, 147.1, 141.1, 129.8, 128.6, 128.5, 128.5, 128.4, 126.2, 60.9, 44.4, 42.0, 35.1, 29.9, 24.8, 14.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd. for $C_{21}H_{25}O_3$ 325.1798; Found 325.17911.

FT-IR (neat): 2933, 1712, 1276, 1178, 1106 cm^{-1}.

ethyl 4-((tetrahydrofuran-2-yl)methyl)benzoate (**29**)[8]



Synthesized following general method 7.0 mg isolated (15%).

Colorless oil.

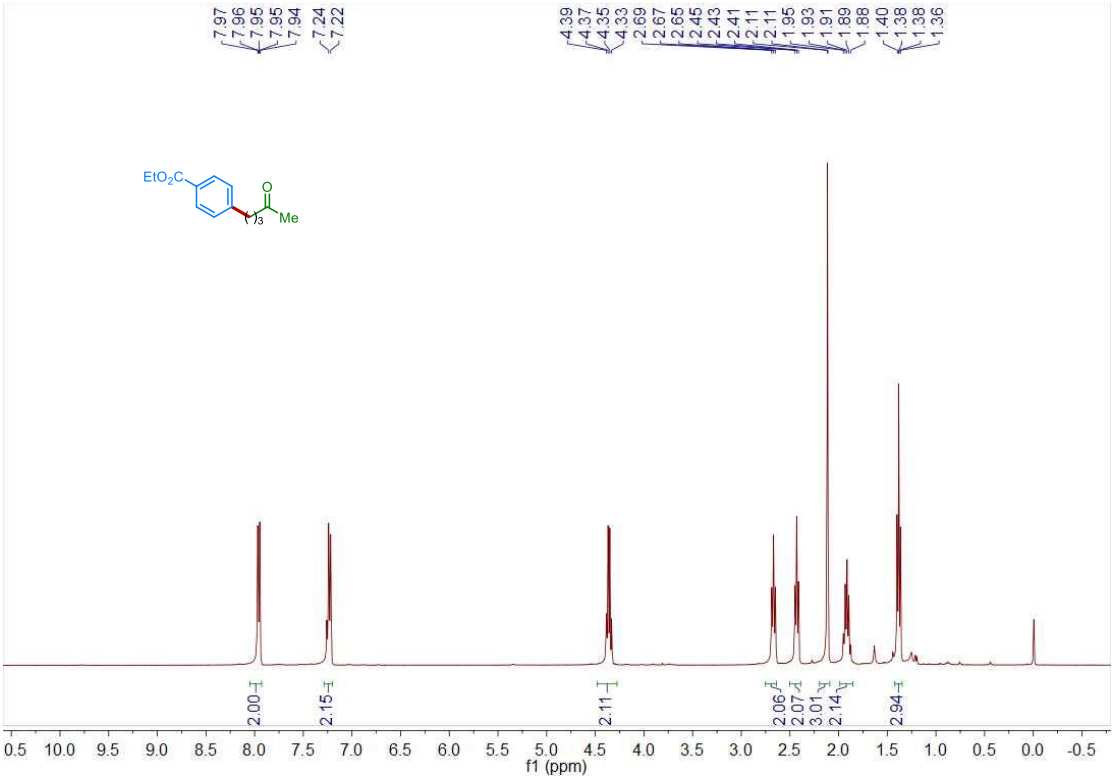
R_f = 0.3 (petroleum ether/EtOAc 10:1)

1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 4.08 (dq, *J* = 7.8, 6.2 Hz, 1H), 3.88 (dt, *J* = 8.2, 6.7 Hz, 1H), 3.82-3.68 (m, 1H), 2.94 (dd, *J* = 13.6, 6.7 Hz, 1H), 2.82 (dd, *J* = 13.6, 6.0 Hz, 1H), 1.98-1.81 (m, 3H), 1.58-1.51 (m, 1H), 1.38 (t, J = 7.1 Hz, 3H).

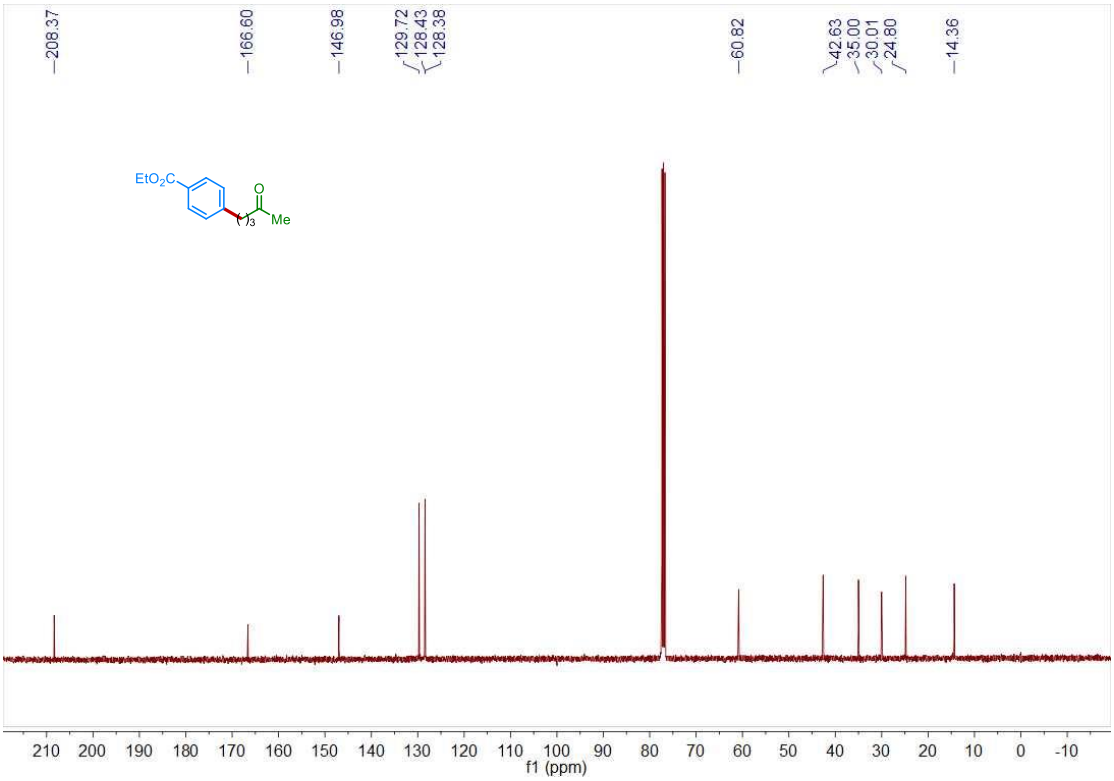
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 144.5, 129.7, 129.4, 128.7, 79.7, 68.1, 60.9, 42.0, 31.2, 25.8, 14.5.

7. NMR spectra

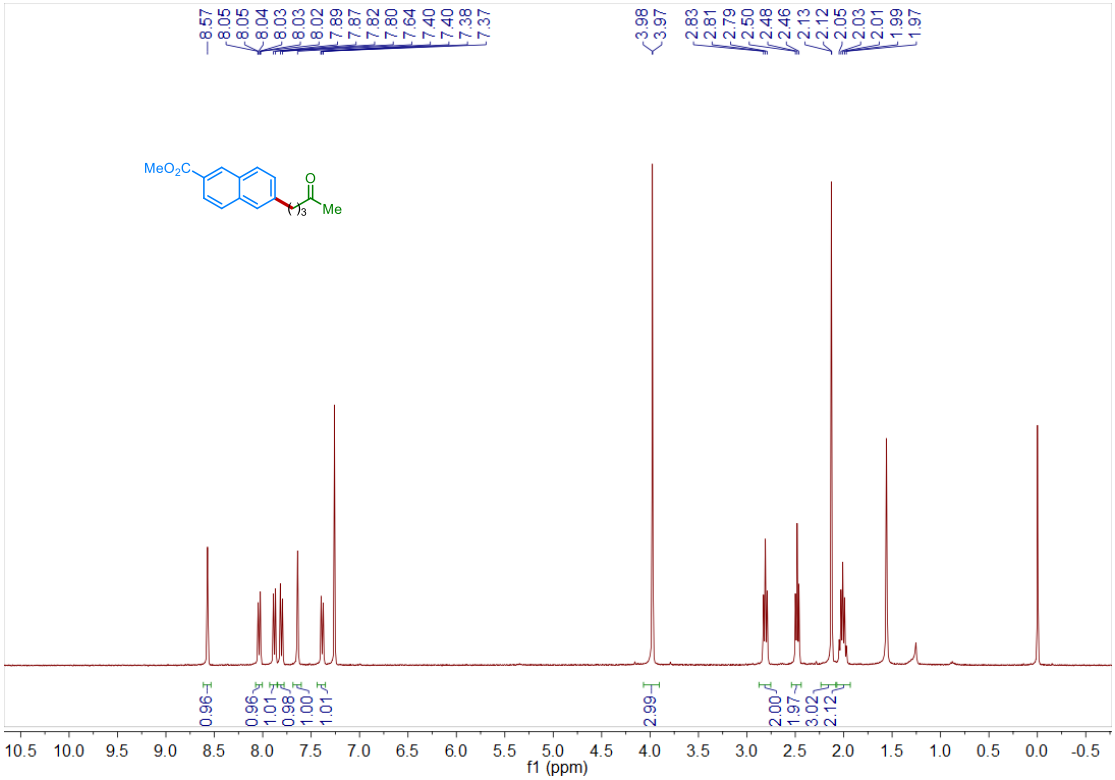
3 ^{1}H-NMR



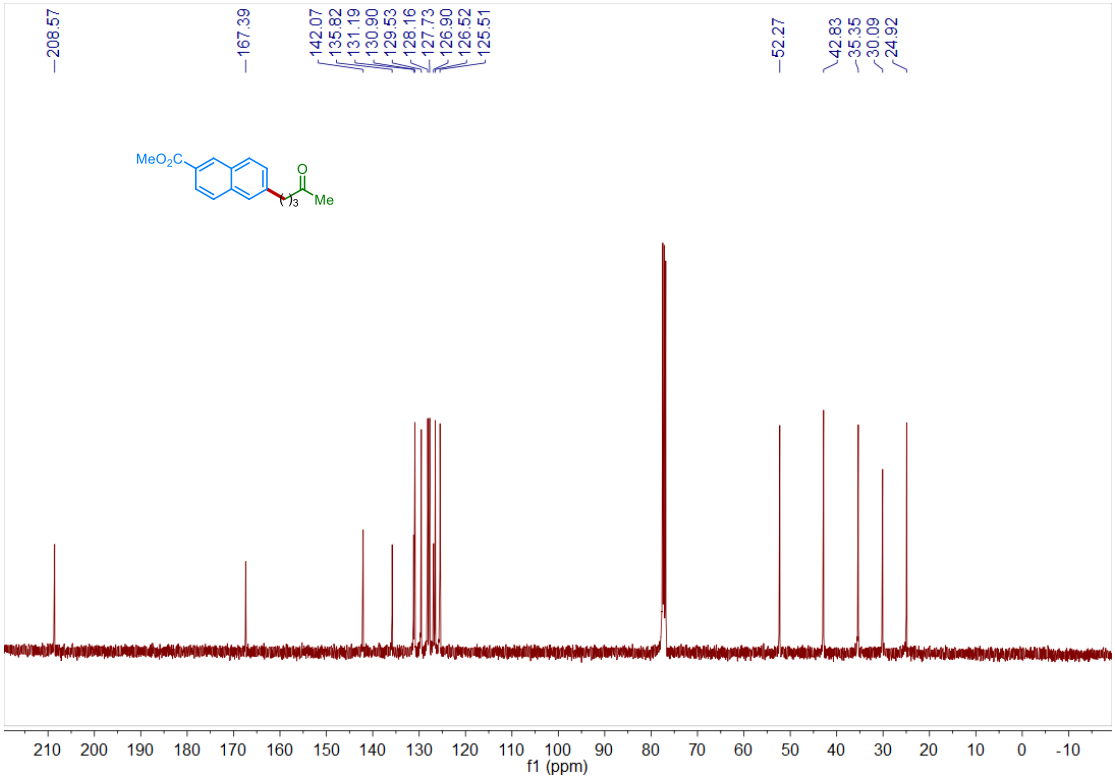
3 ^{13}C-NMR



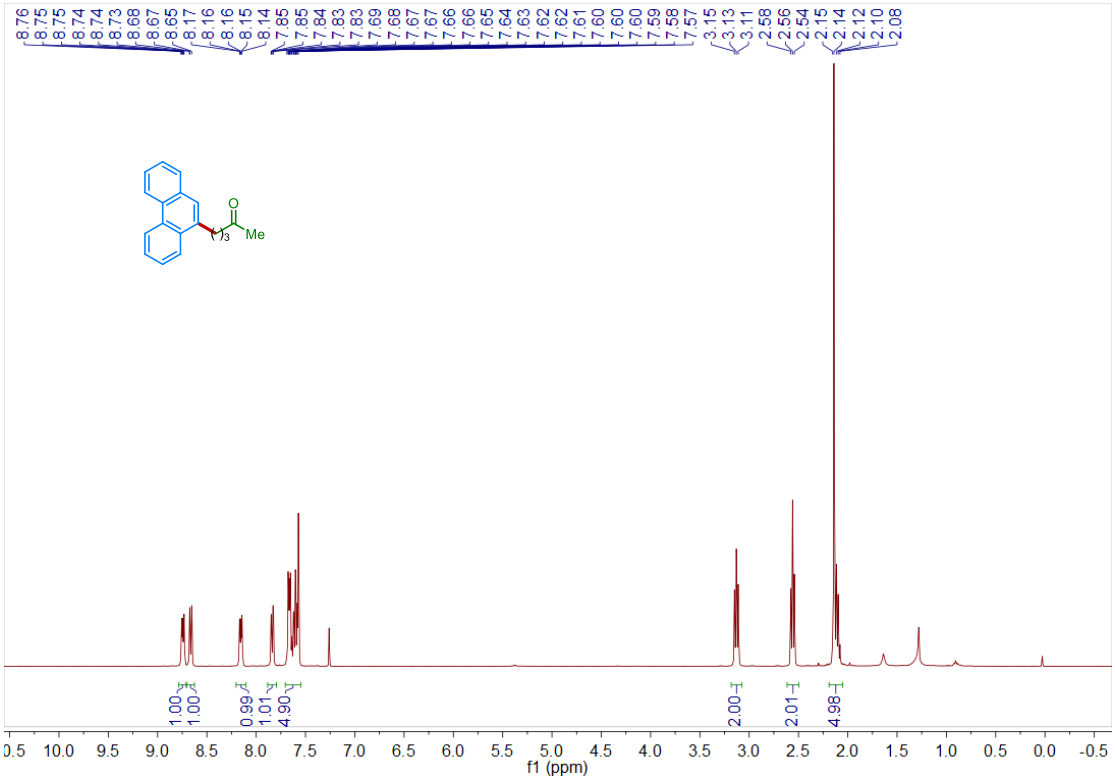
4 ^{1}H-NMR



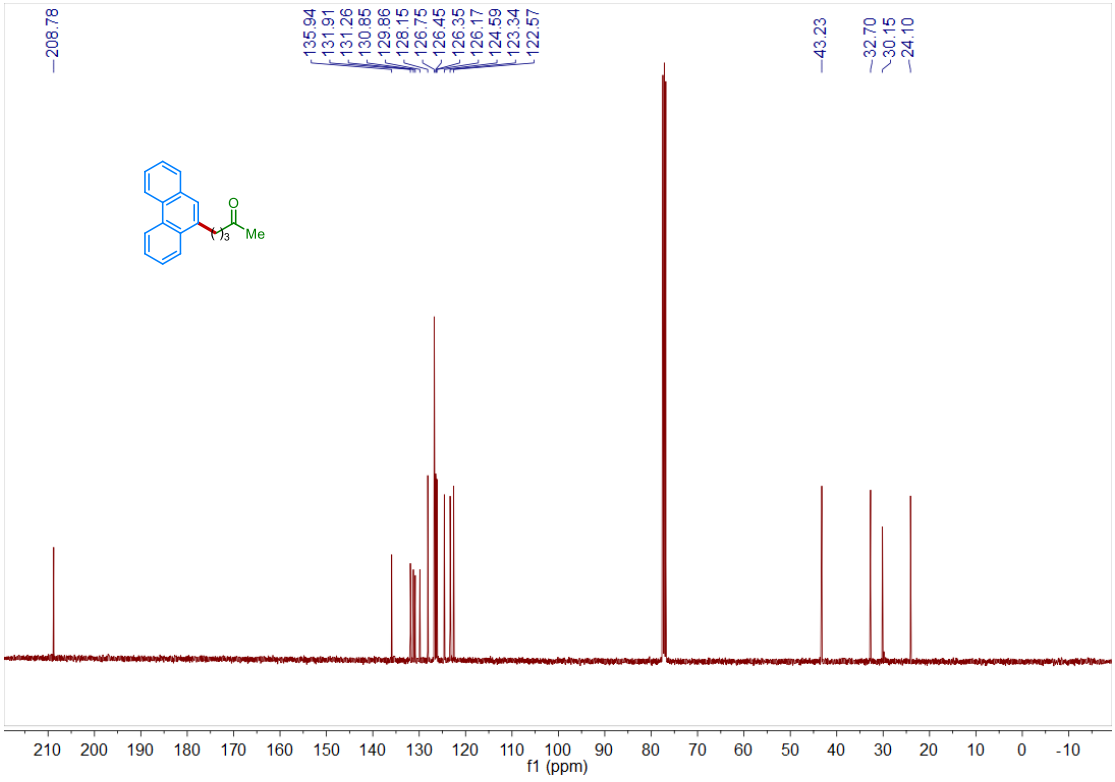
4 ^{13}C-NMR



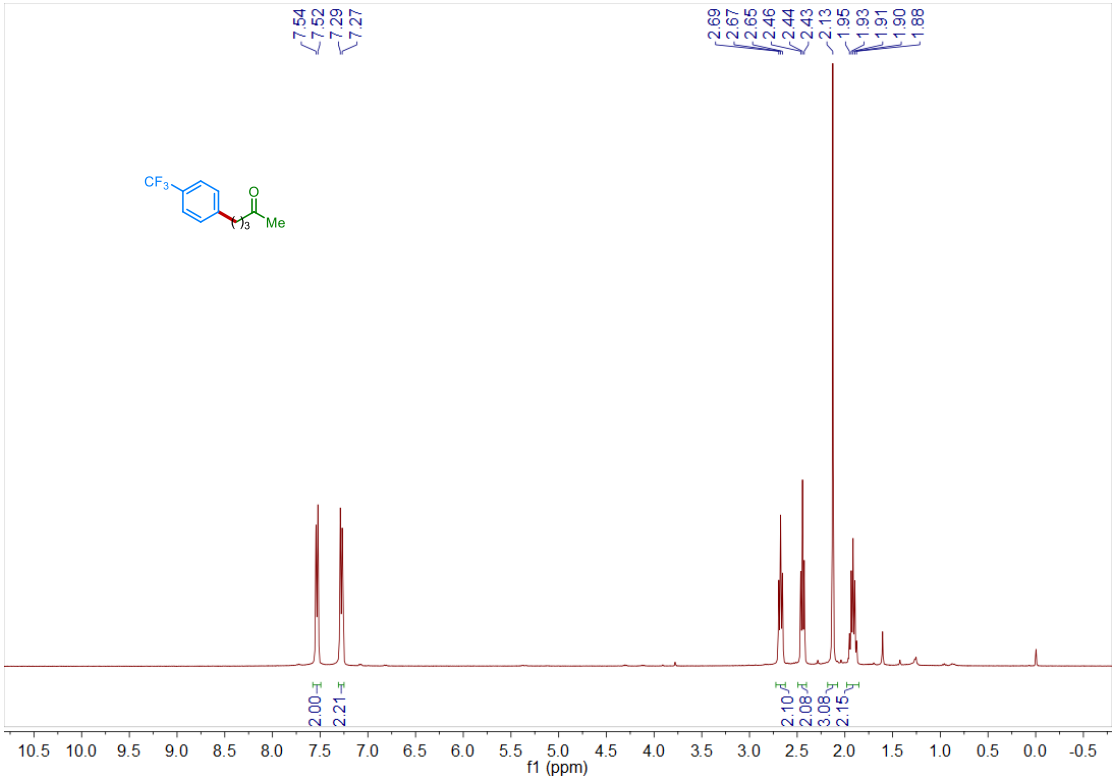
5 ^{1}H-NMR



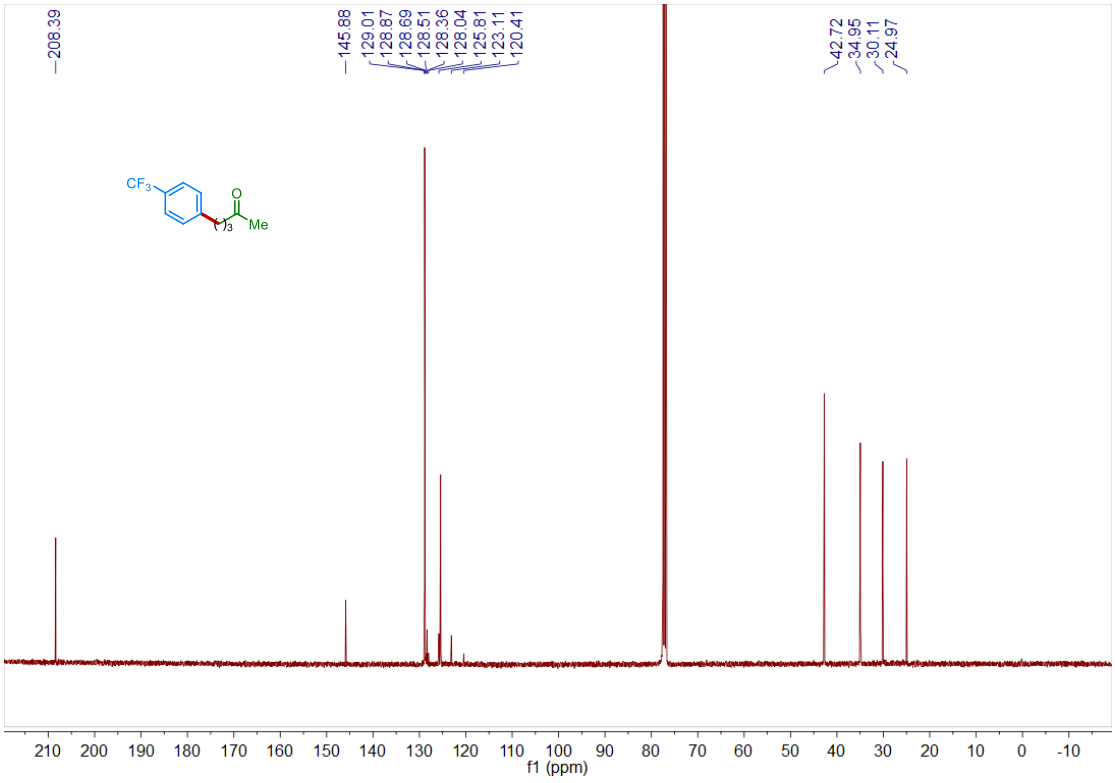
5 ^{13}C-NMR



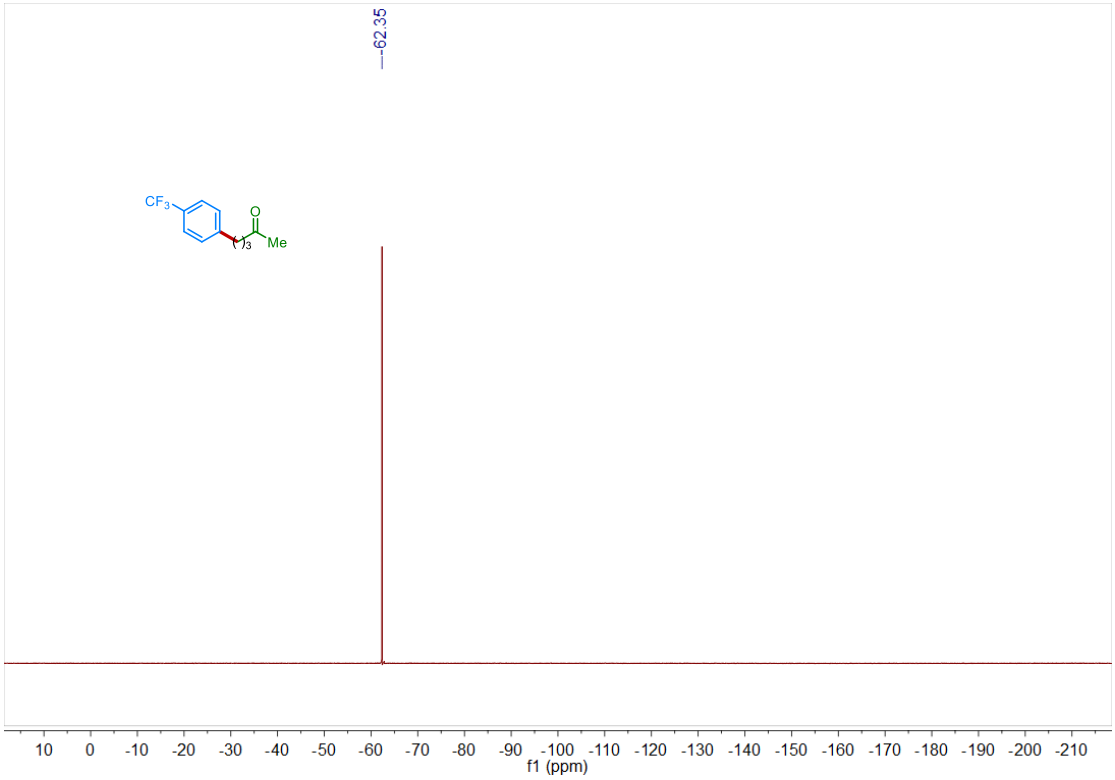
6 ^{1}H-NMR



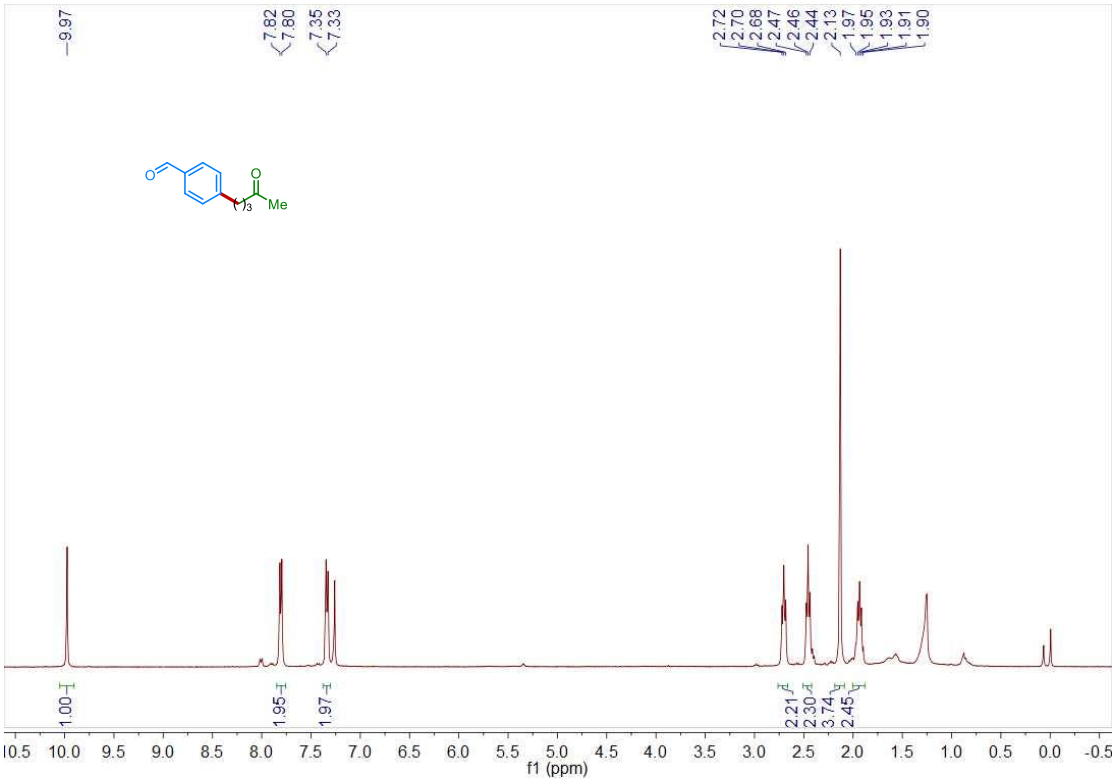
6 ^{13}C-NMR



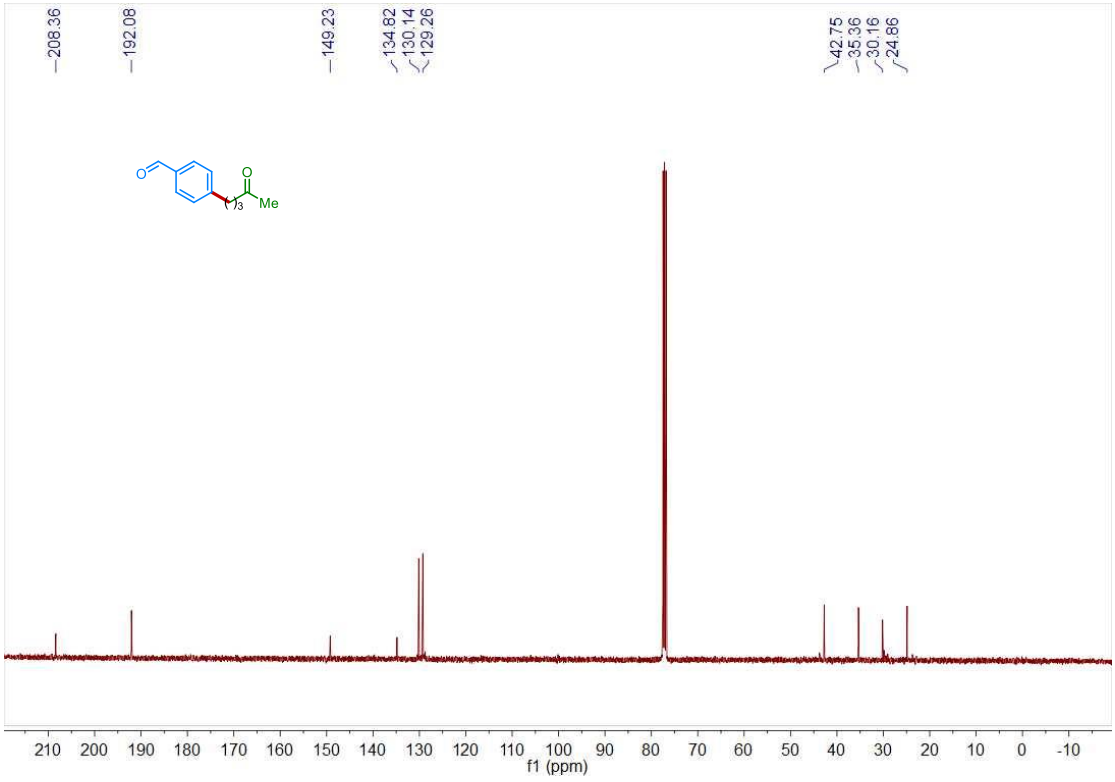
6 ^{19}F-NMR


-62.35
CF3
O
Me
3
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)

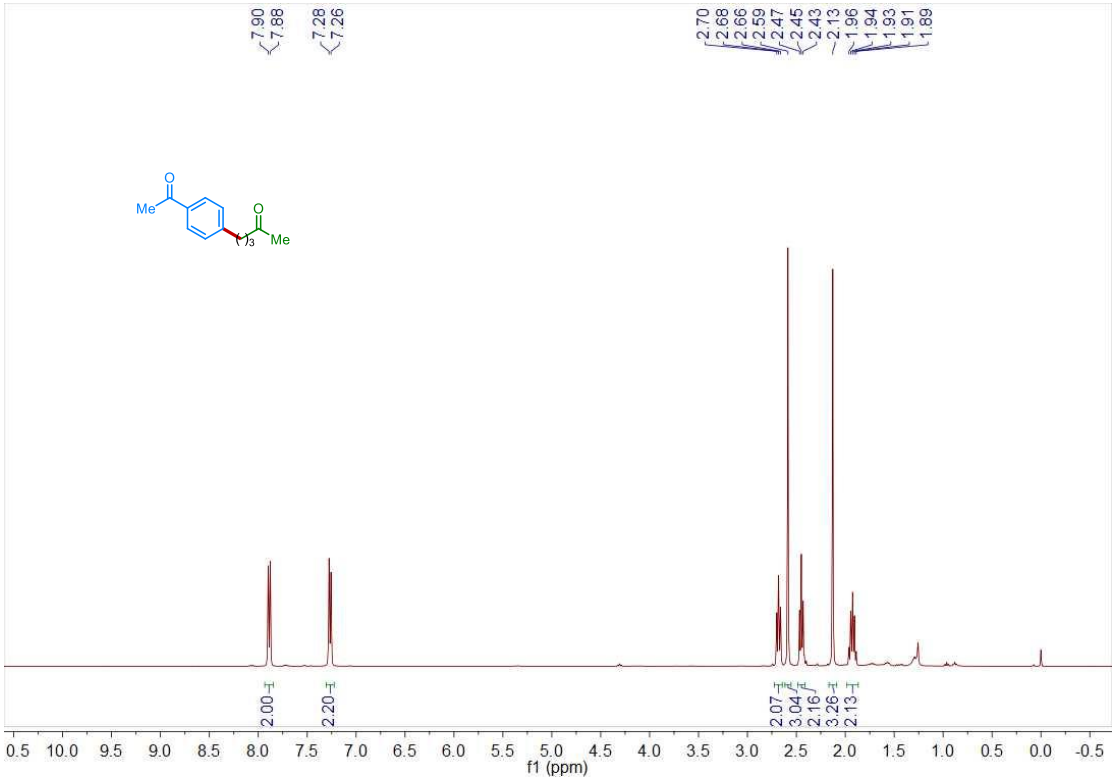
7 ^{1}H-NMR



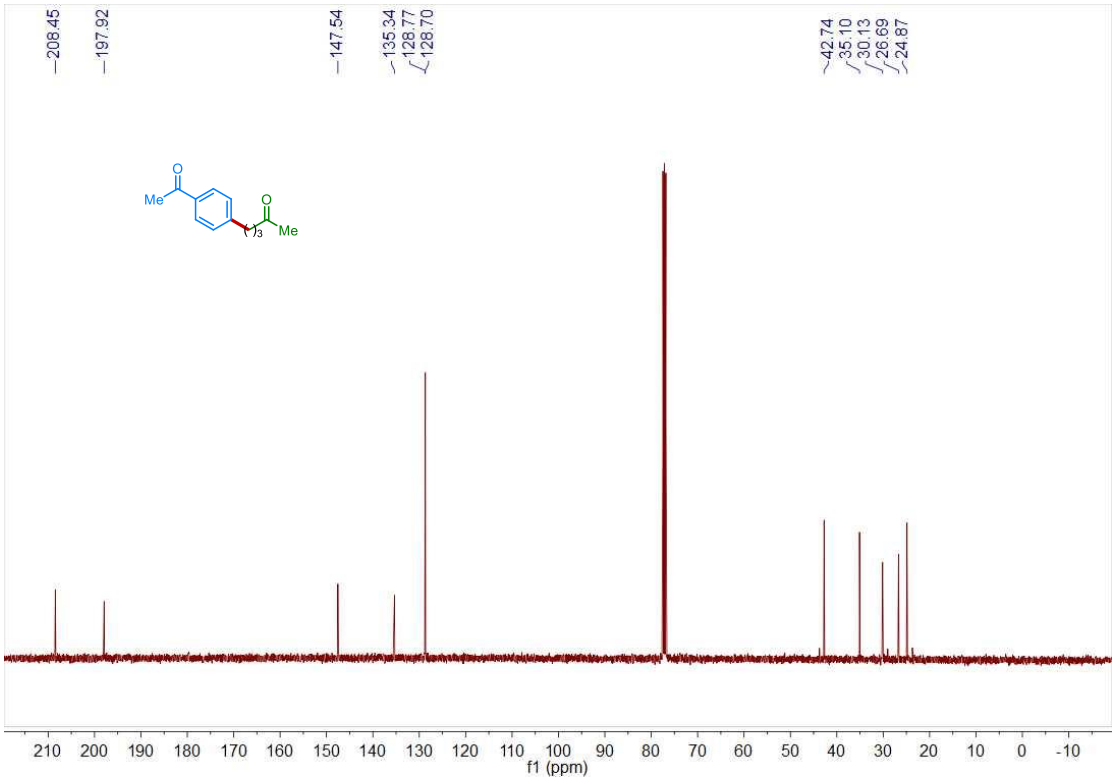
7 ^{13}C-NMR



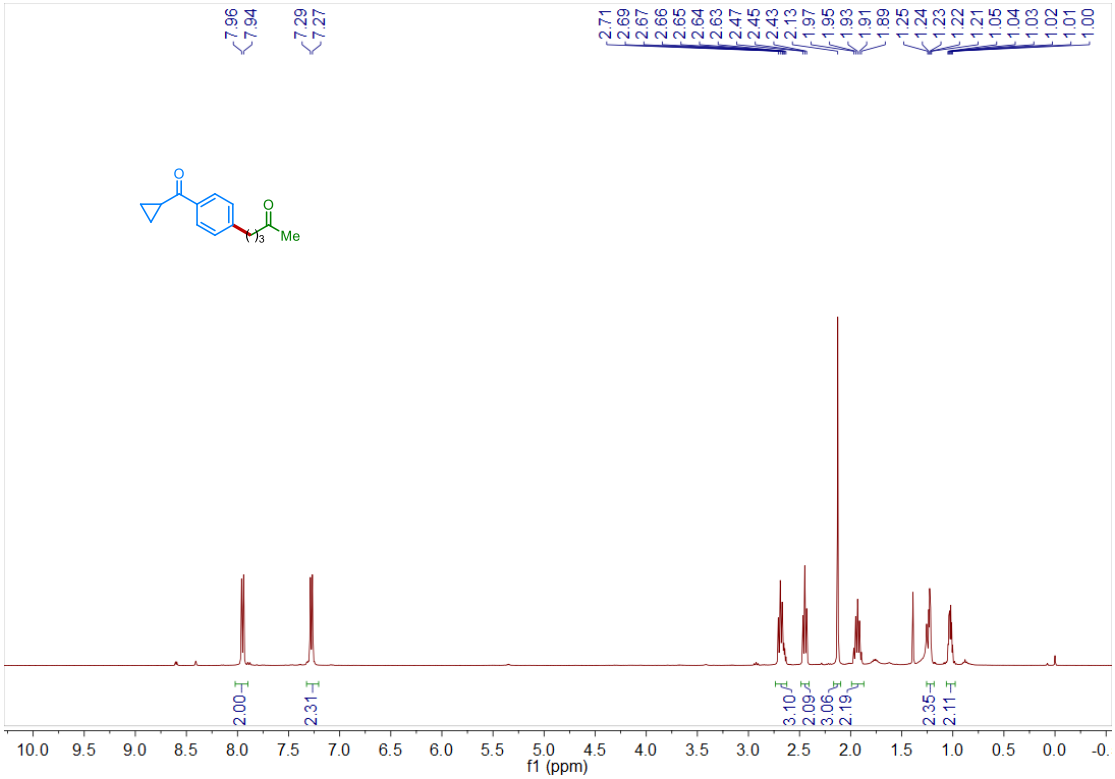
8 ^{1}H-NMR



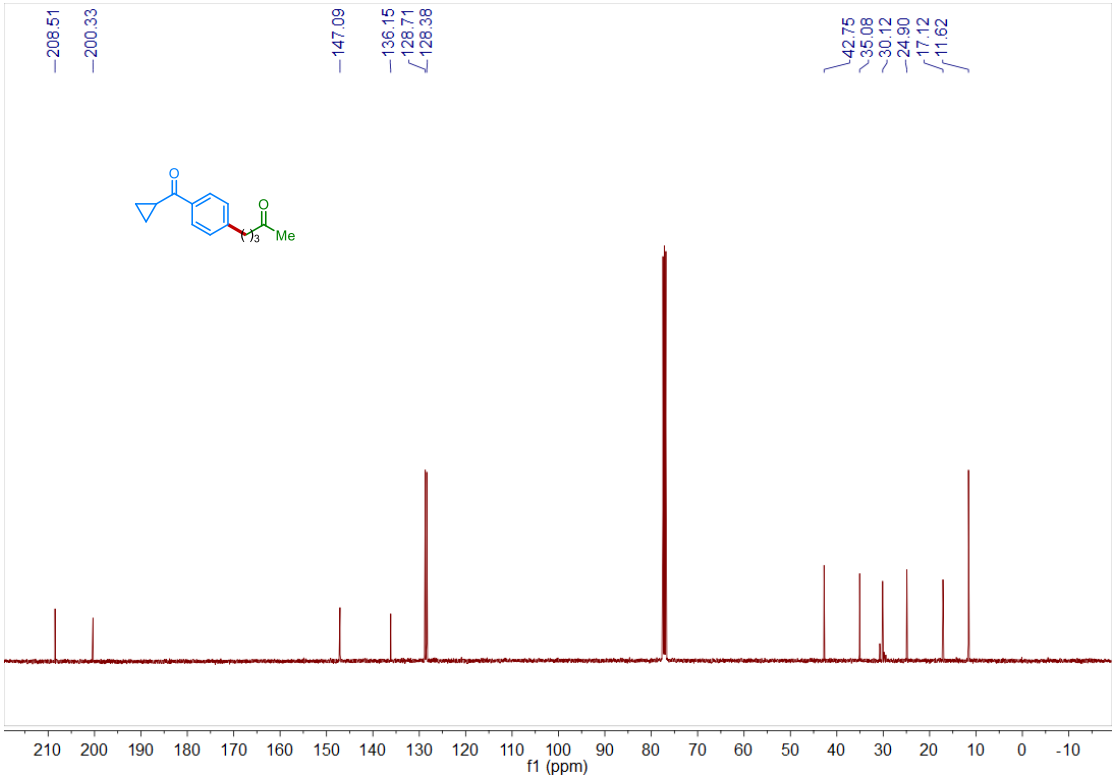
8 ^{13}C-NMR



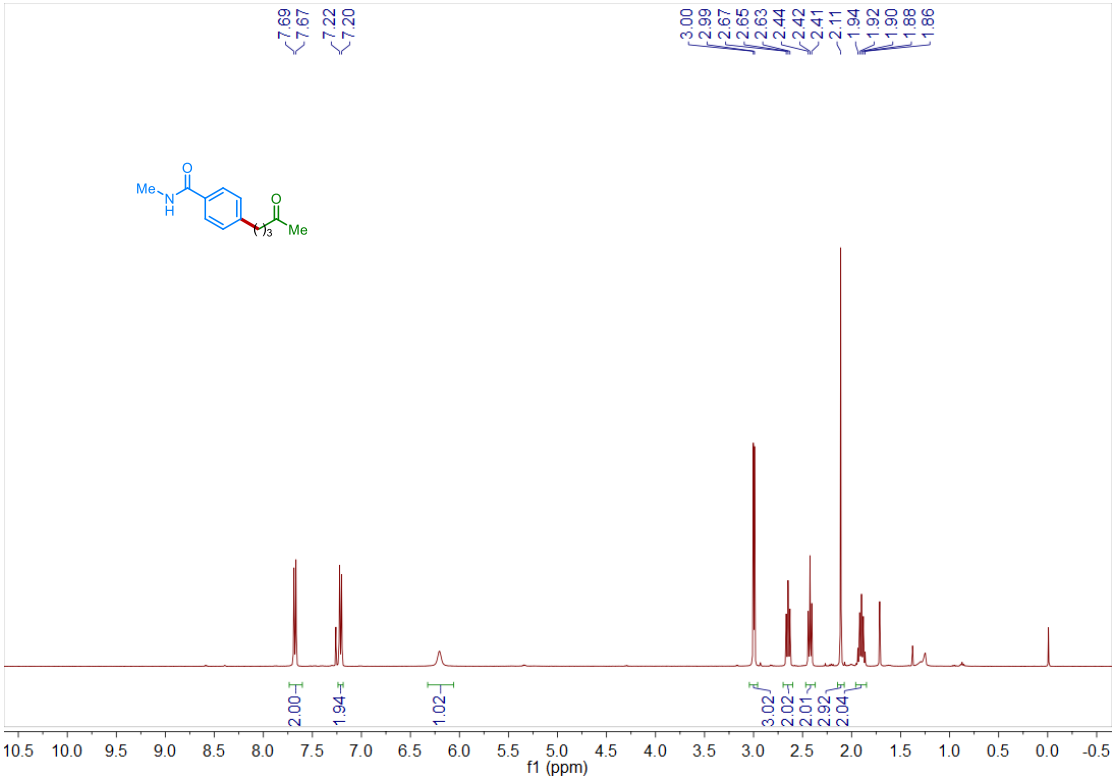
9 ^{1}H-NMR



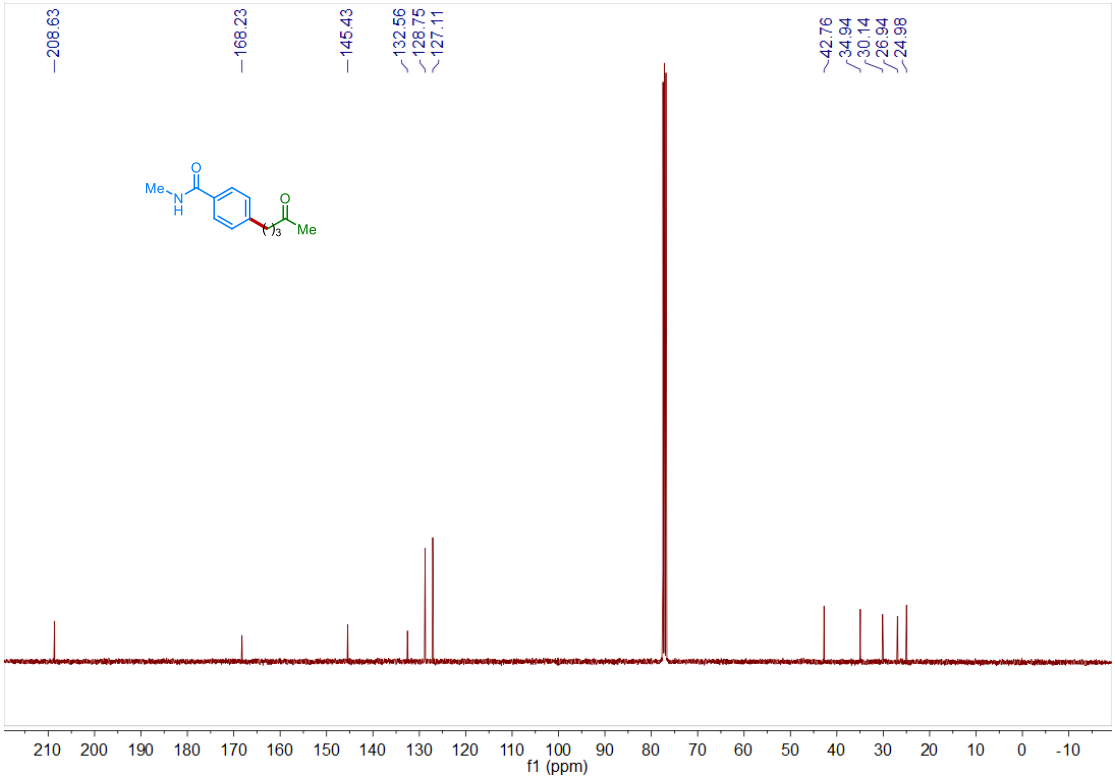
9 ^{13}C-NMR



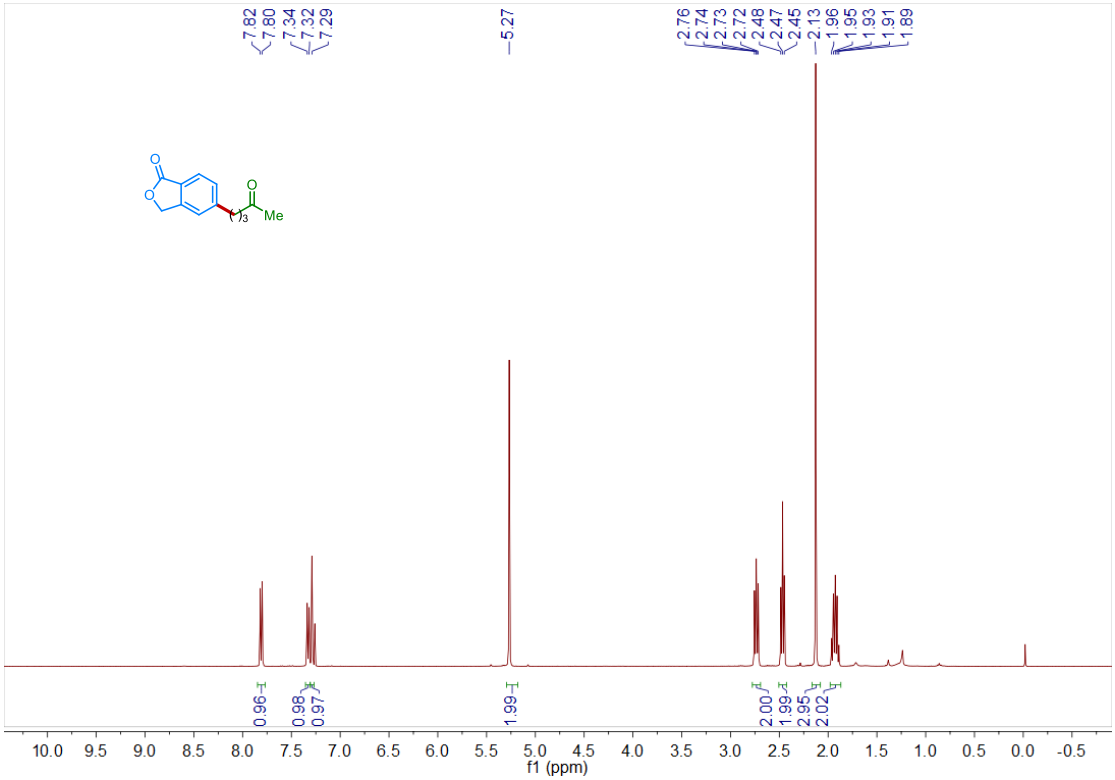
10 ^{1}H-NMR



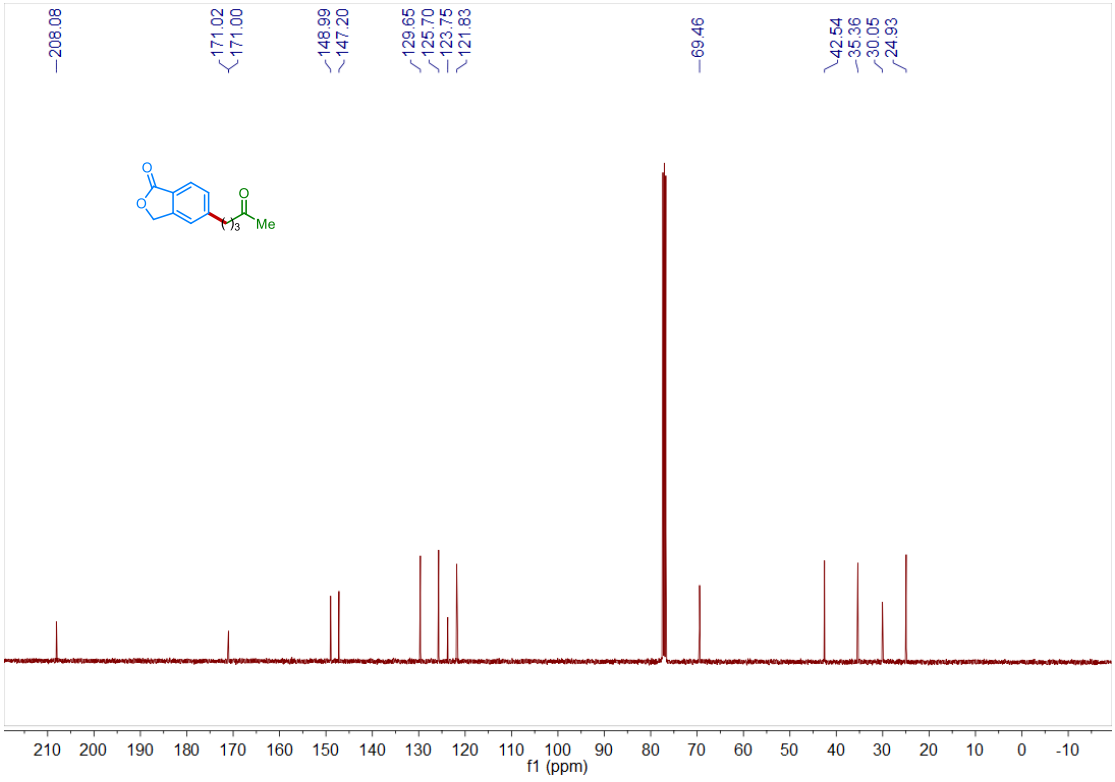
10 ^{13}C-NMR



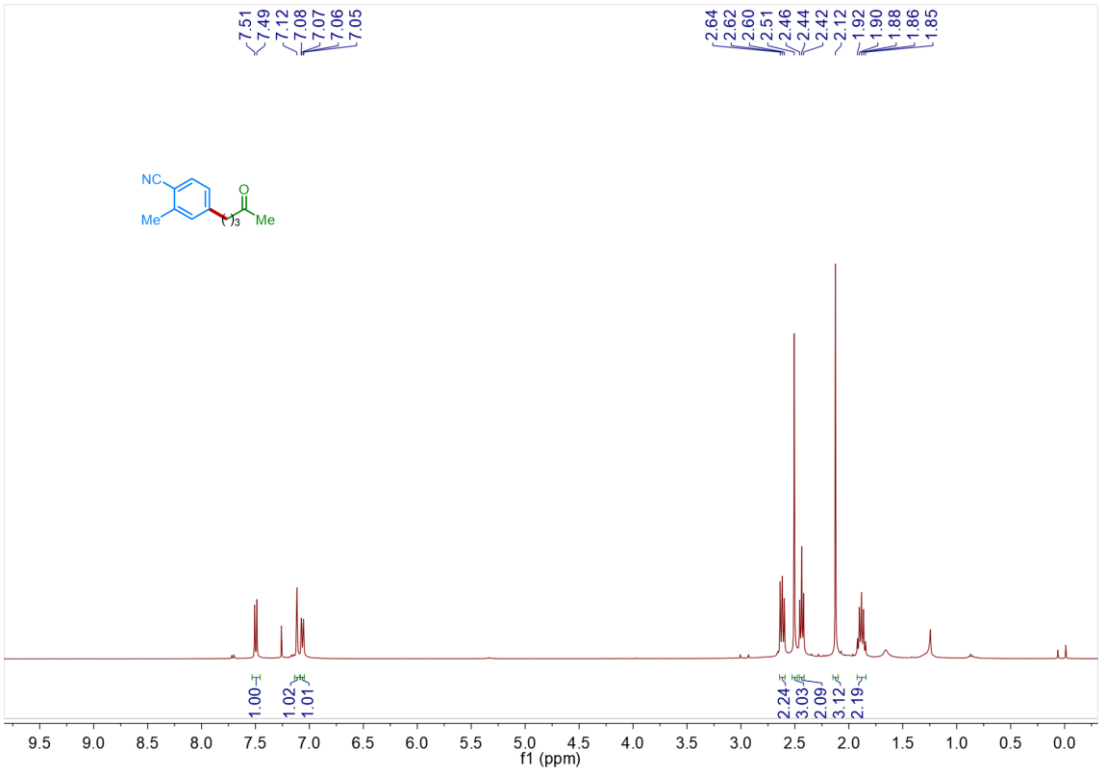
11 ^{1}H-NMR



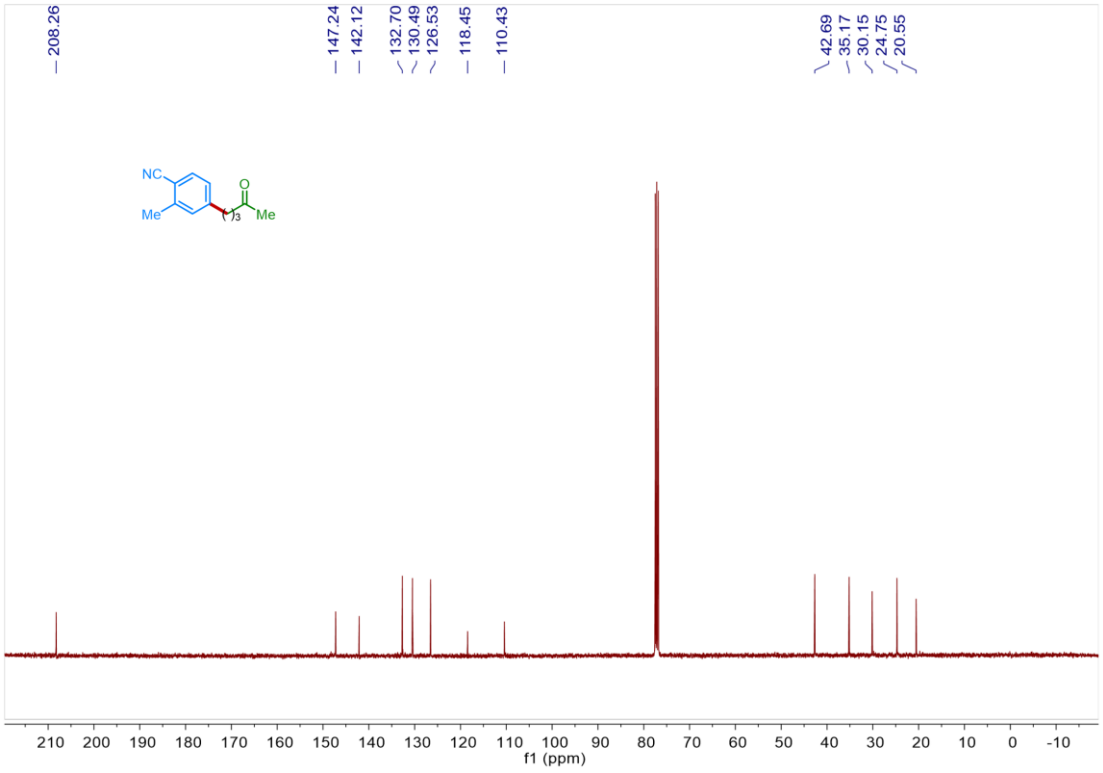
11 ^{13}C-NMR



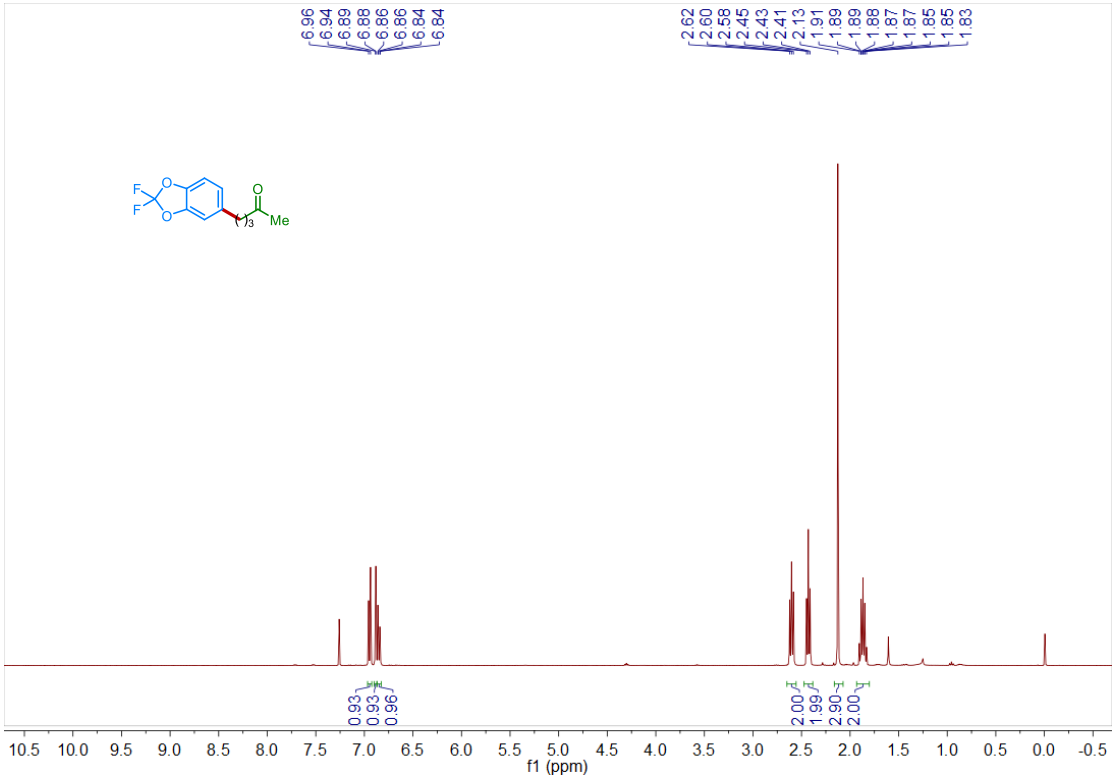
12 ^{1}H-NMR



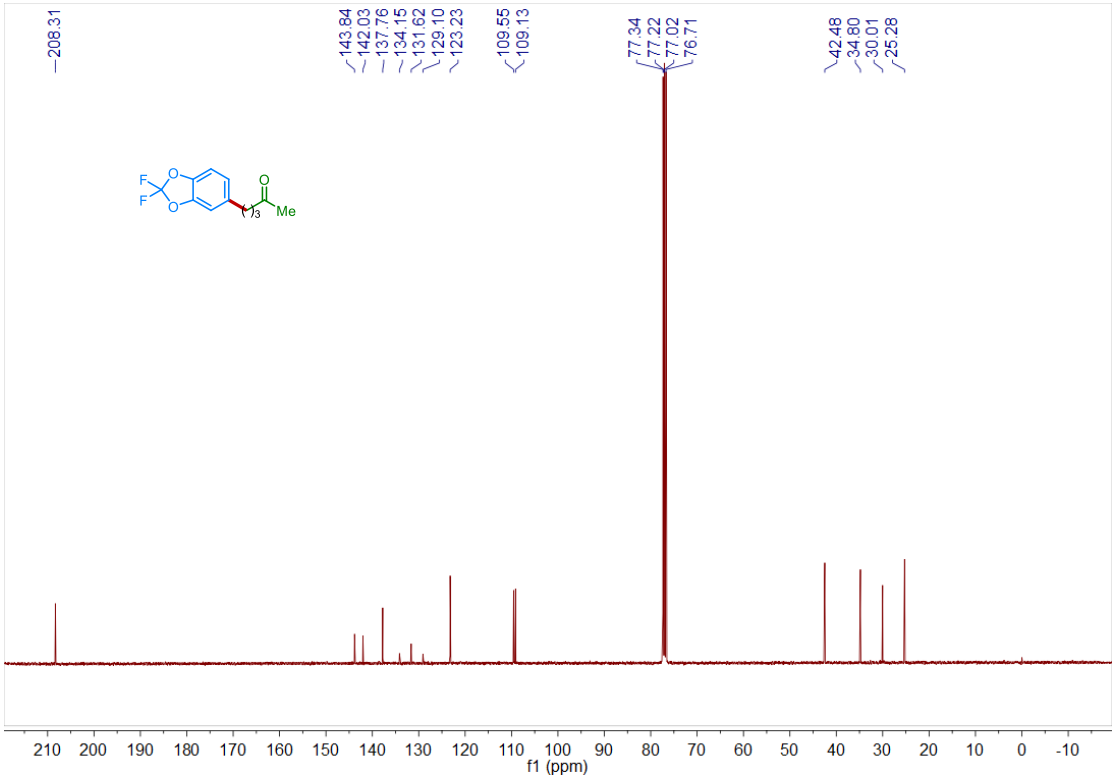
12 ^{13}C-NMR



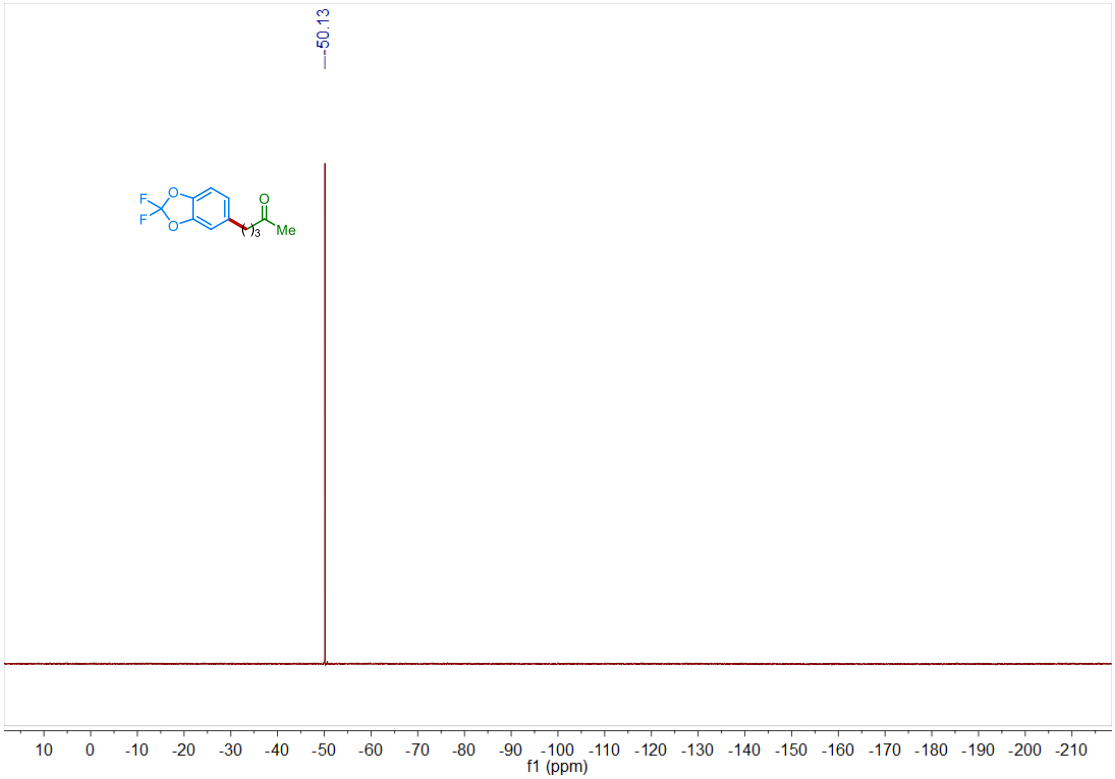
13 ^{1}H-NMR



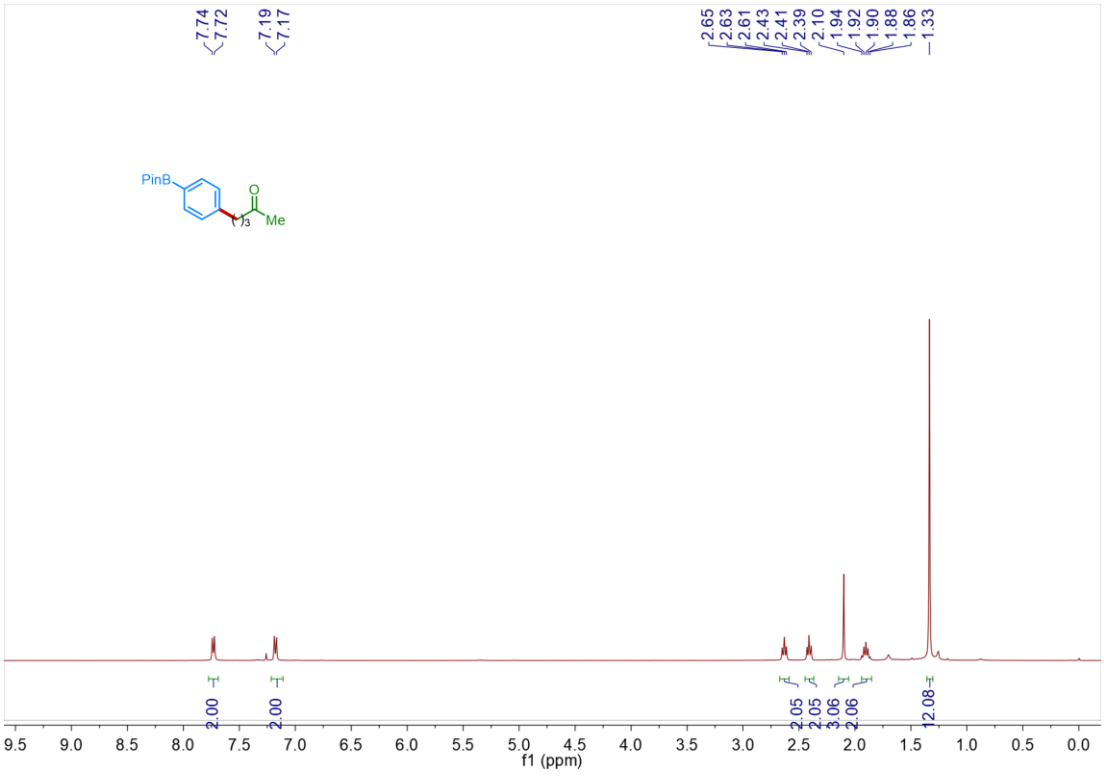
13 ^{13}C-NMR



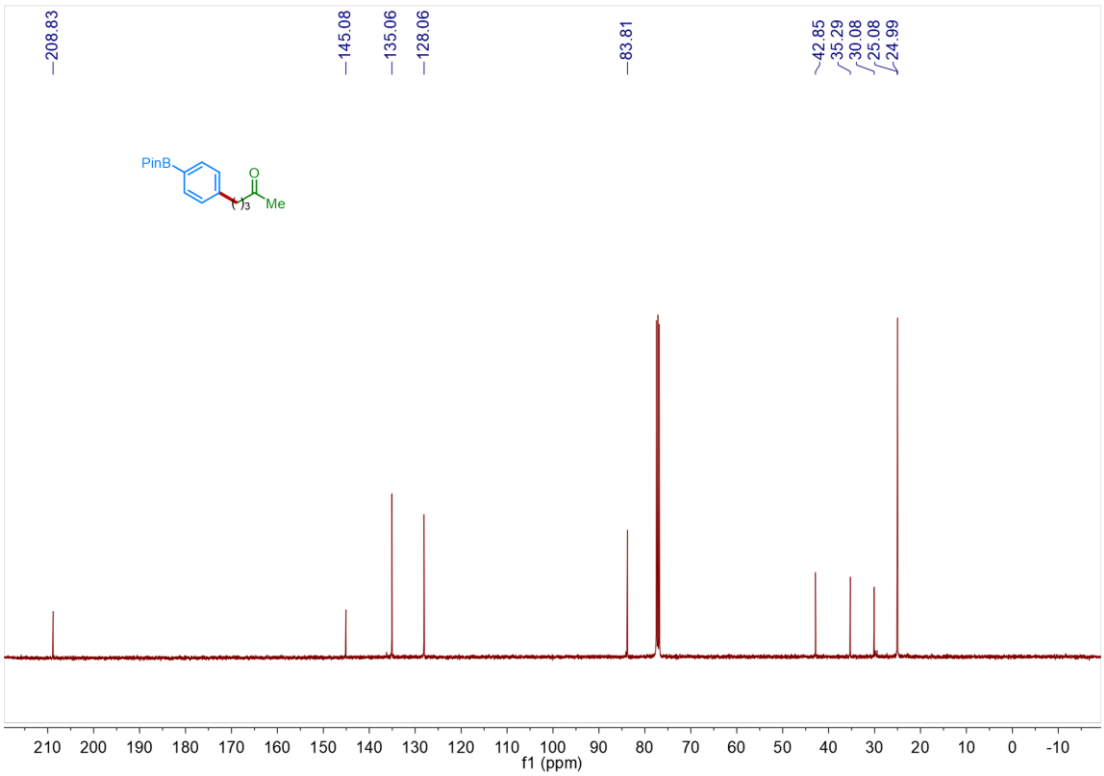
13 ^{19}F-NMR



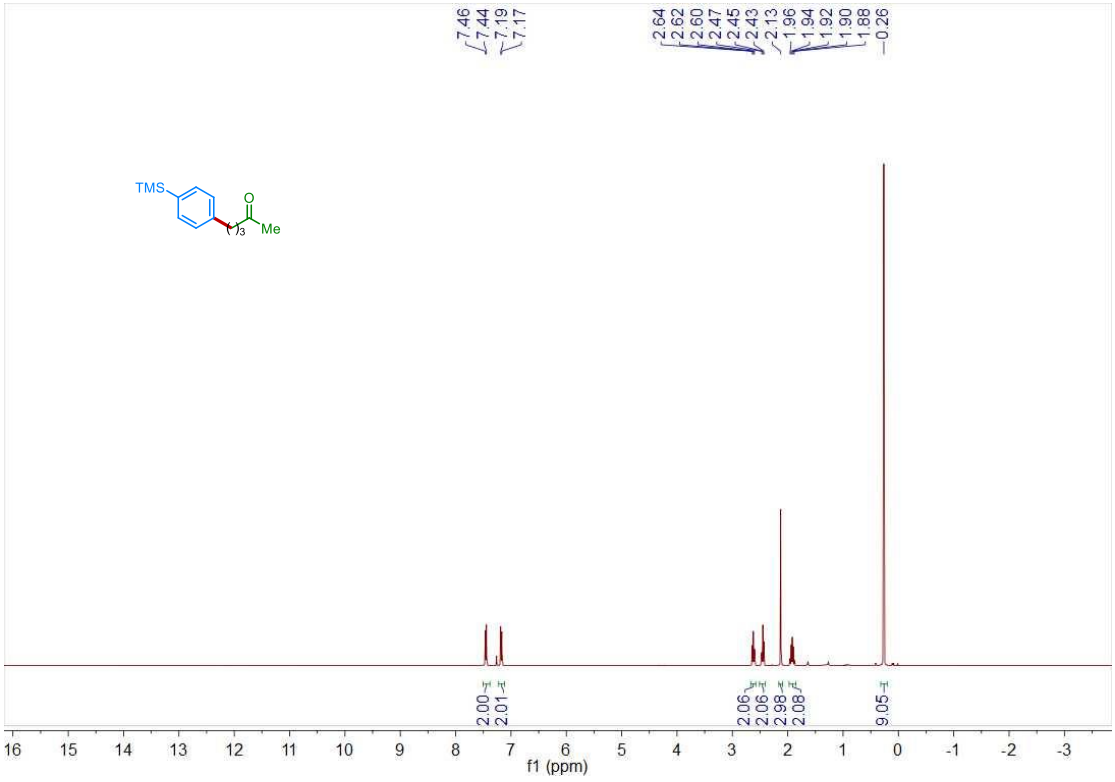
14 ^{1}H-NMR



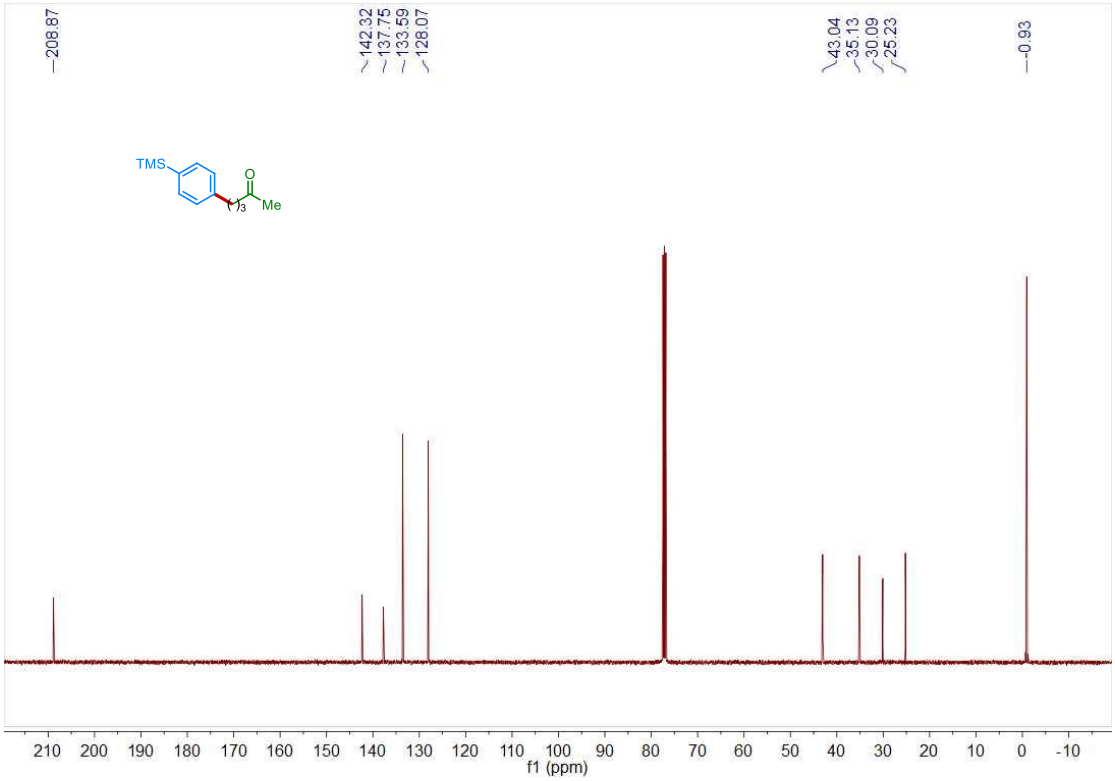
14 ^{13}C-NMR



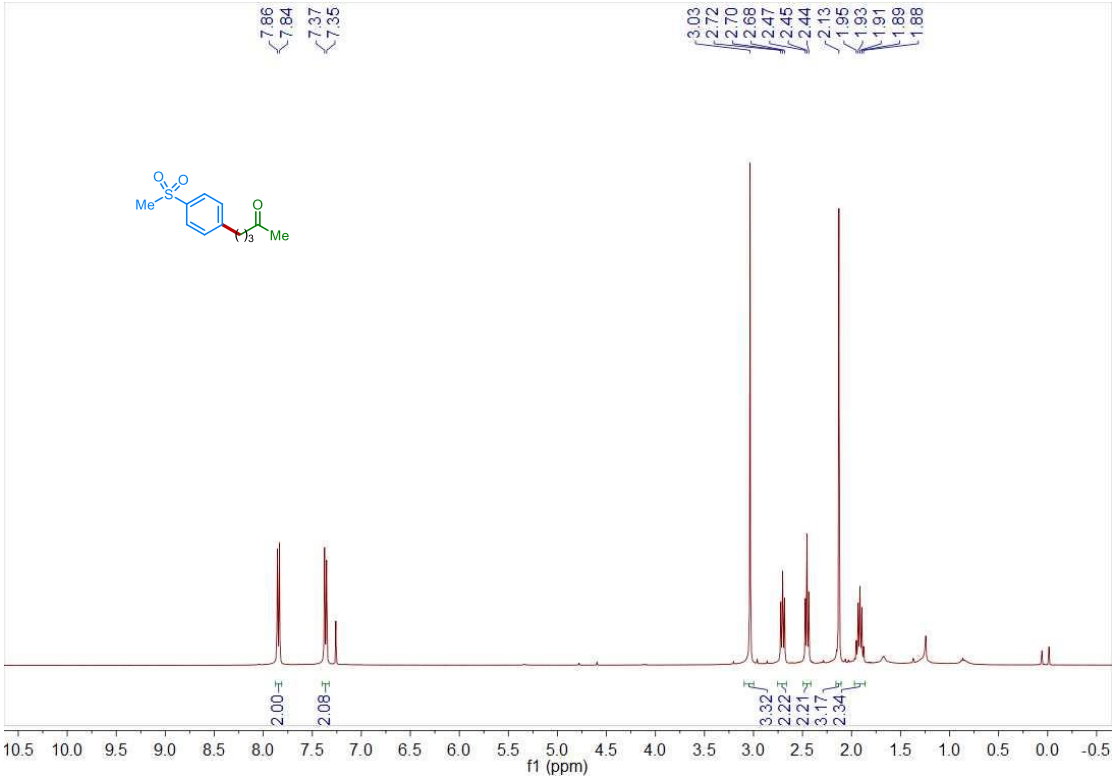
15 ^{1}H-NMR



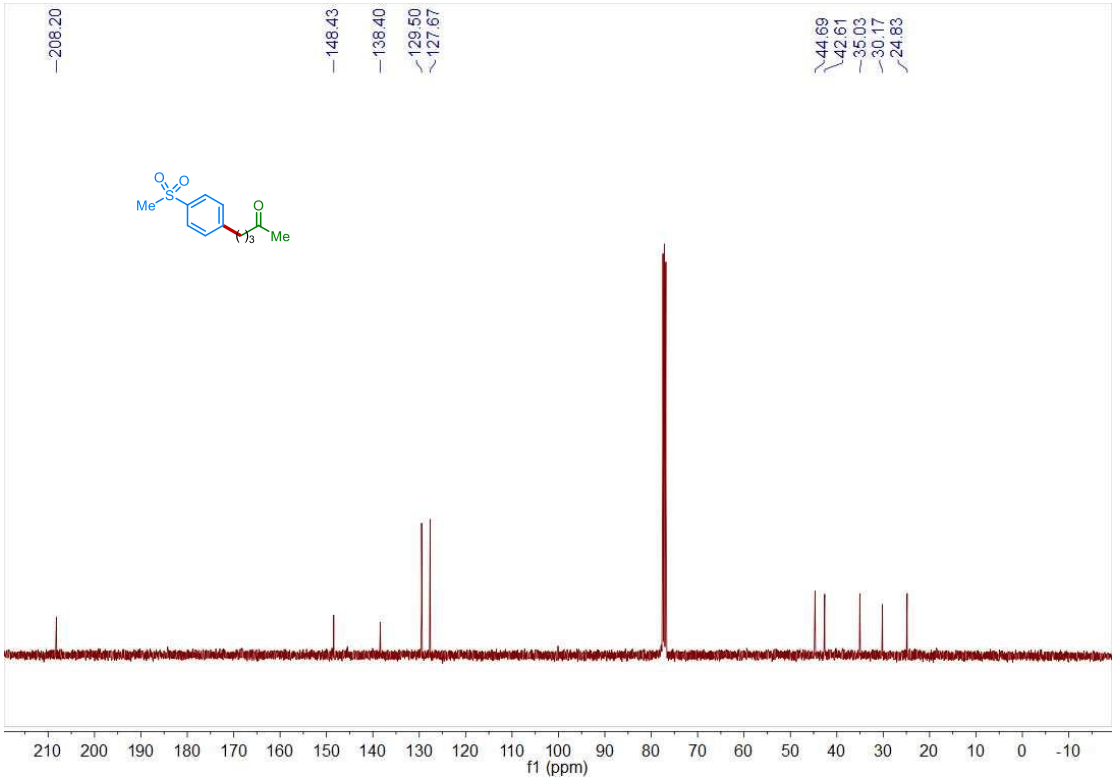
15 ^{13}C-NMR



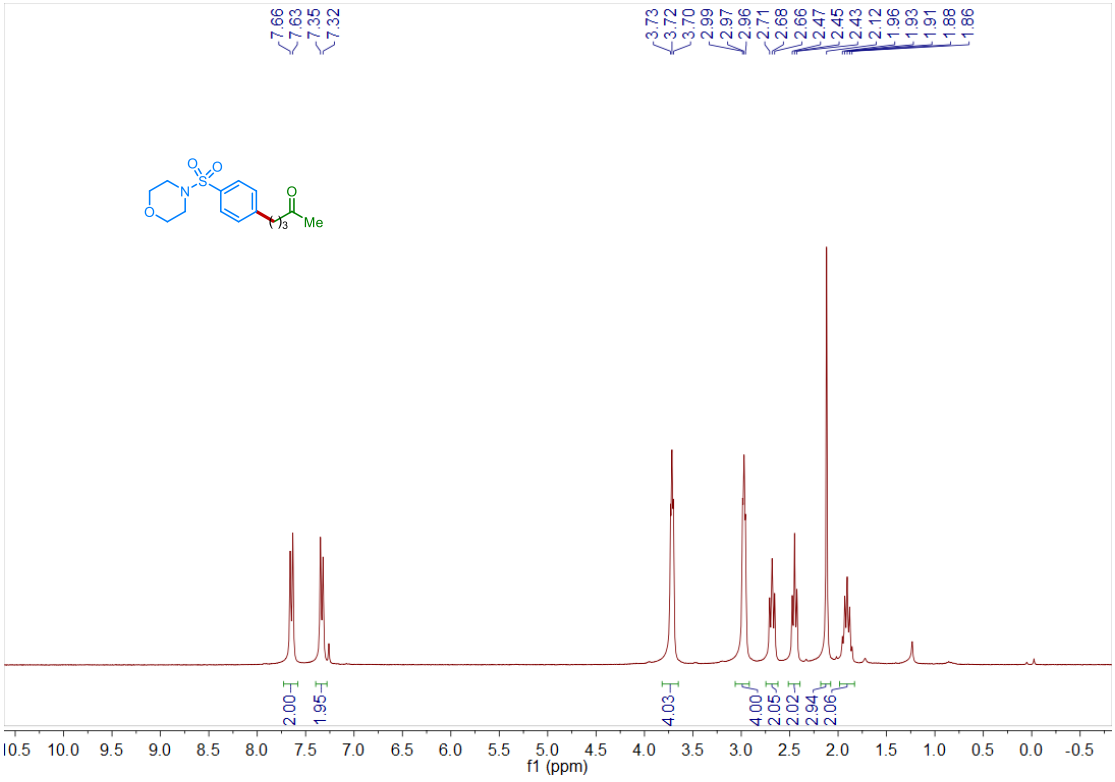
16 ^{1}H-NMR



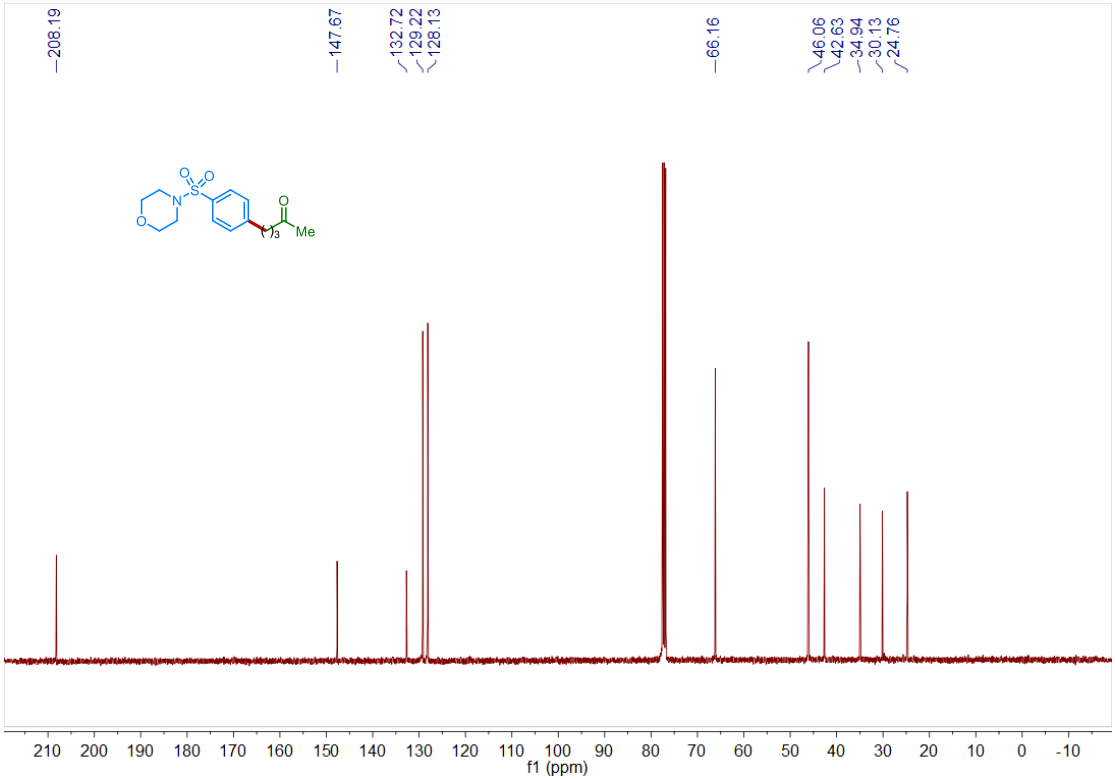
16 ^{13}C-NMR



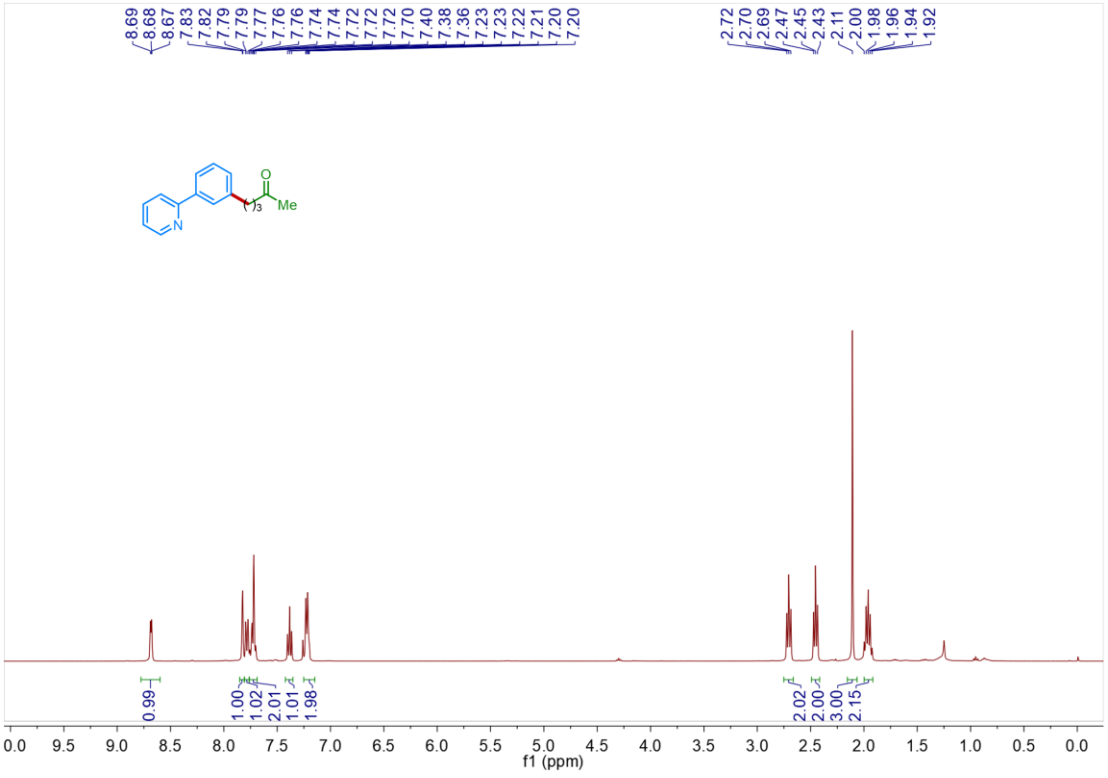
17 ^{1}H-NMR



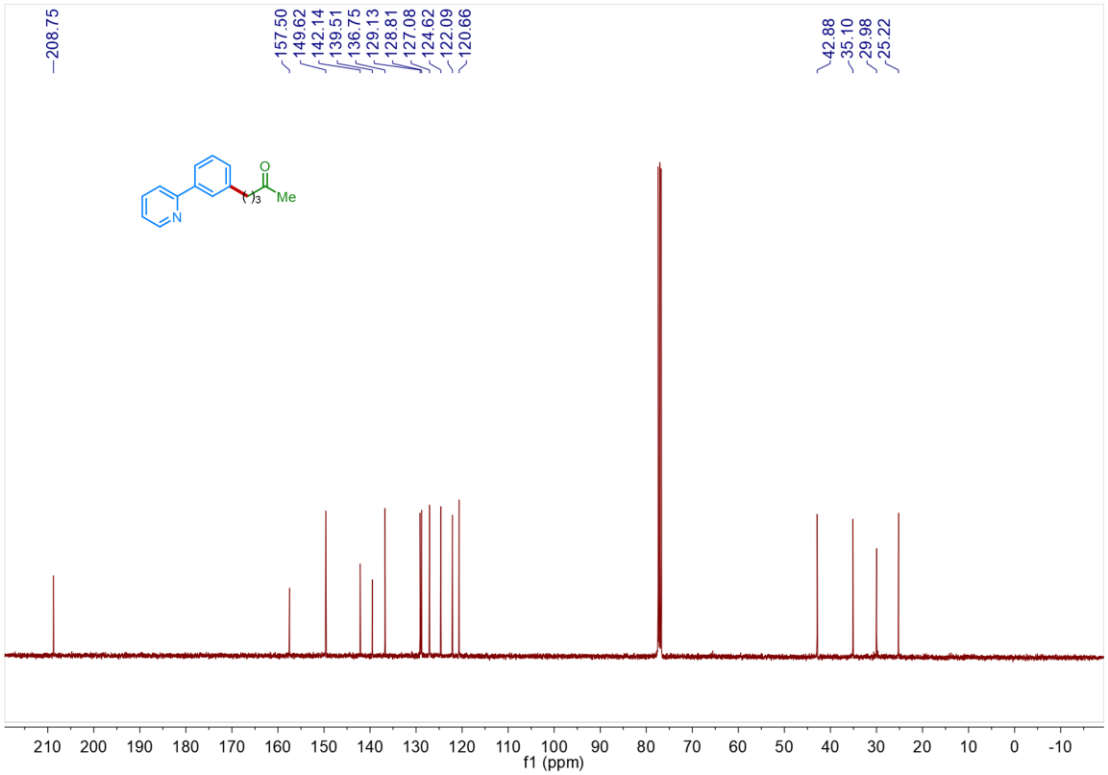
17 ^{13}C-NMR



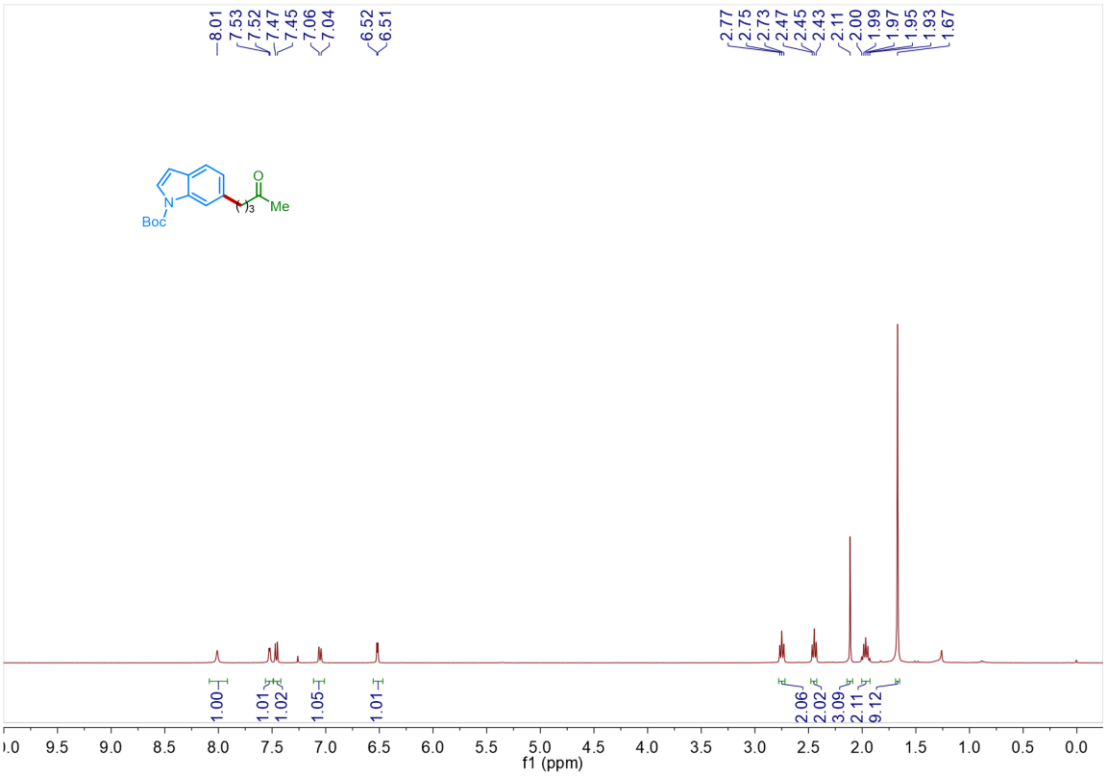
18 ^{1}H-NMR



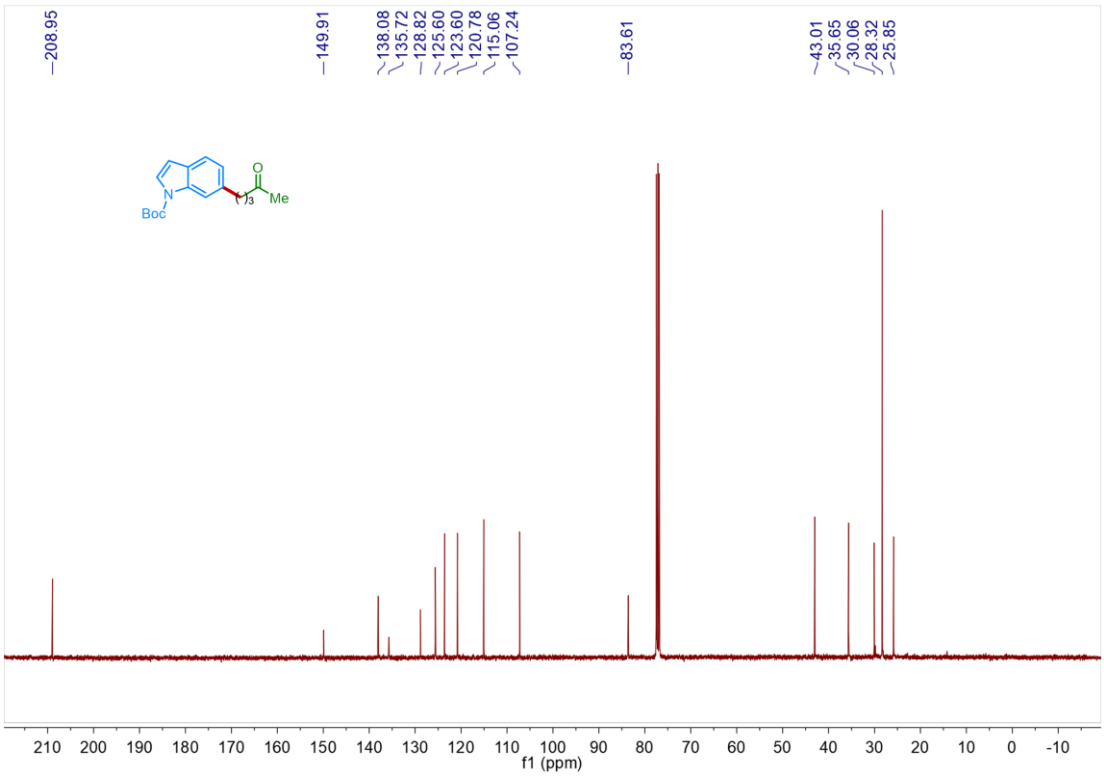
18 ^{13}C-NMR



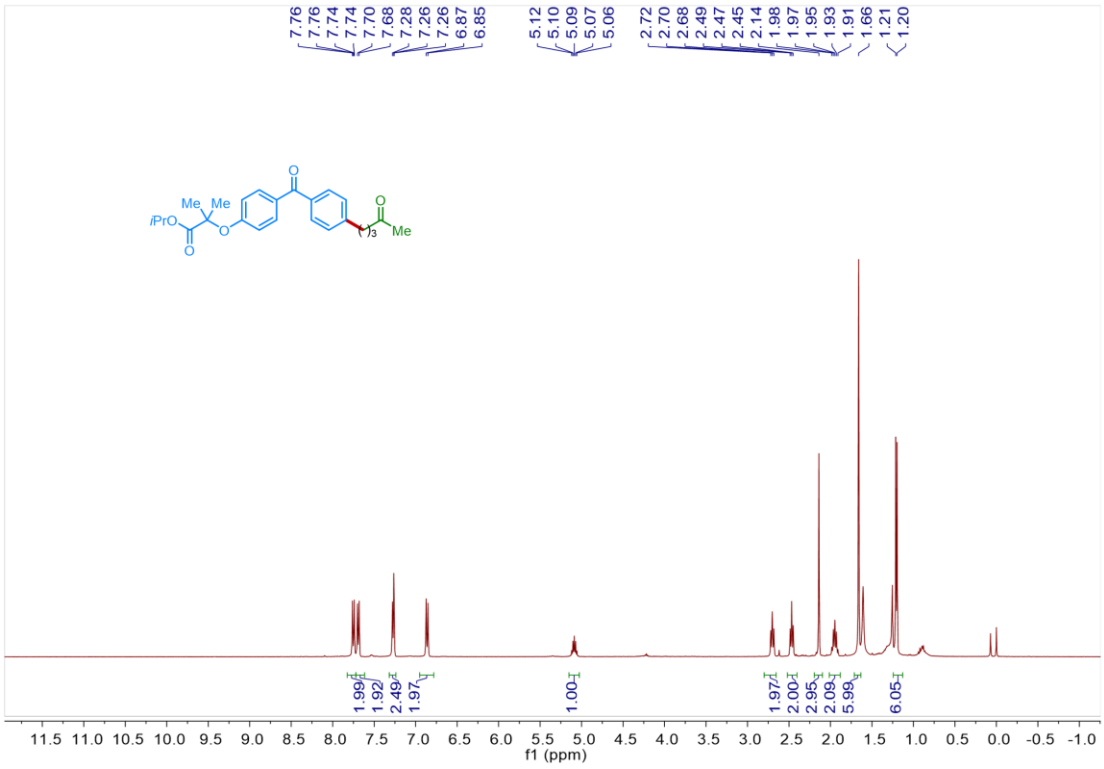
19 ^{1}H-NMR



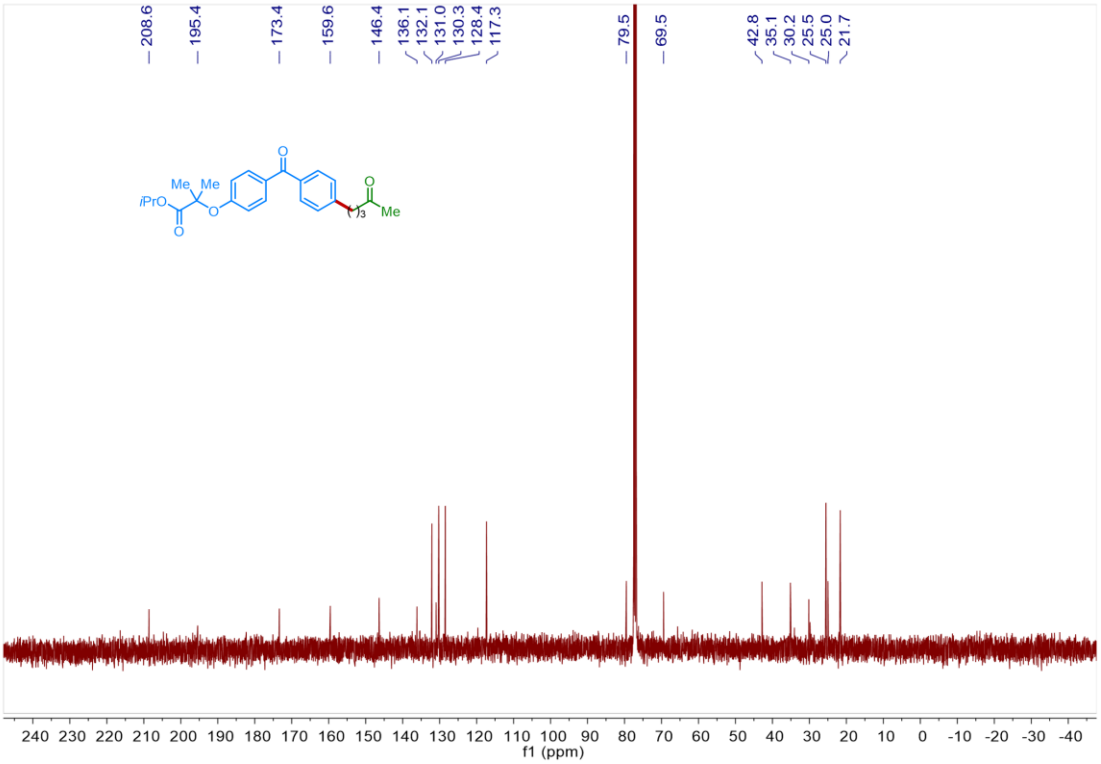
19 ^{13}C-NMR



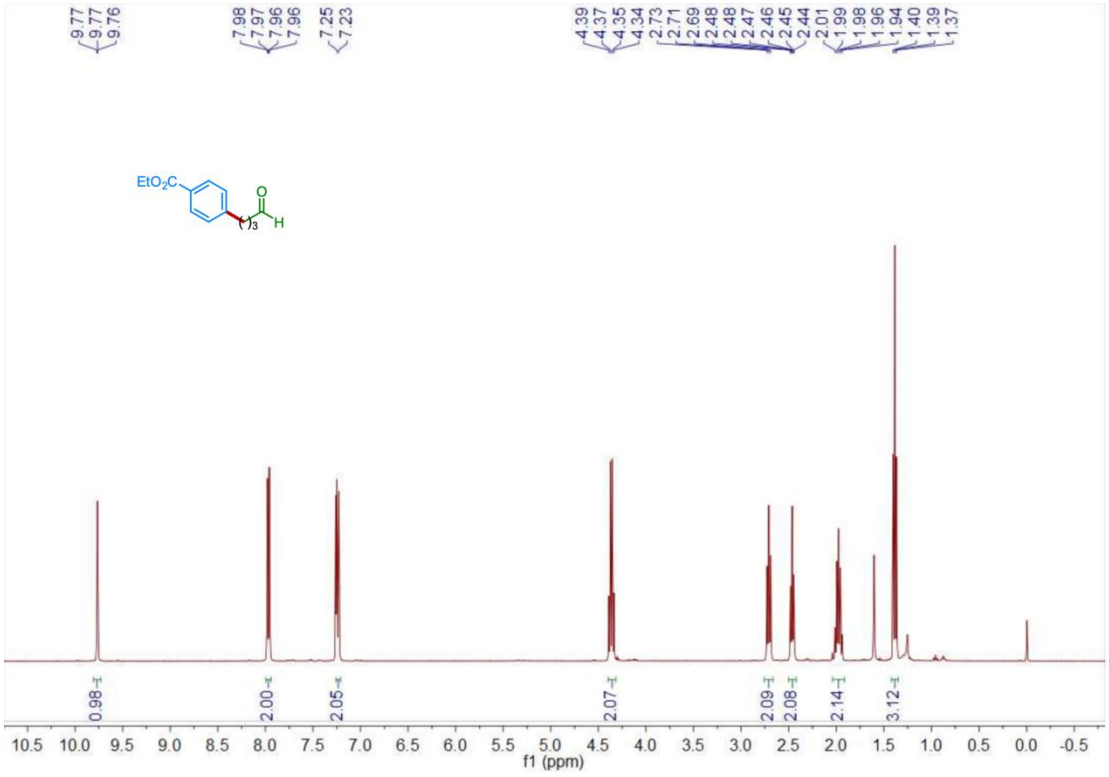
20 ^{1}H-NMR



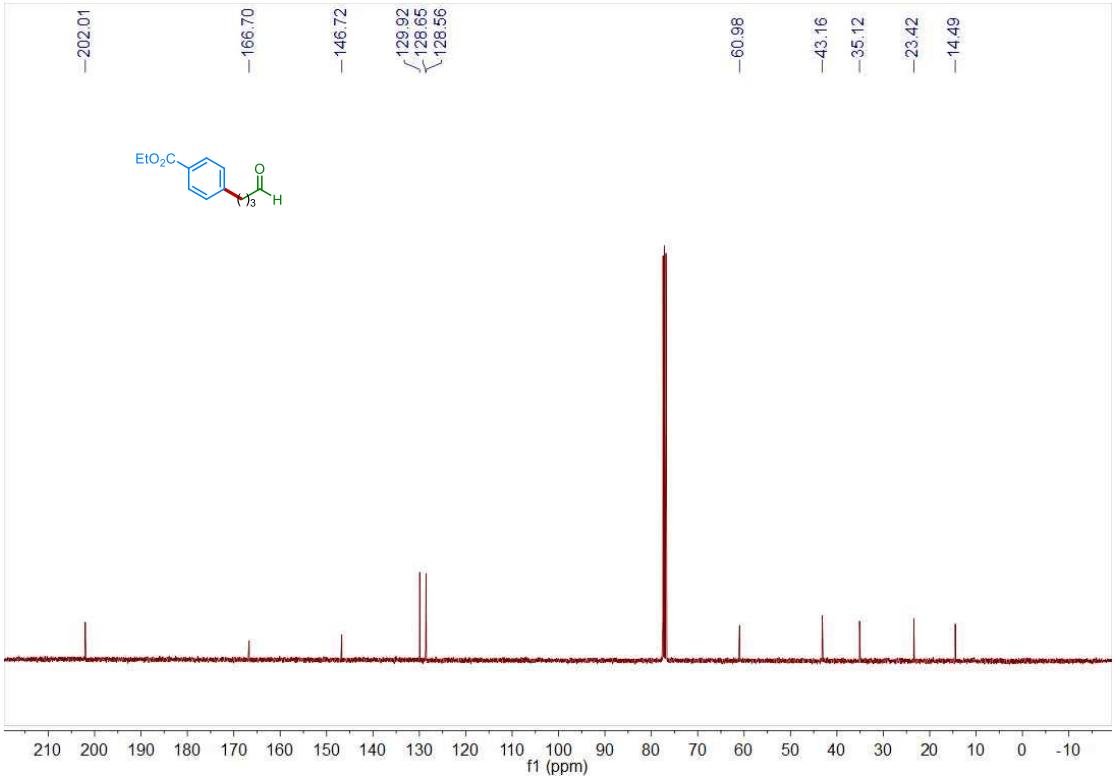
20 ^{13}C-NMR



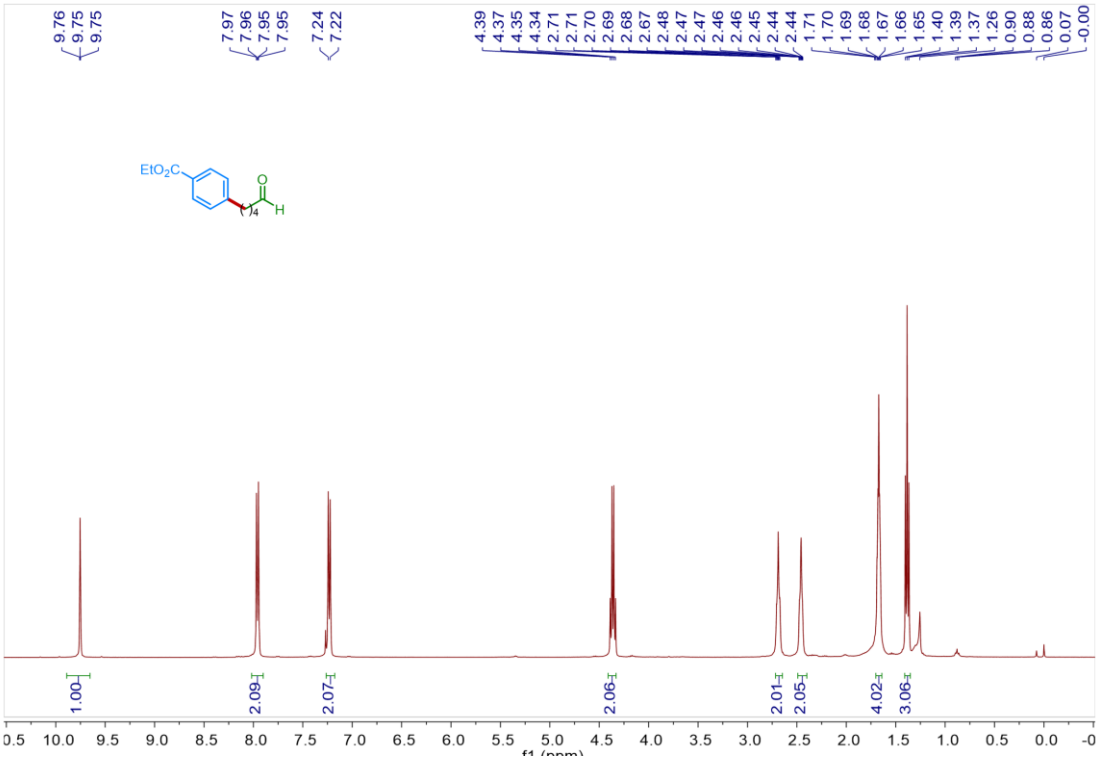
21 ^{1}H-NMR



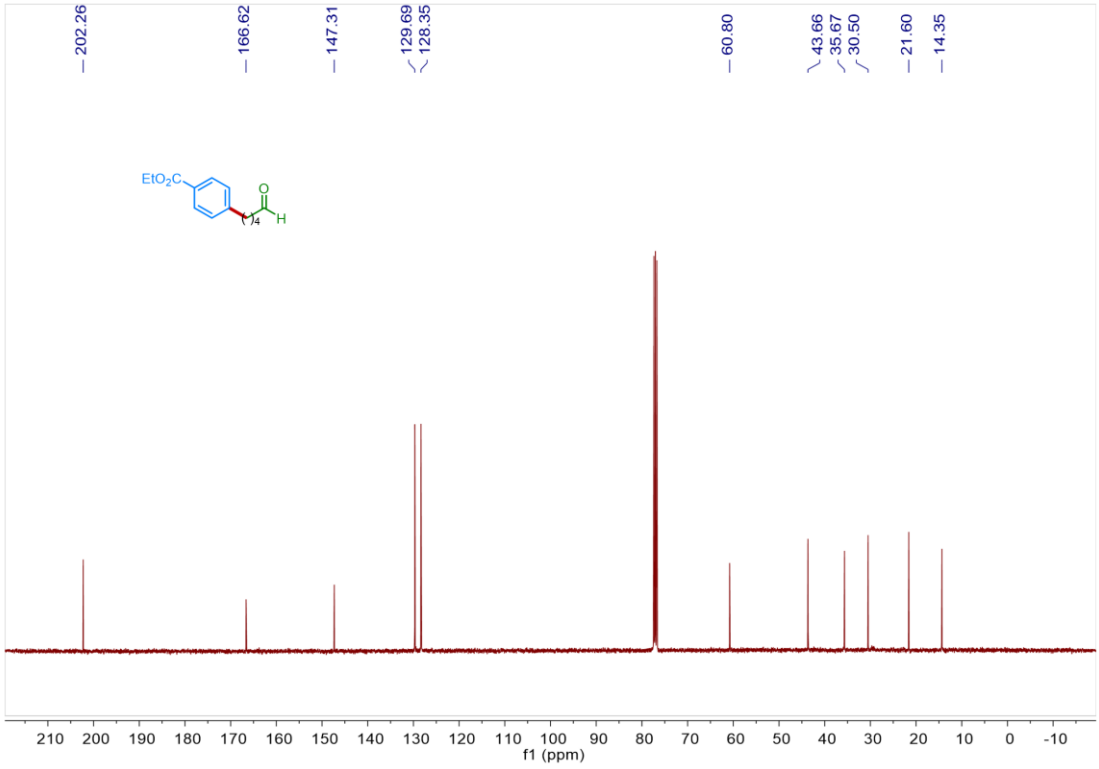
21 ^{13}C-NMR



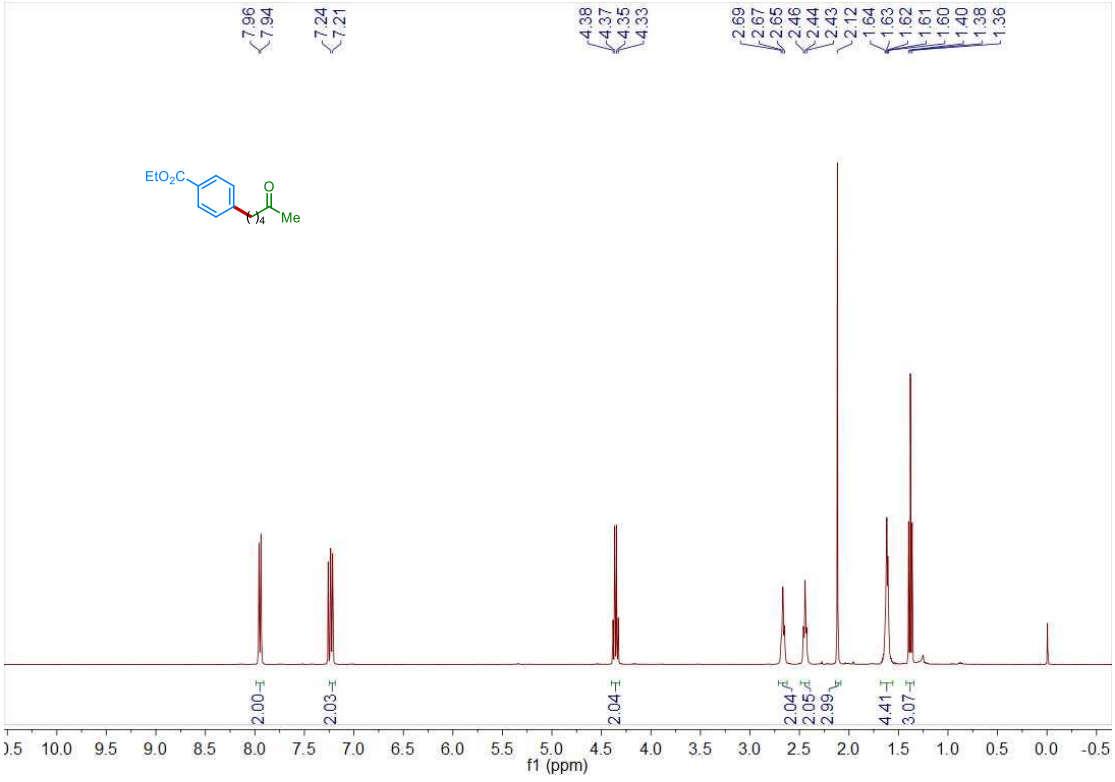
22 ^{1}H-NMR



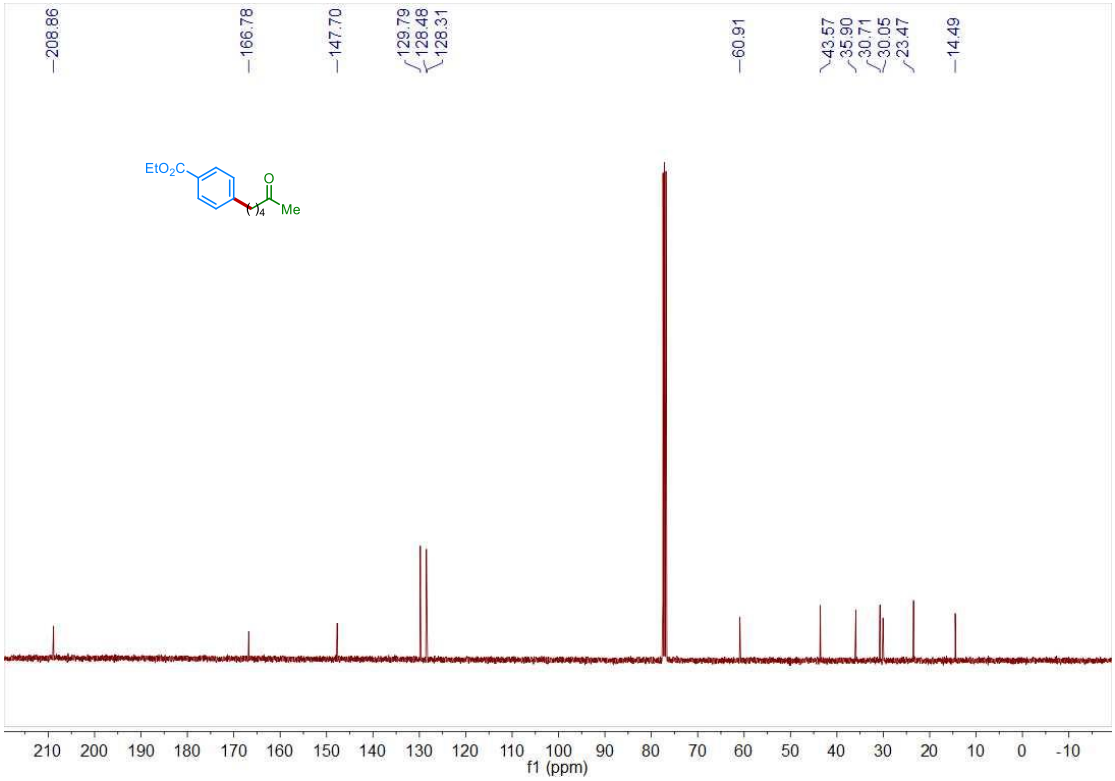
22 ^{13}C-NMR



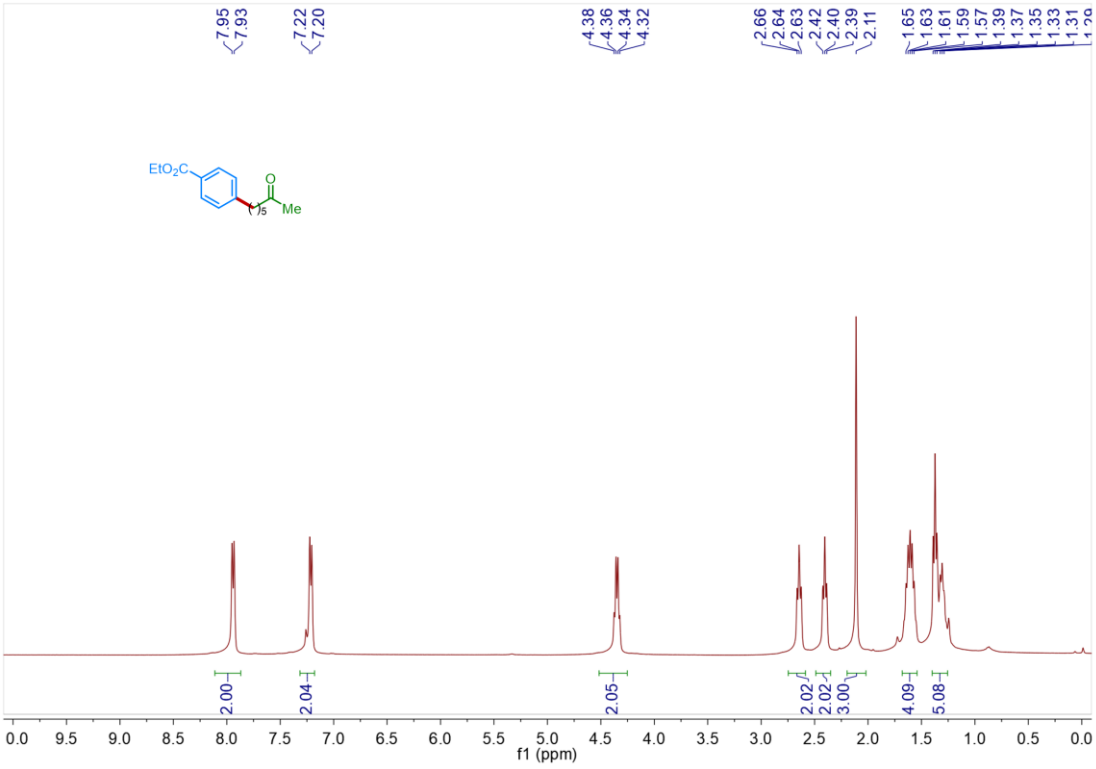
23 ^{1}H-NMR



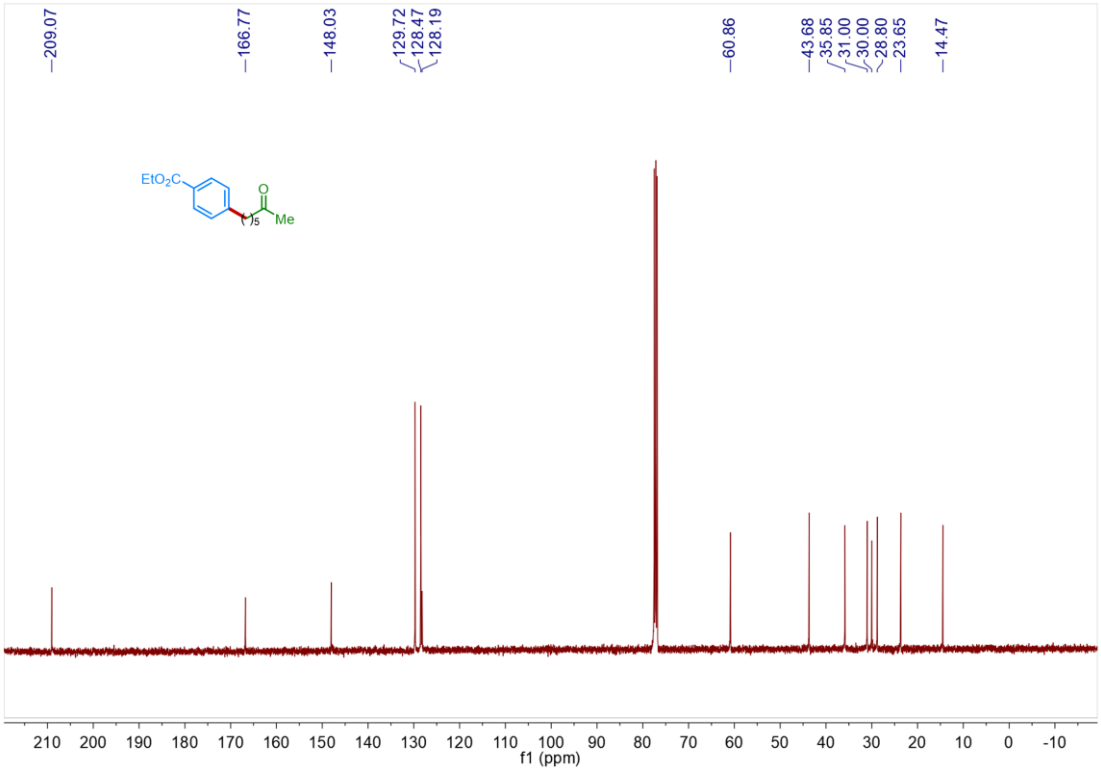
23 ^{13}C-NMR



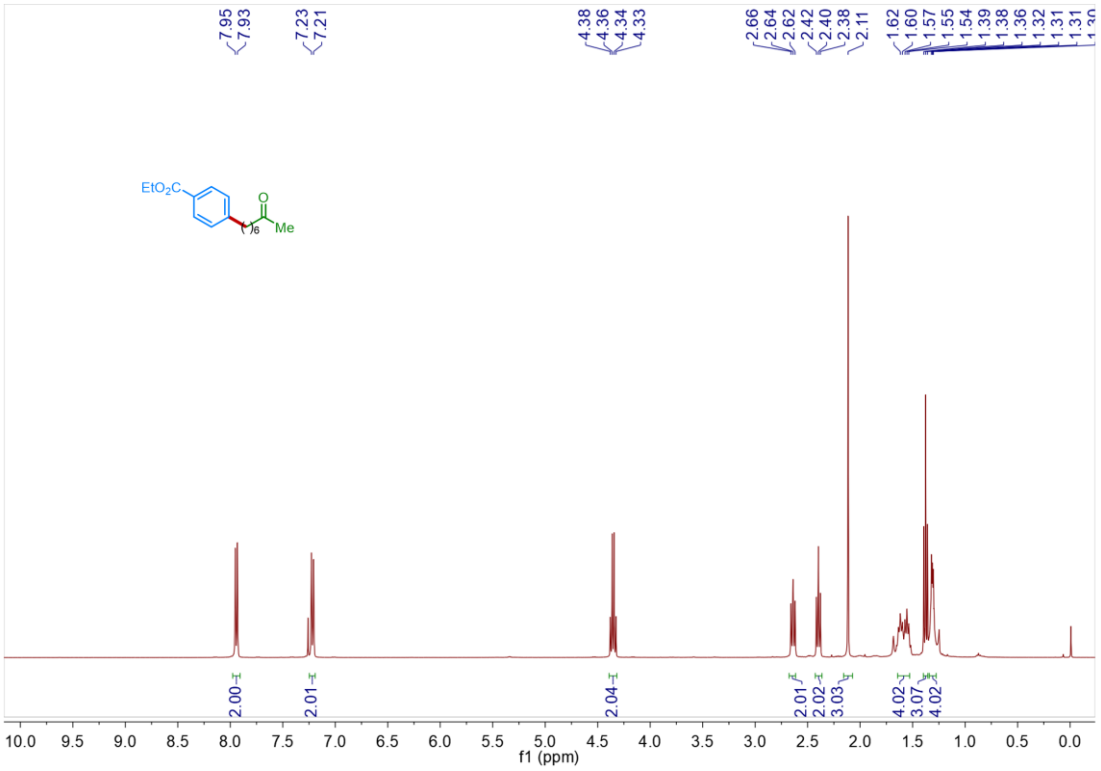
24 ^{1}H-NMR



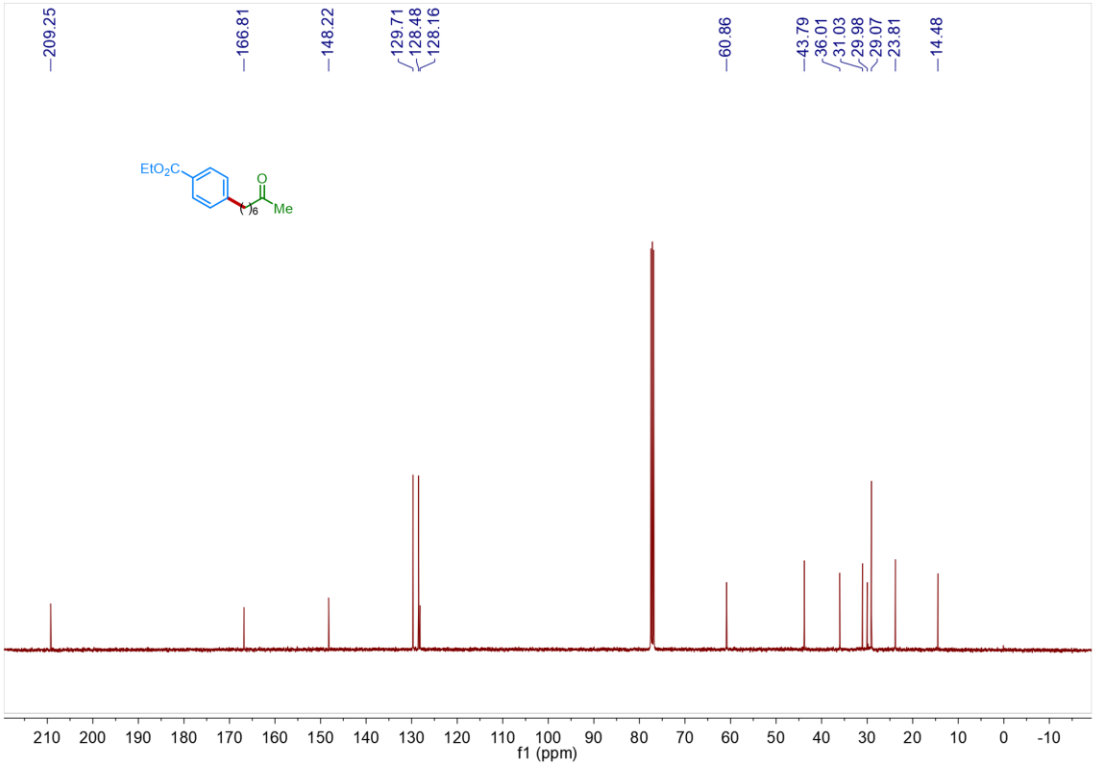
24 ^{13}C-NMR



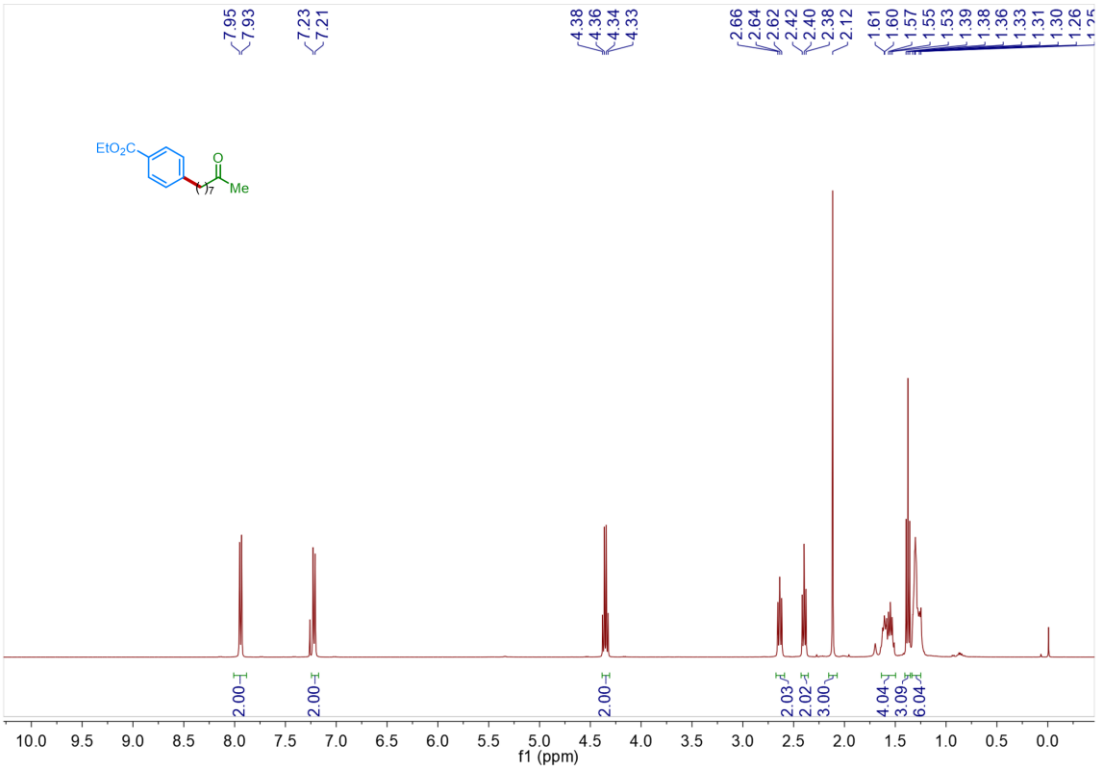
25 ^{1}H-NMR



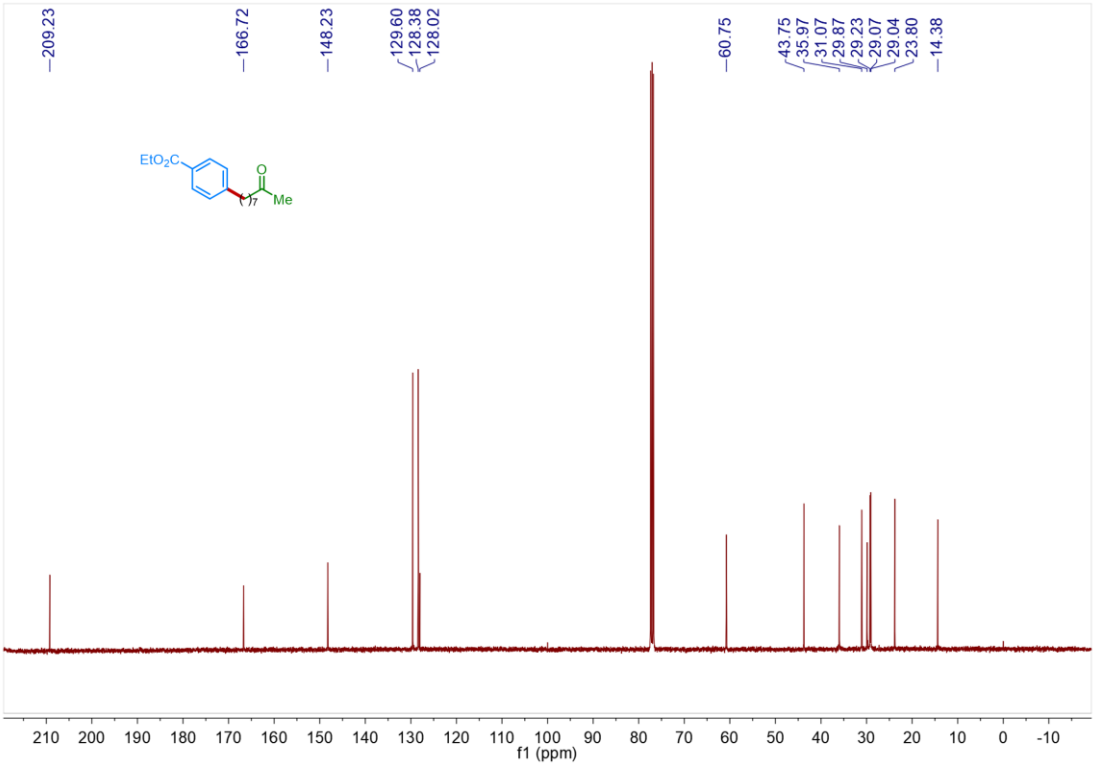
25 ^{13}C-NMR



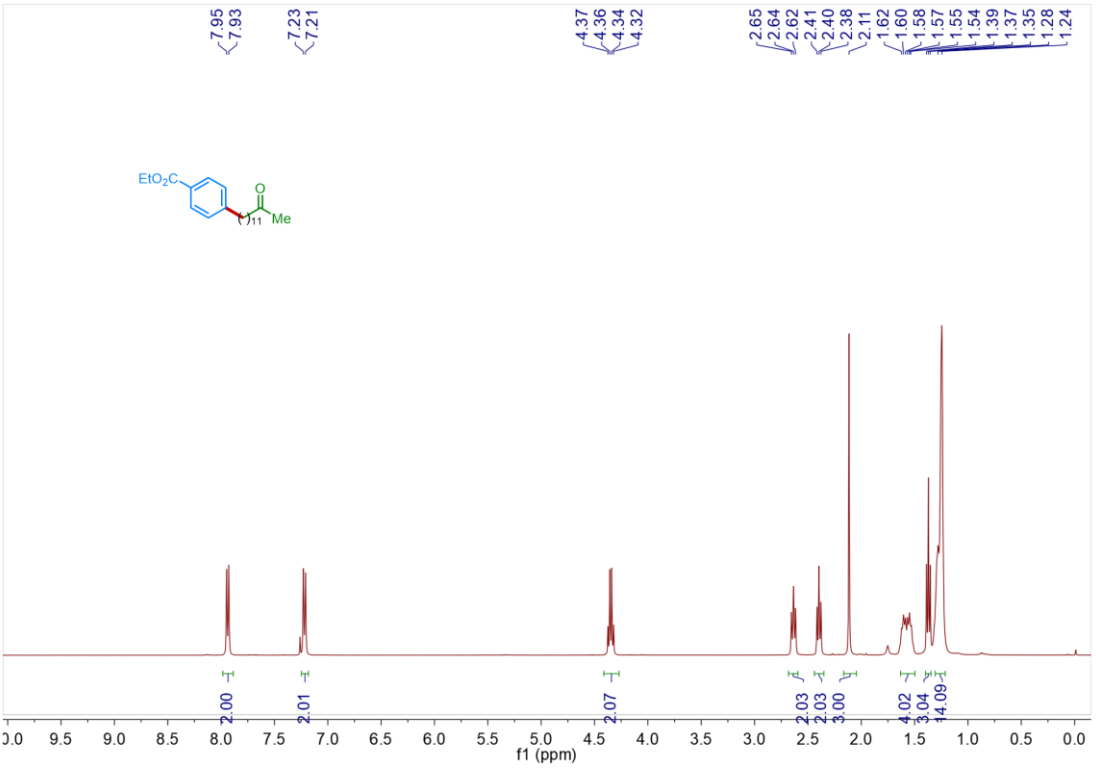
26 ^{1}H-NMR



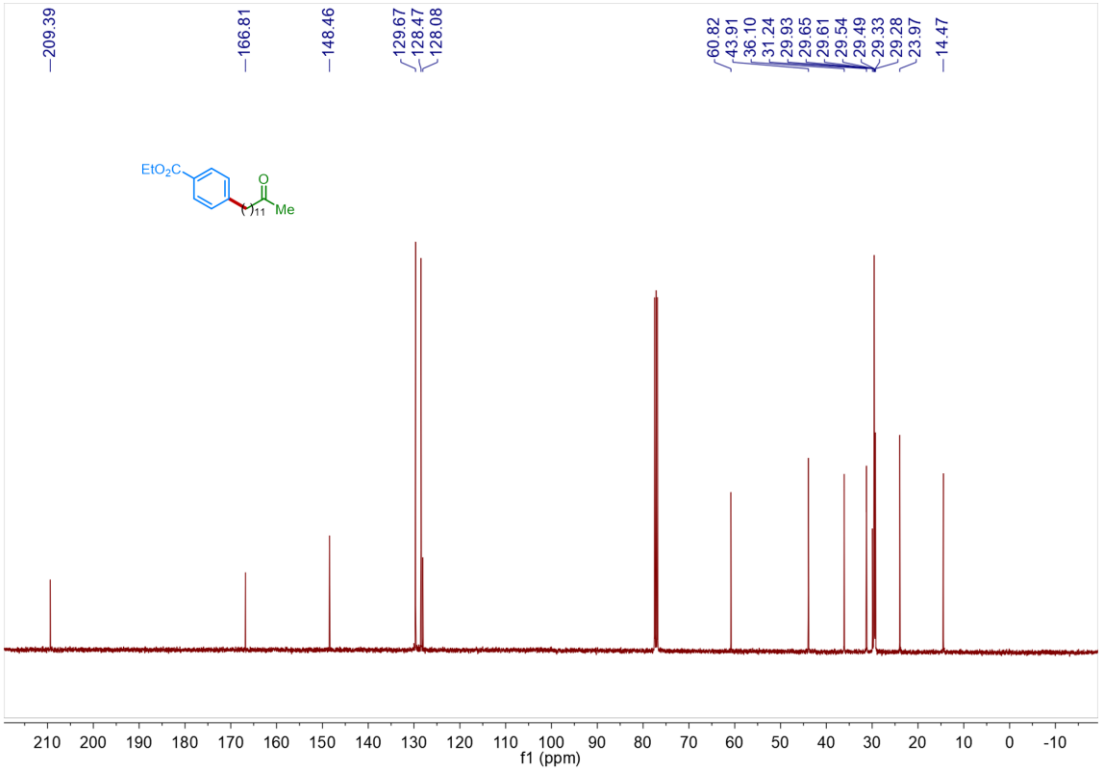
26 ^{13}C-NMR



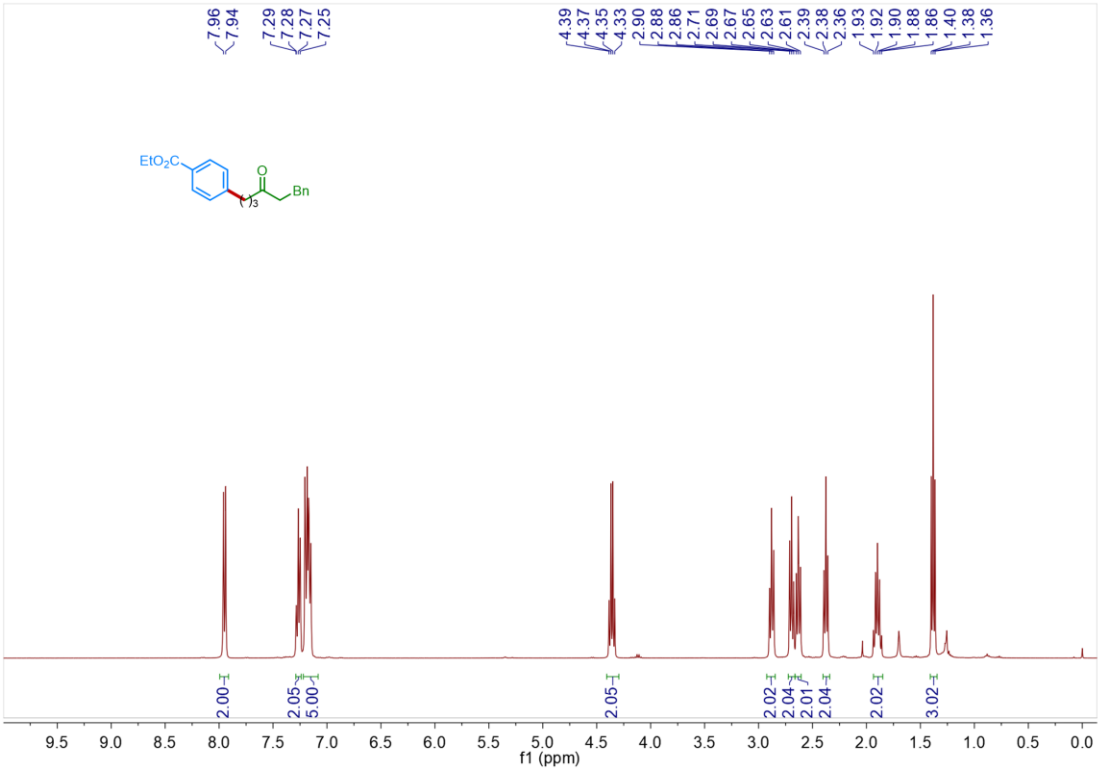
27 ^{1}H-NMR



27 ^{13}C-NMR



28 ^{1}H-NMR



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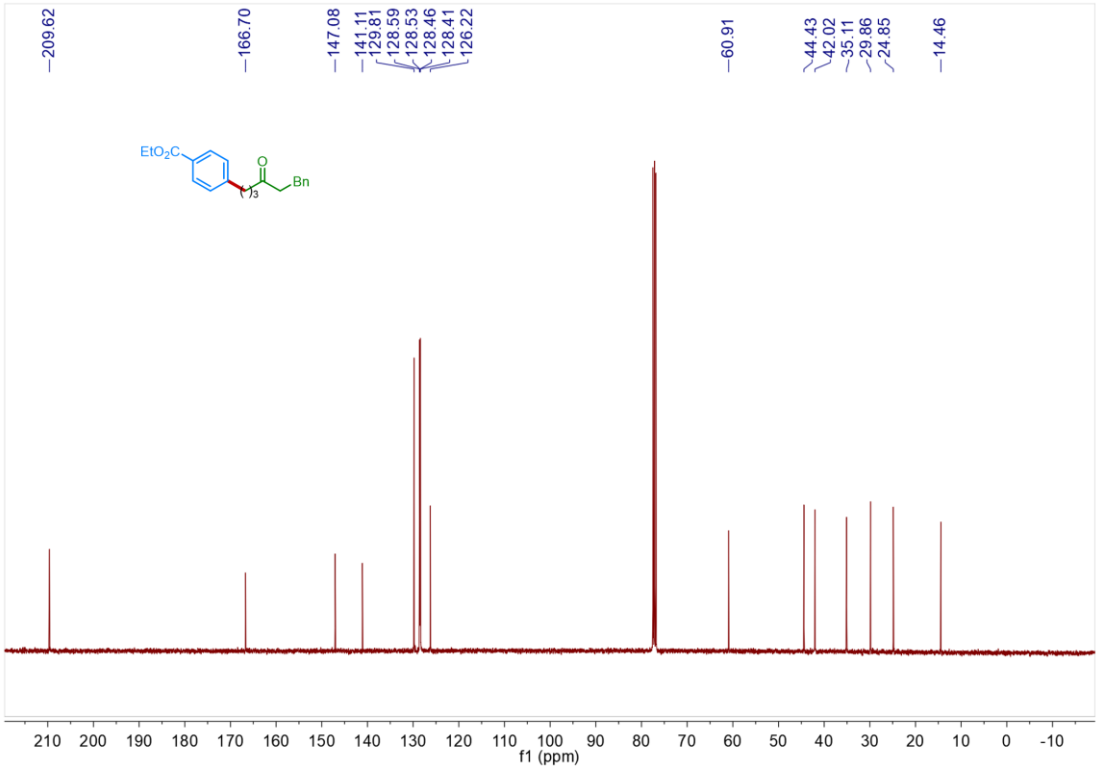
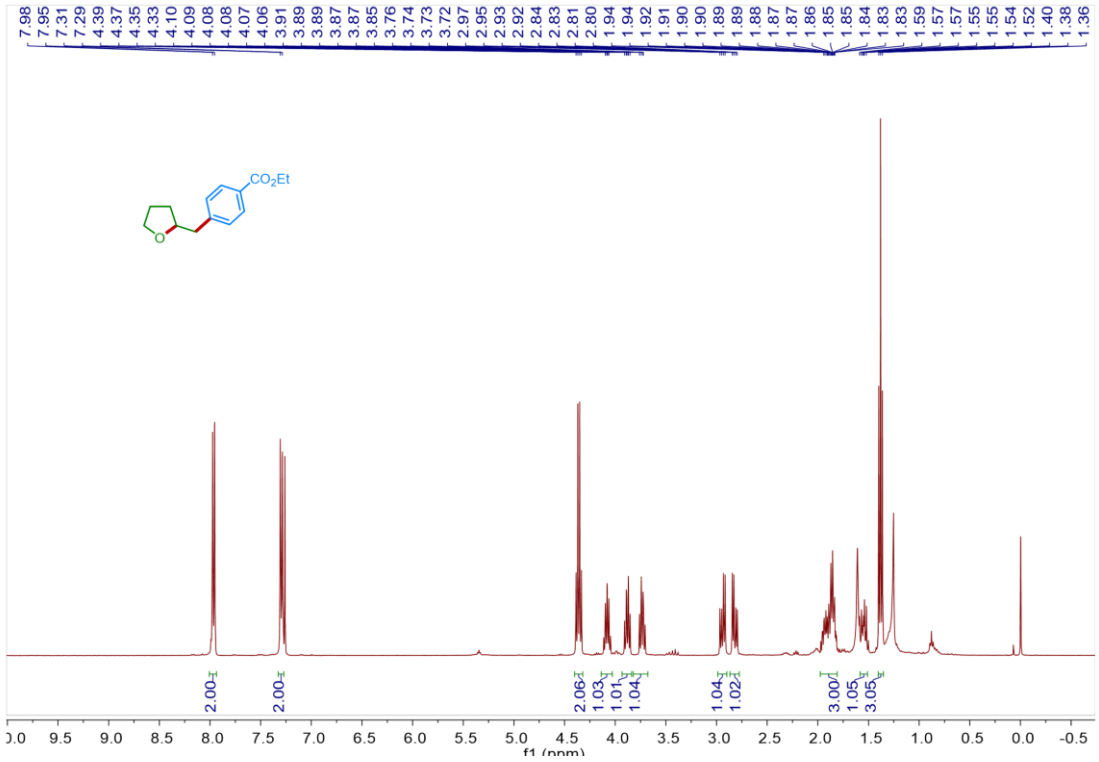


29 ^{1}H-NMR



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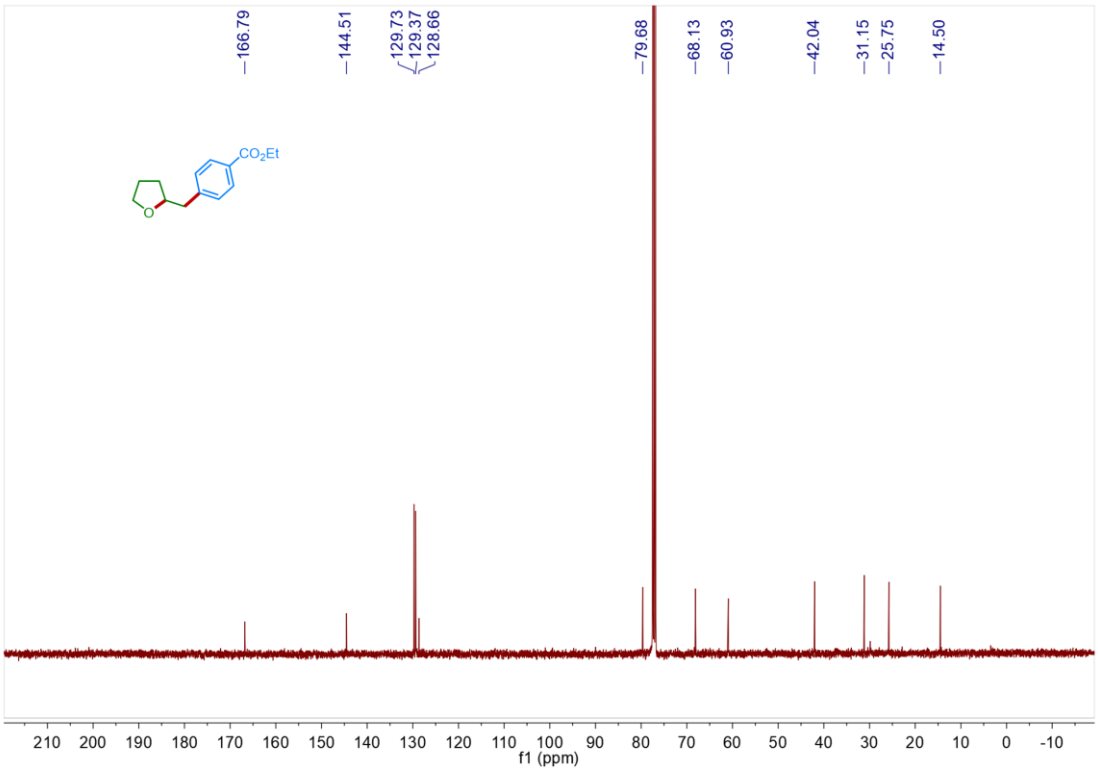

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