Supporting Information

Palladium(II)-Catalyzed Selective Arylation of Tertiary C–H Bonds of Cyclobutylmethyl Ketones Using Transient Directing Groups

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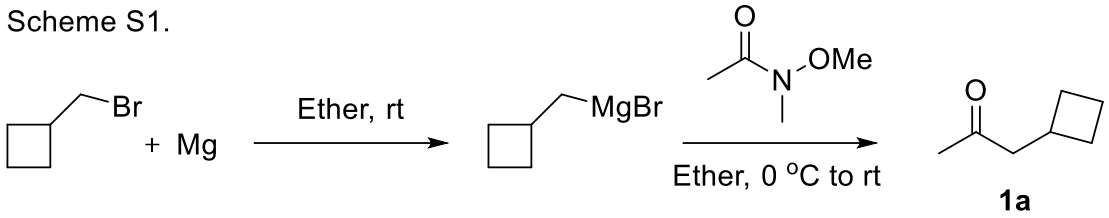
Table of Contents

General Information

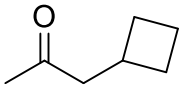
Ketone substrates were obtained from the commercial sources or synthesized following literature procedures. Aryl iodides were obtained from the commercial sources. Solvents were obtained from Sigma-Aldrich, Oakwood and Acros and used directly without further purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Bromocresol Green Stain. ^{1}H NMR was recorded on Bruker DRX-600 instrument (500 MHz, 600 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the literature values of tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q= quartet, p = pentet, m = multiplet, br = broad. coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (125MHz), and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to either the center line of a triplet at 77.16 ppm of chloroform-*d*. High resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

General procedure for the preparation of ketone substrates

Scheme S1.



To a solution of *N*-methoxy-*N*-methylacetamide (10 mmol) in dry ether (50mL) was slowly added the newly prepared (cyclobutylmethyl) magnesium bromide (12 mmol) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 6 h. Upon completion, saturated ammonium chloride (50 mL) solution was slowly added to quench this reaction. The reaction mixture was extracted with diethyl ether (50 mL×2), and the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4, filtered. The solvent was removed under reduced pressure, and the residue was purified by chromatography [Hexane/EtOAc 50:1 to 20:1] to afford **1a** (0.75 g, 67% yield) as a colorless oil.



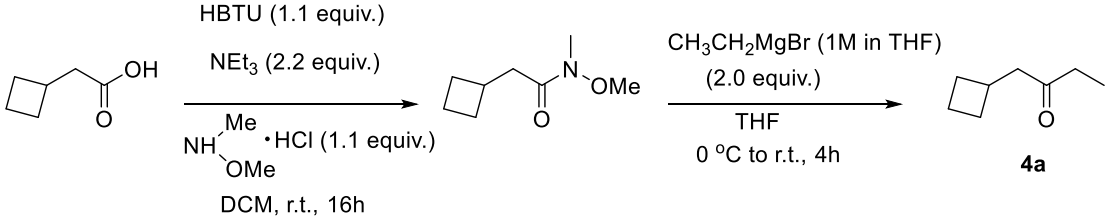
1a

1-cyclobutylpropan-2-one (**1a**)

R_f = 0.63 (petroleum ether/ethyl acetate, 5:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.70–2.62 (m, 1H), 2.52 (d, *J* = 7.4 Hz, 2H), 2.16-2.10 (m, 2H), 2.08 (s, 3H), 1.93-1.79 (m, 2H), 1.68–1.61 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.3, 50.8, 31.1, 29.9, 28.0, 18.5.

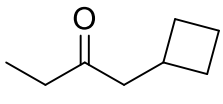
Scheme S2.



The procedure was followed by the literature.[1]

To a solution of 2-cyclobutylacetic acid (5.00 g, 43.8 mmol, 1.0 equiv) and triethylamine (13.4 mL, 96.5 mmol, 2.2 equiv) in dry dichloromethane (150 mL) at 0 ºC was added *N*,*N*,*N′*,*N′*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (18.3 g, 48.2 mmol, 1.1 equiv) and *N*,*O*-dimethylhydroxylamine hydrochloride (4.71 g, 48.2 mmol, 1.1 equiv). The reaction mixture was warmed to room temperature and stirred for 16 hours. Saturated ammonium chloride was added to the mixture and layers separated. The aqueous layer was extracted with dichloromethane (100 mL x 2). The combined organic extracts were washed with brine, dried and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether: ethyl acetate 20:1-5:1, affording 2-cyclobutyl-*N*-methoxy-*N*-methylacetamide as a colorless oil (5.70 g, 36.3 mmol, 83%).

To a solution of 2-cyclobutyl-*N*-methoxy-*N*-methylacetamide (1.57 g, 10 mmol, 1.0 equiv) in dry tetrahydrofuran (40 mL) at 0 ºC was added propyl magnesium bromide (1 M in diethyl ether; 20.0 mL, 20 mmol, 2.0 equiv) dropwise. The reaction mixture was slowly warmed to room temperature and stirred for 4 hours and then slowly quenched with saturated ammonium chloride. The layers were separated and the aqueous layer was extracted with ethyl acetate (50 mL x 2). The combined organic extracts were washed with brine, dried and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel, eluting with petroleum ether: ethyl acetate 20:1-10:1 to afford the title compound **4a** as a colorless oil (0.66 g, 5.2 mmol, 52%).



4a

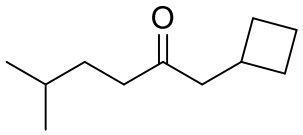
1-cyclobutylbutan-2-one (**4a**)

R_f = 0.60 (petroleum ether/ethyl acetate, 7:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72–2.63 (m, 1H), 2.51 (d, *J* = 7.4 Hz, 2H), 2.37 (q, *J* = 7.3 Hz, 2H), 2.14-2.09 (m, 2H), 1.93-1.80 (m, 2H), 1.67–1.60 (m, 2H), 1.02 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.4, 49.5, 36.1, 31.8, 28.6, 18.7, 7.5.

IR (KBr) v 2975, 2869, 1713, 1459, 1371, 1110, 1024.

HRMS (APCI-FTMS) Calcd for $C_8H_{15}O$ $[M+H]^+$: 127.1118; found: 127.1117.



4d

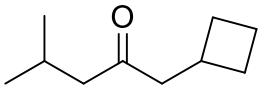
1-cyclobutyl-5-methylhexan-2-one (**4d**)

R_f = 0.58 (petroleum ether/ethyl acetate, 10:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.80 – 2.60 (m, 1H), 2.49 (d, *J* = 7.4 Hz, 2H), 2.39 – 2.28 (m, 2H), 2.13-2.07 (m, 2H), 1.94 – 1.74 (m, 2H), 1.66-1.58 (m, 2H), 1.52-1.48 (m, 1H), 1.42-1.39 (m, 2H), 0.86 (d, *J* = 6.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1, 48.9, 39.9, 31.2, 30.8, 27.9, 26.4, 21.0, 17.7.

IR (KBr) v 2958, 2869, 1714, 1468, 1368, 1260, 1017, 804.

HRMS (APCI-FTMS) Calcd for $C_{11}H_{21}O$ $[M+H]^+$: 169.1587; found: 169.1584.



4e

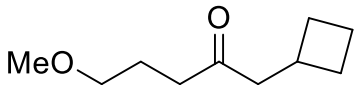
1-cyclobutyl-4-methylpentan-2-one (**4e**)

R_f = 0.56 (petroleum ether/ethyl acetate, 10:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.74 – 2.66 (m, 1H), 2.51 (d, *J* = 7.2 Hz, 2H), 2.26 – 2.24 (m, 2H), 2.16-2.11 (m, 3H), 1.96 – 1.83 (m, 2H), 1.69-1.61 (m, 2H), 0.92 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.1, 52.1, 50.7, 31.4, 28.9, 24.2, 22.7, 19.1.

IR (KBr) v 2958, 2871, 1712, 1468, 1367, 1169, 1047.

HRMS (APCI-FTMS) Calcd for $C_{10}H_{19}O$ $[M+H]^+$: 155.1429; found: 155.1430.



4f

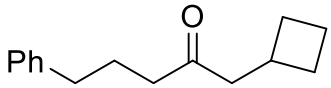
1-cyclobutyl-5-methoxypentan-2-one (**4f**)

R_f = 0.56 (petroleum ether/ethyl acetate, 6:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.36 (t, *J* = 6.0 Hz, 2H), 3.31 (s, 3H), 2.68 (dp, *J* = 15.8, 7.8 Hz, 1H), 2.52 (d, *J* = 7.4 Hz, 2H), 2.45 (t, *J* = 7.2 Hz, 2H), 2.21 – 2.04 (m, 2H), 1.96 – 1.77 (m, 4H), 1.74 – 1.52 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.4, 71.6, 58.3, 49.9, 39.4, 31.2, 28.7, 23.5, 18.5.

IR (KBr) v 2932, 2868, 1712, 1442, 1411, 1371, 1120.

HRMS (APCI-FTMS) Calcd for C11H19O2 [M+H]+: 171.1380; found: 171.1376.



4g

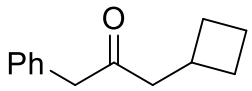
1-cyclobutyl-5-phenylpentan-2-one (**4g**)

R_f = 0.57 (petroleum ether/ethyl acetate, 7:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22-7.18 (m, 2H), 7.12-7.08 (m, 3H), 2.62-2.51 (m, 3H), 2.41 (d, *J* = 7.4 Hz, 2H), 2.29 (t, *J* = 7.3 Hz, 2H), 2.03 (m, 2H), 1.84 – 1.76 (m, 4H), 1.61 – 1.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9, 141.4, 128.5, 128.0, 125.1, 50.1, 41.4, 35.0, 31.6 28.8, 24.8, 19.0.

IR (KBr) v 2935, 2859, 1710, 1496, 1453, 1370, 748, 699.

HRMS (APCI-FTMS) Calcd for $C_{15}H_{21}O$ $[M+H]^+$: 217.1587; found: 217.1584.



4h

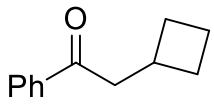
1-cyclobutyl-3-phenylpropan-2-one (**4h**)

R_f = 0.52 (petroleum ether/ethyl acetate, 7:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 7.2 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 2H), 3.64 (s, 2H), 2.71-2.66 (m, 1H), 2.56 (d, *J* = 7.3 Hz, 2H), 2.09 (d, *J* = 8.3 Hz, 2H), 1.95 – 1.83 (m, 1H), 1.83 – 1.74 (m, 1H), 1.63 – 1.53 (m, 2H).^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 134.6, 129.6, 128.8, 127.0, 50.3, 48.8, 31.4, 28.6, 18.5.

IR (KBr) v 2972, 2865, 1714, 1495, 1443, 1366, 746, 699.

HRMS (APCI-FTMS) Calcd for $C_{13}H_{17}O$ $[M+H]^+$: 189.1273; found: 189.1274.



4i

2-cyclobutyl-1-phenylethan-1-one (**4i**)

R_f = 0.50 (petroleum ether/ethyl acetate, 7:1)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 3.09 (d, *J* = 7.2 Hz, 2H), 2.85 (dt, *J* = 15.3, 7.7 Hz, 1H), 2.21 – 2.16 (m, 2H), 1.97 – 1.88 (m, 2H), 1.77 – 1.70 (m, 2H).

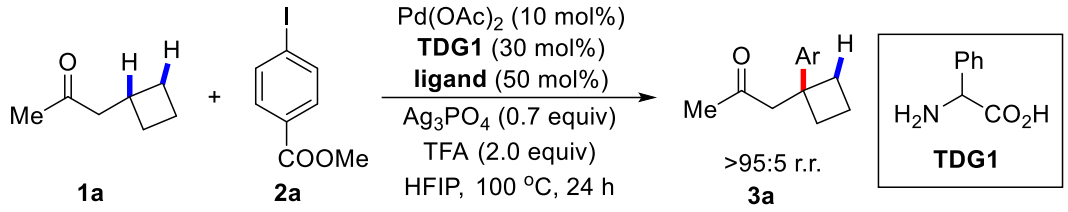
^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 136.5, 132.5, 128.7, 128.2, 46.0, 32.1, 28.9, 18.7.

IR (KBr) v 2972, 2859, 1683, 1598, 1448, 1368, 749, 690.

HRMS (APCI-FTMS) Calcd for $C_{12}H_{15}O$ $[M+H]^+$: 175.1118; found: 175.1117.

Optimization of the Reaction Conditions

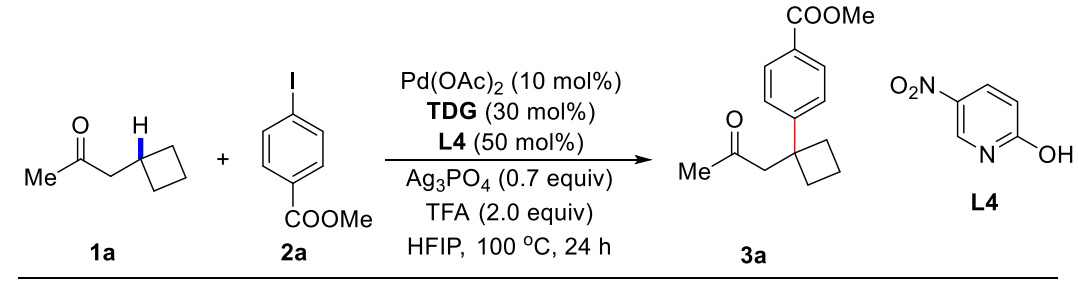
Table S1. Ligand Evaluation[a]

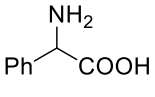
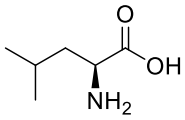
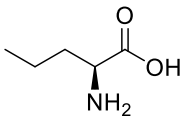
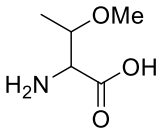
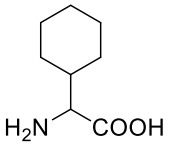
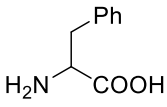
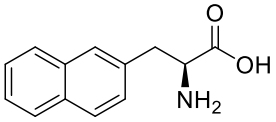
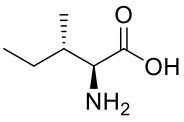
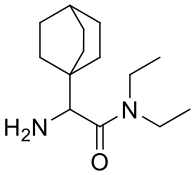
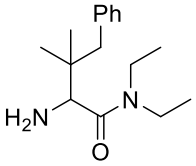
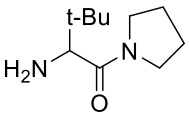
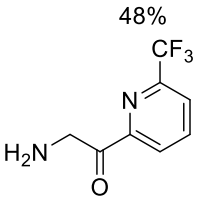
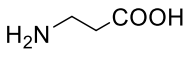
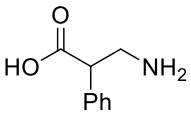
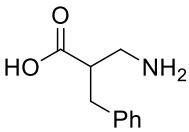
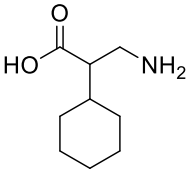


No ligand	**L1**, 29%	**L2**, 45%	**L3**, 33%
5%			
L4, 58%	**L5**, 41%	**L6**, 41%	**L7**, 29%
L8, 31%	**L9**, 41%	**L10**, 40%	**L11**, 55%

[a] Conditions: **1a** (0.2 mmol, 2.0 equiv), methyl 4-iodobenzoate **2a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), **TDG1** (30 mol %), **ligand** (50 mol %), Ag_3PO_4 (70 mol %), HFIP (0.6 mL), 100 °C, under air, 24-48h.

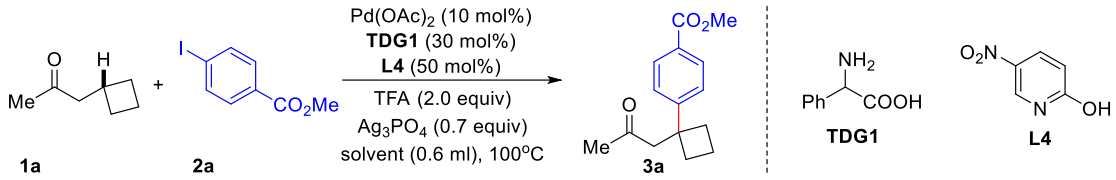
Table S2. TDG Evaluation[a]



			
TDG1	**TDG2**	**TDG3**	**TDG4**
58%	48%	37%	19%
			
TDG5	**TDG6**	**TDG7**	**TDG8**
37%	42%	51%	48%
			
TDG 9	**TDG 10**	**TDG 11**	**TDG 12**
17%	12%	13%	27%
			
TDG13	**TDG14**	**TDG 15**	**TDG 16**
< 5%	< 5%	< 5%	< 5%

[a] Conditions: **1a** (0.2 mmol, 2.0 equiv), methyl 4-iodobenzoate **2a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), **TDG** (30 mol %), **L4** (50 mol %), Ag_3PO_4 (70 mol %), HFIP (0.6 mL), 100 °C, under air, 24-48h.

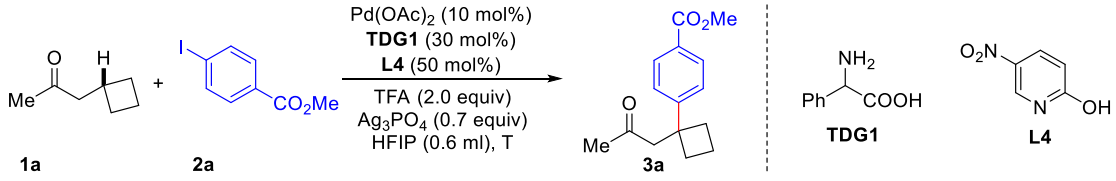
Table S3. Solvents Evaluation[a]



Entry	The ratio of **1a**:**2a**	Solvents (0.6 ml)	Yield (%)
1	**1a**:**2a**=2:1	HFIP:HOAc 9:1	49
2	**1a**:**2a**=2:1	HFIP:HOAc 1:1	32
3	**1a**:**2a**=2:1	HOAc	22
4	**1a**:**2a**=2:1	HFIP:HOAc 19:1 (10 eq H_2O)	25
5	**1a**:**2a**=2:1	HFIP	58

[a] Conditions: **1a** (0.2 mmol, 2.0 equiv), methyl 4-iodobenzoate **2a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), **TDG1** (30 mol %), **L4** (50 mol %), Ag_3PO_4 (70 mol %), Solvent (0.6 mL), 100 °C, under air, 24-48h.

Table S4. Reaction Temperature and the ratio of 1a:2a Evaluation[a]

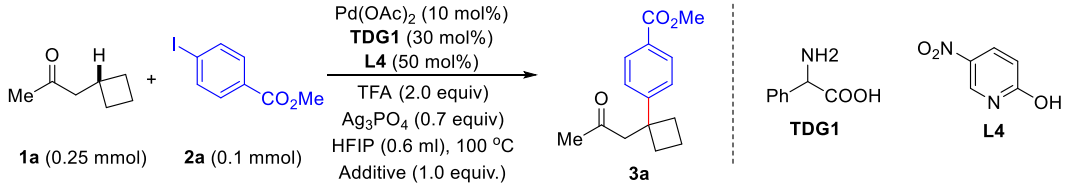


Entry	The ratio of **1a**:**2a**	TDG	T (°C)	Yield (%)
1	**1a**:**2a**=2:1	**TDG1**	90	44
2	**1a**:**2a**=2:1	**TDG1**	100	58
3	**1a**:**2a**=2:1	**TDG1**	110	46

4	**1a**:**2a**=1.5:1	**TDG1**	100	49
5	**1a**:**2a**=2.5:1	**TDG1**	100	71
6	**1a**:**2a**=3:1	**TDG1**	100	70

[a] Conditions: **1a** (X mmol), methyl 4-iodobenzoate **2a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), **TDG1** (30 mol %), **L4** (50 mol %), Ag_3PO_4 (70 mol %), HFIP (0.6 mL), T (°C), under air, 24-48h.

Table S5. Additives Evaluation[a]

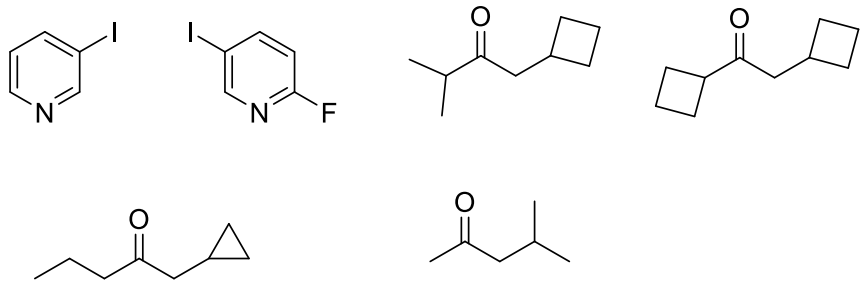


1a (0.25 mmol) **2a** (0.1 mmol) **3a** **TDG1** **L4**

LiOAc	KOAc	NaOAc	CsOAc
46%	62%	55%	72%
Sodium benzoate	Na_2CO_3	Na_3PO_4	CH_3ONa
64%	50%	49%	53%

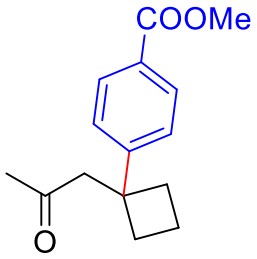
[a] Conditions: **1a** (0.25 mmol, 2.5 equiv), methyl 4-iodobenzoate **2a** (0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol %), **TDG** (30 mol %), **L4** (50 mol %), Ag_3PO_4 (70 mol %), HFIP (0.6 mL), 100 °C, under air, 24-48h.

Table S6. Selected Unsuccessful Substrates



General Procedure for the Pd(II)-Catalyzed Tertiary C-H Arylation of Cyclobutylmethyl ketones

To an oven-dried microwave tube (5 mL) equipped with a magnetic stir bar was added $Pd(OAc)_2$ (0.01 mol, 10 mol%), transient directing groups (**TDG1**, 0.03 mmol, 30 mol %), ligand (**L4**, 0.05 mmol, 50 mol%), ArI (0.1 mmol), Ag_3PO_4 (0.07 mmol, 0.7 equiv.), CsOAc (0.1 mmol, 1.0 equiv.) and solvent (HFIP, 0.6 mL and 0.2 mmol TFA), followed by the ketone substrate (0.25 mmol, 2.5 equiv.). The tube was sealed and stirred at room temperature for 10 min before heating 100 ^oC for 24-48 h under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature and the dark brown suspension was passed through a pad of celite and washed with ethyl acetate (1.0 ml x 3). The resulting solution was concentrated and purified by preparative thin-layer chromatography to afford the desired product.



3a

methyl 4-(1-(2-oxopropyl)cyclobutyl)benzoate (**3a**)

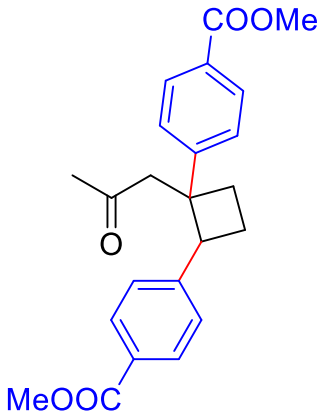
Following the general procedure, **3a** was obtained as a colorless oil, 72% yield.

R_f = 0.50 (petroleum ether/ethyl acetate, 5:1).

^1H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 3.92 (s, 3H), 2.99 (s, 2H), 2.51-2.43 (m, 2H), 2.39-2.34 (m, 2H), 2.18-2.09 (m, 1H), 1.94-1.86 (m, 1H),1.77 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7, 167.4, 154.4, 129.3, 127.7, 126.3, 54.3, 51.7, 45.2, 33.0, 31.5, 15.9.

IR (KBr) v 1716, 1609, 1434, 1277, 1163, 1106, 774, 708.

HRMS (ESI-TOF) Calcd for $C_{15}H_{19}O_3^+[M+H]^+$: 247.1336; found: 247.1334.



3a'

dimethyl 4,4'-(1-(2-oxopropyl)cyclobutane-1,2-diyl)dibenzoate (**3a**')

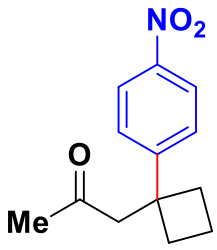
Following the general procedure, **3a**' was obtained as a colorless oil, 3% yield.

R_f = 0.35 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.71 (t, *J* = 12.3 Hz, 1H), 2.85 (d, *J* = 15.5 Hz, 1H), 2.74-2.68 (m, 1H), 2.66-2.41 (m, 3H), 2.22-2.18 (m, 1H), 1.64 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.3, 167.2, 152.9, 144.1, 129.9, 129.8, 128.7, 125.9, 52.3, 52.2, 51.9, 50.1, 48.8, 31.7, 27.3, 20.2.

IR (KBr) v 1717, 1611, 1434, 1275, 1163, 1106, 774, 708.

HRMS (ESI-TOF) Calcd for $C_{23}H_{25}O_5^+$[M+H]$^+$: 381.1702; found: 381.1709.



3b

1-(1-(4-nitrophenyl)cyclobutyl)propan-2-one (**3b**)

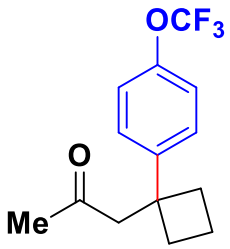
Following the general procedure, **3b** was obtained as a colorless oil, 50% yield.

R_f = 0.42 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.9 Hz, 2H), 7.38 (d, *J* = 8.9 Hz, 2H), 3.04 (s, 2H), 2.48-2.43 (m, 2H), 2.37-2.33 (m, 2H), 2.14-2.07 (m, 1H), 1.92-1.89 (m, 1H), 1.86 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.5, 156.6, 145.9, 127.1, 123.5, 52.9, 44.5, 33.5, 31.5, 15.8.

IR (KBr) v 1715, 1514, 1341, 1163, 1109, 853, 701.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}NO_3^+$[M+H]$^+$: 234.1130; found: 234.1133.



3c

1-(1-(4-(trifluoromethoxy)phenyl)cyclobutyl)propan-2-one (**3c**)

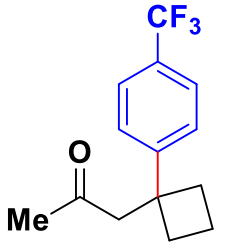
Following the general procedure, **3c** was obtained as a colorless oil, 55% yield.

R_f = 0.36 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 2.94 (s, 2H), 2.44-2.39 (m, 2H), 2.35-2.30 (m, 2H), 2.12-2.04 (m, 1H), 1.89-1.84 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7, 147.4, 147.3, 127.5, 120.7, 120.6 (q, *J* = 255.0 Hz), 54.7, 44.8, 33.4, 31.7, 16.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -60.5 (s, 3F).

IR (KBr) v 1715, 1509, 1358, 1258, 1160, 848, 676.

HRMS (ESI-TOF) Calcd for $C_{14}H_{16}F_3O_2^+$[M+H]$^+$: 273.1102; found: 273.1106.



3d

1-(1-(4-(trifluoromethyl)phenyl)cyclobutyl)propan-2-one (**3d**)

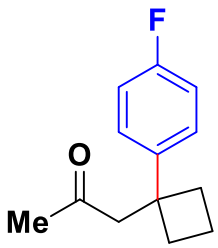
Following the general procedure, **3d** was obtained as a colorless oil, 49% yield.

R_f = 0.51 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 2.98 (s, 2H), 2.47-2.41 (m, 2H), 2.36-2.32 (m, 2H), 2.12-2.06 (m, 1H), 1.90-1.86 (m, 1H), 1.80 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.4, 153.2, 127.1 (q, J_{C-F} = 252.2 Hz), 126.5, 125.2 (q, J_{C-F} = 4.5 Hz), 123.5, 54.6, 45.1, 33.3, 31.6, 16.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.2 (s, 3F).

IR (KBr) v 1720, 1617, 1411, 1358, 1328, 1163, 841.

HRMS (ESI-TOF) Calcd for $C_{14}H_{16}F_3O^+$[M+H]$^+$: 257.1153; found: 257.1148.



3e

1-(1-(4-fluorophenyl)cyclobutyl)propan-2-one (**3e**)

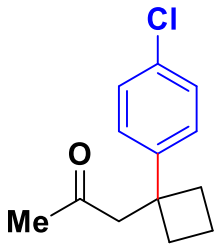
Following the general procedure, **3e** was obtained as a colorless oil, 55% yield.

R_f = 0.56 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 2.91 (s, 2H), 2.41-2.37 (m, 2H), 2.33-2.29 (m, 2H), 2.11-2.05 (m, 1H), 1.88-1.82 (m, 1H), 1.74 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.4, 161.3 (d, J_{C-F} = 166.5 Hz), 144.6 (d, J_{C-F} = 3.0 Hz), 127.5 (d, J_{C-F} = 7.5 Hz), 114.9 (d, J_{C-F} = 21.0 Hz), 54.8, 44.5, 33.5, 31.9, 16.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.7 (s, F).

IR (KBr) v 1715, 1510, 1357, 1222, 1159, 835.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}FO^+$[M+H]$^+$: 207.1185; found: 207.1188.



3f

1-(1-(4-chlorophenyl)cyclobutyl)propan-2-one (**3f**)

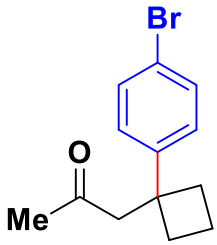
Following the general procedure, **3f** was obtained as a colorless oil, 72% yield.

R_f = 0.50 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 2.92 (s, 2H), 2.42-2.37 (m, 2H), 2.32-2.29 (m, 2H), 2.11-2.04 (m, 1H), 1.88-1.83 (m, 1H), 1.77 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.4, 147.0, 131.6, 128.3, 127.1, 54.4, 44.5, 33.5, 31.7, 15.9.

IR (KBr) v 1715, 1492, 1356, 1161, 1091, 828, 625.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}ClO^+$[M+H]$^+$: 223.0890; found: 223.0893.



3g

1-(1-(4-bromophenyl)cyclobutyl)propan-2-one (**3g**)

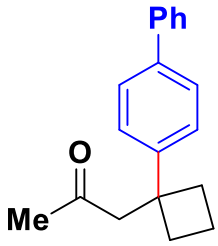
Following the general procedure, **3g** was obtained as a colorless oil, 53% yield.

R_f = 0.41 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 2.92 (s, 2H), 2.43-2.36 (m, 2H), 2.33-2.28 (m, 2H), 2.11-2.00 (m, 1H), 1.88-1.82 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.0, 147.6, 131.2, 127.4, 119.8, 54.8, 44.1, 33.5, 31.6, 16.0.

IR (KBr) v 1718, 1632, 1516, 1490, 1355, 1075, 834.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}BrO^+[M+H]^+$: 267.0385; found: 267.0386.



3h

1-(1-([1,1'-biphenyl]-4-yl)cyclobutyl)propan-2-one (**3h**)

Following the general procedure, **3h** was obtained as a colorless oil, 81% yield.

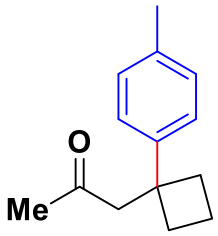
R_f = 0.40 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.57 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.29 (m, 2H), 3.00 (s, 2H), 2.53-2.48 (m, 2H), 2.41-2.37 (m, 2H), 2.15-2.10 (m, 1H), 1.96-1.89 (m, 1H), 1.79 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 208.4, 146.6, 141.1, 138.9, 128.8, 127.2, 127.1, 127.0, 126.4, 54.4, 45.2, 33.1, 31.6, 15.8.

IR (KBr) v 1709, 1485, 1355, 1161, 1007, 838, 766.

HRMS (ESI-TOF) Calcd for $C_{19}H_{21}O^+[M+H]^+$: 265.1592; found: 265.1585.



3i

1-(1-(p-tolyl)cyclobutyl)propan-2-one (**3i**)

Following the general procedure, **3i** was obtained as a colorless oil, 47% yield.

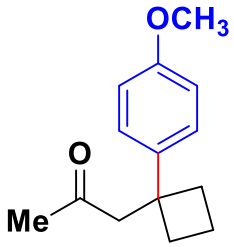
R_f = 0.51 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.12-7.07 (m, 4H), 2.90 (s, 2H), 2.43-2.39 (m, 2H), 2.32-2.29 (m, 2H), 2.30 (s, 3H), 2.09-2.04 (m, 1H), 1.87-1.82 (m, 1H), 1.71 (s,

3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.8, 146.3, 135.2, 129.0, 125.3, 55.5, 44.5, 33.5, 31.7, 21.4, 15.8.

IR (KBr) v 1710, 1513, 1461, 1355, 1236, 1089, 869, 617.

HRMS (ESI-TOF) Calcd for $C_{14}H_{19}O^+$[M+H]$^+$: 203.1436; found: 203.1433.



3j

1-(1-(4-methoxyphenyl)cyclobutyl)propan-2-one (**3j**)

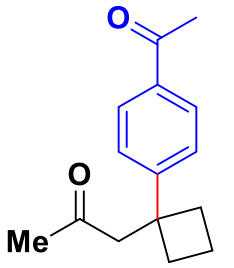
Following the general procedure, **3j** was obtained as a colorless oil, 50% yield.

R_f = 0.43 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H), 2.89 (s, 2H), 2.42-2.37 (m, 2H), 2.32-2.28 (m, 2H), 2.10-2.04 (m, 1H), 1.87-1.82 (m, 1H), 1.70 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.7, 157.7, 140.9, 127.0, 113.7, 55.4, 55.2, 44.9, 33.5, 31.9, 16.1.

IR (KBr) v 1706, 1511, 1462, 1355, 1246, 1177, 830, 662.

HRMS (ESI-TOF) Calcd for $C_{14}H_{19}O_2^+$[M+H]$^+$: 219.1385; found: 219.1388.



3k

1-(1-(4-acetylphenyl)cyclobutyl)propan-2-one (**3k**)

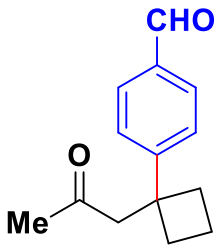
Following the general procedure, **3k** was obtained as a colorless oil, 45% yield.

R_f = 0.36 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 2.99 (s, 2H), 2.58 (s, 3H), 2.47-2.42 (m, 2H), 2.36-2.32 (m, 2H), 2.14-2.06 (m, 1H), 1.89-1.86 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.3, 197.4, 154.0, 134.5, 128.3, 126.5, 54.4, 45.6, 33.1, 31.3, 26.5, 16.2.

IR (KBr) v 1715, 1680, 1604, 1404, 1357, 1269, 1163, 838.

HRMS (ESI-TOF) Calcd for $C_{15}H_{19}O_2^+$[M+H]$^+$: 231.1385; found: 231.1384.



3l

4-(1-(2-oxopropyl)cyclobutyl)benzaldehyde (**3l**)

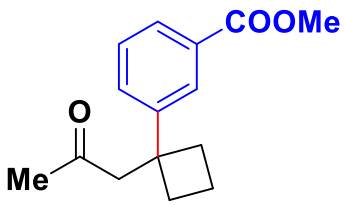
Following the general procedure, **3l** was obtained as a colorless oil, 31% yield.

R_f = 0.45 (petroleum ether/ethyl acetate, 3:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.82 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 3.01 (s, 2H), 2.49-2.44 (m, 2H), 2.38-2.34 (m, 2H), 2.16-2.09 (m, 1H), 1.91-1.84 (m, 1H), 1.80 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.3, 191.8, 156.6, 134.2, 129.4, 126.9, 54.1, 44.9, 33.5, 31.3, 16.2.

IR (KBr) v 1703, 1697, 1606, 1404, 1357, 1271, 1162.

HRMS (ESI-TOF) Calcd for $C_{14}H_{17}O_2^+$[M+H]$^+$: 217.1229; found: 217.1231.



3m

methyl 3-(1-(2-oxopropyl)cyclobutyl)benzoate (**3m**)

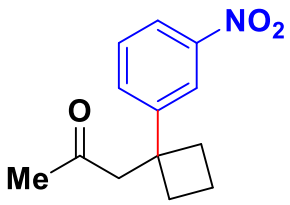
Following the general procedure, **3m** was obtained as a colorless oil, 57% yield.

R_f = 0.46 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.84 (m, 2H), 7.43 (ddd, *J* = 7.7, 1.8, 1.3 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 3.91 (s, 3H), 2.97 (s, 2H), 2.47-2.42 (m, 2H), 2.37-2.32 (m, 2H), 2.14-2.05 (m, 1H), 1.90-1.84 (m, 1H), 1.76 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.3, 167.2, 149.2, 148.1, 130.5, 130.1, 128.3, 126.8, 54.8, 51.9, 45.2, 33.1, 31.3, 15.8.

IR (KBr) v 1719, 1603, 1438, 1357, 1266, 1108, 757, 699.

HRMS (ESI-TOF) Calcd for $C_{15}H_{19}O_3^+$[M+H]$^+$: 247.1334; found: 247.1333.



3n

1-(1-(3-nitrophenyl)cyclobutyl)propan-2-one (**3n**)

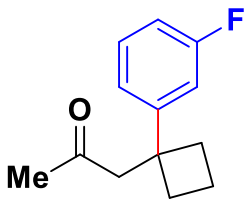
Following the general procedure, **3n** was obtained as a colorless oil, 63% yield.

R_f = 0.40 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (t, *J* = 1.9 Hz, 1H), 8.05 – 7.99 (m, 1H), 7.65 – 7.56 (m, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 3.06 (s, 2H), 2.49-2.43 (m, 2H), 2.38-2.33 (m, 2H), 2.14-2.05 (m, 1H), 1.90-1.88 (m, 1H), 1.90 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 206.5, 151.0, 148.3, 132.7, 128.5, 120.9, 120.5, 53.6, 44.5, 33.5, 31.6, 16.4.

IR (KBr) v 1714, 1524, 1346, 1308, 1098, 736, 690.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}NO_3^+$[M+H]$^+$: 234.1130; found: 234.1134.



3o

1-(1-(3-fluorophenyl)cyclobutyl)propan-2-one (**3o**)

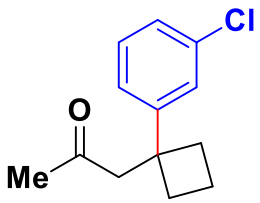
Following the general procedure, **3o** was obtained as a colorless oil, 55% yield.

R_f = 0.51 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.23 (m, 1H), 6.96 (d, *J* = 7.7 Hz, 1H), 6.91 – 6.84 (m, 2H), 2.93 (s, 2H), 2.43-2.38 (m, 2H), 2.34-2.29 (m, 2H), 2.10-2.04 (m, 1H), 1.88-1.86 (m, 1H), 1.76 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.0, 162.9 (d, J_{C-F} = 245.0 Hz), 151.7 (d, J_{C-F} = 6.3 Hz), 129.7 (d, J_{C-F} = 7.5 Hz), 121.7 (d, J_{C-F} = 2.5 Hz), 113.1 (d, J_{C-F} = 21.3 Hz), 112.8 (d, J_{C-F} = 21.3 Hz), 54.8, 45.2, 33.5, 31.3, 15.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.6 (s, F).

IR (KBr) v 1718, 1587, 1486, 1357, 1219, 1160, 783, 708.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}FO^+$[M+H]$^+$: 207.1185; found: 207.1181.



3p

1-(1-(3-chlorophenyl)cyclobutyl)propan-2-one (**3p**)

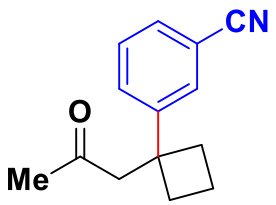
Following the general procedure, **3p** was obtained as a colorless oil, 38% yield.

R_f = 0.43 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 1.9 Hz, 1H), 7.16 – 7.13 (m, 1H), 7.10 – 7.07 (m, 1H), 2.93 (s, 2H), 2.43-2.38 (m, 2H), 2.33-2.29 (m, 2H), 2.10-2.06 (m, 1H), 1.88-1.83 (m, 1H), 1.78 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.2, 151.0, 134.2, 129.7, 126.5, 126.1, 124.3, 54.4, 44.9, 33.1, 30.9, 15.8.

IR (KBr) v 1714, 1595, 1568, 1474, 1415, 1356, 1078, 783, 699.

HRMS (ESI-TOF) Calcd for $C_{13}H_{16}ClO^+$[M+H]$^+$: 223.0890; found: 223.0888.



3q

3-(1-(2-oxopropyl)cyclobutyl)benzonitrile (**3q**)

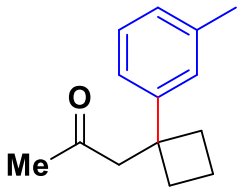
Following the general procedure, **3q** was obtained as a colorless oil, 26% yield.

R_f = 0.47 (petroleum ether/ethyl acetate, 3:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50-7.46 (m, 3H), 7.39 (t, *J* = 7.7 Hz, 1H), 3.00 (s, 2H), 2.44-2.39 (m, 2H), 2.33-2.30 (m, 2H), 2.11-2.07 (m, 1H), 1.90-1.87 (m, 1H), 1.86 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.0, 150.6, 131.0, 130.0, 129.6, 128.9, 119.2, 112.2, 54.3, 44.6, 33.3, 31.5, 16.2.

IR (KBr) v 1715, 1653, 1647, 1558, 1356, 1078.

HRMS (ESI-TOF) Calcd for $C_{14}H_{16}NO^+$[M+H]$^+$: 214.1232; found: 214.1232.



3r

1-(1-(m-tolyl)cyclobutyl)propan-2-one (**3r**)

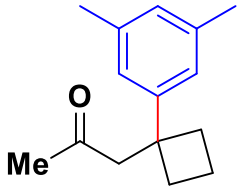
Following the general procedure, **3r** was obtained as a colorless oil, 51% yield.

R_f = 0.47 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.7 Hz, 1H), 6.98 – 6.96 (m, 3H), 2.90 (s, 2H), 2.46-2.41 (m, 2H), 2.32 (s, 3H), 2.34-2.30 (m, 2H), 2.13-2.04 (m, 1H), 1.89-1.82 (m, 1H), 1.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.7, 148.9, 137.7, 128.0, 126.7, 126.6, 122.9, 55.1, 45.4, 33.3, 31.9, 21.7, 16.1.

IR (KBr) v 1705, 1539, 1458, 1354, 1159, 783, 709.

HRMS (ESI-TOF) Calcd for $C_{14}H_{19}O^+$[M+H]$^+$: 203.1436; found: 203.1438.



3s

1-(1-(3,5-dimethylphenyl)cyclobutyl)propan-2-one (**3s**)

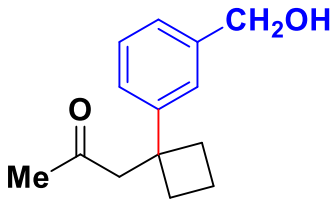
Following the general procedure, **3s** was obtained as a colorless oil, 49% yield.

R_f = 0.53 (petroleum ether/ethyl acetate, 8:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.81 (s, 1H), 6.78 (s, 2H), 2.88 (s, 2H), 2.43-2.40 (m, 2H), 2.30-2.24 (overlapped, 2H), 2.29 (s, 6H), 2.09-2.04 (m, 1H), 1.87-1.83 (m, 1H), 1.69 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.0, 148.8, 137.7, 127.5, 123.6, 55.1, 46.3, 33.2, 31.9, 21.6, 16.0.

IR (KBr) v 1705, 1697, 1633, 1470, 1159, 783, 709.

HRMS (ESI-TOF) Calcd for $C_{15}H_{21}O^+$[M+H]$^+$: 217.1592; found: 217.1598.



3t

1-(1-(3-(hydroxymethyl)phenyl)cyclobutyl)propan-2-one (**3t**)

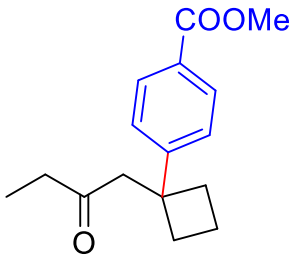
Following the general procedure, **3t** was obtained as a colorless oil, 47% yield.

R_f = 0.59 (petroleum ether/ethyl acetate, 6:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 7.19 - 7.14 (m, 2H), 4.85 (s, 2H), 2.93 (s, 2H), 2.45-2.41 (m, 2H), 2.36-2.32 (m, 2H), 2.13-2.07 (m, 1H), 1.90-1.84 (m, 1H), 1.75 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.6, 150.0, 133.8, 128.7, 126.8, 126.5, 126.4, 76.1, 54.8, 45.4, 33.3, 31.7, 16.1.

IR (KBr) v 1709, 1372, 1287, 1264, 1192, 1101, 795, 687.

HRMS (ESI-TOF) Calcd for $C_{14}H_{17}O^+$[M-OH]$^+$: 201.1279; found: 201.1281.



5a

methyl 4-(1-(2-oxobutyl)cyclobutyl)benzoate (**5a**)

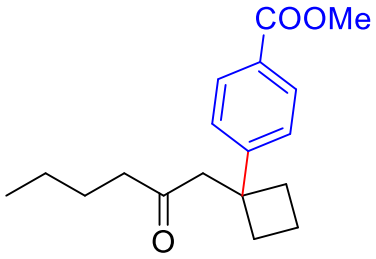
Following the general procedure, **5a** was obtained as a colorless oil, 58% yield.

R_f = 0.51 (petroleum ether/ethyl acetate, 7:1).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 3.90 (s, 3H), 2.93 (s, 2H), 2.43 (q, *J* = 9.5 Hz, 2H), 2.38-2.36 (m, 2H), 2.14 – 2.06 (m, 1H), 1.94 (q, *J* = 7.2 Hz, 2H), 1.88-1.83 (m, 1H), 0.78 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.4, 167.2, 154.6, 129.6, 127.7, 126.0, 53.3, 52.2, 45.6, 37.6, 33.3, 16.2, 7.3.

IR (KBr) v 1718, 1609, 1436, 1278, 1105, 774, 708.

HRMS (ESI-TOF) Calcd for $C_{16}H_{21}O_3^+$[M+H]$^+$: 261.1491; found: 261.1492.



5b

methyl 4-(1-(2-oxohexyl)cyclobutyl)benzoate (**5b**)

Following the general procedure, **5b** was obtained as a colorless oil, 66% yield.

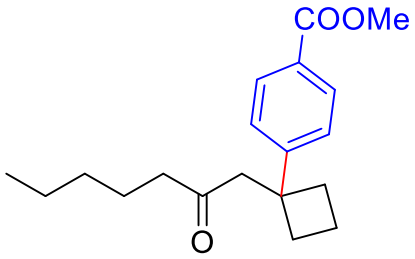
R_f = 0.48 (petroleum ether/ethyl acetate, 10:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 3.89 (s, 3H), 2.91 (s, 2H), 2.46-2.41 (m, 2H), 2.38-2.34 (m, 2H), 2.14-2.07 (m, 1H), 1.96 (t, *J* = 7.4 Hz, 2H), 1.86-1.82 (m, 1H), 1.32-1.26 (m, 2H), 1.11-1.04

(m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 167.2, 154.6, 129.2, 127.6, 126.1, 53.1, 52.4, 44.8, 43.6, 33.3, 24.9, 22.3, 15.9, 13.9.

IR (KBr) v 1718, 1611, 1436, 1278, 1105, 775, 708.

HRMS (ESI-TOF) Calcd for $C_{18}H_{25}O_3^+$[M+H]$^+$: 289.1804; found: 289.1798.



5c

methyl 4-(1-(2-oxoheptyl)cyclobutyl)benzoate (**5c**)

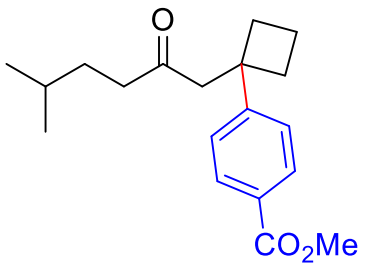
Following the general procedure, **5c** was obtained as a colorless oil, 61% yield.

R_f = 0.53 (petroleum ether/ethyl acetate, 10:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 3.92 (s, 3H), 2.95 (s, 2H), 2.49-2.43 (m, 2H), 2.41-2.36 (m, 2H), 2.16-2.11 (m, 1H), 1.96 (t, *J* = 7.4 Hz, 2H), 1.92-1.84 (m, 1H), 1.36-1.20 (m, 2H), 1.20-1.13 (m, 2H), 1.07-1.01 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 166.2, 154.8, 129.3, 127.4, 126.2, 54.0, 51.7, 45.3, 44.1, 33.5, 30.8, 23.6, 22.0, 16.0, 13.7.

IR (KBr) v 1718, 1609, 1434, 1276, 1105, 775, 709.

HRMS (ESI-TOF) Calcd for $C_{19}H_{27}O_3^+$[M+H]$^+$: 303.1960; found: 303.1965.



5d

methyl 4-(1-(5-methyl-2-oxohexyl)cyclobutyl)benzoate (**5d**)

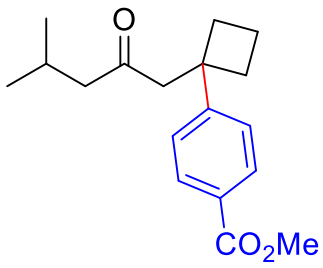
Following the general procedure, **5d** was obtained as a colorless oil, 63% yield.

R_f = 0.47 (petroleum ether/ethyl acetate, 10:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 3H), 2.94 (s, 2H), 2.44 (dd, *J* = 19.9, 9.9 Hz, 2H), 2.40 – 2.31 (m, 2H), 2.17 – 2.03 (m, 1H), 1.98 – 1.91 (m, 2H), 1.88-1.83 (m, 1H), 1.32-1.26 (m, 1H), 1.20 (dd, *J* = 14.9, 7.2 Hz, 2H), 0.72 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 166.9, 154.6, 128.9, 127.8, 125.6, 53.6, 52.1, 45.2, 42.3, 33.4, 32.1, 27.5, 22.3, 15.9.

IR (KBr) v 1721, 1609, 1435, 1278, 1113, 775, 708.

HRMS (APCI-FTMS) Calcd for $C_{19}H_{25}O_3$ $[M-H]^-$: 301.1809; found: 301.1802.



5e

methyl 4-(1-(4-methyl-2-oxopentyl)cyclobutyl)benzoate (**5e**)

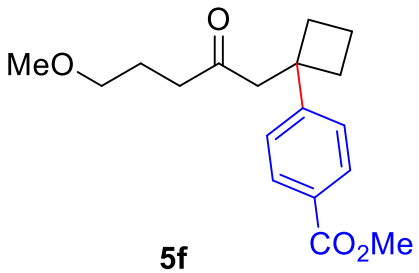
Following the general procedure, **5e** was obtained as a colorless oil, 61% yield.

R_f = 0.49 (petroleum ether/ethyl acetate, 10:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 3.90 (s, 3H), 2.92 (s, 2H), 2.44 (dd, *J* = 19.4, 9.2 Hz, 2H), 2.41 – 2.34 (m, 2H), 2.14 – 2.06 (m, 1H), 1.92-1.86 (m, 4H), 0.70 (d, *J* = 6.2 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 166.9, 154.3, 129.6, 127.4, 125.9, 53.9, 53.4, 52.1, 45.5, 33.3, 24.3, 22.5, 16.1.

IR (KBr) v 1722, 1609, 1435, 1278, 1107, 776, 709.

HRMS (APCI-FTMS) Calcd for $C_{18}H_{25}O_3$ $[M+H]^+$: 289.1798; found: 289.1795.



5f

methyl 4-(1-(5-methoxy-2-oxopentyl)cyclobutyl)benzoate (**5f**)

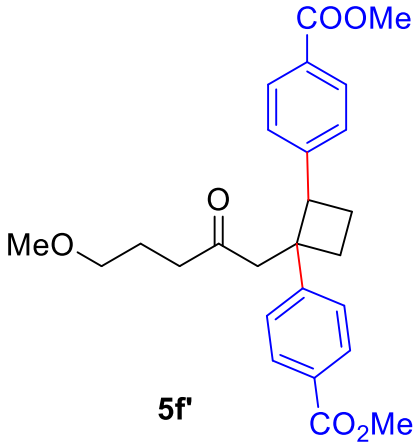
Following the general procedure, **5f** was obtained as a colorless oil, 43% yield.

R_f = 0.49 (petroleum ether/ethyl acetate, 6:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.3 Hz, 2H), 3.90 (s, 3H), 3.20 (s, 3H), 3.18 – 3.16 (m, 2H), 2.96 (s, 2H), 2.47-2.42 (m, 2H), 2.38-2.36 (m, 2H), 2.20 – 1.99 (m, 3H), 1.95 – 1.80 (m, 1H), 1.71 – 1.52 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 166.9, 154.3, 129.6, 127.7, 125.6, 71.3, 58.3, 53.6, 51.7, 46.0, 40.9, 33.6, 23.2, 15.5.

IR (KBr) v 1720, 1609, 1435, 1278, 1105, 775, 708.

HRMS (APCI-FTMS) Calcd for $C_{18}H_{23}O_4$ $[M-H]^-$: 303.1602; found: 303.1596.



5f'

dimethyl 4,4'-(1-(5-methoxy-2-oxopentyl)cyclobutane-1,2-diyl)dibenzoate (**5f'**)

Following the general procedure, **5f'** was obtained as a colorless oil, 2% yield.

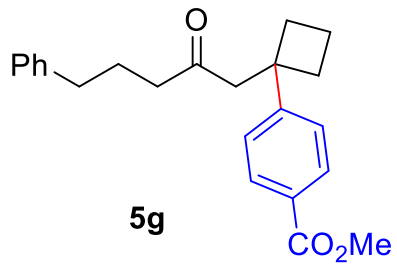
R_f = 0.32 (petroleum ether/ethyl acetate, 6:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.2 Hz, 2H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.71 (t, *J* = 9.2 Hz, 1H), 3.14 (s, 3H), 3.14 – 3.09 (m, 1H), 3.06-3.03 (m, 1H), 2.86 (d,

J = 15.8 Hz, 1H), 2.72 (dd, *J* = 19.4, 9.7 Hz, 1H), 2.51-2.44 (m, 4H), 2.27 – 2.06 (m, 3H), 1.84-1.78 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.9, 208.8, 166.9, 153.5, 144.7, 129.8, 129.0, 128.9, 128.0, 125.9, 71.3, 58.7, 52.3, 52.2, 51.8, 50.1, 47.9, 40.7, 27.7, 23.4, 20.6.

IR (KBr) v 1719, 1611, 1435, 1277, 1106, 775, 708.

HRMS (APCI-FTMS) Calcd for $C_{26}H_{29}O_6$ $[M-H]^-$: 437.1970; found: 437.1962.



5g

methyl 4-(1-(2-oxo-5-phenylpentyl)cyclobutyl)benzoate (**5g**)

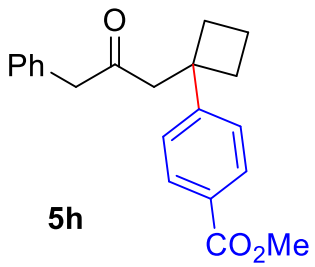
Following the general procedure, **5g** was obtained as a colorless oil, 56% yield.

R_f = 0.50 (petroleum ether/ethyl acetate, 7:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.28 – 7.18 (m, 4H), 7.14 (t, *J* = 7.3 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 2H), 3.90 (s, 3H), 2.90 (s, 2H), 2.54 – 2.28 (m, 6H), 2.11-2.07 (m, 1H), 1.95 (t, *J* = 7.2 Hz, 2H), 1.91 – 1.76 (m, 1H), 1.72 – 1.56 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6, 166.9, 154.6, 140.8, 129.6, 128.5, 128.4, 127.7, 126.1, 126.0, 53.2, 51.7, 45.2, 43.0, 34.3, 33.6, 24.2, 16.2.

IR (KBr) v 1720, 1609, 1435, 1278, 1105, 775, 708.

HRMS (APCI-FTMS) Calcd for $C_{23}H_{25}O_3$ $[M-H]^-$: 349.1809; found: 349.1801.



5h

methyl 4-(1-(2-oxo-3-phenylpropyl)cyclobutyl)benzoate (**5h**)

Following the general procedure, **5h** was obtained as a colorless oil, 48% yield.

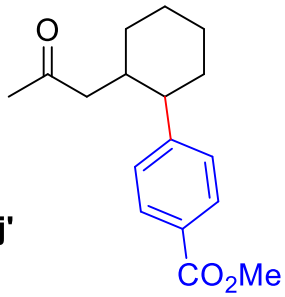
R_f = 0.43 (petroleum ether/ethyl acetate, 7:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 2H), 7.23 (m, 5H), 6.88 (d, *J* = 8.2 Hz, 2H), 3.92 (s, 3H), 3.22 (s, 2H), 2.97 (s, 2H), 2.43 (dd, *J* = 19.9, 10.0 Hz, 2H), 2.37 – 2.27 (m, 2H), 2.11 – 2.01 (m, 1H), 1.89 – 1.80 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 166.7, 153.9, 133.7, 129.5, 129.3, 128.6, 127.6, 126.9, 126.0, 52.3, 52.0, 51.4, 45.5, 33.2, 16.0.

IR (KBr) v 1718, 1632, 1609, 1434, 1278, 1105, 700.

HRMS (APCI-FTMS) Calcd for $C_{21}H_{23}O_3$ $[M+H]^+$: 323.1634; found: 323.1641.



5j'

methyl 4-(2-(2-oxopropyl)cyclohexyl)benzoate (**5j'**)

Following the general procedure, **5j'** was obtained as a colorless oil, 4% yield.

R_f = 0.40 (petroleum ether/ethyl acetate, 5:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 3.90 (s, 3H), 2.30 (t, *J* = 11.2 Hz, 1H), 2.14 (d, *J* = 13.9 Hz, 2H), 2.08-2.02 (m, 1H), 1.92 (s, 3H), 1.92-1.89 (m, 1H), 1.83 – 1.77 (m, 3H), 1.53 – 1.30 (m, 2H), 1.06 (dd, *J* = 25.7, 13.7 Hz, 1H), 0.89-0.84 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 208.7, 166.9, 151.4, 130.1, 128.5, 127.8, 52.1, 50.6, 48.9, 38.6, 35.6, 33.1, 30.7, 26.7, 26.3.

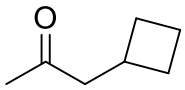
IR (KBr) v 1718, 1647, 1609, 1277, 775, 708.

HRMS (APCI-FTMS) Calcd for $C_{17}H_{23}O_3$ $[M+H]^+$: 275.1641; found: 275.1642.

References

[1] D. K. H. Ho, J. CalleJa, M. J. Gaunt, *Synlett* **2019**, 30, 454-458.

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



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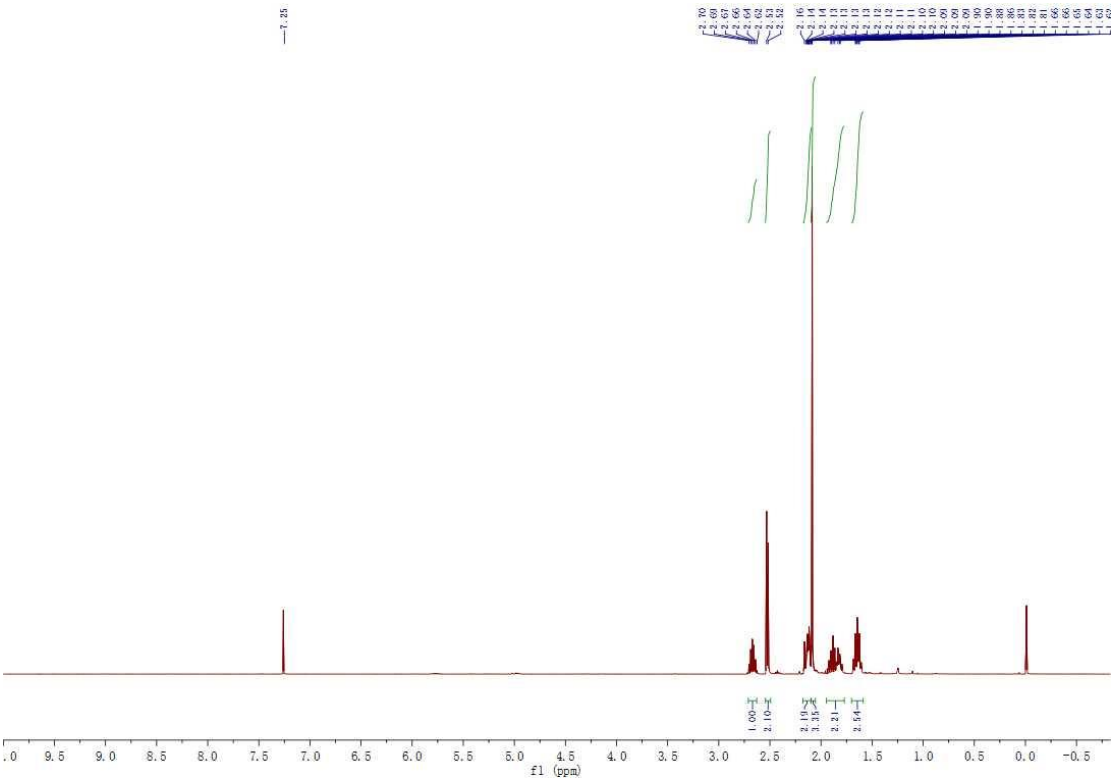

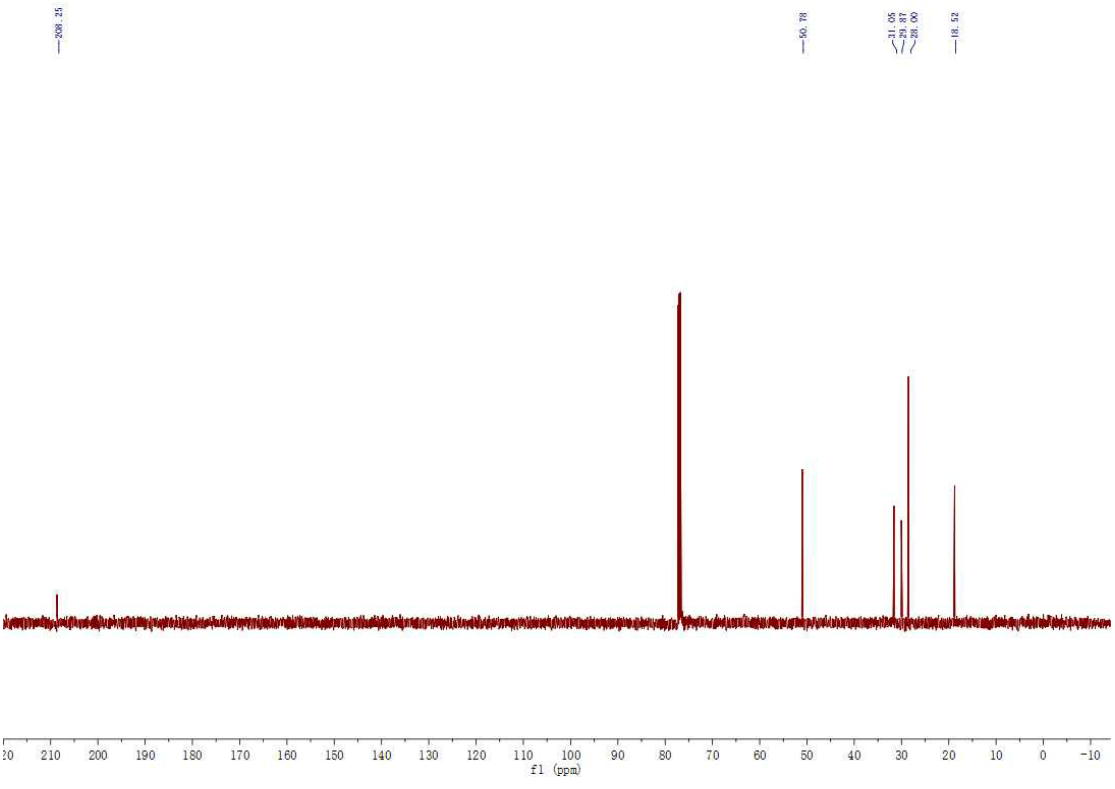

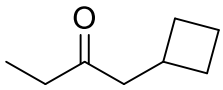

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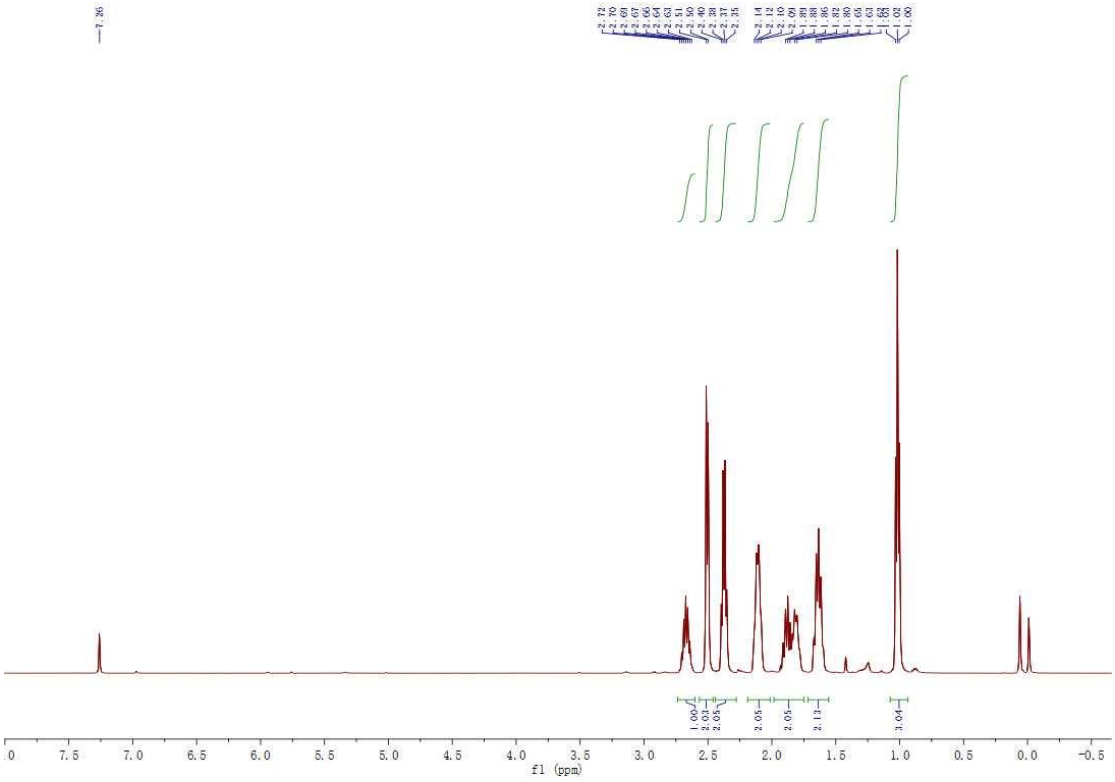

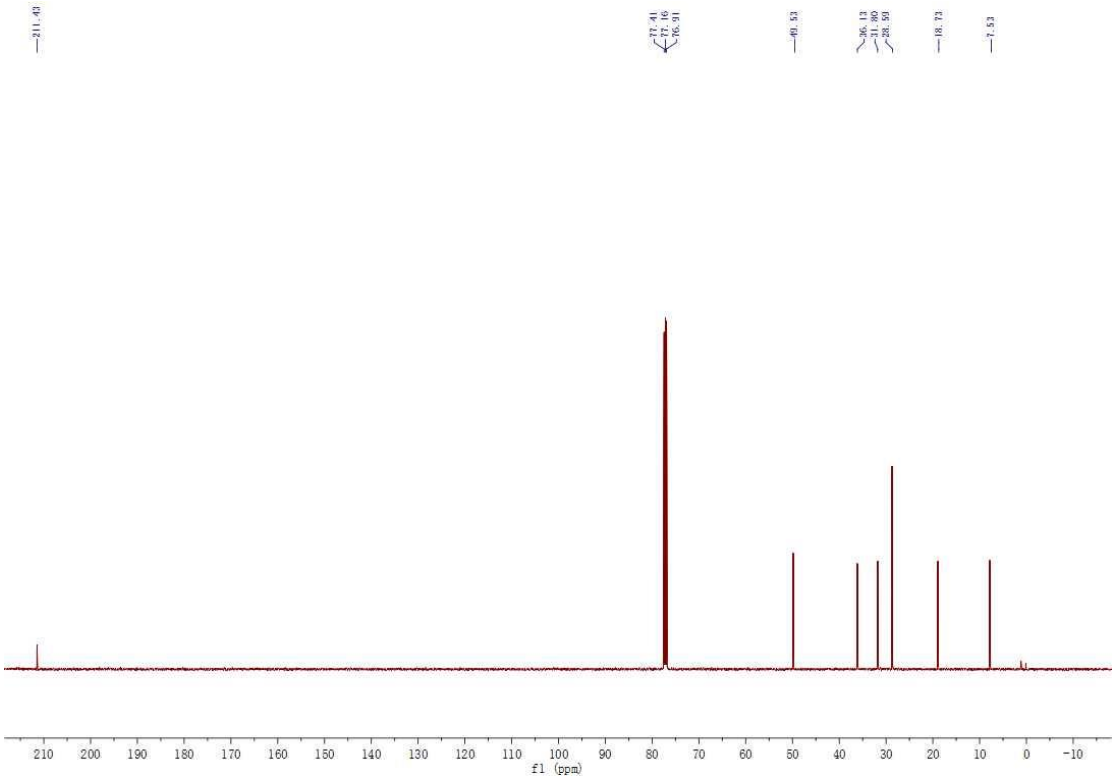

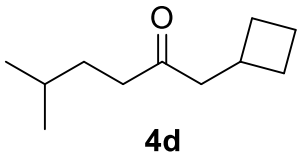

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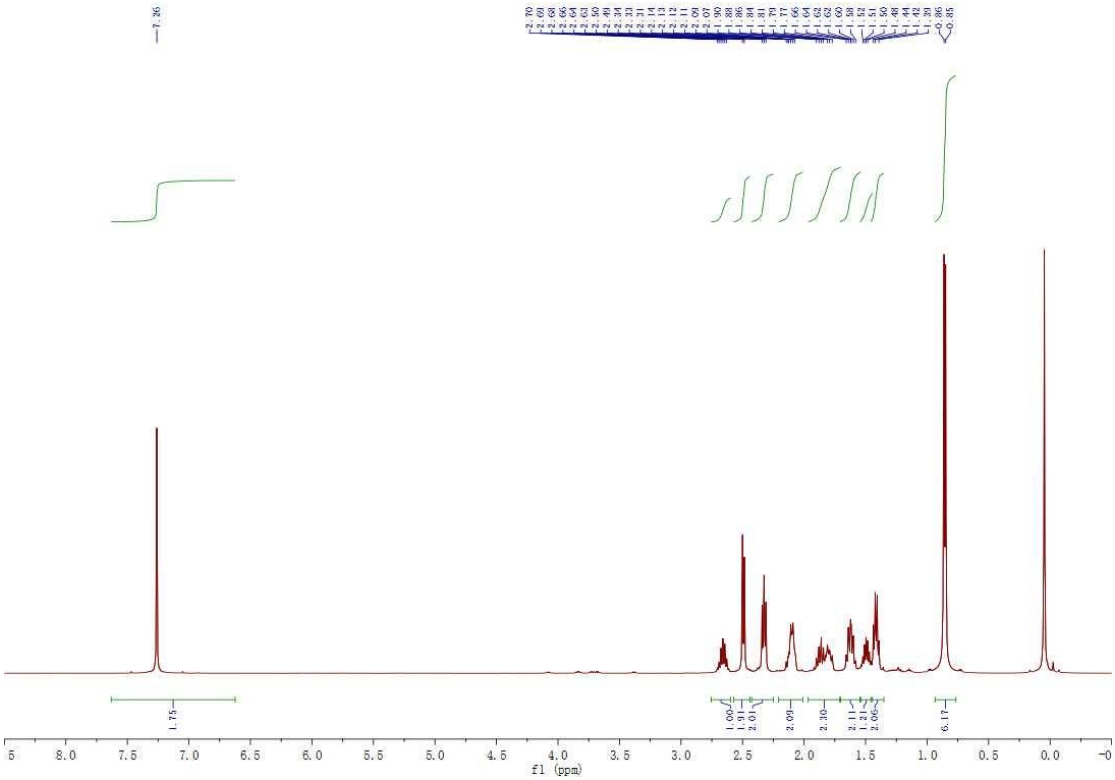

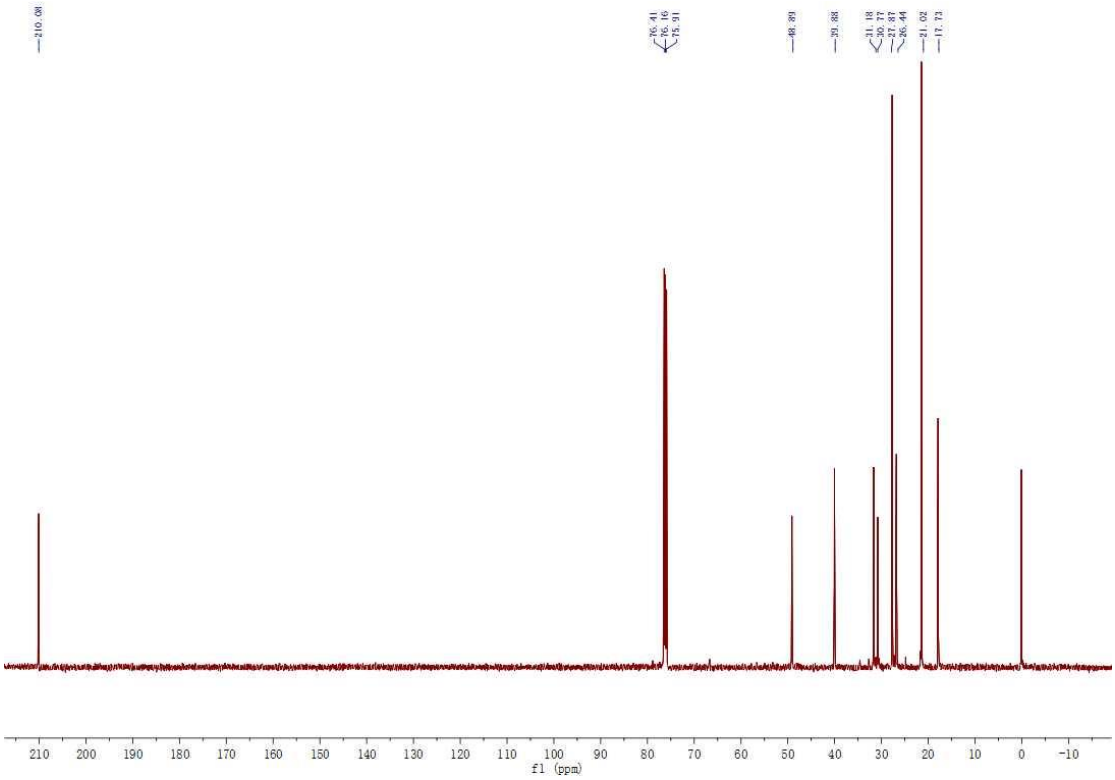

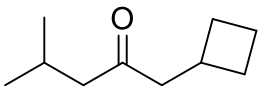

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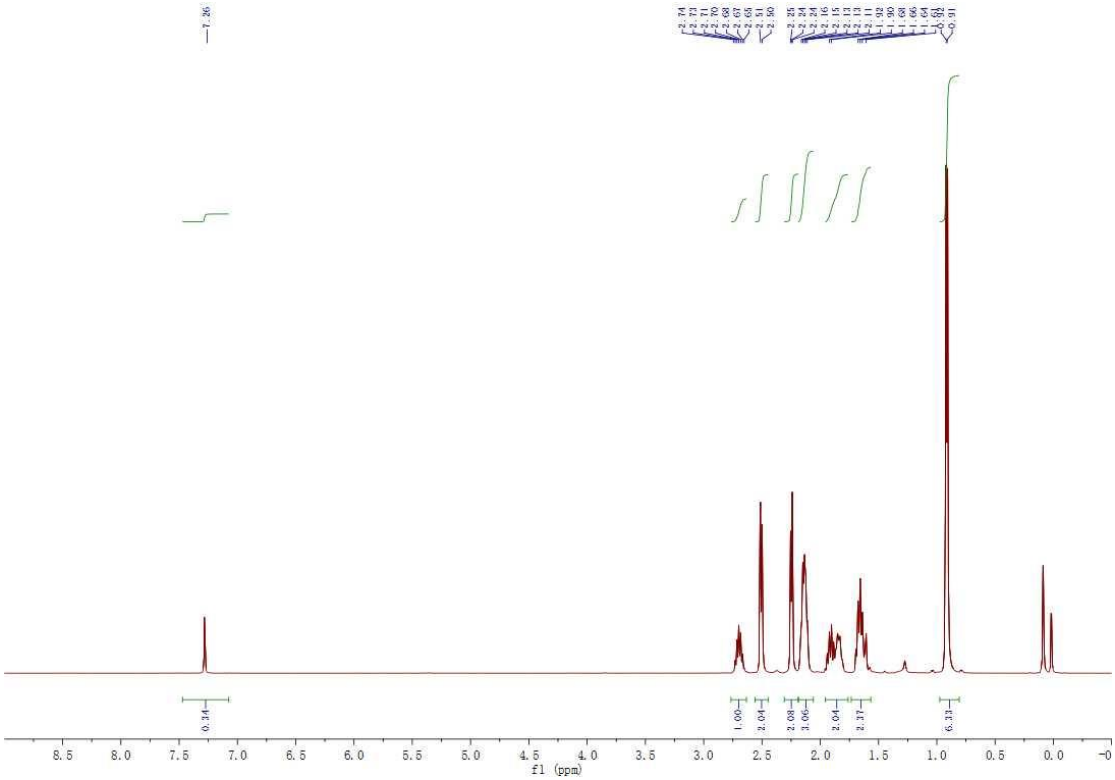

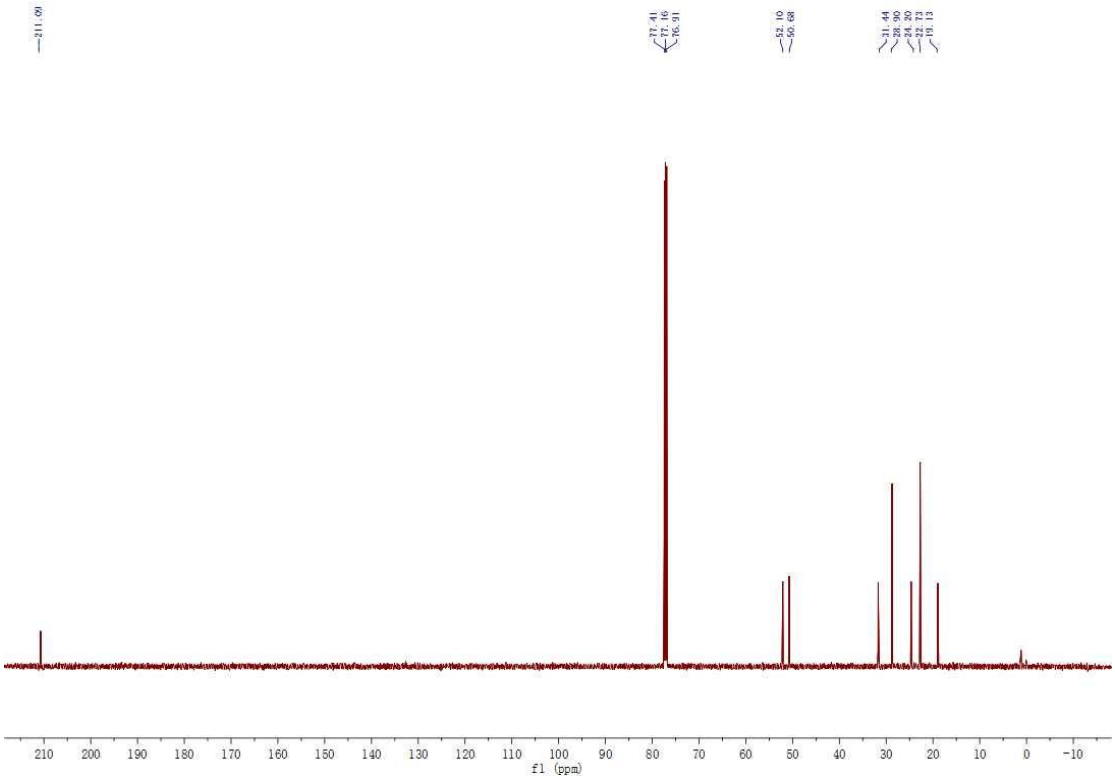

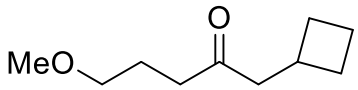

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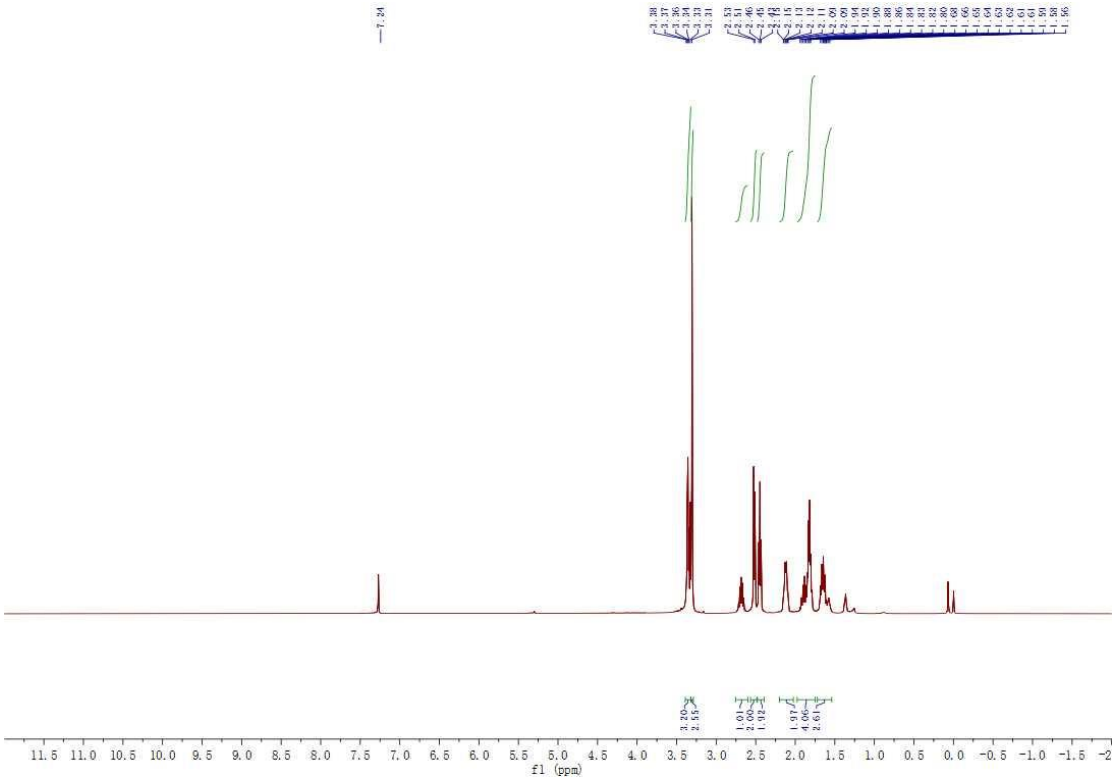

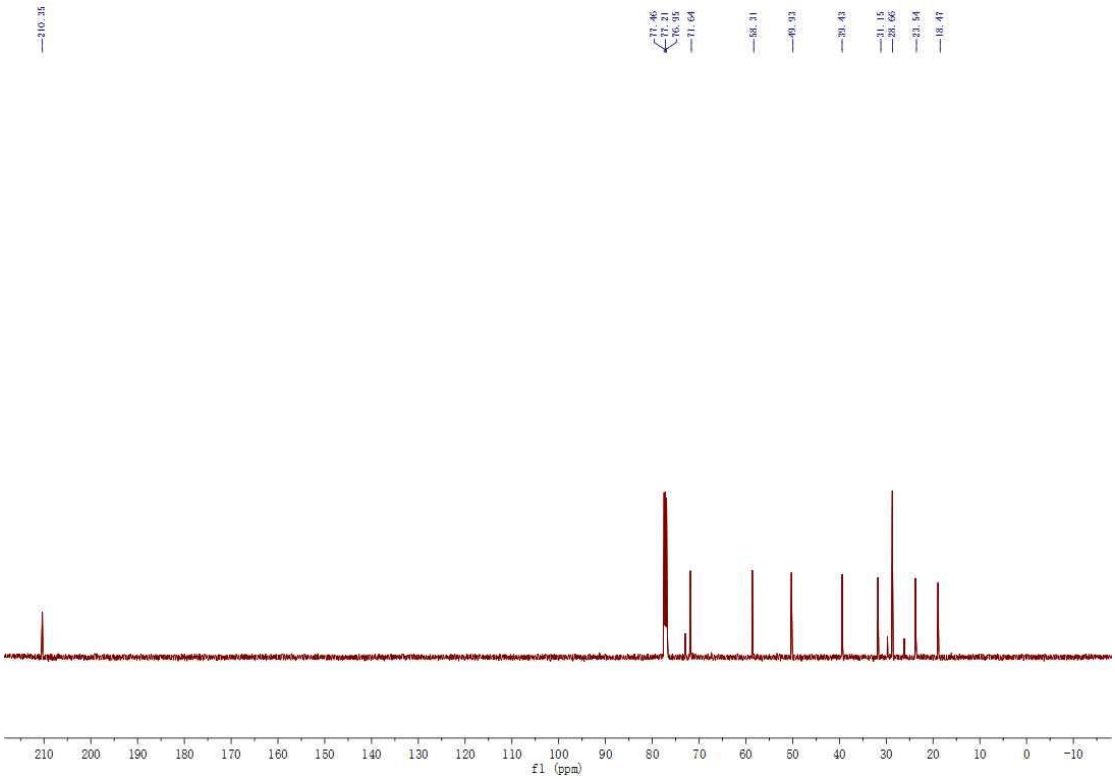

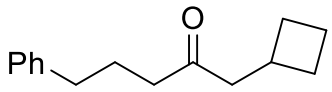

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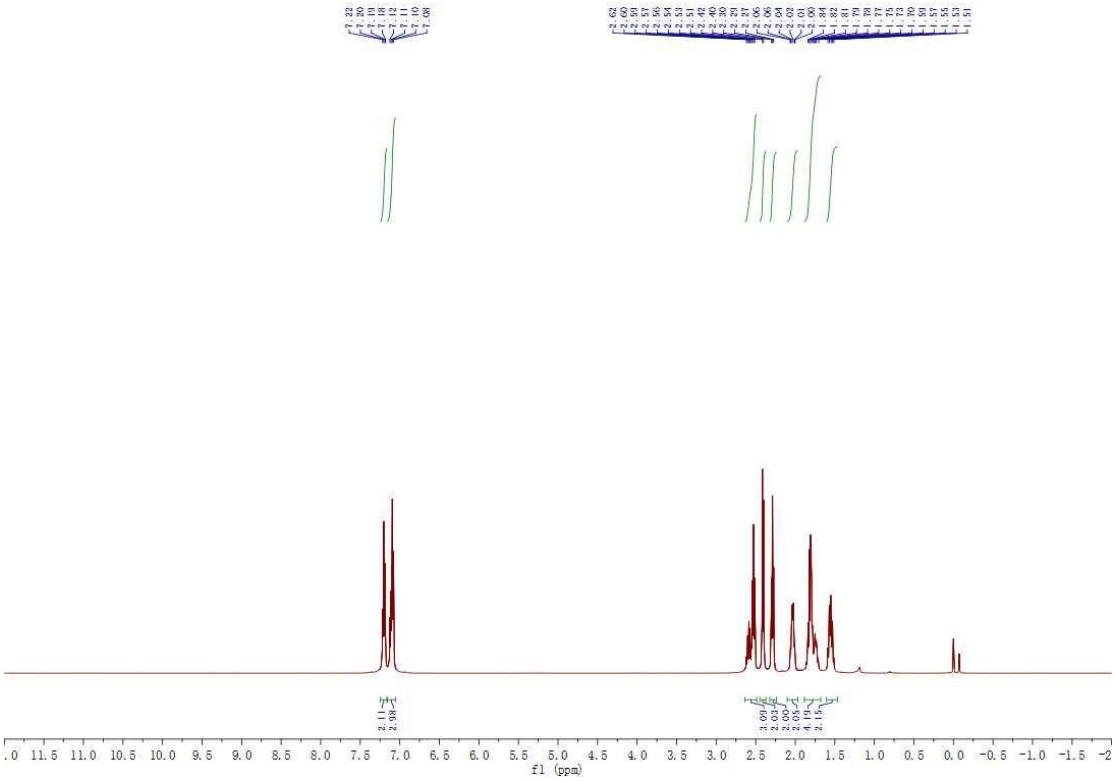

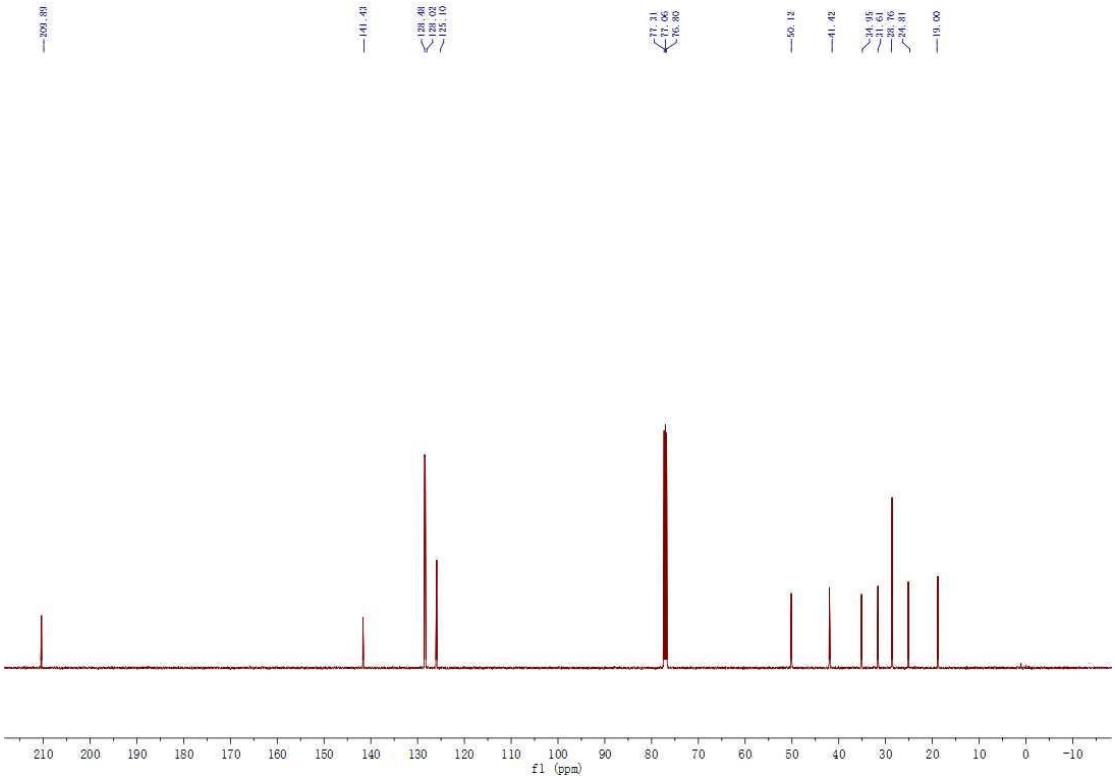

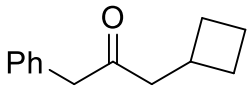

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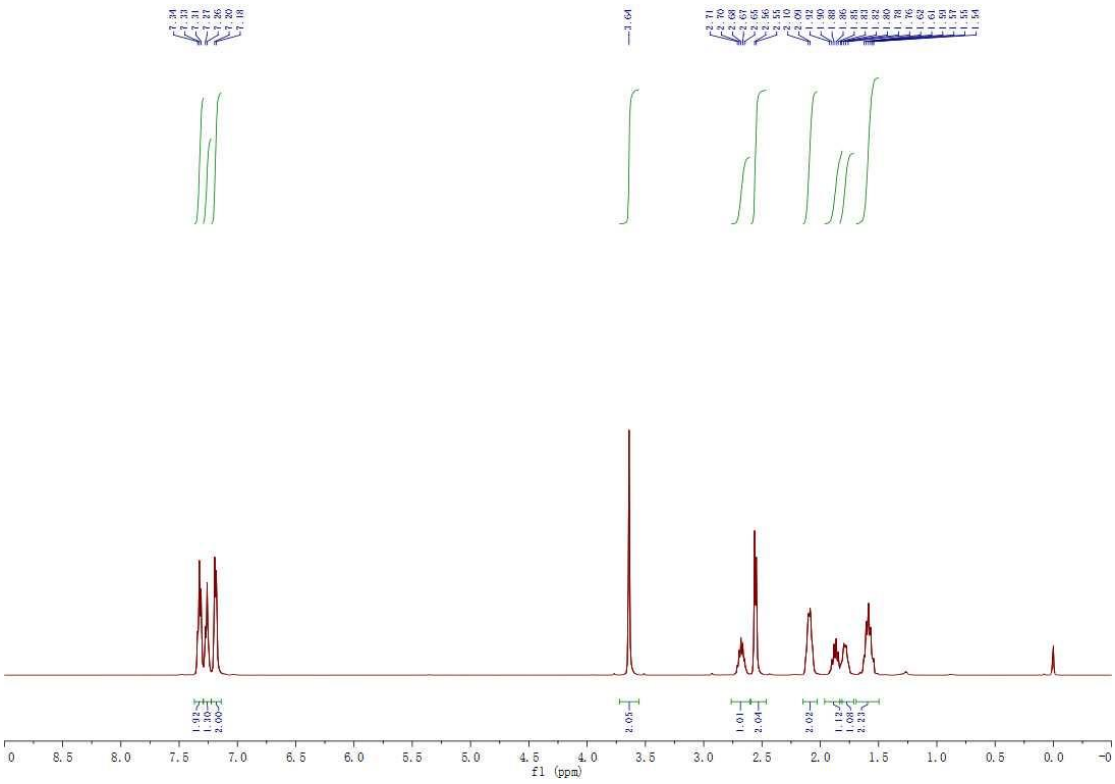

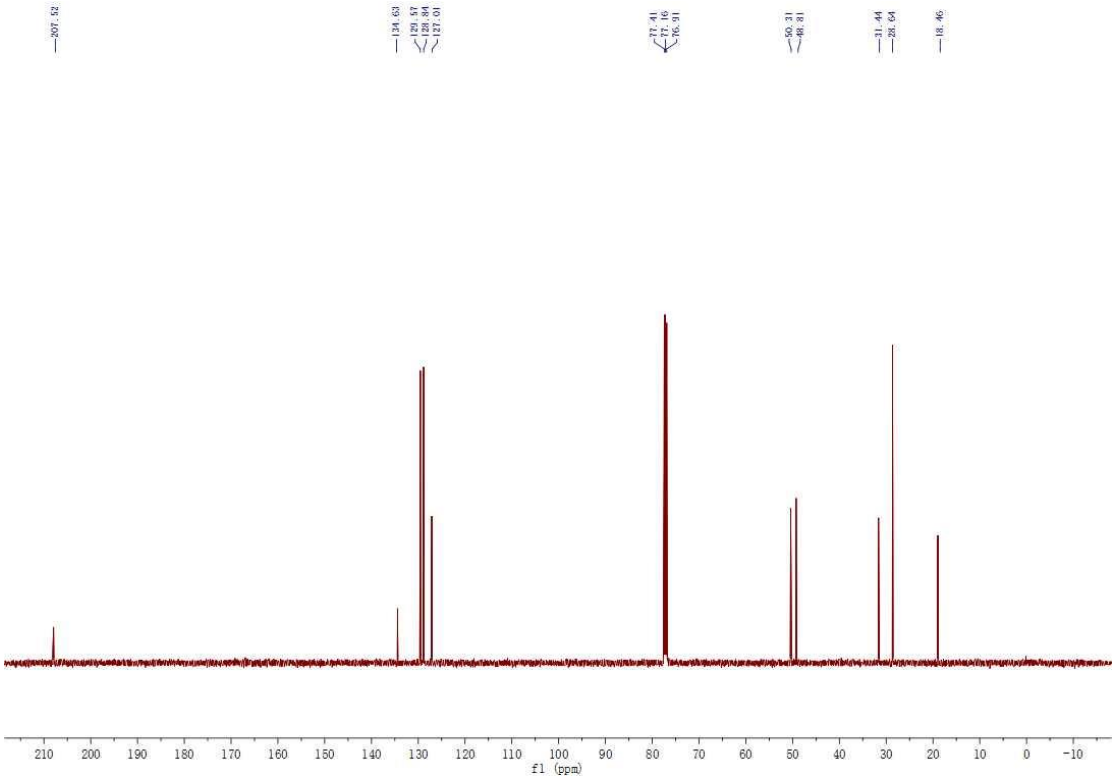

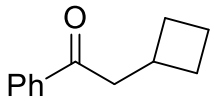

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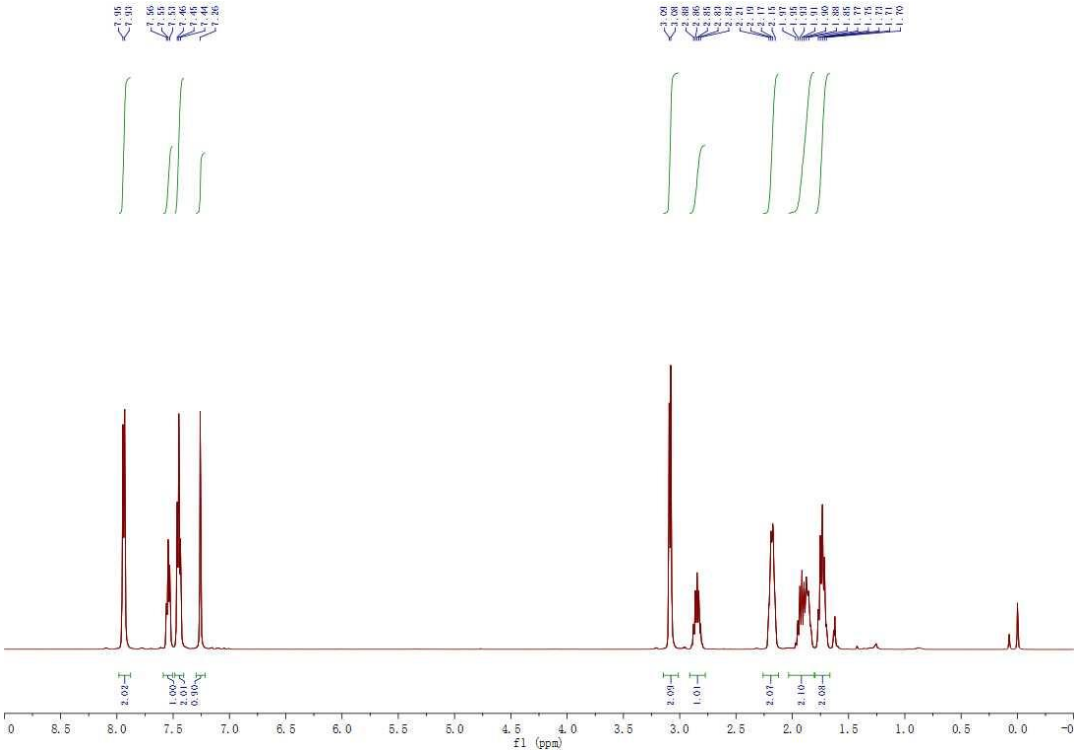

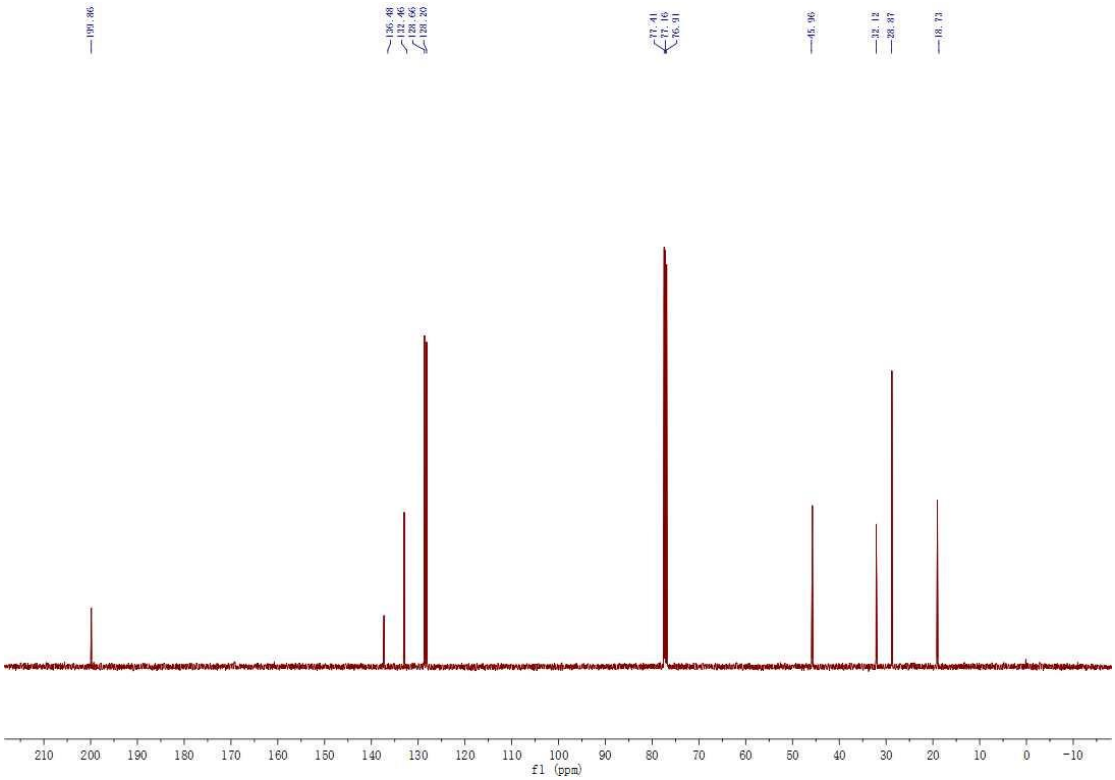

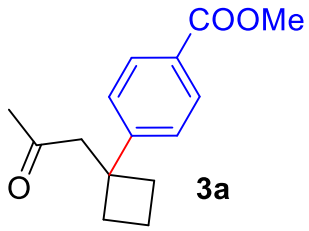

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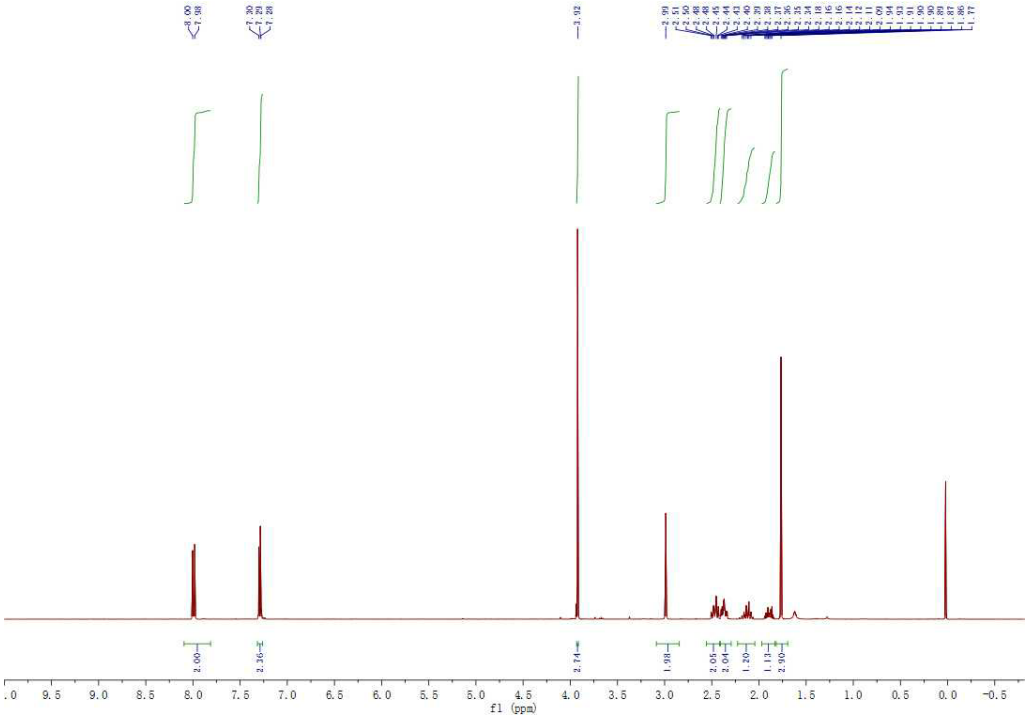
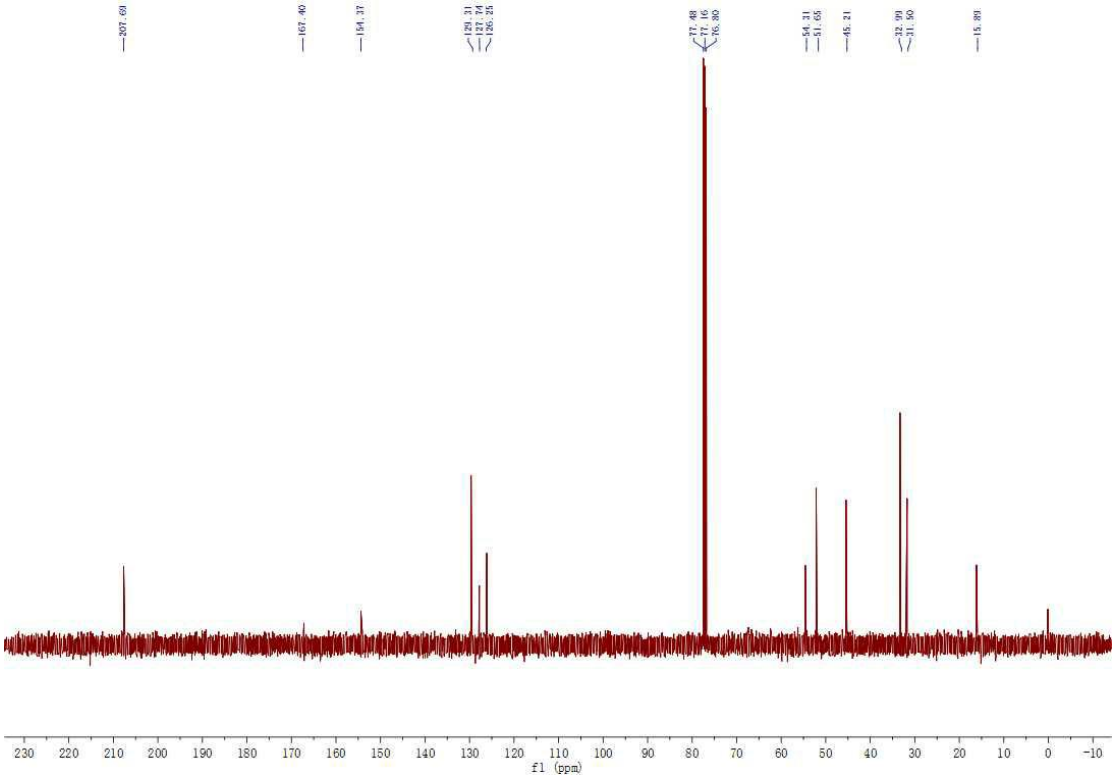
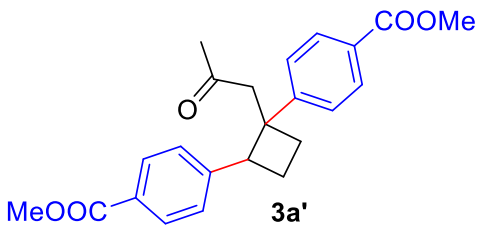
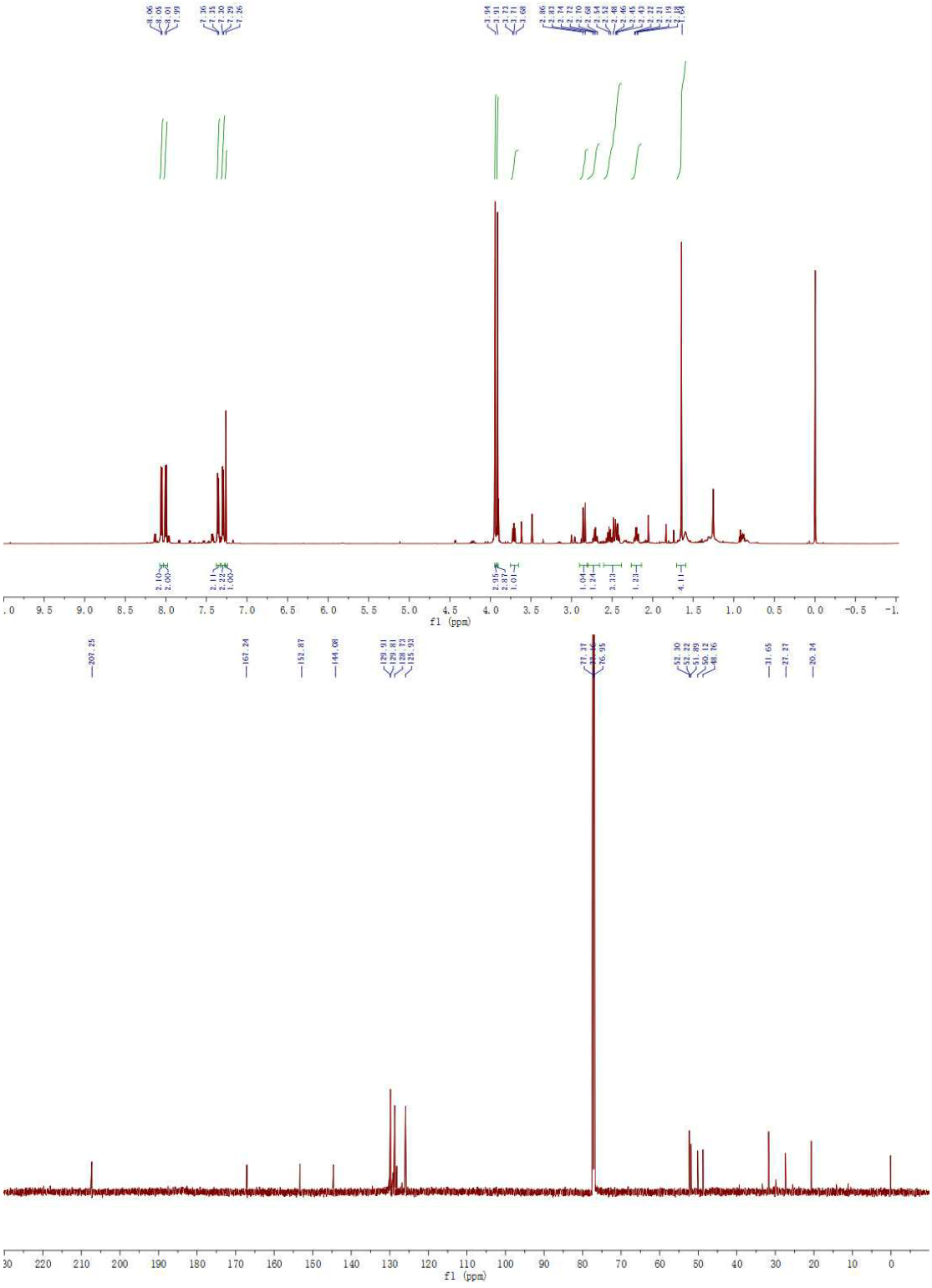
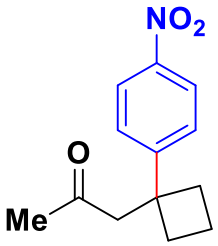






3a'





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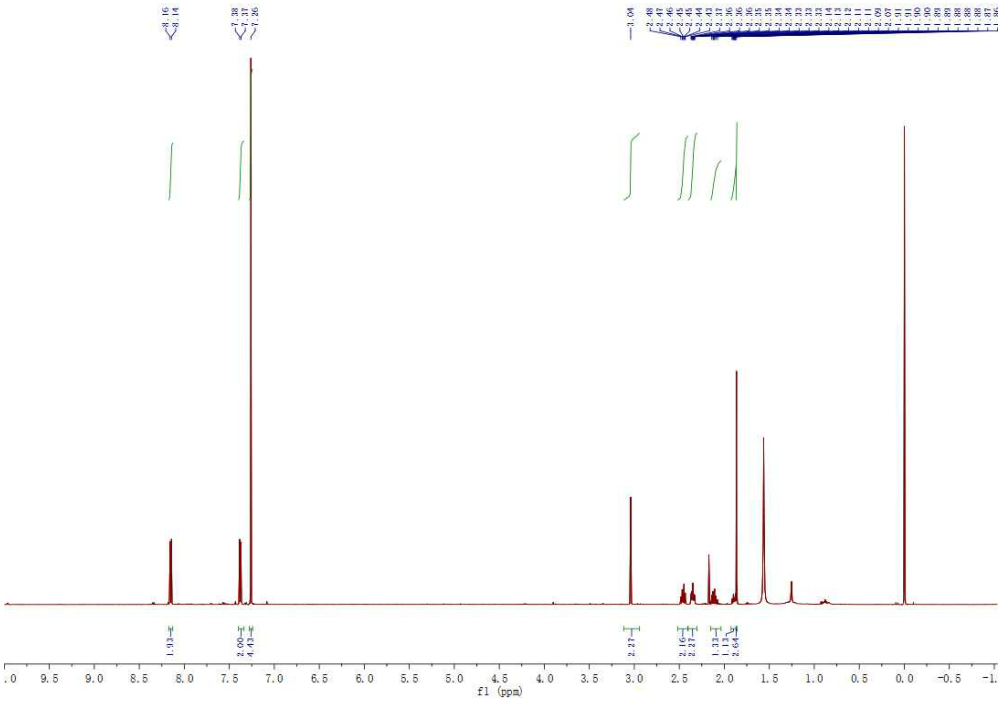

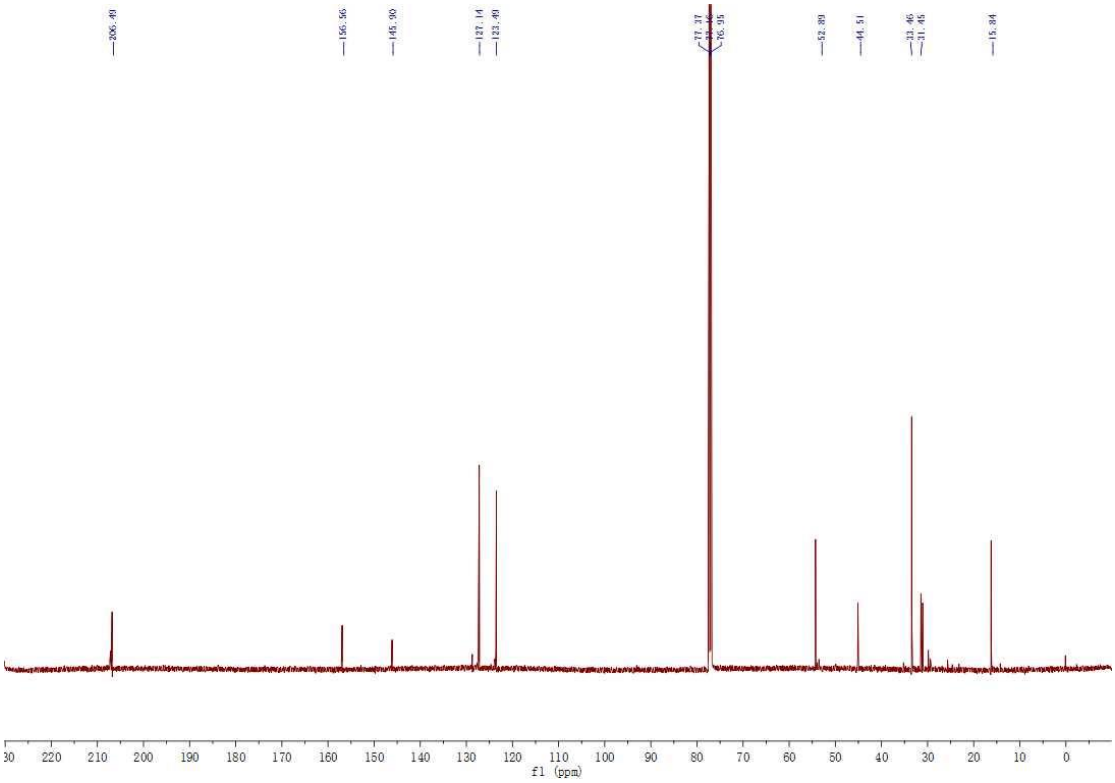

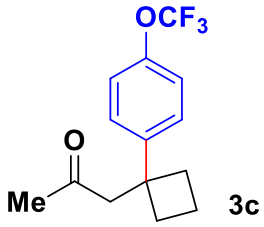
OCF3
O
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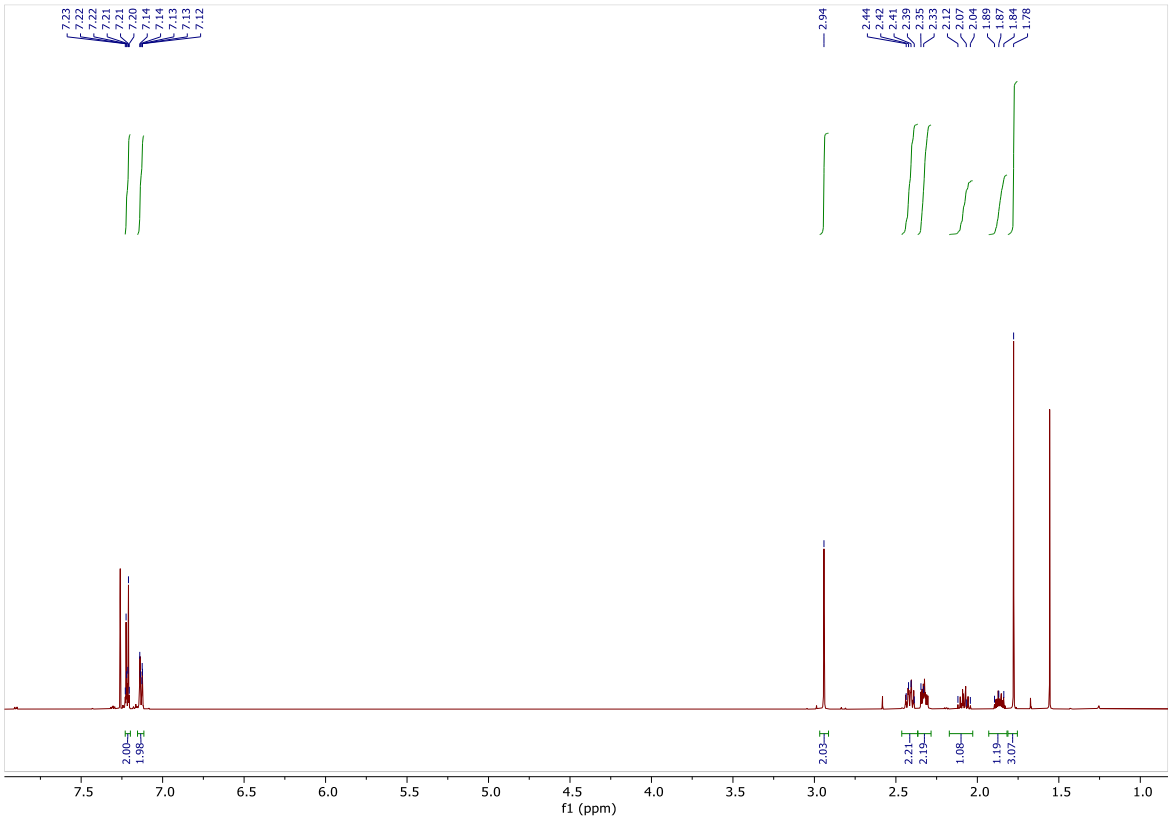
3c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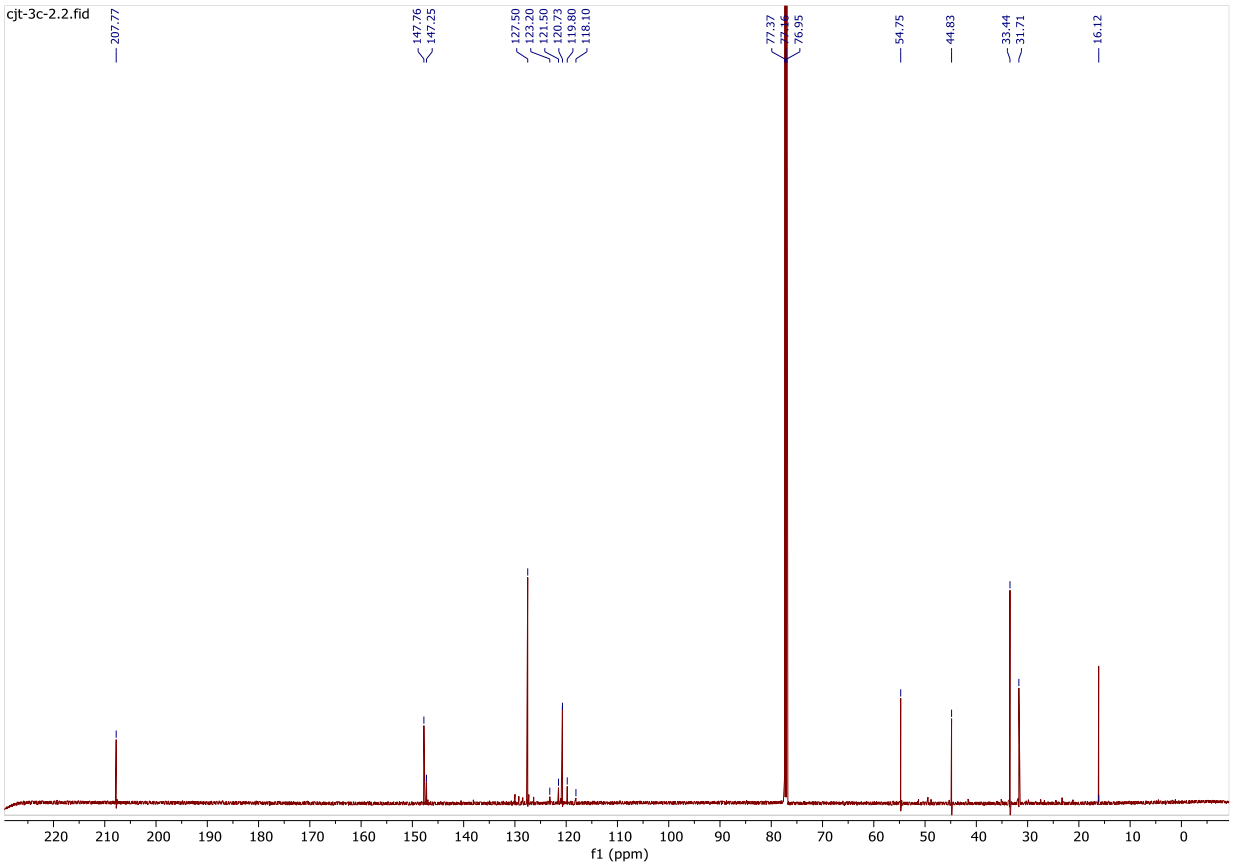
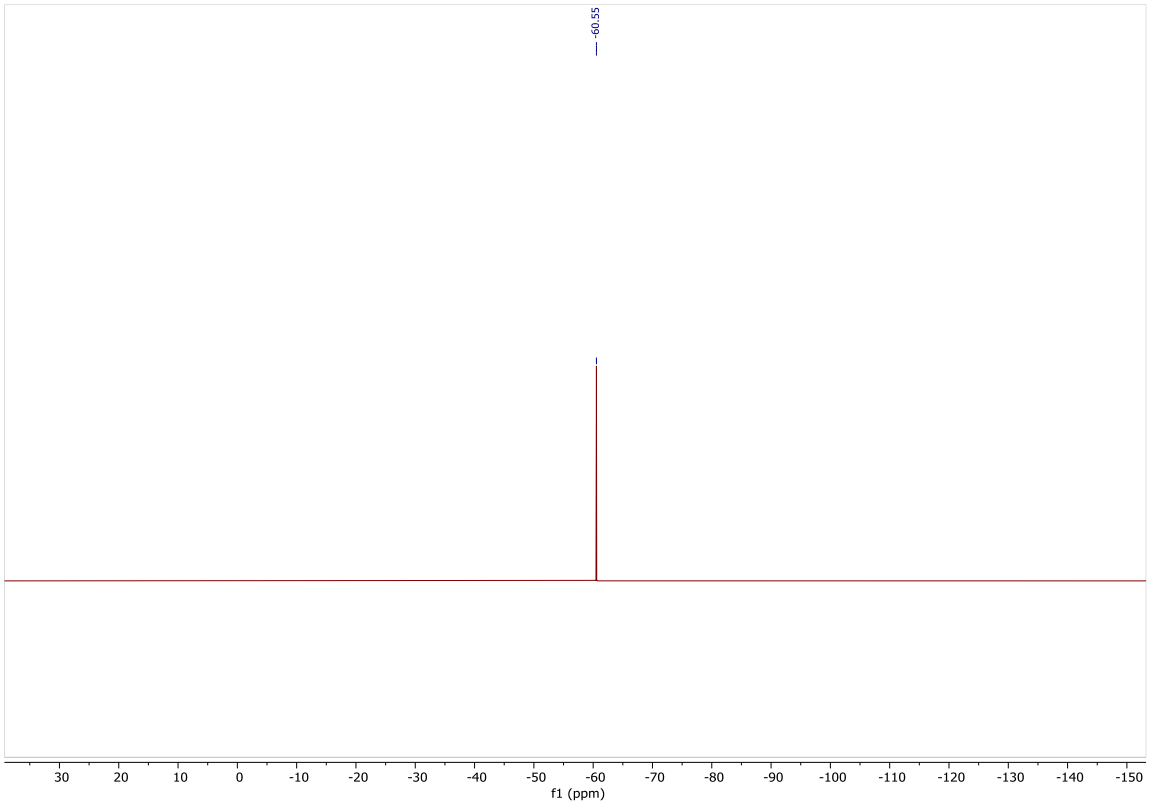
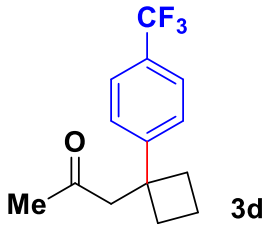
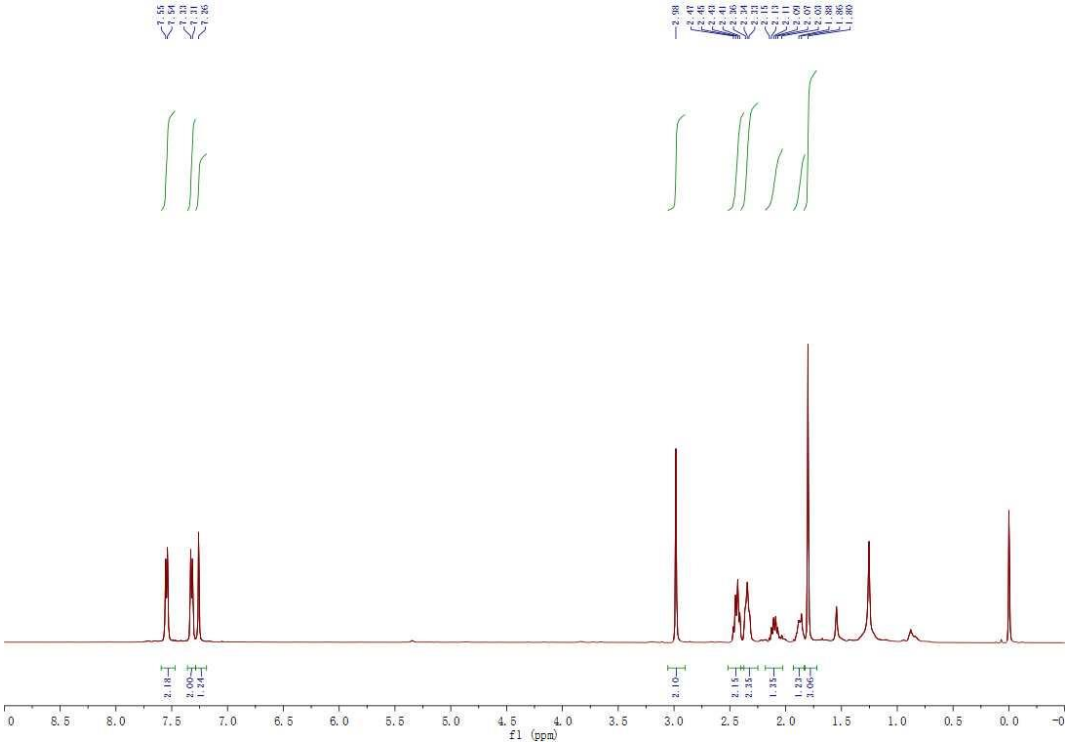


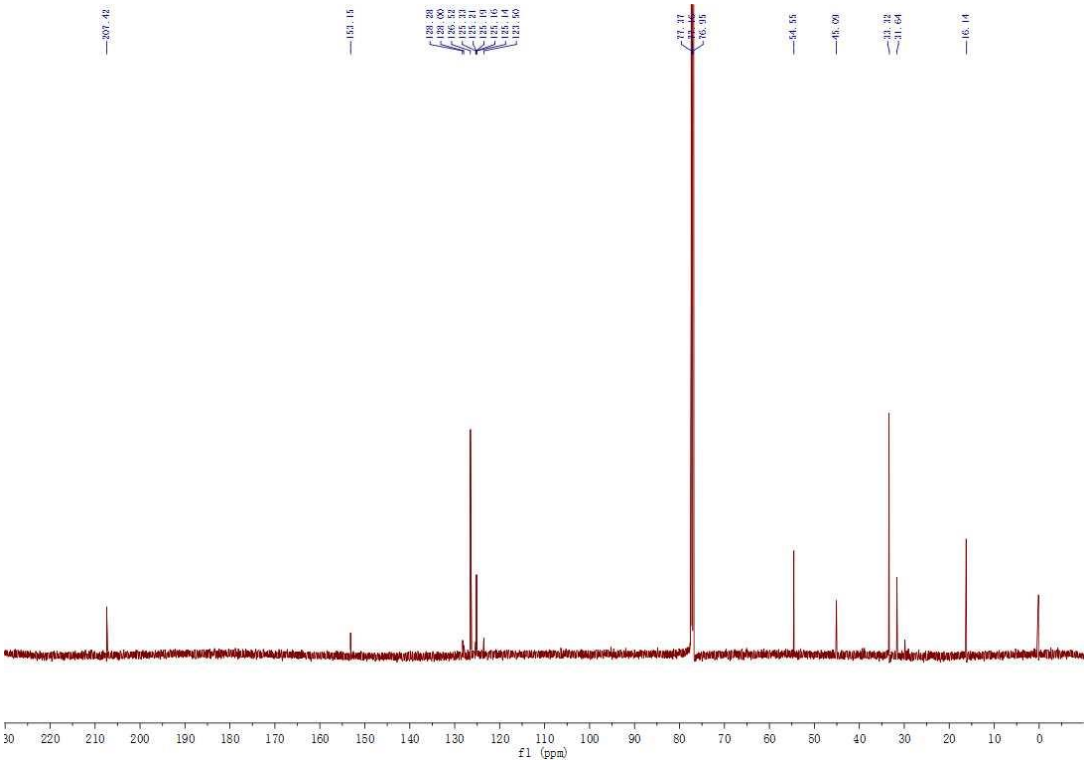
^{19}F NMR of **3c** (376 MHZ, $CDCl_3$)



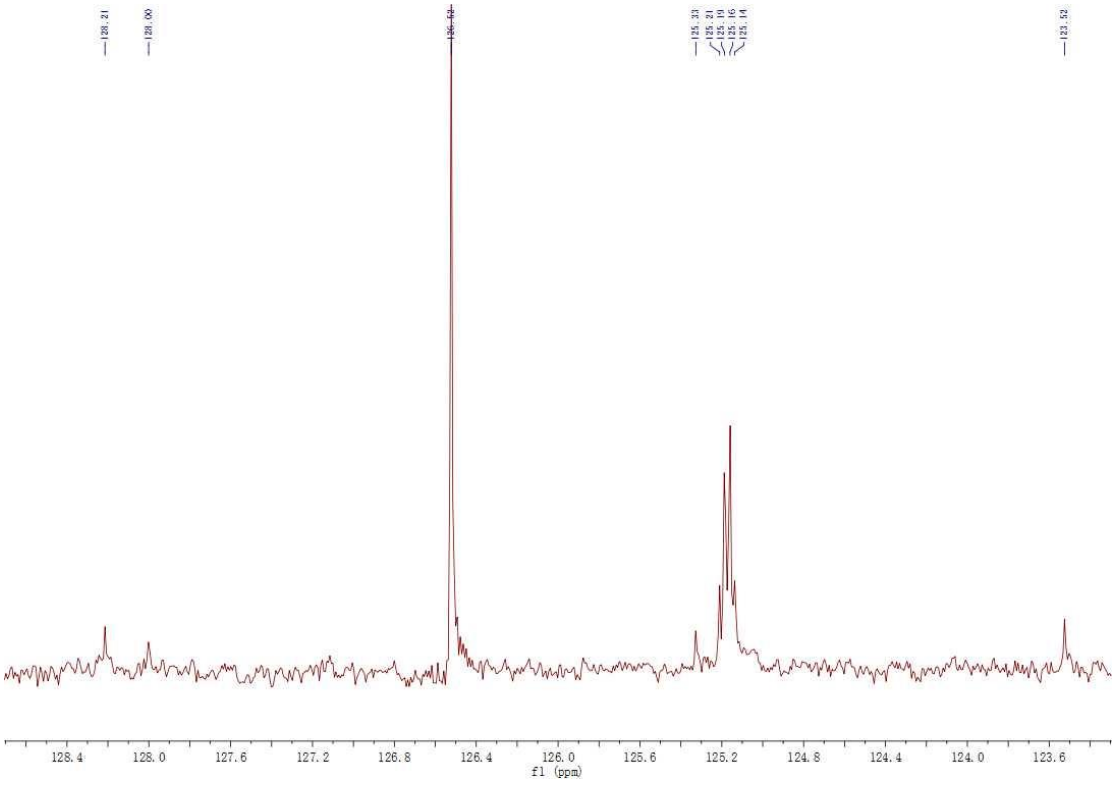


3d

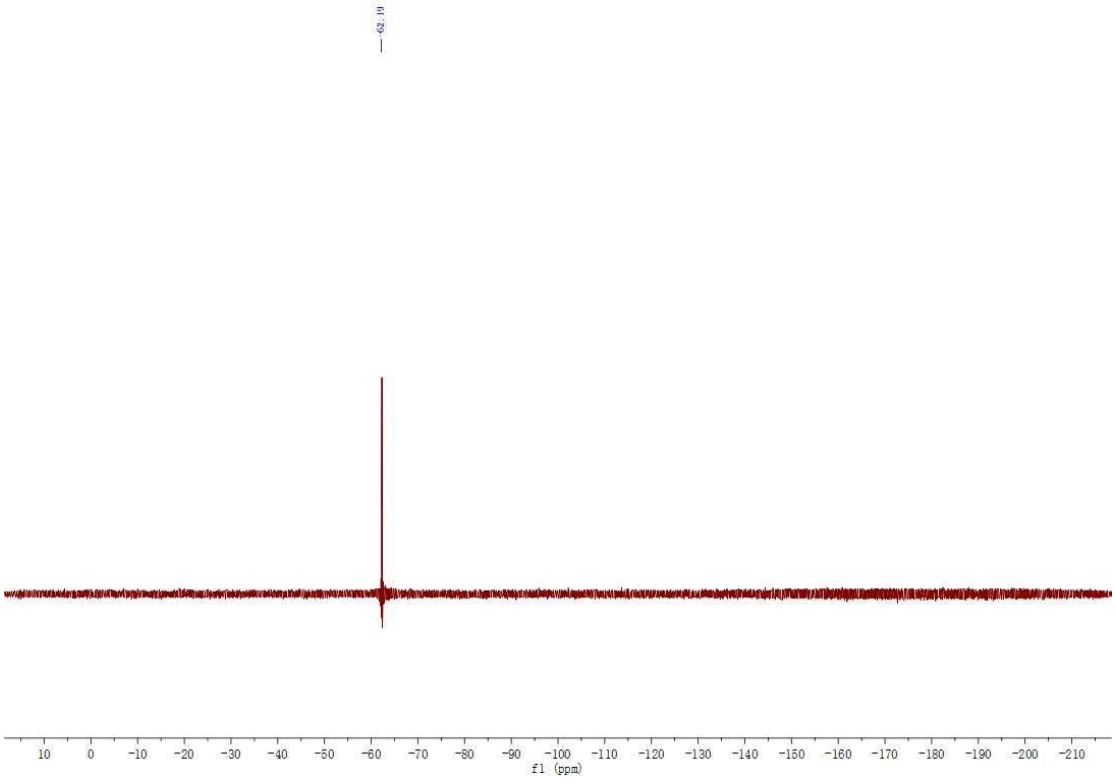


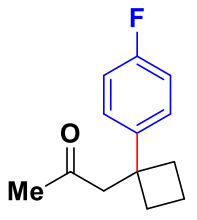


partially enlarged ^{13}C spectrum of **3d**

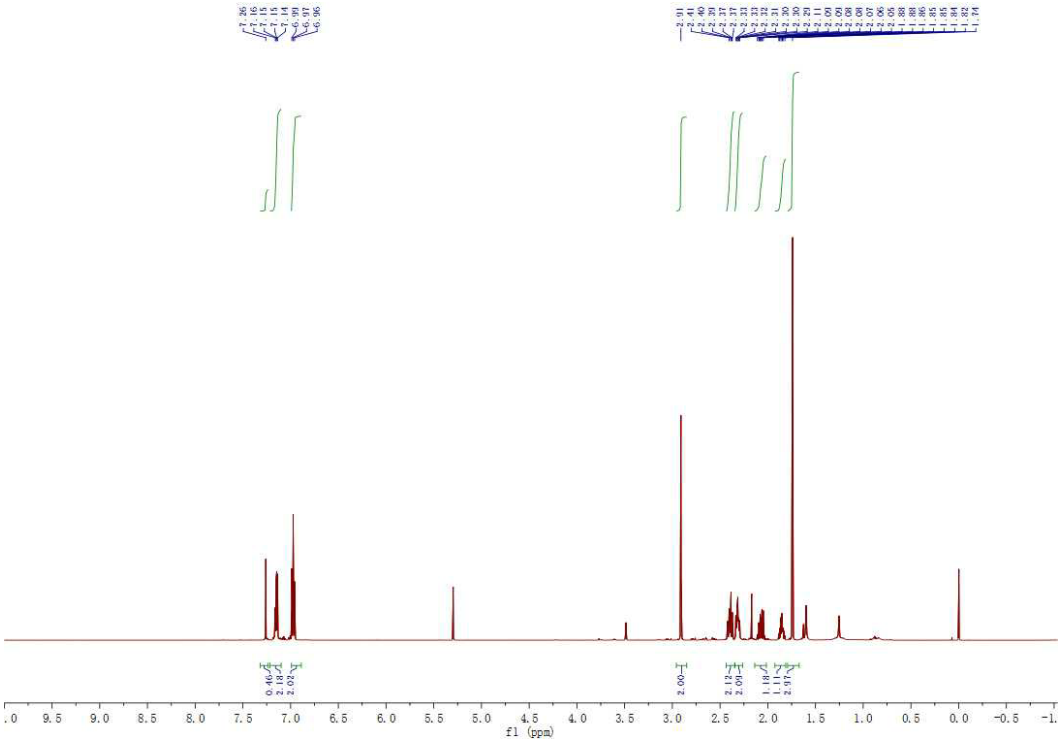


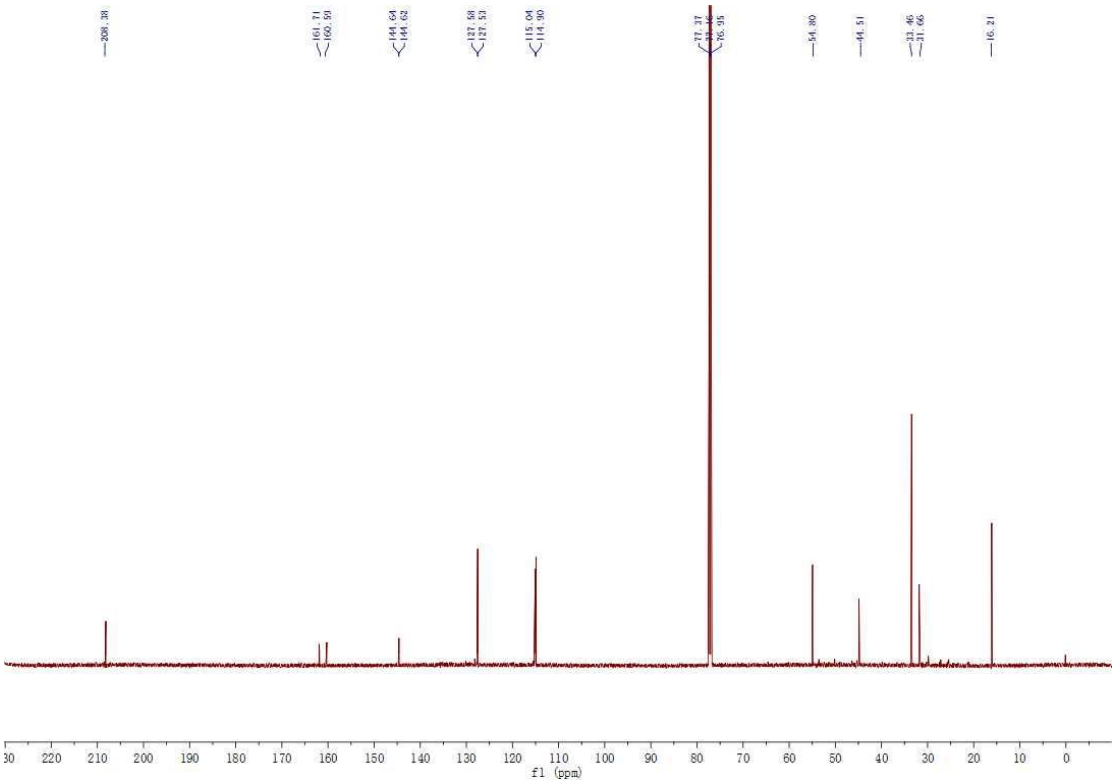
^{19}F NMR of **3d** (376 MHZ, $CDCl_3$)



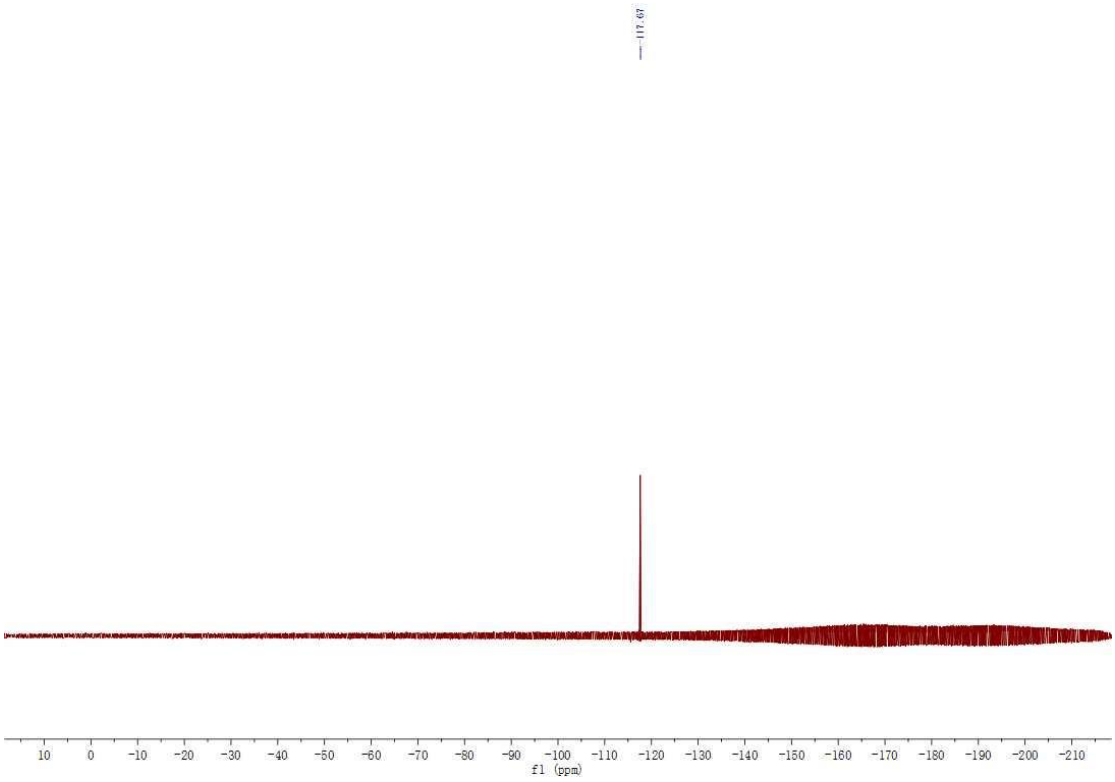


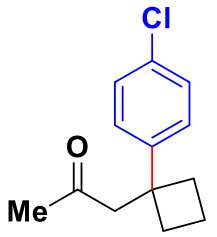
3e





^{19}F NMR of **3e** (376 MHZ, $CDCl_3$)





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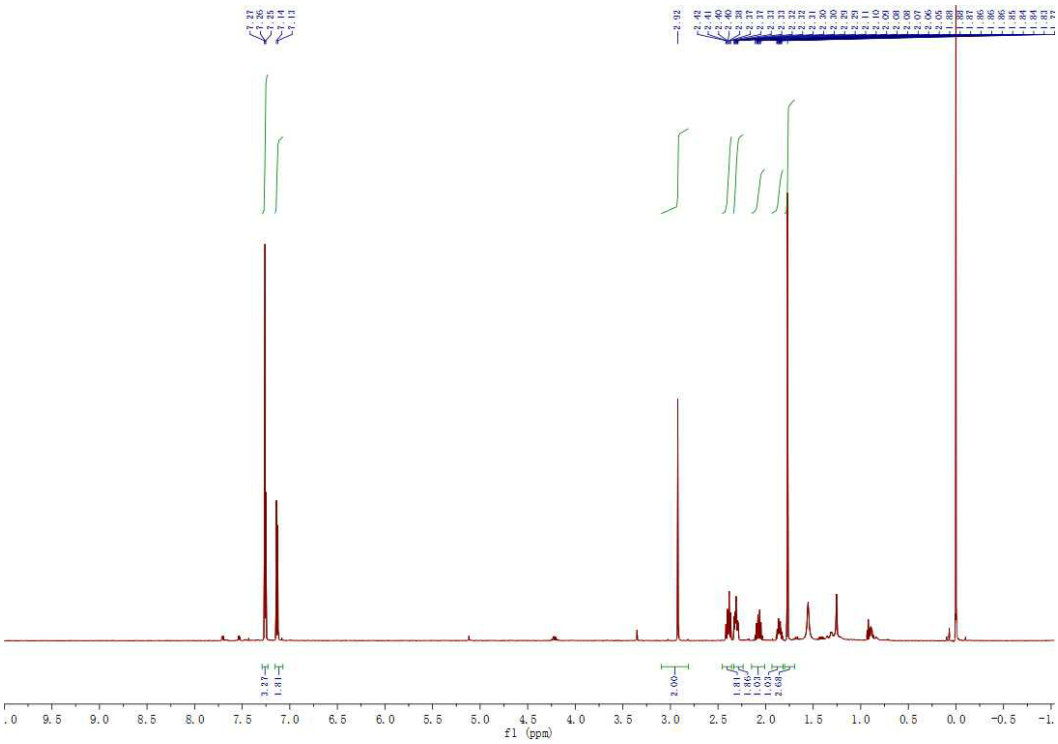
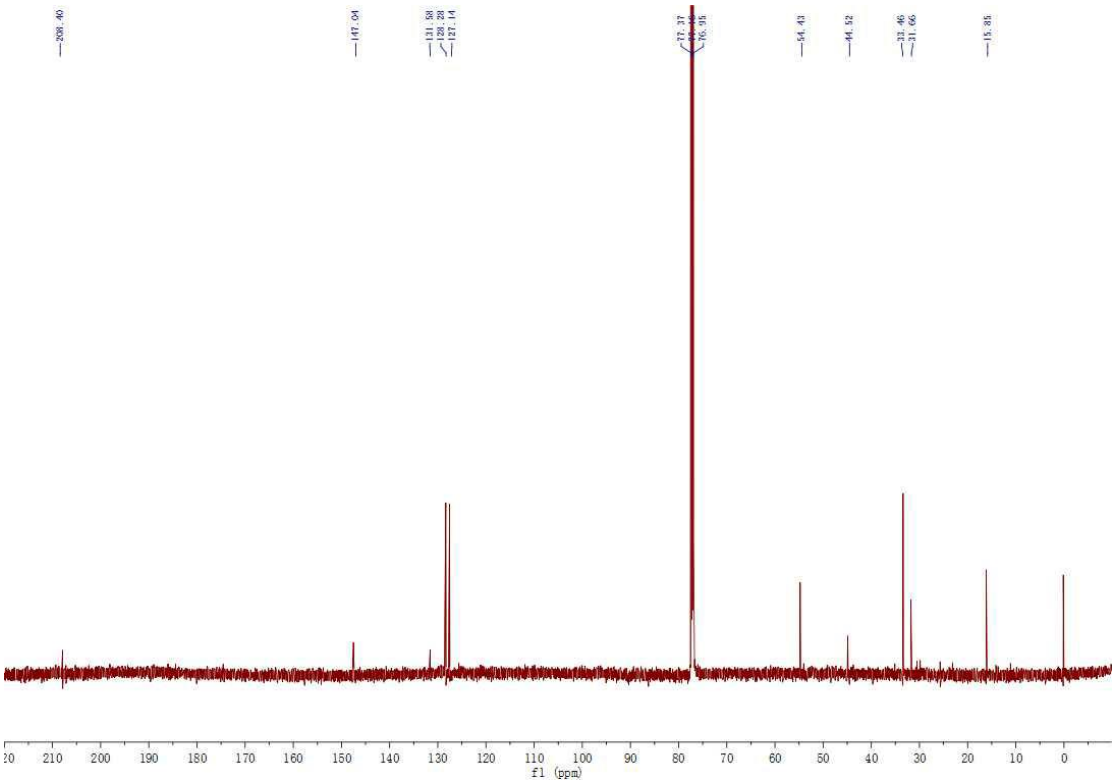
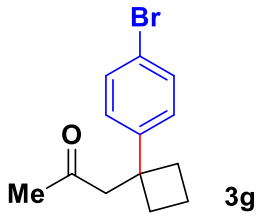
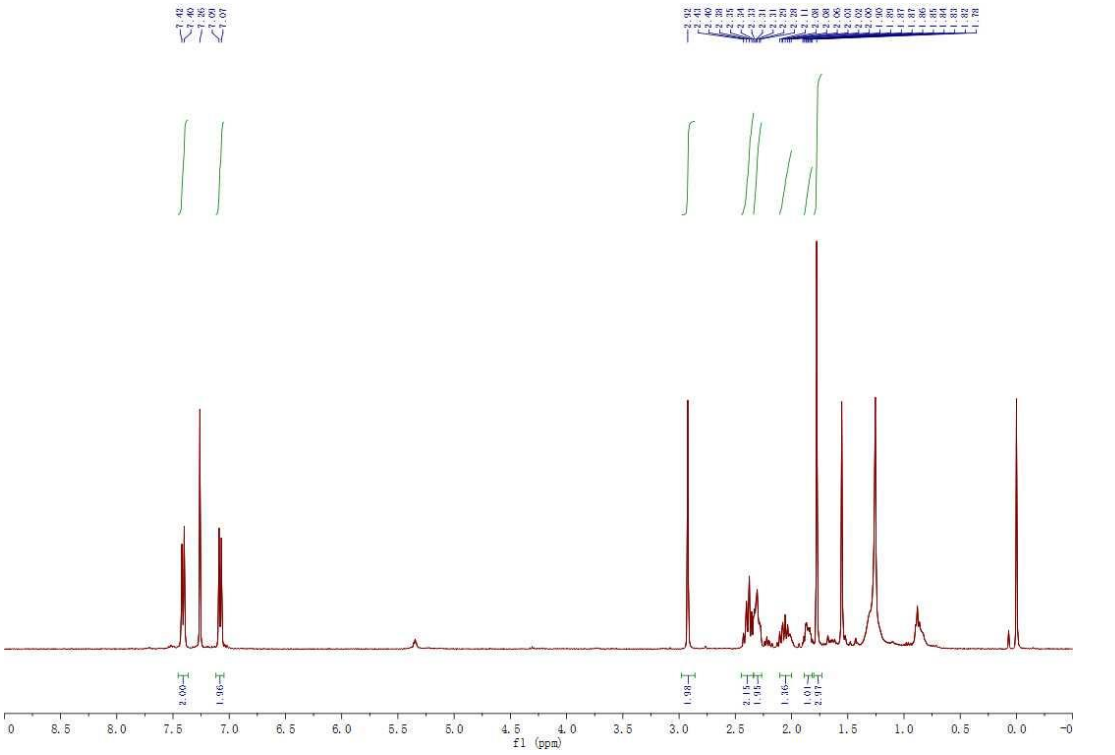
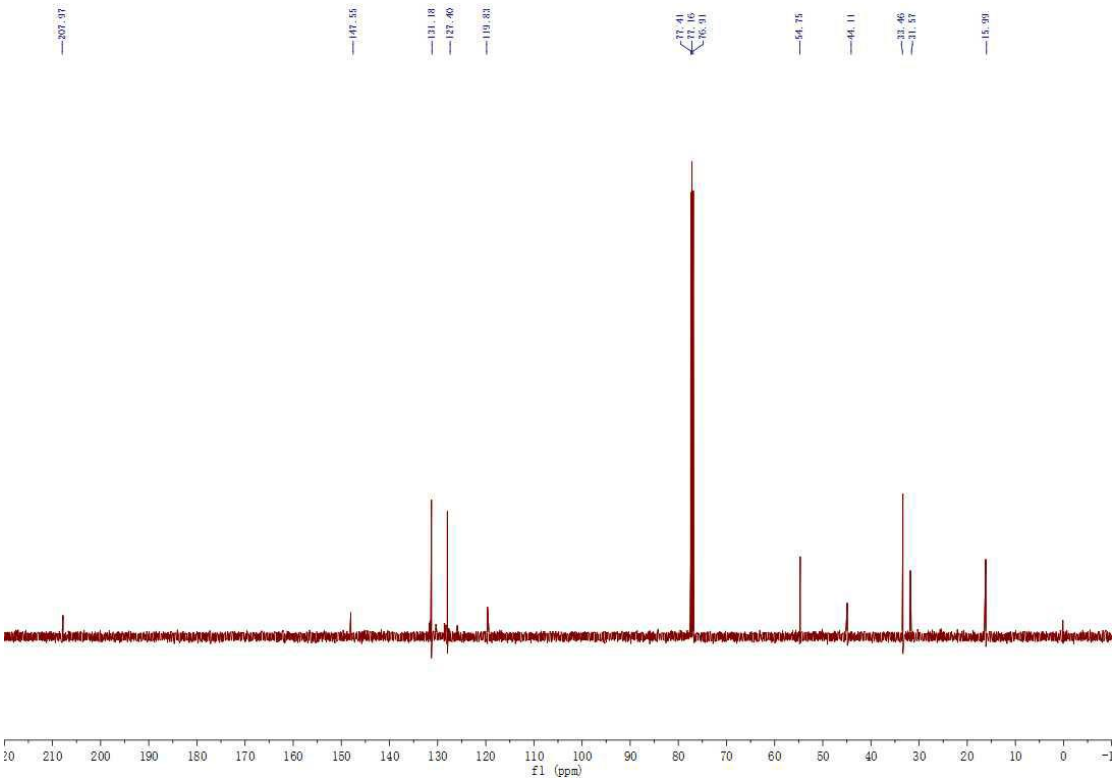


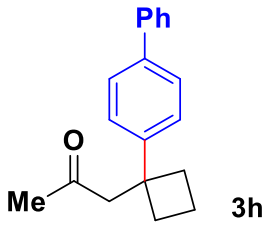




3g







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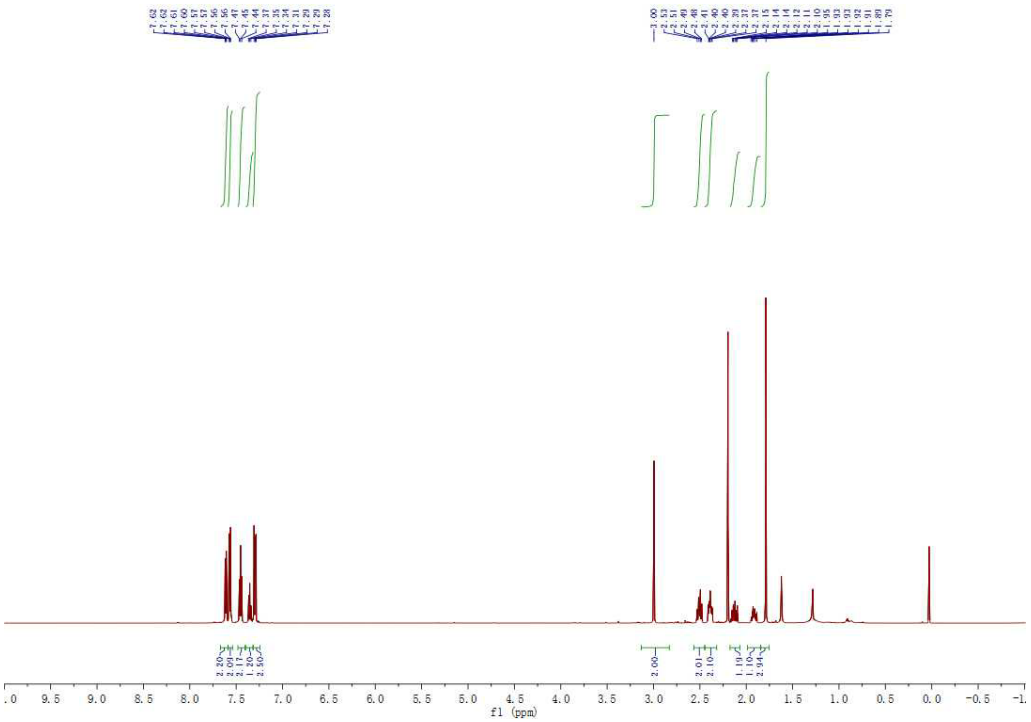

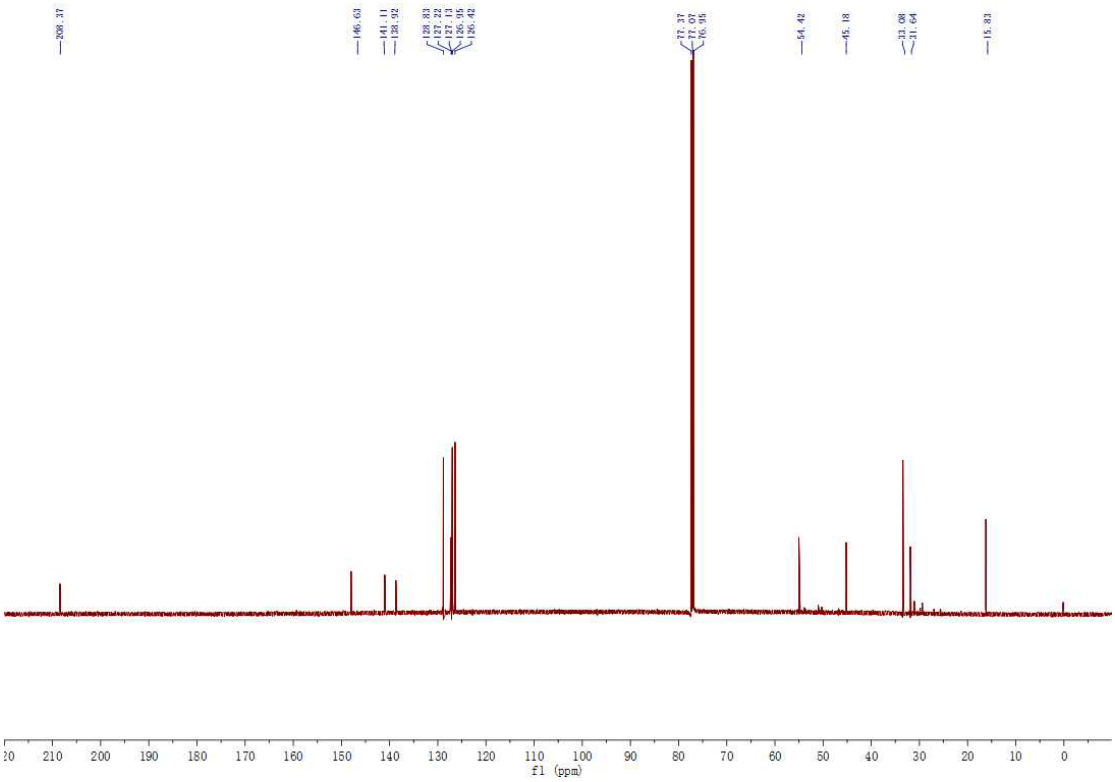

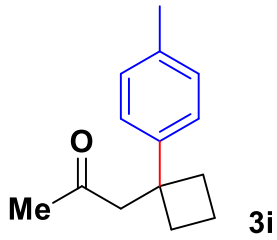

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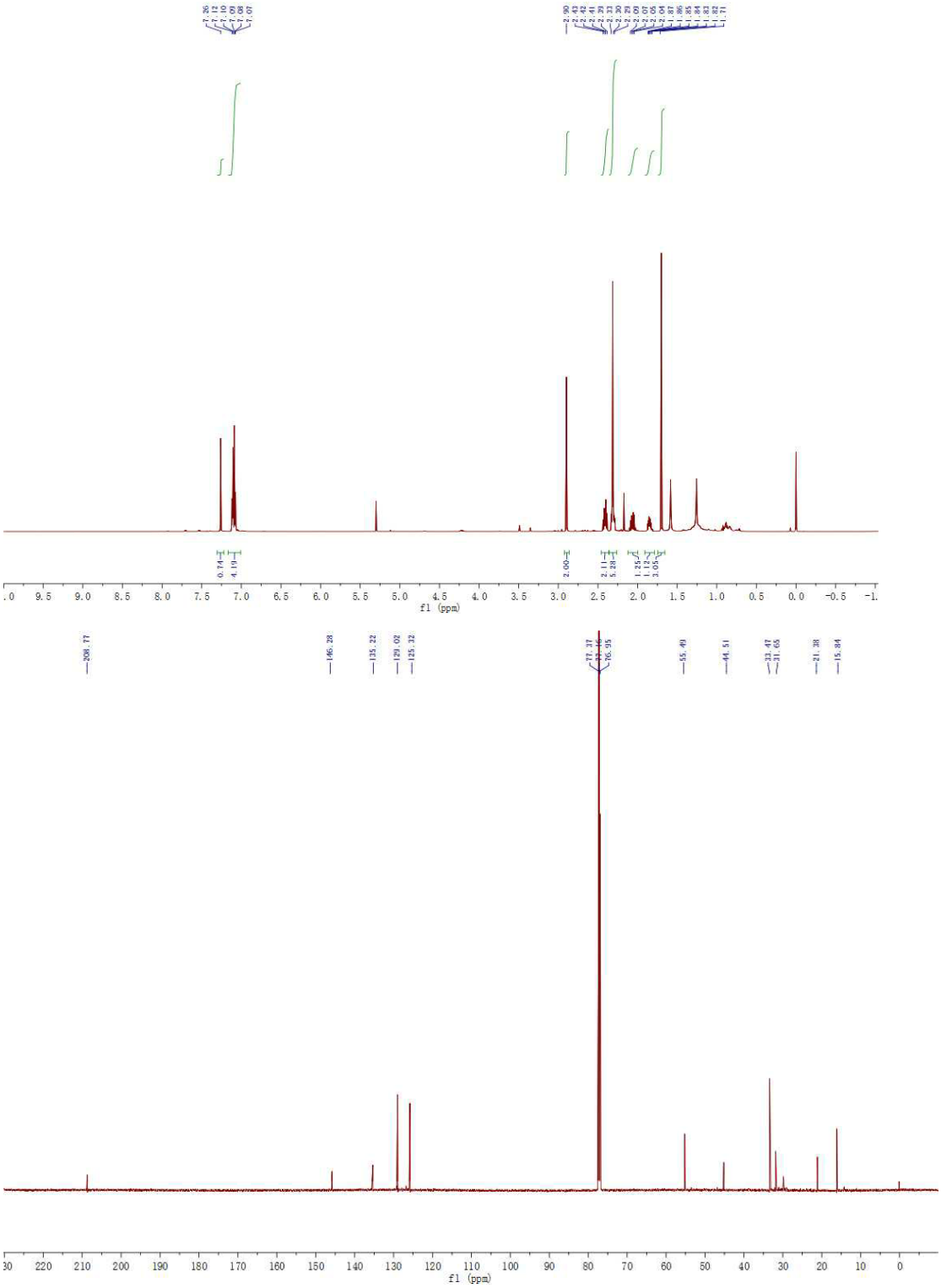

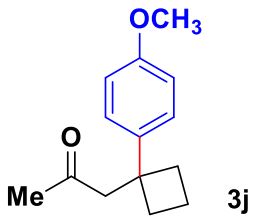

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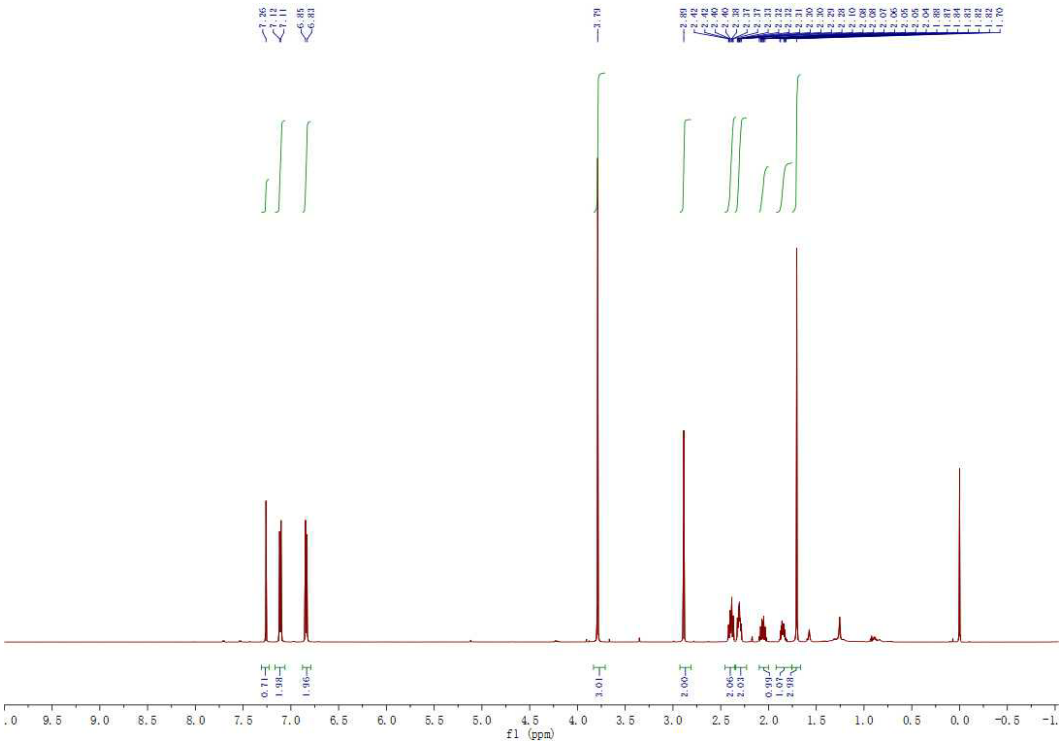
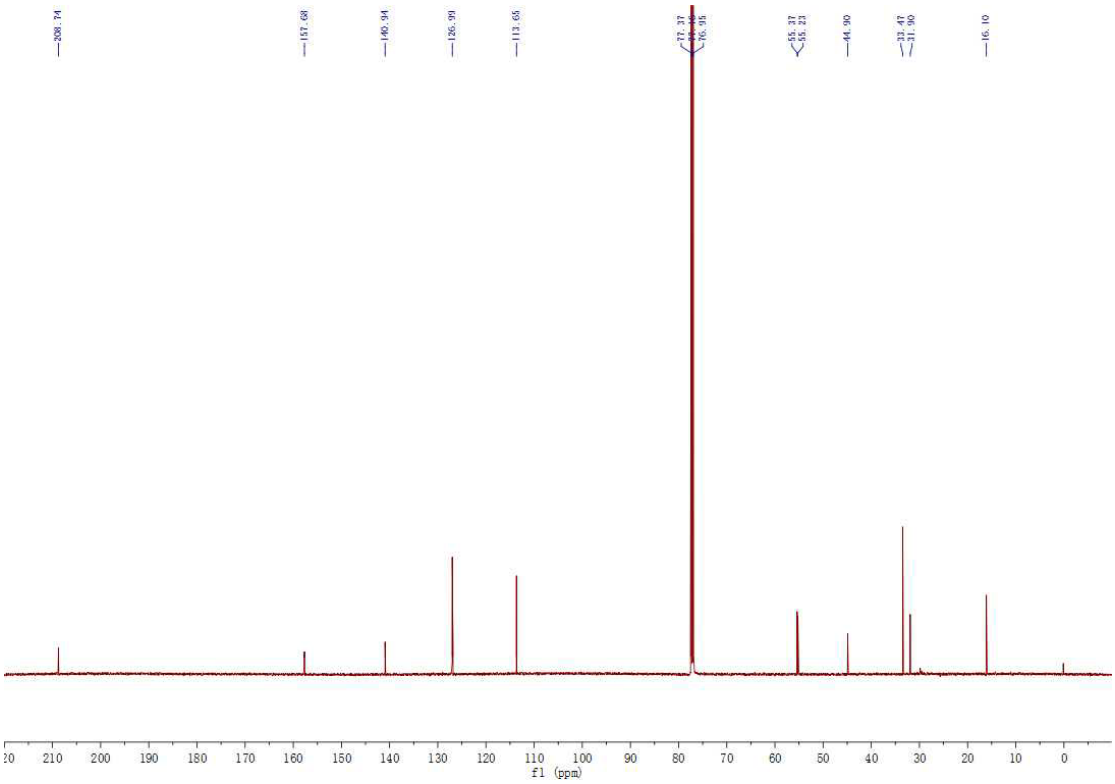
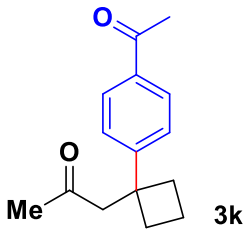
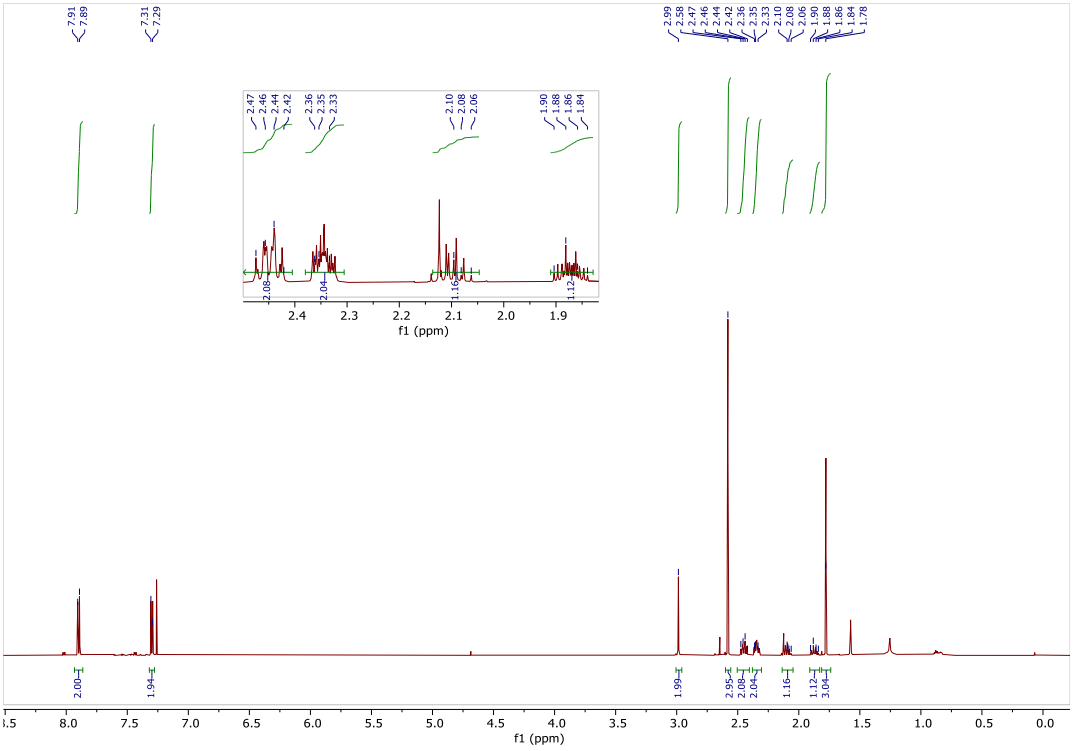





O
O
Me

3k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2.46
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2.42
2.36
2.35
2.33
2.10
2.08
2.06
1.90
1.88
1.86
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f1 (ppm)
2.00
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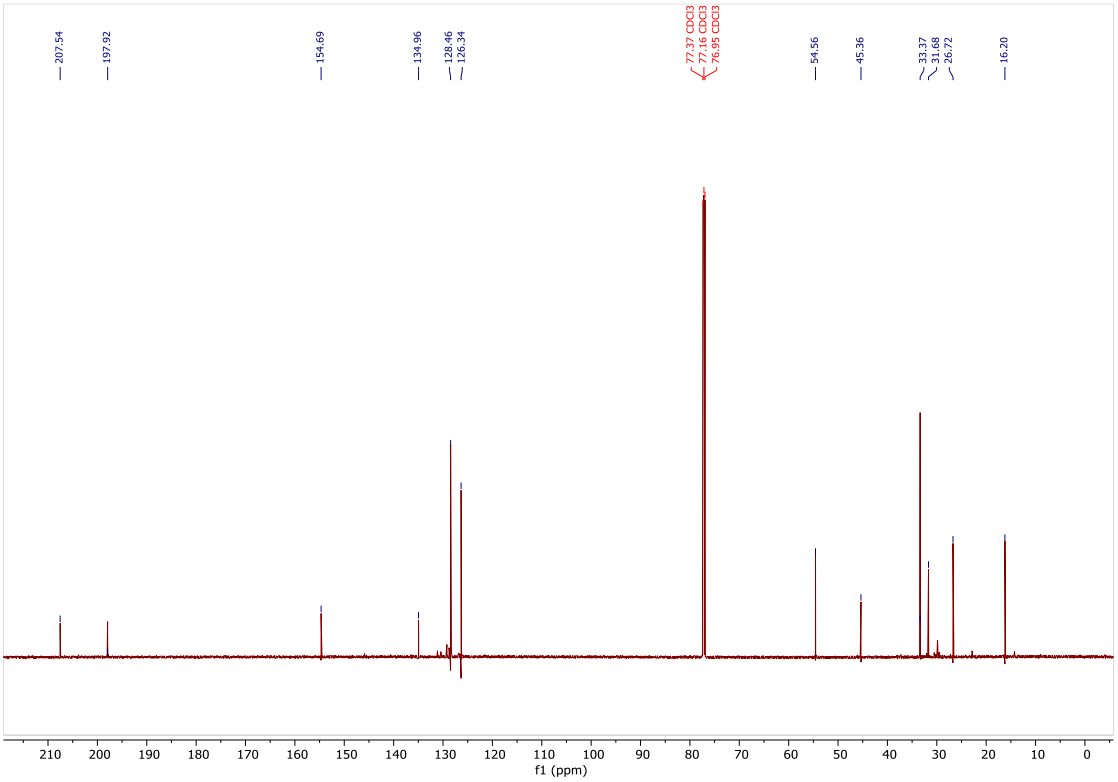
1.99
2.95
2.08
2.04
1.16
1.12
3.04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197.92
154.69
134.96
128.46
126.34
77.37 CDCl3
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31.68
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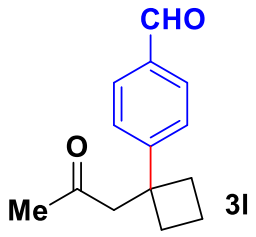
f1 (ppm)



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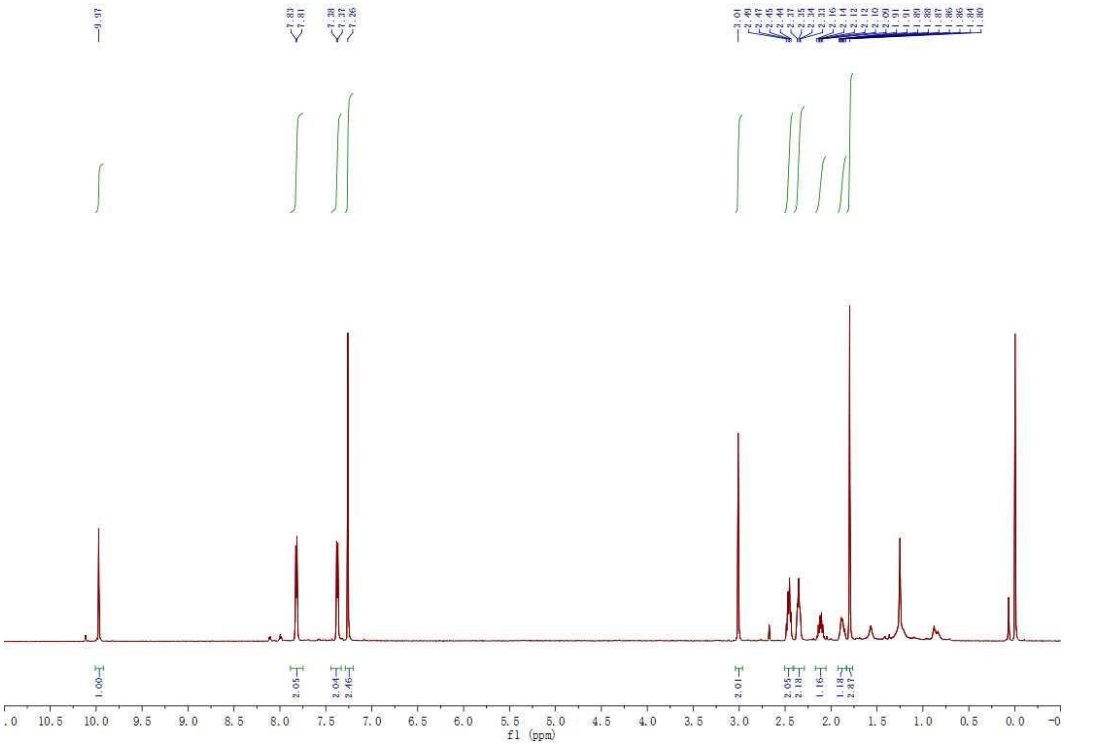
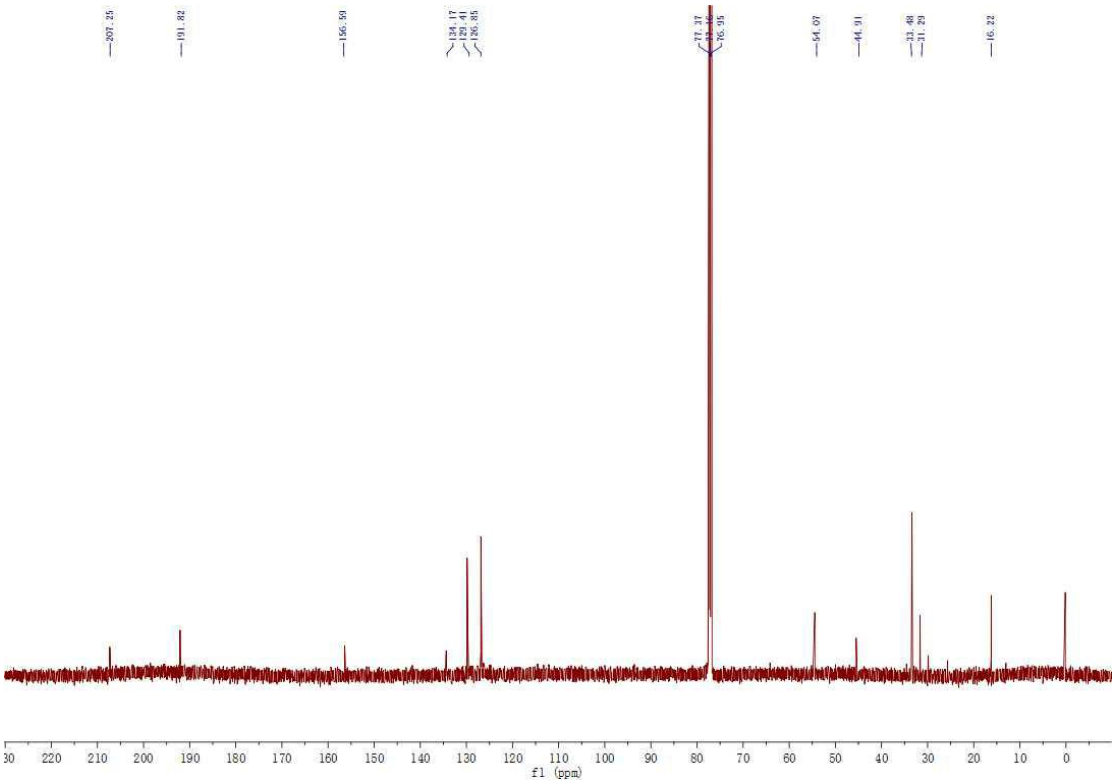
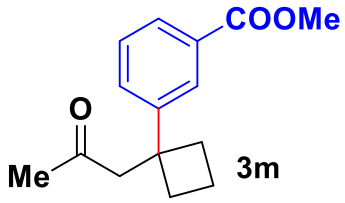
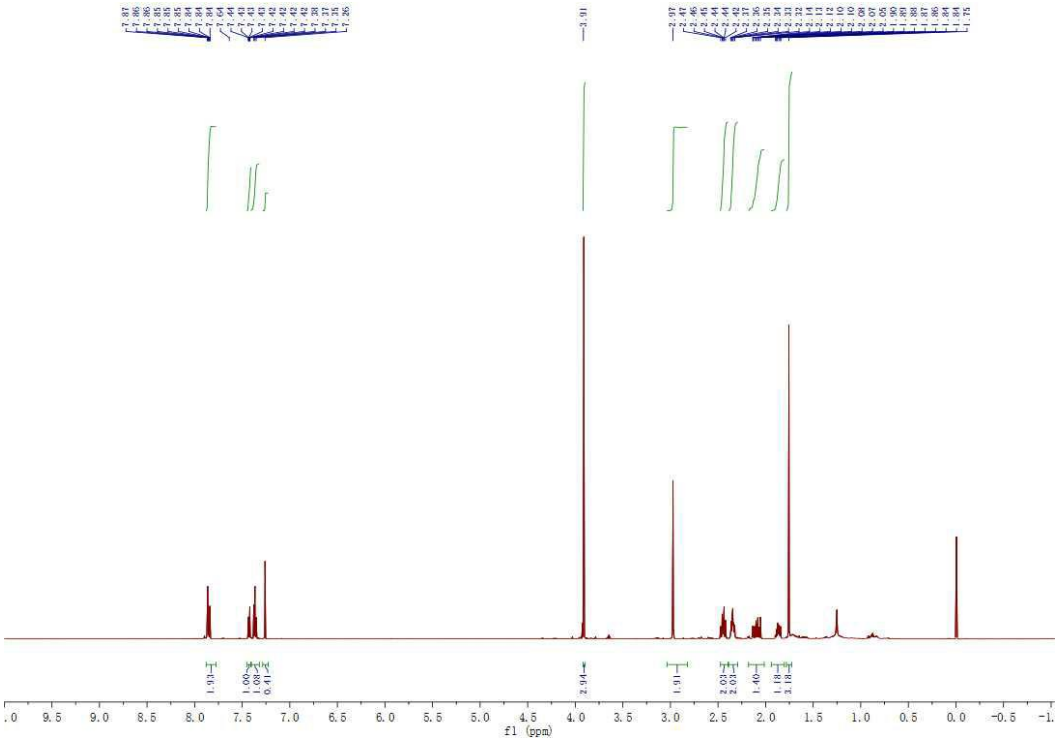





COOMe
O
Me
3m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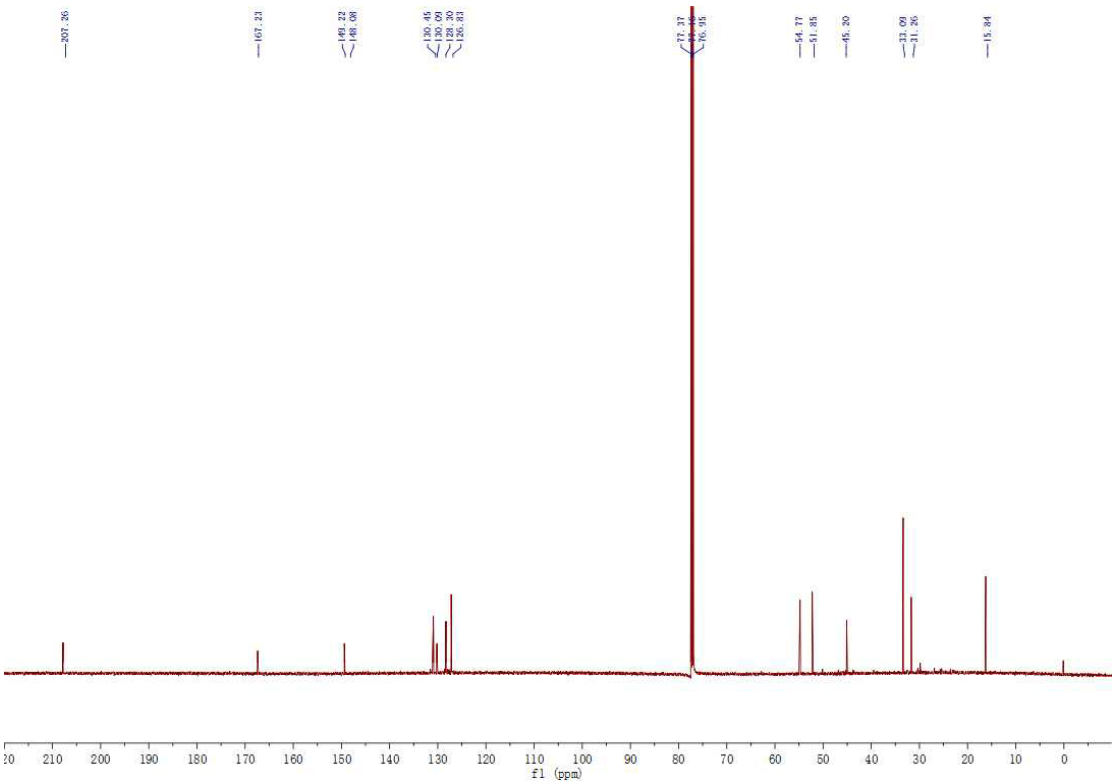
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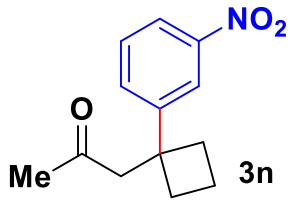
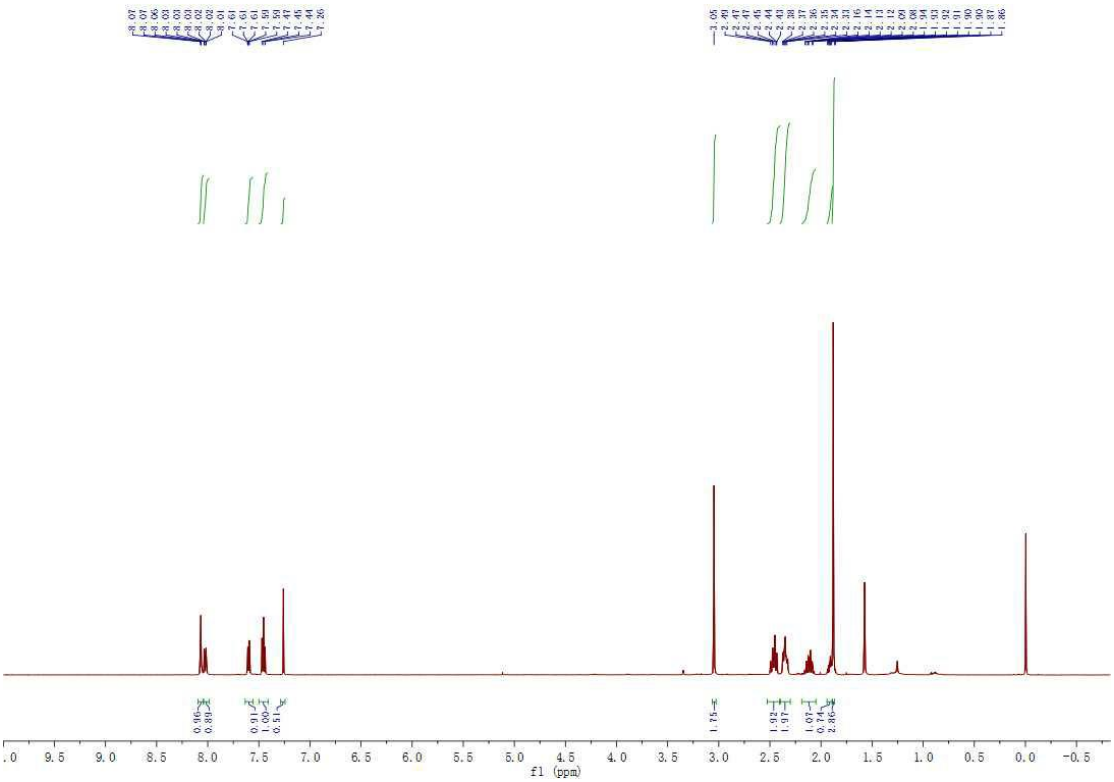

NO2
O
Me
3n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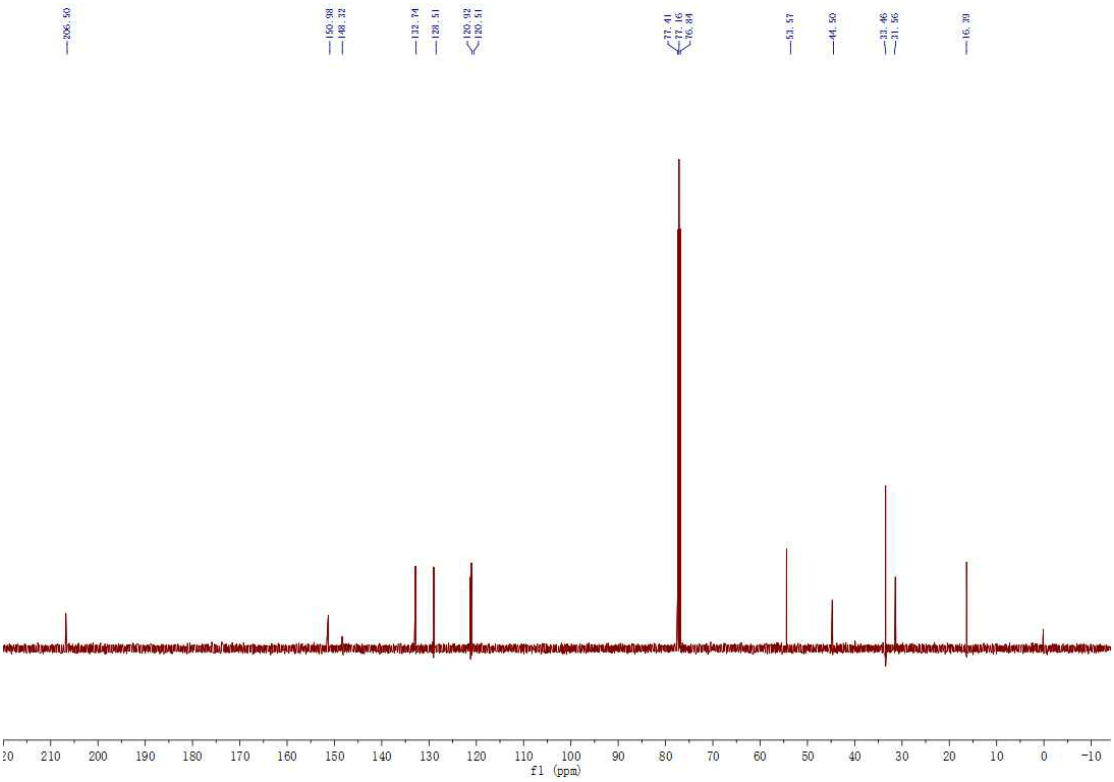
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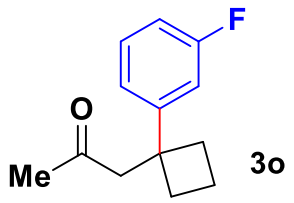
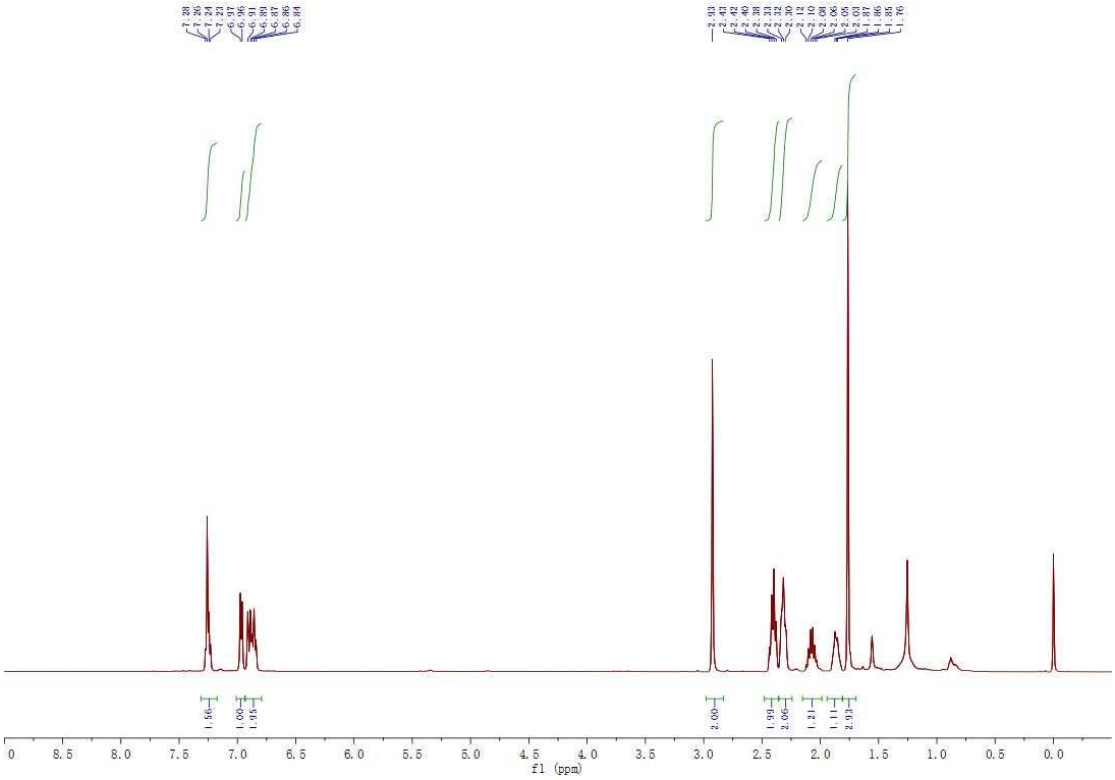
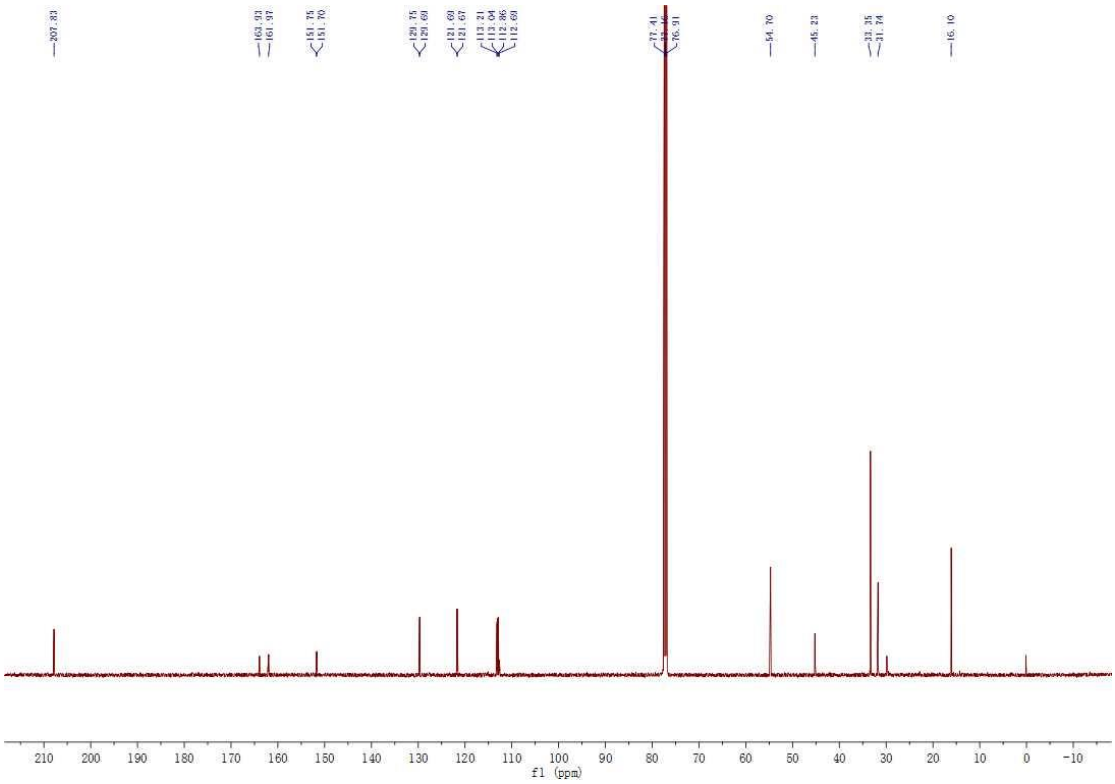
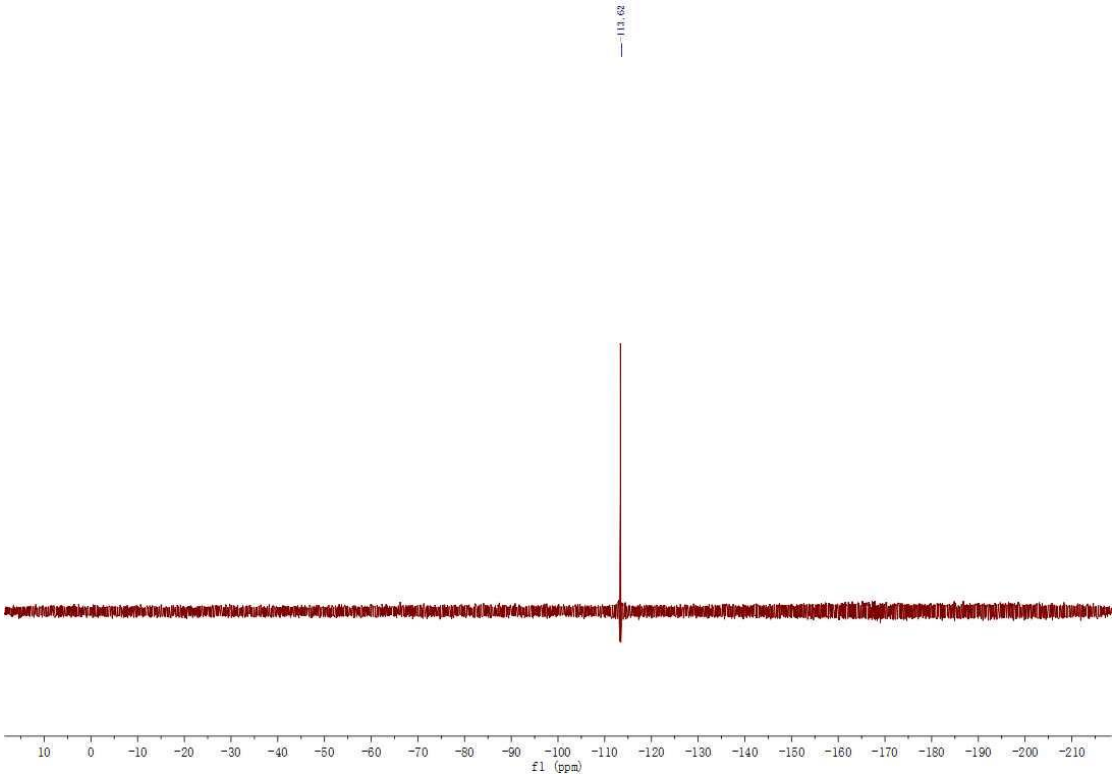


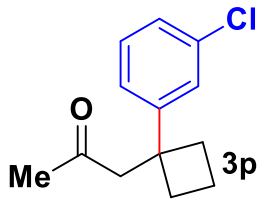
3o

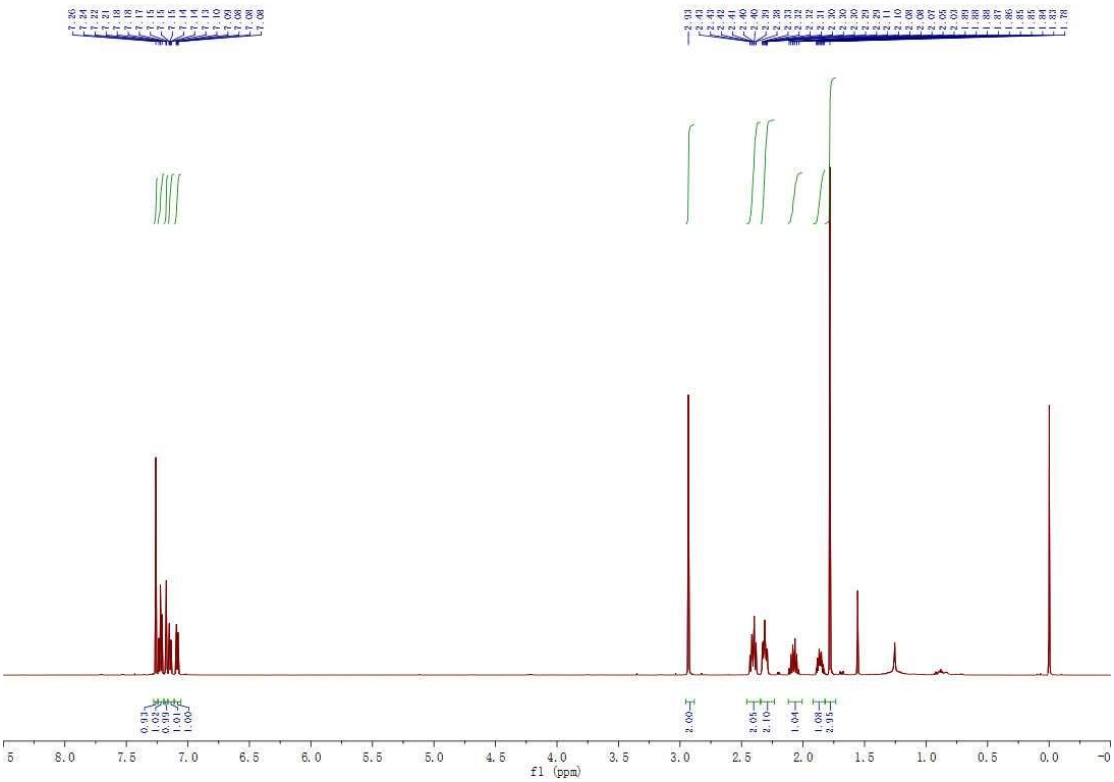




^{19}F NMR of **3o** (376 MHZ, $CDCl_3$)




Cl
O
Me
3p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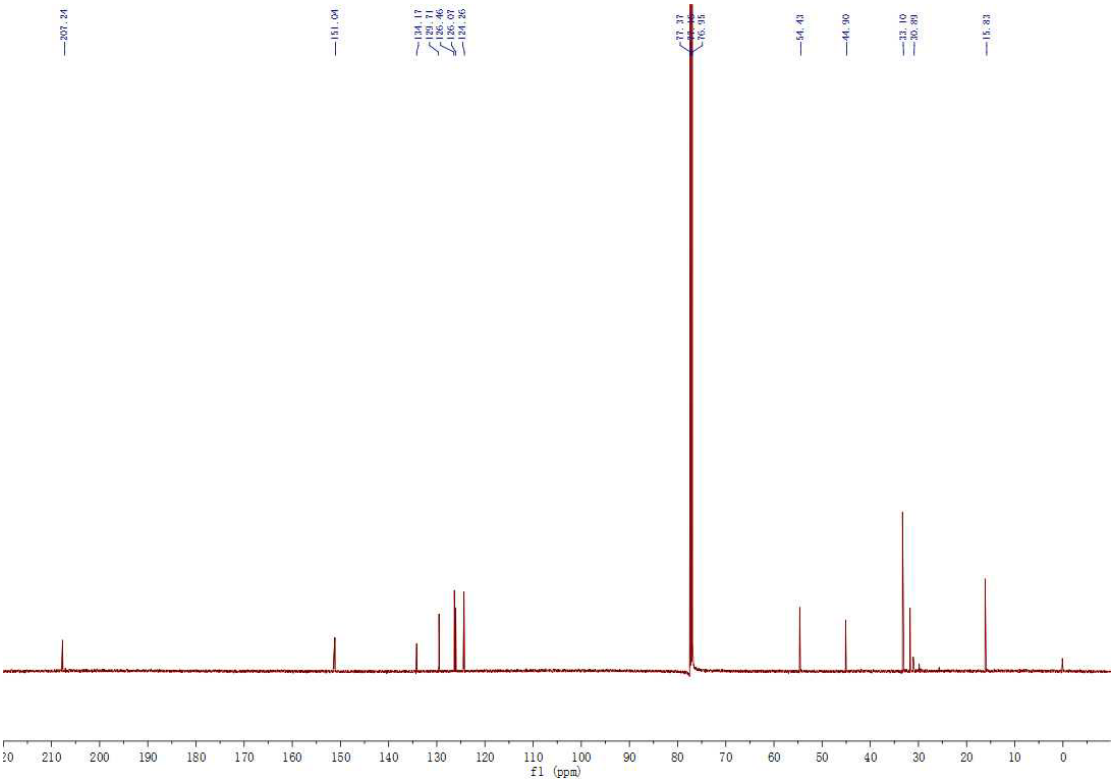
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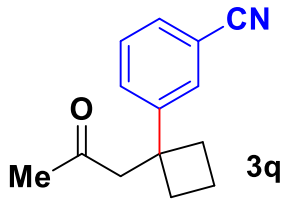

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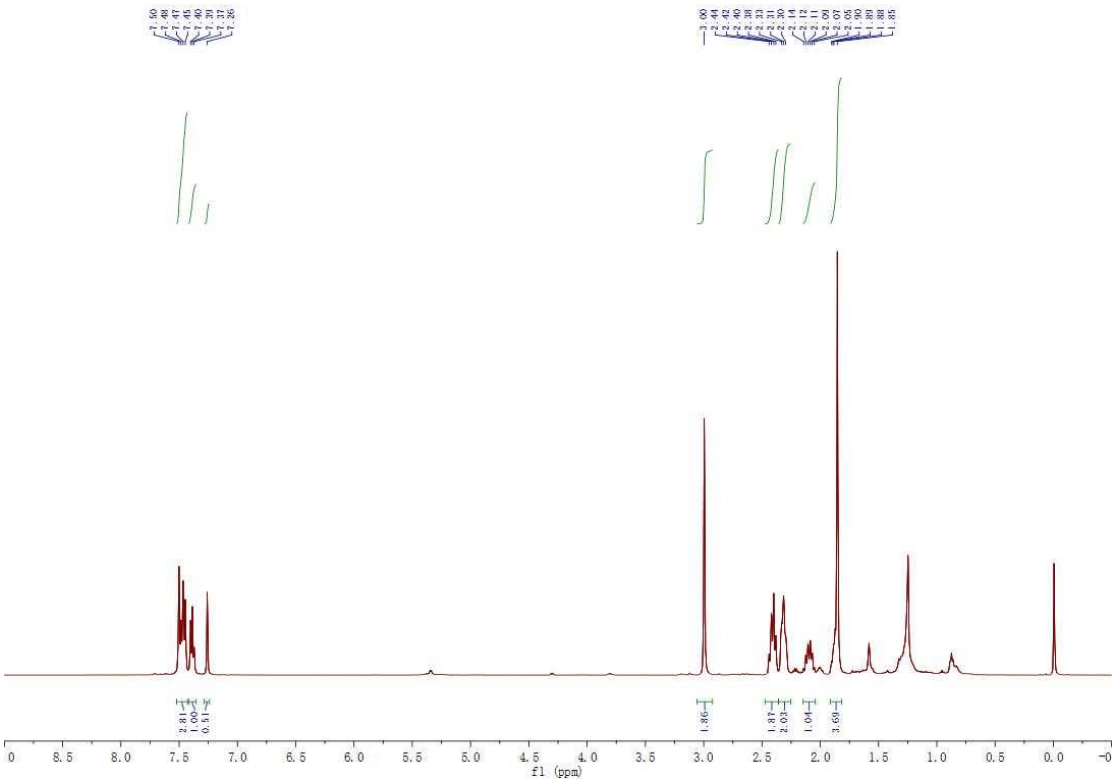
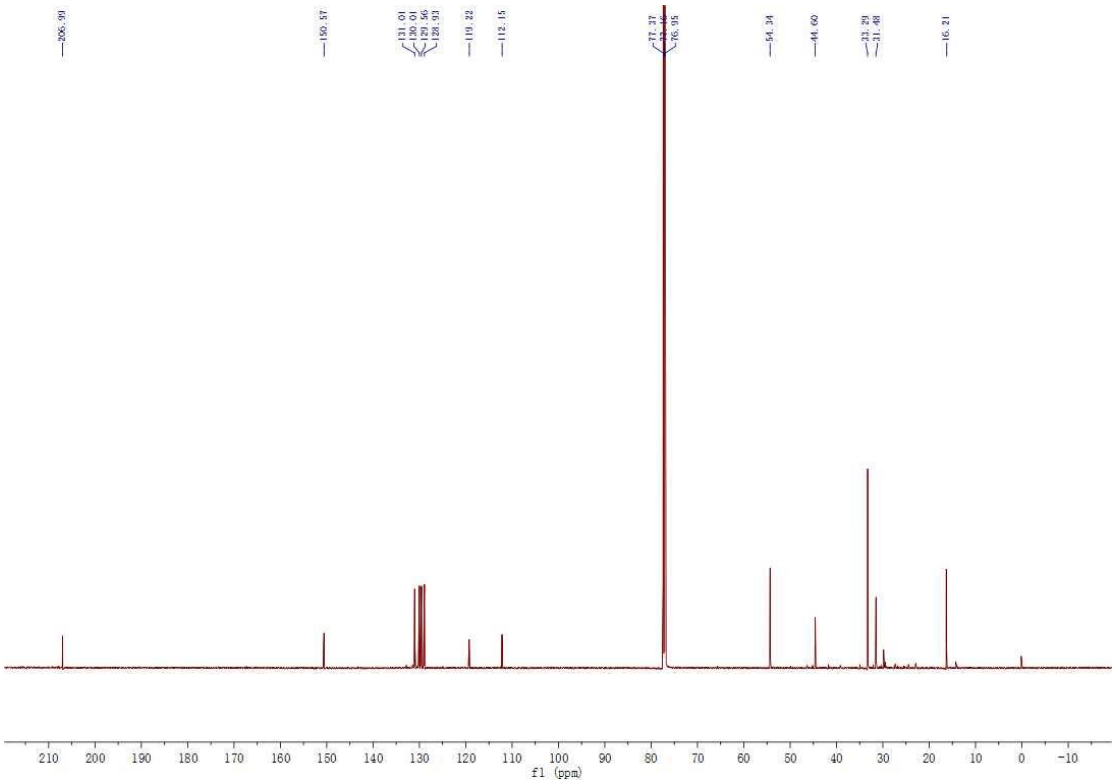
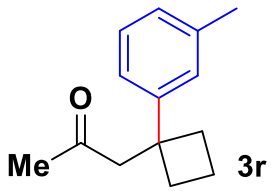
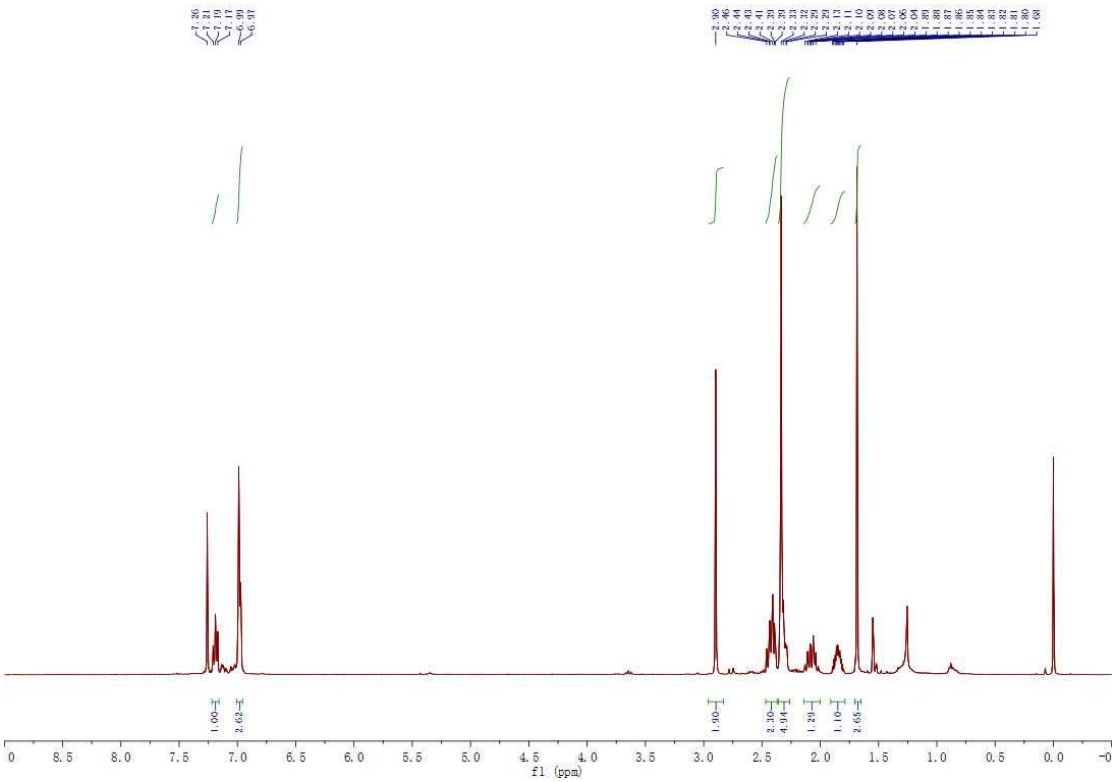





O
Me
3r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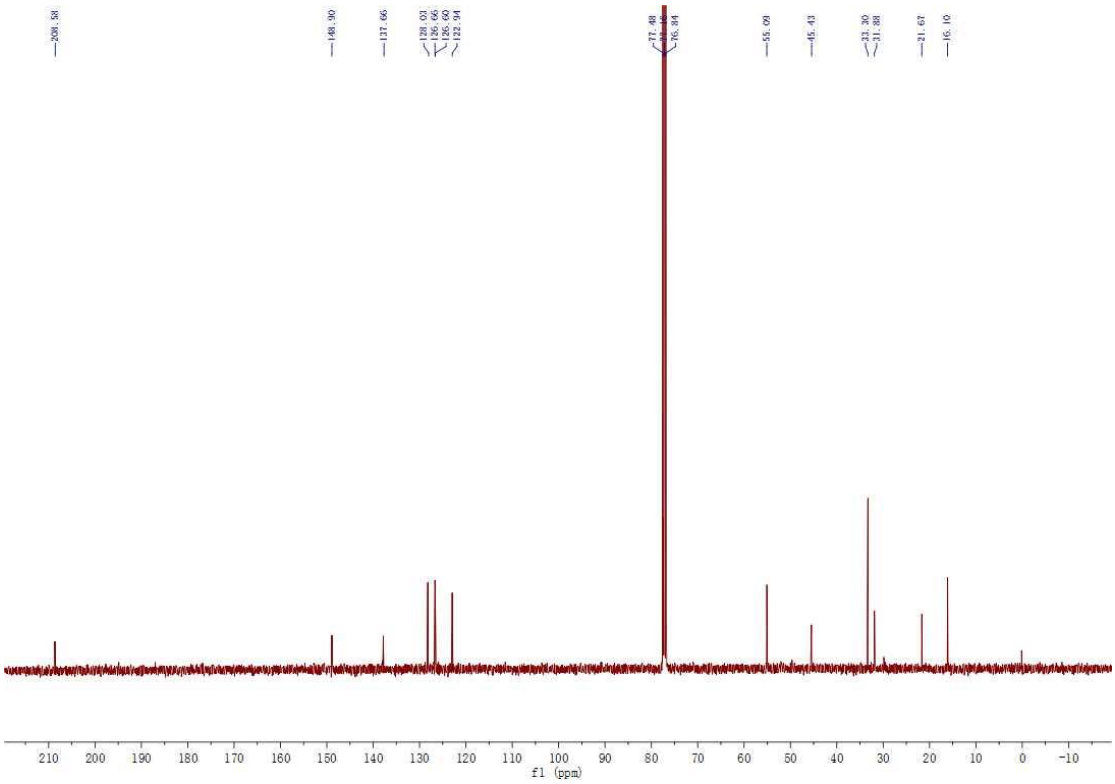
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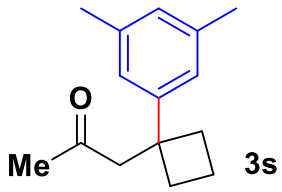

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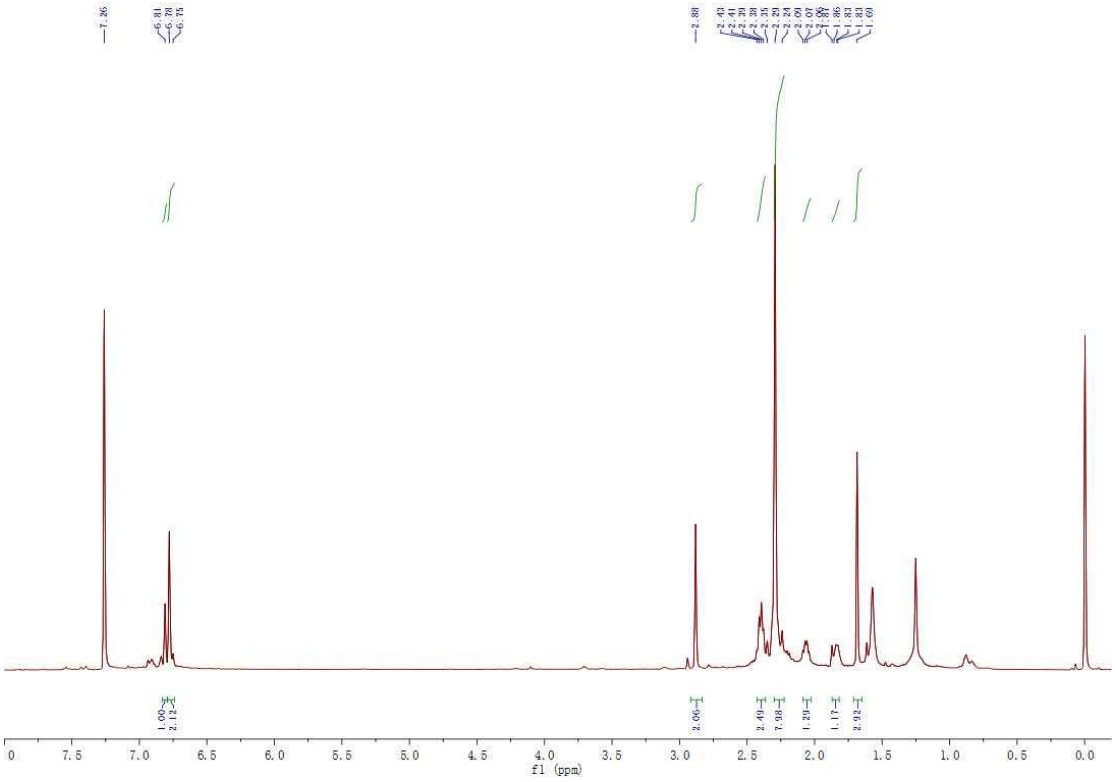

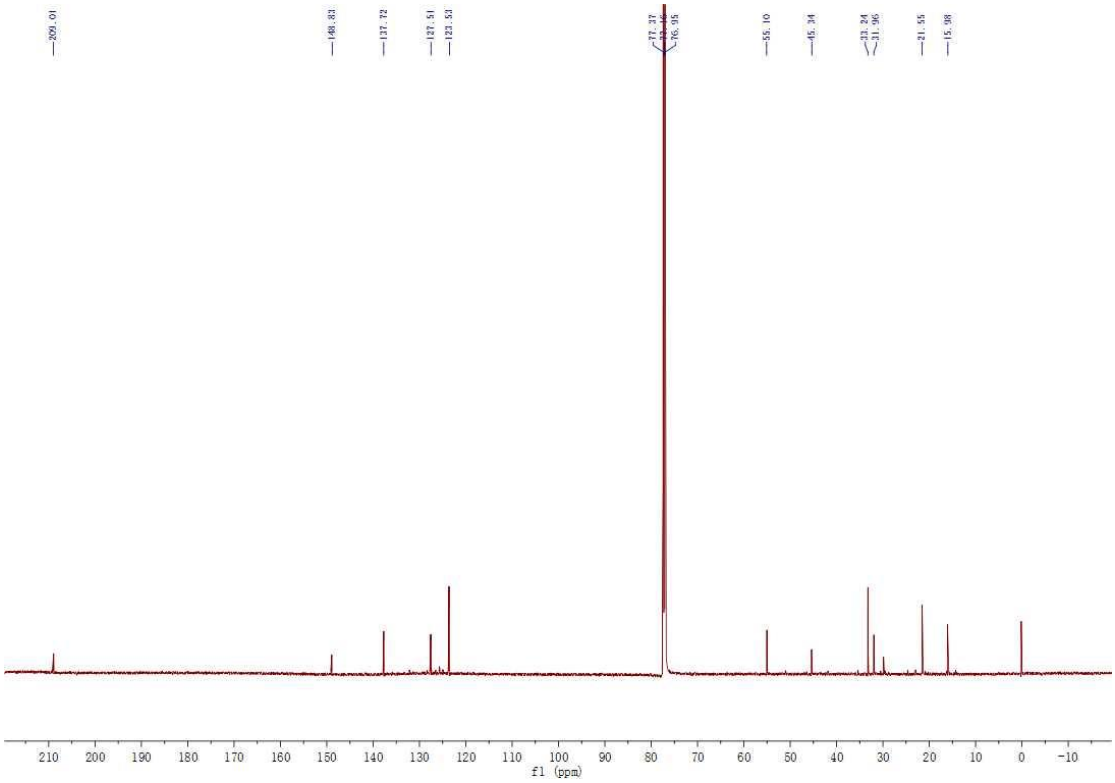

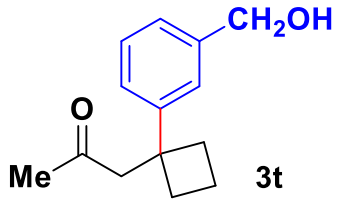

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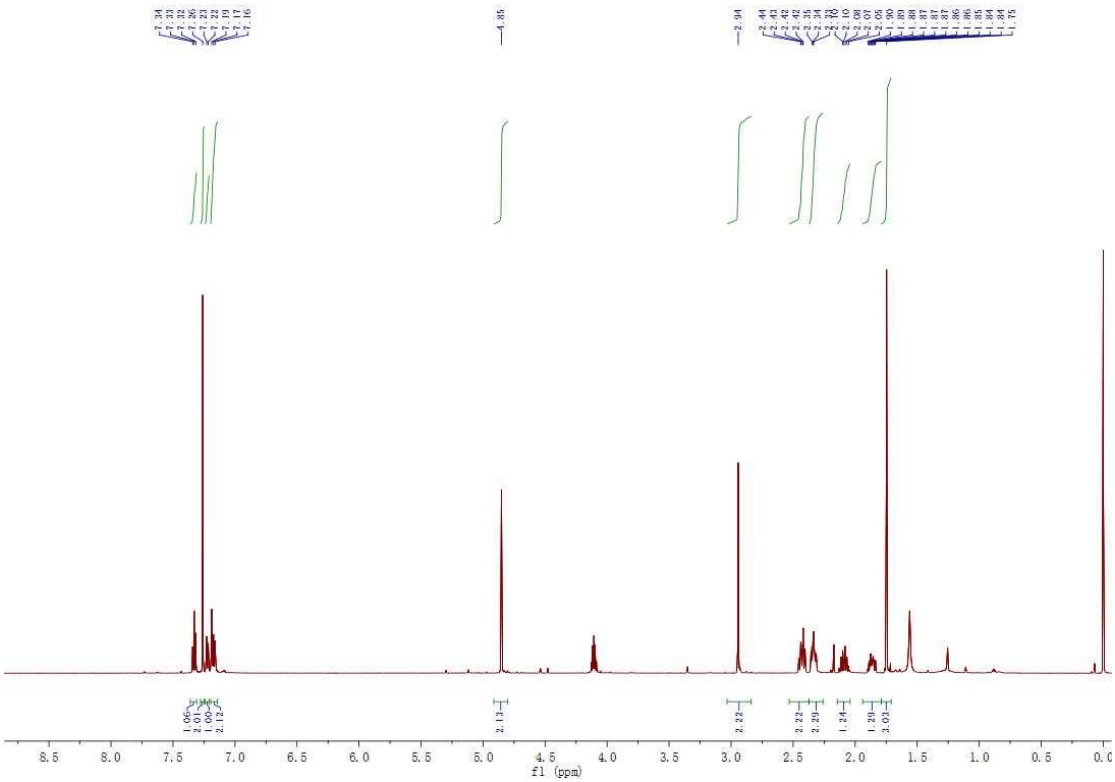

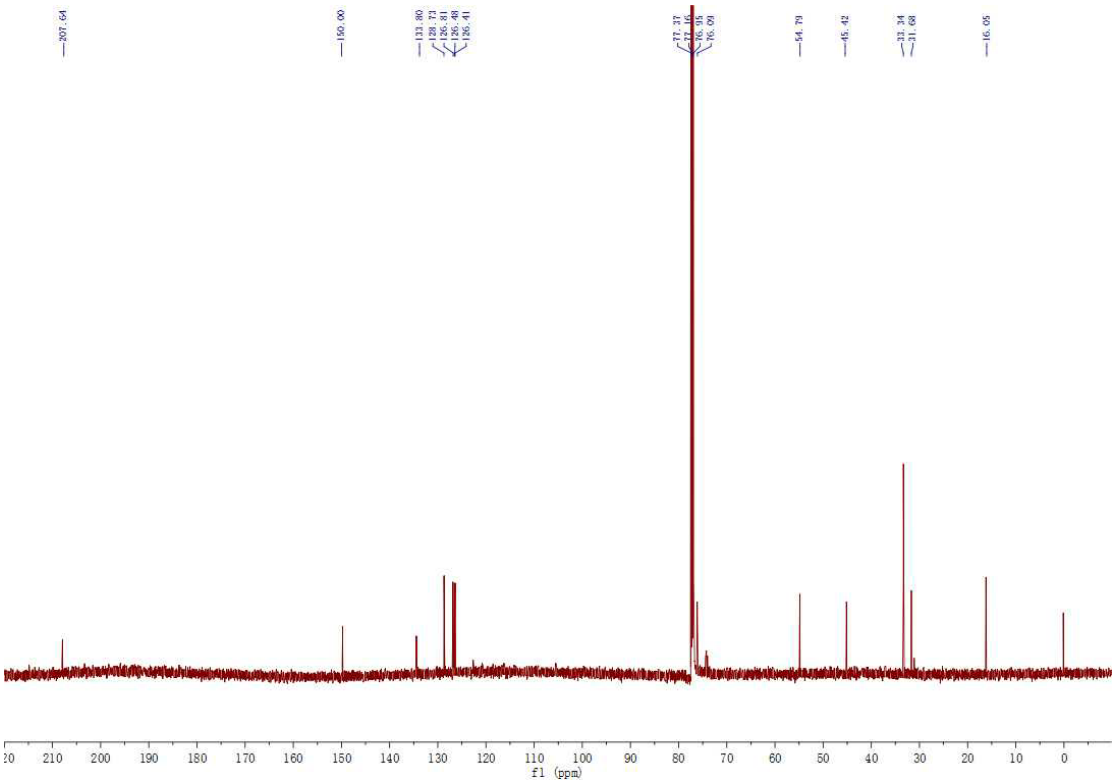

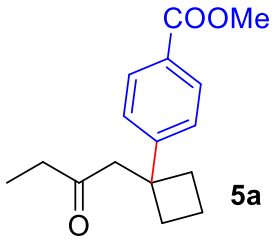

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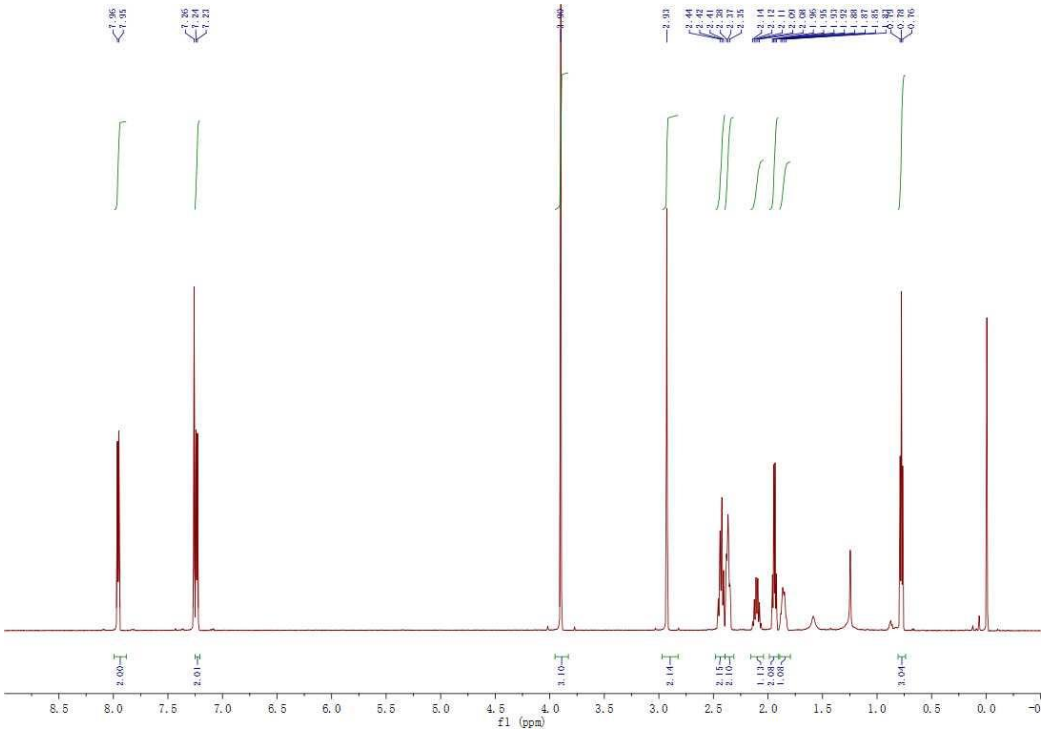

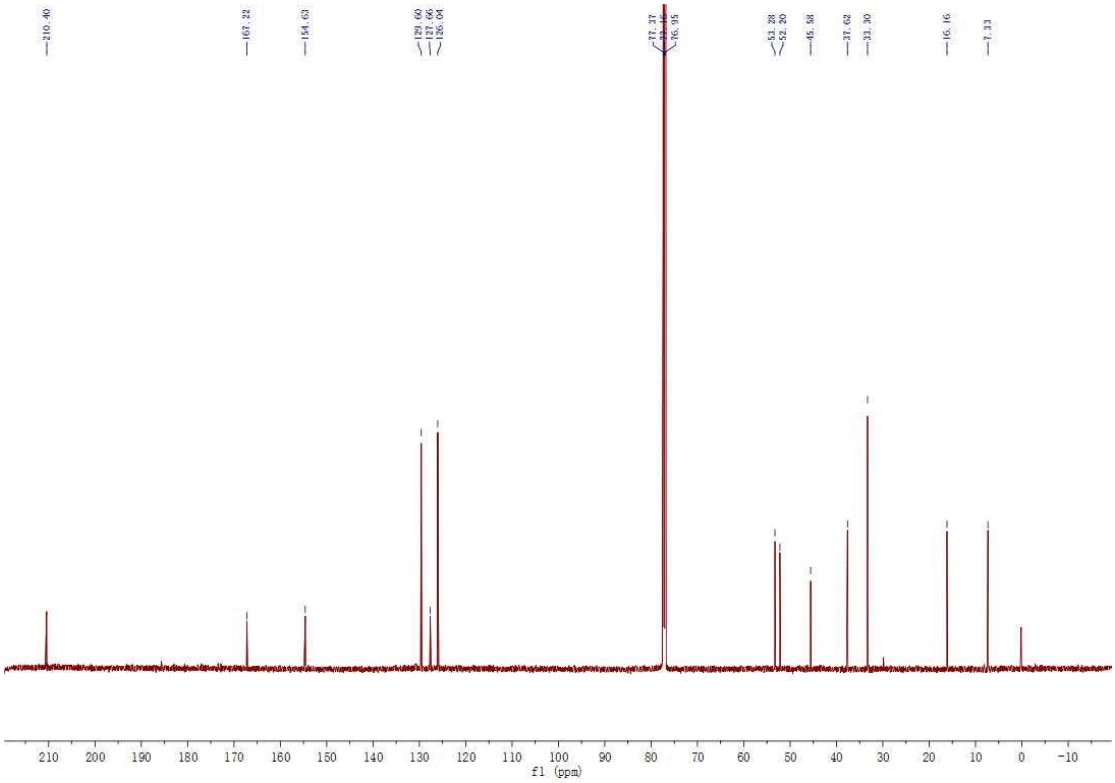

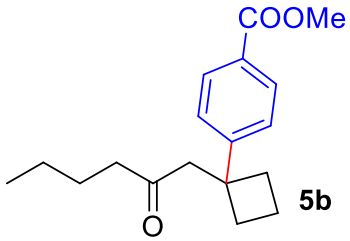

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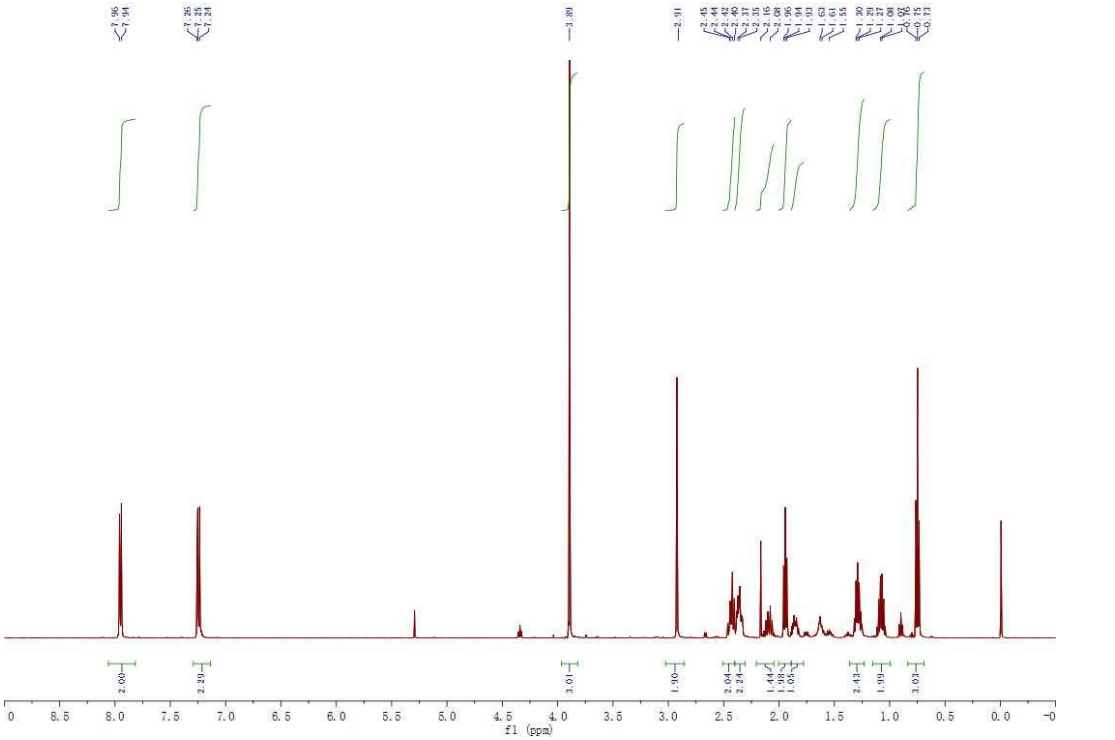

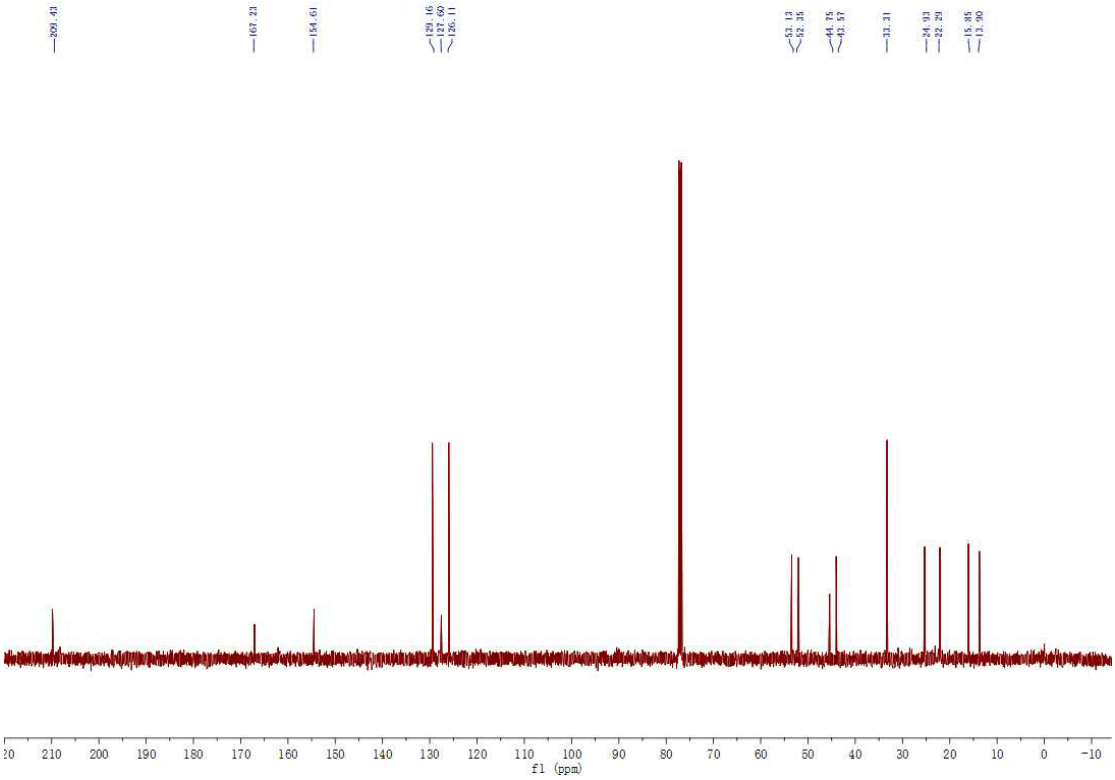

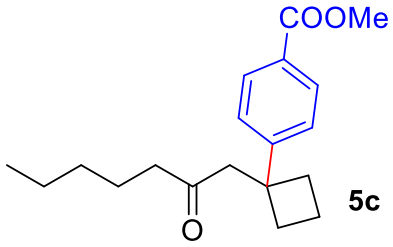

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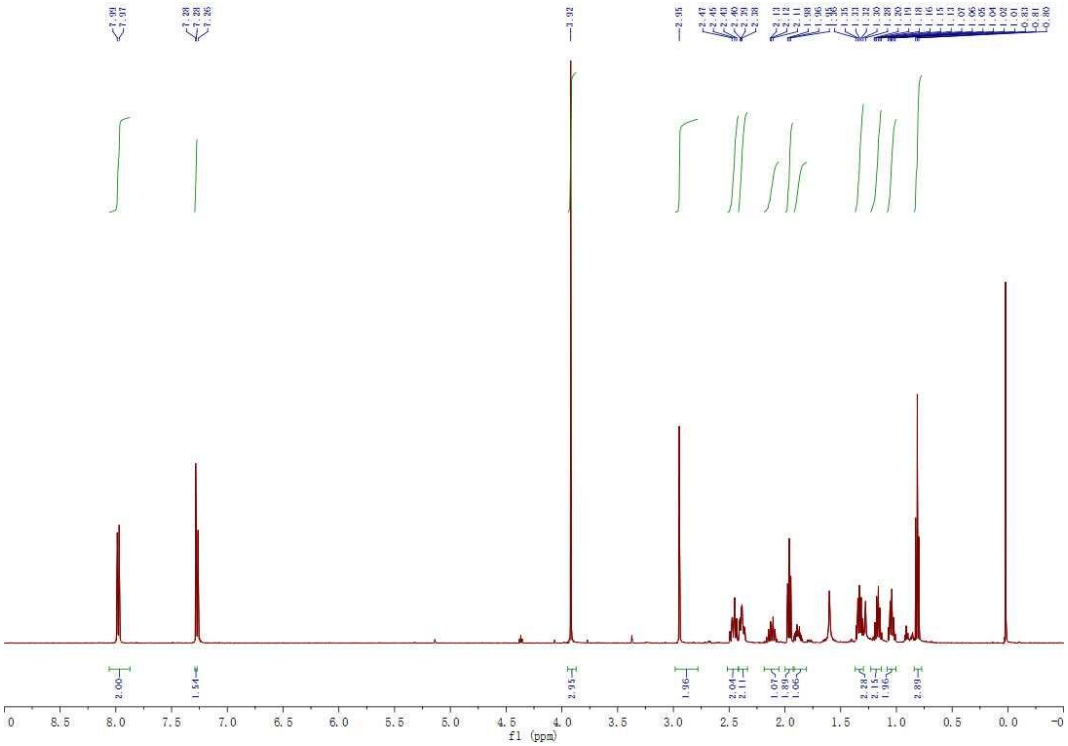

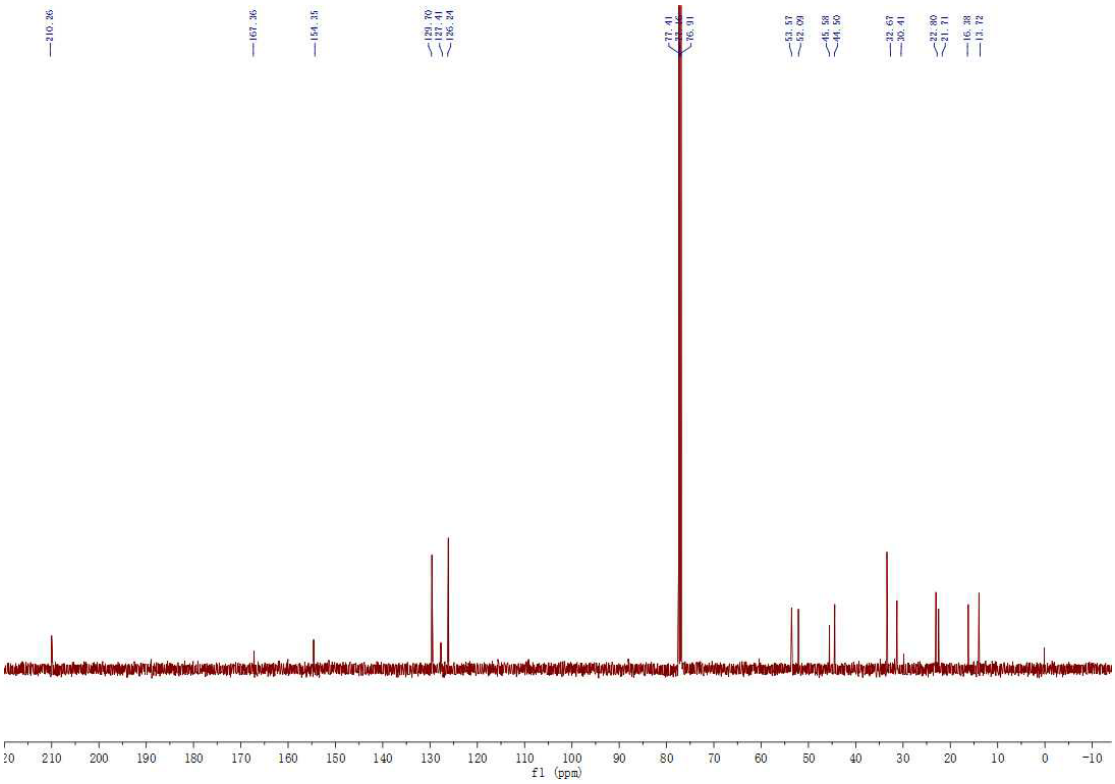

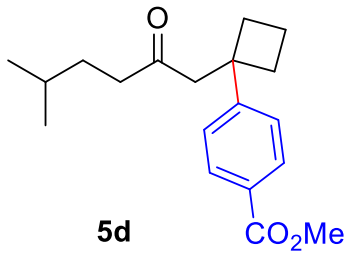

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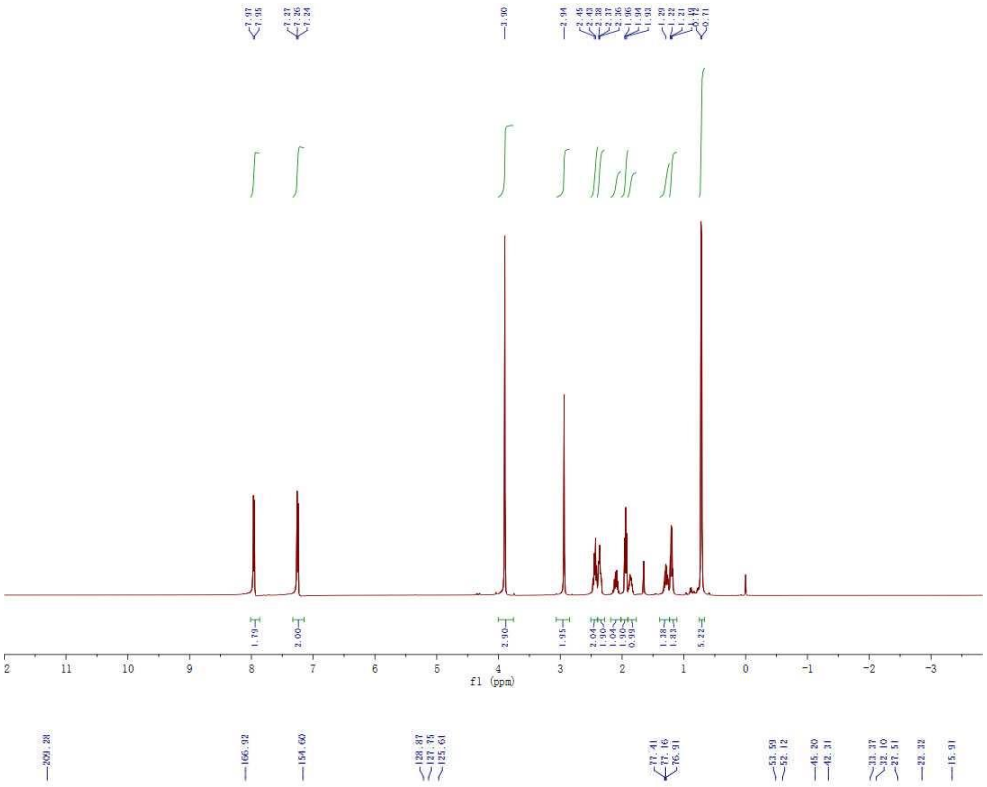

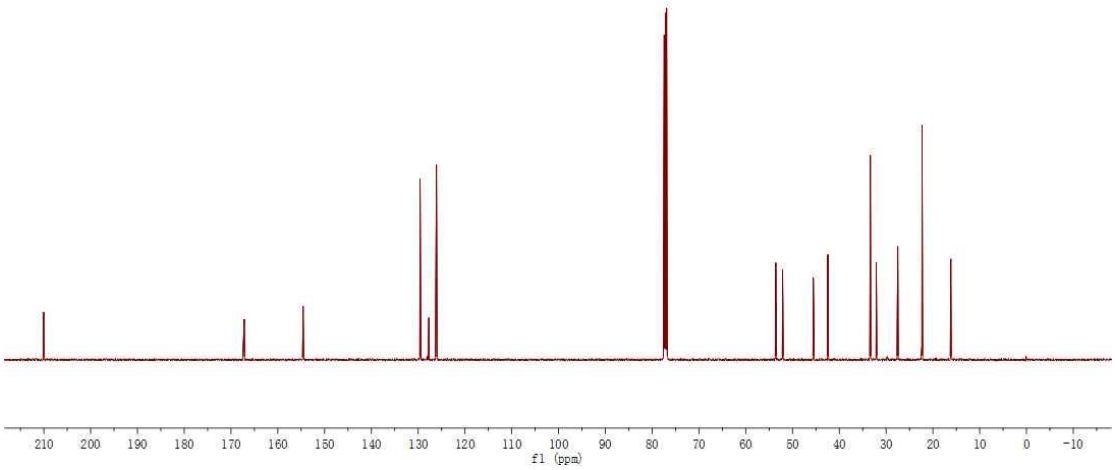

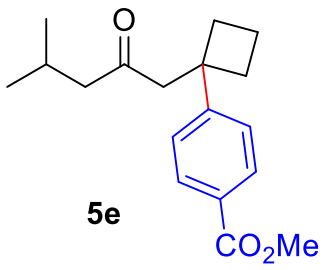

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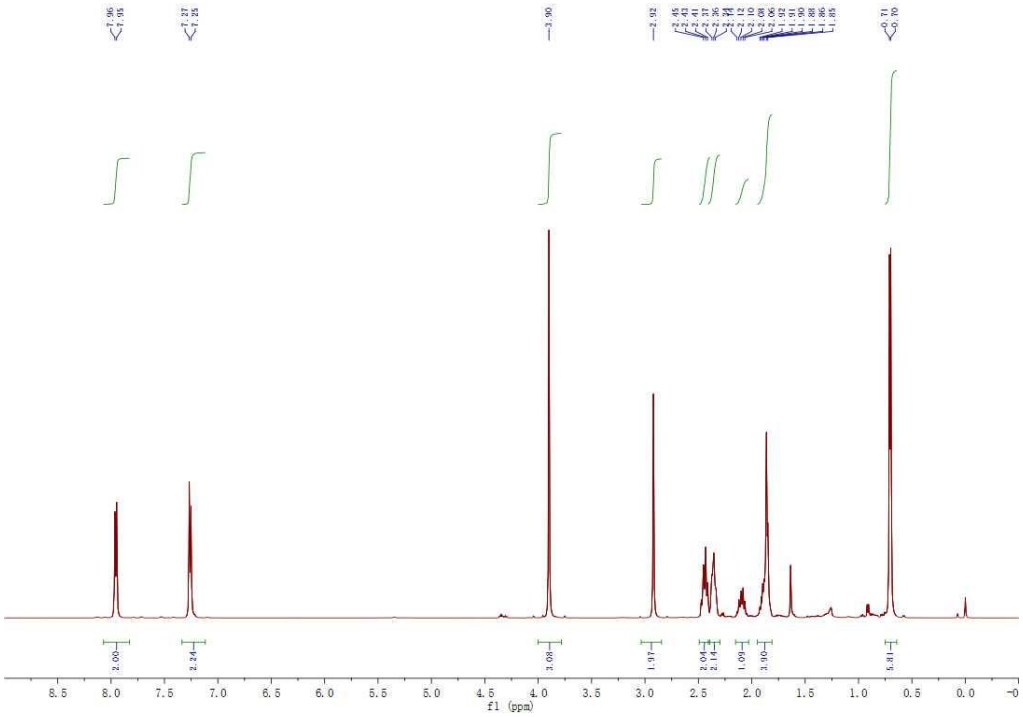

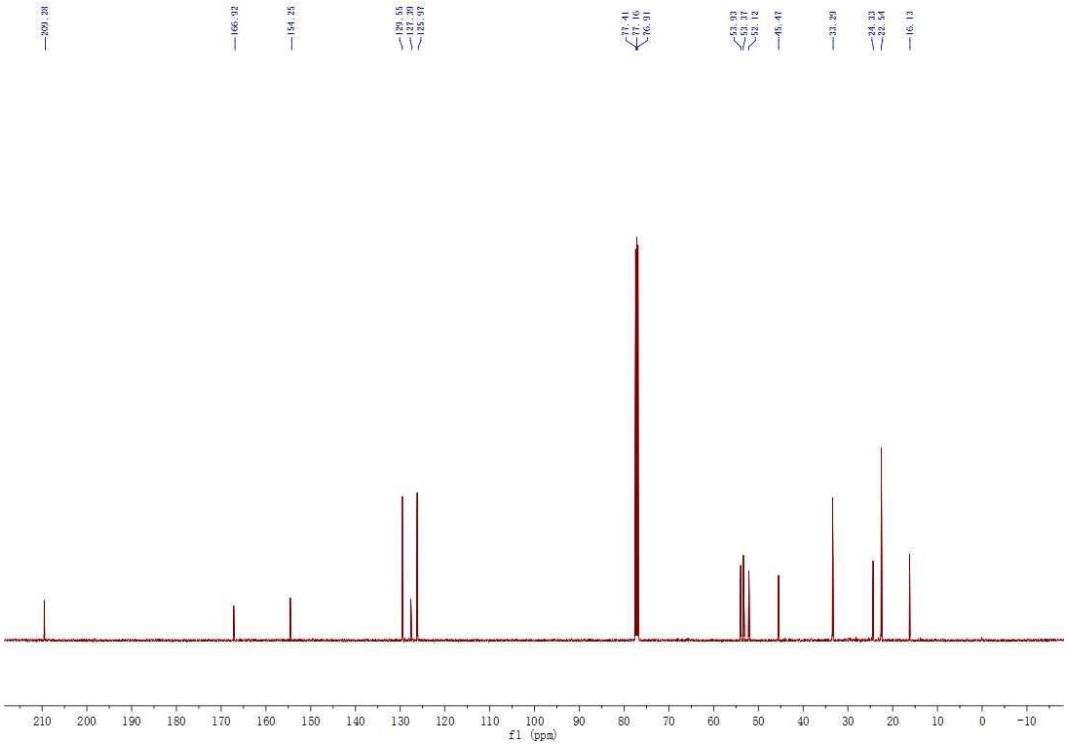

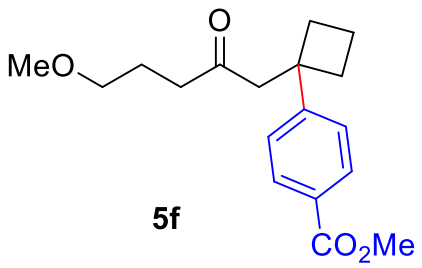

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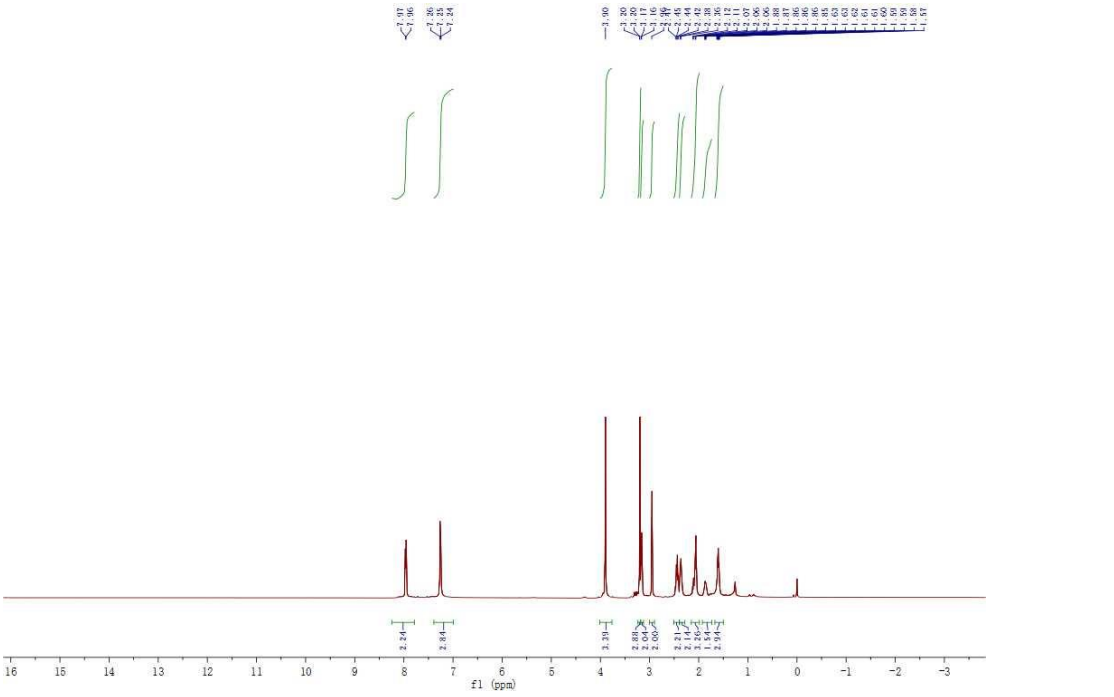
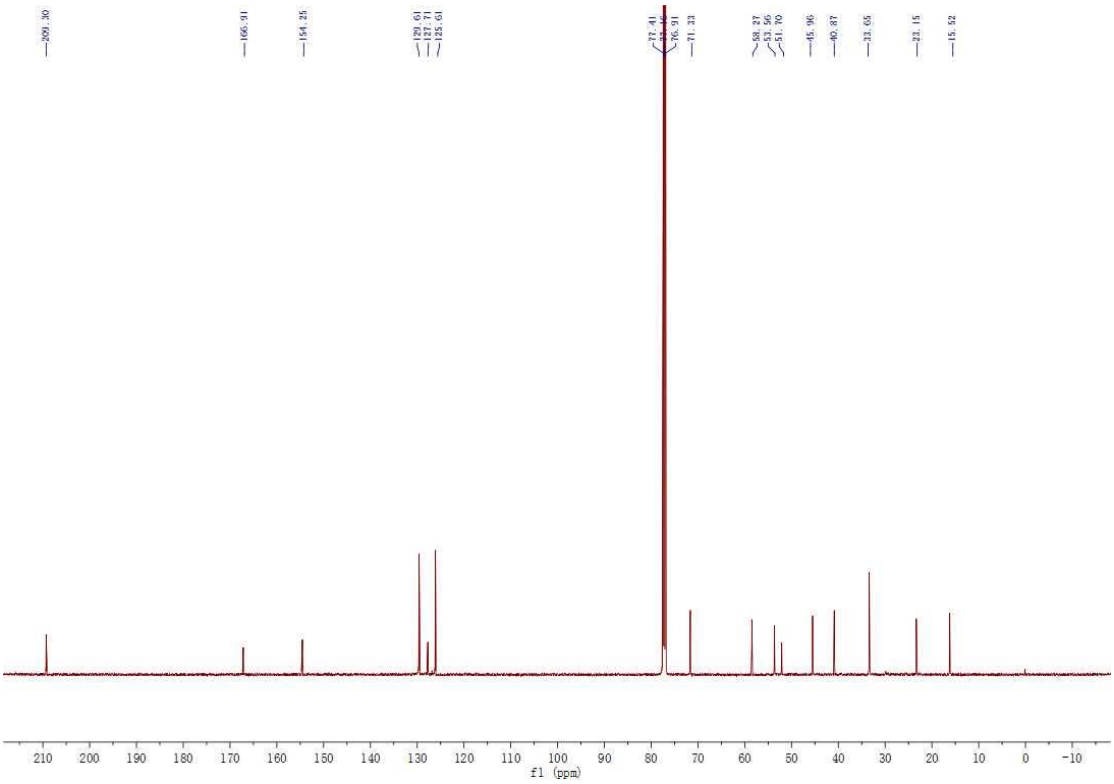
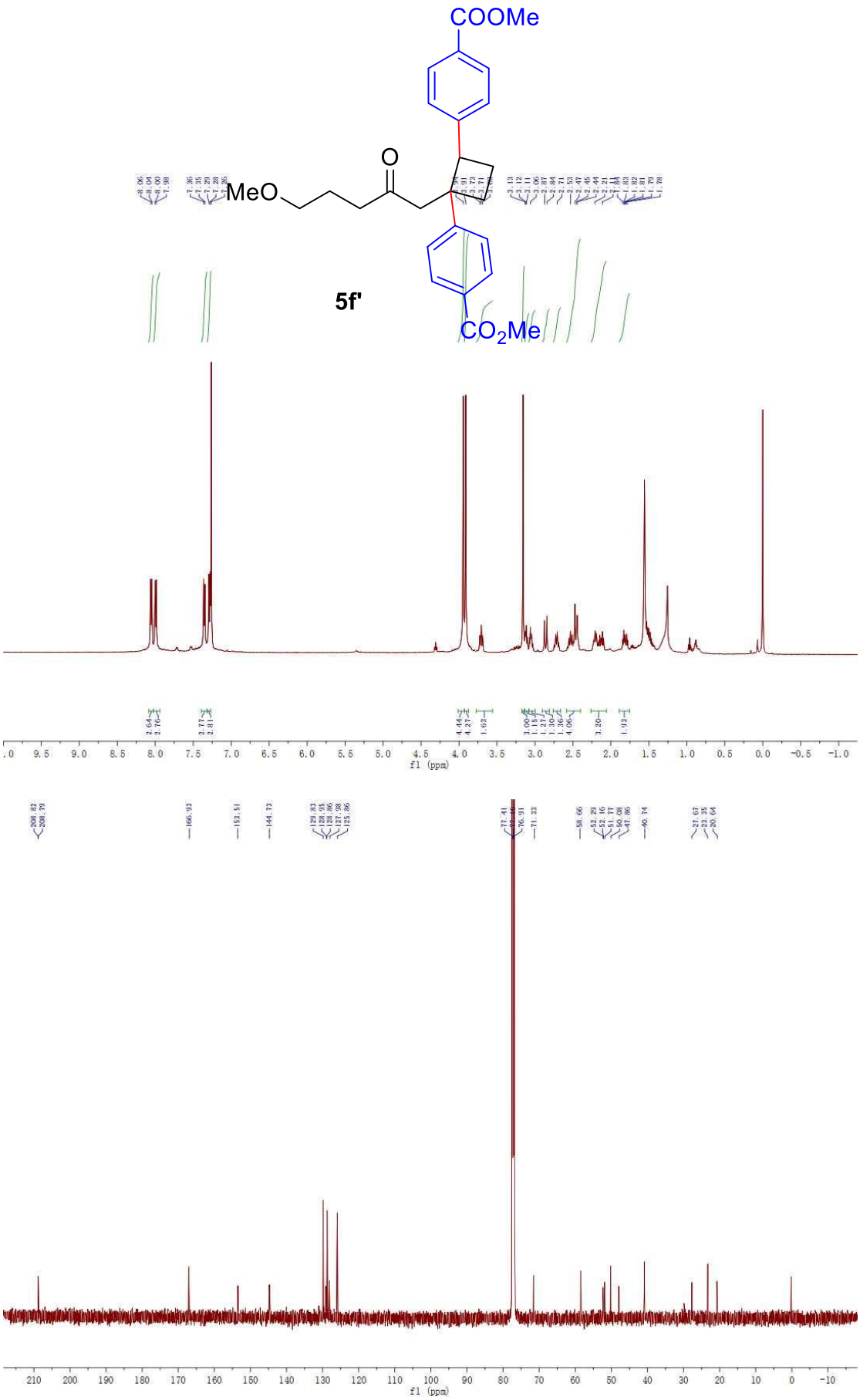
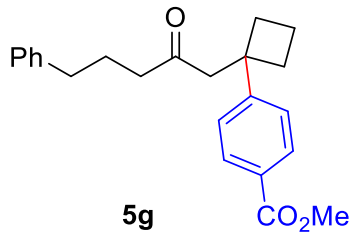
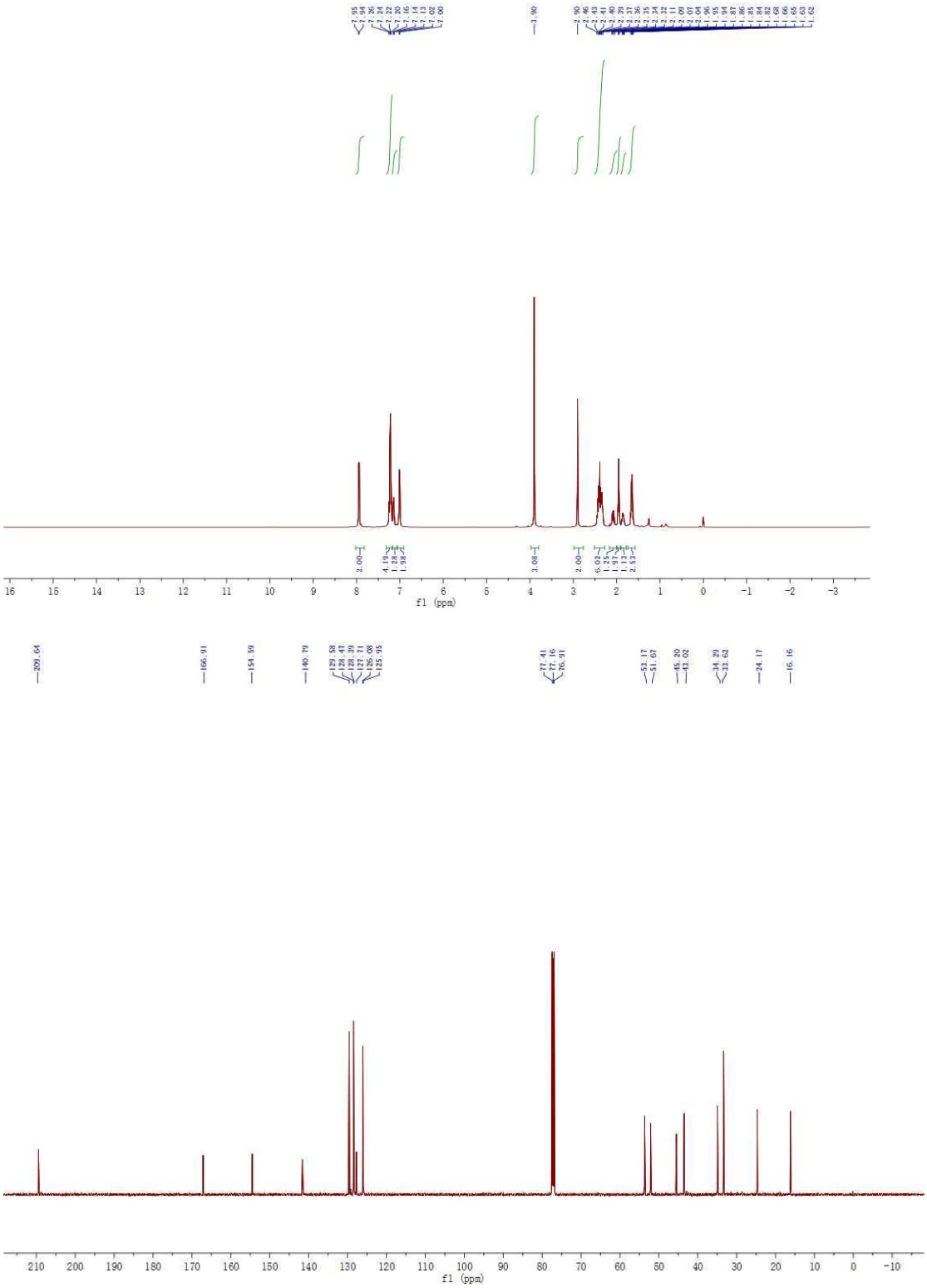


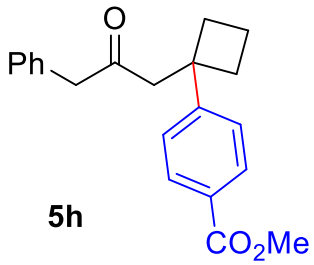



COOMe
O
MeO
5f'
CO2Me
f1 (ppm)
f1 (ppm)

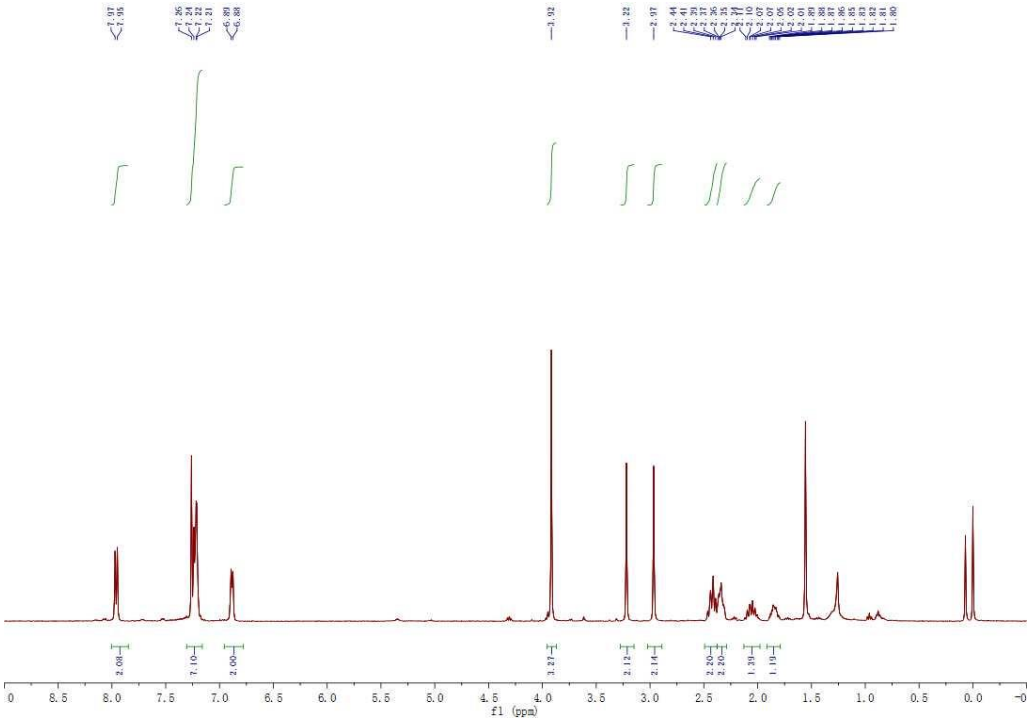


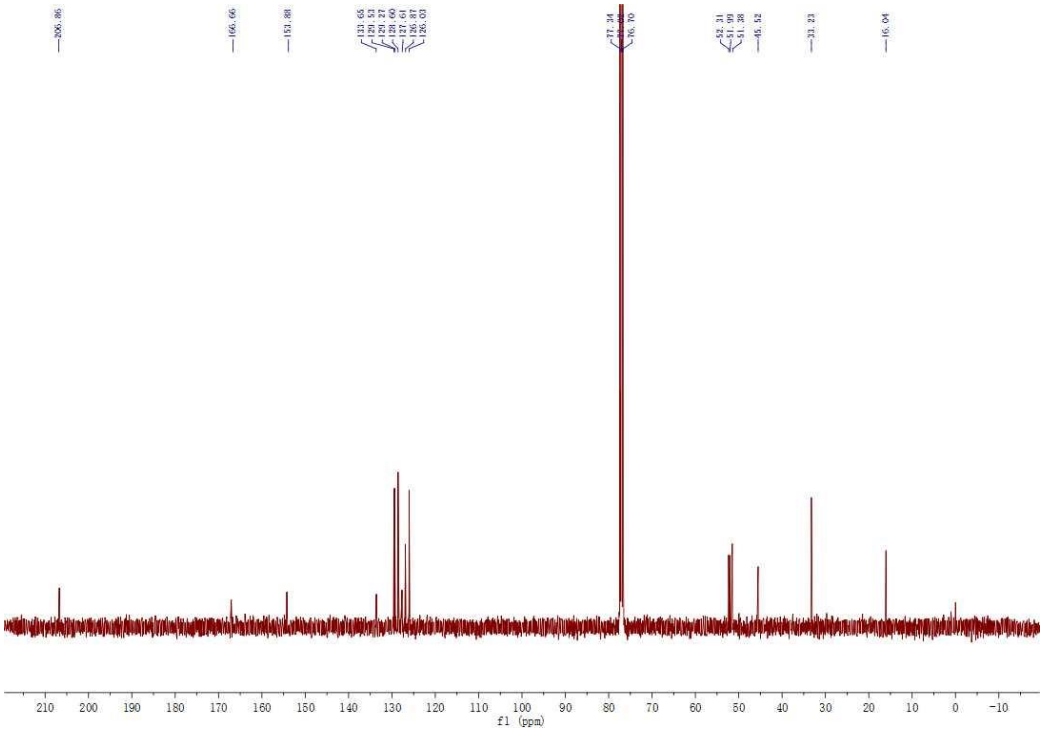
5g

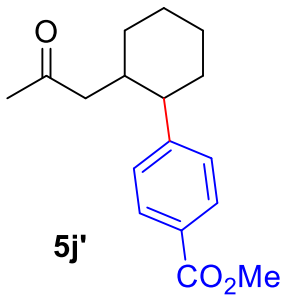




5h







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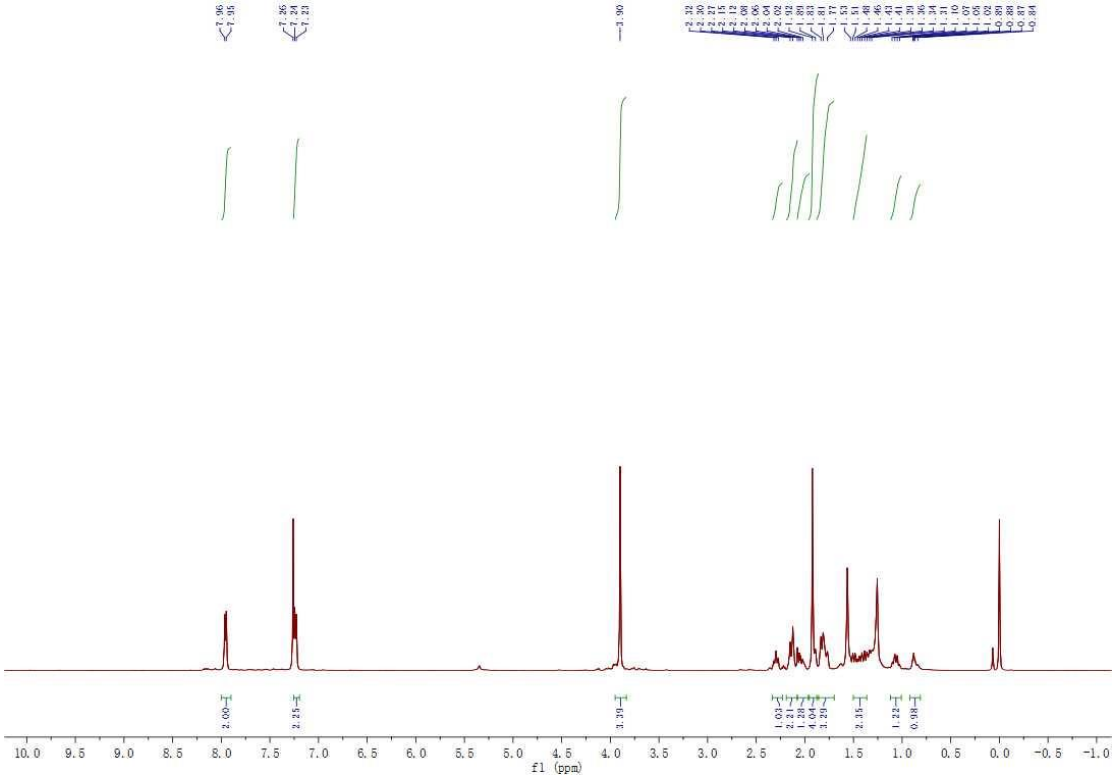

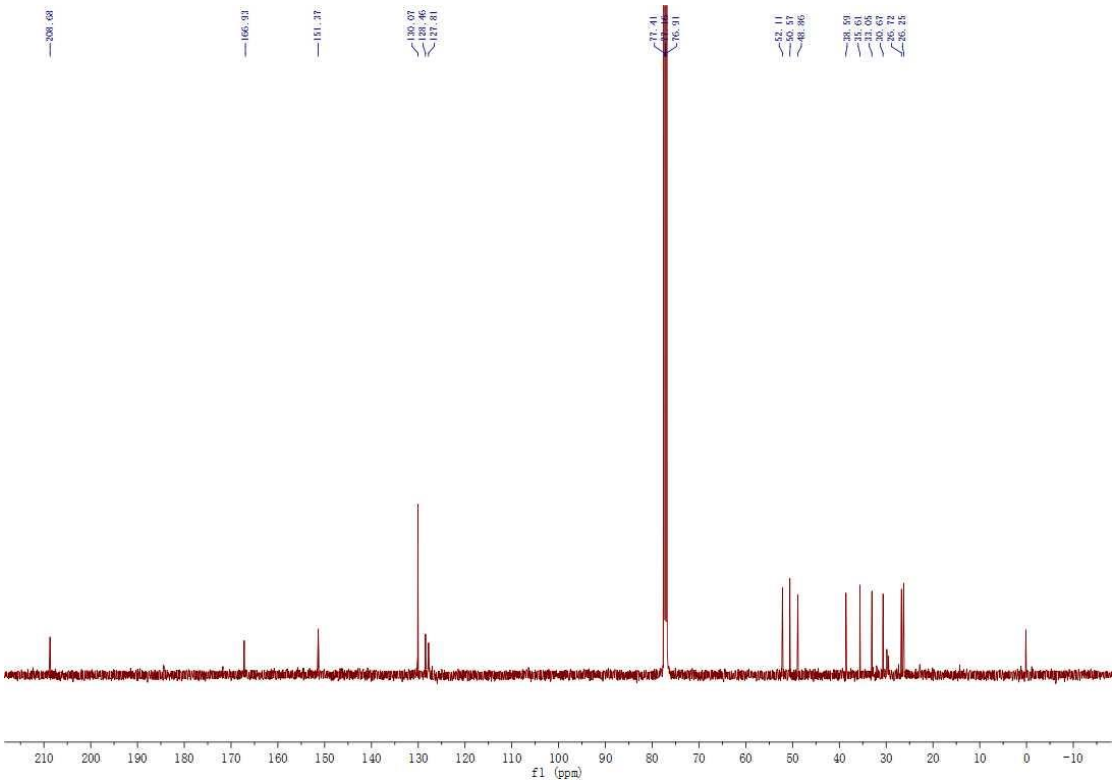

DEPT 135 of **5j'**