Supporting Information

A Unified Strategy for Remote C-H Fluorination of Phenylacetic Acids and Their Homologues at *meta*-Position

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1. General

Chemicals: Unless otherwise stated, all experiments were carried out under air atmosphere. The reagents and solvents were purchased from commercial suppliers and used without further purification unless otherwise noted.

NMR spectroscopy: ^{1}H NMR spectra were acquired on Bruker AVANCE spectrometers (400, 500, or 600 MHz) in $CDCl_3$ with tetramethylsilane (TMS) as the internal reference. ^{13}C NMR spectra were acquired on Bruker AVANCE spectrometers (101, 126 or 151 MHz) in $CDCl_3$ with tetramethylsilane (TMS) as the internal reference. ^{19}F NMR spectra were acquired on Bruker AVANCE spectrometers (376, 470 or 565 MHz) in $CDCl_3$ with tetramethylsilane (TMS) as the internal reference. Chemical shifts (δ) are reported in ppm relative to residual solvent signals: $CHCl_3$ (δ 7.26 ppm for ^{1}H) and $CDCl_3$ (δ 77.16 ppm for ^{13}C). Coupling constants (J) are expressed in Hz. Multiplicity descriptors: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), dd (doublet of doublets), td (triplet of doublets), ddd (doublet of doublet of doublets), m (multiplet), br (broad resonance).

Analytical Techniques:

- **GC**: Agilent 7890B system equipped with an FID detector.
- **GC-MS**: Agilent 6890N GC coupled to a 5973N mass spectrometer, using dodecane as an internal standard.
- **HRMS**: Agilent 6545 Q-TOF LC-MS, Waters GCT Premier TOF mass spectrometer with electron impact (EI) or chemical ionization (CI).
- **XRD:** The Bruker D8 venture uses a room-temperature molybdenum target.

General Procedures: Reagents were weighed under ambient laboratory conditions. Unless specified, reactions were performed in air without inert gas protection.

The separation method for fluorinated products: Initially, crude separation is carried out by column chromatography, followed by separation using preparative Thin-layer chromatography (TLC).

Abbreviations: Petroleum ether (PE), Ethyl acetate (EA), 1,2-Dichloroethane (DCE), Dichloromethane (DCM), Tetrahydrofuran (THF), Triethylamine (Et_3N), Diethyl ether (Et_2O), Trifluoroacetic acid (TFA), N,N-Dicyclohexylcarbodiimide (DCC), 4-Dimethylaminopyridine (DMAP), N-Fluorobenzenesulfonimide (NFSI), Hexafluoroisopropanol (HFIP), Directing Group (DG), Thin-layer chromatography (TLC).

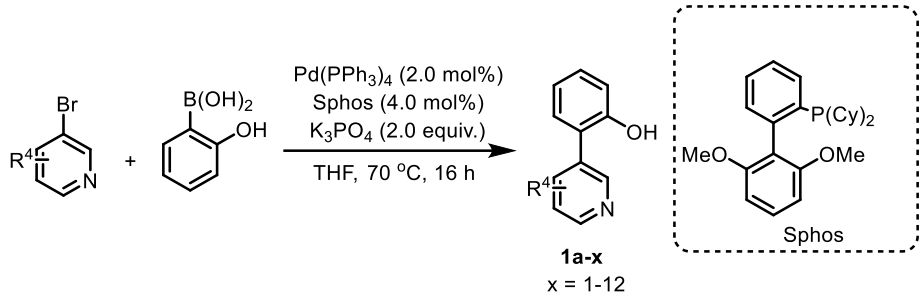
2. Preparation of starting materials

2.1 Preparation of directing-groups

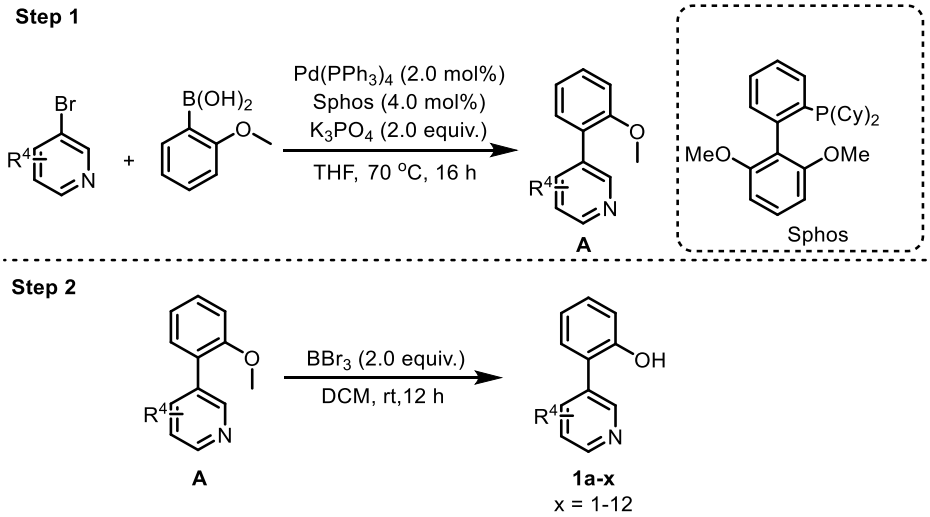
***General method A*[1]**

To a 25 mL Schlenk tube equipped with a magnetic stirring bar, 3-bromopyridine (2.0 mmol), 2-hydroxyphenylboronic acid (3.0 mmol), $Pd(PPh_3)_4$ (2.0 mol%), Sphos (4.0 mol%), K_3PO_4 (4 mmol) were added under N_2, THF (4 mL) was added by use of syringe. After stirring at room temperature for half an hour, then move the reaction to reflux for 16 h. Upon completion, the mixture was quenched with water (10 mL), and extracted with EtOAc (3 × 10 mL). Then the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$, filtrated and concentrated in *vacuo*

to give the crude product, the crude mixture was purified by silica gel chromatography (PE: EA=1:1, *v/v*) to afford the directing group (**1a-x**).



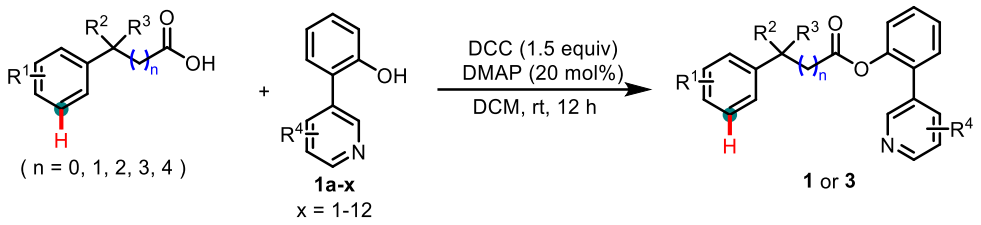
***General method B*[2]**



Step 1: In a 25 mL Schlenk tube equipped with a magnetic stir bar, were added 3-bromopyridine (2.0 mmol, 1.0 equiv.), 2-hydroxyphenylboronic acid (3.0 mmol, 1.5 equiv.), $Pd(PPh_3)_4$ (2.0 mol%), Sphos (4.0 mol%), and K_3PO_4 (4.0 mmol, 2.0 equiv.) under N_2 atmosphere. THF (4 mL) was injected *via* syringe. After stirring at room temperature for 30 minutes, the reaction mixture was heated to reflux for 16 h. Upon completion, the mixture was quenched with ice-cold water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product. The crude material was purified by silica gel chromatography (PE: EA = 3:1, v/v) to afford compound A, which was used directly in the next step.

Step 2: Compound A was dissolved in DCM (50 mL) in a 100 mL round-bottom flask. BBr_3 (4.0 mmol, 2.0 equiv.) was added dropwise at 0 °C. After complete addition, the mixture was stirred at room temperature for 12 h. Upon completion, the reaction was quenched with ice-cold water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (PE: EA = 1:1, v/v) to yield the directing group precursor (**1a-x**).

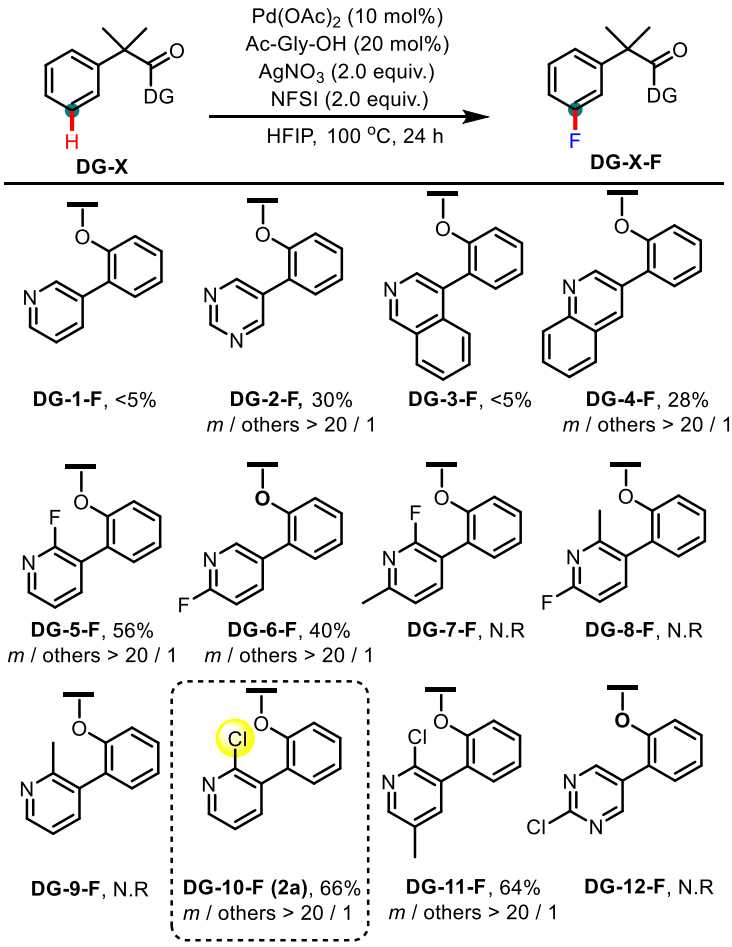
2.2 Preparation of 1 and 3



To a 50 mL round-bottom flask were added 2-phenylisobutyric acid derivative (3 mmol, 1.5 equiv.), directing group (2 mmol, 1.0 equiv.), DCC (3 mmol, 1.5 equiv.), and DMAP (0.4 mmol, 20 mol%). The mixture was dissolved in DCM and stirred at rt for 12 h. After completion, the precipitate was filtered off. The filtrate was washed with saturated brine (3 × 10 mL), and the aqueous layer was extracted with DCM. The combined organic layers were dried, concentrated under reduced pressure, and purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to afford the pure product (**1** or **3**).

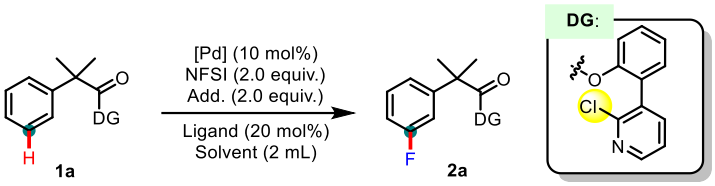
3. Condition screening

Table S1. Preliminary screening of the DGs



Reaction conditions: DG-X (0.2 mmol), $Pd(OAc)_2$ (10 mol%), Ac-Gly-OH (20 mol%), NFSI (2.0 equiv), $AgNO_3$ (2.0 equiv), HFIP (2 mL), 24 h, 100 °C; Yield is determined by GC using dodecane as an internal standard.

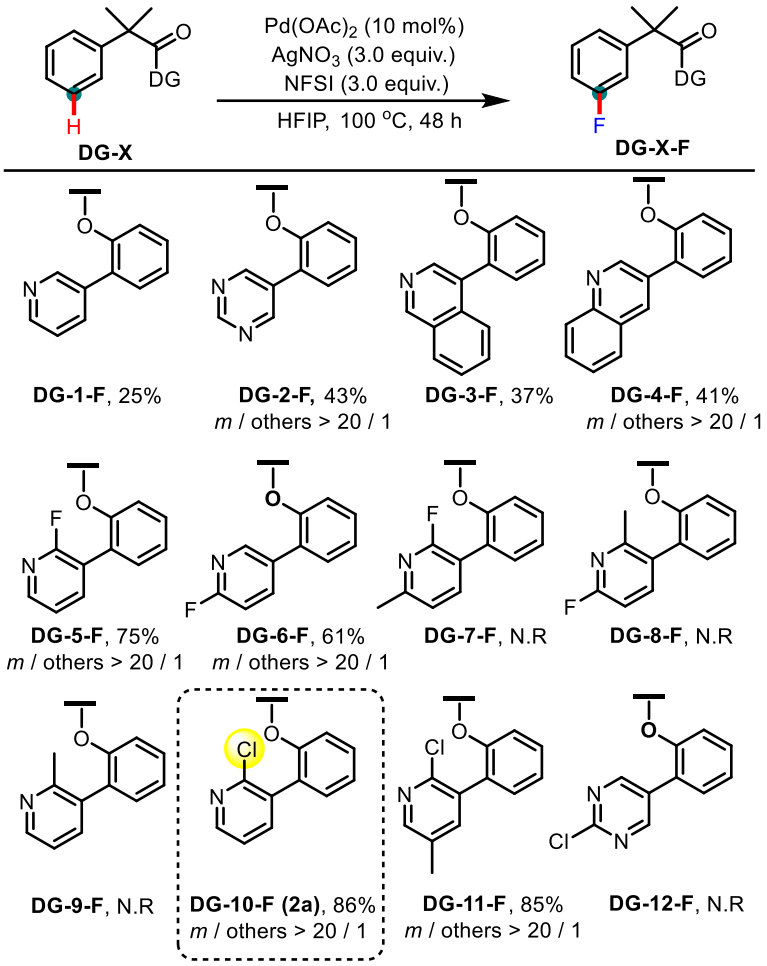
Table S2. Screening of the conditions[a]



Entry	[Pd]	Ligand	Add.	Sol.	Temp. (°C)	Time (h)	Yield (%)
1	$Pd(OAc)_2$	AC-Gly-OH	$AgNO_3$	HFIP	100	24	66
2	$Pd(NO_3)_2·3H_2O$	AC-Gly-OH	$AgNO_3$	HFIP	100	24	16
3	$PdCl_2$	AC-Gly-OH	$AgNO_3$	HFIP	100	24	45
4	$Pd(PPh_3)_4$	AC-Gly-OH	$AgNO_3$	HFIP	100	24	65
5	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	100	24	70
6	$Pd(OAc)_2$	TFA-Gly-OH	$AgNO_3$	HFIP	100	24	60
7	-	-	$AgNO_3$	HFIP	100	24	N.R.
8	$Pd(OAc)_2$	-	-	HFIP	100	24	29
9	$Pd(OAc)_2$	-	AgOAc	HFIP	100	24	20
10	$Pd(OAc)_2$	-	$AgSbF_6$	HFIP	100	24	65
11	$Pd(OAc)_2$	-	KNO_3	HFIP	100	24	31
12[b]	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	100	24	55
13[c]	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	100	24	77
14	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	80	24	55
15	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	120	24	65
16[c]	$Pd(OAc)_2$	-	$AgNO_3$	HFIP	100	24	81
17[d]	**$Pd(OAc)_2$**	**-**	**$AgNO_3$**	**HFIP**	**100**	**48**	**86(72)[e]**
18	$Pd(OAc)_2$	-	$AgNO_3$	TFA	100	24	67
19	$Pd(OAc)_2$	-	$AgNO_3$	AcOH	100	24	20
20	$Pd(OAc)_2$	-	$AgNO_3$	$MeNO_2$	100	24	21
21	$Pd(OAc)_2$	-	$AgNO_3$	DCE	100	24	16

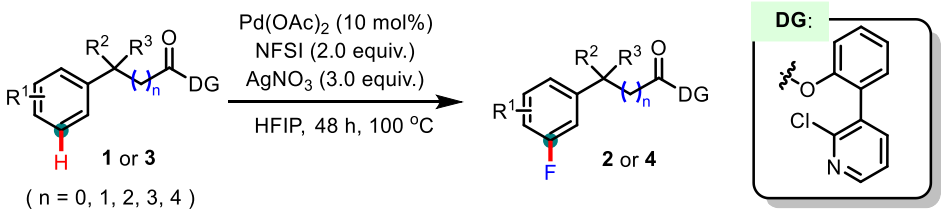
Reaction conditions: [a]**1a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (2.0 equiv), $AgNO_3$ (2.0 equiv), HFIP, 24 h, 100 °C; [b]**1a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (2.0 equiv), $AgNO_3$ (1.0 equiv), HFIP, 24 h, 100 °C; [c]**1a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (2.0 equiv), $AgNO_3$ (3.0 equiv); [d]**1a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (3.0 equiv), $AgNO_3$ (3.0 equiv), HFIP, 48 h, 100 °C; Yield is determined by GC using dodecane as an internal standard; [e]Isolated yield.

Table S3. Re-evaluation of DGs under ligand-free conditions



Reaction conditions: **DG-X** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (3.0 equiv.), $AgNO_3$ (3.0 equiv.), HFIP (2.0 mL), 24 h, 100 °C; Yield is determined by GC using dodecane as an internal standard.

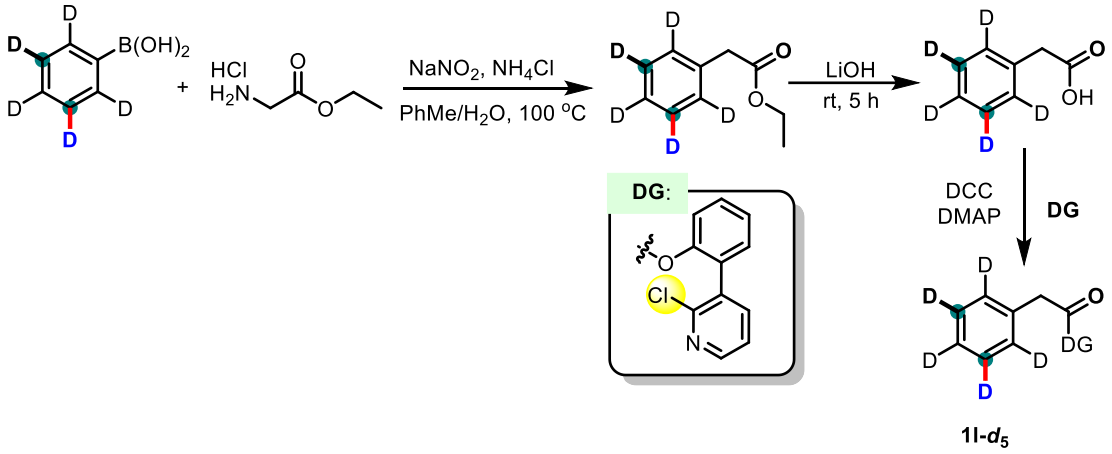
4. Typical experimental procedure



To a 15 mL Schlenk tube were added arenes acid derivative (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (0.4 mmol, 2.0 equiv.), and $AgNO_3$ (0.6 mmol, 3.0 equiv.). HFIP (2.0 mL) was added, and the mixture was stirred at 100 °C for 48 h. After completion, the reaction was cooled to room temperature and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to give the crude product, followed by separation using preparative thin-layer chromatography (TLC).

5. Deuterium-labelling experiments

5.1 Synthesis of deuterated starting material



Into a Schlenk tube were added phenylboronic acid-d_5 (2 mmol), ethyl glycinate hydrochloride (3 mmol, 1.5 equiv.), sodium nitrite (3.6 mmol, 1.8 equiv.), and ammonium chloride (8 mmol, 4.0 equiv.), followed by toluene (9.5 mL) and water (0.5 mL). The mixture was stirred at 100 °C for 24 h, then cooled to room temperature and concentrated under reduced pressure to give a crude product, which was purified by column chromatography (petroleum ether/ethyl acetate = 20:1) to afford ethyl phenylacetate-d_5 in 85% yield (0.34 g). This intermediate was further hydrolyzed with LiOH (1.1 equiv.) in THF to give the target phenylacetic acid-d_5 in 61% yield (0.14 g).

To a 25 mL round-bottom flask were added phenylacetic acid-d_5, directing group (1.2 mmol, 1.2 equiv.), DCC (1.5 mmol, 1.5 equiv.), and DMAP (20 mol%). The mixture was dissolved in DCM and stirred at rt for 12 h. After completion, the precipitate was filtered off. The filtrate was washed with saturated brine (3 × 10 mL), and the aqueous layer was extracted with DCM. The combined organic layers were dried, concentrated under reduced pressure, and purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to afford the pure product **1l-d_5.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.59 - 7.42 (m, 2H), 7.35 (td, *J* = 7.5, 1.2 Hz, 1H), 7.31 - 7.26 (m, 1H), 7.23 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.10 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.63 (s, 2H). (See ***Figure S1*** for details.)

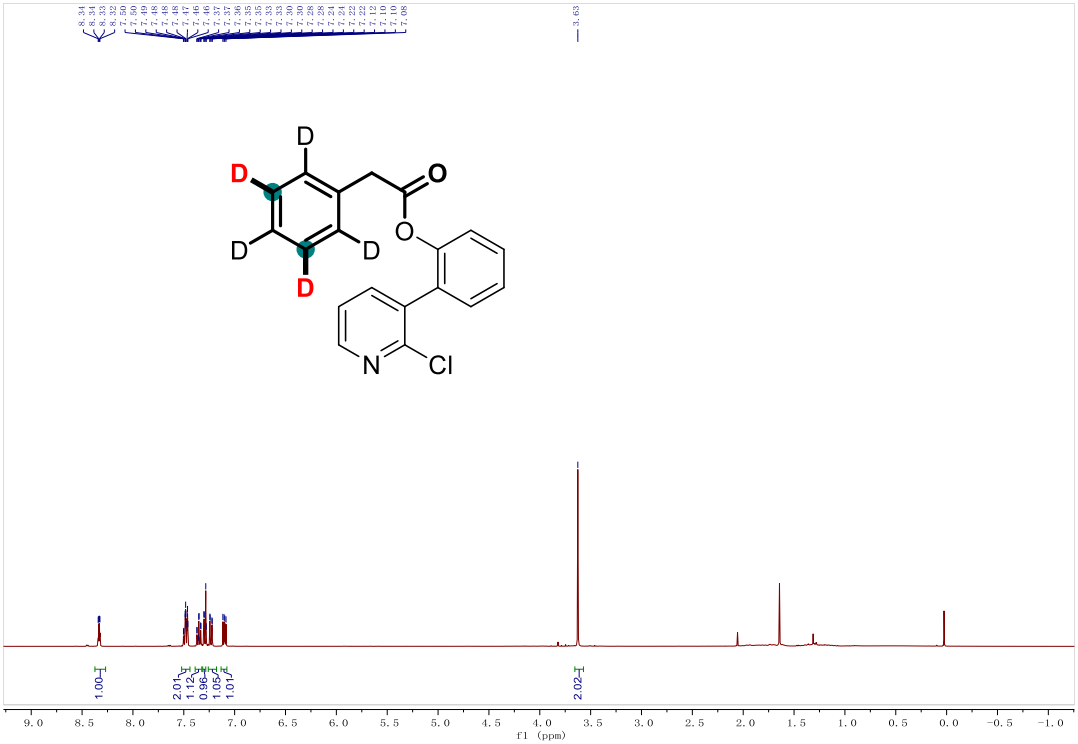
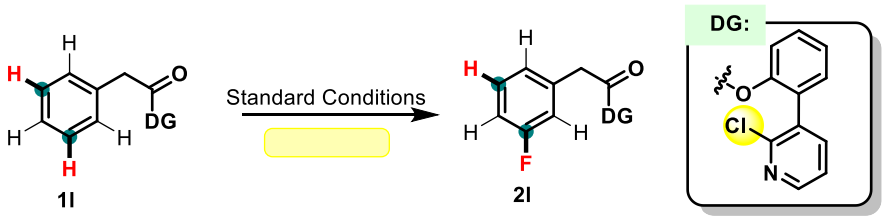
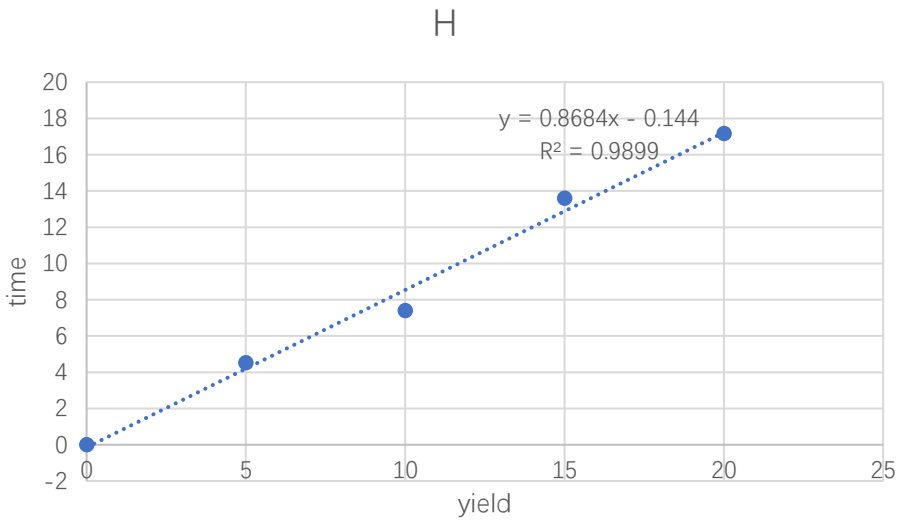


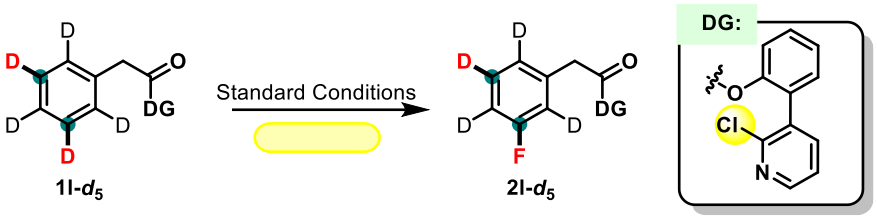
Figure S1 **^{1}H NMR spectrum of 1l-d_5 (400MHz, $CDCl_3$)**



To four 15 mL Schlenk tubes were added **1l** (0.025 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (3.0 equiv), and $AgNO_3$ (3.0 equiv). HFIP (1.0 mL) was added, and the resulting mixture was stirred at 100 °C for 5, 10, 15, and 20 min, respectively. Yields were determined by GC using dodecane as an internal standard.

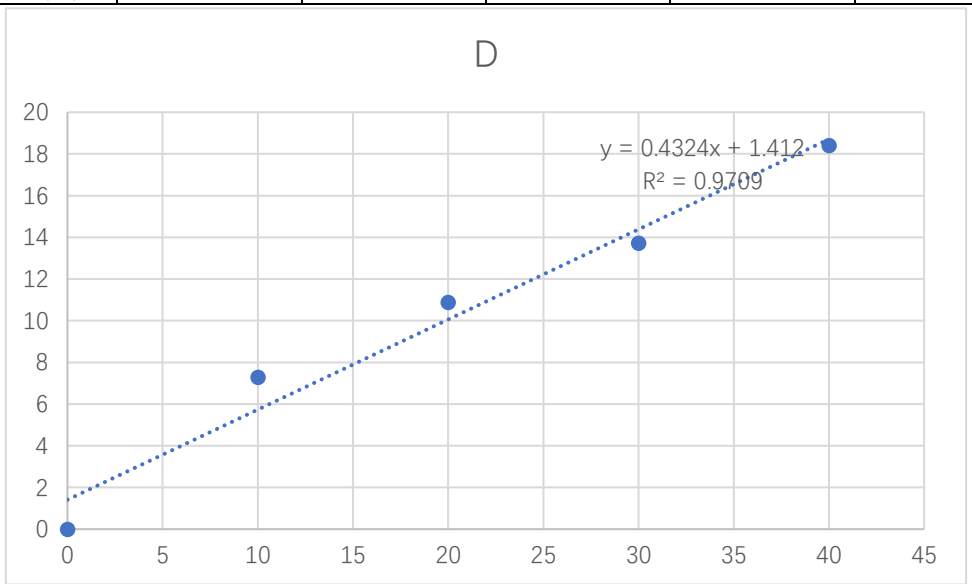
Time (min)	0	5	10	15	20
Yield (%)	0	4.52	7.41	13.6	17.17





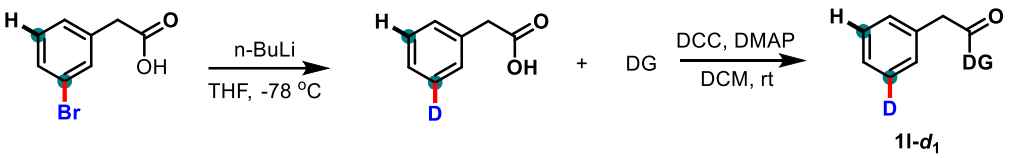
To four 15 mL Schlenk tubes were added **1l-*d*$_5$** (0.025 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (3.0 equiv), and $AgNO_3$ (3.0 equiv). HFIP (1.0 mL) was added, and the resulting mixture was stirred at 100 °C for 10, 20, 30, and 40 min, respectively. Yields were determined by GC using dodecane as an internal standard.

Time (min)	0	10	20	30	40
Yield (%)	0	7.29	10.88	13.73	18.4



On the basis of the above experiments, a KIE value of 2.0 was obtained.

5.2 Synthesis of deuterated starting material



To a solution of 2-(3-bromophenyl) acetic acid[8] (1.0 mmol) in THF (6 mL) at -78 °C was added *n*-BuLi (3.0 mmol, 1.6 M in hexanes, 3.0 equiv.) dropwise. After stirring at -78 °C for 10 min, the mixture was warmed to 0 °C. D_2O (0.6 mL) was added dropwise, and stirring was continued at room temperature for 30 min. The reaction was quenched with H_2O (10 mL). THF and hexanes were removed under reduced pressure, and the aqueous layer was washed with CH_2Cl_2 (3 × 10 mL). The aqueous phase was acidified with conc. aq. HCl to pH ≈ 1 and extracted with CH_2Cl_2 (3 ×10 mL). The combined organic extracts were dried over $MgSO_4$, concentrated under reduced pressure to afford crude product without further purification. Then put it to a 25 mL round-bottom flask, added **DG-10** (1.1 mmol, 1.1 equiv.), DCC (2 mmol, 2.0 equiv.), and DMAP (0.2 mmol, 20 mol%). The mixture was dissolved in DCM and stirred at rt for 12 h. After completion, the precipitate was filtered off. The filtrate was washed with saturated brine (3 × 10 mL), and the aqueous layer was extracted with DCM. The combined organic layers were dried, concentrated under reduced pressure, and purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to afford the pure product **1l-d_1** (0.187 g, yield 58%) (96% D). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.43 (dd, J = 4.8, 1.9 Hz, 1H), 7.62 (dd, J = 7.6, 1.9 Hz, 1H), 7.53 (ddd, J = 8.3, 5.5, 3.7 Hz, 1H), 7.42 - 7.36 (m, 3H), 7.32 (d, J = 8.1 Hz, 1H), 7.23 (dd, J = 4.6, 2.0 Hz, 3H), 7.00 (dd, J = 6.6, 2.9 Hz, 2H), 3.68 (s, 2H). (See ***Figure S2*** for details.)

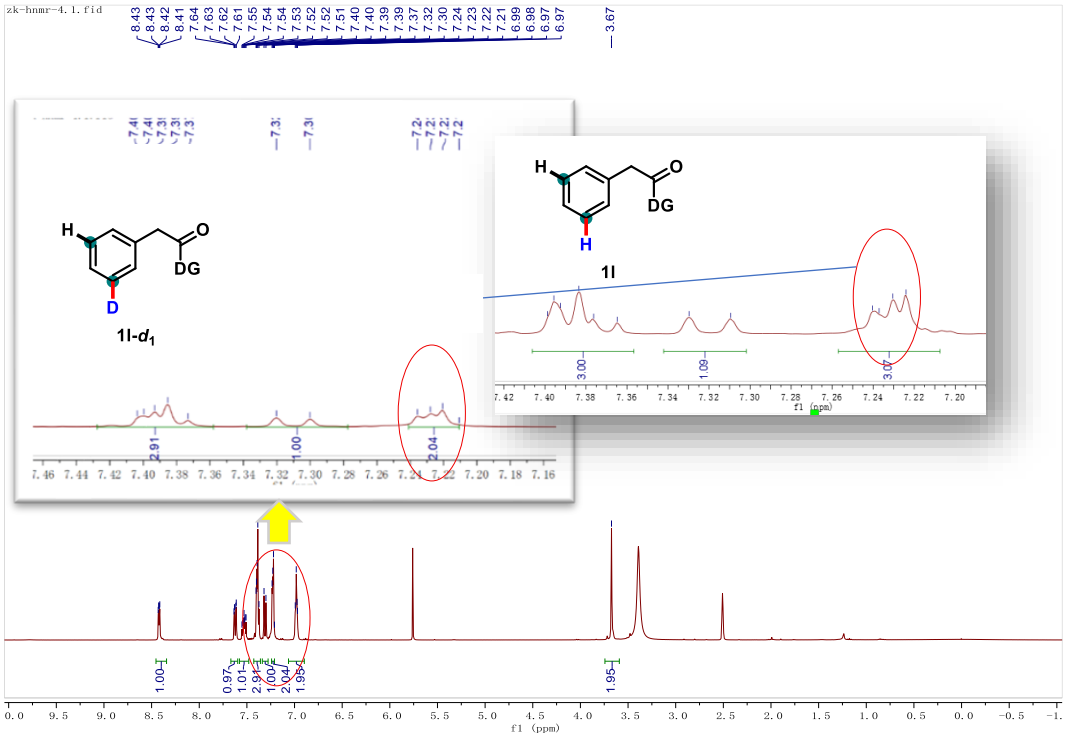
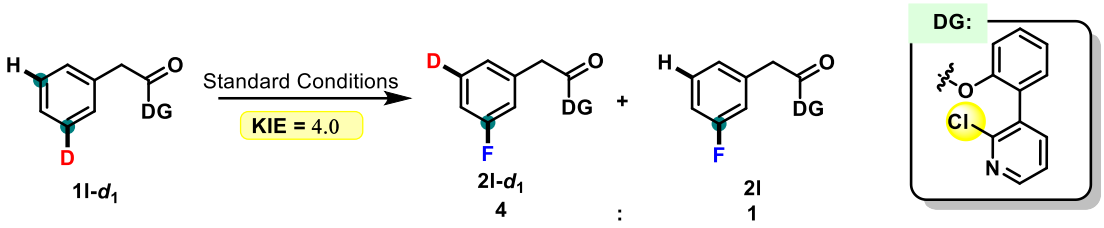


Figure S2 **^{1}H NMR spectrum of 1l-d_1 (400MHz, DMSO-d_6)**

5.3 Deuterium-labelling experiments



To a 15 mL Schlenk tube were added **1l-d_1** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NFSI (0.4 mmol, 2.0 equiv.), and $AgNO_3$ (0.6 mmol, 3.0 equiv.). HFIP (2.0 mL) was added, and the mixture was stirred at 100 °C for 2 h. After completion, the reaction was cooled to room temperature and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to give the crude product, followed by separation using preparative Thin-layer chromatography (PE: EA = 7:1) to afford the pure product (0.019 g, yield 29%). The ratio of **2l** to **2l-d_1** was determined to be 1:4 by ^{1}H NMR analysis, based on the integration of characteristic hydrogen resonances. (See ***Figure S3*** for details.)

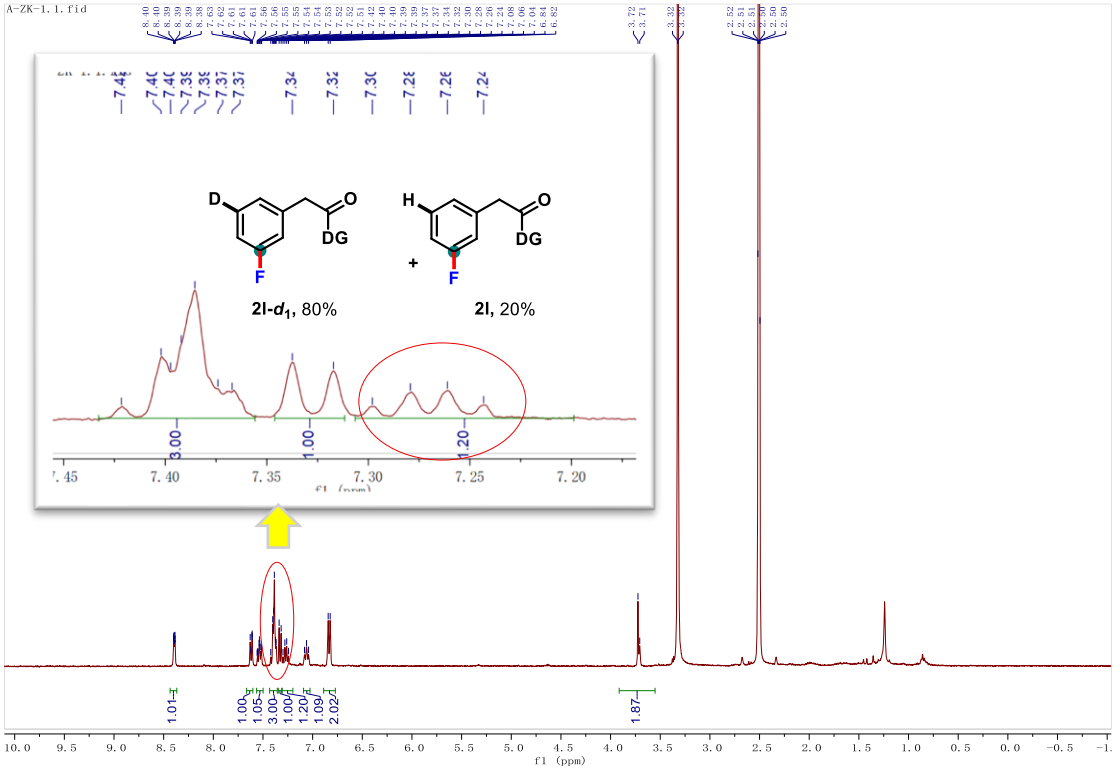


Figure S3 **^{1}H NMR spectrum of 2l & 2l-d_1 (400MHz, DMSO-d_6)**

6. X-Ray analysis for 2h

CCDC numbers 2366841 (**2h**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.uk/data_request/cif.

Single crystals suitable for X-ray crystallography was grown by slow evaporation of the prepared solution in CH_2Cl_2 and petroleum ether at room temperature.

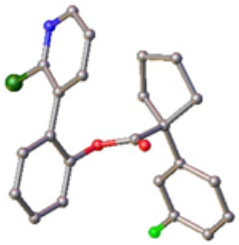


Figure S4. X-ray structure of **2h**

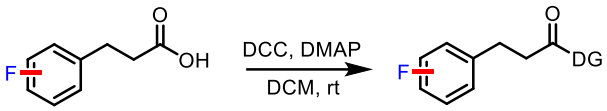
Table 1 Crystal data and structure refinement for 2h.

dentification code	**2h**
Empirical formula	$C_{23}H_{19}ClFNO_2$
Formula weight	395.84
Temperature/K	193.00
Crystal system	monoclinic
Space group	C2/c
a/Å	33.0613(18)
b/Å	7.2094(4)
c/Å	15.6708(8)
α/°	90
β/°	91.011(2)
γ/°	90
Volume/Å^3	3734.6(3)
Z	8
ρ_{calc}g/cm^3	1.408
μ/mm^{-1}	1.350
F(000)	1648.0
Crystal size/mm^3	0.13 × 0.12 × 0.1
Radiation	GaKα (λ = 1.34139)
2Θ range for data collection/°	4.652 to 120.572
Index ranges	-41 ≤ h ≤ 42, -8 ≤ k ≤ 9, -20 ≤ l ≤ 20
Reflections collected	23529
Independent reflections	4123 [R_{int} = 0.0355, R_{sigma} = 0.0237]
Data/restraints/parameters	4123/0/253
Goodness-of-fit on F^2	1.045

Final R indexes [I>=2σ (I)]	R_1 = 0.0378, wR_2 = 0.0957
Final R indexes [all data]	R_1 = 0.0450, wR_2 = 0.1003
Largest diff. peak/hole / e Å^{-3}	0.27/-0.35

7. Determination of the structure of the target compounds

7.1 Synthesis of reference molecules for identifying 4a



To a 25 mL round-bottom flask were added fluoro-substituted 3-phenylpropanoic acid derivatives (3.0 mmol, 1.5 equiv.), directing group (2 mmol, 1.0 equiv.), DCC (4 mmol, 2.0 equiv.), and DMAP (0.4 mmol, 20 mol%). The mixture was dissolved in DCM and stirred at rt for 12 h. After completion, the precipitate was filtered off. The filtrate was washed with saturated brine (3 × 10 mL), and the aqueous layer was extracted with DCM. The combined organic layers were dried, concentrated under reduced pressure, and purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to afford the pure product in 87% yield. (all the fluoro-substituted 3-phenylpropanoic acid derivatives were purchased from Bide Pharmatech Co., Ltd.)

***ortho*-Fluoro-substituted 3-phenylpropanoic acid derivatives:**

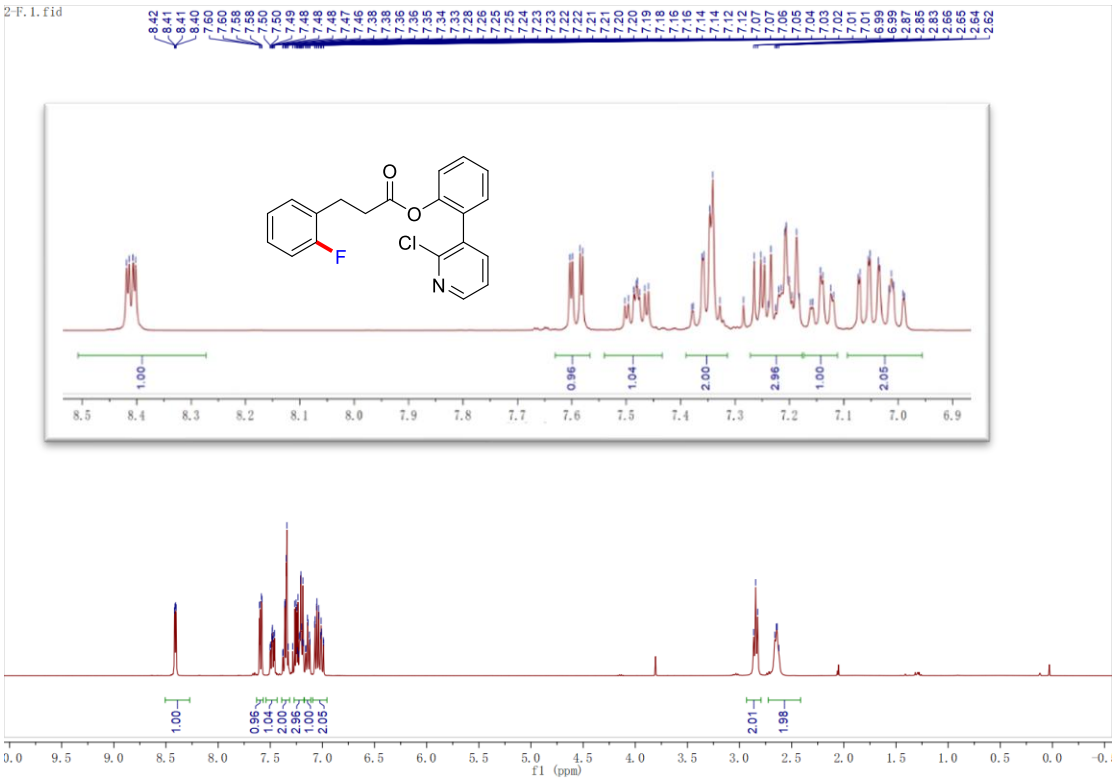


Figure S5 **^{1}H NMR spectrum of *ortho*-fluoride (400 MHz, $CDCl_3$)**

***meta*-Fluoro-substituted 3-phenylpropanoic acid derivatives:**

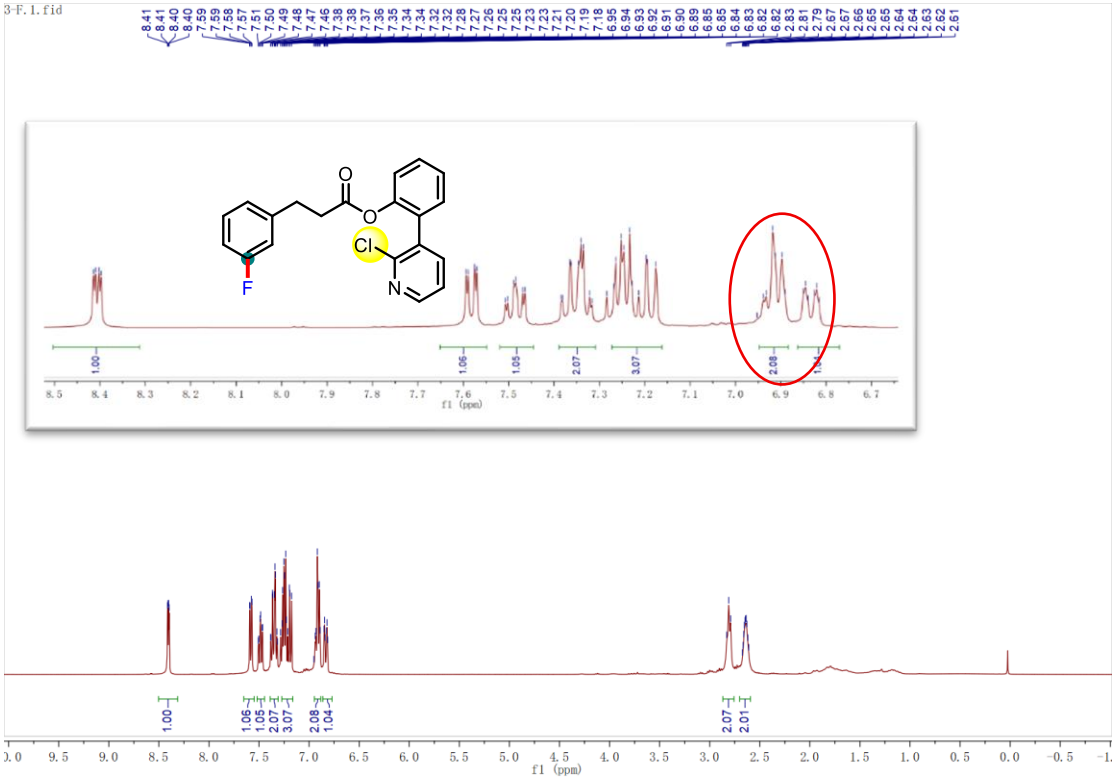


Figure S6 **^{1}H NMR spectrum of *meta*-fluoride (400 MHz, $CDCl_3$)**

***para*-Fluoro-substituted 3-phenylpropanoic acid derivatives:**

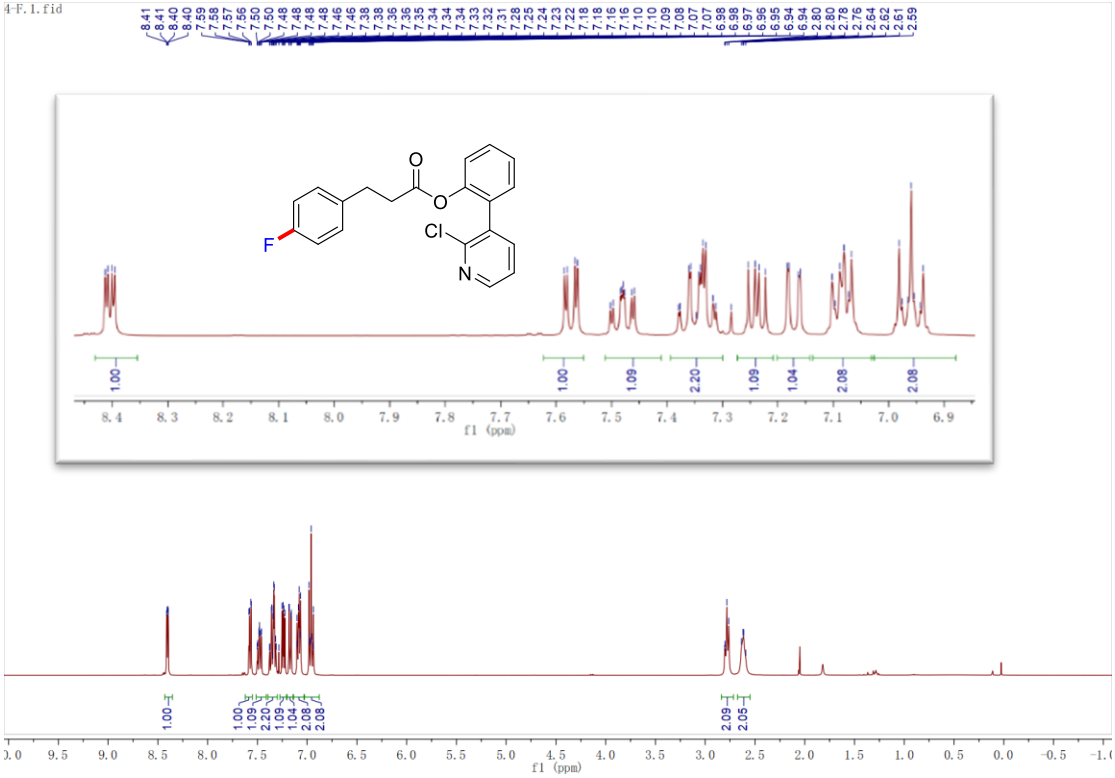


Figure S7 **^{1}H NMR spectrum of *para*-fluoride (400 MHz, $CDCl_3$)**

Upon comparison with the synthesized target product, we found that the *meta*-fluorinated product

exhibits a ^{1}H NMR spectrum completely identical to that of the target. (See ***Figure S5, S6, S7, S8*** for details.)

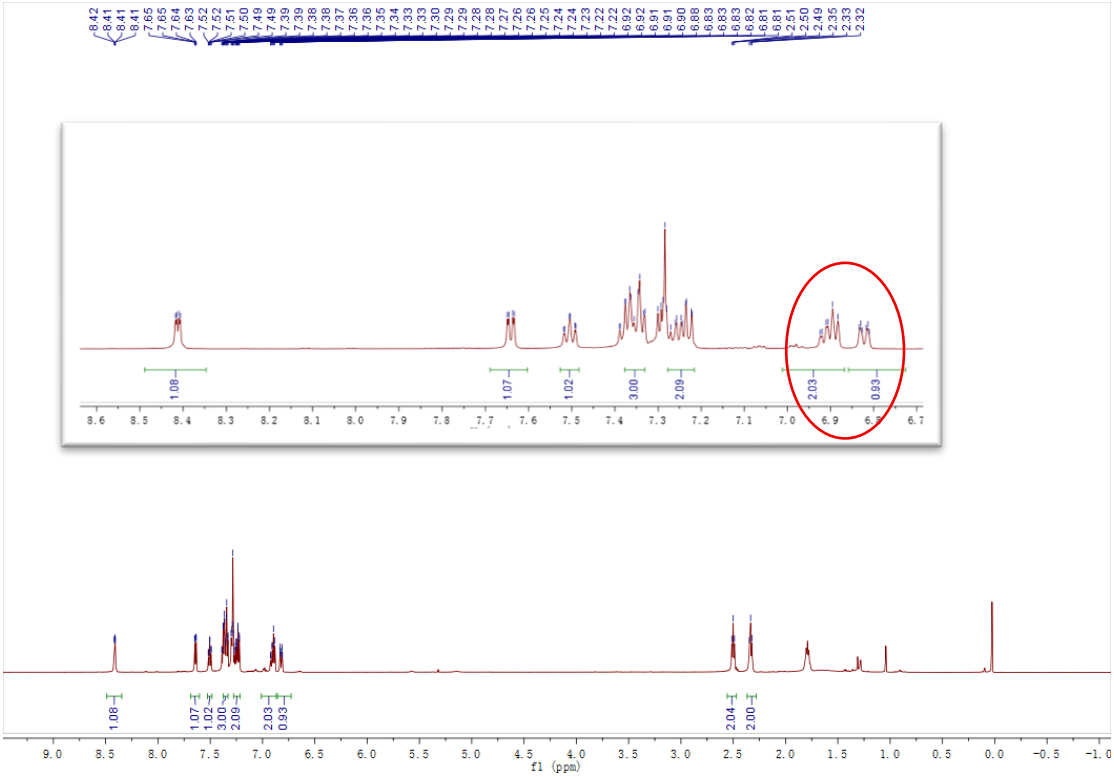
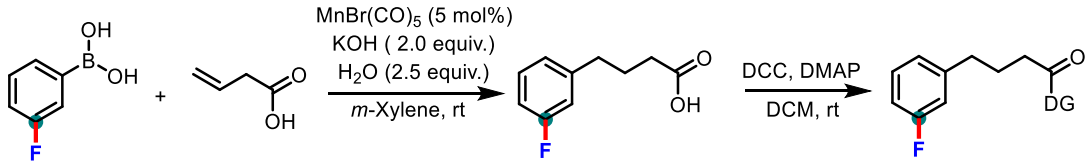


Figure S8 **^{1}H NMR spectrum of 4a (400 MHz, $CDCl_3$)**

7.2 Synthesis of reference molecules for identifying 4h



4h, 20%

Step1[9]**:**

To a 25 mL flask equipped with a magnetic stir bar were added $MnBr(CO)_5$ (5 mol%), alkene (1.0 mmol, 1.0 equiv.), boronic acid (2.0 mmol, 2.0 equiv.), KOH (2.0 mmol, 2.0 equiv.), H_2O (2.5 equiv.), and *m*-xylene (6 mL) under argon. The mixture was stirred at room temperature for 24 h, then concentrated and diluted with 1 M HCl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were concentrated in vacuo to afford the crude intermediate.

Step 2:

This intermediate was transferred to a 25 mL round-bottom flask, followed by addition of **DG-10** (1.1 mmol, 1.1 equiv.), DCC (2.0 mmol, 2.0 equiv.), and DMAP (0.2 mmol, 20 mol%). The mixture was dissolved in DCM and stirred at room temperature for 12 h. After reaction completion, the precipitate was filtered off. The filtrate was washed with saturated brine (3 × 10 mL), and the aqueous layer was back-extracted with DCM. The combined organic phases were dried, concentrated under reduced pressure, and purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to give the pure product in 34% yield.

***meta*-Fluoro-substituted 3-phenylbutyric acid derivatives:**

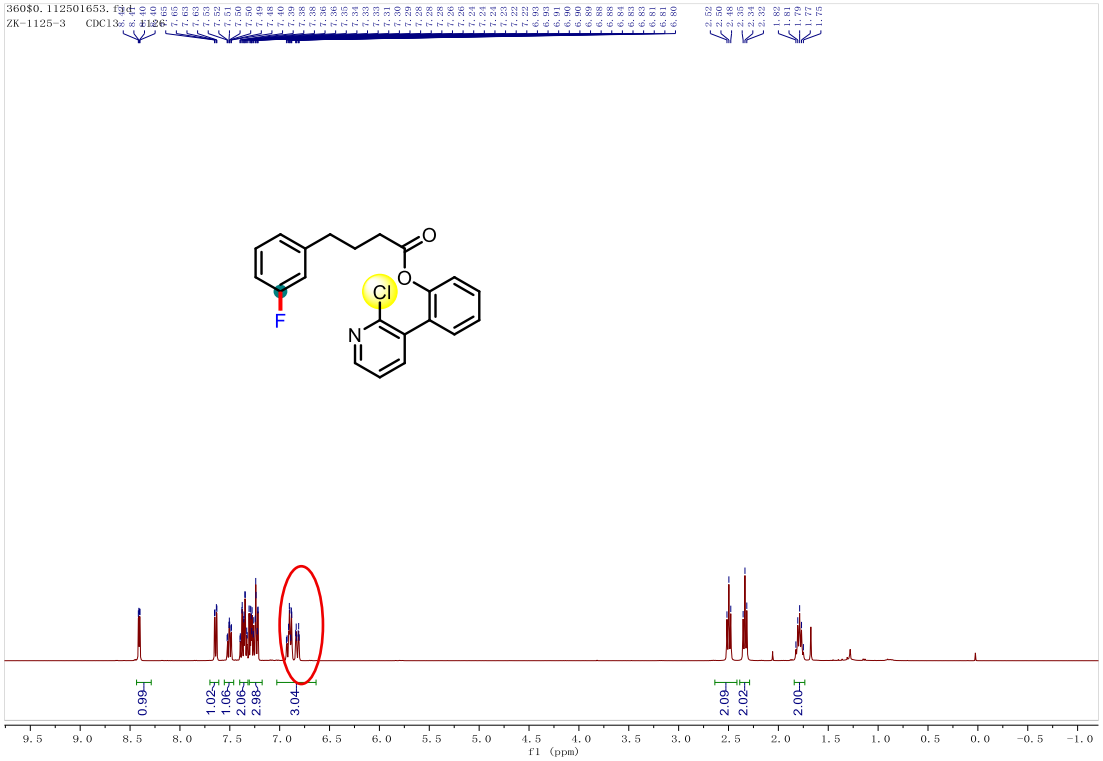


Figure S9 **^{1}H NMR spectrum of *meta*-fluoride (400 MHz, $CDCl_3$)**

Upon comparison with the synthesized target product, we found that the *meta*-fluorinated product exhibits a ^{1}H NMR spectrum completely identical to that of the target. (See ***Figure S9, S10*** for details.)

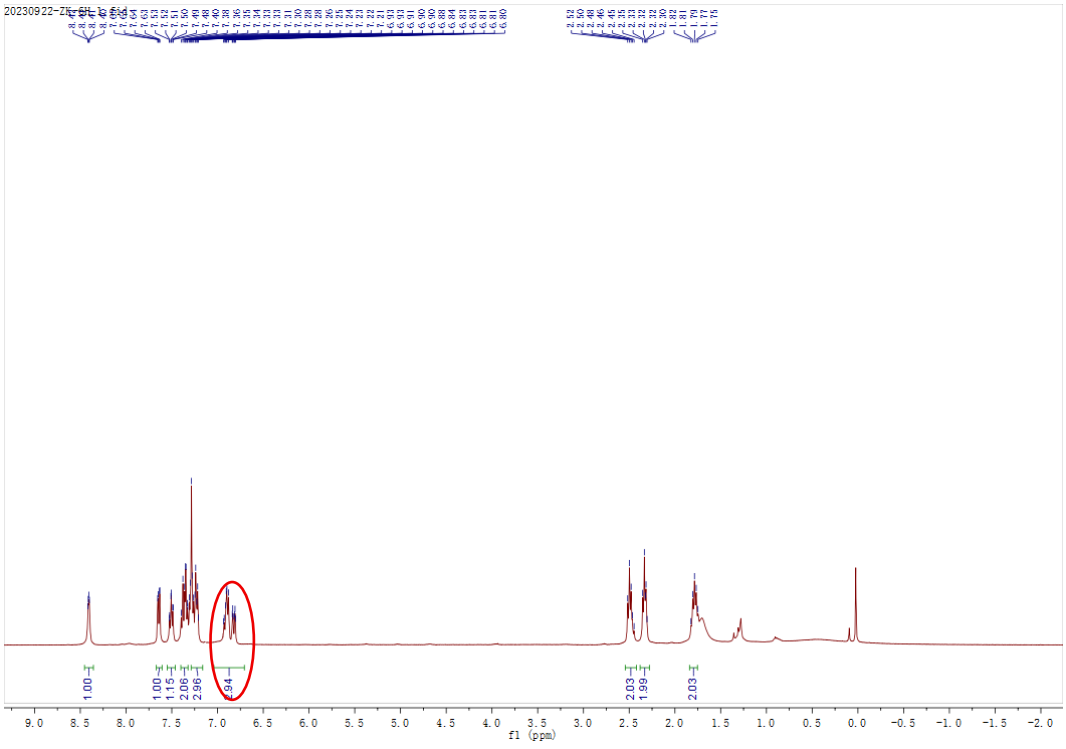
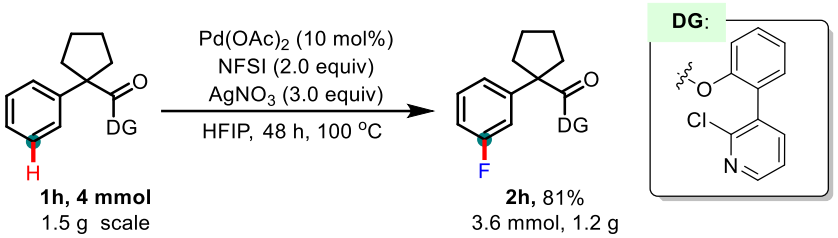


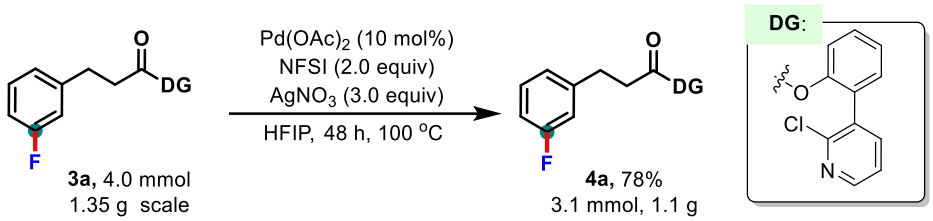
Figure S10 **^{1}H NMR spectrum of 4h (400 MHz, $CDCl_3$)**

8. Further transformation

8.1 Gram-scale reaction

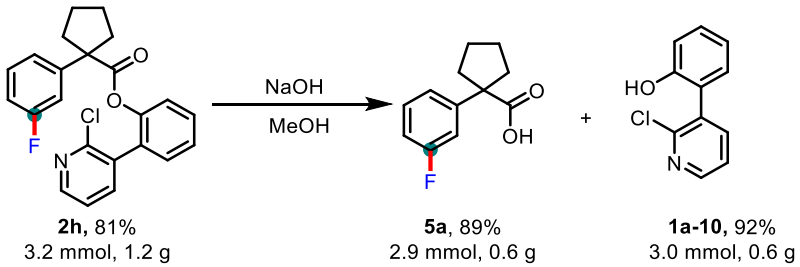


To a 50 mL tube were added **1h** (4.0 mmol, 1.5 g), $Pd(OAc)_2$ (10 mol%), NFSI (2.0 equiv.), and $AgNO_3$ (3.0 equiv.). HFIP (10.0 mL) was added, and the mixture was stirred at 100 °C for 48 h. After completion, the reaction was cooled to room temperature and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) to give the crude product **2h,** followed by separation using preparative Thin-layer chromatography (PE: EA = 7:1) to give the pure product (1.2 g, yield 81%)



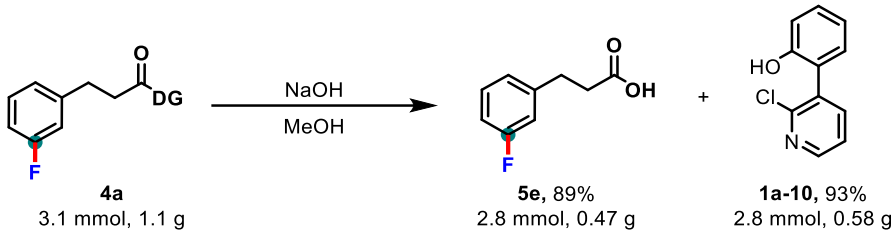
To a 50 mL tube were added **3a** (4.0 mmol, 1.35 g), $Pd(OAc)_2$ (10 mol%), NFSI (2.0 equiv.), and $AgNO_3$ (3.0 equiv.). HFIP (10.0 mL) was added, and the mixture was stirred at 100 °C for 48 h. After completion, the reaction was cooled to room temperature and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel GF254, 200–300 mesh; ethyl acetate/petroleum ether = 1:5) to give the crude product, followed by separation using preparative Thin-layer chromatography (PE: EA = 7:1), affording the pure product **4a** (1.1 g, yield 78%).

8.2 Removal of the directing group



To a 50 mL round-bottom flask were added compound **2h** (3.6 mmol) and NaOH (4.0 equiv). The mixture was dissolved in MeOH (20 mL) and stirred at 70 °C for 24 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was partitioned between ethyl acetate (20 mL) and water (20 mL). The aqueous layer was acidified with HCl to pH 3-4, washed with saturated brine (3 × 5 mL), and extracted with ethyl acetate. The combined organic layers were dried, filtered, and concentrated. Purification by column chromatography (silica gel

GF254, 200-300 mesh; PE: EA = 5:1) afforded pure product **5a** (0.6 g, 72% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.31 - 7.21 (m, 1H), 7.16 (d, J = 7.9 Hz, 1H), 7.10 (dt, J = 10.5, 2.2 Hz, 1H), 6.97 - 6.89 (m, 1H), 2.62 (dd, J = 12.6, 5.2 Hz, 2H), 1.95 - 1.83 (m, 2H), 1.74 (p, J = 3.1 Hz, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.7, 162.7 (d, J = 245.5 Hz), 145.2 (d, J = 7.0 Hz), 129.7 (d, J = 8.3 Hz), 122.8, 114.4 (d, J = 21.7 Hz), 113.9 (d, J = 20.8 Hz), 58.7 (d, J = 1.7 Hz), 36.0 (2C), 23.5 (2C). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -112.99. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 247.1107; found: 247.1110.



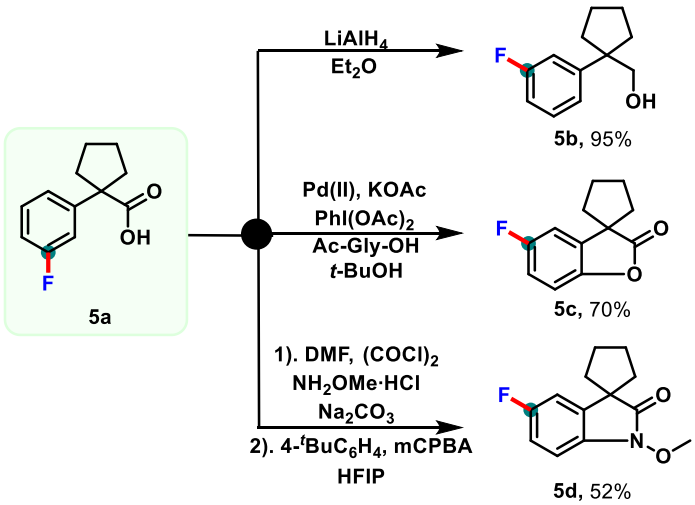
4a
3.1 mmol, 1.1 g

5e, 89%
2.8 mmol, 0.47 g

1a-10, 93%
2.8 mmol, 0.58 g

To a 50 mL round-bottom flask were added compound **4a** (3.1 mmol) and NaOH (4.0 equiv). The mixture was dissolved in MeOH (20 mL) and stirred at 70 °C for 24 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was partitioned between ethyl acetate (20 mL) and water (20 mL). The aqueous layer was acidified with HCl to pH 3-4, washed with saturated brine (3 × 5 mL), and extracted with ethyl acetate. The combined organic layers were dried, filtered, and concentrated. Purification by column chromatography (silica gel GF254, 200–300 mesh; PE: EA = 5:1) afforded pure product **5e** (0.47 g, 70% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.75 (s, 1H), 7.25 (tdd, J = 7.8, 6.2, 1.9 Hz, 1H), 7.02 - 6.95 (m, 1H), 6.94 - 6.85 (m, 2H), 2.95 (t, J = 7.7 Hz, 2H), 2.68 (dd, J = 8.2, 7.2 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 178.8, 163.0 (d, J = 245.6 Hz), 142.7 (d, J = 7.3 Hz), 130.0 (d, J = 8.4 Hz), 123.9, 115.2 (d, J = 21.2 Hz), 113.3 (d, J = 21.1 Hz), 35.2, 30.2 (d, J = 1.7 Hz). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.31. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 191.0479; found: 191.0477.

8.3 Other transformations

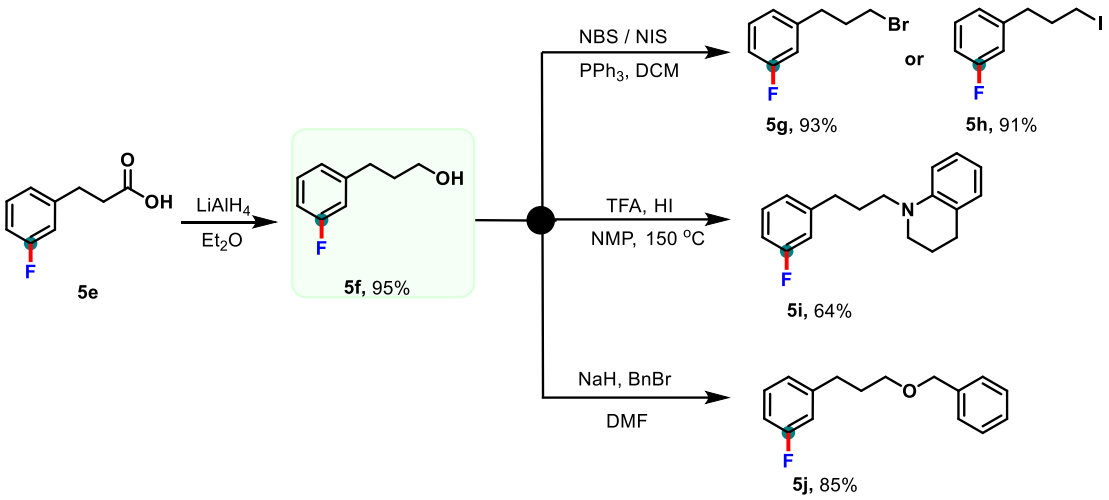


Synthesis of 5b: A magnetically stirred Schlenk tube was charged with compound **5a** (0.2 mmol) and dry Et_2O (1.0 mL). $LiAlH_4$ (0.3 mmol) was added slowly at 0 °C, and the resulting mixture was stirred at this temperature for 6 h. The reaction was quenched by the careful addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate (3 × 2.0 mL). The combined organic

extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, PE: EA = 5:1) yielded compound **5b** (36 mg, 95% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.28 (q, J = 8.4, 7.8 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 7.02 (dd, J = 10.9, 2.3 Hz, 1H), 6.90 (td, J = 8.4, 2.6 Hz, 1H), 3.52 (s, 2H), 1.99 (dd, J = 12.1, 5.9 Hz, 2H), 1.91 - 1.79 (m, 2H), 1.72 (q, J = 4.7, 3.3 Hz, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 162.88 (d, J = 245.3 Hz), 149.82 (d, J = 6.6 Hz), 129.64 (d, J = 8.3 Hz), 122.88, 115.18, 112.97 (d, J = 21.1 Hz), 70.12 (d, J = 2.0 Hz), 53.37 (d, J = 1.7 Hz), 34.39 (2C), 23.82 (2C). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.19. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 217.1005; found: 217.1012.

Synthesis of 5c[3]: To a mixture of compound **5a** (0.2 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 5 mol%), N-protected amino acid (0.06 mmol, 0.3 equiv.), KOAc (39.2 mg, 0.4 mmol, 2.0 equiv.), and $PhI(OAc)_2$ (96.6 mg, 0.3 mmol, 1.5 equiv.) in a 35 mL sealed tube was added ^{t}BuOH (2.0 mL). The tube was sealed with a PTFE-lined cap and stirred at 100 °C under air for 12 h. After cooling to room temperature, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel using a gradient of petroleum ether and dichloromethane to afford the target product **5c** (29 mg, 70% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.04 (ddt, J = 8.6, 4.2, 2.5 Hz, 1H), 7.01 - 6.78 (m, 2H), 2.34 - 2.21 (m, 2H), 2.18 - 2.04 (m, 2H), 2.04 - 1.87 (m, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 181.5, 159.7 (d, J = 242.0 Hz), 148.2, 135.7, 114.7 (d, J = 23.9 Hz), 111.4 (d, J = 8.5 Hz), 110.1 (d, J = 29.6 Hz), 52.7, 39.7 (2C), 26.4 (2C). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -117.92. **HRMS (ESI-TOF):** calcd. [M+Na]+ 229.2056; found: 229.2056.

Synthesis of 5d[4]: To a solution of compound **5a** (1.0 mmol, 1.0 equiv.) in dry DCM (2 mL) at 0 °C were added DMF (0.2 mmol, 0.2 equiv.) and oxalyl chloride (2.0 mmol, 2.0 equiv.). The mixture was stirred at room temperature for 4 h and then concentrated *in vacuo*. The residue was dissolved in toluene (2 mL). Separately, a solution of methoxyamine hydrochloride (2.2 mmol, 1.1 equiv.) and Na_2CO_3 (2.0 mmol, 2.0 equiv.) in toluene/water (v/v = 1:1) was prepared at 0 °C. The two solutions were combined and stirred at room temperature overnight. The mixture was extracted with ethyl acetate, and the organic phase was concentrated to give the crude intermediate. A reaction tube charged with the crude intermediate (0.1 mmol, 1.0 equiv.) and *p*-tert-butyl iodobenzene (20 mol%) was treated with *m*-CPBA (0.13 mmol, 1.3 equiv.) in HFIP (1.0 mL). After stirring at room temperature for 8 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with DCM (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by flash column chromatography (silica gel, petroleum ether/EtOAc gradient) to afford the target product **5c** (122 mg, 52% yield). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.02 - 6.82 (m, 3H), 4.01 (s, 3H), 2.25 - 2.14 (m, 2H), 2.13 - 2.00 (m, 2H), 1.99 - 1.88 (m, 2H), 1.89 - 1.79 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 176.2, 159.7 (d, J = 240.8 Hz), 135.2 (d, J = 1.9 Hz), 134.8 (d, J = 7.8 Hz), 113.8 (d, J = 23.9 Hz), 110.8 (d, J = 24.9 Hz), 107.6 (d, J = 8.1 Hz), 63.4, 52.9 (d, J = 1.8 Hz), 38.0 (2C), 26.6 (2C). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -119.86. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 258.2476; found: 258.2476.



Synthesis of 5f: A magnetically stirred Schlenk tube was charged with compound **5e** (2.8 mmol) and dry Et_2O (15.0 mL). $LiAlH_4$ (4.0 mmol) was added slowly at 0 °C, and the resulting mixture was stirred at this temperature for 6 h. The reaction was quenched by the careful addition of saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate (3 × 2.0 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (silica gel, PE: EA = 5:1) yielded compound **5f** (0.41g, yield 95%). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.22 (td, J = 7.8, 6.0 Hz, 1H), 6.96 (dd, J = 7.6, 1.5 Hz, 1H), 6.93 - 6.83 (m, 2H), 3.65 (t, J = 6.4 Hz, 2H), 2.69 (dd, J = 8.8, 6.8 Hz, 2H), 2.05 (s, 1H), 1.95 - 1.73 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.0 (d, J = 245.2 Hz), 144.5 (d, J = 7.2 Hz), 129.8 (d, J = 8.4 Hz), 124.1 (d, J = 2.6 Hz), 115.2 (dt, J = 20.7, 1.6 Hz), 112.7 (d, J = 21.1 Hz), 61.9 (d, J = 2.3 Hz), 33.9, 31.8. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.81. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 177.0692; found: 177.0684.

Synthesis of 5g[5]: To a solution of **5f** (0.2 mmol) in dry DCM (4 mL) at 0 °C were added PPh_3 (1.2 equiv.) and NBS (1.2 equiv.) sequentially. The mixture was stirred at room temperature for 30 min, concentrated *in vacuo*, and purified by flash column chromatography (silica gel, PE: EA = 5:1) to afford the primary bromide **5g**. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 (dddd, J = 9.0, 7.5, 6.0, 1.6 Hz, 1H), 7.01 - 6.94 (m, 1H), 6.95 - 6.85 (m, 2H), 3.38 (td, J = 6.5, 1.6 Hz, 2H), 2.88 - 2.66 (m, 2H), 2.21 - 2.06 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 162.9 (d, J = 245.6 Hz), 143.1 (d, J = 7.2 Hz), 129.9 (d, J = 8.3 Hz), 124.2 (d, J = 2.9 Hz), 115.4 (d, J = 21.0 Hz), 113.1 (d, J = 21.0 Hz), 33.8, 33.7, 32.8. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.49. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 238.9848; found: 238.9853.

Synthesis of 5h: To a solution of **5f** (0.2mmol) in dry DCM (4 mL) at 0 °C were added PPh_3 (1.2 equiv.) and NIS (1.2 equiv.) sequentially. The mixture was stirred at room temperature for 30 min, concentrated *in vacuo*, and purified by flash column chromatography (silica gel, PE: EA = 5:1) to afford the primary bromide **5h**. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.23 (dddd, J = 9.2, 7.7, 5.8, 1.7 Hz, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.89 (ddd, J = 8.2, 4.3, 2.1 Hz, 2H), 3.14 (td, J = 6.9, 1.8 Hz, 2H), 2.71 (td, J = 7.4, 1.7 Hz, 2H), 2.10 (pd, J = 6.9, 1.8 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.0 (d, J = 245.8 Hz), 143.0 (d, J = 7.2 Hz), 130.0 (d, J = 8.3 Hz), 124.3 (d, J = 2.8 Hz), 115.4 (d, J = 19.6 Hz), 113.1 (d, J = 20.8 Hz), 36.0, 34.6, 6.0. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.32. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 286.9709; found: 286.9716.

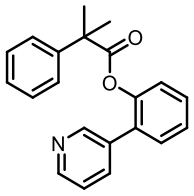
Synthesis of 5i[6]: Under a nitrogen atmosphere, a mixture of the amine (0.5 mmol), alcohol (1.0 mmol), and TFA (0.10 mmol) in NMP (1 mL) was treated with aqueous HI (55%, 0.05 mmol). The

resulting mixture was stirred at 150 °C for the indicated time. After cooling to room temperature, the reaction was quenched and neutralized with saturated aqueous $NaHCO_3$ (10 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine (3 × 20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (silica gel, PE: EA = 7:1) afforded the corresponding product **5i.** **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.25 - 7.18 (m, 1H), 7.05 - 6.84 (m, 5H), 6.55 (t, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 3.25 (q, *J* = 6.3, 5.0 Hz, 4H), 2.74 (t, *J* = 6.4 Hz, 2H), 2.66 (t, *J* = 7.8 Hz, 2H), 2.00 - 1.84 (m, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.0 (d, *J* = 245.3 Hz), 145.2, 144.5 (d, *J* = 7.2 Hz), 129.8 (d, *J* = 8.3 Hz), 129.2, 127.1, 124.0, 122.4, 115.6, 115.2 (d, *J* = 20.9 Hz), 112.8 (d, *J* = 21.0 Hz), 110.5, 50.9, 49.5, 33.2, 28.2, 27.5, 22.3. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.73. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 292.1477; found: 292.1485.

Synthesis of 5j[7]: To a solution of **5f** (0.5 mmol) in DMF (5 mL) was added NaH (60% w/w in mineral oil, 2.0 equiv.) at 0 °C. The mixture was stirred at this temperature for 2 h. Benzyl bromide (1.1 equiv.) was then added, and stirring was continued at room temperature for 9 h. The reaction mixture was concentrated *in vacuo*. The residue was partitioned between Et_2O (10 mL) and water (10 mL). The organic layer was washed with water (10 mL) and brine (5 mL), dried over $MgSO_4$, and concentrated. Purification by flash column chromatography (silica gel, PE: EA = 20:1) afforded **5j** (yield 85%) as a colorless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.33 (dd, *J* = 4.5, 1.8 Hz, 4H), 7.31 - 7.23 (m, 1H), 7.19 (dt, *J* = 10.0, 6.9 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.86 (d, *J* = 9.8 Hz, 2H), 4.49 (d, *J* = 1.8 Hz, 2H), 3.46 (td, *J* = 6.3, 1.8 Hz, 2H), 2.84 - 2.61 (m, 2H), 1.91 (qd, *J* = 8.2, 7.3, 5.3 Hz, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.0 (d, *J* = 245.2 Hz), 144.7 (d, *J* = 7.2 Hz), 138.6, 129.7 (d, *J* = 8.3 Hz), 128.4, 127.7, 127.6, 124.2 (d, *J* = 2.6 Hz), 115.4 (d, *J* = 20.7 Hz), 112.7 (d, *J* = 21.0 Hz), 73.0, 69.3, 32.2, 31.2. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -113.78. **HRMS (ESI-TOF):** calcd. $[M+Na]^+$ 267.1161; found: 267.1154.

9. Characterisation of new compounds

9.1 Characterisation of the starting materials bearing different directing groups



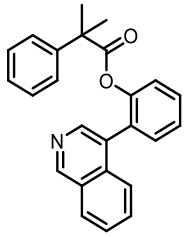
2-(Pyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-1).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.50 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.61 (d, *J* = 2.3 Hz, 1H), 8.56 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.53 (dt, *J* = 7.8, 2.0 Hz, 1H), 7.39 - 7.35 (m, 1H), 7.34 - 7.29 (m, 3H), 7.29 - 7.23 (m, 4H), 7.19 - 7.14 (m, 1H), 7.06 (dd, *J* = 8.1, 1.2 Hz, 1H), 1.54 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.8, 149.7, 148.5, 148.2, 143.5, 136.3, 133.0, 131.5, 130.7, 129.3, 128.6 (2C), 126.9, 126.4, 125.5 (2C), 122.9, 122.6, 46.6, 26.3 (2C).

HRMS (ESI-TOF): calcd. $[M+H]^+$ 318.1489; found: 318.1489.



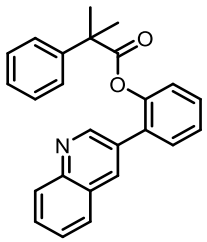
2-(Isoquinolin-4-yl)phenyl 2-methyl-2-phenylpropanoate (DG-3).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.58 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.92 (d, *J* = 2.3 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 2.2 Hz, 1H), 7.81 - 7.73 (m, 2H), 7.59 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.49 - 7.40 (m, 2H), 7.35 (td, *J* = 7.5, 1.2 Hz, 1H), 7.21 - 7.16 (m, 2H), 7.13 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.11 - 7.01 (m, 3H), 1.52 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.0, 151.0, 148.4, 147.2, 143.3, 135.6, 131.6, 131.1, 130.4, 129.6, 129.3, 129.3, 128.3 (2C), 128.1, 127.5, 126.8, 126.8, 126.5, 125.3 (2C), 122.8, 46.6, 26.2 (2C).

HRMS (ESI-TOF): calcd. $[M+H]^+$ 368.1645; found: 368.1654.



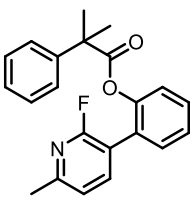
2-(Quinolin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-4).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.58 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.92 (d, *J* = 2.3 Hz, 1H), 8.18 (dt, *J* = 8.3, 1.0 Hz, 1H), 8.04 (d, *J* = 2.3 Hz, 1H), 7.80 - 7.70 (m, 2H), 7.58 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.46 - 7.40 (m, 2H), 7.35 (td, *J* = 7.5, 1.3 Hz, 1H), 7.20 - 7.16 (m, 2H), 7.15 - 7.11 (m, 1H), 7.11 - 7.07 (m, 2H), 7.07 - 7.03 (m, 1H), 1.52 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 175.0, 151.0, 148.4, 147.2, 143.3, 135.6, 131.7, 131.1, 130.4, 129.6, 129.3, 129.3, 128.3 (2C), 128.1, 127.5, 126.8, 126.8, 126.5, 125.3 (2C), 122.8, 46.6, 26.2 (2C).

HRMS (ESI-TOF): calcd. $[M+H]^+$ 368.1645; found: 368.1654.



2-(2-Fluoro-6-methylpyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-7).

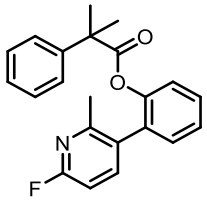
Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired

product as white solid (0.55 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.20 (dd, *J* = 5.0, 1.9 Hz, 1H), 7.63 (ddd, *J* = 9.3, 7.3, 2.0 Hz, 1H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.26 (dd, *J* = 8.3, 4.1 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.13 (td, *J* = 6.0, 5.1, 1.7 Hz, 2H), 1.99 (s, 3H), 1.52 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.9, 160.4 (d, *J* = 240.1 Hz), 147.1, 147.0, 146.9, 142.9, 142.0 (d, *J* = 4.3 Hz), 131.7, 131.2, 128.5, 128.4 (2C), F126.9, 126.0, 125.8 (2C), 121.1 (d, *J* = 4.4 Hz), 120.2 (d, *J* = 31.6 Hz), 46.3, 26.0, 16.3 (2C).

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 372.1370; found: 372.1374.



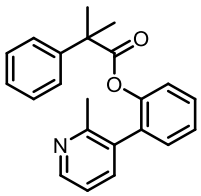
2-(6-Fluoro-2-methylpyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-8).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.55 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.47 (dd, *J* = 9.6, 7.5 Hz, 1H), 7.41 (ddd, *J* = 8.6, 7.1, 2.1 Hz, 1H), 7.34 - 7.30 (m, 2H), 7.30 - 7.28 (m, 2H), 7.28 - 7.23 (m, 3H), 7.11 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.96 - 6.92 (m, 1H), 2.55 (s, 3H), 1.57 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.7, 159.5 (d, *J* = 239.1 Hz), 156.8 (d, *J* = 13.5 Hz), 148.5, 143.5, 142.0 (d, *J* = 4.2 Hz), 131.1, 129.5, 128.4 (2C), 127.3 (d, *J* = 4.3 Hz), 126.7, 126.0, 125.5 (2C), 122.4, 120.4 (d, *J* = 4.3 Hz), 116.1 (d, *J* = 31.4 Hz), 46.6, 26.2 (2C), 23.7.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 372.1370; found: 372.1374.



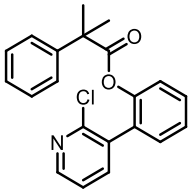
2-(2-Methylpyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-9).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.52 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.51 (dt, *J* = 4.5, 2.1 Hz, 1H), 7.45 - 7.36 (m, 2H), 7.28 (tdd, *J* = 16.0, 7.9, 3.2 Hz, 2H), 7.23 - 7.19 (m, 3H), 7.16 - 7.09 (m, 3H), 7.06 (dd, *J* = 8.2, 3.6 Hz, 1H), 2.25 (s, 3H), 1.40 (d, *J* = 46.6 Hz, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.9, 156.8, 148.4, 148.2, 143.5, 137.5, 133.0, 132.2, 130.6, 129.1, 128.5 (2C), 126.8, 126.2, 125.4 (2C), 122.2, 120.5, 46.5, 26.1 (2C), 22.7.

HRMS (ESI-TOF): calcd. $[M+H]^+$ 332.1645; found: 332.1643.



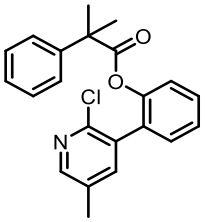
2-(2-Chloropyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-10).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.596 g, 1.7 mmol, 86% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.52 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.46 (td, *J* = 7.8, 1.7 Hz, 1H), 7.33 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 - 7.26 (m, 3H), 7.26 - 7.21 (m, 3H), 7.18 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.12 (dd, *J* = 8.2, 1.1 Hz, 1H), 1.47 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.7, 150.6, 148.9, 148.2, 143.3, 140.0, 132.8, 130.7, 130.6, 129.8, 128.5 (2C), 126.8, 126.0, 125.4 (2C), 122.2, 121.9, 46.5 (2C), 26.0.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 374.0918; found: 374.0928.



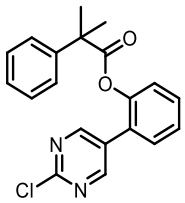
2-(2-Chloro-5-methylpyridin-3-yl)phenyl 2-methyl-2-phenylpropanoate (DG-11).

Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.582 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 2.4 Hz, 1H), 7.44 (td, *J* = 7.8, 1.8 Hz, 1H), 7.36 - 7.28 (m, 3H), 7.27 - 7.20 (m, 4H), 7.14 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.95 - 6.86 (m, 1H), 2.28 (s, 3H), 1.51 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.8, 149.0, 148.2, 147.6, 143.3, 140.8, 132.1, 131.9, 130.7, 129.8, 129.5, 128.5 (2C), 126.8, 126.0, 125.4 (2C), 122.3, 119.8, 115.6, 46.5, 17.5.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 388.1075; found: 388.1084.



2-(2-Chloropyrimidin-5-yl)phenyl 2-methyl-2-phenylpropanoate (DG-12).

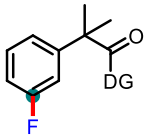
Purification via column chromatography on silica gel (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.563 g, 1.6 mmol, 80% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.46 (s, 2H), 7.49 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.34 - 7.28 (m, 4H), 7.24 - 7.21 (m, 2H), 7.16 (dd, *J* = 8.2, 1.2 Hz, 1H), 1.63 (s, 6H).

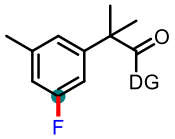
^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.7, 160.1, 158.8 (2C), 148.1, 142.7, 130.5, 130.4, 129.5, 128.6 (2C), 127.3, 126.7, 126.5, 125.2 (2C), 123.1, 46.5, 26.1 (2C).

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 375.0871; found: 375.0873.

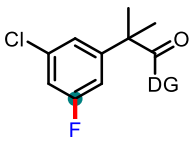
9.2 Characterisation of products



2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluorophenyl)-2-methylpropanoate (2a).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.053 g, 0.144 mmol, 72% yield);
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.38 (dd, J = 4.8, 1.9 Hz, 1H), 7.51 (dd, J = 7.5, 2.0 Hz, 1H), 7.47 (td, J = 7.8, 1.7 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.30 - 7.26 (m, 1H), 7.26 - 7.22 (m, 1H), 7.20 (dd, J = 7.5, 4.8 Hz, 1H), 7.13 (d, J = 8.2 Hz, 1H), 6.99 (dd, J = 7.9, 1.8 Hz, 1H), 6.94 (td, J = 8.3, 2.6 Hz, 1H), 6.90 (dt, J = 10.6, 2.2 Hz, 1H), 1.47 (s, 6H).
^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.1, 162.7 (d, J = 245.8 Hz), 150.6, 148.9, 148.1, 145.9 (d, J = 6.8 Hz), 139.9, 132.7, 130.6, 129.9 (d, J = 8.2 Hz), 129.9, 128.5, 126.1, 122.1, 121.9, 121.2 (d, J = 2.8 Hz), 113.8 (d, J = 21.0 Hz), 112.8 (d, J = 22.5 Hz), 46.4 (d, J = 16.6 Hz), 26.0 (2C).
^{19}F NMR (565 MHz, Chloroform-*d*) δ -112.35.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0824; found: 392.0831.



2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluoro-5-methylphenyl)-2-methylpropanoate (2b).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.050 g, 0.13 mmol, 65% yield);
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.37 (dd, J = 4.8, 1.9 Hz, 1H), 7.51 (dd, J = 7.5, 1.9 Hz, 1H), 7.46 (qd, J = 7.6, 1.8 Hz, 1H), 7.37 - 7.31 (m, 1H), 7.28 - 6.96 (m, 4H), 6.84 - 6.67 (m, 2H), 2.35 (s, 3H), 1.45 (s, 6H).
^{13}C NMR (151 MHz, Chloroform-*d*) δ 174.1, 162.7 (d, J = 244.7 Hz), 150.6, 148.9, 148.1, 140.3 (d, J = 8.5 Hz), 139.9, 132.6, 130.6, 129.8, 128.3, 126.1, 122.4 (d, J = 42.6 Hz), 122.2, 122.0 (d, J = 2.6 Hz), 121.8, 114.5 (d, J = 21.0 Hz), 109.8 (d, J = 22.7 Hz), 46.3 (d, J = 11.8 Hz), 25.9, 21.6, 21.5 (d, J = 1.8 Hz).
^{19}F NMR (565 MHz, Chloroform-*d*) δ -113.67.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 406.0981; found: 406.0986.



2-(2-Chloropyridin-3-yl)phenyl 2-(3-chloro-5-fluorophenyl)-2-methylpropanoate (2c).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.028 g, 0.07

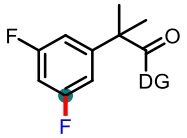
mmol, 35% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.39 (dd, J = 4.8, 2.0 Hz, 1H), 7.56 - 7.44 (m, 2H), 7.35 (td, J = 7.5, 1.1 Hz, 1H), 7.27 (d, J = 1.7 Hz, 1H), 7.22 (dd, J = 7.5, 4.8 Hz, 1H), 7.15 (d, J = 8.2 Hz, 1H), 7.02 - 6.93 (m, 2H), 6.81 (dt, J = 9.9, 2.0 Hz, 1H), 1.47 (s, 6H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.4, 162.5 (d, J = 249.3 Hz), 150.6, 149.0, 147.9, 147.0, 139.8, 135.0 (d, J = 10.9 Hz), 132.5, 130.7, 130.6, 129.9, 126.3, 122.0, 122.0 (d, J = 3.1 Hz), 121.8, 114.9 (d, J = 24.7 Hz), 111.6 (d, J = 22.5 Hz), 46.4, 25.8 (2C).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -110.08.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 426.0434; found: 426.0438.



2-(2-Chloropyridin-3-yl)phenyl 2-(3,5-difluorophenyl)-2-methylpropanoate (2d).

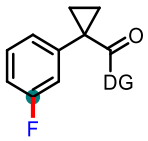
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.023 g, 0.062 mmol, 31% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.39 (dd, J = 4.8, 2.0 Hz, 1H), 7.52 (dd, J = 7.5, 2.0 Hz, 1H), 7.48 (td, J = 7.8, 1.7 Hz, 1H), 7.35 (td, J = 7.5, 1.1 Hz, 1H), 7.30 - 7.25 (m, 2H), 7.23 (dd, J = 7.5, 4.8 Hz, 1H), 7.14 (d, J = 8.2 Hz, 1H), 6.77 - 6.65 (m, 3H), 1.47 (s, 7H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 173.5, 163.7 (d, J = 13.2 Hz), 162.1 (d, J = 13.1 Hz), 150.6, 149.0, 148.0, 147.2 (d, J = 8.4 Hz), 139.8, 132.6, 130.7, 130.6, 129.9, 126.3, 122.0, 121.8, 109.0 (d, J = 5.2 Hz), 108.8 (d, J = 5.5 Hz), 102.5 (t, J = 25.2 Hz), 46.4, 25.8 (2C).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -109.00.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 410.0730; found: 410.0736.



2-(2-Chloropyridin-3-yl)phenyl 1-(3-fluorophenyl)cyclopropane-1-carboxylate (2e).

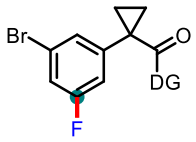
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.055 g, 0.15 mmol, 75% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.50 (dd, J = 4.8, 2.0 Hz, 1H), 7.51 (dd, J = 7.5, 2.0 Hz, 1H), 7.46 (ddd, J = 8.2, 7.4, 1.8 Hz, 1H), 7.35 - 7.30 (m, 2H), 7.27 (dd, J = 7.5, 1.7 Hz, 1H), 7.24 (dd, J = 8.3, 1.2 Hz, 1H), 7.20 (td, J = 8.0, 6.0 Hz, 1H), 6.96 - 6.88 (m, 2H), 6.83 (ddd, J = 9.7, 2.6, 1.6 Hz, 1H), 1.53 (q, J = 3.8 Hz, 2H), 1.18 (q, J = 3.8 Hz, 2H).

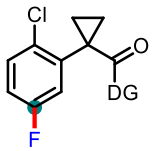
^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.9, 162.3 (d, J = 245.9 Hz), 150.8, 148.9, 148.1, 140.8 (d, J = 7.8 Hz), 140.1, 132.9, 130.5, 130.3, 129.7, 129.6 (d, J = 8.4 Hz), 126.1 (d, J = 2.9 Hz), 126.0, 122.4, 122.0, 117.4 (d, J = 21.5 Hz), 114.3 (d, J = 21.0 Hz), 28.8 (d, J = 2.0 Hz), 17.1(2C).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -113.33.

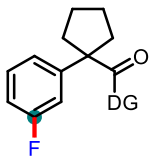
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 390.0668; found: 390.0672.



2-(2-Chloropyridin-3-yl)phenyl 1-(3-bromo-5-fluorophenyl)cyclopropane-1-carboxylate (2f).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.026 g, 0.058 mmol, 29% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.53 - 7.41 (m, 2H), 7.36 - 7.27 (m, 2H), 7.27 - 7.19 (m, 2H), 7.14 - 7.09 (m, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.77 (dt, *J* = 9.2, 1.9 Hz, 1H), 1.52 (q, *J* = 4.2 Hz, 2H), 1.15 (q, *J* = 4.2 Hz, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.24, 162.10 (d, *J* = 250.9 Hz), 150.72, 149.15, 148.01, 142.33 (d, *J* = 8.3 Hz), 140.08, 132.79, 130.57, 130.25, 129.82, 129.42, 126.13, 122.40, 122.06, 118.45 (d, *J* = 2.2 Hz), 118.21, 116.79 (d, *J* = 2.7 Hz), 116.58 (d, *J* = 2.8 Hz), 28.72, 28.70, 17.20.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.77.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 467.9778; found: 467.9783.



2-(2-Chloropyridin-3-yl) phenyl 1-(2-chloro-5-fluorophenyl) cyclopropane-1-carboxylate (2g).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.030 g, 0.074 mmol, 37% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.51 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.46 (td, *J* = 7.7, 1.8 Hz, 1H), 7.34 - 7.26 (m, 4H), 7.26 - 7.24 (m, 1H), 6.94 (ddd, *J* = 8.8, 7.8, 3.0 Hz, 1H), 6.86 (dd, *J* = 8.9, 3.0 Hz, 1H), 1.67 (q, *J* = 3.6 Hz, 2H), 1.20 (q, *J* = 3.6 Hz, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.9, 160.9 (d, *J* = 246.7 Hz), 150.7, 148.9, 148.0, 140.1, 138.4 (d, *J* = 7.8 Hz), 132.9, 131.6 (d, *J* = 3.3 Hz), 130.6, 130.5 (d, *J* = 5.0 Hz), 130.4 (d, *J* = 15.2 Hz), 129.8, 126.0, 122.3, 122.0, 118.6 (d, *J* = 23.2 Hz), 115.8 (d, *J* = 22.7 Hz), 28.1 (d, *J* = 1.6 Hz), 18.2 (2C).
^{19}F NMR (376 MHz, Chloroform-*d*) δ -115.21.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 424.0283; found: 424.0291.

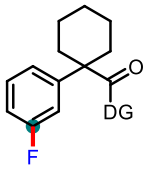


2-(2-Chloropyridin-3-yl)phenyl 1-(3-fluorophenyl)cyclopentane-1-carboxylate (2h).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.065 g, 0.166 mmol, 83% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.47 - 7.39 (m, 2H), 7.32 (td, *J* = 7.5, 1.2 Hz, 1H), 7.27 - 7.18 (m, 2H), 7.14 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.02 (ddd, *J* = 8.1, 3.2, 1.3 Hz, 2H), 6.99 - 6.83 (m, 2H), 2.56 (s, 2H), 1.84 (dt, *J* = 12.8, 8.6 Hz, 2H), 1.73 - 1.60 (m, 2H), 1.52 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.4, 162.5 (d, J = 245.7 Hz), 150.5, 148.9, 148.1, 144.5 (d, J = 7.1 Hz), 139.7, 132.6, 130.7 (d, J = 7.3 Hz), 130.6, 129.9, 129.8 (d, J = 8.2 Hz), 126.1, 122.5 (d, J = 2.9 Hz), 122.3, 121.8, 114.0 (d, J = 9.0 Hz), 113.8 (d, J = 8.0 Hz), 58.9 (d, J = 1.8 Hz), 35.8 (2C), 23.2 (2C).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.71.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 418.0986; found: 418.0992.



2-(2-Chloropyridin-3-yl)phenyl 1-(3-fluorophenyl)cyclohexane-1-carboxylate (2i).

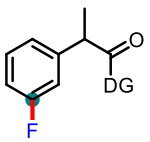
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.071 g, 0.174 mmol, 87% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (dd, J = 4.8, 2.0 Hz, 1H), 7.45 (ddd, J = 10.2, 7.8, 1.9 Hz, 2H), 7.32 (td, J = 7.5, 1.2 Hz, 1H), 7.24 (dtd, J = 8.1, 6.7, 1.7 Hz, 2H), 7.12 (dd, J = 7.5, 4.8 Hz, 1H), 7.09 - 7.03 (m, 2H), 6.98 - 6.88 (m, 2H), 2.56 - 2.31 (m, 2H), 1.77 - 1.48 (m, 4H), 1.46 - 0.99 (m, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8, 162.8 (d, J = 245.4 Hz), 150.5, 148.9, 148.1, 145.1 (d, J = 7.0 Hz), 139.8, 132.6, 130.7 (d, J = 2.3 Hz), 130.7, 129.9 (d, J = 8.3 Hz), 129.8, 126.0, 122.2, 121.8, 121.5 (d, J = 2.8 Hz), 113.9 (d, J = 21.1 Hz), 113.1 (d, J = 22.5 Hz), 50.5 (d, J = 1.7 Hz), 34.3 (2C), 25.3, 23.3 (2C).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.27.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 432.1143; found: 432.1139.



2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluorophenyl)propanoate (2j).

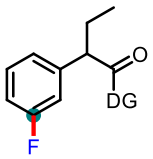
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.051 g, 0.144 mmol, 68% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.32 (s, 1H), 7.47 (qd, J = 7.8, 1.8 Hz, 2H), 7.35 (td, J = 7.5, 1.1 Hz, 1H), 7.28 - 7.16 (m, 3H), 7.13 (dd, J = 7.6, 4.9 Hz, 1H), 7.10 - 6.89 (m, 2H), 6.81 (s, 1H), 3.76 (q, J = 5.2, 3.3 Hz, 1H), 1.40 (d, J = 6.8 Hz, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.8, 162.7 (d, J = 246.1 Hz), 150.4, 148.9, 147.8, 141.4 (d, J = 7.5 Hz), 139.8, 132.4, 130.7 (d, J = 17.7 Hz), 130.1 (d, J = 8.3 Hz), 129.9, 128.7, 127.2 (d, J = 11.6 Hz), 126.2, 123.2, 122.4, 121.8, 114.3 (d, J = 21.1 Hz), 45.0, 17.9.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -112.41.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 378.0668; found: 378.0675.



2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluorophenyl)butanoate (2k).

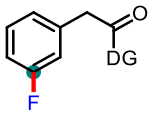
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.050 g, 0.136mmol, 68% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.29 (s, 1H), 7.47 (tt, *J* = 8.7, 4.3 Hz, 1H), 7.35 (td, *J* = 7.6, 1.2 Hz, 1H), 7.27 - 7.19 (m, 2H), 7.12 (d, *J* = 34.0 Hz, 2H), 6.95 (ddd, *J* = 21.6, 10.8, 5.1 Hz, 2H), 6.82 (s, 1H), 3.62 - 3.22 (m, 1H), 2.11 - 1.63 (m, 3H), 1.40 - 1.17 (m, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.7, 162.8 (d, *J* = 246.4 Hz), 148.9, 147.8, 140.2, 139.8, 132.5, 130.7 (d, *J* = 6.6 Hz), 130.1 (d, *J* = 8.3 Hz), 129.9, 128.6, 127.7, 127.2, 126.2, 126.1, 122.4, 121.8, 114.3 (d, *J* = 21.1 Hz), 52.9, 26.1, 11.8.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -112.53.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0824; found: 392.0824.



2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluorophenyl)acetate (2l).

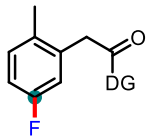
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.035 g, 0.104 mmol, 52% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.49 (dtd, *J* = 8.0, 3.9, 1.6 Hz, 2H), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H), 7.31 - 7.28 (m, 1H), 7.27 - 7.18 (m, 2H), 7.15 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.97 (td, *J* = 8.5, 2.6 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.78 (dt, *J* = 9.6, 2.1 Hz, 1H), 3.62 (s, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.8, 162.7 (d, *J* = 246.4 Hz), 150.4, 149.0, 147.8, 139.8, 134.9 (d, *J* = 7.7 Hz), 132.5, 130.8, 130.6, 130.1 (d, *J* = 8.3 Hz), 129.9, 126.3, 124.8 (d, *J* = 2.9 Hz), 122.4, 121.9, 116.0 (d, *J* = 22.0 Hz), 114.3 (d, *J* = 21.1 Hz), 40.8 (d, *J* = 1.9 Hz).

^{19}F NMR (565 MHz, Chloroform-*d*) δ -112.72.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 364.0511; found: 364.0515.



2-(2-Chloropyridin-3-yl)phenyl 2-(5-fluoro-2-methylphenyl)acetate (2m).

Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.048 g, 0.138 mmol, 69% yield);

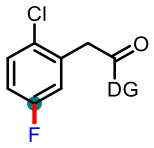
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.49 (dq, *J* = 6.2, 1.9 Hz, 2H), 7.36 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 - 7.27 (m, 1H), 7.25 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.16 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.07 (dd, *J* = 8.4, 5.8 Hz, 1H), 6.87 (td, *J* = 8.4, 2.8 Hz, 1H), 6.72 (dd, *J* = 9.3, 2.7 Hz, 1H), 3.62 (s, 2H), 2.12 (s, 3H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.7, 161.0 (d, *J* = 243.7 Hz), 150.4, 149.0, 147.8, 139.8,

133.1 (d, J = 7.3 Hz), 132.5, 132.2 (d, J = 3.6 Hz), 131.6 (d, J = 7.8 Hz), 130.8, 130.6, 129.9, 126.3, 122.4, 121.9, 116.6 (d, J = 21.7 Hz), 114.3 (d, J = 20.5 Hz), 38.8 (d, J = 1.4 Hz), 18.6.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -117.42.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 378.0668; found: 378.0672.



2-(2-Chloropyridin-3-yl)phenyl 2-(2-chloro-5-fluorophenyl)acetate (2n).

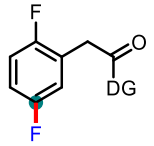
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.021 g, 0.056 mmol, 28% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.37 (d, J = 5.9 Hz, 1H), 7.50 (d, J = 6.5 Hz, 2H), 7.41 - 7.30 (m, 2H), 7.22 (ddt, J = 34.2, 7.7, 3.6 Hz, 2H), 7.01 (t, J = 6.1 Hz, 1H), 6.88 (s, 1H), 6.76 - 6.62 (m, 1H), 3.59 (t, J = 3.7 Hz, 2H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.1, 162.5 (d, J = 249.9 Hz), 150.4, 149.1, 147.7, 139.8, 136.0 (d, J = 9.2 Hz), 135.1 (d, J = 10.4 Hz), 132.4, 130.8, 130.5, 130.0, 126.5, 125.2 (d, J = 3.3 Hz), 122.3, 121.9, 115.4 (d, J = 24.7 Hz), 114.8 (d, J = 21.9 Hz), 40.5.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -110.41.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 398.0121; found: 398.0126.



2-(2-Chloropyridin-3-yl) phenyl 2-(2,5-difluorophenyl) acetate (2o).

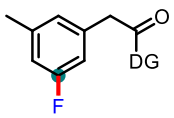
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.024 g, 0.068 mmol, 34% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, J = 4.8, 2.0 Hz, 1H), 7.55 (dd, J = 7.5, 2.0 Hz, 1H), 7.50 (td, J = 7.8, 1.8 Hz, 1H), 7.37 (td, J = 7.5, 1.2 Hz, 1H), 7.32 - 7.28 (m, 1H), 7.27 - 7.22 (m, 2H), 7.03 - 6.90 (m, 2H), 6.76 (ddd, J = 8.6, 5.7, 2.9 Hz, 1H), 3.66 (d, J = 1.4 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.99, 158.36 (dd, J = 242.8, 2.3 Hz), 156.85 (dd, J = 243.0, 2.6 Hz), 150.49, 149.05, 147.83, 140.00, 132.59, 130.86, 130.54, 130.01, 126.42, 122.47, 122.06, 121.69 (dd, J = 18.7, 8.4 Hz), 117.58 (dd, J = 24.5, 4.0 Hz), 116.45 (dd, J = 24.8, 8.8 Hz), 115.76 (dd, J = 23.9, 8.4 Hz), 34.28 (dd, J = 2.8, 1.1 Hz).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -118.64 (d, J = 17.5 Hz), -123.18 (d, J = 17.3 Hz).

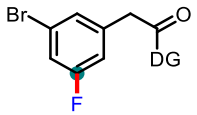
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 382.0422; found: 382.0431.



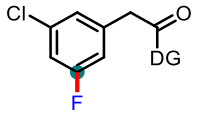
2-(2-Chloropyridin-3-yl)phenyl 2-(3-fluoro-5-methylphenyl)acetate (2p).

Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.044 g, 0.126 mmol, 63% yield);

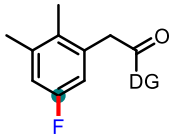
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.36 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.49 (ddd, *J* = 7.8, 4.9, 1.9 Hz, 2H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.25 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.16 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.07 (dd, *J* = 8.4, 5.9 Hz, 1H), 6.88 (td, *J* = 8.4, 2.8 Hz, 1H), 6.72 (dd, *J* = 9.3, 2.7 Hz, 1H), 3.62 (s, 2H), 2.12 (s, 3H).
^{13}C NMR (151 MHz, Chloroform-*d*) δ 168.7, 161.0 (d, *J* = 243.9 Hz), 150.4, 149.0, 147.8, 139.8, 133.1 (d, *J* = 7.6 Hz), 132.5, 132.2 (d, *J* = 3.3 Hz), 131.6 (d, *J* = 8.1 Hz), 130.8, 130.64 129.9, 126.3, 122.4, 121.9, 116.6 (d, *J* = 21.7 Hz), 114.3 (d, *J* = 20.6 Hz), 38.8, 18.6.
^{19}F NMR (565 MHz, Chloroform-*d*) δ -117.43.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 378.0668; found: 378.0671.



2-(2-Chloropyridin-3-yl) phenyl 2-(3-bromo-5-fluorophenyl) acetate (2q).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.022 g, 0.052 mmol, 26% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.38 (td, *J* = 7.5, 1.2 Hz, 1H), 7.30 (d, *J* = 9.8 Hz,1H), 7.24 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.22 - 7.13 (m, 2H), 7.04 (d, *J* = 1.8 Hz, 1H), 6.75 (dt, *J* = 9.0, 1.9 Hz, 1H), 3.59 (s, 2H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.21, 162.46 (d, *J* = 251.1 Hz), 150.43, 149.16, 147.73, 139.89, 136.32 (d, *J* = 8.4 Hz), 132.42, 130.88, 130.58, 130.06, 128.17 (d, *J* = 3.3 Hz), 126.53, 122.66 (d, *J* = 10.2 Hz), 122.38, 121.95, 118.29 (d, *J* = 24.3 Hz), 115.30 (d, *J* = 21.8 Hz), 40.50 (d, *J* = 1.8 Hz).
^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.16.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 441.9622; found: 441.9631.



2-(2-Chloropyridin-3-yl) phenyl 2-(3-chloro-5-fluorophenyl) acetate (2r).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.021g, 0.056 mmol, 29% yield);
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.56 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.50 (td, *J* = 7.8, 1.7 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.32 - 7.28 (m, 3H), 7.25 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.96 (td, *J* = 8.3, 3.0 Hz, 1H), 6.84 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.77 (s, 2H).
^{13}C NMR (151 MHz, Chloroform-*d*) δ 167.7, 161.0 (d, *J* = 247.0 Hz), 150.5, 149.0, 147.8, 140.0, 133.0 (d, *J* = 8.3 Hz), 132.7, 130.8, 130.6 (d, *J* = 8.5 Hz), 130.5, 129.9, 129.4 (d, *J* = 3.3 Hz), 126.3, 122.4, 122.0, 118.2 (d, *J* = 23.5 Hz), 116.0 (d, *J* = 22.6 Hz), 38.9.
^{19}F NMR (565 MHz, Chloroform-*d*) δ -114.91.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 398.0121; found: 398.0128.



2-(2-Chloropyridin-3-yl) phenyl 2-(5-fluoro-2,3-dimethylphenyl) acetate (2s).

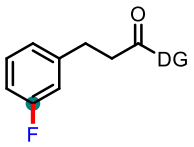
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as white solid (0.037g, 0.102 mmol, 51% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 (dd, J = 4.8, 2.0 Hz, 1H), 7.63 - 7.42 (m, 2H), 7.36 (td, J = 7.5, 1.2 Hz, 1H), 7.32 - 7.22 (m, 2H), 7.14 (dd, J = 7.6, 4.8 Hz, 1H), 6.80 (dd, J = 9.4, 2.8 Hz, 1H), 6.60 (dd, J = 9.2, 2.8 Hz, 1H), 3.64 (s, 2H), 2.26 (s, 3H), 1.97 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.9, 160.3 (d, J = 242.9 Hz), 148.9, 147.8, 139.8, 139.2 (d, J = 7.6 Hz), 132.9 (d, J = 7.8 Hz), 132.5, 130.9, 130.9 (d, J = 3.4 Hz), 130.8, 130.6, 129.9, 126.3, 122.5, 121.8, 115.9 (d, J = 20.5 Hz), 114.4 (d, J = 21.3 Hz), 39.4 (d, J = 1.7 Hz), 20.9, 14.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -118.53.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0830; found: 392.0836.



2-(2-Chloropyridin-3-yl)phenyl 4-(3-fluorophenyl)butanoate (4a).

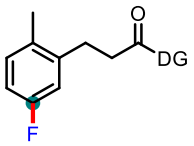
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.058g, 0.158 mmol, 79% yield);

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.41 (dd, J = 4.8, 2.0 Hz, 1H), 7.64 (dd, J = 7.5, 2.0 Hz, 1H), 7.50 (td, J = 7.7, 1.8 Hz, 1H), 7.38 - 7.32 (m, 3H), 7.26 - 7.19 (m, 2H), 6.91 (dt, J = 13.8, 5.1 Hz, 1H), 6.82 (dt, J = 10.1, 2.1 Hz, 1H), 2.50 (t, J = 7.7 Hz, 2H), 2.33 (t, J = 7.3 Hz, 2H), 1.79 (p, J = 7.2 Hz, 1H).

^{13}C NMR (151 MHz, Chloroform-*d*) δ 171.2, 162.9 (d, J = 245.4 Hz), 149.0, 143.5 (d, J = 7.1 Hz), 140.2, 133.0, 130.7, 130.6, 130.0, 129.8 (d, J = 8.3 Hz), 129.0, 128.6, 126.2, 124.0 (d, J = 2.8 Hz), 122.6, 122.1, 115.2 (d, J = 21.0 Hz), 112.9 (d, J = 21.2 Hz), 34.4 (d, J = 1.6 Hz), 33.2, 25.8.

^{19}F NMR (565 MHz, Chloroform-*d*) δ -113.61.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0824; found: 392.0831.



2-(2-Chloropyridin-3-yl)phenyl 3-(5-fluoro-2-methylphenyl)propanoate (4b).

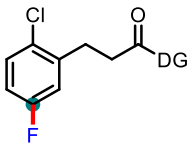
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.066g, 0.18 mmol, 90% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, J = 4.8, 2.0 Hz, 1H), 7.61 (dd, J = 7.5, 2.0 Hz, 1H), 7.51 (ddd, J = 8.2, 7.2, 2.0 Hz, 1H), 7.38 (td, J = 7.4, 1.2 Hz, 1H), 7.34 (dd, J = 7.6, 2.0 Hz, 1H), 7.28 - 7.19 (m, 2H), 7.09 (dd, J = 8.3, 5.9 Hz, 1H), 6.91 - 6.67 (m, 2H), 2.75 (t, J = 7.7 Hz, 2H), 2.65 - 2.52 (m, 2H), 2.22 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 161.2 (d, J = 243.3 Hz), 150.6, 149.0, 147.9, 140.1, 139.9 (d, J = 7.0 Hz), 132.9, 131.5 (d, J = 3.8 Hz), 131.4, 130.8, 130.5, 130.0, 126.3, 122.6, 122.1, 114.9 (d, J = 21.3 Hz), 113.0 (d, J = 20.6 Hz), 33.9, 27.8 (d, J = 1.6 Hz), 18.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.45.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0830; found: 392.0822.



2-(2-Chloropyridin-3-yl)phenyl 3-(2-chloro-5-fluorophenyl)propanoate (4c).

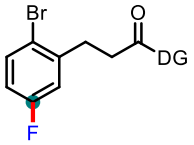
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.045g, 0.116 mmol, 58% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.47 - 8.32 (m, 1H), 7.58 (dd, J = 7.5, 1.9 Hz, 1H), 7.48 (ddd, J = 8.0, 7.1, 2.0 Hz, 1H), 7.42 - 7.26 (m, 2H), 7.26 - 7.16 (m, 3H), 6.94 - 6.82 (m, 2H), 2.87 (t, J = 7.7 Hz, 2H), 2.64 (d, J = 8.2 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.4, 161.2 (d, J = 246.4 Hz), 150.6, 149.0, 147.9, 140.0, 139.4 (d, J = 7.6 Hz), 132.8, 130.8, 130.7, 130.5, 128.7, 126.2, 122.5, 122.0, 117.3 (d, J = 4.9 Hz), 117.1 (d, J = 3.2 Hz), 115.0 (d, J = 3.0 Hz), 114.8 (d, J = 3.0 Hz), 33.3, 28.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.77.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 412.0283; found: 412.0292.



2-(2-Chloropyridin-3-yl)phenyl 3-(2-bromo-5-fluorophenyl)propanoate (4d).

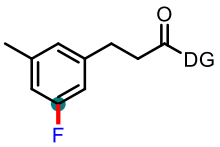
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.033g, 0.078 mmol, 39% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, J = 4.7, 1.9 Hz, 1H), 7.58 (dt, J = 7.5, 1.7 Hz, 1H), 7.51 - 7.41 (m, 2H), 7.39 - 7.30 (m, 2H), 7.26 - 7.17 (m, 2H), 6.90 (dd, J = 9.2, 3.0 Hz, 1H), 6.82 (td, J = 8.3, 2.9 Hz, 1H), 2.87 (t, J = 7.7 Hz, 2H), 2.62 (t, J = 7.7 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.3, 161.9 (d, J = 247.0 Hz), 150.6, 149.1, 147.9, 141.2 (d, J = 7.6 Hz), 140.1, 134.0 (d, J = 8.3 Hz), 132.9, 130.8, 130.5, 130.0, 126.3, 122.6, 122.1, 118.3 (d, J = 3.2 Hz), 117.5 (d, J = 3.5 Hz), 117.3 (d, J = 3.5 Hz), 33.5, 31.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.56.

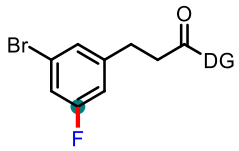
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 455.9778; found: 455.9778.



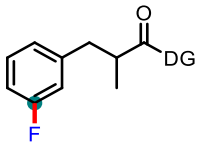
2-(2-Chloropyridin-3-yl)phenyl 3-(3-fluoro-5-methylphenyl)propanoate (4e).

Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.064g, 0.176 mmol, 88% yield);

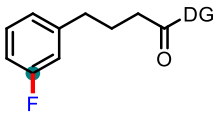
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.59 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.50 (ddd, *J* = 8.2, 7.1, 2.1 Hz, 1H), 7.41 - 7.31 (m, 2H), 7.26 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.19 (dd, *J* = 8.1, 1.2 Hz, 1H), 6.78 - 6.58 (m, 3H), 2.76 (t, *J* = 7.9 Hz, 2H), 2.62 (s, 2H), 2.33 (s, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 162.8 (d, *J* = 245.1 Hz), 150.6, 149.0, 147.9, 141.9 (d, *J* = 7.9 Hz), 140.4 (d, *J* = 8.2 Hz), 140.1, 132.8, 130.8, 130.5, 130.0, 126.2, 124.7 (d, *J* = 2.4 Hz), 122.6, 122.1, 113.9 (d, *J* = 20.9 Hz), 112.1 (d, *J* = 21.3 Hz), 35.2, 30.2 (d, *J* = 1.8 Hz), 21.3 (d, *J* = 1.8 Hz).
^{19}F NMR (376 MHz, Chloroform-*d*) δ -114.44.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0830; found: 392.0826.



2-(2-Chloropyridin-3-yl)phenyl 3-(3-bromo-5-fluorophenyl)propanoate (4f).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.025g, 0.058 mmol, 29% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 4.9, 2.0 Hz, 1H), 7.58 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.50 (td, *J* = 7.7, 1.9 Hz, 1H), 7.44 - 7.31 (m, 2H), 7.26 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.20 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.16 - 7.07 (m, 2H), 6.79 (dt, *J* = 9.3, 2.0 Hz, 1H), 3.02 - 2.40 (m, 4H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.30, 162.60 (d, *J* = 250.7 Hz), 150.59, 149.08, 147.84, 143.89 (d, *J* = 8.0 Hz), 140.07, 132.82, 130.87, 130.51, 130.07, 127.34 (d, *J* = 3.1 Hz), 126.35, 122.54, 122.51 (d, *J* = 10.1 Hz), 122.12, 117.24 (d, *J* = 24.5 Hz), 114.35 (d, *J* = 21.2 Hz), 34.86, 29.88 (d, *J* = 1.8 Hz).
^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.71.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 455.9778; found: 455.9783.



2-(2-Chloropyridin-3-yl)phenyl 3-(3-fluorophenyl)-2-methylpropanoate (4g).
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.055g, 0.15 mmol, 75% yield);
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.60 (s, 1H), 7.54 - 7.41 (m, 1H), 7.41 - 7.29 (m, 2H), 7.25 (td, *J* = 7.9, 6.0 Hz, 2H), 7.14 - 7.01 (m, 1H), 6.99 - 6.89 (m, 2H), 6.84 (dt, *J* = 9.8, 2.1 Hz, 1H), 2.90 (dd, *J* = 13.6, 7.4 Hz, 1H), 2.76 (s, 1H), 2.55 (dd, *J* = 13.5, 7.2 Hz, 1H), 1.62 (d, *J* = 1.7 Hz, 3H).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.8, 162.7 (d, *J* = 245.8 Hz), 150.7, 149.0, 147.9, 141.3 (d, *J* = 7.4 Hz), 140.2, 132.9, 130.7, 130.6, 130.0, 129.8 (d, *J* = 8.4 Hz), 126.2, 124.6 (d, *J* = 2.9 Hz), 122.5, 122.0, 115.8 (d, *J* = 21.1 Hz), 113.4 (d, *J* = 21.0 Hz), 38.7 (d, *J* = 1.8 Hz), 38.7, 16.5.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.38.
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0830; found: 392.0828.



2-(2-Chloropyridin-3-yl)phenyl 4-(3-fluorophenyl)butanoate (4h).

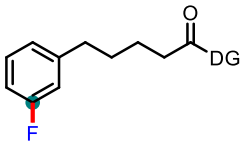
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.039g, 0.108 mmol, 54% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 - 8.26 (m, 1H), 7.64 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.51 (td, *J* = 7.7, 2.0 Hz, 1H), 7.45 - 7.29 (m, 3H), 7.24 (dd, *J* = 10.5, 7.5 Hz, 2H), 7.11 - 6.74 (m, 3H), 2.48 (dt, *J* = 12.9, 7.6 Hz, 2H), 2.33 (t, *J* = 7.3 Hz, 2H), 1.79 (p, *J* = 7.6 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.3, 162.9 (d, *J* = 245.5 Hz), 150.7, 149.0, 147.9, 143.5 (d, *J* = 7.2 Hz), 140.2, 133.0, 130.8, 130.6, 130.0, 129.8 (d, *J* = 8.4 Hz), 126.2, 124.1 (d, *J* = 2.7 Hz), 122.6, 122.1, 115.2 (d, *J* = 20.9 Hz), 112.9 (d, *J* = 21.0 Hz), 34.4 (d, *J* = 1.4 Hz), 33.2, 25.8.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.61.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 392.0830; found: 392.0823.



2-(2-Chloropyridin-3-yl)phenyl 5-(3-fluorophenyl)pentanoate (4i).

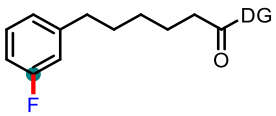
Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.032g, 0.086 mmol, 43% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (dt, *J* = 4.4, 2.1 Hz, 1H), 7.62 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.50 (td, *J* = 7.6, 1.9 Hz, 1H), 7.44 - 7.30 (m, 3H), 7.27 - 7.18 (m, 2H), 7.13 - 6.95 (m, 1H), 6.95 - 6.82 (m, 2H), 2.54 (dt, *J* = 11.3, 7.0 Hz, 2H), 2.41 - 2.27 (m, 2H), 1.47 (dq, *J* = 9.1, 5.0, 3.9 Hz, 4H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.5, 162.9 (d, *J* = 245.2 Hz), 150.6, 148.9, 148.0, 144.4 (d, *J* = 7.0 Hz), 140.2, 133.0, 130.7, 130.0, 129.7 (d, *J* = 8.4 Hz), 128.9, 126.1, 124.0 (d, *J* = 2.7 Hz), 122.6, 122.1, 115.2 (d, *J* = 20.7 Hz), 112.7 (d, *J* = 21.0 Hz), 35.1 (d, *J* = 1.6 Hz), 33.9, 30.2, 24.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.86.

HRMS (ESI-TOF): calcd. $[M+Na]^+$ 406.0986; found: 406.0989.



2-(2-Chloropyridin-3-yl)phenyl 6-(3-fluorophenyl)hexanoate (4j).

Purification via TLC (PE: EA = 7:1, v/v) afforded the desired product as colorless oil (0.027 g, 0.07 mmol, 35% yield);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dq, *J* = 5.0, 3.1, 2.4 Hz, 1H), 7.63 (dt, *J* = 7.4, 1.3 Hz, 1H), 7.50 (ddd, *J* = 8.1, 7.2, 2.0 Hz, 1H), 7.44 - 7.29 (m, 3H), 7.29 - 7.17 (m, 2H), 7.16 - 7.08 (m, 1H), 7.02 - 6.82 (m, 2H), 2.56 (dt, *J* = 11.6, 7.7 Hz, 2H), 2.31 (td, *J* = 7.4, 1.6 Hz, 2H), 1.61 - 1.41 (m, 4H), 1.20 (tt, *J* = 9.9, 6.2 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 161.2 (d, *J* = 243.0 Hz), 150.7, 148.9, 148.0, 144.9 (d, *J* = 7.1 Hz), 140.2, 137.9 (d, *J* = 3.2 Hz), 133.1, 130.7, 130.6, 130.0, 129.7, 129.6, 126.1, 124.0

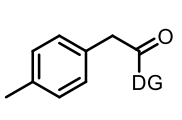
(d, J = 3.0 Hz), 122.6, 122.1, 115.0 (d, J = 21.0 Hz), 112.6 (d, J = 21.1 Hz), 34.7, 34.0 (d, J = 2.3 Hz), 31.0, 28.3, 24.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.98.

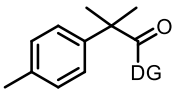
HRMS (ESI-TOF): calcd. $[M+Na]^+$ 420.1143; found: 420.1149.

10. Failed or less successful substrates

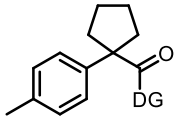
The limitation of the substrate scope was summarized as below. Under the optimized reaction conditions, the para-substituted substrates did not afford the target product, with only starting material recovered (defined as N.R.). This is probably due to significantly increased steric hindrance. In addition, the substrates bearing strong electron-withdrawing groups, such as cyano and carbonyl, were less successful in this reaction, probably because of that the low electron density of target aromatic ring is less favored for the electrophilic C-H palladation. We also tried drug-relevant substrates, however, most of them have a para-substituents, which prohibited the *meta*-C-H fluorination and resulted in only trace of the product.



N.R.



trace



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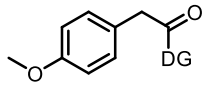

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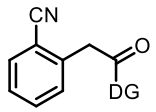

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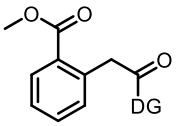

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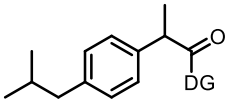

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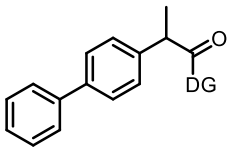

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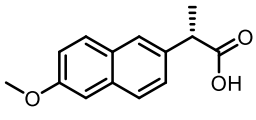
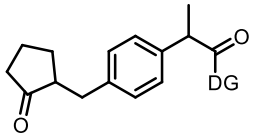
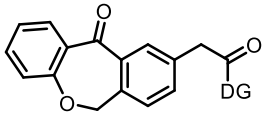


N.R.

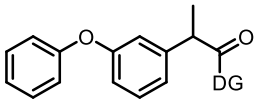


N.R.



N.R.

For the substrate bearing an electron-donating group (e.g. phenoxyl, methoxyl) at the meta-position, poor regioselectivity was observed due to the background electrophilic fluorination, which resulted in a complex mixture of regioisomers and separation was highly challenging.



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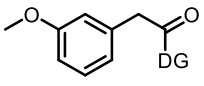

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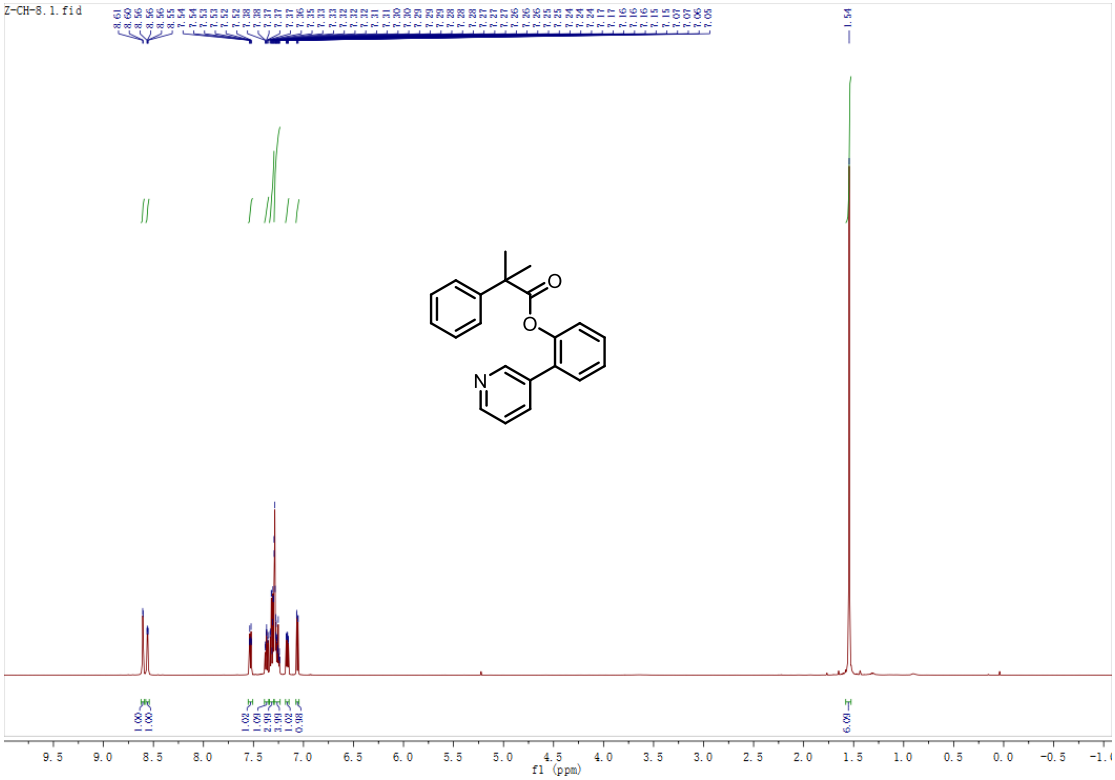
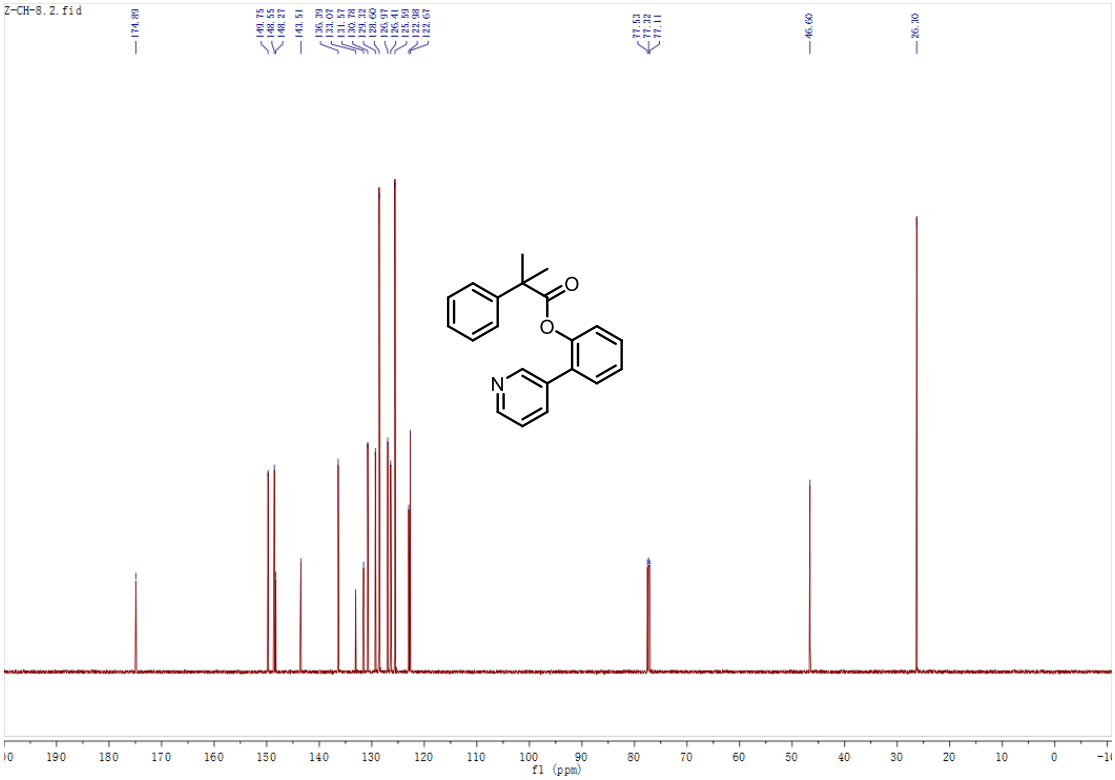
11. Copy of NMR spectra

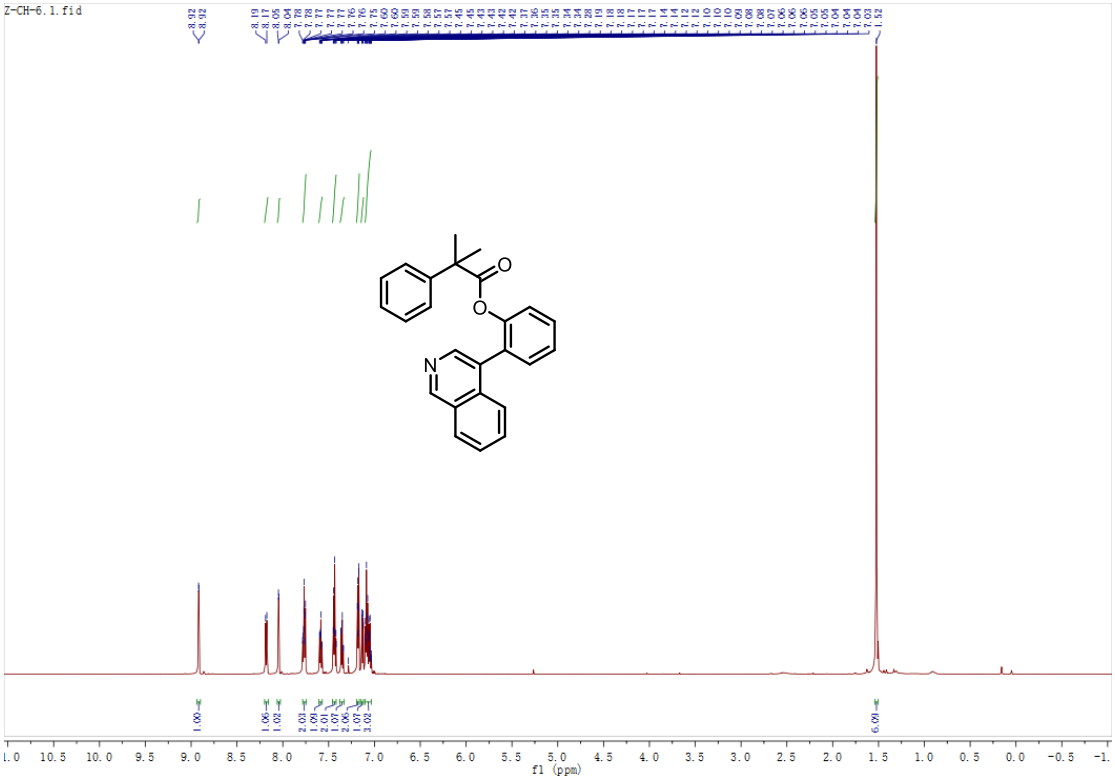
11.1 NMR spectra of the starting materials bearing different directing groups



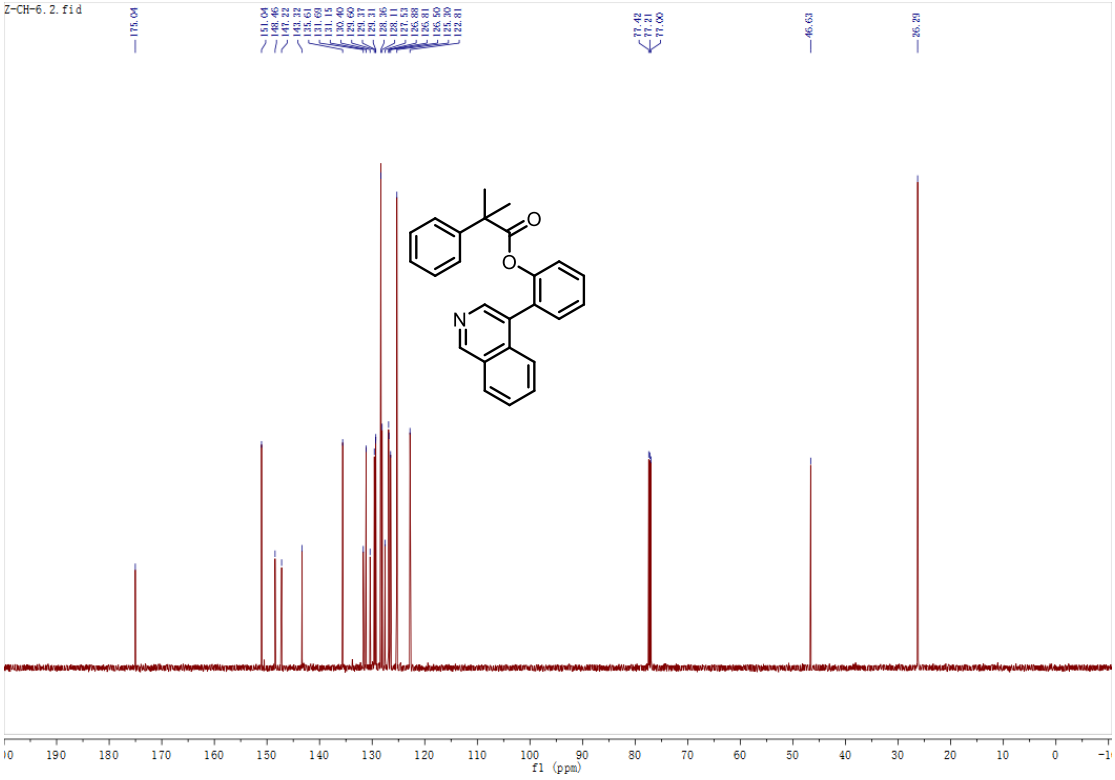
^{1}H NMR spectrum of DG-1 (500 MHz, $CDCl_3$)



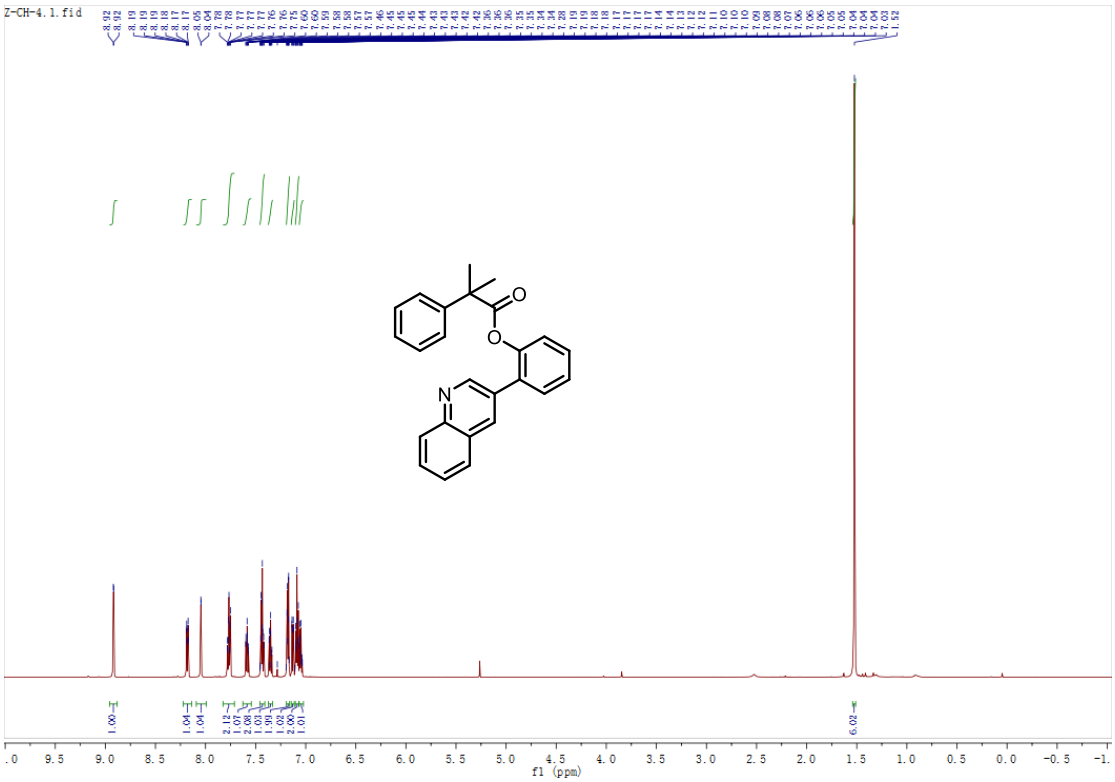
^{13}C NMR spectrum of DG-1 (126 MHz, $CDCl_3$)



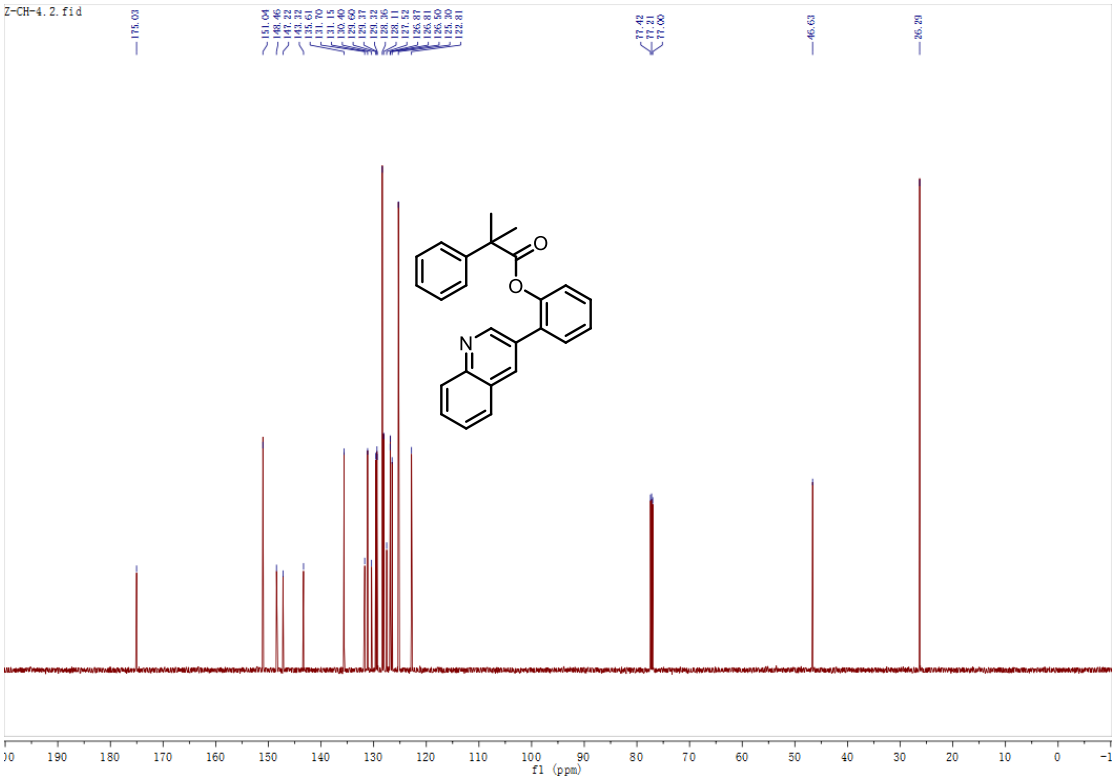
^{1}H NMR spectrum of DG-3(500 MHz, $CDCl_3$)



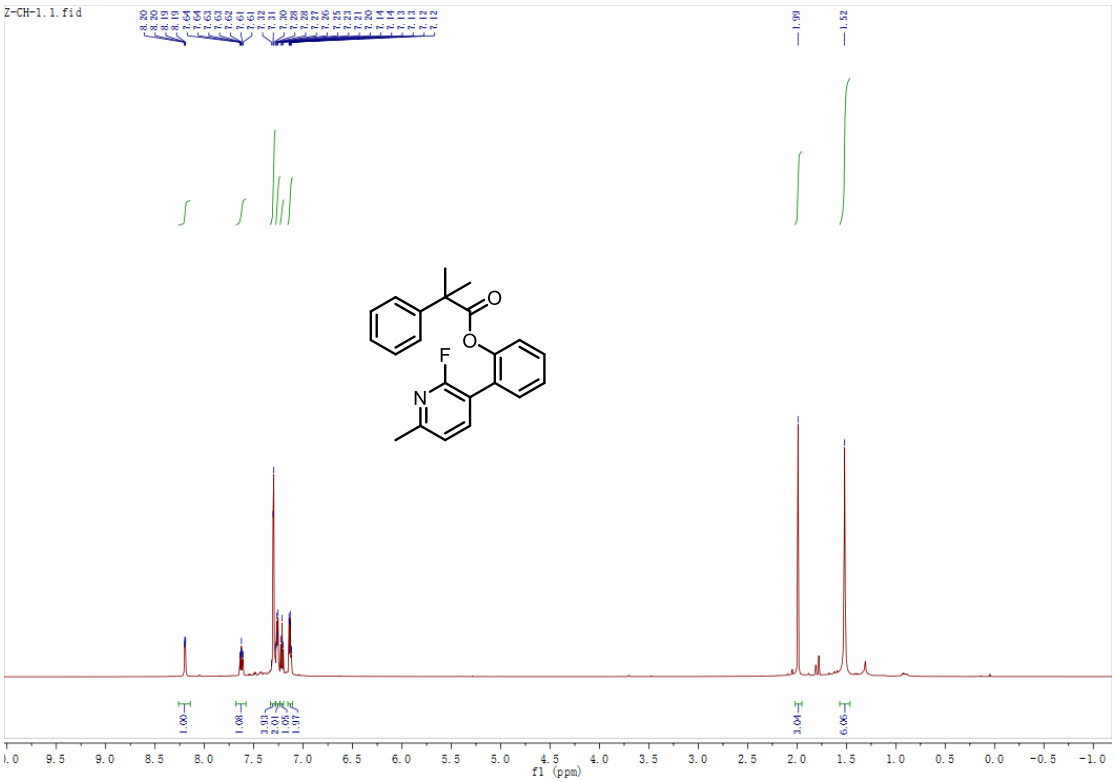
^{13}C NMR spectrum of DG-3 (126 MHz, $CDCl_3$)



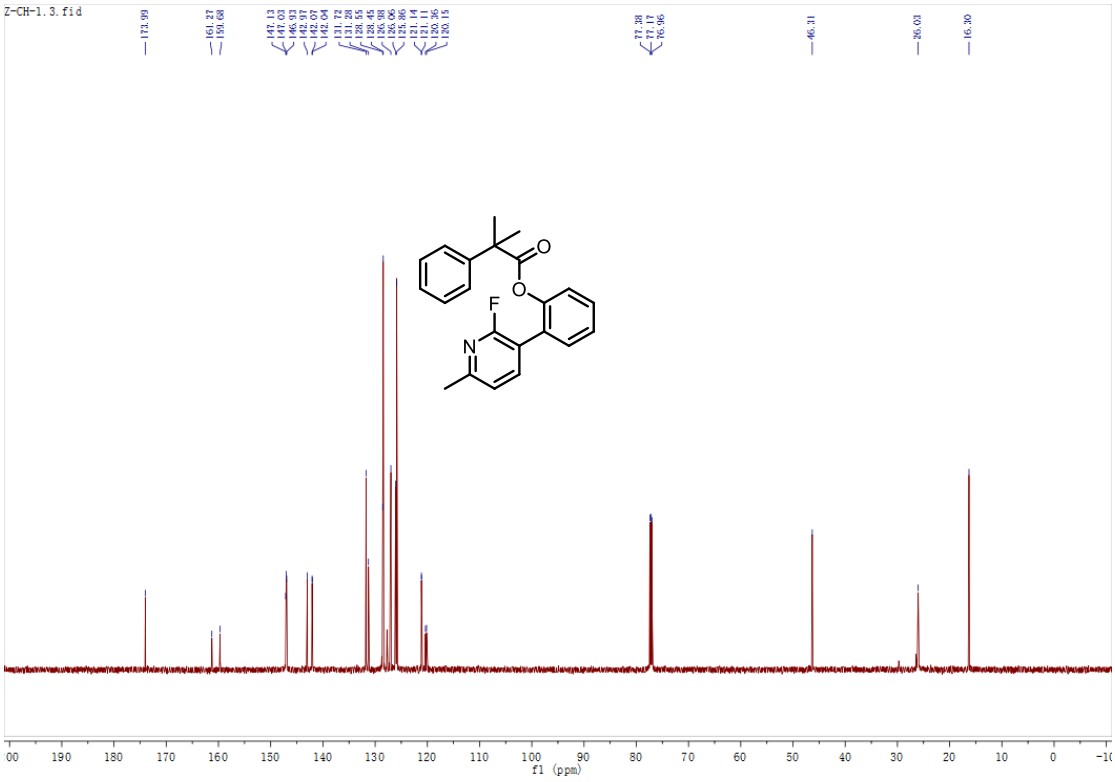
^{1}H NMR spectrum of DG-4 (500 MHz, $CDCl_3$)



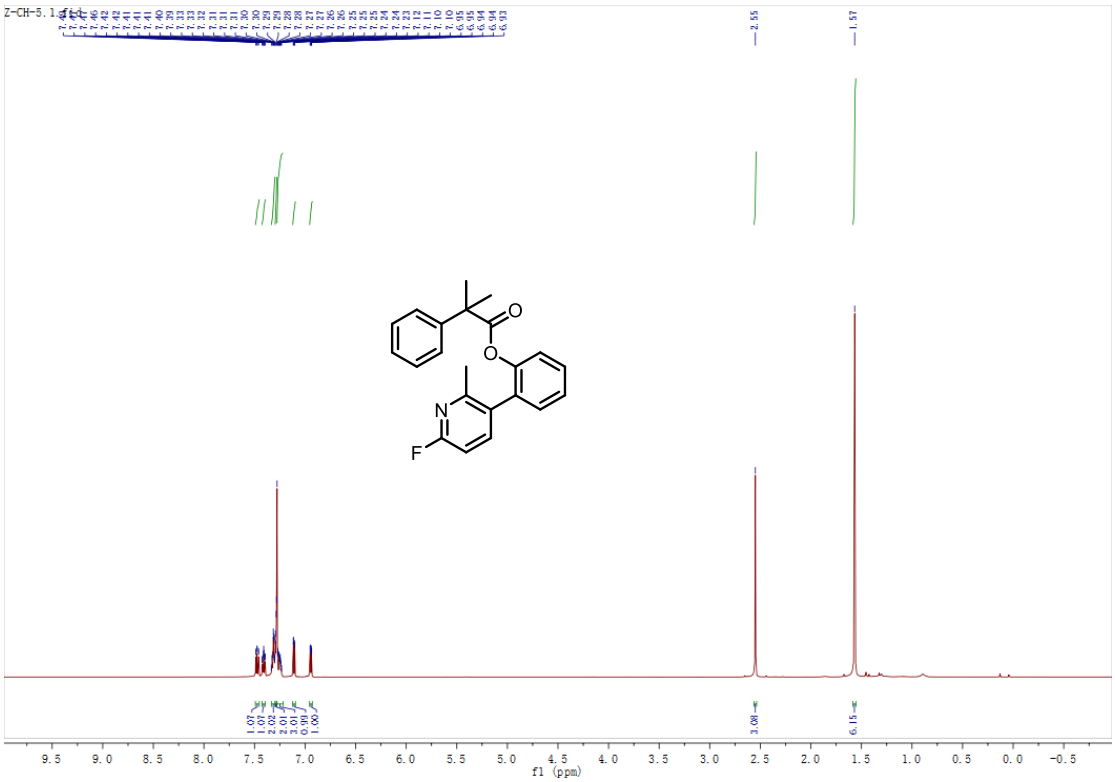
^{13}C NMR spectrum of DG-4 (126 MHz, $CDCl_3$)



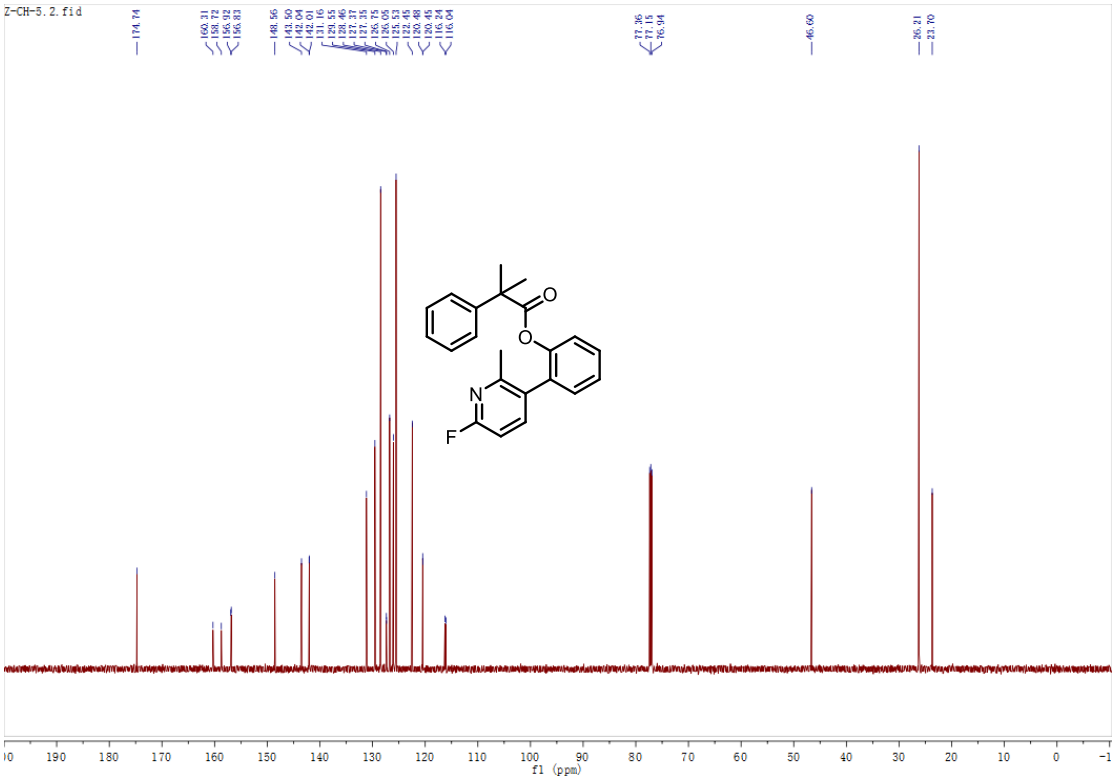
^{1}H NMR spectrum of DG-7 (500 MHz, $CDCl_3$)



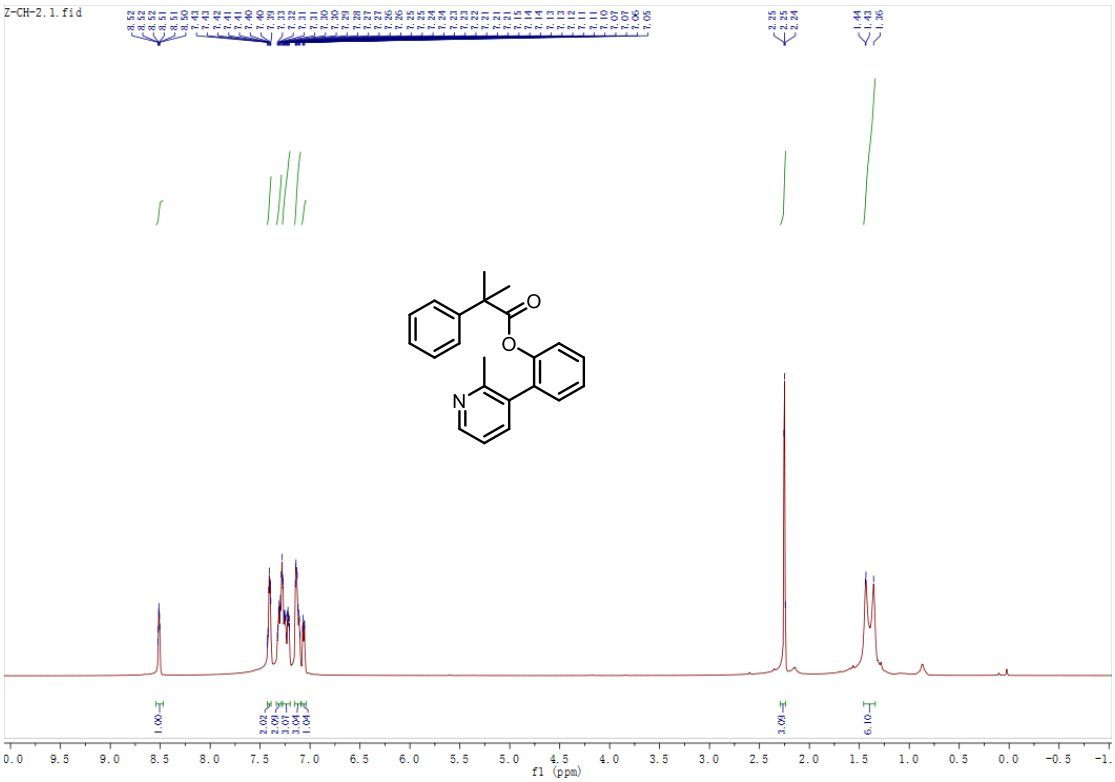
^{13}C NMR spectrum of DG-7 (126 MHz, $CDCl_3$)



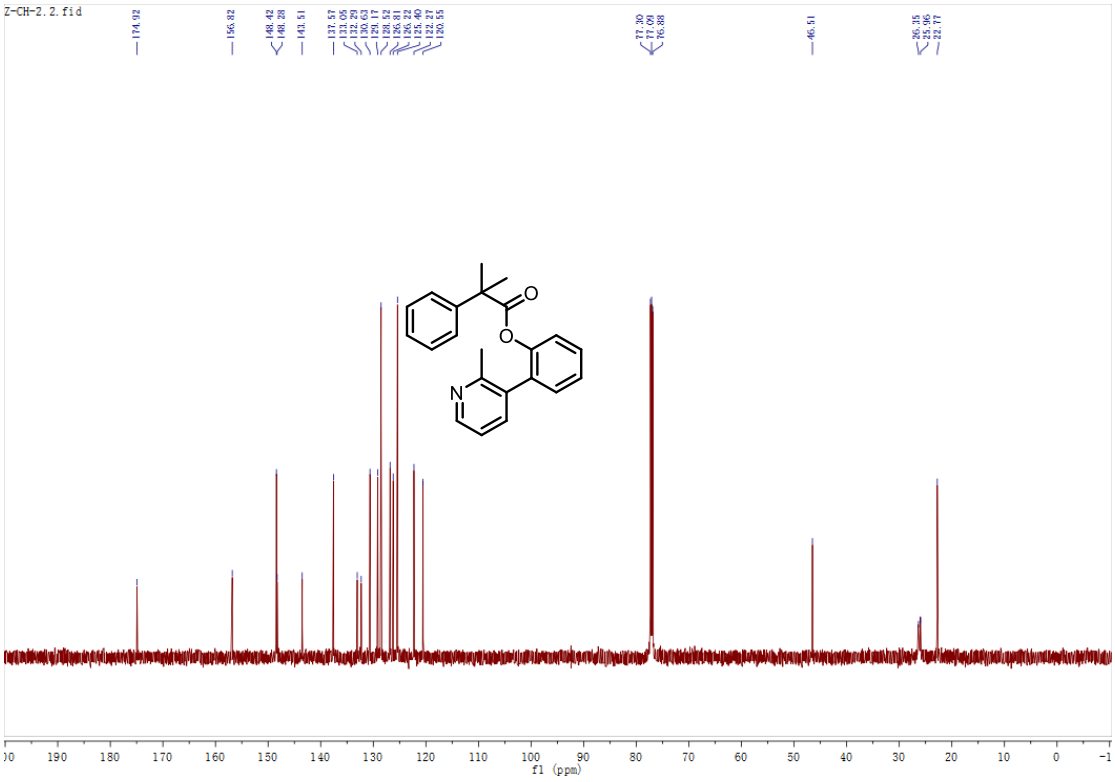
^{1}H NMR spectrum of DG-8 (500 MHz, $CDCl_3$)



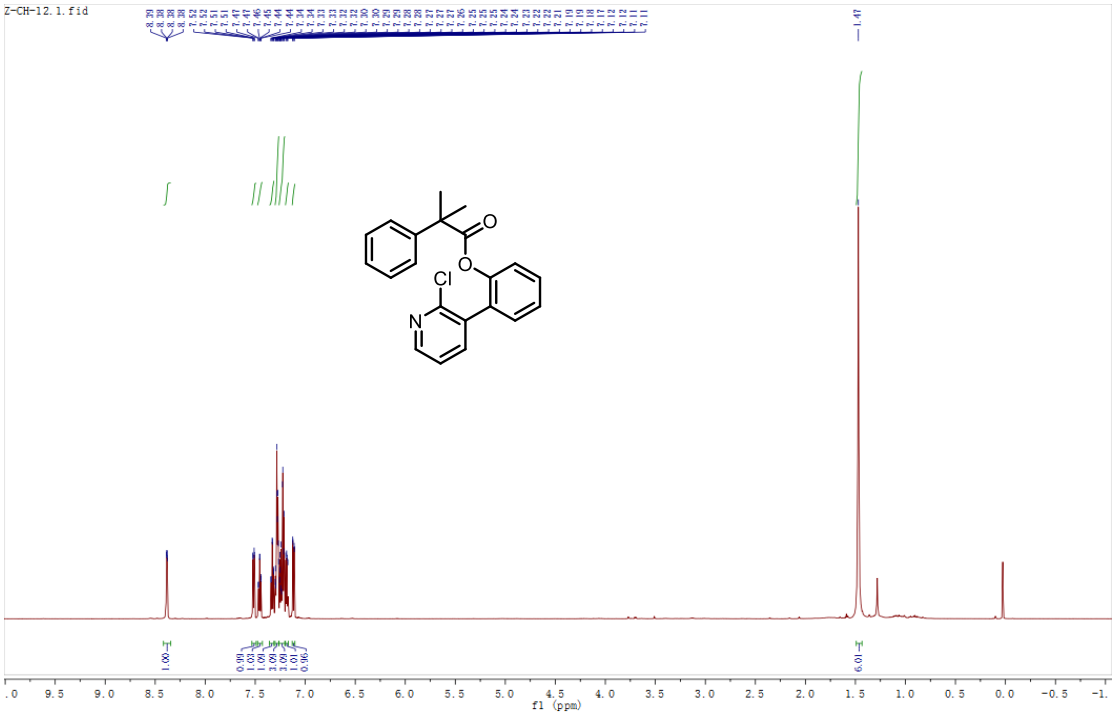
^{13}C NMR spectrum of DG-8 (126 MHz, $CDCl_3$)



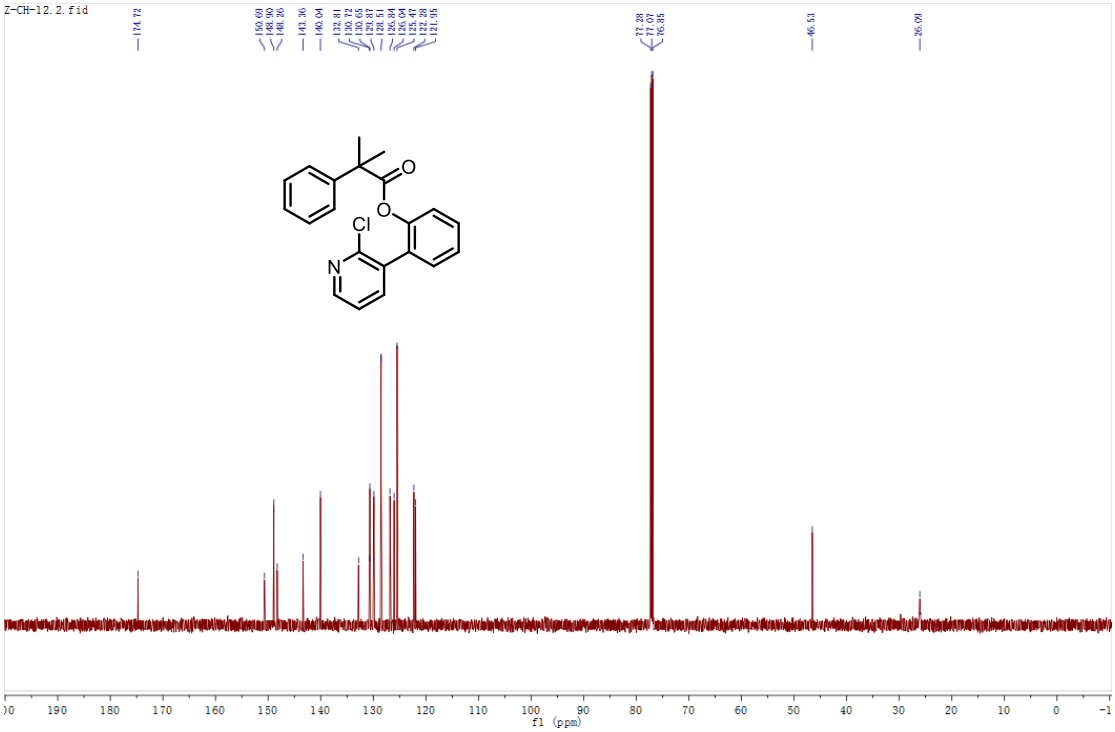
^{1}H NMR spectrum of DG-9 (500 MHz, $CDCl_3$)



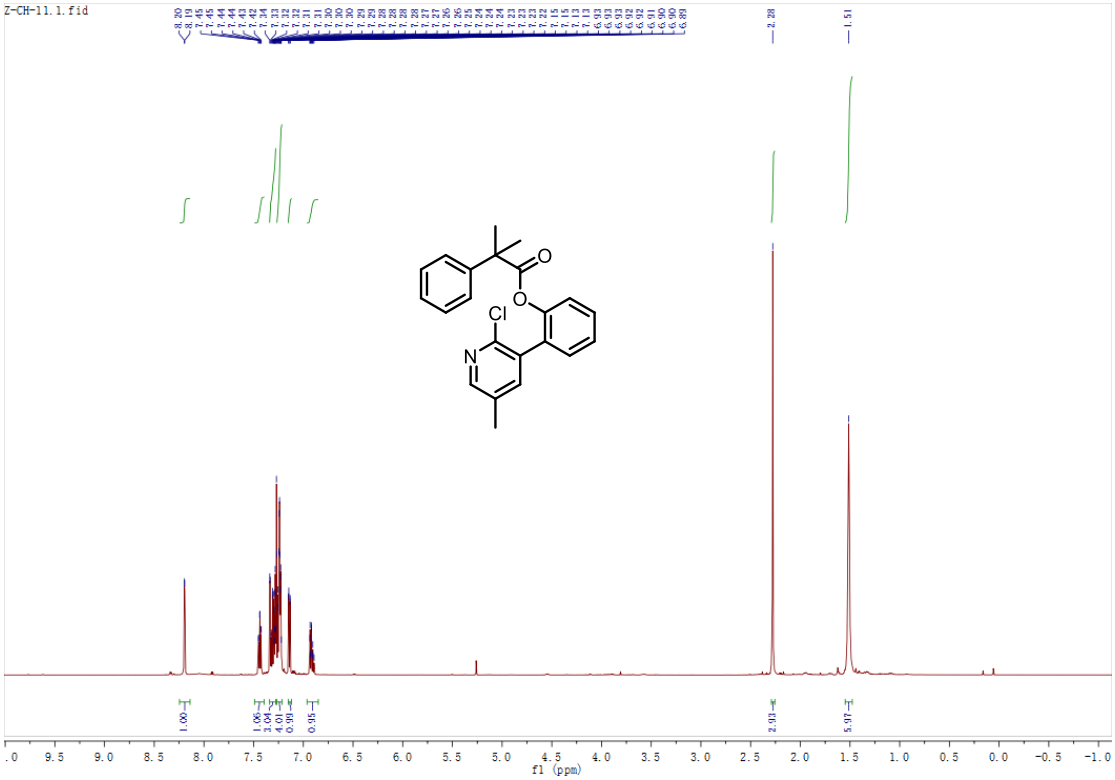
^{13}C NMR spectrum of DG-9 (126 MHz, $CDCl_3$)



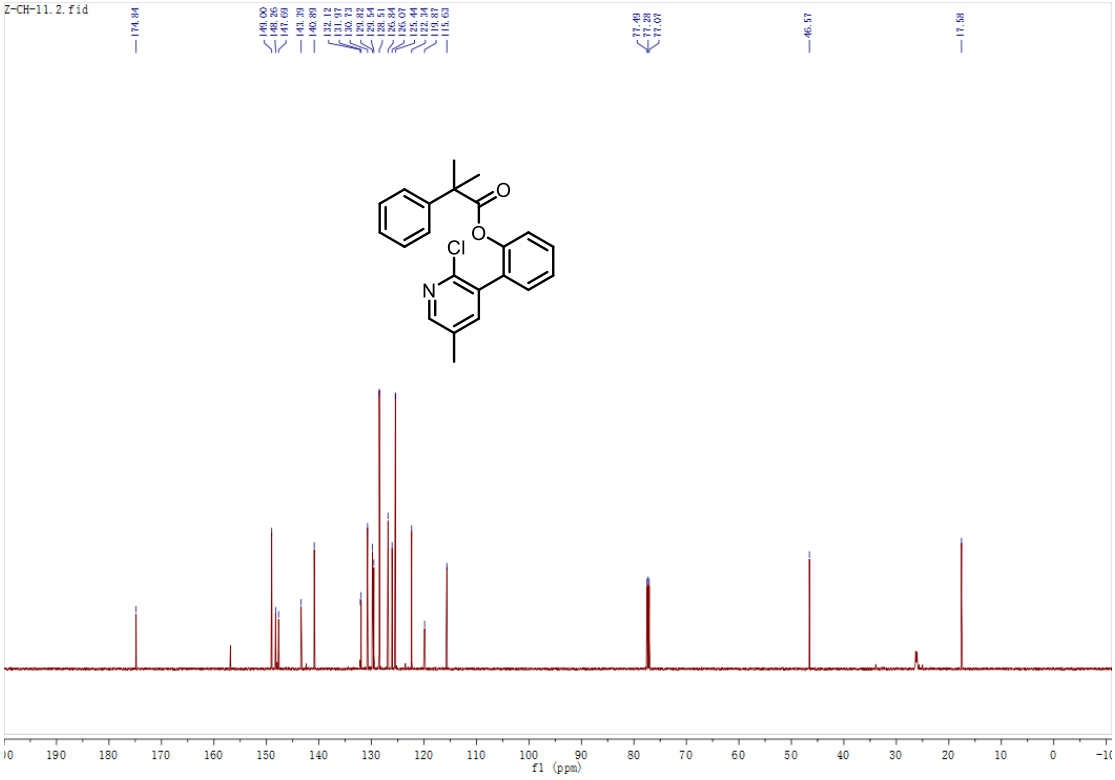
^{1}H NMR spectrum of DG-10 (500 MHz, $CDCl_3$)



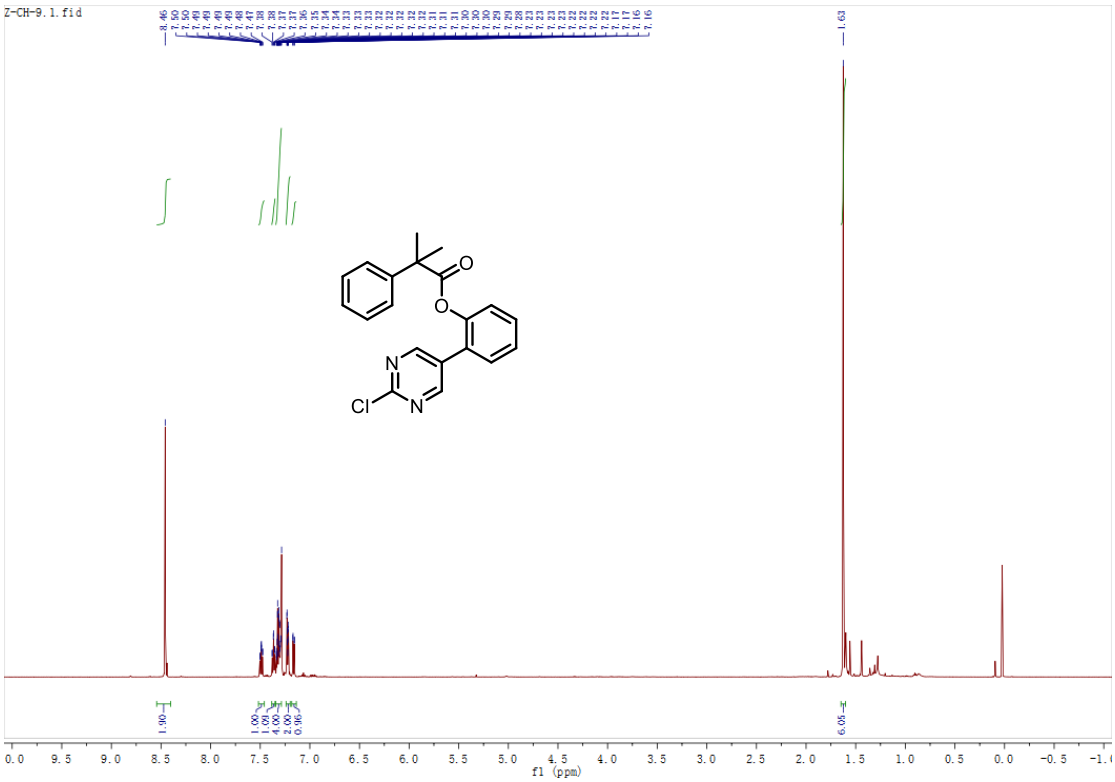
^{13}C NMR spectrum of DG-10 (126 MHz, $CDCl_3$)



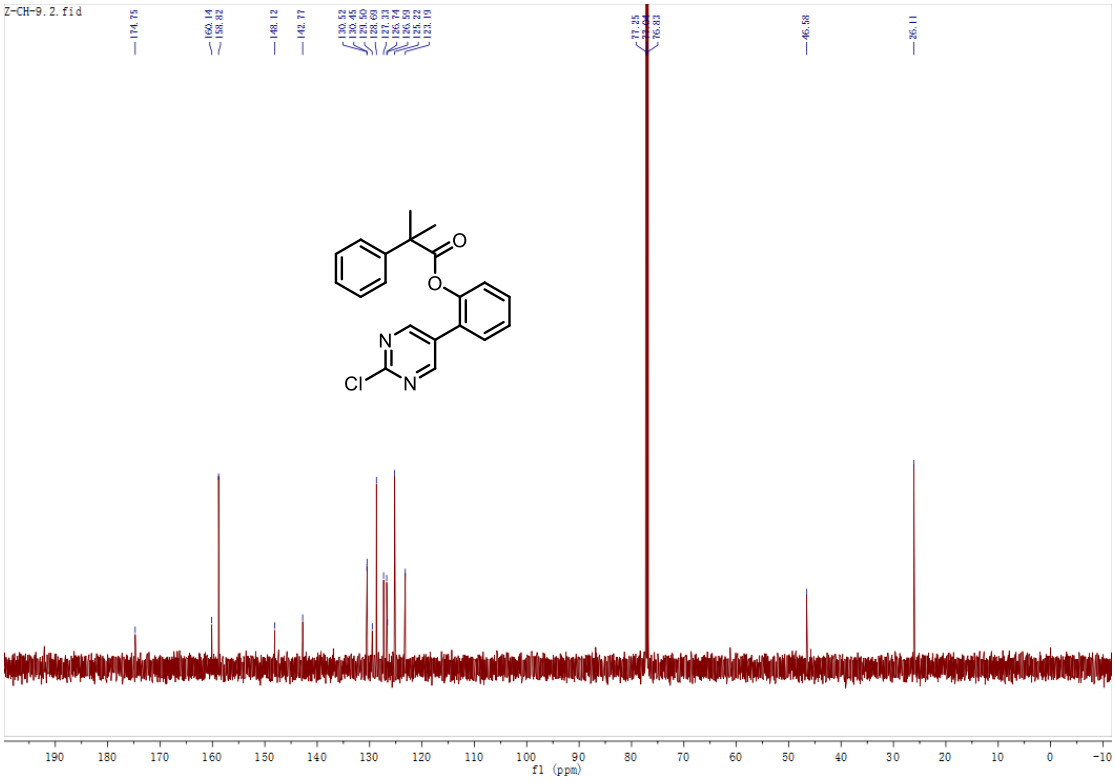
^{1}H NMR spectrum of DG-11 (500 MHz, $CDCl_3$)



^{13}C NMR spectrum of DG-11 (126 MHz, $CDCl_3$)

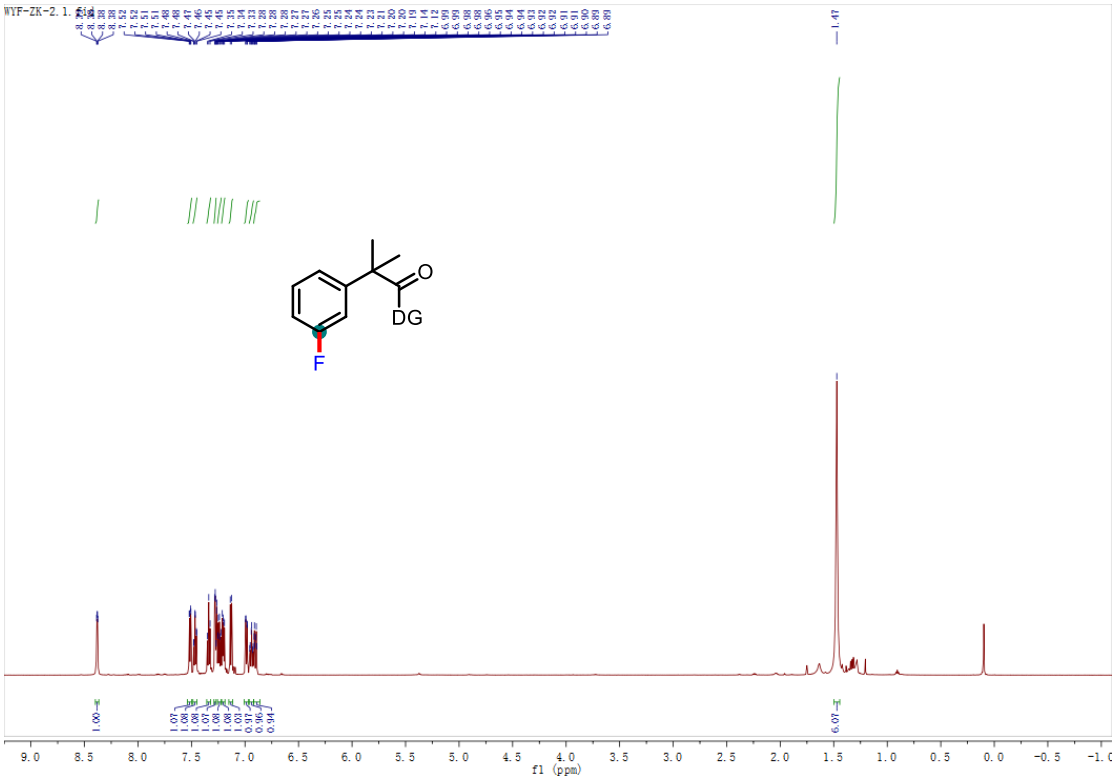


^{1}H NMR spectrum of DG-12 (500 MHz, $CDCl_3$)

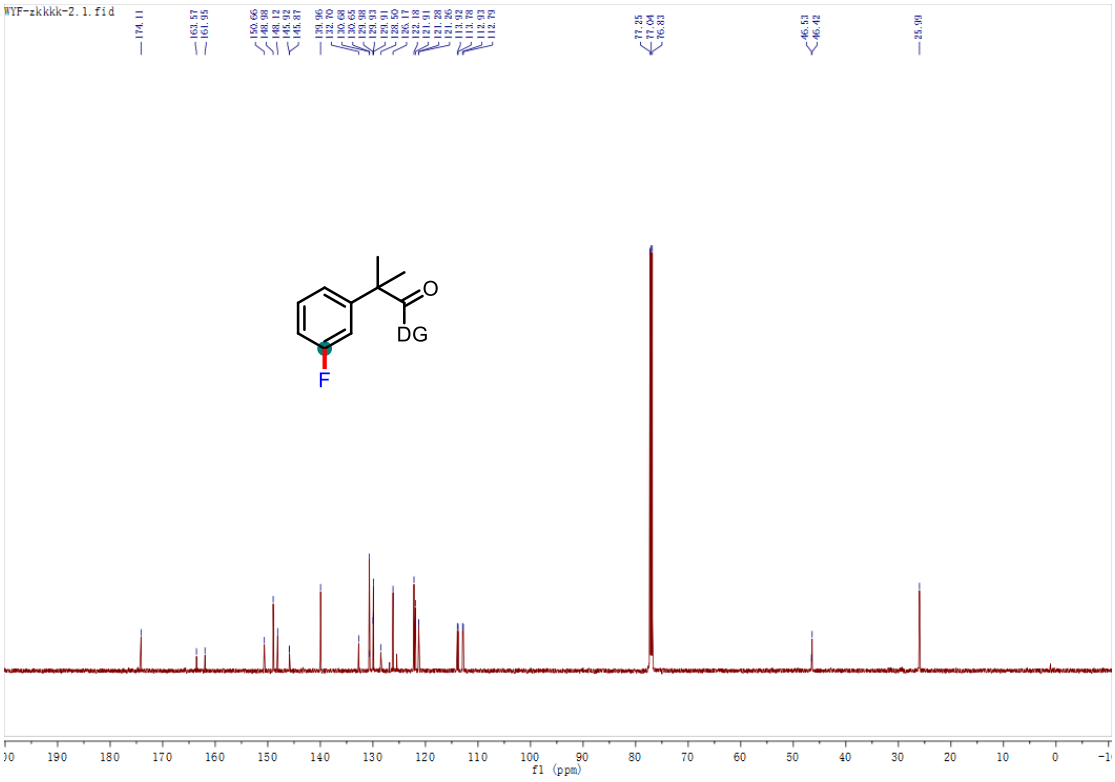


^{13}C NMR spectrum of DG-12 (126 MHz, $CDCl_3$)

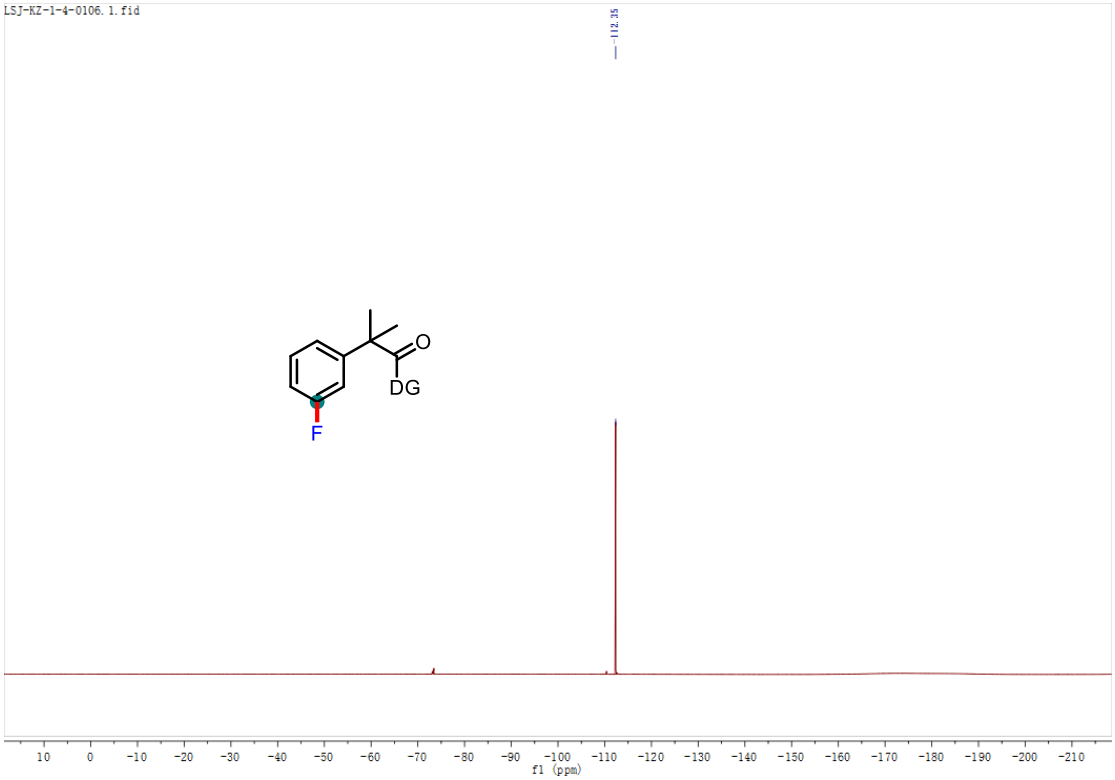
10.2 NMR spectra of products



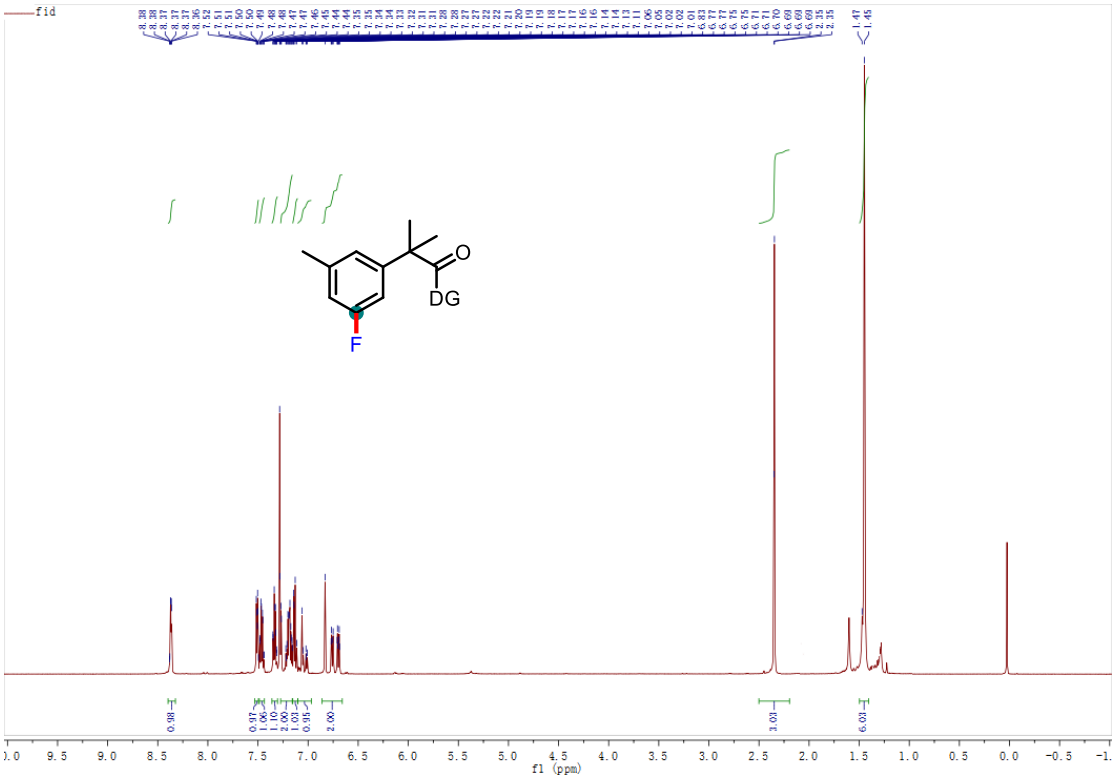
^{1}H NMR spectrum of 2a (600 MHz, $CDCl_3$)



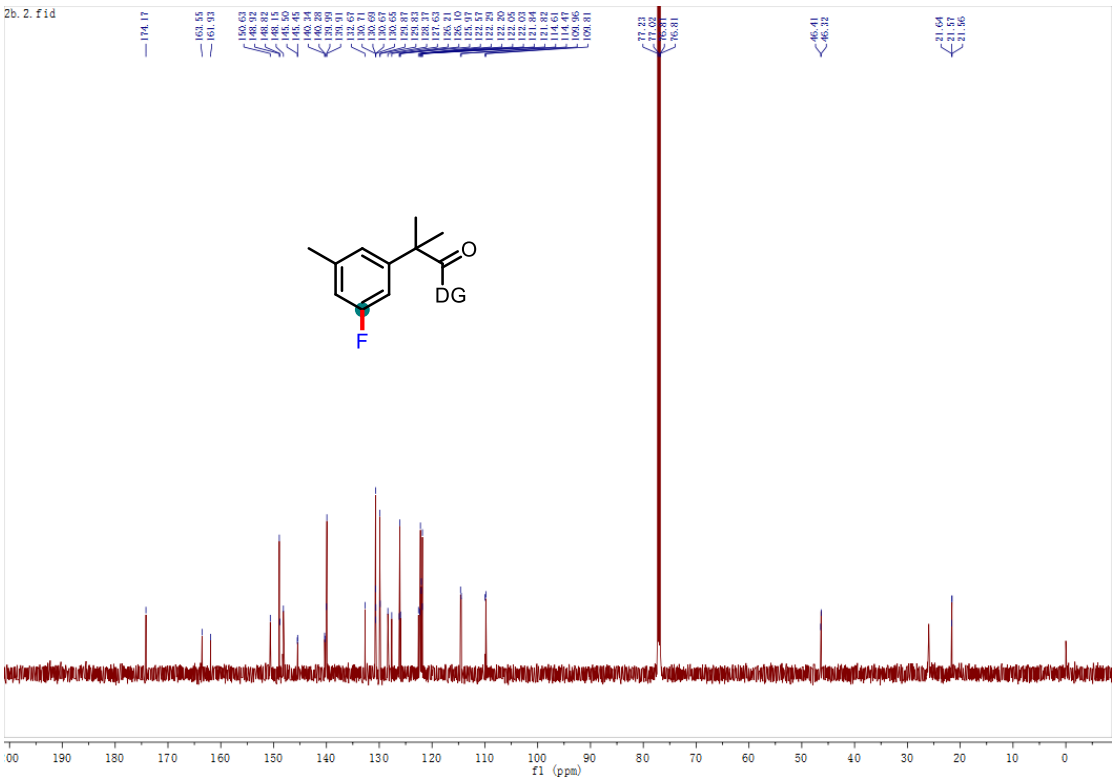
^{13}C NMR spectrum of 2a (151 MHz, $CDCl_3$)



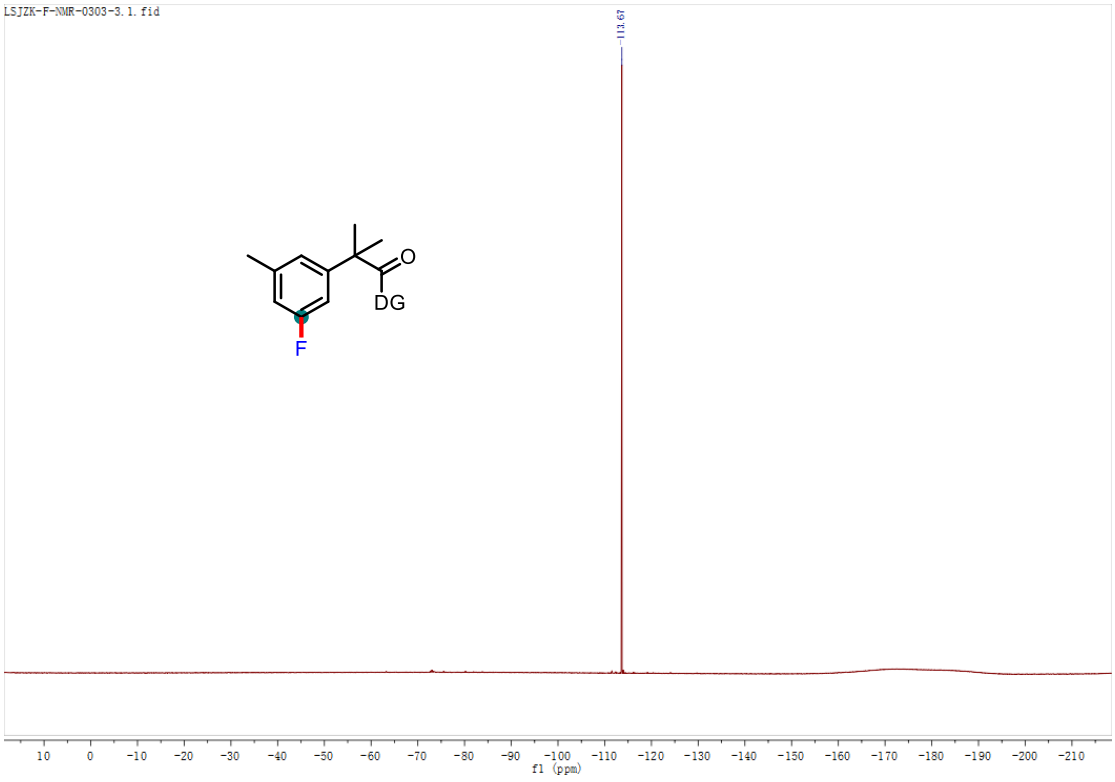
^{19}F NMR spectrum of 2a (565 MHz, $CDCl_3$)



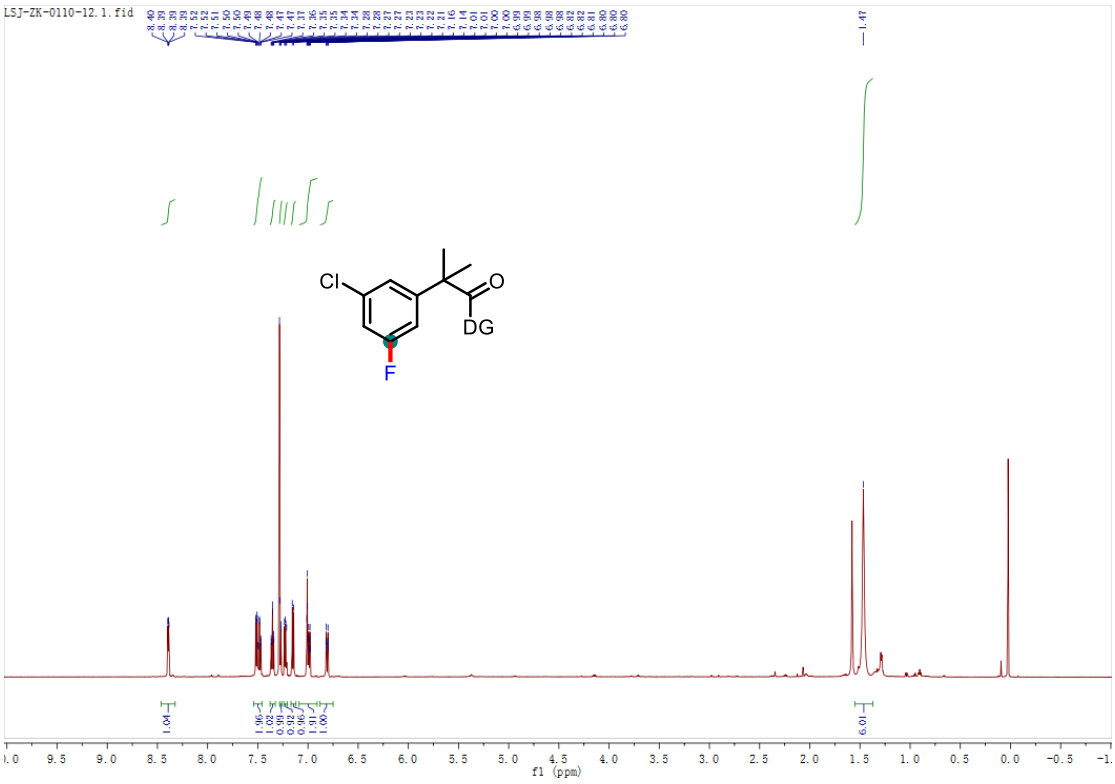
^{1}H NMR spectrum of 2b (600 MHz, $CDCl_3$)



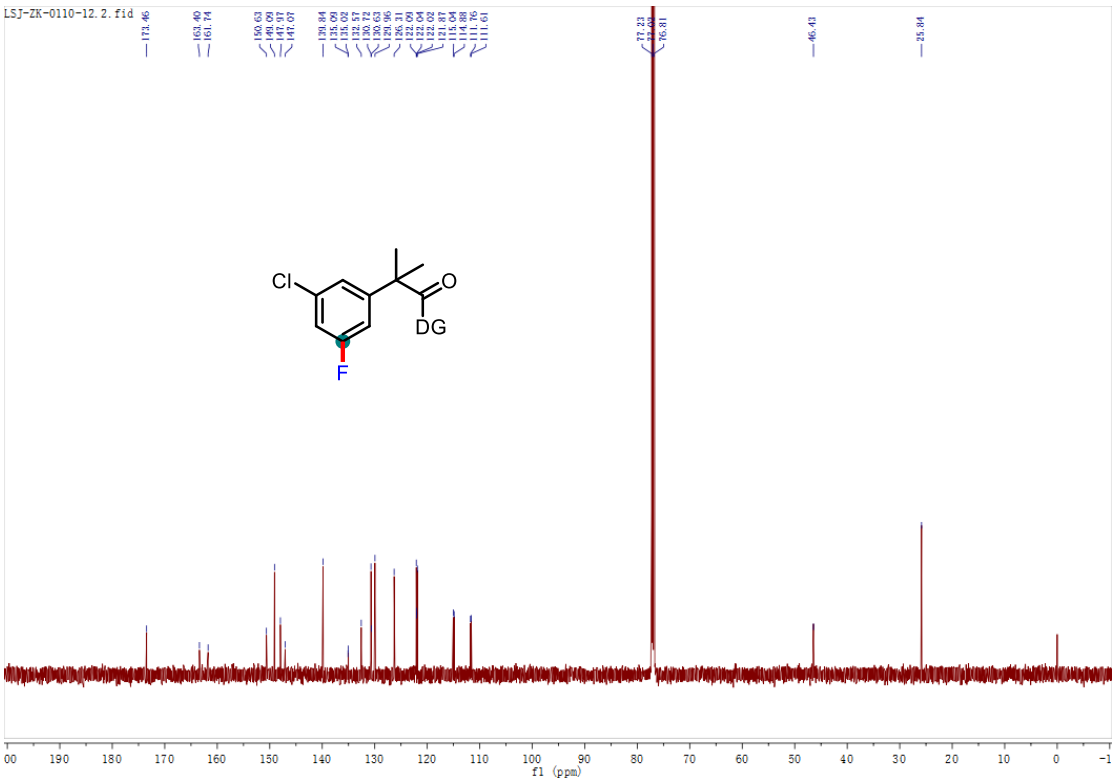
^{13}C NMR spectrum of 2b (151 MHz, $CDCl_3$)



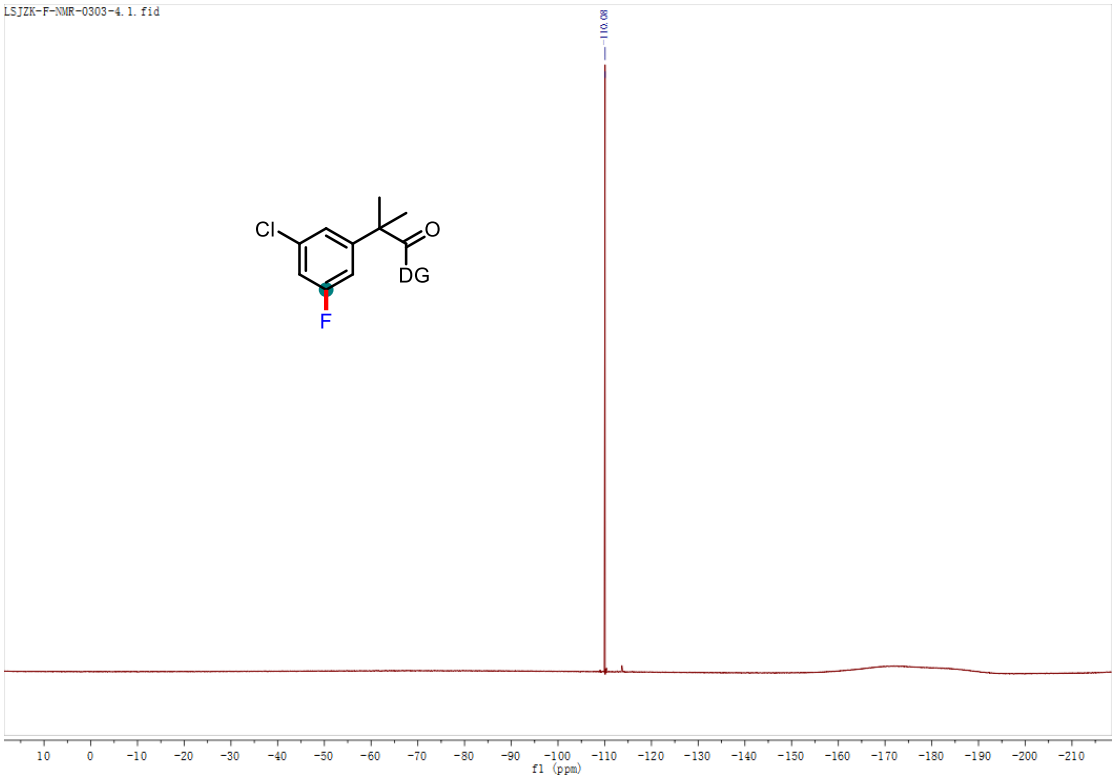
^{19}F NMR spectrum of 2b (565 MHz, $CDCl_3$)



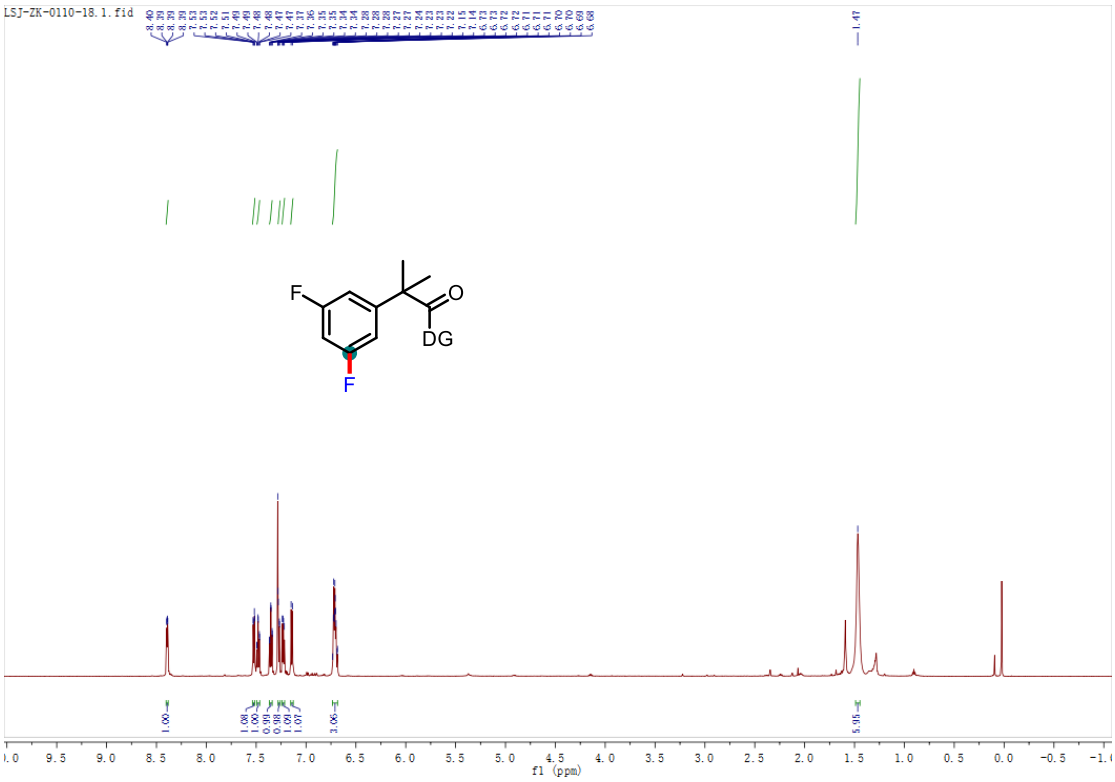
^{1}H NMR spectrum of 2c (600 MHz, $CDCl_3$)



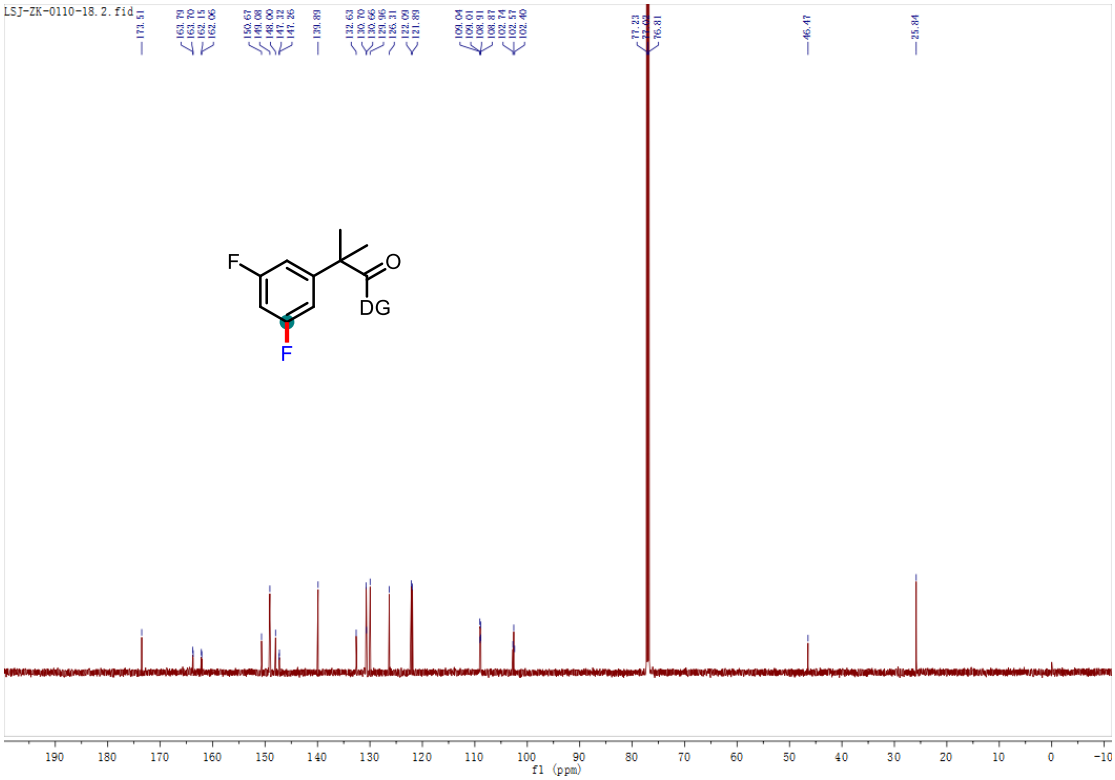
^{13}C NMR spectrum of 2c (151 MHz, $CDCl_3$)



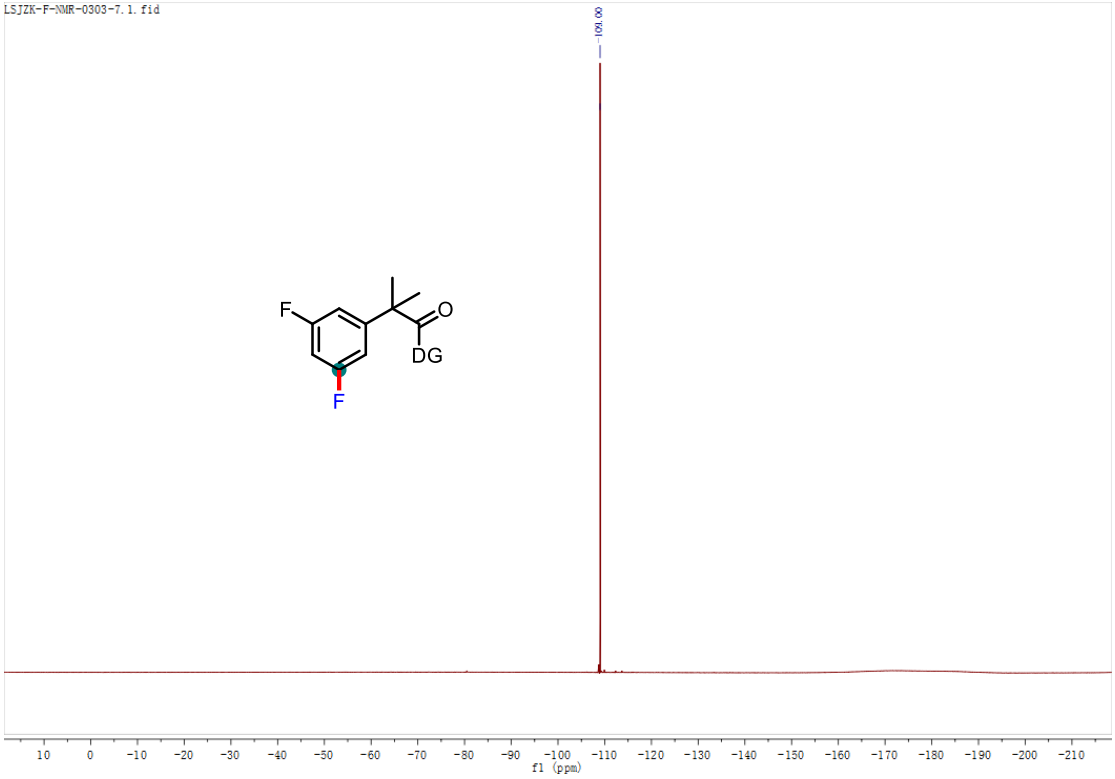
^{19}F NMR spectrum of 2c (565 MHz, $CDCl_3$)



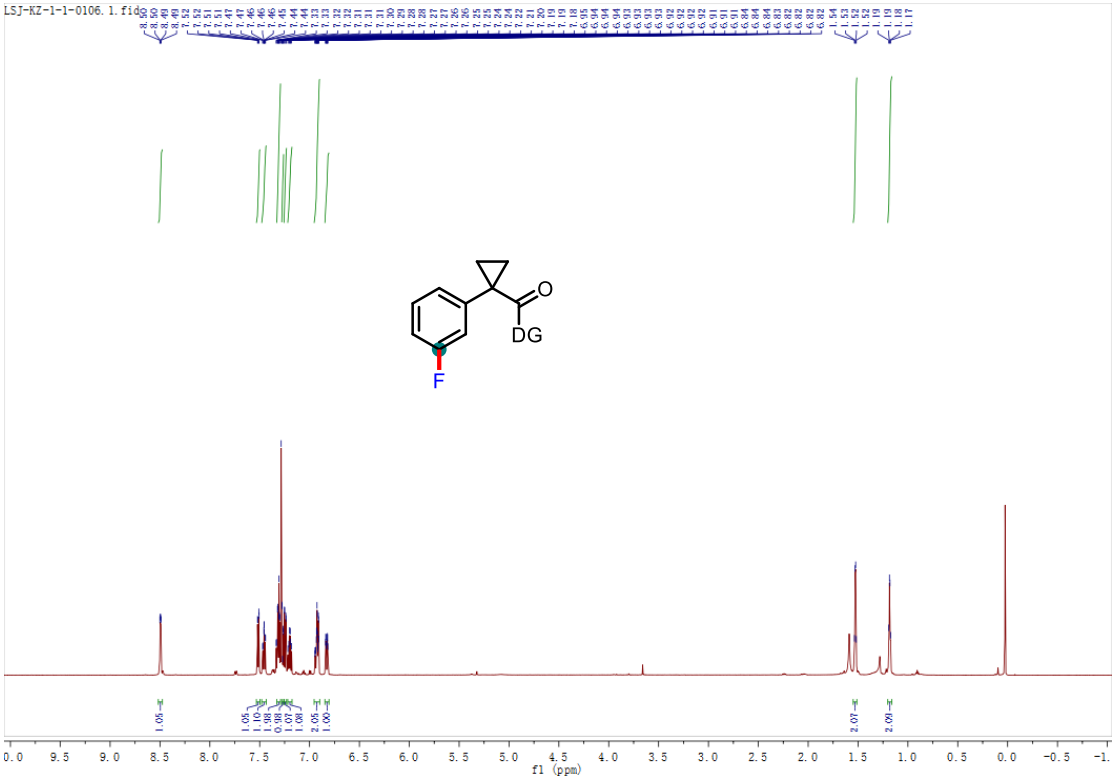
^{1}H NMR spectrum of 2d (600 MHz, $CDCl_3$)



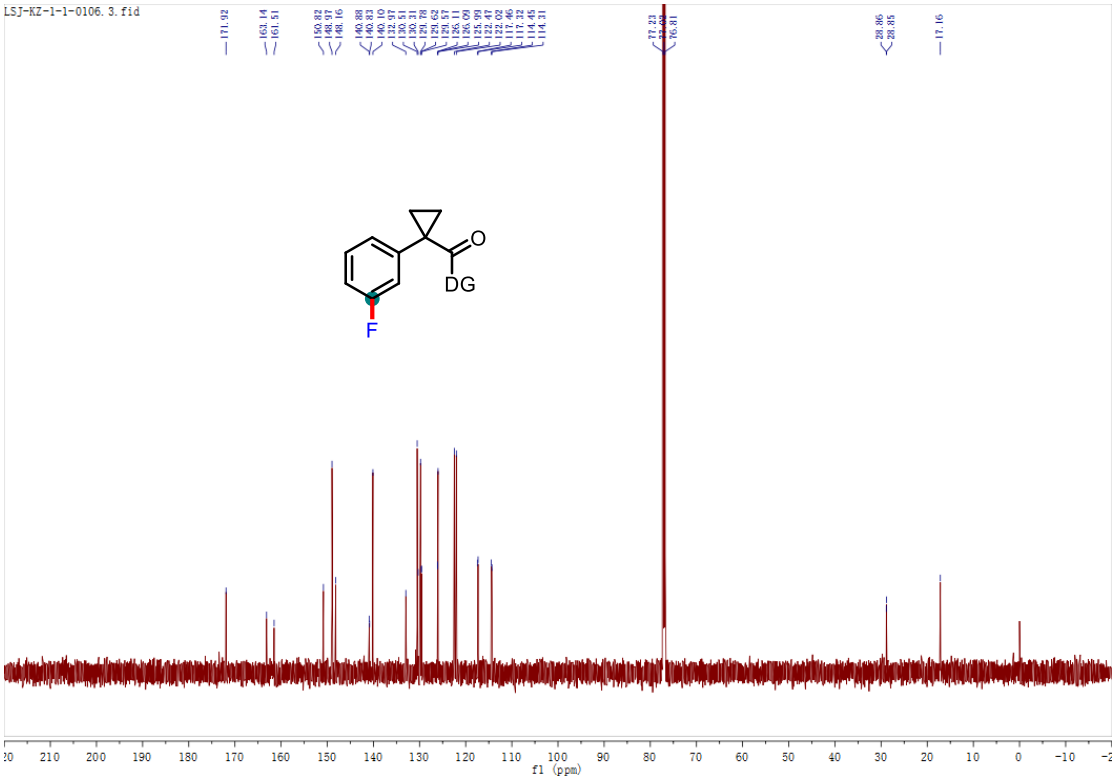
^{13}C NMR spectrum of 2d (151 MHz, $CDCl_3$)



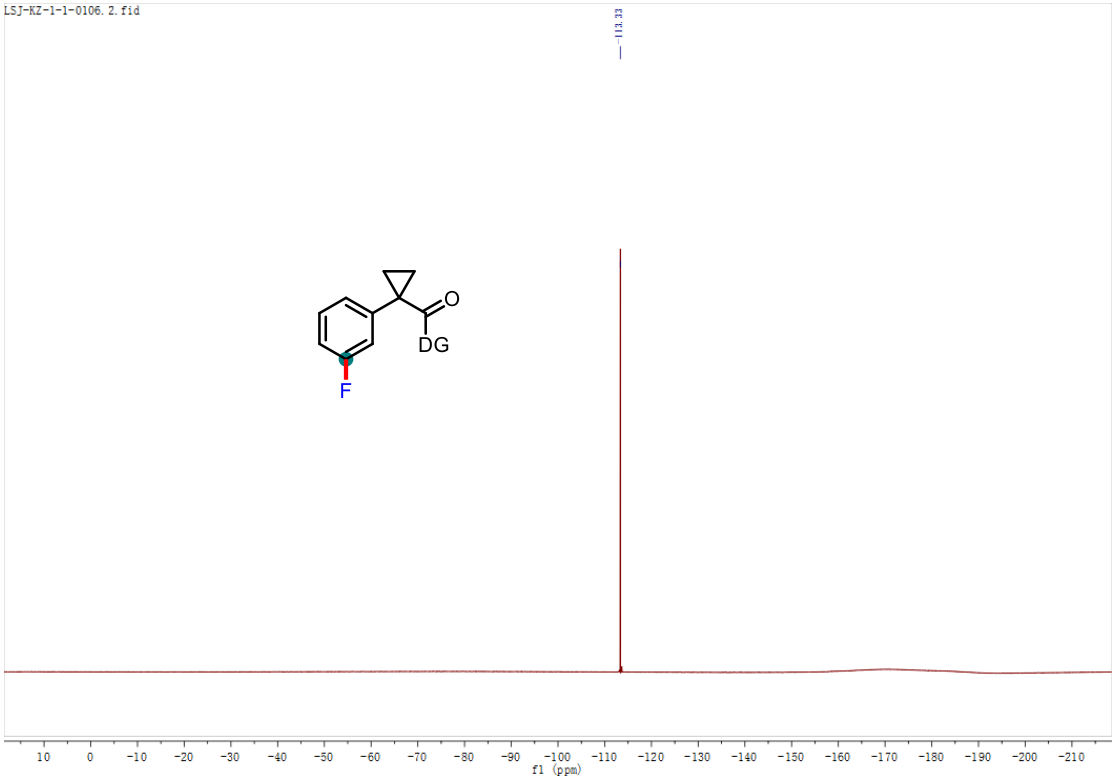
^{19}F NMR spectrum of 2d (565 MHz, $CDCl_3$)



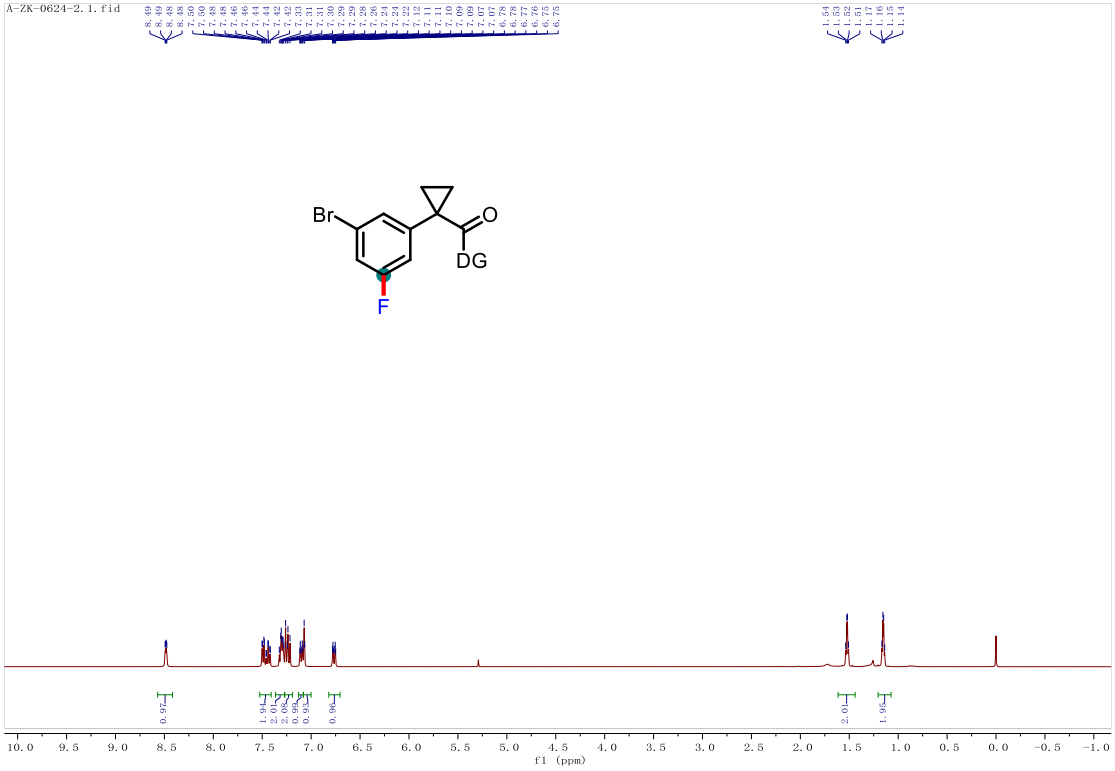
^{1}H NMR spectrum of 2e (600 MHz, $CDCl_3$)



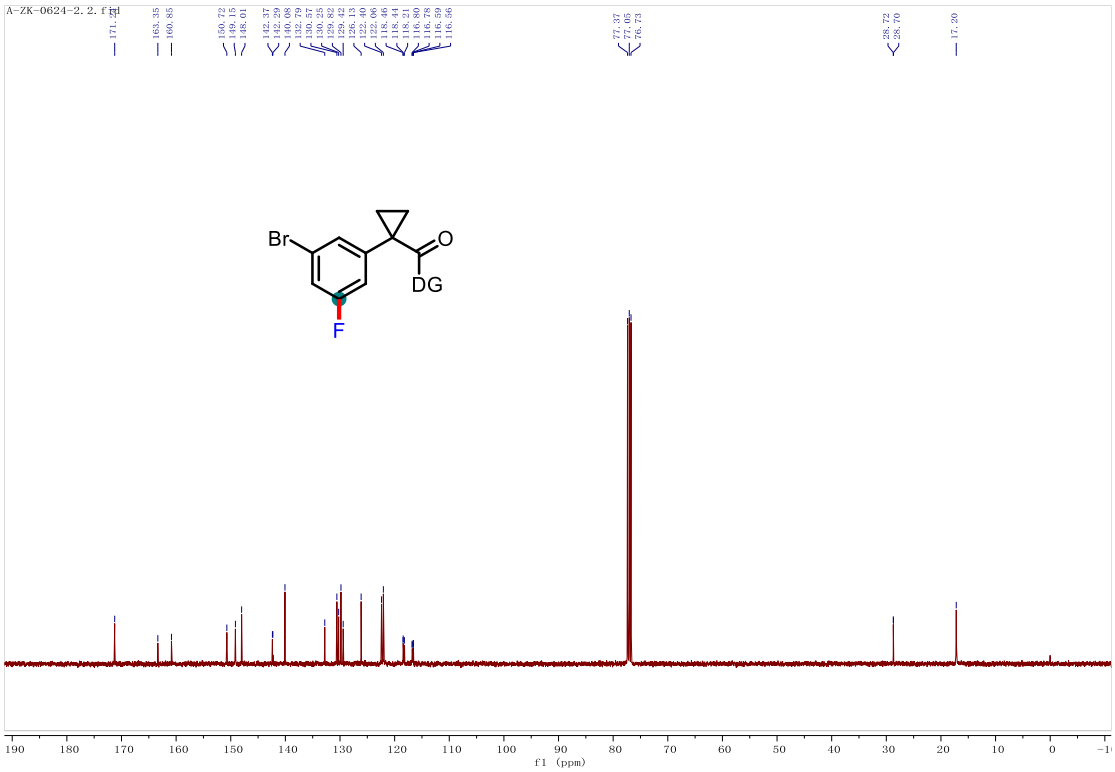
^{13}C NMR spectrum of 2e (151 MHz, $CDCl_3$)



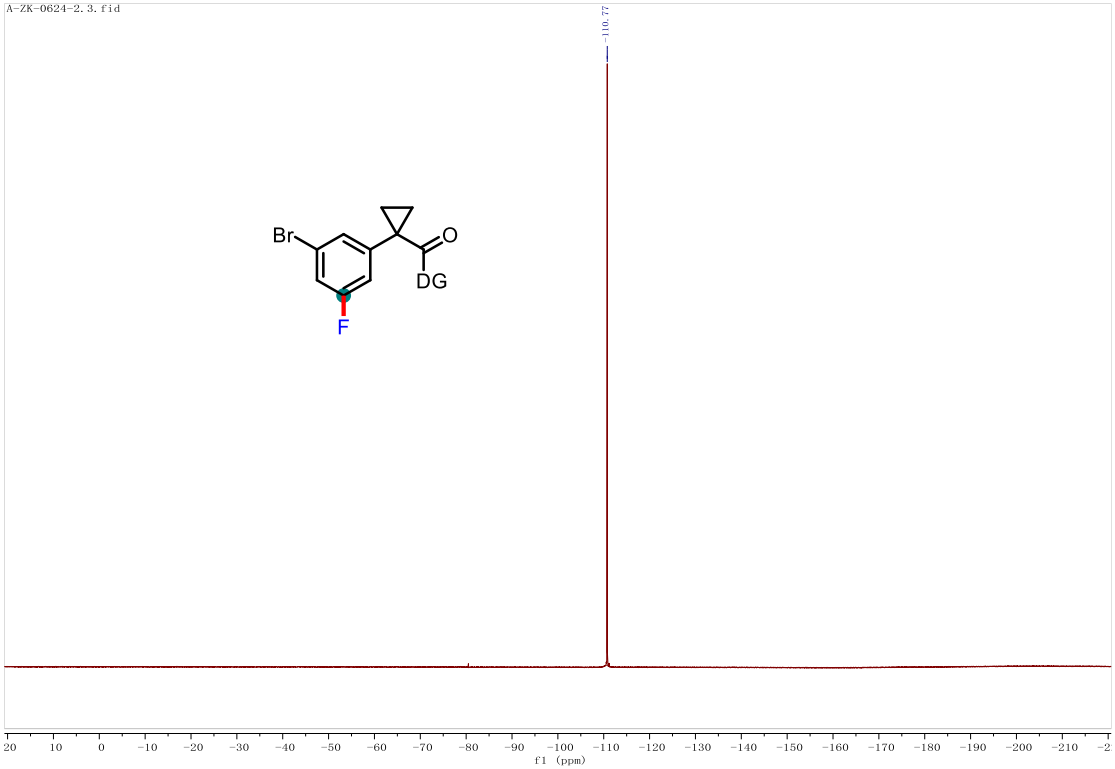
^{19}F NMR spectrum of 2e (565 MHz, $CDCl_3$)



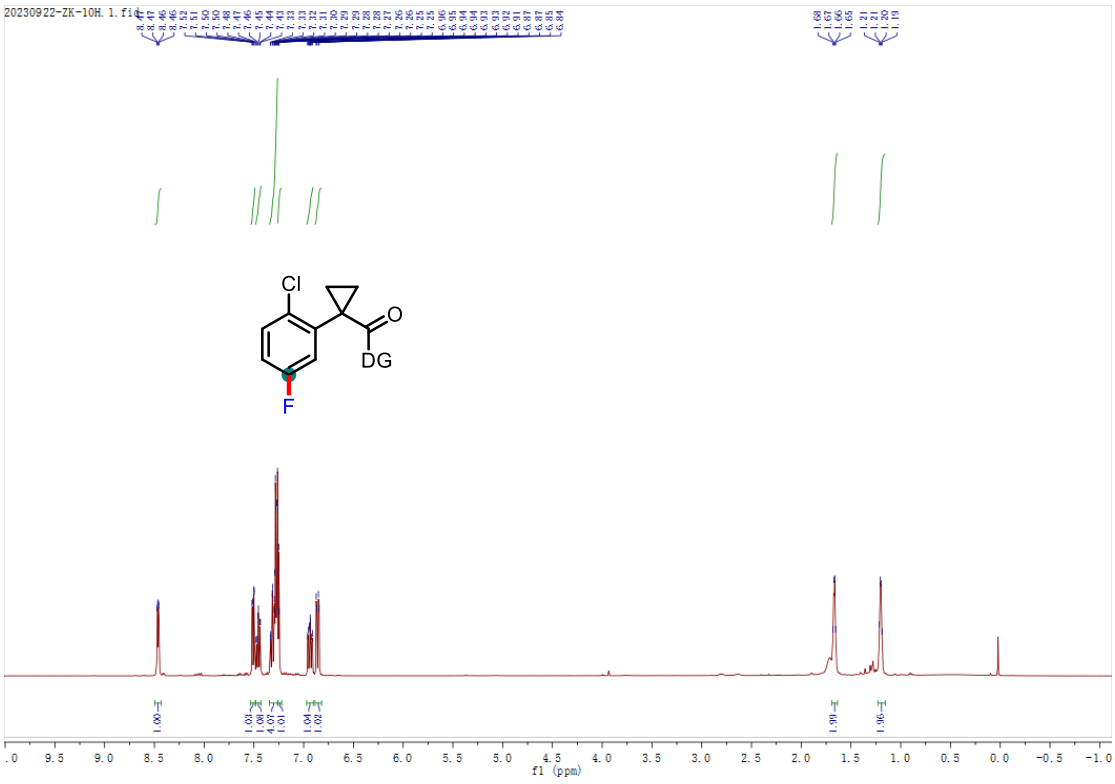
^{1}H NMR spectrum of 2f (400 MHz, $CDCl_3$)



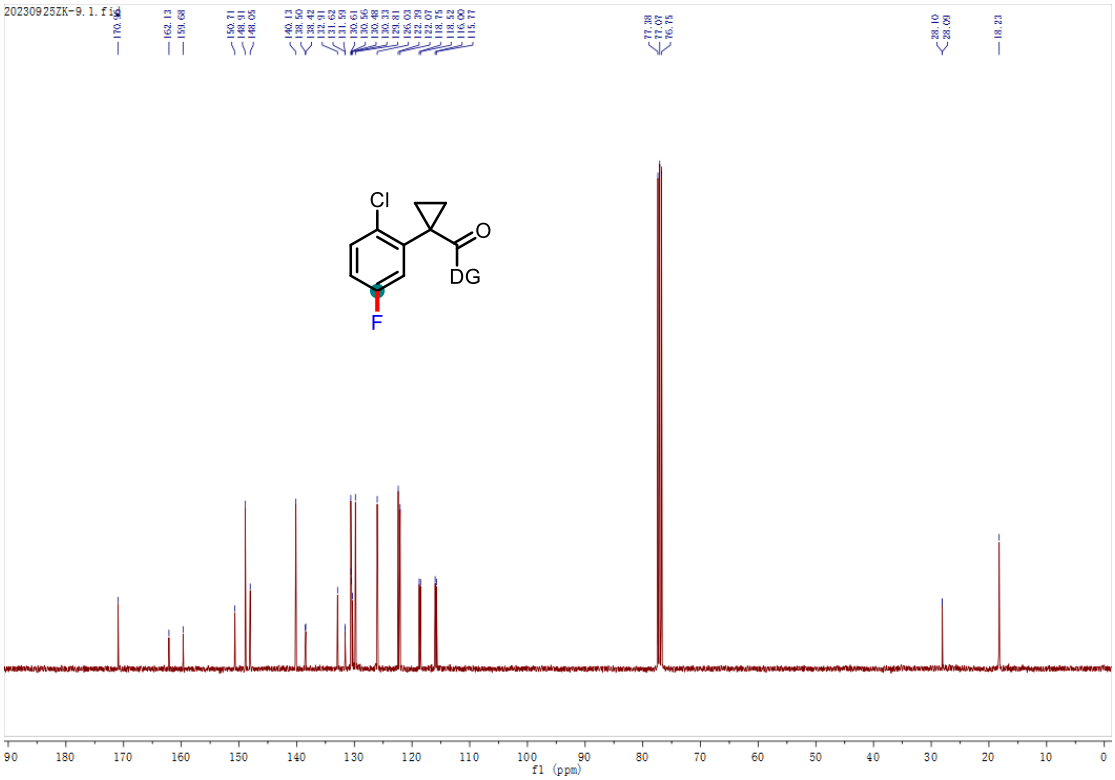
^{13}C NMR spectrum of 2f (101 MHz, $CDCl_3$)



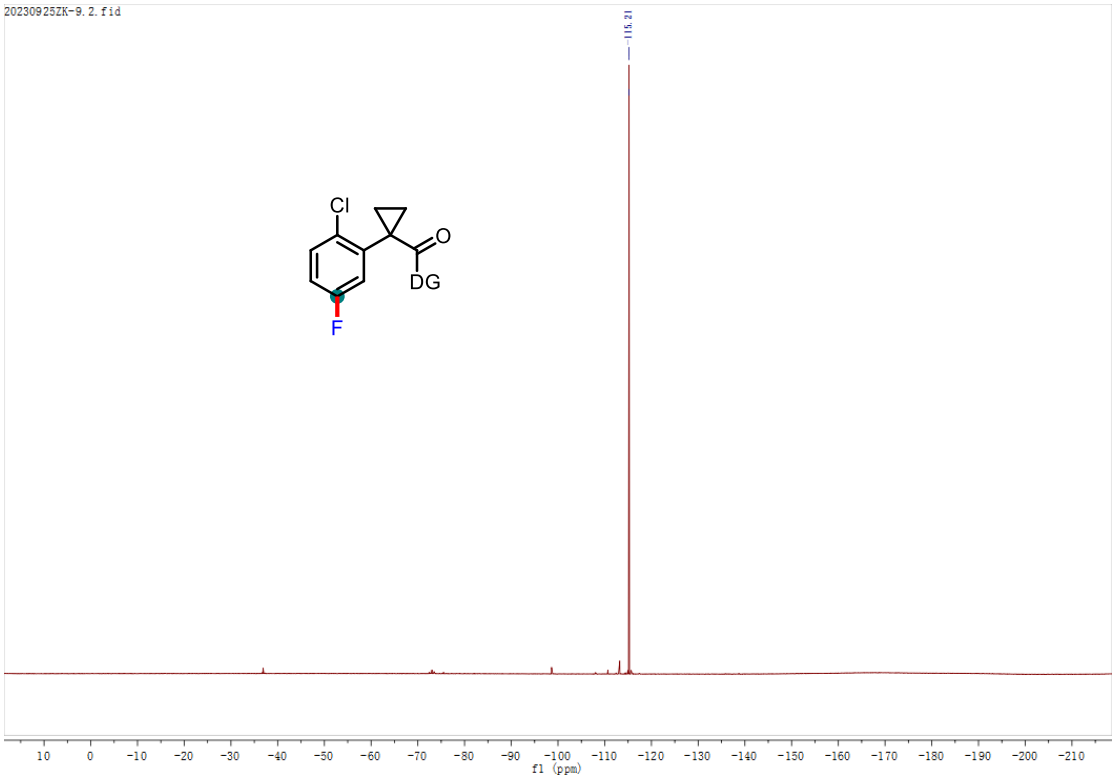
^{19}F NMR spectrum of 2f (376 MHz, $CDCl_3$)



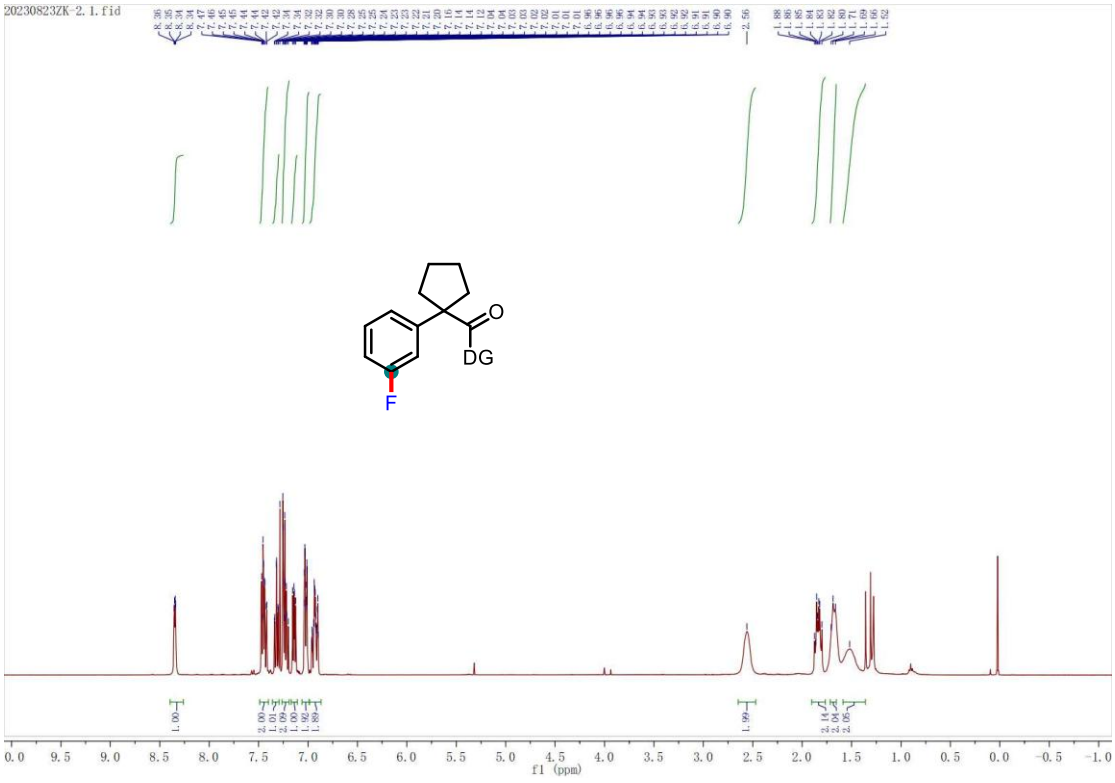
^{1}H NMR spectrum of 2g (400 MHz, $CDCl_3$)



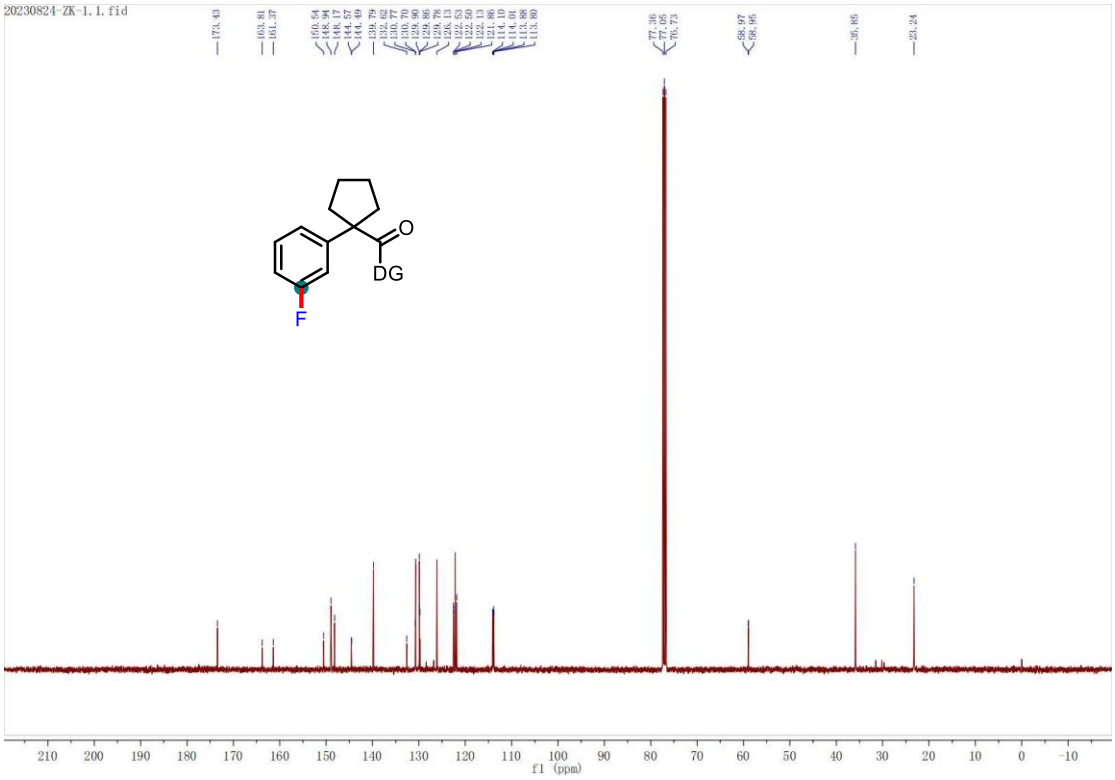
^{13}C NMR spectrum of 2g (101 MHz, $CDCl_3$)



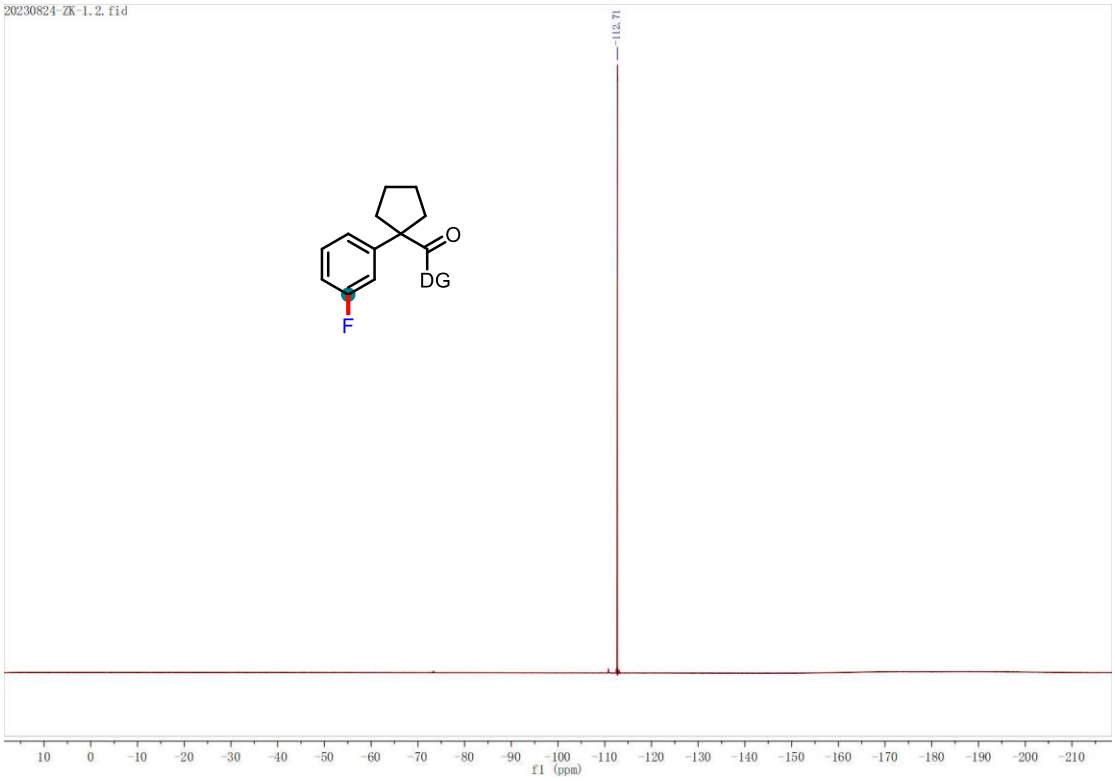
^{19}F NMR spectrum of 2g (376 MHz, $CDCl_3$)



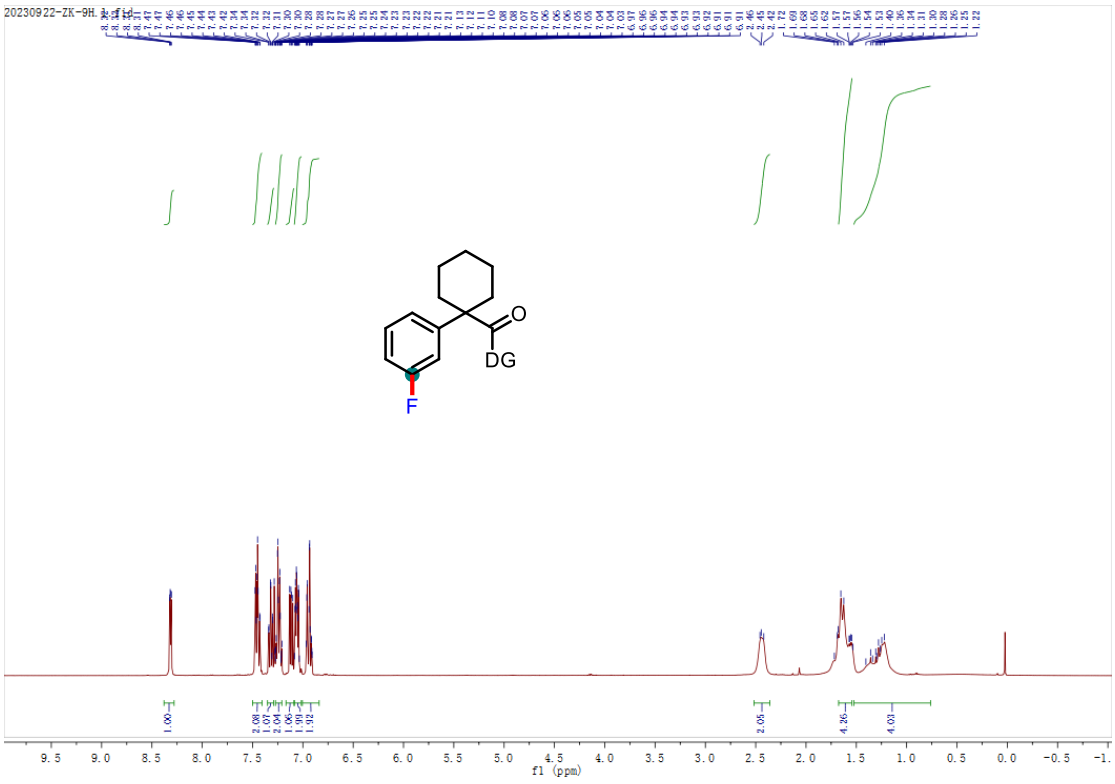
^{1}H NMR spectrum of 2h (400 MHz, $CDCl_3$)



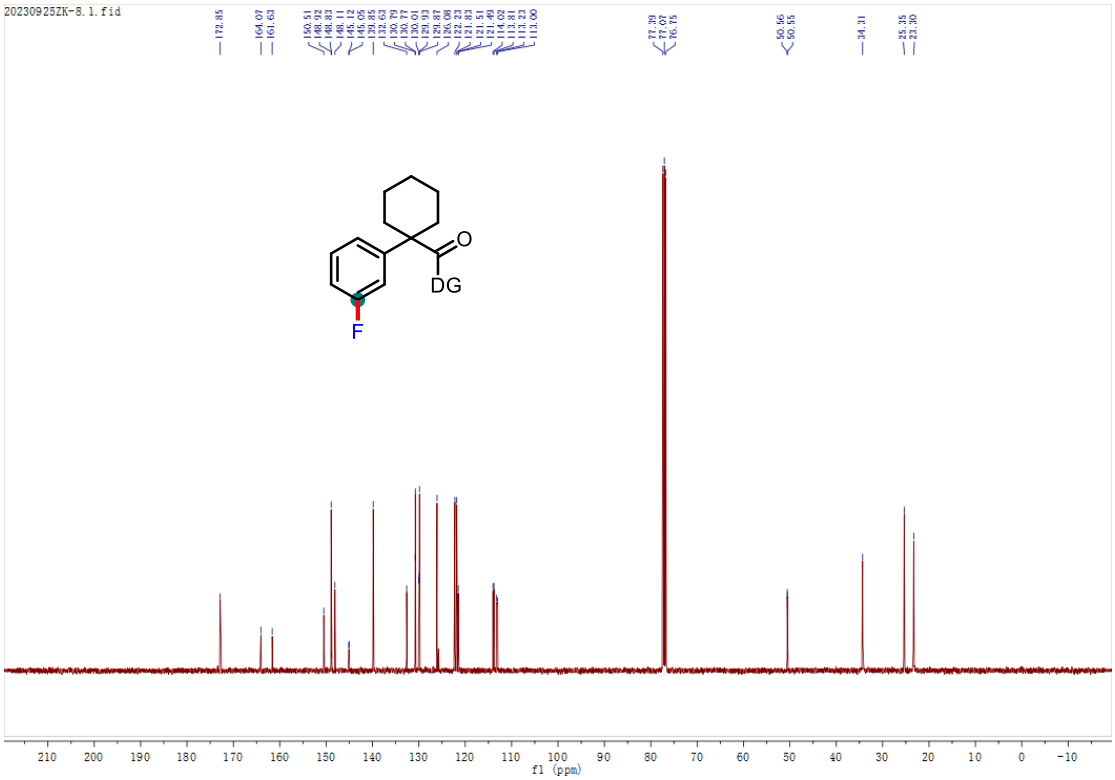
^{13}C NMR spectrum of 2h (101 MHz, $CDCl_3$)



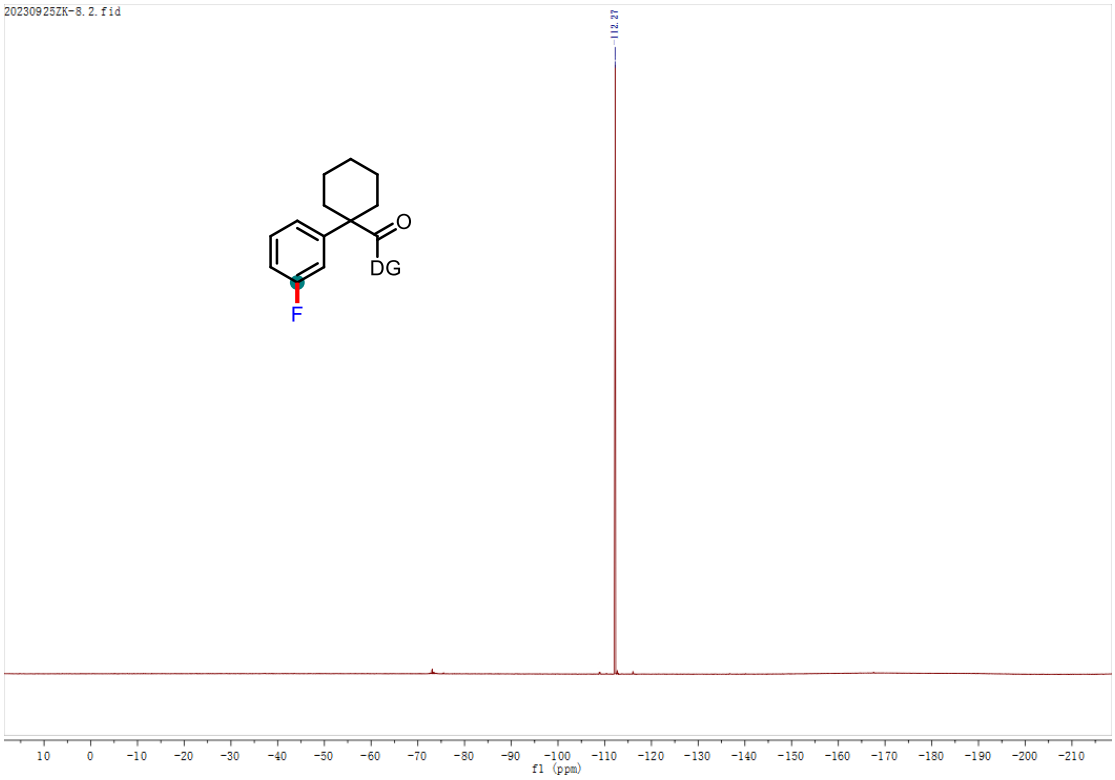
^{19}F NMR spectrum of 2h (376 MHz, $CDCl_3$)



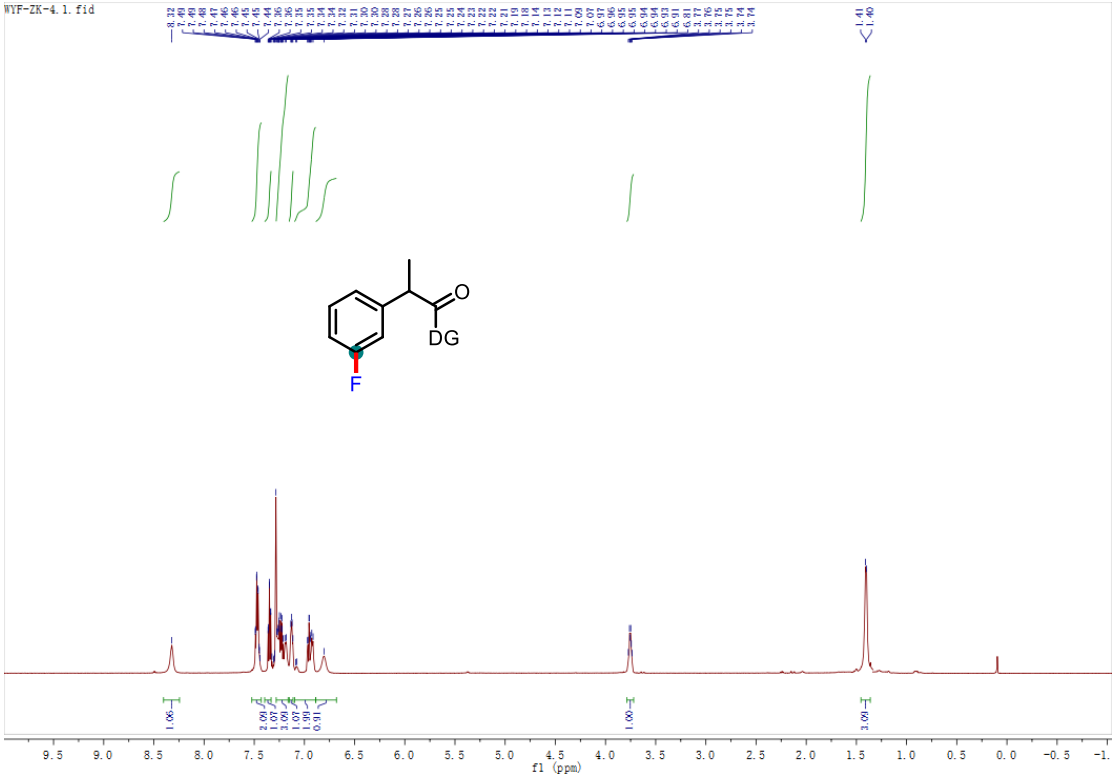
^{1}H NMR spectrum of 2i (400 MHz, $CDCl_3$)



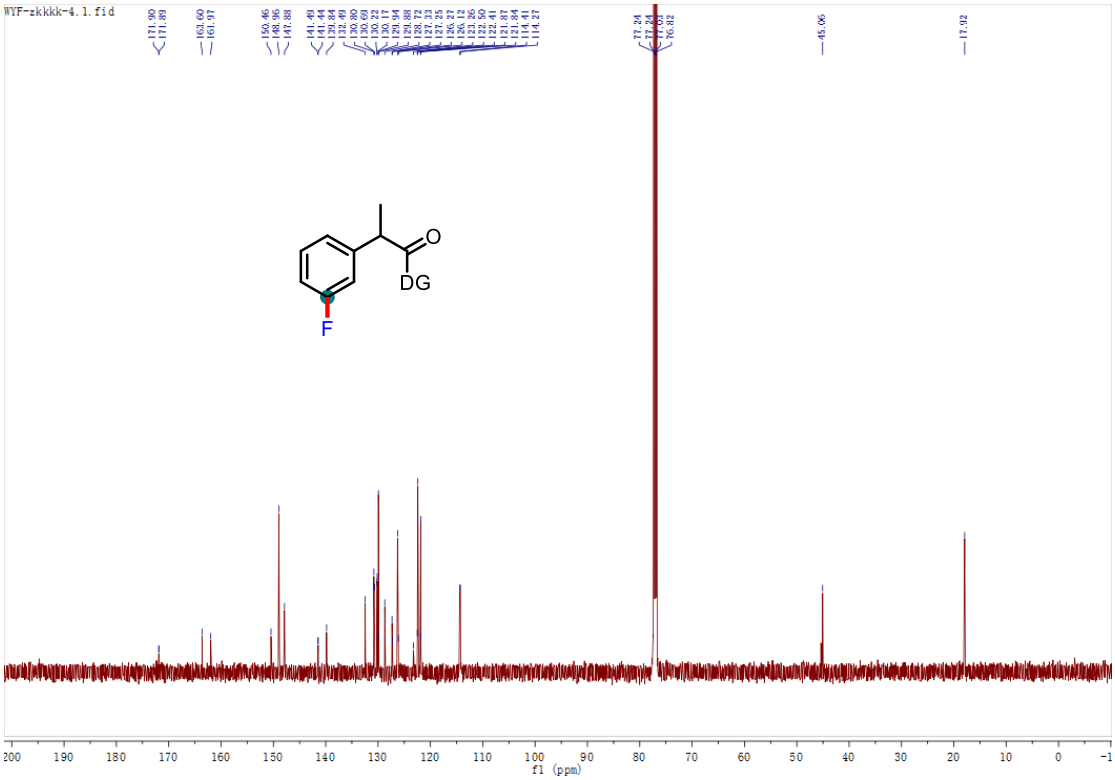
^{13}C NMR spectrum of 2i (101 MHz, $CDCl_3$)



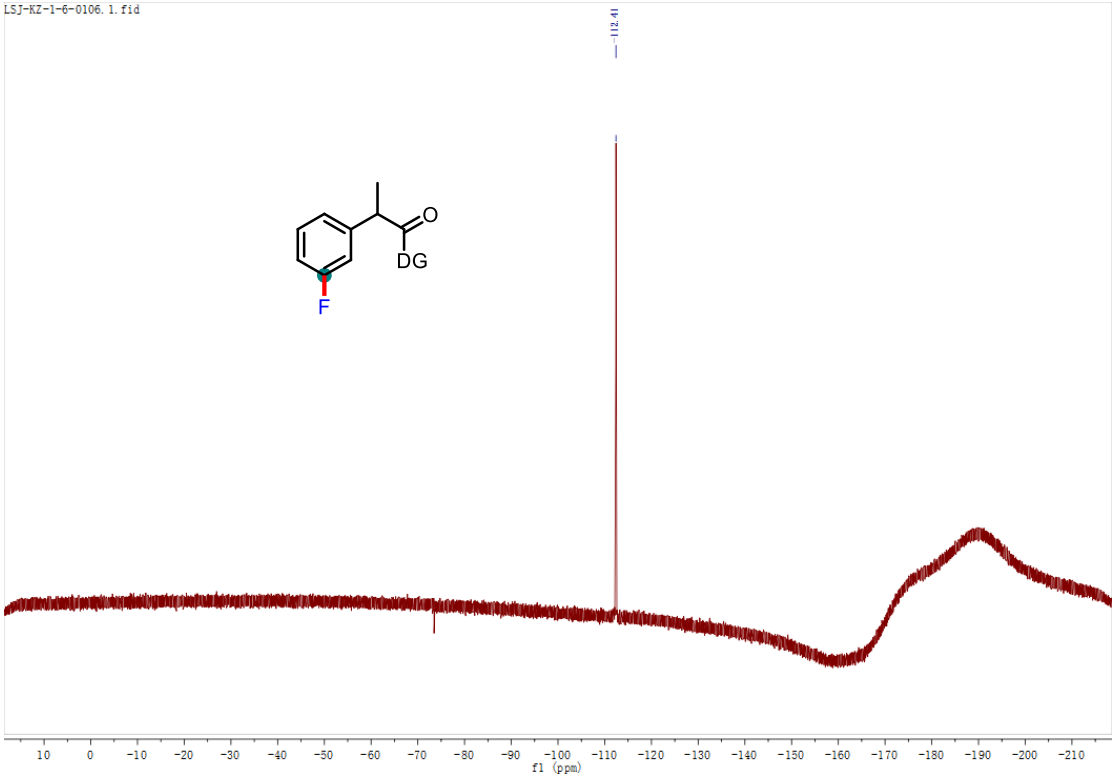
^{19}F NMR spectrum of 2i (376 MHz, $CDCl_3$)



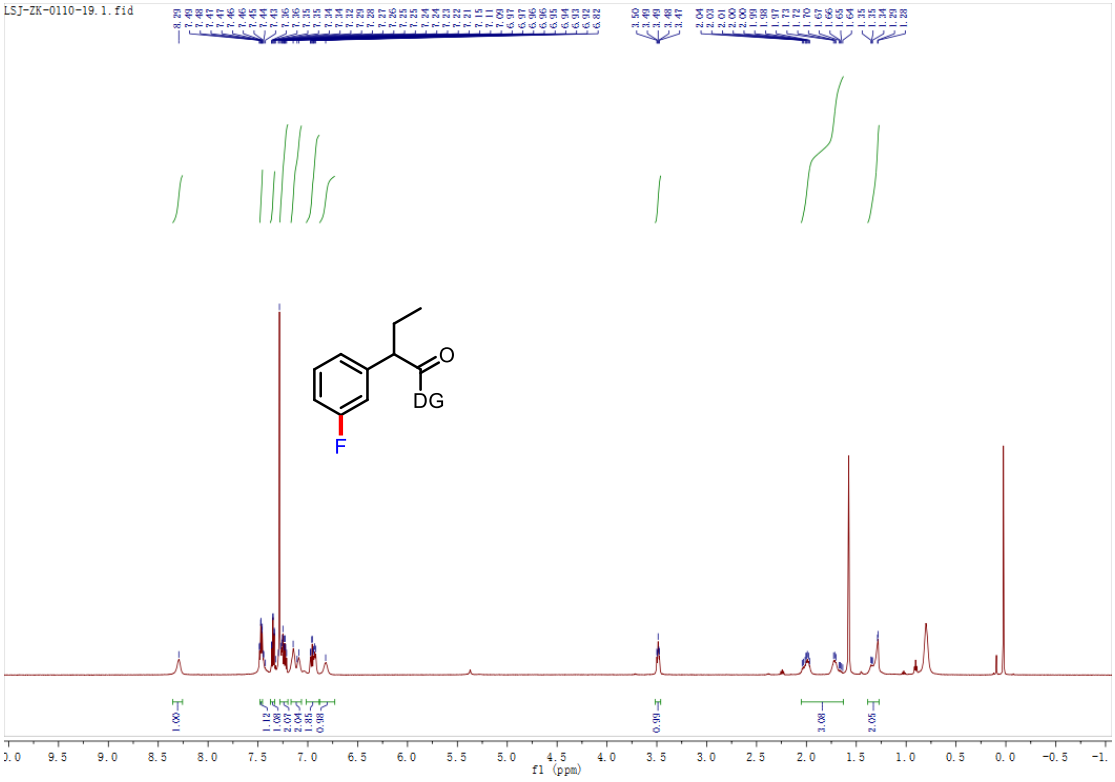
^{1}H NMR spectrum of 2j (600 MHz, $CDCl_3$)



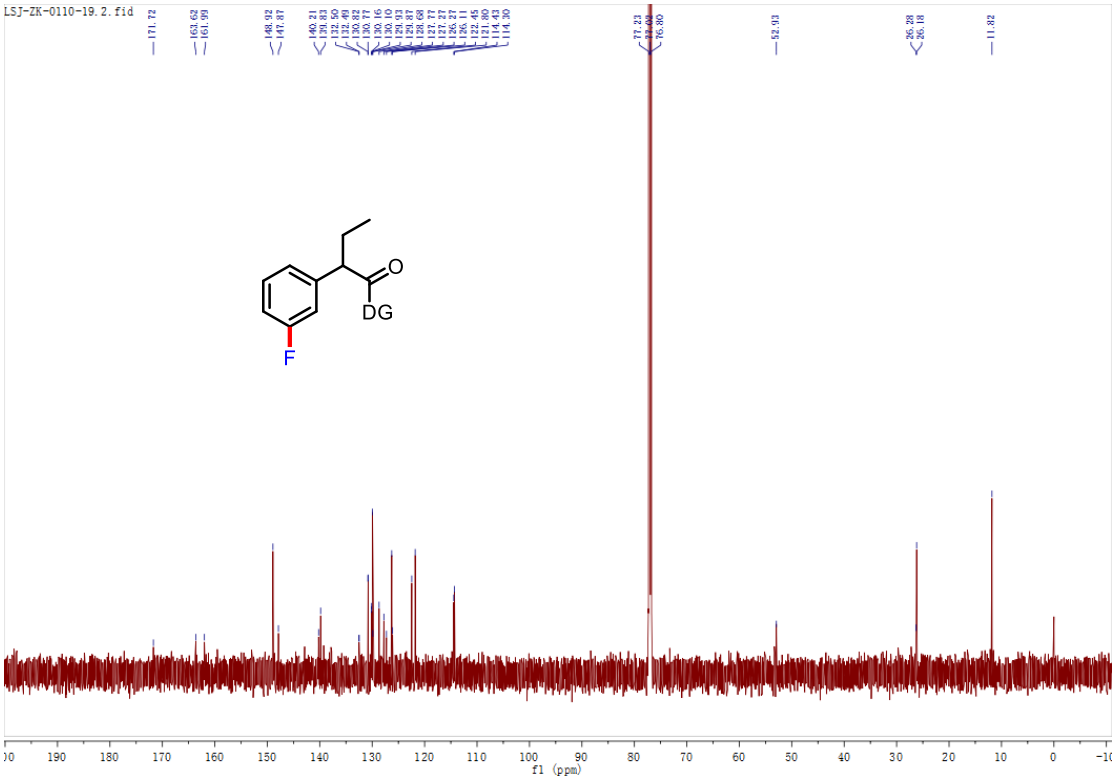
^{13}C NMR spectrum of 2j (151 MHz, $CDCl_3$)



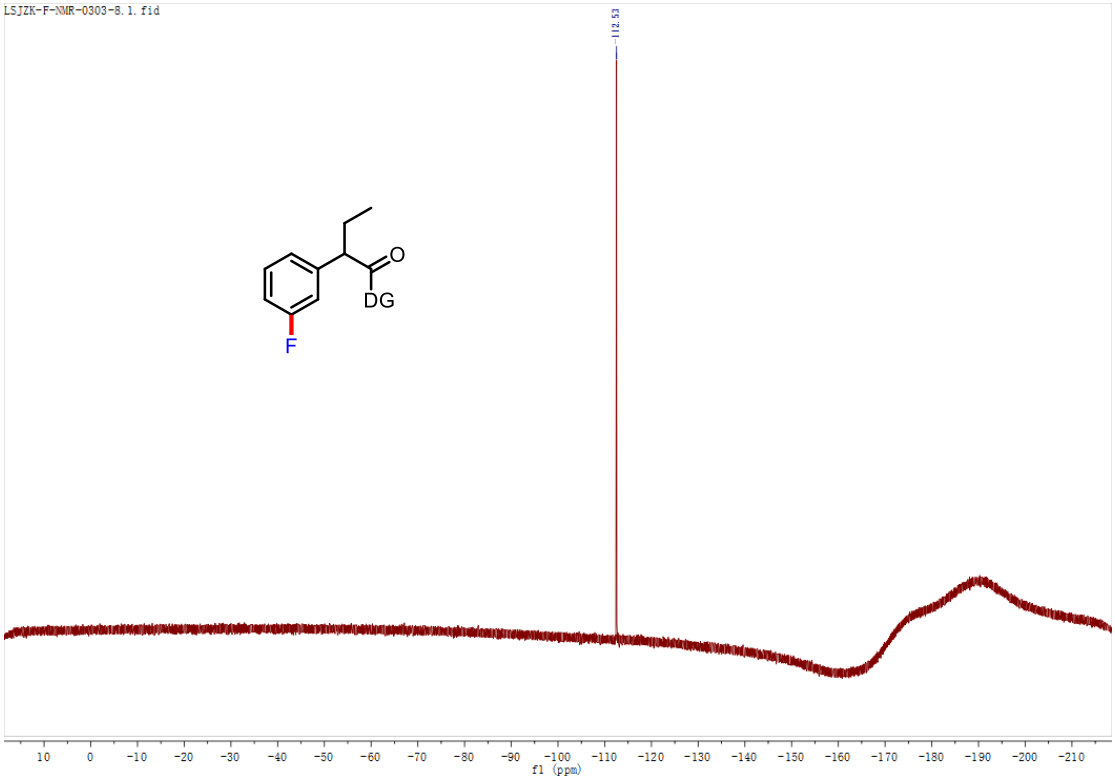
^{19}F NMR spectrum of 2j (565 MHz, $CDCl_3$)



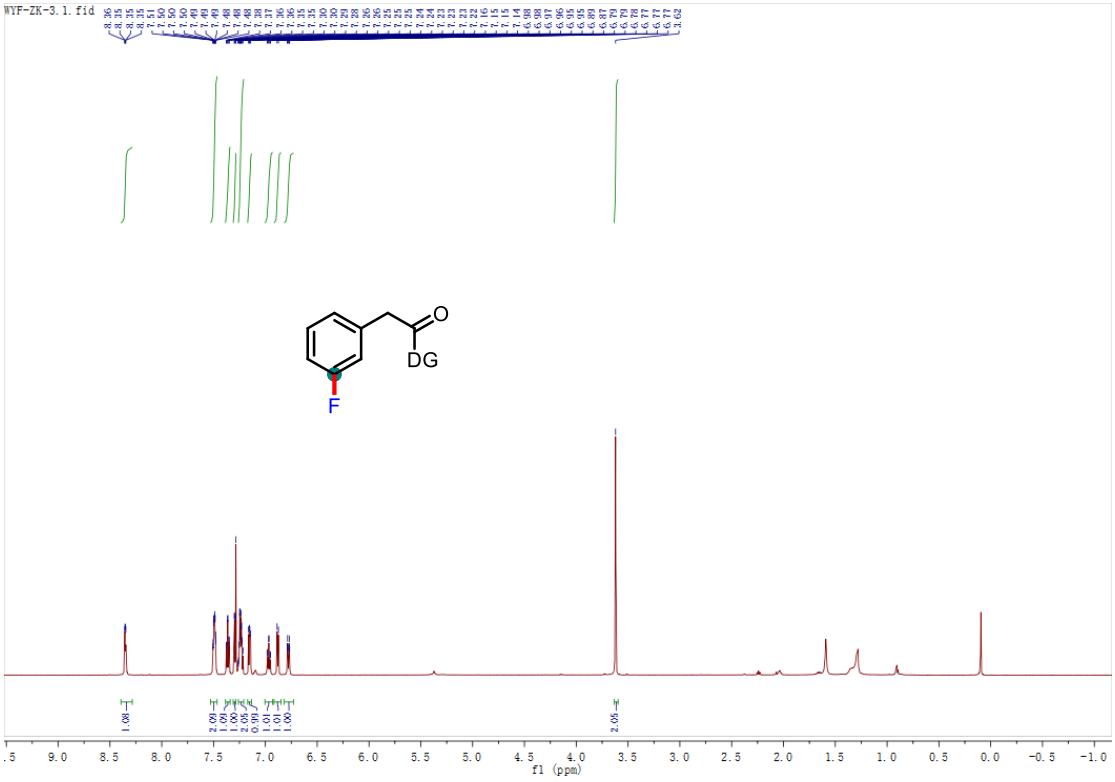
^{1}H NMR spectrum of 2k (600 MHz, $CDCl_3$)



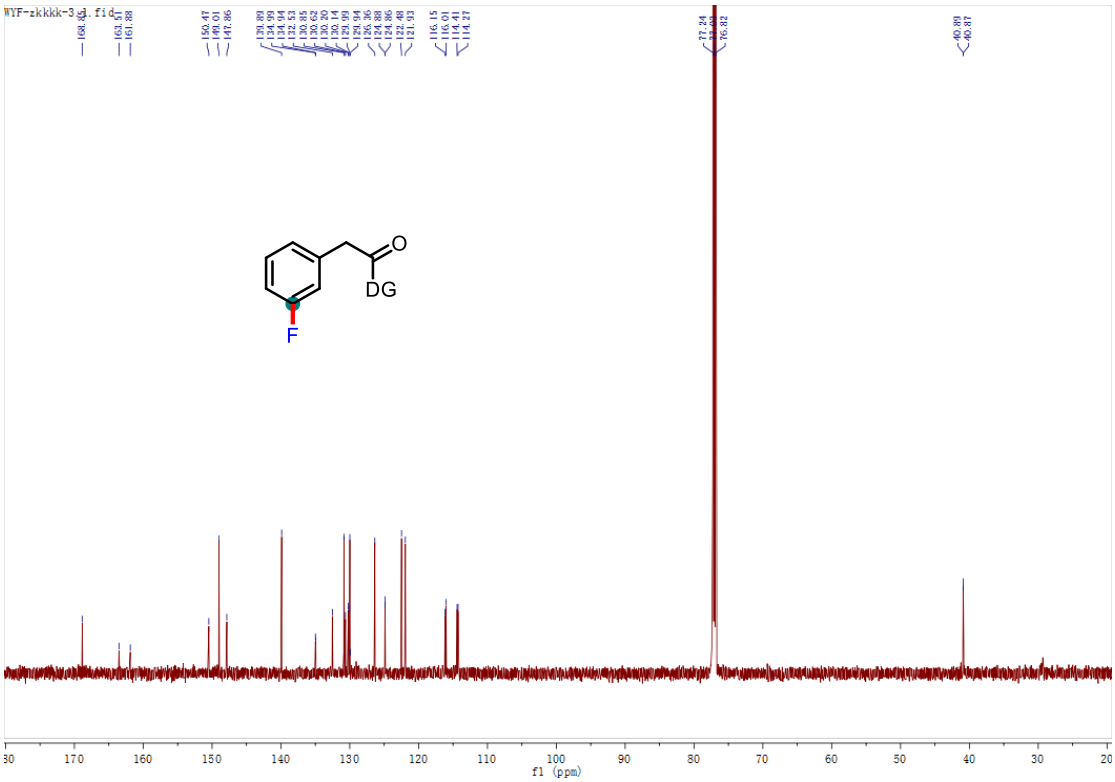
^{13}C NMR spectrum of 2k (151 MHz, $CDCl_3$)



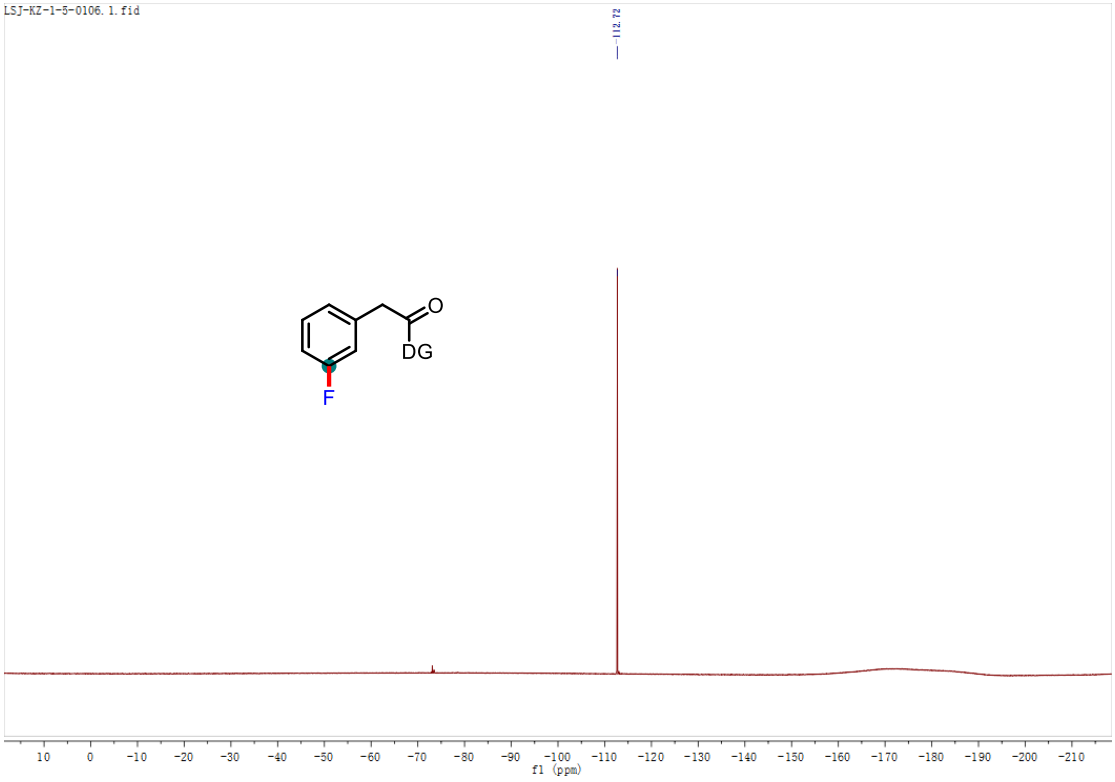
^{19}F NMR spectrum of 2k (565 MHz, $CDCl_3$)



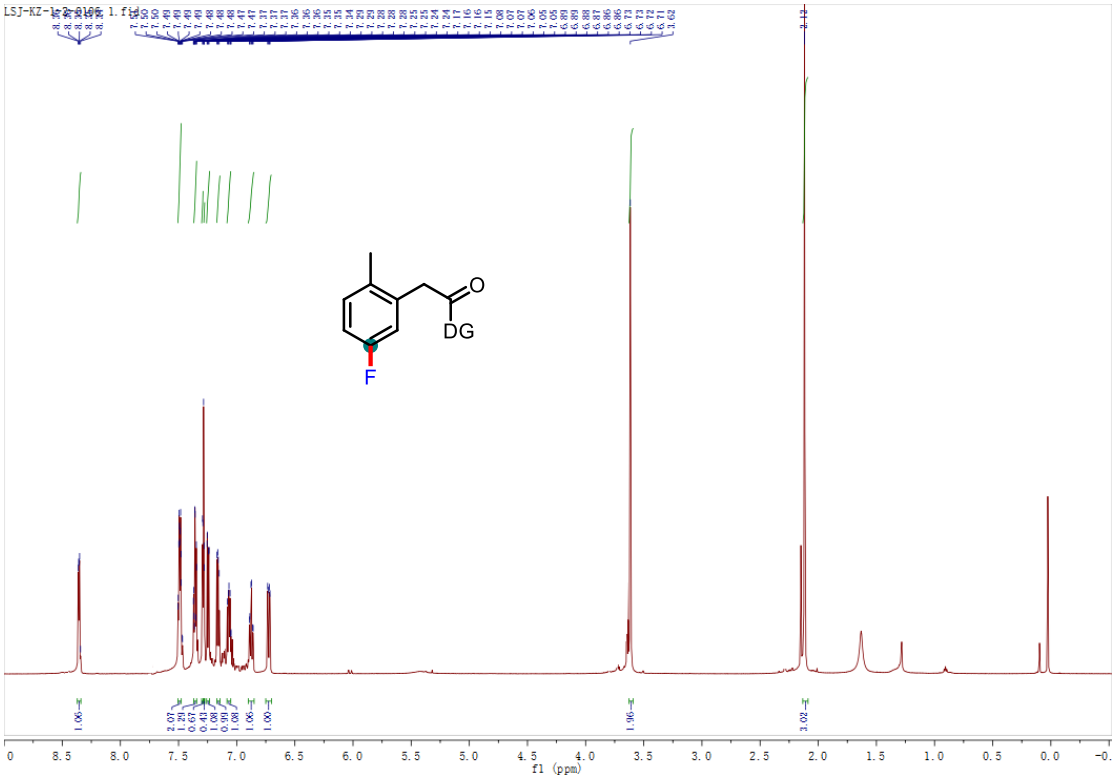
^{1}H NMR spectrum of 2l (600 MHz, $CDCl_3$)



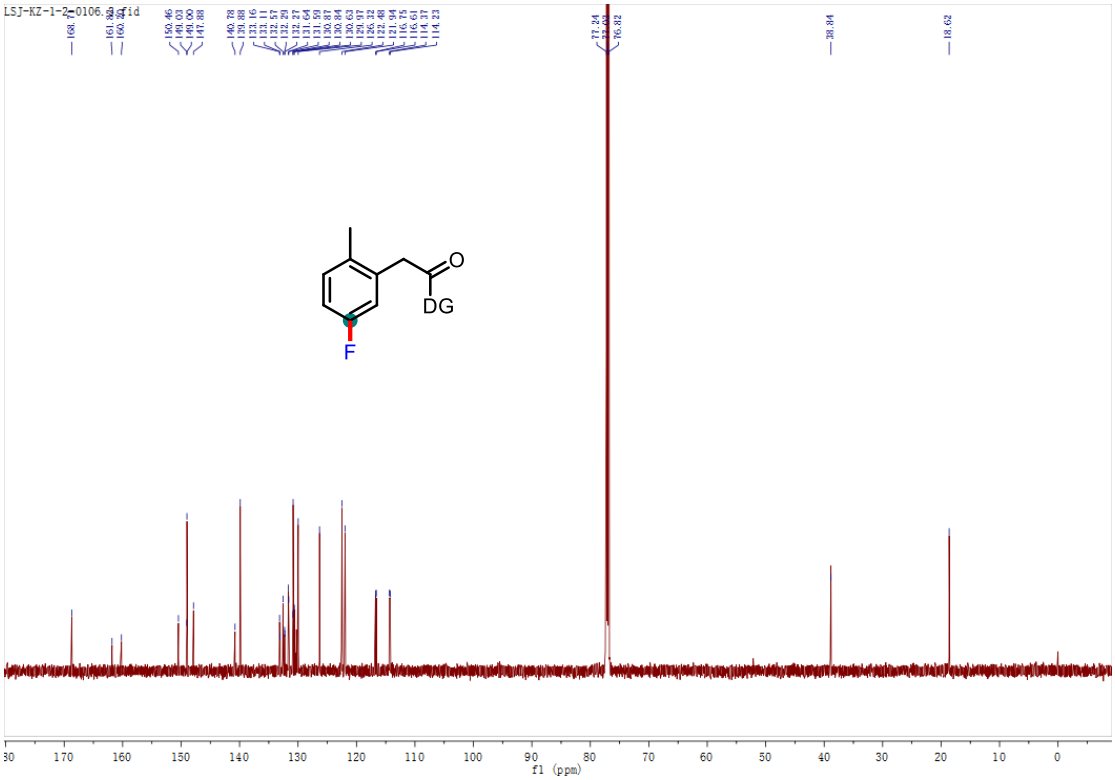
^{13}C NMR spectrum of 2l (151 MHz, $CDCl_3$)



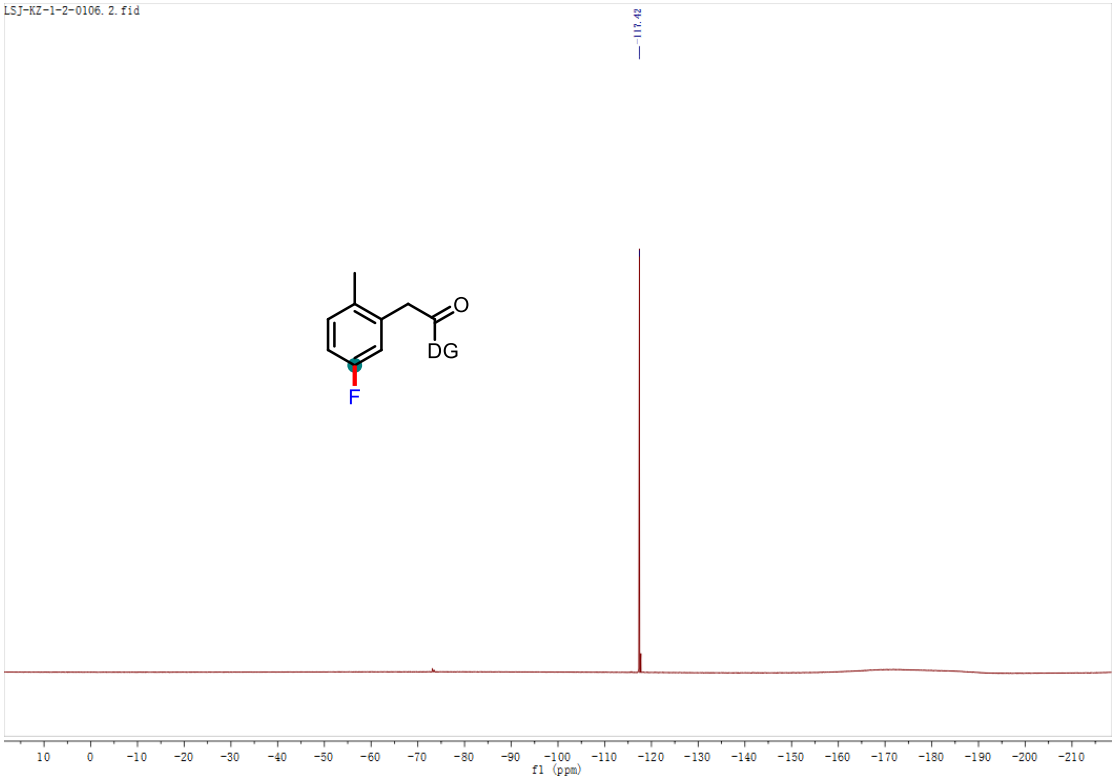
^{19}F NMR spectrum of 2l (565 MHz, $CDCl_3$)



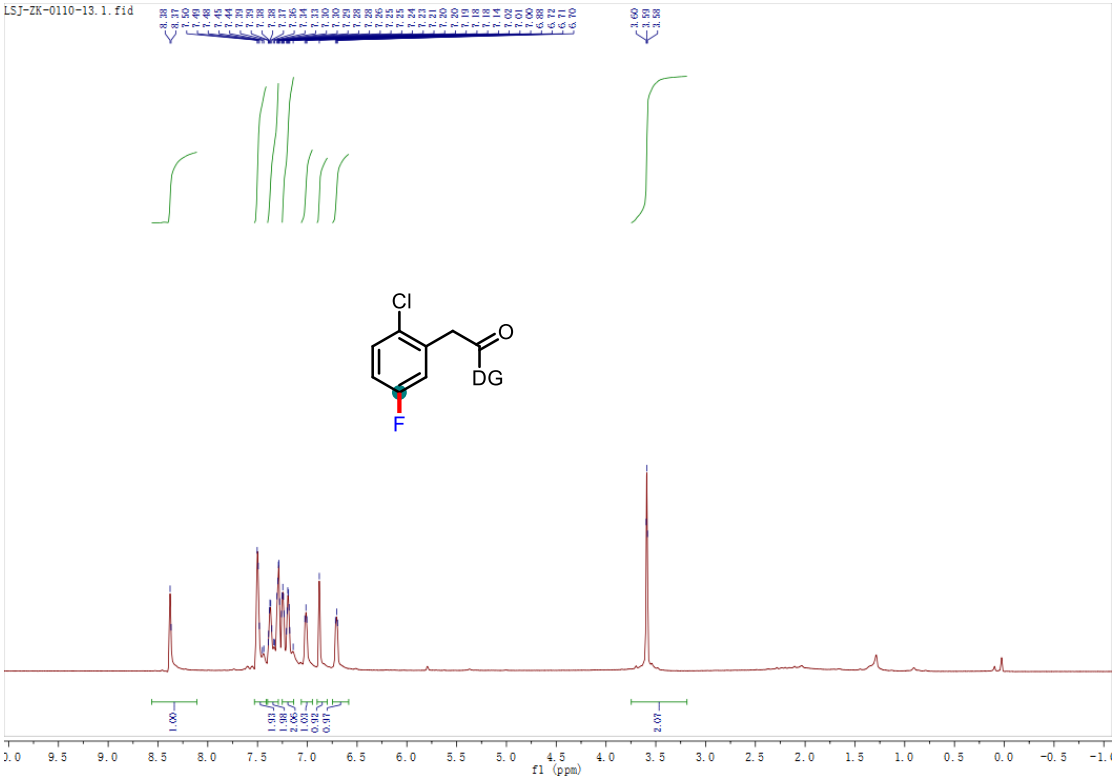
^{1}H NMR spectrum of 2m (600 MHz, $CDCl_3$)



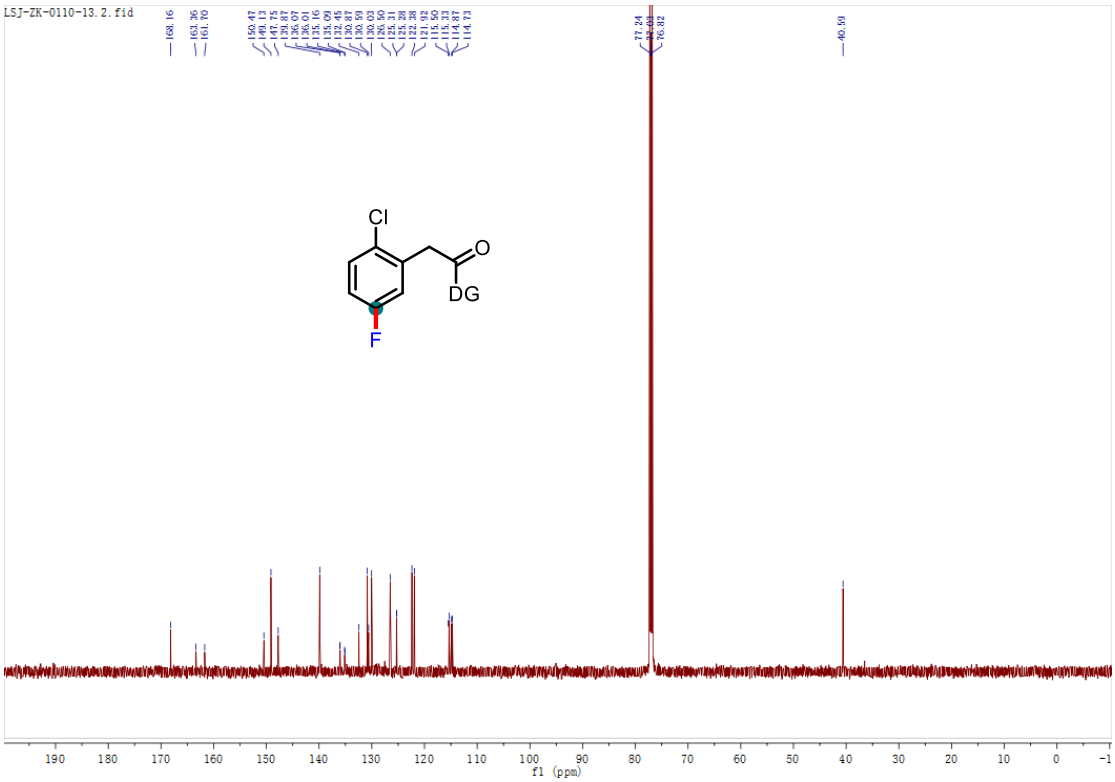
^{13}C NMR spectrum of 2m (151 MHz, $CDCl_3$)



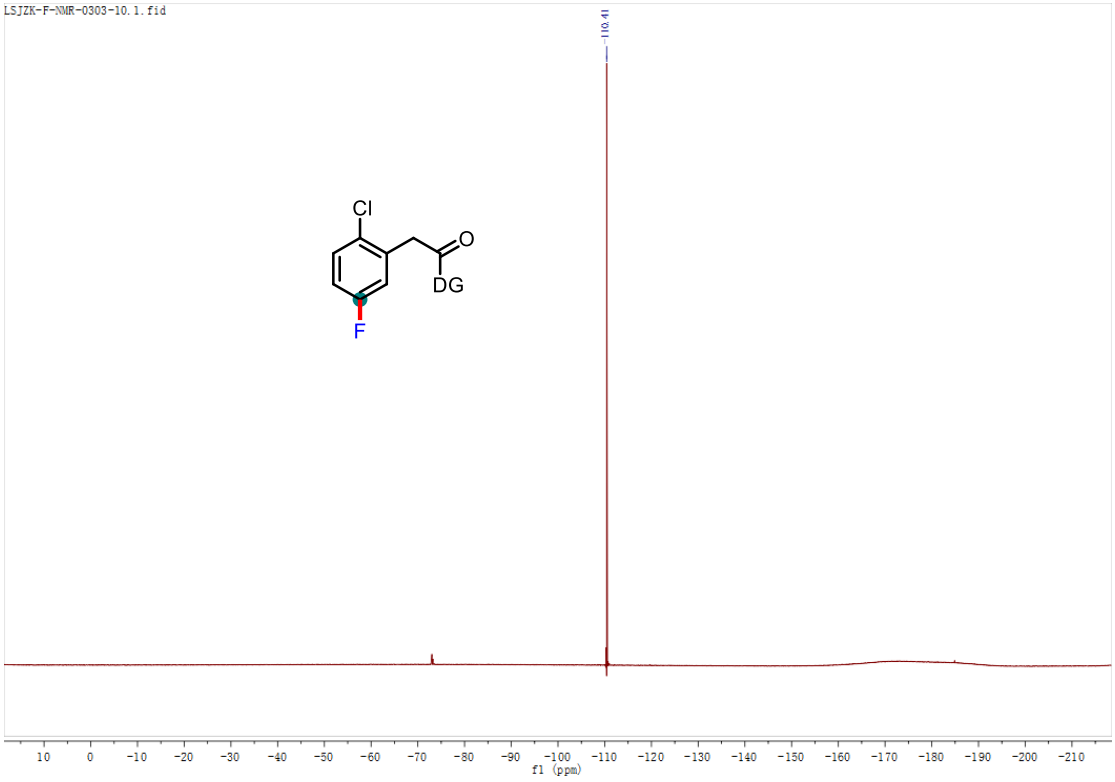
^{19}F NMR spectrum of 2m (565 MHz, $CDCl_3$)



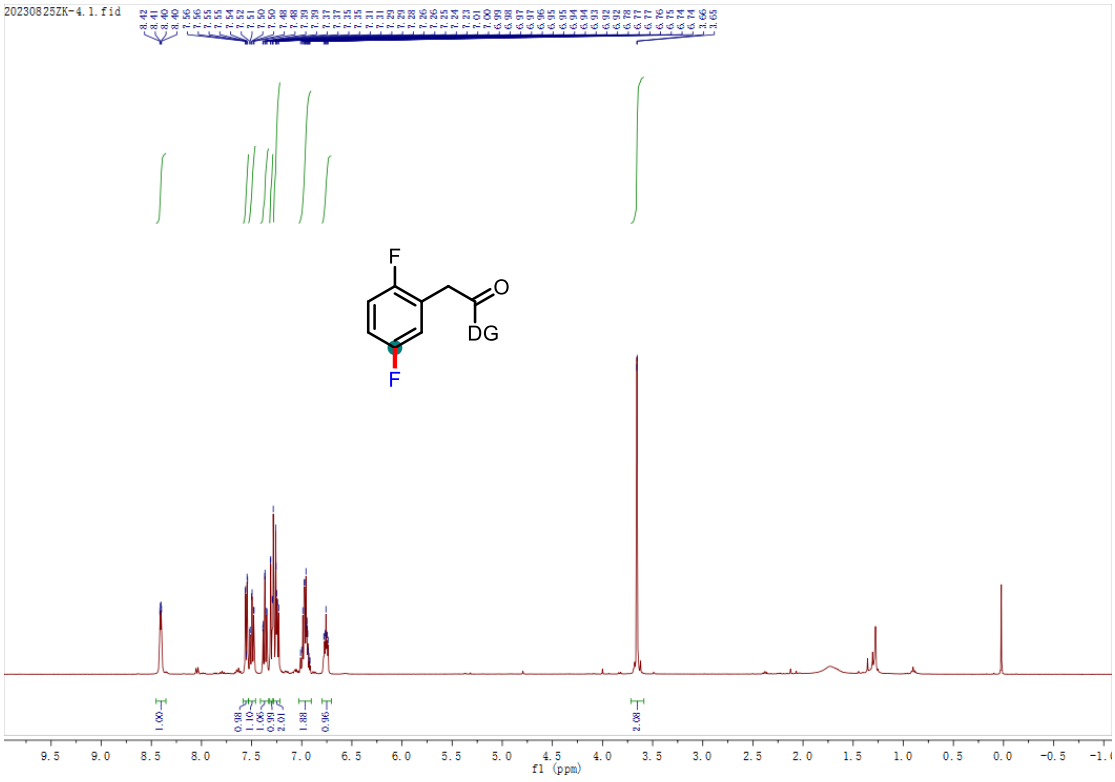
^{1}H NMR spectrum of 2n (600 MHz, $CDCl_3$)



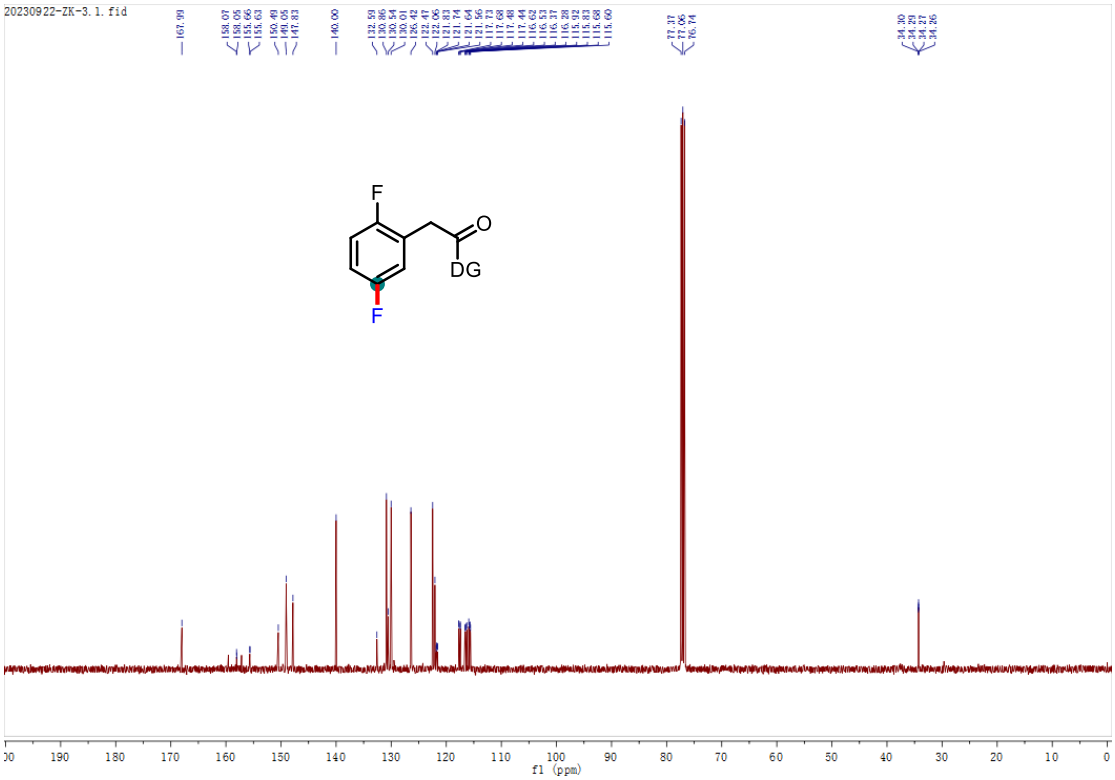
^{13}C NMR spectrum of 2n (151 MHz, $CDCl_3$)



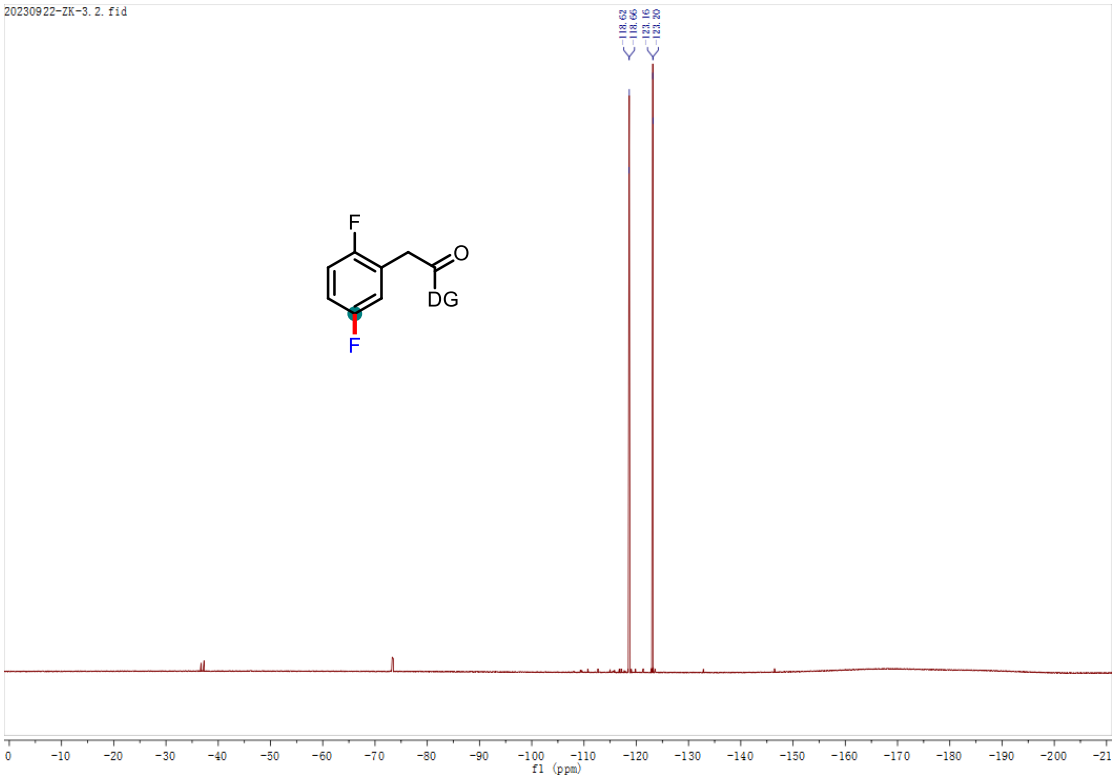
^{19}F NMR spectrum of 2n (565 MHz, $CDCl_3$)



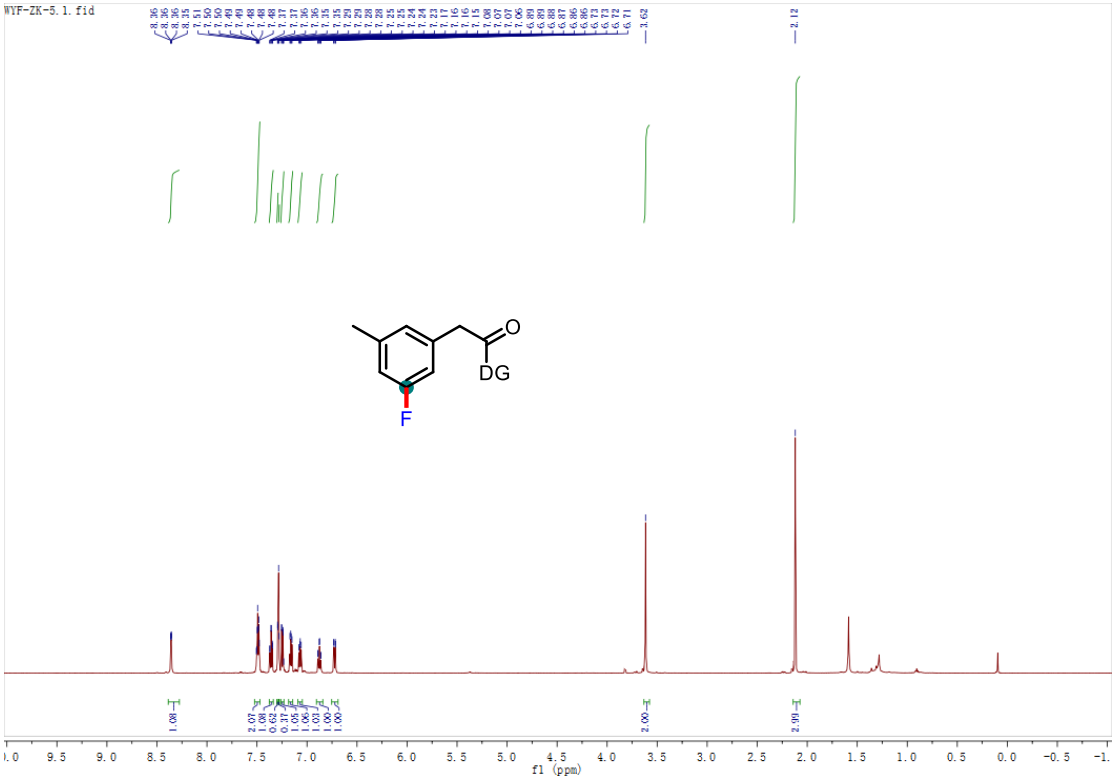
^{1}H NMR spectrum of 2o (400 MHz, $CDCl_3$)



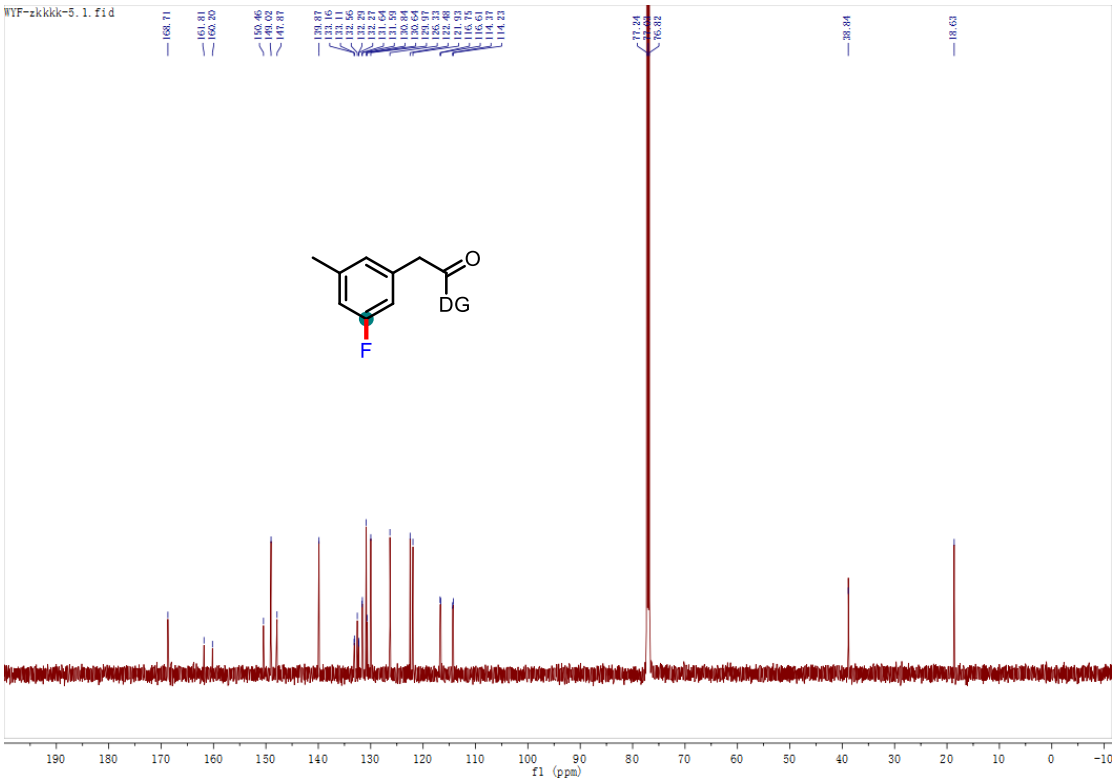
^{13}C NMR spectrum of 2o (101 MHz, $CDCl_3$)



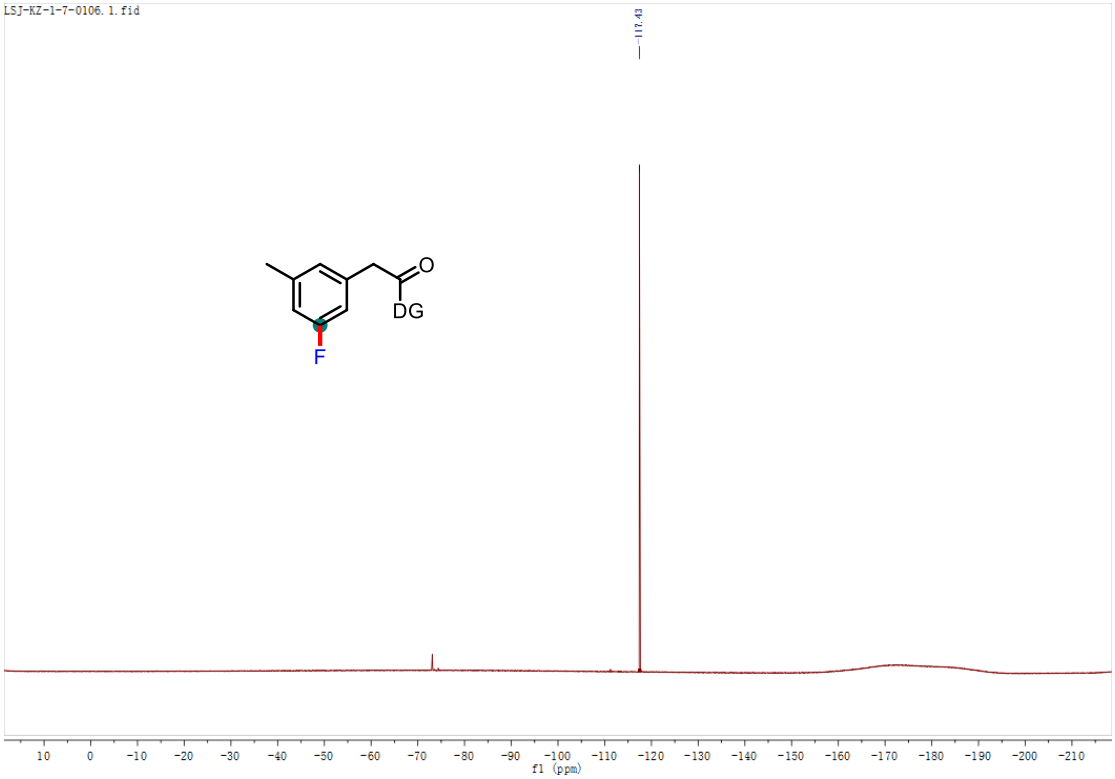
^{19}F NMR spectrum of 2o (376 MHz, $CDCl_3$)



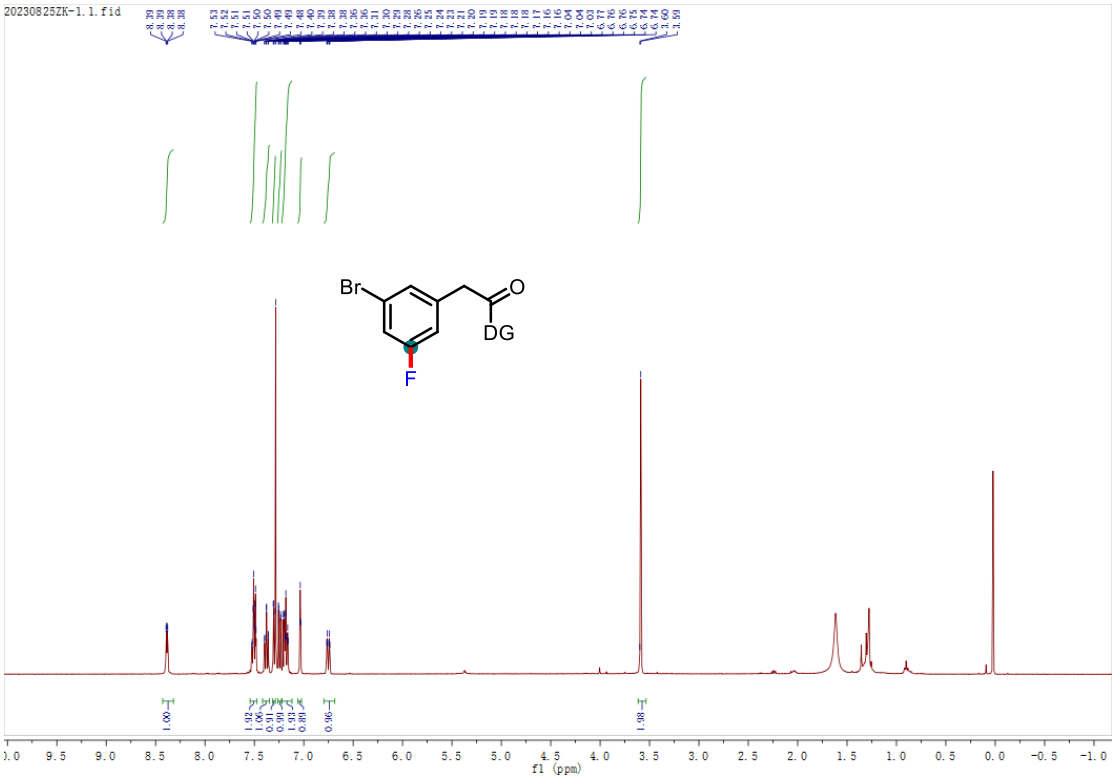
^{1}H NMR spectrum of 2p (600 MHz, $CDCl_3$)



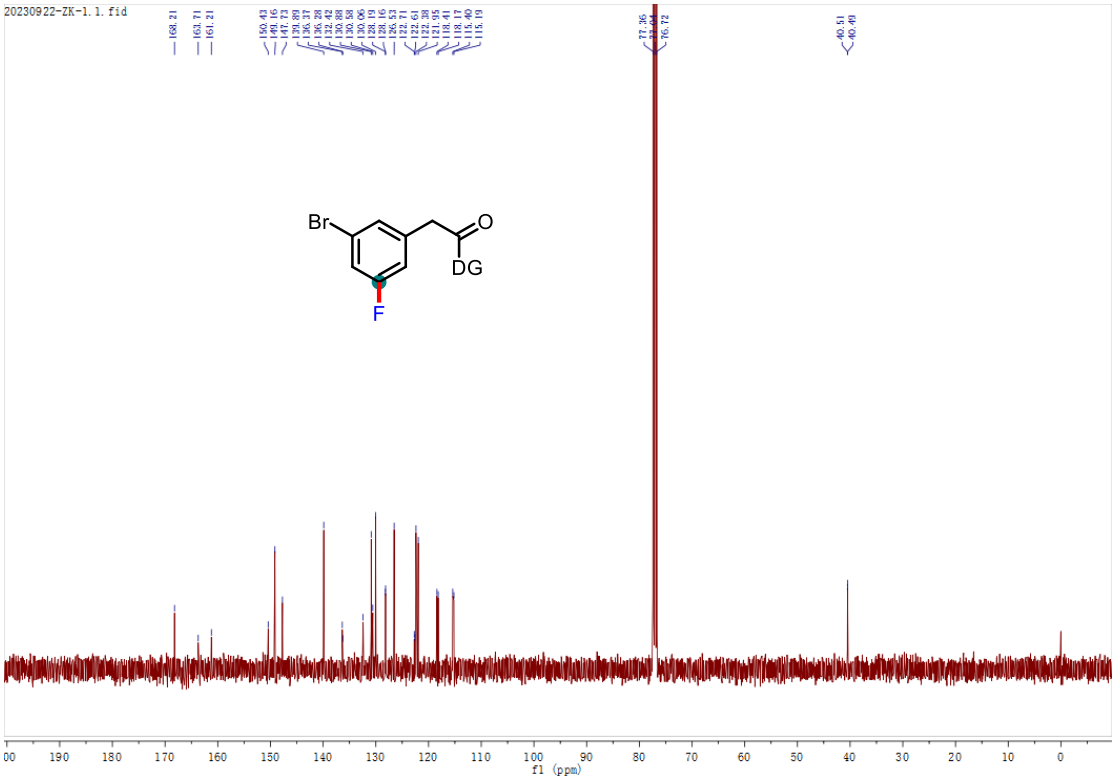
^{13}C NMR spectrum of 2p (151 MHz, $CDCl_3$)



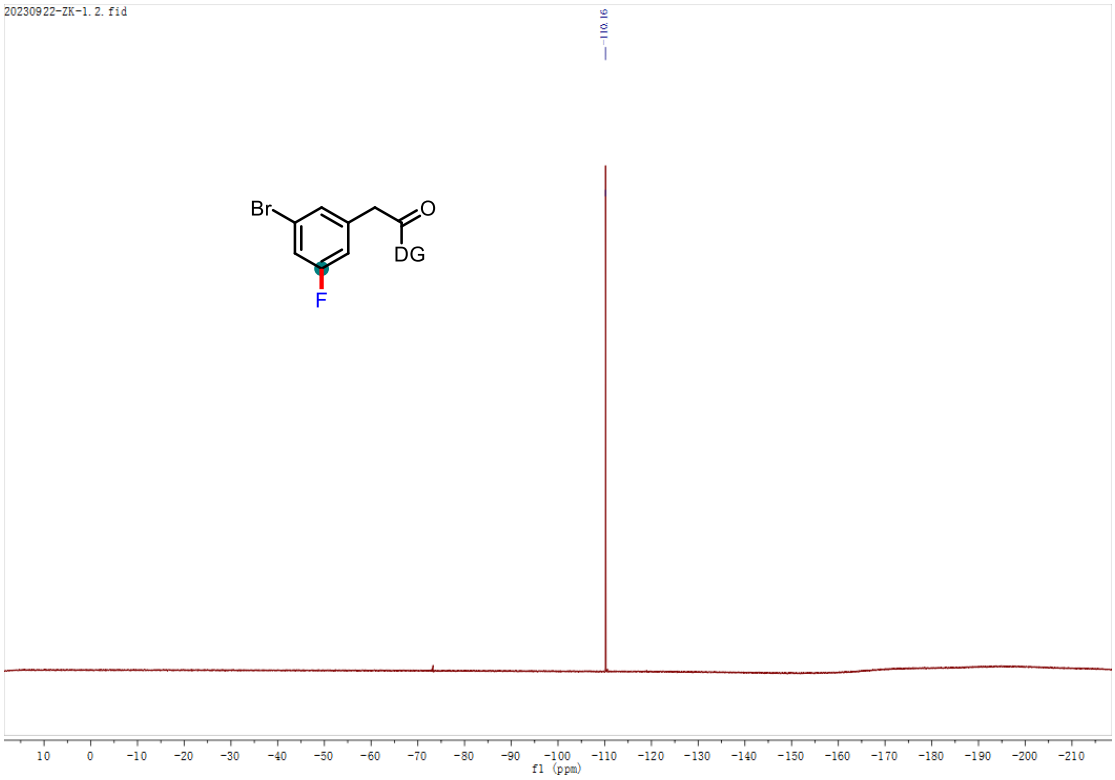
^{19}F NMR spectrum of 2p (565 MHz, $CDCl_3$)



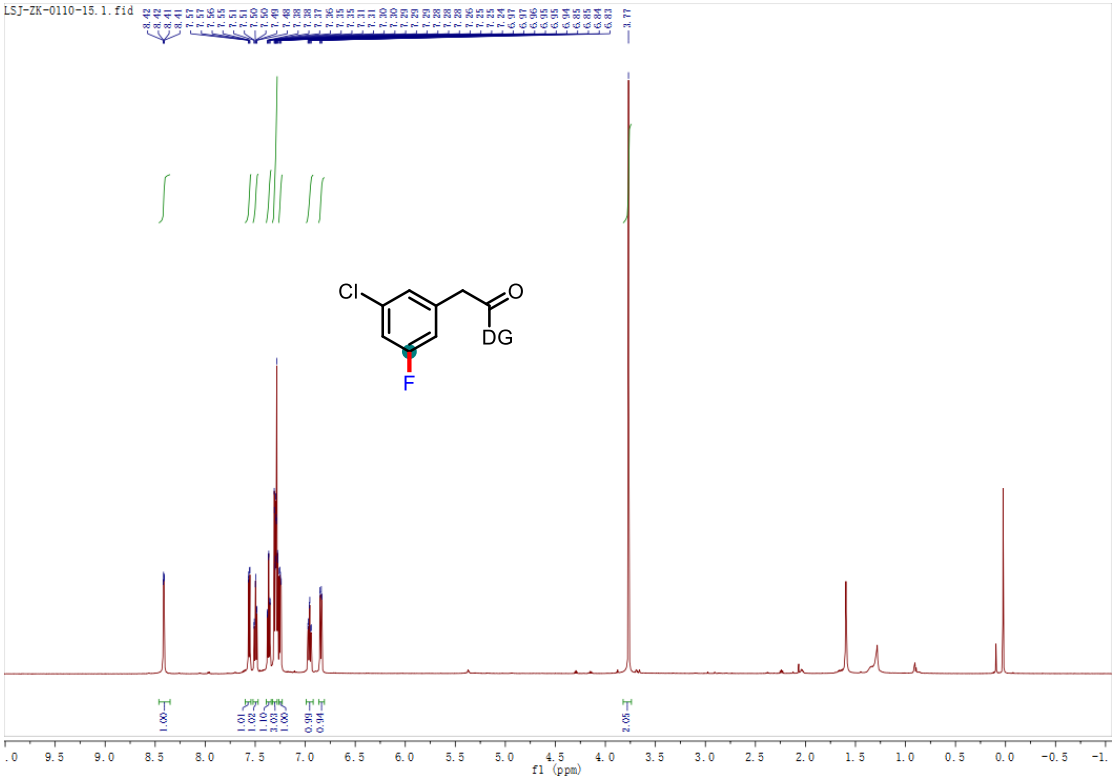
^{1}H NMR spectrum of 2q (400 MHz, $CDCl_3$)



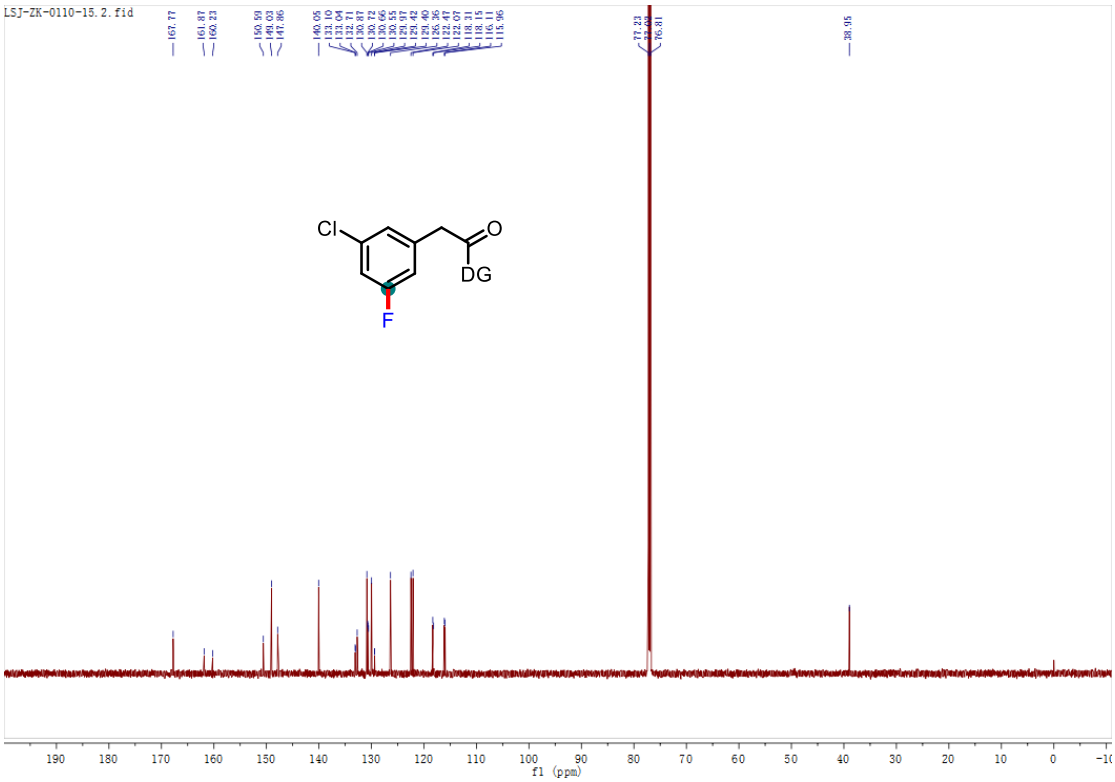
^{13}C NMR spectrum of 2q (101 MHz, $CDCl_3$)



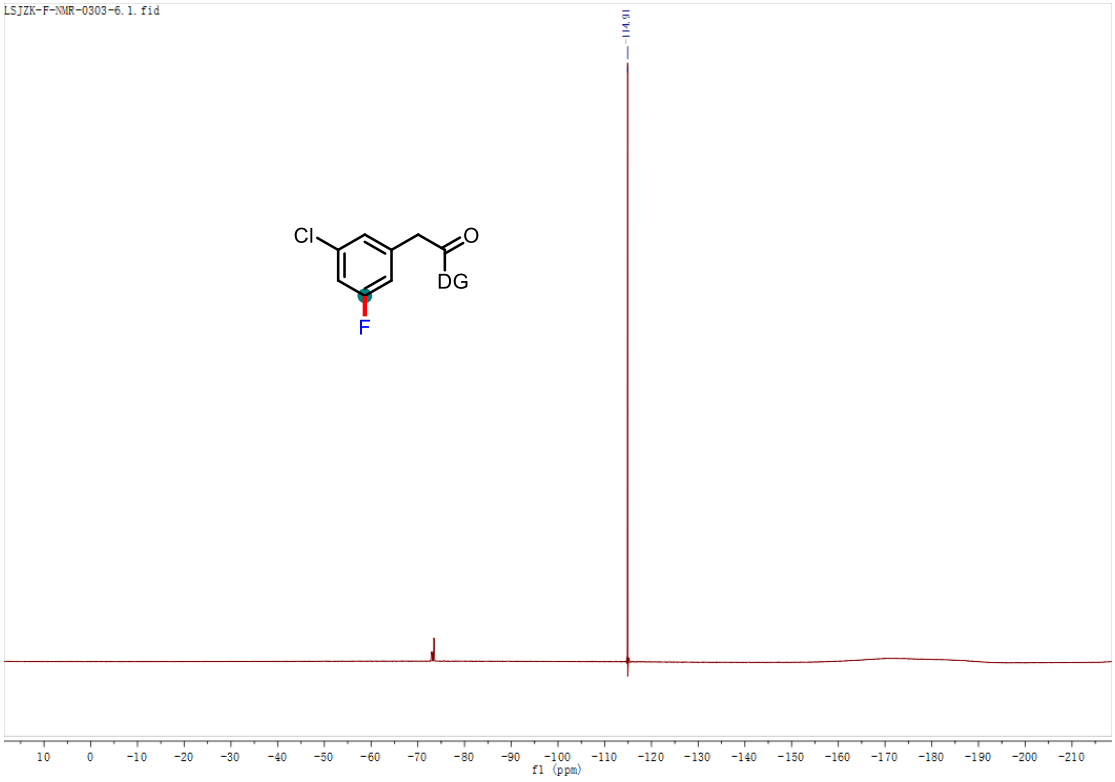
^{19}F NMR spectrum of 2q (376 MHz, $CDCl_3$)



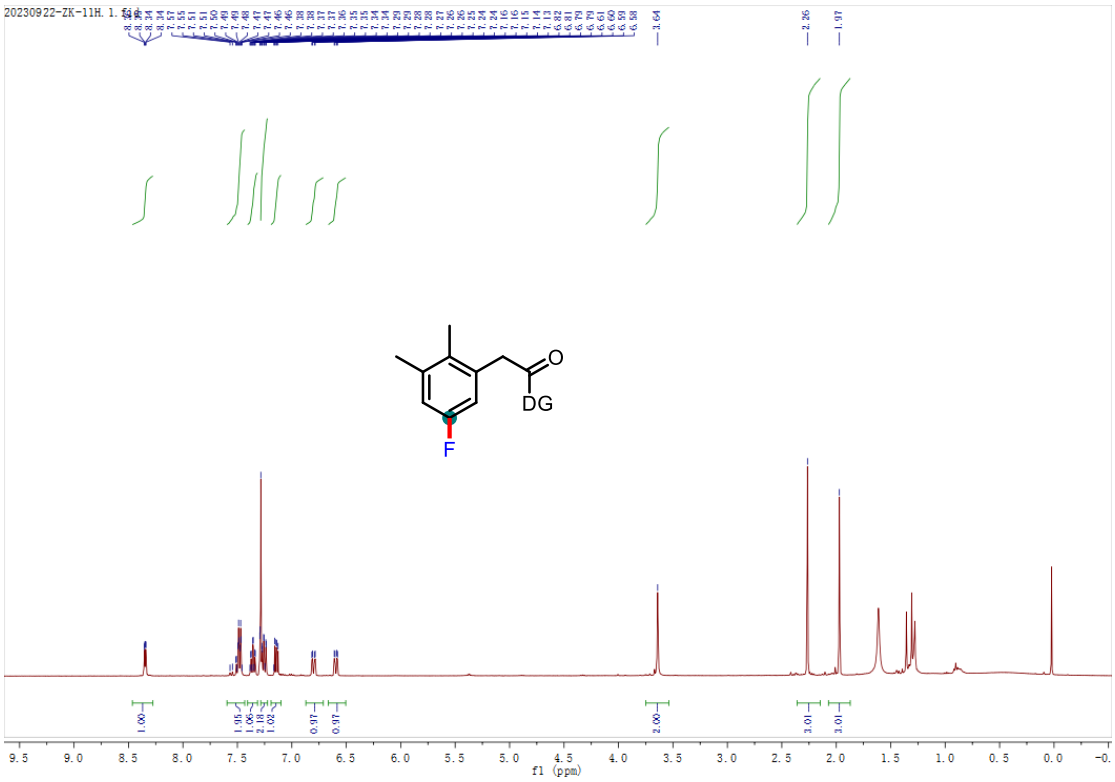
^{1}H NMR spectrum of 2r (600 MHz, $CDCl_3$)



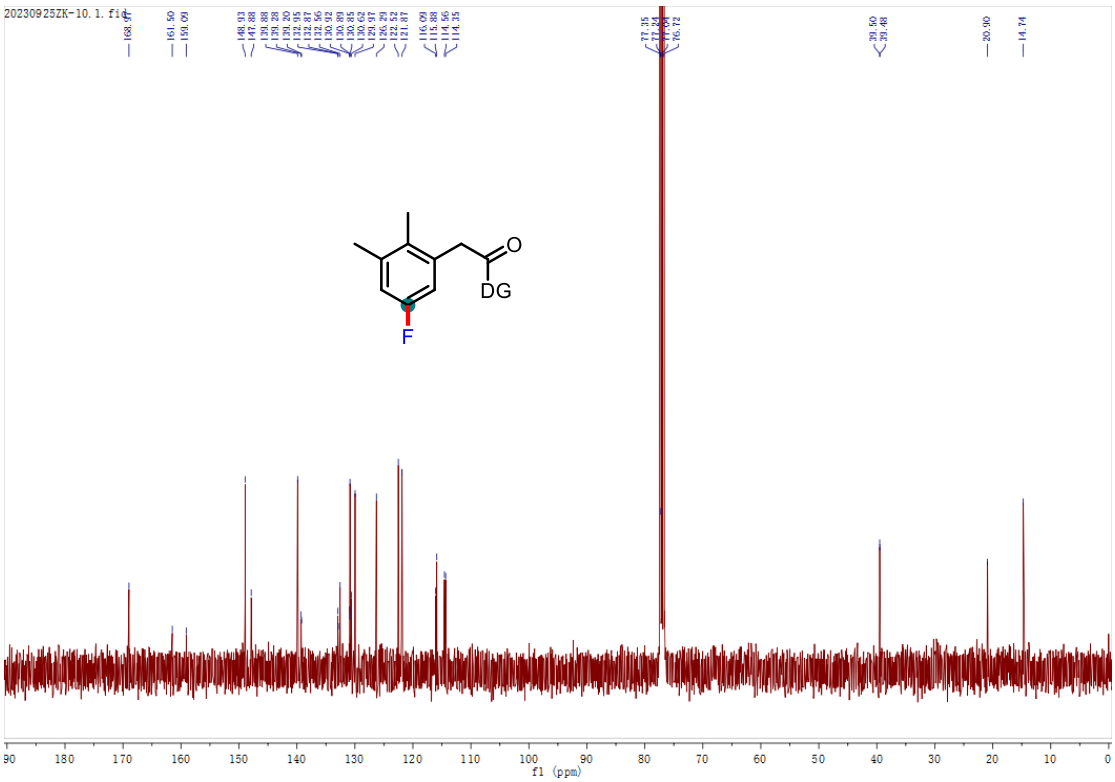
^{13}C NMR spectrum of 2r (151 MHz, $CDCl_3$)



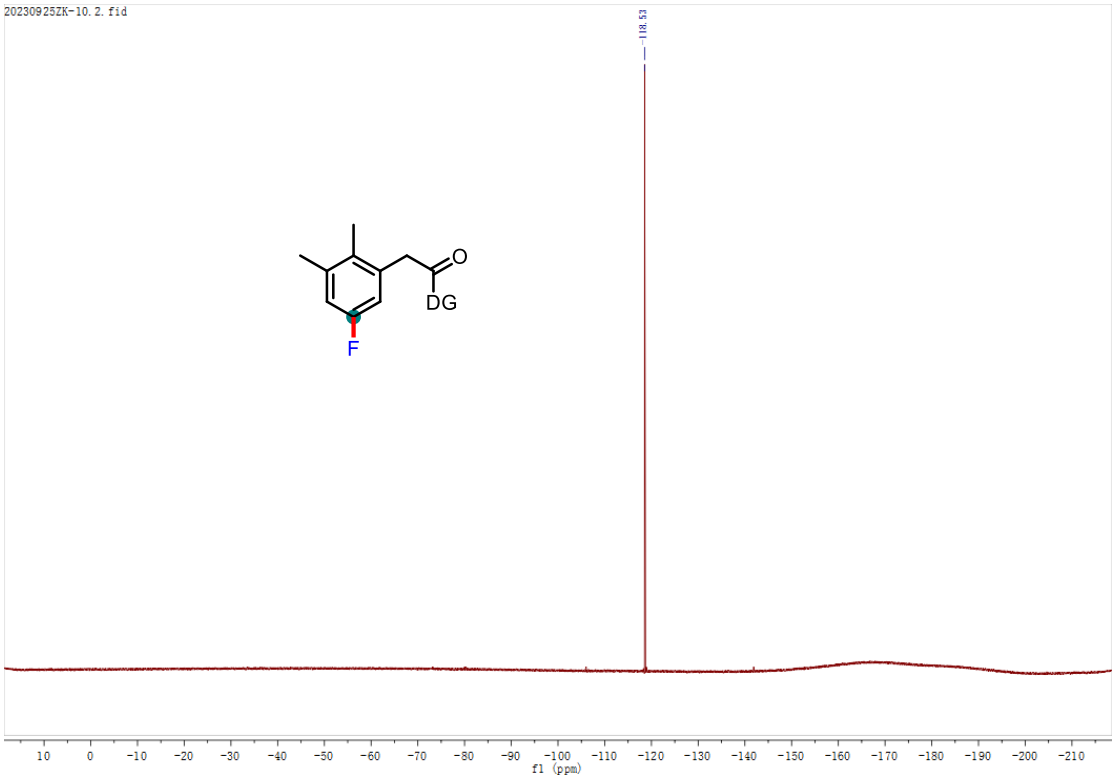
^{19}F NMR spectrum of 2r (565 MHz, $CDCl_3$)



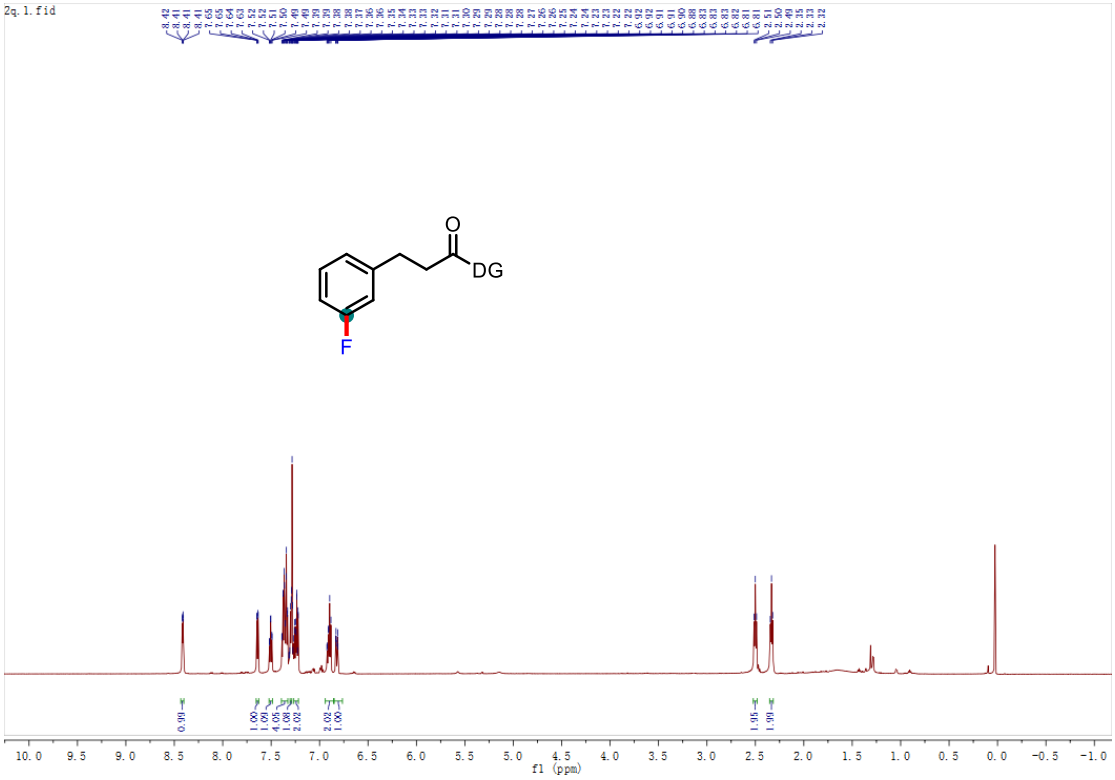
^{1}H NMR spectrum of 2s (400 MHz, $CDCl_3$)



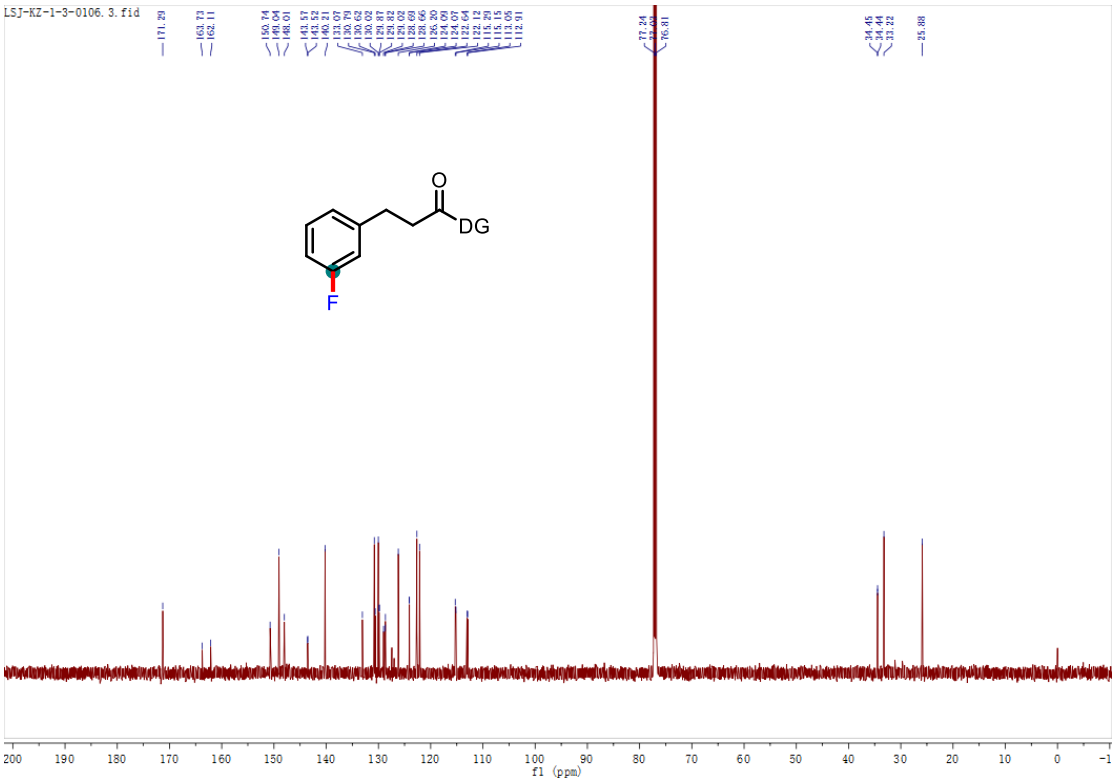
^{13}C NMR spectrum of 2s (101 MHz, $CDCl_3$)



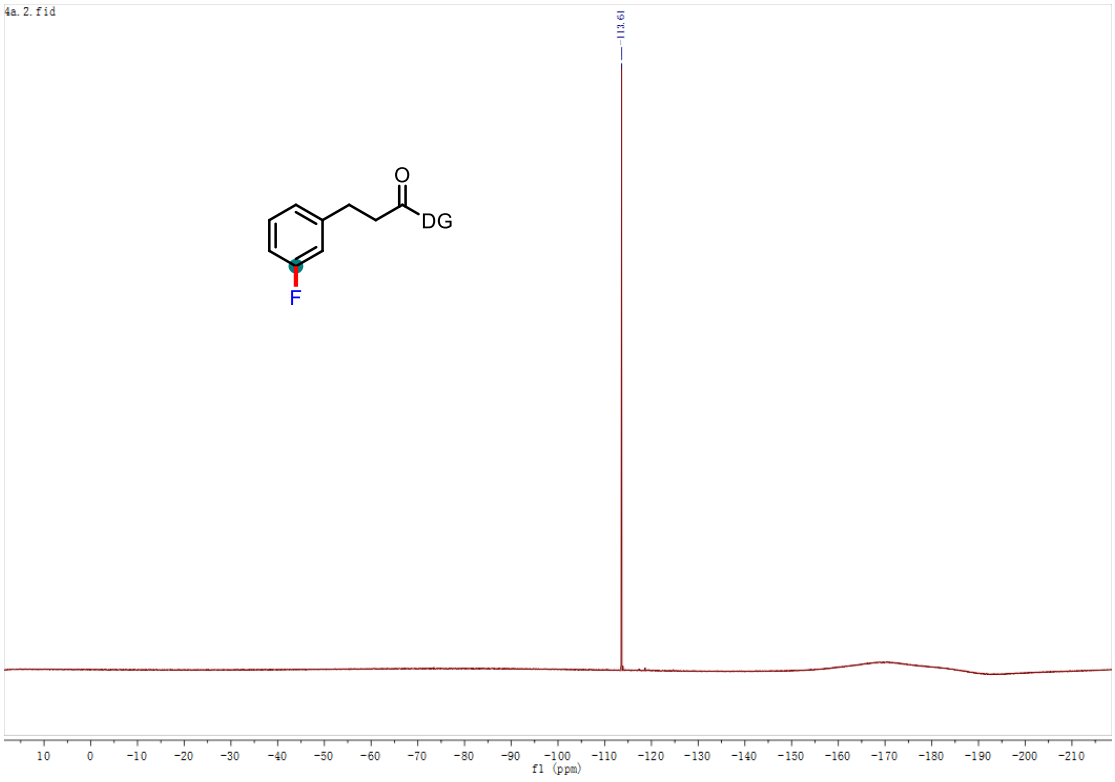
^{19}F NMR spectrum of 2s (376 MHz, $CDCl_3$)



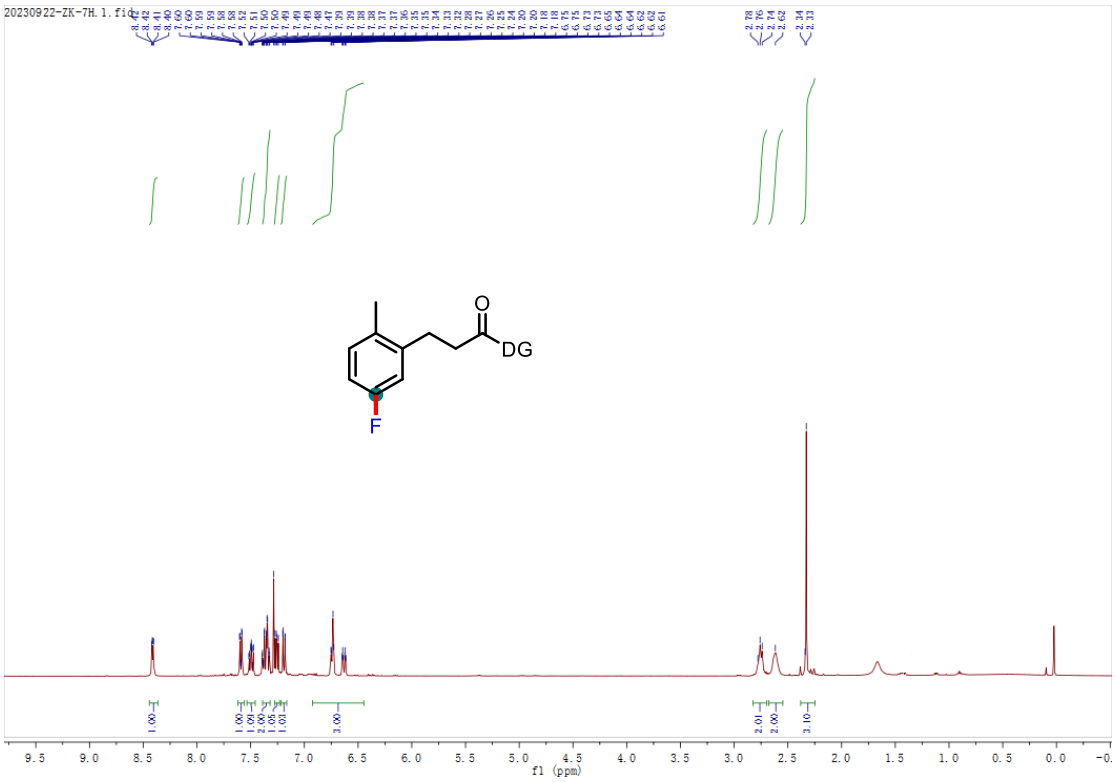
^{1}H NMR spectrum of 4a (600 MHz, $CDCl_3$)



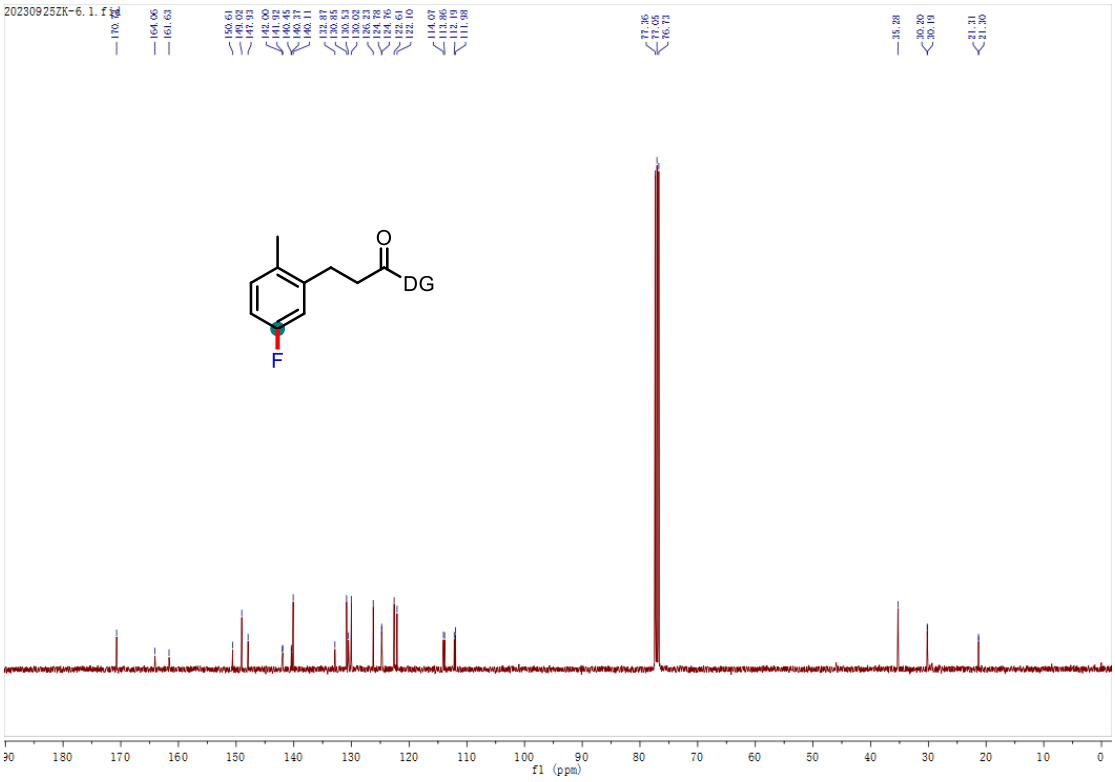
^{13}C NMR spectrum of 4a (151 MHz, $CDCl_3$)



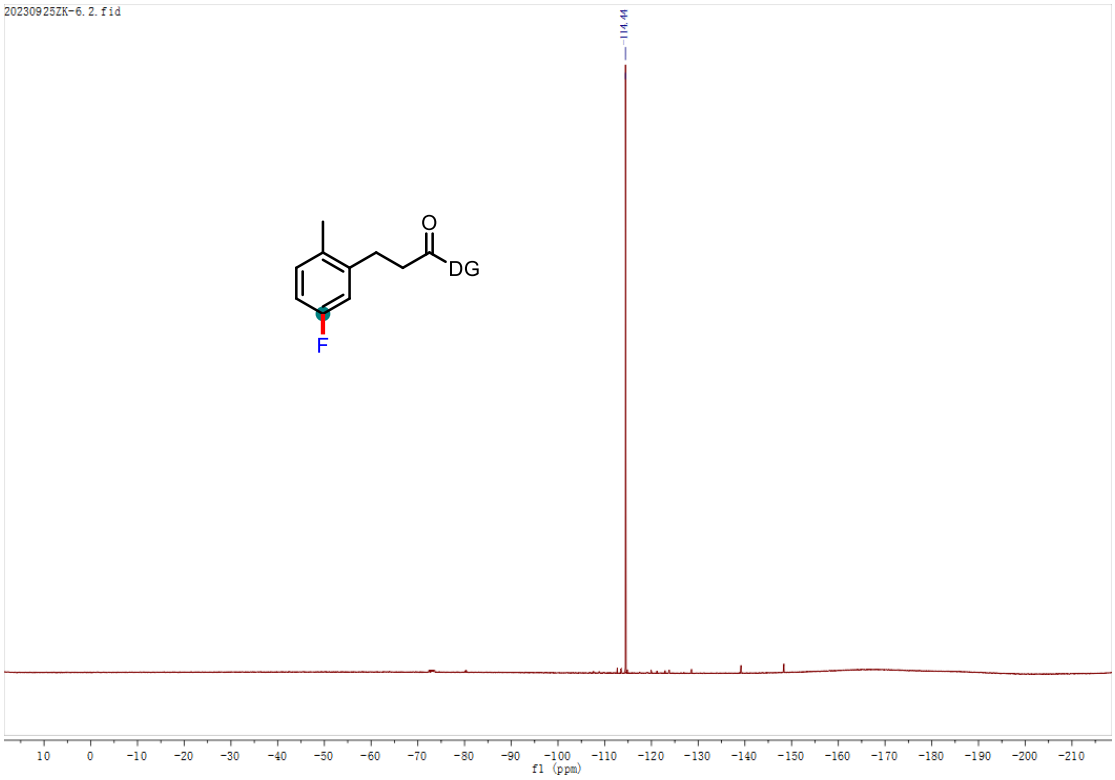
^{19}F NMR spectrum of 4a (565 MHz, $CDCl_3$)



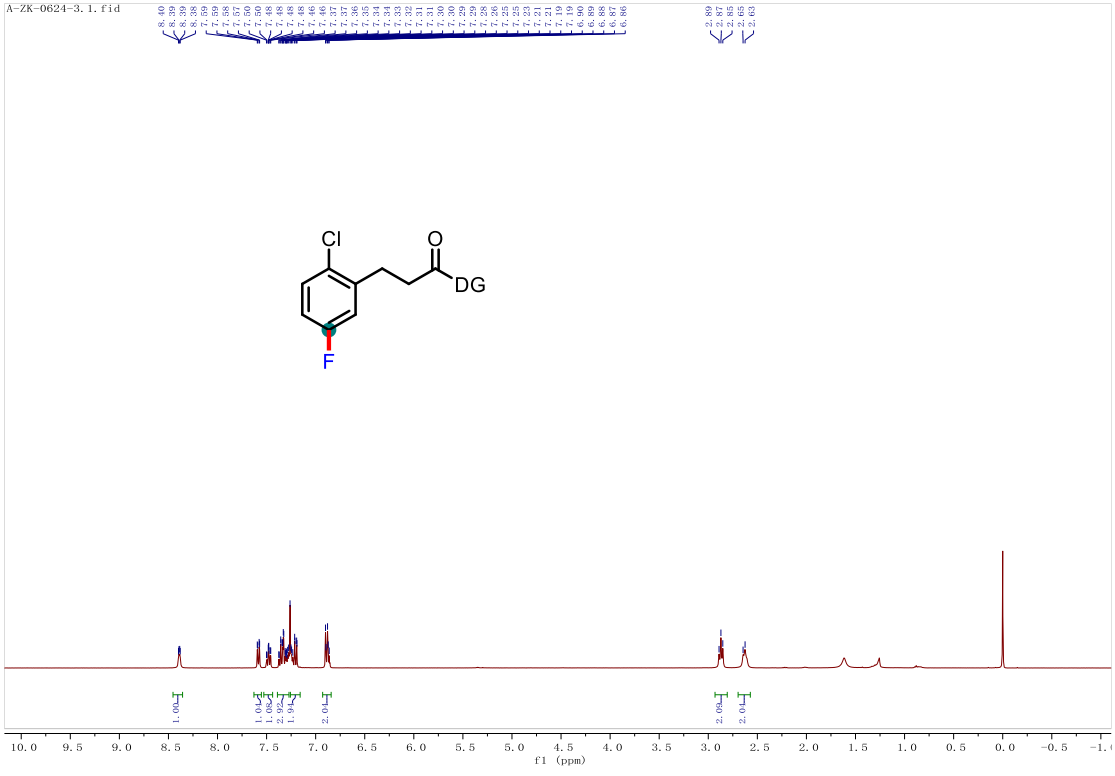
^{1}H NMR spectrum of 4b (400 MHz, $CDCl_3$)



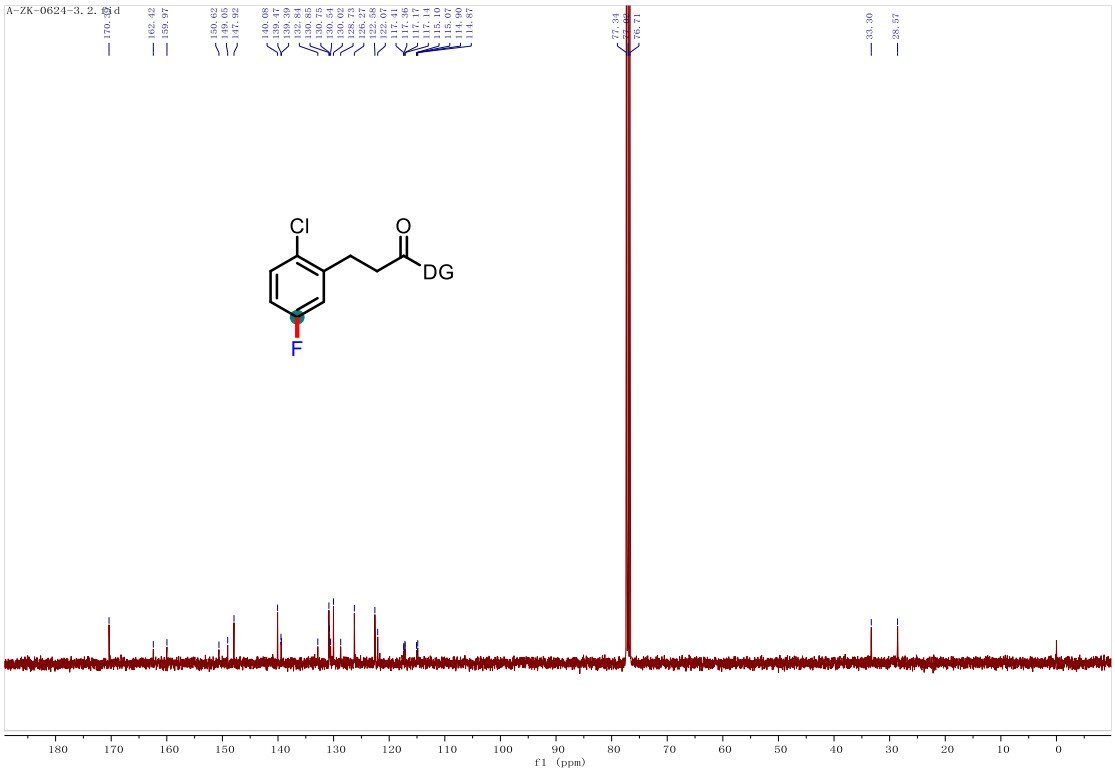
^{13}C NMR spectrum of 4b (101 MHz, $CDCl_3$)



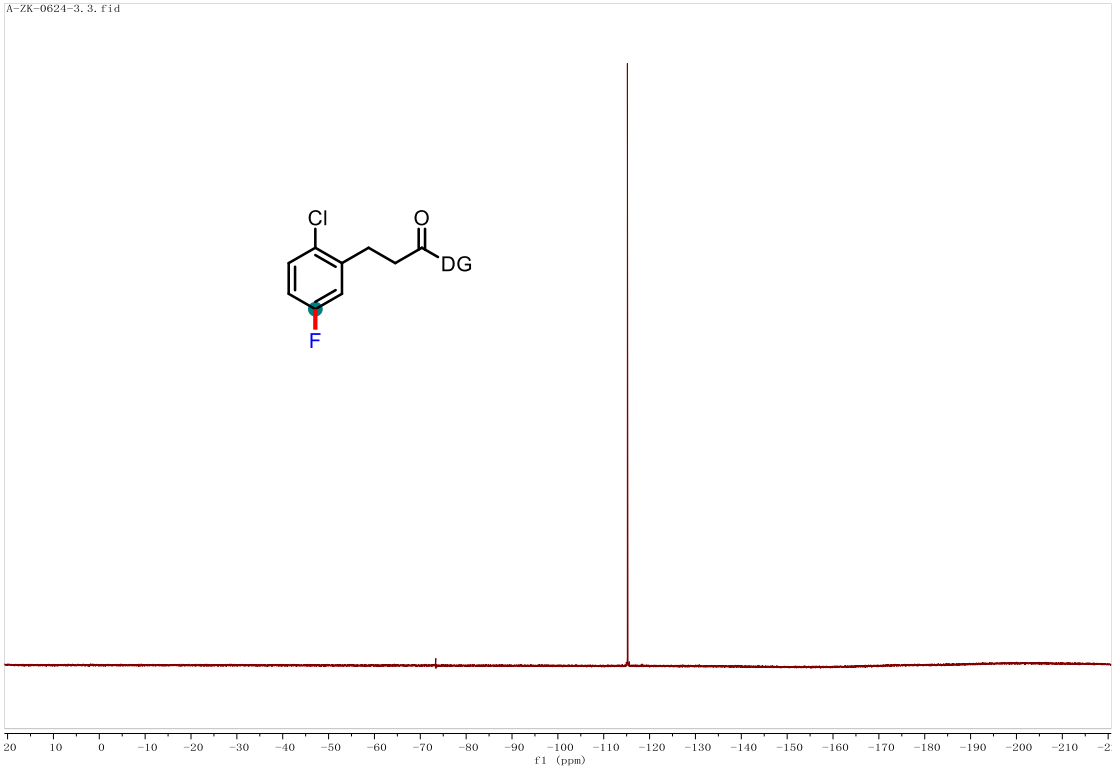
^{19}F NMR spectrum of 4b (376 MHz, $CDCl_3$)



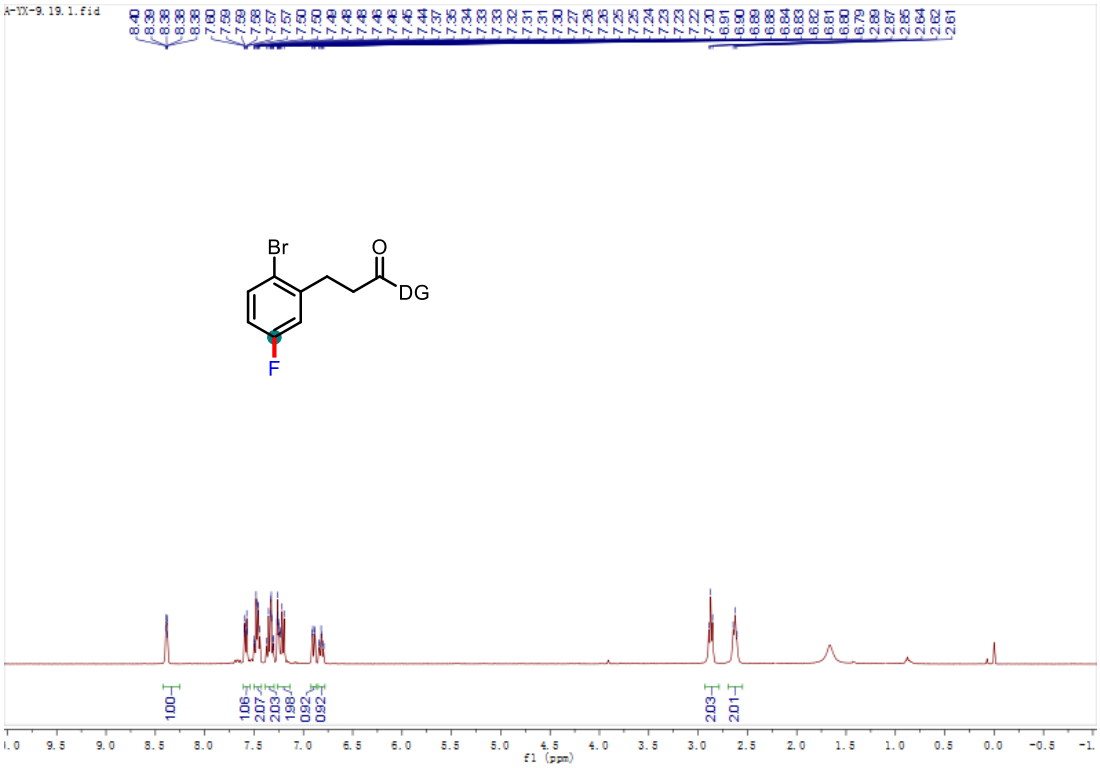
^{1}H NMR spectrum of 4c (400 MHz, $CDCl_3$)



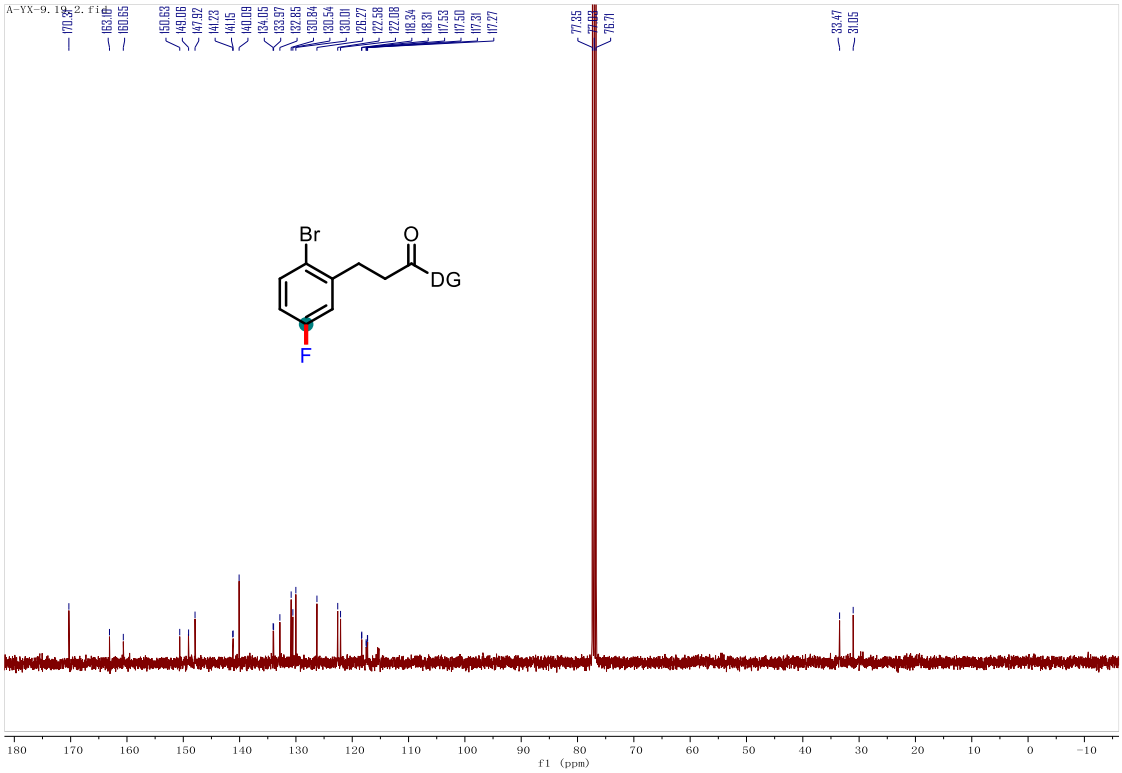
^{13}C NMR spectrum of 4c (101 MHz, $CDCl_3$)



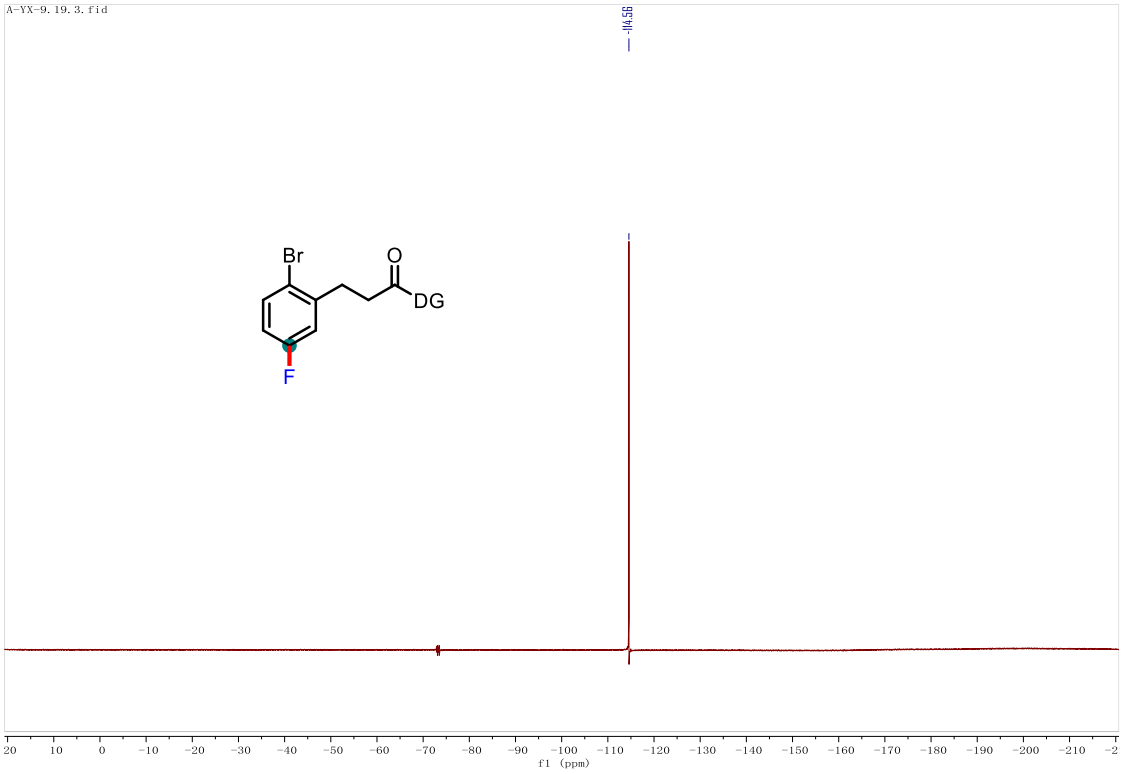
^{19}F NMR spectrum of 4c (376 MHz, $CDCl_3$)



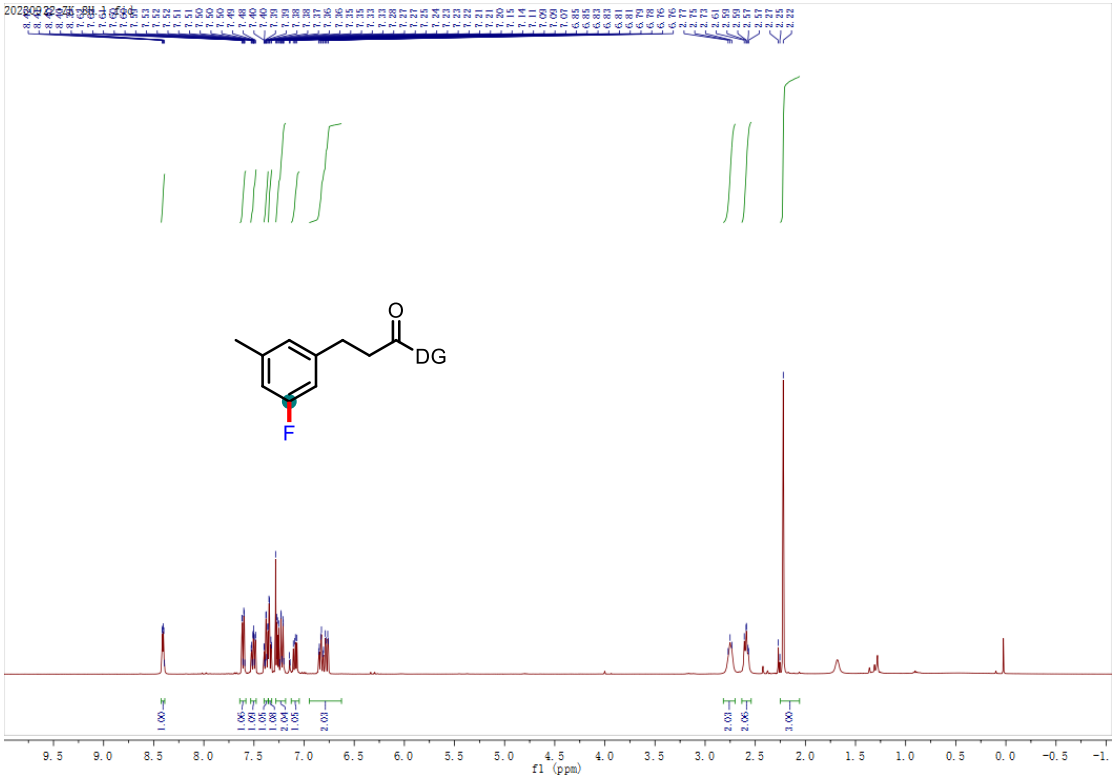
^{1}H NMR spectrum of 4d (400 MHz, $CDCl_3$)



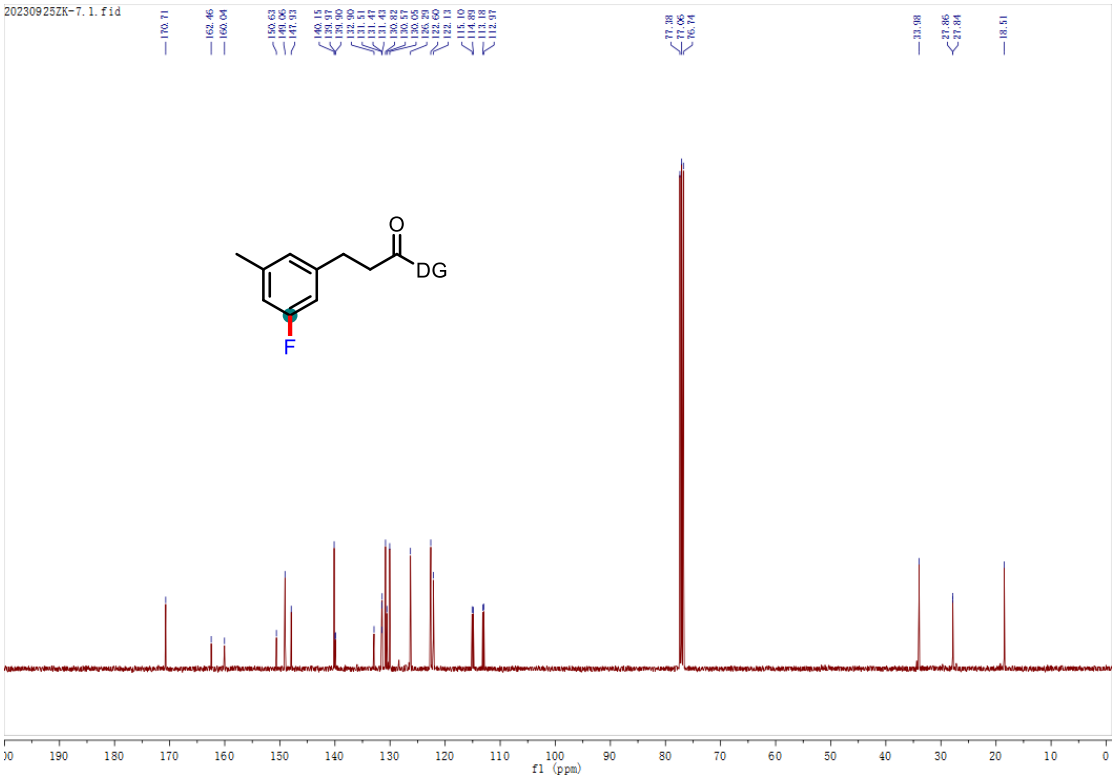
^{13}C NMR spectrum of 4d (101 MHz, $CDCl_3$)



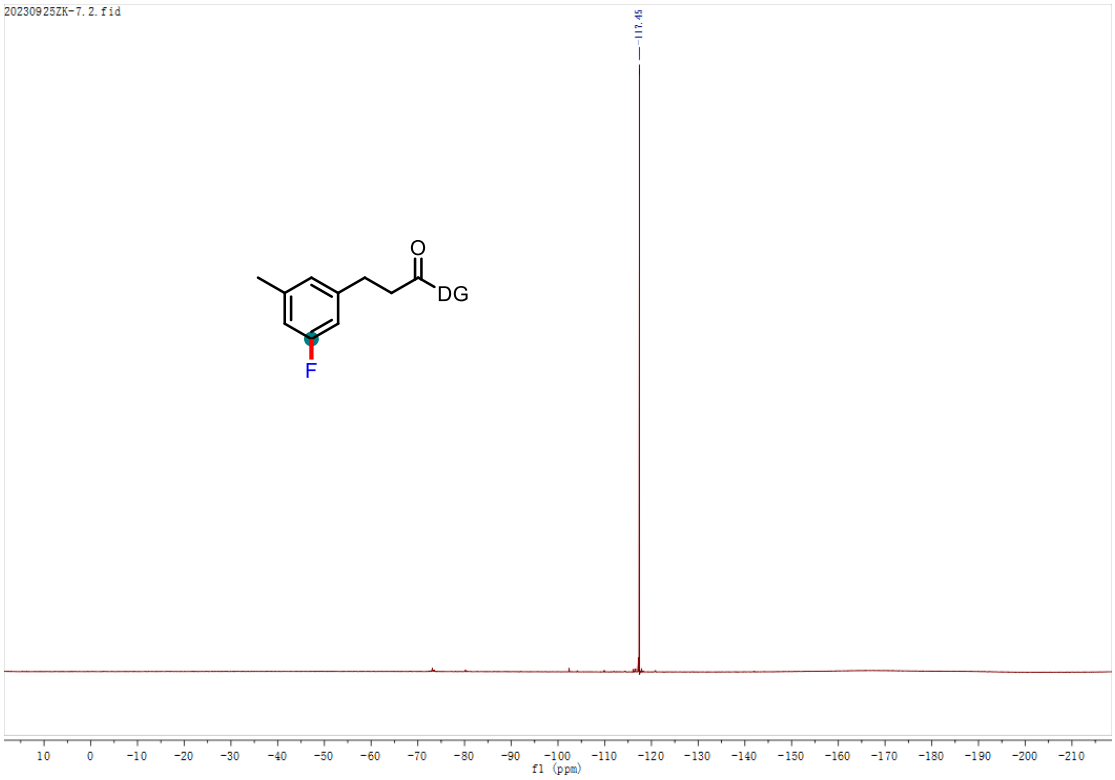
^{19}F NMR spectrum of 4d (376 MHz, $CDCl_3$)



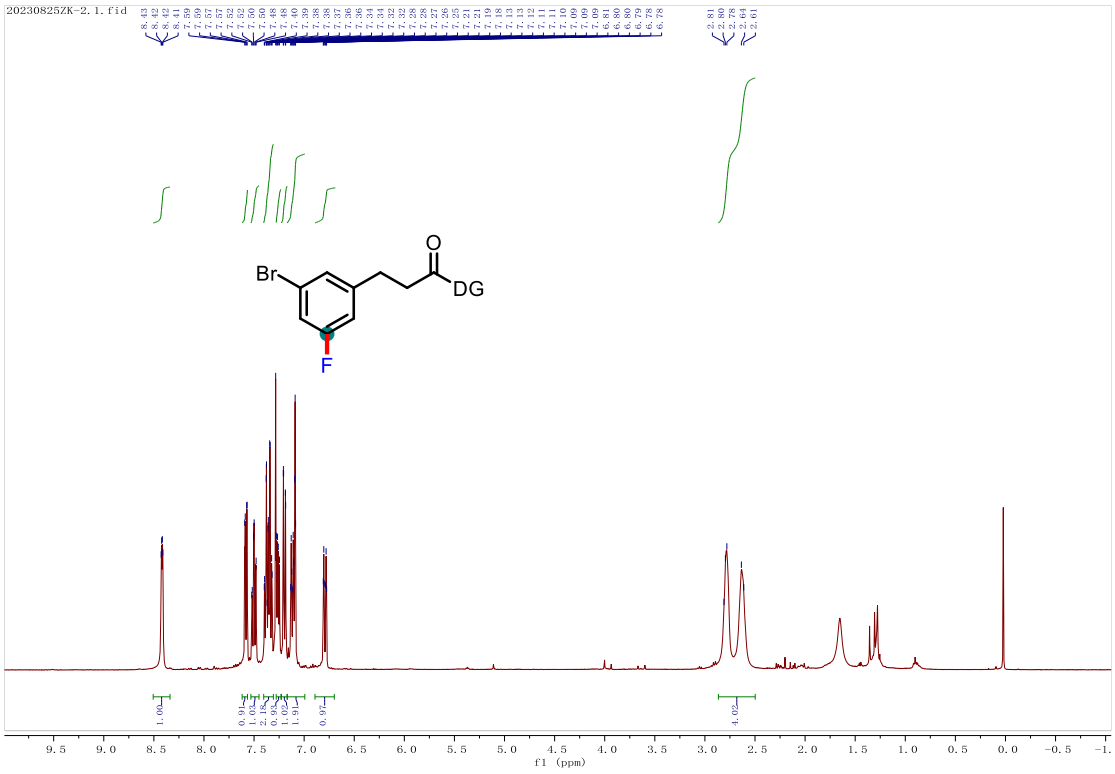
^{1}H NMR spectrum of 4e (400 MHz, $CDCl_3$)



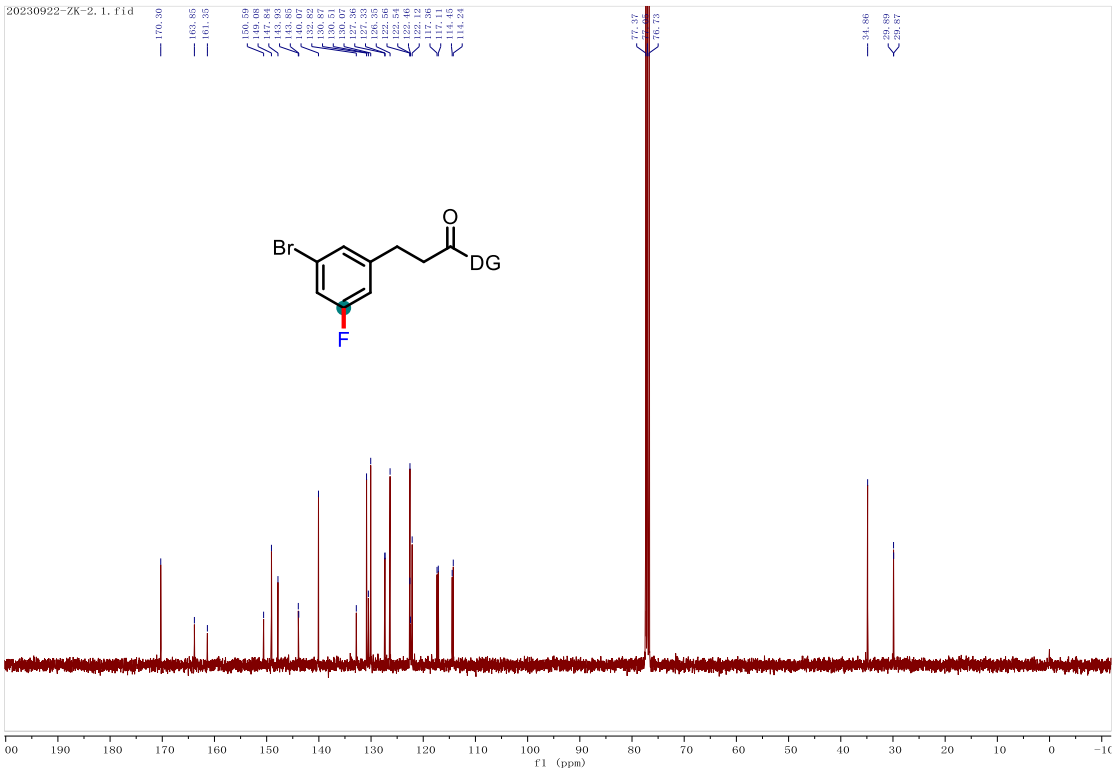
^{13}C NMR spectrum of 4e (101 MHz, $CDCl_3$)



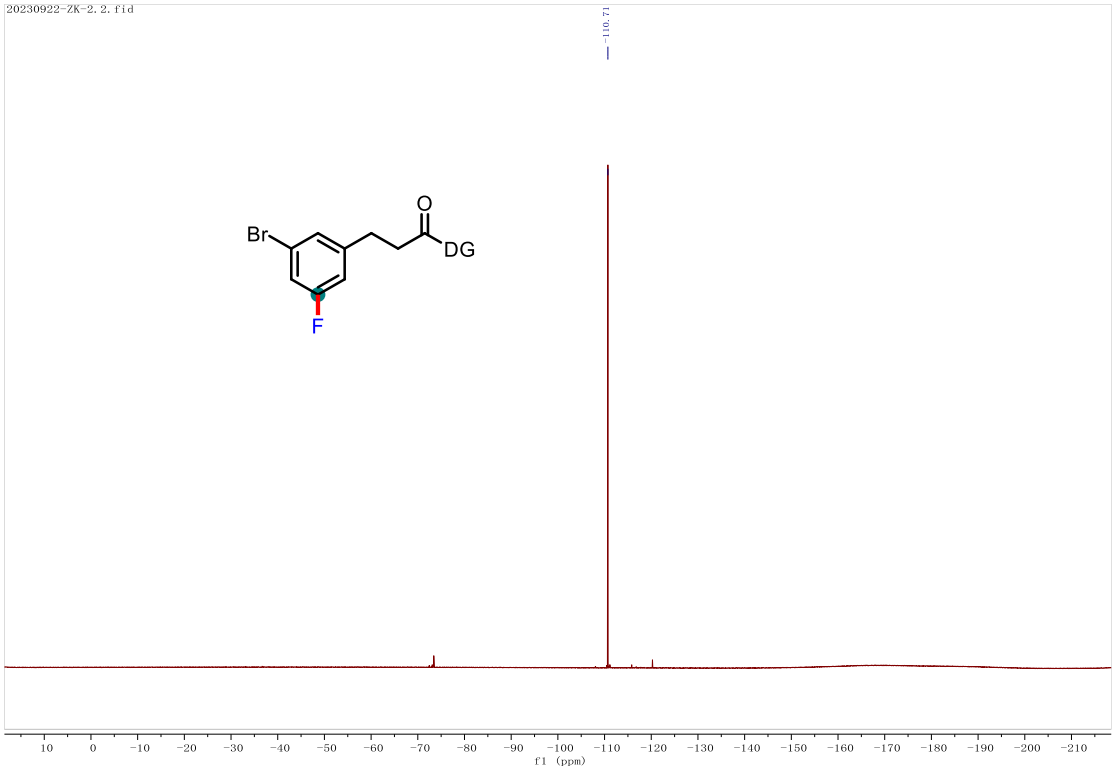
^{19}F NMR spectrum of 4e (376 MHz, $CDCl_3$)



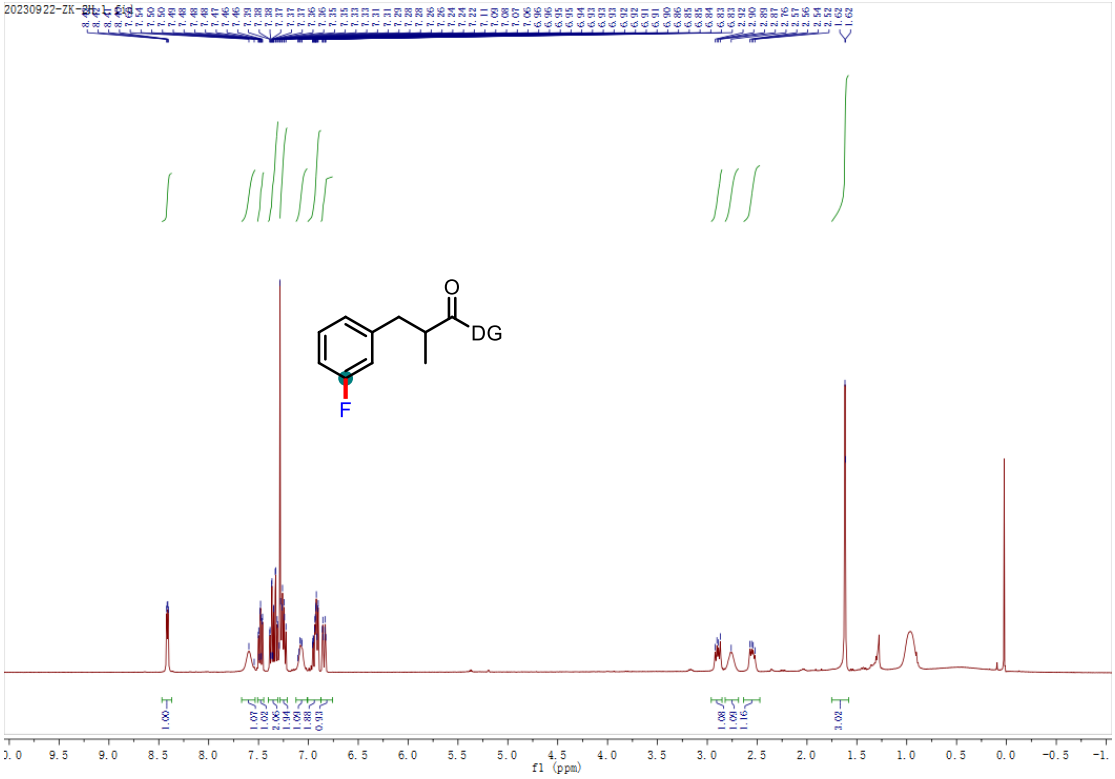
^{1}H NMR spectrum of 4f (400 MHz, $CDCl_3$)



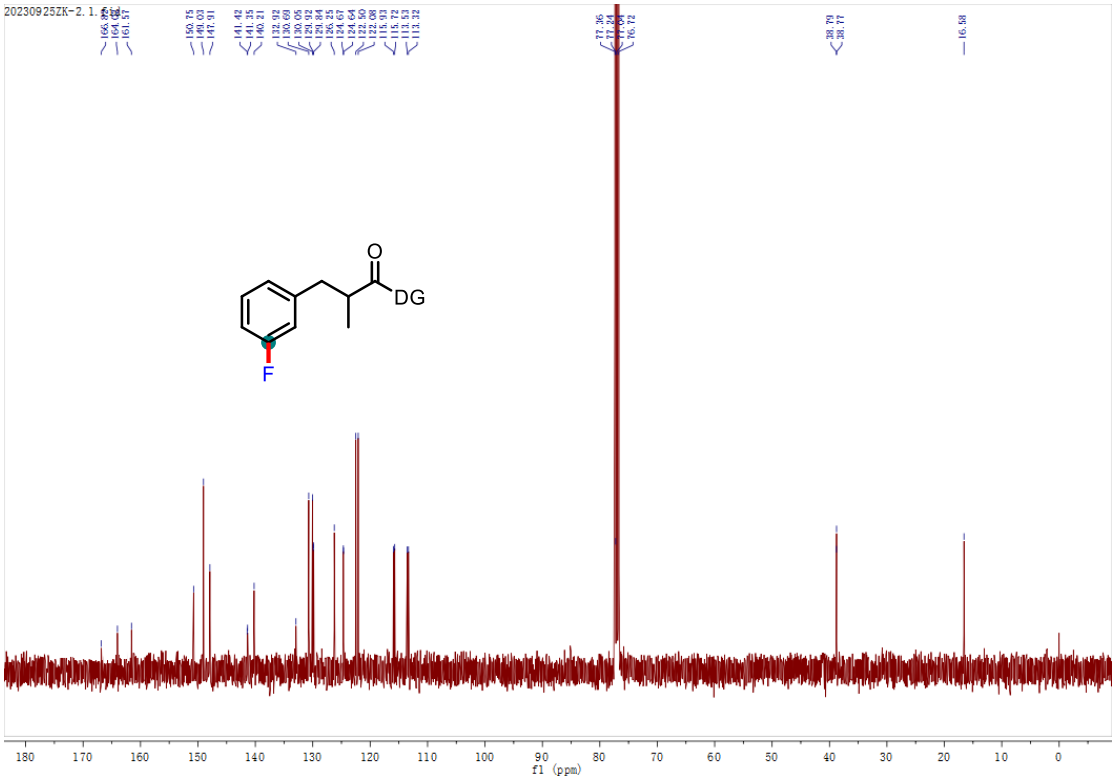
^{13}C NMR spectrum of 4f (101 MHz, $CDCl_3$)



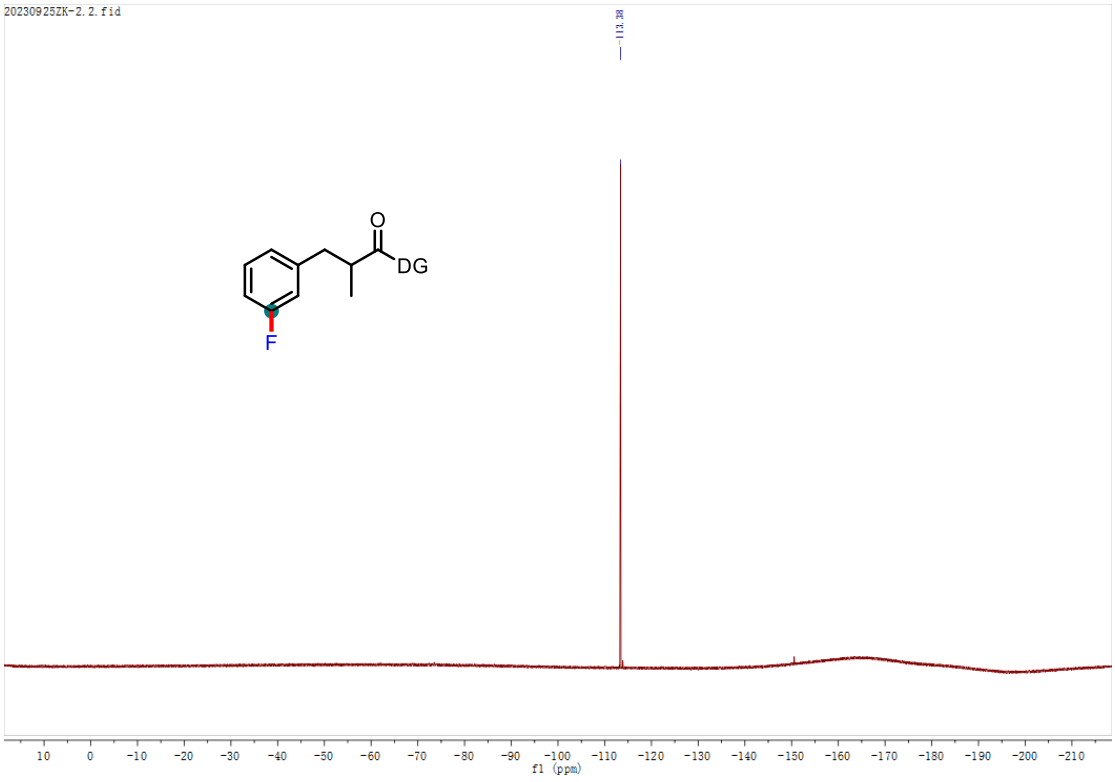
^{19}F NMR spectrum of 4f (376 MHz, $CDCl_3$)



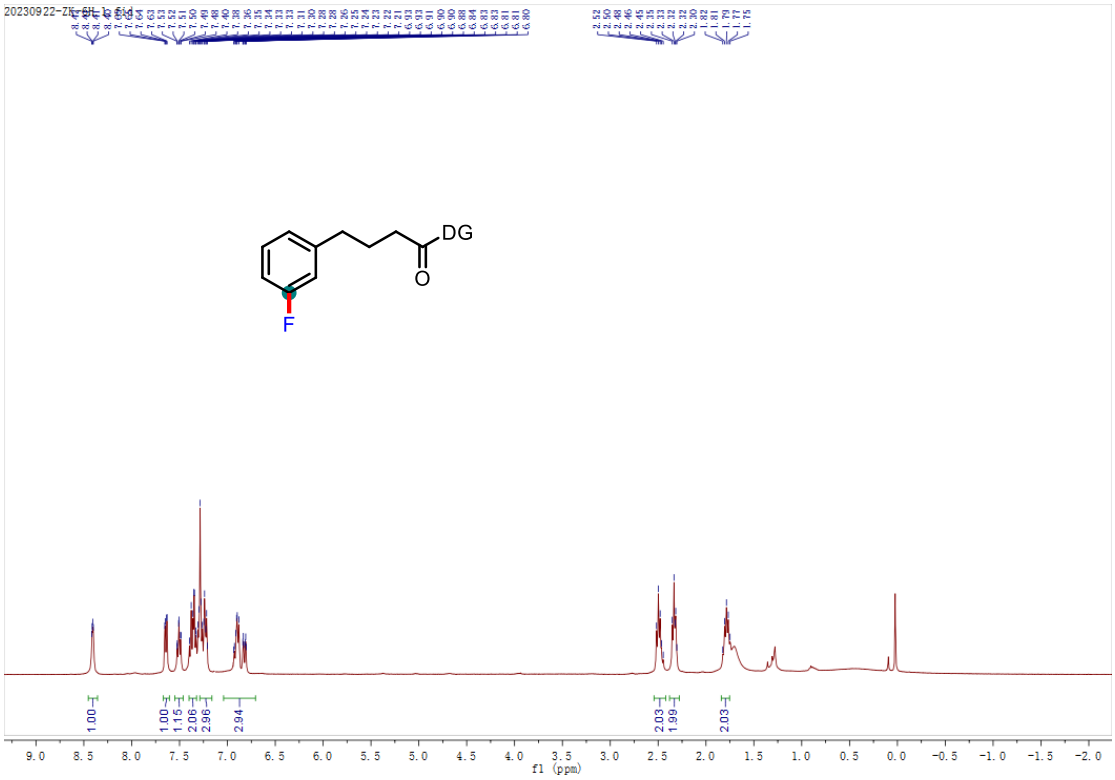
^{1}H NMR spectrum of 4g (400 MHz, $CDCl_3$)



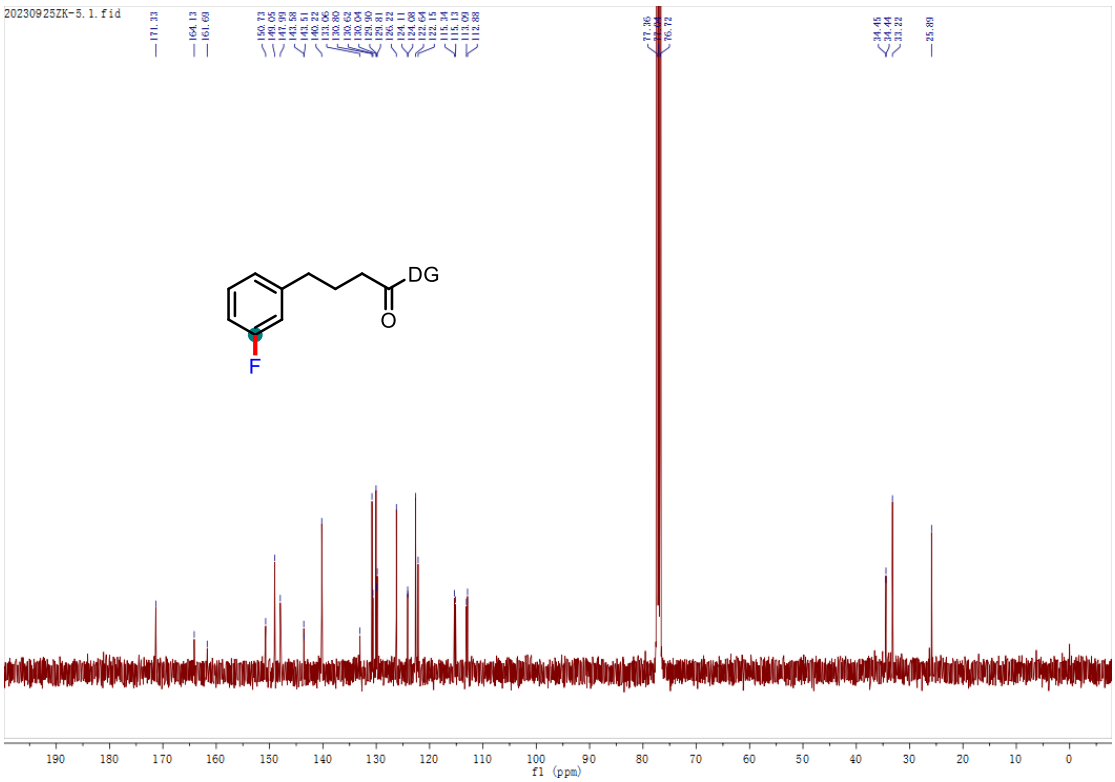
^{13}C NMR spectrum of 4g (101 MHz, $CDCl_3$)



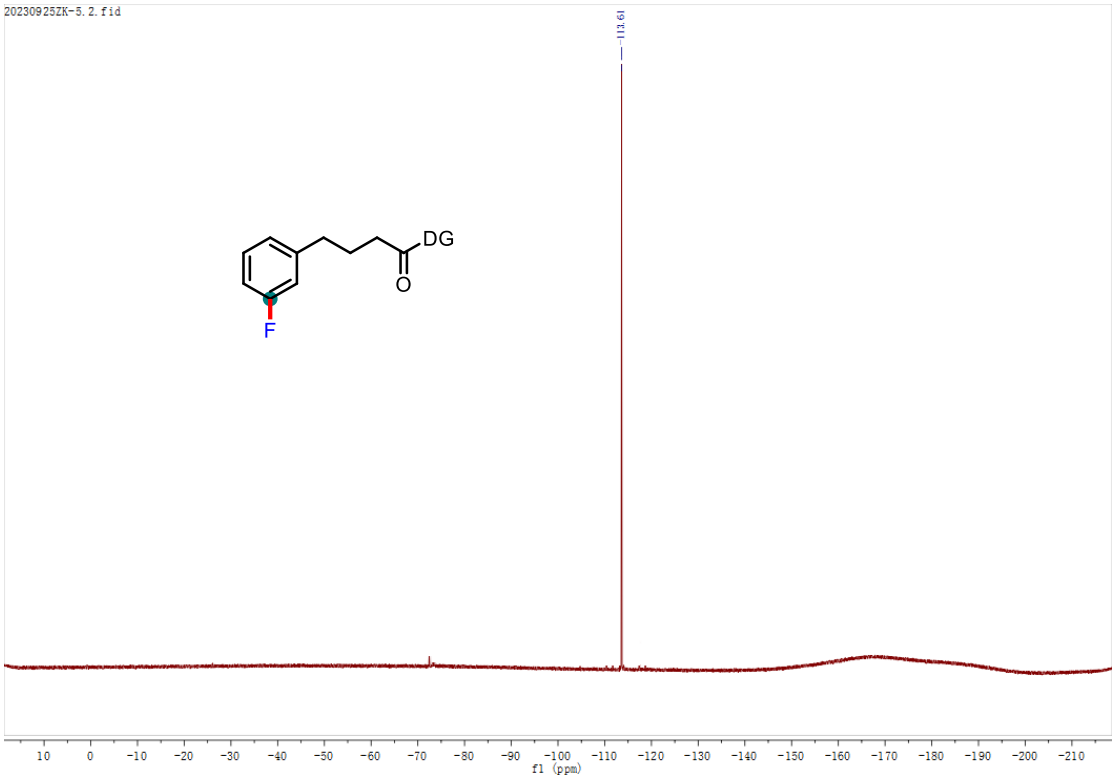
^{19}F NMR spectrum of 4g (376 MHz, $CDCl_3$)



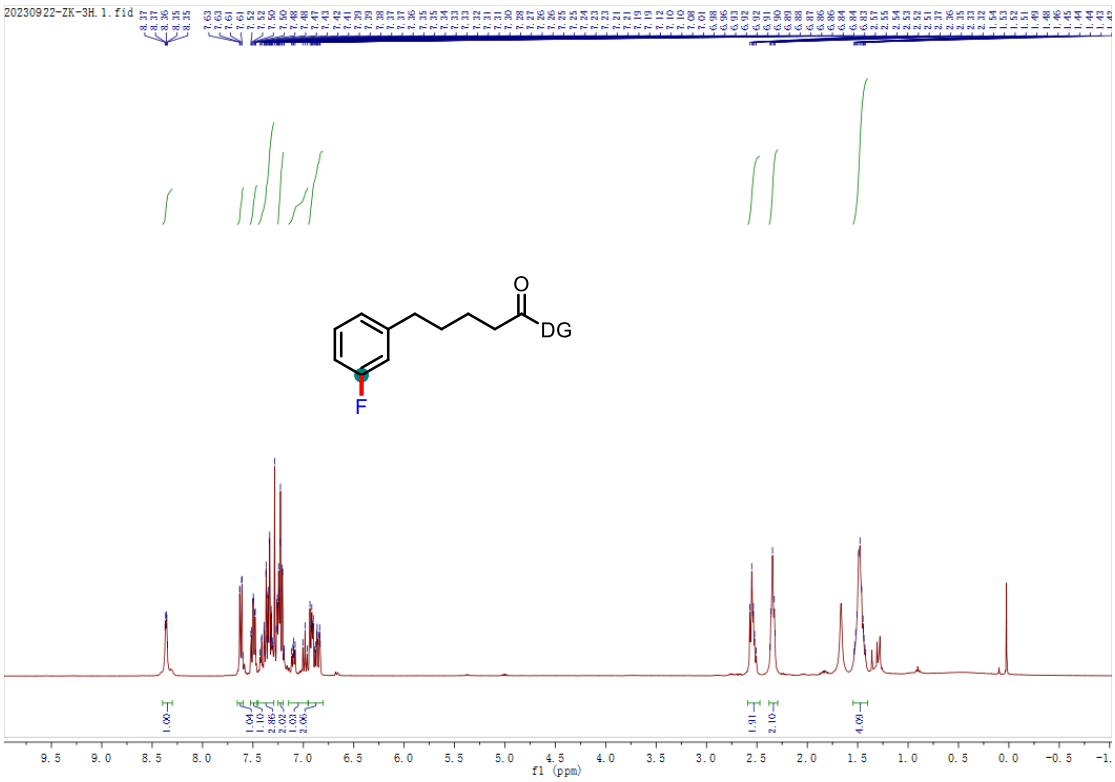
^{1}H NMR spectrum of 4h (400 MHz, $CDCl_3$)



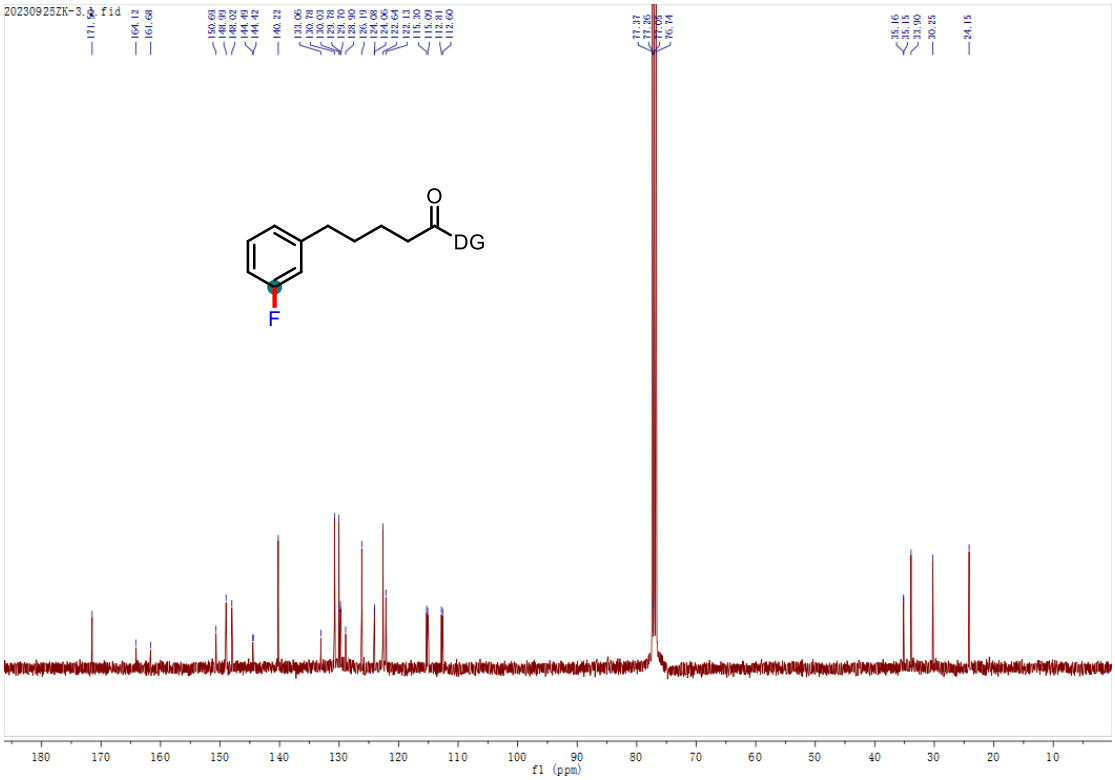
^{13}C NMR spectrum of 4h (101 MHz, $CDCl_3$)



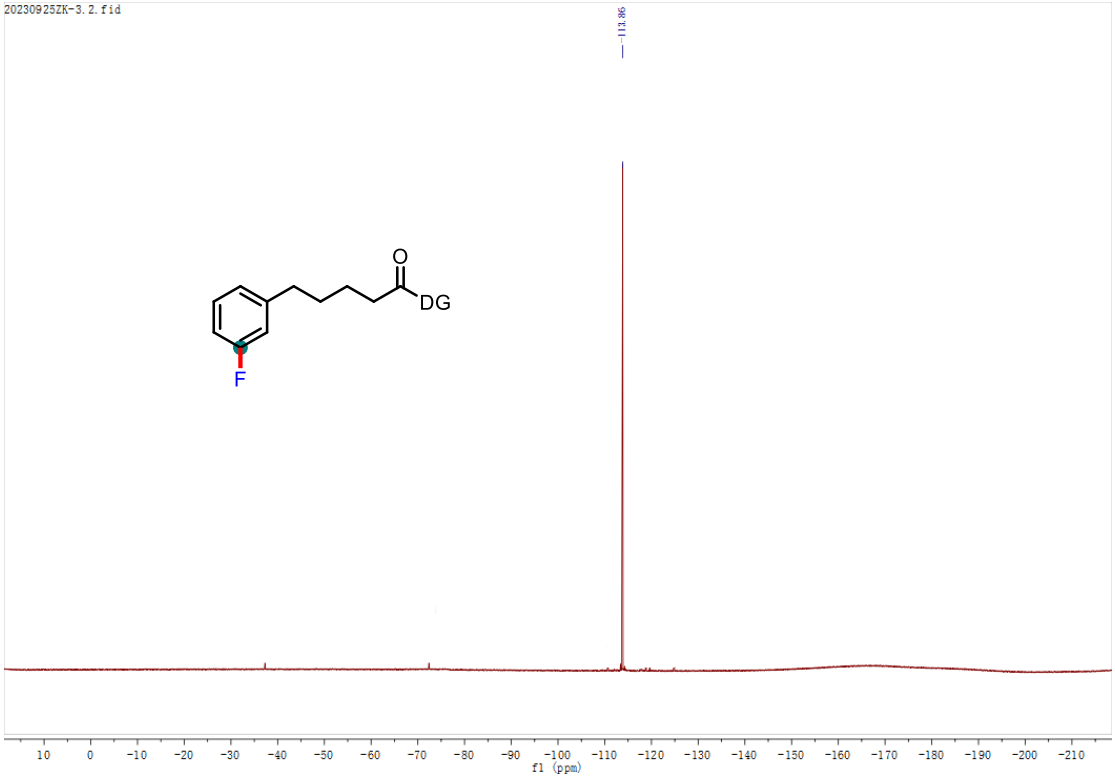
^{19}F NMR spectrum of 4h (376 MHz, $CDCl_3$)



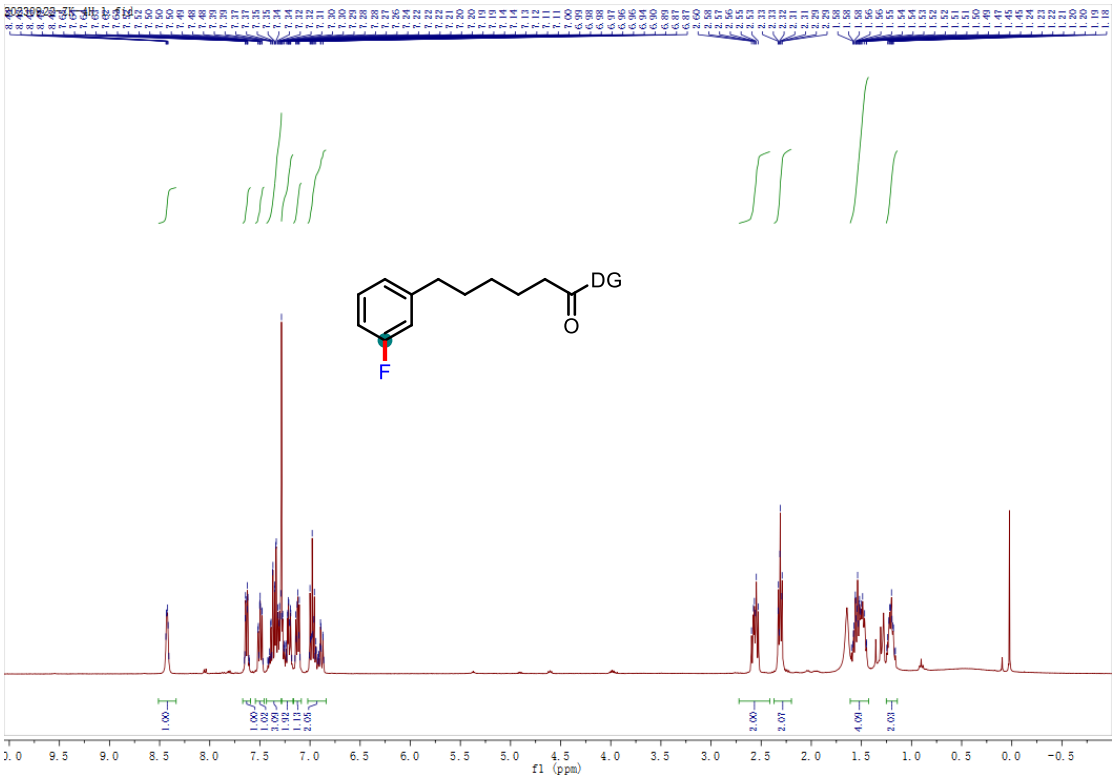
^{1}H NMR spectrum of 4i (400 MHz, $CDCl_3$)



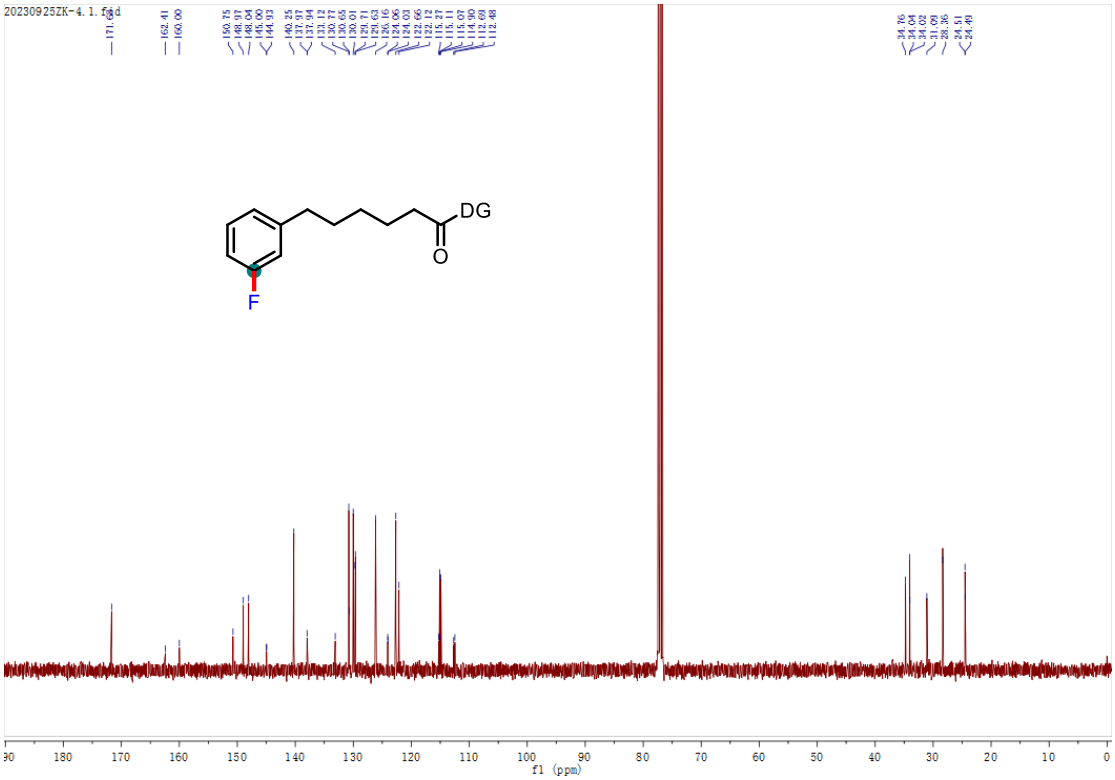
^{13}C NMR spectrum of 4i (101 MHz, $CDCl_3$)



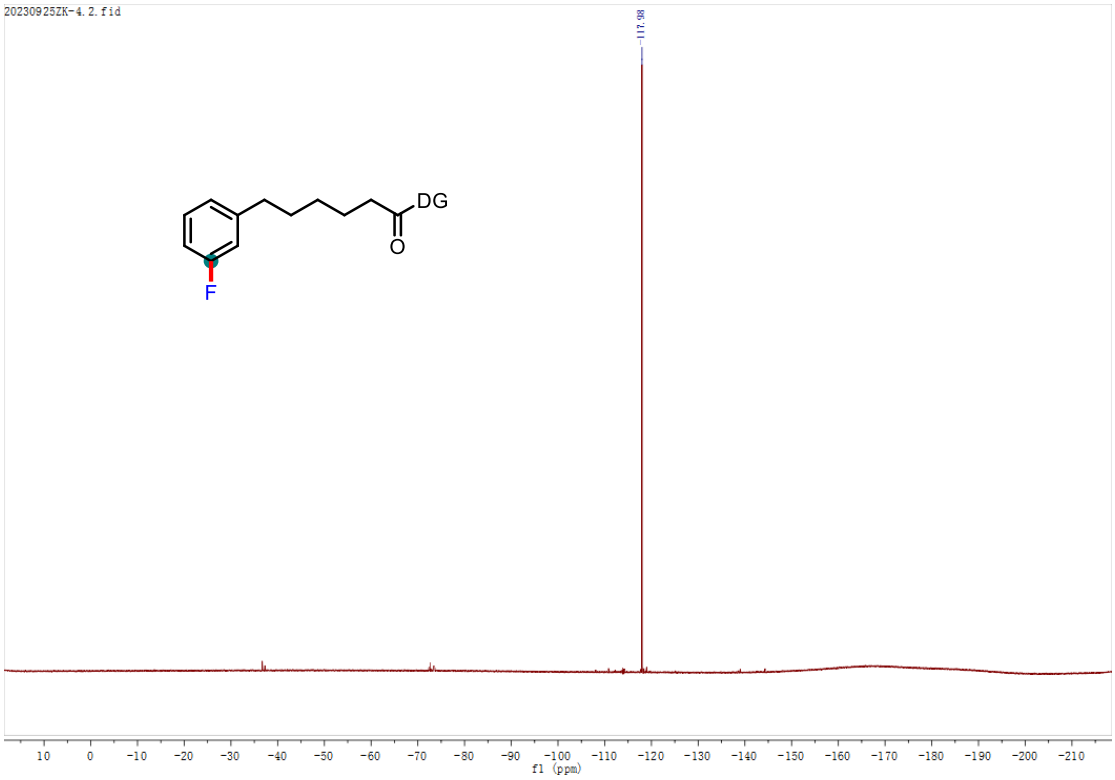
^{19}F NMR spectrum of 4i (376 MHz, $CDCl_3$)



^{1}H NMR spectrum of 4j (400 MHz, $CDCl_3$)

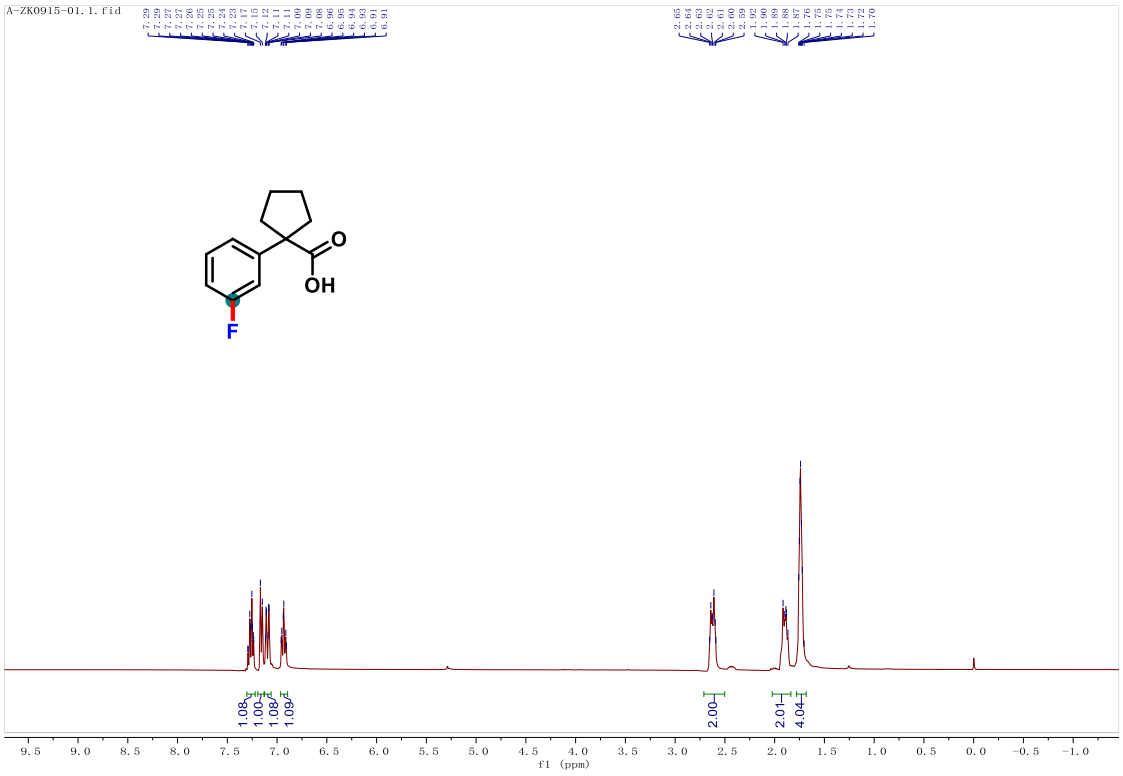


^{13}C NMR spectrum of 4j (101 MHz, $CDCl_3$)

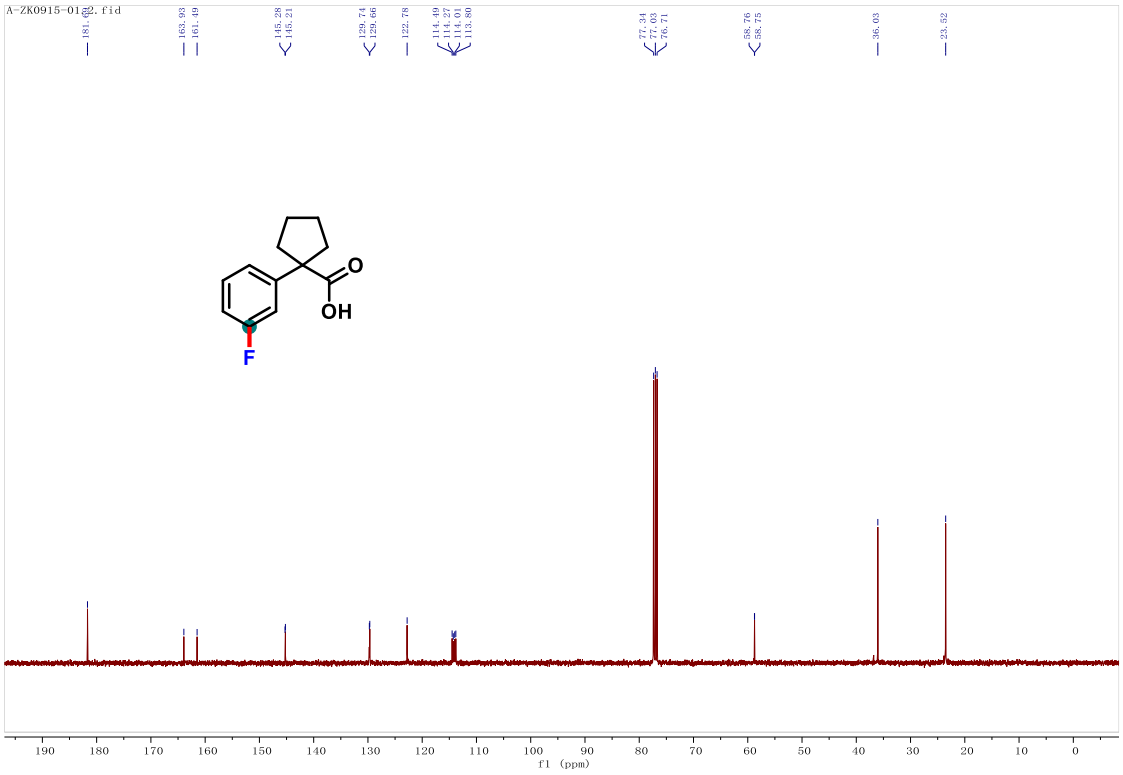


^{19}F NMR spectrum of 4j (376 MHz, $CDCl_3$)

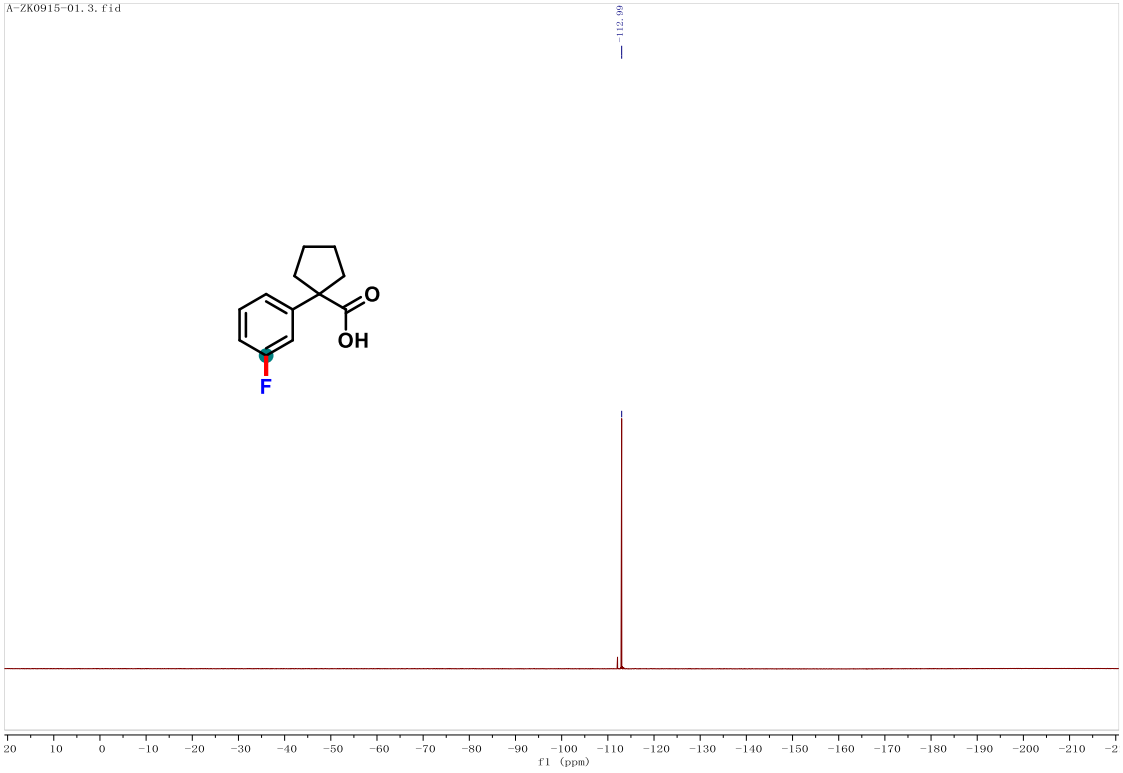
10.3 NMR spectra of transformations



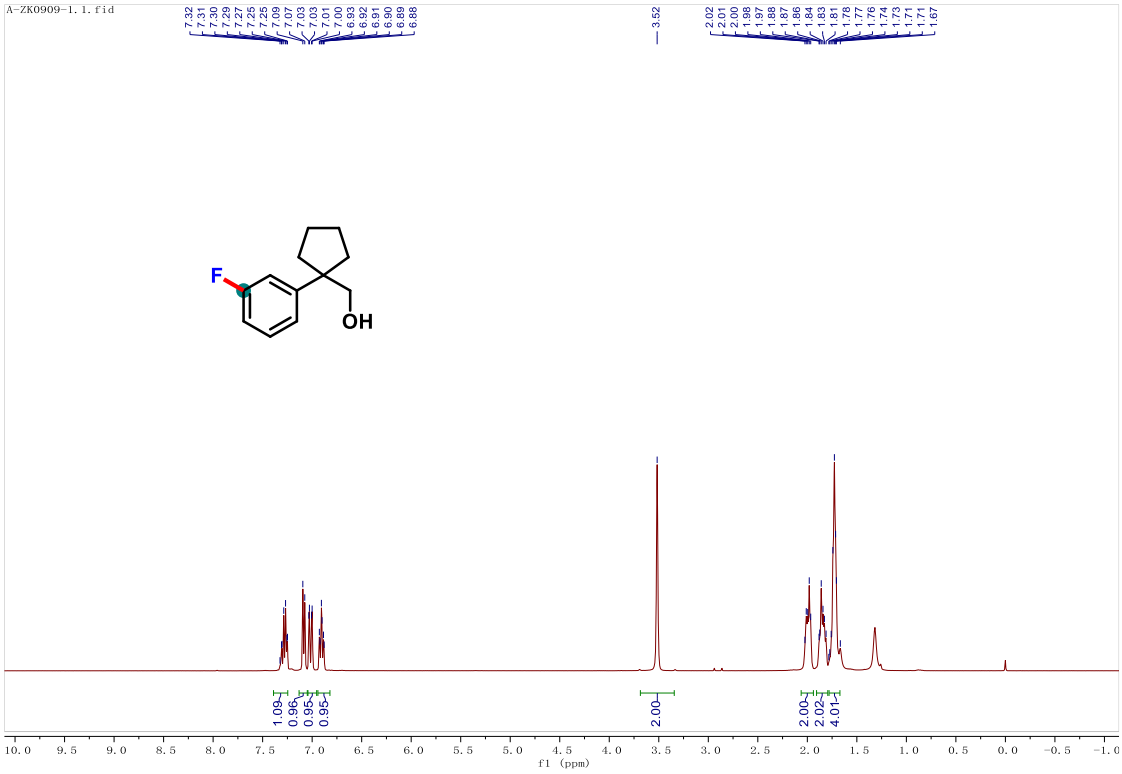
^{1}H NMR spectrum of 5a (400 MHz, $CDCl_3$)



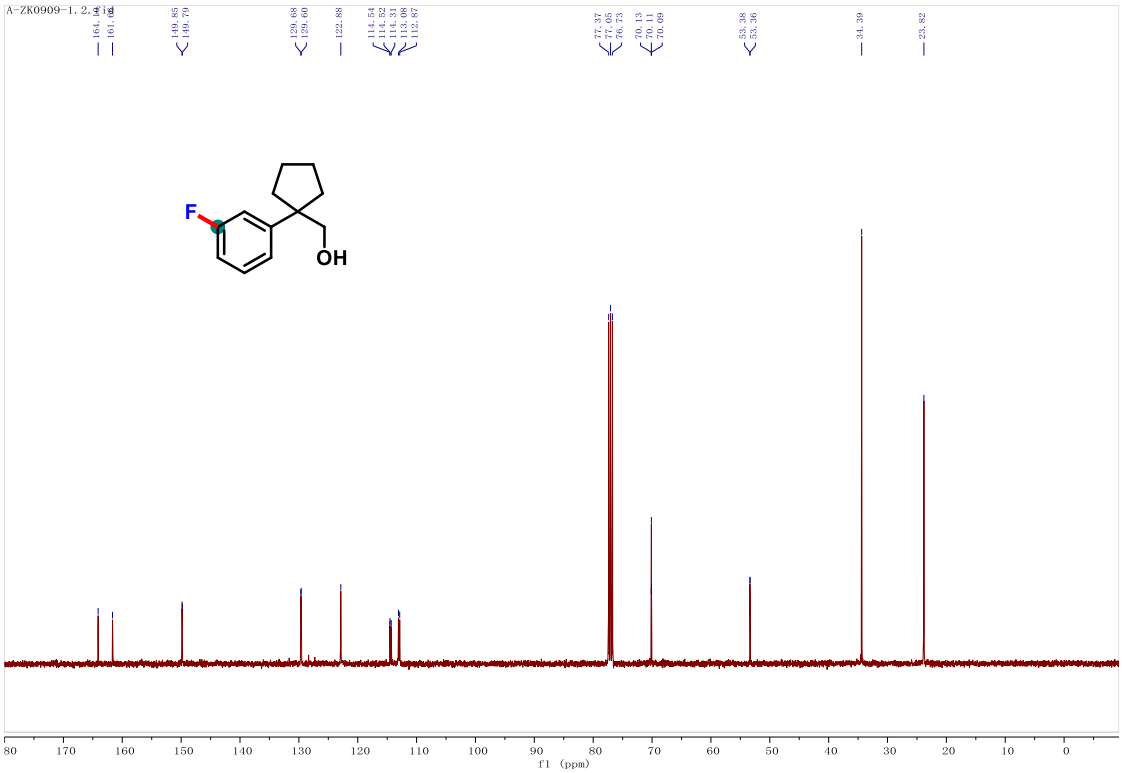
^{13}C NMR spectrum of 5a (101 MHz, $CDCl_3$)



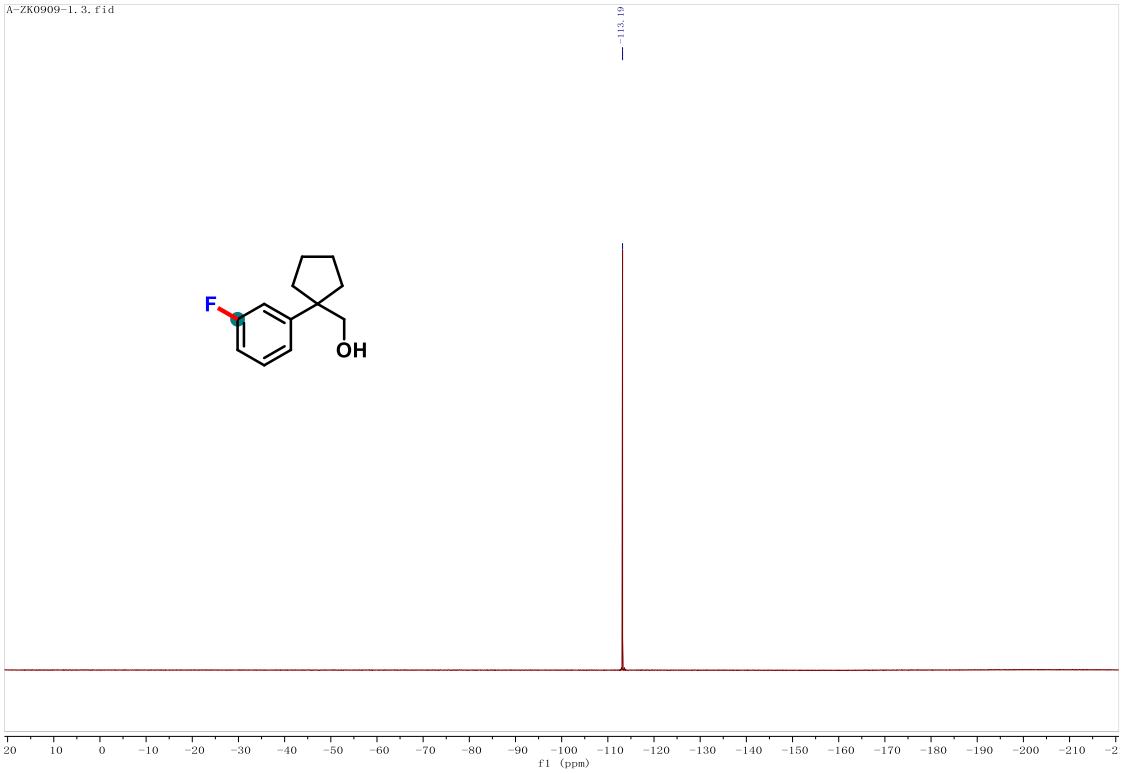
^{19}F NMR spectrum of 5a (376 MHz, $CDCl_3$)



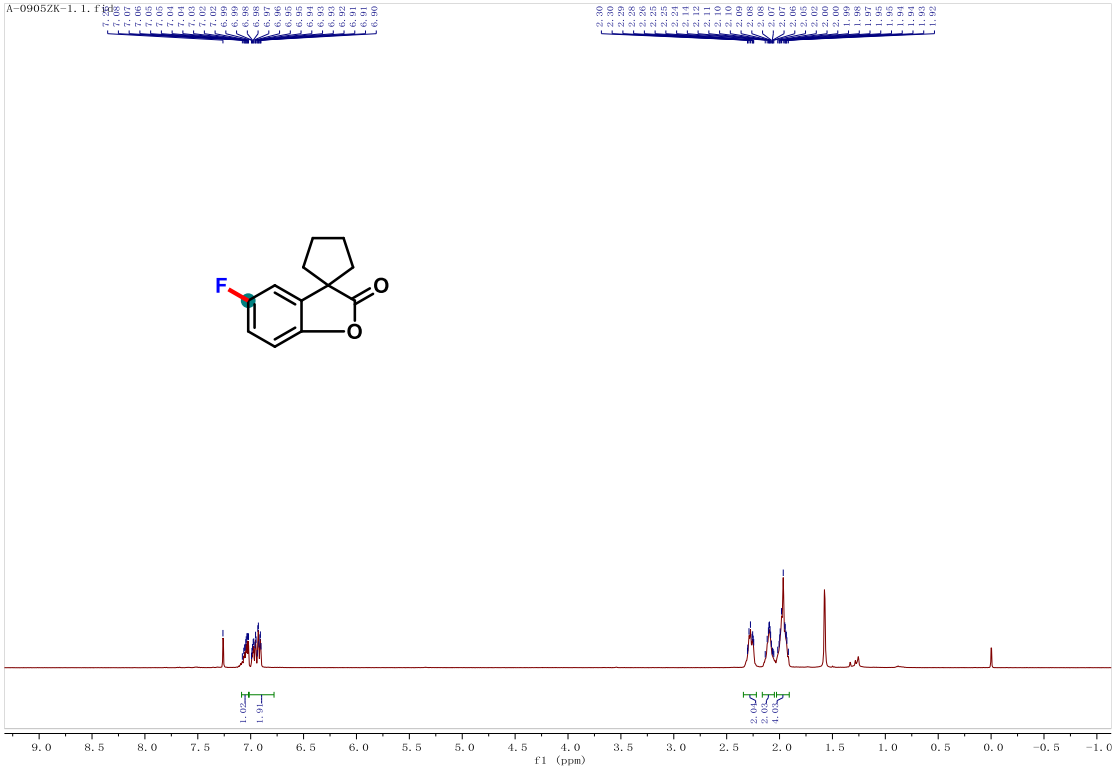
^{1}H NMR spectrum of 5b (400 MHz, $CDCl_3$)



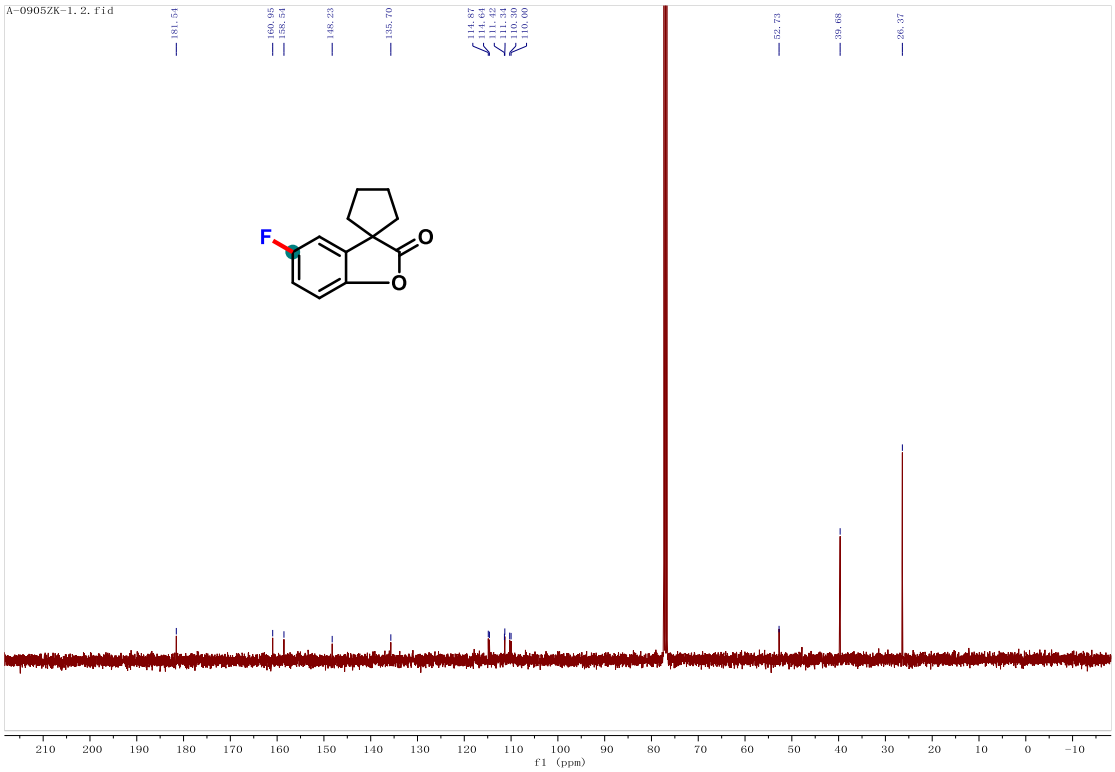
^{13}C NMR spectrum of 5b (101 MHz, $CDCl_3$)



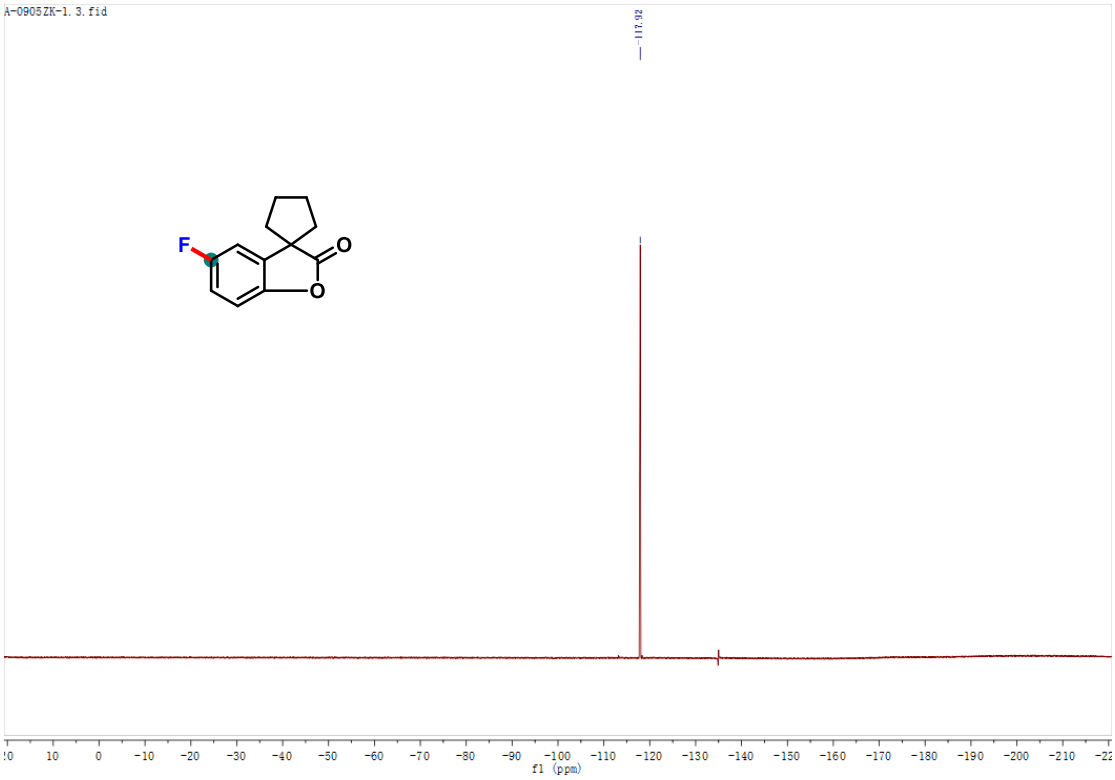
^{19}F NMR spectrum of 5b (376 MHz, $CDCl_3$)



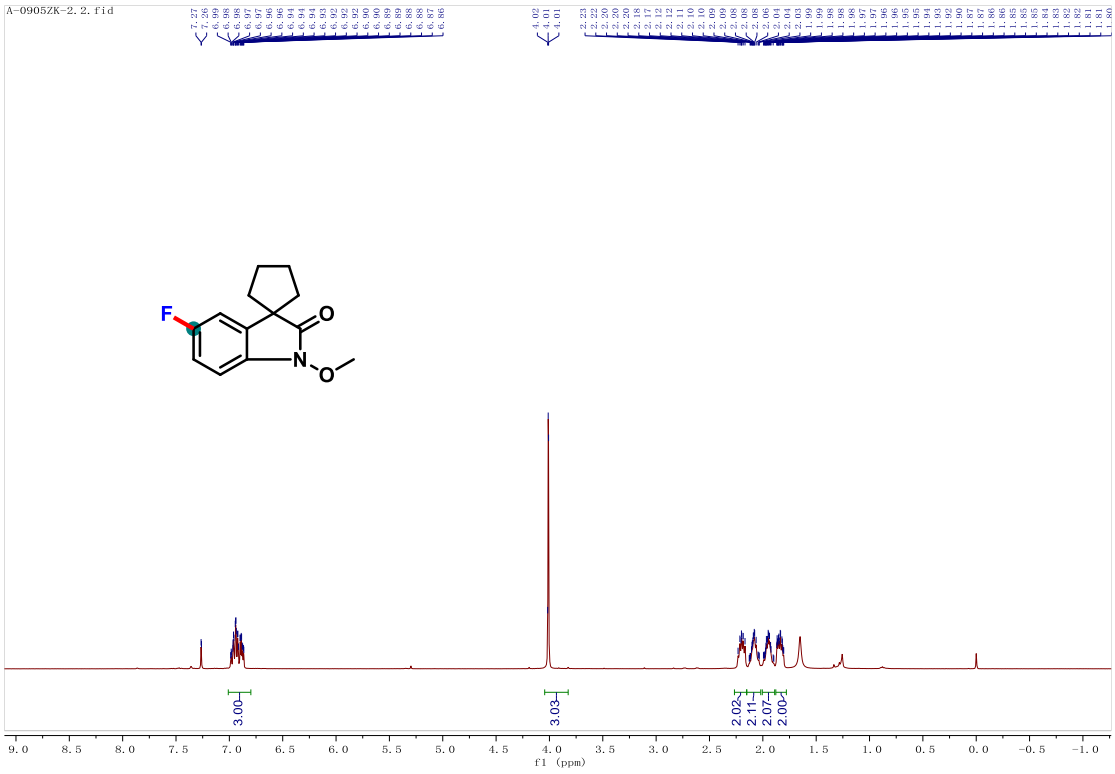
^{1}H NMR spectrum of 5c (400 MHz, $CDCl_3$)



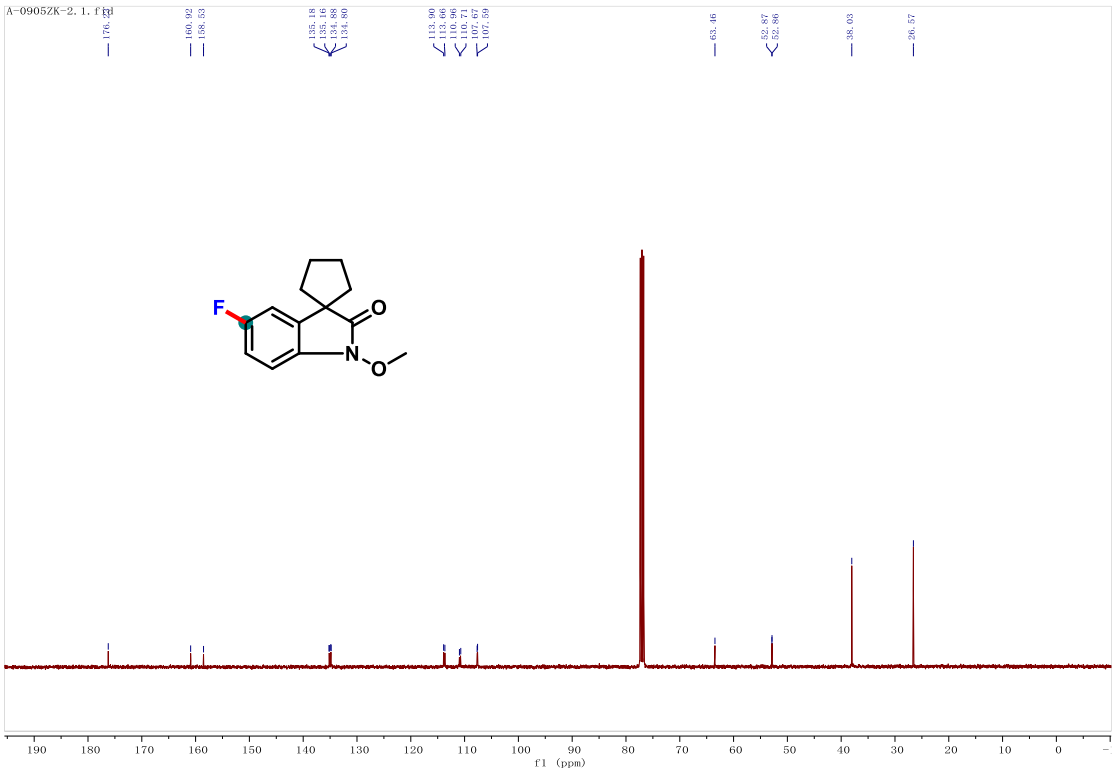
^{13}C NMR spectrum of 5c (101 MHz, $CDCl_3$)



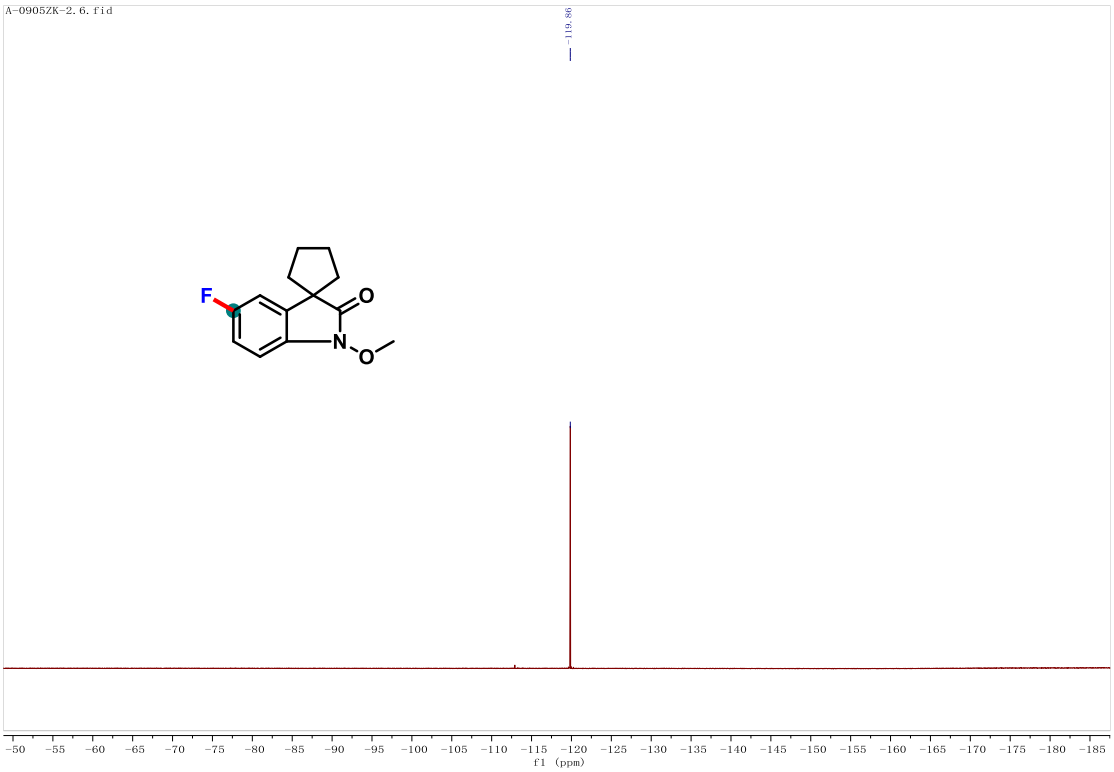
^{19}F NMR spectrum of 5c (376 MHz, $CDCl_3$)



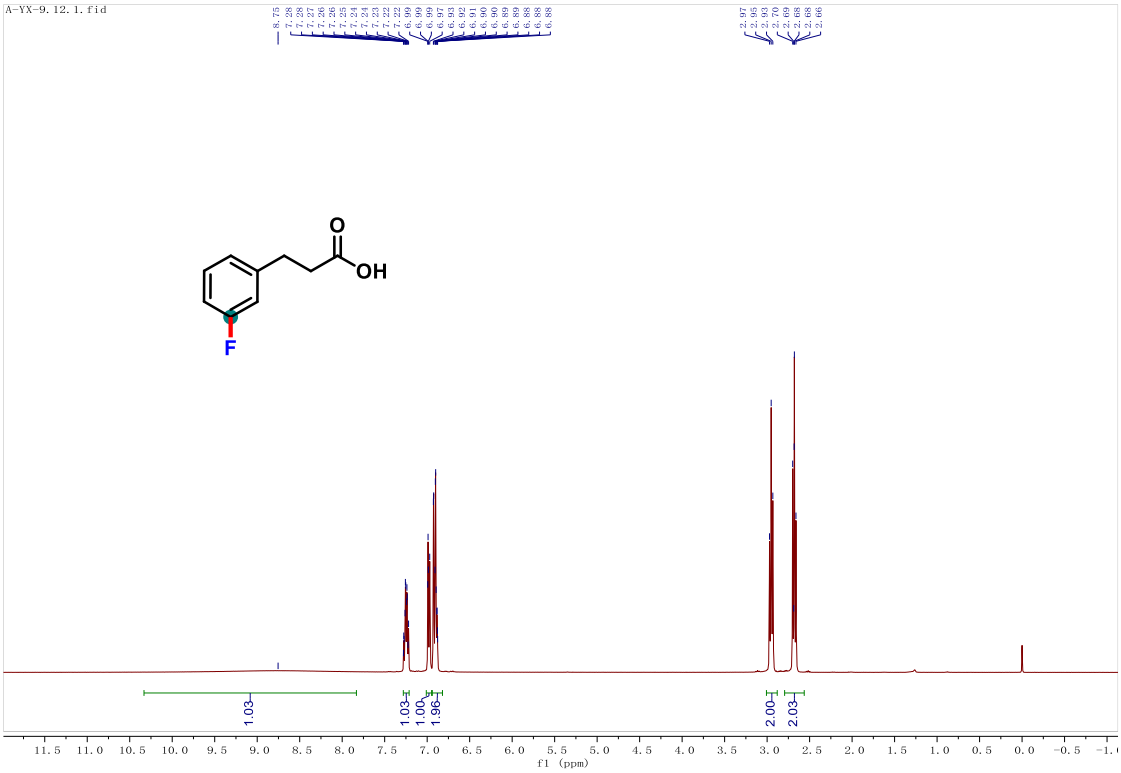
^{1}H NMR spectrum of 5d (400 MHz, $CDCl_3$)



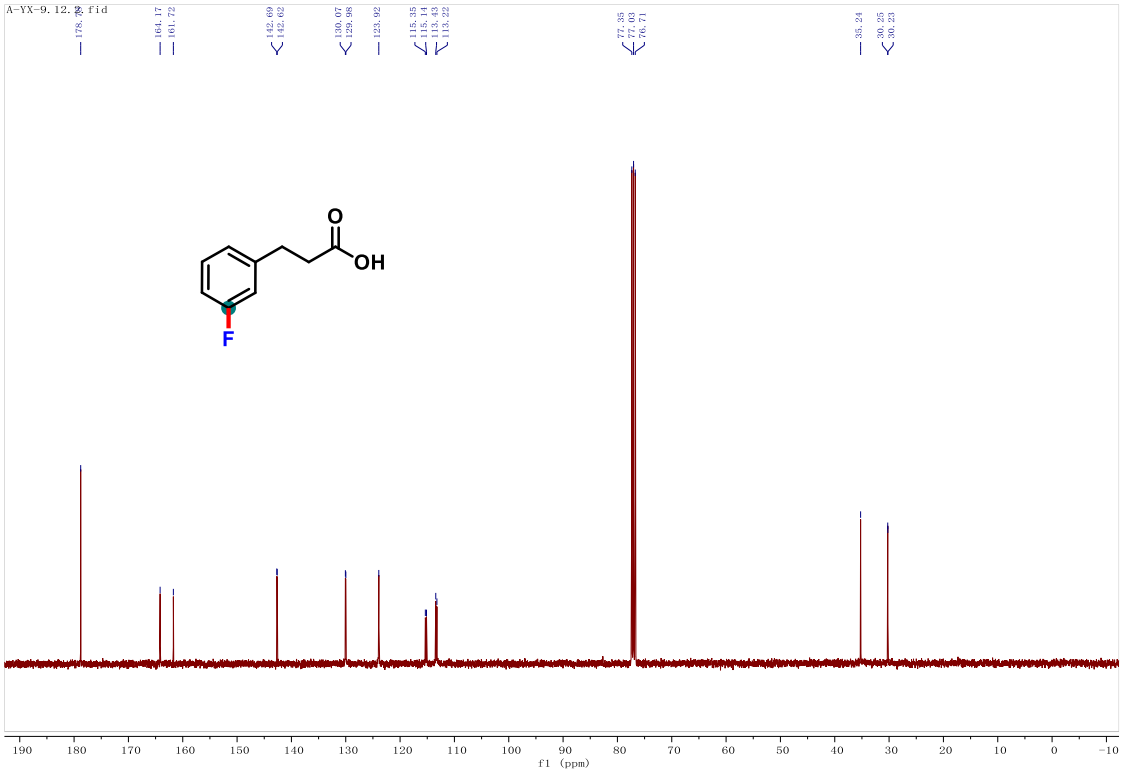
^{13}C NMR spectrum of 5d (101 MHz, $CDCl_3$)



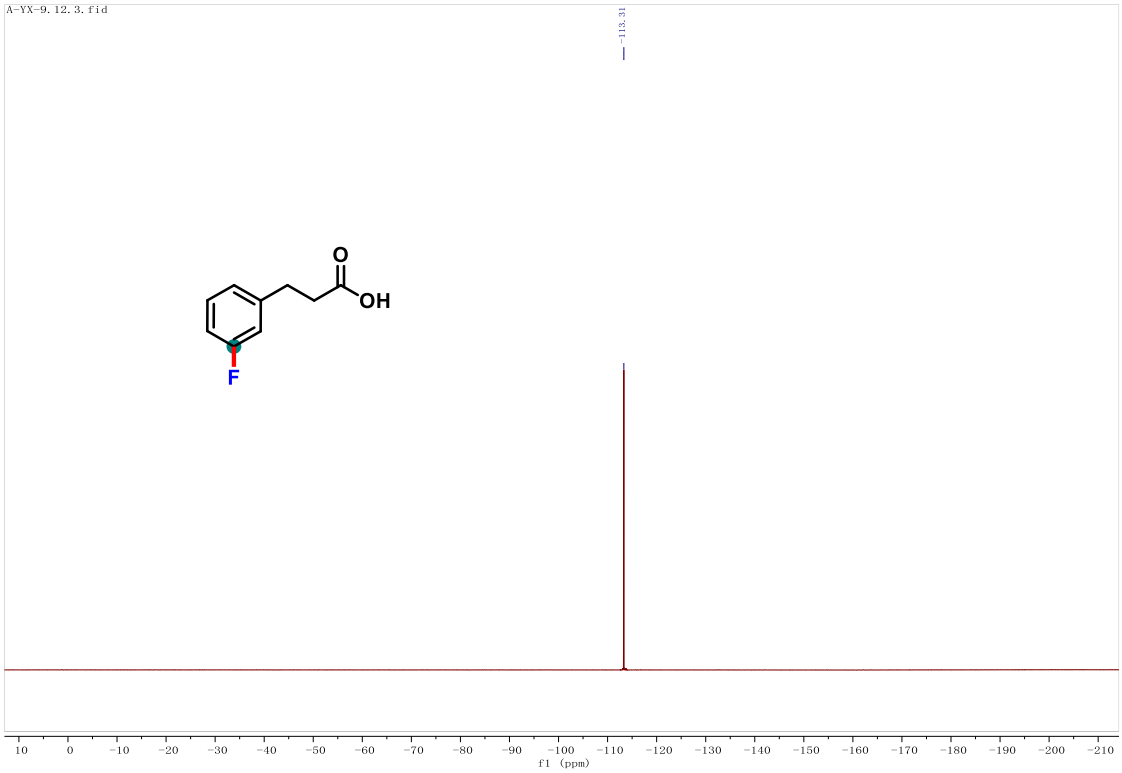
^{19}F NMR spectrum of 5d (376 MHz, $CDCl_3$)



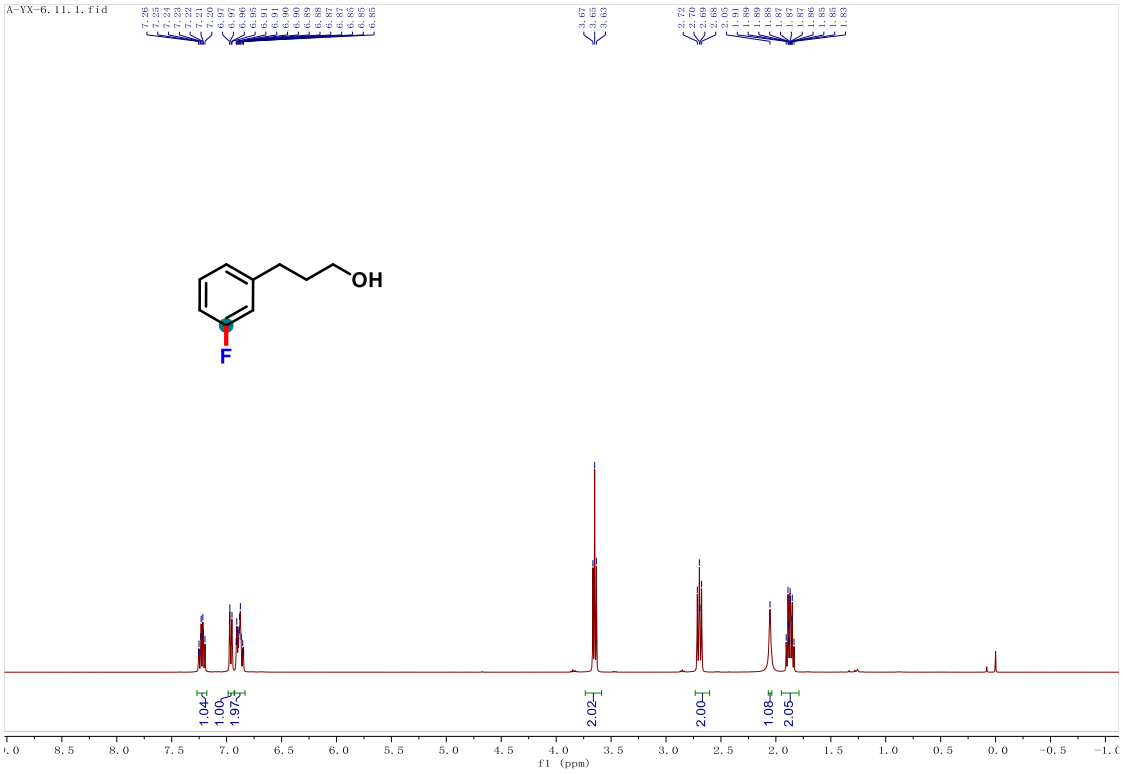
^{1}H NMR spectrum of 5e (400 MHz, $CDCl_3$)



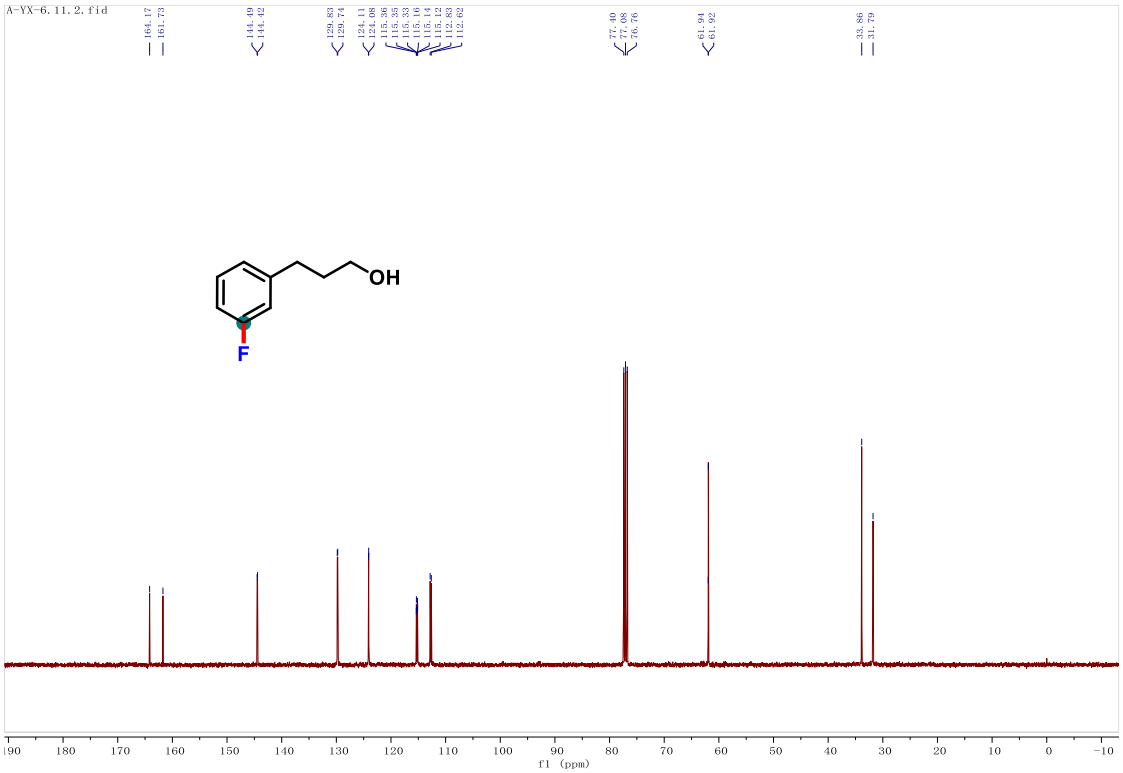
^{13}C NMR spectrum of 5e (101 MHz, $CDCl_3$)



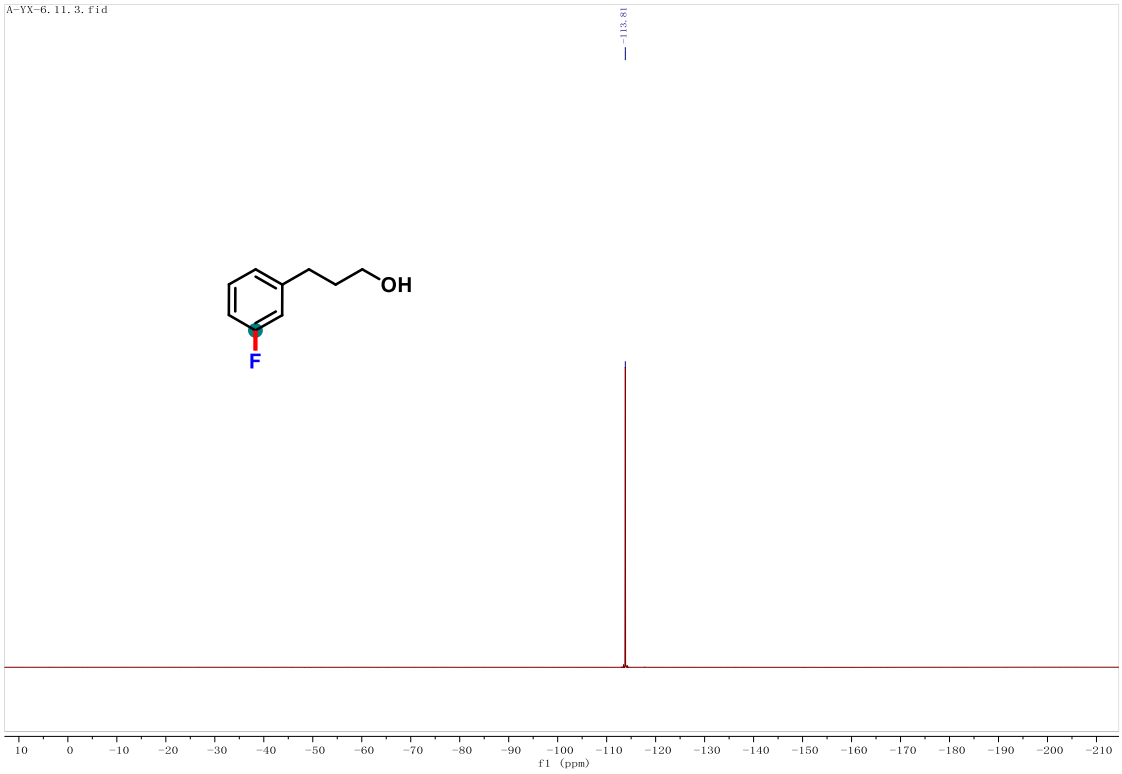
^{19}F NMR spectrum of 5e (376 MHz, $CDCl_3$)



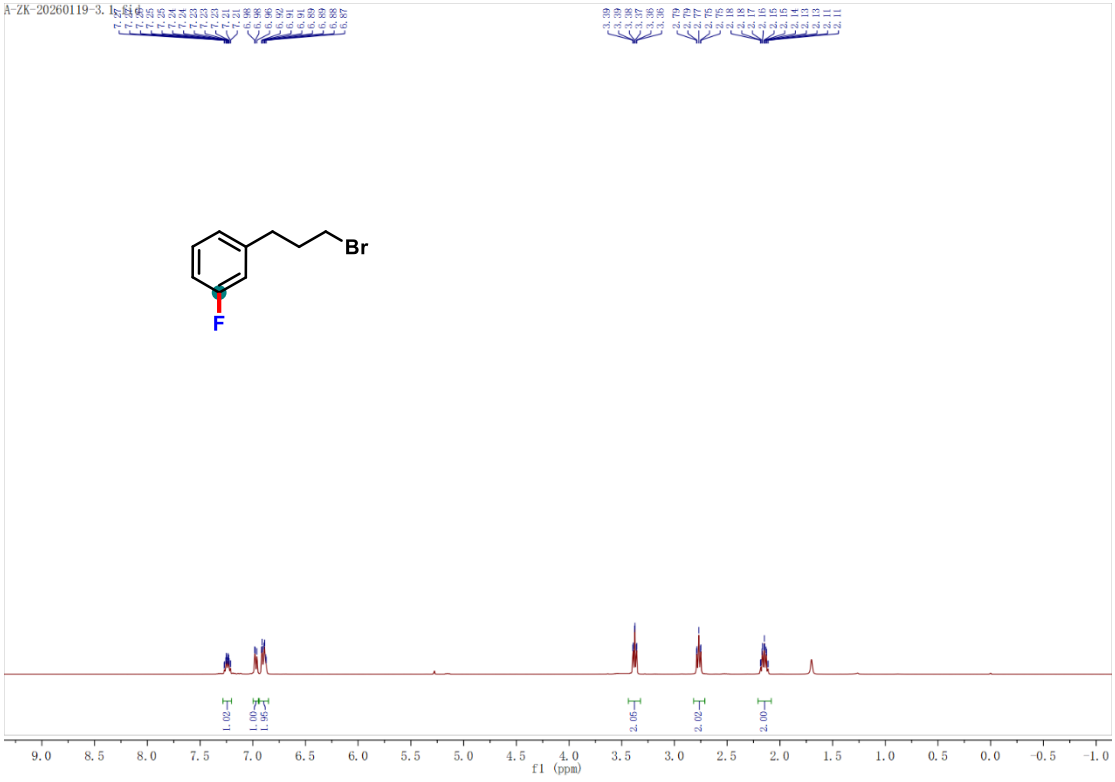
^{1}H NMR spectrum of 5f (400 MHz, $CDCl_3$)



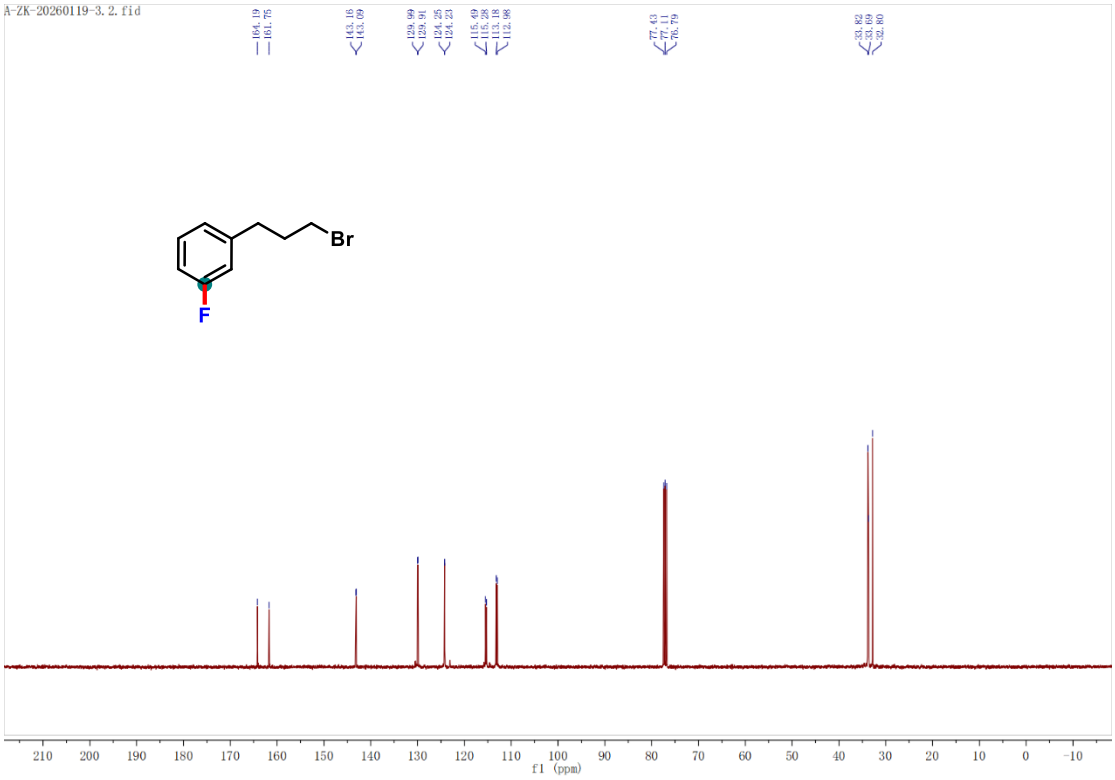
^{13}C NMR spectrum of 5f (101 MHz, $CDCl_3$)



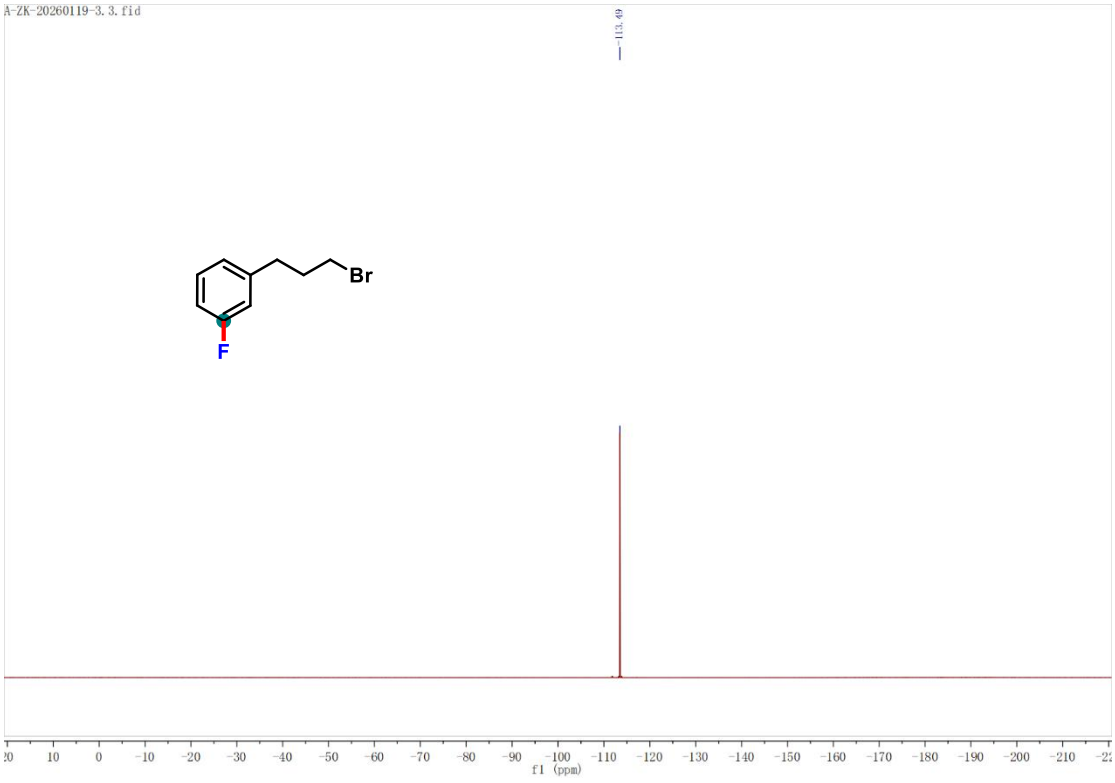
^{19}F NMR spectrum of 5f (376 MHz, $CDCl_3$)



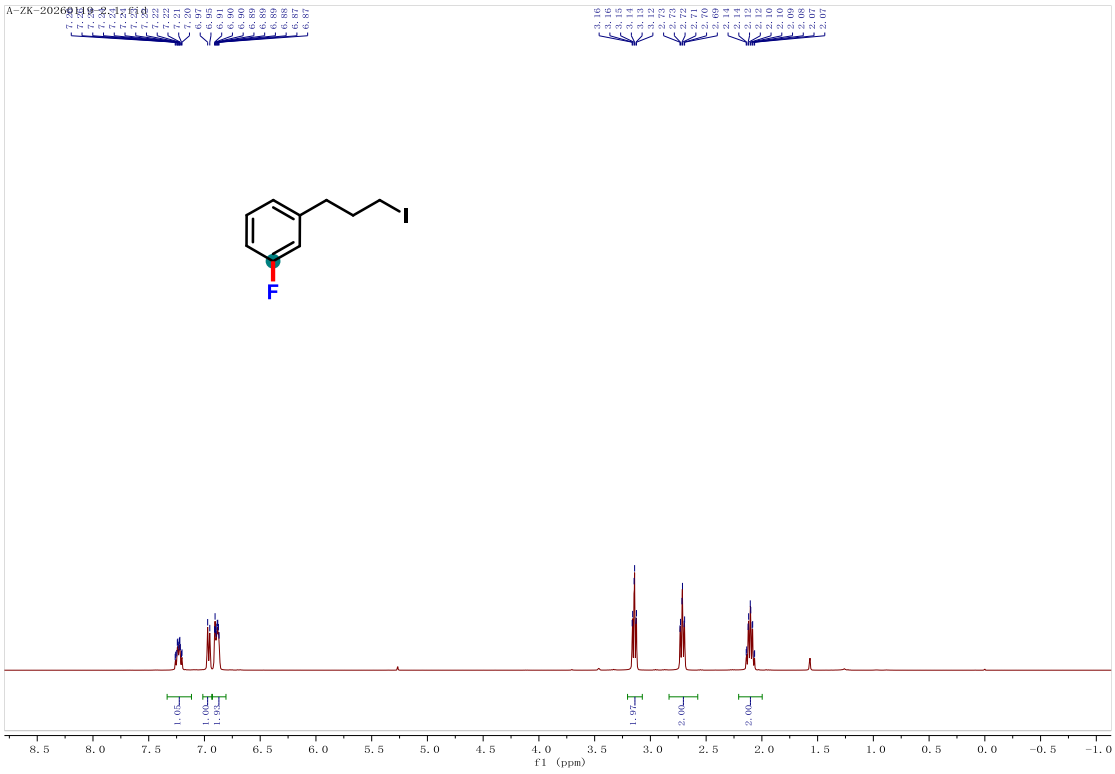
^{1}H NMR spectrum of 5g (400 MHz, $CDCl_3$)



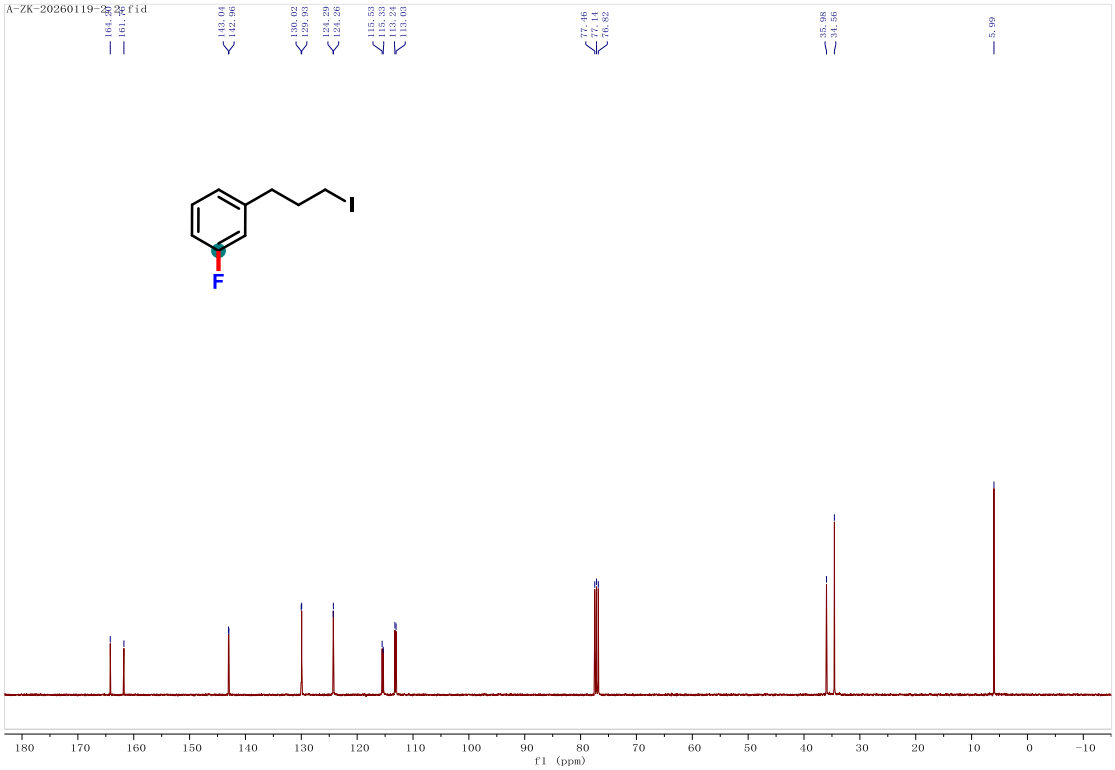
^{13}C NMR spectrum of 5g (101 MHz, $CDCl_3$)



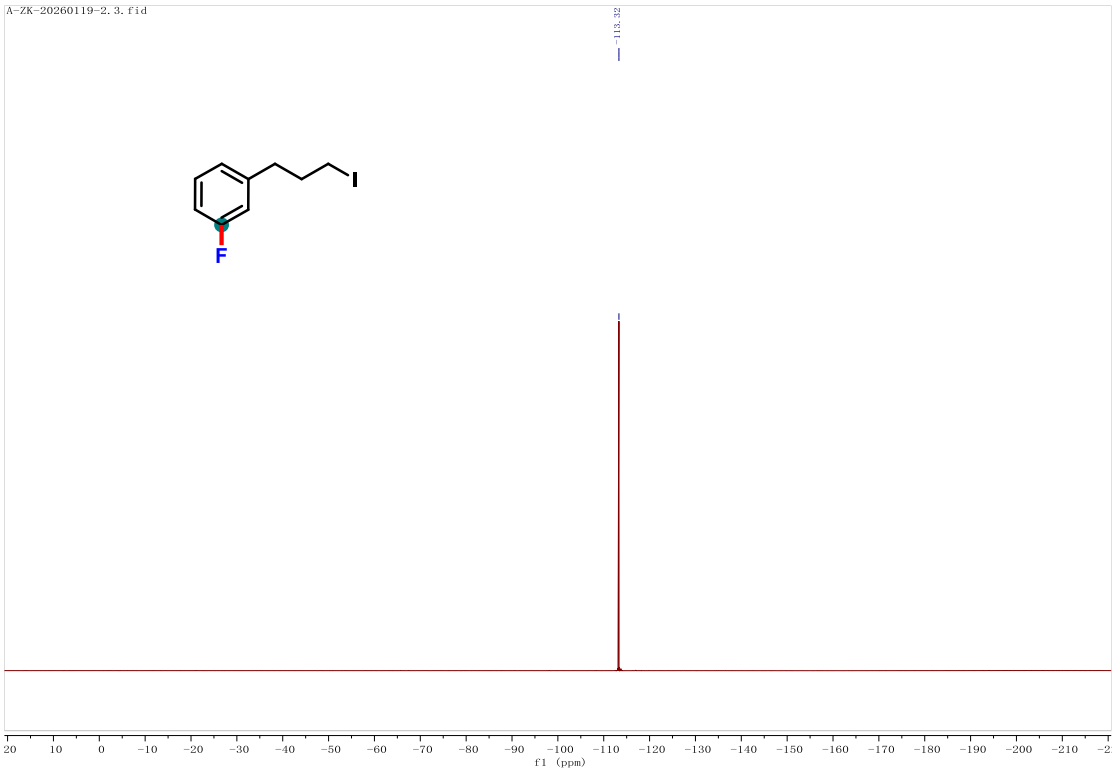
^{19}F NMR spectrum of 5g (376 MHz, $CDCl_3$)



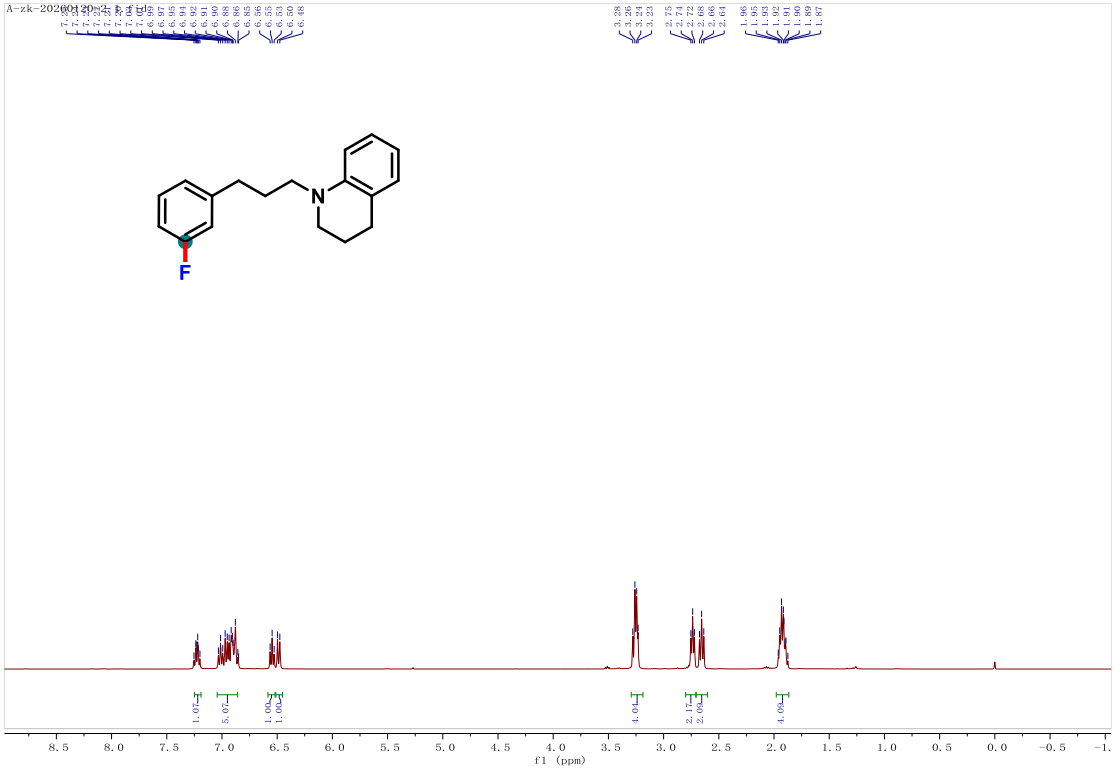
^{1}H NMR spectrum of 5h (400 MHz, $CDCl_3$)



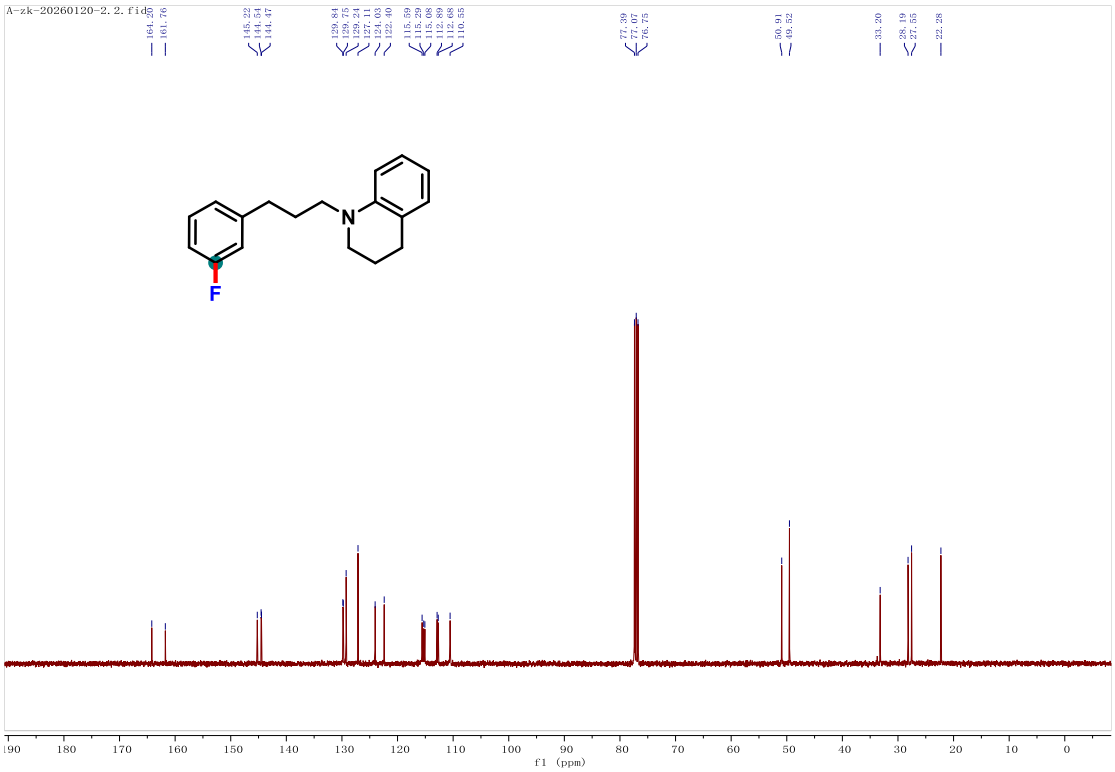
^{13}C NMR spectrum of 5h (101 MHz, $CDCl_3$)



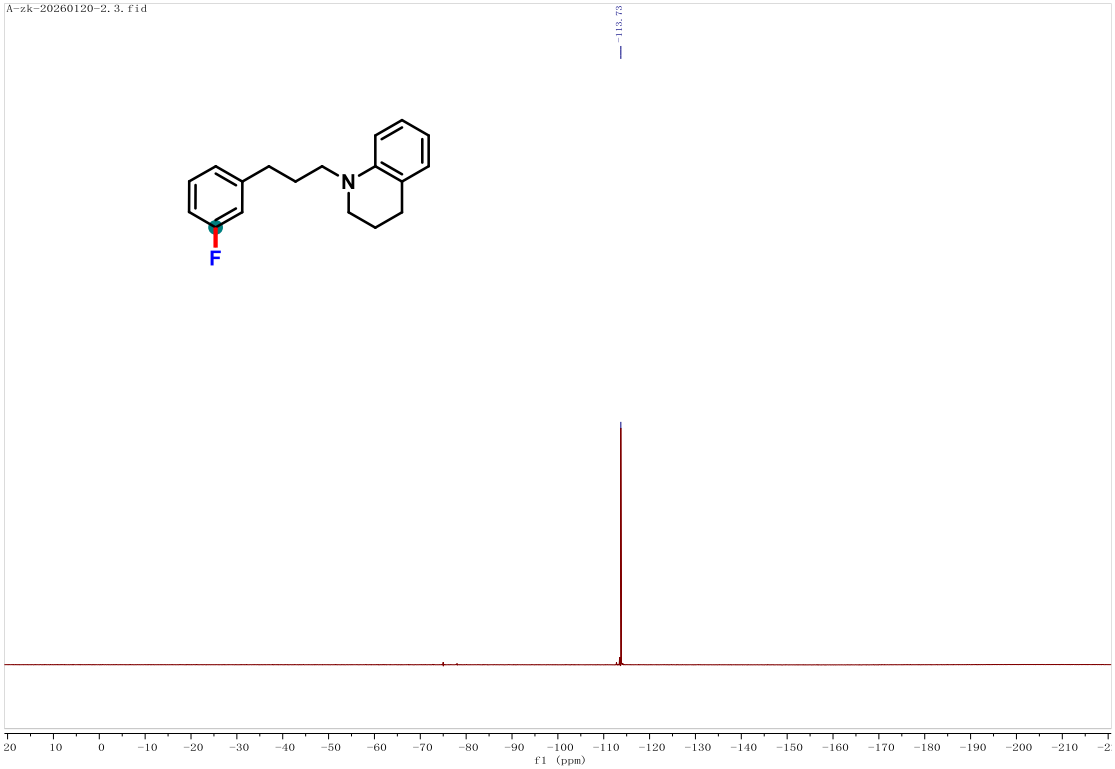
^{19}F NMR spectrum of 5h (376 MHz, $CDCl_3$)



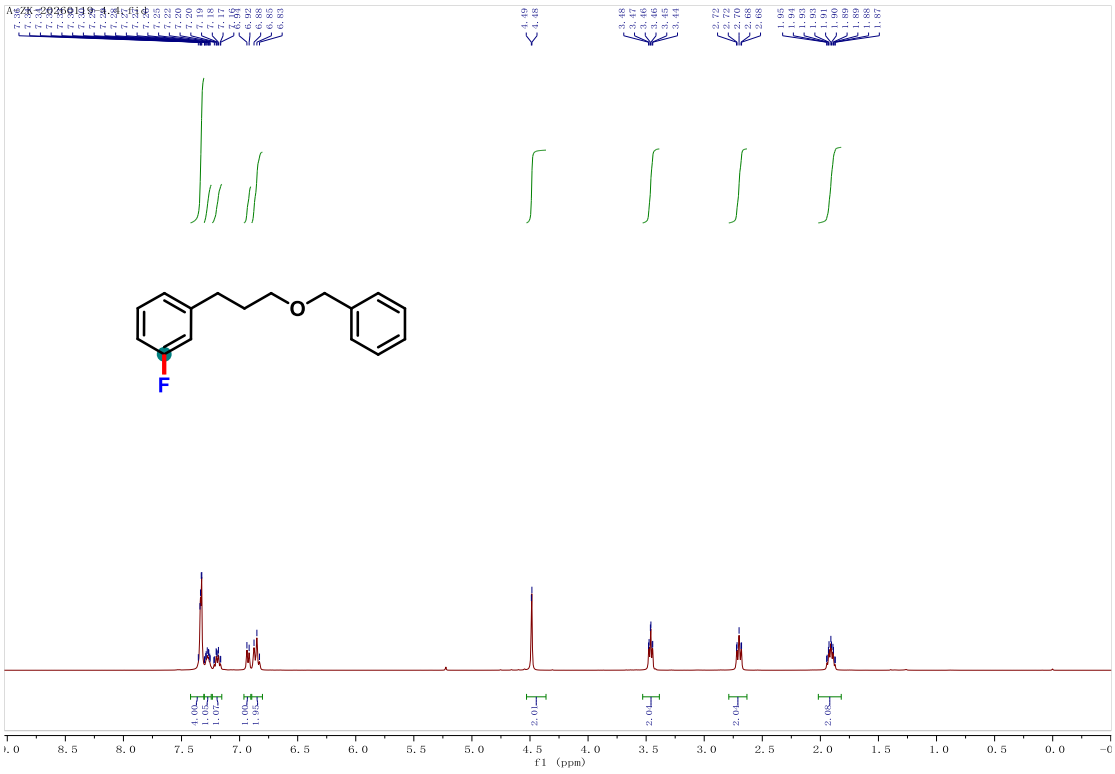
^{1}H NMR spectrum of 5i (400 MHz, $CDCl_3$)



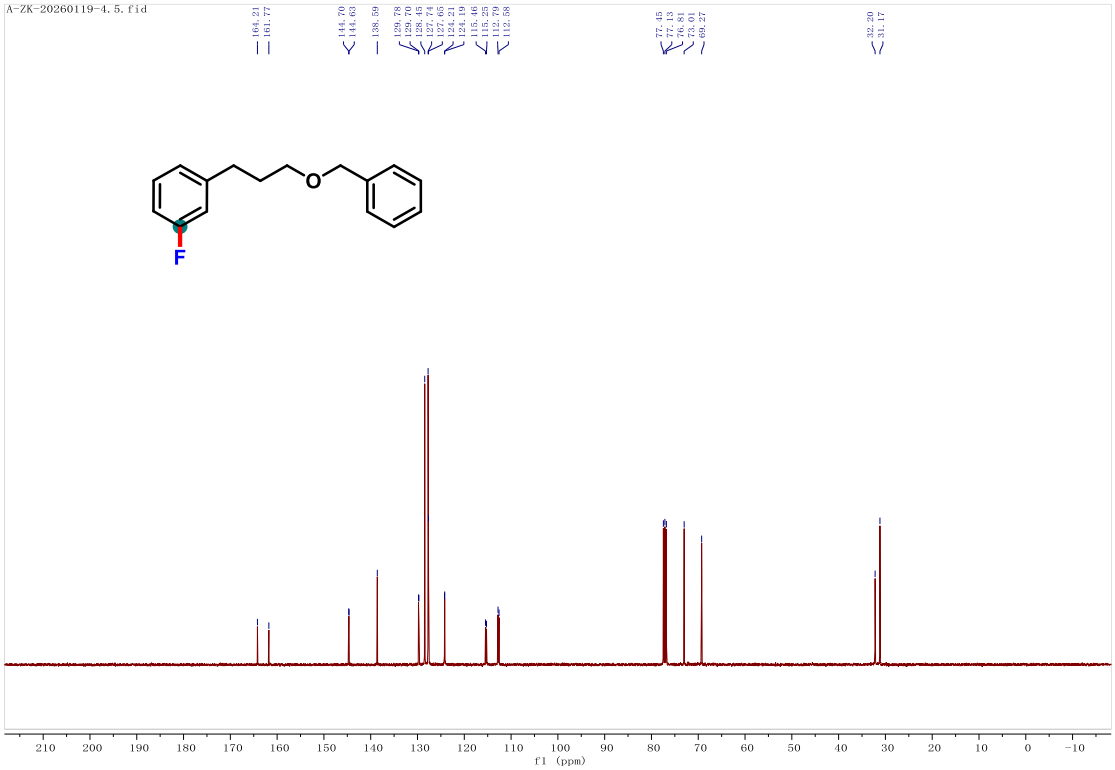
^{13}C NMR spectrum of 5i (101 MHz, $CDCl_3$)



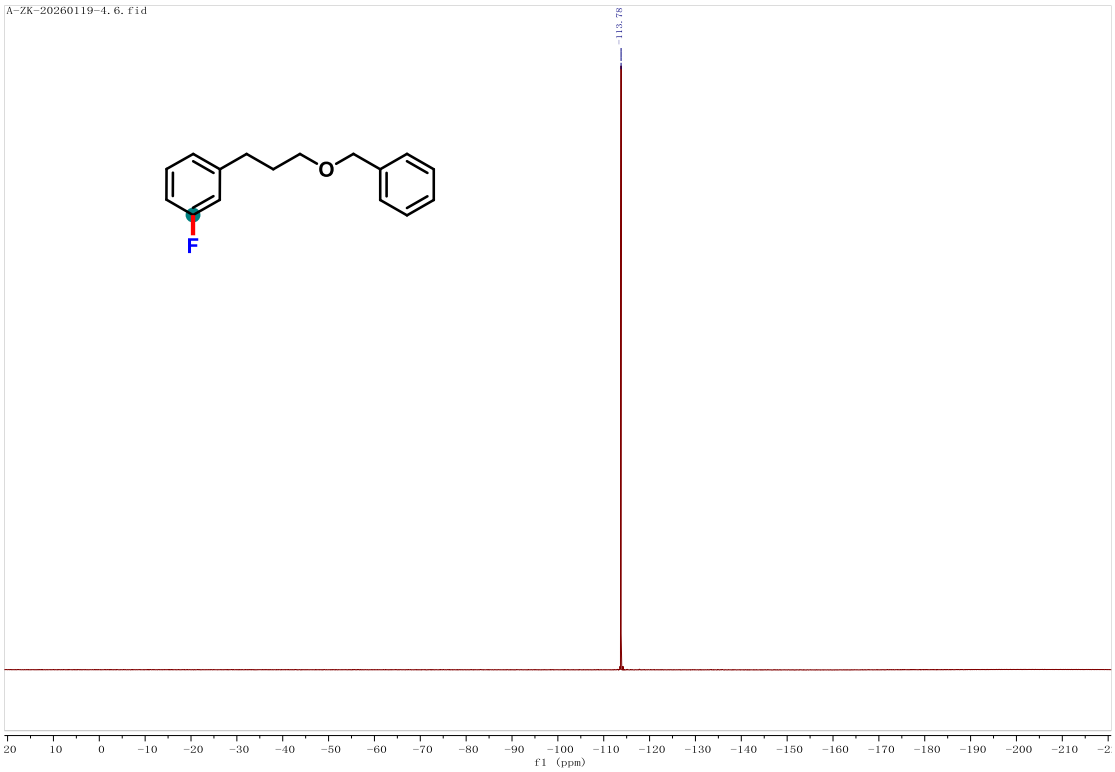
^{19}F NMR spectrum of 5i (376 MHz, $CDCl_3$)



^{1}H NMR spectrum of 5j (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of 5j (101 MHz, $CDCl_3$)



^{19}F NMR spectrum of 5j (376 MHz, $CDCl_3$)

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