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Supporting Information

Modular Synthesis of Conjugated Enamidines and Cascade Annulation toward Benzofuran-3-oxoacetate

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Contents

1. General experimental information

All reactions were performed in Schlenk tubes and bottomed flasks which dried by bake out furnace at 120 °C for 4 h. The preparation of conjugated enamidine derivatives were conducted under N_2 atmosphere by using standard Schlenk techniques for the water-sensitive and air-sensitive substrates. Except the KF were dried by heating 200 °C for 4 h, all reagents purchased from commercial supplier were used without further purified. All solvents were dried over 4 Å molecular sieves before used in transformation. ^{1}H NMR (400 Hz), ^{13}C NMR (100 Hz) and ^{19}F NMR (376 Hz) spectra were measured on a Bruker AV400 nuclear magnetic resonance instrument with TMS signal at 0.0 ppm as internal standard and chemical shifts were reported as the delta scale in ppm which $CDCl_3$ (7.26 ppm) for ^{1}H NMR and $CDCl_3$ (77.16 ppm) for ^{13}C NMR. The multiplicity data were presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The HRMS data were determined by Water SYNAPT G2-Si high-resolution mass spectrometer, and the single crystal structures were determined by Rigaku RAXISRAPID IP X-ray single crystal diffractometer. The reactions were monitored by TLC using a 254 nm UV lamp on a 0.20 mm silica gel 60 F plate and were visualized by I_2. The purification of products was carried out using flash column chromatography on silica gel (200–300 mesh) and the yields were referred chromatographically and spectroscopically pure compounds, unless otherwise noted.

2. General procedure for the synthesis of Aryne precursors

According to reference, we prepared the aryne precursors as shown in the **Fig. 1**:

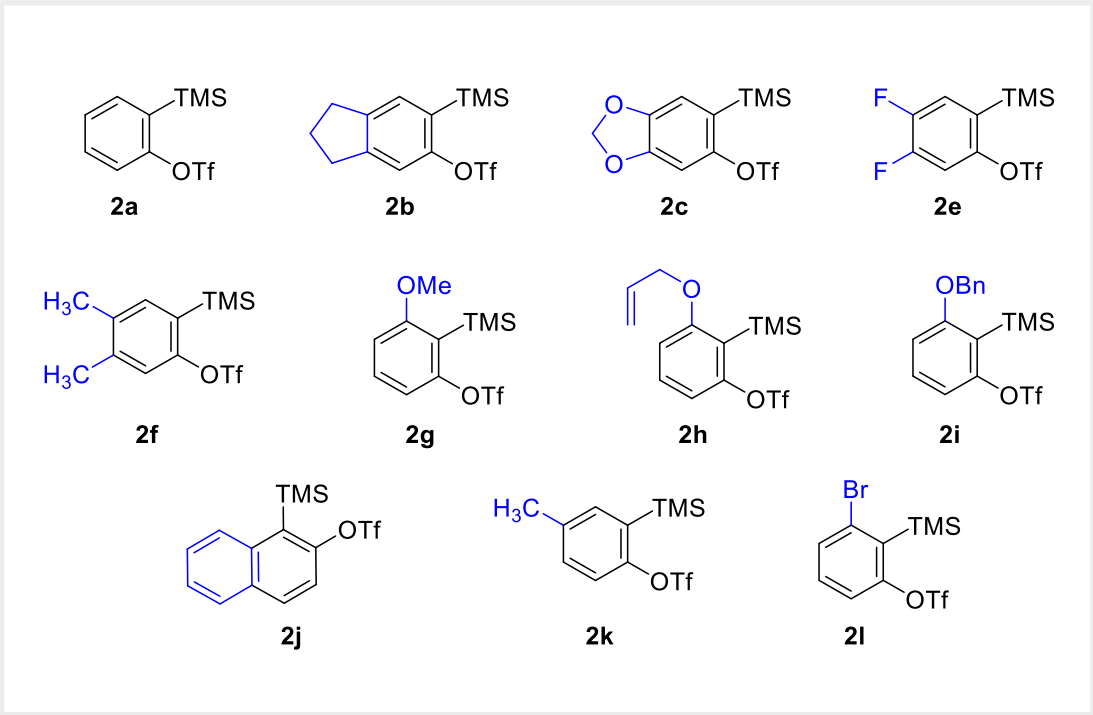
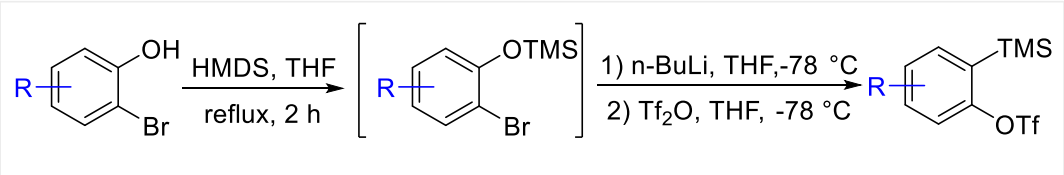


Fig. 1

The substrates **2a-2f, 2j-2l** were prepared via method from reference[1], we chose **2a** as model example to introduce the preparation method.

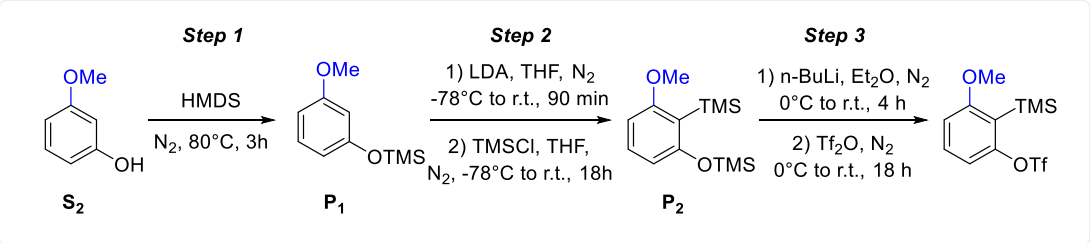


The clean round-bottom flask was heated in 120 °C for 4 h and cool to room temperature under nitrogen. Then, the 2-bromophenol (0.5 g, 2.91 mmol, 1.0 equiv.), hexamethyldisilazane (HMDS, 0.61 ml, 2.94 mmol, 1.01 equiv.) and anhydrous THF (12 mL) were added into the round-bottom flask by syringe, and the mixture was heated to 85 °C and refluxed for 2 h. After the reaction system was cooled to room temperature, concentrated under reduced pressure to remove excess HMDS and THF and a dark brown liquid crude product were obtained, which directly put into the next reaction without further purification.

The solution of crude product dissolved in anhydrous THF was put into the clean and dry round-bottom flask under the atmosphere of N_2, and the mixture system were cooled to -78 °C. Subsequently, the *n*-BuLi (1.6 mol/L in hexane, 2.0 mL, 3.20 mmol, 1.1 equiv.) was added dropwise to the mixture via syringe at -78 °C and stirred a same temperature for 40 min. Then the Tf_2O (0.59 mL, 3.49 mmol, 1.2 equiv.) was added slowly to the flask and stirred for another 1 h at -78 °C. After that, saturated ammonium chloride solution was added to the mixture to quench the reaction at -78 °C and then warmed to room temperature. The aqueous layer was extracted with

ethyl acetate and the combined organic phase was washed with saturated brine solution and dried over Na_2SO_4, the solution was evaporated in vacuo and the crude product was purified by flash chromatography on a silica gel column chromatography (only PE eluent) and a colorless liquid was obtained in 76% yield.

The preparation of aryne precursor **2g**[2]

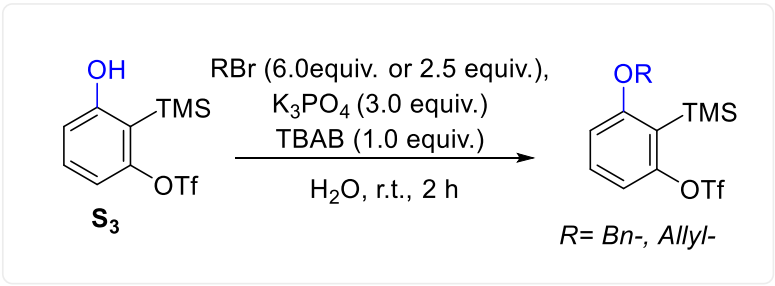


Step 1: To a clean and dry round-bottom flask with a magnetic stir bar was added the 3-methoxyphenol **S2** (0.2 g, 1.61 mmol, 1.0 equiv.) and HMDS (0.51 mL, 2.42 mmol, 1.5 equiv.) under N_2, and the mixture was heated to 80 °C for 3 h. After that, a crude product **P1** was prepared via the mixture concentrated in vacuum.

Step 2: The crude product **P1** was placed in a round-bottom flask which was evacuated and replaced with nitrogen three times, anhydrous THF was added to the mixture and the solution was cooled to -78 °C. After the LDA (1.1 equiv.) added dropwise via syringe at -78 °C and the mixture warm to room temperature stirred for 1.5 h. Then the mixture was cooled to -78 °C again and trimethylchlorosilane (TMSCl, 0.25 mL, 1.93 mmol, 1.2 equiv.) was added to mixture and stirred for 18 h after the temperature returned to r.t.. The mixture was quenched with sat. NH_4Cl solution and extracted with EA for three times, combined organic phase was extracted with sat. NaCl solution and dried over sodium sulfate. After concentrating in reduce pressure, the residue product was loaded on a silica gel column to acquire the pure product **P2**.

Step 3: Under atmosphere of N_2, to the solution of **P2** dissolved in anhydrous Et_2O were added slowly the *n*-BuLi (1.6 mol/L in hexane, 1.06 mL, 1.69mmol, 1.05 equiv.) at 0 °C and then warm to r.t. stirred for 4 h. When the indicated time finished, the Tf_2O (0.33 mL, 1.93 mmol, 1.2 equiv.) was added to the mixture at 0 °C and stirred at r.t. for 18 h. The reaction mixture was quenched with sat. $NaHCO_3$ solution and extracted with Et_2O (three times), the combined organic layer was dried with sodium sulfate and concentrated by rotary evaporator. The pure product **2g** (0.42 g, 80%) was purified by SiO_2 column chromatography as a colorless liquid.

The preparation of aryne precursors **2h** and **2i**[3]



As described earlier, the synthesis of **S₃** was similar with **2a**. Take the preparation of **2h** as an example, 3-hydroxy-2-(trimethylsilyl) phenyl trifluoromethanesulfonate **S₃** (0.6 g, 1.91 mmol, 1.0 equiv.) was suspended in H_2O (19.0 mL) and allyl bromide (1.37g, 11.4 mmol, 6.0 equiv.), and K_3PO_4(1.21g, 5.70 mmol, 3.0 equiv.) and TBAB (0.61g, 1.91mmol, 1.0 equiv.) were put into the mixture at room temperature. After the suspension stirred for 2 h, adding some water to dilute the mixture and extracting with EA for three times. The organic layer was dried over anhydrous Na_2SO_4 and filtered, concentrated in vacuo to provide crude product, which can be purified via the column chromatography to obtain the **2h** (0.46 g, 68%).

3. General procedure for the preparation of Isocyanides

The isocyanide compounds that we prepared are as shown in the **Fig. 2**:

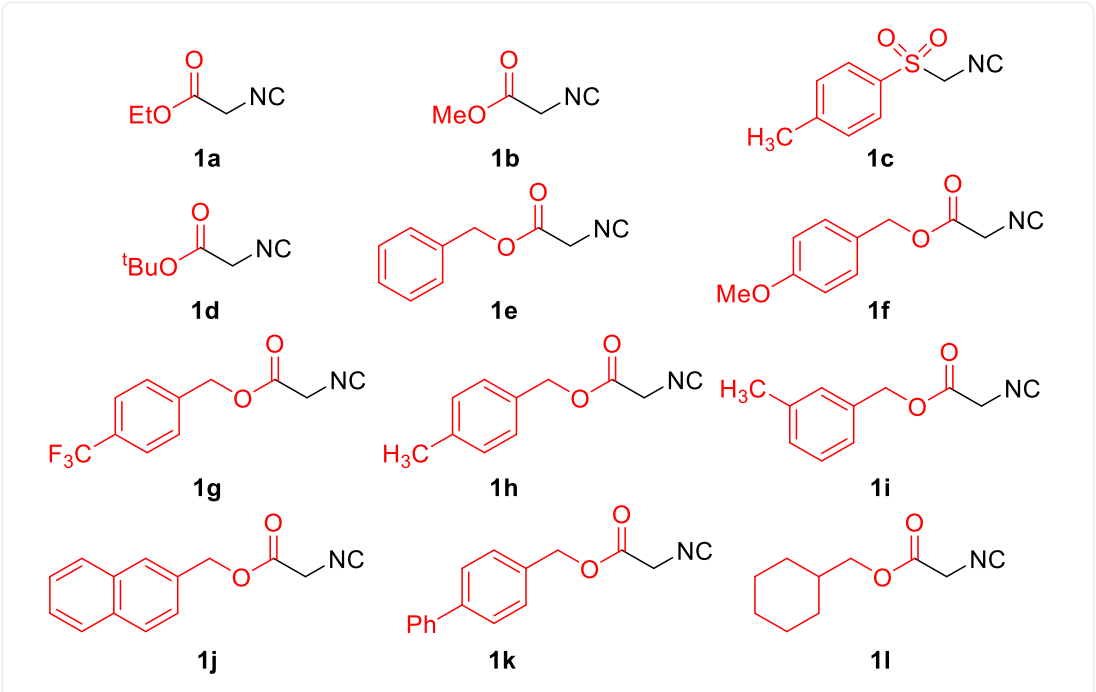
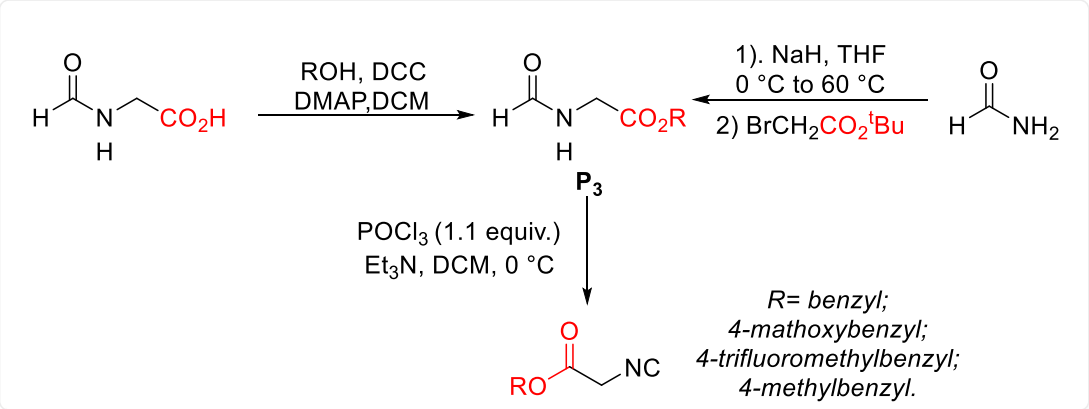


Fig. 2

1a-1c were purchased from commercial sources. The synthesis methods of **1d-1h** were reported in literature[4].

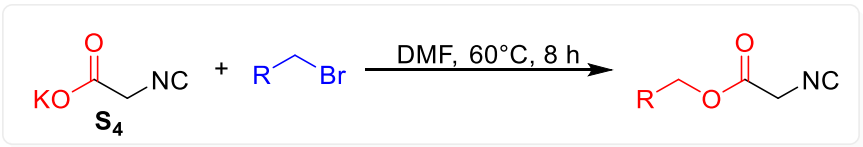


The preparation of **1e**:

Step a: To a stirred suspension of benzyl alcohol (1.4 mL, 13.24 mmol, 1.0 equiv.) and N-formyl glycine (1.5 g, 14.56 mmol, 1.1 equiv.) in CH_2Cl_2 (45 mL) was added the DCC (2.73 g, 13.24 mmol, 1.0 equiv.) and DMAP (0.16 g, 1.32 mmol, 0.1 equiv.) at 0 °C and stirred at room temperature for 16 h. The mixture was filtrated the solid and the filtrate was concentrated in the reduced pressure. The pure product **P₃** was obtained by flash chromatography on a silica gel column chromatography (PE: EA= 1:2) as white solid (78%).

Step b: To a clean round-bottom flask with a magnetic stir bar added the solution of benzyl 2-formamidoaceate **P₃** (2.2 g, 11.29 mmol, 1.0 equiv.) and Et_3N (1.2 mL, 12.42 mmol, 1.1 equiv.) in DCM (36 mL) under N_2, the $POCl_3$(3.8 mL, 27.09 mmol, 1.1 equiv.) was added dropwise slowly to the mixture at 0 °C. After stirred for 1.5 h, the **P₁** has converted completely and the color of mixture became orange. Saturated sodium carbonate solution was added to mixture to quench the reaction and mixture was extracted with DCM for three times, combined organic phase was washed with brine and concentrated in vacuo. Then the progress of purify was eluted by silica gel column to provide the final product **1e**.

We used another method[5] to prepare the isocyanide **1i-1l** via the commercial ethyl isocyanoacetate. The synthesis of **1j** is as follows:

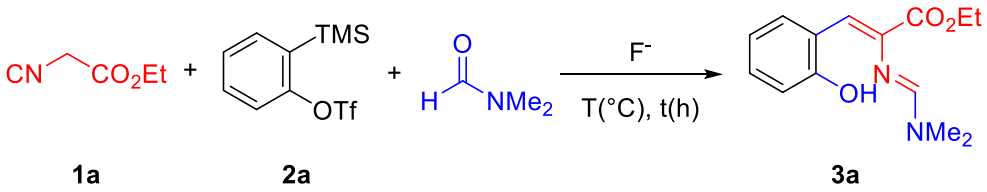


Firstly, to a solution of ethyl isocyanoacetate (2.0 g, 17.50 mmol, 1.2 equiv.) in THF (10 mL) was added the solution of KOH (1.0 g, 15 mmol, 1.0 equiv.) dissolved in H_2O (2.5 mL) at r.t.. And the mixture was stirred for 5 h, the mixture concentrated in vacuo directly and the crude potassium 2-isocyanoacetate was obtained, which washed with Et_2O and dried in reduced pressure to provide pure product potassium 2-isocyanoacetate **S₄**.

Next, to a flask were placed potassium 2-isocyanoacetate **S₄** (0.13g, 1.06 mmol, 1.0 equiv.) and 2-naphthalene bromide (0.24g, 1.09 mmol, 1.03 equiv.), the DMF (1.1 mL) also added to the mixture and stirred at 60 °C for 8 h. After the indicated time finished, the solvent was evaporated in vacuum and the residue was diluted with water, extracted with EA, organic layer was dried over Na_2SO_4, filtrated and concentrated in vacuo, the pure isocyanide **1j** was obtained in yield of 49% by the flash column chromatography with PE: EA (8:1).

4. Detail conditions screening

Table S1 the parameters involve F^- source, Temperature and Time screening of the MCRs reaction



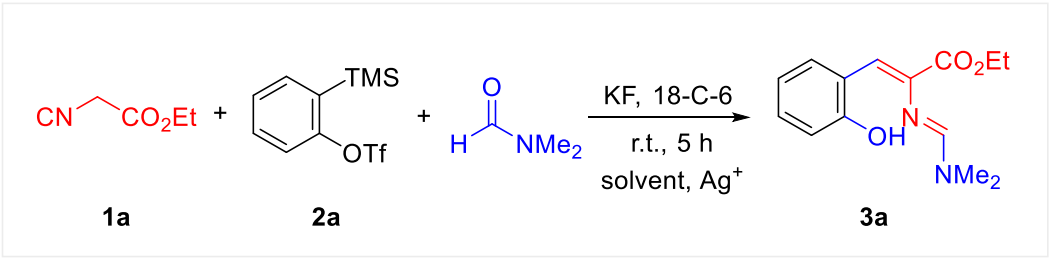
1a **2a** **3a**

F^- source, Temperature and Time screening of the MCRs reaction

Entry	F^- source	T/ °C	t/ h	**3a**, Yield (%)[d]
1	CsF	r. t.	5	49
2	KF	r. t.	5	62
3[a]	KF+18-C-6	r. t.	5	83
4[b]	KF+18-C-6	r. t.	5	58
5[c]	**KF+18-C-6**	**r. t.**	**5**	**85**
6	TBAF • $3H_2O$	r. t.	5	10
7	TBAF (THF)	r. t.	5	trace
8	ZnF_2	r. t.	5	n.r.
9	AgF	r. t.	5	n.r.
10	CuF_2	r. t.	5	n.r.
11	KF+18-C-6	30	5	76
12	KF+18-C-6	40	5	73
13	KF+18-C-6	50	5	71
14	KF+18-C-6	60	5	69
15	KF+18-C-6	80	5	65
16	KF+18-C-6	r. t.	2	30
17	KF+18-C-6	r. t.	3	45
18	KF+18-C-6	r. t.	4	60
20	KF+18-C-6	r .t.	6	56
21	KF+18-C-6	r. t.	8	50
22	KF+18-C-6	r. t.	10	43

General condition: [a]**1a** (0.1 mmol, 1.0 equiv.), **2a** (0.2 mmol, 2.0 equiv.), DMF (0.5 mL, 0.2 M); [b]1.0 equiv of **2a** was used**;** [c]1.5 equiv of **2a** was used**;** [d]Yields of isolated products.

Table S2 Screening conditions of Solvent and Ag^+ for the MCRs reaction



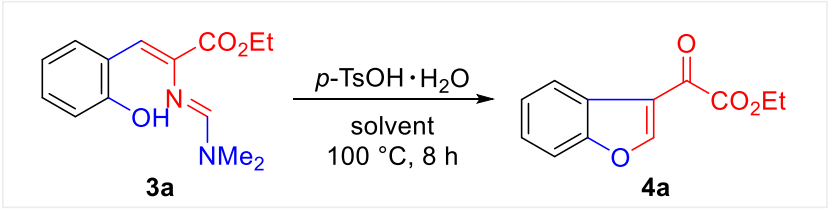
1a **2a** **3a**

Screening conditions of Solvent and Ag^+

Entry	solvent	Ag^+	**3a**, Yield (%)[d]
1[a]	MeCN	---	20
2[b]	MeCN	---	35
3[a]	MeOH	---	n.r.
4[b]	MeOH	---	n.r.
5	THF	---	n.r.
6	Toluene	---	n.r.
7	acetone	---	15
8	DMSO	---	11
9	DCM	---	n.r.
10[c]	DMF	AgOTf	n.r.
11[c]	DMF	$AgBF_4$	17
12[c]	DMF	TFA	n.r.
13[c]	DMF	$AgNO_3$	n.r.
14[c]	DMF	Ag_2O	n.r.
15[c]	DMF	Ag_2CO_3	29
16[c]	DMF	AgOAc	n.r.

General condition: [a]**1a** (0.1 mmol, 1.0 equiv.), **2a** (0.15 mmol, 1.5 equiv.), DMF (7.7 ul, 1.0 equiv.), r.t., 5 h; [b]DMF (77 ul, 10.0 equiv.); [c]**1a** (0.1 mmol, 1.0 equiv.), **2a** (0.15 mmol, 1.5 equiv.), DMF (0.5 mL, 0.2 M), Ag^+(0.1 mmol, 1.0 equiv.), r.t., 5 h; [d]Yields of isolated products.

Table S3 Solvent screening for the synthesis of benzofuran-3-oxocarboxylate



3a **4a**

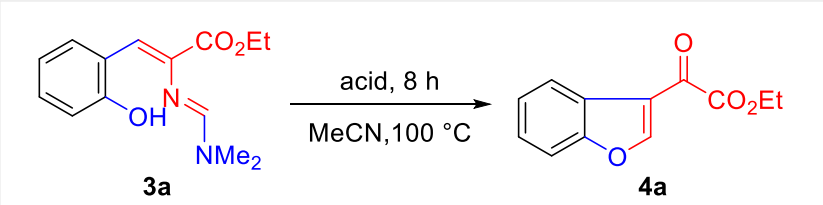
Solvent screening study

Entry	3a	*p*-TsOH•H_2O	solvent	**4a**, Yield (%)[b]
1	**1.0 equiv.**	**2.0 equiv.**	**MeCN**	**82**
2	1.0 equiv.	2.0 equiv.	1,4-dioxane	32

3	1.0 equiv.	2.0 equiv.	DMF	47
4	1.0 equiv.	2.0 equiv.	DMSO	43
5	1.0 equiv.	2.0 equiv.	THF	76
6	1.0 equiv.	2.0 equiv.	DCM	81
7	1.0 equiv.	2.0 equiv.	acetone	72
8	1.0 equiv.	2.0 equiv.	Toluene	59
9	1.0 equiv.	2.0 equiv.	MeOH	0

General condition: **3a** (0.1 mmol, 1.0 equiv.), TsOH•H_2O (0.2 mmol, 2.0 equiv.), solvent (1.0 mL, 0.1 M), 100 °C, 8 h; [b]Yields of isolated products.

Table S4 Acid screening for the synthesis of benzofuran-3-oxocarboxylate

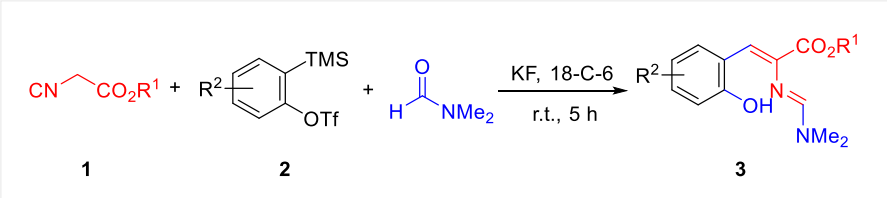


Acid screening study

Entry	3a	acid	solvent	**4a**, Yield (%)[b]
1	1.0 equiv.	CH_3SO_3H	MeCN	26
2	1.0 equiv.	Camphorsulfonic	MeCN	78
3	1.0 equiv.	NH_2SO_3H	MeCN	0
4	1.0 equiv.	TfOH	MeCN	0
5	1.0 equiv.	$NH_2CH_2CH_2SO_3H$	MeCN	0
6	1.0 equiv.	TsOH•H_2O	MeCN	82
7	1.0 equiv.	H_3BO_3	MeCN	0
8	1.0 equiv.	$AlCl_3$	MeCN	trace
9	1.0 equiv.	$BF_3{\cdot}Et_2O$	MeCN	0
10	1.0 equiv.	PFBA	MeCN	0
11	1.0 equiv.	HCF_2COOH	MeCN	trace
12	1.0 equiv.	HCOOH	MeCN	trace

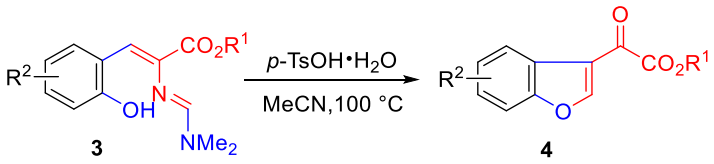
General condition: **3a** (0.1 mmol, 1.0 equiv.), acid (0.2 mmol, 2.0 equiv.), MeCN (0.5 mL, 0.2 M), 100 °C, 8 h; [b]Yields of isolated products.

5. General procedure for conjugated enamidine derivatives



To a clean and dry Schlenk tube with a magnetic stir bar was added the KF (0.023g, 0.4 mmol, 4.0 equiv.) and the system was vacuumized and blow in nitrogen for three times. Then, isocyanide **1** (0.1 mmol, 1.0 equiv.), aryne precursor **2** (0.15 mmol, 1.5 equiv.) and 18-crown-6 (0.026 g, 0.1 mmol, 1.0 equiv.) were added to the tube under the atmosphere of N_2. DMF (0.5 mL) was added to mixture via syringe under N_2 and the mixture was stirred at room temperature for 5 hours. Water (1.0 mL) was added to dilute the mixture and extracted with ethyl acetate for three times, the organic phase was combined and washed with brine, dried over anhydrous Na_2SO_4, filtrate and evaporated in vacuo to provide the crude product. The product was purified by SiO_2 column chromatography (PE: EA= 10: 1).

6. General procedure for the preparation of Benzofuran-3-oxocarboxylates



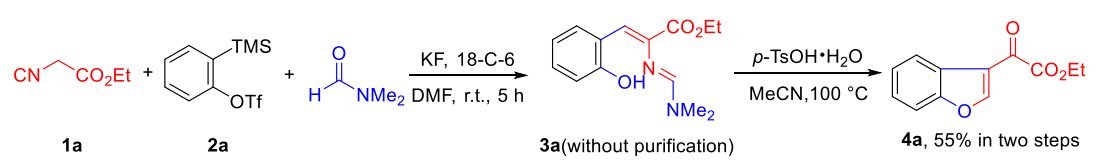
Under N_2, **3** (0.1 mmol, 1.0 equiv.) and TsOH•H_2O (0.2 mmol, 2.0 equiv.) were placed to the Schlenk tube and MeCN (1.0 mL) added to the mixture. Then the mixture heated to 100 °C and stirred for 8 hours. After that, the mixture was concentrated directly under reduced pressure to obtain the crude product. Using PE: EA = 100: 1~ 200: 1 as the eluent via SiO_2 column chromatography to separate and purify and the benzofuran-3-carboxylate products were prepared.

7. One-pot reaction and gram-scale reaction

7.1 One-pot reaction

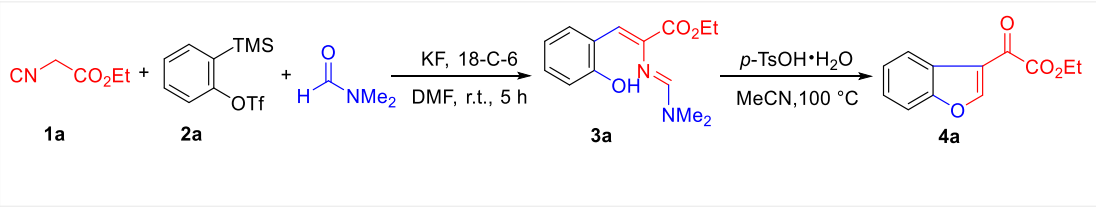
A one-pot reaction was carried out to be demonstrated the practicability of this method. **1a** (33.9 mg, 0.3 mmol, 1.0 equiv.), **2a** (134.1 mg, 0.45mmol, 1.5 equiv.) were dissolved in DMF (1.5

mL), the mixture was stirred at room temperature under the KF (69.7 mg, 1.2 mmol, 4.0 equiv.) and 18-C-6 (79.3 mg, 0.3mmol, 1.0 equiv.) for 5 h. After that, the crude product **3a** was obtained via removing residual DMF in vacuo and put into cyclization reaction without further purification. TsOH•H_2O (114 mg, 0.6 mmol, 2.0 equiv.) and the crude product **3a** were reacted at 100 °C in MeCN (1.5 mL) for 8 h, Ethyl α-oxo-3-benzofuranacetate was obtained in 55% yield (36.0 mg) in total.



7.2 Gram-scale reaction

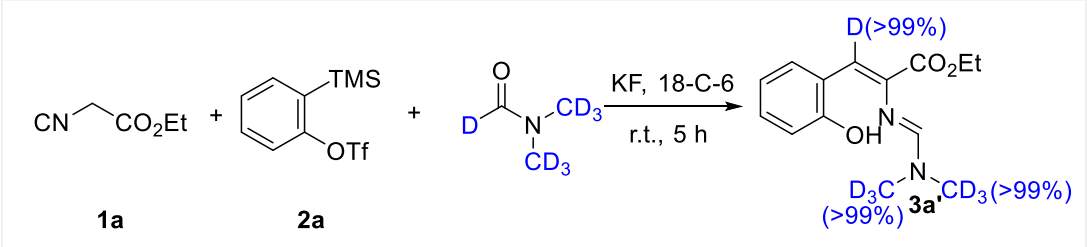
In a typical experiment of enamidine **3a**, **1a** (0.30 g, 2.65 mmol, 1.0 equiv.) and **2a** (1.2 g, 4.0 mmol, 1.5 equiv.) were reacted at the same condition, the **3a** was obtained in yield of 78% (0.54 g) without significantly decrease. And then, **3a** was converted to benzofuran-3-oxoacetate **4a** in the presence of TsOH•H_2O (380 mg, 2.0 mmol, 2.0 equiv.), the yield of **4a** was 63% (0.28 g), while the yield of **4a** in 80% was calculated on the base of recycling raw material **3a**.



8. Mechanistic study experiments

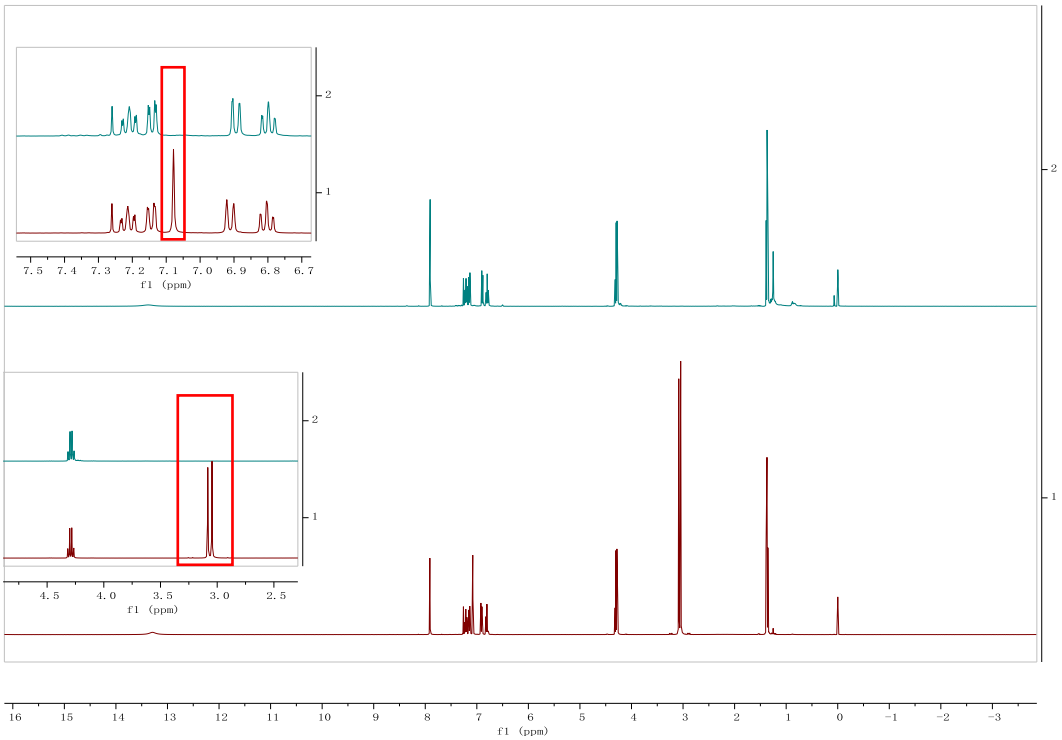
8.1 Deuteration experiment

DMF-d7 was replaced the DMF as the solvent of the three components reaction, and we acquired the deuterated product **3a'** in 85% yield under standard condition.

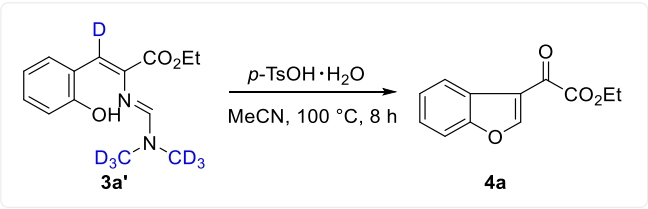


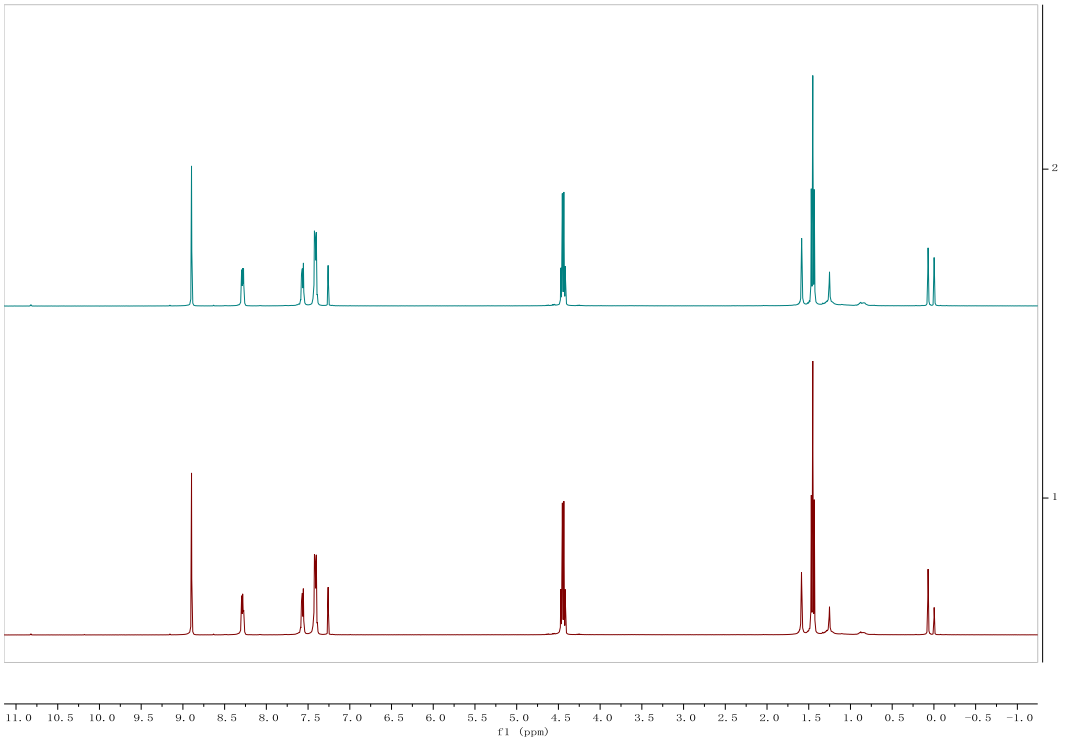
Conditions: **1a** (0.01 mmol, 1.0 equiv.), **2a** (0.015 mmol, 1.5 equiv.), DMF-d7(0.5 ml, 0.2 M), KF (0.04 mmol, 4.0 equiv.), 18-crown-6 (0.01 mmol, 1.0 equiv.), r.t., 5 h.

We found that δ = 3.05 ppm and δ = 3.08 ppm were not appeared the absorption signal via the ^{1}H NMR spectra of the **3a'** compared with the **3a**, which indicated the DMF-d7 take part in this transformation and the methyl hydrogen connected to the nitrogen atom is deuterated hydrogen. In addition, we found there is a deuterated hydrogen on the carbon atom of the C = C bond where the chemical shift value is 7.08 ppm, and we estimated that hydrogen was originated from the carbonyl hydrogen atom of DMF-d7.



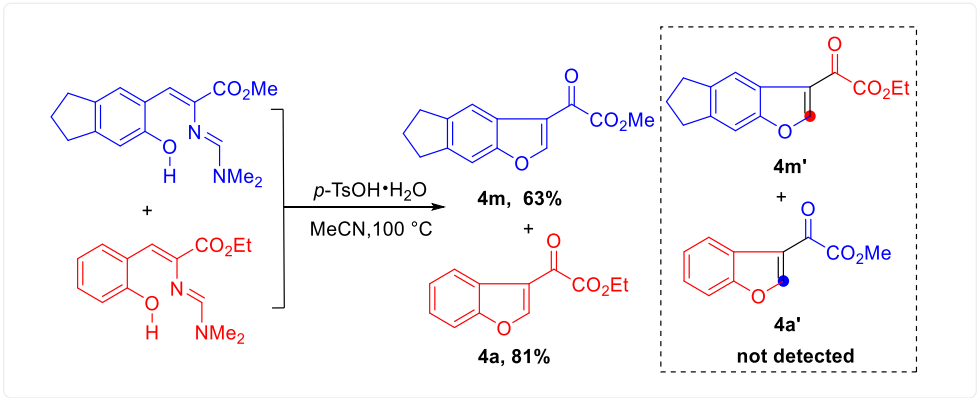
Next, **3a'** was used to obtain the ethyl benzofuran-3-oxoacetate **4a** under acid condition, the product **4a** was prepared in the yield of 81%. Analyzing the ^{1}H NMR data, we realized that the deuterated hydrogen of were disappeared, because **3a'** removed a molecular of H_2O (deuterated) and a molecular of $NH(CD_3)_2$ during the process of cyclization reaction.





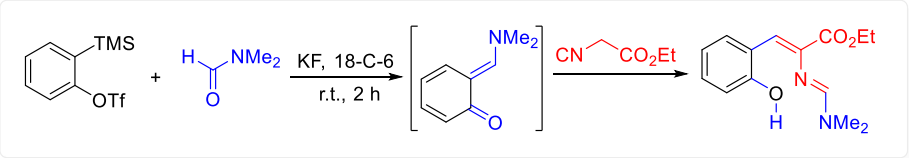
8.2 Cross-over experiment

3a and **3m** were added to Schlenk tube under same condition, **4a** and **4m** were obtained in 81%, 63%, respectively. Surprisingly, the cross-over products **4a'** and **4m'** were not detected, which indicated the cyclization reaction is an intramolecular cyclization process.



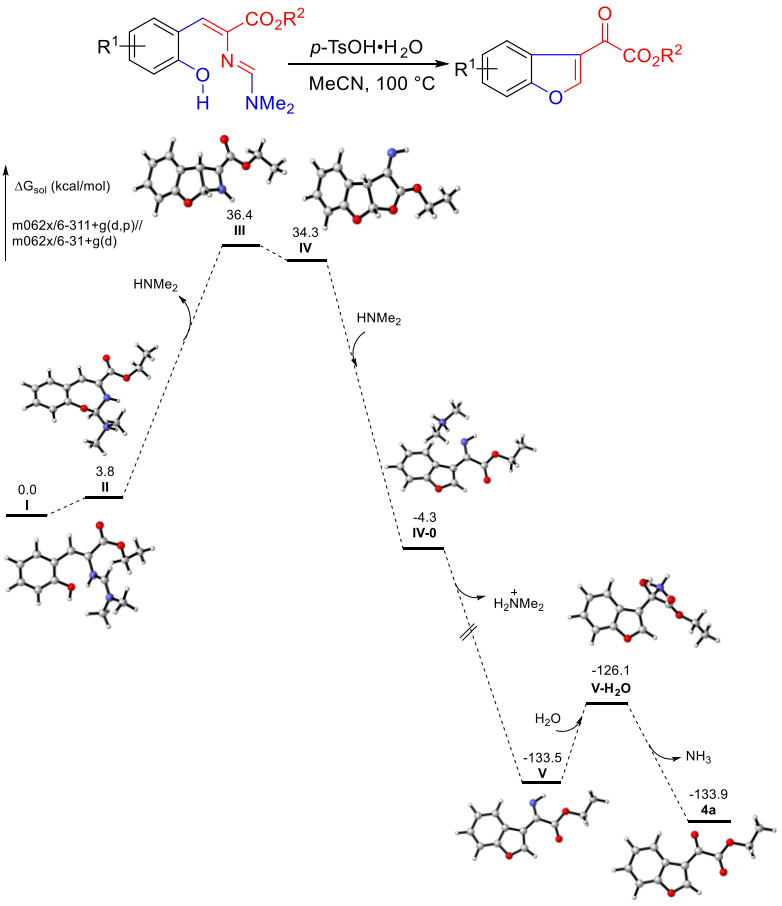
8.3 Step-wise experiment

In N_2 atmosphere, the aryne precursor **1a** and DMF were reacted under the activation of KF and 18-crown-6 stirred at room temperature for 2 h, and then the isocyanide **2a** was added to the mixture under N_2. The **3a** was prepared successfully with the yield of 84%. Reference to previous literature, reaction starts with the cycloaddition reaction of in-situ generated aryne with DMF, and then the isocyanide reacted with the intermediate to proceed the product.



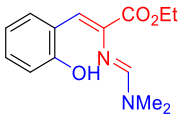
8.4 The DFT Calculation of Benzofuran-3-oxoacetate

The DFT calculations were performed with Gaussian 16. Geometry optimizations of all the minima and transition states were carried out at the M06-2X[6] level of theory with the 6-311+G(d,p) basis set. Vibrational frequencies were computed at the same level to verify that optimized structures are energy minima or transition states and to evaluate zero-point vibrational energies (ZPVE) and thermal corrections at 298 K. Solvent effects in acetonitrile were computed at the M06-2X /6-311+G(d,p) level using the optimized structures.



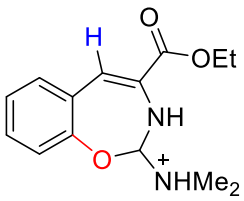
Compounds	TCG	E
I	0.27351	-879.824453
II	0.279663	-879.824494
NHMe2	0.068335	-135.133266
III	0.184537	-744.61251
IV	0.186189	-744.61748
NHMe2	0.068335	-135.133266

IV-0	0.273307	-879.831173
$^{+}NH_2Me2$	0.070162	-135.775672
V	0.170569	-744.228761
H_2O	0.003037	-76.428735
V-H_2O	0.196852	-820.668969
NH_3	0.015735	-56.551885
4a	0.158131	-764.106545



C	-4.8316	1.22712	-1.4763
C	-3.45149	1.05557	-1.5817
C	-2.6475	0.94361	-0.43541
C	-3.27333	1.05857	0.8182
C	-4.64702	1.22051	0.93354
C	-5.42709	1.30154	-0.22234
H	-5.43084	1.31426	-2.37868
H	-2.65604	1.00503	1.711
H	-5.10658	1.29096	1.91357
H	-6.50171	1.43649	-0.15037
C	-1.18983	0.76493	-0.45204
H	-0.64412	1.29427	0.32616
C	1.06156	0.00274	-1.03696
O	1.54577	0.00223	0.07092
O	1.85497	-0.03959	-2.11409
C	1.44641	0.48481	-3.40357
H	1.17171	-0.36088	-4.04005
H	0.57887	1.13798	-3.27548
C	2.62411	1.24251	-3.97644
H	2.36134	1.62334	-4.96737
H	2.88799	2.08702	-3.33476
H	3.49211	0.58568	-4.07534
C	-0.42729	0.00301	-1.25283
N	-0.93929	-0.80221	-2.29905
C	-0.45753	-2.00475	-2.58851
H	0.35612	-2.3937	-1.98187
N	-0.90397	-2.7426	-3.5663
C	-2.00235	-2.27698	-4.4154
H	-1.70799	-1.36553	-4.94462
H	-2.22533	-3.05382	-5.14417
H	-2.89382	-2.09151	-3.80908
C	-0.33267	-4.06359	-3.84081
H	-1.11297	-4.81873	-3.73052

H	0.05391	-4.07732	-4.86135
H	0.47608	-4.26503	-3.13934
O	-2.83108	1.03398	-2.80268
H	-3.47204	1.17916	-3.51777
H	-1.7157	-0.39735	-2.83297

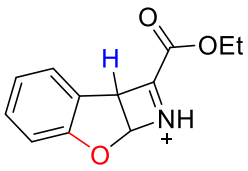


C	-4.87522	0.0863	-0.58884
C	-3.59871	0.11494	-1.10767
C	-2.82925	1.28341	-1.15867
C	-3.42331	2.44509	-0.65139
C	-4.71357	2.44539	-0.11911
C	-5.44082	1.26437	-0.08752
H	-5.41953	-0.85175	-0.58181
H	-2.8516	3.3678	-0.67934
H	-5.13849	3.36675	0.26349
H	-6.44595	1.24166	0.31935
C	-1.47256	1.40177	-1.68551
H	-1.04815	2.4018	-1.68632
C	0.70694	0.8205	-2.64052
O	1.13268	1.95172	-2.63256
O	1.37081	-0.25109	-3.06689
C	2.72913	-0.05232	-3.53857
H	2.91338	-0.91621	-4.17614
H	2.74693	0.8585	-4.13948
C	3.69329	0.01029	-2.37198
H	4.7135	0.10363	-2.75508
H	3.48375	0.87348	-1.73537
H	3.63119	-0.90179	-1.77264
C	-0.66153	0.4547	-2.16408
N	-0.97347	-0.93039	-2.27162
C	-2.06715	-1.58335	-2.02276
O	-3.19745	-1.15912	-1.5747
H	-0.20452	-1.50038	-2.62929
H	-2.06524	-2.65069	-2.21948

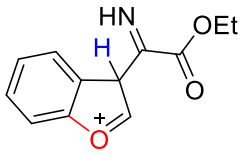
- NHMe2

N	0.18257	-1.10716	0.03923
H	0.55083	-0.58633	-0.75354

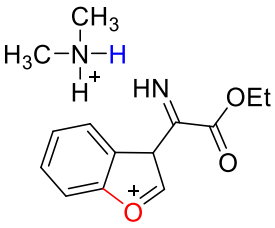
C	0.69447	-2.47166	-0.01409
H	1.78716	-2.4571	-0.03937
H	0.38183	-3.00755	0.88851
H	0.3294	-3.0384	-0.88705
C	-1.27456	-1.07927	-0.01381
H	-1.67544	-1.55337	0.88846
H	-1.62517	-0.04424	-0.03828
H	-1.68732	-1.61174	-0.8871



C	-3.5641	0.21526	-0.26946
C	-2.19077	0.33525	-0.17136
C	-1.56395	1.47588	0.32747
C	-2.32229	2.55581	0.75978
C	-3.71364	2.45737	0.68184
C	-4.31984	1.30512	0.17258
H	-4.0239	-0.68491	-0.66193
H	-1.84369	3.45048	1.14545
H	-4.32922	3.2853	1.01696
H	-5.40249	1.24978	0.11985
C	-0.07322	1.26513	0.25127
H	0.5215	1.49013	1.13604
O	-1.29917	-0.66947	-0.5189
C	-0.01835	-0.16178	-0.41021
H	0.69856	-0.91195	-0.08815
C	0.45614	1.71448	-1.08057
N	0.4408	0.56189	-1.64653
C	0.82509	3.05768	-1.6565
O	0.68481	4.05852	-1.00202
O	1.2759	2.93158	-2.88101
C	1.66238	4.16145	-3.56262
H	2.43548	4.6406	-2.9576
H	0.7813	4.8063	-3.59684
C	2.154	3.77263	-4.93546
H	2.45202	4.67551	-5.4748
H	3.01959	3.10939	-4.86467
H	1.3652	3.2737	-5.50386
H	0.64005	0.27779	-2.60954



C	-3.34971	0.45002	-0.68609
C	-2.02582	0.27592	-0.332
C	-1.19165	1.31935	0.04221
C	-1.67131	2.6212	0.06267
C	-3.00773	2.83292	-0.28841
C	-3.82986	1.76301	-0.65483
H	-3.97524	-0.38833	-0.97158
H	-1.02739	3.44867	0.34527
H	-3.41135	3.83985	-0.27719
H	-4.86418	1.95148	-0.92426
C	0.1715	0.74107	0.36016
H	0.46216	0.83741	1.40857
O	-1.37999	-0.95439	-0.2738
C	-0.04738	-0.72466	-0.07086
H	0.41119	-1.52194	0.50557
C	1.242	1.25469	-0.56743
N	1.90252	2.32134	-0.47568
C	1.33918	0.22209	-1.65507
O	0.64156	-0.81904	-1.42769
O	2.04685	0.37809	-2.68448
C	2.10542	-0.69742	-3.70998
H	1.0778	-0.86266	-4.03565
H	2.48885	-1.58142	-3.19855
C	3.00868	-0.19747	-4.80503
H	3.07149	-0.97064	-5.57511
H	2.60683	0.71142	-5.2578
H	4.01377	-0.00392	-4.42442
H	2.55173	2.44176	-1.2614



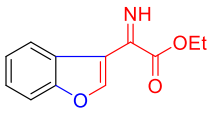
C	-4.93671	0.25707	-0.10044
C	-3.88274	-0.26803	-0.83623
C	-2.86303	0.50299	-1.40424
C	-2.91072	1.89837	-1.26768
C	-3.95609	2.44884	-0.5348

C	-4.94957	1.64028	0.04909
H	-5.70253	-0.38019	0.32829
H	-2.15929	2.53172	-1.72943
H	-4.01075	3.52592	-0.41185
H	-5.74791	2.10524	0.61851
C	-1.98338	-0.45278	-2.05437
H	-0.26991	1.64255	-0.62099
O	-3.6813	-1.59265	-1.11381
C	-2.54862	-1.6765	-1.84738
H	-2.24889	-2.67034	-2.14276
C	-0.70915	-0.13533	-2.69011
N	-0.0828	0.9292	-2.36404
C	-0.16201	-1.11439	-3.72596
O	-0.72905	-2.13648	-4.03504
O	0.99473	-0.70377	-4.21893
C	1.61549	-1.55633	-5.21217
H	0.91447	-1.66951	-6.04288
H	1.78268	-2.53539	-4.75627
C	2.90422	-0.88978	-5.63314
H	3.40113	-1.50902	-6.38476
H	2.7085	0.09344	-6.06894
H	3.57788	-0.77319	-4.78018
H	0.78347	1.03159	-2.89921
N	-0.03596	1.78397	0.38828
H	-0.33163	2.73087	0.64261
C	-0.76703	0.78827	1.22167
H	-1.83489	0.99828	1.1677
H	-0.55531	-0.20646	0.82721
H	-0.4149	0.87033	2.24965
C	1.44532	1.67438	0.50787
H	1.73466	0.6695	0.20001
H	1.90286	2.41573	-0.14566
H	1.7296	1.85085	1.54448

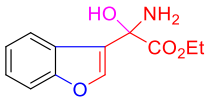
NH_2Me

N	0.14865	-1.1532	-0.47196
H	0.30676	-0.93345	-1.45253
C	0.68992	-2.47356	-0.18091
H	1.76661	-2.48472	-0.37378
H	0.53431	-2.69767	0.87928
H	0.21542	-3.27892	-0.76734
C	-1.27841	-1.08708	-0.18793
H	-1.44281	-1.30474	0.8724
H	-1.65044	-0.07791	-0.38727

H	-1.87402	-1.80744	-0.77443
H	0.73076	-0.34057	2.93467



C	-3.79187	0.93631	0.86957
C	-2.69974	0.46378	0.1543
C	-1.73668	1.28177	-0.447
C	-1.868	2.67375	-0.33009
C	-2.95406	3.17257	0.38154
C	-3.90303	2.31918	0.97379
H	-4.51173	0.25962	1.3176
H	-1.13953	3.33411	-0.78468
H	-3.07434	4.24683	0.48384
H	-4.73728	2.74603	1.52176
C	-0.79627	0.36628	-1.07605
O	-2.40486	-0.85339	-0.06736
C	-1.26755	-0.88471	-0.80242
H	-0.90478	-1.86647	-1.06074
C	0.39573	0.75665	-1.83003
N	0.69359	1.98983	-1.96607
C	1.25286	-0.35162	-2.43897
O	0.98821	-1.53058	-2.36676
O	2.31766	0.14034	-3.05751
C	3.20246	-0.81662	-3.68416
H	2.62402	-1.37955	-4.42122
H	3.55475	-1.50684	-2.9134
C	4.33242	-0.03679	-4.31566
H	5.02379	-0.73109	-4.80086
H	3.95142	0.65656	-5.07011
H	4.88338	0.52891	-3.55964
H	1.55126	2.08756	-2.51589

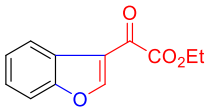


C	-3.59793	0.85113	1.10771
C	-2.61268	0.44996	0.21264
C	-1.66557	1.31619	-0.3452
C	-1.69254	2.67318	0.00804
C	-2.66875	3.09849	0.90069
C	-3.60885	2.20075	1.44379
H	-4.31386	0.14604	1.51682
H	-0.96823	3.36465	-0.40916
H	-2.71055	4.14459	1.18857

H	-4.35716	2.56883	2.1389
C	-0.84619	0.48487	-1.20584
O	-2.41985	-0.81876	-0.25065
C	-1.35316	-0.76721	-1.1009
H	-1.07952	-1.70341	-1.56154
C	0.31116	0.99879	-2.01363
N	-0.19738	1.90835	-3.04151
C	1.09645	-0.14007	-2.69863
O	0.58712	-1.12059	-3.19355
O	2.39305	0.14843	-2.77333
C	3.2259	-0.77006	-3.51936
H	2.83947	-0.82188	-4.54057
H	3.13567	-1.757	-3.05903
C	4.63995	-0.23974	-3.46566
H	5.29981	-0.91152	-4.02135
H	4.69938	0.7546	-3.91621
H	4.99392	-0.18309	-2.43284
H	0.56486	2.22982	-3.63931
O	1.14559	1.70978	-1.13148
H	2.00756	1.84722	-1.5592
H	-0.86739	1.42293	-3.63685

NH_3

N	-0.19294	0.51304	0.00001
H	0.19346	-0.42853	0.
H	0.19347	0.98377	0.81543
H	0.19345	0.98378	-0.81545



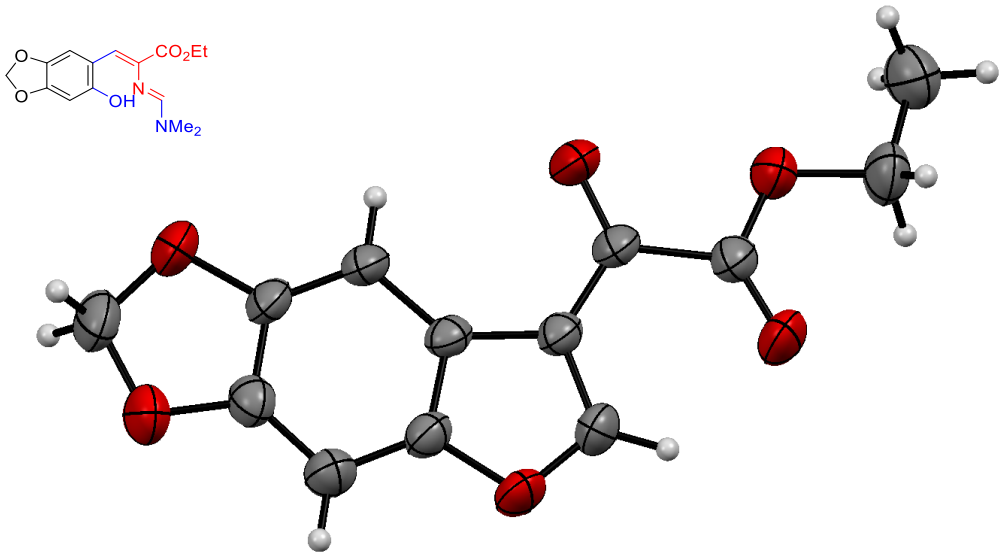
C	-3.92658	0.97131	0.62172
C	-2.83239	0.48091	-0.07634
C	-1.67922	1.22016	-0.35418
C	-1.59944	2.54629	0.09189
C	-2.68288	3.06289	0.7946
C	-3.82892	2.2897	1.0564
H	-4.80068	0.35846	0.81345
H	-0.71921	3.14667	-0.10729
H	-2.64574	4.08767	1.15094
H	-4.65387	2.72908	1.60821
C	-0.81619	0.31228	-1.09161
O	-2.71518	-0.78529	-0.59414
C	-1.51163	-0.86257	-1.19035
H	-1.26963	-1.80878	-1.64873
C	0.5028	0.65119	-1.61096

C	1.30185	-0.45111	-2.34132
O	0.96874	-1.61521	-2.35168
O	2.37572	0.04047	-2.92794
C	3.20804	-0.90913	-3.63509
H	2.59447	-1.39541	-4.39803
H	3.54097	-1.66565	-2.91964
C	4.36163	-0.13733	-4.23268
H	5.01472	-0.82583	-4.77573
H	4.00005	0.62137	-4.93172
H	4.9479	0.35184	-3.45035
O	0.98975	1.75797	-1.48323
H_2O			
O	-2.54049	-0.71615	0.
H	-1.57343	-0.67758	0.
H	-2.82694	0.20831	0.

9. X-Ray data of the 3c and 4c

The single crystals of the compound **3c** was grown in a mixture solvent of n-hexane and ethyl acetate. The **4c** was prepared by evaporation of chloroform. The crystallographic data of compounds were collected room temperature on a Bruker SMAR.T. APEX II CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å). Structure was solved by the direct method using the SHELXS97. All nonhydrogen atoms were refined by full-matrix least squares on F2 using SHELXL-2014/7. All H atoms were placed at calculated ideal positions using a riding model approach. The OR.T.EP diagram was generated using the Mercury. CDCC 2072987, 2076653 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

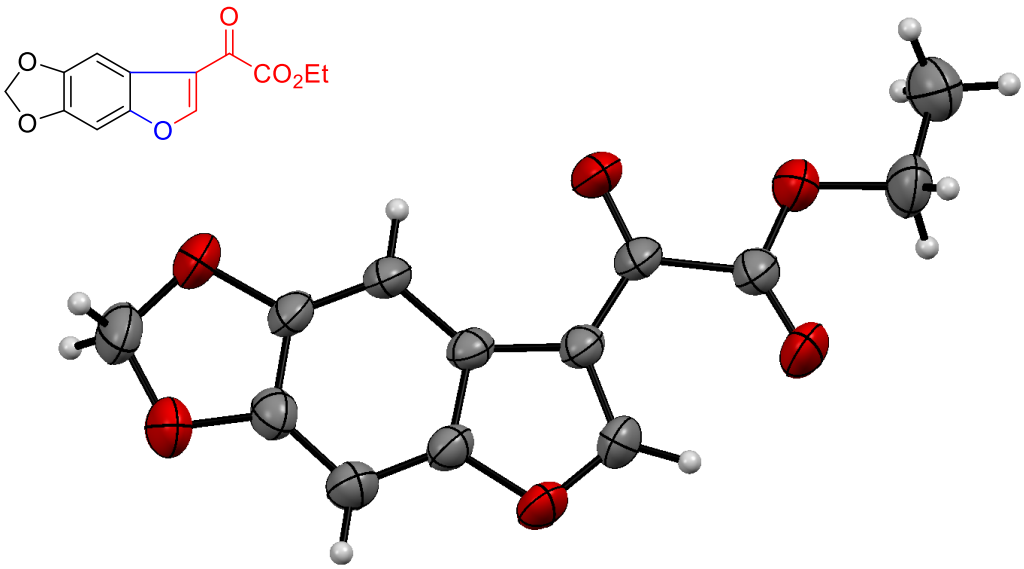
Compound **3c**



Identification code	**3c**
Empirical formula	$C_{15}H_{18}N_2O_5$
Formula weight	306.31
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_{1/n}$
Unit cell dimensions	a = 7.7482(6) Å, α = 90°
	b = 17.8486(11) Å, β= 93.153 (7)°
	c = 10.7825(8) Å, γ = 90°
Volume	1488.90(18) $Å^3$
Z	4
Density (calculated)	1.366 Mg/m^3
Absorption coefficient	0.104 mm^{-1}
F(000)	648
Crystal size	0.160 x 0.140 x 0.120 mm^3
Theta range for data collection	3.326 to 25.498°
Index ranges	-9<=h<=9, -21<=k<=21, -13<=l<=13
Reflections collected	17131
Independent reflections	2772 [R(int) = 0.0913]
Completeness to theta = 25.242°	99.9 %
Absorption correction	None
Refinement method	Full-matrix least-squares on

	F^2
Data / restraints / parameters	2772 / 0 / 204
Goodness-of-fit on F^2	1.100
Final R indices [I>2sigma(I)]	R1 = 0.1055, wR2 = 0.2729
R indices (all data)	R1 = 0.1178, wR2 = 0.2805
Extinction coefficient	n/a
Largest diff. peak and hole	0.484 and -0.327 e.$Å^{-3}$

Compound **4c**

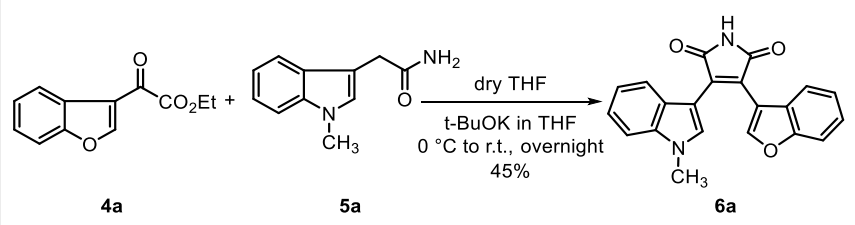


Identification code	**4c**
Empirical formula	$C_{13}H_{10}O_6$
Formula weight	262.21
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 8.499(2) Å; α= 90°
	b = 12.440(3) Å; β= 104.08(3)°
	c = 11.520(3) Å; γ= 90°
Volume	1181.4(5) $Å^3$
Z	4
Density (calculated)	1.474 Mg/m^3
Absorption coefficient	0.119 mm^{-1}
F(000)	544
Crystal size	0.240 x 0.220 x 0.210 mm^3

Theta range for data collection	3.275 to 25.493°
Index ranges	-10<=h<=10, -14<=k<=15, -13<=l<=13
Reflections collected	9342
Independent reflections	2195 [R(int) = 0.0836]
Completeness to theta = 25.242°	99.8 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2195 / 0 / 173
Goodness-of-fit on F^2	1.037
Final R indices [I>2sigma(I)]	R1 = 0.0512, wR2 = 0.1279
R indices (all data)	R1 = 0.0796, wR2 = 0.1505
Extinction coefficient	n/a
Largest diff. peak and hole	0.171 and -0.287 e.$Å^{-3}$

10. The preparation of GSK-3β and the ^{1}H, ^{13}C NMR data

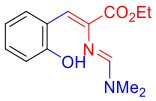
According to reference reported by Kozikowski[7], we take the synthesis of **5a** as an example, the procedure was depicted as follows:



To a suspension of **4a** (57 mg, 0.26 mmol, 1.0 equiv.) and **5a** (50 mg, 0.26 mmol, 1.0 equiv.) in dry THF (2.5 mL, 0.1 M) was added slowly the *t*-BuOK (1.02 mL, 1.0 M in dry THF) at 0 °C, and then the mixtures was warmed to room temperature and stirred overnight. After the raw material was converted completely, the 12 N HCl was added into mixture to quenched the reaction and the mixture was diluted with EA. The organic phase was washed with saturated $NaHCO_3$, NaCl solution and died with Na_2SO_4. The crude product was obtained via evaporating in vacuo, then crude product was purified by column chromatography (PE: EA = 5: 1) as an orange solid.

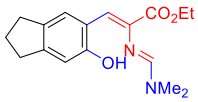
11. IR, ^{1}H, ^{13}C and ^{19}F NMR data of conjugated enamidines derivatives.

ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl)acrylate (3a)



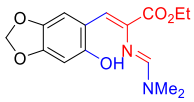
Purified by flash column chromatography (PE: EA= 10:1, v:v), yellow solid (22.3 mg, 85%), m.p.: 78–79 °C; **IR (neat)**: ν =2922, 1697, 1629, 1596, 1114, 752 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.29 (s, 1H), 7.91 (s, 1H), 7.23–7.19 (m, 1H), 7.14 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.08 (s, 1H), 6.91 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.80 (td, *J* = 7.4, 1.3 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.08 (s, 3H), 3.05 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.8, 157.5, 154.8, 133.1, 131.1, 130.6, 127.1, 122.8, 119.2, 118.9, 61.4, 41.4, 35.2, 14.5; **HRMS (ESI)** m/z calcd for $C_{14}H_{19}N_2O_3^+$ $[M+H]^+$ 263.1390, found 263.1390.

ethyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl) acrylate (3b)



Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (21.8 mg, 72%); m.p.:106–108 °C; **IR (neat)**: ν =2922, 2848, 1696, 1608, 1100, 864 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.03 (bs, 1H), 7.88 (s, 1H), 7.09 (s, 1H), 6.99 (s, 1H), 6.79 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.06 (s, 3H), 3.02 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.08–2.00(m, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 156.2, 154.6, 148.0, 134.8, 130.3, 127.9, 127.8, 120.7, 114.8, 61.3, 41.3, 35.1, 33.2, 31.8, 26.0, 14.5; **HRMS (ESI)** m/z calcd for $C_{17}H_{23}N_2O_3^+$ $[M+H]^+$ 303.1703, found 303.1706.

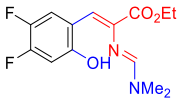
ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl) acrylate (3c)



Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (23.2 mg, 75%); m.p.: 105–110 °C; **IR (neat)**: ν =2920, 2848, 1645, 1262, 1091, 1012 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.36 (bs, 1H), 7.90 (s, 1H), 6.97 (s, 1H), 6.57 (s, 1H), 6.44 (s, 1H), 5.88 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.05 (s, 3H), 3.04 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.8, 154.5, 154.1, 150.1, 140.6, 129.4, 127.2, 114.7, 110.3, 101.3, 100.5, 61.3, 41.4, 35.2, 14.5; **HRMS (ESI)** m/z calcd for $C_{15}H_{19}N_2O_5^+$ $[M+H]^+$ 307.1288, found 307.1289.

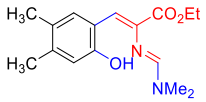
Ethyl (Z)-3-(4,5-difluoro-2-hydroxyphenyl)-2-(((E)-(dimethylamino)methylene)amino) acrylate

(3d)



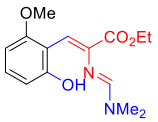
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (26.8 mg, 90%); m.p.: 61–63 °C; **IR (neat)**: ν =2925, 2812, 1700, 1643, 1247, 1021, 837 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.69 (bs, 1H), 7.91 (s, 1H), 6.91 (dd, J = 11.6, 9.2 Hz, 1H), 6.89 (s, 1H) 6.65 (dd, *J* = 12.2, 7.2 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.06 (s, 3H), 3.06 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -135.13 (ddd, *J* = 22.0, 12.0, 9.0 Hz), -151.37 (ddd, *J* = 22.8, 11.4, 7.1 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -135.13 (d, *J* = 22.8 Hz), -151.38 (d, *J* = 22.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 154.8, 154.5 (d, *J*=10.3 Hz), 151.5 (dd, *J* = 249.8, 14.0 Hz), 143.6 (dd, *J* = 237.5, 13.4 Hz), 131.4 (d, *J* = 1.9 Hz), 124.9, 119.4 (d, *J* = 17.7 Hz), 118.7, 107.4 (d, *J* = 18.6 Hz), 61.6, 41.6, 35.3, 14.4; **HRMS (ESI)** m/z calcd for $C_{14}H_{17}F_2N_2O_3^+$ $[M+H]^+$ 299.1202, found 299.1205.

ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxy-4,5-dimethylphenyl) acrylate (3e)



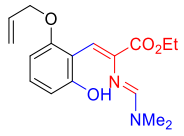
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (25.2 mg, 87%); m.p.: 73–75 °C; **IR (neat)**: ν =2919, 2848, 1695, 1604, 1107, 864 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.05 (bs, 1H), 7.89 (s, 1H), 7.04 (s, 1H), 6.90 (s, 1H), 6.72 (s, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.06 (s, 3H), 3.03 (s, 3H), 2.20 (s, 3H), 2.15 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 155.2, 154.7, 139.9, 133.8, 130.4, 127.4, 126.9, 120.2, 120.0, 61.3, 41.4, 35.2, 19.9, 18.7, 14.5; **HRMS (ESI)** m/z calcd for $C_{16}H_{23}N_2O_3^+$ $[M+H]^+$ 291.1703, found 291.1702.

ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxy-6-methoxyphenyl) acrylate (3f)



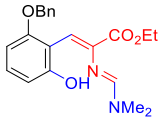
Purified by flash column chromatography (PE: EA= 10:1, v: v), white solid (22.2 mg, 76%); m.p.: 87–89 °C; **IR (neat)**: ν =2920, 2849, 1698, 1632, 1105, 788 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.95 (bs, 1H), 7.86 (s, 1H), 7.52 (s, 1H), 7.18 (t, *J* = 8.2 Hz, 1H), 6.59 (d, *J* = 8.3 Hz, 1H), 6.38 (dd, *J* = 8.1, 1.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.04 (s, 3H), 3.02 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.9, 158.8, 158.7, 154.7, 131.2, 130.6, 121.2, 112.7, 112.4, 100.8, 61.4, 55.9, 41.3, 35.1, 14.5; **HRMS (ESI)** m/z calcd for $C_{15}H_{21}N_2O_4^+$ $[M+H]^+$ 293.1496, found 293.1496.

ethyl (Z)-3-(2-(allyloxy)-6-hydroxyphenyl)-2-(((E)-(dimethylamino)methylene)amino)acrylate (3g)



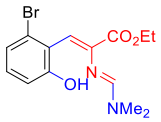
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (26.4 mg, 83%); m.p.: 66–68 °C; **IR (neat)**: ν =2925, 2866, 1703, 1453, 1244, 1105, 765 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.08 (s, 1H),7.89 (s, 1H), 7.64 (s, 1H), 7.15 (t, *J* = 8.2 Hz, 1H), 6.59 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.36 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.08 (ddt, *J* = 17.3, 10.6, 4.7 Hz, 1H), 5.50 (dq, *J* = 17.2, 1.8 Hz, 1H), 5.28 (dq, *J* = 10.6, 1.6 Hz, 1H), 4.56 (dt, *J* = 4.7, 1.7 Hz, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.05 (s, 3H), 3.03 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H)；**^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 158.8, 157.8, 154.7, 133.5, 131.0, 130.6, 121.3, 116.6, 113.1, 112.4, 102.2, 69.1, 61.3, 41.3, 35.2, 14.4; **HRMS (ESI)** m/z calcd for $C_{17}H_{23}N_2O_4^+$ $[M+H]^+$ 319.1652, found 319.1647.

ethyl (Z)-3-(2-(benzyloxy)-6-hydroxyphenyl)-2-(((E)-(dimethylamino)methylene)amino) acrylate (3h)



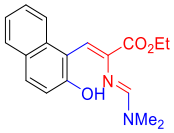
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (29.5 mg, 80%); m.p.: 124–129 °C; **IR (neat)**: ν =2922, 2862, 1700, 1628, 1250, 1111, 762 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.71 (s, 1H), 7.48 (d, *J* = 7.1 Hz, 2H), 7.42–7.35 (m, 2H), 7.35–7.28 (m, 1H), 7.17 (t, *J* = 8.2 Hz, 1H), 6.62 (d, *J* = 8.2 Hz, 1H), 6.45 (dd, *J* = 8.1, 1.0 Hz, 1H), 5.11 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.07 (s, 3H), 3.04 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 158.8, 158.0, 154.6, 137.5, 130.8, 130.7, 128.6 (2C), 127.8, 127.0 (2C), 121.4, 113.1, 112.6, 102.5, 70.5, 61.3, 41.4, 35.2, 14.4; **HRMS (ESI)** m/zcalcd for $C_{21}H_{25}N_2O_4^+$ $[M+H]^+$ 369.1809, found 369.1809.

ethyl (Z)-3-(2-bromo-6-hydroxyphenyl)-2-(((E)-(dimethylamino)methylene)amino)acrylate (3i)

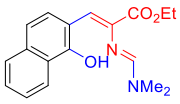


Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (23.2 mg, 68%); m.p.: 79-85 °C ; **IR (neat)**: ν =2958, 1706, 1631, 1444, 1259, 1096, 801 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.44 (s, 1H), 7.13 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 6.90 (dd, *J* = 8.1, 1.2 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.05 (s, 3H), 3.03 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 158.6, 154.9, 132.4, 130.6, 126.0, 125.5, 123.8, 123.4, 119.0, 61.7, 41.5, 35.2, 14.4; **HRMS (ESI)** m/z calcd for $C_{14}H_{17}BrN_2O_3^+$ $[M+H]^+$ 341.0495, found 341.0490.

ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(1-hydroxynaphthalen-2-yl)acrylate and ethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxynaphthalen-1-yl)acrylate (3j/3j')

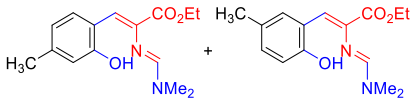


Purified by flash column chromatography (PE: EA= 8:1, v: v), yellow solid (18.7 mg, 60%); m.p.: 75–76 °C; **IR (neat)**: ν =2922, 1700, 1619, 1457, 1111, 804 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.5 Hz, 1H), 7.90 (s, 1H), 7.85 (s, 1H), 7.77–7.72 (m, 2H), 7.51–7.46 (m, 1H), 7.34–7.30 (m, 1H), 7.19 (d, J = 8.9 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 3.06 (s, 3H), 3.04 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 156.3, 154.7, 133.9, 132.0, 131.1, 128.7, 128.5, 126.6, 123.1, 123.0, 123.0, 122.1, 114.7, 61.5, 41.3, 35.1, 14.5; **HRMS (ESI)** m/z calcd for $C_{18}H_{21}N_2O_3^+$ $[M+H]^+$ 313.1547, found 313.1545.



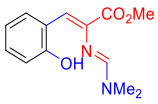
Purified by flash column chromatography (PE: EA= 15:1, v: v), yellow liquid (8.7 mg, 18%); **IR (neat)**: ν =2931, 2854, 1700, 1631, 1253, 1108, 816 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 (d, J = 7.3 Hz, 1H), 7.97 (s, 1H), 7.70 (d, J = 7.2 Hz,1H), 7.48 – 7.37 (m, 2H), 7.25 – 7.18 (m, 3H), 4.31 (q, J = 7.1 Hz, 2H), 3.17 (s, 3H), 3.06 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.8, 154.7, 154.4, 135.3, 130.4, 130.0, 128.2, 127.5, 127.1, 127.0, 124.9, 124.1, 118.2, 115.8, 61.4, 41.5, 35.3, 14.5; **HRMS (ESI)** m/z calcd for $C_{18}H_{21}N_2O_3^+$$[M+H]^+$ 313.15467, found 313.15408.

ethyl (E)-2-(((dimethylamino)methylene)amino)-3-(2-hydroxy-4-methylphenyl)propanoate compound with ethyl (E)-2-(((dimethylamino)methylene)amino)-3-(2-hydroxy-5-methylphenyl) propanoate (3k/3k')



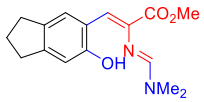
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow liquid (20.3 mg, 73%); **IR (neat)**: ν =2917, 2856, 1700, 1399, 1274, 1095, 797 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.03 (d, J = 8.1 Hz, 2H), 6.73 (s, 1H), 6.62 (d, J = 8.1 Hz, 1H), 4.28 (q, J = 7.2 Hz, 3H), 3.07 (s, 3H), 3.04 (s, 2H), 2.29 (s, 3H), 1.37 (t, J = 7.1, Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.0, 157.3, 154.7, 133.1, 131.5, 130.3, 127.4, 120.1, 119.6, 119.0, 61.3, 41.4, 35.2, 21.4, 14.5; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.05 (d, J = 4.3 Hz, 2H), 6.95 (s, 1H), 6.82 (d, J = 8.2 Hz, 1H), 4.28 (q, J = 7.1, Hz, 3H), 3.07 (s, 3H), 3.04 (s, 2H), 2.25 (s, 3H), 1.37 (t, J = 7.1, Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.9, 155.1, 154.8, 141.3, 133.1, 131.2, 127.9, 127.2, 122.4, 112.0, 61.4, 41.4, 35.2, 20.4, 14.5; **HRMS (ESI)** m/z calcd for $C_{15}H_{20}N_2O_3^+$ $[M+H]^+$ 277.1547, found 277.1546.

methyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl)acrylate (3l)



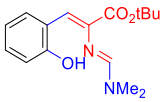
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (16.4 mg, 66%); m.p.: 94–96 °C; **IR (neat)**: ν =2946, 1706, 1631, 1471, 1268, 1117, 754 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.34 (s, 1H), 7.88 (s, 1H), 7.21 (td, *J* = 7.2, 1.7 Hz, 1H), 7.13 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.07 (s, 1H), 6.90 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.80 (td, *J* = 7.4, 1.2 Hz, 1H), 3.83 (s, 3H), 3.07 (s, 3H), 3.03 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.3, 157.5, 154.8, 133.1, 130.9, 130.7, 127.3, 122.7, 119.2, 118.9, 52.3, 41.4, 35.2; **HRMS (ESI)** m/z calcd for $C_{13}H_{17}N_2O_3^+$ $[M+H]^+$ 249.1234, found 249.1236.

Methyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl)acrylate (3m)



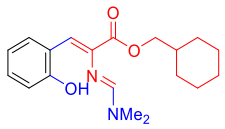
Purified by flash column chromatography (PE: EA= 12:1, v: v), yellow solid (19.0 mg, 66%); m.p.: 120–122 °C; **IR (neat)**: ν =2958, 2851, 1694, 1628, 1256, 1105, 864 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.03 (bs, 1H), 7.87 (s, 1H), 7.08 (s, 1H), 6.98 (s, 1H), 6.79 (s, 1H), 3.82 (s, 3H), 3.06 (s, 3H), 3.03 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.08–2.00 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.4, 156.2, 154.6, 148.2, 134.8, 130.1, 128.1, 127.9, 120.6, 114.9, 52.3, 41.4, 35.2, 33.2, 31.9, 26.0; **HRMS (ESI)** m/z calcd for $C_{16}H_{21}N_2O_3^+$ $[M+H]^+$ 289.1547, found 289.1570.

***tert*-butyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl)acrylate (3n)**

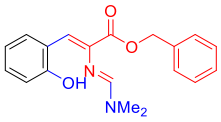


Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (22.0 mg, 76%); m.p.: 76–77 °C; **IR (neat)**: ν =2973, 2806, 1697, 1477, 1277, 1117, 751 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.24 (s, 1H), 7.87 (s, 1H), 7.20 (td, *J* = 7.3, 1.8 Hz, 1H), 7.13 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.01 (s, 1H), 6.90 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.80 (td, *J* = 7.4, 1.2 Hz, 1H), 3.07 (s, 3H), 3.04 (s, 3H), 1.56 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.0, 157.3, 154.7, 132.9, 132.3, 130.3, 126.3, 123.0, 119.2, 118.8, 81.7, 41.3, 35.1, 28.3(3C); **HRMS (ESI)** m/z calcd for $C_{16}H_{23}N_2O_3^+$ $[M+H]^+$ 291.1703, found 291.1705.

cyclohexylmethyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl) acrylate (3o)



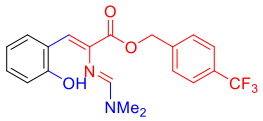
Purified by flash column chromatography (PE: EA= 15:1, v: v), yellow liquid (18.5 mg, 56%); **IR (neat)**: ν =2928, 2851, 1700, 1631, 1471 , 1117, 754 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.35 (bs, 1H), 7.90 (s, 1H), 7.22 (td, *J* = 8.4, 1.7 Hz 1H), 7.15 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.07 (s, 1H), 6.90 (dd, *J* = 8.0 Hz, 1H), 6.81 (t, *J* = 7.7 Hz, 1H), 4.04 (d, *J* = 6.3 Hz, 2H), 3.08 (s, 3H), 3.04 (s, 3H), 1.84–1.73 (m, 5H), 1.31–1.22 (m, 4H), 1.08–1.01 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.9, 157.4, 154.8, 133.2, 131.2, 130.6, 127.0, 122.8, 119.3, 118.9, 70.5, 41.4, 37.3, 35.2, 29.9(2C), 26.5, 25.8(2C); **HRMS (ESI)** m/z calcd for $C_{19}H_{27}N_2O_3^+$ $[M+H]^+$ 331.2016, found 331.2046.



benzyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl)acrylate (3p)

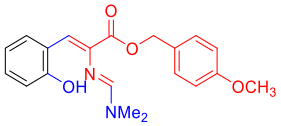
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (23.0 mg, 71%); m.p.: 66–68 °C; **IR (neat)**: ν =2922, 2851, 1709, 1634, 1462, 1117, 751 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.27 (s, 1H), 7.90 (s, 1H), 7.46–7.32 (m, 5H), 7.21 (td, *J* = 8.3, 1.7 Hz, 1H), 7.14–7.12 (m, *J* = 7.3 Hz, 2H), 6.90 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.79 (td, *J* = 8.2, 1.2 Hz, 1H), 5.28 (s, 2H), 3.08 (s, 3H), 3.02 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 157.6, 154.8, 136.1, 133.3, 130.9, 130.8, 128.8 (2C), 128.5, 128.3 (2C), 127.7, 122.7, 119.3, 118.9, 67.1, 41.4, 35.2; **HRMS (ESI)** m/z calcd for $C_{19}H_{21}N_2O_3^+$ $[M+H]^+$ 325.1547, found 325.1541.

4-(trifluoromethyl)benzyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxy-phenyl)acrylate (3q)



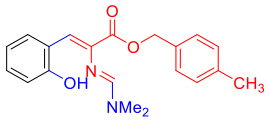
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (19.6 mg, 50%); m.p.: 84–85°C; **IR (neat)**: ν =2934, 2815, 1703, 1643, 1268, 1096, 754 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.24 (bs, 1H), 7.90 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.23 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 7.16 (s, 1H), 7.14 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.91 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.81 (td, *J* = 7.4, 1.2 Hz, 1H), 5.32 (s, 2H), 3.08 (s, 3H), 3.04 (s, 3H); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -62.59; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.59; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.4, 157.6, 154.8, 140.1, 133.2, 131.0, 130.6 (q, *J* = 32.3 Hz), 130.5, 128.2(2C), 128.0, 125.8 (q, *J* = 3.8 Hz), 124.1(q, *J* = 272.3 Hz), 122.8, 122.6, 119.3, 119.0, 66.1, 41.4, 35.2; **HRMS (ESI)** m/z calcd for $C_{20}H_{20}F_3N_2O_3^+$ $[M+H]^+$ 393.1421, found 393.1414.

4-methoxybenzyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl) acrylate (3r)



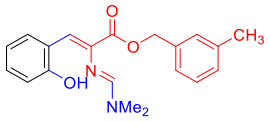
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (21.2 mg, 60%); m.p.: 84–86 °C; **IR (neat)**: ν =2928, 1700, 1631, 1381, 1253, 1114, 754 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.28 (s, 1H), 7.89 (s, 1H), 7.38–7.34 (m, 2H), 7.22–7.18 (m, 1H), 7.12 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.08 (s, 1H), 6.93–6.88 (m, 3H), 6.78 (td, *J* = 7.4, 1.3 Hz, 1H), 5.21 (s, 2H), 3.82 (s, 3H), 3.07 (s, 3H), 3.02 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 159.8, 157.5, 154.8, 133.2, 131.1, 130.7, 130.2, 128.2, 127.5, 122.8, 119.2, 118.9, 114.1, 114.1, 66.9, 55.5, 41.4, 35.2, 29.8; **HRMS (ESI)** m/z calcd for $C_{20}H_{22}N_2O_4Na^+$ $[M+Na]^+$ 377.1472, found 377.1470.

4-methylbenzyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl) acrylate (3s)



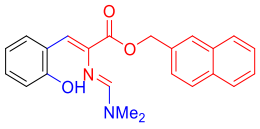
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (19.6 mg, 58%); m.p.: 131–132 °C; **IR (neat)**: ν =2925, 2806, 1700, 1631, 1265, 1114, 757 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.23–7.19 (m, 3H), 7.13–7.11 (m, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 5.24 (s, 2H), 3.08 (s, 3H), 3.02 (s, 3H), 2.37 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 157.5, 154.8, 138.3, 133.2, 133.0, 130.9, 130.7, 129.4 (2C), 128.4 (2C), 127.6, 122.7, 119.2, 118.9, 67.0, 41.4, 35.2, 21.4; **HRMS (ESI)**m/z calcd for $C_{20}H_{23}N_2O_3^+$ $[M+H]^+$ 339.1703, found 339.1702.

3-methylbenzyl (Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxyphenyl) acrylate (3t)



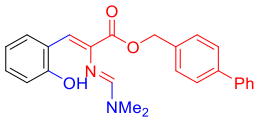
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow liquid (18.5 mg, 55%); **IR (neat)**: ν =2925, 2857, 1700, 1634, 1262, 1117, 751 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.24 (bs, 1H), 7.92 (s, 1H), 7.33–7.25 (m, 1H), 7.24–7.19 (m, 3H), 7.18–7.11 (m, 3H), 6.94 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.4 Hz, 1H), 5.24 (s, 2H), 3.10 (s, 3H), 3.04 (s, 3H), 2.38 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.6, 157.3, 154.7, 138.5, 135.9, 133.2, 130.9, 130.5, 129.2, 129.0, 128.7, 127.8, 125.4, 122.6, 119.2, 119.0, 67.2, 41.6, 35.4, 21.6; **HRMS (ESI)** m/z calcd for $C_{20}H_{23}N_2O_3^+$ $[M+H]^+$ 339.1703, found 339.1737.

naphthalen-2-ylmethyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxy-phenyl)acrylate (3u)



Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (18.7 mg, 50%); m.p.: 85–86 °C; **IR (neat)**: ν =2925, 2857, 1700, 1468, 1259, 1117, 748 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.32 (bs, 1H), 7.92–7.84 (m, 5H), 7.55–7.49 (m, 3H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.18 (s, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 5.44 (s, 2H), 3.08 (s, 3H), 3.02 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.6, 157.5, 154.8, 133.4, 133.3, 133.3, 133.2, 130.8, 128.6, 128.1, 127.9, 127.7, 127.5, 126.5, 126.5, 125.9, 122.7, 119.3, 118.9, 67.3, 41.5, 35.3; **HRMS (ESI)** m/z calcd for $C_{23}H_{23}N_2O_3^+$ $[M+H]^+$ 375.1703, found 375.1735.

[1,1'-biphenyl]-4-ylmethyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(2-hydroxy-phenyl)acrylate (3v)

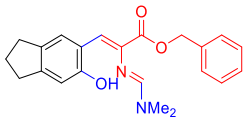


Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (19.2 mg, 48%); m.p.: 115–117 °C; **IR (neat)**: ν =2922, 2854, 1703, 1634, 1471, 1265, 1111, 760 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.35 (s, 1H), 7.92 (s, 1H), 7.65–7.59 (m, 4H), 7.52 – 7.50 (m, 2H), 7.48–7.44 (m, 2H), 7.39–7.35 (m, 1H), 7.25–7.21 (td, *J* = 7.2, 1.7 Hz, 1H), 7.18 (s, 1H), 7.15 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 6.81 (td, *J* = 7.4, 1.3 Hz, 1H), 5.33 (s, 2H), 3.09 (s, 3H), 3.03 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.6, 157.5, 154.8, 141.4, 140.7, 135.0, 133.2, 130.8, 130.8, 128.9(2C), 128.8(2C), 127.7, 127.6, 127.5(2C), 127.2(2C), 122.7, 119.3, 118.9, 66.8, 41.4, 35.2. **HRMS (ESI)** m/z calcd for $C_{25}H_{25}N_2O_3^+$ $[M+H]^+$ 401.1860, found 401.1861.

(E)-N'-((E)-2-(2-hydroxyphenyl)-1-tosylvinyl)-N,N-dimethylformimidamide (3w)

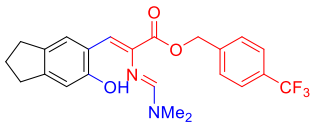
Purified by flash column chromatography (PE: EA= 8:1, v: v), colorless solid (22.7 mg, 66%); m.p.: 93–94 °C; **IR (neat)**: ν =2922, 2854, 1628, 1474, 1262, 1146, 754 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 8.08 (s, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.25–7.15 (m, 3H), 6.85 (t, *J* = 8.2 Hz, 2H), 3.06 (s, 3H), 2.97 (s, 3H), 2.43 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 156.6, 155.0, 144.4, 139.8, 137.8, 133.1, 131.1, 129.9(2C), 127.8(2C), 124.9, 121.0, 119.6, 119.2, 41.5, 34.9, 21.7; **HRMS (ESI)** m/z calcd for $C_{18}H_{21}N_2O_3S^+$ $[M+H]^+$ 345.1267 found 345.1271.

benzyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl)acrylate (3bp)



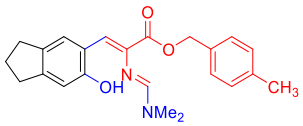
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (23.6 mg, 65%); m.p.: 144–146 °C; **IR (neat)**: ν =2925, 2848, 1700, 1637, 1477, 1259, 1099, 795 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.05 (s, 1H), 7.88 (s, 1H), 7.44–7.36 (m, 5H), 7.16 (s, 1H), 6.98 (s, 1H), 6.81 (s, 1H), 5.27 (s, 2H), 3.06 (s, 3H), 3.01 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.03 (dt, *J* = 14.8, 7.4 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 156.2, 154.6, 148.2, 136.1, 134.8, 129.9, 128.7(2C), 128.4(2C), 128.2(2C), 128.0, 120.5, 114.9, 67.0, 41.4, 35.2, 33.2, 31.8, 26.0; **HRMS (ESI)** m/z calcd for $C_{22}H_{25}N_2O_3^+$ $[M+H]^+$ 365.1860, found 365.1887.

4-(trifluoromethyl)benzyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl)acrylate (3bq)



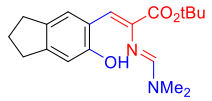
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (21.2 mg, 49%); m.p.: 123–126 °C; **IR (neat)**: ν =2958, 2848, 1703, 1640 , 1256, 1111, 822 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.05 (s, 1H), 7.88 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.18 (s, 1H), 6.98 (s, 1H), 6.81 (s, 1H), 5.31 (s, 2H), 3.07 (s, 3H), 3.02 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.04 (dt, *J* = 14.6, 7.3 Hz, 2H); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -62.55; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.55; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.5, 156.3, 154.6, 148.5, 140.2, 134. 9, 130.5 (q, *J* = 32.5 Hz), 129.6, 128.8, 128.1(2C), 128.0, 125.7 (q, *J* = 3.8 Hz), 124.1(q, *J* = 272.1 Hz), 120.4, 114.9, 66.0, 41.4, 35.2, 33.2, 31.8, 26.0; **HRMS (ESI)** m/z calcd for $C_{23}H_{24}F_3N_2O_3^+$ $[M+H]^+$ 433.1734, found 433.1732.

4-methylbenzyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl)acrylate (3bs)



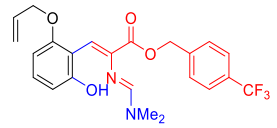
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow solid (29.1 mg, 77%); m.p.: 130-132 °C; **IR (neat)**: ν =2922, 2851, 1697, 1634, 1471, 1096, 801 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.05 (bs, 1H), 7.87 (s, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.13 (s, 1H), 6.97 (s, 1H), 6.79 (s, 1H), 5.22 (s, 2H), 3.06 (s, 3H), 3.01 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.79 (t, *J* = 7.3 Hz, 2H), 2.37 (s, 3H), 2.03 (dt, *J* = 14.6, 7.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.8, 156.2, 154.6, 148.2, 138.2, 134.8, 133.1, 130.0, 129.4(2C), 128.4(2C), 128.2, 128.0, 120.6, 114.8, 66.9, 41.3, 35.2, 33.2, 31.8, 26.0, 21.4; **HRMS (ESI)** m/z calcd for $C_{23}H_{27}N_2O_3^+$ $[M+H]^+$ 379.2016, found 379.2047.

ter.t.-butyl(Z)-2-(((E)-(dimethylamino)methylene)amino)-3-(6-hydroxy-2,3-dihydro-1H-inden-5-yl)acrylate (3bn)



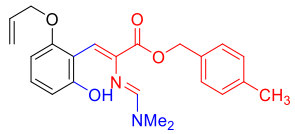
Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow liquid (22.1 mg, 67%); **IR (neat)**: ν =2928, 2848, 1694, 1634, 1283, 1102, 851 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.97 (bs, 1H), 7.84 (s, 1H), 7.02 (s, 1H), 6.98 (s, 1H), 6.79 (s, 1H), 3.05 (s, 3H), 3.02 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.80 (t, *J* = 7.3 Hz, 2H), 2.04 (dt, *J* = 14.8, 7.4 Hz, 2H), 1.55 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.1, 156.1, 154.6, 147.7, 134.7, 131.5, 127.7, 127.1, 120.9, 114.9, 81.5, 41.3, 35.1, 33.2, 31.9, 28.4(3C), 26.0; **HRMS (ESI)** m/z calcd for $C_{19}H_{27}N_2O_3^+$ $[M+H]^+$ 331.2016, found 331.2011.

4-(trifluoromethyl)benzyl (Z)-3-(2-(allyloxy)-6-hydroxyphenyl)-2-(((E)-(dimethylamino) methylene)amino)acrylate (3gq)



Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow liquid (22.4 mg, 50%); **IR (neat)**: ν =2920, 2851, 1706, 1634, 1259, 1099, 816 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.09 (s, 1H), 7.89 (s, 1H), 7.73 (s, 1H), 7.64 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.17 (t, *J* = 8.2 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 6.36 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.03 (ddt, *J* = 17.3, 10.6, 4.9 Hz, 1H), 5.40 (dq, *J* = 17.2, 1.8 Hz, 1H), 5.32 (s, 2H), 5.18 (dq, *J* = 10.5, 1.6 Hz, 1H), 4.53 (dt, *J* = 4.9, 1.7 Hz, 2H), 3.05 (s, 3H), 3.03 (s, 3H); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -62.57; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.57; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.5, 158.9, 157.8, 154.6, 140.2 (q, *J* = 1.4 Hz), 133.4, 130.9, 130.4, 130.3(q, *J* = 32.7 Hz), 128.0(2C), 125.7 (q, *J* = 3.7 Hz, 2C), 124.2(q, *J* = 272.3 Hz), 122.2, 116.9, 112.9, 112.4, 102.1, 69.2, 66.0, 41.4, 35.2; **HRMS (ESI)** m/z calcd for $C_{23}H_{24}F_3N_2O_4^+$ $[M+H]^+$ 449.1683, found 449.1718.

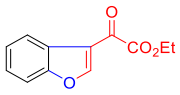
4-methylbenzyl (Z)-3-(2-(allyloxy)-6-hydroxyphenyl)-2-(((E)-(dimethylamino)methylene) amino)acrylate (3gs)



Purified by flash column chromatography (PE: EA= 10:1, v: v), yellow liquid (26.4 mg, 67%); **IR (neat)**: ν =2920, 2849, 1700, 1634, 1248, 1107, 802 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.12 (bs, 1H), 7.88 (s, 1H), 7.69 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 8.1 Hz, 1H), 6.58 (d, *J* = 8.2 Hz, 1H), 6.35 (dd, *J* = 8.2, 1.0 Hz, 1H), 6.03 (ddt, *J* = 17.3, 10.6, 4.8 Hz, 1H), 5.40 (dq, *J* = 17.4, 1.7 Hz, 1H), 5.24 (s, 2H), 5.18 (dq, *J* = 10.6, 1.6 Hz, 1H), 4.52 (dt, *J* = 4.9, 1.7 Hz, 2H), 3.05 (s, 3H), 3.02 (s, 3H), 2.36 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.7, 158.8, 157.8, 154.6, 138.0, 133.4, 133.2, 130.7, 129.3(2C), 128.2(2C), 121.9, 116.8, 113.0, 112.4, 102.1, 69.2, 66.9, 41.3, 35.2, 29.8, 21.4; **HRMS (ESI)** m/z calcd for $C_{23}H_{26}N_2O_4Na^+$$[M+Na]^+$ 417.1785, found 417.1782.

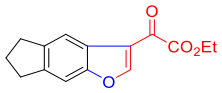
12. IR,^{1}H,^{13}C and ^{19}F NMR data of Benzofuran-3-oxoacetate derivatives

ethyl 2-(benzofuran-3-yl)-2-oxoacetate (4a)[8]



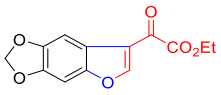
Purified by flash column chromatography (PE: EA= 100:1, v: v), white liquid (17.8 mg, 82%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.31 –8.26 (m, 1H), 7.59–7.54 (m, 1H), 7.47–7.36 (m, 2H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.6, 161.2, 156.1, 155.2, 126.4, 125.2, 124.3, 123.0, 118.8, 111.7, 62.9, 14.2; **HRMS (ESI)** m/z calcd for $C_{12}H_{10}O_4Na^+$ $[M+Na]^+$ 241.0471, found 241.0472.

ethyl 2-(6,7-dihydro-5H-indeno[5,6-b]furan-3-yl)-2-oxoacetate (4b)



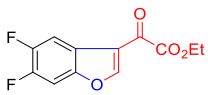
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (21.1 mg, 82%); m.p.: 67–69 °C; **IR (neat)**: ν =2922, 2847, 1729, 1672, 1110, 795 cm^{-1}. **^{1}H NMR** (400 MHz, CDCl3) δ 8.79 (s, 1H), 8.06 (s, 1H), 7.37 (s, 1H), 4.43 (q, J = 7.1 Hz, 2H), 3.17–2.88 (m, 4H), 2.15 (dt, J = 14.6, 7.3 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl3) δ 178.7, 161.4, 155.9, 154.9, 143.7, 141.9, 122.8, 118.8, 117.7, 107.4, 62.8, 33.2, 32.6, 26.6, 14.2; **HRMS (ESI)** m/z calcd for $C_{15}H_{14}O_4Na$+ [M+Na]+ 281.0784, found 281.0809.

ethyl 2-([1,3]dioxolo[4,5-f]benzofuran-7-yl)-2-oxoacetate (4c)



Purified by flash column chromatography (PE: EA= 100:1, v: v), yellow solid (17.8 mg, 68%); m.p.: 114–115 °C; **IR (neat)**: ν =2911, 2848, 1729, 1670, 1143, 834 cm^{-1} .**^{1}H NMR** (400 MHz, CDCl3) δ 8.75 (s, 1H), 7.63 (s, 1H), 7.01 (s, 1H), 6.03 (s, 2H), 4.42 (q, J = 7.1 Hz, 2H), 1.44 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, CDCl3) δ 178.6, 161.2, 155.2, 150.6, 147.6, 146.5, 119.2, 117.8, 102.0, 101.2, 93.6, 62.8, 14.2; **HRMS (ESI)** m/z calcd for $C_{13}H_{10}O_6Na$+ [M+Na]+ 285.0370, found 285.0397.

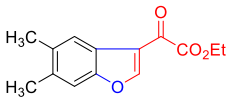
ethyl 2-(5,6-difluorobenzofuran-3-yl)-2-oxoacetate (4d)



Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (16.8 mg, 66%); m.p.:

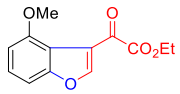
99–101 °C; **IR (neat)**: ν =2922, 2852, 1731, 1669, 1014, 794 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.06 (dd, *J* = 9.8, 7.9 Hz, 1H), 7.40 (dd, *J* = 9.3, 6.2 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -136.19 (dt, *J* = 20.0, 8.6 Hz), -139.78 (ddd, *J* = 20.0, 9.7, 6.2 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -136.19 (d, *J* = 20.0 Hz), -139.79 (d, *J* = 19.8 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.1, 160.8, 157.1 (d, *J* = 3.6 Hz), 151.1 (d, *J* = 16.4 Hz), 150.0 (d, *J* = 10.9 Hz), 148.7, 120.1 (d, *J* = 9.5 Hz), 118.8, 110.1 (d, *J* = 21.7 Hz), 101.2 (d, *J* = 22.6 Hz), 63.1, 14.2; **HRMS (ESI)** m/z calcd for $C_{12}H_8F_2O_4Na^+$ $[M+Na]^+$ 277.0283, found 277.0284.

ethyl 2-(5,6-dimethylbenzofuran-3-yl)-2-oxoacetate (4e)



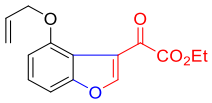
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (16.7 mg, 68%); m.p.: 72–73°C; **IR (neat)**: ν =2921, 2849, 1730, 1672, 1063, 828 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.01 (s, 1H), 7.33 (s, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 2.38 (s, 7H), 1.45 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.7, 161.4, 155.6, 154.3, 135.7, 134.1, 122.8, 122.0, 118.7, 112.0, 62.8, 20.7, 20.2, 14.2; **HRMS (ESI)** m/z calcd for $C_{14}H_{14}O_4Na^+$ $[M+Na]^+$ 269.0784, found 269.0808.

ethyl 2-(4-methoxybenzofuran-3-yl)-2-oxoacetate (4f)



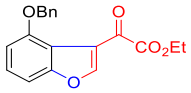
Purified by flash column chromatography (PE: EA= 100:1, v: v), yellow liquid (17.3 mg, 70%); **IR (neat)**: ν =2985, 2836, 1729, 1691, 1075, 805 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 7.18 (d, *J* = 8.2 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.40 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 1.40 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 180.3, 162.8, 157.0, 154.5, 152.8, 127.2, 119.8, 113.6, 105.7, 105.0, 62.5, 56.0, 14.2; **HRMS (ESI)** m/z calcd for $C_{13}H_{12}O_5Na^+$ $[M+Na]^+$ 271.0577, found 271.0577.

ethyl 2-(4-(allyloxy)benzofuran-3-yl)-2-oxoacetate (4g)



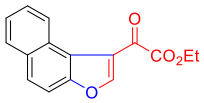
Purified by flash column chromatography (PE: EA= 100:1, v: v), white liquid (22.7 mg, 83%); **IR (neat)**: ν =2984, 2866, 1732, 1684, 1111, 777 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.30 (t, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.3, 0.7 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 6.12 (ddt, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.53 (dq, *J* = 17.3, 1.6 Hz, 1H), 5.32 (dq, *J* = 10.6, 1.5 Hz, 1H), 4.67 (dt, *J* = 5.2, 1.6 Hz, 2H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.9, 162.6, 157.1, 153.5, 153.1, 132.9, 127.1, 119.9, 118.0, 113.9, 107.0, 105.1, 70.0, 62.6, 14.1; **HRMS (ESI)** m/z calcd for $C_{15}H_{14}O_5Na^+$ $[M+Na]^+$ 297.0733, found 297.0736.

ethyl 2-(4-(benzyloxy)benzofuran-3-yl)-2-oxoacetate (4h)



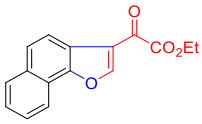
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (22.6 mg, 70%); m.p.: 124–126 °C; **IR (neat)**: ν =2985, 2859, 1729, 1688, 1114, 777 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.34–7.26 (m, 2H), 7.19 (d, *J* = 8.2 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.22 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.9, 162.7, 157.2, 153.5, 153.1, 136.6, 128.7(2C), 128.0, 127.4(2C), 127.1, 119.9, 114.0, 107.4, 105.2, 70.9, 62.5, 14.1; **HRMS (ESI)** m/z calcd for $C_{19}H_{16}O_5Na^+$ $[M+Na]^+$ 347.0890, found 347.0891.

ethyl 2-(naphtho[1,2-b]furan-3-yl)-2-oxoacetate (4i)



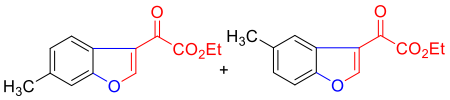
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (19.3 mg, 72%); m.p.: 73-75 °C; **IR (neat)**: ν =2919, 1731, 1672, 1014, 825 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.34 – 8.29 (m, 2H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.6 Hz, 1H), 7.67 – 7.62 (m, 1H), 7.59 - 7.55 (m, 1H), 4.47 (q, *J* = 7.2 Hz, 3H), 1.47 (t, *J* = 7.1 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.9, 161.3, 154.7, 151.2, 132.4, 128.6, 127.1, 126.4, 125.8, 120.9, 120.5, 120.2, 120.1, 119.8, 62.9, 14.2; **HRMS (ESI)** m/z calcd for $C_{16}H_{12}O_4Na^+$ $[M+Na]^+$ 291.0628, found 291.0654.

ethyl 2-(naphtho[2,1-b]furan-1-yl)-2-oxoacetate (4j)



Purified by flash column chromatography (PE: EA= 200:1, v: v), white solid (17.4 mg, 65%); m.p.: 86-88 °C; **IR (neat)**: ν =2920, 1728, 1679, 1039, 801 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.45 – 9.36 (m, 1H), 8.91 (s, 1H), 7.94 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.58 – 7.53 (m, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.6, 162.8, 156.6, 154.1, 131.7, 128.8(2C), 128.2, 127.5, 127.0, 125.7, 121.4, 119.0, 112.0, 62.9, 14.2; **HRMS (ESI)** m/z calcd for $C_{16}H_{12}O_4Na^+$ $[M+Na]^+$ 291.0628, found 291.0653.

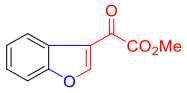
ethyl 2-(5-methylbenzofuran-3-yl)-2-oxoacetate and ethyl 2-(6-methylbenzofuran-3-yl)-2-oxoacetate (4k/4k')



Purified by flash column chromatography (PE: EA= 100:1, v: v), yellow liquid (15.1 mg, 65%); **IR (neat)**: ν =2921, 2848, 1785, 1645, 1054, 783 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.06 (d, *J* = 1.7 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.20 (d, *J* = 4.5 Hz, 1H), 4.43 (q, *J* = 7.1 Hz,

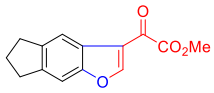
2H), 2.48 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.5, 161.3, 156.3, 155.7, 136.8, 126.6, 122.3, 121.7, 118.8, 111.8, 62.8, 21.8, 14.2; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.35 (s, 1H), 7.22 (d, J = 3.2 Hz, 2H), 4.43 (q, J = 7.1 Hz, 2H), 2.48 (s, 3H), 1.44 (t, J = 7.2, Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.6, 161.3, 155.7, 153.7, 135.0, 127.5, 124.3, 122.7, 118.6, 111.2, 62.8, 21.5, 14.2; **HRMS (ESI)** m/z calcd for $C_{13}H_{12}O_4Na^+$ $[M+Na]^+$ 255.0628, found 255.0653.

methyl 2-(benzofuran-3-yl)-2-oxoacetate (4l)[9]



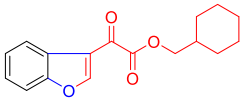
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (15.3 mg, 75%); m.p.: 73–75 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.31–8.26 (m, 1H), 7.61–7.53 (m, 1H), 7.47–7.37 (m, 2H), 3.99 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.1, 161.6, 156.3, 155.2, 126.4, 125.2, 124.2, 123.0, 118.8, 111.7, 53.4; **HRMS (ESI)** m/z calcd for $C_{11}H_8O_4Na^+$ $[M+Na]^+$ 227.0315, found 227.0315.

methyl 2-(6,7-dihydro-5H-indeno[5,6-b]furan-3-yl)-2-oxoacetate (4m)



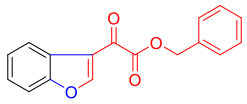
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (16.1 mg, 66%); m.p.: 73–75 °C; **IR (neat)**: ν =2922, 1774, 1648, 1054, 834 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.06 (s, 1H), 7.38 (s, 1H), 3.98 (s, 3H), 3.01 (t, J = 6.9 Hz, 4H), 2.20–2.11 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.2, 161.8, 156.0, 154.9, 143.8, 141.9, 122.7, 118.8, 117.7, 107.4, 53.3, 33.2, 32.6, 26.6; **HRMS (ESI)** m/z calcd for $C_{14}H_{12}O_4Na^+$ $[M+Na]^+$ 267.0628, found 267.0655.

cyclohexylmethyl 2-(benzofuran-3-yl)-2-oxoacetate (4n)



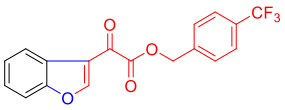
Purified by flash column chromatography (PE: EA= 150:1, v: v), white solid (22.0 mg, 77%); m.p.: 52–53 °C; **IR (neat)**: ν =2923, 2852, 1727, 1675, 1084, 746 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.32–8.24 (m, 1H), 7.61–7.54 (m, 1H), 7.46–7.37 (m, 2H), 4.18 (d, J = 6.3 Hz, 2H), 1.87–1.67 (m, 6H), 1.34–1.23 (m, 3H), 1.13–0.98 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.6, 161.4, 156.1, 155.2, 126.3, 125.2, 124.3, 122.9, 118.9, 111.7, 71.7, 37.1, 29.7(2C), 26.3, 25.7(2C); **HRMS (ESI)** m/z calcd for $C_{17}H_{18}O_4Na^+$ $[M+Na]^+$ 309.1097, found 309.1097.

benzyl 2-(benzofuran-3-yl)-2-oxoacetate (4o)



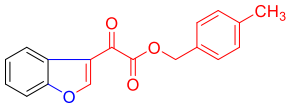
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (17.9 mg, 64%); m.p.: 88–90 °C; **IR (neat)**: ν =2961, 2848, 1729, 1673, 1111, 801 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.31–8.23 (m, 1H), 7.58–7.53 (m, 1H), 7.50–7.46 (m, 2H), 7.44–7.37 (m, 5H), 5.41 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.1, 161.0, 156.1, 155.2, 134.6, 129.0, 128.9(2C), 128.8(2C), 126.4, 125.2, 124.2, 122.9, 118.8, 111.7, 68.3; **HRMS (ESI)** m/z calcd for $C_{16}H_{12}O_4Na^+$ $[M+Na]^+$ 303.0628, found 303.0657.

4-(trifluoromethyl)benzyl 2-(benzofuran-3-yl)-2-oxoacetate (4p)



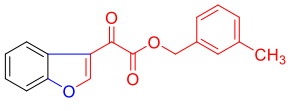
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (18.8 mg, 54%); m.p.:90–91 °C; **IR (neat)**: ν =2922, 2846, 1735, 1679, 1122, 751 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.31–8.22 (m, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.62–7.55 (m, 3H), 7.46–7.39 (m, 2H), 5.44 (s, 2H); **^{19}F{^{1}H} NMR** (376 MHz, $CDCl_3$) δ -62.69; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.69; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 177.7, 160.8, 156.2, 155.2, 138.5, 130.5(q, J = 32.5Hz), 128.7(2C), 126.5, 125.91 (q, J = 3.8 Hz, 2C), 125.4, 124.2, 124.1(q, J = 241.2 Hz), 122.7, 118.8, 111.8, 67.2; **HRMS (ESI)** m/z calcd for $C_{18}H_{11}F_3O_4Na^+$ $[M+Na]^+$ 371.0502, found 371.0502.

4-methylbenzyl 2-(benzofuran-3-yl)-2-oxoacetate (4q)



Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (23.5 mg, 80%); m.p.:70–71 °C; **IR (neat)**: ν =2921, 1728, 1674, 1083, 747 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.31–8.22 (m, 1H), 7.62–7.51 (m, 1H), 7.46–7.33 (m, 4H), 7.21 (d, J = 7.8 Hz, 2H), 5.37 (s, 2H), 2.37 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.2, 161.0, 156.1, 155.2, 138.9, 131.6, 129.6(2C), 129.0(2C), 126.3, 125.2, 124.3, 122.9, 118.8, 111.7, 68.3, 21.4; **HRMS (ESI)** m/z calcd for $C_{18}H_{14}O_4Na^+$ $[M+Na]^+$ 317.0784, found 317.0785.

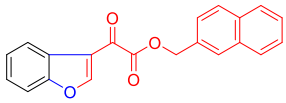
3-methylbenzyl 2-(benzofuran-3-yl)-2-oxoacetate (4r)



Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (21.2 mg, 72%); m.p.:79–81 °C; **IR (neat)**: ν =2922, 1735, 1676, 1125, 751 cm^{-1}.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.36–8.18 (m, 1H), 7.65–7.50 (m, 1H), 7.43–7.38 (m, 2H), 7.32–7.25 (m, 3H), 7.18 (d, J = 7.0 Hz, 1H), 5.37 (s, 2H), 2.38 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.2, 161.0, 156.1, 155.2, 138.7, 134.5, 129.7, 129.5, 128.8, 126.3, 125.9, 125.2, 124.3, 122.9, 118.8, 111.7, 68.4,

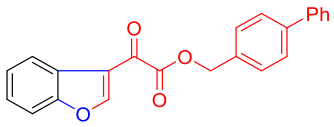
21.5; **HRMS (ESI)** m/z calcd for $C_{18}H_{14}O_4Na^+$ $[M+Na]^+$ 317.0784, found 317.0785.

naphthalen-2-ylmethyl 2-(benzofuran-3-yl)-2-oxoacetate (4s)



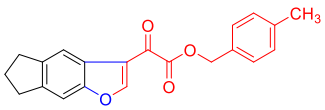
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (20.8 mg, 63%); m.p.: 129–130 °C; **IR (neat)**: ν =2961, 1732, 1658, 1087, 751 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.33–8.23 (m, 1H), 7.96 (s, 1H), 7.91–7.83 (m, 3H), 7.59–7.49 (m, 4H), 7.44–7.37 (m, 2H), 5.57 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.1, 161.0, 156.2, 155.2, 133.5, 133.3, 132.0, 128.8, 128.2(2C), 127.9, 126.7, 126.6, 126.4, 126.0, 125.2, 124.2, 122.9, 118.8, 111.7, 68.5; **HRMS (ESI)** m/z calcd for $C_{21}H_{14}O_4Na^+$ $[M+Na]^+$ 353.0784, found 353.0785.

[1,1'-biphenyl]-4-ylmethyl 2-(benzofuran-3-yl)-2-oxoacetate (4t)



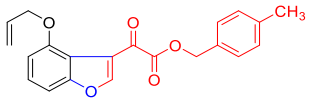
Purified by flash column chromatography (PE: EA= 100:1, v: v), white solid (23.5 mg, 66%); m.p.: 119–121 °C; **IR (neat)**: ν =2920, 1741, 1661, 1122, 733 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.31–8.25 (m, 1H), 7.66–7.53 (m, 7H), 7.49–7.40 (m, 4H), 7.39–7.34 (m, 1H), 5.45 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.1, 161.0, 156.2, 155.2, 141.9, 140.6, 133.5, 129.3(2C), 129.0(2C), 127.7, 127.6(2C), 127.3(2C), 126.4, 125.2, 124.2, 122.9, 118.8, 111.7, 68.1; **HRMS (ESI)** m/z calcd for $C_{23}H_{16}O_4Na^+$ $[M+Na]^+$ 379.0941, found 379.0942.

4-methylbenzyl 2-(6,7-dihydro-5H-indeno[5,6-b]furan-3-yl)-2-oxoacetate (4bs)



Purified by flash column chromatography (PE: EA= 100:1), white solid (20.0 mg, 60%); m.p.: 84–86 °C; **IR (neat)**: ν =2961, 1729, 1676, 1108, 804 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.04 (s, 1H), 7.37 (d, J = 7.9 Hz, 1H), 7.20 (d, J = 7.8 Hz, 2H), 5.36 (s, 2H), 3.00 (t, J = 7.4 Hz, 4H), 2.37 (s, 3H), 2.15 (dt, J = 14.6, 7.3 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.4, 161.2, 155.8, 154.9, 143.7, 141.9, 138.9, 131.7, 129.6(2C), 129.0(2C), 122.7, 118.8, 117.7, 107.4, 68.2, 33.2, 32.6, 26.6, 21.4; **HRMS (ESI)** m/z calcd for $C_{21}H_{18}O_4Na^+$ $[M+Na]^+$ 357.1097, found 357.1099.

4-methylbenzyl 2-(4-(allyloxy)benzofuran-3-yl)-2-oxoacetate (4gs)



Purified by flash column chromatography (PE: EA= 100:1, v: v), light yellow liquid (22.4 mg, 64%); **IR (neat)**: ν =2985, 1729, 1682, 1122, 804 cm^{-1} .**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.33–7.28 (m, 3H), 7.17 (dd, *J* = 8.2, 3.6 Hz, 3H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.10 (ddt, *J* = 17.3, 10.5, 5.2 Hz, 1H), 5.52 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.36 – 5.28 (m, 3H), 4.63 (dt, *J* = 5.2, 1.7 Hz, 2H), 2.35 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.7, 162.5, 157.1, 153.5, 153.1, 138.7, 132.9, 131.7, 129.5(2C), 128.8(2C), 127.1, 119.9, 118.1, 113.8, 107.0, 105.1, 69.9, 68.0, 21.4; **HRMS (ESI)** m/z calcd for $C_{21}H_{18}O_5Na^+$ $[M+Na]^+$ 373.1046, found 373.1044.

13. References

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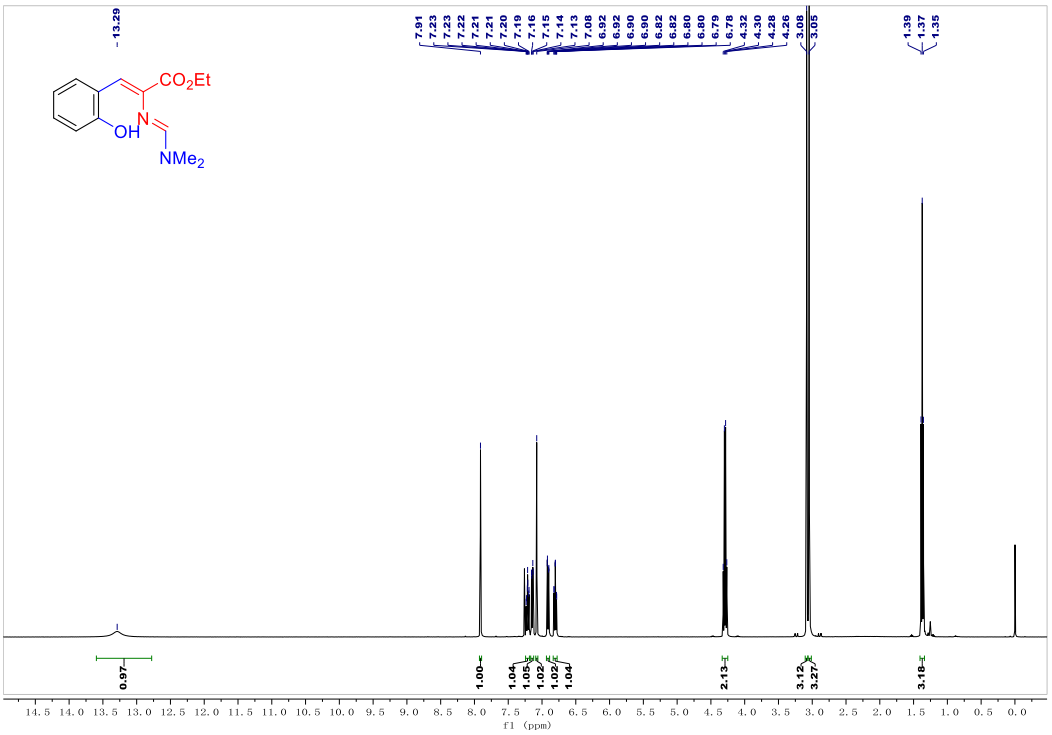
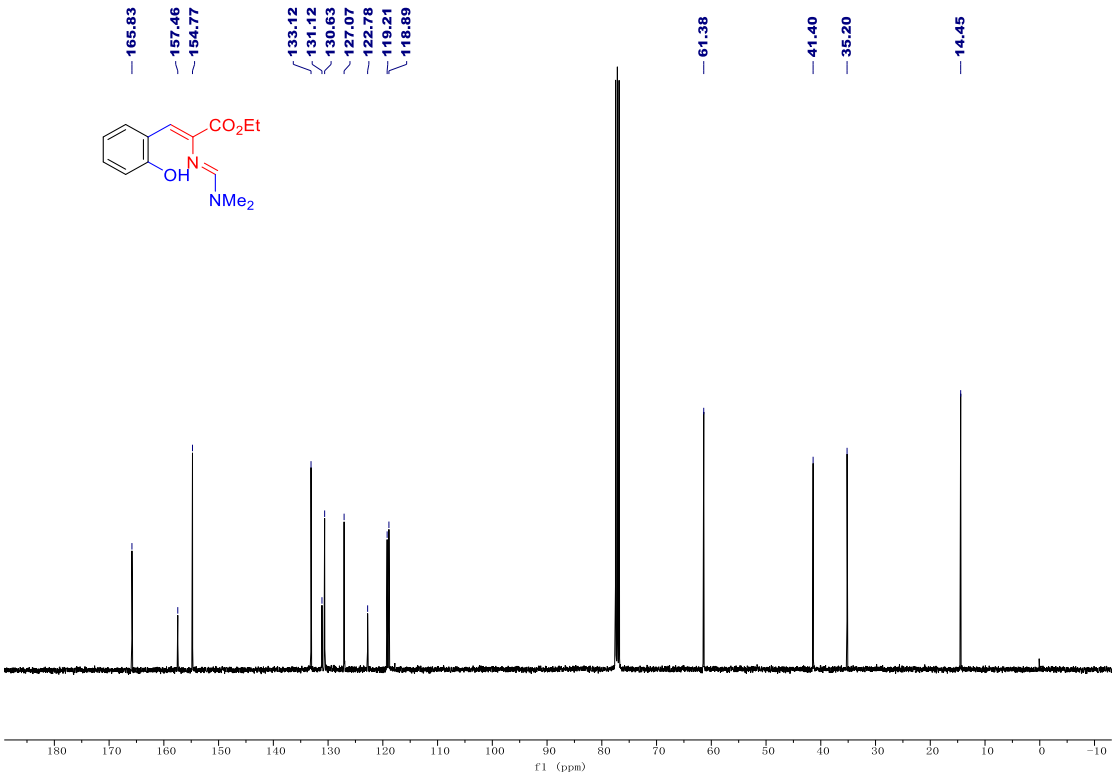
14. ^{1}H, ^{13}C and ^{19}F NMR Spectra of conjugated enamidines derivatives.

3a ^{1}H NMR



3a ^{13}C NMR



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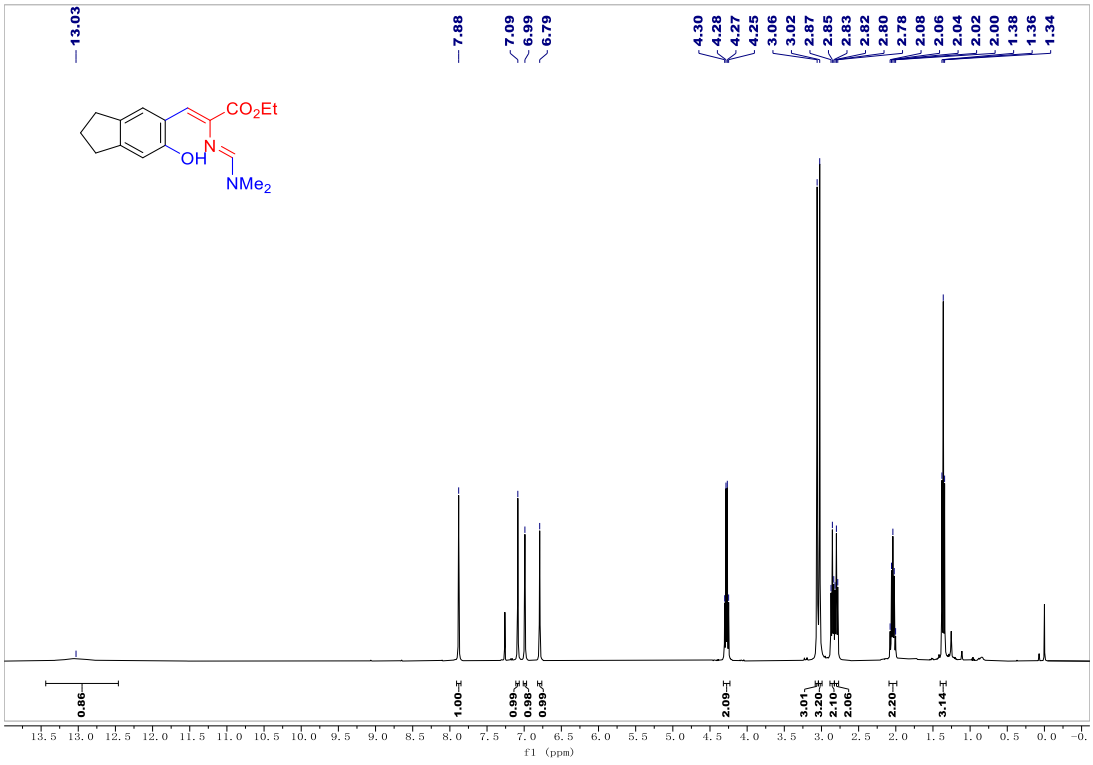

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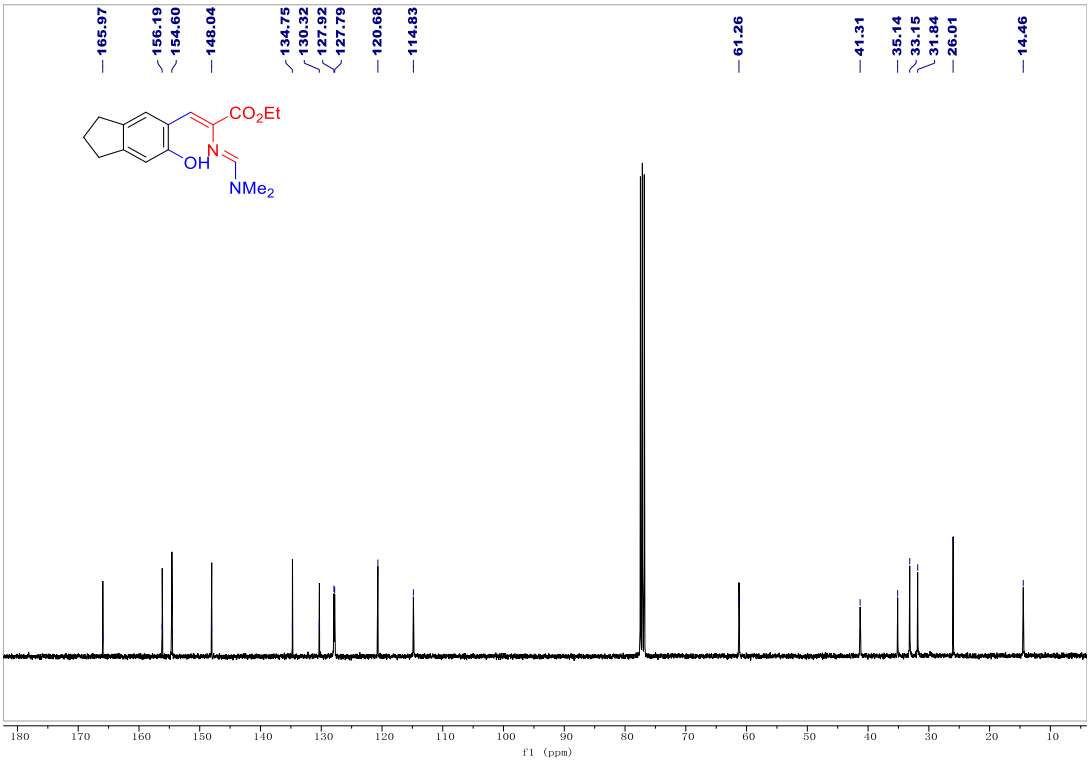

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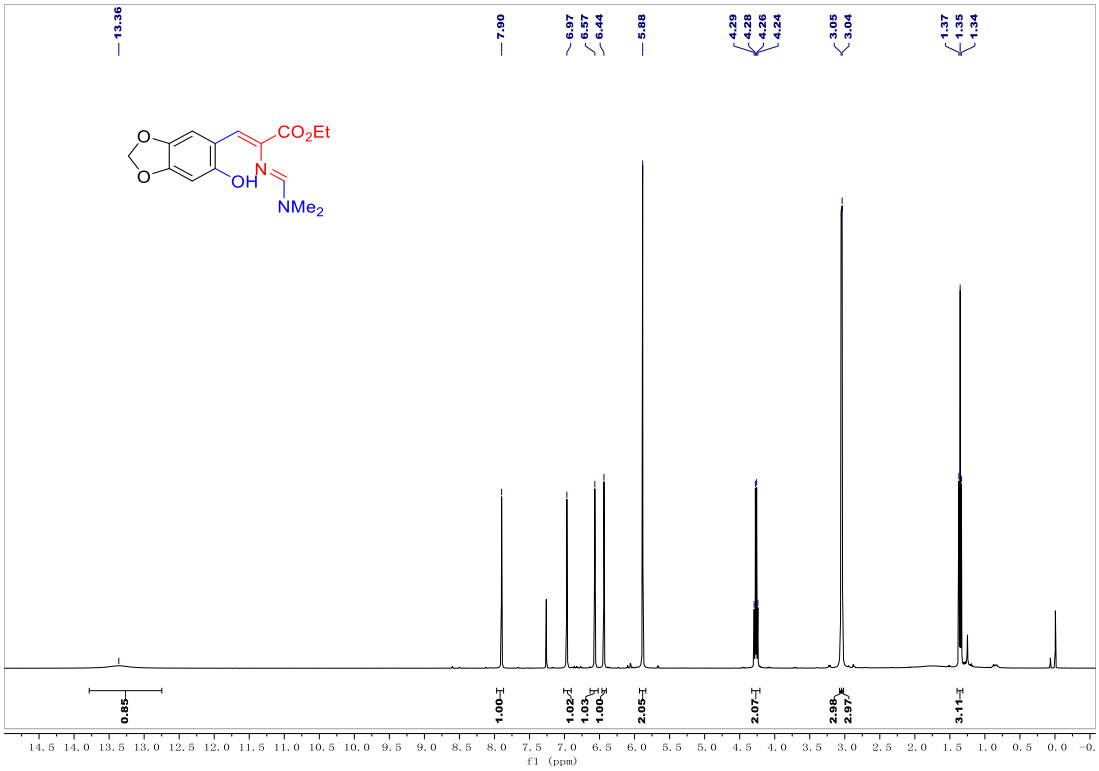

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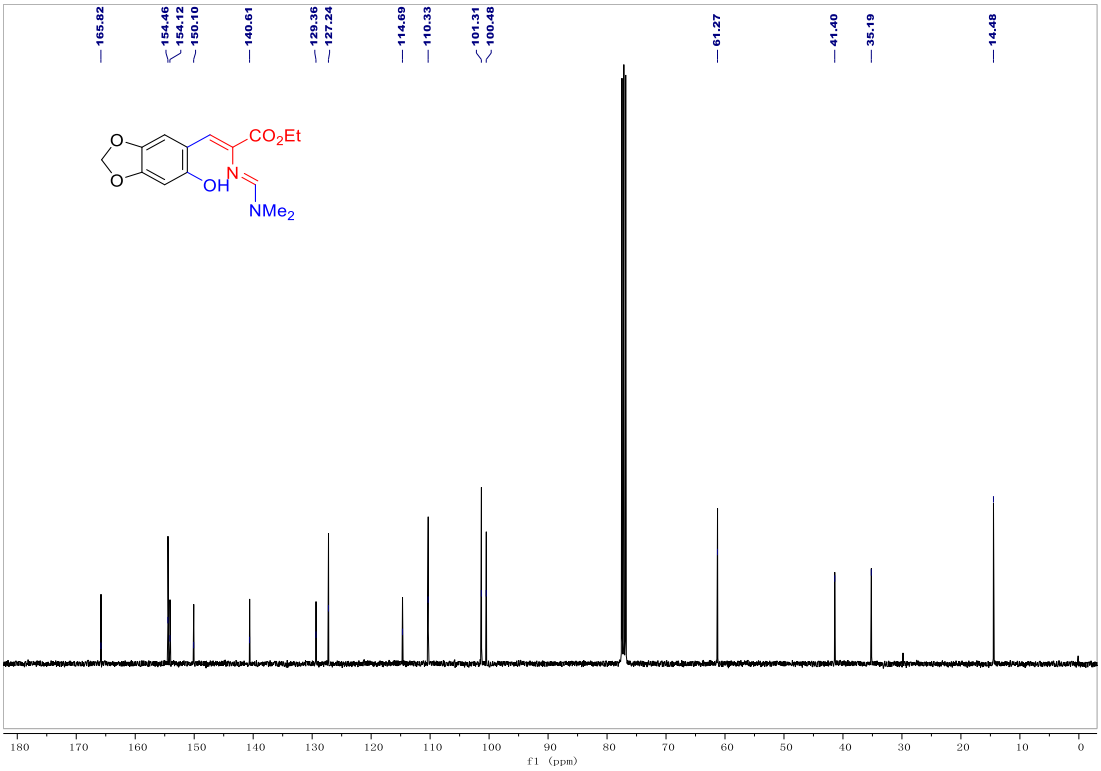
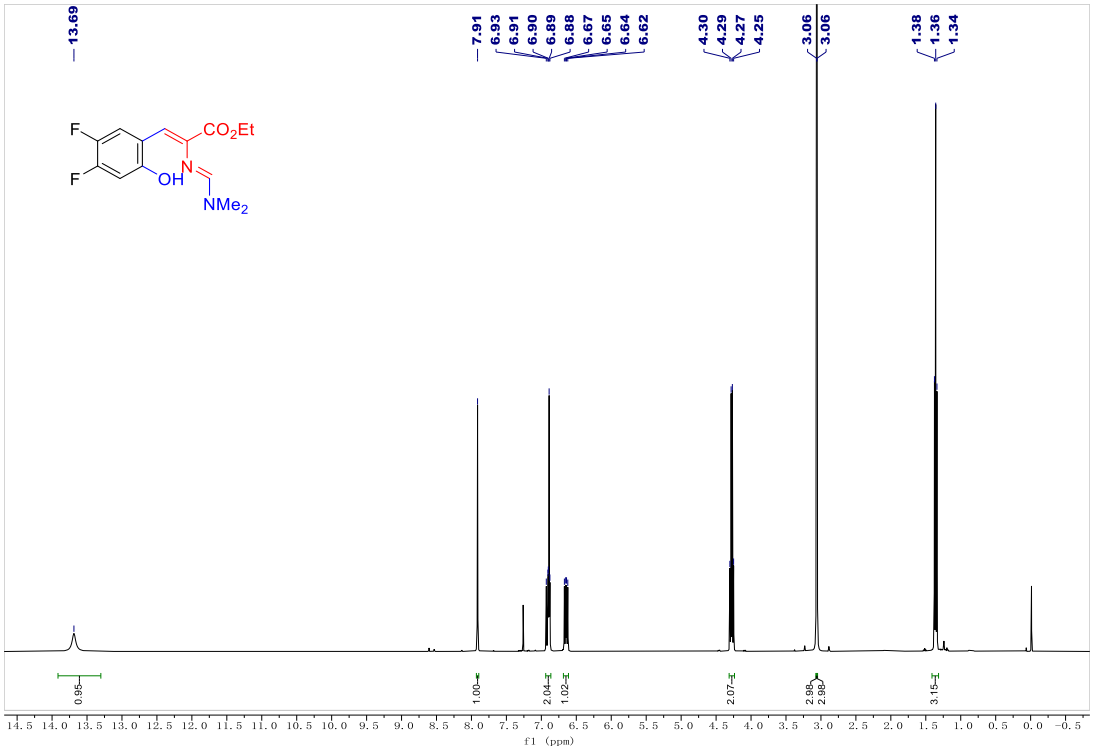
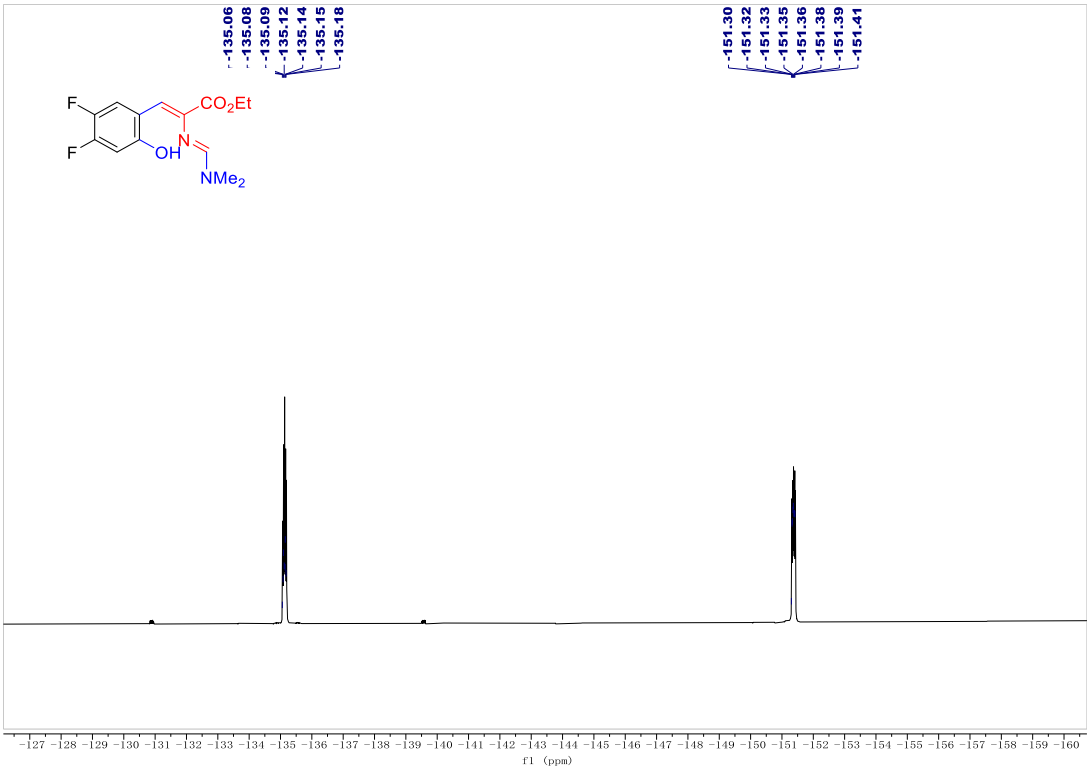


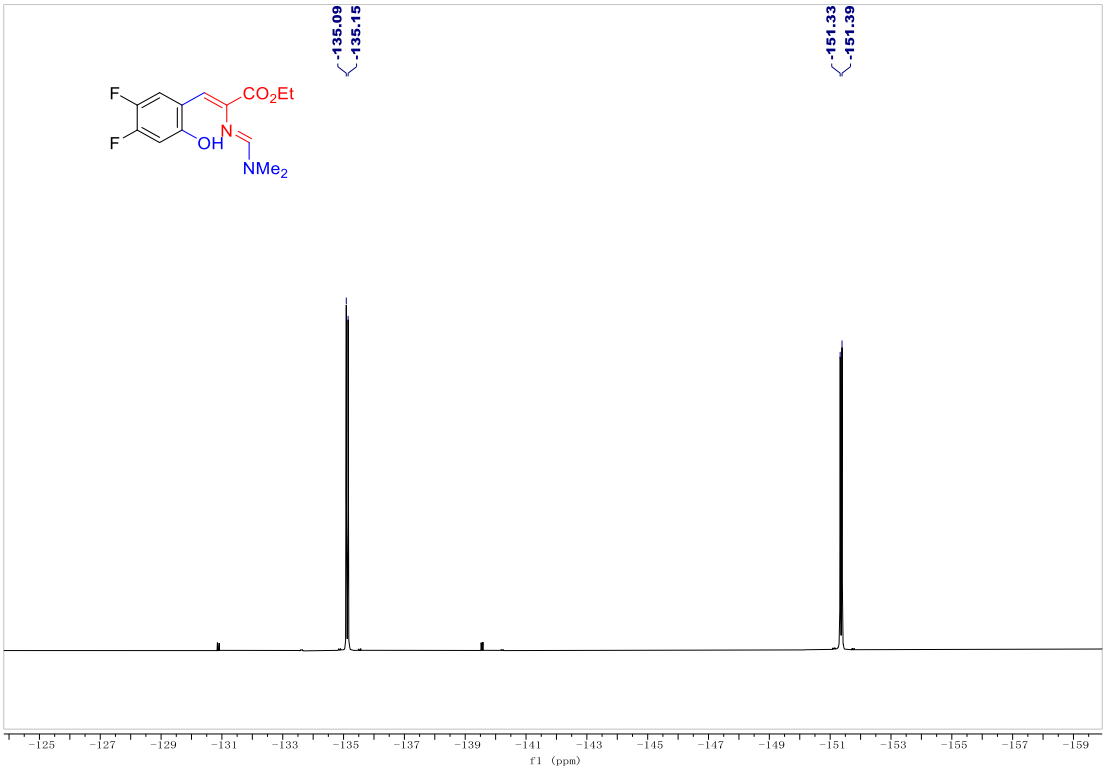
3d ^{1}H NMR



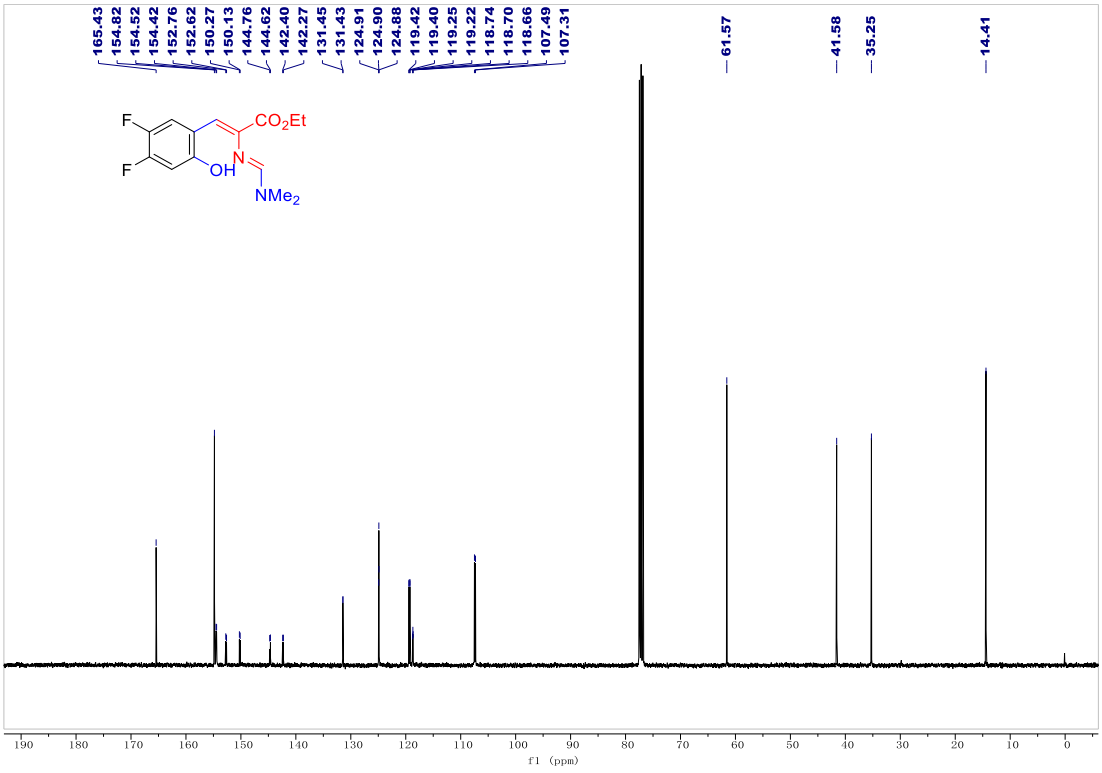
3d ^{19}F{1H} NMR



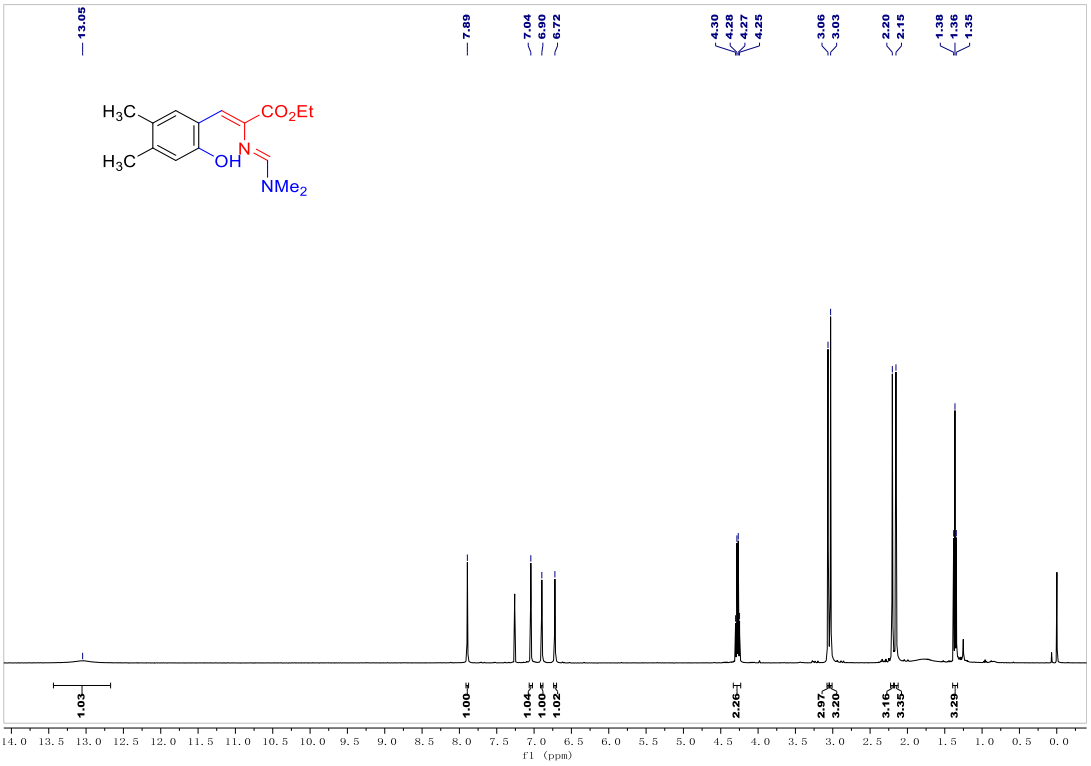
3d ^{19}F NMR



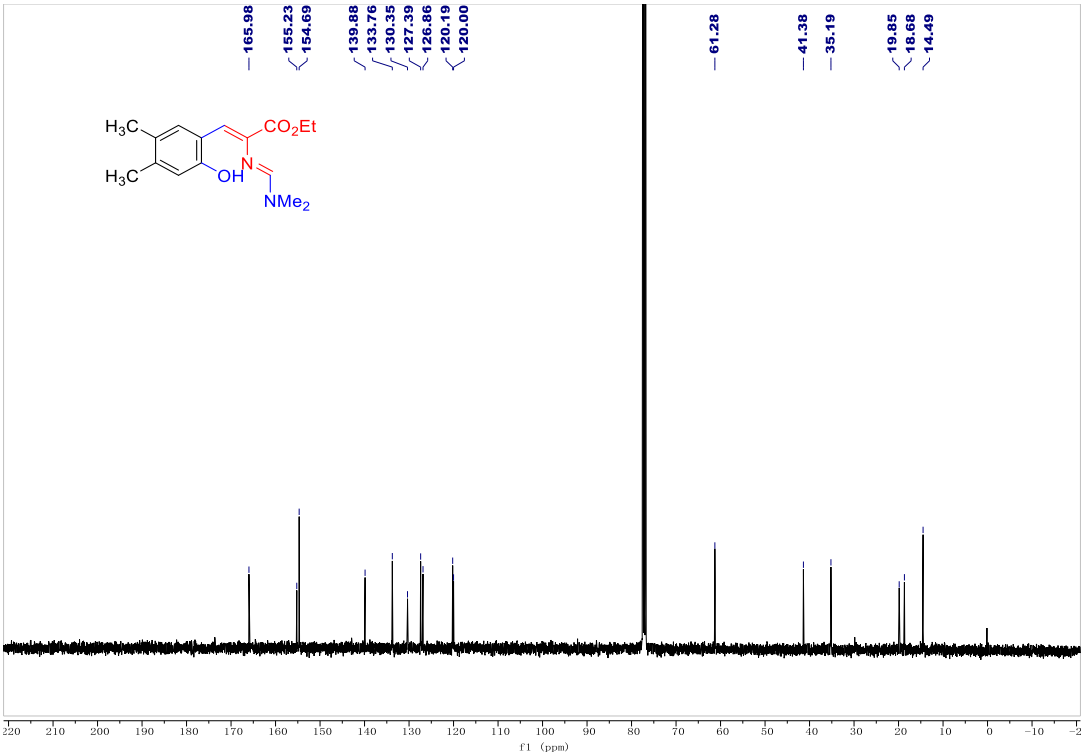
3d ^{13}C NMR



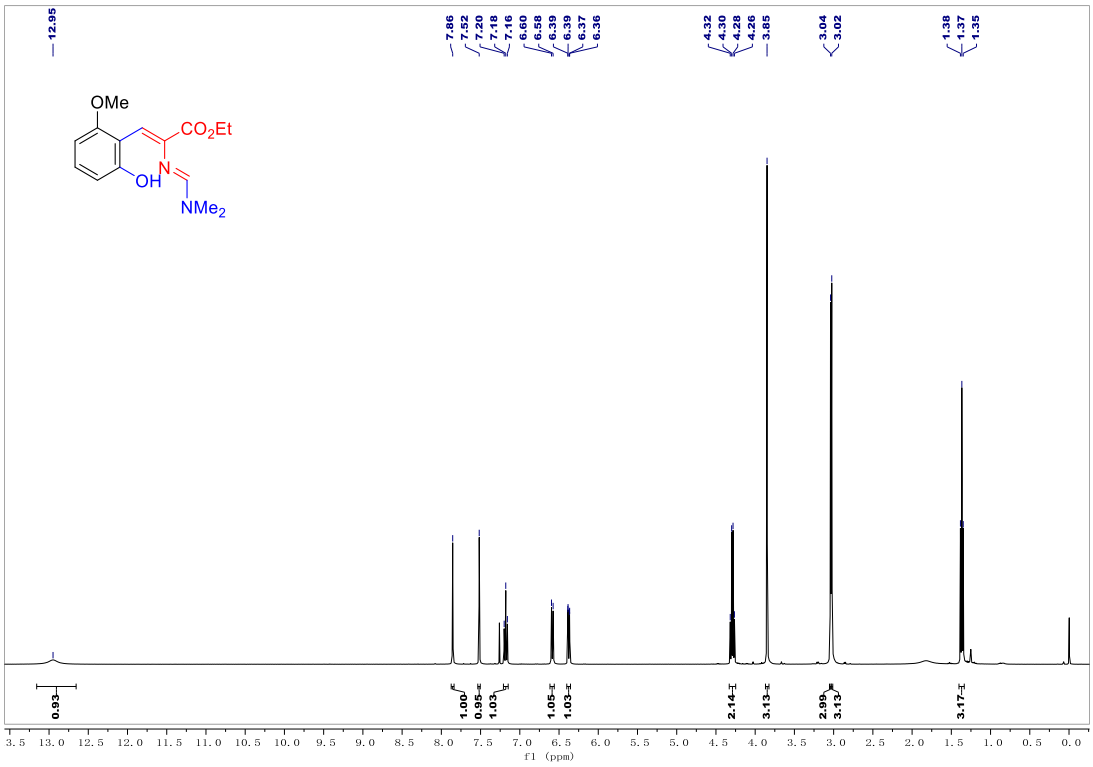
3e ^{1}H NMR



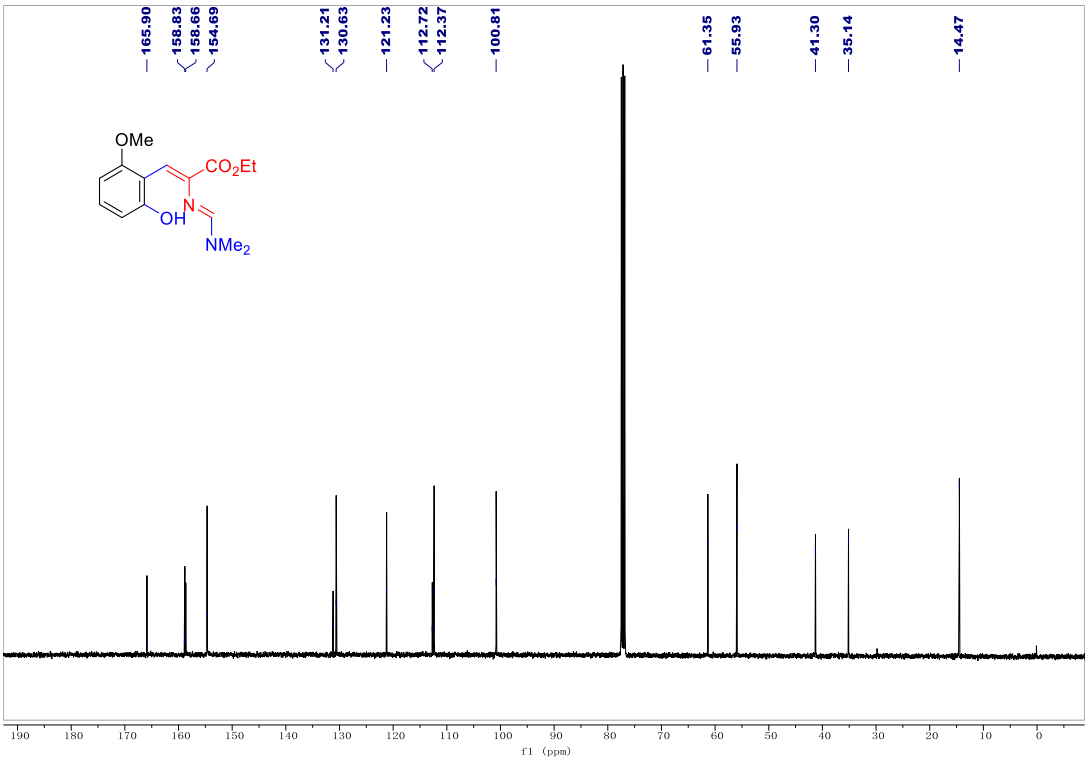
3e ^{13}C NMR



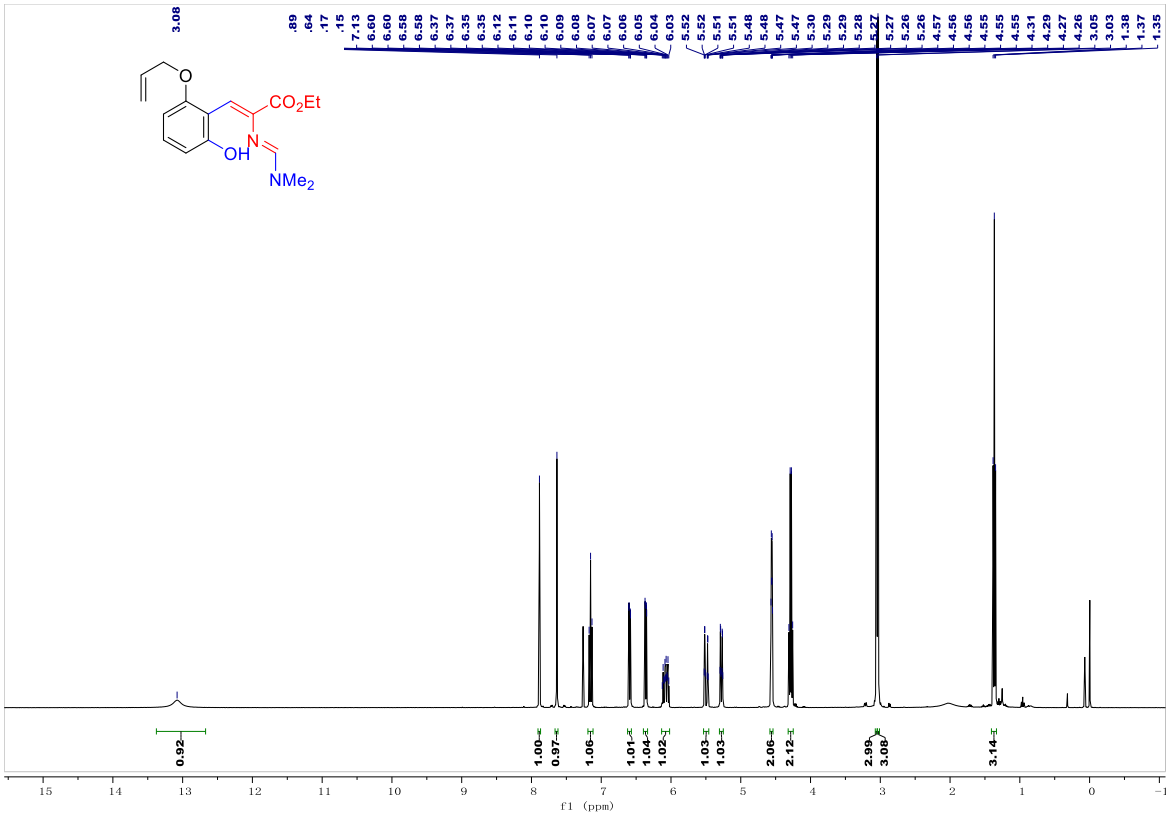
3f ^{1}H NMR



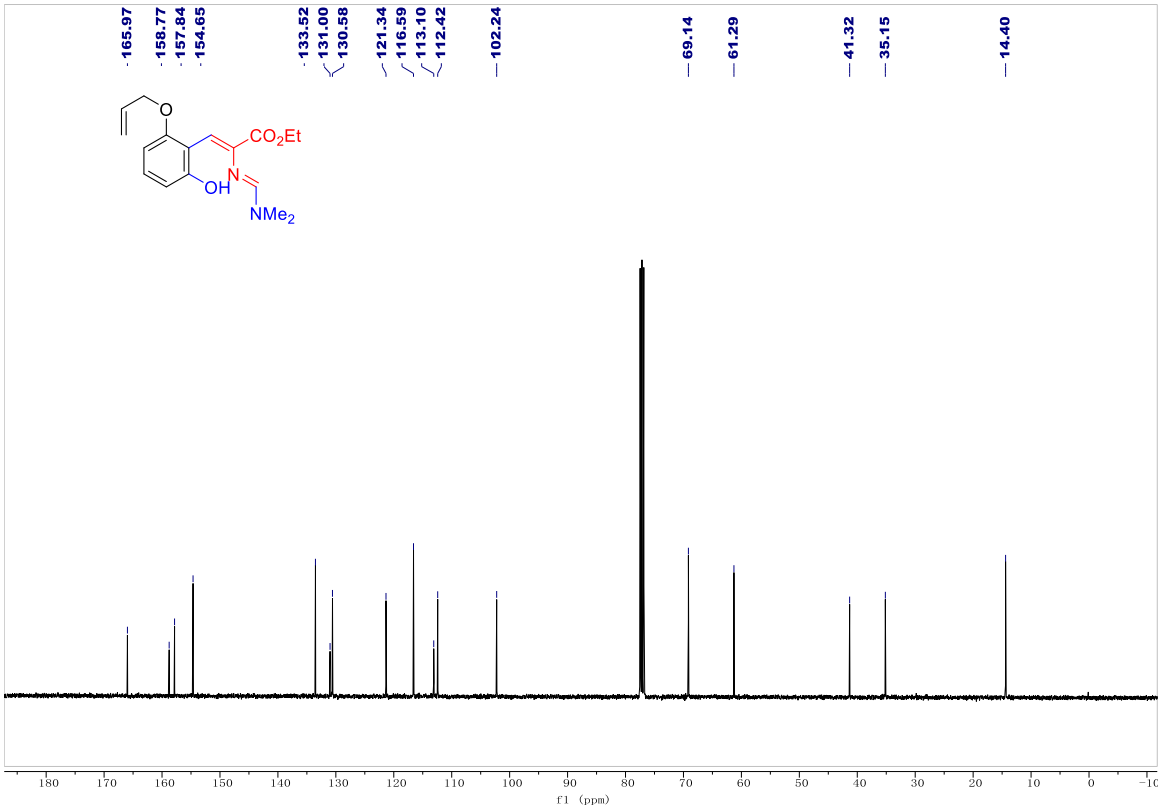
3f ^{13}C NMR



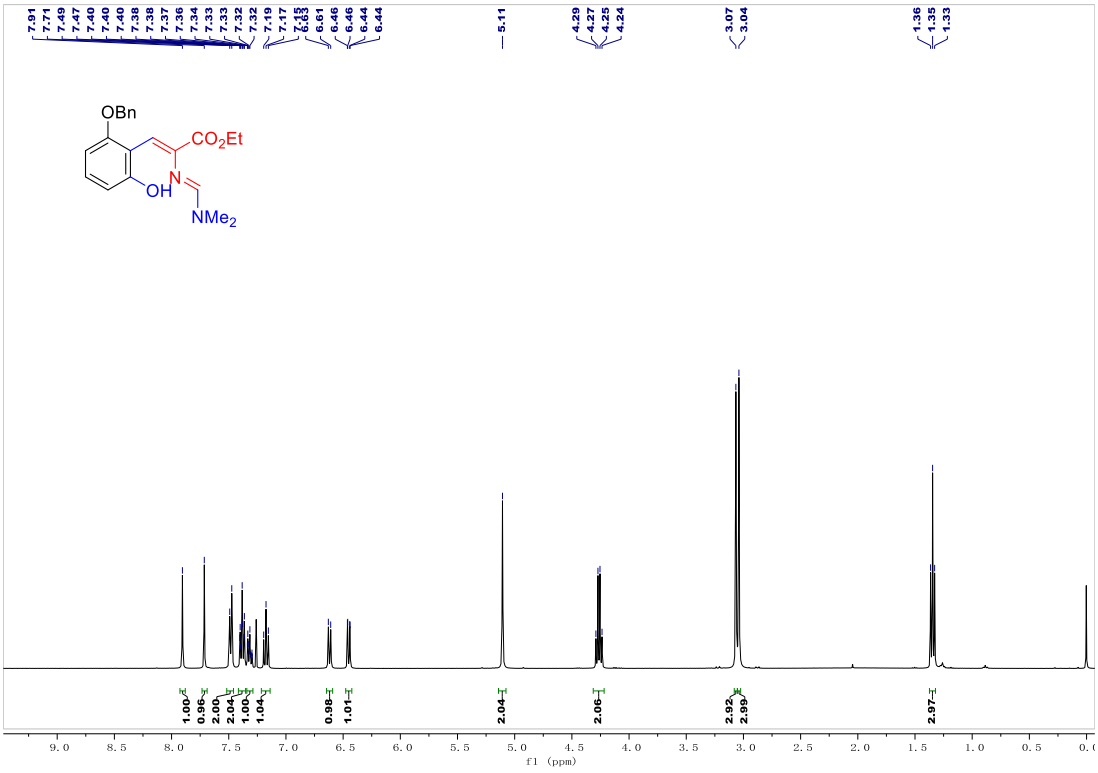
3g ^{1}H NMR



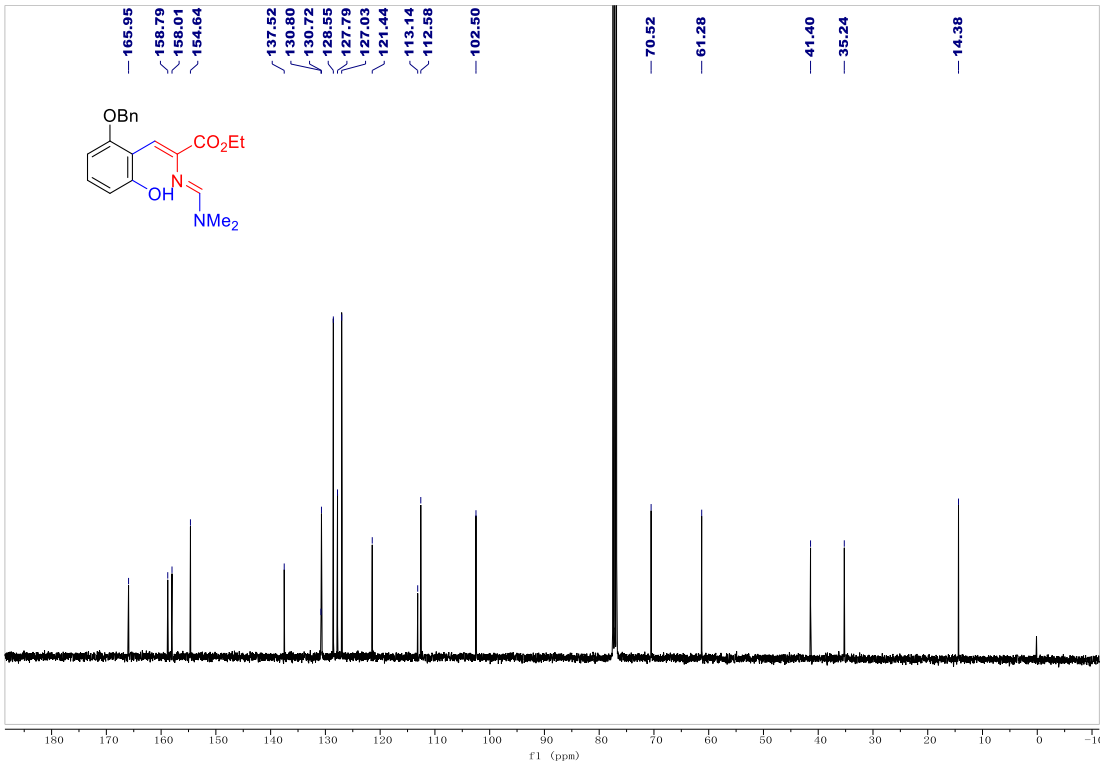
3g ^{13}C NMR



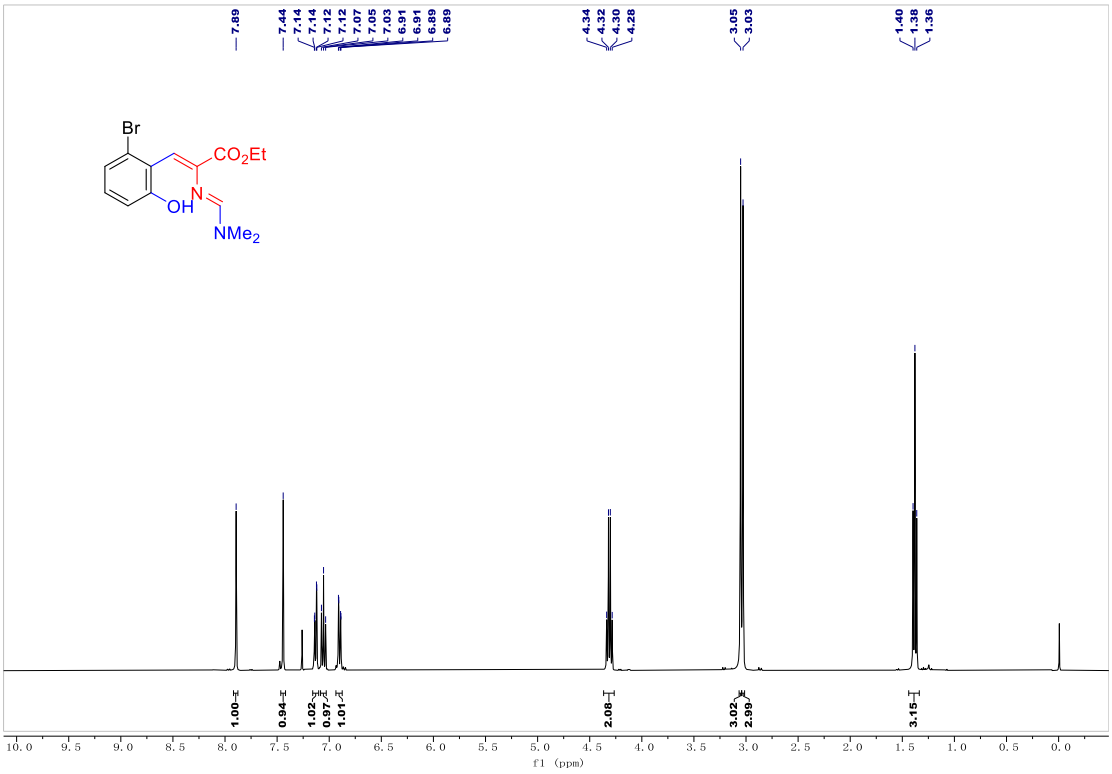
3h ^{1}H NMR



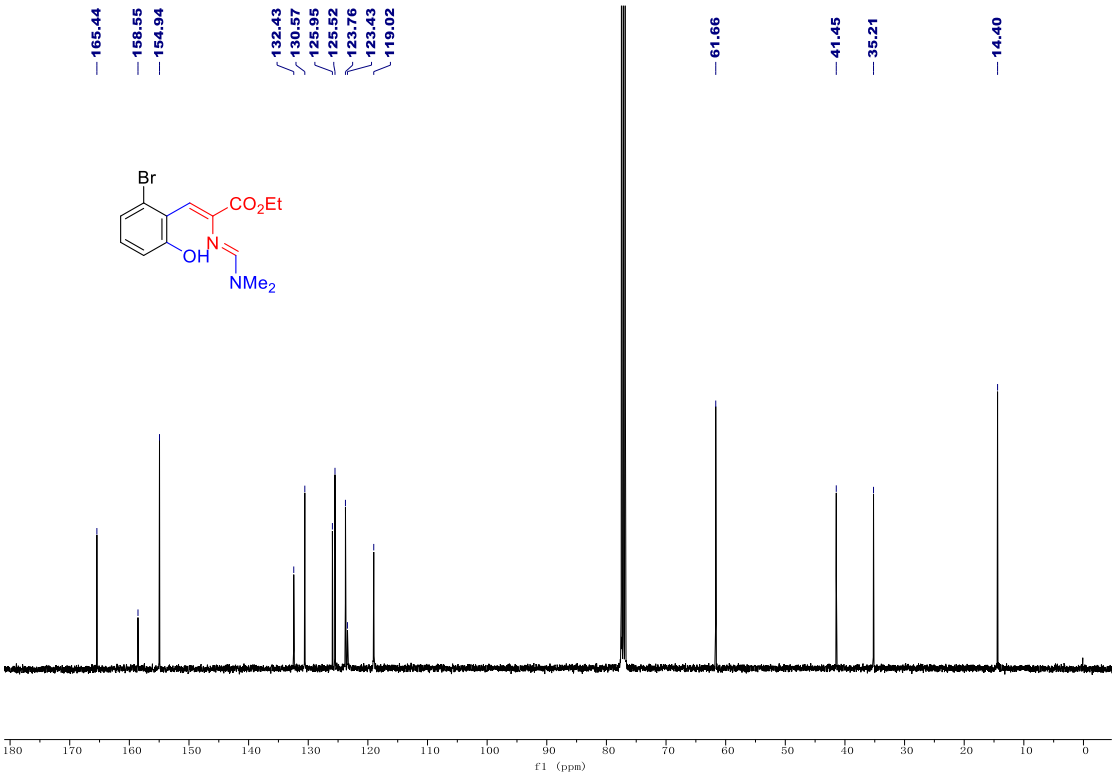
3h ^{13}C NMR



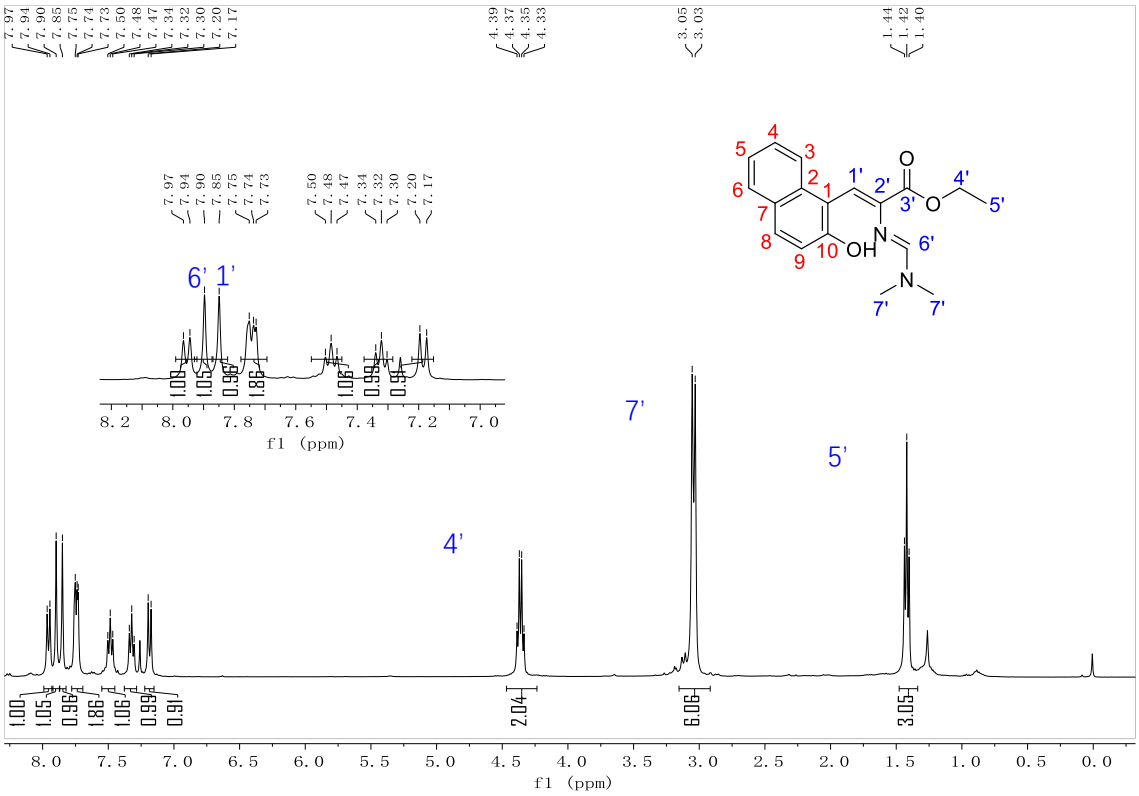
3i ^{1}H NMR



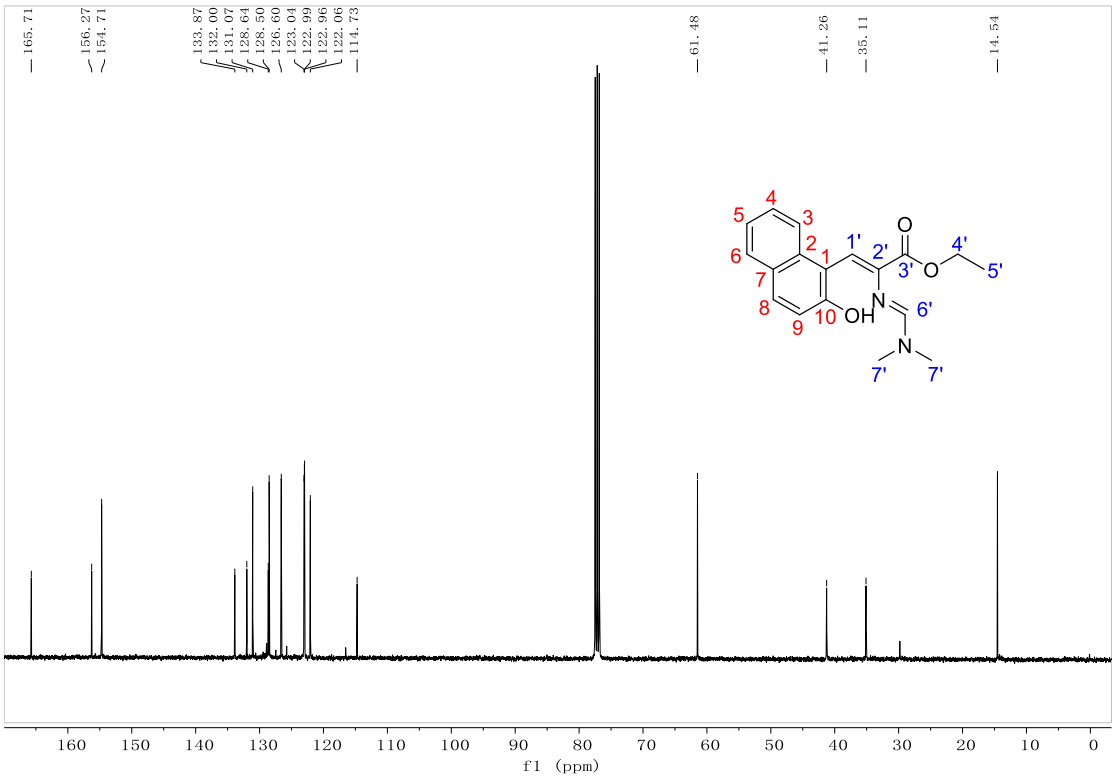
3i ^{13}C NMR



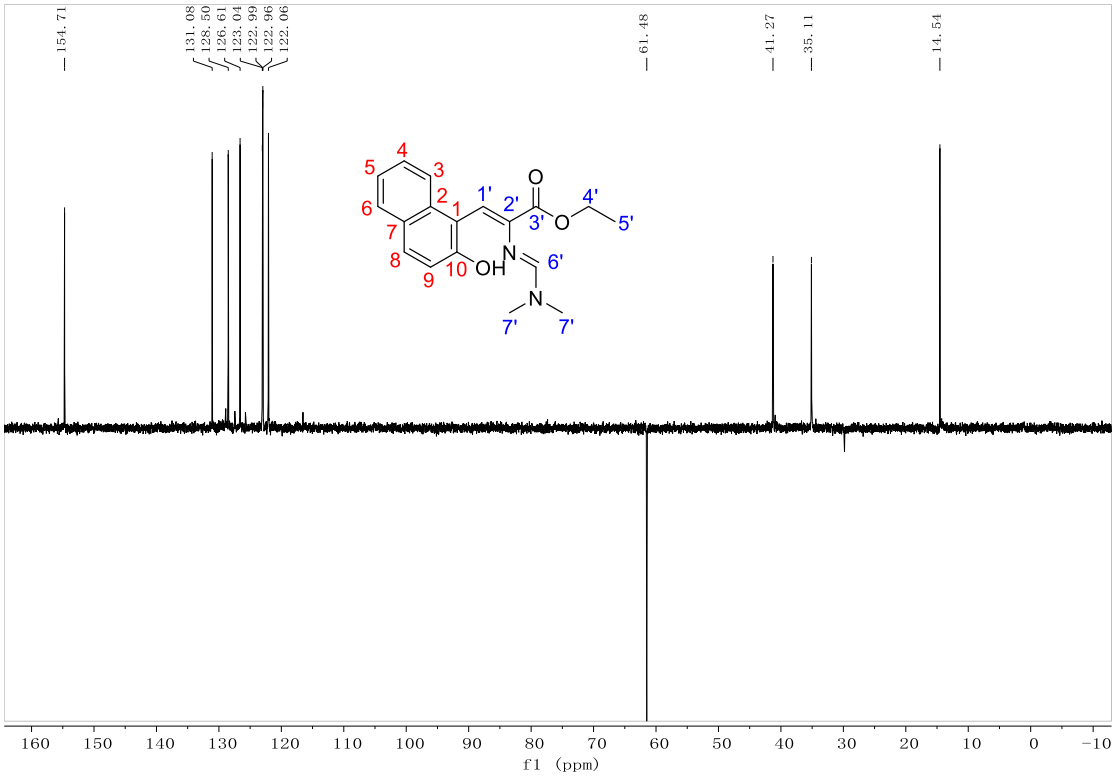
^{1}H NMR (400 MHz, $CDCl_3$) of 3j



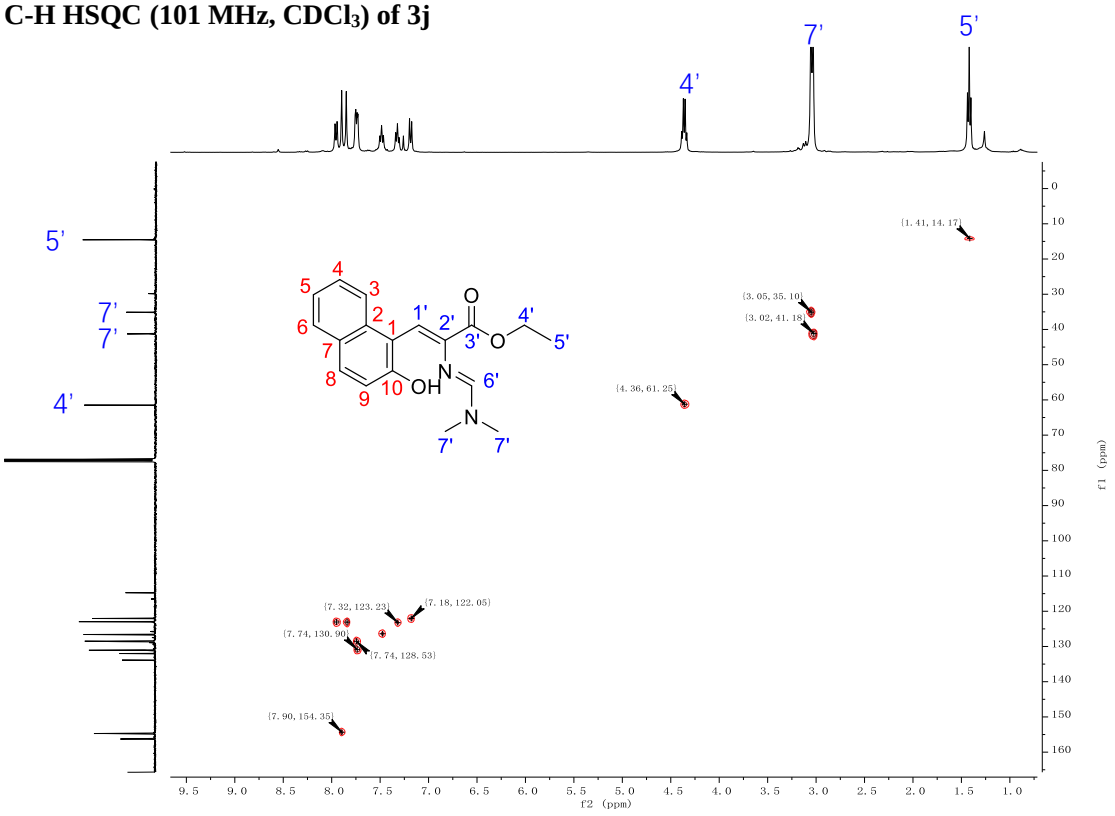
^{13}C NMR (101 MHz, $CDCl_3$) of 3j



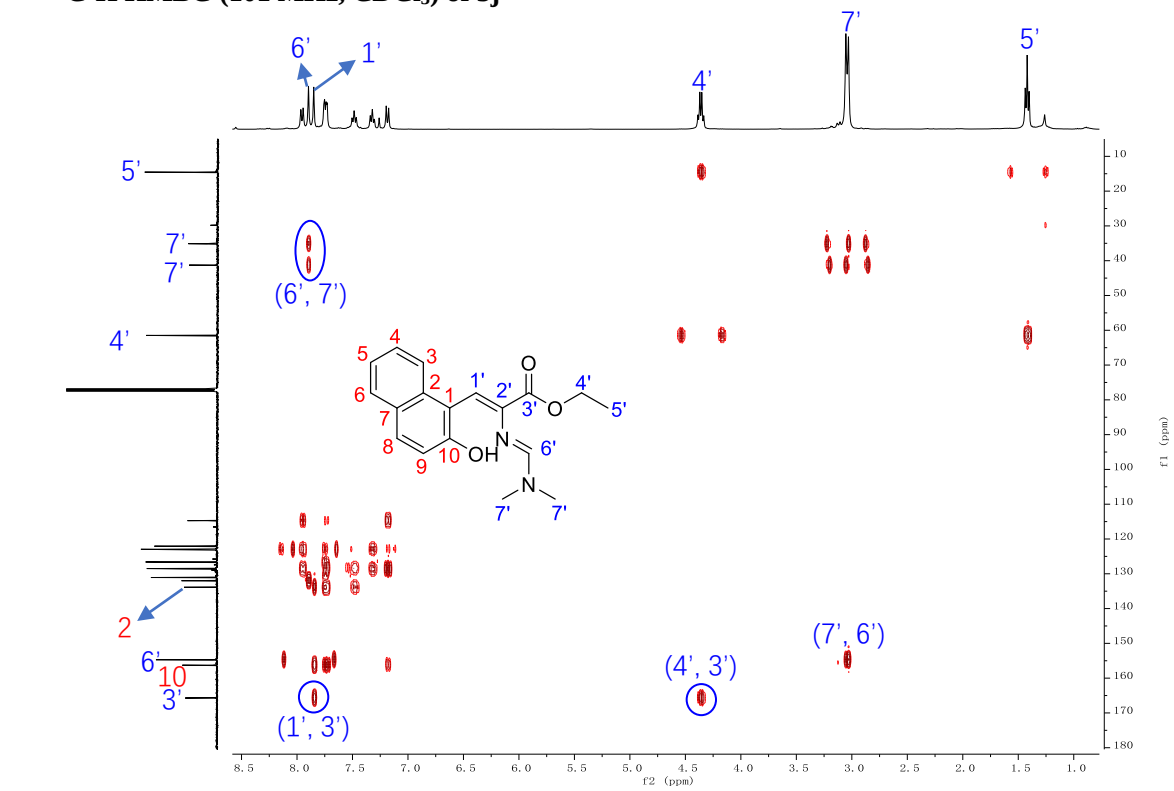
DEPT 135°（101 MHz, $CDCl_3$) of 3j

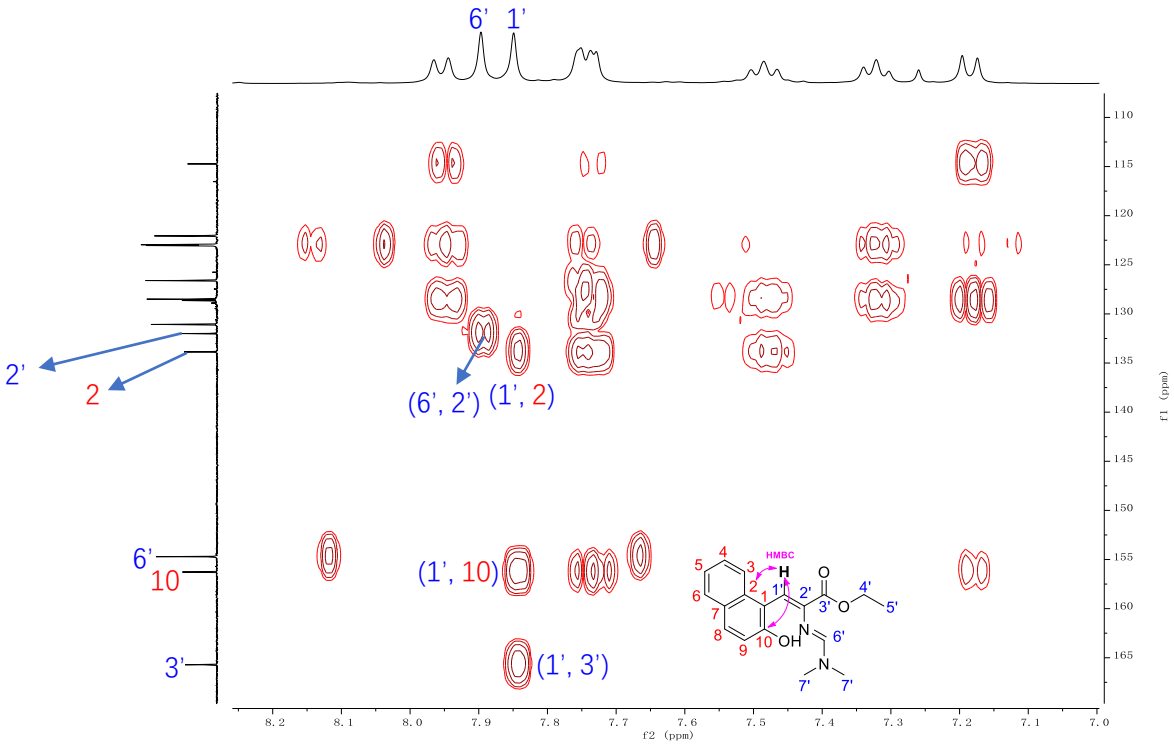


C-H HSQC (101 MHz, $CDCl_3$) of 3j

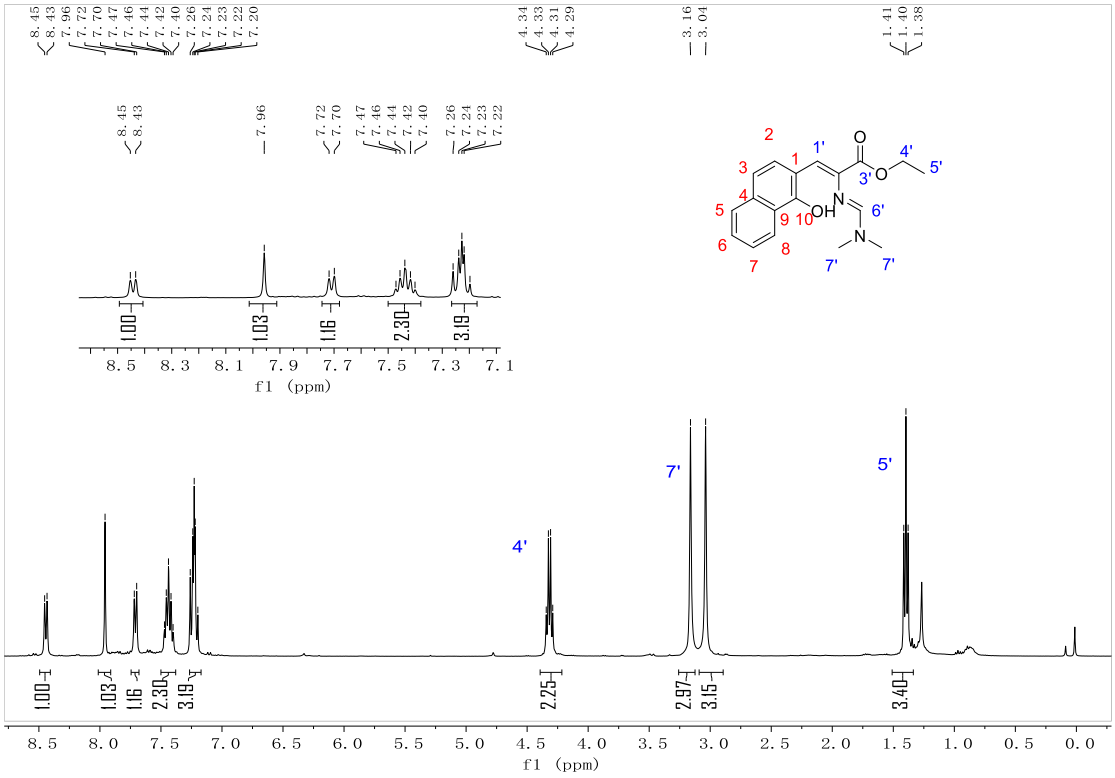


C-H HMBC (101 MHz, $CDCl_3$) of 3j

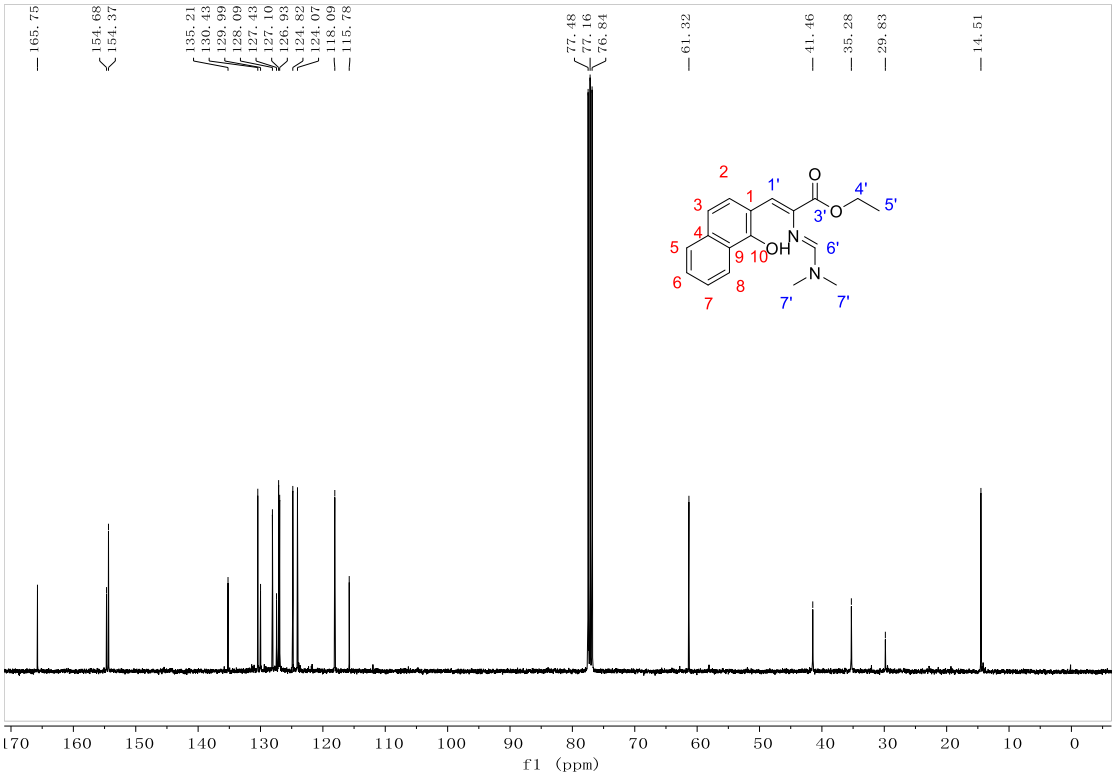




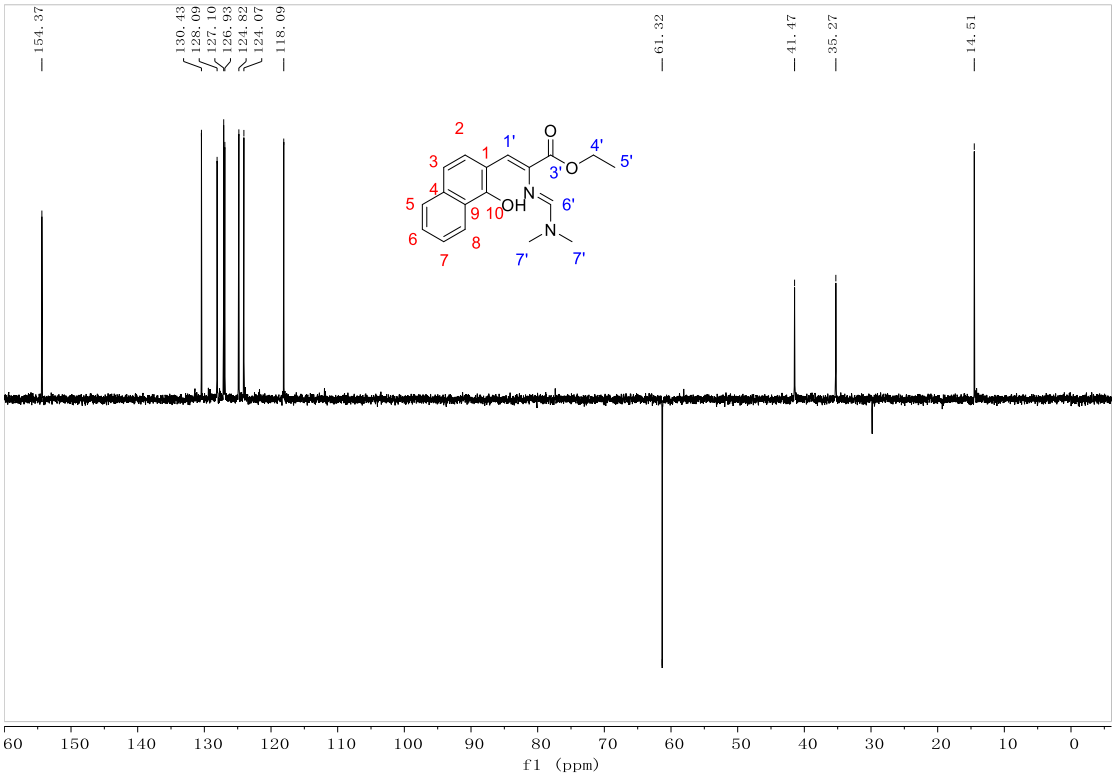
^{1}H NMR (400 MHz, $CDCl_3$) of 3j’



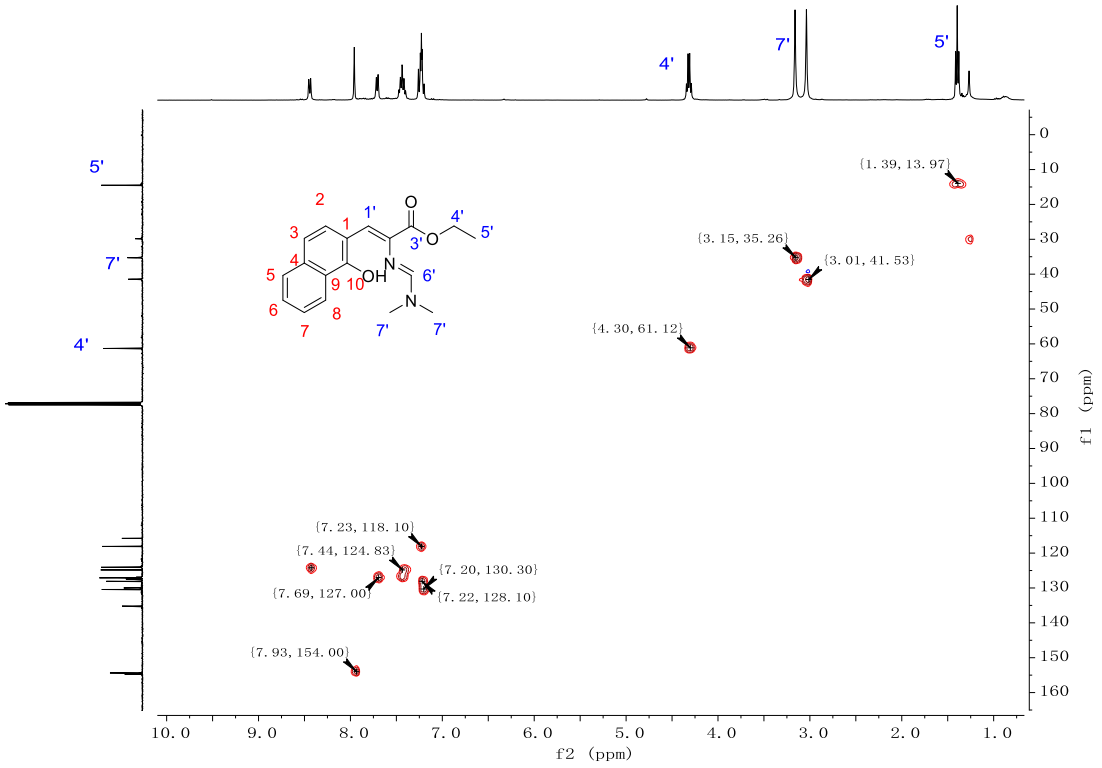
^{13}C NMR (101 MHz, $CDCl_3$) of 3j’



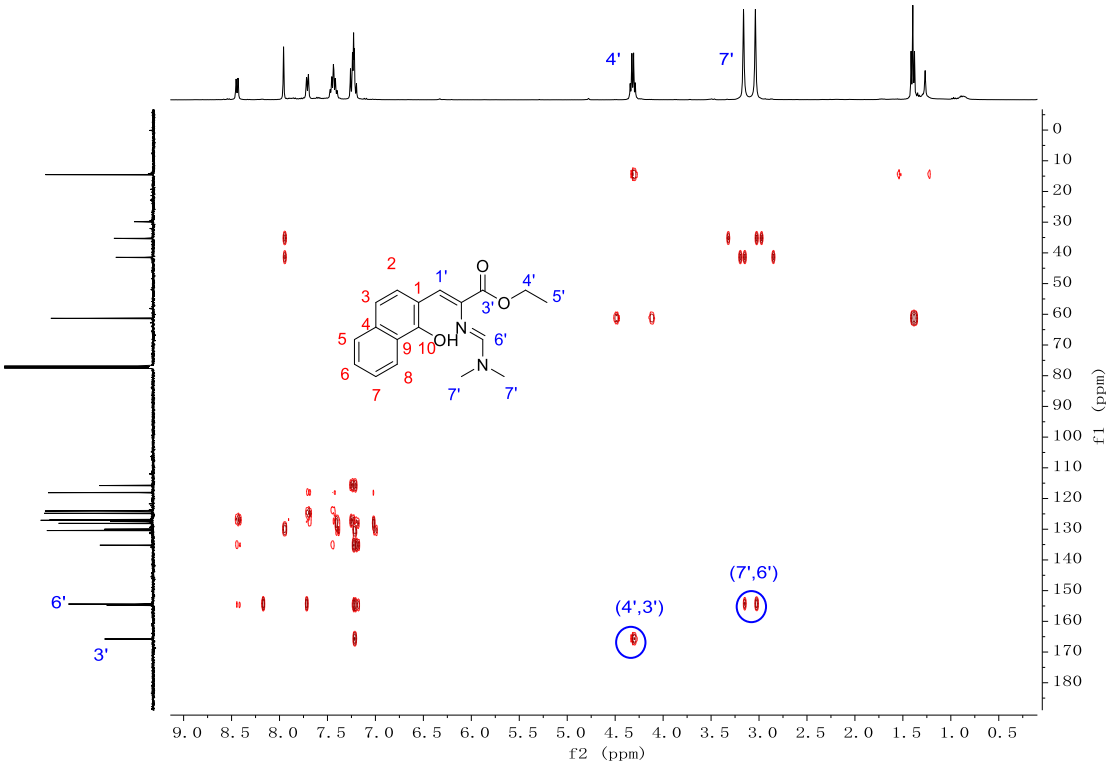
DEPT 135° (101 MHz, $CDCl_3$) of 3j

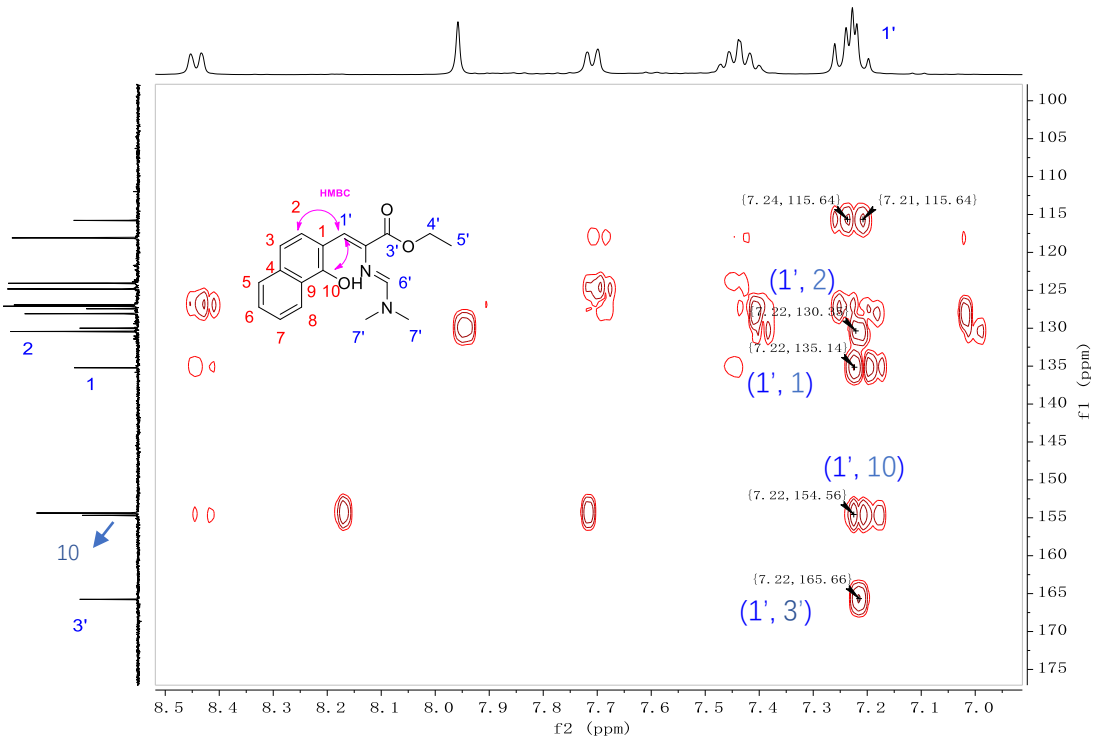


C-H HSQC (101 MHz, $CDCl_3$) of 3j

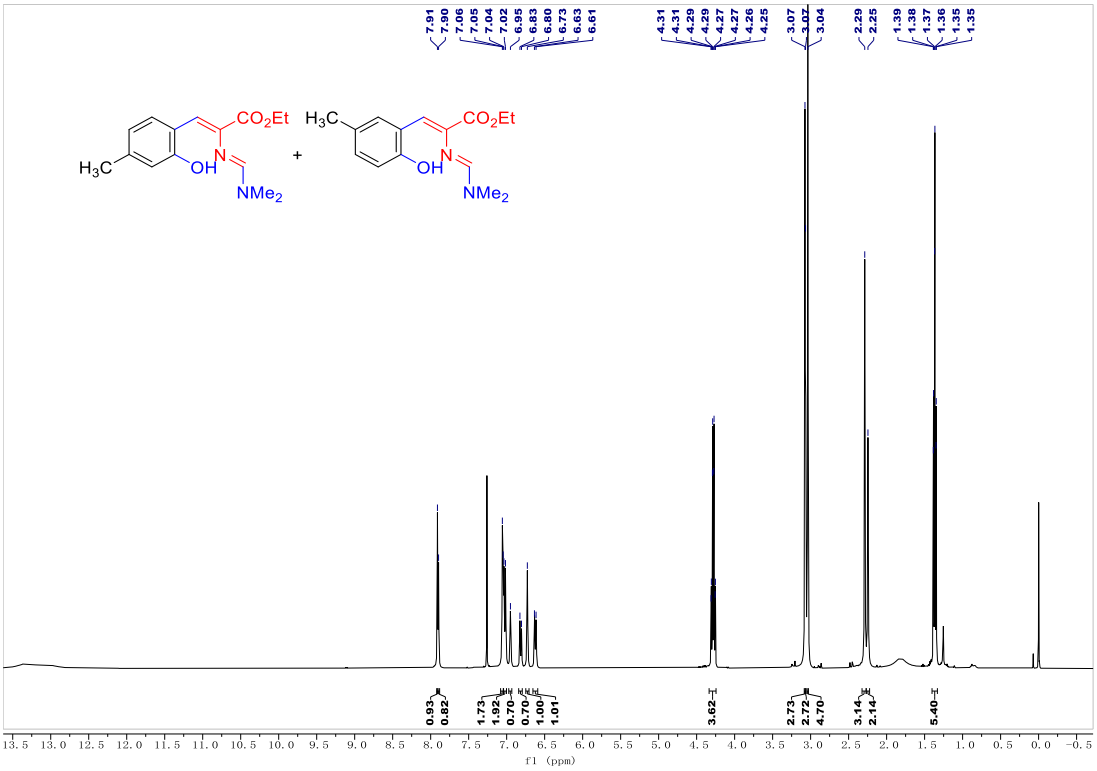


C-H HMBC (101 MHz, $CDCl_3$) of 3j

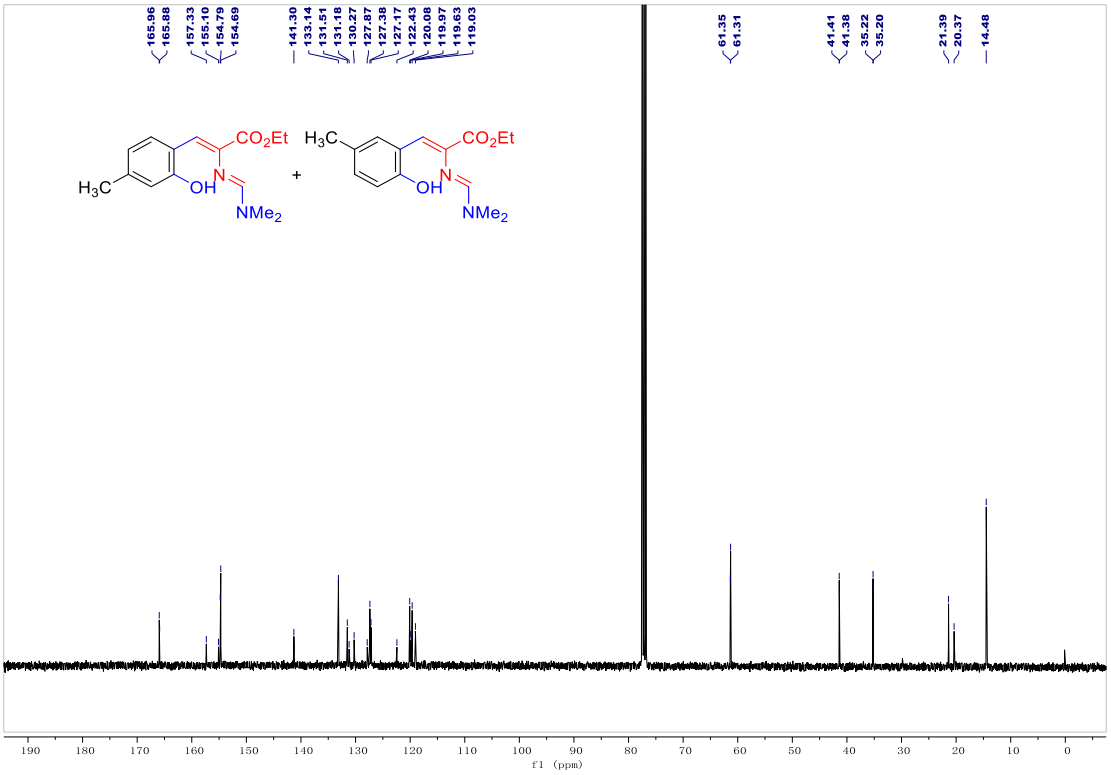




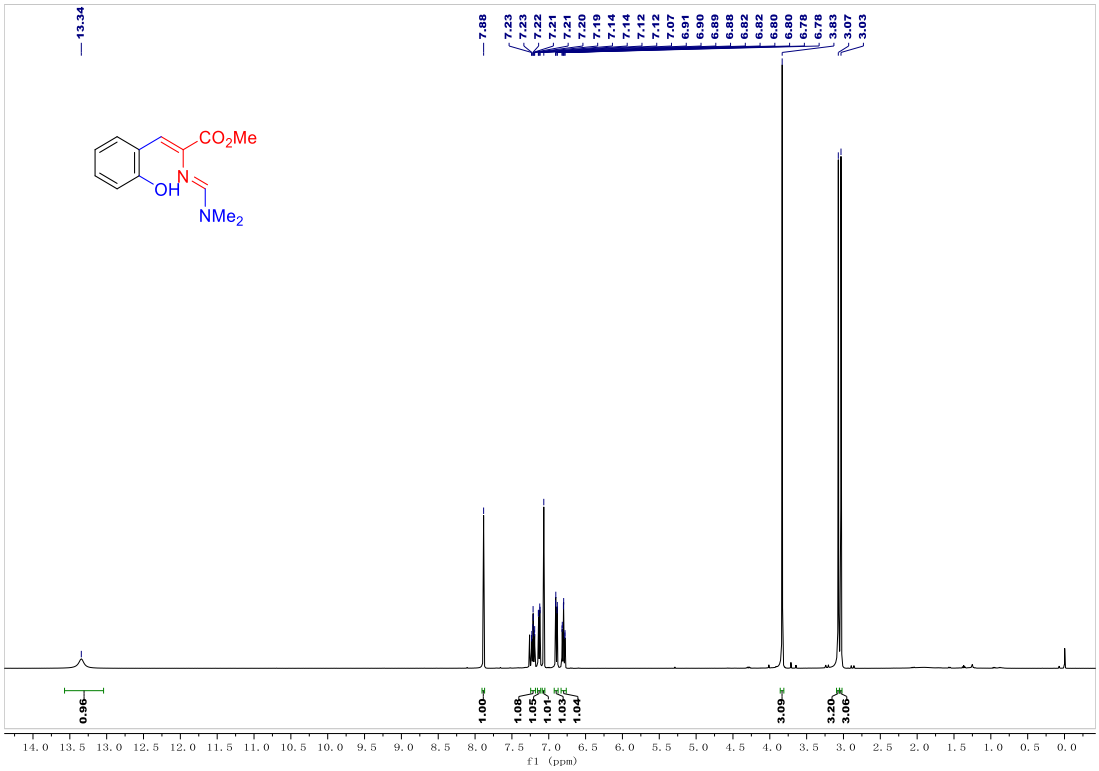
3k/3k' ^{1}H NMR



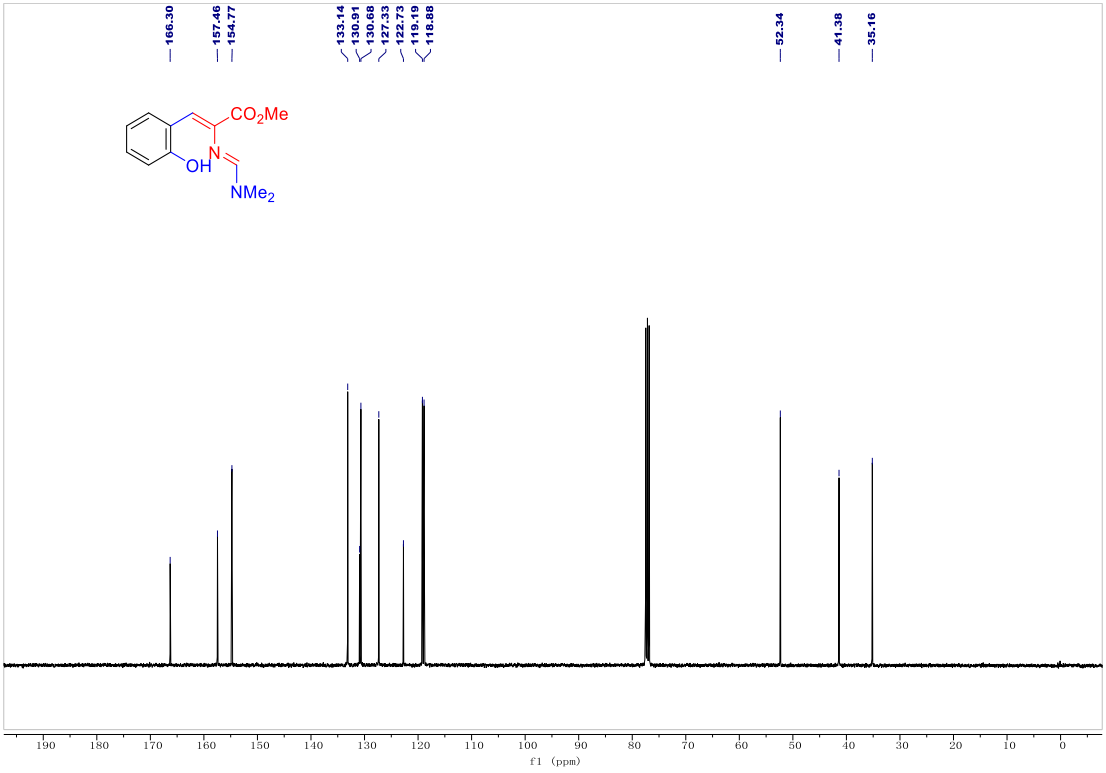
3k/3k' ^{13}C NMR



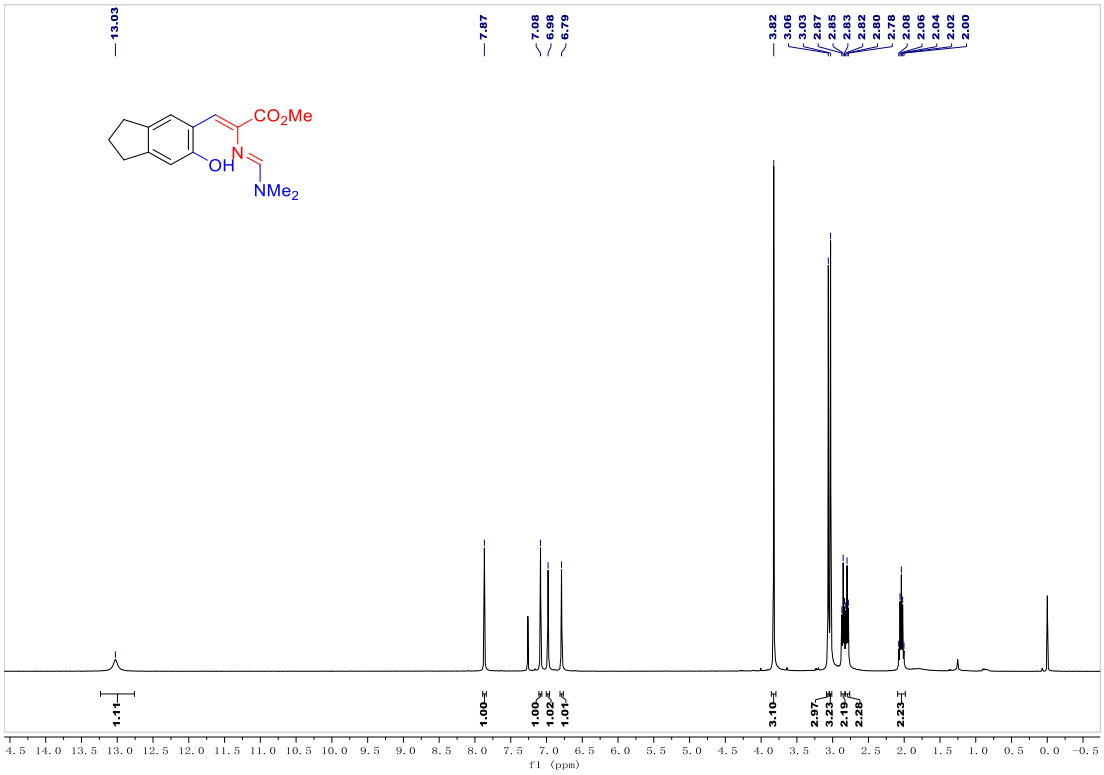
3l ^{1}H NMR



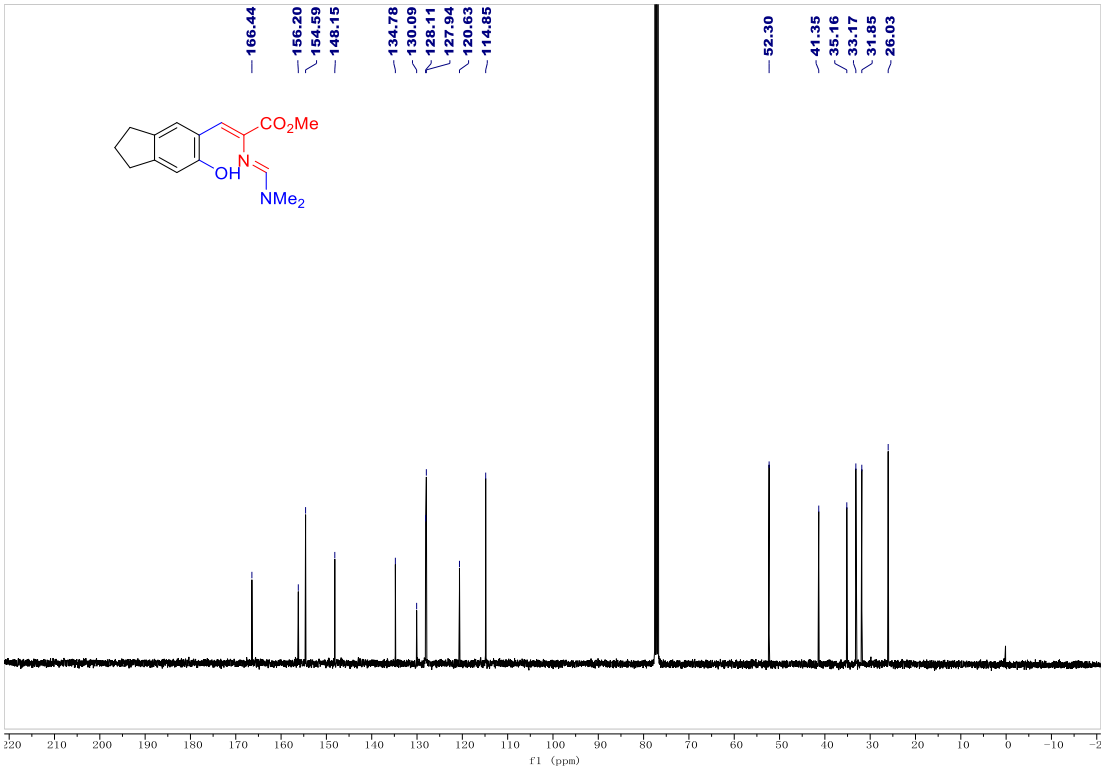
3l ^{13}C NMR



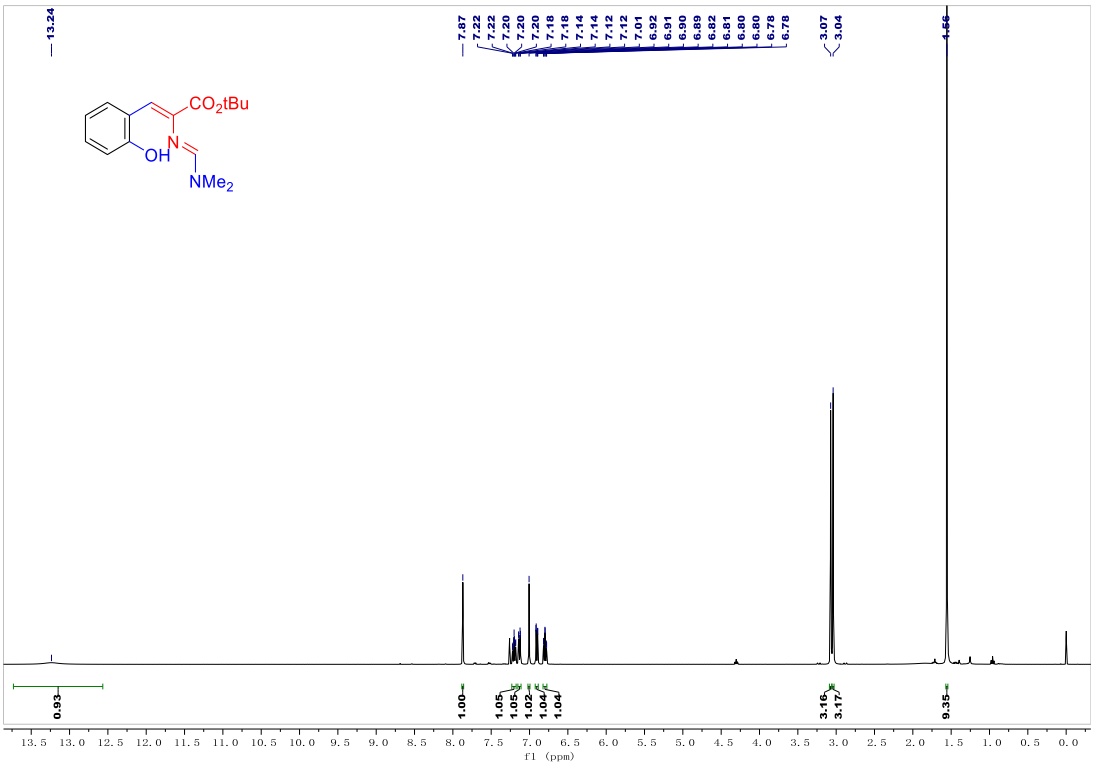
3m ^{1}H NMR



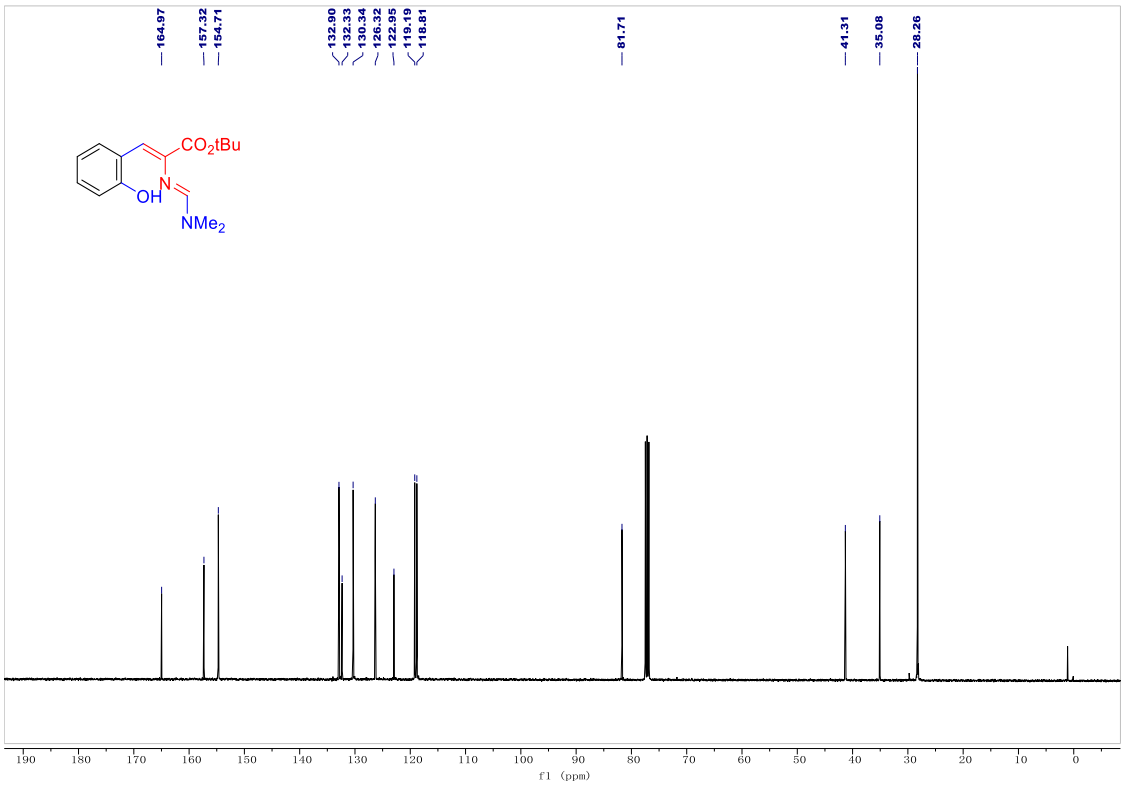
3m ^{13}C NMR



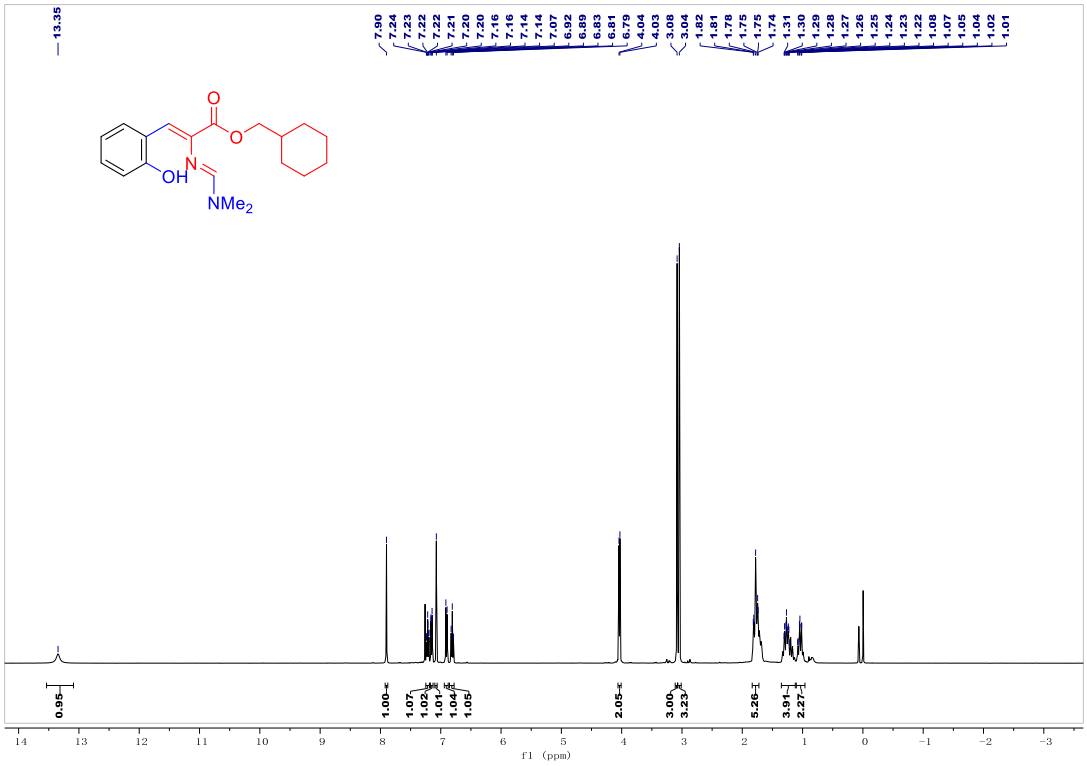
3n ^{1}H NMR



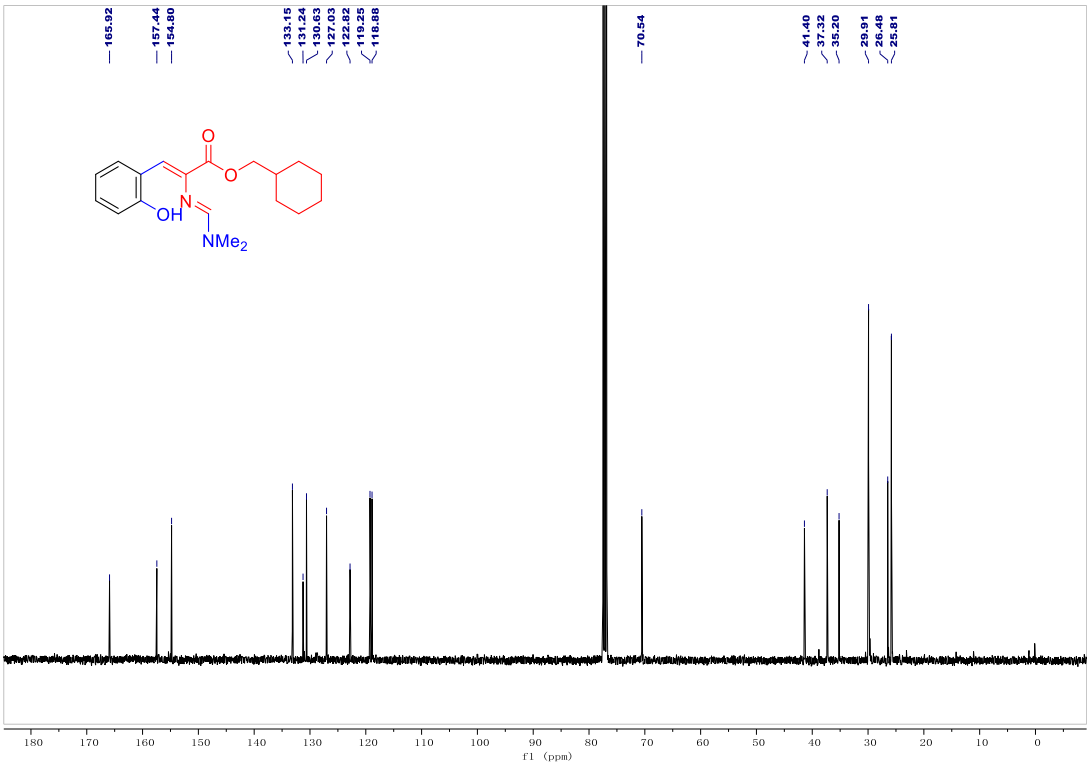
3n ^{13}C NMR



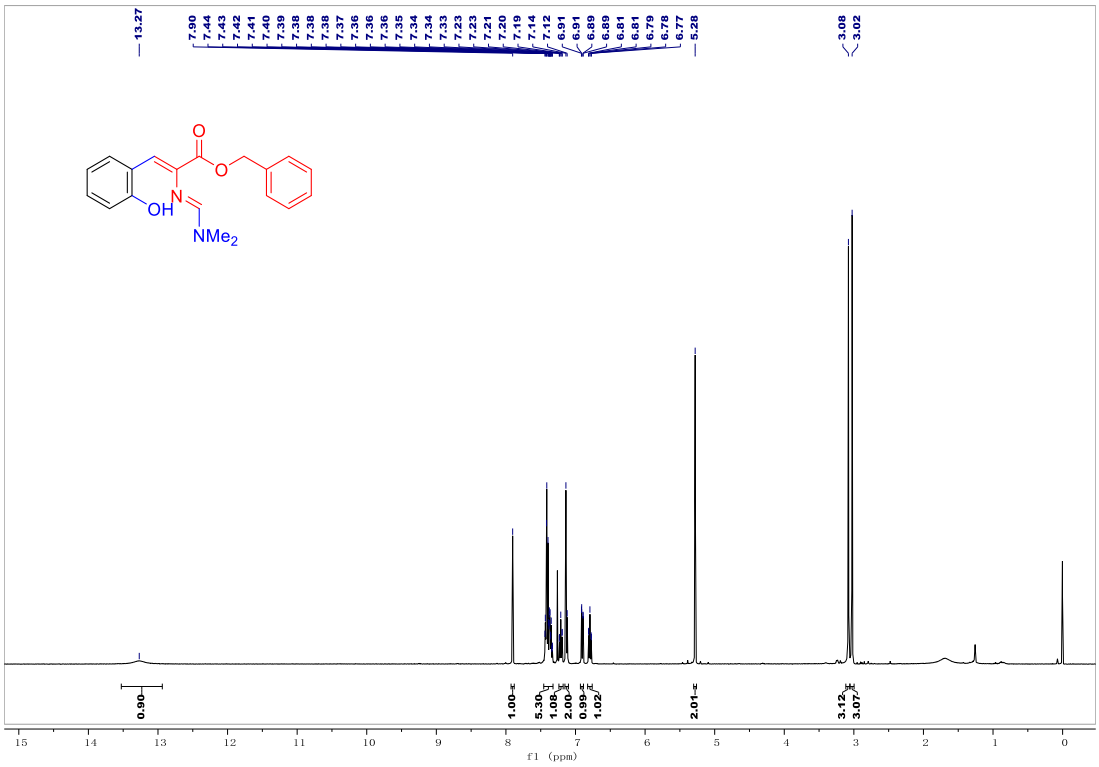
3o ^{1}H NMR



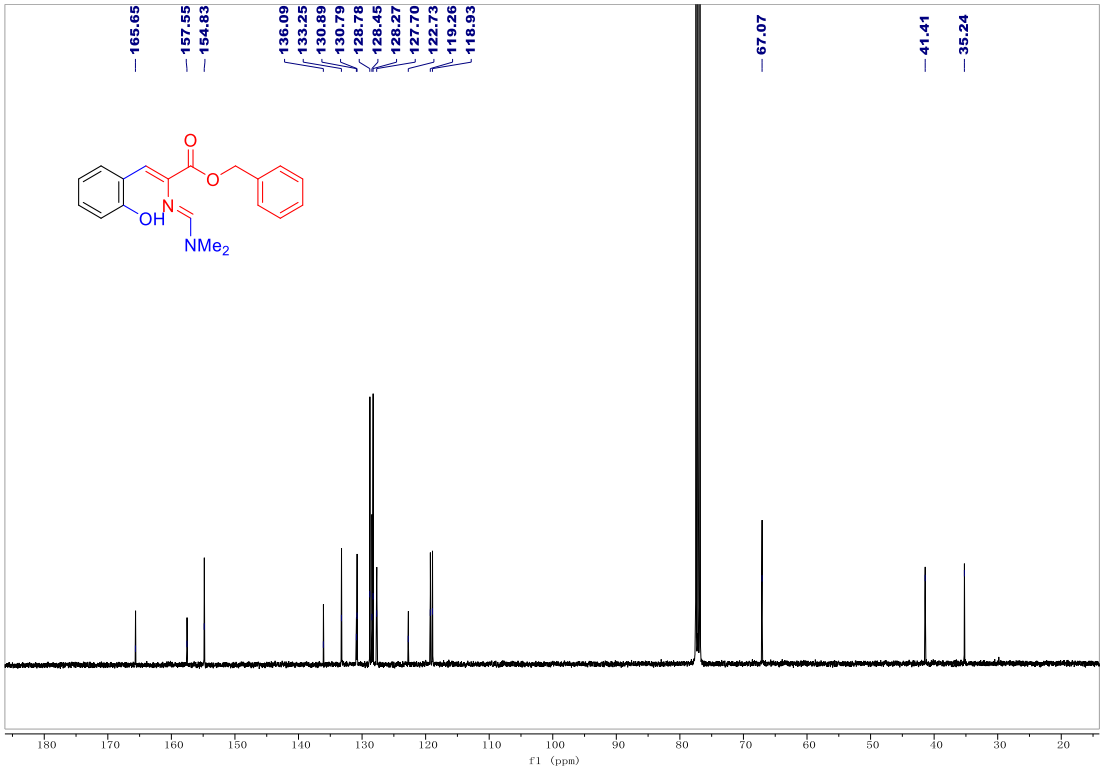
3o ^{13}C NMR



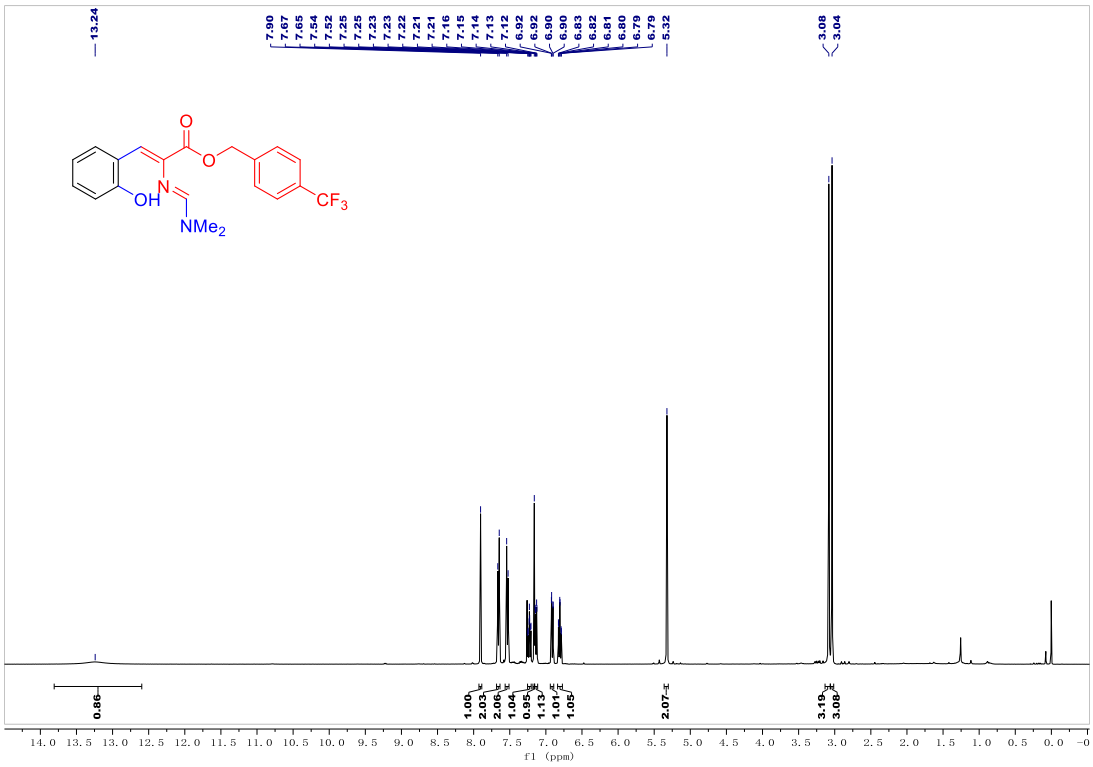
3p ^{1}H NMR



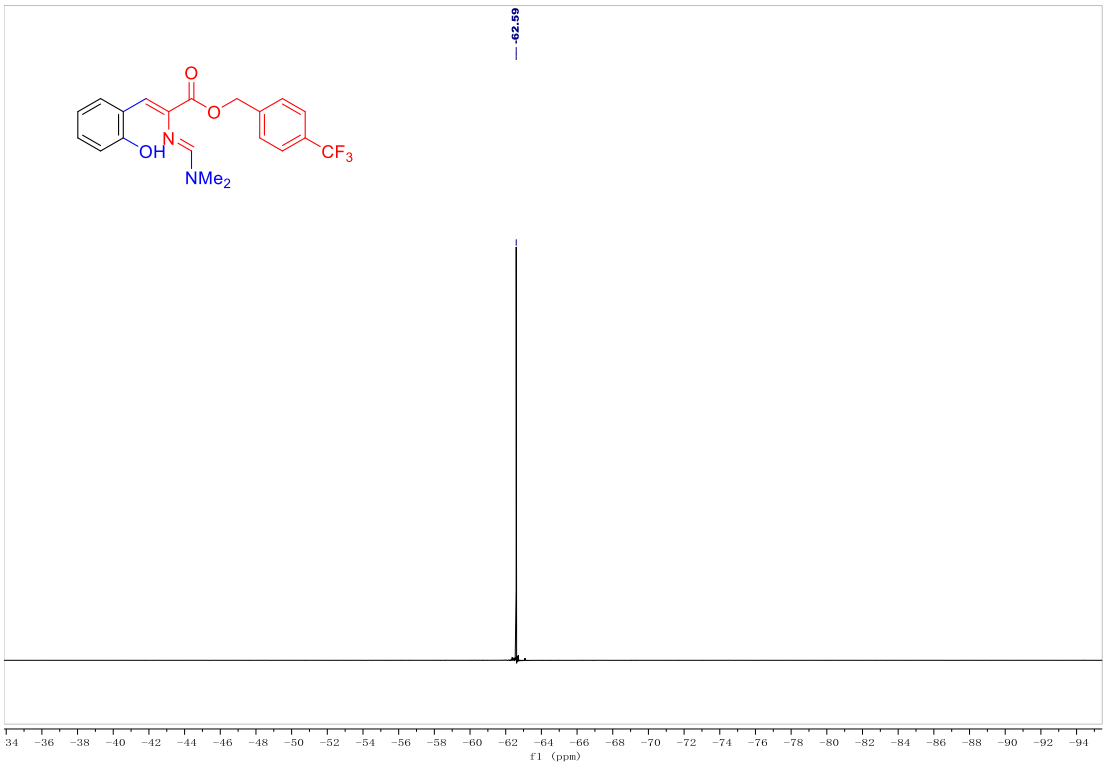
3p ^{13}C NMR



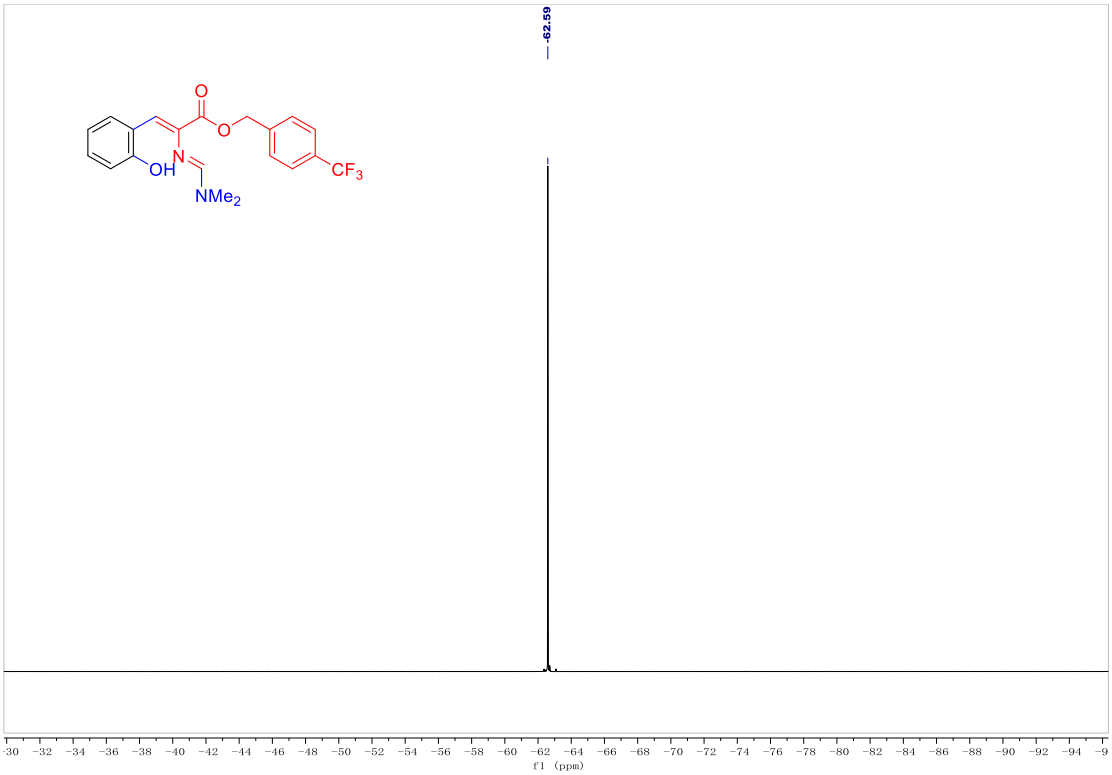
3q ^{1}H NMR



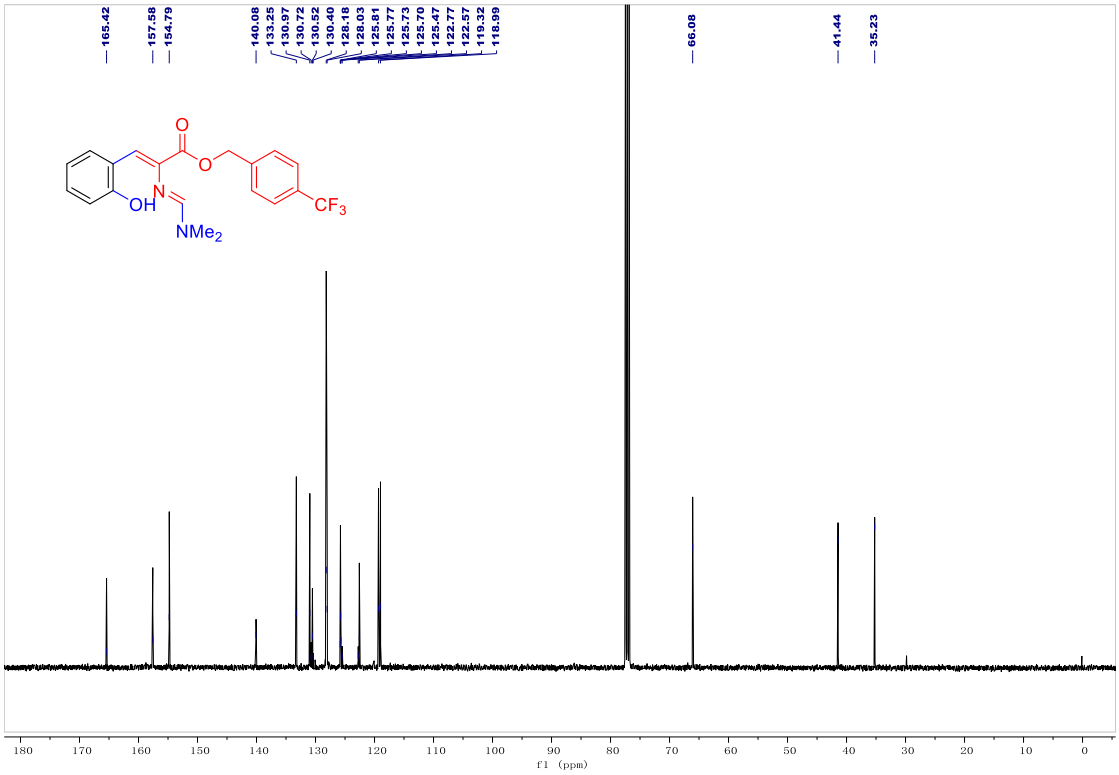
3q ^{19}F{^{1}H} NMR



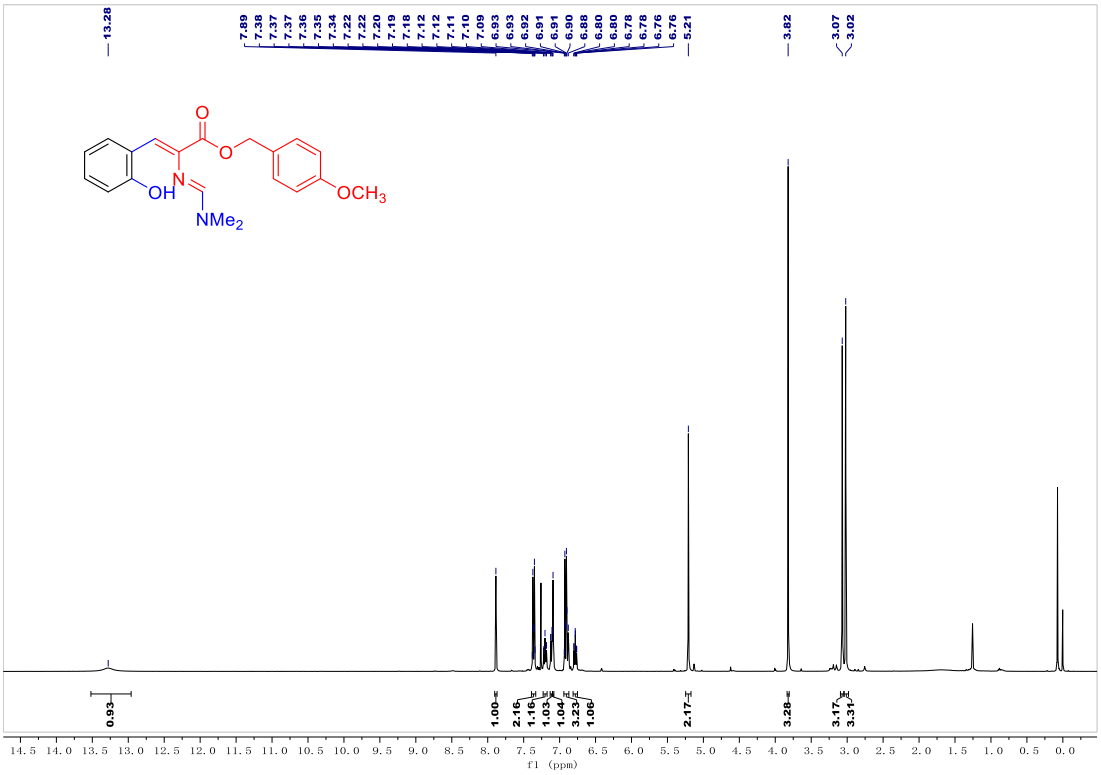
3q ^{19}F NMR



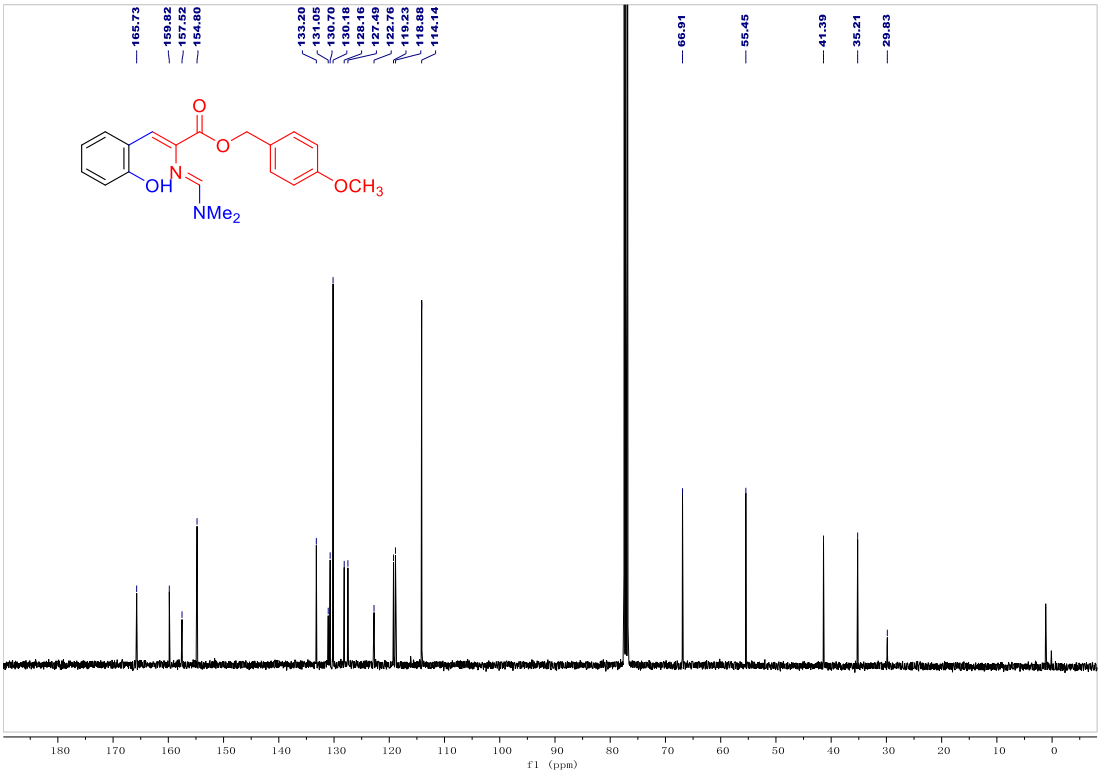
3q ^{13}C NMR



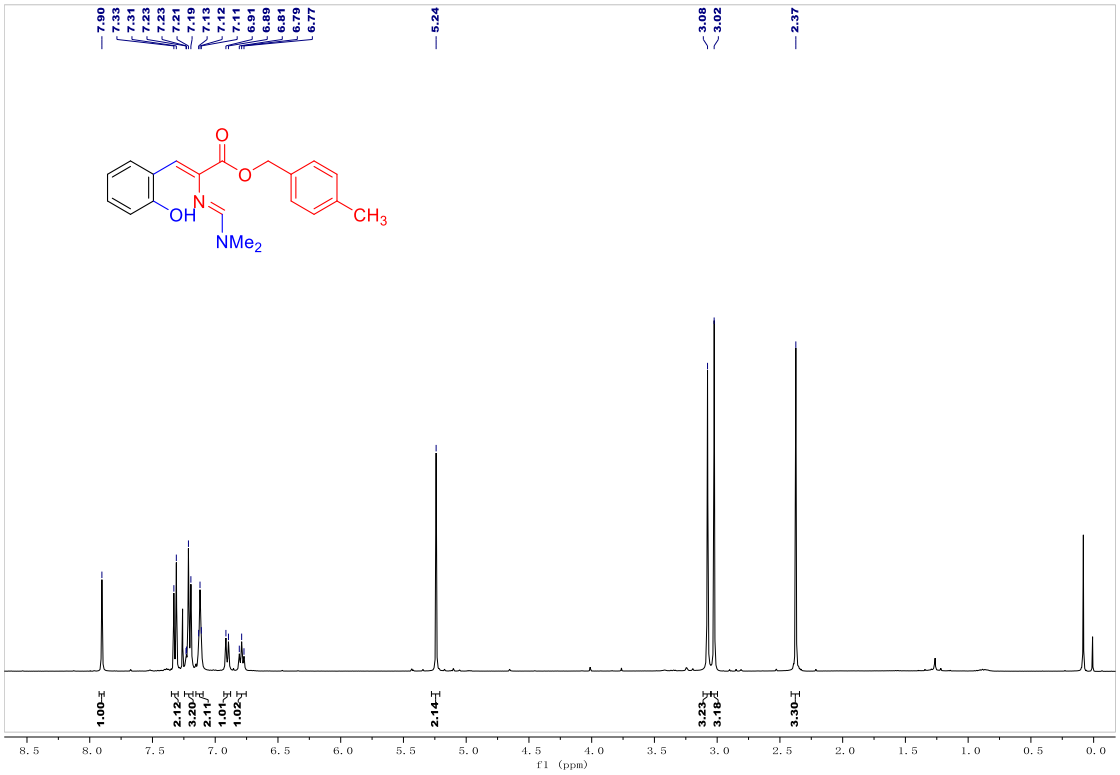
3r ^{1}H NMR



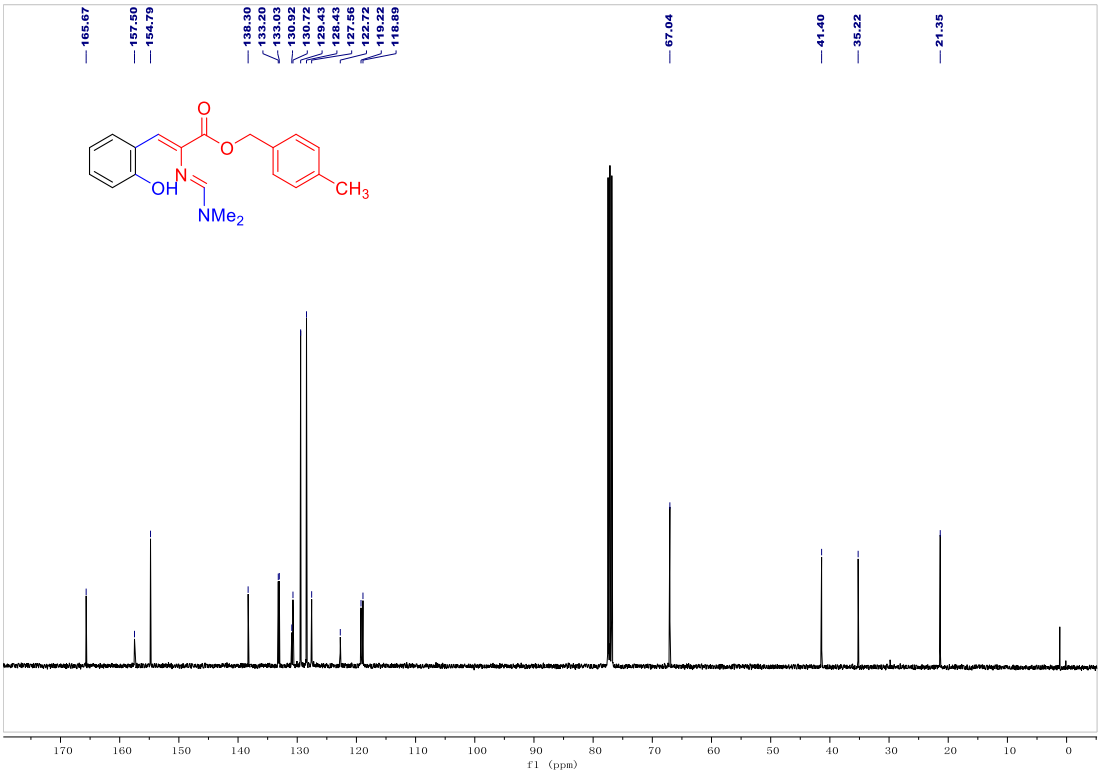
3r ^{13}C NMR



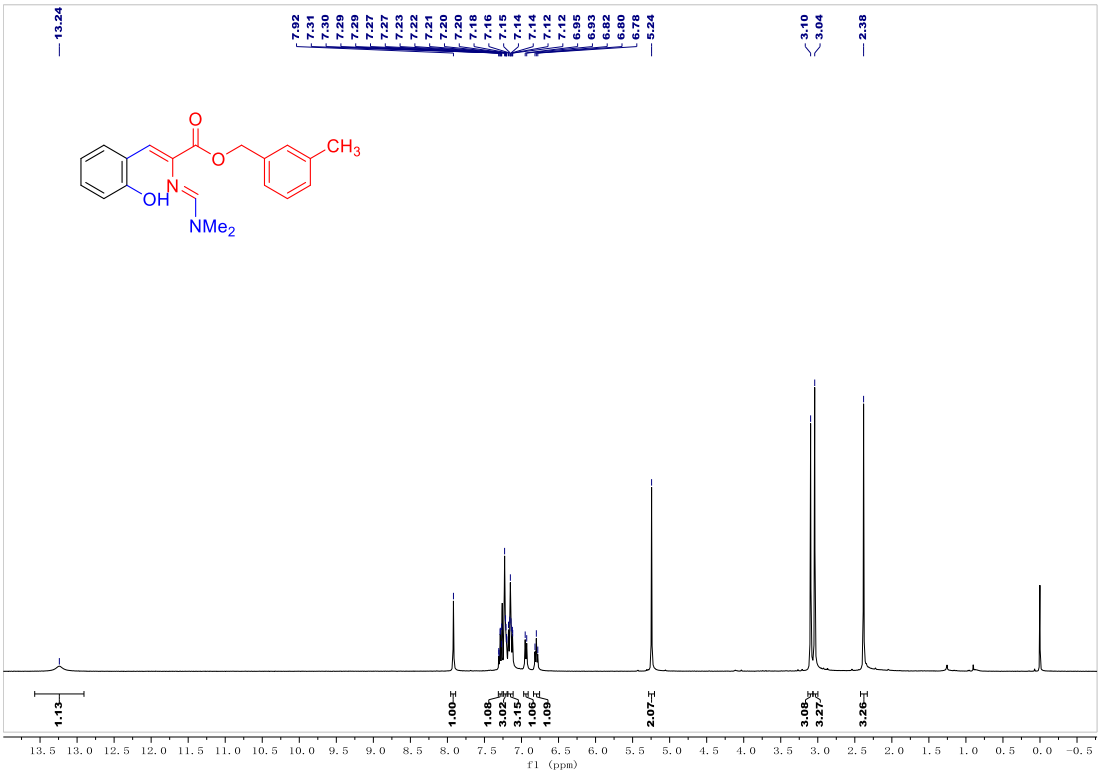
3s ^{1}H NMR



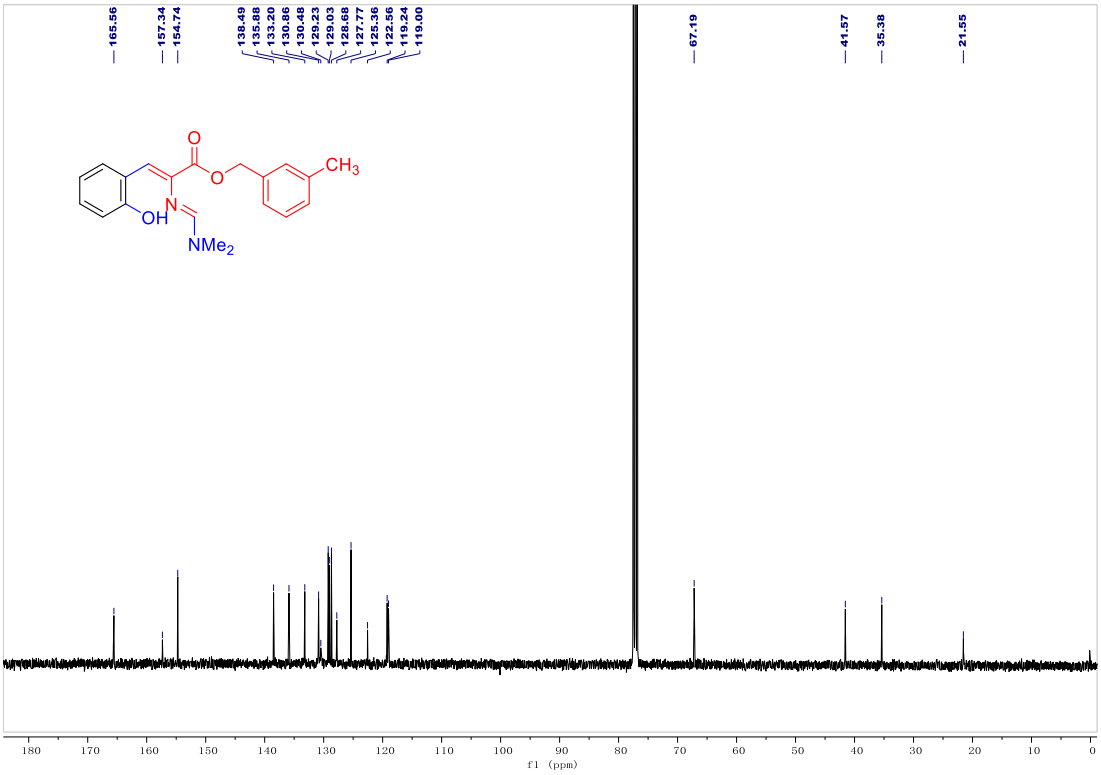
3s ^{13}C NMR



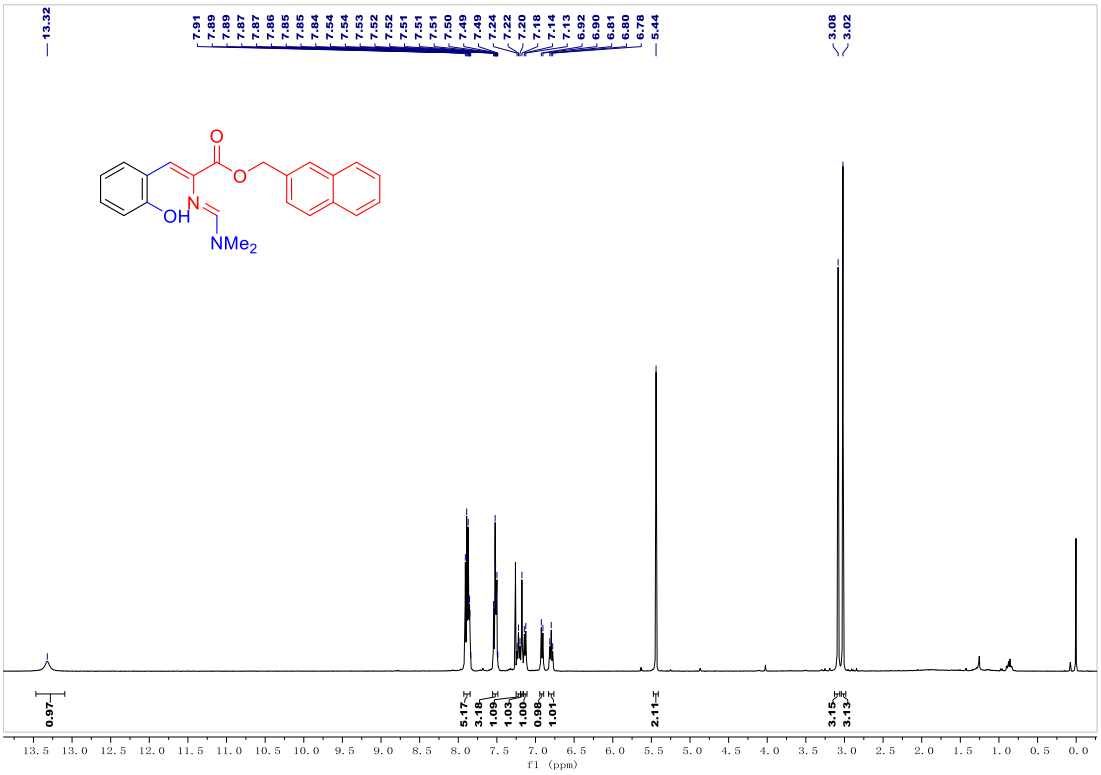
3t ^{1}H NMR



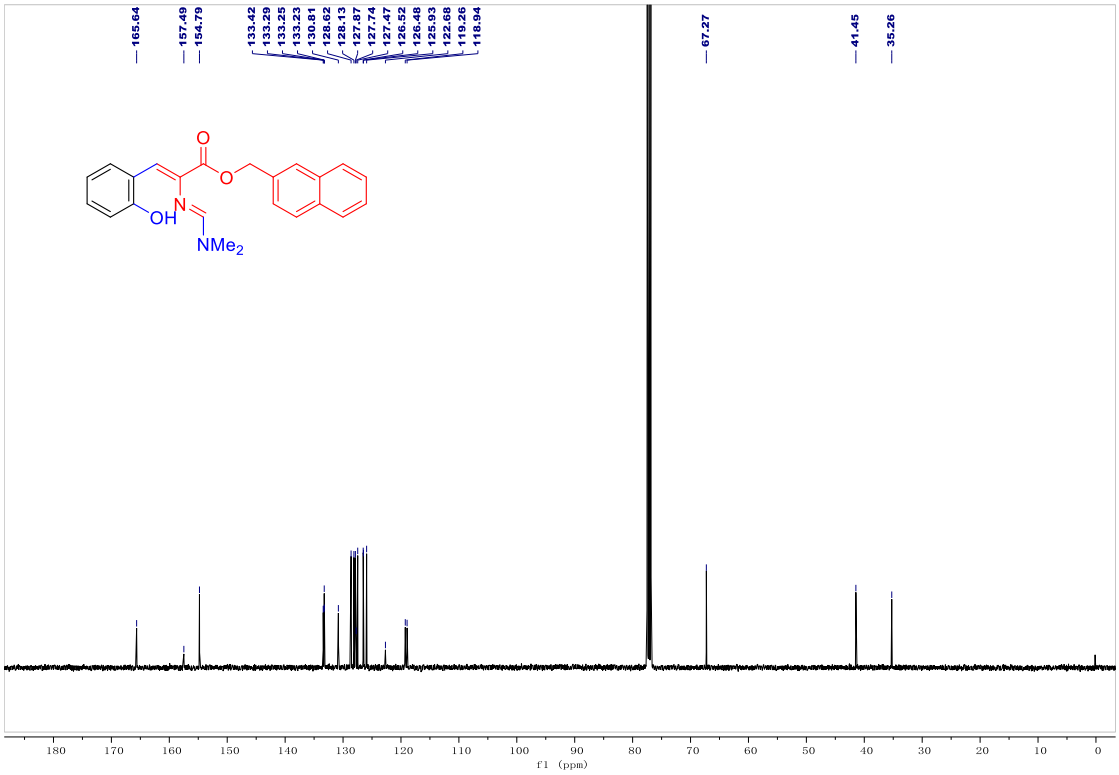
3t ^{13}C NMR



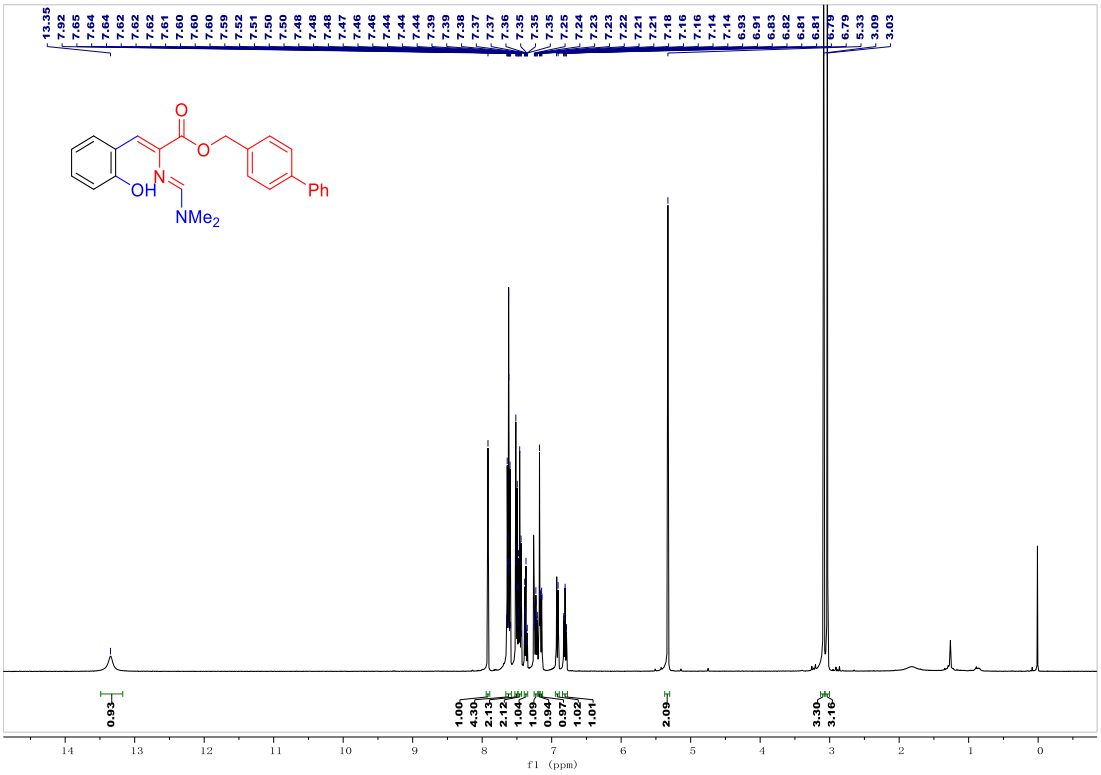
3u ^{1}H NMR



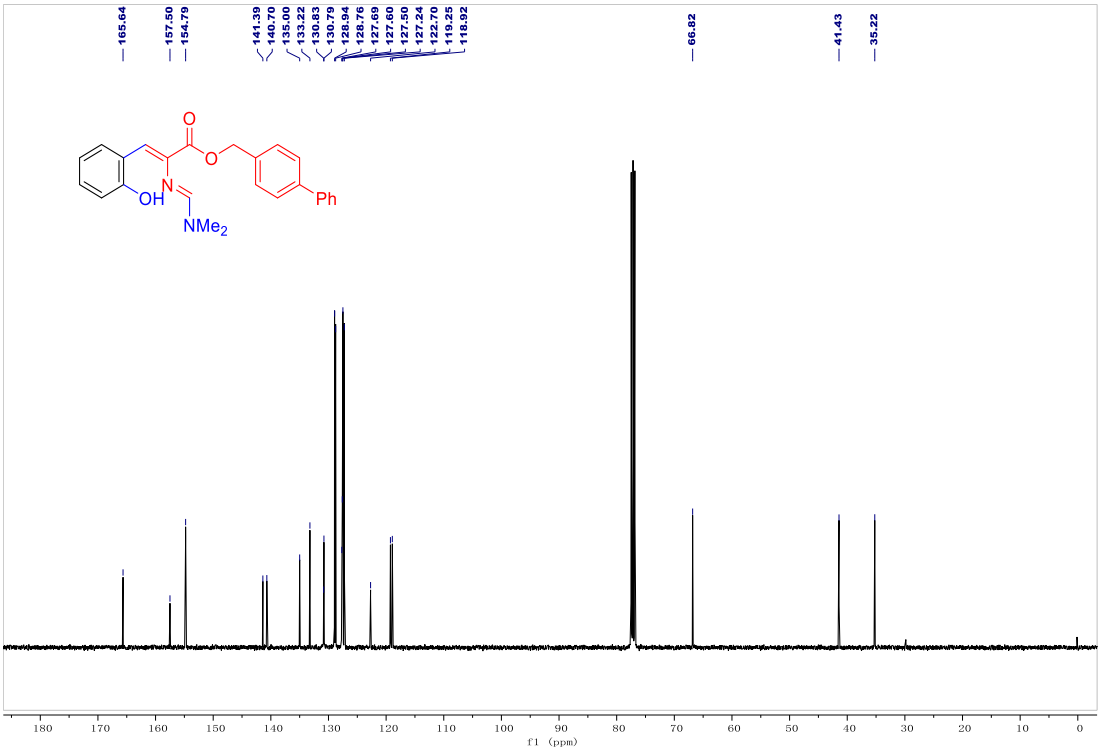
3u ^{13}C NMR



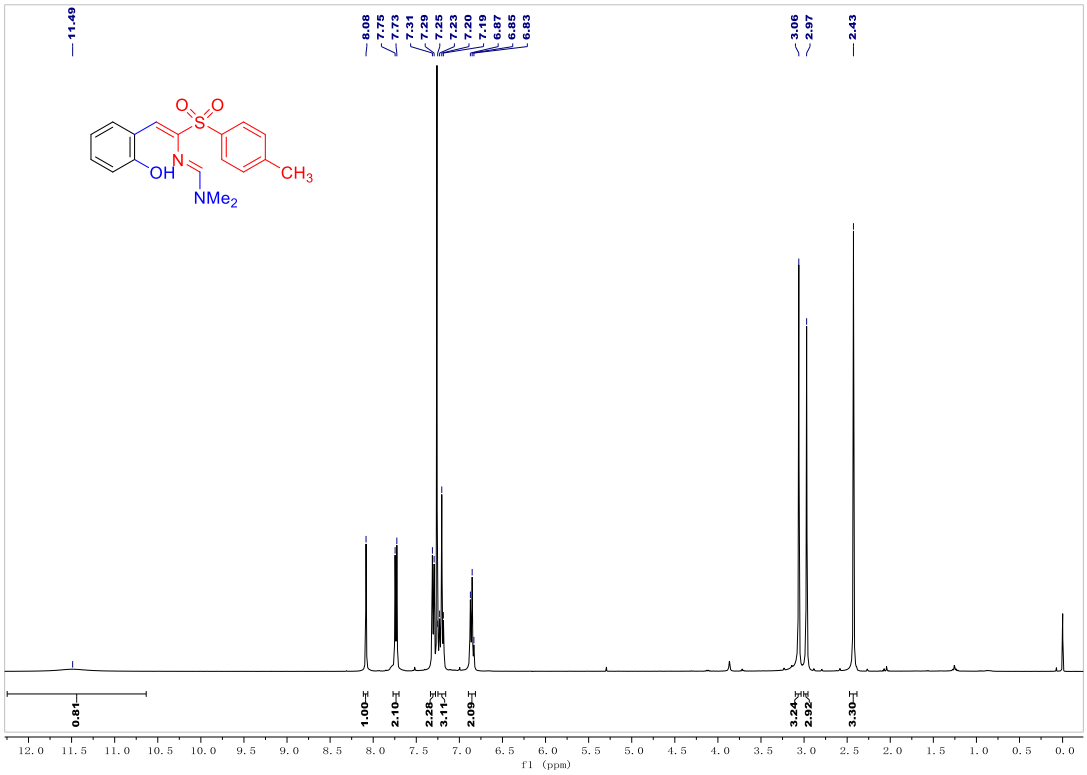
3v ^{1}H NMR



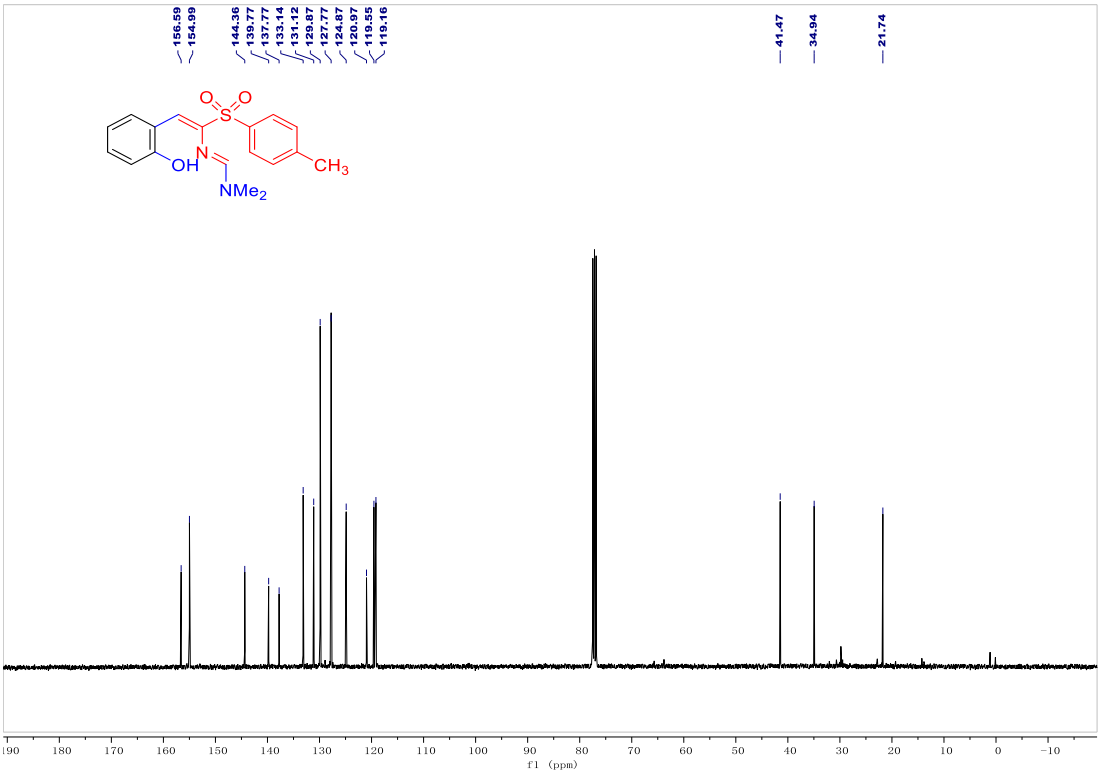
3v ^{13}C NMR



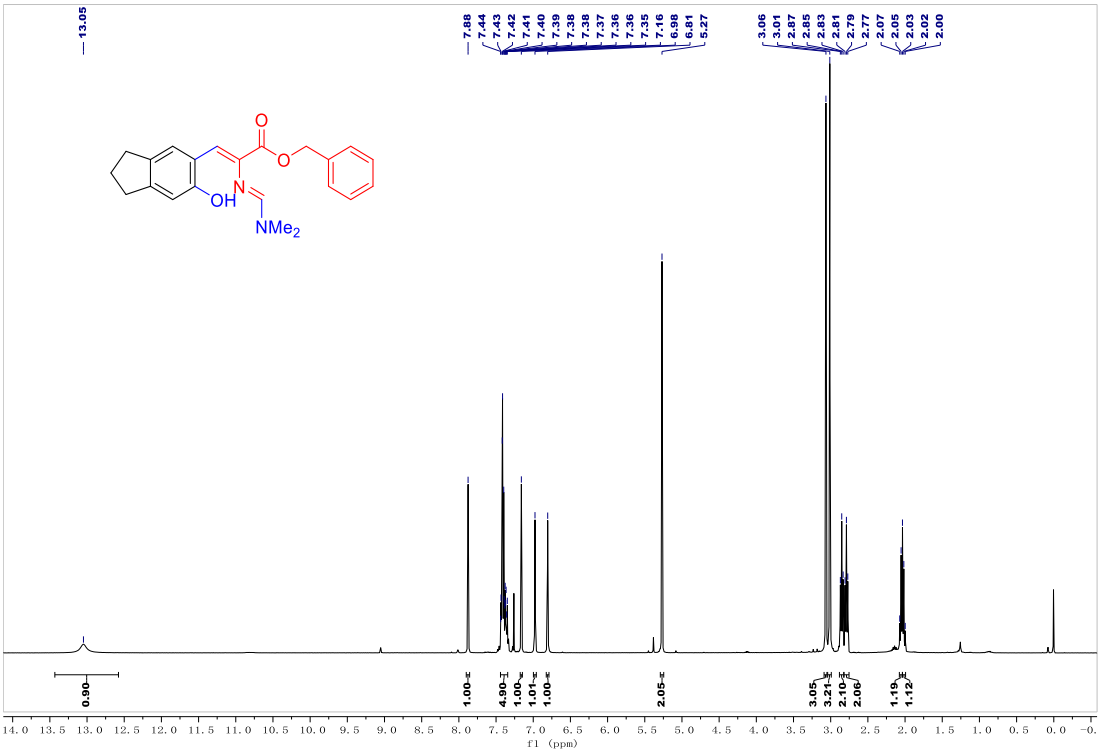
3w ^{1}H NMR



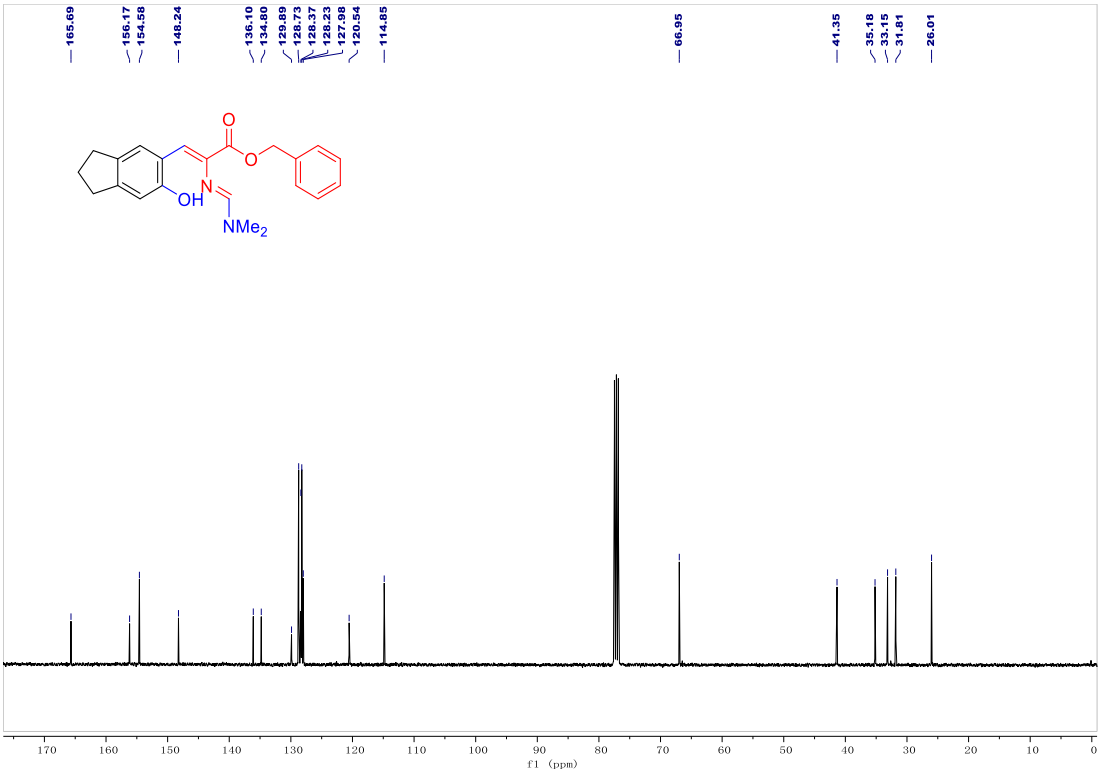
3w ^{13}C NMR



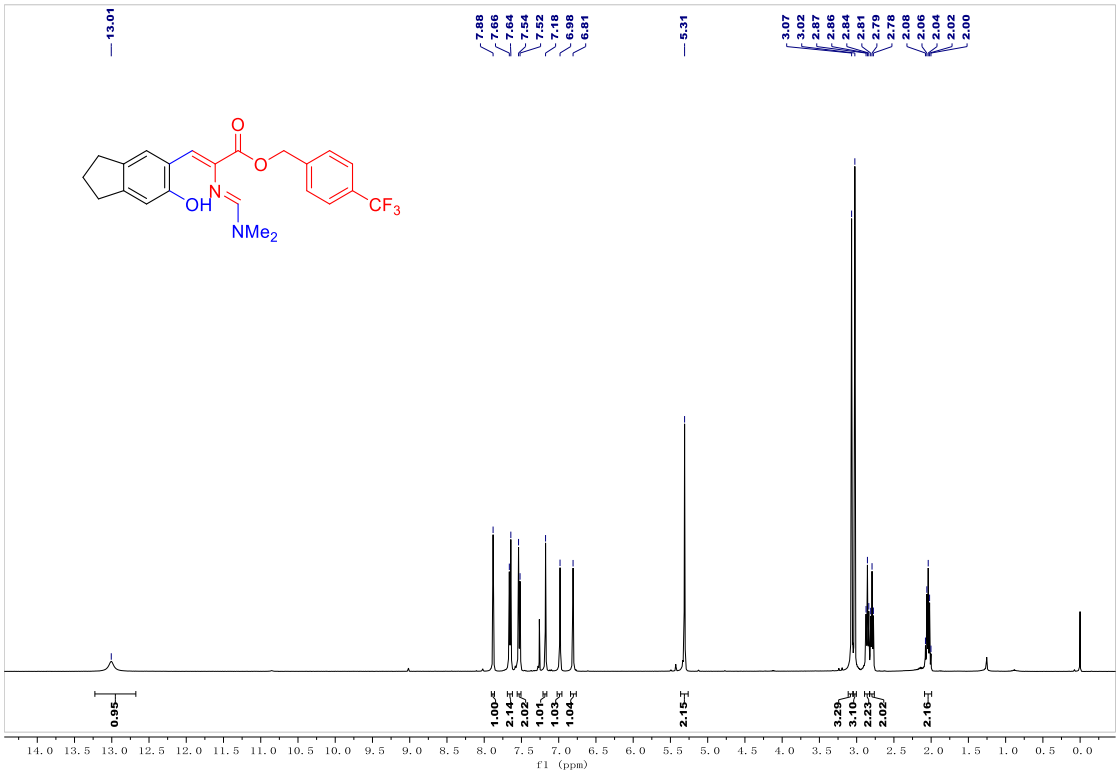
3bp ^{1}H NMR



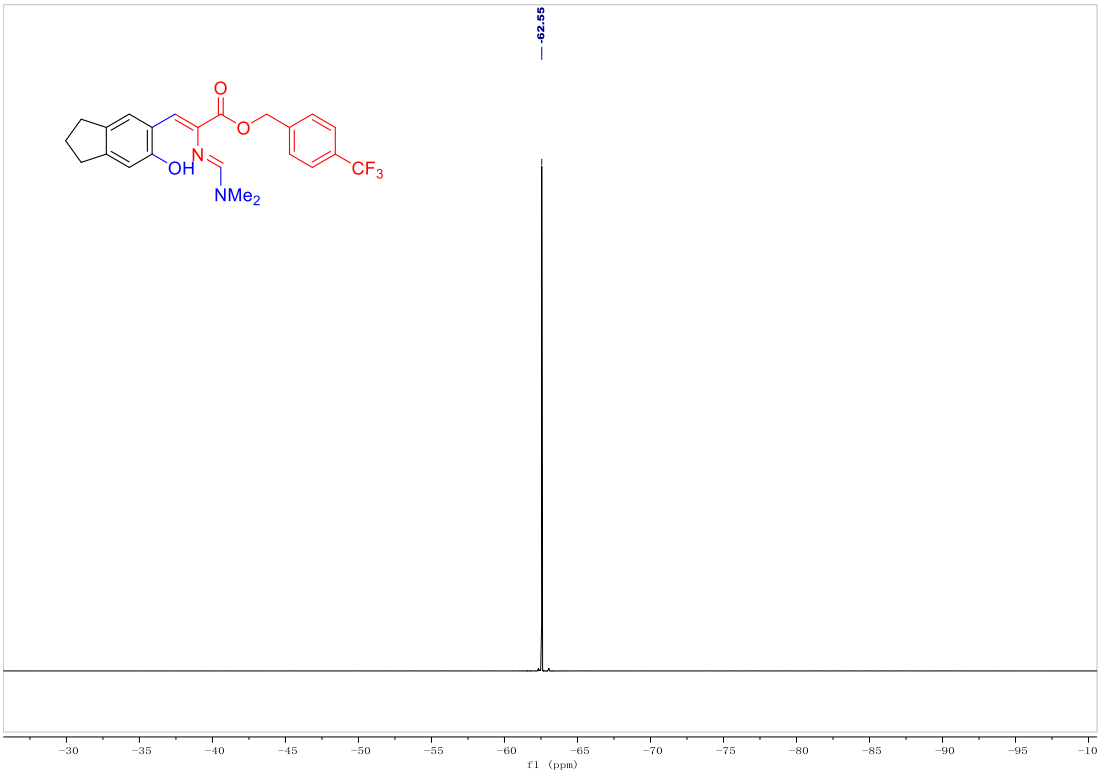
3bp ^{13}C NMR



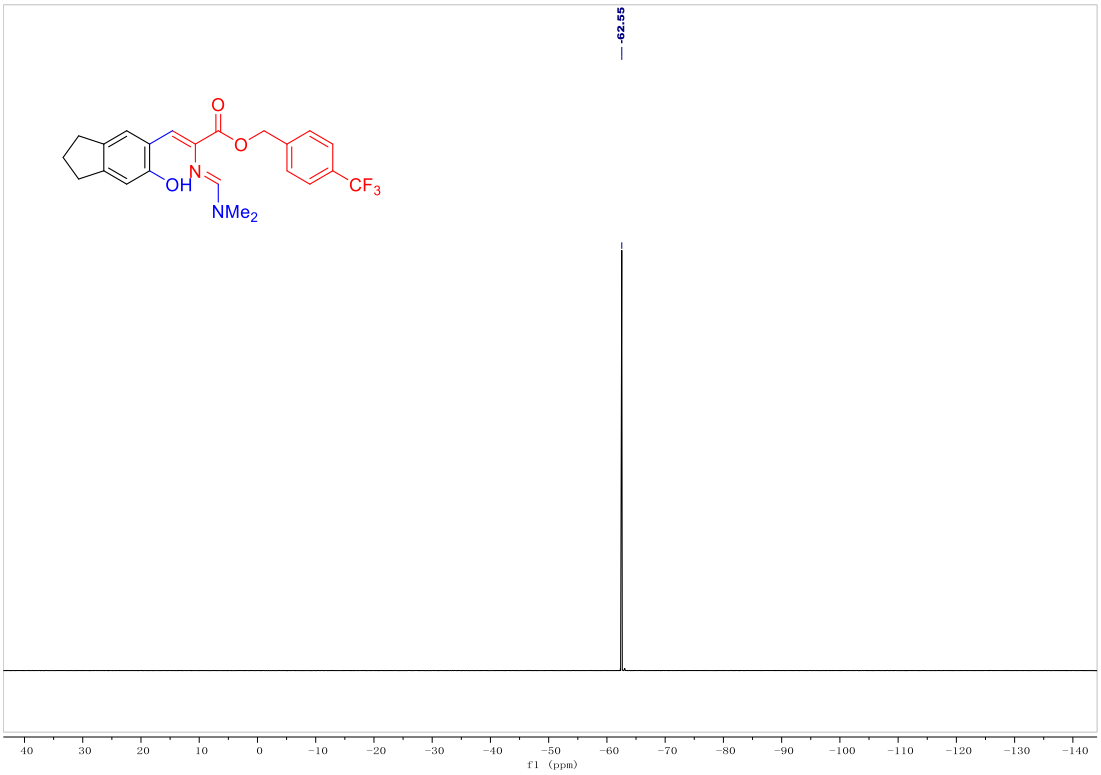
3bq ^{1}H NMR



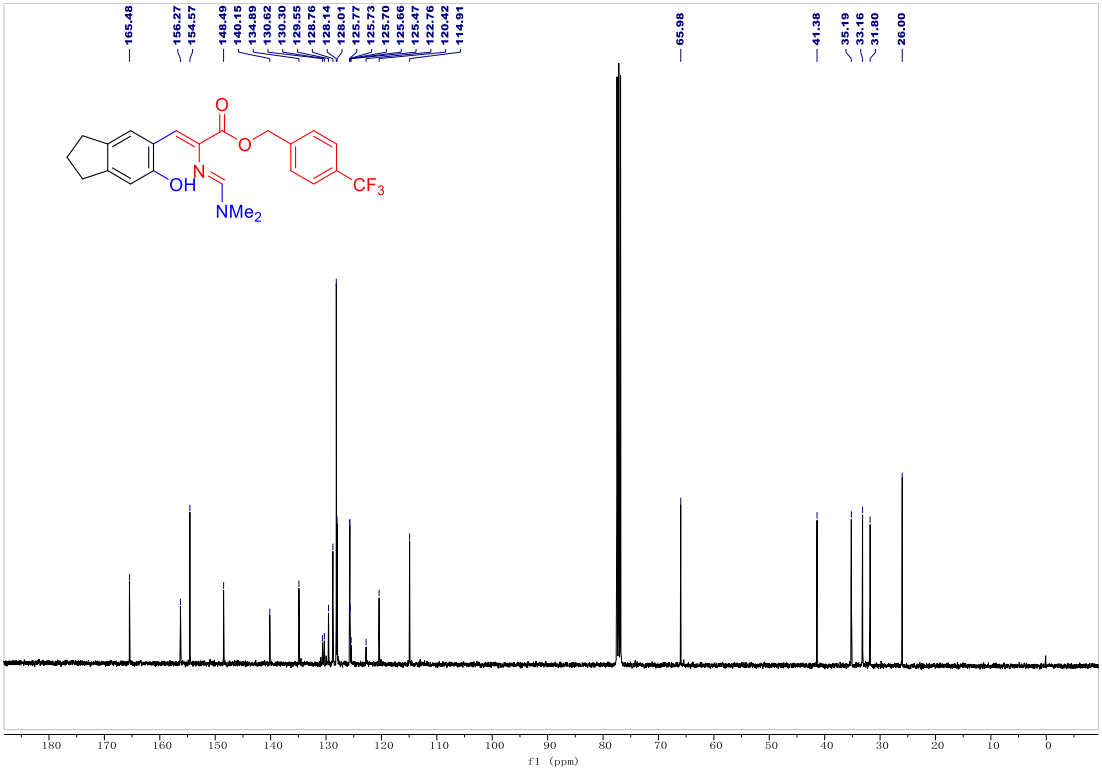
3bq ^{19}F{^{1}H} NMR



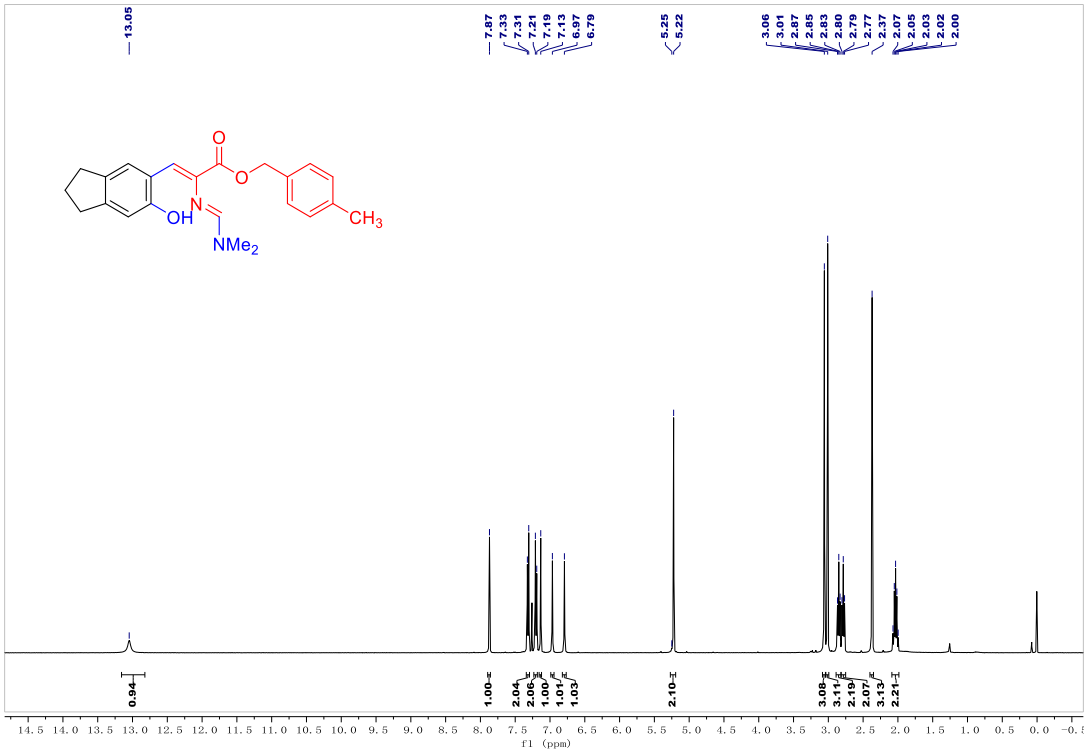
3bq ^{19}F NMR



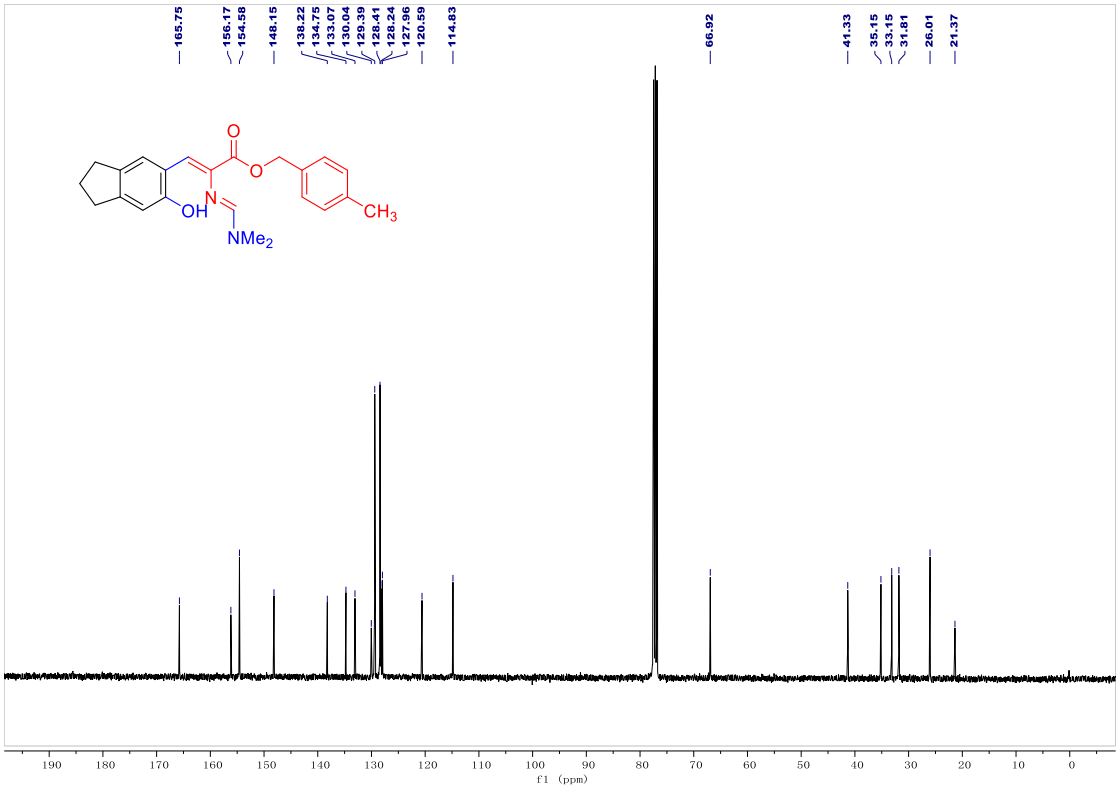
3bq ^{13}C NMR



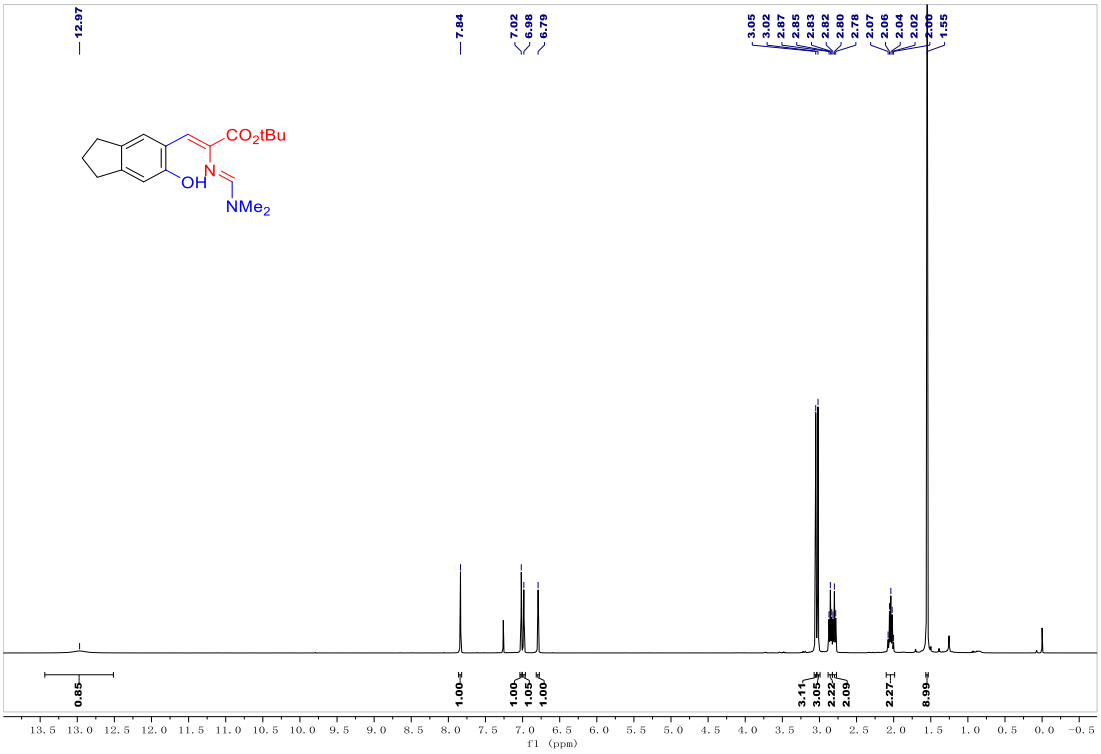
3bs ^{1}H NMR



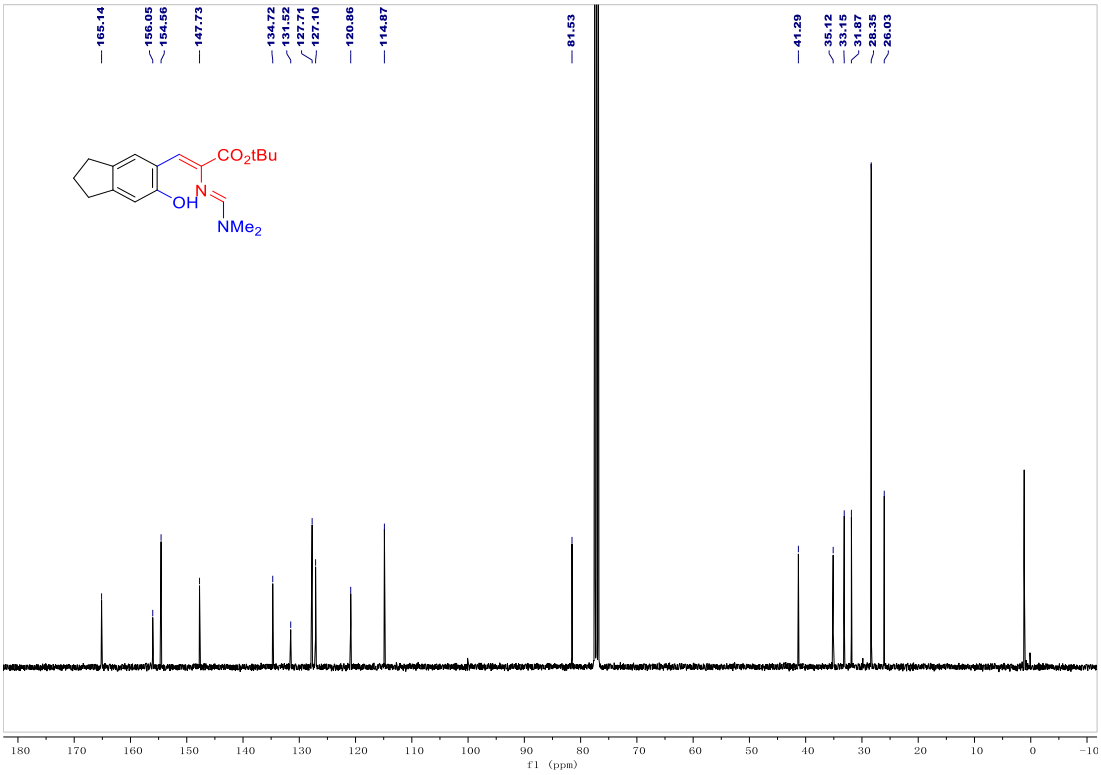
3bs ^{13}C NMR



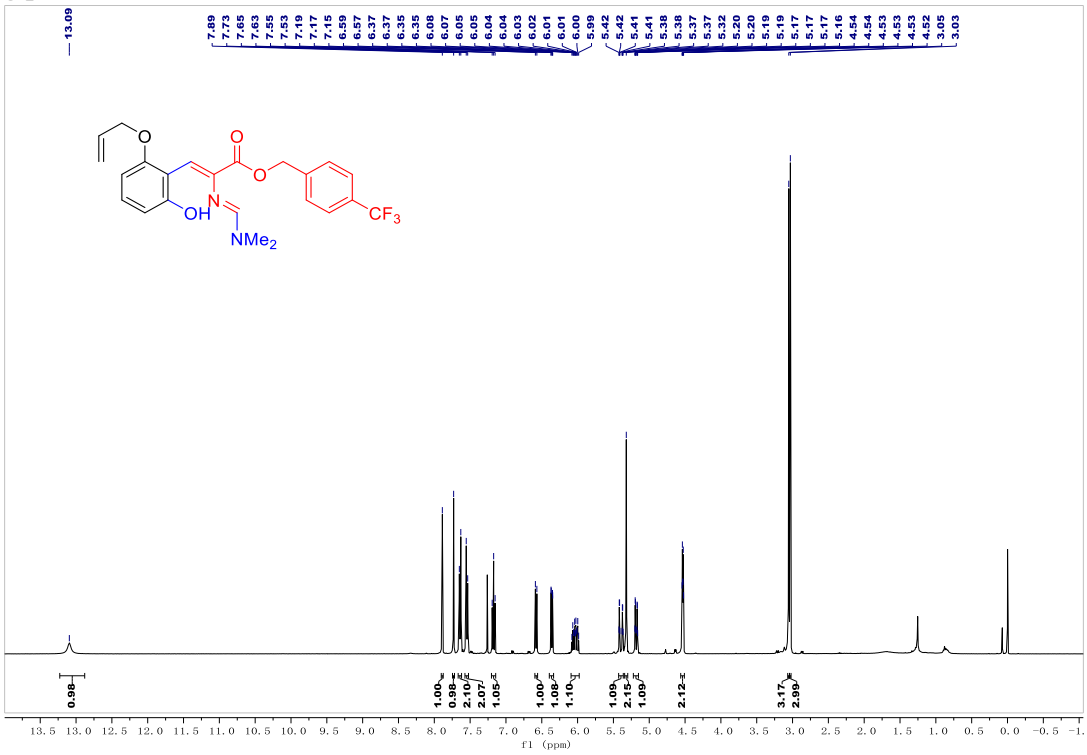
3bn ^{1}H NMR



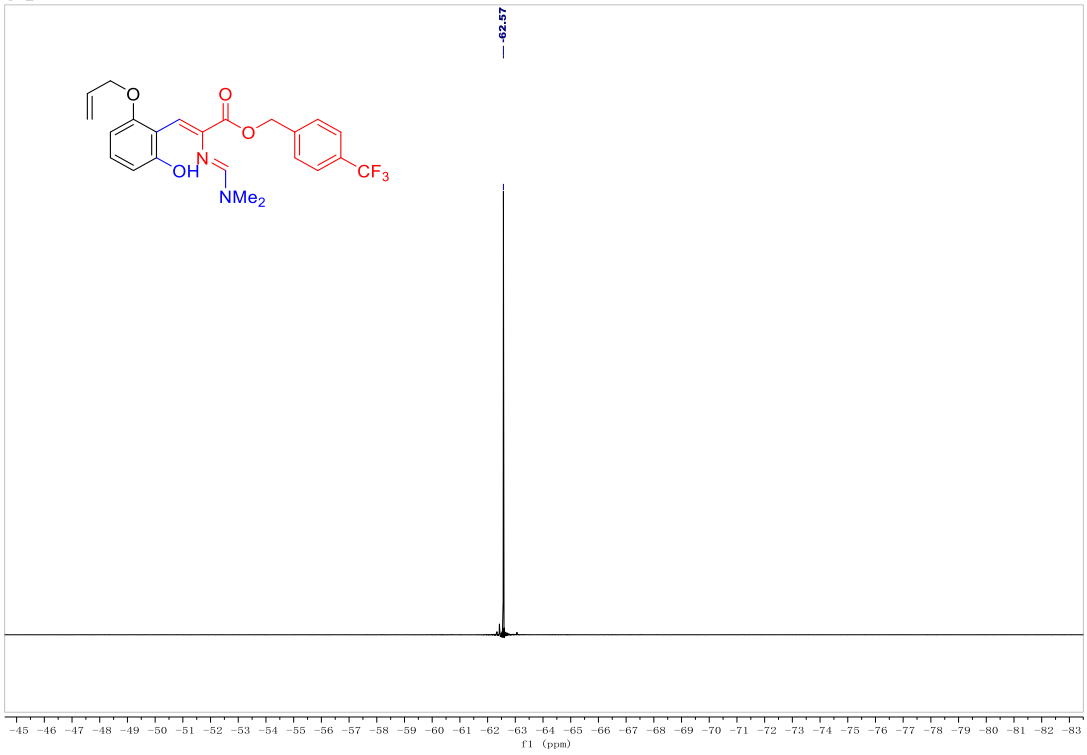
3bn ^{13}C NMR



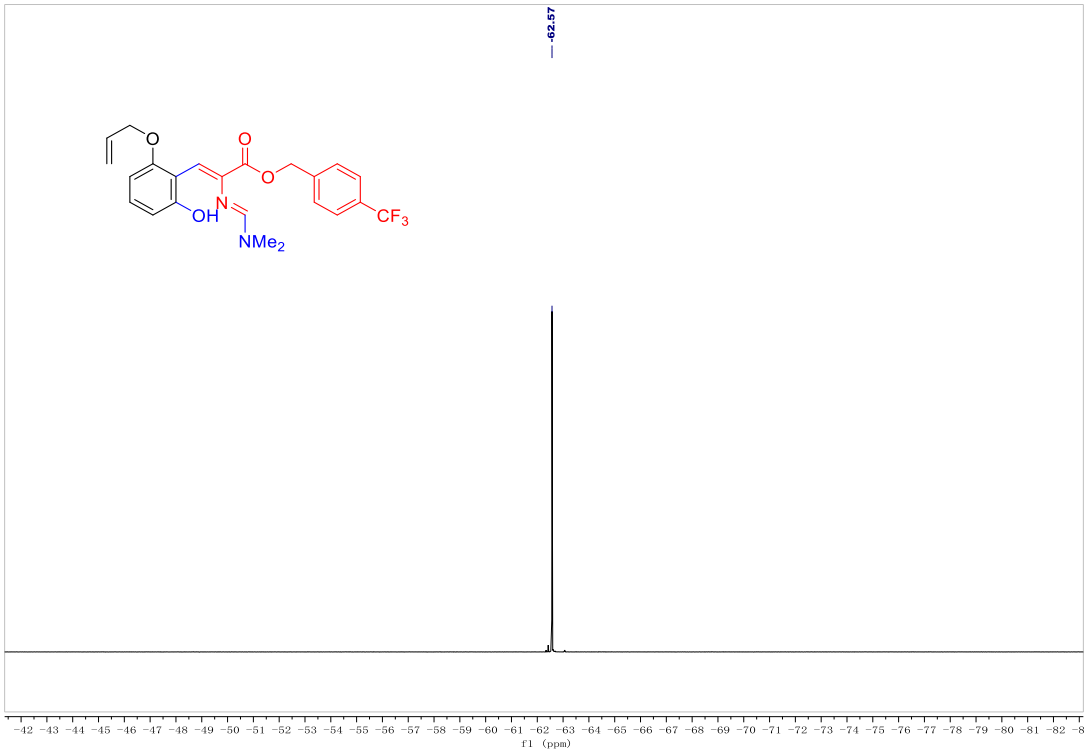
3gq ^{1}H NMR



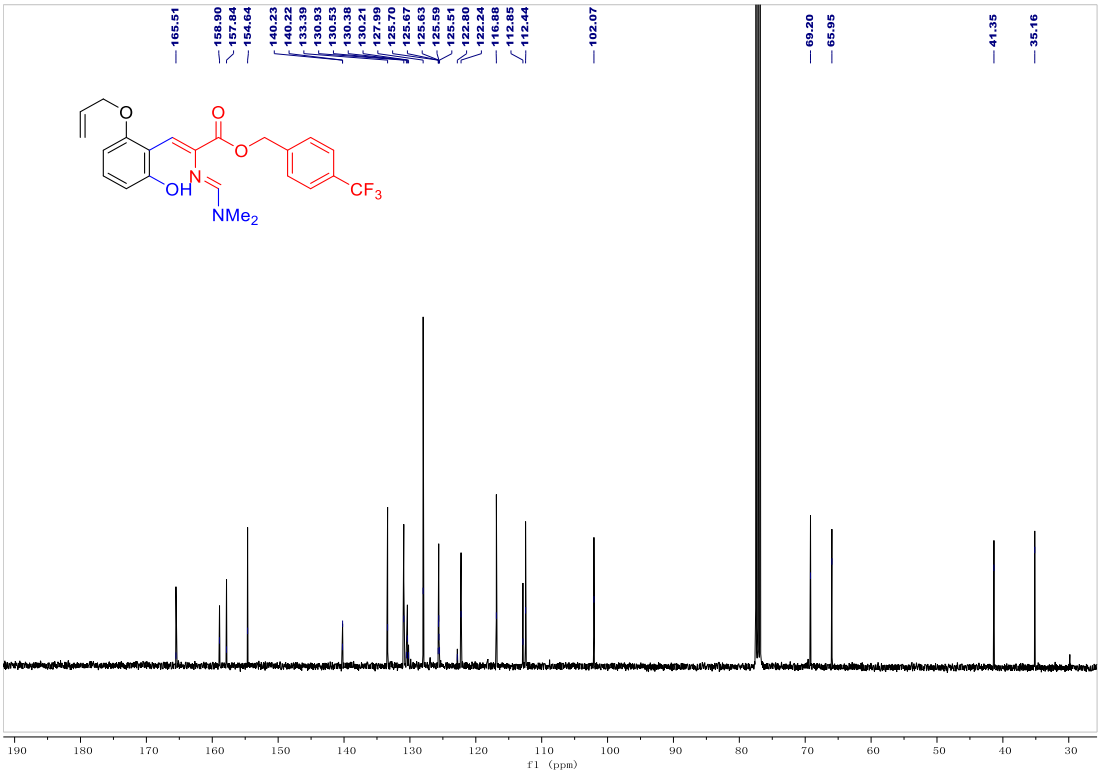
3gq ^{19}F{^{1}H} NMR



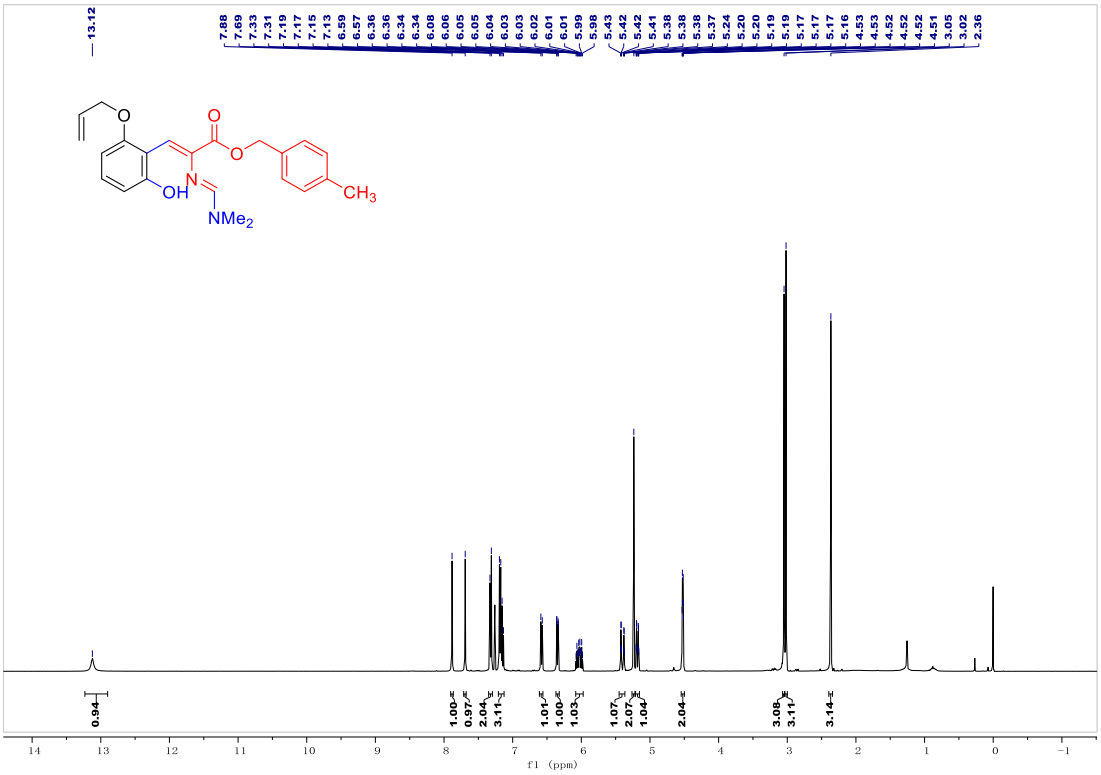
3gq ^{19}F NMR



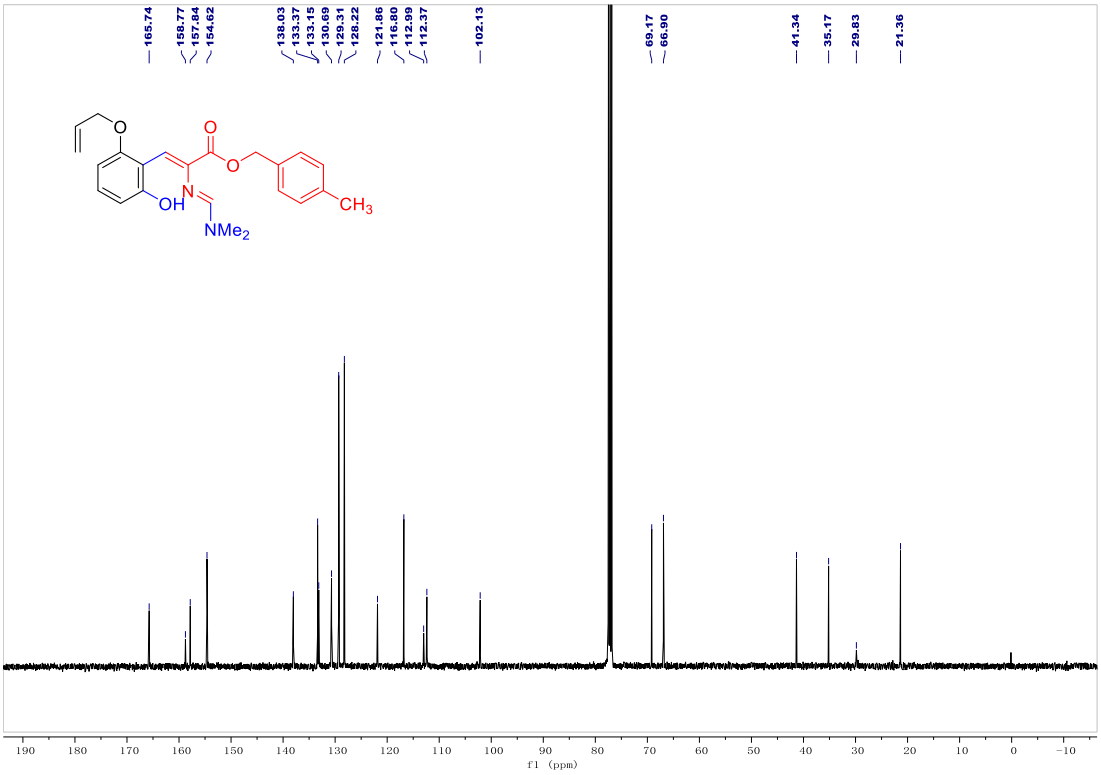
3gq ^{13}C NMR



3gs ^{1}H NMR

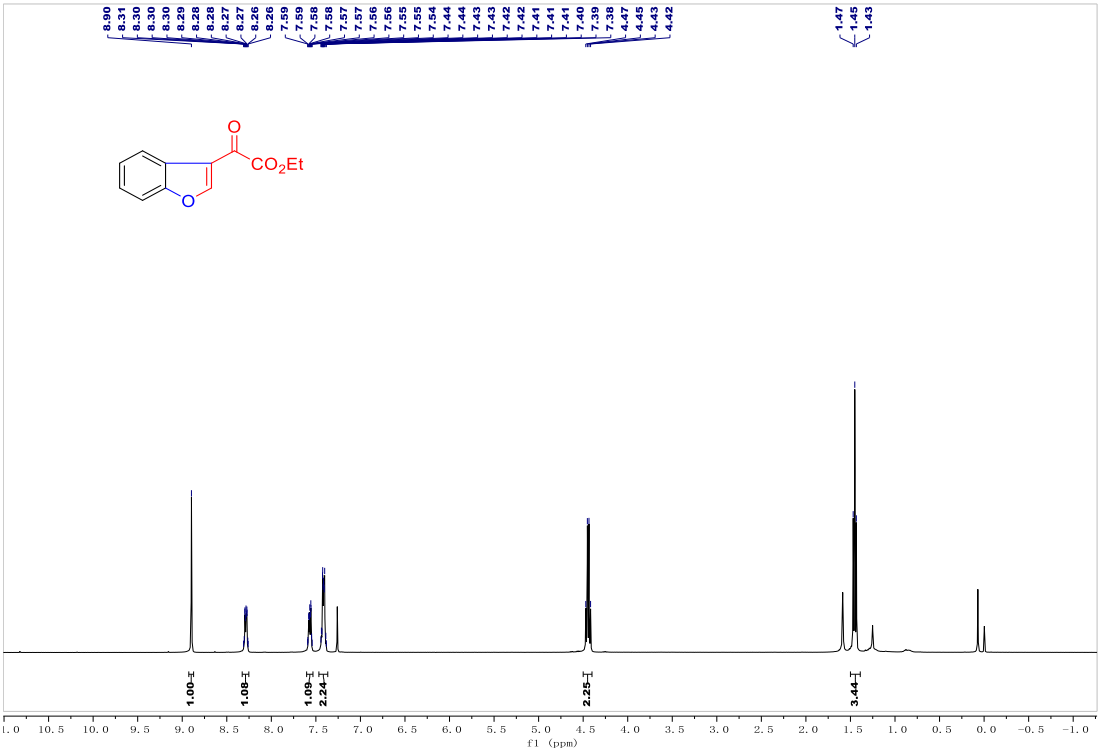


3gs ^{13}C NMR

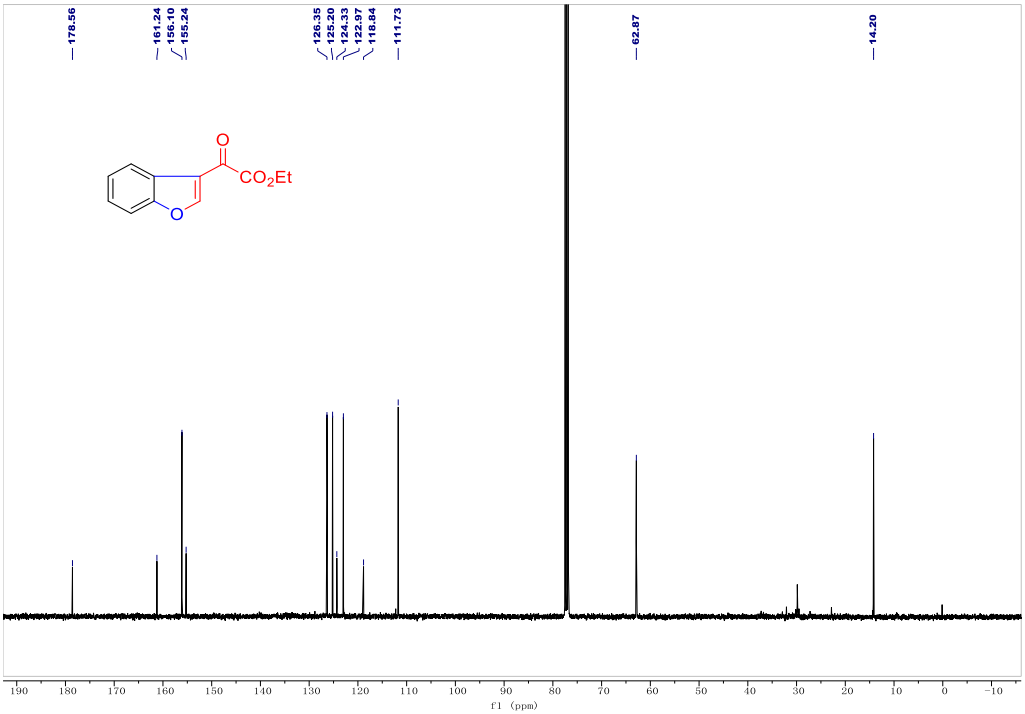


^{1}H, ^{13}C and ^{19}F NMR Spectra of Benzofuran-3-oxocarboxylate derivatives

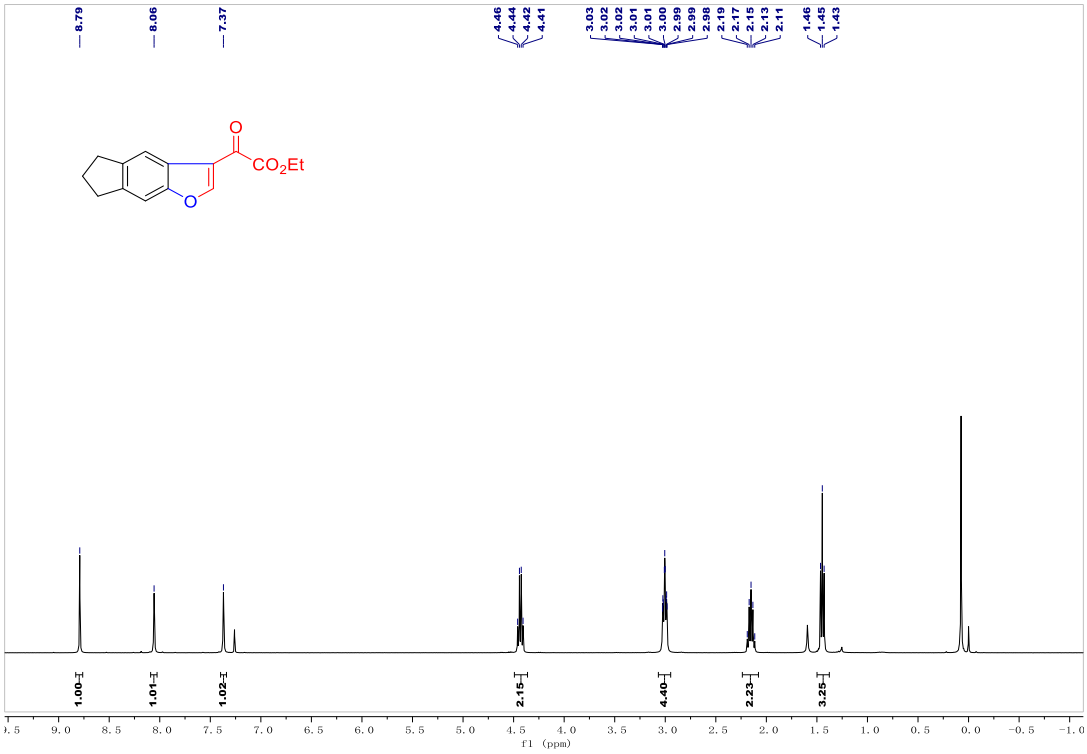
4a ^{1}H NMR



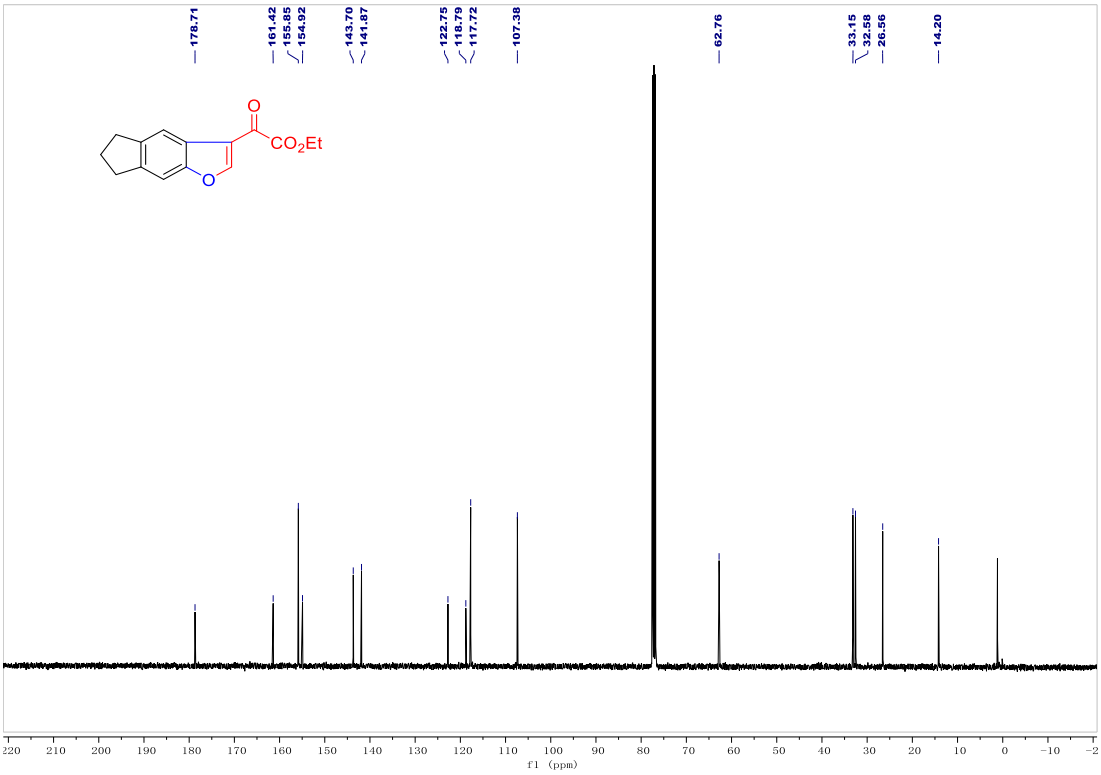
4a ^{13}C NMR



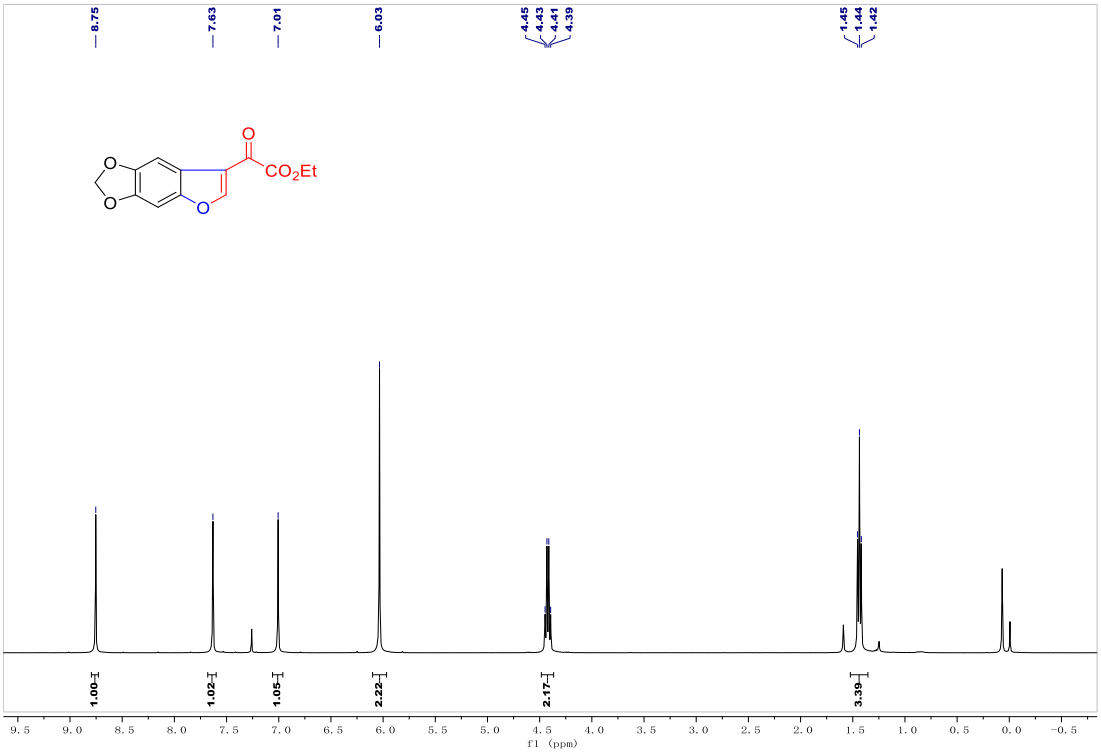
4b ^{1}H NMR



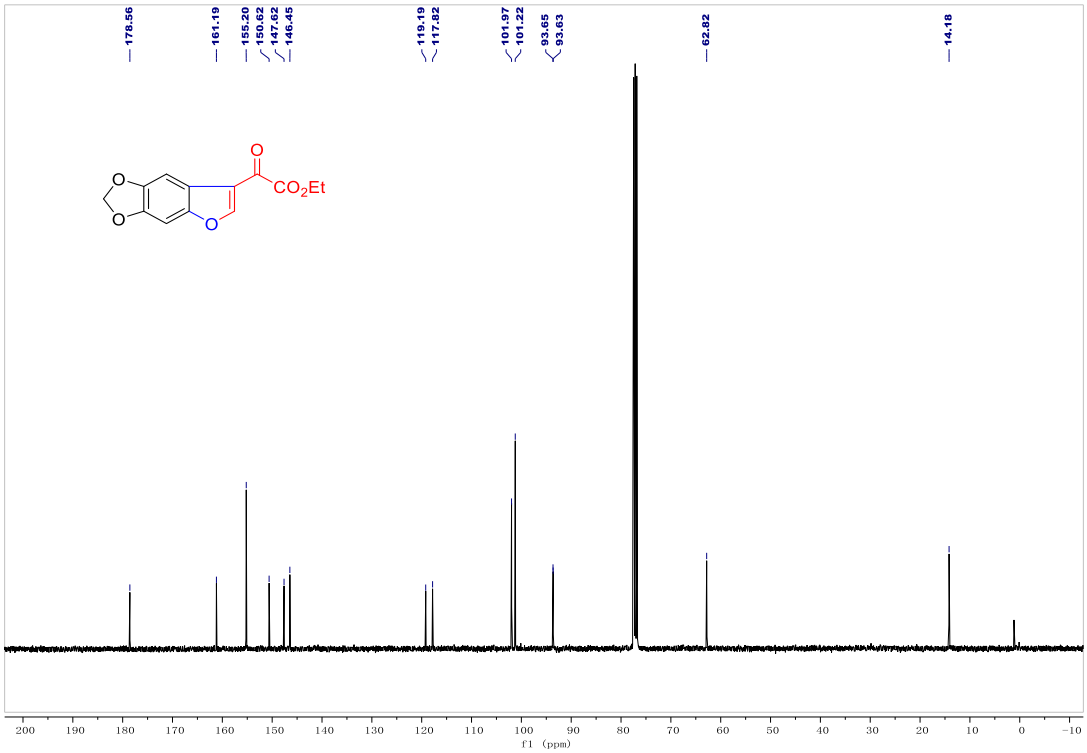
4b ^{13}C NMR



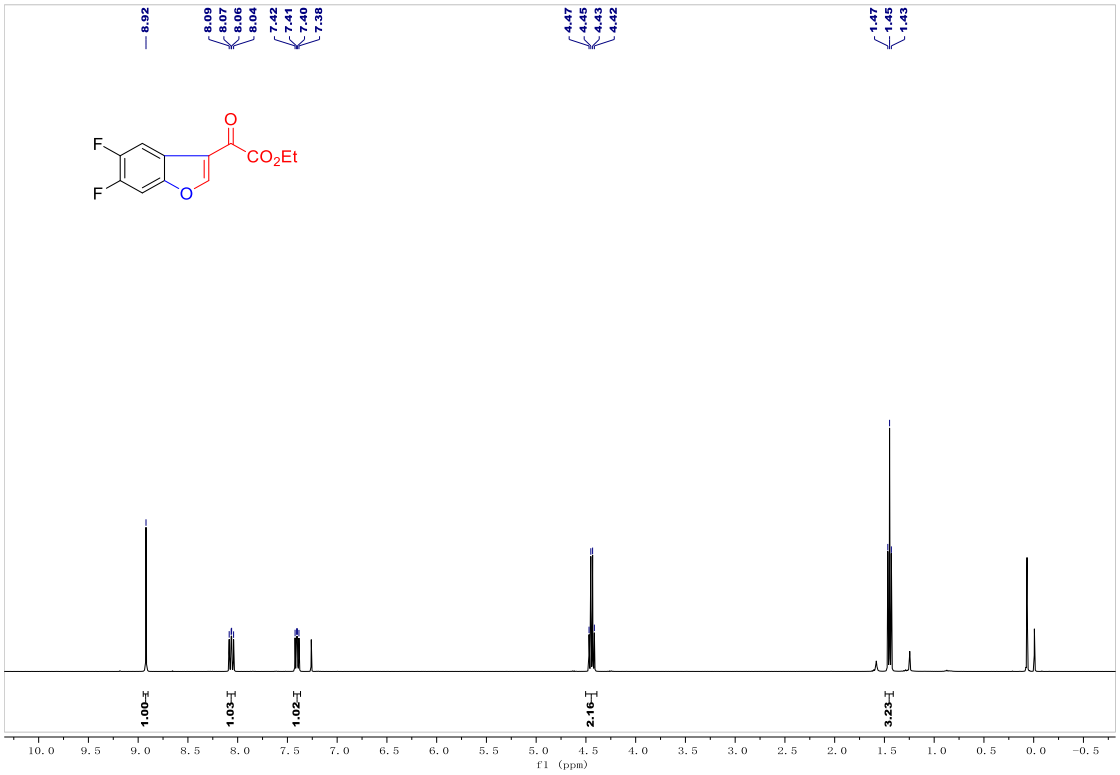
4c ^{1}H NMR



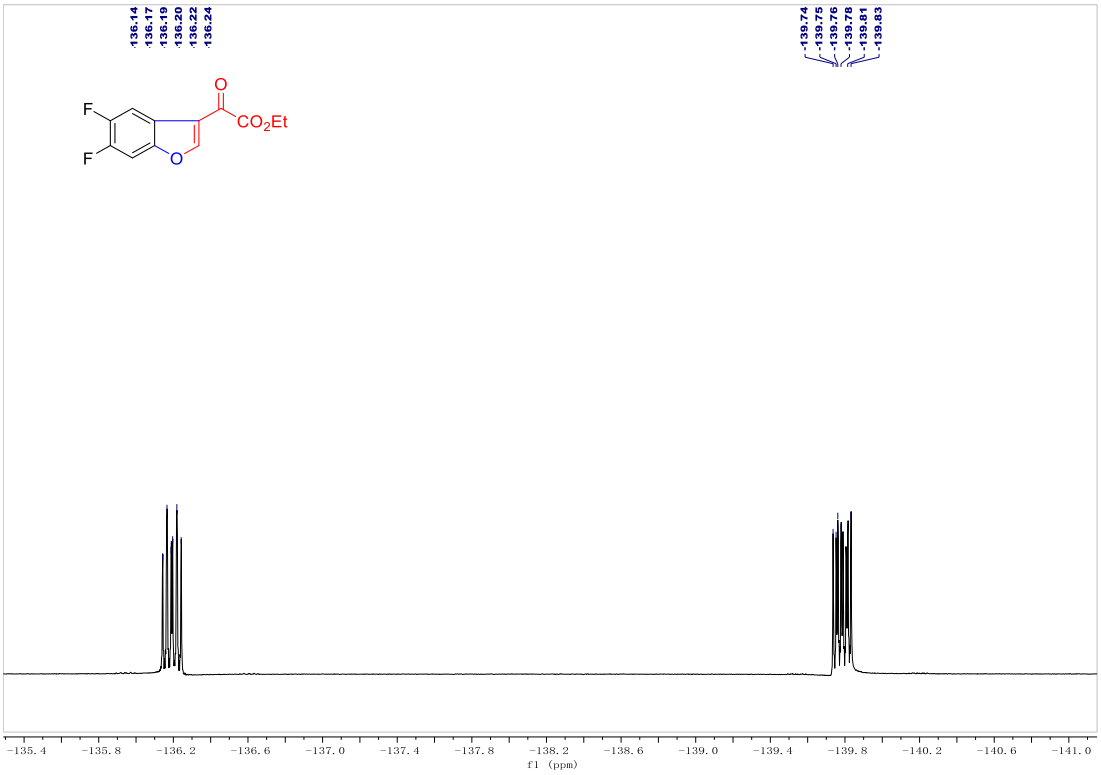
4c ^{13}C NMR



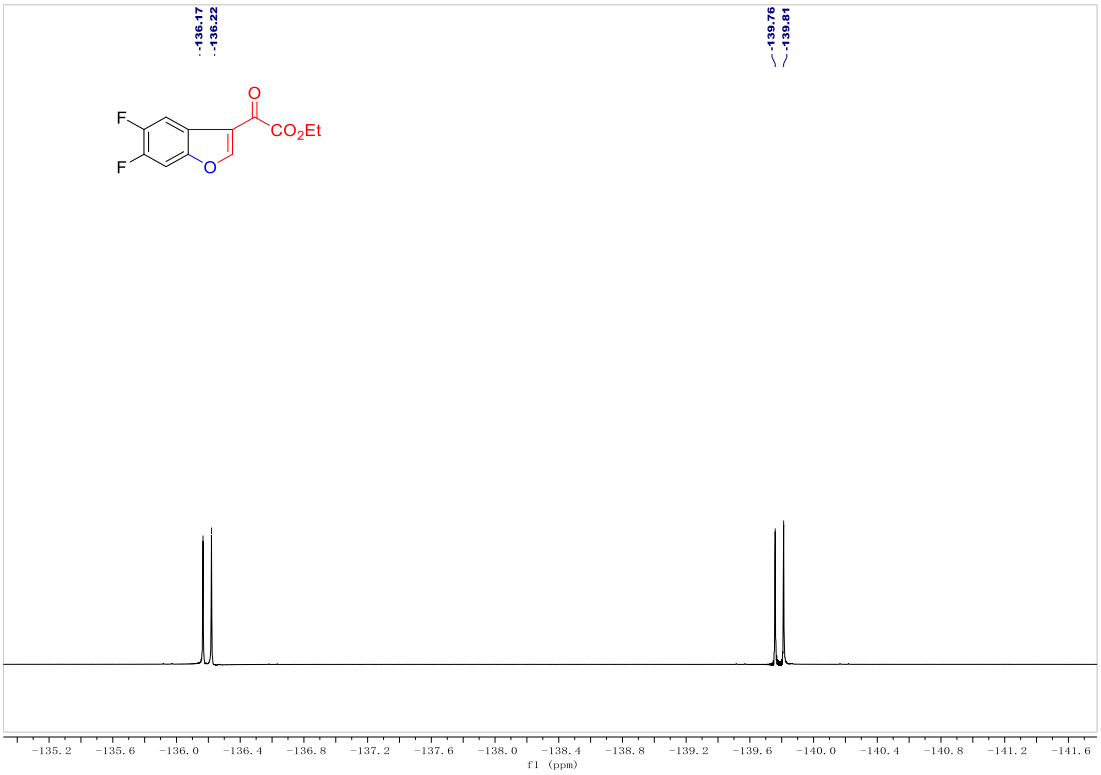
4d ^{1}H NMR



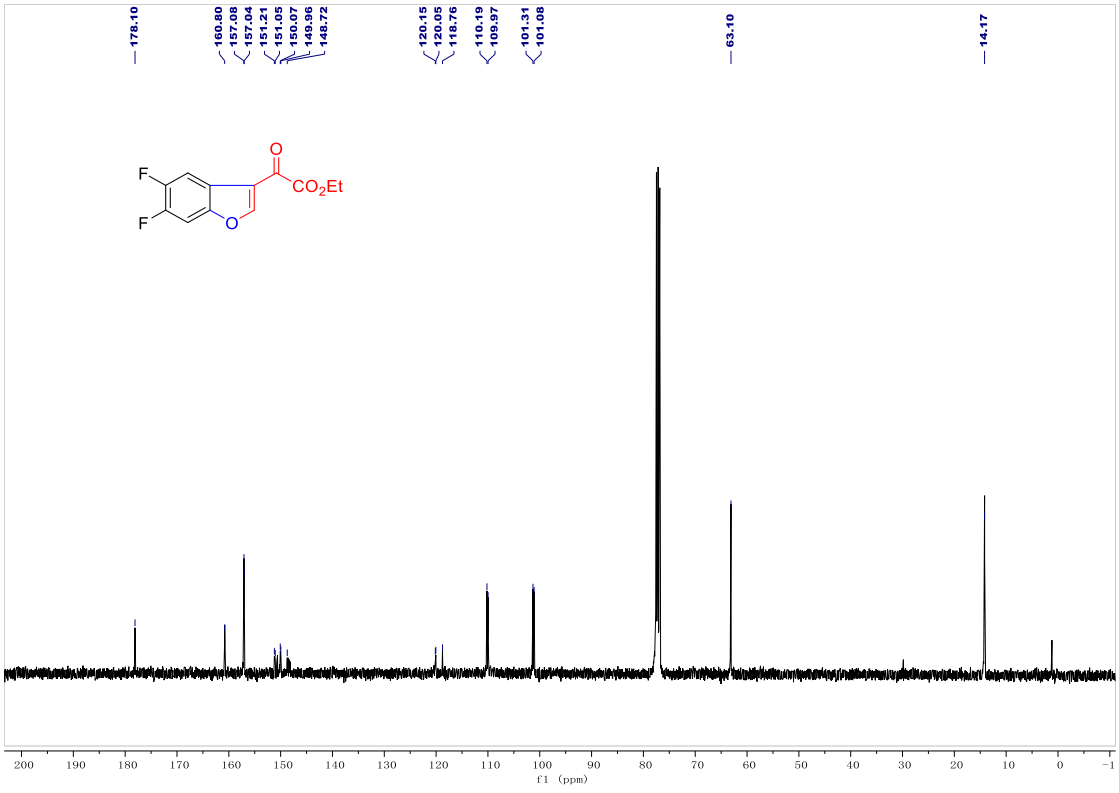
4d ^{19}F{^{1}H} NMR



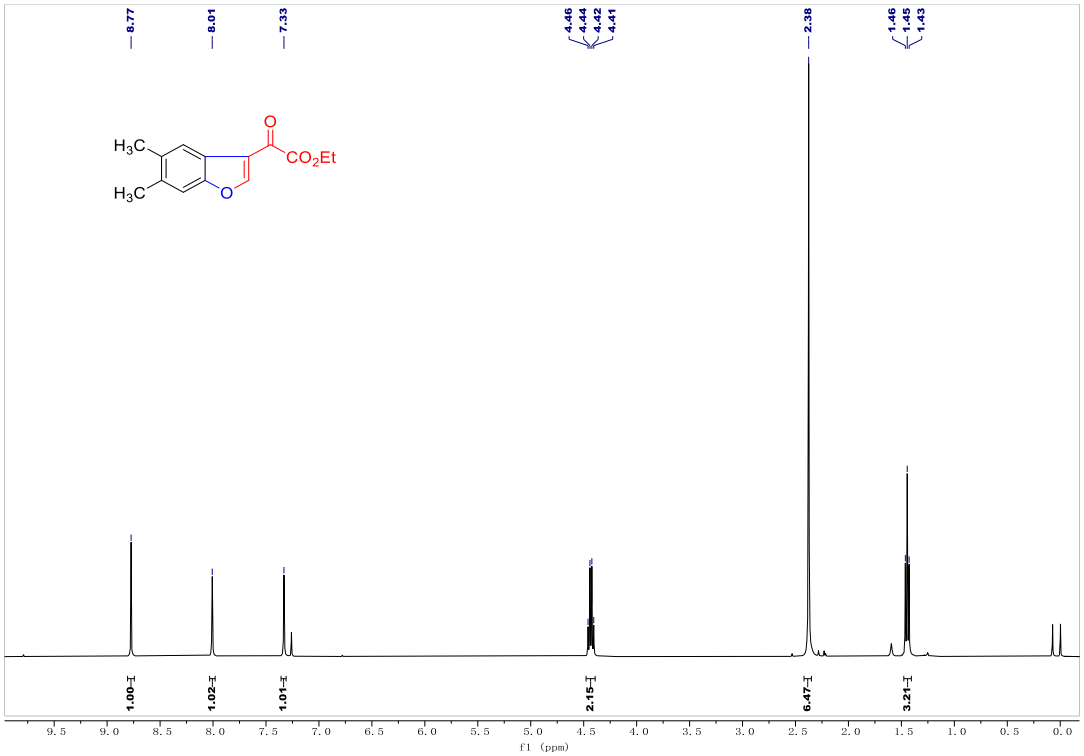
4d ^{19}F NMR



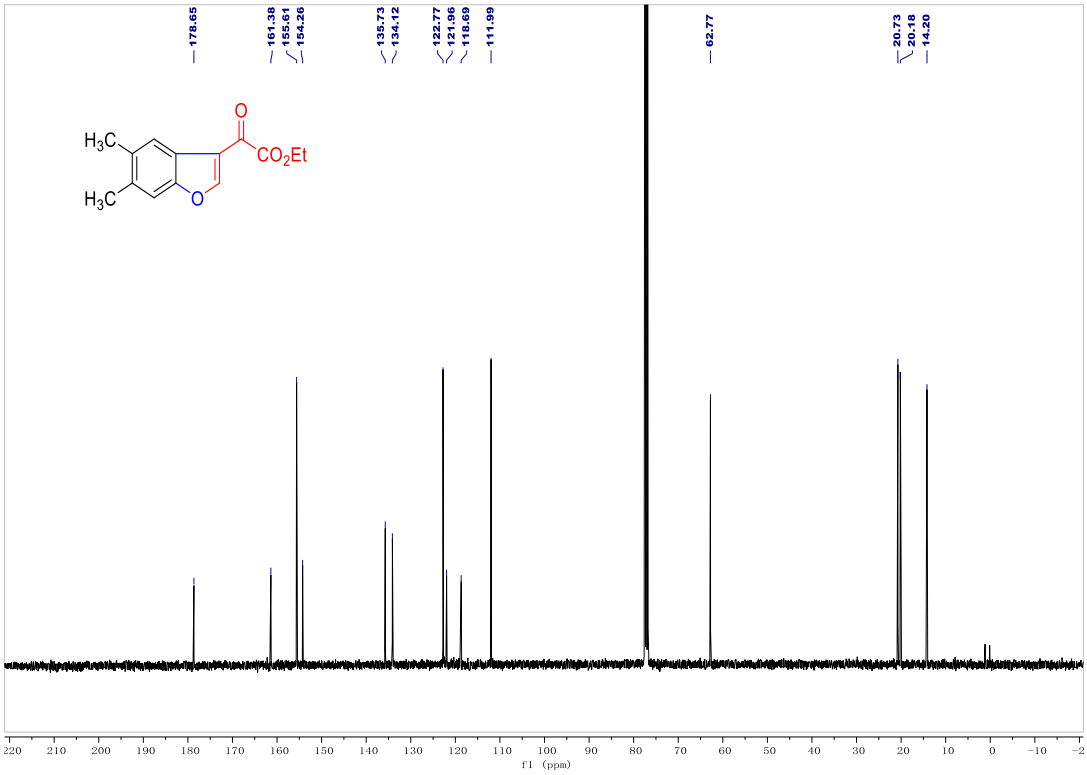
4d ^{13}C NMR



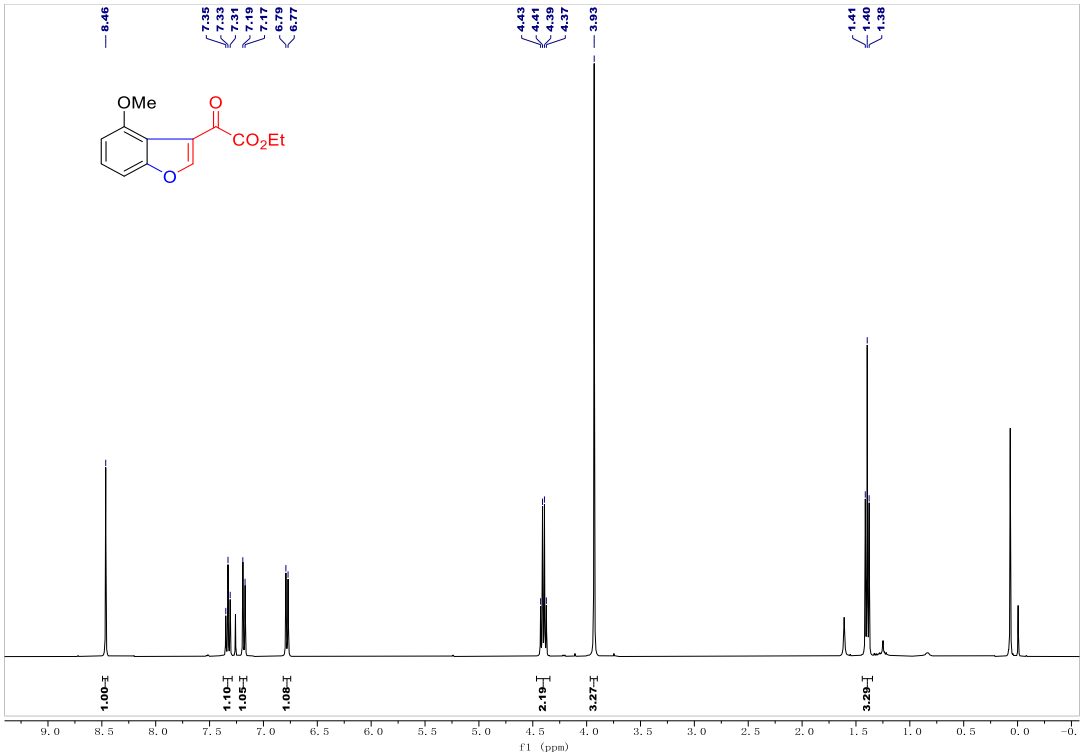
4e ^{1}H NMR



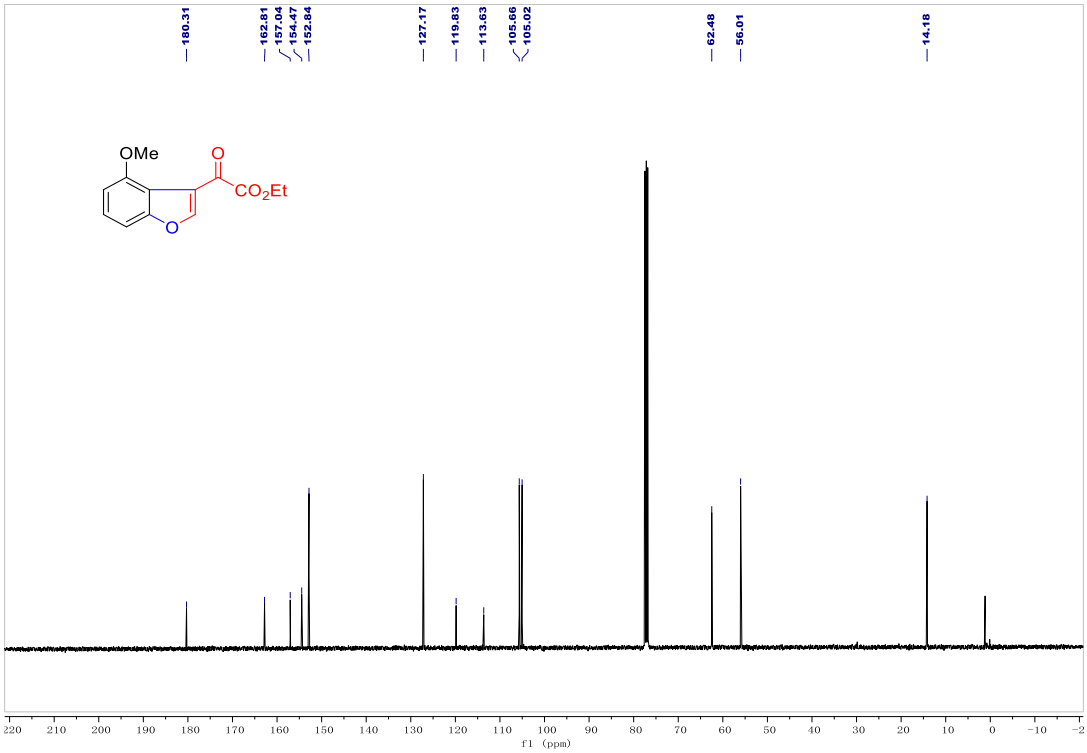
4e ^{13}C NMR



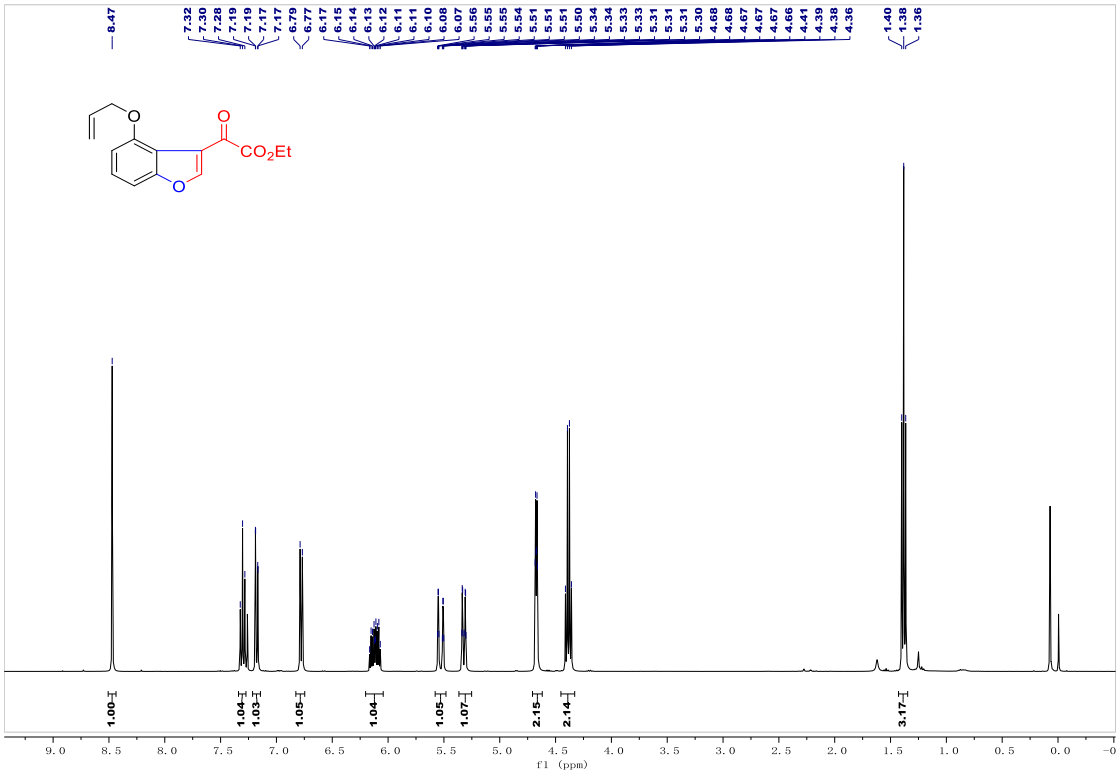
4f ^{1}H NMR



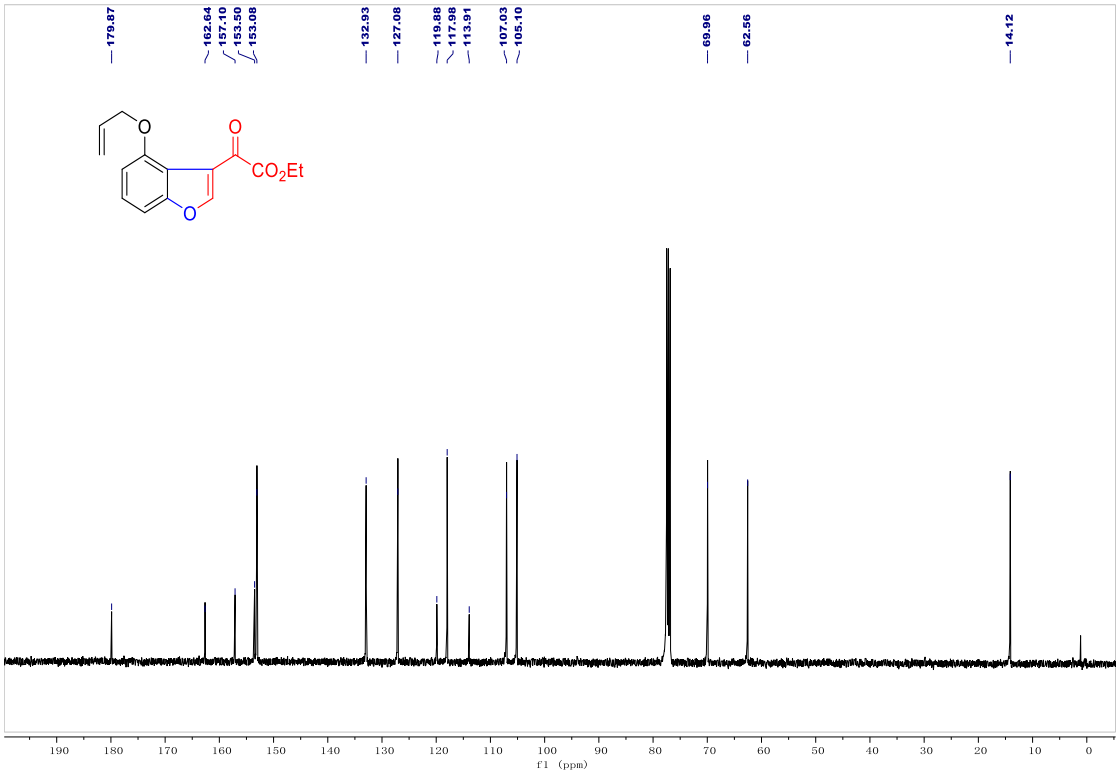
4f ^{13}C NMR



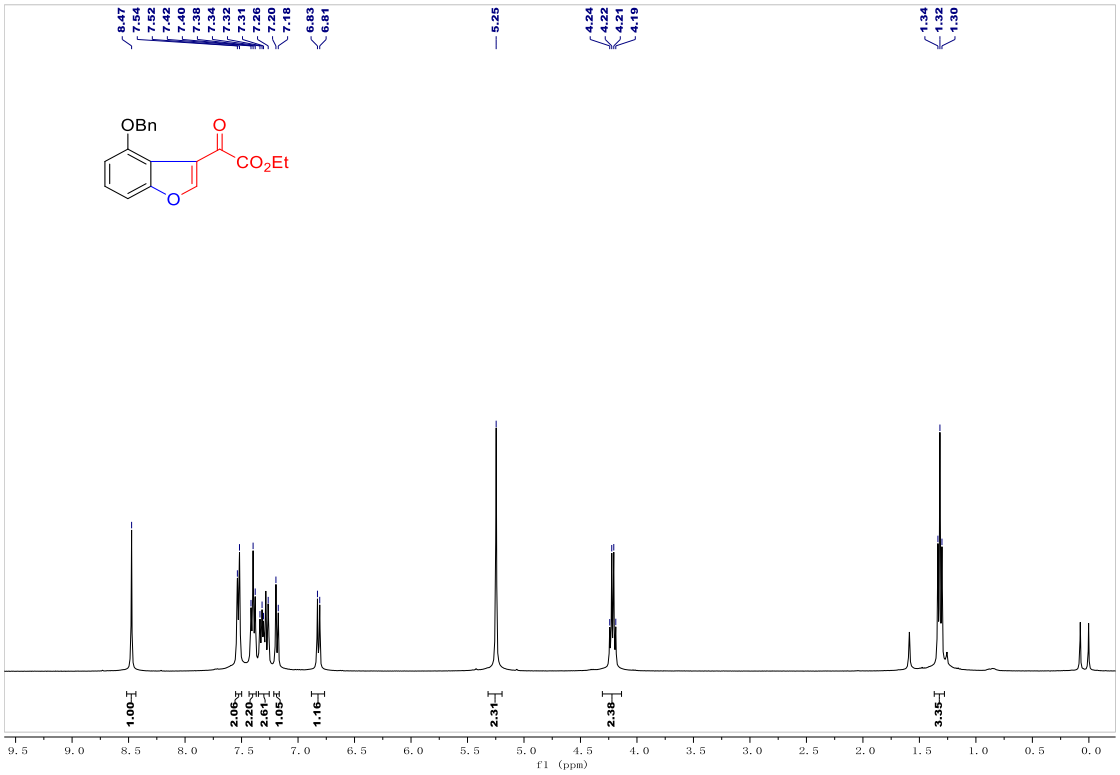
4g ^{1}H NMR



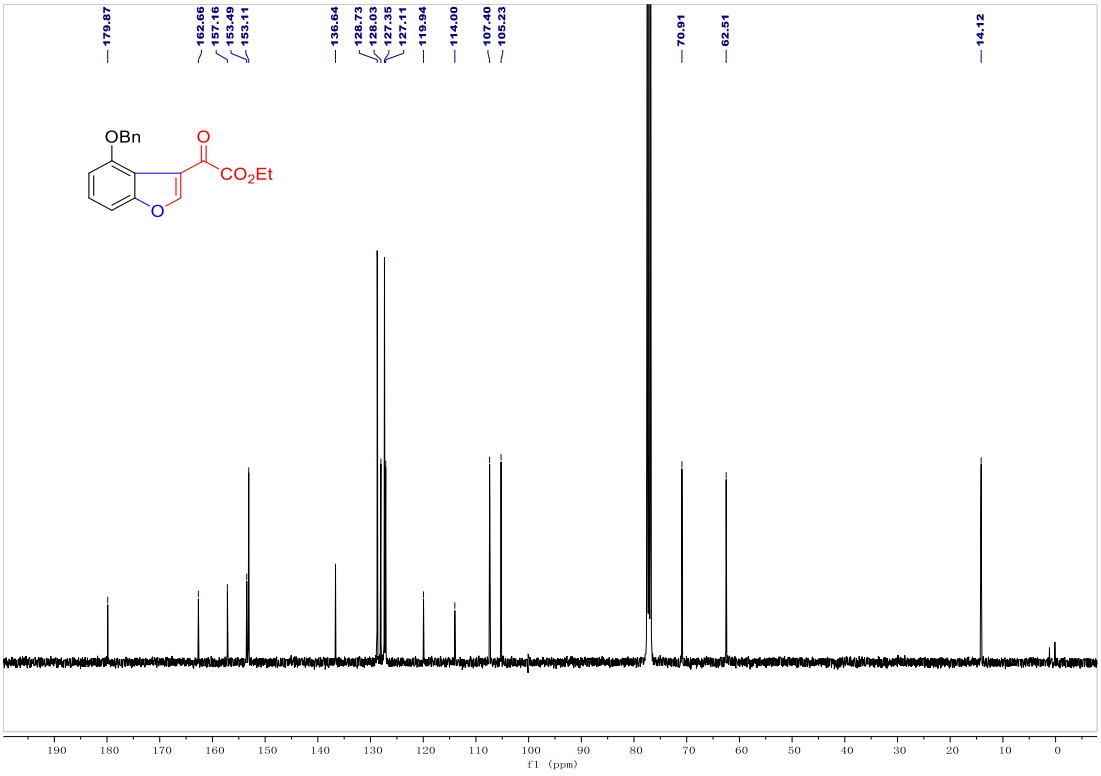
4g ^{13}C NMR



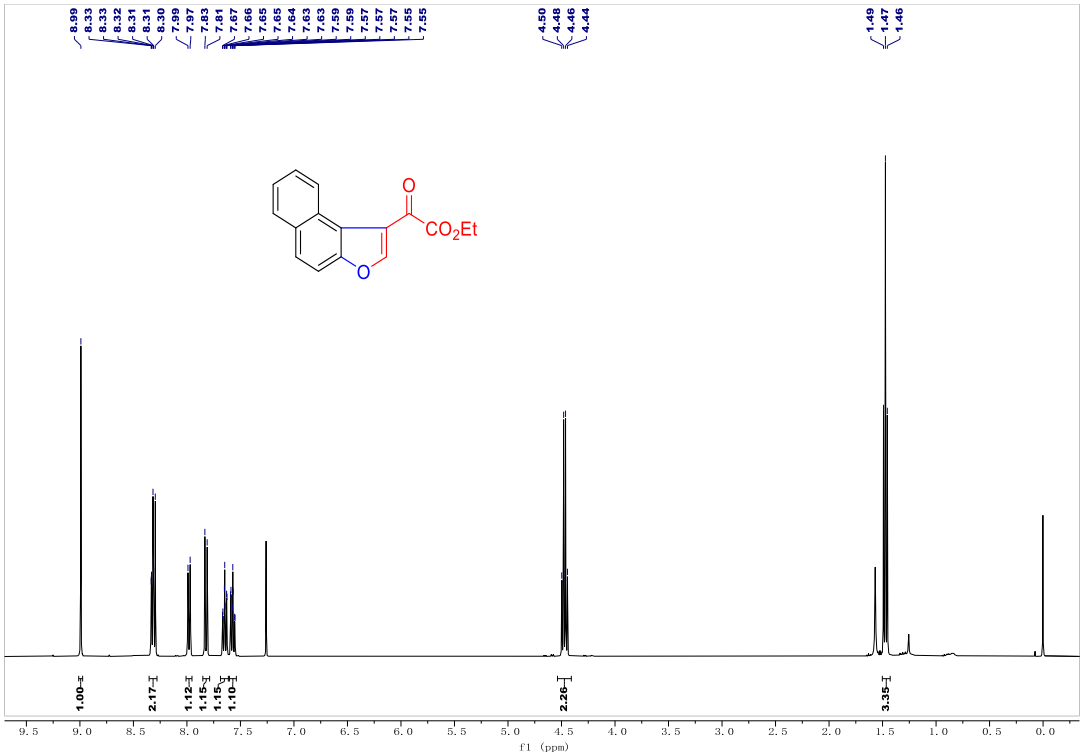
4h ^{1}H NMR



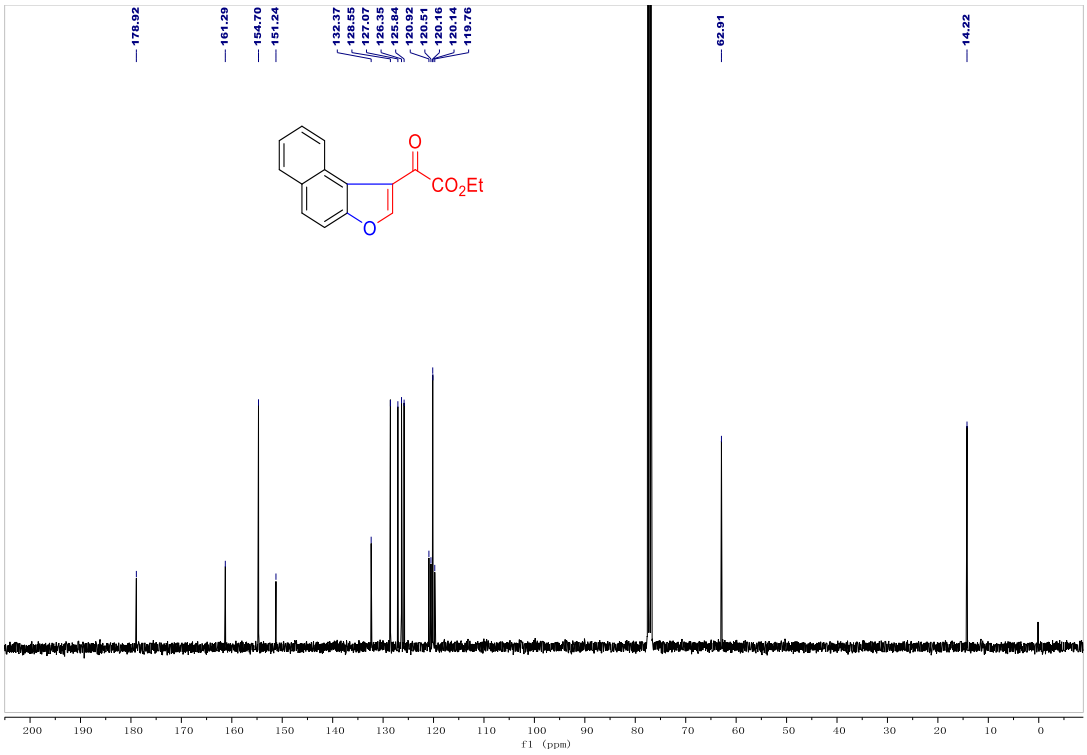
4h ^{13}C NMR



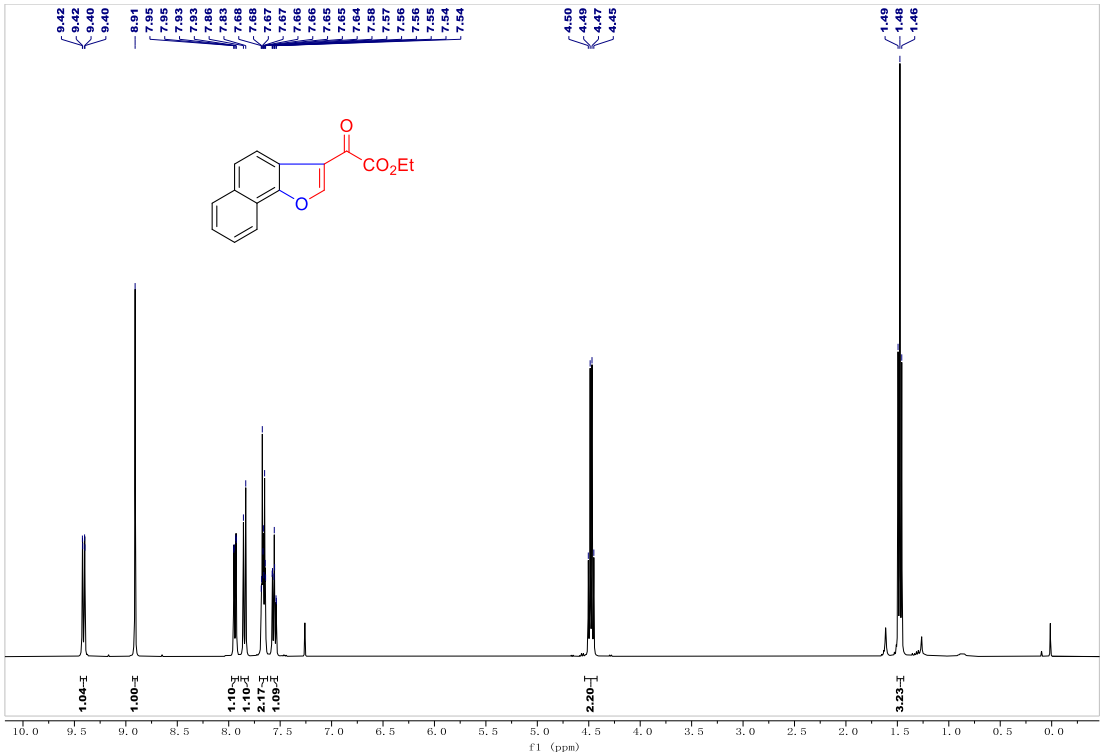
4i ^{1}H NMR



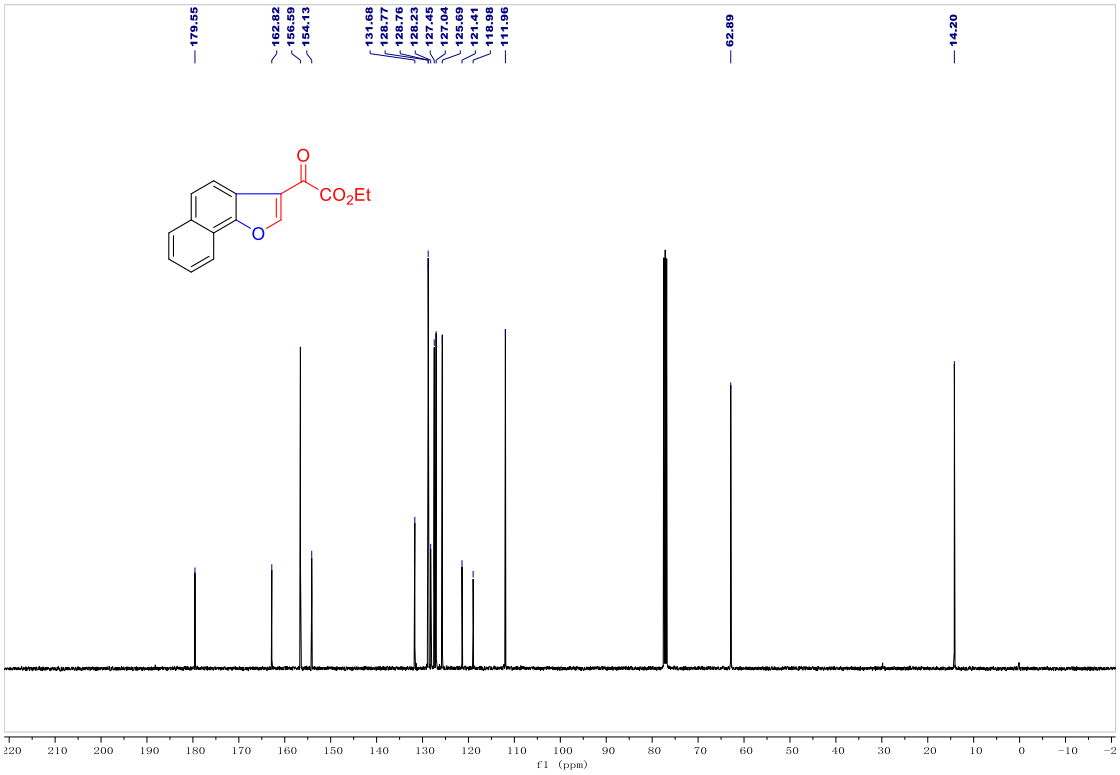
4i ^{13}C NMR



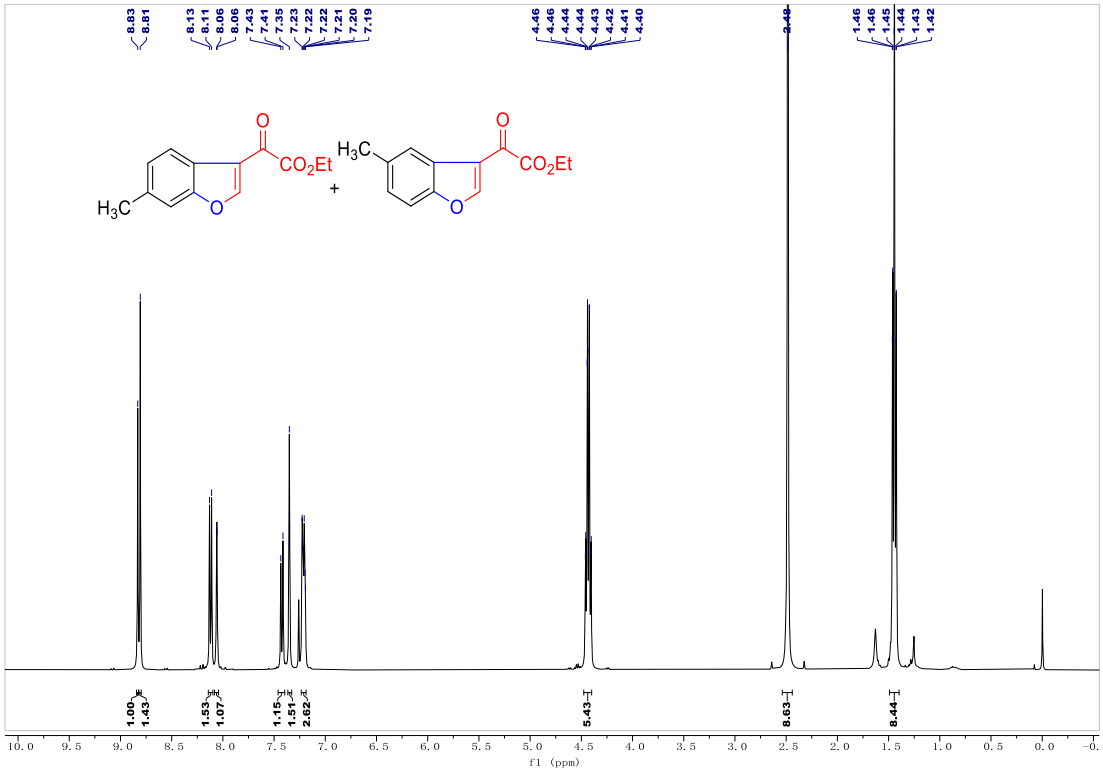
4j ^{1}H NMR



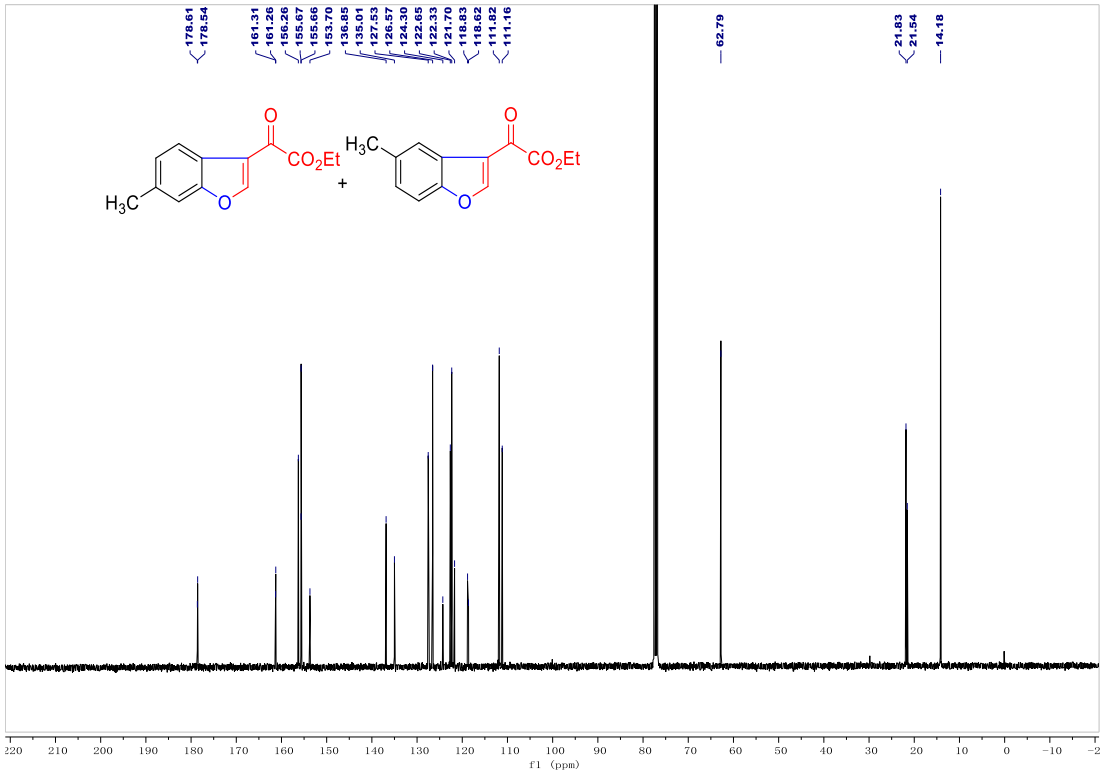
4j ^{13}C NMR



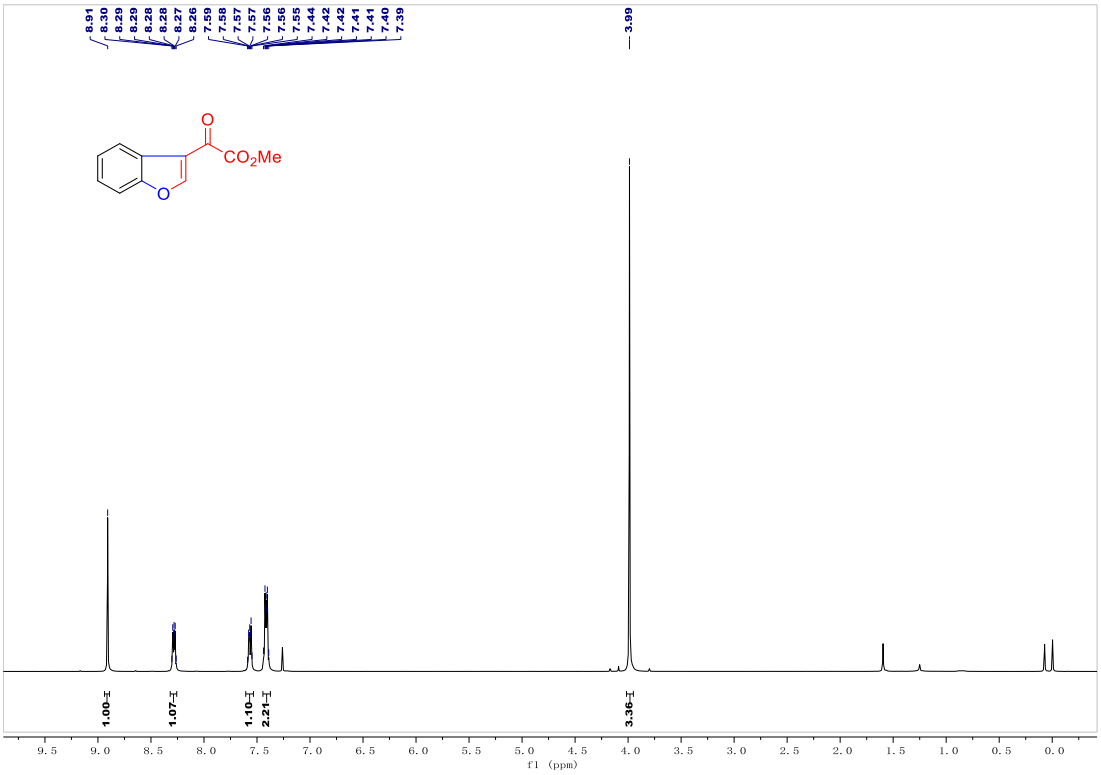
4k/4k' ^{1}H NMR



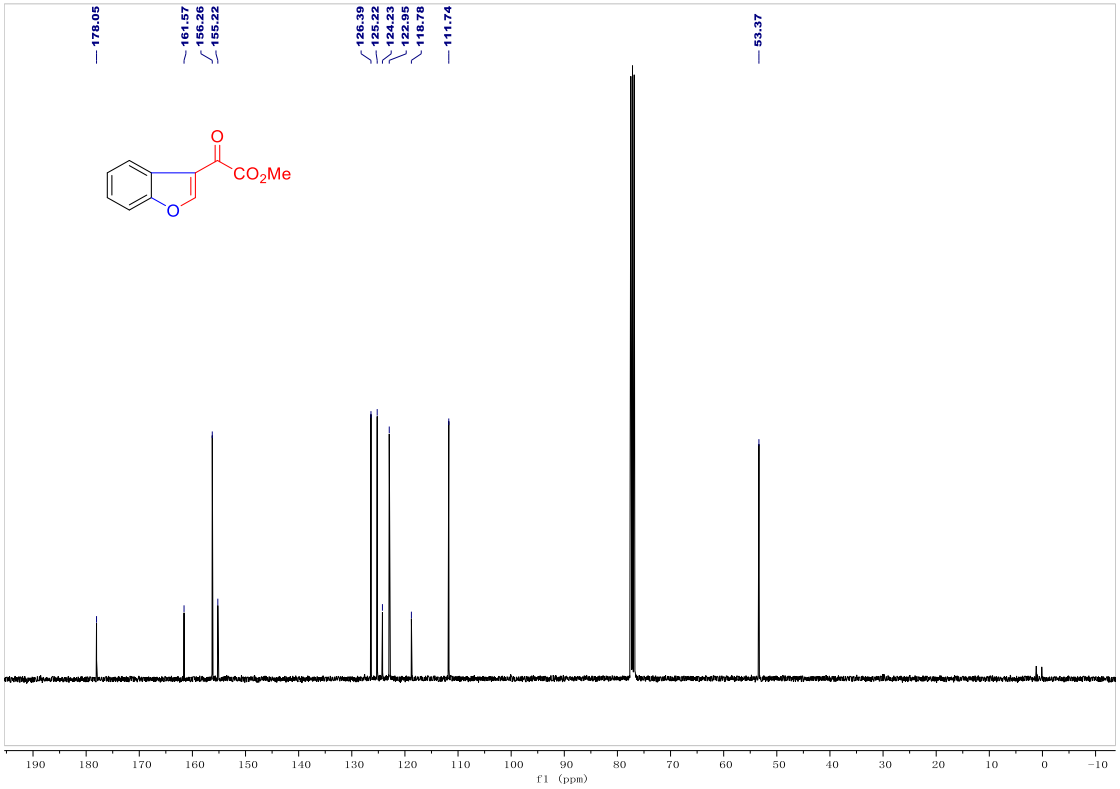
4k/4k' ^{13}C NMR



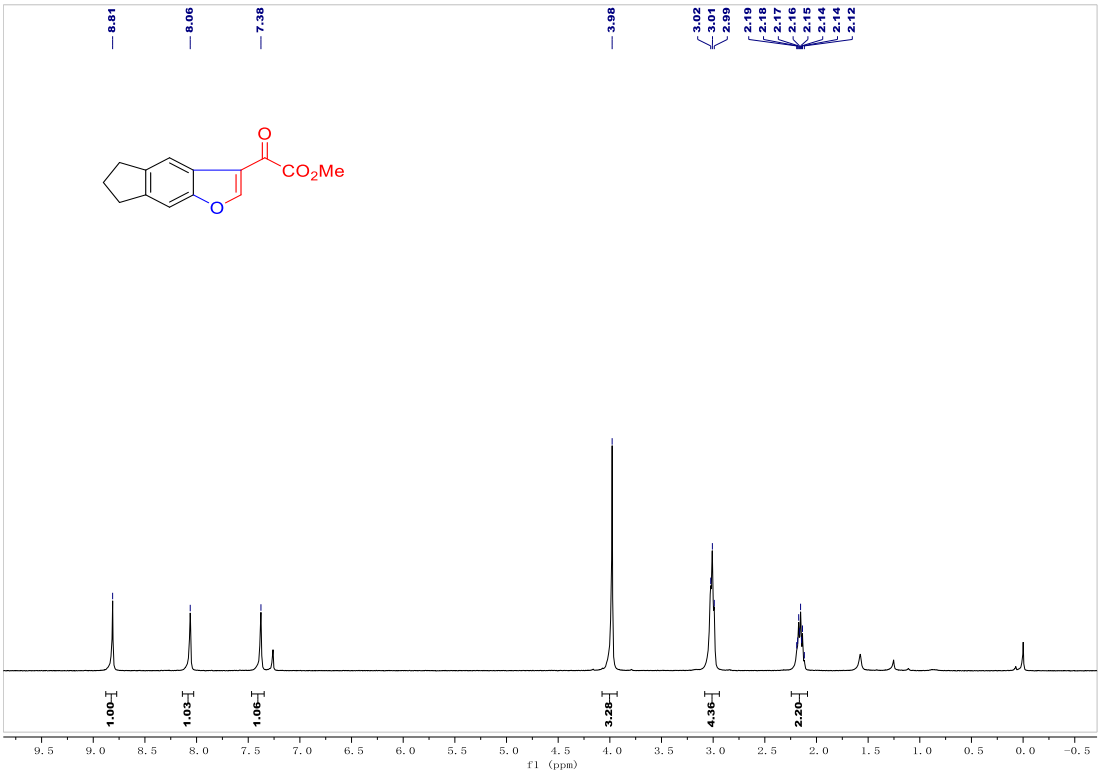
4l ^{1}H NMR



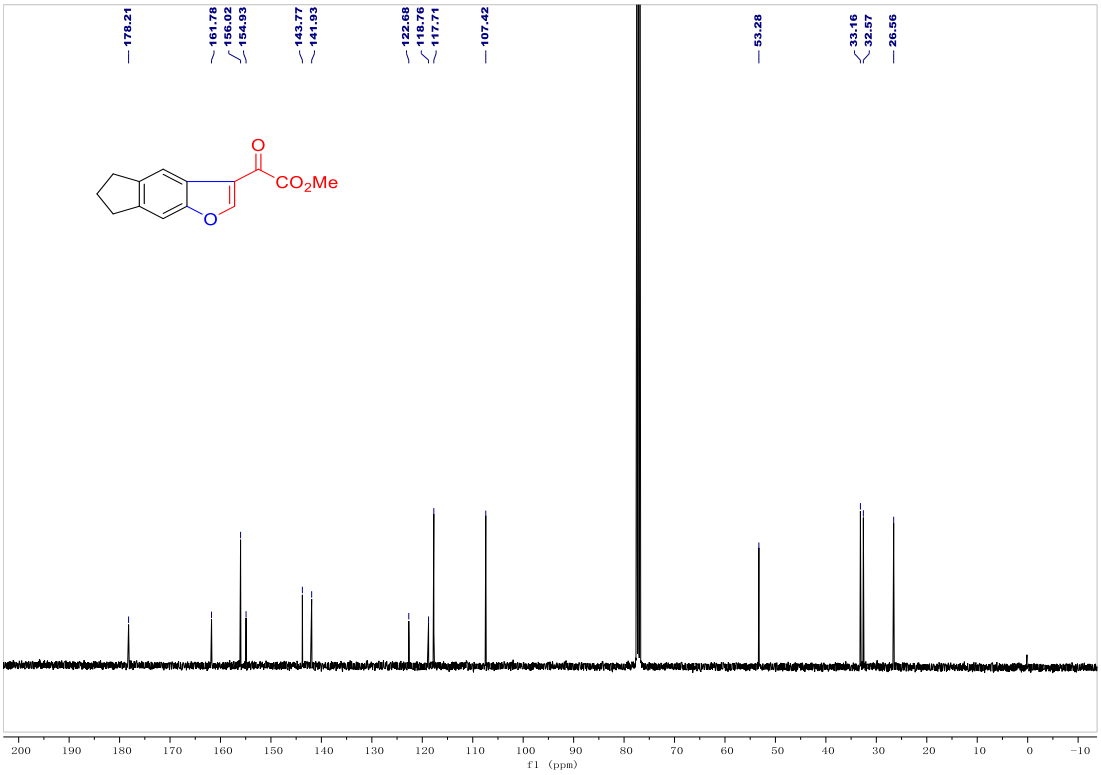
4l ^{13}C NMR



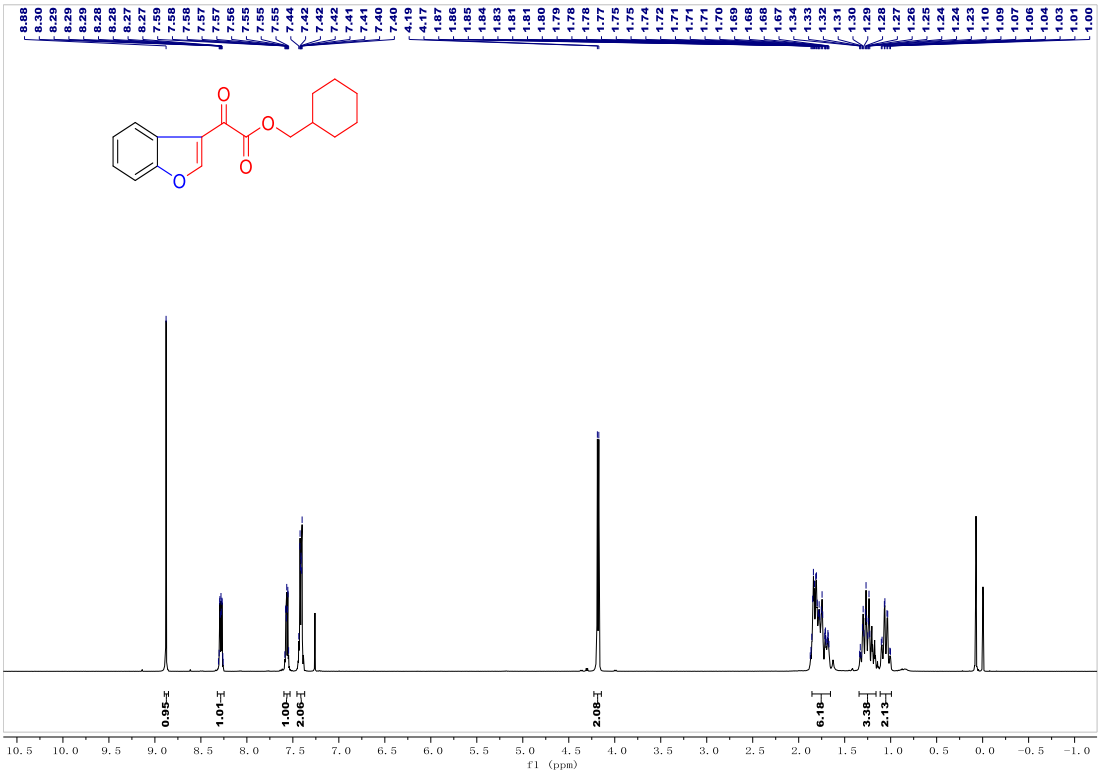
4m ^{1}H NMR



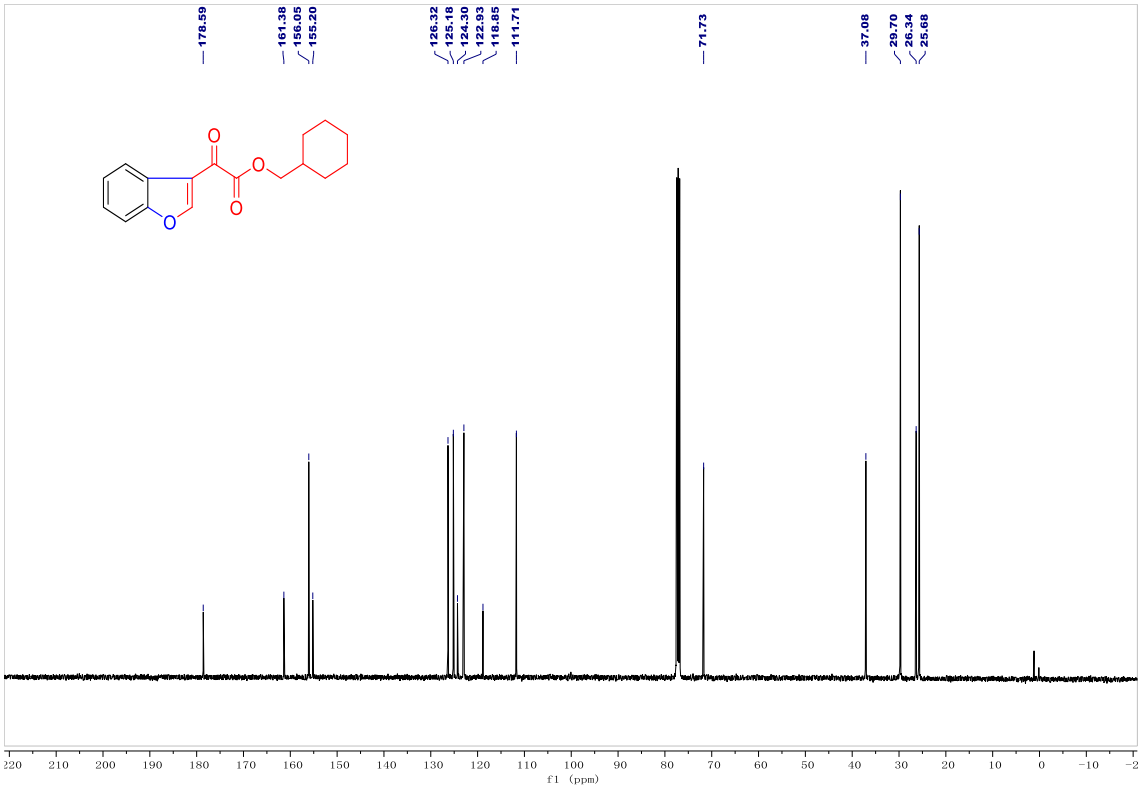
4m ^{13}C NMR



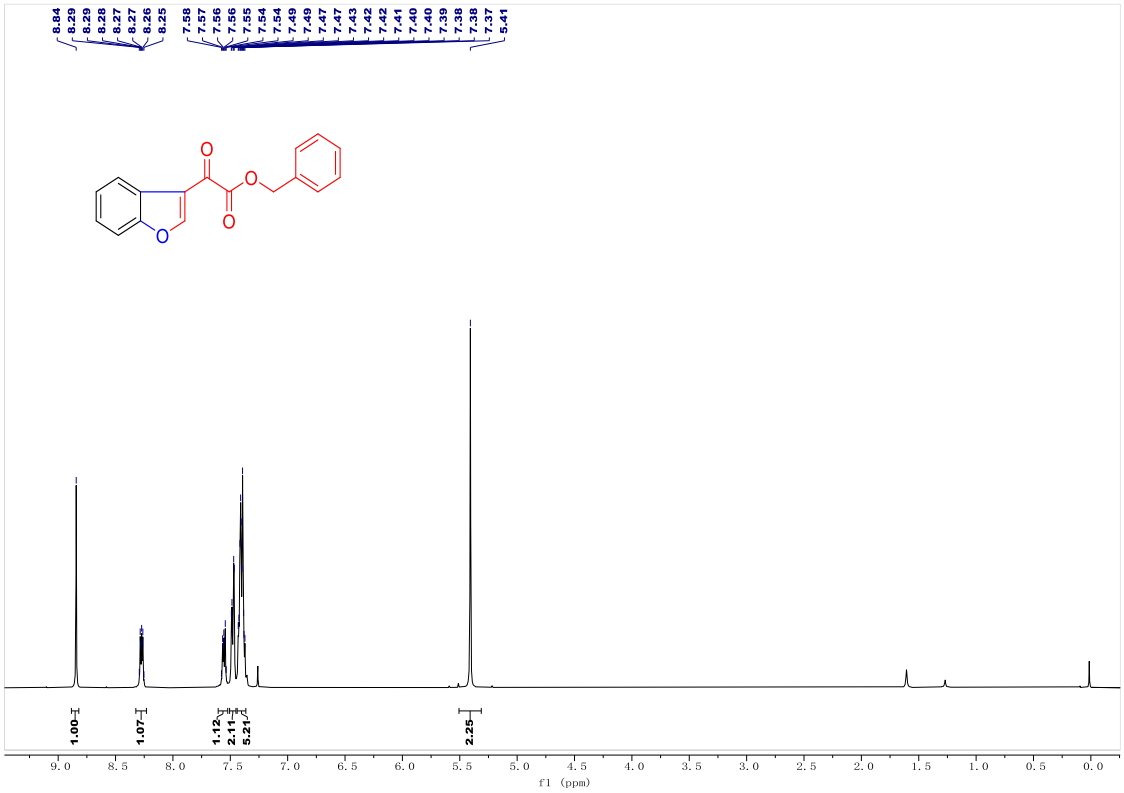
4n ^{1}H NMR



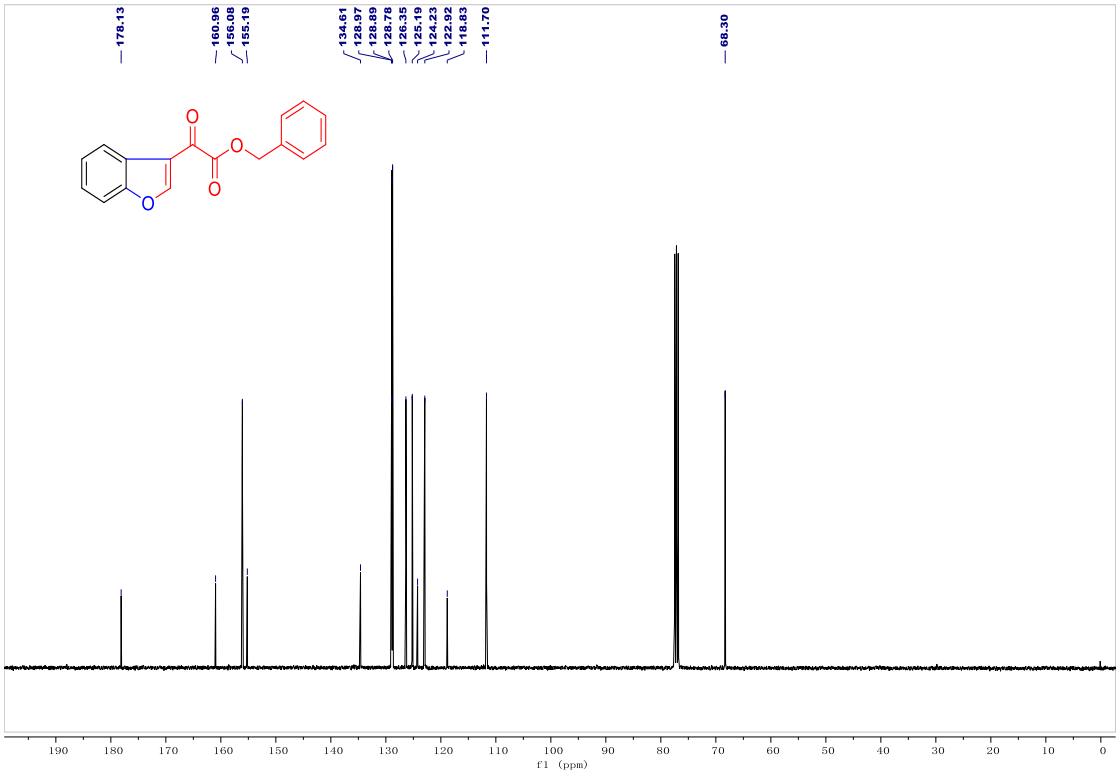
4n ^{13}C NMR



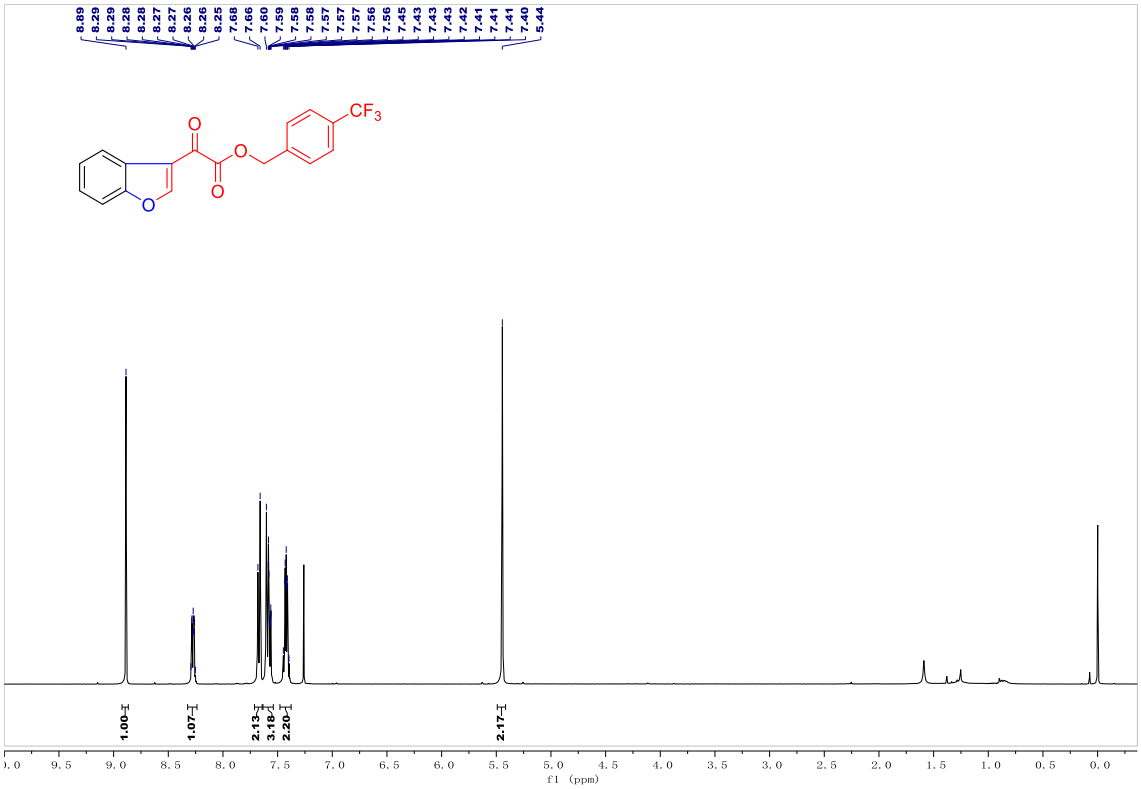
4o ^{1}H NMR



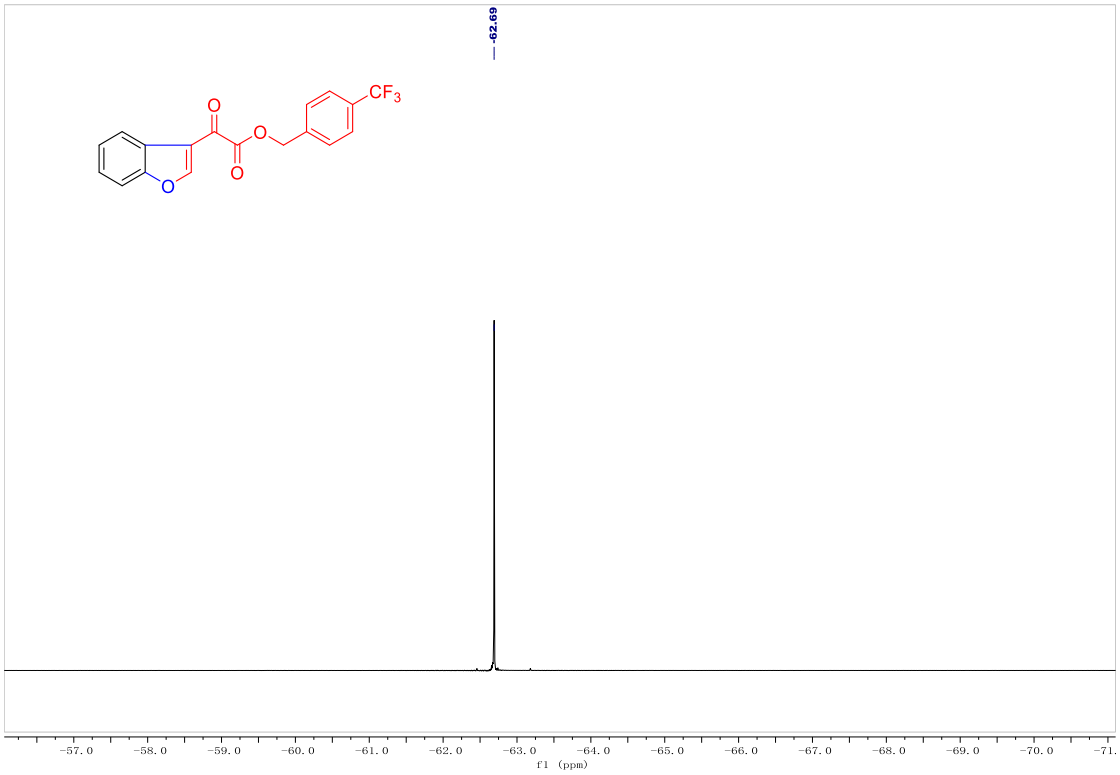
4o ^{13}C NMR



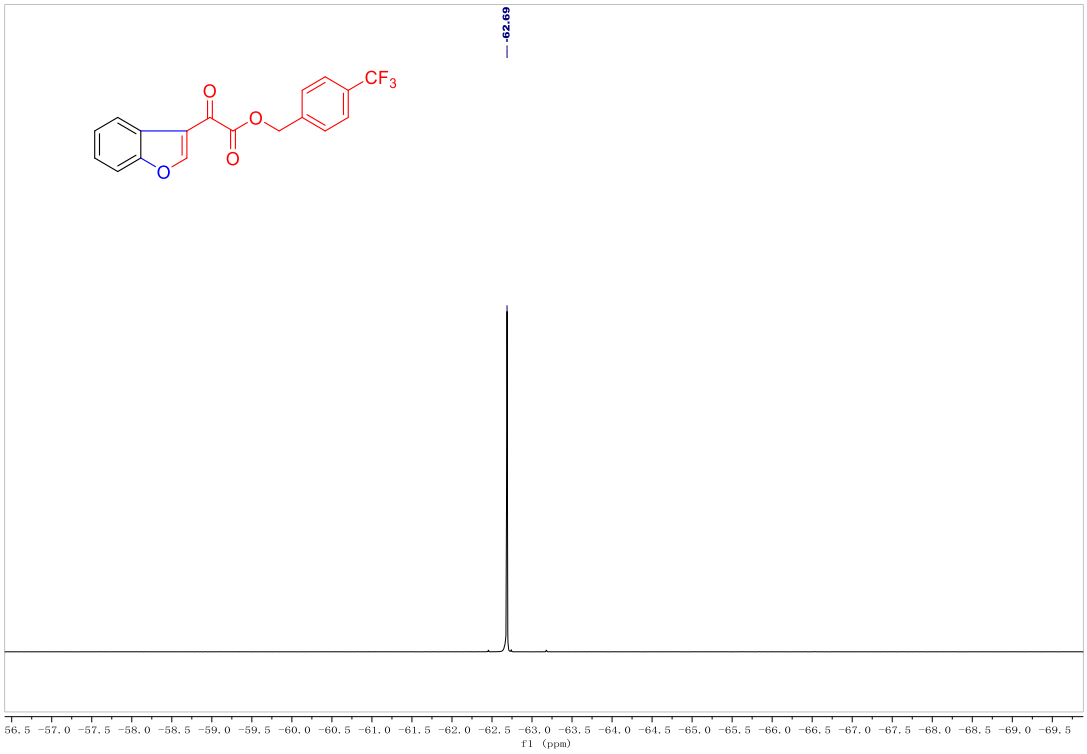
4p ^{1}H NMR



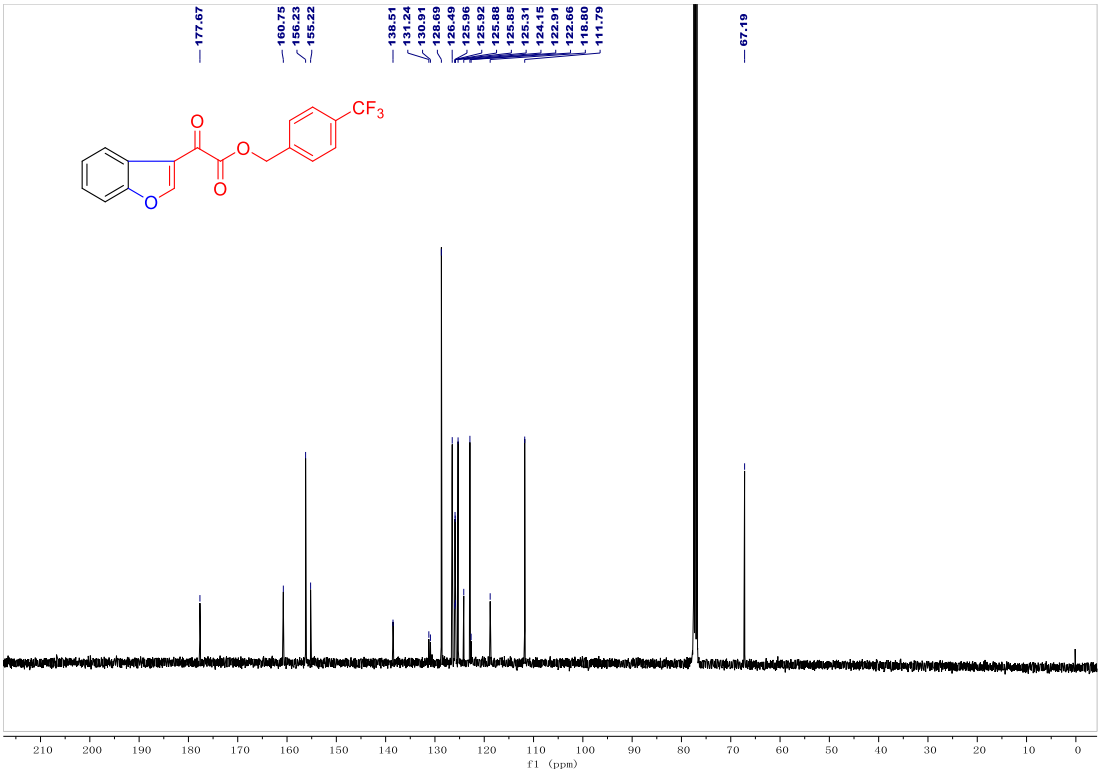
4p ^{19}F{^{1}H} NMR



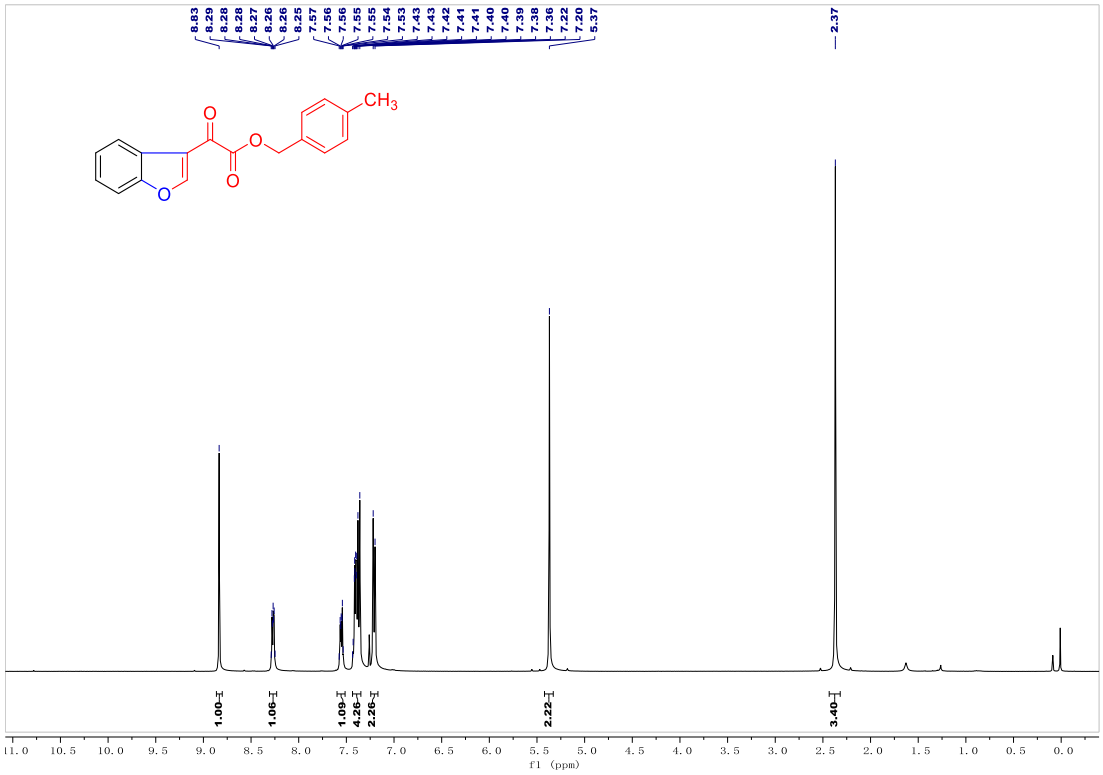
4p ^{19}F NMR



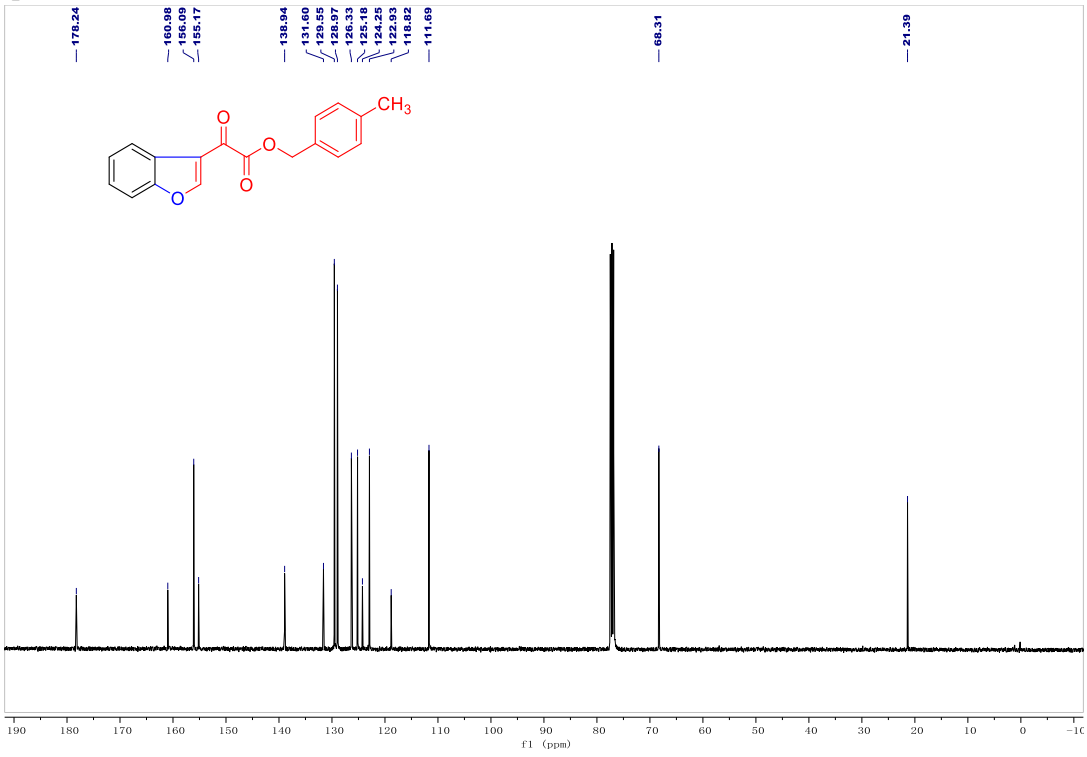
4p ^{13}C NMR



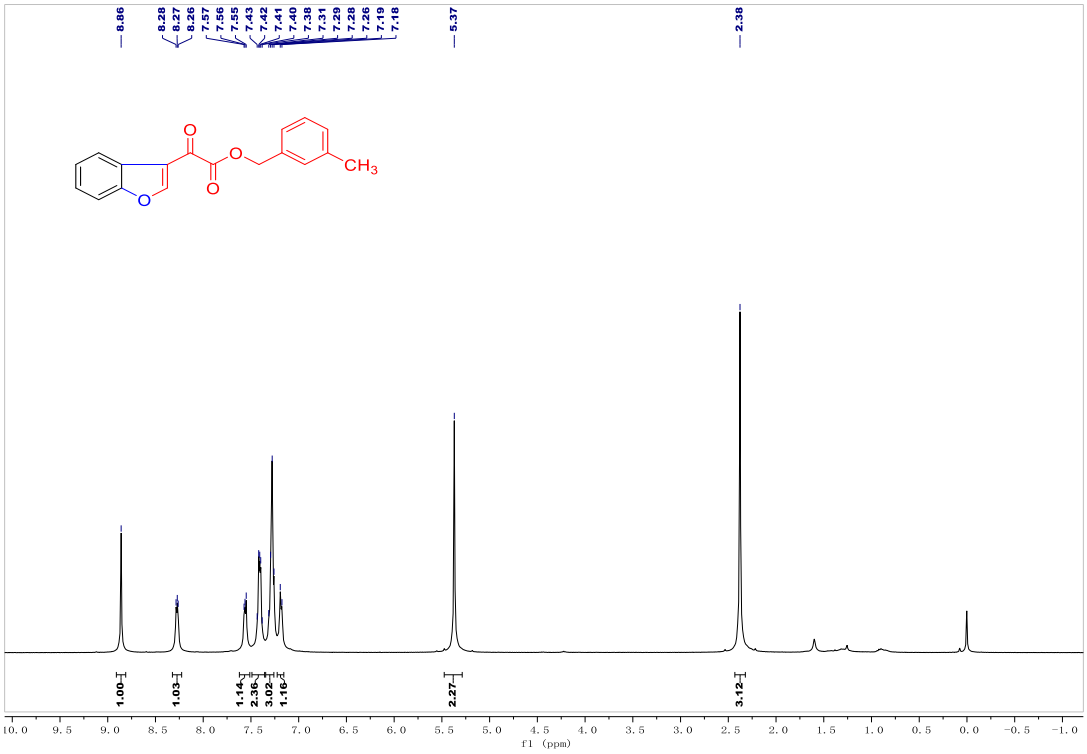
4q ^{1}H NMR



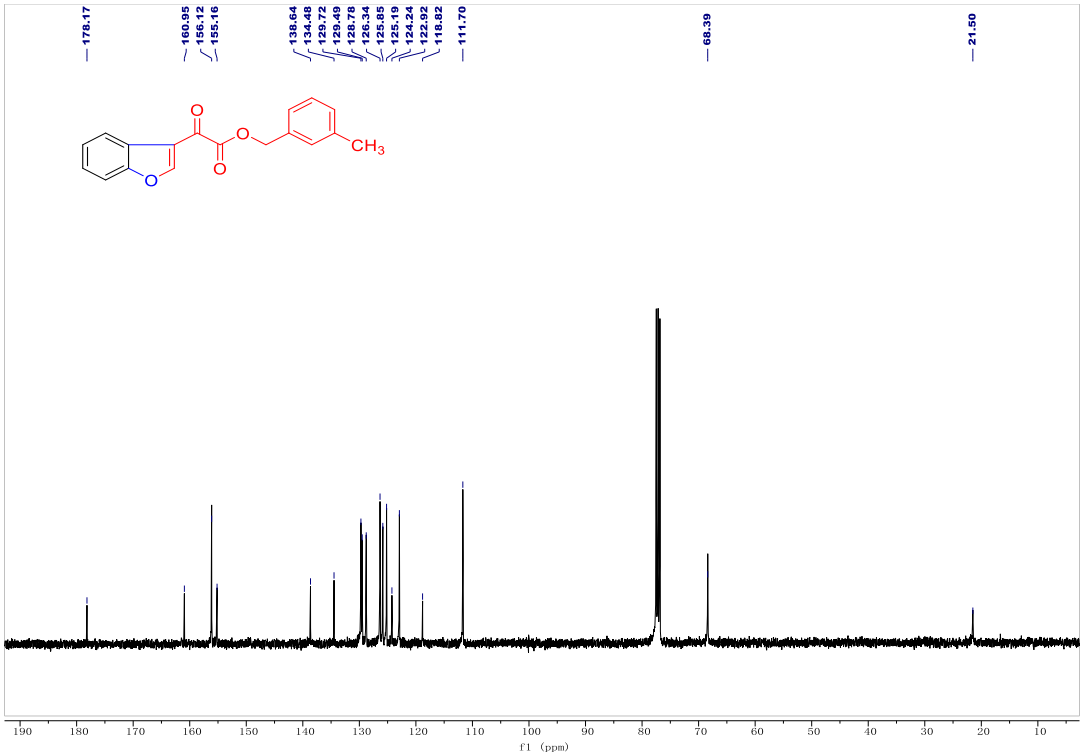
4q ^{13}C NMR



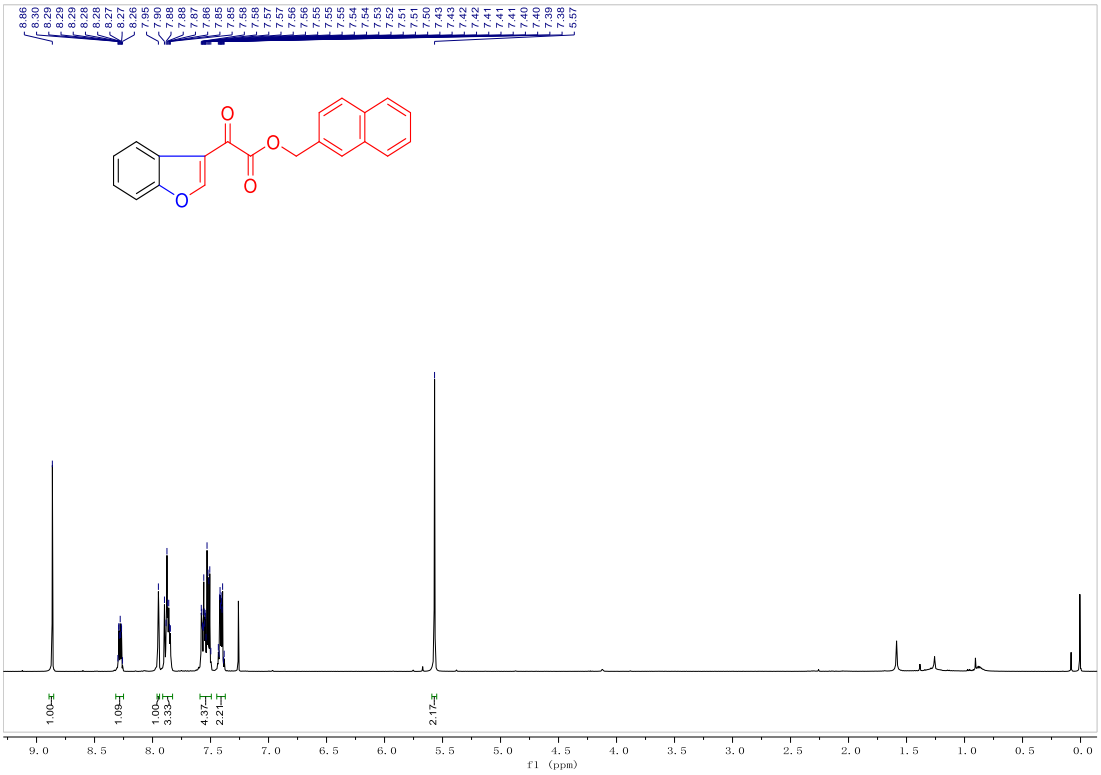
4r ^{1}H NMR



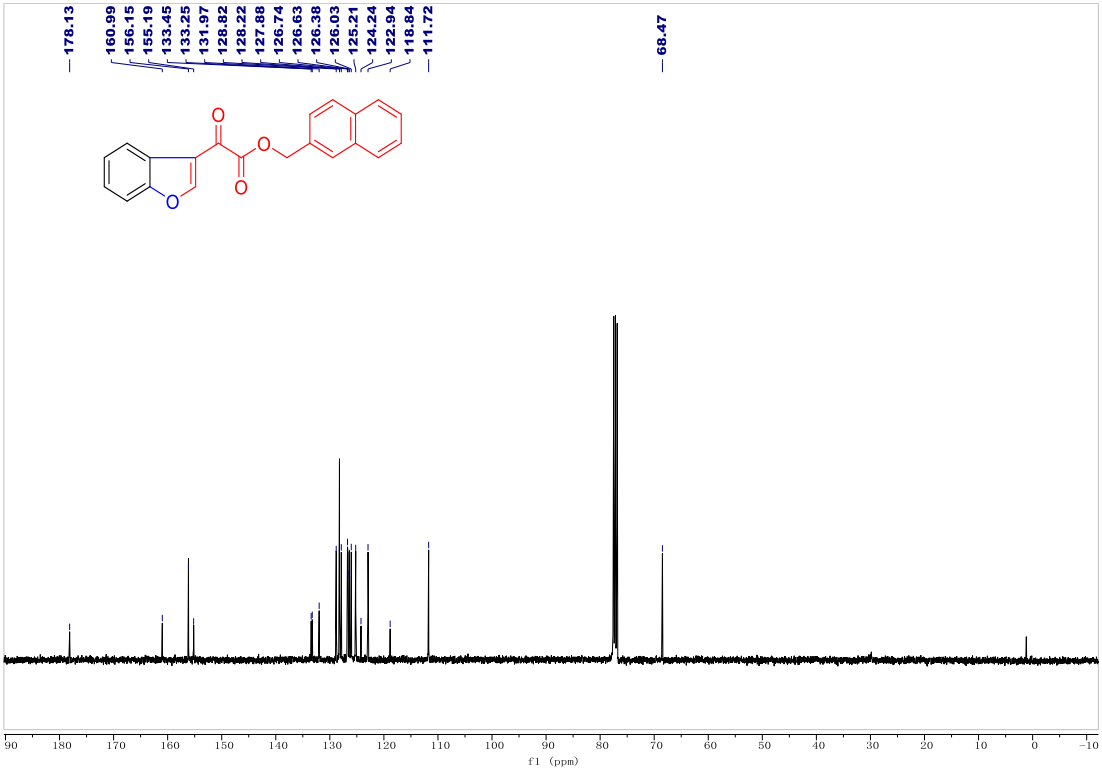
4r ^{13}C NMR



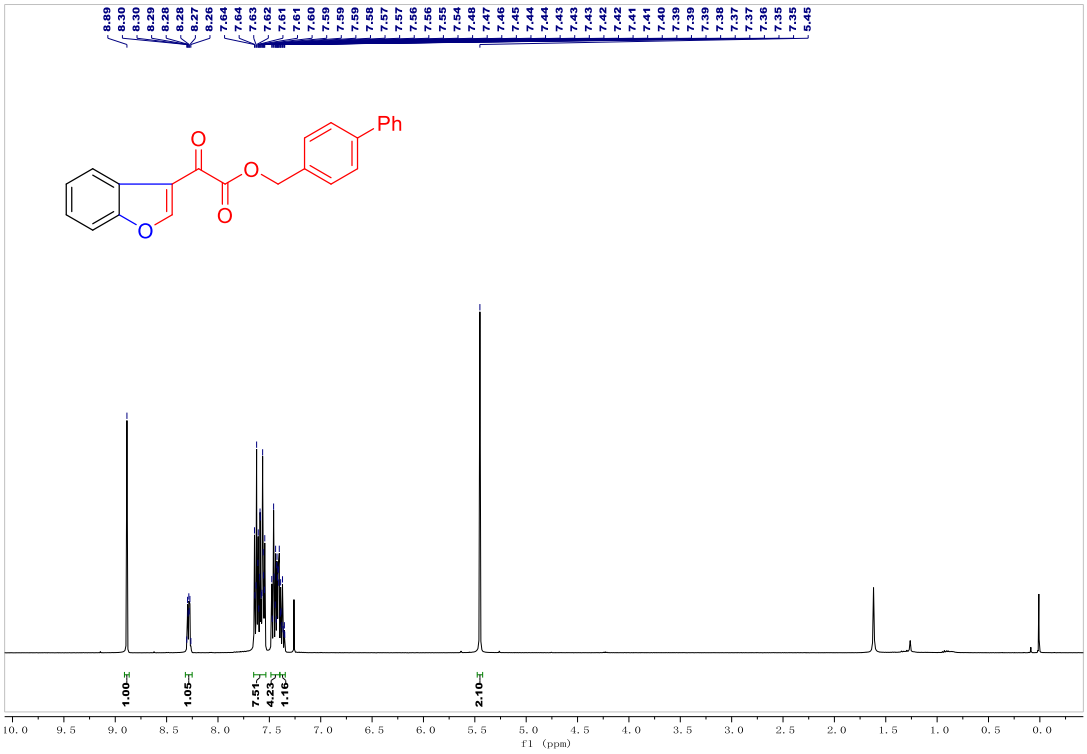
4s ^{1}H NMR



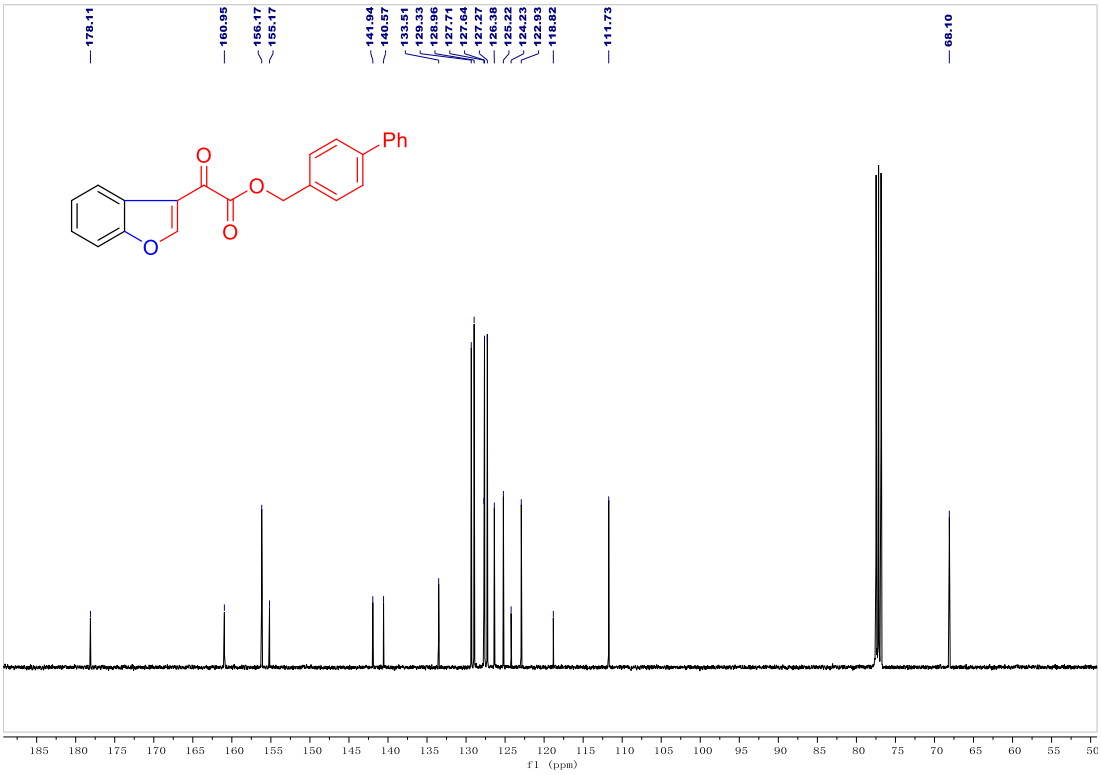
4s ^{13}C NMR



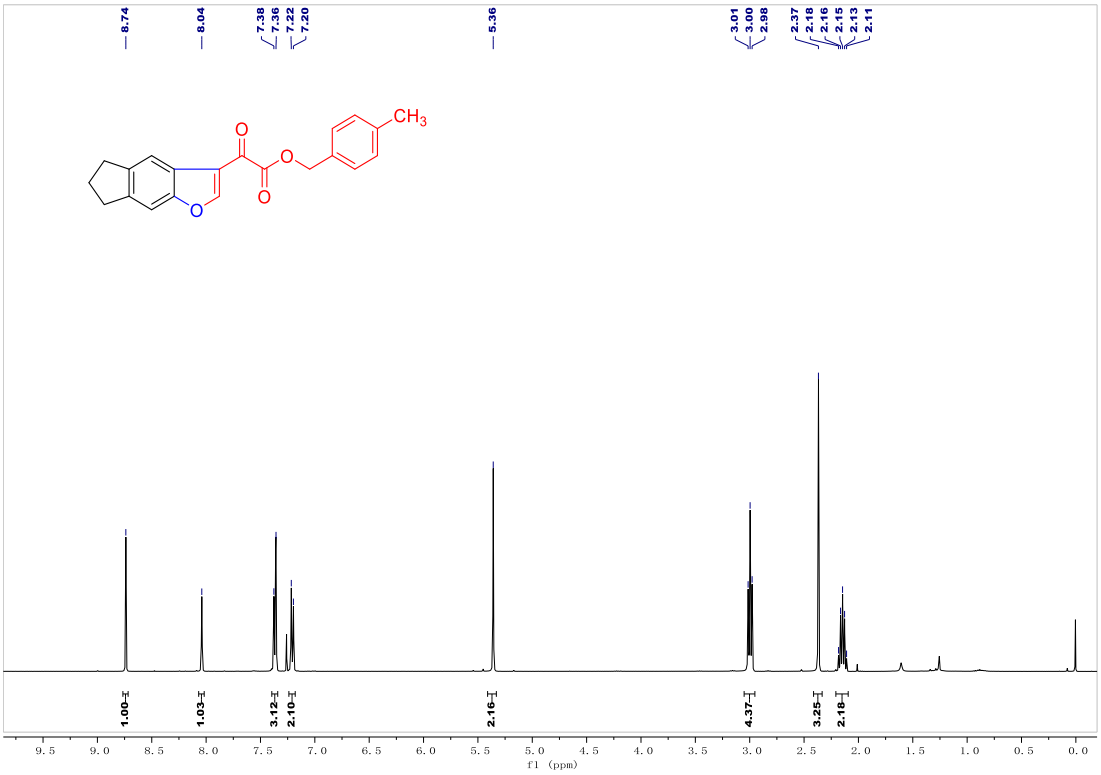
4t ^{1}H NMR



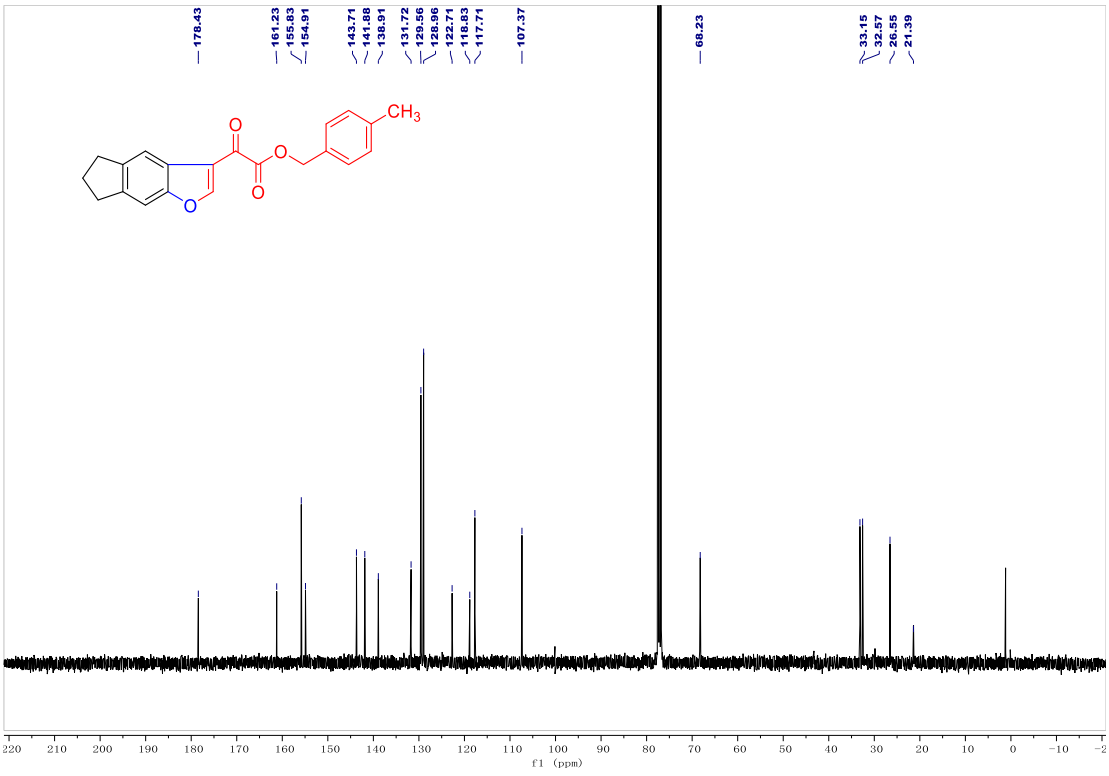
4t ^{13}C NMR



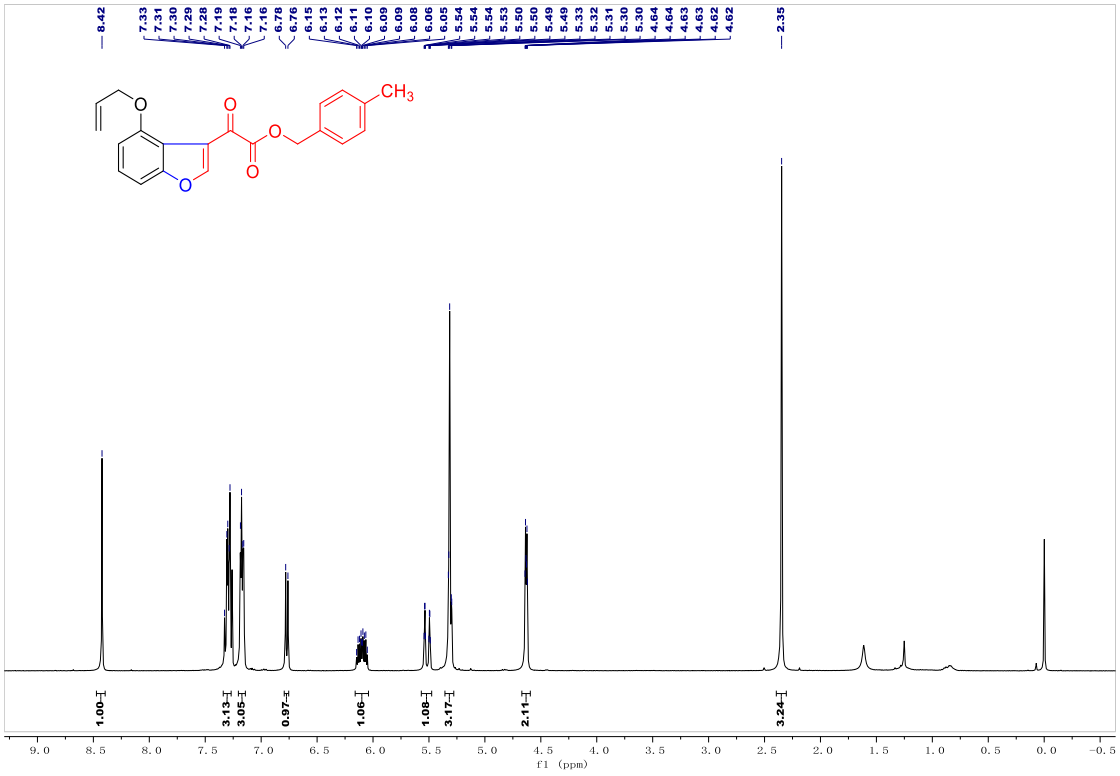
4bs ^{1}H NMR



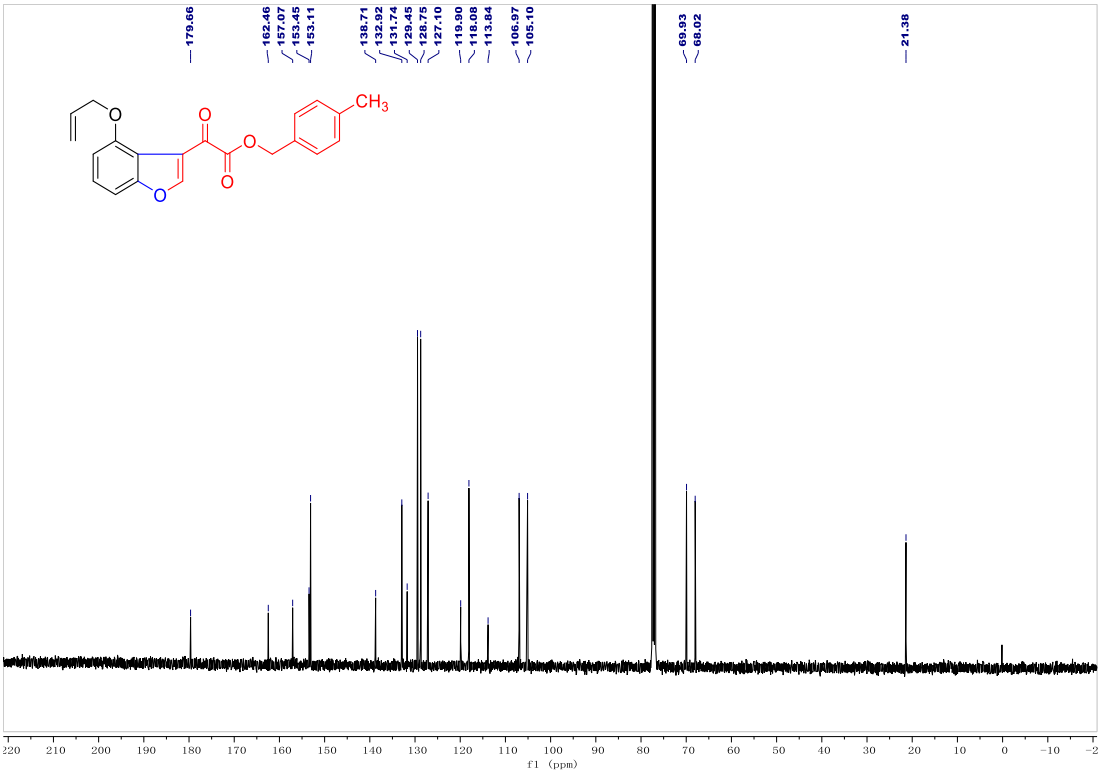
4bs ^{13}C NMR



4gs ^{1}H NMR

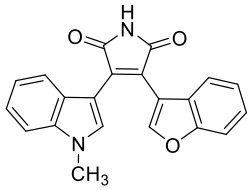


4gs ^{13}C NMR



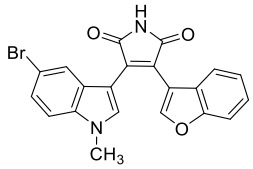
15. ^{1}H, ^{13}C NMR data and ^{1}H, ^{13}C NMR Spectra of GSK-3β 6a, 6b[7]

3-Benzofuran-3-yl-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione (6a)



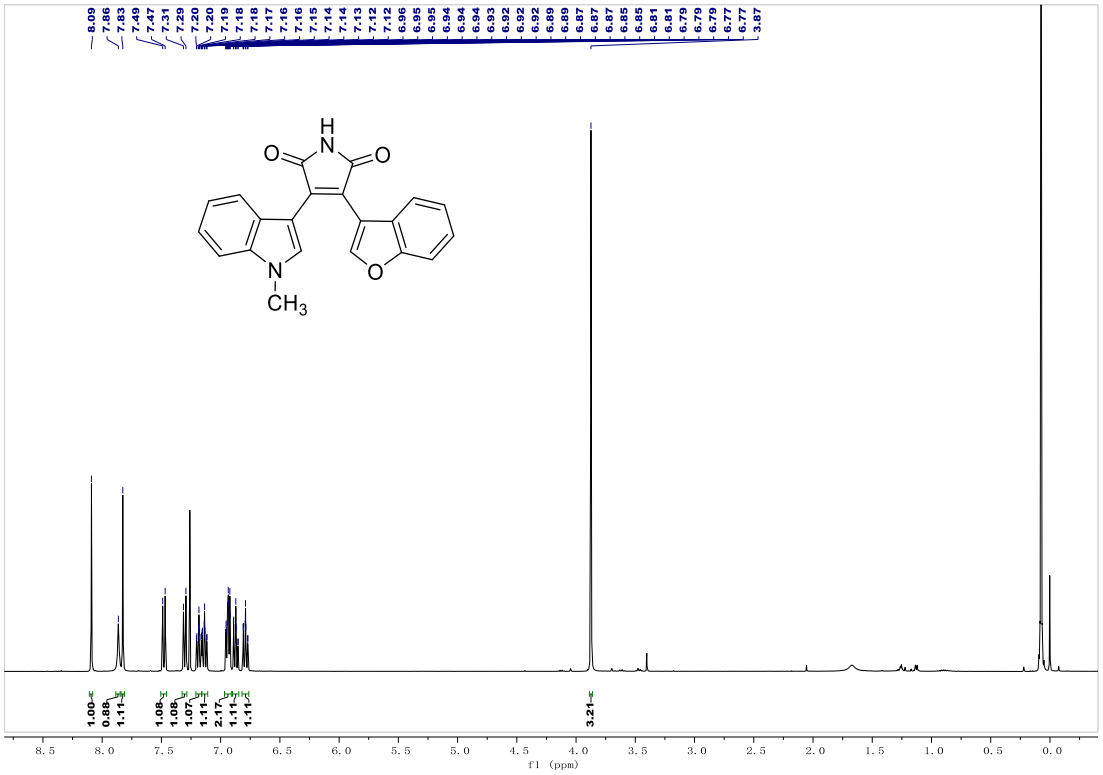
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.86 (s, 1H), 7.83 (s, 1H), 7.48 (d, *J* = 8.3 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.16 – 7.11 (m, 1H), 6.97 – 6.91 (m, 2H), 6.89 – 6.85 (m, 1H), 6.81 – 6.77 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.2, 155.0, 147.2, 137.1, 134.0, 132.5, 126.0, 125.6, 124.9, 122.9, 122.9, 122.8, 122.4, 122.0, 120.9, 111.9, 111.5, 109.8, 105.1, 33.7.

3-Benzofuran-3-yl-4-(5-bromo-1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione (6b)



^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.80 (s, 1H), 7.75 (s, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.15 (d, *J* = 8.6 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 6.89 – 6.83 (m, 1H), 6.82 – 6.77 (m, 1H), 3.83 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.3, 170.8, 155.1, 147.3, 135.7, 134.6, 131.9, 127.6, 125.8, 125.3 , 125.1, 124.7, 123.8, 122.9, 122.0, 114.4, 111.7, 111.6, 111.2, 104.6, 33.8.

^{1}H NMR ($CDCl_3$, 400 Hz) of **6a**



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