Supporting Information

Rhodium-Catalyzed C-H carboxymethylation of anilines with Vinylene Carbonate

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1. General information

Chemicals and reagents were purchased from commercial suppliers and used without special instructions. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker 400 MHz instrument in $CDCl_3$ using TMS as internal standard, operating at 400 MHz and 101 MHz, respectively. Chemical shifts (d) are expressed in ppm and coupling constants J are given in Hz. Abbreviations are as follows: s (singlet), d (doublet), t (triplet), m (multiplet). High resolution mass spectra (HRMS) were obtained on Agilent 6520 LC/MS with ESI source. Unless otherwise noted, the purification was performed using column chromatography on silica gel.

2. General Procedure for Synthesis of Products

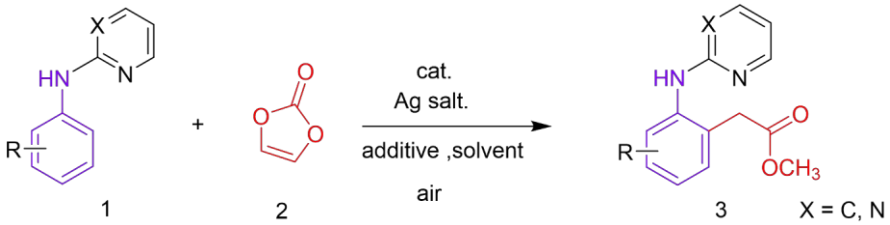
General procedure for the synthesis of pyridinyl arylamines[1-3]

1,4-Dioxane (10 mL), KO^{t}Bu (505 mg, 4.5 mmol), 2-bromo-pyridine (3.0 mmol), and arylamine (3.6 mmol) were added in turn to a round bottom flask charged with $Pd_2(dba)_3$ (54mg, 0.06 mmol), 1,3-bis(2,6-diisopropylphenyl) imidazolium chloride (iPr·HCl) (48 mg, 4 mol%), and a magnetic stirring bar. The flask tube was placed in a 105 °C oil bath and was stirred for 12 h. The mixture was then allowed to cool to room temperature. The mixture was diluted with water then extracted with diethyl ether. The extracts were combined, washed with brine, and then dried over Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash chromatography (petroleum ether/ethyl acetate (10:1)).

General procedure for the synthesis of pyrimidyl arylamines[1-3]

To an oven-dried flask charged with aniline (977.8 mg, 10.5 mmol, 150 mol %), 2-chloropyrimidine (801.7 mg, 7.0 mmol, 100 mol %) and acetic acid (7 mL) in 1,4-dioxane (19 mL) was added. The reaction mixture was stirred at 110℃ for 24 h and monitored by TLC. Upon completion, the mixture was extracted with CH_2Cl_2 (3 × 20 mL) and washed with brine. The organic layer was dried over Mg_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (n-hexanes/EtOAc) to give N-phenylpyrimidin-2-amine (990.6 mg) in 88% yield.

General Procedure for the Rhodium-Catalyzed C-H carboxymethylation of anilines with Vinylene Carbonate

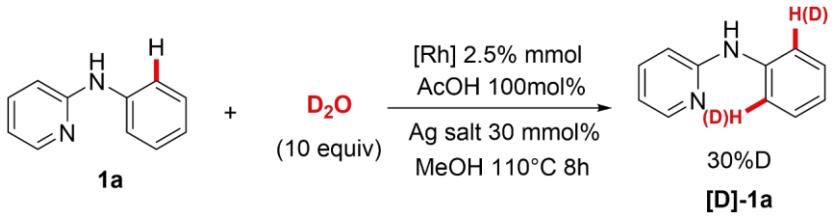


1 2 3 X = C, N

A mixture of (0.2 mmol) N-phenylpyridin-2-amine or N-phenylpyrimidin-2-amine, $[Cp^*RhCl_2]_2$ (0.005 mmol, 2.5 mol %)，AgOTf (30 mol%) and AcOH (0.2 mmol, 100 mol%) was taken in a 25 mL pressure tube. To this reaction mixture, MeOH (2.0 mL) and vinylene carbonate (0.3 mmol) were added, and the closed reaction mixture was allowed to stirred at 110 °C for 8 h. After completion, as indicated by TLC and dilution with dichloromethane, then filtered through Celite and silica gel. The solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel using petroleum ether/ethyl acetate as the eluent to afford the desired compound **3**.

3. Mechanistic Investigation

H/D Exchange of N-(2-pyridyl)-aniline (1a)



A mixture of N-(2-pyridyl)-aniline **1a** (34.0 mg, 0.2 mmol), D_2O (40.0 mg, 2.0 mmol, 10.0 equiv), [Cp* $RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), AgOTf (30 mol%) and AcOH (0.2 mmol, 100 mol%) in MeOH (2.0 mL) was allowed to stir at 110 °C for 8h. After completion, the mixture was cooled to room temperature and then purified by column chromatography on silica gel (petroleum ether/ethyl acetate=15:1) to afford the desired products **[D]-1a** as white solid. The ratio of H/D exchange (H/D = 30%) was determined by ^{1} H-NMR analysis (Figure S-1).

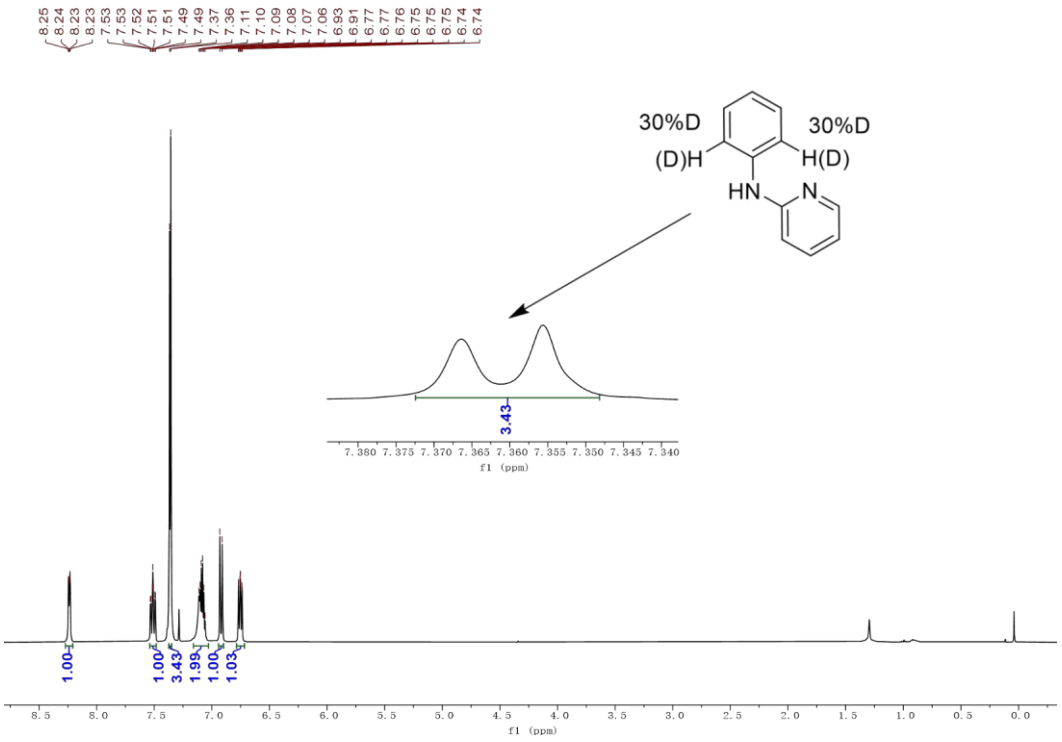
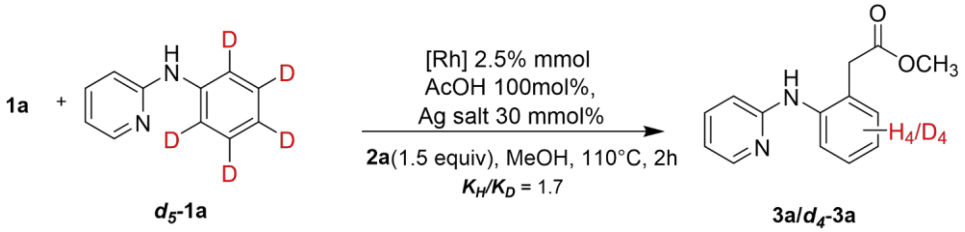


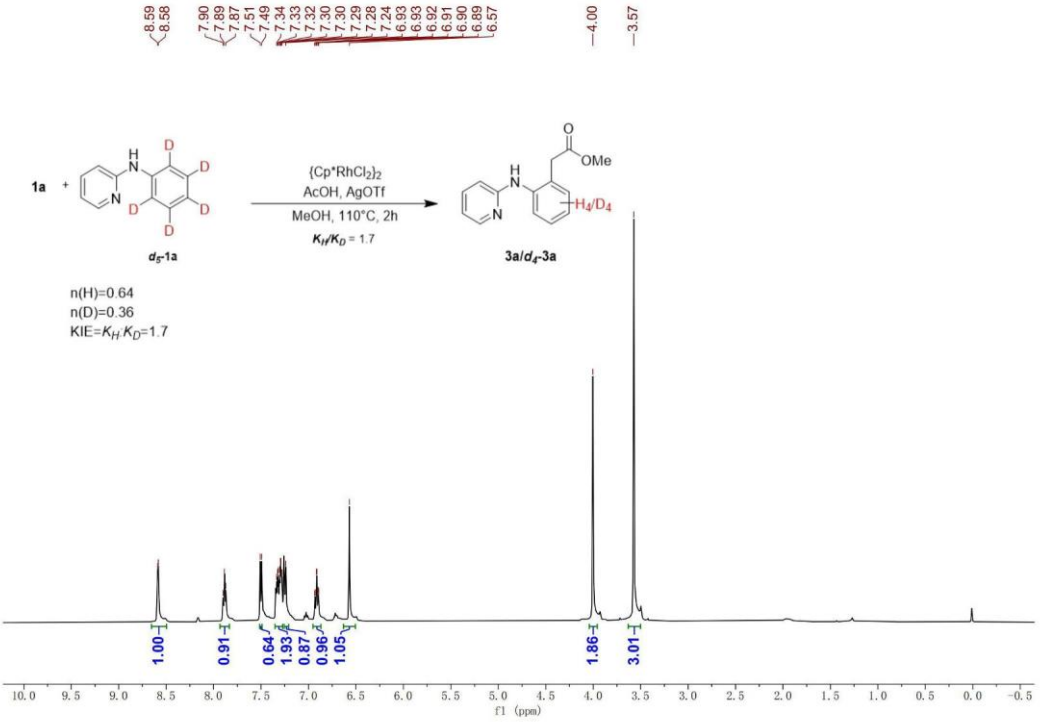
Figure S-1 The ^{1}H NMR spectra of **[D]-1a** (400 MHz, $CDCl_3$).

Kinetic isotope effect of the transformation about 1a/d5-1a



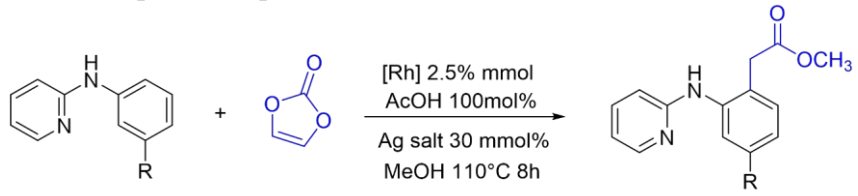
A mixture of N-(2-pyridyl)-aniline **1a** (34 mg, 0.2 mmol), ***d5*-1a** (37 mg, 0.2 mmol), vinylene carbonate **2** (0.3 mmol), [Cp* $RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), AgOTf (30 mol%) and AcOH (0.2 mmol, 100 mol%) in MeOH (2.0 mL) was allowed to stir at 110 °C for

8h. After completion, the mixture was cooled to room temperature and then purified by column chromatography on silica gel (PE/EtOAc = 15:1) to afford the desired products **3a** and ***d*$_4$-3a** as white solid. The deuterium incorporation was determined to be k_H/k_D = 1.7 by ^{1}H NMR.



The ^{1}H NMR spectra of ***d*$_4$-3a** (400 MHz, $CDCl_3$).

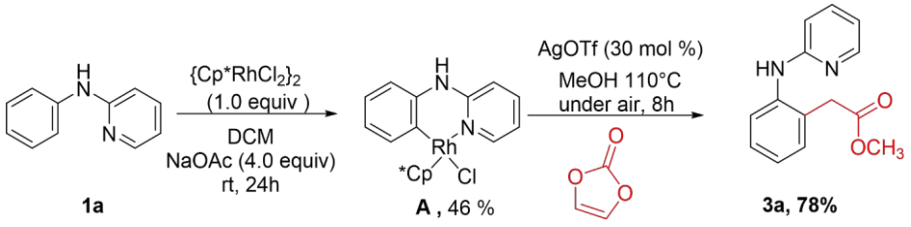
Intermolecular competition experiments



1j(R= Me) **: 1k**(R=CF_3)=1:1 **1j**(R= Me) : **1k**(R=CF_3)=1.33

A mixture of N-(3-methoxyphenyl) pyridin-2-amine **1j** (0.2 mmol), N-(3-trifluoromethyl) pyridin-2-amine **1k** (0.2 mmol), vinylene carbonate (0.3 mmol), [Cp* $RhCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), AgOTf (30 mol%) and AcOH (0.2 mmol), in MeOH (2.0 mL) was allowed to stir at 110 °C for 8 h. After completion, the mixture was cooled to room temperature and then purified by column chromatography on silica gel (petroleum ether/ethyl acetate=10:1) to afford the desired products **3ja** /**3ka** = 1.33.

Procedure for the Preparation of rhodium intermediate[4]



A 15 mL pressure tube was filled with [Cp* $RhCl_2]_2$ (89 mg), N-phenylpyridine-2-amine **1a** (50 mg) and DCM (2.0 mL). The reaction mixture was stirred at 80°C for 5 h, then filtered with a sintered crucible and washed with DCM solvent (10.0 mL) to obtain pure complex **A** (46% yield). The pure complex **A** was then mixed with vinylene carbonate **2**, 30 mol% AgOTf ,100 mol% AcOH in MeOH (2.0 mL) and stir at 110 ℃ for 8 h. After that, the reaction tube is cooled to room temperature and then purified by column chromatography on silica gel (petroleum ether/ethyl acetate=5:1) to afford the desired products **3a** (78% yield).

Rh intermediate A

Yield 46%; A reddish brown solid; M.p: 285–286 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H), 8.77 (s, 1H), 7.49 (ddd, *J* = 8.7, 7.0, 1.8 Hz, 1H), 7.39 – 7.33 (m, 2H), 7.23 (s, 1H), 7.14 – 7.06 (m, 2H), 6.73 (ddd, *J* = 7.1, 5.9, 1.3 Hz, 1H), 1.55 (s, 15H). The ESI-HRMS for Rh-intermediate A (calcd. for $C_{21}H_{24}ClN_2RhNa$ $[M + Na]^+$ 465.0581; found 465.0586.

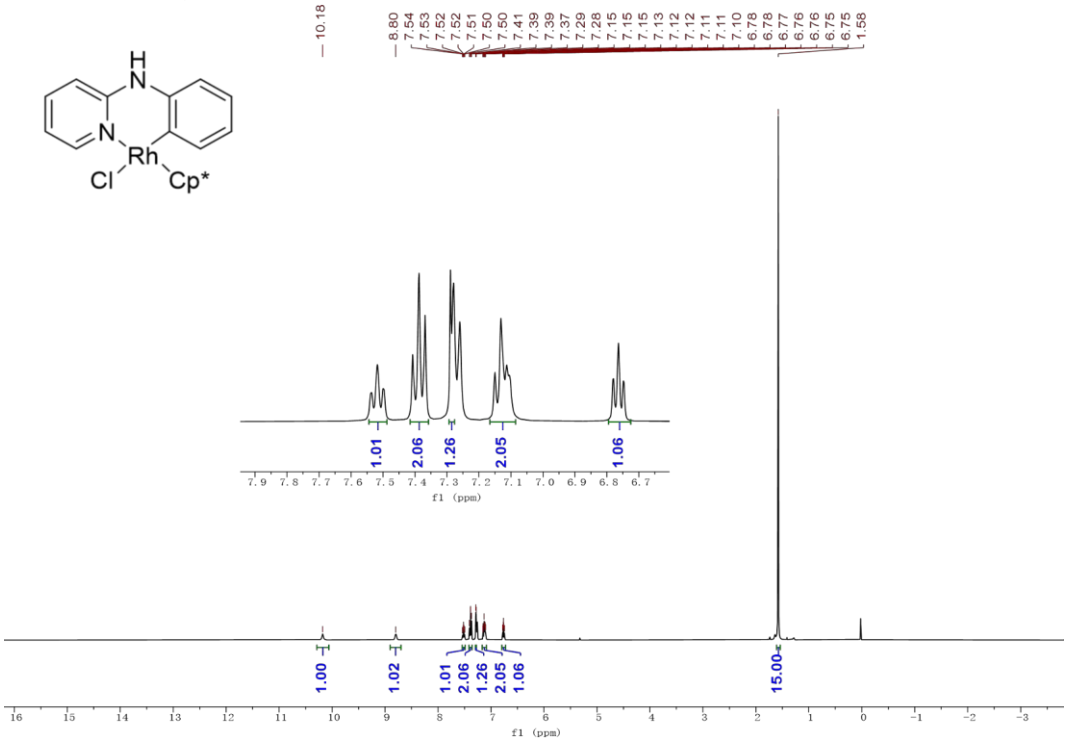
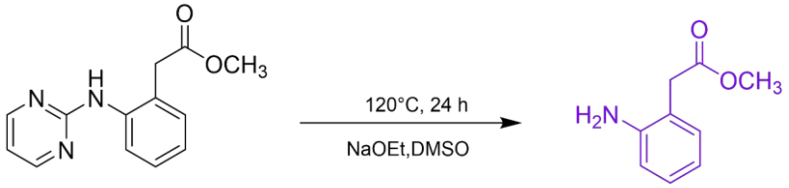


Figure S-3 The ^{1}H NMR spectra of Complex **A**. (400 MHz, DMSO-d_6).

4. Scale-up Reactions and Remove of Directing Group

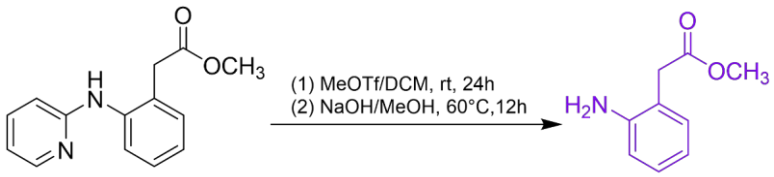
Removal of Directing Group[5-6]



6a, 88%

A mixture of **3aa** (0.50 mmol), NaOEt (102 mg, 1.50 mmol) and DMSO (2.0 mL) was stirred at 120 °C under a nitrogen atmosphere for 24 h. After cooling to ambient temperature, the reaction mixture was diluted with EtOAc (75 mL) and washed with brine (2 × 30 mL). The aqueous phase was extracted with EtOAc (2 × 30 mL), and the combined organic phase was dried over Na_2SO_4. After filtration and evaporation of the solvents in vacuum, the crude product was purified by column chromatography on silica gel (n-hexane/EtOAc: 20/1) to

yield **6a** (72 mg, 88%) as a yellow oil.



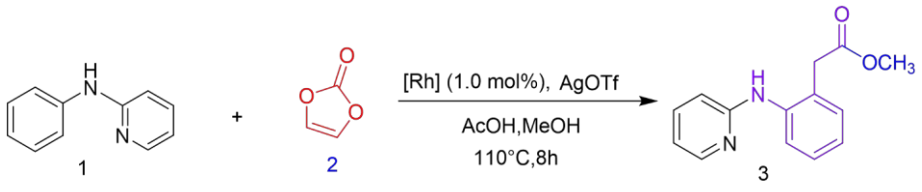
6a, 58%

To a solution of **3aa** (0.14 g, 0.50 mmol, 1.0 equiv) in DCM (2.0 mL) was added MeOTf (113 μL, 1.0 mmol, 2.0 equiv) dropwise. And the mixture was stirred for 1h at room temp. Solvent was removed under reduced pressure. The residue was then dissolved in iPrOH (2.0 mL). A mixed solution of hydrazine/acetic acid (5.2 mL/1.5 mL) was added. The resulting solution was heated to 170 °C and stirred for 2 days. After the mixture was cooled to rt, we analyzed the crude mixture, besides desired product, it mainly includes the unconverted starting material 3aa, and no by-products were produced. The mixture quenched with water (20 mL) and extracted with EtOAc (3x15 mL). The combined organic layers were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (n-hexane/EtOAc: 20/1) to afford **6a** (58 %) as a yellow oil.

methyl 2-(2-aminophenyl)acetate (6a)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.6 Hz, 2H), 6.80 – 6.69 (m, 2H), 4.04 (s, 2H), 3.69 (s, 3H), 3.58 (s, 2H).

Scale-up Reactions



N-phenylpyridin-2-amine **1a** (6.0 mmol), vinylene carbonate **2** (9.0 mmol), (2.5 mol %), [Cp* $RhCl_2$]$_2$(1.0 mol%), AgOTf (30 mol%) , AcOH (100 mol%) and MeOH (10.0 mL) were added to a test tube. The reaction mixture was stirred at 110℃ under air for 8 h. Upon completion, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel using petroleum ether/ethyl acetate as the eluent to afford the product **3aa** in 70% yield.

References

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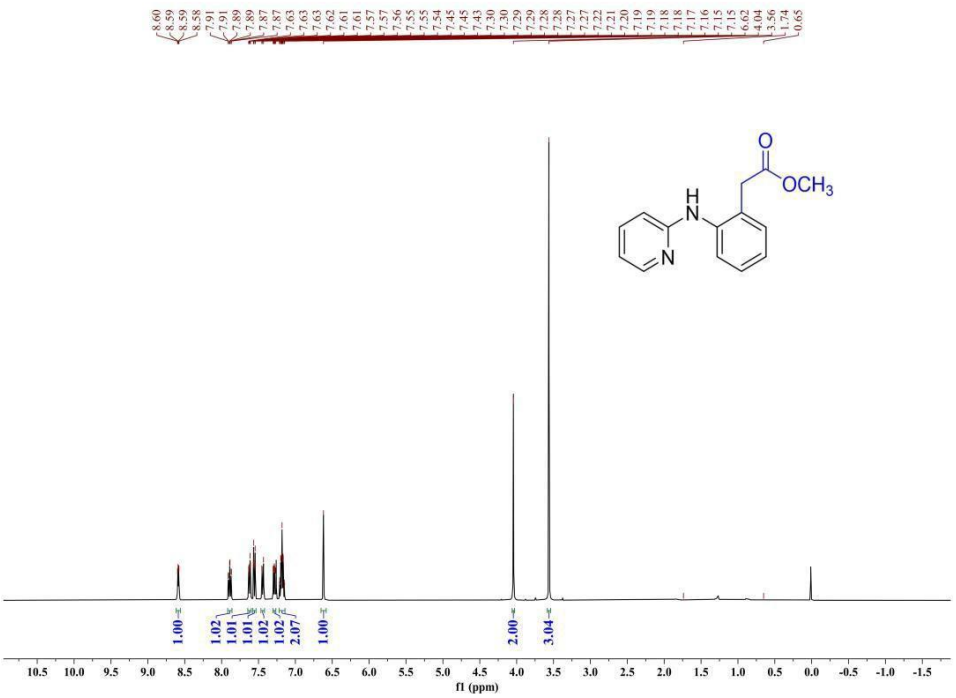
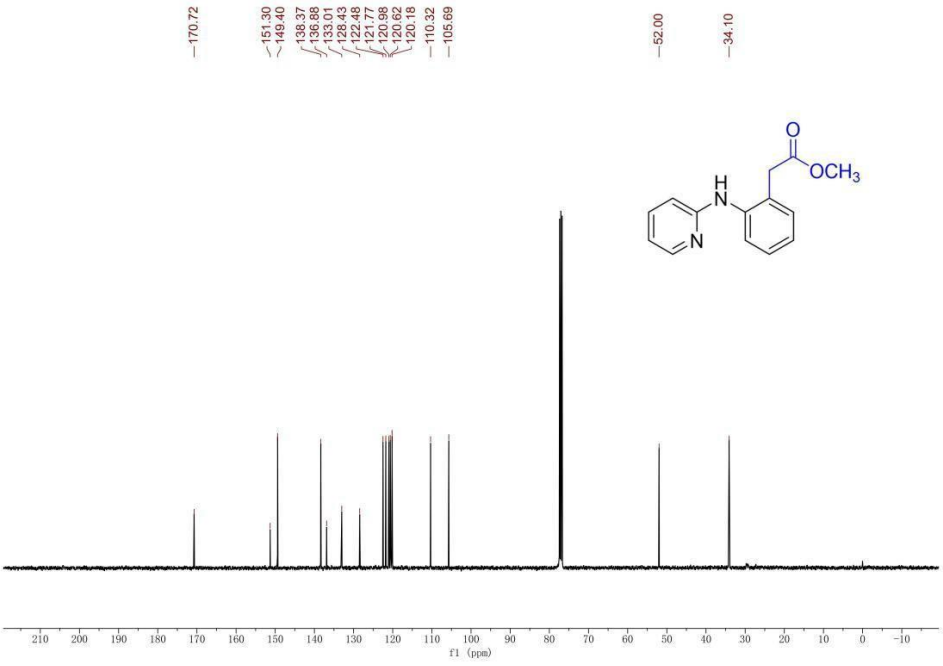
4. B. Ramesh and M. Jeganmohan. *Org. Lett.*, 2017, **19**, 6000-6003.
5. Z.-J. Wu, F. Su, W. Lin, J. Song, T.-B. Wen, H.-J. Zhang and H.-C. Xu. *Angew. Chem. Int. Ed.*, 2019, **58**, 16770-16774.
6. Ackermann L, Lygin A V. *Org. Lett*., 2012, **14**(3): 764-767.

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

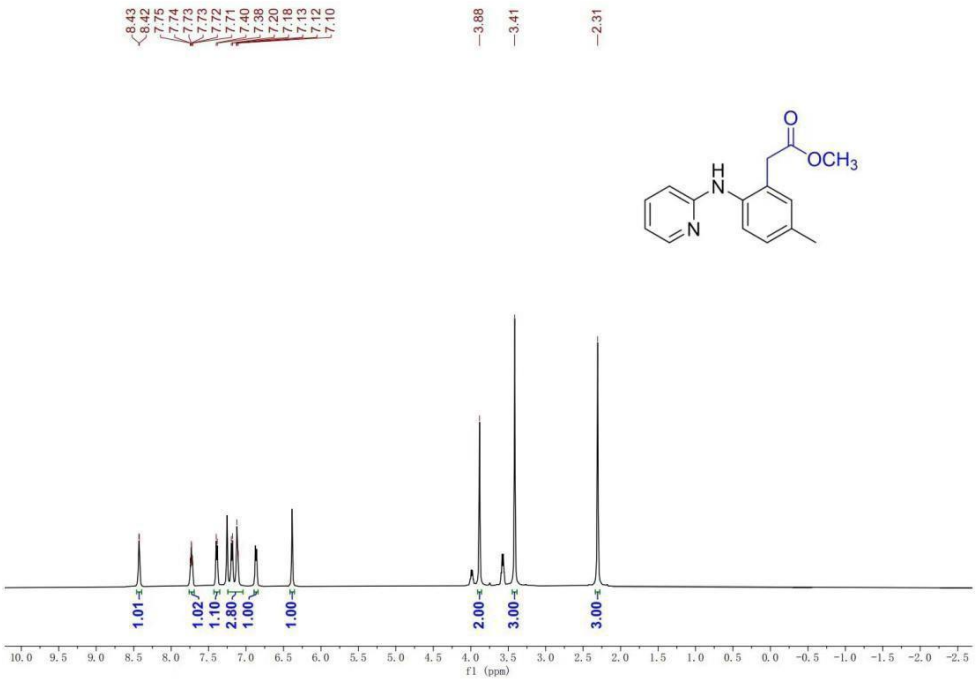
^{1}H NMR of 3aa



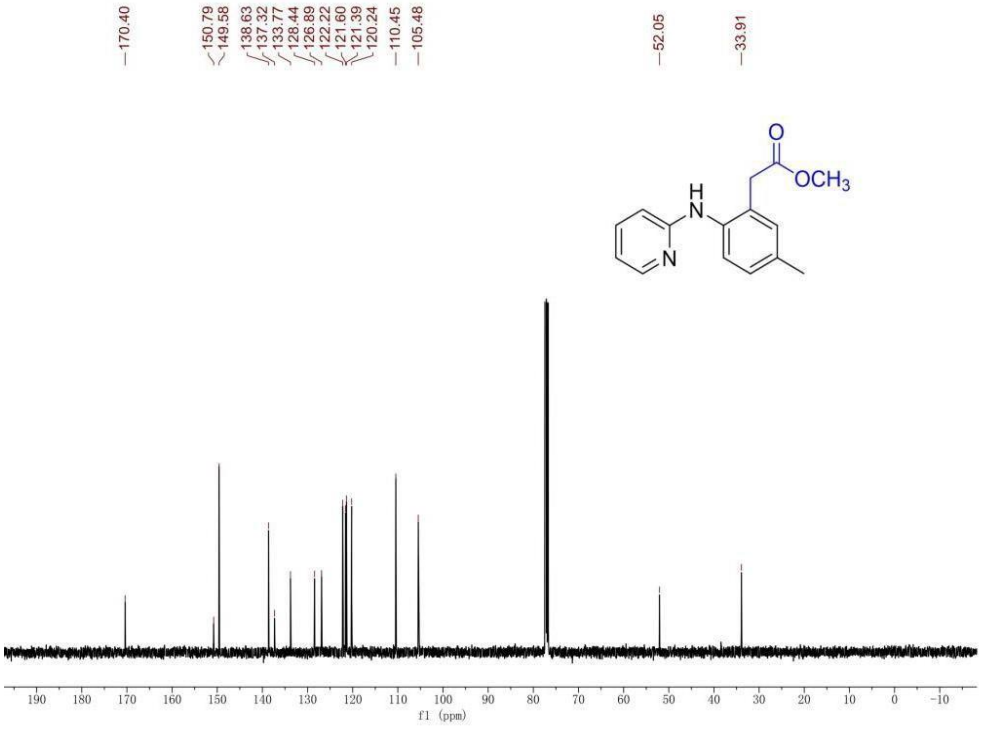
^{13}C NMR of 3aa



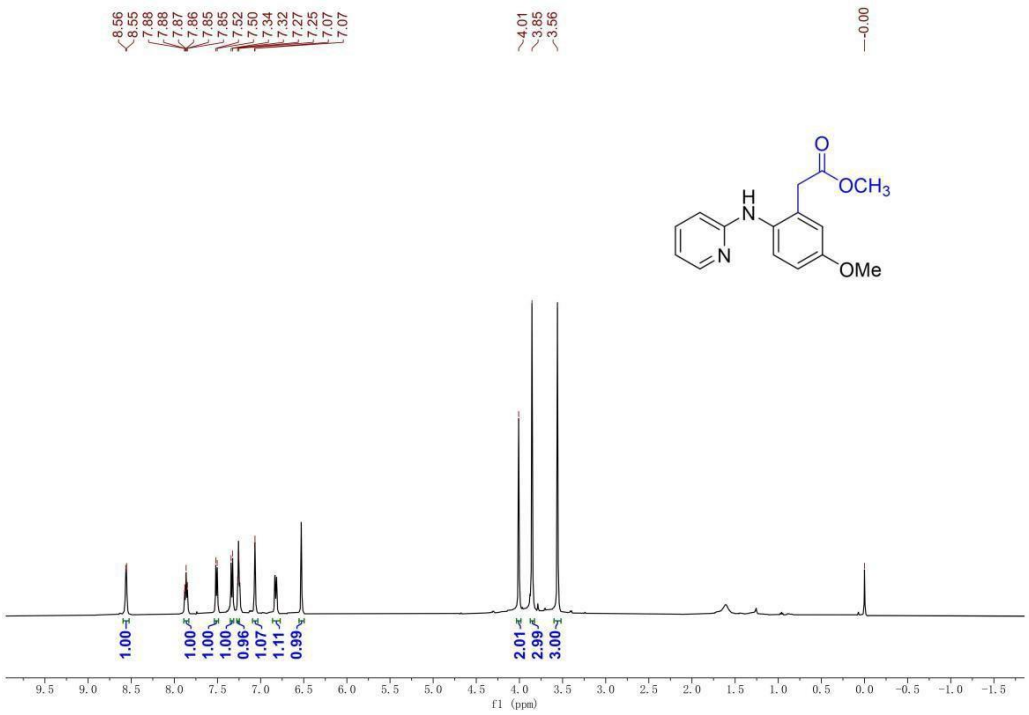
^{1}H NMR of 3b



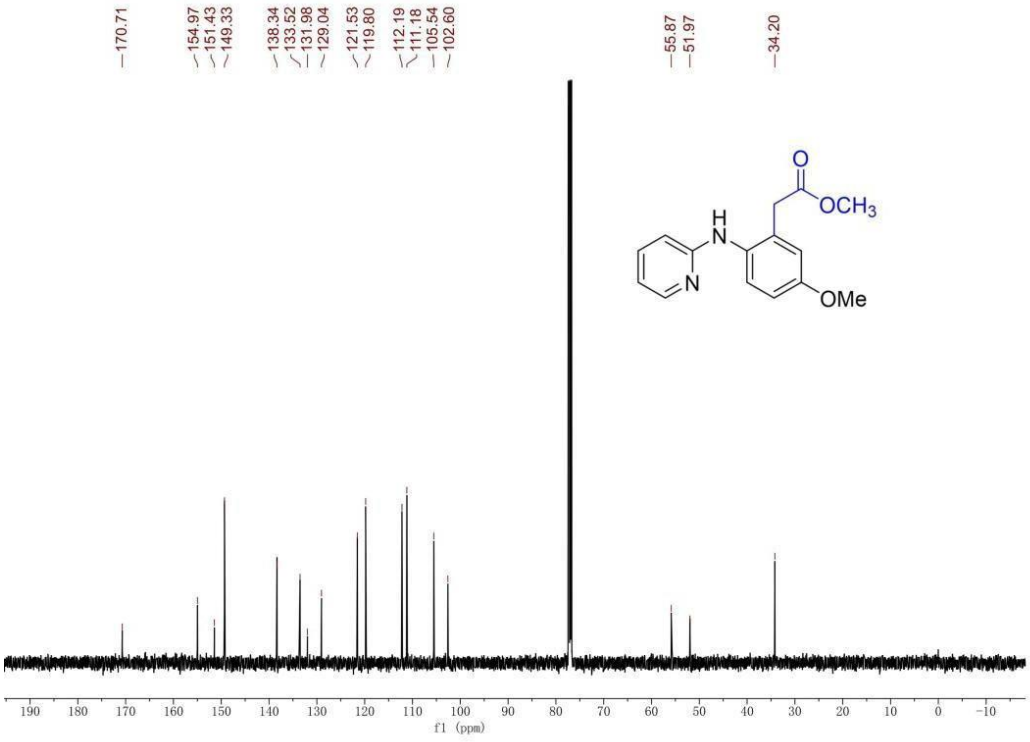
^{13}C NMR of 3b



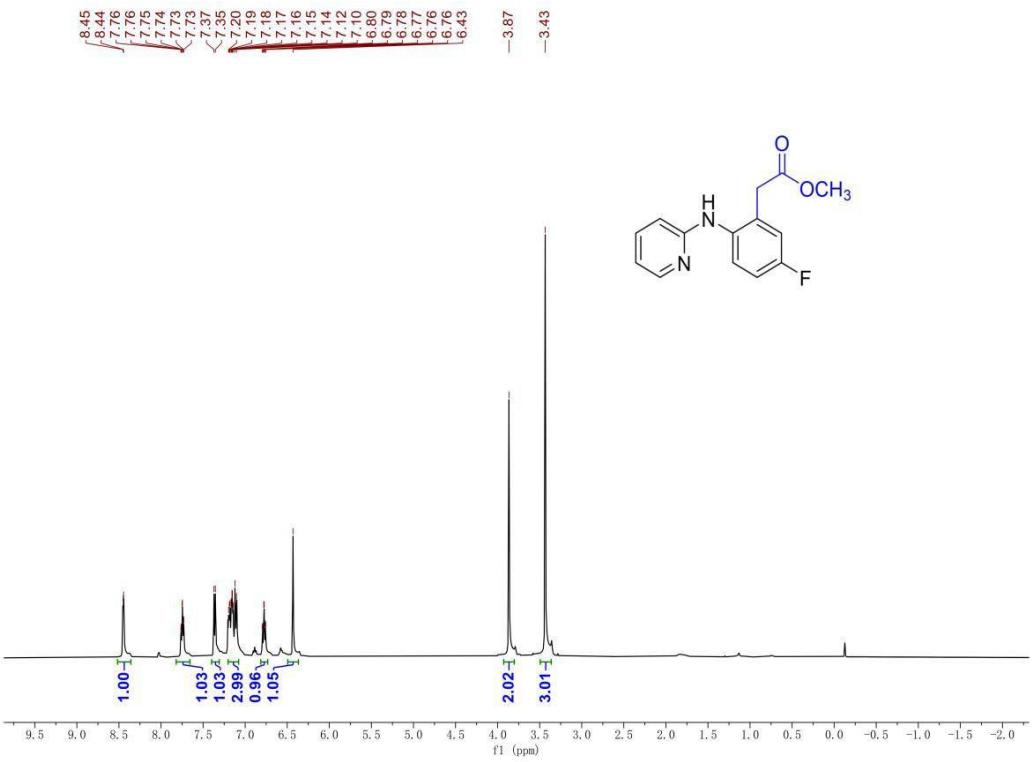
^{1}H NMR of 3c



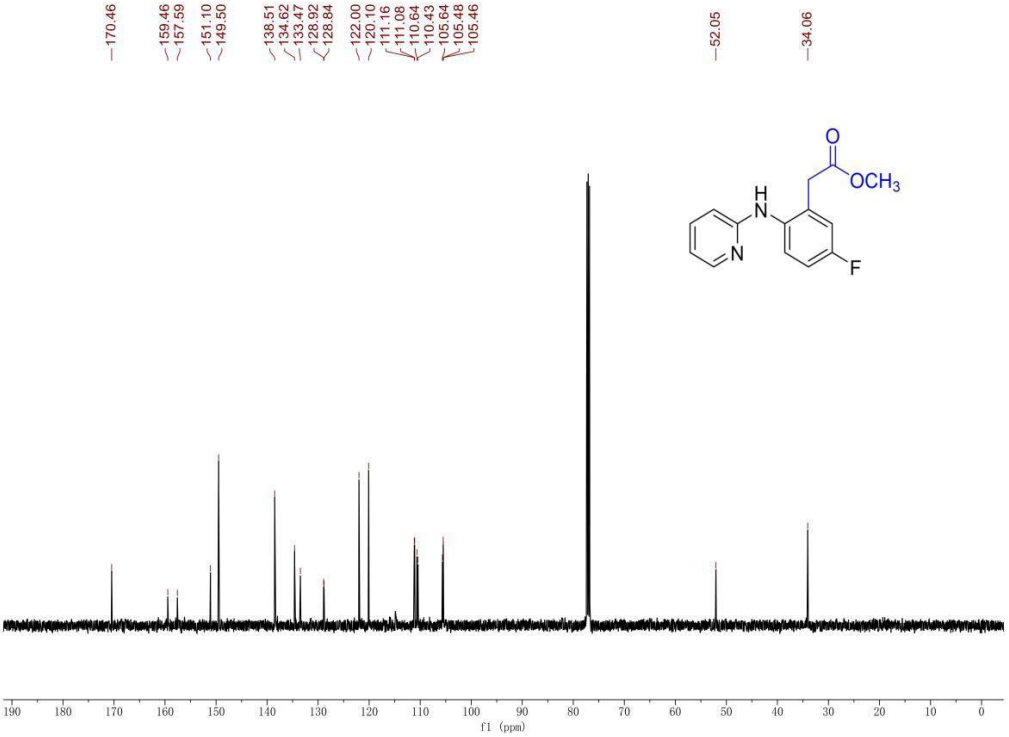
^{13}C NMR of 3c



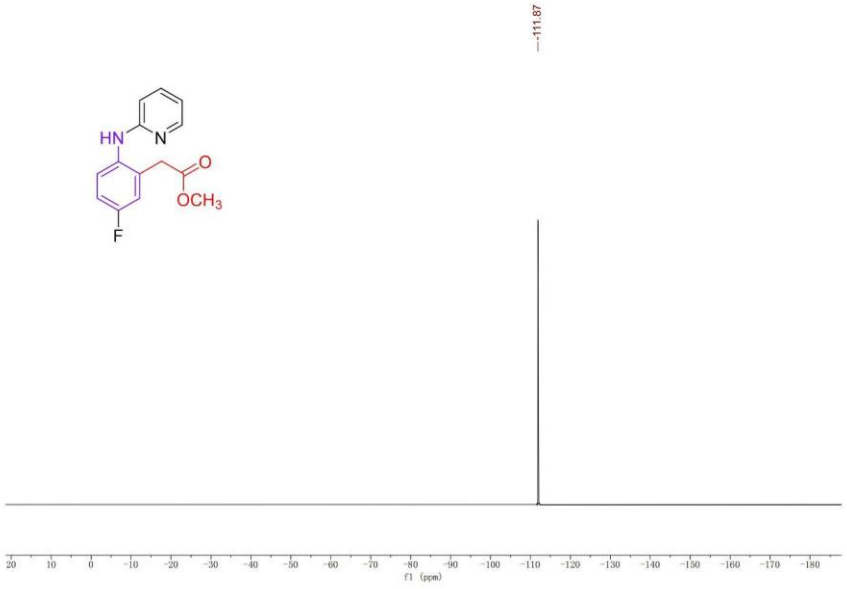
^{1}H NMR of 3d



^{13}C NMR of 3d



^{19}F NMR spectra of 3d



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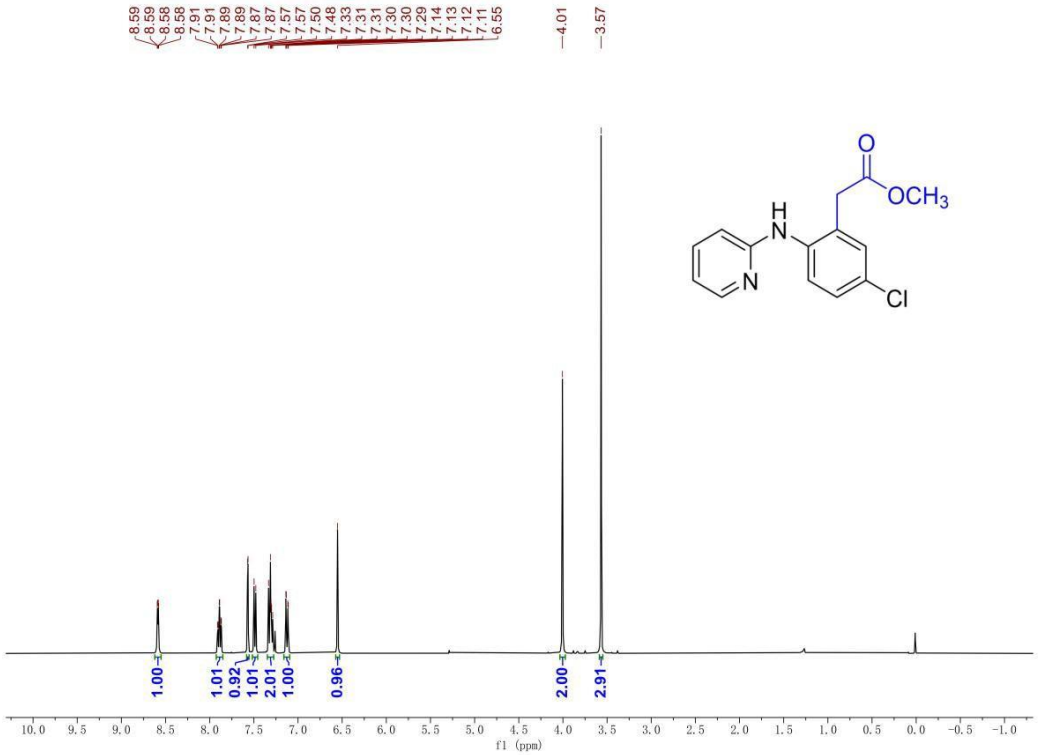

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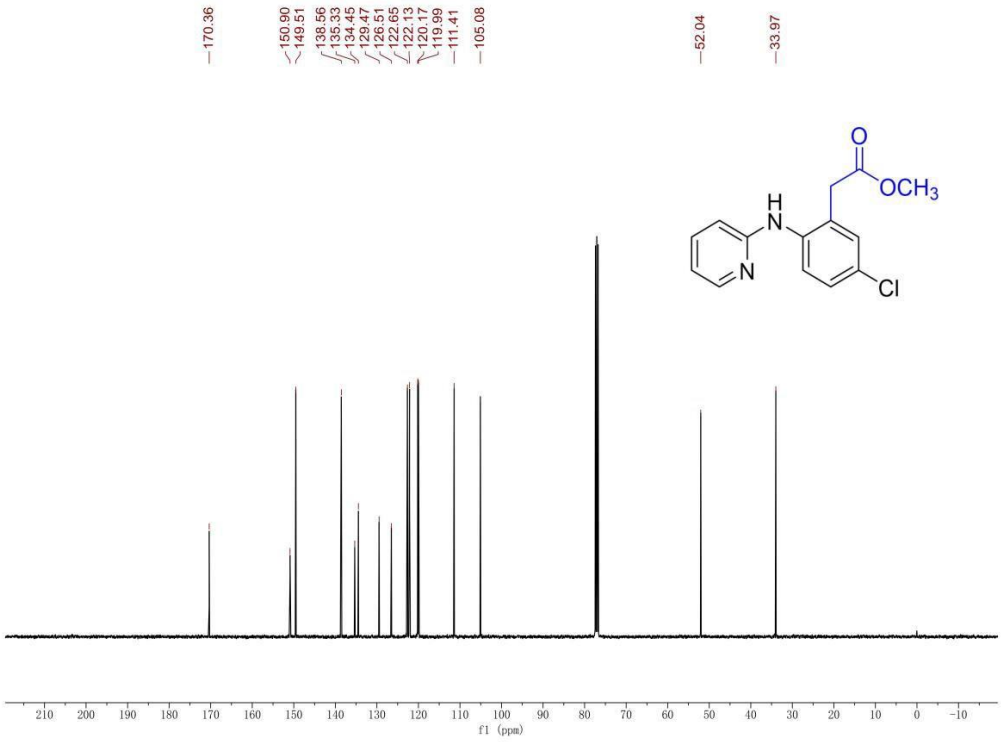
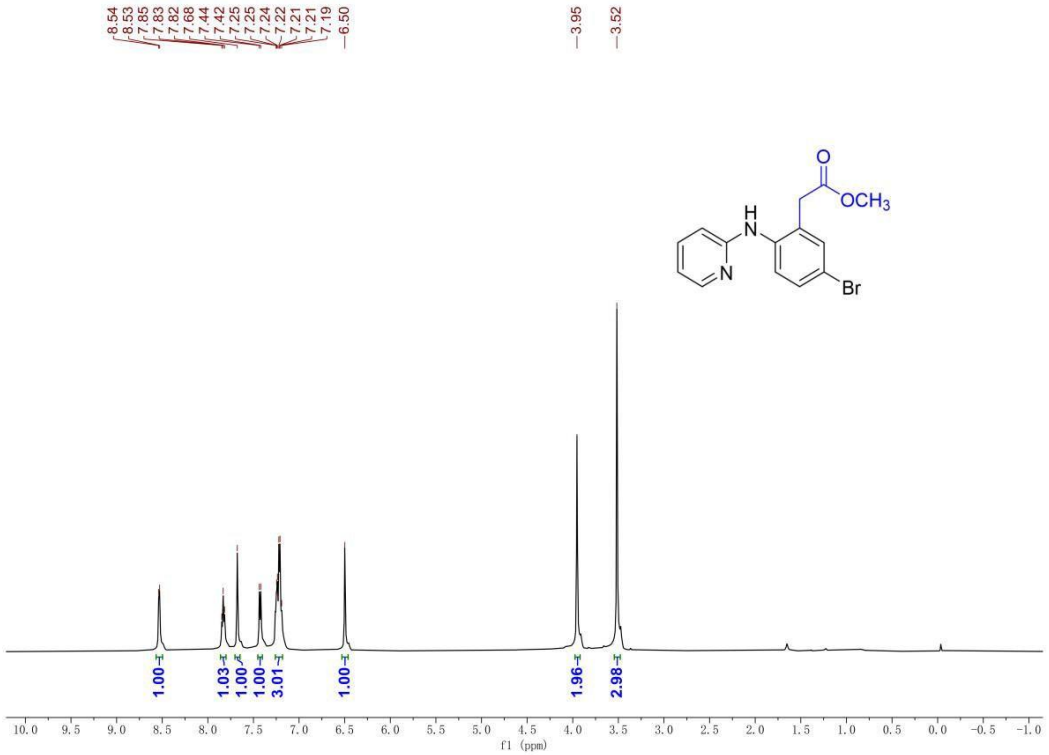
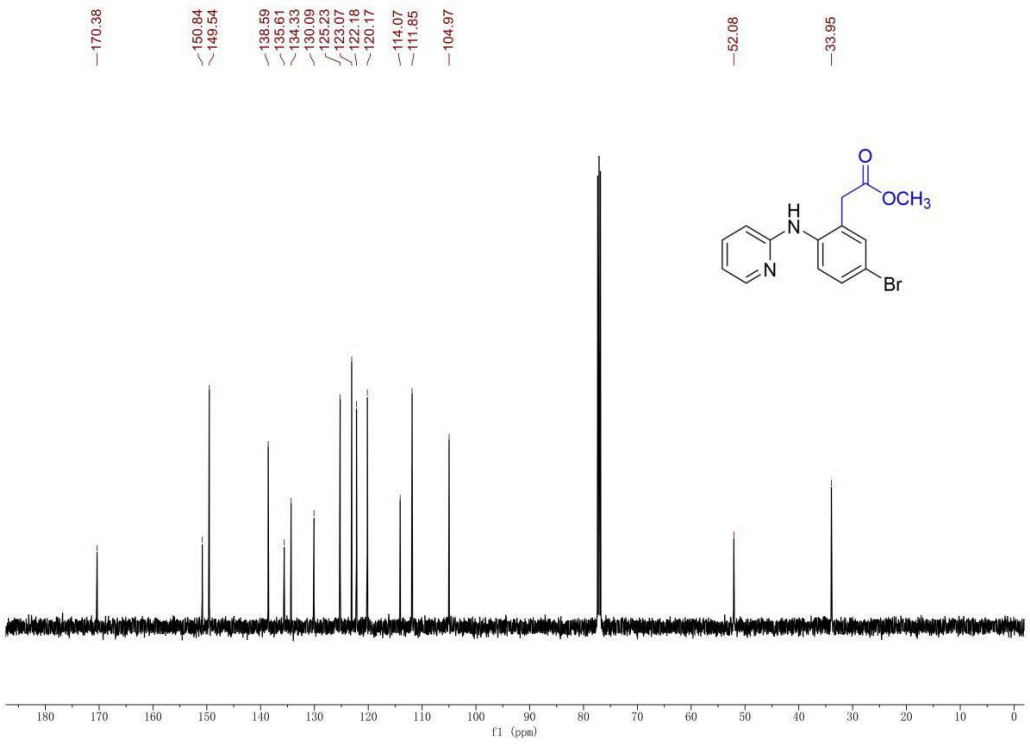


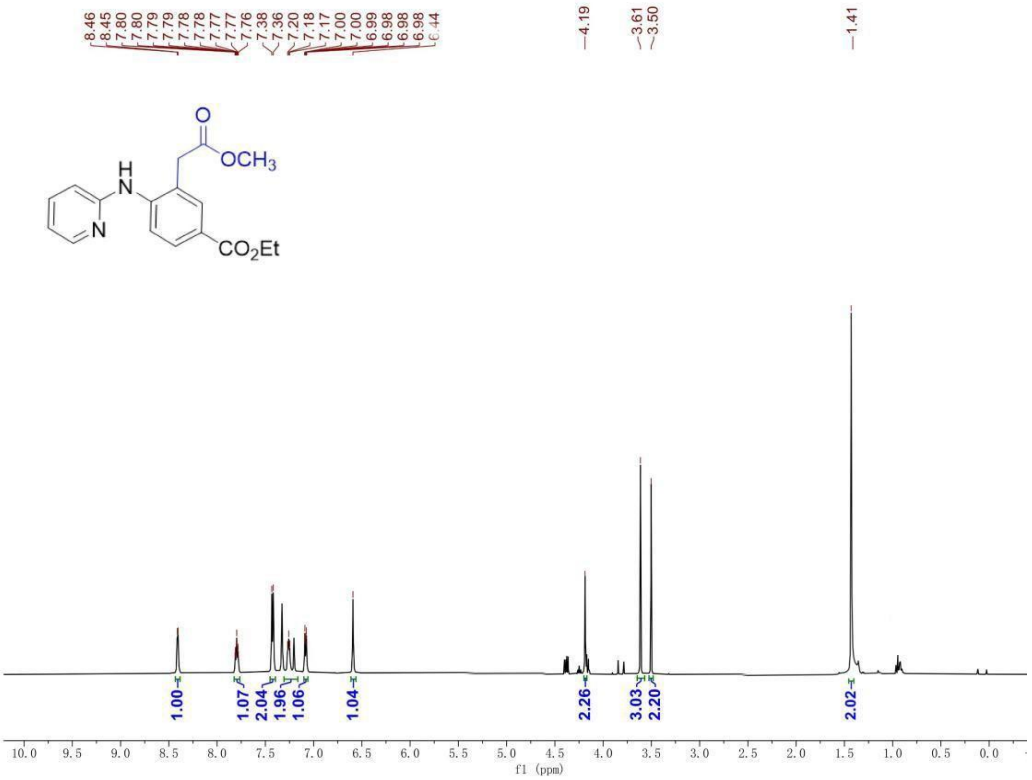
^{1}H NMR of 3f



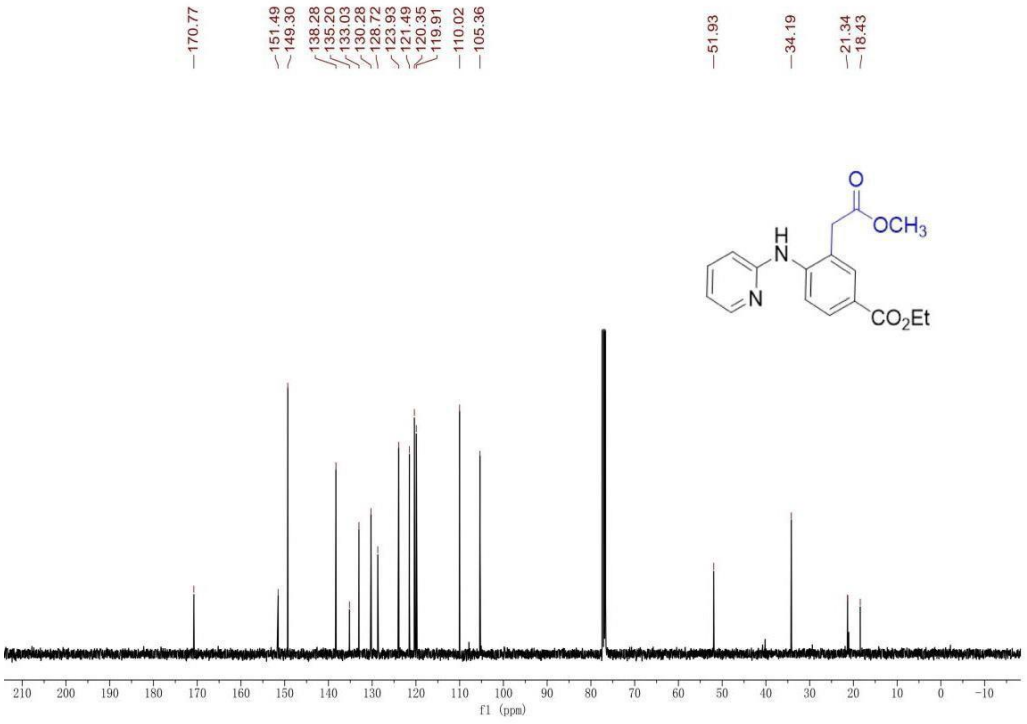
^{13}C NMR of 3f



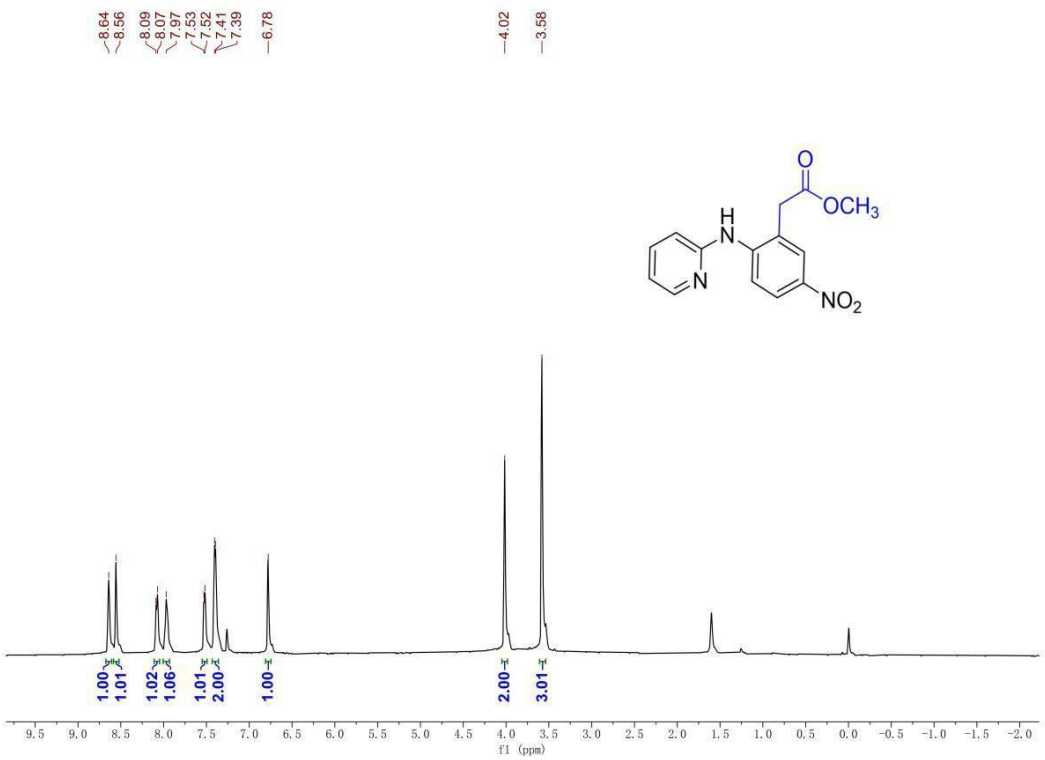
^{1}H NMR of 3g



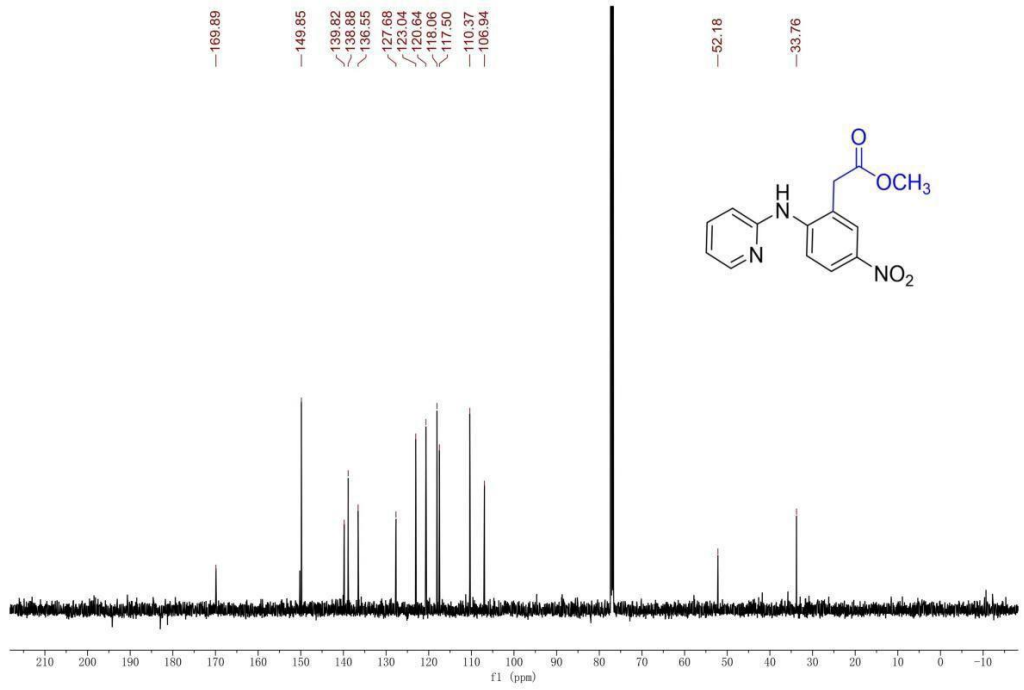
^{13}C NMR of 3g



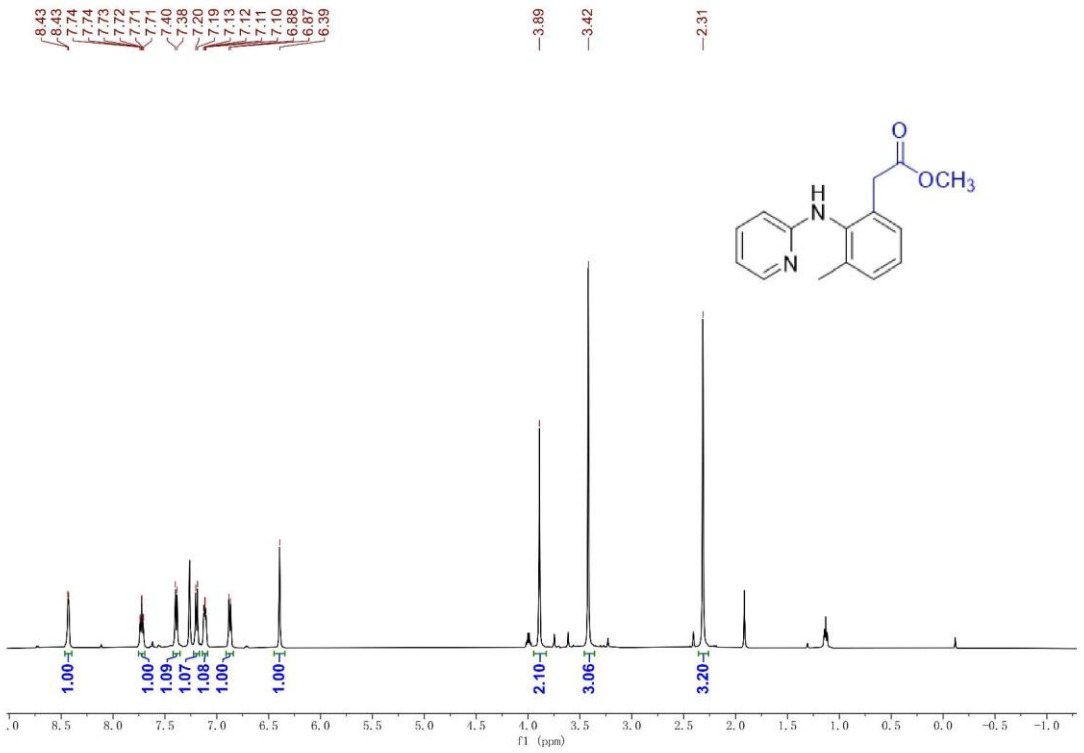
^{1}H NMR of 3h



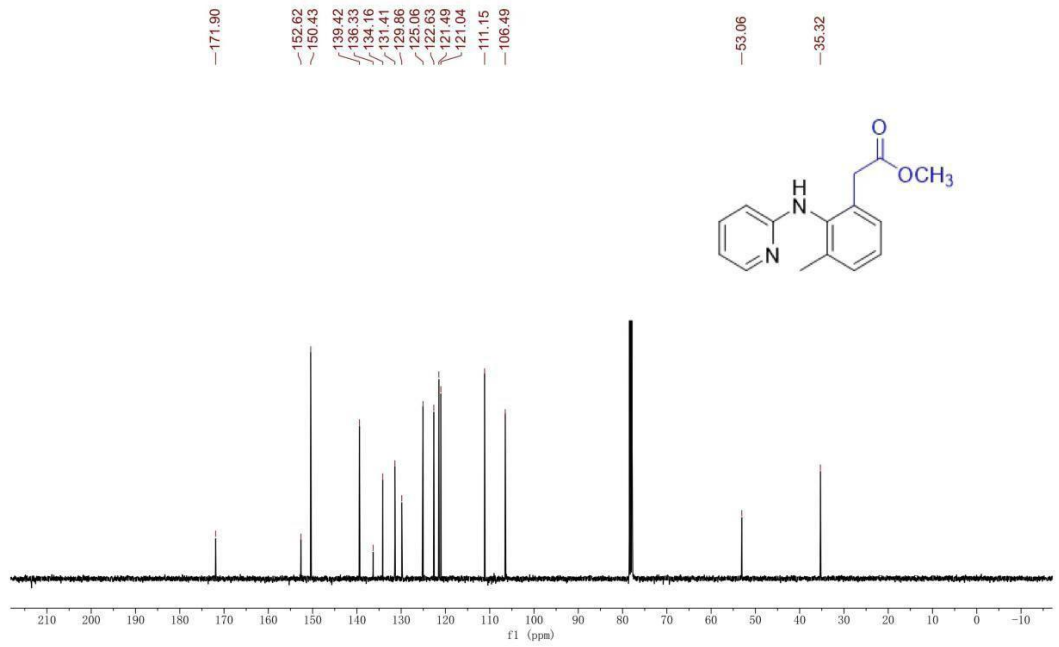
^{13}C NMR of 3h



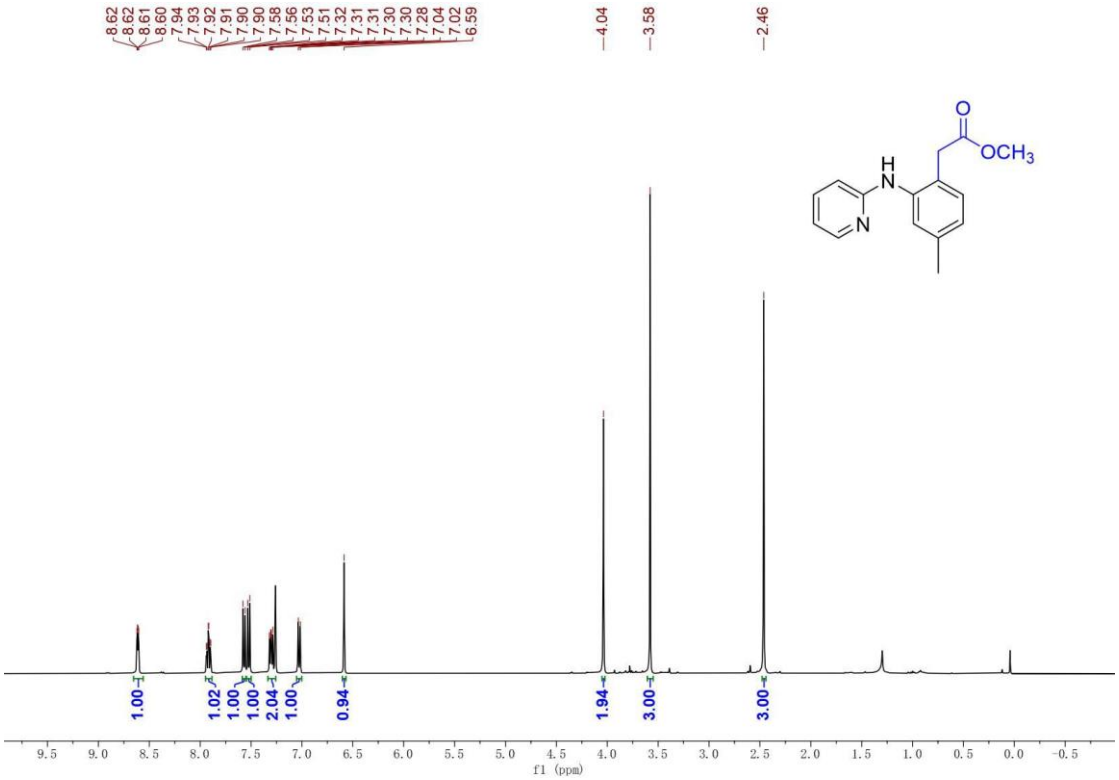
^{1}H NMR of 3i



^{13}C NMR of 3i



^{1}H NMR of 3j



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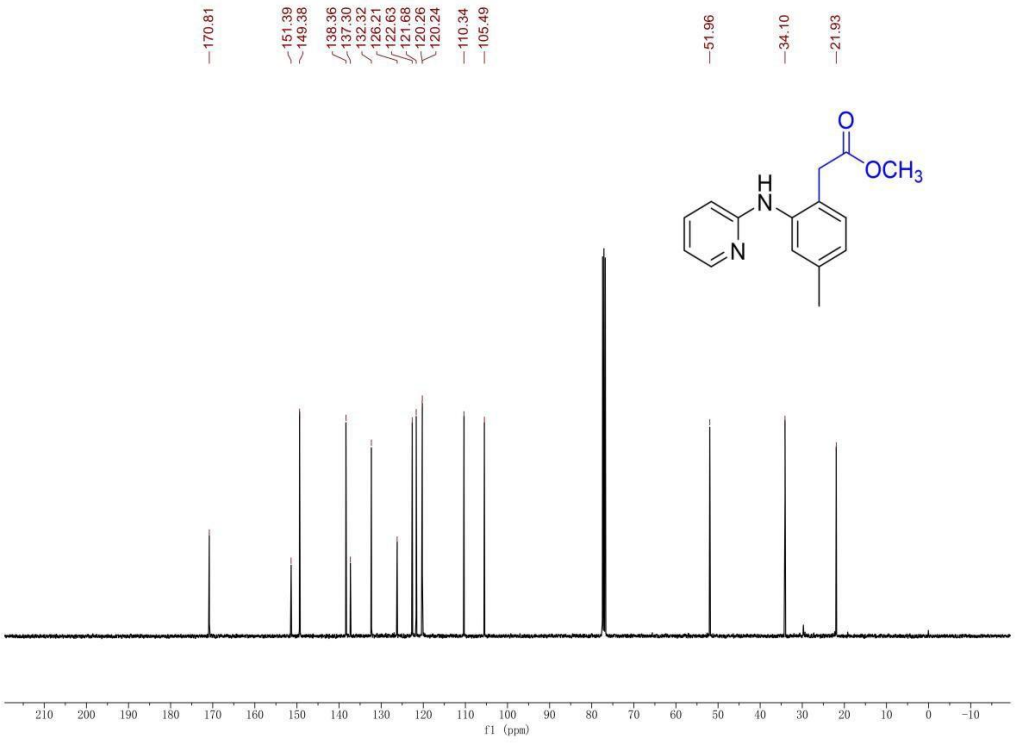
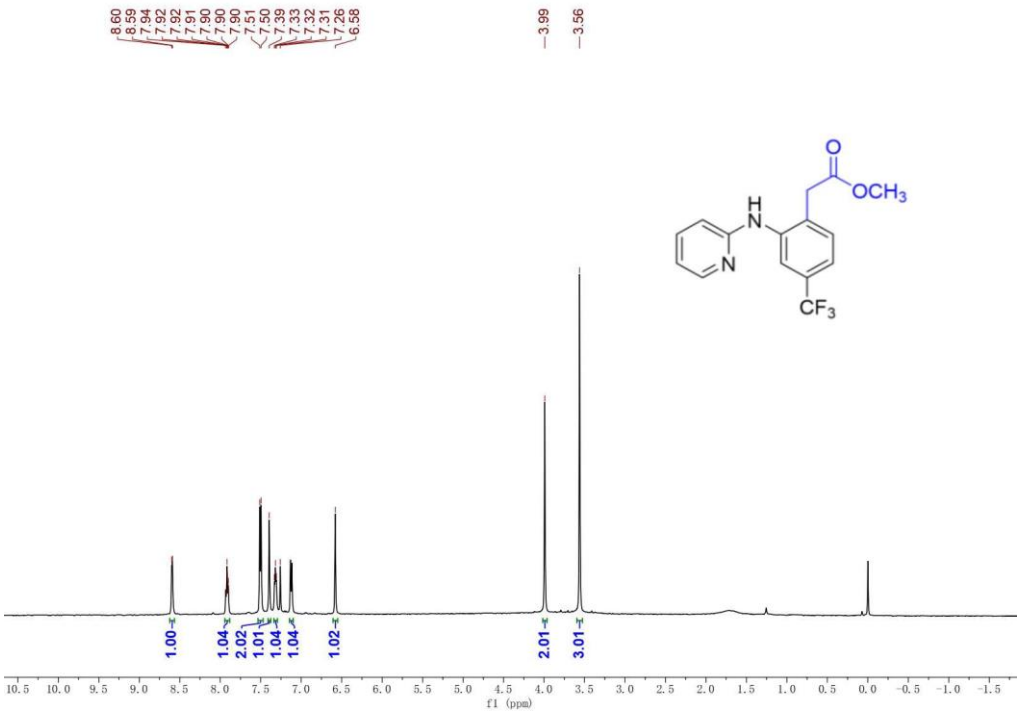
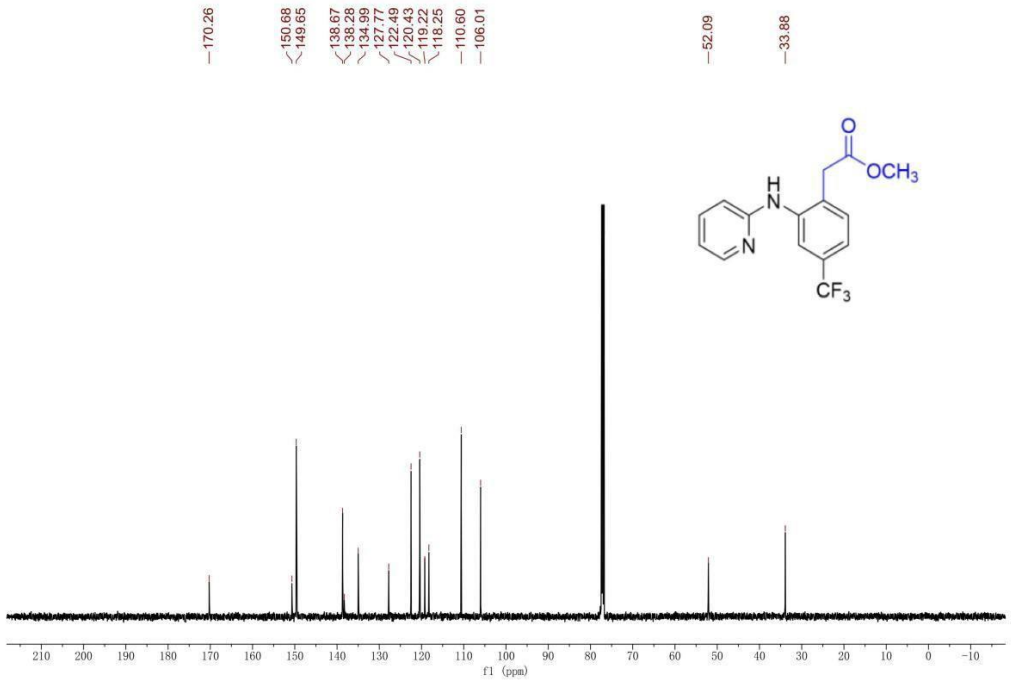


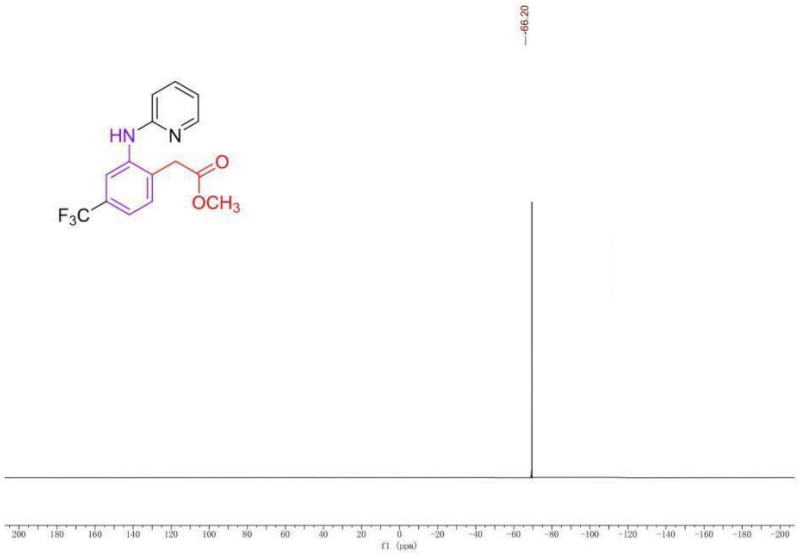
^{1}H NMR of 3k



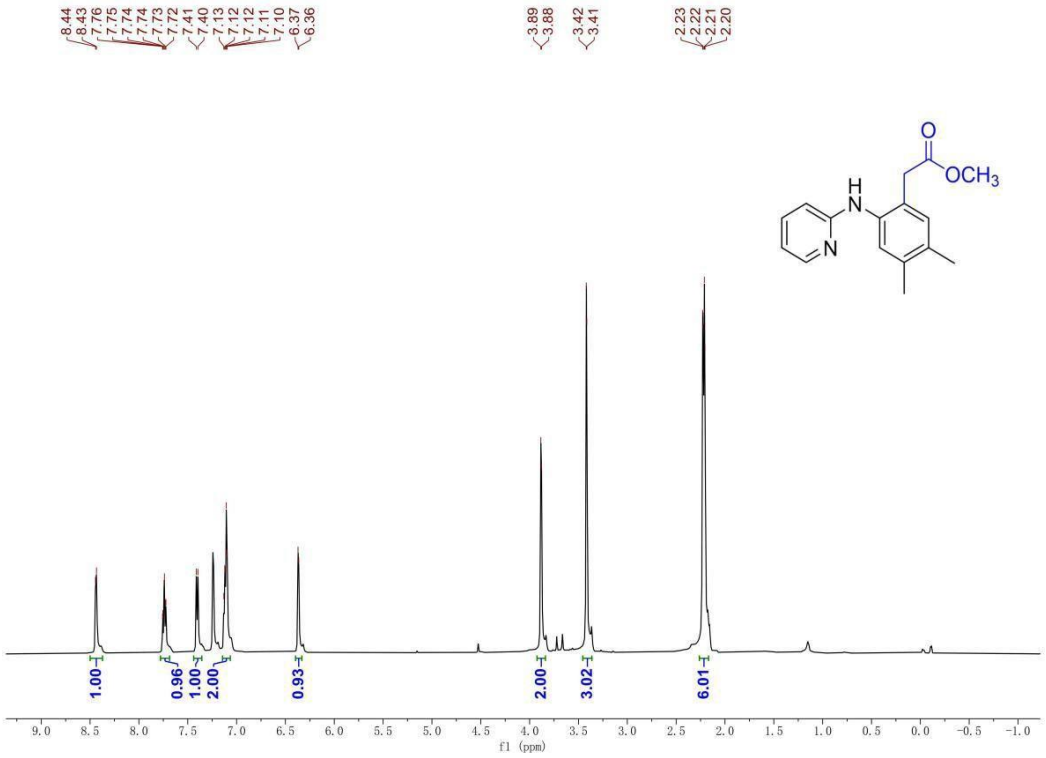
^{13}C NMR of 3k



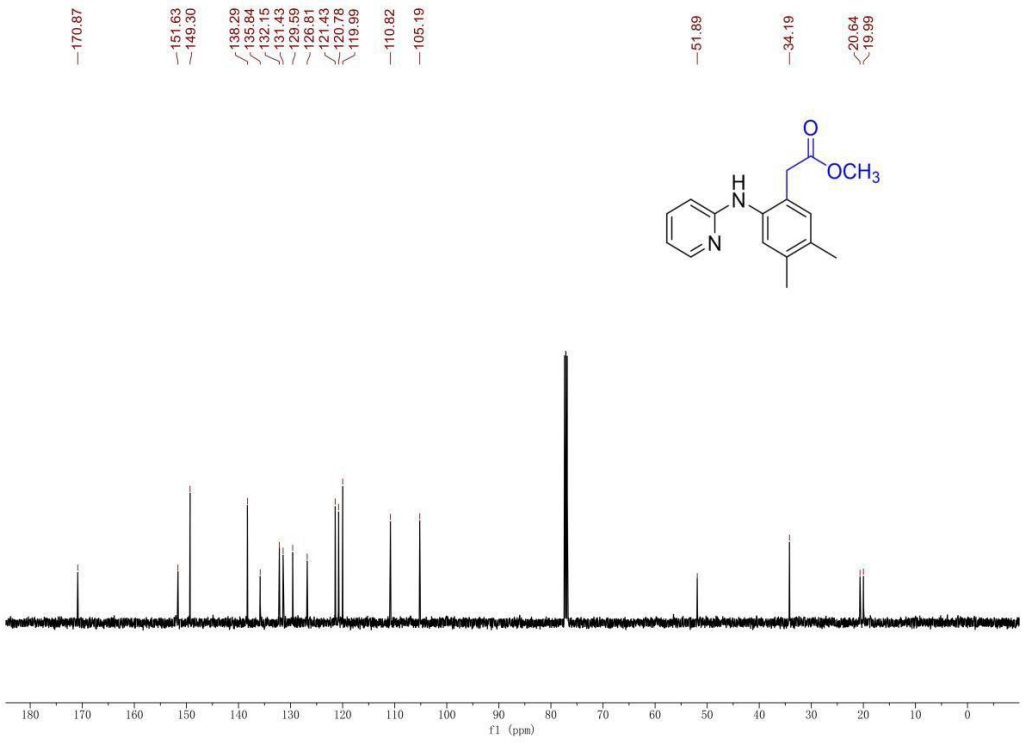
^{19}F NMR spectra of 3k



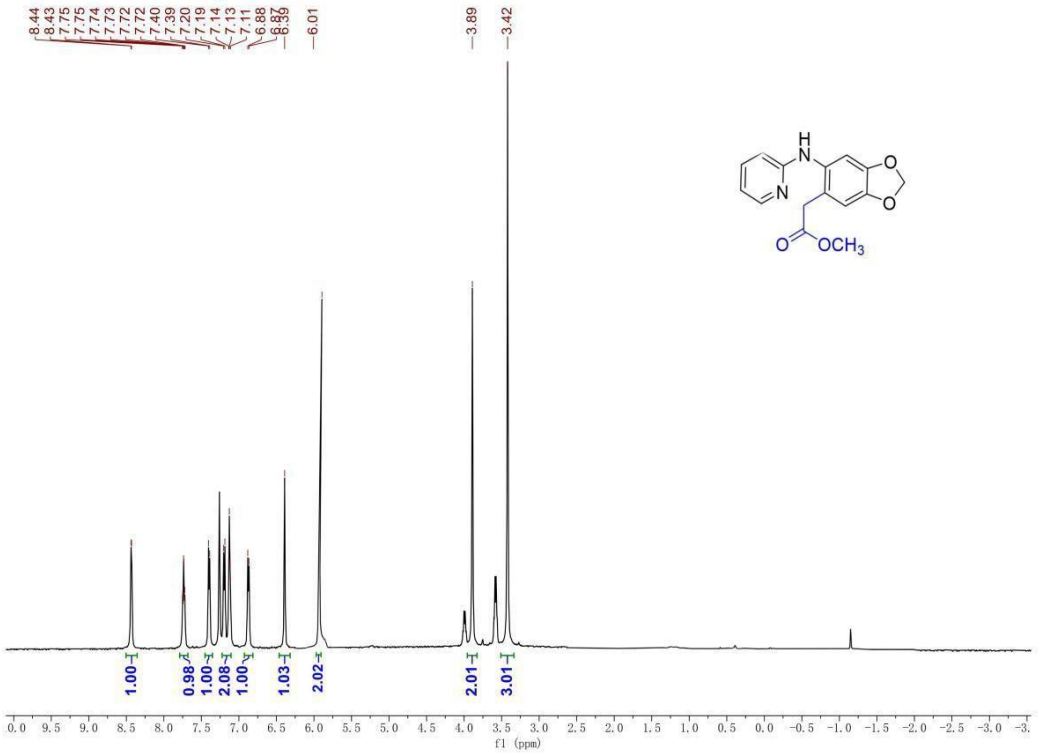
^{1}H NMR of 3l



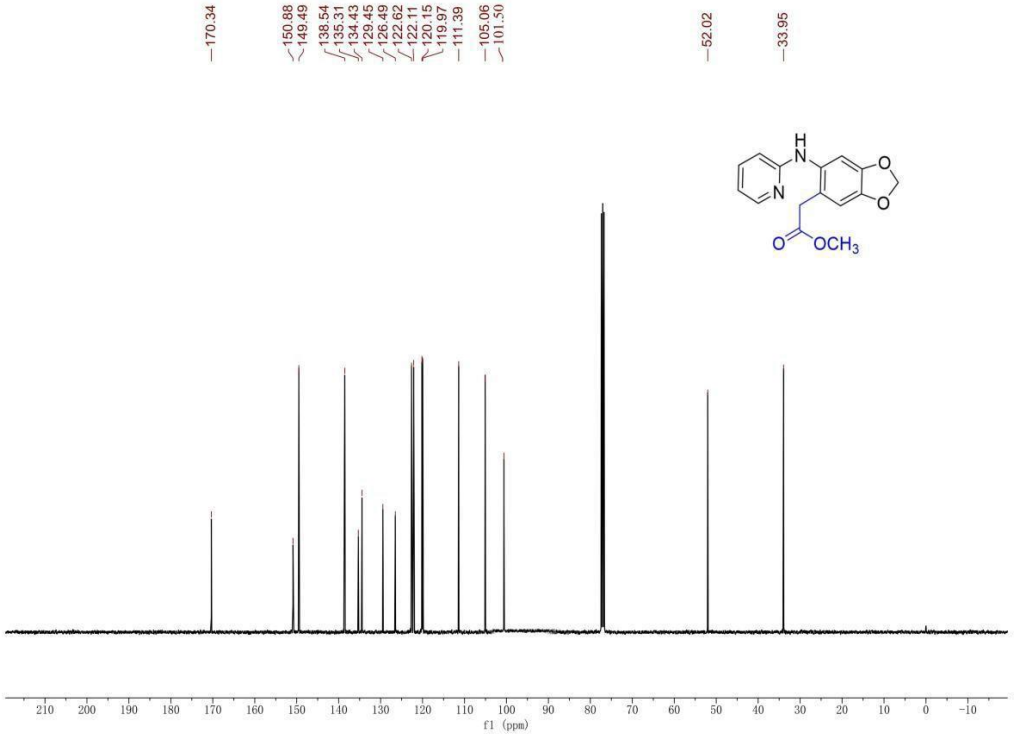
^{13}C NMR of 3l



^{1}H NMR of 3m



^{13}C NMR of 3m



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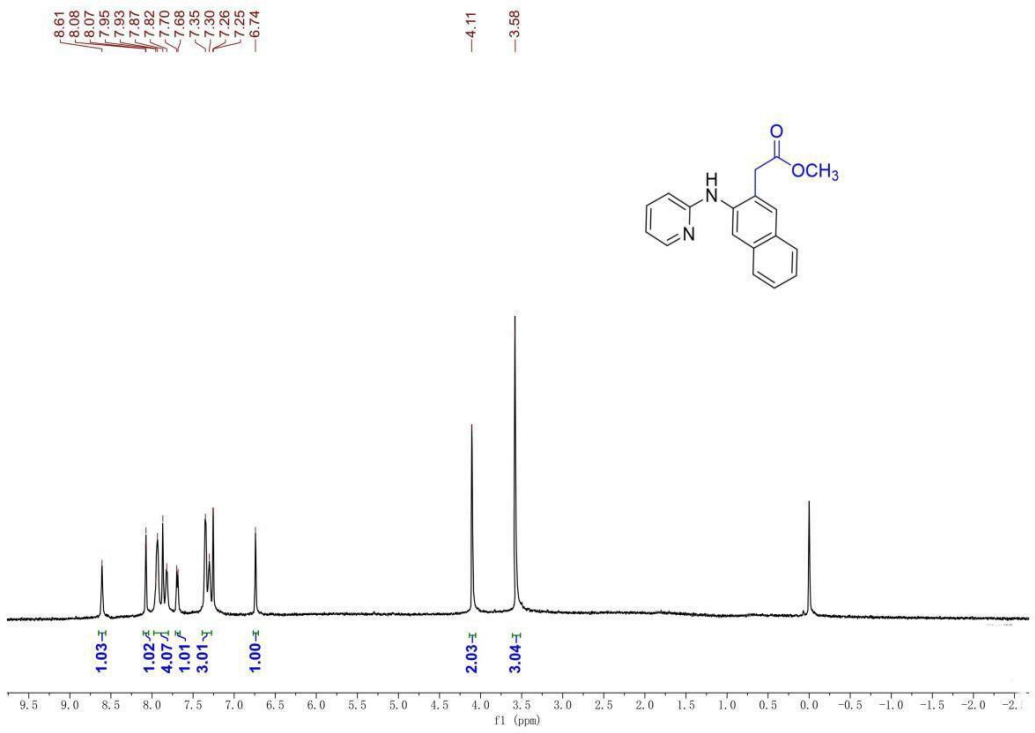
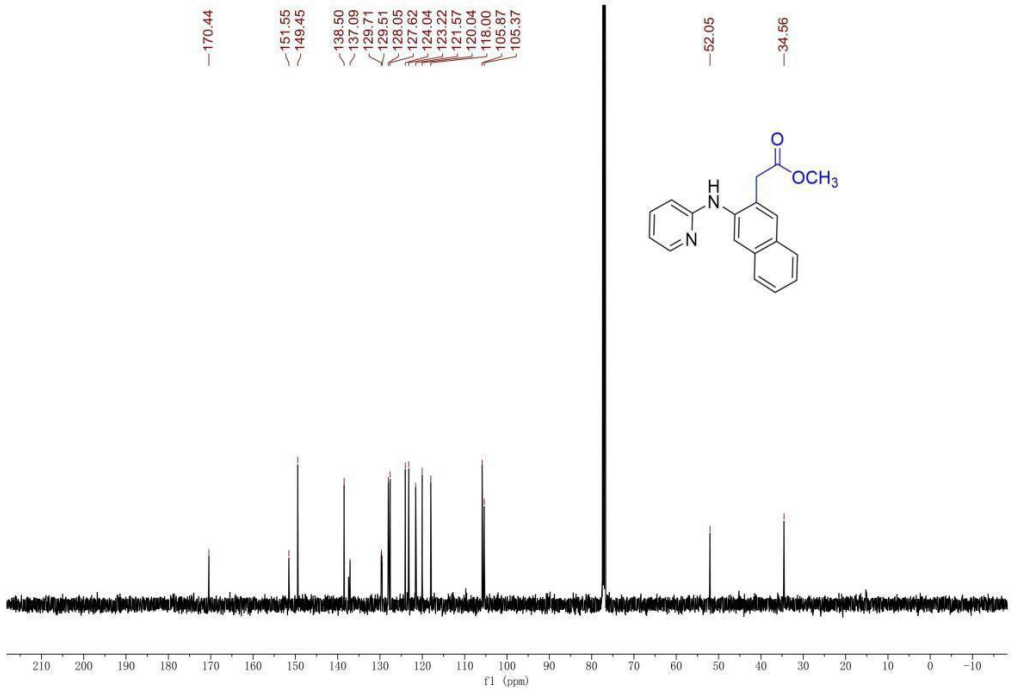
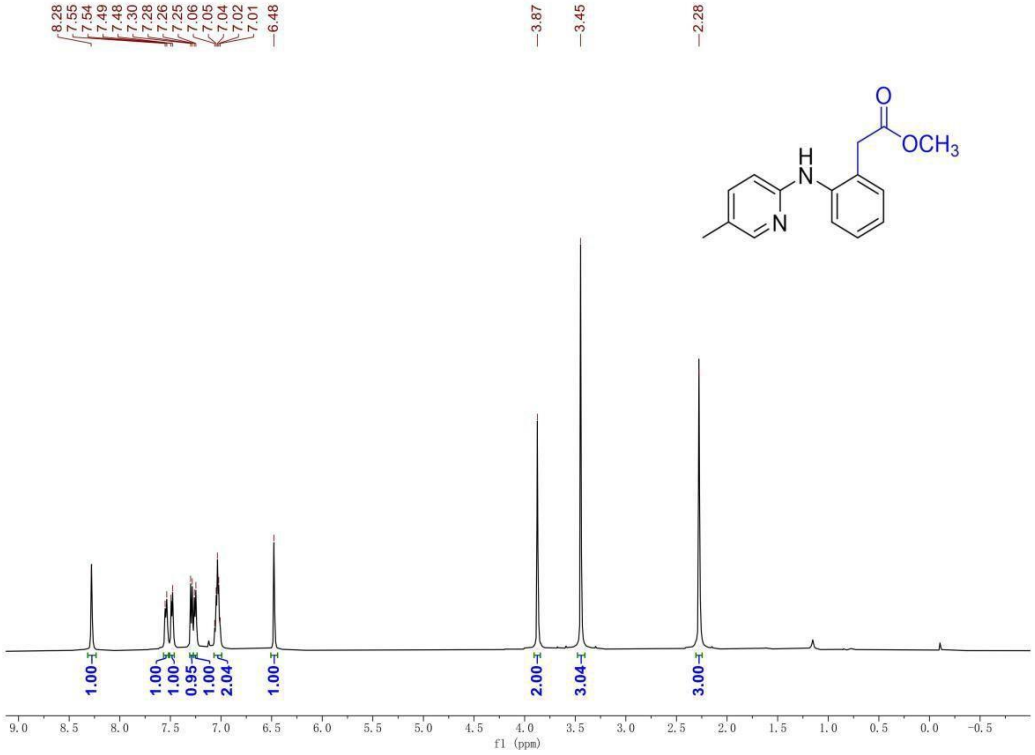


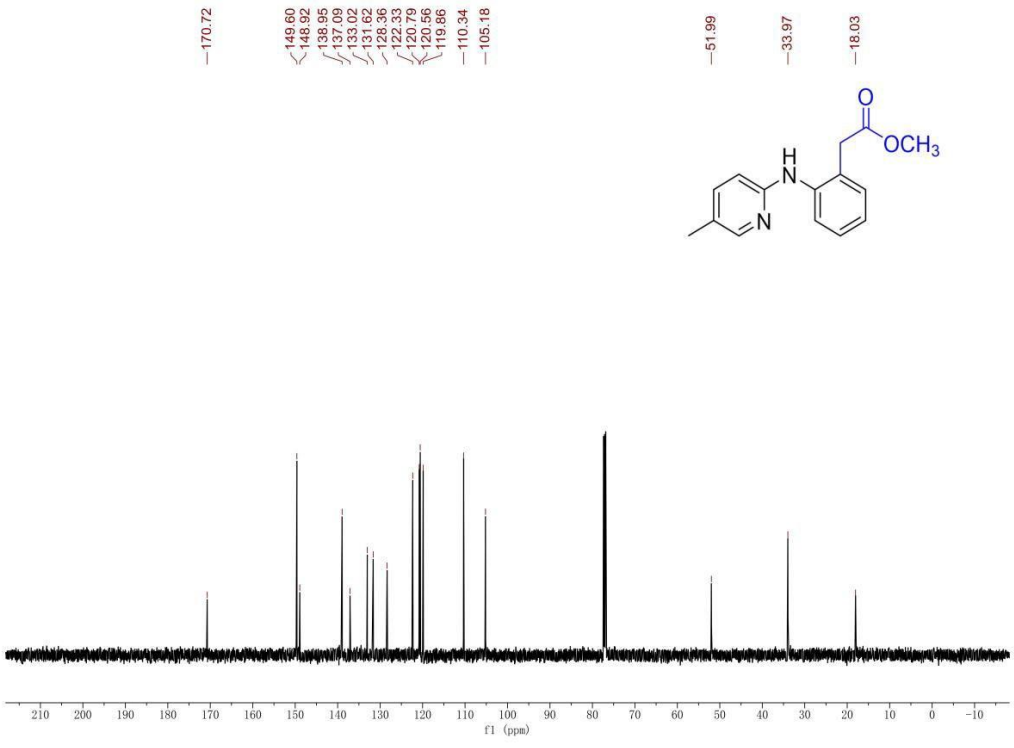
^{13}C NMR of 3n



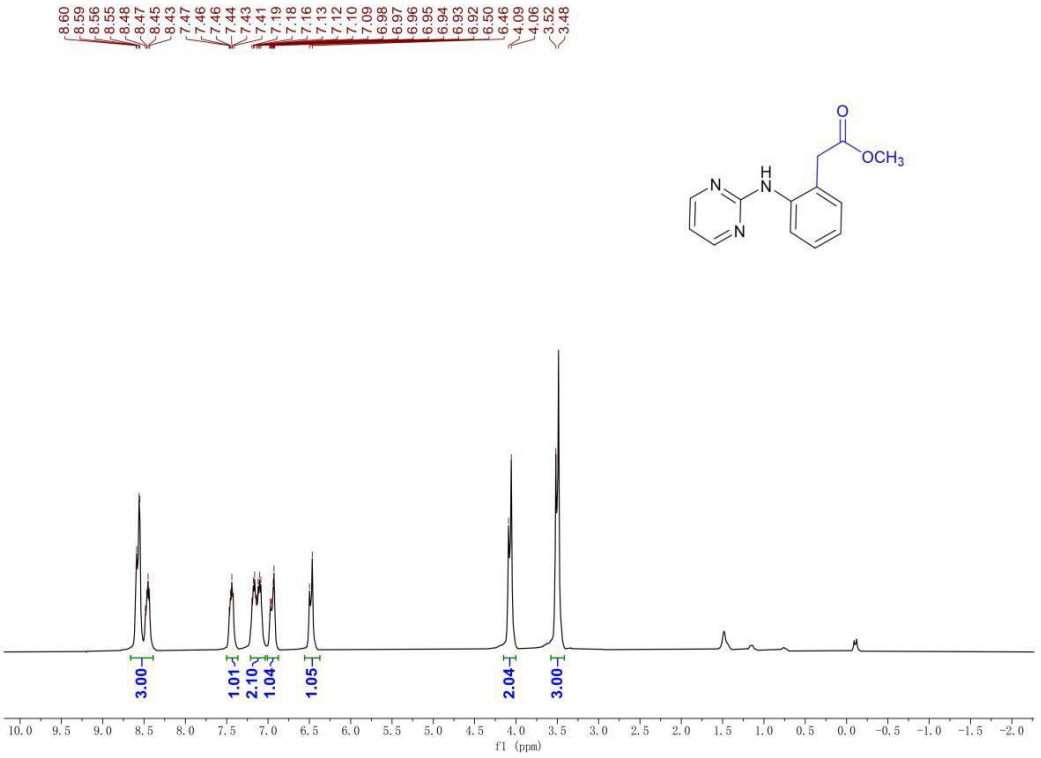
^{1}H NMR of 3o



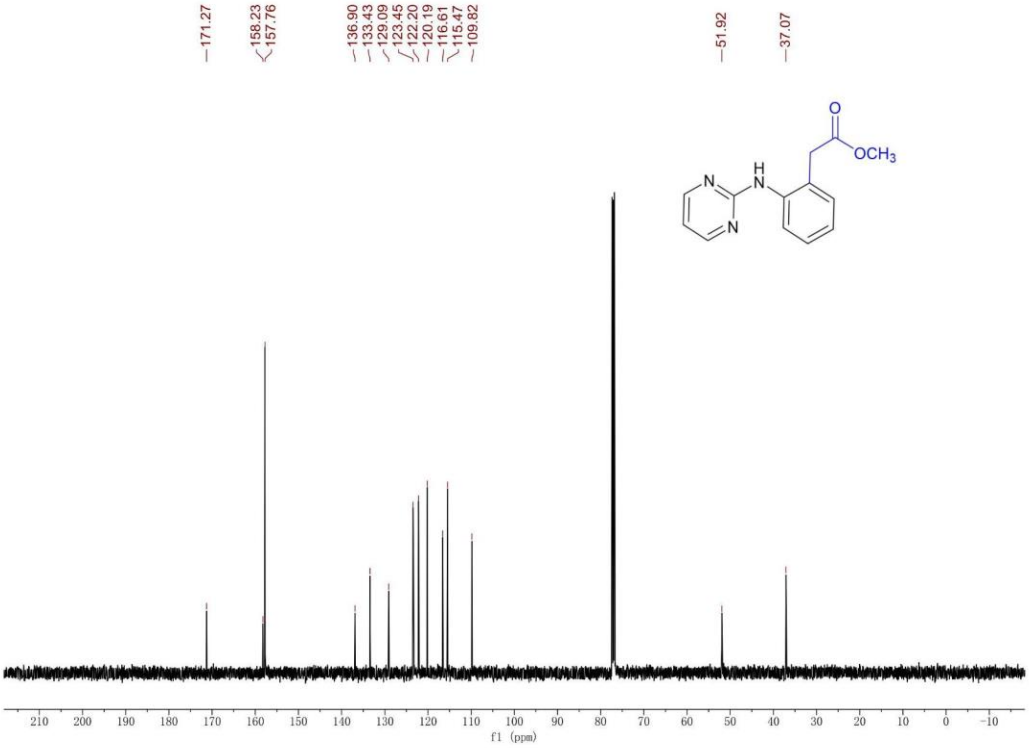
^{13}C NMR of 3o



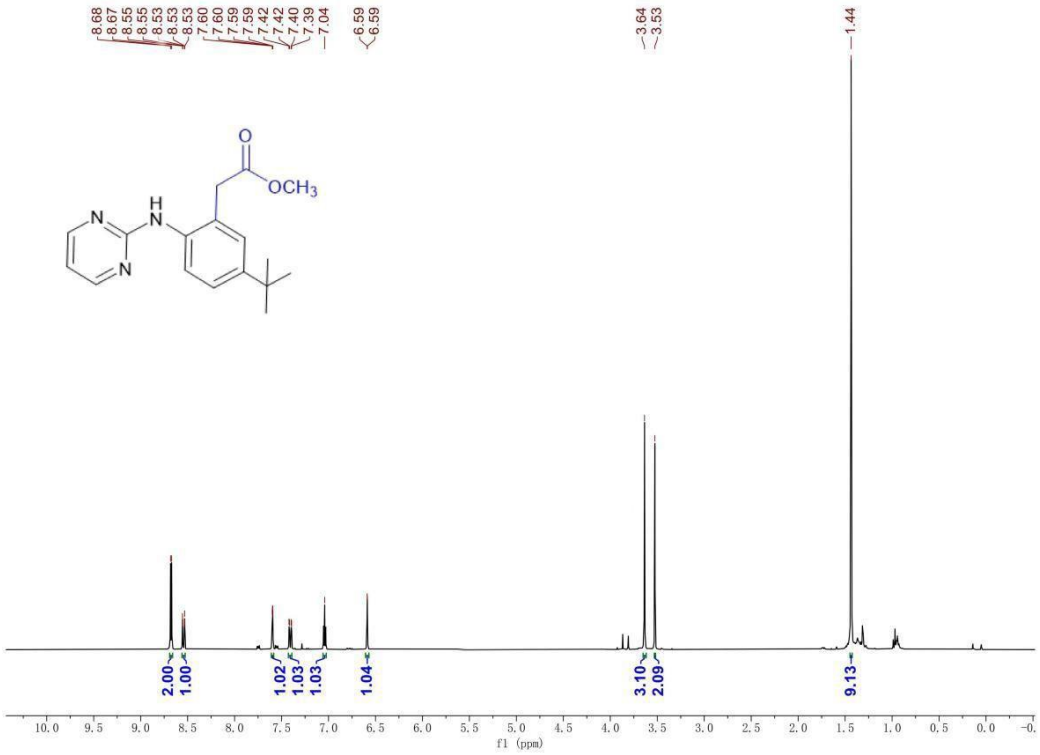
^{1}H NMR of 4a



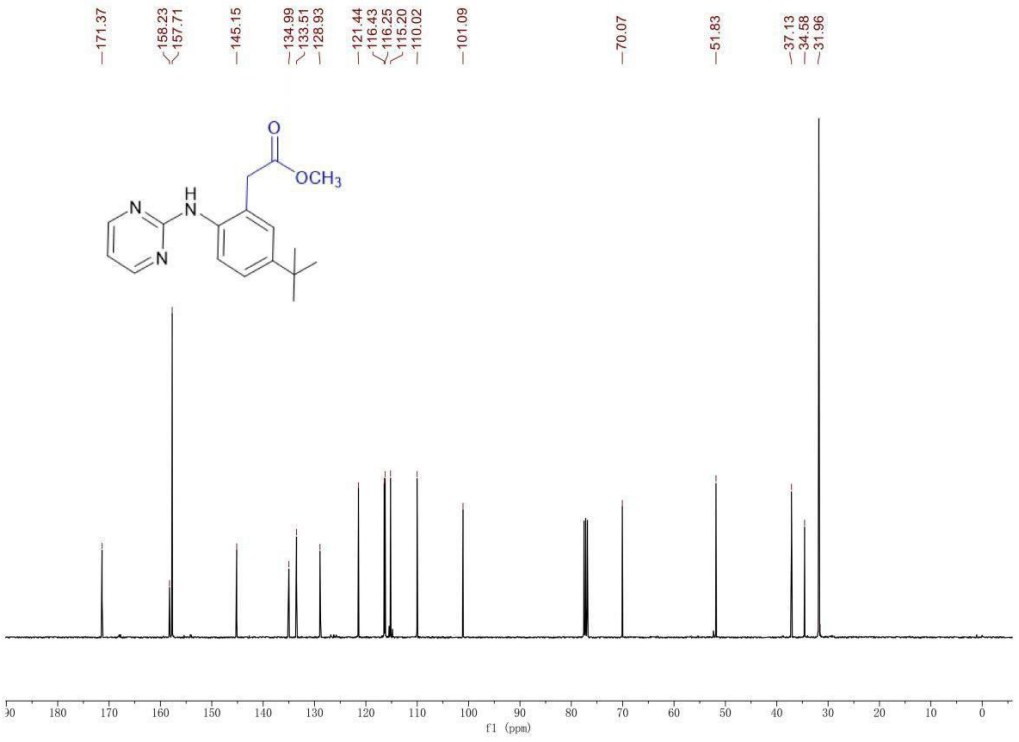
^{13}C NMR of 4a



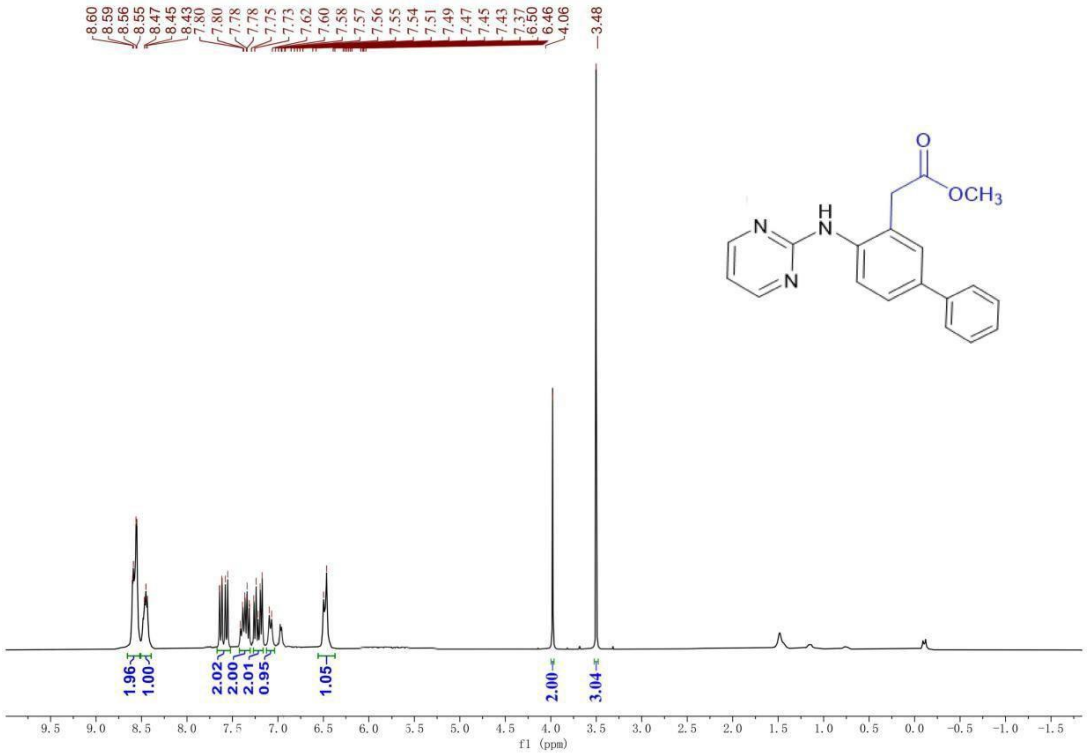
^{1}H NMR of 4b



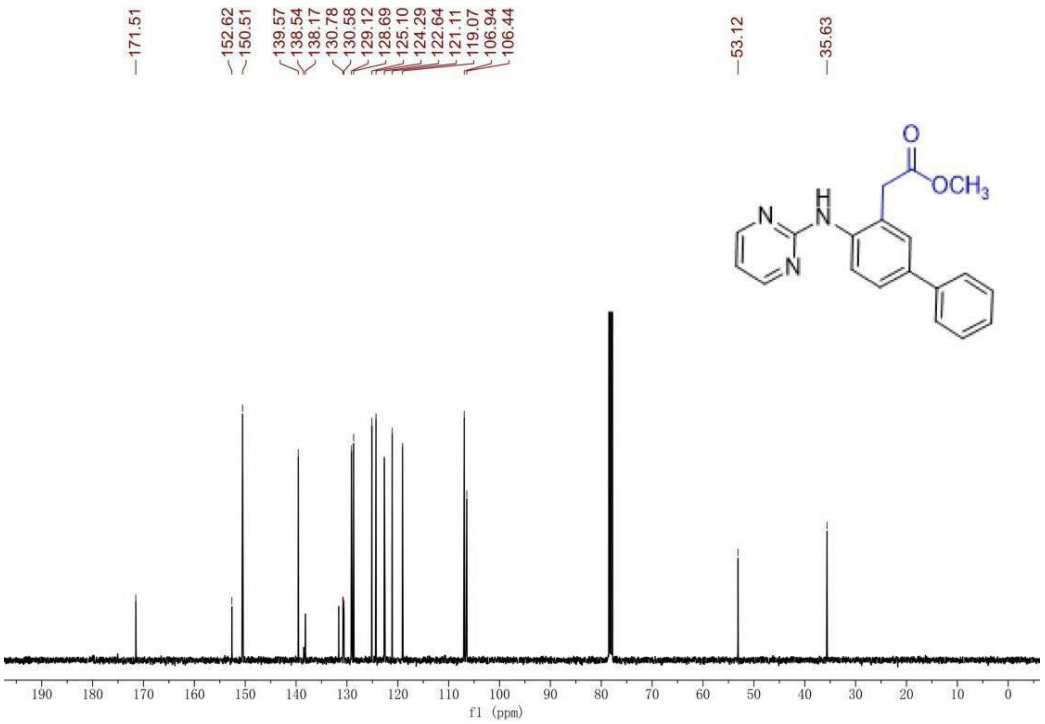
^{13}C NMR of 4b



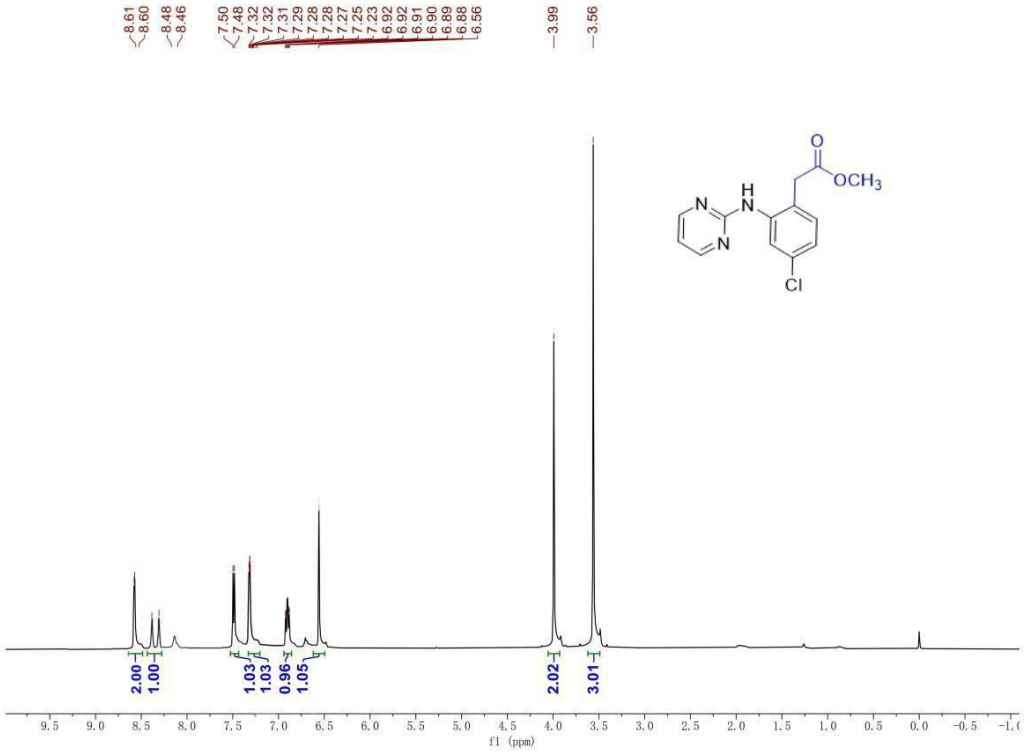
^{1}H NMR of 4c



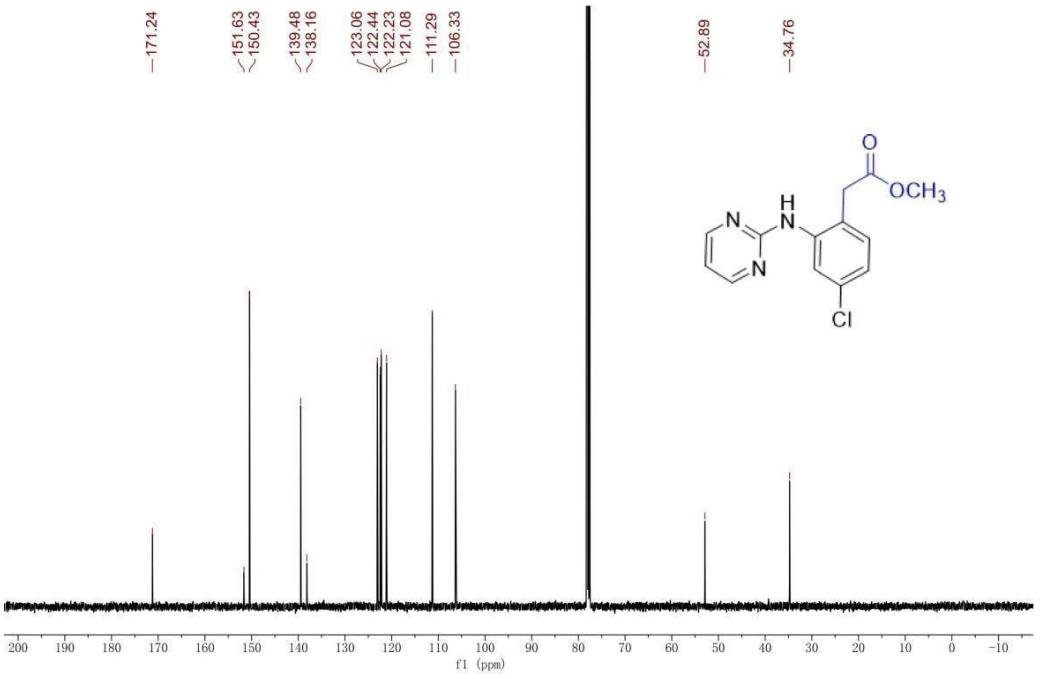
^{13}C NMR of 4c



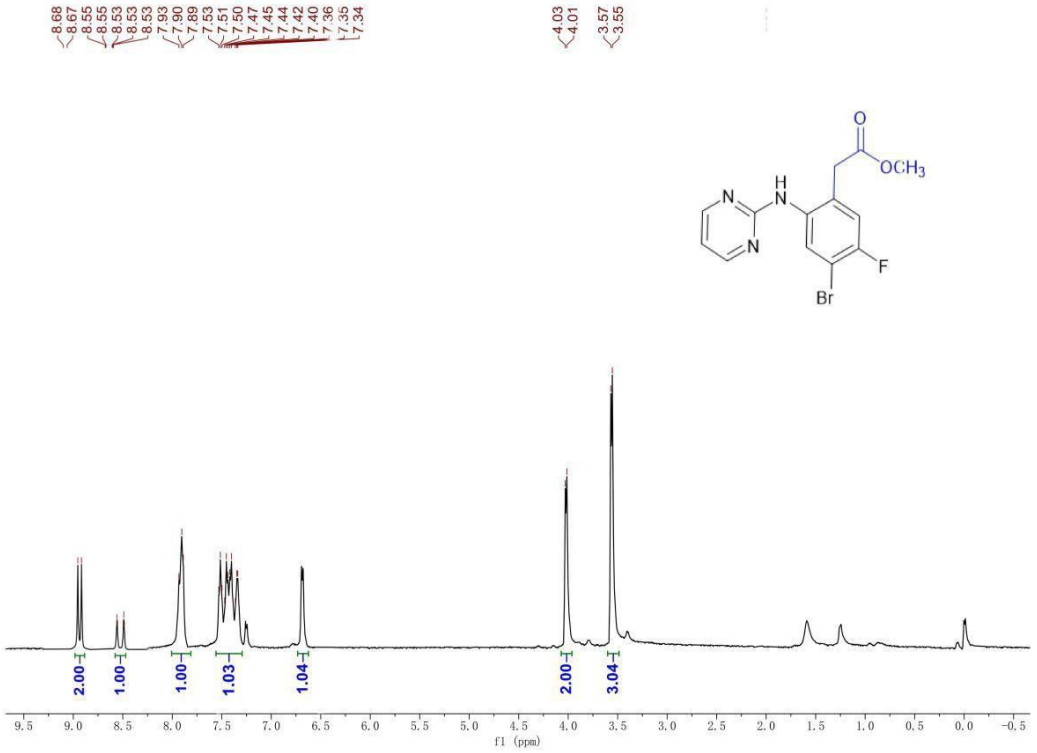
^{1}H NMR of 4d



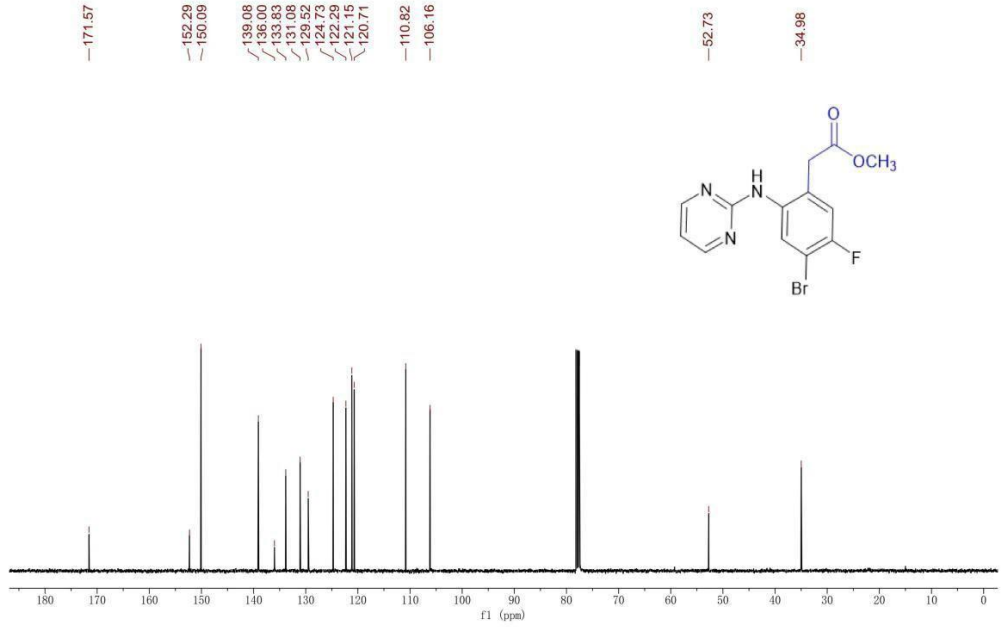
^{13}C NMR of 4d



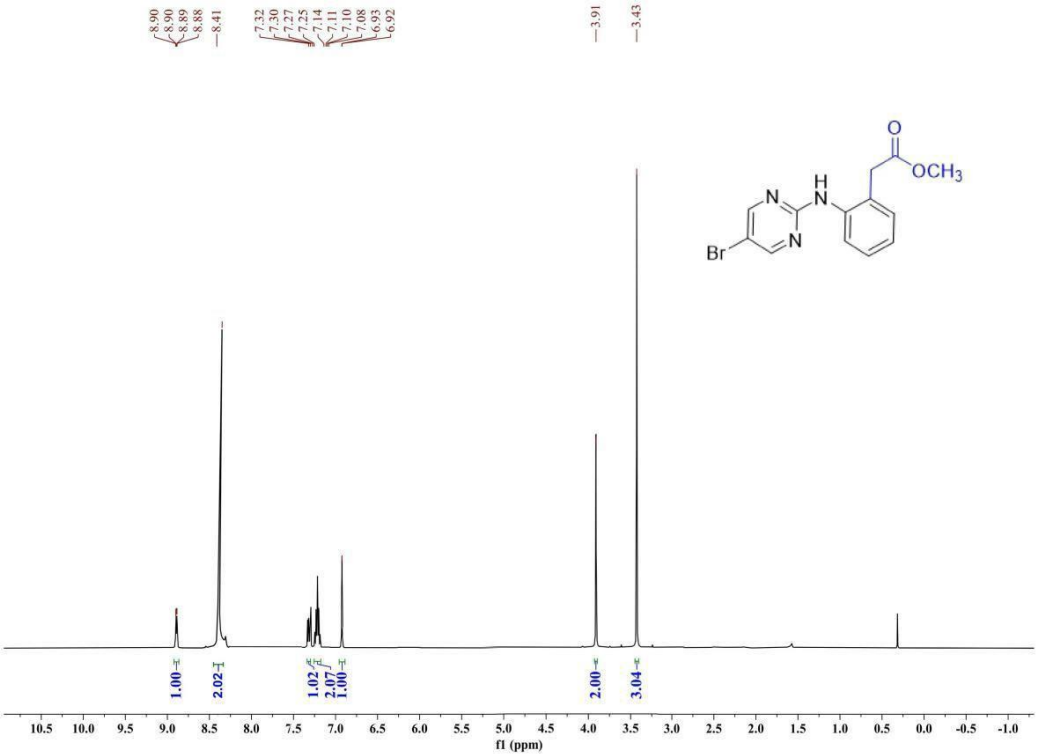
^{1}H NMR of 4e



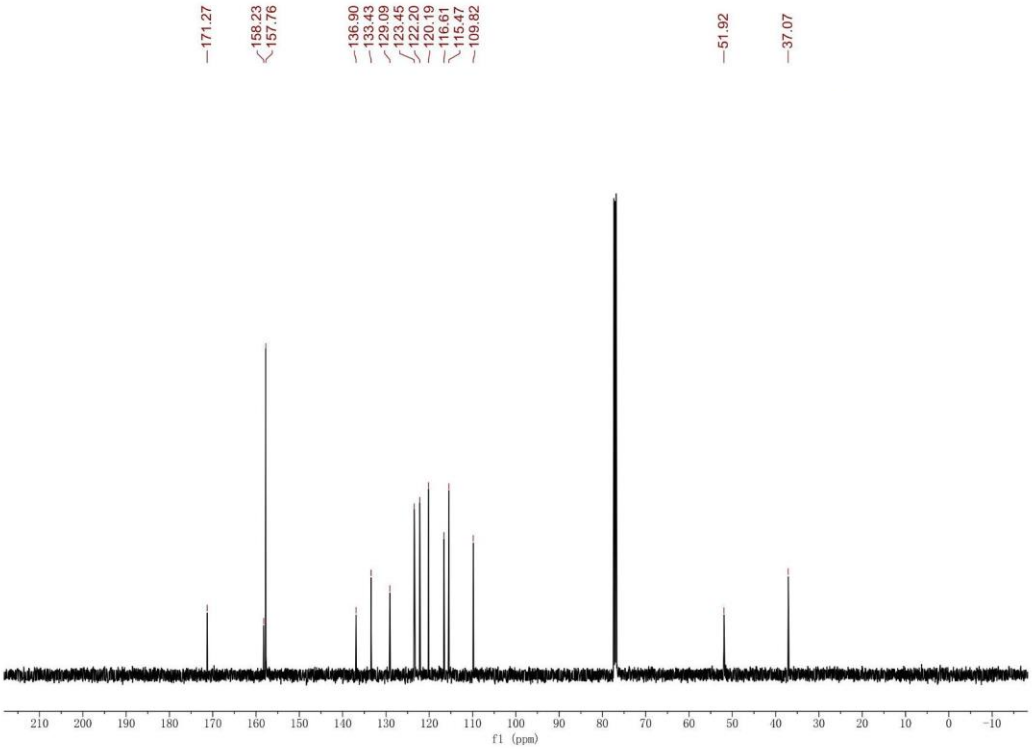
^{13}C NMR of 4e



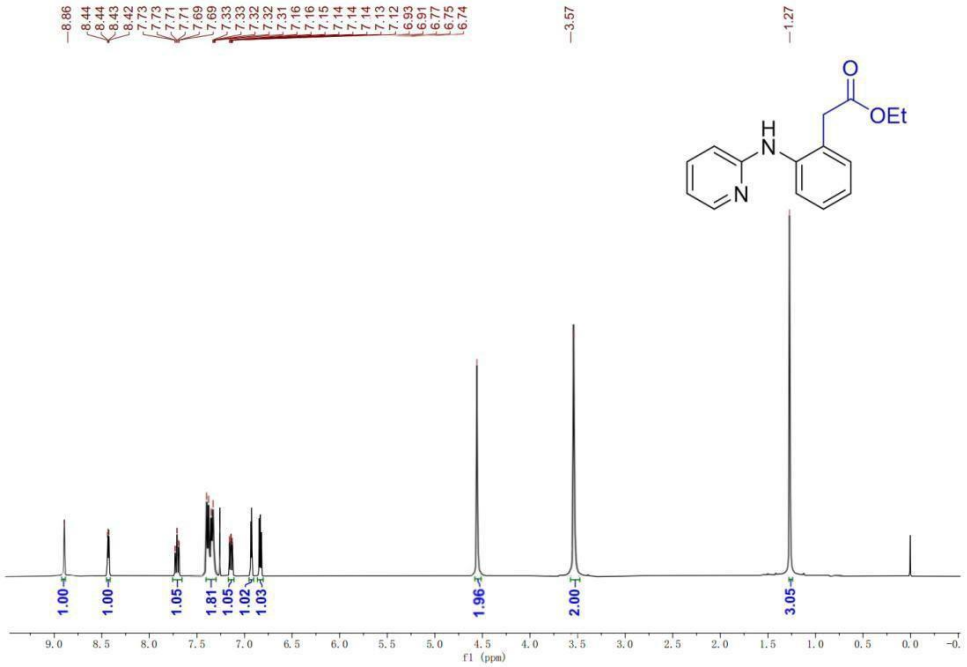
^{1}H NMR of 4f



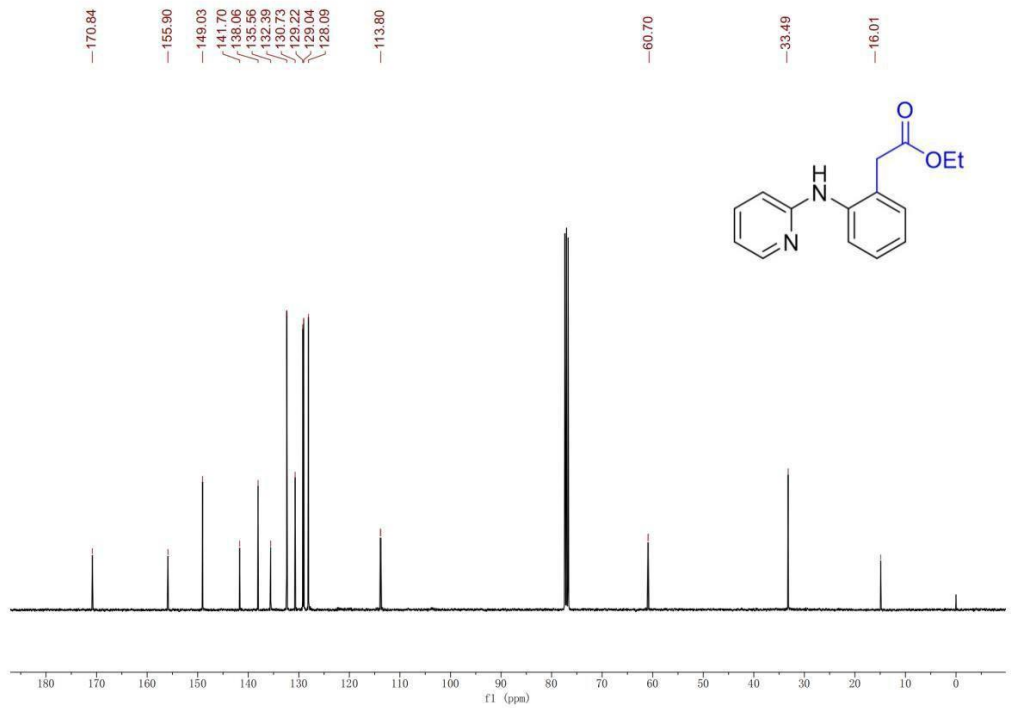
^{13}C NMR of 4f



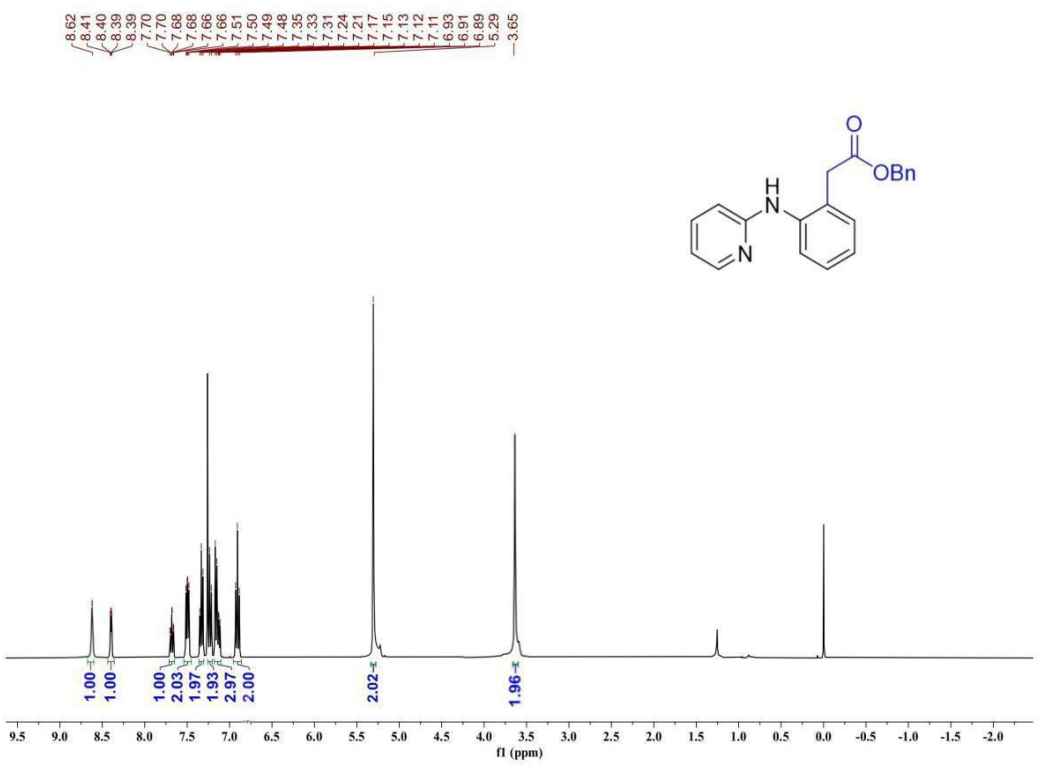
^{1}H NMR of 5a



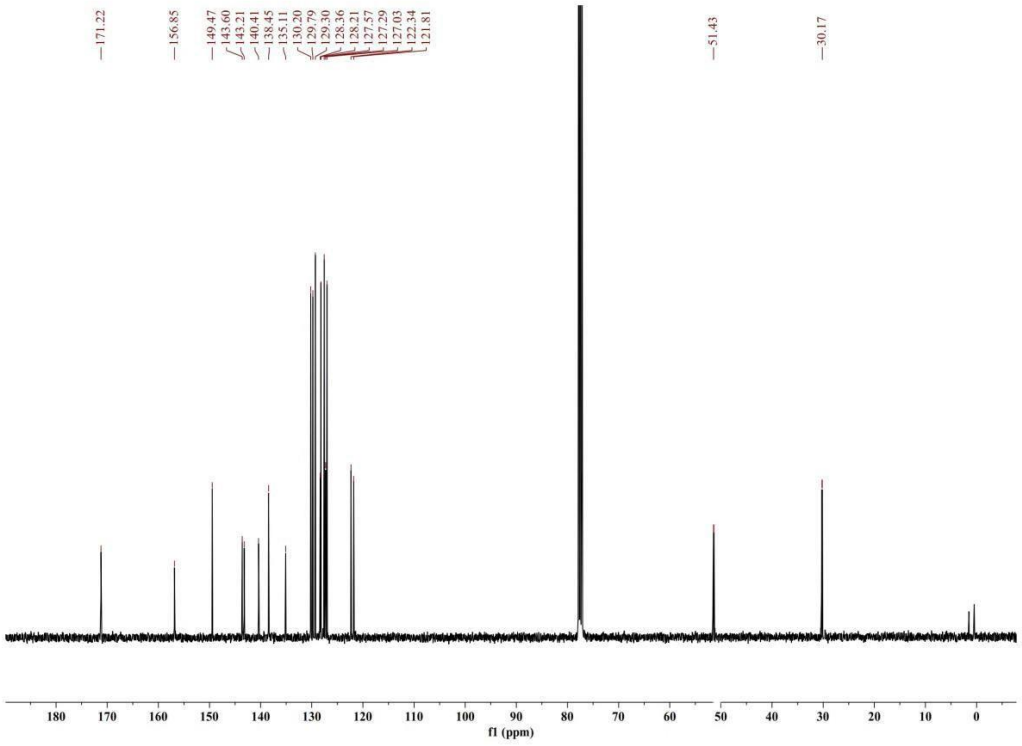
^{13}C NMR of 5a



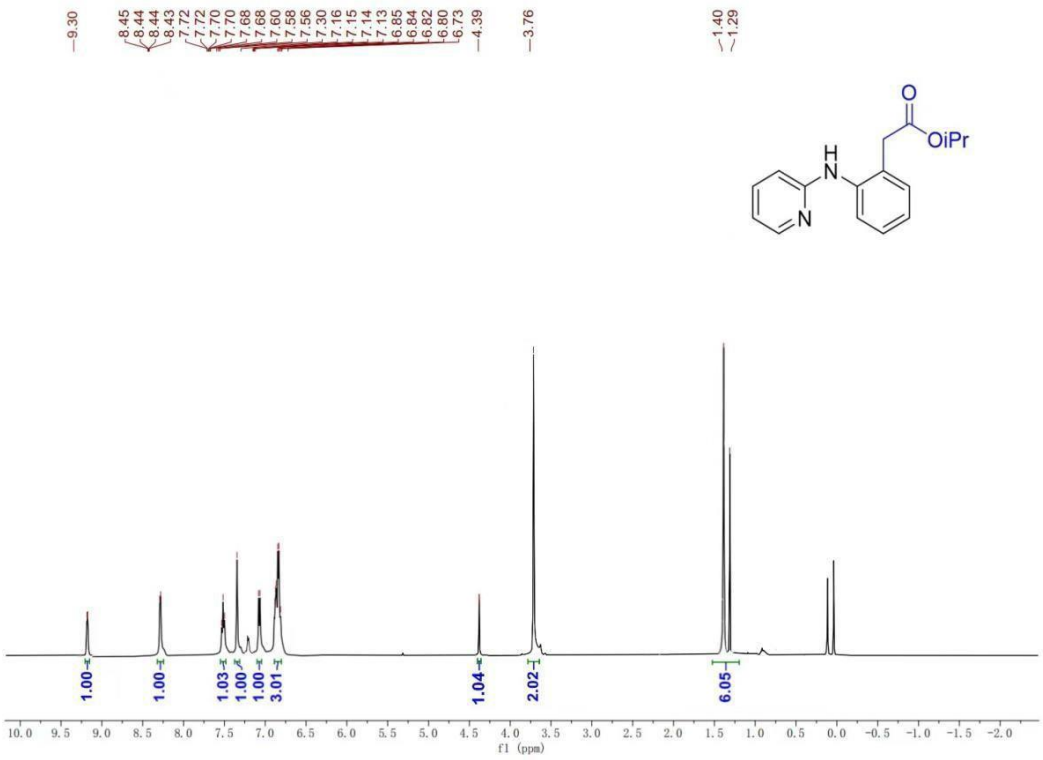
^{1}H NMR of 5b



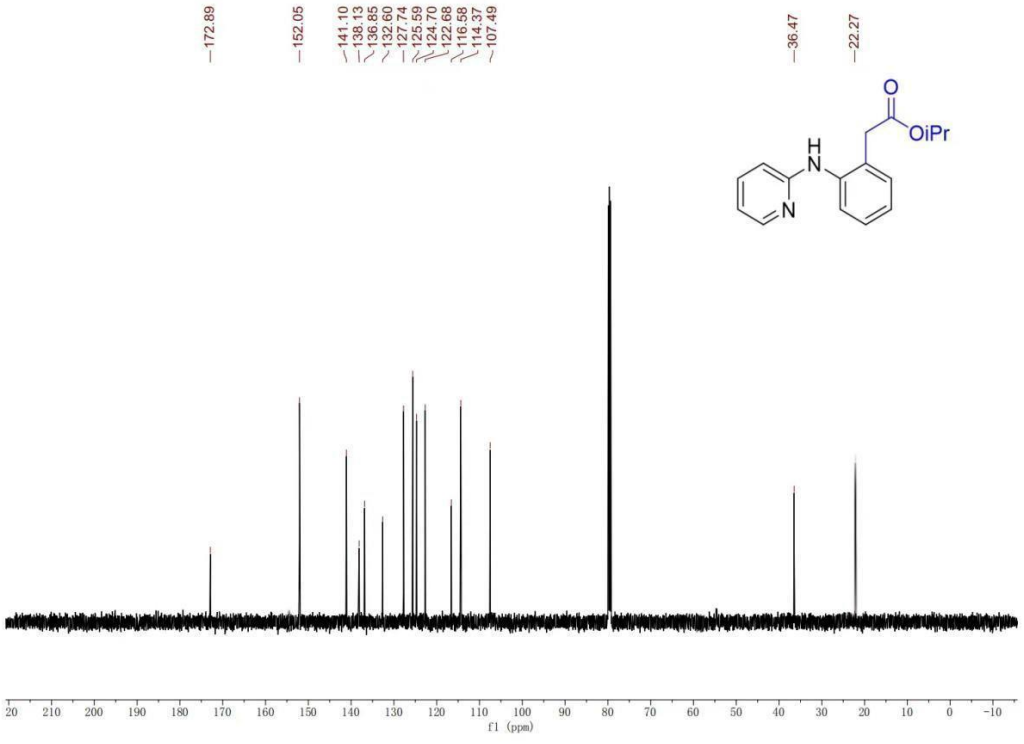
^{13}C NMR of 5b

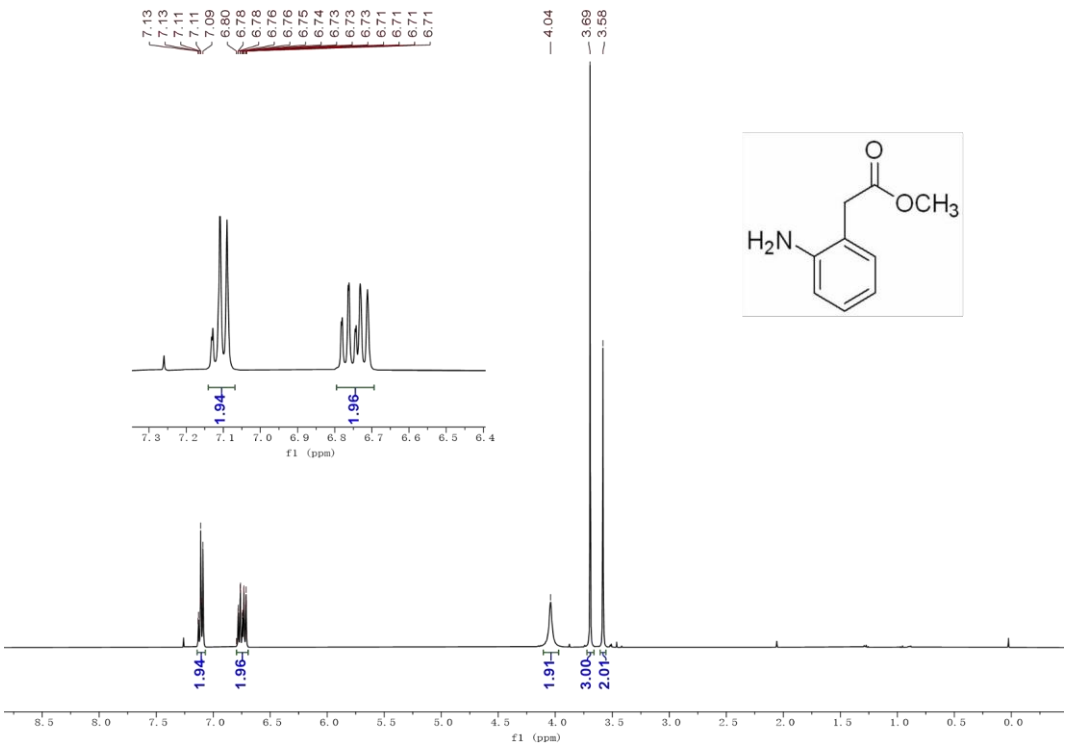


^{1}H NMR of 5c

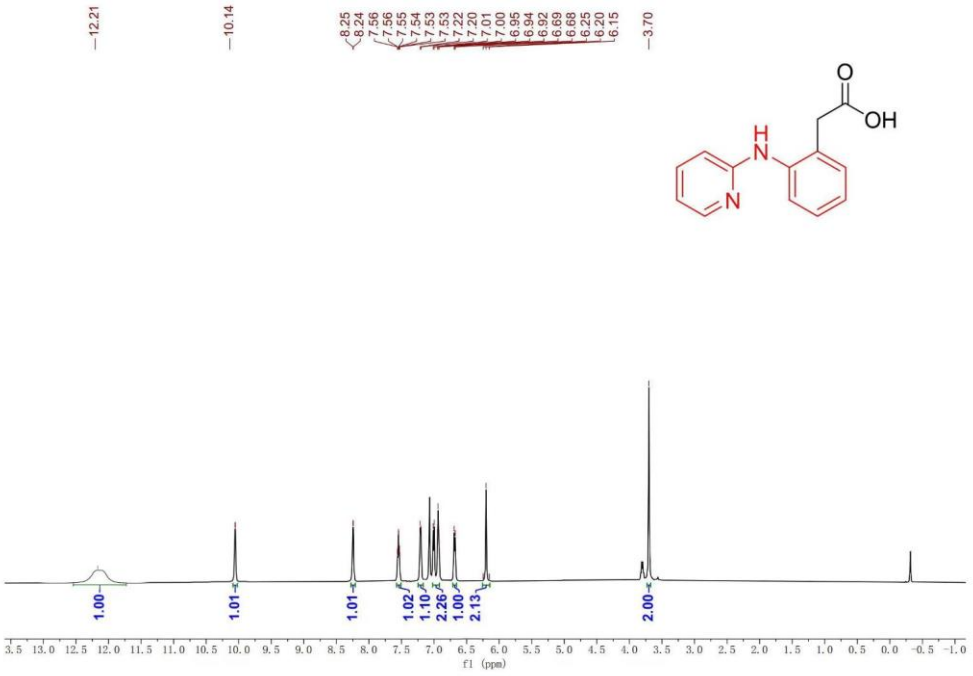


^{13}C NMR of 5c




7.13
7.13
7.11
7.11
7.09
6.80
6.78
6.78
6.76
6.76
6.75
6.74
6.73
6.73
6.73
6.71
6.71
6.71
6.71
4.04
3.69
3.58
O
OCH3
H2N
1.94
1.96
1.94
1.96
1.91
3.00
2.01
f1 (ppm)

^{1}H NMR of 7


12.21
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8.24
7.56
7.56
7.55
7.54
7.53
7.53
7.22
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7.00
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3.70
O
OH
H
N
N
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1.01
1.01
1.02
1.10
2.26
1.00
2.13
2.00
f1 (ppm)