Supporting Information

Cobalt-Catalyzed Enantioselective Reductive Addition of Ketimine with Cyclopropyl Chloride to Construct the Chiral Amino Esters Bearing Cyclopropyl Fragments

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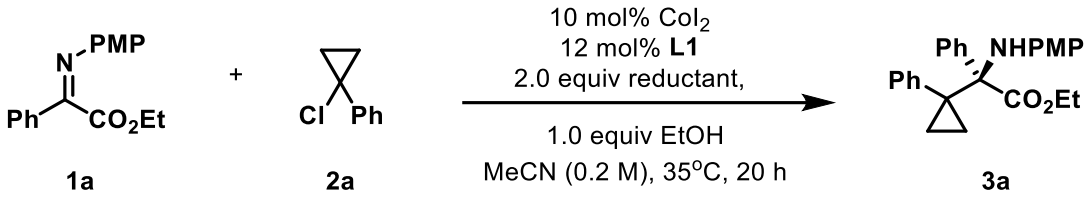
General Information

All reactions were carried out in dried glassware under nitrogen atmosphere and anhydrous conditions unless otherwise indicated. All manipulations of air-sensitive or moisture-sensitive compounds were performed in a glovebox under an atmosphere of nitrogen. Solvents such as toluene and THF were distilled from sodium/benzophenone, while DCM was distilled over CaH_2. CoI_2 was purchased from Adamas. Indium was purchased from Leyan; Zinc powder (Adamas, 200 mesh) was activated with hydrochloric acid before it was used; Manganese powder (325 mesh) was purchased from Alfa Aesar; MeCN was purchased from Meryer (99.9%, SuperDry, with molecular sieves, Water ≤ 50 ppm (by K.F.)

Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.20 mm Huanghai silica gel plates (HSGF 254) using UV light as the visualizing agent, $KMnO_4$ and PMA with heat as the developing agents. All new compounds were characterized by means of ^1H NMR, ^{13}C NMR and HRMS. NMR spectra were recorded using a Bruker AVANCE III 400 MHz NMR spectrometer and can be found at the end of the paper. High-resolution mass spectra (HRMS) were recorded on Q-Exactive plus mass spectrometer (Thermo Fisher, USA). HPLC was performed on SHIMADZU LC-2030 Plus. Optical rotations were recorded on digital automatic polarimeter (WZZ-2S). All ^1H NMR data are reported in δ units, parts per million (ppm), and were calibrated relative to the signals for residual chloroform (7.26 ppm) in deuterochloroform ($CDCl_3$). All ^{13}C NMR data are reported in ppm relative to $CDCl_3$ (77.16 ppm). The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, m = multiplet.

Conditions Screening

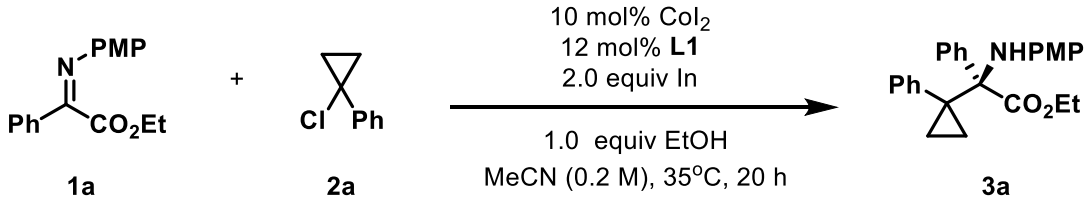
Table S1. Investigation of reductant



Entry	reductant	Conversion of 1a (%)	yield of 3a (%)	ee (%)
1	Mn	100	43	99
2	Zn	85	30	99
3	In	42	24	99
4[a]	Mn	100	16	99

Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol, 1.5 equiv), CoI_2 (0.01 mmol, 10 mol %), **L1** (0.012 mmol ,12 mol %), EtOH (0.1 mmol, 1.0 equiv), reductant (0.2 mmol, 2.0 equiv), MeCN (0.5 mL, 0.2 M) under 35 °C for 20 hours. The yields were determined by ^1H NMR using CH_2Br_2 as an internal standard, and ee values were determined by chiral HPLC analysis on a chiral stationary phase. [a]without EtOH.

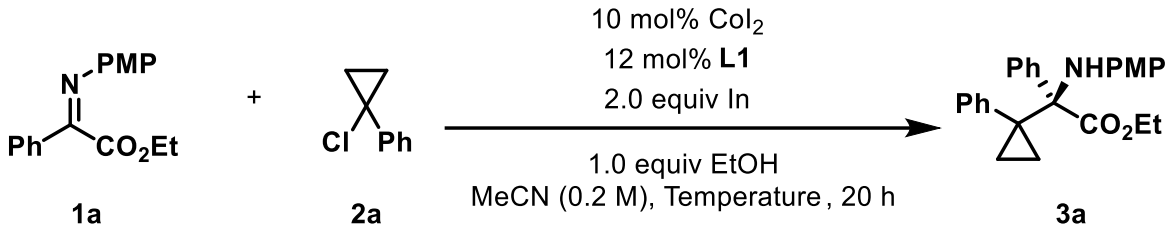
Table S2. Investigation of other parameters



Entry	Variation	yield of 3a (%)	ee (%)
1	none	24	99
2	48 h	29	99
3	50 °C	80	99
4	2.0 equiv **2a**	24	99
5	MeCN (0.4 M)	31	99

Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol, 1.5 equiv), CoI_2 (0.01 mmol, 10 mol %), **L1** (0.012 mmol, 12 mol %), EtOH (0.1 mmol, 1.0 equiv), In (0.2 mmol, 2.0 equiv), MeCN (0.5mL, 0.2 M) under 35 °C for 20 hours. The yields were determined by ^1H NMR using CH_2Br_2 as an internal standard, and ee values were determined by chiral HPLC analysis on a chiral stationary phase.

Table S3. Investigation of Temperature

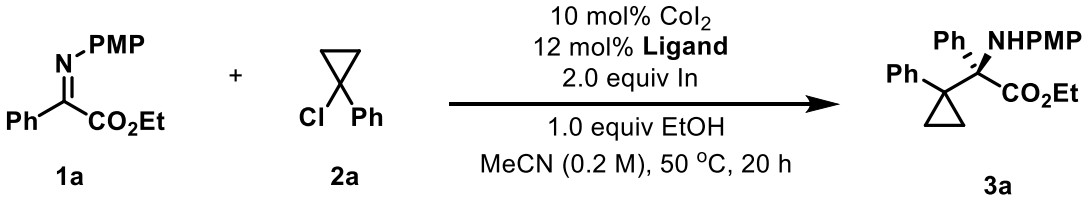


1a 2a 3a

Entry	Temperature	yield of 3a (%)	ee (%)
1	35 °C	24	99
2	50 °C	80	99
3	80 °C	84	97

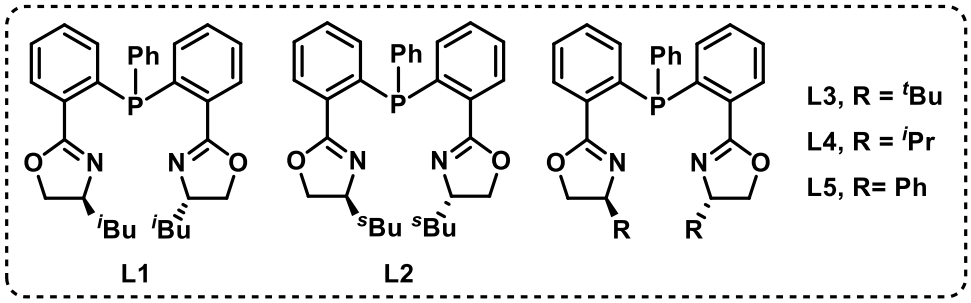
Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol, 1.5 equiv), CoI_2 (0.01 mmol, 10 mol %), **L1** (0.012 mmol, 12 mol %), EtOH (0.1 mmol, 1.0 equiv), In (0.2 mmol, 2.0 equiv), MeCN (0.5 mL, 0.2 M) for 20 hours. The yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard, and ee values were determined by chiral HPLC analysis on a chiral stationary phase.

Table S4. Investigation of ligand



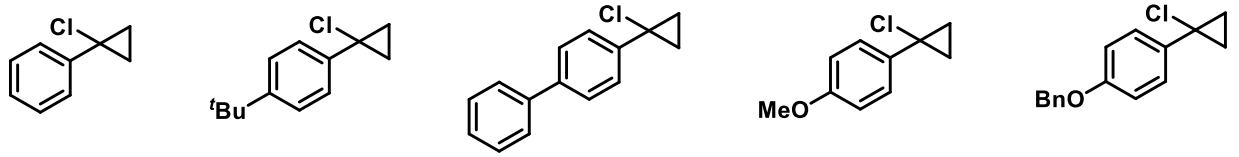
1a 2a 3a

Entry	Ligand	yield of 3a (%)	ee (%)
1	**L1**	80	99
2	**L2**	83	99
3	**L3**	57	97
4	**L4**	80	97
5	**L5**	69	99

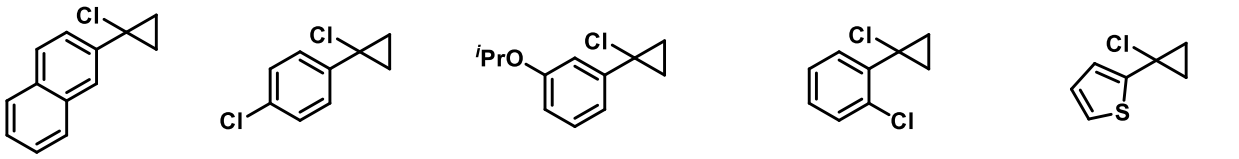


Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol, 1.5 equiv), CoI_2 (0.01 mmol, 10 mol %), **Ligand** (0.012 mmol, 12 mol %), EtOH (0.1 mmol, 1.0 equiv), In (0.2 mmol, 2.0 equiv), MeCN (0.5 mL, 0.2 M) under 50 ^oC for 20 hours. The yields were determined by ^1H NMR using CH_2Br_2 as an internal standard, and ee values were determined by chiral HPLC analysis on a chiral stationary phase.

Experimental Procedures and Characterization Data for Substrates



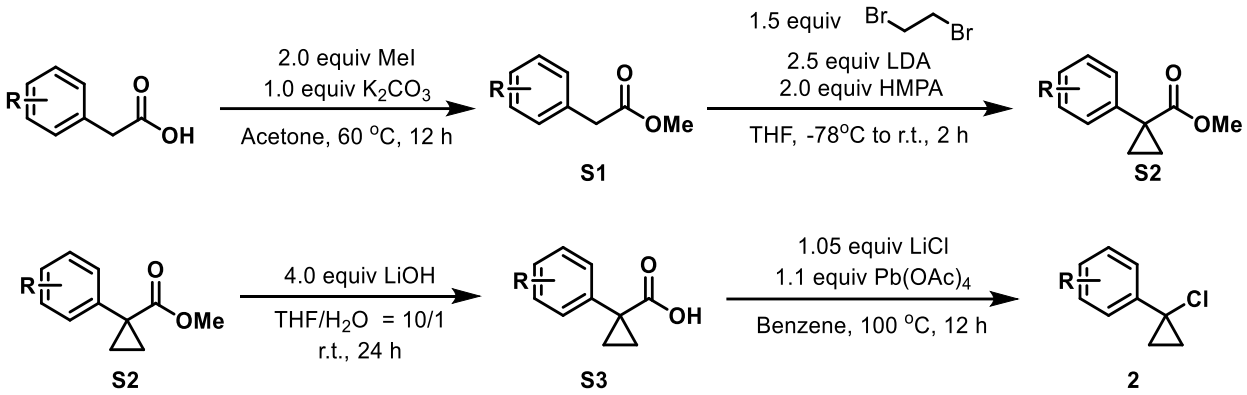
2a **2b** **2c** **2d** **2e**



2f **2g** **2h** **2i** **2j**

Compounds **2a**[1] and **2d**[2] were synthesized according to the literature.

General procedure A for cyclopropyl chloride compounds synthesis



A round bottomed flask was charged with phenyl acetic acid (1.0 equiv), potassium carbonate (1.0 equiv), MeI (2.0 equiv) and acetone (0.5 M) at room temperature. The resulting mixture was heated at 60 ℃ and stirred for 12 h. After a complete conversion, the mixture was concentrated under reduce pressure and the residue was diluted in water, extracted by DCM. The combined organic solution was then dried over Na_2SO_4, filtered, concentrated under reduced pressure and the crude product **S1** was used without further purification.

The above crude product **S1** (1.0 equiv) was dissolved in dry THF (0.2 M) and cooled to -78 ℃ under nitrogen atmosphere. A solution of LDA (1.0 M in THF, 1.5 equiv) was added slowly and allowed to stir at -78 ℃ for 30 min. The resulting mixture was warmed to 0 ℃ and HMPA (2.0 equiv) was added slowly. After stirring for 30 min at 0 ℃, 1,2-dibromoethane (1.5 equiv) was added dropwise to the solution, stirred for 30 min at 0 ℃ and then stirred for 30 min at room temperature. After a complete conversion (monitored by TLC), the reaction was quenched with

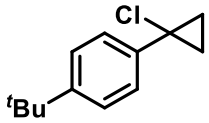
saturated aqueous NH_4Cl, extracted with EtOAc, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography to afford the product **S2**.

To a solution of **S2** (1.0 equiv) in THF/H_2O (v/v = 10/1, 0.5 M) was added LiOH (4.0 equiv). The reaction mixture was stirred at room temperature overnight. After completion, the reaction was diluted with water and acidified with 2M HCl to pH = 1. The aqueous was extracted with EtOAc, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting acid **S3** was used without further purification.

To a solution of **S3** (1.0 equiv) in benzene (0.33 M) was added LiCl (1.05 equiv) and $Pb(OAc)_4$ (1.1 equiv) under nitrogen atmosphere, and then the mixture was stirred at room temperature until it became nearly homogeneous. Next, the resulting reaction was stirred for 12 h at 100 ℃. After completion, the mixture was quenched with saturated aqueous $NaHCO_3$, filtered and the the filter cake was washed with EtOAc. The aqueous was extracted with EtOAc, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified via silica gel column chromatography to give cyclopropyl chloride **2**.

Characterization data for cyclopropyl chloride substrates:

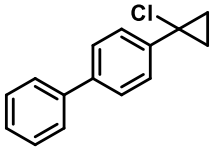
1-(Tert-butyl)-4-(1-chlorocyclopropyl)benzene (2b)



General procedure A was followed on 2.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2b** as a colorless oil (188 mg, 36%). $\mathbf{R_f}$ = 0.83 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.29 (m, 4H), 1.41–1.37 (m, 2H), 1.26 (s, 9H), 1.23–1.20 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 150.9, 139.2, 127.5, 125.5, 43.4, 34.7, 31.4, 17.5;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{18}Cl^+$: 209.1092; found: 209.1095.

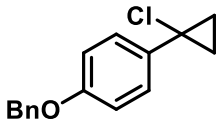
4-(1-Chlorocyclopropyl)-1,1'-biphenyl (2c) HJT-4-137



General procedure A was followed on 1.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2c** as a white solid (155 mg, 45%). $\mathbf{R_f}$ = 0.65 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.55 (m, 6H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 1.56–1.52 (m, 2H), 1.38–1.35 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 140.8, 140.7, 128.9, 128.1, 127.6, 127.3, 127.2, 43.3, 17.8;
HRMS (ESI): $[M+K]^+$ Calcd for $C_{15}H_{13}ClK^+$: 267.0337; found: 267.0329.

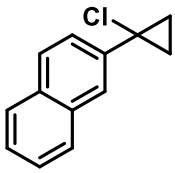
1-(Benzyloxy)-4-(1-chlorocyclopropyl)benzene (2e)



General procedure A was followed on 2.4 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2e** as a white solid (175 mg, 28%). $\mathbf{R_f}$ = 0.35 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.38 (m, 6H), 7.37–7.33 (m, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 5.07 (s, 2H), 1.46–1.43 (m, 2H), 1.26–1.23 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 137.0, 134.8, 129.5, 128.7, 128.1, 127.6, 114.8, 70.2, 43.5, 17.3;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{16}H_{16}ClO^+$: 259.0884; found: 259.0884.

2-(1-Bhlorocyclopropyl)naphthalene (2f)



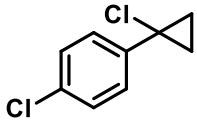
General procedure A was followed on 2.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2f** as a white solid (195 mg, 38%). $\mathbf{R_f}$ = 0.77 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 2.0 Hz, 1H), 7.85–7.82 (m, 3H), 7.61 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.53–7.47 (m, 2H), 1.58–1.55 (m, 2H), 1.43–1.40 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 133.2, 132.9, 128.5, 128.2, 127.7, 126.5, 126.4, 126.3, 126.0, 43.8, 17.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{13}H_{12}Cl^+$: 203.0622; found: 203.0624.

1-Chloro-4-(1-chlorocyclopropyl)benzene (2g)



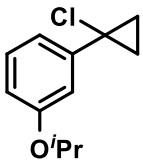
General procedure A was followed on 2.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2g** as a colourless oil (207 mg, 44%). $\mathbf{R_f}$ = 0.83 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 1.50–1.47 (m, 2H), 1.29–1.25 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 133.7, 129.2, 128.7, 42.7, 17.8;

HRMS (ESI): $[M+H]^+$ Calcd for $C_9H_9Cl_2^+$: 187.0076; found: 187.0082.

1-Chloro-2-(1-chlorocyclopropyl)benzene (2h)



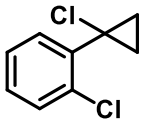
General procedure A was followed on 2.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2h** as a colourless oil (302 mg, 57%). $\mathbf{R_f}$ = 0.68 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (t, *J* = 8.0 Hz, 1H), 7.00–6.97 (m, 2H), 6.77 (ddd, *J* = 8.4, 2.8, 0.8 Hz, 1H), 4.55 (sept, *J* = 6.0 Hz, 1H), 1.45–1.42 (m, 2H), 1.33 (d, *J* = 6.0 Hz, 6H), 1.29–1.25 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 158.0, 143.7, 129.6, 119.6, 115.6, 114.9, 69.9, 43.4, 22.1, 17.8;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{12}H_{16}ClO^+$: 211.0884; found: 211.0882.

1-Chloro-2-(1-chlorocyclopropyl)benzene (2i)



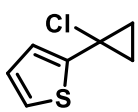
General procedure A was followed on 1.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2i** as a colourless oil (111 mg, 40%). $\mathbf{R_f}$ = 0.63 (PE);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.48 (m, 1H), 7.44–7.39 (m, 1H), 7.30–7.23 (m, 2H), 1.56–1.53 (m, 2H), 1.32–1.29 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 136.2, 131.2, 130.3, 129.8, 127.0, 42.0, 17.3;

HRMS (ESI): $[M+H]^+$ Calcd for $C_9H_9Cl_2^+$: 187.0076; found: 187.0079.

2-(1-Chlorocyclopropyl)thiophene (2j)



General procedure A was followed on 2.5 mmol scale and purification by flash column chromatography on silica gel (PE) to afforded **2j** as a colorless oil (265 mg, 67%). $\mathbf{R_f}$ = 0.79 (PE);

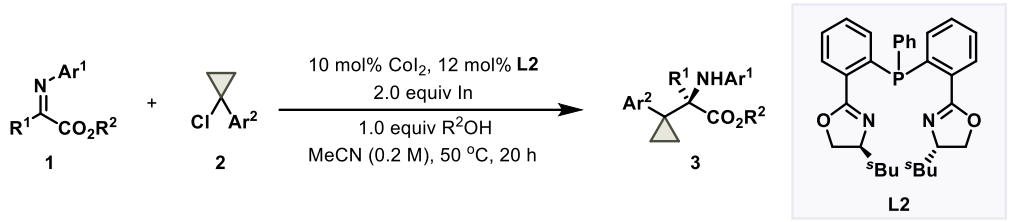
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (dd, *J* = 5.2, 1.6 Hz, 1H), 6.97 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.93 (dd, *J* = 5.2, 3.6 Hz, 1H), 1.78 (q, *J* = 4.4 Hz, 2H), 1.41 (q, *J* = 4.0 Hz, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): 142.4, 127.2, 126.5, 125.4, 23.5, 20.3;

HRMS (ESI): $[M+Na]^+$ Calcd for $C_7H_7ClSNa^+$: 180.9849; found: 180.9842.

Experimental Procedures of Synthetic Method and Characterization Data for Products

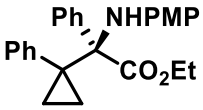
General procedure B for Cobalt-Catalyzed Enantioselective Reductive Addition of Ketimine with Cyclopropyl Chloride to Construct the Chiral Amino Acids Bearing Cyclopropyl Fragments



To an oven-dried 8 mL vial equipped with a magnetic stir bar were added ligand **L2** (12 mol%), In (2.0 equiv) and imine **1** (1.0 equiv). Then the vial was transferred into the glovebox, CoI_2 (10 mol%), MeCN (0.2 M), cyclopropyl chloride compounds **2** (1.5 equiv) and R^2OH (1.0 equiv) were added in sequence (To avoid transesterification between imine **1** and alcohol, the type of alcohol should be the same as that of protecting group of α-imino ester). The reaction vial was capped and stirred at 50 °C for 20 hours. After completion, the reaction mixture was filtered through a pad of silica gel and the filter cake was washed with EtOAc. The resulted filtrate was then concentrated under reduced pressure to give the crude product, which was purified by silica gel flash column chromatography to afford products **3**.

Characterization data for products:

Ethyl (*R*)-2-((4-methoxyphenyl)amino)-2-phenyl-2-(1-phenylcyclopropyl)acetate (3a)



General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3a** as a white solid (62.2 mg, 78%); $\mathbf{R}_f$ = 0.69 (PE/EtOAc = 10/1);

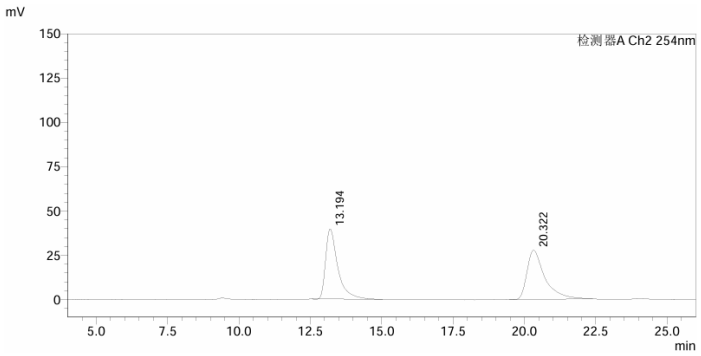
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.76 (m, 2H), 7.24–7.26 (m, 3H), 7.19–7.13 (m, 5H), 6.55 (d, *J* = 8.8 Hz, 2H), 6.21 (d, *J* = 9.2 Hz, 2H), 4.58 (bs, 1H), 4.03 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.90 (dq, *J* = 10.4, 7.2 Hz, 1H), 3.64 (s, 3H), 1.27–1.24 (m, 1H), 1.03–1.00 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.86–0.79 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.7, 152.2, 142.2, 140.5, 137.5, 131.8, 129.8, 127.8, 127.42, 127.39, 127.3, 116.6, 114.0, 70.2, 61.0, 55.7, 35.7, 13.8, 10.9, 10.5.

HRMS (ESI): $[M+H]^+$ Calcd for $C_{26}H_{28}NO_3^+$: 402.2064; found: 402.2064;

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 13.520 min (minor), t_{R2} = 20.607 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 105.45 (c = 0.27, CH_2Cl_2).

<Chromatogram>



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
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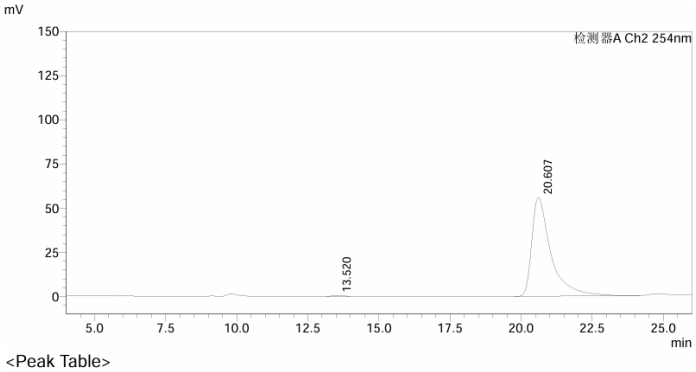
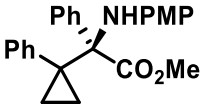


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.520	10627	432	0.404		M
2	20.607	2619292	55776	99.596		M
总计		2629919	56208			

Methyl (*R*)-2-((4-methoxyphenyl)amino)-2-phenyl-2-(1-phenylcyclopropyl)acetate (3b)



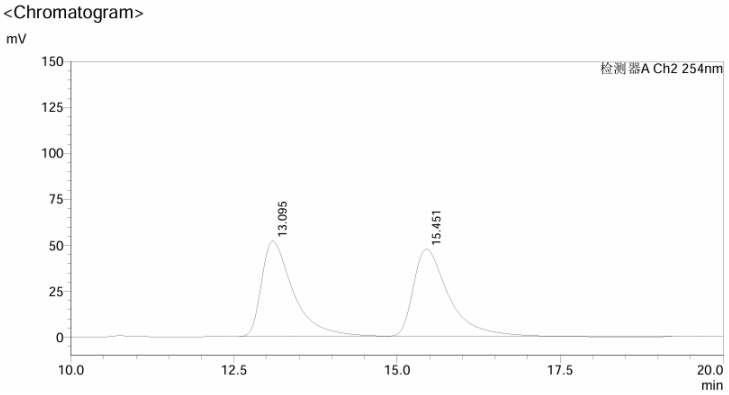
General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3a** as a white solid (62.7 mg, 81%); $\mathbf{R_f}$ = 0.60 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80–7.77 (m, 2H), 7.27–7.25 (m, 3H), 7.22–7.16 (m, 5H), 6.56 (d, *J* = 9.2 Hz, 2H), 6.21 (d, *J* = 8.8 Hz, 2H), 4.61 (bs, 1H), 3.66 (s, 3H), 3.52 (s, 3H), 1.23 (dt, *J* = 9.6, 3.2 Hz, 1H), 1.00 (dt, *J* =10.0, 2.8 Hz, 1H), 0.87–0.80 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 152.1, 142.1, 140.1, 137.1, 131.7, 129.7, 127.9, 127.48, 127.46, 127.4, 116.5, 114.0, 70.2, 55.6, 51.9, 35.7, 10.8, 10.5;

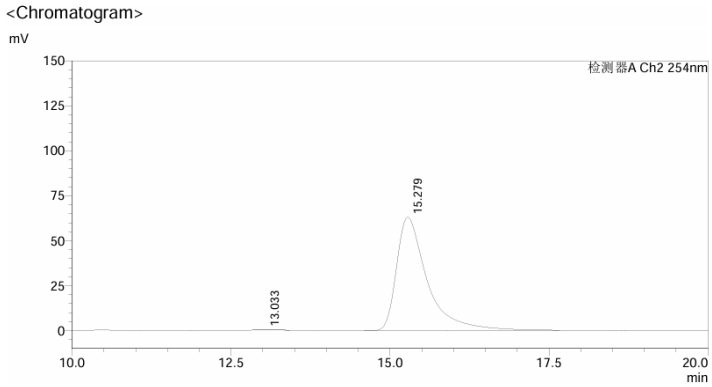
HRMS (ESI): $[M+H]^+$ Calcd for $C_{25}H_{26}NO_3^+$: 388.1907; found: 388.1907;

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 13.033 min (minor), t_{R2} = 15.279 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 109.09 (c = 0.15, CH_2Cl_2).



<Peak Table>
检测器A Ch2 254nm

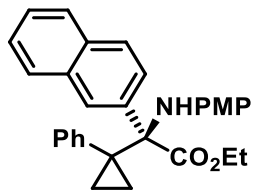
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.095	1770609	51918	49.835		M
2	15.451	1782339	47451	50.165		V M
总计		3552948	99369			



<Peak Table>
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.033	6017	334	0.284		M
2	15.279	2111195	62893	99.716		M
总计		2117212	63227			

Ethyl (*R*)-2-((4-methoxyphenyl)amino)-2-(naphthalen-2-yl)-2-(1-phenylcyclopropyl)acetate (3c)



General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~15/1) to afford **3c** as a white solid (70.5 mg, 78%); $\mathbf{R}_f$ = 0.69 (PE/EtOAc = 10/1);

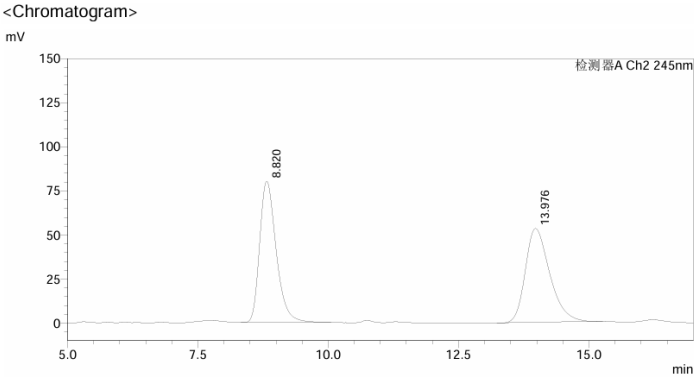
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.92 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.83–7.79 (m, 2H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.50–7.43 (m, 2H), 7.21–7.17 (m, 5H), 6.52 (d, *J* = 8.8 Hz, 2H), 6.24 (d, *J* = 8.8 Hz, 2H), 4.67 (bs, 1H), 4.07 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.93 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.63 (s, 3H), 1.31–1.28 (m, 1H), 1.05–1.02 (m, 1H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.88–0.82 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 152.2, 142.1, 140.5, 135.1, 132.9, 132.7, 131.8, 129.1, 128.9, 127.90, 127.85, 127.4, 127.3, 126.7, 126.2, 125.7, 116.7, 114.0, 70.2, 61.0, 55.6, 35.6, 13.8, 11.0, 10.4;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{30}H_{30}NO_3^+$: 452.2220; found: 452.2220;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 245 nm, t_{R1} = 8.518 min (minor), t_{R2} = 13.514 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 105.45 (c = 0.15, CH_2Cl_2).

<Chromatogram>

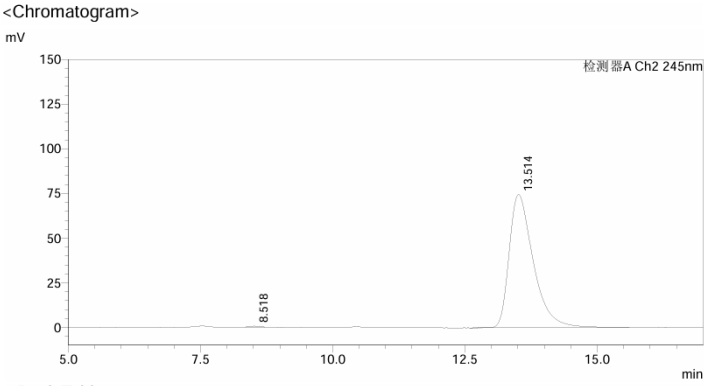


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.820	1765129	80031	50.447		M
2	13.976	1733864	53191	49.553		M
总计		3498993	133222			

<Chromatogram>

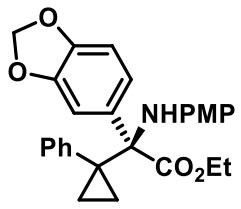


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.518	6441	510	0.271		M
2	13.514	2366716	74519	99.729		M
总计		2373157	75030			

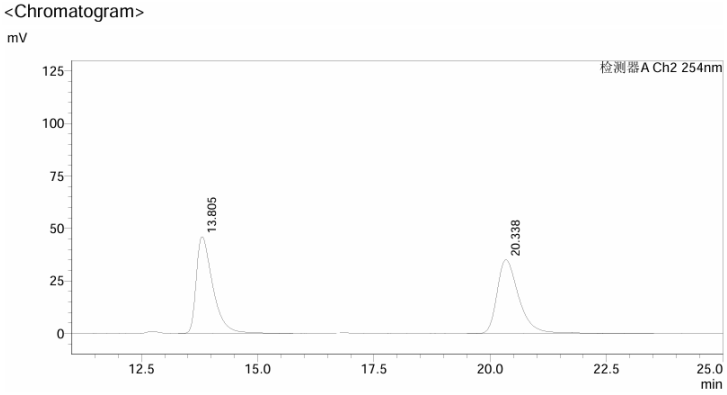
Ethyl (*R*)-2-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxyphenyl)amino)-2-(1-phenylcyclopropyl)acetate (3d)



General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3d** as a white solid (76.4 mg, 86%); $\mathbf{R_f}$ = 0.68 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 2.0 Hz, 1H), 7.27 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.22–7.17 (m, 5H), 6.67 (d, *J* = 8 Hz, 1H), 6.56 (d, *J* = 9.2 Hz, 2H), 6.23 (d, *J* = 8.8 Hz, 2H), 5.93 (abq, *J* = 4.8, 1.2 Hz, 2H), 4.56 (bs, 1H), 4.01 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.87 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.65 (s, 3H), 1.25–1.22 (m, 1H), 1.02–0.98 (m, 1H), 0.88 (t, *J* = 7.2 Hz, 3H), 0.83–0.81 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 152.2, 147.1, 146.7, 142.2, 140.5, 131.8, 131.2, 127.9, 127.3, 123.4, 116.6, 114.0, 110.6, 107.1, 101.0, 69.9, 61.0, 55.7, 36.8, 13.7, 10.8, 10.4;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{28}NO_5^+$: 446.1962; found: 446.1960;
HPLC (Chiralpak IBN): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 254 nm, t_{R1} = 13.369 min (major), t_{R2} = 19.766 min (minor); 99% ee; $[\alpha]_D^{33.5}$ = 63.75 (c = 0.11, CH_2Cl_2).

<Chromatogram>

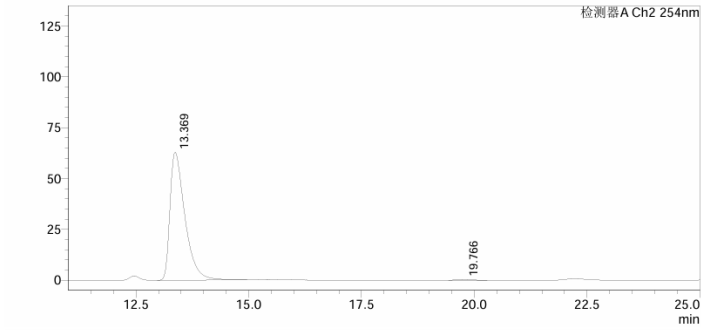


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.805	1132855	46075	49.968		M
2	20.338	1134295	35098	50.032		M
总计		2267150	81173			

<Chromatogram>

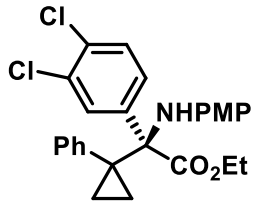


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.369	1452311	62865	99.557		M
2	19.766	6469	261	0.443		M
总计		1458780	63126			

Ethyl (*R*)-2-(3,4-dichlorophenyl)-2-((4-methoxyphenyl)amino)-2-(1-phenylcyclopropyl)acetate (3e)



General procedure B was followed using **2a** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3e** as a colorless oil (29.3 mg, 62%); $\mathbf{R_f}$ = 0.49 (PE/EtOAc = 10/1);

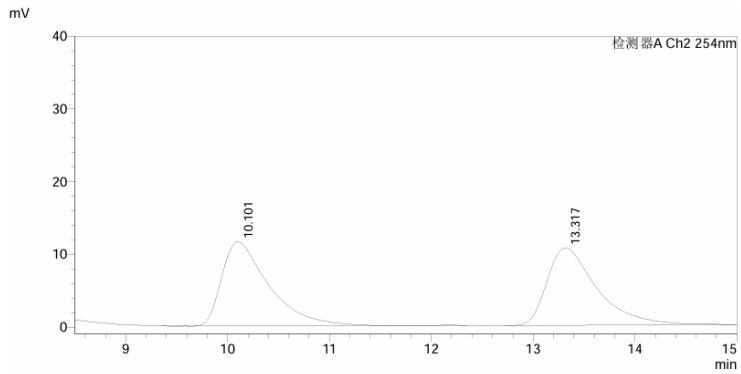
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 2.4 Hz, 1H), 7.51 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.21–7.15 (m, 3H), 7.08–7.05 (m, 2H), 6.57 (d, *J* = 9.2 Hz, 2H), 6.20 (d, *J* = 9.2 Hz, 2H), 4.53 (bs, 1H), 4.02 (dq, *J* = 10.4, 7.2 Hz, 1H), 3.91 (dq, *J* = 10.8, 7.2 Hz, 1H), 3.66 (s, 3H), 1.30–1.26 (m, 1H), 1.07–1.02 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.93–0.83 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 152.6, 141.4, 139.7, 138.5, 131.9, 131.8, 131.5, 131.4, 129.3, 129.2, 127.9, 127.6, 116.5, 114.2, 69.6, 61.4, 55.7, 35.9, 13.8, 11.2, 10.4;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{26}H_{26}Cl_2NO_3^+$: 470.1284; found: 470.1284;

HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 10.735 min (minor), t_{R2} = 13.475 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 276.67 (c = 0.06, CH_2Cl_2).

<Chromatogram>

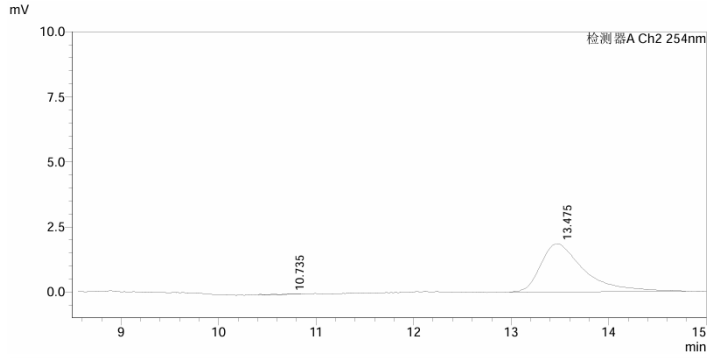


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.101	370519	11563	50.508		M
2	13.317	363071	10642	49.492		M
总计		733589	22205			

<Chromatogram>

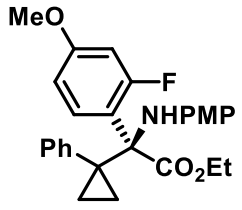


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.735	8	16	0.013		M
2	13.475	57635	1861	99.987		M
总计		57643	1877			

Ethyl (*S*)-2-(2-fluoro-4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-2-(1-phenylcyclopropyl)acetate (3f)

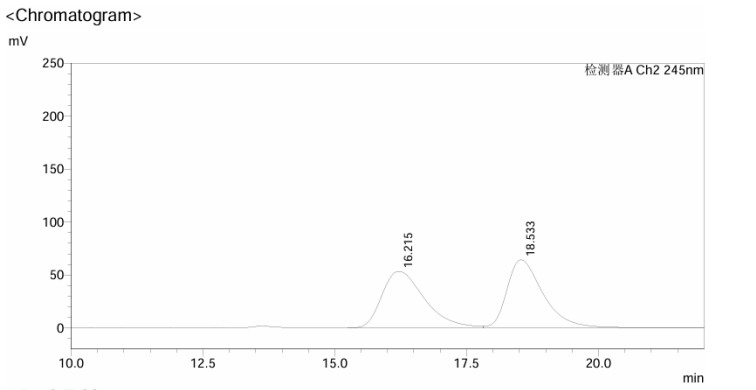


General procedure B was followed using **2a** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3f** as a colorless oil (30.5 mg, 68%); $\mathbf{R}_f$ = 0.50 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23–7.20 (m, 2H), 7.11 (t, *J* = 8.8 Hz, 1H), 7.06–7.04 (m, 3H), 6.61 (d, *J* = 8.8 Hz, 2H), 6.55 (dd, *J* = 13.2, 2.4 Hz, 1H), 6.44 (d, *J* = 9.2 Hz, 2H), 6.33 (dd, *J* = 8.8, 2.4 Hz, 1H), 4.66 (bs, 1H), 3.96 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 3.68 (s, 3H), 1.78–1.73 (m, 1H), 1.32–1.26 (m, 1H), 1.18–1.13 (m, 1H), 0.97 (t, *J* = 6.8 Hz, 3H), 0.88–0.83 (m, 1H);

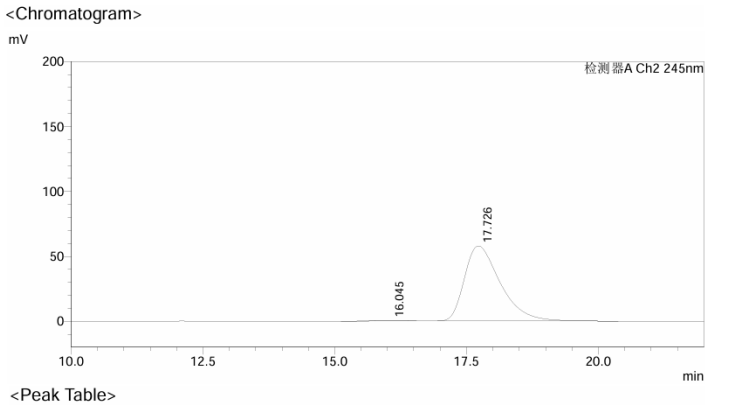
^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 161.5 (d, $J_{C\text{-}F}$ = 246.5 Hz), 160.4 (d, $J_{C\text{-}F}$ = 11.5 Hz), 152.9, 143.2, 140.2, 131.28 (d, $J_{C\text{-}F}$ = 7.8 Hz), 131.25, 127.4, 126.7, 118.6 (d, $J_{C\text{-}F}$ = 12.7 Hz), 117.3, 114.1, 108.2 (d, $J_{C\text{-}F}$ = 2.5 Hz), 102.0 (d, $J_{C\text{-}F}$ = 27.6 Hz), 71.1 (d, $J_{C\text{-}F}$ = 4.2 Hz), 61.3, 55.7, 55.6, 34.5, 13.9, 13.5 (d, $J_{C\text{-}F}$ = 6.5 Hz), 10.3;

^{19}F NMR (376 MHz, $CDCl_3$) δ -100.6;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{29}FNO_4^+$: 450.2075; found: 450.2074;
HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 245 nm, t_{R1} = 16.045 min (minor), t_{R2} = 17.726 min (major); 98% ee; $[\alpha]_D^{33.5}$ = 25.11 (c = 0.31, CH_2Cl_2).



<Peak Table>
检测器A Ch2 245nm

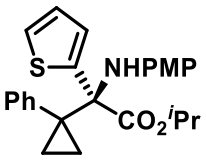
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	16.215	2996379	53384	49.336		
2	18.533	3077058	64224	50.664		SV
总计		6073436	117608			



<Peak Table>
检测器A Ch2 245nm

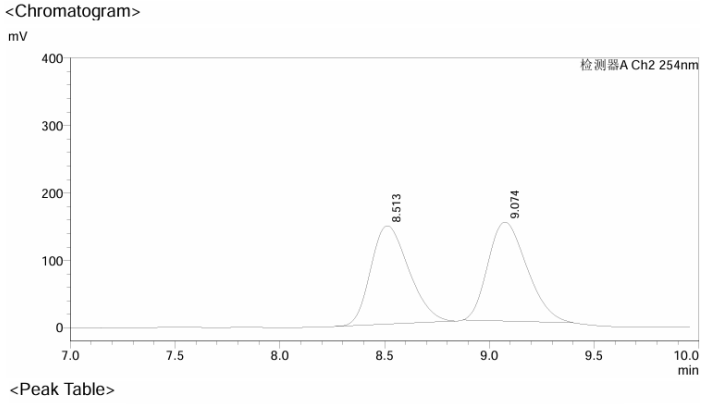
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	16.045	22980	516	0.830		M
2	17.726	2745322	57815	99.170		M
总计		2768302	58331			

Isopropyl (*R*)-2-((4-methoxyphenyl)amino)-2-(1-phenylcyclopropyl)-2-(thiophen-2-yl)acetate (3g)



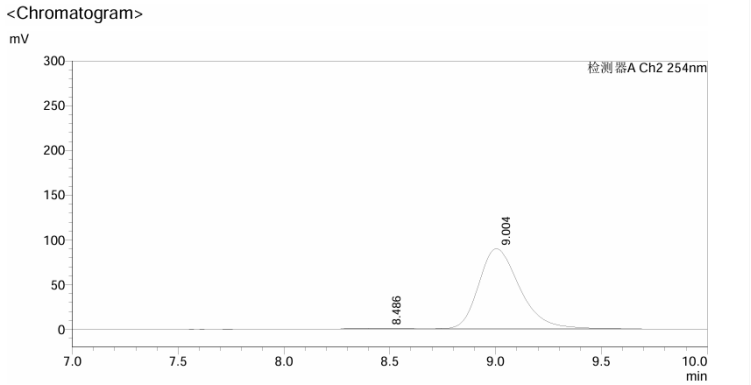
General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3g** as a white solid (46.0 mg, 55%); $\mathbf{R_f}$ = 0.54 (PE/EtOAc = 10/1);
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.19 (m, 6H), 7.14 (dd, *J* = 4.0, 1.6 Hz, 1H), 6.88 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.56 (d, *J* = 8.8 Hz, 2H), 6.26 (d, *J* = 9.2 Hz, 2H), 4.86 (sept, *J* = 6.4 Hz, 1H), 4.64 (bs, 1H), 3.65 (s, 3H), 1.31–1.26 (m, 1H), 1.13–1.08 (m, 1H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H), 0.90–0.76 (m, 5H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 152.5, 142.0, 141.8, 140.2, 131.9, 128.4, 128.0, 127.6, 126.3, 126.0, 116.6, 114.0, 69.6, 69.1, 55.7, 35.8, 21.6, 21.2, 11.1, 11.0;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{25}H_{28}NO_3S^+$: 422.1784; found: 422.1781;

HPLC (Chiralpak IBN): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 254 nm, t_{R1} = 8.486 min (minor), t_{R2} = 9.004 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 47.78 (c = 0.12, CH_2Cl_2).



<Peak Table>
检测器A Ch2 254nm

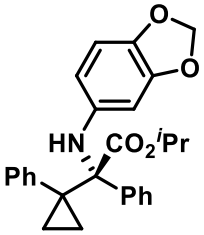
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.513	1834792	145668	49.209		M
2	9.074	1893757	146749	50.791		M
总计		3728549	292416			



<Peak Table>
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.486	5270	483	0.438		M
2	9.004	1198976	89480	99.562		M
总计		1204245	89963			

Isopropyl (*R*)-2-(benzo[d][1,3]dioxol-5-ylamino)-2-phenyl-2-(1-phenylcyclopropyl)acetate (3h)



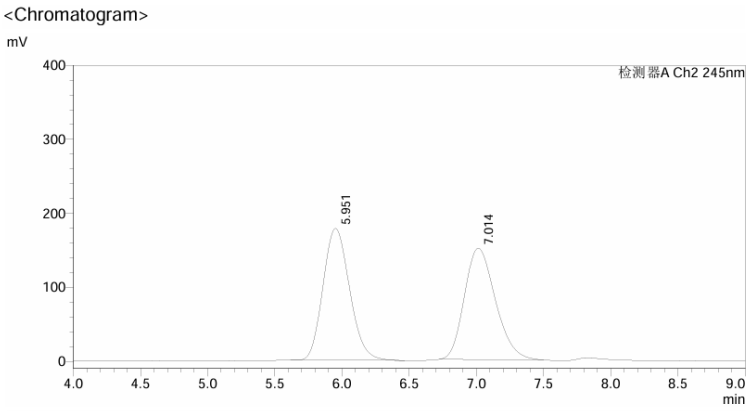
General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3h** as a white solid (77.9 mg, 91%); $\mathbf{R_f}$ = 0.53 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.71 (m, 2H), 7.22–7.16 (m, 3H), 7.13–7.07 (m, 5H), 6.39 (d, *J* = 8.4 Hz, 1H), 5.91 (d, *J* = 2.4 Hz, 1H), 5.71 (s, 2H), 5.66 (dd, *J* = 8.4, 2.8 Hz, 1H), 4.85 (sept, *J* = 6.4 Hz, 1H), 4.59 (bs, 1H), 1.29–1.25 (m, 1H), 1.03–1.00 (m, 4H), 0.82–0.78 (m, 5H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 147.5, 142.3, 142.2, 139.7, 137.6, 131.9, 129.7, 127.7, 127.37, 127.35, 127.2, 107.9, 107.5, 100.5, 98.4, 70.3, 69.1, 35.9, 21.7, 21.3, 11.0, 10.5;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{28}NO_4^+$: 430.2013; found: 430.2012;

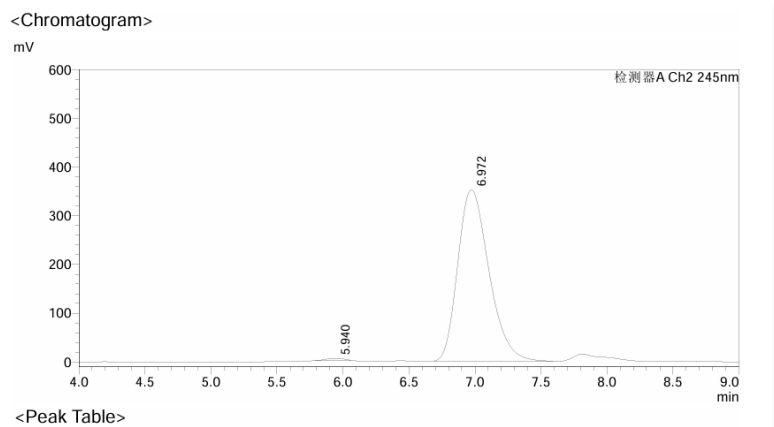
HPLC (Chiralpak IA): *n*-Hexane/EtOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 245 nm, t_{R1} = 5.940 min (minor), t_{R2} = 6.972 min (major); 98% ee; $[\alpha]_D^{33.5}$ = 84.58 (c = 0.16, CH_2Cl_2).



<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.951	2458032	178230	50.409		M
2	7.014	2418143	150491	49.591		M
总计		4876175	328722			

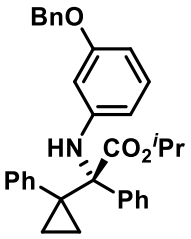


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.940	38916	4163	0.670		M
2	6.972	5768133	351608	99.330		M
总计		5807049	355772			

Esopropyl (*R*)-2-((3-(benzyloxy)phenyl)amino)-2-phenyl-2-(1-phenylcyclopropyl)acetate (3i)



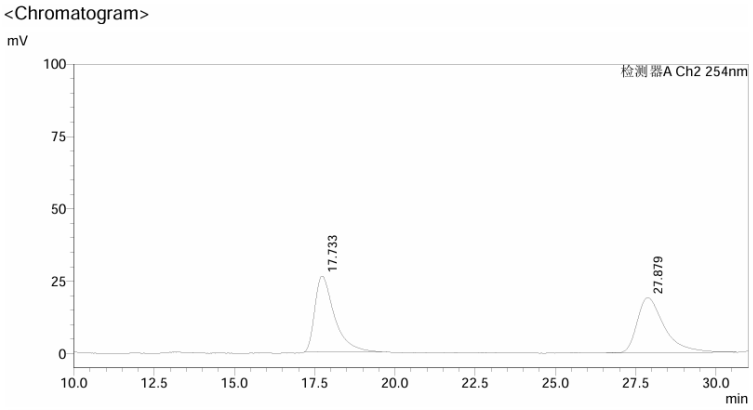
General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3i** as a colorless oil (84.3 mg, 86%); $\mathbf{R_f}$ = 0.63 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.68 (m, 2H), 7.25–7.20 (m, 5H), 7.18–7.13 (m, 3H), 7.08–7.02 (m, 5H), 6.74 (t, *J* = 8.0 Hz, 1H), 6.16 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.85 (t, *J* = 2.4 Hz, 1H), 5.79 (dd, *J* = 8.0, 2.0 Hz, 1H), 4.75–4.68 (m, 4H),1.22–1.19 (m, 1H), 0.96–0.93 (m, 1H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.77–0.70 (m, 2H), 0.64 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 159.2, 148.2, 142.1, 137.5, 137.4, 131.9, 129.7, 129.1, 128.5, 127.8, 127.8, 127.5, 127.40, 127.36, 127.2, 108.9, 104.5, 102.6, 70.0, 69.7, 69.1, 35.7, 21.6, 21.1, 10.9, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{33}H_{34}NO_3^+$: 492.2533; found: 492.2533;

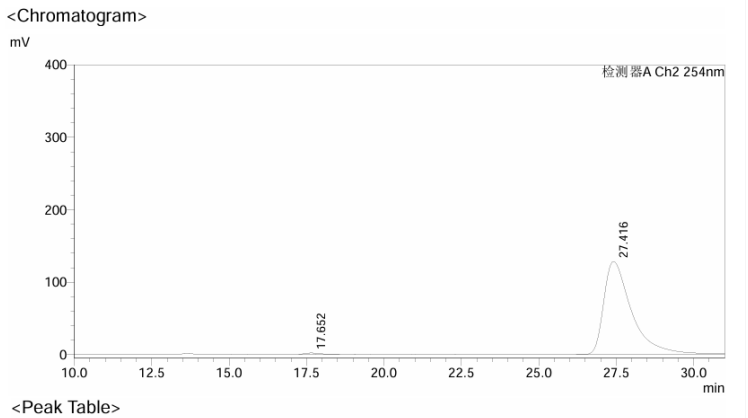
HPLC (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 17.652 min (major), t_{R2} = 27.416 min (minor); 98% ee; $[\alpha]_D^{33.5}$ = 313.04 (c = 0.15, CH_2Cl_2).



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	17.733	1117297	26253	49.910		M
2	27.879	1121343	19057	50.090		M
总计		2238641	45310			

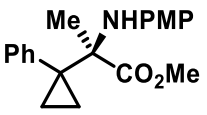


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	17.652	74152	2030	0.883		M
2	27.416	8320095	128604	99.117		M
总计		8394247	130634			

Methyl (*R*)-2-((4-methoxyphenyl)amino)-2-(1-phenylcyclopropyl)propanoate (3j)



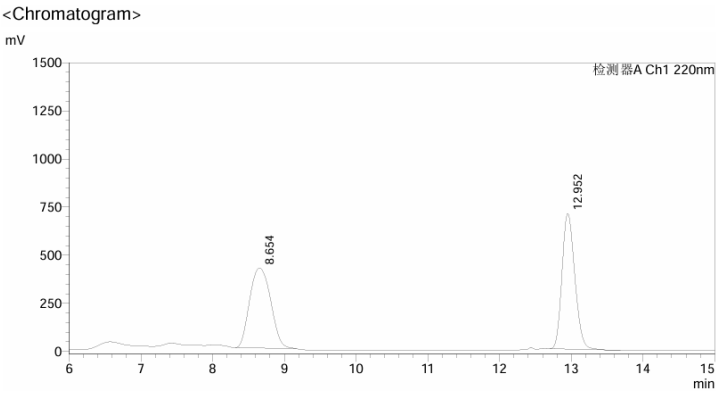
General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3j** as a white solid (31.2 mg, 46%); $\mathbf{R_f}$ = 0.67 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.34 (m, 2H), 7.29–7.21 (m, 3H), 6.74–6.69 (m, 4H), 3.94 (bs, 1H), 3.74 (s, 3H), 3.61 (s, 3H), 1.32 (s, 3H), 1.29–1.26 (m, 1H), 1.21–1.18 (m, 1H), 0.88–0.80 (m, 2H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.8, 154.7, 142.8, 138.6, 131.9, 127.9, 127.2, 122.8, 114.2, 64.8, 55.6, 52.0, 33.9, 20.0, 10.2, 9.9;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{20}H_{24}NO_3^+$: 326.1751; found: 326.1751;

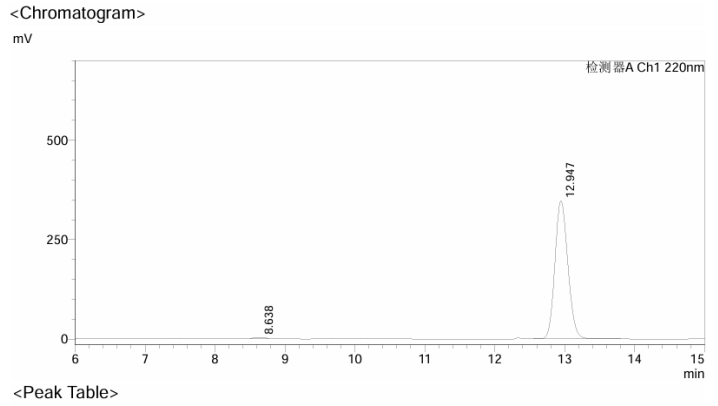
HPLC (Chiralpak IBN): *n*-Hexane/EtOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 220 nm, t_{R1} = 8.638 min (minor), t_{R2} = 12.947 min (major); 99% ee; $[\alpha]_D^{33.5}$ = -37.62 it! (c = 0.14, CH_2Cl_2).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.654	8487438	415308	49.286		M
2	12.952	8733450	704381	50.714		M
总计		17220888	1119689			

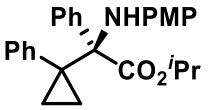


<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.638	10300	973	0.231		M
2	12.947	4439874	346358	99.769		M
总计		4450174	347331			

Isopropyl (*R*)-2-((4-methoxyphenyl)amino)-2-phenyl-2-(1-phenylcyclopropyl)acetate (3k)



General procedure B was followed using **2a** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3k** as a white solid (74.8 mg, 90%); $\mathbf{R_f}$ = 0.70 (PE/EtOAc = 10/1);

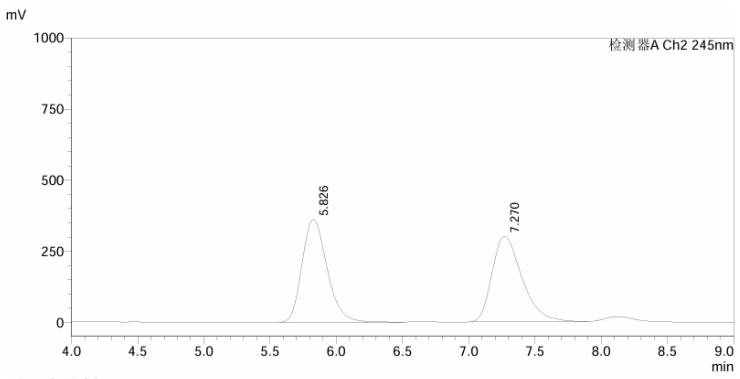
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78–7.76 (m, 2H), 7.24–7.20 (m, 3H), 7.18–7.11 (m, 5H), 6.56 (d, *J* = 9.2 Hz, 2H), 6.25 (d, *J* = 8.8 Hz, 2H), 486 (sept, *J* = 6.4 Hz, 1H), 4.59 (bs, 1H), 3.65 (s, 3H), 1.35–1.32 (m, 1H), 1.11–1.06 (m, 1H), 1.04 (d, *J* = 6.0 Hz, 3H), 0.87–0.82 (m, 2H), 0.77 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 152.2, 142.3, 140.8, 137.9, 131.9, 129.7, 127.7, 127.32, 127.25, 127.1, 116.6, 114.0, 70.2, 69.0, 55.7, 35.9, 21.6, 21.2, 11.1, 10.4;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{30}NO_3^+$: 416.2220; found: 416.2220;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 245 nm, t_{R1} = 5.622 min (minor), t_{R2} = 7.057 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 62.25 (c = 0.27, CH_2Cl_2).

<Chromatogram>

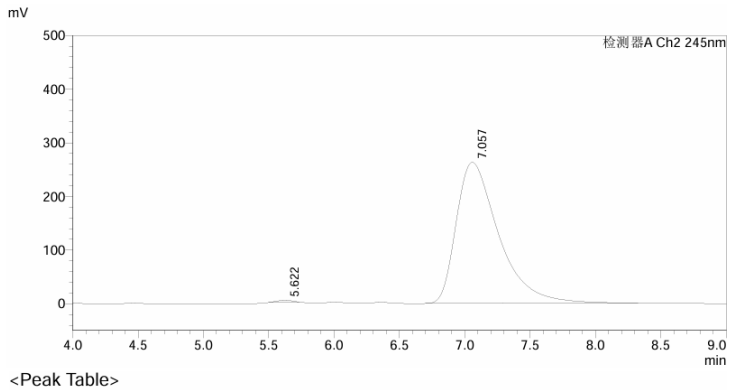


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.826	4726003	360502	50.133		M
2	7.270	4700895	300028	49.867		M
总计		9426899	660531			

<Chromatogram>

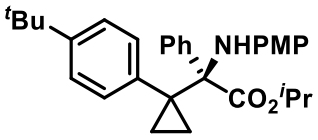


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.622	29588	3486	0.496		M
2	7.057	5931068	262761	99.504		M
总计		5960656	266247			

Isopropyl (*R*)-2-(1-(4-(tert-butyl)phenyl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate (3l)



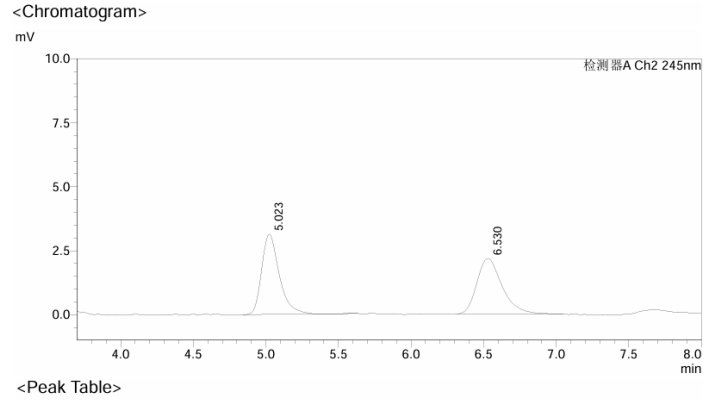
General procedure B was followed using **2b** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3l** as a white solid (40.2 mg, 85%); $\mathbf{R_f}$ = 0.67 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81–7.78 (m, 2H), 7.23–7.21 (m, 3H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.54 (d, *J* = 9.2 Hz, 2H), 6.20 (d, *J* = 8.8 Hz, 2H), 4.80 (sept, *J* = 6.4 Hz, 1H), 4.61 (bs, 1H), 3.64 (s, 3H), 1.27 (s, 9H), 1.21–1.18 (m, 1H), 0.97–0.94 (m, 1H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.80–0.77 (m, 2H), 0.75 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 152.1, 150.1, 140.9, 139.2, 137.6, 131.4, 129.8, 127.34, 127.27, 124.7, 116.6, 113.9, 70.2, 68.8, 55.8, 35.2, 34.5, 31.4, 21.6, 21.2, 10.6, 10.5;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{31}H_{38}NO_3^+$: 472.2846; found: 472.2846;

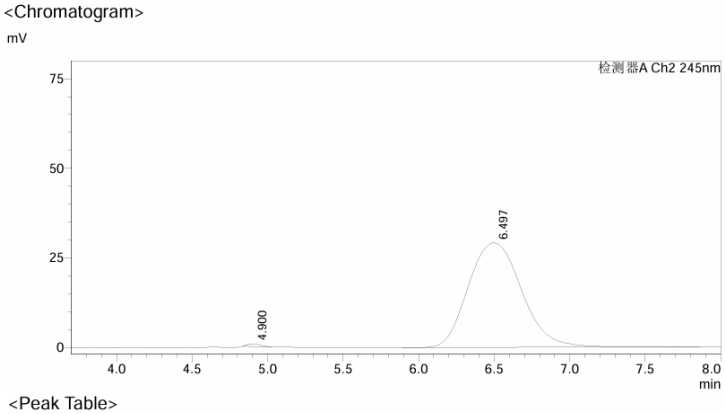
HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 245 nm, t_{R1} = 4.900 min (minor), t_{R2} = 6.497 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 118.00 (c = 0.1, CH_2Cl_2).



<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.023	26127	3134	49.914		M
2	6.530	26217	2167	50.086		M
总计		52343	5300			

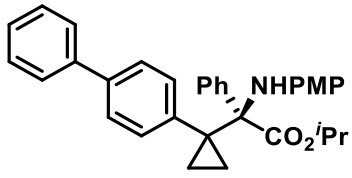


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	4.900	4488	773	0.621		M
2	6.497	717737	29176	99.379		M
总计		722225	29948			

Isopropyl (*R*)-2-(1-([1,1'-biphenyl]-4-yl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate (3m)



General procedure B was followed using **2c** as an electrophile on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3m** as a white solid (91.8 mg, 93%); $\mathbf{R_f}$ = 0.75 (PE/EtOAc = 10/1);

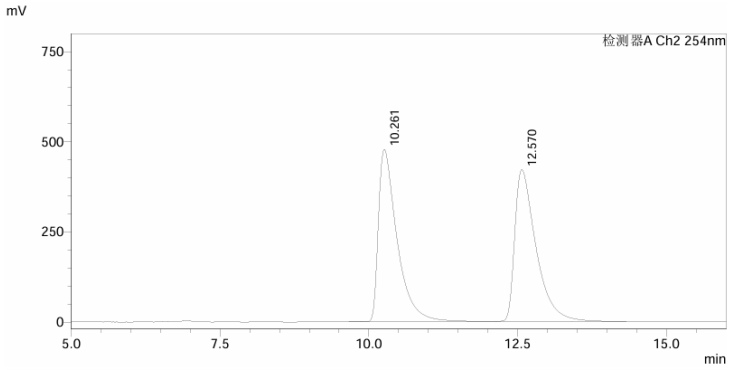
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80–7.78 (m, 2H), 7.55 (d, *J* = 6.8 Hz, 2H), 7.44–7.38 (m, 4H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.25–7.23 (m, 3H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 6.26 (d, *J* = 8.8 Hz, 2H), 4.87 (sept, *J* = 6.4 Hz, 1H), 4.61 (bs, 1H), 3.65 (s, 3H), 1.37–1.34 (m, 1H), 1.13–1.08 (m, 1H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.91–0.84 (m, 2H), 0.78 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 152.3, 141.4, 140.80, 140.79, 139.9, 137.9, 132.3, 129.8, 128.9, 127.4, 127.3, 127.1, 126.4, 116.7, 114.0, 70.2, 69.1, 55.7, 35.6, 21.7, 21.2, 11.1, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{33}H_{34}NO_3^+$: 492.2533; found: 492.2533;

HPLC (Chiralpak IBN): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 254 nm, t_{R1} = 10.233 min (minor), t_{R2} = 11.995 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 111.82 (c = 0.37, CH_2Cl_2).

<Chromatogram>

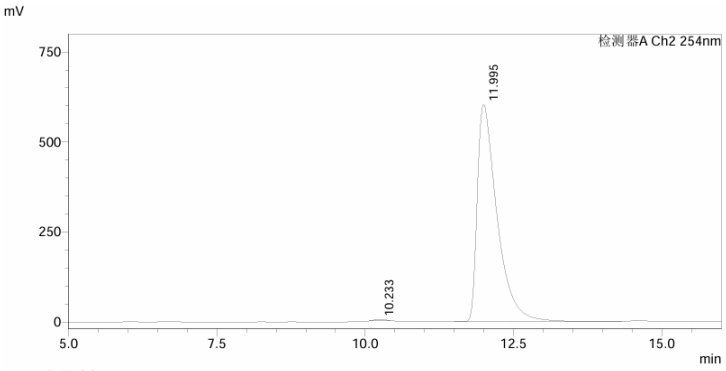


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.261	10423469	478304	50.037		M
2	12.570	10408213	420586	49.963		M
总计		20831682	898890			

<Chromatogram>

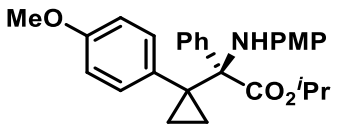


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.233	42840	3246	0.304		M
2	11.995	14050330	603929	99.696		M
总计		14093171	607175			

Isopropyl (*R*)-2-((4-methoxyphenyl)amino)-2-(1-(4-methoxyphenyl)cyclopropyl)-2-phenylacetate (3n)



General procedure B was followed using **2d** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3n** as a white solid (38.8 mg, 87%); $\mathbf{R_f}$ = 0.56 (PE/EtOAc = 10/1);

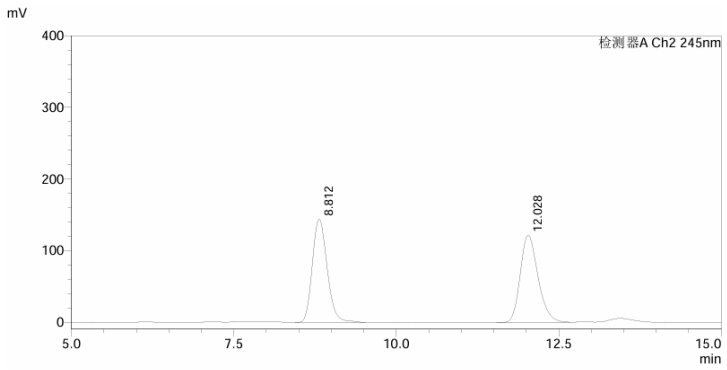
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.72 (m, 2H), 7.23–7.21 (m, 3H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 6.54 (d, *J* = 9.2 Hz, 2H), 6.22 (d, *J* = 8.8 Hz, 2H), 4.85 (sept, *J* = 6.4 Hz, 1H), 4.51 (bs, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 1.30–1.26 (m, 1H), 1.10–1.03 (m, 4H), 0.81–0.74 (m, 5H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 158.6, 152.2, 140.9, 138.0, 134.3, 132.9, 129.7, 127.3, 127.2, 116.6, 114.0, 113.0, 70.2, 69.0, 55.7, 55.3, 35.1, 21.7, 21.2, 11.3, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{28}H_{32}NO_4^+$: 446.2326; found: 446.2326;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 245 nm, t_{R1} = 8.666 min (minor), t_{R2} = 11.702 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 93.89 (c = 0.12, CH_2Cl_2).

<Chromatogram>

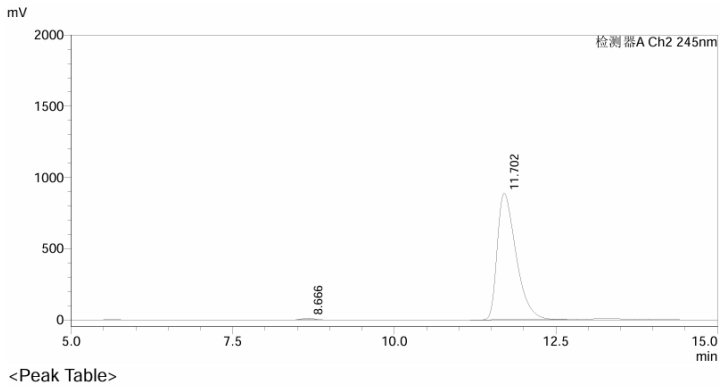


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.812	2298895	144162	49.798		M
2	12.028	2317517	121924	50.202		M
总计		4616412	266086			

<Chromatogram>

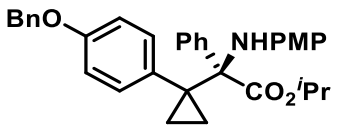


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.666	77447	7340	0.432		M
2	11.702	17867788	886016	99.568		M
总计		17945235	893356			

Isopropyl (*R*)-2-(1-(4-(benzyloxy)phenyl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate (3o)



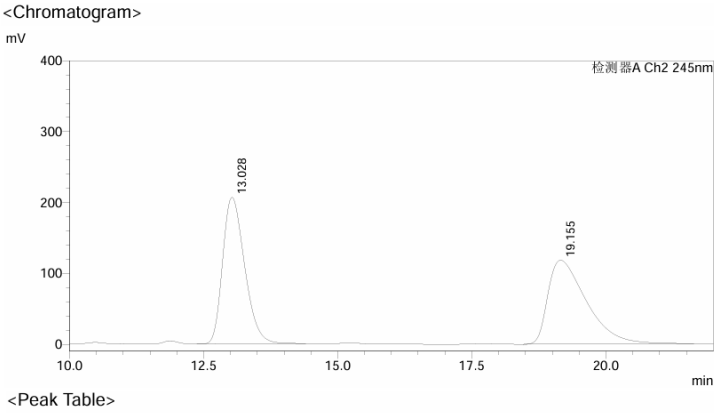
General procedure B was followed using **2e** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3o** as a white solid (46.3 mg, 89%); $\mathbf{R_f}$ = 0.56 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75–7.72 (m, 2H), 7.42–7.32 (m, 5H), 7.23–7.21 (m, 3H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 6.22 (d, *J* = 8.8 Hz, 2H), 5.00 (s, 2H), 4.84 (sept, *J* = 6.4 Hz, 1H), 4.52 (bs, 1H), 3.65 (s, 3H), 1.30–1.27 (m, 1H), 1.07–1.00 (m, 4H), 0.81–0.78 (m, 2H), 0.77 (d, *J* = 6.0 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 157.8, 152.2, 140.9, 138.0, 137.1, 134.6, 132.9, 129.7, 128.7, 128.1, 127.6, 127.4, 127.2, 116.7, 114.00, 113.98, 70.2, 70.1, 69.0, 55.7, 35.1, 21.7, 21.2, 11.3, 10.6;

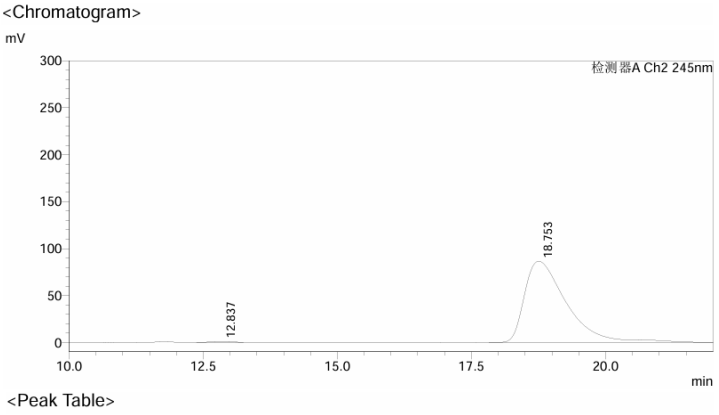
HRMS (ESI): $[M+H]^+$ Calcd for $C_{34}H_{36}NO_4^+$: 522.2639; found: 522.2639;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 40 °C, λ = 245 nm, t_{R1} = 12.837 min (minor), t_{R2} = 18.753 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 107.55 (c = 0.33, CH_2Cl_2).



<Peak Table>
检测器A Ch2 245nm

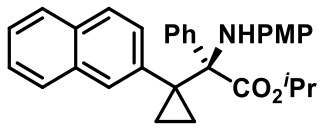
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.028	5926637	206724	50.112		M
2	19.155	5900203	118229	49.888		M
总计		11826839	324954			



<Peak Table>
检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	12.837	30911	1164	0.647		M
2	18.753	4743158	86549	99.353		M
总计		4774069	87713			

Isopropyl (*R*)-2-((4-methoxyphenyl)amino)-2-(1-(naphthalen-2-yl)cyclopropyl)-2-phenylacetate (3p)



General procedure B was followed using **2f** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3p** as a white solid (41.3 mg, 89%); $\mathbf{R_f}$ = 0.67 (PE/EtOAc = 10/1);

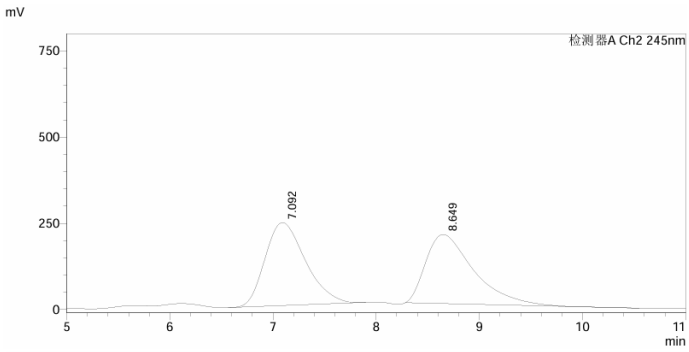
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81–7.74 (m, 3H), 7.72–7.70 (m, 1H), 7.63–7.60 (m, 2H), 7.47–7.42 (m, 2H), 7.24–7.19 (m, 4H), 6.55 (d, *J* = 9.2 Hz, 2H), 6.24 (d, *J* = 8.8 Hz, 2H), 4.88 (sept, *J* = 6.4 Hz, 1H), 4.65 (bs, 1H), 3.64 (s, 3H), 1.43–1.40 (m, 1H), 1.15 (dt, *J* = 9.6, 2.8 Hz, 1H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.94–0.92 (m, 2H), 0.77 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 152.2, 140.7, 139.8, 137.9, 132.9, 132.5, 131.1, 129.8, 129.7, 127.9, 127.6, 127.41, 127.35, 127.1, 126.0, 116.7, 114.0, 70.2, 69.1, 55.7, 35.9, 21.6, 21.2, 11.3, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{31}H_{32}NO_3^+$: 466.2377; found: 466.2377;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 245 nm, t_{R1} = 7.112 min (minor), t_{R2} = 8.693 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 82.35 (c = 0.11, CH_2Cl_2).

<Chromatogram>



<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.092	6520981	240293	50.286		M
2	8.649	6446830	200184	49.714		M
总计		12967811	440476			

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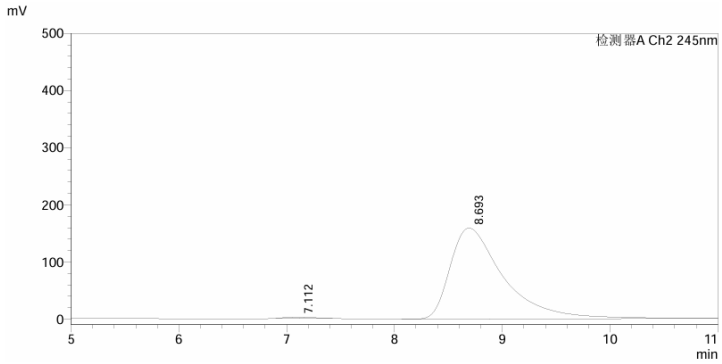
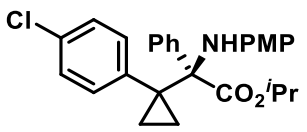


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.112	35976	2008	0.648		M
2	8.693	5512689	159080	99.352		M
总计		5548664	161088			

Isopropyl (*R*)-2-(1-(4-chlorophenyl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate (3q)



General procedure B was followed using **2g** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3q** as a white solid (36.0 mg, 80%); $\mathbf{R_f}$ = 0.65 (PE/EtOAc = 10/1);

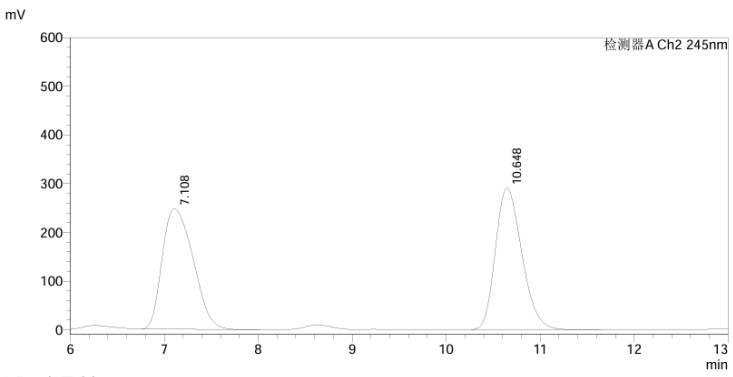
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68–7.66 (m, 2H), 7.22–7.18 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.56 (d, *J* = 9.2 Hz, 2H), 6.26 (d, *J* = 8.8 Hz, 2H), 4.85 (sept, *J* = 6.4 Hz, 1H), 4.45 (bs, 1H), 3.65 (s, 3H), 1.42–1.38 (m, 1H), 1.67–1.12 (m, 1H), 1.08 (d, *J* = 6.0 Hz, 3H), 0.86–0.79 (m, 2H), 0.77 (d, *J* = 6.0 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 152.5, 140.9, 140.6, 137.9, 133.2, 132.9, 129.6, 127.7, 127.41, 127.37, 116.8, 114.1, 70.2, 69.2, 55.7, 35.6, 21.7, 21.2, 11.4, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{29}Cl_1N_1O_3^+$: 450.1830; found: 450.1830;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 245 nm, t_{R1} = 7.245 min (minor), t_{R2} = 10.526 min (major); 98% ee; $[\alpha]_D^{33.5}$ = 122.67 (c = 0.2, CH_2Cl_2).

<Chromatogram>

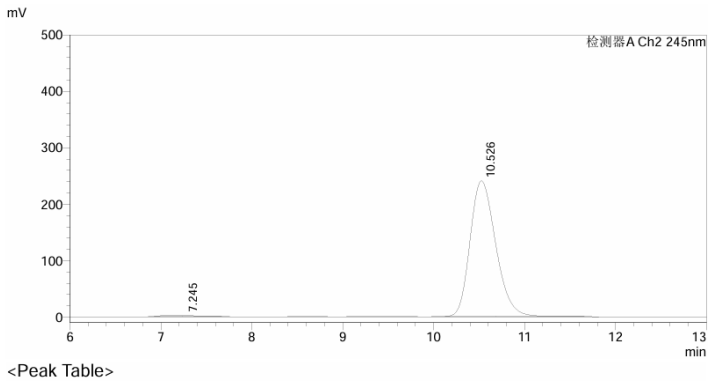


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.108	5631437	247260	49.765		M
2	10.648	5684519	290641	50.235		M
总计		11315956	537901			

<Chromatogram>

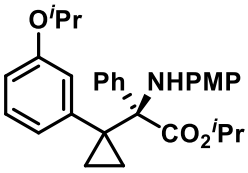


<Peak Table>

检测器A Ch2 245nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.245	40455	1322	0.850		M
2	10.526	4717342	240256	99.150		M
总计		4757796	241579			

Esopropyl (*R*)-2-(1-(3-isopropoxyphenyl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate (3r)



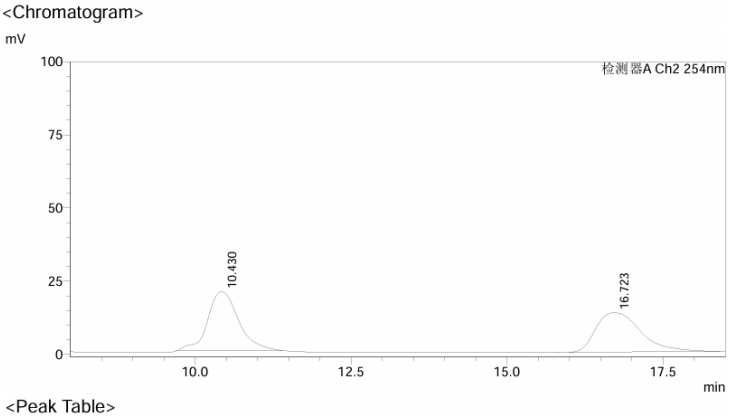
General procedure B was followed using **2h** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3r** as a white solid (32.8 mg, 69%); $\mathbf{R}_f$ = 0.56 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78–7.76 (m, 2H), 7.24–7.21 (m, 3H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.68 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.61 (t, *J* = 2.4 Hz, 1H), 6.54 (d, *J* = 9.2 Hz, 2H), 6.21 (d, *J* = 8.8 Hz, 2H), 4.84 (sept, *J* = 6.0 Hz, 1H), 4.60 (bs, 1H), 4.36 (sept, *J* = 6.0 Hz, 1H), 3.64 (s, 3H), 1.30–1.25 (m, 7H), 1.02 (d, *J* = 6.0 Hz, 3H), 1.00–0.97 (m, 1H), 0.84–0.80 (m, 2H), 0.75 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 157.3, 152.1, 143.7, 140.9, 137.8, 129.8, 128.6, 127.4, 127.3, 124.2, 119.7, 116.6, 115.0, 114.0, 70.1, 70.0, 69.0, 55.7, 35.8, 22.2, 21.7, 21.2, 11.1, 10.6;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{30}H_{36}NO_4^+$: 474.2639; found: 474.2636;

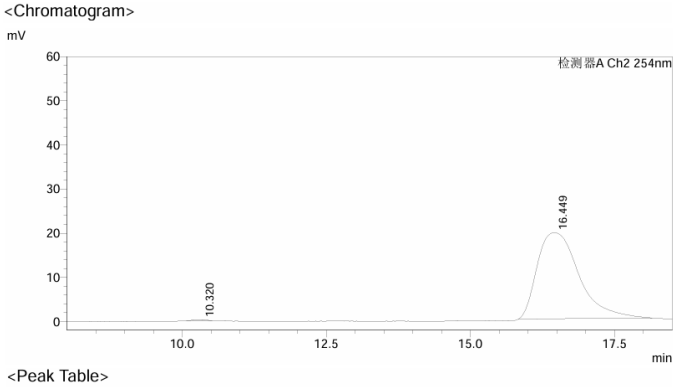
HPLC (Chiralcel AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 10.320 min (minor), t_{R2} = 16.449 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 228.64 (c = 0.15, CH_2Cl_2).



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.430	700318	20097	50.942		M
2	16.723	674406	13407	49.058		M
总计		1374724	33504			

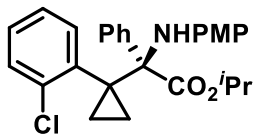


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.320	2192	129	0.222		M
2	16.449	984125	19454	99.778		M
总计		986317	19582			

Isopropyl (*R*)-2-(1-(2-chlorophenyl)cyclopropyl)-2-((4-methoxyphenyl)amino)-2-phenylacetate （3s）



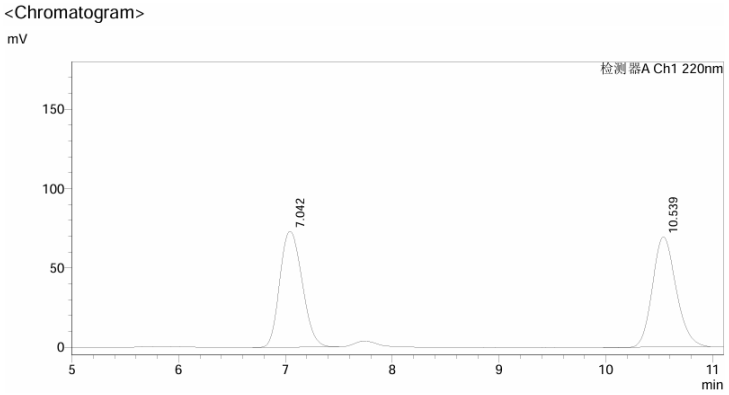
General procedure B was followed using **2i** as an electrophile on 0.2 mmol scale for 40 hours. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3s** as a white solid (52.3 mg, 58%); $\mathbf{R}_f$ = 0.67 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, DMSO-d6): δ 7.83–7.56 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.23–7.84 (m, 6H),6.55 (d, *J* = 8.0 Hz, 2H), 6.21 (d, *J* = 8.0 Hz, 2H), 5.62 (bs, 1H), 4.66 (sept, *J* = 6.0 Hz, 1H), 3.54 (s, 3H), 1.23–1.18 (m, 1H), 0.93–0.84 (m, 6H), 0.63 (s, 3H);

^{13}C NMR (100 MHz, DMSO-d_6): δ 171.0, 151.6, 140.4, 139.5, 137.8, 135.7, 135.0, 129.7, 129.4, 128.7, 127.3, 127.0, 126.3, 115.9, 113.8, 70.8, 68.5, 55.2, 32.9, 21.2, 20.7, 13.1;

HRMS (ESI): $[M+H]^+$ Calcd for $C_{27}H_{29}ClNO_3^+$: 450.1830; found: 450.1828;

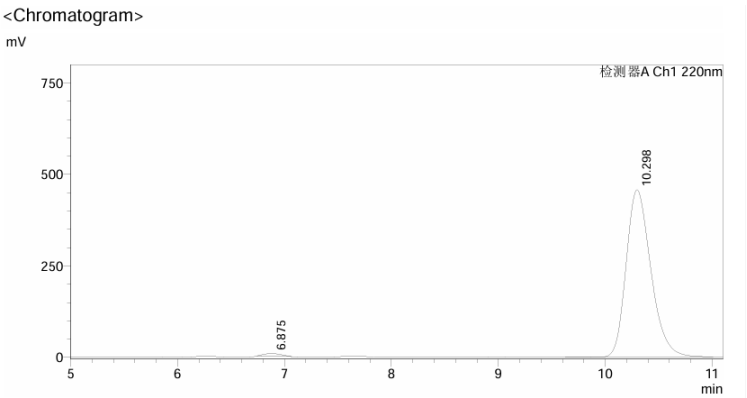
HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 ºC, λ = 220 nm, t_{R1} = 6.875 min (minor), t_{R2} = 10.298 min (major); 98% ee; $[\alpha]_D^{33.5}$ = 119.41 (c = 0.11, CH_2Cl_2).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.042	1063658	73059	50.022		M
2	10.539	1062738	69362	49.978		M
总计		2126395	142421			

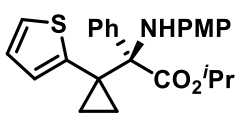


<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	6.875	84720	7338	1.135		M
2	10.298	7379732	457737	98.865		M
总计		7464452	465075			

Isopropyl (*R*)-2-((4-methoxyphenyl)amino)-2-phenyl-2-(1-(thiophen-2-yl)cyclopropyl)acetate (3t)



General procedure B was followed using **2j** as an electrophile on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford **3t** as a white solid (32.7 mg, 78%); $\mathbf{R_f}$ = 0.57 (PE/EtOAc = 10/1);

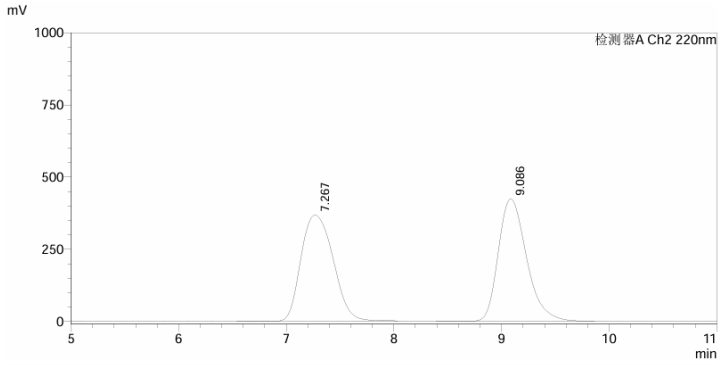
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74–7.70 (m, 2H), 7.26–7.22 (m, 3H), 7.06 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.76 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.70 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.57 (d, *J* = 9.2 Hz, 2H), 6.28 (d, *J* = 8.8 Hz, 2H), 4.90 (sept, *J* = 6.4 Hz, 1H), 4.64 (bs, 1H), 3.66 (s 3H), 3.70–3.66 (m, 4H), 1.42–1.36 (m, 1H), 1.17–1.12 (m, 1H), 1.09 (d, *J* = 6.0 Hz, 3H), 1.04–0.95 (m, 2H), 0.85 (d, *J* = 6.4 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ171.7, 152.3, 146.5, 140.7, 137.7, 129.6, 128.6, 127.5, 125.9, 125.1, 116.7, 114.0, 70.6, 69.3, 55.7, 30.8, 21.7, 21.2, 13.2, 12.7.

HRMS (ESI): $[M+H]^+$ Calcd for $C_{25}H_{28}NO_3S^+$: 422.1784; found: 422.1783;

HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 220 nm, t_{R1} = 7.319 min (minor), t_{R2} = 9.320 min (major); 98% ee; $[\alpha]_D^{33.5}$ = 188.08 (c = 0.17, CH_2Cl_2).

<Chromatogram>

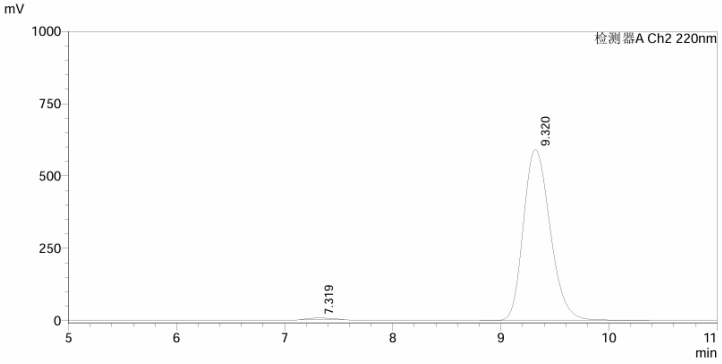


<Peak Table>

检测器A Ch2 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.267	7594369	366887	49.845		M
2	9.086	7641546	422273	50.155		M
总计		15235915	789160			

<Chromatogram>



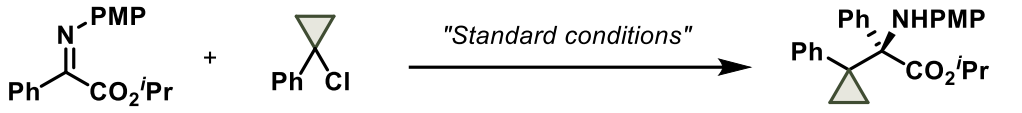
<Peak Table>

检测器A Ch2 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.319	87796	5595	0.861		M
2	9.320	10104452	590808	99.139		M
总计		10192248	596404			

Synthetic Applications

(A) Gram-scale reaction

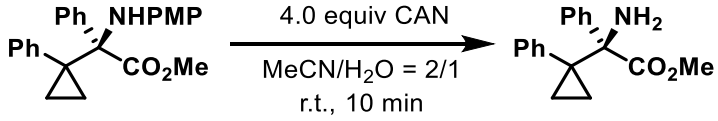


1b **2a** **3k,** 1.07 g, 86%, 99% ee

To an oven-dried 100 mL Schlenk tube equipped with a magnetic stir bar were added ligand **L2** (0.36 mmol, 12 mol%), In (6.0 mmol, 2.0 equiv) and imine **1a** (3.0 mmol, 1.0 equiv). Then the vial was transferred into the glovebox, CoI_2 (0.3 mmol, 10 mol%), MeCN (0.2 M), cyclopropyl chloride compounds **2a** (4.5 mmol, 1.5 equiv) and ^{i}PrOH (3.0 mmol, 1.0 equiv) were added in sequence. The reaction vial was capped and stirred at 50 °C for 20 hours. After completion, the reaction mixture was filtered through a pad of silica gel and the filter cake was washed with EtOAc. The resulted filtrate was concentrated under reduced pressure to give the crude product, which was purified by silica gel flash column chromatography (silica gel, PE/EtOAc = 20/1~10/1) to afford **3a** as a white solid (1.07 g, 86%, 99% ee)

(B) Derivatization of products

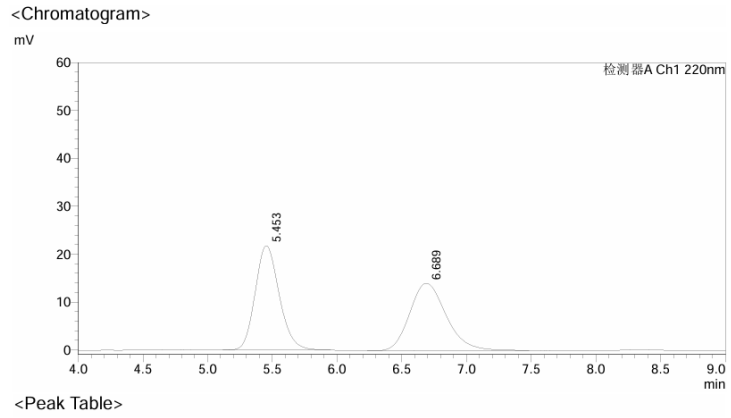
Isopropyl (*R*)-2-amino-2-phenyl-2-(1-phenylcyclopropyl)acetate (4)



3b **4**

To a solution of **3b** (0.5 mmol, 1.0 equiv) in MeCN (5.0 mL) was added CAN (2.0 mmol, 4.0 equiv) in H_2O (2.5 mL) dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 10 min. After completion, the reaction mixture was diluted with H_2O and extracted with DCM for 3 times. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude product, which was purified by silica gel flash column chromatography (silica gel, PE/EtOAc = 10/1~5/1) to afford **4** as a dark red oil (134 mg, 95%, 99% ee), $\boldsymbol{R_f}$ = 0.48 (PE/EtOAc = 8/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.43 (d, *J* = 6.8 Hz, 2H), 7.35–7.29 (m, 3H), 7.25–7.19 (m, 3H), 3.72 (s, 3H), 1.89 (bs, 2H), 0.97–0.90 (m, 1H), 0.88–0.83 (m, 1H), 0.69–0.62 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 142.8, 139.2, 132.3, 128.0, 127.82, 127.79, 127.2, 67.9, 52.3, 33.0, 10.7, 9.0;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{18}H_{20}NO_2^+$: 282.1489; found: 282.1487;
HPLC (Chiralpak IA): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, T = 30 °C, λ = 220 nm, tR1 = 5.472 min (major), tR2 = 6.715 min (minor); 99% ee; $[\alpha]_D^{33.5}$ = -21.36 (c = 0.29, CH_2Cl_2).



<Peak Table>

检测器A Ch1 220nm

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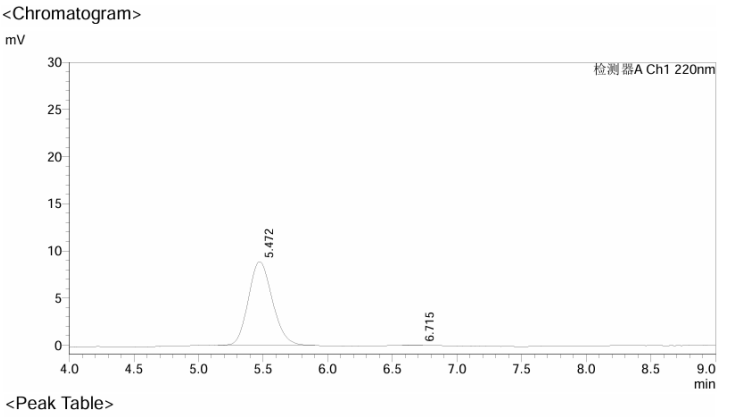
2	6.689	275042	14085	49.627		M
总计		554214	35824			

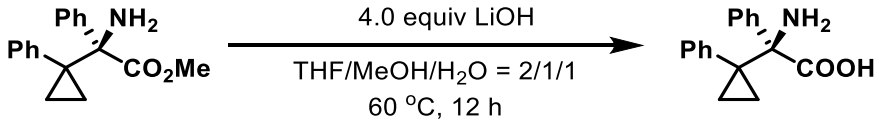


<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.472	114171	8872	99.926		M
2	6.715	84	15	0.074		M
总计		114255	8887			

(*R*)-2-amino-2-phenyl-2-(1-phenylcyclopropyl)acetic acid (5)



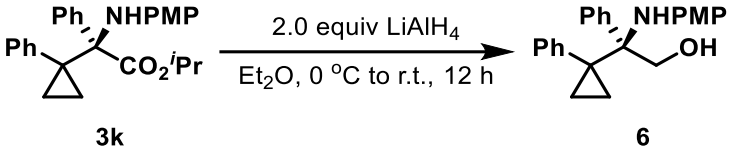
4 **5**

To a solution of **4** (0.036 mmol, 1.0 equiv) in mixed solvent (THF/MeOH/H_2O = 2/1/1, 0.025 M) was added LiOH (0.144 mmol, 4.0 equiv). The resulting mixture was stirred at 60 °C overnight. After completion, the reaction was diluted with H_2O and then acidified with 1M HCl to pH = 1. The aqueous was washed with EtOAc for 3 times and concentrated under reduced pressure. The residue was dissolved in MeOH, filtered, and the filter cake was washed with MeOH. The resulting filtrate was concentrated in vacuo to afford a white solid **5** (9.2 mg, 96%).

^{1}H NMR (400 MHz, CD_3OD): δ 7.75 (d, *J* = 7.2 Hz, 1H), 7.53–7.46 (m, 5H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.33–7.29 (m, 2H), 1.13–1.07 (m, 1H), 1.02–0.86 (m, 3H);

^{13}C NMR (100 MHz, CD_3OD): δ 170.4, 140.5, 136.2, 133.1, 130.8, 130.3, 129.5, 129.4, 129.1, 128.4, 128.0, 126.0, 68.9, 31.6, 11.8, 10.6;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{17}H_{18}NO_2^+$: 268.1332; found: 268.1330;

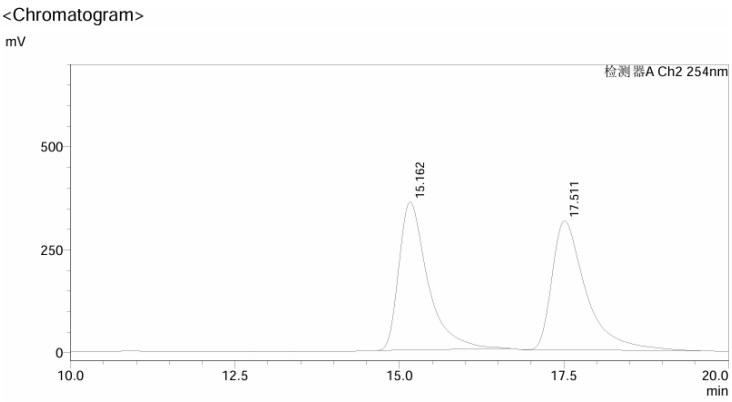
(*R*)-2-((4-methoxyphenyl)amino)-2-phenyl-2-(1-phenylcyclopropyl)ethan-1-ol (6)



3k **6**

To a solution of **3k** (0.1 mmol, 1.0 equiv) in Et_2O (1.0 mL, 0.1 M) was added $LiAlH_4$ (0.2 mmol, 2.0 equiv) at 0 °C, and then the resulting mixture was slowly warmed to room temperature. After stirring for 12 h at room temperature, the reaction was quenched with 1M HCl, extracted with EtOAc for 3 times. The combined organic layers were dried over Na_2SO_4 and then filtered. After removal of the solvent, the residue was purified by silica gel flash column chromatography (silica gel, PE/EtOAc = 5/1) to afford colorless oil **6** (33.9mg, 94%, 99% ee). $\boldsymbol{R_f}$ = 0.43 (PE/EtOAc = 5/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.24 (m, 3H), 7.22–7.13 (m, 5H), 7.08–7.02 (m, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 6.34 (d, *J* = 8.4 Hz, 2H), 4.28–4.19 (m, 2H), 4.08 (bs, 1H), 3.67 (s, 3H), 1.94 (bs, 1H), 1.36–1.22 (m, 2H), 0.87–0.77 (m, 2H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 143.0, 141.8, 139.1, 132.3, 127.9, 127.8, 127.7, 127.1, 127.0, 117.6, 114.6, 63.6, 62.9, 55.7, 34.6, 10.6, 9.0;
HRMS (ESI): $[M+H]^+$ Calcd for $C_{24}H_{26}NO_2^+$: 360.1958; found: 360.1958;
HPLC (Chiralpak AD-H): n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 14.865 min (minor), t_{R2} = 17.170 min (major); 99% ee; $[\alpha]_D^{33.5}$ = 85.38 (c = 0.16, CH_2Cl_2).



<Peak Table>
检测器A Ch2 254nm

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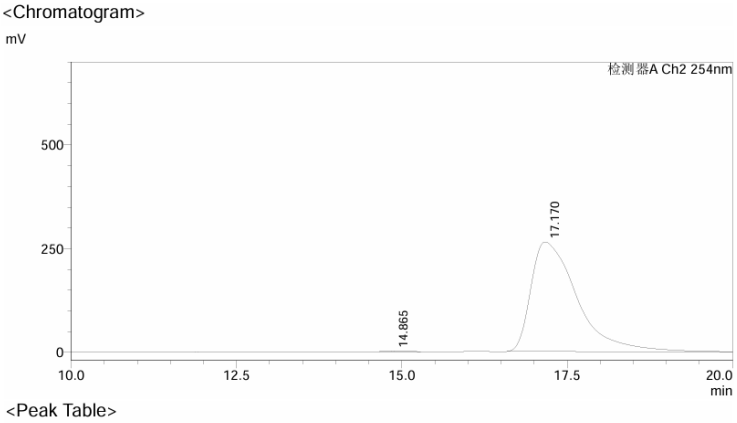
2	17.511	11251711	312843	50.532		M
总计		22266530	671528			

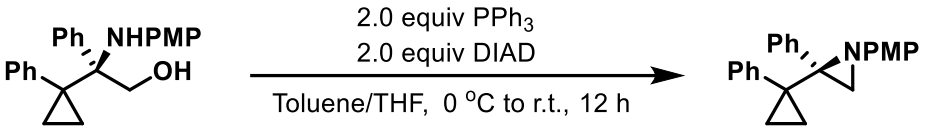


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	14.865	32744	1434	0.254		M
2	17.170	12880401	264432	99.746		M
总计		12913145	265866			

(*R*)-1-(4-methoxyphenyl)-2-phenyl-2-(1-phenylcyclopropyl)aziridine (7)

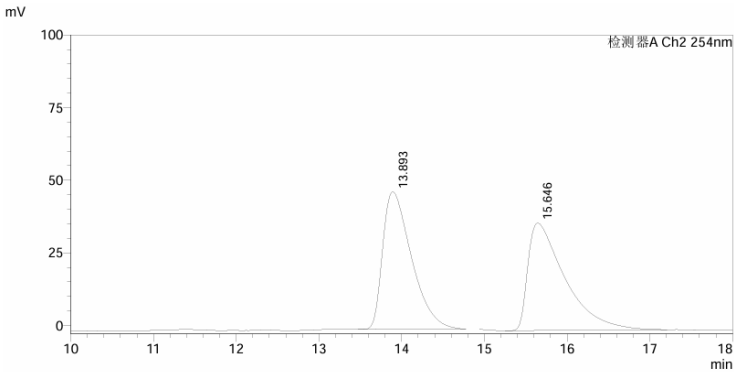


6 **7**

To a solution of **6** (0.1 mmol, 1.0 equiv) in THF (1.0 mL, 0.1 M) was added PPh_3 (0.105 mmol, 1.05 equiv) and DIAD (2.0 M in toluene, 2.0 equiv) at 0 °C under nitrogen atmosphere. The resulting mixture was stirred at room temperature for 12 hours. After completion, the reaction was quenched with H_2O, filtered through a pad of diatomite and the filter cake was washed with EtOAc. The resulting mixture was extracted with EA for three times and the combined organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the crude product, which was purified by silica gel flash column chromatography (silica gel, PE/EtOAc = 20/1) to afford white solid **7**(26.4mg, 77%, 95% ee). $\boldsymbol{R_f}$ = 0.80 (PE/EtOAc = 10/1);

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18–7.11 (m, 6H), 7.07–6.99 (m, 4H), 6.62–6.56 (m, 4H), 3.65 (s, 3H), 2.96 (s, 1H), 2.73 (s, 1H), 1.51–1.47 (m, 1H), 1.44–1.39 (m, 2H), 0.57–0.53 (m, 1H);
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 143.8, 142.3, 136.2, 129.8, 128.7, 128.0, 127.6, 127.1, 125.8, 122.1, 113.8, 55.5, 51.3, 36.6, 29.5, 13.2, 11.3.
HRMS (ESI): $[M+H]^+$ Calcd for $C_{24}H_{24}NO_1^+$: 342.1852; found: 342.1852;
HPLC (Chiralpak IBN): *n*-Hexane/*i*-PrOH = 99.5/0.5, flow rate 1.0 mL/min, T = 30 °C, λ = 254 nm, t_{R1} = 13.803 min (major), t_{R2} = 15.994 min (minor); 95% ee; $[\alpha]_D^{33.5}$ = -66.55 (c = 0.37, CH_2Cl_2).

<Chromatogram>

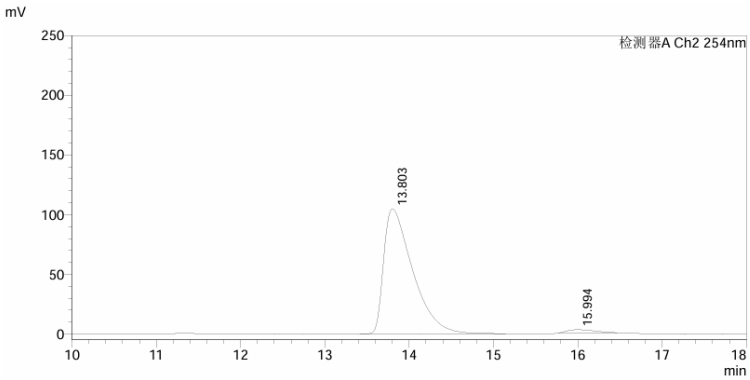


<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.893	1144665	47333	49.928		M
2	15.646	1147966	36952	50.072		M
总计		2292632	84285			

<Chromatogram>



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	13.803	2494646	104656	97.672		M
2	15.994	59457	2663	2.328		M
总计		2554103	107319			

Crystallographic Data

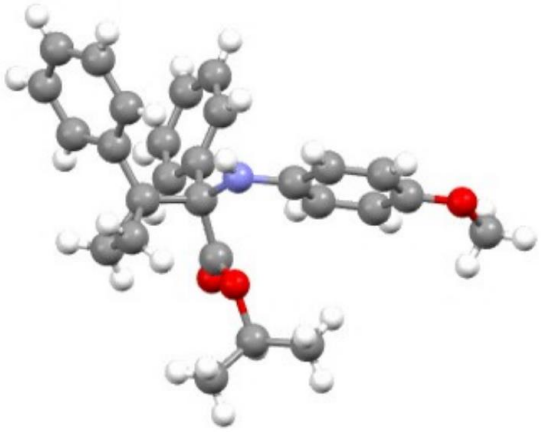


Fig S1. Crystal data and structure refinement for 3k (CCDC 2355497)

Identification code	240507cyf	
Empirical formula	C27 H29 N O3	
Formula weight	415.51	
Temperature	170.00 K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	P212121	
Unit cell dimensions	a = 11.3423(2) Å	α= 90 °.
	b = 13.4728(2) Å	β= 90 °.
	c = 14.6164(2) Å	γ = 90 °.
Volume	2233.57(6) Å3	
Z	4	
Density (calculated)	1.236 Mg/m3	
Absorption coefficient	0.403 mm-1	
F(000)	888	
Crystal size	0.17 x 0.17 x 0.05 mm3	
Theta range for data collection	3.882 to 54.890 °.	
Index ranges	-13<=h<=13, -15<=k<=16, -16<=l<=17	
Reflections collected	28341	
Independent reflections	4228 [R(int) = 0.0429]	
Completeness to theta = 53.594 °	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7508 and 0.6486	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	4228 / 0 / 283	
Goodness-of-fit on F2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0295, wR2 = 0.0790	
R indices (all data)	R1 = 0.0299, wR2 = 0.0794	
Absolute structure parameter	0.05(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.306 and -0.353 e.Å-3	

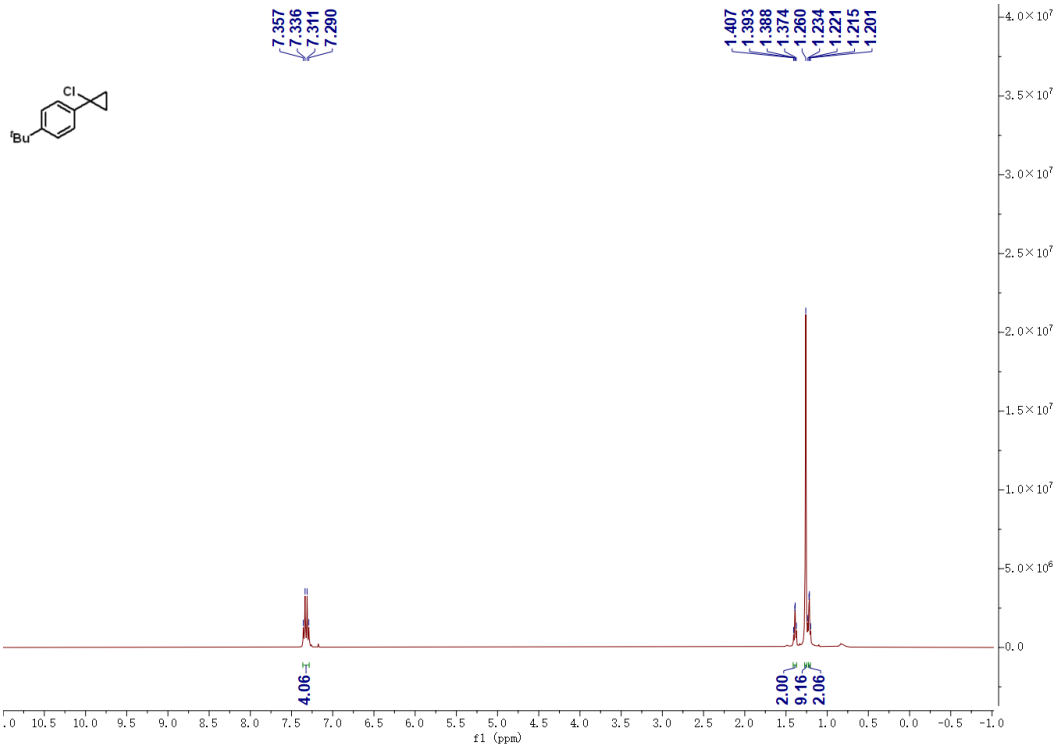
References

1. C. A. Ogle, P. A. Riley, J. J. Dorchak and J. L. Hubbard, *The Journal of Organic Chemistry*, 1988, **53**, 4409-4412.

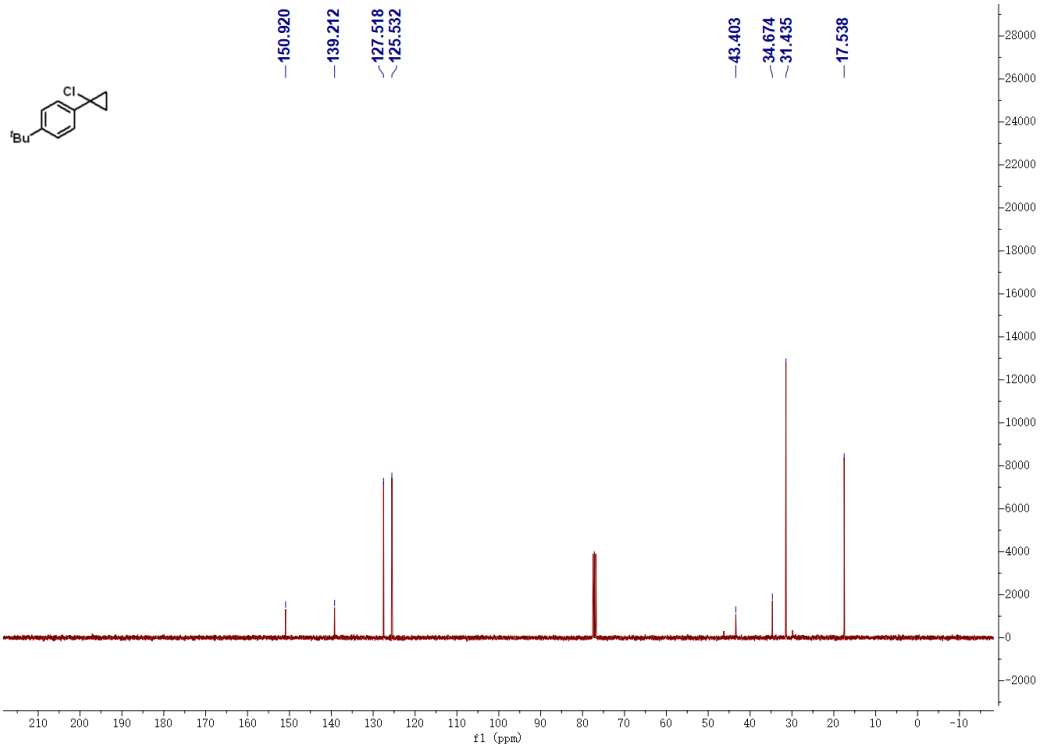
2. J. R. Van der Vecht, H. Steinberg and T. J. De Boer, *Recueil des Travaux Chimiques des Pays-Bas*, 1976, **95**, 149-152.

NMR Spectrum

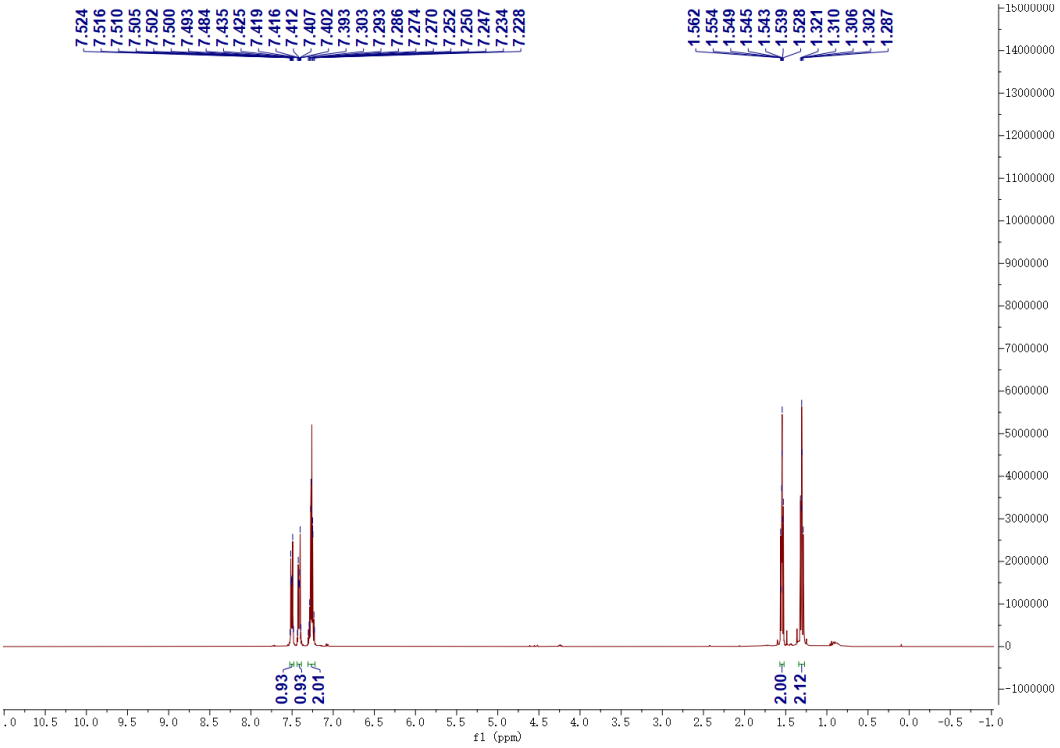
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2b**



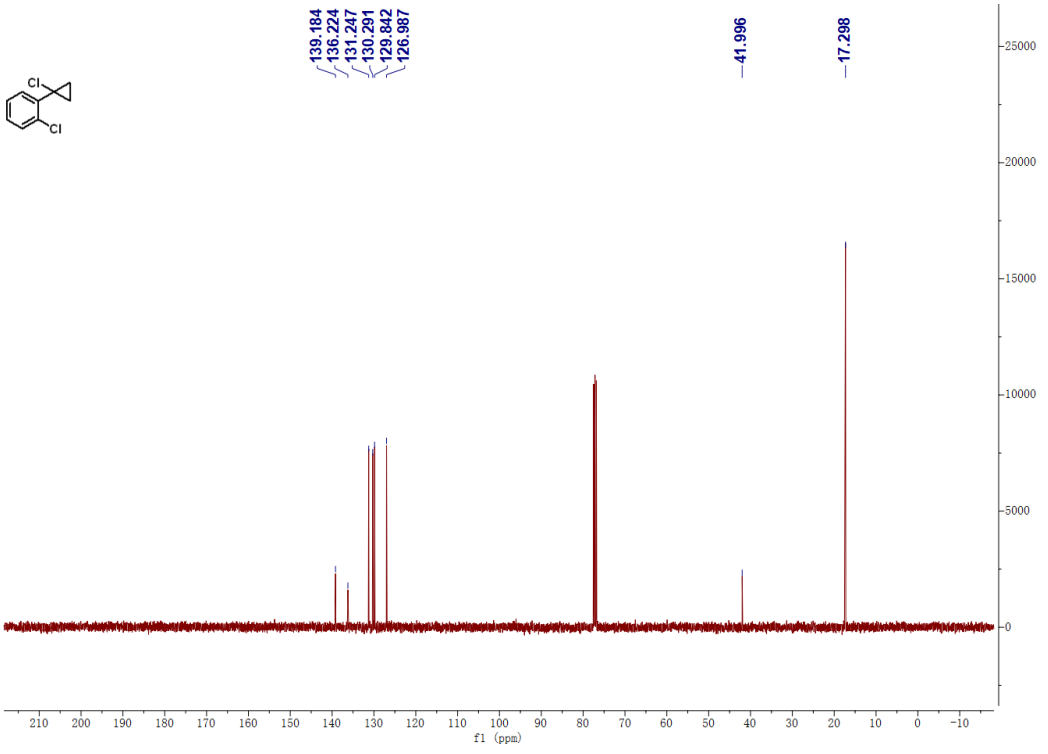
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2b**



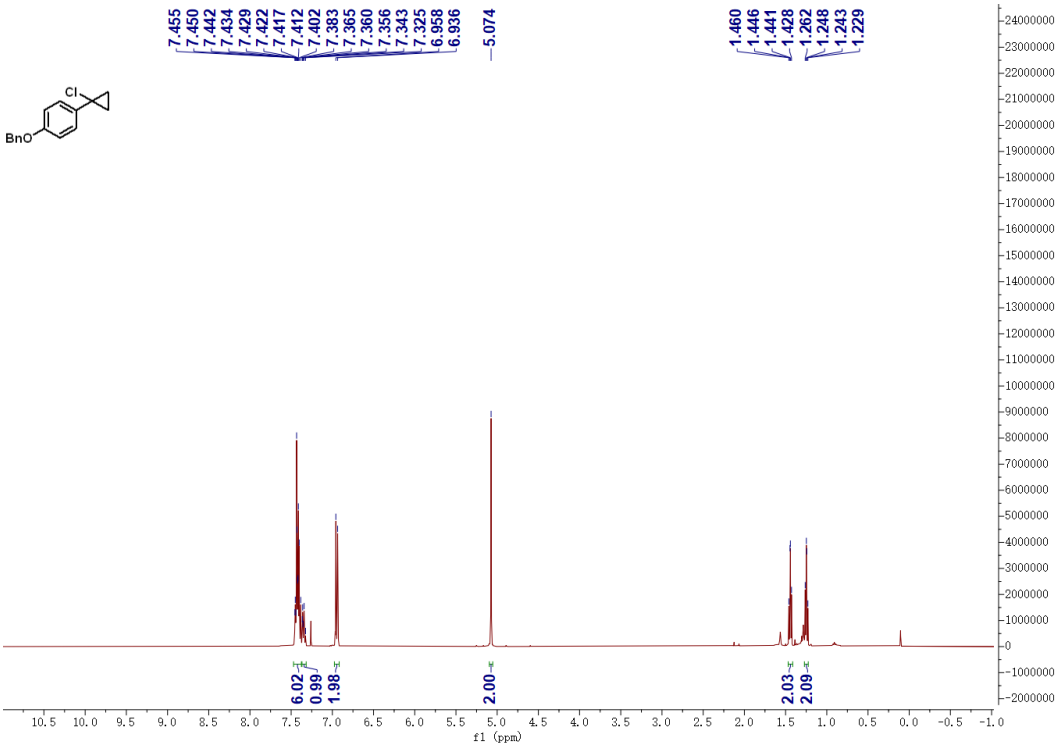
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2c**



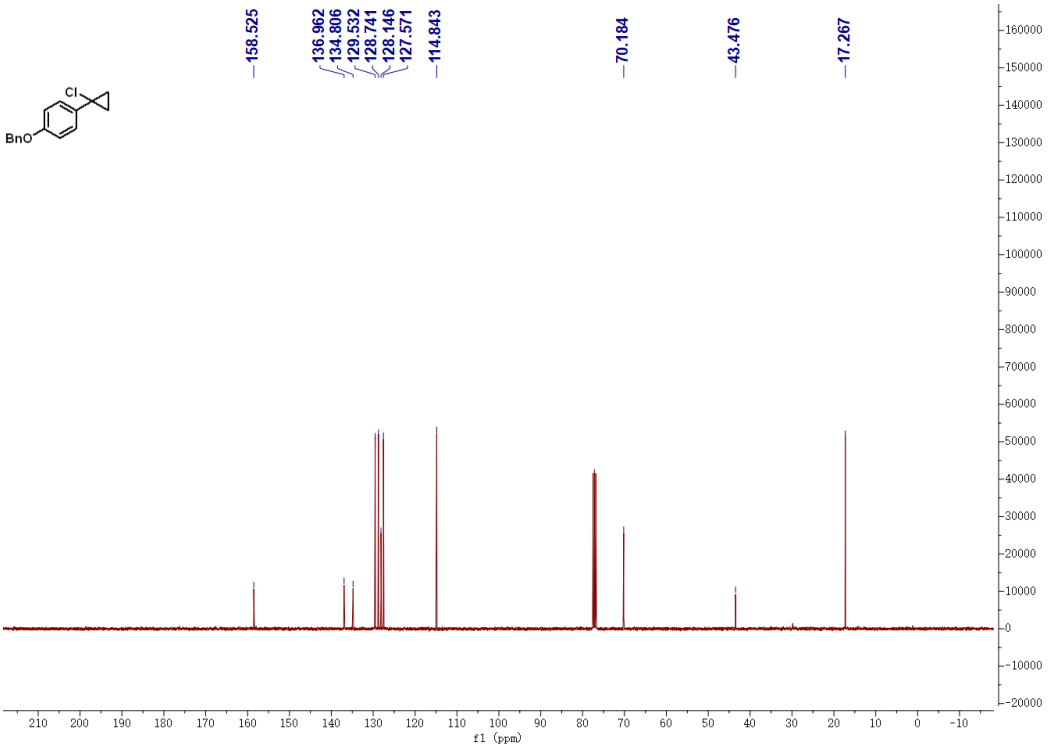
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2c**



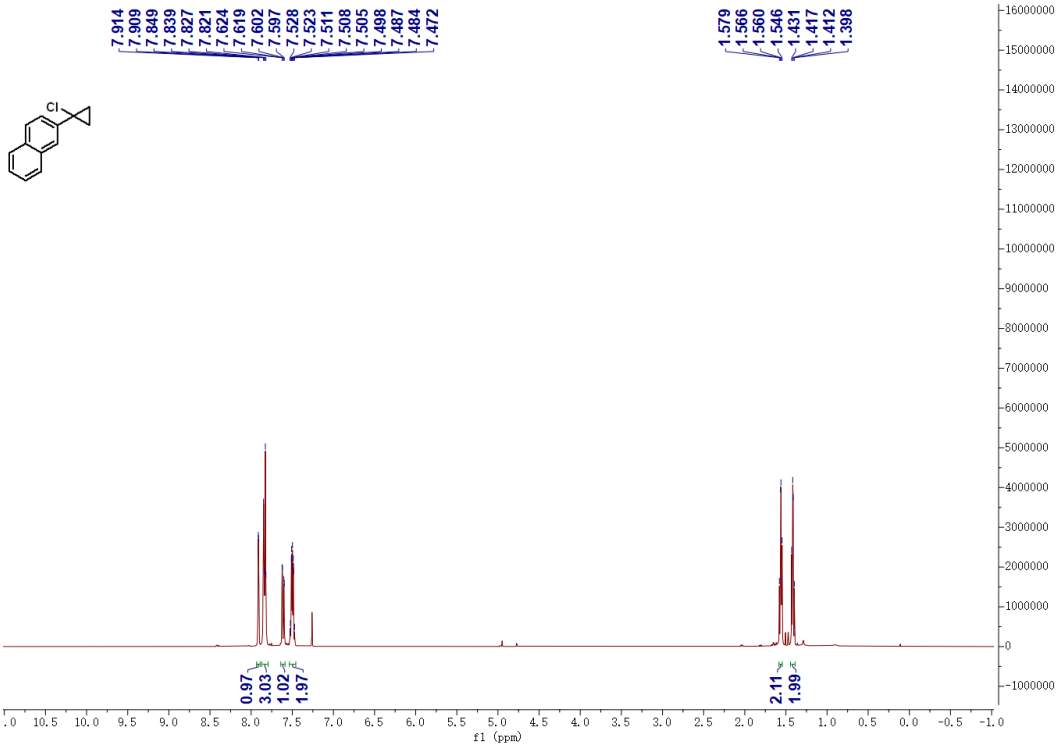
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2e**



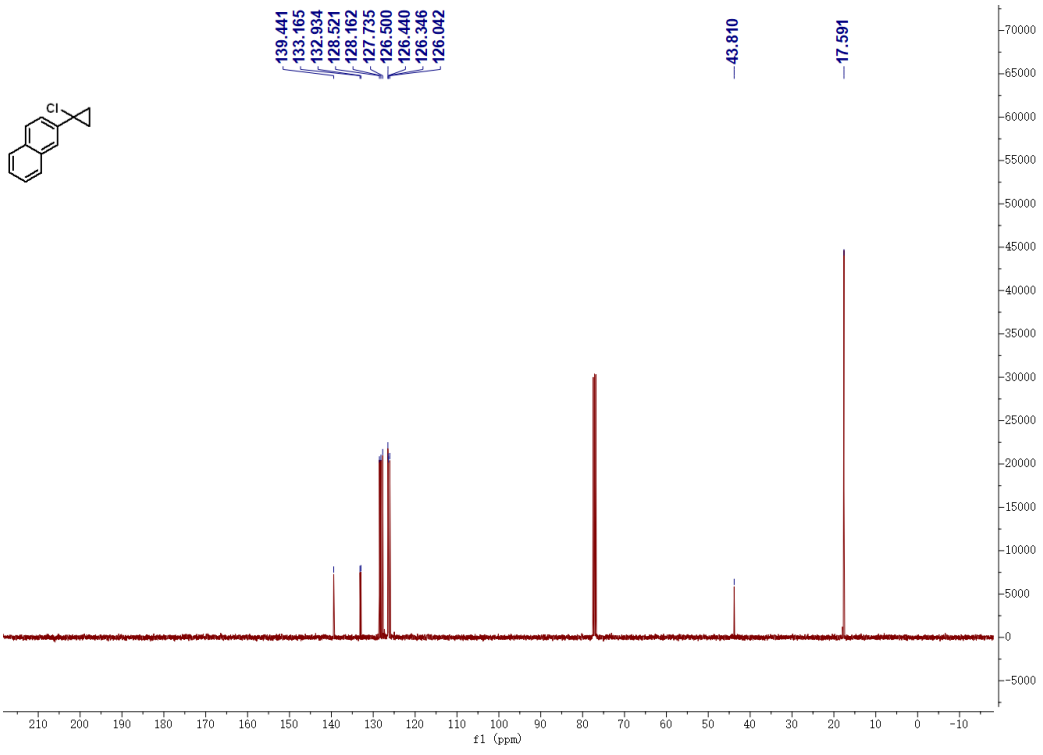
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2e**



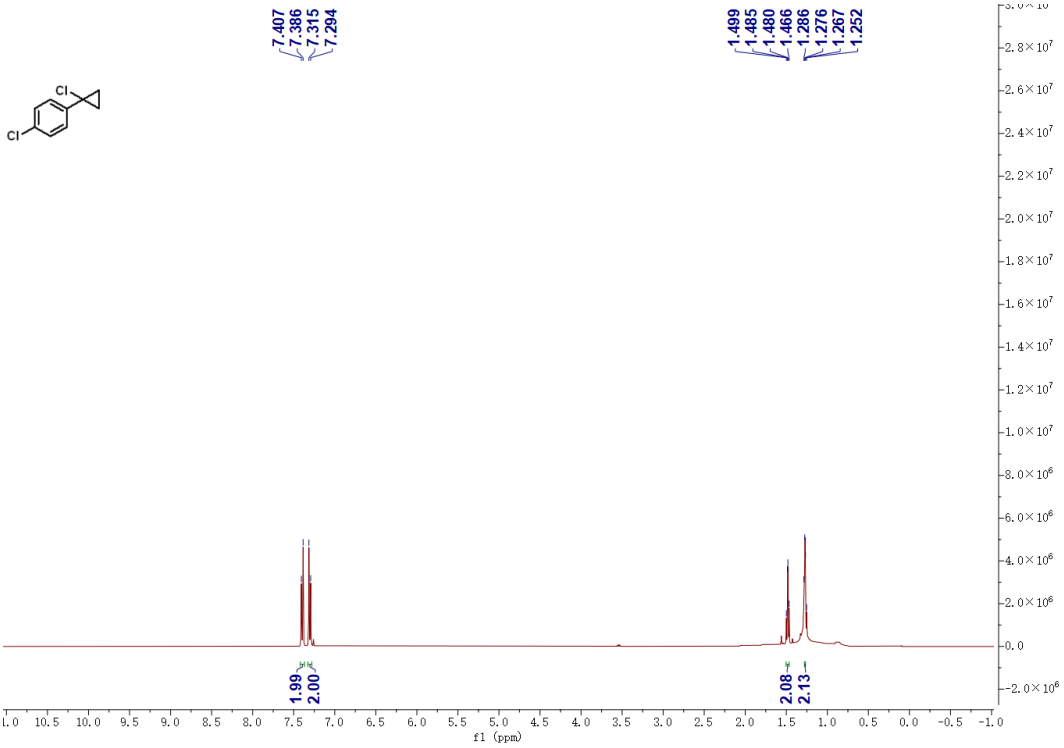
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2f**



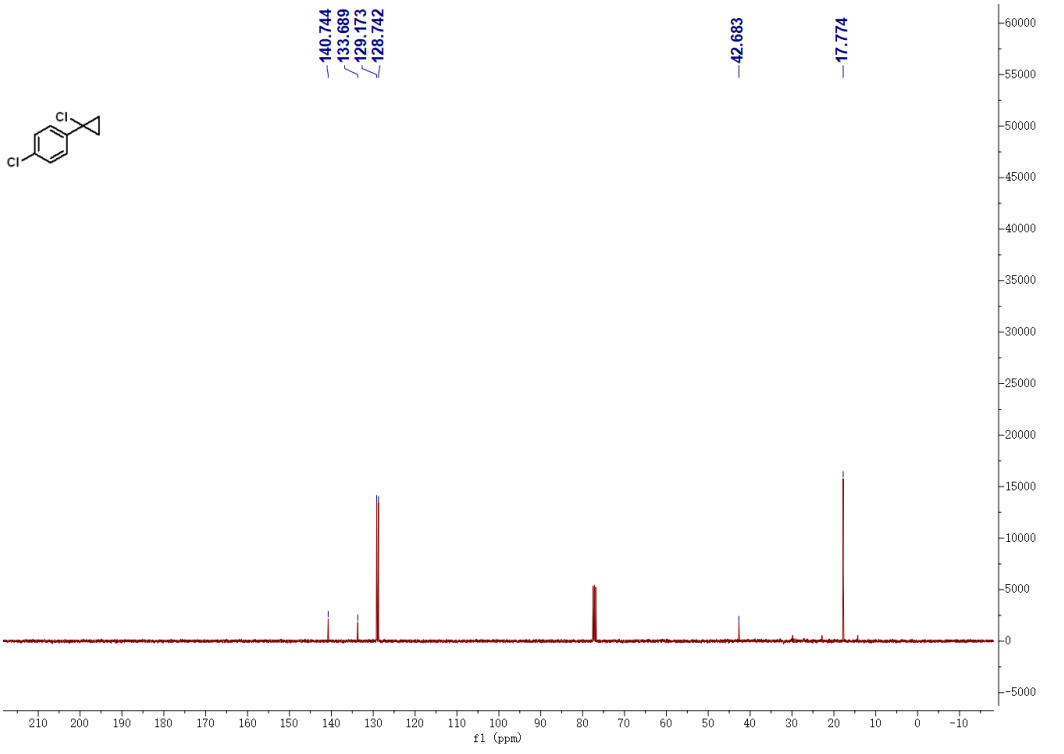
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2f**



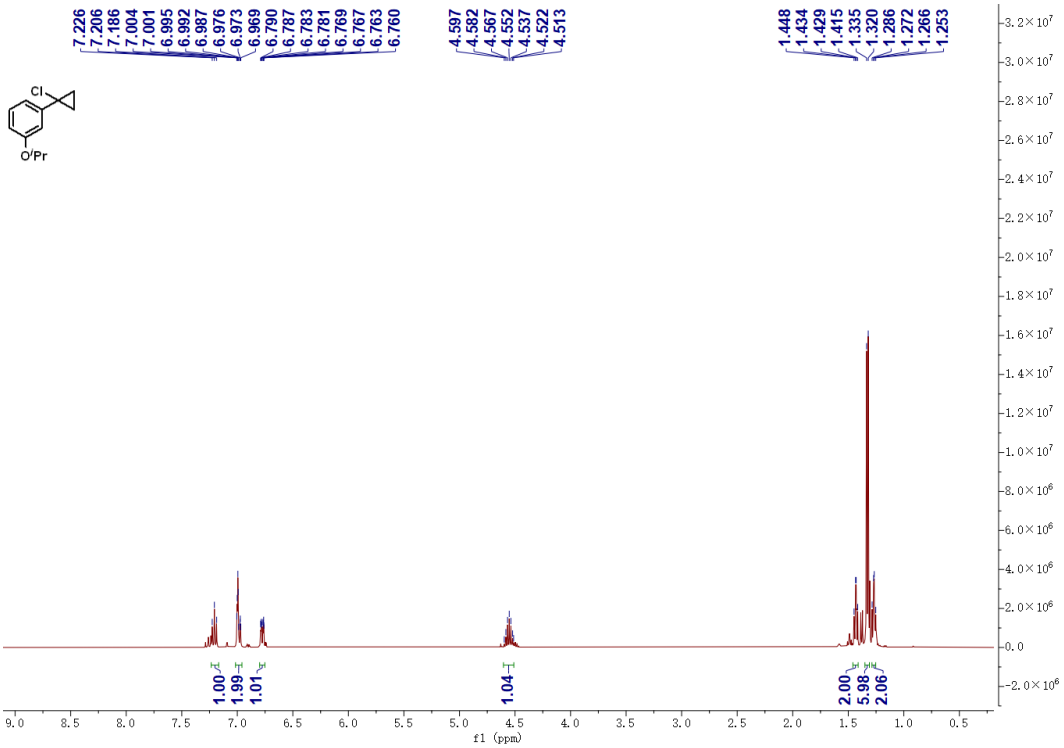
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2g**



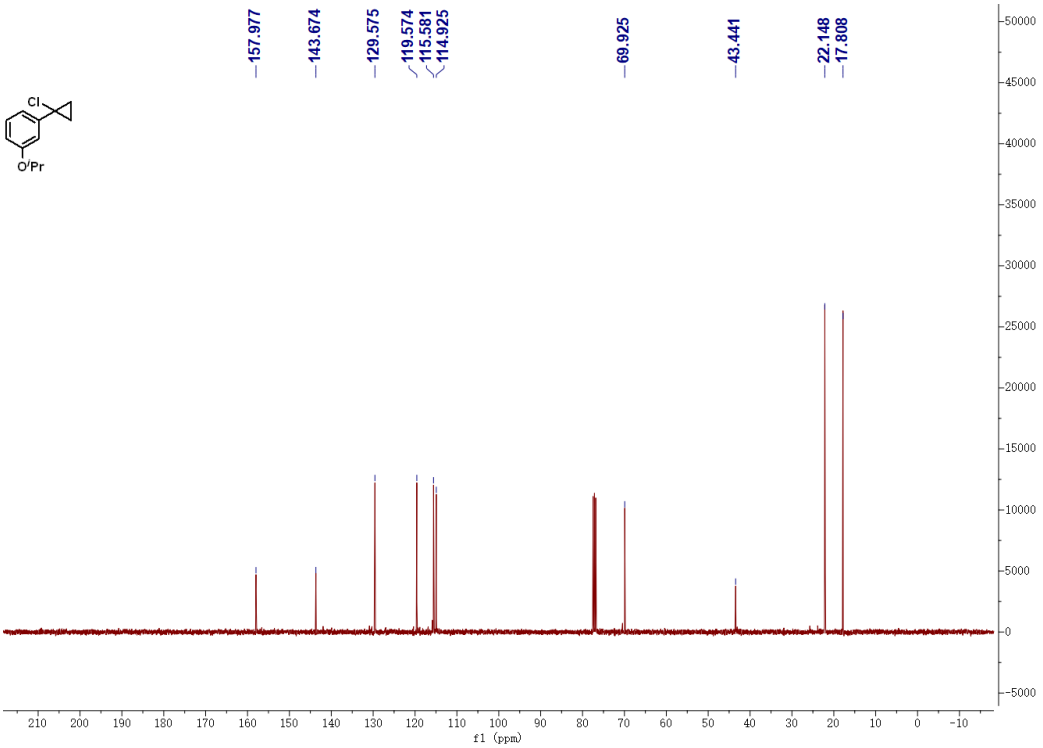
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2g**



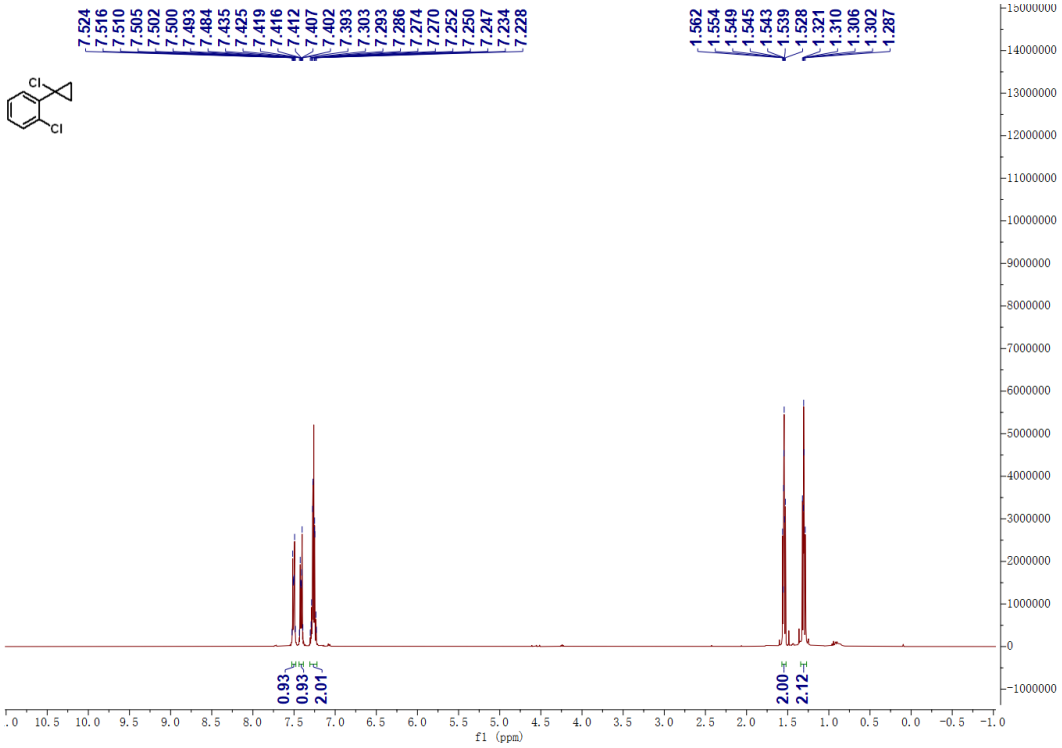
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2h**



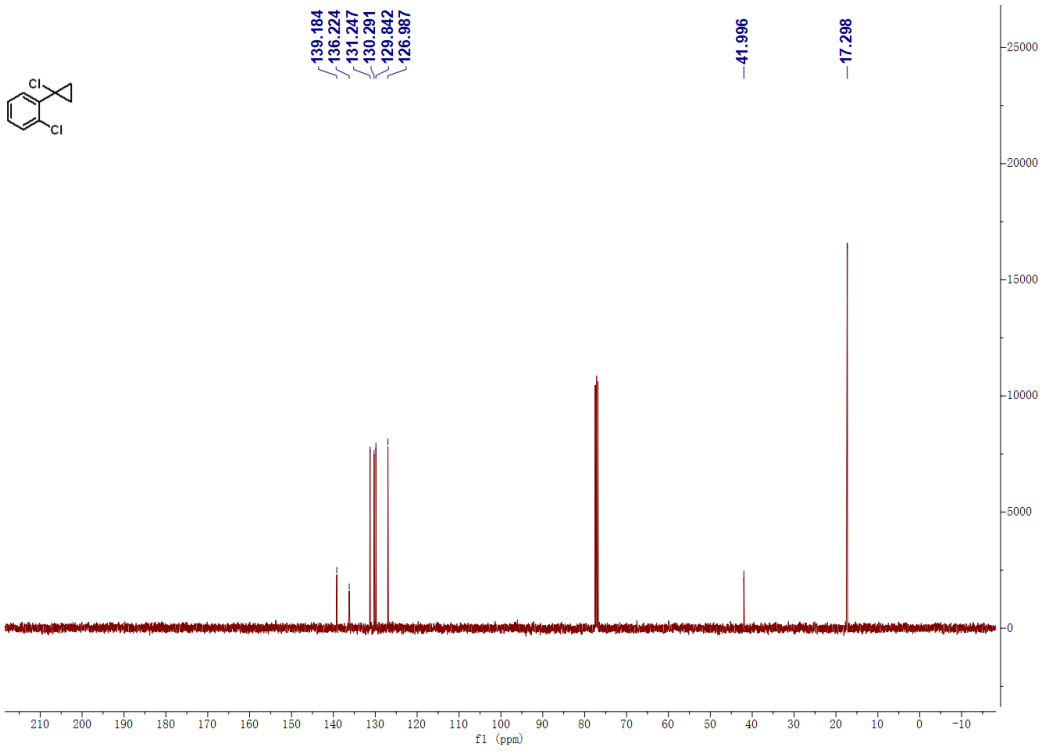
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2h**



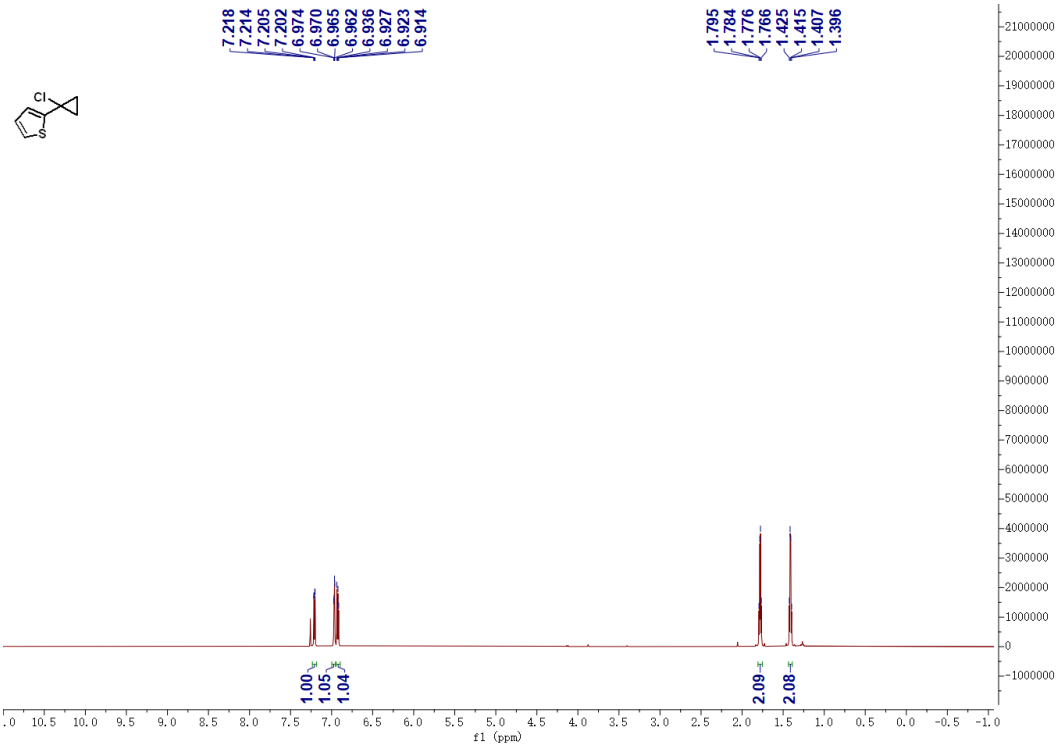
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2i**



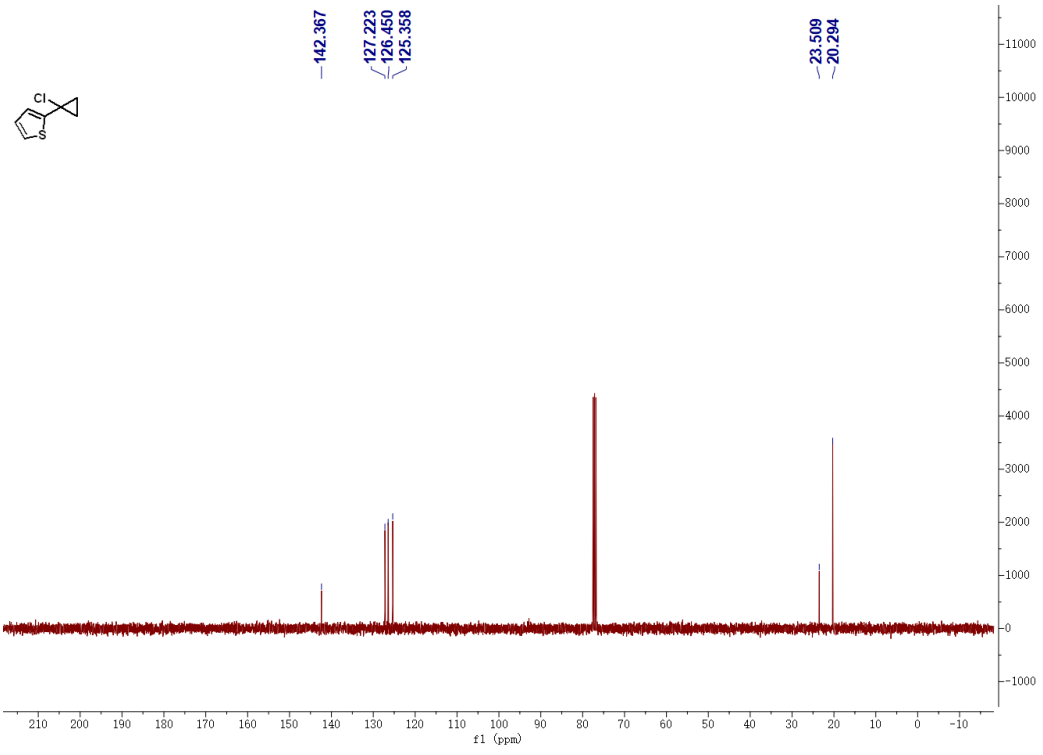
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2i**



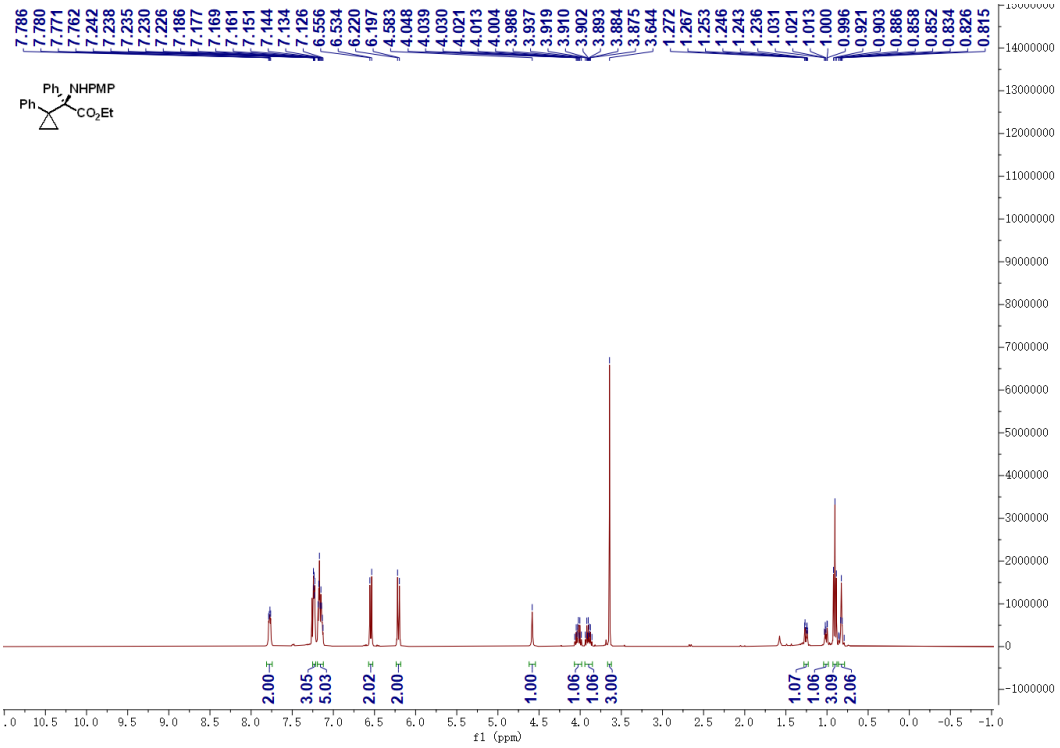
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **2g**



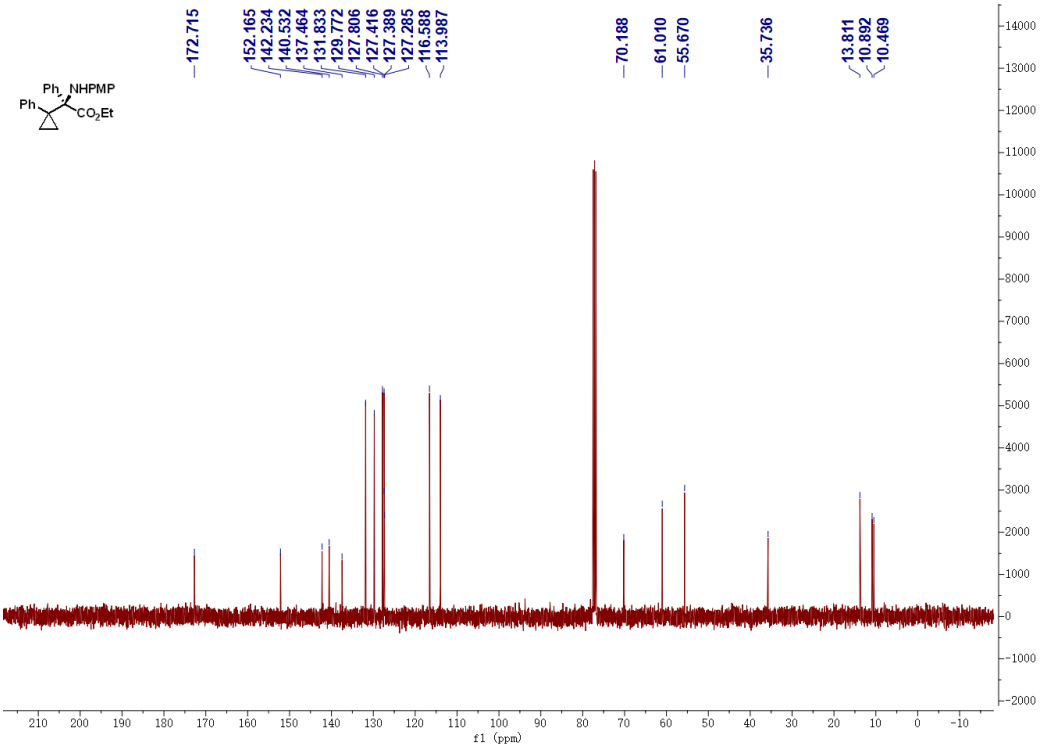
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **2g**



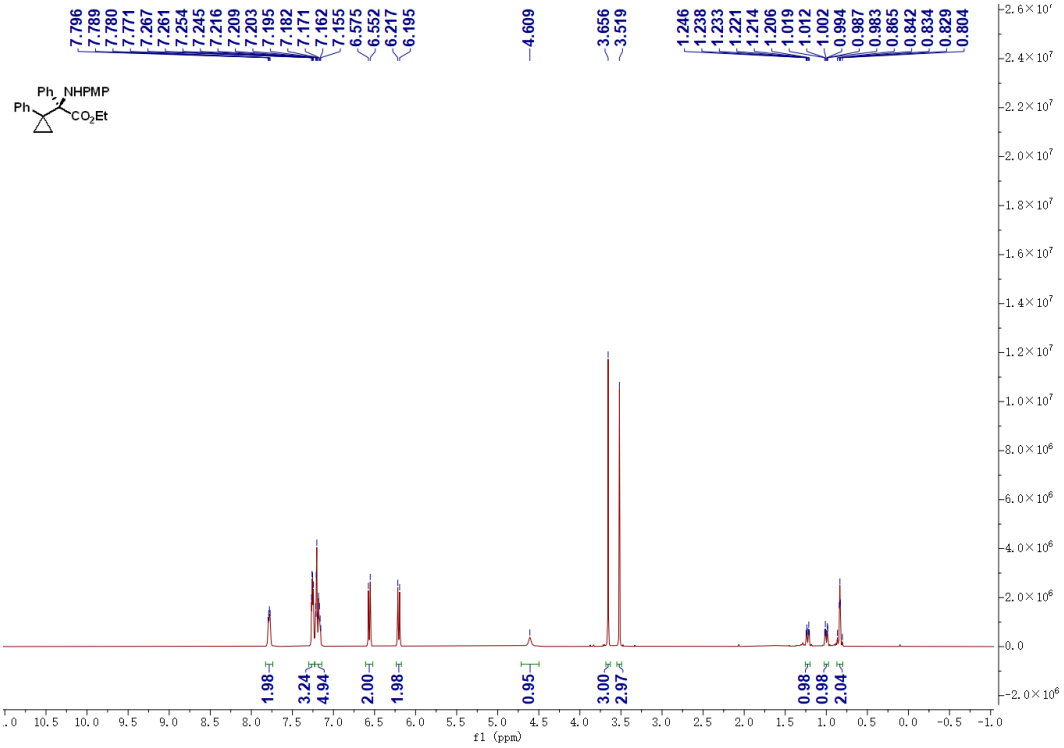
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3a**



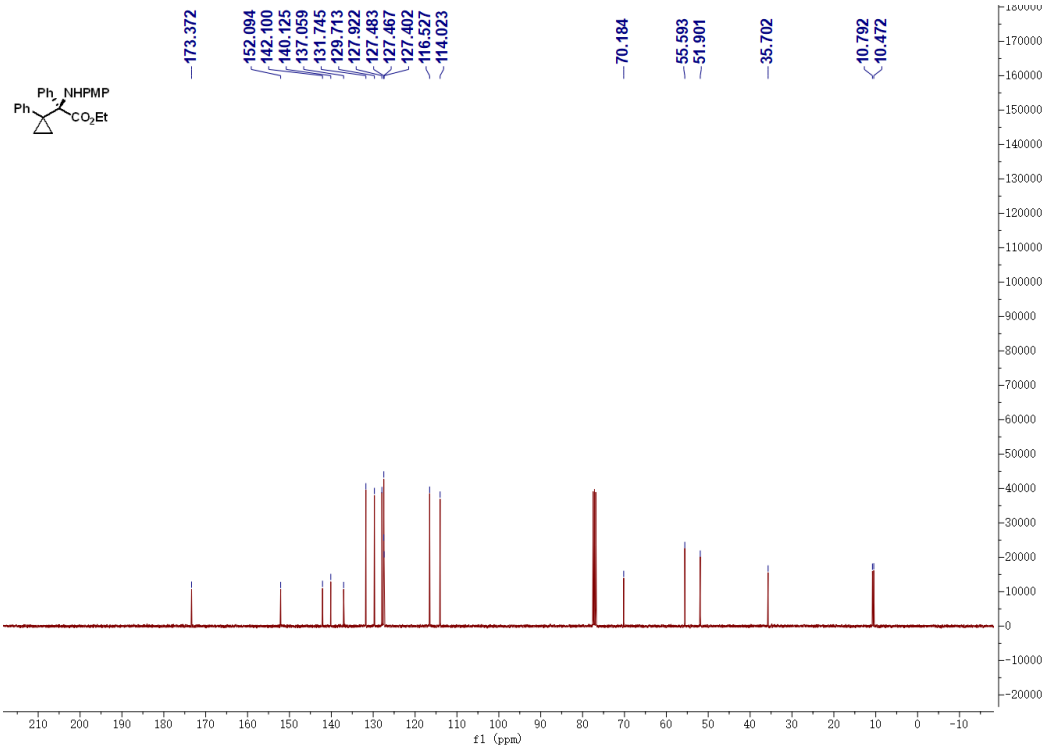
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3a**



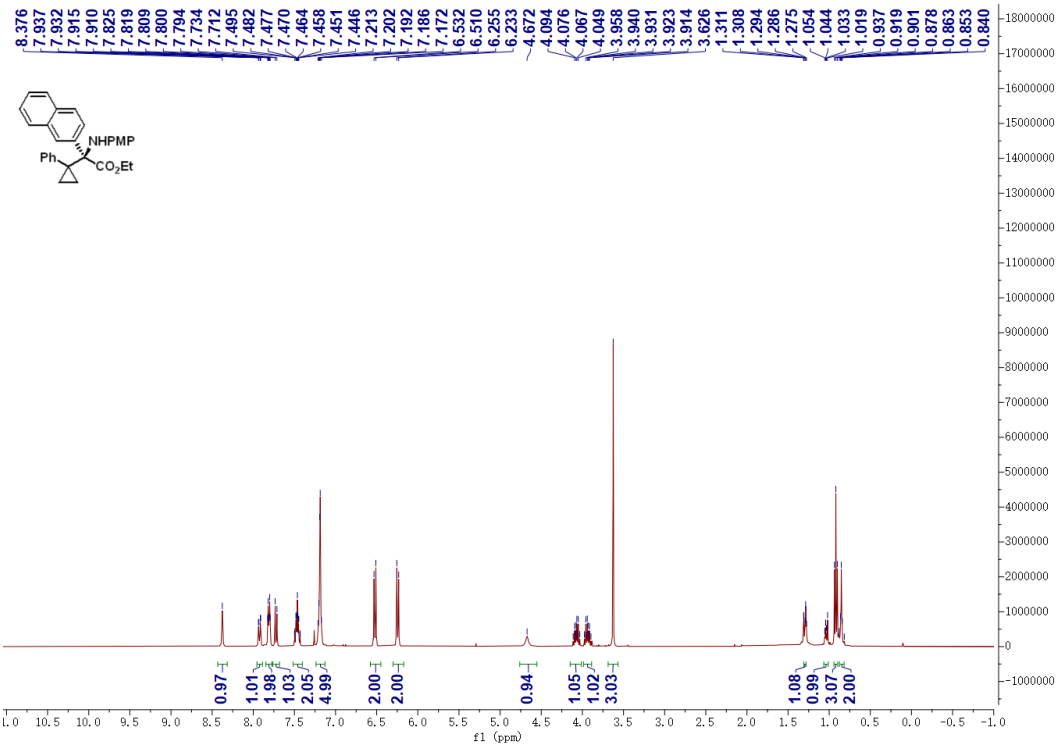
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3b**



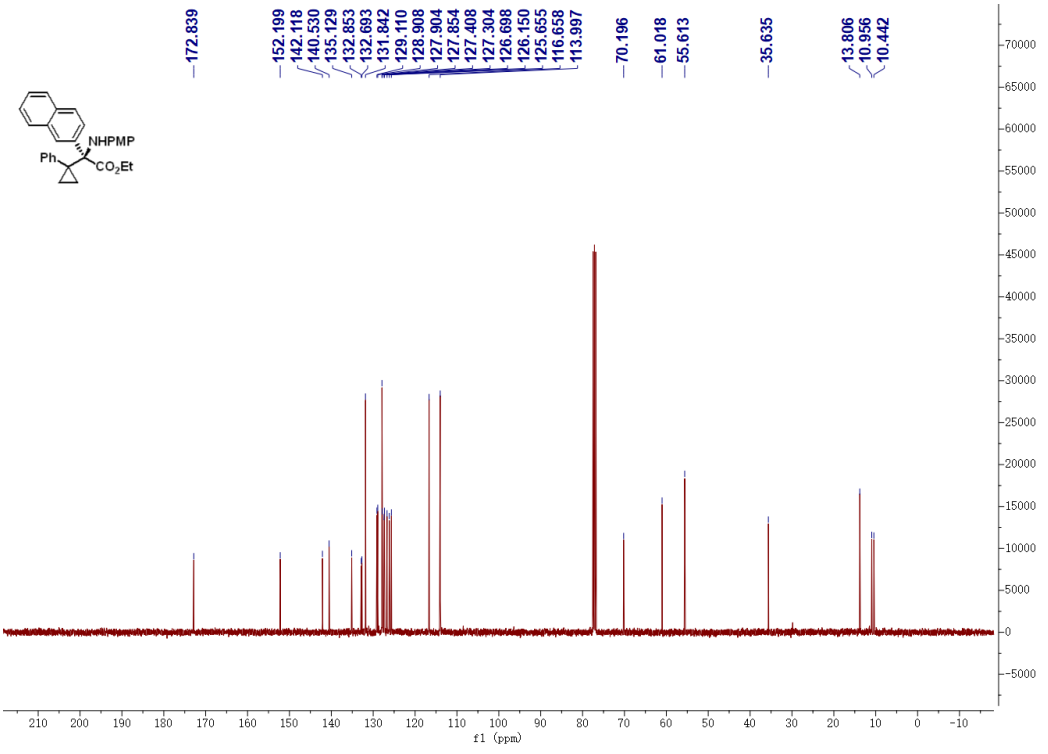
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3b**



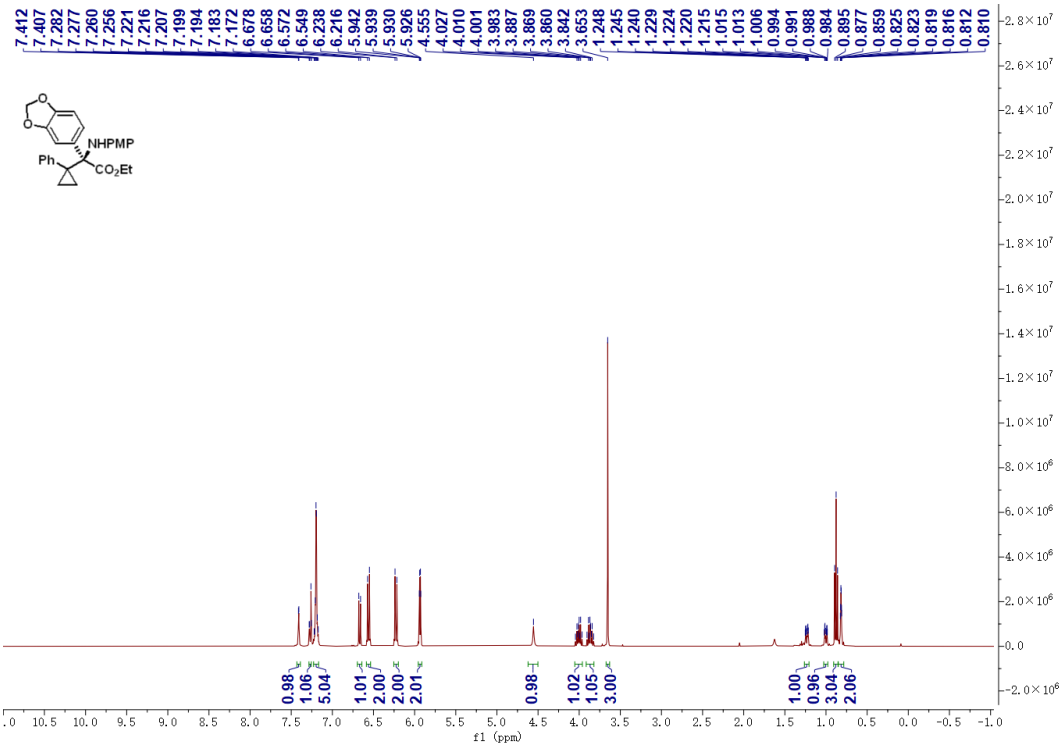
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3c**



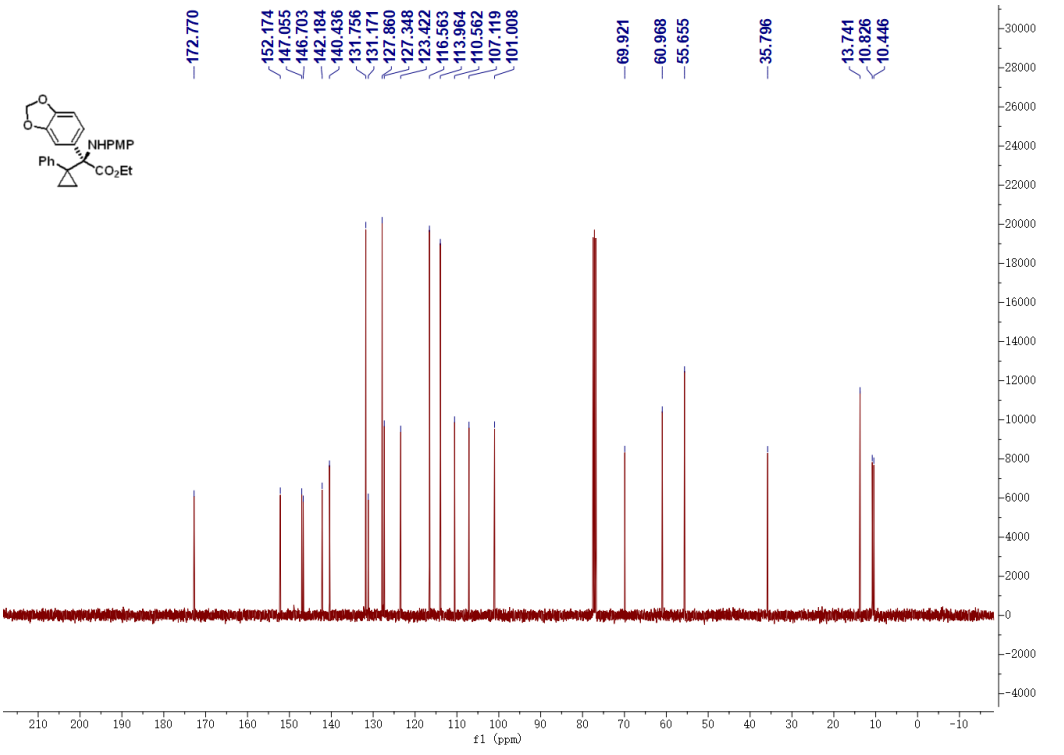
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3c**



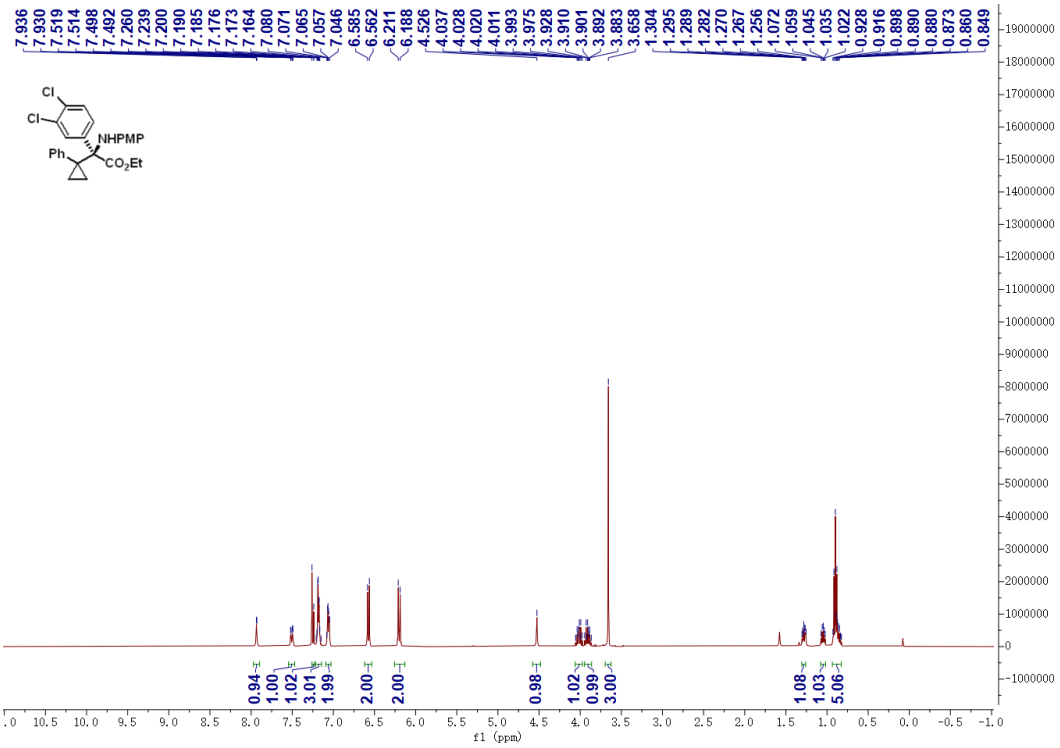
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3d**



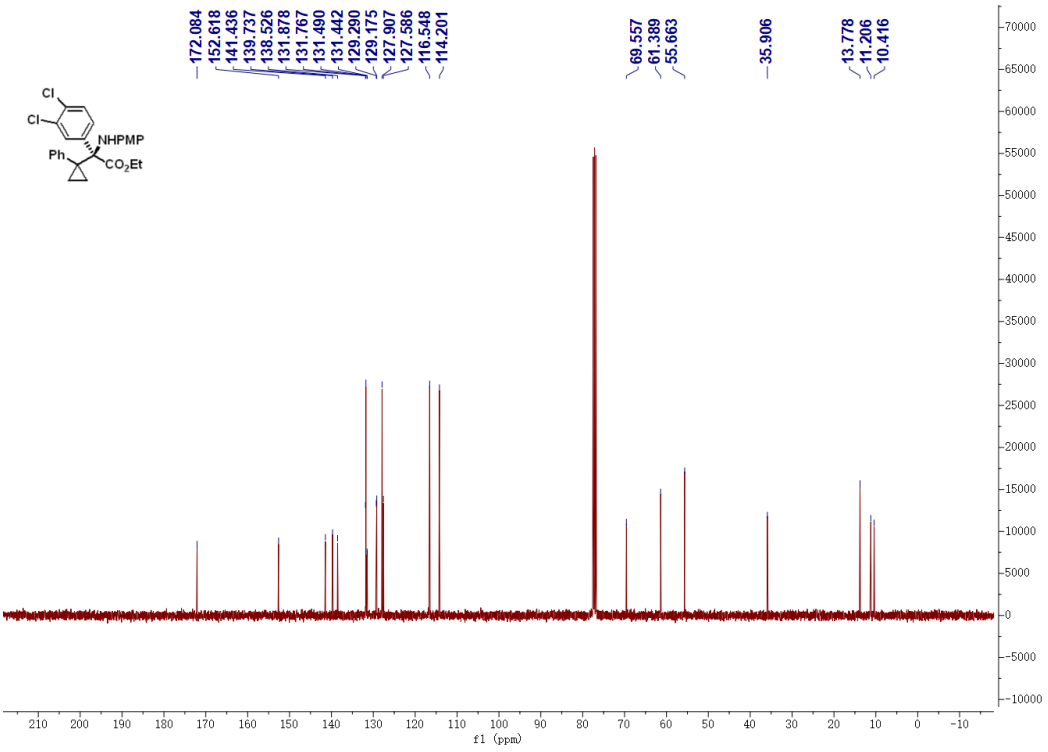
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3d**



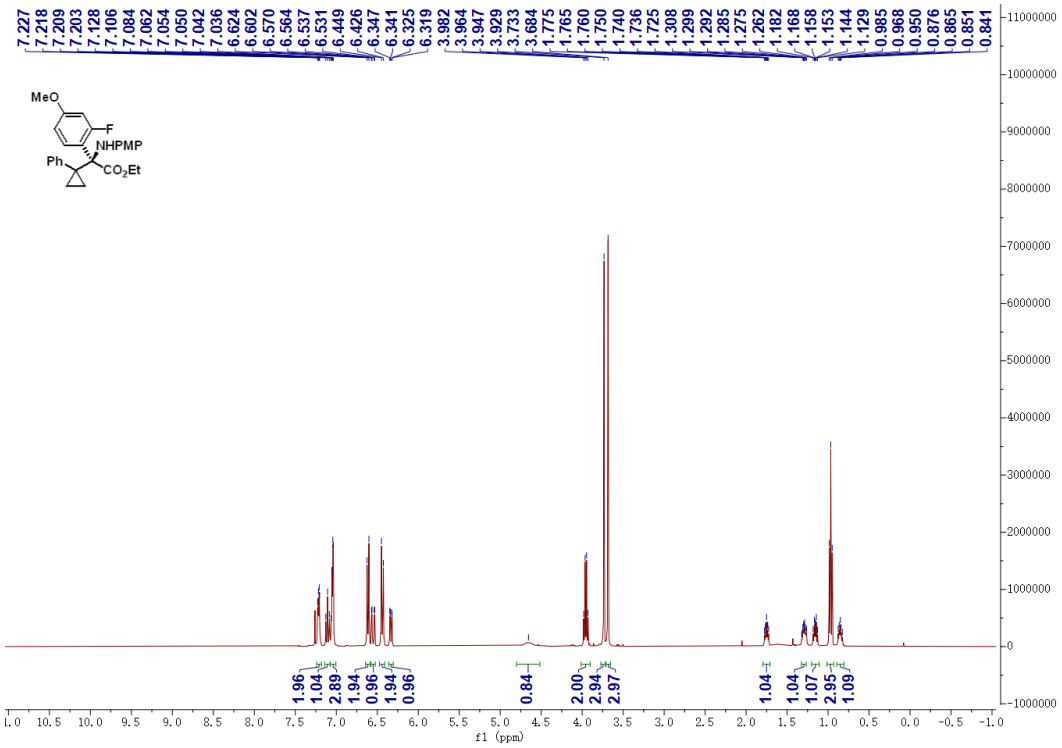
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3e**



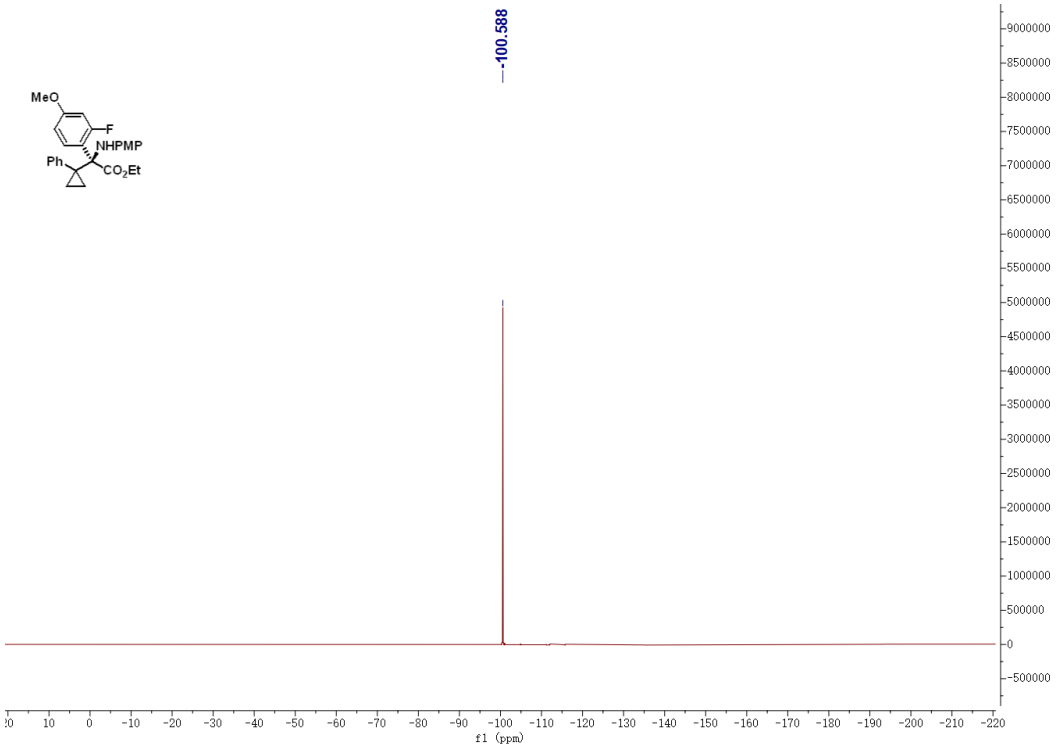
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3e**



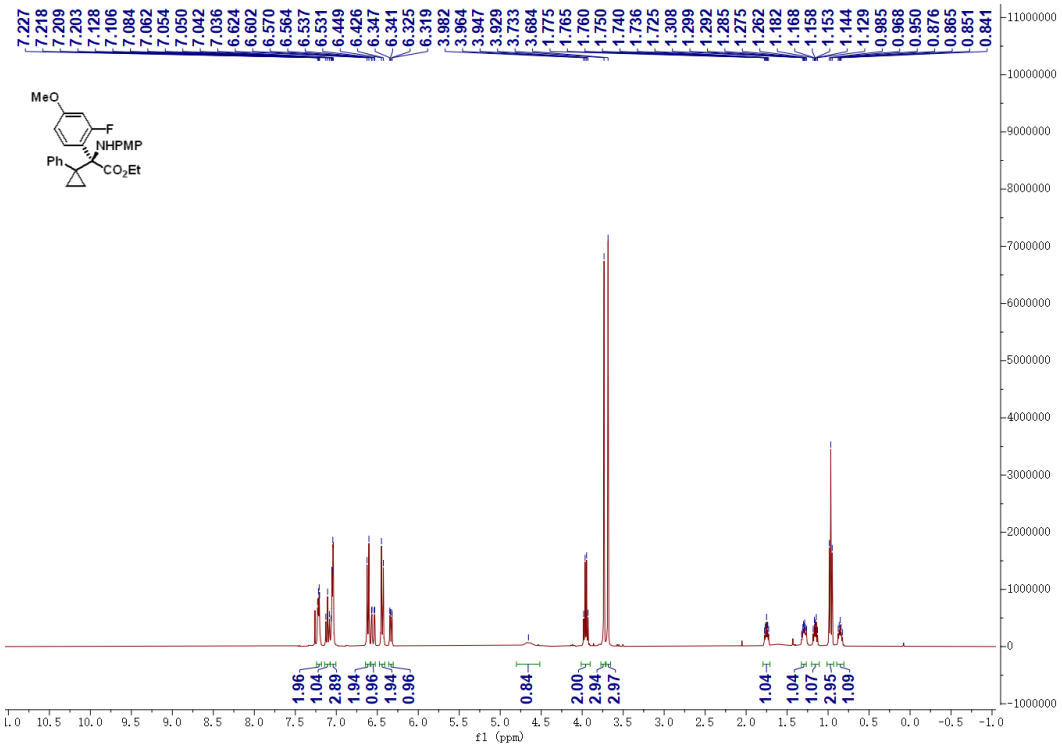
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3f**



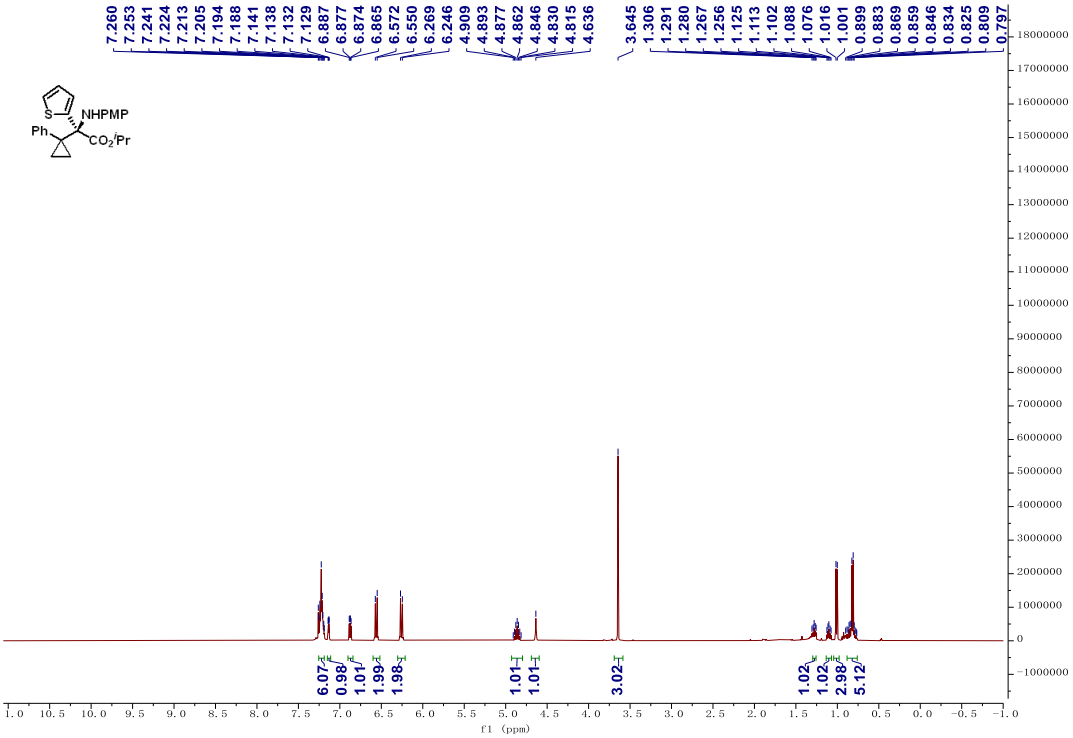
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3f**



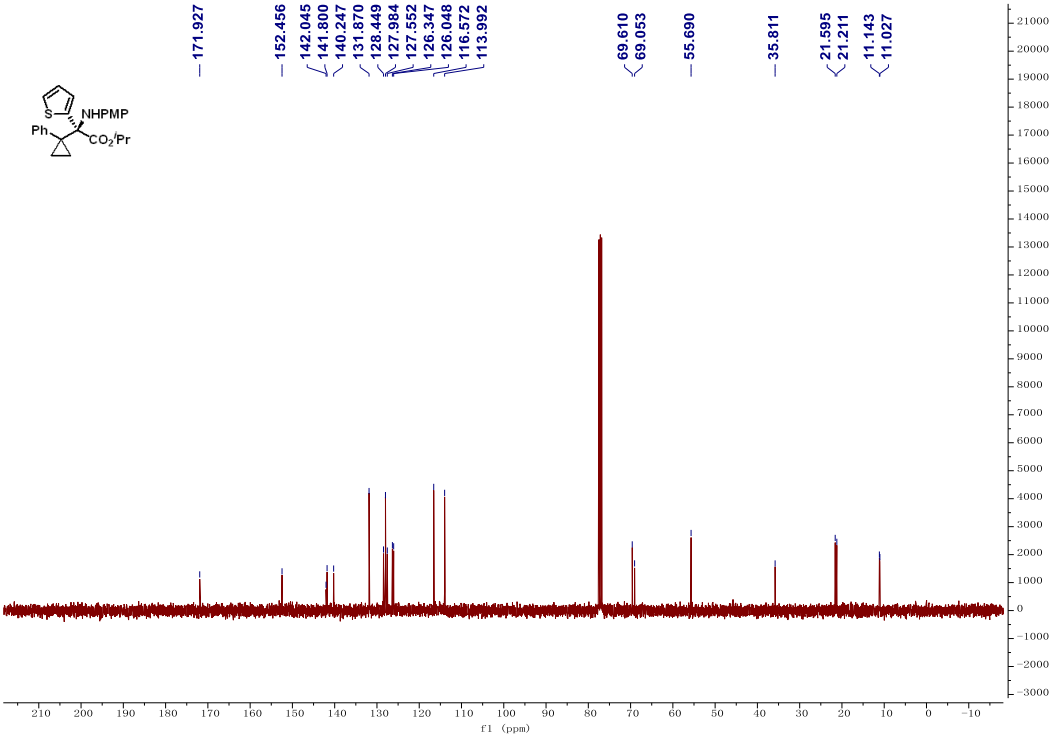
^{19}F NMR-spectrum (376 MHz, $CDCl_3$) of **3a**



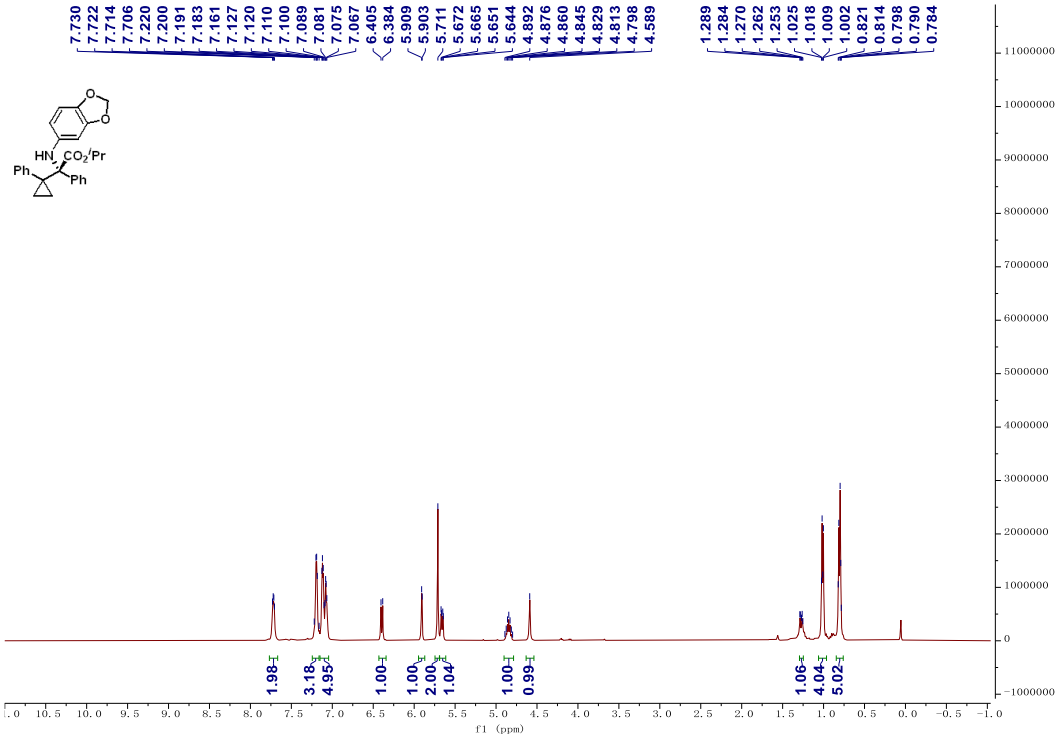
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3g**



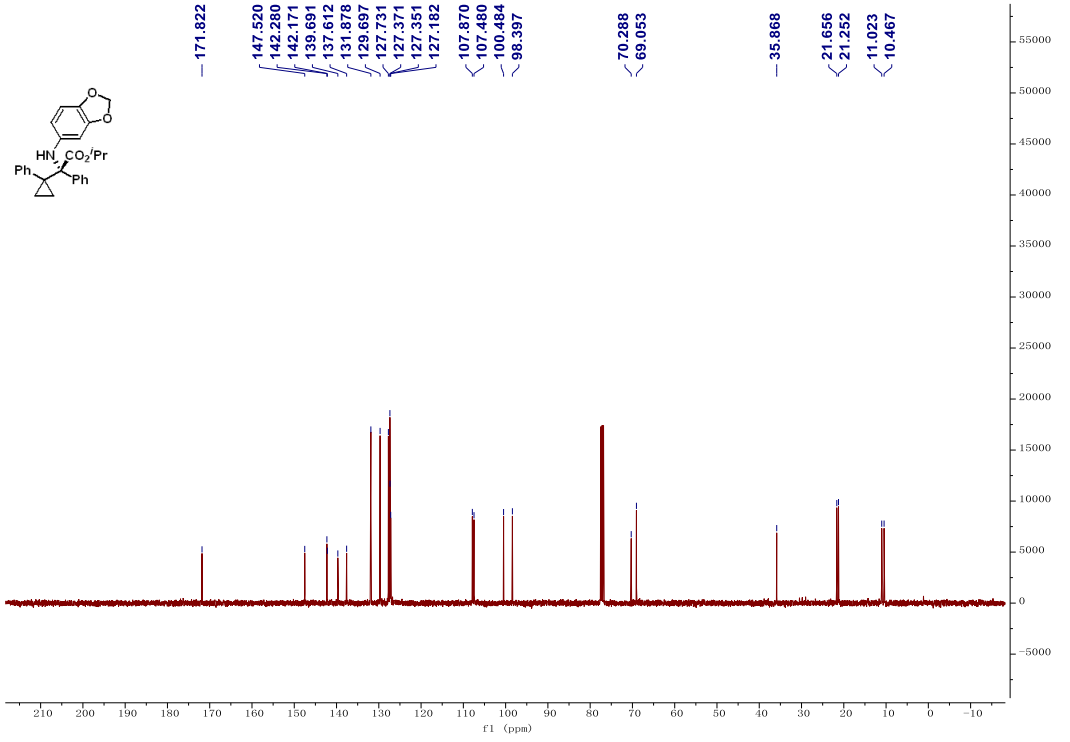
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3g**



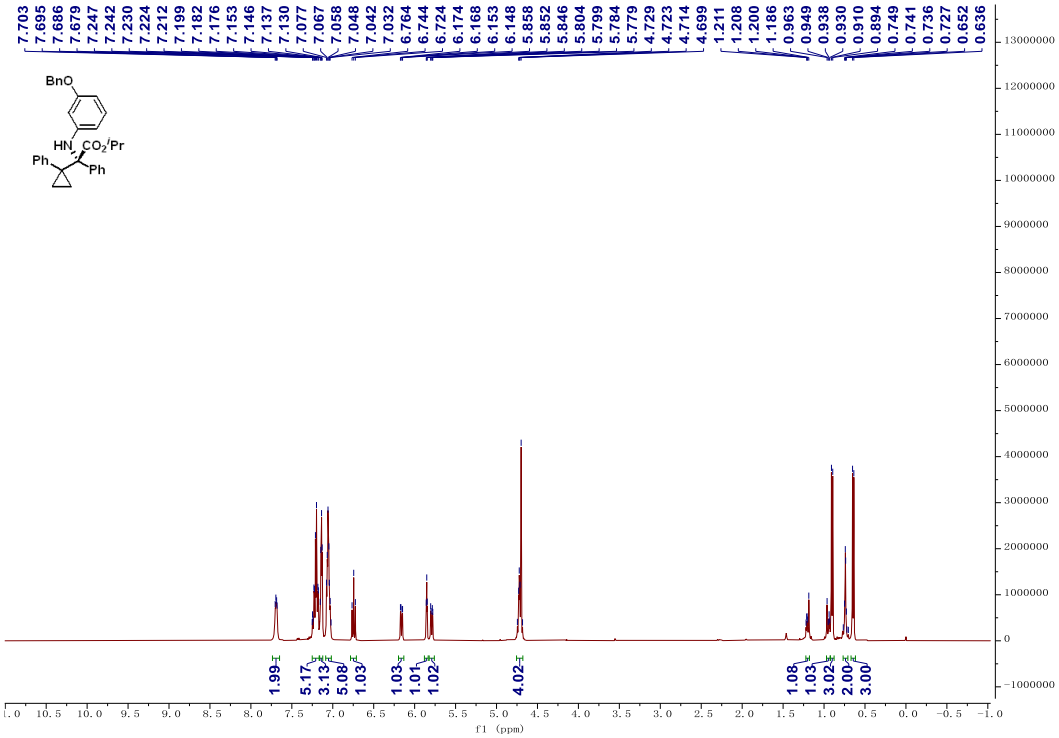
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3h**



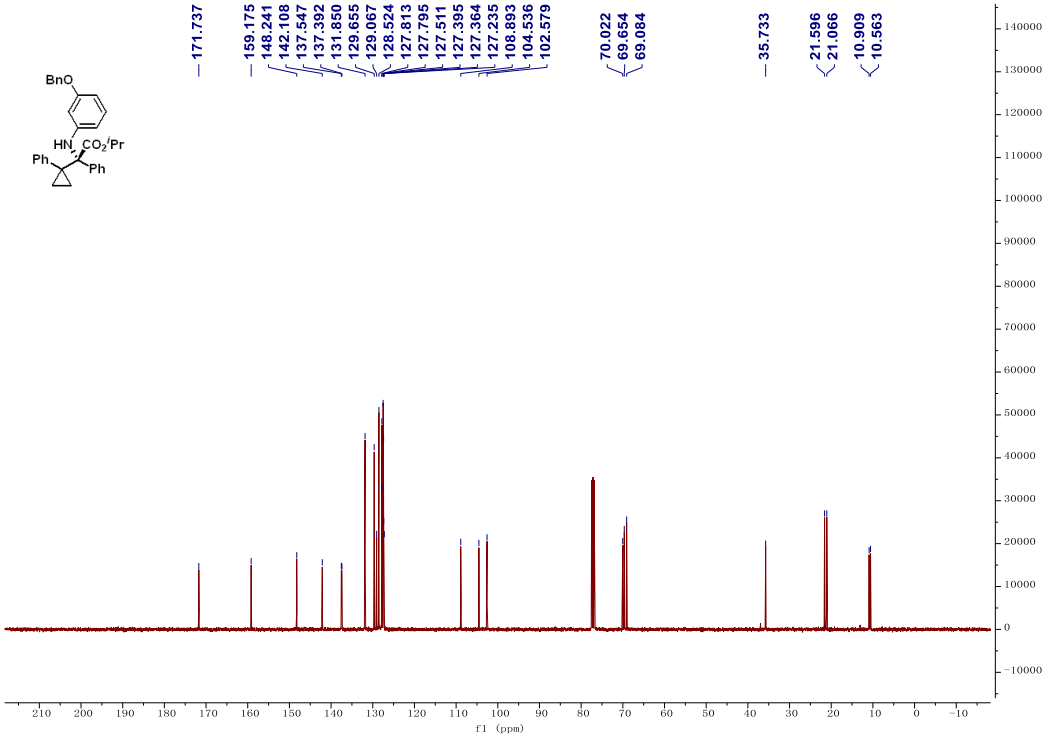
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3h**



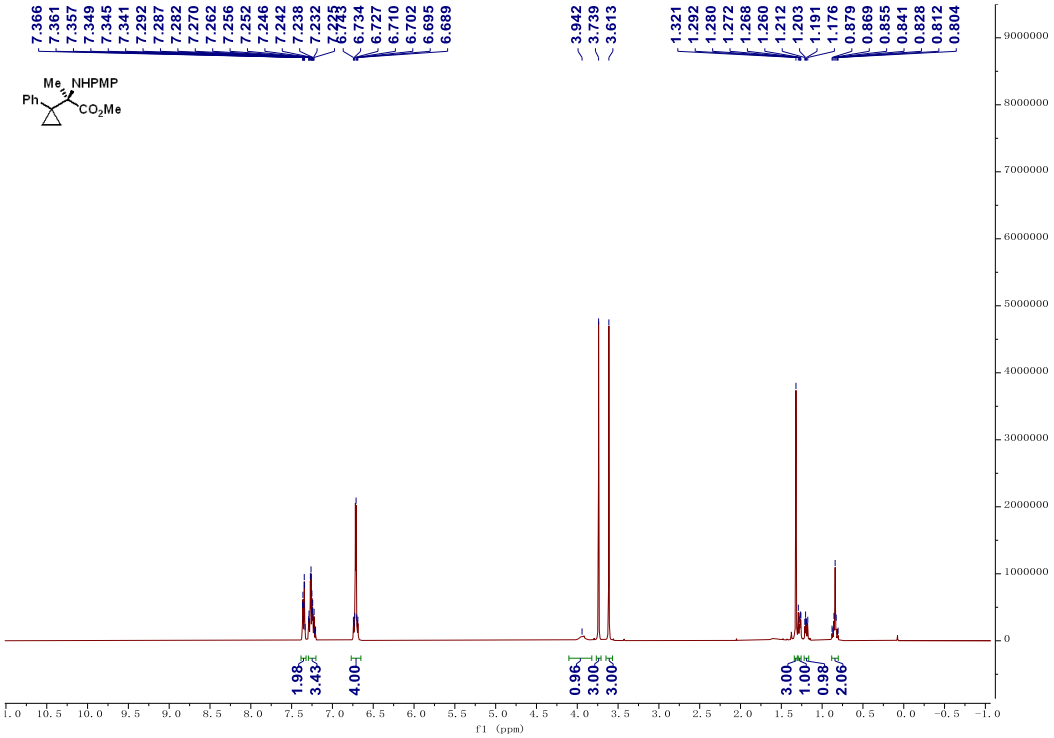
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3i**



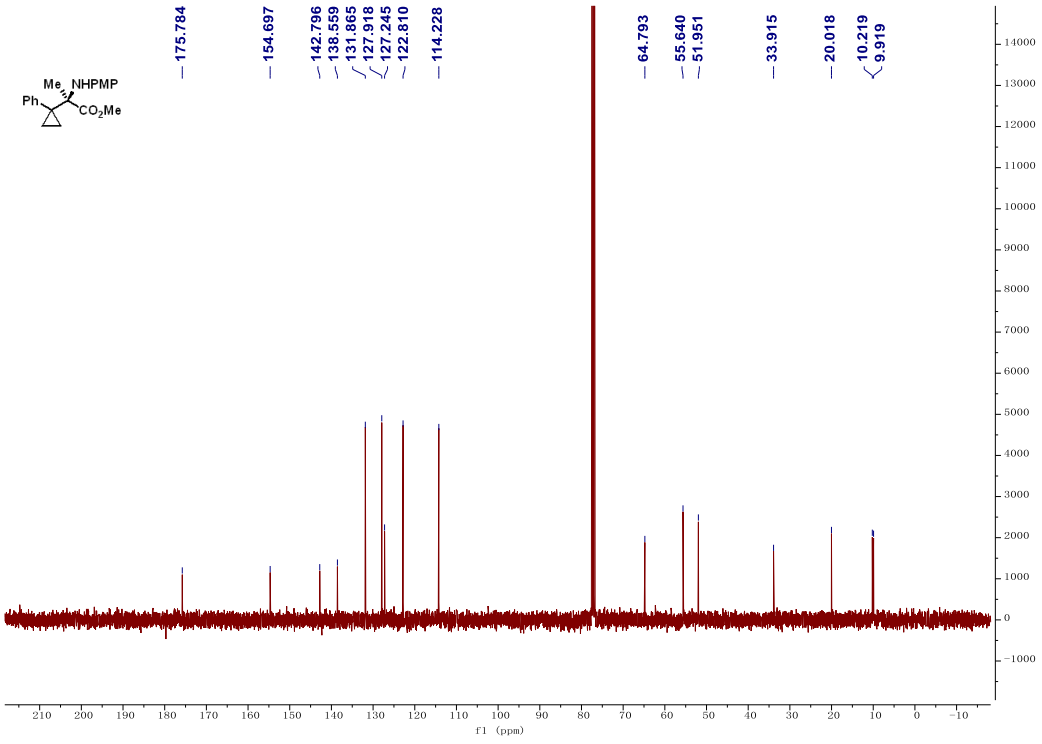
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3i**



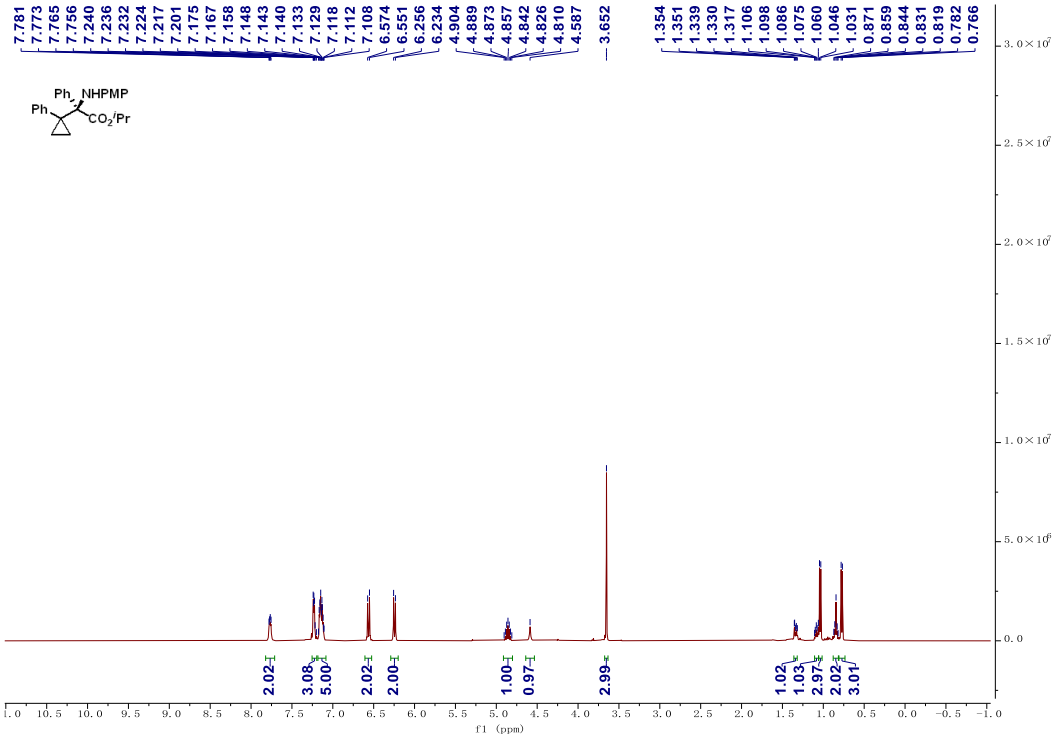
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3j**



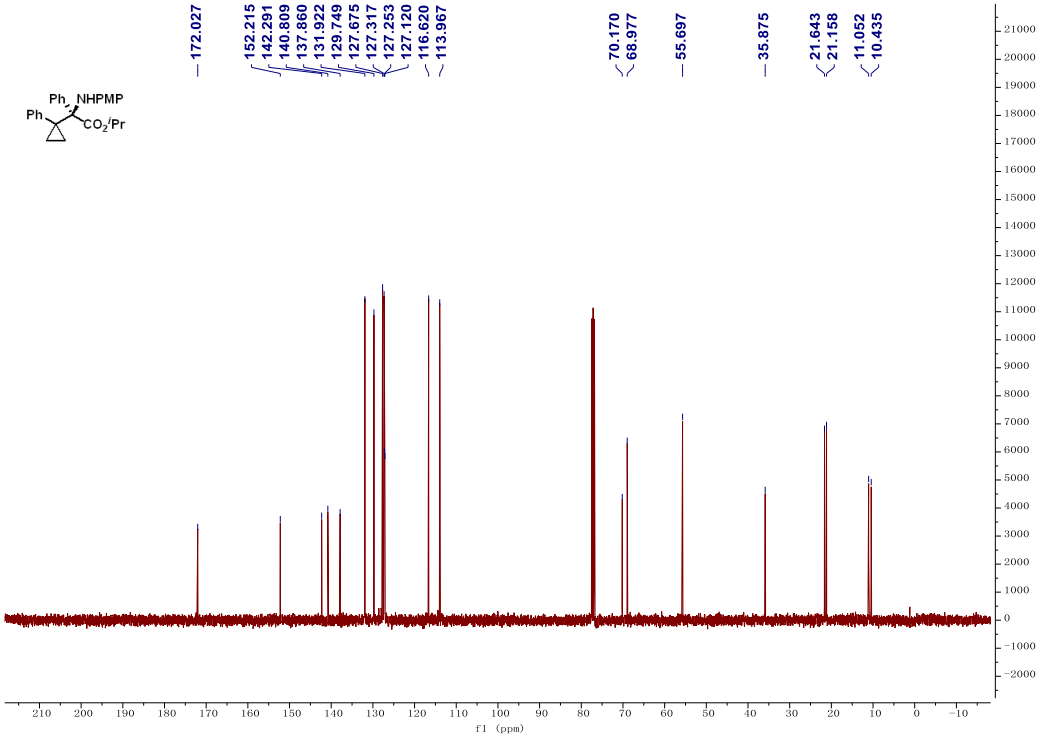
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3j**



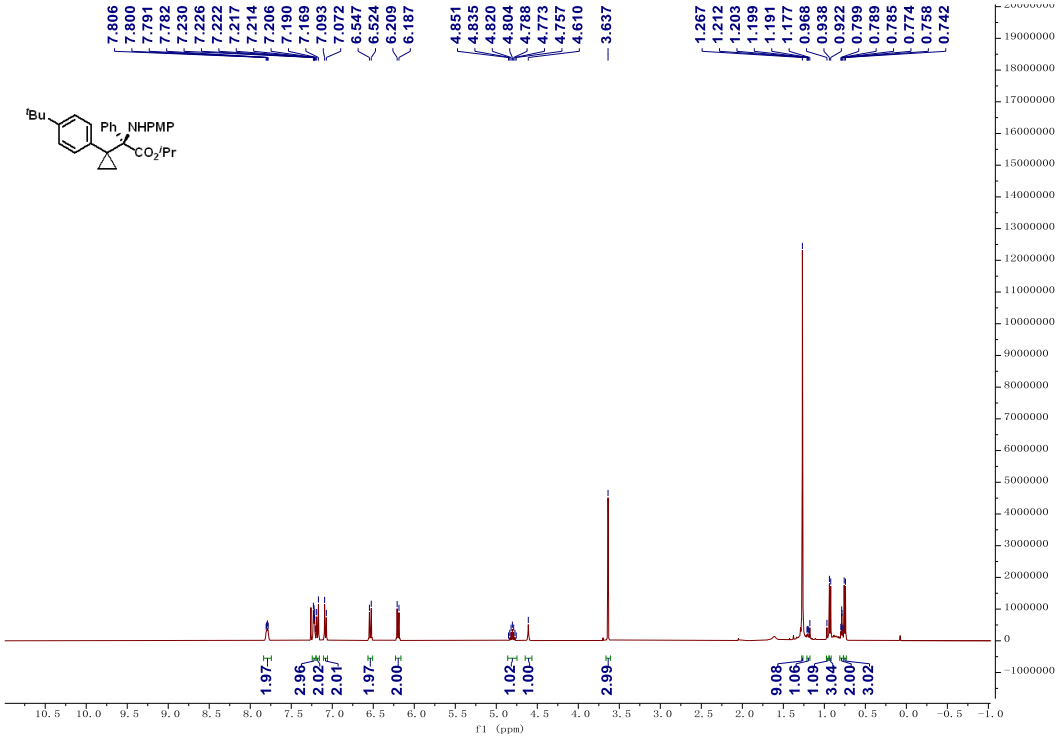
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3k**



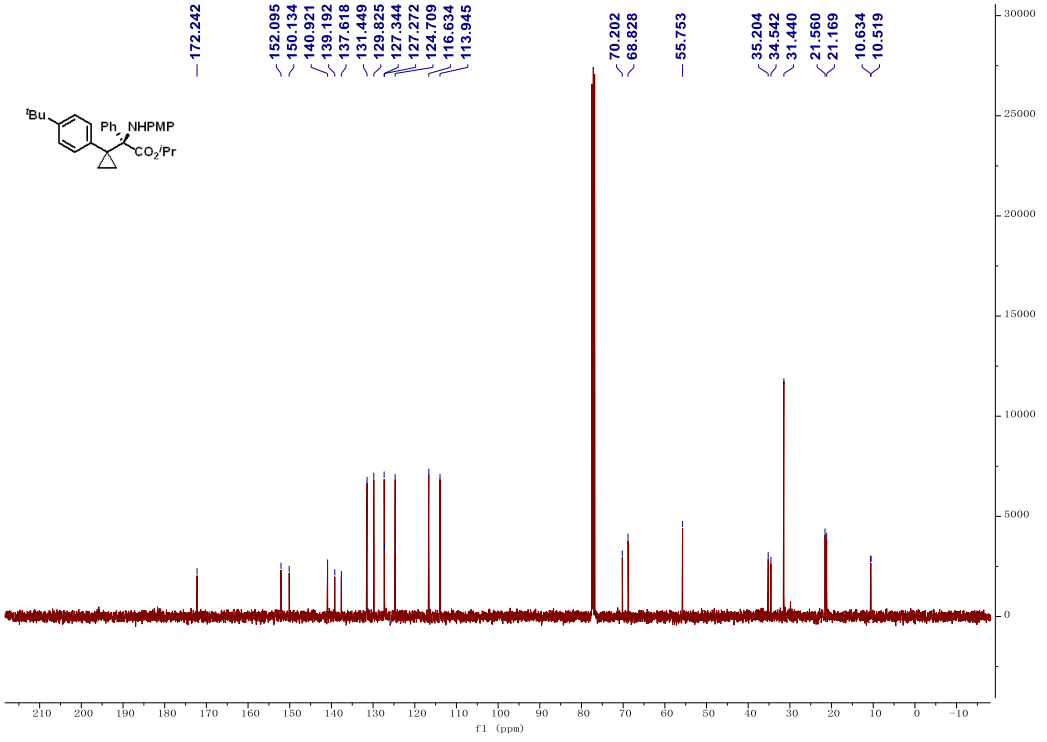
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3k**



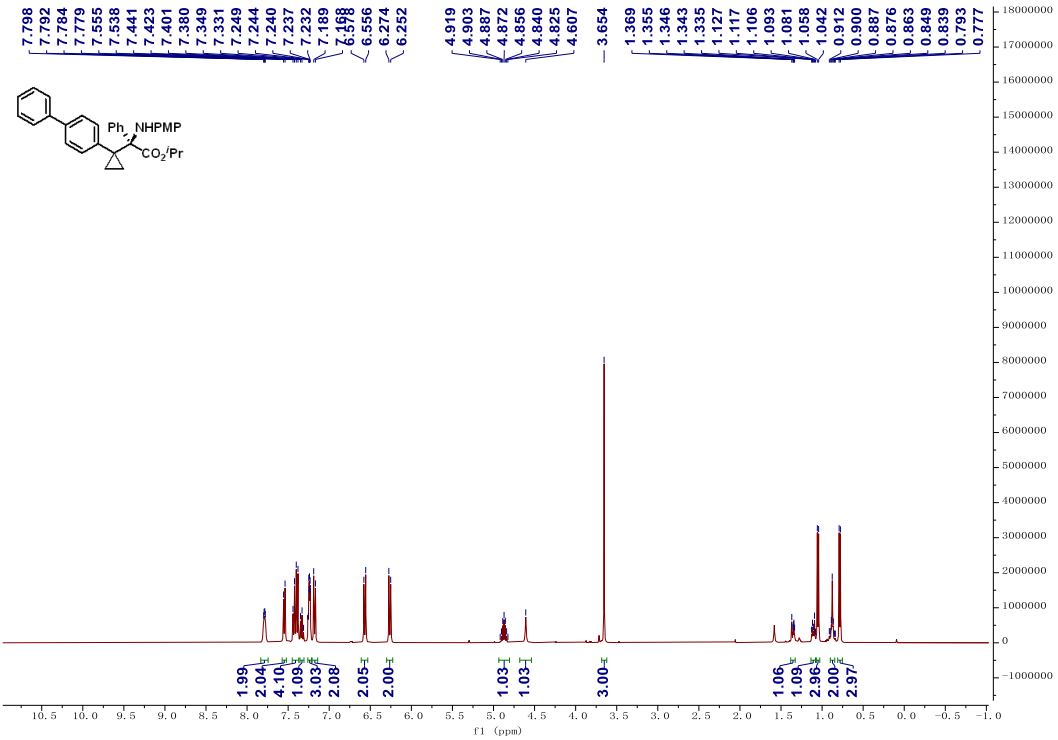
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3l**



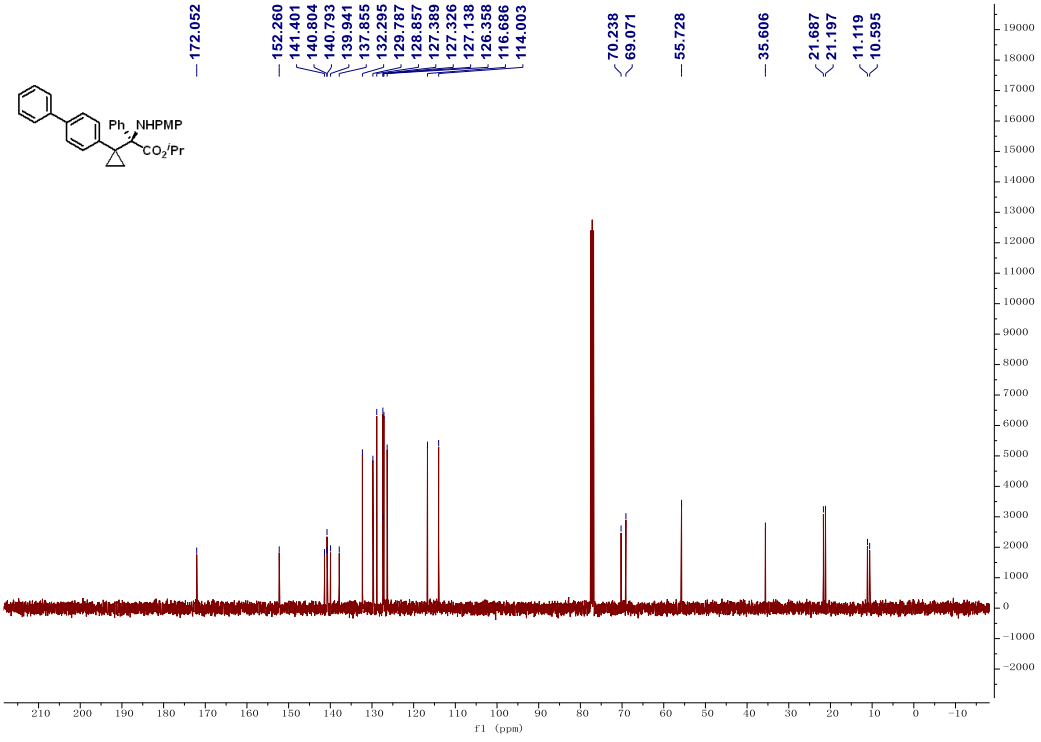
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3l**



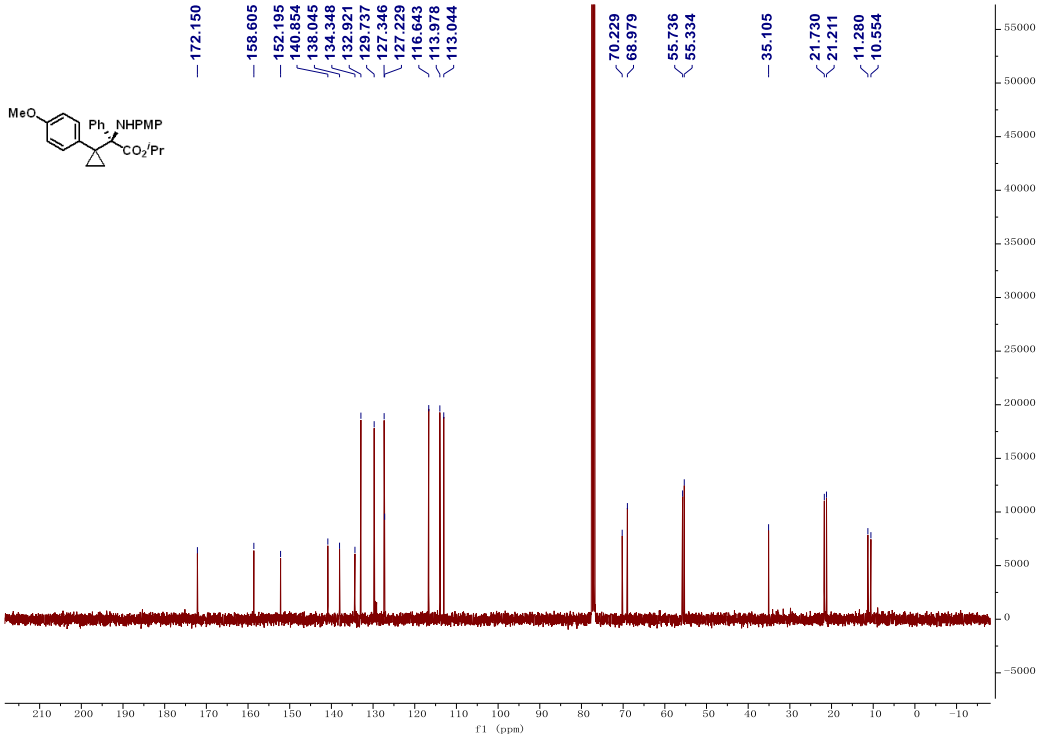
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3m**



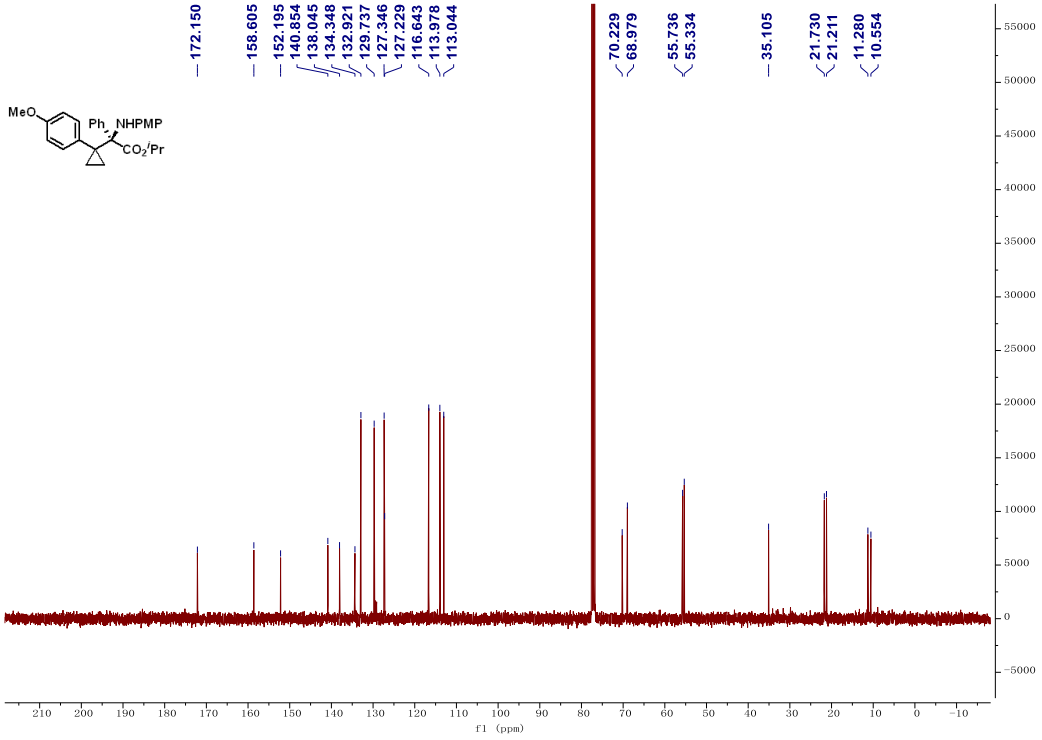
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3m**



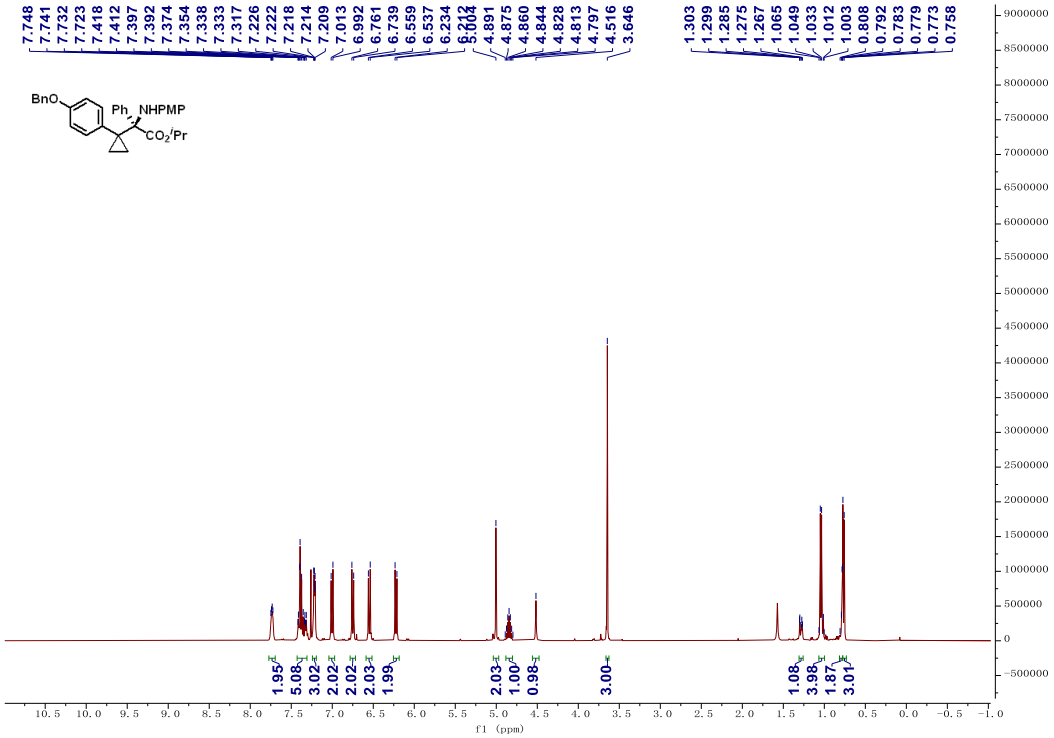
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3n**



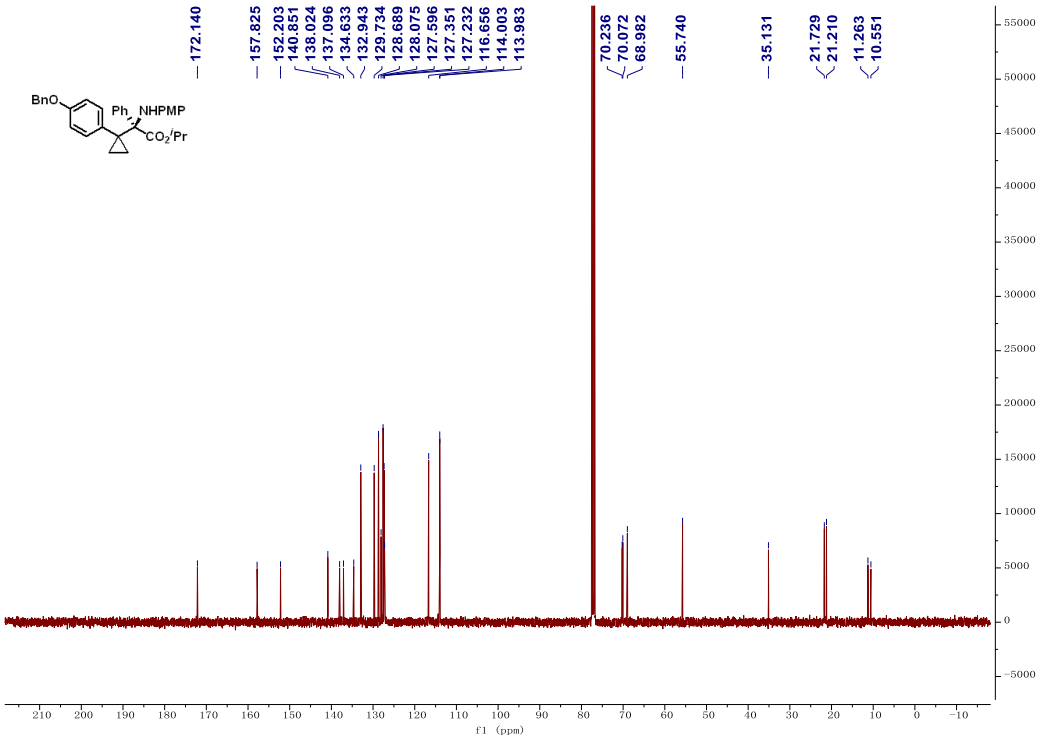
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3n**



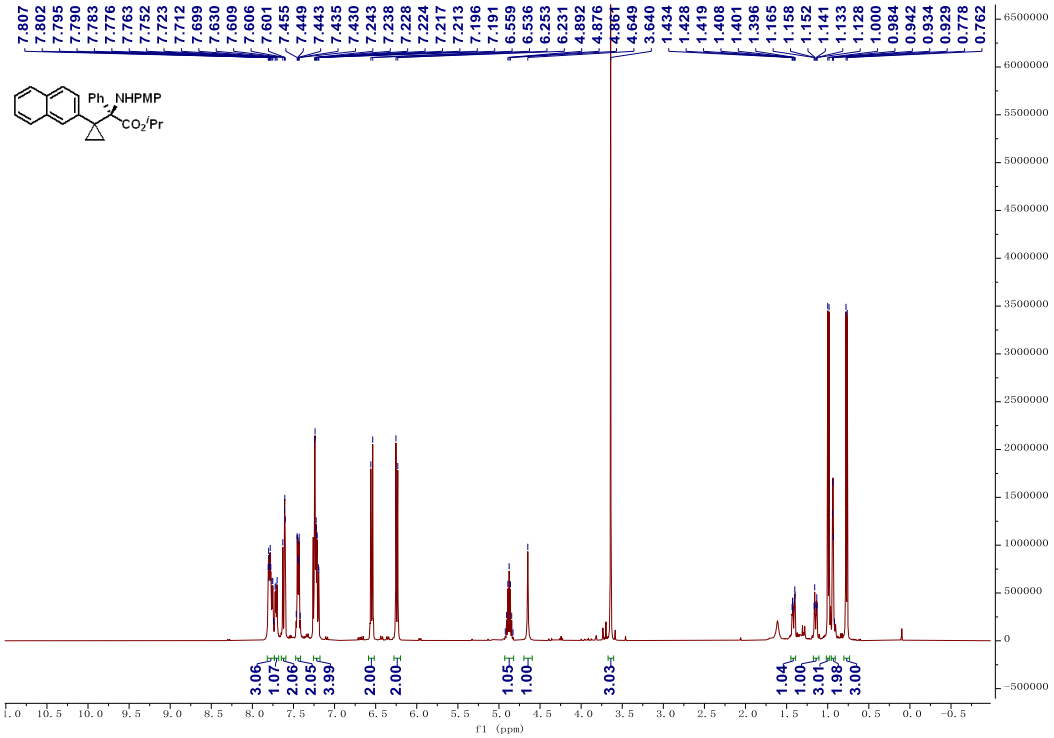
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3o**



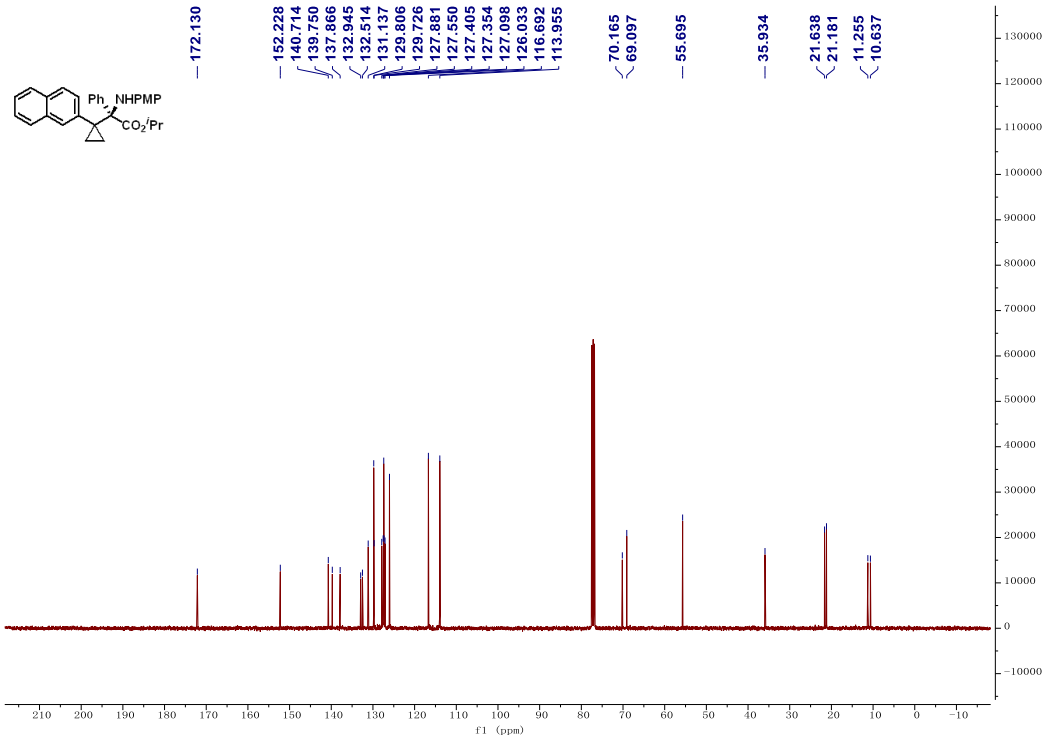
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3o**



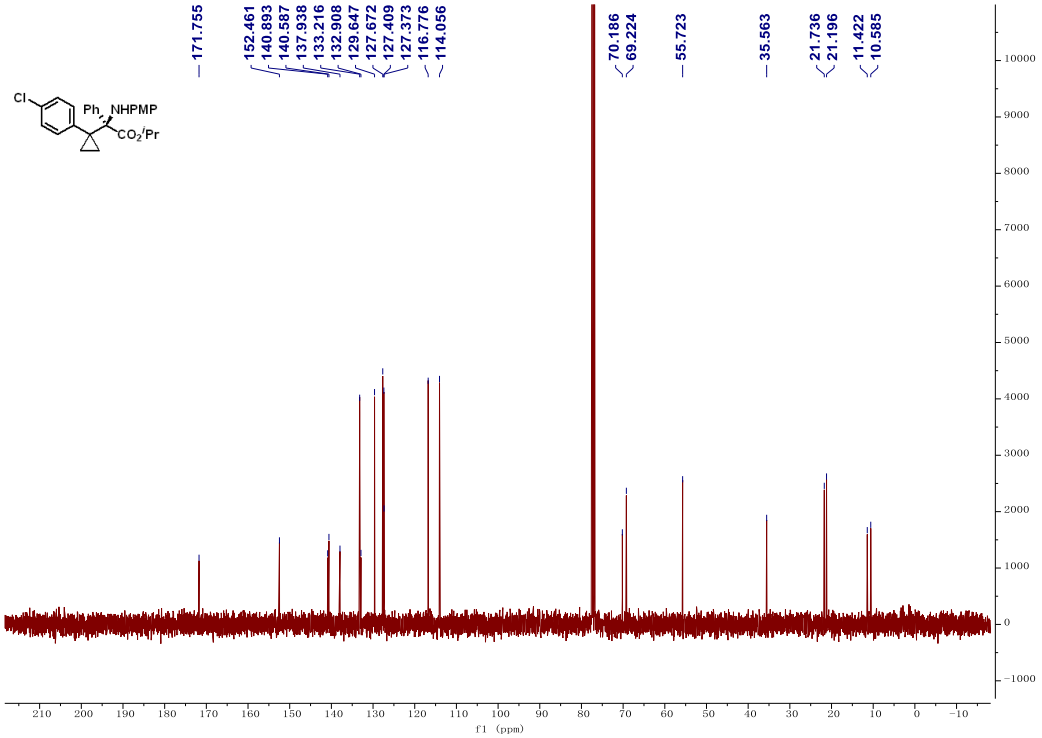
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3p**



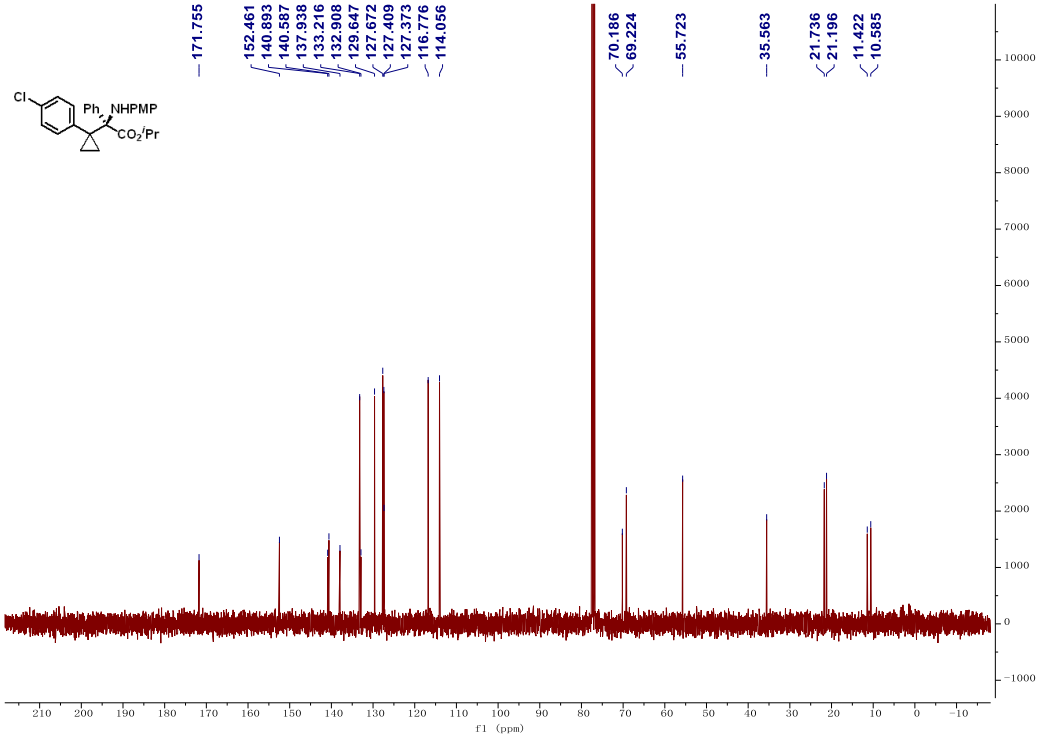
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3p**



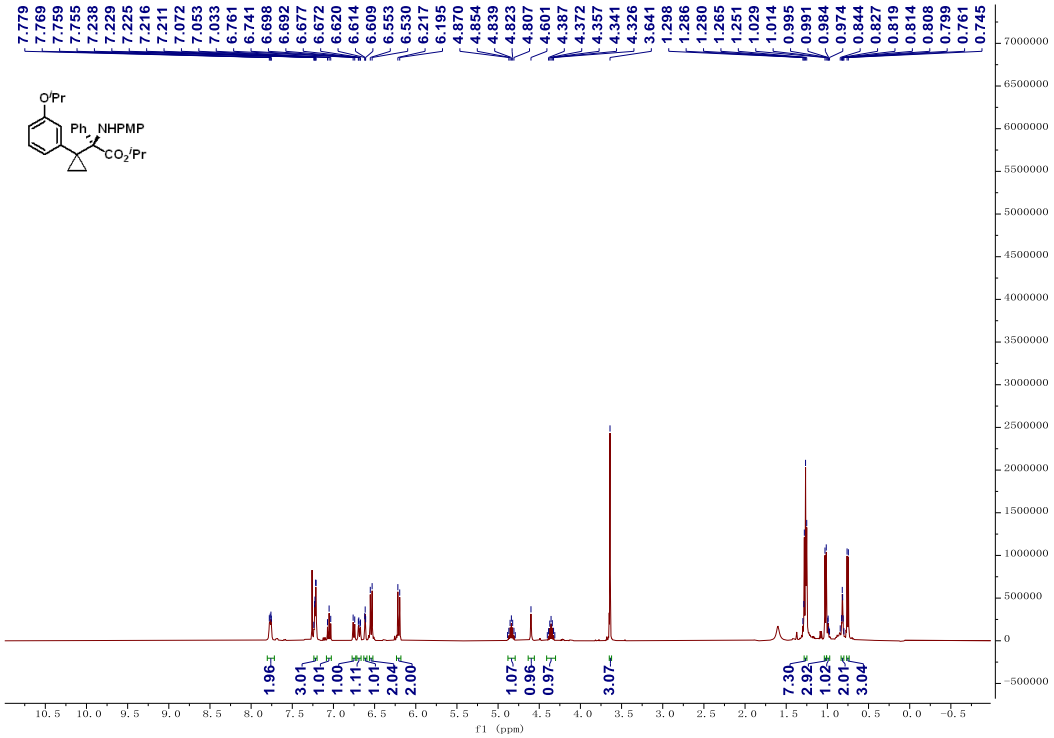
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3q**



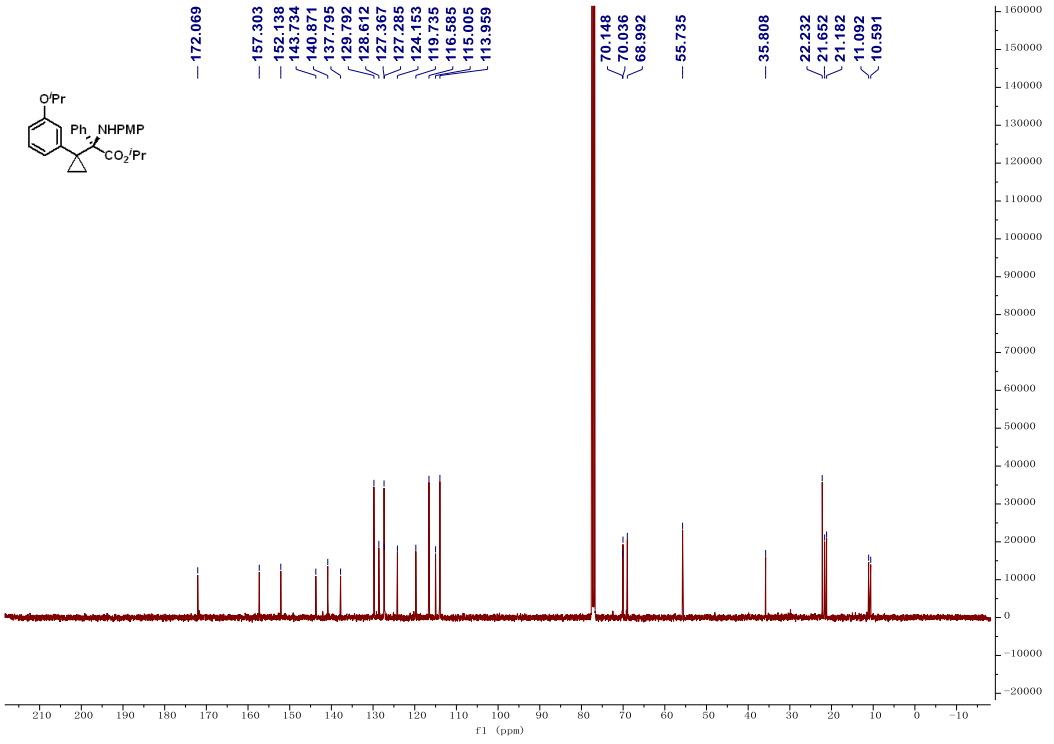
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3q**



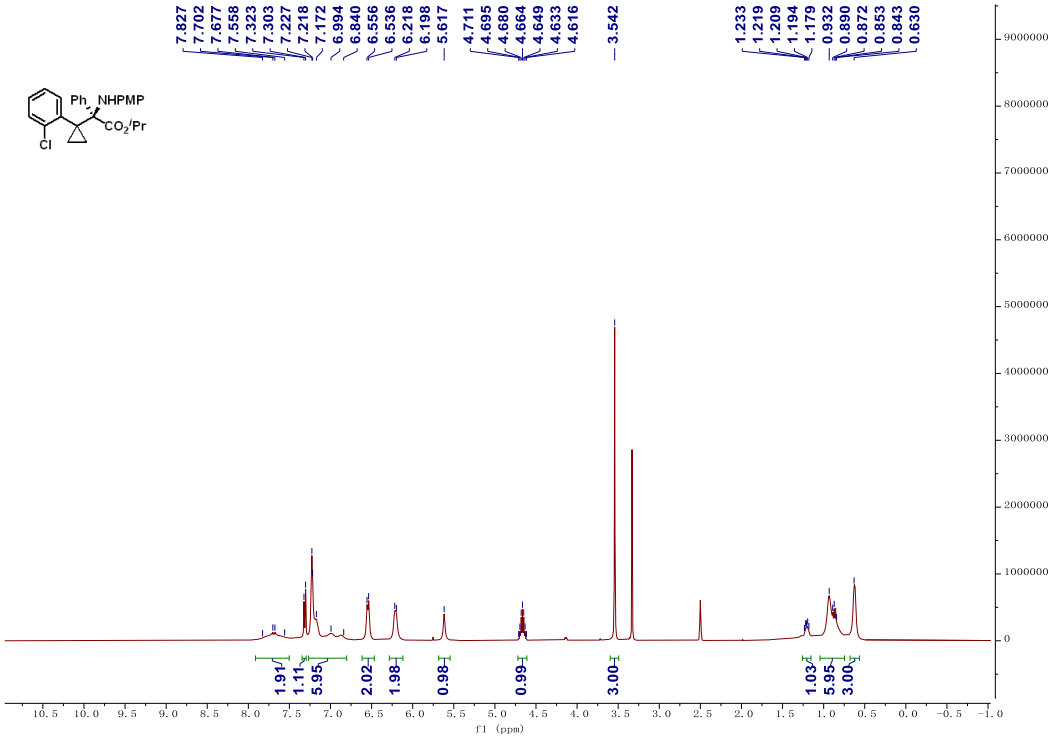
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3r**



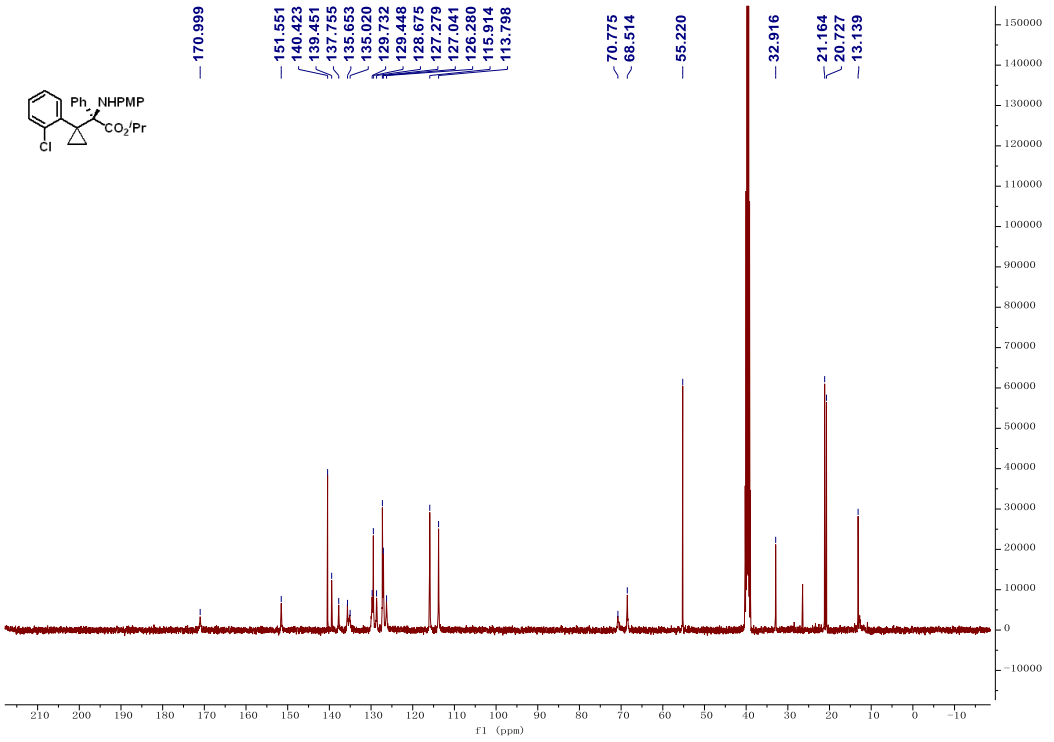
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3r**



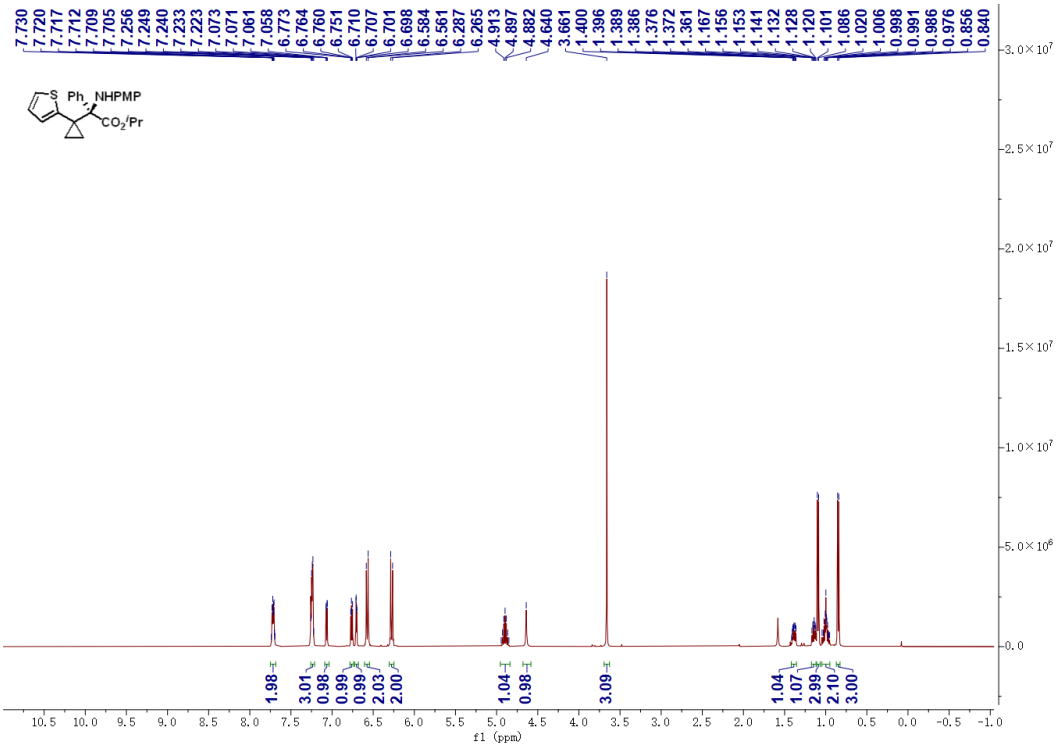
^{1}H NMR-spectrum (400 MHz, DMSO-d_6) of **3s**



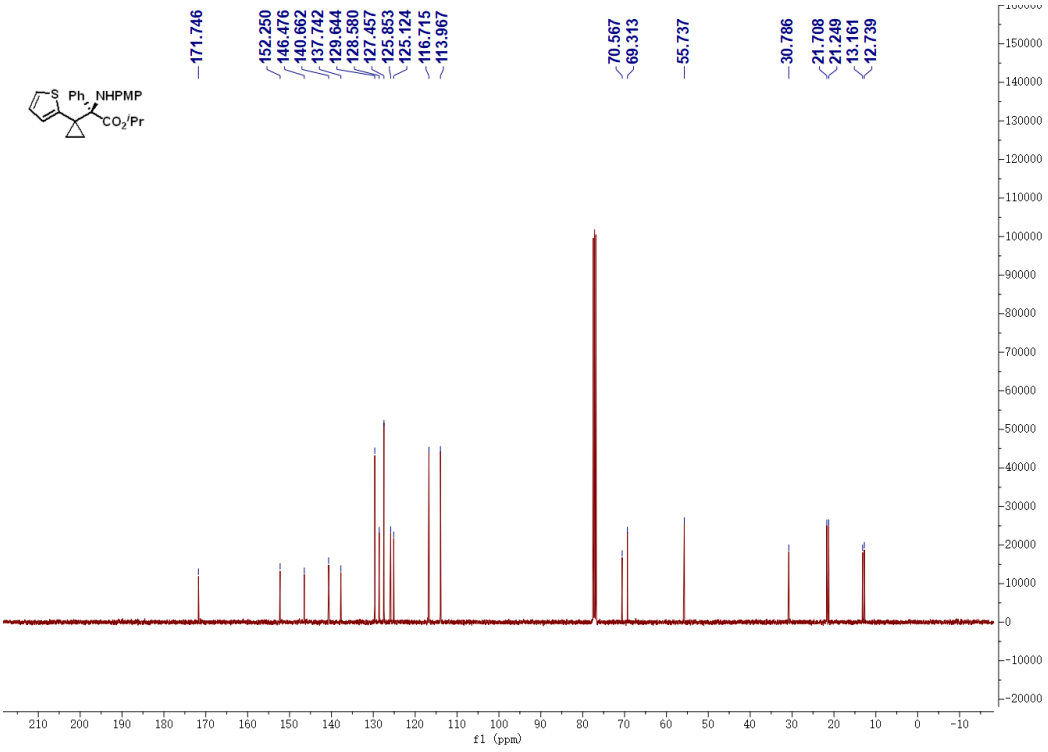
^{13}C NMR-spectrum (100 MHz, DMSO-d_6) of **3s**



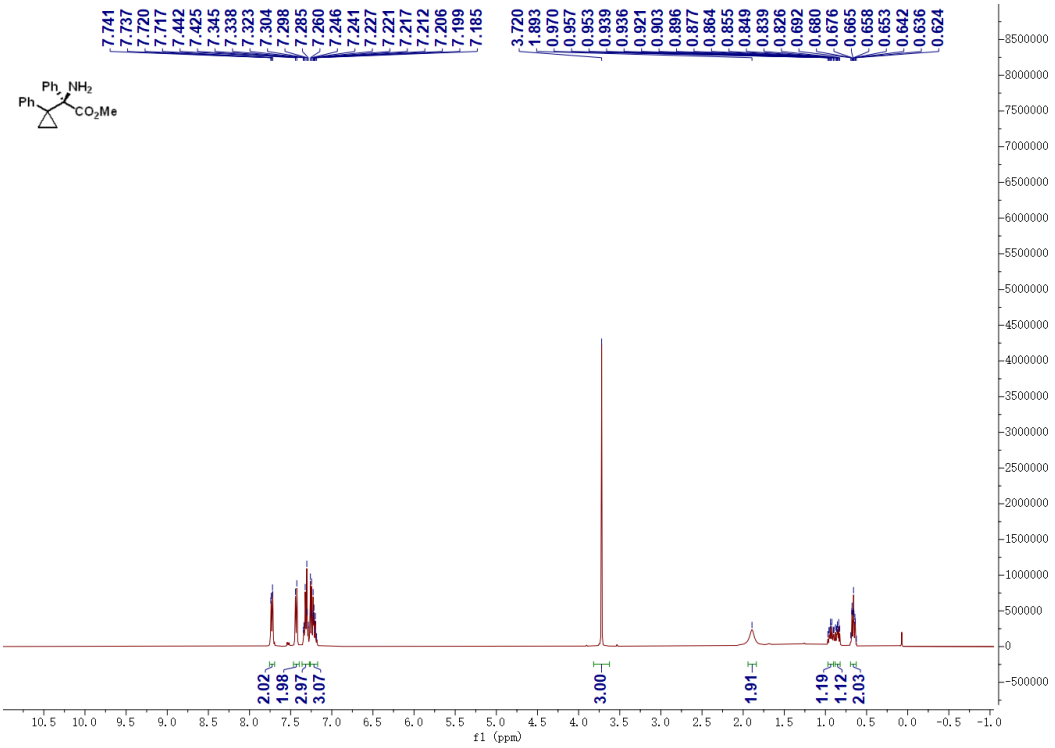
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **3t**



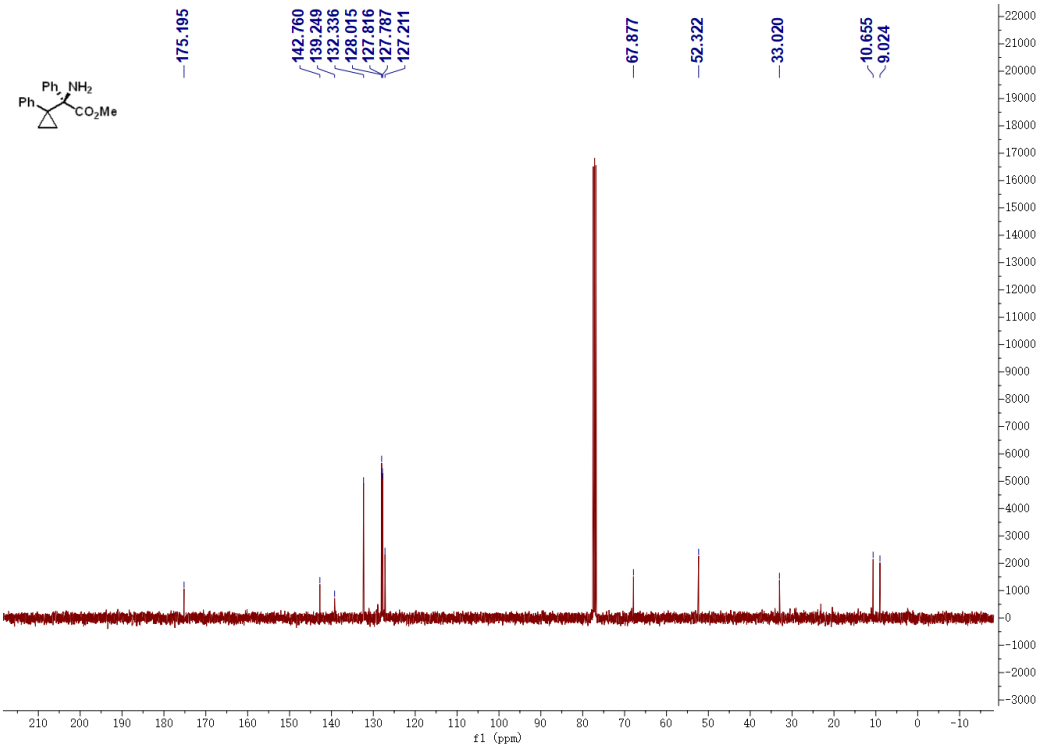
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **3t**



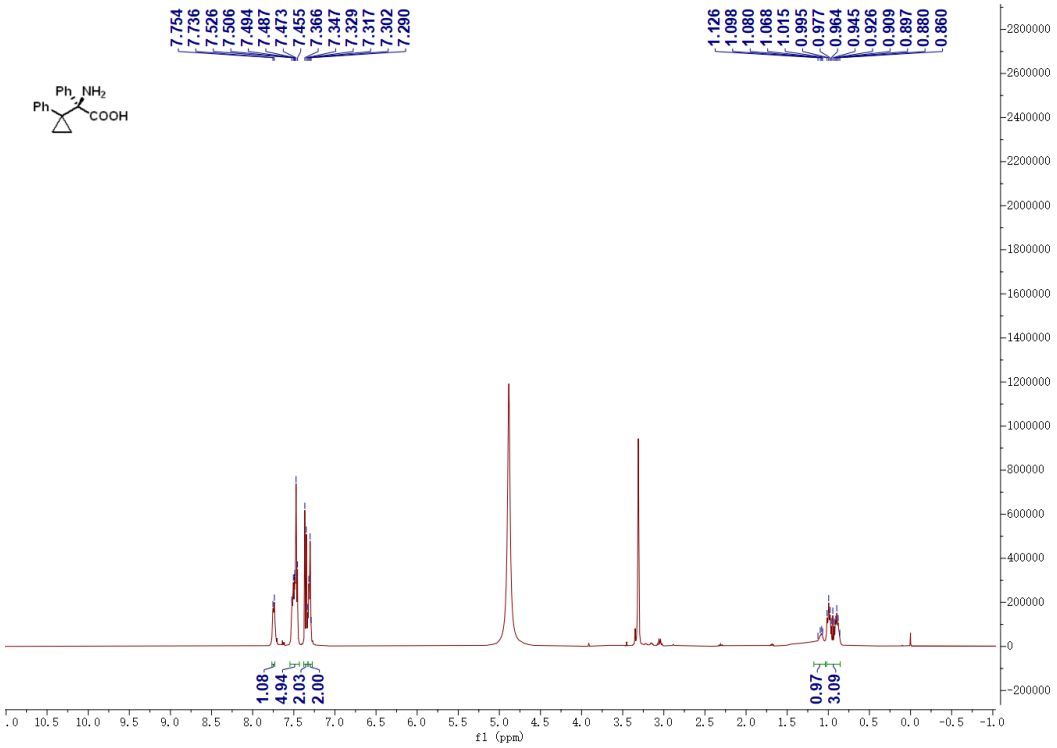
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4**



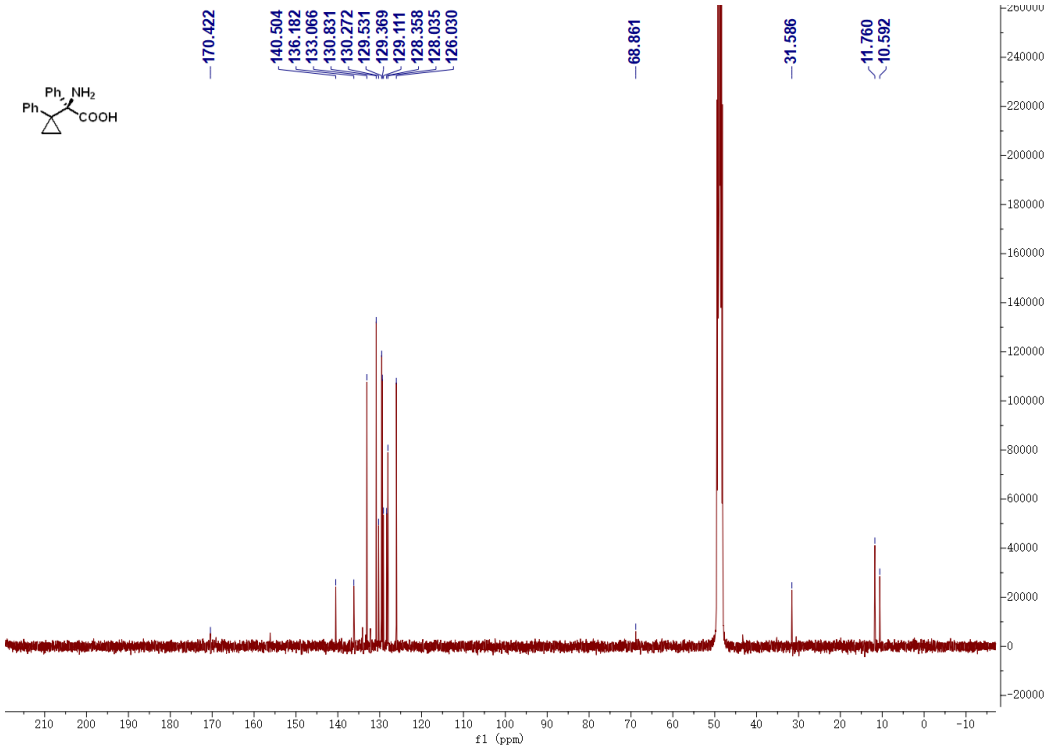
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4**



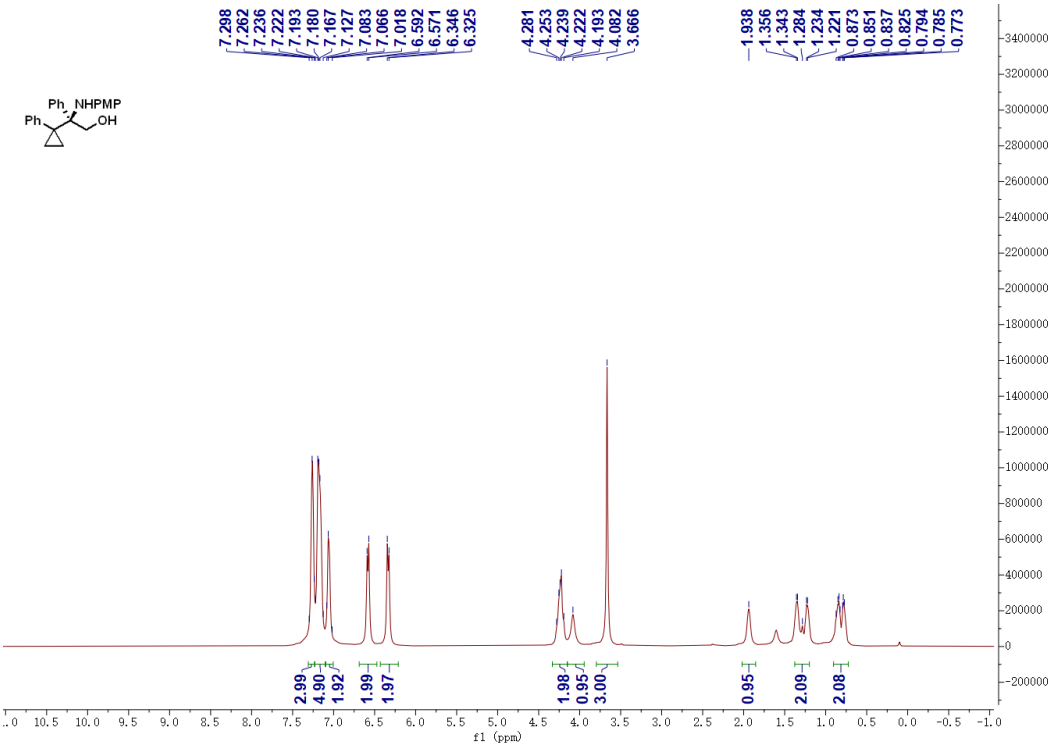
^{1}H NMR-spectrum (400 MHz, CD_3OD) of **5**



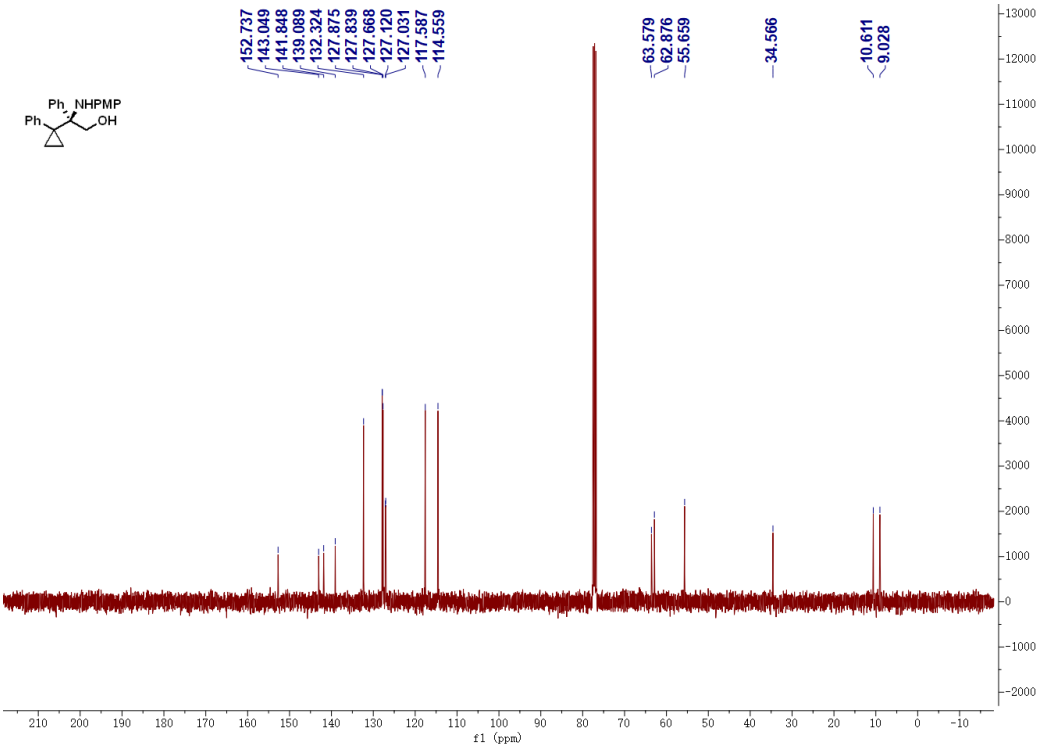
^{13}C NMR-spectrum (100 MHz, CD_3OD) of **5**



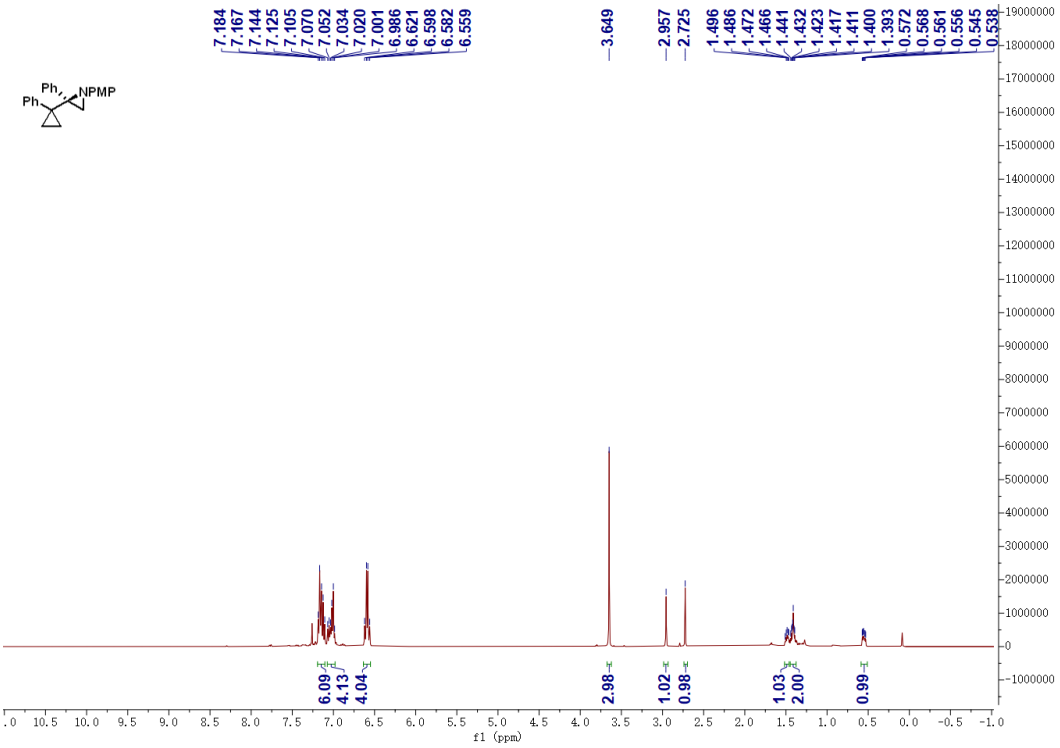
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **6**



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



^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **7**



^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **7**