Supplementary Information

Cobalt-Catalyzed Asymmetric Three-Component Reductive Addition of Alkyne with Alkyl Halides and Imines.

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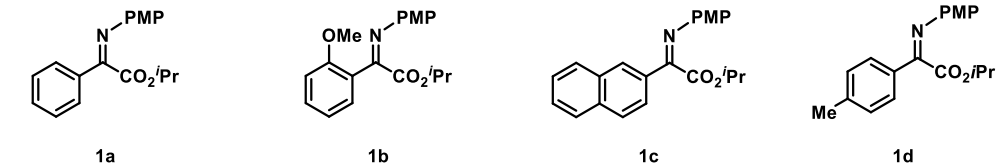
Table of Contents

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 THF were distilled from benzophenone. CoI_2 was purchased from Adamas and 9dingchem. Manganese powder was purchased from Alfa Aesar; isopropyl alcohol was purchased from Meryer. 2-Iodo-2-methylpropane was purchased from TCI. Compounds **2a**-**2f**, **2i**-**2l** and other commercially available reagents were purchased from Bidepharm, Adamas-beta China, Energy Chemical and were used as received. 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 and PMA with heat as the developing agents. All new compounds were characterized by means of ^{1}H NMR and ^{13}C NMR. HPLC was performed on SHIMADZU LC-2030 Plus. Optical rotations were recorded on digital automatic polarimeter (WZZ-2S). X-ray analysis was performed on Bruker D8 Venture diffractometer. 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). All ^{1}H 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) and were obtained with 1H decoupling. The following abbreviations or combinations thereof were used to explain the multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sept = septet, m = multiplet.

Information of substrates

The list of imines:

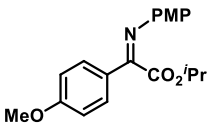


1a

1b

1c

1d



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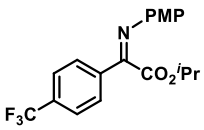

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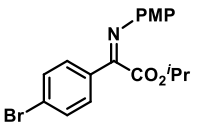

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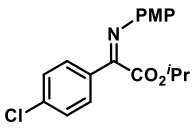

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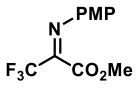

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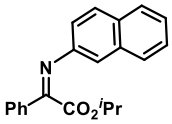

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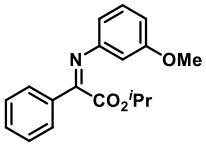

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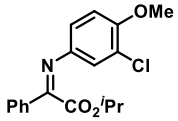

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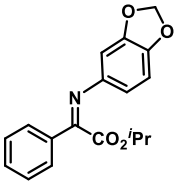

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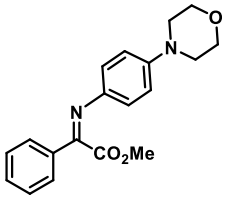

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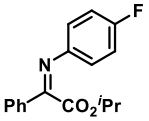
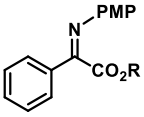


1o

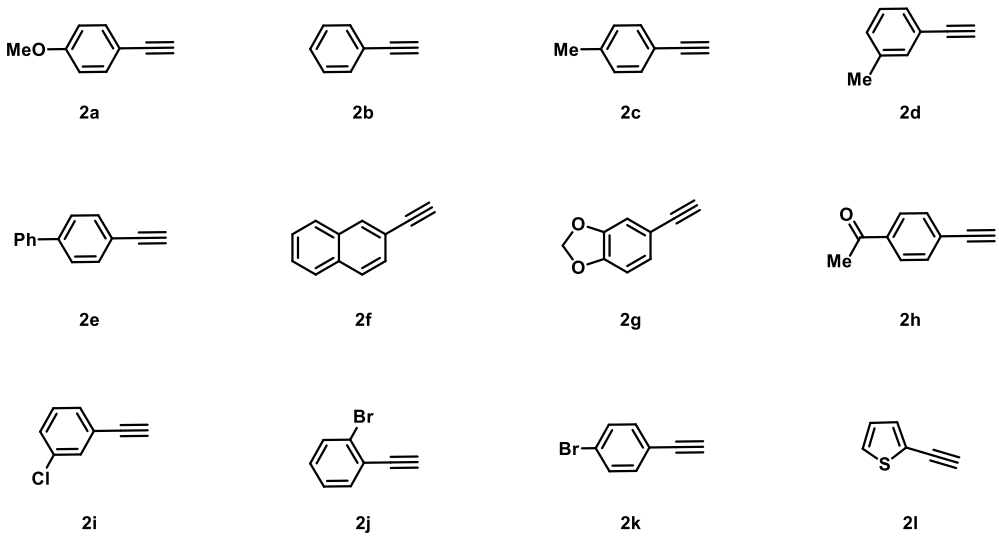


1p, R = Me
1q, R = Et

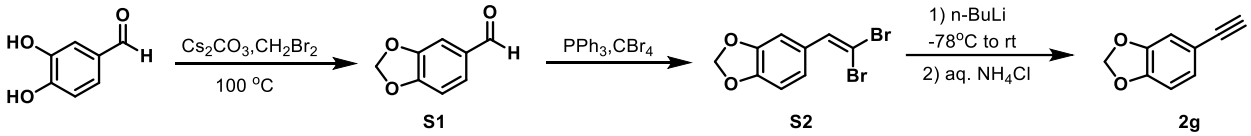
Preparation of imines:

p-Anisidine (1.05 equiv), the appropriate a-keto esters (1 equiv) and TsOH (0.05 equiv) were dissolved in toluene (30-50 mL) in a round bottle flask. The flask was equipped with a reflux condenser. The mixture was heated to reflux for 24 h after which the solvent was removed in vacuo. The crude products were purified by column chromatography using 20:1~5:1 (v/v) petroleum ether and ethyl acetate as eluent. The products were further purified by recrystallization if necessary. Compounds **1a**[1], **1b**[2], **1c**[1], **1d**[1], **1e**[1], **1f**[1], **1g**[1], **1h**[1], **1i**[3], **1k**[2], **1o**[2], **1p**[4], **1q**[4] were synthesized according to the literature.

The list of alkynes:



Preparation of 2g:



Benzo[*d*] [1, 3] dioxole-5-carbaldehyde (S1)

A 250 mL flask was charged with 3,4-dihydroxybenzaldehyde (10.0 g, 72.5 mmol), cesium carbonate (59.0 g, 181.0 mmol), *N*, *N*-dimethylformamide (125 mL) and dibromomethane (25 g, 145 mmol). The mixture was stirred at 100 °C for 24 h. The reaction mixture was poured into 300 mL water, and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, filtration and concentration. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 30/1) to afford **S1** (7.3 g, 48.6 mmol, 67% yield) as a yellow oil.

5-(2,2-Dibromovinyl)benzo[d][1,3]dioxole (S2)

Carbon tetrabromide (11.1 g, 33.0 mmol) was dissolved with 50 mL of dichloromethane in a flask under argon. Triphenylphosphine (17.3 g, 66.0 mmol) was dissolved in 100 mL of dichloromethane in a flask under argon. The first solution was slowly added to the second one at 0 °C under vigorous stirring. The resulting mixture was stirred for 15 min at 0 °C. Benzo[*d*][1,3]dioxole-5-carbaldehyde (**S1**) (5.0 g, 33.0 mmol) was dissolved with 40 mL dichloromethane in a flask under argon, and then slowly added to the previous mixture. After 2 h of stirring at rt, 100 mL of water were added to the mixture which was then extracted with dichloromethane. The organic extract was dried over Na_2SO_4. Filtration and concentration in vacuo to give a crude material which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate =30/1) to afford **S2** (4.2 g, 13.9 mmol, 42% yield) as a yellow oil.

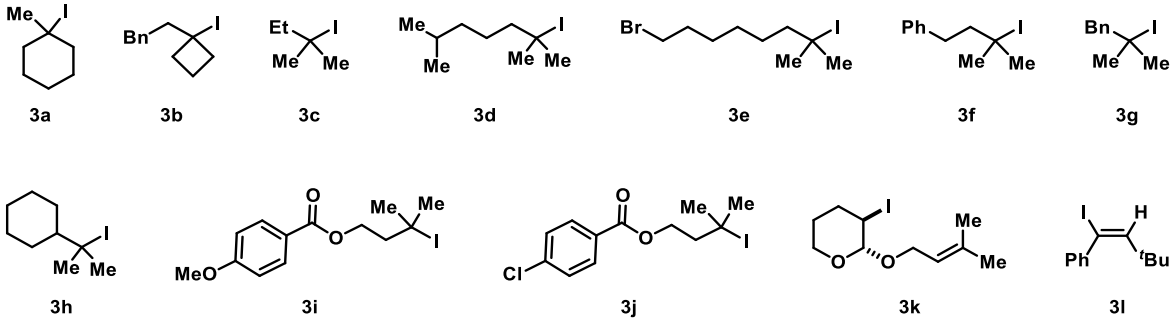
5-Ethynylbenzo[d][1,3]dioxole (2g)

5-(2,2-Dibromovinyl)benzo[d][1,3]dioxole (**S2**) (4.0 g, 13.1 mmol) was dissolved under argon with 80 mL of dry THF. The solution was cooled down to -78 °C. n-BuLi (2.0M in hexane,

19.6 mL, 39.3 mmol) was added dropwise. The mixture was stirred 1 h at -78 °C, and then allowed to reach room temperature. The excess of n-BuLi was quenched with aqueous NH_4Cl. 80 mL of water were added and then the mixture was extracted with dichloromethane. The organic extract was dried over Na_2SO_4. Filtration and concentration in vacuo gave **2g** (1.4 g, 9.7 mmol, 74% yield) as a yellow oil.

Compounds **2g**[5] and **2h**[6] were synthesized according to the literature.

The list of alkyl iodides:



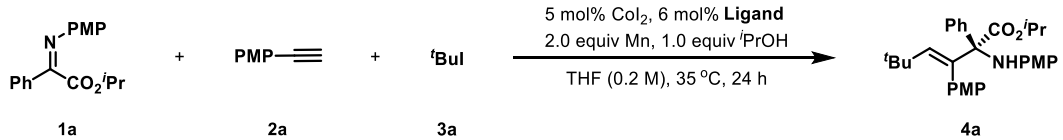
General procedure for preparing alkyl iodides:

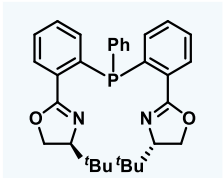
A 200-mL oven-dried round-bottom flask equipped with a stir bar was charged with triphenylphosphine (1.2 equiv) and imidazole (1.3 equiv), then DCM (non-anhydrous) was added under nitrogen. The flask was then placed in an ice-bath. After 5 min of stirring, iodine (1.2 equiv) was added, and the reaction was stirred for another 15 min. The alcohol (1.0 equiv) was then added. After 30 min, the ice bath was removed and reaction stirred at rt for the indicated time under nitrogen. To quench the reaction, water was added and the layers were separated. The aqueous layer was washed with DCM and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered through glass frit. The solvent was removed under reduced pressure and the crude product was purified by flash silica gel column chromatography.

Compounds **3a**[7], **3b**[8], **3c**[9], **3d**[10], **3e**[8], **3f**[11], **3g**[12], **3i**[13], **3k**[14] and **3l**[15] were synthesized according to the literature.

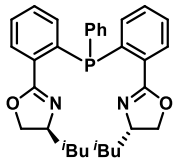
Conditions screening

Table S1. Investigation of chiral NPN ligands

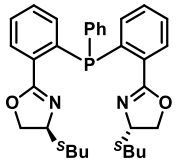




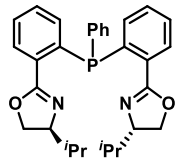
L1, 57%, 97% *ee*



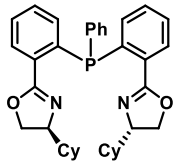
L2, 36%, 98% *ee*



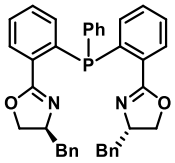
L3, 39%, 97% *ee*



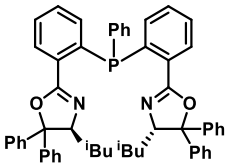
L4, 35%, 96% *ee*



L5, 33%, 94% *ee*



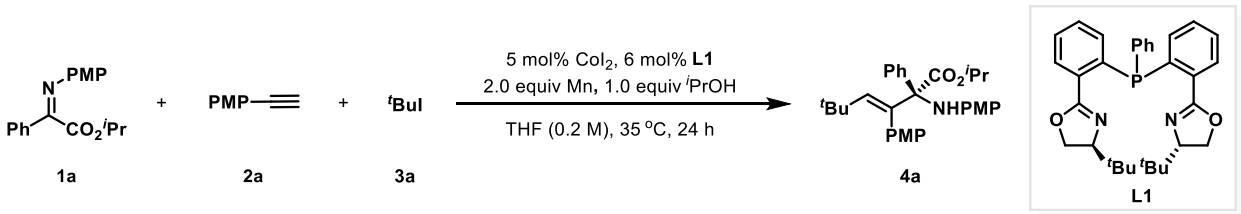
L6, 16%, 91% *ee*



L7, 21%, 89% *ee*

Reaction condition: **1a** (1.0 equiv, 0.10 mmol), **2a** (3.0 equiv, 0.30 mmol), **3a** (1.5 equiv, 0.15 mmol), CoI_2 (5 mol%, 0.005 mmol), **L1** (6 mol%, 0.012 mmol), Mn (2.0 equiv, 0.2 mmol), ^{i}PrOH (1.0 equiv, 0.1 mmol), THF (0.2 M, 0.5 mL), stirred at 35 ^{o}C for 24 h. The yields were determined by ^{1}H NMR using mesitylene as the internal standard and the ee values were determined by chiral HPLC analysis on a chiral stationary phase.

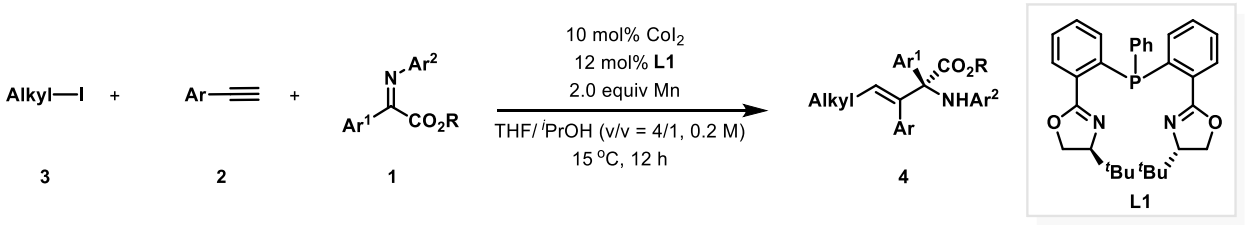
Table S2. Screening of other parameters



Entry	Deviation from above	Yield (%)	*ee* (%)
1	none	57	97
2	1.0 equiv **2a**, 1.5 equiv **3a** and 2.0 equiv **1a**	29	87
3	2.0 equiv **3a**	70	98
4	10 mol% CoI, 12 mol% **L1**	69	98
5	2.0 equiv **3a**, 10 mol% CoI, 12 mol% **L1**	73	98
6[a]	THF/^{i}PrOH=4/1	80	98
7[a,b]	15 °C instead of 35 °C	82 (79)[c]	99

Reaction condition: **1a** (1.0 equiv, 0.10 mmol), **2a** (3.0 equiv, 0.30 mmol), **3a** (1.5 equiv, 0.15 mmol), CoI_2 (5 mol%, 0.005 mmol), **L1** (6 mol%, 0.012 mmol), Mn (2.0 equiv, 0.2 mmol), ^{i}PrOH (1.0 equiv, 0.1 mmol), THF (0.2 M, 0.5 mL), stirred at 35 °C for 24 h. The yields were determined by ^{1}H NMR using mesitylene as the internal standard and the ee values were determined by chiral HPLC analysis on a chiral stationary phase. [a]10 mol% CoI_2, 12 mol% **L1**, 2.0 equiv **3a**. [b]THF/^{i}PrOH (v/v = 4/1, 0.2 M), 12 h; [c]Isolated yield in the parentheses.

Experimental procedures of cobalt-catalyzed asymmetric three-component reductive addition of alkyne

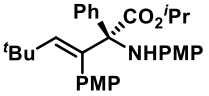


3 2 1 4

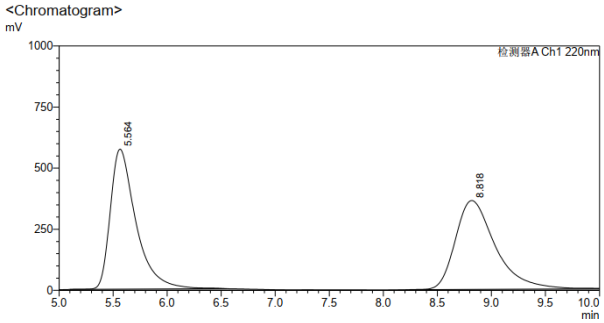
To a dried 8-mL vial were added ligand (12 mol%), Mn (2.0 equiv) and imine **1** (1.0 equiv). Then the vial was transferred into the glovebox. CoI_2 (10 mol%), THF, alkyne **2** (3.0 equiv) and alkyl iodide **3** (2.0 equiv) were added in sequence and ^{i}PrOH was added finally. The reaction vial was capped and stirred at 15 °C for required time. 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 **4**.

Characterization data for products:

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4a)



General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4a** as a yellow oil (38.5 mg, 79%). $\mathbf{R_f}$ = 0.50 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.35–7.29 (m, 3H), 7.17–7.05 (m, 1H), 6.72–6.65 (m, 5H), 6.45 (d, *J* = 8.8 Hz, 2H), 5.90 (s, 1H), 5.02 (s, 1H), 4.77 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.07 (d, *J* = 6.0 Hz, 3H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 158.9, 152.0, 143.0, 139.2, 137.9, 133.8, 130.6, 129.7, 127.44, 127.41, 117.3, 114.2, 112.5, 74.4, 69.9, 55.8, 55.2, 34.0, 31.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{38}NO_4^+$:488.2795; found: 488.2782. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 5.385 min (major), t_{R2} = 8.419 min (minor); 99% *ee*. **$[\alpha]_D^{16.0}$** = - 25.87 (c = 1.43, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

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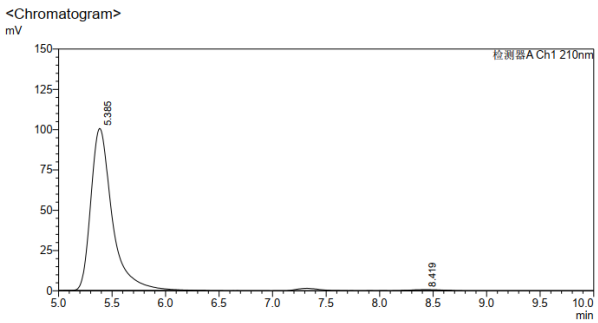
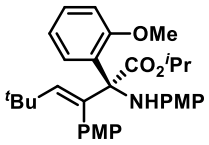
总计		18895008	936868				



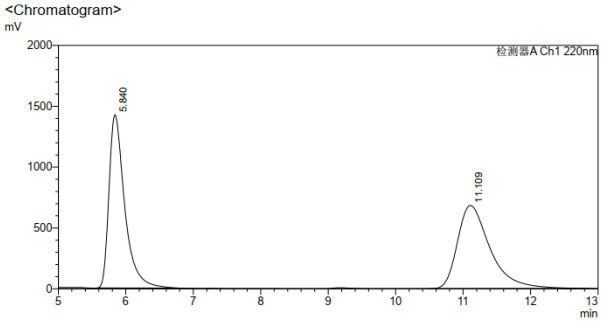
<Peak Table>
检测器A Ch1 210nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.385	1395158	100529	99.339		M	
2	8.419	9290	578	0.661		M	
总计		1404448	101107				

Isopropyl (*S*,*E*)-2-(2-methoxyphenyl)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethylhex-3-enoate (4b)

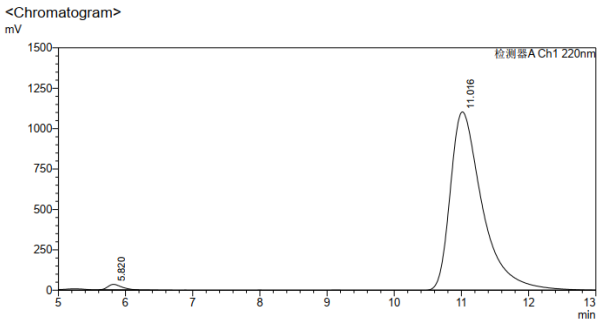


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4b** as a brown oil (86.3 mg, 83%). $\mathbf{R_f}$ = 0.28 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.27–7.23 (m, 1H), 6.96 (td, *J* = 7.6, 1.2 Hz, 3H), 6.73–6.69 (m, 3H), 6.53 (d, *J* = 9.2 Hz, 2H), 6.42 (d, *J* = 9.2 Hz, 2H), 6.15 (s, 1H), 4.82 (sept, *J* = 6.4 Hz, 1H), 4.67 (s, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 3.54 (s, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H), 0.84 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.4, 158.5, 157.4, 152.5, 143.7, 140.1, 135.8, 132.3, 130.9, 130.6, 129.5, 129.0, 119.6, 118.8, 113.4, 112.2, 111.1, 73.1, 68.5, 55.6, 55.2, 54.8, 33.9, 31.2, 21.5, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{40}NO_5^+$:518.2901; found: 518.2890. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 5.820 min (minor), t_{R2} = 11.016 min (major); 97% *ee*. **$[\alpha]_D^{16.0}$** = - 1.66 (c = 8.36, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.840	23051311	1422348	50.019		M	
2	11.109	23033982	683843	49.981		M	
总计		46085293	2106191				

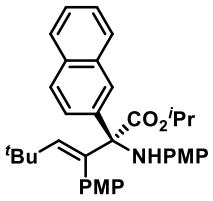


<Peak Table>
检测器A Ch1 220nm

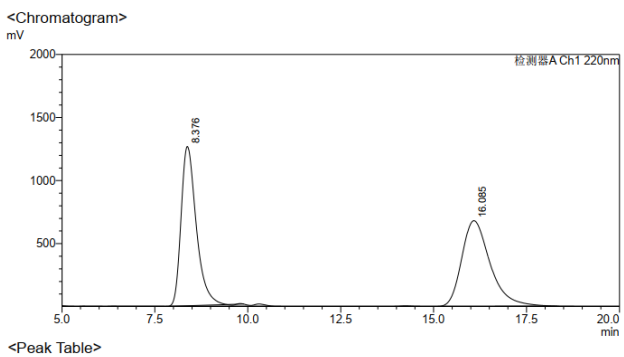
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.820	480416	33568	1.287		M	
2	11.016	36837804	1106201	98.713		M	
总计		37318220	1139769				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-(naphthalen-2-yl)hex-3-enoate (4c)

General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4c** as a yellow solid (53.9 mg, 50%). $\mathbf{R_f}$ =

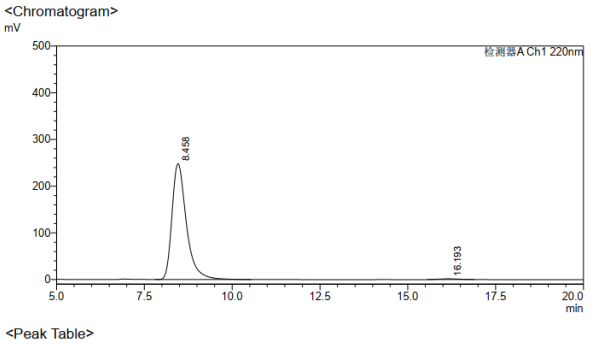


0.49 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.99 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.53–7.44 (m, 2H), 7.20–7.13 (m, 1H), 6.76–6.67 (m, 5H), 6.53 (d, *J* = 9.2 Hz, 2H), 5.94 (s, 1H), 5.17 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.76 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 158.9, 152.1, 143.7, 139.2, 135.7, 133.5, 133.0, 132.8, 129.7, 129.0, 128.8, 127.4, 126.4, 126.3, 125.8, 117.6, 114.2, 112.5, 74.7, 70.1, 55.7, 55.2, 34.0, 31.1, 21.6, 21.5; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{35}H_{40}NO_4^+$: 538.2952; found: 538.2941. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 8.458 min (major), t_{R2} = 16.193 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = 2.86 (c = 4.48, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

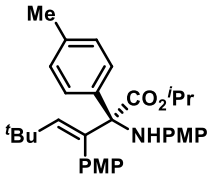
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.376	35900199	1264485	49.656		M	
2	16.085	36398216	680963	50.344		M	
总计		72298414	1945448				



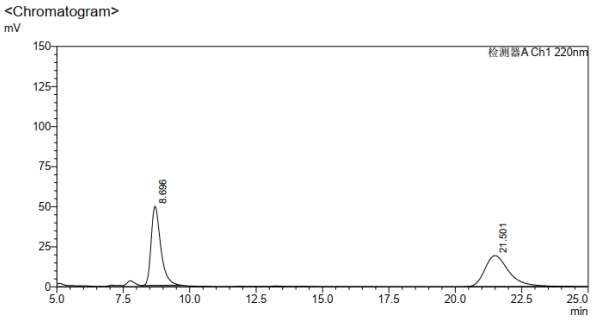
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.458	7078025	248262	99.110		M	
2	16.193	63560	1545	0.890		M	
总计		7141585	249806				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-(p-tolyl)hex-3-enoate (4d)



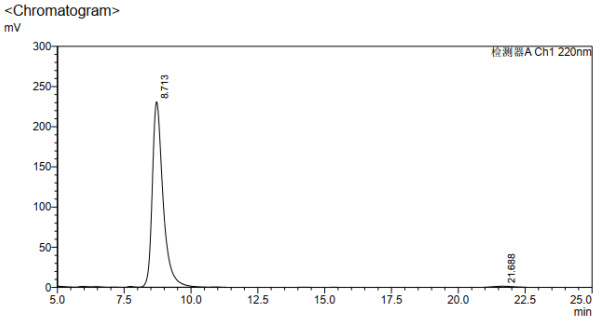
General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4d** as a colorless oil (36.7 mg, 73%). **R_f** = 0.28 (PE/Acetone = 15/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.08–7.06 (m, 1H), 6.71–6.60 (m, 5H), 6.45 (d, *J* = 8.8 Hz, 2H), 5.91 (s, 1H), 5.03 (s, 1H), 4.76 (sept, *J* = 6.4 Hz, 1H), 3.77 (s, 3H), 3.71 (s, 3H), 2.37 (s, 3H), 1.08 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.4, 158.8, 151.9, 143.0, 139.3, 137.1, 134.7, 133.7, 130.6, 129.9, 128.2, 117.3, 114.1, 112.4, 74.2, 69.9, 55.8, 55.2, 33.9, 31.1, 21.6, 21.4, 21.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{40}NO_4^+$: 502.2952; found: 502.2943. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 8.713 min (major), t_{R2} = 21.688 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = 1.91 (c = 7.75, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.696	1236358	49287	50.070		M	
2	21.501	1232894	19386	49.930		M	
总计		2469253	68673				

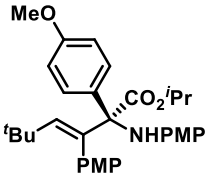


<Peak Table>

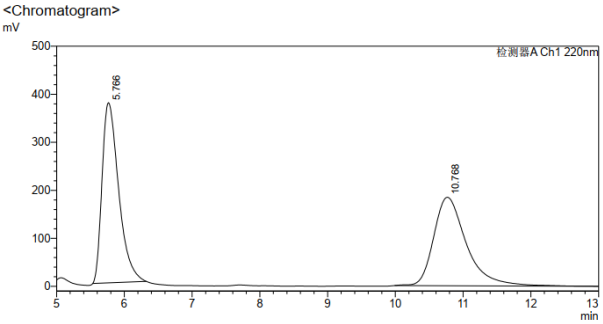
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.713	6471551	230584	98.973		M	
2	21.688	67145	1327	1.027		M	
总计		6538696	231911				

Isopropyl (*R*,*E*)-2,3-bis(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethylhex-3-enoate (4e)



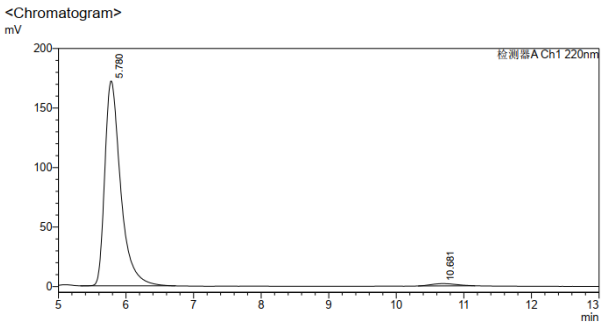
General procedure was followed with on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/Acetone = 40/1) to afford **4e** as a red solid (28.9 mg, 56%). $\mathbf{R_f}$ = 0.63 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.8 Hz, 2H), 7.17–7.02 (m, 1H), 6.86 (d, *J* = 9.2 Hz, 2H), 6.72–6.66 (m, 5 H), 6.45 (d, *J* = 9.2 Hz, 2H), 5.90 (s, 1H), 5.02 (s, 1H), 4.77 (sept, *J* = 6.4 Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 3.72 (s, 3H), 1.09 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.4, 158.9, 158.8, 151.9, 142.9, 139.3, 133.7, 131.9, 129.8, 129.6, 117.3, 114.2, 112.7, 112.5, 73.9, 69.9, 55.8, 55.3, 55.2, 34.0, 31.2, 21.6, 21.5; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{40}NO_5^+$: 518.2901; found: 518.2898. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 90/10, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 5.780 min (major), t_{R2} = 10.681 min (minor); 97% *ee*. **$[\alpha]_D^{16.0}$** = 9.64 (c = 1.93, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.766	6390876	375113	50.915		M	
2	10.768	6161252	184135	49.085		M	
总计		12552128	559248				

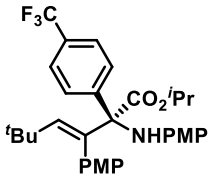


<Peak Table>

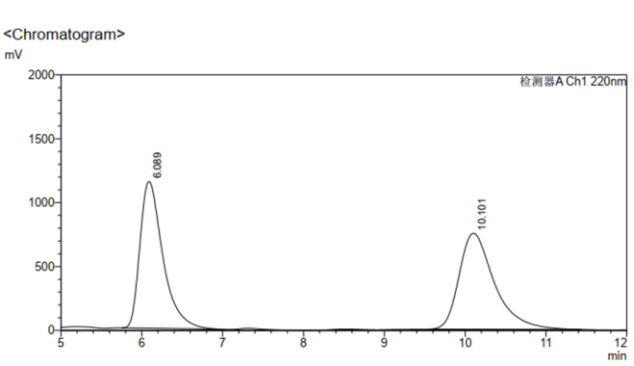
检测器A Ch1 220nm

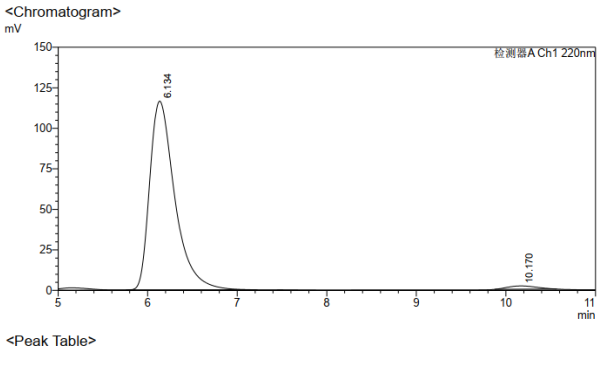
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.780	2808825	172196	98.285		M	
2	10.681	49021	1907	1.715		M	
总计		2857845	174103				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-(4-(trifluoromethyl)phenyl)hex-3-enoate (4f)



General procedure was followed with on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4f** as a yellow oil (25.8 mg, 46%). $\mathbf{R_f}$ = 0.41 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.12–7.06 (m, 1H), 6.77–6.50 (m, 5H), 6.38 (d, *J* = 8.8 Hz, 2H), 5.82 (s, 1H), 4.95 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.03 (d, *J* = 6.4 Hz, 6H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.7, 159.1, 152.3, 143.1, 142.6, 138.8, 134.4, 130.9, 129.6 (q, $J_{C\text{-}F}$ = 31.8 Hz), 129.0, 124.4 (q, $J_{C\text{-}F}$ = 270.2 Hz), 124.3 (q, $J_{C\text{-}F}$ = 3.8 Hz), 117.2, 114.3, 112.7, 74.3, 70.2, 55.8, 55.3, 34.1, 31.1, 21.5, 21.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -62.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{37}F_3NO_4^+$: 556.2669; found: 556.2661. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.134 min (major), t_{R2} = 10.170 min (minor); 96% *ee*. **[α]$_D^{16.0}$** = 9.60 (c = 1.25, $CHCl_3$).





<Peak Table>

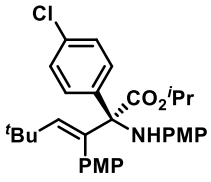
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.089	22569718	1148497	49.724		M	
2	10.101	22820186	751343	50.276		M	
总计		45389904	1899840				

检测器A Ch1 220nm

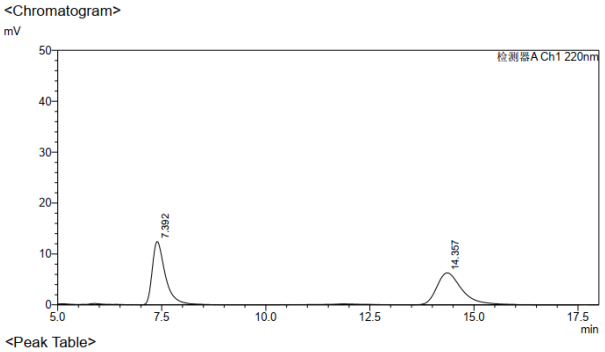
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.134	2270424	116419	98.030		M	
2	10.170	45623	2029	1.970		M	
总计		2316047	118448				

Isopropyl (*R*,*E*)-2-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethylhex-3-enoate (4g)



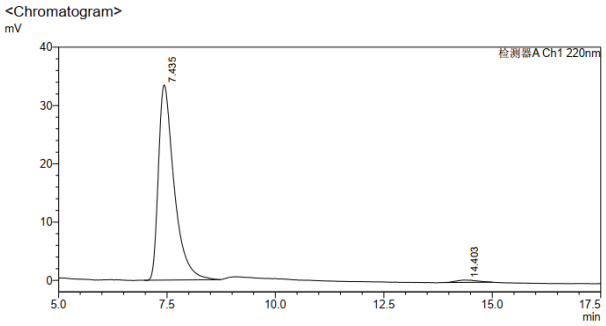
General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4g** as a yellow oil (32.9 mg, 63%). $\mathbf{R_f}$ = 0.41 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.8 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 2H), 7.10–7.08 (m, 1H), 6.72–6.66 (m, 4H), 6.59–6.53 (m, 1H), 6.40 (d, *J* = 9.2 Hz, 2H), 5.83 (s, 1H), 4.96 (s, 1H), 4.78 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.05 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.0 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.0, 159.0, 152.3, 143.1, 139.0, 136.8, 134.2, 133.5, 132.2, 129.4, 127.7, 117.4, 114.3, 112.7, 74.1, 70.2, 55.9, 55.3, 34.1, 31.2, 21.7, 21.6; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{37}ClNO_4^+$: 522.2406; found: 522.2406. **HPLC** (Chiralpak

AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 7.435 min (major), t_{R2} = 14.403 min (minor); 97% *ee*. **[α]$_D^{16.0}$** = 3.74 (c = 2.99, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

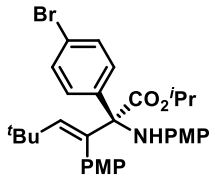
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.392	267687	12396	50.083		M	
2	14.357	266800	6271	49.917		M	
总计		534486	18667				



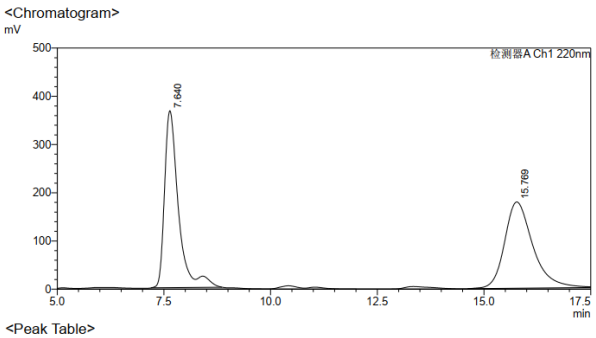
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.435	845072	33505	98.516		M	
2	14.403	12725	388	1.484		M	
总计		857798	33893				

Isopropyl (*R*,*E*)-2-(4-bromophenyl)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethylhex-3-enoate (4h)

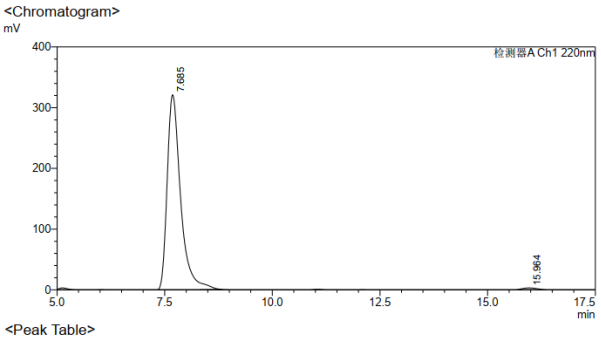


General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4h** as a white solid (23.7 mg, 42%). **R_f** = 0.49 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.8 Hz, 2H), 7.45 (d, *J* = 8.8 Hz, 2H), 7.13–7.05 (m, 1H), 6.74–6.65 (m, 5H), 6.40 (d, *J* = 9.2 Hz, 2H), 5.83 (s, 1H), 4.95 (s, 1H), 4.78 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.05 (d, *J* = 6.0 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.8, 159.0, 152.2, 143.0, 138.9, 137.3, 134.0, 132.4, 130.5, 129.3, 121.8, 117.3, 114.2, 112.6, 74.0, 70.1, 55.8, 55.2, 34.0, 31.1, 21.6, 21.5; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{37}BrNO_4^+$: 566.1900; found: 566.1890. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 7.685 min (major), t_{R2} = 15.964 min (minor); 96% *ee*. **[α]$_D^{16.0}$** = 18.76 (c = 1.61, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

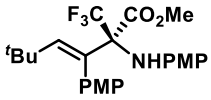
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.640	8305014	366894	50.069		M	
2	15.769	8282187	178929	49.931		M	
总计		16587201	545823				



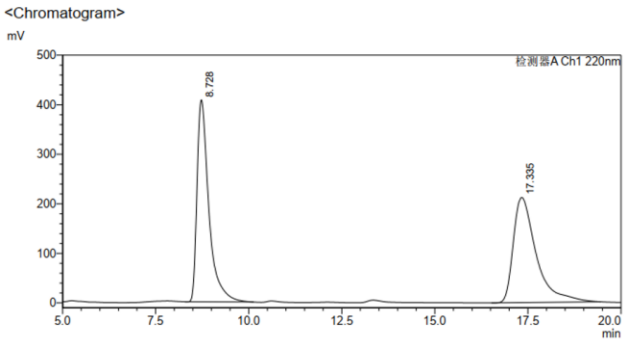
<Peak Table>
检测器A Ch1 220nm

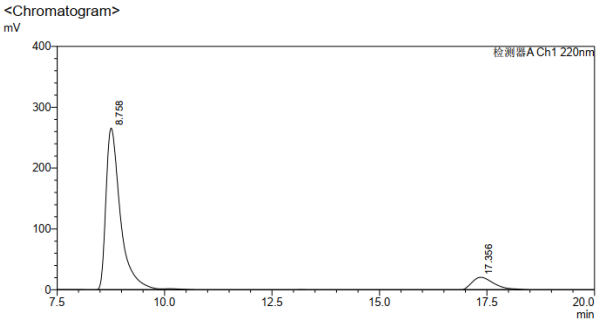
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.685	7000242	321859	98.065		M	
2	15.964	138134	4520	1.935		M	
总计		7138376	326379				

Methyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-(trifluoromethyl)hex-3-enoate (4i)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1 to PE/Et_2O = 20/1) to afford **4i** as a yellow oil (57.3 mg, 63%). $\mathbf{R_f}$ = 0.38 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.07–7.03 (m, 1H), 6.96–6.92 (m, 1H), 6.84–6.80 (m, 2H), 6.72 (d, *J* = 9.2 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 6.03 (q, *J* = 1.6 Hz, 1H), 4.20 (s, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.67 (s, 3H), 0.83 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.0, 159.6, 153.5, 145.8, 137.9, 132.7, 129.9, 126.8, 124.9 (q, $J_{C\text{-}F}$ = 287.1 Hz), 118.3, 114.3, 113.2, 72.1 (q, $J_{C\text{-}F}$ = 26.2 Hz), 55.7, 55.3, 53.3, 34.4, 30.7; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -69.0; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{24}H_{29}F_3NO_4^+$: 452.2043; found: 452.2033. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 8.758 min (major), t_{R2} = 17.356 min (minor); 73% *ee*. **$[\alpha]_D^{16.0}$** = 1.13 (c = 4.76, $CHCl_3$).





<Peak Table>

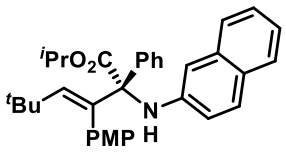
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.728	9075537	407464	50.024		M	
2	17.335	9066686	212142	49.976		M	
总计		18142222	619605				

检测器A Ch1 220nm

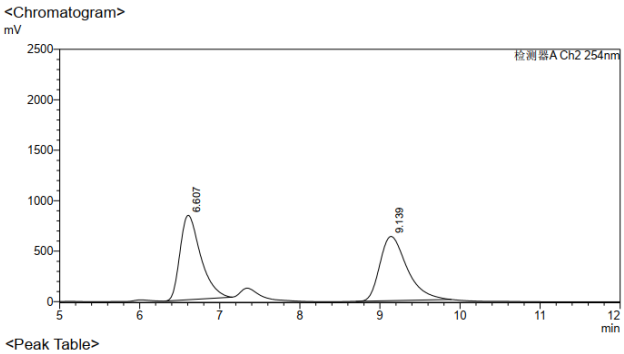
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.758	6398279	266375	86.689		M	
2	17.356	982410	22792	13.311		M	
总计		7380689	289167				

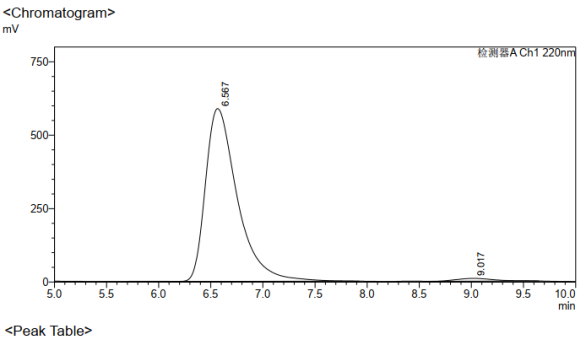
Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-5,5-dimethyl-2-(naphthalen-2-ylamino)-2-phenylhex-3-enoate (4j)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4j** as a yellow oil (85.1 mg, 84%). $\mathbf{R_f}$ = 0.58 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.38–7.28 (m, 4H), 7.19 (t, *J* = 8.0 Hz, 2H), 6.98 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.75–6.58 (m, 4H), 6.12 (s, 1H), 5.59 (s, 1H), 4.85 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 1.17 (d, *J* = 6.4 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 3H), 0.80 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 158.9, 144.1, 142.5, 136.6, 134.6, 132.7, 130.7, 129.6, 128.6, 127.7, 127.6, 127.5, 127.4, 126.3, 126.1, 122.1, 119.9, 112.5, 109.3, 74.3, 70.4, 55.2, 34.0, 31.1, 21.7, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{34}H_{38}NO_3^+$: 508.2846; found: 508.2840. **HPLC** (Chiralpak AD-H): *n*-

Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.657 min (major), t_{R2} = 9.017 min (minor); 96% *ee*. **[α]D$^{16.0}$** = - 93.40 (c = 4.95, $CHCl_3$).





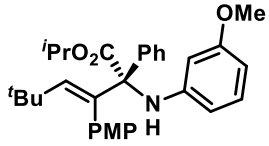
<Peak Table>
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.607	15007557	836046	49.900		M	
2	9.139	15068007	636201	50.100		M	
总计		30075564	1472247				

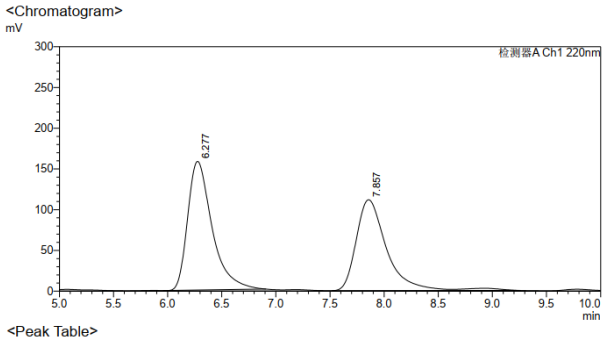
<Peak Table>
检测器A Ch1 220nm

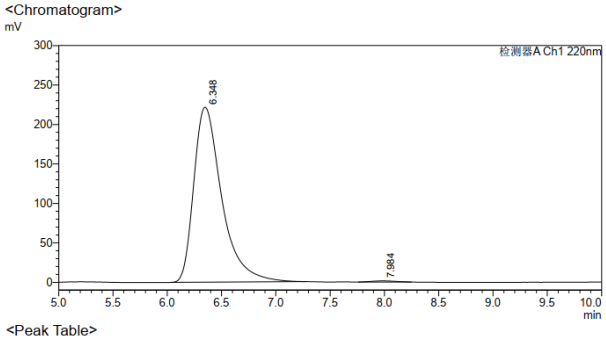
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.567	12485750	588140	98.131		M	
2	9.017	237861	9501	1.869		M	
总计		12723612	597641				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4k)



General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4k** as a colorless oil (39.9 mg, 82%). **R_f** = 0.46 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76–7.73 (m, 2H), 7.34–7.28 (m, 3H,) 7.14–7.10 (m, 1H), 6.99 (t, *J* = 8.4 Hz, 1H), 6.72–6.61 (m, 3H), 6.26 (dd, *J* = 7.6, 2.0 Hz, 1H), 6.14 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.08 (t, *J* = 2.4 Hz, 1H), 5.96 (s, 1H), 5.30 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.68 (s, 3H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.76 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 160.2, 158.9, 146.4, 143.4, 137.2, 133.5, 130.6, 129.7, 129.2, 127.5, 127.4, 112.5, 109.5, 102.7, 102.5, 74.1, 70.1, 55.2, 55.1, 34.0, 31.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{38}NO_4^+$: 488.2795; found: 488.2791. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.348 min (major), t_{R2} = 7.984 min (minor); 99% *ee*. **[α]D$^{16.0}$** = - 26.44 (c = 1.80, $CHCl_3$).





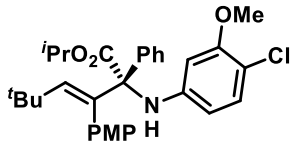
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.277	2480923	157942	52.921		M	
2	7.857	2207075	111610	47.079		M	
总计		4687998	269552				

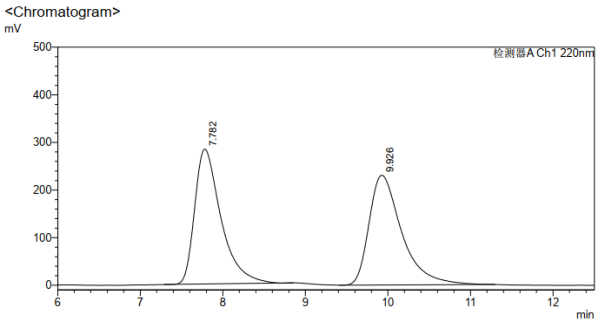
<Peak Table>
检测器A Ch1 220nm

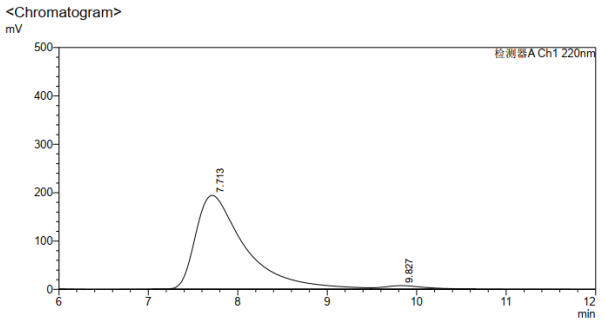
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.348	3974093	221796	99.450		M	
2	7.984	21971	1433	0.550		M	
总计		3996064	223229				

Isopropyl (*R*,*E*)-2-((3-chloro-4-methoxyphenyl)amino)-3-(4-methoxyphenyl)-5,5-dimethyl-2-phenylhex-3-enoate (4l)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4l** as a yellow oil (87.7 mg, 84%). $\mathbf{R}_f$ = 0.65 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.37–7.31 (m, 3H), 7.12–7.04 (m, 1H), 6.74–6.72 (m, 4H), 6.58 (d, *J* = 2.8 Hz, 1H), 6.41 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.94 (s, 1H), 5.19 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.77 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 158.9, 147.2, 143.8, 139.7, 137.1, 133.0, 130.5, 129.5, 127.6, 127.5, 122.5, 118.0, 115.2, 113.4, 112.5, 74.2, 70.2, 56.9, 55.1, 34.0, 31.1, 21.6, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{37}ClNO_4^+$: 522.2406; found: 522.2396. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 7.713 min (major), t_{R2} = 9.827 min (minor); 94% *ee*. **[α]$_D^{16.0}$** = -31.58 (c = 9.88, $CHCl_3$).





<Peak Table>

检测器A Ch1 220nm

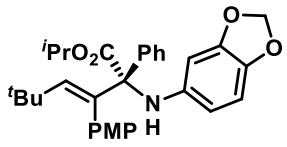
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.782	6277174	283241	49.713		M	
2	9.926	6349532	230530	50.287		M	
总计		12626706	513771				

<Peak Table>

检测器A Ch1 220nm

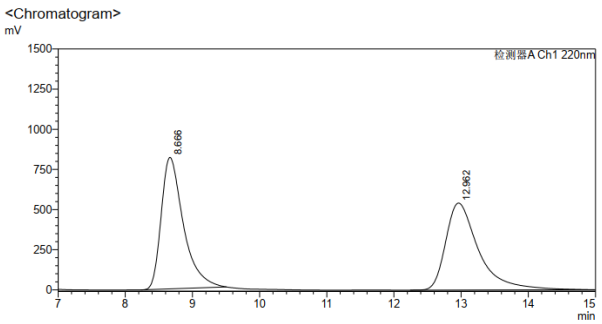
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.713	7437606	193697	97.161		M	
2	9.827	217308	6935	2.839		V M	
总计		7654914	200632				

Isopropyl (*R*,*E*)-2-(benzo[d][1,3]dioxol-5-ylamino)-3-(4-methoxyphenyl)-5,5-dimethyl-2-phenylhex-3-enoate (4m)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4m** as a brown oil (79.6 mg, 79%). $\mathbf{R}_f$ = 0.58 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78–7.75 (m, 2H), 7.36–7.30 (m, 3H), 7.16–7.08 (m, 1H), 6.75–6.74 (m, 3H), 6.59, (d, *J* = 8.4 Hz, 1H), 6.14 (d, *J* = 2.4 Hz, 1H), 5.96 (dd, *J* = 8.0 Hz, 2.0 Hz, 1H), 5.92 (s, 1H), 5.81 (q, *J* = 1.6 Hz, 2H), 5.14 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.76 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 158.9, 147.6, 143.4, 140.5, 139.4, 137.6, 133.4, 130.6, 129.7, 127.5, 127.4, 112.5, 108.22, 108.16, 100.5, 99.1, 74.4, 70.0, 55.2, 34.0, 31.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{36}NO_5^+$: 502.2588; found: 502.2580. **HPLC** (Chiralpak AD-H): *n*-

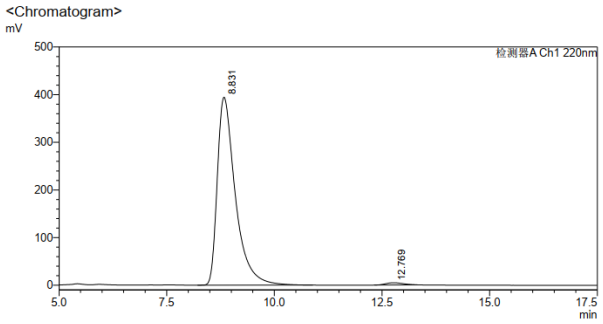
Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 8.831 min (major), t_{R2} = 12.769 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = - 0.33 (c = 6.57, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.666	18828952	818839	50.440		M	
2	12.962	18500612	541512	49.560		M	
总计		37329564	1360351				

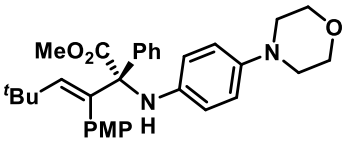


<Peak Table>

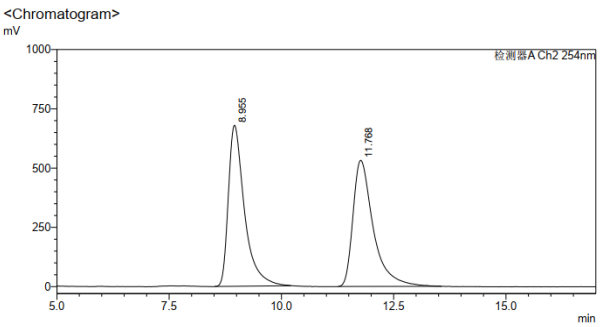
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.831	11505385	394452	98.836		M	
2	12.769	135498	4721	1.164		M	
总计		11640883	399173				

Methyl (*R*,*E*)-3-(4-methoxyphenyl)-5,5-dimethyl-2-((4-morpholinophenyl)amino)-2-phenylhex-3-enoate (4n)



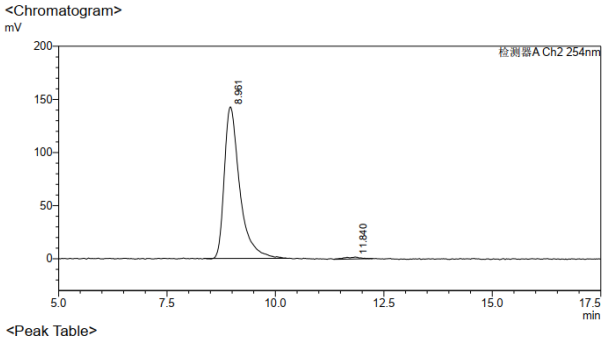
General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 5/1) to afford **4n** as a yellow oil (30.1 mg, 59%). $\mathbf{R}_f$ = 0.26 (PE/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.37–7.31 (m, 3H), 7.05–7.00 (m, 1H), 6.80–6.74 (m, 5H), 6.48 (d, *J* = 8.8 Hz, 2H), 5.92 (s, 1H), 5.19 (s, 1H), 3.84 (t, *J* = 4.4 Hz, 4H), 3.78 (s, 3H), 3.53 (s, 3H), 3.02 (dd, *J* = 5.6, 3.2 Hz, 4H), 0.72 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.1, 158.7, 143.4, 143.1, 139.0, 137.1, 132.7, 131.8, 130.7, 129.8, 127.5, 117.3, 117.2, 112.5, 74.3, 67.1, 55.1, 52.7, 50.9, 33.9, 31.0; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{39}N_2O_4^+$: 515.2904; found: 515.2896. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, rt, λ = 254 nm, t_{R1} = 8.961 min (major), t_{R2} = 11.840 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = - 69.67 (c = 3.35, $CHCl_3$).



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.955	16987102	679271	50.326		M	
2	11.768	16766860	532134	49.674		M	
总计		33753962	1211405				

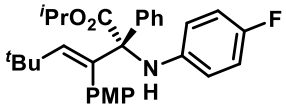


<Peak Table>

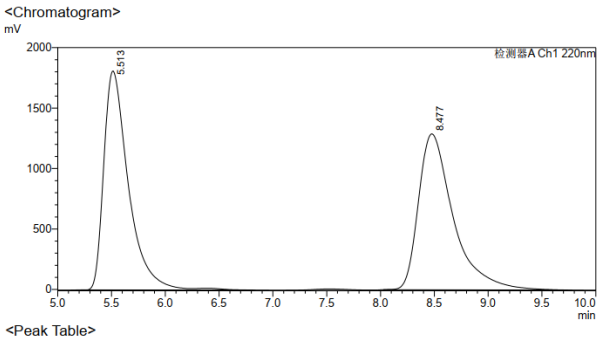
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.961	3522350	142522	98.757		M	
2	11.840	44329	1814	1.243		M	
总计		3566679	144336				

Isopropyl (*R*,*E*)-2-((4-fluorophenyl)amino)-3-(4-methoxyphenyl)-5,5-dimethyl-2-phenylhex-3-enoate (4o)

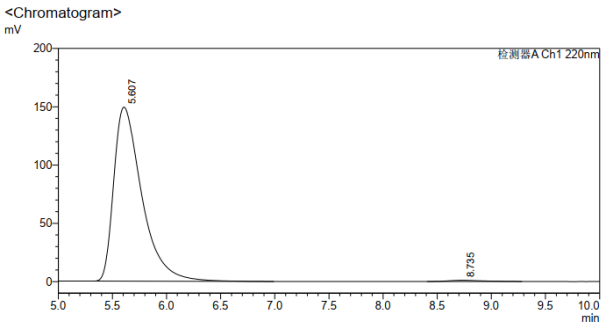


General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4o** as a colorless oil (32.1 mg, 68%). $\mathbf{R_f}$ = 0.51 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75–7.71 (m, 2H), 7.36–7.28 (m, 3H), 7.16–7.07 (m, 1H), 6.82–6.73 (m, 4H), 6.61–6.53 (m, 1H), 6.45–6.40 (m, 2H), 5.91 (s, 1H), 5.17 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 1.09 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 158.9, 155.8 (d, $J_{C\text{-}F}$ = 233.5 Hz), 143.2, 141.3 (d, $J_{C\text{-}F}$ = 2.1 Hz), 137.3, 133.4, 130.4, 129.4, 127.5, 127.4, 116.8 (d, $J_{C\text{-}F}$ = 7.2 Hz), 114.9 (d, $J_{C\text{-}F}$ = 21.9 Hz), 112.5, 74.1, 70.1, 55.2, 55.1, 34.0, 31.1, 21.6, 21.3; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -128.1; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{35}FNO_3^+$: 476.2595; found: 476.2591. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 5.607 min (major), t_{R2} = 8.735 min (minor); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 20.07 (c = 2.68, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

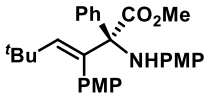
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.513	28927104	1809632	49.962		M	
2	8.477	28971303	1288936	50.038		M	
总计		57898407	3098569				



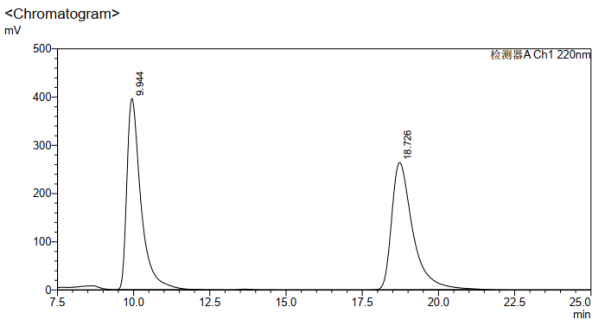
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.607	2699206	149337	99.211		M	
2	8.735	21461	991	0.789		M	
总计		2720667	150328				

Methyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4p)



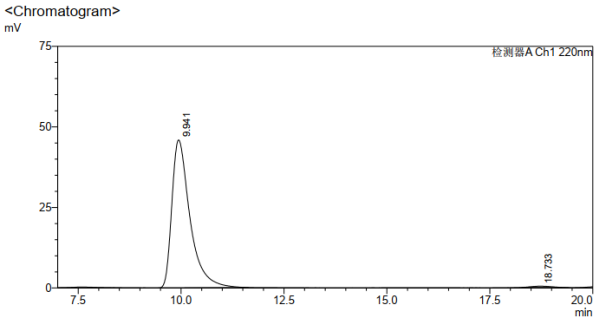
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4p** as a yellow oil (67.3 mg, 73%). $\mathbf{R_f}$ = 0.68 (PE/EtOAc = 40/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83–7.80 (m, 2H), 7.38–7.30 (m, 3H), 7.07–7.02 (m, 1H), 6.75–6.69 (m, 5H), 6.47 (d, *J* = 8.8 Hz, 2H), 5.93 (s, 1H), 5.17 (s, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.54 (s, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.2, 158.8, 152.0, 143.5, 138.8, 137.2, 132.8, 131.9, 130.8, 129.9, 127.6, 117.5, 114.2, 112.6, 74.5, 55.7, 55.2, 52.8, 34.0, 31.1; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{29}H_{34}NO_4^+$:460.2482; found: 460.2482. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 9.941 min (major), t_{R2} = 18.733 min (minor); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 75.54 (c = 5.88, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.944	12680541	396351	49.954		M	
2	18.726	12703813	263902	50.046		M	
总计		25384354	660253				

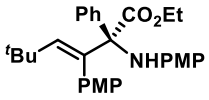


<Peak Table>

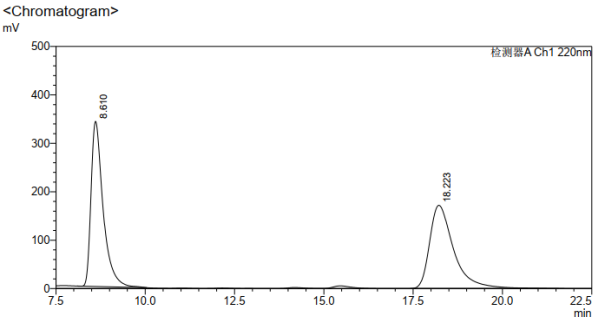
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.941	1408569	45966	98.928		M	
2	18.733	15263	443	1.072		M	
总计		1423833	46409				

Ethyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4q)



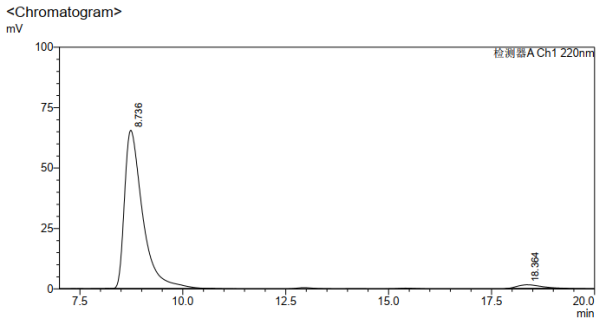
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4q** as a brown solid (60.4 mg, 64%). $\mathbf{R_f}$ = 0.38 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82–7.79 (m, 2H), 7.37–7.29 (m, 3H), 7.09–7.04 (m, 1H), 6.74–6.68 (m, 5H), 6.47 (d, *J* = 8.8 Hz, 2H), 5.92 (s, 1H), 5.13 (s, 1H), 4.04–3.87 (m, 2H), 3.78 (s, 3H), 3.73 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.7, 158.8, 152.0, 143.4, 139.0, 137.5, 133.2, 132.3, 130.7, 129.8, 127.52, 127.51, 117.5, 114.1, 112.5, 74.4, 62.0, 55.7, 55.2, 34.0, 31.1, 13.9; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{36}NO_4^+$:474.2639; found: 474.2630. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 8.736 min (major), t_{R2} = 18.364 min (minor); 94% *ee*. **$[\alpha]_D^{16.0}$** = - 61.32 (c = 3.62, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.610	8034961	340948	49.910		M	
2	18.223	8063984	171855	50.090		M	
总计		16098945	512803				

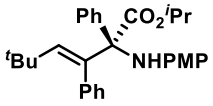


<Peak Table>

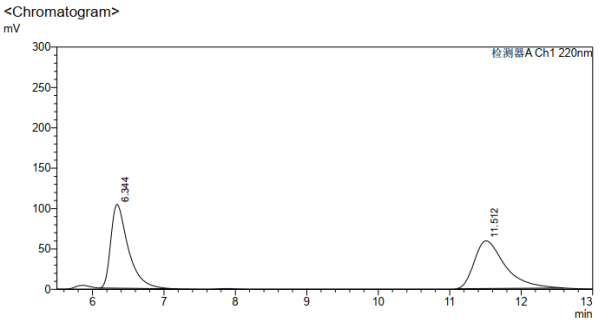
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.736	2004544	65473	96.958		M	
2	18.364	62886	1550	3.042		M	
总计		2067430	67023				

Isopropyl (*R*,*E*)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2,3-diphenylhex-3-enoate (4r)



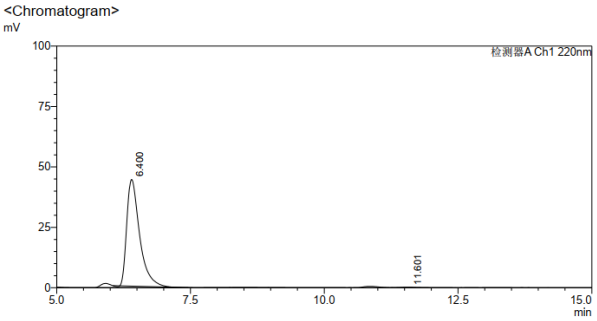
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) then PTLC (Tol:THF = 2000/1) to afford **4r** as a yellow oil (82.3 mg, 90%). $\mathbf{R}_f$ = 0.53 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.36–7.30 (m, 3H), 7.23–7.21 (m, 4H), 6.69 (d, *J* = 8.8 Hz, 3H), 6.46 (d, *J* = 8.8 Hz, 2H), 5.92 (s, 1H), 5.05 (s, 1H), 4.76 (sept, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 1.07 (d, *J* = 6.0 Hz, 3H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 152.0, 142.8, 139.2, 137.9, 137.7, 134.1, 130.6, 127.5, 127.4, 127.3, 117.4, 114.2, 74.3, 70.0, 55.8, 34.0, 31.1, 21.5, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{36}NO_3^+$:458.2690; found: 458.2680. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.400 min (major), t_{R2} = 11.601 min (minor); 99% *ee*. **$[\alpha]_D^{16.0}$** = - 19.32 (c = 3.83, $CHCl_3$). While *tert*-butyl bromide was used as an electrophile, **4r** was obtained in only 16% yield with 46% ee.



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.344	1768187	103622	49.977		M	
2	11.512	1769846	58935	50.023		M	
总计		3538032	162557				

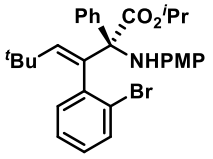


<Peak Table>

检测器A Ch1 220nm

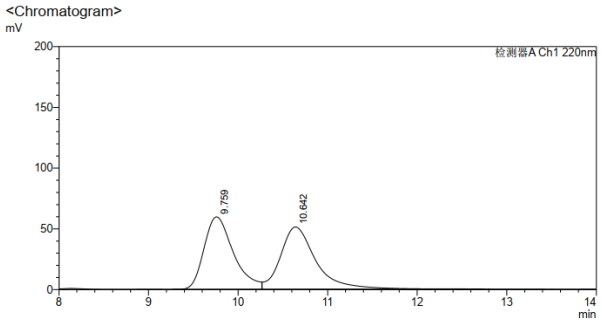
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.400	733812	44135	99.466		M	
2	11.601	3942	220	0.534		M	
总计		737754	44355				

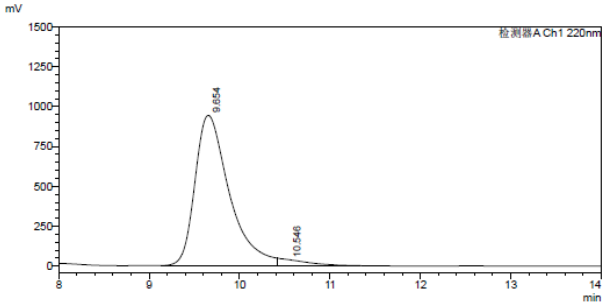
Isopropyl (*R*,*E*)-3-(2-bromophenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4s)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4s** as a yellow oil (63.6 mg, 59%). $\mathbf{R}_f$ = 0.61 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75–7.72 (m, 2H), 7.54 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35–7.27 (m, 3H), 7.21 (td, *J* = 7.6, 1.2 Hz, 1H), 7.13 (td, *J* =7.6, 1.2 Hz, 1H), 7.07 (dd, *J* = 7.2, 1.6 Hz, 1H), 6.58 (d, *J* = 9.2 Hz, 2H), 6.39 (d, *J* = 8.8 Hz, 2H), 5.63 (s, 1H), 4.88 (s, 1H), 4.60 (sept, *J* = 6.4 Hz, 1H), 3.67 (s, 3H), 0.78 (d, *J* = 6.0 Hz, 3H), 0.76 (d, *J* = 6.4 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 152.6, 146.7, 141.9, 140.9, 139.8, 137.5, 132.5, 132.3, 129.8, 129.1, 127.6, 127.2, 127.0, 126.5, 117.2, 114.0, 74.8, 69.2, 55.8, 34.6, 29.7, 21.2, 21.1; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{35}BrNO_3^+$:536.1795; found: 536.1788. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH =

98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 9.654 min (major), t_{R2} = 10.546 min (minor); 93% *ee*. **[α]$_D^{16.0}$** = 9.03 (c = 2.79, $CHCl_3$).





<Peak Table>

检测器A Ch1 220nm

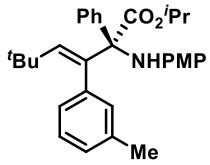
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.759	1361517	59650	49.083		M	
2	10.642	1412378	51246	50.917		V M	
总计		2773895	110896				

<Peak Table>

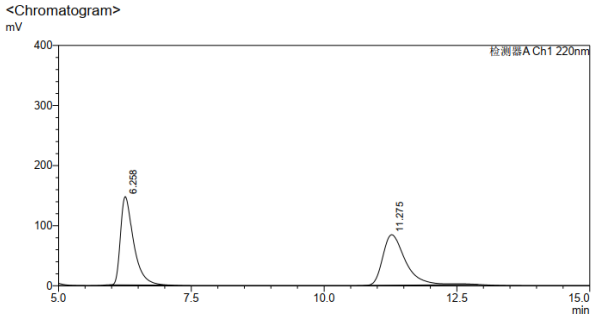
检测器A Ch1 220nm

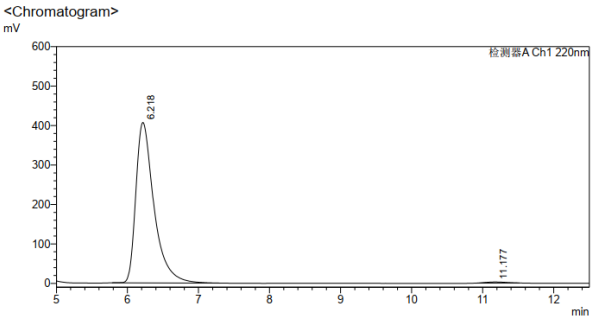
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.654	24862361	941634	96.583		M	
2	10.546	879735	37161	3.417		V M	
总计		25742096	978796				

Isopropyl (*R*,*E*)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenyl-3-(m-tolyl)hex-3-enoate (4t)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) then PTLC (Tol:THF = 2000/1) to afford **4t** as a yellow oil (87.6 mg, 93%). **R_f** = 0.62 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.35–7.29 (m, 3H), 7.10–7.02 (m, 3H), 6.68 (d, *J* = 9.2 Hz, 2H), 6.52–6.43 (m, 3H), 5.88 (s, 1H), 5.03 (s, 1H), 4.76 (sept, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 2.31–2.19 (m, 3H), 1.06 (d, *J* = 6.4 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 3H), 0.73 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 151.9, 142.4, 139.1, 137.9, 137.3, 134.1, 130.6, 127.9, 127.32, 127.26, 117.3, 114.0, 74.2, 69.8, 55.7, 33.9, 31.0, 21.4, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{38}NO_3^+$:472.2846; found: 472.2841. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.218 min (major), t_{R2} = 11.177 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = - 4.62 (c = 1.30, $CHCl_3$).





<Peak Table>

检测器A Ch1 220nm

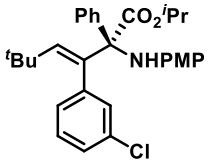
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.258	2519590	146873	50.016		M	
2	11.275	2517953	84190	49.984		M	
总计		5037544	231063				

<Peak Table>

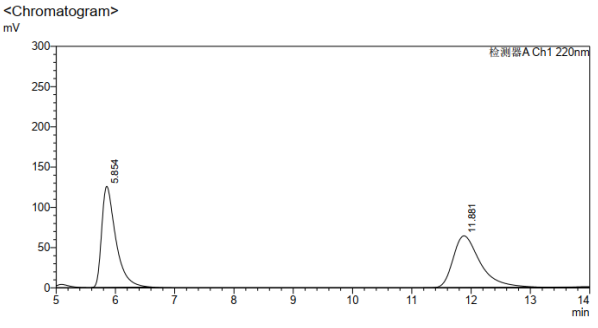
检测器A Ch1 220nm

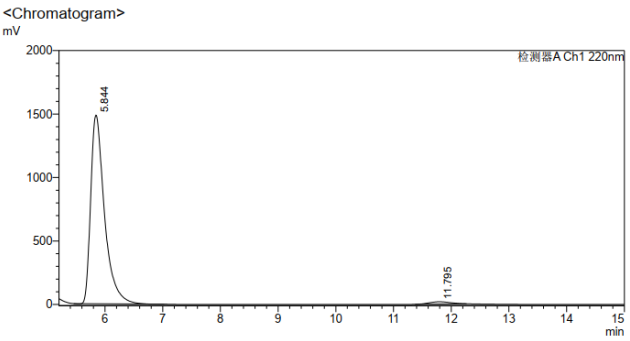
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.218	7213457	406729	99.224		M	
2	11.177	56386	2700	0.776		M	
总计		7269843	409428				

Isopropyl (*R*,*E*)-3-(3-chlorophenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4u)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) then PTLC (Tol:THF = 2000/1) to afford **4u** as a yellow oil (67.6 mg, 69%). $\mathbf{R_f}$ = 0.53 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 6.8 Hz, 2H), 7.37–7.31 (m, 3H), 7.22–7.10 (m, 3H), 6.72–6.67 (m, 3H), 6.48 (d, *J* = 8.8 Hz, 2H), 5.96 (s, 1H), 5.15 (s, 1H), 4.76 (sept, *J* = 6.4 Hz, 1H), 3.73 (s, 3H), 1.15 (s, 3H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.7, 152.0, 144.0, 139.6, 138.6, 137.2, 131.8, 130.5, 128.5, 127.6, 127.4, 127.3, 117.4, 114.1, 74.1, 70.3, 55.7, 34.0, 31.0, 21.4, 21.2; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{35}ClNO_3^+$:492.2300; found: 492.2293. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 5.844 min (major), t_{R2} = 11.795 min (minor); 96% *ee*. **$[\alpha]_D^{16.0}$** = - 43.46 (c = 1.56, $CHCl_3$).





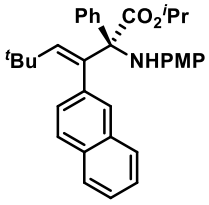
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.854	2070215	125515	50.119		M	
2	11.881	2060410	64376	49.881		M	
总计		4130625	189891				

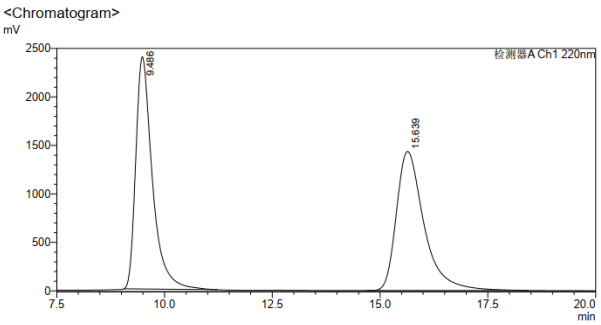
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5.844	24638502	1486304	98.191		M	
2	11.795	453829	17762	1.809		M	
总计		25092330	1504066				

Isopropyl (*R*,*E*)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-3-(naphthalen-2-yl)-2-phenylhex-3-enoate (4v)

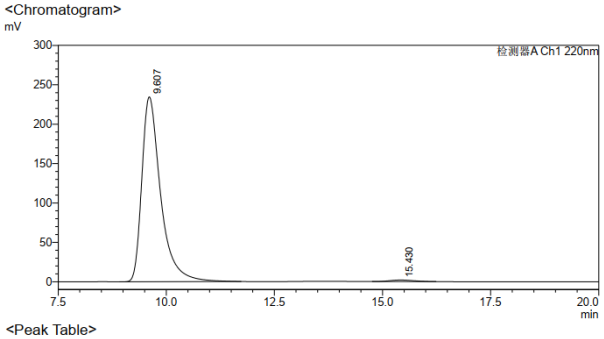


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4v** as a yellow oil (94.6 mg, 93%). $\mathbf{R_f}$ = 0.56 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85–7.80 (m, 3H), 7.68–7.65 (m, 2H), 7.47–7.32 (m, 6H), 7.18–6.85 (m, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 6.05 (s, 1H), 5.12 (s, 1H), 4.76 (sept, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 1.10 (d, *J* = 6.4 Hz, 3H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.77 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.0, 152.1, 143.2, 139.1, 137.8, 132.7, 132.4, 130.7, 130.4, 129.5, 129.0, 128.3, 127.7, 127.6, 127.5, 126.6, 125.9, 117.4, 114.2, 74.5, 70.0, 55.8, 34.1, 31.2, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{34}H_{38}NO_3^+$:508.2846; found: 508.2840. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 9.607 min (major), t_{R2} = 15.430 min (minor); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 50.40 (c = 5.69, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

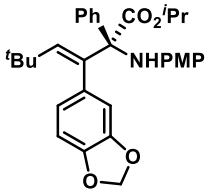
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.486	64178358	2393663	50.098		M	
2	15.639	63926626	1433611	49.902		M	
总计		128104984	3827274				



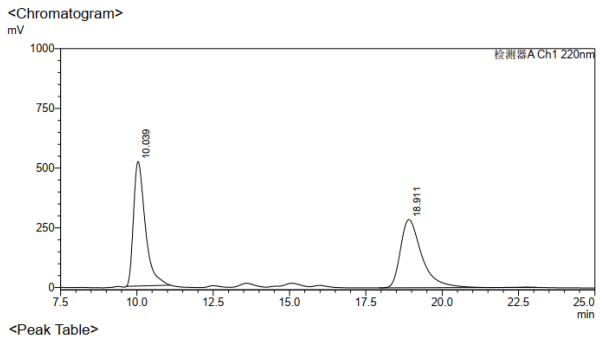
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.607	7101681	234655	98.935		M	
2	15.430	76431	1966	1.065		M	
总计		7178112	236621				

Isopropyl (*R*,*E*)-3-(benzo[d][1,3]dioxol-5-yl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4w)

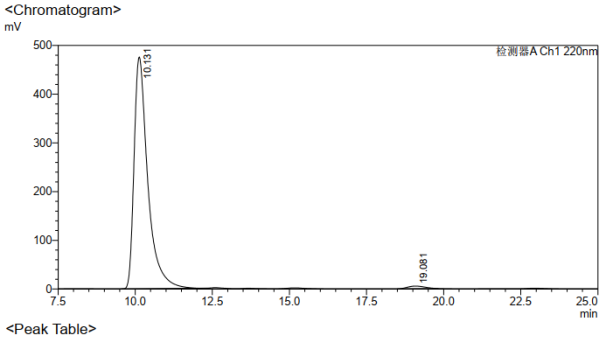


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4w** as a yellow oil (56.0 mg, 56%). $\mathbf{R_f}$ = 0.45 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.2 Hz, 2H), 7.36–7.30 (m, 3H), 6.69–6.66 (m, 4H), 6.45 (d, *J* = 8.8 Hz, 2H), 6.20–6.16 (m, 1H), 5.94–5.90 (m, 3H), 5.07 (s, 1H), 4.80 (sept, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.77 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 152.0, 146.8, 143.3, 139.0, 137.8, 131.0, 130.6, 127.5, 127.4, 117.4, 116.4, 114.2, 113.9, 111.1, 106.8, 100.9, 74.3, 70.0, 55.8, 34.1, 31.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{36}NO_5^+$:502.2588; found: 502.2581. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 10.131 min (major), t_{R2} = 19.081 min (minor); 97% *ee*. **$[\alpha]_D^{16.0}$** = - 49.78 (c = 4.05, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

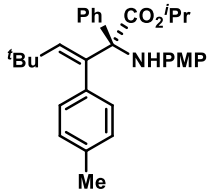
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.039	13964563	521060	50.197		M	
2	18.911	13855066	285075	49.803		M	
总计		27819629	806135				



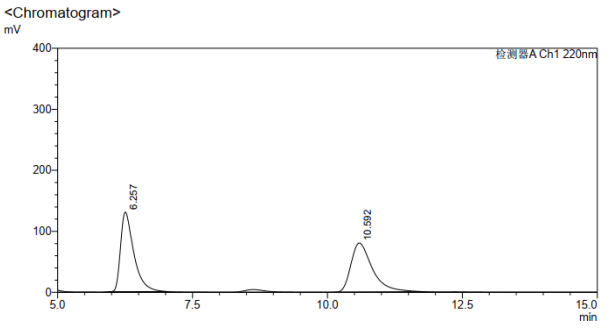
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	10.131	14644215	475544	98.530		M	
2	19.081	218408	5531	1.470		M	
总计		14862623	481075				

Isopropyl (*R*,*E*)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenyl-3-(p-tolyl)hex-3-enoate (4x)



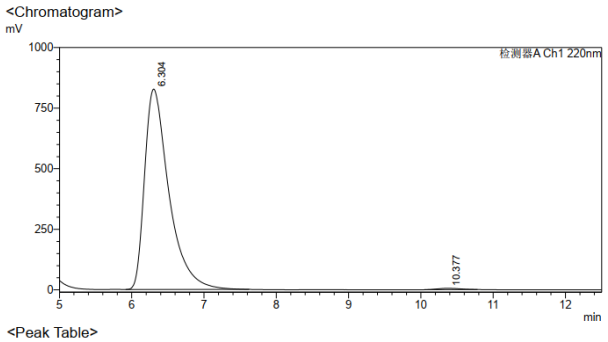
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) then PTLC (Tol:THF = 2000/1) to afford **4x** as a yellow oil (86.7 mg, 92%). $\mathbf{R_f}$ = 0.62 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 6.8 Hz, 2H), 7.35–7.29 (m, 3H), 7.02–6.96 (m, 3H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.56–6.53 (m, 1H), 6.44 (d, *J* = 8.8 Hz, 2H), 5.90 (s, 1H), 5.00 (s, 1H), 4.77 (sept, *J* = 6.4 Hz, 1H), 3.71 (s, 3H), 2.31 (s, 3H), 1.07 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ172.2, 152.0, 142.5, 139.3, 138.0, 136.9, 134.5, 134.4, 130.6, 128.0, 127.40, 127.37, 117.3, 114.1, 74.3, 69.9, 55.8, 33.9, 31.1, 21.5, 21.4, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{31}H_{38}NO_3^+$:472.2846; found: 472.2837. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.304 min (major), t_{R2} = 10.377 min (minor); 99% *ee*. **$[\alpha]_D^{16.0}$** = - 24.80 (c = 3.21, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.257	2225233	130364	50.060		M	
2	10.592	2219927	80397	49.940		M	
总计		4445160	210761				

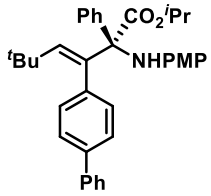


<Peak Table>

检测器A Ch1 220nm

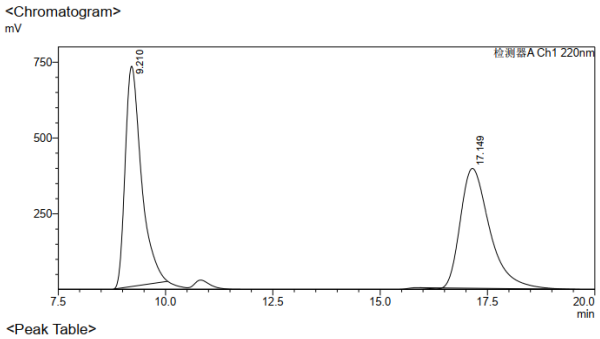
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.304	19380494	826501	99.382		M	
2	10.377	120604	5472	0.618		M	
总计		19501098	831973				

Isopropyl (*R*,*E*)-3-([1,1'-biphenyl]-4-yl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4y)



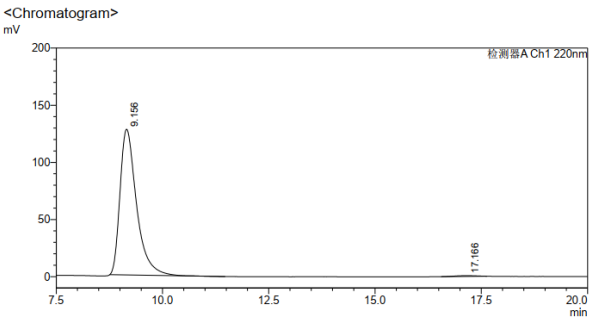
General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4y** as a yellow oil (49.6 mg, 93%). $\mathbf{R_f}$ = 0.59 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.46–7.31 (m, 9H), 6.92–6.80 (m, 1H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.51 (d, *J* = 8.8 Hz, 2H), 5.98 (s, 1H), 5.11 (s, 1H), 4.80 (sept, *J* = 6.4 Hz, 1H), 3.74 (s, 3H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.79 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 152.0, 143.1, 140.9, 139.9, 139.1, 137.8, 136.8, 133.8, 130.7, 128.8, 127.53, 127.47, 127.4, 127.1, 125.5, 117.4, 114.2, 74.3, 70.1, 55.8, 34.0, 31.2, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{36}H_{40}NO_3^+$:534.3003; found:

534.2994. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 9.156 min (major), t_{R2} = 17.166 min (minor); 99% *ee*. **[α]$_D^{16.0}$** = - 74.66 (c = 3.82, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

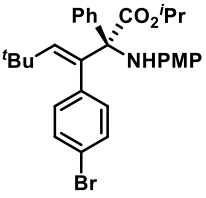
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.210	19113481	726065	50.399		M	
2	17.149	18810889	394905	49.601		M	
总计		37924370	1120970				



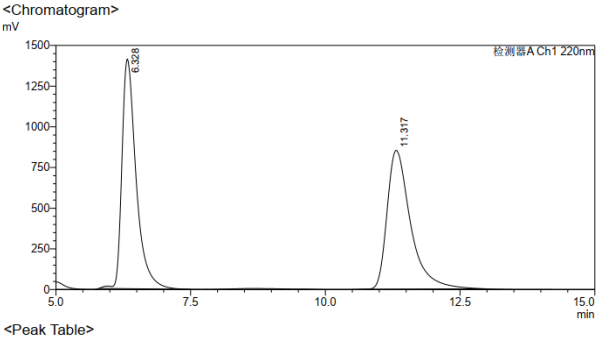
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.156	3451286	127543	99.333		M	
2	17.166	23163	661	0.667		M	
总计		3474449	128204				

Isopropyl (*R*,*E*)-3-(4-bromophenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4z)

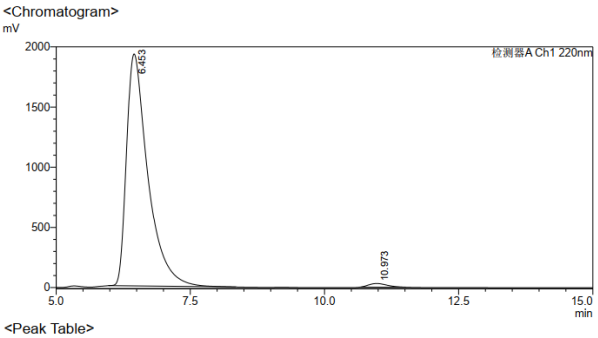


General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) then PTLC (Tol:THF = 2000/1) to afford **4z** as a yellow oil (52.0 mg, 96%). **R_f** = 0.68 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.36–7.28 (m, 5H), 7.08–7.04 (m, 1H), 6.71–6.58 (m, 3H), 6.46 (d, *J* = 8.8 Hz, 2H), 5.96 (s, 1H), 5.03 (s, 1H), 4.77 (sept, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 1.09 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 152.1, 143.6, 138.8, 137.4, 136.8, 132.6, 130.6, 130.2, 127.7, 127.5, 121.6, 117.4, 114.2, 74.1, 70.2, 55.8, 34.0, 31.1, 21.6, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{30}H_{35}BrNO_3^+$:536.1795; found: 536.1788. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.453 min (major), t_{R2} = 10.973 min (minor); 98% *ee*. **[α]$_D^{16.0}$** = - 36.40 (c = 1.00, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

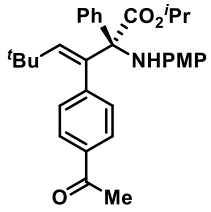
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.328	25795068	1410172	49.912		M	
2	11.317	25886331	853267	50.088		M	
总计		51681398	2263440				



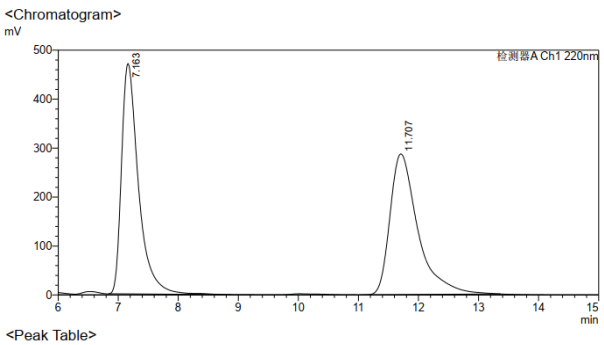
<Peak Table>
检测器A Ch1 220nm

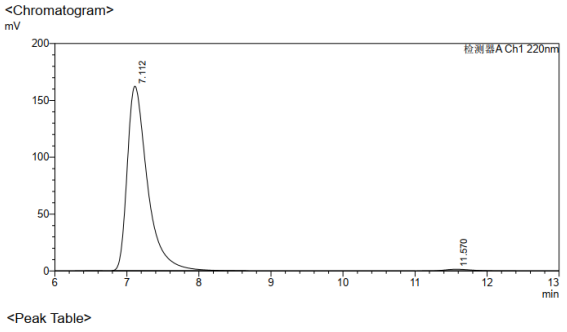
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.453	53482810	1927520	98.712		M	
2	10.973	697832	29633	1.288		M	
总计		54180642	1957153				

Isopropyl (*R*,*E*)-3-(4-acetylphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhex-3-enoate (4aa)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 30/1) to afford **4aa** as a white solid (78.4 mg, 79%). $\mathbf{R}_f$ = 0.24 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78–7.73 (m, 4H), 7.37–7.29 (m, 4H), 6.88–6.84 (m, 1H), 6.70 (d, *J* = 9.2 Hz, 2H), 6.48 (d *J* = 8.8 Hz, 2H), 6.00 (s, 1H), 5.07 (s, 1H), 4.75 (sept, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 2.58 (s, 3H), 1.09 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H), 0.74 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.0, 171.8, 152.2, 143.5, 143.4, 138.7, 137.3, 136.0, 132.8, 130.5, 127.7, 127.5, 117.4, 114.2, 74.1, 70.3, 55.7, 34.0, 31.1, 26.7, 21.5, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{38}NO_4^+$:500.2795; found: 500.2787. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 7.112 min (major), t_{R2} = 11.570 min (minor); 97% *ee*. **$[\alpha]_D^{16.0}$** = -75.50 (c = 6.22, $CHCl_3$).





<Peak Table>

检测器A Ch1 220nm

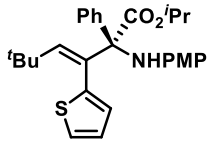
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.163	9234738	470357	49.839		M	
2	11.707	9294507	287368	50.161		M	
总计		18529245	757724				

<Peak Table>

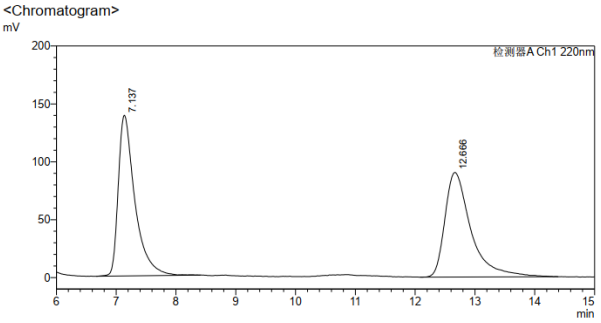
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.112	3172937	162210	98.546		M	
2	11.570	46799	1643	1.454		M	
总计		3219737	163853				

Isopropyl (*R*,*Z*)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenyl-3-(thiophen-2-yl)hex-3-enoate (4ab)

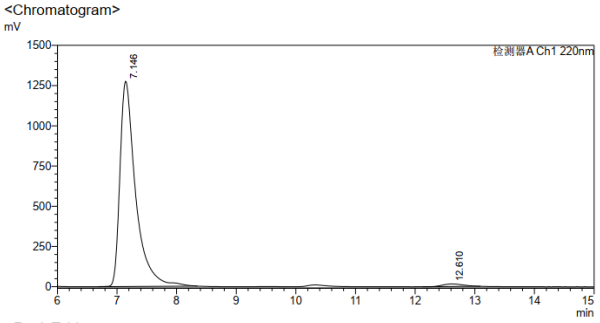


General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4ab** as a yellow solid (34.0 mg, 73%). $\mathbf{R}_f$ = 0.66 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78–7.75 (m, 2H), 7.37–7.29 (m, 3H), 7.22 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.87 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.68 (d, *J* = 9.2 Hz, 2H), 6.64 (d, *J* = 3.2 Hz, 1H), 6.47 (d, *J* = 8.8 Hz, 2H), 6.07 (s, 1H), 5.19 (s, 1H), 4.81 (sept, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.80 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.0, 152.1, 147.0, 138.5, 137.4, 137.3, 130.6, 129.6, 127.7, 127.6, 125.9, 125.6, 117.8, 114.0, 74.4, 70.2, 55.8, 34.2, 30.6, 21.5, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{28}H_{34}NO_3S^+$:464.2254; found: 464.2254. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 7.146 min (major), t_{R2} = 12.610 min (minor); 97% *ee*. **$[\alpha]_D^{16.0}$** = - 33.77 (c = 1.38, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

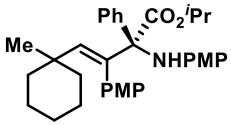
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.137	2679631	138718	49.511		M	
2	12.666	2732549	90292	50.489		M	
总计		5412180	229010				



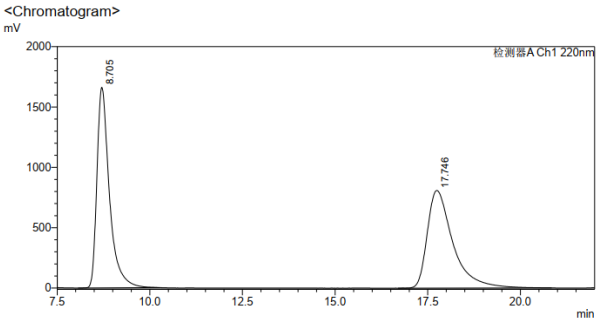
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7.146	23344972	1274955	98.383		M	
2	12.610	383631	16200	1.617		M	
总计		23728603	1291155				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-4-(1-methylcyclohexyl)-2-phenylbut-3-enoate (4ac)

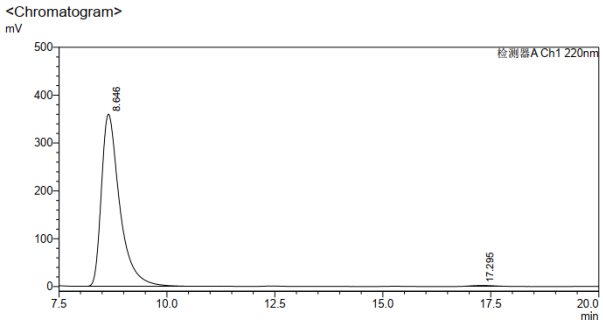


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4ac** as a yellow oil (92.7 mg, 88%). $\mathbf{R_f}$ = 0.36 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.2 Hz, 2H), 7.37–7.30 (m, 3H), 7.17–7.15 (m, 1H), 6.72–6.61 (m, 5H), 6.48 (d, *J* = 8.8 Hz, 2H), 5.91 (s, 1H), 5.00 (s, 1H), 4.81 (sept, *J* = 6.4 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 1.40–1.22 (m, 8H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.97–0.91 (m, 2H), 0.77 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 158.5, 151.6, 141.6, 138.9, 137.6, 135.3, 131.7, 130.3, 129.4, 127.1, 127.0, 116.9, 113.9, 112.2, 74.2, 69.6, 66.9, 55.4, 54.8, 39.7, 38.8, 36.9, 25.8, 22.8, 22.5, 21.3, 21.1; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{34}H_{42}NO_4^+$: 528.3108; found: 528.3099. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 8.646 min (major), t_{R2} = 17.295 min (minor); 99% *ee*. **[α]$_D^{16.0}$** = - 24.13 (c = 8.62, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.705	38934614	1660712	50.034		M	
2	17.746	38882310	808698	49.966		M	
总计		77816924	2469410				

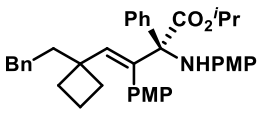


<Peak Table>
检测器A Ch1 220nm

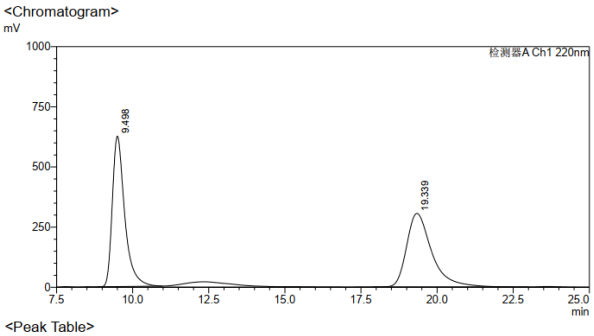
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8.646	10552182	359475	99.575		M	
2	17.295	45029	1506	0.425		M	
总计		10597211	360981				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-4-(1-phenethylcyclobutyl)-2-phenylbut-3-enoate (4ad)

General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4ad** as a yellow oil (48.6 mg, 41%). $\mathbf{R_f}$ =

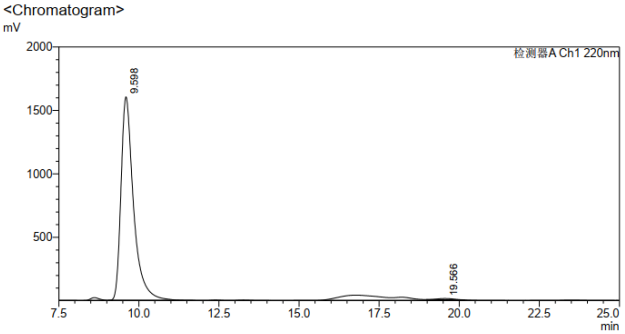


0.30 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86–7.83 (m, 2H), 7.37–7.28 (m, 5H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.15–7.13 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.74–6.67 (m, 4H), 6.53 (d, *J* = 8.8 Hz, 2H), 6.02 (s, 1H), 5.11 (s, 1H), 4.77 (sept, *J* = 6.4 Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 2.59–2.44 (m, 2H), 1.86–1.52 (m, 8H), 1.04 (d, *J* = 6.0 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 165.7, 159.0, 152.1, 140.7, 139.3, 138.9, 137.7, 135.7, 131.0, 130.6, 129.2, 129.1, 128.8, 127.6, 127.5, 117.4, 114.2, 112.6, 74.5, 70.1, 63.1, 55.7, 55.2, 41.8, 36.3, 29.7, 29.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{39}H_{44}NO_4^+$: 590.3265; found: 590.3255. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, rt, flow rate 1 mL/min, λ = 220 nm, t_{R1} = 9.598 min (major), t_{R2} = 19.566 min (minor); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 20.11 (c = 1.79, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

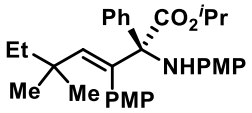
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.498	17709476	625112	50.136		M	
2	19.339	17613110	305671	49.864		M	
总计		35322586	930783				



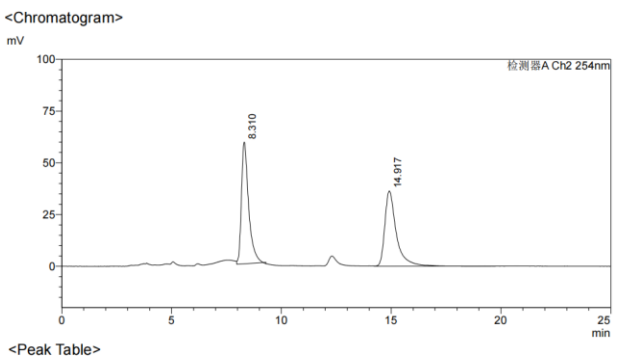
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9.598	43672429	1603478	99.151		M	
2	19.566	374043	9957	0.849		M	
总计		44046472	1613435				

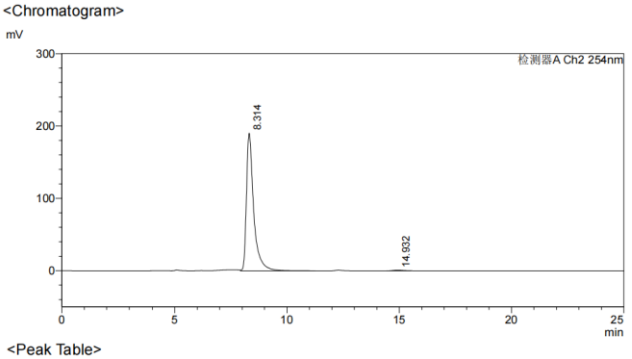
Isopropyl-(*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhept-3-enoate (4ae)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1~20/1)) to afford **4ae** as a yellow oil (53.2 mg, 53%). **R_f** = 0.14 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 6.4 Hz, 2H), 7.35–7.29 (m, 3H), 7.15–7.10 (m, 1H), 6.81–6.57 (m, 5H), 6.44 (d, *J* = 8.8 Hz, 2H), 5.82 (s, 1H), 4.97 (s, 1H), 4.79 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.16 (dt, *J* = 7.6, 7.2 Hz, 2H), 1.08 (d, *J* = 6.4 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.74 (t, *J* = 7.6 Hz, 3H), 0.66 (s, 3H), 0.61 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 158.8, 152.0, 141.8, 139.3, 138.0, 135.1, 130.6, 129.7, 127.41, 127.37, 117.2, 114.2, 112.4, 74.4, 69.9, 55.8, 55.2, 37.3, 36.9, 28.9, 27.9, 21.6, 21.4, 9.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{32}H_{39}NO_4^+$: 502.2952; found: 502.2948. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 °C, λ = 254 nm, t_{R1} = 8.314 min (major), t_{R2} = 14.932 min (minor); 98% *ee*. **$[\alpha]_D^{19.0}$** = -35.78 (c = 0.49, $CHCl_3$).

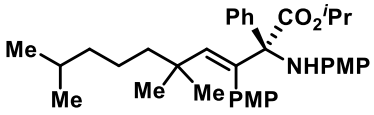


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.310	1333006	58768	50.168		M
2	14.917	1324086	36392	49.832		S
总计		2657092	95159			

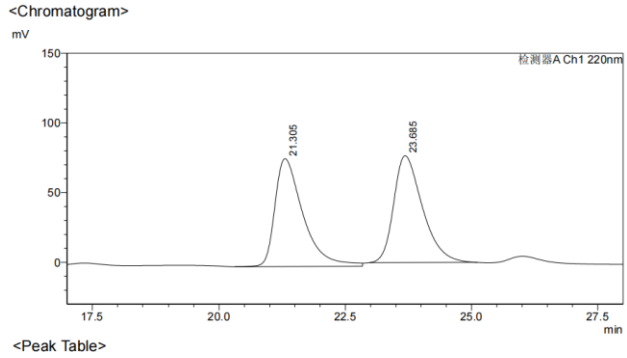


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.314	4267387	190216	99.288		S
2	14.932	30622	941	0.712		V M
总计		4298009	191157			

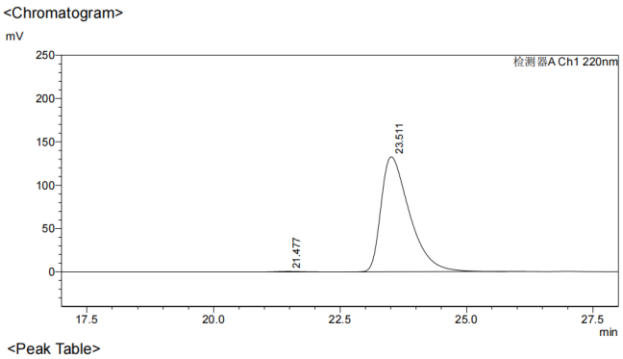
Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5,9-trimethyl-2-phenyldec-3-enoate (4af)



General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1~30/1) to afford **4af** as a yellow oil (35.5 mg, 64%). $\mathbf{R_f}$ = 0.55 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 6.0 Hz, 2H), 7.34–7.29 (m, 3H), 7.11 (bs, 1H), 6.76–6.58 (m, 5H), 6.44 (d, *J* = 8.8 Hz, 2H), 5.83 (s, 1H), 4.98 (s, 1H), 4.78 (sept, *J* = 6.0 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 1.49 (sept, *J* = 6.4 Hz, 1H), 1.54–1.44 (m, 1H), 1.19–1.00 (m, 12H), 0.87 (d, *J* = 8.4 Hz, 6H), 0.69 (s, 3H), 0.61 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 158.8, 152.0, 142.1, 139.2, 138.0, 134.7, 130.6, 129.7, 127.43, 127.38, 117.2, 114.2, 112.4, 74.4, 69.9, 55.7, 55.2, 44.8, 39.8, 37.2, 29.7, 28.4, 28.1, 22.84, 22.79, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{36}H_{47}NO_4^+$: 558.3578; found: 558.3578. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 ºC, λ = 220 nm, t_{R1} = 21.477 min (minor), t_{R2} = 23.511 min (major); 99% *ee*. **$[\alpha]_D^{14.0}$** = -30.42 (c = 1.71, $CHCl_3$).

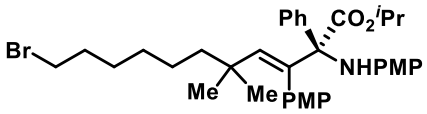


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	21.305	3010216	77397	49.713		
2	23.685	3045025	76677	50.287		M
总计		6055242	154074			

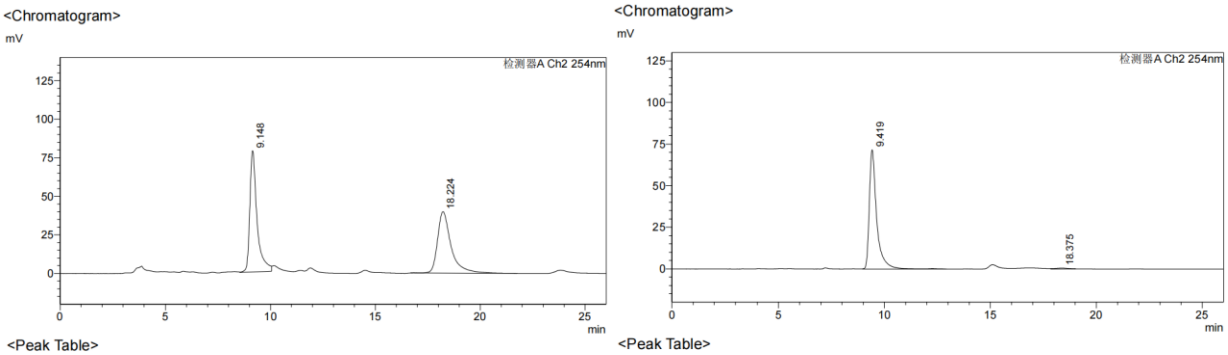


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	21.477	23792	653	0.453		
2	23.511	5225644	132678	99.547		M
总计		5249436	133331			

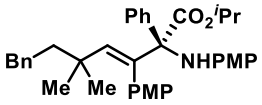
Isopropyl (*R*,*E*)-11-bromo-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylundec-3-enoate (4ag)



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1~30/1) to afford **4ag** as a yellow oil (38.6 mg, 30%). $\mathbf{R_f}$ = 0.22 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 6.4 Hz, 2H), 7.35–7.29 (m, 3H), 7.11 (bs, 1H), 6.76–6.59 (m, 5H), 6.44 (d, *J* = 8.8 Hz, 2H), 5.81 (s, 1H), 4.98 (s, 1H), 4.78 (sept, *J* = 6.4 Hz, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 3.41 (t, *J* = 6.8 Hz, 2H), 1.82 (sept, *J* = 6.8 Hz, 2H), 1.35 (quint, *J* = 6.8 Hz, 2H), 1.11–0.99 (m, 12H), 0.69 (s, 3H), 0.65 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.2, 158.9, 152.0, 141.9, 139.2, 138.0, 134.9, 130.6, 129.6, 127.5, 127.4, 117.3, 114.2, 112.5, 74.4, 69.9, 55.7, 55.2, 44.2, 37.1, 34.2, 32.9, 29.52, 29.48, 28.7, 28.3, 24.8, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{36}H_{46}BrNO_4^+$: 636.2683; found: 636.2683. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 °C, λ = 254 nm, t_{R1} = 9.419 min (major), t_{R2} = 18.375 min (minor); 98% *ee*. **$[\alpha]_D^{19.0}$** = -25.61 (c = 0.76, $CHCl_3$).

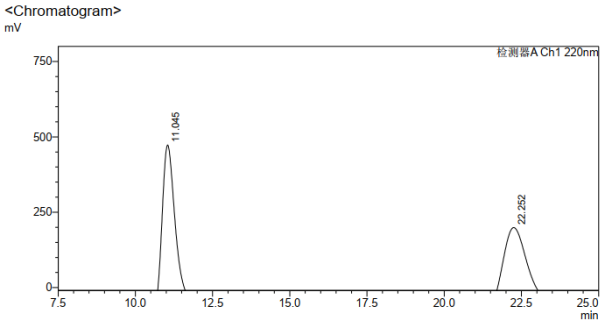


Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2,7-diphenylhept-3-enoate (4ah)



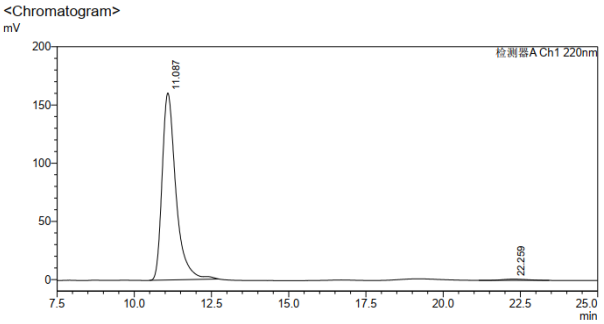
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4ah** as a brown oil (63.2 mg, 55%). $\mathbf{R_f}$ = 0.40 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85–7.82 (m, 2H), 7.39–7.28 (m, 5H), 7.18 (t, *J* = 7.2 Hz, 2H), 7.10 (d, *J* = 6.8 Hz, 2H), 6.75–6.67 (m, 5H), 6.48 (d, *J* = 8.8 Hz, 2H), 5.94 (s, 1H), 5.03 (s, 1H), 4.81 (sept, *J* = 6.4 Hz, 1H), 3.79 (s, 3H), 3.69 (s, 3H), 2.51–2.45 (m, 2H), 1.47–1.42 (m, 2H), 1.11 (d, *J* = 6.0 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H), 0.78 (s, 3H), 0.72 (3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 158.9, 152.0, 143.3, 141.7, 139.1, 138.0, 135.4, 132.3, 130.6, 129.5, 128.4, 128.3, 127.54, 127.48,

125.7, 117.3, 114.2, 112.5, 74.5, 70.0, 55.7, 55.2, 46.6, 37.3, 31.6, 29.5, 28.3, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{38}H_{44}NO_4^+$: 578.3265; found: 578.3251. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 11.087 min (minor), t_{R2} = 22.259 min (major); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 86.75 (c = 0.83, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

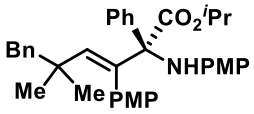
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.045	17073253	548724	50.151		M	
2	22.252	16970625	276785	49.849		M	
总计		34043879	825509				



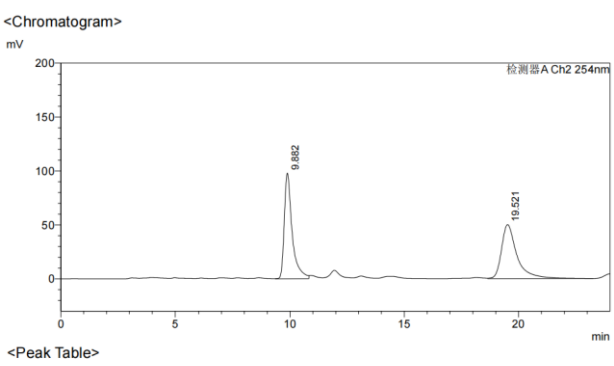
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	11.087	4990247	160665	98.808		M	
2	22.259	60183	1054	1.192		M	
总计		5050430	161718				

Isopropyl (*R*,*E*)-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2,6-diphenylhex-3-enoate (4ai)

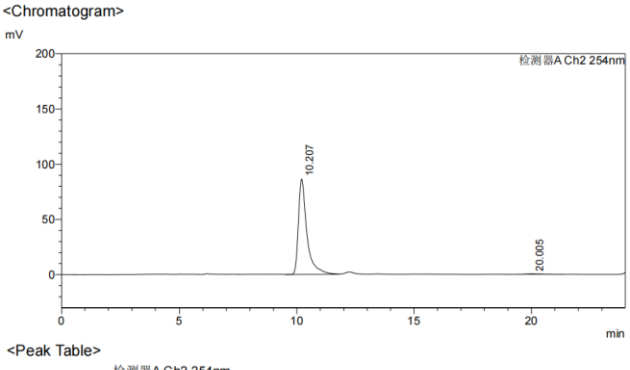


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1~20/1) to afford **4ai** as a yellow oil (78.6 mg, 70%). $\mathbf{R_f}$ = 0.24 (PE/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.34–7.25 (m, 6H), 7.09–7.06 (m, 2H), 6.72 (bs, 1H), 6.64 (d, *J* = 9.2 Hz, 4H), 6.53 (bs, 1H), 6.40 (d, *J* = 9.2 Hz, 2H), 5.91 (s, 1H), 4.96 (bs, 1H), 4.75 (sept, *J* = 6.4 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 2.50 (s, 2H), 1.05 (d, *J* = 6.4 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 3H), 0.72 (s, 3H), 0.56 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.1, 158.8, 152.0, 141.2, 139.2, 139.1, 137.9, 135.4, 130.8, 130.5, 129.5, 127.8, 127.4, 126.1, 117.2, 114.2, 112.3, 74.2, 69.9, 55.8, 55.2, 50.4, 38.5, 29.9, 27.8, 21.6, 21.5; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{37}H_{41}NO_4^+$: 564.3108; found: 564.3109. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 ºC, λ = 254 nm, t_{R1} = 10.207 min (major), t_{R2} = 20.005 min (minor); 98% *ee*. **$[\alpha]_D^{19.0}$** = -37.01 (c = 0.29, $CHCl_3$).



<Peak Table>
检测器A Ch2 254nm

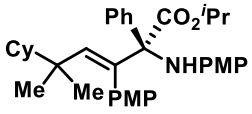
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	9.882	2342754	97935	49.902		V M
2	19.521	2351953	50053	50.098		S M
总计		4694707	147988			



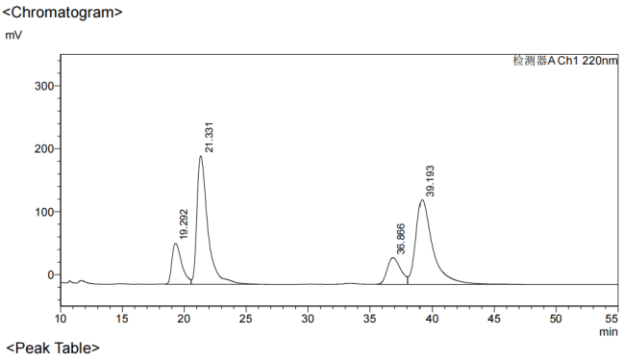
<Peak Table>
检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	10.207	2177117	86297	98.967		M
2	20.005	22723	440	1.033		M
总计		2199840	86737			

Isopropyl (*R*,*E*)-5-cyclohexyl-3-(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5-methyl-2-phenylhex-3-enoate (4aj)

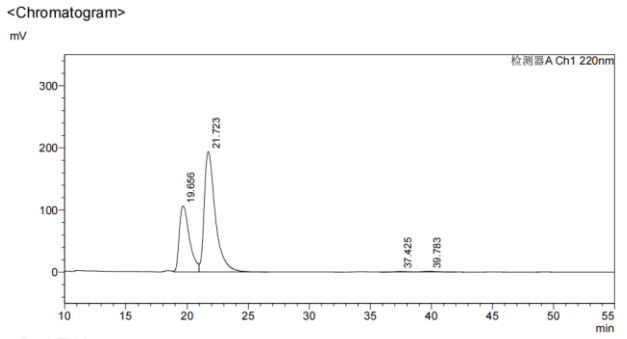


General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1) to afford **4aj** as a yellow oil (81.9 mg, 74%). $\mathbf{R_f}$ = 0.29 (PE/EtOAc = 50/1); Product was isolated as a 2:1 mixture of rotamers. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 6.8 Hz, 0.7H), 7.75 (d, *J* = 7.2 Hz, 1.3H), 7.34–7.28 (m, 3H), 7.11 (bs, 1H), 6.77 (bs, 1H), 6.67–6.64 (m, 3H), 6.57–6.52 (m, 1H), 6.42 (d, *J* = 8.4 Hz, 2H), 5.84 (s, 0.3H), 5.82 (s, 0.7H), 4.89–4.75 (m, 2H), 3.79 (s, 1H), 3.78 (s, 2H), 3.71 (s, 2H), 3.69 (s, 1H), 1.73–1.58 (m, 4H), 1.13–0.79 (m, 14H), 0.71 (d, *J* = 6.8 Hz, 1H), 0.63 (s, 2H), 0.53 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.3, 158.8, 151.9, 142.2, 140.6, 139.4, 138.4, 138.2, 134.8, 130.6, 130.5, 129.8, 127.4, 127.3, 117.1, 117.0, 114.3, 114.2, 112.4, 74.5, 69.8, 55.81, 55.76, 55.2, 49.1, 43.5, 40.2, 33.0, 32.5, 32.1, 28.0, 27.9, 27.2, 26.9, 26.54, 26.49, 25.3, 22.8, 22.5, 21.6, 21.54, 21.47, 18.1, 17.7; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{36}H_{45}NO_4^+$: 556.3421; found: 556.3416. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 °C, λ = 220 nm, t_{R1} = 19.656 min (major), t_{R2} = 21.723 min (major), t_{R3} = 37.425 min (minor), t_{R4} = 39.783 min (minor); 98% *ee*, 98% *ee*. **$[\alpha]_D^{19.0}$** = -9.84 (c = 0.21, $CHCl_3$).



<Peak Table>
检测器A Ch1 220nm

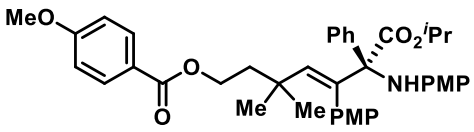
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	19.292	3566595	64870	11.259		
2	21.331	12445235	203914	39.288		V
3	36.866	3195805	42301	10.089		
4	39.193	12469070	134204	39.364		SV
总计		31676704	445289			



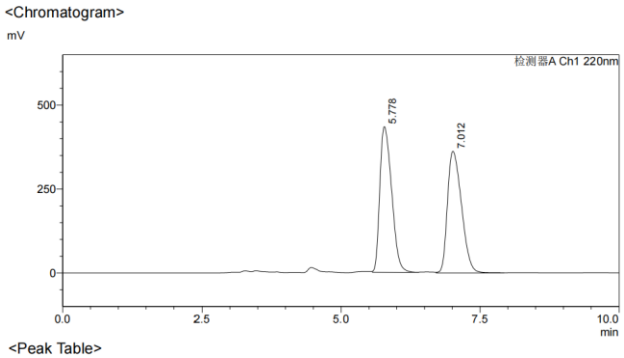
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	19.656	6148489	106354	33.038		
2	21.723	12266166	193851	65.911		SV
3	37.425	81383	1028	0.437		M
4	39.783	114260	1339	0.614		V M
总计		18610298	302572			

Isopropyl (*R*,*E*)-3,7-bis(4-methoxyphenyl)-2-((4-methoxyphenyl)amino)-5,5-dimethyl-2-phenylhept-3-enoate (4ak)



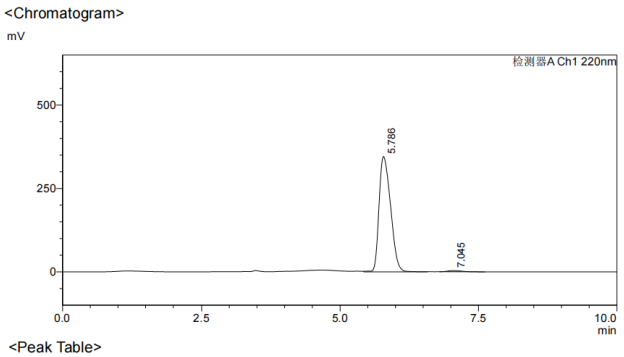
General procedure was followed on 0.2 mmol scale with **3i** (1.75 equiv) as an electrophile. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 50/1~20/1) to afford **4ak** as a yellow oil (81.0 mg, 62%). $\mathbf{R}_f$ = 0.18 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 9.2 Hz, 2H), 7.79 (d, *J* = 6.8 Hz, 2H), 7.36–7.28 (m, 3H), 7.13 (bs, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.74–6.55 (m, 5H), 6.47 (d, *J* = 8.8 Hz, 2H), 5.91 (s, 1H), 5.05 (bs, 1H), 4.79 (sept, *J* = 6.8 Hz, 1H), 4.17 (t, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.68 (s, 3H), 1.64–1.53 (m, 2H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.01 (d, *J* = 6.0 Hz, 3H), 0.81 (s, 3H), 0.76 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.0, 166.3, 163.3, 158.9, 152.0, 140.7, 138.9, 137.7, 135.6, 131.6, 130.5, 129.2, 127.54, 127.49, 123.0, 117.3, 114.2, 113.6, 112.5, 74.4, 70.1, 62.5, 55.6, 55.5, 55.1, 42.0, 36.2, 29.8, 28.9, 21.5, 21.3; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{39}H_{45}NO_5^+$: 652.3269; found: 652.3269. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1 mL/min, 30 °C, λ = 220 nm, t_{R1} = 5.786 min (major), t_{R2} = 7.045 min (minor); 97% *ee*. **[α]$_D^{14.0}$** = -13.41 (c = 2.12, $CHCl_3$).



<Peak Table>

检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.778	6425111	434050	50.093		M
2	7.012	6401187	362641	49.907		M
总计		12826299	796691			

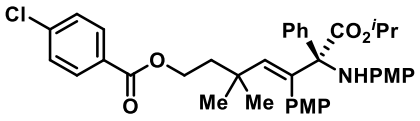


<Peak Table>

检测器A Ch1 220nm

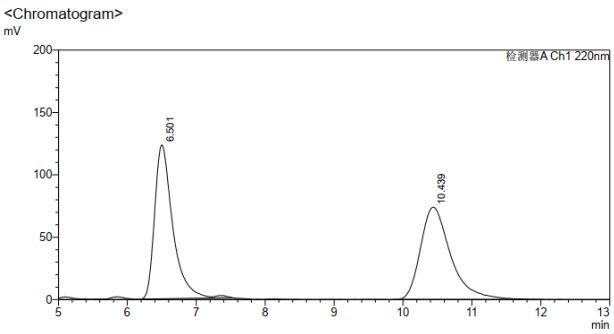
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	5.786	5015052	345745	98.735		M
2	7.045	64252	3639	1.265		M
总计		5079303	349384			

(*R*,*E*)-7-isopropoxy-5-(4-methoxyphenyl)-6-((4-methoxyphenyl)amino)-3,3-dimethyl-7-oxo-6-phenylhept-4-en-1-yl 4-chlorobenzoate (4al)



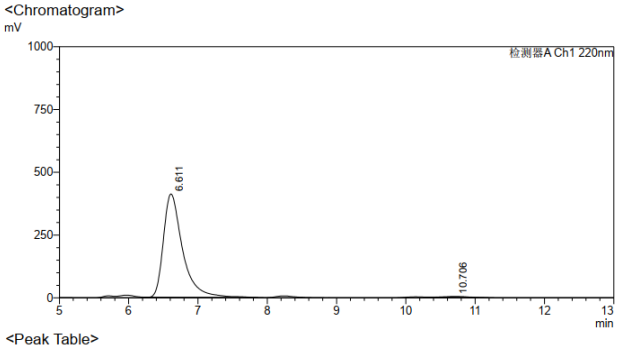
General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EtOAc = 40/1) to afford **4al** as a yellow oil (57.0 mg, 43%). $\mathbf{R}_f$ = 0.38 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 6.8 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.36–7.30 (m, 3H), 7.14–7.11 (m, 1H), 6.73–6.67 (m, 5H), 6.46 (d, *J* = 9.2 Hz, 2H), 5.89 (s, 1H), 5.04 (s, 1H), 4.78 (sept, *J* = 6.4 Hz, 1H), 4.14 (t, *J* = 6.8 Hz, 2H), 3.75 (s, 3H), 3.67 (s, 3H), 1.56 (t, *J* = 7.6 Hz, 2H), 1.10 (d, *J* = 6.4 Hz, 3H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.80 (s, 3H), 0.76 (3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.9, 165.7, 159.0, 152.1, 140.7,

139.3, 138.9, 137.7, 135.7, 131.0, 130.6, 129.2, 129.1, 128.8, 127.6, 127.5, 117.4, 114.2, 112.6, 74.5, 70.1, 63.1, 55.7, 55.2, 41.8, 36.3, 29.7, 29.1, 21.6, 21.4; **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{39}H_{43}ClNO_6^+$: 656.2773; found: 656.2765. **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 85/15, flow rate 1 mL/min, rt, λ = 220 nm, t_{R1} = 6.611 min (major), t_{R2} = 10.706 min (minor); 98% *ee*. **$[\alpha]_D^{16.0}$** = - 6.01 (c = 3.46, $CHCl_3$).



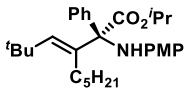
<Peak Table>
检测器A Ch1 220nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.501	2253748	123393	49.895		M	
2	10.439	2263221	74072	50.105		M	
总计		4516969	197466				

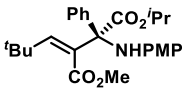


<Peak Table>
检测器A Ch1 220nm

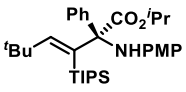
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6.611	7893389	411245	99.079		M	
2	10.706	73405	3595	0.921		M	
总计		7966795	414840				



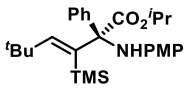
N.D.



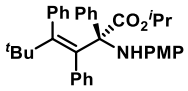
N.D.



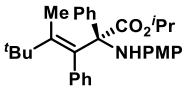
N.D.



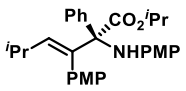
N.D.



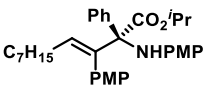
N.D.



N.D.



N.D.

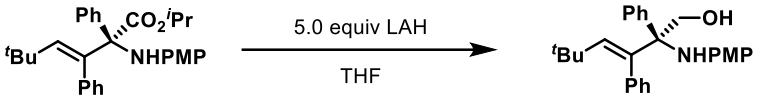


N.D.

Figure S1. The failed substrate scope.

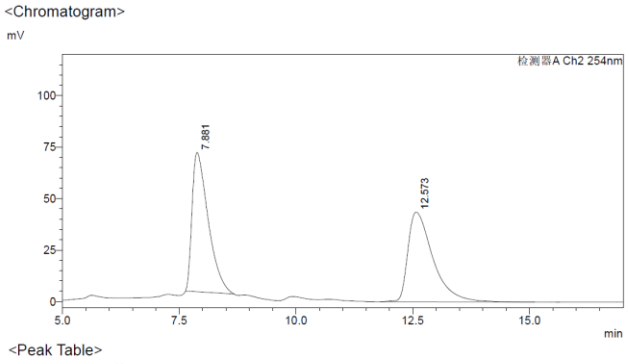
Synthetic Application

(a) Reduction of ester moiety

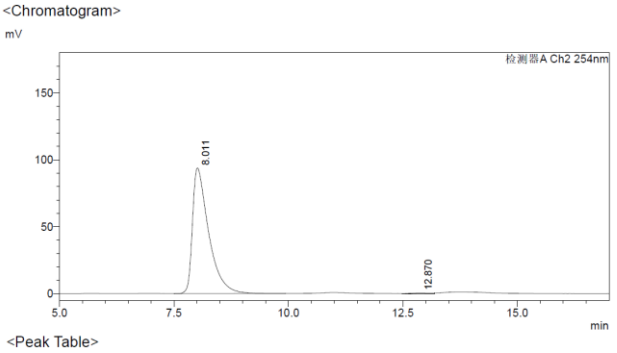


4r **5**, 97%, 99% ee

To a solution of starting material **4r** (0.1 mmol, 1.0 equiv.) in anhydrous THF (3.0 mL) under nitrogen atmosphere at 0 °C was added $LiAlH_4$ (0.5 mmol, 5.0 equiv.). The reaction mixture was stirred and allowed to warm to room temperature overnight until TLC analysis indicated complete consumption of the starting material. After completion, the reaction mixture was diluted with H_2O and extracted with EtOAc for 3 times. The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/EtOAc = 10/1~5/1) to afford **5** as a colorless oil (39.1 mg, 97%, 99% ee). $\mathbf{R_f}$ = 0.18 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.2 Hz, 2H), 7.37–7.27 (m, 3H), 7.22–7.14 (m, 3H), 6.97 (bs, 1H), 6.70 (d, *J* = 9.2 Hz, 2H), 6.67–6.65 (m, 1H), 6.61 (d, *J* = 8.8 Hz, 2H), 6.00 (s, 1H), 4.25 (bs, 1H), 3.94 (d, *J* = 11.6 Hz, 1H), 3.73–3.71 (m, 4H), 0.77 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.8, 142.2, 141.7, 139.5, 138.5, 137.3, 130.5, 130.4, 128.4, 128.3, 127.4, 127.3, 127.3, 127.1, 118.7, 114.3, 68.9, 65.8, 55.7, 33.9, 31.2. **HRMS (ESI):** $[M+H]^+$ Calcd for $C_{27}H_{32}NO_2^+$: 402.2428; found: 402.2423; **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, rt, λ = 254 nm, t_{R1} = 8.011 min (major), t_{R2} = 12.870 min (minor); 99% *ee*.

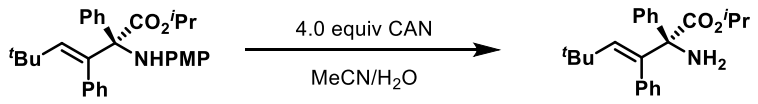


Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	7.881	1627836	67642	50.157		M
2	12.573	1617668	43543	49.843		M
总计		3245504	111185			



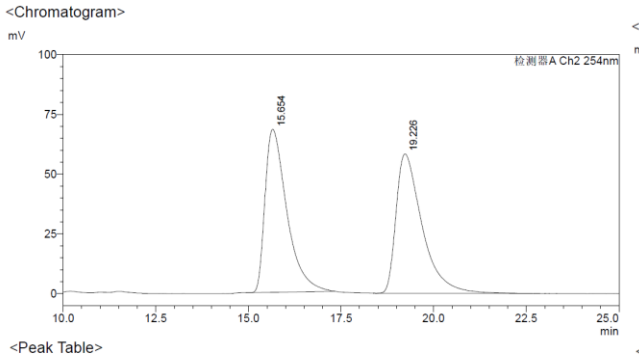
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	8.011	2307025	93870	99.324		M
2	12.870	15696	546	0.676		M
总计		2322721	94416			

(b) Deprotection of amine group



4r **6**, 75%, 98% ee

To a round-bottomed vial charged with **4r** (0.05 mmol, 1.0 equiv) in MeCN/H_2O = 3/2 (1.0 mL) was added CAN (0.2 mmol, 4.0 equiv). The mixture was stirred at 0 ℃ for 5 min. After completion, the reaction mixture was quenched with the addition of H_2O and extracted with EtOAc for 3 times, then sat. aq. $NaHCO_3$ was added and the resulting mixture was extracted with EtOAc for another 3 times. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford crude product, which was purified by preparative thin-layer chromatography (PE/EtOAc = 5/1) to give **6** as a colorless oil (13.2 mg, 75%, 98% ee). $\mathbf{R_f}$ = 0.30 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.36–7.28 (m, 3H), 7.23–7.22 (m, 3H), 7.07 (bs, 2H), 5.50 (s, 1H), 5.04 (sept, *J* = 6.4 Hz, 1H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.78 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 173.7, 142.0, 141.7, 140.0, 137.6, 131.1, 128.5, 127.8, 127.5, 127.5, 127.4, 70.6, 69.6, 33.9, 31.1, 21.8. **HRMS (ESI):** $[M+H]^+$ Calcd for $C_{23}H_{30}NO_2^+$: 352.2271; found: 352.2269; **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 254 nm, t_{R1} = 15.356 min (major), t_{R2} = 18.777 min (minor); 98% *ee*.



Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
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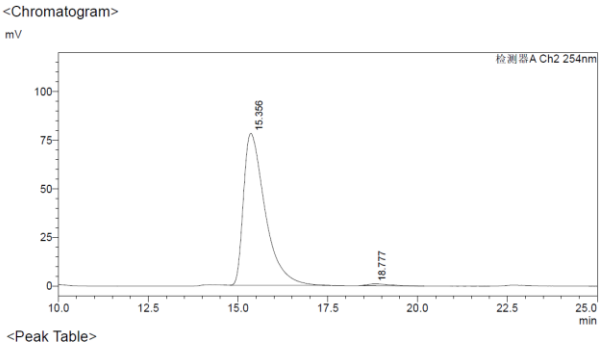
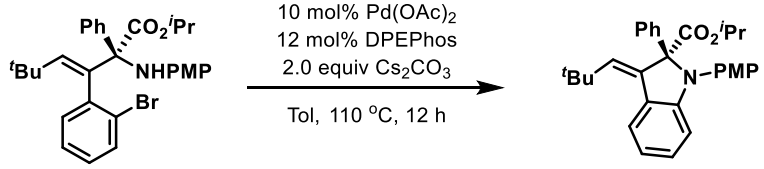
2	19.226	2853927	58268	50.502		M
总计		5651060	126446			



Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	15.356	3273613	78142	98.883		M
2	18.777	36970	898	1.117		M
总计		3310582	79040			

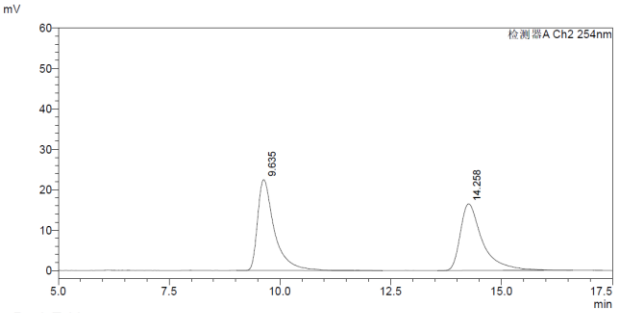
(c) Intramolecular C-N coupling



4s **7**, 93%, 93% ee

To a dried 8-mL vial were added $Pd(OAc)_2$ (10 mol%), DPEPhos (12 mol%), Cs_2CO_3 (2.0 equiv). The via was then evacusted and backfilled with nitrogen (repeat three times). Toluene was added under N2 atmosphere. The reaction vial was sealed and stirred at 110 °C for 12 h. 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 (PE/EA = 20/1) to afford products **7** as a colorless oil (21.2 mg, 93%). $\mathbf{R_f}$ = 0.52 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.0 Hz, 1H), 7.23–7.20 (m, 5H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* =7.2 Hz, 2H), 6.75–6.68 (m, 3H), 6.33 (d, *J* = 8.0 Hz, 1H), 5.78 (s, 1H), 5.12 (sept, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 1.33 (s, 9H), 1.20 (d, *J* = 6.4 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.2, 157.6, 153.4, 141.8, 140.1, 137.9, 132.7, 130.2, 129.7, 129.4, 127.5, 127.4, 127.3, 122.3, 117.1, 113.9, 107.7, 82.6, 68.9, 55.3, 32.1, 29.8, 21.5; **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, rt, λ = 254 nm, t_{R1} = 9.810 min (major), t_{R2} = 14.754 min (minor); 93% *ee*.



<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
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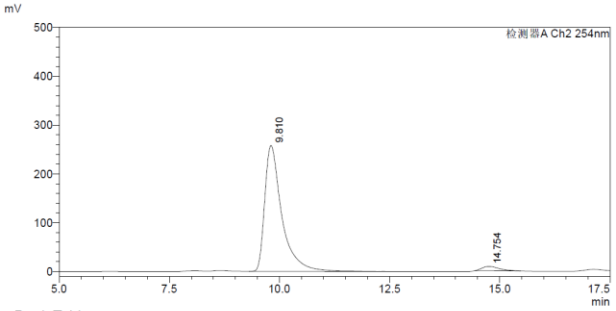
2	14.258	573538	16508	49.199		M
总计		1165750	39014			



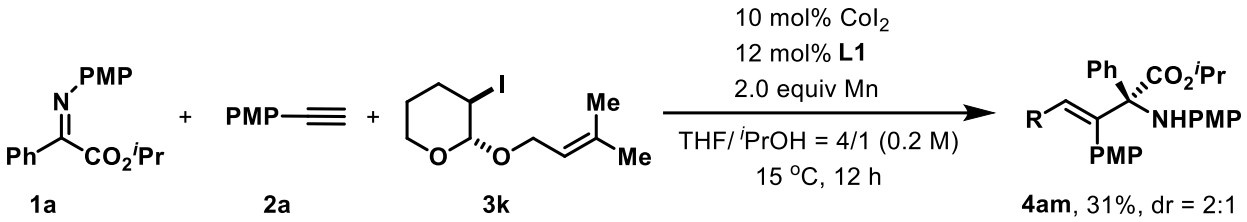
<Peak Table>

检测器A Ch2 254nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark
1	9.810	6959385	257823	96.705		M
2	14.754	237162	8905	3.295		M
总计		7196548	266728			

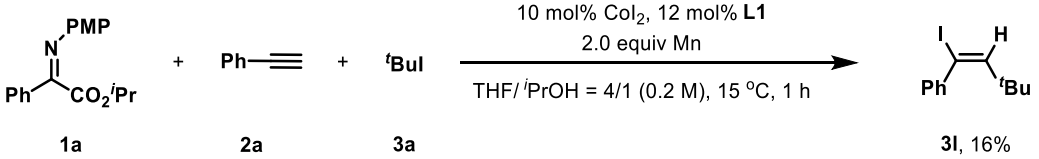
Mechanism Studies

(A) Radical cyclization experiment



General procedure was followed on 0.2 mmol scale. The reaction mixture was purified by flash column chromatography (PE/EA = 5:1) to afford **4am** as a yellow oil (37.2 mg, 31%, 2:1 dr). $\mathbf{R_f}$ = 0.34 (PE/EtOAc = 5/1); The product was isolated as a 5.5:1 mixture of rotamers. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.79–7.77 (m,1.4H), 7.75–7.73 (m, 0.6H), 7.35–7.29 (m, 3H), 7.11–7.03 (m, 1H), 6.78–6.64 (m, 5H), 6.44–6.38 (m, 2H), 5.96–5.90 (m, 1H), 5.17–4.95 (m, 2H), 4.83–4.74 (m, 1H), 3.40–4.10 (m, 10H), 2.15–2.02 (m, 1H), 1.98–1.87 (m, 1H), 1.80–1.73 (m, 1H), 1.56–1.29 (m, 3H), 1.13–1.06 (m, 3H), 1.02–0.98 (m, 3H), 0.73–0.56 (m, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 172.0, 171.9, 171.9, 159.1, 159.0, 159.0, 158.9, 152.2, 152.1, 152.1, 152.0, 140.3, 140.3, 140.2, 140.2, 139.1, 139.1, 139.0, 138.4, 138.0, 137.7, 137.5, 136.0, 135.9, 135.4, 132.3, 132.1, 131.8, 131.5, 130.6, 130.5, 130.3, 130.2, 129.6, 129.4, 129.3, 127.7, 127.7, 127.6, 127.5, 117.3, 117.2, 114.2, 112.7, 112.7, 112.6, 112.5, 102.5, 102.4, 101.4, 101.3, 74.5, 74.4, 74.1, 74.1, 70.2, 70.1, 70.1, 70.0, 65.6, 65.4, 64.2, 64.0, 60.9, 60.9, 55.8, 55.8, 55.7, 55.2, 52.4, 51.9, 50.3, 50.1, 39.4, 39.4, 39.1, 39.0, 37.6, 37.6, 37.2, 37.0, 28.9, 28.2, 28.1, 28.0, 27.7, 26.9, 26.6, 25.4, 25.3, 25.1, 23.5, 23.4, 21.6, 21.6, 21.48, 21.46, 21.43, 21.40, 21.36, 21.2, 21.1. **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{37}H_{46}NO_6^+$: 600.3320; found: 600.3310.

(B) Control experiment



General procedure was followed on 0.1 mmol scale with a reaction time of 1 h at 15 ℃ ice bath. The imine **1a** was largely remained by TLC analysis. Compound **3l**[16] was observed in 16% uncorrected GC yield and confirmed by GC-MS.

```
File       :D:\yfchen group\HLT\HLT-6-130-1H.D
Operator   :
Acquired   : 22 Apr 2023  09:56     using AcqMethod Mathod C.M
Instrument :    GCMSD
Sample Name: HLT-6-130-1H
Misc Info  :
Vial Number: 8
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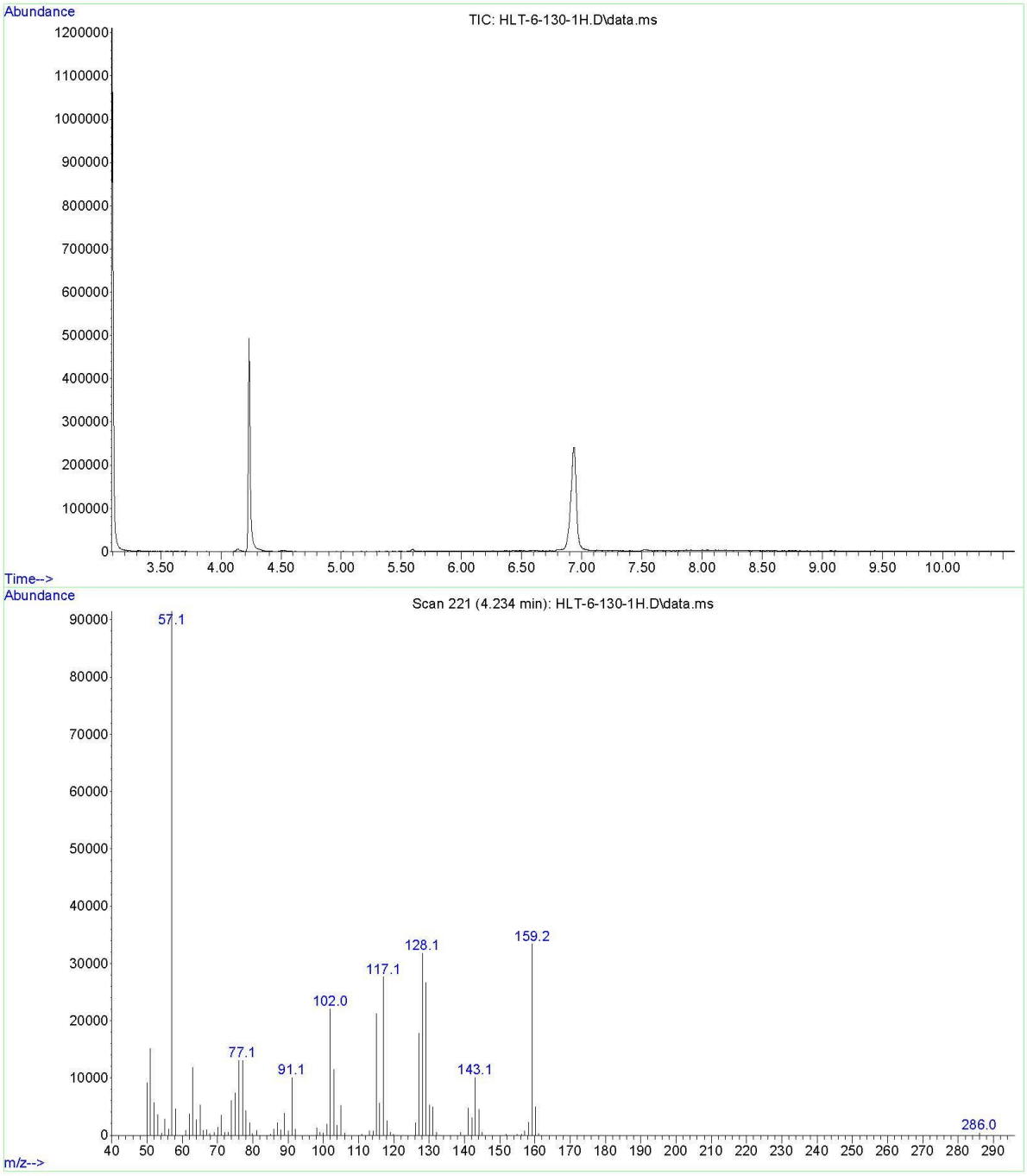
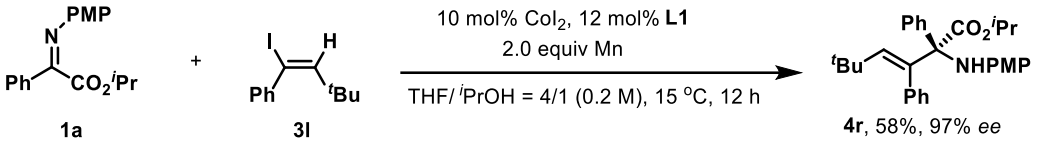
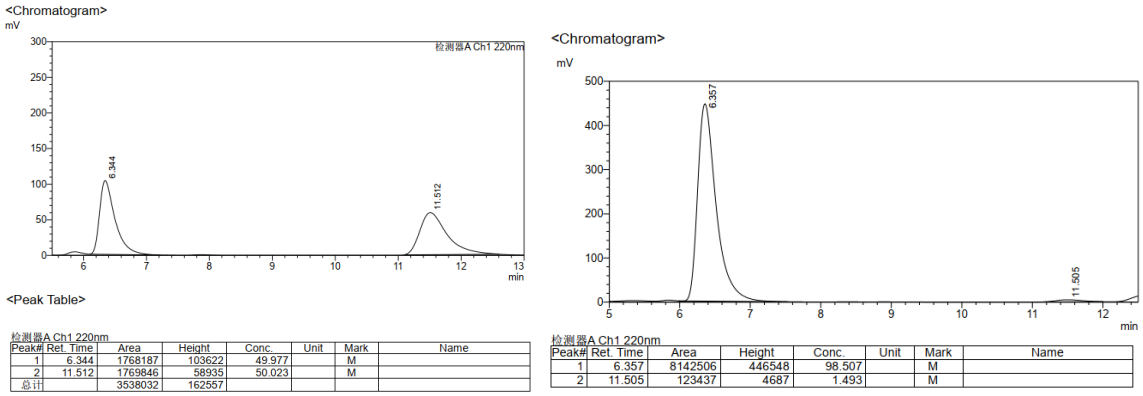


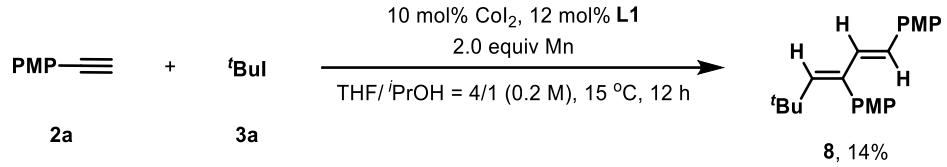
(C) Reaction with alkenyl iodide



To a dried 8-mL vial were added **L1** (0.012 mmol, 12 mol%), Mn (0.2 mmol, 2.0 equiv) and imine **1a** (0.1 mmol, 1.0 equiv). Then the vial was transferred into the glovebox. CoI_2 (0.01 mmol, 10 mol%), THF (0.4 ml) and alkenyl iodide **3l** (0.2 mmol, 2.0 equiv) were added in sequence and ^{i}PrOH (0.1 ml) was added finally. The reaction vial was capped and stirred at 15 °C for 12 h. 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 **4r** as a yellow oil (26.5 mg, 58%). **HPLC** (Chiralpak AD-H): *n*-Hexane/*i*-PrOH = 98/2, flow rate 1.0 mL/min, rt, λ = 220 nm, t_{R1} = 6.400 min (major), t_{R2} = 11.601 min (minor); 97% *ee*.



(D) Reaction without imine



General procedure was followed on 0.1 mmol scale. The reaction mixture was purified by flash column chromatography (PE) to afford **8** as a yellow oil (9.2 mg, 14%). $\mathbf{R_f}$ = 0.67 (PE/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.22 (d, *J* = 8.4 Hz, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 16.4 Hz, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 5.80 (s, 1H), 5.74 (d, *J* = 16.0 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 0.92 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.9, 158.6, 144.3, 138.9, 134.6, 131.3, 131.1, 130.8, 128.5, 127.5, 114.0, 113.3, 55.4, 55.3, 34.0, 31.5. **HRMS (ESI)**: $[M+H]^+$ Calcd for $C_{22}H_{27}O_2^+$: 323.2006; found: 323.2008.

Crystallographic Data

Compound **4aa** is dissolved in acetone to form a supersaturated solution, which is then left to stand at 25 °C for 5 days, allowing crystals to slowly precipitate.

Single-crystal X-ray diffraction data for **4aa** were collected on a Bruker D8 Venture diffractometer with a graphite-monochromated Ga Kα radiation (λ = 1.34139 Å) at 213 K. Empirical absorption correction was performed using the SADABS program. The structure was solved by direct methods and refined by full-matrix least-squares procedures on F^2 using SHELXTL2018 and solved with the Superflip structure solution program using charge flipping and refined with the XL refinement package using least-squares minimization that is included in Olex2. All of the non-hydrogen atoms were refined anisotropically. All of the hydrogen atoms on carbons were generated and refined in ideal positions.

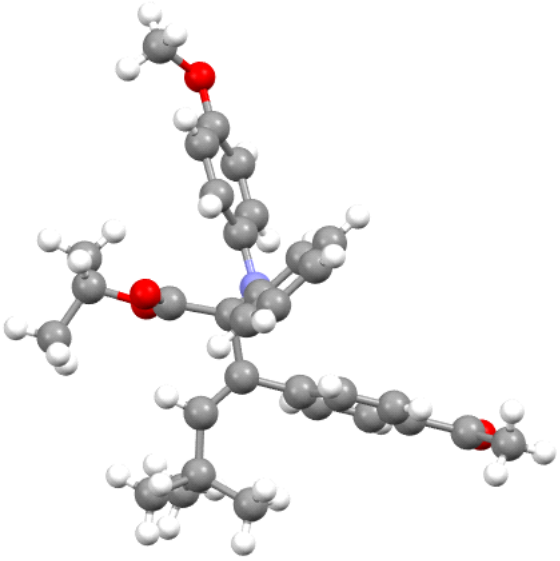


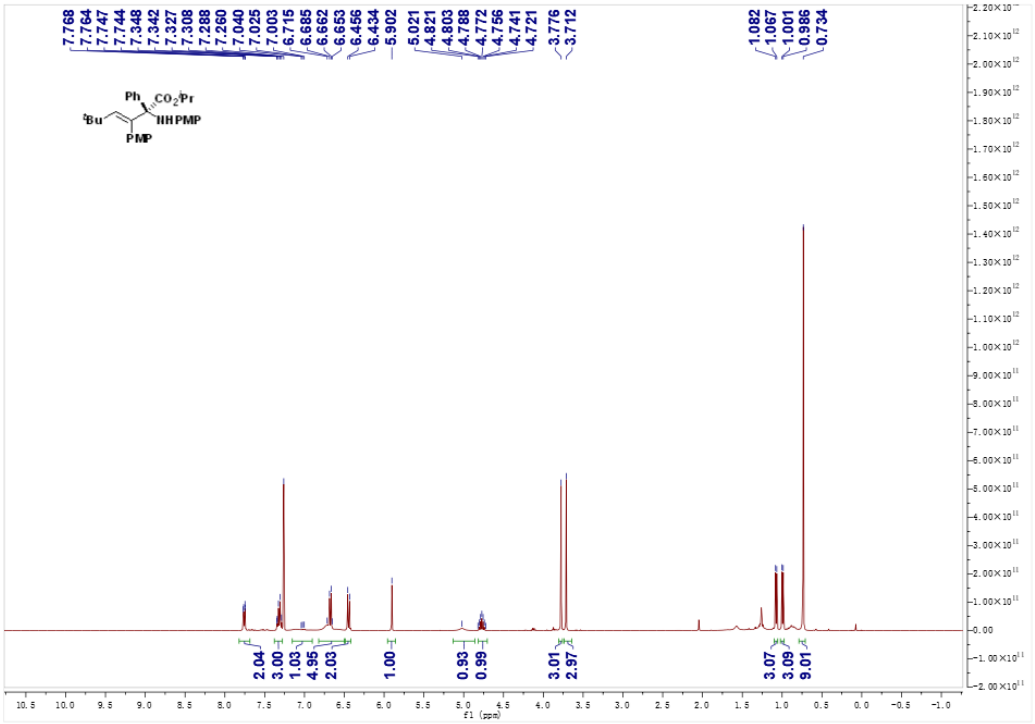
Fig. S2 Crystal data and structure refinement for **4aa** (CCDC 2255872)

Empirical formula	C32 H37 N O4	
Formula weight	499.62	
Temperature	213 K	
Wavelength	1.34139 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 2	
Unit cell dimensions	a = 10.8470(4) Å	α = 90°.
	b = 27.3287(9) Å	β = 90°.
	c = 10.7209(4) Å	γ = 90°.
Volume	3178.0(2) $Å^3$	
Z	4	
Density (calculated)	1.044 Mg/m^3	
Absorption coefficient	0.344 mm^{-1}	

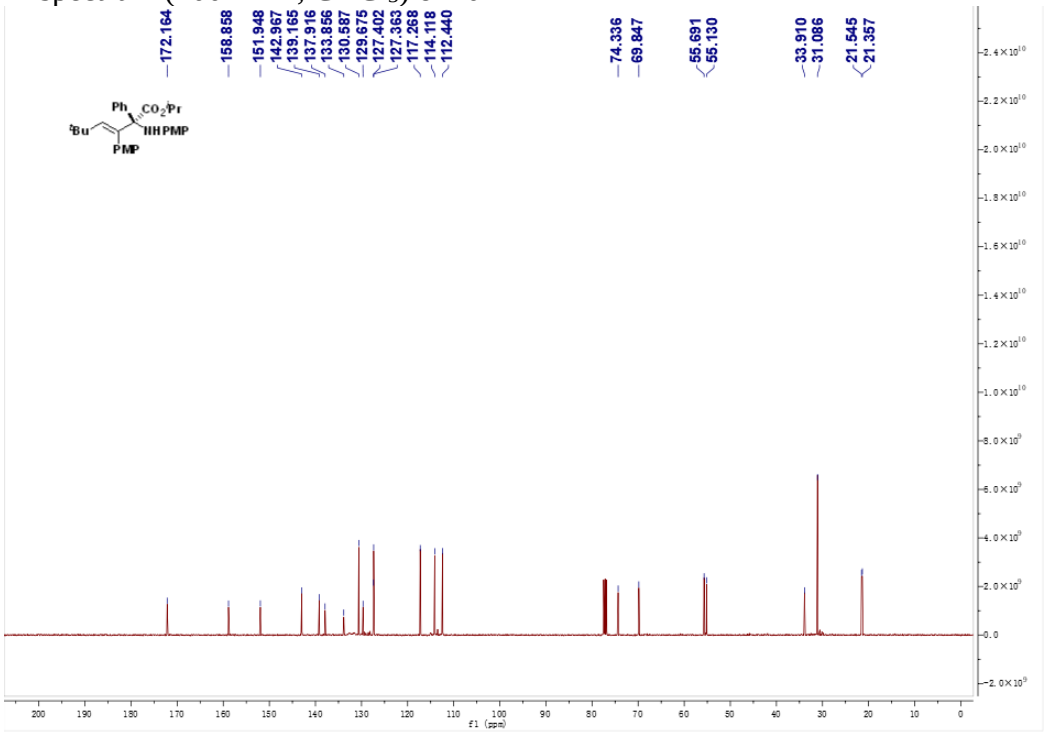
F(000)	1072
Crystal size	0.12 x 0.09 x 0.06 mm^3
Theta range for data collection	6.662 to 55.092°.
Index ranges	-13<=h<=10, -33<=k<=33, -13<=l<=13
Reflections collected	33038
Independent reflections	5970 [R(int) = 0.0425]
Completeness to theta = 53.594°	97.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7508 and 0.5744
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5970 / 0 / 341
Goodness-of-fit on F^2	1.417
Final R indices [I>2sigma(I)]	R1 = 0.0550, wR2 = 0.1654
R indices (all data)	R1 = 0.0580, wR2 = 0.1684
Absolute structure parameter	-0.06(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.464 and -0.220 $e.Å^{-3}$

NMR spectra

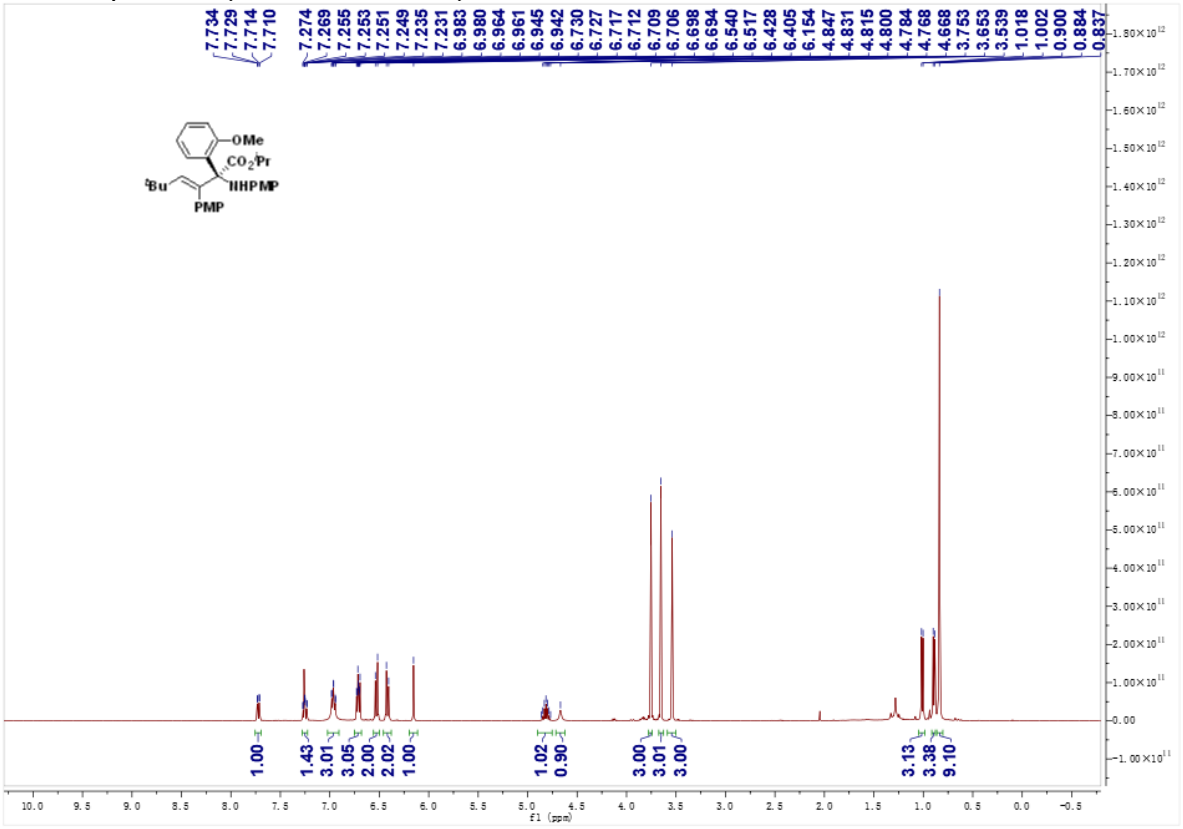
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4a**



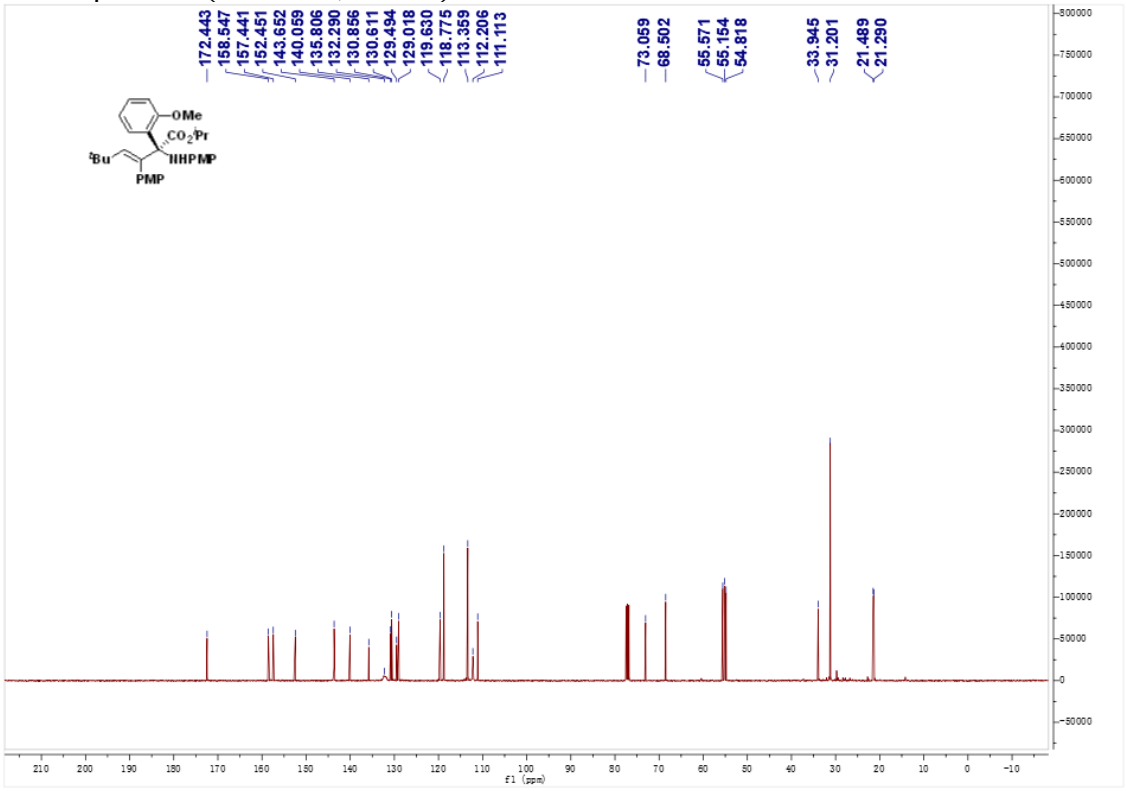
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4a**



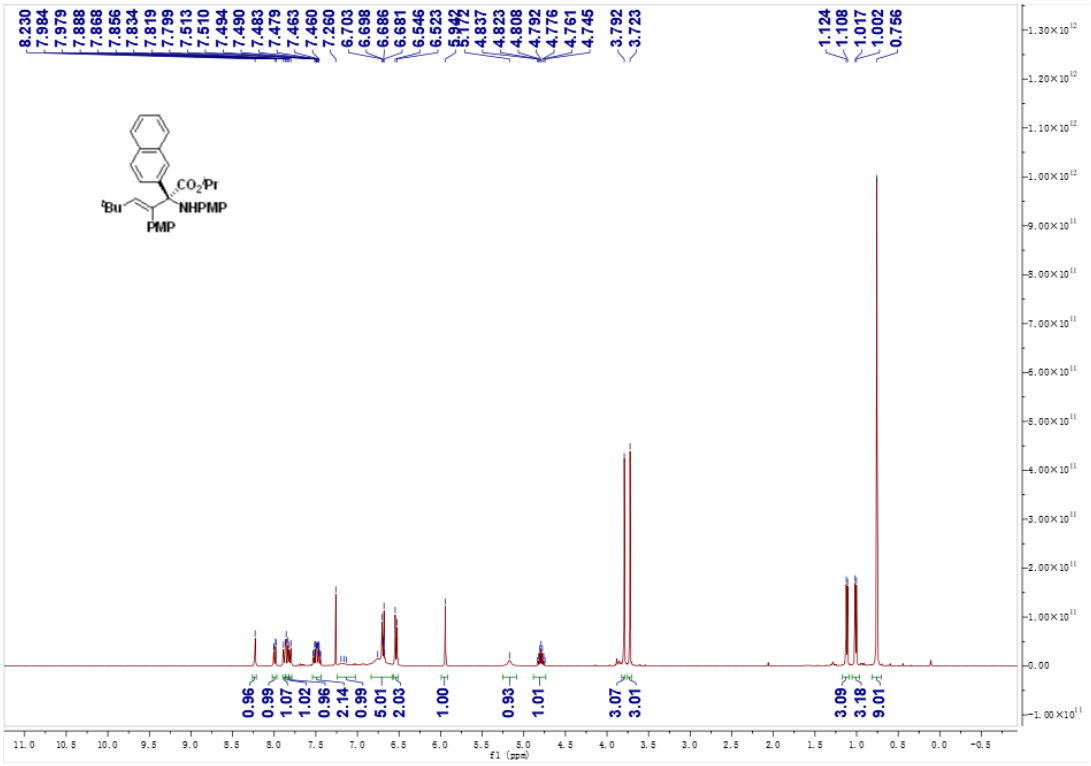
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4b**



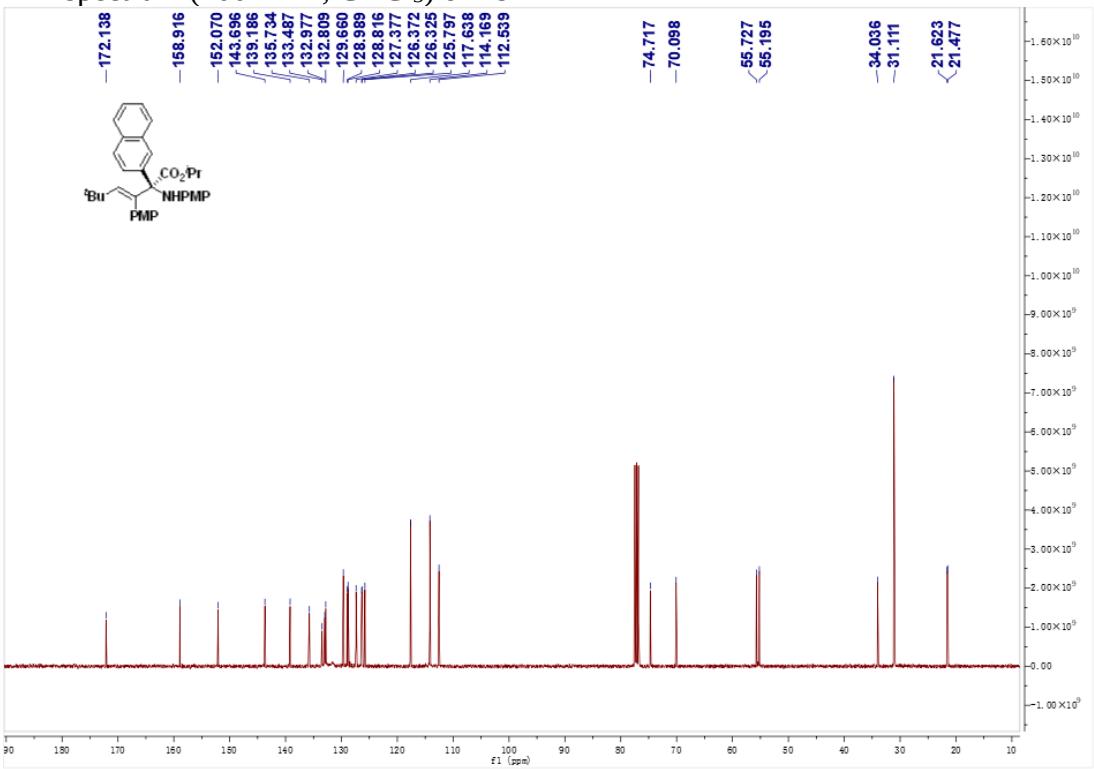
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4b**



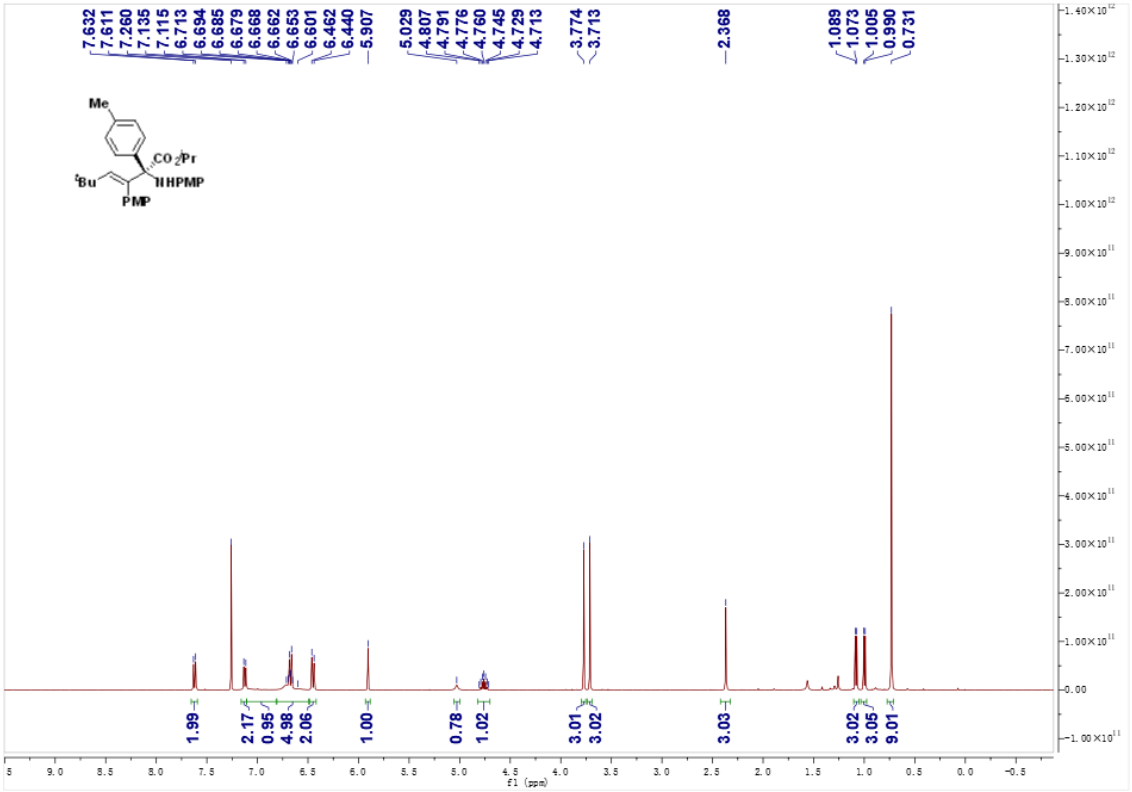
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4c**



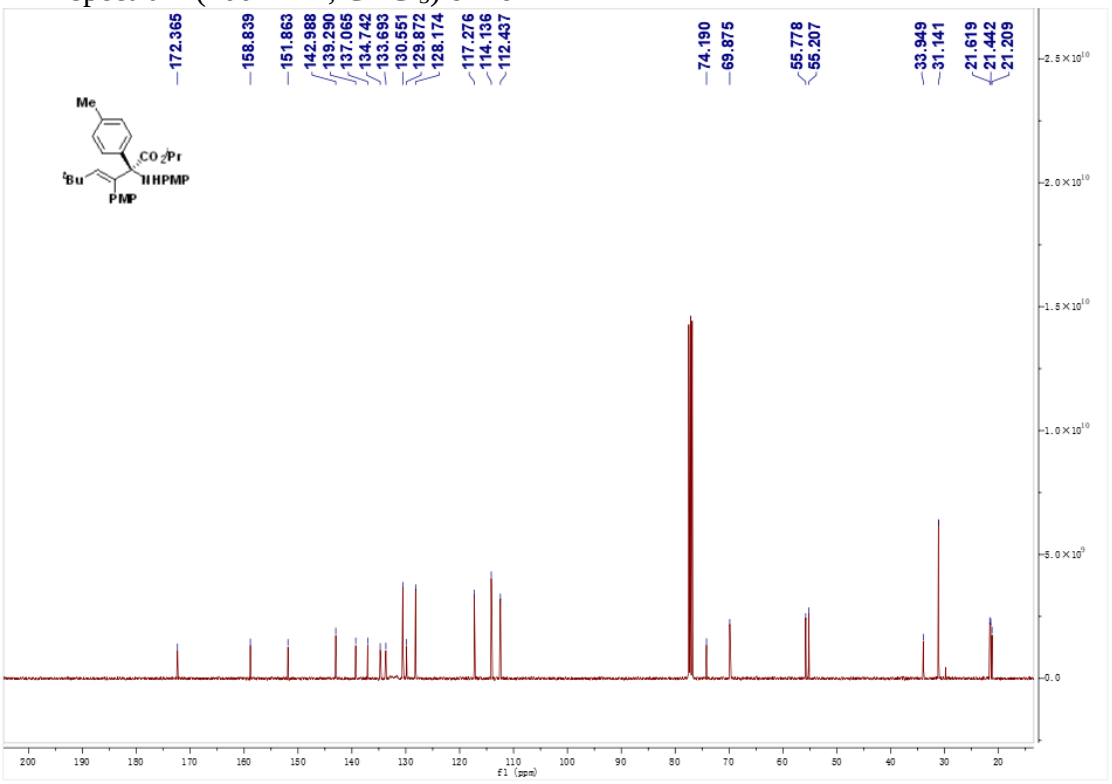
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4c**



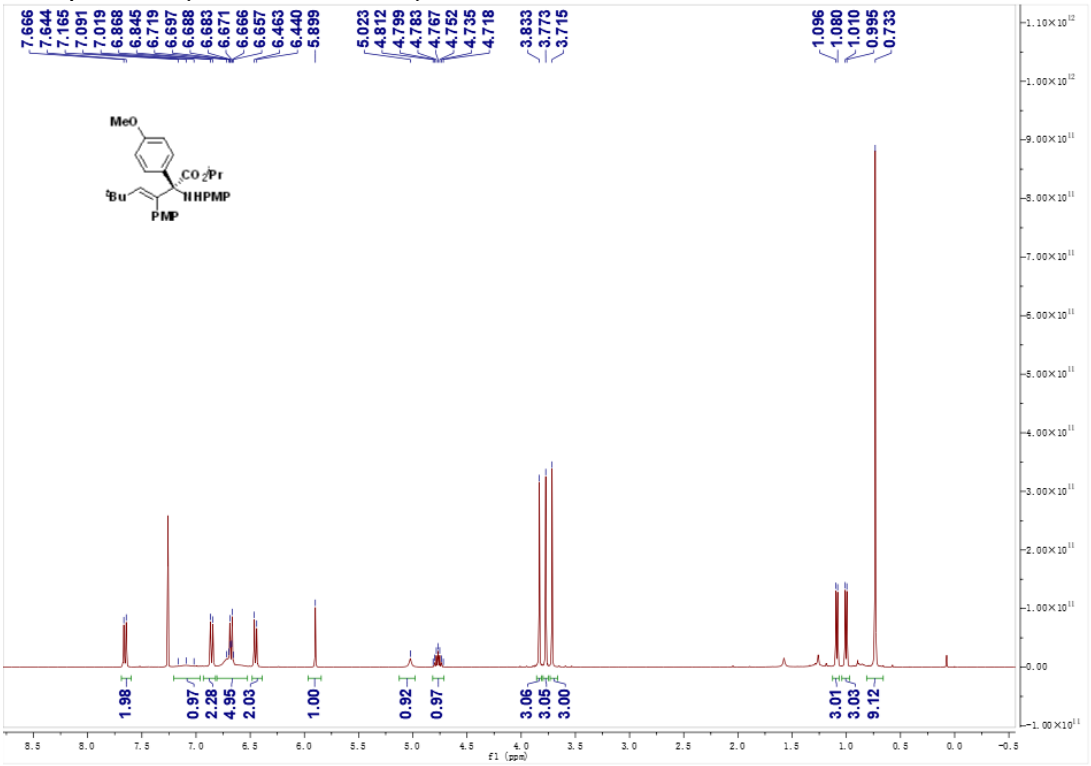
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4d**



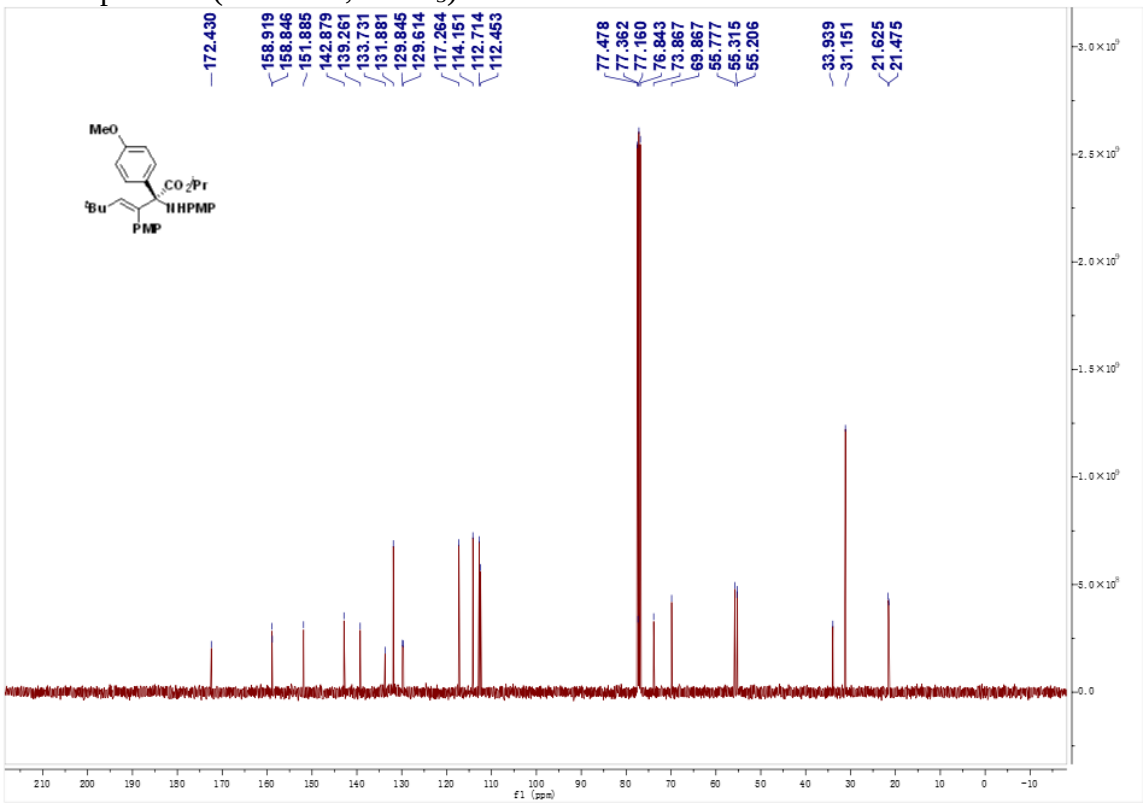
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4d**



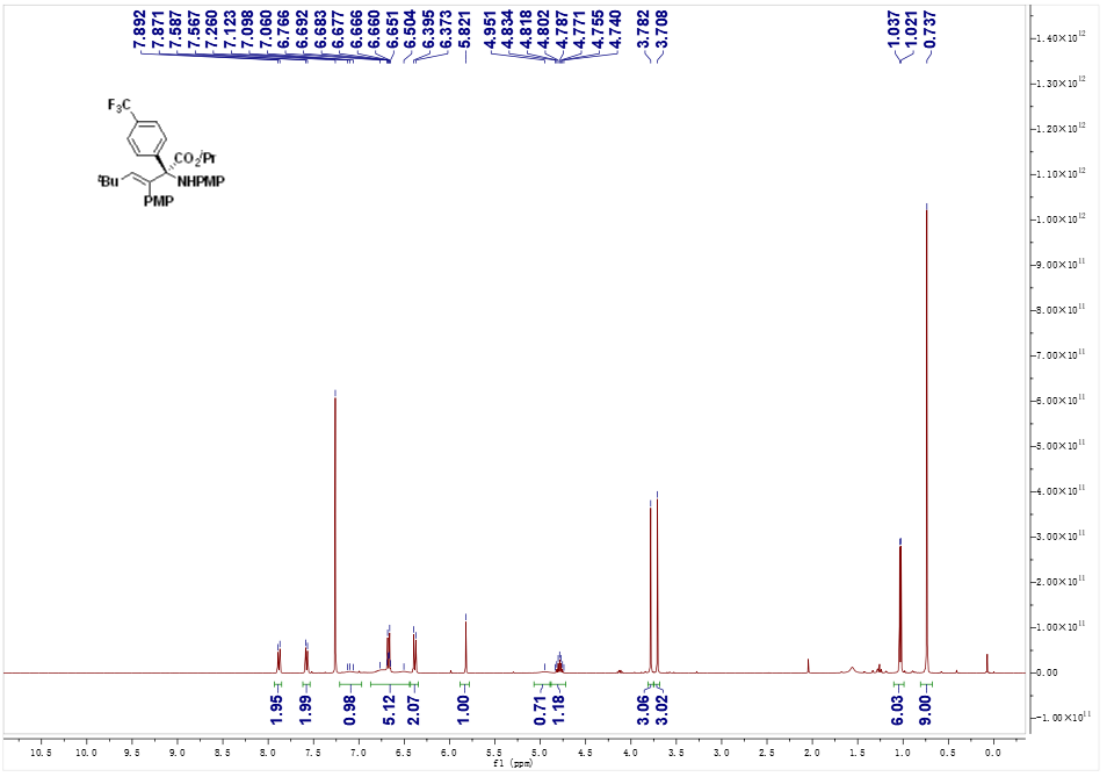
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4e**



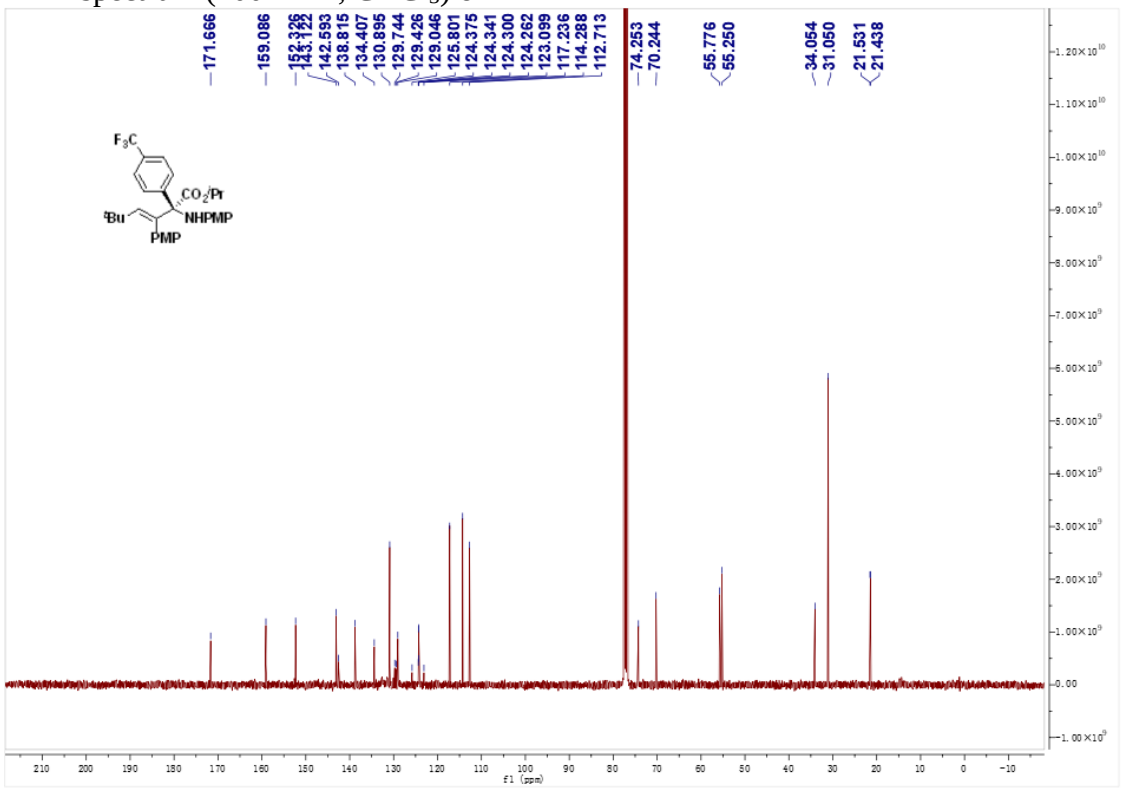
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4e**



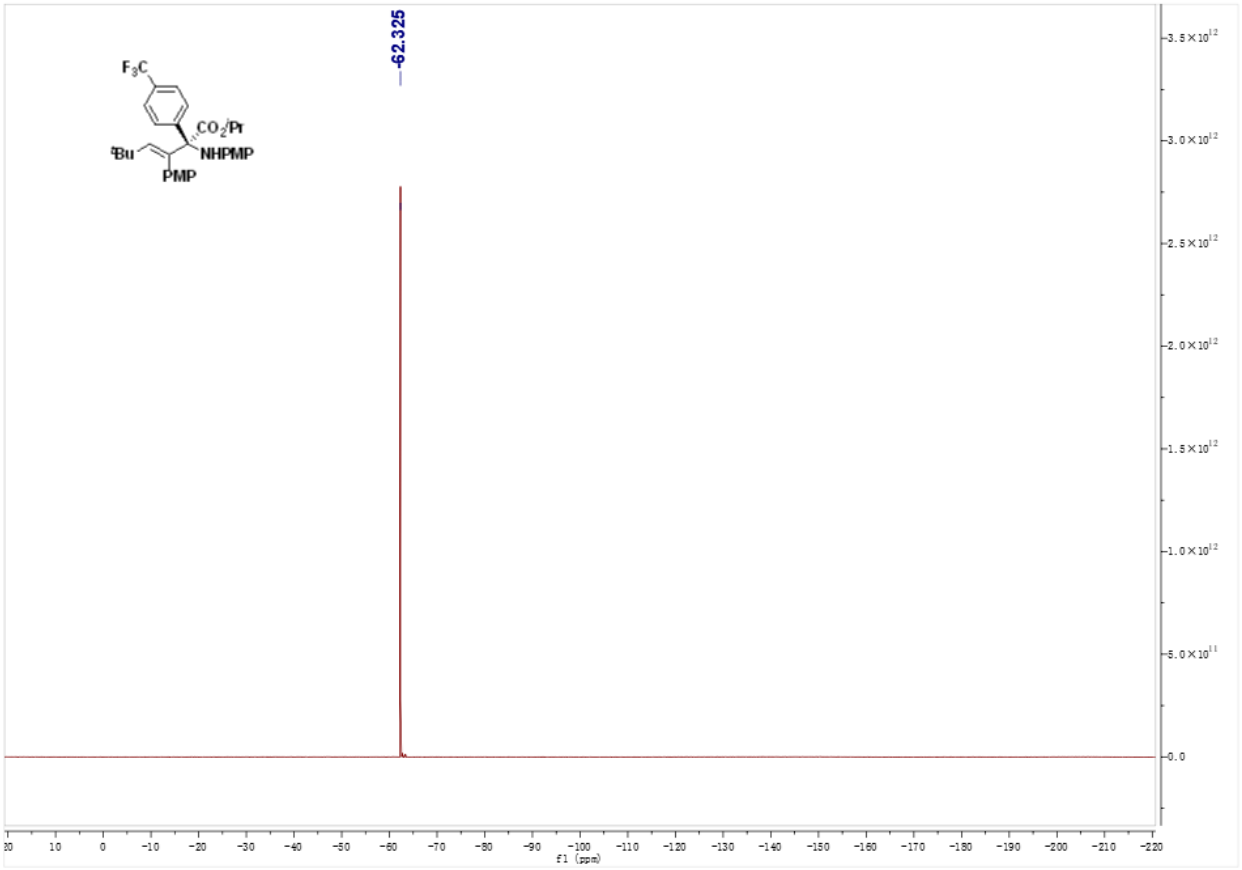
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4f**



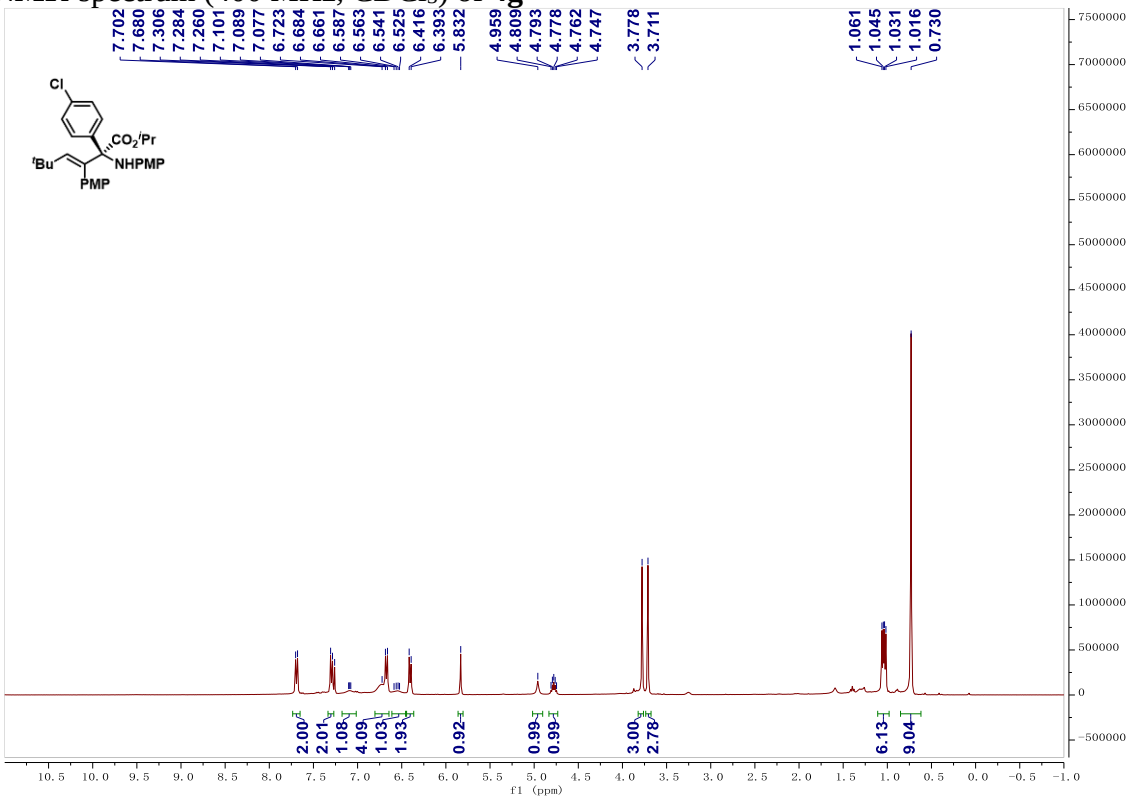
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4f**



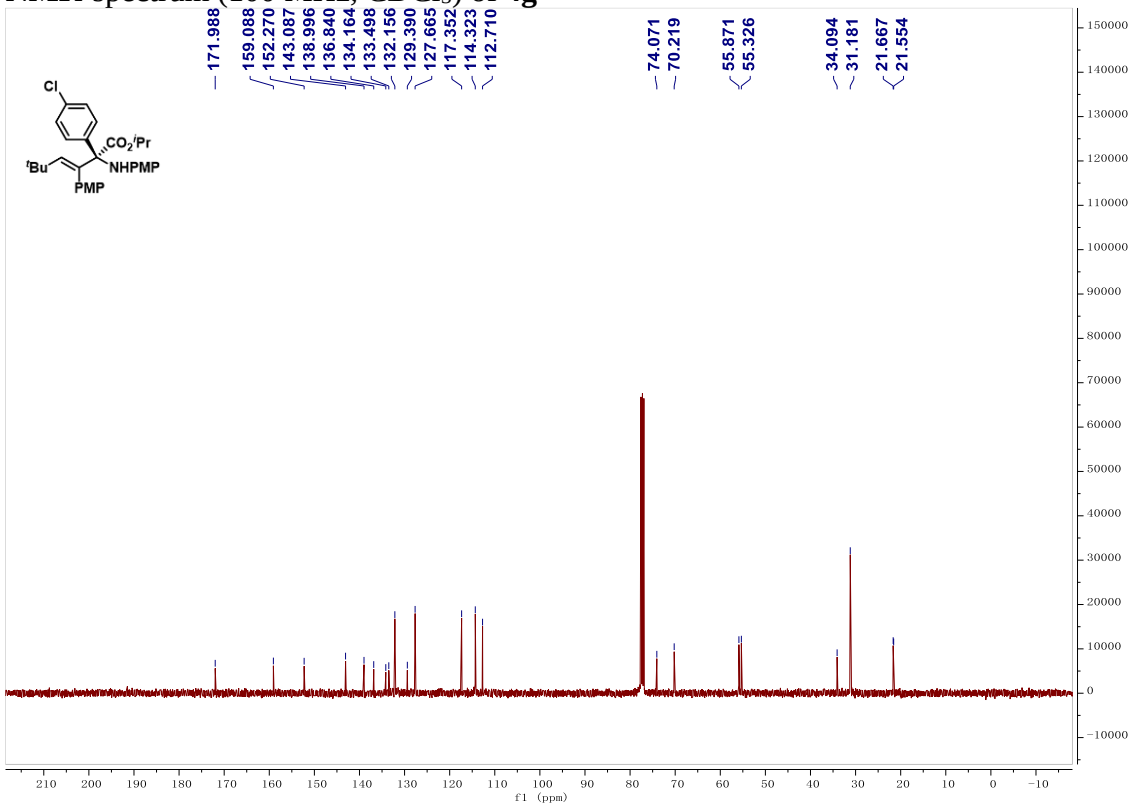
^{19}F NMR-spectrum (376 MHz, $CDCl_3$) of **4f**



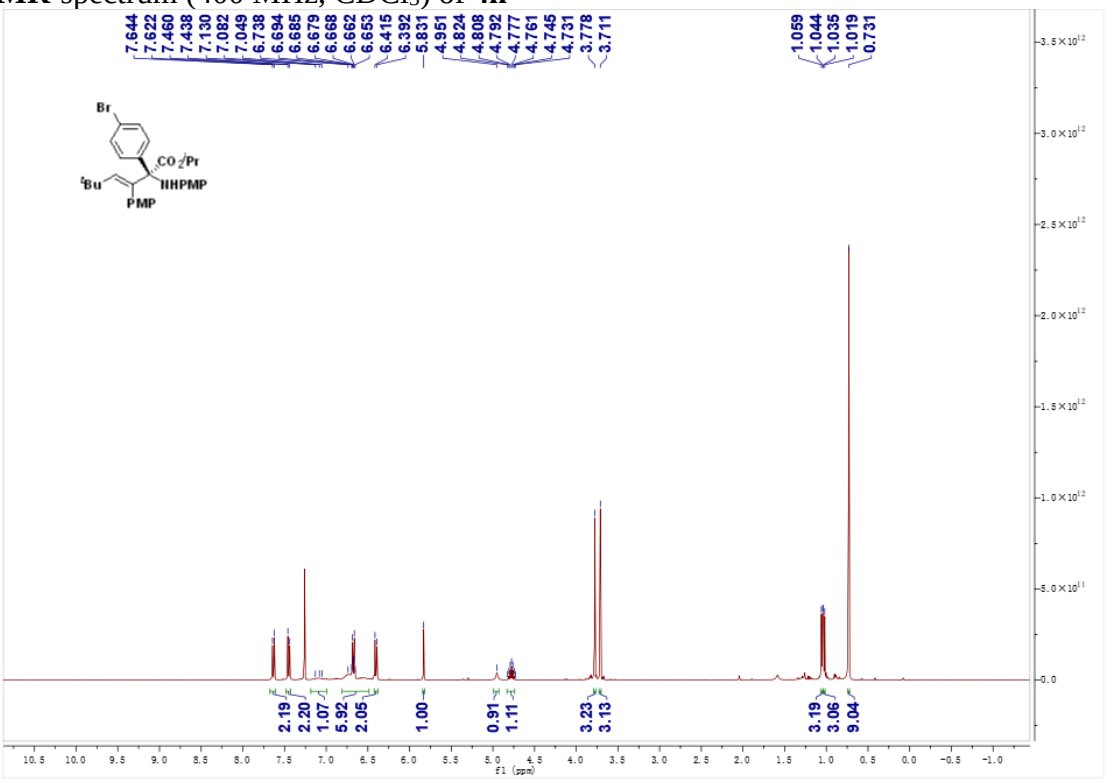
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4g**



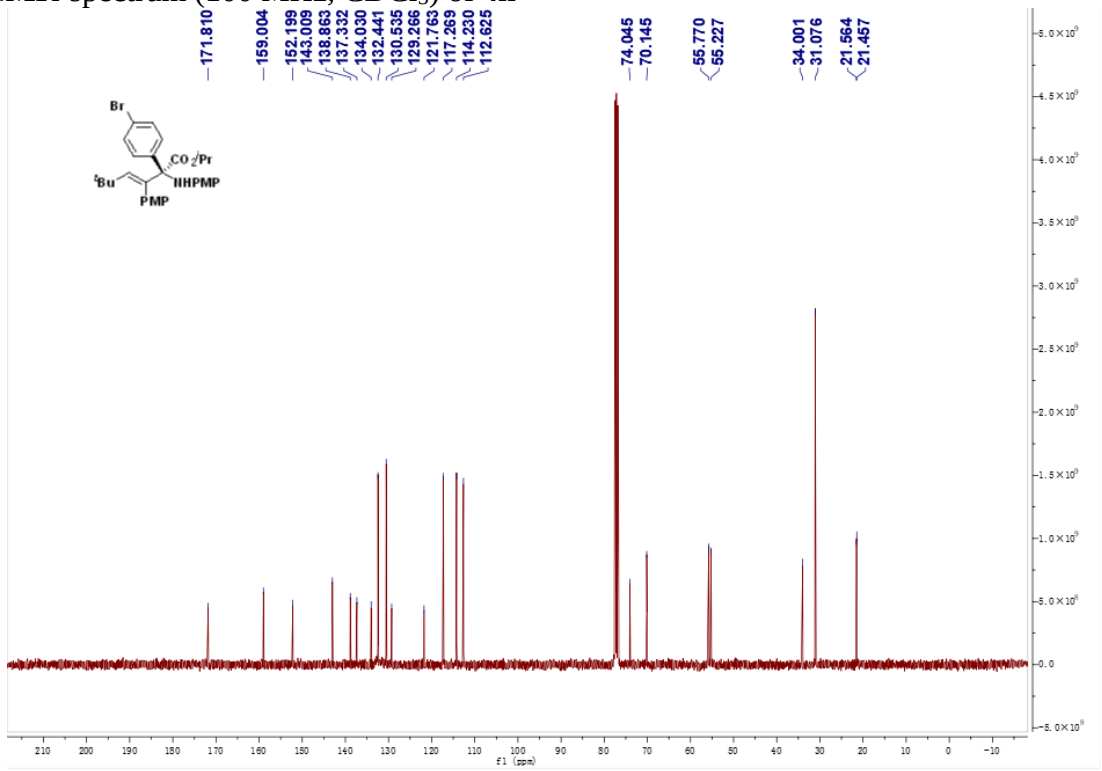
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4g**



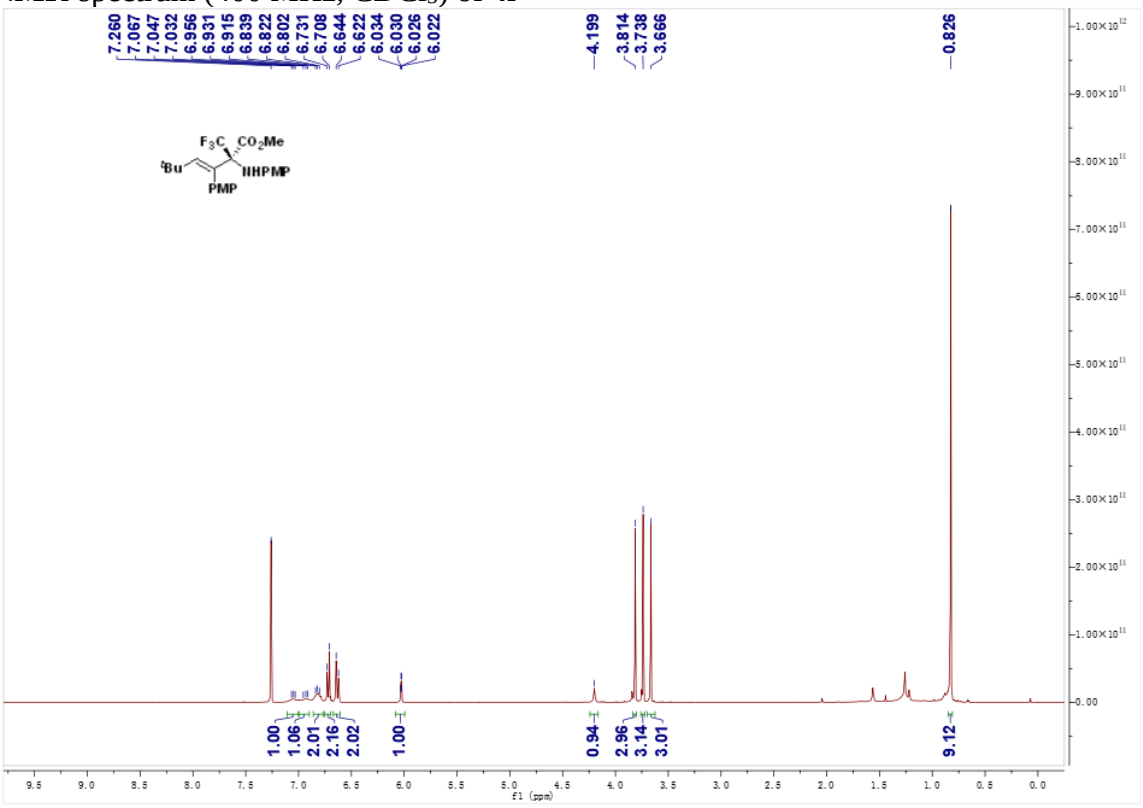
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4h**



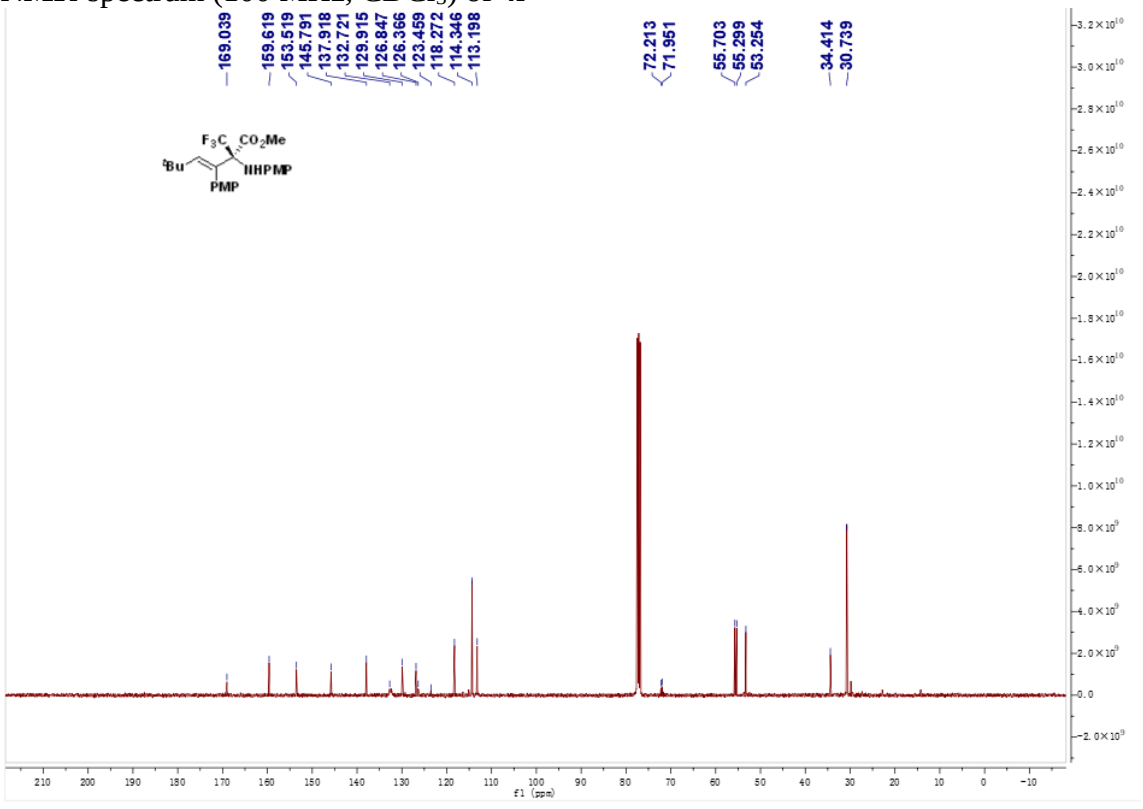
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4h**



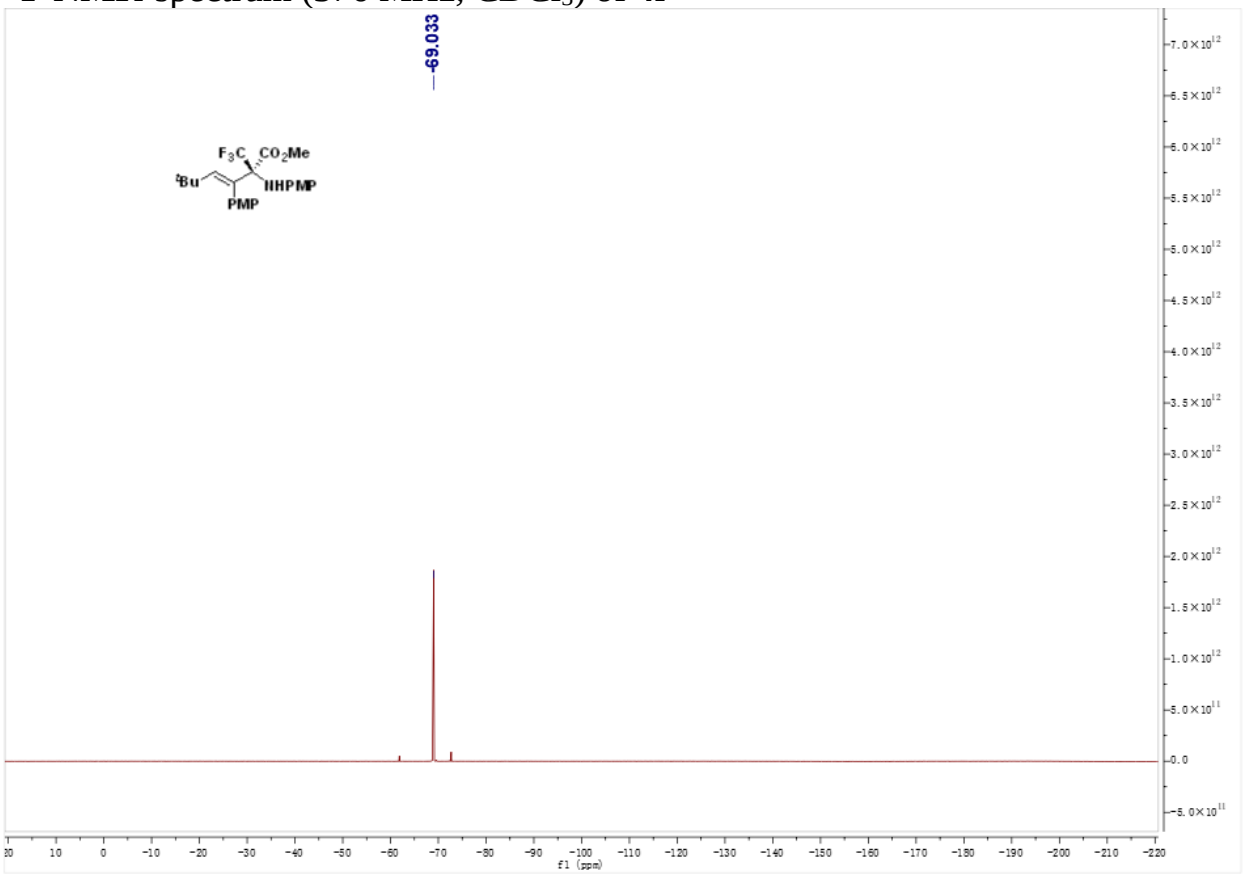
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4i**



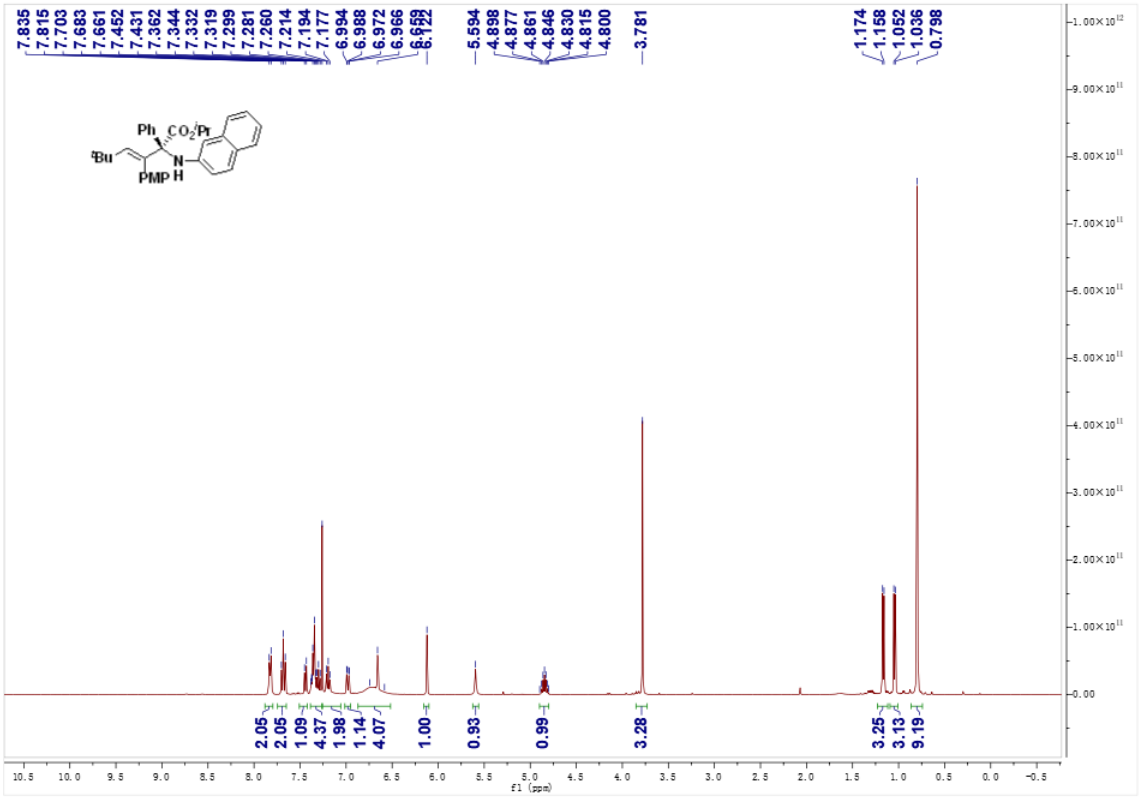
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4i**



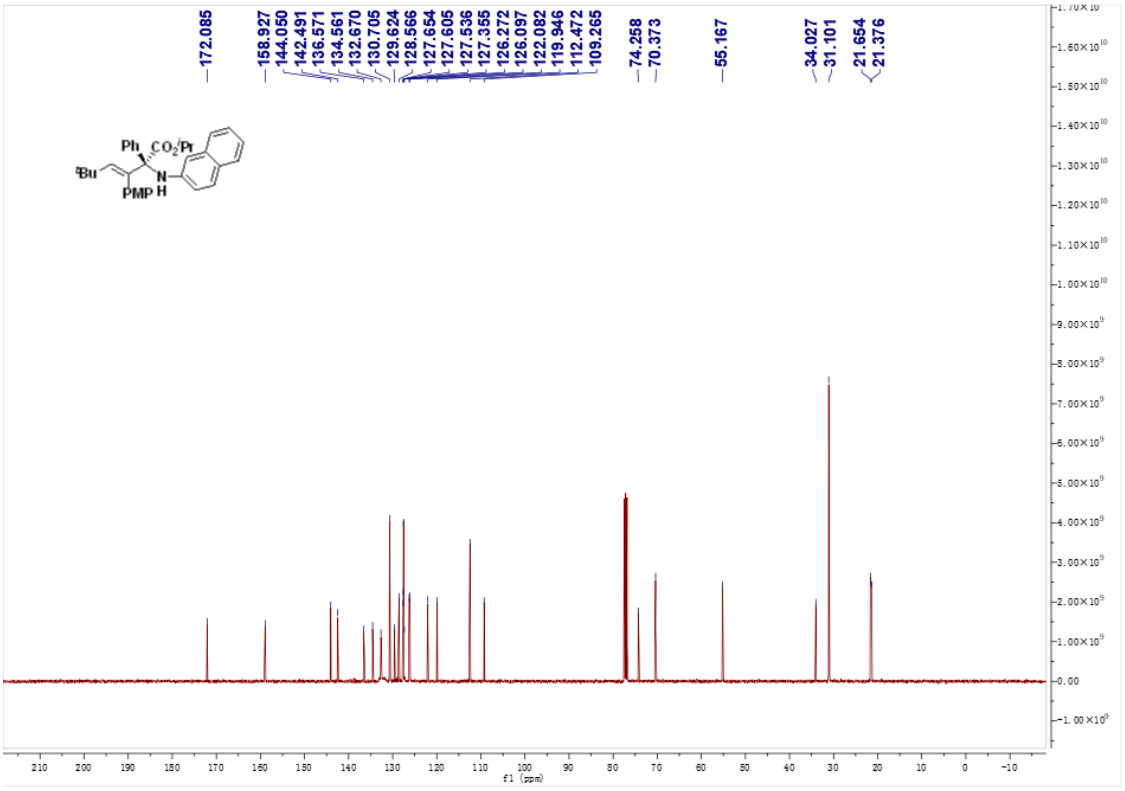
^{19}F NMR-spectrum (376 MHz, $CDCl_3$) of **4i**



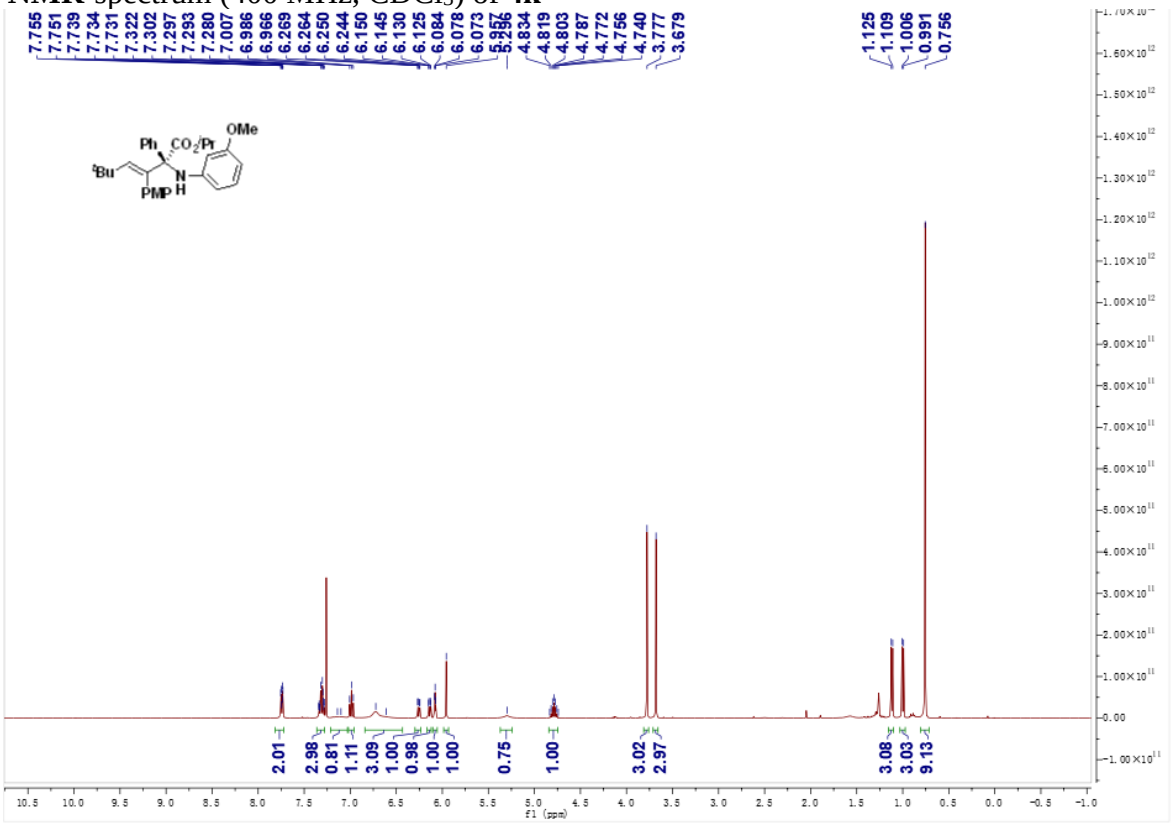
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4j**



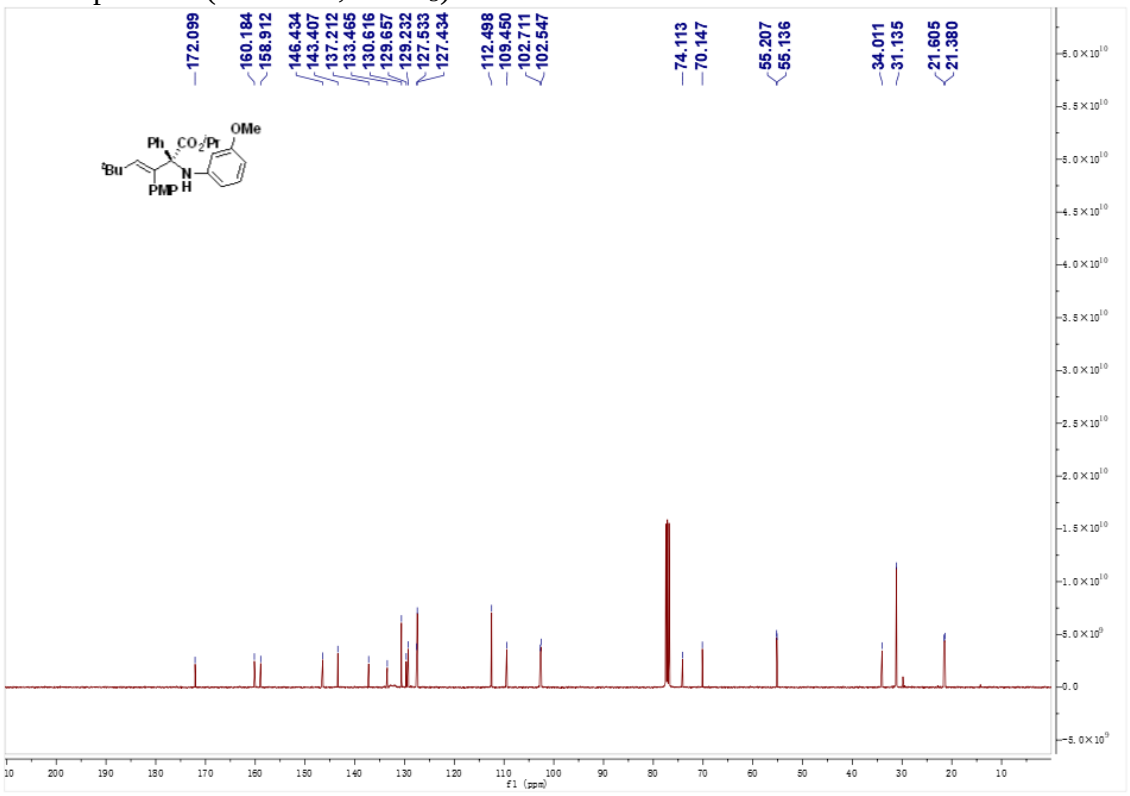
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4j**



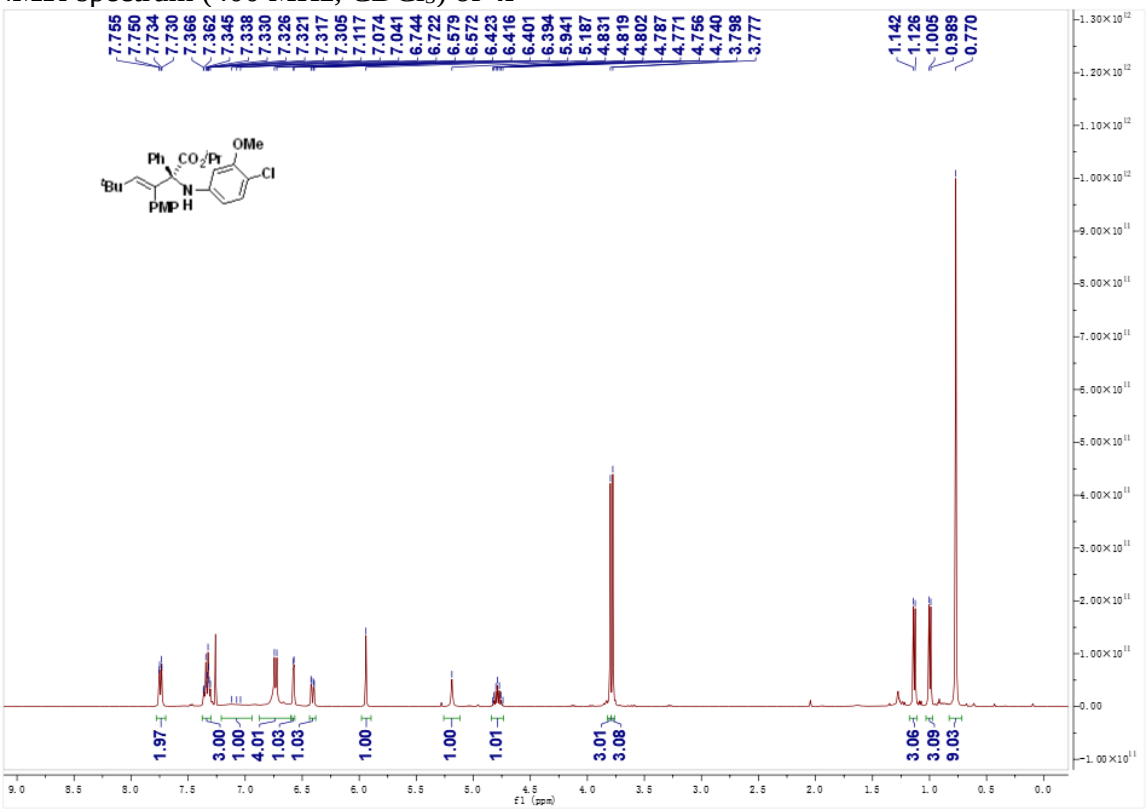
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4k**



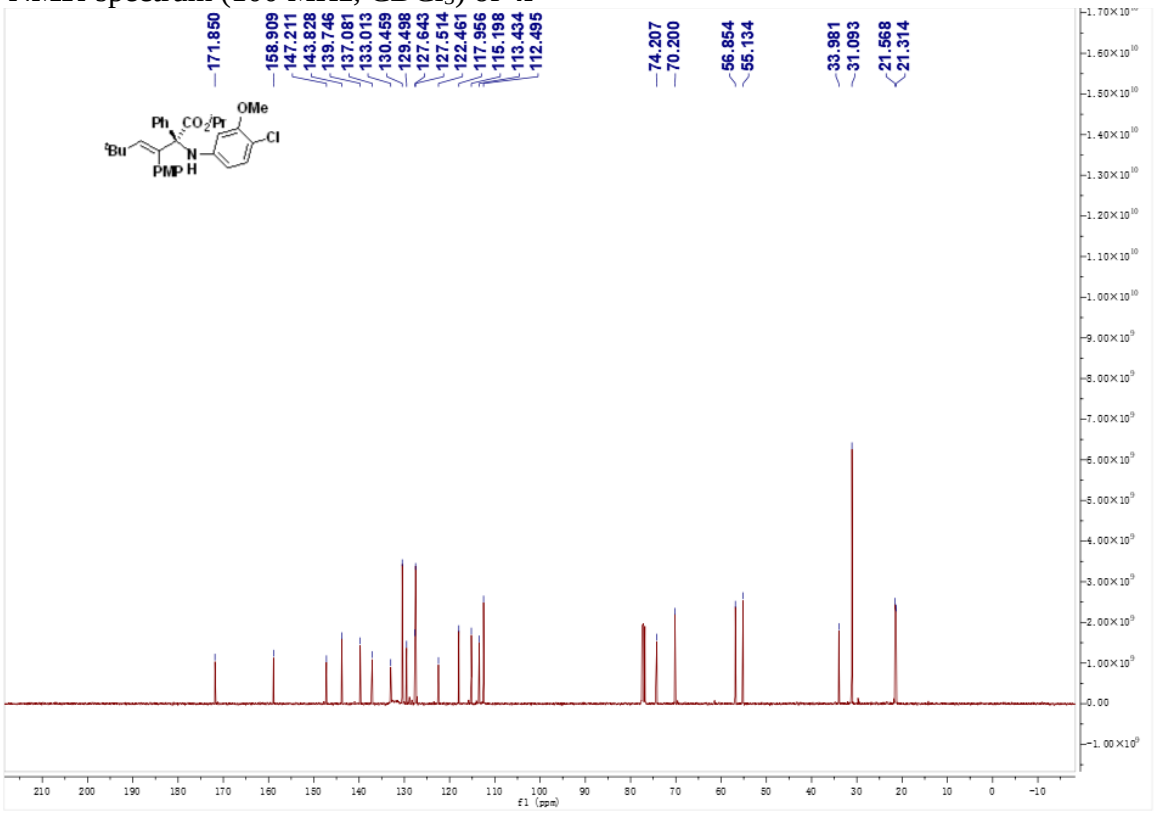
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4k**



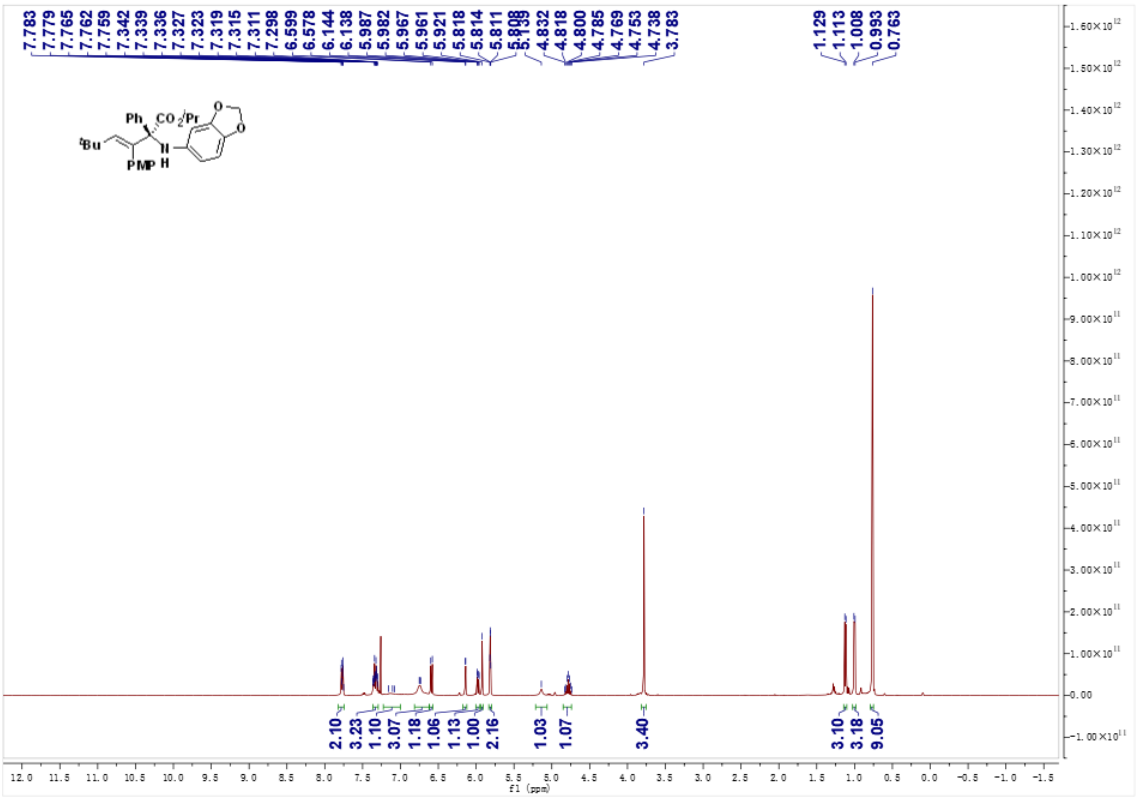
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4l**



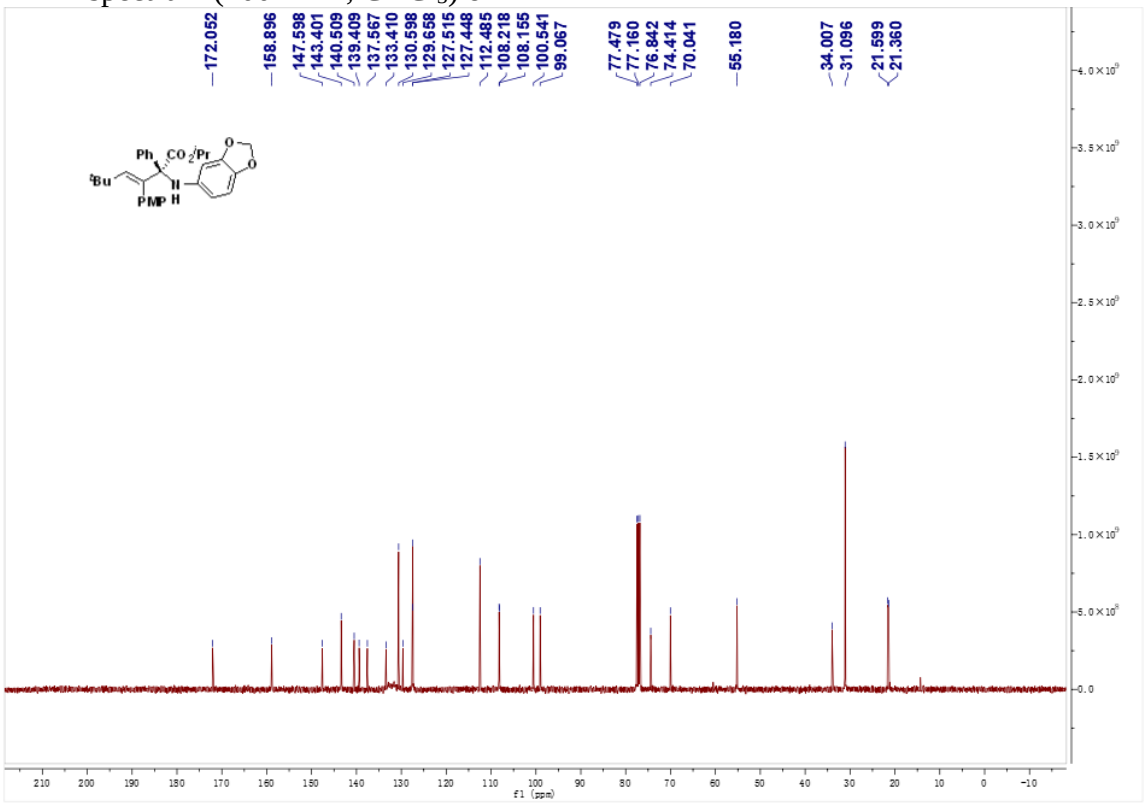
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4l**



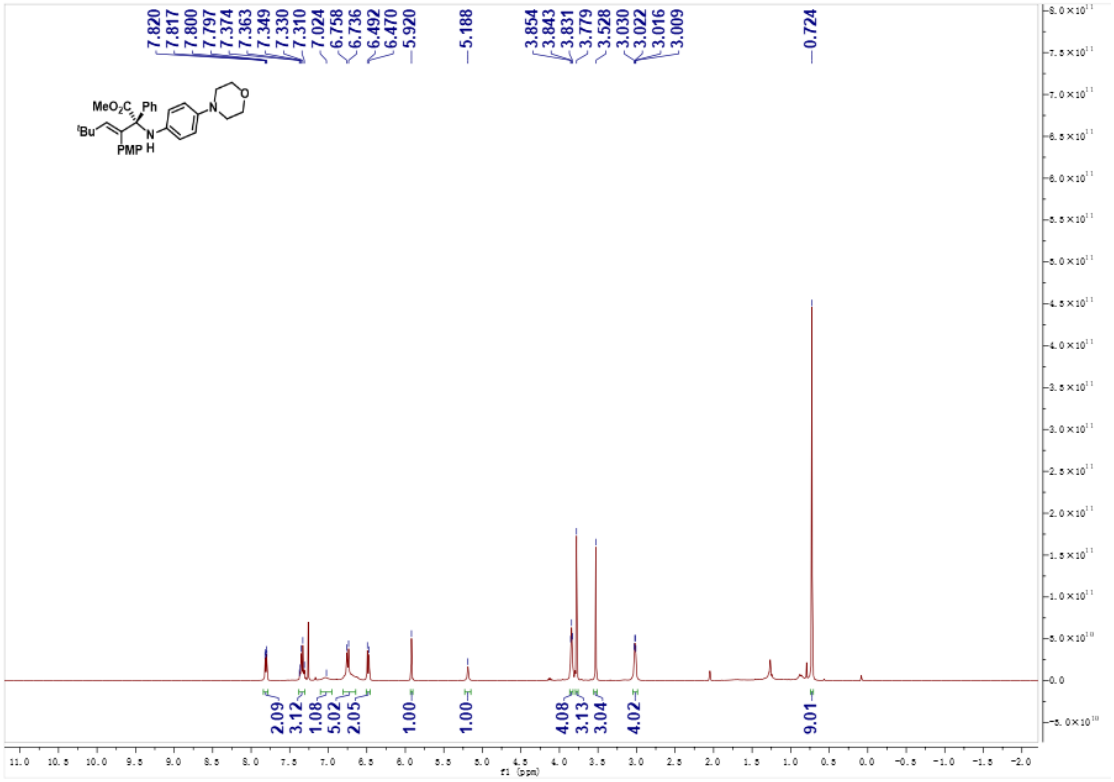
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4m**



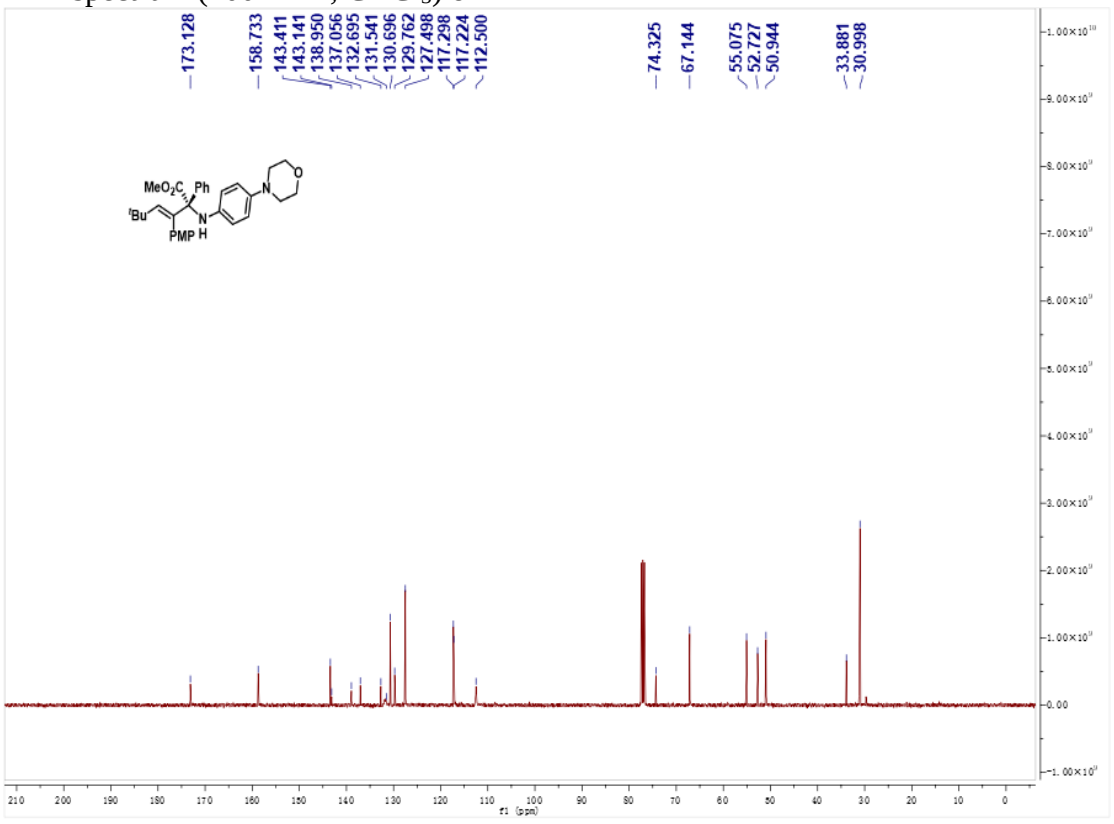
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4m**



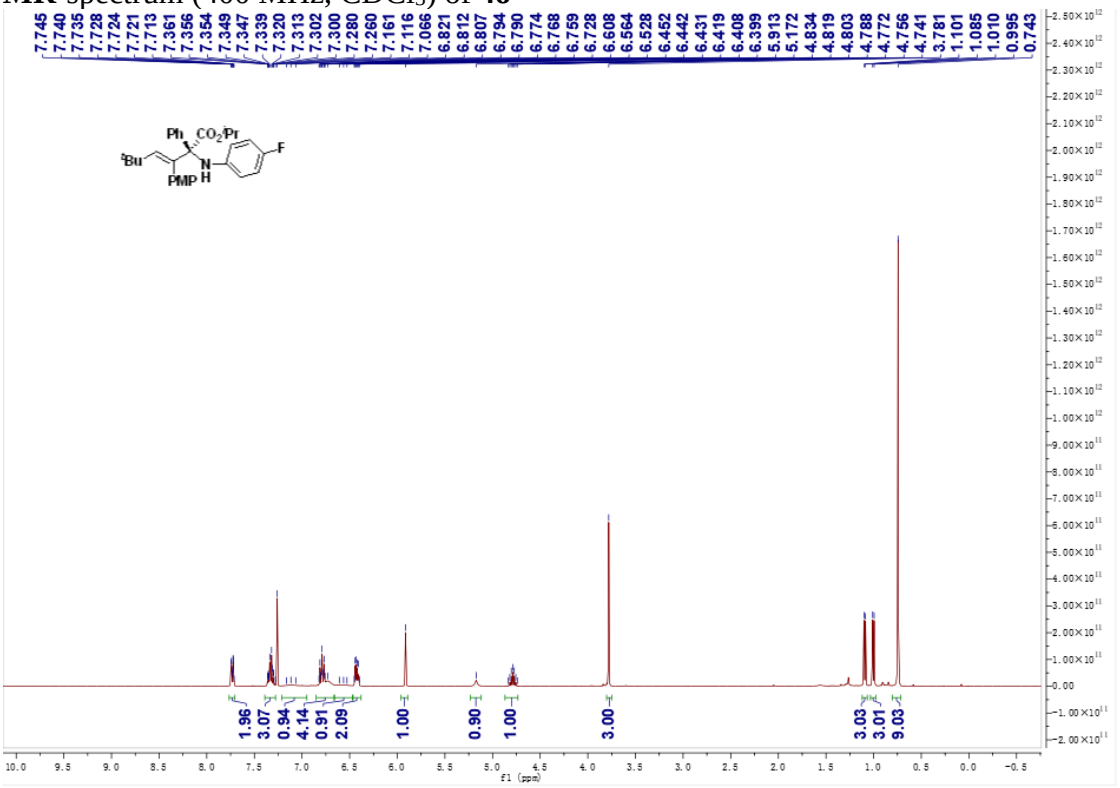
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4n**



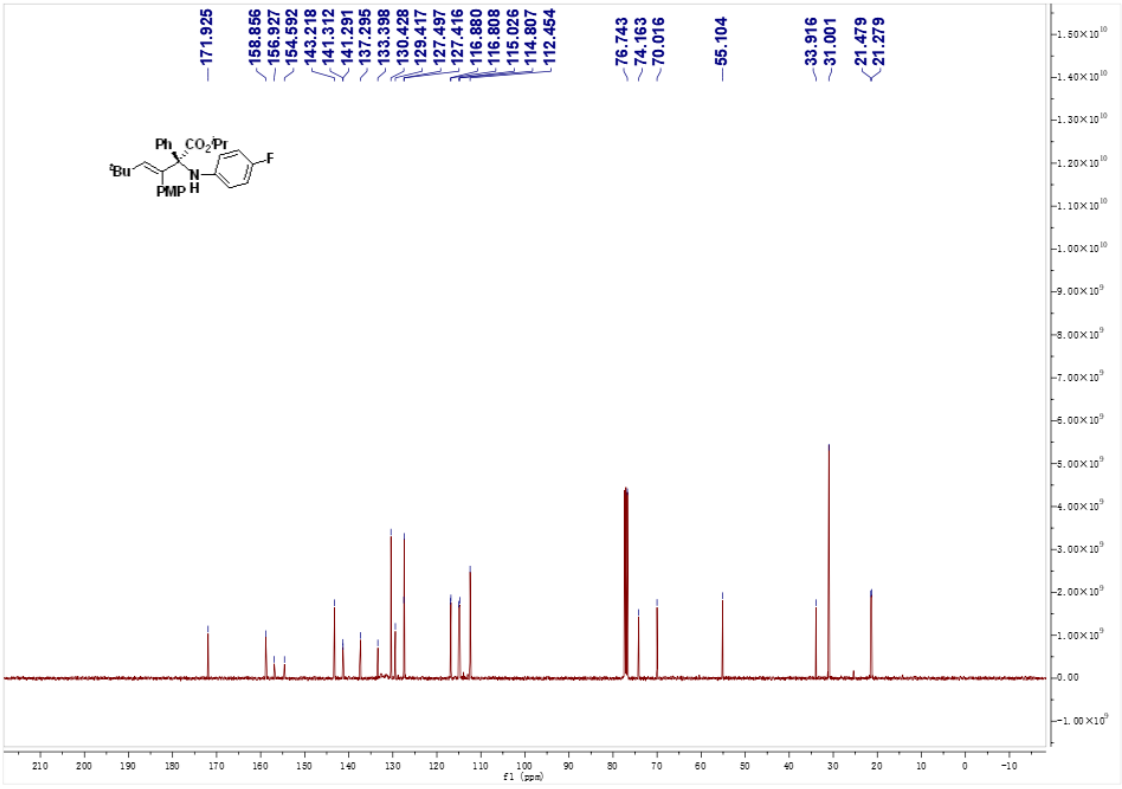
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4n**



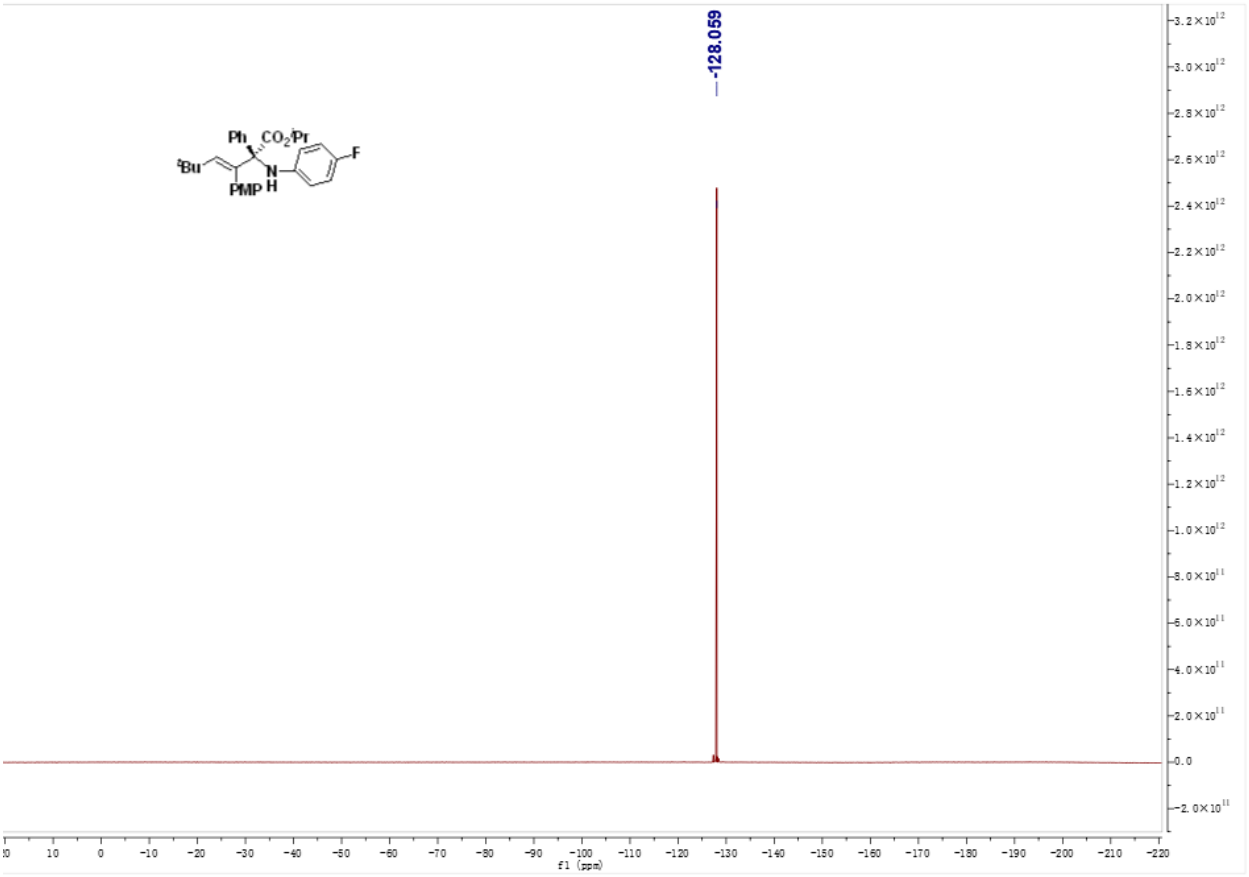
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4o**



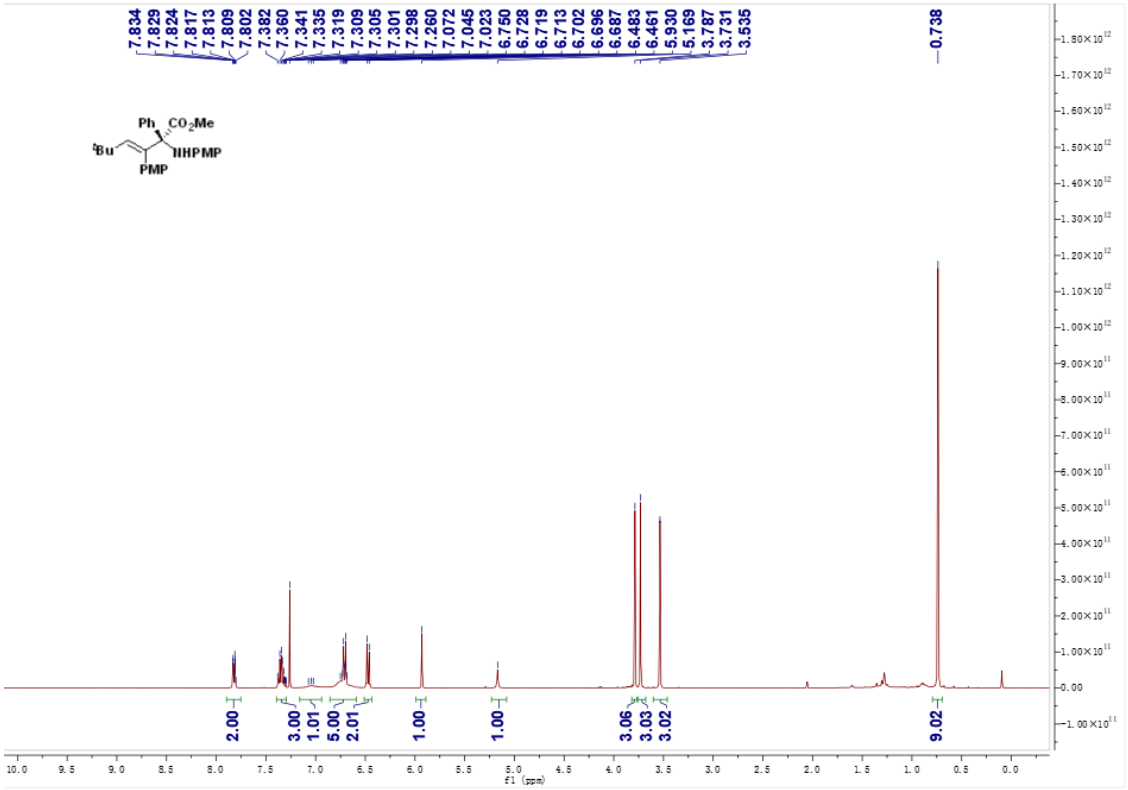
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4o**



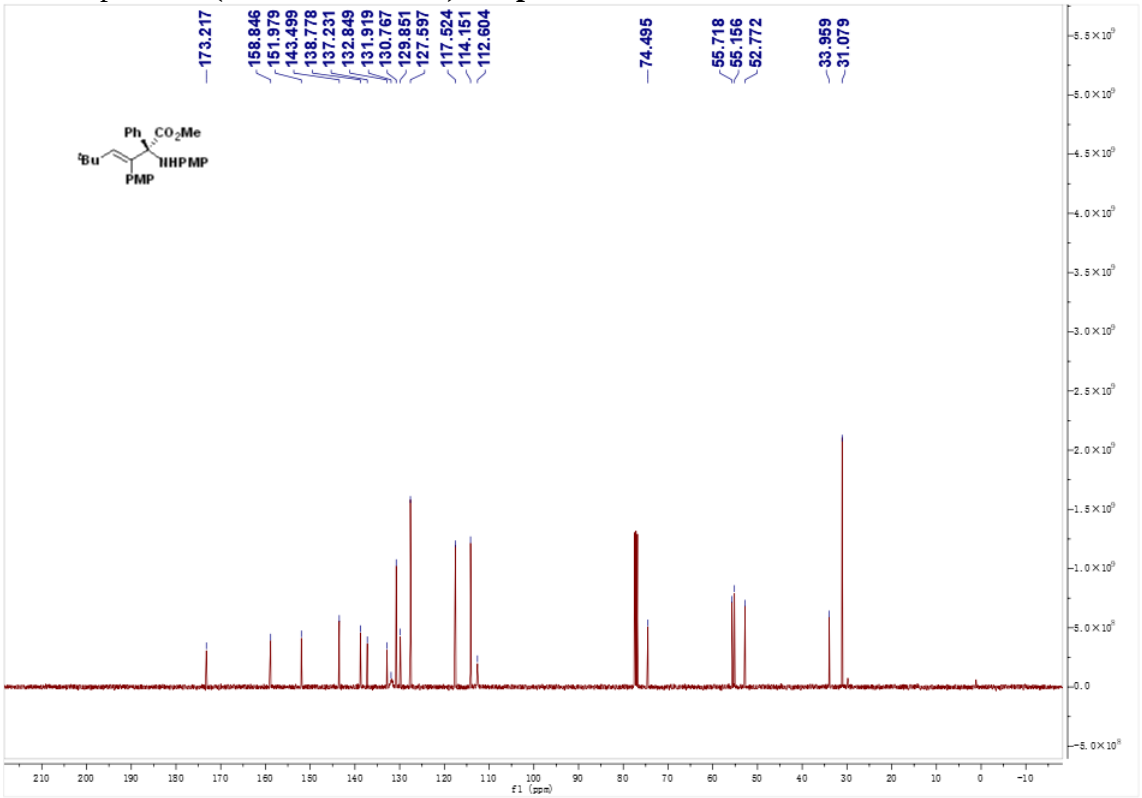
^{19}F NMR-spectrum (376 MHz, $CDCl_3$) of **4o**



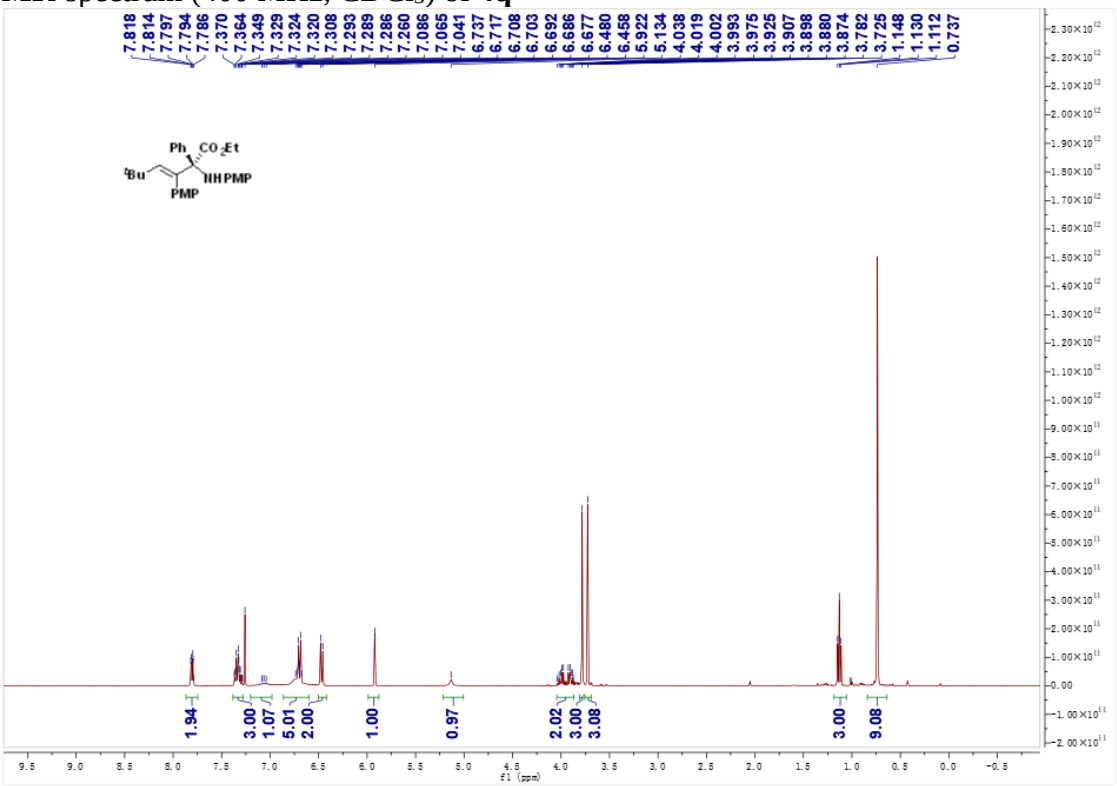
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4p**



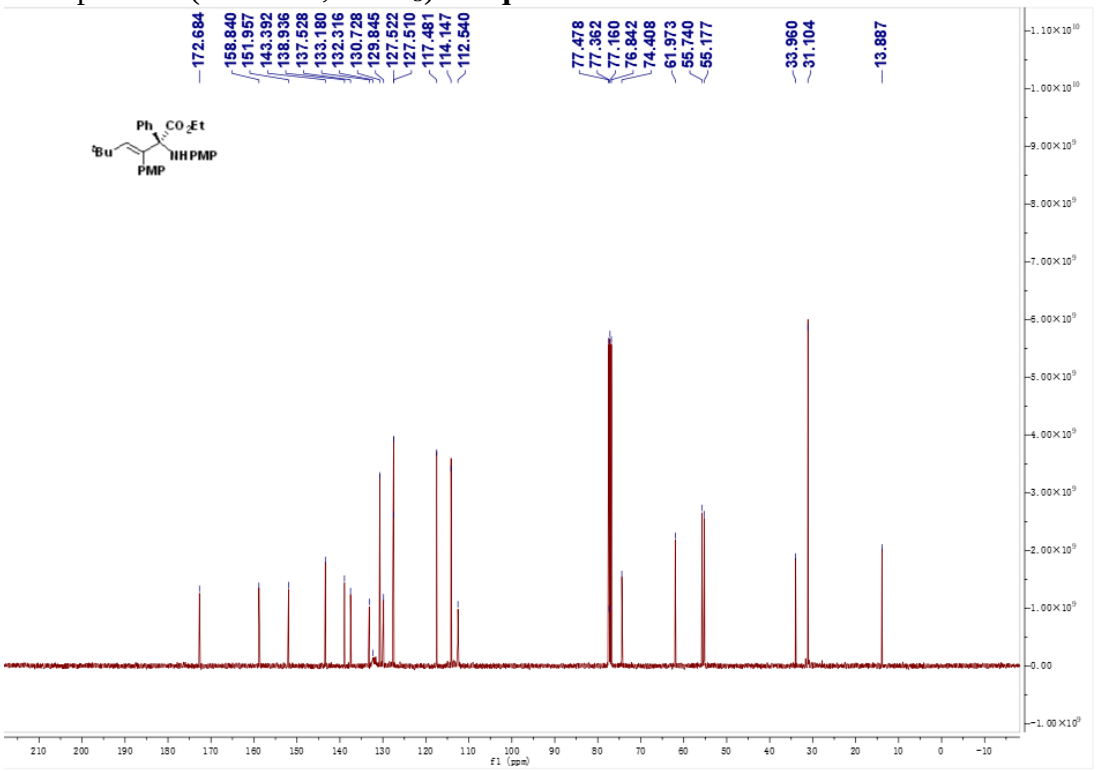
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4p**



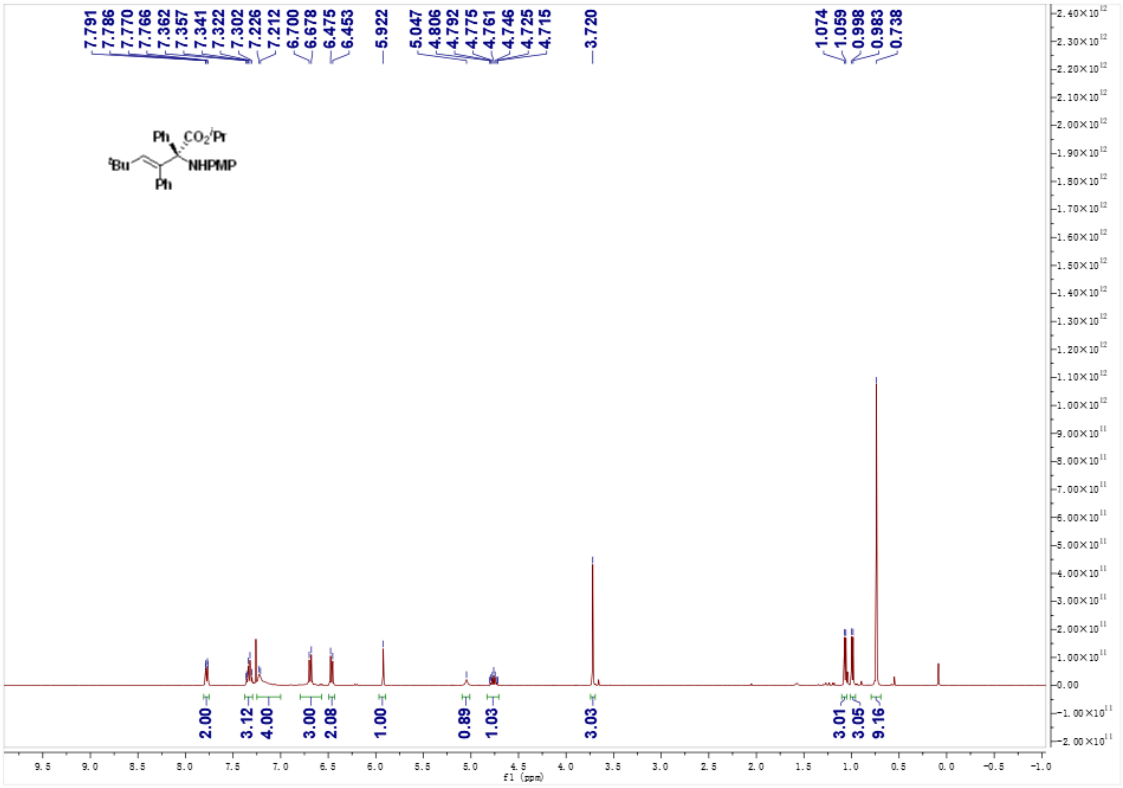
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4q**



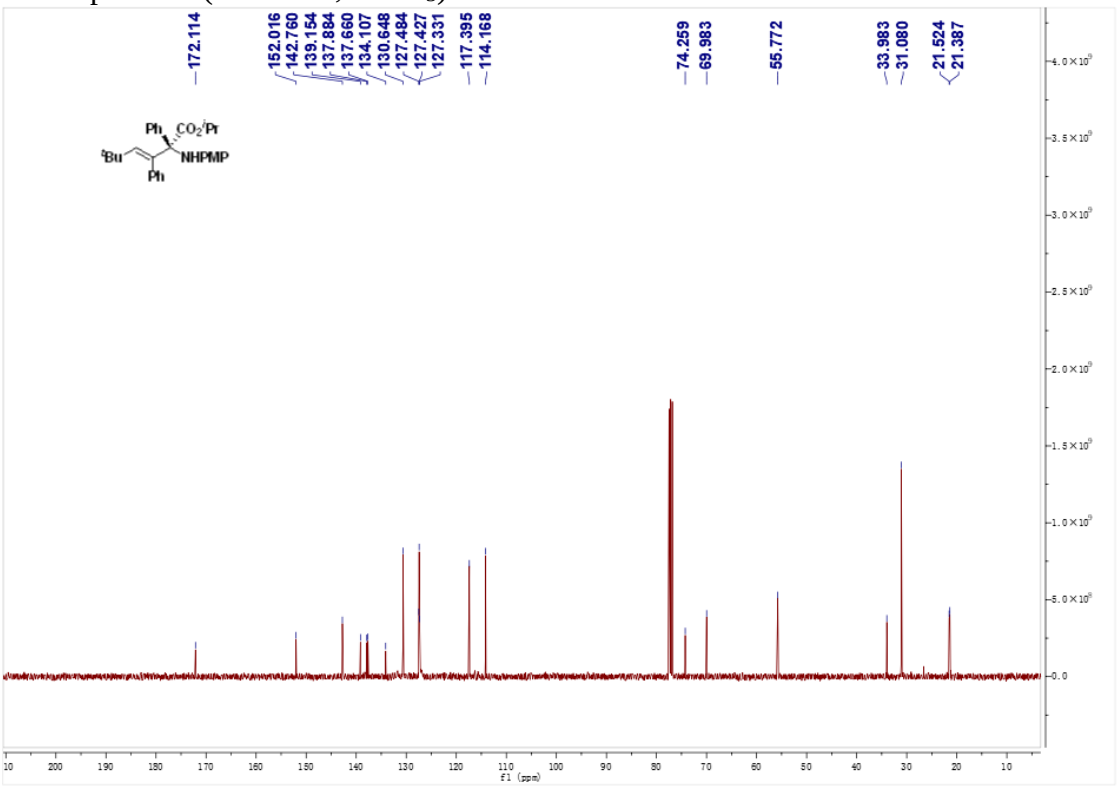
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4q**



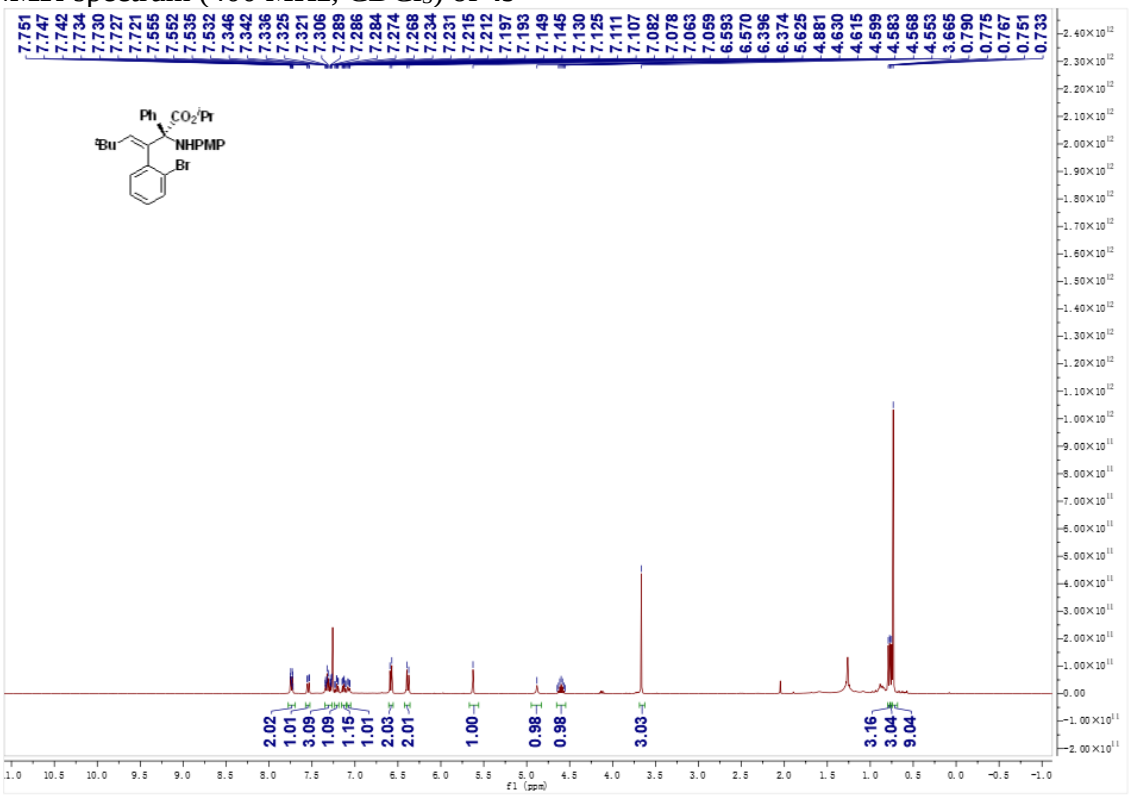
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4r**



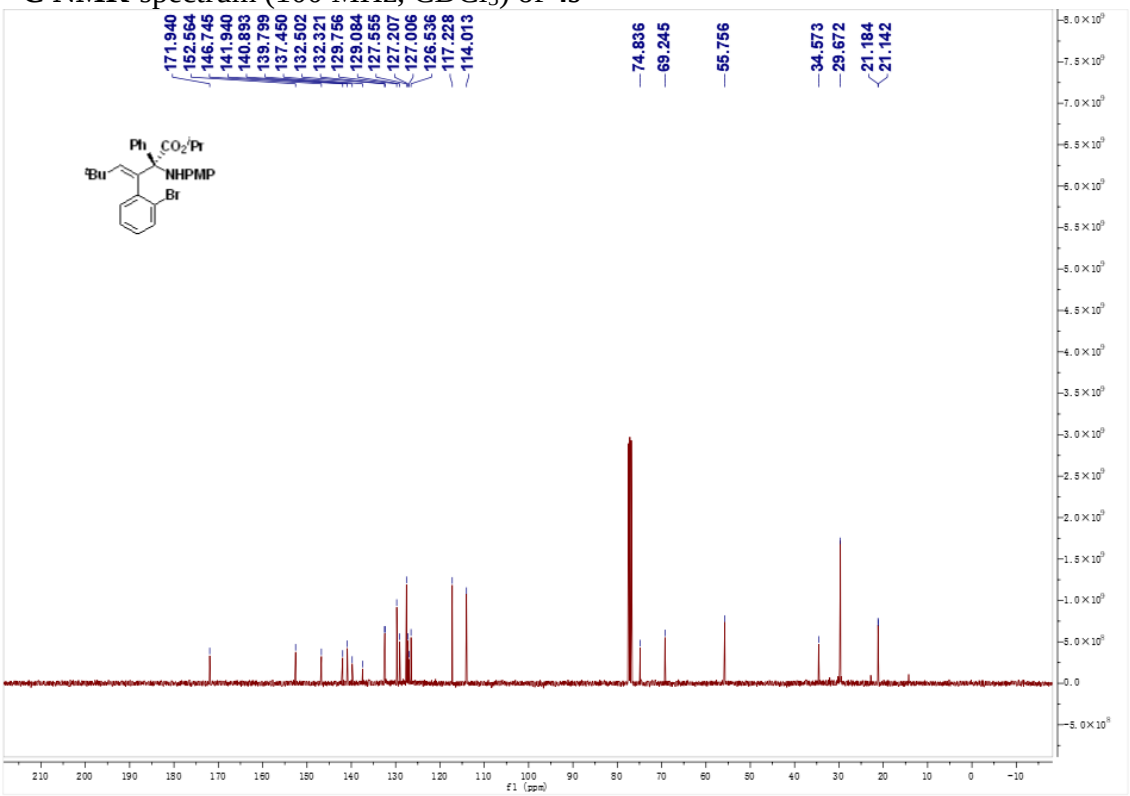
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4r**



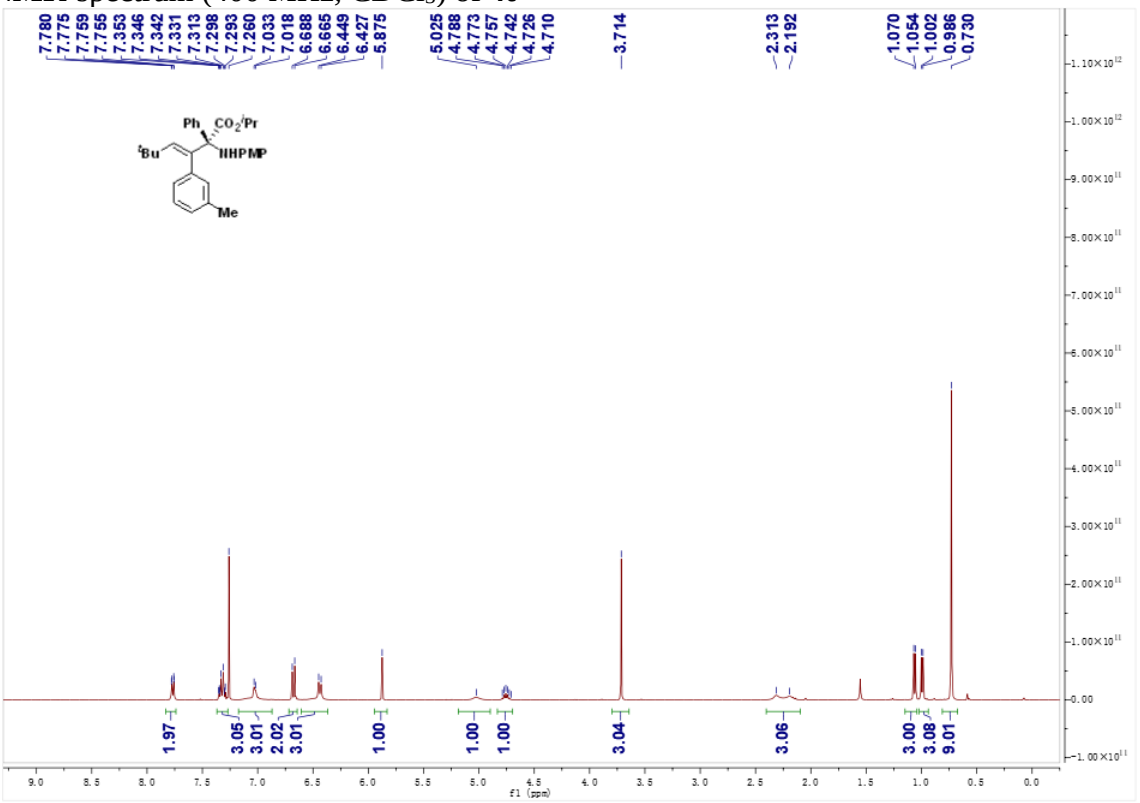
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4s**



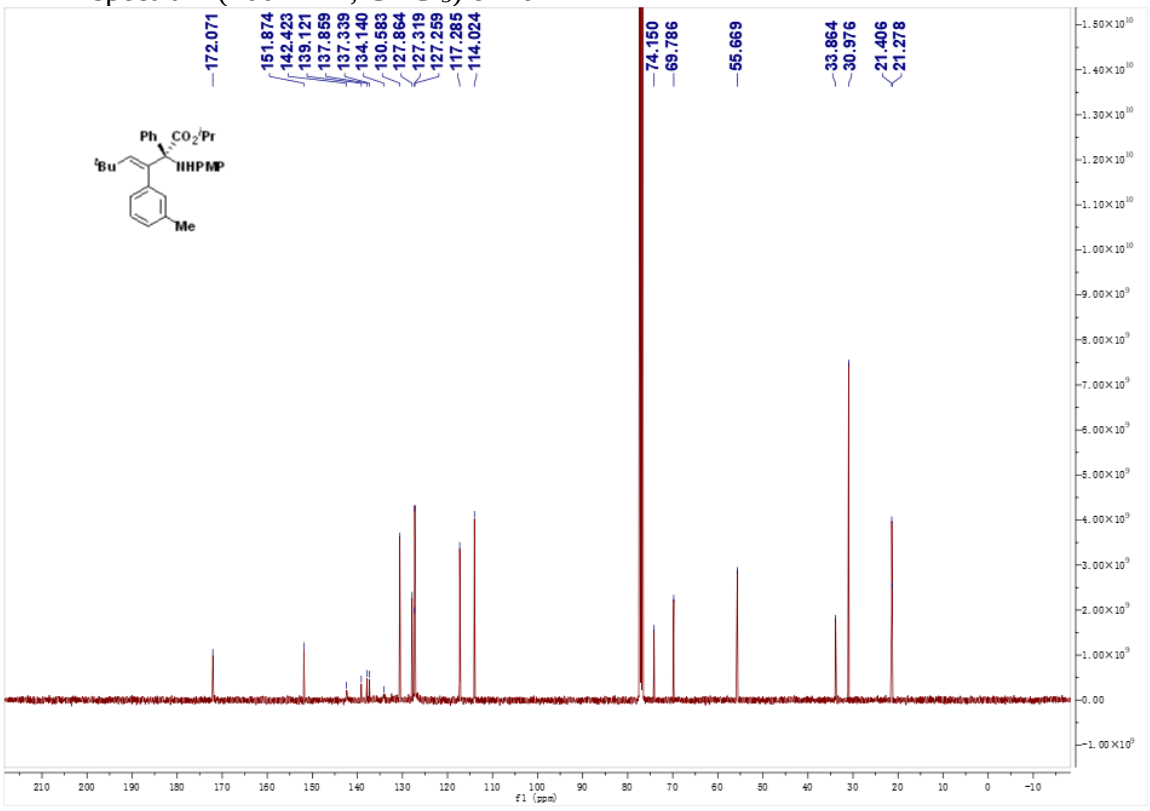
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4s**



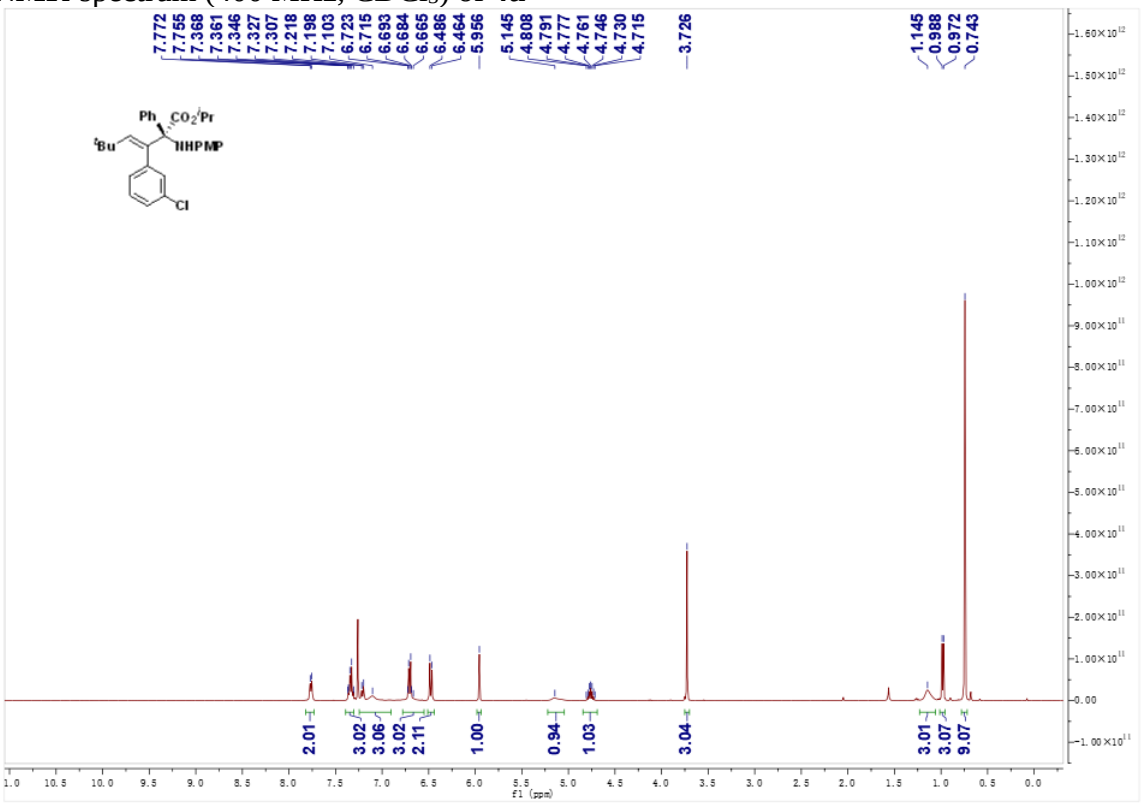
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4t**



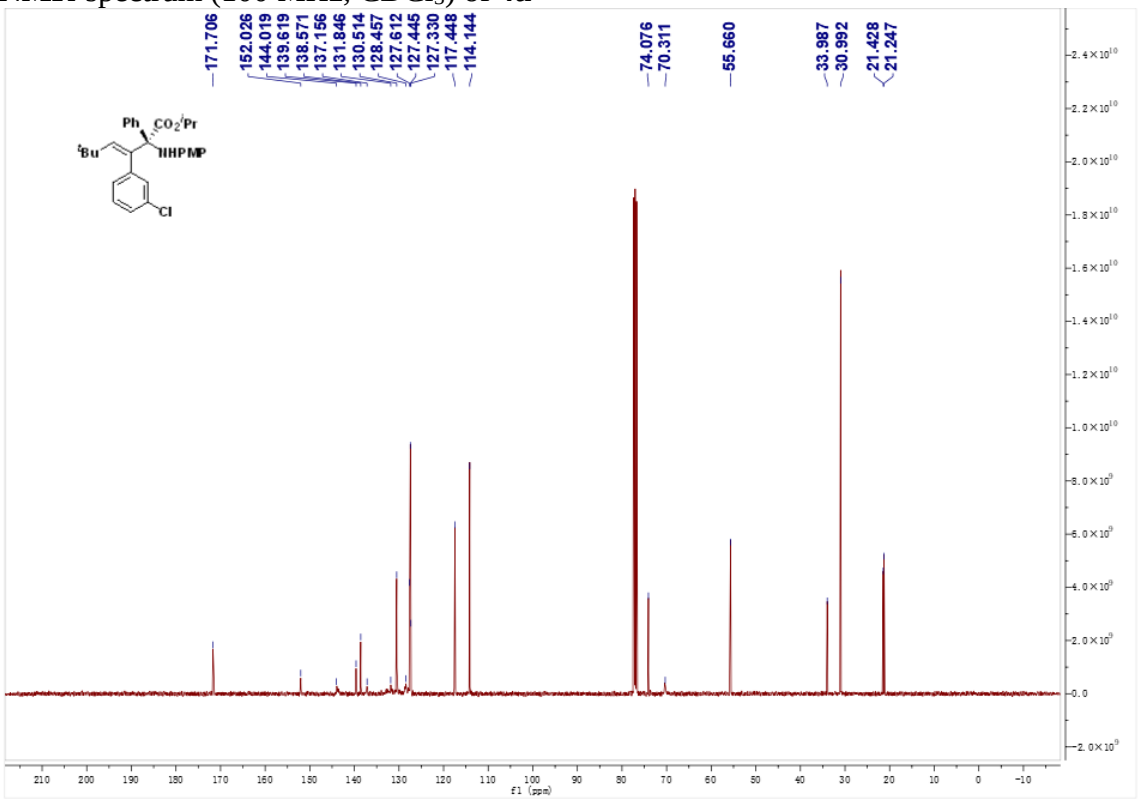
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4t**



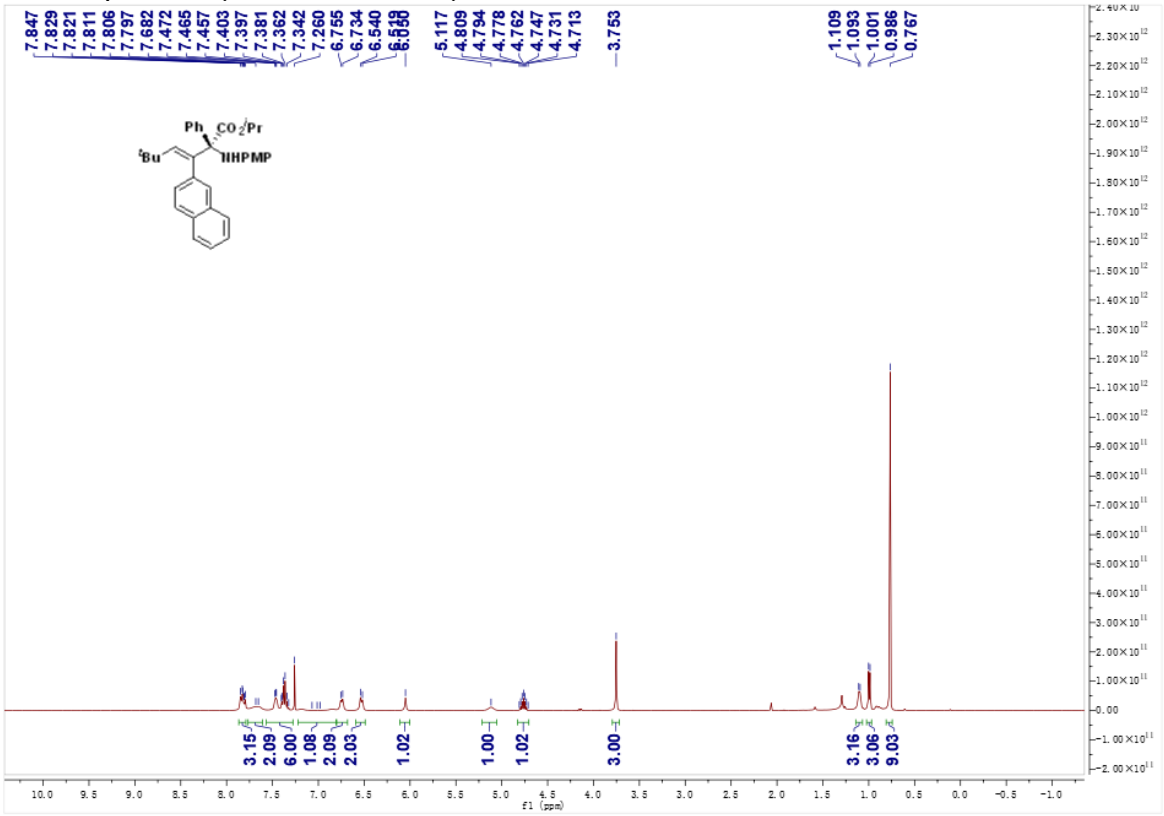
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4u**



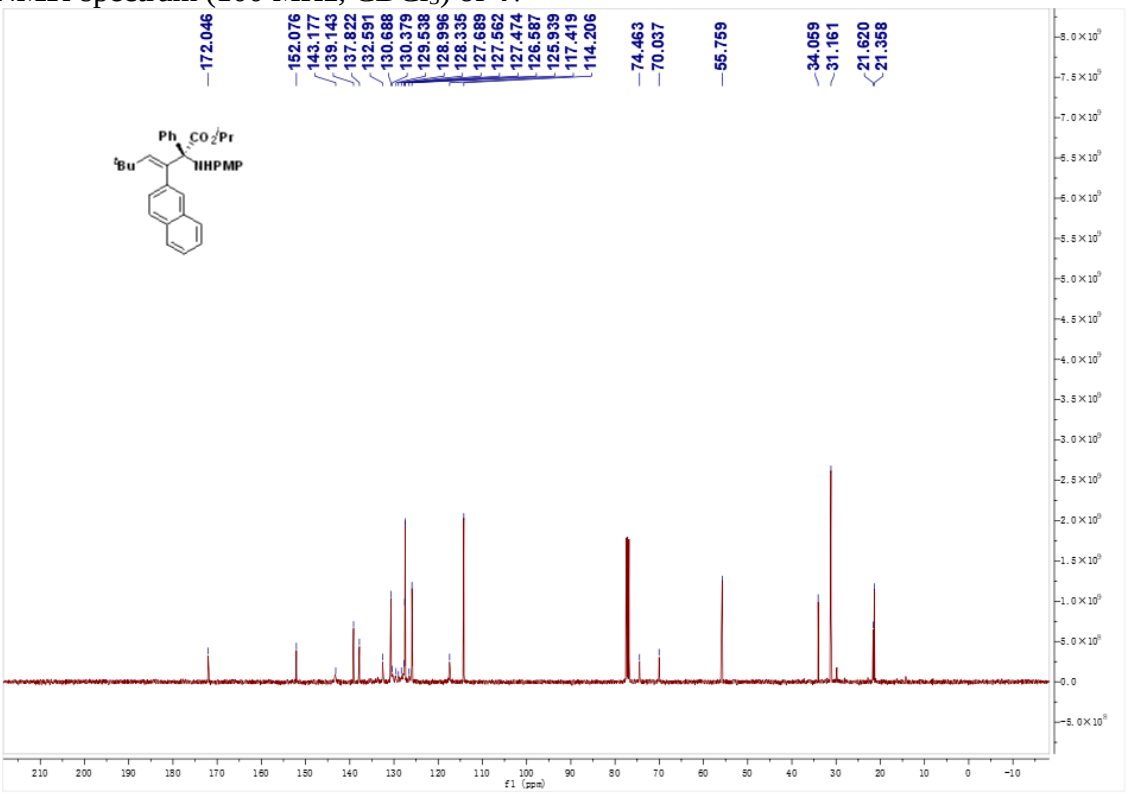
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4u**



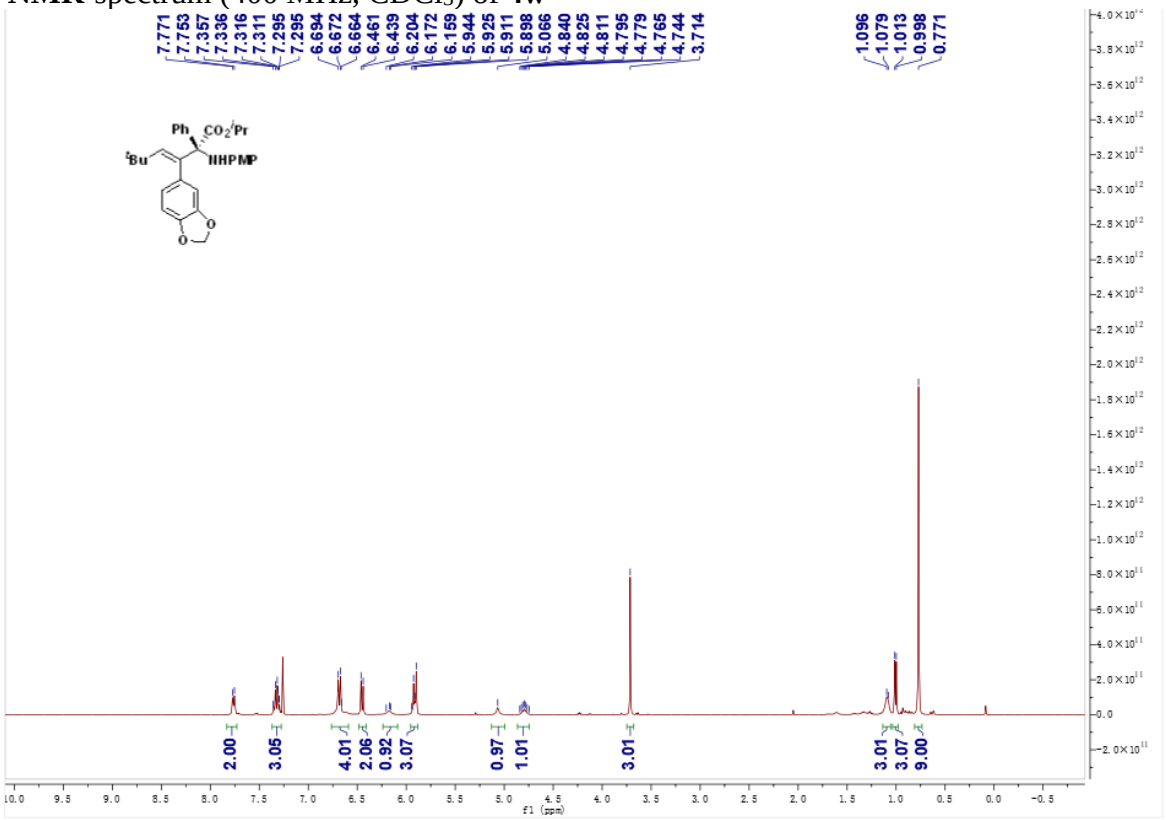
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4v**



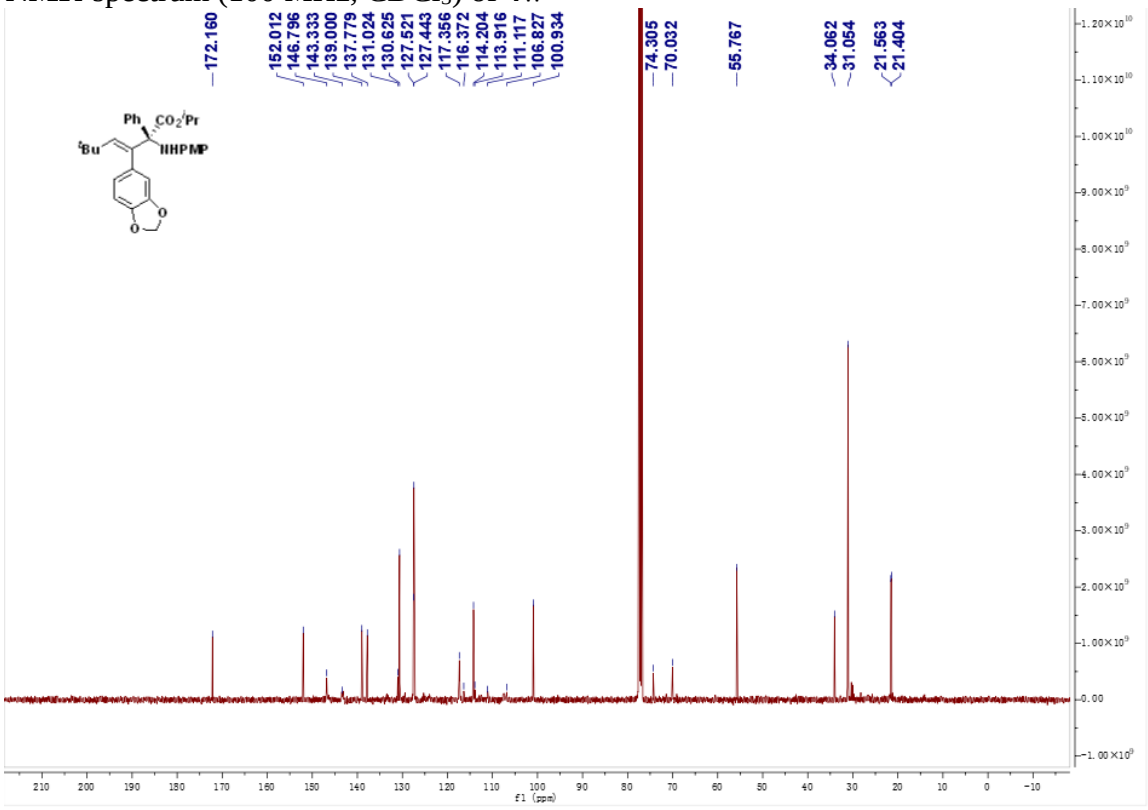
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4v**



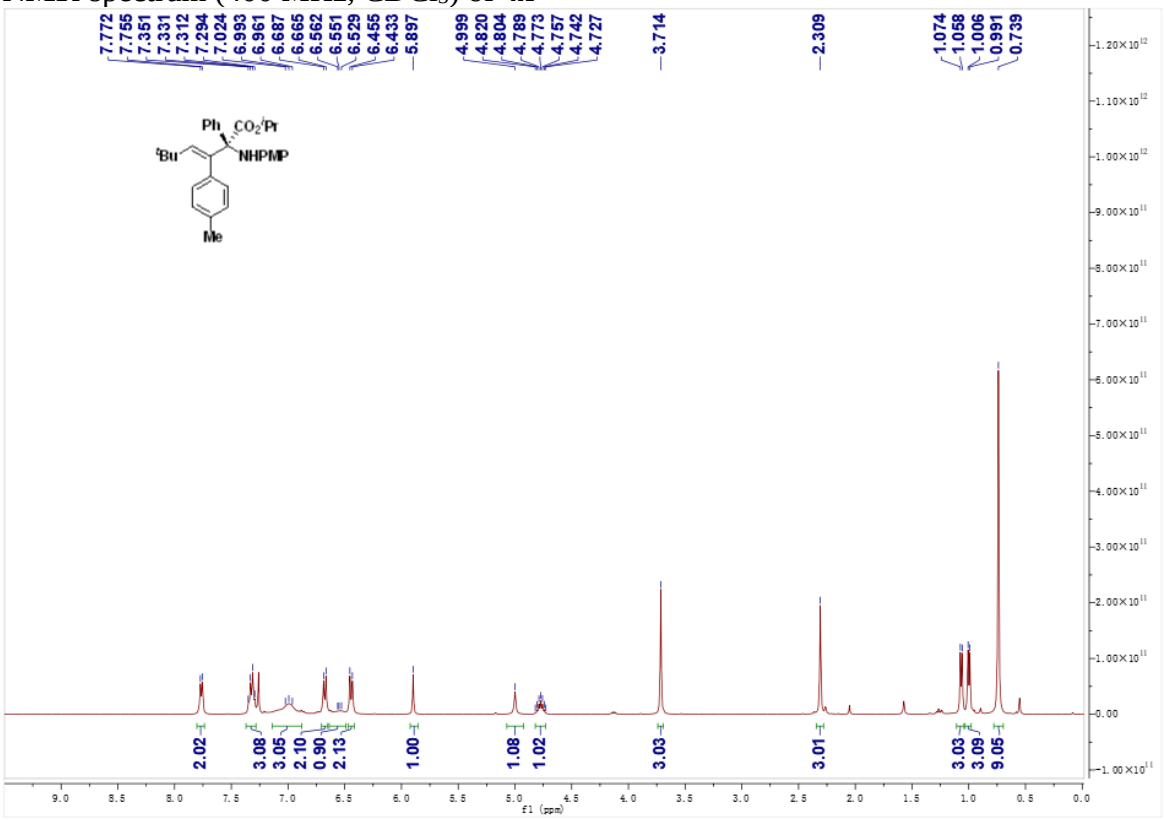
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4w**



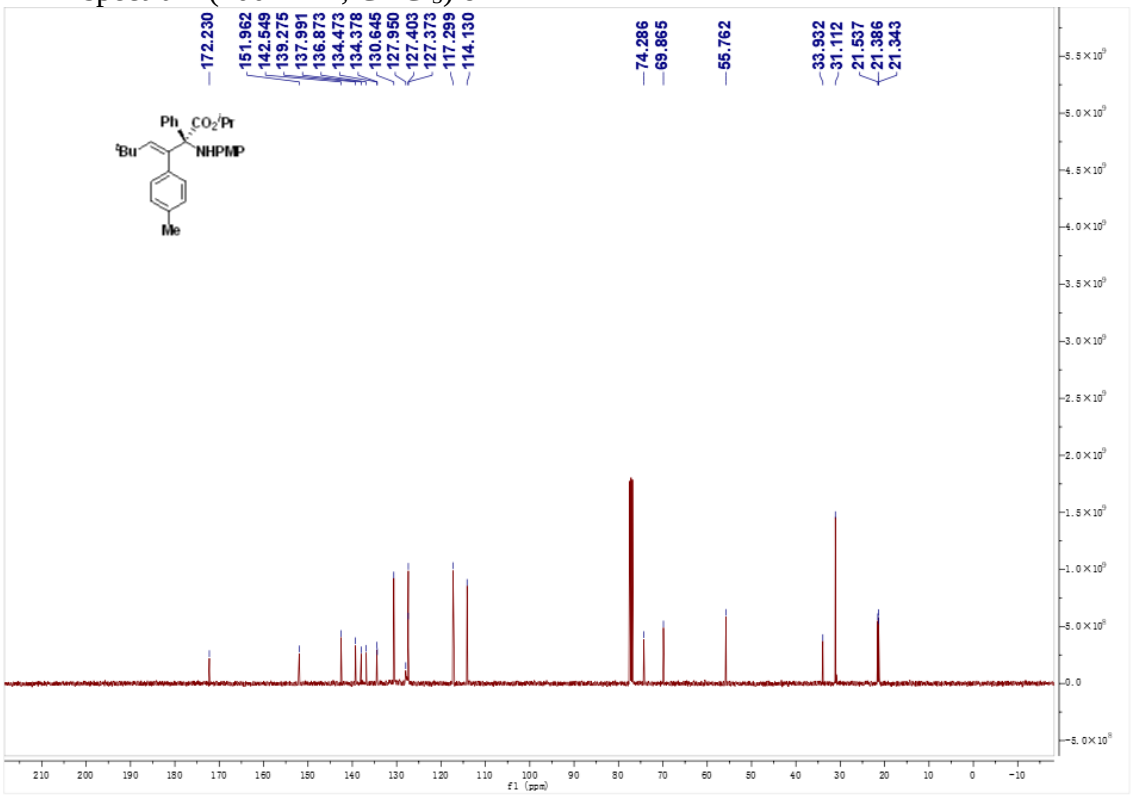
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4w**



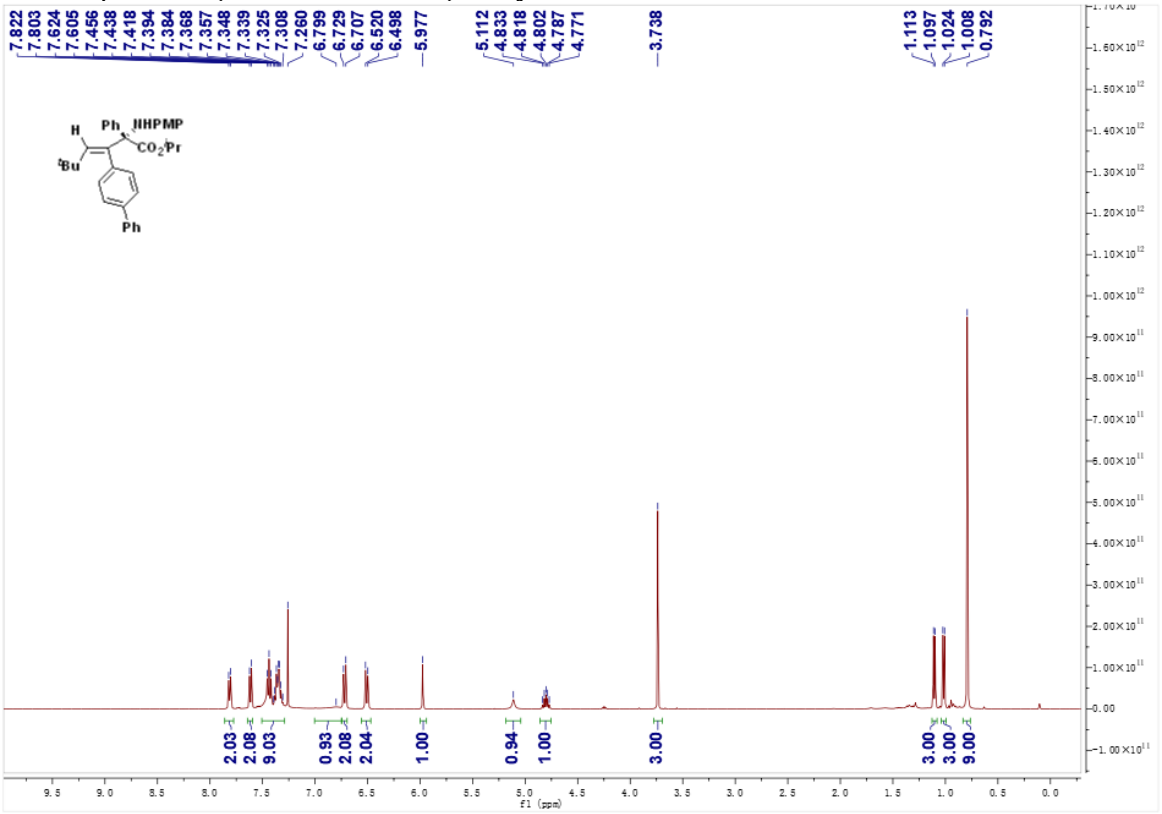
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4x**



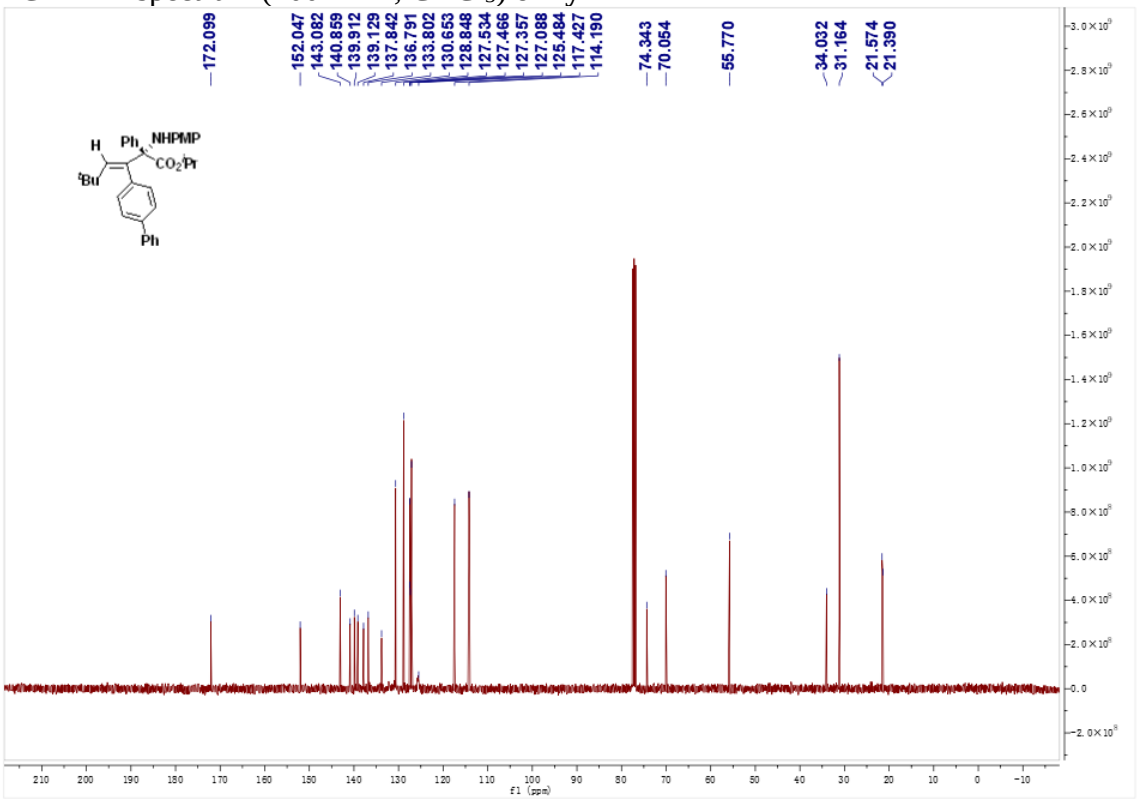
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4x**



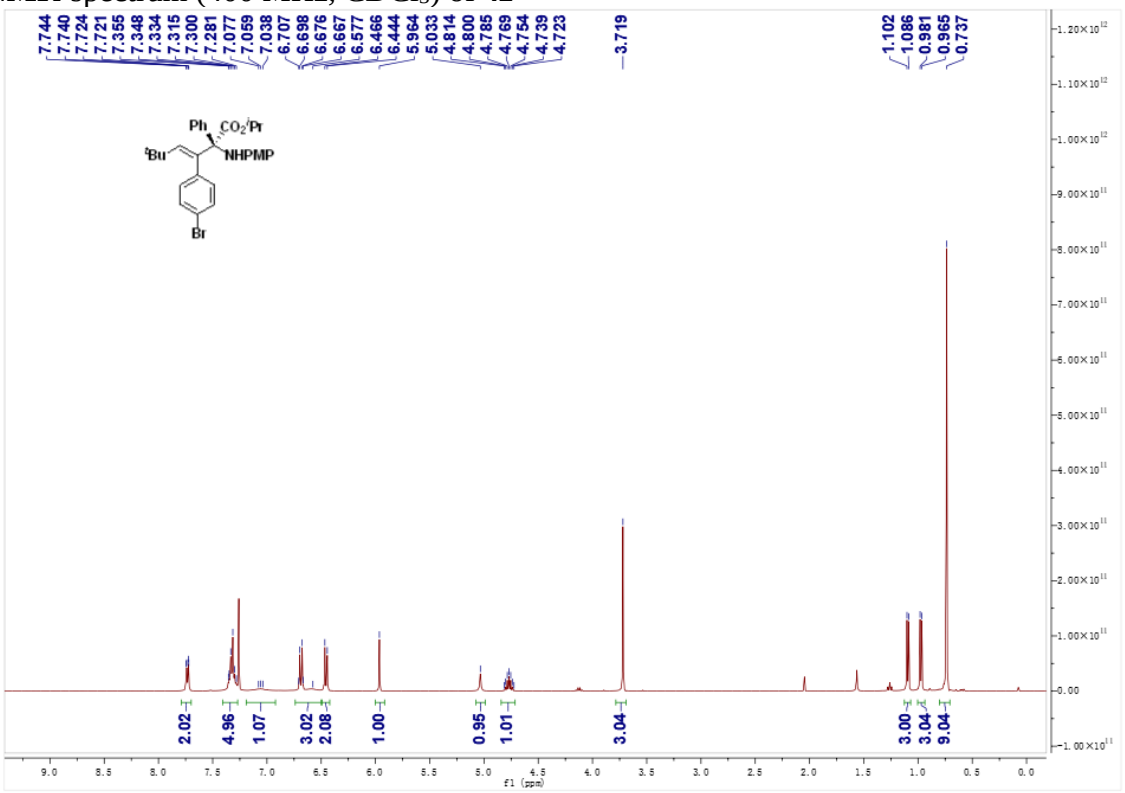
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4y**



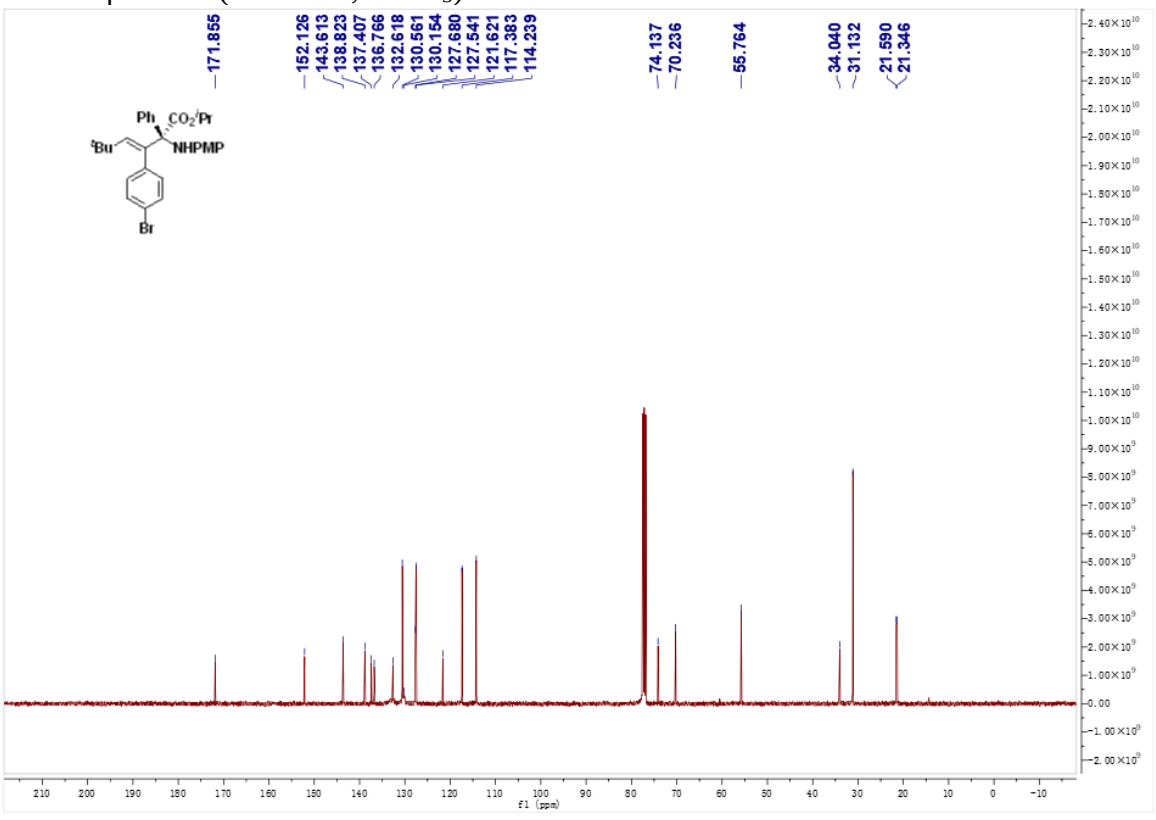
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4y**



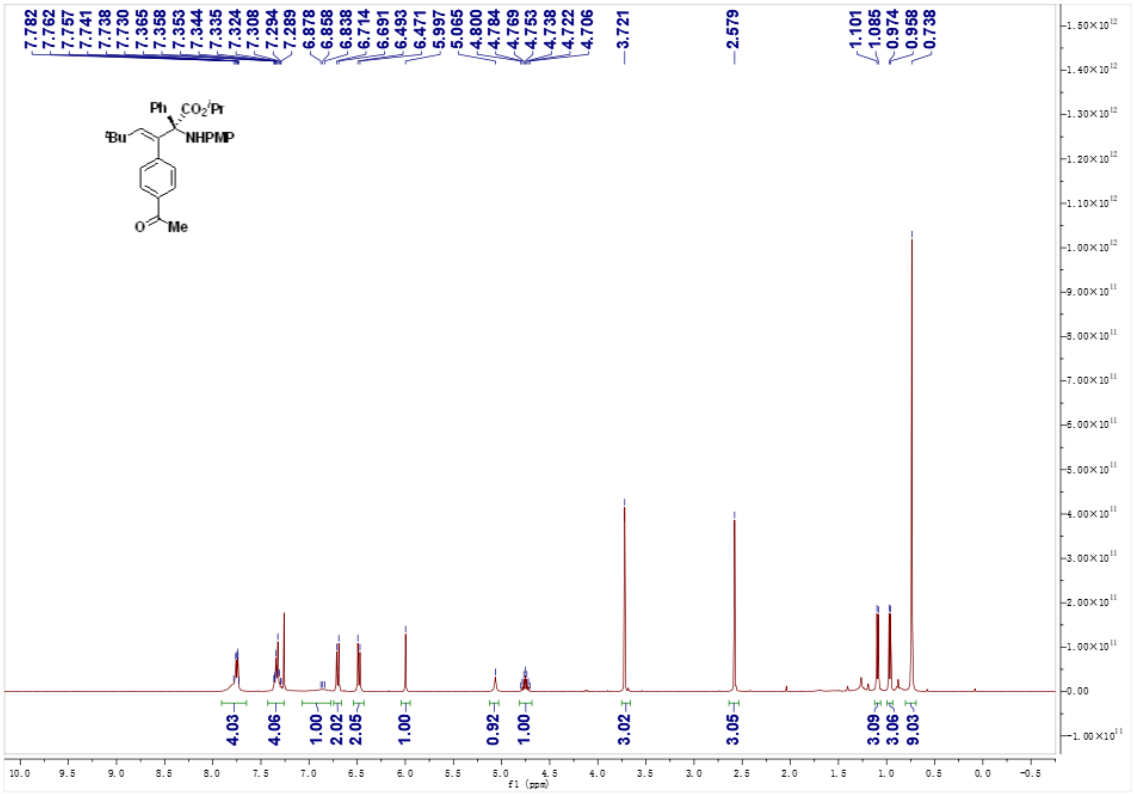
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4z**



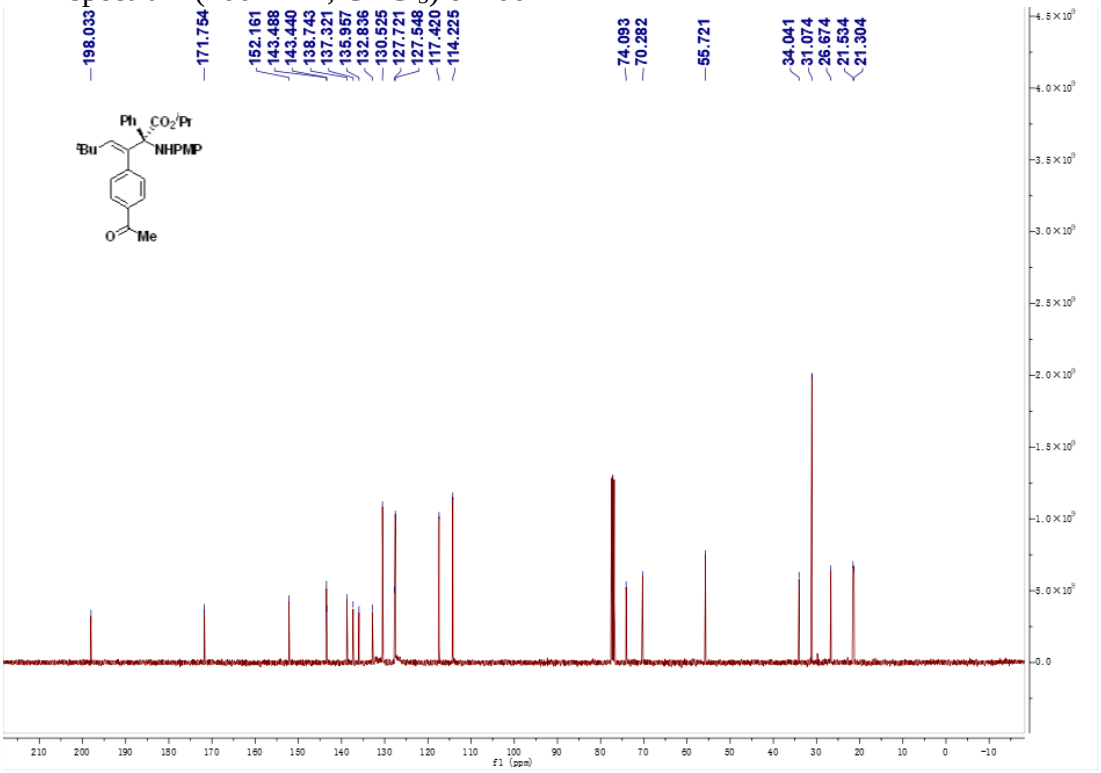
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4z**



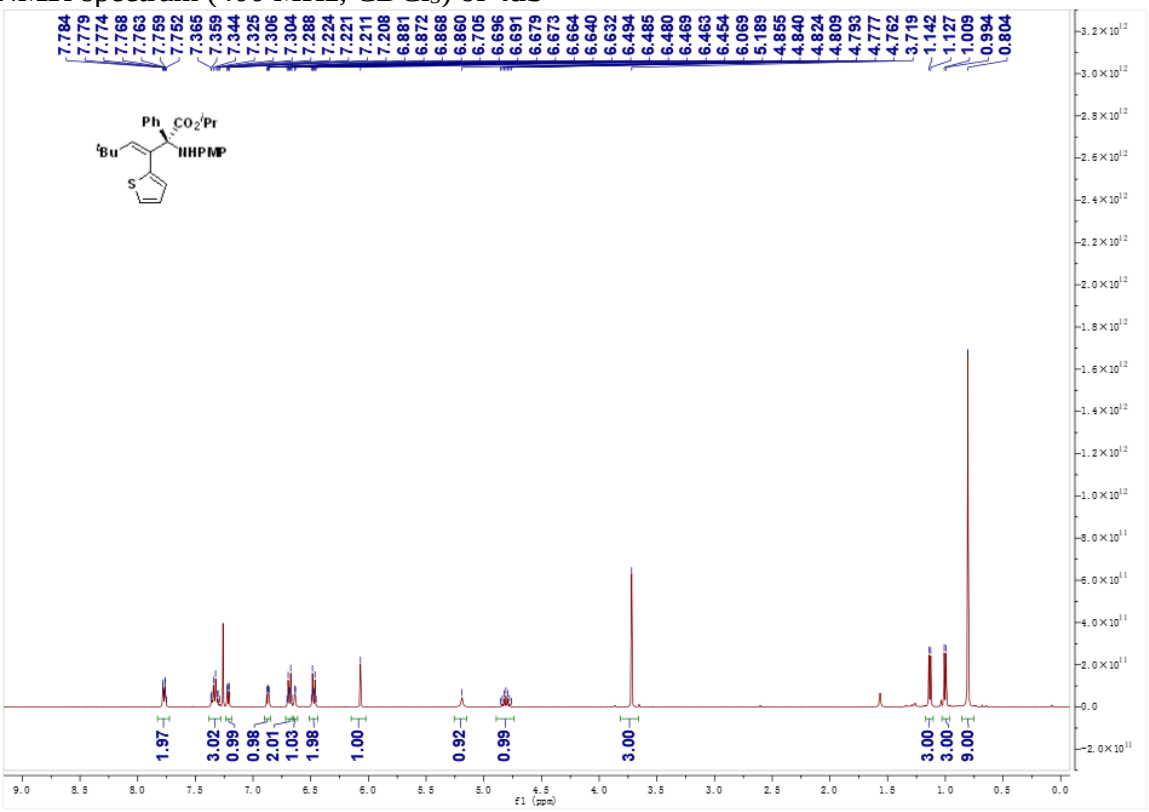
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4aa**



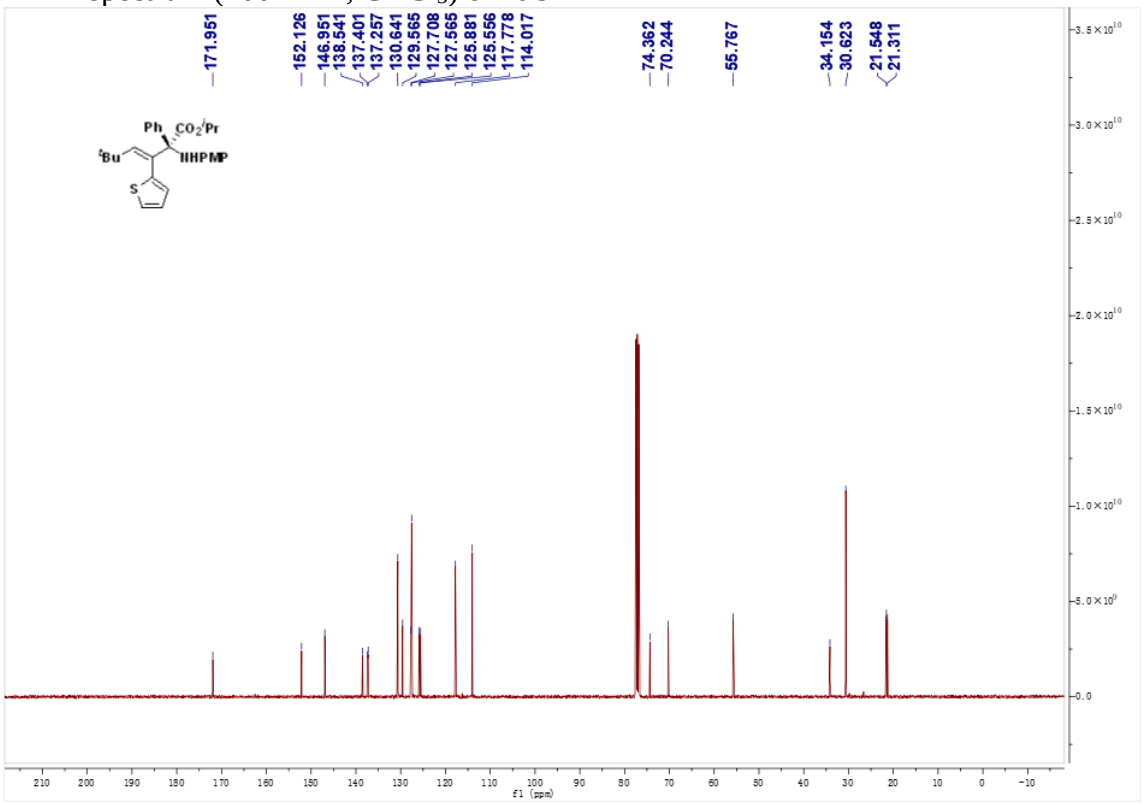
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4aa**



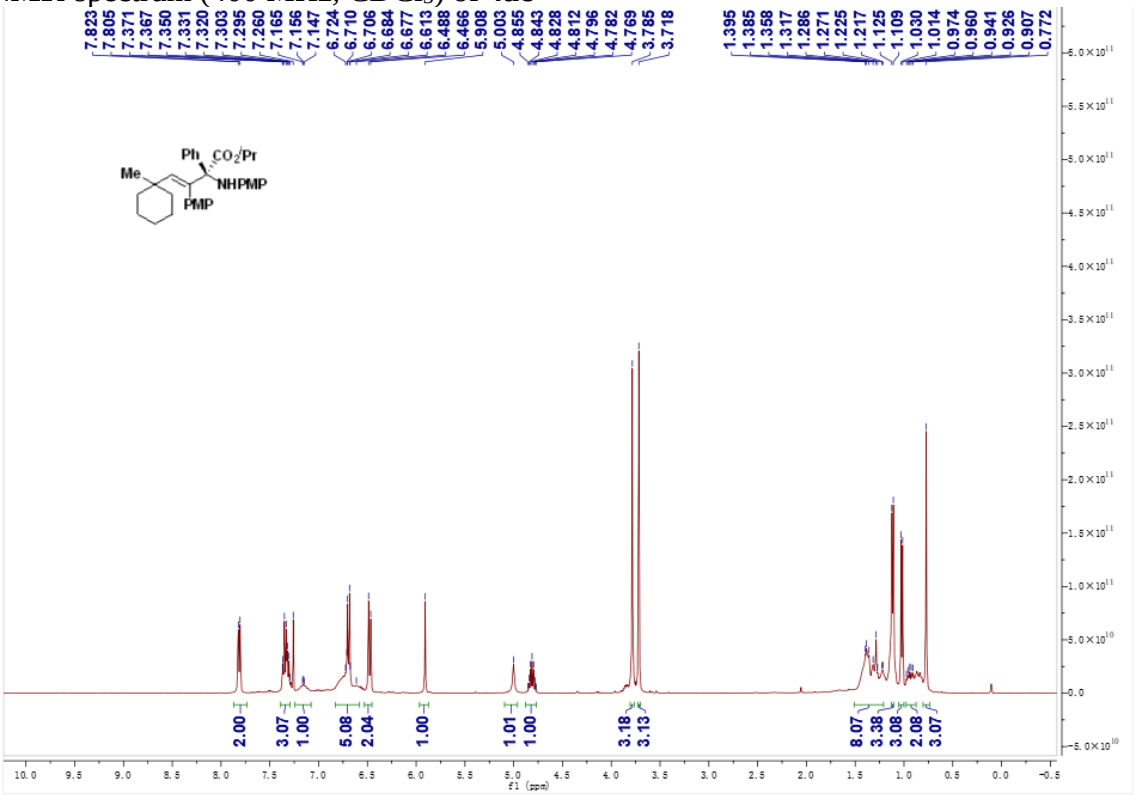
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ab**



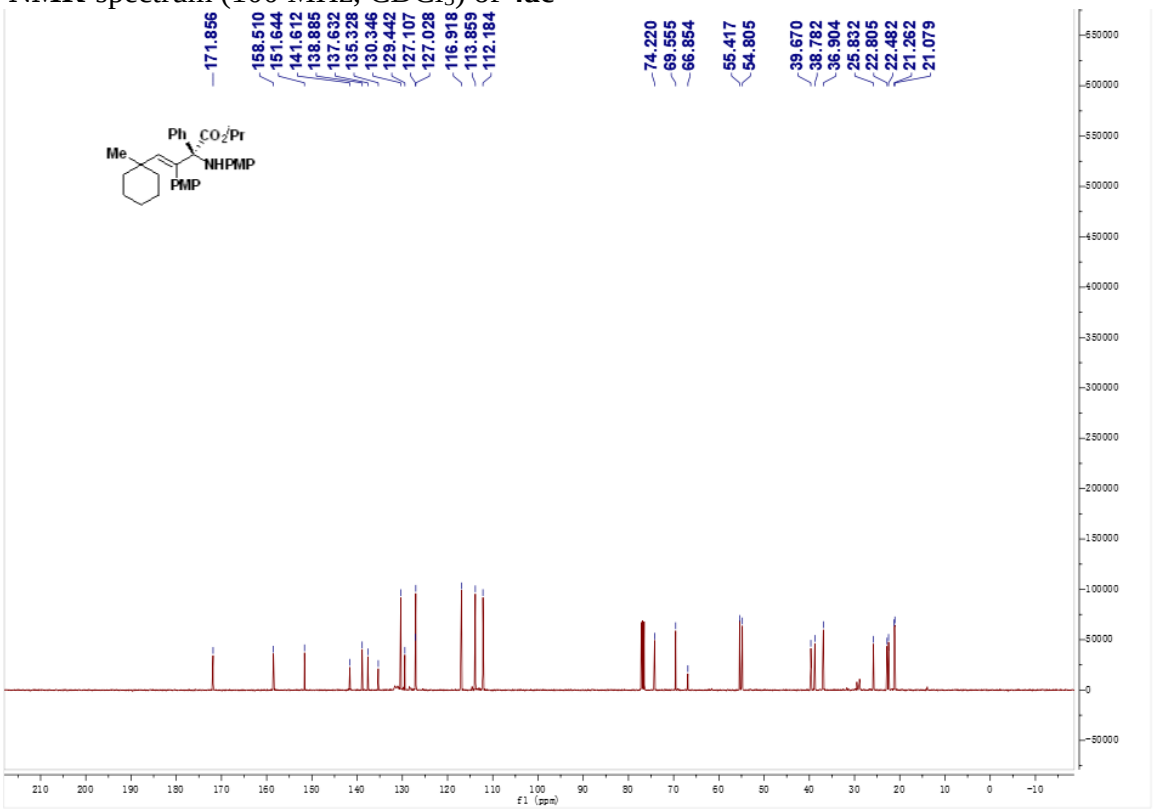
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ab**



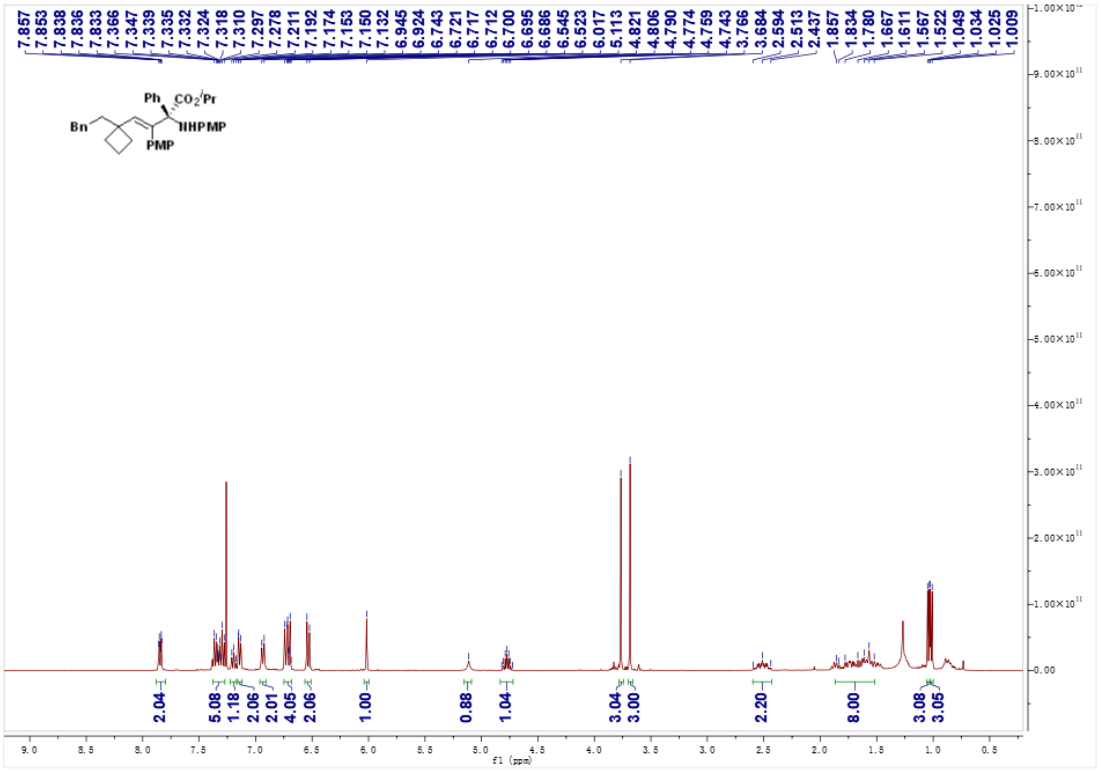
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ac**



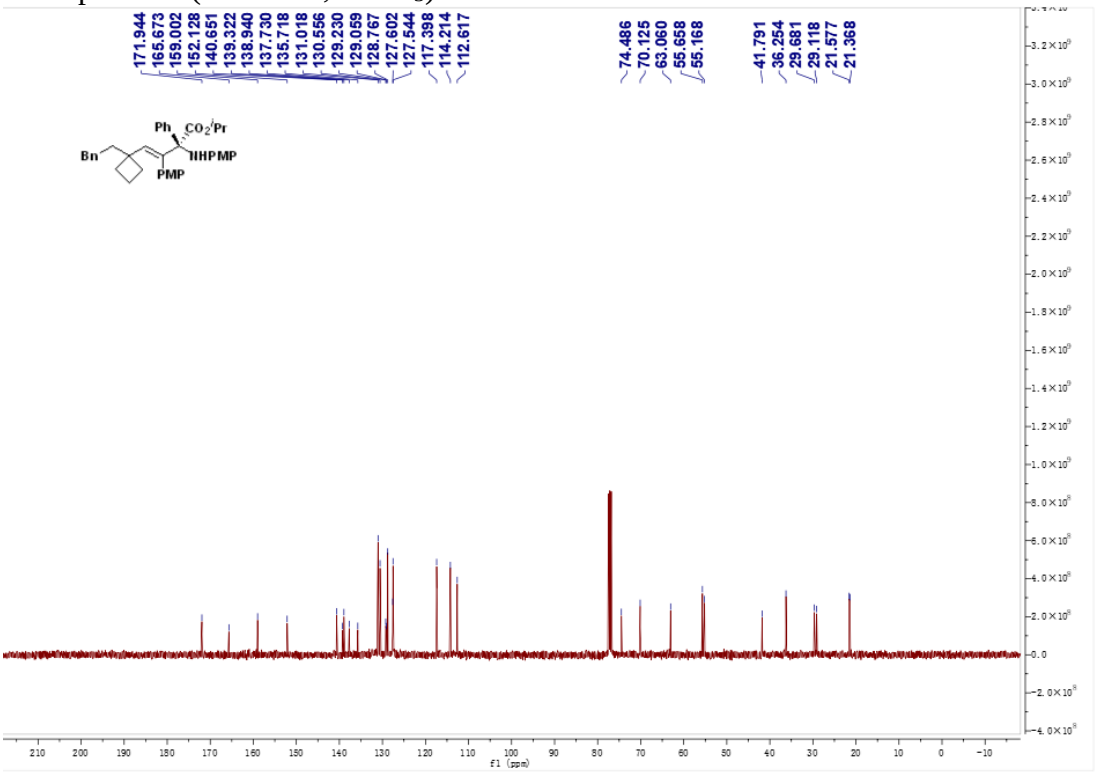
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ac**



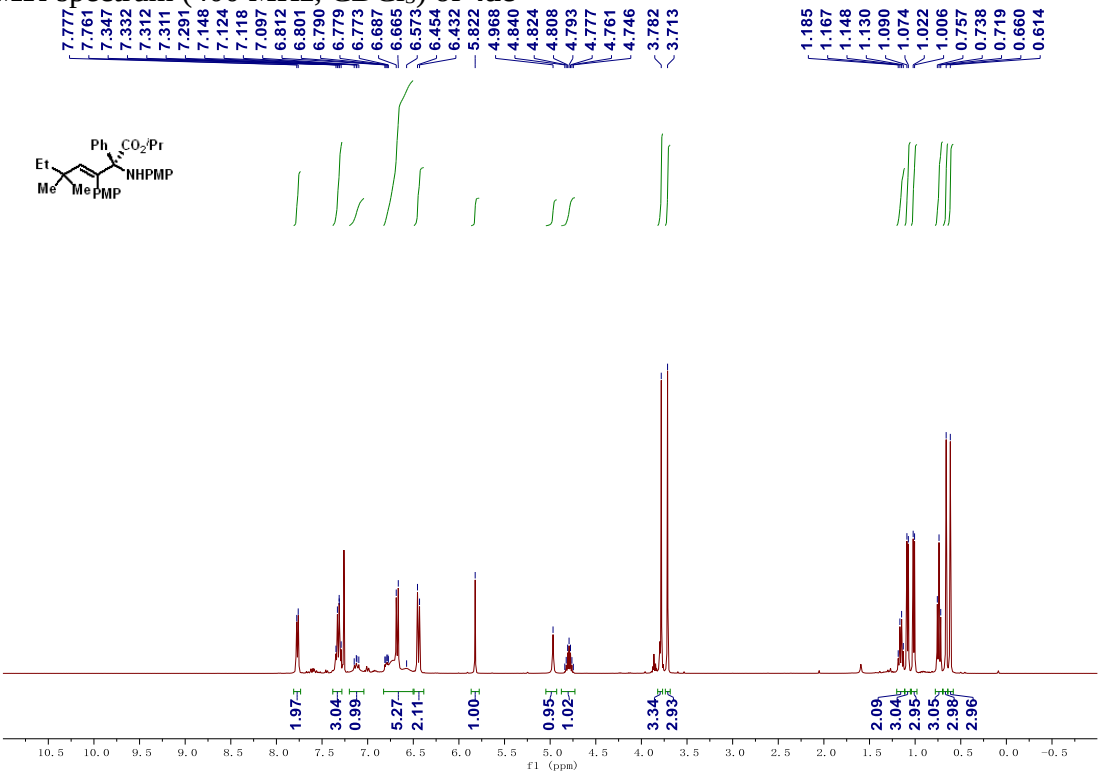
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ad**



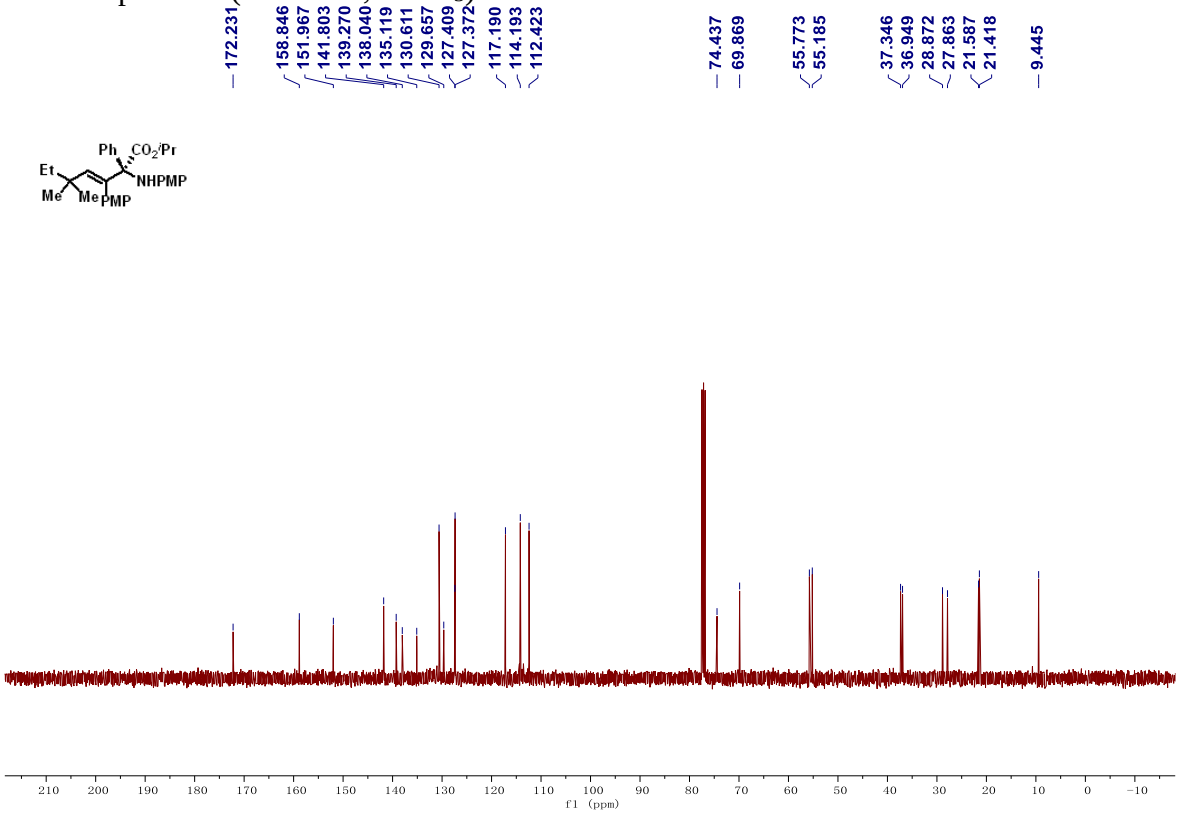
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ad**



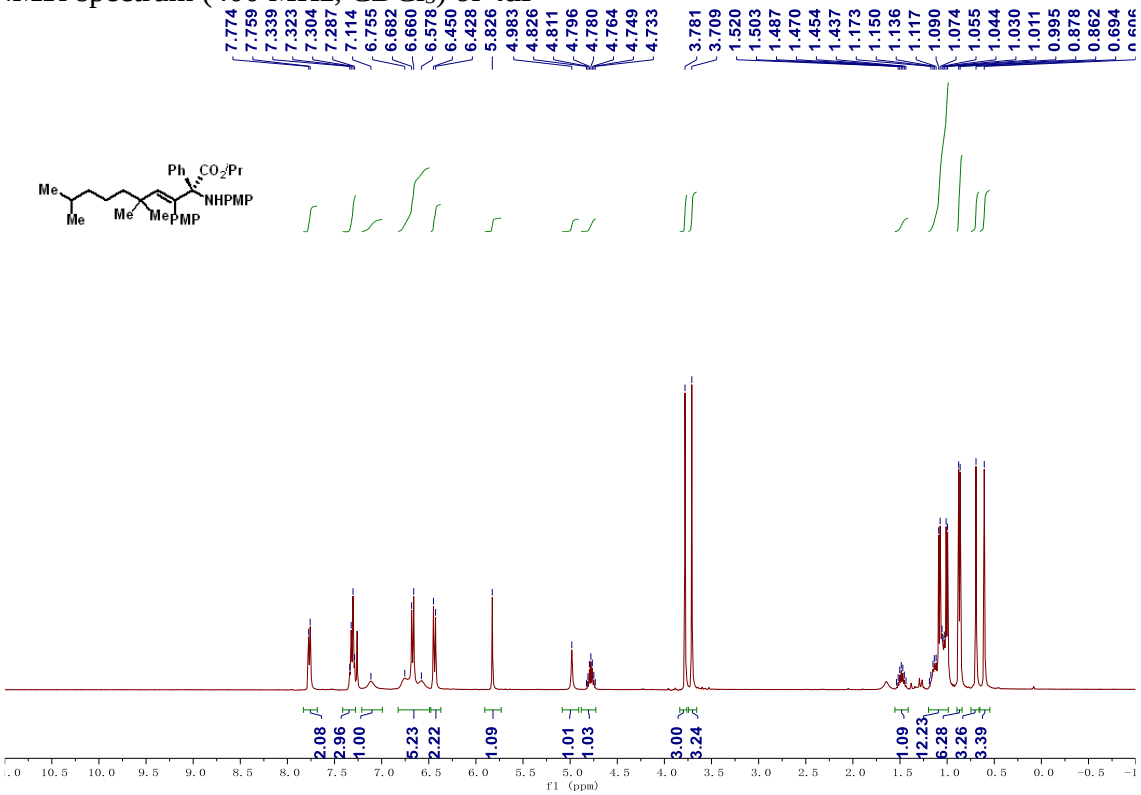
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ae**



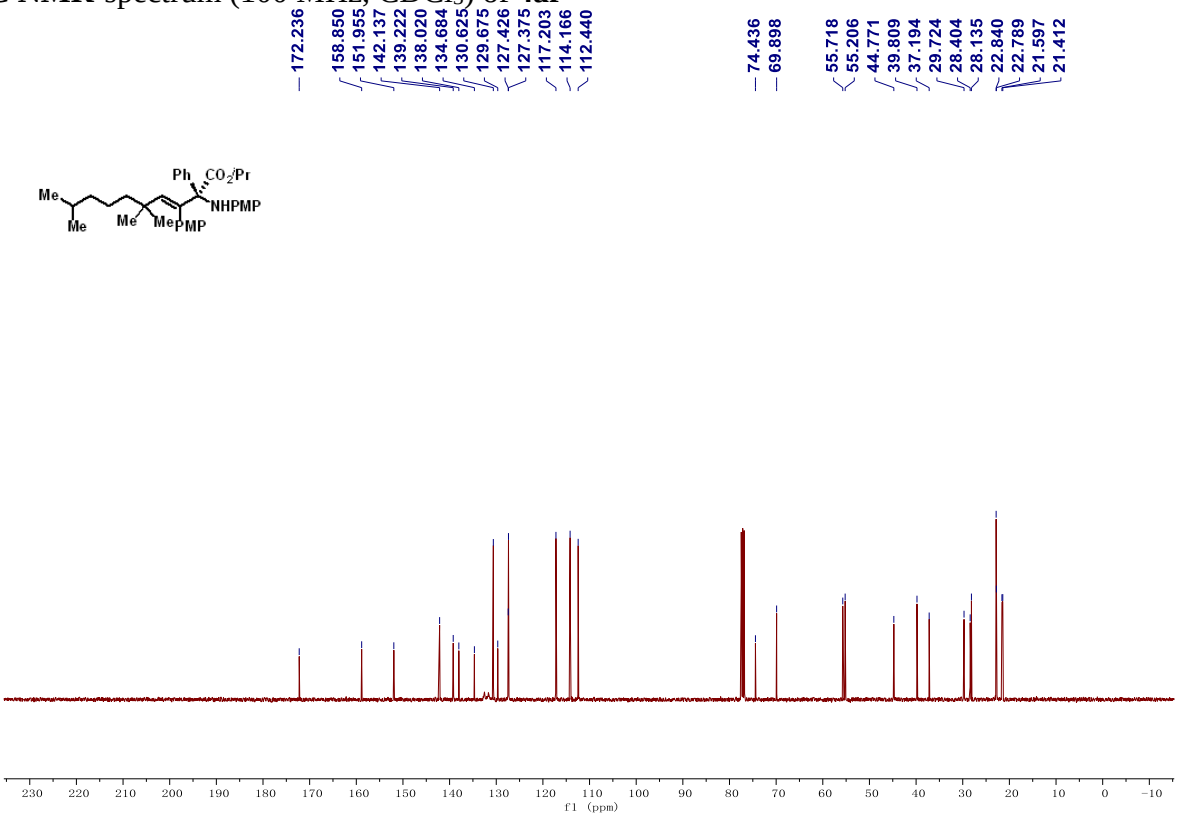
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ae**



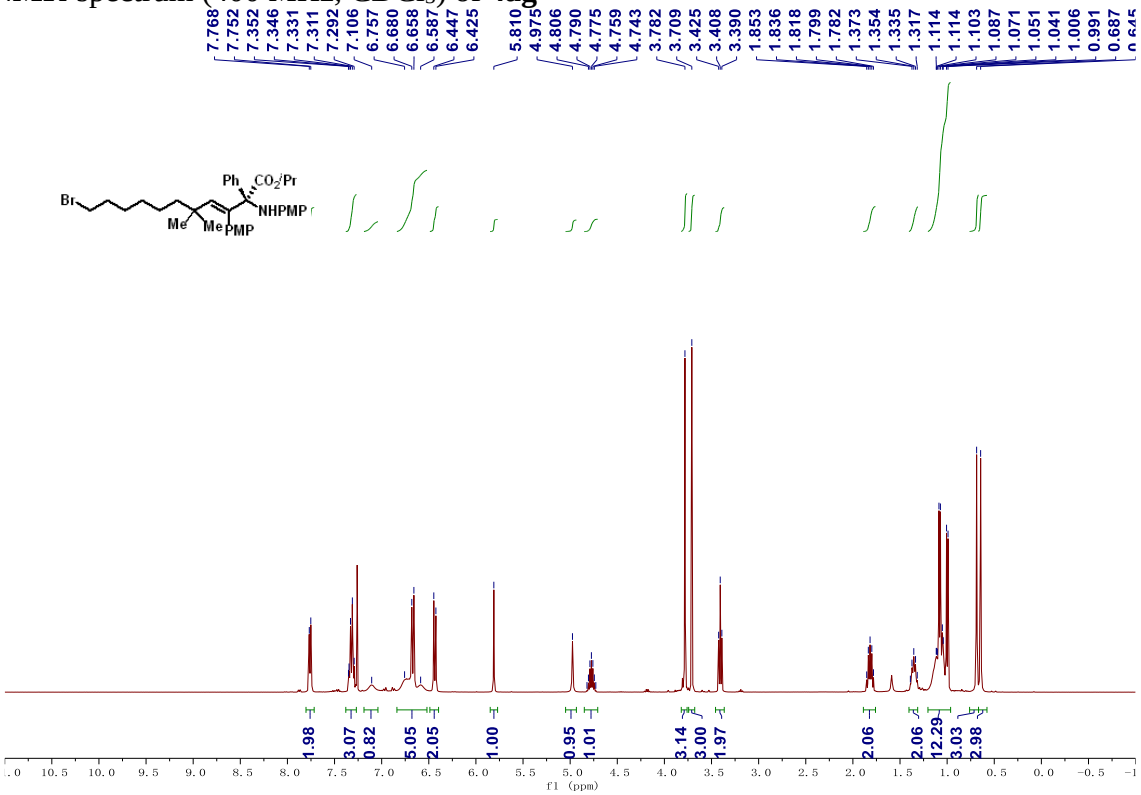
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4af**



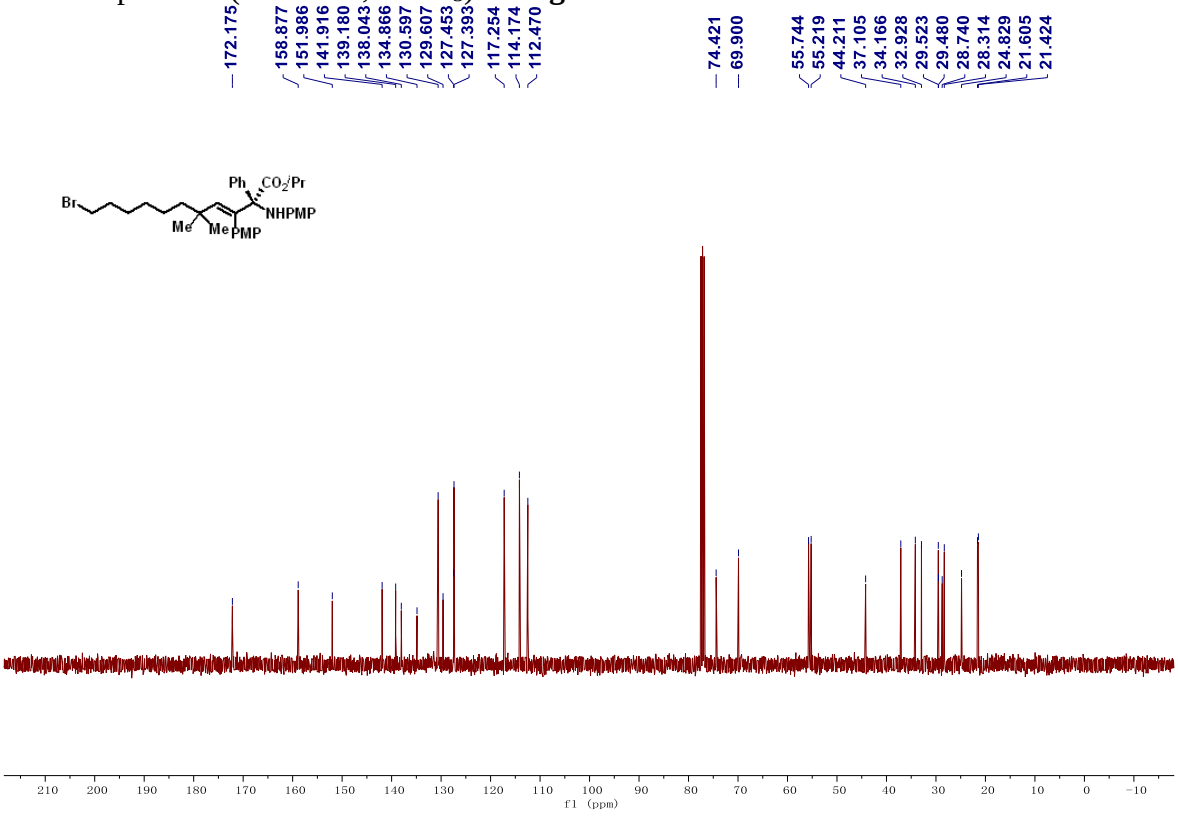
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4af**



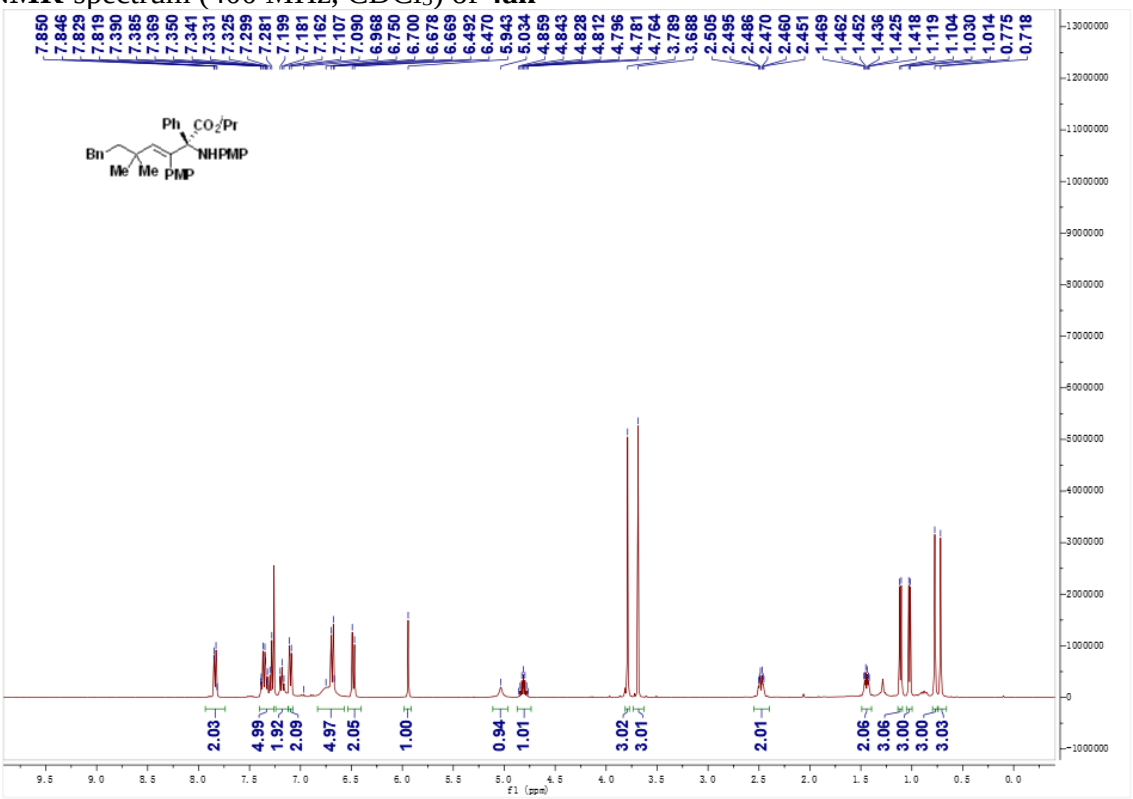
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ag**



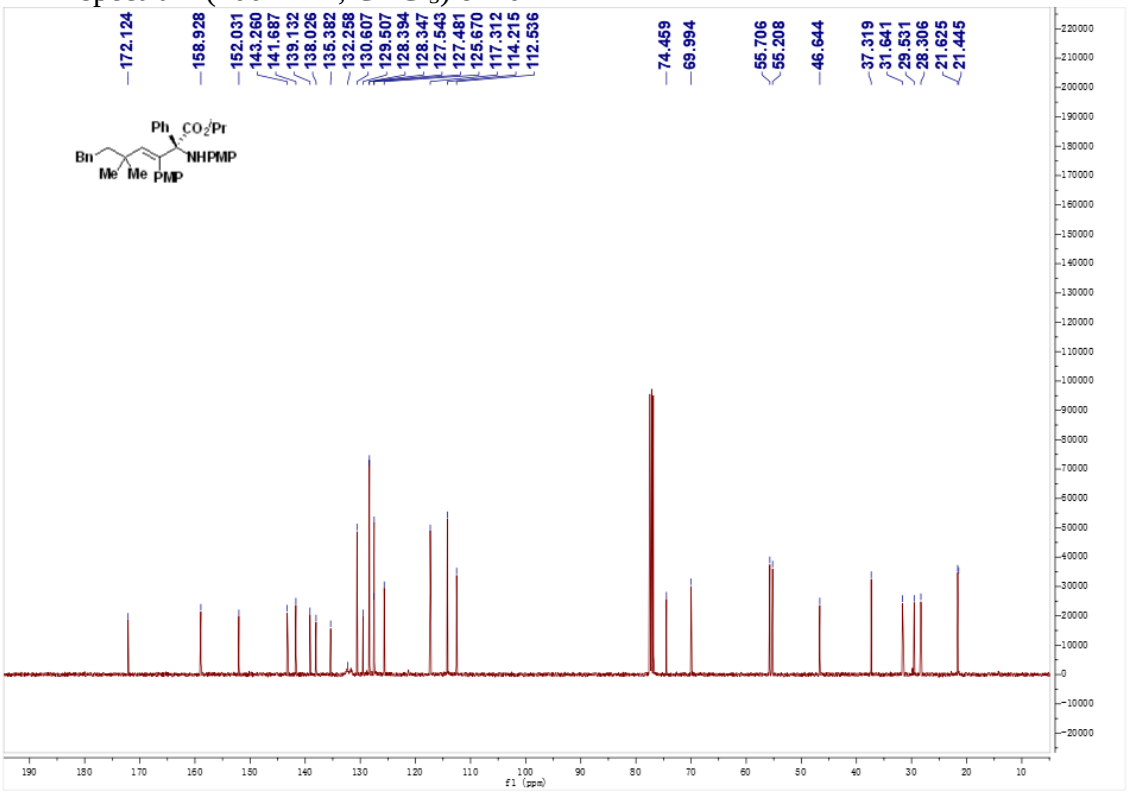
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ag**



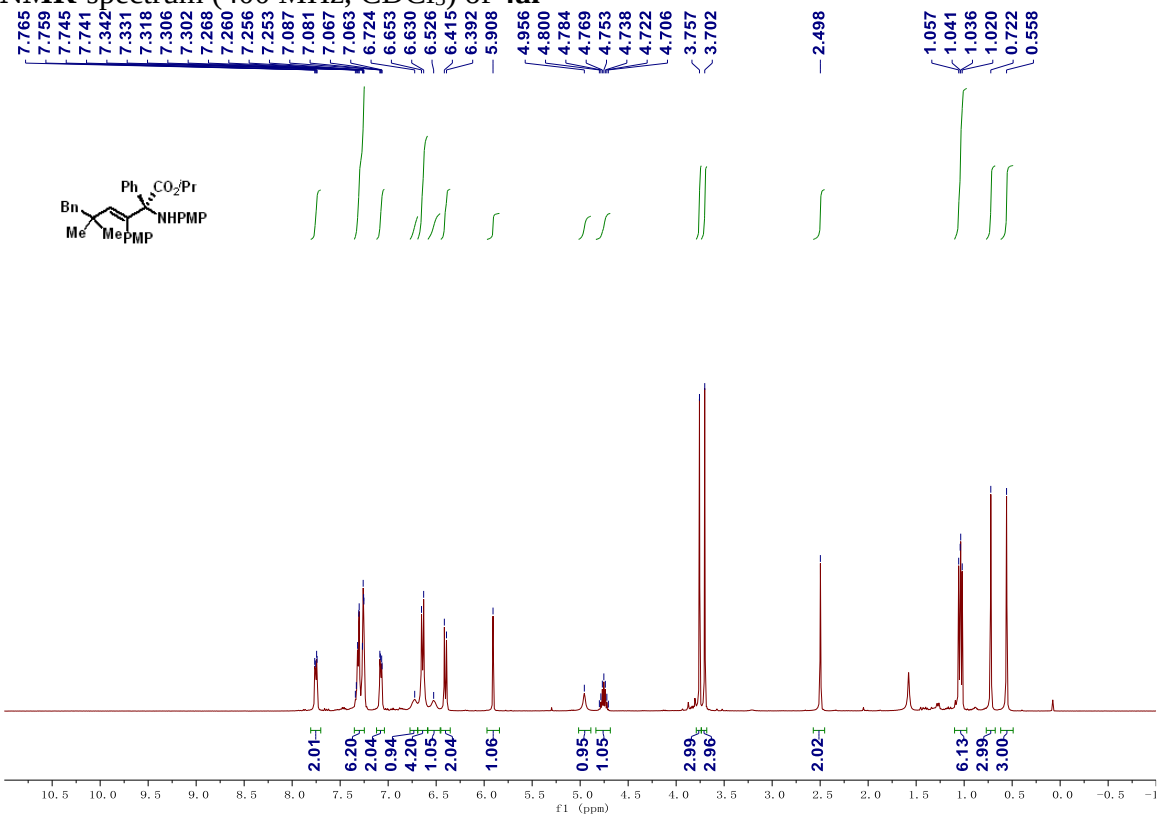
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ah**



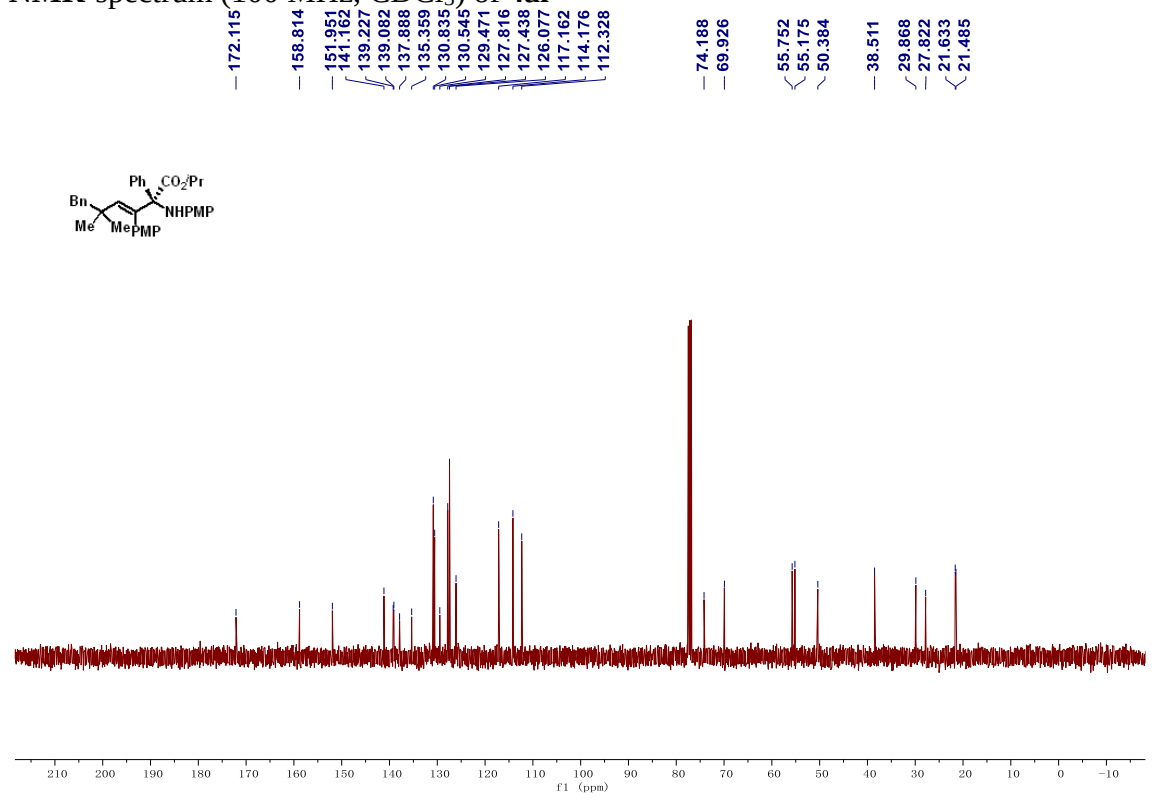
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ah**



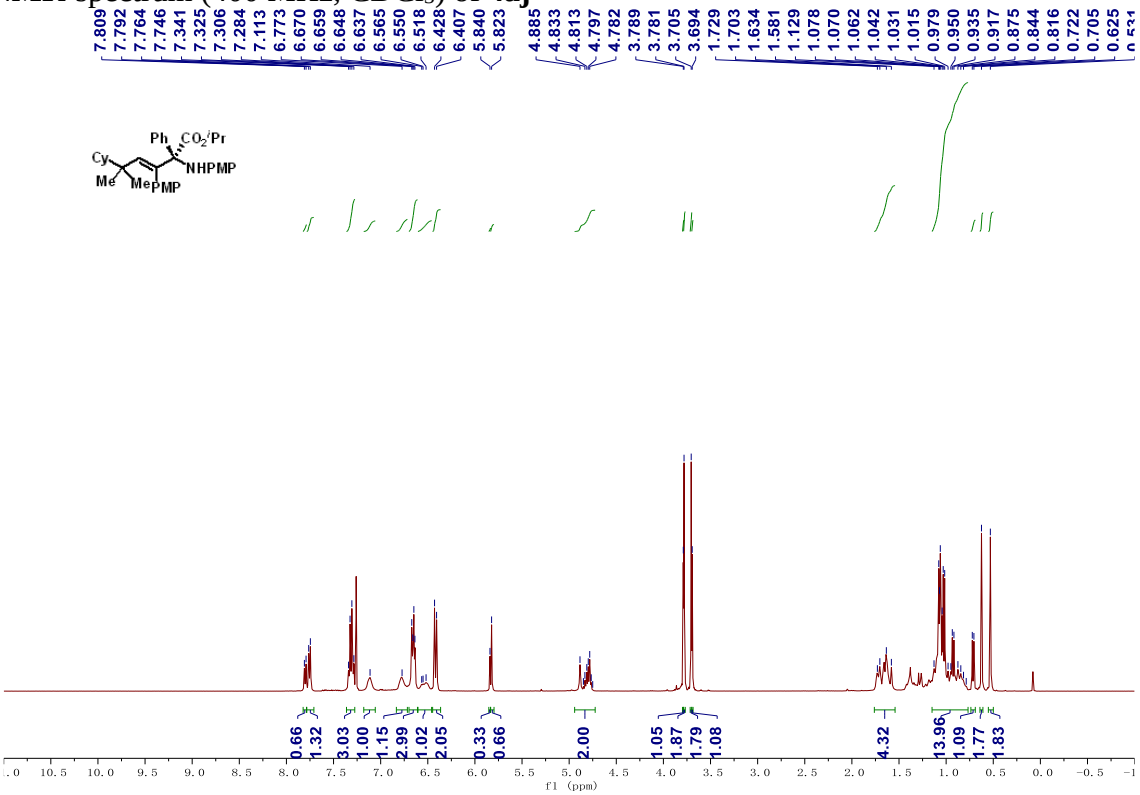
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ai**



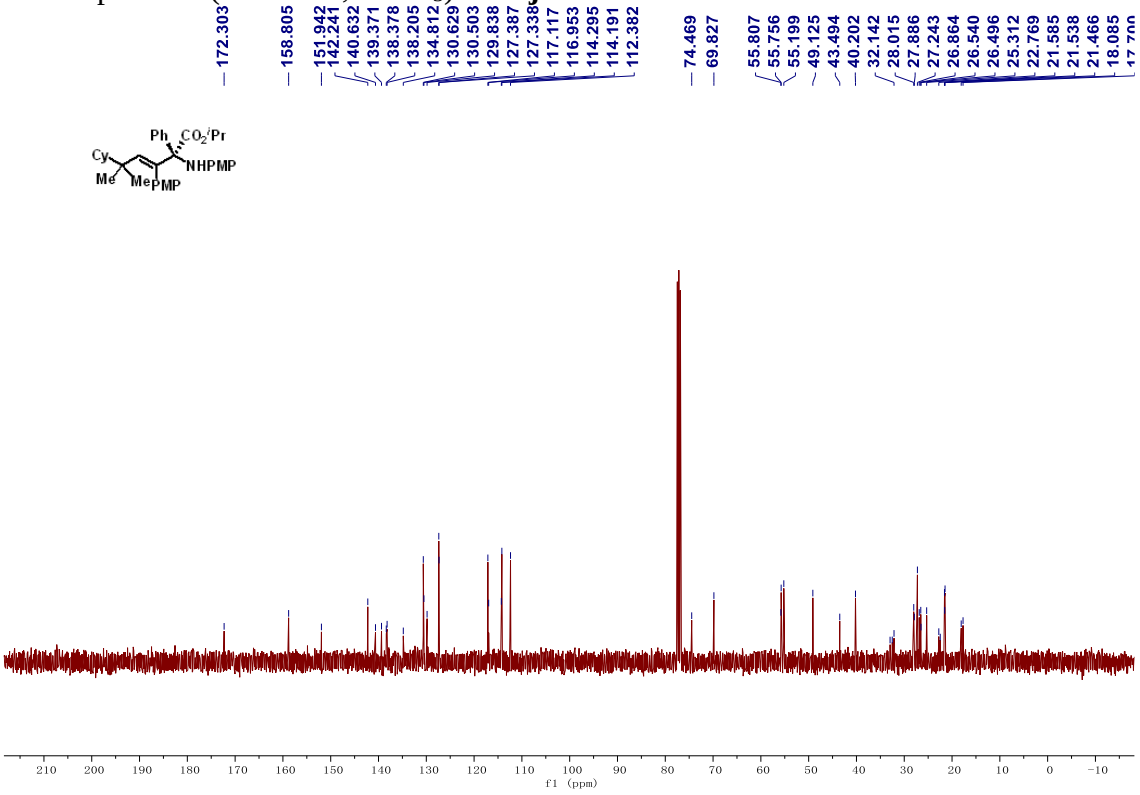
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ai**



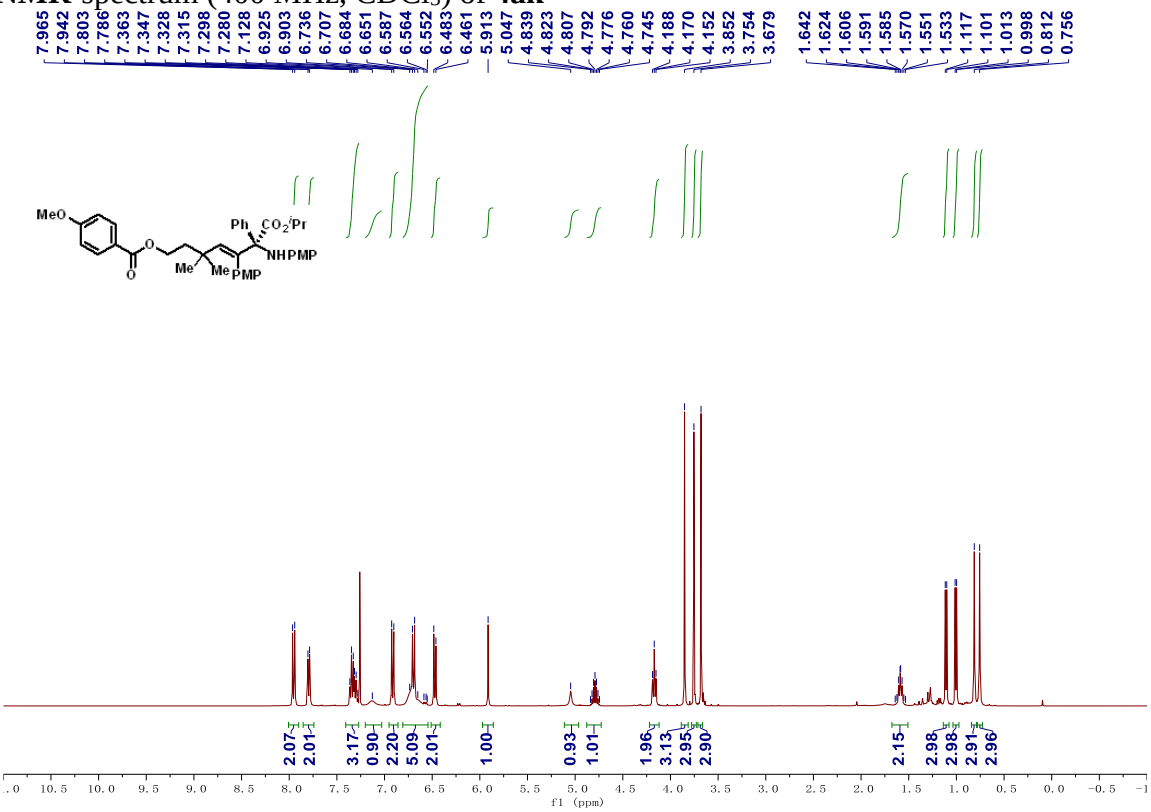
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4aj**



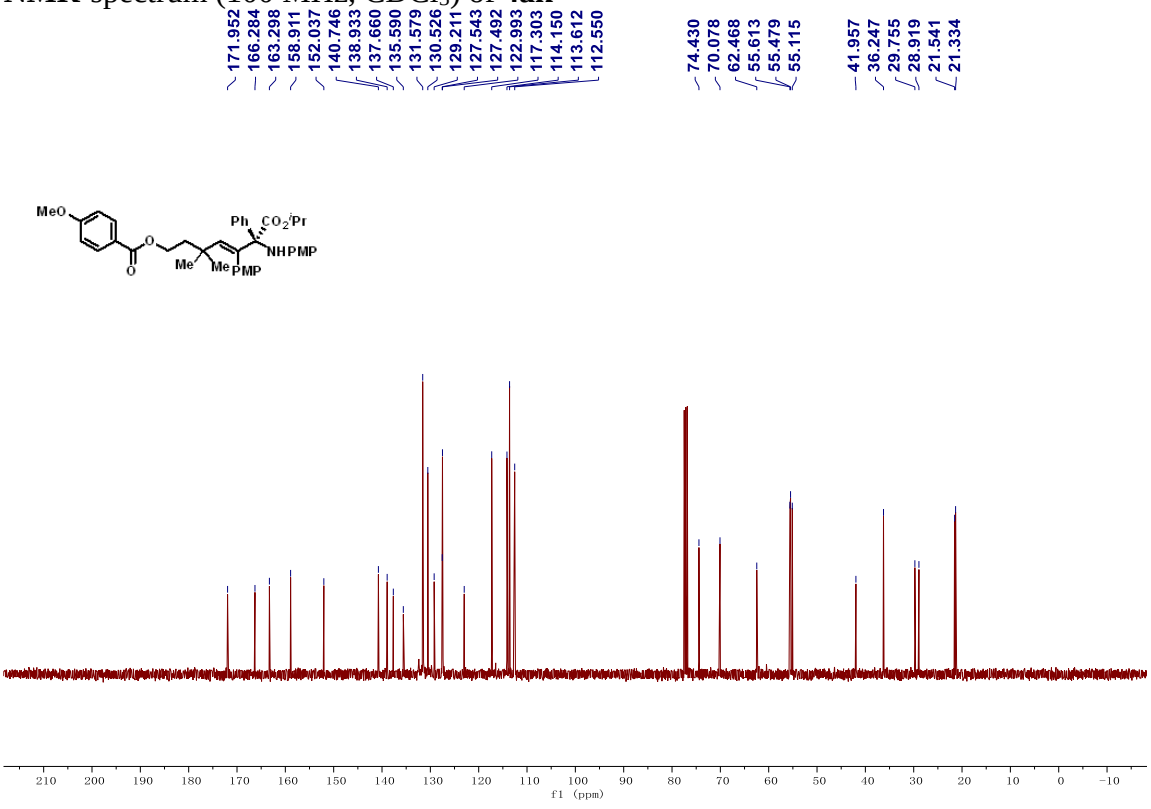
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4aj**



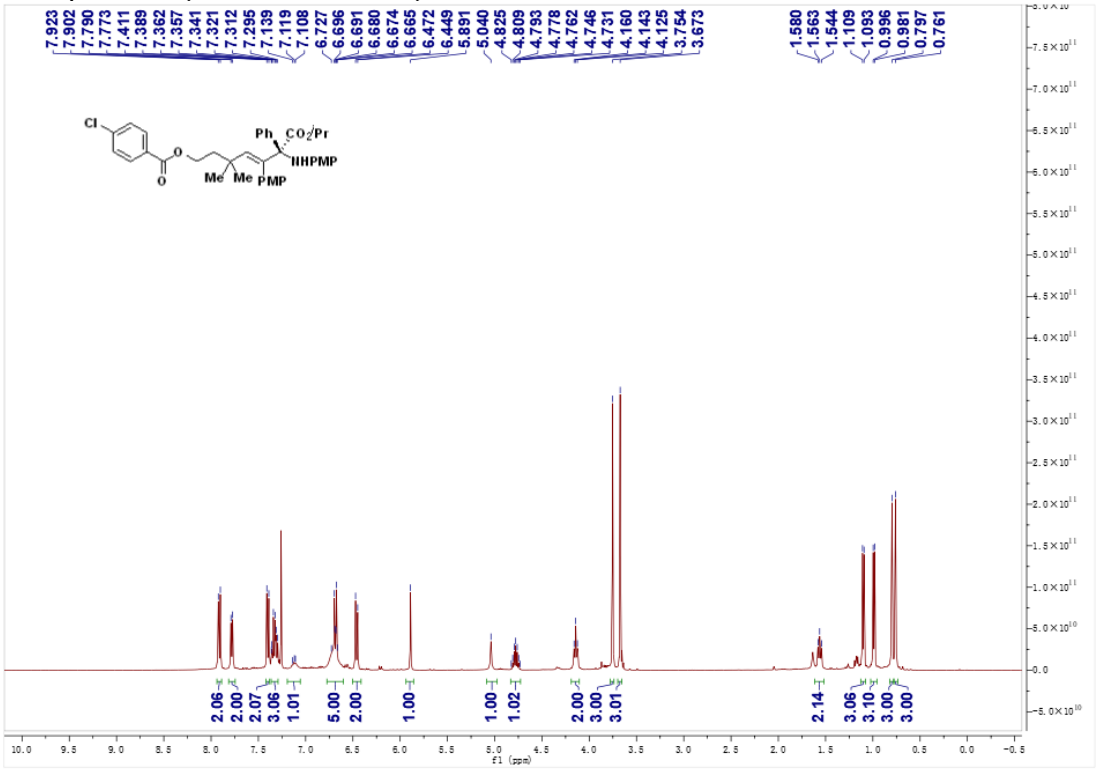
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4ak**



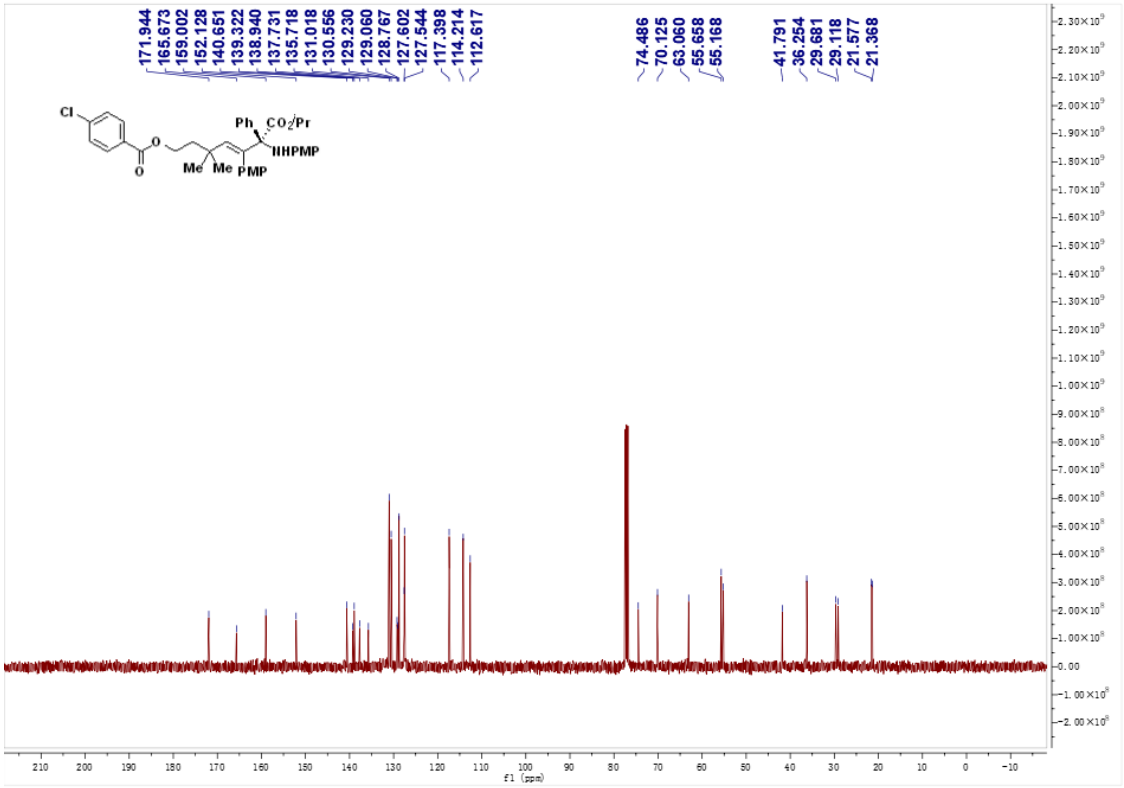
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4ak**



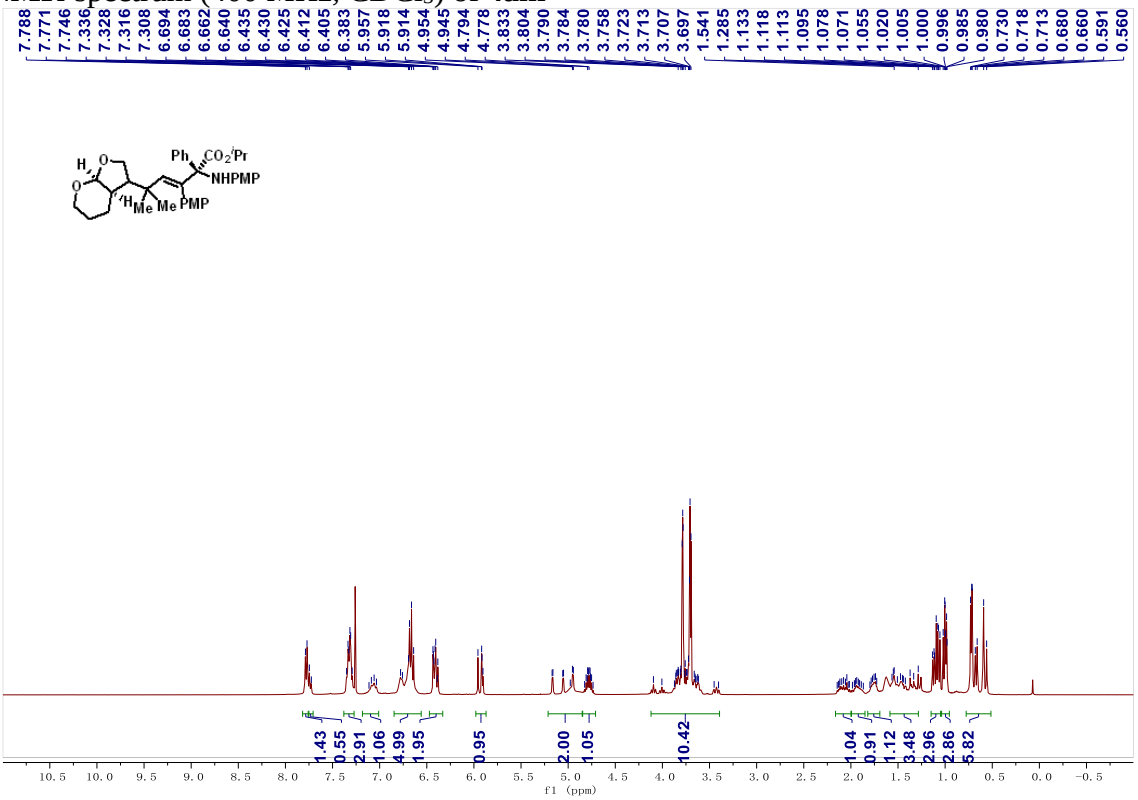
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4al**



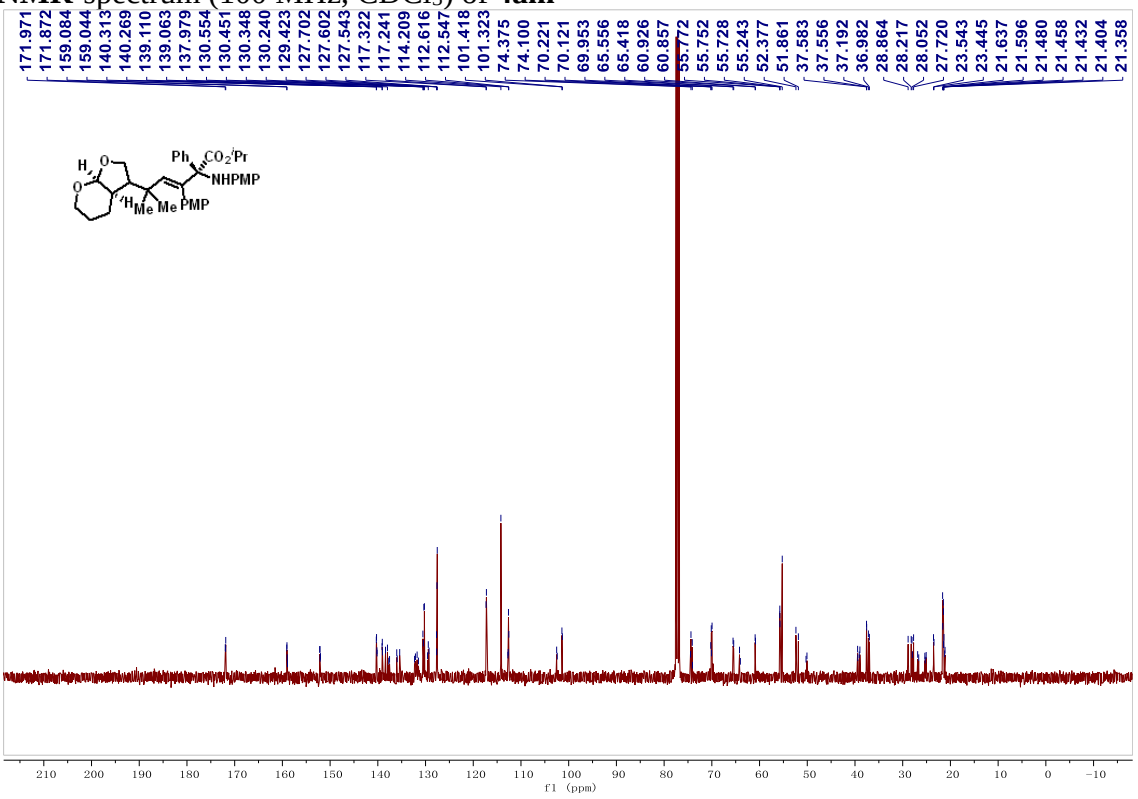
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4al**



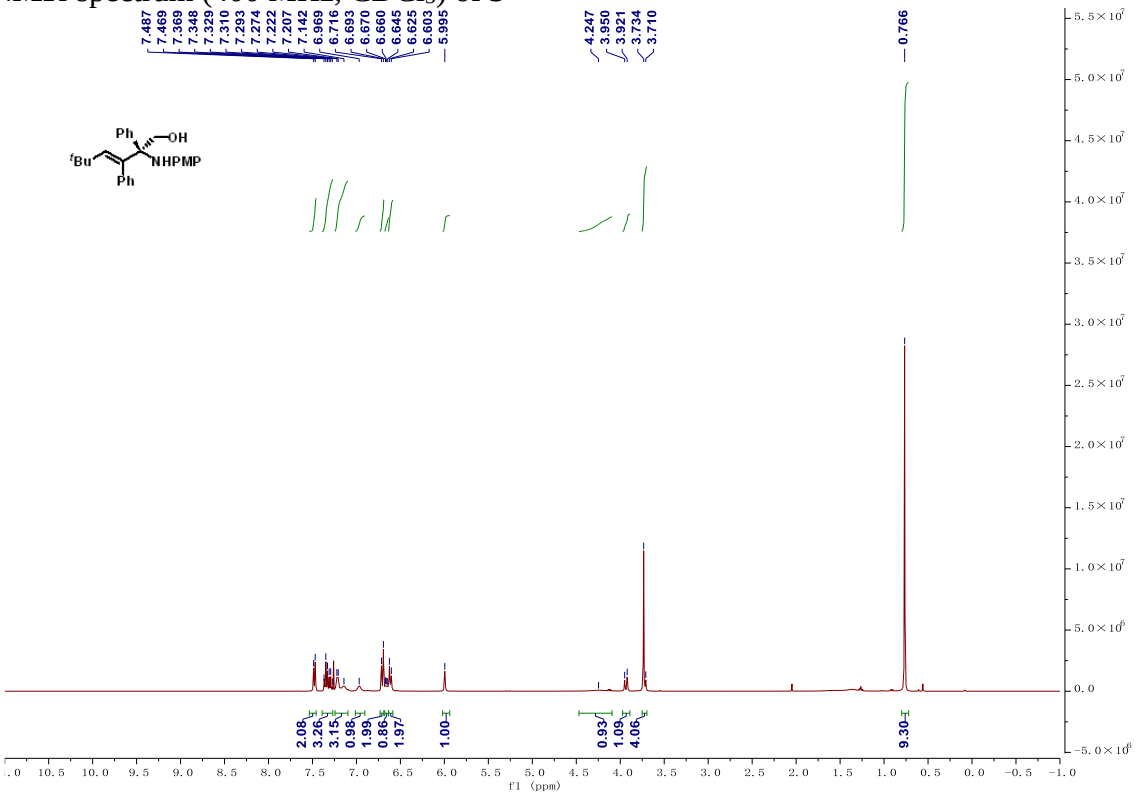
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **4am**



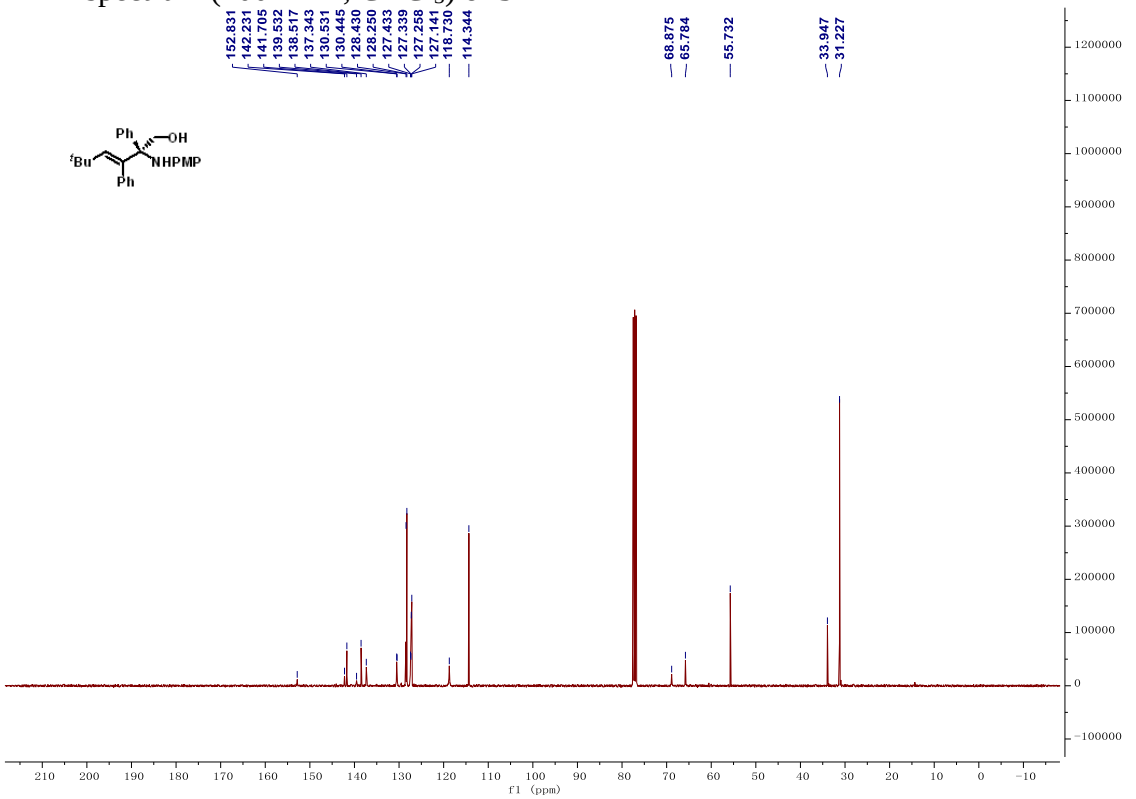
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **4am**



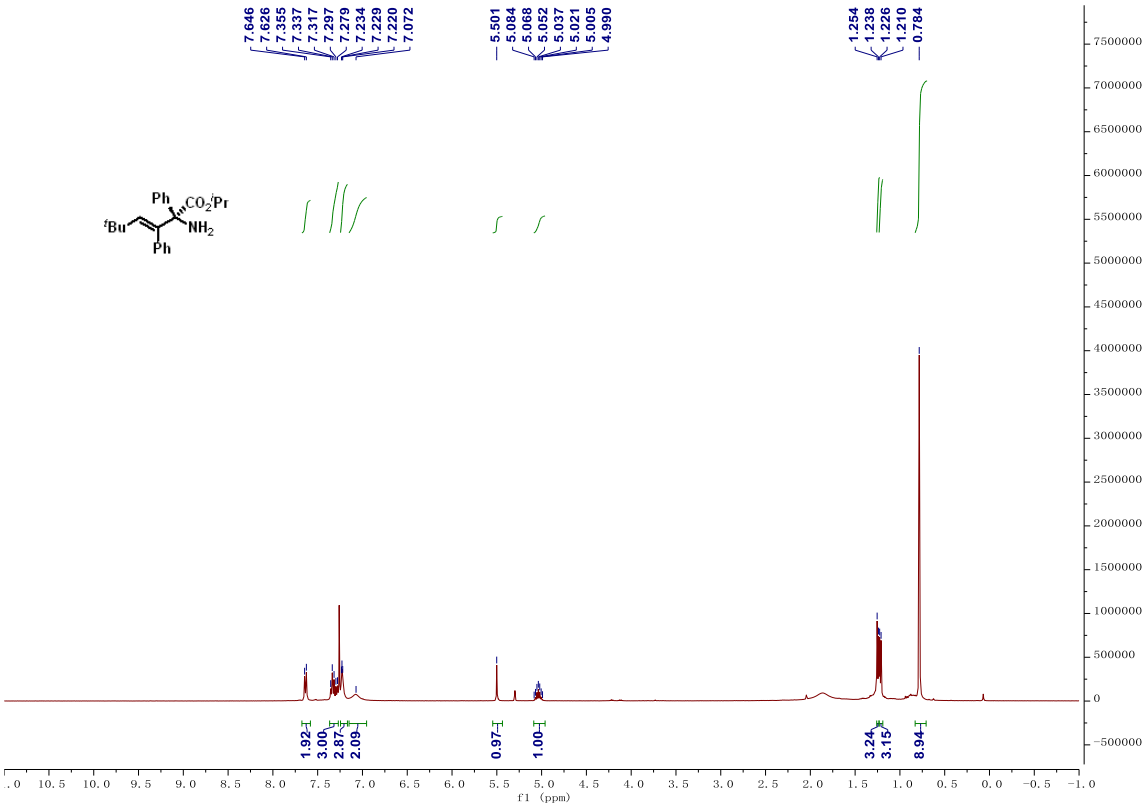
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **5**



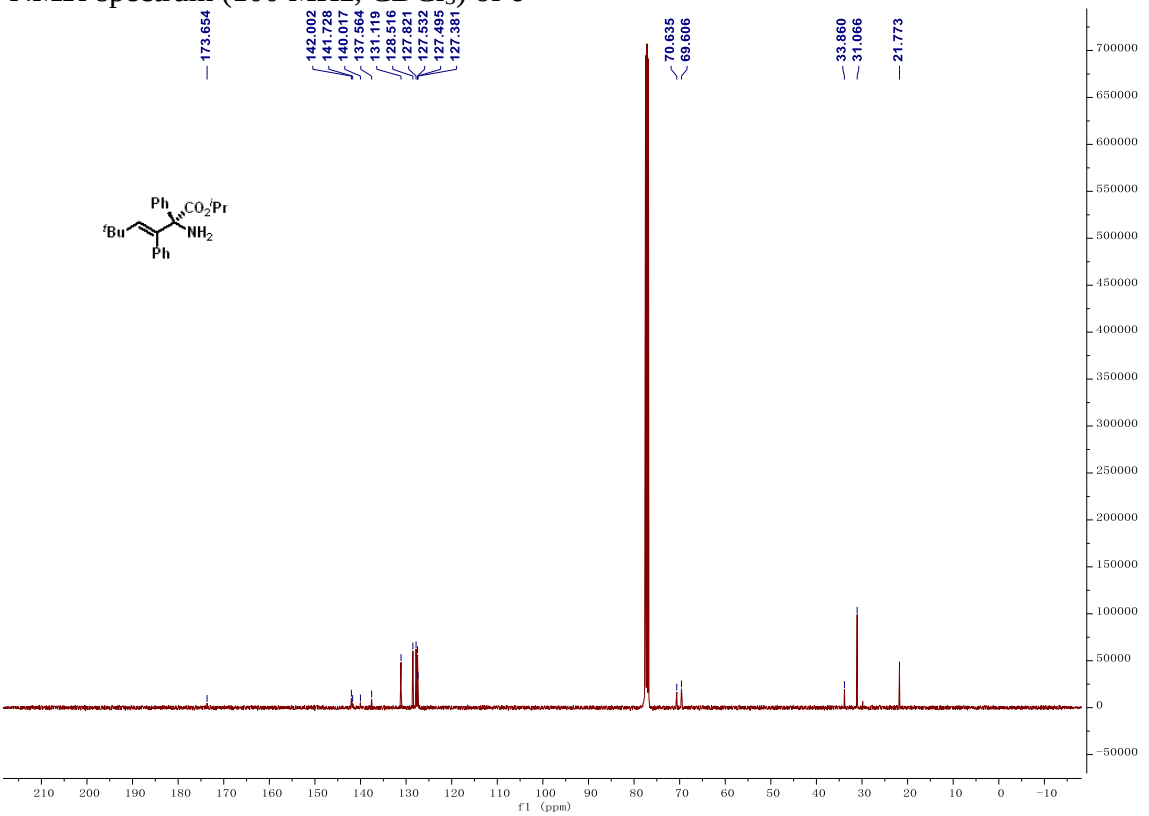
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **5**



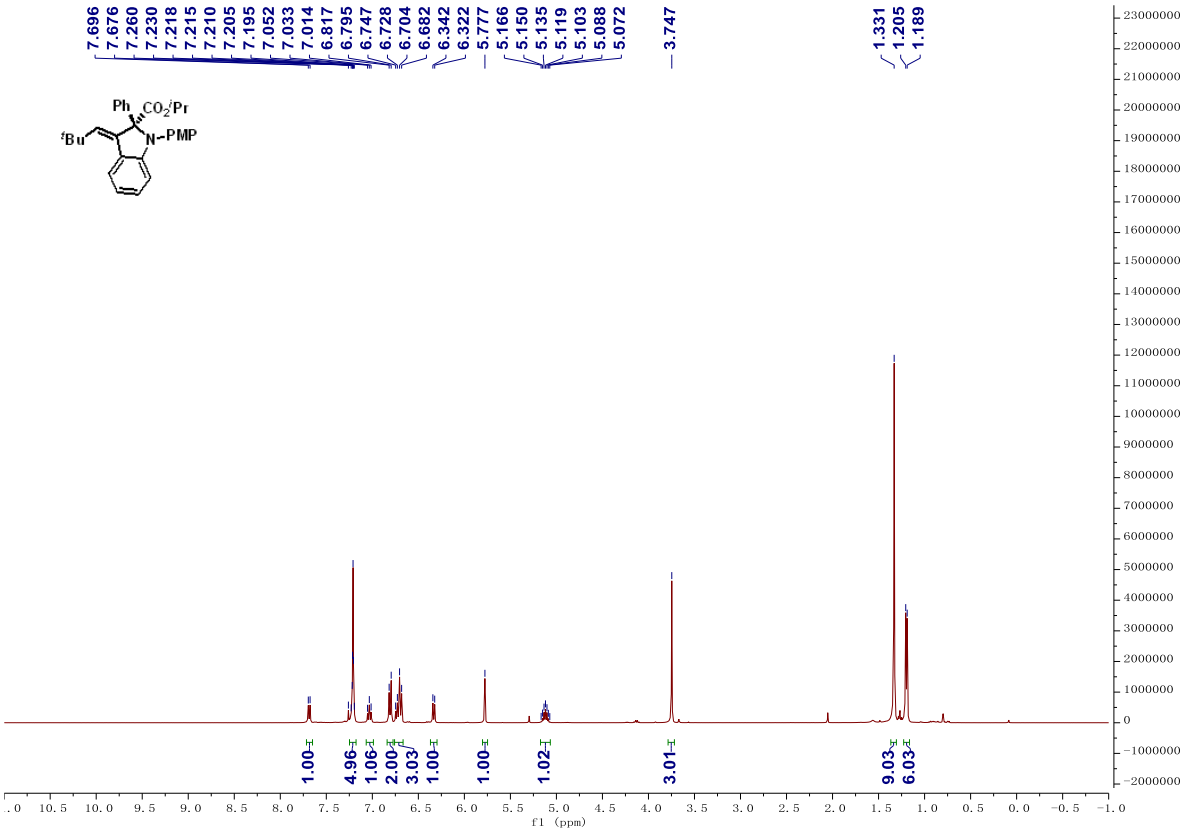
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **6**



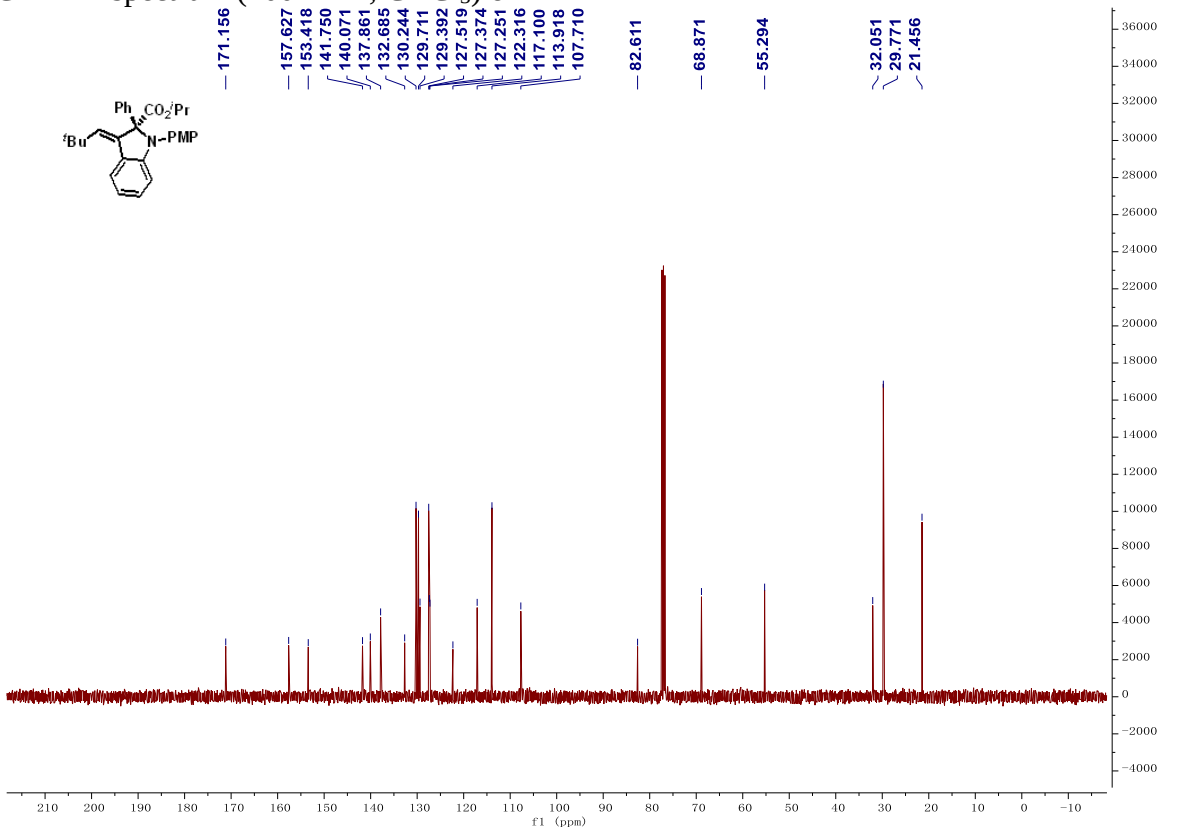
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **6**



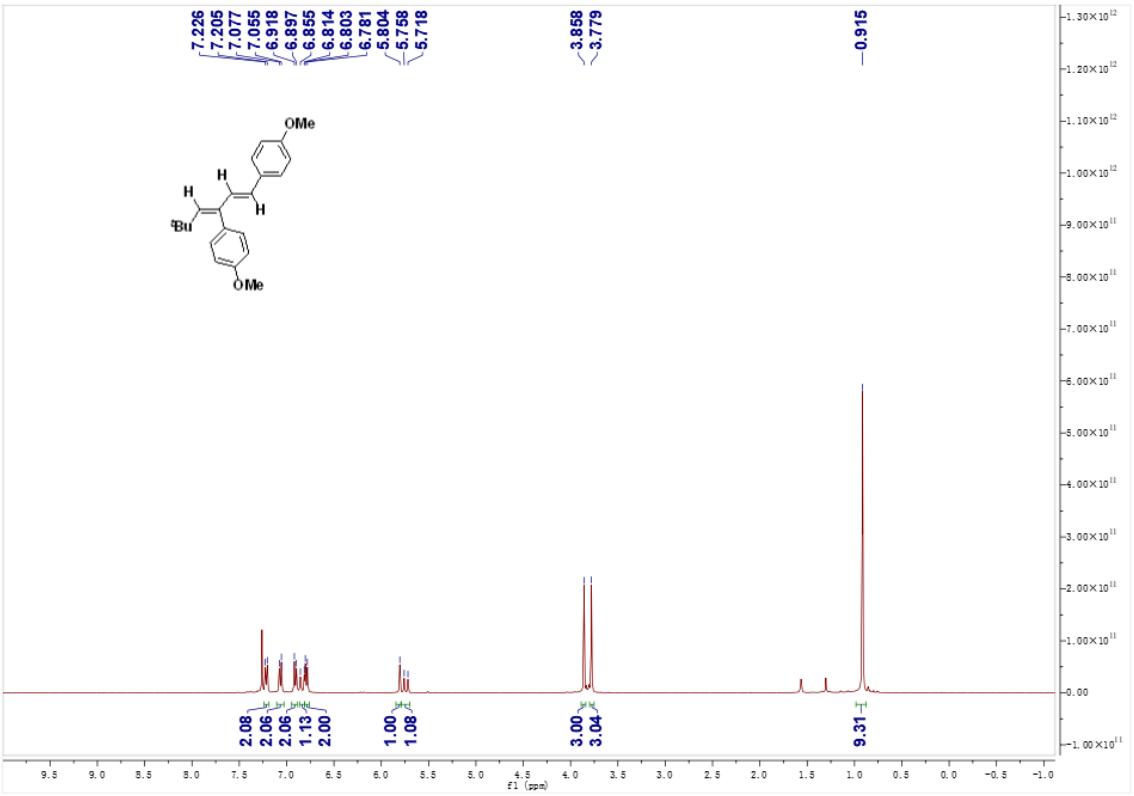
^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **7**



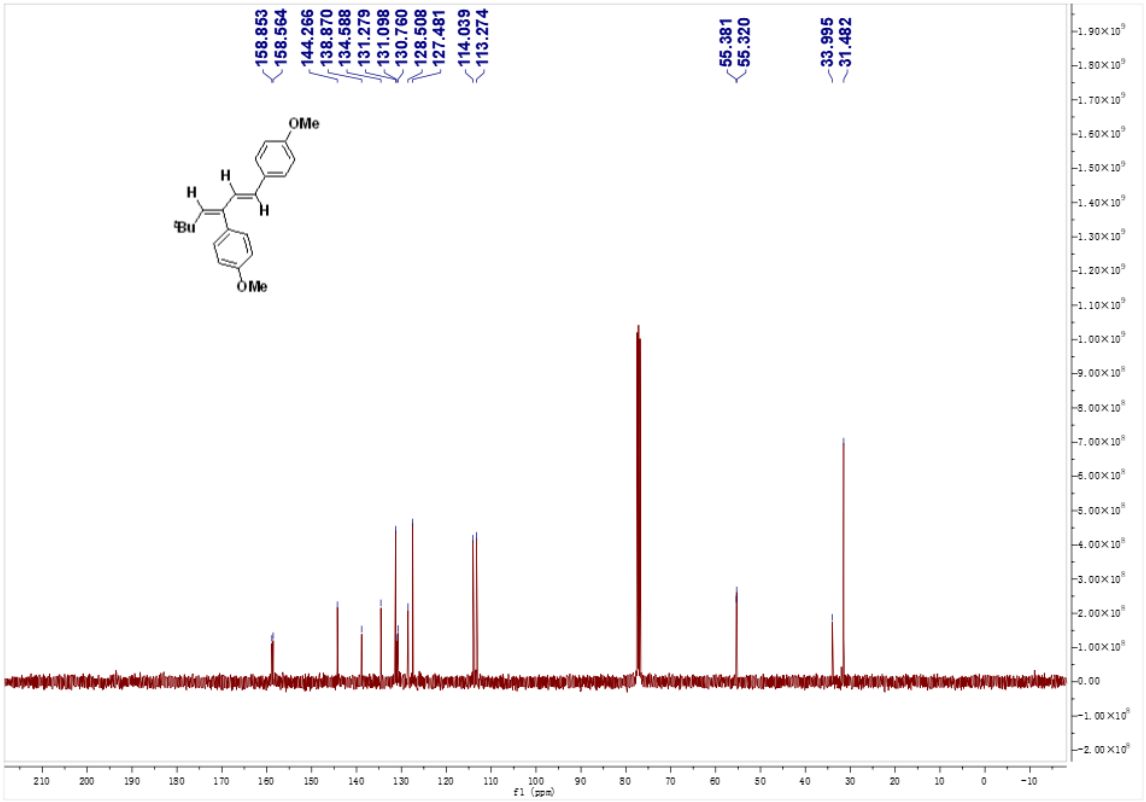
^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **7**



^{1}H NMR-spectrum (400 MHz, $CDCl_3$) of **8**



^{13}C NMR-spectrum (100 MHz, $CDCl_3$) of **8**



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