Supporting Information

Design, Synthesis and Application of Bipyridine-N,N'-dioxides Catalysts in Asymmetric Synthesis of Chiral Cyclopropanes

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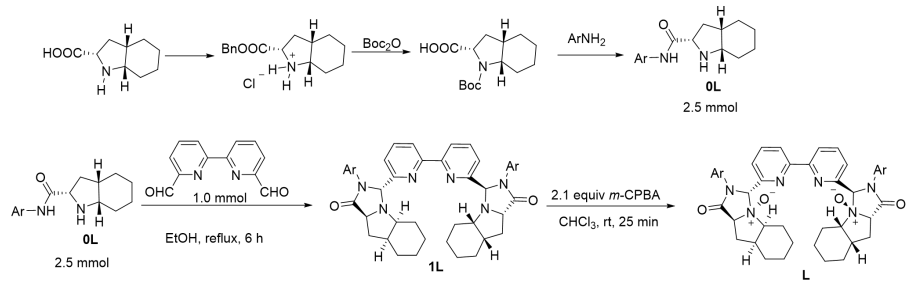
I General Information

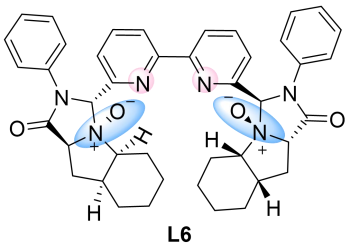
Commercially available materials were used as received, unless otherwise noted, all reactions and manipulations involving air- or moisture-sensitive compounds were performed using standard Schlenk technique. Without special instructions, the heating reactions used are all using an oil bath. Reactions were checked by TLC analysis and plates were visualized with short-wave UV light (254 nm). The ^{1}H, ^{13}C NMR and ^{19}F spectra were obtained in $CDCl_3$ & CD_3OD using a Bruker-BioSpin AVANCE III HD NMR spectrometer at 400 MHz, 101 MHz and 376 MHz respectively. Chemical shifts are reported in parts per million (δ value) calibrated against the residual solvent peak. The determination of e.e. was performed via chiral HPLC analysis using Shimadzu LC-20A HPLC workstation. HPLC analysis of the compounds was done using chiralcel IC column using hexane and isopropanol as eluent, and the column temperature is 40 °C. The Rudolph Autopol V polarimeter was employed to gauge the optical rotation. The melting point was measured by Shanghai Instrument electrooptical SGW X-4A micro melting point instrument. High resolution mass spectra(HRMS) were recorded on Thermo Scientific Q Exactive mass spectrometry equipped with an APCI source. Crystal structure data was collected on a SuperNova, Dual, Cu at zero, Atlas diffractometer. The following abbreviations are used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

II Synthesis of Ligands

1 General procedure L6 for synthesis of hiral Bipyridine-N,N'-dioxides Catalysts.[1-3]



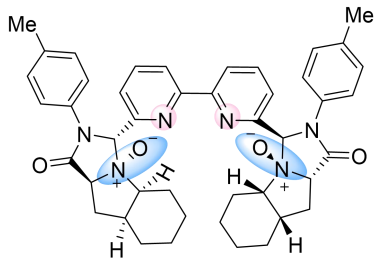
The synthesis of compound amide **0L** was referred to Reference 1. In a sealed tube equipped with a magnetic stirring bar, [2,2'-bipyridine]-6,6'-dicarbaldehyde (1.0 mmol) and **0L** (2.5 mmol, 2.5 equiv.) were added. Then, anhydrous ethanol (6.0 mL) was added and the reaction was heated with stirring at reflux for 6 h. After completion of the reaction, as indicated by TLC, the aftertreatment residue was purified by flash column chromatography to give the intermediate **1L**. Then, the intermediate and m-chloroperoxybenzoic acid (2.1 equiv.) was added to the reaction tube, and an appropriate amount of trichloromethane was added to dissolve the reaction system. After stirring at room temperature for 25 minutes, the reaction liquid was treated and purified by column chromatography (200-300 mesh, EtOAc/MeOH v/v = 20:1-10:1 as the eluent) to obtain a white solid **L**.



L6

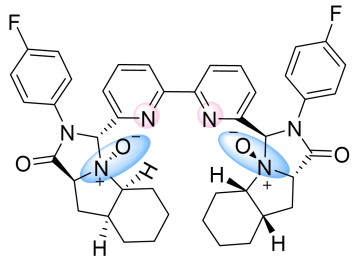
L6: White solid (783.1 mg, 45% yield); >20:1 dr; mp 168.6-170.2 ℃. ^{1}H NMR (400 MHz, CD_3OD) δ = 8.30 (d, *J* = 7.9 Hz, 2H), 7.88 (t, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 3H), 7.17 (t, *J* = 7.9 Hz, 4H), 7.04 (t, *J* = 7.4 Hz, 2H), 6.90 (s, 2H), 4.76 (dd, *J* = 10.3, 6.1 Hz, 2H), 3.89 (dt, *J* = 11.8, 5.4 Hz, 2H), 3.33 (p, *J* = 6.1 Hz, 2H), 2.47 (ddd, *J* = 12.8, 10.2, 8.2 Hz, 2H), 2.29 (td, *J* = 12.8, 6.2 Hz, 3H), 1.83 (d, *J* = 3.5 Hz, 1H), 1.79 (s, 2H), 1.76 – 1.62 (m, 3H), 1.52 – 1.47 (m, 2H), 1.46

– 1.23 (m, 4H), 1.23 – 1.08 (m, 3H). ^{13}C NMR (101 MHz, CD_3OD) δ = 170.96, 156.52, 152.54, 139.19, 136.33, 130.34, 128.30, 127.79, 123.35, 122.79, 85.72, 85.62, 77.30, 37.02, 28.64, 25.86, 25.42, 25.13, 21.11. HRMS (APCI) m/z calcd for $C_{42}H_{45}N_6O_4^+$(M+H)$^+$: 697.3497, found 697.3461.



L7

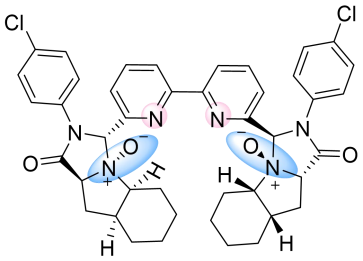
L7: White solid (796.9 mg, 44% yield); >20:1 dr; mp 202.6-204.2 °C. ^{1}H NMR (400 MHz, CD_3OD) δ = 8.32 (d, *J* = 7.9 Hz, 2H), 7.89 (t, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 4H), 6.93 (d, *J* = 8.2 Hz, 4H), 6.86 (s, 2H), 4.76 (dd, *J* = 10.3, 6.1 Hz, 2H), 3.89 (dt, *J* = 11.8, 5.3 Hz, 2H), 3.39 – 3.26 (m, 2H), 2.50 – 2.43 (m, 2H), 2.38 – 2.23 (m, 4H), 2.05 (s, 6H), 1.88 – 1.64 (m, 6H), 1.56 – 1.39 (m, 4H), 1.39 – 1.26 (m, 2H), 1.20 (t, *J* = 12.9 Hz, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ = 170.89, 156.54, 152.58, 139.16, 137.98, 133.71, 130.78, 128.30, 123.44, 122.75, 85.79, 85.69, 77.34, 37.05, 28.60, 25.90, 25.43, 25.15, 21.13, 20.88. HRMS (APCI) m/z calcd for $C_{44}H_{49}N_6O_4^+$(M+H)$^+$: 725.3810, found 725.3798.



L8

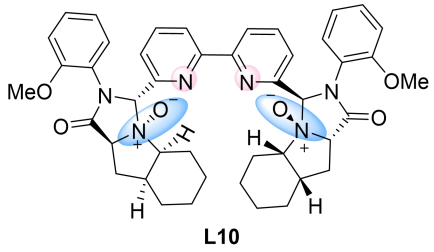
L8: White solid (768.9 mg, 42% yield); >20:1 dr; mp 179.7-181.3 °C. ^{1}H NMR (400 MHz, CD_3OD) δ = 8.32 (d, *J* = 7.9 Hz, 2H), 7.92 (t, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 7.39 (dd, *J* = 8.9, 4.7 Hz, 4H), 6.93 (t, *J* = 8.6 Hz, 4H), 6.89 (s, 2H), 4.77 (dd, *J* = 10.3, 6.1 Hz, 2H), 3.91 (dt, *J* = 12.0, 5.4 Hz, 2H), 3.41 – 3.29 (m, 2H), 2.49 (dt, *J* = 12.6, 9.1 Hz, 2H), 2.40 – 2.24 (m, 4H), 1.87 – 1.68 (m, 6H), 1.57 – 1.45 (m, 4H), 1.35 (d, *J* = 13.3 Hz, 2H), 1.21 (d, *J* = 12.8 Hz, 2H).^{13}C NMR (101 MHz, CD_3OD) δ

=170.98, 163.28, 160.83, 156.53, 152.36, 139.29, 132.44, 128.45, 125.90, 125.81, 122.85, 117.17, 116.94, 85.75, 77.20, 37.05, 28.58, 25.88, 25.41, 25.16, 21.11. ^{19}F NMR (376 MHz, CD_3OD) δ = 116.02. HRMS (APCI) m/z calcd for $C_{42}H_{43}F_2N_6O_4^+(M+H)^+$: 733.3308, found 733.3295.



L9

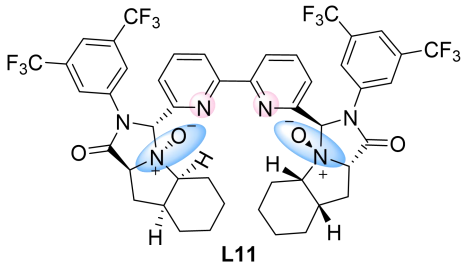
L9: White solid (802.5 mg, 42% yield); >20:1 dr; mp 158.3-159.9 °C. ^{1}H NMR (400 MHz, CD_3OD) δ = 8.29 (d, *J* = 7.9 Hz, 2H), 7.92 (t, *J* = 7.8 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 4H), 7.08 (d, *J* = 8.5 Hz, 4H), 6.90 (s, 2H), 4.74 (dd, *J* = 10.3, 6.1 Hz, 2H), 3.89 (dt, *J* = 11.9, 5.3 Hz, 2H), 3.37 – 3.28 (m, 2H), 2.48 (dt, *J* = 12.6, 9.1 Hz, 2H), 2.30 – 2.25 (m, 4H), 1.84 – 1.69 (m, 6H), 1.49 (d, *J* = 14.4 Hz, 2H), 1.41 (dd, *J* = 12.8, 2.9 Hz, 2H), 1.38 – 1.29 (m, 2H), 1.19 (t, *J* = 12.9 Hz, 2H).^{13}C NMR (101 MHz, CD_3OD) δ =170.91, 156.53, 152.27, 139.28, 135.03, 132.81, 130.29, 128.47, 124.46, 122.92, 85.76, 85.26, 77.18, 37.01, 28.67, 25.85, 25.36, 25.13, 21.11.HRMS (APCI) m/z calcd for $C_{42}H_{43}Cl_2N_6O_4^+(M+H)^+$: 765.2717, found 765.2709.



L10

L10: White solid (716.7 mg, 38% yield); >20:1 dr; mp 184.2-185.8 °C. ^{1}H NMR (400 MHz, CD_3OD) δ = 8.38 (d, *J* = 7.9 Hz, 2H), 7.87 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.17 – 7.12 (m, 2H), 7.07 – 7.02 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.80 (s, 2H), 6.60 (t, *J* = 7.7 Hz, 2H), 3.93 (dt, *J* = 11.9, 5.5 Hz, 2H), 3.80 (s, 6H), 3.39 – 3.31 (m, 2H), 2.63 (d, *J* = 12.6 Hz, 2H), 2.50 – 2.40 (m, 2H), 2.28 (td, *J* = 12.6, 6.5 Hz, 2H), 1.99 – 1.83 (m, 5H), 1.80 – 1.71 (m, 2H), 1.63 – 1.52 (m, 4H), 1.41 – 1.23 (m,

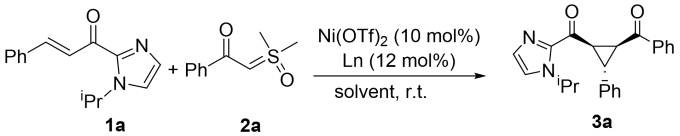
5H).[13]C NMR (101 MHz, CD_3OD) δ =171.51, 156.44, 155.66, 152.48, 139.05, 130.73, 130.03, 128.15, 123.76, 122.52, 121.55, 113.31, 85.91, 85.71, 77.04, 56.14, 37.06, 28.09, 26.04, 25.42, 25.24, 20.99. HRMS (APCI) m/z calcd for $C_{44}H_{49}N_6O_6^+$ $(M+H)^+$: 757.3708, found 757.3692.

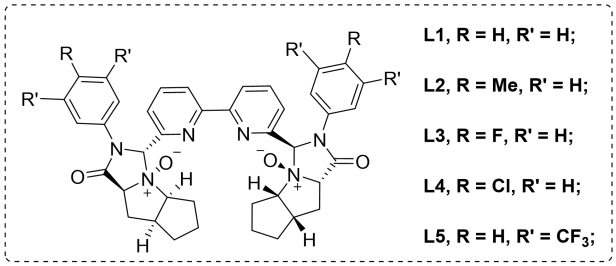


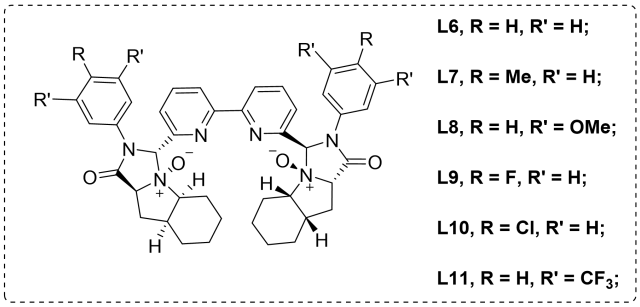
L11

L11: White solid (847.3 mg, 35% yield); >20:1 dr; mp 145.4-147.0 °C. [1]H NMR (400 MHz, CD_3OD) δ = 8.27 (d, *J* = 8.0 Hz, 2H), 8.03 (s, 4H), 7.98 (t, *J* = 7.7 Hz, 2H), 7.72 (d, *J* = 7.6 Hz, 2H), 7.51 (s, 2H), 7.20 (s, 2H), 4.78 (dd, *J* = 10.3, 6.2 Hz, 2H), 3.94 (dt, *J* = 12.0, 5.4 Hz, 2H), 3.41 – 3.32 (m, 2H), 2.54 (dt, *J* = 12.5, 8.9 Hz, 2H), 2.40 – 2.28 (m, 4H), 1.88 – 1.71 (m, 6H), 1.53 (d, *J* = 13.6 Hz, 2H), 1.47 – 1.35 (m, 4H), 1.23 (t, *J* = 12.8 Hz, 2H). [13]C NMR (101 MHz, CD_3OD) δ =171.51, 156.46, 151.52, 139.49, 138.31, 133.70, 133.37, 128.84, 125.40, 122.95, 122.69, 122.60, 120.32, 85.97, 84.66, 77.08, 37.07, 28.71, 25.82, 25.21, 25.12, 21.03. [19]F NMR (376 MHz, CD_3OD) δ = 64.7. HRMS (APCI) m/z calcd for $C_{46}H_{41}F_{12}N_6O_4^+$$(M+H)^+$: 969.2992, found 969.2972.

III Optimization of Reaction Conditions[a]







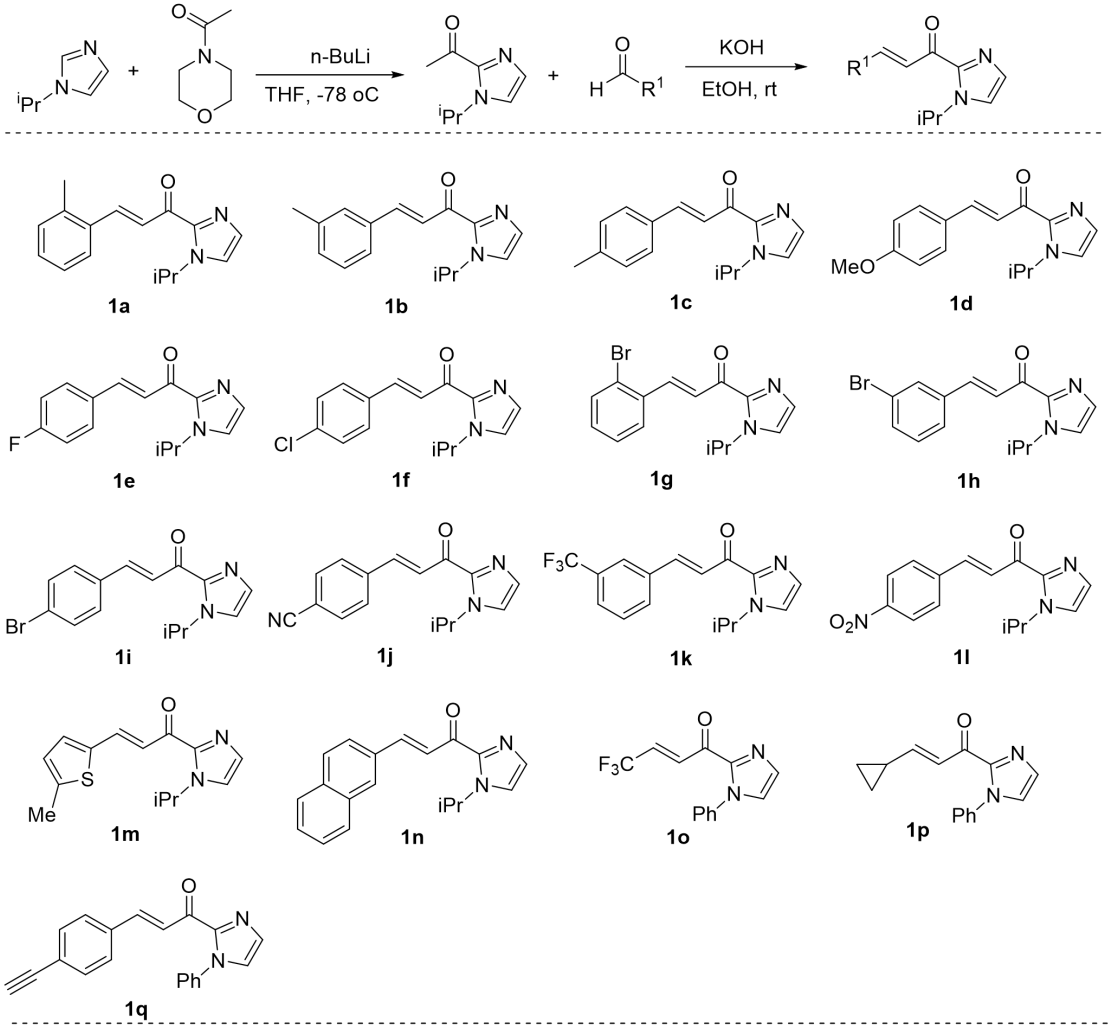
Entry	Ligand	Solvent	Yield(%)[b]	Ee(%)[c]	Dr[d]
1	L1	DCM	88	52	>20:1
2	L2	DCM	90	24	>20:1
3	L3	DCM	91	48	>20:1
4	L4	DCM	85	40	>20:1
5	L5	DCM	84	6	>20:1
6	L6	DCM	95	86	>20:1
7	L7	DCM	90	89	>20:1
8	L8	DCM	90	57	>20:1
9	L9	DCM	92	83	>20:1
10	L10	DCM	93	86	>20:1
11	L11	DCM	94	33	>20:1
12	L7	DCE	94	82	>20:1
13	L7	$CHCl_3$	92	52	>20:1
14	L7	THF	95	85	>20:1
15	L7	CH_3CN	96	88	>20:1
16	L7	Acetone	96	91	>20:1
17	L7	CB	94	33	>20:1
18	L7	MeOH	80	10	>20:1
19	L7	EtOH	86	43	>20:1
20	L7	Butanone	94	90	>20:1
21	L7	NMP	-	-	-
22[d]	L7	Acetone	87	89	>20:1
23[e]	L7	Acetone	79	91	>20:1

24[f]	L7	Acetone	86	85	>20:1

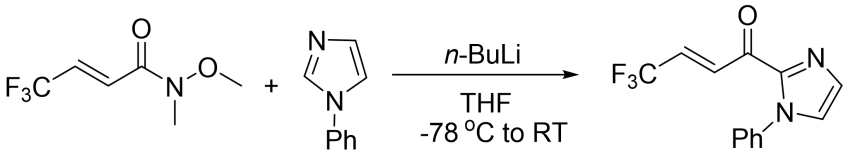
[a]Reaction conditions: $Ni(OTf)_2$ (10 mol%), **L1-L11** (12 mol%), **1a** (0.10 mmol), and **2a** (0.12 mmol) in 2.0 mL of Acetone at 25 ℃. [b]Isolated yield after flash chromatography. [c]Determined by HPLC analysis [d]Determined by ^1H NMR analysis. [d]$Ni(ClO_4)_2·6H_2O$ (10 mol%). [e]$Cu(OTf)_2$ (10 mol%). [f]$Zn(OTf)_2$ (10 mol%). [d]$Ni(ClO_4)_2·6H_2O$ (10 mol%). [e]$Cu(OTf)_2$ (10 mol%). [f]$Zn(OTf)_2$ (10 mol%).

IV Synthesis of Substrates

4-1 Synthesis of Compounds 1(α,β-unsaturated 2-acylimidazoles)[4]

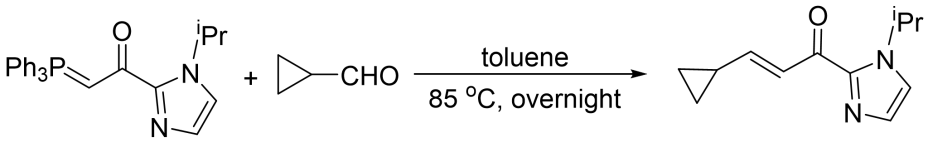


α,β-unsaturated 2-acylimidazoles **1a-1n, 1q** were prepared according to a reported procedure. Accordingly, 2-acetyl-imidazole (10.0 mmol, 1.0 equiv.) and EtOH (20 mL) were added to a 50 mL a round-bottom flask followed by the aromatic aldehyde (10.5 mmol, 1.05 equiv.) and NaOH (11.0 mmol, 1.1 equiv.). The solution was stirred until the substrates consumption (detected by TLC). Saturated NaCl (30 mL) and H_2O (10 mL) were added and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by a flash column chromatography on silica gel to give the desired products.



1o

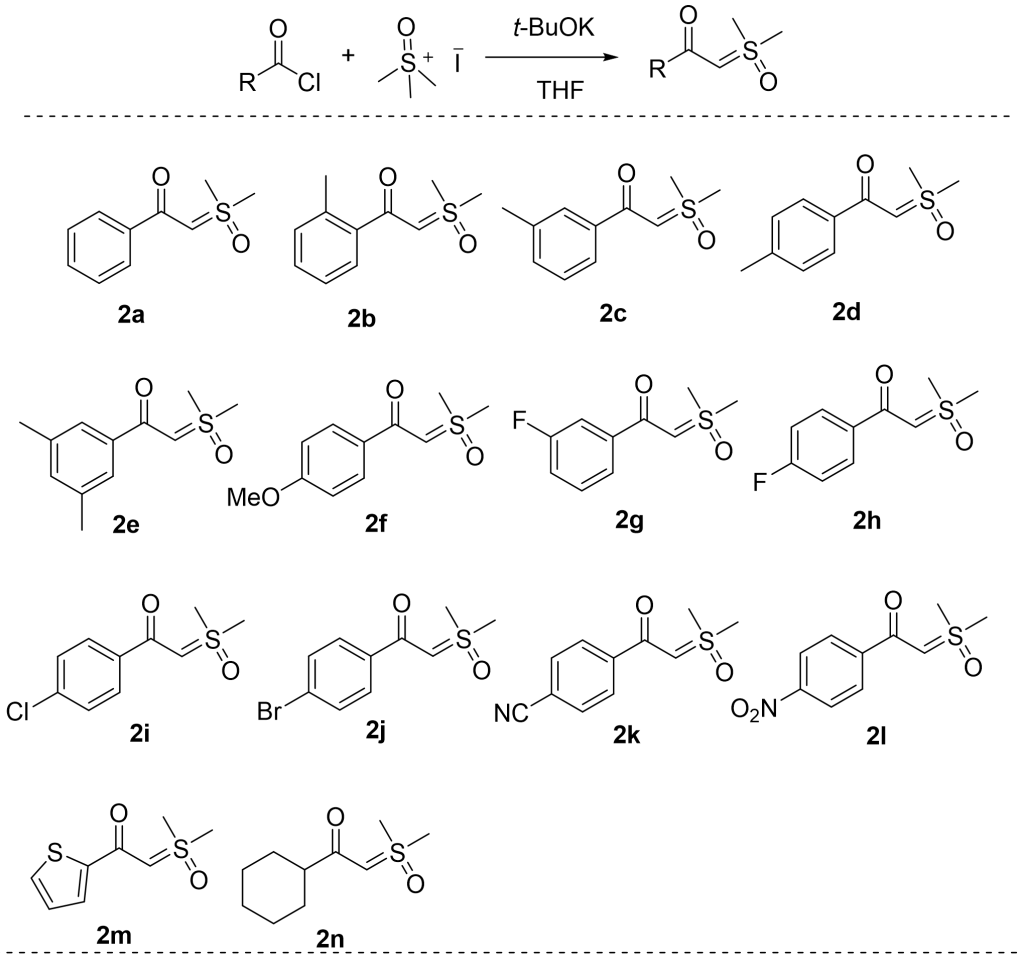
Following the general procedure[6], to a suitable vacuum flame-dried flask under N_2 was added N-benzylimidazole (1.44 g, 0.01 mol, 1.0 equiv.) to 30 mL THF. The flask was cooled to -78 °C for 20-30 min before a titrated 10 mL *n*-butyllithium (2.5 M in hexanes) (1.5 equiv.) was added in drops to the flask. The reaction was stirred at -78 °C for about 5 minutes. The bath was removed and the reaction was allowed to warm to r.t. over a 30 minutes period. The reaction was cooled back down to -78 °C for 20 minutes before the corresponding Weinreb amide (1.0 equiv.) was added to the solution in THF. The reaction was stirred at -78 °C for 2 h. The reaction was quenched with water and then extracted with EtOAc for three times. The organic layer was washed with brine, and dried with Na_2SO_4. The drying agent was concentrated and directly purified by silica gel column chromatography (with ethyl acetate-petroleum ether as the eluent) to afford the desired products **1o**.



1p

Following the general procedure[5], to a solution of Wittig reagent (1.03 g, 2.5 mmol) in toluene (12.6 mL) at room temperature was added cyclopropanecarboxaldehyde (350.5 mg, 5.0 mmol). The reaction was stirred at 85 °C overnight. After the solvent was removed in vacuo, the residue was purified by flash chromatography on silica gel (EtOAc/hexane = 1/5 to 1/3) to produce the unsaturated alkenes as a mixture of *E*:*Z* isomers. Then, to a solution of purified alkene in CH_2Cl_2 (0.2 M) at room temperaturewas added DMAP (30.5 mg, 0.25 mmol). The reaction was sealed and stored at 4 °C (fridge) for 24 hours. After isomerization, the solution was passed through a short silica columnto afford **1p** as colorless oil (306.4 mg, yield: 60%).

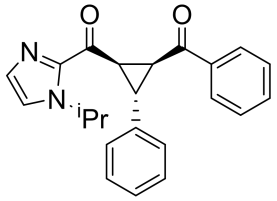
4-2 synthesis of Compounds 2 (sulfoxonium ylides).[7]



All the sulfoxonium ylides are known and the synthesis method is as follows. Potassium tert-butoxide (27.2 mmol, 3 g, 4.0 equiv.) and anhydrous THF (27.0 mL) were added to a 100 mL Schlenk tube under argon atmosphere. Then, trimethylsulfoxonium iodide (20.4 mmol, 4.48 g, 3.0 equiv.) was added in one portion. The suspension was heated at reflux(oil bath) for 3 hours. After that, the mixture was cooled to 0 °C, followed by slow addition of the acyl chloride (6.8 mmol, 1.0 equiv.). The mixture was stirred overnight at room temperature. The solvent was removed on a rotary evaporator. Then 80 mL H_2O was added and the mixture was extracted with DCM (8 ×20 mL). The organic phase was combined and dried over Na_2SO_4. The crude product was concentrated on a rotary evaporator and purified by flash column chromatography on silica gel (200-300 mesh, MeOH/EA v/v = 1:15 - 1:10) to afford the desired product **(2a-2n)**.

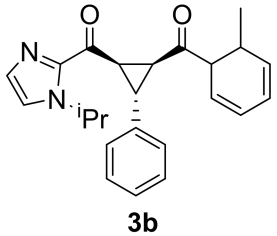
V Asymmetric Cycloaddition Reactions

General Procedure: fitted with a magnetic stirring bar, was charged with $Ni(OTf)_2$ (3.6 mg, 10 mol%) in an Ar setting, followed by the addition of **L7** (8.0 mg,12 mol%) and Acetone (1.0 mL, 0.1 M), with the mixture being stirred at room temperature for an hour. Following this, **1** (0.10 mmol, 1.0 equiv.) and **2** (0.12 mmol, 1.2 equiv.) were added.The reaction mixture was stirred at 25 °C for indicated time (monitored by TLC) under argon. the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford chiral products.



3a

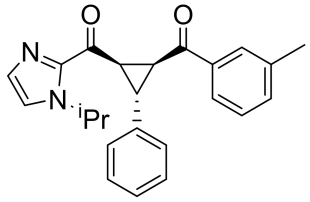
(1*R*,2*S*,3*S*)-2-benzoyl-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3a). pale yellow oil (34.4 mg, 96% yield). HPLC: 91% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 7.64 min, tr (minor) = 6.87 min. $[\alpha]_D^{26}$ = +7.0 (c = 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.29 (t, *J* = 7.3 Hz, 2H), 7.24 (dd, *J* = 10.4, 1.3 Hz, 2H), 7.22 – 7.18 (m, 4H), 7.17 (d, *J* = 1.1 Hz, 1H), 7.16 – 7.09 (m, 3H), 5.52 (p, *J* = 6.7 Hz, 1H), 3.82 (dd, *J* = 9.7, 6.3 Hz, 1H), 3.38 (t, *J* = 6.3 Hz, 1H), 2.84 (d, *J* = 2.5 Hz, 1H), 1.42 (dd, *J* = 6.8, 1.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 204.24, 186.23, 142.70, 141.01, 138.53, 129.91, 128.64, 128.44, 128.32, 126.97, 126.57, 126.03, 49.32, 45.22, 40.33, 37.33, 30.70, 29.65, 23.69, 23.52. HRMS (APCI) m/z calcd for $C_{23}H_{23}N_2O_2^+$ $(M+H)^+$: 359.1766, found 359.1761.



3b

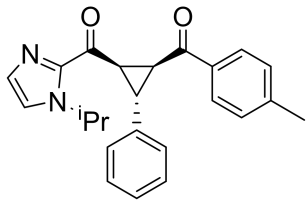
(1*R*,2*S*,3*S*)-2-(6-methylcyclohexa-2,4-diene-1-carbonyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3b). yellow oil (35.7 mg, 95% yield). HPLC:

92% ee (Chiralpak IA column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 7.84 min, tr (minor) = 5.7 min. $[\alpha]_D^{26}$ = +6.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.48 (d, *J* = 7.1 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 8.9 Hz, 1H), 7.21 – 7.15 (m, 3H), 7.00 (s, 2H), 5.83 (s, 1H), 5.15 – 5.09 (m, 1H), 5.01 (p, *J* = 6.7 Hz, 1H), 4.85 (s, 1H), 3.25 (d, *J* = 15.0 Hz, 1H), 3.07 (s, 1H), 2.61 (ddd, *J* = 15.3, 9.5, 5.3 Hz, 1H), 2.39 (s, 1H), 1.31 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 197.58, 185.99, 142.91, 138.85, 138.75, 137.70, 131.86, 131.52, 129.88, 129.66, 128.74, 127.02, 126.70, 125.62, 121.27, 47.93, 42.14, 38.88, 32.38, 23.63, 23.51, 21.16. HRMS (APCI) m/z calcd for $C_{24}H_{27}N_2O_2^+$ $(M+H)^+$: 375.2023, found 375.2017.



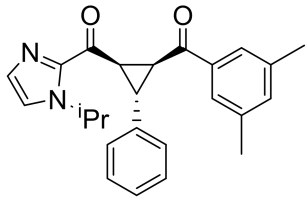
3c

(1*R*,2*S*,3*S*)-2-(3-methylbenzoyl)-3-phenylcyclopropyl-(isopropyl-1H-imidazol-2-yl)methanone (**3c**).yellow oil (35.6 mg, 95 % yield). HPLC: 83% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.85 min, tr (minor) = 7.38 min. $[\alpha]_D^{26}$ = +9.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 – 7.78 (m, 2H), 7.38 – 7.31 (m, 4H), 7.27 – 7.22 (m, 3H), 7.20 (dd, *J* = 13.8, 1.1 Hz, 2H), 5.41 (p, *J* = 6.7 Hz, 1H), 4.19 (dd, *J* = 9.7, 6.1 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 1H), 3.30 (dd, *J* = 9.7, 6.6 Hz, 1H), 2.33 (s, 3H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.21 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.29, 186.13, 143.00, 138.81, 138.39, 137.20, 133.93, 129.94, 129.16, 128.76, 127.06, 126.87, 125.89, 121.31, 49.29, 38.79, 36.81, 30.43, 23.55, 21.38. HRMS (APCI) m/z calcd for $C_{24}H_{27}N_2O_2^+$ $(M+H)^+$: 375.2021, found 375.2019.



3d

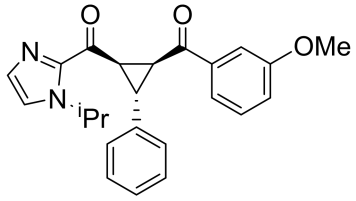
(1*R*,2*S*,3*S*)-2-(4-methylbenzoyl)-3-phenylcyclopropyl)-(isopropyl-1H-imidazol-2-yl)methanone (3d). yellow solid (33.8 mg, 95% yield), mp 101.4-102.3 ℃. HPLC: 81% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 13.74 min, tr (minor) = 9.23 min. $[\alpha]_D^{26}$ = +15.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 3.1 Hz, 4H), 7.16 (d, *J* = 12.1 Hz, 2H), 7.09 (d, *J* = 7.2 Hz, 3H), 5.35 (p, *J* = 6.7 Hz, 1H), 4.09 (dd, *J* = 9.7, 6.0 Hz, 1H), 3.48 (t, *J* = 6.3 Hz, 1H), 3.23 (dd, *J* = 9.7, 6.6 Hz, 1H), 2.28 (s, 3H), 1.30 (d, *J* = 6.7 Hz, 3H), 1.15 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.65, 186.19, 143.95, 142.99, 138.84, 134.74, 130.34, 129.90, 129.24, 128.75, 127.03, 126.85, 121.28, 49.70, 38.72, 37.30, 30.48, 23.55, 21.76. HRMS (APCI) m/z calcd for $C_{24}H_{27}N_2O_2^+$ $(M+H)^+$: 375.2022, found 375.2020.



3e

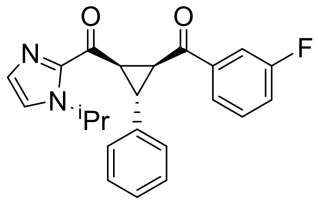
(1*R*,2*S*,3*S*)-2-(3,5-dimethylbenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanonepale (3e). yellow oil (37.1 mg, 96% yield). HPLC: 88% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 6.70 min, tr (minor) = 4.89 min. $[\alpha]_D^{26}$ = +28.4 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.63 (s, 2H), 7.33 (d, *J* = 4.8 Hz, 4H), 7.26 – 7.14 (m, 3H), 7.11 (s, 1H), 5.40 (p, *J* = 6.7 Hz, 1H), 4.19 (dd, *J* = 9.8, 6.1 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 1H), 3.29 (dd, *J* = 9.8, 6.5 Hz, 1H), 2.27 (s, 6H), 1.37 (d, *J* = 6.7 Hz, 3H), 1.20 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.38, 186.08, 143.98, 138.85, 138.17, 137.22, 134.79, 130.39, 129.22, 126.98, 126.84, 126.45, 121.24,

49.24, 40.39, 37.55, 30.22, 24.73, 21.22. HRMS (APCI) m/z calcd for $C_{25}H_{27}N_2O_2^+$ $(M+H)^+$: 387.2002, found 387.2000.



3f

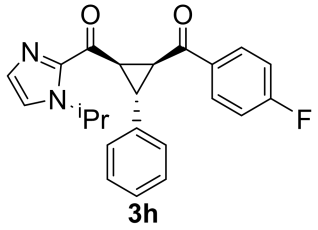
(1*R*,2*S*,3*S*)-2-(3-methoxybenzoyl)-3-phenylcyclopropyl)-(1-isopropyl-1H-imidazol-2-yl)methanone (3f). pale yellow solid (37.3 mg, 96% yield); mp 93.3-94.8 °C. HPLC:80% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C,tr (major) = 10.06 min, tr (minor) = 7.19 min. $[\alpha]_D^{26}$ = +17.3 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 – 7.96 (m, 2H), 7.32 (d, *J* = 5.3 Hz, 4H), 7.28 – 7.21 (m, 2H), 7.18 (s, 1H), 6.86 – 6.82 (m, 2H), 5.43 (p, *J* = 6.7 Hz, 1H), 4.16 (dd, *J* = 9.7, 6.0 Hz, 1H), 3.81 (s, 3H), 3.55 (t, *J* = 6.3 Hz, 1H), 3.28 (dd, *J* = 9.7, 6.6 Hz, 1H), 1.37 (d, *J* = 6.7 Hz, 3H), 1.23 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 194.35, 186.59, 150.34, 144.40, 141.67, 138.86, 130.87, 129.53, 128.89, 126.80, 125.30, 121.79, 49.40, 38.31, 36.60, 33.58, 30.94, 24.21. HRMS (APCI) m/z calcd for $C_{24}H_{25}N_2O_2^+$ $(M+H)^+$: 389.1803, found 389.1805.



3g

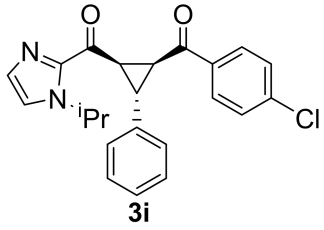
(1*R*,2*S*,3*S*)-2-(3-fluorobenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3g). pale yellow solid (34.7 mg, 92% yield); mp 87.3-88.9 °C. HPLC: 83% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 6.45 min, tr (minor) = 5.54 min. $[\alpha]_D^{26}$ = +31.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.02 (m, 2H), 7.35 – 7.29 (m, 4H), 7.26 – 7.23 (m, 2H), 7.18 (d, *J* = 1.1 Hz, 1H), 7.08 – 7.01 (m, 2H), 5.42 (p, *J* = 6.7 Hz, 1H), 4.20 (dd, *J* = 9.7, 6.1 Hz, 1H), 3.56 (t, *J* = 6.3 Hz, 1H), 3.26 (dd, *J* = 9.7, 6.6 Hz, 1H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$)

δ =192.55, 186.00, 167.10, 164.56, 142.86, 138.55, 133.63, 131.19, 130.02, 128.80, 127.15, 126.83, 121.47, 115.77, 115.55, 49.32, 38.49, 36.69, 30.49, 23.57, 23.50. ^{19}F NMR (376 MHz, $CDCl_3$) δ = 105.32. HRMS (APCI) m/z calcd for $C_{23}H_{22}FN_2O_2^+$ $(M+H)^+$: 376.1601, found 376.1599.



3h

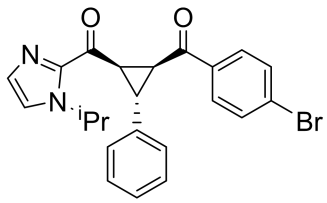
(1*R*,2*S*,3*S*)-2-(4-fluorobenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3h). pale yellow solid (34.7 mg, 92% yield)**;** mp 87.3-88.9 °C. HPLC: 80% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C,tr (major) = 7.67 min, tr (minor) = 5.84 min. $[\alpha]_D^{26}$ = +15.1 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.07 – 8.01 (m, 2H), 7.33 (dd, *J* = 8.2, 2.0 Hz, 4H), 7.26 (s, 1H), 7.23 (d, *J* = 1.1 Hz, 1H), 7.18 (d, *J* = 1.1 Hz, 1H), 7.07 – 7.02 (m, 2H), 5.42 (p, *J* = 6.7 Hz, 1H), 4.20 (dd, *J* = 9.7, 6.1 Hz, 1H), 3.56 (t, *J* = 6.3 Hz, 1H), 3.26 (dd, *J* = 9.7, 6.6 Hz, 1H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 192.55, 186.00, 167.10, 164.56, 142.86, 138.55, 133.63, 131.19, 130.02, 128.80, 127.15, 126.83, 121.47, 115.77, 115.55, 49.32, 38.49, 36.69, 30.49, 23.57, 23.50. ^{19}F NMR (376 MHz, $CDCl_3$) δ = 105.34. HRMS (APCI) m/z calcd for $C_{23}H_{22}FN_2O_2^+$ $(M+H)^+$: 376.1600, found 376.1602.



3i

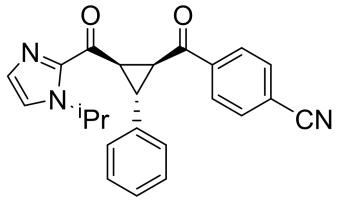
(1*R*,2*S*,3*S*)-2-(4-chlorobenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3i). pale yellow solid (36.5 mg, 93% yield); mp 87.8-89.6 °C. HPLC: 66% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.40 min, tr (minor) = 6.78 min. $[\alpha]_D^{26}$ = +14.3 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 – 7.93 (m, 2H), 7.36 – 7.30 (m, 6H), 7.28 – 7.23 (m, 2H), 7.18 (d, *J* = 1.0 Hz, 1H), 5.40 (p, *J* = 6.7 Hz, 1H), 4.20 (dd, *J* =

9.6, 6.0 Hz, 1H), 3.55 (t, *J* = 6.3 Hz, 1H), 3.25 (dd, *J* = 9.7, 6.6 Hz, 1H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ =192.97, 186.53, 142.81, 139.58, 138.46, 135.50, 130.04, 129.99, 128.87, 128.80, 127.17, 126.82, 49.32, 38.41, 36.75, 30.52, 23.54, 23.51. HRMS (APCI) m/z calcd for $C_{23}H_{22}ClN_2O_2^+$ $(M+H)^+$: 393.1301, found 393.1300.



3j

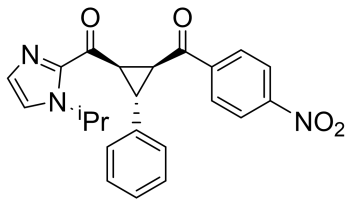
(1*R*,2*S*,3*S*)-2-(4-bromobenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3j). pale yellow solid (41.5 mg, 95% yield); mp 134.4-135.6 °C. HPLC: 71% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.32 min, tr (minor) = 7.77min. $[\alpha]_D^{26}$ = +15.6 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.87 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 20.8 Hz, 5H), 7.21 (d, *J* = 21.2 Hz, 2H), 5.40 (p, *J* = 6.7 Hz, 1H), 4.20 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.55 (t, *J* = 6.3 Hz, 1H), 3.24 (dd, *J* = 9.6, 6.6 Hz, 1H), 1.37 (d, *J* = 6.6 Hz, 3H), 1.24 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.16, 185.88, 142.79, 138.43, 135.89, 131.85, 130.08, 130.04, 128.79, 128.33, 127.16, 126.80, 121.52, 49.32, 38.36, 36.75, 30.52, 23.52. HRMS (APCI) m/z calcd for $C_{23}H_{22}BrN_2O_2^+$ $(M+H)^+$: 437.0801, found 437.0799.



3k

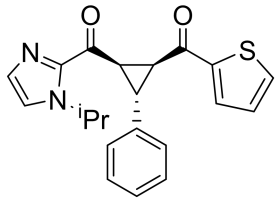
(1*S*,2*R*,3*S*)-3-phenylcyclopropane-1-carbonyl-2-(1-isopropyl-1H-imidazole-2-carbonyl)benzonitril (3k). yellow oil (35.3 mg, 96% yield). HPLC: 75% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) =14.67 min, tr (minor) = 10.77 min. $[\alpha]_D^{26}$ = +19.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.10 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.38 – 7.25 (m, 6H), 7.19 (s, 1H), 5.39 (p, *J* = 6.7 Hz, 1H), 4.24 (dd, *J* = 9.6, 6.1 Hz, 1H),

3.56 (t, *J* = 6.3 Hz, 1H), 3.25 (dd, *J* = 9.6, 6.5 Hz, 1H), 1.38 (d, *J* = 6.7 Hz, 3H), 1.23 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ =193.17, 185.63, 142.60, 140.13, 138.06, 133.06, 130.18, 128.90, 128.85, 127.32, 126.78, 121.74, 118.05, 116.29, 49.36, 38.16, 37.06, 31.43, 23.55, 23.45. HRMS (APCI) m/z calcd for $C_{24}H_{22}N_3O_2^+$ $(M+H)^+$: 384.1604, found 384.1602.



3l

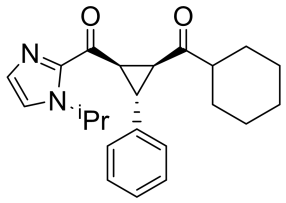
(1*R*,2*S*,3*S*)-2-(4-nitrobenzoyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3l). yellow oil (36.3 mg, 96% yield). HPLC: 99% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 12.27 min, tr (minor) = 9.36 min. $[\alpha]_D^{26}$ = +31.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.57 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.46 – 7.08 (m, 8H), 7.03 (dd, *J* = 5.0, 3.8 Hz, 1H), 5.47 (p, *J* = 6.7 Hz, 1H), 4.11 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 1H), 3.28 (dd, *J* = 9.6, 6.4 Hz, 1H), 1.40 (d, *J* = 6.7 Hz, 3H), 1.28 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.07, 185.90, 164.07, 161.61, 142.79, 139.31, 139.25, 138.42, 130.26, 130.18, 130.06, 128.80, 127.18, 126.81, 124.41, 124.38, 121.50, 120.26, 120.05, 115.27, 115.05, 49.32, 38.40, 36.86, 30.68, 23.55, 23.48. HRMS (APCI) m/z calcd for $C_{23}H_{22}N_3O_4^+$ $(M+H)^+$: 403.1500, found 403.1499.



3m

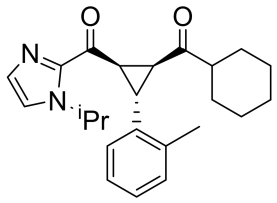
(1*R*,2*S*,3*S*)-2-phenyl-3-(thiophene-2-carbonyl)cyclopropyl)-(1-isopropyl-1H-imidazol-2-yl)methanone (3m). yellow oil (34.3 mg, 94% yield). HPLC: 42% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.81 min, tr (minor) = 7.34 min. $[\alpha]_D^{26}$ = +30.7 (c = 0.1, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.77 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.57 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.35 – 7.29 (m, 4H), 7.24 (d, *J* = 6.2 Hz, 2H), 7.17 (s, 1H), 7.03 (dd, *J* = 5.0, 3.8 Hz, 1H), 5.47 (p, *J* = 6.7 Hz, 1H), 4.11 (dd, *J* = 9.6, 6.2 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 1H), 3.28 (dd, *J* = 9.6, 6.4 Hz, 1H), 1.40 (d, *J* = 6.7 Hz, 3H), 1.28 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 186.71, 185.86, 144.37, 142.96, 138.97, 133.73, 132.62, 129.94, 128.76, 128.10, 127.12, 126.83, 121.35, 49.32, 38.79, 36.50, 30.62, 23.61, 23.49. HRMS (APCI) m/z calcd for $C_{21}H_{21}N_2O_2S^+$ $(M+H)^+$: 365.1200, found 365.1203.



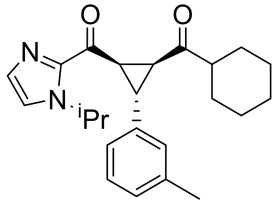
3n

(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-phenylcyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (3n). colourless solid (35.4 mg, 97% yield); mp 67.1-68.8 °C. HPLC: 99% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.40 min, tr (minor) = 7.14 min. $[\alpha]_D^{26}$ = +4.9 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 – 7.27 (m, 2H), 7.27 – 7.22 (m, 4H), 7.17 (d, *J* = 1.1 Hz, 1H), 5.55 (p, *J* = 6.7 Hz, 1H), 3.80 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.38 (t, *J* = 6.3 Hz, 1H), 2.87 (dd, *J* = 9.7, 6.3 Hz, 1H), 2.54 – 2.46 (m, 1H), 1.84 – 1.61 (m, 5H), 1.43 (dd, *J* = 6.7, 4.4 Hz, 6H), 1.34 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.85, 185.94, 142.85, 138.86, 129.78, 128.70, 126.94, 126.65, 121.16, 51.43, 49.33, 39.35, 37.44, 30.91, 28.33, 28.21, 25.94, 25.68, 23.80, 23.56. HRMS (APCI) m/z calcd for $C_{23}H_{29}N_2O_2^+$ $(M+H)^+$: 365.2211, found 365.2209.



4a

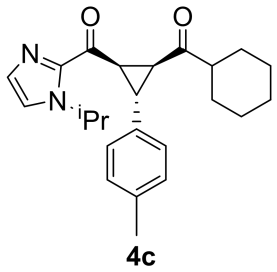
(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(o-tolyl)cyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (4a). colourless solid (37.1 mg, 98% yield); mp 65.8-67.6 °C. HPLC: 99% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 7.11 min, tr (minor) = 5.76 min. $[\alpha]_D^{26}$ = +2.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 (s, 1H), 7.18 – 7.13 (m, 4H), 7.10 (d, *J* = 4.4 Hz, 1H), 5.56 (p, *J* = 6.7 Hz, 1H), 3.77 (dd, *J* = 9.6, 6.7 Hz, 1H), 3.43 (t, *J* = 6.6 Hz, 1H), 2.83 (dd, *J* = 9.6, 6.5 Hz, 1H), 2.55 – 2.47 (m, 1H), 2.38 (s, 3H), 1.77 (dd, *J* = 43.6, 29.8 Hz, 5H), 1.44 (dd, *J* = 11.8, 6.7 Hz, 6H), 1.36 – 1.15 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.19, 186.28, 142.86, 138.15, 136.78, 130.09, 129.80, 127.10, 126.08, 125.85, 121.17, 51.54, 49.33, 37.69, 36.54, 28.90, 28.47, 28.25, 25.95, 25.71, 25.68, 23.86, 23.54, 19.76. HRMS (APCI) m/z calcd for $C_{24}H_{31}N_2O_2^+$ $(M+H)^+$: 379.2301, found 379.2303.



4b

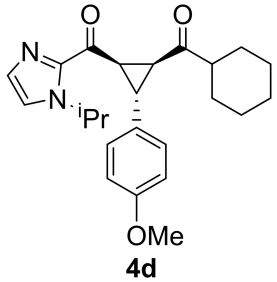
(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(m-tolyl)cyclopropyl)-(1-isopropyl-1H-imidazol-2-yl)methanone (4b). colourless solid (36.0 mg, 95% yield); mp 67.9-69.2 °C. HPLC: 93% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 10.47 min, tr (minor) = 8.63 min. $[\alpha]_D^{26}$ = +6.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.18 (s, 1H), 7.14 – 7.08 (m, 2H), 6.96 (d, *J* = 5.5 Hz, 3H), 5.47 (p, *J* = 6.7 Hz, 1H), 3.72 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.27 (t, *J* = 6.3 Hz, 1H), 2.79 (dd, *J* = 9.7, 6.3 Hz, 1H), 2.46 – 2.37 (m, 1H), 2.25 (s, 3H), 1.76 – 1.53 (m, 5H), 1.36 (dd, *J* = 6.7, 4.1 Hz, 6H), 1.27 – 1.07 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.88, 185.97, 142.86, 138.78, 138.35, 129.75, 128.58, 127.69, 127.21, 123.73, 121.12, 51.41, 49.31, 39.43, 37.47, 30.45, 28.31, 28.21, 25.94,

25.68, 25.66, 23.78, 23.56, 21.48. HRMS (APCI) m/z calcd for $C_{24}H_{31}N_2O_2^+$ $(M+H)^+$: 379.2300, found 379.2298.



4c

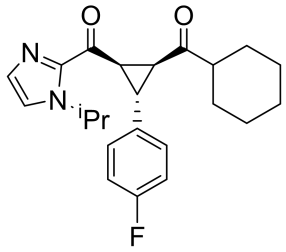
(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(p-tolyl)cyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (4c). colourless oil (36.0 mg, 95% yield). HPLC: 91% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 12.22 min, tr (minor) = 9.72 min. $[\alpha]_D^{26}$ = +3.5 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.27 – 7.25 (m, 1H), 7.17 (s, 1H), 7.12 (s, 4H), 5.55 (p, *J* = 6.7 Hz, 1H), 3.77 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.34 (t, *J* = 6.3 Hz, 1H), 2.83 (dd, *J* = 9.6, 6.3 Hz, 1H), 2.53 – 2.44 (m, 1H), 2.32 (s, 3H), 1.85 – 1.61 (m, 5H), 1.43 (dd, *J* = 6.7, 4.4 Hz, 6H), 1.30 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.01, 186.13, 158.69, 142.90, 130.86, 129.75, 127.78, 121.11, 114.13, 55.43, 51.42, 49.31, 39.30, 37.34, 30.07, 28.34, 28.22, 25.96, 25.16, 23.80, 23.57. HRMS (APCI) m/z calcd for $C_{24}H_{31}N_2O_2^+$ $(M+H)^+$: 379.2299, found 379.2298.



4d

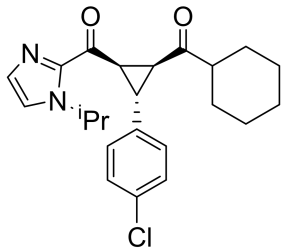
(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(4-methoxyphenyl)cyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (4d). colourless oil (36.3 mg, 92% yield). HPLC: 90% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.54 min, tr (minor) = 7.96 min. $[\alpha]_D^{26}$ = +18.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25 (s, 1H), 7.18 – 7.13 (m, 3H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.55 (p, *J* = 6.7 Hz, 1H), 3.79 (s, 3H), 3.75 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.33 (t, *J* = 6.4 Hz, 1H), 2.80 (dd, *J* = 9.6, 6.3 Hz, 1H), 2.49 (td, *J* = 10.9, 5.4 Hz, 1H),

1.83 – 1.60 (m, 5H), 1.43 (dd, *J* = 6.7, 5.3 Hz, 6H), 1.27 – 1.15 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 186.13, 158.69, 142.90, 130.86, 129.75, 127.78, 121.11, 114.13, 55.43, 51.42, 49.31, 39.30, 37.34, 30.07, 28.34, 28.22, 25.96, 25.69, 23.80, 23.57. HRMS (APCI) m/z calcd for $C_{24}H_{31}N_2O_3^+$ $(M+H)^+$: 395.2297, found 395.2299.



4e

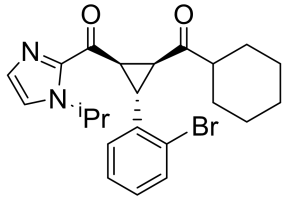
(1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(4-fluorophenyl)cyclopropyl-(1-isopropyl-1H-imidazol-2-yl)methanone (4e). colourless oil (36.0 mg, 94% yield). HPLC: 99% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 11.99 min, tr (minor) = 9.43 min. $[\alpha]_D^{26}$ = +3.6 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 (dd, *J* = 7.2, 2.2 Hz, 2H), 7.27 (s, 1H), 7.17 (dd, *J* = 5.2, 2.4 Hz, 3H), 5.53 (p, *J* = 6.6 Hz, 1H), 3.78 (dd, *J* = 9.8, 6.4 Hz, 1H), 3.34 (t, *J* = 6.3 Hz, 1H), 2.85 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.52 – 2.44 (m, 1H), 1.69 (s, 5H), 1.43 (t, *J* = 6.7 Hz, 6H), 1.36 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.41, 185.40, 142.72, 141.32, 130.22, 130.08, 129.91, 129.61, 125.57, 122.85, 121.35, 51.46, 49.39, 39.14, 37.47, 29.71, 28.33, 28.19, 25.93, 25.66, 23.81, 23.56. ^{19}F NMR (376 MHz, $CDCl_3$) δ =114.46. HRMS (APCI) m/z calcd for $C_{23}H_{28}FN_2O_2^+$ $(M+H)^+$: 383.2100, found 383.2099.



4f

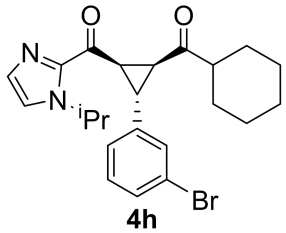
(1*R*,2*S*,3*S*)-2-(4-chlorophenyl)-3-cyclopropyl-(1-isopropyl-1H-imidazole-2-carbonyl)(cyclohexyl)methanone (4f). colourless solid (38.3 mg, 96% yield); mp 113.8-115.7 °C. HPLC: 90% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH

= 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.91min, tr (minor) = 7.84 min. $[\alpha]_D^{26}$ = +13.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 – 7.26 (m, 3H), 7.18 – 7.14 (m, 3H), 5.53 (p, *J* = 6.7 Hz, 1H), 3.77 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.34 (t, *J* = 6.3 Hz, 1H), 2.82 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.52 – 2.44 (m, 1H), 1.81 (d, *J* = 42.8 Hz, 5H), 1.43 (t, *J* = 6.6 Hz, 6H), 1.28 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.55, 185.57, 142.75, 137.43, 132.70, 129.87, 128.83, 128.06, 121.31, 51.45, 49.38, 39.16, 37.39, 29.72, 28.34, 28.17, 25.92, 25.66, 23.80, 23.55. HRMS (APCI) m/z calcd for $C_{23}H_{28}ClN_2O_2^+$ $(M+H)^+$: 399.1797, found 399.1800.



4g

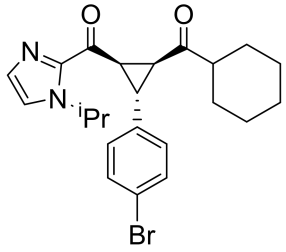
(1*R*,2*S*,3*S*)-2-(2-bromophenyl)-3-(1-isopropyl-1H-imidazole-2-carbonyl)cyclopropyl)(cyclohexyl)methanone (4g). yellow oil (43.3 mg, 98% yield). HPLC: 98% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.60 min, tr (minor) = 8.26 min. $[\alpha]_D^{26}$ = +10.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 7.9 Hz, 1H), 7.26 (d, *J* = 5.8 Hz, 2H), 7.18 – 7.10 (m, 3H), 5.57 (p, *J* = 6.7 Hz, 1H), 3.80 (dd, *J* = 9.7, 6.7 Hz, 1H), 3.57 (t, *J* = 6.5 Hz, 1H), 2.76 (dd, *J* = 9.7, 6.4 Hz, 1H), 2.60 – 2.51 (m, 1H), 1.81 (d, *J* = 47.2 Hz, 5H), 1.44 (dd, *J* = 10.3, 6.7 Hz, 6H), 1.31 – 1.15 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.72, 185.69, 142.85, 138.18, 132.86, 129.78, 128.66, 127.98, 127.57, 126.18, 121.19, 51.45, 49.35, 38.06, 36.54, 31.45, 28.38, 28.29, 25.96, 25.74, 25.64, 23.81, 23.59. HRMS (APCI) m/z calcd for $C_{23}H_{28}BrN_2O_2^+$ $(M+H)^+$: 443.1300, found 443.1298.



4h

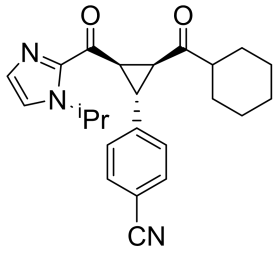
(1*S*,2*S*,3*R*)-2-(3-bromophenyl)-3-(1-isopropyl-1H-imidazole-2-carbonyl)cyclopropyl)(cyclohexyl)methanone (4h). yellow oil (42.0 mg, 95% yield). HPLC: 90% ee

(Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.44 min, tr (minor) = 7.60 min. $[\alpha]_D^{26}$ = +14.0 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 (d, *J* = 2.7 Hz, 2H), 7.27 (s, 1H), 7.17 (dd, *J* = 5.5, 2.4 Hz, 3H), 5.53 (p, *J* = 6.6 Hz, 1H), 3.78 (dd, *J* = 9.8, 6.4 Hz, 1H), 3.34 (t, *J* = 6.3 Hz, 1H), 2.85 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.53 – 2.45 (m, 1H), 1.82 – 1.61 (m, 5H), 1.43 (t, *J* = 6.8 Hz, 6H), 1.31 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.40, 185.39, 142.71, 141.31, 130.22, 130.07, 129.90, 129.60, 125.56, 122.84, 121.35, 51.45, 49.38, 39.14, 37.47, 29.71, 28.33, 28.18, 25.92, 25.66, 23.80, 23.55. HRMS (APCI) m/z calcd for $C_{23}H_{28}BrN_2O_2^+$ $(M+H)^+$: 443.1299, found 443.1297.



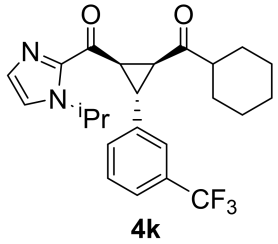
4i

((1*S*,2*S*,3*R*)-2-(4-bromophenyl)-3-(1-isopropyl-1H-imidazole-2-carbonyl)cyclopropyl)(cyclohexyl)methanon (4i). colourless solid (42.0 mg, 95% yield); mp 115.3-116.9℃. HPLC: 93% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.41 min, tr (minor) = 8.22 min. $[\alpha]_D^{26}$ = +3.2 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ =7.42 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 1.1 Hz, 1H), 7.17 (d, *J* = 1.0 Hz, 1H), 7.12 – 7.08 (m, 2H), 5.53 (p, *J* = 6.7 Hz, 1H), 3.77 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.33 (t, *J* = 6.3 Hz, 1H), 2.82 (dd, *J* = 9.7, 6.2 Hz, 1H), 2.52 – 2.44 (m, 1H), 1.84 – 1.59 (m, 5H), 1.43 (t, *J* = 6.6 Hz, 6H), 1.31 – 1.17 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.50, 185.51, 142.71, 137.96, 131.75, 129.87, 128.41, 121.31, 120.69, 51.42, 49.36, 39.11, 37.34, 29.75, 28.32, 28.15, 25.91, 25.64, 23.78, 23.53. HRMS (APCI) m/z calcd for $C_{23}H_{28}BrN_2O_2^+$ $(M+H)^+$: 443.1296, found 443.1298.



4j

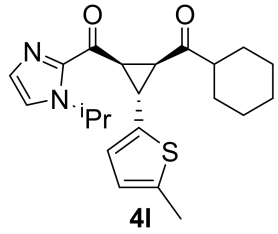
((1*S*,2*S*,3*R*)-2-(4-yclohexanecarbonyl)-3-(1-isopropyl-1H-imidazole-2-carbonyl)cyclopropyl)benzonitrile (4j). yellow oil (35.1mg, 90% yield). HPLC: 90% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 23.41 min, tr (minor) = 15.26 min. $[\alpha]_D^{26}$ = +24.8 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.28 (s, 1H), 7.18 (s, 1H), 5.52 (p, *J* = 6.7 Hz, 1H), 3.83 (dd, *J* = 9.9, 6.4 Hz, 1H), 3.40 (t, *J* = 6.3 Hz, 1H), 2.89 (dd, *J* = 9.9, 6.2 Hz, 1H), 2.53 – 2.45 (m, 1H), 1.83 – 1.61 (m, 5H), 1.44 (t, *J* = 6.8 Hz, 6H), 1.30 – 1.17 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.02, 184.90, 144.65, 142.55, 132.53, 129.99, 127.40, 121.56, 118.85, 110.69, 51.46, 49.45, 39.23, 37.70, 29.89, 28.31, 28.12, 25.87, 25.61, 25.60, 23.78, 23.51. HRMS (APCI) m/z calcd for $C_{24}H_{28}N_3O_2^+$ $(M+H)^+$: 390.2101, found 390.2099.



4k

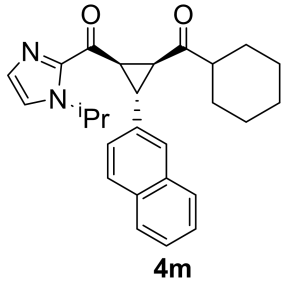
((1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(3-(trifluoromethyl)phenyl)cyclopropyl)(1-isopropyl-1H-imidazol-2-yl)methanone (4k). colourless solid (41.9 mg, 97% yield); mp 86.7-87.5 °C. HPLC: 90% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.10 min, tr (minor) = 7.47 min. $[\alpha]_D^{26}$ = +10.4 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.28 (s, 1H), 7.18 (s, 1H), 5.53 (p, *J* = 6.7 Hz, 1H), 3.84 (dd, *J* = 9.8, 6.4 Hz, 1H), 3.42 (t, *J* = 6.3 Hz, 1H), 2.89 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.54 – 2.45 (m, 1H), 1.90 – 1.64 (m, 5H), 1.44 (t, *J* = 6.4 Hz, 6H), 1.31 – 1.14 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.31, 185.26, 143.10, 142.66,

129.93, 126.97, 125.71, 125.67, 125.63, 125.59, 121.41, 51.46, 49.40, 39.20, 37.55, 29.82, 28.32, 28.14, 25.89, 25.63, 25.62, 23.77, 23.62, 23.51. ^{19}F NMR (376 MHz, $CDCl_3$) δ = 62.37. HRMS (APCI) m/z calcd for $C_{24}H_{28}F_3N_2O_2^+$ $(M+H)^+$: 433.1999, found 433.2001.



4l

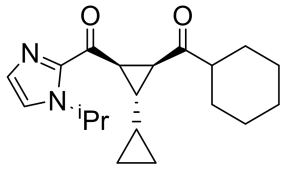
((1*S*,2*R*,3*S*)-2-(cyclohexanecarbonyl)-3-(5-methylthiophen-2-yl)cyclopropyl)(1-isopropyl-1H-imidazol-2-yl)methanone (4l). yellow oil (34.6 mg, 90% yield). HPLC: 64% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 14.78 min, tr (minor) = 11.58 min. $[\alpha]_D^{26}$ = -9.6 (c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26 (s, 1H), 7.17 (s, 1H), 6.69 (d, *J* = 3.4 Hz, 1H), 6.55 (d, *J* = 3.5 Hz, 1H), 5.53 (p, *J* = 6.6 Hz, 1H), 3.74 (dd, *J* = 9.7, 6.3 Hz, 1H), 3.45 (t, *J* = 6.2 Hz, 1H), 2.82 (dd, *J* = 9.7, 6.1 Hz, 1H), 2.42 (s, 3H), 1.91 – 1.66 (m, 5H), 1.43 (dd, *J* = 8.2, 6.7 Hz, 6H), 1.32 – 1.13 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.62, 185.54, 142.77, 140.33, 138.27, 129.86, 125.07, 124.33, 121.21, 51.43, 49.35, 40.00, 38.26, 28.31, 28.17, 26.22, 25.97, 25.70, 25.68, 23.82, 23.58, 15.46. HRMS (APCI) m/z calcd for $C_{22}H_{29}N_2O_2S^+$ $(M+H)^+$: 385.1904, found 385.1905.



4m

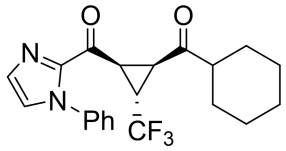
((1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(naphthalen-2-yl)cyclopropyl)(1-isopropyl-1H-imidazol-2-yl)methanone (4m). yellow oil (39.8 mg, 96% yield). HPLC: 98% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.80 min, tr (minor) = 8.72 min. $[\alpha]_D^{26}$ = -3.6 (c = 0.1,

CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ = 8.30 (d, *J* = 8.1 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 7.4 Hz, 1H), 7.57 – 7.47 (m, 2H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 6.3 Hz, 1H), 7.19 (s, 1H), 5.62 (p, *J* = 6.6 Hz, 1H), 3.93 (d, *J* = 8.1 Hz, 2H), 2.95 – 2.90 (m, 1H), 2.58 – 2.50 (m, 1H), 1.92 – 1.58 (m, 5H), 1.46 (dd, *J* = 12.1, 6.7 Hz, 6H), 1.38 – 1.13 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.33, 186.27, 142.85, 134.73, 133.65, 133.04, 129.88, 128.53, 127.86, 126.51, 126.06, 125.40, 124.42, 123.94, 121.25, 51.67, 49.36, 37.51, 36.32, 28.55, 28.33, 28.17, 25.94, 25.73, 25.64, 23.90, 23.52. HRMS (APCI) m/z calcd for $C_{27}H_{31}N_2O_2^+$ $(M+H)^+$: 4152301, found 415.2299.



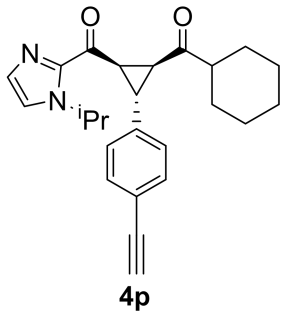
4n

((1*S*,2*R*,3*S*)-3-(cyclohexanecarbonyl)-[1,1'-bi(cyclopropan)]-2-yl)(1-isopropyl-1H-imidazol-2-yl)methanone (4n). colourless oil (29.6 mg, 90% yield). HPLC: 81% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 10.51 min, tr (minor) = 7.57 min. $[\alpha]_D^{26}$ = +13.2 (c = 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.23 (d, *J* = 1.1 Hz, 1H), 7.16 (d, *J* = 1.1 Hz, 1H), 5.51 (p, *J* = 6.7 Hz, 1H), 3.26 (dd, *J* = 9.5, 6.3 Hz, 1H), 2.46 – 2.36 (m, 2H), 2.33 – 2.25 (m, 1H), 1.87 – 1.65 (m, 5H), 1.41 (dd, *J* = 12.3, 6.7 Hz, 6H), 1.32 – 1.14 (m, 5H), 0.99 – 0.91 (m, 1H), 0.49 (dd, *J* = 5.2, 4.4 Hz, 2H), 0.27 – 0.22 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 208.71, 186.91, 142.97, 129.61, 120.93, 51.39, 49.35, 49.23, 35.93, 34.42, 29.37, 28.42, 28.28, 25.99, 25.73, 23.81, 23.58, 11.36, 3.56, 3.48. HRMS (APCI) m/z calcd for $C_{20}H_{29}FN_2O_2^+$ $(M+H)^+$: 329.2199, found 329.2197.



4o

((1*S*,2*R*,3*S*)-2-(cyclohexanecarbonyl)-3-(trifluoromethyl)cyclopropyl)(1-phenyl-1H-imidazol-2-yl)methanone (4o). colourless solid (33.2 mg, 85% yield); mp 69.2-71.3 °C. HPLC: 75% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 6.98 min, tr (minor) = 6.11 min. $[\alpha]_D^{26}$ = -7.0(c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.45 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.32 – 7.28 (m, 3H), 7.20 (d, *J* = 1.0 Hz, 1H), 3.62 (dd, *J* = 10.2, 6.2 Hz, 1H), 2.95 – 2.85 (m, 2H), 2.52 – 2.46 (m, 1H), 1.86 – 1.65 (m, 5H), 1.34 – 1.18 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 205.88, 181.62, 142.65, 137.90, 131.14, 130.21, 129.17, 129.02, 128.27, 127.51, 126.09, 125.87, 123.31, 51.42, 31.00, 30.41, 28.16, 27.90, 25.84, 25.58, 25.52. ^{19}F NMR (376 MHz, $CDCl_3$) δ = 66.6. HRMS (APCI) m/z calcd for $C_{21}H_{22}F_3N_2O_2^+$ $(M+H)^+$: 391.1599, found 391.1602.

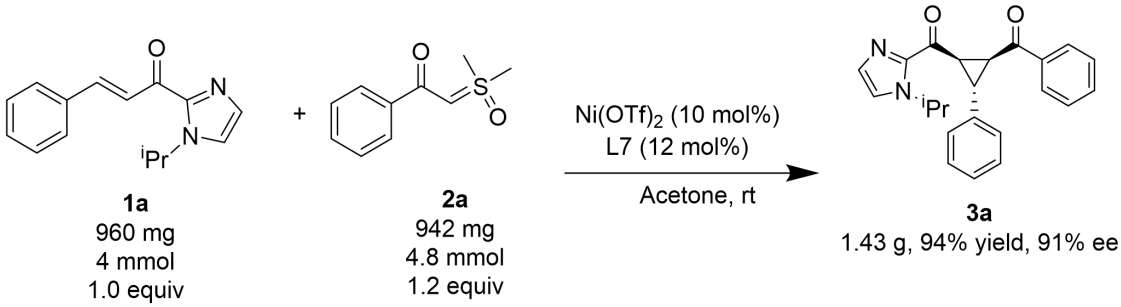


4p

((1*R*,2*S*,3*S*)-2-(cyclohexanecarbonyl)-3-(4-ethynylphenyl)cyclopropyl)(1-isopropyl-1H-imidazol-2-yl)methanone (4p). colourless oil (35.7 mg, 92% yield). HPLC: 90% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 80:20, flow rate: 1.0 mL/min, 40 °C, tr (major) = 8.31 min, tr (minor) = 5.75 min. $[\alpha]_D^{26}$ = +15.6(c = 0.1, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.43 (d, *J* = 8.3 Hz, 2H), 7.26 (s, 1H), 7.20 – 7.16 (m, 3H), 5.53 (p, *J* = 6.7 Hz, 1H), 3.80 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.36 (t, *J* = 6.3 Hz, 1H), 3.07 (s, 1H), 2.85 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.53 – 2.45 (m, 1H), 1.87 – 1.63 (m, 5H), 1.45 – 1.40 (m, 6H), 1.34 – 1.16 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.47, 185.51, 142.72, 139.81, 132.44, 129.84, 126.60, 121.28, 120.64, 83.48,

51.41, 49.34, 49.21, 39.29, 37.48, 30.17, 28.30, 28.15, 25.90, 25.63, 23.77, 23.52. HRMS (APCI) m/z calcd for $C_{25}H_{29}N_2O_2^+$ $(M+H)^+$: 389.2199, found 389.2202.

VI Gram-scale Experiments and Synthetic Transformations

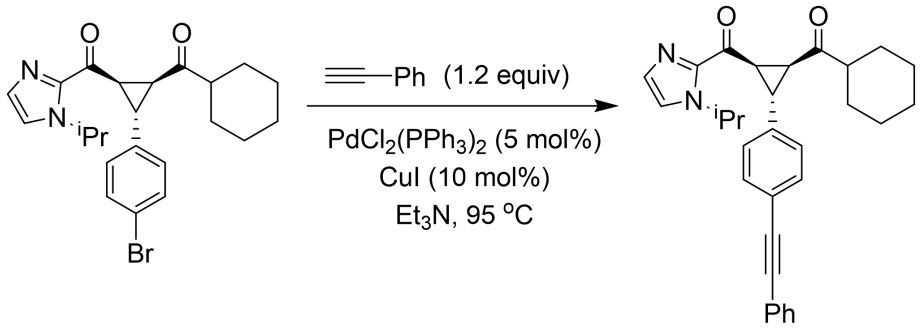


1a
960 mg
4 mmol
1.0 equiv

2a
942 mg
4.8 mmol
1.2 equiv

3a
1.43 g, 94% yield, 91% ee

An oven-dried 100 mL Schlenk tube, fitted with a magnetic stirring bar, was charged with $Ni(OTf)_2$ (144 mg, 10 mol%) in an Ar setting, followed by the addition of **L7** (320 mg, 12 mol%) and Acetone (40 mL, 0.1 M), with the mixture being stirred at room temperature for an hour. Following this, **1a** (960 mg, 4.0 mmol, 1.0 equiv.) and **2a** (942 mg, 4.8 mmol, 1.2 equiv.) were added.The reaction mixture was stirred at 25°C for indicated time (monitored by TLC) under argon. the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 10:1 to 5:1) to afford products the respective products **3a** (yellow oil, 1430 mg, 94% yield, 91% ee).

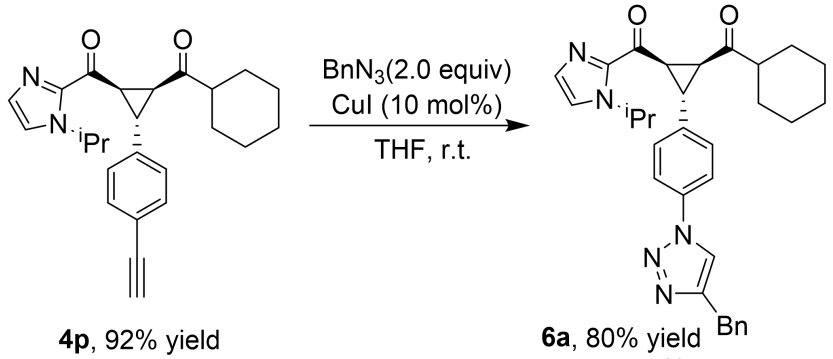


4j, 95% yield
dr>20:1, 93% ee

5a, 60% yield
dr>20:1, 84% ee

To a dry flask under argon containing **4j** (44.2 mg, 0.1 mmol, 1.0 equiv.) was sequentially added Et_3N (1.0 mL), phenyl acetylene (13.0 μL, 0.12 mmol, 1.2 equiv.), $PdCl_2(PPh_3)_2$ (2.0 mg, 0.005 mmol, 0.05 equiv.), CuI (2.0 mg, 0.01 mmol, 0.1 equiv.). The mixture was stirred for 12 h at 95 °C in a pre-heated oil bath. Then the mixture was filtered through a pad of celite. Removal of solvent under reduced pressure afforded a residue which is purified by column chromatography on silica gel eluting with ethyl-acetate: hexane (10 – 12 %) to afford compound **5a** with 60% yield. HPLC: 84% ee (Chiralpak IA column, λ = 254 nm, n-hexane/i-PrOH = 70:30, flow rate: 1.0

mL/min, 40 °C, tr (major) = 13.53 min, tr (minor) = 7.19 min. $[\alpha]_D^{26}$ = +5.6 (c = 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.48 – 7.43 (m, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.25 (m, 3H), 7.19 (s, 1H), 7.15 – 7.10 (m, 3H), 5.47 (p, *J* = 6.7 Hz, 1H), 3.75 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.31 (t, *J* = 6.3 Hz, 1H), 2.80 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.42 (t, *J* = 10.9 Hz, 1H), 1.79 – 1.57 (m, 5H), 1.36 (dd, *J* = 6.7, 5.4 Hz, 6H), 1.27 – 1.10 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.56, 185.61, 142.77, 139.22, 131.93, 131.69, 129.85, 128.45, 128.35, 126.66, 123.35, 121.85, 121.28, 89.72, 89.26, 51.44, 49.36, 39.40, 37.52, 30.31, 28.33, 28.19, 25.93, 25.66, 23.79, 23.55. HRMS (APCI) m/z calcd for $C_{31}H_{33}N_2O_2^+$ $(M+H)^+$: 465.2504, found 465.2506.



4p, 92% yield
dr>20:1, 90%ee

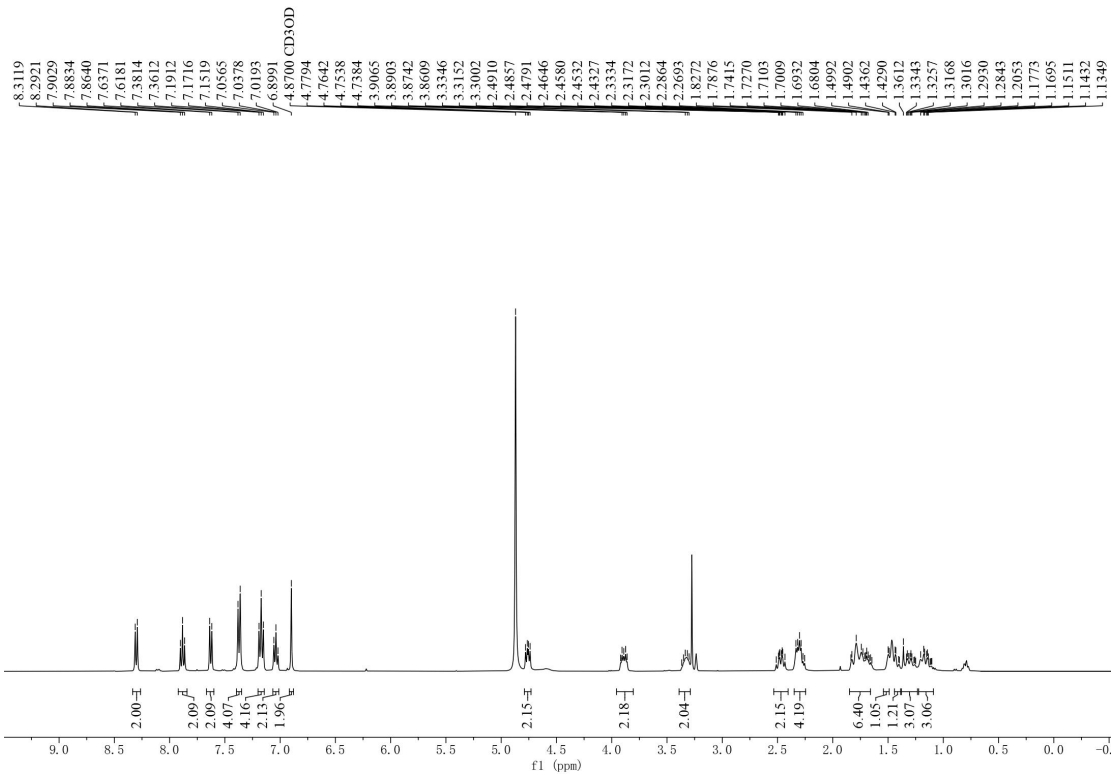
6a, 80% yield
dr>20:1, 87%ee

An oven-dried 25 mL Schlenk tube was charged with **4p** (38.8 mg, 0.1 mmol), benzylazide (55.7 mg, 0.4 mmol), and CuI (19.0 mg, 10 mol%) in THF (1 mL, 1.0 M solution). The reaction was stirred at room temperature for 30 min, concentrated in vaccum. The concentrate was then purified by silica gel chromatography (PE/EtOAc = 5/1-2:1) to afford **6a** colorless oil (80% yield).HPLC: 87% ee (Chiralpak IC column, λ = 254 nm, n-hexane/i-PrOH = 70:30, flow rate: 1.0 mL/min, 40 °C, tr (major) = 9.24 min, tr (minor) = 8.09 min. $[\alpha]_D^{26}$ = +10.6 (c = 0.1, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.65 (d, *J* = 8.3 Hz, 2H), 7.60 (s, 1H), 7.27 (d, *J* = 7.1 Hz, 3H), 7.23 – 7.14 (m, 5H), 7.08 (s, 1H), 5.53 – 5.40 (m, 3H), 3.74 (dd, *J* = 9.7, 6.4 Hz, 1H), 3.30 (t, *J* = 6.3 Hz, 1H), 2.79 (dd, *J* = 9.8, 6.2 Hz, 1H), 2.46 – 2.36 (m, 1H), 1.78 – 1.49 (m, 5H), 1.33 (t, *J* = 6.3 Hz, 6H), 1.24 – 1.06 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 207.54, 185.59, 171.08, 147.76, 142.64, 138.72, 134.70, 129.71, 129.20, 129.10, 128.71, 128.02, 126.94, 125.85, 121.18, 119.53, 60.34, 54.15, 51.26, 49.20, 39.25,

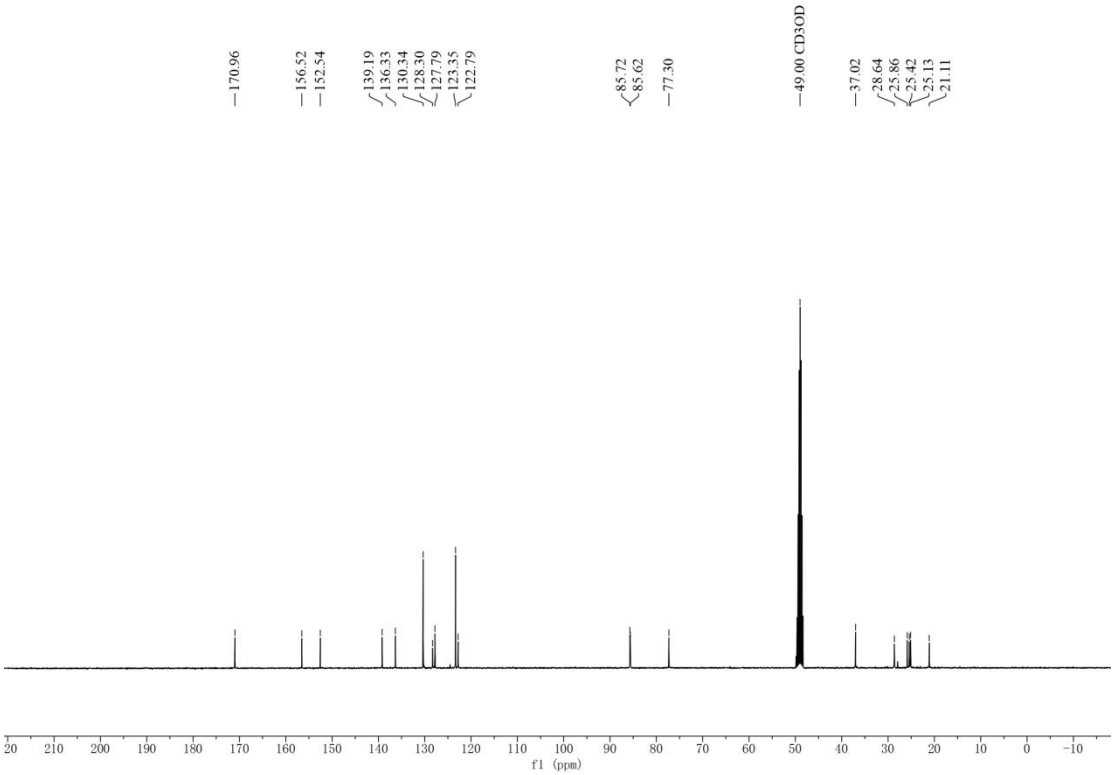
37.33, 30.09, 28.18, 28.06, 25.79, 25.51, 23.64, 23.39, 21.02, 14.18. HRMS (APCI) m/z calcd for $C_{32}H_{36}N_5O_2^+$ $(M+H)^+$: 522.2824, found 522.2823.

VII NMR Spectra

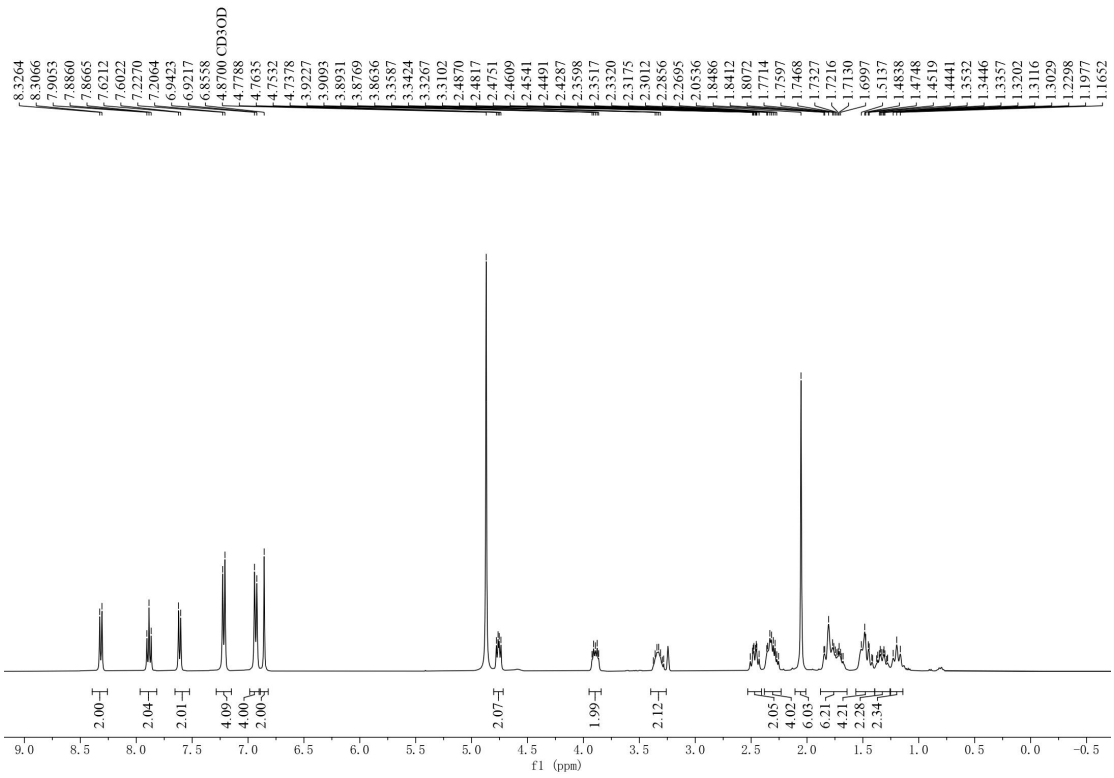
^{1}H NMR-L6 (400 MHz,) CD_3OD



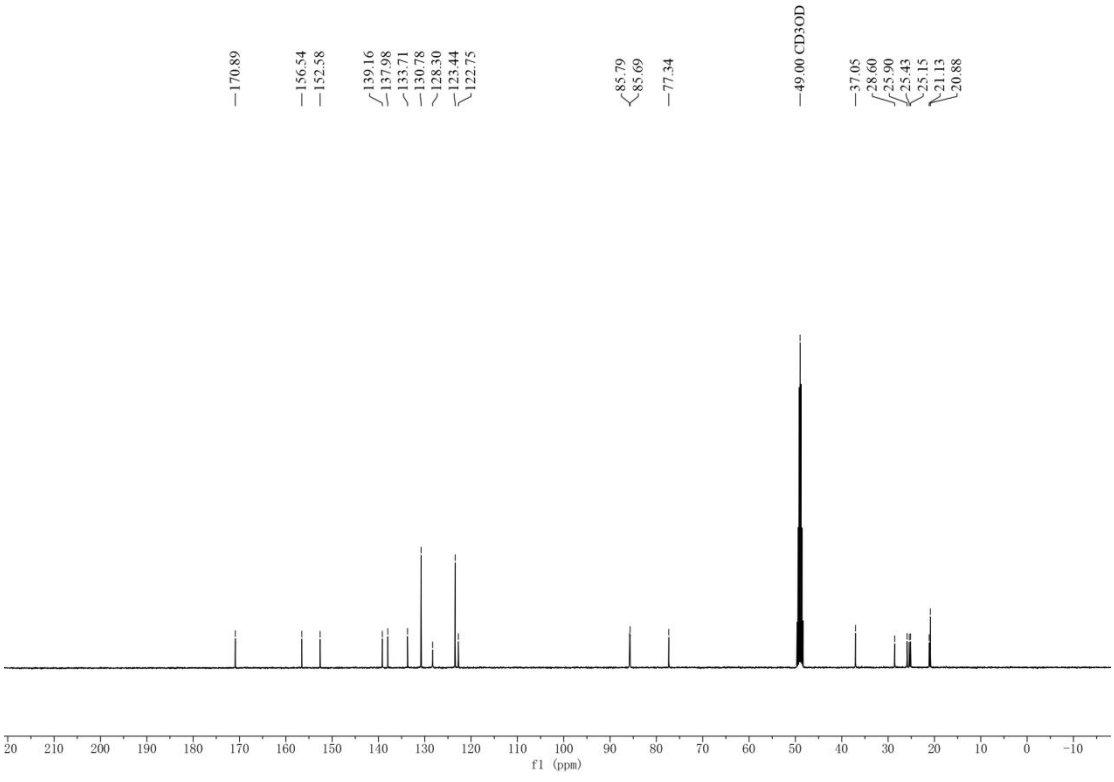
^{13}C NMR-L6 (101 MHz, CD_3OD)



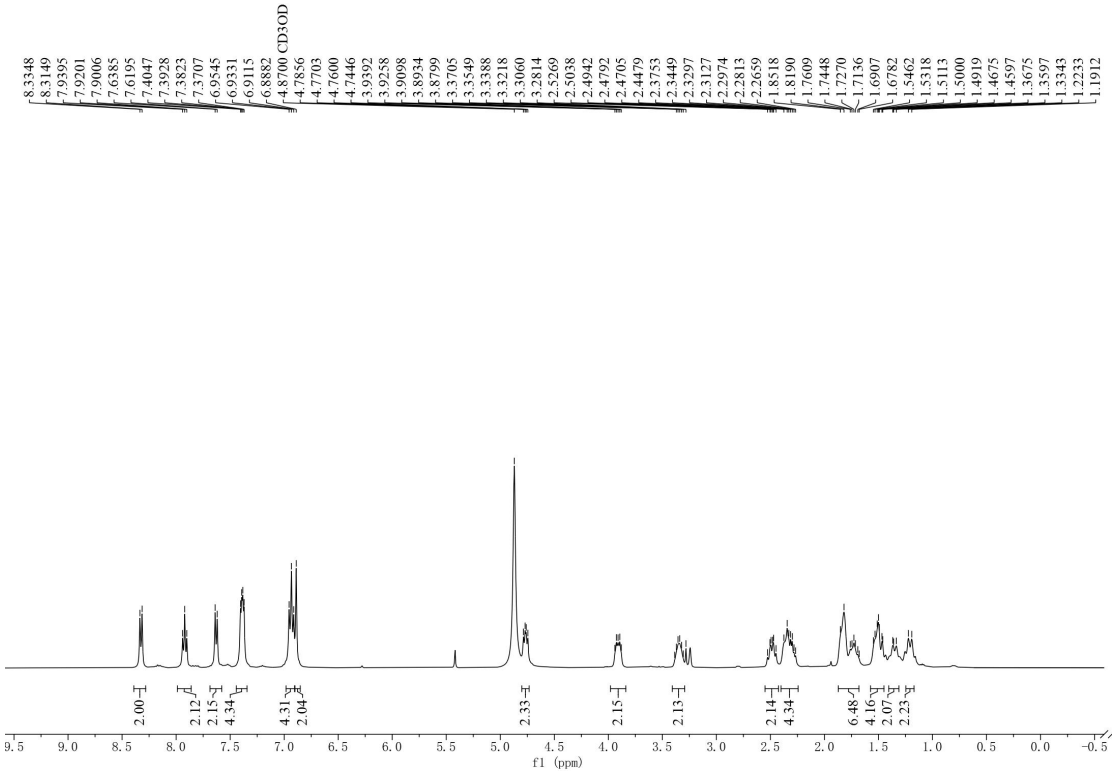
^{1}H NMR-L7 (400 MHz, CD_3OD)



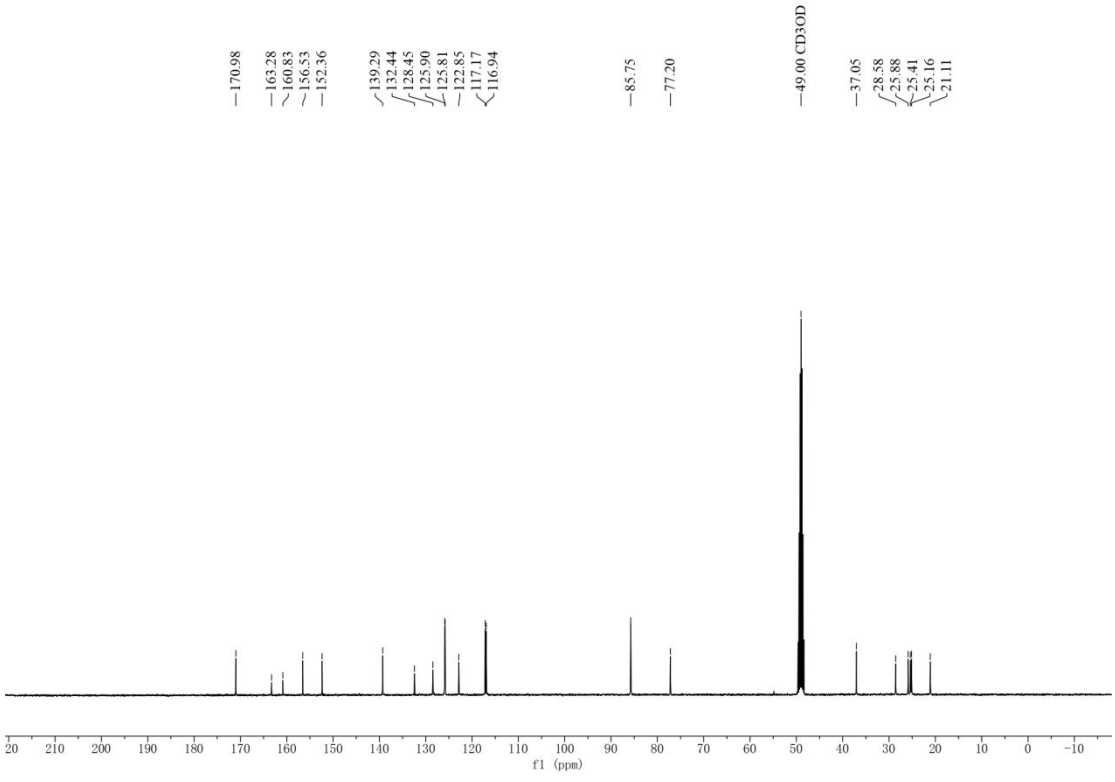
^{13}C NMR-L7 (101 MHz, CD_3OD)



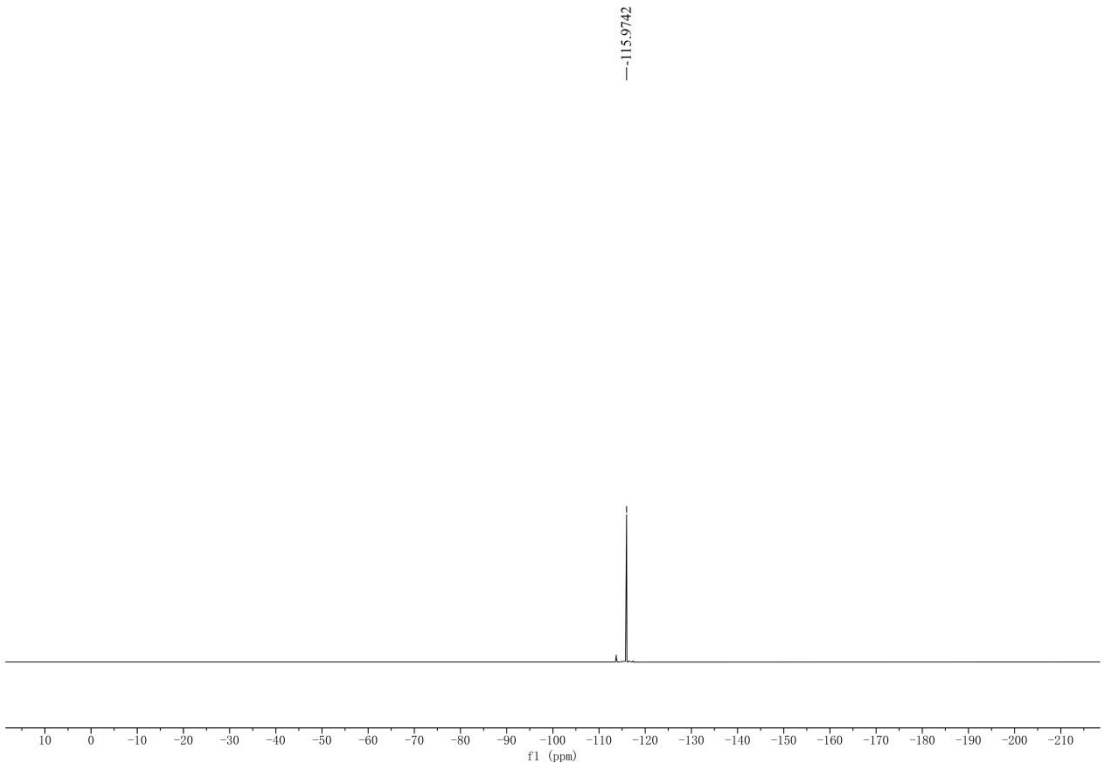
^{1}H NMR-L8 (400 MHz, CD_3OD)



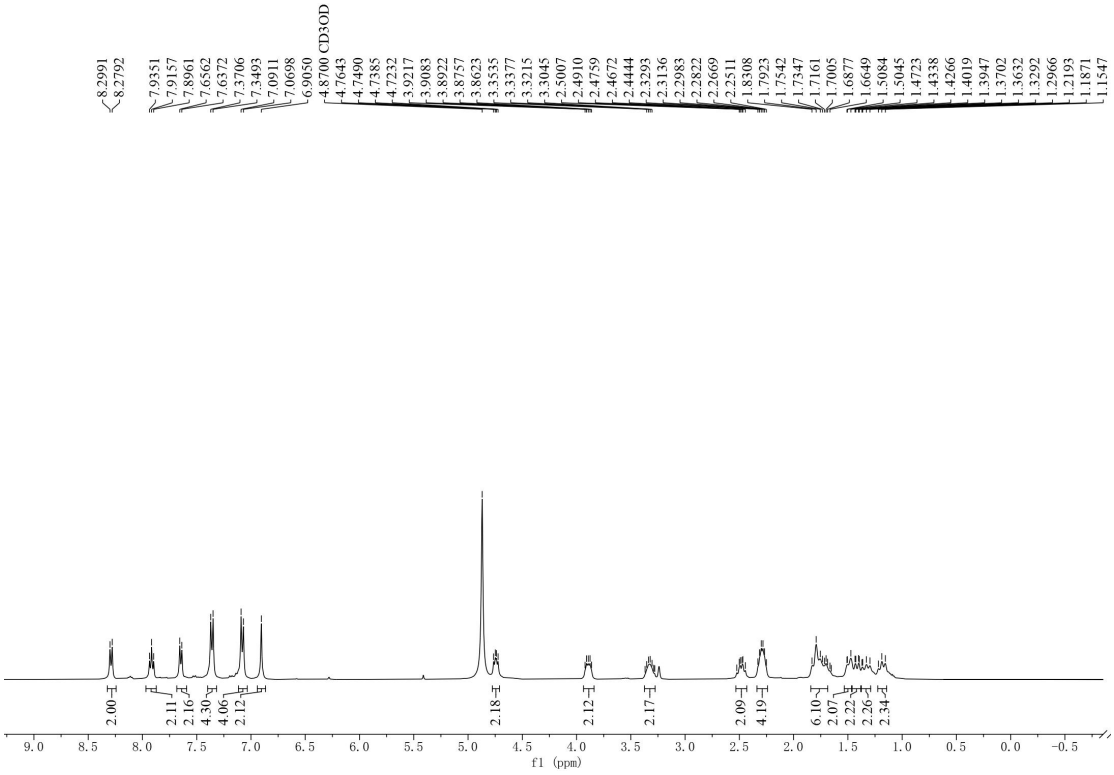
^{13}C NMR-L8 (101 MHz, CD_3OD)



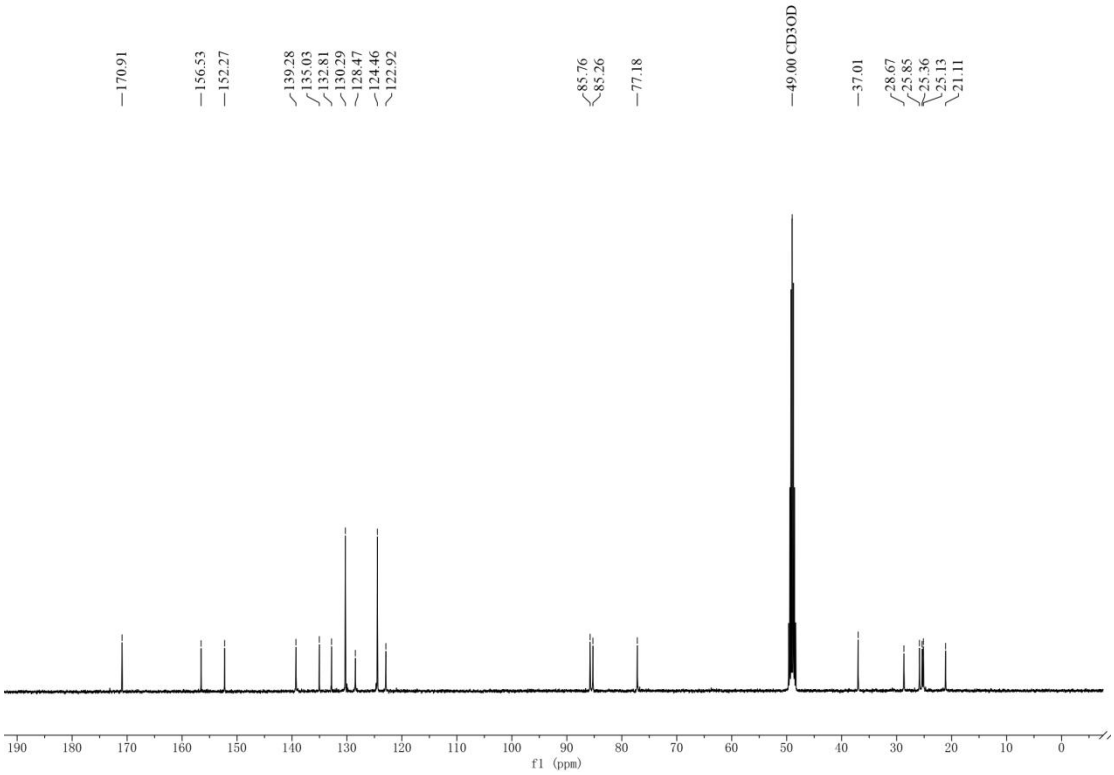
^{19}F NMR-L8 (376 MHz, CD_3OD)



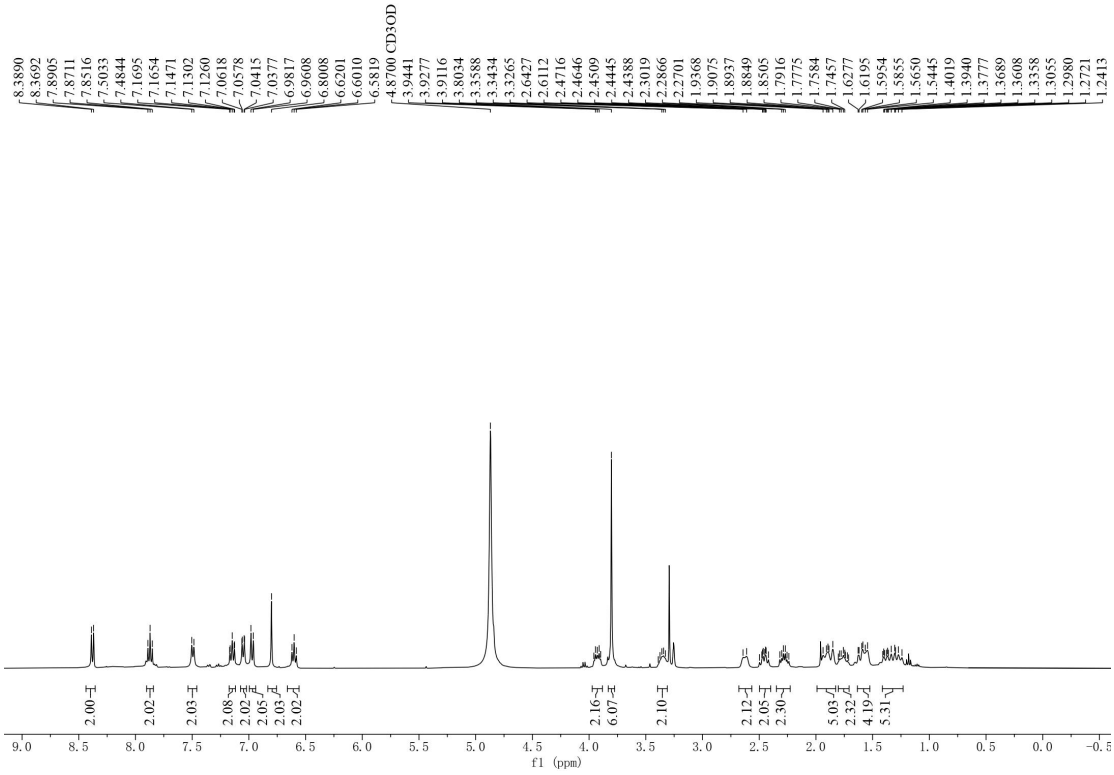
^{1}H NMR-L9 (400 MHz, CD_3OD)



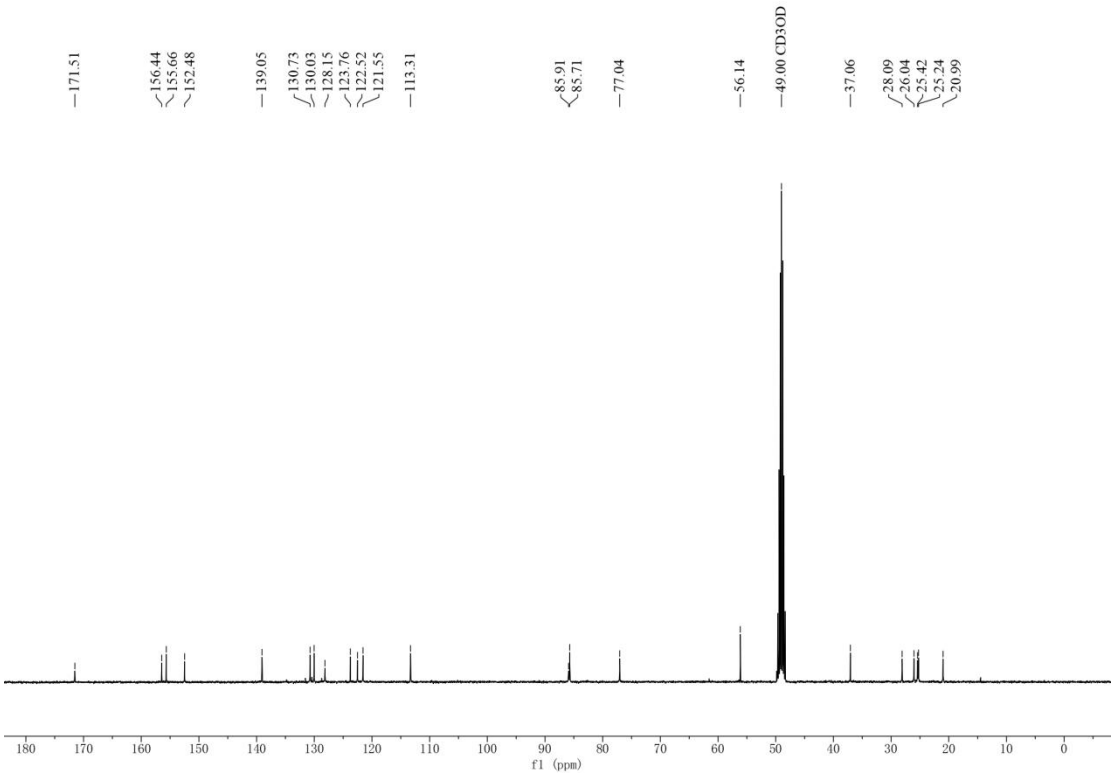
^{13}C NMR-L9 (101 MHz, CD_3OD)



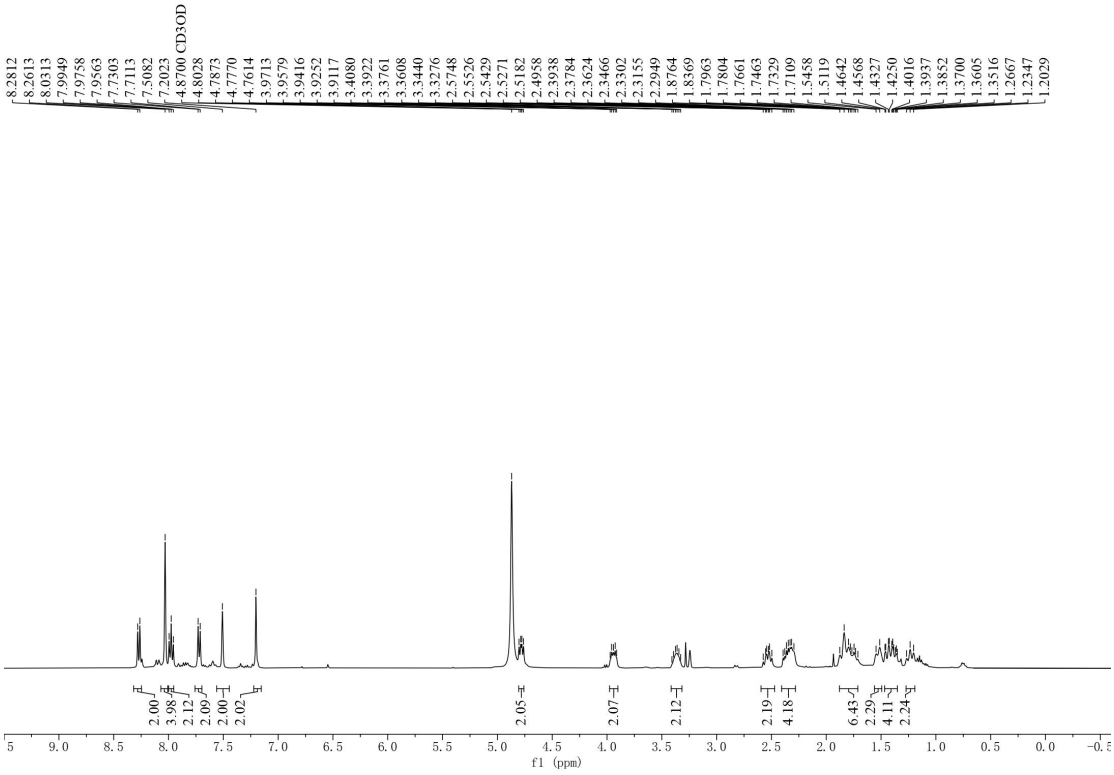
^{1}H NMR-L10 (400 MHz, CD_3OD)



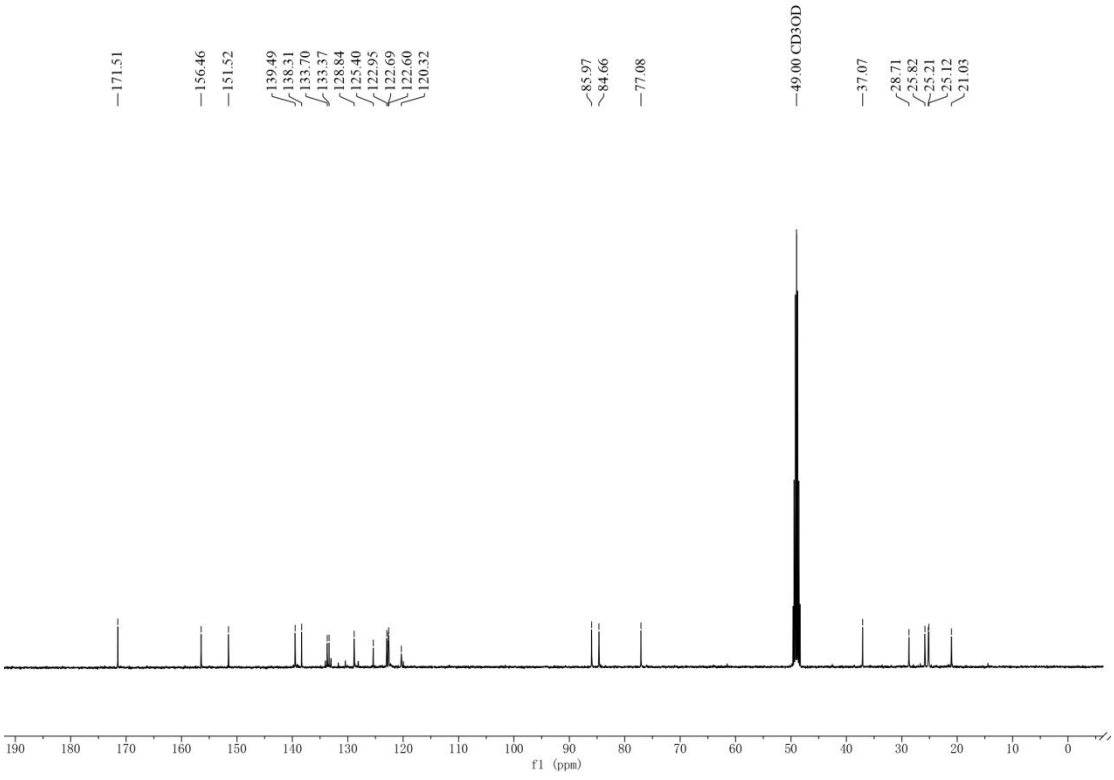
^{13}C NMR-L10 (100 MHz, CD_3OD)



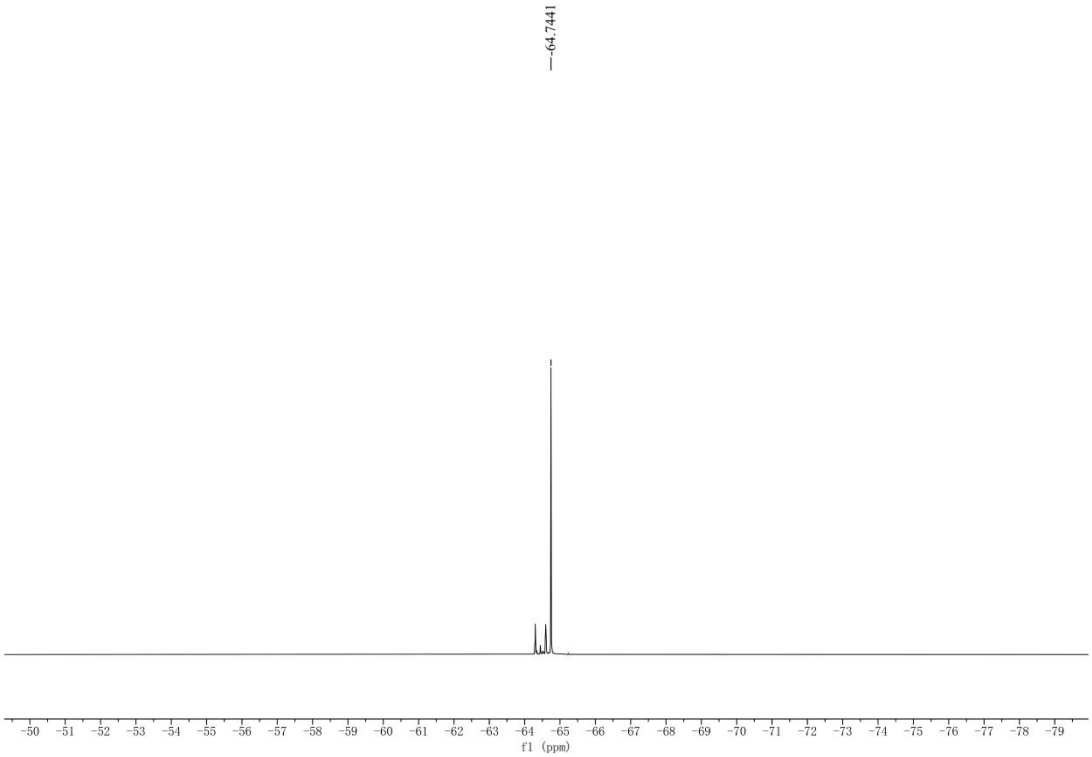
^{1}H NMR-L11 (400 MHz, CD_3OD)



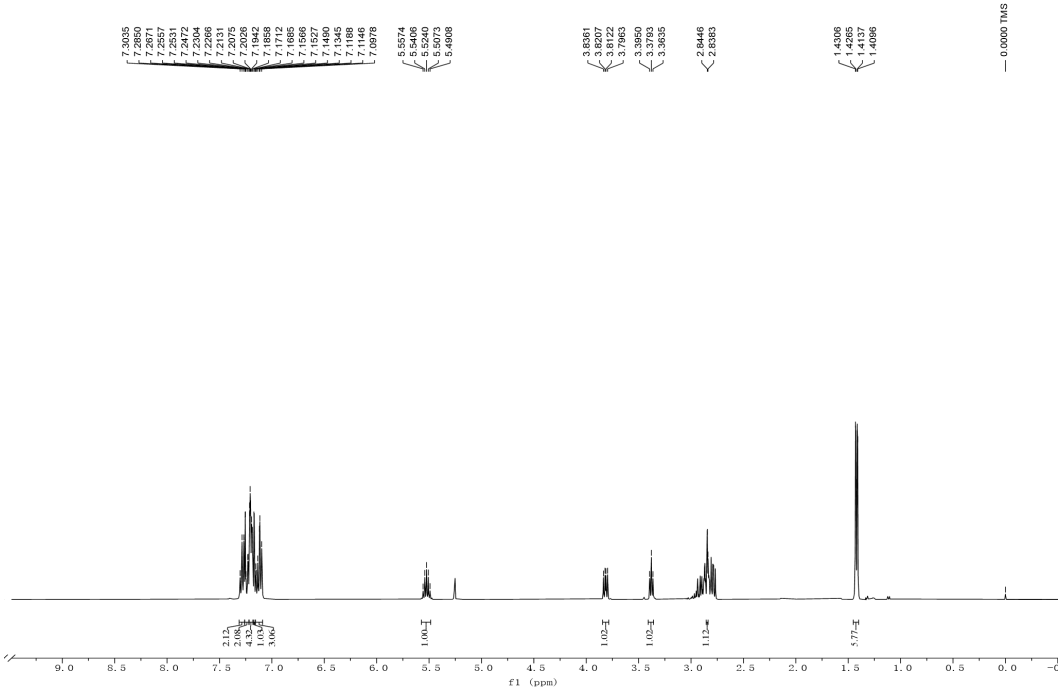
^{13}C NMR-L11 (101 MHz, CD_3OD)



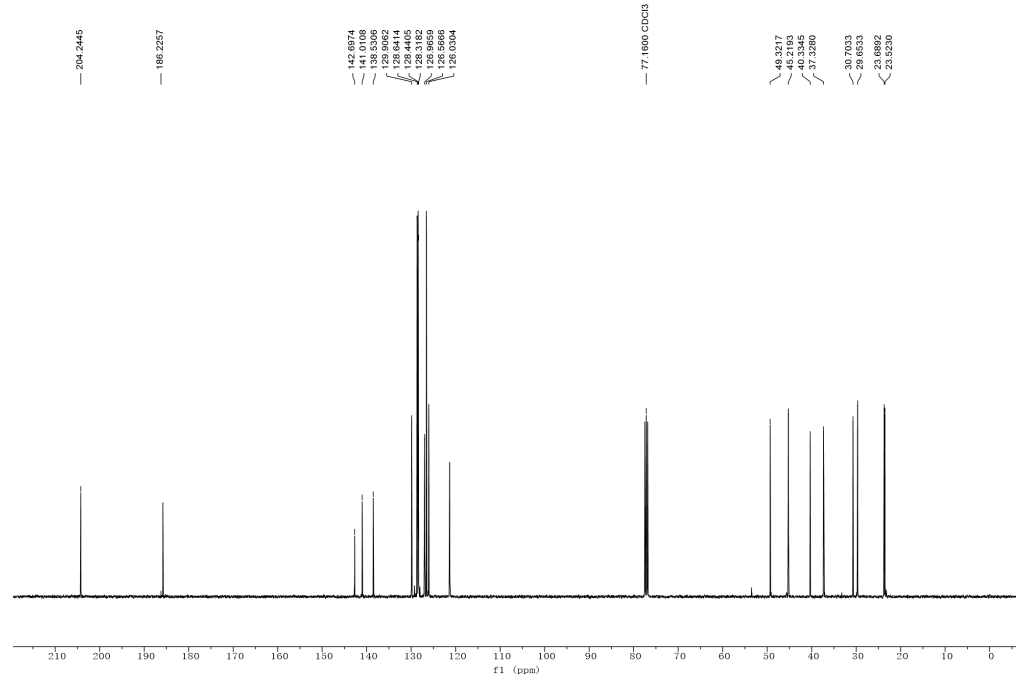
^{19}F NMR-L11 (376 MHz, CD_3OD)



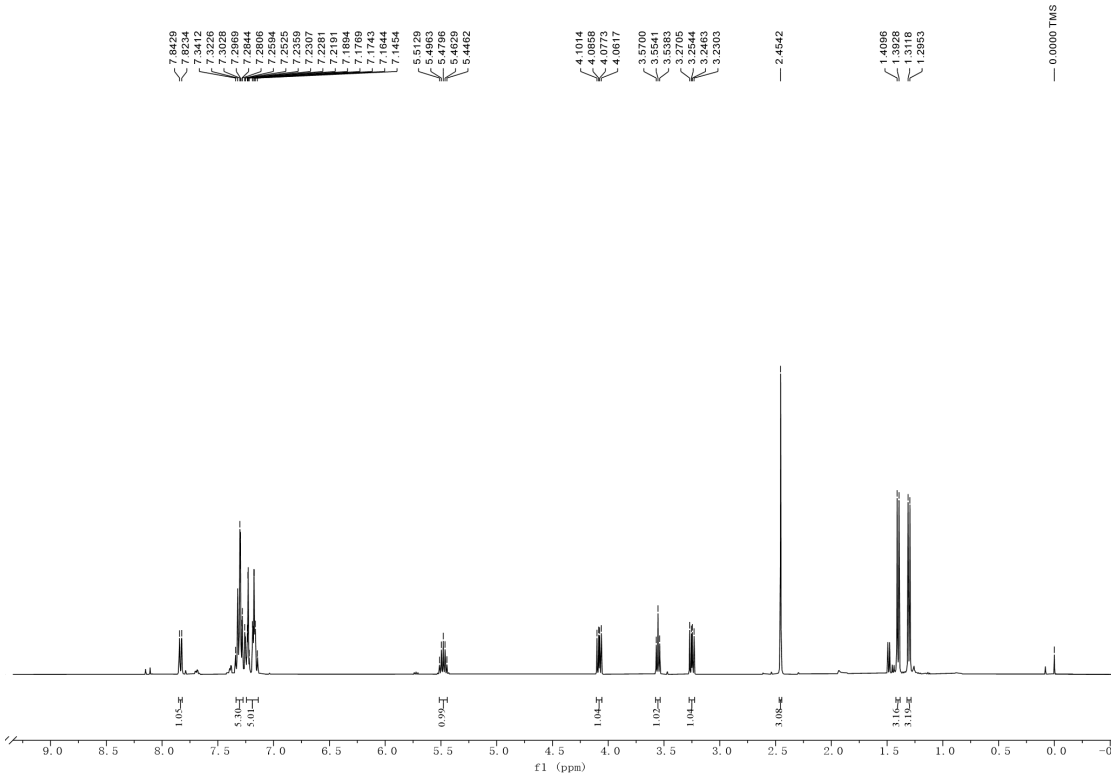
^{1}H NMR-3a (400 MHz, $CDCl_3$)



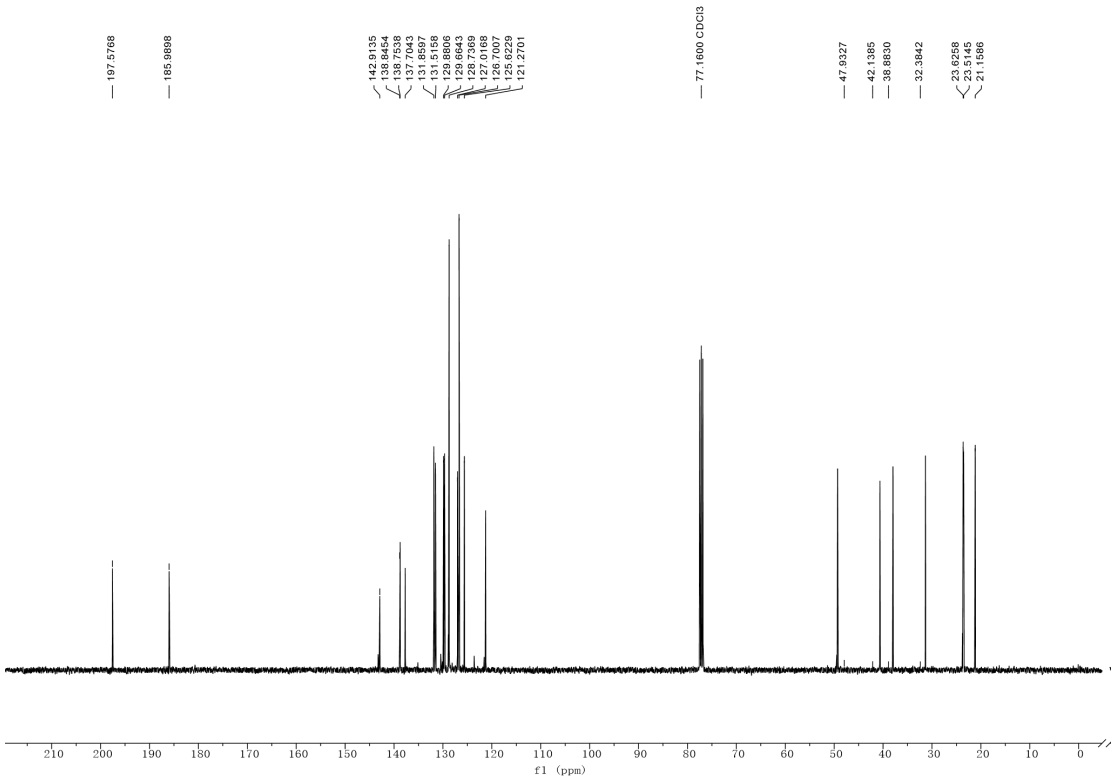
^{13}C NMR-3a (101 MHz, $CDCl_3$)



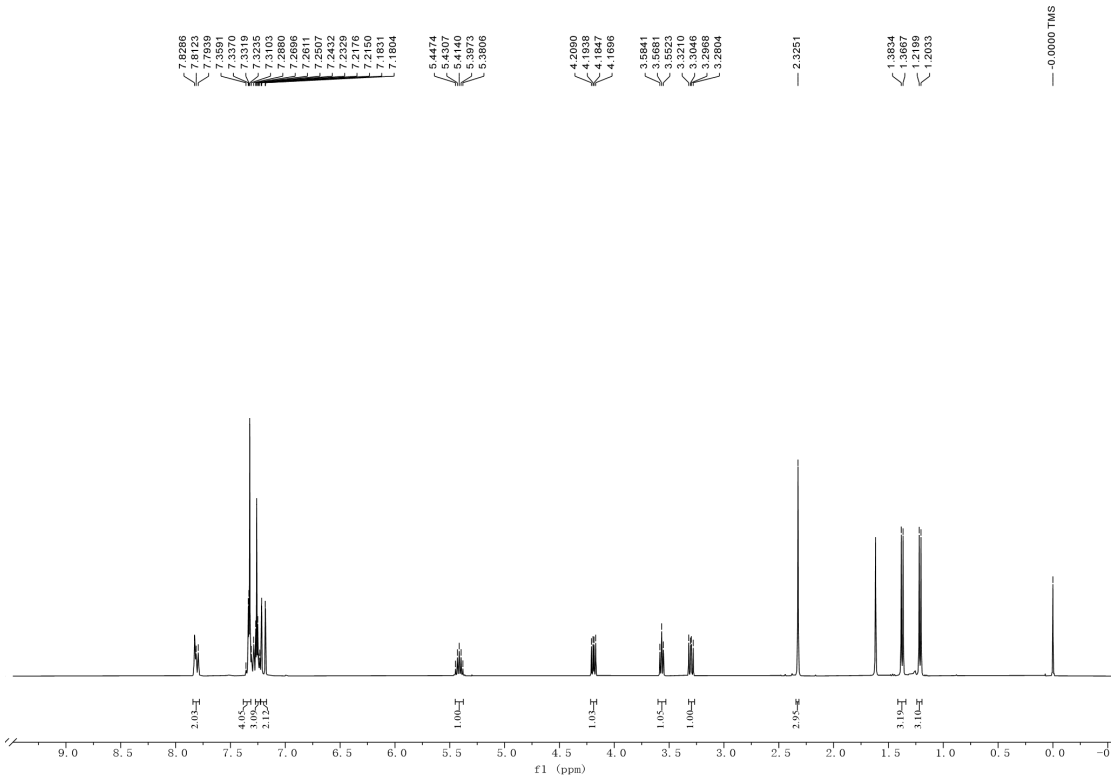
^{1}H NMR-3b (400 MHz, $CDCl_3$)



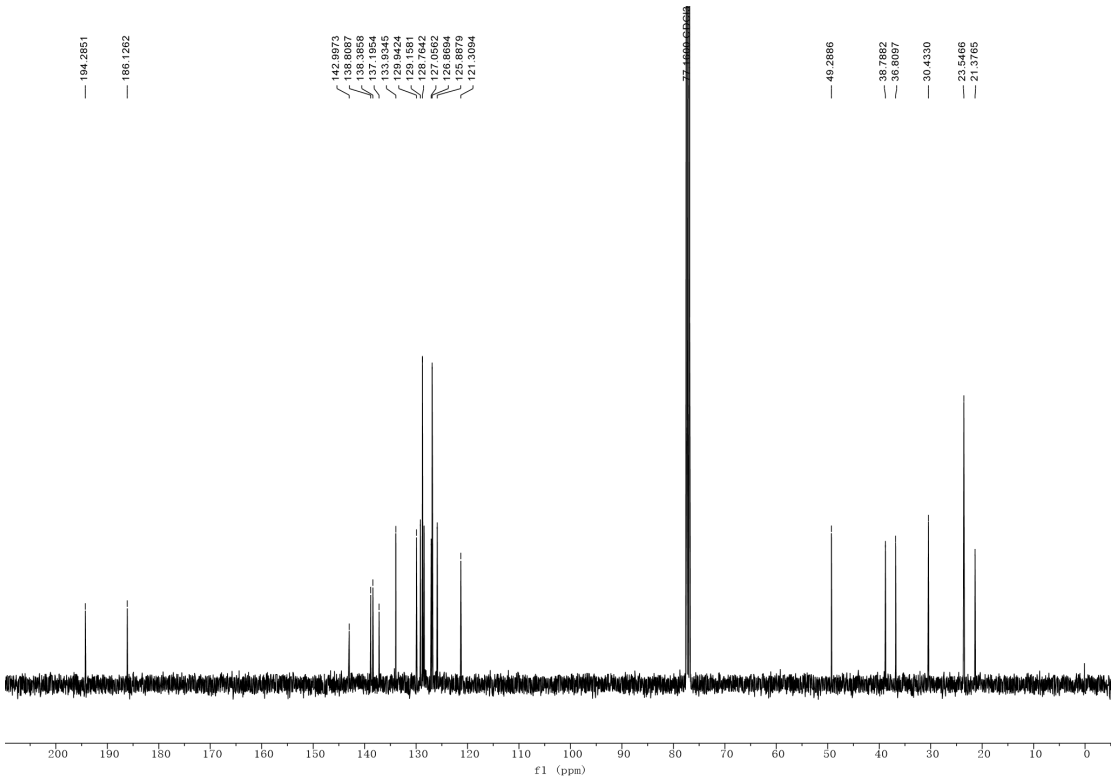
^{13}C NMR-3b (101 MHz, $CDCl_3$)



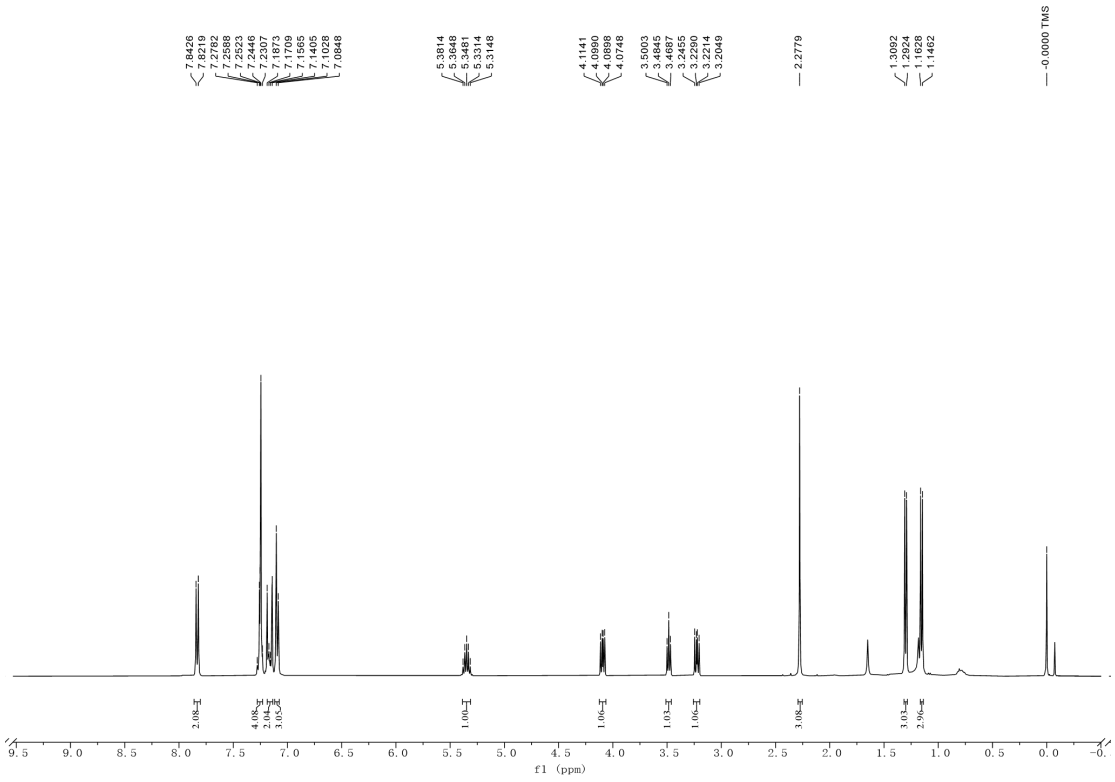
^{1}H NMR-3c (400 MHz, $CDCl_3$)



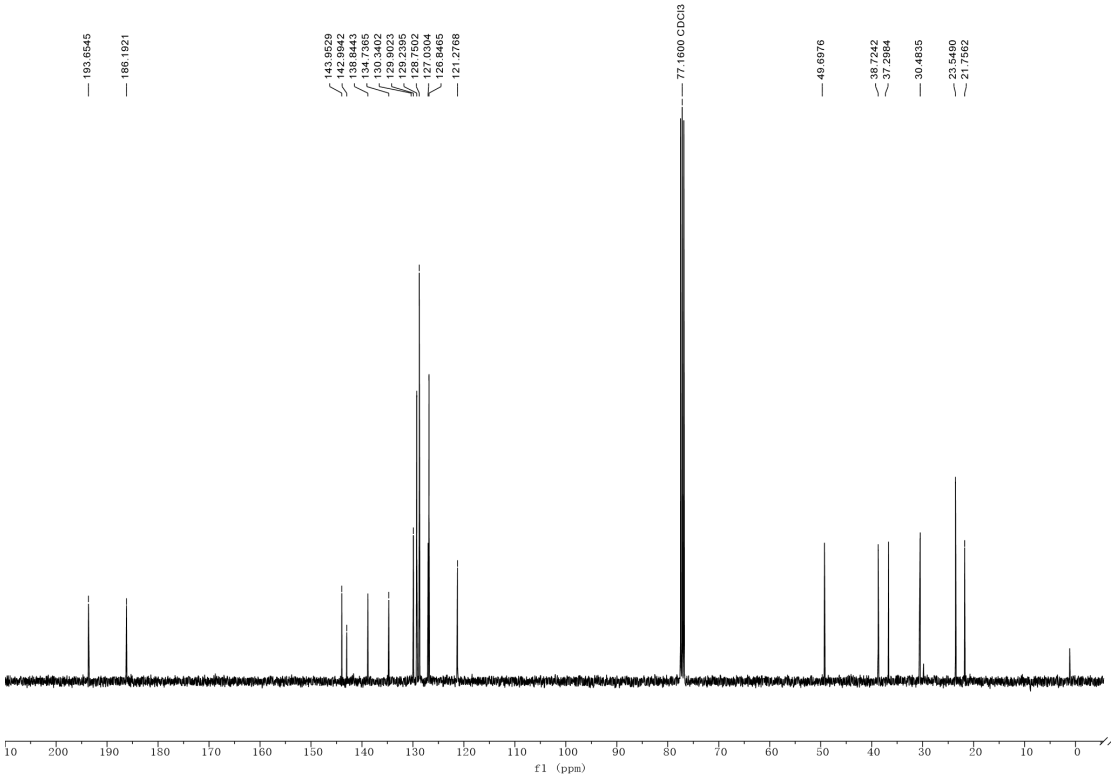
^{13}C NMR-3c (101 MHz, $CDCl_3$)



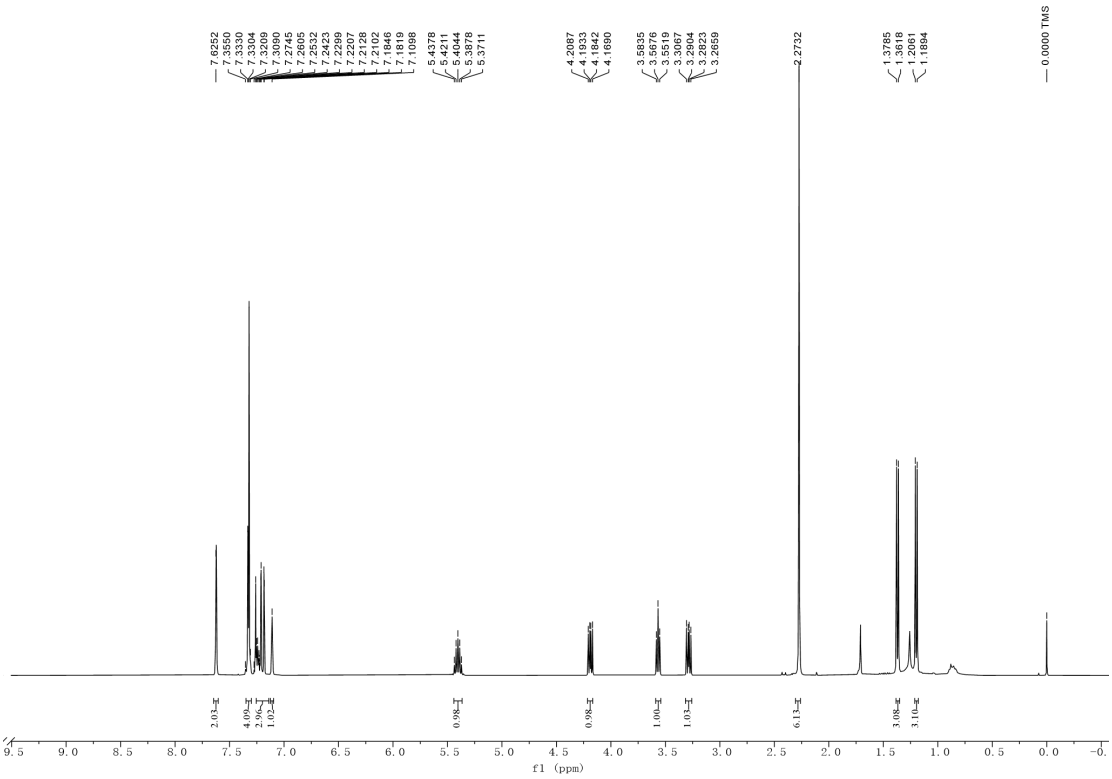
^{1}H NMR-3d (400 MHz, $CDCl_3$)



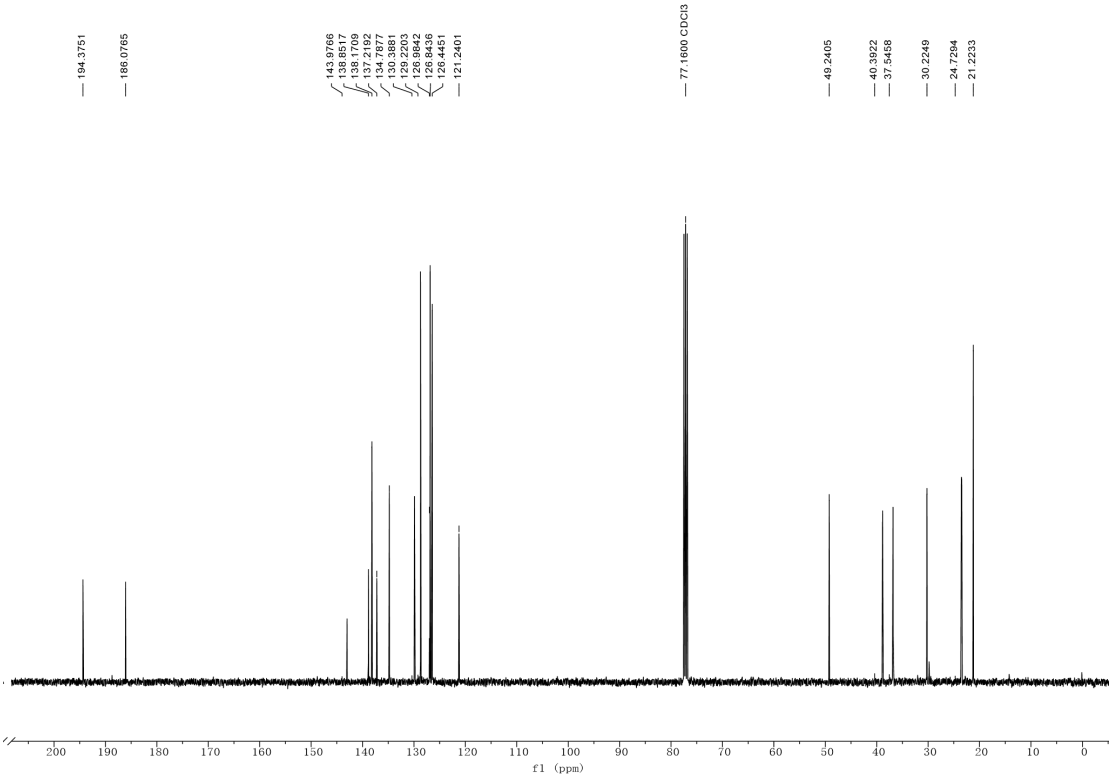
^{13}C NMR-3d (101 MHz, $CDCl_3$)



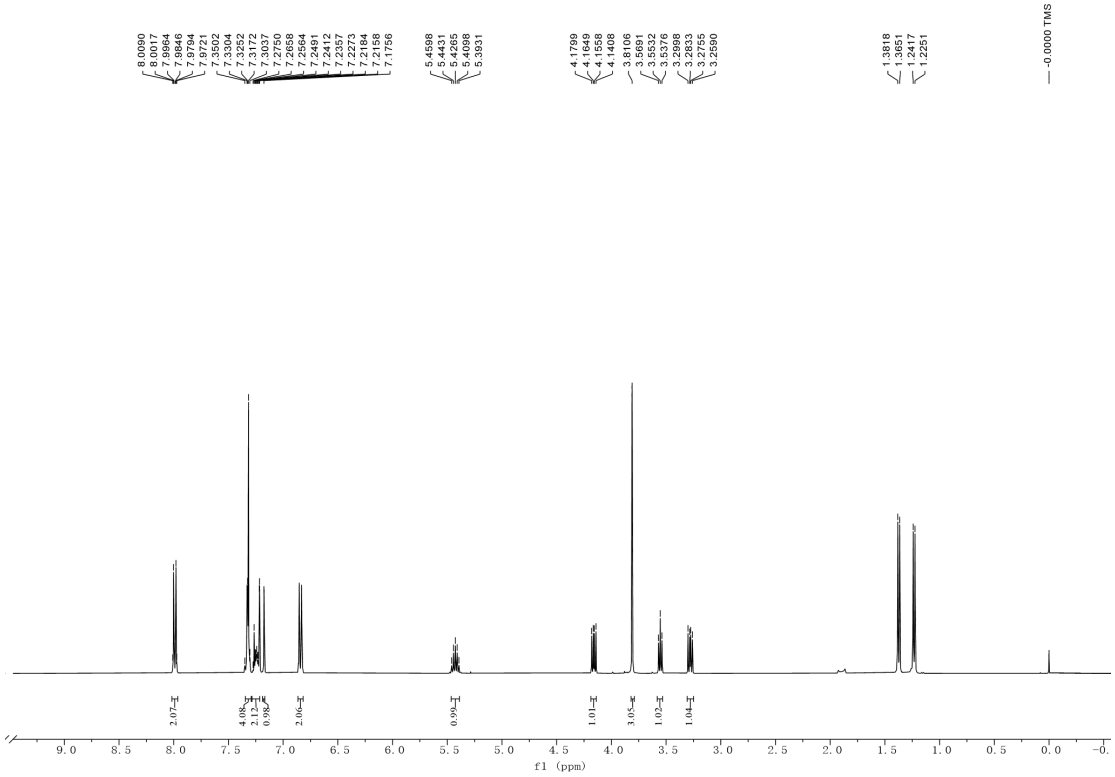
^{1}H NMR-3e (400 MHz, $CDCl_3$)



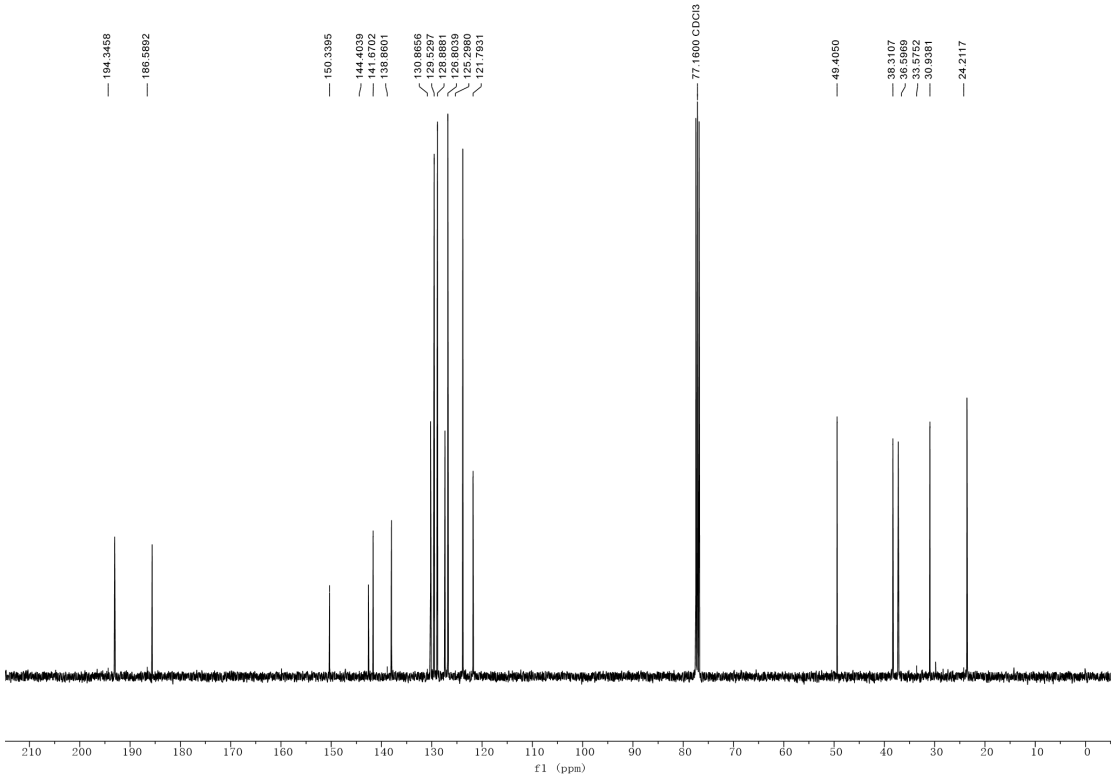
^{13}C NMR-3e (101MHz, $CDCl_3$)



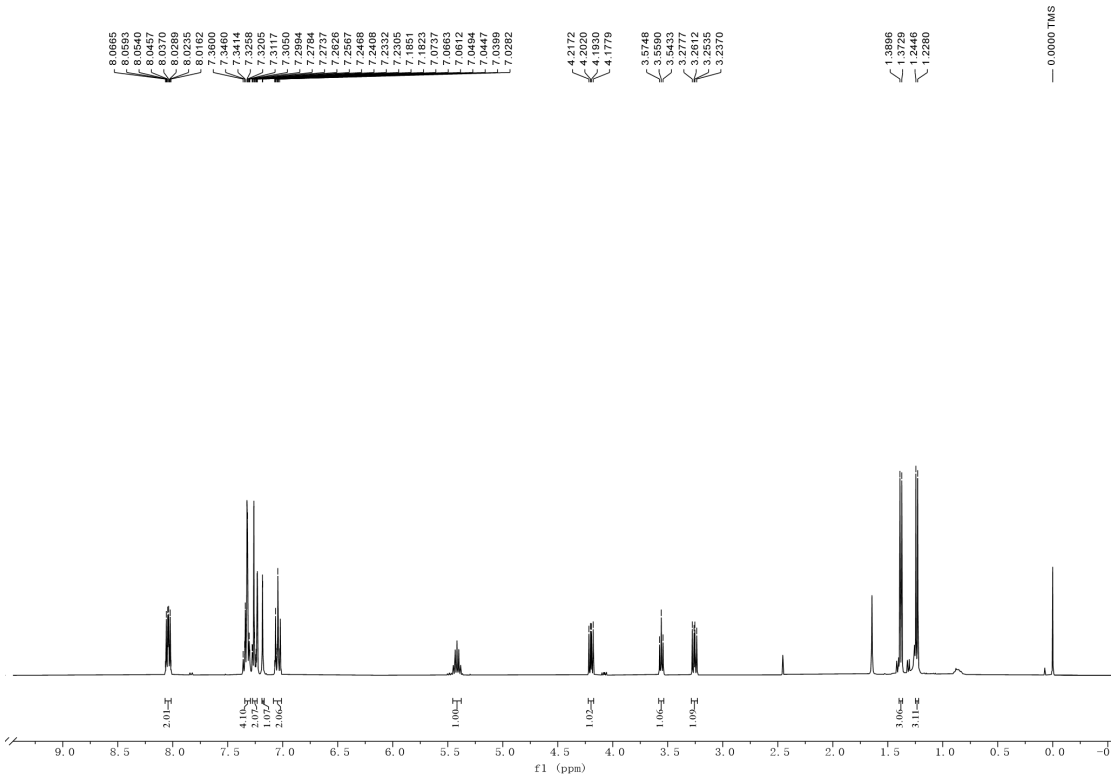
^{1}H NMR-3f (400 MHz, $CDCl_3$)



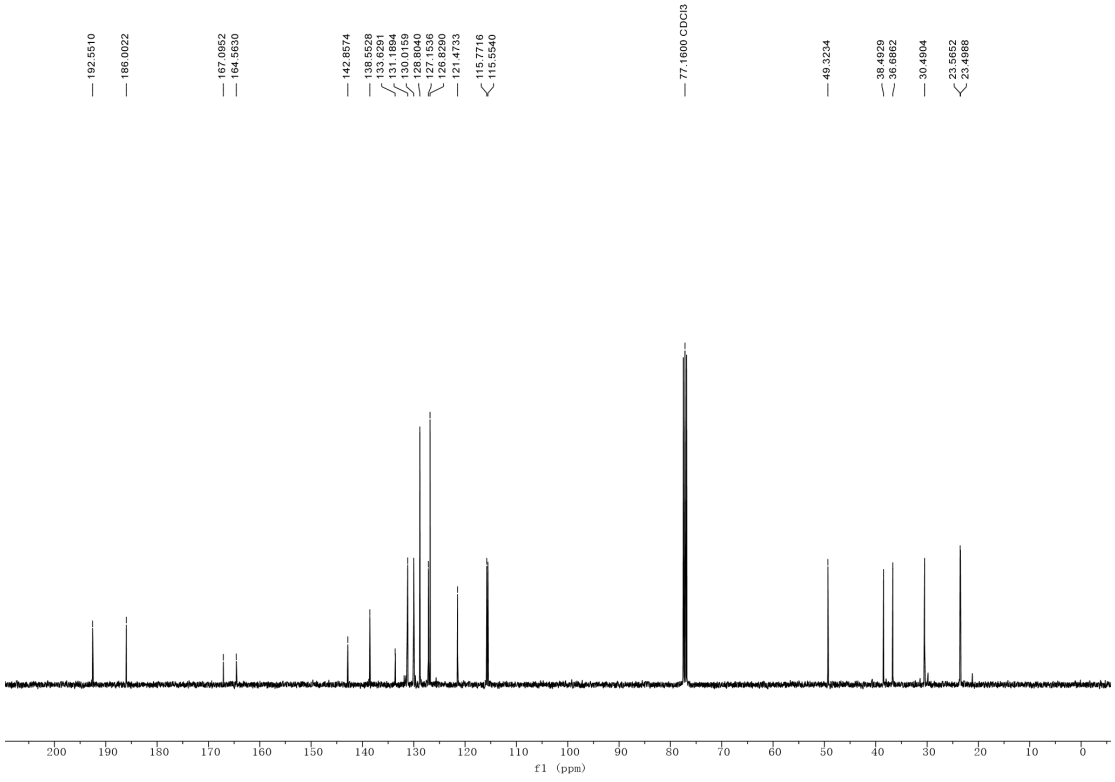
^{13}C NMR-3f (101 MHz, $CDCl_3$)



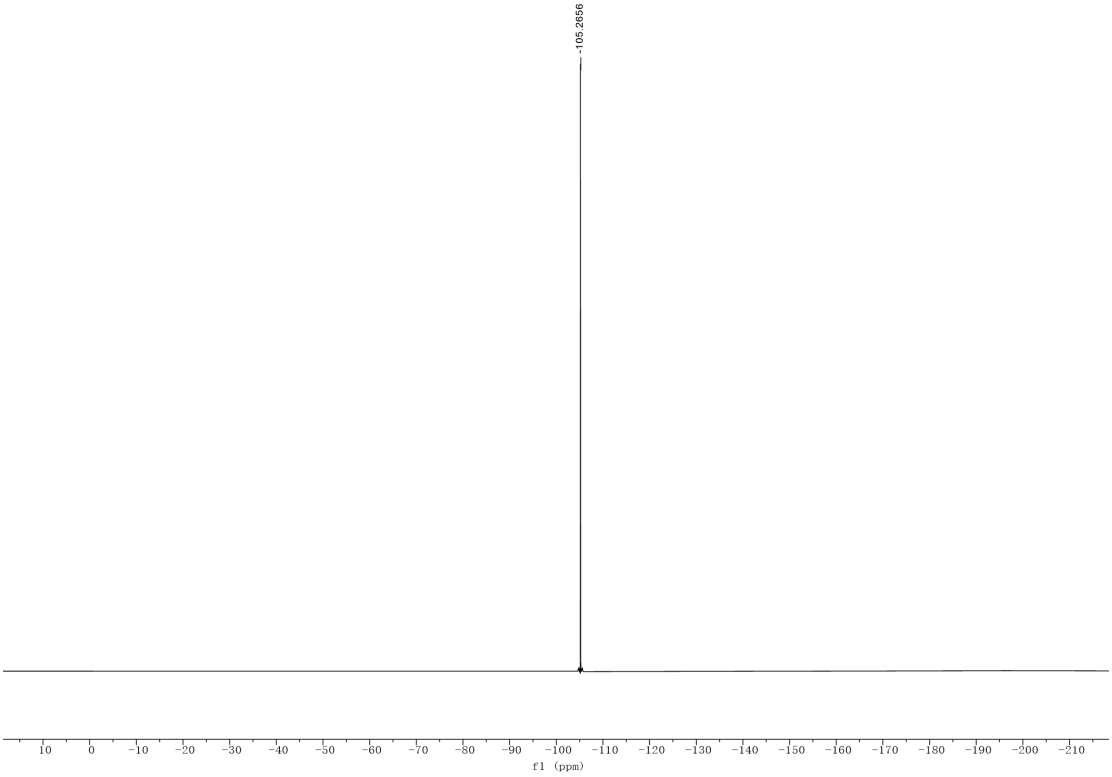
^{1}H NMR-3g (400 MHz, $CDCl_3$)



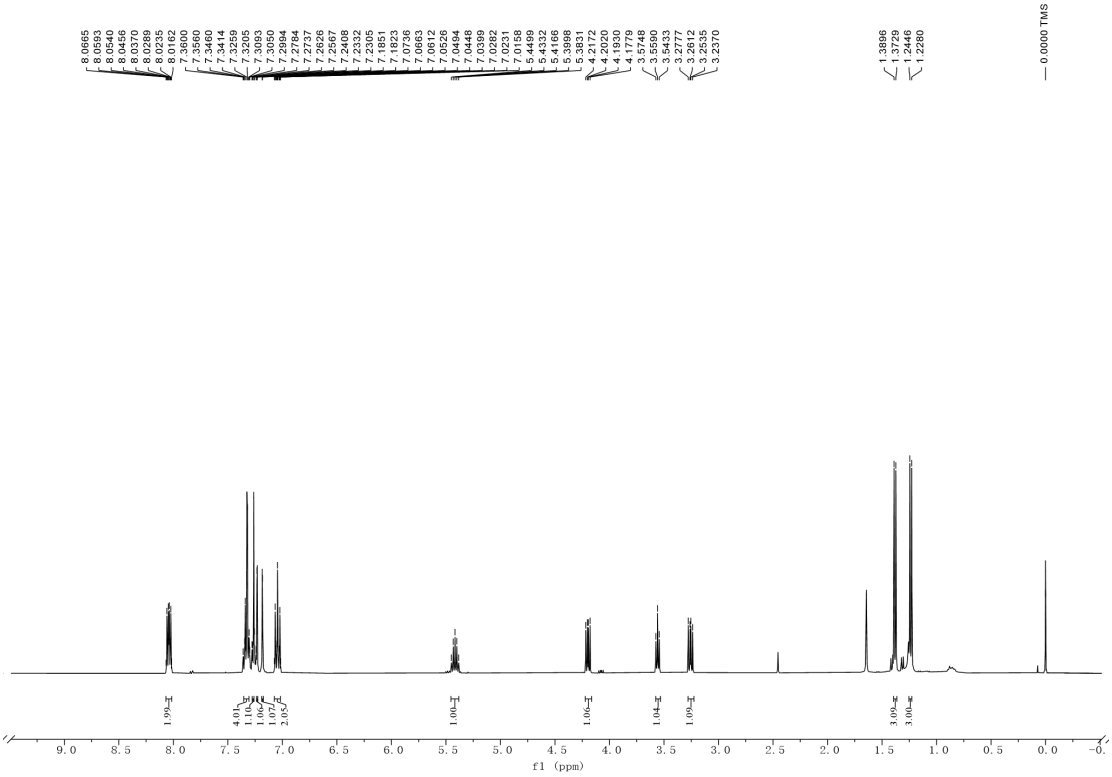
^{13}C NMR-3g (101 MHz, $CDCl_3$)



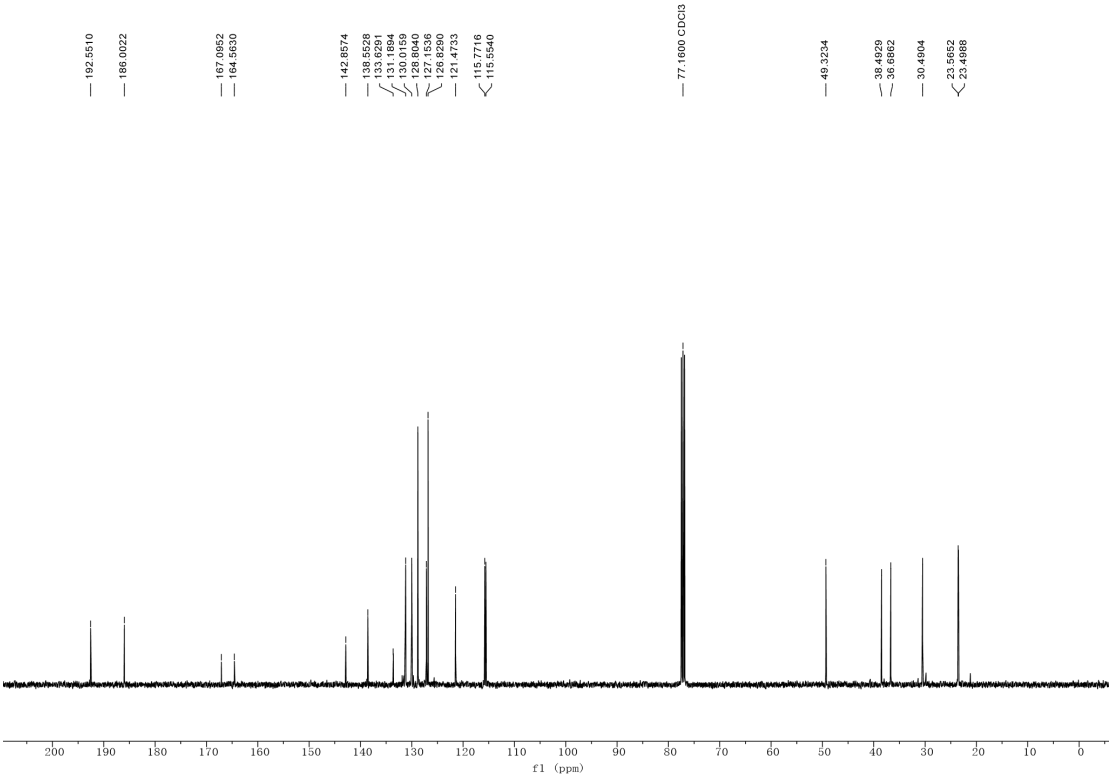
^{19}F NMR-3g (376 MHz, $CDCl_3$)



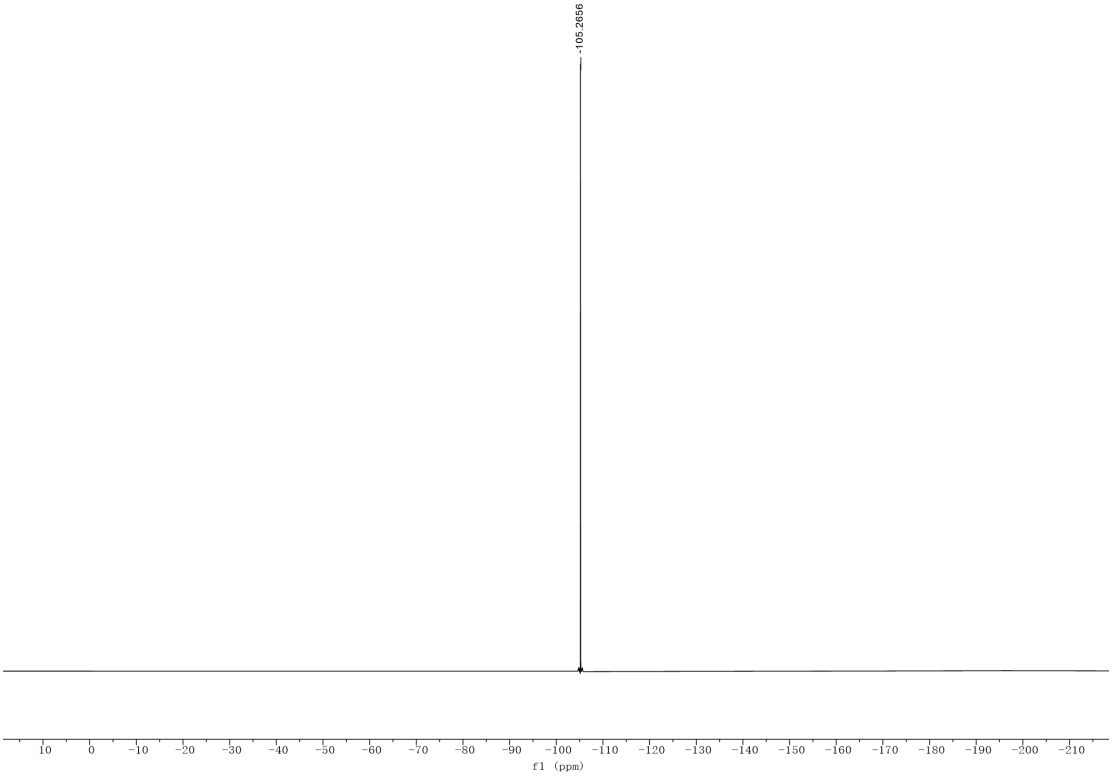
^{1}H NMR-3h (400 MHz, $CDCl_3$)



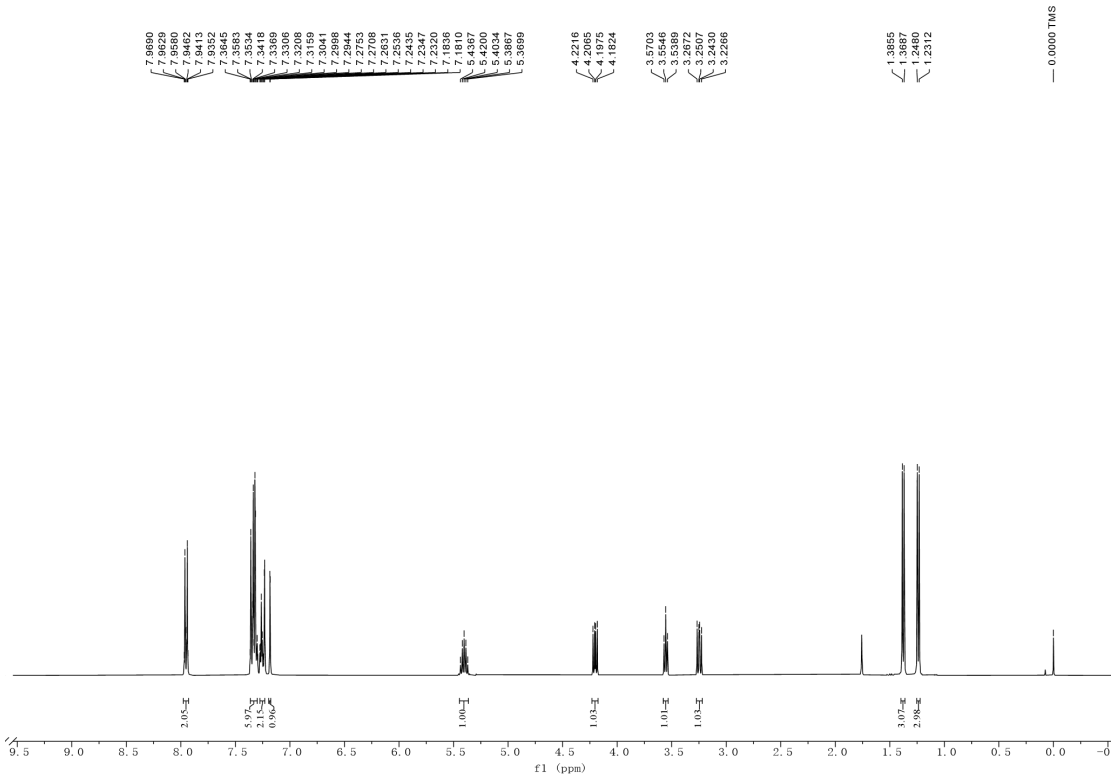
^{13}C NMR-3h (101 MHz, $CDCl_3$)



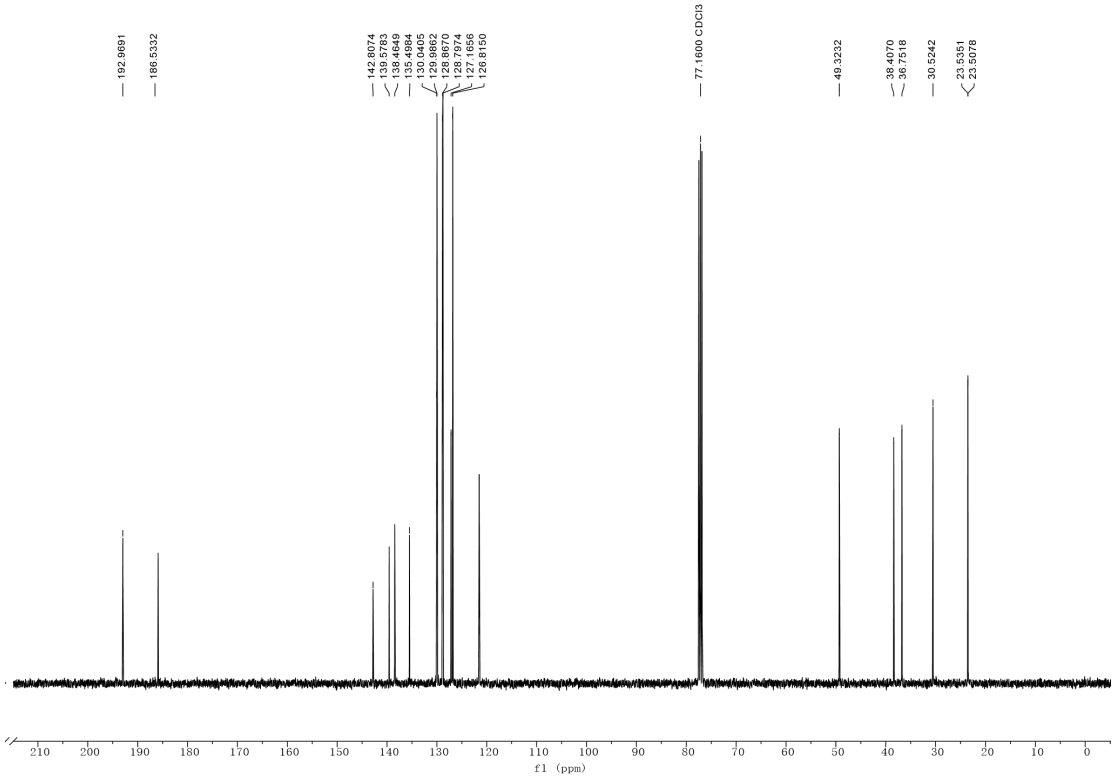
^{19}F NMR-3h (376 MHz, $CDCl_3$)



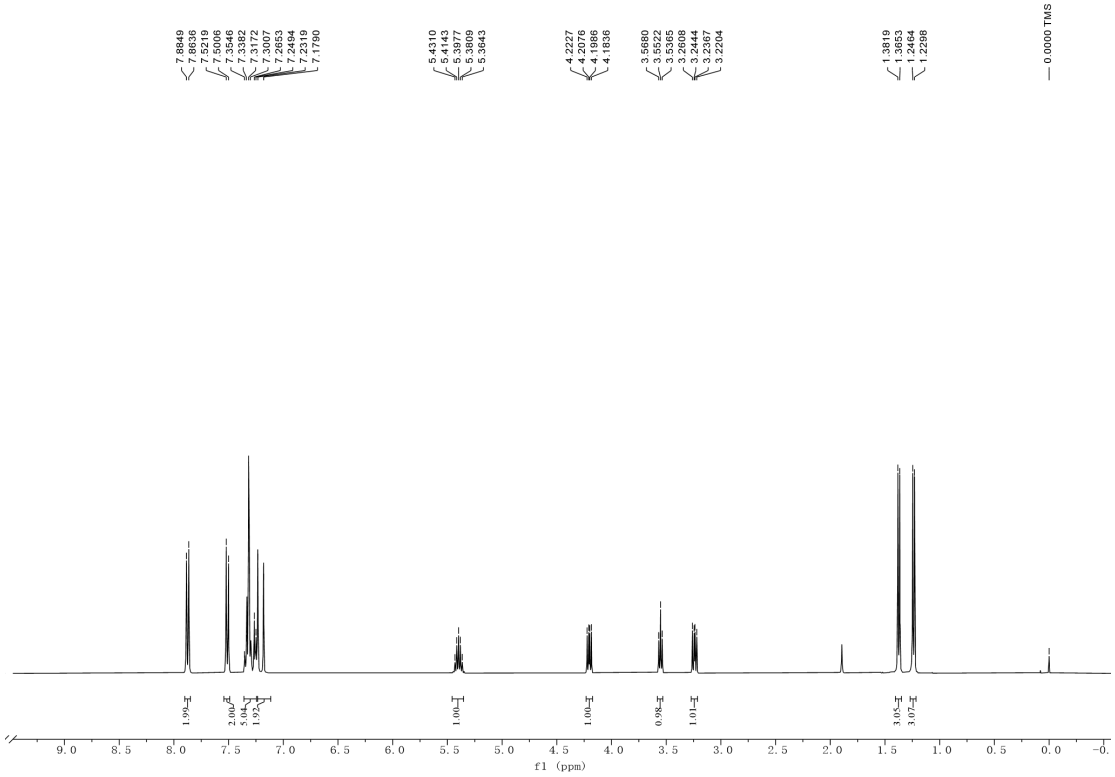
^{1}H NMR-3i (400 MHz, $CDCl_3$)



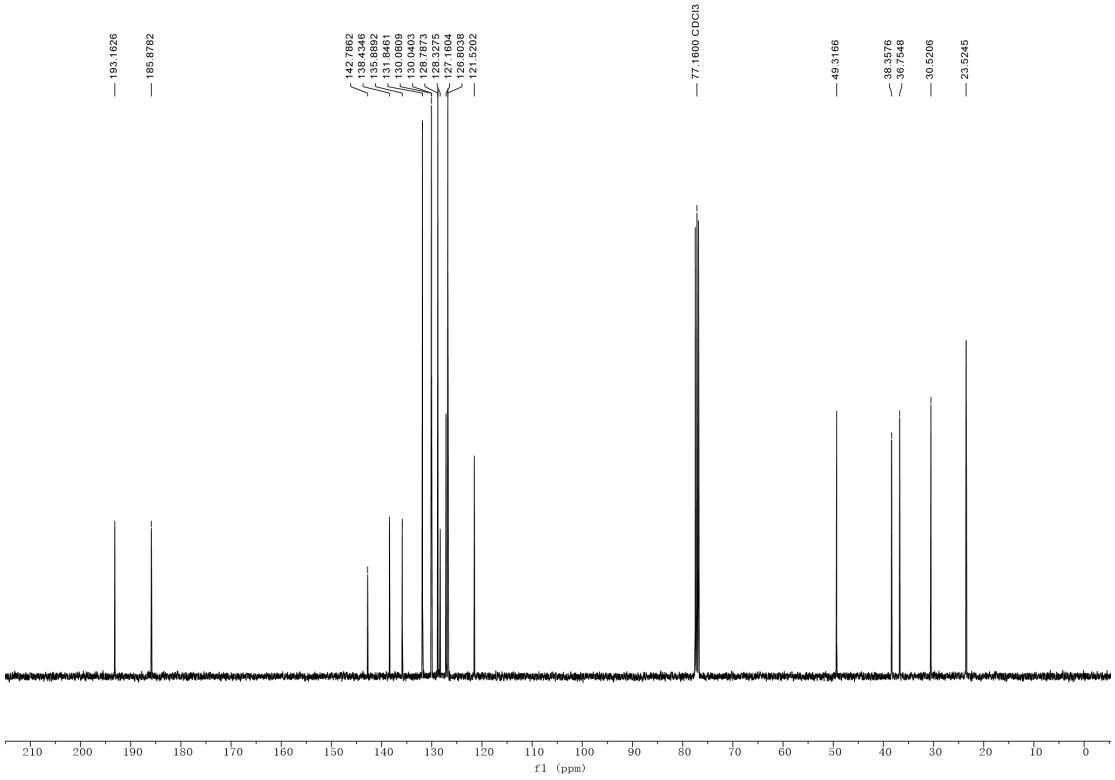
^{13}C NMR-3i (101 MHz, $CDCl_3$)



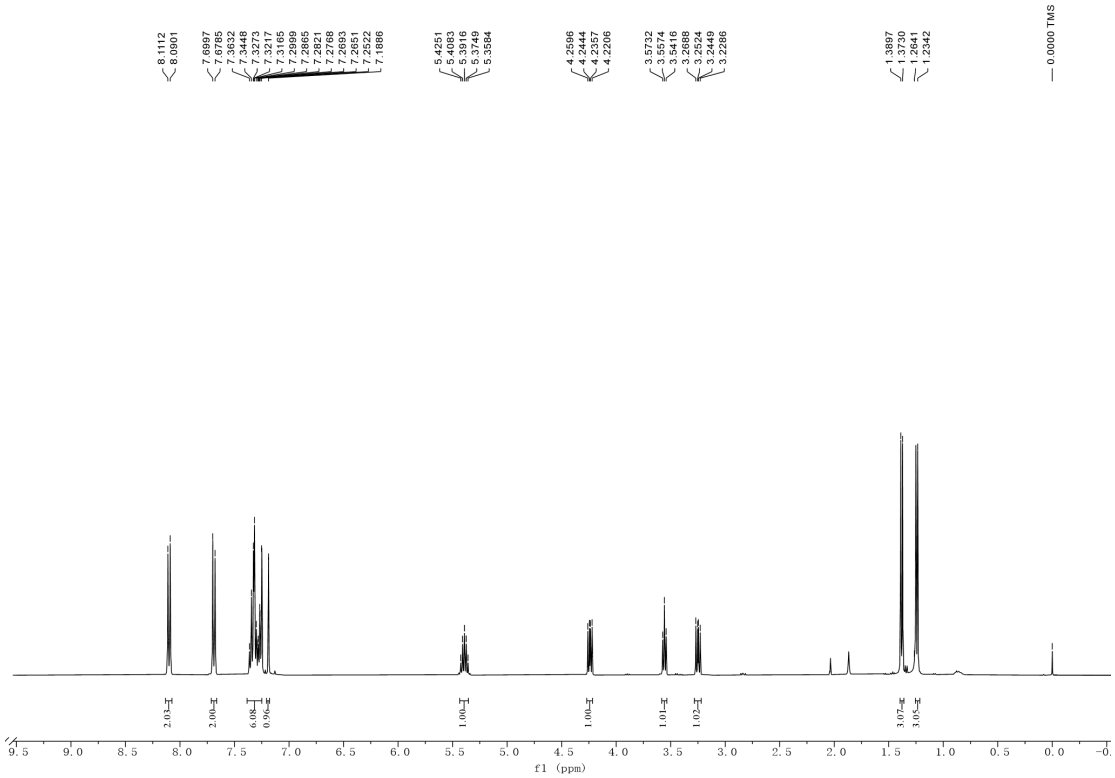
^{1}H NMR-3j (400 MHz, $CDCl_3$)



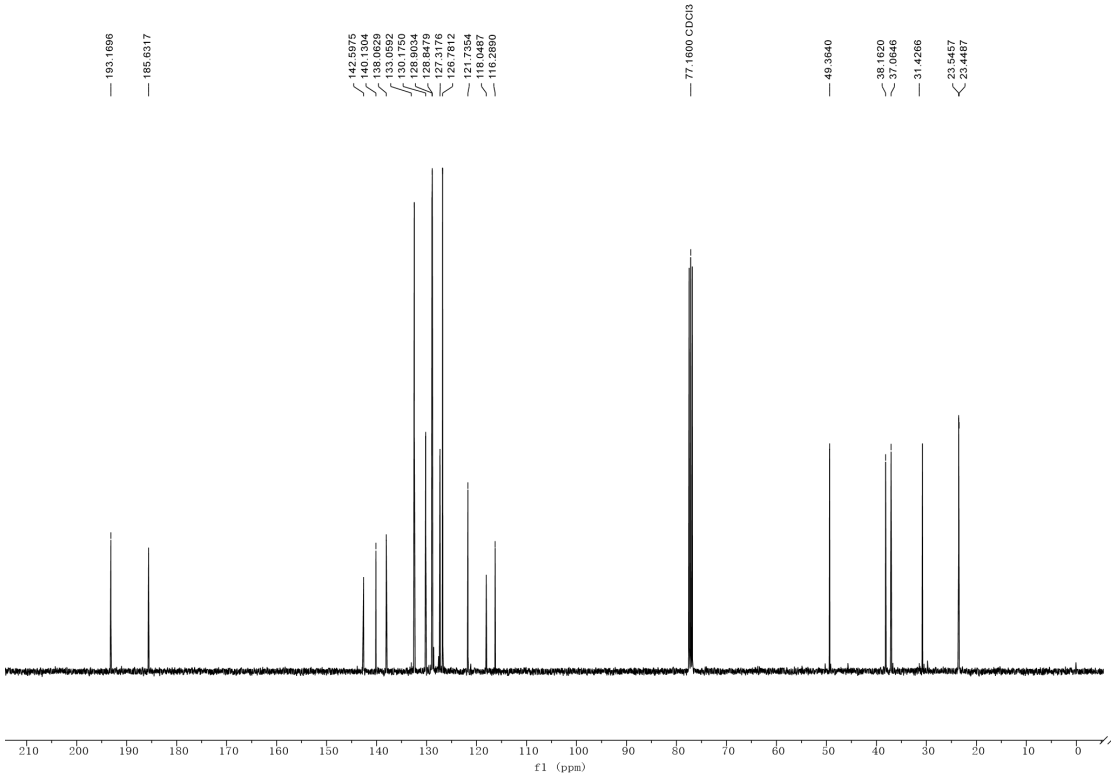
^{13}C NMR-3j (101 MHz, $CDCl_3$)



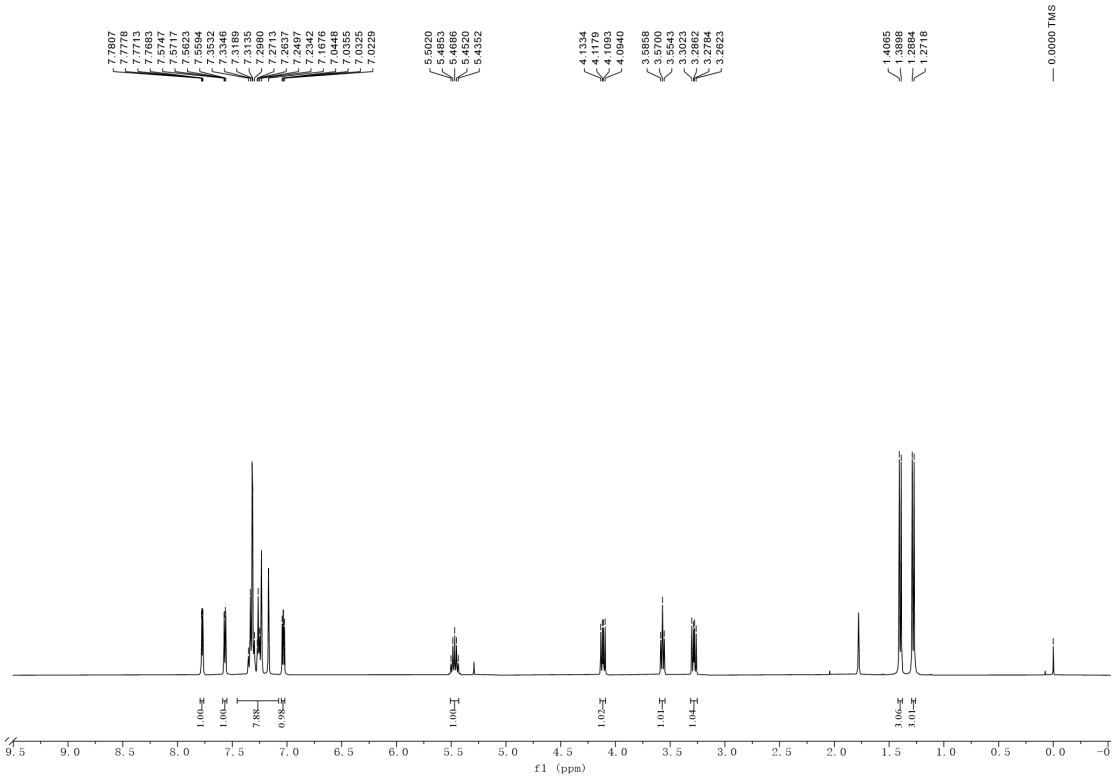
^{1}H NMR-3k (400 MHz, $CDCl_3$)



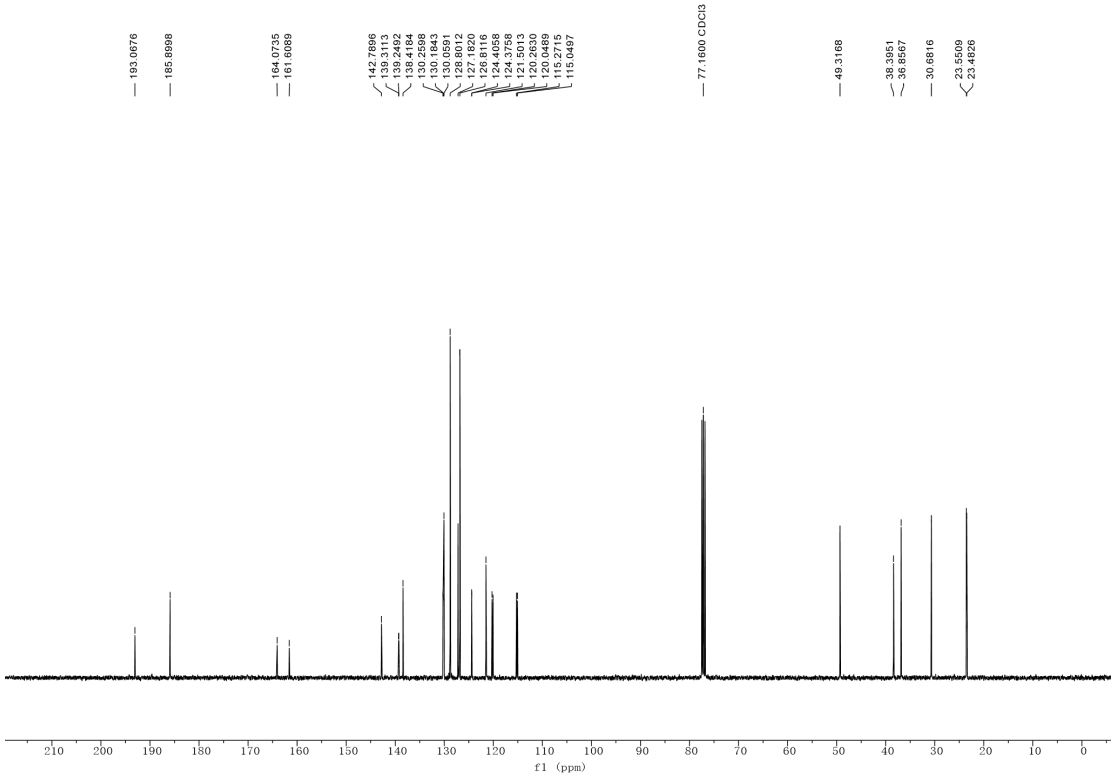
^{13}C NMR-3k (101 MHz, $CDCl_3$)



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



^{13}C NMR-3l (101 MHz, $CDCl_3$)



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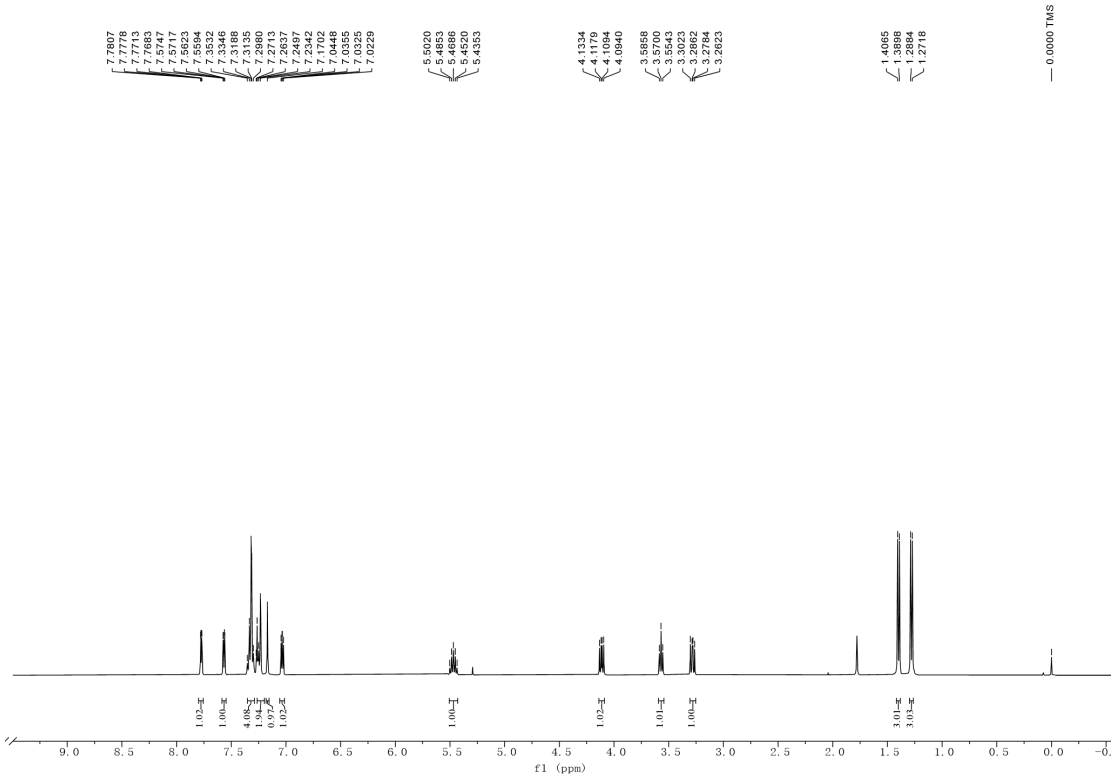
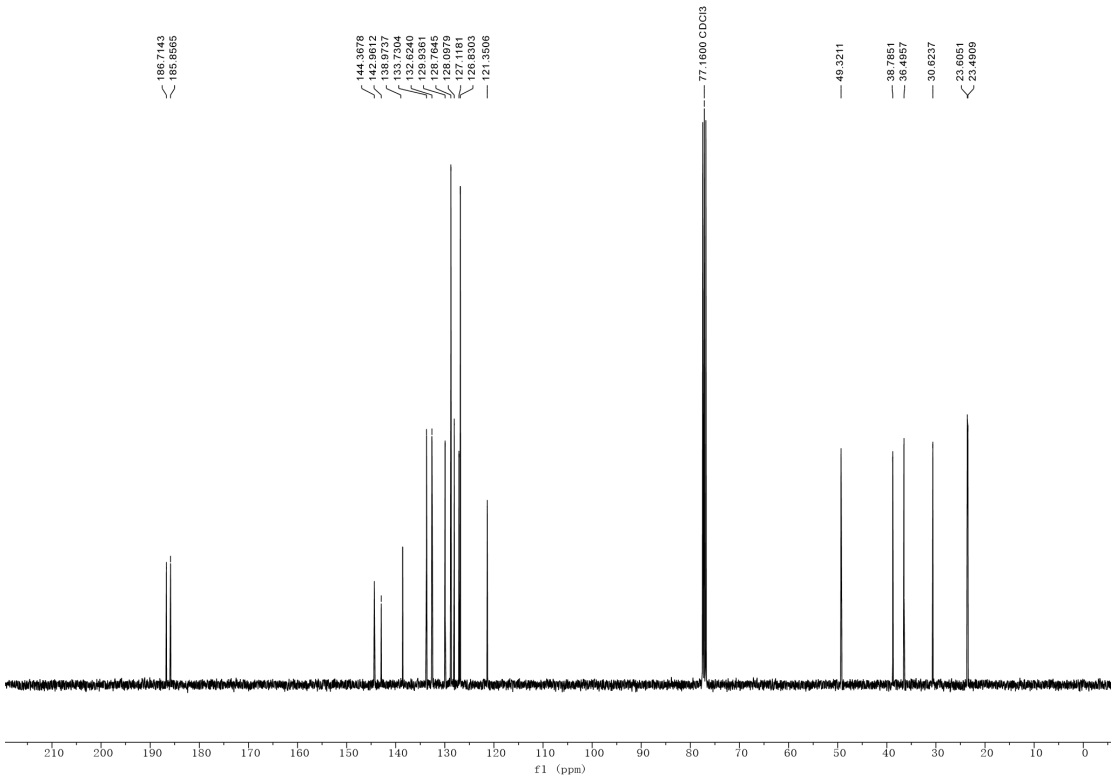
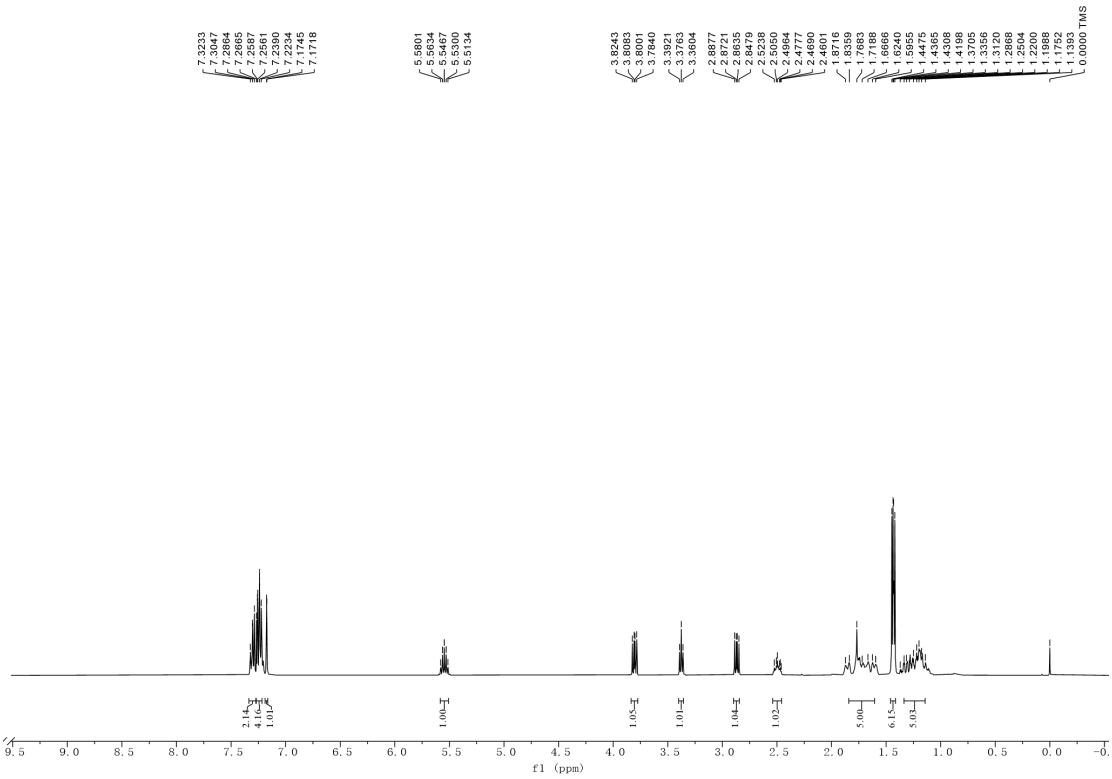


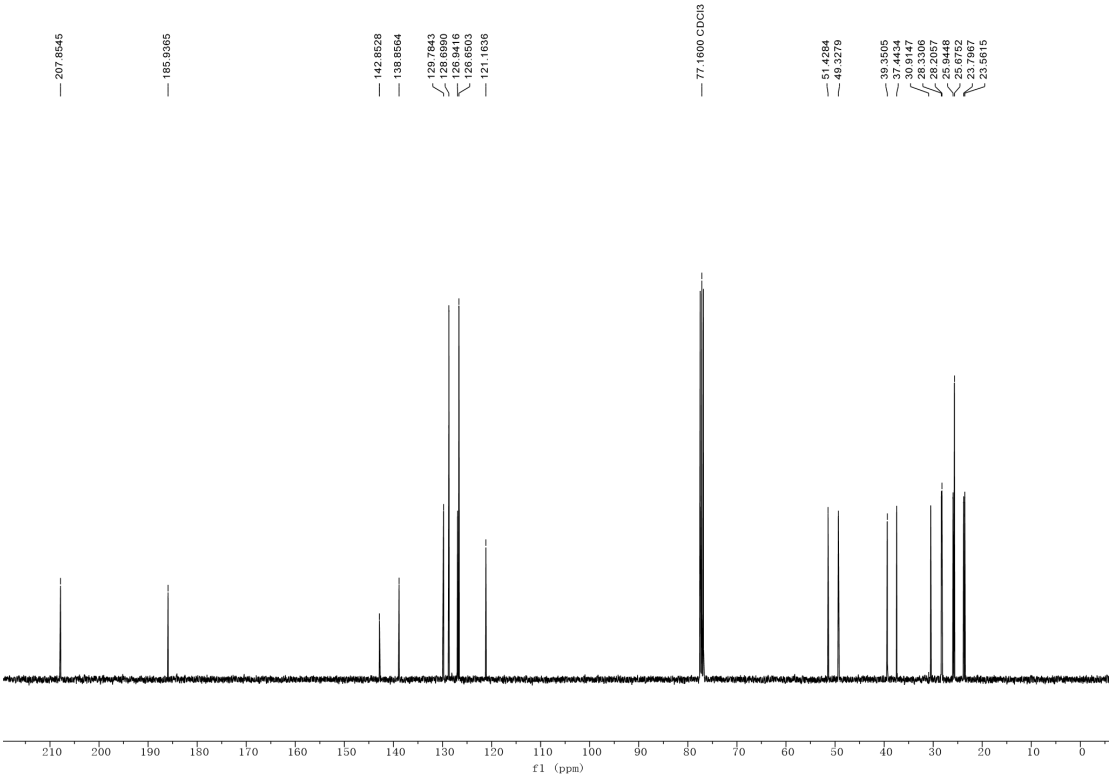
^{13}C NMR-3m (101 MHz, $CDCl_3$)



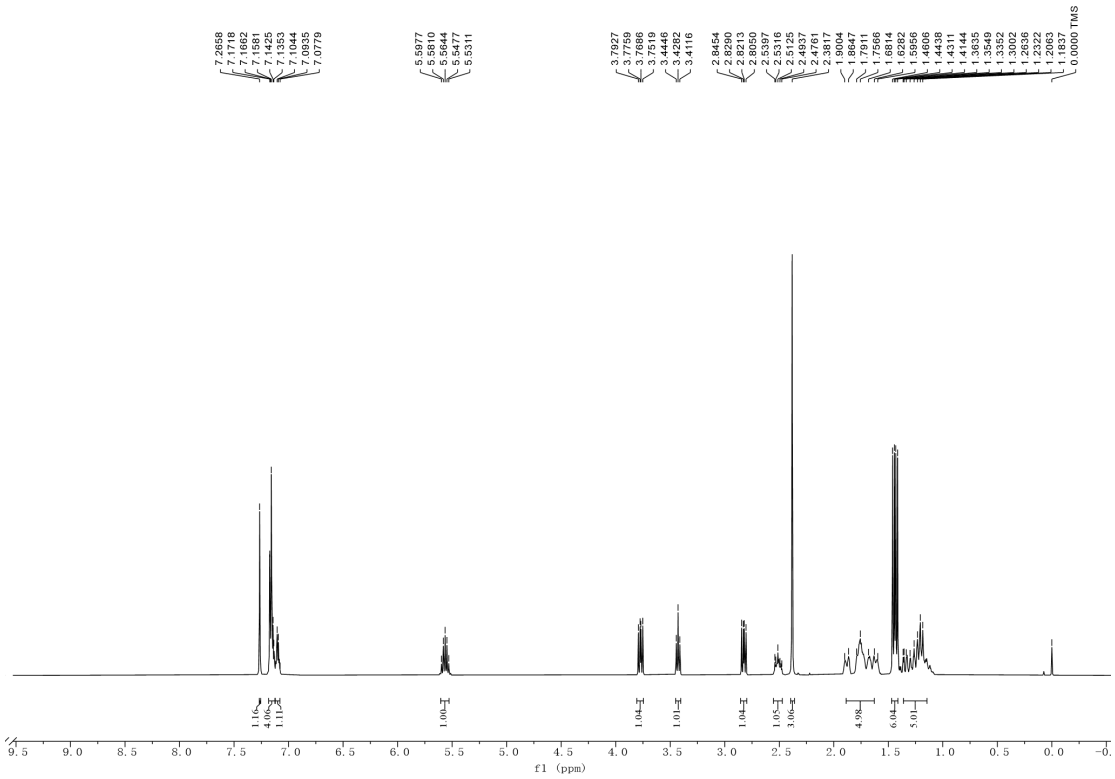
^{1}H NMR-3n (400 MHz, $CDCl_3$)



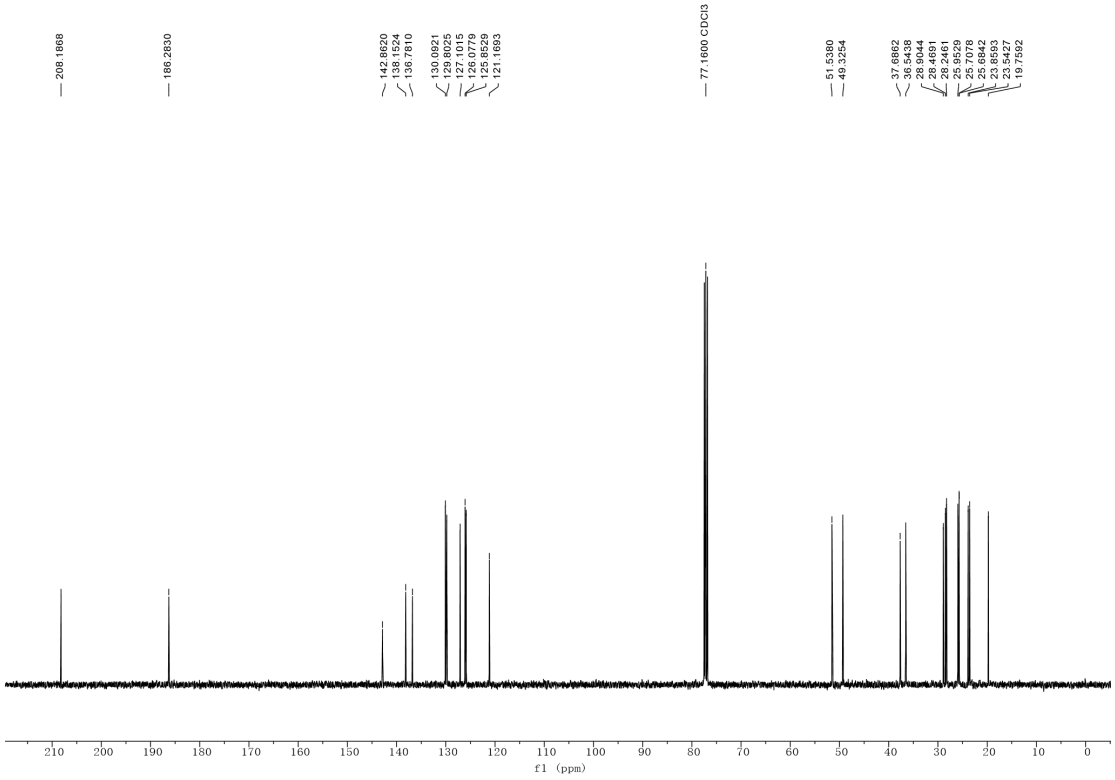
^{13}C NMR-3n (101 MHz, $CDCl_3$)



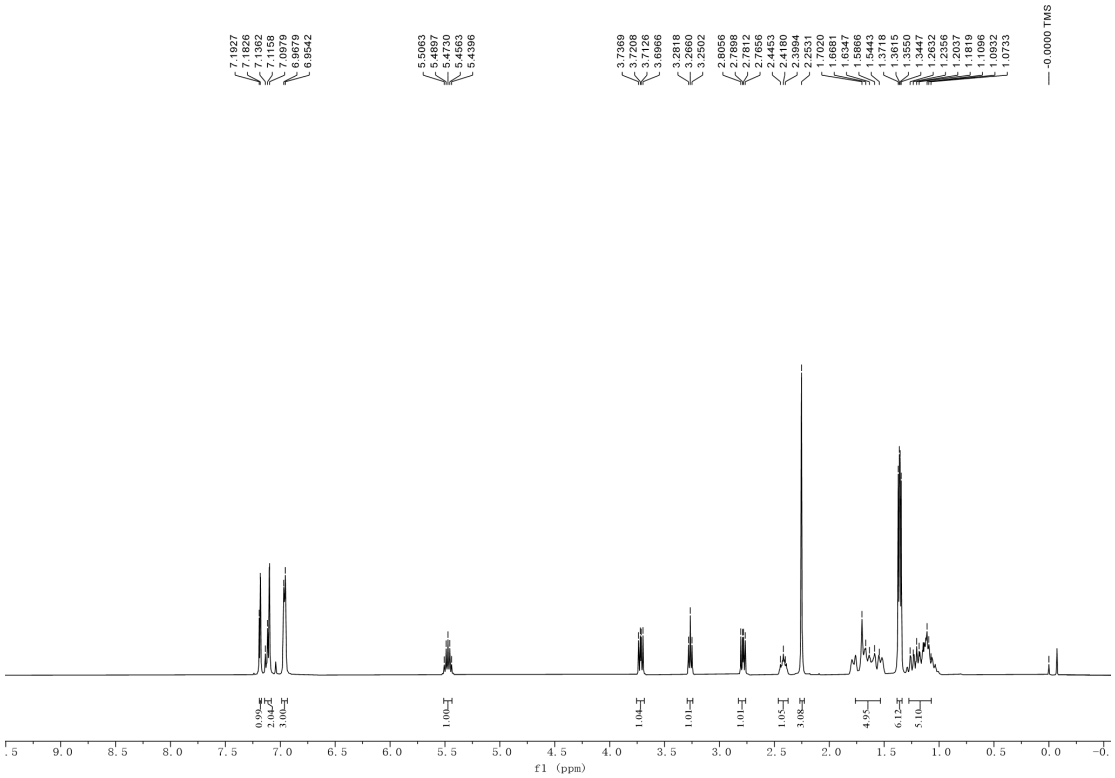
^{1}H NMR-4a (400 MHz, $CDCl_3$)



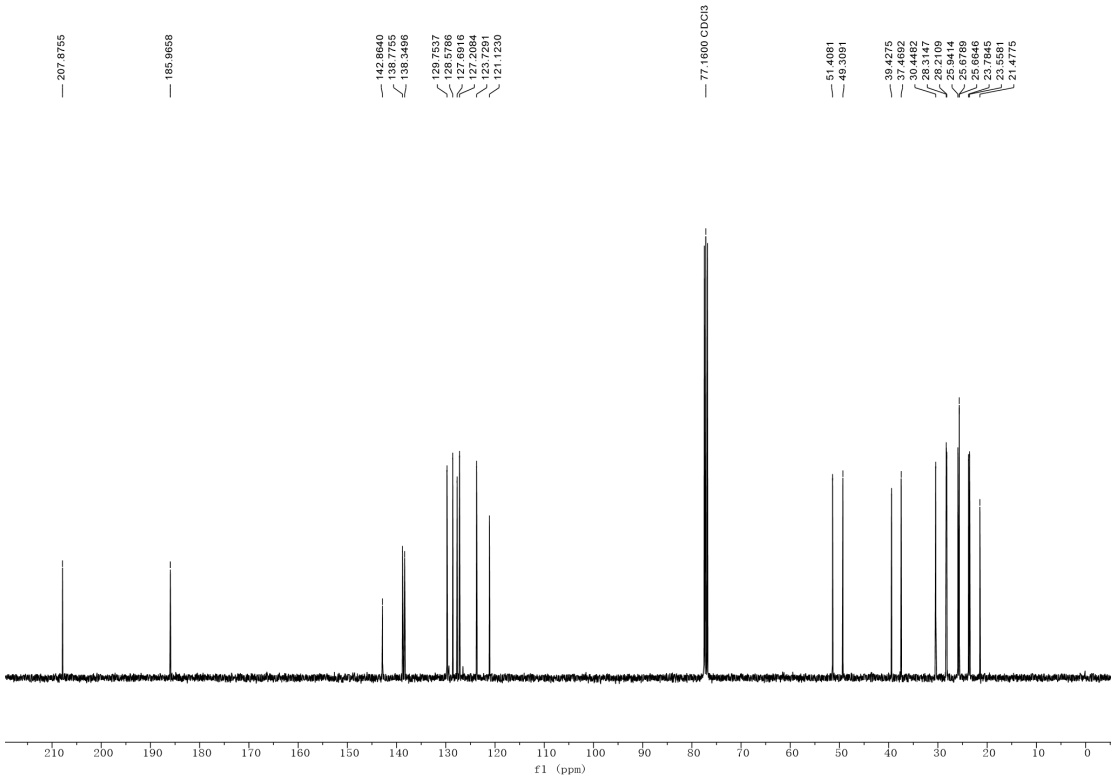
^{13}C NMR-4a (101 MHz, $CDCl_3$)



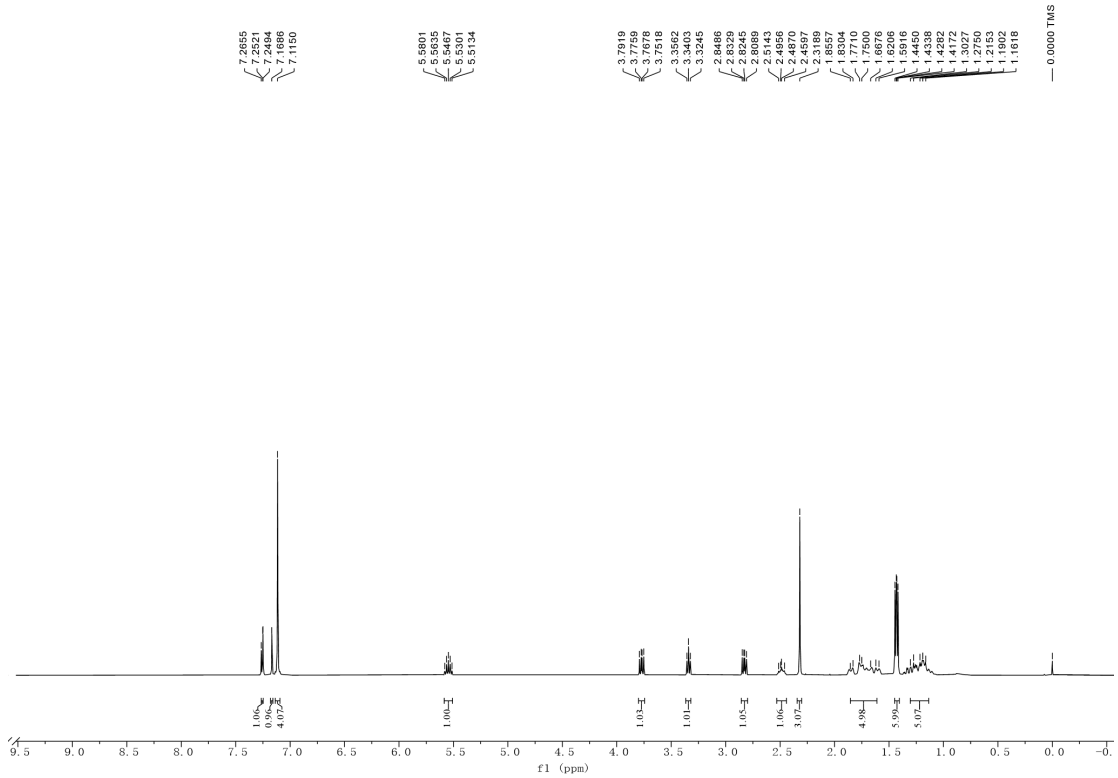
^{1}H NMR-4b (400 MHz,$CDCl_3$)



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



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



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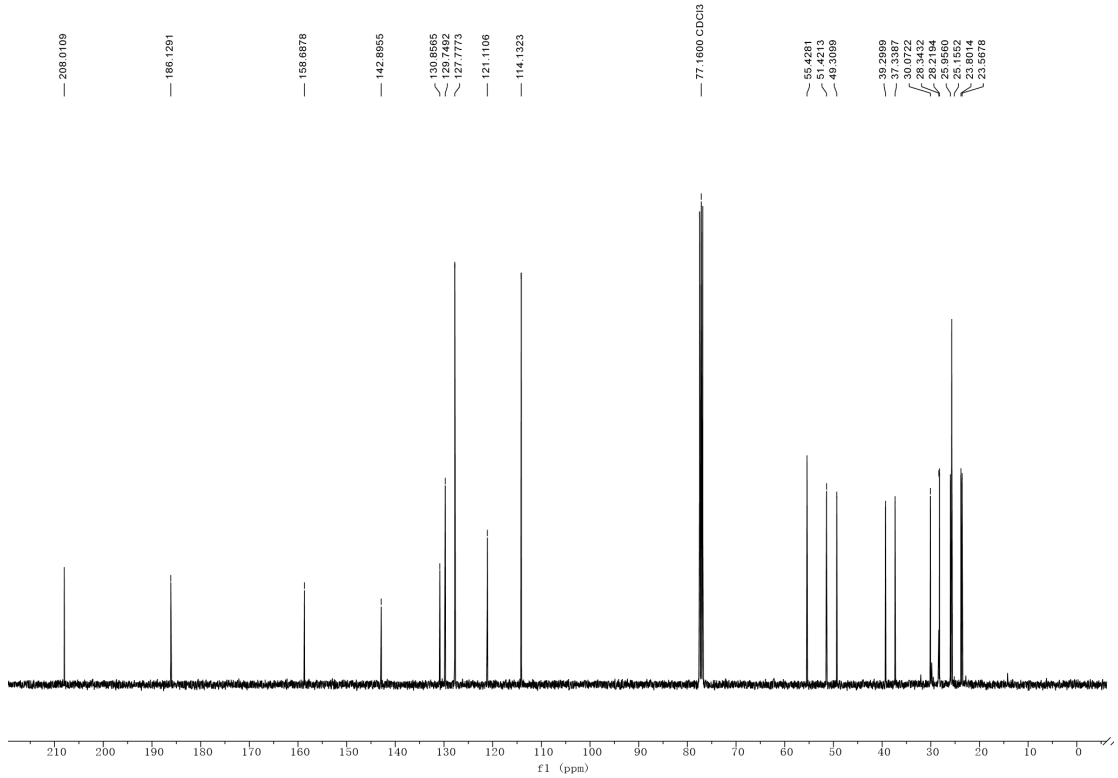

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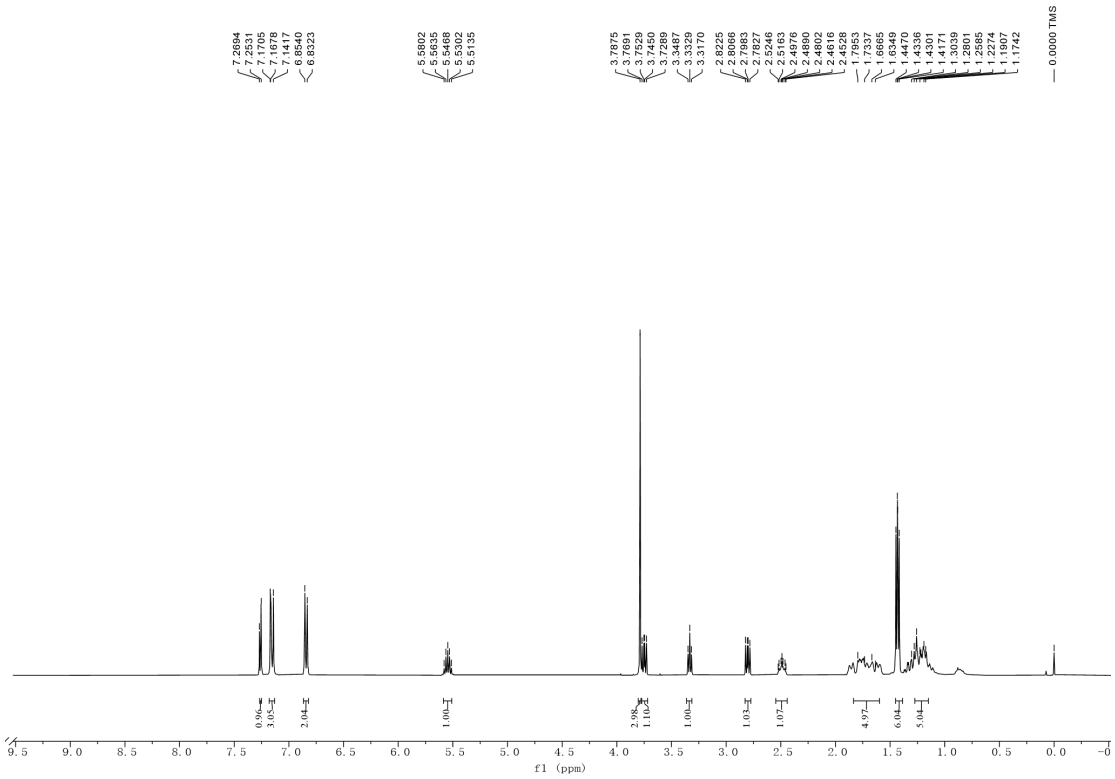
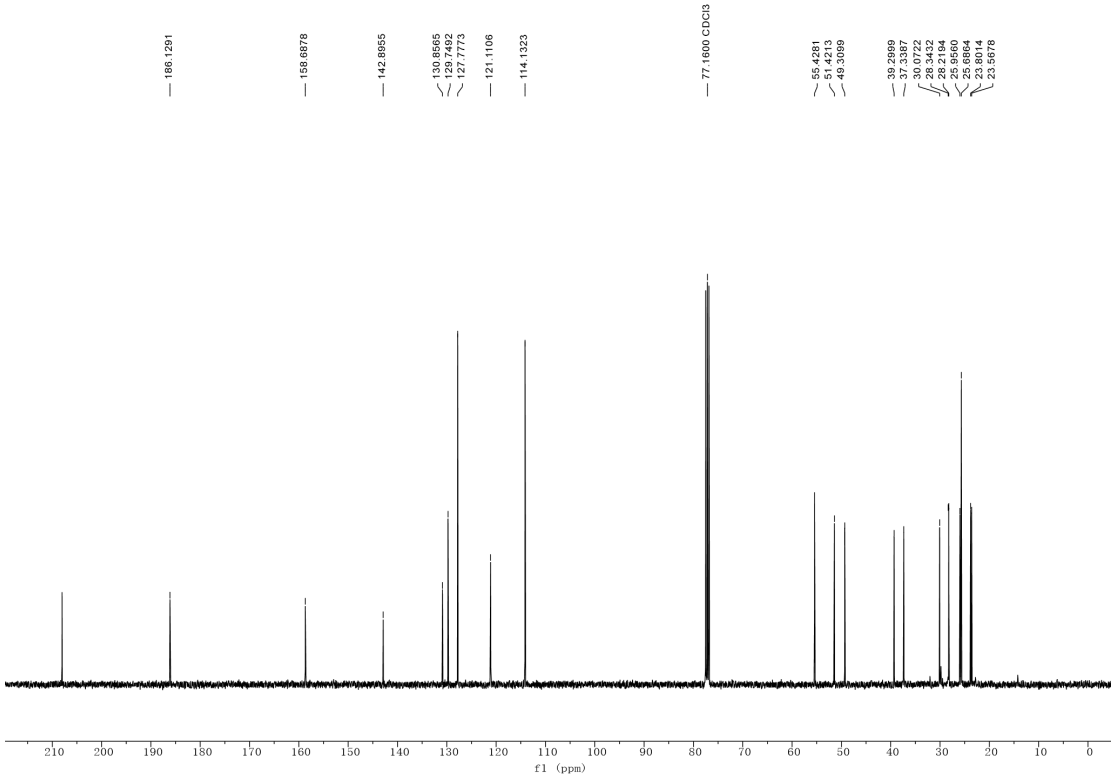
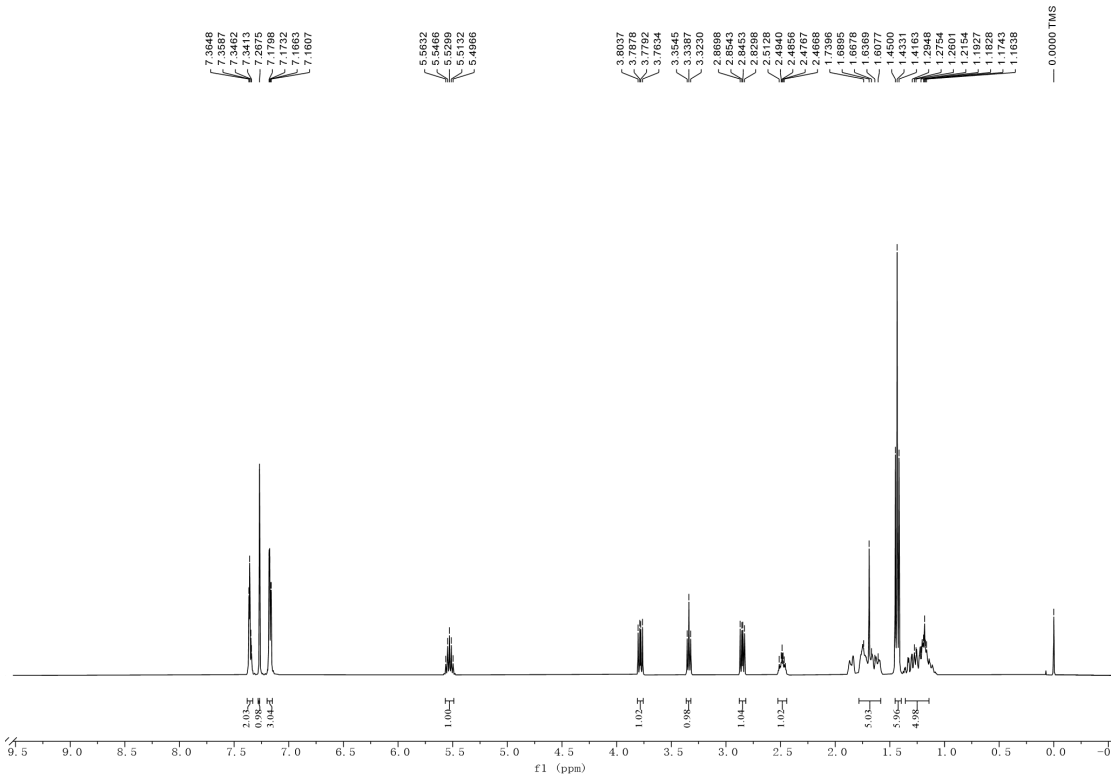


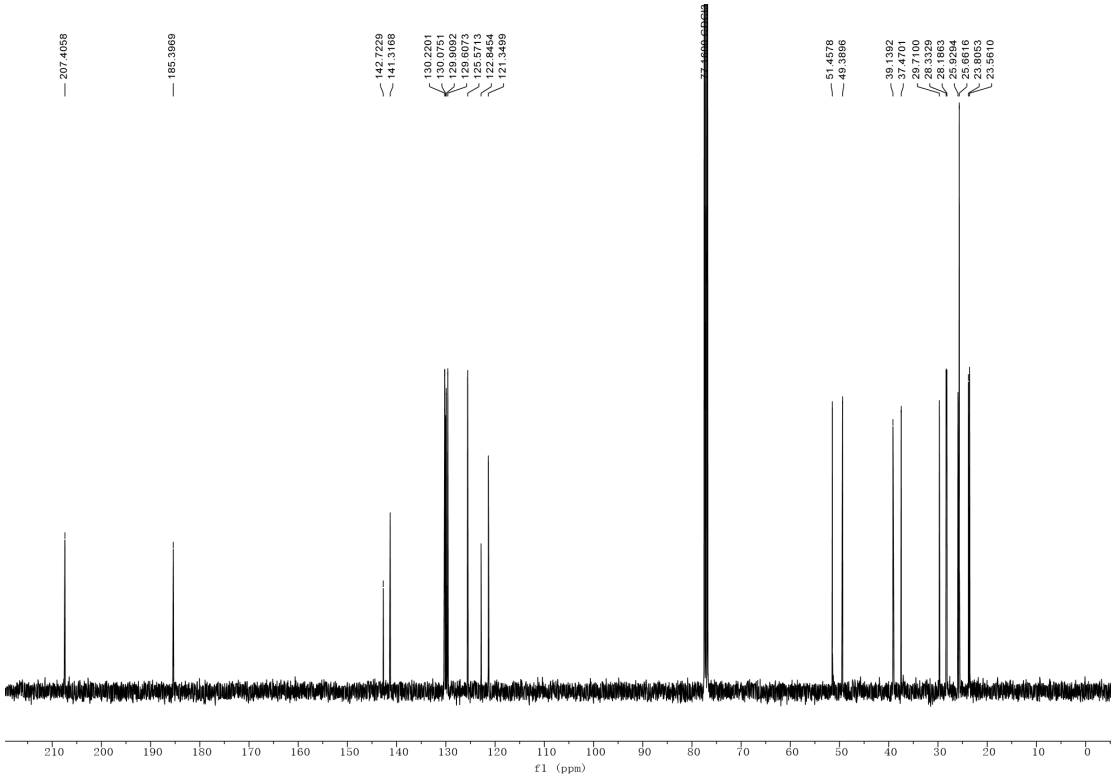
^{13}C NMR-4d (101 MHz, $CDCl_3$)



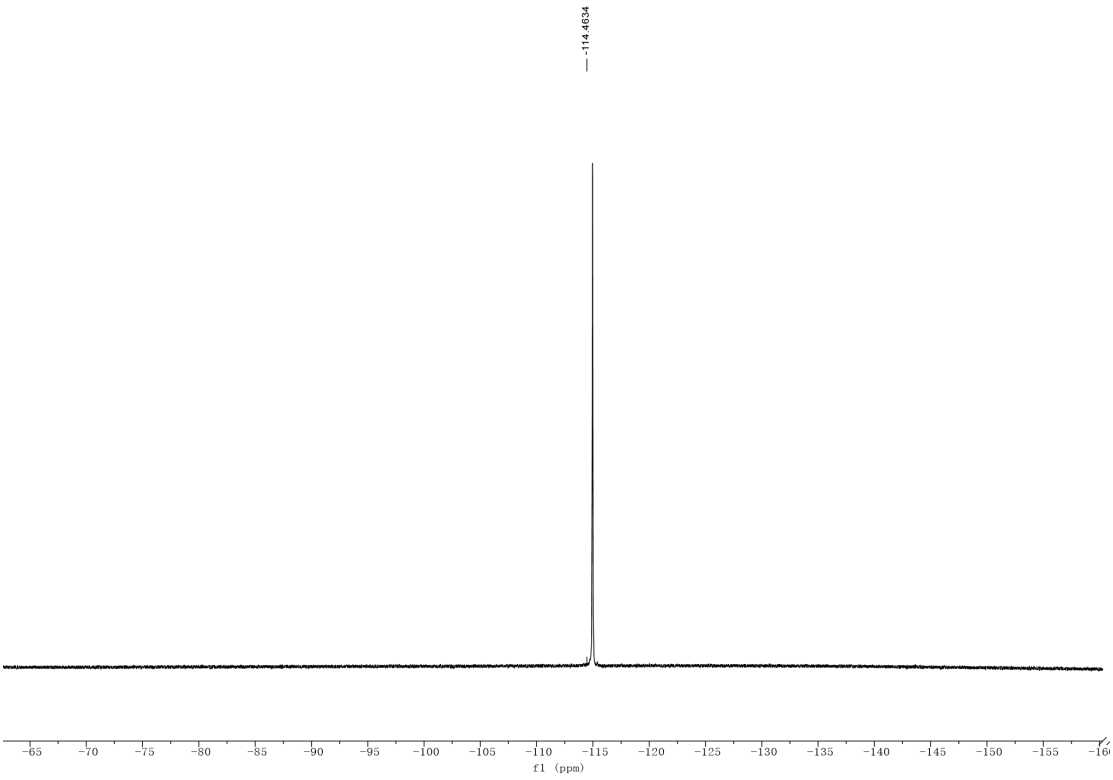
^{1}H NMR-4e (400 MHz, $CDCl_3$)



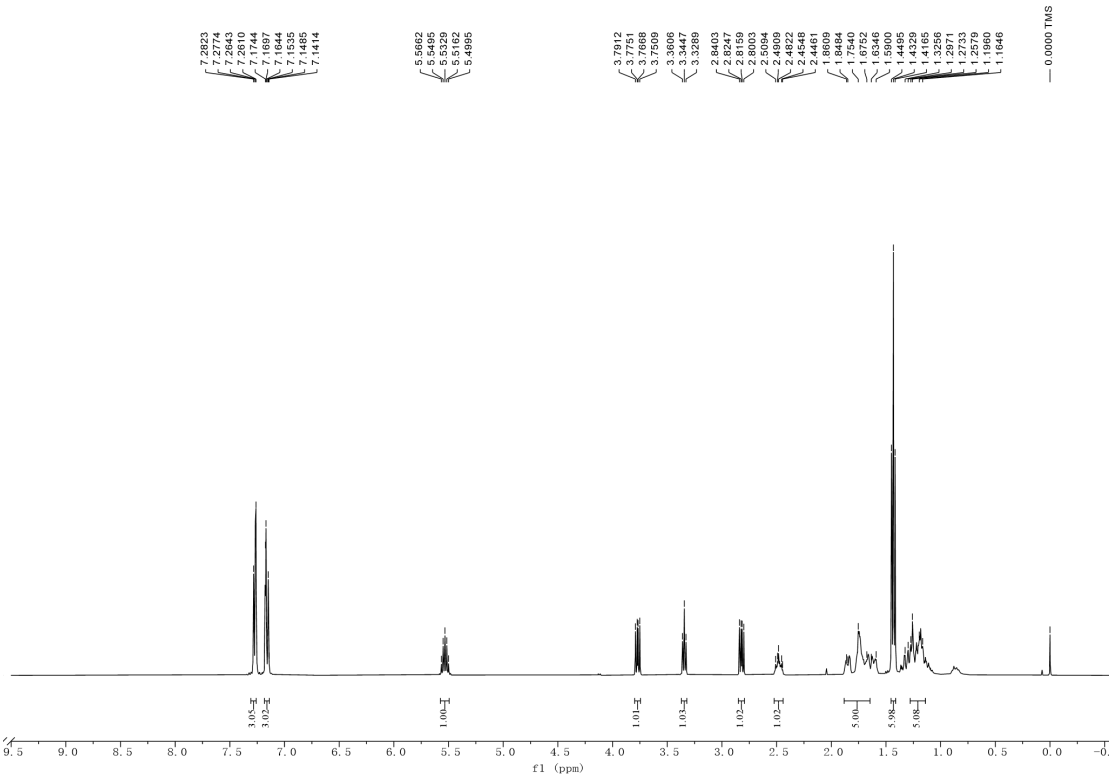
^{13}C NMR-4e (101 MHz,$CDCl_3$)



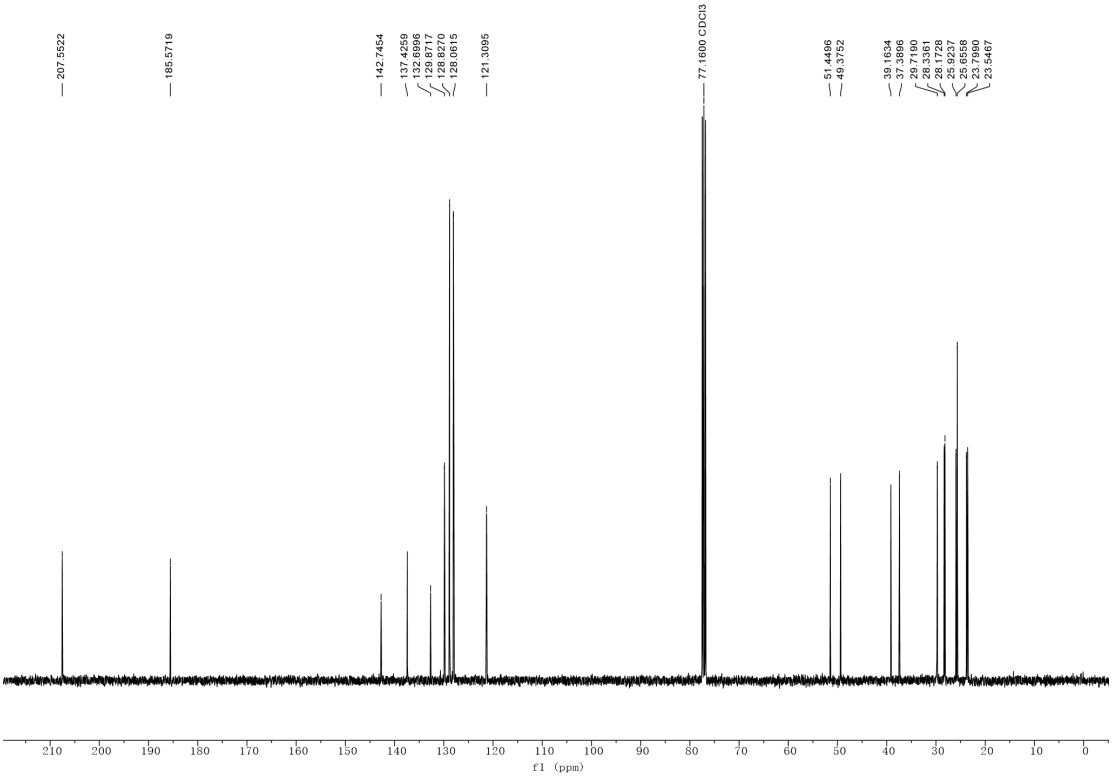
^{19}F NMR-4e (376 MHz, $CDCl_3$)



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



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



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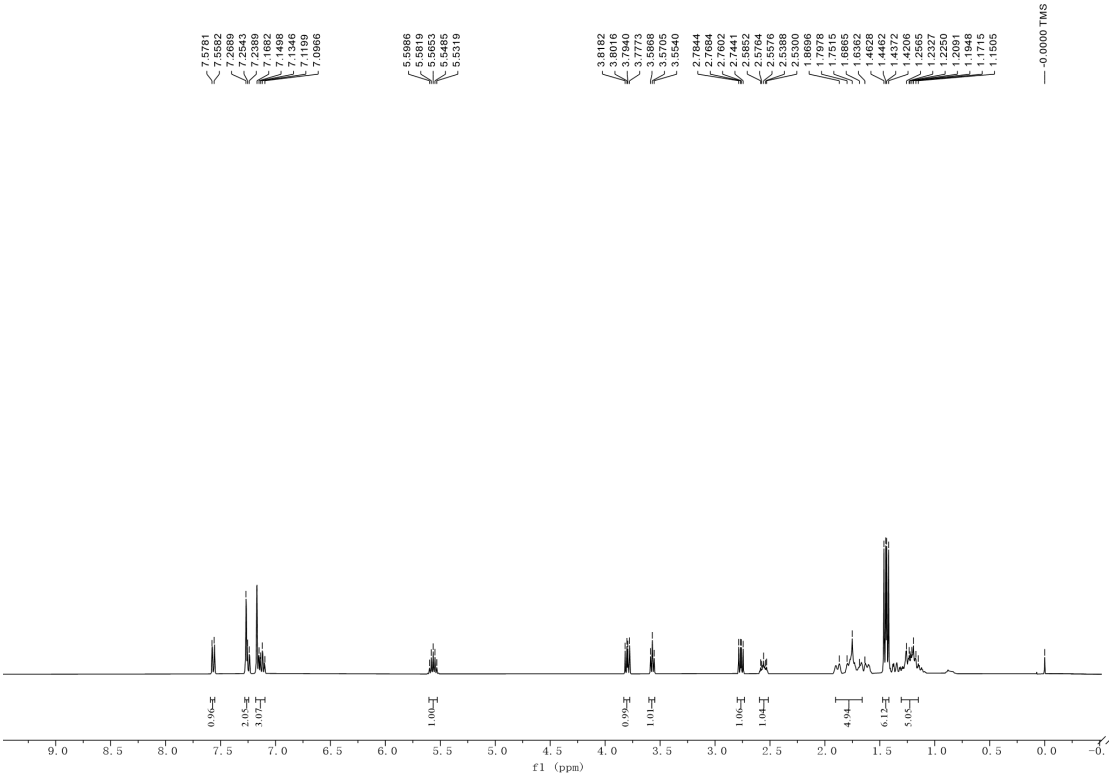
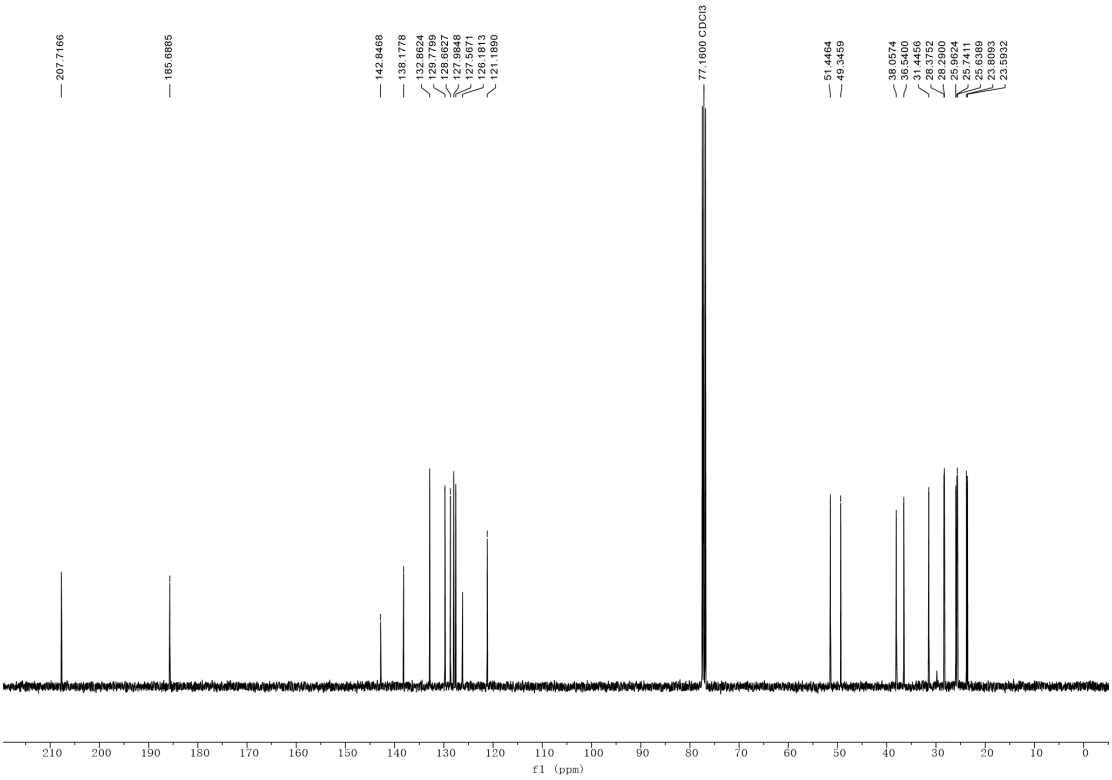
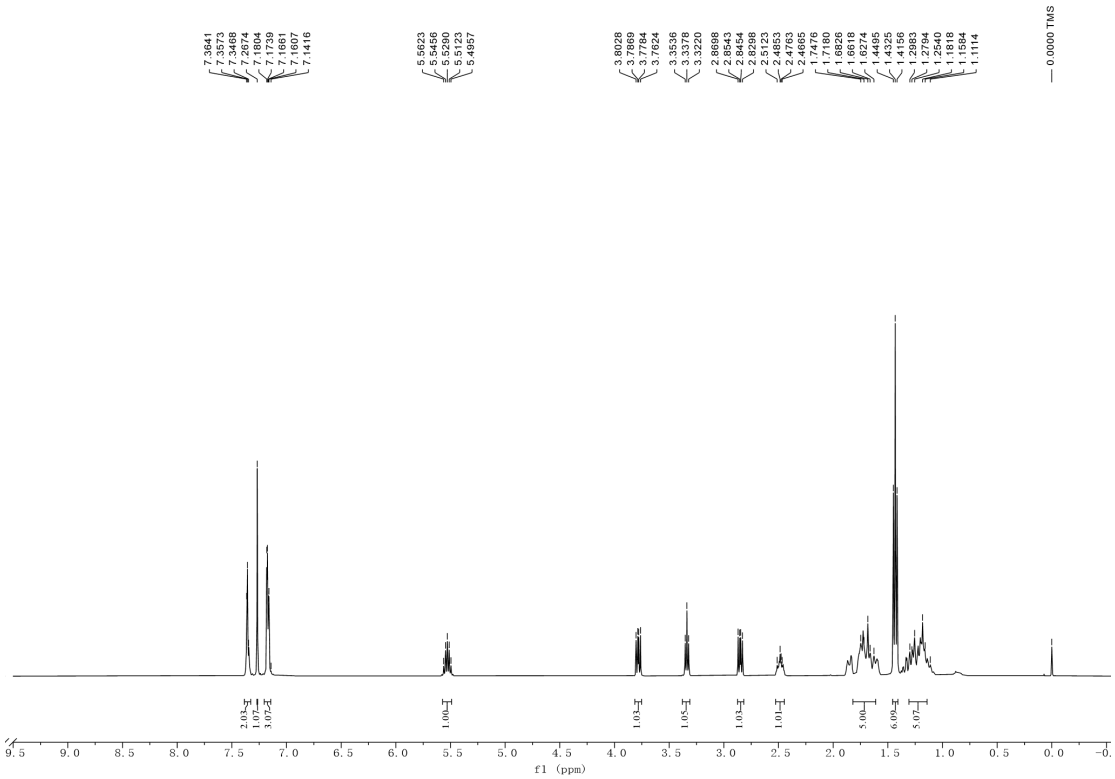


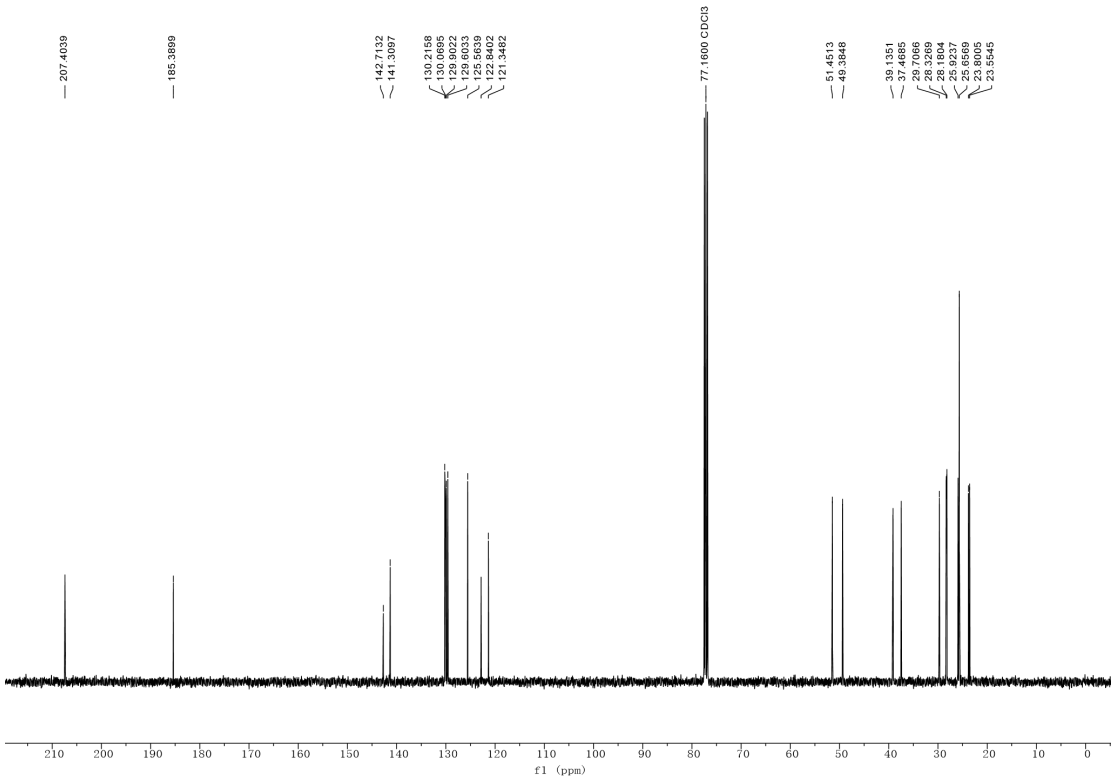
^{13}C NMR-4g (101 MHz, $CDCl_3$)



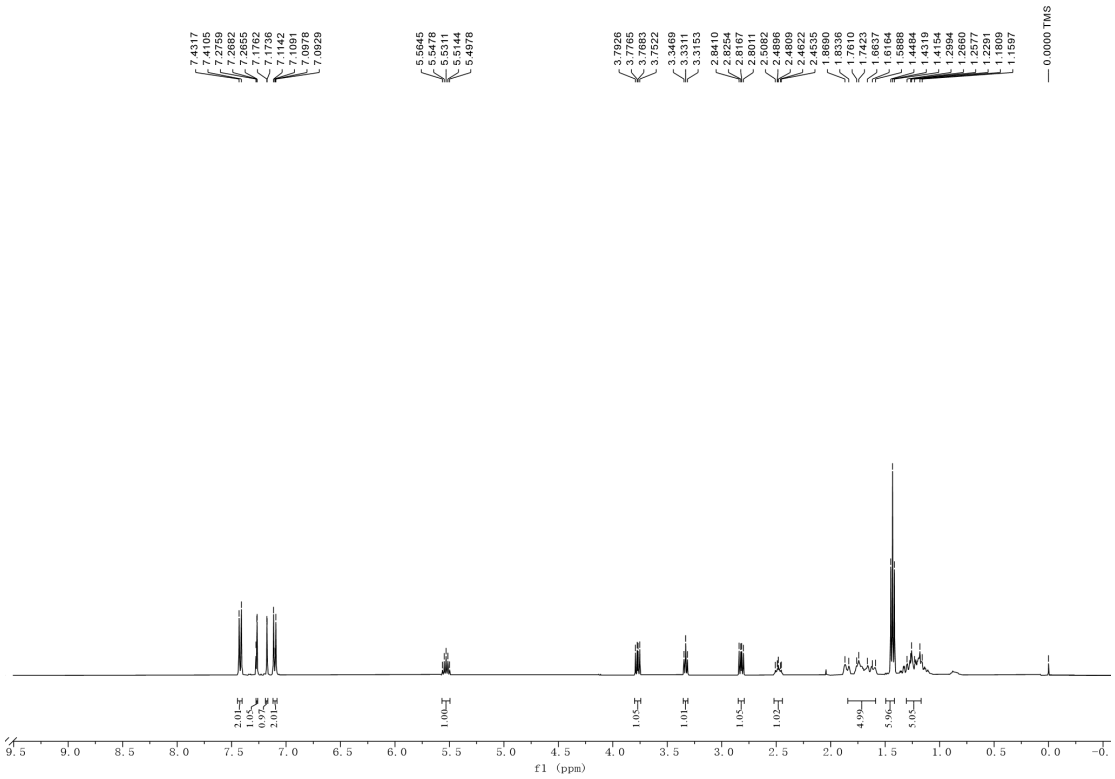
^{1}H NMR-4h (400 MHz, $CDCl_3$)



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



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



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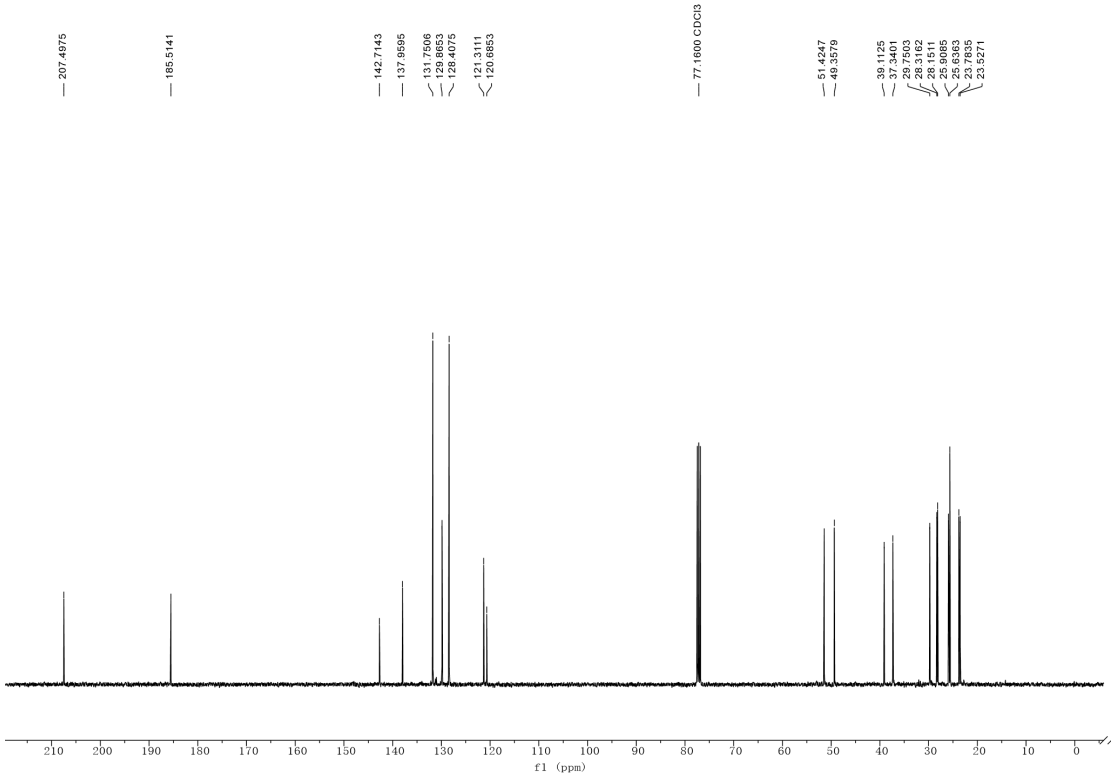
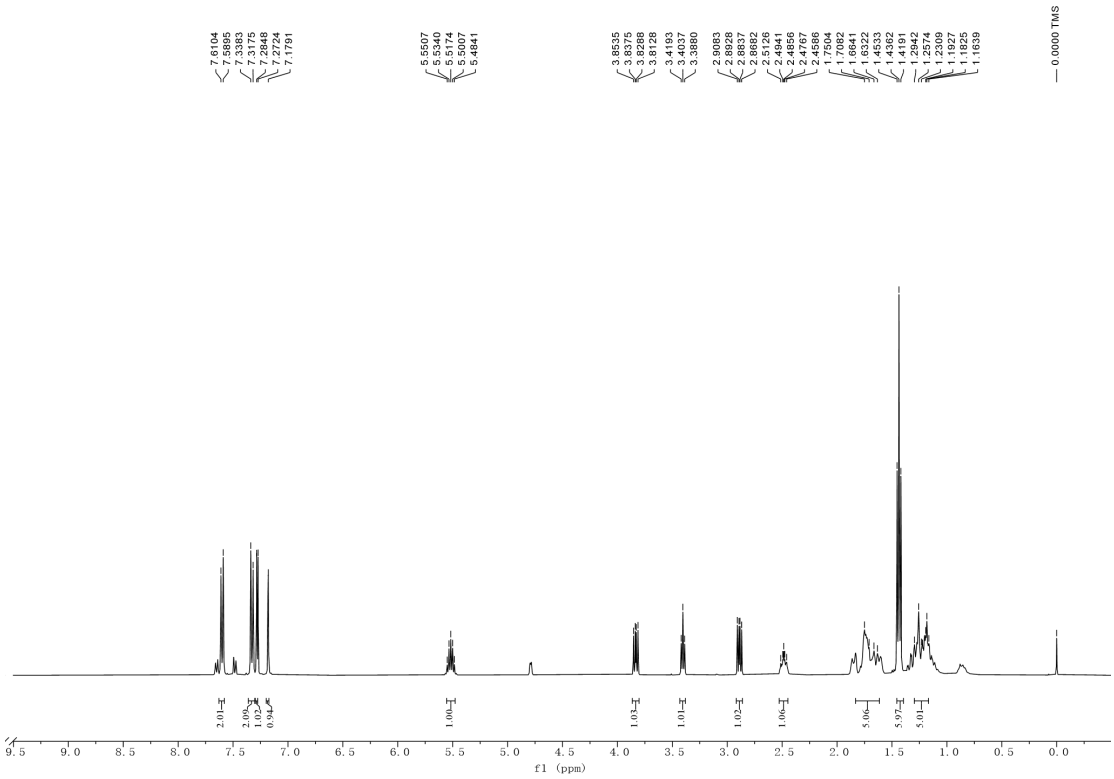
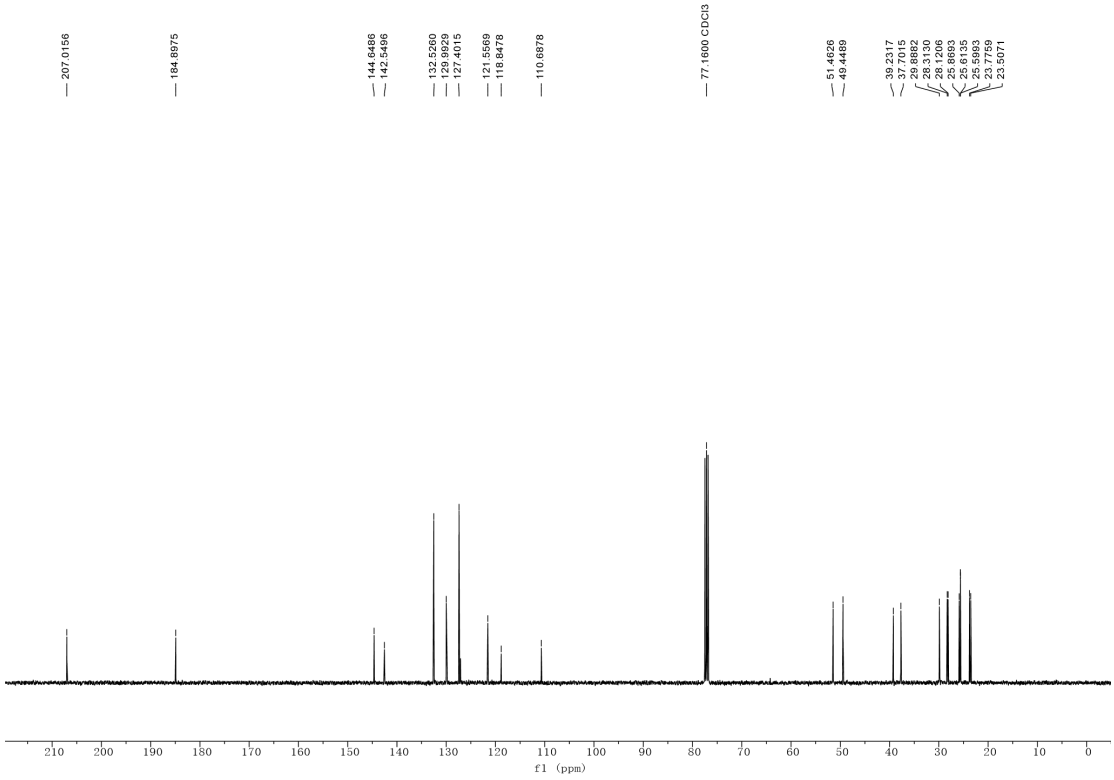


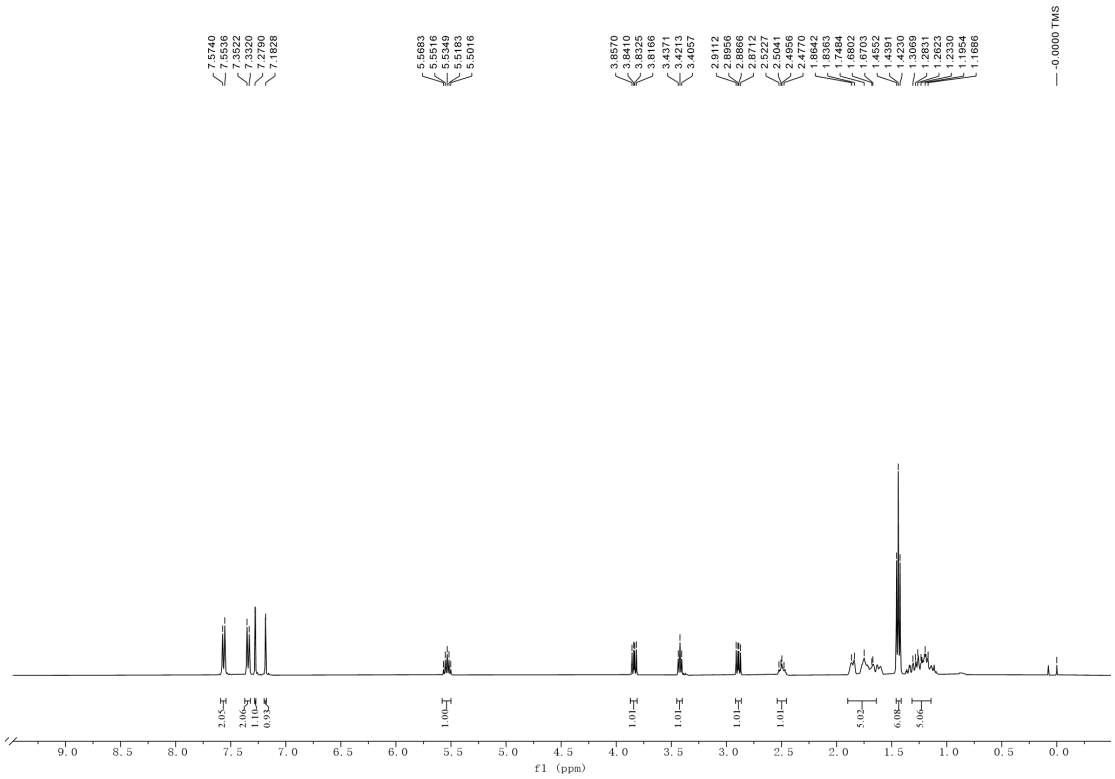
^{1}H NMR-4j (400 MHz, $CDCl_3$)



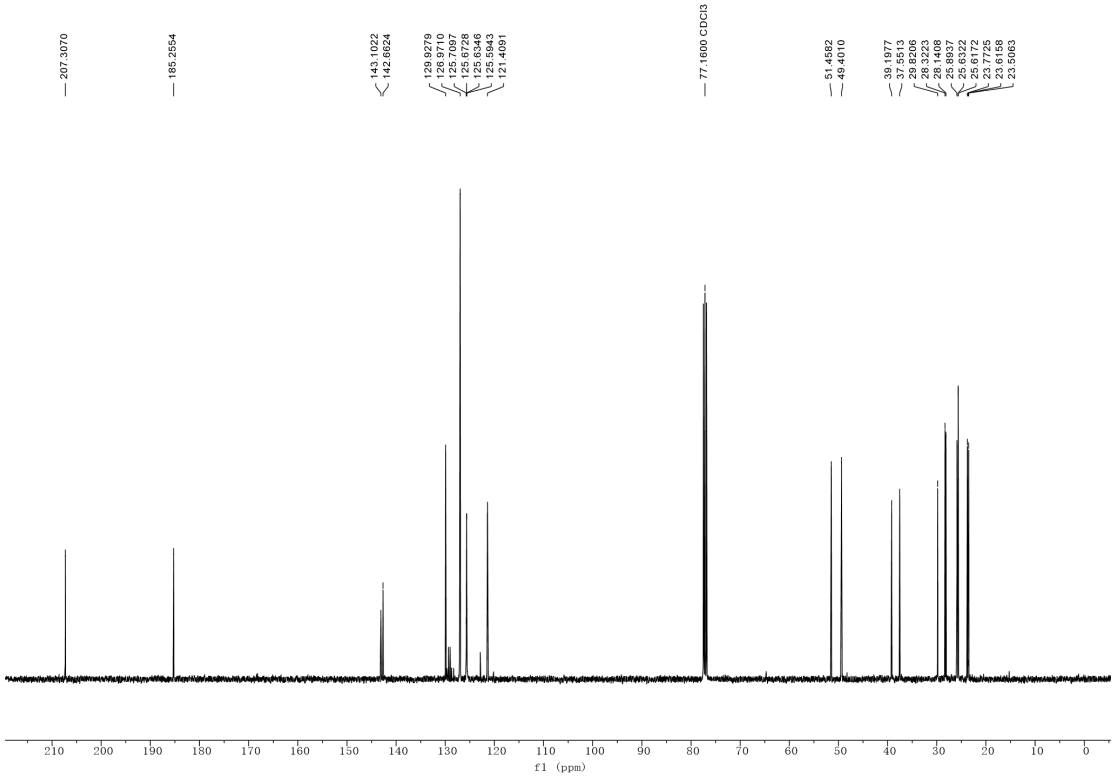
^{13}C NMR-4j (101 MHz, $CDCl_3$)



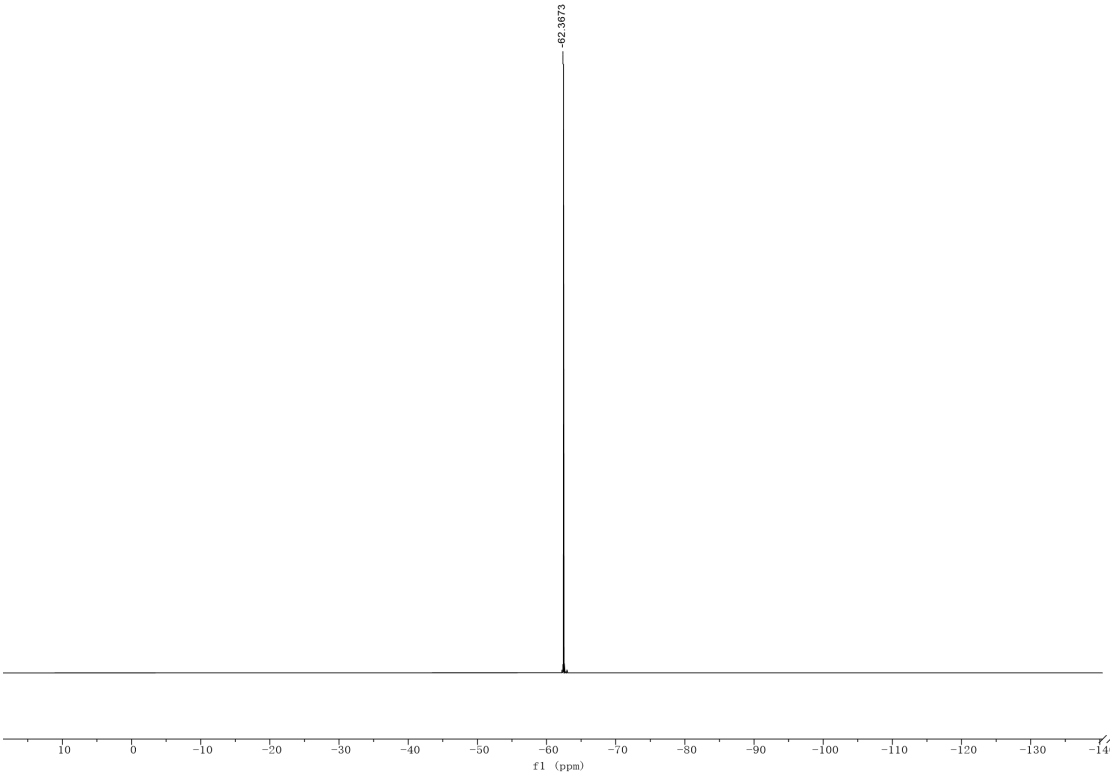
^{1}H NMR-4k (400 MHz, $CDCl_3$)



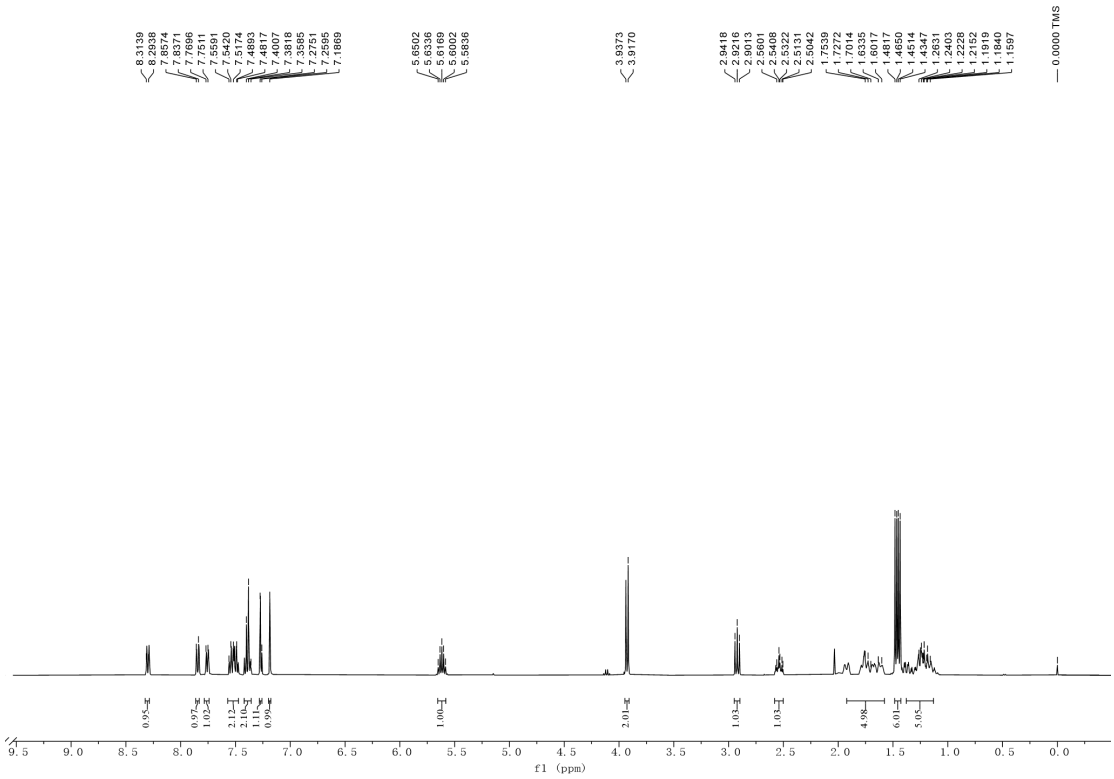
^{13}C NMR-4k (101 MHz, $CDCl_3$)



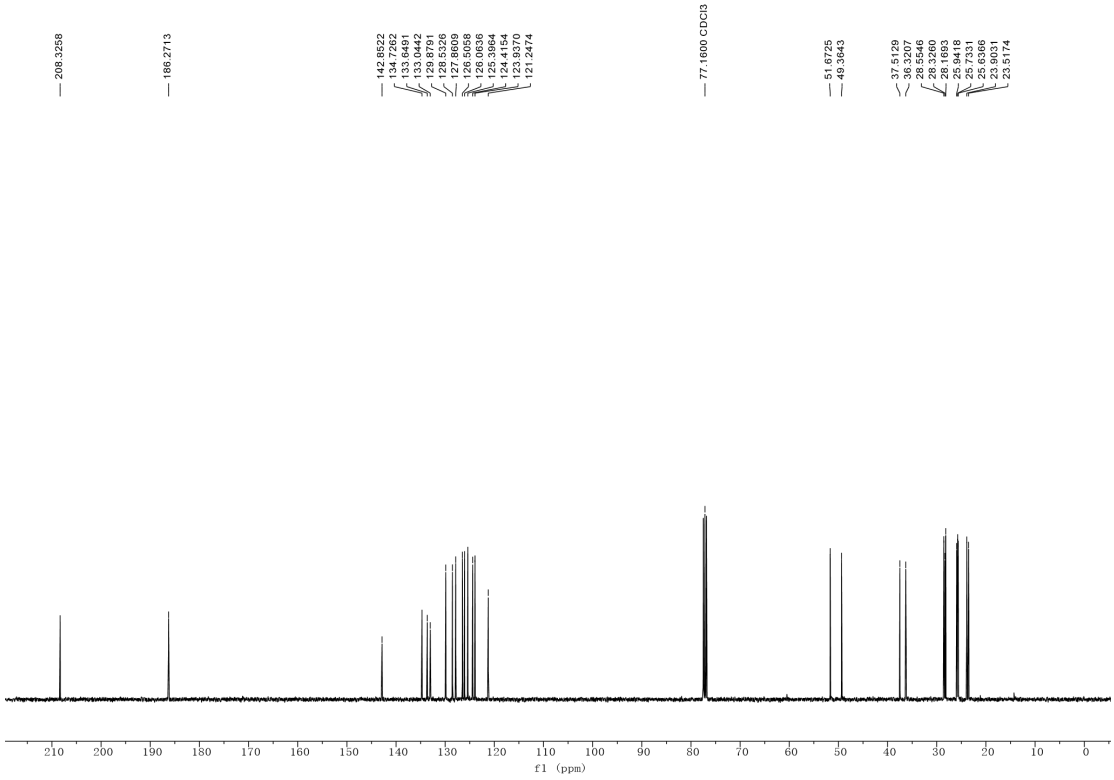
^{19}F NMR-4k (376 MHz, $CDCl_3$)



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



^{13}C NMR-4l (101 MHz,$CDCl_3$)



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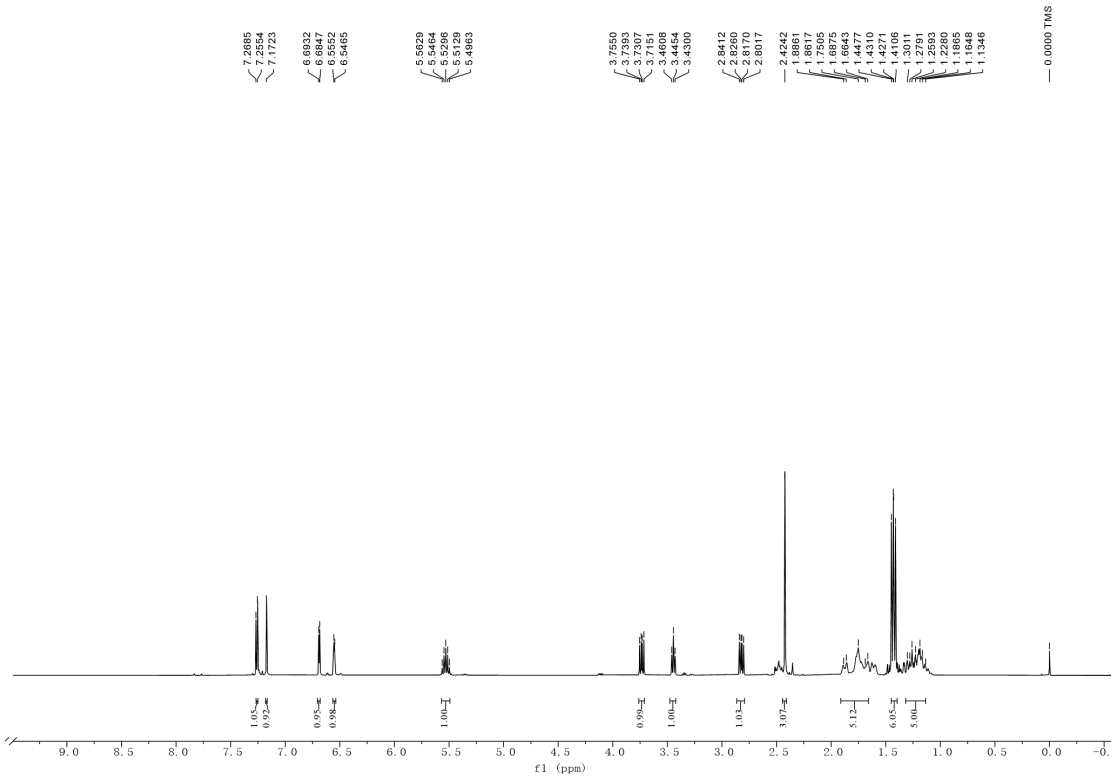
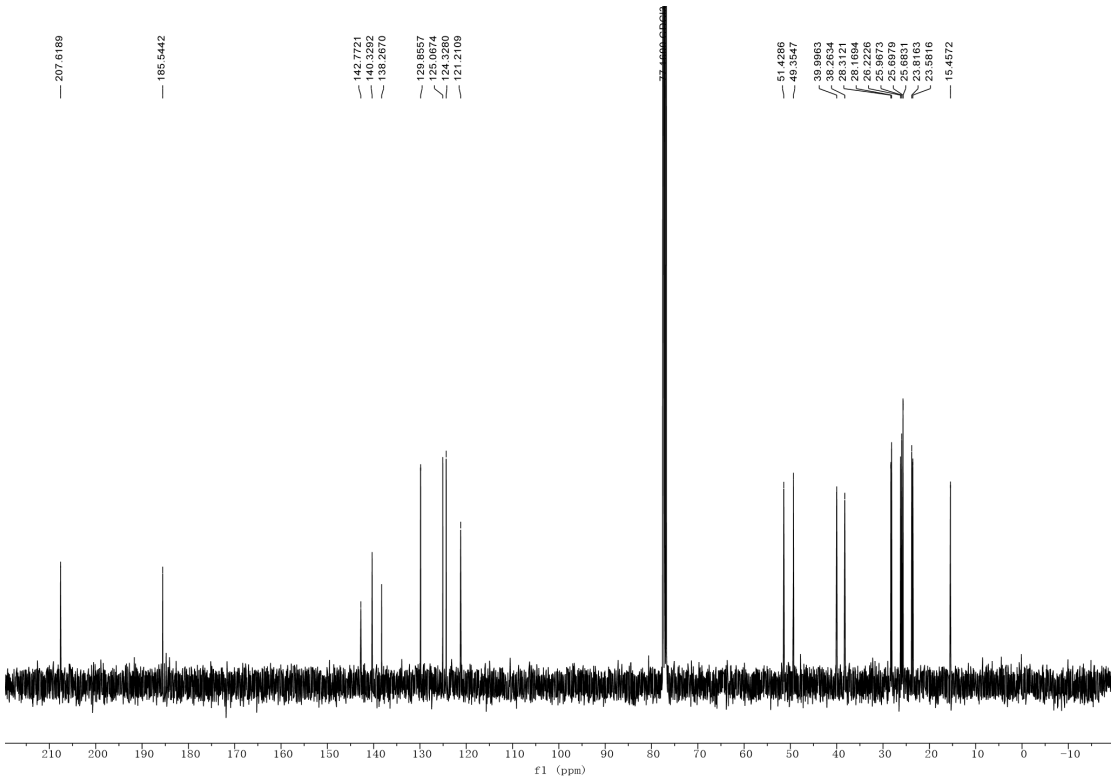


^{13}C NMR-4m (101 MHz, $CDCl_3$)



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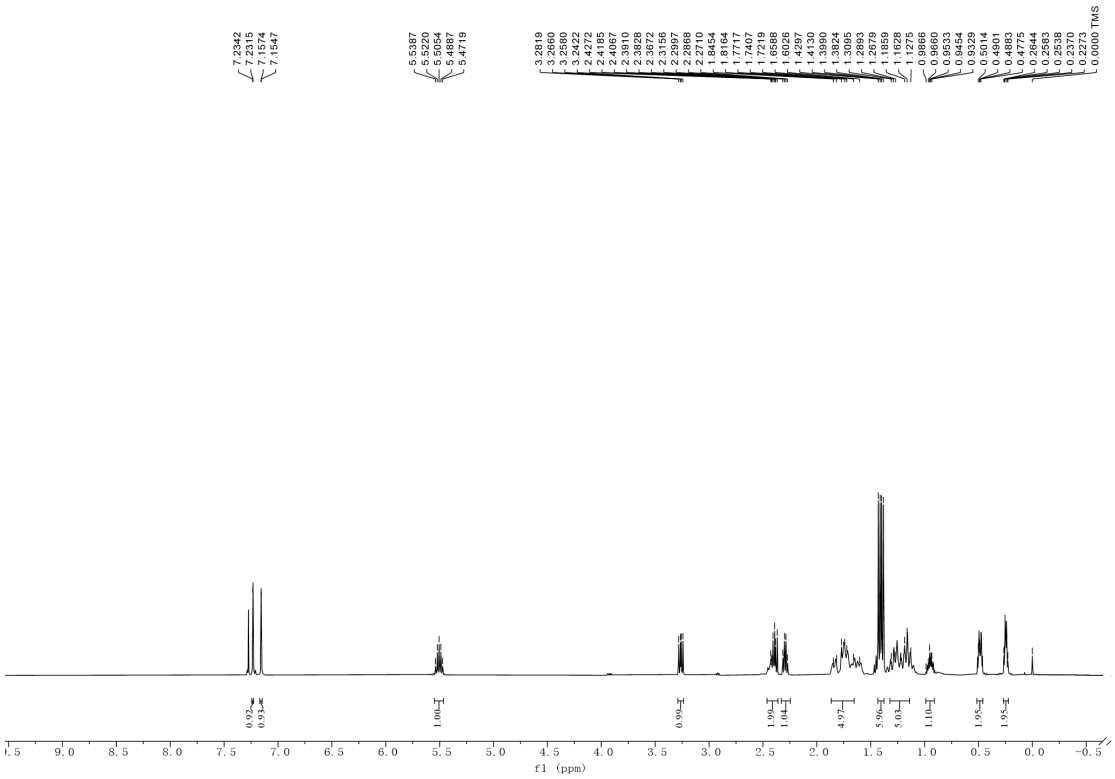
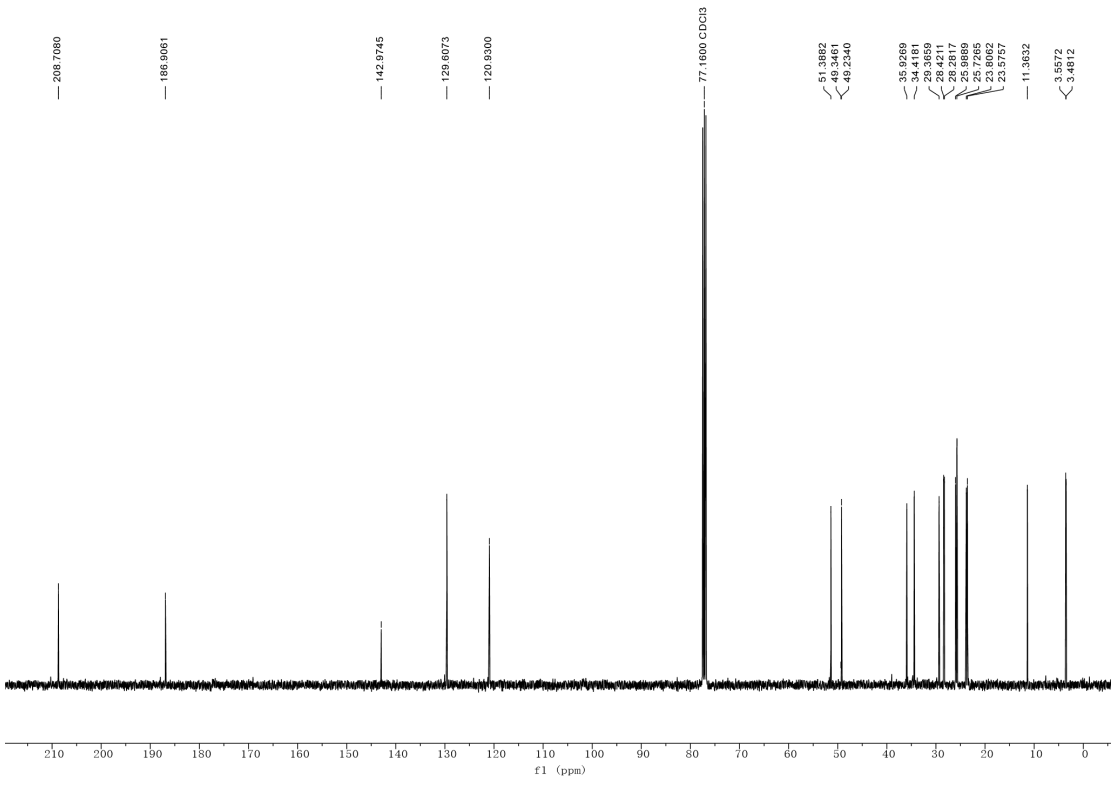
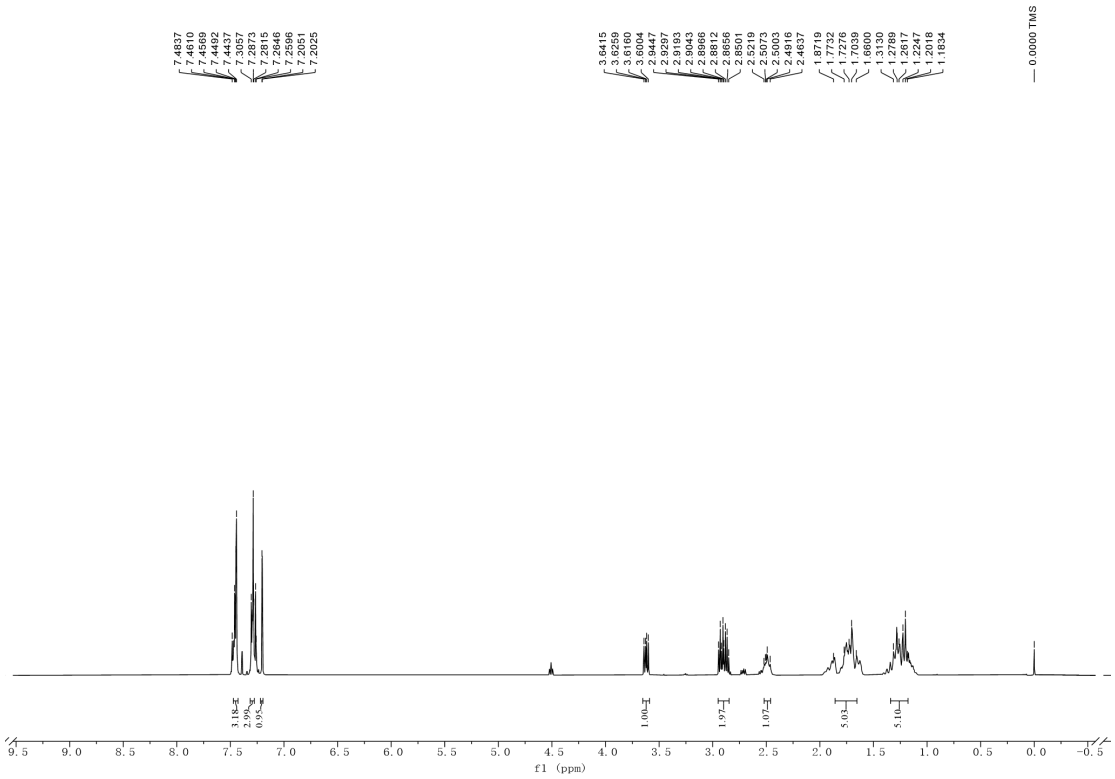


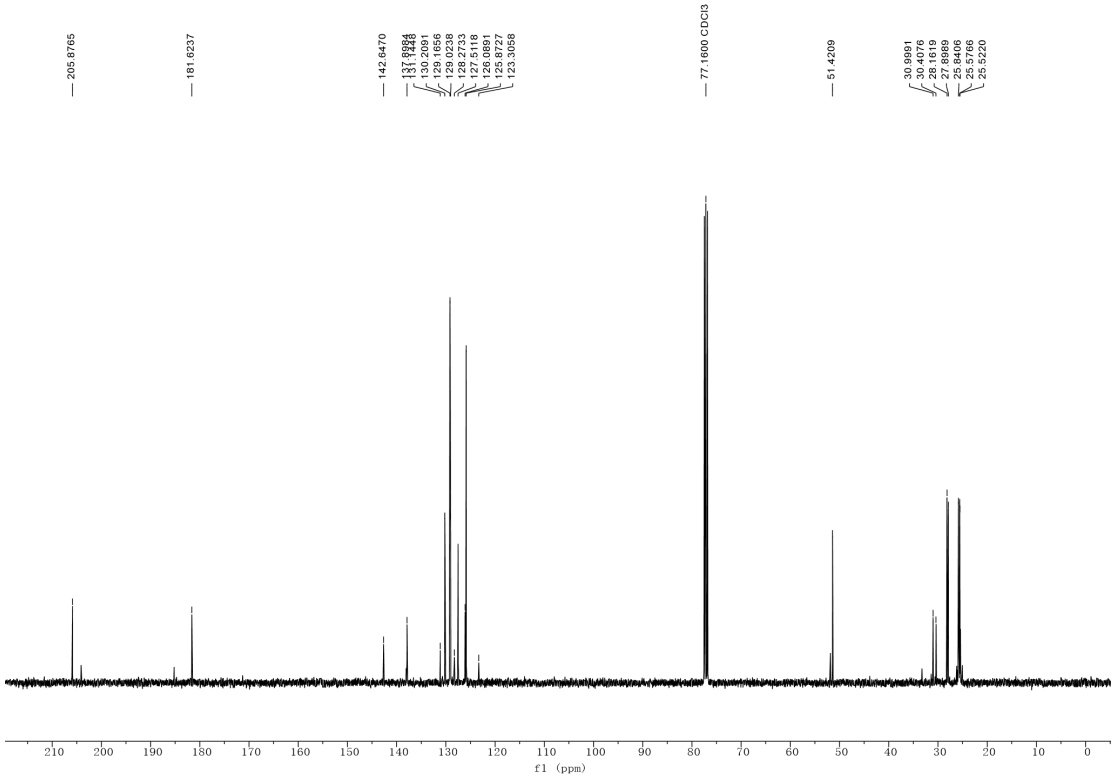
^{13}C NMR-4n (101 MHz, $CDCl_3$)



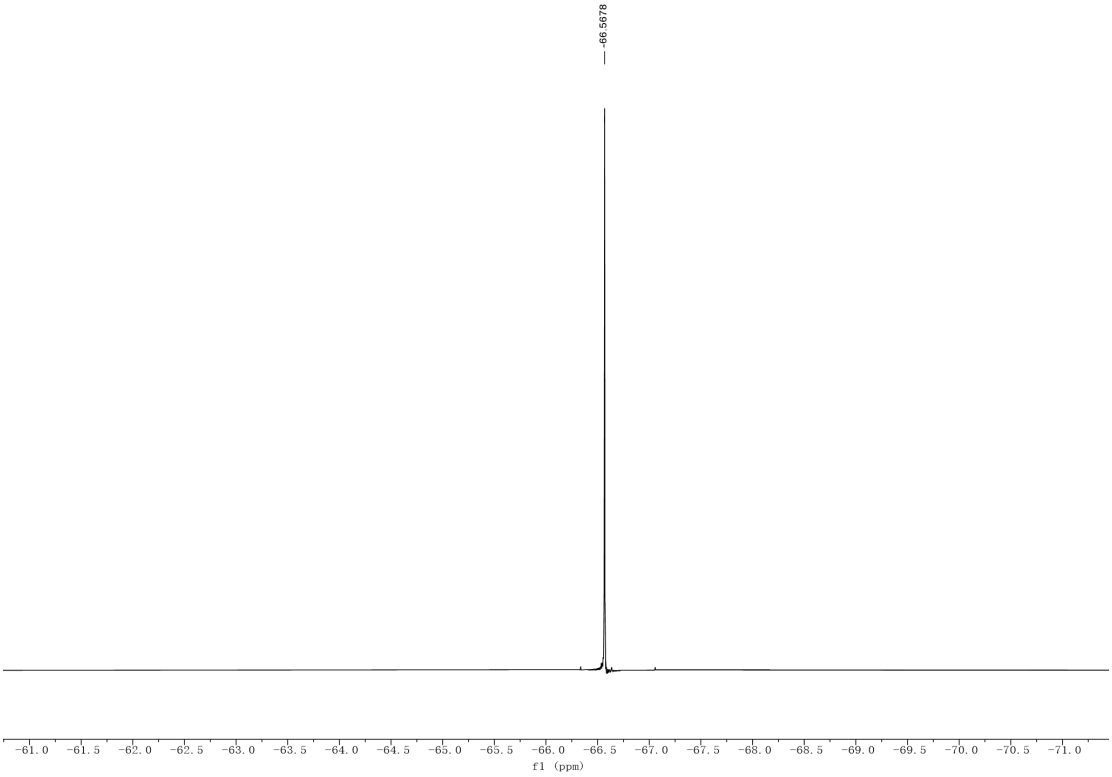
^{1}H NMR-4o (400 MHz, $CDCl_3$)



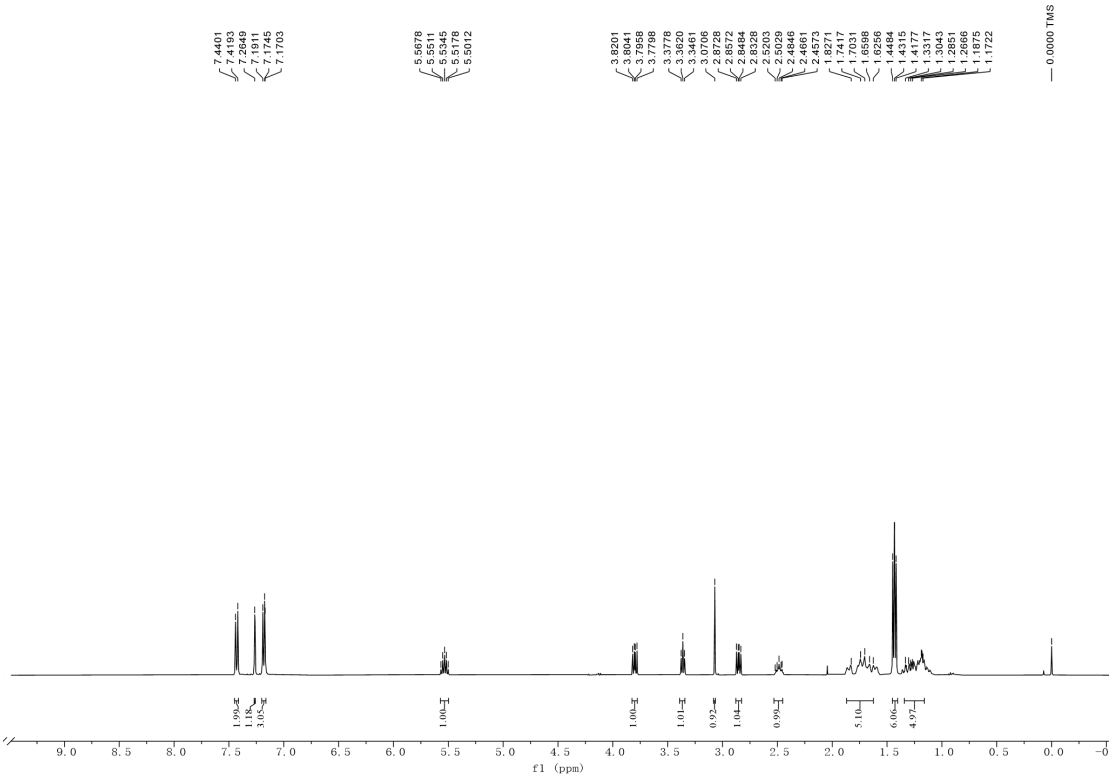
^{13}C NMR-4o (101 MHz, $CDCl_3$



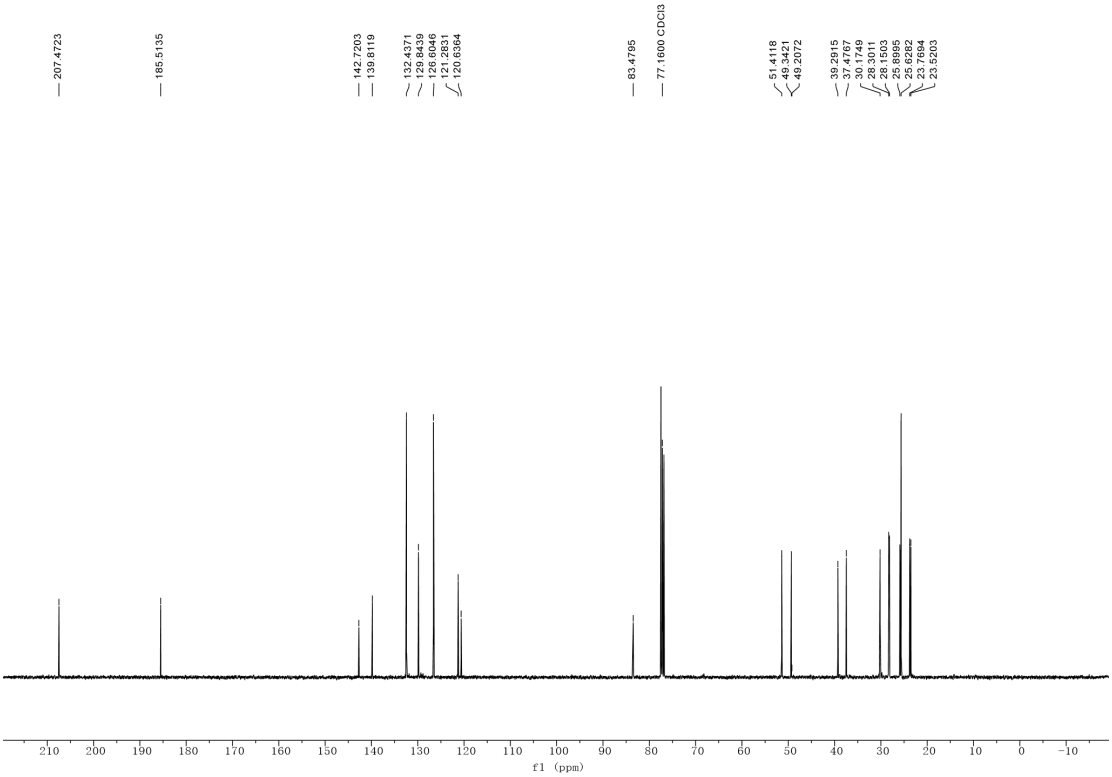
^{19}F NMR-4o (376 MHz, $CDCl_3$)



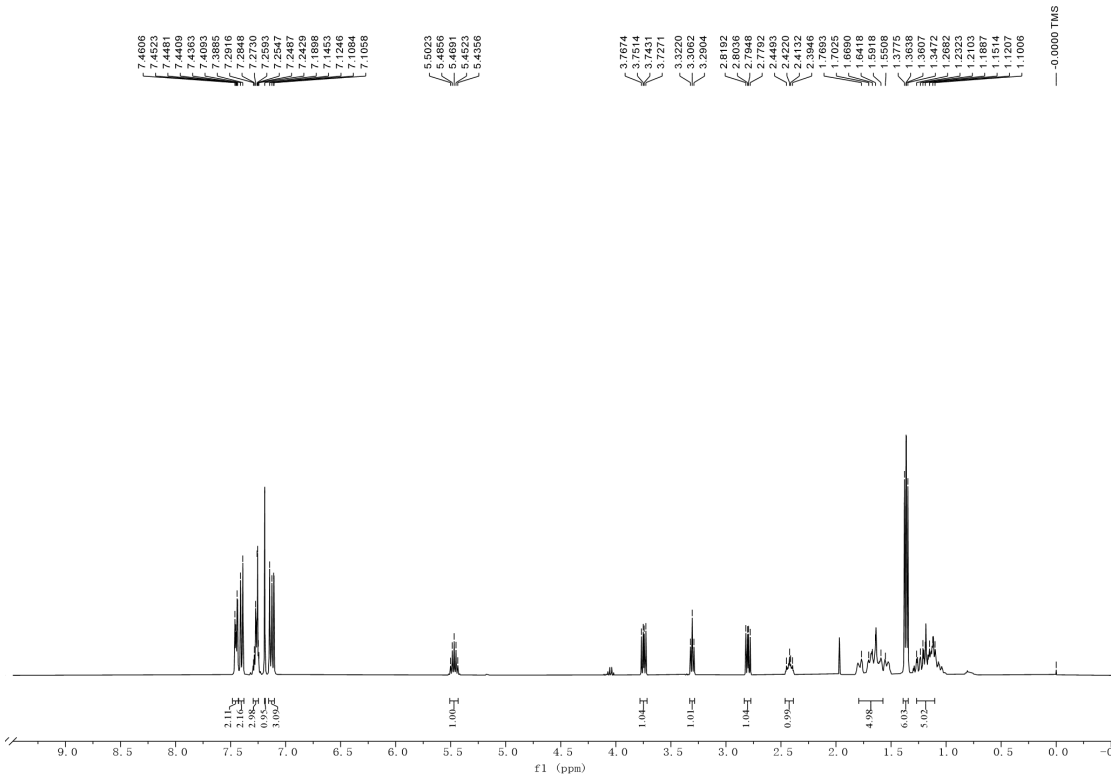
^{1}H NMR-4p (400 MHz, $CDCl_3$)



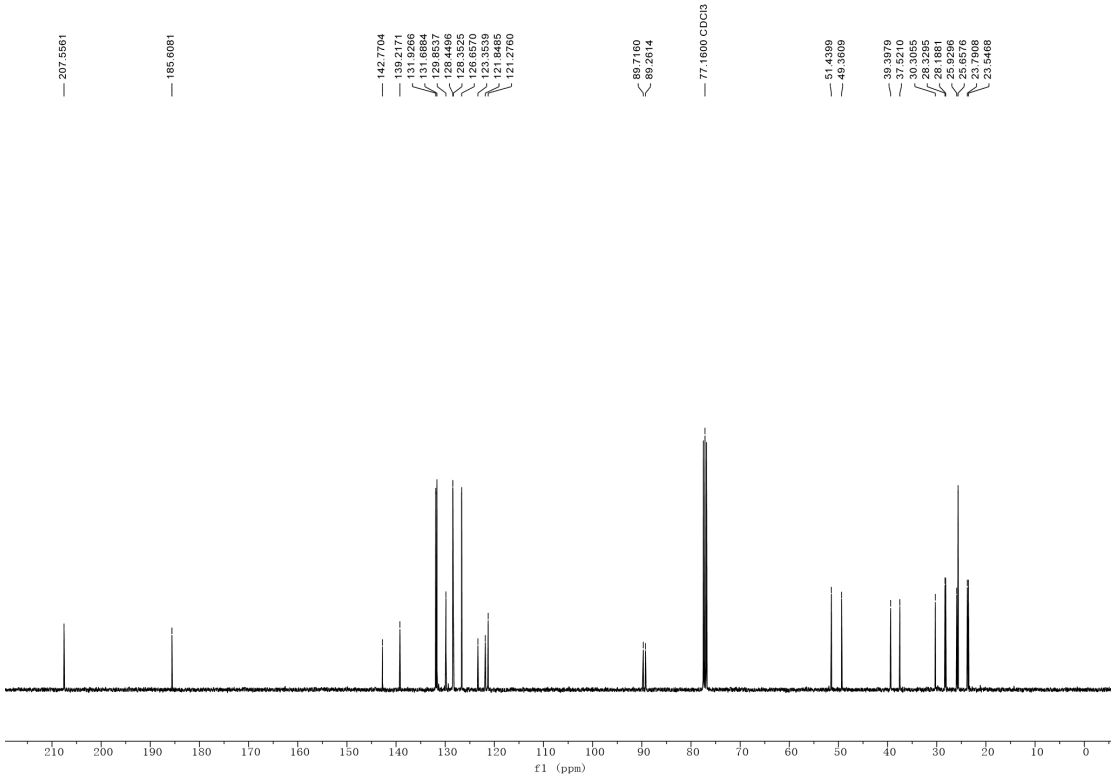
^{13}C NMR-4p (101 MHz,$CDCl_3$)



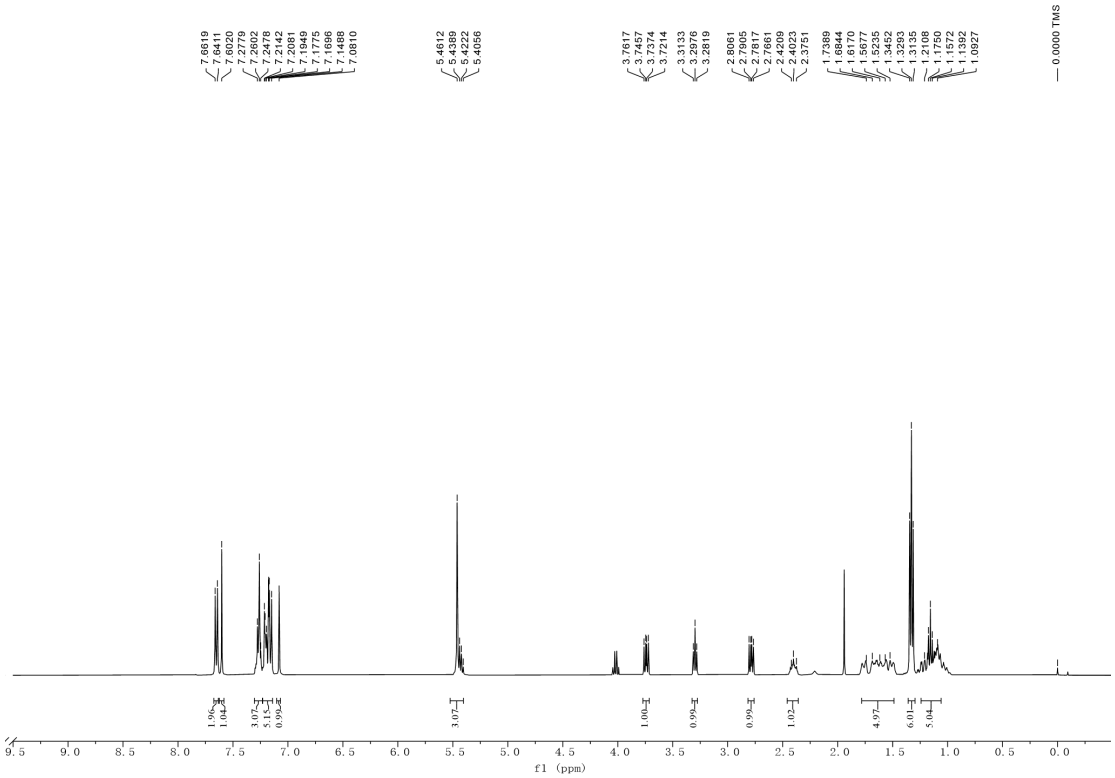
^{1}H NMR-5a (400 MHz, $CDCl_3$)



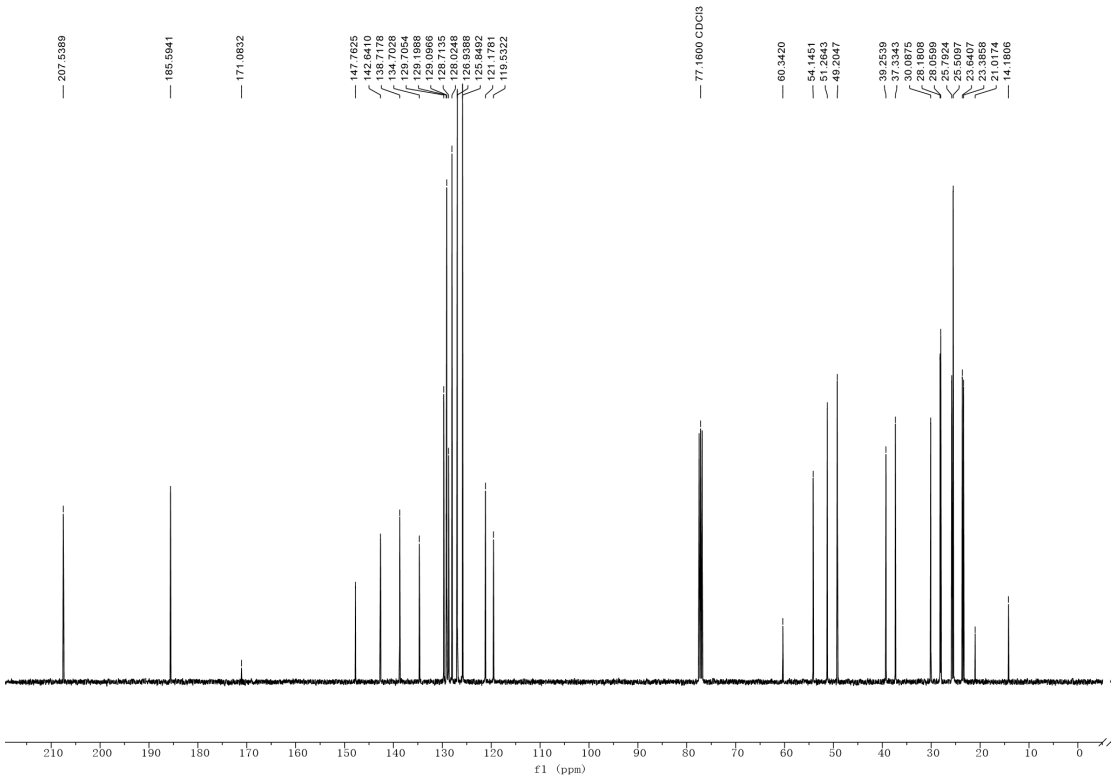
^{13}C NMR-5a (101 MHz, $CDCl_3$)



^{1}H NMR-6a (400 MHz, $CDCl_3$)

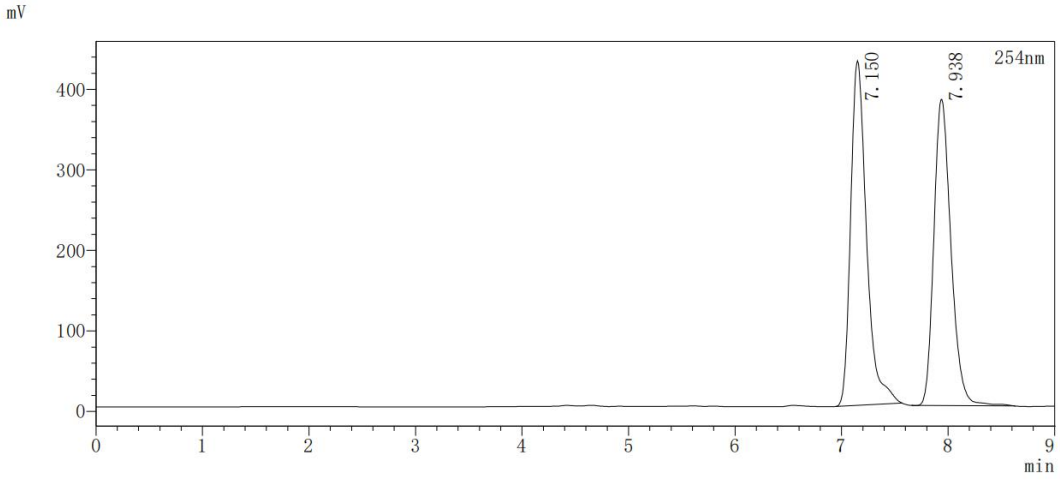


^{13}C NMR-6a (101 MHz, $CDCl_3$)



VIII HPLC Traces on Chiral Stationary Phase

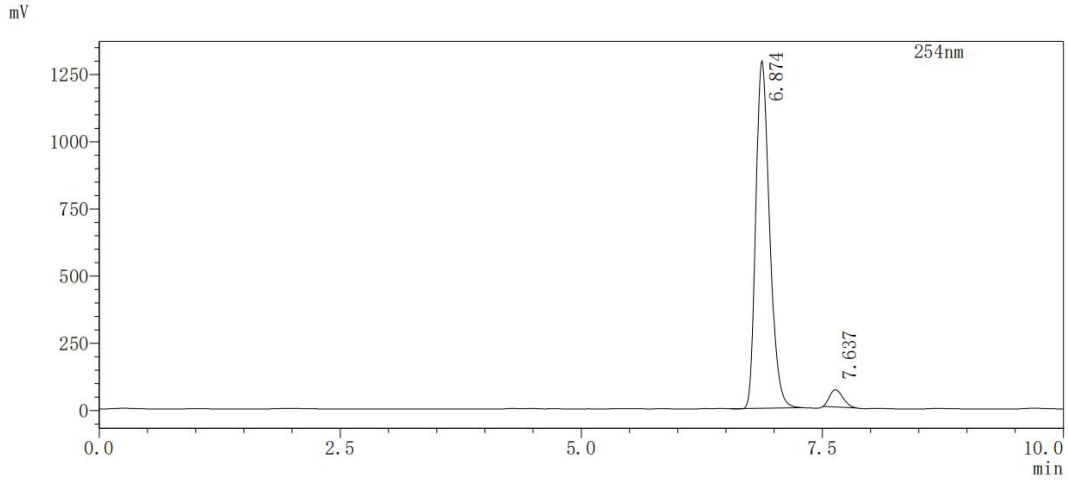
racemic-3a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.150	4431199	427891	50.978
2	7.938	4261187	380437	49.022
Total		8692385	808327	100.000

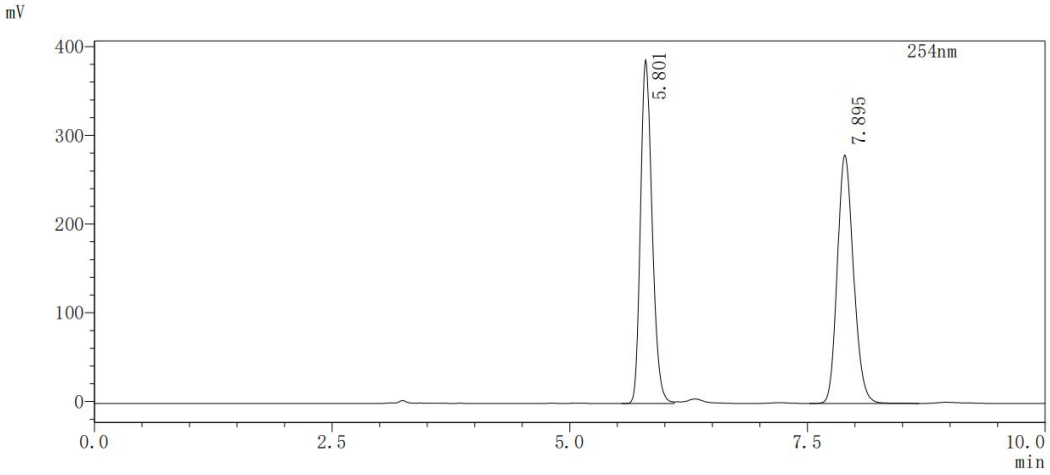
chiral-3a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.874	12882806	1293020	95.458
2	7.637	613032	64071	4.542
Total		13495838	1357091	100.000

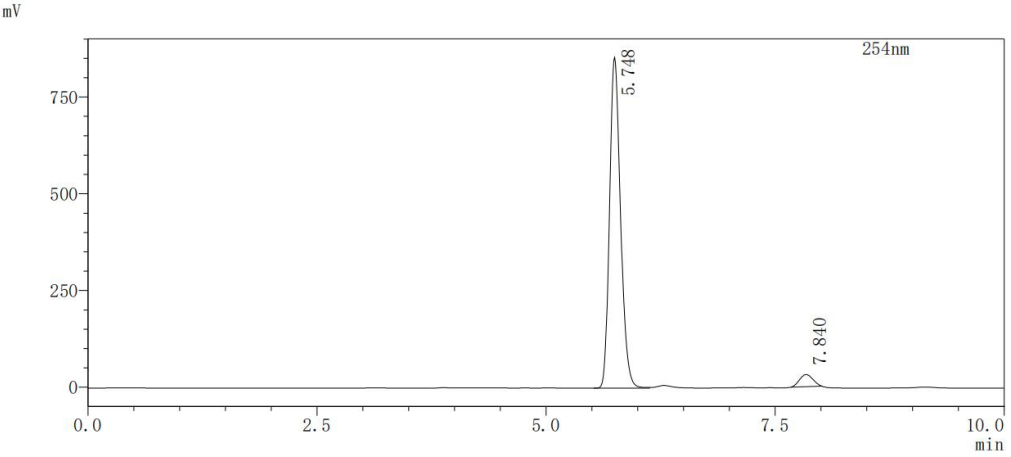
racemic-3b



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.801	3287387	386969	49.724
2	7.895	3323894	279969	50.276
Total		6611281	666938	100.000

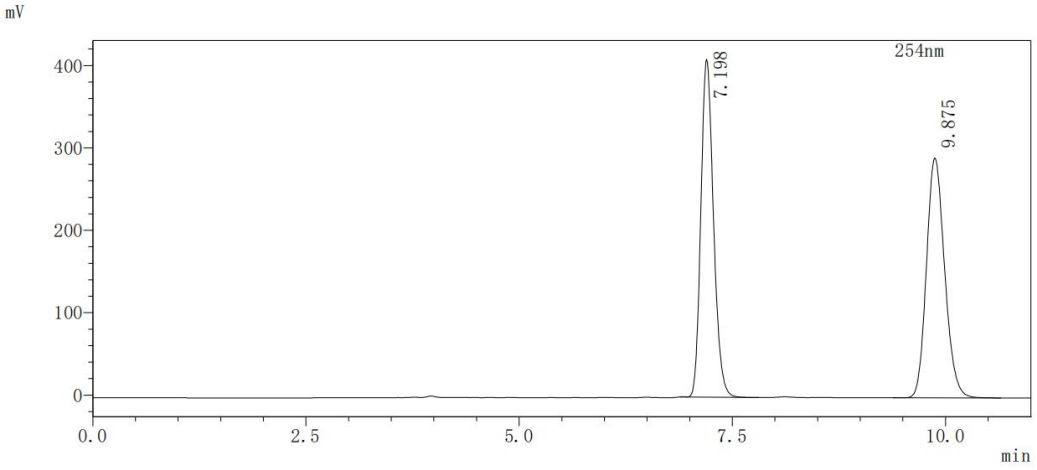
chiral-3b



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.748	7154201	854720	95.814
2	7.840	312541	30885	4.186
Total		7466742	885605	100.000

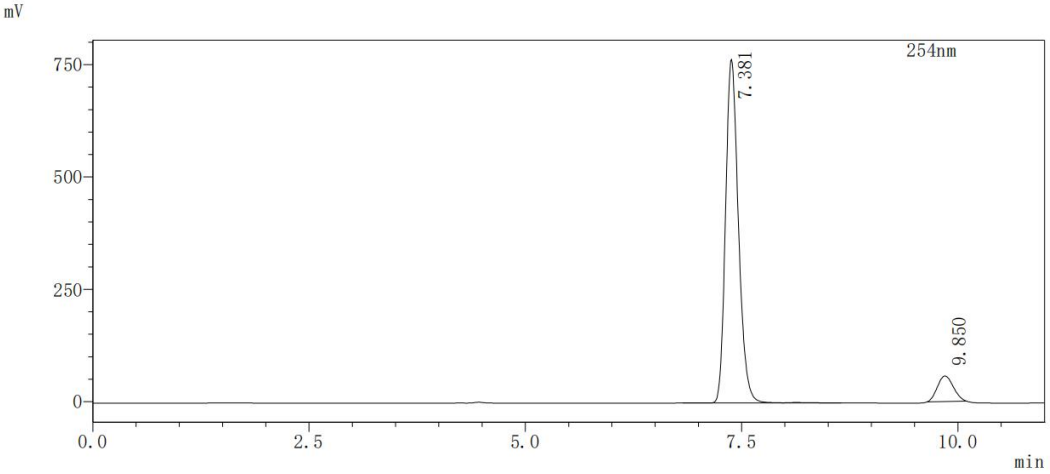
racemic-3c



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.198	4217333	409764	49.379
2	9.875	4323440	291164	50.621
Total		8540773	700927	100.000

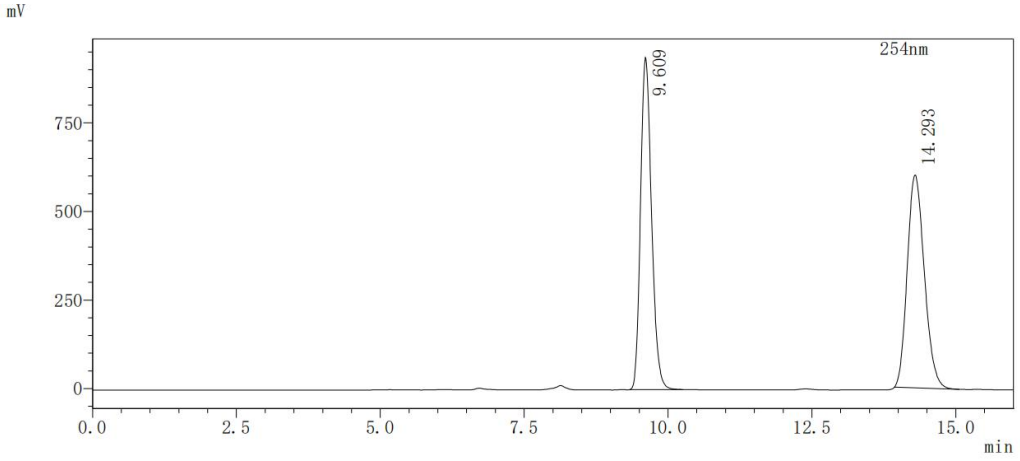
chiral-3c



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.381	7915016	764406	91.509
2	9.850	734464	57231	8.491
Total		8649480	821637	100.000

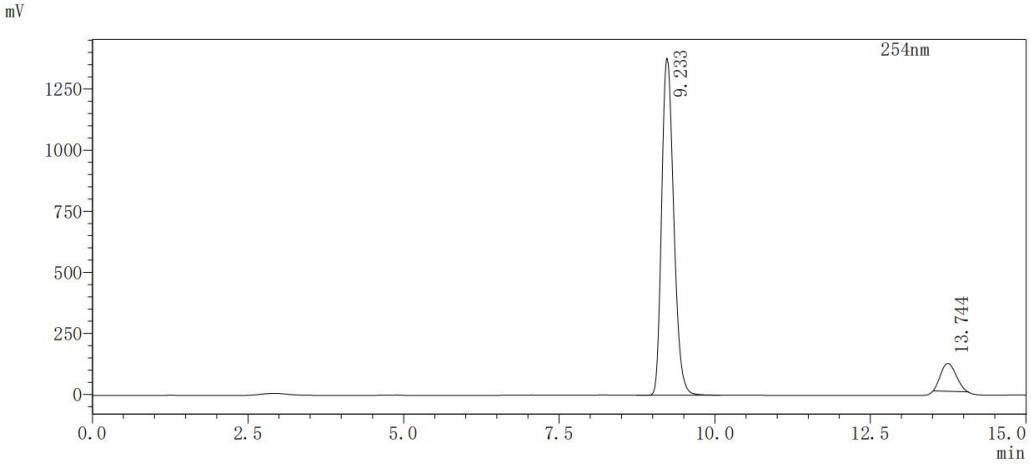
racemic-3d



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.609	12474531	937230	50.092
2	14.293	12428629	600893	49.908
Total		24903160	1538123	100.000

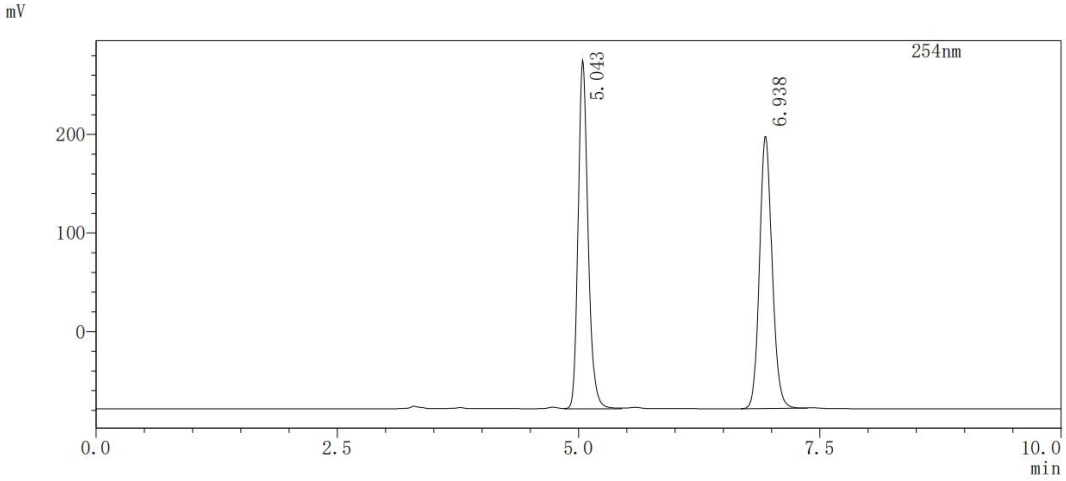
chiral-3d



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.233	18584314	1378770	90.472
2	13.744	1957295	113781	9.528
Total		20541609	1492551	100.000

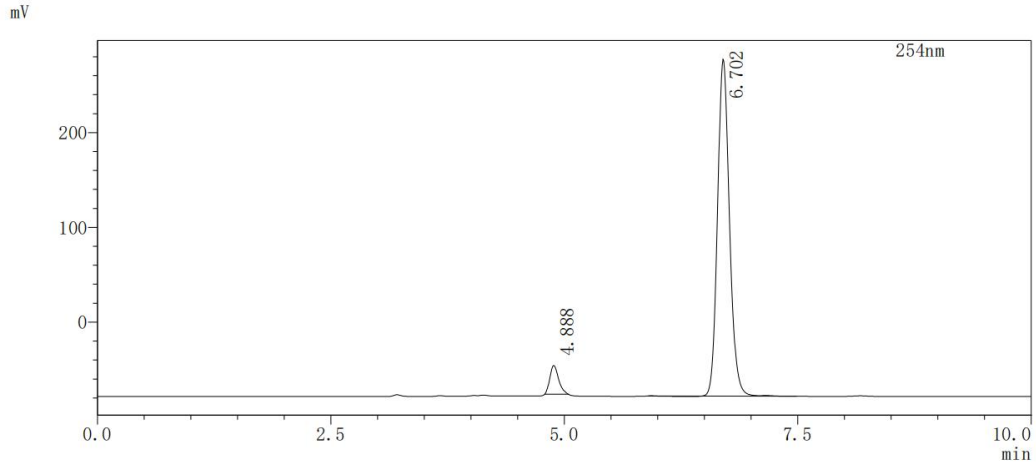
racemic-3e



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.043	2529123	353738	50.158
2	6.938	2513229	275788	49.842
Total		5042352	629526	100.000

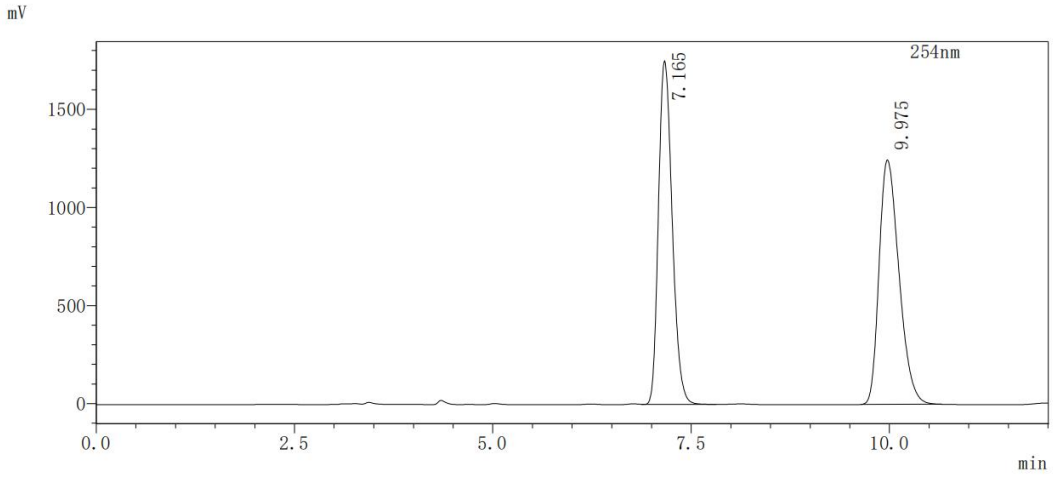
chiral-3e



254nm

Peak#	Ret. Time	Area	Height	Area%
1	4.888	197790	30235	5.904
2	6.702	3152155	355368	94.096
Total		3349945	385603	100.000

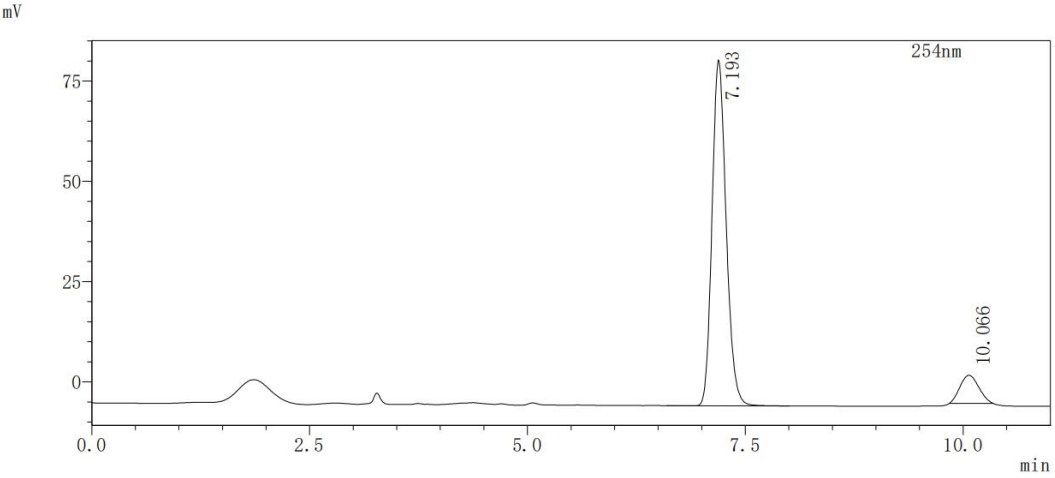
racemic-3f



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.165	21070958	1751103	49.218
2	9.975	21740420	1247047	50.782
Total		42811378	2998150	100.000

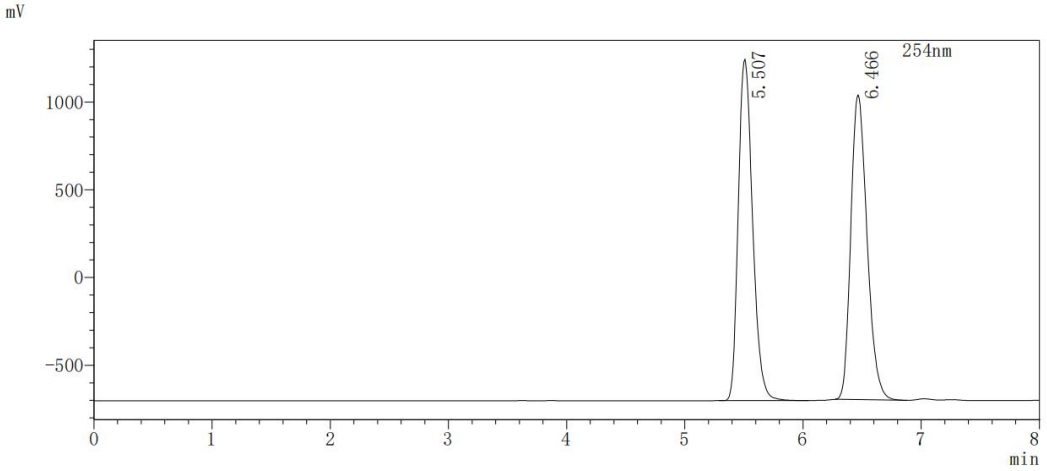
chiral-3f



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.193	972408	86205	90.290
2	10.066	104577	7007	9.710
Total		1076985	93212	100.000

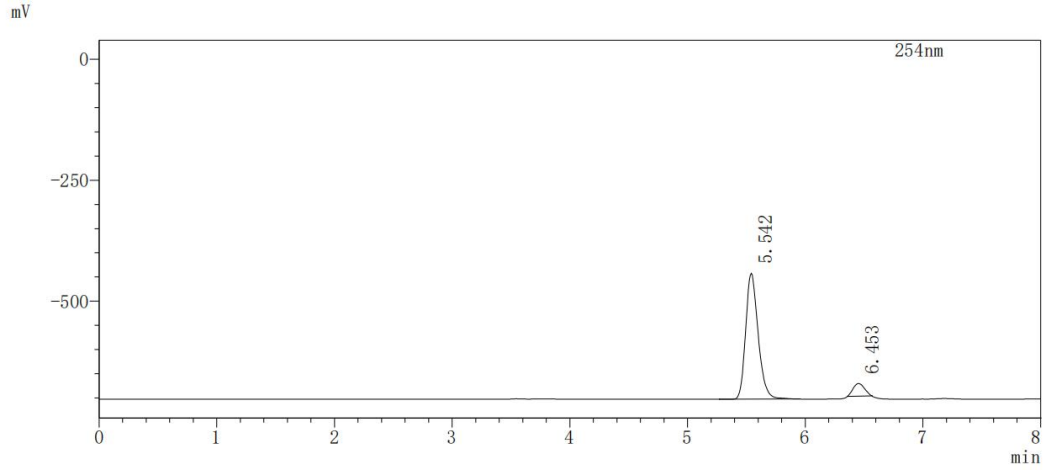
racemic-3g



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.507	16365731	1944008	49.673
2	6.466	16581254	1734591	50.327
Total		32946985	3678599	100.000

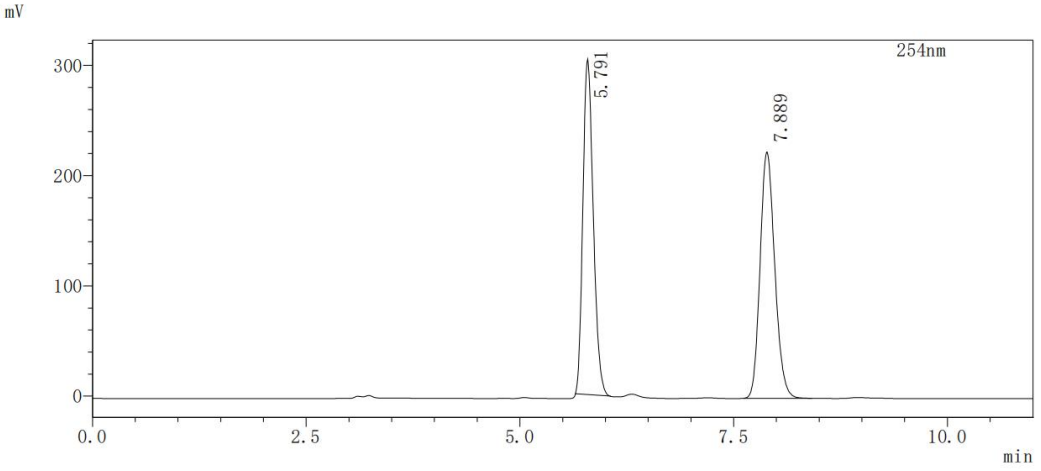
chiral-3g



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.542	1920565	260332	91.479
2	6.453	178905	26299	8.521
Total		2099470	286631	100.000

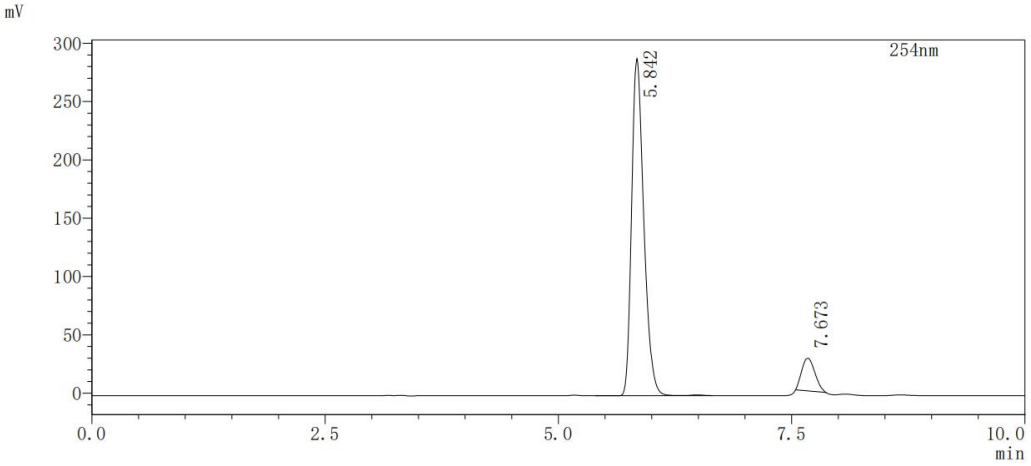
racemic-3h



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.791	2573642	304342	49.107
2	7.889	2667254	223385	50.893
Total		5240895	527727	100.000

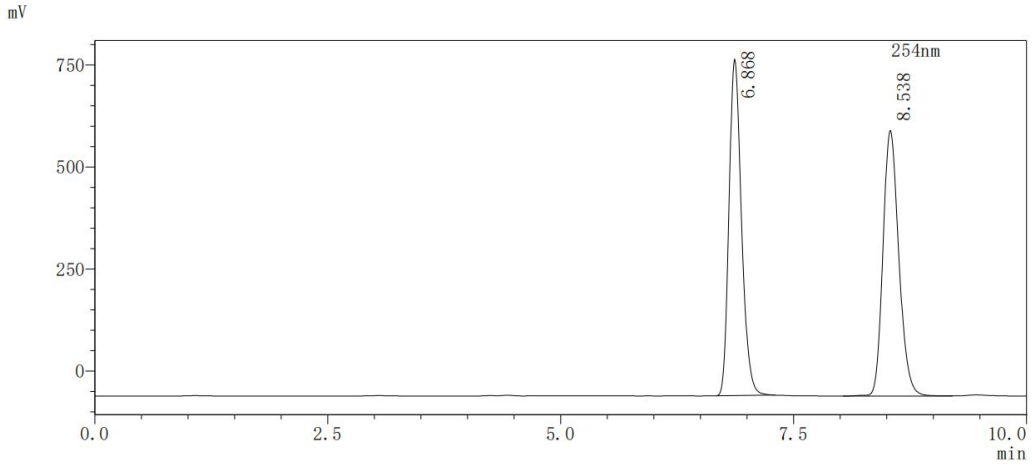
chiral-3h



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.842	2623864	288844	90.542
2	7.673	274098	28034	9.458
Total		2897962	316878	100.000

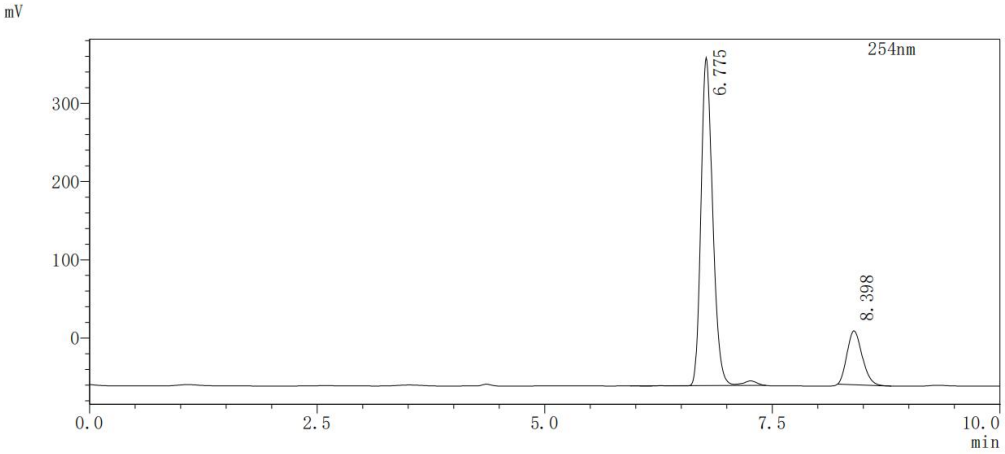
racemic-3i



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.868	7680333	823497	49.894
2	8.538	7712905	650235	50.106
Total		15393238	1473731	100.000

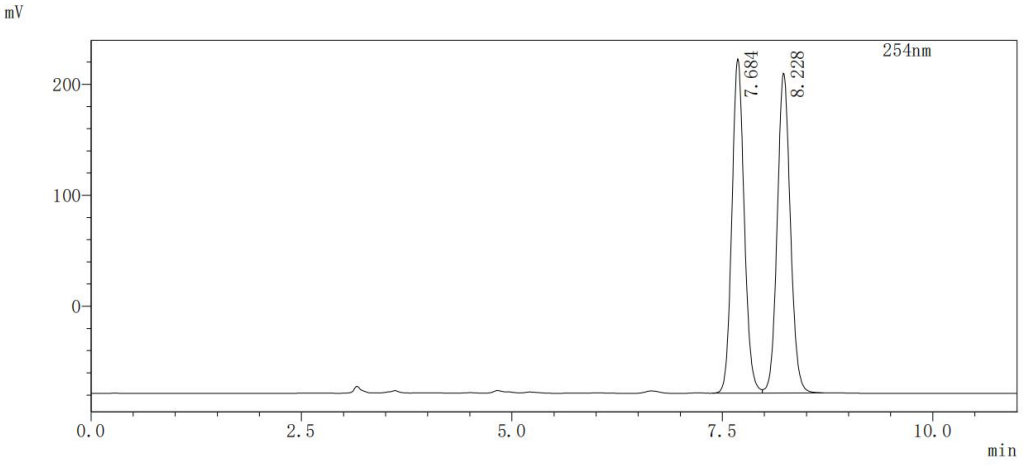
chiral-3i



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.775	3802371	419131	82.643
2	8.398	798606	68891	17.357
Total		4600977	488021	100.000

racemic-3j

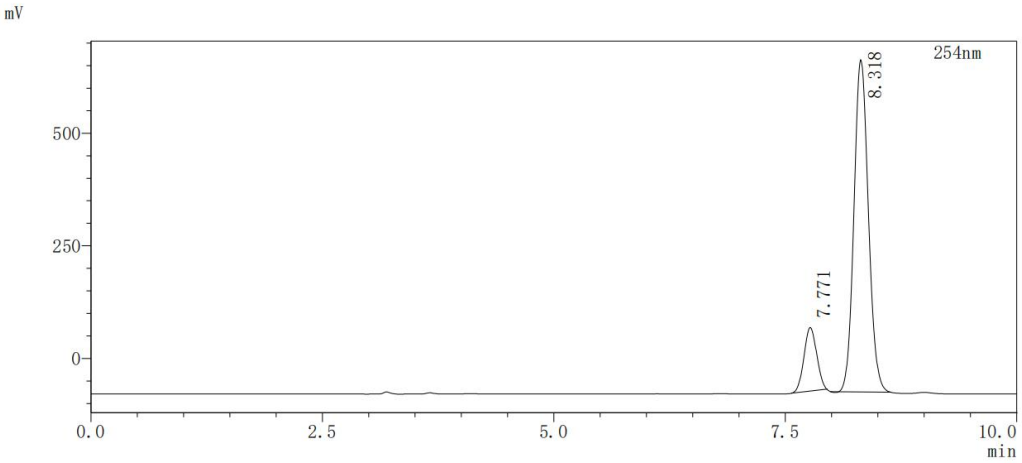


254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.684	3072639	301156	49.583
2	8.228	3124363	288218	50.417
Total		6197002	589374	100.000

c

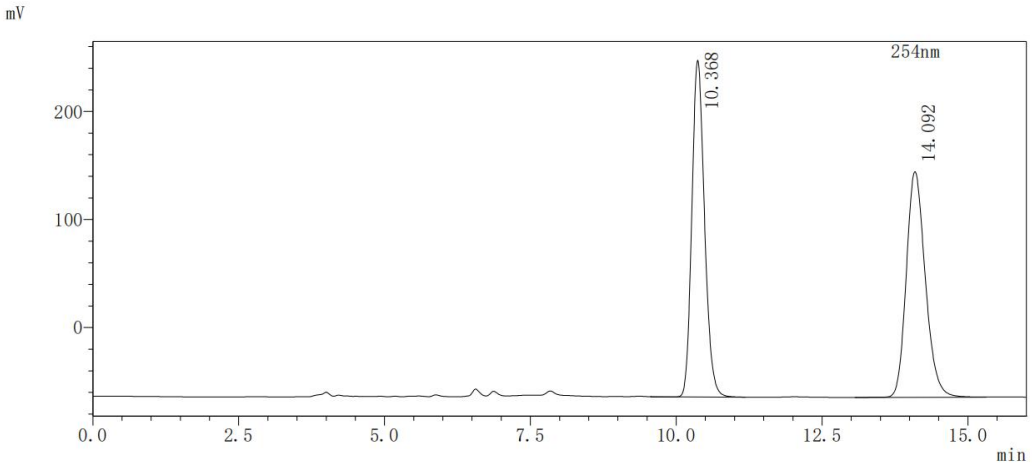
hiral-3j



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.771	1353653	141061	14.495
2	8.318	7984896	737006	85.505
Total		9338548	878067	100.000

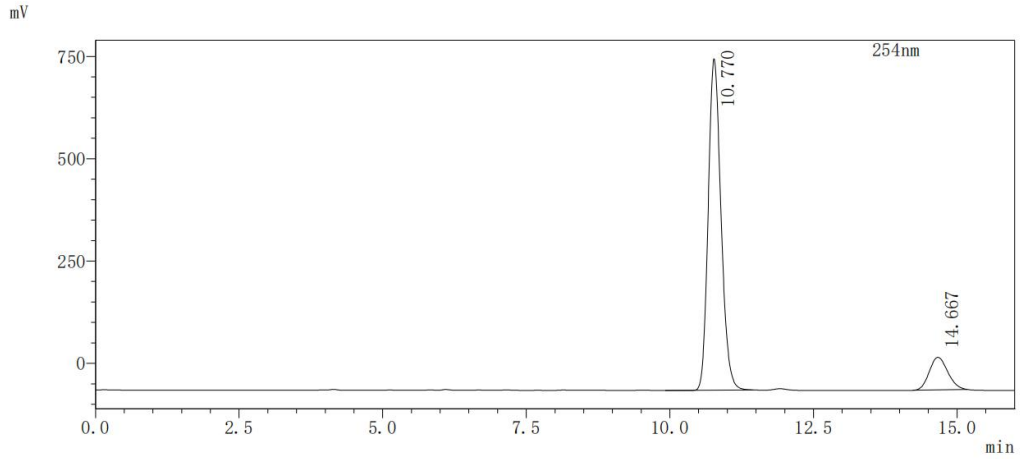
racemic-3k



254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.368	4710131	311569	49.809
2	14.092	4746338	208889	50.191
Total		9456469	520458	100.000

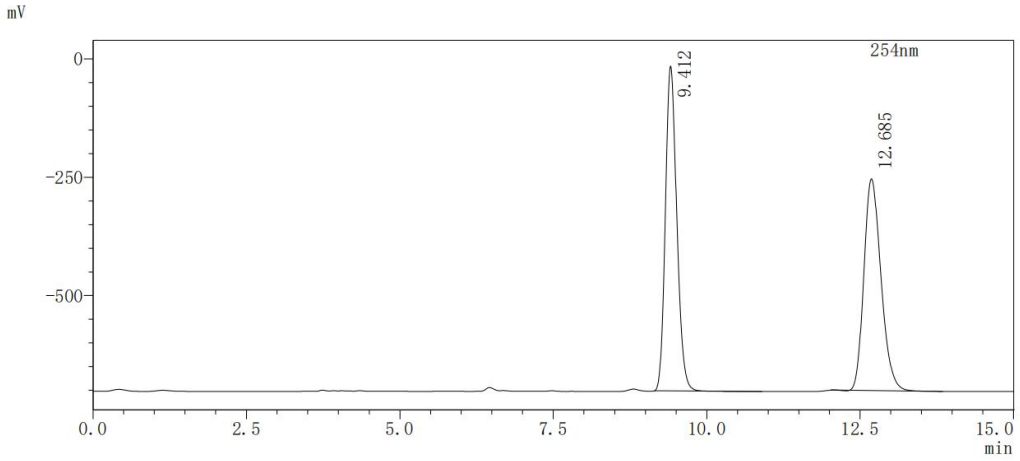
chiral-3k



254nm

Peak#	Ret. Time	Area	Height	Area%
1	10.770	12522993	809713	87.571
2	14.667	1777358	79600	12.429
Total		14300351	889313	100.000

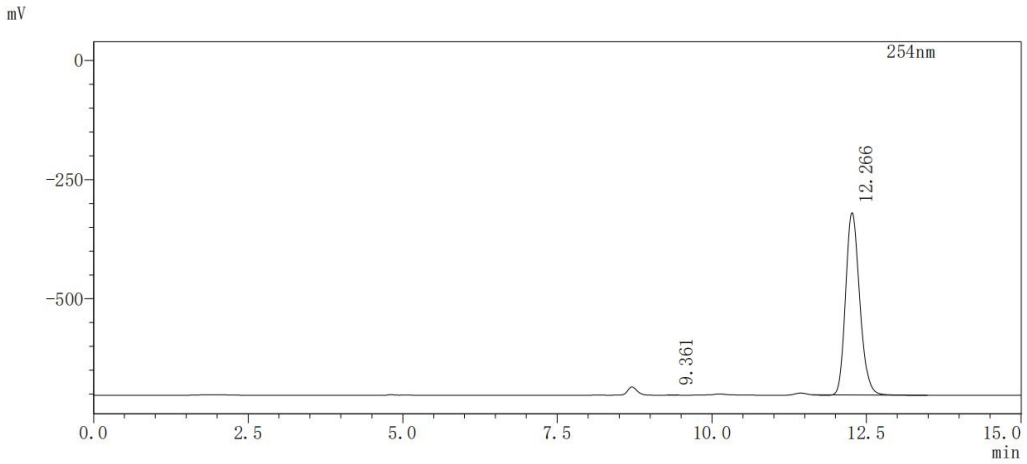
racemic-3l



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.412	8862778	685674	50.526
2	12.685	8678115	447209	49.474
Total		17540892	1132882	100.000

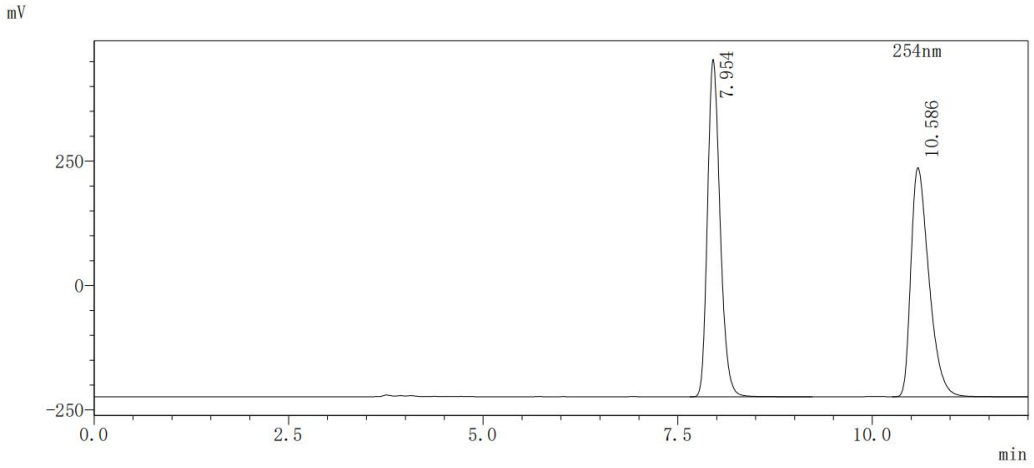
chiral-3l



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.361	1625	266	0.027
2	12.266	6051896	382763	99.973
Total		6053521	383029	100.000

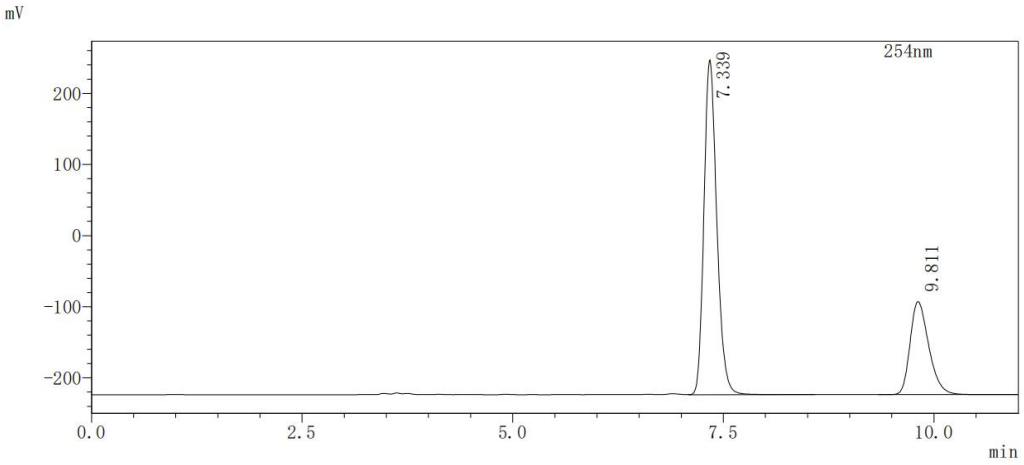
racemic-3m



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.954	7645148	677558	50.733
2	10.586	7424283	460395	49.267
Total		15069431	1137954	100.000

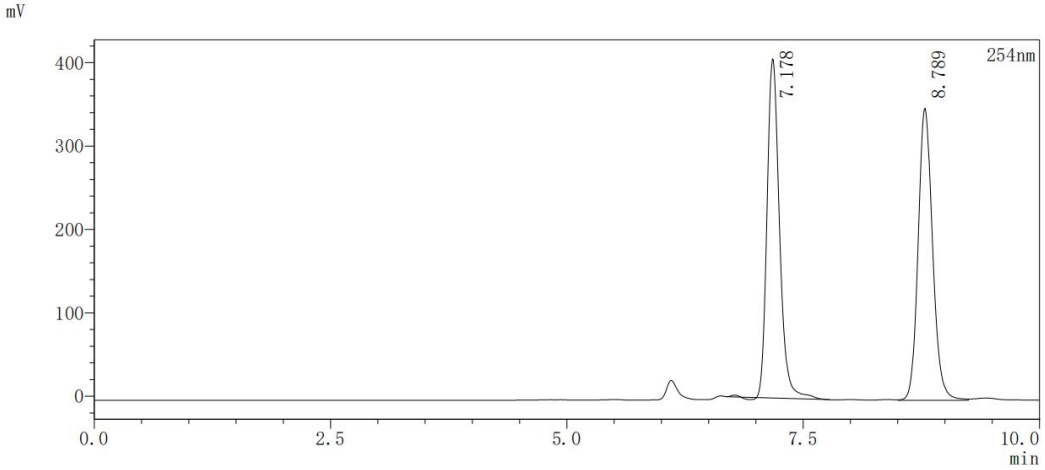
chiral-3m



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.339	4989216	470590	71.135
2	9.811	2024527	130814	28.865
Total		7013743	601404	100.000

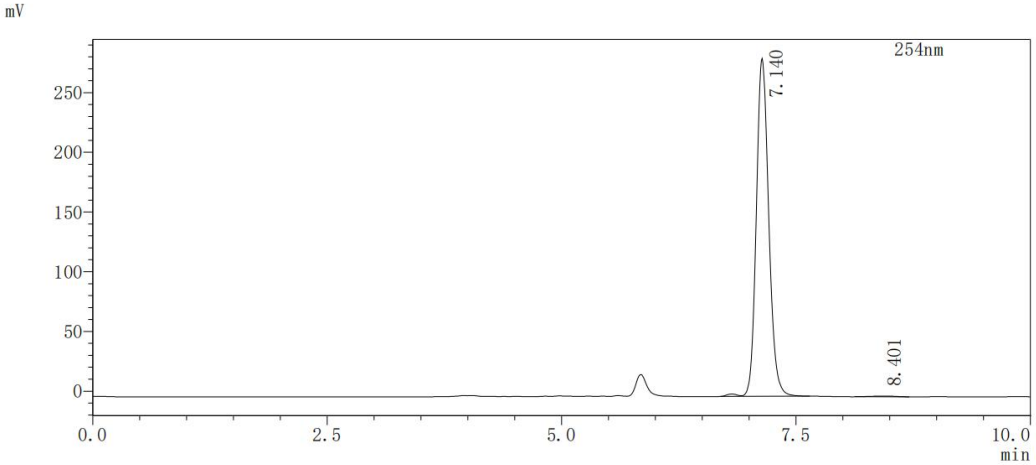
racemic-3n



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.178	3719229	406568	49.943
2	8.789	3727653	349980	50.057
Total		7446882	756548	100.000

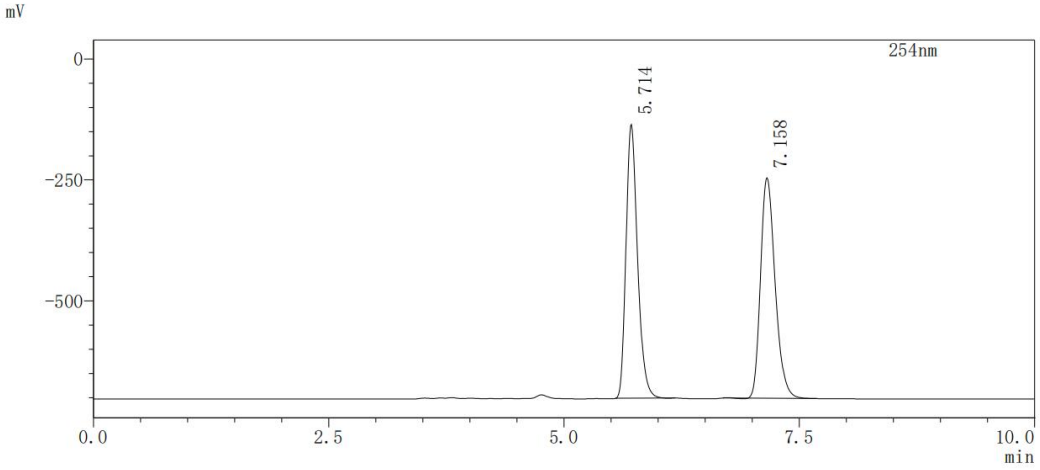
chiral-3n



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.140	2617675	283102	99.594
2	8.401	10682	591	0.406
Total		2628357	283693	100.000

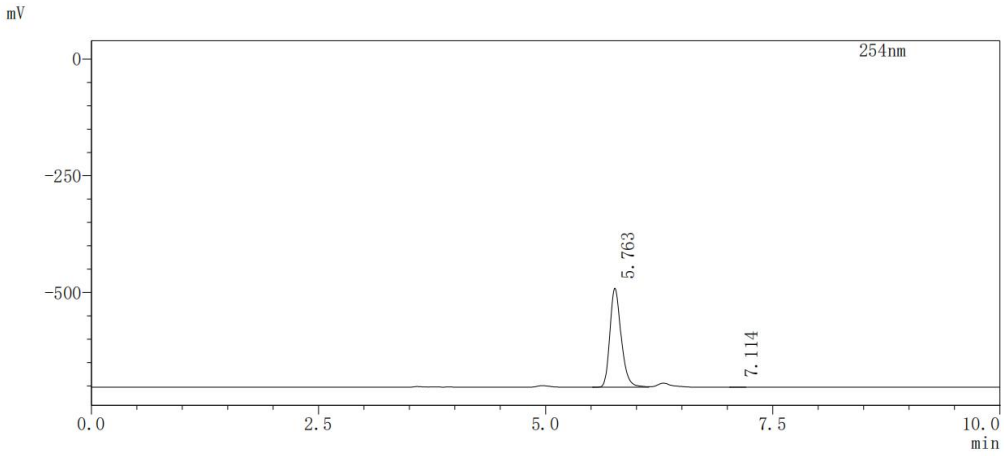
racemic-4a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.714	4829622	566101	49.633
2	7.158	4901103	455593	50.367
Total		9730724	1021695	100.000

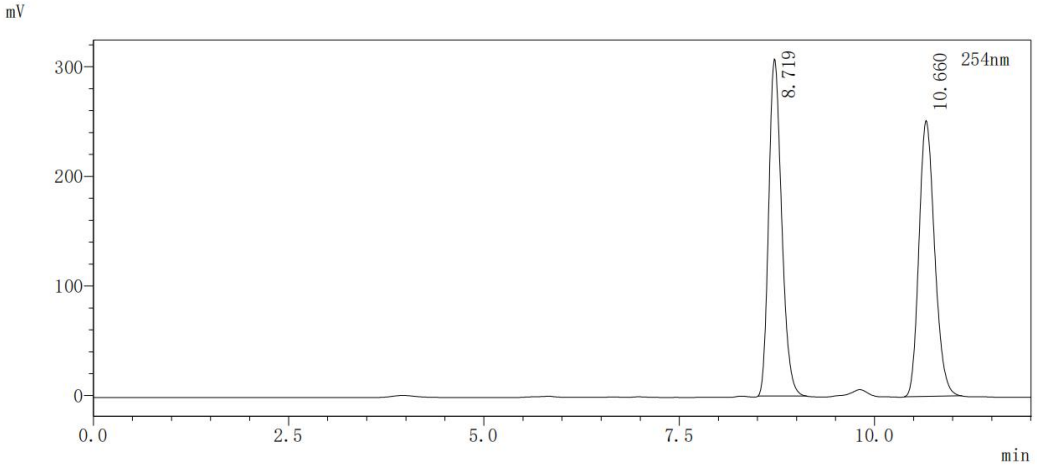
chiral-4a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.763	1841903	211764	99.991
2	7.114	159	30	0.009
Total		1842062	211793	100.000

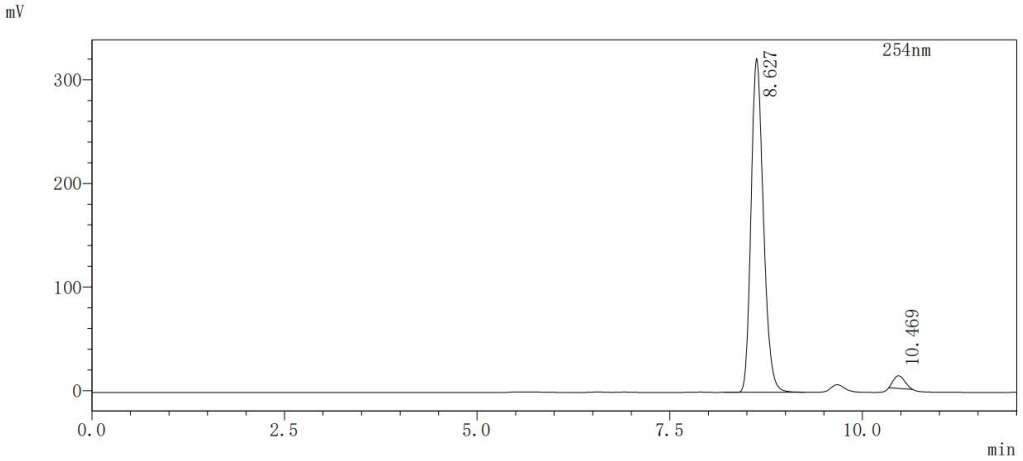
racemic-4b



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.719	3544780	307516	50.263
2	10.660	3507630	251673	49.737
Total		7052410	559189	100.000

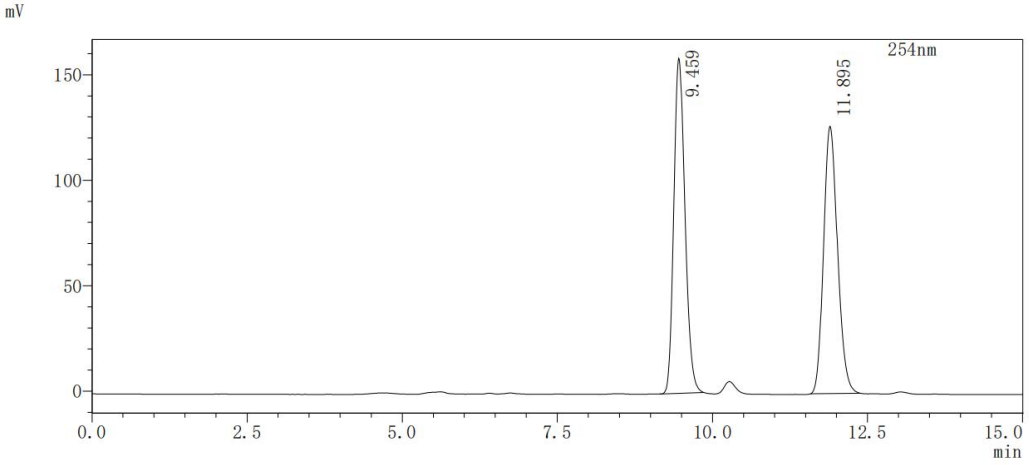
chiral-4d



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.627	3590911	322109	96.675
2	10.469	123517	12193	3.325
Total		3714428	334301	100.000

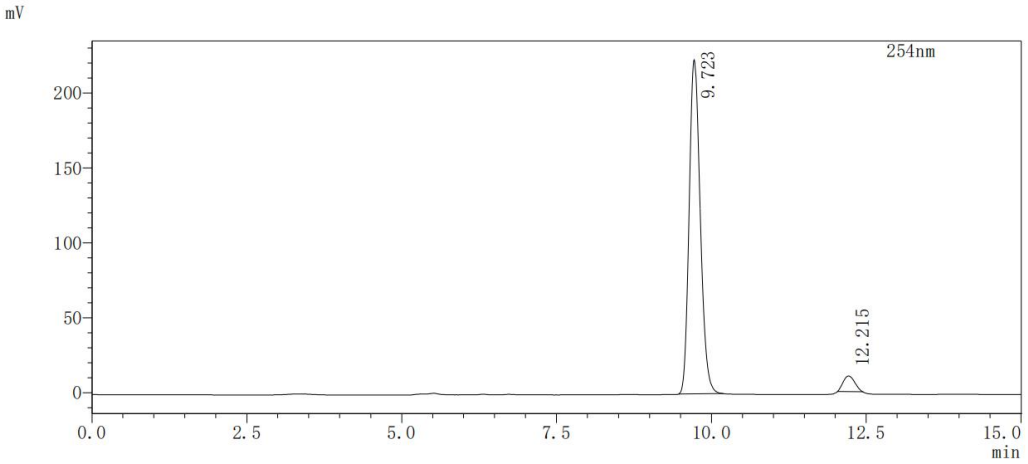
racemic-4c



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.459	1993129	158867	50.067
2	11.895	1987820	126617	49.933
Total		3980949	285484	100.000

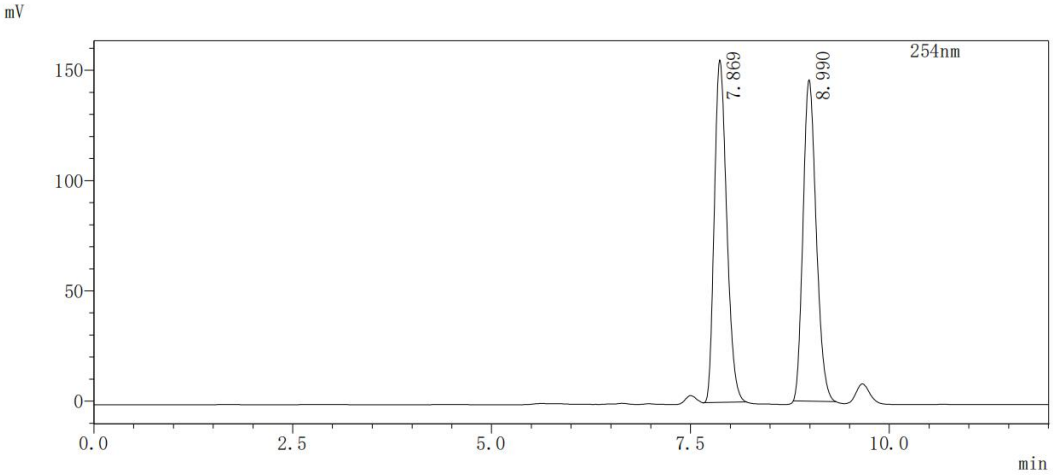
chiral-4c



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.723	2775214	223037	95.350
2	12.215	135327	10456	4.650
Total		2910541	233493	100.000

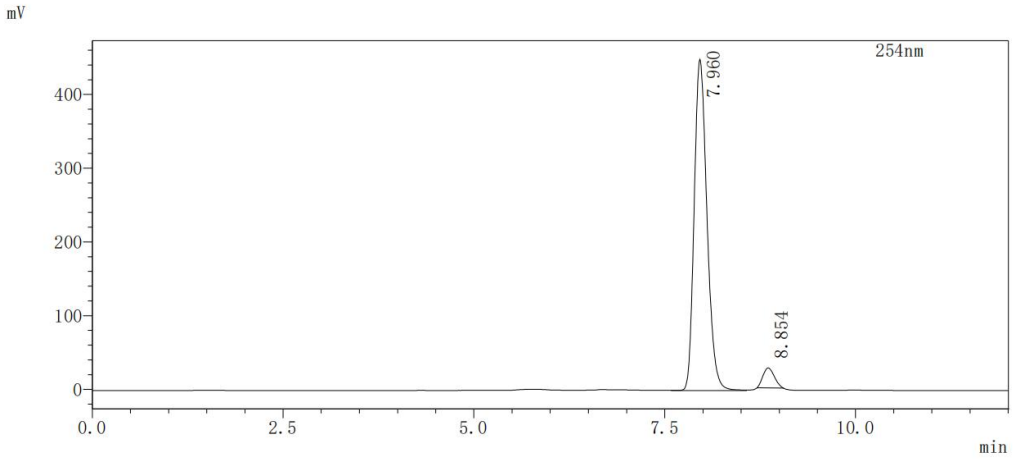
racemic-4d



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.869	1684906	155204	50.066
2	8.990	1680496	145650	49.934
Total		3365402	300854	100.000

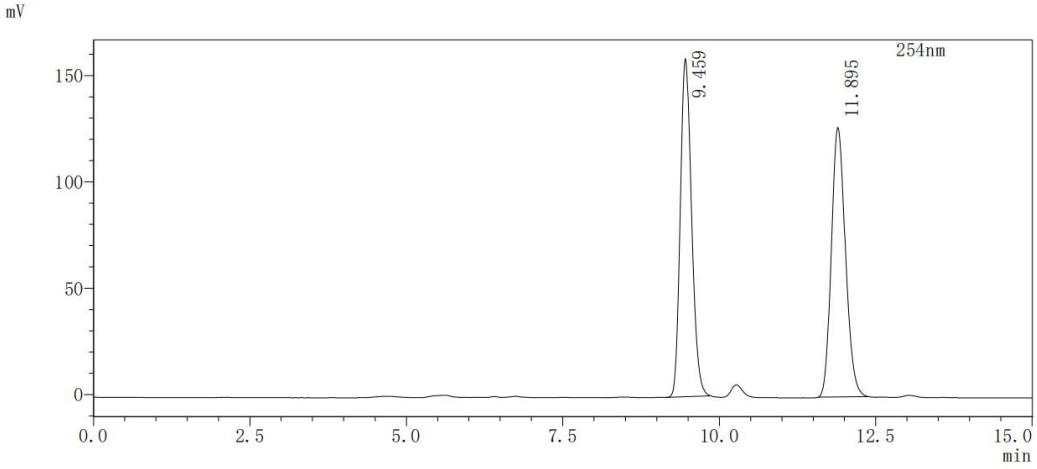
chiral-4d



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.960	5231858	449260	94.944
2	8.854	278605	26874	5.056
Total		5510463	476133	100.000

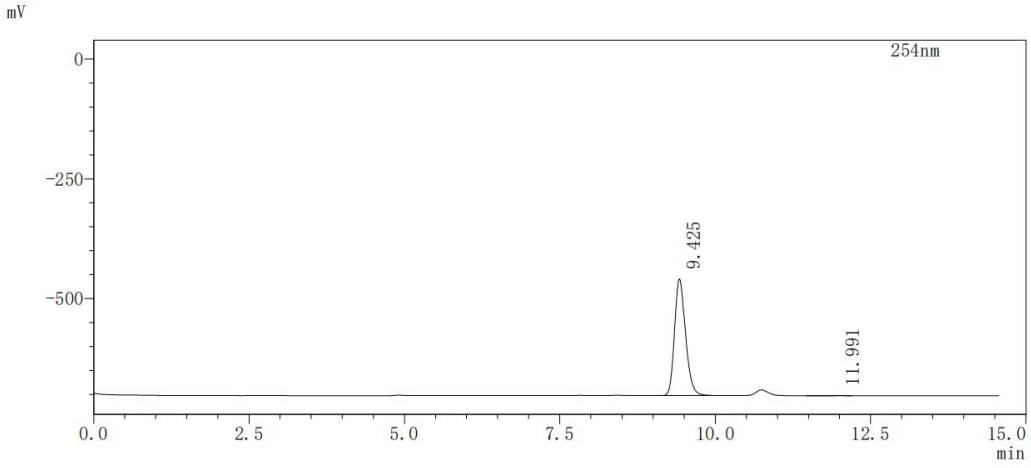
racemic-4e



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.459	1993129	158867	50.067
2	11.895	1987820	126617	49.933
Total		3980949	285484	100.000

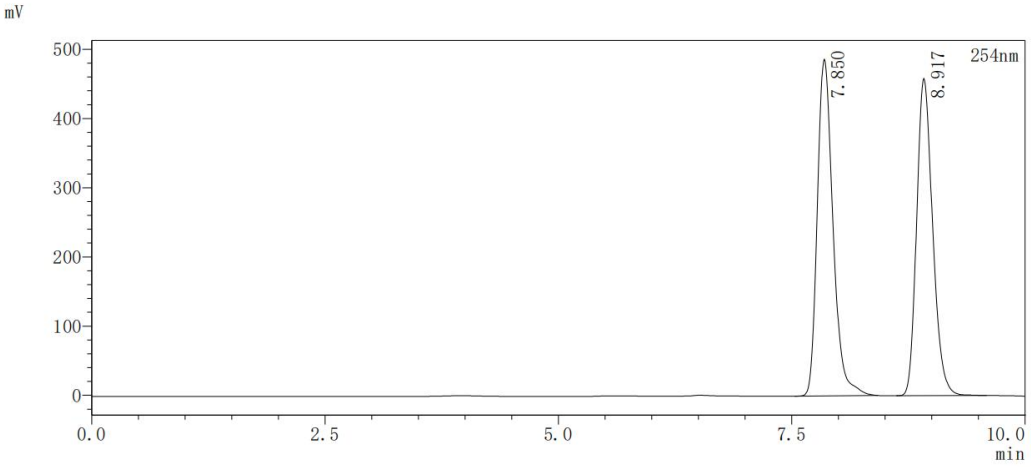
chiral-4e



254nm

Peak#	Ret. Time	Area	Height	Area%
1	9.425	2995646	243309	99.974
2	11.991	778	179	0.026
Total		2996423	243488	100.000

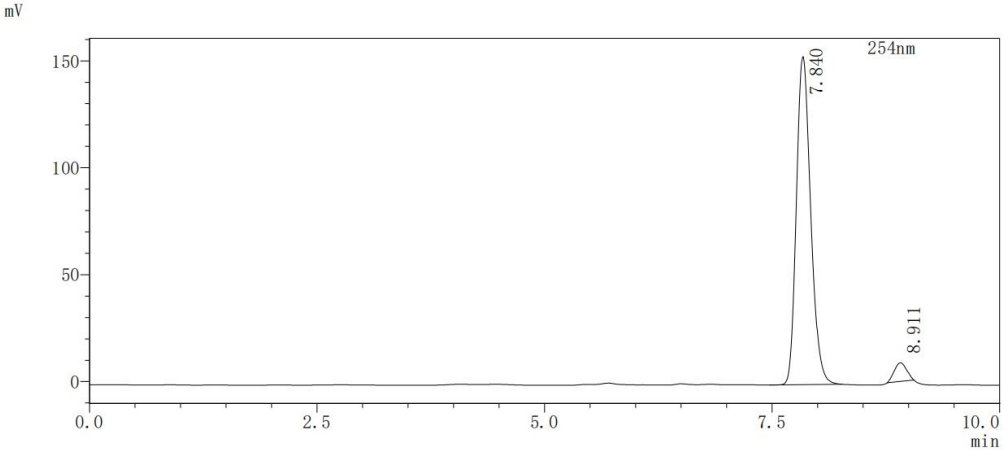
racemic-4f



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.850	5692783	486555	50.974
2	8.917	5475241	458407	49.026
Total		11168024	944962	100.000

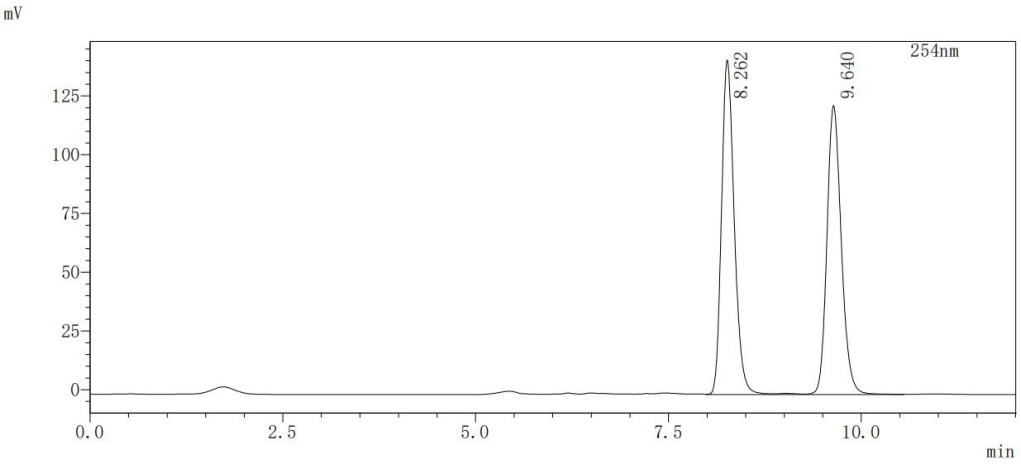
chiral-4f



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.840	1676152	153356	95.350
2	8.911	81746	8666	4.650
Total		1757899	162022	100.000

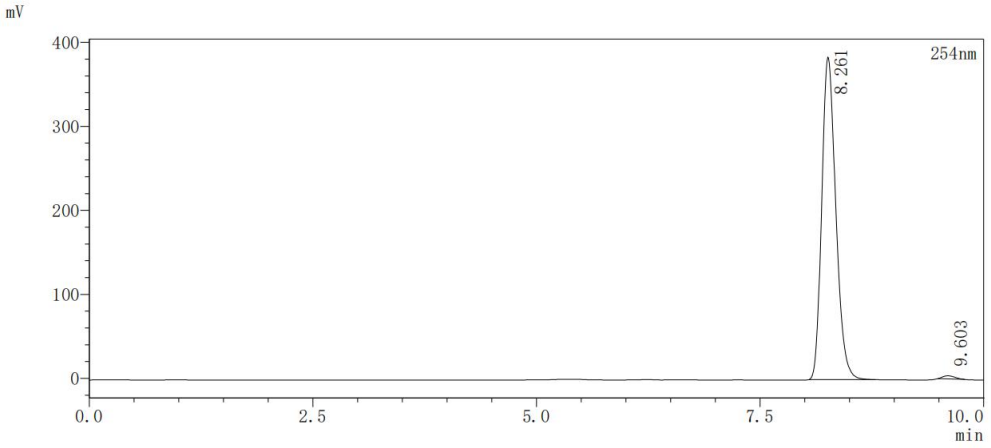
racemic-4g



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.262	1640413	142278	50.734
2	9.640	1592925	122968	49.266
Total		3233337	265246	100.000

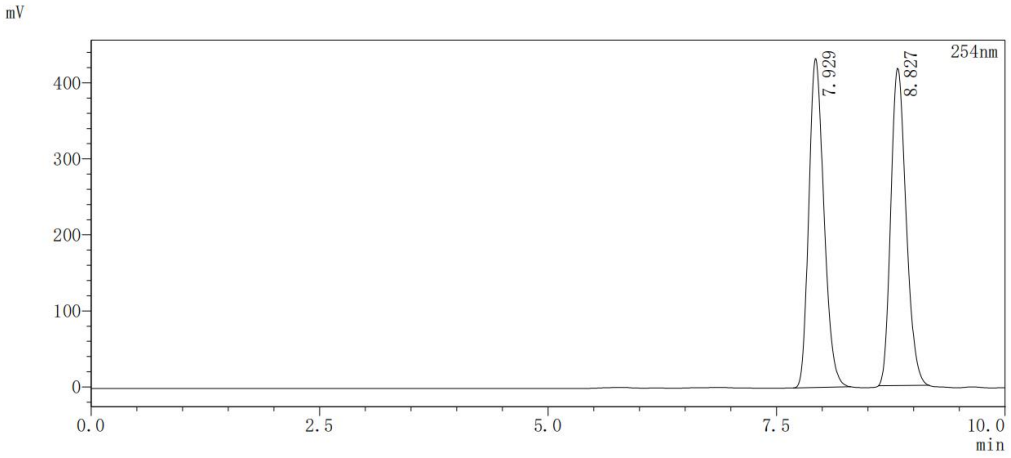
chiral-4g



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.261	4202106	383750	99.184
2	9.603	34589	3690	0.816
Total		4236695	387440	100.000

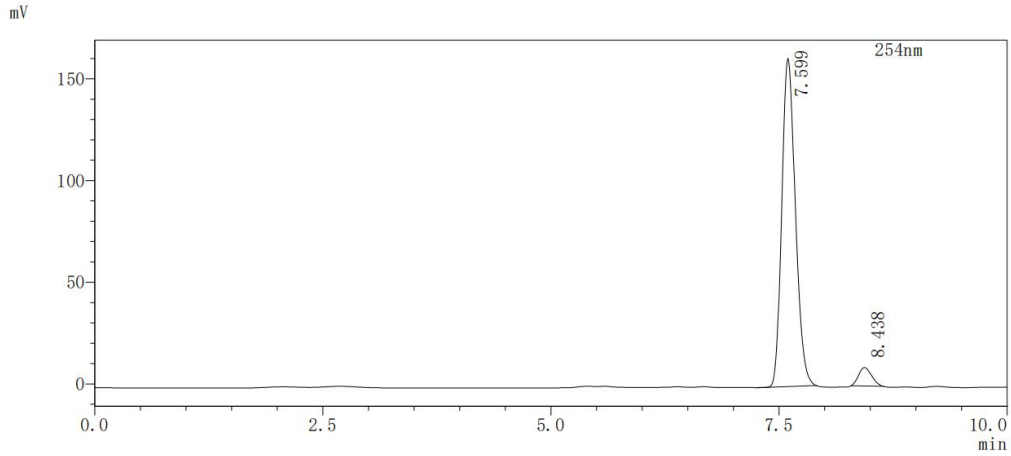
racemic-4h



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.929	4979137	432596	50.591
2	8.827	4862724	417229	49.409
Total		9841861	849825	100.000

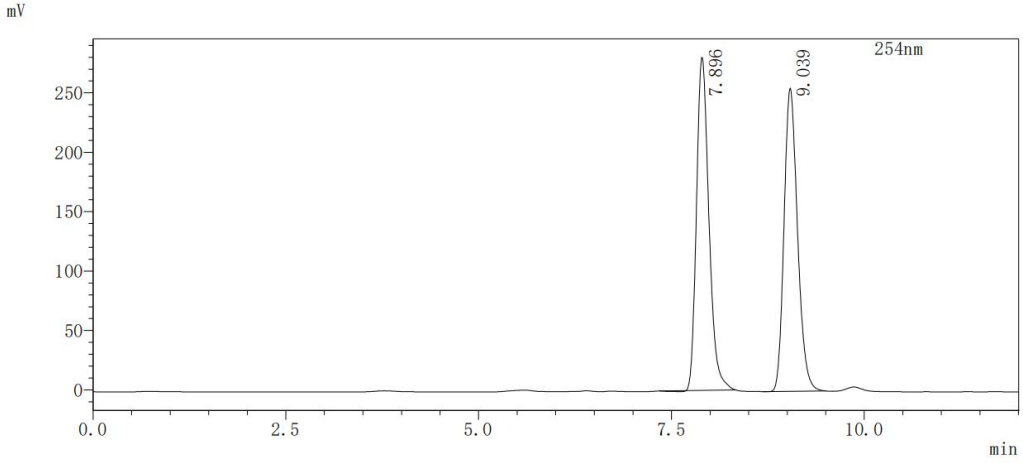
chiral-4h



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.599	1674841	161271	94.870
2	8.438	90568	9094	5.130
Total		1765409	170366	100.000

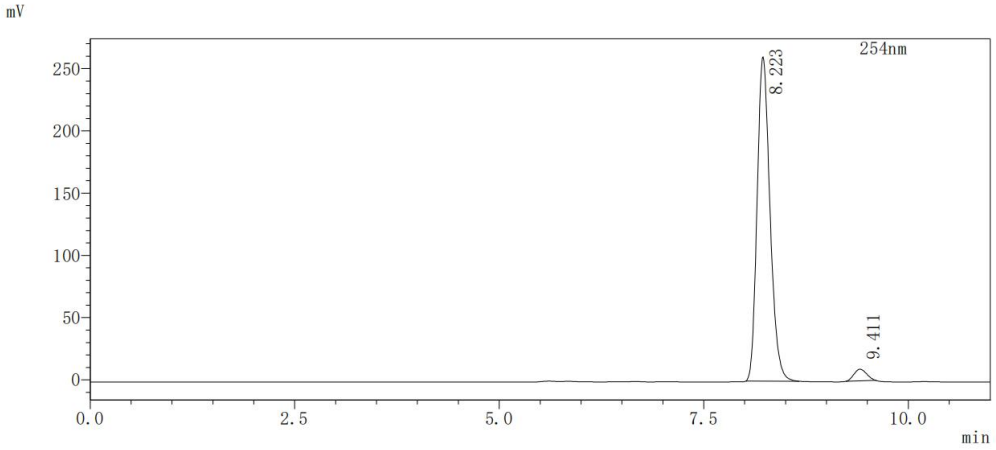
racemic-4i



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.896	3141610	280133	50.344
2	9.039	3098655	255074	49.656
Total		6240264	535208	100.000

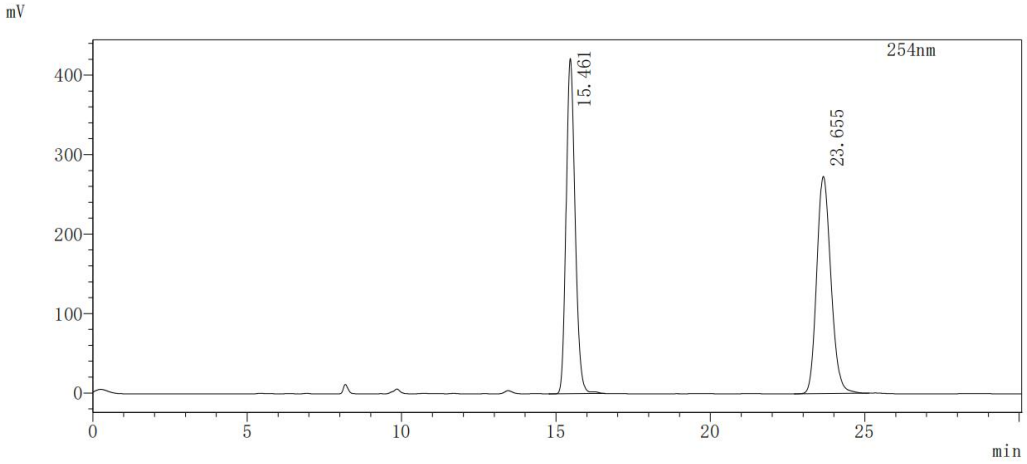
chiral-4i



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.223	2850008	260388	96.612
2	9.411	99957	9305	3.388
Total		2949965	269693	100.000

racemic-4j

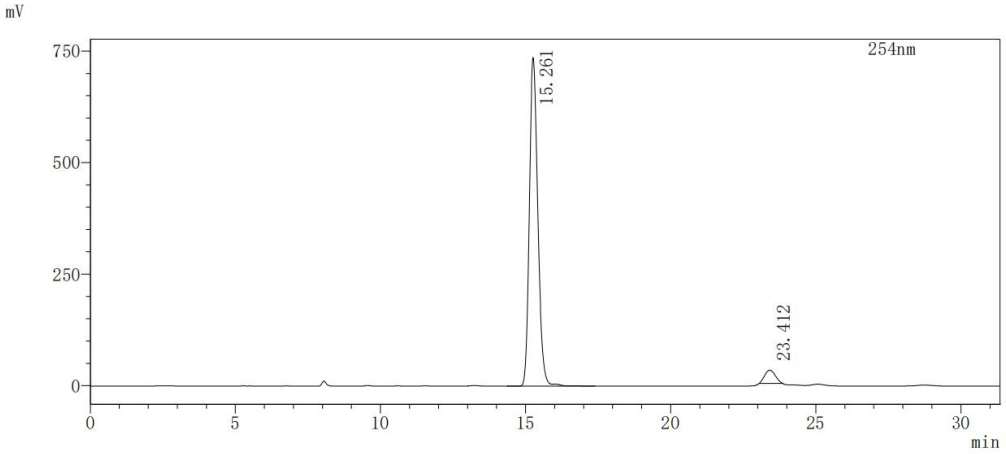


254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.461	8546259	421746	49.449
2	23.655	8736741	273404	50.551
Total		17282999	695151	100.000

c

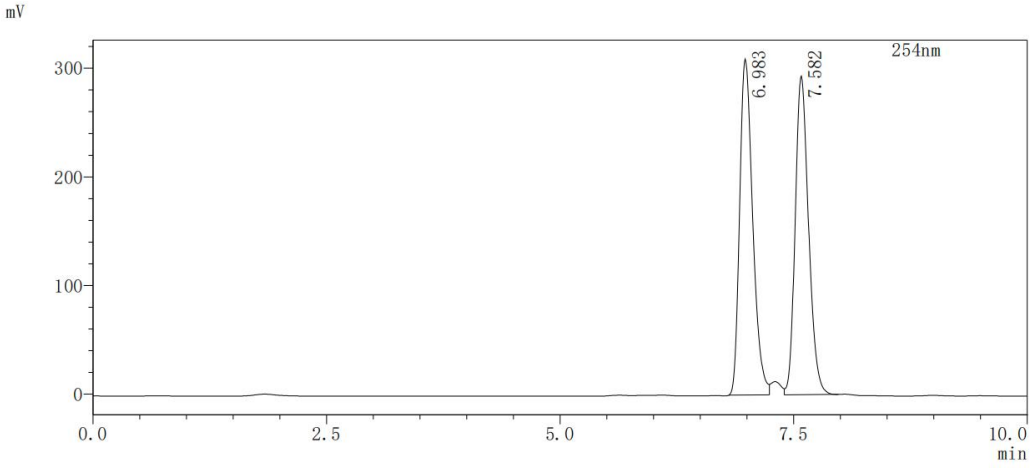
hiral-4j



254nm

Peak#	Ret. Time	Area	Height	Area%
1	15.261	14881934	736543	95.162
2	23.412	756603	29540	4.838
Total		15638537	766083	100.000

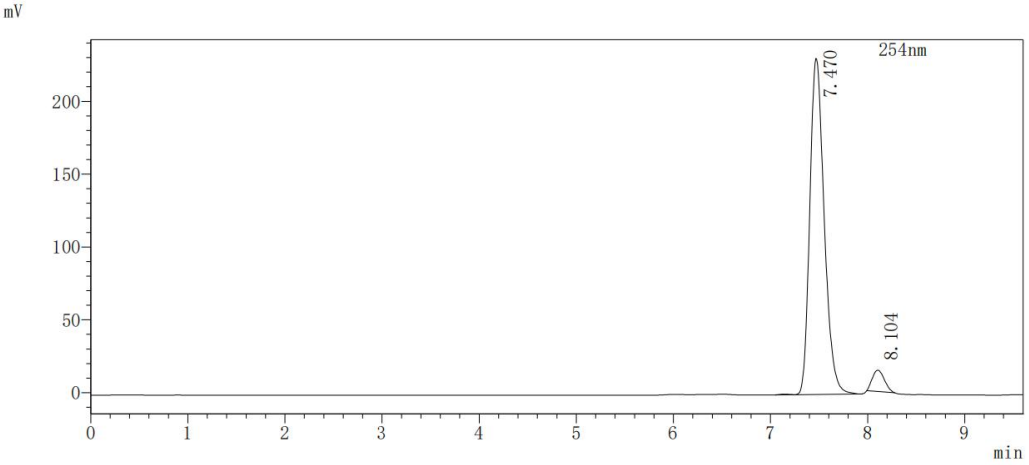
racemic-4k



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.983	3007296	309437	50.700
2	7.582	2924232	293390	49.300
Total		5931528	602827	100.000

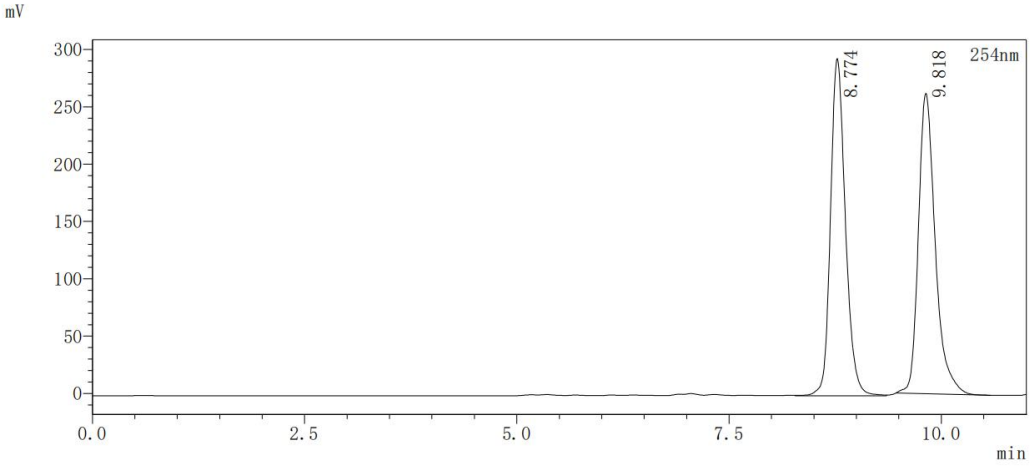
chiral-4k



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.470	2379971	230607	94.991
2	8.104	125489	14531	5.009
Total		2505460	245137	100.000

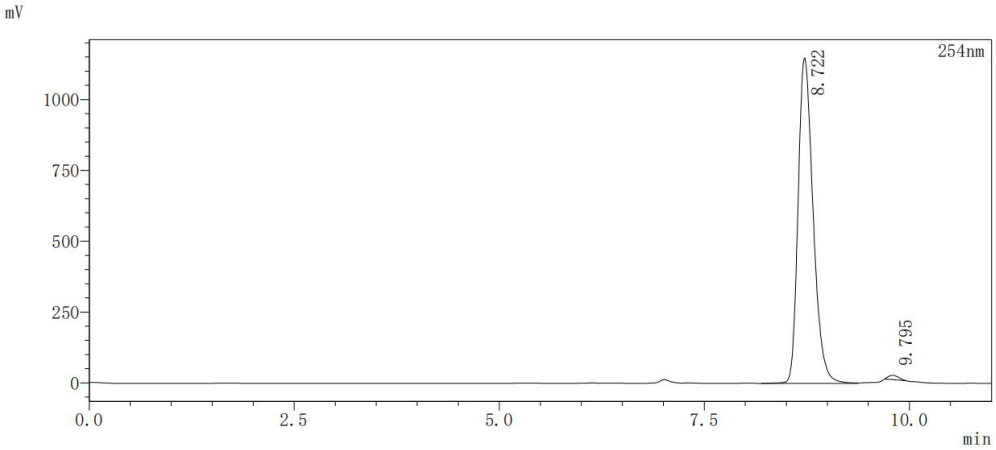
racemic-4l



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.774	3596258	294026	49.877
2	9.818	3613960	261958	50.123
Total		7210218	555984	100.000

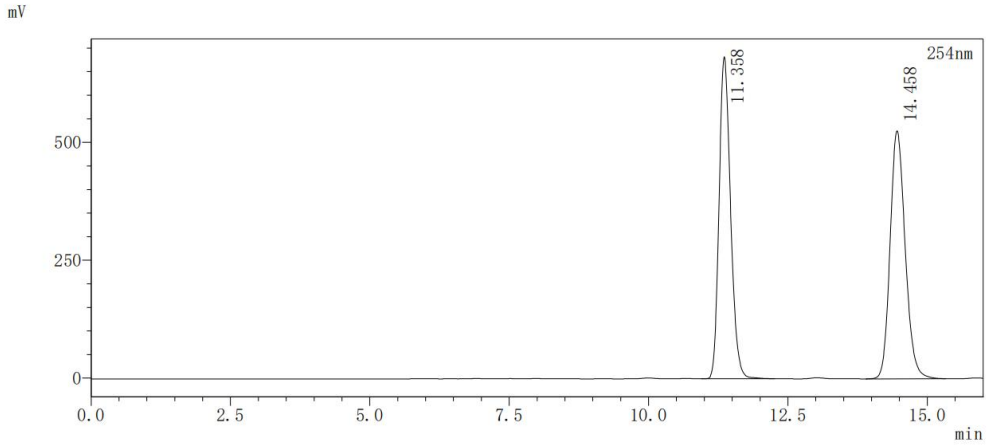
chiral-4l



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.722	14666368	1148954	99.093
2	9.795	134275	15359	0.907
Total		14800643	1164314	100.000

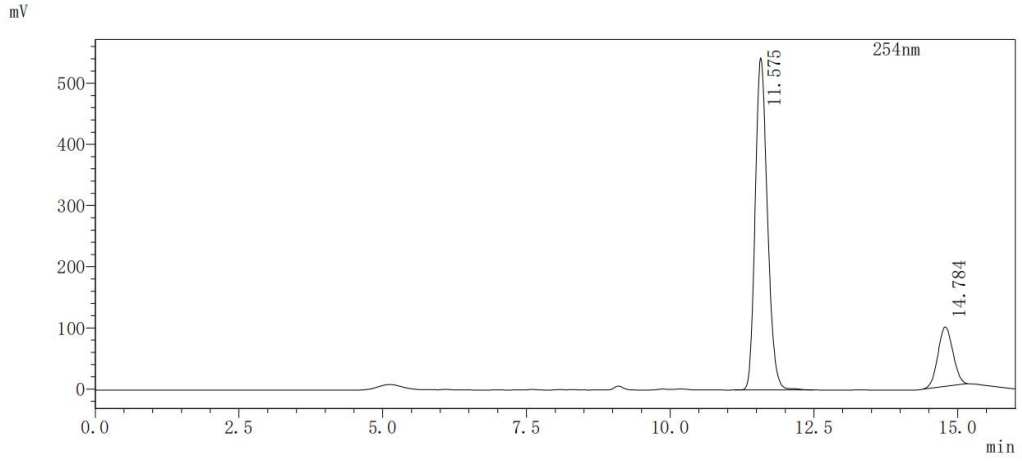
racemic-4m



254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.358	9793540	682695	49.689
2	14.458	9916315	526082	50.311
Total		19709855	1208778	100.000

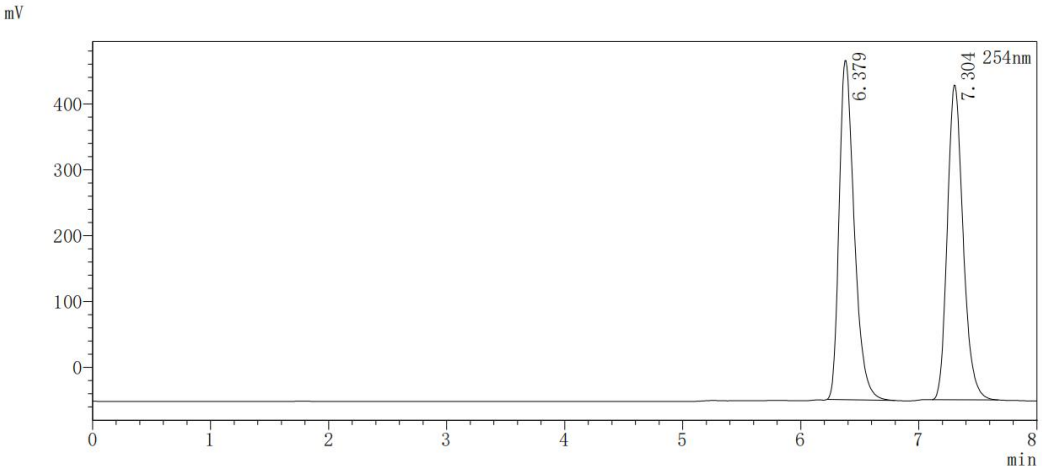
chiral-4m



254nm

Peak#	Ret. Time	Area	Height	Area%
1	11.575	8054239	542802	82.097
2	14.784	1756424	97073	17.903
Total		9810662	639876	100.000

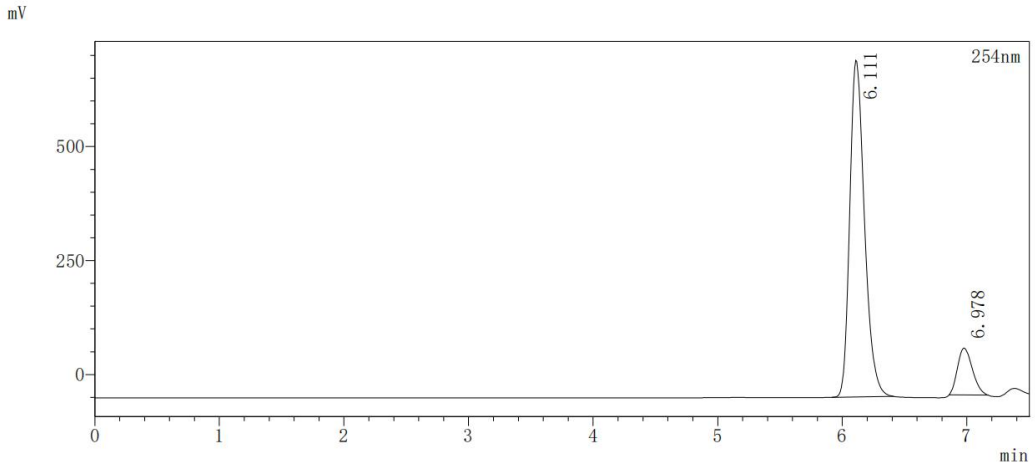
racemic-4n



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.379	4569228	514357	50.772
2	7.304	4430241	477287	49.228
Total		8999469	991644	100.000

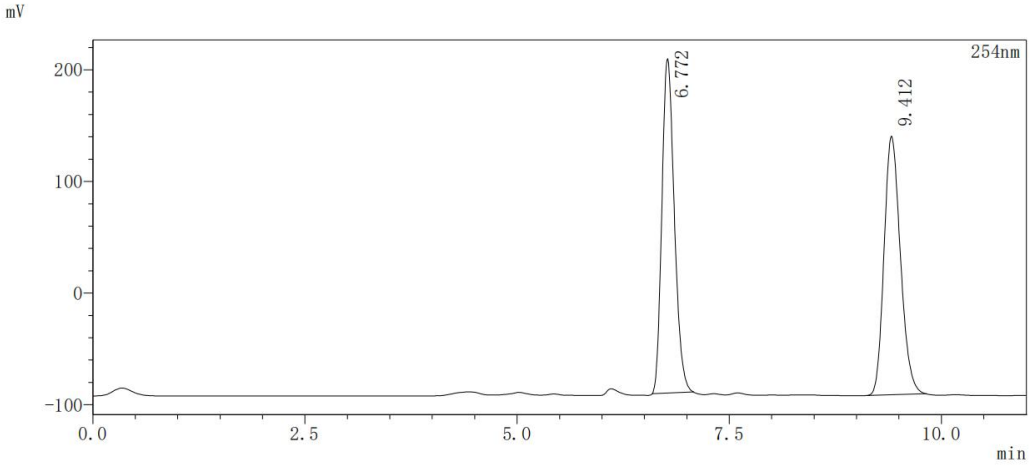
chiral-4n



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.111	6076777	738491	87.692
2	6.978	852895	102700	12.308
Total		6929672	841191	100.000

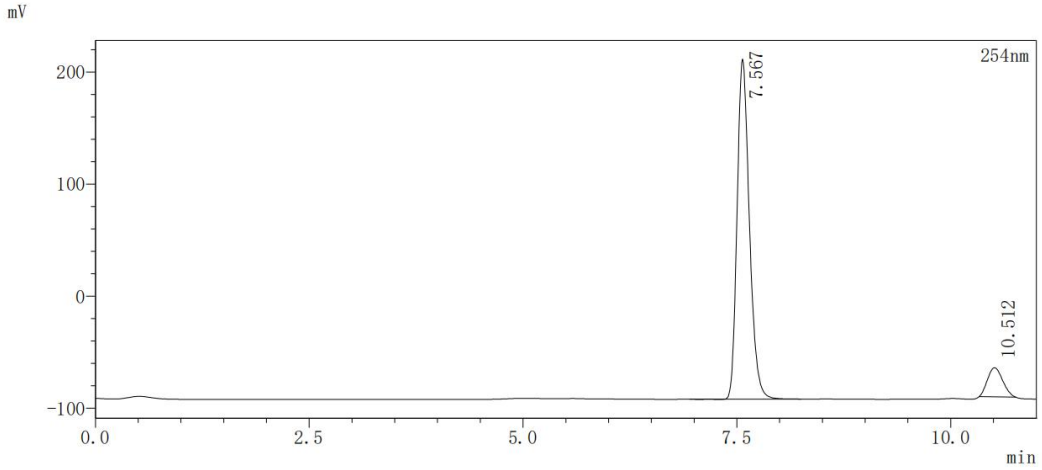
racemic-4o



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.772	3054865	299355	49.598
2	9.412	3104416	231453	50.402
Total		6159281	530808	100.000

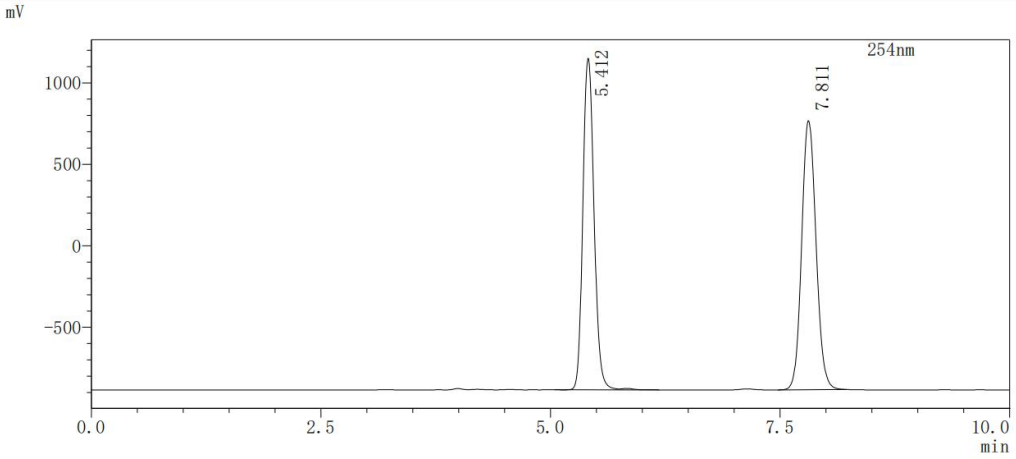
chiral-4o



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.567	3034315	303068	90.476
2	10.512	319398	25972	9.524
Total		3353713	329041	100.000

racemic-4p

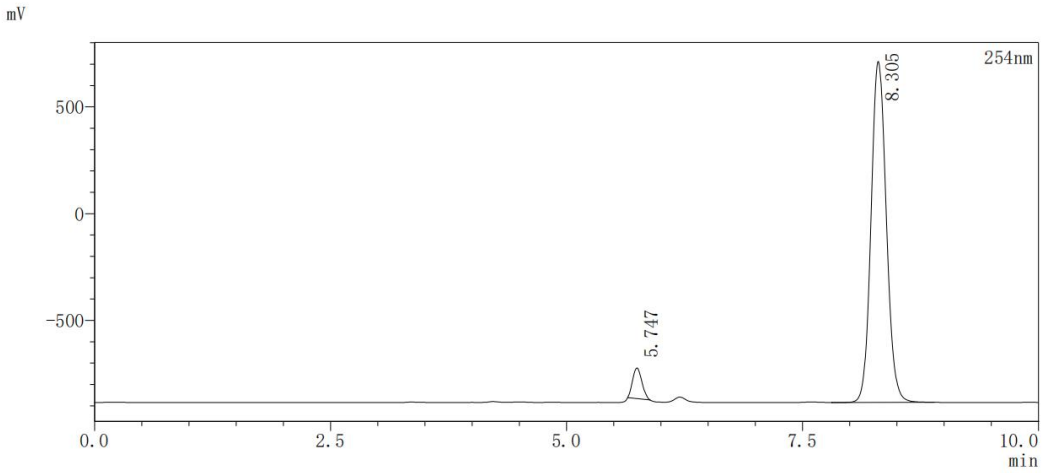


254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.412	17361434	2034474	49.109
2	7.811	17991660	1651747	50.891
Total		35353094	3686220	100.000

c

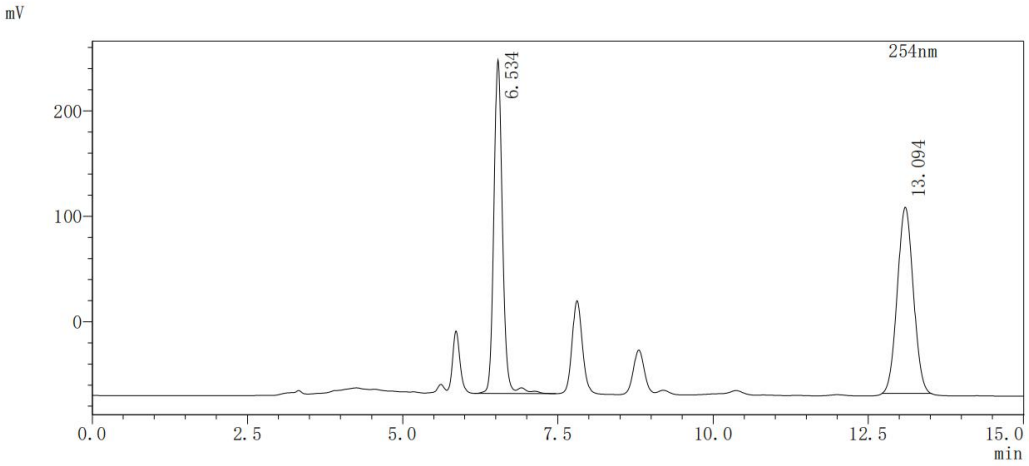
hiral-4p



254nm

Peak#	Ret. Time	Area	Height	Area%
1	5.747	979644	143099	5.167
2	8.305	17979243	1596424	94.833
Total		18958887	1739522	100.000

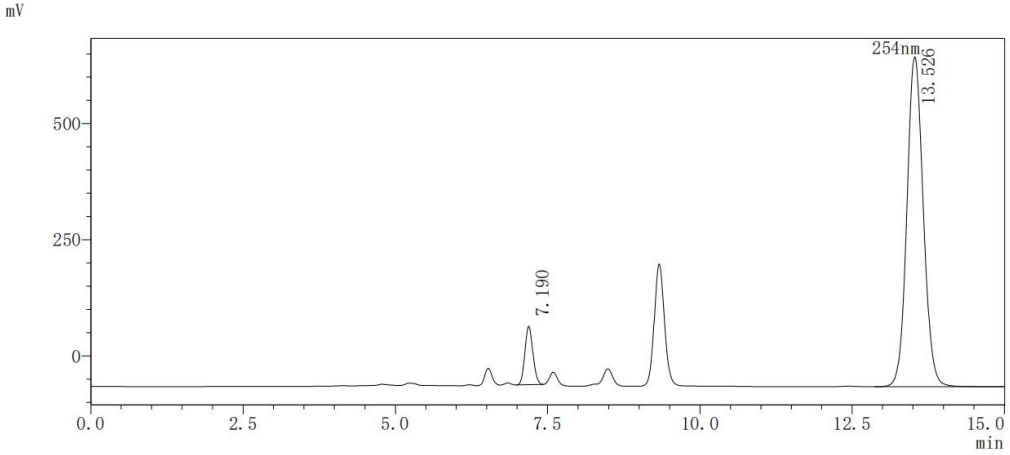
racemic-5a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	6.534	3048010	316246	49.030
2	13.094	3168613	176432	50.970
Total		6216623	492677	100.000

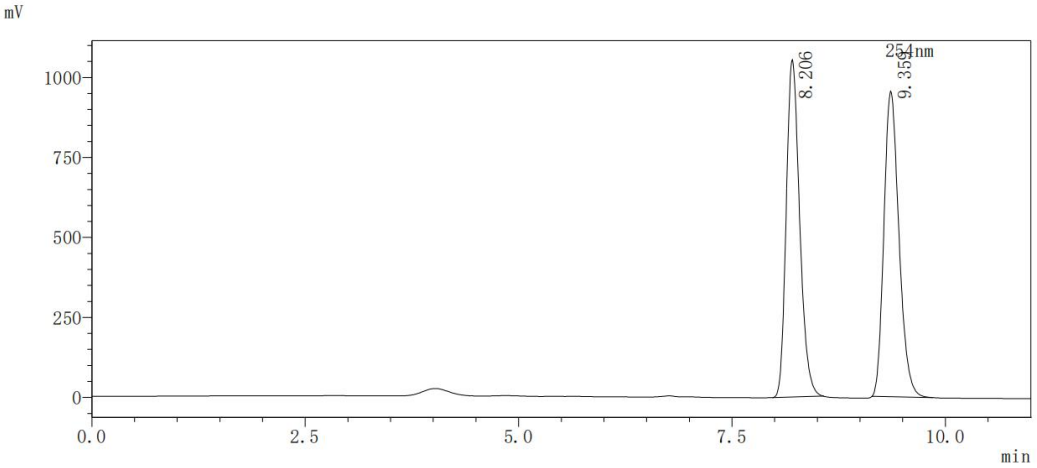
chiral-5a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	7.190	1146471	125763	7.935
2	13.526	13301874	710114	92.065
Total		14448345	835877	100.000

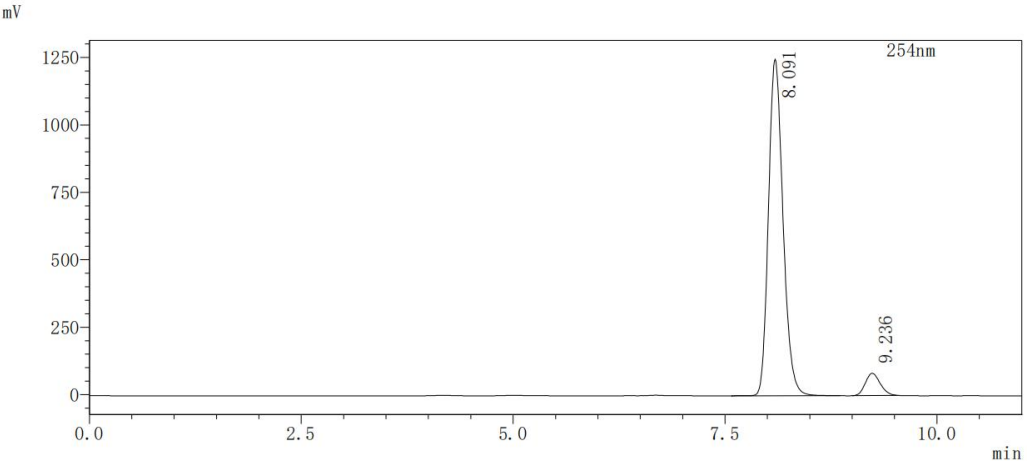
racemic-6a



254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.206	11524420	1054584	49.638
2	9.359	11692536	954462	50.362
Total		23216955	2009046	100.000

chiral-6a

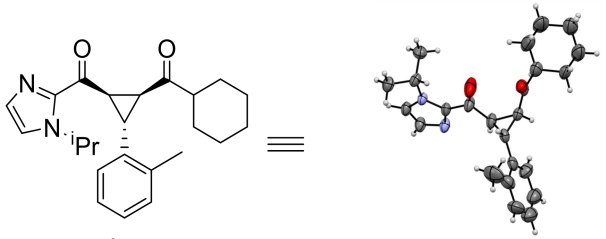


254nm

Peak#	Ret. Time	Area	Height	Area%
1	8.091	14894845	1247881	93.685
2	9.236	1003987	82461	6.315
Total		15898831	1330342	100.000

IX Single Crystal X-Ray Diffraction of 4a

Crystal data and structure refinement for **4a**. The method for crystal growth: mixture of Petroleum ether and ethyl acetate, at room tempretrue. X-ray derived ORTEP of **4a** with thermal ellipsoids shown at the 35% probability level.



4a

CCDC: 2378265

Identification code	**4a**	
Empirical formula	C24 H30 N2 O2	
Formula weight	378.50	
Temperature	173.0 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 10.483(2) Å	a= 90°
	b = 9.2579(13) Å	b= 112.815(13)°
	c = 12.006(2) Å	g = 90°
Volume	1074.0(3) $Å^3$	
Z	2	
Density (calculated)	1.170 Mg/m^3	
Absorption coefficient	0.583 mm^{-1}	
F(000)	408	
Crystal size	0.17 x 0.09 x 0.07 mm^3	
Theta range for data collection	3.994 to 72.228°	
Index ranges	-10<=h<=12, -11<=k<=11, -14<=l<=14	
Reflections collected	11154	
Independent reflections	4065 [R(int) = 0.0947]	
Completeness to theta = 67.679°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7536 and 0.5954	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4065 / 19 / 245	
Goodness-of-fit on F^2	1.090	
Final R indices [I>2sigma(I)]	R1 = 0.0704, wR2 = 0.1832	

R indices (all data)	R1 = 0.1206, wR2 = 0.2112
Absolute structure parameter	0.0(8)
Extinction coefficient	n/a
Largest diff. peak and hole	0.427 and -0.295 e.Å^{-3}

X References

(1) W. Li, X.-H. Liu, X.-Y. Hao, Y.-F. Cai, L.-L. Lin, X.-M.Feng, A Catalytic Asymmetric Ring-Expansion Reaction of Isatins and α-Alkyl-α-Diazoesters: Highly Efficient Synthesis of Functionalized 2-Quinolone Derivatives. *Angew. Chem.* 2012, **124**, 8772-8775.

(2) X.-H. L.-L. Liu, Lin, X.-M. Feng,Chiral *N,N*-dioxide ligands: synthesis, coordination chemistry and asymmetric catalysis. *Org. Chem. Front.* 2014, **1**, 298-302.

(3) R.-M. Liu, Y.-H. Wang, Z.-Y. Chen, L. Zhang, Q.-H. Shi, Y. Zhou,Y.-P. Tian, X.-L. Liu, New tertiary amine-derived C2-symmetric chiral pyridine-N,N'-dioxide ligands and their applications in asymmetric catalysis. *Org. Chem. Front.* 2022, **9**, 6881–6887; (b) Z.-Y. Chen, P. Hu, X.-R. Wang, K.-L. Xu, Y.-H.Wang, Y.-P. Tian, Y. Zhou, X.-L. Liu, Design and Synthesis of Rigid-Featured Tertiary AmineDerived C2-Symmetric Chiral Furan-N,N'-dioxide Ligands. *Eur. J. Org. Chem.* 2023, **26**, e202300764.

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