Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Brønsted Acid-catalyzed Dynamic Kinetic Resolution of *in situ* Formed Acyclic N,O-hemiaminals: Cascade Synthesis of Chiral Cyclic N,O-aminals

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Contents

A. General information:

The ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz or 500 MHz for ^{1}H and at 101 MHz or 125 MHz for ^{13}C. The chemical shifts (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents ($CDCl_3$ at 7.26 ppm ^{1}H NMR, 77.16 ppm ^{13}C NMR). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High-resolution mass spectra (HRMS) were obtained from the Waters Q-Tof Ultima Global. X-ray data were obtained from Zhongke chemical technology service center. Optical rotations are reported as follows: $[\alpha]_D^{20}$ (c in g per 100 mL, solvent: $CHCl_3$).

Note: NMR signals containing common solvent contaminants were list. H_2O in $CDCl_3$ at 1.56 ppm ^{1}H NMR; Ethyl acetate in $CDCl_3$ at 2.05 (s), 4.12 (q), 1.26 (t) ppm ^{1}H NMR; Dichloromethane in $CDCl_3$ at 5.30 (s) ppm ^{1}H NMR.

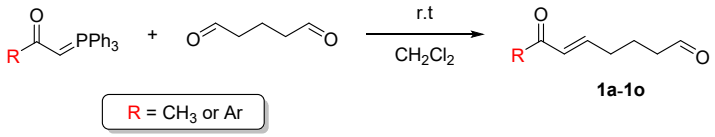
All the reactions were set up under air and using freshly distilled solvents, without any precautions to exclude moisture, unless otherwise noted open air chemistry on the bench-top. Chromatographic purification of products was accomplished using force-flow chromatography (FC) on silica gel (300-400 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck pre-coated TLC plates (silica gel 60 GF254, 0.25 mm) were used, using UV light as the visualizing agent and a phosphomolybdic acid or basic aqueous potassium permanganate ($KMnO_4$) as stain developing solutions. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

HPLC analyses on chiral stationary phase were performed on a Hitachi Chromaster. Daicel Chiralpak IA, IC, ID, or AD columns with *n*-hexane/*i*-PrOH as the eluent were used. HPLC traces were compared to racemic samples which prepared by mixture of two enantiomeric final products obtained using (*S*) and (*R*) catalyst.

Commercial reagents and solvents were purchased from Sigma Aldrich, Fluka, Energy Chemical and Alfa Aesar used as received, without further purification.

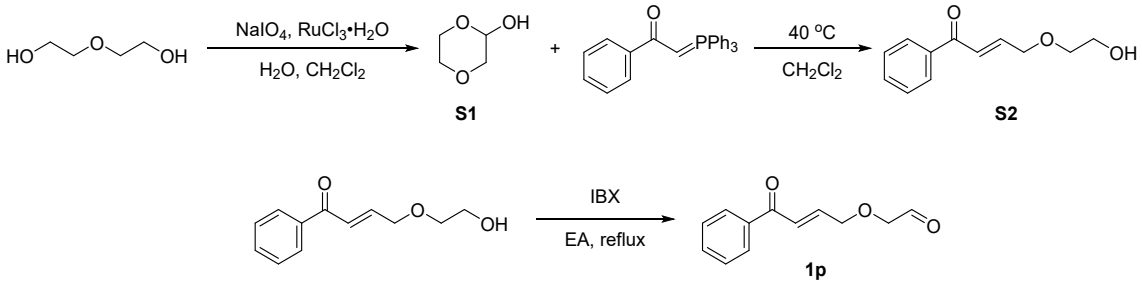
B. General procedures for the synthesis of starting materials:

General procedure for synthesis of (E)-7-substituted-7-oxohept-5-enals 1a-1o: [1]



The required phosphorane (1.0 equiv) was dissolved in CH_2Cl_2 (0.5 M) and added dropwise to a solution of glutaraldehyde (50% aqueous solution, 3.0 equiv) at room temperature. Then the reaction mixture was allowed to stir at room temperature for 48 h. Upon completion, the reaction mixture was washed with water and CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1 to 8:1) to afford the corresponding products **1a-1o** in good yields. All these products are known compounds.

Procedure for synthesis of (E)-2-((4-oxo-4-phenylbut-2-en-1-yl)oxy)acetaldehyde 1p: [2-3]



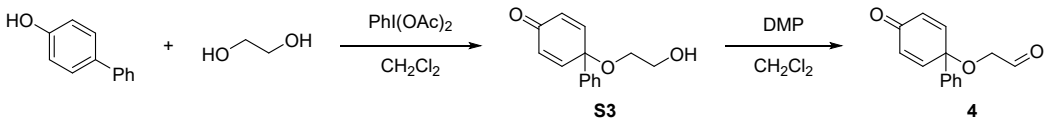
Step 1: To the solution of diethylene glycol (10 mmol, 1.0 equiv) were added $NaIO_4$ (2.14 g, 10 mmol), $RuCl_3 \cdot H_2O$ (7 mg, 0.034 mmol) in CH_2Cl_2 (10 mL). The solution was stirred at 40 °C for 10 min. Water (0.54 g, 30 mmol) was added and stirred overnight. After the reaction, the reaction mixture was filtered through a celite and washed with

CH_2Cl_2. The filtrate was concentrated and column chromatography (petroleum ether/ethyl acetate = 1:1) to hemiacetal **S1** (521 mg, 50%) as orange oil.

Step 2: The ylide reagent (1.9 g, 5 mmol) was added to the solvent of hemiacetal **S1** in CH_2Cl_2 (10 mL). The result mixture was stirred at room temperature for 48 h until no **S1** remained. After evaporation of the solvent, the reside was purified by column chromatography (petroleum ether/ethyl acetate = 3:1) to afford **S2** as orange oil.

Step 3: To the solvent of **S2** (1.0 equiv) in ethyl acetate, IBX (1.4 g, 1.0 equiv) was added and the reaction mixture stirred at 80 °C for about 10 h. After the reaction, the reaction mixture was filtered through a celite, concentrated and purified by column chromatography (petroleum ether/ethyl acetate = 1:1) to provide **1p** (300 mg, 30% for 2 steps) as a yellow oil.

Procedure for synthesis of 2-((4-oxo-[1,1'-biphenyl]-1(4H)-yl)oxy)acetaldehyde 4:[4]



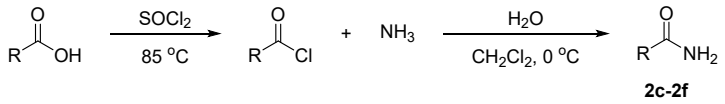
Step 1: Ethylene glycol (33.4 ml, 600 mmol) was added to the solution of 4-phenylphenol (20 mmol) in CH_2Cl_2 (30 mL). Then $PhI(OAc)_2$ (9.7 g, 30 mmol) was added slowly over 5 min. The solution was then allowed to stir at room temperature for further 1 h. The solution was concentrated in vacuo and the residue was subjected to column chromatography (petroleum ether/ethyl acetate = 2:1) to provide **S3** (2.2 g, 47%) as orange oil.

Step 2: In a flame-dried round bottom flask, **S3** (1.0 equiv) was dissolved in CH_2Cl_2 (0.5 M), Dess Martin periodinane (1.5 equiv) was added to the solution directly and the solution was then allowed to stir at room temperature for 1 h. The solution was filtered through celite and then concentrated in vacuo and the residue was subjected to column chromatography (petroleum ether/ethyl acetate = 2:1) to provide **4** (1.9 g, 89%) as a yellow oil.

Synthesis of amides：

Amides **2a**-**2b**, **2g**-**2k, 2m-2p** and **2r**-**2s** were obtained from commercial sources and used without further purification. Other amides were prepared according to the following procedures.

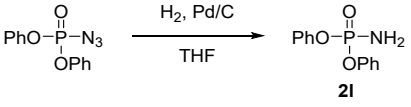
Procedure A: [5]



In a dry round bottom flask, acid (4 mmol) and $SOCl_2$ (3 mL) were added. The mixture was heated to reflux for 2 h. Then removed the excess $SOCl_2$ and got the crude acyl chloride. It was used to undergo the next step without further purification.

The synthesis of amide was conducted similar to a literature-known procedure. A solution of acyl chloride (prepared above or commercial) in anhydrous CH_2Cl_2 (0.5 M) was added dropwise to an aqueous ammonia solution (25 w%, 10 equiv) at 0 °C. The resulting two-phase system was stirred vigorously at room temperature for 18 h. The reaction mixture was diluted with water, extracted with CH_2Cl_2. The organic layer was combined and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and colorless solid was recrystallization from ethyl acetate to afford the desired primary amides **2c**-**2f** in excellent yields.

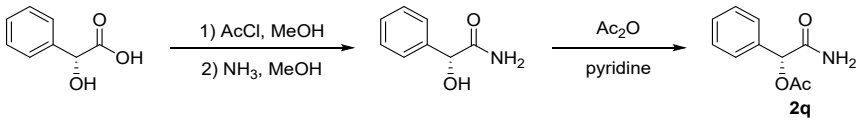
Procedure B:[6-7]



The synthesis of diphenylphosphoryl amide was conducted similar to a literature-known procedure. Diphenylphosphoryl azide (275 mg, 1 mmol) was dissolved in dry THF (5 mL) and 10% Pd/C (27 mg) was added. The complex was placed in atmospheric pressure of hydrogen and stirred for 5 h at room temperature. After the reaction was complete, Pd/C was filtered through celite and the filtrate was concentrated under reduced pressure. The

crude product was filtered with dichloromethane to give pure product as a white solid **2l** (170 mg, 68%).

Procedure C:[8]



2q

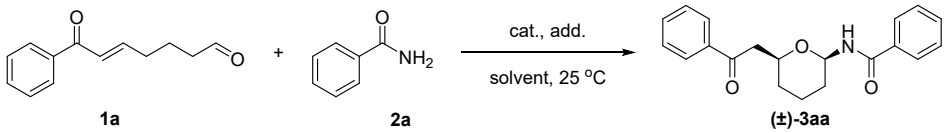
Step 1: The synthesis of (*R*)-acetoxy mandelamide was conducted similar to a literature-known procedure. (*R*)-mandelic acid (456 mg) was dissolved in 10 mL MeOH and cooled to 0 °C. Acetyl chloride (0.57 mL) was added and the solution was allowed to warm to room temperature and stirred for 24 h. Concentration in vacuo gave a colorless liquid, which was dissolved in 5 mL NH_3 (in MeOH) and the solution was stirred at 80 °C for 24 h. Concentration in vacuo gave a white solid, which was recrystallized from hot EtOH to yield (*R*)-mandelamide as a white solid (228 mg, 50%).

Step 2: Under a nitrogen atmosphere, (*R*)-mandelamide (228 mg) was dissolved in 8 mL pyridine. Acetic anhydride (0.4 mL) was added and the solution was stirred for 18 h. Concentration in vacuo gave an off-white solid, which was recrystallized from hot EtOH to yield white crystal **2q** (148 mg, 51%).

All materials were known compounds and the characterization data were in accordance with those reported in the literatures. [1-8]

C. Optimization of racemic cyclic N,O-aminals:

Table S1. Optimization of catalyst, solvent and additive



Entry[a]	Cat.	Sol.	V (mL)	Add.	T (h)	Y (%)[b]	dr[c]
1	TsOH	DCE	0.2	-	4	75	>20:1
2	TfOH	DCE	0.2	-	5	68	>20:1
3	MsOH	DCE	0.2	-	5	68	>20:1
4	TFA	DCE	0.2	-	10	29	>20:1
5	$Zn(OTf)_2$	DCE	0.2	-	>10	9	>20:1
6	$SnCl_2$	DCE	0.2	-	10	24	>20:1
7	$Ti(O\textit{i}\text{-}Pr)_4$	DCE	0.2	-	NR	-	-
8	DPP	DCE	0.2	-	10	66	>20:1
9	TsOH	CH_3CN	0.2	-	5	29	>20:1
10	TsOH	toluene	0.2	-	4	42	>20:1
11	TsOH	acetone	0.2	-	4	13	>20:1
12	TsOH	MTBE	0.2	-	4	37	>20:1
13	TsOH	DCM	0.2	-	4	56	>20:1
14	TsOH	Et_2O	0.2	-	5	46	>20:1
15	TsOH	THF	0.2	-	10	39	>20:1
16	TsOH	EA	0.2	-	10	51	>20:1
17[d]	TsOH	DCE	0.2	Na_2SO_4	4	62	>20:1
18[d]	TsOH	DCE	0.2	$MgSO_4$	3.5	58	>20:1
19[d]	TsOH	DCE	0.2	3 Å MS	4	59	>20:1
20[d]	TsOH	DCE	0.2	4 Å MS	NR	-	-
21[d]	TsOH	DCE	0.2	5 Å MS	NR	-	-

[*a*] Unless otherwise specified, all reactions were carried out using **1a** (0.05 mmol, 1.0 equiv), **2a** (0.06 mmol, 1.2 equiv) in solvent (0.2 mL) with cat. (20 mol%) at 25 °C. After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **(±)-3aa** as a white solid. [*b*] Isolated yield of **(±)-3aa**. [*c*] Determined by ^{1}H NMR. [*d*] The reactions ran with additive (10 mg).

DCE = 1,2-Dichloroethane

DCM = Dichloromethane

MTBE = Methyl-*tert*-butylether

THF = Tetrahydrofuran

EA = Ethyl acetate

TsOH = *p*-Toluenesulfonic acid

TfOH = Trifluoromethanesulfonic acid

MsOH = Methanesulfonic acid

TFA = Trifluoroacetic acid

$Zn(OTf)_2$ = Zinc trifluoromethanesulfonate

$Ti(O\textit{i}\text{-}Pr)_4$ = Titanium tetraisopropanolate

DPP = Diphenyl phosphate

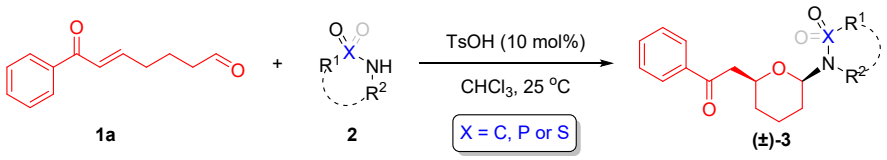
NR = No reaction

Table S2. Optimization of other conditions

Entry[*a*]	Scale (mmol)	Loading of cat. (equiv)	Sol.	V (mL)	T (h)	Y (%)[*b*]	dr[*c*]
1[*d*]	0.05	0.2	DCE	0.2	5	75	>20:1
2	0.1	0.2	DCE	0.2	6	59	>20:1
3	0.1	0.1	DCE	0.2	10	59	>20:1
4	0.1	0.1	DCE	0.5	10	72	>20:1
5	0.1	0.1	$CHCl_3$	0.5	10	77	>20:1

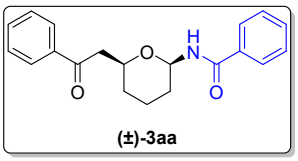
[*a*] Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1.0 equiv), **2a** (0.12 mmol, 1.2 equiv) in solvent with TsOH at 25 °C. After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **(±)-3aa** as a white solid. [*b*] Isolated yield of **(±)-3aa**. [*c*] Determined by ^{1}H NMR. [*d*] The reaction was carried out using **1a** (0.05 mmol, 1.0 equiv), **2a** (0.06 mmol, 1.2 equiv) in DCE (0.2 mL) with TsOH (0.2 equiv) at 25 °C.

D. Scope of racemic cyclic N,O-aminals:

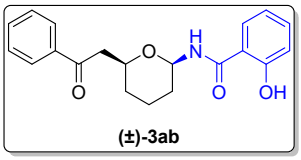


General procedure: A glass vial equipped with a magnetic stirring bar was charged with (*E*)-7-oxo-7-phenylhept-5-enal **1a** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1a** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 7:1 to 1:1) to afford **(±)-3** in good to excellent yield for NMR.

Note: The synthesis of **3ag** and **3ah** were charged with DPP (10 mol%) as catalyst. The synthesis of **3an** and **3ao** were charged with **1a** (2.0 equiv) and amide **2** (1.0 equiv) at 25 °C. The synthesis of **3as** was charged at 0 °C.

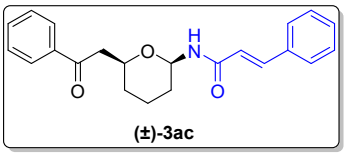


(±)-3aa was obtained as a white solid 25 mg in 77% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.81 – 7.76 (m, 2H), 7.58 – 7.52 (m, 1H), 7.51 – 7.37 (m, 5H), 6.67 (d, *J* = 8.8 Hz, 1H), 5.41 (ddd, *J* = 10.9, 8.8, 2.1 Hz, 1H), 4.26 – 4.16 (m, 1H), 3.35 (dd, *J* = 16.3, 4.7 Hz, 1H), 3.07 (dd, *J* = 16.3, 7.9 Hz, 1H), 1.96 – 1.87 (m, 2H), 1.83 (ddq, *J* = 13.2, 4.0, 2.0 Hz, 1H), 1.73 (tdd, *J* = 13.3, 10.9, 3.8 Hz, 1H), 1.50 – 1.39 (m, 1H), 1.29 – 1.18 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.6, 166.5, 137.0, 134.0, 133.2, 131.8, 128.6, 128.5, 128.2, 127.2, 78.9, 73.9, 45.2, 31.4, 30.6, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{22}NO_3^+$ 324.1594, found 324.1590. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



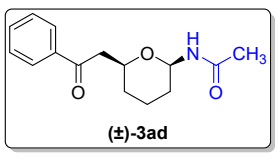
(±)-3ab

(±)-3ab was obtained as a white solid 19 mg in 56% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 7/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.11 (s, 1H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.49 – 7.31 (m, 4H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 8.6 Hz, 1H), 5.45 – 5.32 (m, 1H), 4.22 (dt, *J* = 11.0, 6.2 Hz, 1H), 3.34 (dd, *J* = 16.5, 5.1 Hz, 1H), 3.07 (dd, *J* = 16.4, 7.4 Hz, 1H), 1.99 – 1.88 (m, 2H), 1.88 – 1.81 (m, 1H), 1.76 – 1.65 (m, 1H), 1.54 – 1.39 (m, 1H), 1.27 (qd, *J* = 13.0, 4.0 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.5, 169.3, 161.9, 137.0, 134.6, 133.3, 128.6, 128.2, 125.7, 118.7, 113.8, 78.5, 74.0, 45.1, 31.3, 30.6, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{22}NO_4^+$ 340.1543, found 340.1538. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3ac

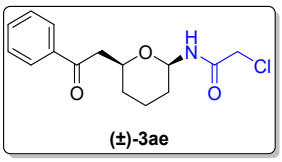
(±)-3ac was obtained as a white solid 20 mg in 57% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.65 (d, *J* = 15.6 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.51 – 7.42 (m, 4H), 7.36 (dd, *J* = 5.1, 2.0 Hz, 3H), 6.35 (d, *J* = 15.6 Hz, 1H), 6.07 (d, *J* = 9.0 Hz, 1H), 5.35 (ddd, *J* = 10.9, 9.0, 2.2 Hz, 1H), 4.21 (dddd, *J* = 10.2, 7.2, 4.7, 2.0 Hz, 1H), 3.35 (dd, *J* = 16.3, 4.8 Hz, 1H), 3.08 (dd, *J* = 16.3, 7.8 Hz, 1H), 1.96 – 1.79 (m, 3H), 1.79 – 1.65 (m, 1H), 1.45 – 1.33 (m, 1H), 1.30 – 1.19 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.6, 164.9, 142.2, 137.0, 134.68, 133.2, 129.9, 128.9, 128.6, 128.2, 127.9, 120.3, 78.5, 73.8, 45.2, 31.4, 30.6, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{22}H_{24}NO_3^+$ 350.1751, found 350.1753. The diastereomeric ratio was determined by NMR ***dr* = 10:1**.



(±)-3ad

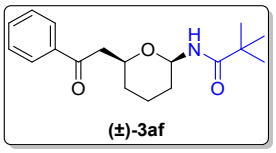
(±)-3ad was obtained as a white solid 16 mg in 61% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1). **^{1}H NMR** (400

MHz, $CDCl_3$) δ 7.94 (dt, J = 8.5, 1.7 Hz, 2H), 7.57 (tq, J = 6.8, 1.7 Hz, 1H), 7.46 (tt, J = 6.6, 1.4 Hz, 2H), 5.92 (d, J = 9.1 Hz, 1H), 5.19 (ddd, J = 11.1, 9.1, 2.3 Hz, 1H), 4.15 (dddd, J = 10.9, 7.8, 4.7, 2.0 Hz, 1H), 3.32 (dd, J = 16.4, 4.8 Hz, 1H), 3.07 (dd, J = 16.3, 7.9 Hz, 1H), 1.99 (s, 3H), 1.93 – 1.85 (m, 1H), 1.85 – 1.77 (m, 2H), 1.66 (tt, J = 13.1, 3.8 Hz, 1H), 1.26 (dtdd, J = 42.4, 13.0, 11.0, 4.2 Hz, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.6, 169.3, 137.0, 133.2, 128.6, 128.2, 78.2, 73.7, 45.2, 31.3, 30.6, 23.6, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{15}H_{20}NO_3^+$ 262.1438, found 262.1436. The diastereomeric ratio was determined by NMR ***dr* = 5:1**.



(±)-3ae

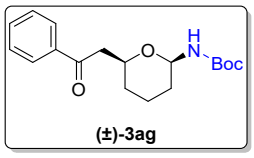
(±)-3ae was obtained as a white solid 16 mg in 54% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.60 – 7.53 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 6.92 (d, J = 8.5 Hz, 1H), 5.19 (ddd, J = 11.0, 8.9, 2.3 Hz, 1H), 4.17 (dddd, J = 11.1, 7.3, 4.9, 2.0 Hz, 1H), 4.04 (d, J = 1.8 Hz, 2H), 3.34 (dd, J = 16.5, 5.0 Hz, 1H), 3.07 (dd, J = 16.5, 7.6 Hz, 1H), 1.92 (dtd, J = 13.6, 4.1, 2.1 Hz, 1H), 1.88 – 1.79 (m, 2H), 1.69 (dddd, J = 17.0, 13.2, 8.3, 3.9 Hz, 1H), 1.39 (tdd, J = 12.8, 10.8, 4.2 Hz, 1H), 1.24 (tdd, J = 13.0, 11.0, 4.0 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.5, 165.2, 137.0, 133.2, 128.6, 128.2, 78.6, 74.0, 45.0, 42.5, 31.1, 30.5, 22.5 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{15}H_{19}ClNO_3^+$ 296.1048, found 296.1054. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3af

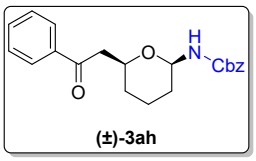
(±)-3af was obtained as a colorless oil 17 mg in 56% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (t, J = 5.9 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 6.00 (d, J = 8.5 Hz, 1H), 5.25 – 5.12 (m, 1H), 4.14 (dd, J = 11.2, 5.8 Hz, 1H), 3.34 (dd, J = 16.2, 4.7 Hz, 1H), 3.07 (dd, J = 16.1, 8.0 Hz, 1H), 1.93 – 1.86 (m, 1H), 1.81 (d, J = 13.0 Hz, 2H), 1.75 – 1.63 (m, 1H), 1.35 – 1.25 (m, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.9,

177.7, 137.1, 133.1, 128.6, 128.2, 78.6, 73.9, 45.2, 38.7, 31.4, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{26}NO_3^+$ 304.1907, found 304.1910. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



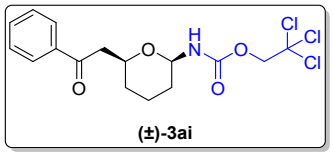
(±)-3ag

(±)-3ag was obtained as a colorless oil 15 mg in 47% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, J = 8.1 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.05 (s, 1H), 4.91 (s, 1H), 4.12 (s, 1H), 3.37 (dd, J = 16.3, 4.7 Hz, 1H), 3.16 – 3.02 (m, 1H), 1.89 (d, J = 13.9 Hz, 1H), 1.85 – 1.76 (m, 2H), 1.69 (ddd, J = 13.3, 8.6, 4.6 Hz, 1H), 1.44 (s, 9H), 1.30 (t, J = 10.8 Hz, 1H), 1.18 (dd, J = 18.7, 6.9 Hz, 1H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.8, 154.5, 137.1, 133.1, 128.6, 128.2, 80.0, 73.5, 66.5, 45.3, 31.2, 30.6, 28.3, 22.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{26}NO_4^+$ 320.1856, found 320.1853. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

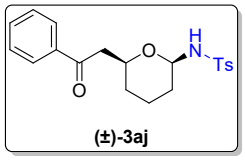


(±)-3ah

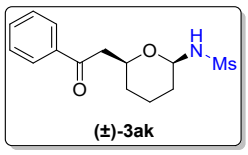
(±)-3ah was obtained as a white solid 19 mg in 54% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 5/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.58 – 7.52 (m, 1H), 7.45 (m, 2H), 7.37 – 7.31 (m, 5H), 5.32 – 5.22 (m, 1H), 5.17 – 5.04 (m, 2H), 4.98 (t, J = 10.1 Hz, 1H), 4.17 – 4.10 (m, 1H), 3.35 (dd, J = 16.5, 4.7 Hz, 1H), 3.07 (dd, J = 16.5, 8.1 Hz, 1H), 1.94 – 1.75 (m, 3H), 1.75 – 1.56 (m, 1H), 1.44 – 1.25 (m, 1H), 1.24 – 1.10 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.7, 155.2, 137.1, 136.2, 133.2, 128.6, 128.5, 128.2, 80.4, 73.5, 67.0, 45.2, 31.2, 30.5, 22.8 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{21}H_{24}NO_4^+$ 354.1700, found 354.1703. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3ai was obtained as a colorless oil 32 mg in 81% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dt, *J* = 7.2, 1.5 Hz, 2H), 7.58 – 7.53 (m, 1H), 7.45 (dd, *J* = 8.3, 6.9 Hz, 2H), 5.53 (d, *J* = 9.5 Hz, 1H), 5.07 – 4.86 (m, 1H), 4.76 (d, *J* = 12.1 Hz, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 4.21 – 4.08 (m, 1H), 3.33 (dd, *J* = 16.3, 5.1 Hz, 1H), 3.06 (dd, *J* = 16.4, 7.6 Hz, 1H), 1.97 – 1.73 (m, 3H), 1.73 – 1.61 (m, 1H), 1.36 (ddd, *J* = 20.1, 10.4, 3.5 Hz, 1H), 1.24 (ddt, *J* = 15.4, 11.1, 3.5 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.7, 153.5, 137.1, 133.2, 128.6, 128.2, 95.2, 80.5, 74.6, 73.7, 45.0, 31.1, 30.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. $C_{16}H_{19}Cl_3NO_4^+$ 394.0374, found 394.0376. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

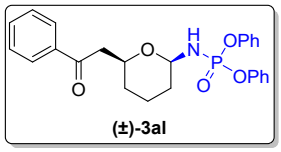


(±)-3aj was obtained as a white solid 23 mg in 62% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 2H), 7.73 – 7.67 (m, 2H), 7.61 – 7.55 (m, 1H), 7.46 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.04 (d, *J* = 8.1 Hz, 2H), 5.11 (d, *J* = 10.1 Hz, 1H), 4.82 (td, *J* = 10.4, 2.1 Hz, 1H), 4.13 – 3.99 (m, 1H), 2.97 (dd, *J* = 16.8, 6.5 Hz, 1H), 2.71 (dd, *J* = 16.7, 5.4 Hz, 1H), 2.18 (s, 3H), 1.88 (ddq, *J* = 11.6, 7.1, 2.9, 2.4 Hz, 2H), 1.73 – 1.57 (m, 2H), 1.38 – 1.09 (m, 2H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.1, 143.0, 138. 8, 137.1, 133.2, 129.2, 128.6, 128.1, 127.2, 82.7, 73.1, 44.4, 31.7, 30.1, 22.9, 21.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{24}NO_4S^+$ 374.1421, found 374.1421. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



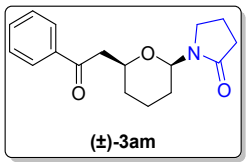
(±)-3ak was obtained as a colorless oil 18 mg in 61% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.1 Hz, 2H), 7.60 – 7.55 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 5.05 (d,

J = 10.4 Hz, 1H), 4.70 (td, *J* = 10.6, 2.2 Hz, 1H), 4.16 (ddd, *J* = 8.9, 3.8, 1.9 Hz, 1H), 3.28 (dd, *J* = 15.8, 8.4 Hz, 1H), 3.01 – 2.91 (m, 1H), 2.81 (s, 3H), 1.98 – 1.82 (m, 2H), 1.75 – 1.64 (m, 3H), 1.36 – 1.27 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.8, 137.0, 133.4, 128.7, 128.2, 82.5, 73.9, 44.5, 42.9, 31.2, 30.3, 22.8 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{14}H_{20}NO_4S^+$ 298.1108, found 298.1107. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3al

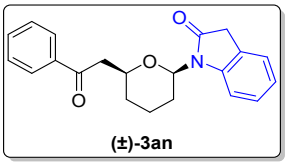
(±)-3al was obtained as a white solid 37 mg in 82% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.58 – 7.53 (m, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.37 – 7.28 (m, 3H), 7.27 – 7.18 (m, 5H), 7.16 (tt, *J* = 7.3, 1.2 Hz, 1H), 7.13 – 7.08 (m, 1H), 4.67 (tdd, *J* = 10.6, 8.1, 2.3 Hz, 1H), 4.14 (dtd, *J* = 11.2, 6.3, 2.0 Hz, 1H), 3.83 (dd, *J* = 12.3, 10.8 Hz, 1H), 3.22 (dd, *J* = 16.4, 5.8 Hz, 1H), 2.96 (dd, *J* = 16.4, 6.6 Hz, 1H), 1.90 – 1.83 (m, 1H), 1.78 (dd, *J* = 12.8, 3.0 Hz, 1H), 1.76 – 1.71 (m, 1H), 1.64 (qt, *J* = 13.3, 3.9 Hz, 1H), 1.35 – 1.26 (m, 2H), 1.26 – 1.18 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.8, 150.7, 150.6, 137.1, 133.2, 129.6, 129.5, 128.6, 128.2, 125.0, 124.9, 120.5, 120.5, 120.4, 82.0, 73.7, 44.9, 33.2, 30.3, 23.0 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{25}H_{27}NO_5P^+$ 452.1621, found 452.1628. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3am

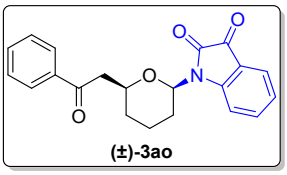
(±)-3am was obtained as a colorless oil 18 mg in 63% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.58 – 7.51 (m, 1H), 7.44 (dd, *J* = 8.4, 7.0 Hz, 2H), 5.24 (dd, *J* = 9.8, 3.5 Hz, 1H), 4.14 (dddd, *J* = 11.1, 7.4, 5.0, 2.1 Hz, 1H), 3.45 (ddd, *J* = 9.5, 7.7, 6.4 Hz, 1H), 3.36 (dt, *J* = 9.5, 6.9 Hz, 1H), 3.27 (dd, *J* = 15.9, 5.0 Hz, 1H), 3.04 (dd, *J* = 15.9, 7.5 Hz, 1H), 2.41 – 2.32 (m, 2H), 2.01 – 1.94 (m, 2H), 1.90 (dp, *J* = 13.1, 3.1 Hz, 1H), 1.82 – 1.73 (m, 1H), 1.67 (dtd, *J* = 12.9, 8.5, 3.9 Hz, 1H), 1.56 (ddt, *J* = 12.5, 10.2, 4.7 Hz, 2H), 1.20 (tdd, *J* = 12.7, 11.1, 4.1 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.9, 175.0, 137.2, 133.1,

128.5, 128.3, 79.7, 74.2, 45.1, 42.5, 31.6, 30.6, 28.4, 22.6, 18.1 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{17}H_{22}NO_3^+$ 288.1594, found 288.1596. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



(±)-3an

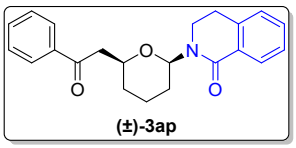
(±)-3an was obtained as a colorless oil 14 mg in 42% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 6/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.91 (m, 2H), 7.55 – 7.50 (m, 1H), 7.40 (dd, *J* = 8.4, 7.1 Hz, 2H), 7.26 – 7.18 (m, 3H), 7.01 (td, *J* = 7.4, 1.4 Hz, 1H), 5.65 (dd, *J* = 11.4, 2.6 Hz, 1H), 4.25 (dddd, *J* = 11.1, 7.3, 5.4, 2.1 Hz, 1H), 3.52 (s, 2H), 3.36 (dd, *J* = 16.2, 5.4 Hz, 1H), 3.12 (dd, *J* = 16.2, 6.9 Hz, 1H), 2.20 (tdd, *J* = 12.9, 11.2, 4.2 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.89 (ddq, *J* = 13.2, 3.8, 1.9 Hz, 1H), 1.81 (tt, *J* = 13.2, 3.9 Hz, 1H), 1.73 – 1.67 (m, 1H), 1.43 (tdd, *J* = 12.8, 11.1, 4.0 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.6, 174.0, 142.5, 137.1, 133.2, 128.5, 128.3, 127.5, 124.4, 124.3, 122.2, 112.0, 80.9, 75.0, 45.0, 36.0, 30.7, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{21}H_{22}NO_3^+$ 336.1594, found 336.1593. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



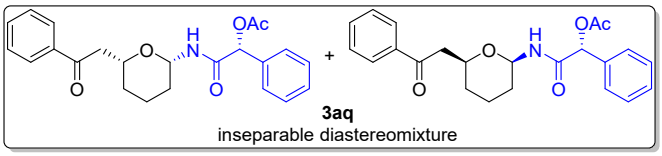
(±)-3ao

(±)-3ao was obtained as a yellow solid 14 mg in 40% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.60 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.41 (dd, *J* = 8.4, 7.0 Hz, 2H), 7.27 (d, *J* = 4.4 Hz, 1H), 7.11 (dd, *J* = 7.6, 0.9 Hz, 1H), 5.55 (dd, *J* = 11.4, 2.4 Hz, 1H), 4.28 (dtd, *J* = 11.7, 6.1, 2.1 Hz, 1H), 3.34 (dd, *J* = 16.3, 5.9 Hz, 1H), 3.13 (dd, *J* = 16.3, 6.1 Hz, 1H), 2.22 (tdd, *J* = 13.8, 11.0, 4.3 Hz, 1H), 2.13 – 1.99 (m, 1H), 1.94 – 1.71 (m, 3H), 1.56 – 1.40 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.4, 183.1, 156.9, 149.6, 138.2, 137.0, 133.3, 128.6, 128.2, 125.3, 123.7, 117.7, 113.8, 81.5, 75.0, 44.6, 30.4,

27.5, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{21}H_{20}NO_4^+$ 350.1387, found 350.1389. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

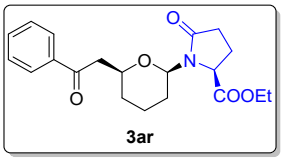


(±)-3ap was obtained as a colorless oil 16 mg in 46% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.97 (dq, *J* = 8.6, 1.8 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.47 – 7.37 (m, 3H), 7.32 (td, *J* = 7.6, 1.3 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 5.86 (dd, *J* = 10.9, 2.5 Hz, 1H), 4.22 (dddd, *J* = 12.4, 7.3, 5.5, 1.9 Hz, 1H), 3.60 (ddd, *J* = 12.0, 6.7, 5.1 Hz, 1H), 3.44 (ddd, *J* = 12.3, 9.4, 4.8 Hz, 1H), 3.28 (dd, *J* = 15.4, 5.4 Hz, 1H), 3.08 (dd, *J* = 15.4, 6.9 Hz, 1H), 2.87 (qdd, *J* = 15.7, 6.4, 4.9 Hz, 2H), 1.99 – 1.89 (m, 1H), 1.83 – 1.74 (m, 2H), 1.72 – 1.64 (m, 1H), 1.61 – 1.52 (m, 1H), 1.34 – 1.24 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.2, 163.7, 138.5, 137.4, 133.1, 131.8, 129.5, 128.6, 128.5, 128.4, 127.0, 126.8, 81.3, 74.7, 45.2, 39.7, 30.7, 28.4, 28.0, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{22}H_{24}NO_3^+$ 350.1751, found 350.1750. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



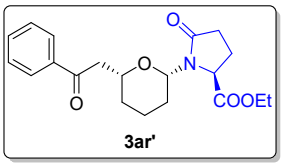
3aq was obtained as a colorless oil 20 mg in 51% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.90 (m, 2H), 7.59 – 7.53 (m, 1H), 7.43 (dddd, *J* = 20.1, 10.1, 6.9, 5.0 Hz, 4H), 7.36 – 7.32 (m, 3H), 6.60 (dd, *J* = 31.9, 9.0 Hz, 1H), 6.08 (d, *J* = 3.4 Hz, 1H), 5.19 (dddd, *J* = 11.0, 8.9, 4.0, 2.2 Hz, 1H), 4.19 – 4.06 (m, 1H), 3.31 (ddd, *J* = 16.0, 5.8, 4.9 Hz, 1H), 3.10 – 3.00 (m, 1H), 2.16 (d, *J* = 1.0 Hz, 3H), 1.84 (ddt, *J* = 29.7, 13.8, 3.4 Hz, 3H), 1.67 (qt, *J* = 13.0, 3.8 Hz, 1H), 1.44 – 1.28 (m, 1H), 1.26 – 1.14 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.8, 197.6, 169.1, 169.0, 167.6, 137.1, 137.0, 135.5, 135.3, 133.2, 133.2, 129.1, 129.0, 128.8, 128.8 128.6, 128.6, 128.6, 128.2, 128.2, 127.7, 127.4, 78.5, 75.3, 75.2, 74.2, 74.1, 45.1, 45.0, 31.3, 30.5, 30.5, 22.5, 22.5, 21.1, 21.0

ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{23}H_{26}NO_5^+$ 396.1805, found 396.1803. The diastereomeric ratio was determined by NMR ***dr* = 1:1**.



3ar

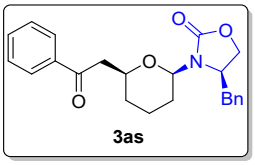
3ar was obtained as a colorless oil 4 mg in 11% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 7.4, 1.7 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.27 – 5.21 (m, 1H), 4.24 (dd, J = 8.9, 1.7 Hz, 1H), 4.10 (ddt, J = 21.5, 10.8, 7.1 Hz, 2H), 3.99 (dq, J = 10.8, 7.1 Hz, 1H), 3.24 (dd, J = 16.4, 5.6 Hz, 1H), 2.90 (dd, J = 16.4, 6.9 Hz, 1H), 2.67 (dt, J = 16.6, 9.9 Hz, 1H), 2.36 (ddd, J = 16.6, 9.6, 2.1 Hz, 1H), 2.22 (dq, J = 13.1, 9.6 Hz, 1H), 2.04 (ddt, J = 13.2, 9.4, 1.9 Hz, 1H), 1.95 – 1.86 (m, 1H), 1.76 – 1.60 (m, 5H), 1.21 (t, J = 7.1 Hz, 3H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.2, 174.9, 172.6, 137.0, 133.2, 128.6, 128.1, 81.1, 74.1, 61.1, 57.1, 44.9, 30.6, 30.3, 28.5, 23.5, 22.4, 14.1 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{26}NO_5^+$ 360.1805, found 360.1803. **$[\alpha]_D^{20}$** -8.91 (c = 0.78 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 240 nm, t_{major} = 48.43 min, t_{minor} = 44.37 min, **er >99.9:0.1**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



3ar'

3ar' was obtained as a colorless oil 7 mg in 19% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 1/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 2H), 7.60 – 7.53 (m, 1H), 7.49 – 7.42 (m, 2H), 5.28 (dd, J = 11.3, 2.1 Hz, 1H), 4.36 – 4.30 (m, 1H), 4.26 – 4.11 (m, 3H), 3.28 (dd, J = 15.9, 5.4 Hz, 1H), 3.01 (dd, J = 15.8, 7.1 Hz, 1H), 2.65 – 2.49 (m, 1H), 2.38 – 2.20 (m, 2H), 2.04 – 1.94 (m, 1H), 1.92 – 1.81 (m, 1H), 1.80 – 1.72 (m, 1H), 1.72 – 1.57 (m, 2H), 1.32 – 1.14 (m, 5H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.8, 175.4, 173.3, 137.2, 133.1, 128.5, 128.3, 80.2, 74.4, 61.4, 56.3, 45.1, 30.6, 30.0, 29.0, 24.5, 22.7, 14.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{26}NO_5^+$ 360.1805, found 360.1811. **$[\alpha]_D^{20}$** -10.86 (c = 0.70 in $CHCl_3$). The enantiomeric ratio was determined

by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 240 nm, t_{major} = 36.29 min, t_{minor} = 34.07 min, **er >99.7:0.3.** The diastereomeric ratio was determined by NMR ***dr* >20:1**.

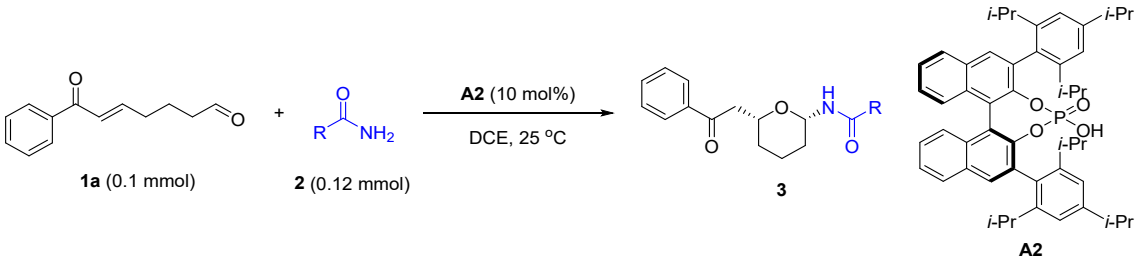


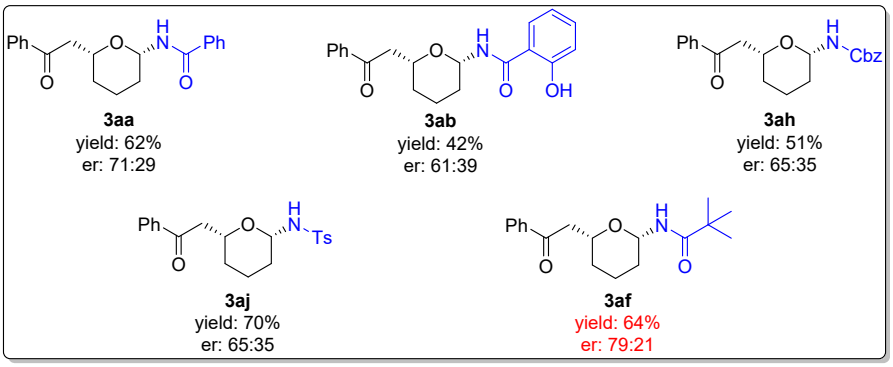
3as

3as was obtained as a colorless oil 28 mg in 74% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 – 7.92 (m, 2H), 7.59 – 7.50 (m, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.21 (m, 3H), 7.17 – 7.10 (m, 2H), 5.05 (dd, *J* = 10.6, 2.7 Hz, 1H), 4.22 – 3.93 (m, 4H), 3.29 (td, *J* = 16.2, 4.6 Hz, 2H), 3.08 (dd, *J* = 15.8, 6.8 Hz, 1H), 2.60 (dd, *J* = 14.0, 9.5 Hz, 1H), 2.01 (dq, *J* = 13.7, 3.4 Hz, 1Hk), 1.92 – 1.64 (m, 4H), 1.31 (tdd, *J* = 14.5, 11.9, 4.9 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.0, 157.0, 137.2, 136.2, 133.2, 129.2, 128.8, 128.6, 128.3, 127.0, 82.8, 74.7, 66.6, 54.5, 44.8, 39.9, 30.6, 28.5, 22.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{23}H_{26}NO_4^+$ 380.1856, found 380.1857. **$[\alpha]_D^{20}$** -27.03 (*c* = 1.44 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IB column [*n*-hexane/*i*-PrOH = 65/35, 1 mL/min], λ = 205 nm, t_{major} = 7.55 min, t_{minor} = 8.70 min, **er >99.9:0.1**. The diastereomeric ratio was determined by ^{1}H NMR ***dr* >20:1.**

E. Optimization of the synthesis of chiral N,O-aminals:

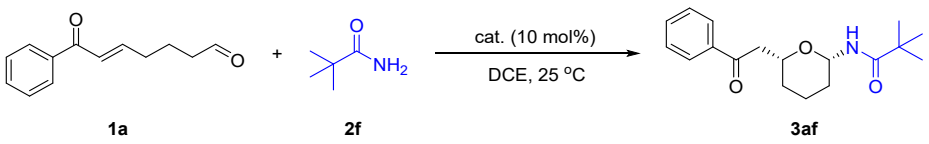
Scheme S1. Screening of amides



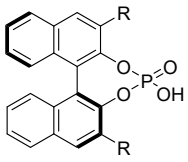


General procedure: All reactions were carried out using **1a** (0.1 mmol, 1.0 equiv), **2** (0.12 mmol, 1.2 equiv) in DCE (0.5 mL) with **A2** (10 mol%) at 25 °C. After workup, the mixture was purified by column chromatography on silica gel to afford product **3** for HPLC analysis. And pivalic amide **2f** was chosen to optimize other conditions.

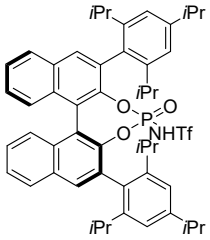
Table S3. Screening of catalysts



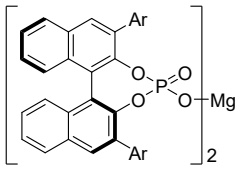
1a **2f** **3af**



A1: R = 2,4,6-$(CH_3)_3C_6H_2$
A2: R = 2,4,6-$(i\text{Pr})_3C_6H_2$
A3: R = 9-anthracenyl
A5: R = Ph
A6: R = 4-$t\text{Bu}C_6H_4$
A7: R = 3,5-$(CH_3)_2C_6H_3$
A8: R = 2,4,6-$Cy_3C_6H_2$
A9: R = 4-PhC_6H_4
A10: R = 1-naphthaleny
A11: R = 2-naphthaleny
A12: R = $Si(Ph)_3$

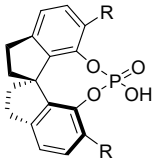


A4

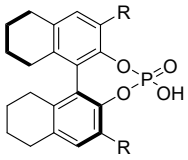


Ar = 2,4,6-$(i\text{Pr})_3C_6H_2$

A13



A'1: R = 2,4,6-$(i\text{Pr})_3C_6H_2$
A'2: R = Ph
A'3: R = 3,5-$(t\text{Bu})_2C_6H_3$



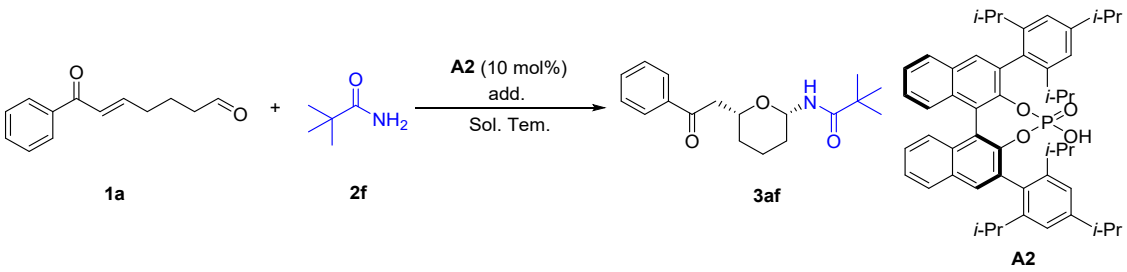
A''1: R = 2,4,6-$(i\text{Pr})_3C_6H_2$
A''2: R = Ph
A''3: R = 4-$t\text{Bu}C_6H_4$

entry[a]	Cat.	T (d)	Y (%)[b]	er[c]	dr[d]
1	**A1**	2	36	69:31	>20:1
2	**A2**	2	64	79:21	>20:1
3	**A3**	2	64	66:34	>20:1
4	**A4**	2	<5	66:34	>20:1
5	**A5**	1	76	58:42	>20:1
6	**A6**	1	64	57:43	>20:1
7	**A7**	2	46	62:38	>20:1
8	**A8**	2	54	72:28	>20:1
9	**A9**	2	64	55:45	>20:1
10	**A10**	2	86	57:43	>20:1
11	**A11**	2	57	59:41	>20:1
12	**A12**	-	NR	-	--
13	**A13**	2	<5	78:22	>20:1
14	**A'1**	2	20	53:47	>20:1

15	**A'2**	2	50	57.5:42.5	>20:1
16	**A'3**	-	NR	-	-
17	**A''1**	2	60	75:25	>20:1
18	**A''2**	2	40	57:43	>20:1
19	**A''3**	2	40	54:46	>20:1

[*a*] Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1.0 equiv), **2f** (0.12 mmol, 1.2 equiv) in DCE (0.5 mL) with cat. (10 mol%) at 25 ^{o}C. After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **3af** as a white solid. [*b*] Isolated yield of **3af**. [*c*] Determined by HPLC analyses of isolated compound **3af** on chiral stationary phases. [*d*] Determined by ^{1}H NMR.

Table S4. Optimization of other reaction conditions

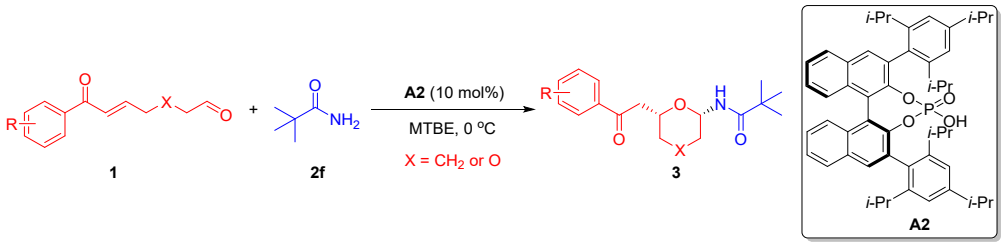


entry[a]	Tem. (°C)	Sol.	Add.	T (d)	Y (%)[b]	er[c]	dr[d]
1[e]	25	DCE	-	2	50	77:23	>20:1
2	25	DCE	-	2	78	79:21	>20:1
3[f]	25	DCE	-	2	71	79:21	>20:1
4	0	DCE	-	6	57	90:10	>20:1
5	-20	DCE	-	6	<5	93:7	>20:1
6	40	DCE	-	2	70	73:27	>20:1
7	0	DCM	-	6	29	87:13	>20:1
8	0	toluene	-	6	64	90:10	>20:1
9	0	$PhOCH_3$	-	6	52	90:10	>20:1
10	0	Et_2O	-	6	29	88:12	>20:1
11	0	EA	-	-	<5	87:13	>20:1
12	0	CH_3CN	-	-	NR	-	-
13	0	acetone	-	-	trace	-	-
14	0	THF	-	-	NR	-	-
15	0	MTBE	-	6	59	95:5	>20:1
16	0	MTBE +Et_2O	-	6	66	93:7	>20:1
17	0	MTBE	$FeCl_3$ (20 mol%)	6	40	64:36	>20:1

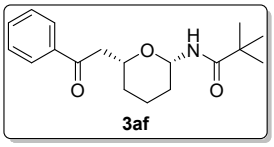
18	0	MTBE	3 Å MS (5 mg)	6	29	92:8	>20:1
19	0	MTBE	4 Å MS (5 mg)	6	50	93:7	>20:1
20	0	MTBE	4 Å MS (10 mg)	6	20	90:10	>20:1
21	0	MTBE	4 Å MS (20 mg)	-	NR	-	-
22	0	MTBE	5 Å MS (5 mg)	6	36	89:11	>20:1
23	0	MTBE	$MgSO_4$ (5 mg)	6	57	94:6	>20:1
24	0	MTBE	Na_2SO_4 (5 mg)	6	64	91:9	>20:1
25	0	MTBE	$(CF_3)_2CHOH$ (20 mol%)	6	50	91:9	>20:1
26	0	MTBE	$(CH_2OH)_2$ (20 mol%)	6	50	93:7	>20:1
27	0	MTBE	H_2O (1.0 equiv)	6	40	93:7	>20:1
28[g]	0	MTBE	-	6	77	89:11	>20:1
29[h]	0	MTBE	-	6	21	92:8	>20:1
30[i]	0	MTBE	-	9	47	95:5	>20:1

[*a*] Unless otherwise specified, all reactions were carried out using **1a** (0.1 mmol, 1.0 equiv), **2f** (0.12 mmol, 1.2 equiv) in solvent (0.5 mL) with **A2** (10 mol%). After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **3af** as a white solid. [*b*] Isolated yield of **3af**. [*c*] Determined by HPLC analyses of isolated compound **3af** on chiral stationary phases. [*d*] Determined by ^{1}H NMR. [*e*] Reactions were carried out using **1a** (0.2 mmol, 2.0 equiv) and **2f** (0.1 mmol, 1.0 equiv). [*f*] Reactions were carried out using **1a** (0.1 mmol, 1.0 equiv) and **2f** (0.2 mmol, 2.0 equiv). [*g*] Reactions were carried out in MTBE (0.2 mL). [*h*] Reactions were carried out in MTBE (1.0 mL). [*i*] Reactions were carried out with **A2** (5 mol%).

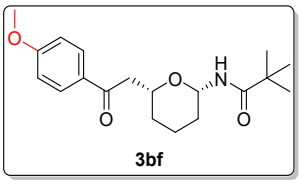
F. Scope of chiral reaction conditions:



General procedure: A glass vial equipped with a magnetic stirring bar was charged with (*E*)-7-oxo-7-phenylhept-5-enal **1** (0.1 mmol, 1.0 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in MTBE (0.5 mL) with **A2** (10 mol%) at 0 °C. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4:1 to 2:1) to afford **3** for NMR and HPLC analysis.

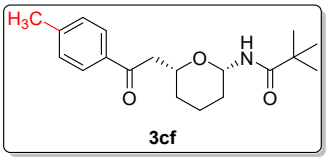


3af was obtained as a white solid 18 mg in 59% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (t, J = 5.9 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 6.00 (d, J = 8.5 Hz, 1H), 5.25 – 5.12 (m, 1H), 4.14 (dd, J = 11.2, 5.8 Hz, 1H), 3.34 (dd, J = 16.2, 4.7 Hz, 1H), 3.07 (dd, J = 16.1, 8.0 Hz, 1H), 1.93 – 1.86 (m, 1H), 1.81 (d, J = 13.0 Hz, 2H), 1.75 – 1.63 (m, 1H), 1.35 – 1.25 (m, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.9, 177.7, 137.1, 133.1, 128.6, 128.2, 78.6, 73.9, 45.2, 38.7, 31.4, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{26}NO_3^+$ 304.1907, found 304.1905. **$[\alpha]_D^{20}$** 24.33 (c = 3.53 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 15.26 min, t_{minor} = 20.48 min, **er = 95:5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



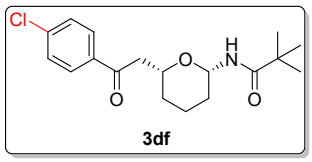
3bf

3bf was obtained as a colorless oil 17 mg in 51% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.7 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 5.97 (d, J = 8.5 Hz, 1H), 5.16 (t, J = 9.3 Hz, 1H), 4.11 (s, 1H), 3.87 (s, 3H), 3.29 (dd, J = 15.9, 4.4 Hz, 1H), 3.01 (dd, J = 15.9, 8.2 Hz, 1H), 1.88 (d, J = 13.4 Hz, 1H), 1.80 (d, J = 12.9 Hz, 2H), 1.73 – 1.63 (m, 1H), 1.28 (dt, J = 18.5, 5.5 Hz, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.3, 177.7, 163.5, 130.6, 130.3, 113.7, 78.6, 74.1, 55.5, 45.0, 38.7, 31.4, 30.7, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{28}NO_4^+$ 334.2013, found 334.2014. **$[\alpha]_D^{20}$** 15.82 (c = 1.52 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 27.10 min, t_{minor} = 32.84 min, **er = 92:8**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



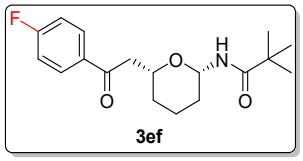
3cf

3cf was obtained as a white solid 16 mg in 50% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 5.97 (d, J = 8.6 Hz, 1H), 5.20 – 5.11 (m, 1H), 4.16 – 4.07 (m, 1H), 3.31 (dd, J = 16.0, 4.5 Hz, 1H), 3.03 (dd, J = 16.0, 8.2 Hz, 1H), 2.40 (s, 3H), 1.87 (dd, J = 11.4, 4.8 Hz, 1H), 1.79 (d, J = 13.2 Hz, 2H), 1.72 – 1.60 (m, 1H), 1.35 – 1.21 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.4, 177.6, 143.9, 134.6, 129.2, 128.3, 78.6, 74.0, 45.1, 38.6, 31.4, 30.6, 27.4, 22.7, 21.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{28}NO_3^+$ 318.2064, found 318.2058. **$[\alpha]_D^{20}$** 18.78 (c = 0.62 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 65/35, 1 mL/min], λ = 240 nm, t_{major} = 16.13 min, t_{minor} = 19.81 min, **er = 95:5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



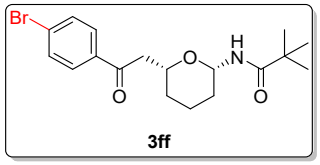
3df

3df was obtained as a yellow oil 26 mg in 77% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.6 Hz, 2H), 7.42 (d, J = 8.6 Hz, 2H), 5.96 (d, J = 8.6 Hz, 1H), 5.15 (ddd, J = 10.9, 9.0, 2.1 Hz, 1H), 4.09 (dddd, J = 9.7, 7.0, 4.8, 1.8 Hz, 1H), 3.28 (dd, J = 16.0, 4.8 Hz, 1H), 3.02 (dd, J = 16.0, 7.7 Hz, 1H), 1.94 – 1.84 (m, 1H), 1.84 – 1.74 (m, 2H), 1.75 – 1.61 (m, 1H), 1.38 – 1.20 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.7, 177.7, 139.5, 135.5, 129.7, 128.8, 78.5, 73.9, 45.2, 38.7, 31.2, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{25}ClNO_3^+$ 338.1517, found 338.1520. **$[\alpha]_D^{20}$** 28.06 (c = 1.14 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 11.67 min, t_{minor} = 16.04 min, **er = 93:7**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



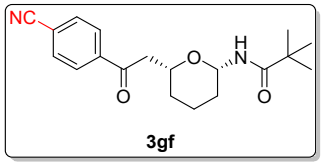
3ef

3ef was obtained as a white solid 20 mg in 62% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (ddd, J = 8.9, 5.2, 2.5 Hz, 2H), 7.15 – 7.09 (m, 2H), 5.97 (d, J = 8.6 Hz, 1H), 5.19 – 5.12 (m, 1H), 4.11 (dd, J = 9.5, 4.1 Hz, 1H), 3.29 (dd, J = 16.0, 4.7 Hz, 1H), 3.03 (dd, J = 16.0, 7.7 Hz, 1H), 1.92 – 1.85 (m, 1H), 1.83 – 1.76 (m, 2H), 1.68 (dt, J = 13.1, 3.8 Hz, 1H), 1.37 – 1.22 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.3, 177.7, 167.0, 164.5, 133.6, 131.0, 130.9, 115.7, 115.5, 78.5, 73.9, 45.2, 38.7, 31.3, 30.6, 27.4 22.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{25}FNO_3^+$ 322.1813, found 322.1819. **$[\alpha]_D^{20}$** 19.74 (c = 1.51 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 12.25 min, t_{minor} = 16.09 min, **er = 94:6**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



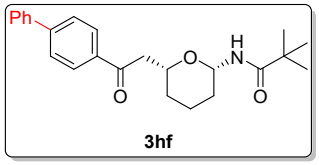
3ff

3ff was obtained as a white solid 24 mg in 63% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.6 Hz, 2H), 7.58 (d, J = 8.6 Hz, 2H), 5.95 (d, J = 8.6 Hz, 1H), 5.20 – 5.09 (m, 1H), 4.16 – 4.03 (m, 1H), 3.28 (dd, J = 16.0, 4.8 Hz, 1H), 3.01 (dd, J = 16.0, 7.6 Hz, 1H), 1.95 – 1.84 (m, 1H), 1.84 – 1.76 (m, 2H), 1.74 – 1.61 (m, 1H), 1.35 – 1.22 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.9, 177.7, 135.9, 131.8, 129.8, 128.3, 78.5, 73.8, 45.2, 38.7, 31.2, 30.6, 27.4, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{25}BrNO_3^+$ 382.1012, found 382.1013. **$[\alpha]_D^{20}$** 40.27 (c = 0.89 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 11.95 min, t_{minor} = 16.67 min, **er = 95:5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



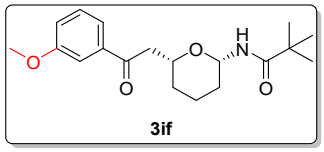
3gf

3gf was obtained as a colorless oil 12 mg in 37% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (d, J = 8.1 Hz, 2H), 7.74 (d, J = 8.1 Hz, 2H), 5.92 (d, J = 8.6 Hz, 1H), 5.12 (t, J = 9.8 Hz, 1H), 4.08 (dt, J = 11.1, 5.9 Hz, 1H), 3.28 (dd, J = 15.9, 5.1 Hz, 1H), 3.04 (dd, J = 15.9, 7.0 Hz, 1H), 1.90 (d, J = 13.5 Hz, 1H), 1.78 (d, J = 12.7 Hz, 2H), 1.67 (d, J = 12.9 Hz, 1H), 1.33 – 1.20 (m, 2H), 1.16 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.9, 177.7, 140.2, 132.4, 128.7, 118.0, 116.3, 78.5, 73.8, 45.5, 38.7, 31.1, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{25}N_2O_3^+$ 329.1860, found 329.1860. **$[\alpha]_D^{20}$** 15.17 (c = 0.77 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 240 nm, t_{major} = 17.66 min, t_{minor} = 24.69 min, **er = 95:5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



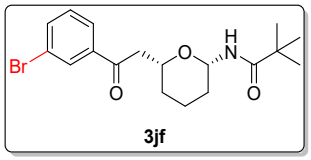
3hf

3hf was obtained as a colorless oil 14 mg in 37% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.65 – 7.59 (m, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.40 (dd, J = 8.3, 6.3 Hz, 1H), 5.97 (d, J = 8.7 Hz, 1H), 5.18 (ddd, J = 10.9, 9.0, 2.1 Hz, 1H), 4.15 (dt, J = 6.1, 3.5 Hz, 1H), 3.37 (dd, J = 16.0, 4.6 Hz, 1H), 3.09 (dd, J = 16.0, 8.0 Hz, 1H), 1.94 – 1.85 (m, 1H), 1.85 – 1.76 (m, 2H), 1.71 (t, J = 3.8 Hz, 1H), 1.37 – 1.21 (m, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.4, 177.6, 145.8, 139.9, 135.8, 128.9, 128.8, 128.2, 127.2, 127.2, 78.6, 74.0, 45.3, 38.6, 31.4, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{24}H_{30}NO_3^+$ 380.2220, found 380.2229. **$[\alpha]_D^{20}$** 35.32 (c = 0.77 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 210 nm, t_{major} = 13.67 min, t_{minor} = 18.93 min, **er = 92:8**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



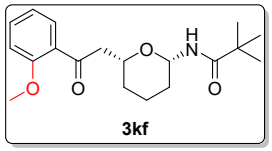
3if

3if was obtained as a white solid 20 mg in 60% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, J = 7.6 Hz, 1H), 7.46 (s, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.09 (dd, J = 8.1, 2.5 Hz, 1H), 5.95 (d, J = 8.5 Hz, 1H), 5.21 – 5.11 (m, 1H), 4.12 (dt, J = 11.0, 5.6 Hz, 1H), 3.84 (s, 3H), 3.31 (dd, J = 16.2, 4.6 Hz, 1H), 3.05 (dd, J = 16.2, 8.0 Hz, 1H), 1.88 (d, J = 13.5 Hz, 1H), 1.80 (d, J = 14.0 Hz, 2H), 1.72 – 1.64 (m, 1H), 1.35 – 1.21 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.6, 177.7, 159.8, 138.5, 129.5, 120.9, 119.7, 112.3, 78.6, 73.9, 55.4, 45.3, 38.7, 31.4, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{28}NO_4^+$ 334.2013, found 334.2010. **$[\alpha]_D^{20}$** 25.19 (c = 0.87 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 210 nm, t_{major} = 14.80 min, t_{minor} = 17.91 min, **er = 93:7**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



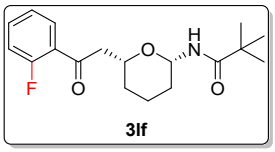
3jf

3jf was obtained as a colorless oil 18 mg in 47% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (t, J = 1.7 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.67 (ddd, J = 7.9, 1.8, 0.9 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 5.96 (d, J = 8.7 Hz, 1H), 5.15 (ddd, J = 10.9, 9.0, 2.2 Hz, 1H), 4.10 (dddd, J = 9.5, 7.1, 5.0, 1.9 Hz, 1H), 3.27 (dd, J = 16.0, 5.0 Hz, 1H), 3.02 (dd, J = 16.1, 7.4 Hz, 1H), 1.95 – 1.85 (m, 1H), 1.84 – 1.74 (m, 2H), 1.75 – 1.62 (m, 1H), 1.35 – 1.21 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.6, 177.7, 138.9, 135.9, 131.4, 130.1, 126.8, 122.9, 78.5, 73.8, 45.2, 38.7, 31.3, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{25}BrNO_3^+$ 382.1012, found 382.1010. **$[\alpha]_D^{20}$** 19.96 (c = 0.75 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 11.06 min, t_{minor} = 17.72 min, **er = 94:6**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



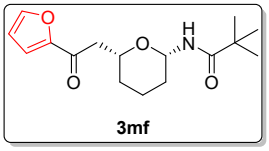
3kf

3kf was obtained as a colorless oil 18 mg in 54% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.7, 1.7 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.03 – 6.89 (m, 2H), 5.97 (d, J = 8.5 Hz, 1H), 5.17 – 5.06 (m, 1H), 4.06 (dt, J = 5.6, 3.0 Hz, 1H), 3.89 (s, 3H), 3.32 (dd, J = 16.4, 4.9 Hz, 1H), 3.11 (dd, J = 16.4, 8.0 Hz, 1H), 1.89 – 1.82 (m, 1H), 1.78 (d, J = 14.4 Hz, 2H), 1.65 (qd, J = 13.1, 3.9 Hz, 1H), 1.28 (ddt, J = 23.6, 12.6, 5.4 Hz, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.0, 177.5, 158.4, 133.4, 130.2, 120.6, 111.4, 78.6, 74.1, 55.5, 50.4, 38.6, 31.4, 30.6, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{28}NO_4^+$ 334.2013, found 334.2015. **$[\alpha]_D^{20}$** 20.45 (c = 0.69 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 65/35, 1 mL/min], λ = 240 nm, t_{major} = 22.98 min, t_{minor} = 26.57 min, **er = 87:13**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



3lf

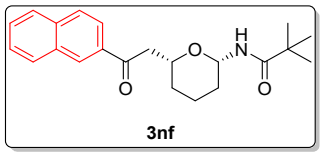
3lf was obtained as a colorless oil 18 mg in 56% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (td, J = 7.6, 1.8 Hz, 1H), 7.50 (dddd, J = 8.3, 7.1, 5.0, 1.8 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.14 – 7.08 (m, 1H), 5.93 (d, J = 8.4 Hz, 1H), 5.12 (td, J = 9.9, 8.9, 2.1 Hz, 1H), 4.16 – 4.06 (m, 1H), 3.29 (ddd, J = 16.9, 5.5, 2.7 Hz, 1H), 3.11 (ddd, J = 16.9, 7.2, 2.8 Hz, 1H), 1.88 (dd, J = 13.6, 2.6 Hz, 1H), 1.79 (d, J = 13.7 Hz, 2H), 1.68 (dt, J = 13.2, 3.8 Hz, 1H), 1.34 – 1.21 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.3, 177.6, 134.5, 134.4, 130.6, 130.6, 126.0, 124.5, 124.4, 116.7, 116.5, 78.6, 73.6, 50.0, 50.0, 38.6, 31.4, 30.7, 27.4, 22.7 ppm. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.0 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{25}FNO_3^+$ 322.1813, found 322.1815. **$[\alpha]_D^{20}$** 12.64 (c = 0.50 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 240 nm, t_{major} = 10.80 min, t_{minor} = 15.10 min, **er = 92.5:7.5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



3mf

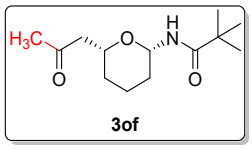
3mf was obtained as a colorless oil 14 mg in 48% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 1H), 7.21 – 7.18 (m, 1H), 6.52 (dd, J = 3.6, 1.7 Hz, 1H), 5.96 (d, J = 8.5 Hz, 1H), 5.15 (ddd, J = 10.9, 8.9, 2.2 Hz, 1H), 4.08 (dddd, J = 11.1, 7.4, 5.3, 1.7 Hz, 1H), 3.16 (dd, J = 15.3, 5.3 Hz, 1H), 2.92 (dd, J = 15.3, 7.6 Hz, 1H), 1.88 (ddd, J = 13.6, 5.8, 3.1 Hz, 1H), 1.81 – 1.73 (m, 2H), 1.65 (ddd, J = 17.0, 8.6, 3.8 Hz, 1H), 1.32 – 1.21 (m, 2H), 1.18 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 186.5, 177.6, 152.8, 146.5, 117.7, 112.2, 78.6, 73.7, 45.2, 38.7, 31.3, 30.6, 27.4, 22.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{16}H_{24}NO_4^+$ 294.1700, found 294.1711. **$[\alpha]_D^{20}$** 20.09 (c = 0.29 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ

= 240 nm, t_{major} = 21.53 min, t_{minor} = 31.77 min, **er = 93.5:6.5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



3nf

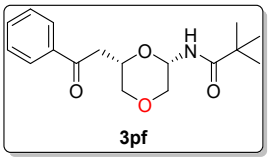
3nf was obtained as a colorless oil 20 mg in 57% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.01 (dd, J = 8.6, 1.7 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.87 (dd, J = 8.3, 4.5 Hz, 2H), 7.63 – 7.51 (m, 2H), 5.98 (d, J = 8.7 Hz, 1H), 5.19 (ddd, J = 10.8, 8.9, 2.1 Hz, 1H), 4.19 (dddd, J = 11.0, 6.1, 4.7, 2.3 Hz, 1H), 3.47 (dd, J = 16.0, 4.6 Hz, 1H), 3.20 (dd, J = 16.0, 8.0 Hz, 1H), 1.91 – 1.78 (m, 3H), 1.68 (ddd, J = 16.5, 8.4, 3.6 Hz, 1H), 1.38 – 1.23 (m, 2H), 1.17 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.8, 177.7, 135.6, 134.5, 132.5, 130.1, 129.6, 128.51, 128.4, 127.8, 126.8, 123.9, 78.6, 74.0, 45.3, 38.7, 31.4, 30.7, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{22}H_{28}NO_3^+$ 354.2064, found 354.2063. **$[\alpha]_D^{20}$** 42.79 (c = 1.05 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 19.19 min, t_{minor} = 26.10 min, **er = 93.5:6.5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



3of

3of was obtained as a white solid 10 mg in 41% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.97 (d, J = 8.0 Hz, 1H), 5.13 (ddd, J = 10.9, 9.0, 2.1 Hz, 1H), 3.99 – 3.89 (m, 1H), 2.68 (dd, J = 15.8, 6.9 Hz, 1H), 2.51 (dd, J = 15.8, 6.1 Hz, 1H), 2.17 (s, 3H), 1.92 – 1.85 (m, 1H), 1.78 (d, J = 12.3 Hz, 1H), 1.70 – 1.59 (m, 2H), 1.34 – 1.25 (m, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.1, 177.9, 78.5, 73.6, 50.2, 38.7, 31.0, 30.5, 30.4, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{13}H_{24}NO_3^+$ 242.1751, found 242.1756. **$[\alpha]_D^{20}$** 6.46 (c = 0.42 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak

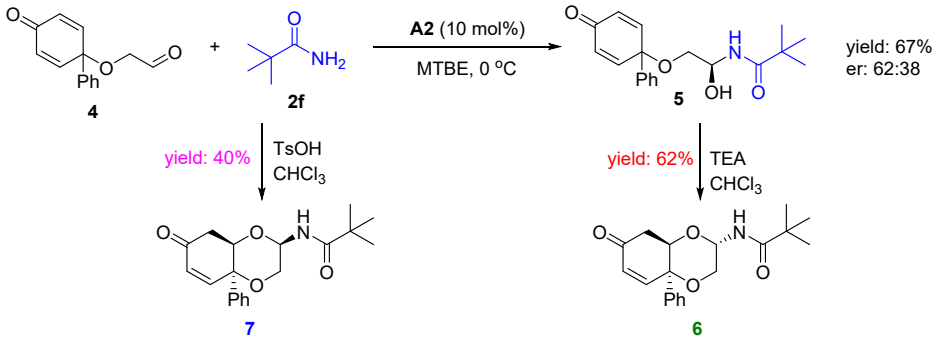
AD-H column [*n*-hexane/*i*-PrOH = 95/5, 1 mL/min], λ = 202 nm, t_{major} = 17.92 min, t_{minor} = 21.95 min, **er = 70:30**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.



3pf

3pf was obtained as a colorless oil 22 mg in 72% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.61 – 7.54 (m, 1H), 7.50 – 7.43 (m, 2H), 5.80 (d, *J* = 8.9 Hz, 1H), 5.42 (ddd, *J* = 9.9, 8.9, 2.9 Hz, 1H), 4.40 (dddd, *J* = 10.3, 7.6, 4.8, 2.6 Hz, 1H), 3.97 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.85 (dd, *J* = 11.1, 2.9 Hz, 1H), 3.30 (dd, *J* = 16.7, 4.8 Hz, 1H), 3.22 (dd, *J* = 11.4, 10.2 Hz, 1H), 3.17 (dd, *J* = 11.1, 9.8 Hz, 1H), 2.98 (dd, *J* = 16.7, 7.9 Hz, 1H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.6, 178.0, 136.7, 133.4, 128.7, 128.2, 75.7, 71.8, 69.8, 68.8, 40.8, 38.9, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{17}H_{24}NO_4^+$ 306.1700, found 306.1701. **$[\alpha]_D^{20}$** 33.35 (*c* = 0.83 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak AD-H column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 240 nm, t_{major} = 5.51 min, t_{minor} = 4.98 min, **er = 97.5:2.5**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

G. Other reactions of hemiaminal by desymmetrization:

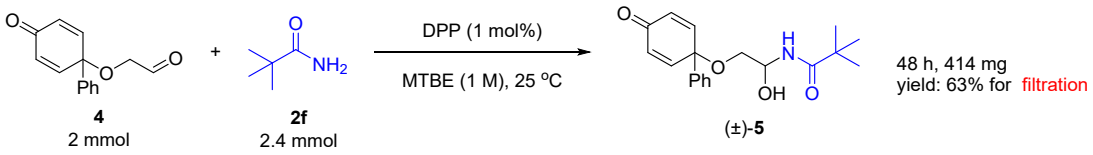


A glass vial equipped with a magnetic stirring bar was charged with **4** (0.1 mmol, 1.0 equiv), **2f** (0.12 mmol, 1.2 equiv) and **A2** (0.01 mmol, 0.1 equiv) in MTBE (0.5 mL) at 0 °C. The reaction stirred at 0 °C until the material **4** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2.5:1) to afford **5** (22 mg, 67%, 62:38 er) as a white solid.

To the solution of **5** (0.05 mmol, 1.0 equiv) in $CHCl_3$ (0.2 mL), TEA (0.02 mmol, 0.4 equiv) was added at 25 °C. The reaction stirred at 25 °C for about 24 h until the material **5** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **(±)-6** (10 mg, 62%) as a white solid.

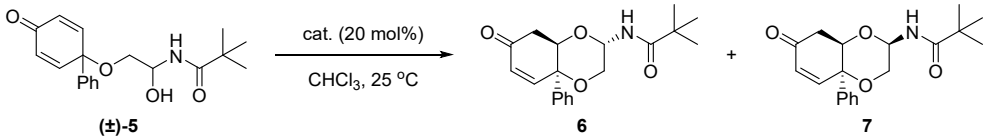
A glass vial equipped with a magnetic stirring bar was charged with **4** (0.1 mmol, 1.0 equiv), **2f** (0.12 mmol, 1.2 equiv) and TsOH (0.01 mmol, 0.1 equiv) in $CHCl_3$ (0.5 mL) at 25 °C. The reaction stirred at 25 °C for about 18 h until the material **4** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **(±)-7** (13 mg, 40%) as a white solid.

Large scale reaction for synthesis of racemic 5 by filtration:

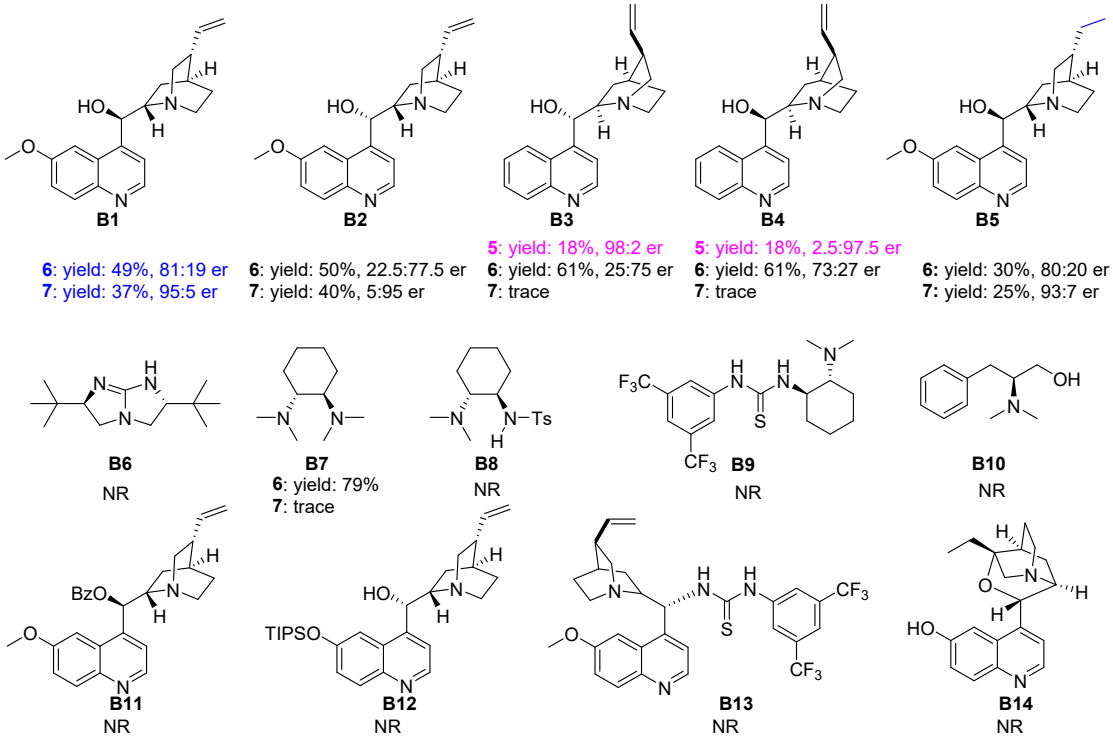


A glass vial equipped with a magnetic stirring bar was charged with **4** (2 mmol, 1.0 equiv), **2f** (2.4 mmol, 1.2 equiv) and DPP (0.02 mmol, 0.01 equiv) in MTBE (2 mL) at 25 °C and stirred until the material **4** disappeared. After completion of the reaction, the reaction mixture was purified by filtration to afford **(±)-5** (414 mg, 63%) as a white solid.

H. Optimization of oxa-Michael reaction:



Scheme S2. Screening of catalysts

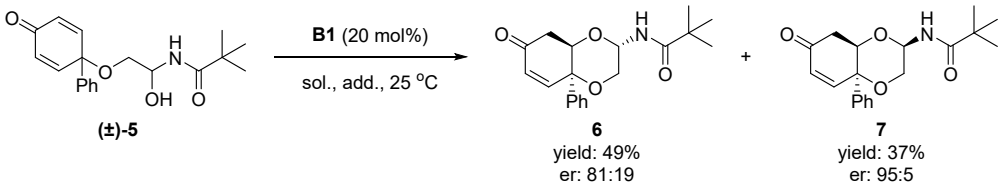


All reactions were carried out using **5** (0.1 mmol, 1.0 equiv), cat. (0.02 mmol, 0.2 equiv) in $CHCl_3$ (0.5 mL). After workup, the mixture was purified by column chromatography on

silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **6** and **7** as white solids for HPLC analysis.

When **B3** and **B4** were used as the catalysts for the reaction, the amount of compound **7** is trace and **5** could be recycled with excellent stereoselectivity. And the absolute configurations of chiral **5**, **6** and **7** were confirmed by chemical correlation and reported literature. [9]

Table S5. Screening of other conditions

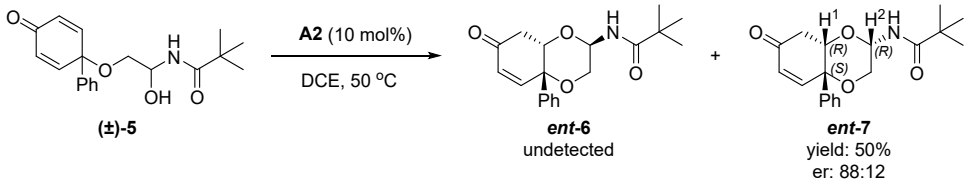


entry[a]	Add.	Sol.	yield of **6** (%)[b]	er of **6**[c]	yield of **7** (%)[b]	er of **7**[c]	dr(**6**/**7**)[d]
1	-	DCM	54	77:23	25	83:17	>20:1/>20:1
2	-	DCE	45	83:17	33	94:6	>20:1/>20:1
3	-	$CHCl_3$	49	81:19	37	95:5	>20:1/>20:1
4	-	toluene	-	-	NR	-	-
5	-	CH_3CN	trace	-	trace	-	-
6	-	THF	trace	-	trace	-	-
7	-	EA	-	-	NR	-	-
8	-	MTBE	-	-	NR	-	-
9	-	Et_2O	-	-	NR	-	-
10	-	1,4-dioxane	-	-	NR	-	-
11	HFIP (0.8 equiv)	$CHCl_3$	44	70:30	25	70:30	>20:1/>20:1

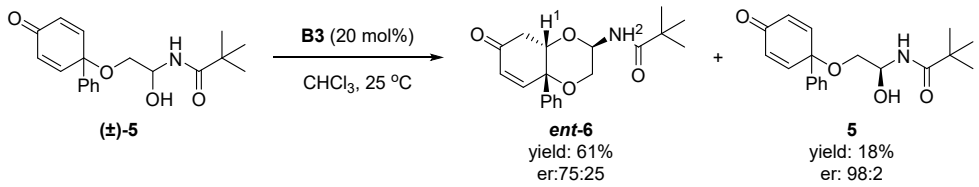
12	4 Å MS (10 mg)	$CHCl_3$	38	83:17	19	93:7	>20:1/>20:1

[*a*] Unless otherwise specified, all reactions were carried out using **(±)-5** (0.1 mmol, 1.0 equiv), **B1** (0.02 mmol, 0.2 equiv) in solvent (0.5 mL) with additive at 25 °C. After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **6** and **7** as white solids. [*b*] Isolated yield of product. [*c*] Determined by HPLC analyses of isolated compounds on chiral stationary phases. [*d*] Determined by ^{1}H NMR.

I. Determination of absolute configurations of 6 and 7:



To the solution of **(±)-5** (0.1 mmol, 1.0 equiv) in MTBE (0.5 mL), phosphoric acid **A2** (10 mol%) was added at 25 °C. Then the reaction stirred at 50 °C until the material **5** consumed completely for about 48 h. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product ***ent*-7** as a white solid (16 mg, 50%, 88:12 er). The absolute configuration of ***ent*-7** was confirmed by analyzed. The relative configuration of ***ent*-7** was confirmed by NOESY (H^1-H^2, Ph-H^2) and according to the reported reference: similar reaction without amide catalyzed by same catalyst **A2** (*J. Am. Chem. Soc.* **2010**, *132*, 4056-4057)[9], the absolute configurations of phenyl group and H^1 are (*S*) and (*R*) on the *cis*-orientation.

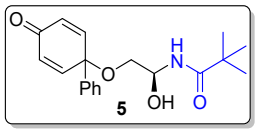


To the solution of (±)-**5** (0.1 mmol, 1.0 equiv) in MTBE (0.5 mL), **B2** (10 mol%) was added at 25 °C. Then the reaction stirred at 25 °C for about 3 d. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford

product ***ent*-6** a white solid (20 mg, 61%, 75:25 er). And **5** was recyclized in 18% yield with 98:2 er. The relative configuration of ***ent*-6** was confirmed by NOESY (H^1-H^2, Ph-H^2). The absolute configuration of ***ent*-6** was confirmed according to the configuration of **5**.

According to the absolute configuration of ***ent*-6** and ***ent*-7**, the absolute configuration of **6** and **7** could be confirmed.

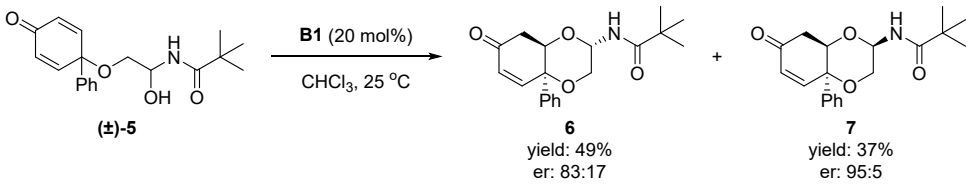
J. The characterization data of 5-7:



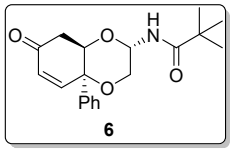
5

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.40 – 7.32 (m, 3H), 6.88 – 6.78 (m, 2H), 6.67 (d, J = 7.4 Hz, 1H), 6.45 – 6.38 (m, 2H), 5.54 (dt, J = 7.4, 4.5 Hz, 1H), 3.69 (d, J = 4.4 Hz, 2H), 1.23 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.2, 179.8, 149.5, 149.3, 137.8, 130.2, 130.1, 129.0, 128.6, 125.6, 76.4, 73.3, 66.5, 38.8, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{24}NO_4^+$ 330.1700, found 330.1694.

Catalyzed by B3: $[\alpha]_D^{20}$ 26.50 (c = 0.25 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IA column [n-hexane/i-PrOH = 80/20, 1 mL/min], λ = 230 nm, t_{major} = 5.29 min, t_{minor} = 5.80 min, **er = 98:2**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

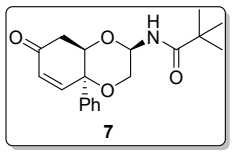


The solvent of racemic **5** (0.1 mmol, 1.0 equiv) was added **B1** (0.02 mmol, 0.2 equiv) in solvent (0.5 mL) at 25 °C. After workup, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford product **6** and **7** as white solids.



6

6 was obtained as a white solid 16 mg in 49% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 2.5/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.37 (m, 5H), 7.05 (d, J = 8.4 Hz, 1H), 6.75 (dd, J = 10.4, 2.8 Hz, 1H), 6.53 (dd, J = 10.4, 1.0 Hz, 1H), 5.54 (dd, J = 8.3, 2.4 Hz, 1H), 4.38 – 4.20 (m, 2H), 3.82 (d, J = 12.2 Hz, 1H), 2.59 – 2.38 (m, 2H), 1.31 (s, 9H) ppm. **^{13}C NMR** (125 MHz, $CDCl_3$) δ 195.3, 178.0, 146.5, 138.1, 134.0, 129.1, 129.0, 126.2, 77.3, 72.3, 72.1, 65.0, 40.1, 39.1, 27.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{24}NO_4^+$ 330.1700, found 330.1702. **$[\alpha]_D^{20}$** -10.19 (c = 0.71 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IA column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 210 nm, t_{major} = 6.67 min, t_{minor} = 5.40 min, **er = 83: 17**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



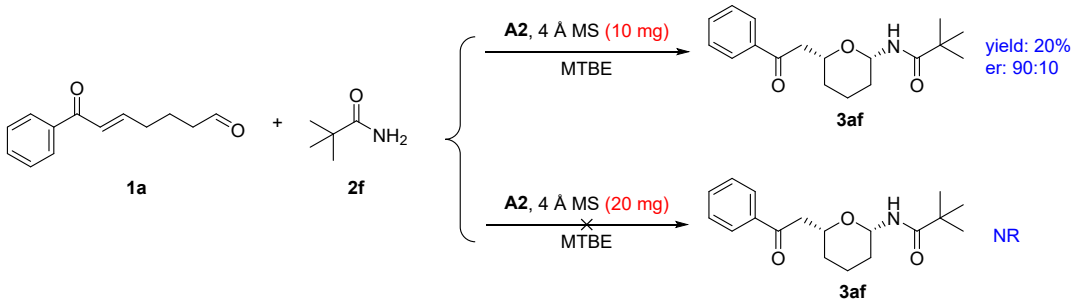
7

7 was obtained as a white solid 12 mg in 37% yield after column chromatography on silica gel (petroleum ether/ethyl acetate = 3/1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 – 7.50 (m, 2H), 7.47 – 7.33 (m, 3H), 6.75 (dd, J = 10.4, 2.8 Hz, 1H), 6.50 (dd, J = 10.4, 1.1 Hz, 1H), 5.90 (d, J = 8.9 Hz, 1H), 5.61 (ddd, J = 10.0, 8.9, 2.8 Hz, 1H), 4.28 (q, J = 3.0 Hz, 1H), 3.97 (dd, J = 11.4, 2.8 Hz, 1H), 3.63 (dd, J = 11.4, 10.0 Hz, 1H), 2.61 – 2.38 (m, 2H), 1.21 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.3, 178.4, 148.1, 137.7, 133.3, 129.0, 128.8, 126.8, 79.5, 75.9, 75.6, 65.3, 40.9, 38.9, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{24}NO_4^+$ 330.1700, found 330.1701. **$[\alpha]_D^{20}$** -98.88 (c = 0.46 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [n-hexane/i-PrOH = 65/35, 1 mL/min], λ = 205 nm, t_{major} = 6.35 min, t_{minor} = 11.27 min, **er = 95:5**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

K. Control experiments:

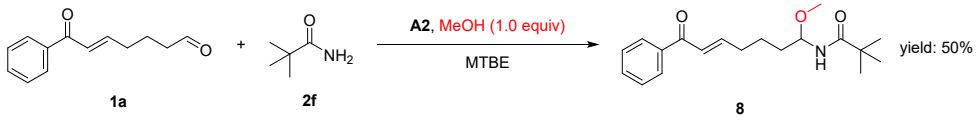
To gain further insight into the reaction mechanism, extensive control experiments were carried out as followed.

(1) The reaction of 1a and 2f with 4 Å MS as additive to identify the importance of H_2O.



To the solution of (*E*)-7-oxo-7-phenylhept-5-enal **1a** (0.1 mmol, 1.0 equiv), amide **2f** (0.12 mmol, 1.2 equiv) in MTBE (0.5 mL) with phosphoric acid **A2** (10 mol%), 4 Å MS (10 mg) was added at 0 °C. After stirred at 0 °C for 7 d, the product **3af** was obtained in 20% yield with 90:10 er. Both yield and stereoselectivity of **3af** reduced obviously (yield: 20% vs 59%, 90:10 vs 95:5 er; contrast to reaction without 4 Å MS). When increase the amount of 4 Å MS to 20 mg, no reaction proceeded even moved to 25 °C.

(2) The reaction of 1a and 2f with MeOH as additive to identify the N-acetylimine intermediate.

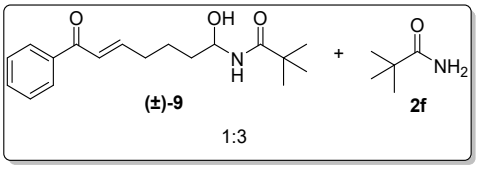


To the solution of (*E*)-7-oxo-7-phenylhept-5-enal **1a** (0.05 mmol, 1.0 equiv) and amide **2f** (0.06 mmol, 1.2 equiv) in MTBE (0.2 mL) with **A2** (10 mol%), MeOH (1.0 equiv) was added at 25 °C. After completion of the reaction (about 24 h), the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1). Acyclic aminal **8** was isolated as a colorless oil (9 mg, 50%) without generation of cyclic **3af**,

which suggested that the formation of N-acyliminium might be involved in the reaction process.

8: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 8.3, 1.4 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.03 (dt, J = 15.4, 6.8 Hz, 1H), 6.89 (dt, J = 15.3, 1.4 Hz, 1H), 5.71 (d, J = 9.6 Hz, 1H), 5.17 (dt, J = 10.0, 6.2 Hz, 1H), 3.32 (s, 3H), 2.40 – 2.30 (m, 2H), 1.74 – 1.56 (m, 4H), 1.23 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.8, 178.8, 148.9, 137.9, 132.7, 128.5, 128.2, 126.4, 80.8, 55.8, 35.2, 32.3, 27.6, 27.4, 23.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{28}NO_3^+$ 318.2064, found 318.2063. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

(3) The reaction of hemiaminal (±)-9 and amide 2f: an attempt to identify the dynamic dynamic resolution and the importance of H_2O.



The racemic hemiaminal **9** was prepared according to the procedure in known literature.[12] The mixture of **9** and **2f** was obtained in the ratio of 1:3 purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1).

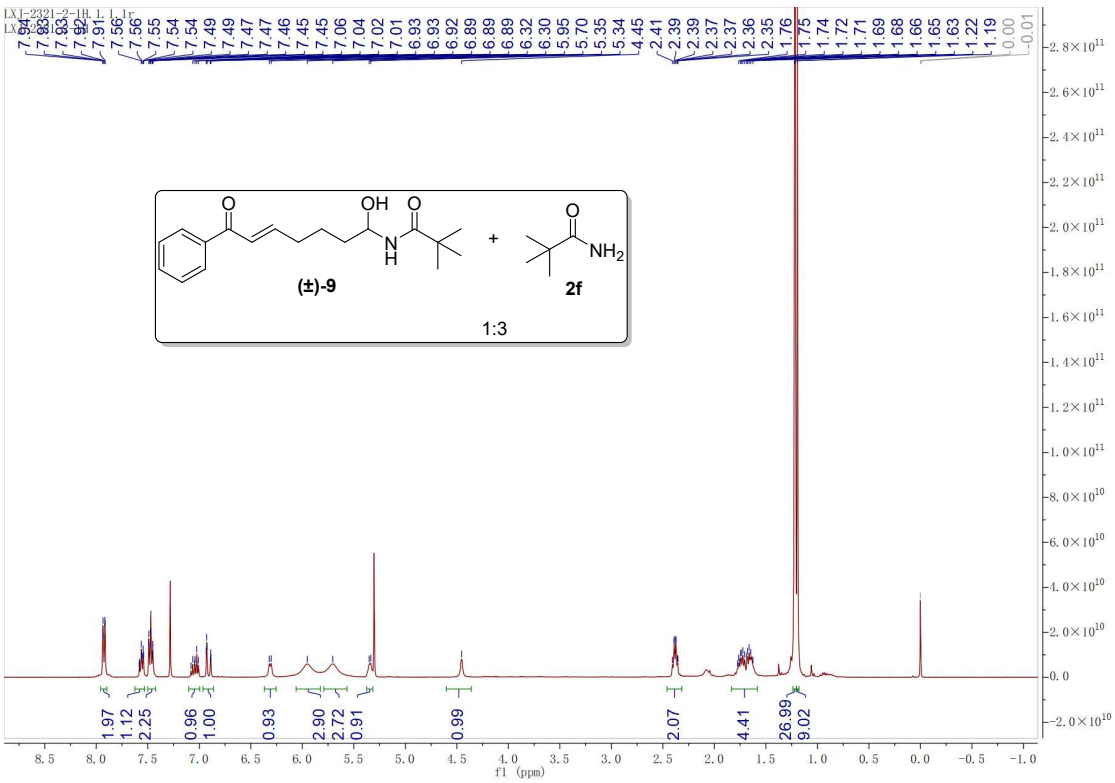
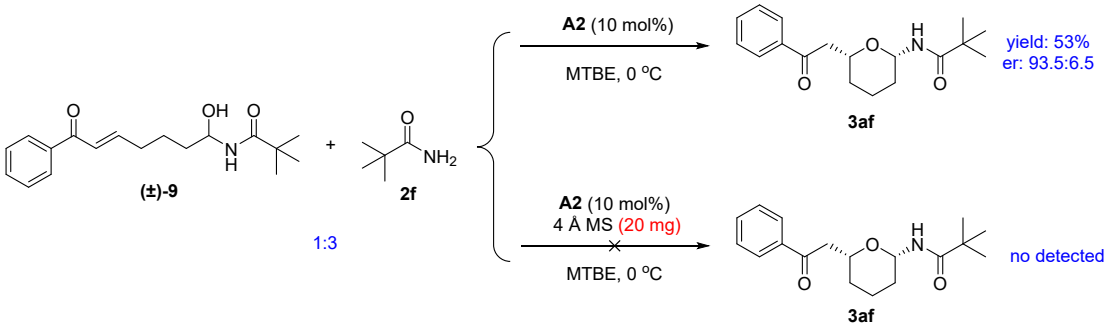
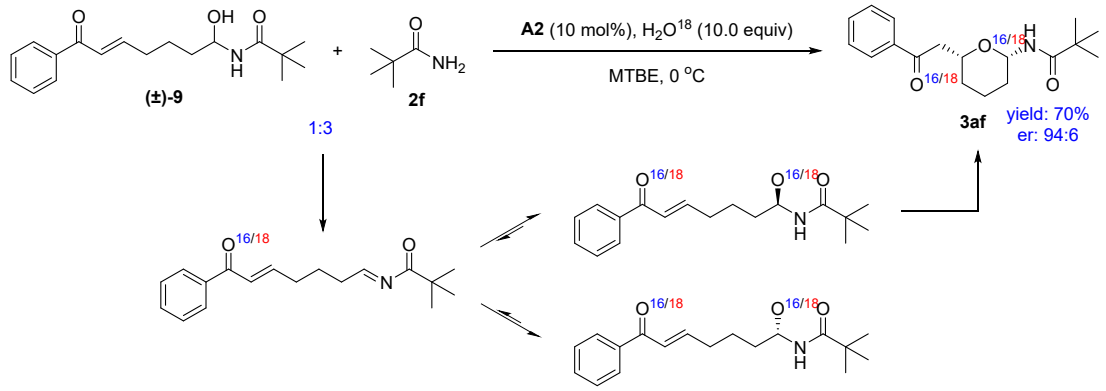


Figure S1. the mixture of **(±)-9** and **2f** in the ratio of 1:3



The solvent of mixture **(±)-9** (0.1 mmol, 1.0 equiv) and **2f** (1:3) in MTBE (0.5 mL) was added **A2** (10 mol%) at 0 °C. After the reaction completion, the reaction was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **3af** in 53% yield with 93.5:6.5 er. Meanwhile, with the addition of 4 Å MS (20 mg), the starting **(±)-9** disappeared, but neither product **3af** or material **(±)-9** was detected. That means hemiaminal **(±)-9** can't return to material **1a**.

(4) The reaction of hemiaminal (±)-9 and amide 2f: an attempt to identify (*R*)-I undergoes rapid conversion to II, and then (*S*)-I is formed.



The solvent of mixture **(±)-9** (0.1 mmol, 1.0 equiv) and **2f** (1:3) in MTBE (0.5 mL) was added H_2O^{18} (10.0 equiv) and **A2** (10 mol%) at 0 °C. After the reaction completion, the reaction was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **3af** and O^{18} labeled **3af** in 70% yield with 94:6 er, which was detected by ^{13}CNMR and LC-MS.

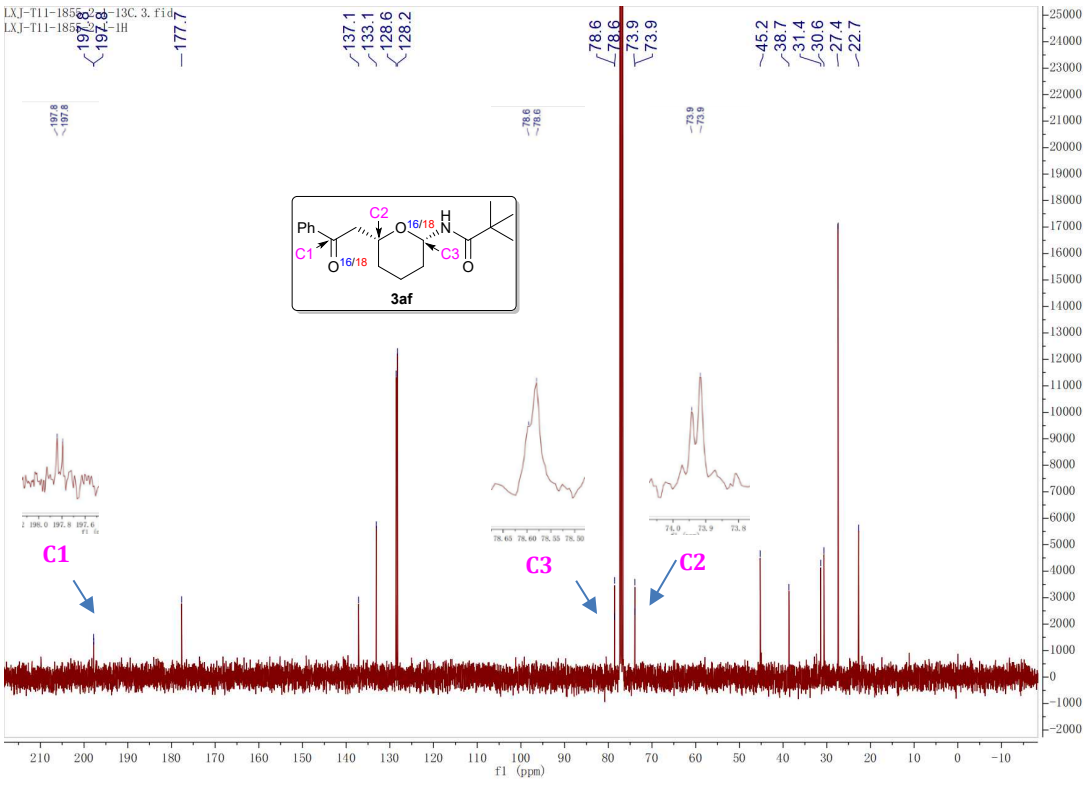


Figure S2. ^{13}C NMR of $O^{16/18}$ labeled **3af** (400 MHz, $CDCl_3$)

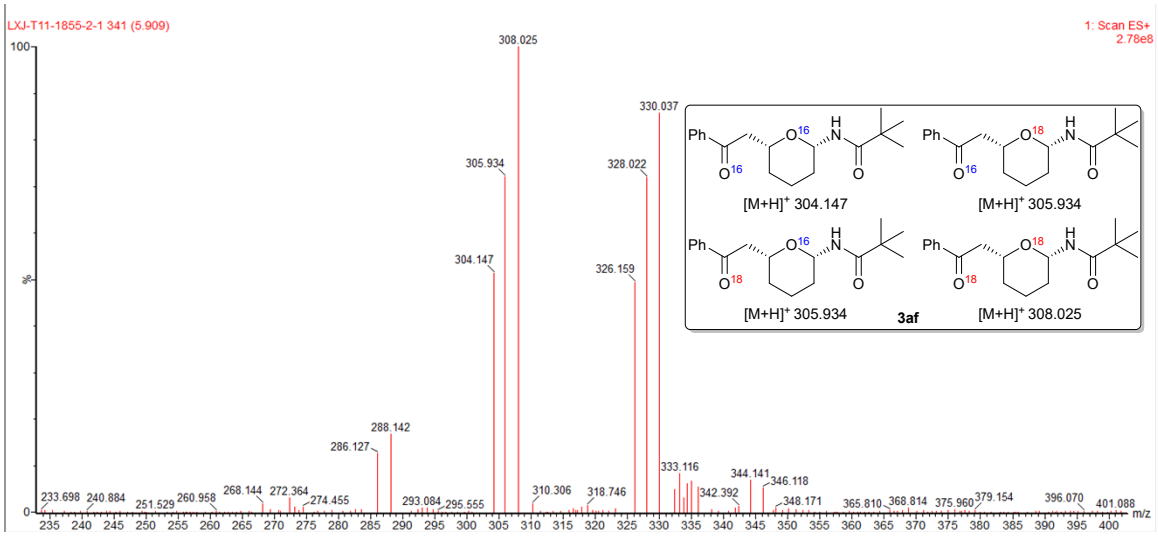
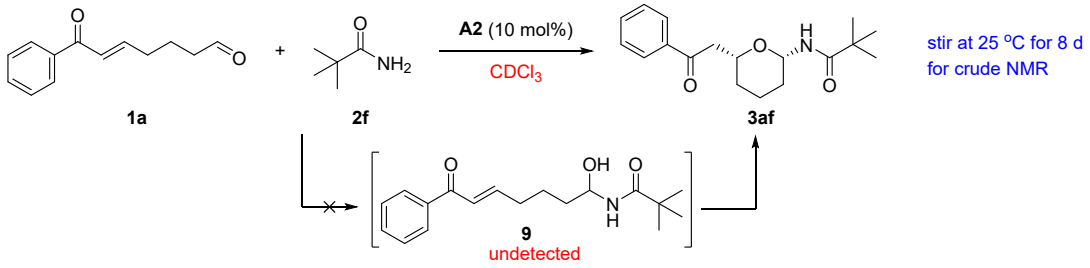


Figure S3. The LC-MS spectrum of $O^{16/18}$ labeled **3af**

(5) ^{1}H NMR of the reaction mixture: an attempt to identify the hemiaminal 9 intermediate.



A 4 mL vial was charged with **1a** (0.1 mmol, 1.0 equiv), amide **2f** (0.12 mmol, 1.2 equiv) and **A2** (10 mol%) in $CDCl_3$ (0.5 mL) at 25 °C. Due to the amount of water in $CDCl_3$ is trace, the reaction became slow. After stirred at 25 °C for 8 d, the reaction solvent was transferred to the nuclear magnetic tube for crude NMR.

According to the crude NMR for the reaction of **1a** and **2f**, N,O-aminal **3af** generated in single configuration, while no hemiaminal **9** was detected, means that the hemiaminal **9** is unstable under acid condition.

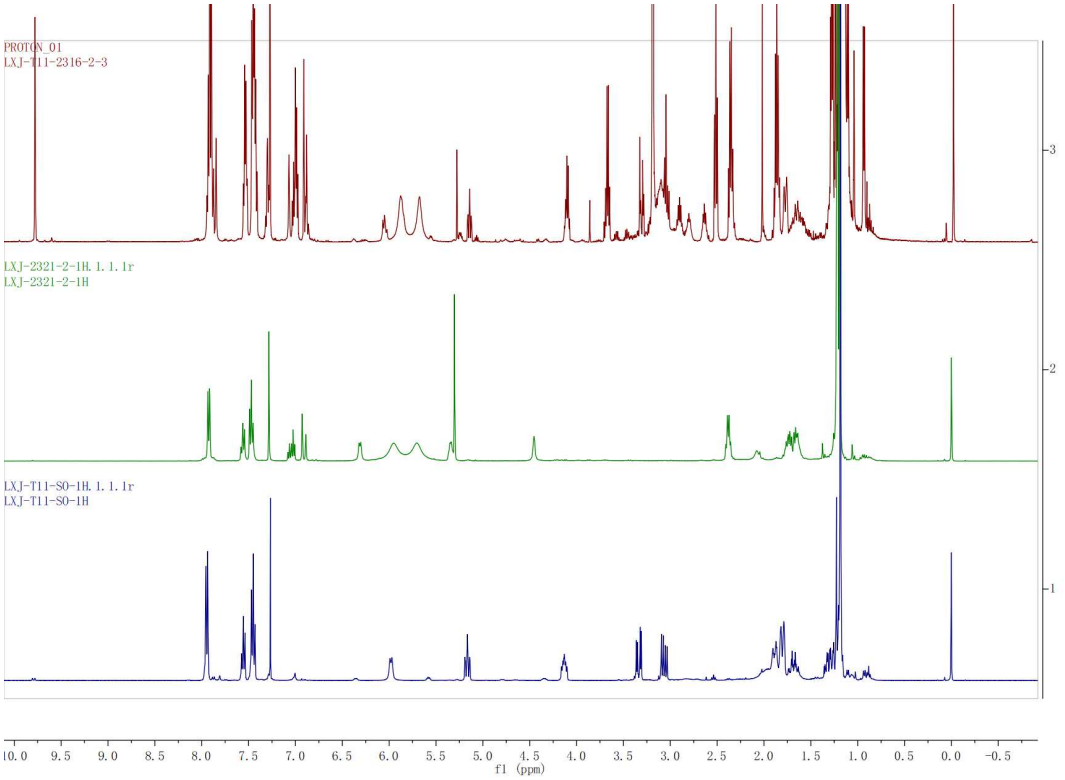
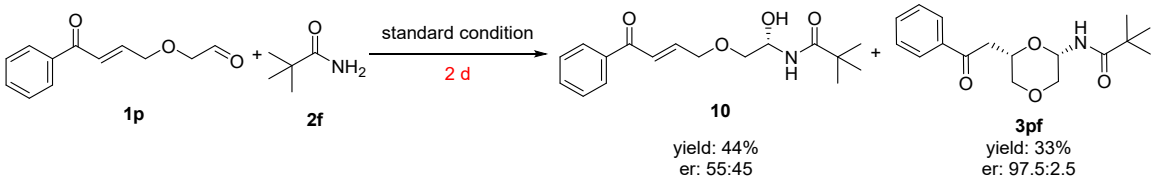


Figure S4. Red: crude NMR of **1a** and **2f** under standard conditions; Green: the ^{1}H NMR of hemiaminal **9** and **2f**; Blue: the ^{1}H NMR of product **3af.**

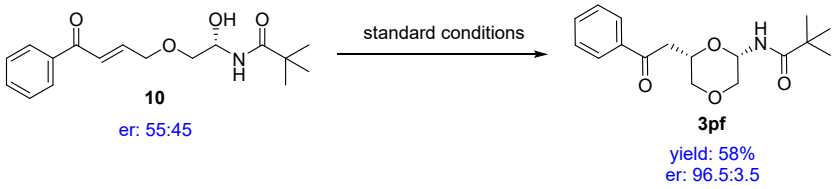
(6) Quenching reaction of 1p and 2f under standard conditions: an attempt to identify the hemiaminal intermediate.



Quench the reaction of **1p** (0.1 mmol, 1.0 equiv) and **2f** (0.12 mmol, 1.2 equiv) after 2 d under standard condition (10 mol% **A2**, 0.5 mL MTBE, 0 °C) by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1 to 2:1) to afford **10** as a colorless oil (12 mg, 40%, 55.5:44.5 er) and **3pf** as a colorless oil (10 mg, 33%, 97.5:2.5 er). If the reaction stirred at 0 °C for 7 d, hemiaminal **10** could be consumed completely and transformed to **3af** (22 mg, 72 %, 97.5:2.5 er).

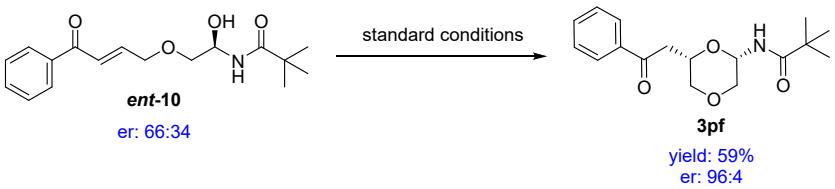
10: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96 (d, J = 7.6 Hz, 2H), 7.60 – 7.55 (m, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.18 (dt, J = 15.5, 2.0 Hz, 1H), 7.03 (dt, J = 15.6, 4.2 Hz, 1H), 6.75 (d, J = 6.8 Hz, 1H), 5.60 (s, 1H), 5.50 (dt, J = 7.5, 3.9 Hz, 1H), 4.43 – 4.33 (m, 2H), 3.77 – 3.65 (m, 2H), 1.22 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.6, 178.0, 136.7, 133.4, 128.7, 128.2, 75.7, 71.8, 69.8, 68.8, 40.8, 38.9, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{17}H_{24}NO_4^+$ 306.1700, found 306.1704. The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak AD-H column [*n*-hexane/*i*-PrOH = 85/15, 1 mL/min], λ = 250 nm, t_{major} = 12.95 min, t_{minor} = 13.66 min, **er = 55:45**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

(7) The reaction of 10 under standard conditions: an attempt to identify the dynamic kinetic resolution



Hemiaminal **10** (12 mg, 0.04 mmol, 1.0 equiv) was redissolved in MTBE (0.16 mL), then **A2** (10 mol%) was added to the solvent at 0 °C. After the reaction finished (**10** was consumed monitored by TLC), the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **3af** as a colorless oil (7 mg, 58%, 96.5:3.5 er). These reactions mean that the hemiaminal **10** was the intermediate with poor enantioselectivity during the tandem reaction.

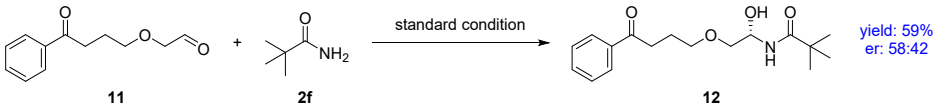
(8) The reaction of *ent*-10 in standard condition.



Ent-**10** was obtained in 50% yield with 66:34 er by recrystallization of *ent*-**10** with 58:42 from ether and *n*-hexane. Resubject hemiaminal *ent*-**10** (*R*:*S* = 66:34) to the standard

reaction condition for about 7 d. Then **3pf** was obtained in 59% with 96:4 er, which means that *ent*-1**0** could turn to **10** through imide **II**, and the reaction process is a DKR.

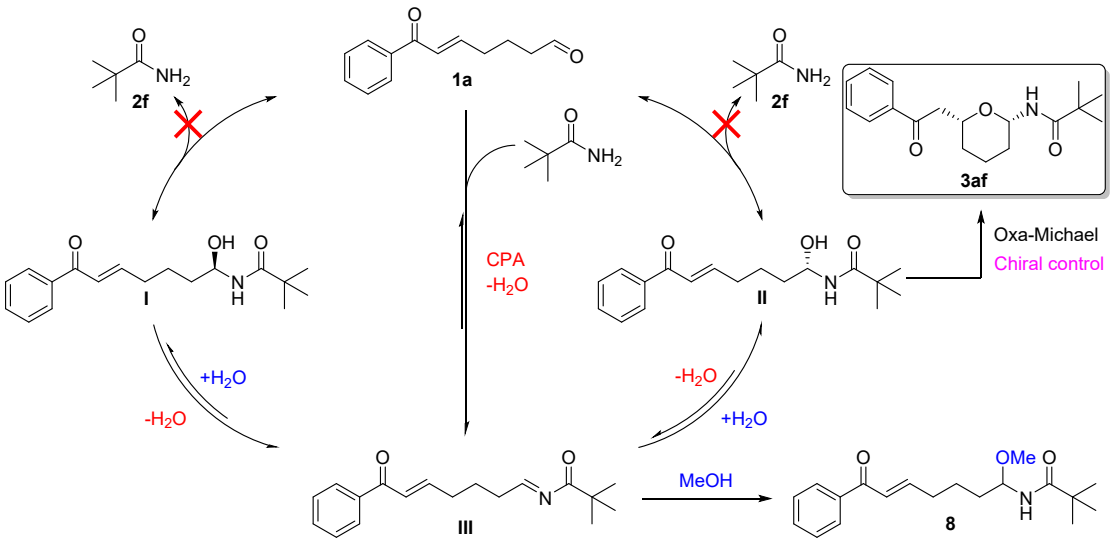
(9) The reaction of 11 and amide 2f under standard conditions to identify the poor stereoselectivity of first step.



11 2f 12

To a solvent of **11** (0.1 mmol, 1.0 equiv), amide **2f** (0.12 mmol, 1.2 equiv) was added under standard condition (10 mol% **A2**, 0.2 mL MTBE, 0 °C). After the reaction completion, the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **12** as a colorless oil (18 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.0 Hz, 2H), 7.61 – 7.53 (m, 1H), 7.46 (t, J = 7.7 Hz, 2H), 6.72 (d, J = 6.7 Hz, 1H), 5.41 (dt, J = 7.3, 4.0 Hz, 1H), 3.85 (s, 1H), 3.66 – 3.54 (m, 4H), 3.08 (t, J = 7.1 Hz, 2H), 2.07 (p, J = 6.7 Hz, 2H), 1.19 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 199.8, 180.1, 136.8, 133.1, 128.6, 128.0, 73.2, 71.8, 70.9, 38.7, 35.0, 27.3, 24.2 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{17}H_{26}NO_4^+$ 308.1856, found 308.1856. The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak AD-H column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 240 nm, t_{major} = 17.41 min, t_{minor} = 22.52 min, **er = 58:42**. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

L. The possible mechanism for asymmetric reaction:



Scheme S3. Proposed mechanism

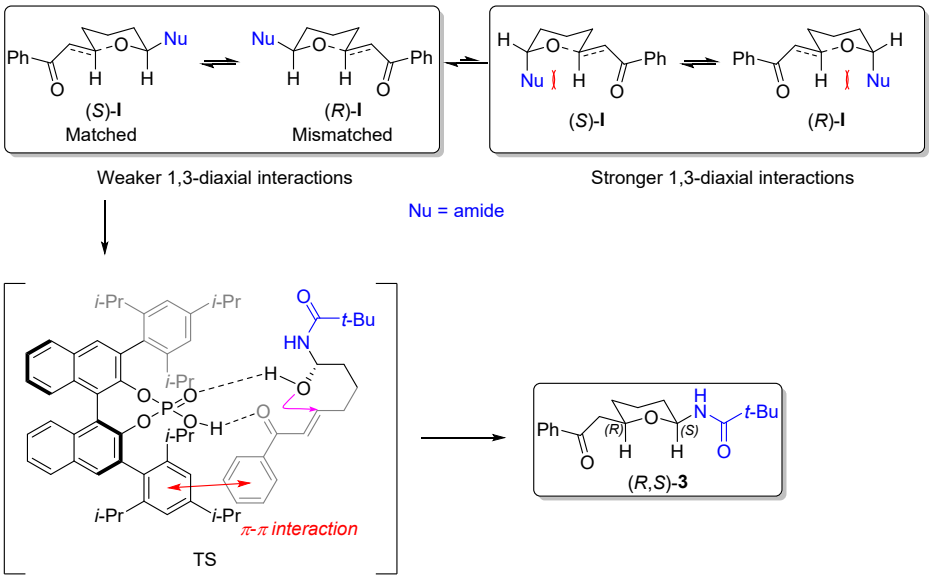


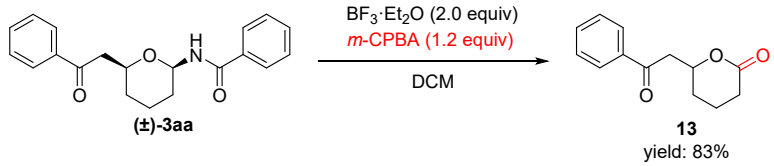
Figure S5. Proposed TS of the reaction

The proposed mechanism of this acid-catalyzed reaction sequence is provided in **Scheme S3**. The reaction of **1a** and **2f** led to hemiaminals **I** and **II** with poor enantioselectivities, which was quite unstable and transformed into N-acetylimine **C** after elimination of H_2O; the formation of **C** can be evidenced by the reaction with MeOH to access aminal **8**. Under the reaction conditions, the water, which was proved to be crucial for this reaction to occur, will attack **III** to regenerate hemiaminal **I**/**II**. Then, hemiaminal **II** could undergo a

subsequent intramolecular oxa-Michael addition from the substrate/catalyst matched chair-like conformation, resulting in **3af** bearing two stereogenic centres with a favorable *cis* configuration. At this stage, hemiaminal **I** was converted into **II** by a dynamic kinetic resolution, where N-acetylimine **III** can be considered as the intermediate. And the transient state of the reaction was shown in **Figure S5**. These two substituents of cycloadducts are bigger groups compared with H group. When they are on the *cis*-orientation, they could be equatorial position in a six-membered oxacycle, enabling weaker 1,3-diaxial interactions.

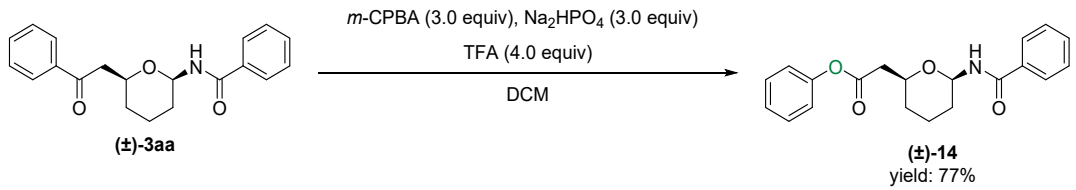
M. Synthetic transformations:

6-(2-oxo-2-phenylethyl)tetrahydro-2*H*-pyran-2-one 13:



To a solvent of **(±)-3aa** (32 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL) with a magnetic rotor was added *m*-CPBA (0.12 mmol, 1.2 equiv) and $BF_3{\cdot}Et_2O$ (0.2 mmol, 2.0 equiv) at 25 °C and stirred until the reaction completed (detected by TLC) for about 9 h. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **13** (18 mg, 83%) as a colorless crystalline solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 2H), 7.63 – 7.56 (m, 1H), 7.52 – 7.45 (m, 2H), 4.99 (dddd, *J* = 10.6, 7.2, 5.3, 3.1 Hz, 1H), 3.56 (dd, *J* = 17.3, 5.3 Hz, 1H), 3.19 (dd, *J* = 17.3, 7.2 Hz, 1H), 2.66 (dtd, *J* = 17.5, 6.4, 1.0 Hz, 1H), 2.50 (dt, *J* = 17.5, 7.9 Hz, 1H), 2.17 (dtdd, *J* = 13.8, 4.7, 3.1, 1.0 Hz, 1H), 1.96 (tdd, *J* = 7.9, 7.1, 5.7 Hz, 2H), 1.65 – 1.59 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.4, 171.4, 136.6, 133.6, 128.8, 128.1, 76.5, 44.3, 29.3, 27.9, 18.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{13}H_{15}O_3^+$ 219.1016, found 219.1017. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

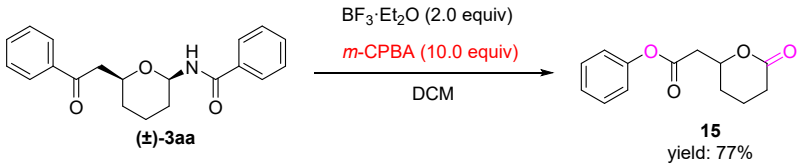
phenyl 2-(6-benzamidotetrahydro-2*H*-pyran-2-yl)acetate (±)-14:



To a solvent of **(±)-3aa** (32 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL) with a magnetic rotor was added *m*-CPBA (0.3mmol, 3.0 equiv), Na_2HPO_4 (0.3 mmol, 3.0 equiv) and TFA (0.4 mmol, 4.0 equiv) at 25 °C and stirred until the reaction completed (detected by TLC) for about 3 d. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **(±)-14** (26 mg, 77%) as a colorless oil. **^{1}H NMR** (400

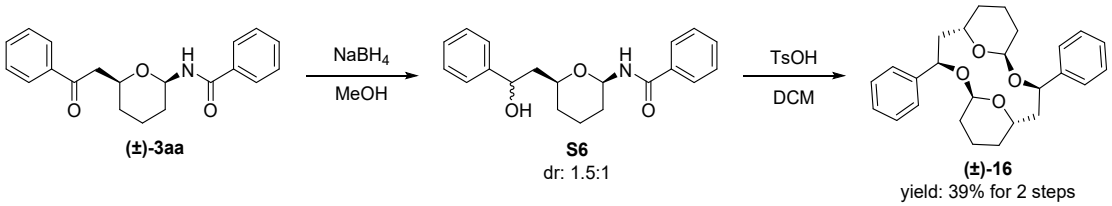
MHz, $CDCl_3$) δ 7.80 (d, J = 8.4 Hz, 2H), 7.54 – 7.47 (m, 1H), 7.43 (dd, J = 8.2, 6.7 Hz, 2H), 7.38 – 7.31 (m, 2H), 7.23 – 7.16 (m, 1H), 7.09 (d, J = 6.6 Hz, 2H), 6.60 (d, J = 9.0 Hz, 1H), 5.45 (ddd, J = 10.8, 9.0, 2.1 Hz, 1H), 4.23 – 4.08 (m, 1H), 2.82 (dd, J = 14.9, 7.3 Hz, 1H), 2.72 (dd, J = 14.9, 6.1 Hz, 1H), 1.96 (ddt, J = 16.6, 11.9, 2.7 Hz, 2H), 1.80 – 1.71 (m, 2H), 1.54 – 1.41 (m, 1H), 1.41 – 1.27 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 166.6, 150.7, 134.0, 131.9, 129.4, 128.6, 127.1, 125.9, 121.7, 78.8, 74.0, 41.5, 31.2, 30.3, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{20}H_{22}NO_4^+$ 340.1543, found 340.1550. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

phenyl 2-(6-oxotetrahydro-2*H*-pyran-2-yl)acetate 15:



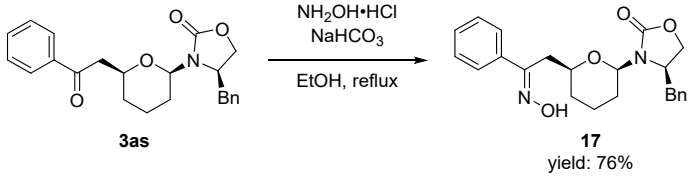
To a solvent of **(±)-3aa** (32 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL) with a magnetic rotor was added *m*-CPBA (1.0mmol, 10.0 equiv) and $BF_3{\cdot}Et_2O$ (0.2 mmol, 2.0 equiv) at 25 °C and stirred until the reaction completed (detected by TLC) for about 36 h. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **15** (18 mg, 77%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.36 (m, 2H), 7.26 – 7.22 (m, 1H), 7.13 – 7.08 (m, 2H), 4.86 (dddd, J = 11.1, 6.8, 6.0, 3.2 Hz, 1H), 3.03 (dd, J = 16.3, 6.9 Hz, 1H), 2.86 (dd, J = 16.3, 6.0 Hz, 1H), 2.65 (dddd, J = 17.8, 6.7, 5.4, 1.1 Hz, 1H), 2.51 (ddd, J = 17.7, 8.7, 7.2 Hz, 1H), 2.15 – 2.07 (m, 1H), 2.05 – 1.88 (m, 2H), 1.78 – 1.63 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 168.4, 150.4, 129.5, 126.1, 121.5, 76.2, 40.6, 29.3, 27.5, 18.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{13}H_{15}O_4^+$ 235.0965, found 235.0964. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

3,11-diphenyl-2,10,17,18-tetraoxatricyclo[11.3.1.15,9]octadecane (±)-16:



To a solvent of **(±)-3aa** (48 mg, 0.15 mmol) in MeOH (1.0 mL) with a magnetic rotor was added $NaBH_4$ (0.23 mmol, 1.5 equiv) at 0 °C and stirred for 0.5 h. After the reaction completed (detected by TLC for about 2 h), the reaction mixture was extracted with ethyl acetate (3 x 3mL) and water (3 x 3mL). Combined the organic layer, dried with Na_2SO_4, filtered and the solvent was removed under vacuum. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford **S6** (46 mg, 94%). To a solvent of **S6** in dry CH_2Cl_2 (0.5 mL) was added TsOH (4.0 equiv) at 25 °C. After the reaction completed (detected by TLC), the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 25:1) to afford **(±)-16** (12 mg, 39% for 2 steps) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 8H), 7.28 – 7.22 (m, 2H), 5.18 (dd, *J* = 11.5, 1.8 Hz, 2H), 4.77 (d, *J* = 3.7 Hz, 2H), 4.50 (tt, *J* = 11.4, 1.9 Hz, 2H), 2.04 – 1.88 (m, 2H), 1.82 (ddd, *J* = 14.5, 11.5, 1.5 Hz, 2H), 1.75 – 1.55 (m, 10H), 1.38 – 1.24 (m, 2H). ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.8, 128.3, 127.1, 126.5, 95.5, 74.1, 66.3, 45.3, 31.3, 30.0, 19.2 ppm. **HRMS**: $[M+Na]^+$ *calcd*. For $C_{26}H_{32}NaO_4^+$ 431.2193, found 431.2180. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

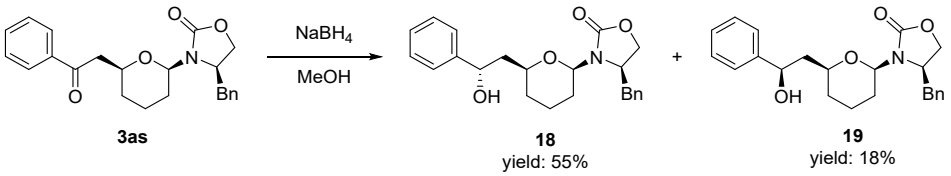
(*R*)-4-benzyl-3-((2*R*,6*S*)-6-((*E*)-2-(hydroxyimino)-2-phenylethyl)tetrahydro-2*H*-pyran-2-yl)oxazolidin-2-one 17:



To a solvent of **3as** (20 mg, 0.05 mmol) in EtOH (0.5 mL) with a magnetic rotor was added $NaHCO_3$ (0.075 mmol, 1.5 equiv) and $NH_2OH{\cdot}HCl$ (0.075 mmol, 1.5 equiv) at room

temperature. Then the reaction stirred at 80 °C for 12 h. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford **17** (15 mg, 76%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.66 – 7.60 (m, 2H), 7.35 – 7.27 (m, 5H), 7.26 – 7.21 (m, 1H), 7.13 – 7.08 (m, 2H), 4.98 (dd, *J* = 10.4, 2.9 Hz, 1H), 4.08 – 3.97 (m, 2H), 3.97 – 3.87 (m, 2H), 3.20 (dd, *J* = 14.1, 3.5 Hz, 1H), 3.14 (dd, *J* = 13.3, 5.8 Hz, 1H), 3.02 (dd, *J* = 13.3, 7.1 Hz, 1H), 2.44 (dd, *J* = 14.1, 9.7 Hz, 1H), 2.01 – 1.91 (m, 1H), 1.81 – 1.66 (m, 3H), 1.59 (dt, *J* = 13.0, 4.1 Hz, 1H), 1.36 – 1.26 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.1, 136.4, 136.3, 129.2, 129.1, 128.8, 128.4, 127.0, 126.7, 82.7, 75.4, 66.7, 54.4, 39.8, 32.8, 30.6, 28.4, 22.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{23}H_{27}N_2O_4^+$ 395.1965, found 395.1976. **$[\alpha]_D^{20}$** -12.75 (*c* = 0.54 in $CHCl_3$). The diastereomeric ratio was determined by NMR ***dr* >20:1**.

(*R*)-4-benzyl-3-((2*R*,6*S*)-6-((*S*)-2-hydroxy-2-phenylethyl)tetrahydro-2*H*-pyran-2-yl)oxazolidin-2-one 18 and (*R*)-4-benzyl-3-((2*R*,6*S*)-6-((*R*)-2-hydroxy-2-phenylethyl)tetrahydro-2*H*-pyran-2-yl)oxazolidin-2-one 19:

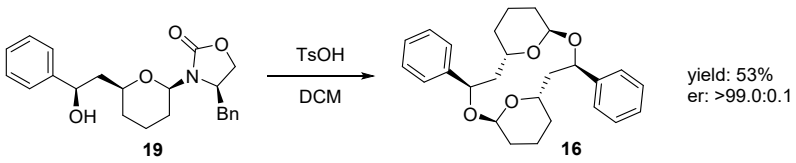


To a solvent of **3as** (76 mg, 0.2 mmol) in MeOH (1.0 mL) with a magnetic rotor was added $NaBH_4$ (0.3 mmol, 1.5 equiv) at 0 °C and stirred for 1 h. After the reaction completed (detected by TLC), the reaction mixture was extracted with ethyl acetate (3 x 3mL) and water (3 x 3mL). Combined the organic layer, dried with Na_2SO_4, filtered and the solvent was removed under vacuum. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford **18** (42 mg, 55%) as a colorless oil and **19** (14 mg, 18%) as a colorless oil for NMR.

18: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 4H), 7.27 (t, *J* = 6.6 Hz, 2H), 7.21 (d, *J* = 7.6 Hz, 2H), 5.13 (dd, *J* = 10.5, 2.8 Hz, 1H), 4.99 (dd, *J* = 8.8, 4.2 Hz, 1H), 4.19 – 4.02 (m, 3H), 3.79 – 3.68 (m, 1H), 3.47 (dd, *J* = 14.0, 3.5 Hz, 1H), 3.40 (s, 1H),

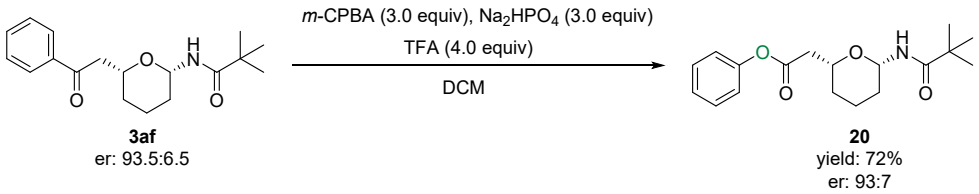
2.82 – 2.66 (m, 1H), 2.08 – 1.94 (m, 2H), 1.80 (tq, *J* = 9.3, 2.7 Hz, 3H), 1.66 (dt, *J* = 12.9, 4.0 Hz, 1H), 1.62 – 1.54 (m, 1H), 1.34 – 1.23 (m, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 144.3, 136.1, 129.2, 129.0, 128.4, 127.4, 127.2, 125.9, 82.5, 78.1, 73.4, 66.8, 54.6, 45.3, 40.4, 31.0, 28.3, 22.8 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{23}H_{28}NO_4^+$ 382.2013, found 382.2017. **$[\alpha]_D^{20}$** -26.84 (*c* = 1.83 in $CHCl_3$). The diastereomeric ratio was determined by NMR ***dr* >20:1**.

19: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 6H), 7.29 – 7.26 (m, 2H), 7.24 – 7.19 (m, 2H), 5.08 (dd, *J* = 9.9, 3.4 Hz, 1H), 5.02 (dd, *J* = 7.6, 3.3 Hz, 1H), 4.12 (qq, *J* = 7.7, 3.6 Hz, 3H), 3.76 (ddt, *J* = 11.5, 9.0, 2.6 Hz, 1H), 3.42 (dd, *J* = 14.3, 3.3 Hz, 1H), 2.87 – 2.60 (m, 1H), 1.99 (dt, *J* = 14.6, 4.7 Hz, 2H), 1.90 (ddd, *J* = 14.4, 7.6, 2.9 Hz, 1H), 1.85 – 1.75 (m, 2H), 1.67 (ddd, *J* = 21.0, 10.4, 4.2 Hz, 2H), 1.58 – 1.51 (m, 1H), 1.35 (ddd, *J* = 13.3, 11.4, 4.2 Hz, 1H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.3, 144.6, 136.1, 129.2, 128.9, 128.4, 127.1, 127.1, 125.7, 82.5, 75.4, 71.2, 66.7, 54.6, 44.4, 40.2, 30.7, 28.4, 22.9 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{23}H_{28}NO_4^+$ 382.2013, found 382.2015. **$[\alpha]_D^{20}$** 16.06 (*c* = 0.58 in $CHCl_3$). The diastereomeric ratio was determined by NMR ***dr* >20:1**.



To a solvent of **19** (14 mg, 1.0 equiv) in dry CH_2Cl_2 (0.5 mL) was added TsOH (4.0 equiv) at 25 °C. After the reaction completed (detected by TLC for 4 h), the mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 25:1) to afford **16** (4 mg, 53%) as a white solid. **$[\alpha]_D^{20}$** 135.18 (*c* = 0.42 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 90/10, 1 mL/min], λ = 210 nm, t_{major} = 3.60 min, t_{minor} = 4.22 min, **er**: **>99.9:0.1**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

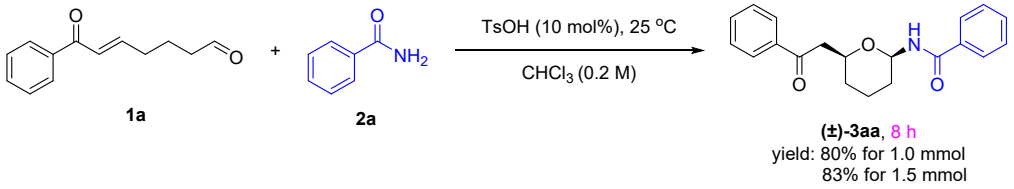
phenyl 2-((2*R*,6*S*)-6-pivalamidotetrahydro-2*H*-pyran-2-yl)acetate 20:



To a solvent of **3af** (30 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL) with a magnetic rotor was added *m*-CPBA (0.3mmol, 3.0 equiv), Na_2HPO_4 (0.3 mmol, 3.0 equiv) and TFA (0.4 mmol, 4.0 equiv) at 25 °C and stirred until the reaction completed (detected by TLC) for about 3 d. The mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **20** (23 mg, 72%) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (t, J = 7.9 Hz, 2H), 7.24 – 7.18 (m, 1H), 7.07 (d, J = 7.5 Hz, 2H), 6.04 (d, J = 8.8 Hz, 1H), 5.23 (ddd, J = 11.1, 8.9, 2.3 Hz, 1H), 4.10 (dddd, J = 11.3, 7.8, 6.0, 2.0 Hz, 1H), 2.79 (dd, J = 14.7, 7.5 Hz, 1H), 2.70 (dd, J = 14.7, 6.1 Hz, 1H), 1.94 (ddd, J = 11.0, 4.6, 2.1 Hz, 1H), 1.85 – 1.76 (m, 2H), 1.69 (td, J = 9.2, 4.6 Hz, 1H), 1.39 – 1.26 (m, 2H), 1.20 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.8, 169.6, 150.7, 129.4, 125.8, 121.7, 78.5, 74.0, 41.6, 38.7, 31.0, 30.3, 27.4, 22.7 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{18}H_{26}NO_4^+$ 320.1856, found 320.1866. **$[\alpha]_D^{20}$** 10.55 (c = 1.96 in $CHCl_3$). The enantiomeric ratio was determined by HPLC analysis on Daicel Chiralpak IC column [*n*-hexane/*i*-PrOH = 70/30, 1 mL/min], λ = 205 nm, t_{major} = 11.67 min, t_{minor} = 11.08 min, **er = 93:7**. The diastereomeric ratio was determined by ^{1}H NMR, ***dr* >20:1**.

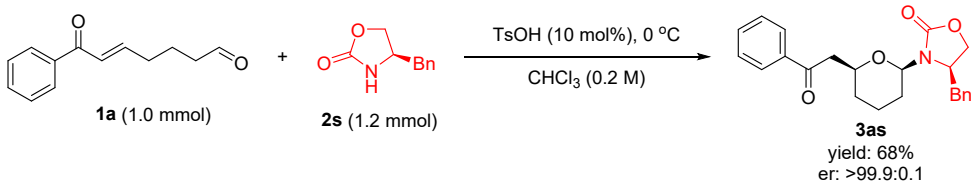
N. Large scale reaction:

N1: Large scale for the synthesis of racemic 3aa:



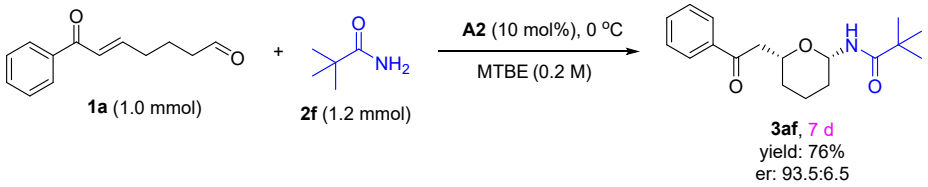
A glass vial equipped with a magnetic stirring bar was charged with (*E*)-7-oxo-7-phenylhept-5-enal **1a** (1.0 mmol or 1.5 mmol, 1.0 equiv), TsOH (0.1 equiv) and amide **2a** (1.2 equiv) in $CHCl_3$ (0.2 M) and the resultant solution was stirred at 25 °C until the material **1a** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **(±)-3aa** as a white solid (258 mg, 80% for 1.0 mmol; 402 mg, 83% for 1.5 mmol).

N2: Large scale for the synthesis of 3as:



A glass vial equipped with a magnetic stirring bar was charged with (*E*)-7-oxo-7-phenylhept-5-enal **1a** (1.0 mmol, 1.0 equiv), TsOH (0.1 equiv) and amide **2s** (1.2 equiv) in $CHCl_3$ (5 mL) and the resultant solution was stirred at 0 °C until the material **1a** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford **3as** as a colorless oil (258 mg, 68%, >99.9:0.1 er).

N3: Large scale for the synthesis of 3af:

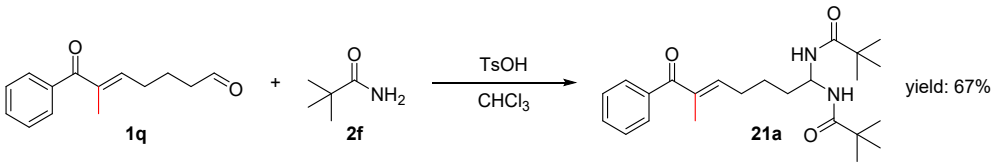


A glass vial equipped with a magnetic stirring bar was charged with (*E*)-7-oxo-7-phenylhept-5-enal **1a** (1.0 mmol, 1.0 equiv), **A2** (10 mol%.) and amide **2f** (1.2 equiv) in $CHCl_3$ (5 mL) and the resultant solution was stirred at 0 °C until the material **1a** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **3af** as a colorless oil (230 mg, 76%, 93.5:6.5 er).

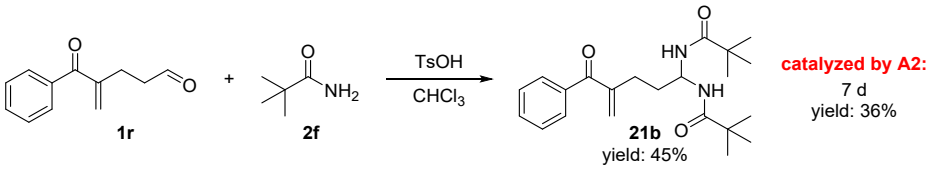
O. Failed substrates:

O1. Diamides compound:

Diamides compound was obtained when aldehyde **1q**-**1u** was used as material to react with amide **2f** catalyzed by TsOH (10 mol%) or **A2**(10 mol%).

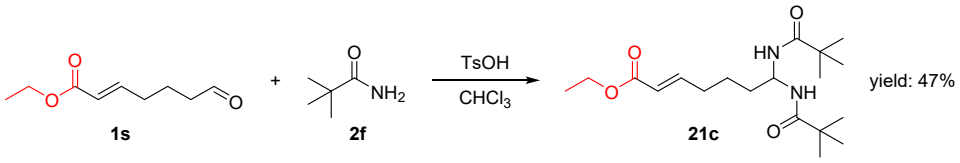


A glass vial equipped with a magnetic stirring bar was charged with **1q** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1q** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **21a** (16 mg, 67%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (dt, J = 6.9, 1.5 Hz, 2H), 7.55 – 7.46 (m, 1H), 7.45 – 7.37 (m, 2H), 6.97 (d, J = 7.7 Hz, 2H), 6.23 (tq, J = 7.3, 1.3 Hz, 1H), 5.05 (p, J = 7.6 Hz, 1H), 2.29 (q, J = 7.4 Hz, 2H), 1.99 (dd, J = 8.8, 6.9 Hz, 5H), 1.42 (tt, J = 10.3, 6.5 Hz, 2H), 1.15 (s, 18H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.9, 179.2, 145.4, 138.6, 137.0, 131.4, 129.3, 128.1, 58.5, 38.8, 33.1, 28.5, 27.3, 25.3, 12.6 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{24}H_{37}N_2O_3^+$ 401.2799, found 401.2791. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

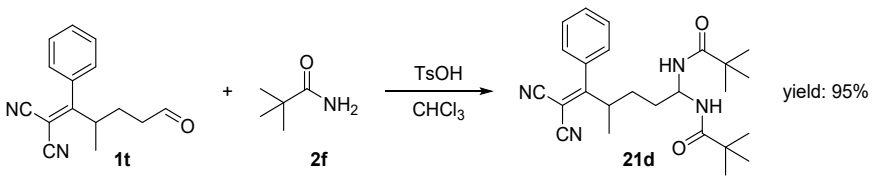


A glass vial equipped with a magnetic stirring bar was charged with **1r** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1r** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford **21b** (10 mg, 45%) as a white solid. The product **32b** also could be obtained (8 mg, 36%) catalyzed by **A2** (10 mol%)

for about 7 d. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 – 7.72 (m, 2H), 7.57 – 7.52 (m, 1H), 7.45 (t, J = 7.8 Hz, 2H), 7.05 (d, J = 7.5 Hz, 2H), 5.95 (d, J = 1.1 Hz, 1H), 5.72 (s, 1H), 5.13 (p, J = 7.5 Hz, 1H), 2.48 (t, J = 7.5 Hz, 2H), 2.17 (q, J = 7.5 Hz, 2H), 1.19 (s, 18H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.5, 179.2, 146.6, 137.6, 132.3, 129.6, 128.3, 127.8, 58.2, 38.9, 32.5, 28.5, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{22}H_{33}N_2O_3^+$ 373.2486, found 373.2488. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

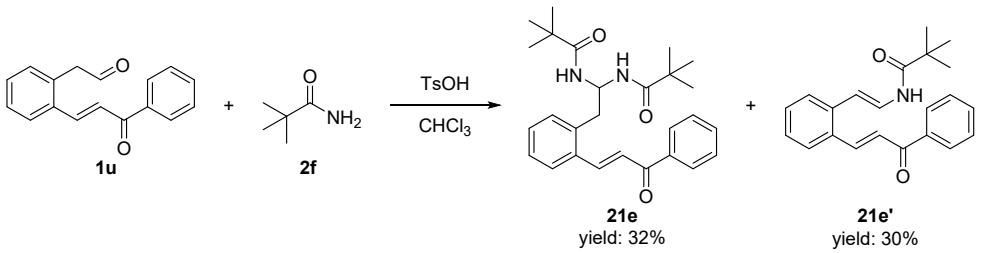


A glass vial equipped with a magnetic stirring bar was charged with **1s** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1s** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **21c** (10 mg, 47%) as a white solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.90 (p, J = 7.7, 6.9 Hz, 3H), 5.80 (d, J = 15.7 Hz, 1H), 5.05 (p, J = 7.7 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 2.21 (q, J = 7.4 Hz, 2H), 1.97 (q, J = 7.8 Hz, 2H), 1.45 (p, J = 7.5 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H), 1.15 (t, J = 1.3 Hz, 18H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.2, 166.6, 148.3, 121.8, 60.2, 58.4, 38.8, 32.8, 31.5, 27.3, 24.7, 14.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{19}H_{35}N_2O_4^+$ 355.2591, found 355.2591. The diastereomeric ratio was determined by NMR ***dr* >20:1**.



A glass vial equipped with a magnetic stirring bar was charged with **1t** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1t** disappeared. After

completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2.5:1) to afford **21d** (24 mg, 95%) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.43 (m, 3H), 7.23 – 7.15 (m, 2H), 6.93 (dd, *J* = 7.7, 2.4 Hz, 2H), 5.04 (p, *J* = 7.6 Hz, 1H), 3.28 (dt, *J* = 7.7, 6.7 Hz, 1H), 2.14 – 1.92 (m, 2H), 1.60 – 1.36 (m, 2H), 1.20 (d, *J* = 6.9 Hz, 3H), 1.14 (s, 9H), 1.13 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.1, 179.4, 133.9, 130.7, 129.0, 126.9, 111.9, 111.8, 87.7, 58.2, 41.4, 38.8, 31.4, 31.3, 27.3, 18.8 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{25}H_{35}N_4O_2^+$ 423.2755, found 423.2756. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

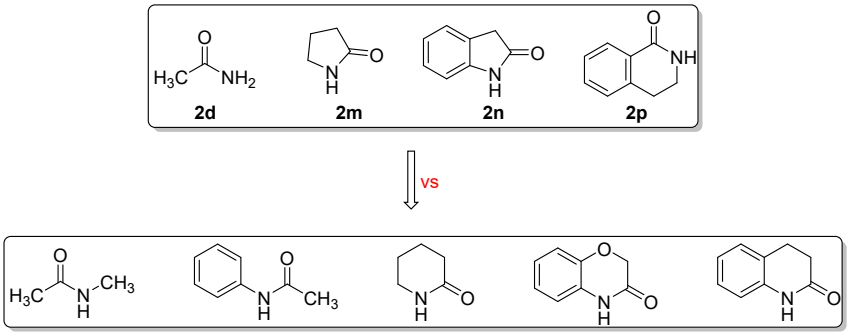


A glass vial equipped with a magnetic stirring bar was charged with **1u** (0.1 mmol, 1.0 equiv), TsOH (1.7 mg, 0.1 equiv) and amide **2f** (0.12 mmol, 1.2 equiv) in $CHCl_3$ (0.5 mL) and the resultant solution was stirred at 25 °C until the material **1u** disappeared. After completion of the reaction, the reaction mixture was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford **21e** (14 mg, 32%) as a white solid and **21e'** (10 mg, 30%) as a yellow solid.

21e: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 15.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.73 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.56 – 7.46 (m, 3H), 7.37 – 7.27 (m, 2H), 7.25 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 2H), 5.30 (p, *J* = 7.6 Hz, 1H), 3.47 (d, *J* = 7.6 Hz, 2H), 1.09 (s, 18H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.3, 179.1, 141.5, 138.1, 137.6, 134.2, 132.9, 131.6, 130.2, 128.7, 128.6, 127.5, 126.8, 124.2, 59.2, 38.8, 36.7, 27.3 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{27}H_{35}N_2O_3^+$ 435.2642, found 435.2648. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

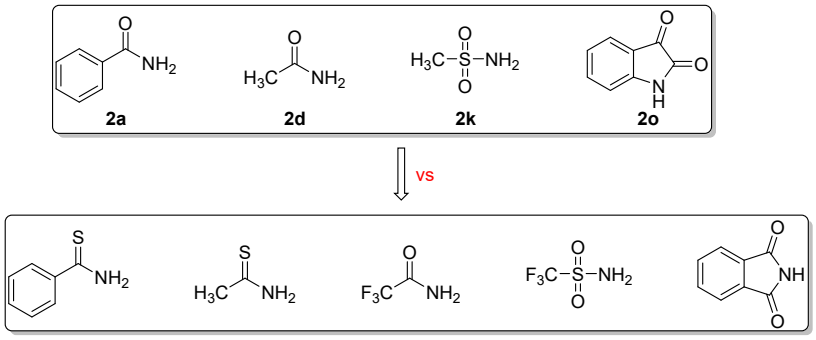
21e': **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (d, J = 15.4 Hz, 1H), 8.07 – 8.02 (m, 2H), 7.67 (dd, J = 7.9, 1.3 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.56 – 7.44 (m, 6H), 7.38 – 7.33 (m, 1H), 7.29 – 7.22 (m, 1H), 6.52 (d, J = 14.3 Hz, 1H), 1.30 (s, 9H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.1, 175.9, 142.3, 137.0, 133.0, 132.3, 130.6, 128.7, 128.5, 126.9, 126.9, 126.1, 125.7, 123.3, 108.9, 38.9, 27.4 ppm. **HRMS**: $[M+H]^+$ *calcd*. For $C_{22}H_{24}NO_2^+$ 334.1802, found 334.1812. The diastereomeric ratio was determined by NMR ***dr* >20:1**.

O2. Amides with no products formed:



Scheme S4. amides with larger steric hindrance

Compared to amides **2d**, **2m**, **2n** and **2p**, the reactions of **1a** and amides with larger steric hindrance all failed, that **1a** disappeared and amides remained without product (**Scheme S4**).

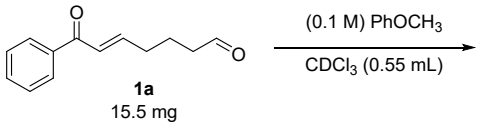


Scheme S5. amides with more acidic N-H

Compared to amides **2a**, **2e**, **2d** and **2s**, the reactions of **1a** and amides with more acidic N-H all failed, that **1a** disappeared and amides remained without product (**Scheme S5**).

P. The stability of 1a in present of A2:

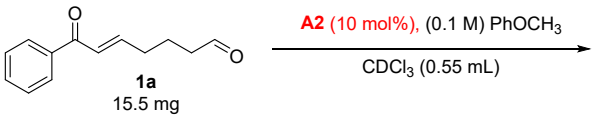
A: 1a in $CDCl_3$ (with 0.1 M $PhOCH_3$ as internal standard)



1a
15.5 mg

A: 1a (15.5 mg) was dissolved in $CDCl_3$ (0.55 mL) containing $PhOCH_3$ (0.1 M) as internal standard. The mixture was used for crude NMR to get the purification of **1a** without **A2** after 12 h, 36 h, 60 h at room temperature.

B: 1a, **A2** (10 mol%) in $CDCl_3$ (with 0.1 M $PhOCH_3$ as internal standard)



1a
15.5 mg

B: To the solution of **1a** (15.5 mg) in $CDCl_3$(0.55 mL) containing $PhOCH_3$ (0.1 M) as internal standard, **A2** (10 mol%) was added. The mixture was used for crude NMR to get the purification of **1a** in present of **A2** after 12 h, 36 h, 60 h at room temperature.

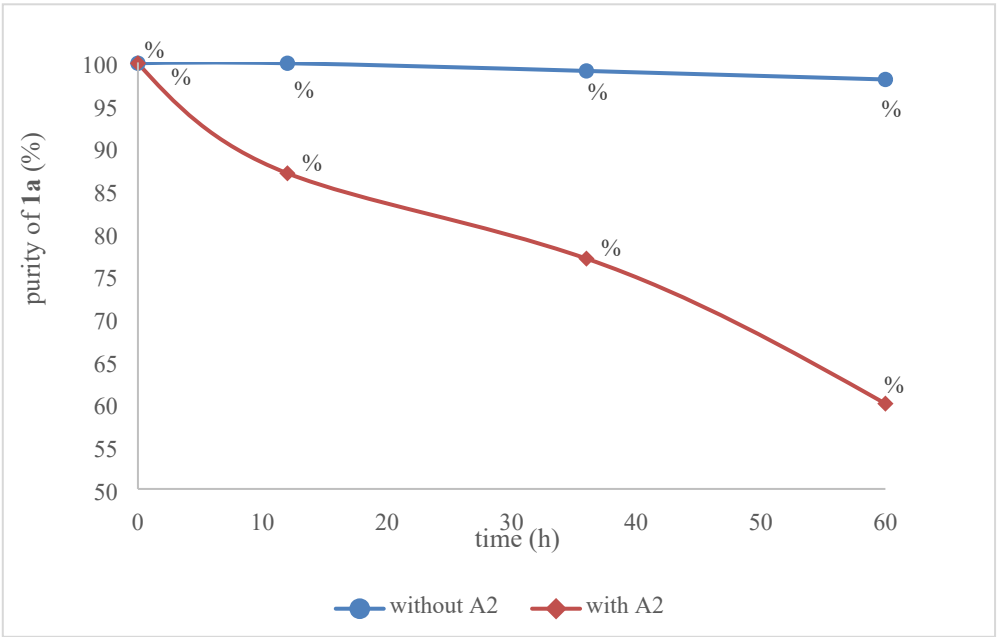
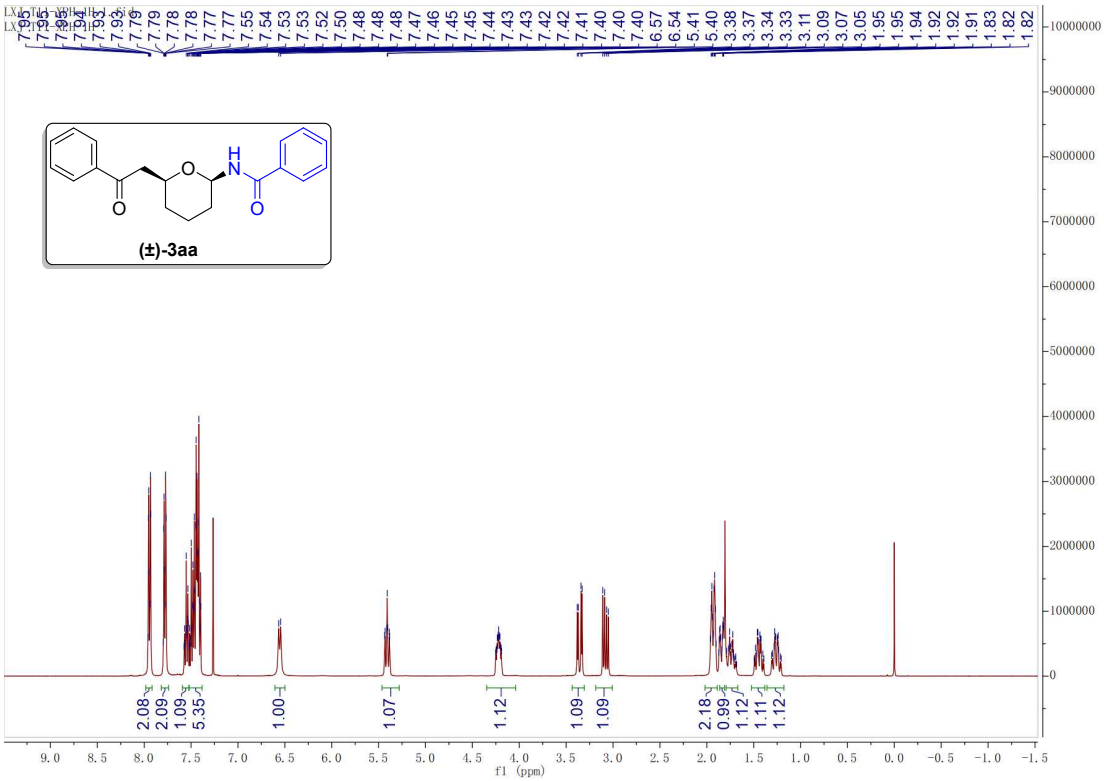


Figure S6. Purity of **1a** vs. time in $CDCl_3$.

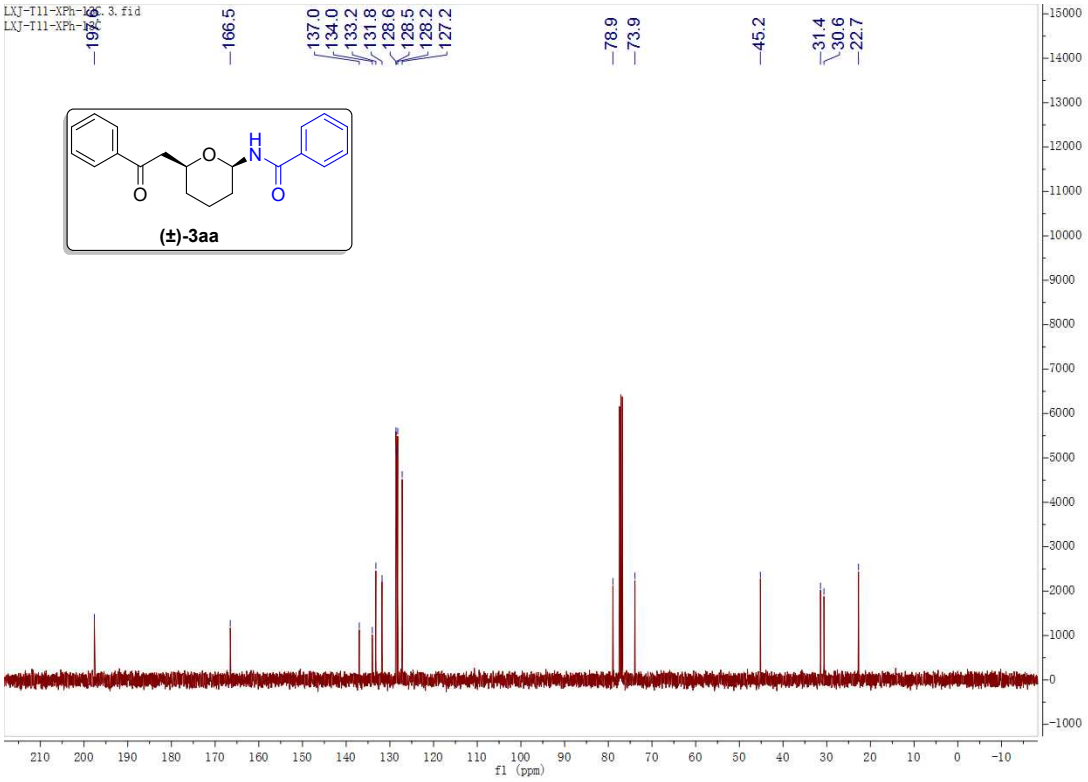
As shown on Figure S6, the purity of **1a** decreased sharply with **A2** means that **1a** is unstable in present of **A2**. Thus the reaction yield of **1** and **2f** is just moderate.

Q. NMR spectra and HPLC traces:

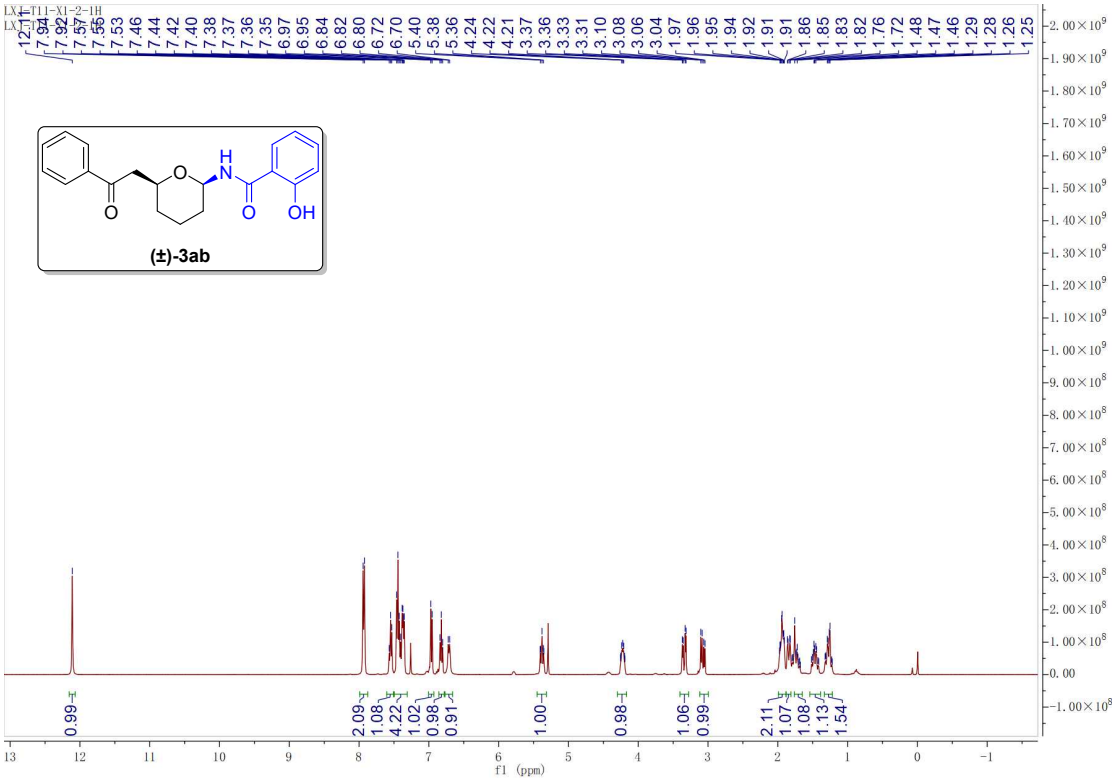
The ^{1}H NMR spectrum of (±)-3aa (400 MHz, $CDCl_3$)



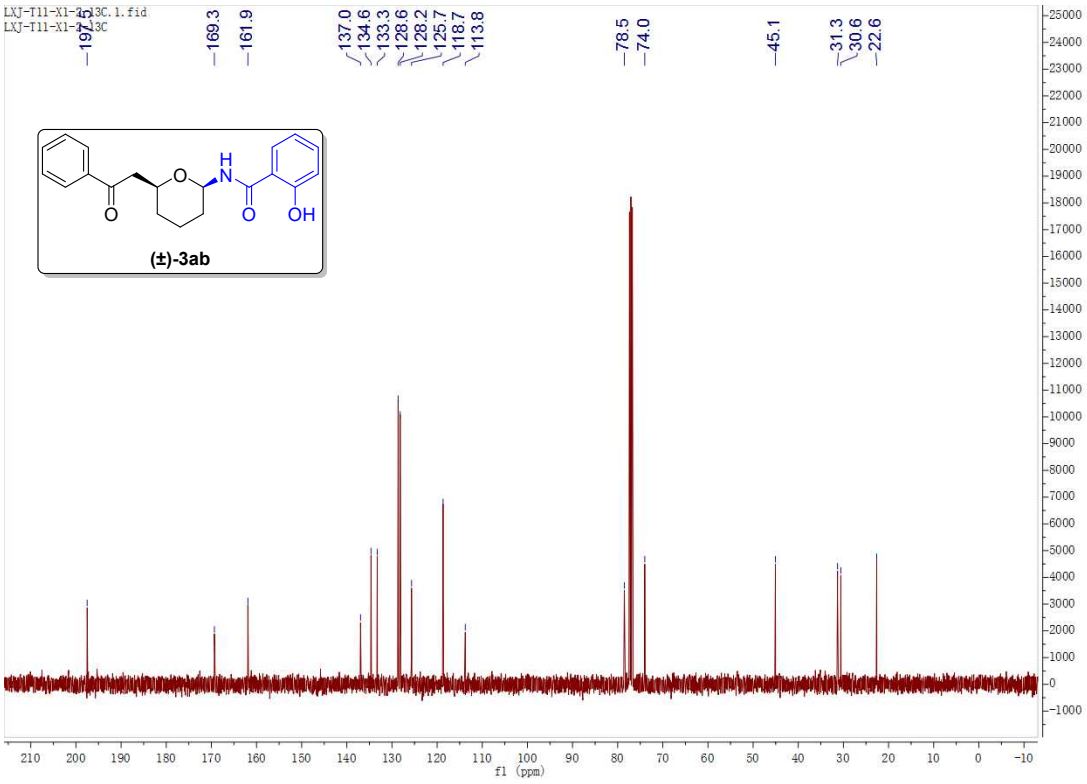
The ^{13}C NMR spectrum of (±)-3aa (101 MHz, $CDCl_3$)



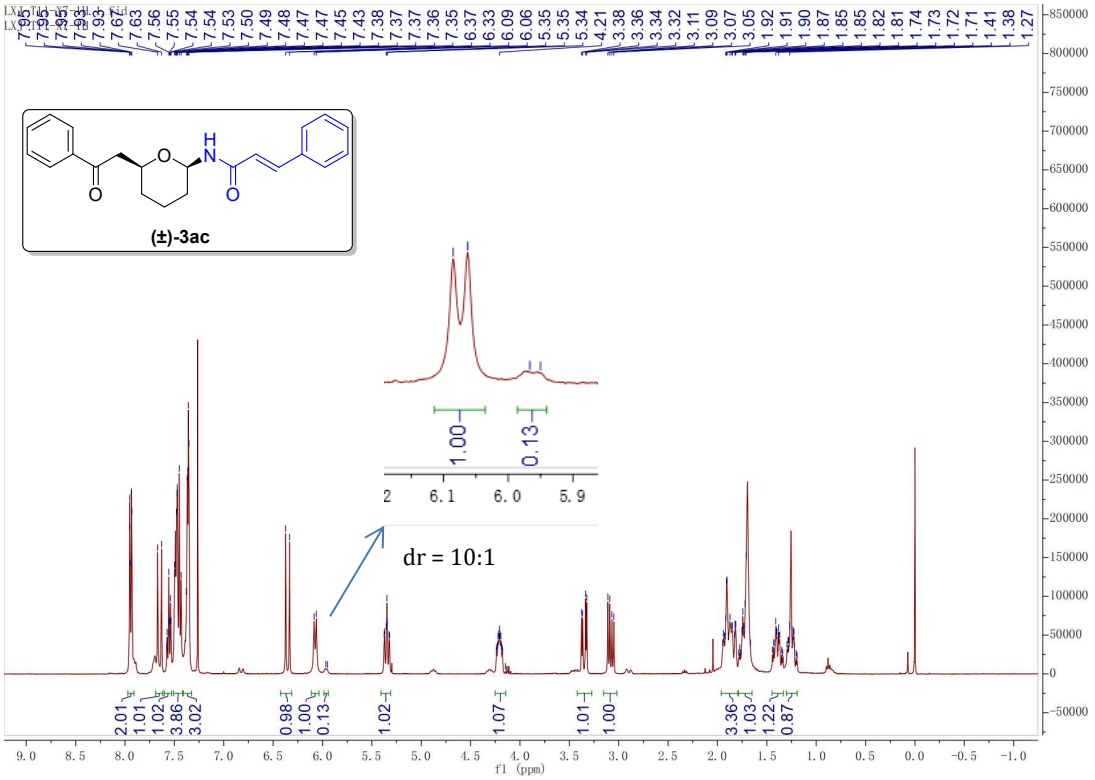
The ^{1}H NMR spectrum of (±)-3ab (400 MHz, $CDCl_3$)



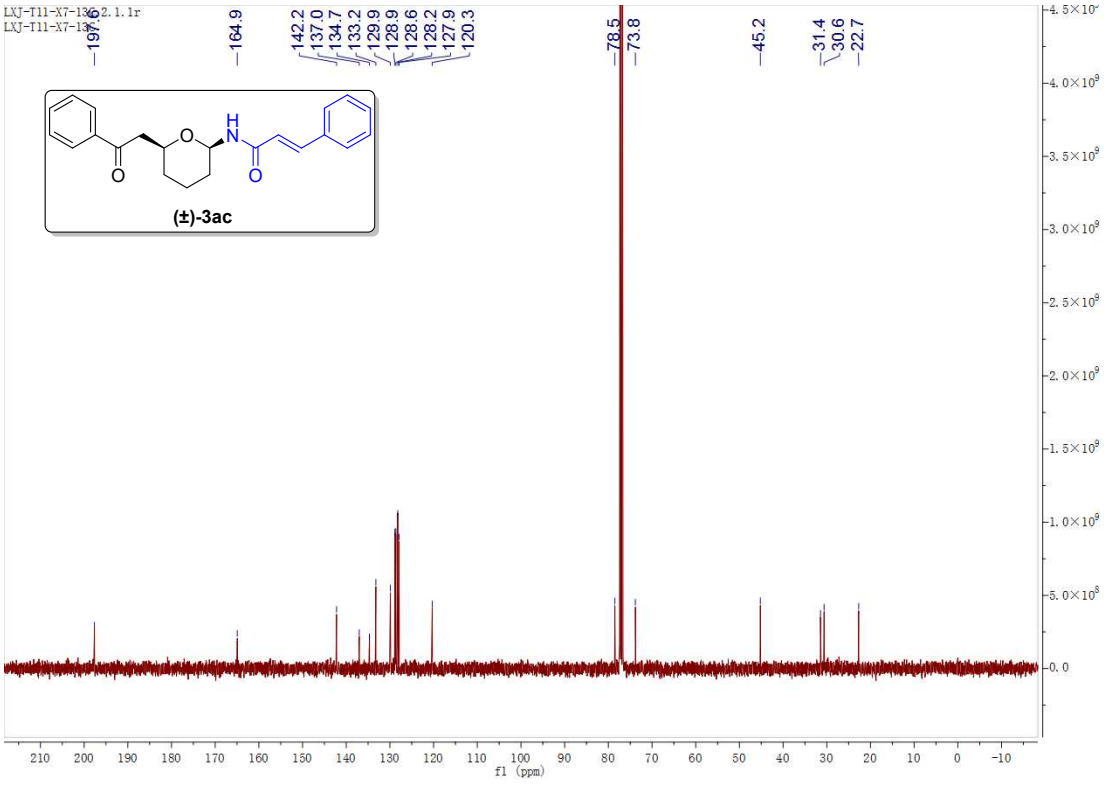
The ^{13}C NMR spectrum of (±)-3ab (101 MHz, $CDCl_3$)



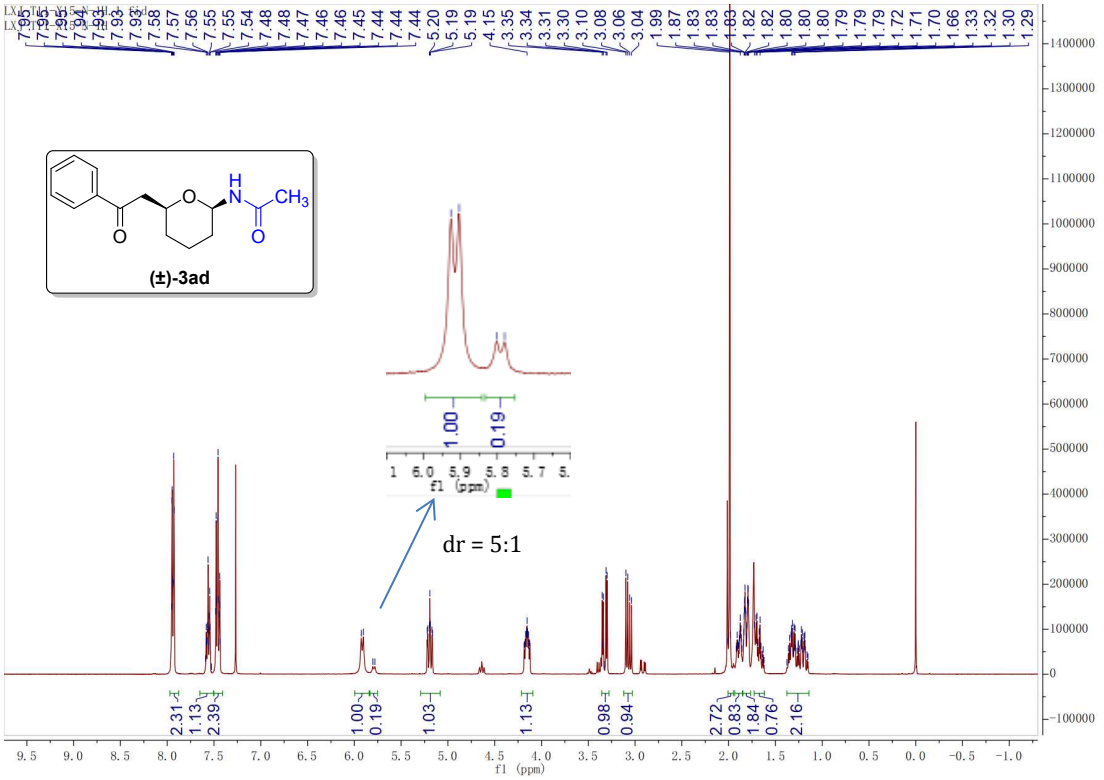
The ^{1}H NMR spectrum of (±)-3ac (400 MHz, $CDCl_3$)



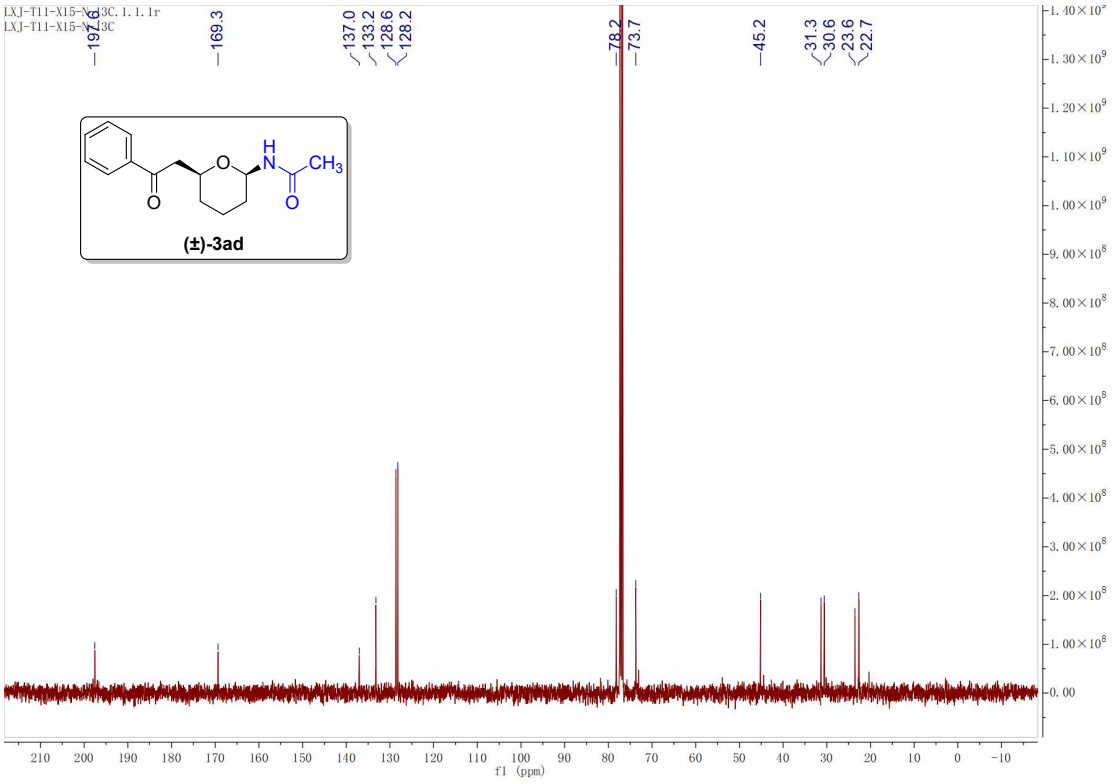
The ^{13}C NMR spectrum of (±)-3ac (101 MHz, $CDCl_3$)



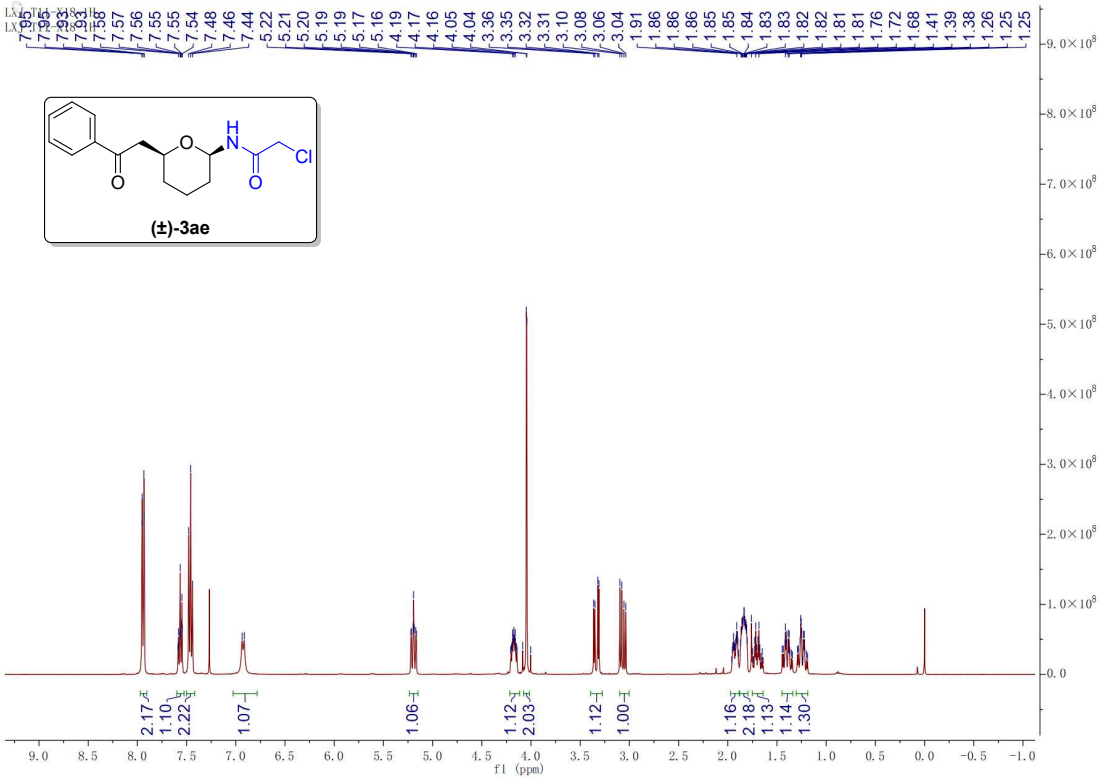
The ^{1}H NMR spectrum of (±)-3ad (400 MHz, $CDCl_3$)



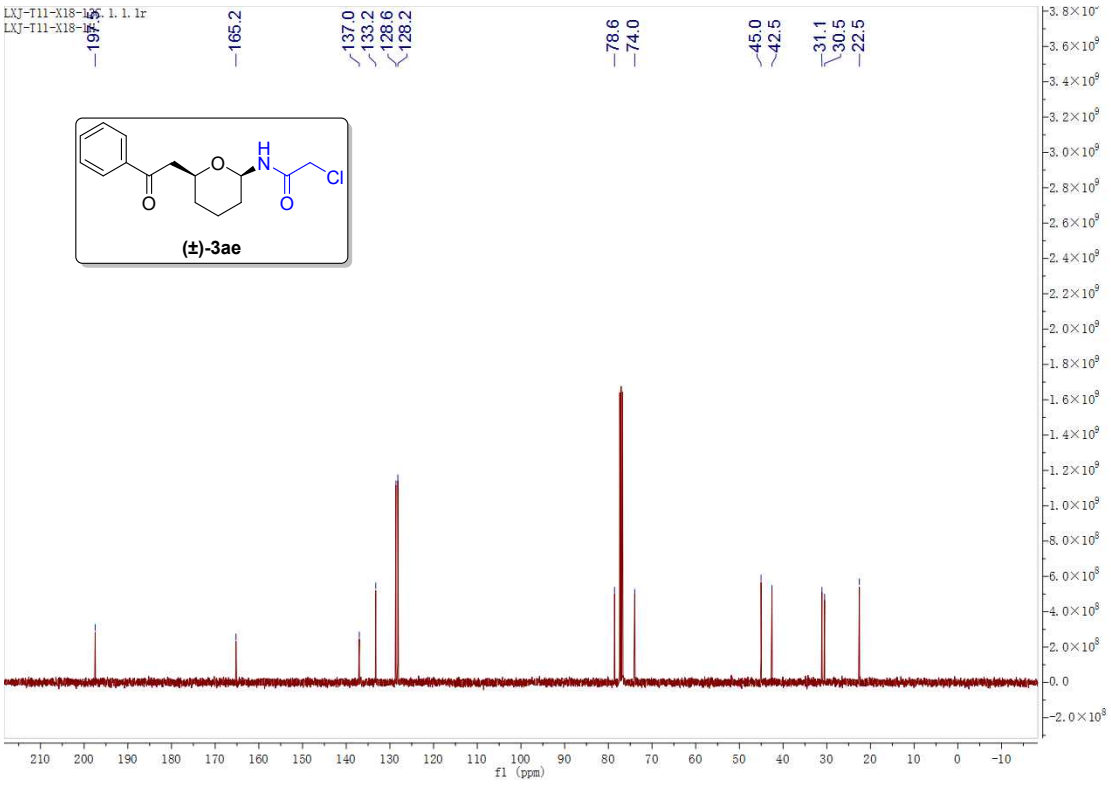
The ^{13}C NMR spectrum of (±)-3ad (101 MHz, $CDCl_3$)



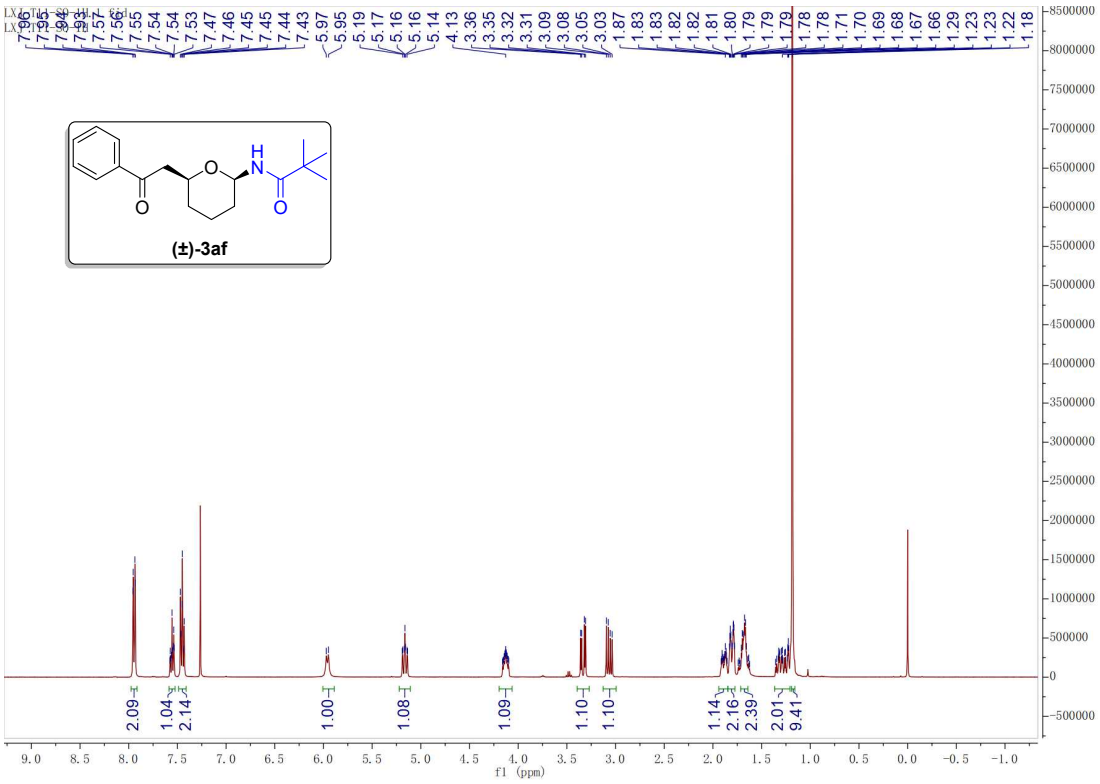
The ^{1}H NMR spectrum of (±)-3ae (400 MHz, $CDCl_3$)



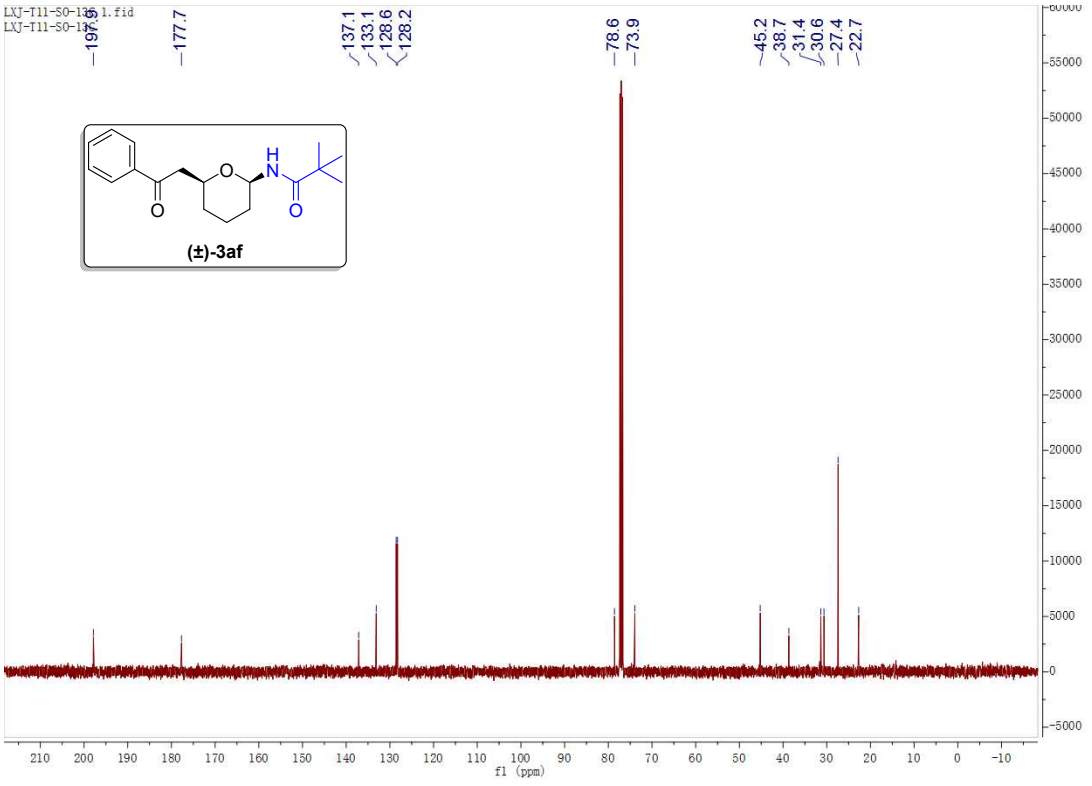
The ^{13}C NMR spectrum of (±)-3ae (101 MHz, $CDCl_3$)


LXJ-T11-X18-1H. 1. 1. 1r
LXJ-T11-X18-13C. 1. 1. 1r
197.5
165.2
137.0
133.2
128.6
128.2
78.6
74.0
45.0
42.5
31.1
30.5
22.5
H
N
O
O
Cl
(±)-3ae
f1 (ppm)

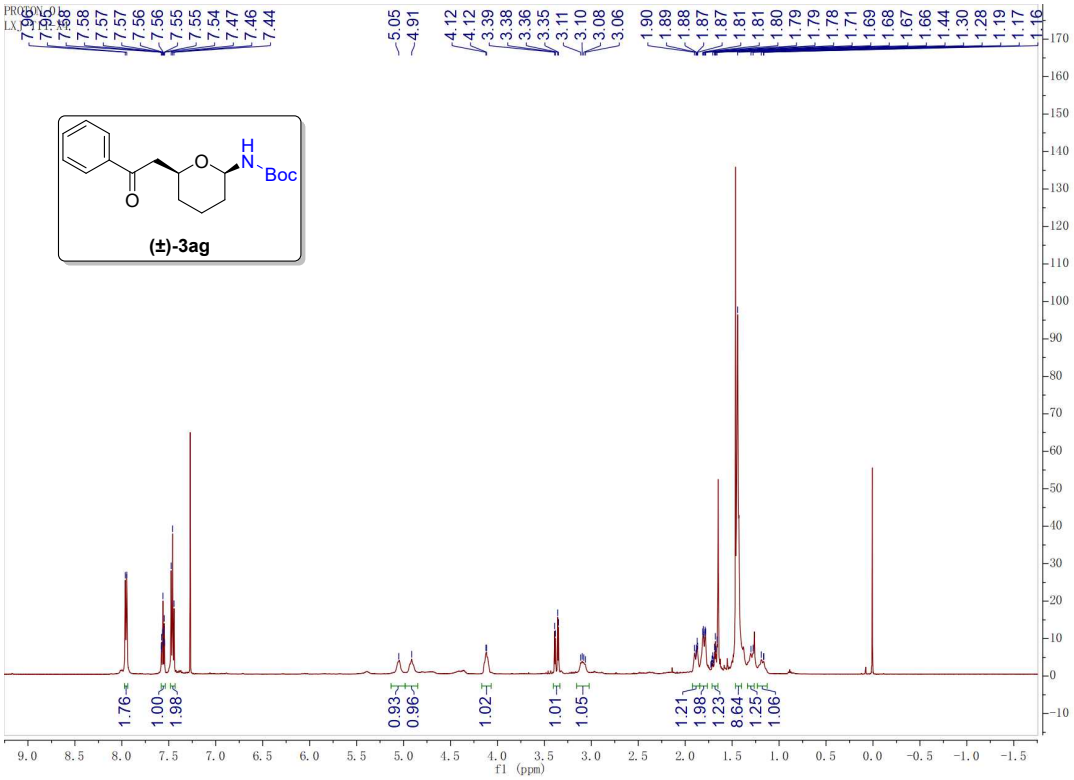
The ^{1}H NMR spectrum of (±)-3af (400 MHz, $CDCl_3$)



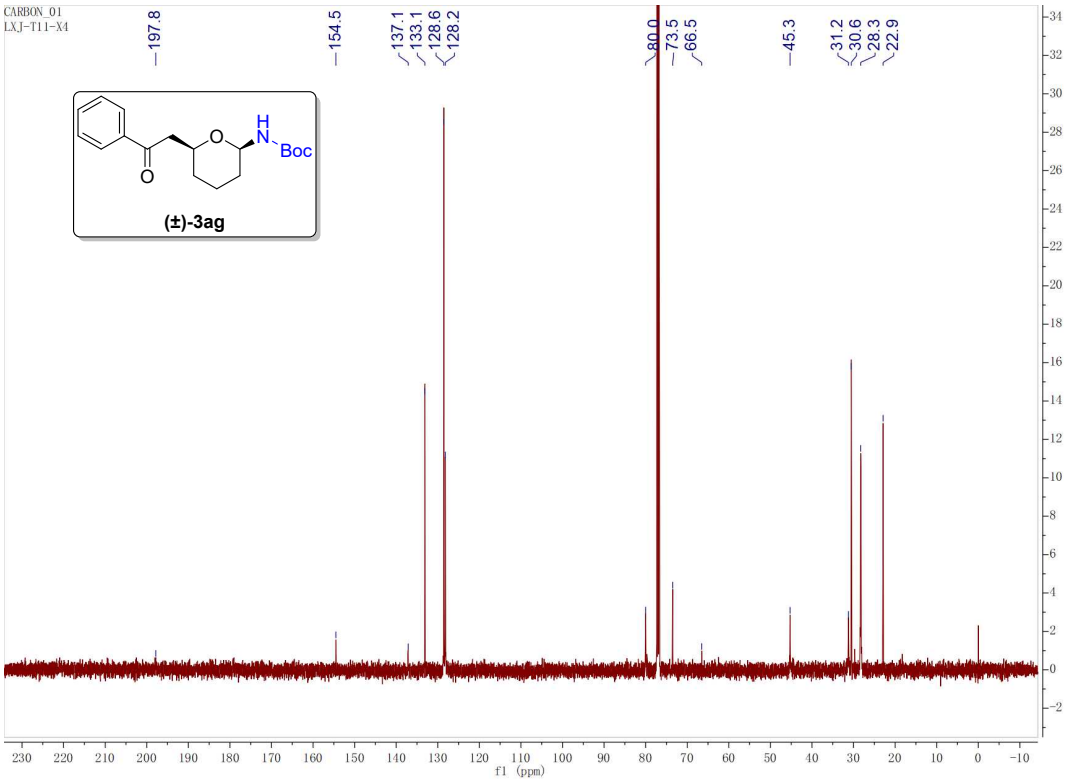
The ^{13}C NMR spectrum of (±)-3af (101 MHz, $CDCl_3$)



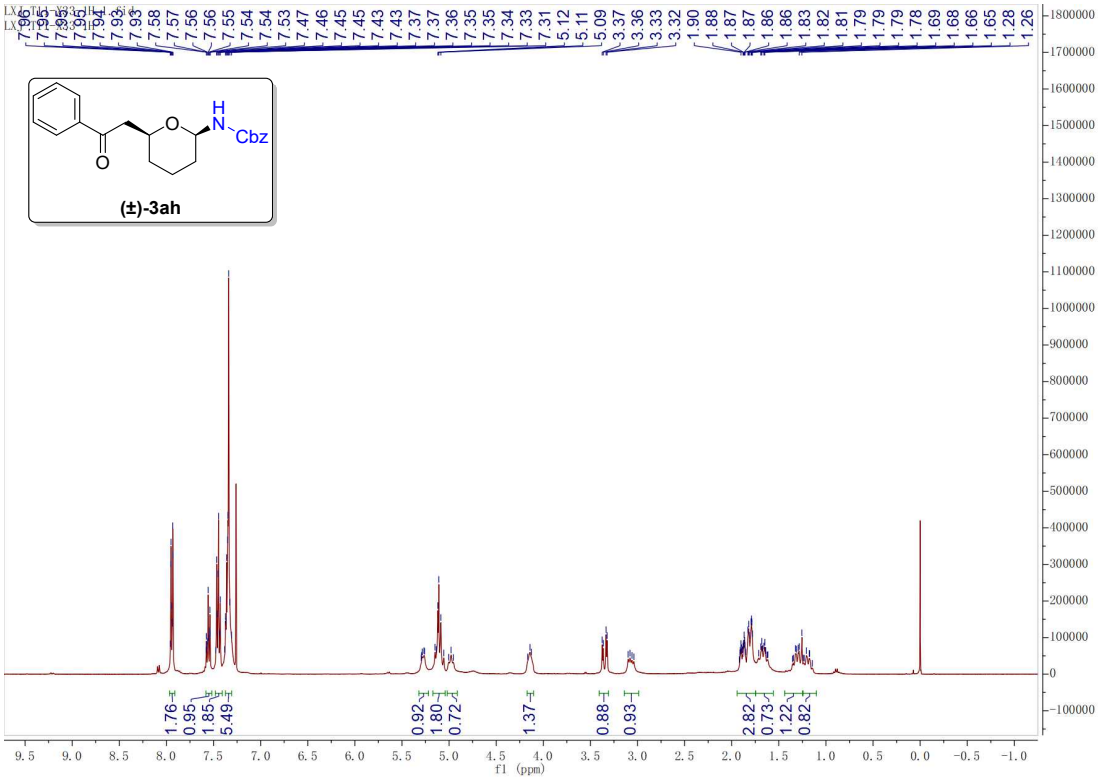
The ^{1}H NMR spectrum of (±)-3ag (500 MHz, $CDCl_3$)



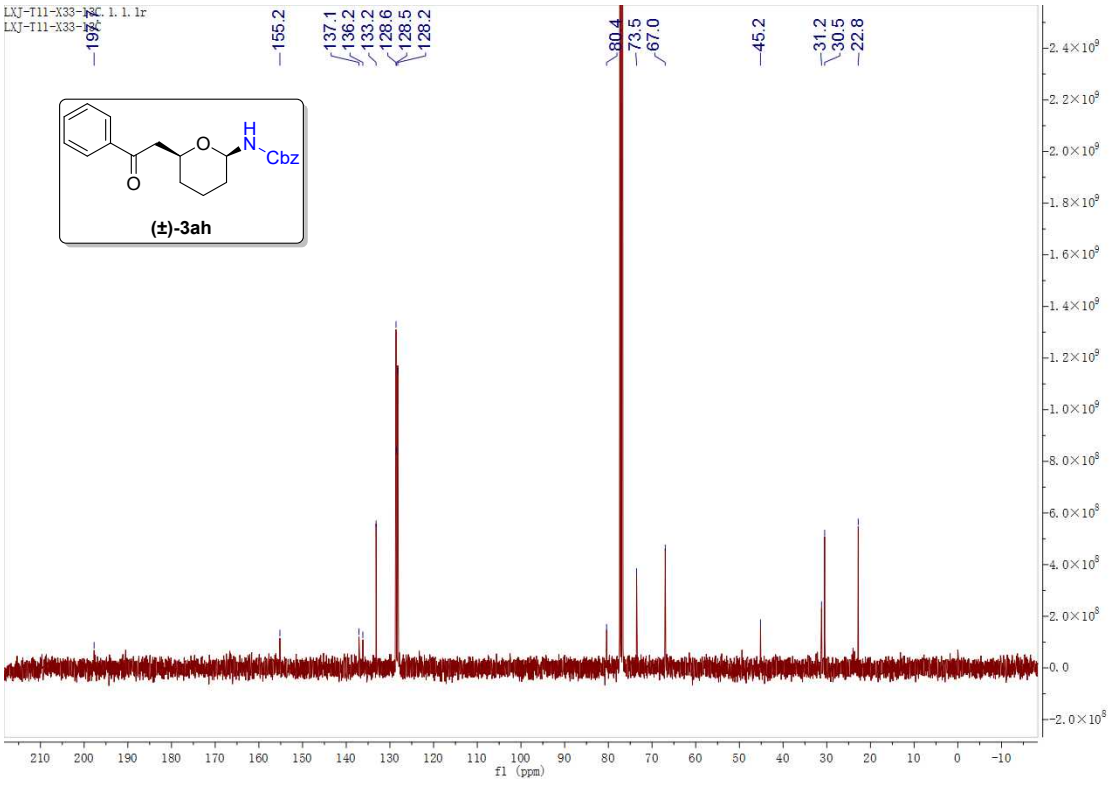
The ^{13}C NMR spectrum of (±)-3ag (125 MHz, $CDCl_3$)



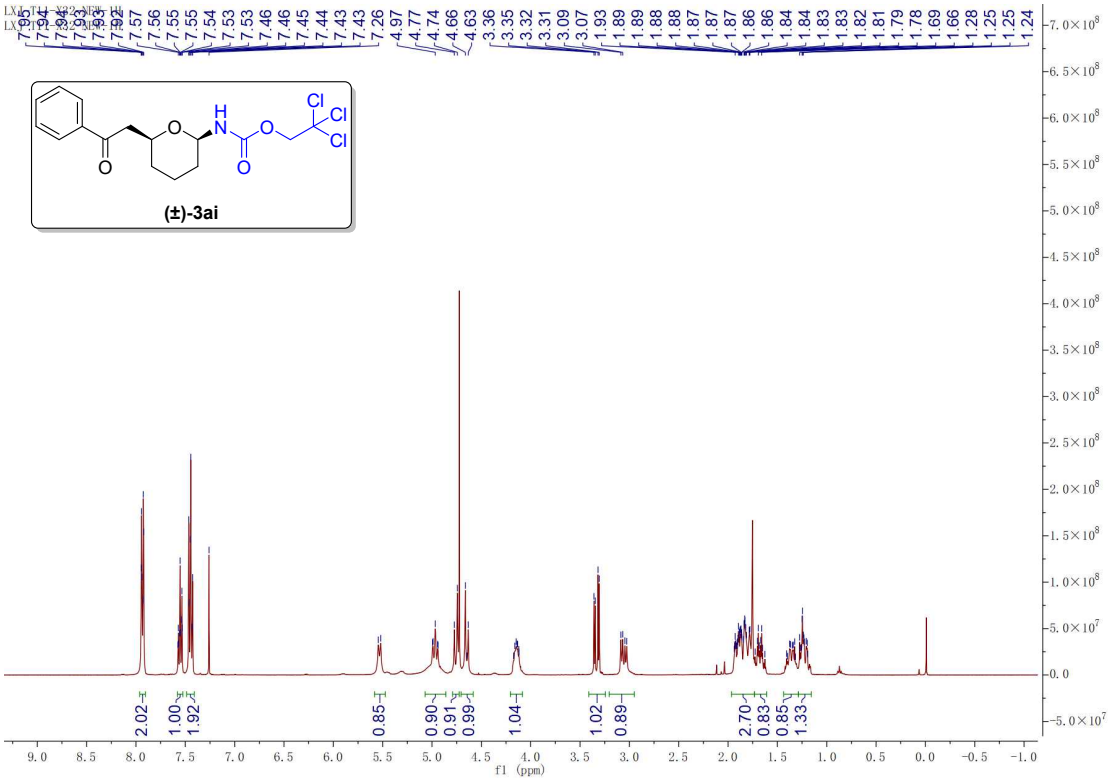
The ^{1}H NMR spectrum of (±)-3ah (400 MHz, $CDCl_3$)



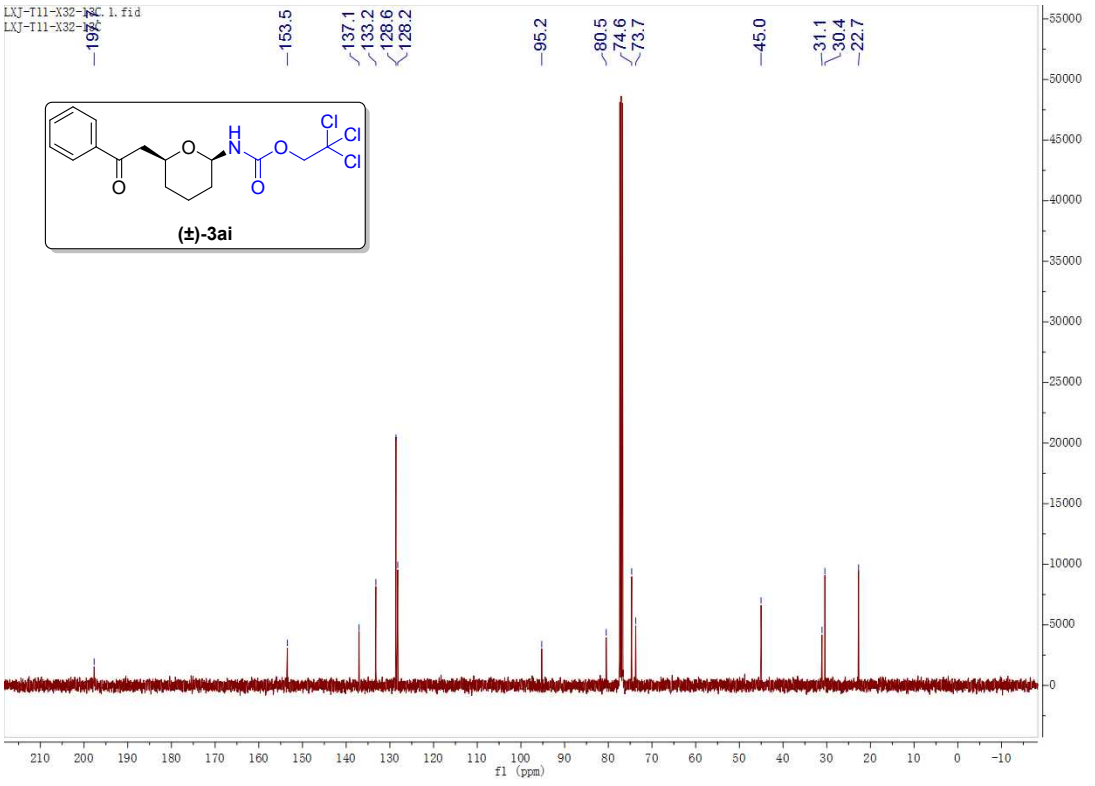
The ^{13}C NMR spectrum of (±)-3ah (101 MHz, $CDCl_3$)



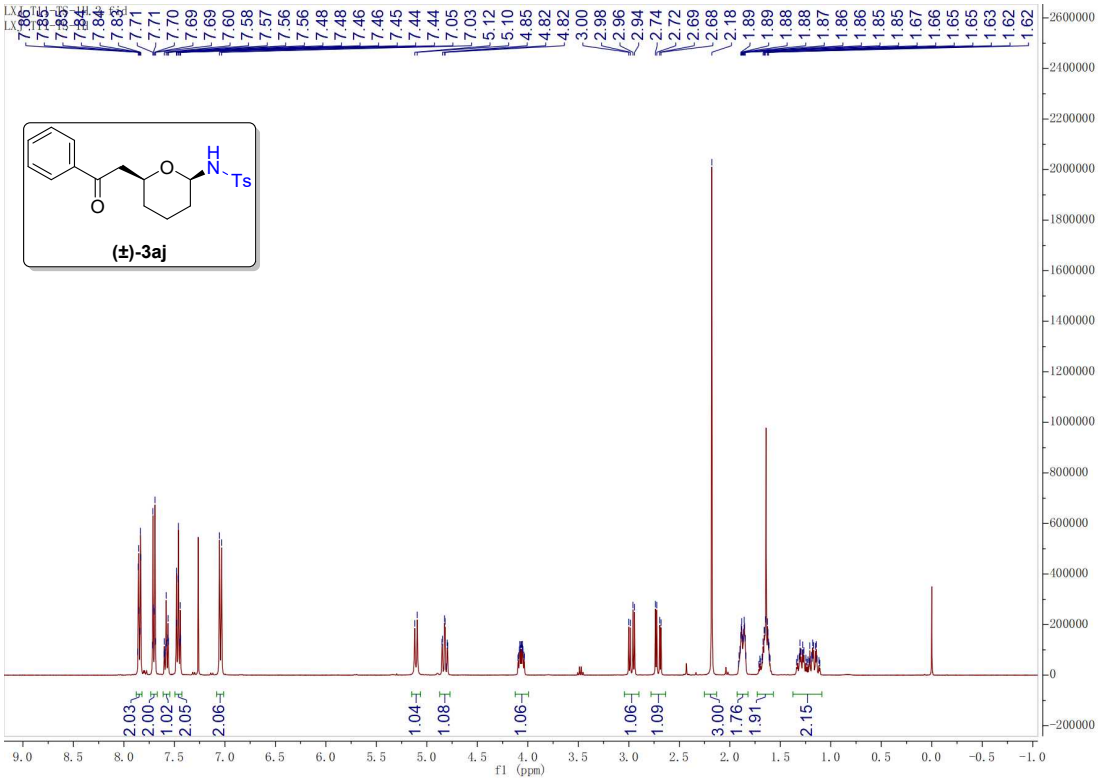
The ^{1}H NMR spectrum of (±)-3ai (400 MHz, $CDCl_3$)



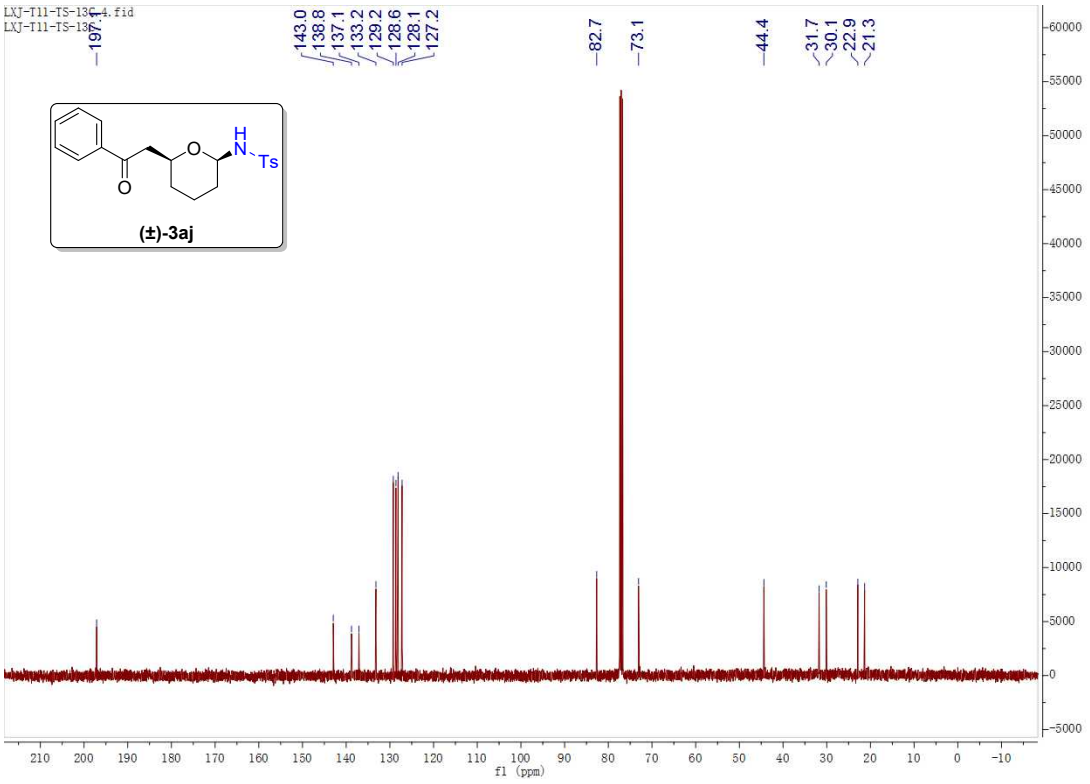
The ^{13}C NMR spectrum of (±)-3ai (101 MHz, $CDCl_3$)



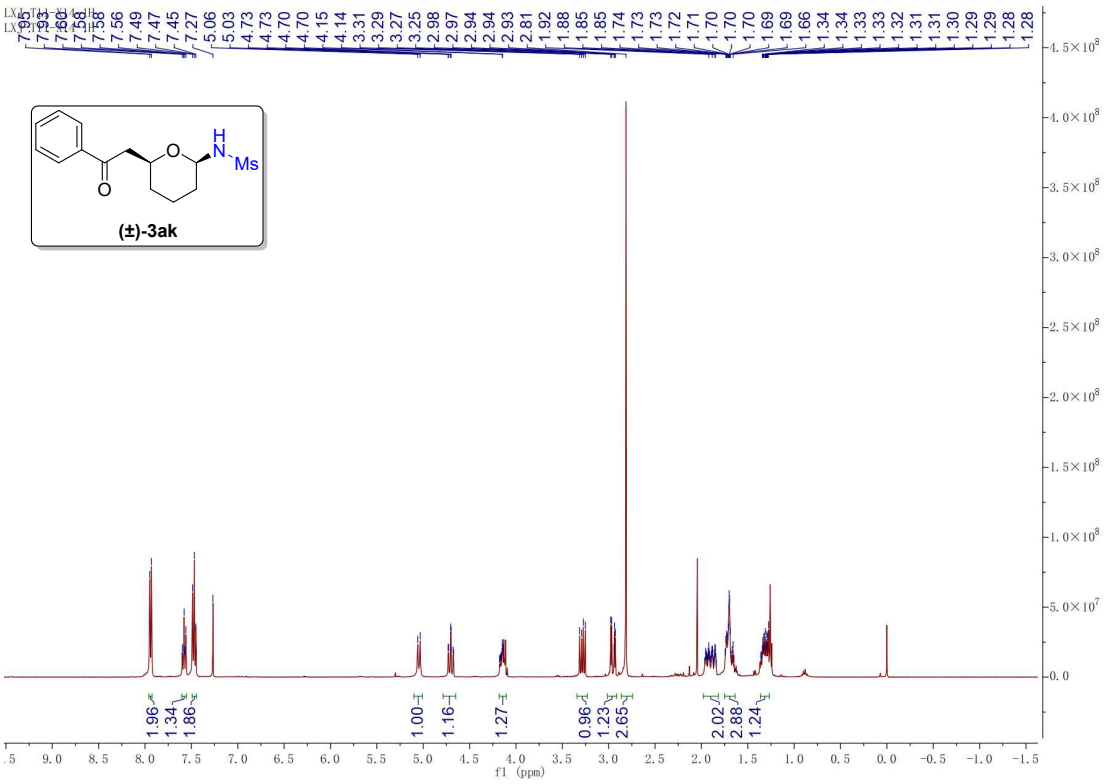
The ^{1}H NMR spectrum of (±)-3aj (400 MHz, $CDCl_3$)



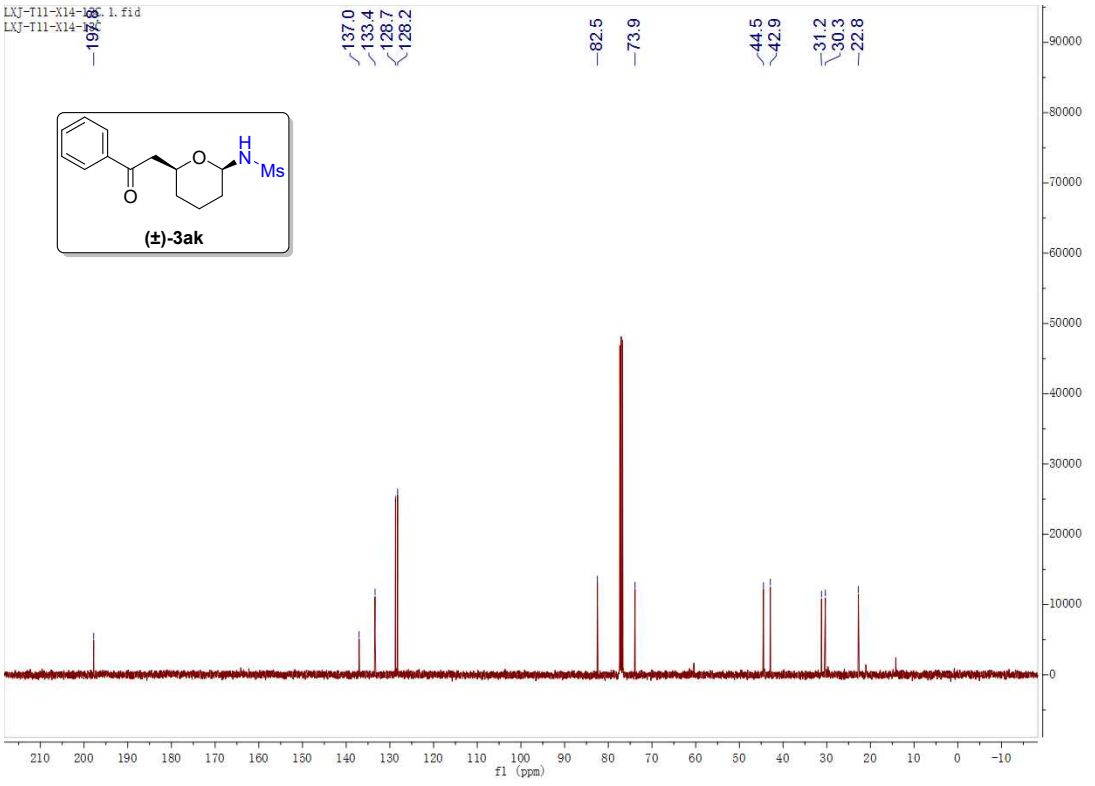
The ^{13}C NMR spectrum of (±)-3aj (101 MHz, $CDCl_3$)



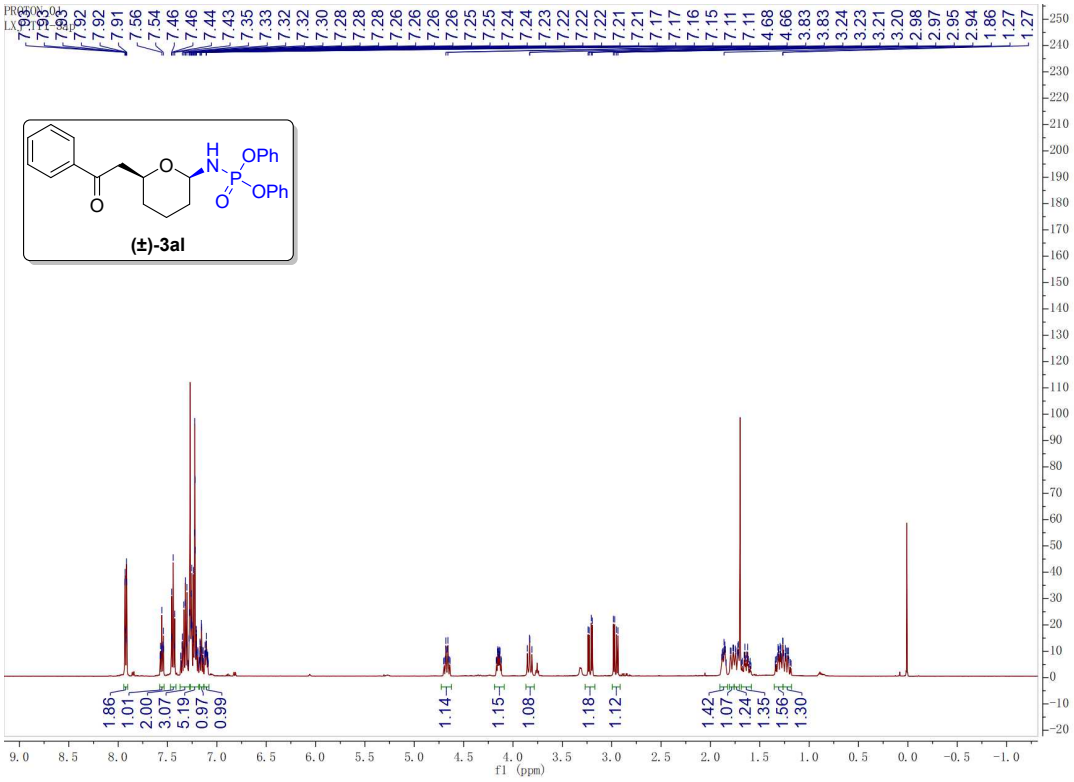
The ^{1}H NMR spectrum of (±)-3ak (400 MHz, $CDCl_3$)



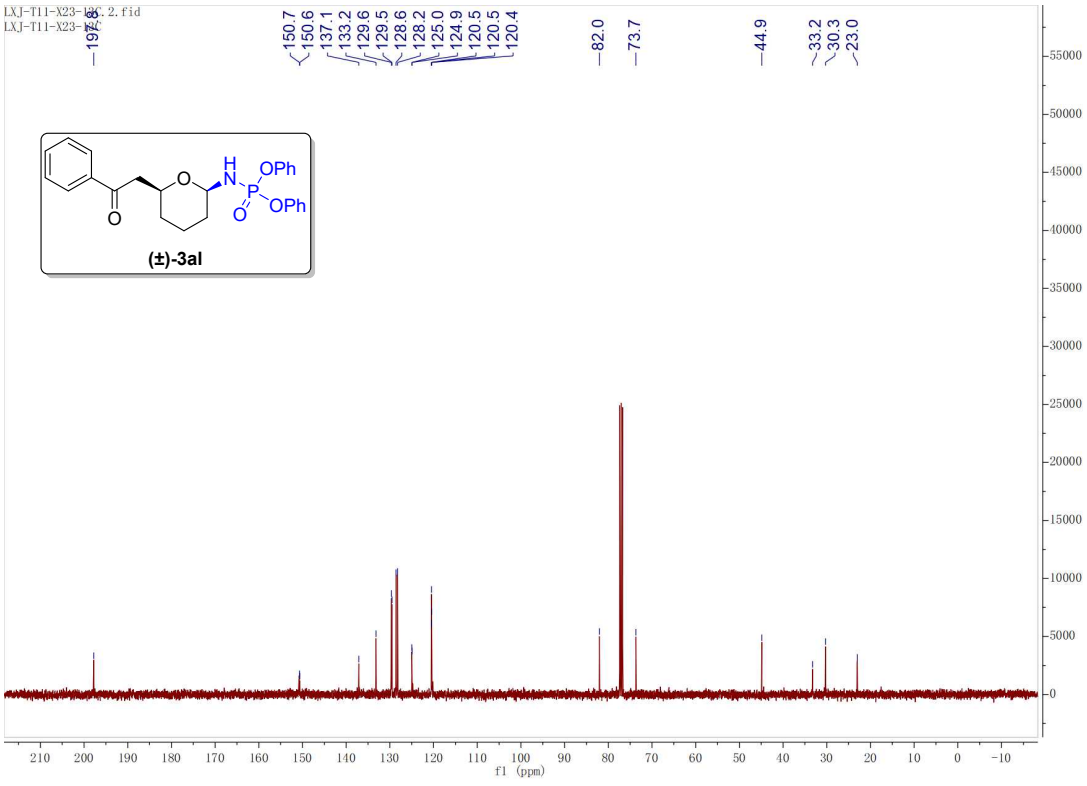
The ^{13}C NMR spectrum of (±)-3ak (101 MHz, $CDCl_3$)



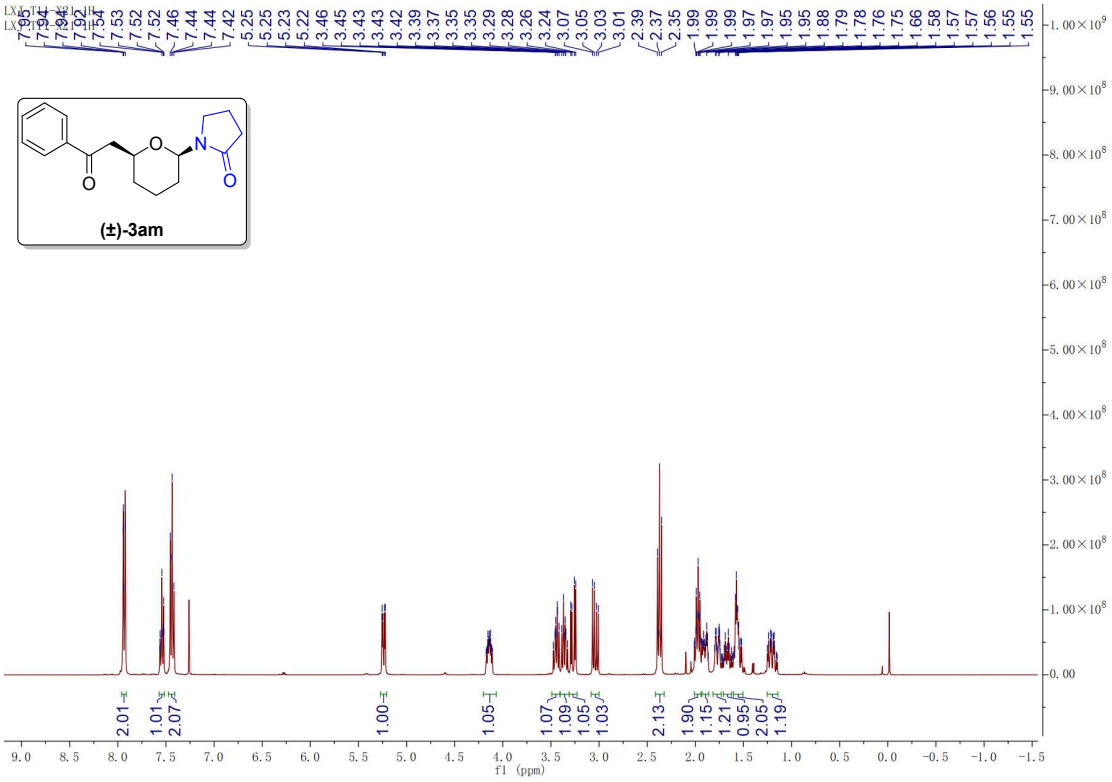
The ^{1}H NMR spectrum of (±)-3al (500 MHz, $CDCl_3$)



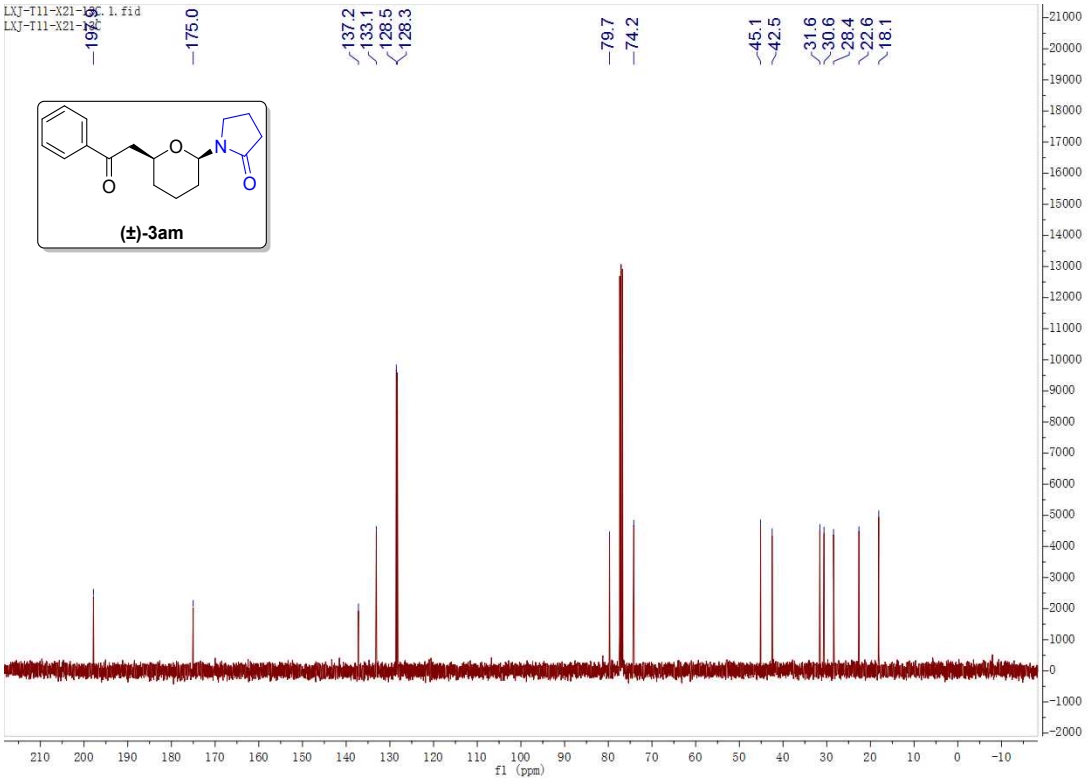
The ^{13}C NMR spectrum of (±)-3al (101 MHz, $CDCl_3$)



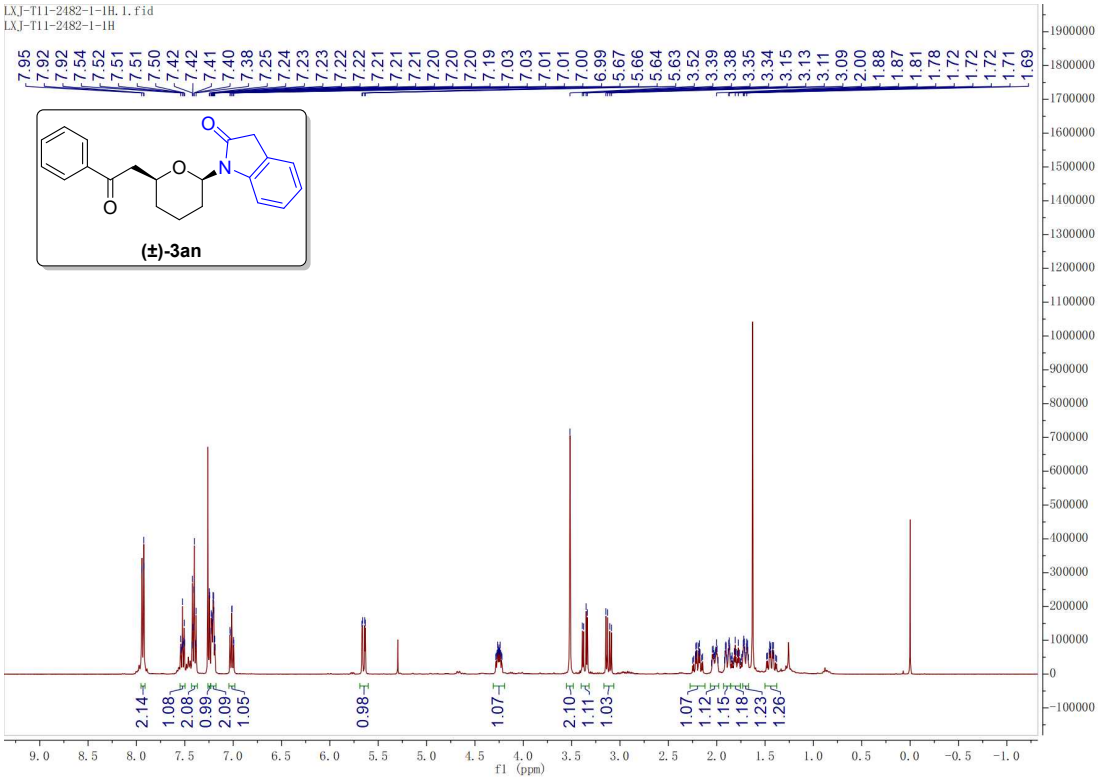
The ^{1}H NMR spectrum of (±)-3am (400 MHz, $CDCl_3$)



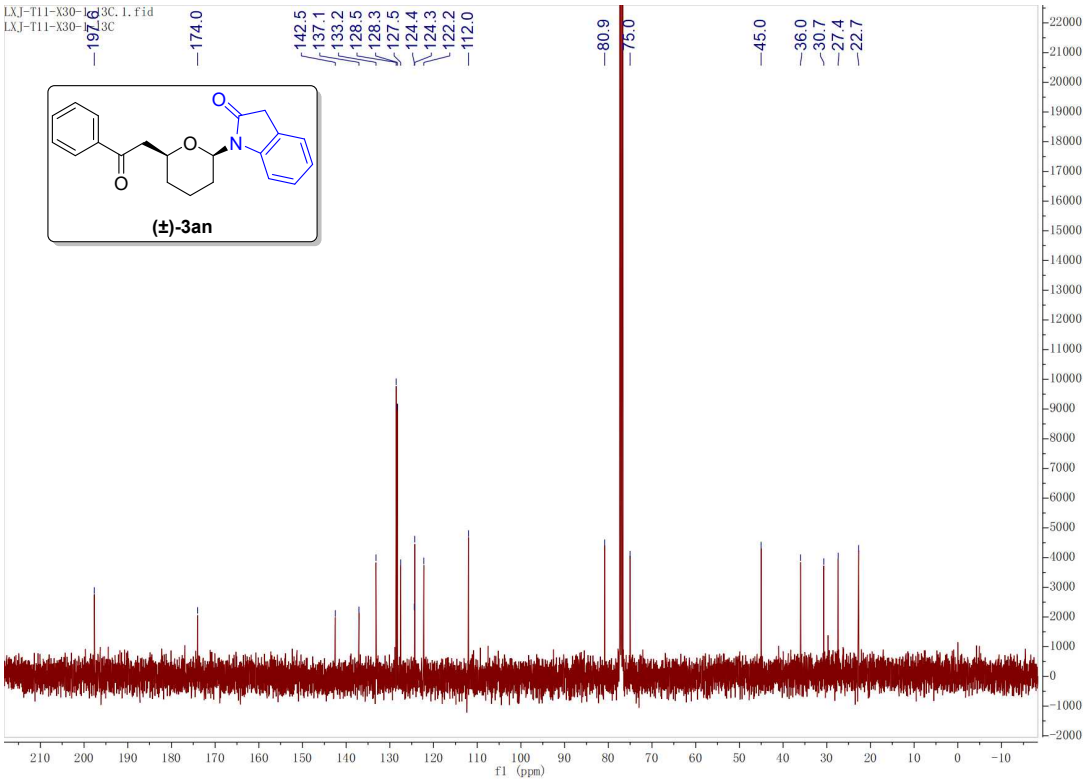
The ^{13}C NMR spectrum of (±)-3am (101 MHz, $CDCl_3$)



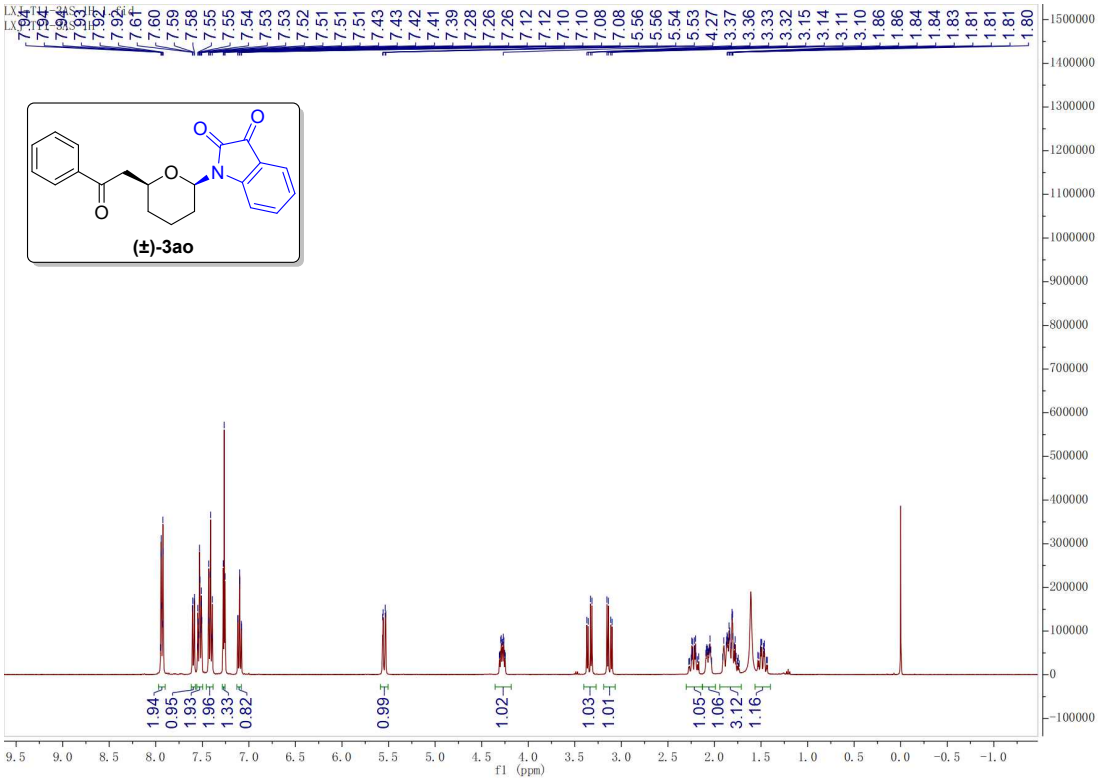
The ^{1}H NMR spectrum of (±)-3an (400 MHz, $CDCl_3$)



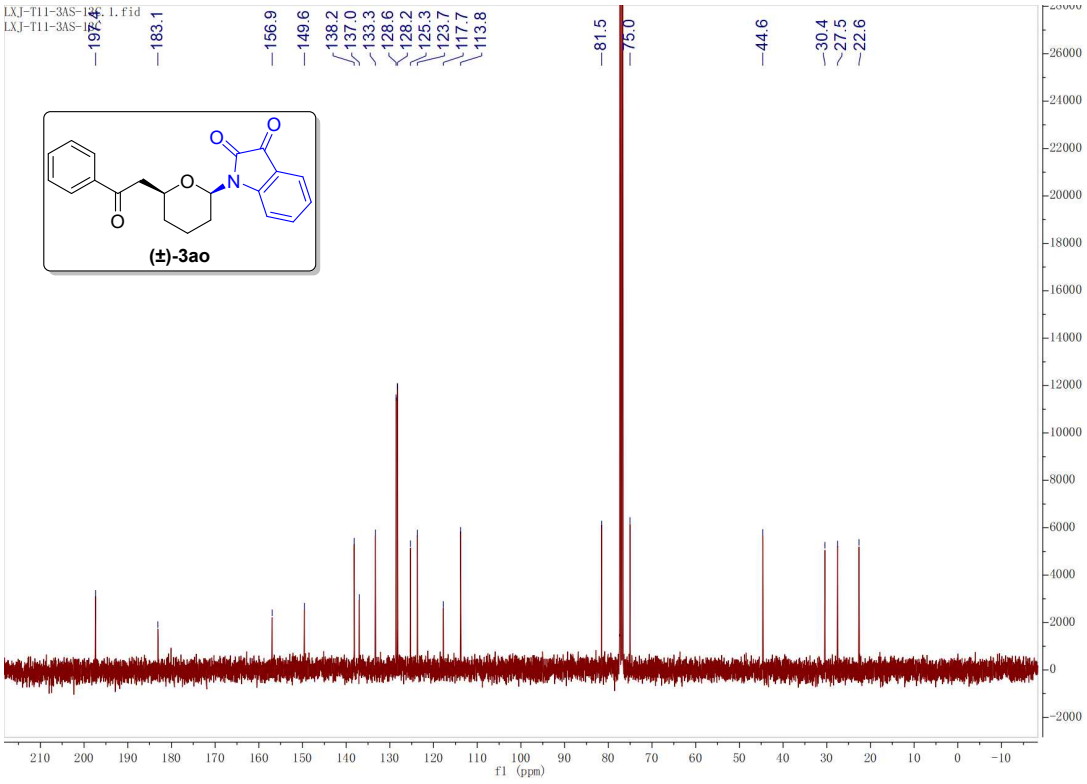
The ^{13}C NMR spectrum of (±)-3an (101 MHz, $CDCl_3$)



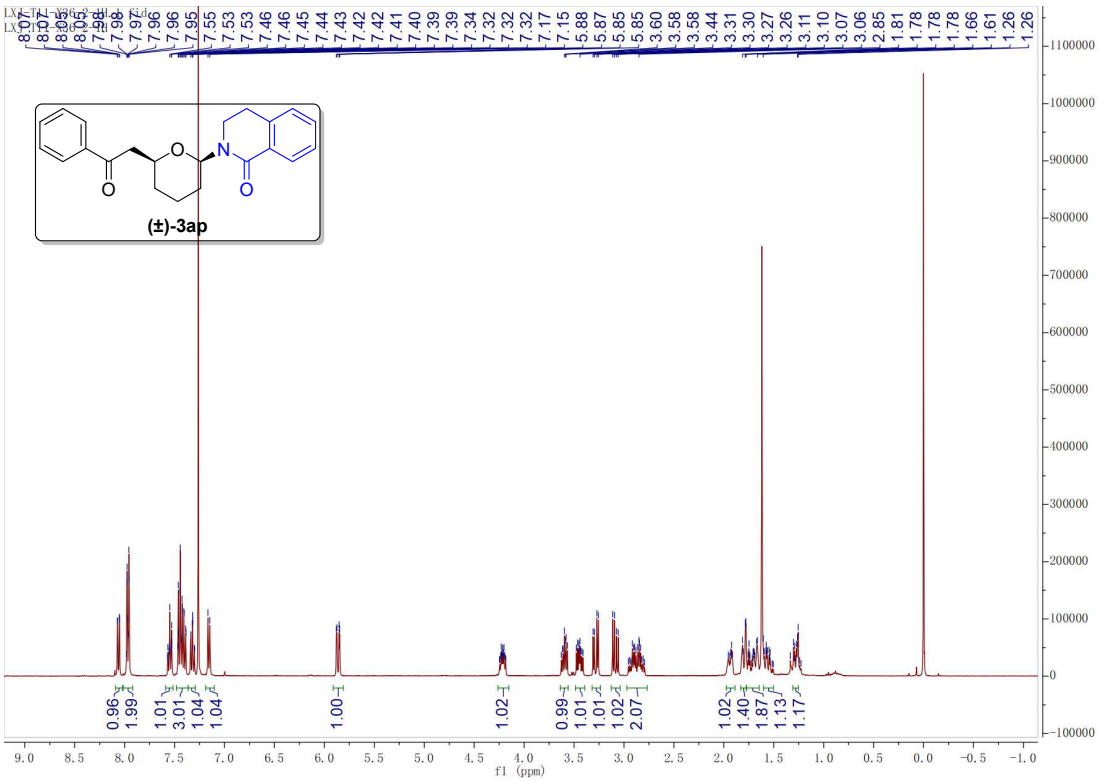
The ^{1}H NMR spectrum of (±)-3ao (400 MHz, $CDCl_3$)



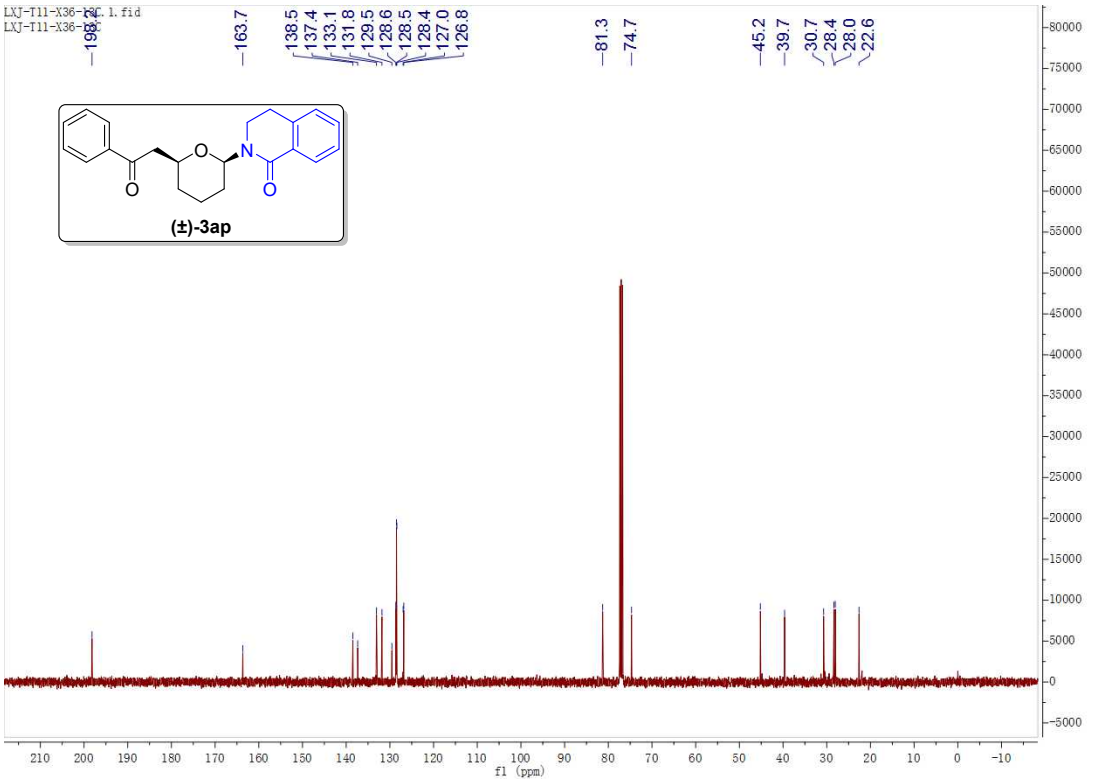
The ^{13}C NMR spectrum of (±)-3ao (101 MHz, $CDCl_3$)



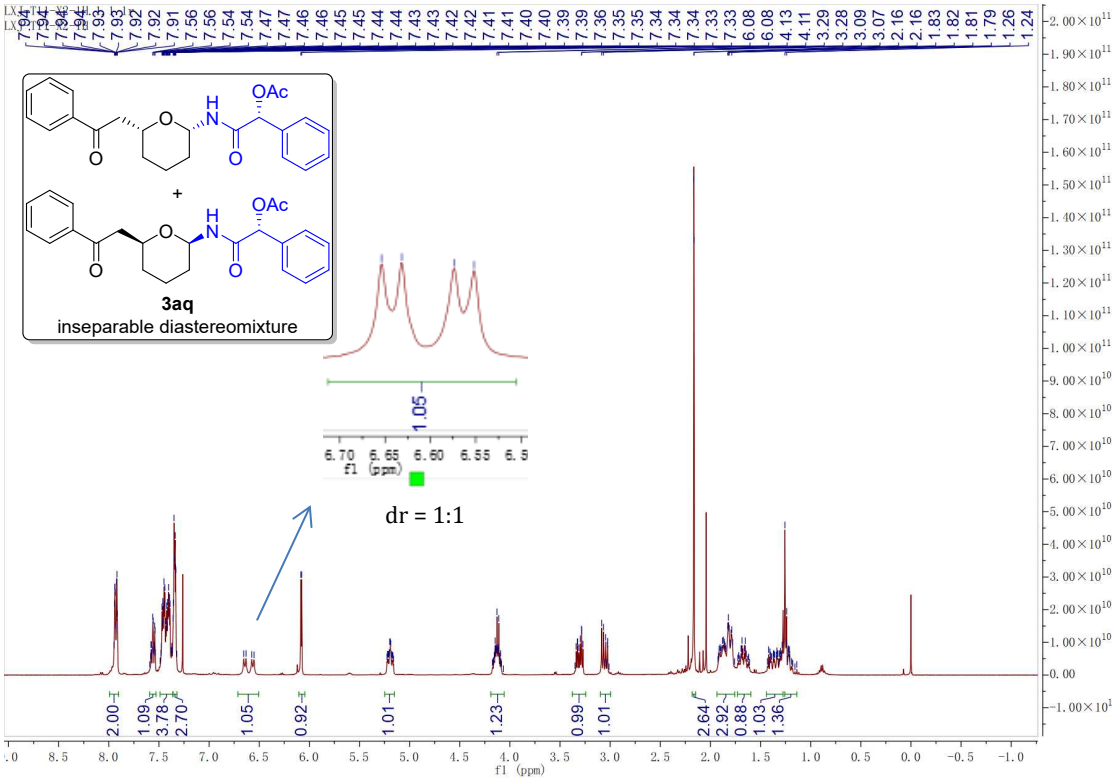
The ^{1}H NMR spectrum of (±)-3ap (400 MHz, $CDCl_3$)



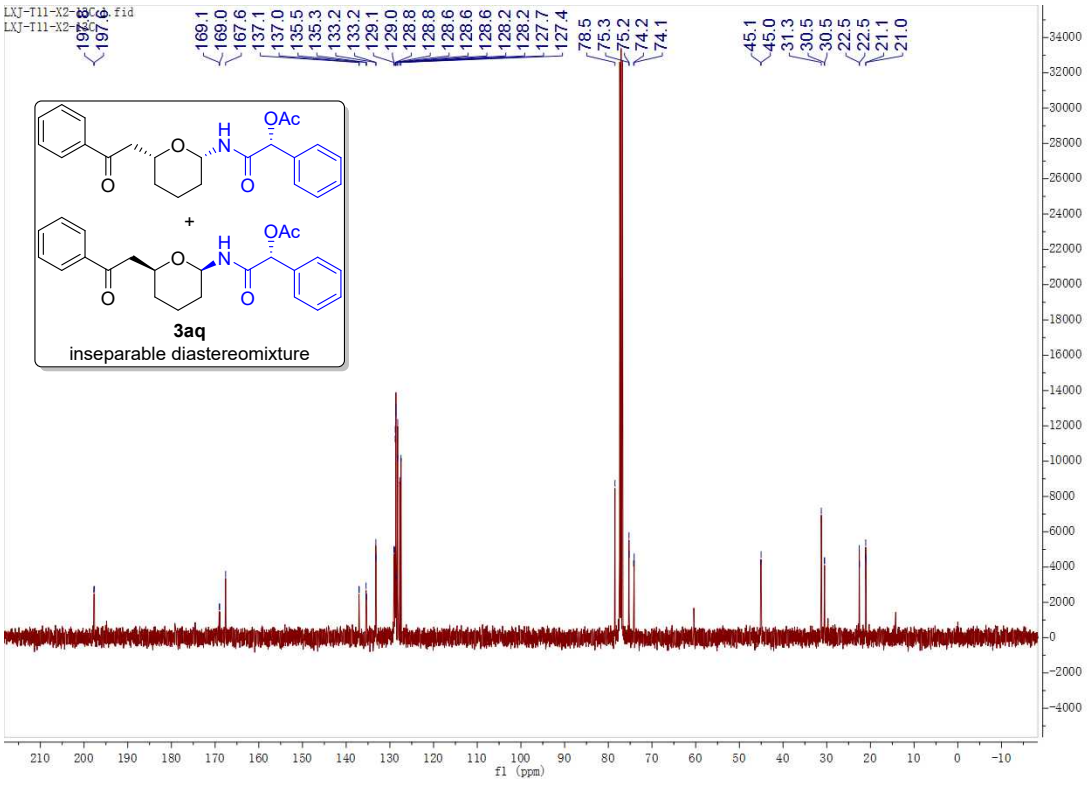
The ^{13}C NMR spectrum of (±)-3ap (101 MHz, $CDCl_3$)



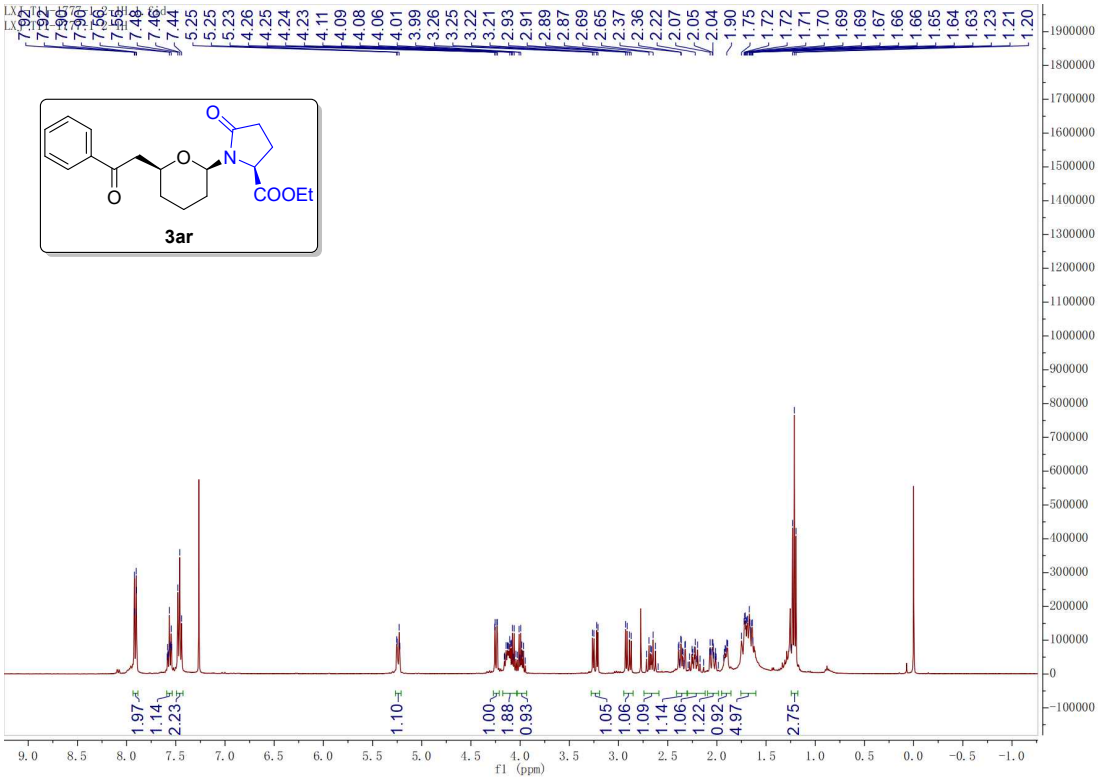
The ^{1}H NMR spectrum of 3aq (400 MHz, $CDCl_3$)



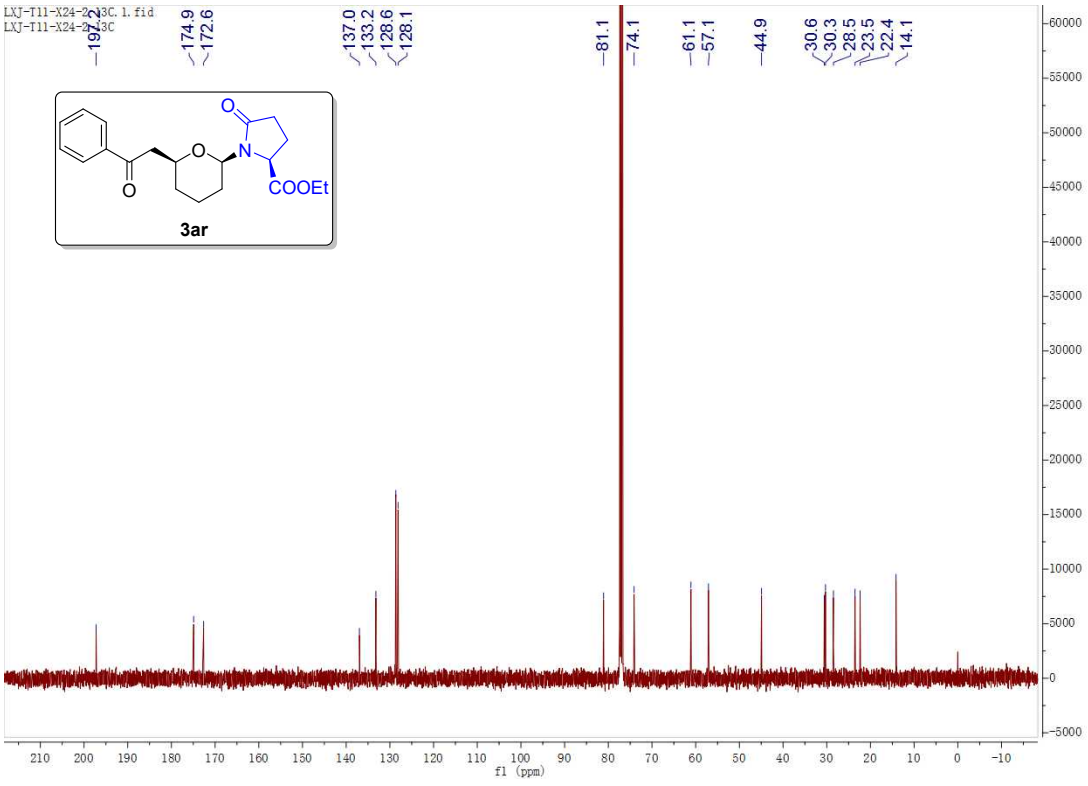
The ^{13}C NMR spectrum of 3aq (101 MHz, $CDCl_3$)



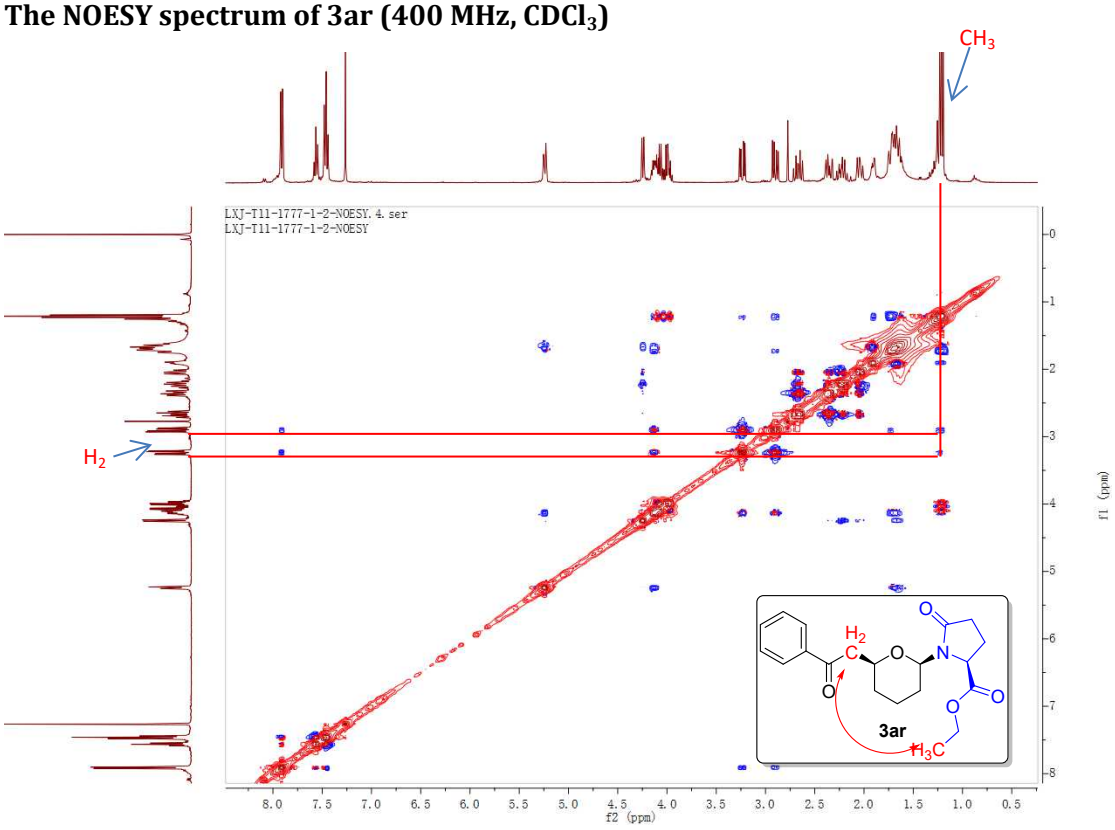
The ^{1}H NMR spectrum of 3ar (400 MHz, $CDCl_3$)



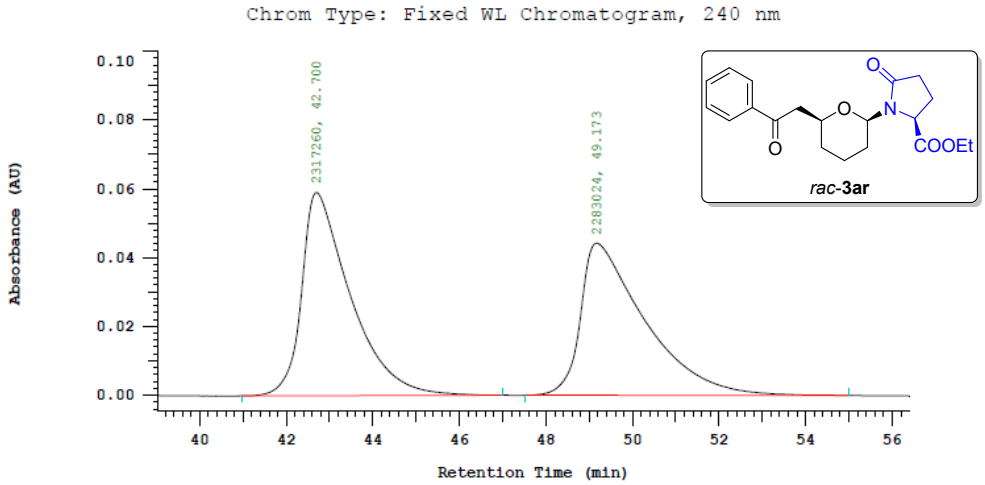
The ^{13}C NMR spectrum of 3ar (101 MHz, $CDCl_3$)



The NOESY spectrum of 3ar (400 MHz, $CDCl_3$)



The HPLC of racemic 3ar



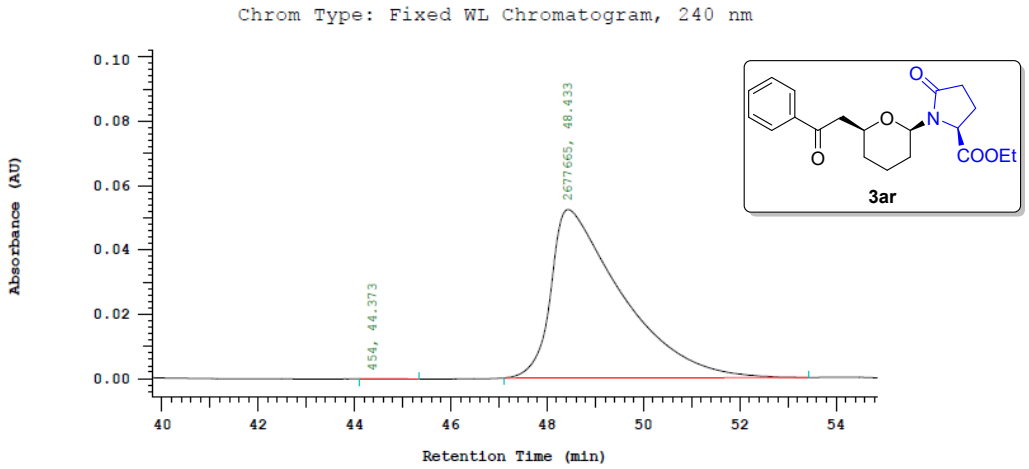
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	42.700	2317260	50.372	BB
2	49.173	2283024	49.628	BB
		4600284	100.000	

The HPLC of chiral 3ar



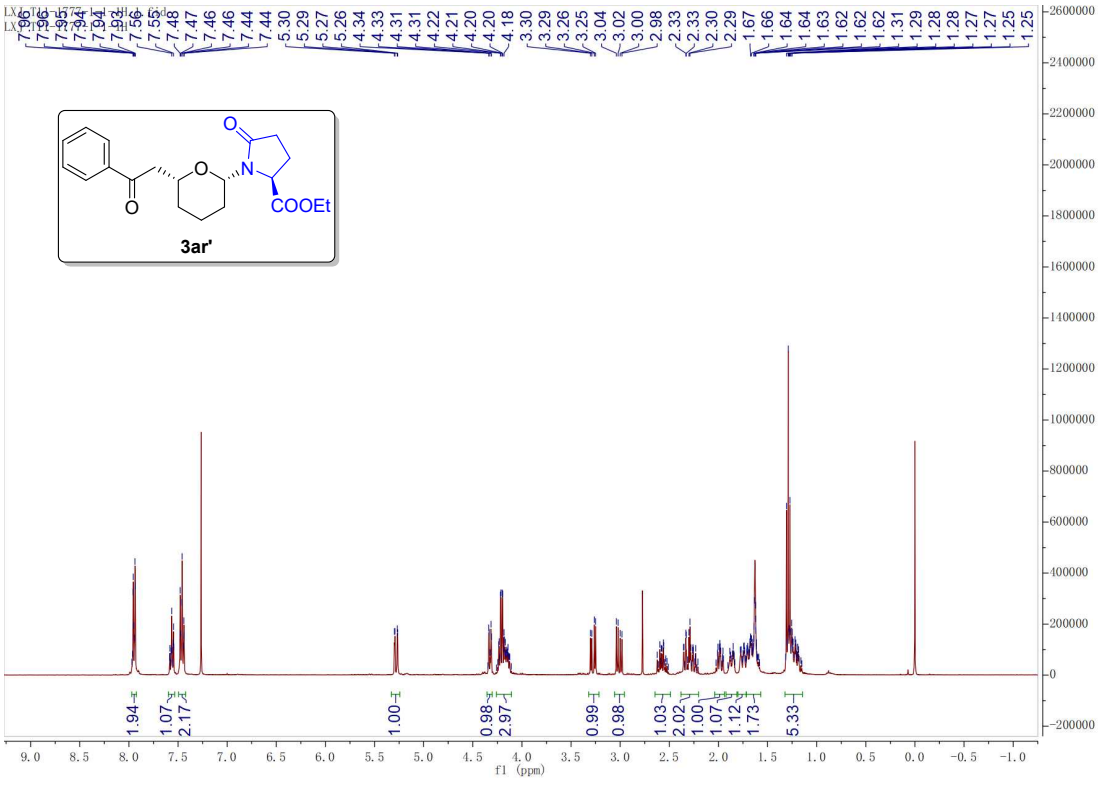
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

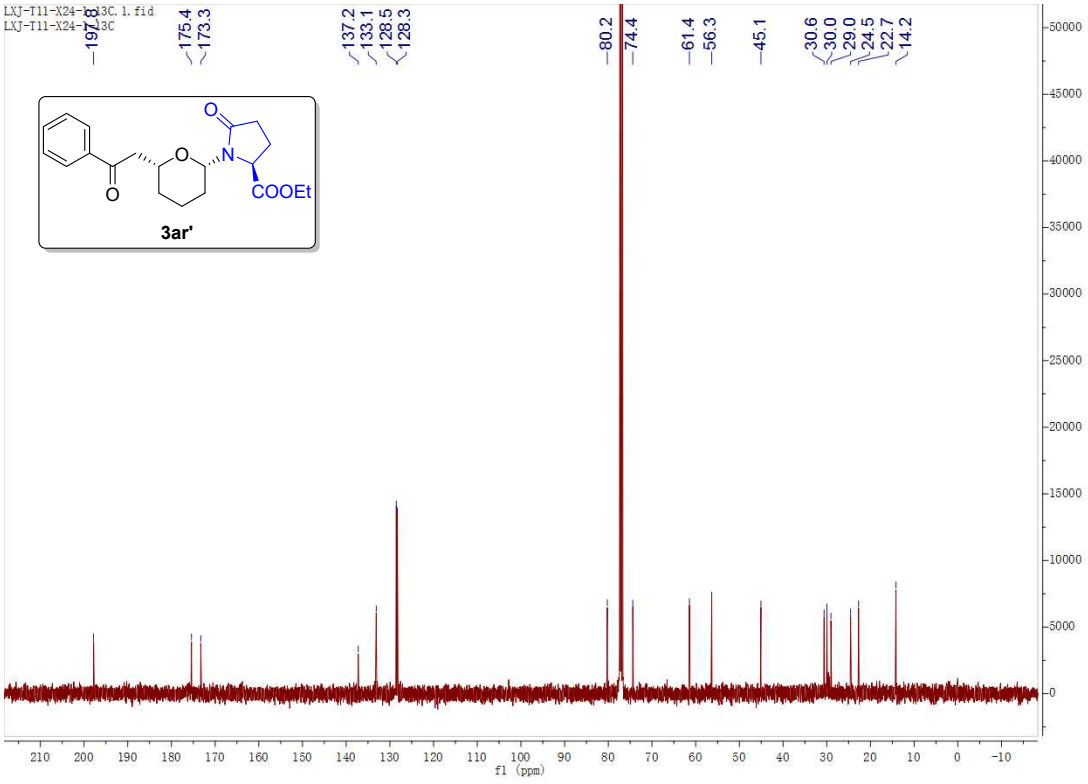
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	44.373	454	0.017	BB
2	48.433	2677665	99.983	BB
		2678119	100.000	

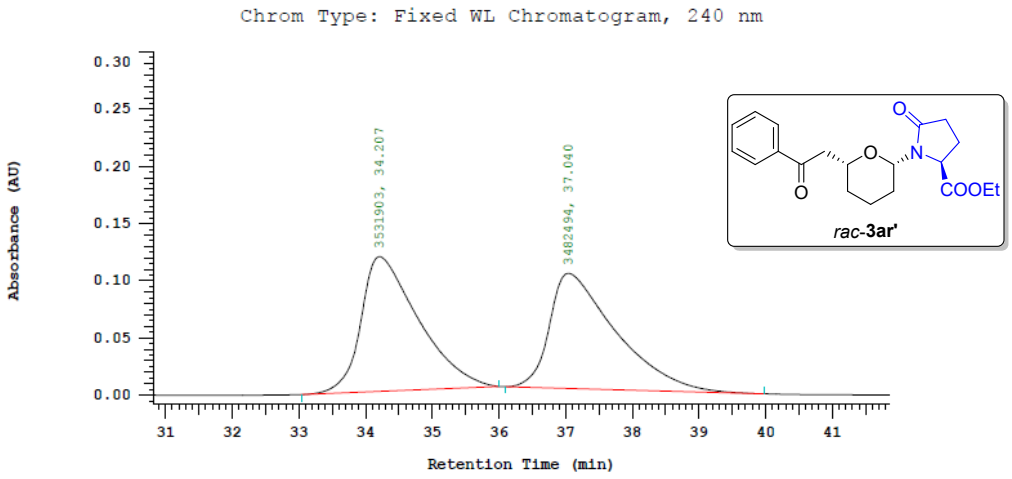
The ^{1}H NMR spectrum of 3ar' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3ar' (101 MHz, $CDCl_3$)



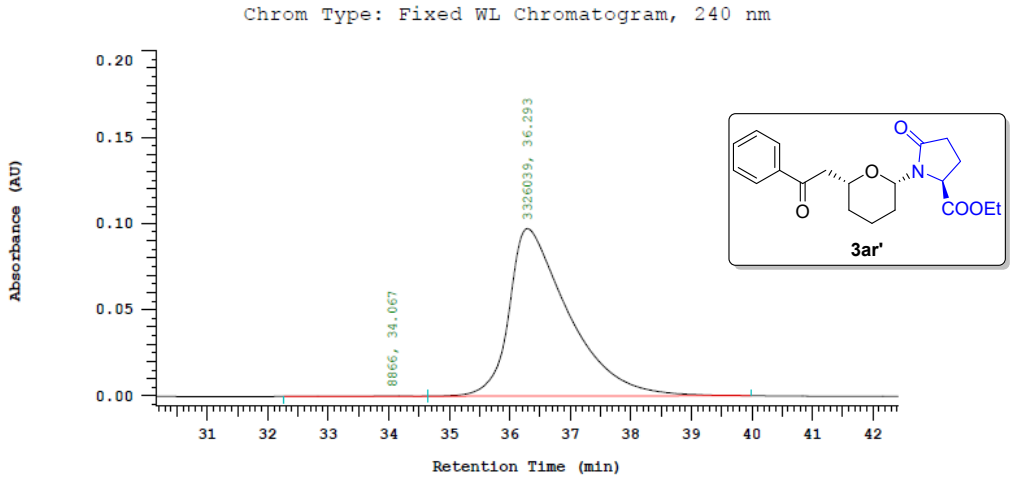
The HPLC of racemic 3ar'



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	34.207	3531903	50.352	BB
2	37.040	3482494	49.648	BB
		7014397	100.000	

The HPLC of chiral 3ar'



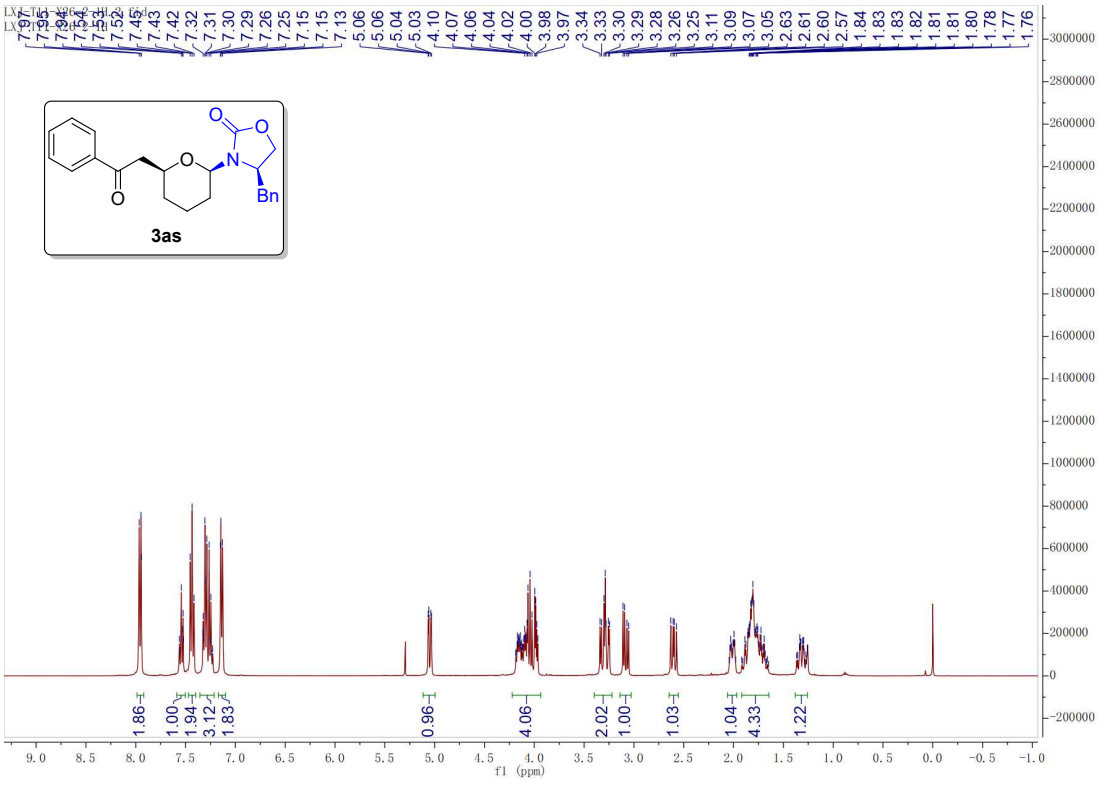
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

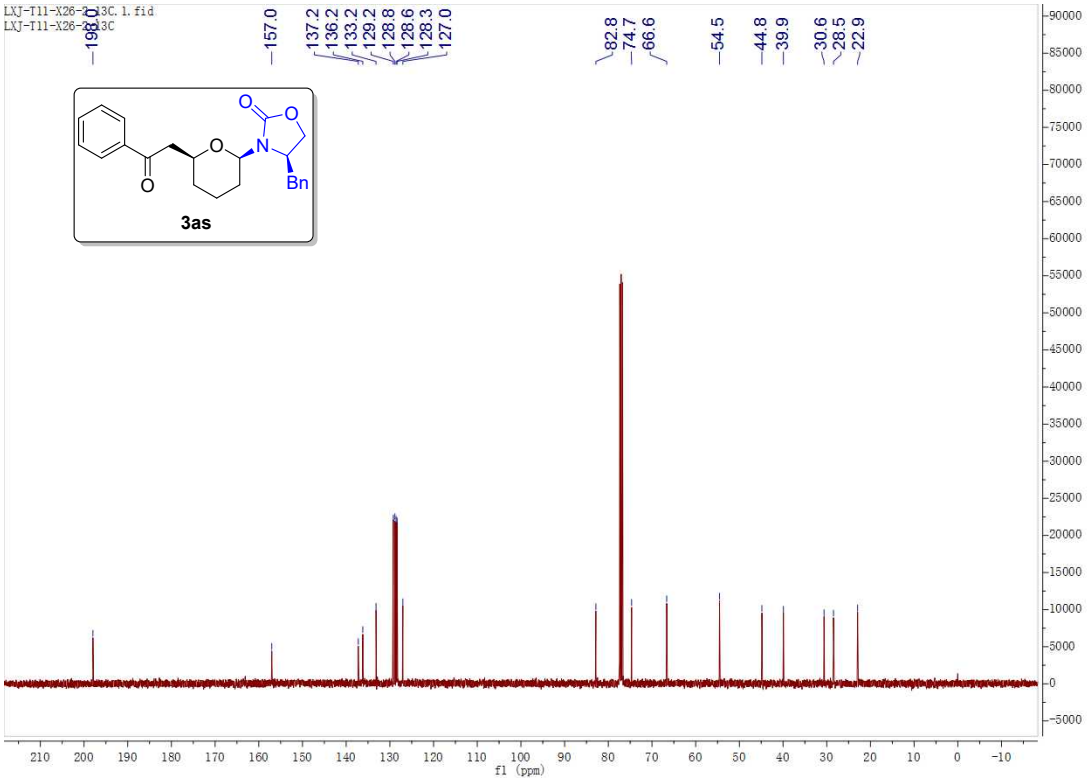
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	34.067	8866	0.266	BV
2	36.293	3326039	99.734	VB
		3334905	100.000	

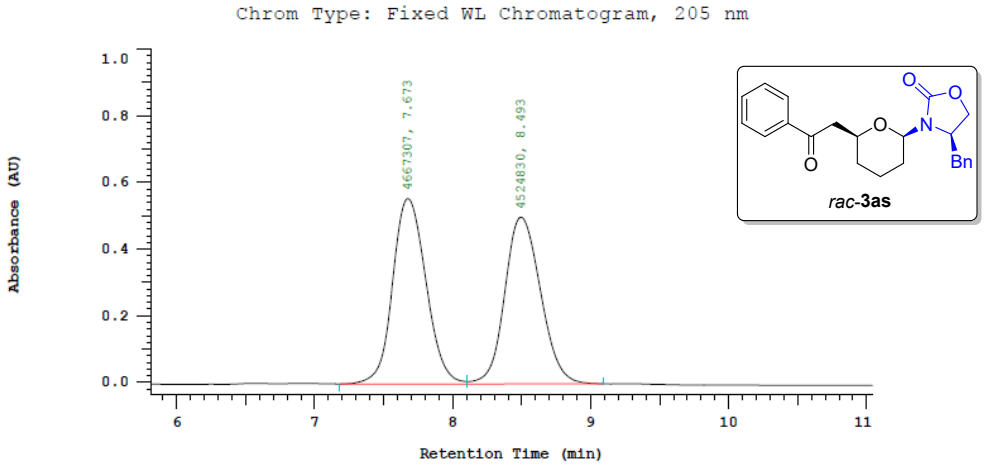
The ^{1}H NMR spectrum of 3as(400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3as (101 MHz, $CDCl_3$)



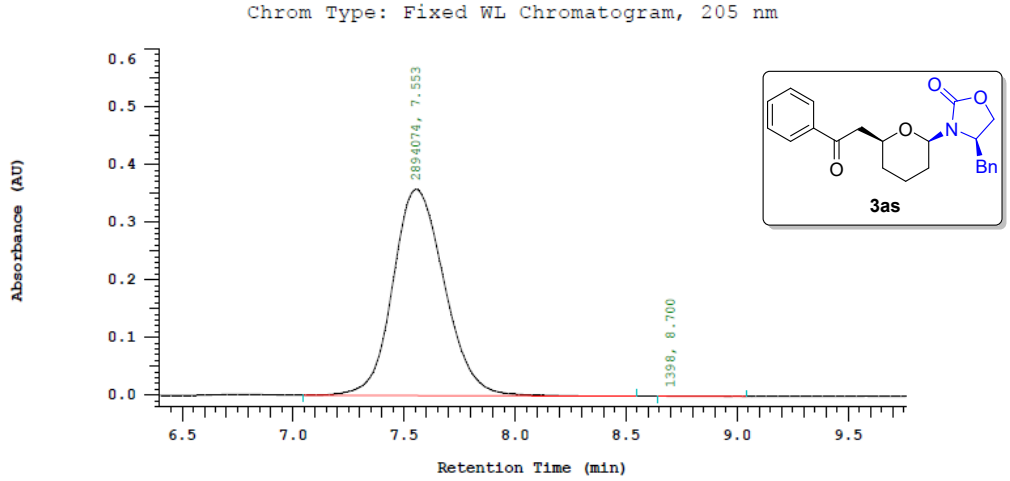
The HPLC of racemic 3as



Chrom Type: Fixed WL Chromatogram, 205 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.673	4667307	50.775	BV
2	8.493	4524830	49.225	VB
		9192137	100.000	

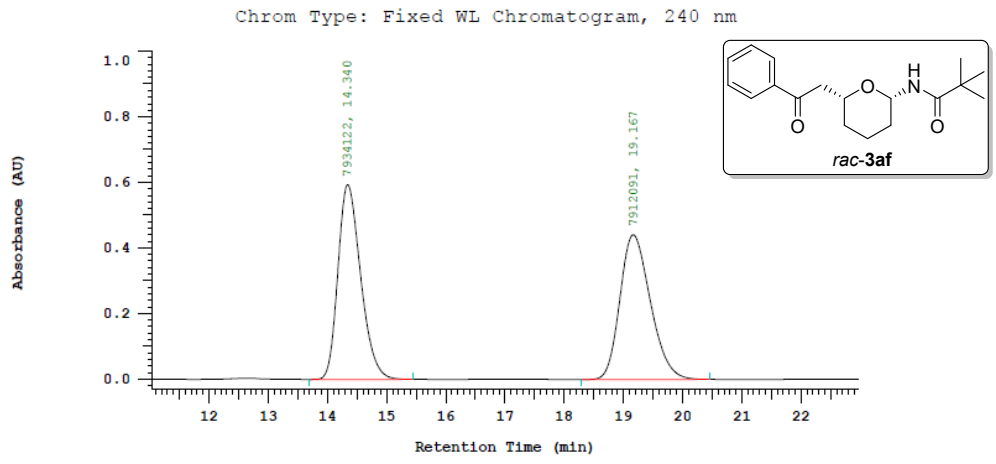
The HPLC of chiral 3as



Chrom Type: Fixed WL Chromatogram, 205 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	7.553	2894074	99.952	BB
2	8.700	1398	0.048	BB
		2895472	100.000	

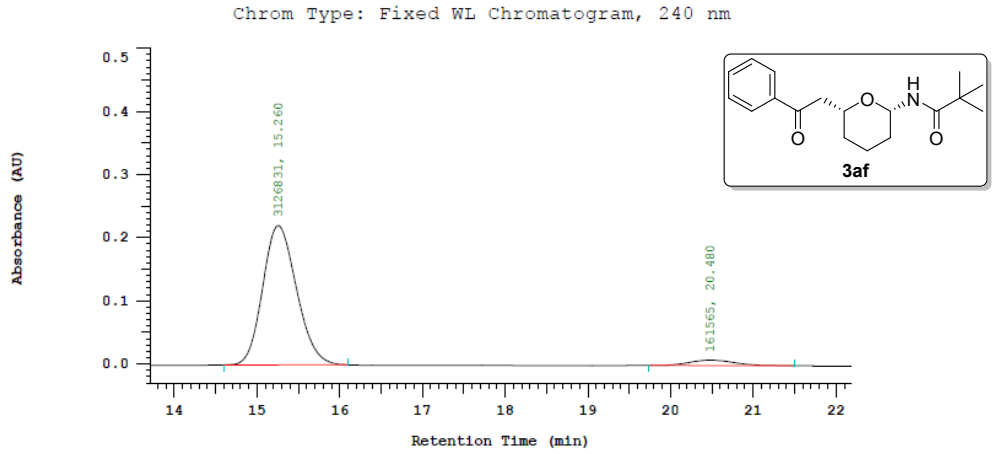
The HPLC of racemic 3af



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.340	7934122	50.070	BB
2	19.167	7912091	49.930	BB
		15846213	100.000	

The HPLC of chiral 3af



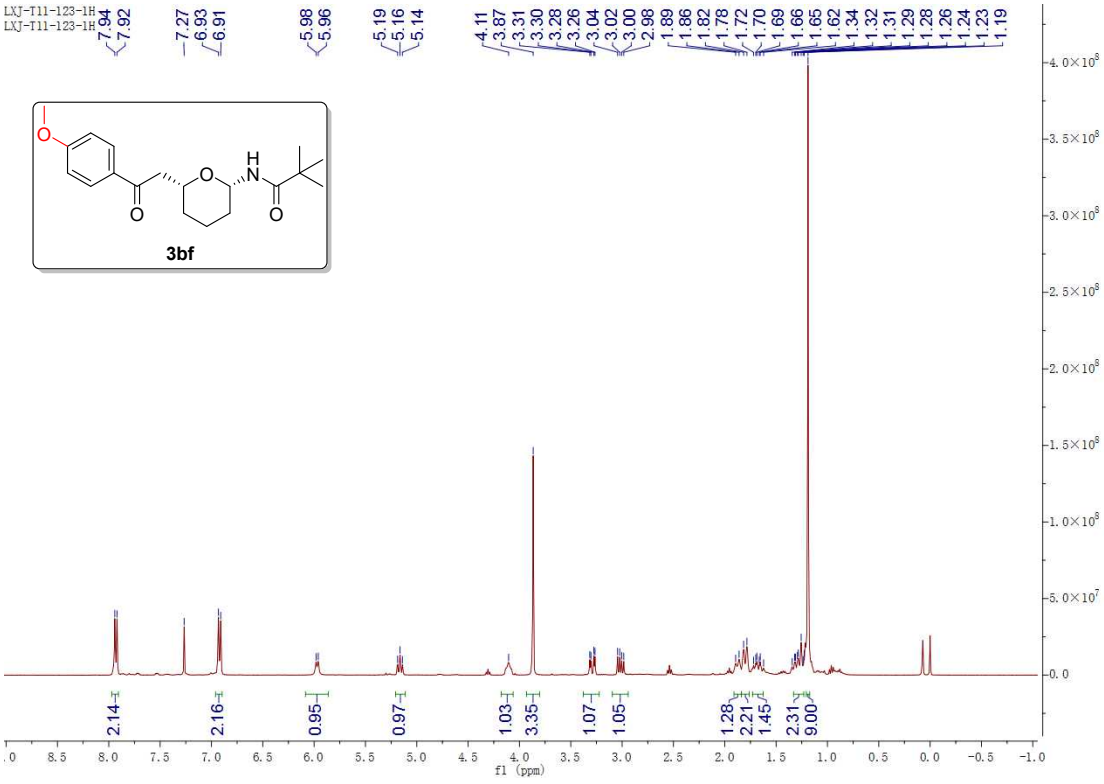
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

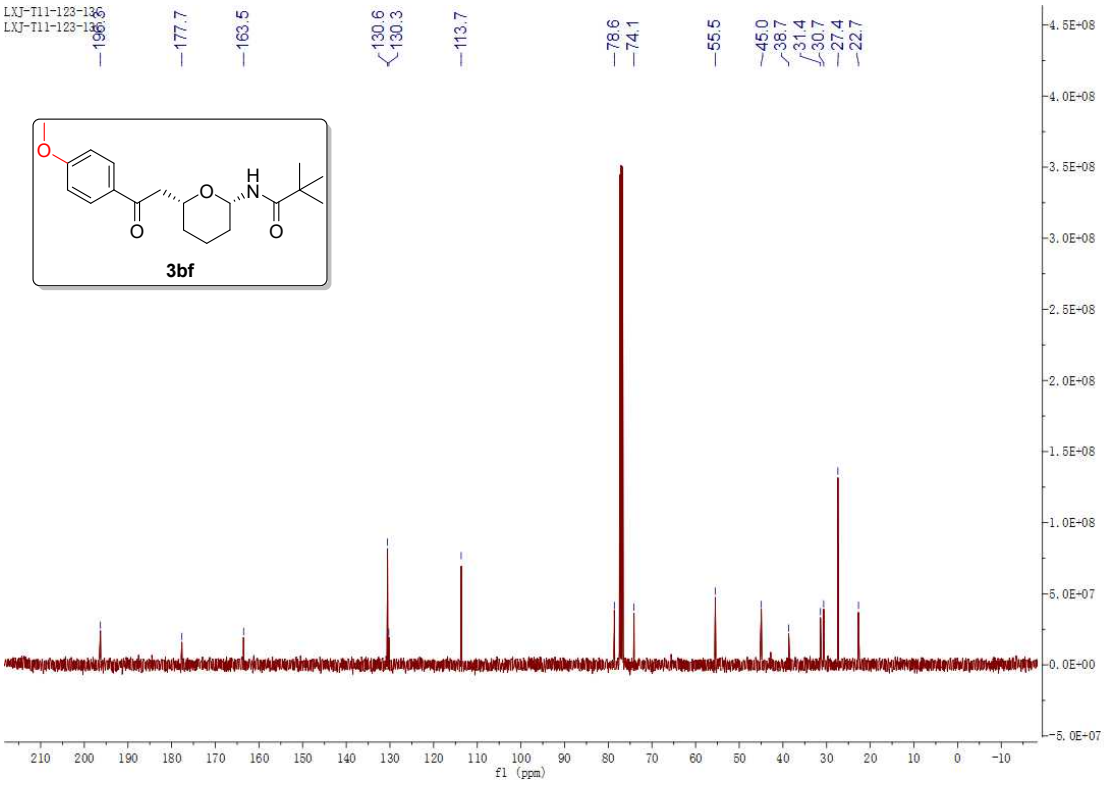
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	15.260	3126831	95.087	BB
2	20.480	161565	4.913	BB
		3288396	100.000	

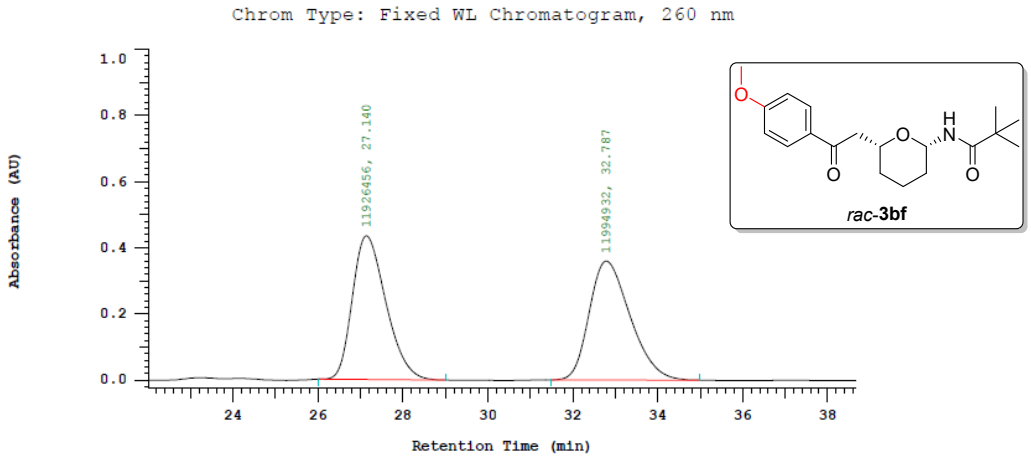
The ^{1}H NMR spectrum of 3bf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3bf (101 MHz, $CDCl_3$)



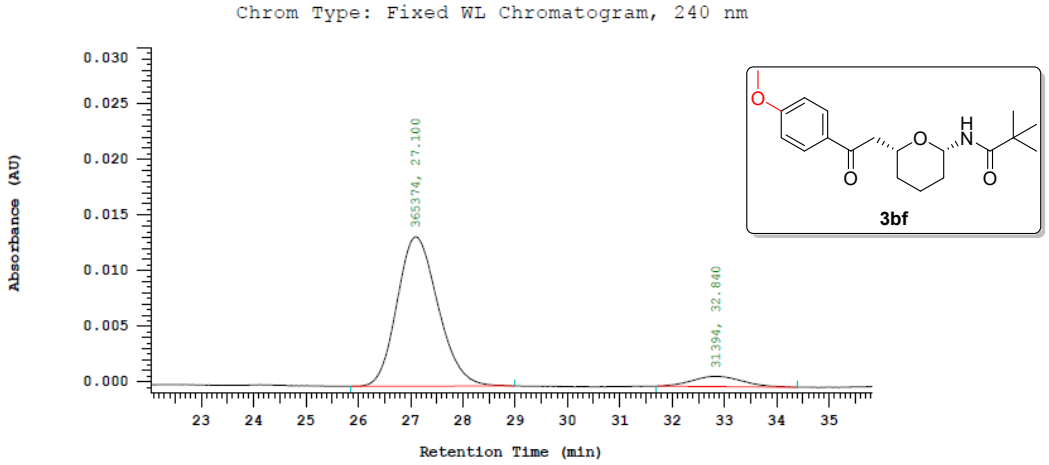
The HPLC of racemic 3bf



Chrom Type: Fixed WL Chromatogram, 260 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	27.140	11926456	49.857	BB
2	32.787	11994932	50.143	BB
		23921388	100.000	

The HPLC of chiral 3bf



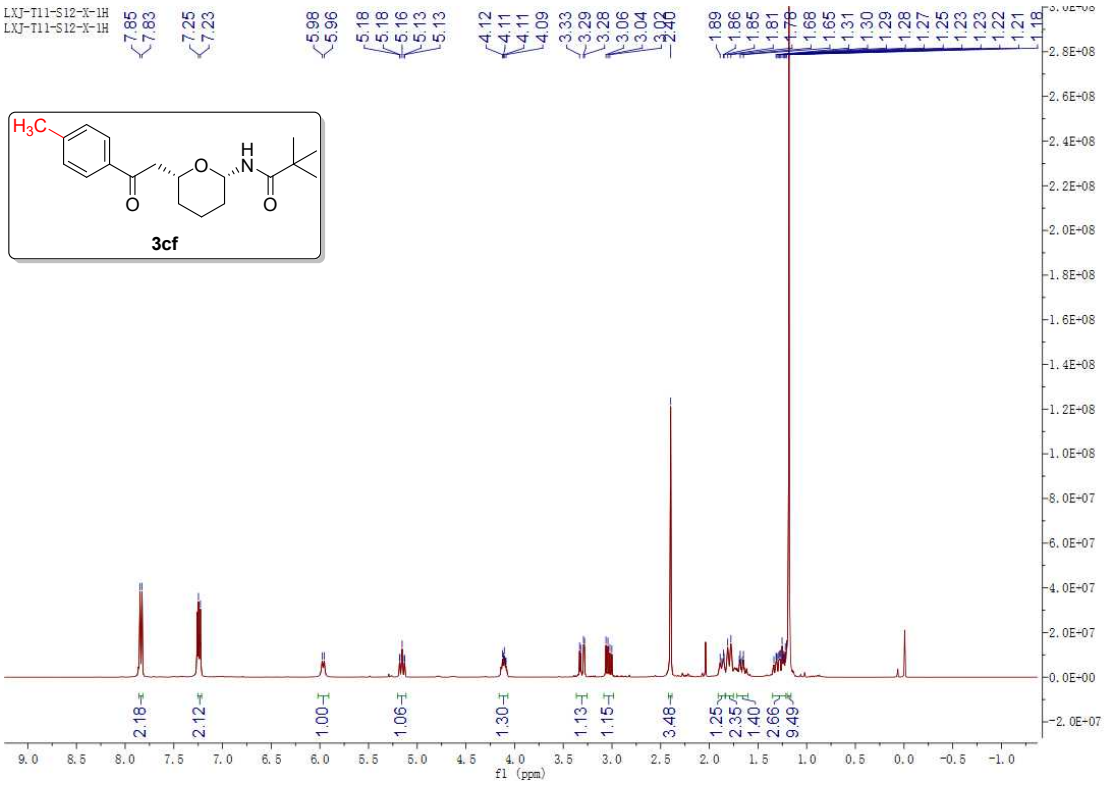
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

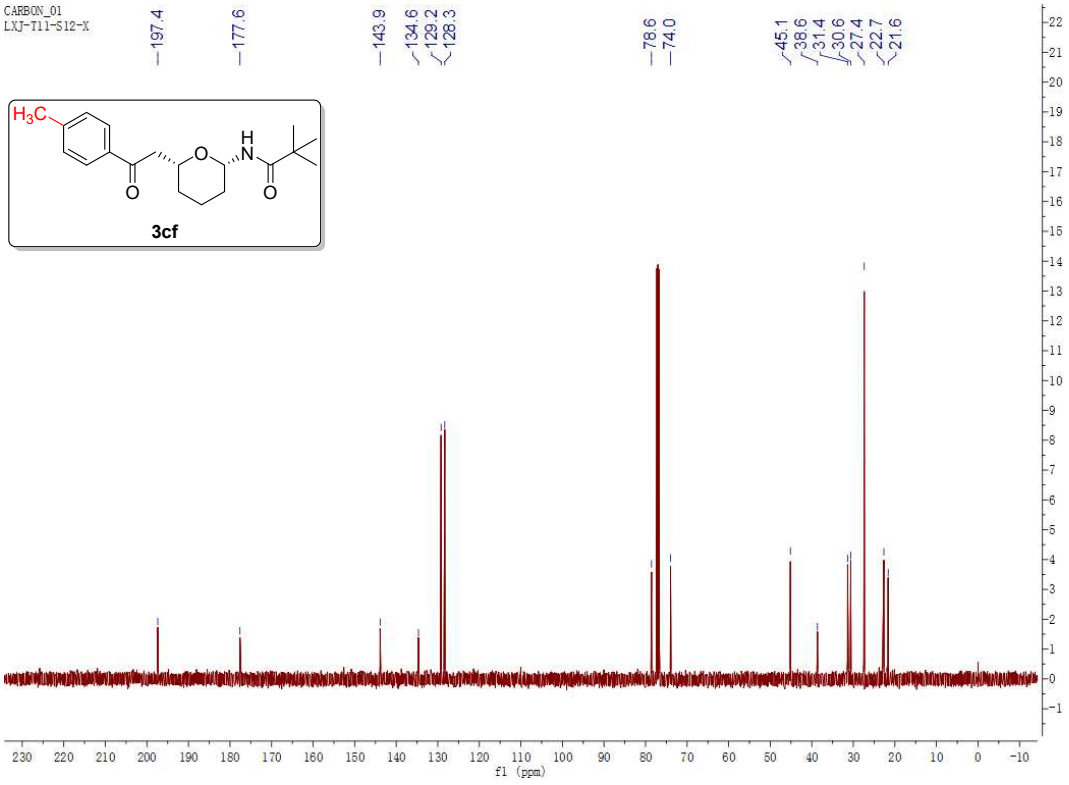
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	27.100	365374	92.088	BB
2	32.840	31394	7.912	BB
		396768	100.000	

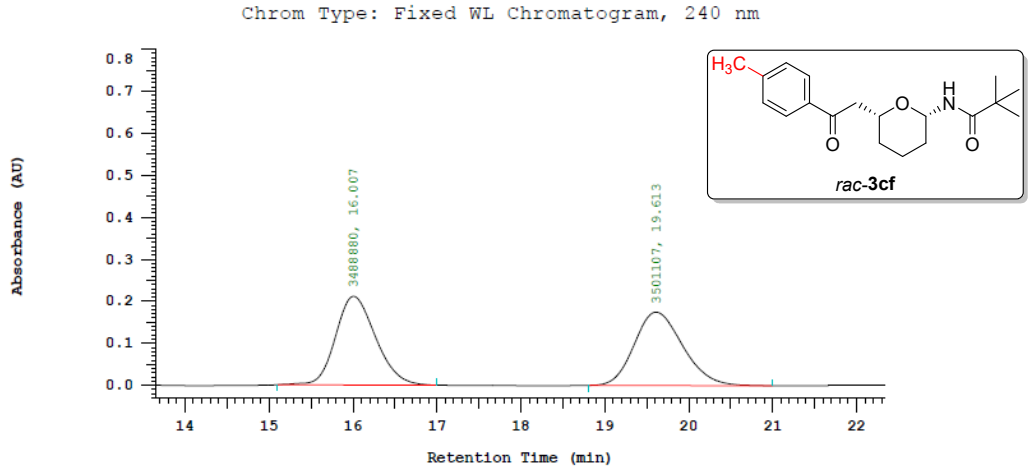
The ^{1}H NMR spectrum of 3cf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3cf (125 MHz, $CDCl_3$)



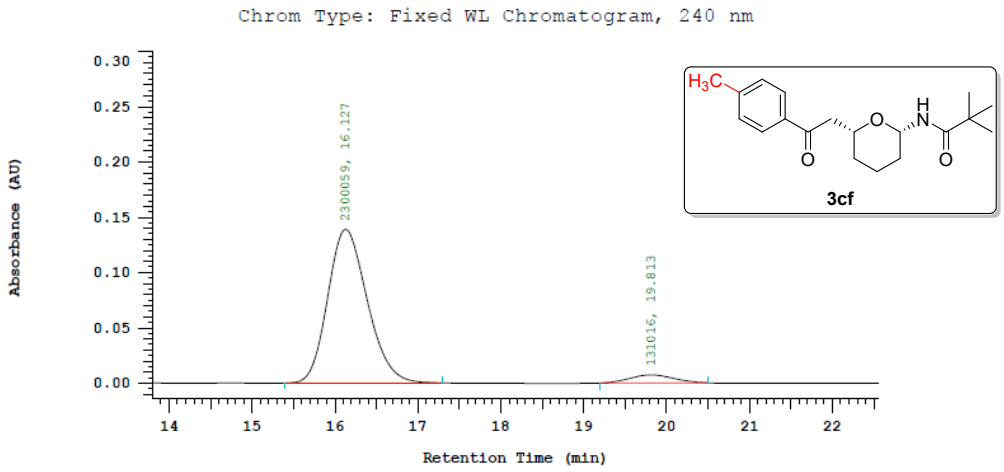
The HPLC of racemic 3cf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.007	3488880	49.913	BB
2	19.613	3501107	50.087	BB
		6989987	100.000	

The HPLC of chiral 3cf



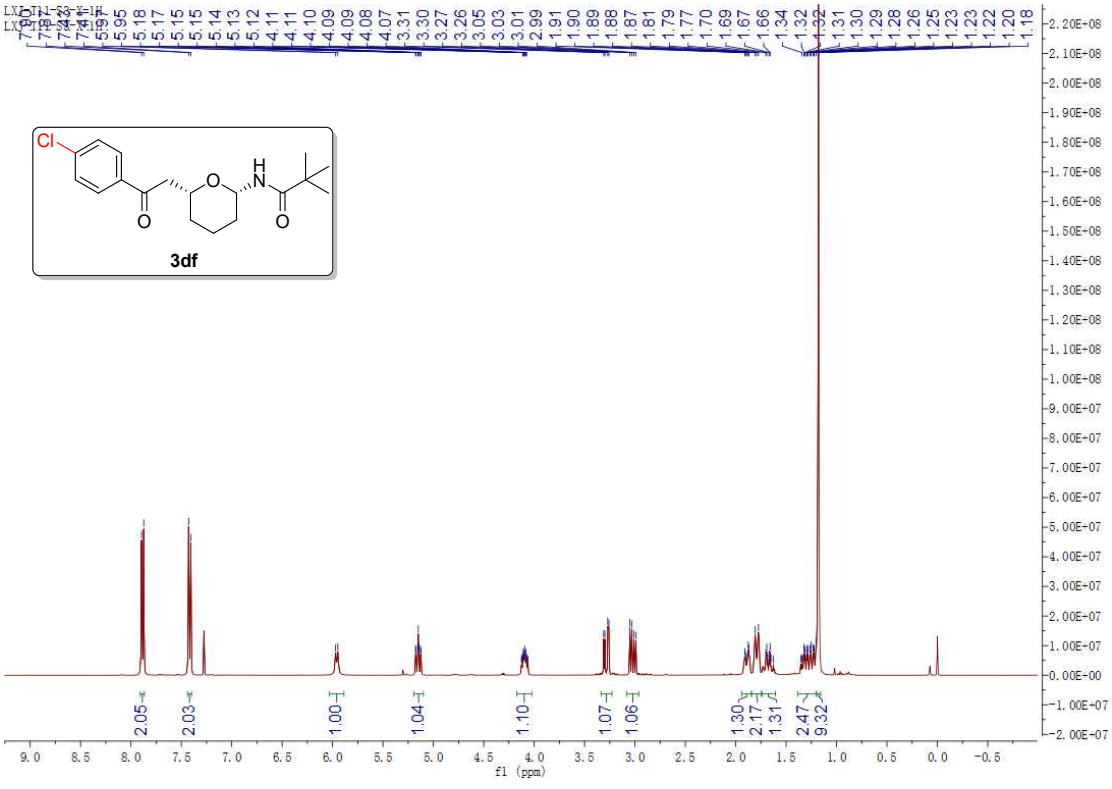
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

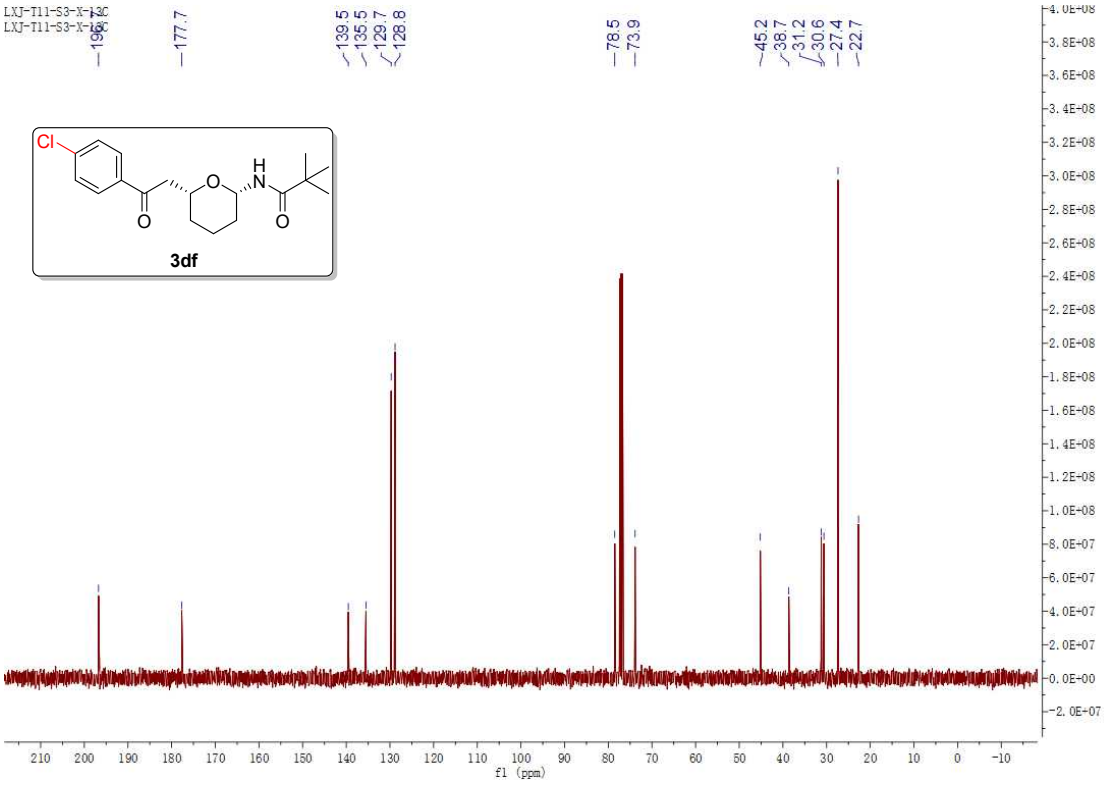
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	16.127	2300059	94.611	BB
2	19.813	131016	5.389	BB
		2431075	100.000	

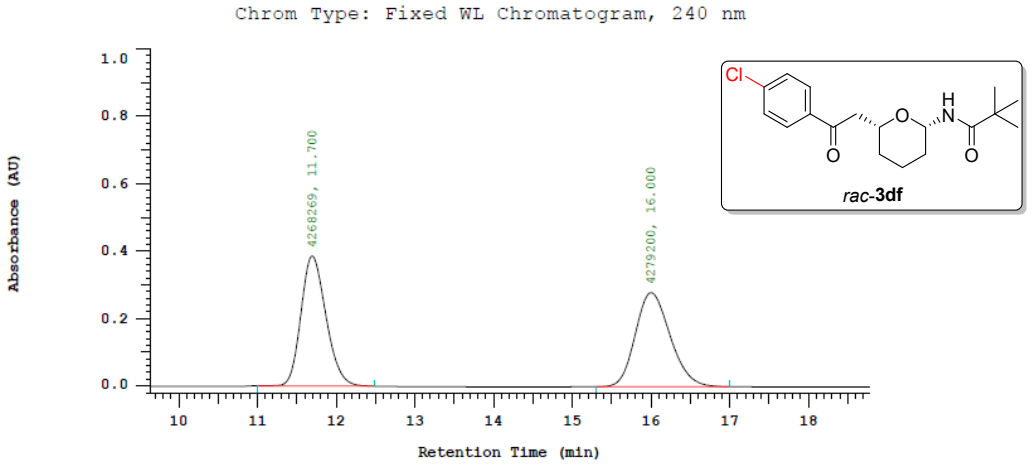
The ^{1}H NMR spectrum of 3df (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3df (101 MHz, $CDCl_3$)



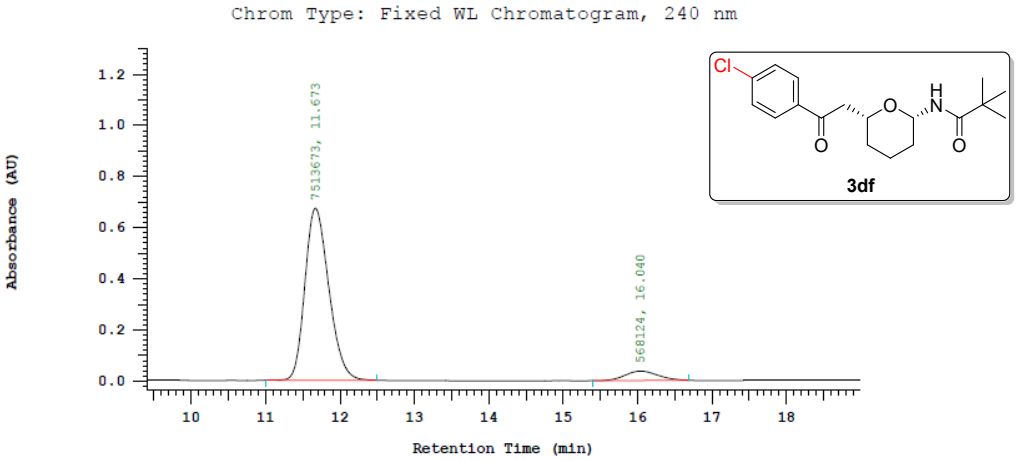
The HPLC of racemic 3df



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.700	4268269	49.936	BB
2	16.000	4279200	50.064	BB
		8547469	100.000	

The HPLC of chiral 3df



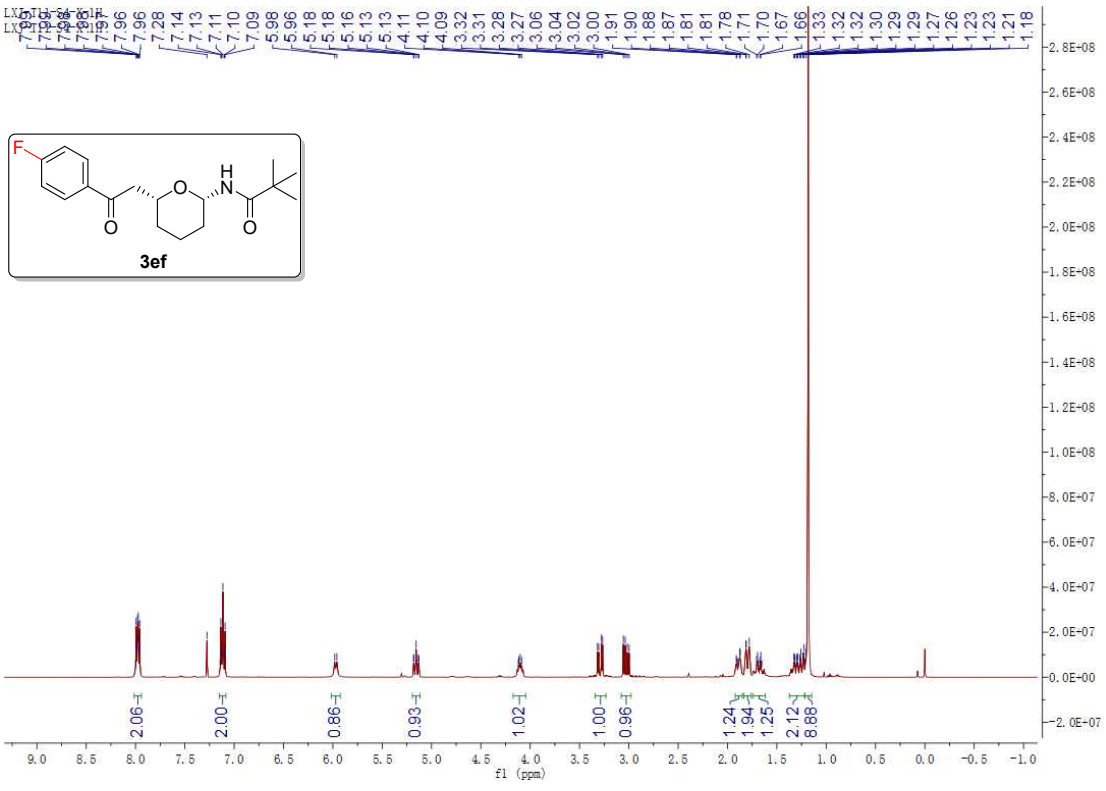
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

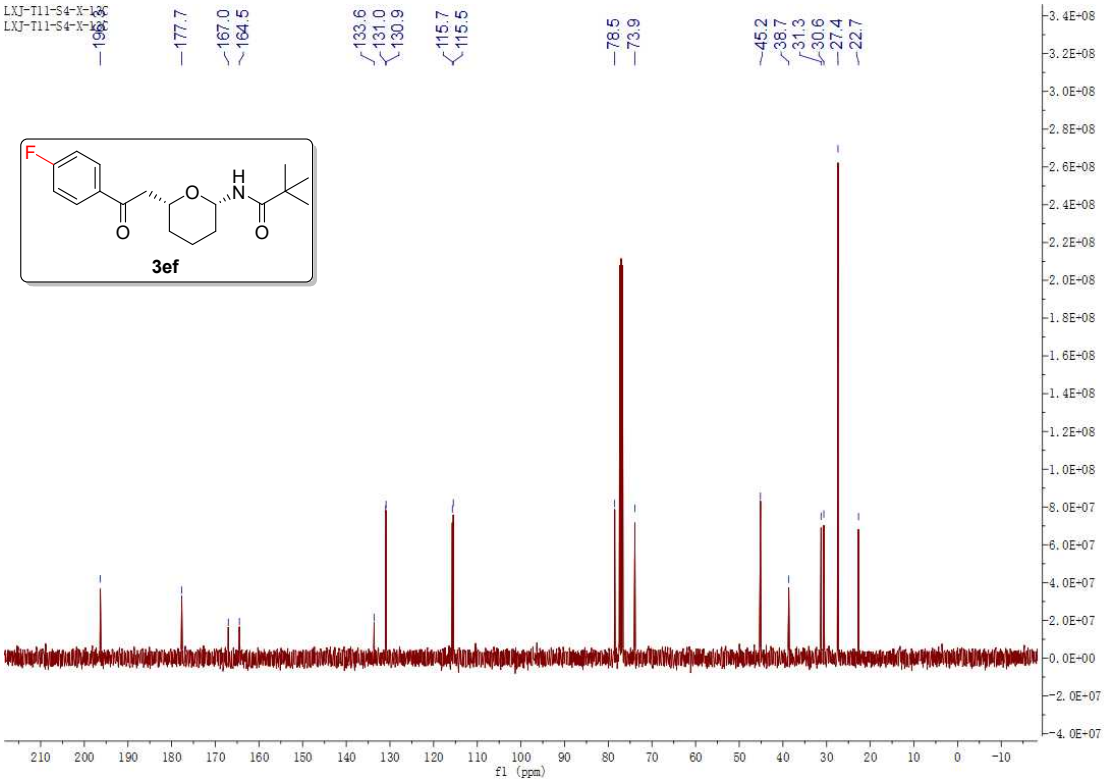
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.673	7513673	92.970	BB
2	16.040	568124	7.030	BB
		8081797	100.000	

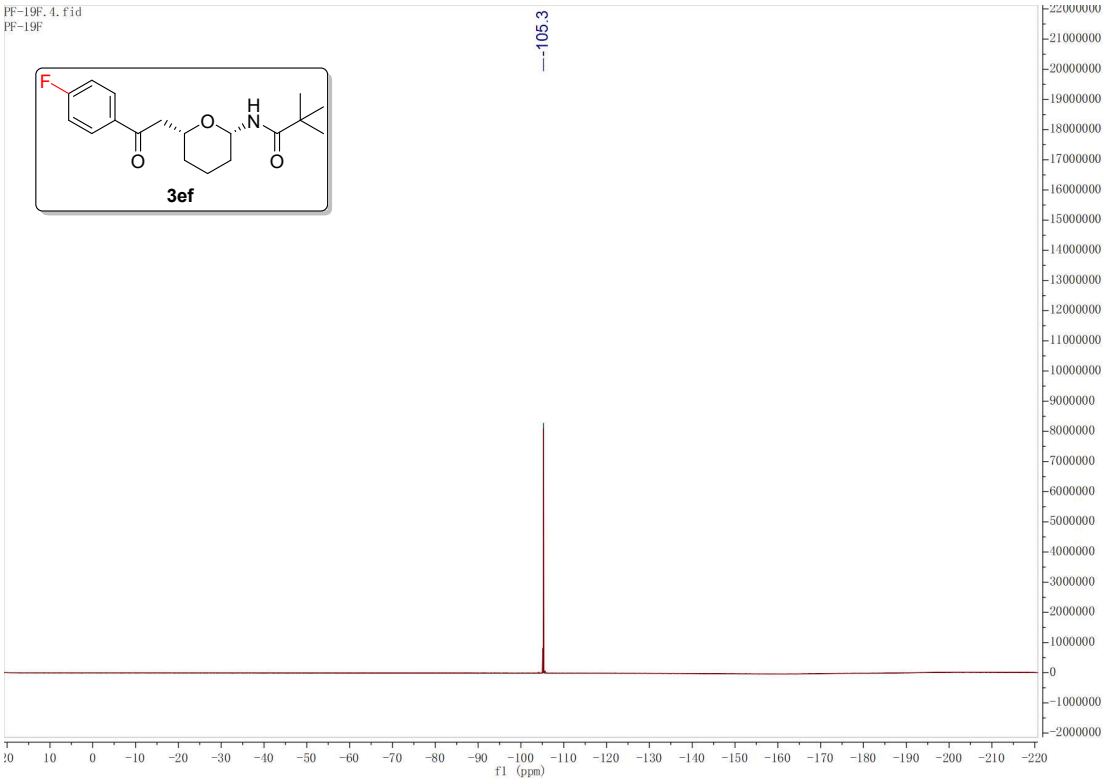
The ^{1}H NMR spectrum of 3ef (400 MHz, $CDCl_3$)



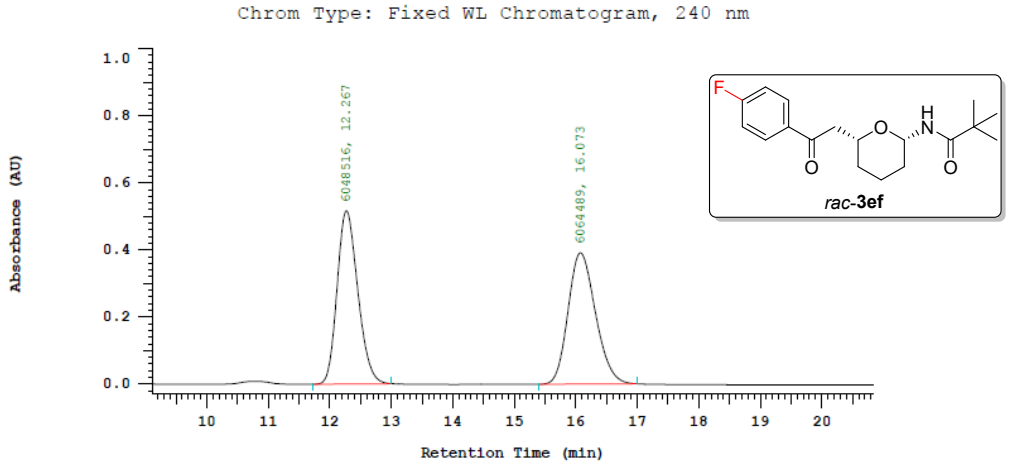
The ^{13}C NMR spectrum of 3ef (101 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 3ef (376 MHz, $CDCl_3$)



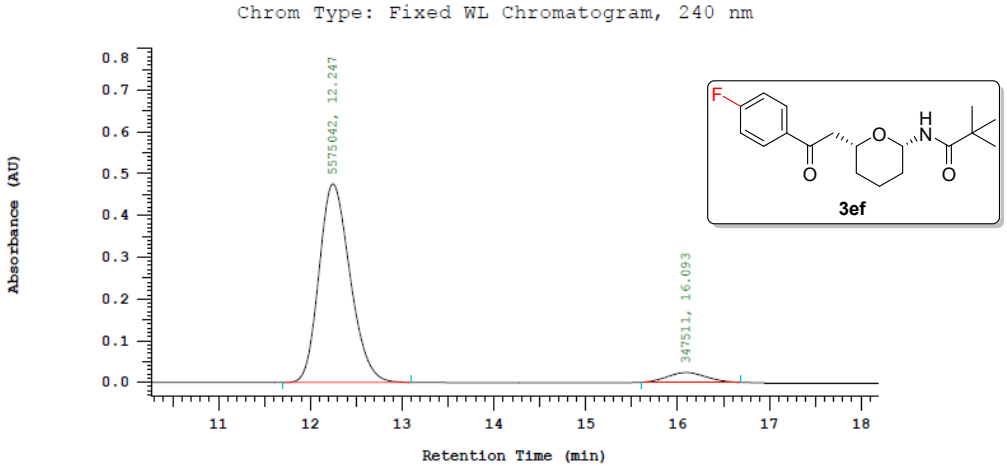
The HPLC of racemic 3ef



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.267	6048516	49.934	BB
2	16.073	6064489	50.066	BB
		12113005	100.000	

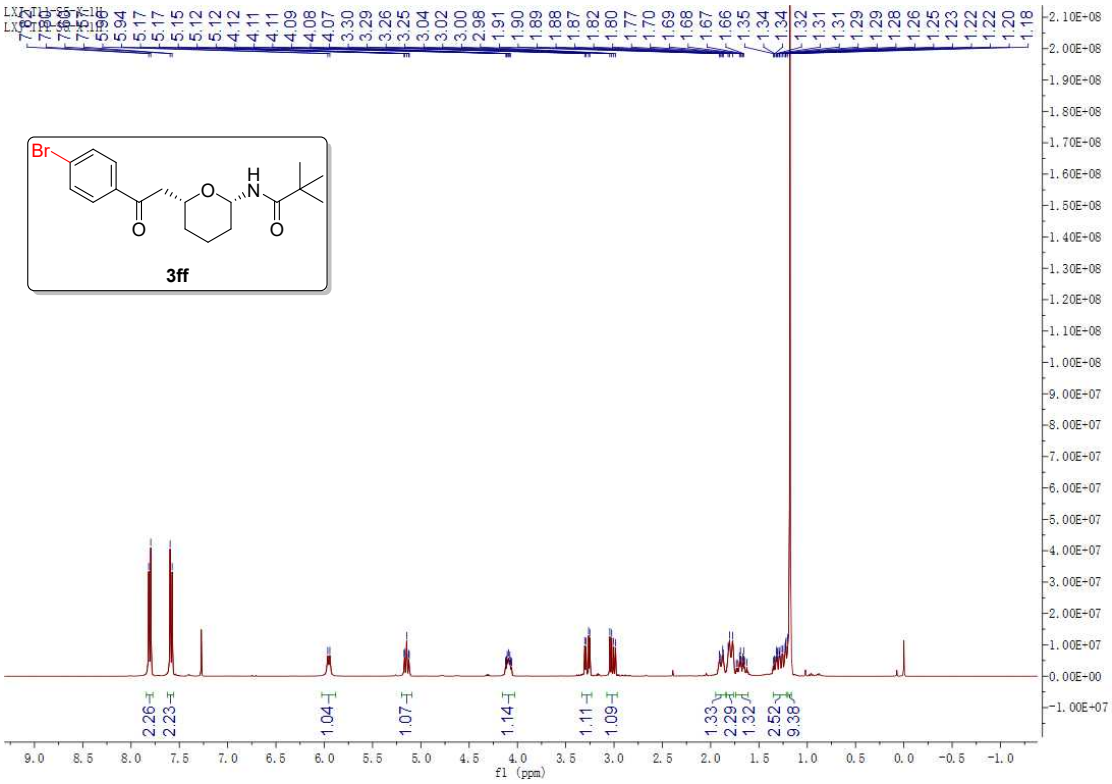
The HPLC of chiral 3ef



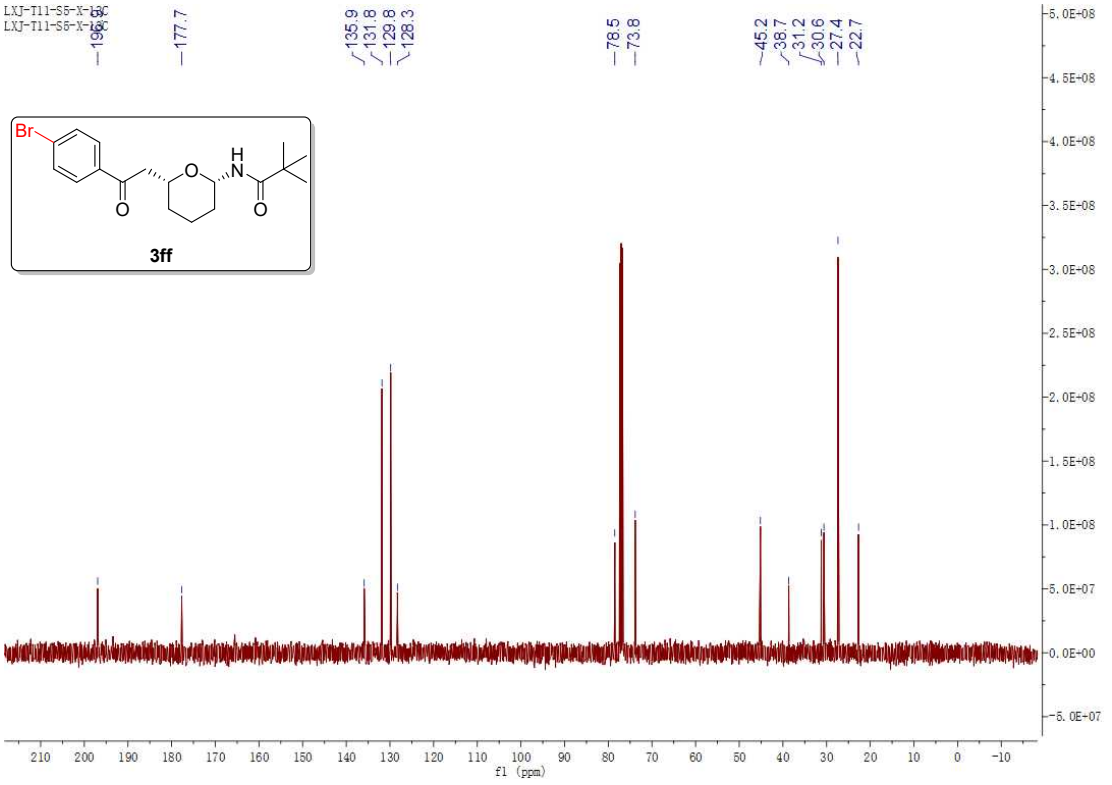
Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.247	5575042	94.132	BB
2	16.093	347511	5.868	BB
		5922553	100.000	

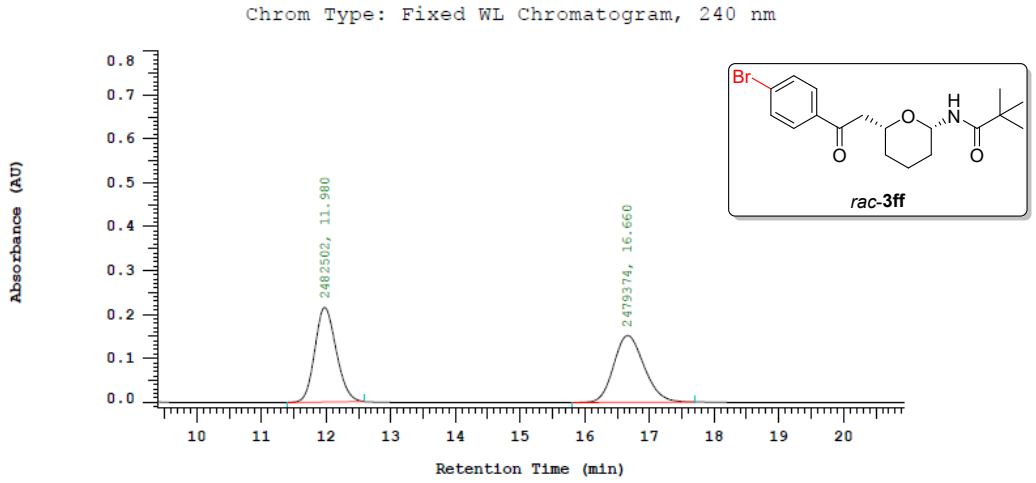
The ^{1}H NMR spectrum of 3ff (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3ff (101 MHz, $CDCl_3$)



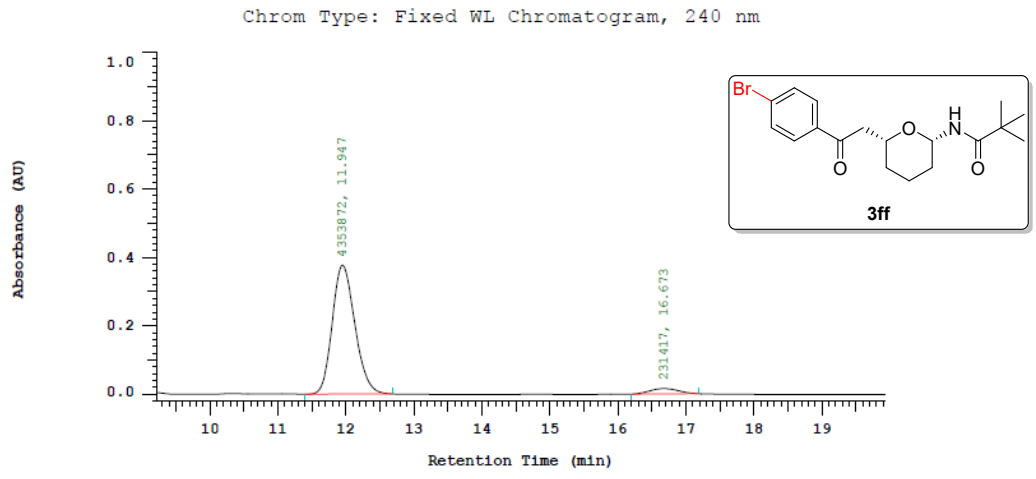
The HPLC of racemic 3ff



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.980	2482502	50.032	BB
2	16.660	2479374	49.968	BB
		4961876	100.000	

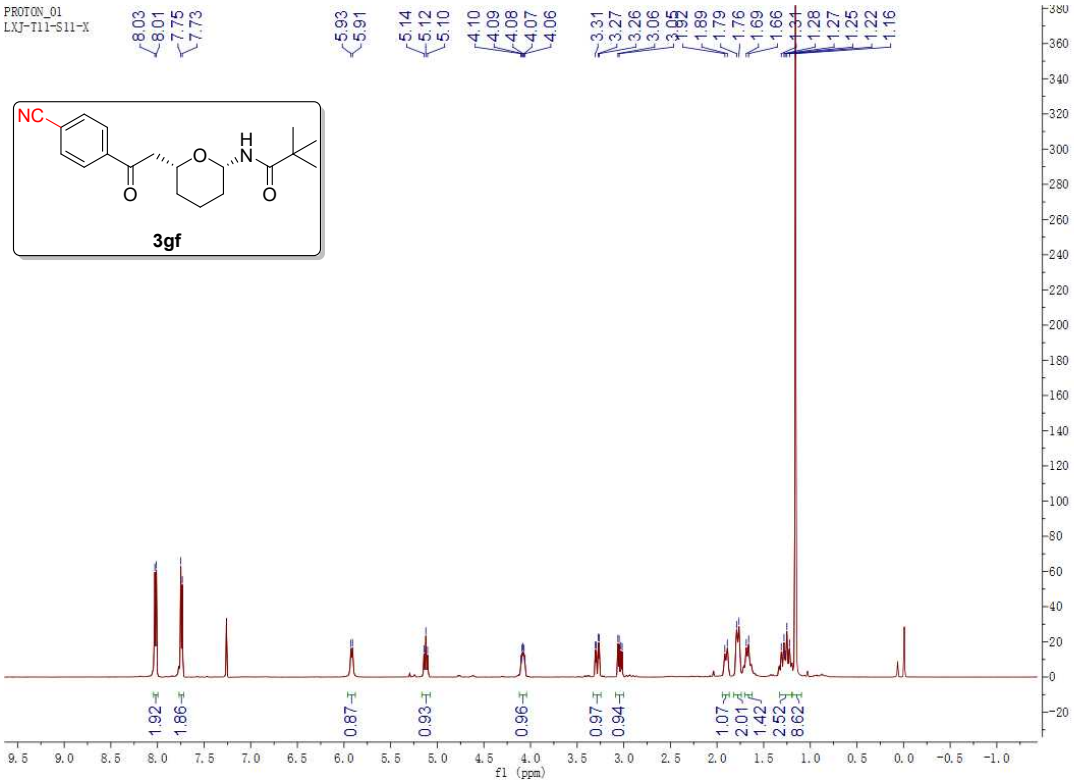
The HPLC of chiral 3ff



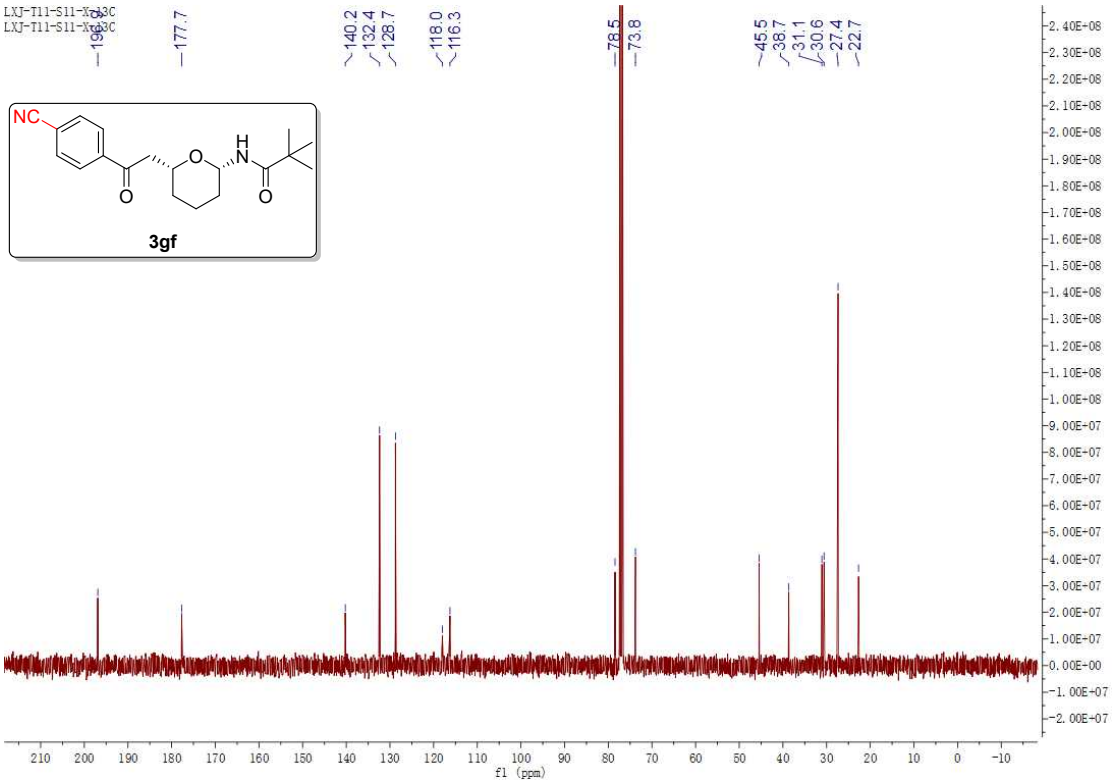
Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.947	4353872	94.953	BB
2	16.673	231417	5.047	BB
		4585289	100.000	

The ^{1}H NMR spectrum of 3gf (500 MHz, $CDCl_3$)

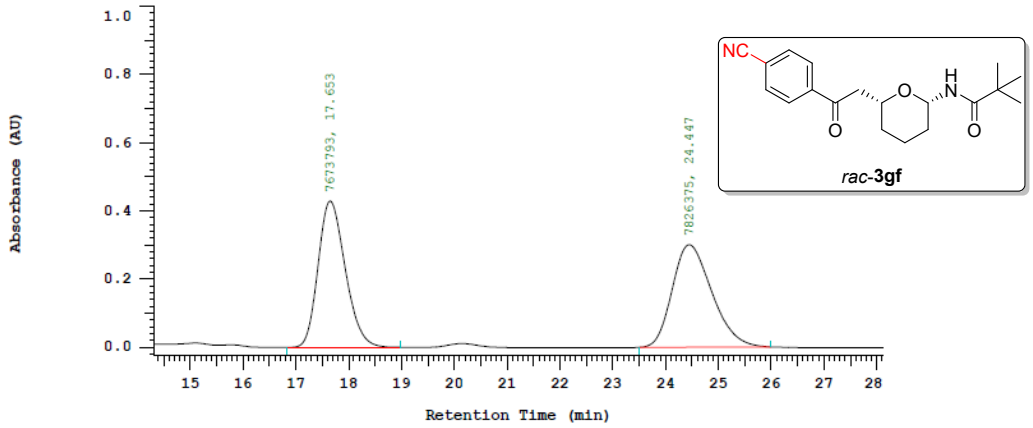


The ^{13}C NMR spectrum of 3gf (101 MHz, $CDCl_3$)



The HPLC of racemic 3gf

Chrom Type: Fixed WL Chromatogram, 240 nm



Chrom Type: Fixed WL Chromatogram, 240 nm

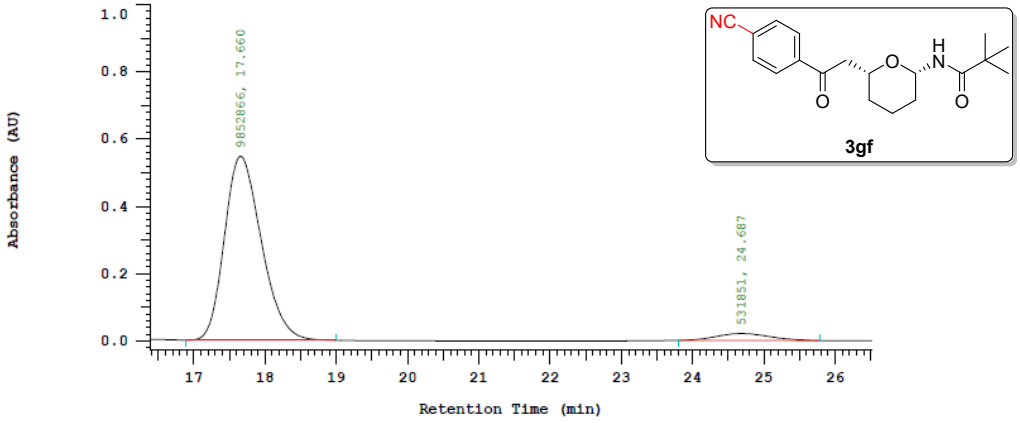
Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.653	7673793	49.508	BB
2	24.447	7826375	50.492	BB
		15500168	100.000	

The HPLC of chiral 3gf

Chrom Type: Fixed WL Chromatogram, 240 nm



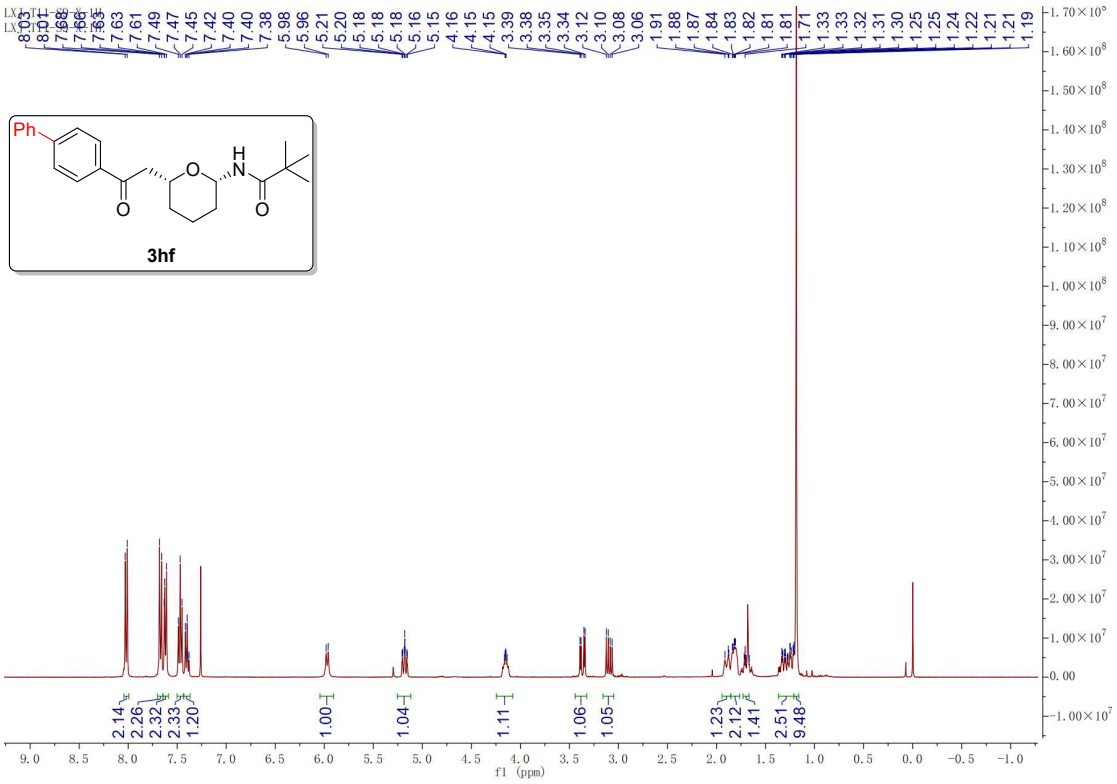
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

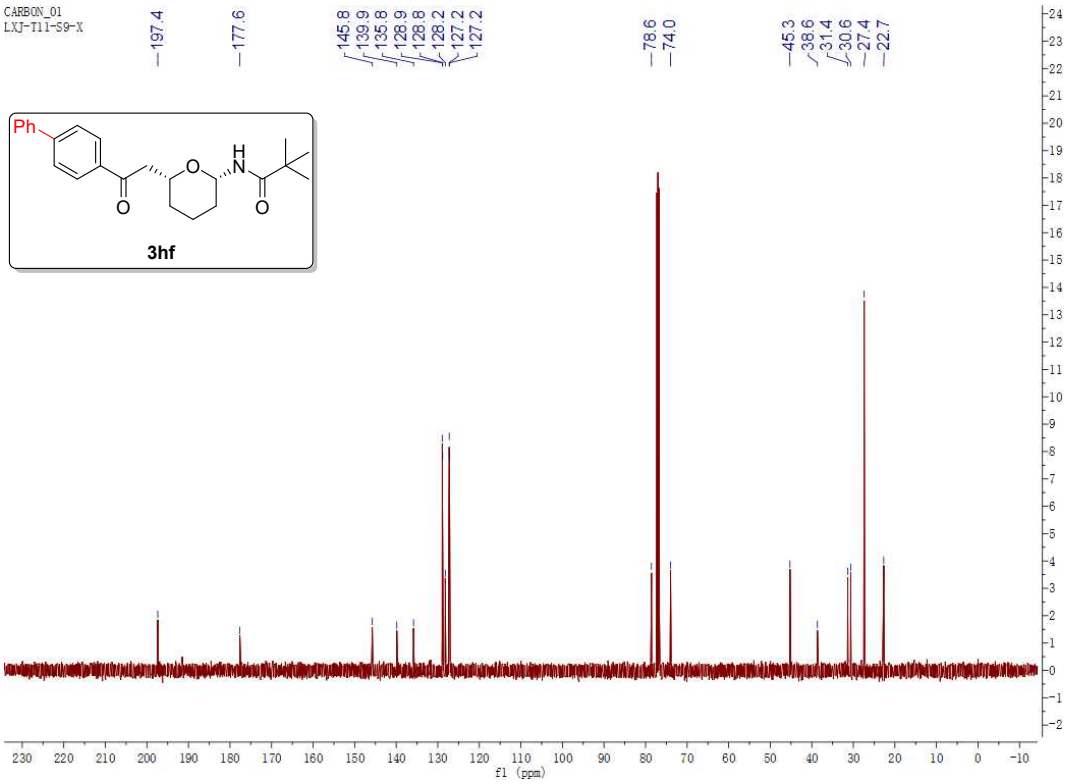
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.660	9852866	94.879	BB
2	24.687	531851	5.121	BB
		10384717	100.000	

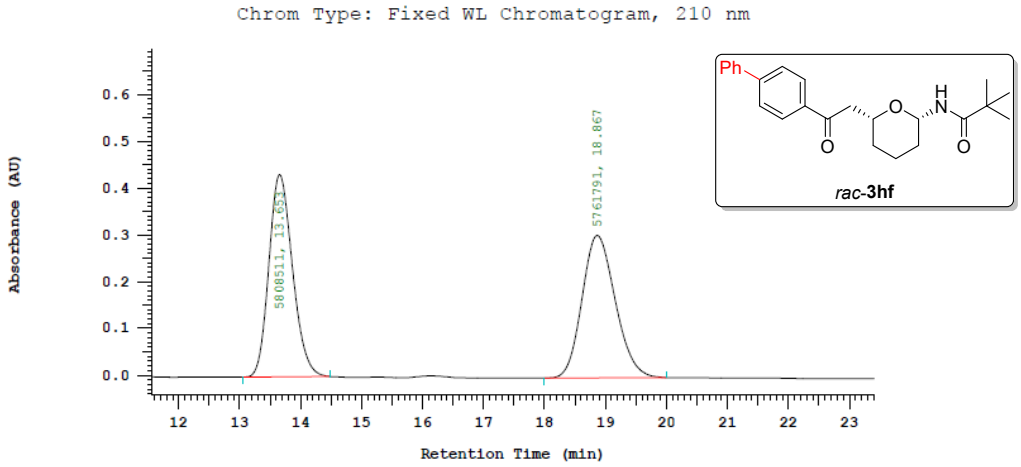
The ^{1}H NMR spectrum of 3hf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3hf (125 MHz, $CDCl_3$)



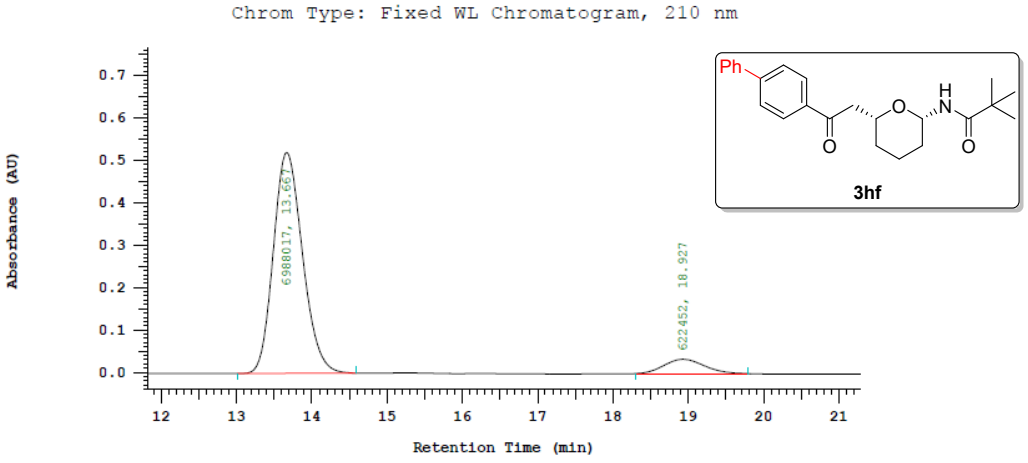
The HPLC of racemic 3hf



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.653	5808511	50.202	BB
2	18.867	5761791	49.798	BB
		11570302	100.000	

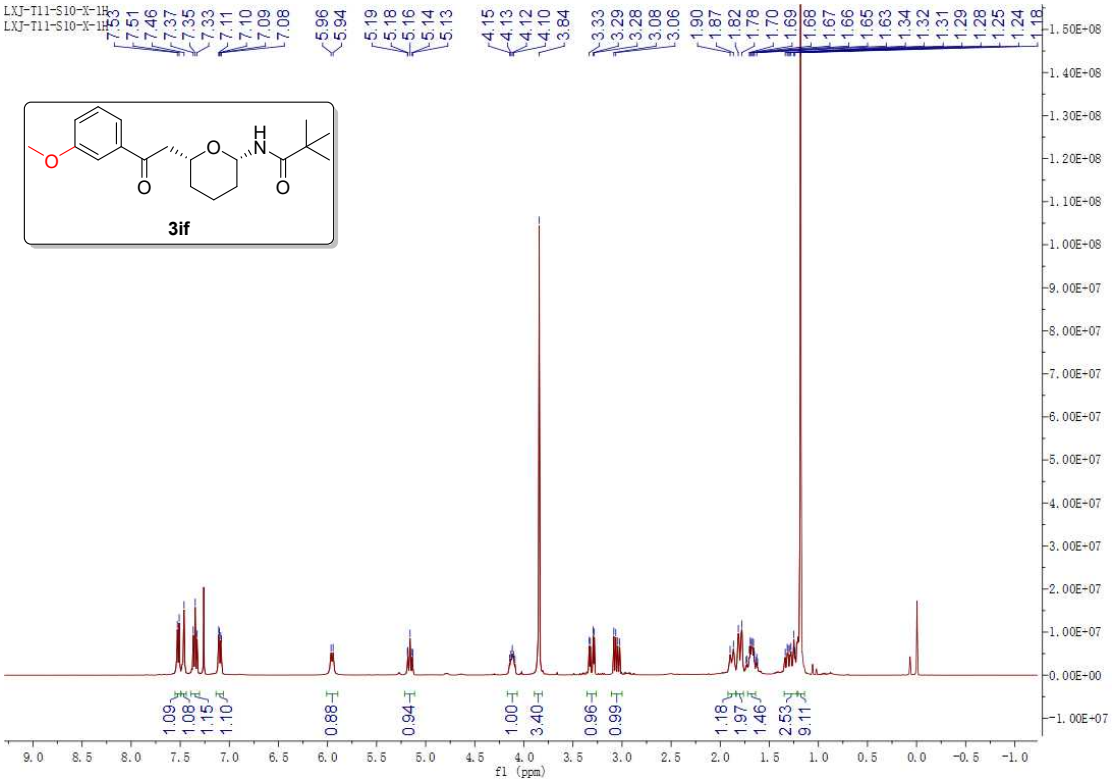
The HPLC of chiral 3hf



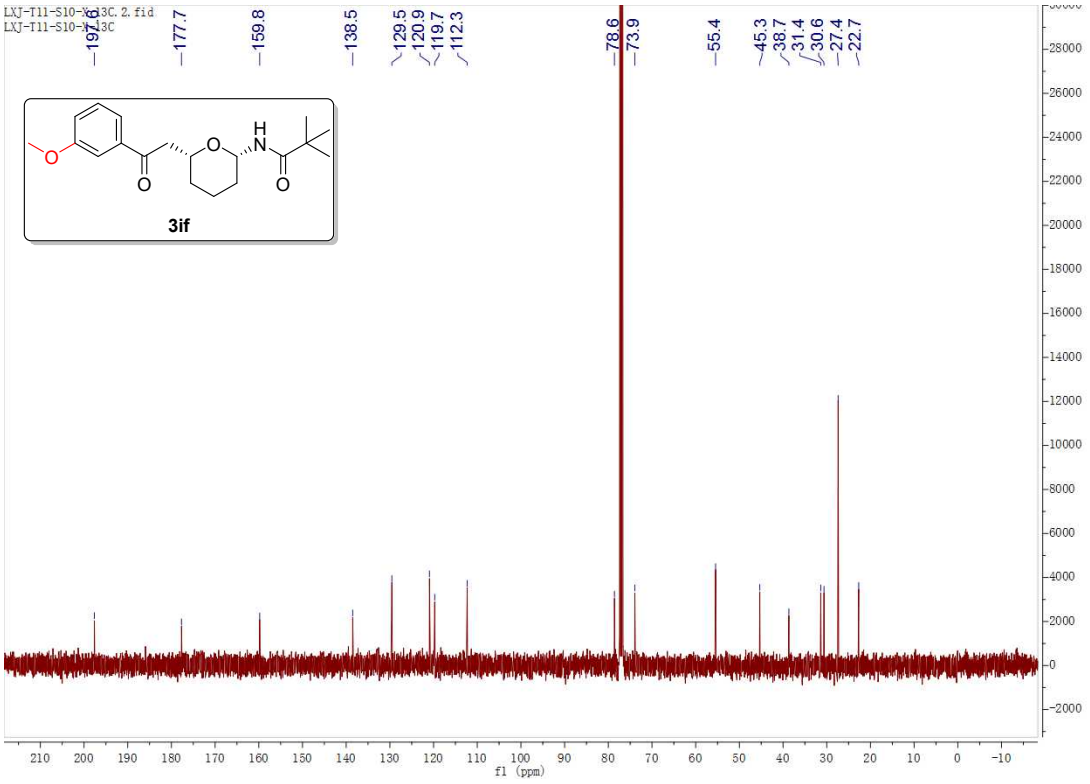
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.667	6988017	91.821	BB
2	18.927	622452	8.179	BB
		7610469	100.000	

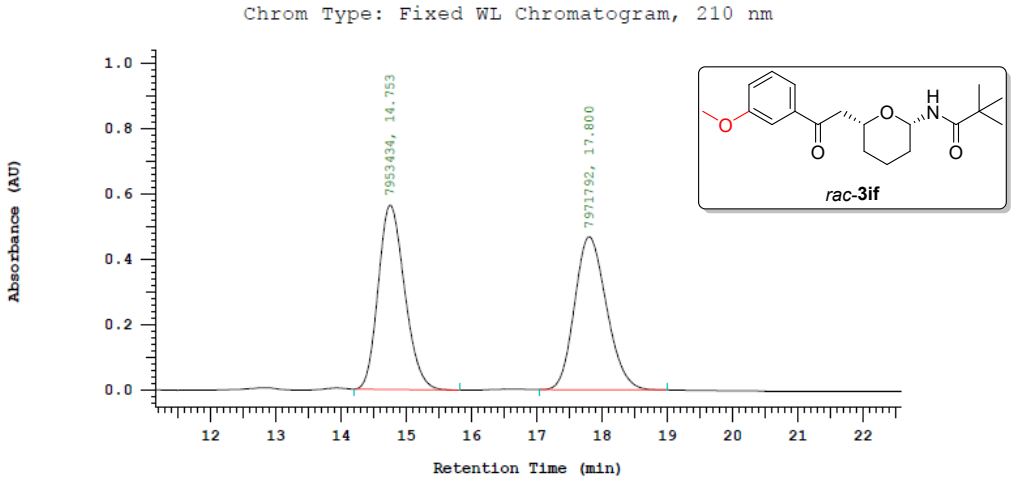
The ^{1}H NMR spectrum of 3if (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3if (101 MHz, $CDCl_3$)



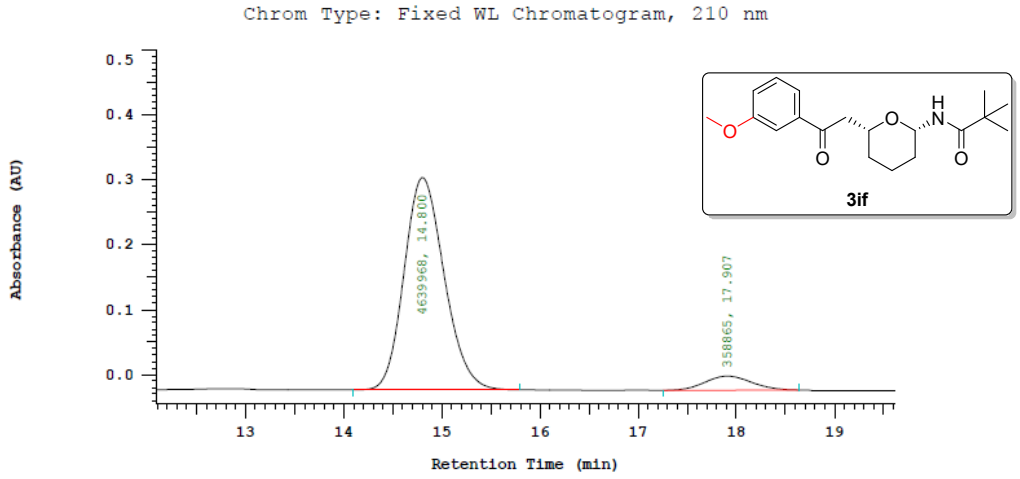
The HPLC of racemic 3if



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.753	7953434	49.942	BB
2	17.800	7971792	50.058	BB
		15925226	100.000	

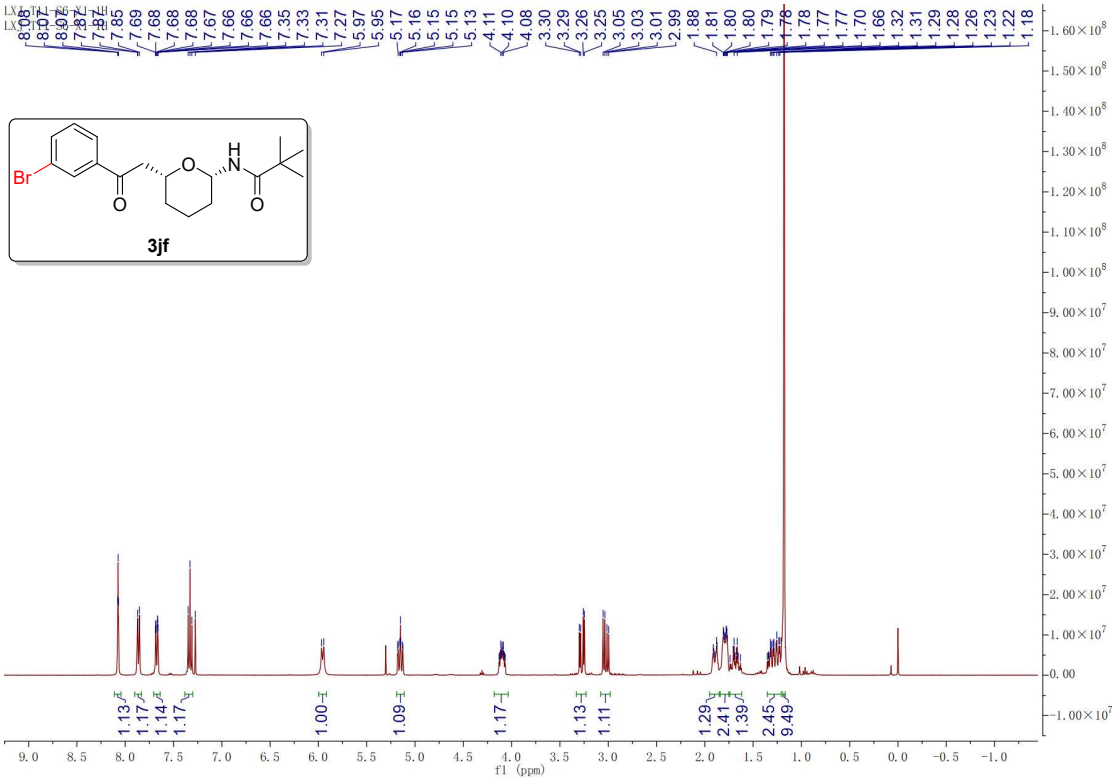
The HPLC of chiral 3if



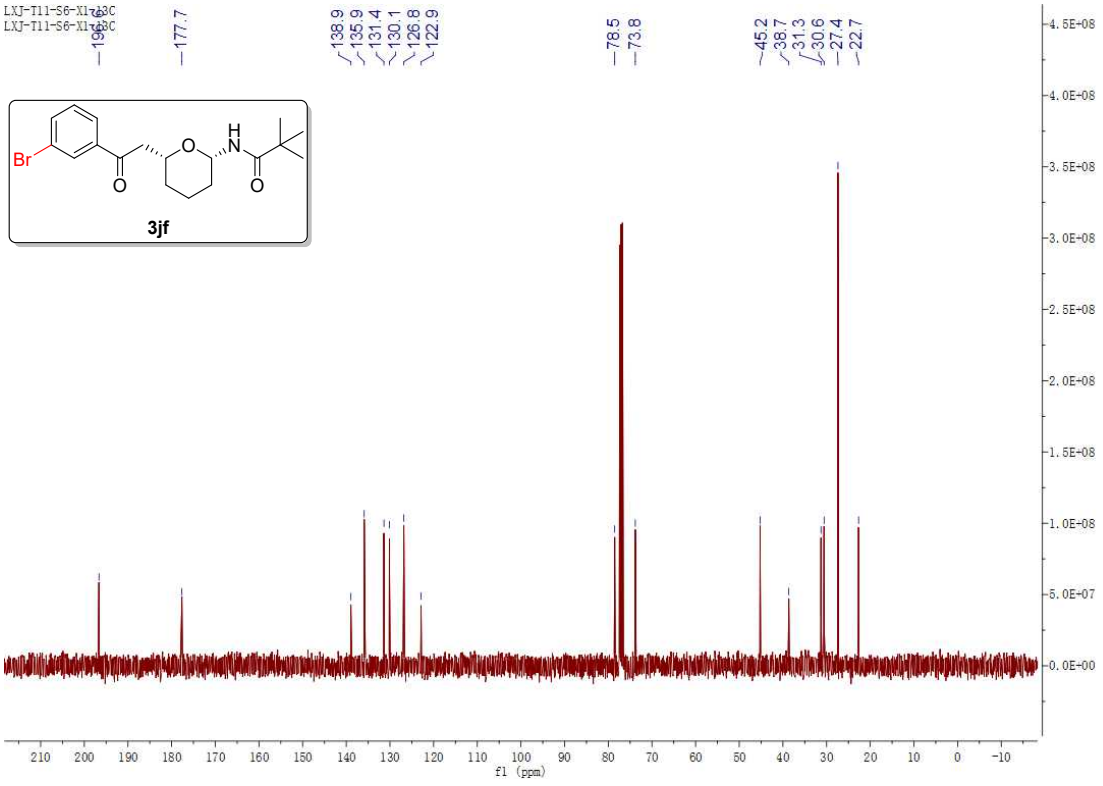
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	14.800	4639968	92.821	BB
2	17.907	358865	7.179	BB
		4998833	100.000	

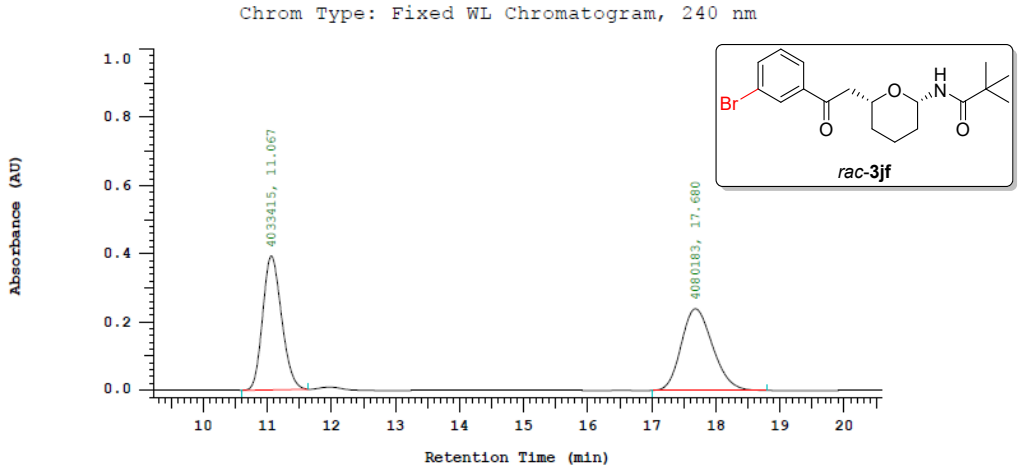
The ^{1}H NMR spectrum of 3jf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3jf (101 MHz, $CDCl_3$)



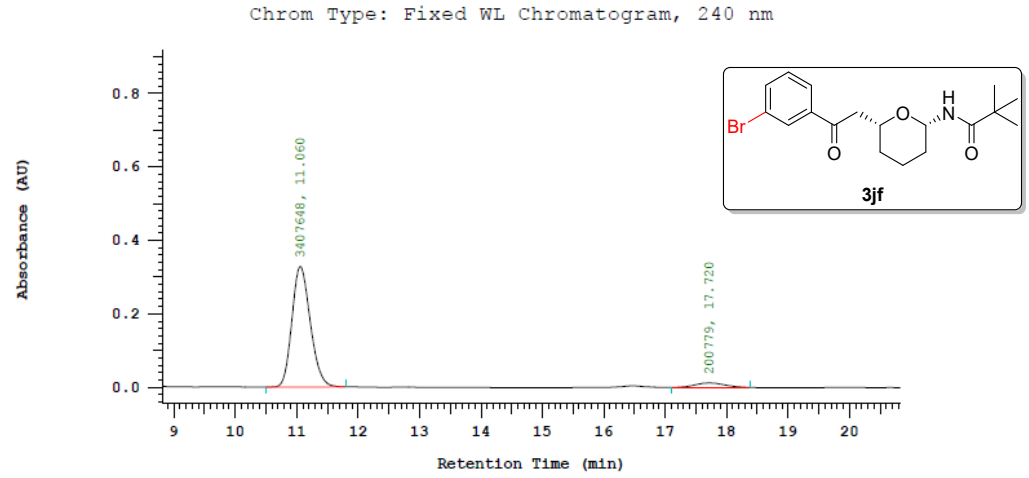
The HPLC of racemic 3jf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.067	4033415	49.712	BB
2	17.680	4080183	50.288	BB
		8113598	100.000	

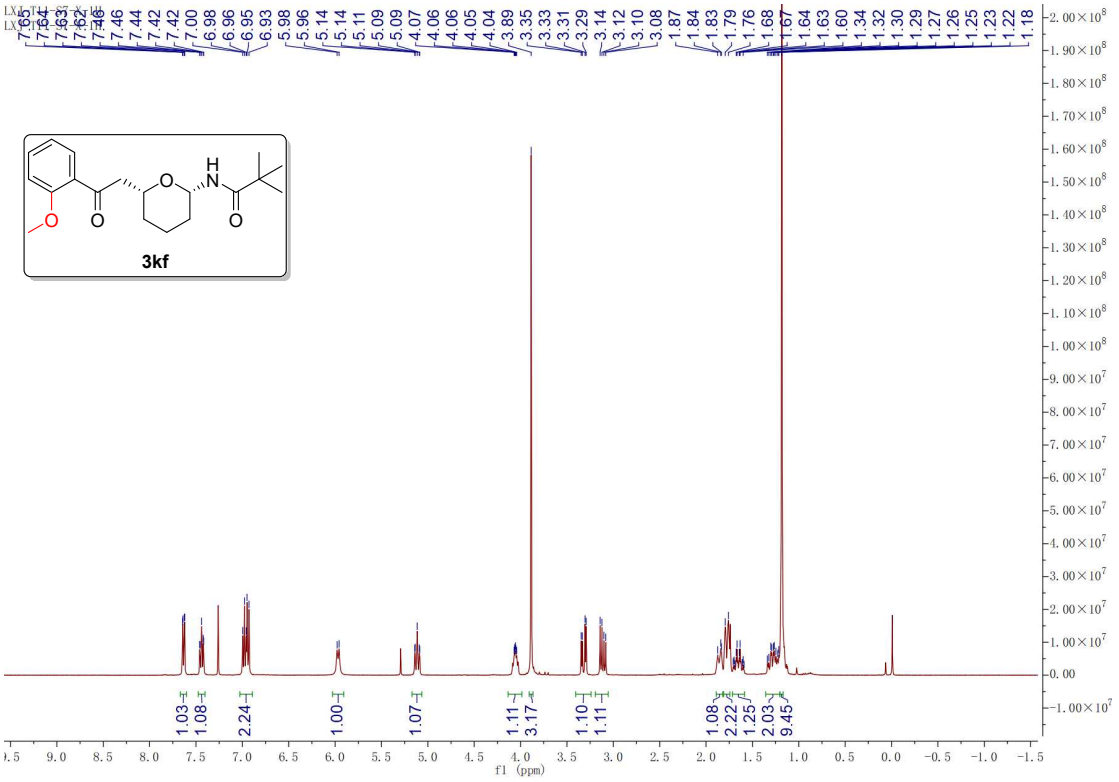
The HPLC of chiral 3jf



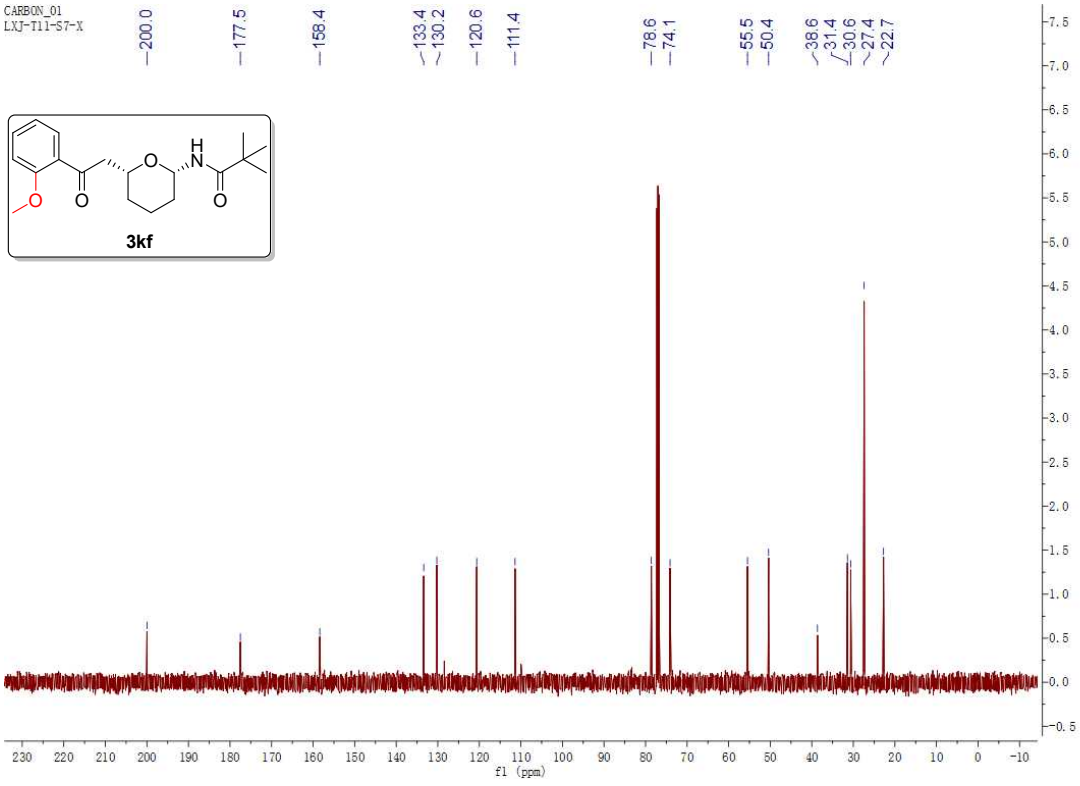
Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.060	3407648	94.436	BB
2	17.720	200779	5.564	BB
		3608427	100.000	

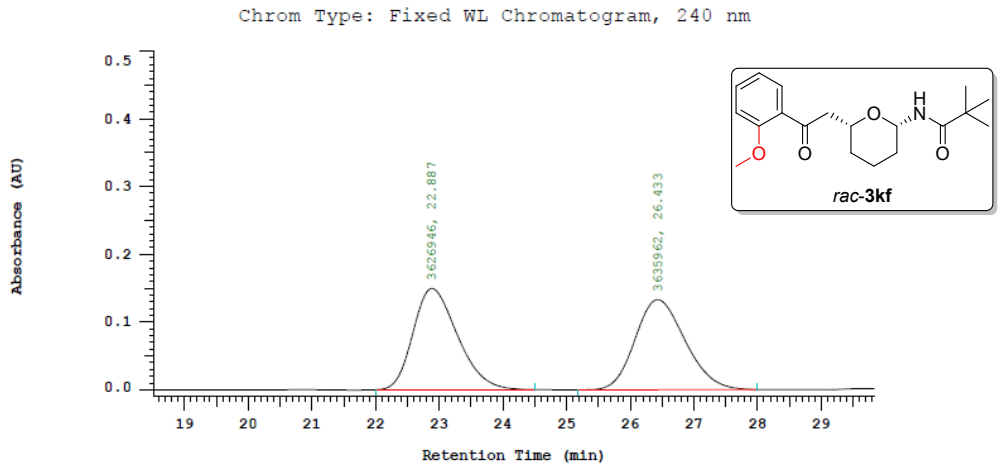
The ^{1}H NMR spectrum of 3kf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3kf (125 MHz, $CDCl_3$)



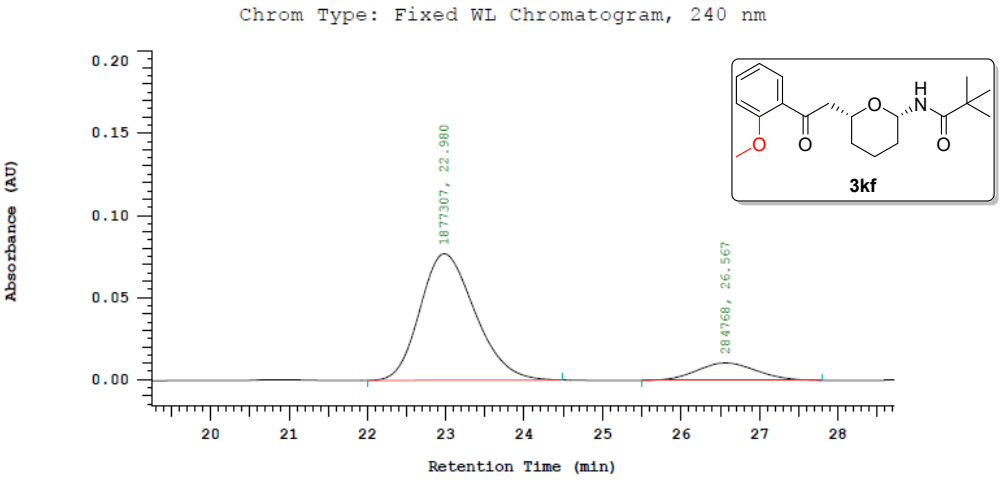
The HPLC of racemic 3kf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.887	3626946	49.938	BB
2	26.433	3635962	50.062	BB
		7262908	100.000	

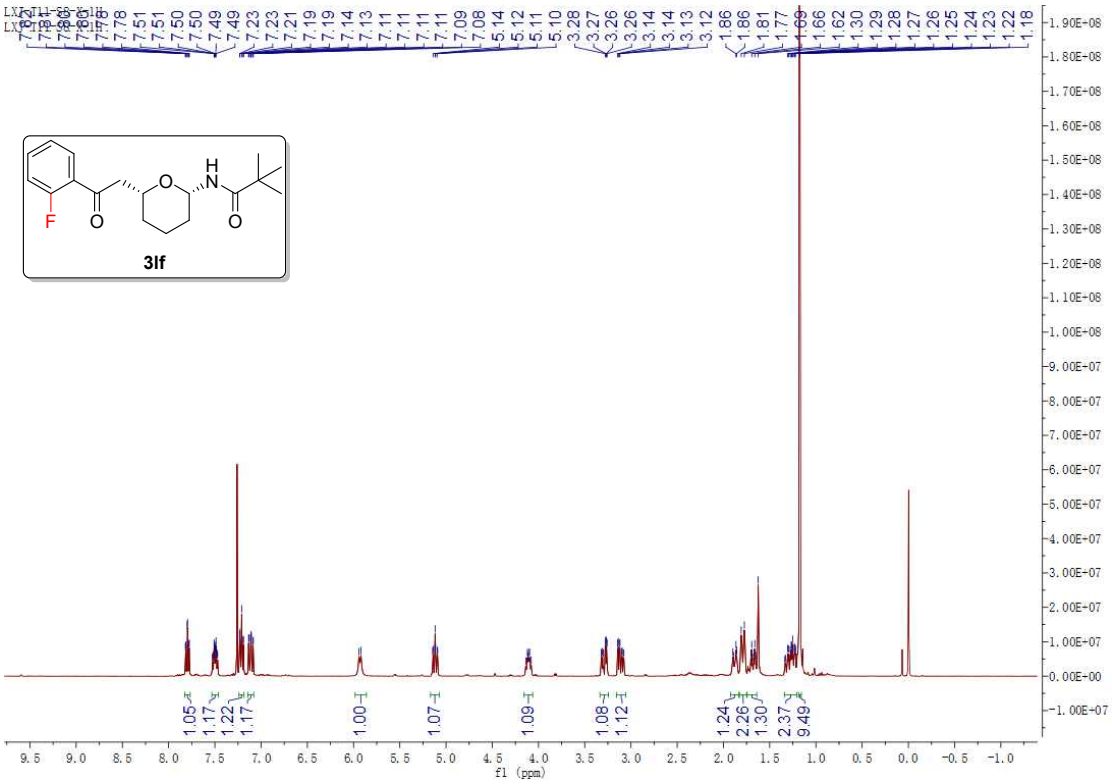
The HPLC of chiral 3kf



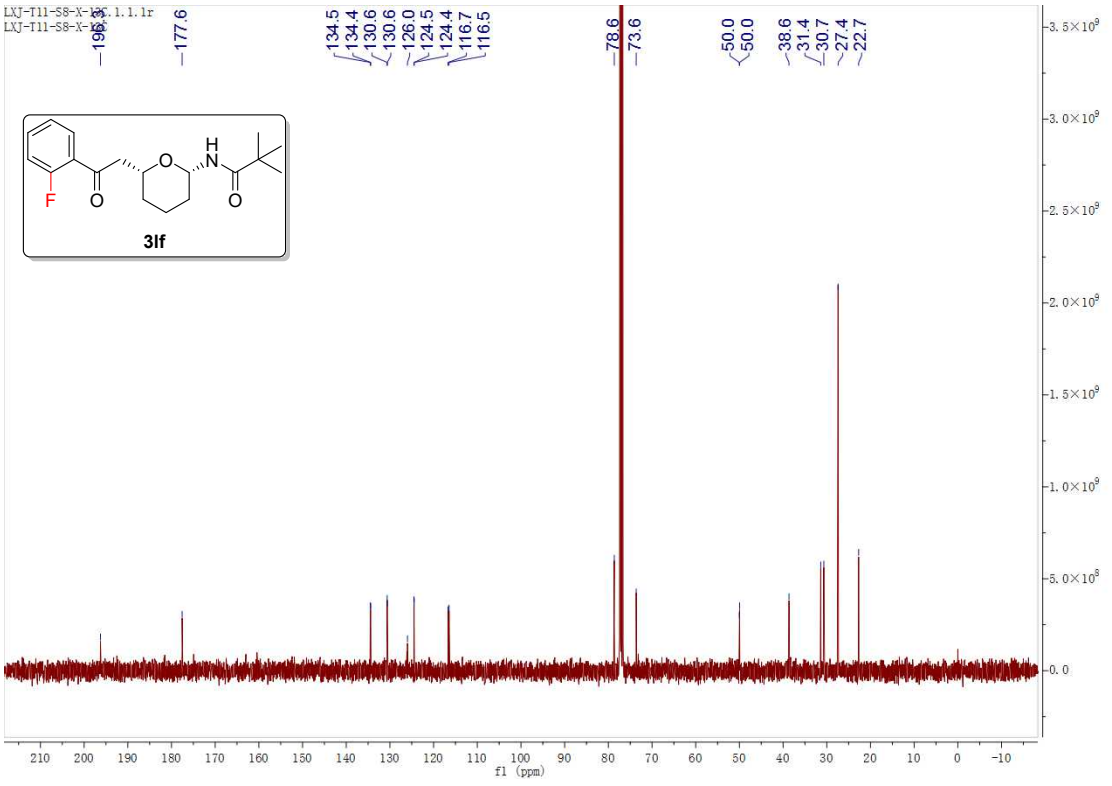
Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	22.980	1877307	86.829	BB
2	26.567	284768	13.171	BB
		2162075	100.000	

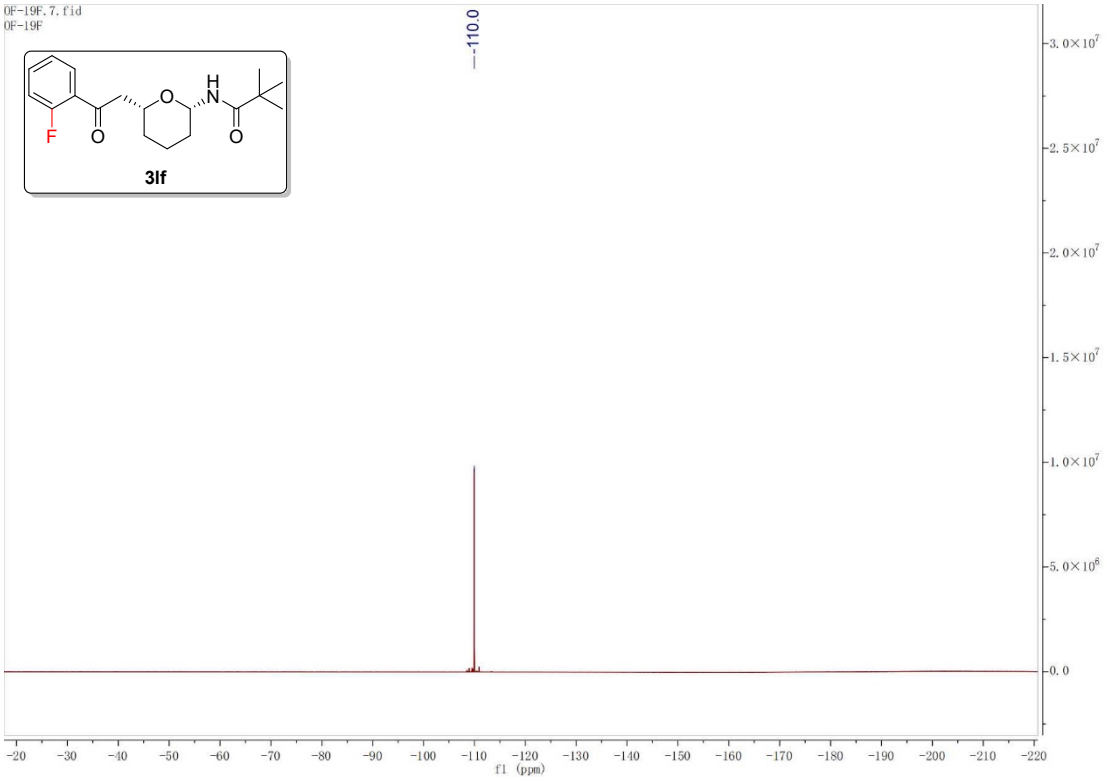
The ^{1}H NMR spectrum of 3lf (400 MHz, $CDCl_3$)



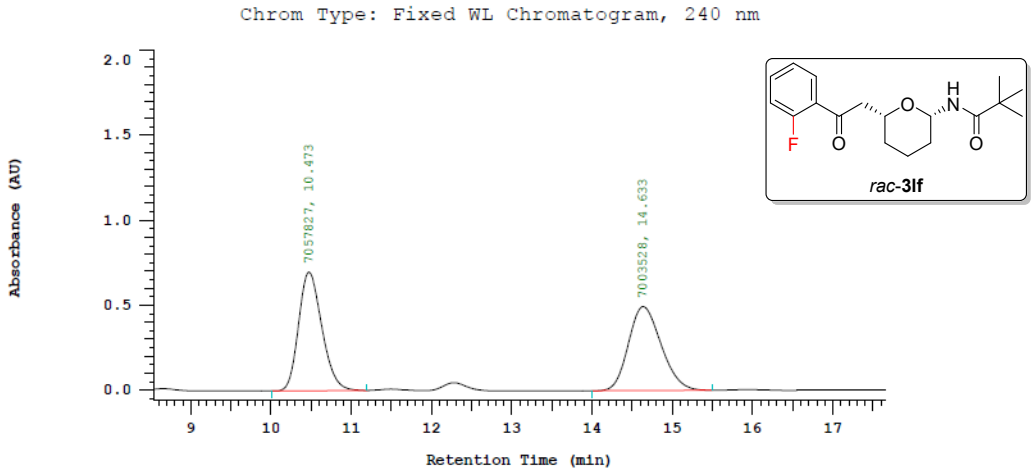
The ^{13}C NMR spectrum of 3lf (101 MHz, $CDCl_3$)



The ^{19}F NMR spectrum of 3lf (376 MHz, $CDCl_3$)



The HPLC of racemic 3lf



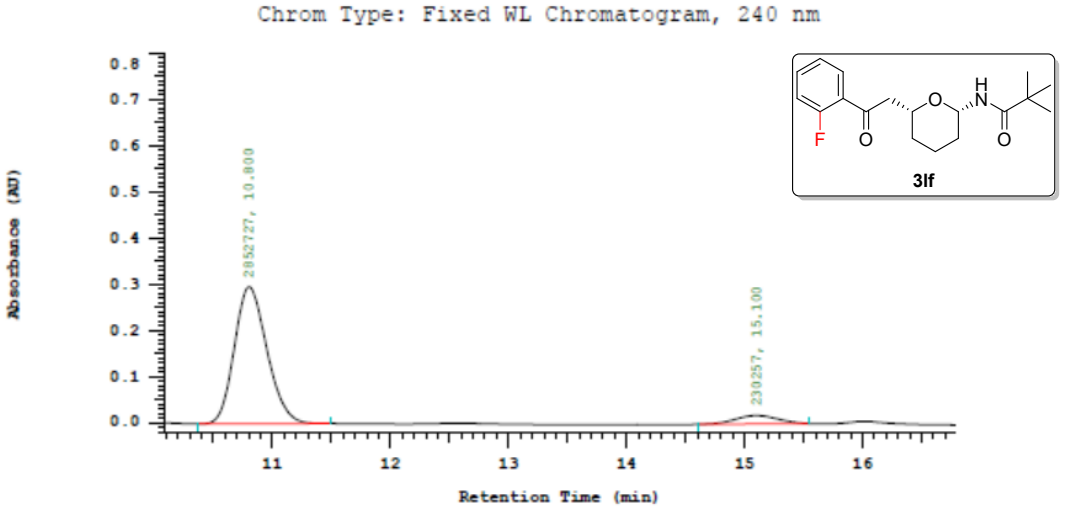
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.473	7057827	50.193	BB
2	14.633	7003528	49.807	BB
		14061355	100.000	

The HPLC of chiral 3lf



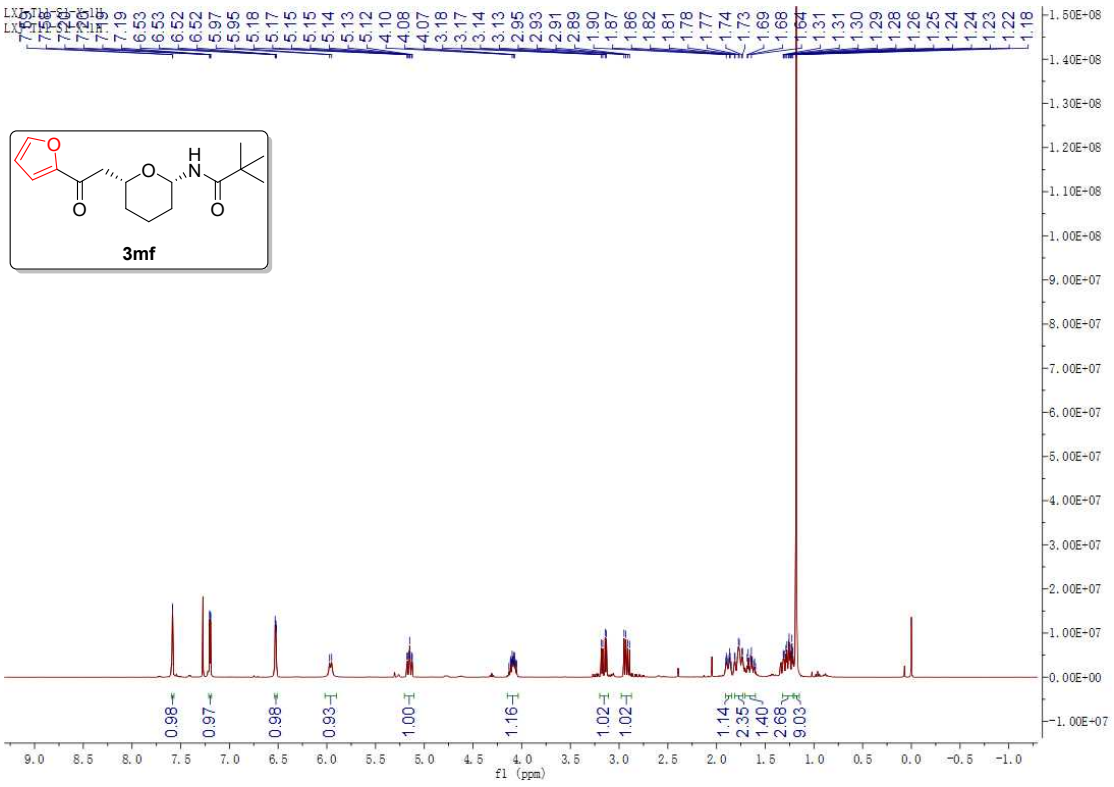
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

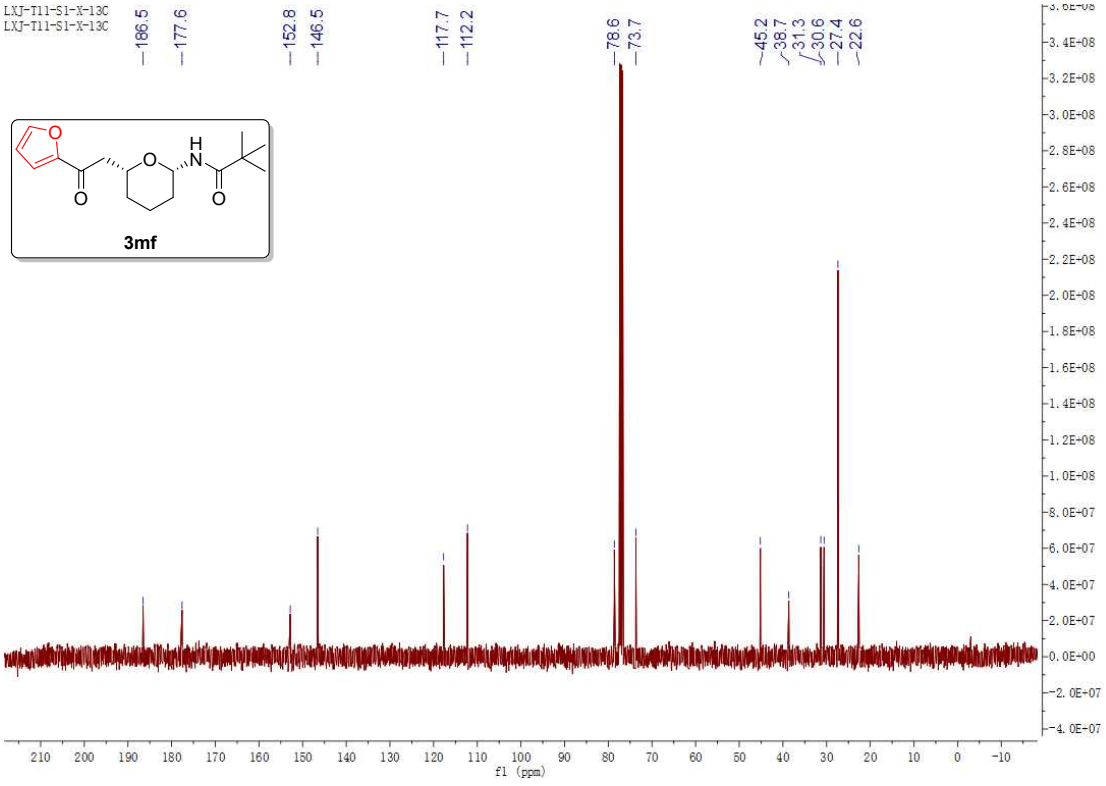
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	10.800	2852727	92.531	BB
2	15.100	230257	7.469	BB
		3082984	100.000	

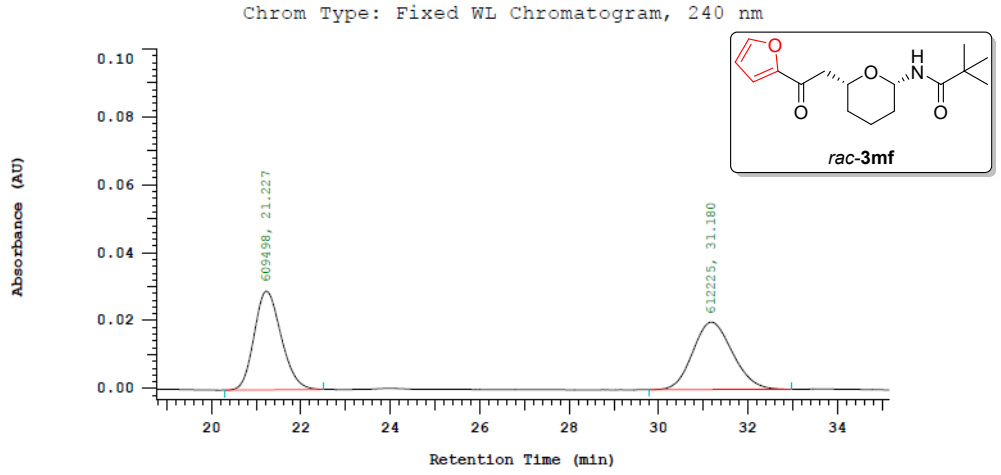
The ^{1}H NMR spectrum of 3mf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3mf (101 MHz, $CDCl_3$)



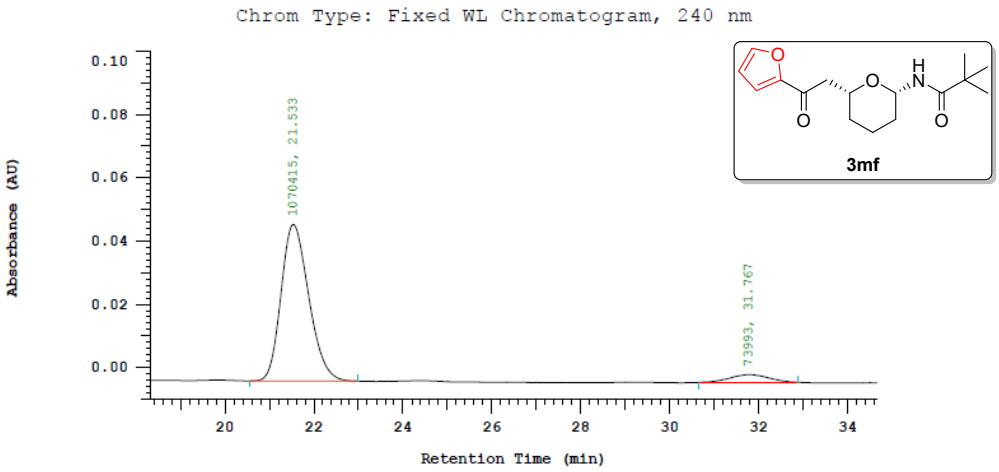
The HPLC of racemic 3mf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	21.227	609498	49.888	BB
2	31.180	612225	50.112	BB
		1221723	100.000	

The HPLC of chiral 3mf



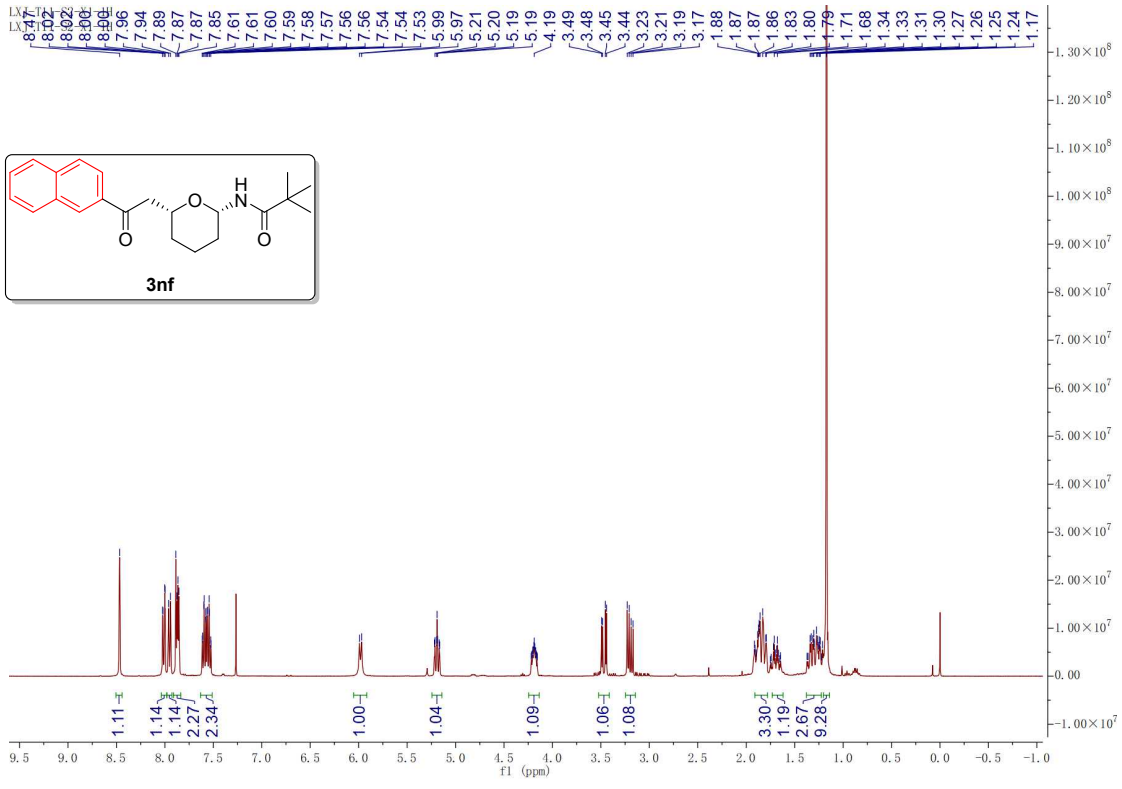
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

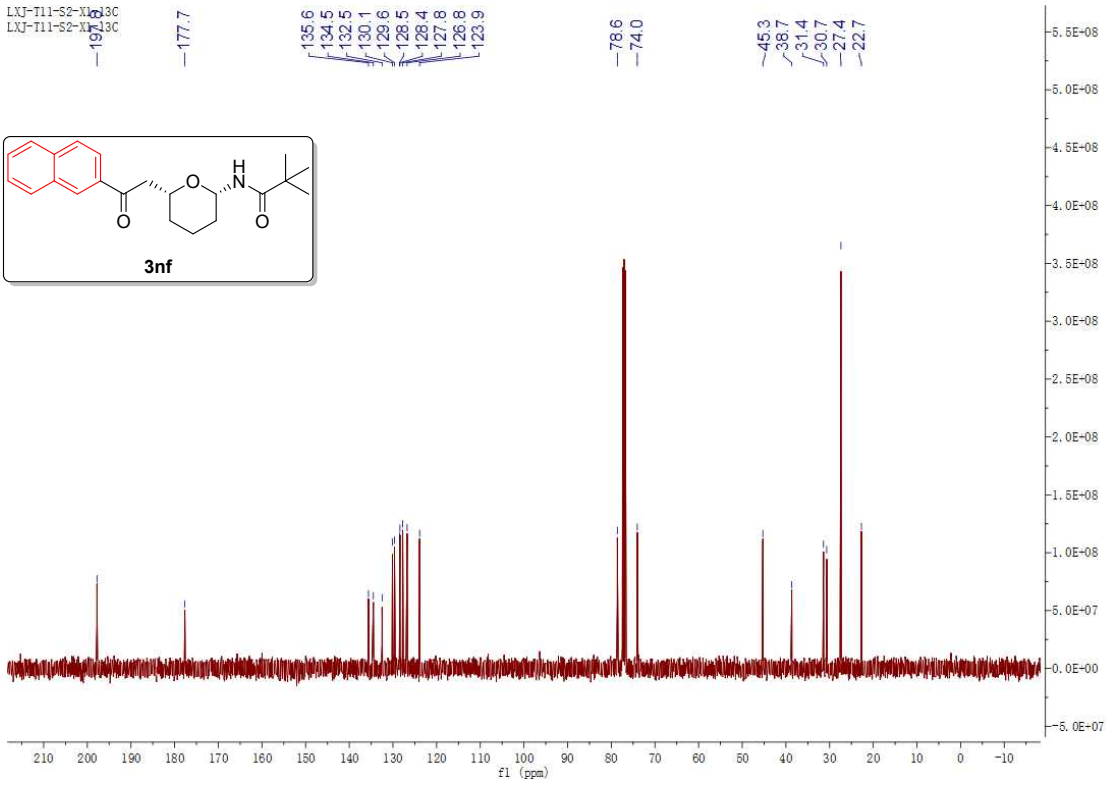
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	21.533	1070415	93.534	BB
2	31.767	73993	6.466	BB
		1144408	100.000	

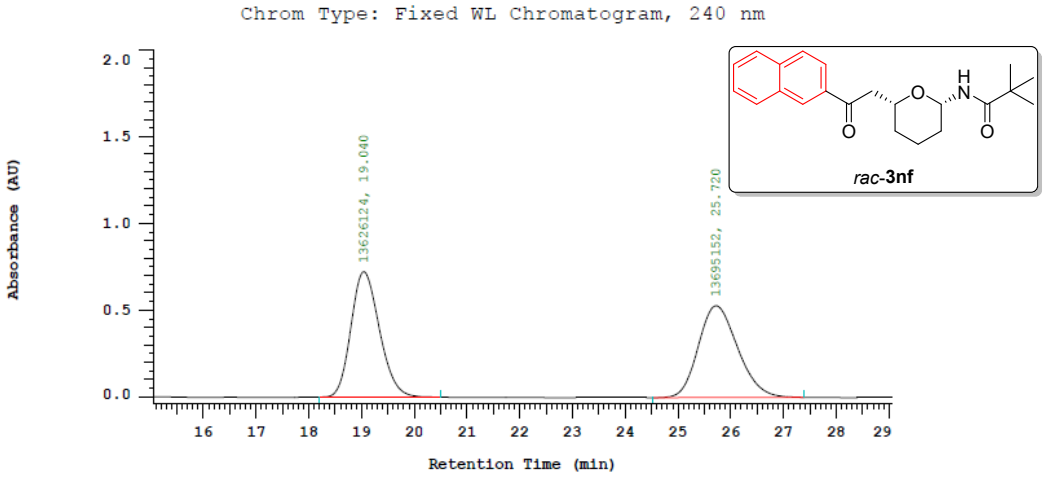
The ^{1}H NMR spectrum of 3nf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3nf (101 MHz, $CDCl_3$)



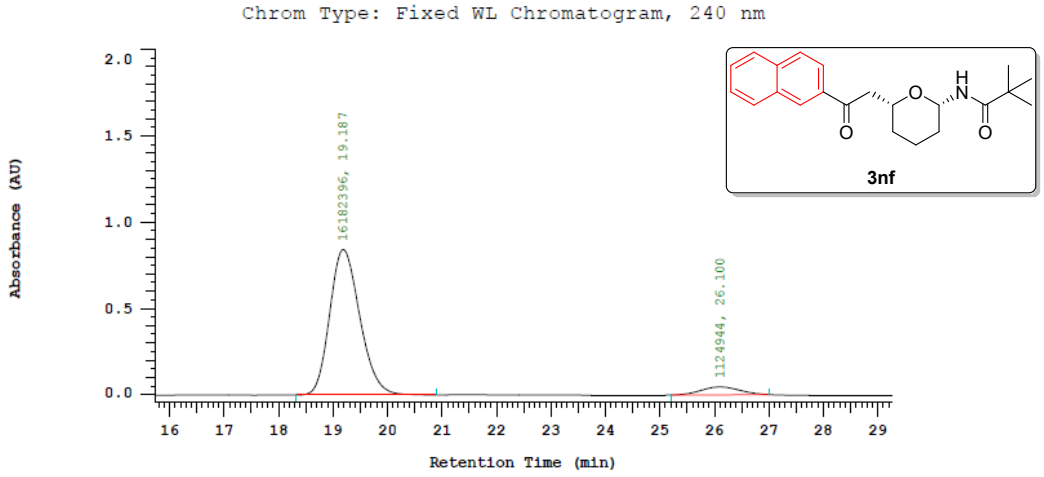
The HPLC of racemic 3nf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	19.040	13626124	49.874	BB
2	25.720	13695152	50.126	BB
		27321276	100.000	

The HPLC of chiral 3nf



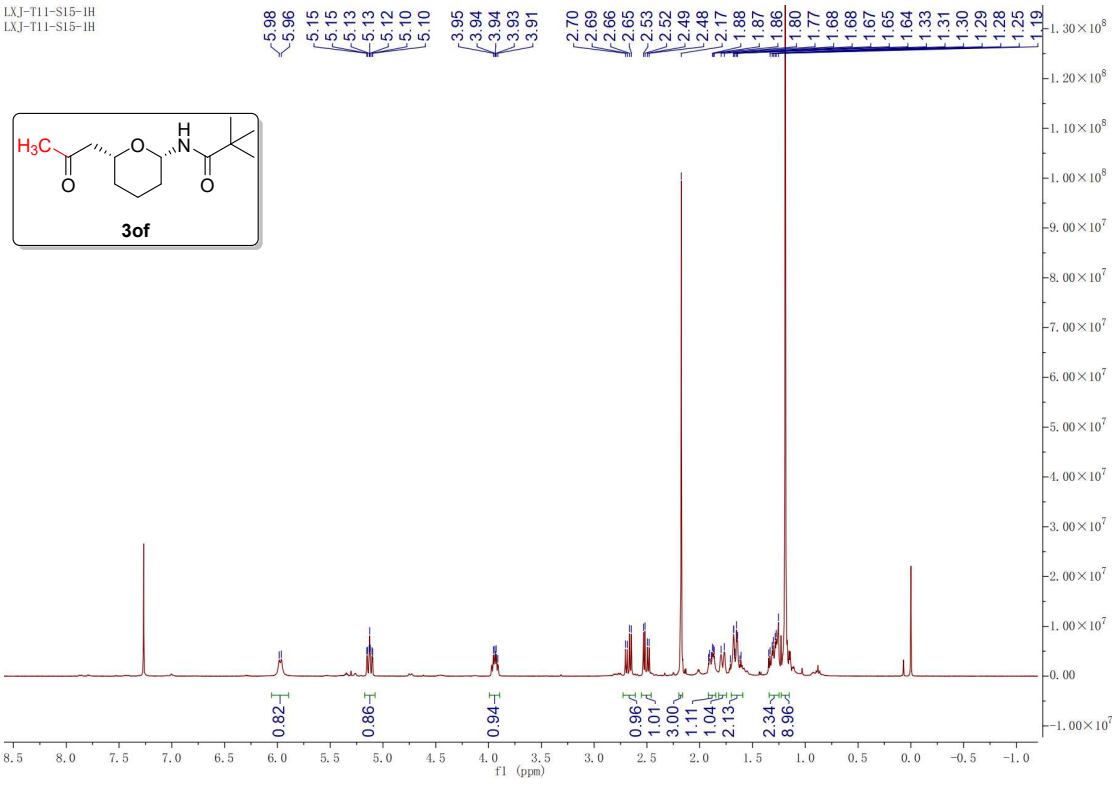
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

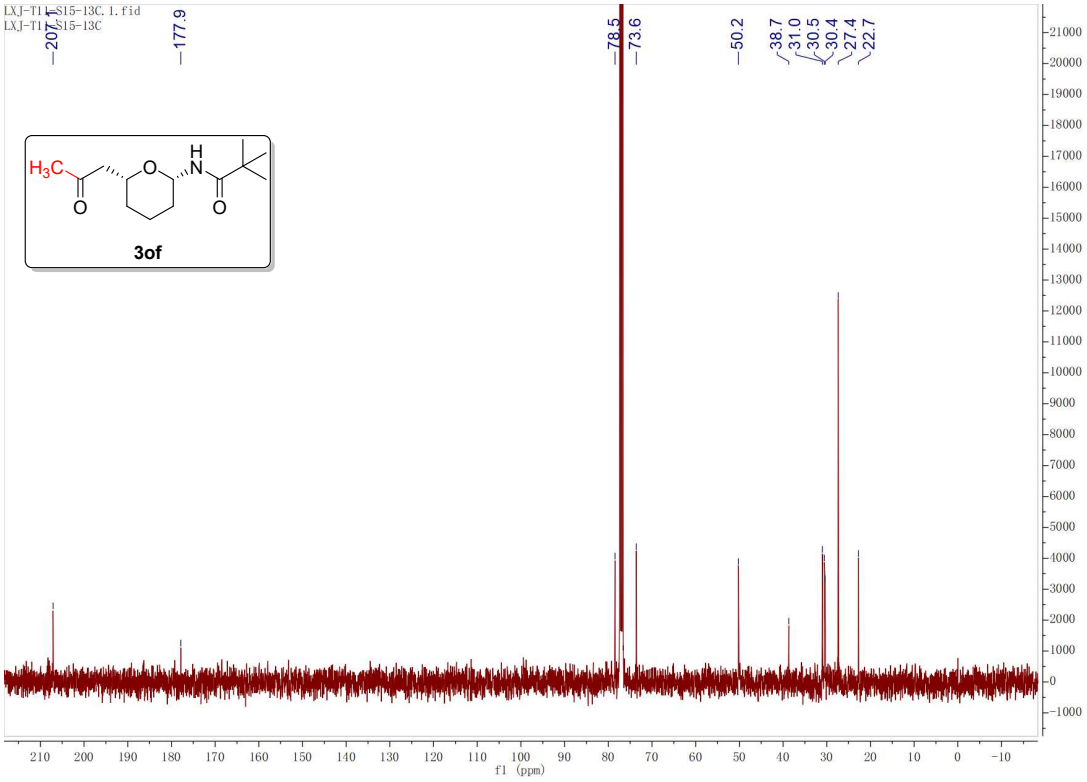
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	19.187	16182396	93.500	BB
2	26.100	1124944	6.500	BB
		17307340	100.000	

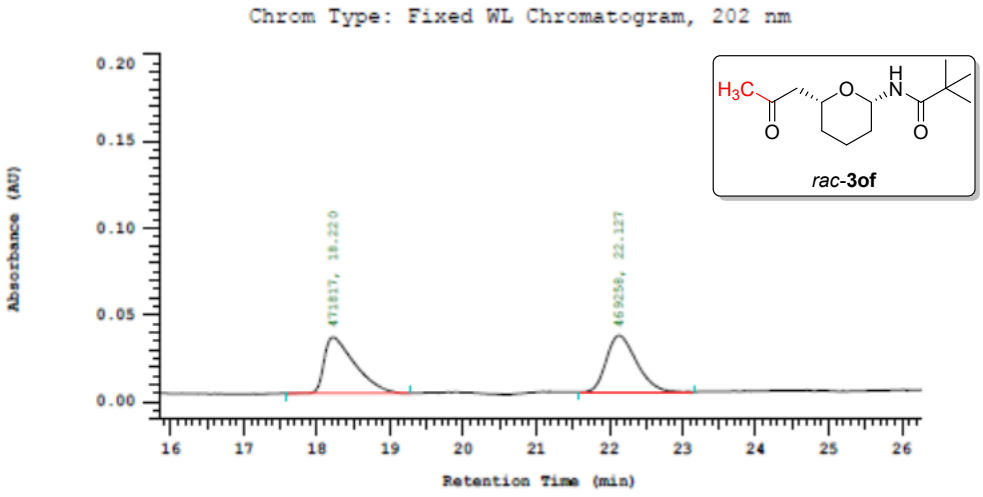
The ^{1}H NMR spectrum of 3of (400 MHz, $CDCl_3$)



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



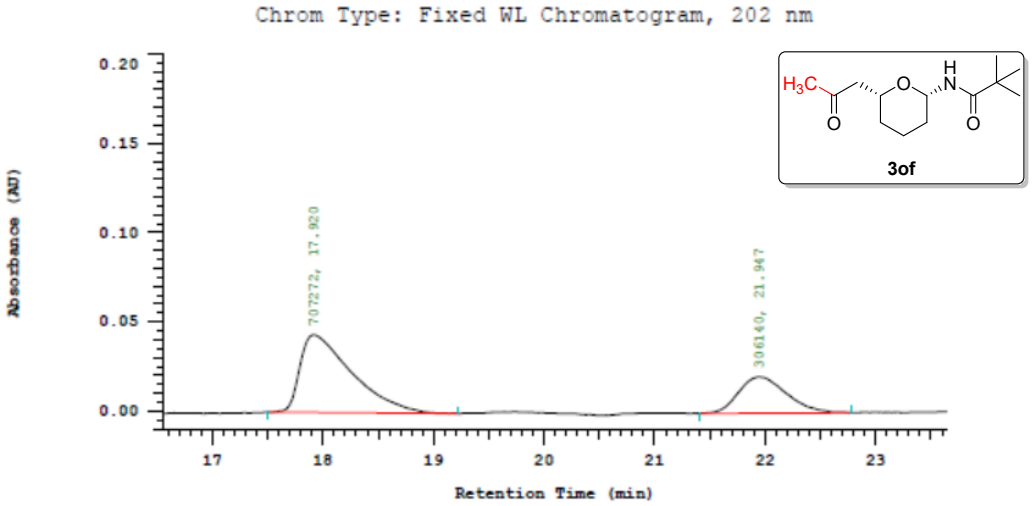
The HPLC of racemic 3of



Chrom Type: Fixed WL Chromatogram, 202 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	18.220	471817	50.136	BB
2	22.127	469258	49.864	BB
		941075	100.000	

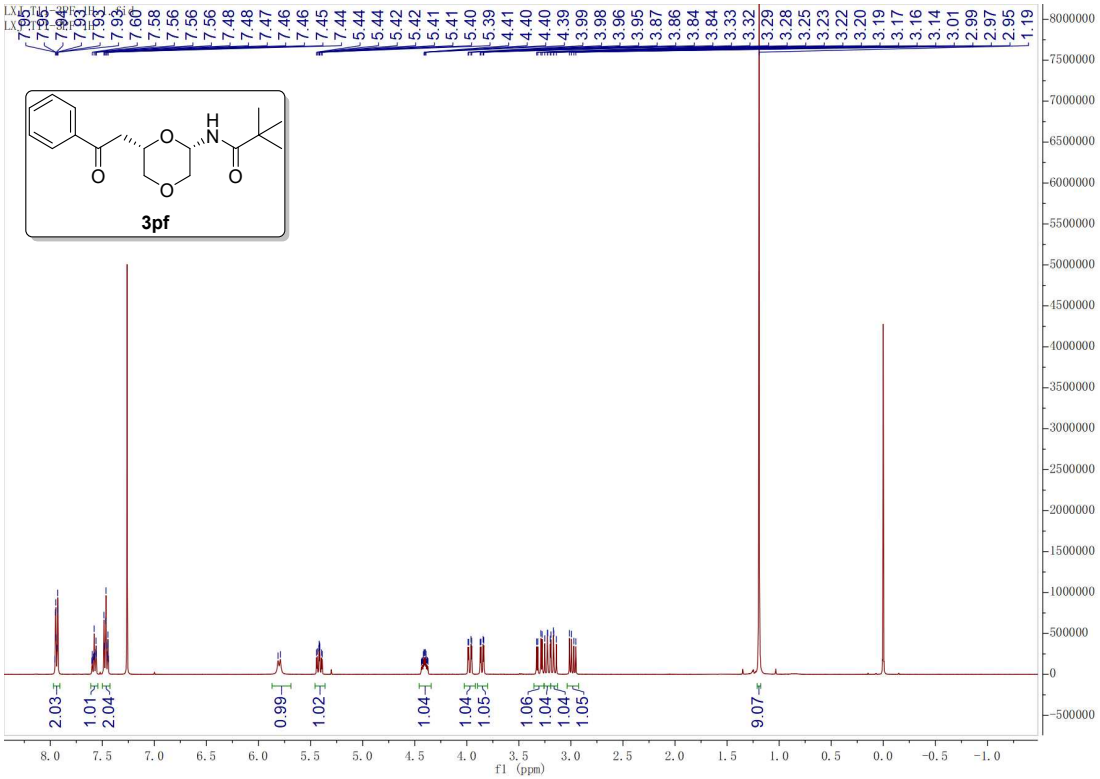
The HPLC of chiral 3of



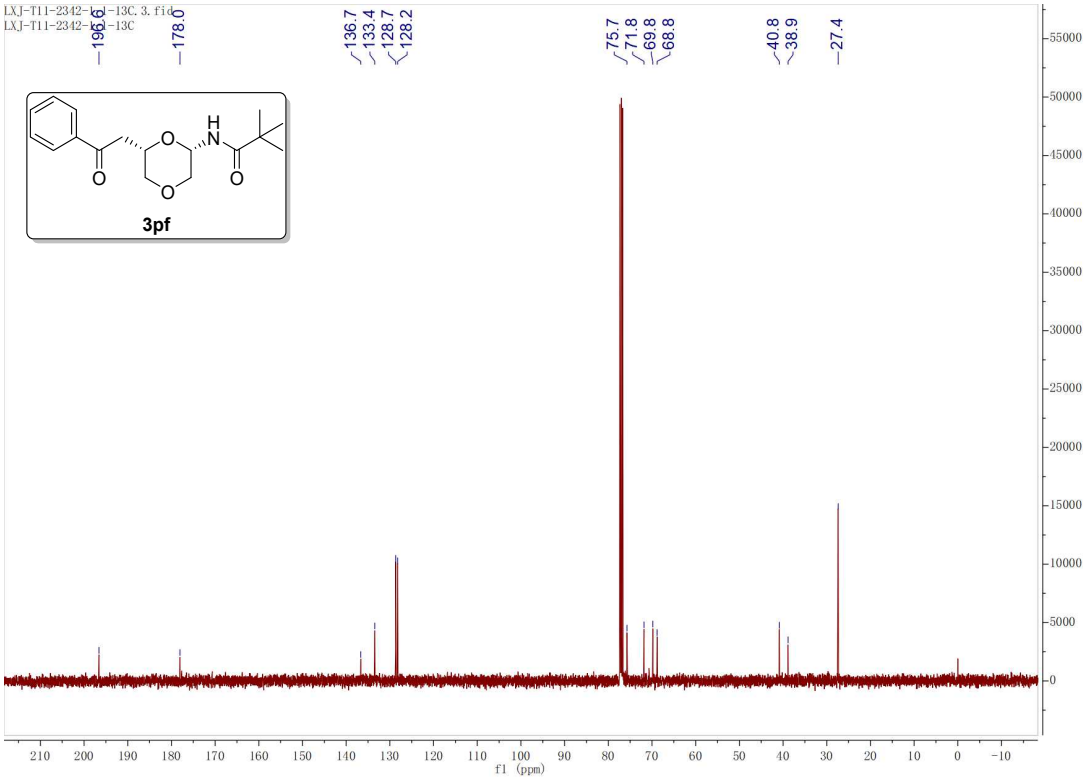
Chrom Type: Fixed WL Chromatogram, 202 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.920	707272	69.791	BB
2	21.947	306140	30.209	BB
		1013412	100.000	

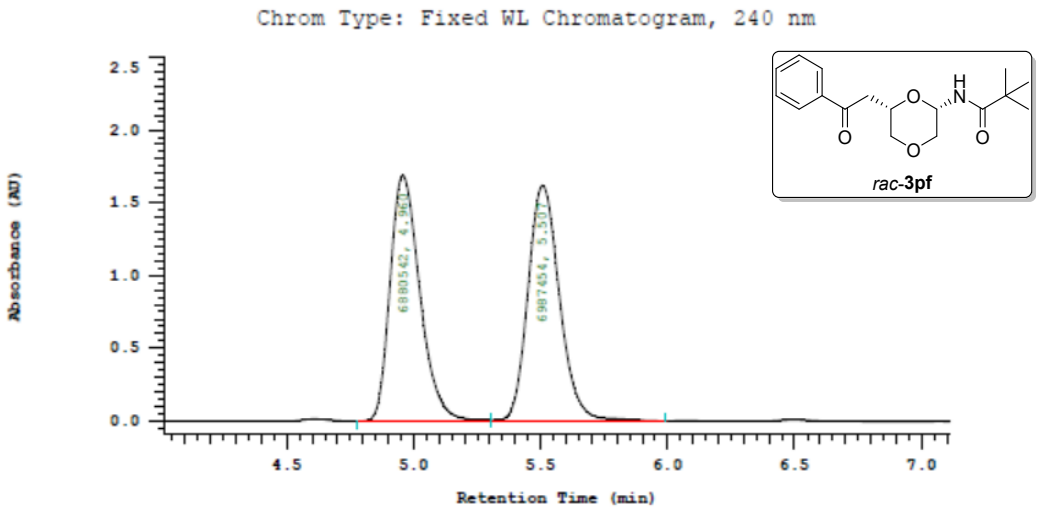
The ^{1}H NMR spectrum of 3pf (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 3pf (101 MHz, $CDCl_3$)



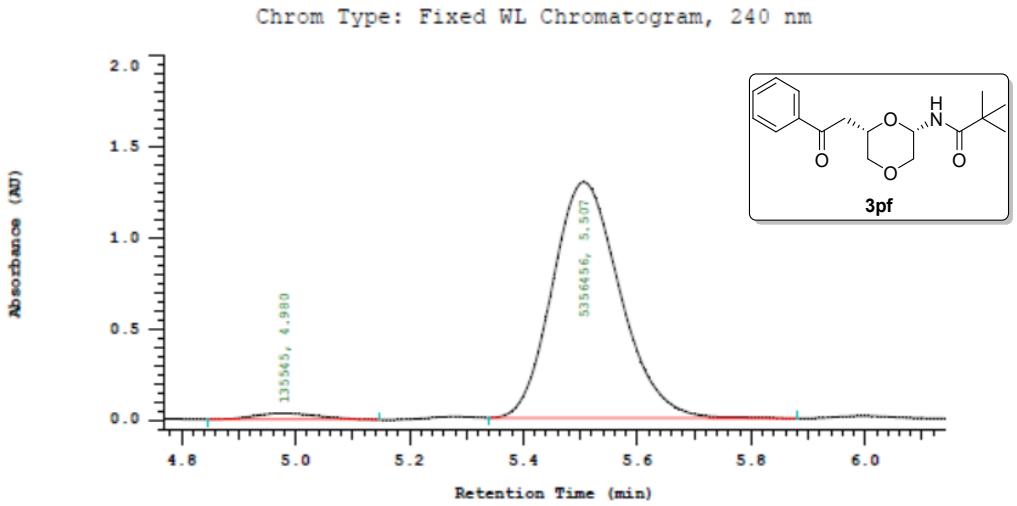
The HPLC of racemic 3pf



Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	4.960	6880542	49.615	BV
2	5.507	6987454	50.385	VB
		13867996	100.000	

The HPLC of chiral 3pf



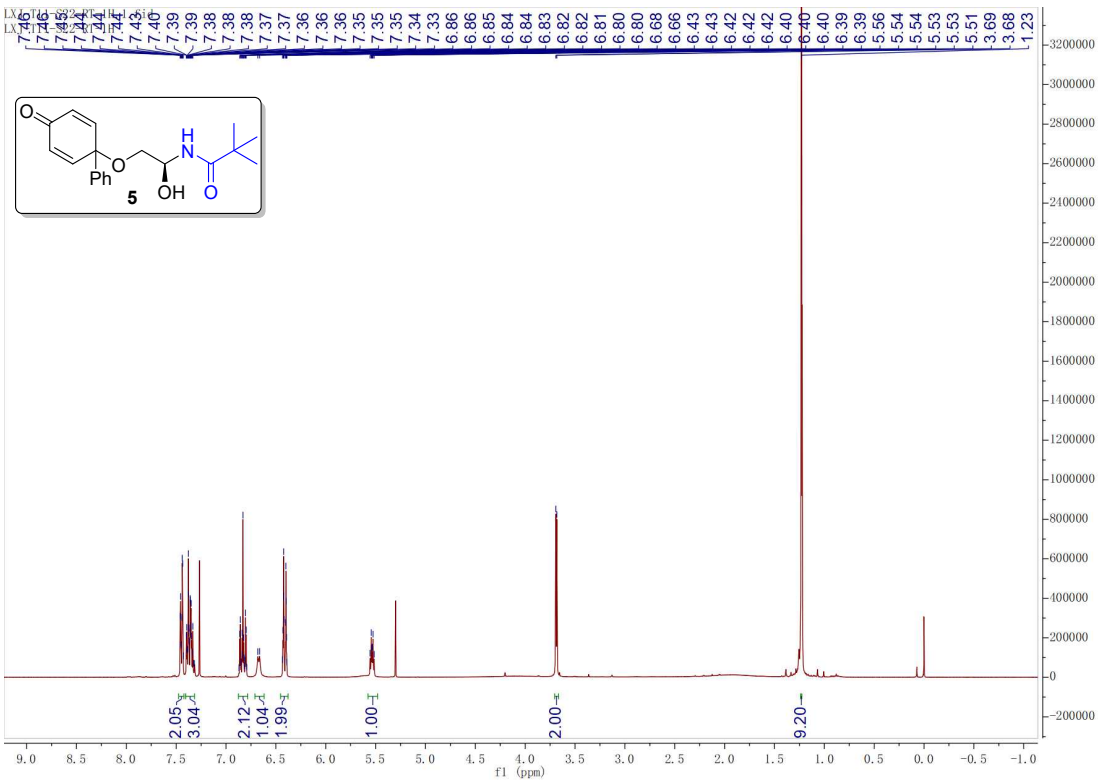
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

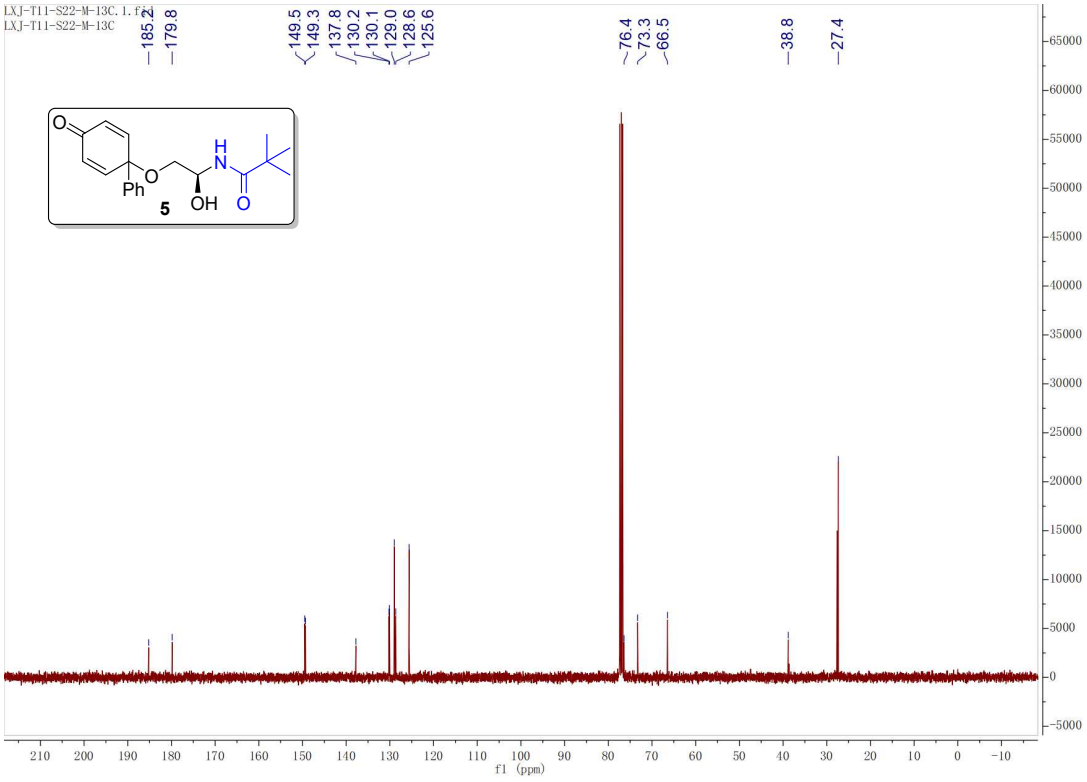
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	4.980	135545	2.468	BB
2	5.507	5356456	97.532	BB
		5492001	100.000	

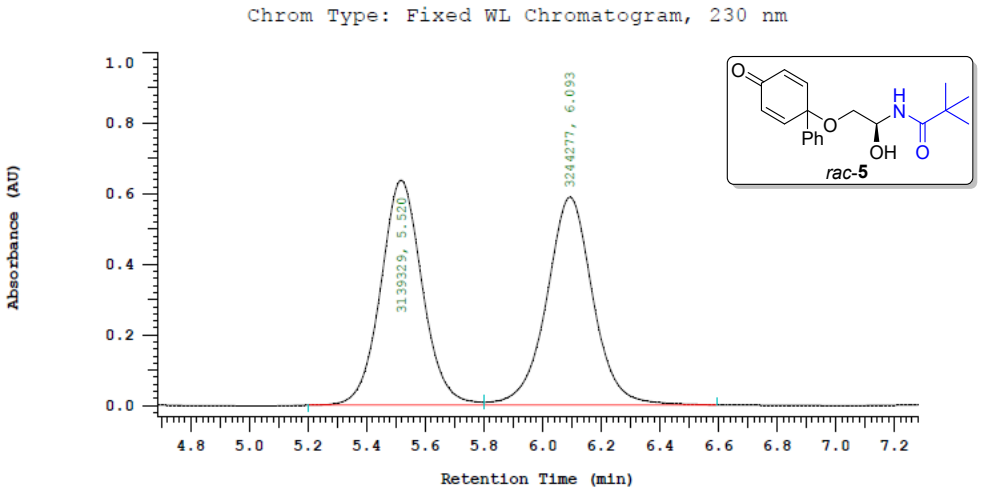
The ^{1}H NMR spectrum of 5 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 5 (101 MHz, $CDCl_3$)



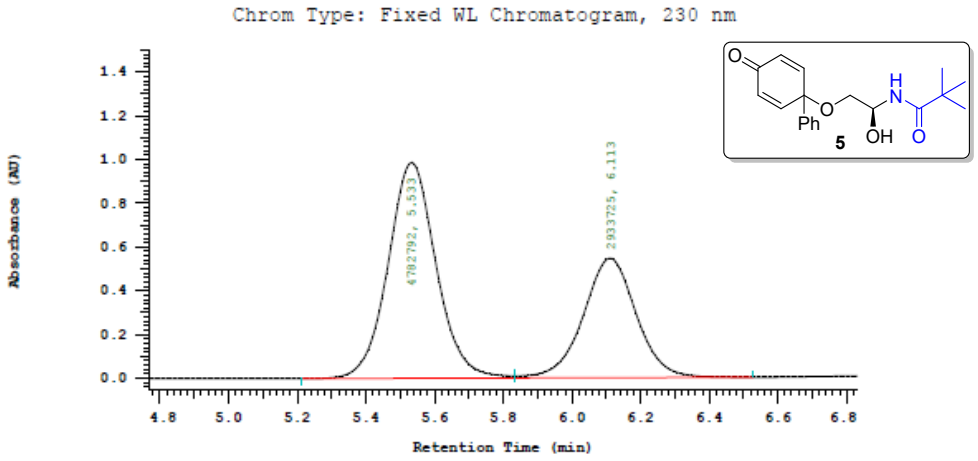
The HPLC of racemic 5



Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.520	3139329	49.178	BV
2	6.093	3244277	50.822	VB
		6383606	100.000	

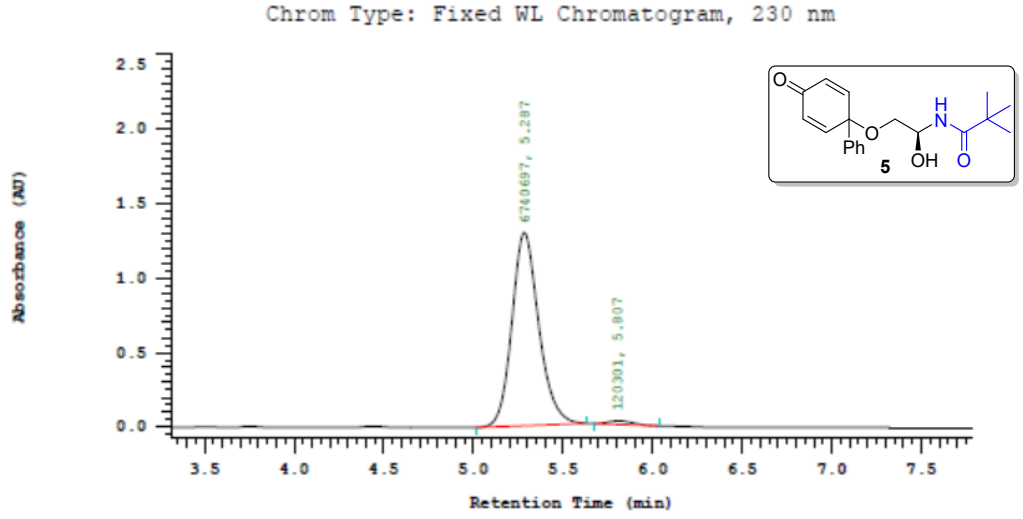
The HPLC of chiral 5 (catalyzed by A2)



Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.533	4782792	61.981	BV
2	6.113	2933725	38.019	VB
		7716517	100.000	

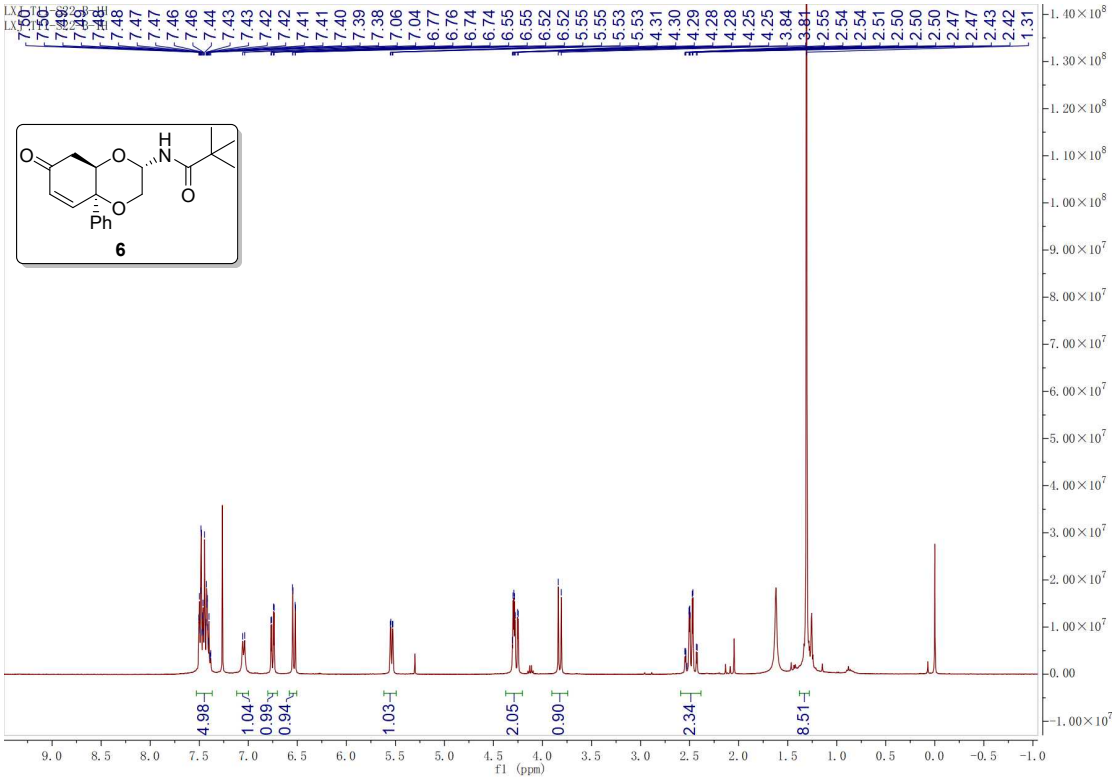
The HPLC of chiral 5 (catalyzed by B3)



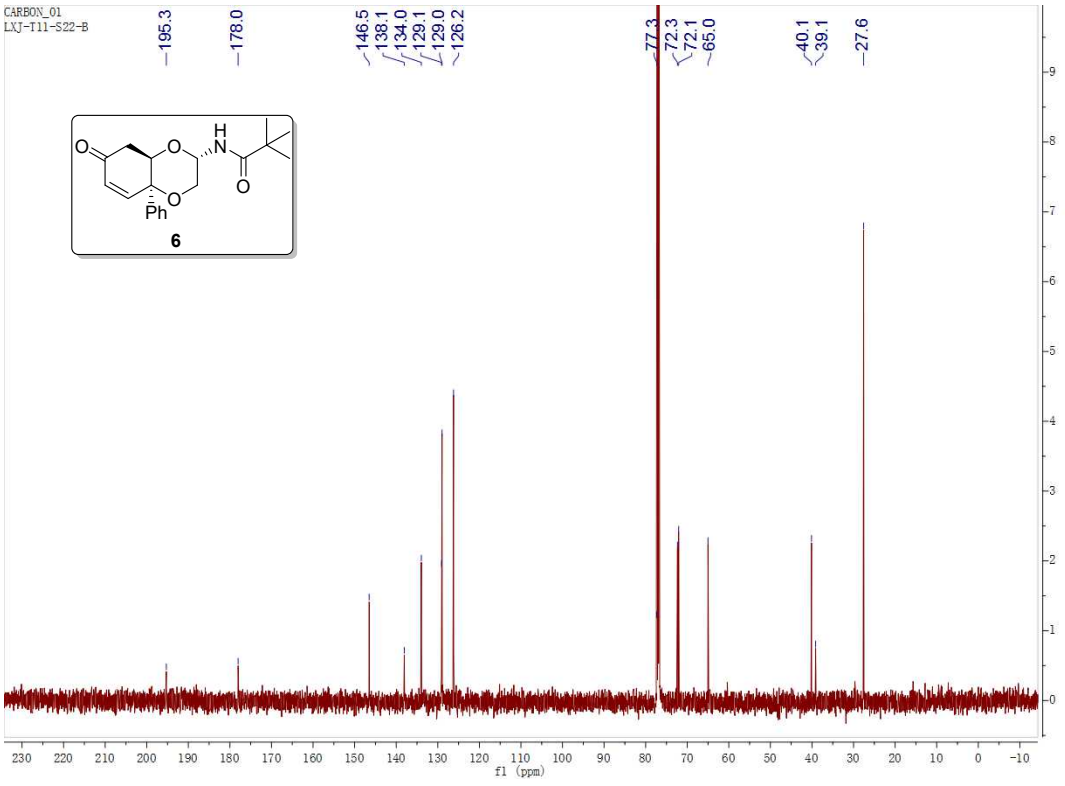
Chrom Type: Fixed WL Chromatogram, 230 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.287	6740697	98.247	BB
2	5.807	120301	1.753	BB
		6860998	100.000	

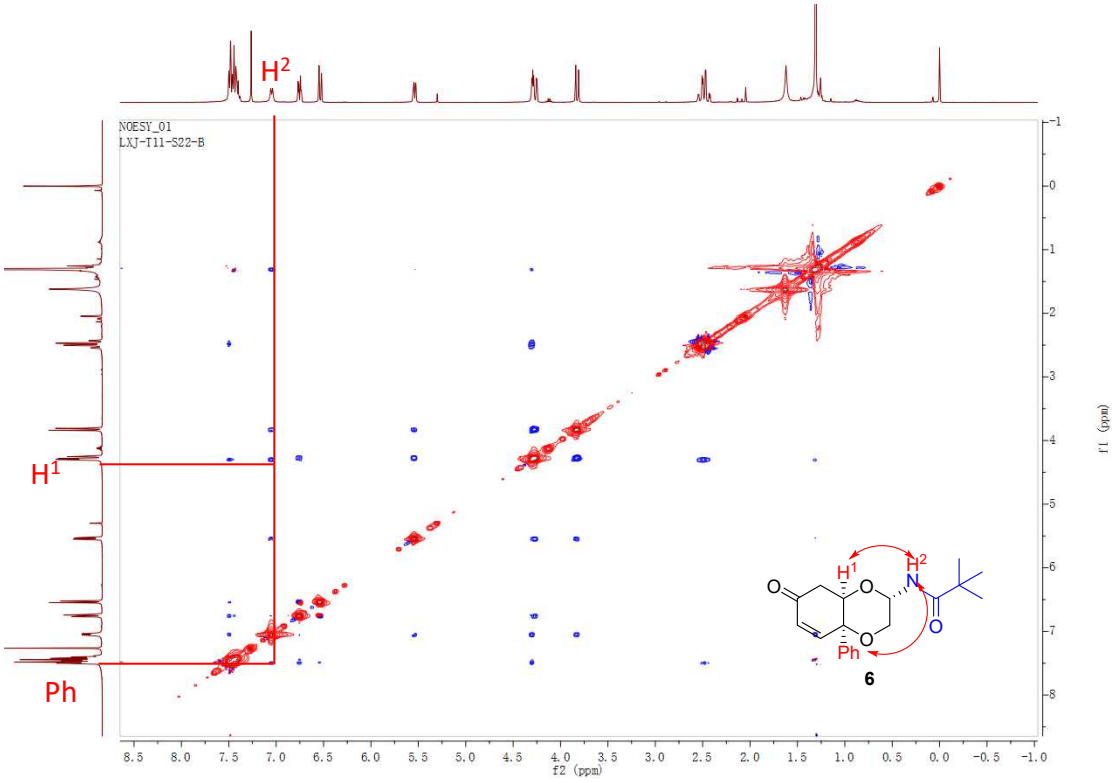
The ^{1}H NMR spectrum of 6 (400 MHz, $CDCl_3$)



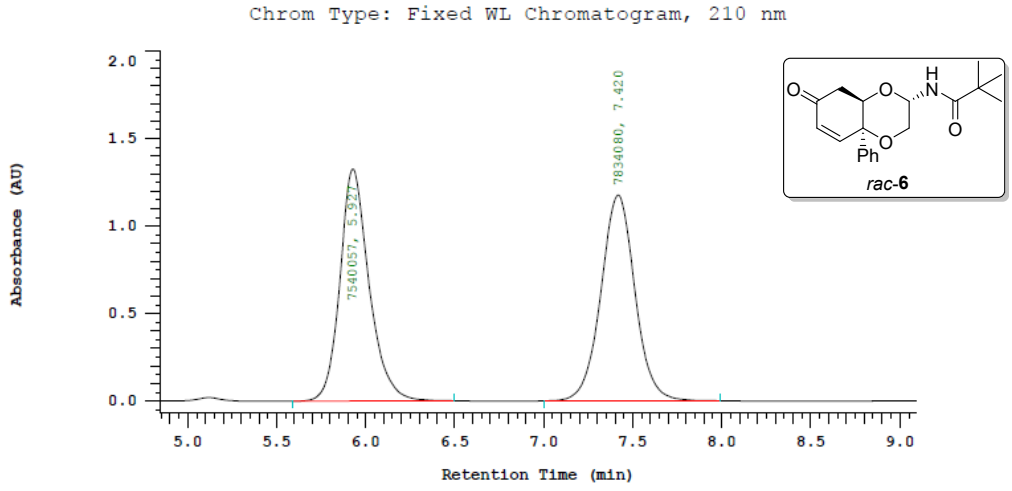
The ^{13}C NMR spectrum of 6 (125 MHz, $CDCl_3$)



The noesy spectrum of 6 (500 MHz, $CDCl_3$)



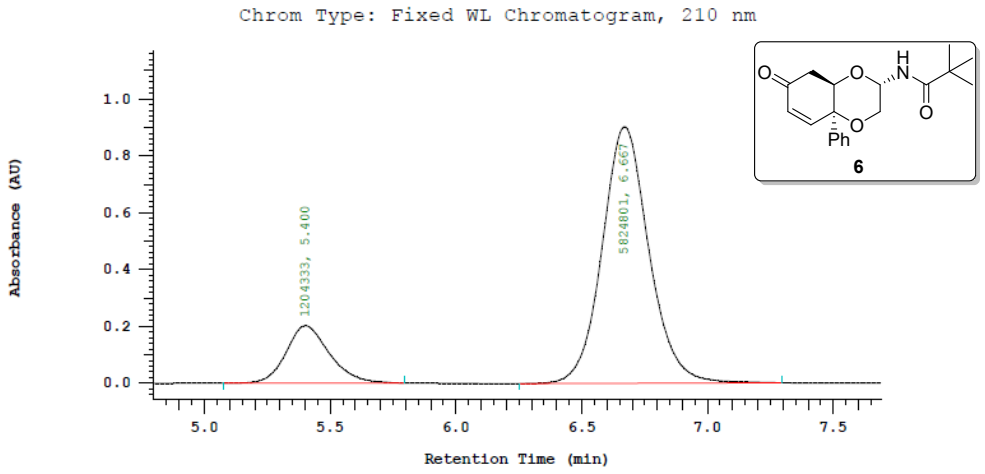
The HPLC of racemic 6



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.927	7540057	49.044	BB
2	7.420	7834080	50.956	BB
		15374137	100.000	

The HPLC of chiral 6



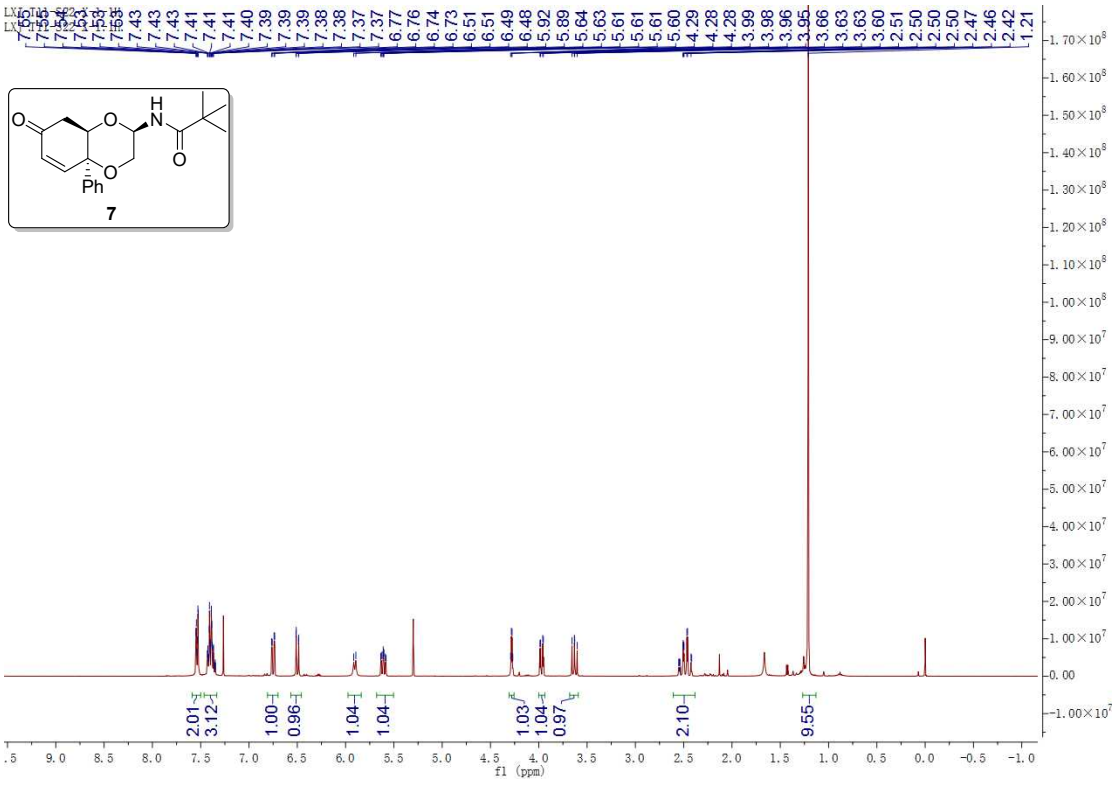
Chrom Type: Fixed WL Chromatogram, 210 nm

Peak Quantitation: AREA

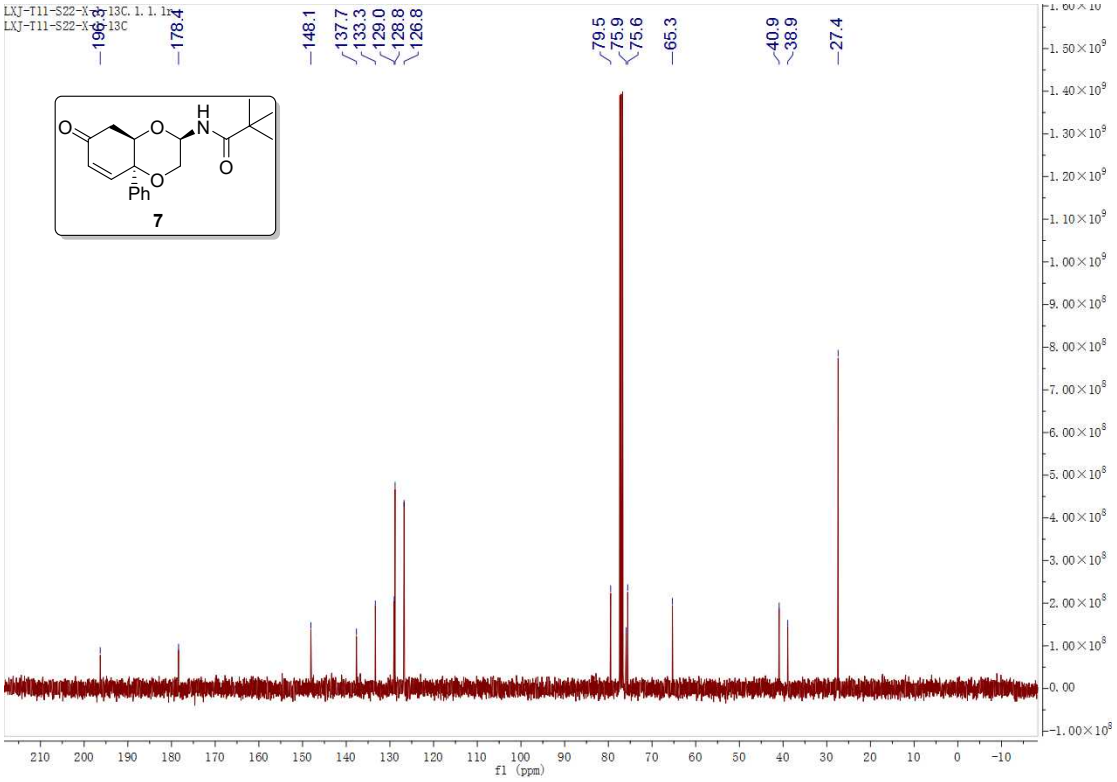
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	5.400	1204333	17.133	BB
2	6.667	5824801	82.867	BB
		7029134	100.000	

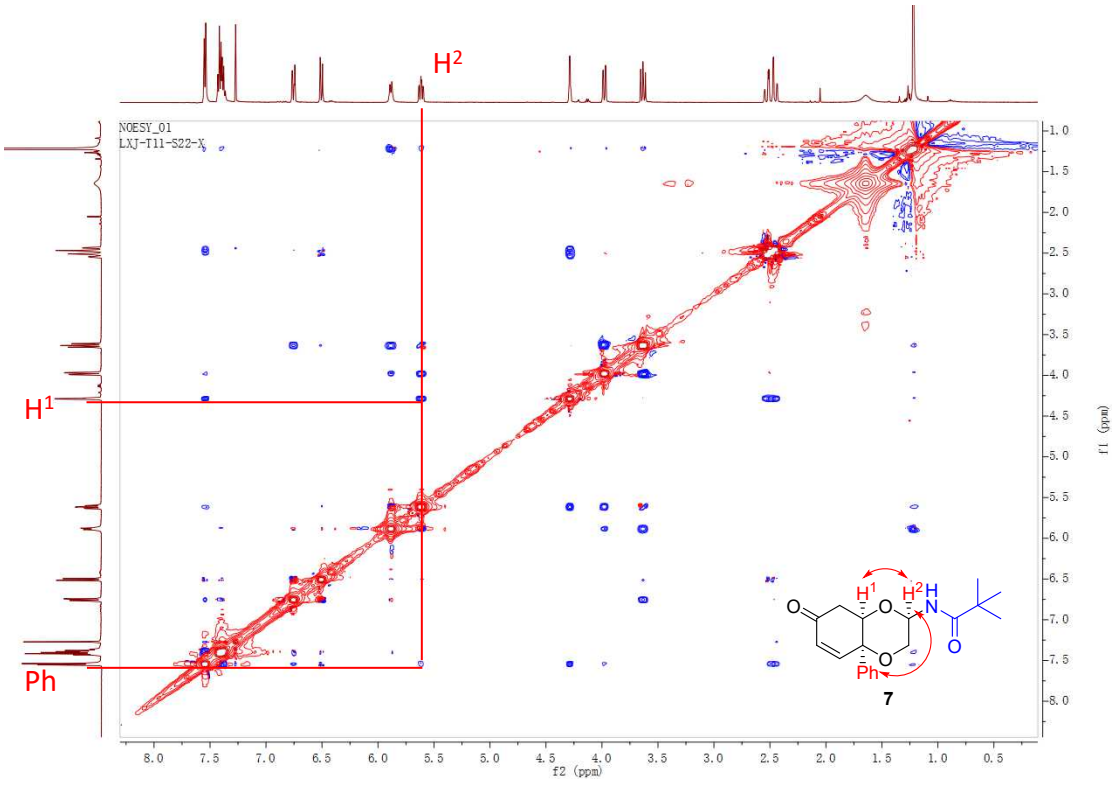
The ^{1}H NMR spectrum of 7 (400 MHz, $CDCl_3$)



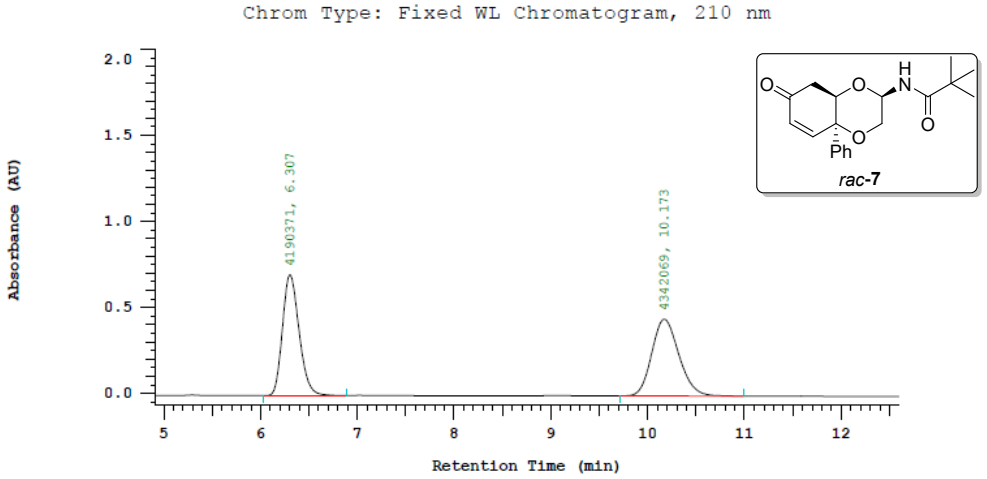
The ^{13}C NMR spectrum of 7 (400 MHz, $CDCl_3$)



The noesy spectrum of 7 (500 MHz, $CDCl_3$)



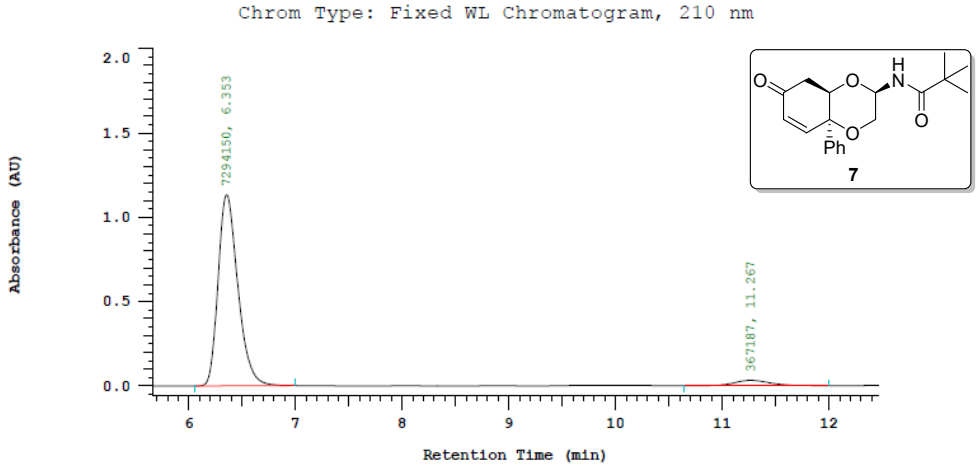
The HPLC of racemic 7



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.307	4190371	49.111	BB
2	10.173	4342069	50.889	BB
		8532440	100.000	

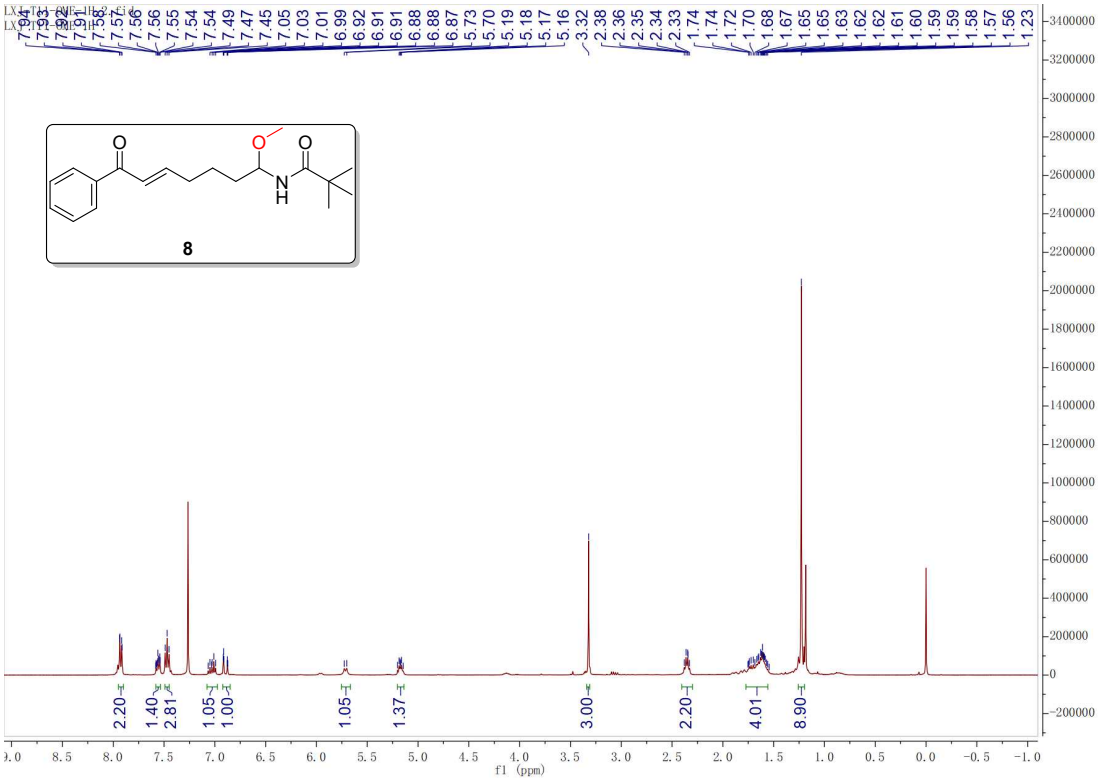
The HPLC of chiral 7



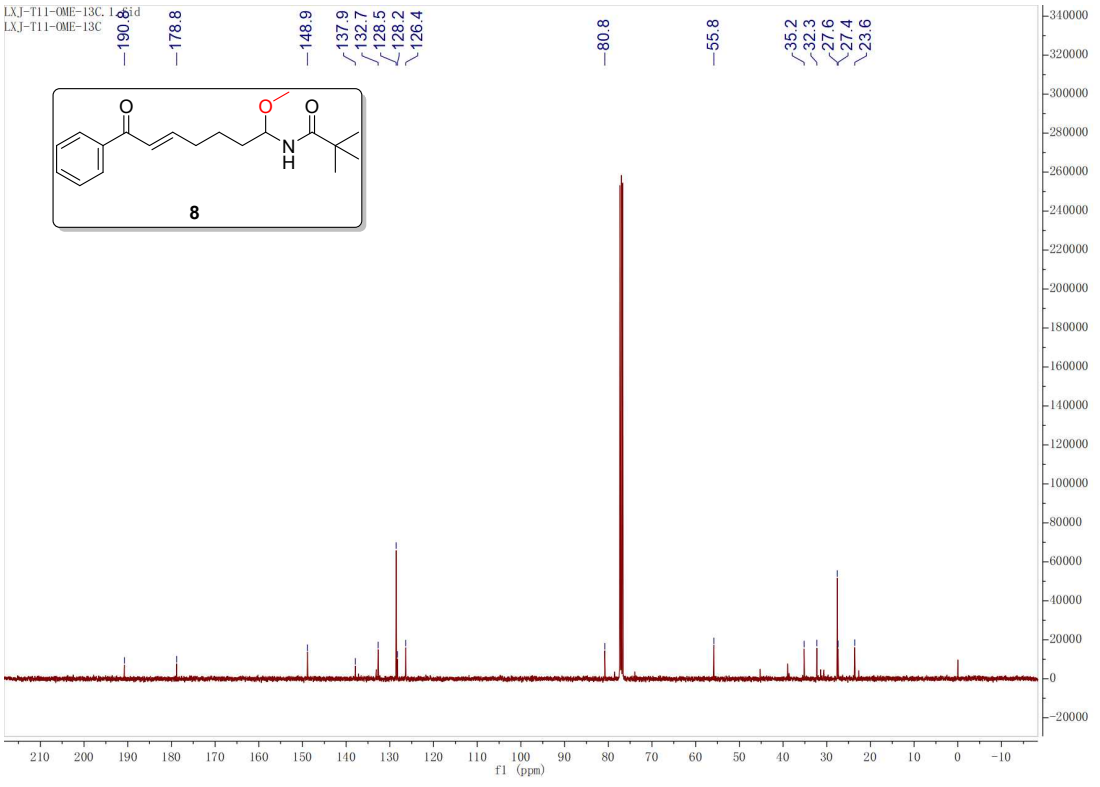
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	6.353	7294150	95.207	BB
2	11.267	367187	4.793	BB
		7661337	100.000	

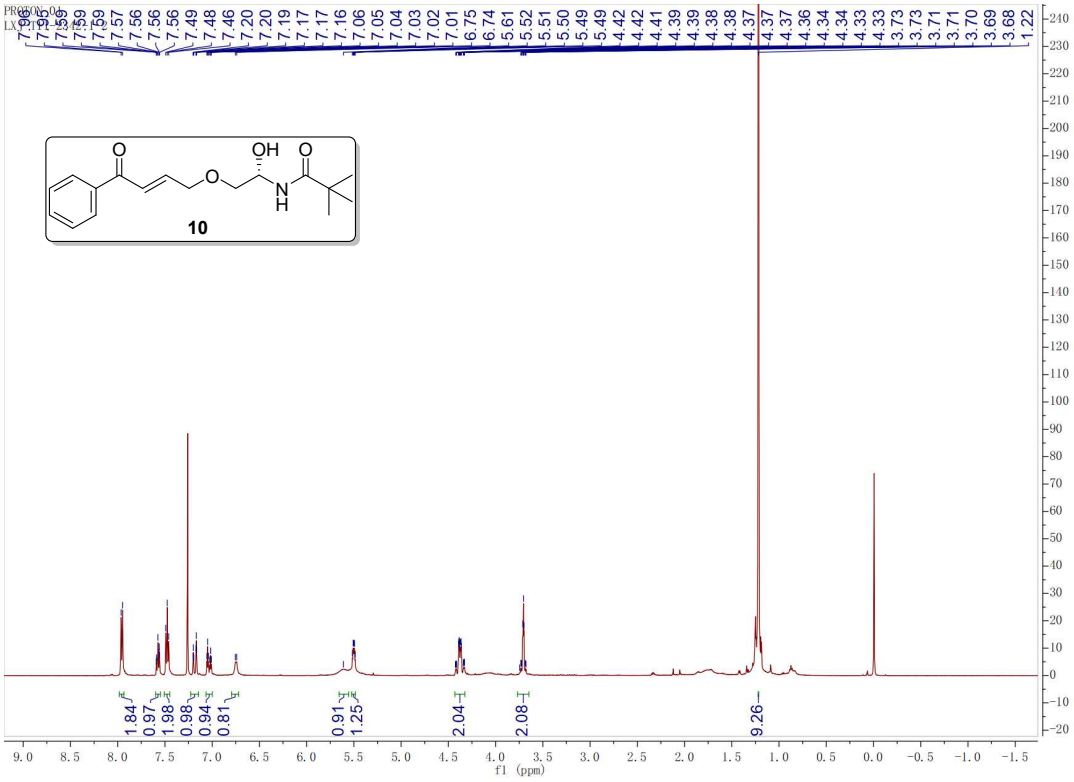
The ^{1}H NMR spectrum of 8 (400 MHz, $CDCl_3$)



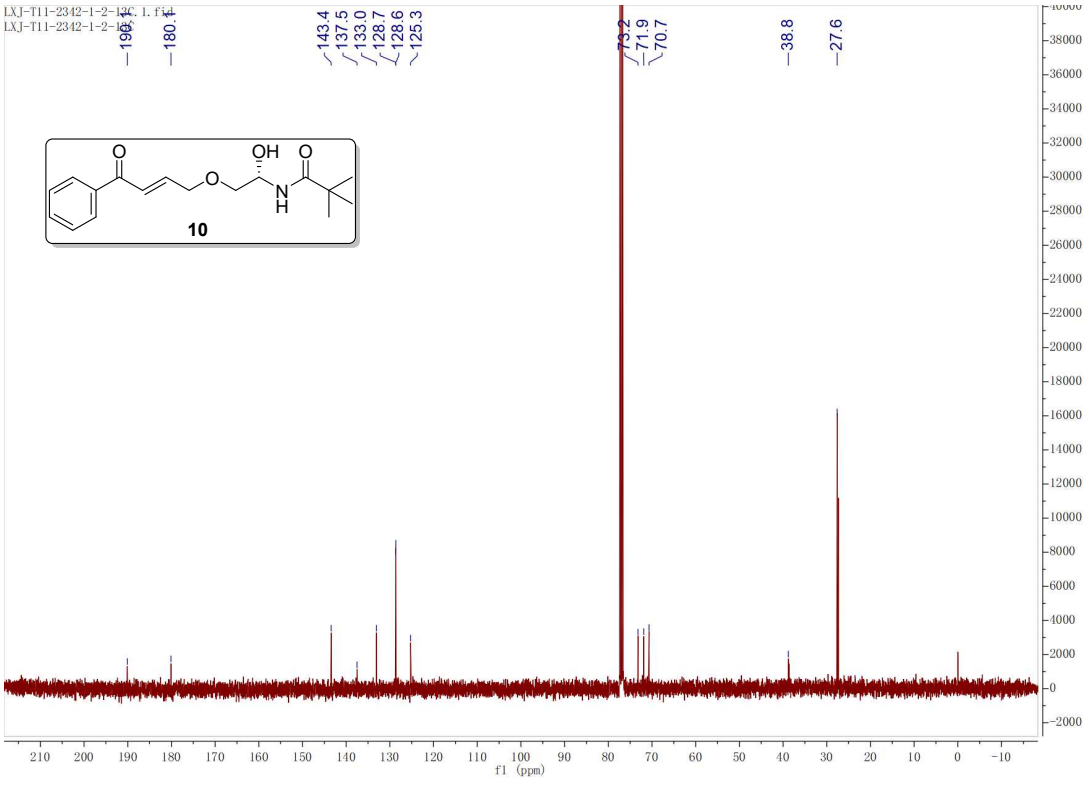
The ^{13}C NMR spectrum of 8 (101 MHz, $CDCl_3$)



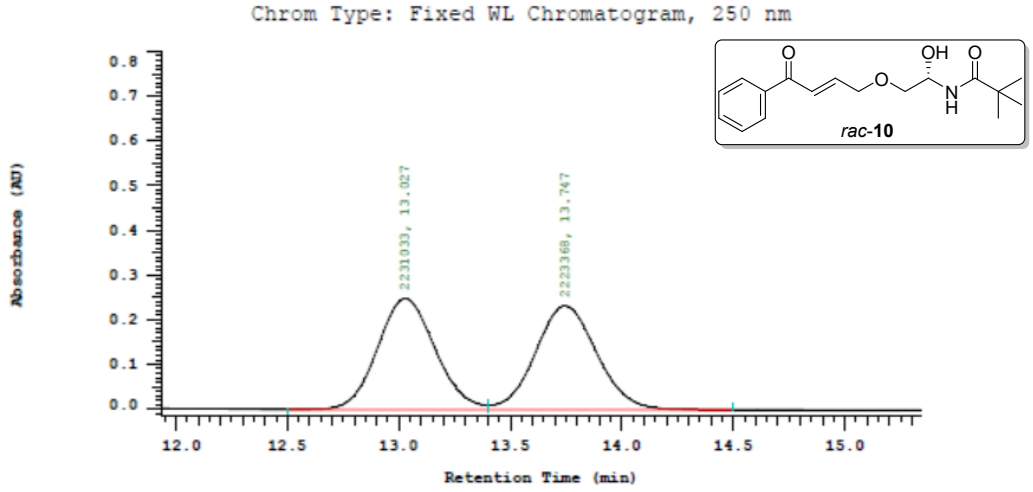
The ^{1}H NMR spectrum of 10 (500 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 10 (101 MHz, $CDCl_3$)



The HPLC of racemic 10



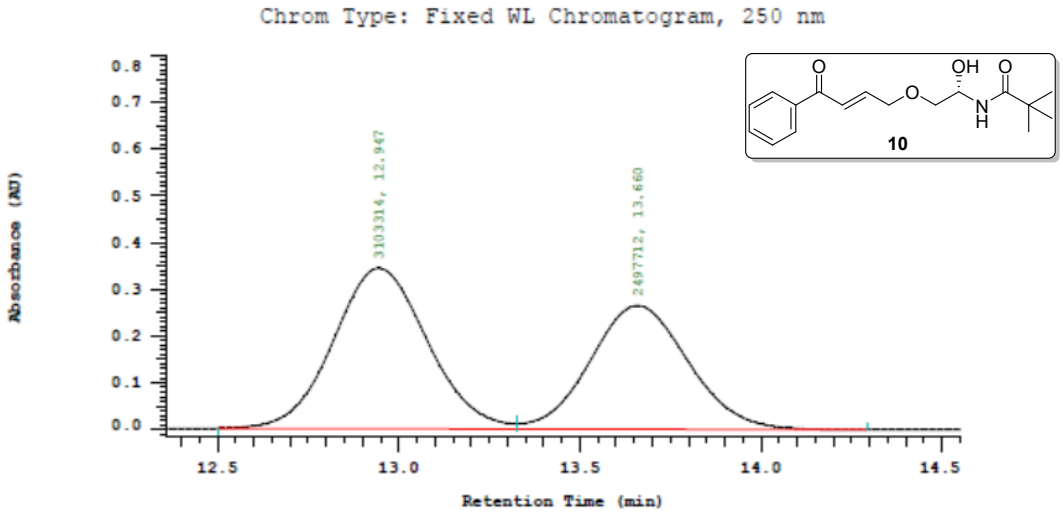
Chrom Type: Fixed WL Chromatogram, 250 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	13.027	2231033	50.086	BV
2	13.747	2223368	49.914	VB
		4454401	100.000	

The HPLC of chiral 10



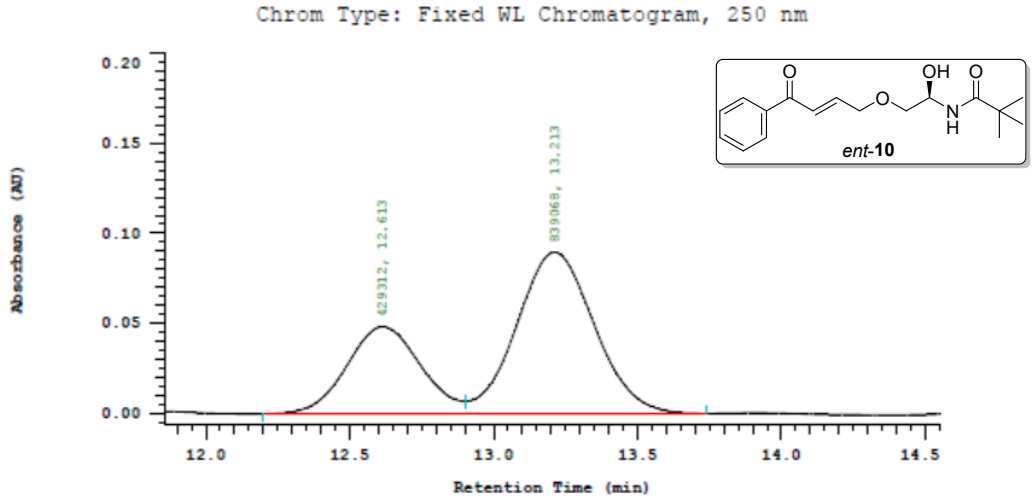
Chrom Type: Fixed WL Chromatogram, 250 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.947	3103314	55.406	BV
2	13.660	2497712	44.594	VB
		5601026	100.000	

The HPLC of chiral *ent*-10



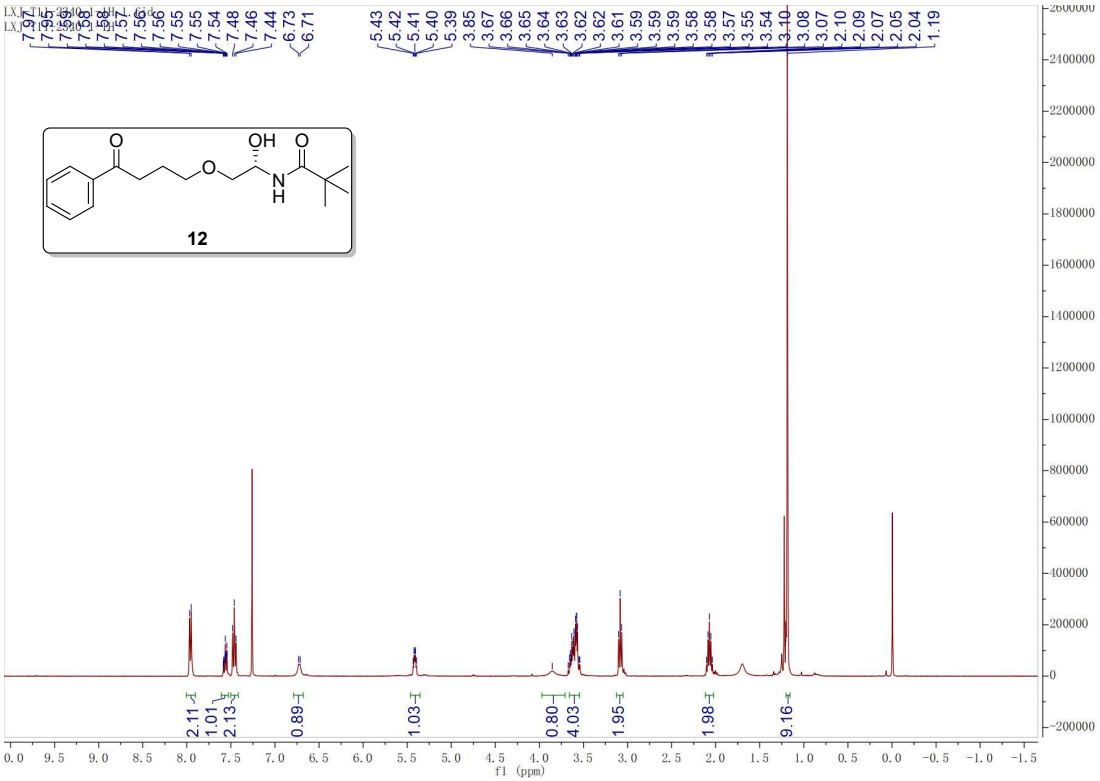
Chrom Type: Fixed WL Chromatogram, 250 nm

Peak Quantitation: AREA

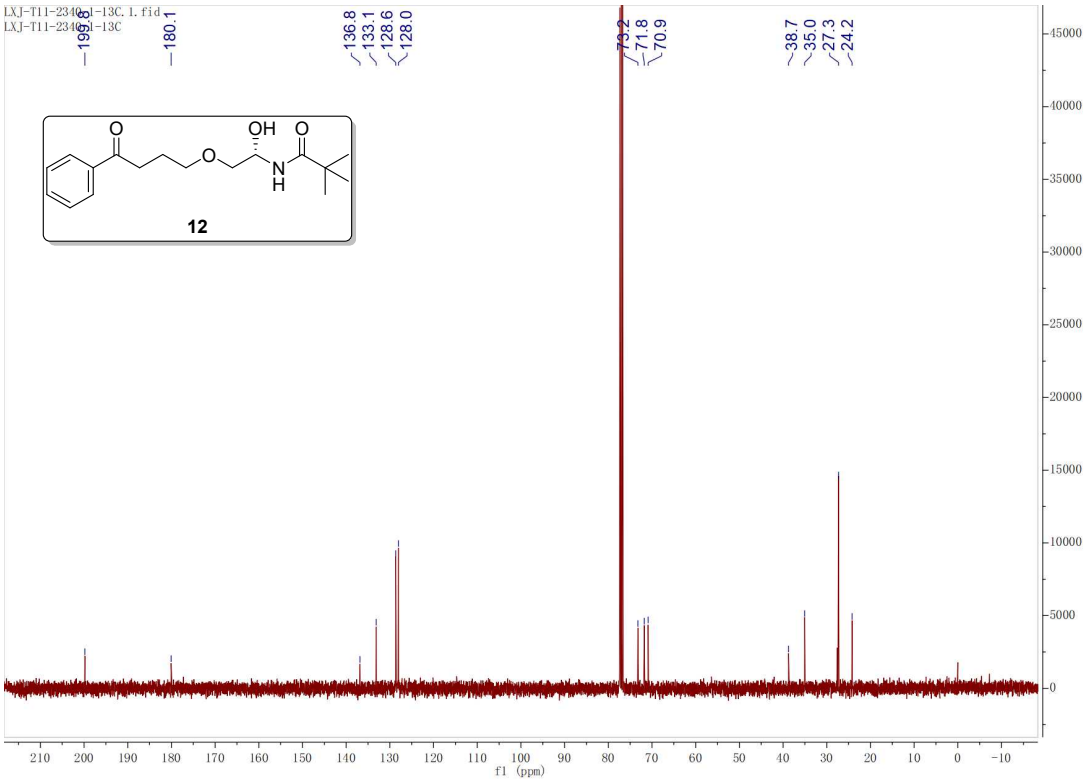
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	12.613	429312	33.847	BV
2	13.213	839068	66.153	VB
		1268380	100.000	

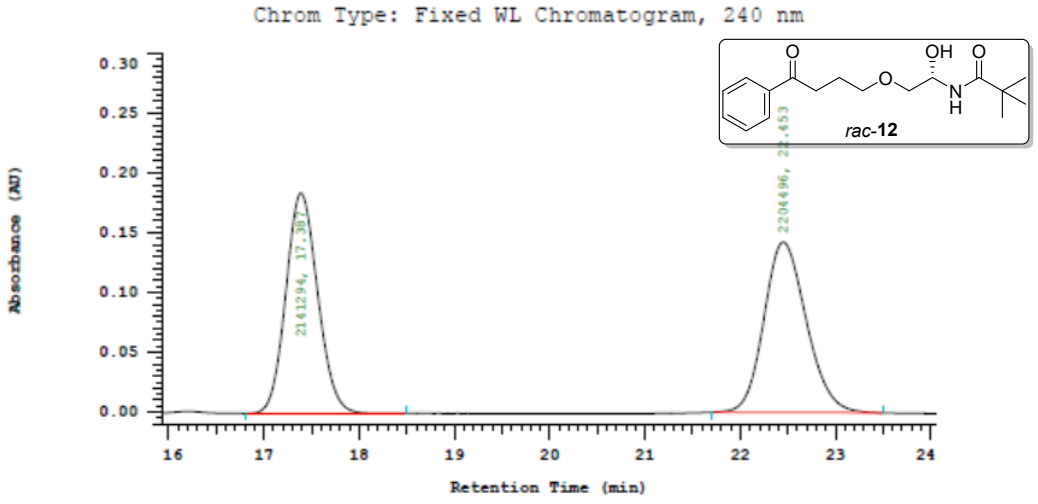
The ^{1}H NMR spectrum of 12 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 12 (101 MHz, $CDCl_3$)



The HPLC of racemic 12



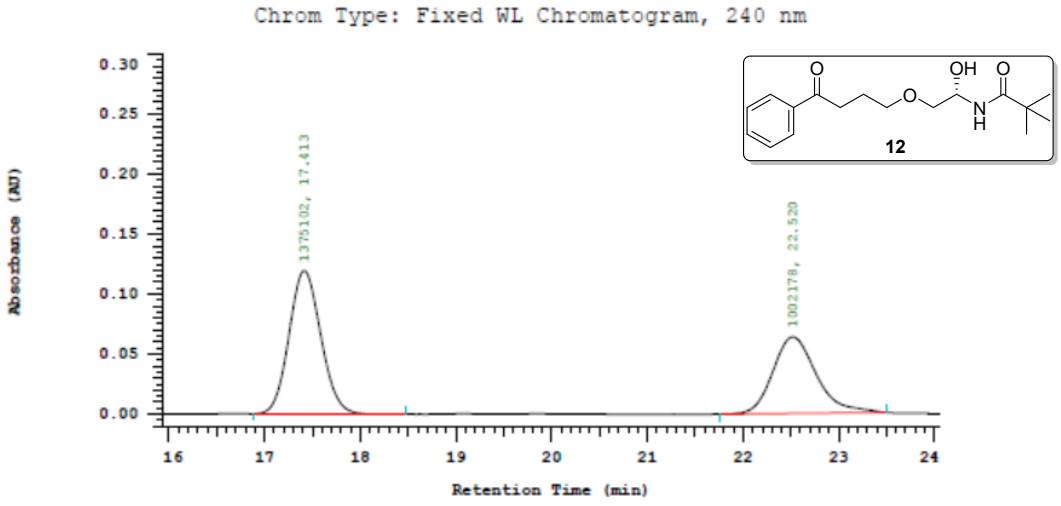
Chrom Type: Fixed WL Chromatogram, 240 nm

Peak Quantitation: AREA

Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.387	2141294	49.273	BB
2	22.453	2204496	50.727	BB
		4345790	100.000	

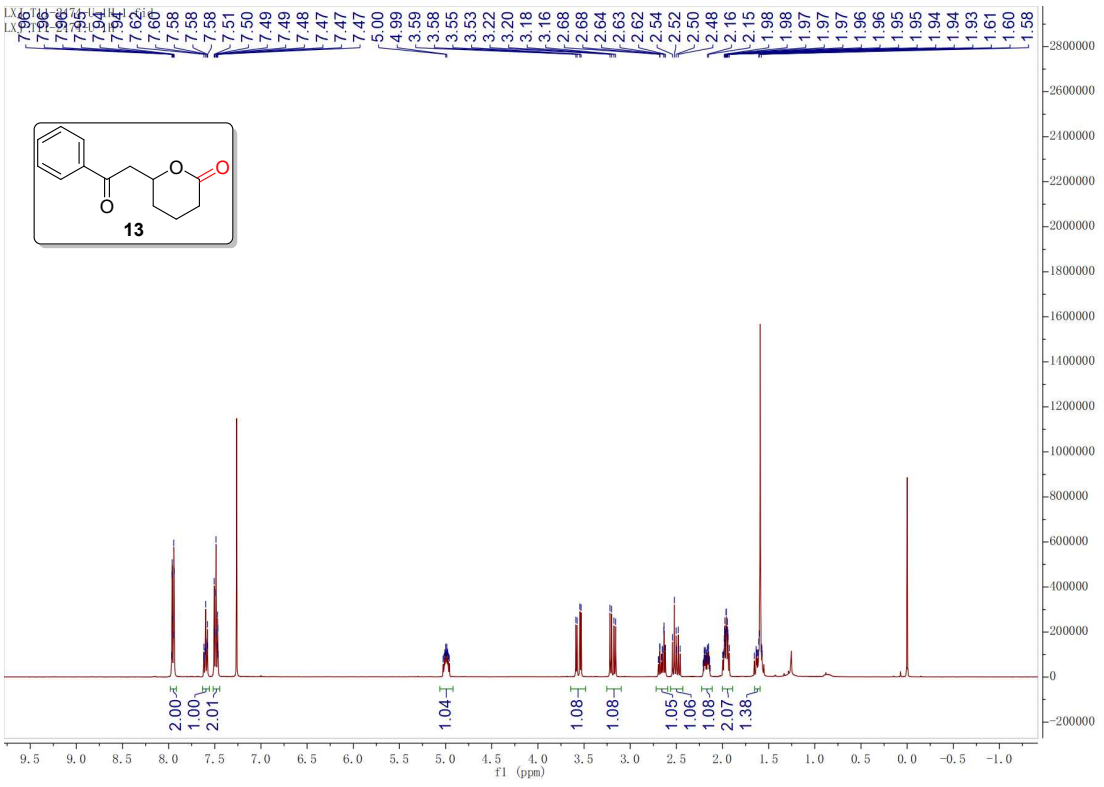
The HPLC of chiral 12



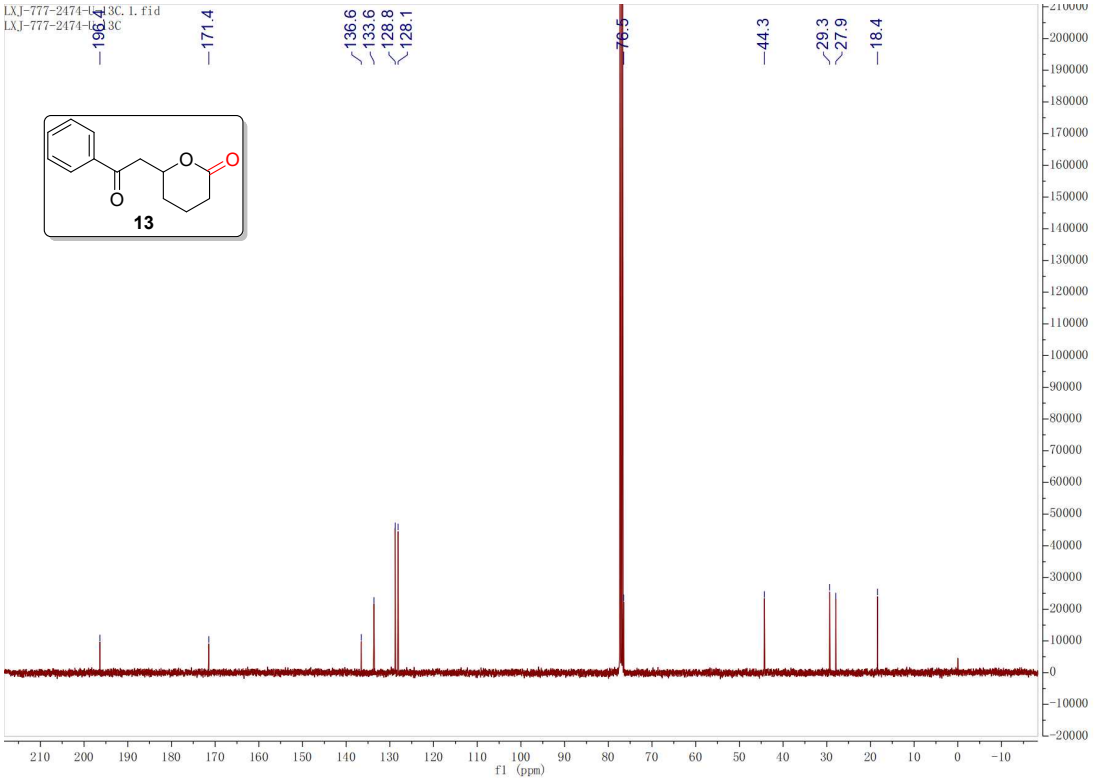
Chrom Type: Fixed WL Chromatogram, 240 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	17.413	1375102	57.843	BB
2	22.520	1002178	42.157	BB
		2377280	100.000	

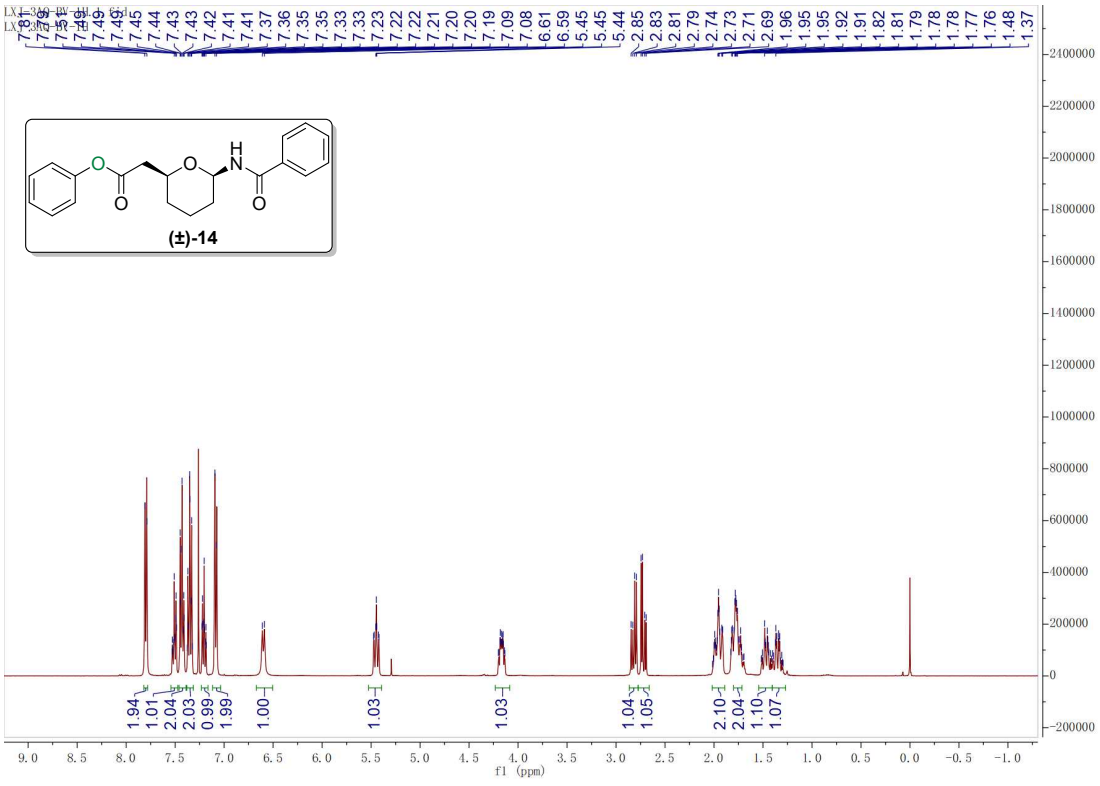
The ^{1}H NMR spectrum of 13 (400 MHz, $CDCl_3$)



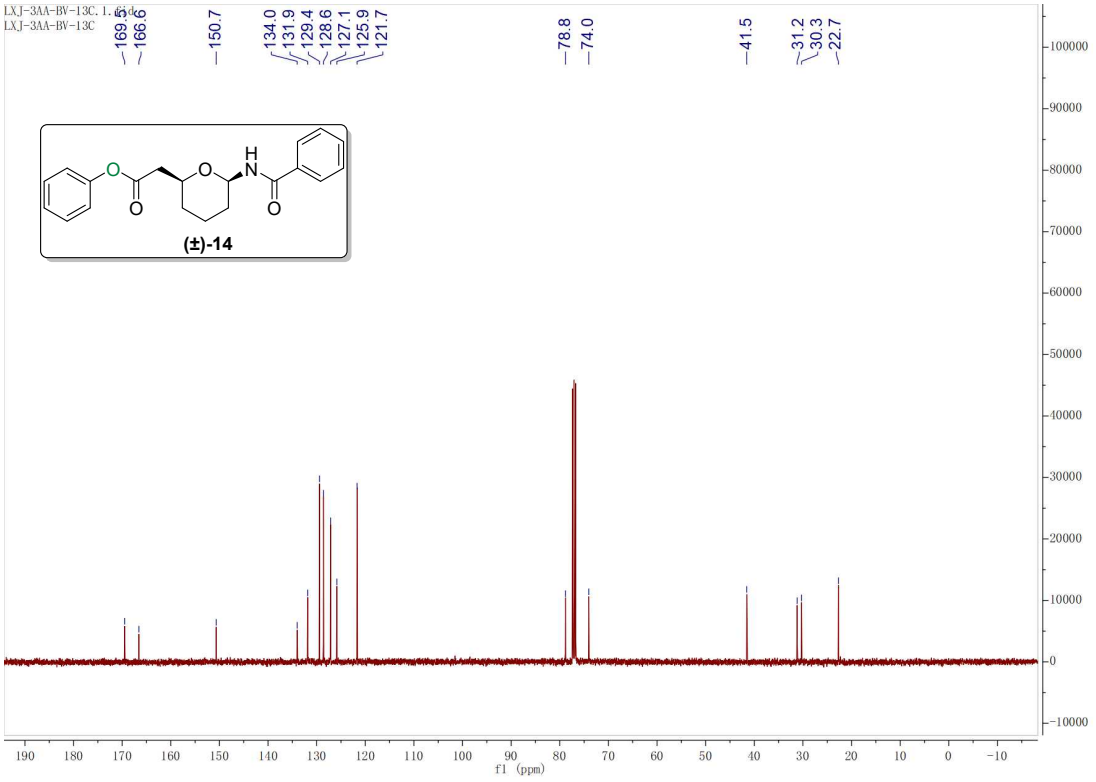
The ^{13}C NMR spectrum of 13 (101 MHz, $CDCl_3$)



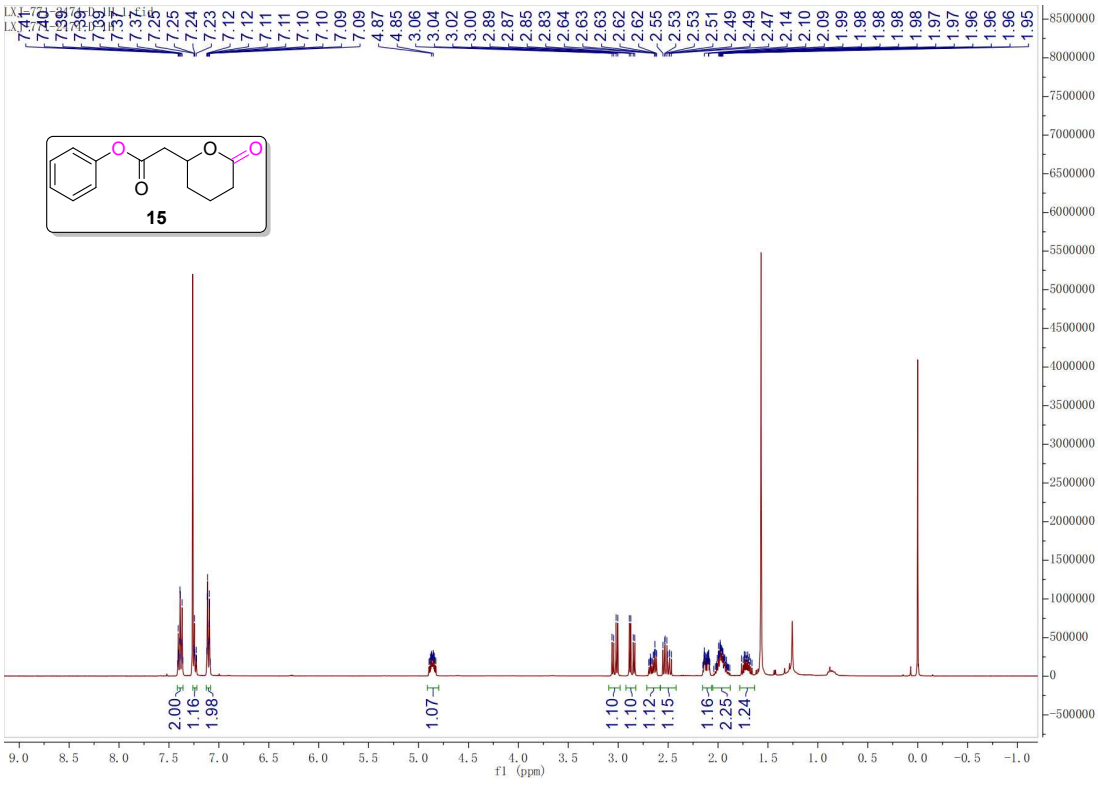
The ^{1}H NMR spectrum of (±)-14 (400 MHz, $CDCl_3$)



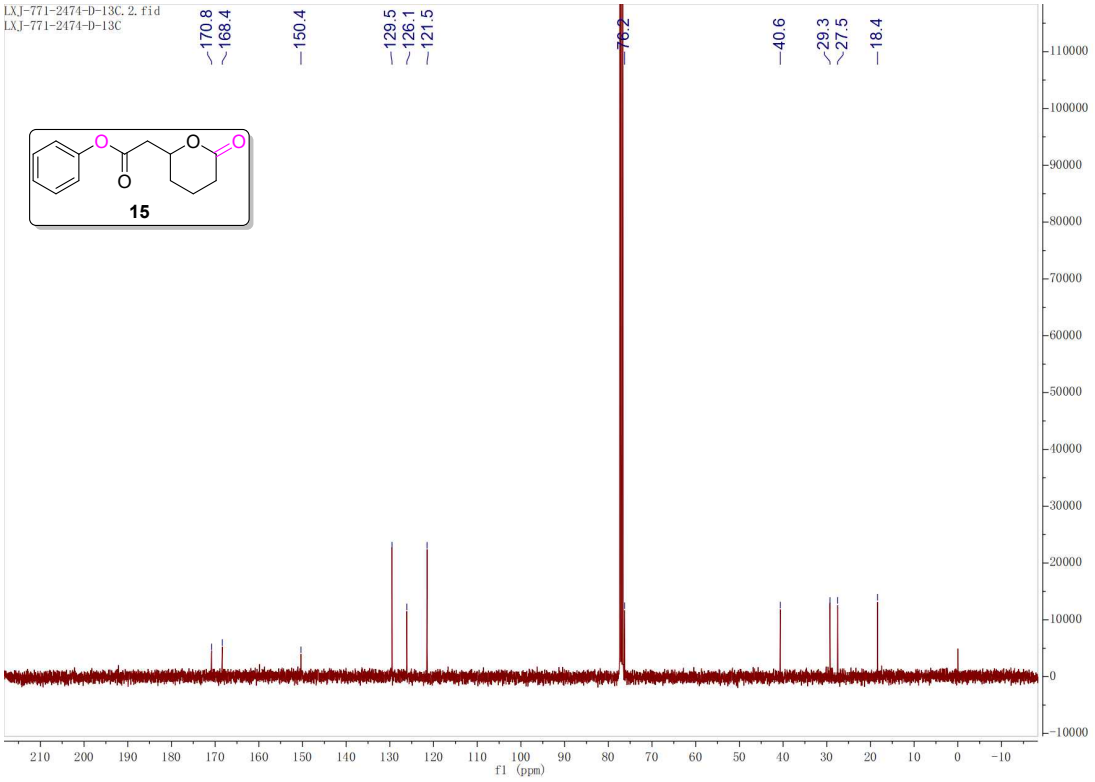
The ^{13}C NMR spectrum of (±)-14 (101 MHz, $CDCl_3$)



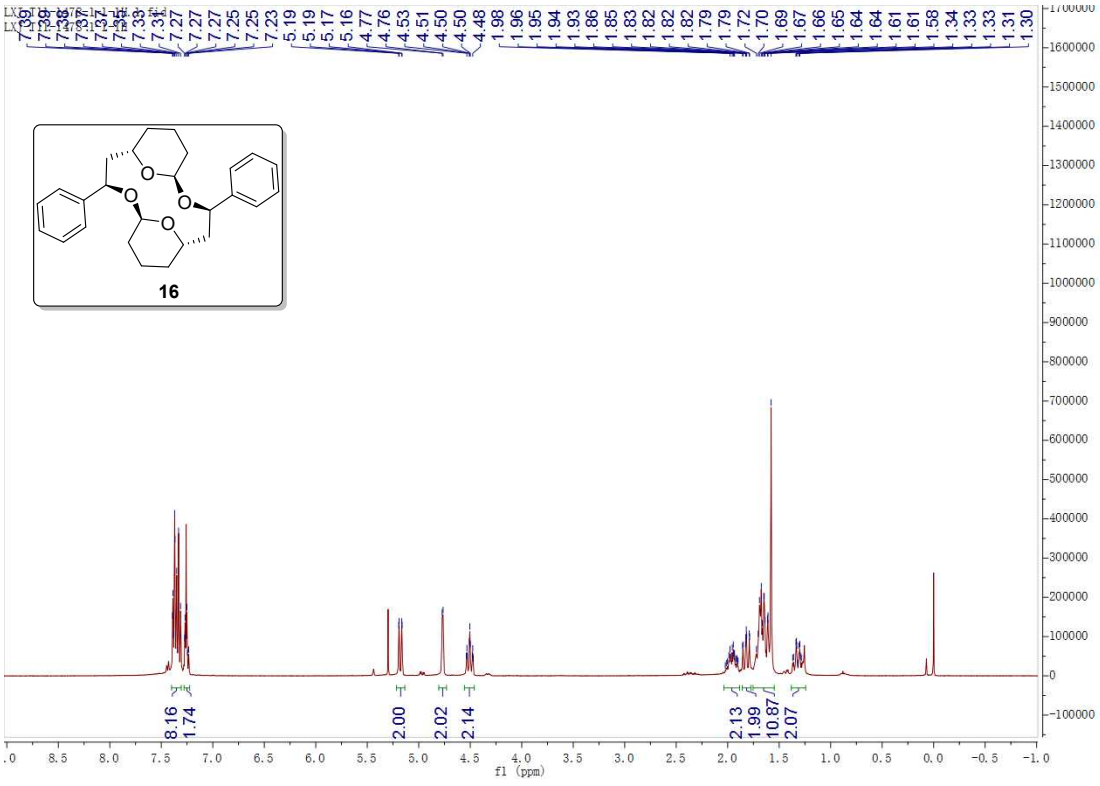
The ^{1}H NMR spectrum of 15 (400 MHz, $CDCl_3$)



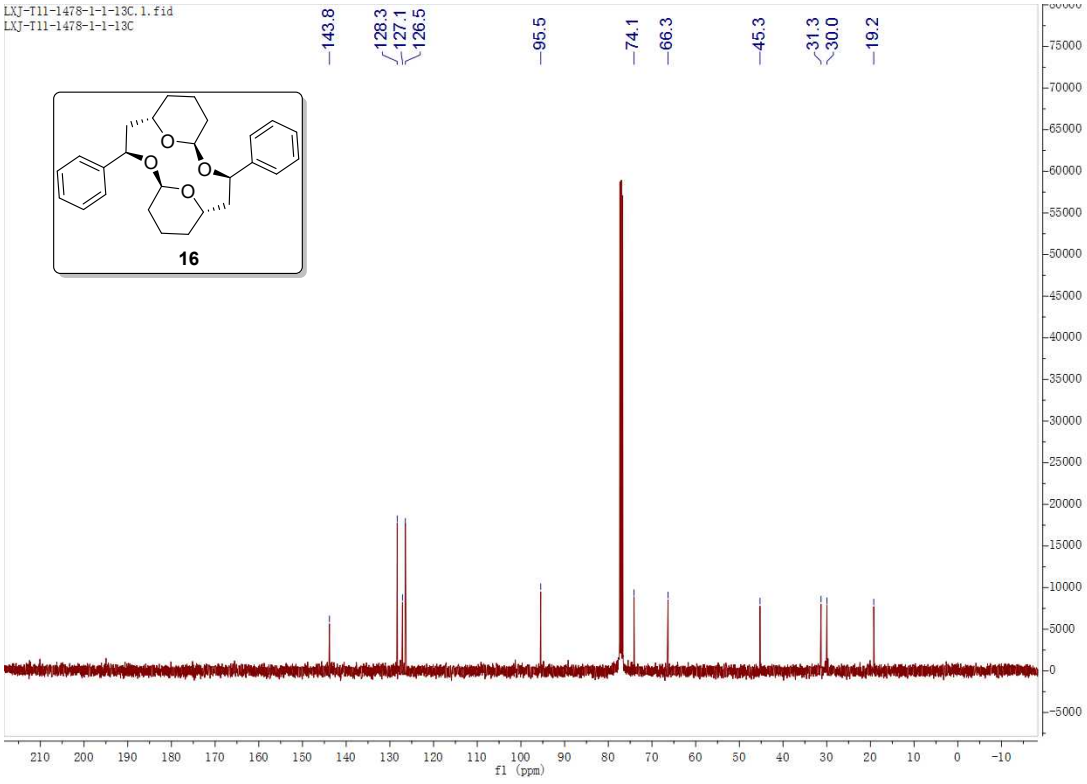
The ^{13}C NMR spectrum of 15 (101 MHz, $CDCl_3$)



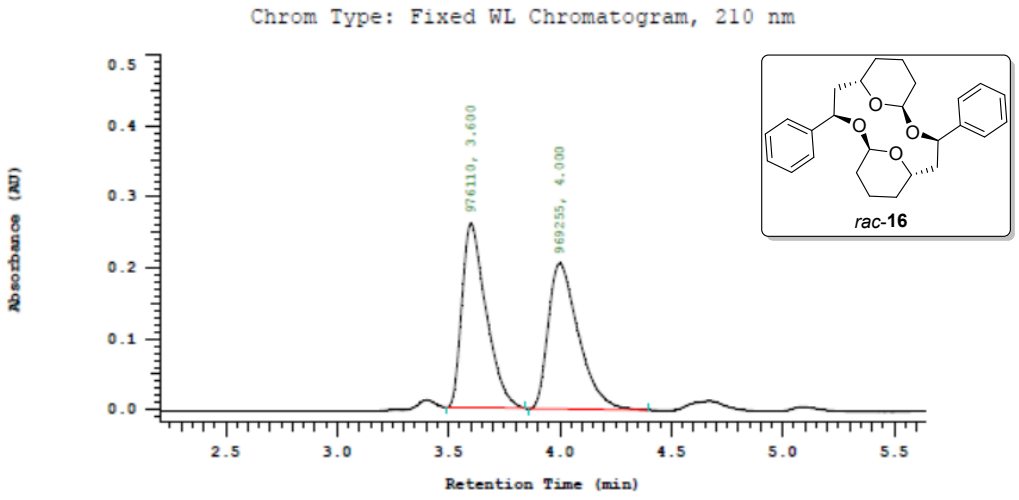
The ^{1}H NMR spectrum of 16 (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 16 (101 MHz, $CDCl_3$)



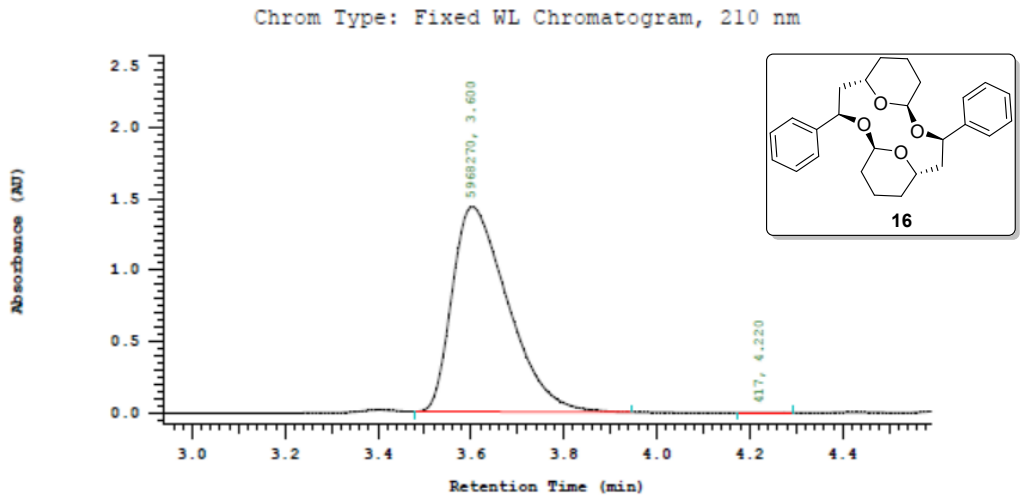
The HPLC of racemic 16



Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	3.600	976110	50.176	BB
2	4.000	969255	49.824	BB
		1945365	100.000	

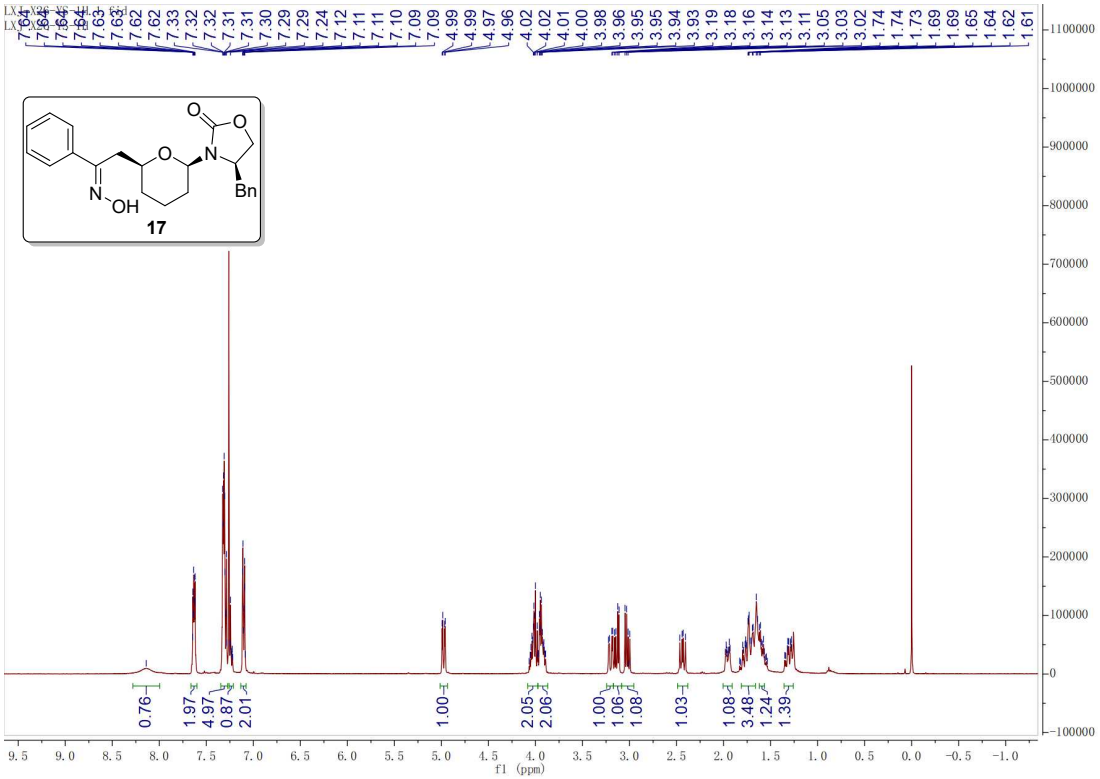
The HPLC of chiral 16



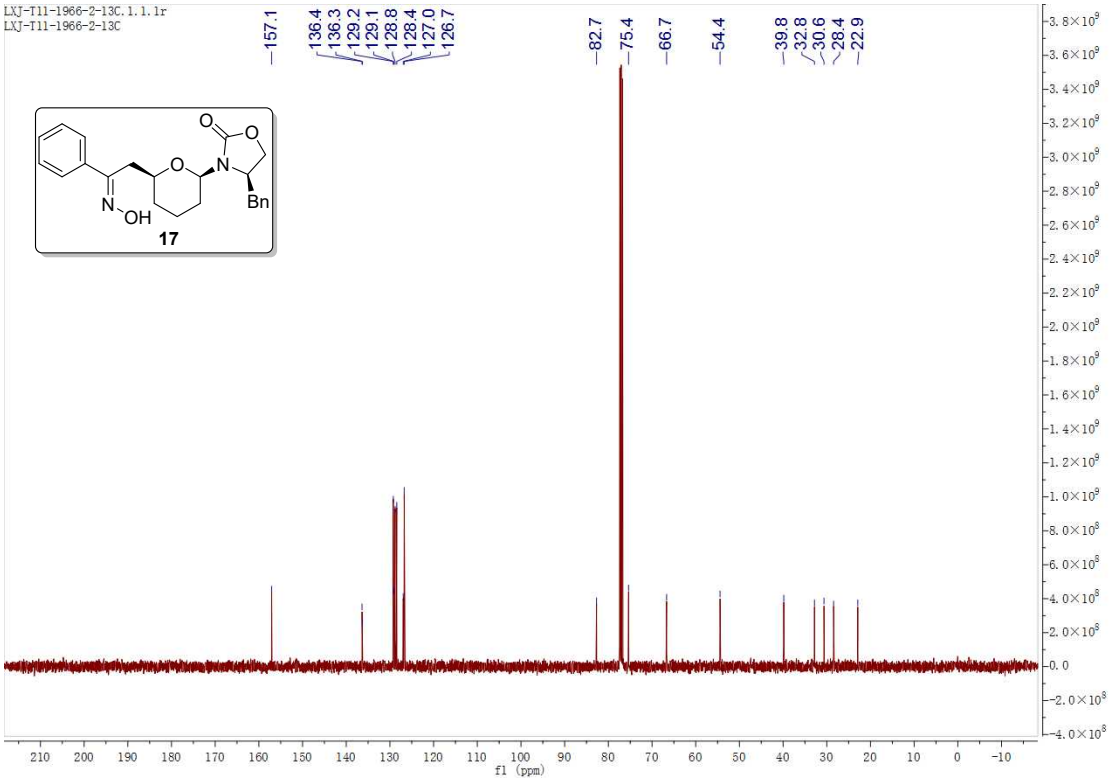
Chrom Type: Fixed WL Chromatogram, 210 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	3.600	5968270	99.993	BB
2	4.220	417	0.007	BB
		5968687	100.000	

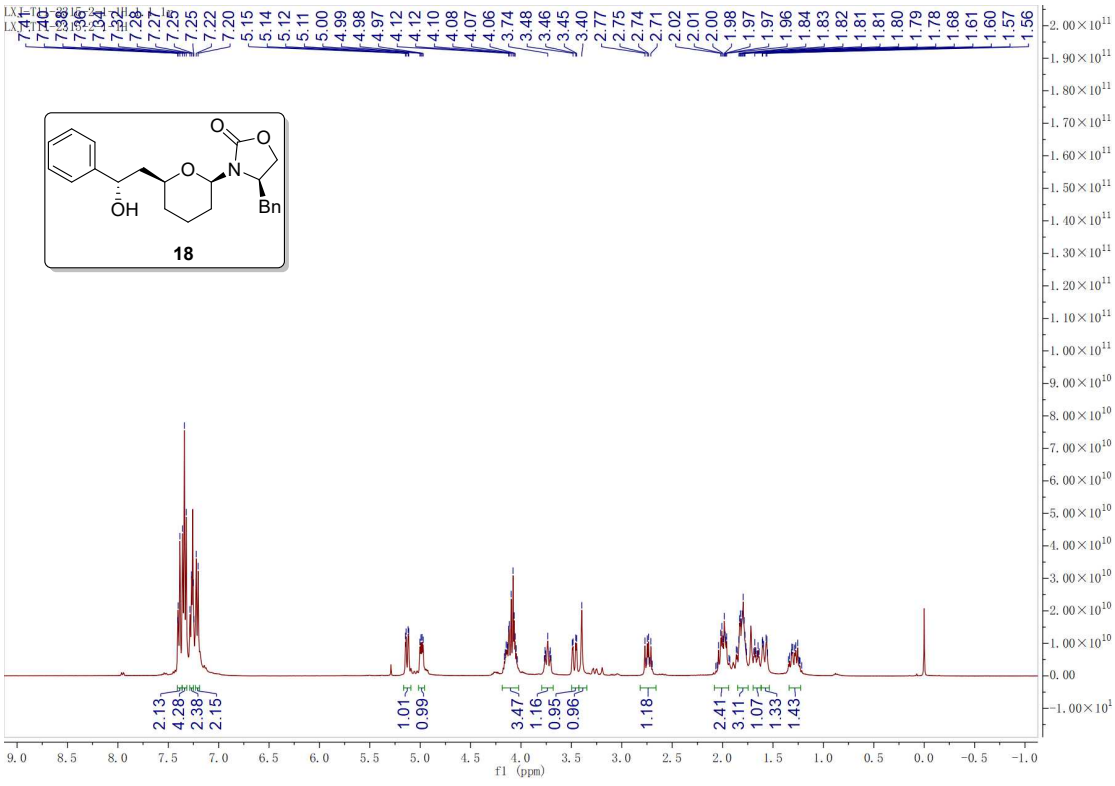
The ^{1}H NMR spectrum of 17 (400 MHz, $CDCl_3$)



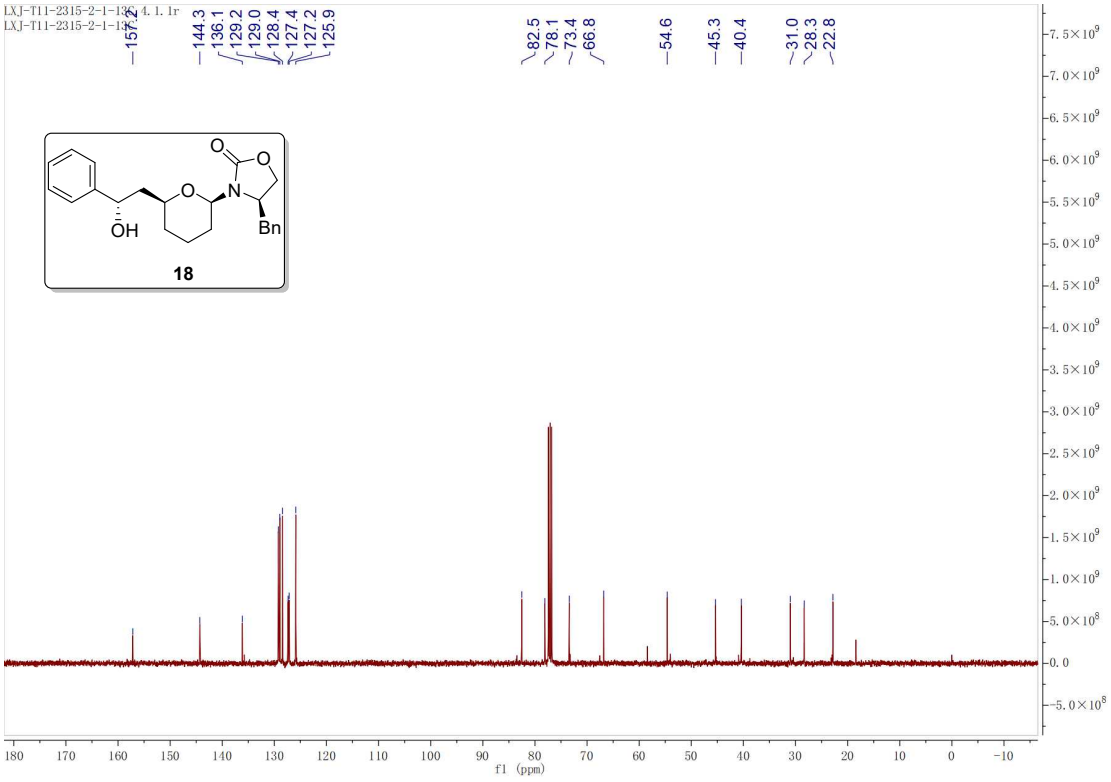
The ^{13}C NMR spectrum of 17 (101 MHz, $CDCl_3$)



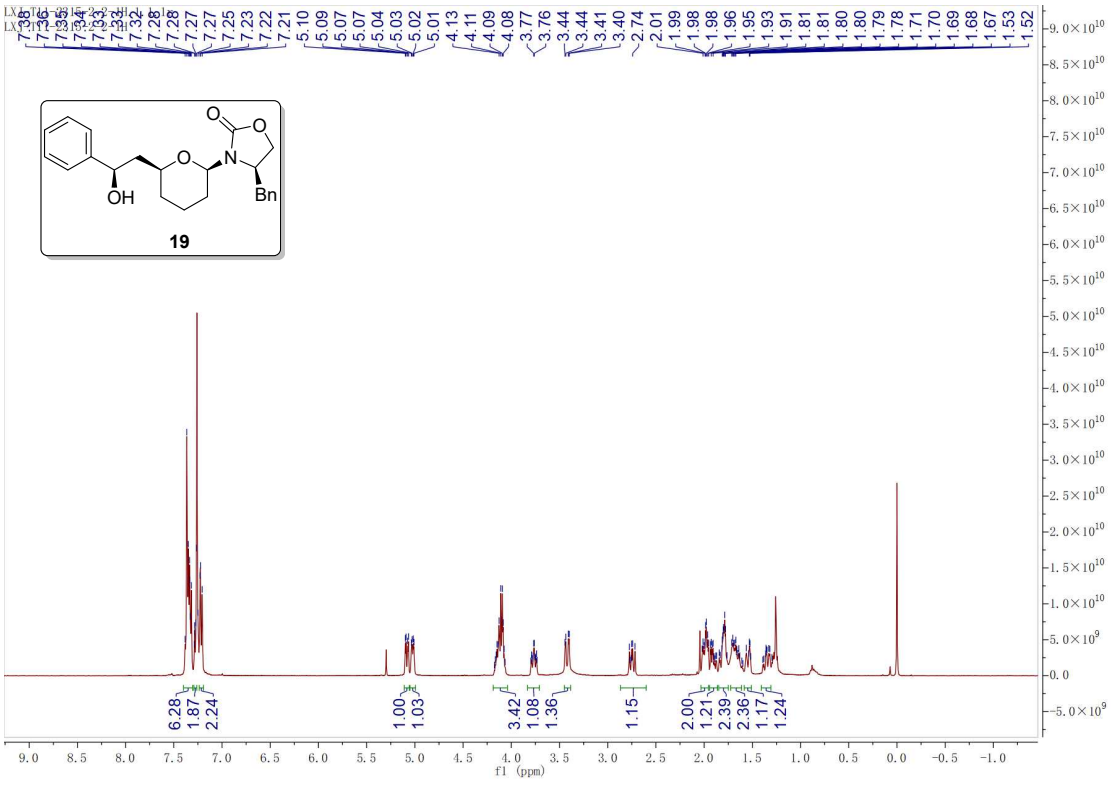
The ^{1}H NMR spectrum of 18 (400 MHz, $CDCl_3$)



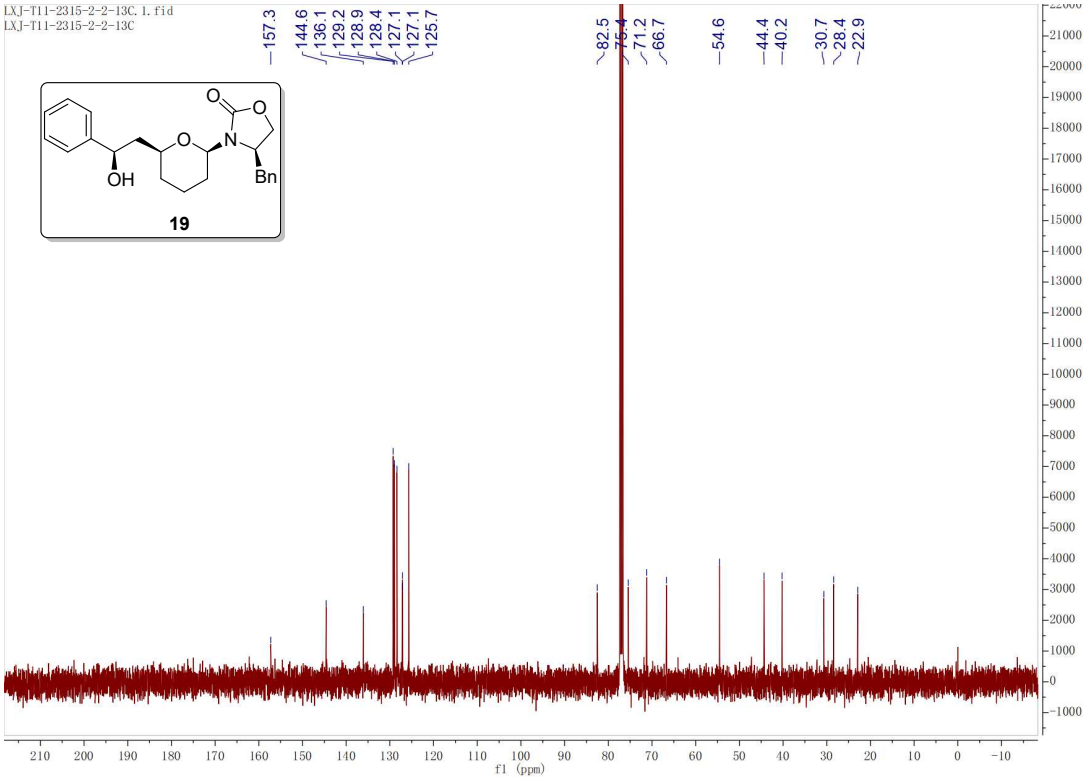
The ^{13}C NMR spectrum of 18 (101 MHz, $CDCl_3$)



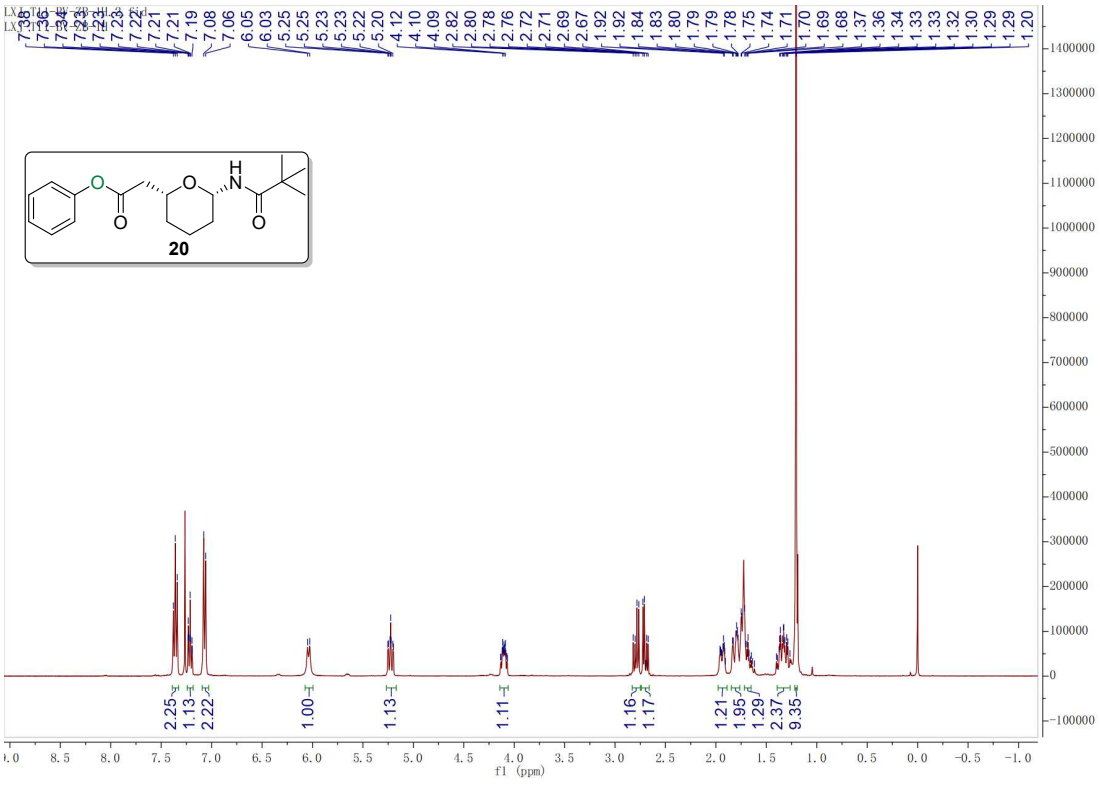
The ^{1}H NMR spectrum of 19 (400 MHz, $CDCl_3$)



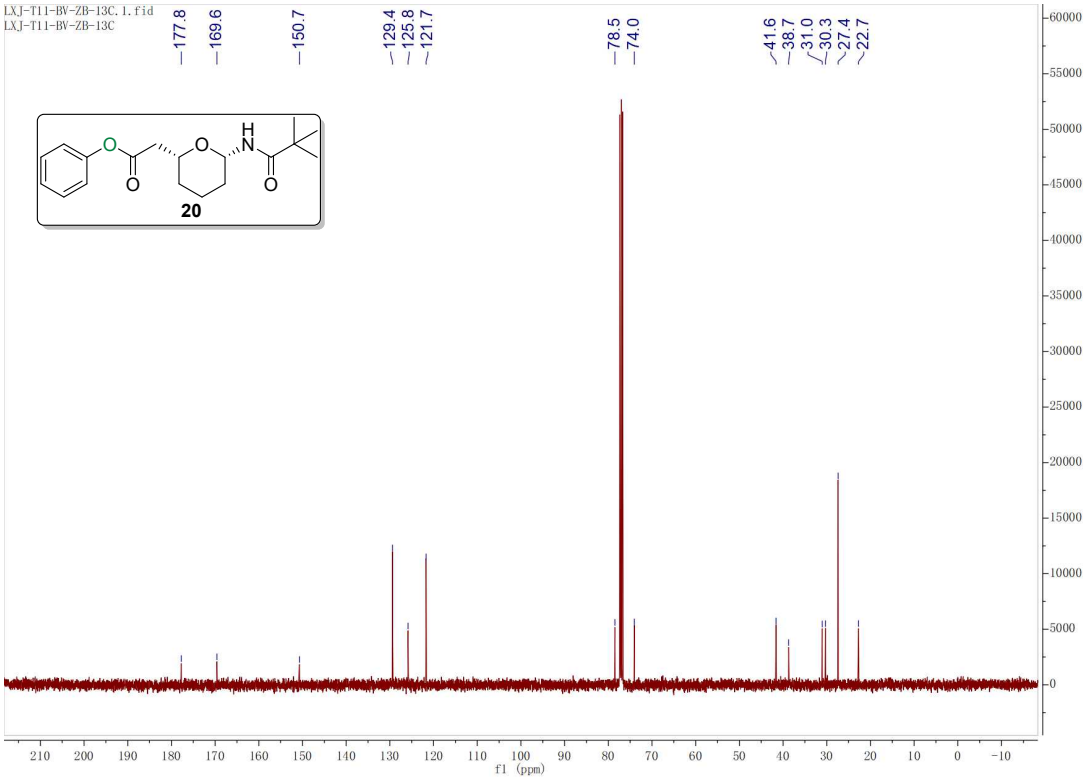
The ^{13}C NMR spectrum of 19 ($CDCl_3$)



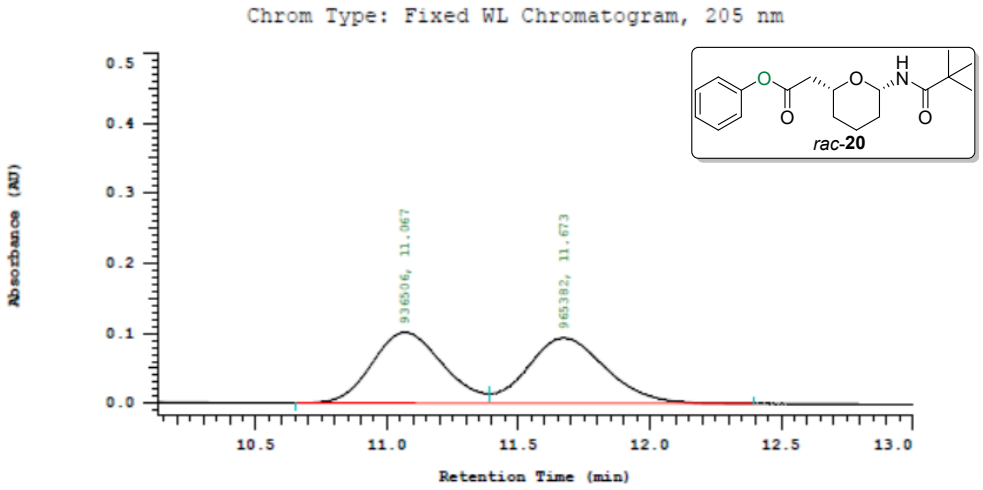
The ^{1}H NMR spectrum of 20 ($CDCl_3$)



The ^{13}C NMR spectrum of 20 (101 MHz, $CDCl_3$)



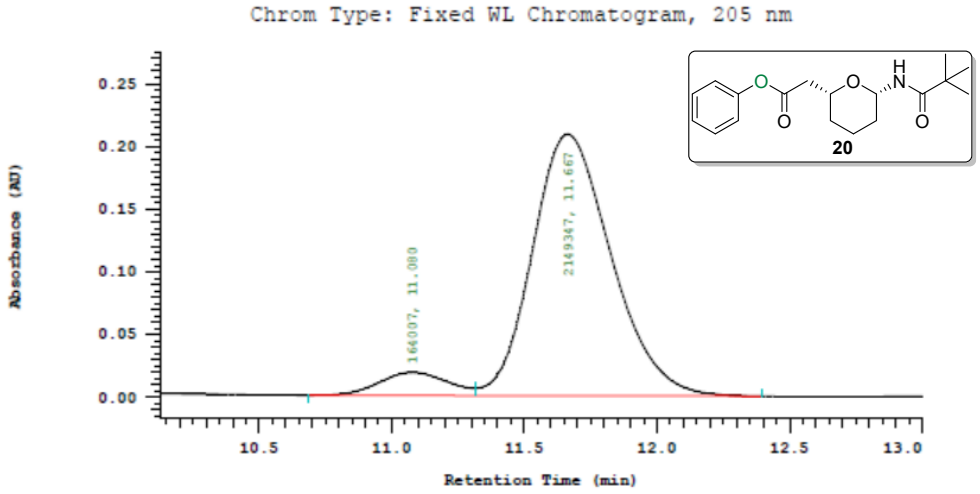
The HPLC of racemic 20



Chrom Type: Fixed WL Chromatogram, 205 nm
Peak Quantitation: AREA
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.067	936506	49.241	BV
2	11.673	965382	50.759	VB
		1901888	100.000	

The HPLC of chiral 20



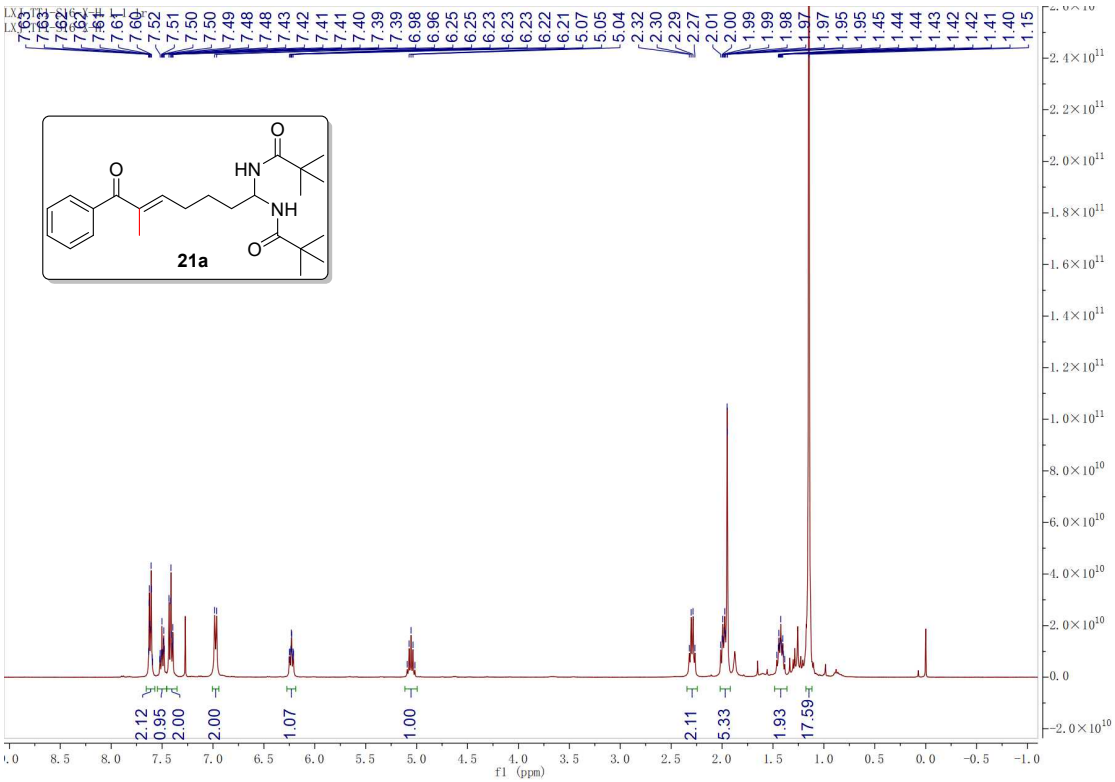
Chrom Type: Fixed WL Chromatogram, 205 nm

Peak Quantitation: AREA

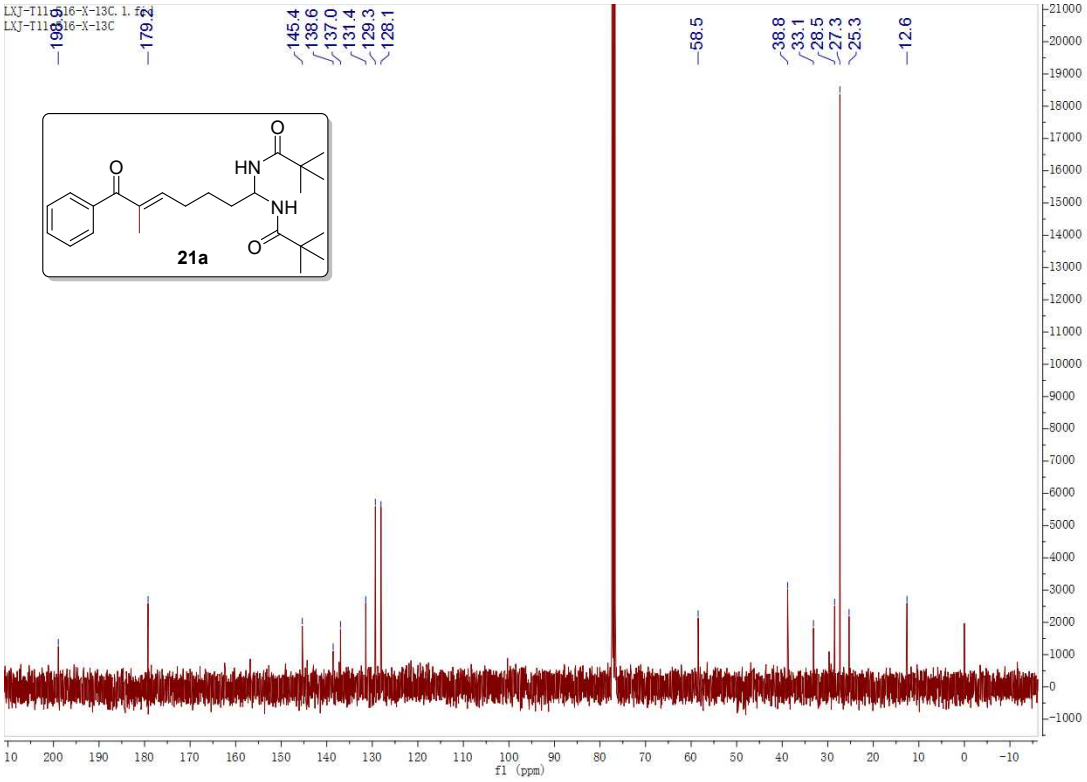
Calculation Method: AREA%

No.	RT	Area	Area %	BC
1	11.080	164007	7.090	BV
2	11.667	2149347	92.910	VB
		2313354	100.000	

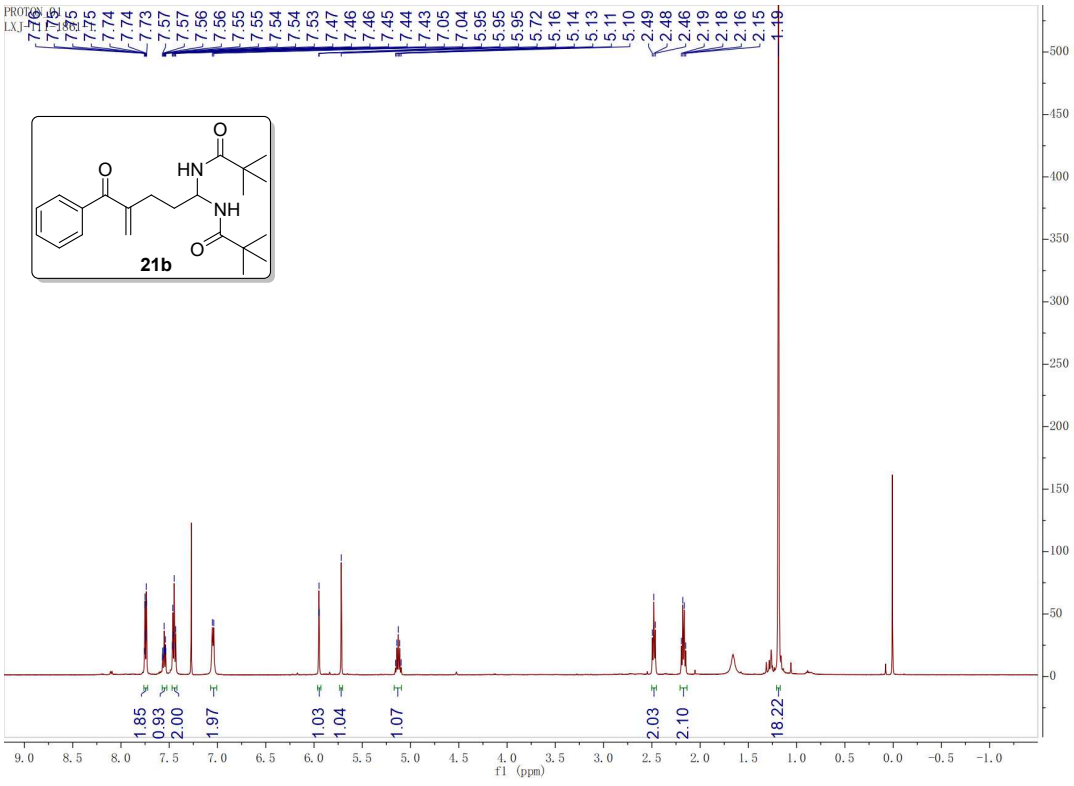
The ^{1}H NMR spectrum of 21a (400 MHz, $CDCl_3$)



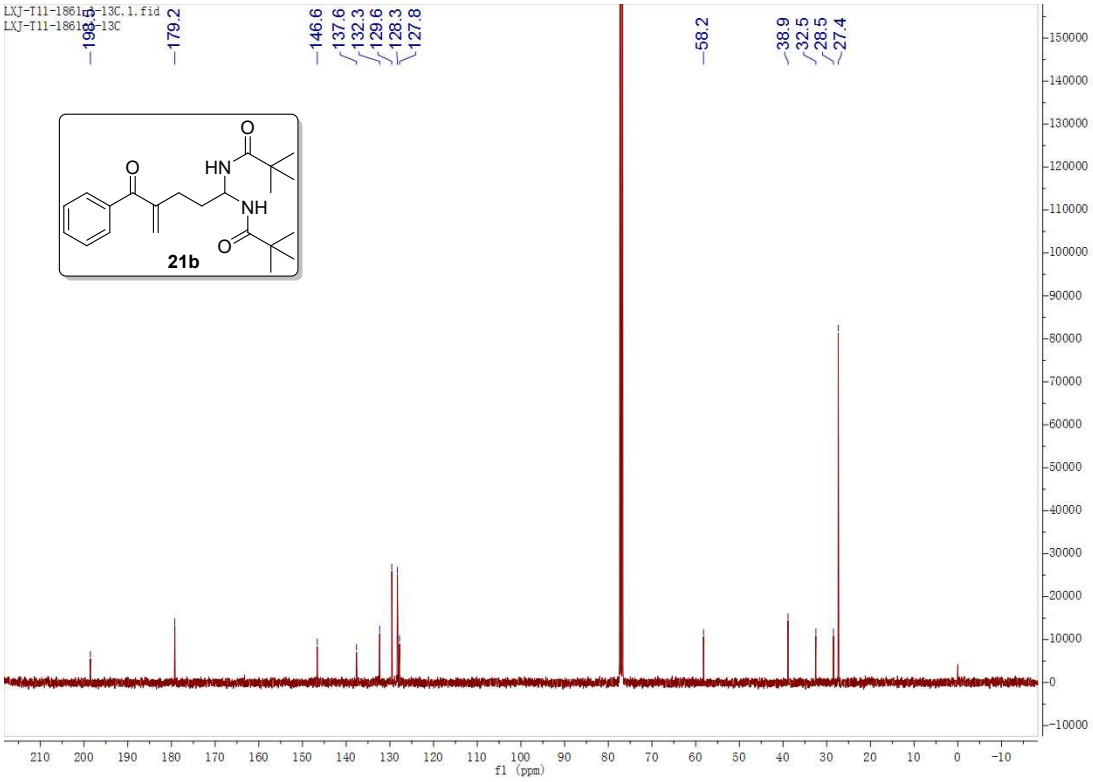
The ^{13}C NMR spectrum of 21a (101 MHz, $CDCl_3$)



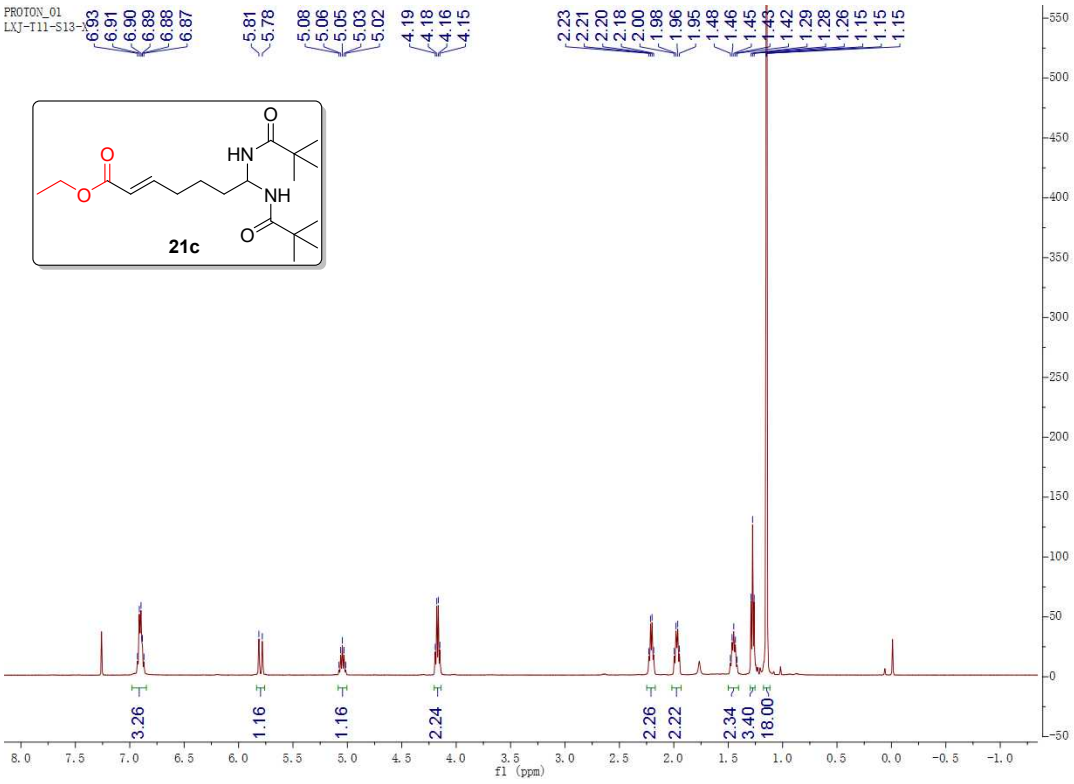
The ^{1}H NMR spectrum of 21b (500 MHz, $CDCl_3$)



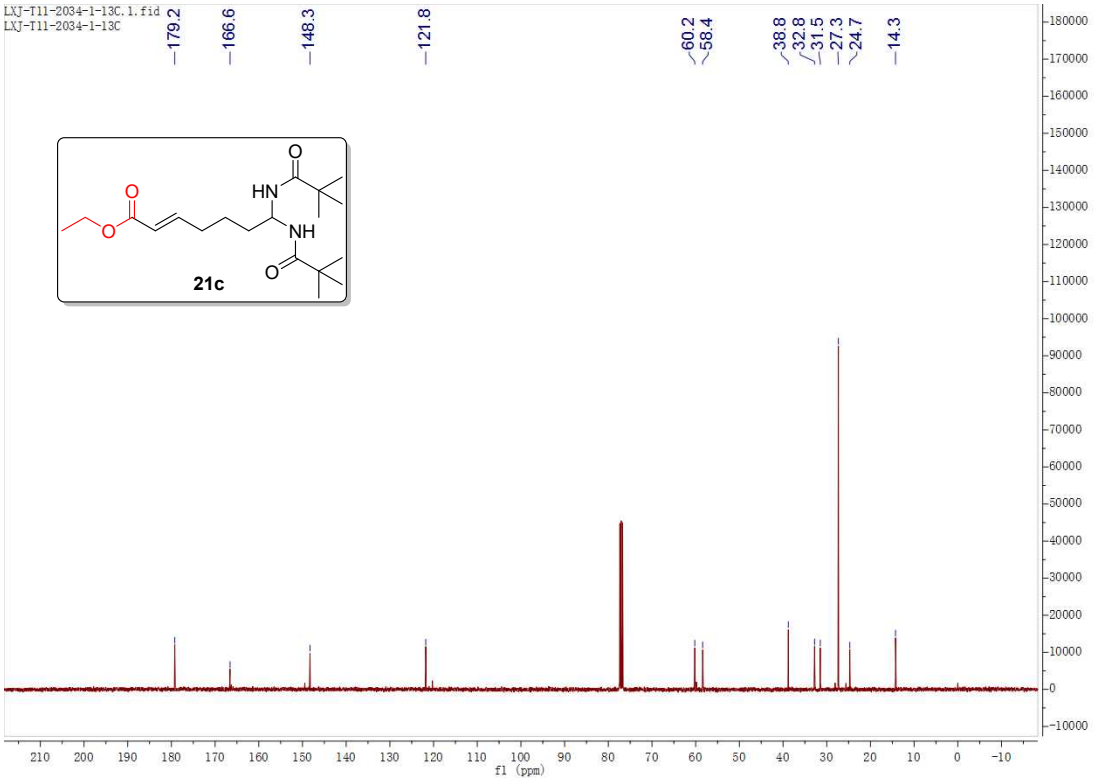
The ^{13}C NMR spectrum of 21b (101 MHz, $CDCl_3$)



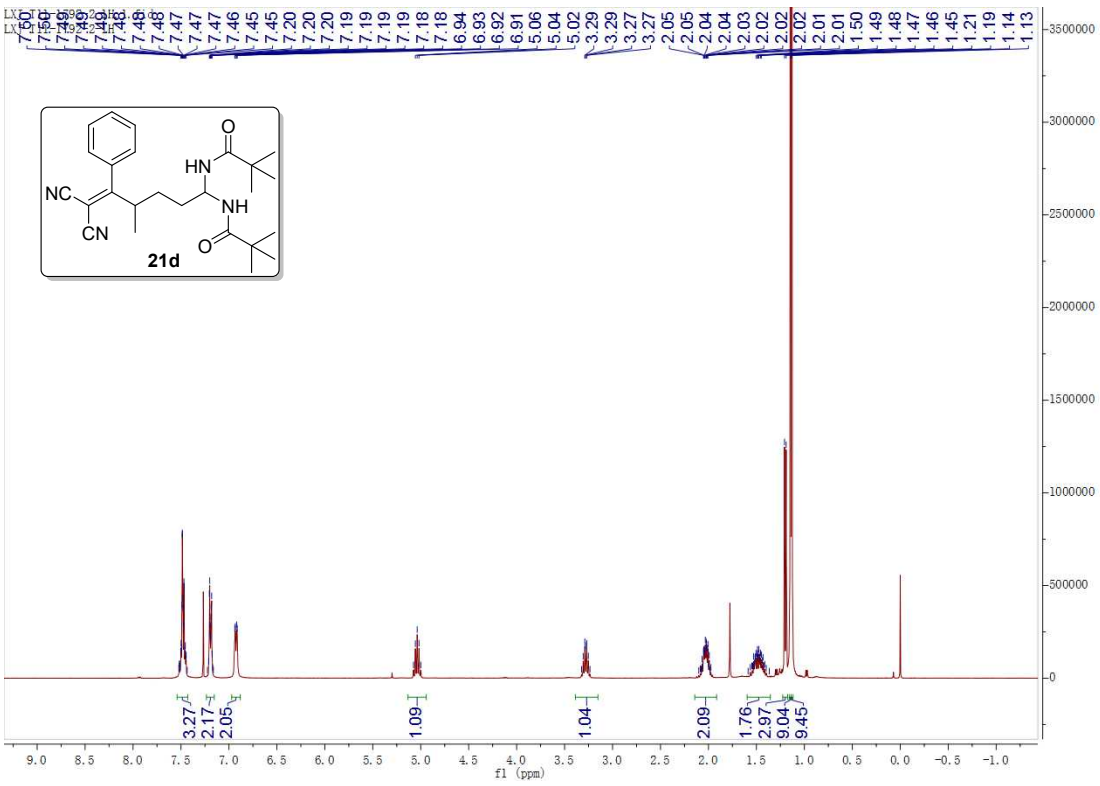
The ^{1}H NMR spectrum of 21c (500 MHz, $CDCl_3$)



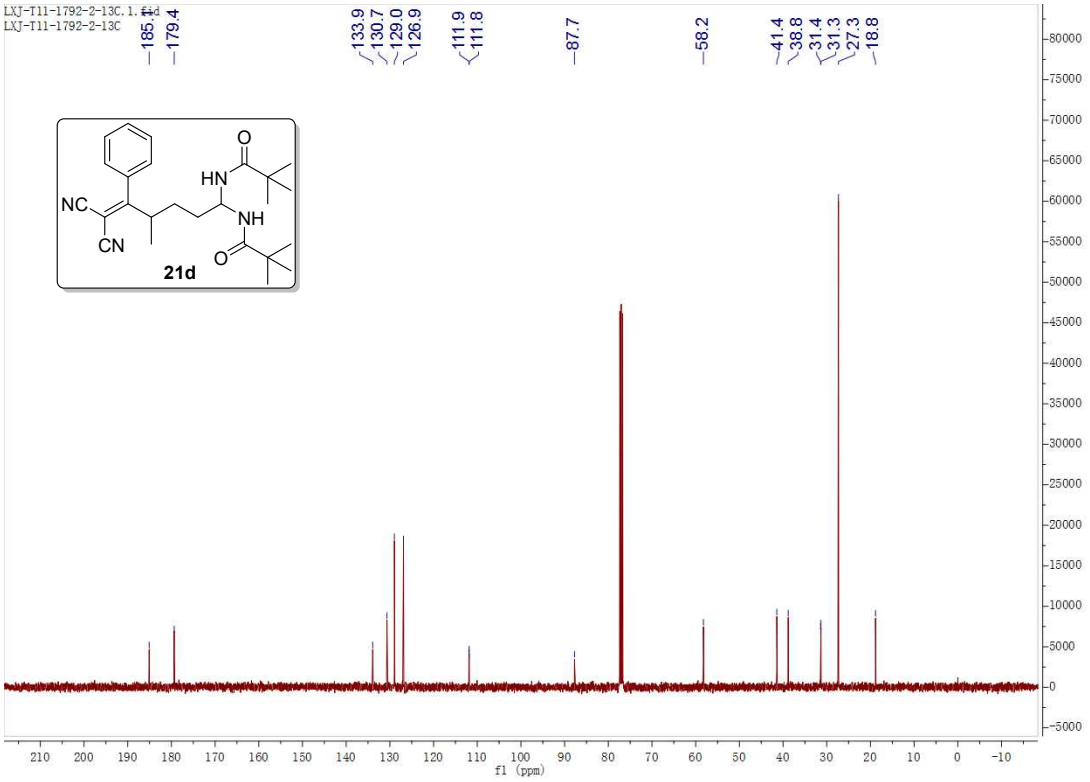
The ^{13}C NMR spectrum of 21c (101 MHz, $CDCl_3$)



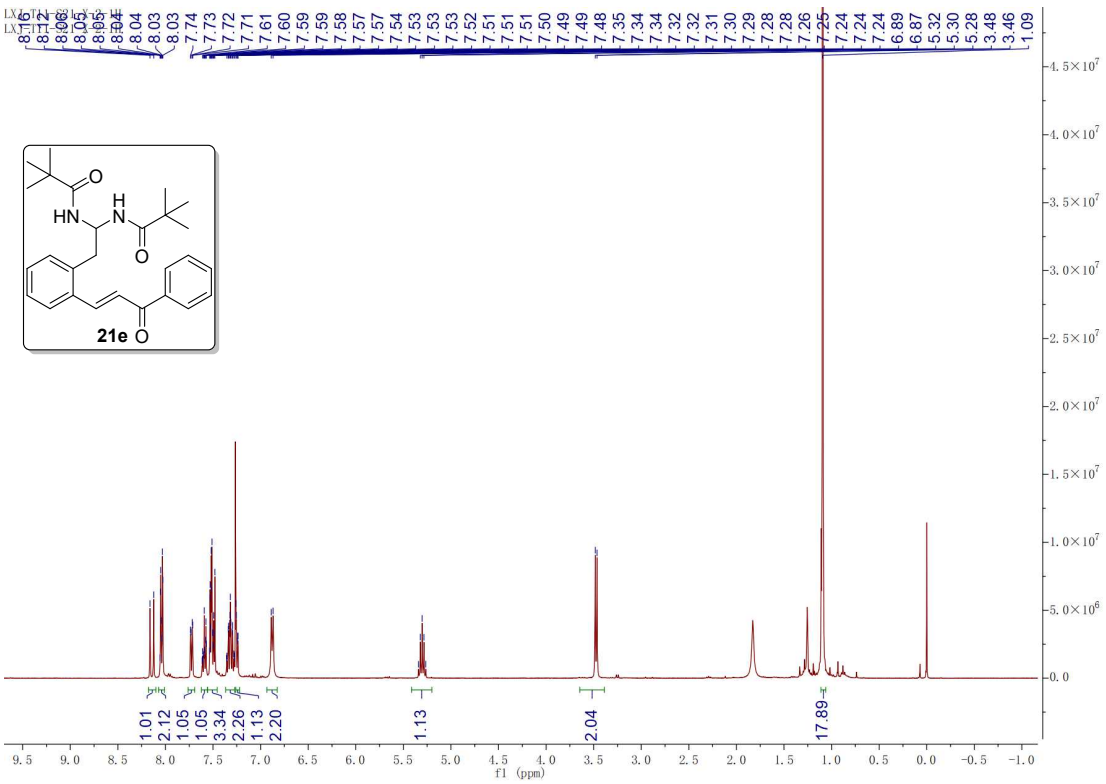
The ^{1}H NMR spectrum of 21d (400 MHz, $CDCl_3$)



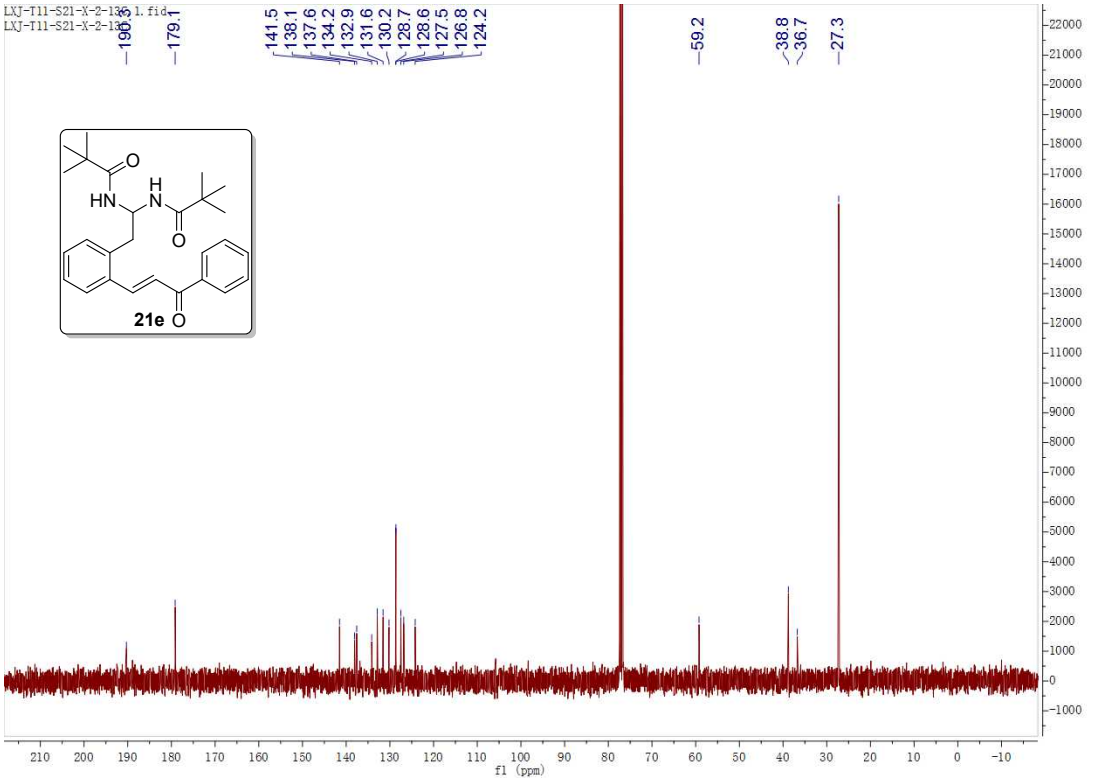
The ^{13}C NMR spectrum of 21d (101 MHz, $CDCl_3$)



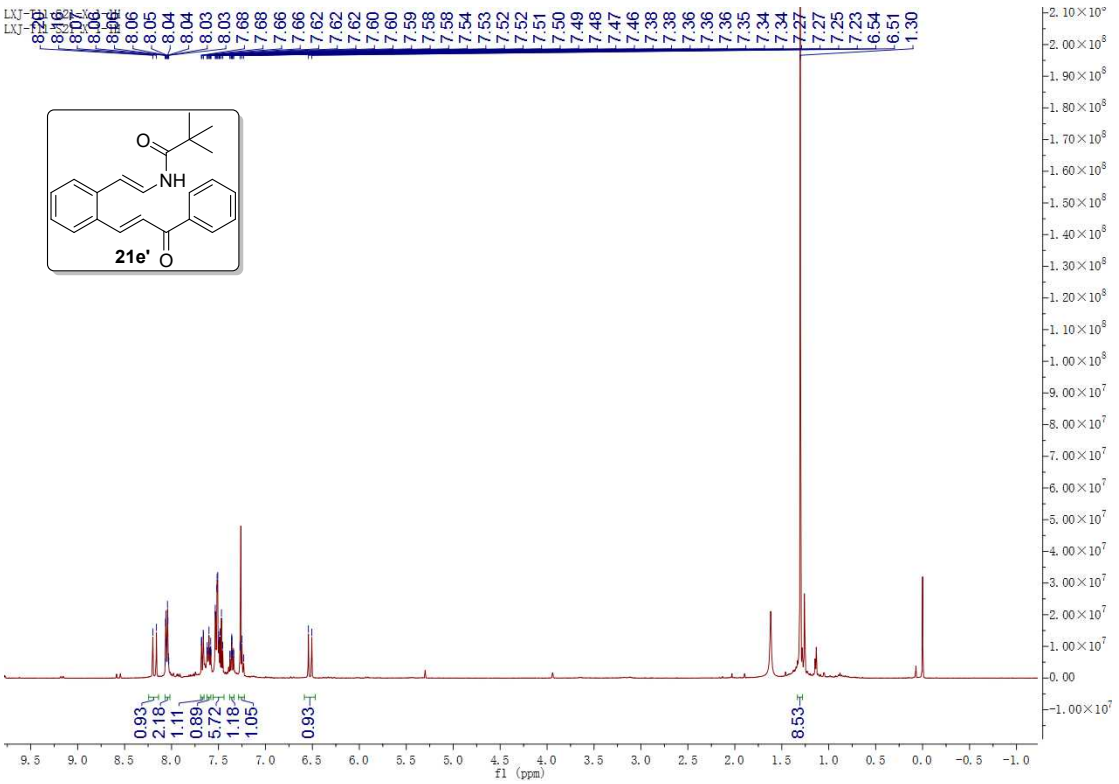
The 1H NMR spectrum of 21e (400 MHz, CDCl3)



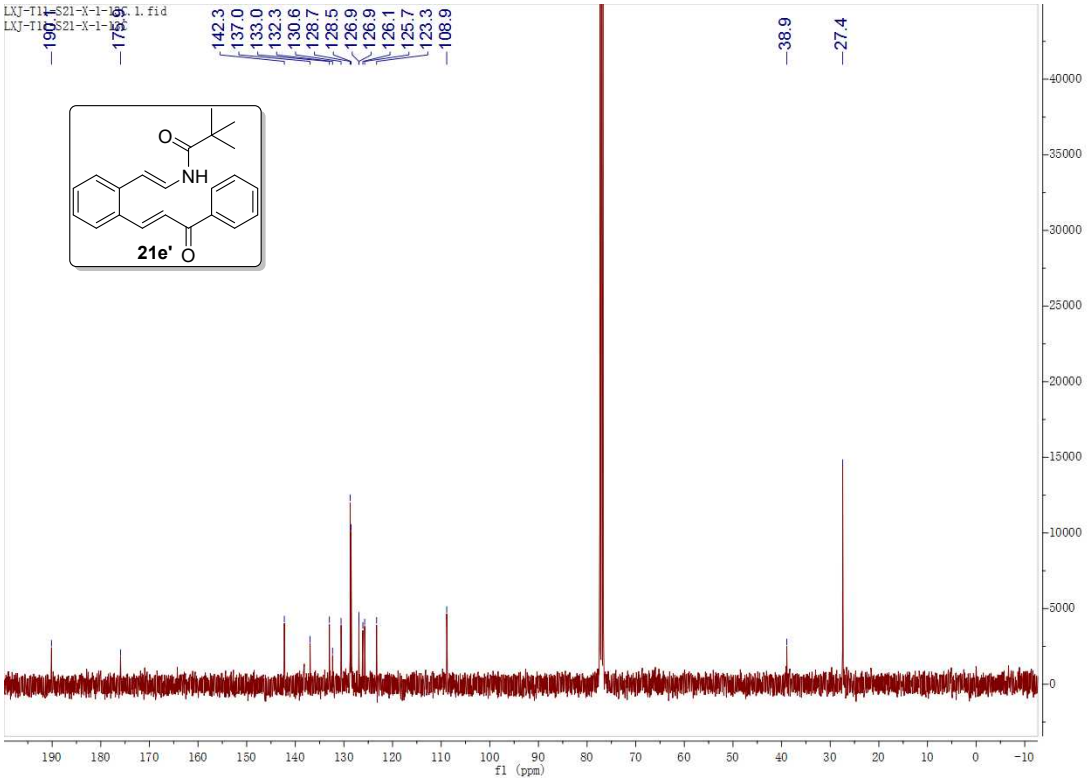
The ^{13}C NMR spectrum of 21e (101 MHz, $CDCl_3$)



The ^{1}H NMR spectrum of 21e' (400 MHz, $CDCl_3$)



The ^{13}C NMR spectrum of 21e' (101 MHz, $CDCl_3$)



R. Single crystal X-Ray diffraction data:

The absolute configuration of compound **3af** (CCDC 2092457), **17** (CCDC 2092460) and the relative configuration of **(±)-3aj** (CCDC 2092458), **(±)-16** (CCDC 2092459) were unambiguously assigned by single crystal X-ray analysis. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.].

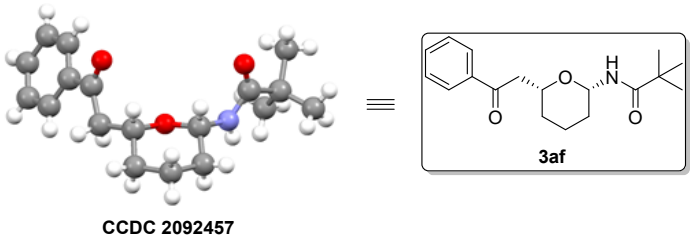


Table **S6**. Crystal data and structure refinement for **3af** (CCDC 2092457)

Identification code	exp_11382
Empirical formula	C9 H12.50 N0.50 O1.50
Formula weight	151.69
Temperature	293(2) K
Wavelength	1.54184 Å
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 5.63303(18) Å α = 90 °
	b = 9.7271(3) Å β = 90 °
	c = 32.2704(12) Å γ = 90 °
Volume	1768.20(11) $Å^3$
Z	8
Density (calculated)	1.140 Mg/m^3
Absorption coefficient	0.615 mm^{-1}
F(000)	656
Crystal size	0.120 x 0.120 x 0.110 mm^3
Radiation	CuKα (λ = 1.54184)
Theta range for data collection	2.739 to 67.218 °
Index ranges	-6<=h<=3, -10<=k<=11, -36<=l<=38
Reflections collected	3735

Independent reflections	2694 [R(int) = 0.0161]
Completeness to theta = 67.218°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.96380
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2694 / 648 / 234
Goodness-of-fit on F^2	1.068
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1232
R indices (all data)	R1 = 0.0479, wR2 = 0.1274
Absolute structure parameter	-0.12(14)
Extinction coefficient	0.0128(12)
Largest diff. peak and hole	0.220 and -0.136 e. $Å^{-3}$

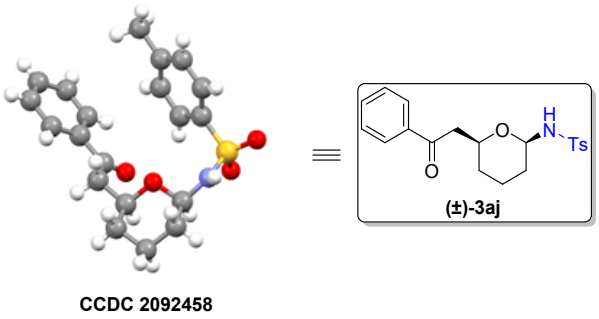


Table **S7**. Crystal data and structure refinement for **(±)-3aj** (CCDC 2092458)

Identification code	exp_11421
Empirical formula	C20 H23 N O4 S
Formula weight	373.45
Temperature	293(2) K
Wavelength	1.54184 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 8.3710(8) Å α = 72.860(11) ° b = 11.0434(13) Å β = 70.943(10) ° c = 11.6957(15) Å γ = 76.348(9) °
Volume	964.8(2) $Å^3$
Z	2
Density (calculated)	1.286 Mg/m^3
Absorption coefficient	1.694 mm^{-1}

F(000)	396
Crystal size	0.120 x 0.120 x 0.110 mm^3
Radiation	CuKα (λ = 1.54184)
Theta range for data collection	4.116 to 67.249 °
Index ranges	-10<=h<=8, -12<=k<=13, -12<=l<=13
Reflections collected	5734
Independent reflections	3337 [R(int) = 0.0345]
Completeness to theta = 67.249°	96.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.80462
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3337 / 1 / 236
Goodness-of-fit on F^2	0.941
Final R indices [I>2sigma(I)]	R1 = 0.0672, wR2 = 0.2758
R indices (all data)	R1 = 0.1008, wR2 = 0.3122
Extinction coefficient	n/a
Largest diff. peak and hole	0.283 and -0.580 e. $Å^{-3}$

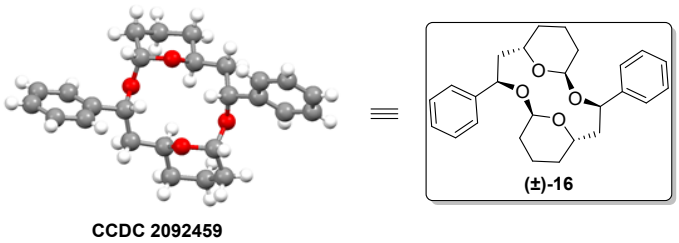
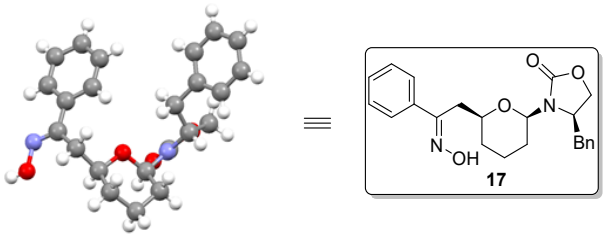


Table **S8**. Crystal data and structure refinement for **(±)-16** – CCDC 2092459

Identification code	HX-LXJ-1478-H-300K	
Empirical formula	C26 H32 O4	
Formula weight	408.51	
Temperature	299.99(10) K	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 16.4248(9) Å	α = 90 °
	b = 13.2124(7) Å	β = 106.465(6) °
	c = 10.8402(6) Å	γ = 90 °
Volume	2256.0(2) $Å^3$	
Z	4	

Density (calculated)	1.203 Mg/m^3
Absorption coefficient	0.080 mm^{-1}
F(000)	880.0
Crystal size	0.18 × 0.12 × 0.11 mm^3
Radiation	MoKα (λ = 0.71073)
Theta range for data collection	4.024 to 50.014 °
Index ranges	-19<=h<=19, -15<=k<=15, -12<=l<=11
Reflections collected	7456
Independent reflections	1993 [R(int) = 0.0187, R(sigma) = 0.0183]
Data / restraints / parameters	1993/0/136
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0343, wR2 = 0.0835
R indices (all data)	R1 = 0.0410, wR2 = 0.0888
Largest diff. peak and hole	0.11 and -0.15 e. $Å^{-3}$



CCDC 2092460

Table **S9**. Crystal data and structure refinement for **17** (CCDC 2092460)

Identification code	11912	
Empirical formula	C23 H26 N2 O4	
Formula weight	394.46	
Temperature	293(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 6.3340(3) Å	α = 90 °
	b = 16.7436(8) Å	β = 100.883(6) °
	c = 10.0625(6) Å	γ = 90 °
Volume	1047.97(10) $Å^3$	
Z	2	
Density (calculated)	1.250 Mg/m^3	

Absorption coefficient	0.696 mm^{-1}
F(000)	420
Crystal size	0.120 x 0.120 x 0.110 mm^3
Radiation	CuKα (λ = 1.54178)
Theta range for data collection	4.474 to 67.230 °
Index ranges	-7<=h<=7, -17<=k<=19, -11<=l<=12
Reflections collected	3598
Independent reflections	2712 [R(int) = 0.0378]
Completeness to theta = 67.230°	99.8 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2712 / 1 / 263
Goodness-of-fit on F^2	1.008
Final R indices [I>2sigma(I)]	R1 = 0.0486, wR2 = 0.0986
R indices (all data)	R1 = 0.0727, wR2 = 0.1131
Absolute structure parameter	-0.1(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.136 and -0.174 e. $Å^{-3}$

S. Reference:

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