Supporting Information

Construction of chiral γ-lactam scaffolds *via* asymmetric cascade [3+2] annulation of *N*-alkoxyacrylamides catalyzed by a chiral-at-metal rhodium complex

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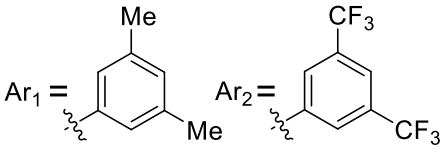
Contents

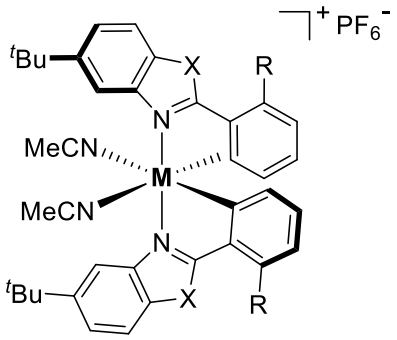
1. General Information

All non-aqueous reactions were performed in oven-dried glassware and standard Schlenk tubes under an atmosphere of argon. Dichloromethane (DCM) and 1,2-dichloroethane (DCE) were distilled from CaH_2 under inert atmosphere. Tetrahydrofuran (THF) and toluene were distilled from sodium and benzophenone under inert atmosphere. All other solvents and reagents were used as received unless otherwise noted. Thin layer chromatography was performed using silica gel 60 F-254 precoated plates (0.2~0.3 mm) and visualized by short-wave UV (254 nm) irradiation, potassium permanganate, or iodine stain. Column chromatography was performed with silica gel (200-300 mesh, Yantai Jiangyou Silica Gel Development Co., Ltd). The ^{1}H, ^{13}C and ^{19}F NMR spectra were obtained in $CDCl_3$ using a Bruker-BioSpin AVANCE III HD 400 NMR spectrometer, respectively. Chemical shifts (δ) for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, and integration. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (δ 77.00 ppm) as the internal standard. Optical rotation was recorded on INESA SGW-1 polarimeter at concentrations of 0.5 g/100 mL or 1.0 g/100 mL. Enantiomeric excess was determined by HPLC analysis on Chiralpak column (Daicel Chemical Industries, LTD) on Shimadzu Essentia LC-16. High-resolution mass spectra were recorded on a Bruker Impact II UHR TOF LC/MS Mass Spectrometry.

2. Synthesis of Catalysts

catalyst	M	X	R
Δ-Rh1	Rh	O	Ar_1
Δ-Rh2	Rh	O	Ar_2
Δ-Rh3	Rh	O	H
Δ-RhS	Rh	S	H
Δ-IrO	Ir	O	H



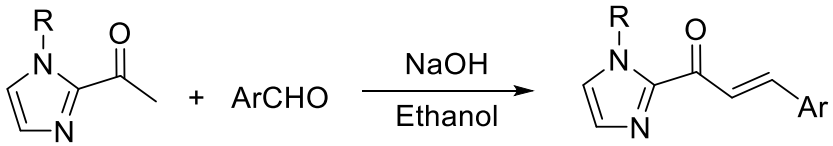


catalyst

Racemic rhodium catalyst ***rac*-Rh3** and chiral catalyst **Δ-Rh3** were prepared according to reported procedures developed by Meggers' group.[1] **Δ-Rh1**[2], **Δ-Rh2**[3] **Δ-RhS**[4] and **Δ-IrO**[5] were synthesized according to published procedures.

3. Synthesis of Substrates

3.1 Synthesis of α,β-unsaturated 2-acylimidazoles



α,β-unsaturated 2-acylimidazoles **1** were prepared by *Aldol* reaction according to a reported procedure.[3] 2-acetyl-imidazole (10.0 mmol, 1.0 eq.) and ethanol (50 mL) were added to a 100 mL round-bottom flask followed by the aromatic aldehyde (12 mmol, 1.2 eq.) and NaOH (5 mmol, 0.5 eq.). The solution was stirred at room temperature until the substrates consumption (detected by TLC). The reaction mixture was then quenched with saturated aqueous NH_4Cl and the mixture was extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with 50 mL brine and dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by a flash column chromatography on silica gel to afford the desired product **1**.

1p was prepared according to published procedures.[5]

3.2 Sythesis of *N*-alkoxyacrylamides 2

The *N*-alkoxyacrylamides **2** were prepared according to a reported method.[6]

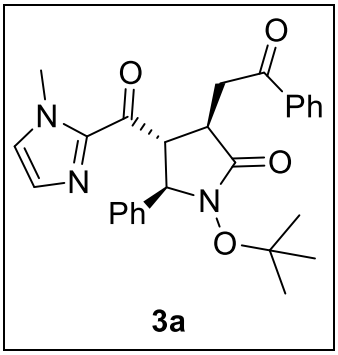
4. Asymmetric [3+2] Annulation Reactions

4.1 Synthesis of racemic products as HPLC references

General Procedure: A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazoles **1** (0.20 mmol), *N*-alkoxyacrylamides **2** (0.24 mmol) and racemic catalyst *rac*-**Rh3** (3.3 mg, 2.0 mol%). The tube was purged with argon, then dry MeCN (1.0 mL) and triethylamine (0.04 mmol) were added successively. The reaction mixture was stirred at 30°C for 12~48 hours (monitored by TLC) under argon. After the reaction was completed, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 6:1 to 3:1) to afford racemic products as HPLC reference for determination of enantiomeric excess.

4.2 Substrate Scope

General Procedure: A dried 25 mL Schlenk tube was charged with α,β-unsaturated 2-acylimidazoles **1** (0.20 mmol), *N*-alkoxyacrylamides **2** (0.24 mmol) and chiral catalyst **Δ-Rh3** (3.3 mg, 2.0 mol%). The tube was purged with argon, then dry MeCN (1.0 mL) and triethylamine (5.6 uL, 0.04 mmol) were added successively. The reaction mixture was stirred at 30°C for 12~48 hours (monitored by TLC) under argon. After the reaction was completed, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 6:1 to 3:1) to afford chiral products.



3a

According to the general procedure, **3a** was obtained as white solid (87.3 mg, 95% yield), m.p. 150.2–152.2℃.

Enantiomeric excess was determined by HPLC analysis, ee = 97%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor)= 10.308 min, t_r(major)=15.971 min.

$[\alpha]_D^{20}$ = +86.4^o (c=0.5, CH_2Cl_2).

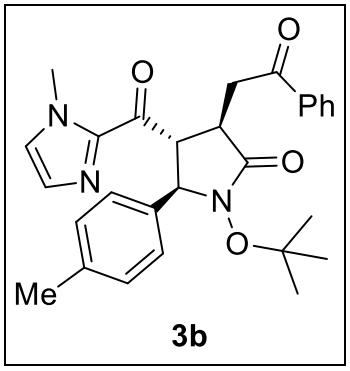
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.53 – 7.48 (m, 1H), 7.41 – 7.32 (m, 6H), 7.30 – 7.27 (m, 1H), 6.97 (d, *J* = 1.0 Hz, 1H), 6.83 (d, *J* = 1.0 Hz, 1H), 5.22 (d, *J* = 6.0 Hz, 1H), 4.37 (dd, *J* = 7.6, 5.9 Hz, 1H), 4.06 (s, 3H), 3.76 – 3.67 (m, 1H), 3.48 (ddd, *J* = 9.4, 7.6, 3.0 Hz, 1H), 3.32 (dd, *J* = 18.1, 9.4 Hz, 1H), 1.21 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.49, 189.63, 173.13, 142.76, 139.05, 136.48, 133.03, 129.46, 128.65, 128.40, 128.17, 127.95, 127.68, 127.65, 84.54, 64.94, 53.60, 39.91, 38.02, 36.17, 27.63.

HRMS (ESI) calcd for $C_{27}H_{30}N_3O_4$ $[M+H]^+$: 460.2216; found: 460.2218.

In the scale-up synthesis, a dried 50 mL flask was charged with α,β-unsaturated 2-acylimidazoles **1a** (636.8 mg, 3.0 mmol), *N*-alkoxyacrylamides **2a** (890.2 mg, 3.6 mmol) and chiral catalyst **Δ-Rh3** (24.9 mg, 1.0 mol%). The tube was purged with argon, then dry MeCN (15.0 mL) and triethylamine (83.4 uL, 0.6 mmol) were added successively. The reaction mixture was stirred at 30^{o}C for 24 hours (monitored by TLC) under argon. After the reaction was completed, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (petroleum ether/ EtOAc = 6:1 to 3:1) to afford **3a** (1.24 g, 90% yield). Enantiomeric excess was determined by HPLC analysis, ee = 97%. In addition, when catalyst loading was reduced to 0.5 mol%, **3a** could be afforded in 87% yield with

95% ee after 36 hours. Remarkably, when as low as 0.2 mol% of **Δ-Rh3** was employed, **3a** still could be obtained in 75% yield with 94% ee after 72 hours.



3b

According to the general procedure, **3b** was obtained as white solid (87.1 mg, 92% yield), m.p. 117.3–118.1℃.

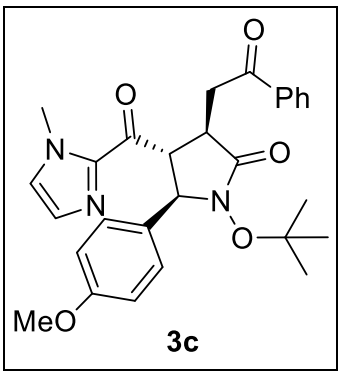
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor)= 11.922 min, t_r(major)=20.335 min.

$[\alpha]_D^{20}$ = +99.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.54 – 7.46 (m, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.27 (s, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 6.96 (s, 1H), 6.82 (s, 1H), 5.17 (d, *J* = 5.8 Hz, 1H), 4.36 (t, *J* = 6.9 Hz, 1H), 4.04 (s, 3H), 3.72 (dd, *J* = 18.1, 3.2 Hz, 1H), 3.52 – 3.43 (m, 1H), 3.31 (dd, *J* = 17.9, 9.5 Hz, 1H), 2.31 (s, 3H), 1.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.54, 189.75, 173.14, 142.82, 137.87, 136.53, 135.97, 133.00, 129.42, 129.33, 128.38, 127.94, 127.59, 84.47, 64.77, 53.64, 39.97, 38.09, 36.12, 27.64, 21.15.

HRMS (ESI) calcd for $C_{28}H_{32}N_3O_4$ $[M+H]^+$: 474.2363; found: 474.2366.



3c

According to the general procedure, **3c** was obtained as colorless oil (88.2 mg, 90% yield).

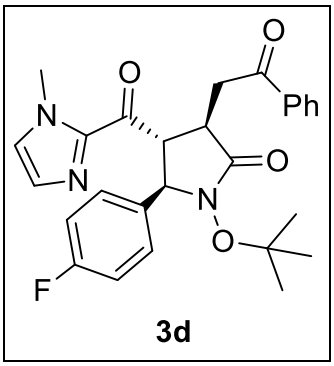
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =15.117 min, t_r(major)=31.042 min.

$[\alpha]_D^{20}$ = +101.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 2H), 7.53 – 7.48 (m, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.33 – 7.29 (m, 2H), 6.96 (s, 1H), 6.89 – 6.84 (m, 2H), 6.82 (d, *J* = 0.9 Hz, 1H), 5.16 (d, *J* = 6.4 Hz, 1H), 4.38 (dd, *J* = 8.0, 6.3 Hz, 1H), 4.05 (s, 3H), 3.78 (s, 3H), 3.73 (dd, *J* = 18.1, 2.8 Hz, 1H), 3.45 (ddd, *J* = 9.4, 7.9, 2.8 Hz, 1H), 3.33 (dd, *J* = 18.1, 9.4 Hz, 1H), 1.20 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.59, 189.76, 173.16, 159.50, 142.90, 136.52, 133.07, 130.82, 129.46, 129.08, 128.43, 127.97, 127.69, 114.03, 84.46, 64.54, 55.27, 53.63, 39.85, 38.25, 36.18, 27.70.

HRMS (ESI) calcd for $C_{28}H_{32}N_3O_5$ $[M+H]^+$: 490.2342; found: 490.2335.



3d

According to the general procedure, **3d** was obtained as white solid (80.2 mg, 84% yield), m.p. 139.6–140.4°C.

Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor)= 14.097 min, t_r(major)= 22.008 min.

$[\alpha]_D^{20}$ = +75.2 (c=0.5, CH_2Cl_2);

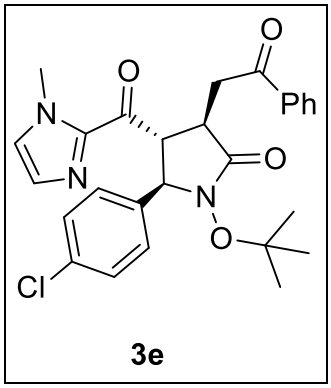
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.76 (m,2H), 7.54 – 7.49 (m, 1H), 7.39 (ddd, *J* = 7.3, 5.9, 1.7 Hz, 4H), 7.04 (t, *J* = 8.7 Hz, 2H), 6.98 (s, 1H), 6.83 (d, *J* = 0.9 Hz, 1H), 5.20 (d, *J* = 6.2 Hz, 1H), 4.41 – 4.36 (m, 1H), 4.06 (s, 3H), 3.73 (dd, *J* = 18.2, 2.8 Hz,

1H), 3.45 (ddd, *J* = 10.6, 7.8, 2.8 Hz, 1H), 3.32 (dd, *J* = 18.0, 9.4 Hz, 1H), 1.21 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.48, 189.47, 173.08, 163.83, 161.37, 142.80, 136.46, 134.75, 133.13, 129.55, 129.50, 128.46, 127.97, 127.79, 115.74, 115.52, 84.67, 64.37, 53.64, 39.68, 38.08, 36.20, 27.68.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.93.

HRMS (ESI) calcd for $C_{27}H_{29}FN_3O_4$ $[M+H]^+$: 478.2132; found: 478.2134.



3e

According to the general procedure, **3e** was obtained as white solid (93.8 mg, 95% yield), m.p. 129.2–131.2℃.

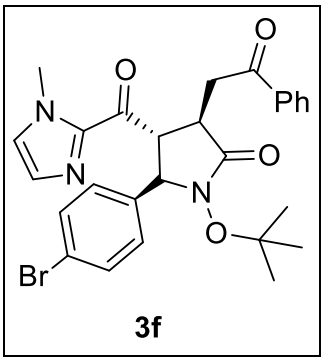
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =13.069 min, t_r(major)=22.545 min.

$[\alpha]_D^{20}$ = +114.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.76 (m, 2H), 7.55 – 7.50 (m, 1H), 7.44 – 7.29 (m, 6H), 6.98 (d, *J* = 0.9 Hz, 1H), 6.84 (d, *J* = 1.0 Hz, 1H), 5.20 (d, *J* = 6.0 Hz, 1H), 4.34 (dd, *J* = 7.7, 6.0 Hz, 1H), 4.06 (s, 3H), 3.73 (dd, *J* = 18.3, 3.0 Hz, 1H), 3.46 (ddd, *J* = 9.4, 7.8, 3.1 Hz, 1H), 3.29 (dd, *J* = 18.2, 9.4 Hz, 1H), 1.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.45, 189.36, 173.05, 142.72, 137.66, 136.44, 134.03, 133.15, 129.59, 129.13, 128.91, 128.47, 127.98, 127.82, 84.77, 64.42, 53.58, 39.70, 37.95, 36.20, 27.68.

HRMS (ESI) calcd for $C_{27}H_{29}ClN_3O_4$ $[M+H]^+$: 494.1826; found: 494.1821.



3f

According to the general procedure, **3f** was obtained as white solid (87.4 mg, 88% yield), m.p. 161.9–163.5℃.

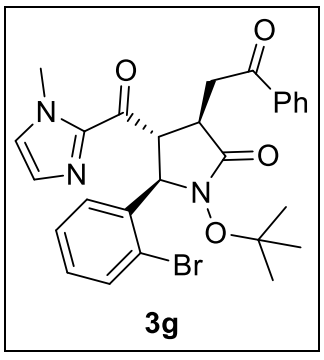
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =12.803 min, t_r(major)=24.089 min.

$[\alpha]_D^{20}$=+99.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, J = 8.4, 1.3 Hz, 2H), 7.54 – 7.45 (m, 3H), 7.44 – 7.35 (m, 2H), 7.31 – 7.27 (m, 2H), 6.99 (d, J = 1.0 Hz, 1H), 6.84 (d, J = 0.9 Hz, 1H), 5.18 (d, J = 6.0 Hz, 1H), 4.33 (dd, J = 7.7, 5.9 Hz, 1H), 4.06 (s, 3H), 3.72 (dd, J = 18.2, 3.0 Hz, 1H), 3.46 (ddd, J = 9.3, 7.6, 2.9 Hz, 1H), 3.28 (dd, J = 18.3, 9.4 Hz, 1H), 1.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.46, 189.34, 173.06, 142.69, 138.22, 136.43, 133.16, 131.86, 129.60, 129.45, 128.48, 127.98, 127.85, 122.22, 84.80, 64.49, 53.52, 39.70, 37.93, 36.21, 27.68.

HRMS (ESI) calcd for $C_{27}H_{29}BrN_3O_4$ $[M+H]^+$: 538.1311; found: 538.1312.



3g

According to the general procedure, **3g** was obtained as white solid (84.4 mg, 82% yield), m.p. 158.2–159.3℃.

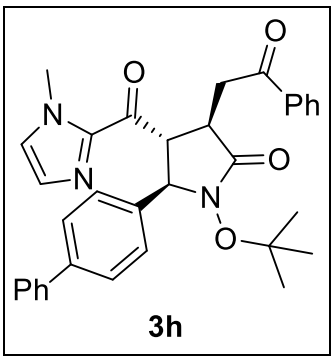
Enantiomeric excess was determined by HPLC analysis, ee = 85%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =14.841 min, t_r(major)=18.910 min.

$[\alpha]_D^{20}$ = +74.7 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 4H), 7.17 – 7.12 (m, 1H), 7.01 (s, 1H), 6.84 (s, 1H), 5.78 – 5.69 (m, 1H), 4.23 (d, *J* = 12.8 Hz, 1H), 4.08 (s, 3H), 3.66 – 3.58 (m, 1H), 3.47 (dd, *J* = 7.4, 4.3 Hz, 1H), 3.32 (d, *J* = 16.5 Hz, 1H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.06, 189.63, 172.58, 136.68, 132.97, 129.45, 129.39, 128.40, 128.05, 127.86, 127.70, 122.84, 84.98, 67.96, 52.80, 40.39, 38.38, 36.15, 27.56, 25.61.

HRMS (ESI) calcd for $C_{27}H_{29}BrN_3O_4$ $[M+H]^+$: 538.1311; found: 538.1314.



3h

According to the general procedure, **3h** was obtained as white solid (101.8 mg, 95% yield), m.p. 72.4-73.3°C.

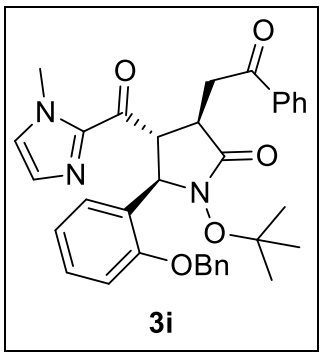
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =16.032 min, t_r(major)=51.722 min.

$[\alpha]_D^{20}$ = +79.3 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.76 (m, 2H), 7.59 – 7.56 (m, 4H), 7.51 – 7.30 (m, 8H), 6.98 (s, 1H), 6.85 (d, *J* = 1.0 Hz, 1H), 5.28 (d, *J* = 1.3 Hz, 1H), 4.41 (dd, *J* = 7.5, 5.7 Hz, 1H), 4.06 (s, 3H), 3.74 (dd, *J* = 18.2, 3.0 Hz, 1H), 3.51 (ddd, *J* = 9.4, 7.5, 3.1 Hz, 1H), 3.34 (dd, *J* = 18.2, 9.5 Hz, 1H), 1.25 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.62, 189.76, 173.26, 142.88, 141.09, 140.70, 138.28, 136.62, 133.14, 129.61, 128.86, 128.52, 128.16, 128.06, 127.78, 127.47, 127.15, 84.76, 68.07, 64.84, 53.71, 40.04, 38.08, 36.26, 27.77, 25.72.

HRMS (ESI) calcd for $C_{33}H_{34}N_3O_4$ $[M+H]^+$: 536.2549; found: 536.2545.



3i

According to the general procedure, **3i** was obtained as pale yellow oil (85.0 mg, 75% yield).

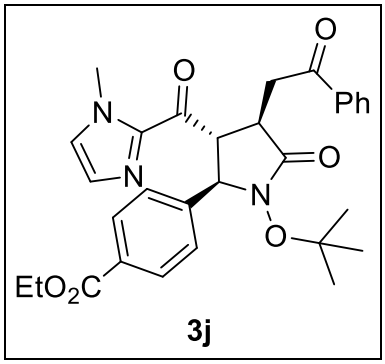
Enantiomeric excess was determined by HPLC analysis, ee = 94%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) = 12.423 min, t_r(major)= 31.706 min.

$[\alpha]_D^{20}$ = +65.4 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 3H), 7.30 – 7.20 (m, 6H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.94 – 6.90 (m, 3H), 5.55 (s, 1H), 5.04 (d, *J* = 11.6 Hz, 1H), 4.91 (d, *J* = 11.2 Hz, 1H), 4.47 (s, 1H), 3.88 (s, 3H), 3.58 (d, *J* = 14.8 Hz, 1H), 3.38 – 3.27 (m, 2H), 1.33 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.71, 190.65, 172.65, 156.23, 142.09, 136.68, 132.86, 129.03, 128.30, 128.04, 127.69, 127.34, 120.84, 111.96, 84.57, 70.00, 52.38, 40.70, 38.35, 36.13, 27.62.

HRMS (ESI) calcd for $C_{34}H_{36}N_3O_5$ $[M+H]^+$: 565.2638; found: 565.2644.



3j

According to the general procedure, **3j** was obtained as white solid (101.0 mg, 95% yield), m.p. 76.6-78.3℃.

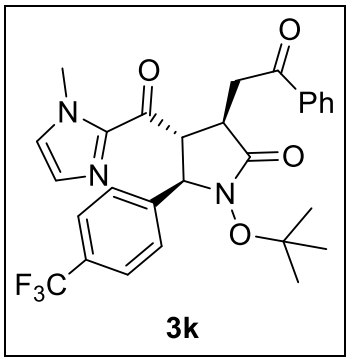
Enantiomeric excess was determined by HPLC analysis, ee = 95%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =15.429 min, t_r(major)=39.266 min.

$[\alpha]_D^{20}$ = +51.0 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.97 (m, 2H), 7.80 – 7.73 (m, 2H), 7.48 (t, *J* = 8.1 Hz, 3H), 7.37 (t, *J* = 7.7 Hz, 2H), 6.98 (s, 1H), 6.83 (s, 1H), 5.27 (d, *J* = 5.7 Hz, 1H), 4.39 – 4.31 (m, 3H), 4.06 (s, 3H), 3.72 (dd, *J* = 18.3, 3.1 Hz, 1H), 3.48 (td, *J* = 7.8, 7.0, 3.9 Hz, 1H), 3.27 (dd, *J* = 18.3, 9.4 Hz, 1H), 1.37 (t, *J* = 8.0 Hz, 3H), 1.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.38, 189.25, 173.03, 166.28, 144.22, 142.61, 136.39, 133.11, 130.34, 129.95, 129.58, 128.43, 127.95, 127.81, 127.61, 84.81, 64.74, 61.01, 53.49, 39.76, 37.84, 36.15, 27.62, 14.32.

HRMS (ESI) calcd for $C_{30}H_{34}N_3O_6$ $[M+H]^+$: 532.2291; found: 532.2287.



3k

According to the general procedure, **3k** was obtained as white solid (76.0 mg, 72% yield), m.p. 134.4-135.2℃.

Enantiomeric excess was determined by HPLC analysis, ee = 93%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =8.733 min, t_r(major)=15.312 min.

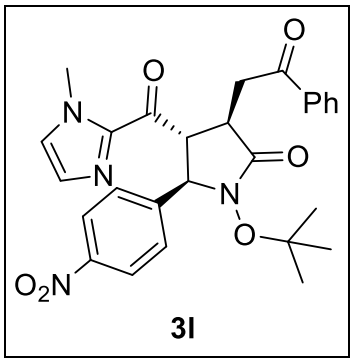
$[\alpha]_D^{20}$ = +63.8 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.52 (dd, *J* = 14.7, 7.7 Hz, 3H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.00 (s, 1H), 6.84 (s, 1H), 5.29 (d, *J* = 5.7 Hz, 1H), 4.35 – 4.30 (m, 1H), 4.06 (s, 3H), 3.72 (dd, *J* = 18.2, 3.2 Hz, 1H), 3.52 – 3.45 (m, 1H), 3.27 (dd, *J* = 18.2, 9.3 Hz, 1H), 1.23 (d, *J* = 1.3 Hz, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.35, 189.15, 172.95, 143.39, 142.56, 136.37, 133.16, 129.62, 128.45, 127.94, 127.89, 125.70, 125.67, 84.95, 64.51, 53.44, 39.61, 37.73, 36.17, 27.61.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.58.

HRMS (ESI) calcd for $C_{28}H_{29}F_3N_3O_4$ $[M+H]^+$: 528.2120; found: 528.2117.



3l

According to the general procedure, **3l** was obtained as pale yellow oil (87.5 mg, 87% yield).

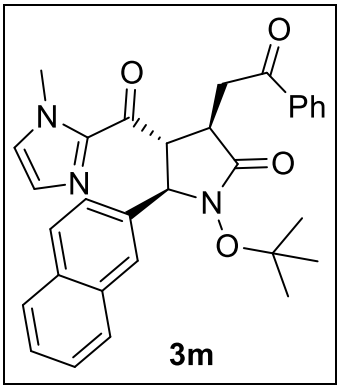
Enantiomeric excess was determined by HPLC analysis, ee = 95%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) = 22.673 min, t_r(major)= 34.114 min.

$[\alpha]_D^{20}$ = +64.0 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.02 (s, 1H), 6.87 (s, 1H), 5.34 (d, *J* = 5.7 Hz, 1H), 4.37 (dd, J = 7.6, 5.7 Hz, 1H), 4.08 (s, 3H), 3.74 (dd, J = 18.3, 3.0 Hz, 1H), 3.51 – 3.44 (m, 1H), 3.28 (dd, J = 18.3, 9.2 Hz, 1H), 1.23 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.29, 188.80, 172.84, 147.81, 146.75, 142.41, 136.35, 133.23, 129.55, 128.63, 128.48, 127.94, 123.93, 85.08, 64.39, 53.27, 39.39, 37.71, 36.18, 27.63.

HRMS (ESI) calcd for $C_{27}H_{29}N_4O_6$ $[M+H]^+$: 504.2032; found: 504.2027.



3m

According to the general procedure, **3m** was obtained as white solid (71.3 mg, 70% yield), m.p. 66.3-67.0℃.

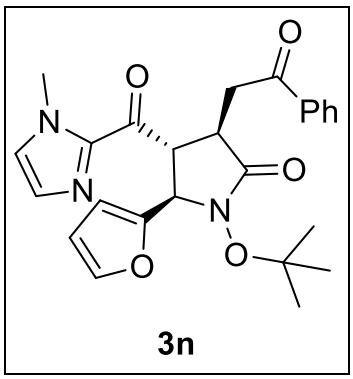
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =13.211 min, t_r(major)=25.706 min.

$[\alpha]_D^{20}$ = +89.6 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.74 (m, 6H), 7.57 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.53 – 7.44 (m, 3H), 7.39 – 7.34 (m, 2H), 6.95 (d, *J* = 0.9 Hz, 1H), 6.79 (d, *J* = 1.0 Hz, 1H), 5.42 (d, *J* = 6.1 Hz, 1H), 4.50 – 4.45 (m, 1H), 4.06 (s, 3H), 3.76 (dd, *J* = 18.2, 3.1 Hz, 1H), 3.53 (ddd, *J* = 9.4, 7.9, 2.9 Hz, 1H), 3.37 (dd, *J* = 18.3, 9.4 Hz, 1H), 1.22 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.54, 189.60, 172.98, 142.82, 136.50, 136.48, 133.21, 133.15, 133.01, 129.47, 128.74, 128.38, 128.06, 127.96, 127.70, 127.65, 127.02, 126.20, 126.17, 125.04, 84.73, 65.12, 53.84, 39.86, 38.26, 36.14, 27.68.

HRMS (ESI) calcd for $C_{31}H_{32}N_3O_4$ $[M+H]^+$: 510.2343; found: 510.2347.



3n

According to the general procedure, **3n** was obtained as white solid (72.8 mg, 81% yield), m.p. 138.2-140.3℃.

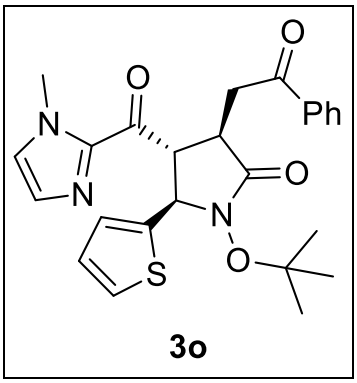
Enantiomeric excess was determined by HPLC analysis, ee = 95%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =16.858 min, t_r(major)=25.028 min.

$[\alpha]_D^{20}$ = +77.6 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 2H), 7.55 – 7.50 (m, 1H), 7.43 – 7.38 (m, 3H), 6.97 (s, 1H), 6.83 (d, *J* = 1.0 Hz, 1H), 6.42 (d, *J* = 4.0 Hz, 1H), 6.32-6.28 (m, 1H), 5.10 (d, *J* = 6.8 Hz, 1H), 4.65 (t, *J* = 7.4 Hz, 1H), 4.04 (s, 3H), 3.79 – 3.66 (m, 1H), 3.53 (dd, *J* = 17.9, 9.3 Hz, 1H), 3.44 (ddd, *J* = 9.4, 7.8, 2.9 Hz, 1H), 1.19 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.53, 189.18, 174.14, 150.05, 143.07, 142.81, 136.53, 133.02, 129.51, 128.40, 127.96, 127.66, 110.80, 110.45, 84.04, 58.20, 49.24, 40.09, 38.48, 36.08, 27.34.

HRMS (ESI) calcd for $C_{25}H_{28}N_3O_5$ $[M+H]^+$: 450.2219; found: 450.2216.



3o

According to the general procedure, **3o** was obtained as white solid (76.4 mg, 82% yield), m.p. 145.7-146.3℃.

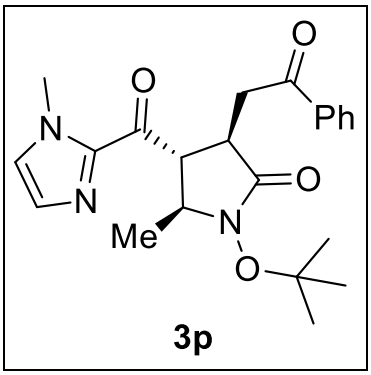
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =18.240 min, t_r(major)=26.487 min.

$[\alpha]_D^{20}$ = +78.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 2H), 7.54 – 7.49 (m, 1H), 7.42 – 7.36 (m, 2H), 7.29 – 7.26 (m, 1H), 7.15 (dd, *J* = 3.5, 1.5 Hz, 1H), 6.98 – 6.93 (m, 2H), 6.84 (d, *J* = 1.0 Hz, 1H), 5.39 (d, *J* = 6.8 Hz, 1H), 4.57 (t, *J* = 7.1 Hz, 1H), 4.05 (s, 3H), 3.78 – 3.68 (m, 1H), 3.49 – 3.40 (m, 2H), 1.21 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.42, 189.03, 173.38, 142.87, 141.58, 136.49, 133.07, 129.60, 129.57, 129.55, 128.44, 128.42, 128.39, 127.96, 127.73, 127.60, 126.81, 126.00, 84.37, 60.28, 53.24, 39.90, 38.59, 36.08, 27.53.

HRMS (ESI) calcd for $C_{25}H_{28}N_3O_4S$ $[M+H]^+$: 466.1800; found: 466.1801.



3p

According to the general procedure, **3p** was obtained as pale yellow oil (52.5 mg, 66% yield).

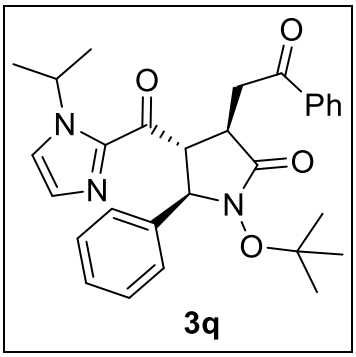
Enantiomeric excess was determined by HPLC analysis, ee = 93%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =12.880 min, t_r(major)=18.788 min.

$[\alpha]_D^{20}$ = +82.4 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.53 – 7.47 (m, 1H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.02 (s, 1H), 6.93 (d, *J* = 0.9 Hz, 1H), 4.06 (s, 3H), 4.05-3.98 (m, 2H), 3.72 (dd, *J* = 18.2, 3.1 Hz, 1H), 3.41 (ddd, *J* = 10.4, 7.5, 3.1 Hz, 1H), 3.23 (dd, *J* = 18.3, 9.7 Hz, 1H), 1.42 (d, *J* = 6.1 Hz, 3H), 1.34 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.66, 190.39, 172.51, 143.07, 136.47, 133.09, 129.40, 128.44, 127.94, 127.69, 84.25, 57.25, 52.28, 40.19, 37.33, 36.17, 27.68, 19.29.

HRMS (ESI) calcd for $C_{22}H_{28}N_3O_4$ $[M+H]^+$: 398.2080; found: 398.2077.



3q

According to the general procedure, **3q** was obtained as pale yellow oil (89.7 mg, 92% yield).

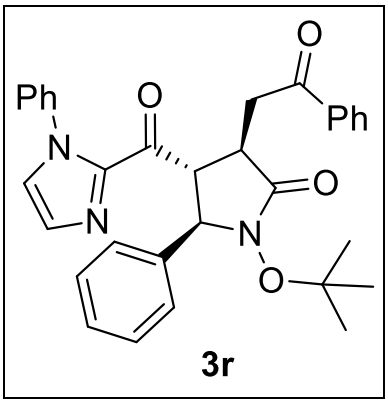
Enantiomeric excess was determined by HPLC analysis, ee = 90%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =8.146 min, t_r(major)=13.091 min.

$[\alpha]_D^{20}$ = +102.3 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.43 – 7.33 (m, 6H), 7.32 – 7.27 (m, 1H), 7.20 (s, 1H), 6.84 (s, 1H), 5.62 (p, *J* = 6.7 Hz, 1H), 5.25 (d, *J* = 6.0 Hz, 1H), 4.47 – 4.41 (m, 1H), 3.72 (dd, *J* = 18.2, 3.0 Hz, 1H), 3.52 (ddd, *J* = 10.5, 7.6, 2.9 Hz, 1H), 3.34 (dd, *J* = 18.2, 9.5 Hz, 1H), 1.55 (d, *J* = 6.7 Hz, 3H), 1.46 (d, *J* = 6.6 Hz, 3H), 1.23 (d, *J* = 1.6 Hz, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.31, 189.66, 173.14, 142.10, 139.06, 136.47, 132.98, 129.90, 128.62, 128.37, 128.13, 127.91, 127.71, 121.87, 84.54, 65.04, 54.18, 49.38, 39.86, 38.14, 27.62, 23.60, 23.55.

HRMS (ESI) calcd for $C_{29}H_{34}N_3O_4$ $[M+H]^+$: 488.2549; found: 488.2546.



3r

According to the general procedure, **3r** was obtained as white solid (78.4 mg, 88% yield), m.p. 119.2-120.0℃.

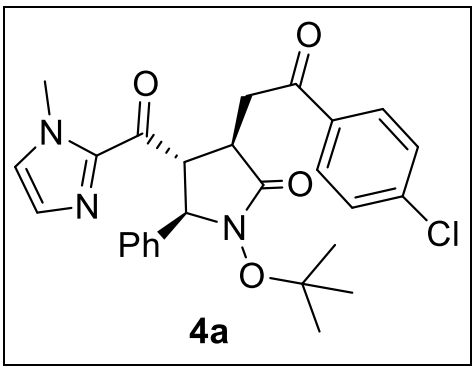
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =10.520 min, t_r(major)=16.595 min.

$[\alpha]_D^{20}$=+123.2 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.56 – 7.46 (m, 6H), 7.42 – 7.37 (m, 2H), 7.35 – 7.27 (m, 5H), 7.07 (d, *J* = 1.0 Hz, 1H), 6.84 (d, *J* = 1.1 Hz, 1H), 5.21 (d, *J* = 6.7 Hz, 1H), 4.41 (dd, *J* = 8.4, 6.7 Hz, 1H), 3.81 – 3.76 (m, 1H), 3.52 – 3.40 (m, 2H), 1.17 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.58, 188.15, 172.34, 142.96, 138.72, 138.25, 136.41, 133.08, 129.83, 129.10, 128.90, 128.60, 128.41, 128.18, 127.96, 127.81, 127.59, 125.89, 84.63, 67.96, 64.64, 54.70, 40.13, 38.31, 27.61, 25.61.

HRMS (ESI) calcd for $C_{32}H_{32}N_3O_4$ $[M+H]^+$: 522.2303; found:522.2306.



4a

According to the general procedure, **4a** was obtained as white solid (91.9 mg, 93% yield), m.p. 130.3-131.2℃.

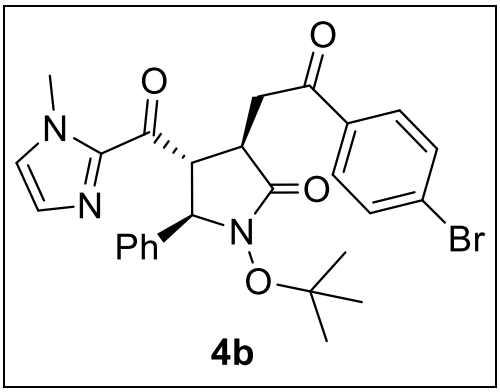
Enantiomeric excess was determined by HPLC analysis, ee = 95%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =20.756 min, t_r(major)=41.041 min.

$[\alpha]_D^{20}$ = +59.0 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 2H), 7.42 – 7.32 (m, 6H), 7.32 – 7.28 (m, 1H), 6.99 (s, 1H), 6.83 (s, 1H), 5.25 (d, J = 6.1 Hz, 1H), 4.42 – 4.36 (m, 1H), 4.06 (s, 3H), 3.69 (dd, J = 18.0, 3.2 Hz, 1H), 3.46 (td, J = 8.4, 7.8, 3.1 Hz, 1H), 3.32 (dd, J = 18.0, 9.1 Hz, 1H), 1.23 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.34, 189.46, 172.84, 142.73, 139.44, 138.93, 134.83, 129.46, 129.38, 128.73, 128.67, 128.22, 127.72, 127.69, 84.61, 64.83, 53.58, 39.77, 38.14, 36.16, 27.62.

HRMS (ESI) calcd for $C_{27}H_{29}ClN_3O_4$ $[M+H]^+$: 494.2846; found: 494.2844.



4b

According to the general procedure, **4b** was obtained as white solid (79.7 mg, 74% yield), m.p. 74.3-75.1℃.

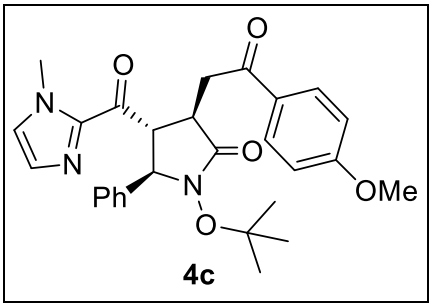
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =23.936 min, t_r(major)=46.675 min.

$[\alpha]_D^{20}$ = +64.3 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCI_3$) δ 7.65 (dd, J = 8.6, 1.8 Hz, 2H), 7.54 (dd, J = 8.6, 1.8 Hz, 2H), 7.42 – 7.33 (m, 4H), 7.32 – 7.27 (m, 1H), 6.98 (s, 1H), 6.83 (s, 1H), 5.25 (d, J = 6.1 Hz, 1H), 4.42 – 4.35 (m, 1H), 4.05 (d, J = 1.7 Hz, 3H), 3.68 (dd, J = 18.0, 3.1 Hz, 1H), 3.46 (td, J = 8.3, 7.7, 3.1 Hz, 1H), 3.31 (dd, J = 18.0, 9.1 Hz, 1H), 1.23 (d, J = 1.7 Hz, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.55, 189.45, 172.82, 142.73, 138.92, 135.24, 131.73, 129.49, 128.67, 128.22, 128.18, 127.73, 127.70, 84.61, 64.82, 53.58, 39.75, 38.14, 36.16, 27.62.

HRMS (ESI) calcd for $C_{27}H_{29}BrN_3O_4$ $[M+H]^+$: 538.1341; found: 538.1336.



4c

According to the general procedure, **4c** was obtained as colorless oil (90.1 mg, 92% yield).

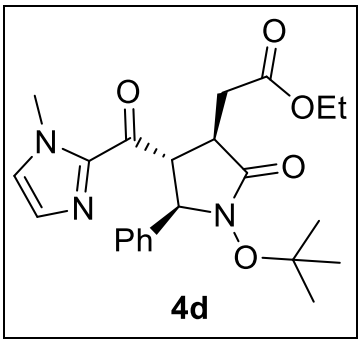
Enantiomeric excess was determined by HPLC analysis, ee = 96%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =17.594 min, t_r(major)=34.992 min.

$[\alpha]_D^{20}$ = +67.8 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCI_3$) δ 7.79 – 7.73 (m, 2H), 7.42 – 7.33 (m, 4H), 7.31 – 7.26 (m, 1H), 6.98 (s, 1H), 6.89 – 6.82 (m, 3H), 5.21 (d, J = 5.9 Hz, 1H), 4.40 – 4.35 (m, 1H), 4.06 (s, 3H), 3.84 (s, 3H), 3.68 (dd, J = 18.0, 3.1 Hz, 1H), 3.50 (ddd, J = 10.5, 7.5, 3.1 Hz, 1H), 3.26 (dd, J = 18.0, 9.6 Hz, 1H), 1.23 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.90, 189.72, 173.35, 163.41, 142.75, 139.11, 130.20, 129.59, 129.41, 128.63, 128.13, 127.64, 127.62, 113.54, 84.54, 65.05, 55.42, 53.60, 39.52, 38.00, 36.14, 27.61.

HRMS (ESI) calcd for $C_{28}H_{32}N_3O_5$ $[M+H]^+$: 490.2312; found: 490.2316.



4d

According to the general procedure, **4d** was obtained as white solid (81.2 mg, 95% yield), m.p. 119.2-120.3℃.

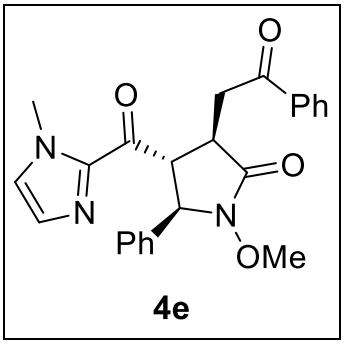
Enantiomeric excess was determined by HPLC analysis, ee = 84%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =10.704 min, t_r(major)=21.090 min.

$[\alpha]_D^{20}$ = +61.2 (c=1.0, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 5H), 7.07 (d, J = 2.9 Hz, 2H), 5.14 (d, J = 5.4 Hz, 1H), 4.43 – 4.38 (m, 1H), 4.02 (s, 3H), 4.00 – 3.90 (m, 2H), 3.23 (ddd, J = 9.2, 7.1, 4.3 Hz, 1H), 2.98 (dd, J = 17.3, 4.3 Hz, 1H), 2.64 (dd, J = 17.4, 9.2 Hz, 1H), 1.20 (s, 9H), 1.13 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 189.66, 172.42, 171.48, 142.51, 139.00, 129.65, 128.66, 128.17, 127.93, 127.52, 84.48, 64.87, 60.62, 52.69, 38.64, 36.15, 35.40, 27.56, 14.00.

HRMS (ESI) calcd for $C_{23}H_{30}N_3O_5$ $[M+H]^+$: 428.2185; found: 428.2188.



4e

According to the general procedure, **4e** was obtained as white solid (73.5 mg, 88% yield), m.p. 149.0-150.9℃.

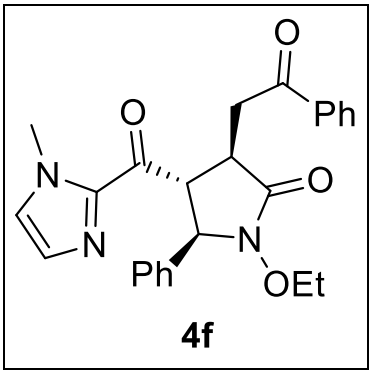
Enantiomeric excess was determined by HPLC analysis, ee = 92%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =28.522 min, t_r(major)=32.210 min.

$[\alpha]_D^{20}$ = +72.0 (c=1.0, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.76 (m, 2H), 7.55 – 7.48 (m, 3H), 7.43 – 7.28 (m, 5H), 6.89 (d, *J* = 0.9 Hz, 1H), 6.67 (d, *J* = 1.0 Hz, 1H), 5.23 (d, *J* = 8.7 Hz, 1H), 4.49 (dd, *J* = 9.8, 8.7 Hz, 1H), 4.01 (s, 3H), 3.75 (dd, *J* = 18.5, 2.7 Hz, 1H), 3.68 (s, 3H), 3.54 (dd, *J* = 18.5, 8.7 Hz, 1H), 3.30 (ddd, *J* = 9.8, 8.6, 2.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.37, 188.83, 171.24, 143.23, 137.66, 136.45, 133.06, 129.40, 128.78, 128.71, 128.39, 127.94, 127.90, 127.86, 127.61, 63.04, 62.43, 52.96, 40.14, 39.16, 36.07.

HRMS (ESI) calcd for $C_{24}H_{24}N_3O_4$ $[M+H]^+$: 418.1767; found: 418.1769.



4f

According to the general procedure, **4f** was obtained as white solid (65.6 mg, 76% yield), m.p. 117.8-119.1℃.

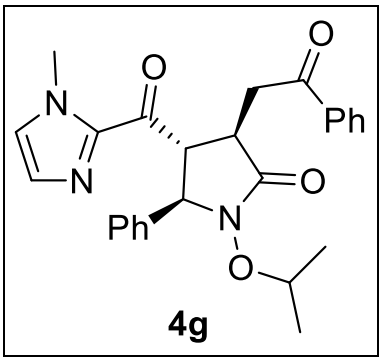
Enantiomeric excess was determined by HPLC analysis, ee = 92%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =27.213 min, t_r(major)=31.737 min.

$[\alpha]_D^{20}$ = +80.3 (c=0.5, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 2H), 7.55 – 7.47 (m, 3H), 7.43 – 7.28 (m, 5H), 6.89 (s, 1H), 6.68 (s, 1H), 5.21 (d, *J* = 8.6 Hz, 1H), 4.50 (t, *J* = 9.1 Hz, 1H), 4.01 (s, 4H), 3.79 – 3.66 (m, 2H), 3.52 (dd, *J* = 18.4, 8.8 Hz, 1H), 3.30 (td, *J* = 9.3, 2.6 Hz, 1H), 1.12 (t, *J* = 8.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.44, 188.98, 171.37, 143.24, 137.74, 136.50, 133.03, 129.38, 128.71, 128.64, 128.38, 128.00, 127.95, 127.91, 127.58, 71.20, 62.94, 52.82, 40.05, 39.24, 36.07, 13.61.

HRMS (ESI) calcd for $C_{25}H_{26}N_3O_4$ $[M+H]^+$: 432.1923; found: 432.1917.



4g

According to the general procedure, **4g** was obtained as white solid (75.7 mg, 85% yield), m.p. 120.5-122.4℃.

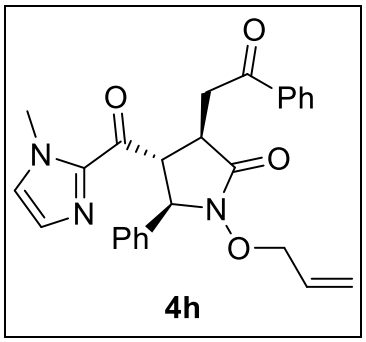
Enantiomeric excess was determined by HPLC analysis, ee = 92%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =27.387 min, t_r(major)=20.234 min.

$[\alpha]_D^{20}$ = +80.7 (c=0.5, CH_2Cl_2)；

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.57 – 7.47 (m, 3H), 7.44 – 7.28 (m, 5H), 6.91 (d, *J* = 1.1 Hz, 1H), 6.71 (d, *J* = 1.0 Hz, 1H), 5.18 (d, *J* = 8.4 Hz, 1H), 4.55 (dd, *J* = 9.4, 8.4 Hz, 1H), 4.01 (s, 3H), 3.91 (p, *J* = 6.2 Hz, 1H), 3.72 (td, *J* = 18.3, 2.8 Hz, 1H), 3.50 (dd, *J* = 18.3, 8.8 Hz, 1H), 3.32 (td, *J* = 8.9, 2.7 Hz, 1H), 1.22 (d, *J* = 6.1 Hz, 3H), 1.00 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.48, 189.15, 171.99, 143.20, 137.83, 136.53, 133.01, 129.39, 128.67, 128.61, 128.38, 128.18, 127.92, 127.59, 77.69, 63.74, 52.47, 39.87, 39.30, 36.09, 21.26, 20.75.

HRMS (ESI) calcd for $C_{26}H_{28}N_3O_4$ $[M+H]^+$: 446.2080; found: 446.2074.



4h

According to the general procedure, **4h** was obtained as white solid (71.8 mg, 81% yield), m.p. 130.8-131.6℃.

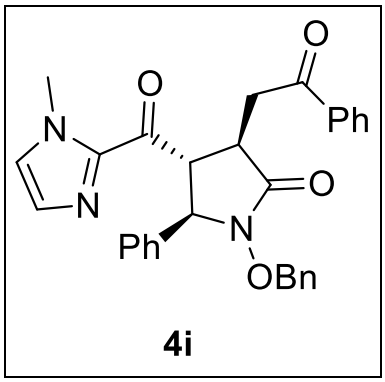
Enantiomeric excess was determined by HPLC analysis, ee = 90%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =29.316 min, t_r(major)=34.337 min.

$[\alpha]_D^{20}$ = +65.3 (c=1.0, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.76 (m, 2H), 7.55 – 7.47 (m, 3H), 7.43 – 7.28 (m, 5H), 6.89 (s, 1H), 6.67 (d, *J* = 0.9 Hz, 1H), 5.92 – 5.77 (m, 1H), 5.27 – 5.18 (m, 3H), 4.49 (dd, *J* = 9.7, 8.6 Hz, 1H), 4.41 (ddt, *J* = 11.5, 6.9, 1.1 Hz, 1H), 4.21 (ddt, *J* = 11.5, 6.2, 1.2 Hz, 1H), 4.01 (s, 3H), 3.79 – 3.67 (m, 1H), 3.52 (dd, *J* = 18.4, 8.8 Hz, 1H), 3.36 – 3.28 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.38, 188.84, 171.29, 143.26, 137.54, 136.47, 133.03, 132.17, 129.38, 128.73, 128.69, 128.38, 128.06, 127.90, 127.56, 120.55, 76.55, 63.15, 52.97, 39.96, 39.25, 36.07.

HRMS (ESI) calcd for $C_{26}H_{26}N_3O_4$ $[M+H]^+$: 444.1923; found: 444.1927.



4i

According to the general procedure, **4i** was obtained as white solid (71.1 mg, 72% yield), m.p. 182.6-183.4℃.

Enantiomeric excess was determined by HPLC analysis, ee = 82%, Chiralpak column ADH, λ=254 nm, *n*-hexane/*i*-PrOH=70:30, flow rate: 0.8 mL/min, 25°C, t_r(minor) =68.919 min, t_r(major)=53.030 min.

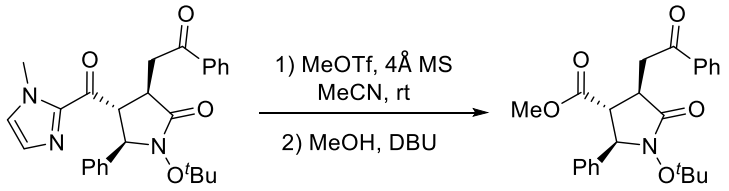
$[\alpha]_D^{20}$=+68.3 (c=1.0, CH_2Cl_2);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.55 – 7.50 (m, 1H), 7.49 – 7.45 (m, 2H), 7.43 – 7.37 (m, 2H), 7.36 – 7.31 (m, 3H), 7.31 – 7.26 (m, 3H), 7.18 – 7.14 (m, 2H), 6.88 (s, 1H), 6.67 (s, 1H), 5.08 (dd, *J* = 9.3, 8.0 Hz, 2H), 4.67 (d, *J* = 9.9 Hz, 1H), 4.50 (dd, *J* = 9.7, 8.6 Hz, 1H), 4.00 (s, 3H), 3.75 (dd, *J* = 18.4, 2.7 Hz, 1H), 3.53 (dd, *J* = 18.4, 8.7 Hz, 1H), 3.35 – 3.28 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.42, 188.75, 171.15, 143.23, 137.58, 136.50, 134.79, 133.03, 129.48, 129.36, 128.75, 128.67, 128.39, 128.35, 128.14, 127.93, 127.51, 77.64, 63.30, 52.98, 39.98, 39.16, 36.07.

HRMS (ESI) calcd for $C_{30}H_{28}N_3O_4$ $[M+H]^+$: 494.2080; found: 494.2076.

5. Synthetic Transformation



3a
97% ee, dr > 20:1

5, 85% yield
97% ee, dr > 20:1

4 Å MS (100 mg) was added to a solution of **3a** (46.0 mg, 0.1 mmol) in dry CH_3CN (1.0 mL) under argon atmosphere. The suspension was stirred vigorously under a positive pressure of argon for 2 hours at 25°C. Then methyl trifluoromethansulfonate (45.3 uL, 0.4 mmol, 4.0 eq.) was added. After being stirred at 25°C for 12 hours, MeOH (0.55 mL) and DBU (22.4 uL, 0.15 mmol, 1.5 eq.) were subsequently added. After being stirred at 25°C for 30 min, the reaction mixture was concentrated and the residue was subjected to a silica gel flash chromatography (petroleum ether/ EtOAc = 10:1 to 4:1) to afford product **5** as colorless oil (33.6 mg, 85% yield).

Enantiomeric excess was determined by HPLC analysis, ee = 97%, Chiralpak column ADH, λ = 254 nm, *n*-hexane/*i*-PrOH = 70:30, flow rate: 0.8 mL/min, 25°C, t_r(major) = 47.760 min, t_r(minor) = 56.418 min. $[\alpha]_D^{20}$=+73.2 (c=0.5, CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.39 – 7.29 (m, 5H), 5.04 (d, *J* = 6.4 Hz, 1H), 3.74 – 3.64 (m, 4H), 3.37 (td, *J* = 8.3, 3.1 Hz, 1H), 3.22 (dd, *J* = 18.0, 8.4 Hz, 1H), 3.09 – 3.04 (m, 1H), 1.19 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.09, 172.53, 172.39, 138.66, 136.39, 133.39, 128.74, 128.64, 128.42, 128.06, 127.67, 84.70, 65.66, 52.53, 51.02, 38.85, 37.83, 27.66, 27.61.

HRMS (ESI) calcd for $C_{24}H_{28}NO_5$ $[M+H]^+$: 410.2080; found: 410.2084.

6. ^{1}H NMR and ^{13}C NMR Spectra

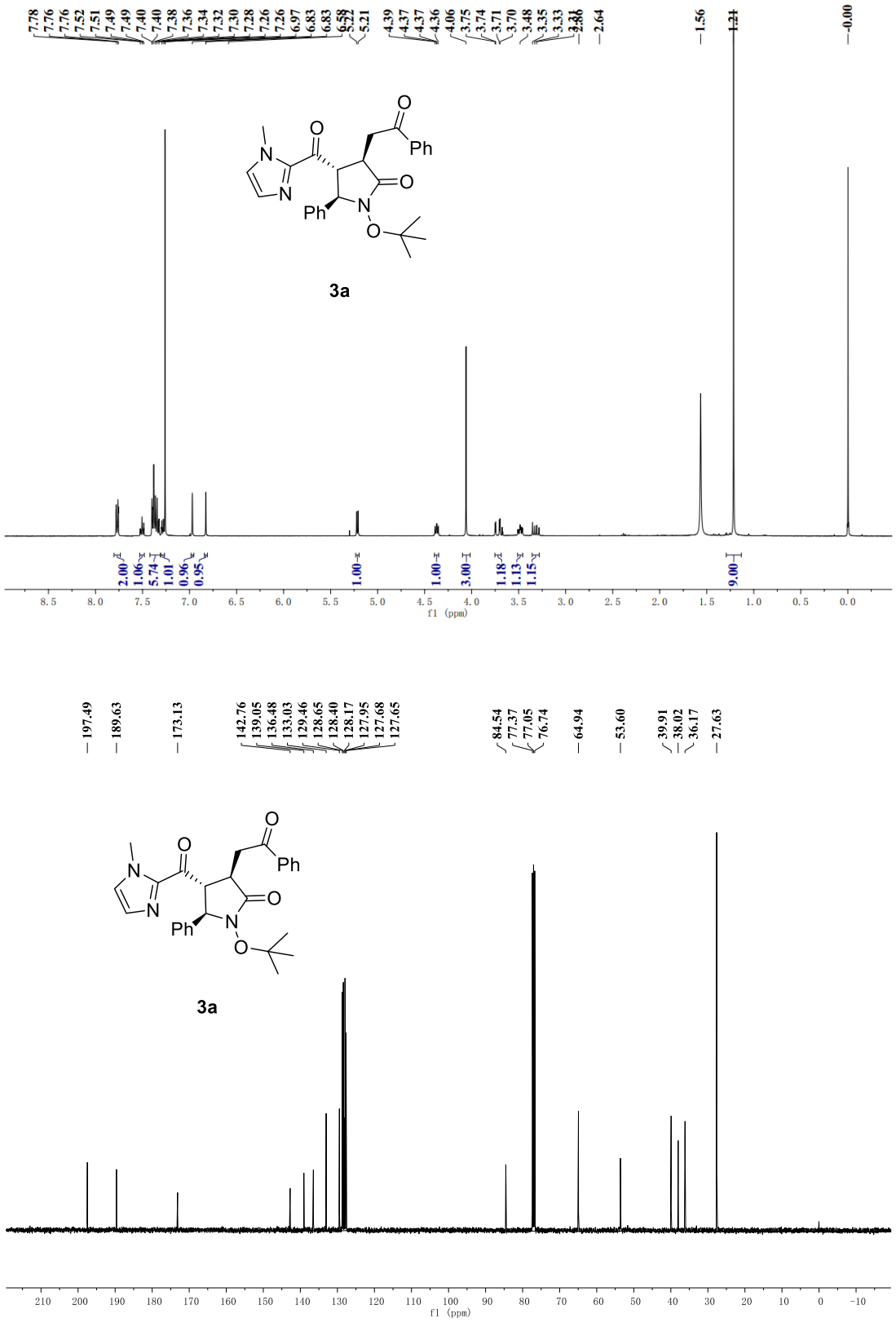


Figure S1. ^{1}H and ^{13}C NMR spectrum of **3a**.

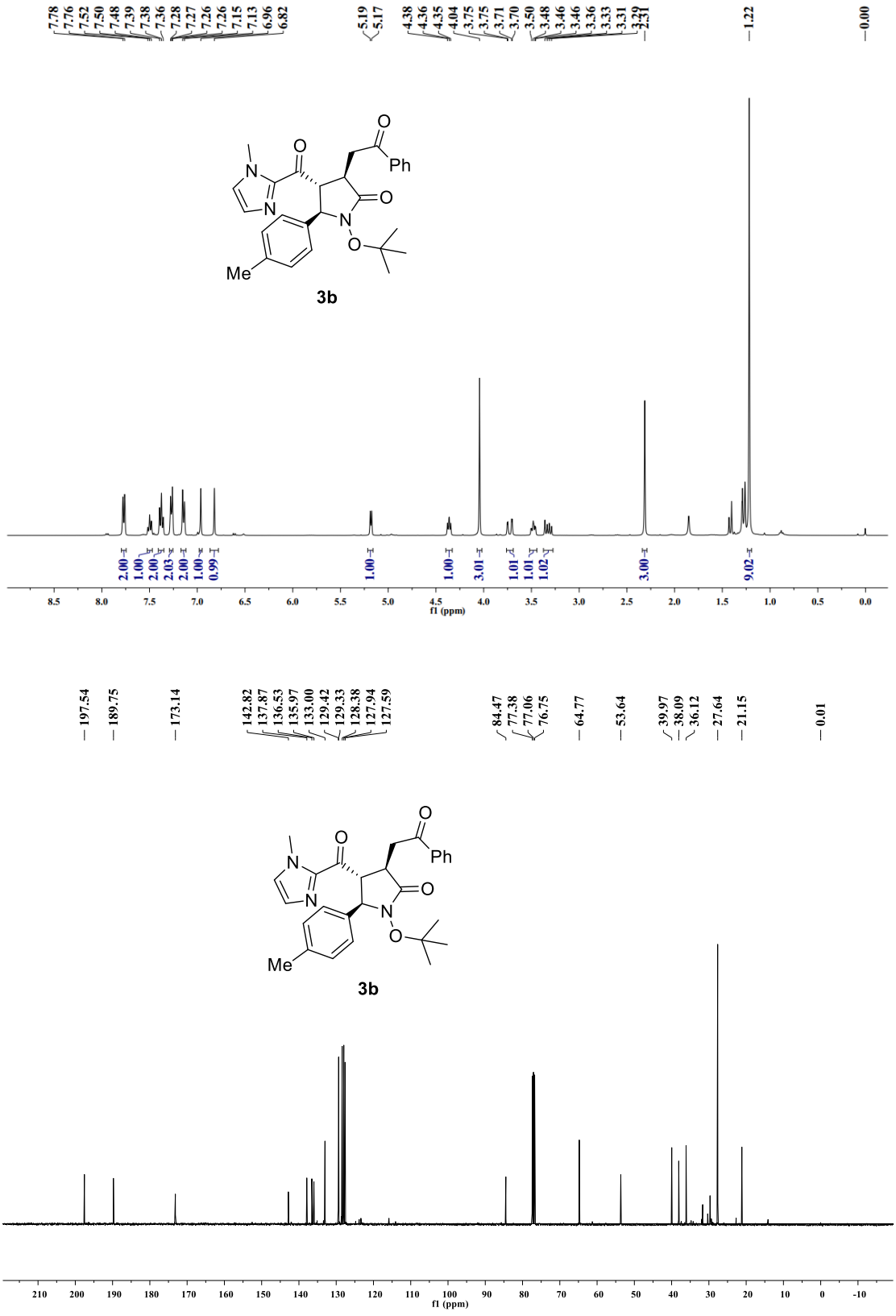


Figure S2. ^{1}H and ^{13}C NMR spectrum of **3b**.

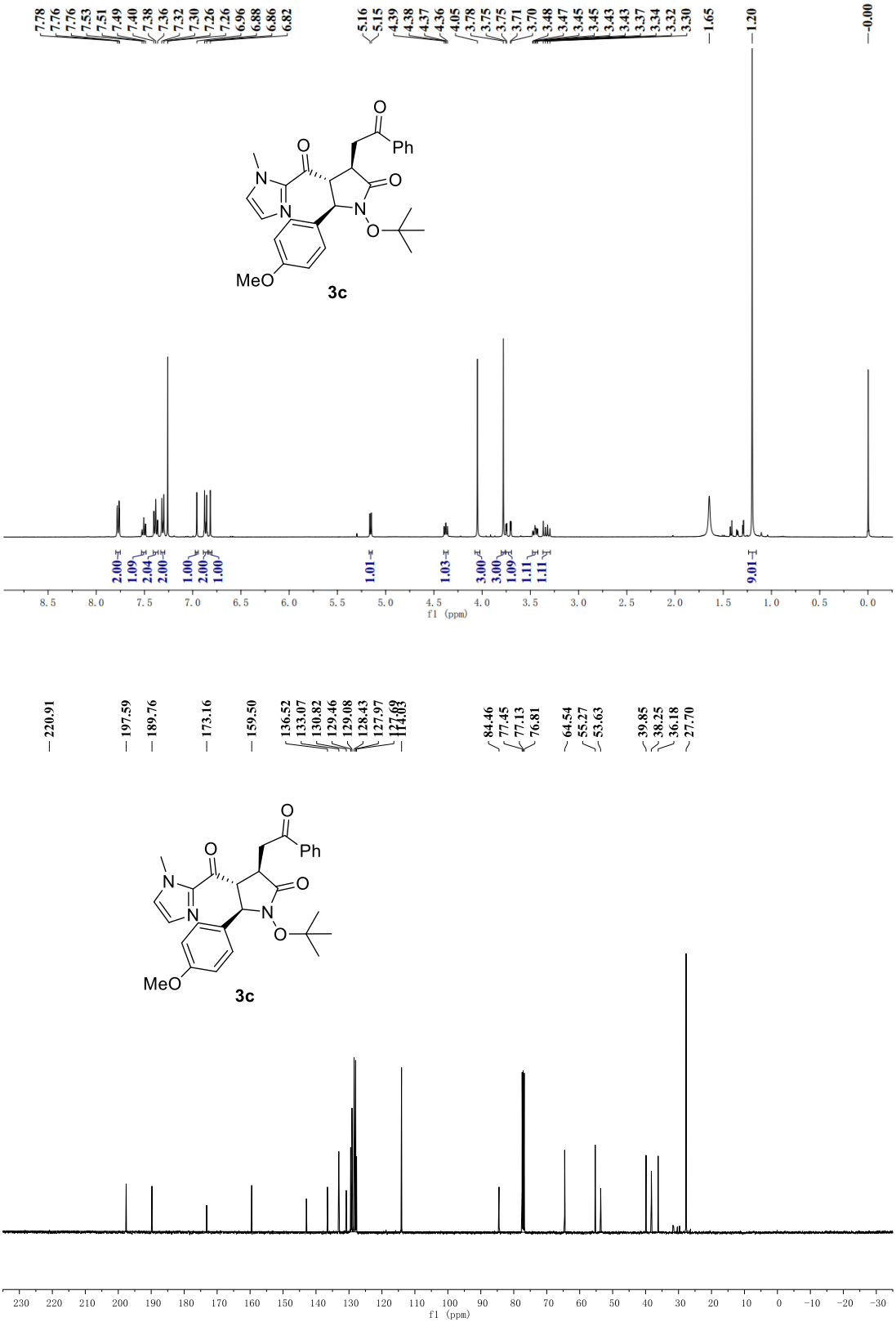
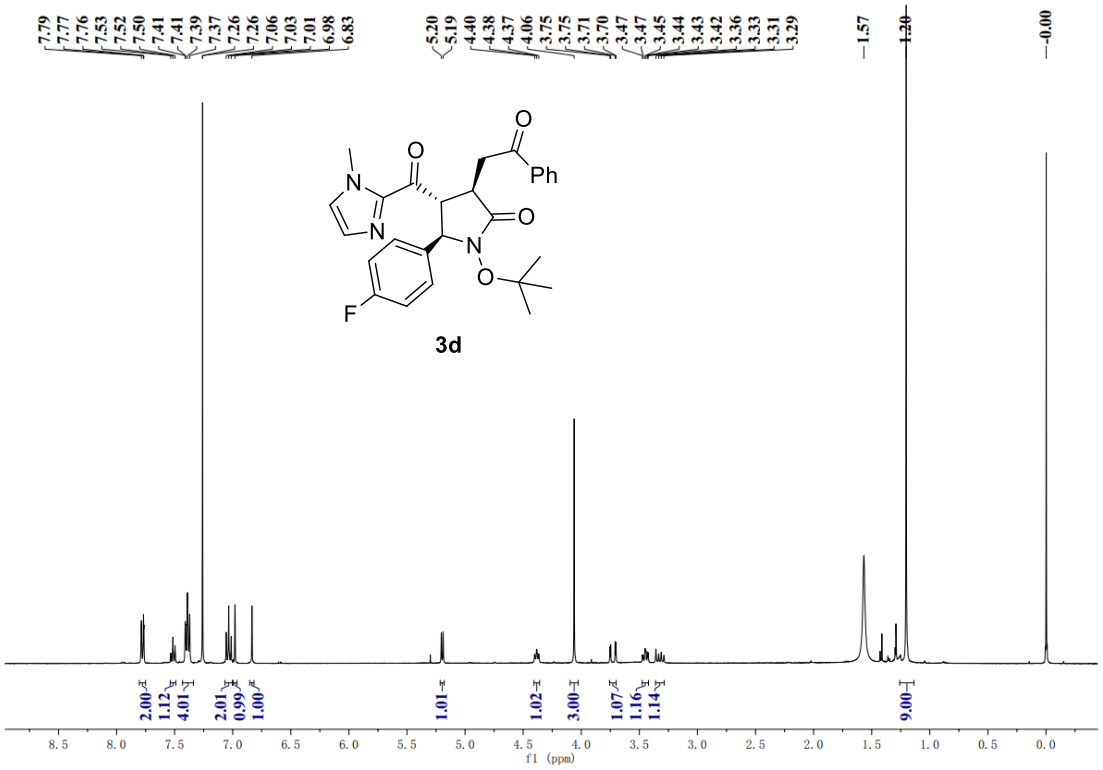
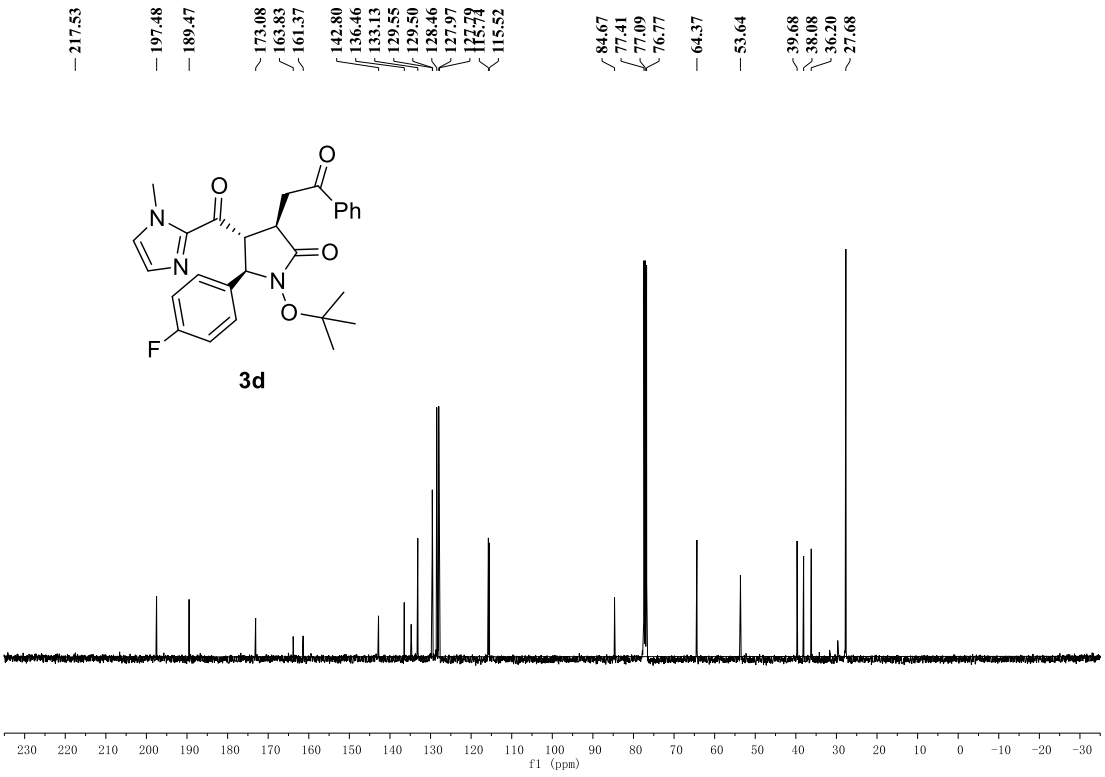


Figure S3. ^{1}H and ^{13}C NMR spectrum of **3c**.


7.79
7.77
7.76
7.53
7.52
7.50
7.41
7.41
7.39
7.37
7.26
7.26
7.06
7.03
7.01
6.98
6.83
5.20
5.19
4.40
4.38
4.37
4.06
3.75
3.75
3.71
3.70
3.47
3.47
3.45
3.44
3.43
3.42
3.36
3.33
3.31
3.29
1.57
1.20
0.00
O
O
Ph
N
N
O
O
F
2.00
1.12
4.01
2.01
0.99
1.00
1.01
1.02
3.00
1.07
1.16
1.14
9.00
f1 (ppm)

3d


217.53
197.48
189.47
173.08
163.83
161.37
142.80
136.46
133.13
129.55
129.50
128.46
127.97
127.79
127.74
115.52
84.67
77.41
77.09
76.77
64.37
53.64
39.68
38.08
36.20
27.68
O
O
Ph
N
N
O
O
F
f1 (ppm)

3d

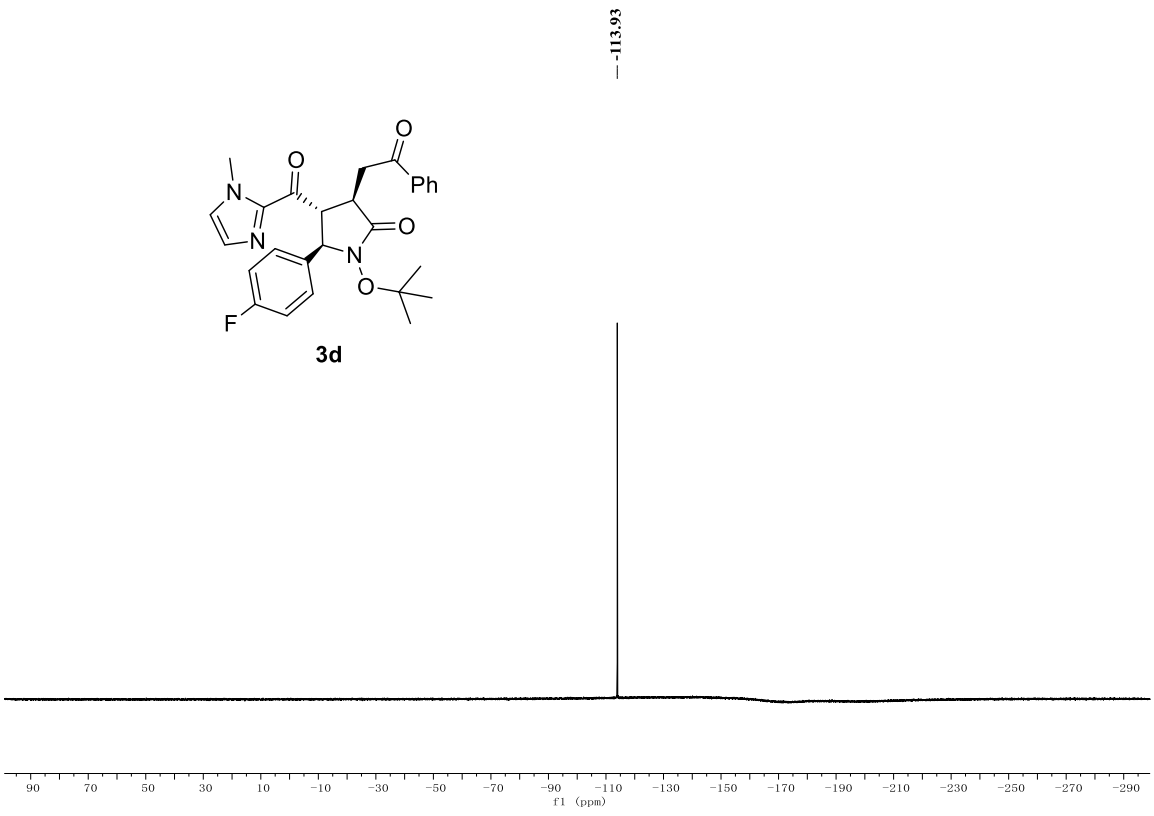


Figure S4. ^{1}H, ^{13}C and ^{19}F NMR spectrum of **3d**.

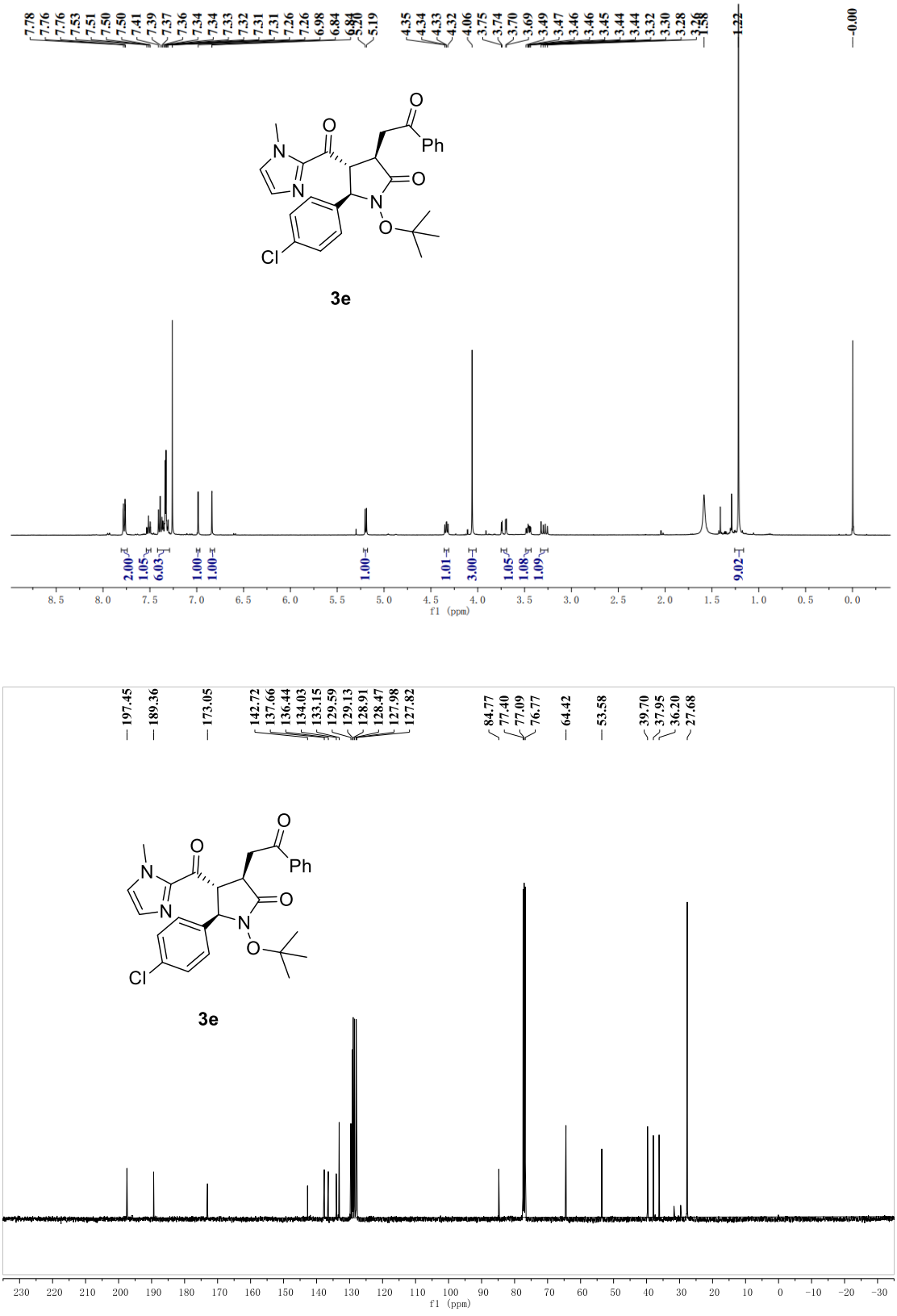


Figure S5. ^{1}H and ^{13}C NMR spectrum of **3e**.

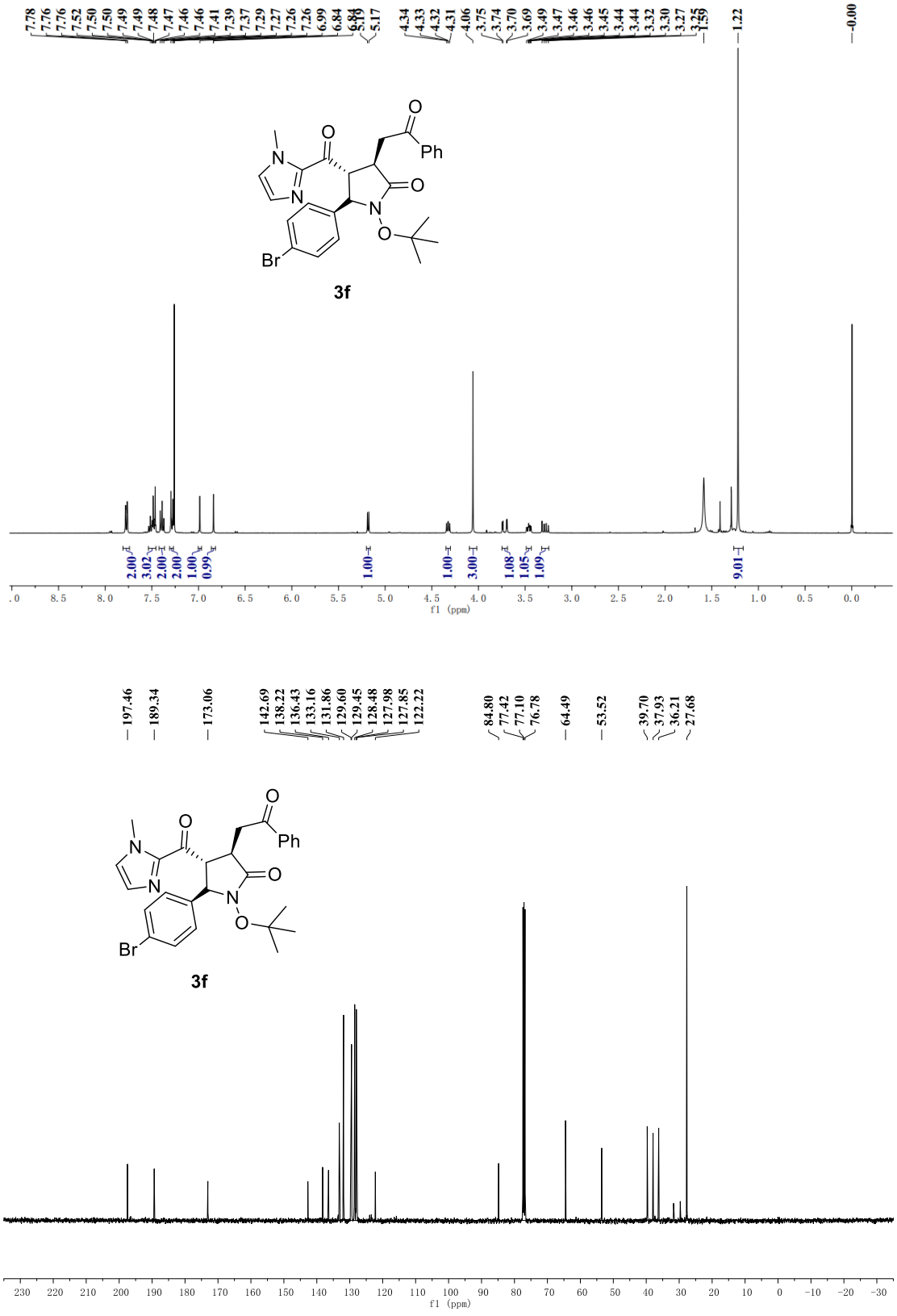


Figure S6. ^{1}H and ^{13}C NMR spectrum of **3f**.

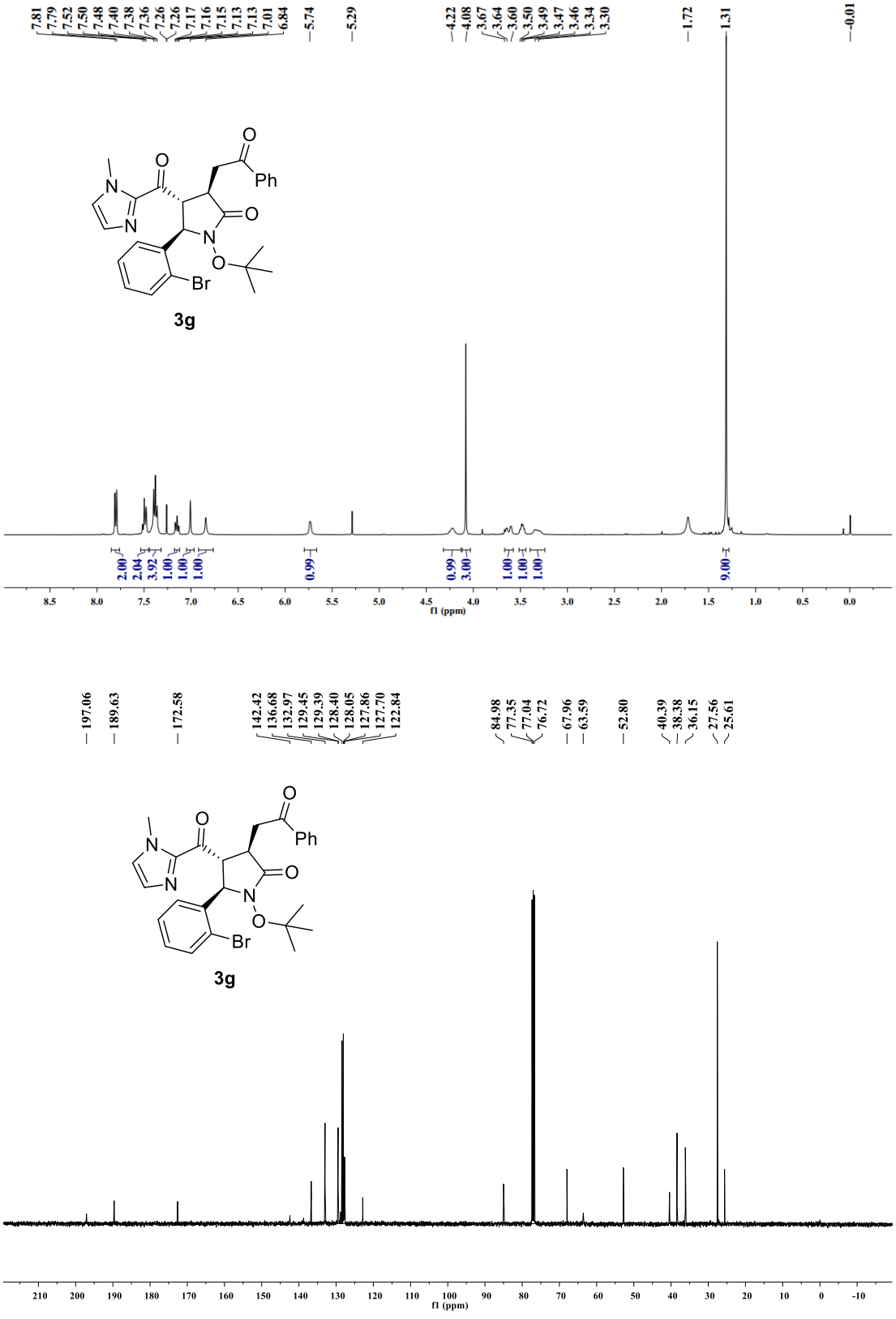


Figure S7. ^{1}H and ^{13}C NMR spectrum of **3g**.

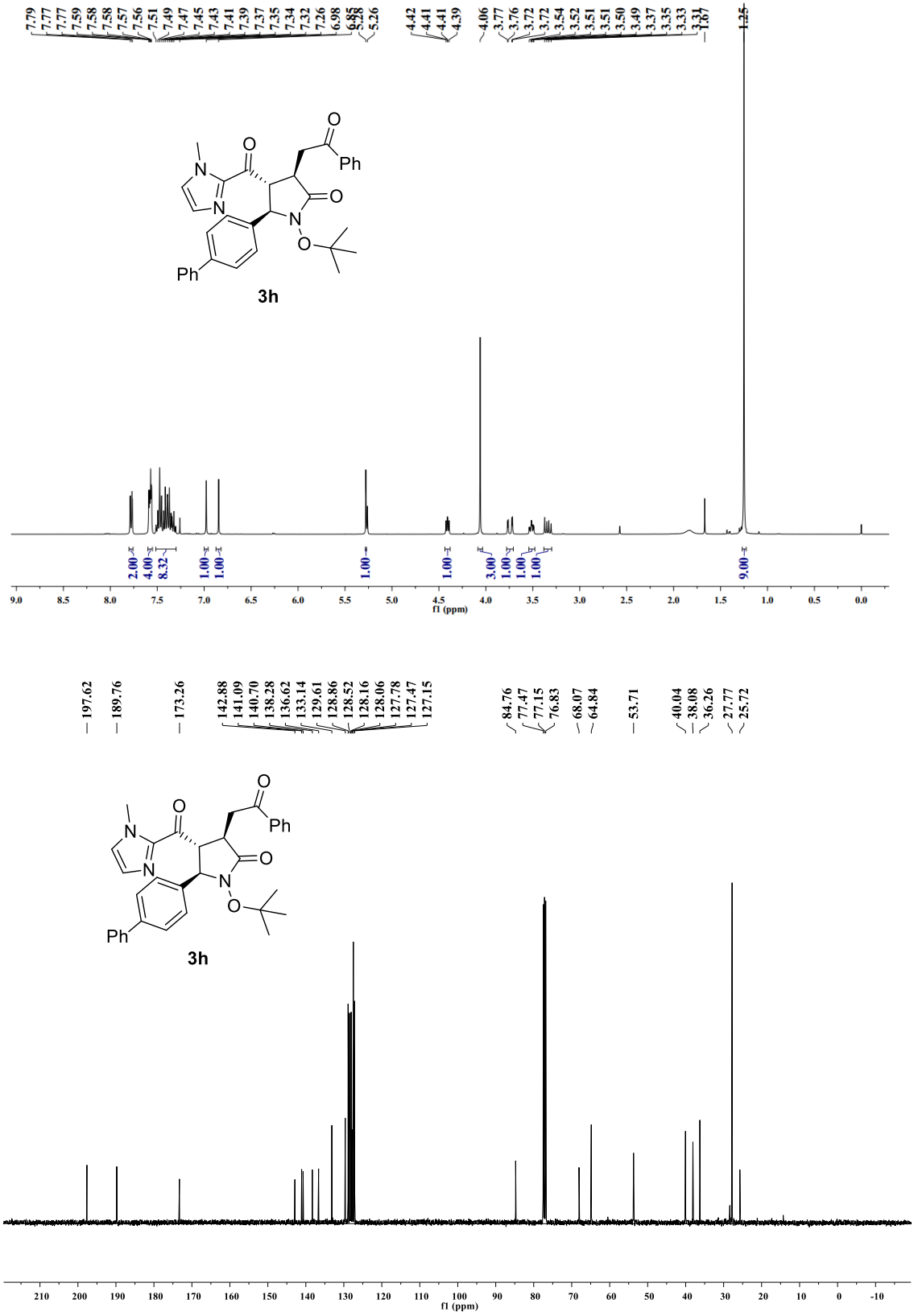


Figure S8. ^{1}H and ^{13}C NMR spectrum of **3h**.

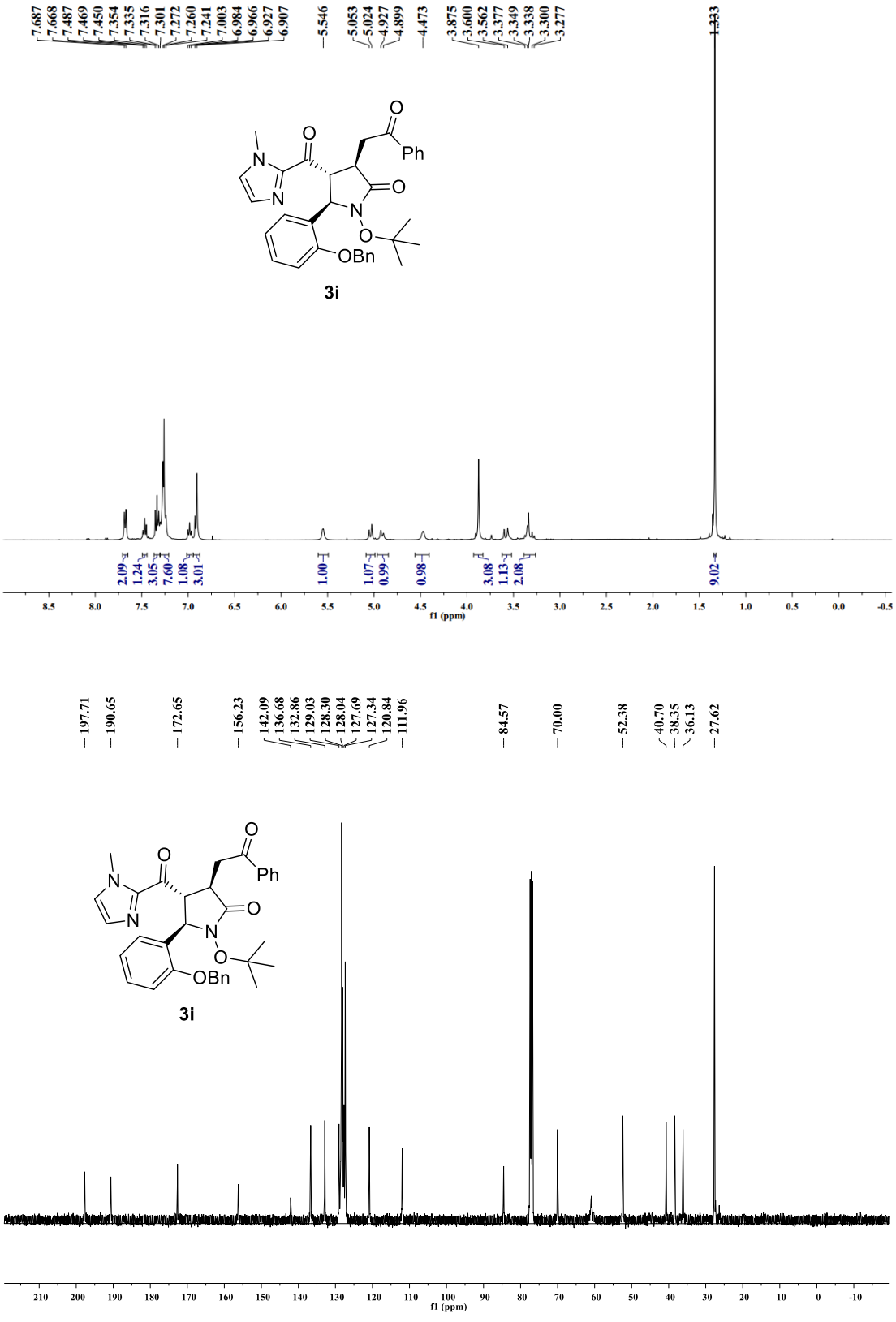


Figure S9. ^{1}H and ^{13}C NMR spectrum of **3i**.

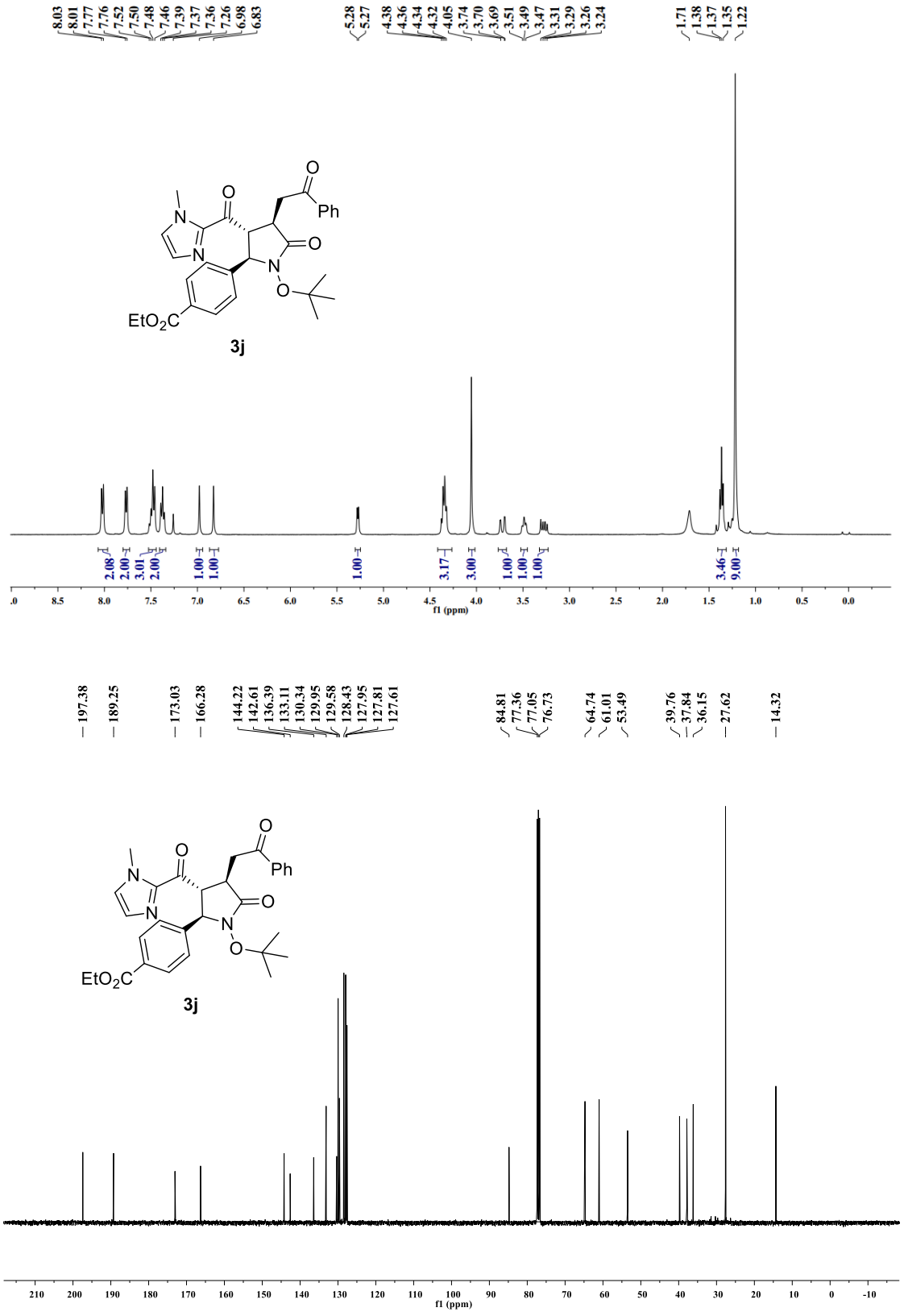
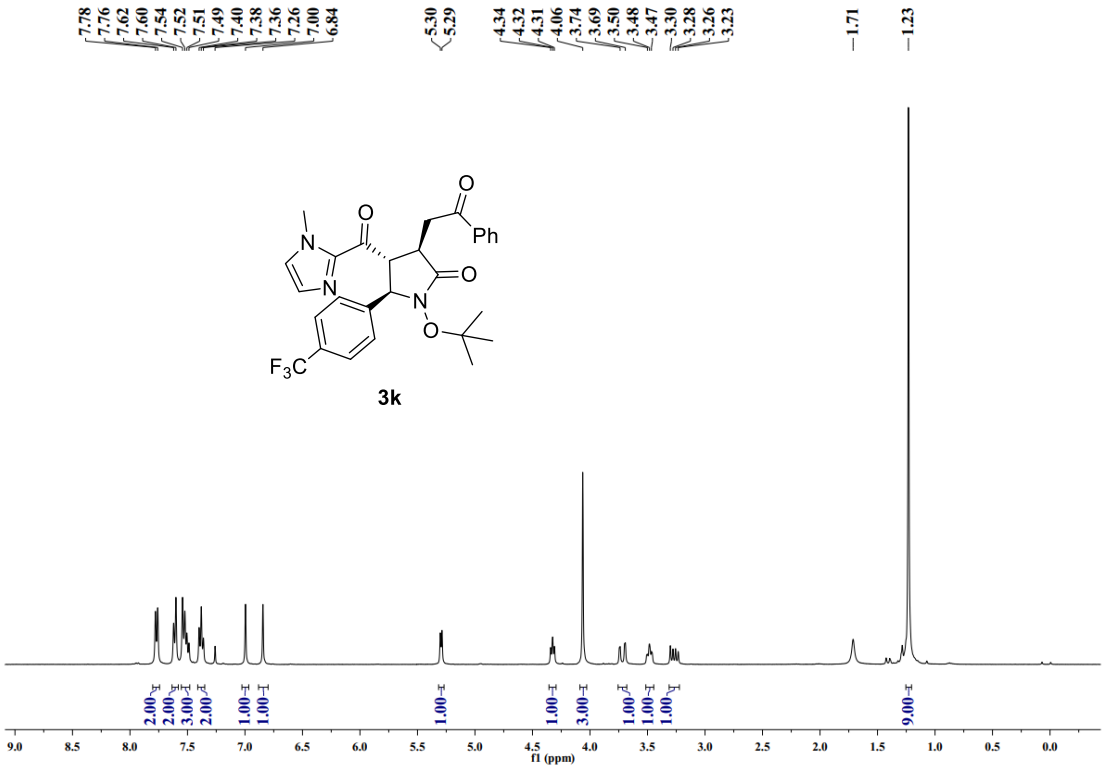


Figure S10. ^{1}H and ^{13}C NMR spectrum of **3j**.


7.78
7.76
7.62
7.60
7.54
7.52
7.51
7.49
7.40
7.38
7.36
7.26
7.00
6.84
5.30
5.29
4.34
4.32
4.31
4.06
3.74
3.69
3.50
3.48
3.47
3.30
3.28
3.26
3.23
1.71
1.23
O
Ph
O
N
N
O
N
O
F3C
3k
2.00
2.00
3.00
2.00
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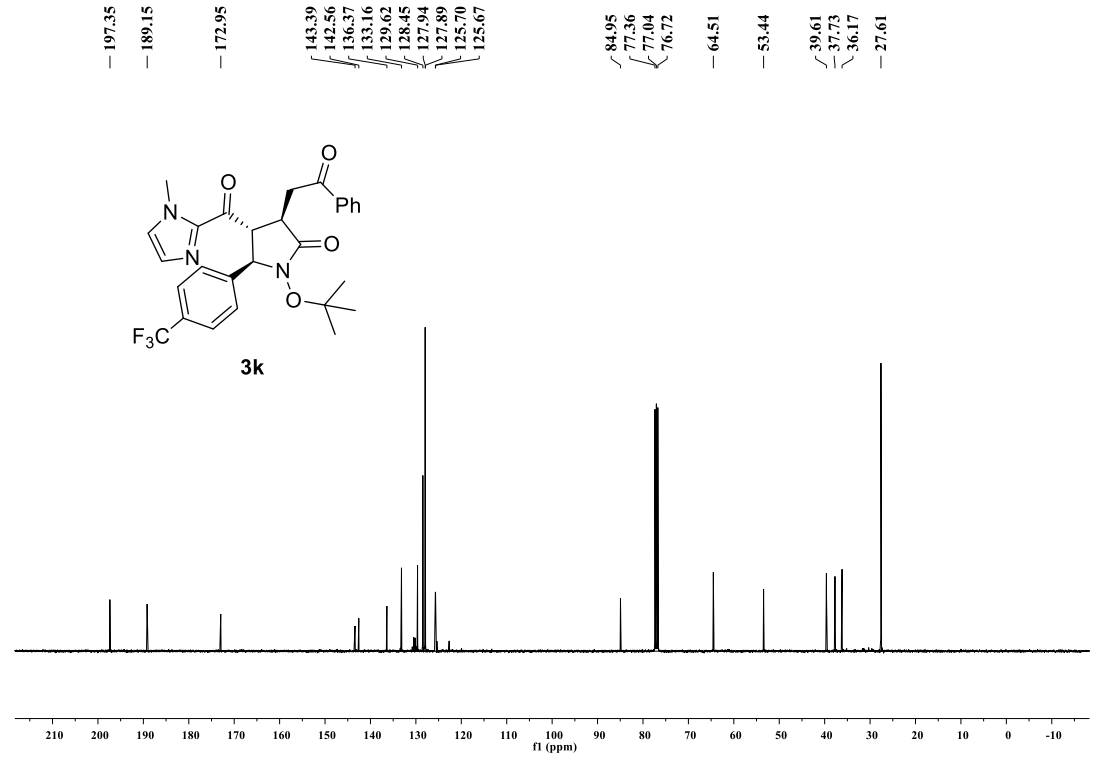
1.00
3.00
1.00
1.00
1.00
9.00
f1 (ppm)


197.35
189.15
172.95
143.39
142.56
136.37
133.16
129.62
128.45
127.94
127.89
125.70
125.67
84.95
77.36
77.04
76.72
64.51
53.44
39.61
37.73
36.17
27.61
O
Ph
O
N
N
O
N
O
F3C
3k
f1 (ppm)

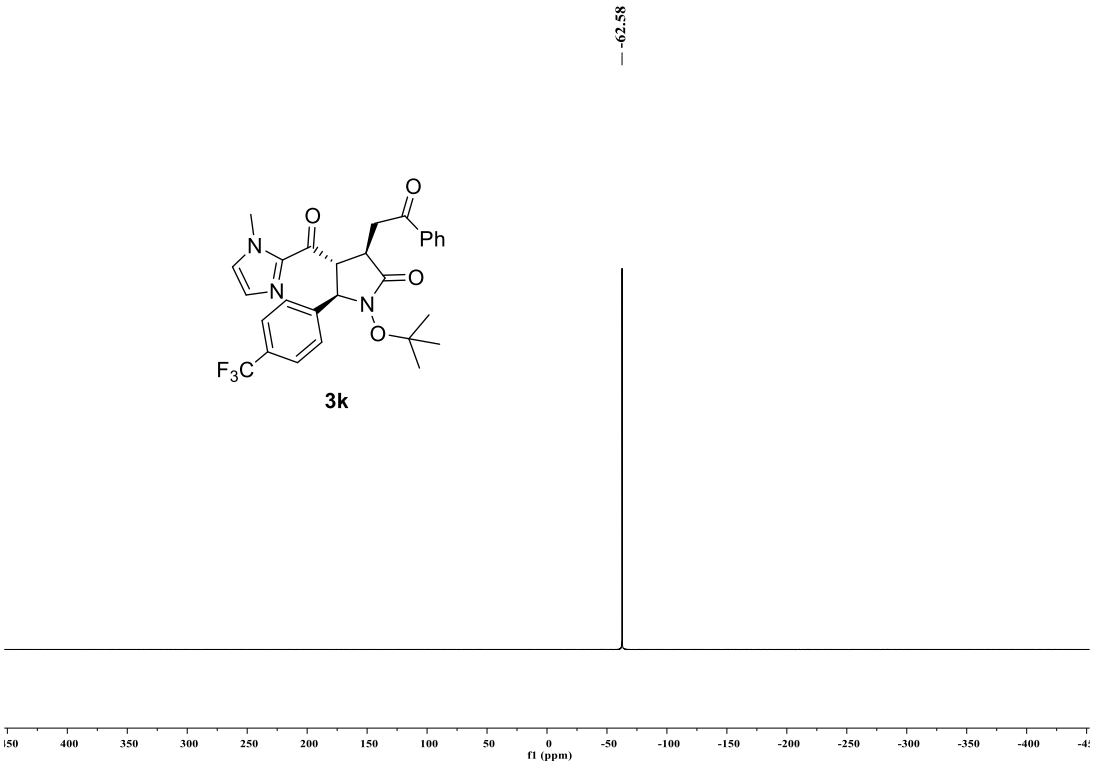


Figure S11. ^{1}H, ^{13}C NMR and ^{19}F NMR spectrum of **3k**.

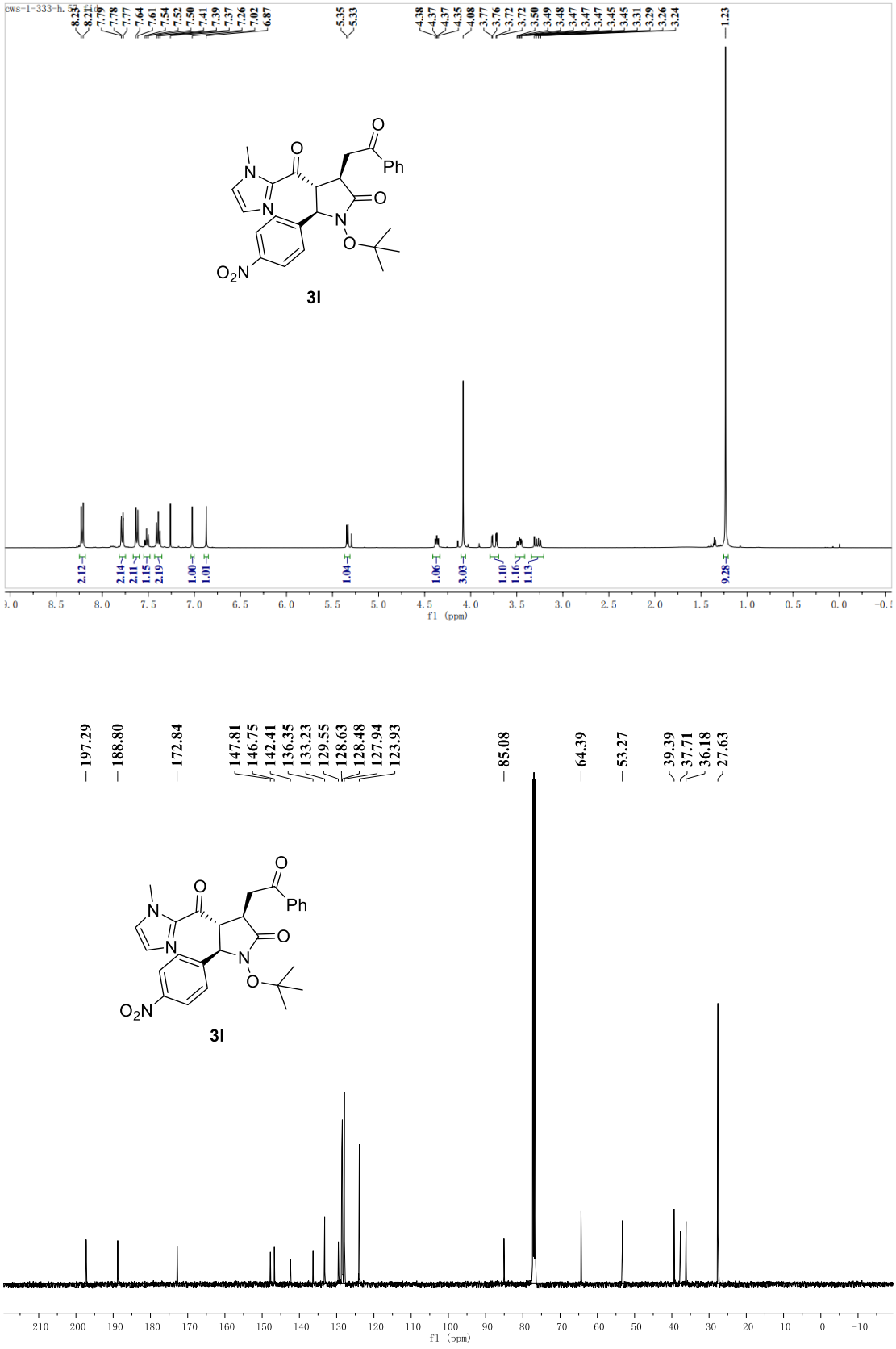


Figure S12. ^{1}H and ^{13}C NMR spectrum of **3l**.

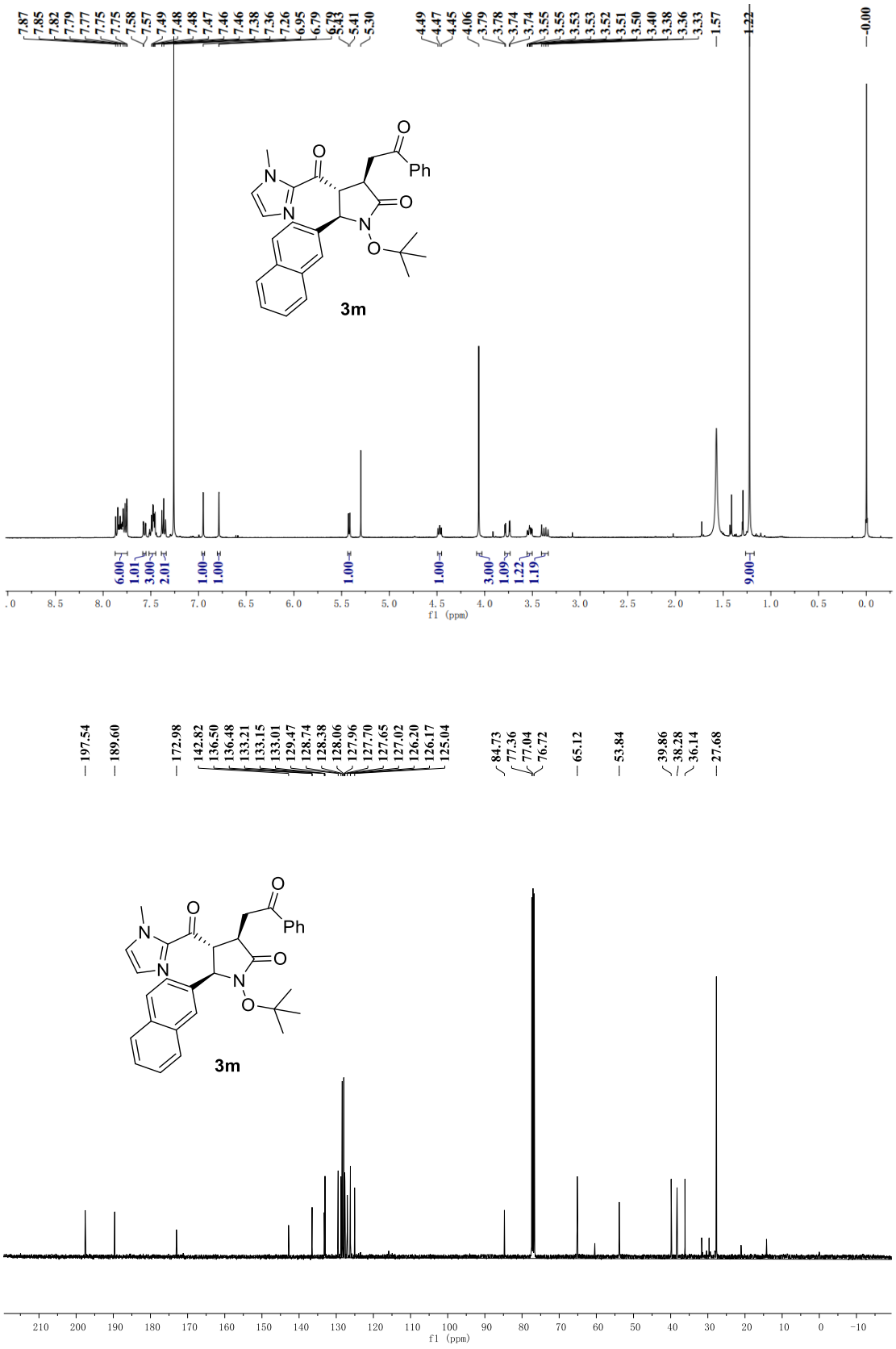


Figure S13. ^{1}H and ^{13}C NMR spectrum of **3m**.

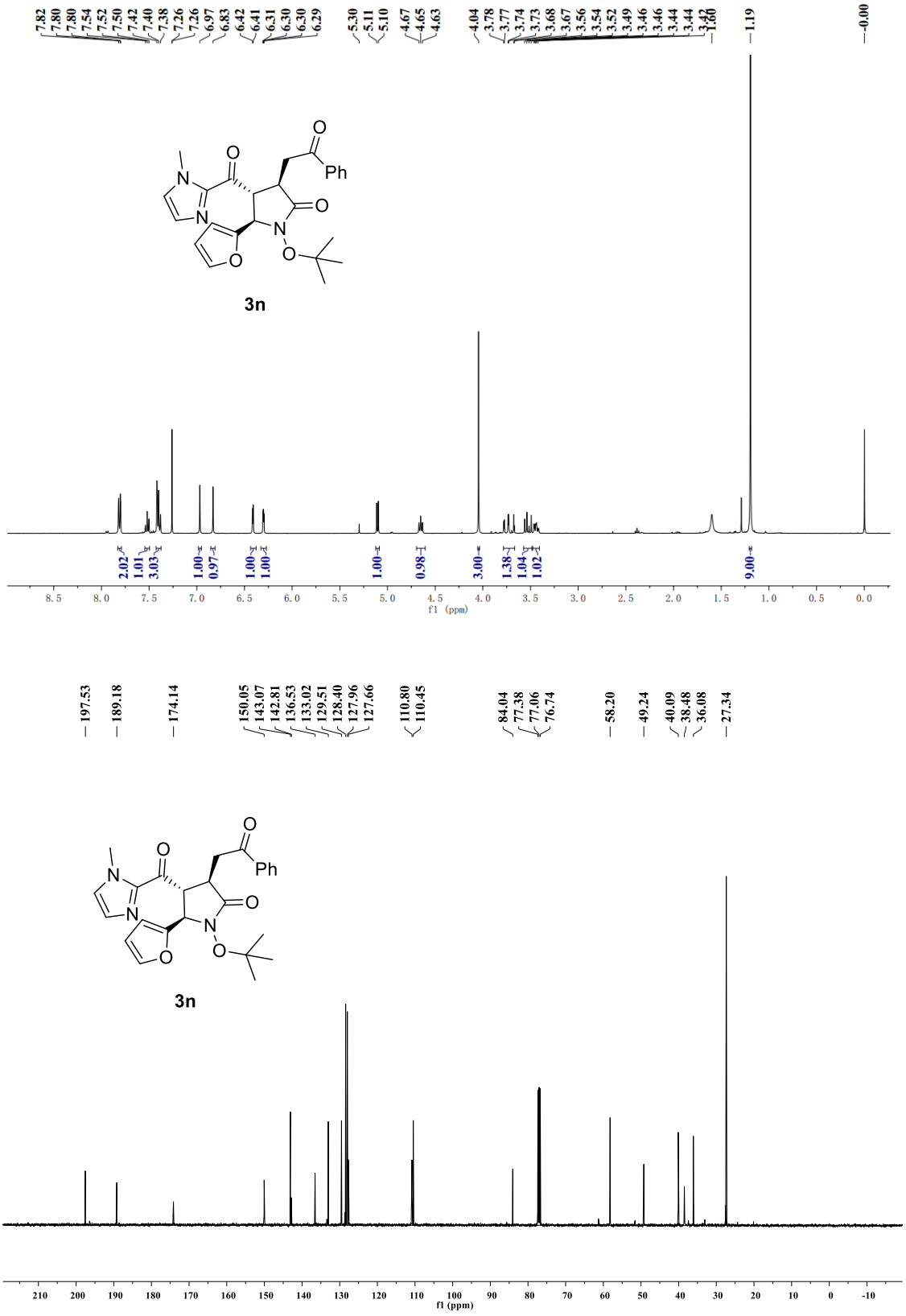


Figure S14. ^{1}H and ^{13}C NMR spectrum of **3n**.

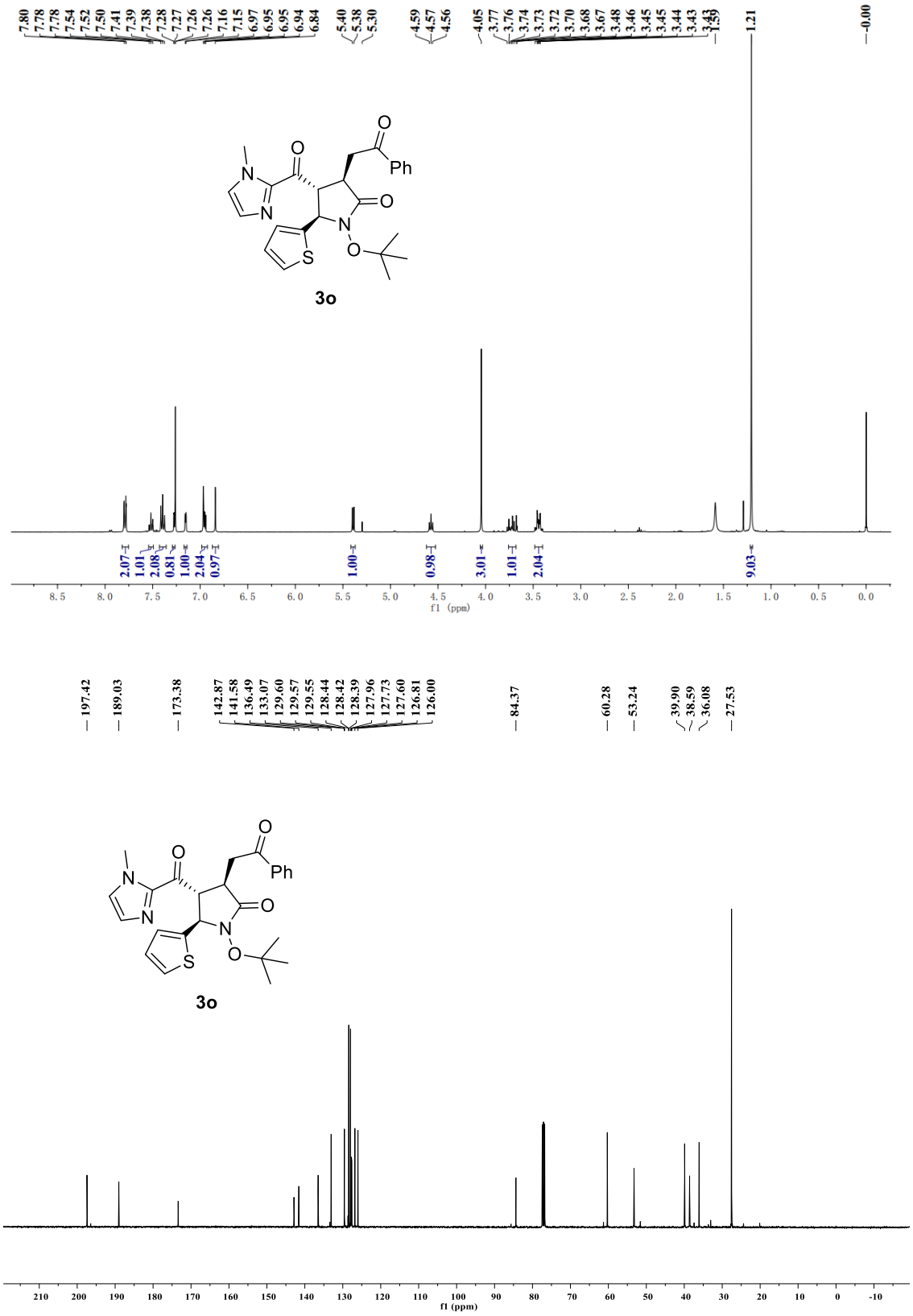


Figure S15. ^{1}H and ^{13}C NMR spectrum of **3o**.

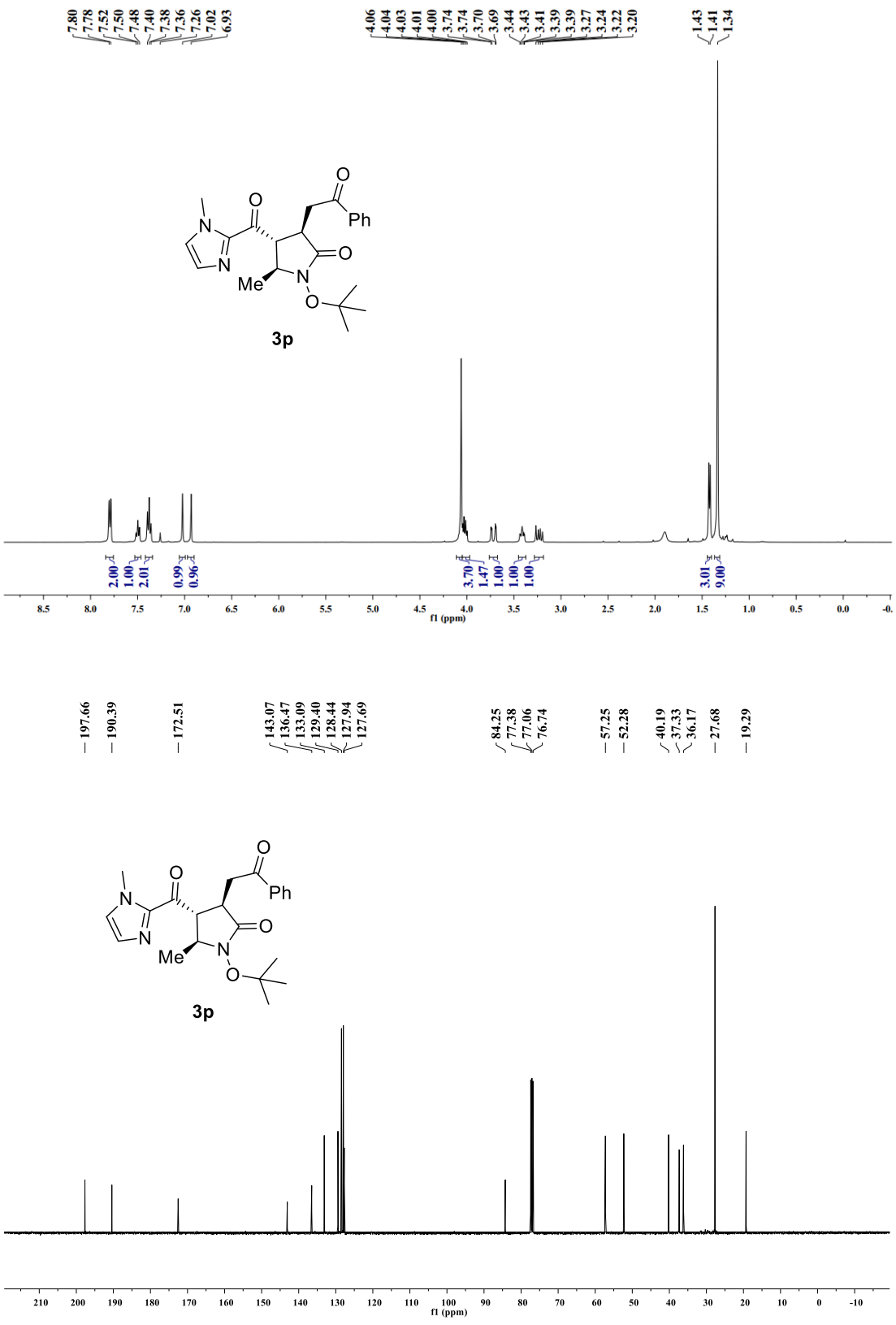


Figure S16. ^{1}H and ^{13}C NMR spectrum of **3p**.

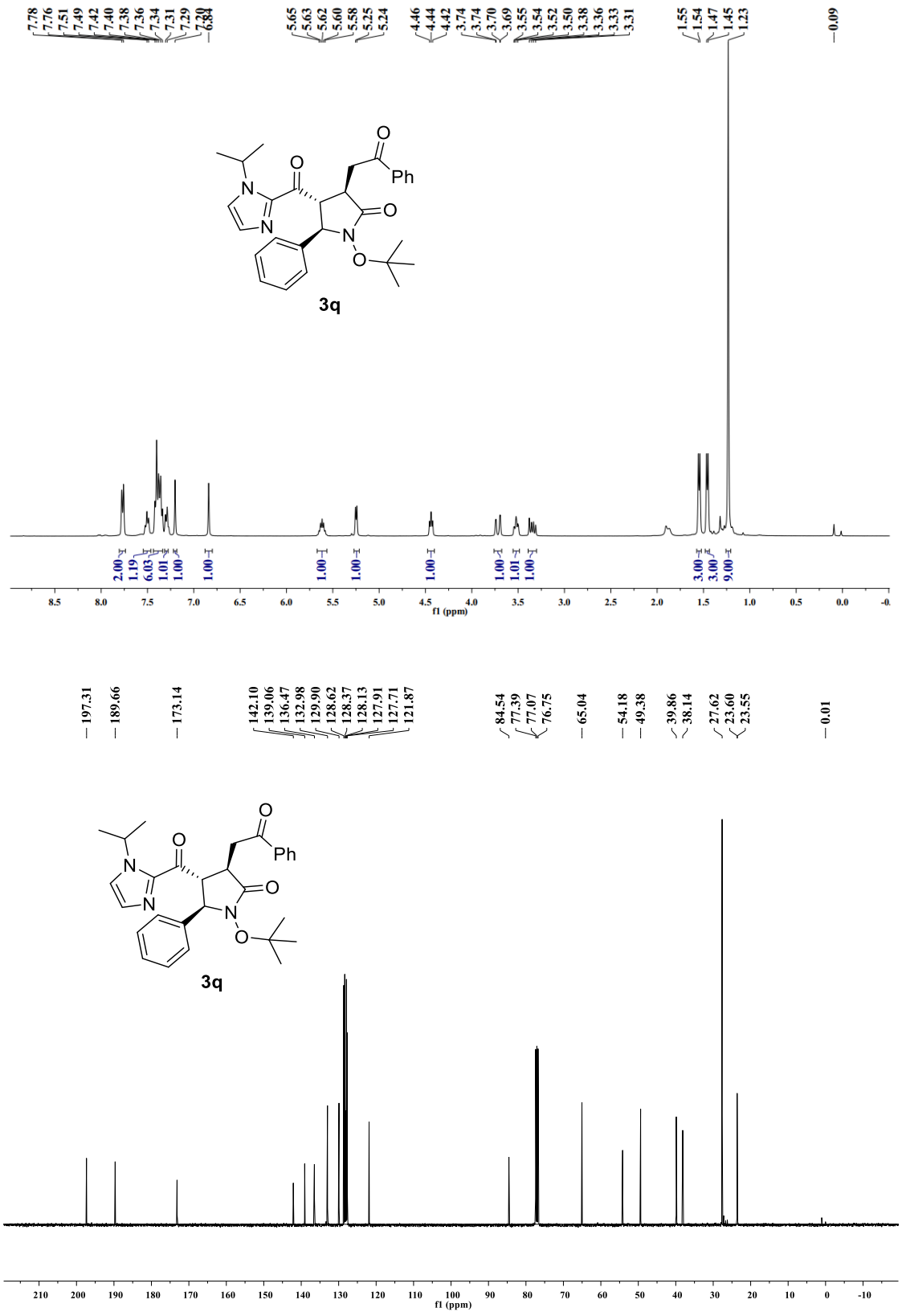


Figure S17. ^{1}H and ^{13}C NMR spectrum of **3q**.

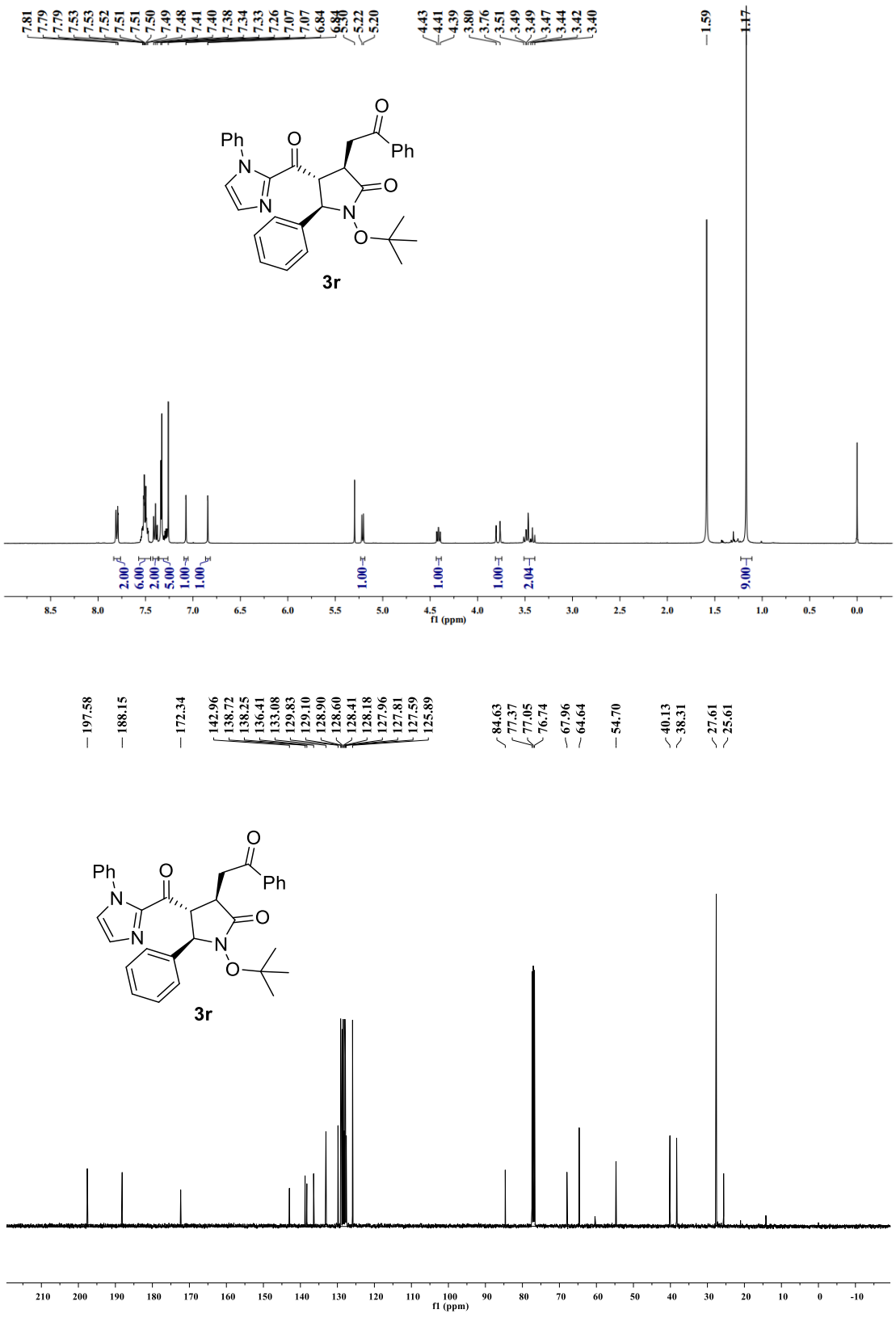


Figure S18. ^{1}H and ^{13}C NMR spectrum of **3r.**

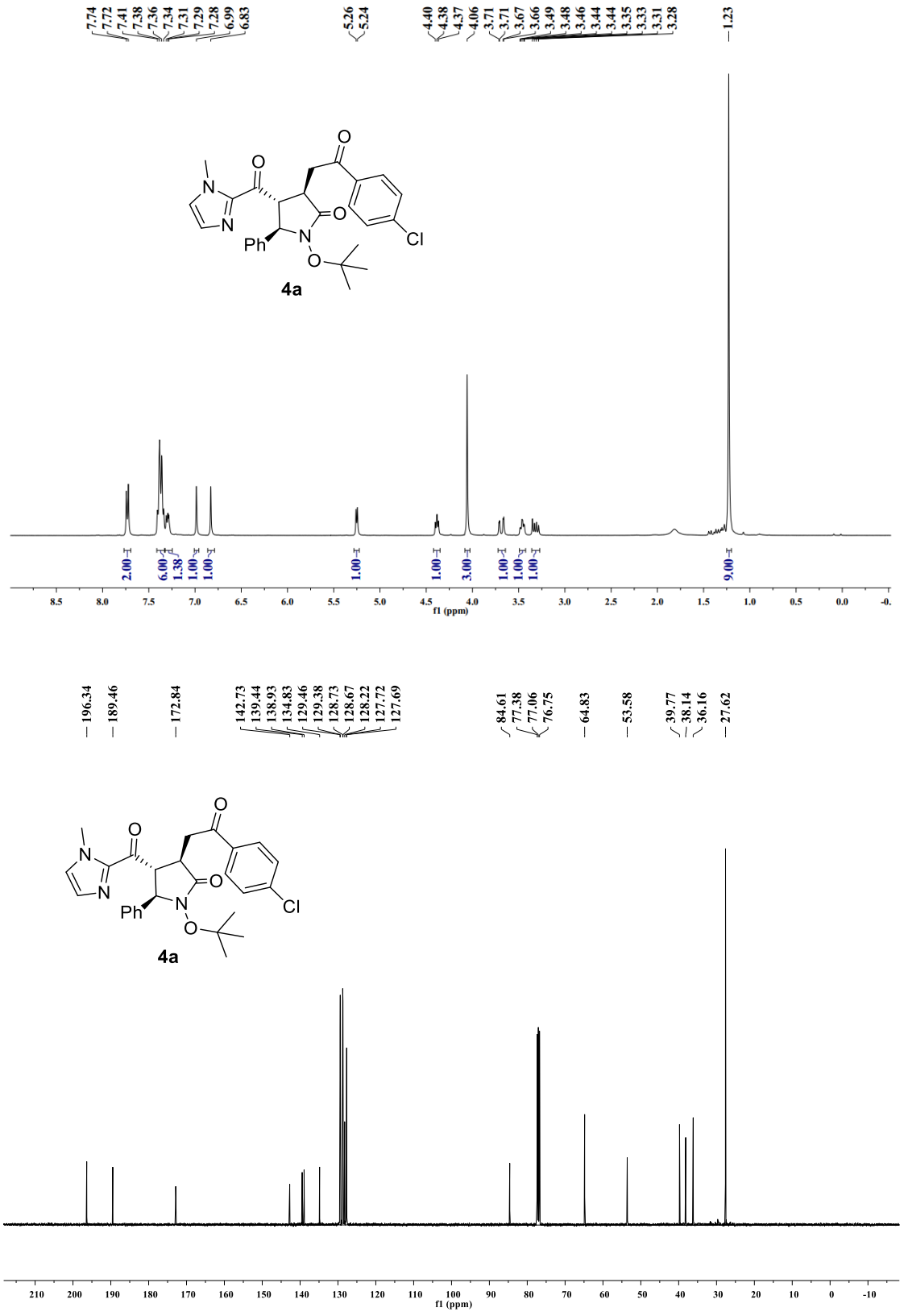


Figure S19. ^{1}H and ^{13}C NMR spectrum of **4a**.

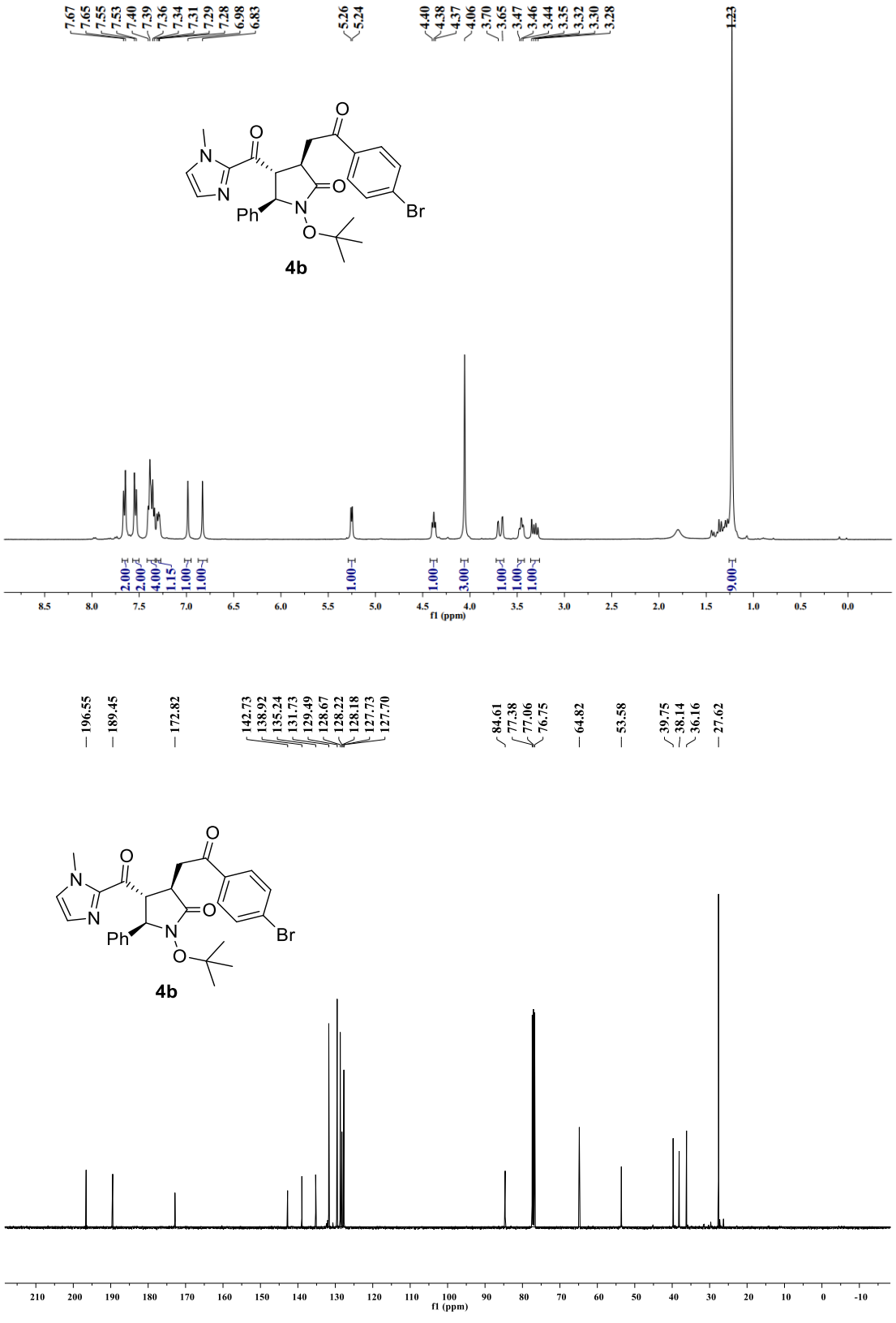


Figure S20. ^{1}H and ^{13}C NMR spectrum of **4b**.

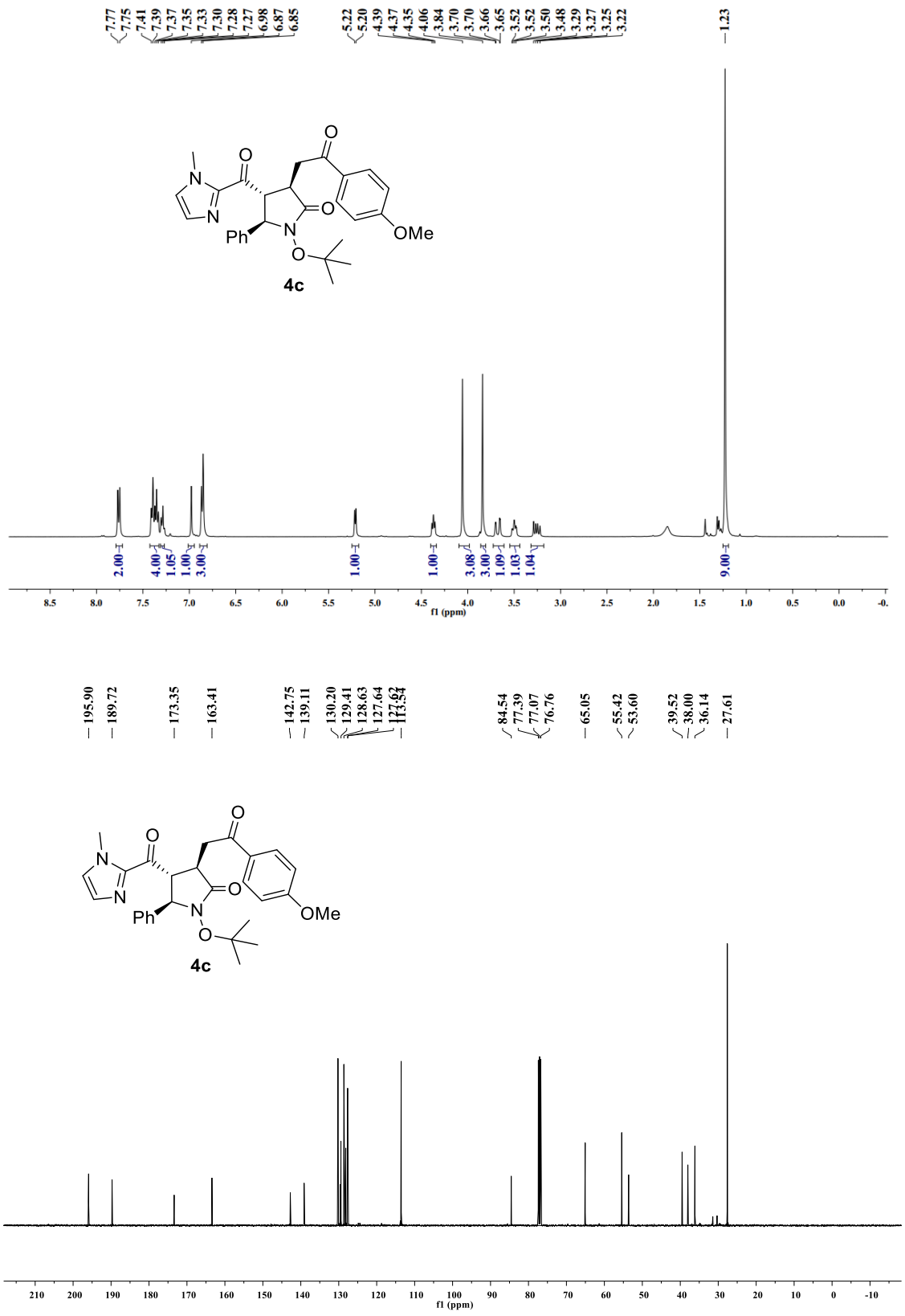


Figure S21. ^{1}H and ^{13}C NMR spectrum of **4c**.

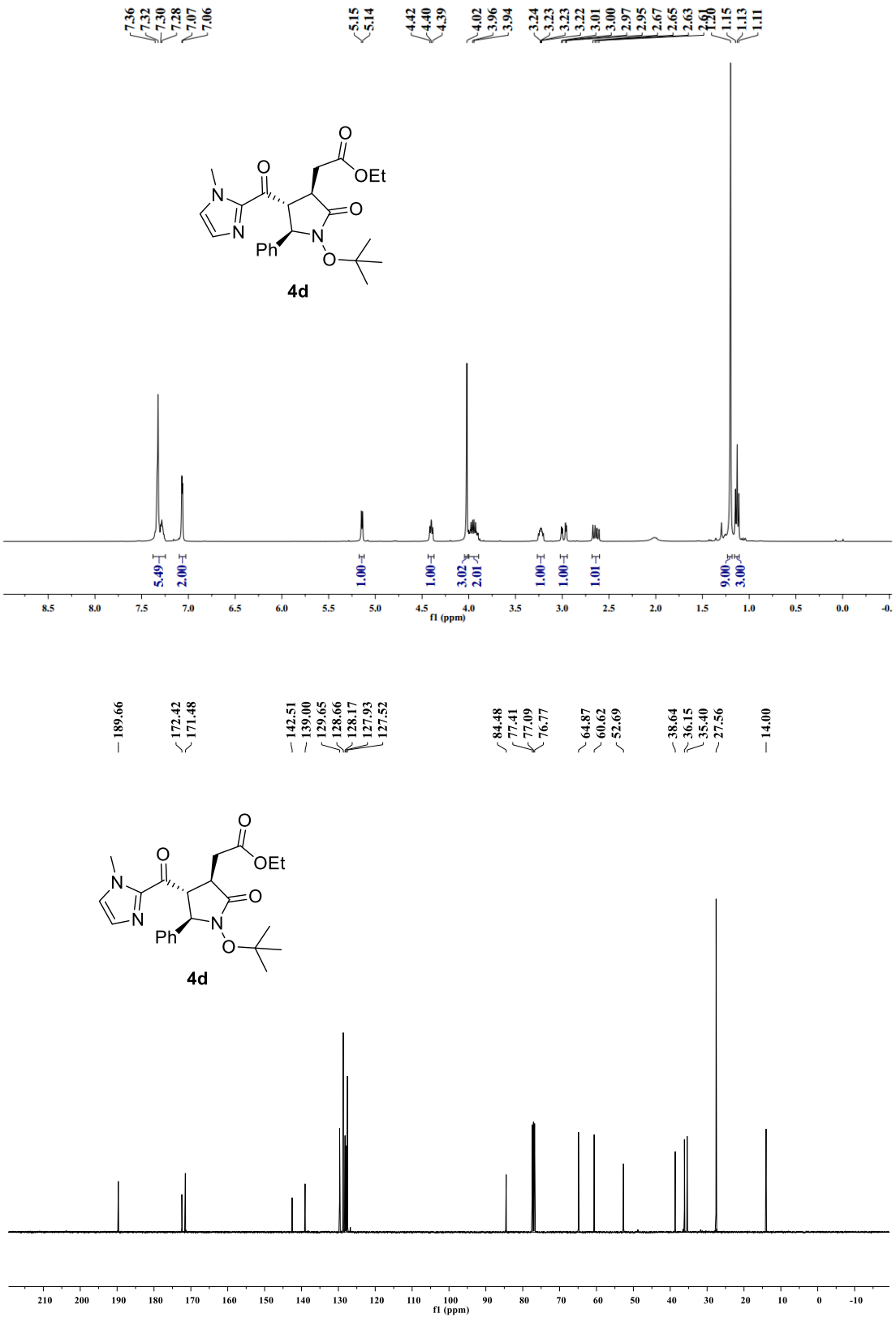


Figure S22. ^{1}H and ^{13}C NMR spectrum of **4d**.

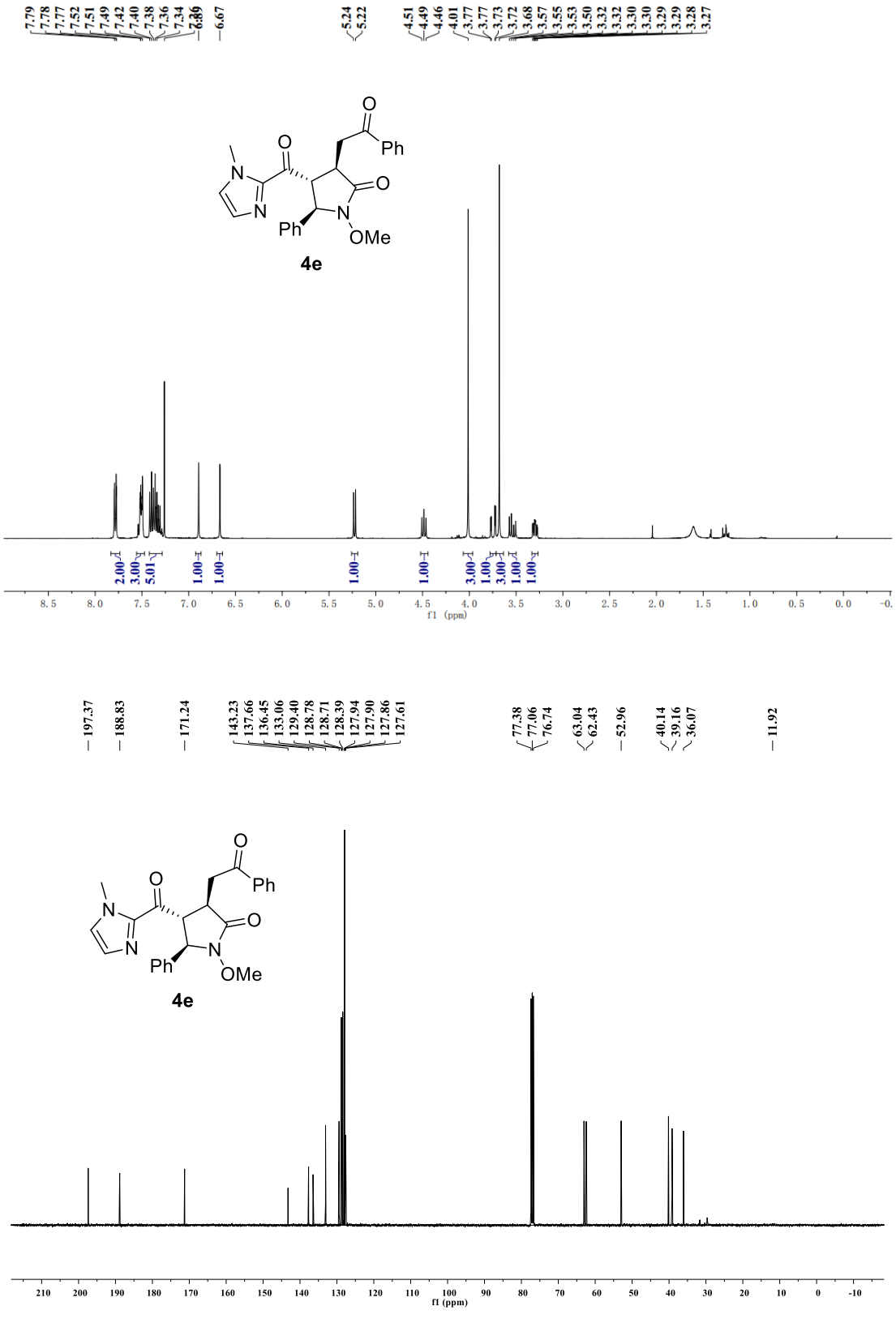


Figure S23. ^{1}H and ^{13}C NMR spectrum of **4e**.

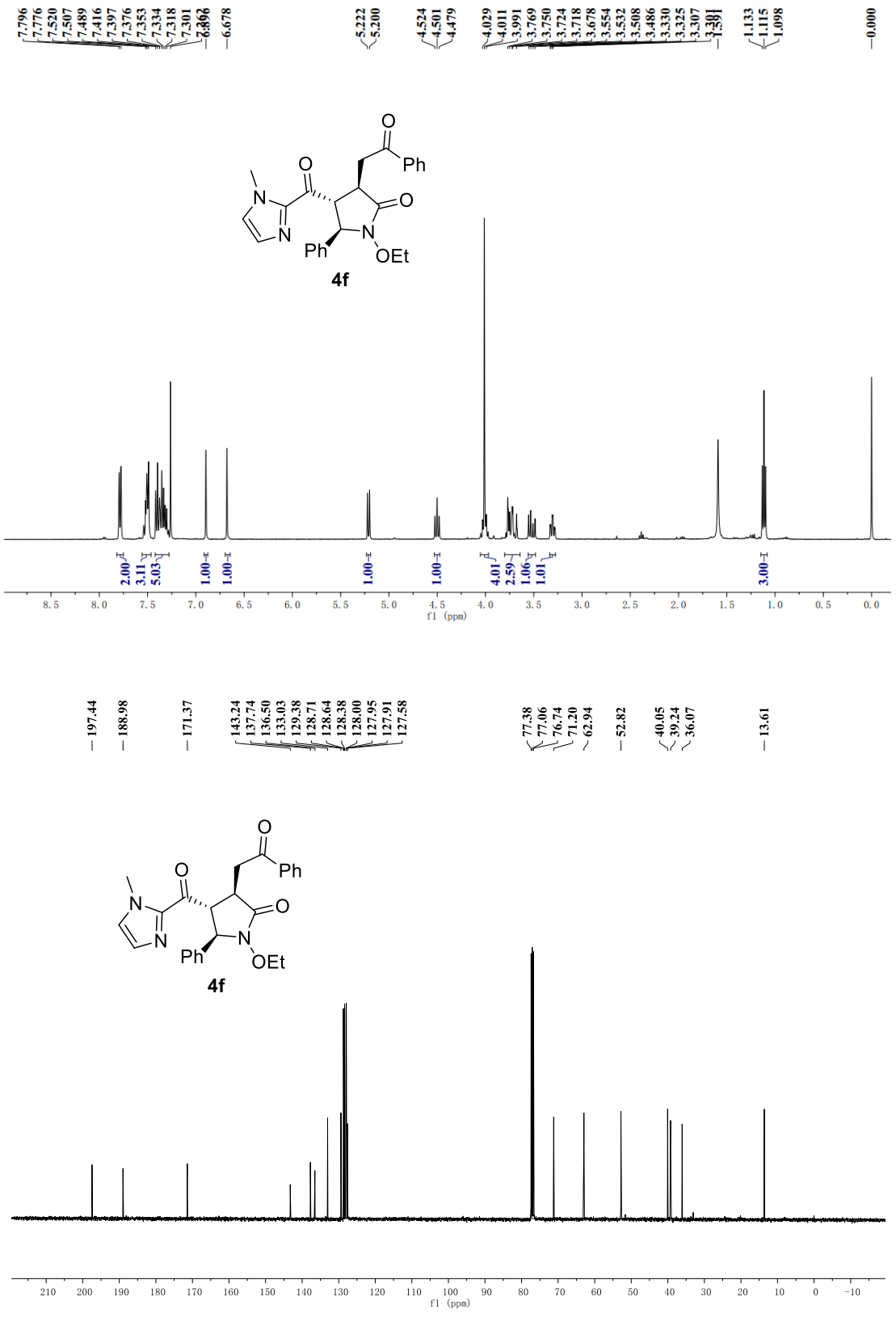


Figure S24. ^{1}H, ^{13}C NMR spectrum of **4f**.

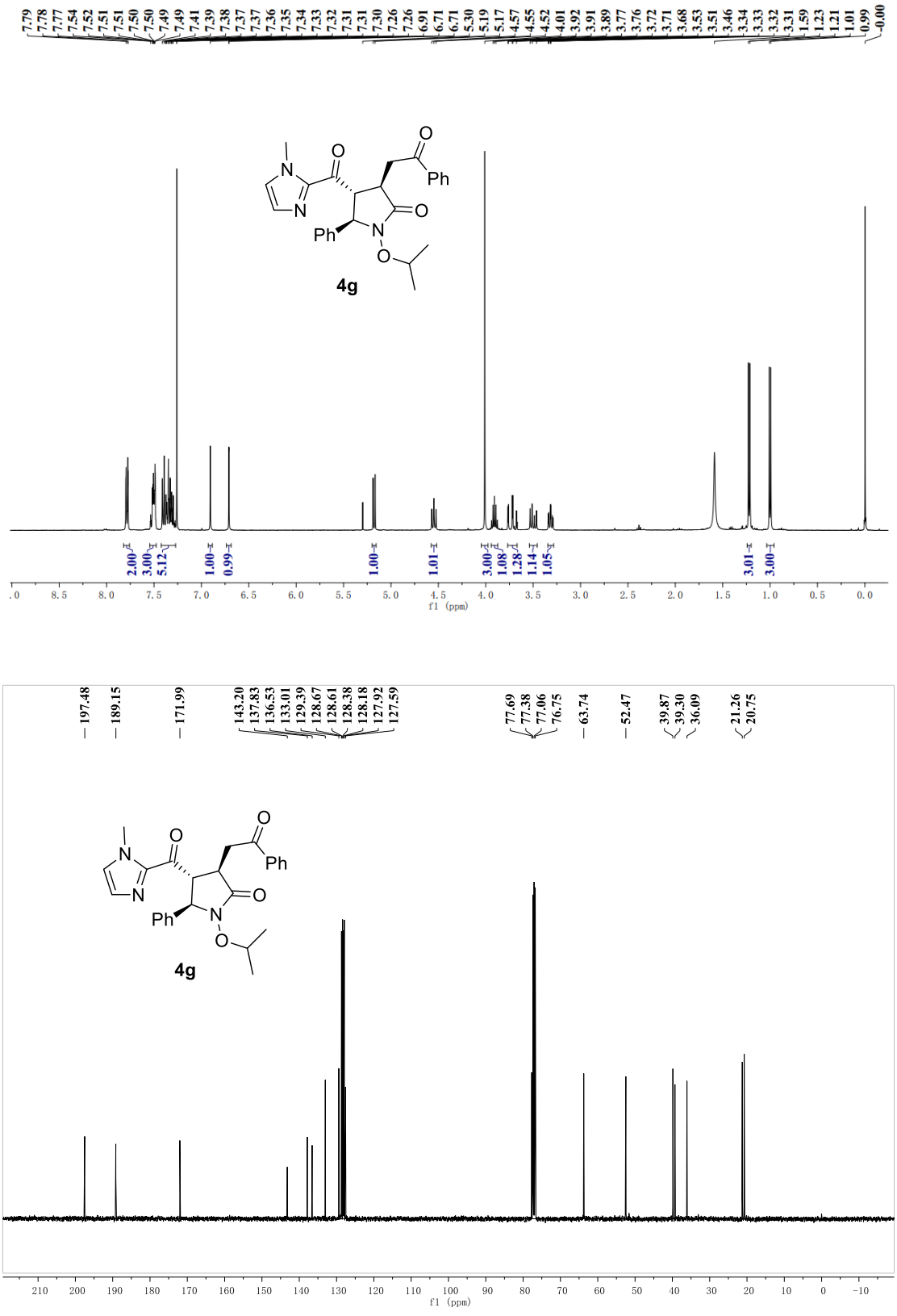


Figure S25. ^{1}H and ^{13}C NMR spectrum of **4g**.

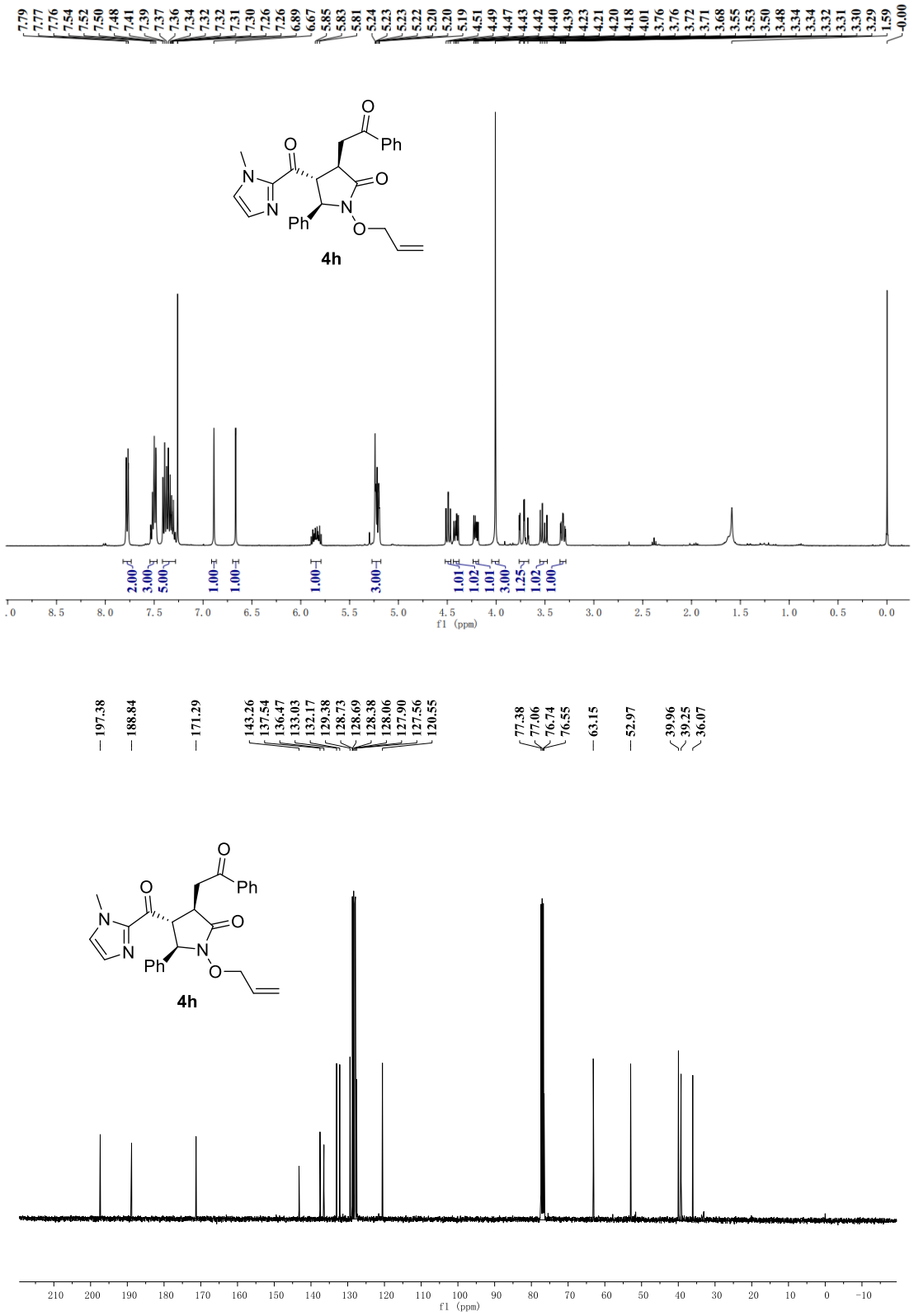


Figure S26. ^{1}H and ^{13}C NMR spectrum of **4h**.

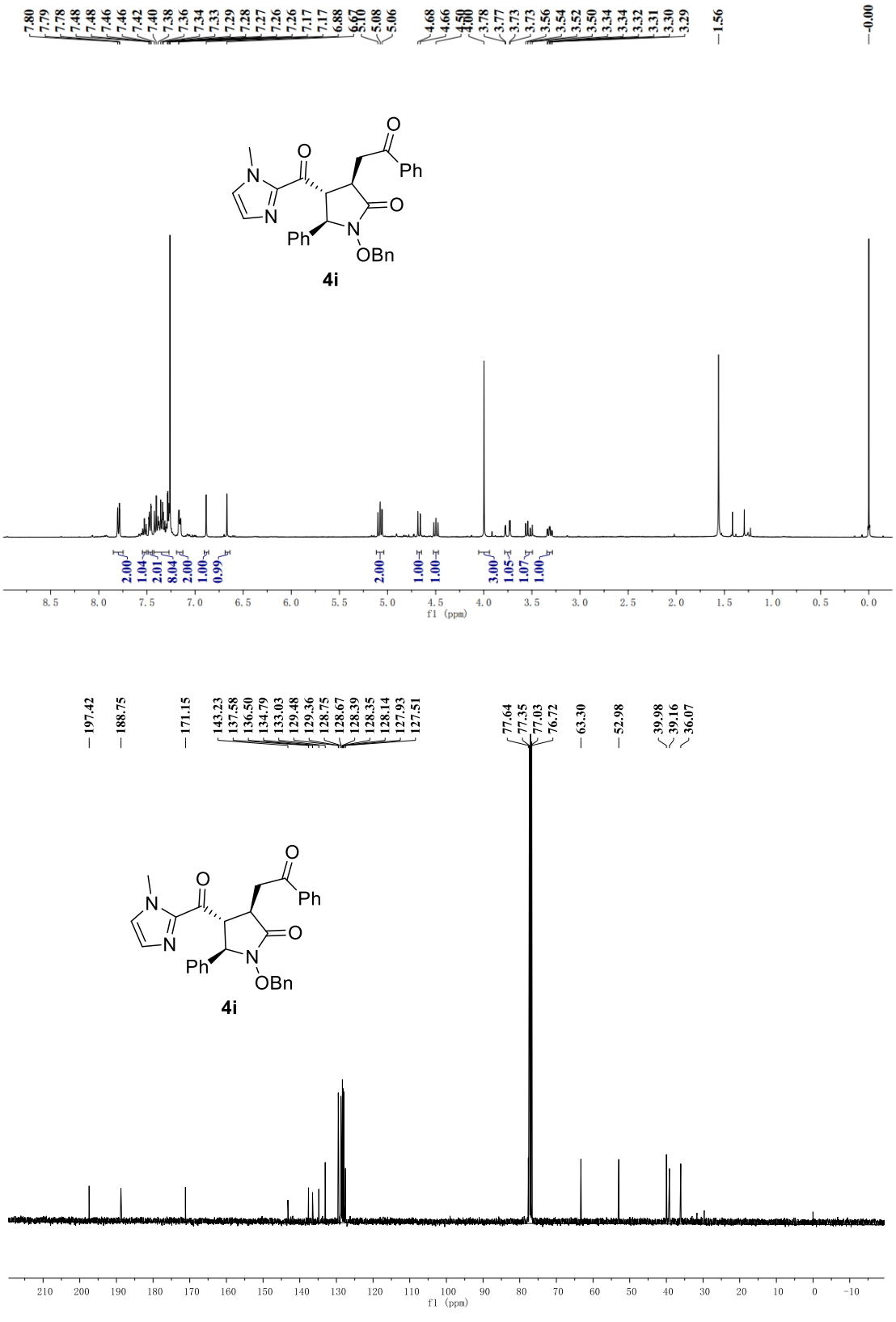


Figure S27. ^{1}H and ^{13}C NMR spectrum of **4i**.

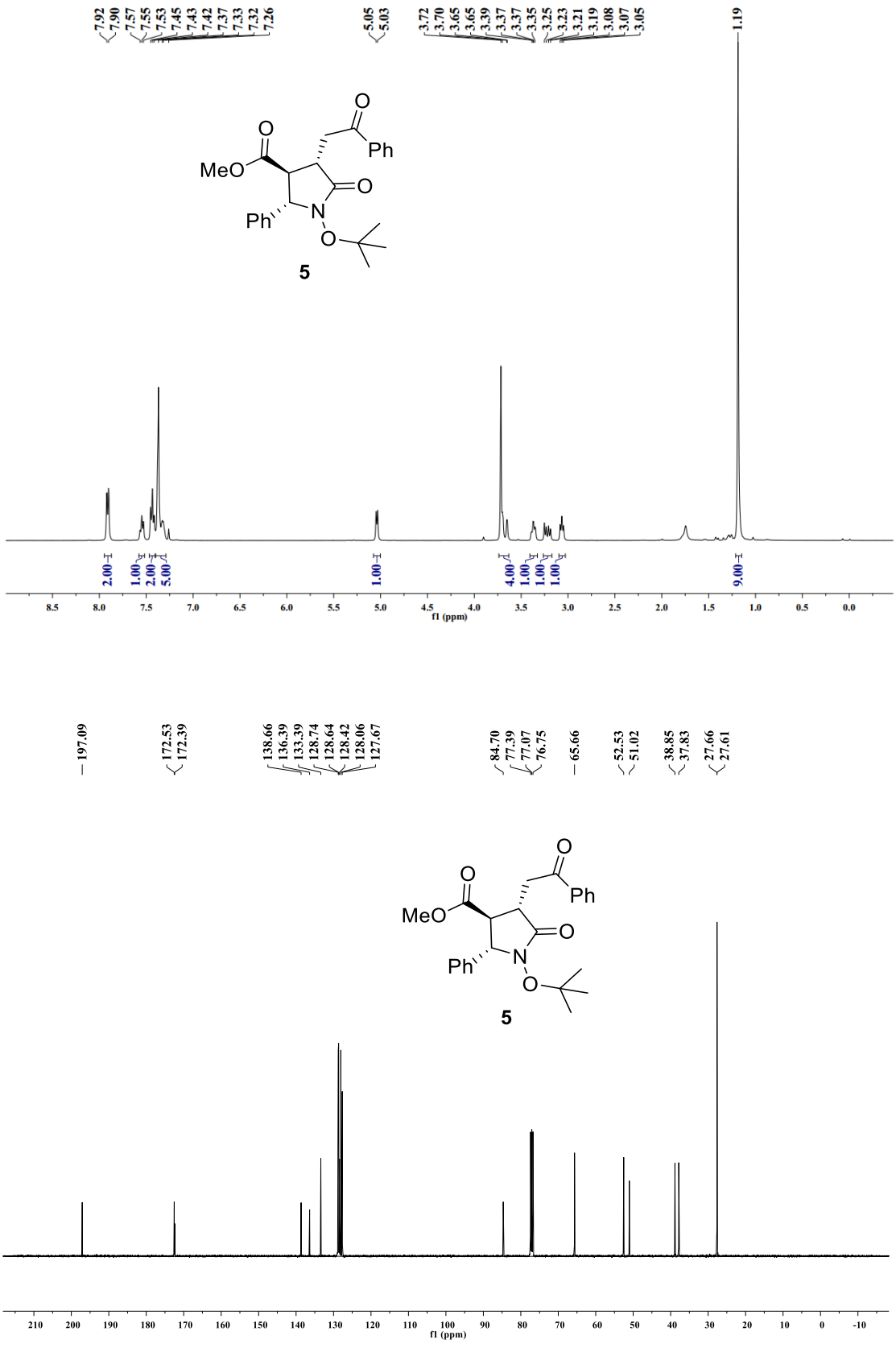
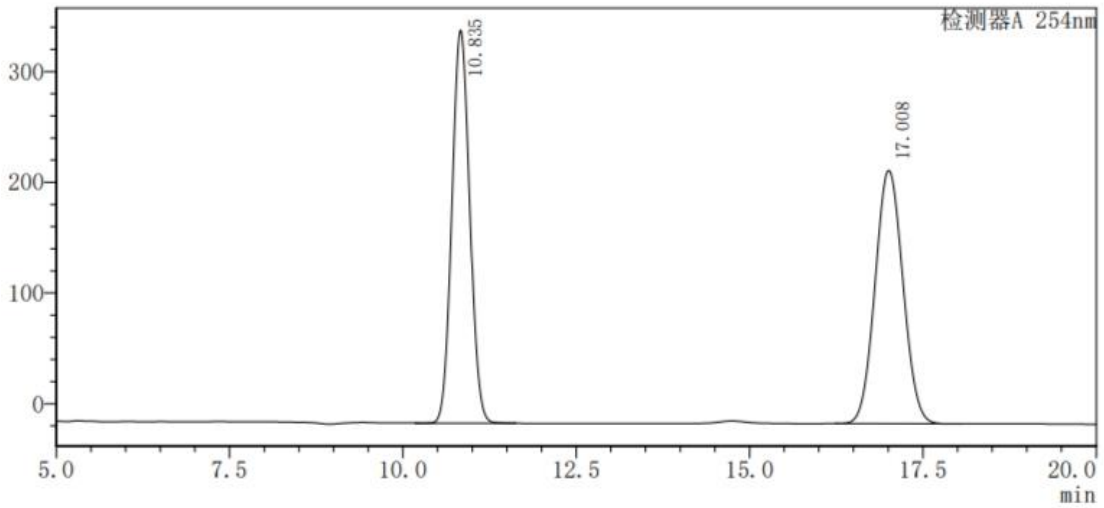


Figure S28. ^{1}H and ^{13}C NMR spectrum of **5**.

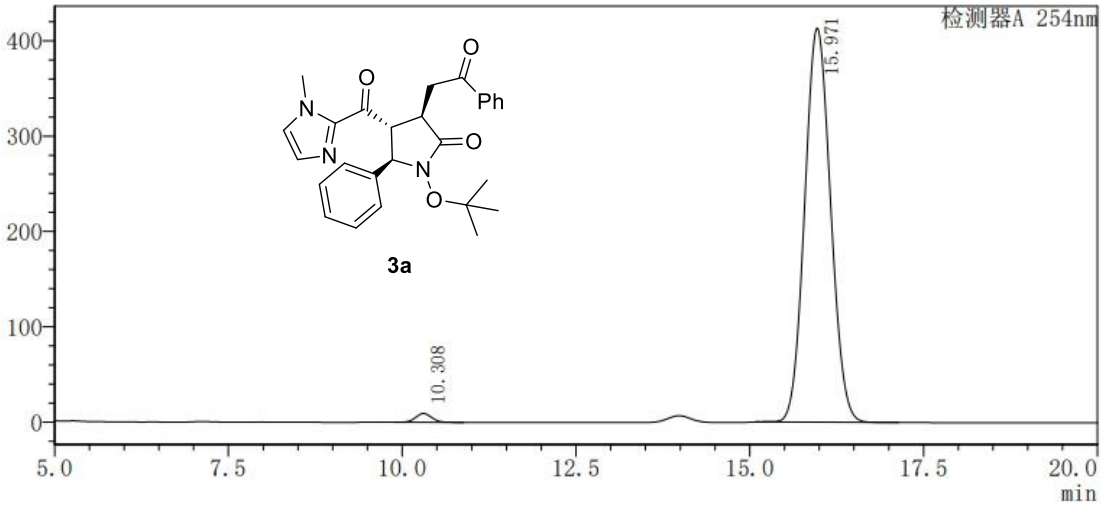
7. HPLC Traces on Chiral Stationary Phase



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.835	6318824	354965	49.853
2	17.008	6356151	228717	50.147
总计		12674974	583682	100.000



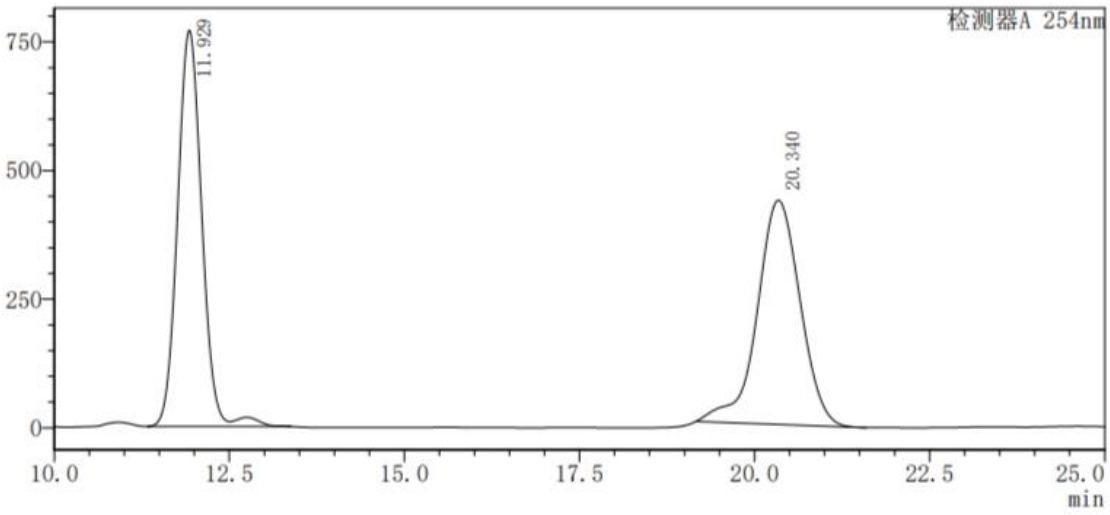
3a

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.308	148274	9199	1.364
2	15.971	10724884	413375	98.636
总计		10873158	422574	100.000

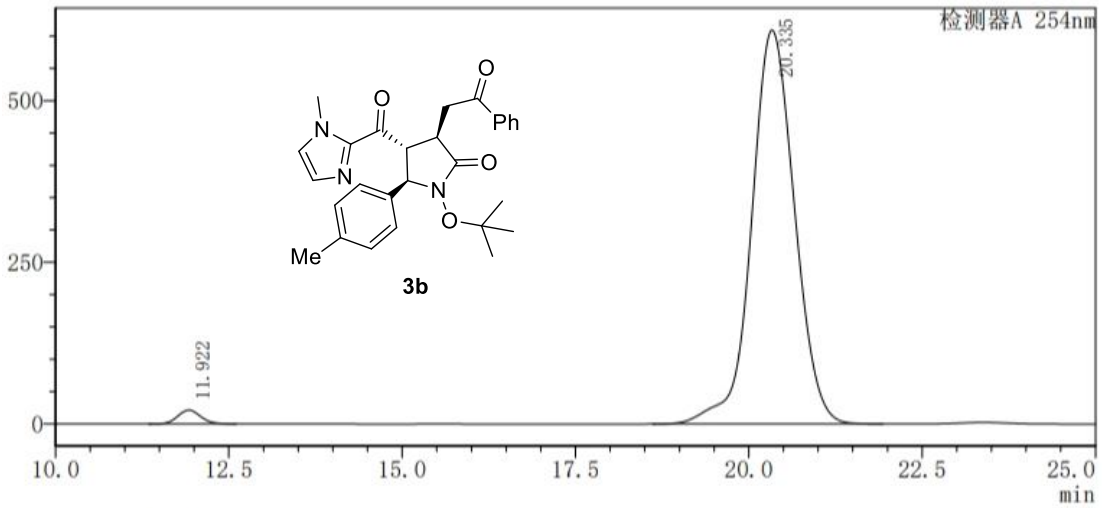
Figure S29. HPLC traces of racemic (reference) and chiral **3a**, Area integration = 98.6: 1.4 (97% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	11.929	18613649	770053	49.921
2	20.340	18672770	435964	50.079
总计		37286419	1206017	100.000



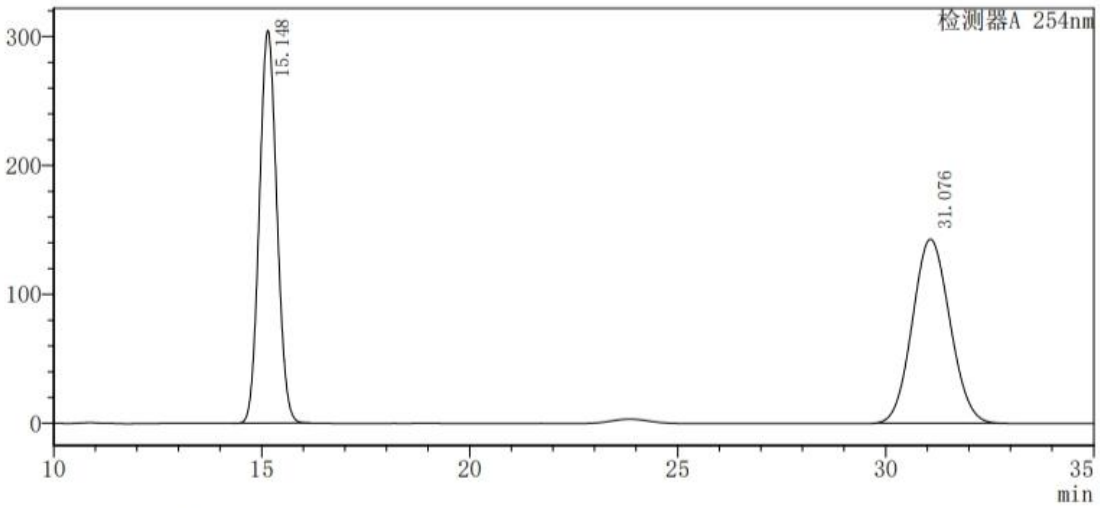
3b

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	11.922	492446	21405	1.837
2	20.335	26315230	609206	98.163
总计		26807677	630611	100.000

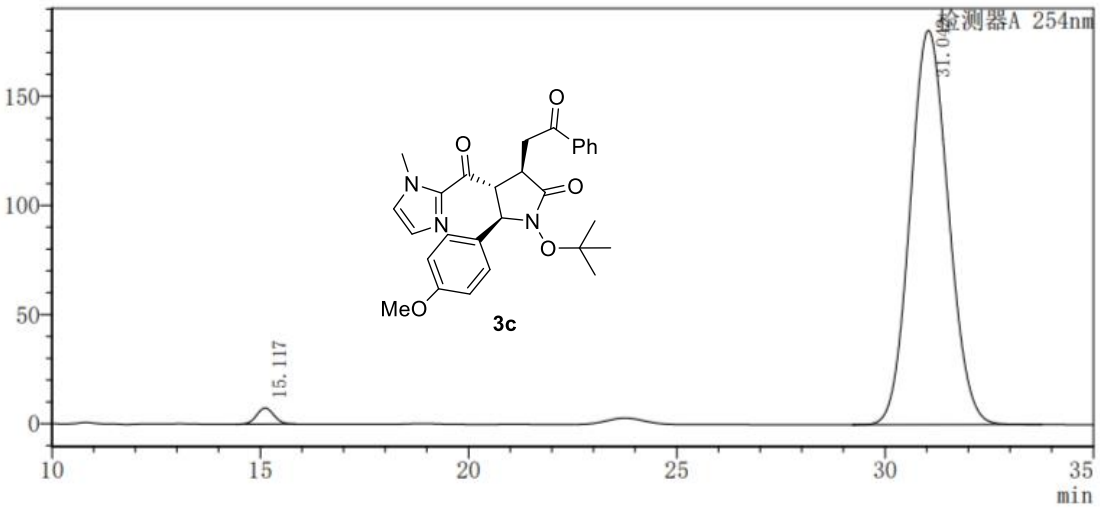
Figure S30. HPLC traces of racemic (reference) and chiral **3b**. Area integration = 98.1:1.9 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	15.148	8912056	304769	49.879
2	31.076	8955236	142823	50.121
总计		17867292	447592	100.000



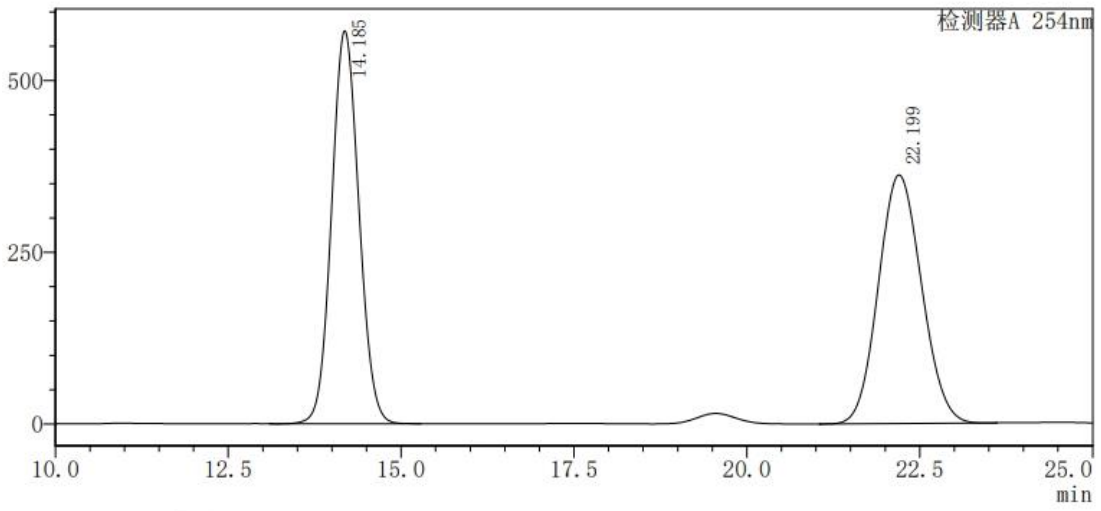
3c

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	15.117	211508	7367	1.807
2	31.042	11496183	180542	98.193
总计		11707691	187909	100.000

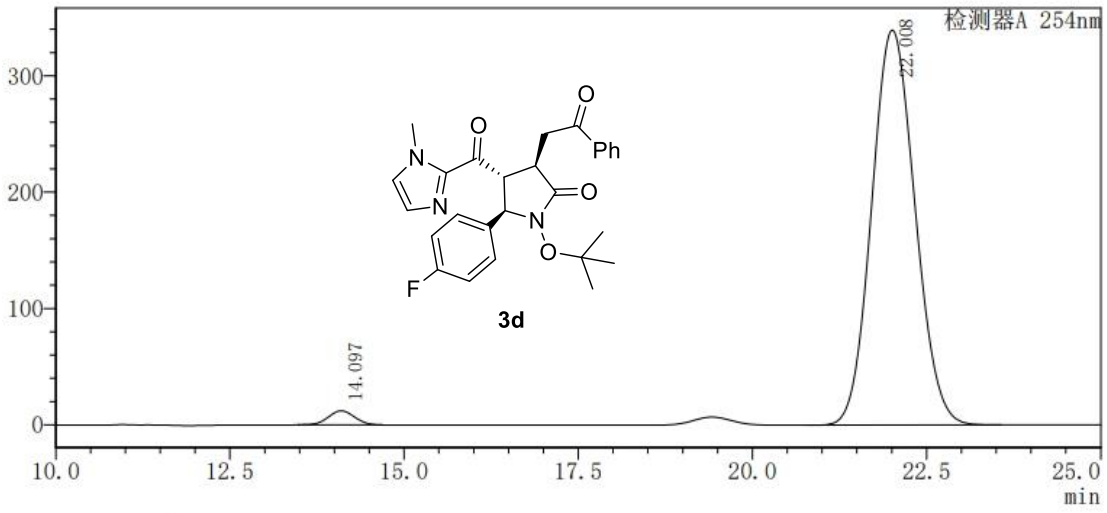
Figure S31. HPLC traces of racemic (reference) and chiral **3c**. Area integration = 98.2:1.8 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	14.185	15751226	572119	50.136
2	22.199	15665507	361818	49.864
总计		31416733	933937	100.000



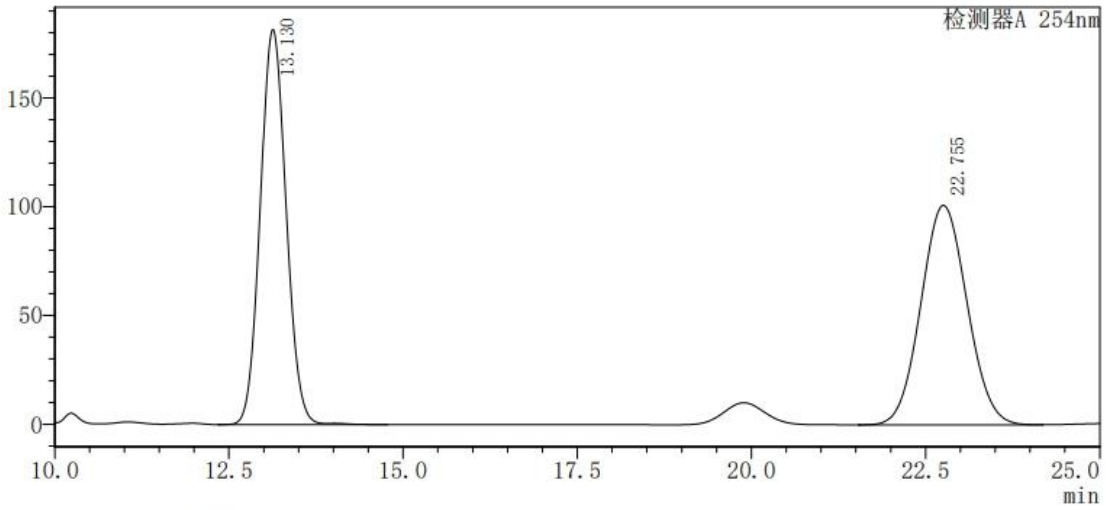
3d

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	14.097	319596	12107	2.138
2	22.008	14631125	339504	97.862
总计		14950721	351611	100.000

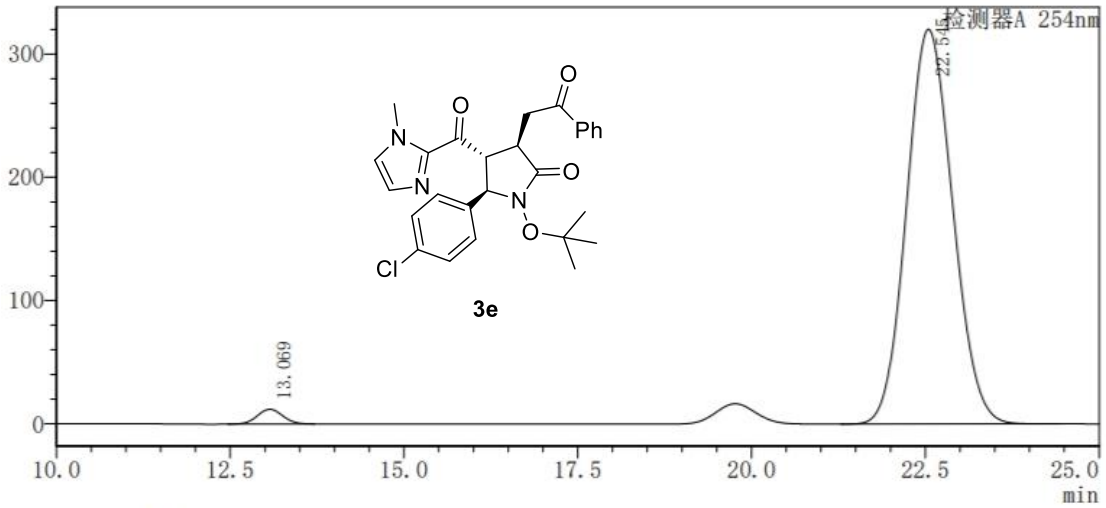
Figure S32. HPLC traces of racemic (reference) and chiral **3d**. Area integration = 97.9:2.1 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	13.130	4663797	181690	50.007
2	22.755	4662553	100927	49.993
总计		9326350	282617	100.000



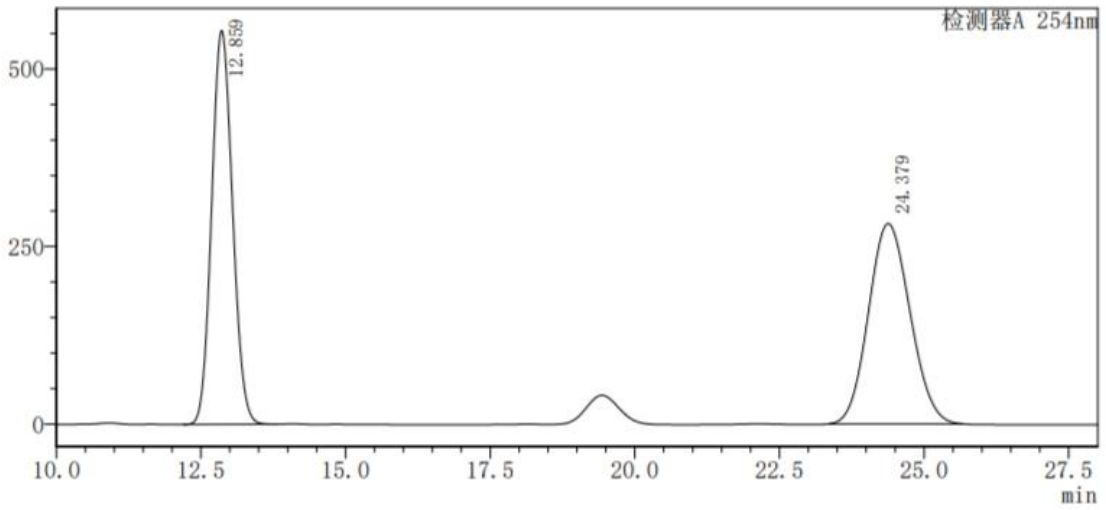
3e

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	13.069	301334	11975	1.998
2	22.545	14779547	320220	98.002
总计		15080880	332195	100.000

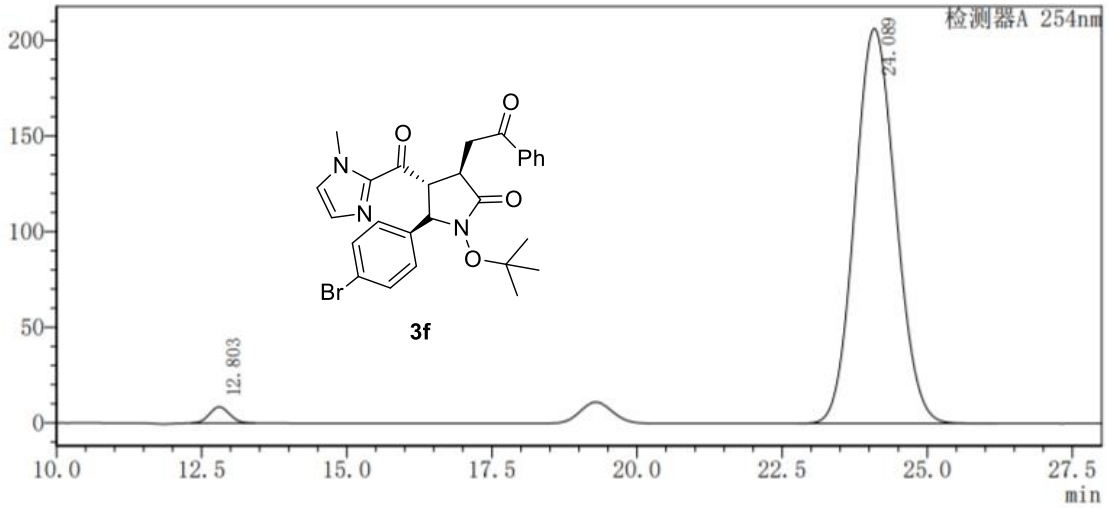
Figure S33. HPLC traces of racemic (reference) and chiral **3e**. Area integration = 98.0:2.0 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	12.859	13929652	554398	49.738
2	24.379	14076270	281717	50.262
总计		28005921	836115	100.000



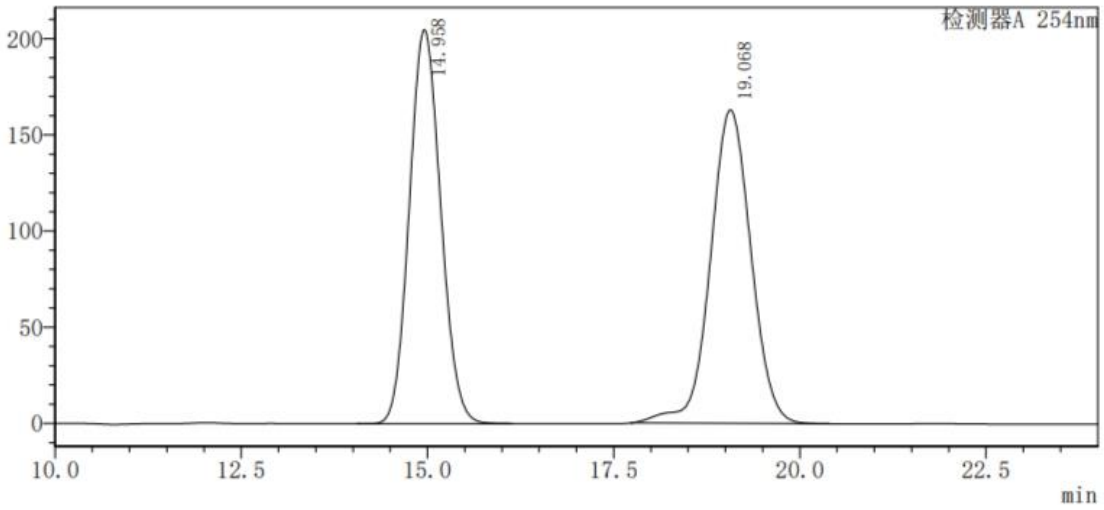
3f

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	12.803	205187	8452	1.989
2	24.089	10108930	206484	98.011
总计		10314118	214935	100.000

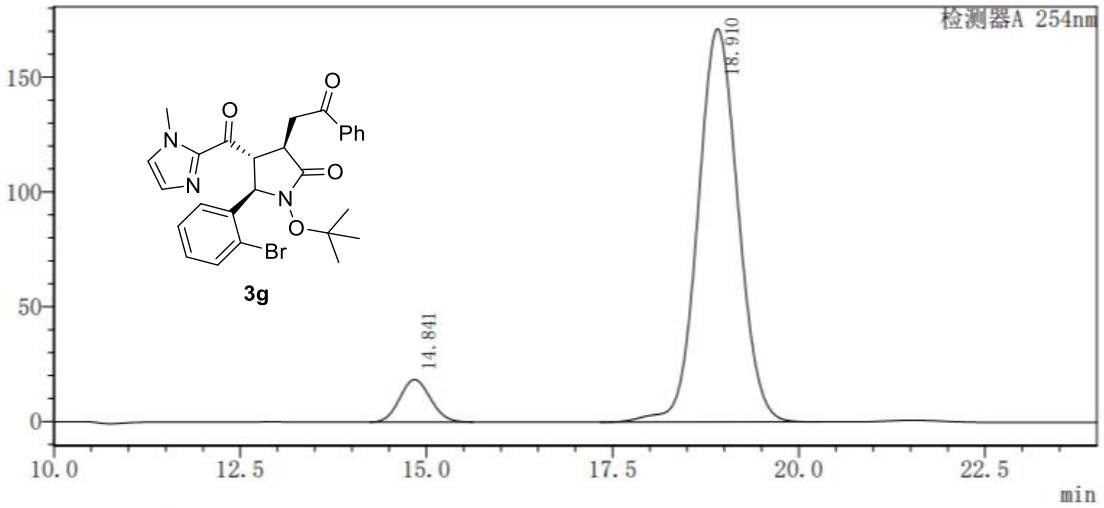
Figure S34. HPLC traces of racemic (reference) and chiral **3f**. Area integration = 98.0:2.0 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	14.958	6009167	204796	49.238
2	19.068	6195179	162943	50.762
总计		12204346	367738	100.000



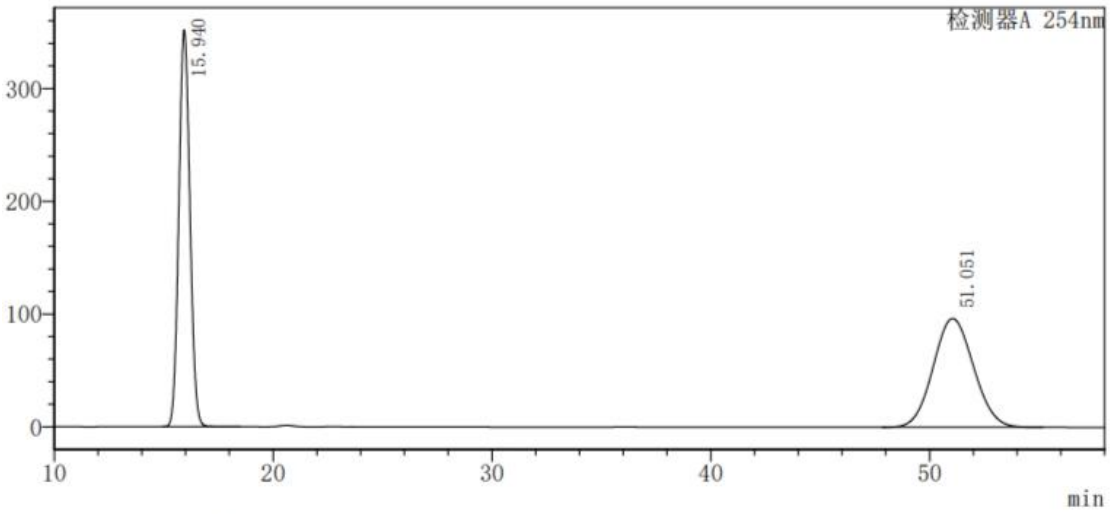
3g

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	14.841	531796	18502	7.640
2	18.910	6429115	171286	92.360
总计		6960911	189787	100.000

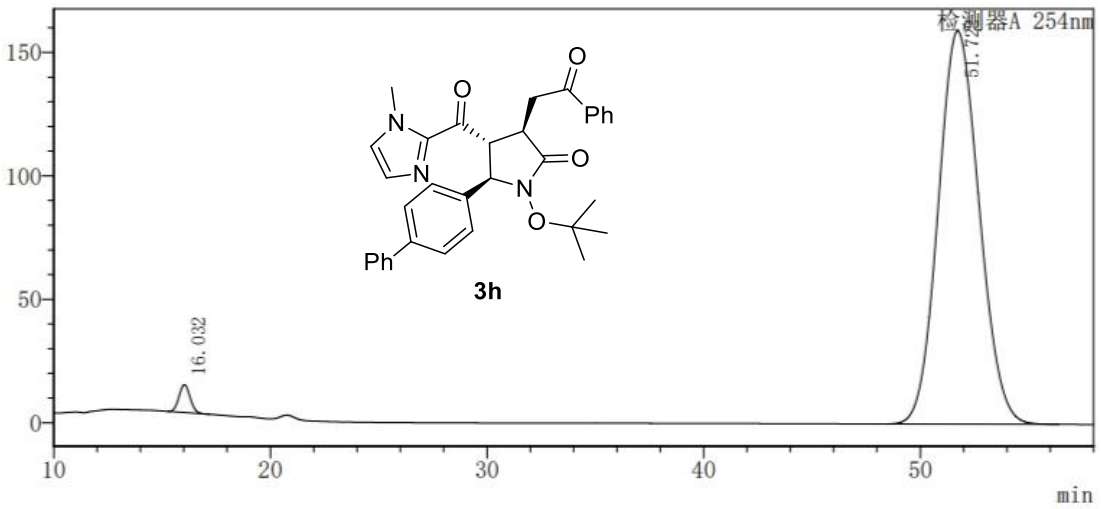
Figure S35. HPLC traces of racemic (reference) and chiral **3g**. Area integration = 92.4:7.6 (85% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	15.940	12378718	351925	49.978
2	51.051	12389705	96473	50.022
总计		24768424	448399	100.000



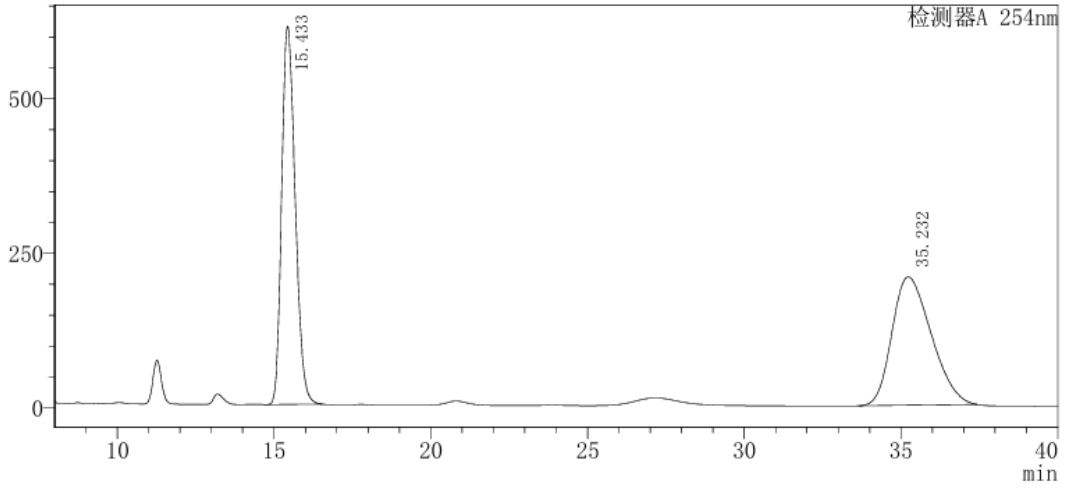
3h

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	16.032	401089	11262	1.879
2	51.722	20941338	159280	98.121
总计		21342426	170542	100.000

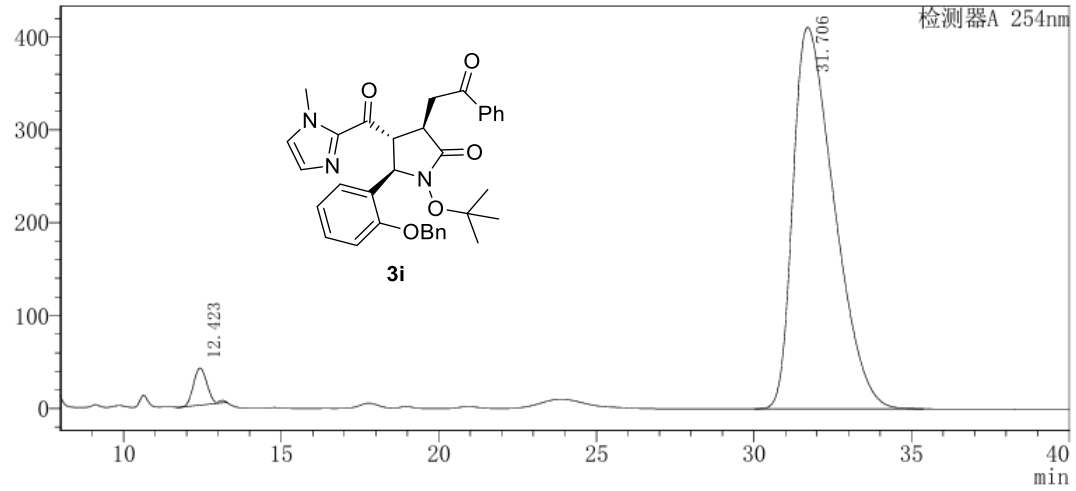
Figure S36. HPLC traces of racemic (reference) and chiral **3h**. Area integration = 98.1:1.9 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	15.433	18340084	611749	50.396
2	35.232	18051733	207535	49.604
总计		36391817	819284	100.000



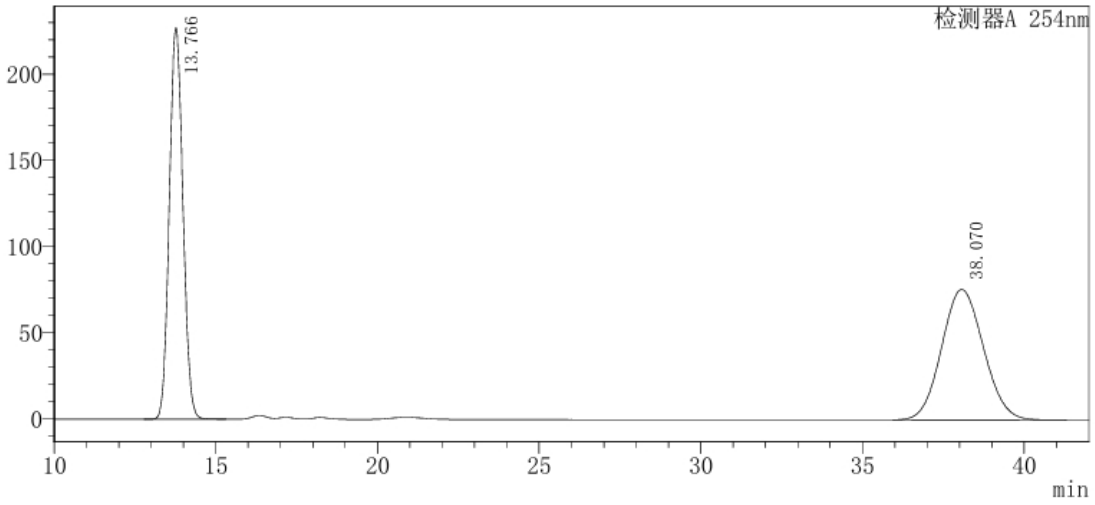
3i

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	12.423	1206043	39844	3.132
2	31.706	37295663	410876	96.868
总计		38501707	450720	100.000

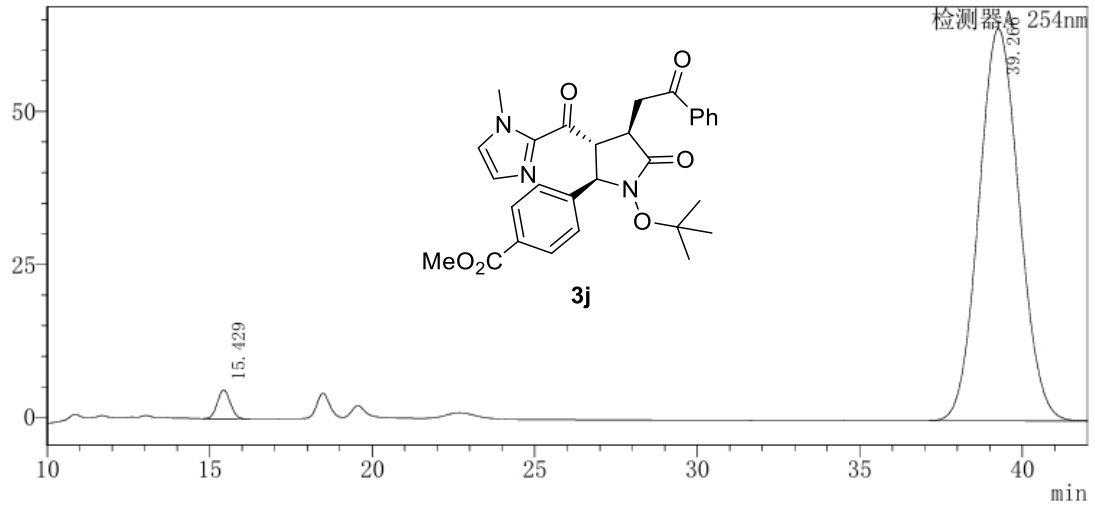
Figure S37. HPLC traces of racemic (reference) and chiral **3i**. Area integration = 96.9:3.1 (94% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	13.766	6642538	227011	49.377
2	38.070	6810067	75667	50.623
总计		13452605	302678	100.000



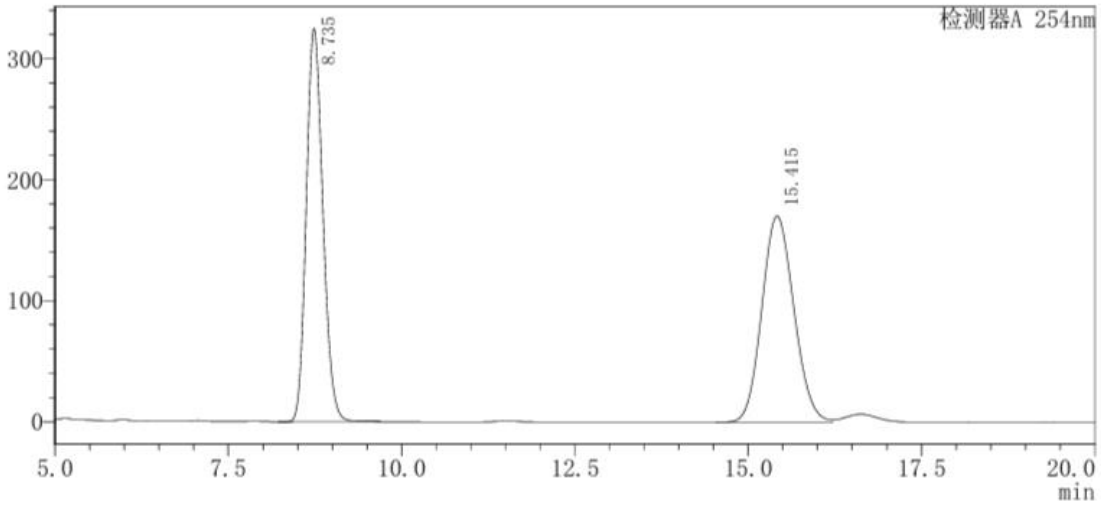
3j

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	15.429	130857	4699	2.309
2	39.266	5537514	64056	97.691
总计		5668371	68755	100.000

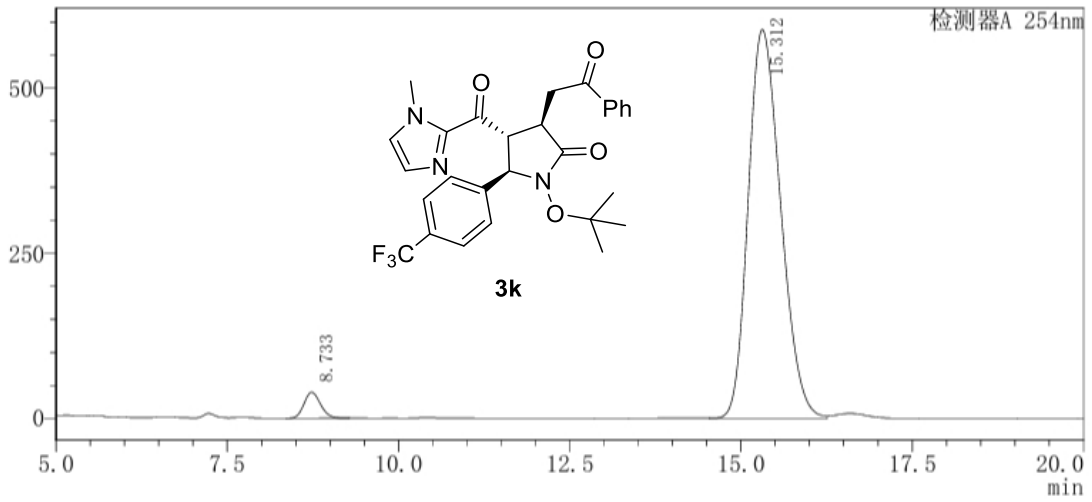
Figure S38. HPLC traces of racemic (reference) and chiral **3j**. Area integration = 97.7:2.3 (95% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	8.735	5435124	325148	49.775
2	15.415	5484237	170478	50.225
总计		10919361	495626	100.000

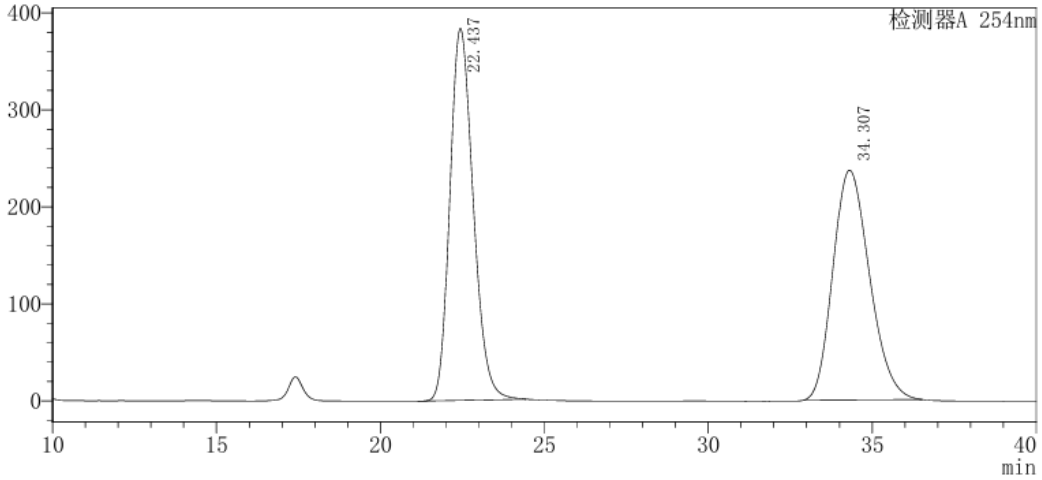


〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	8.733	656708	39378	3.264
2	15.312	19461717	588647	96.736
总计		20118426	628025	100.000

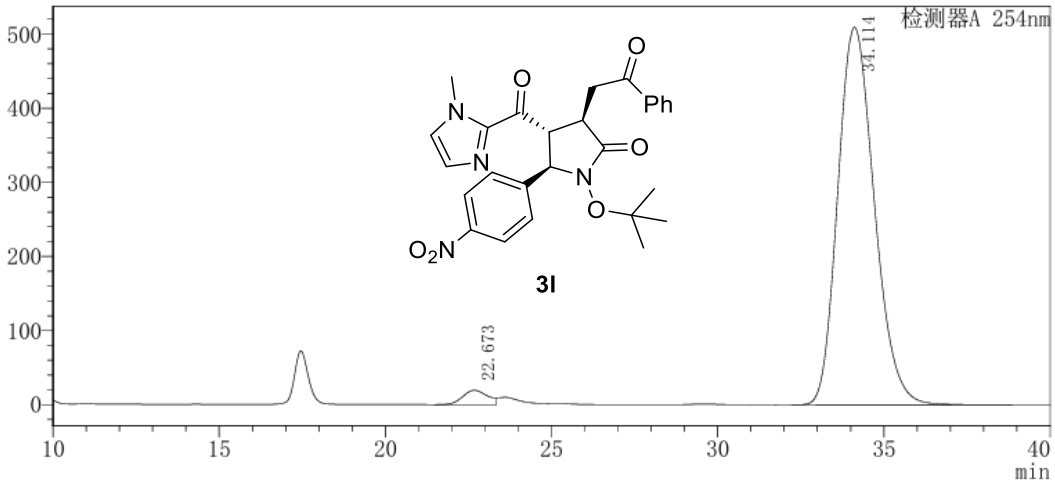
Figure S39. HPLC traces of racemic (reference) and chiral **3k**. Area integration = 96.7:3.3 (93% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	22.437	18937409	383187	50.814
2	34.307	18330893	236724	49.186
总计		37268302	619912	100.000



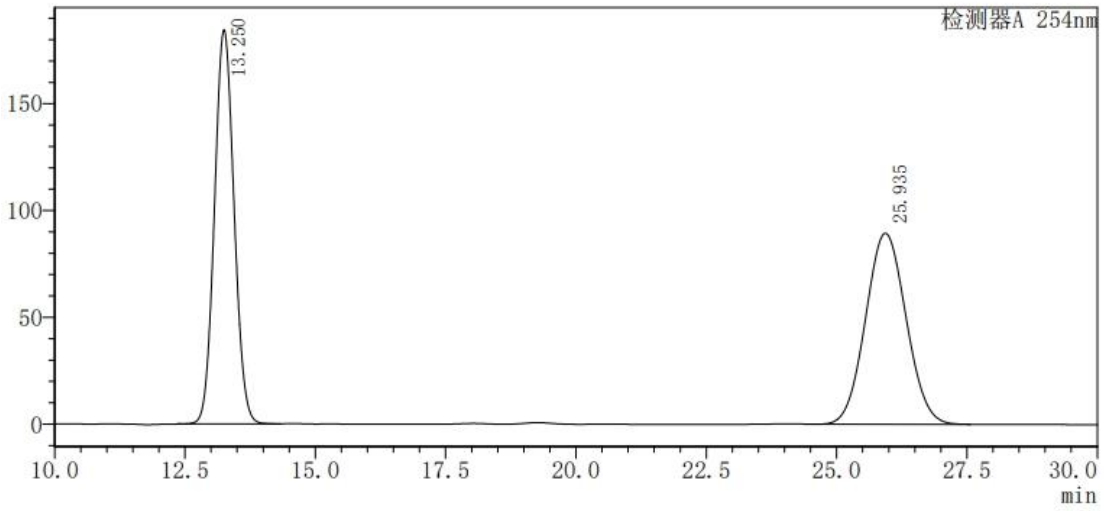
3l

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	22.673	1007612	19376	2.533
2	34.114	38771400	509319	97.467
总计		39779012	528695	100.000

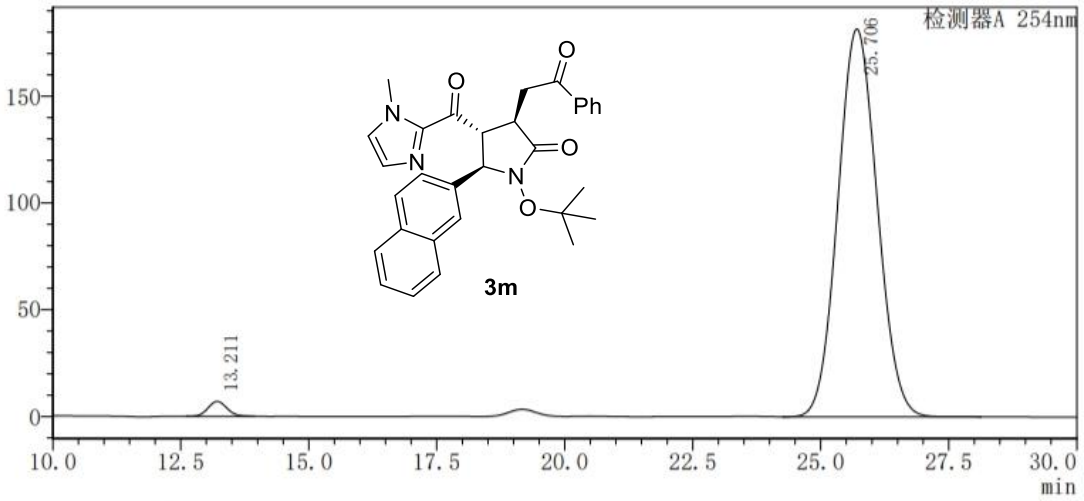
Figure S40. HPLC traces of racemic (reference) and chiral **3l**. Area integration = 97.5:2.5 (95% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	13.250	4829362	184605	50.017
2	25.935	4826083	89409	49.983
总计		9655445	274014	100.000



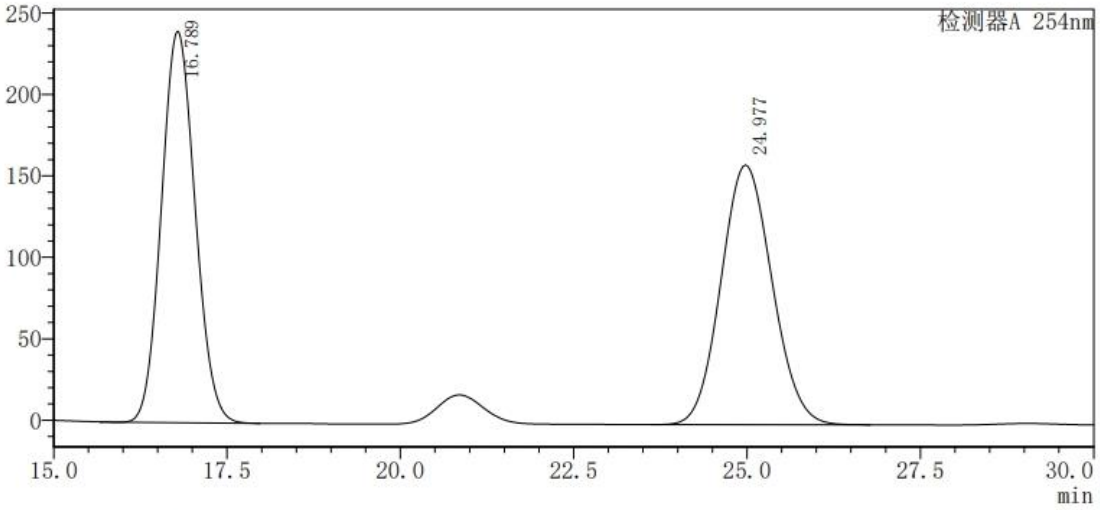
3m

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	13.211	178807	6955	1.809
2	25.706	9703693	181684	98.191
总计		9882501	188640	100.000

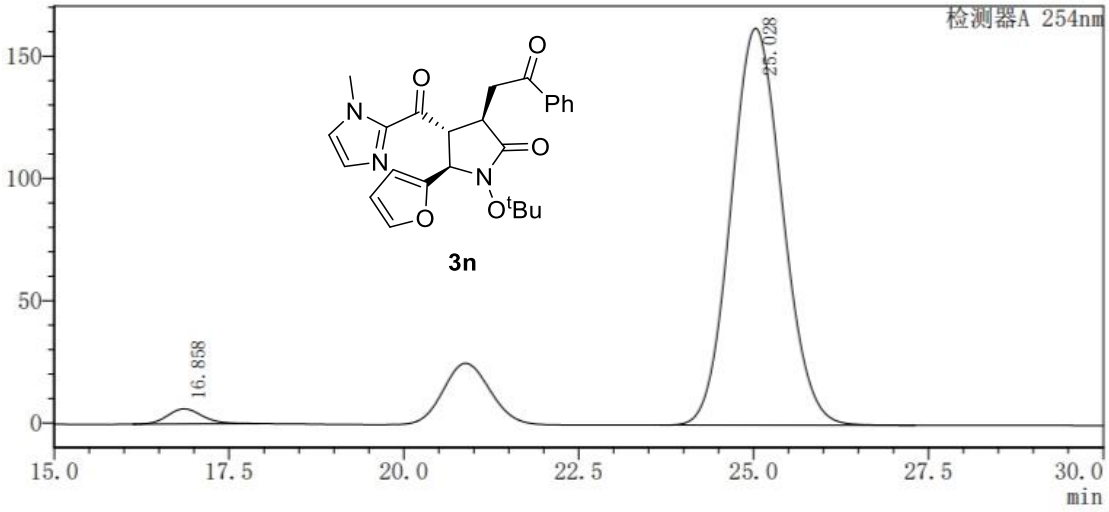
Figure S41. HPLC traces of racemic (reference) and chiral **3m**. Area integration = 98.2:1.8 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	16.789	8135826	240259	49.851
2	24.977	8184548	159326	50.149
总计		16320374	399585	100.000



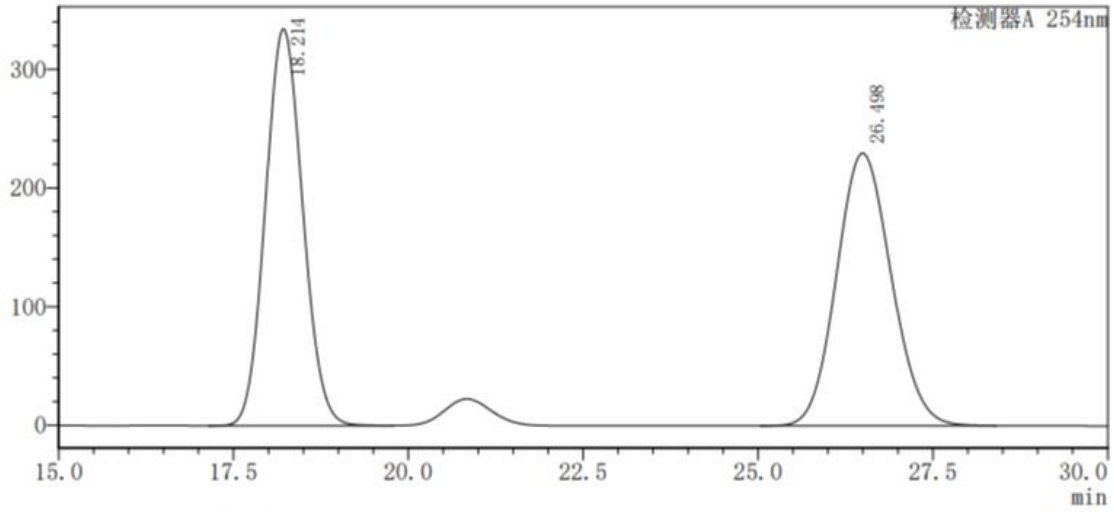
3n

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	16.858	214564	6170	2.512
2	25.028	8325903	162204	97.488
总计		8540467	168374	100.000

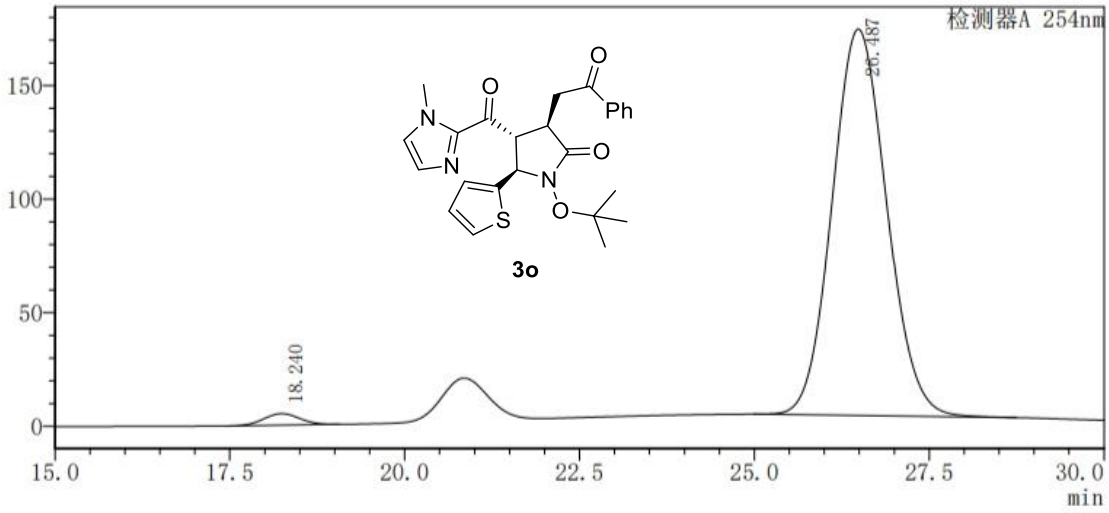
Figure S42. HPLC traces of racemic (reference) and chiral **3n**. Area integration = 2.5:97.5 (95% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	18.214	12398747	334421	49.811
2	26.498	12492770	229704	50.189
总计		24891518	564125	100.000



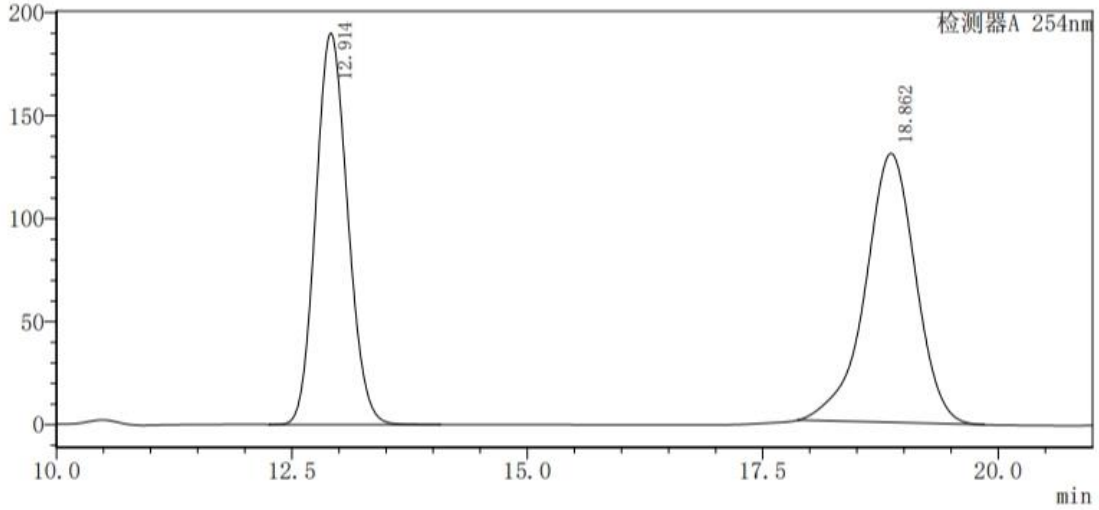
3o

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	18.240	181918	5092	1.931
2	26.487	9241004	170202	98.069
总计		9422922	175293	100.000

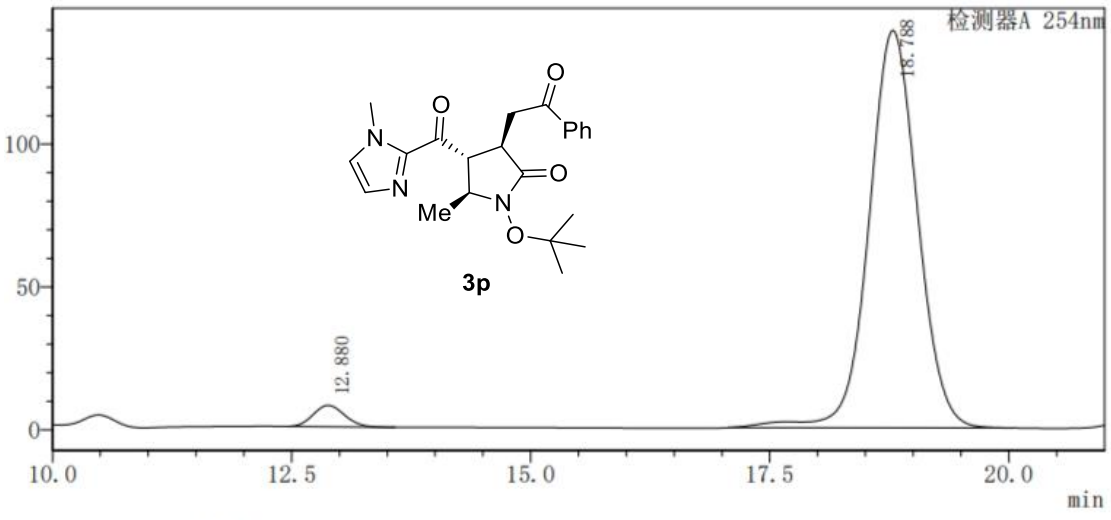
Figure S43. HPLC traces of racemic (reference) and chiral **3o**. Area integration =98.0:2.0 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	12.914	4476348	189967	47.961
2	18.862	4856922	130539	52.039
总计		9333270	320506	100.000



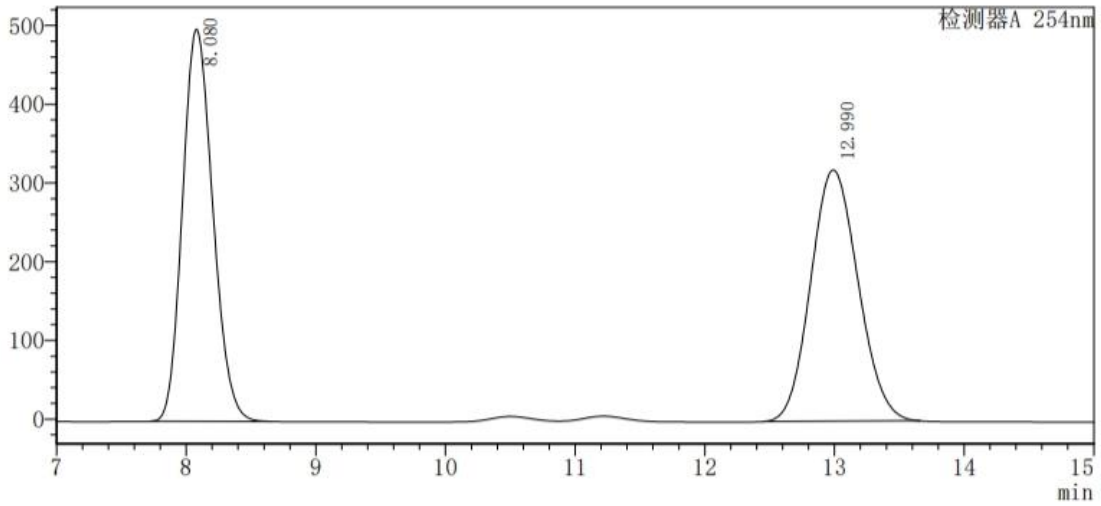
3p

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	12.880	170250	7488	3.339
2	18.788	4929137	139089	96.661
总计		5099387	146577	100.000

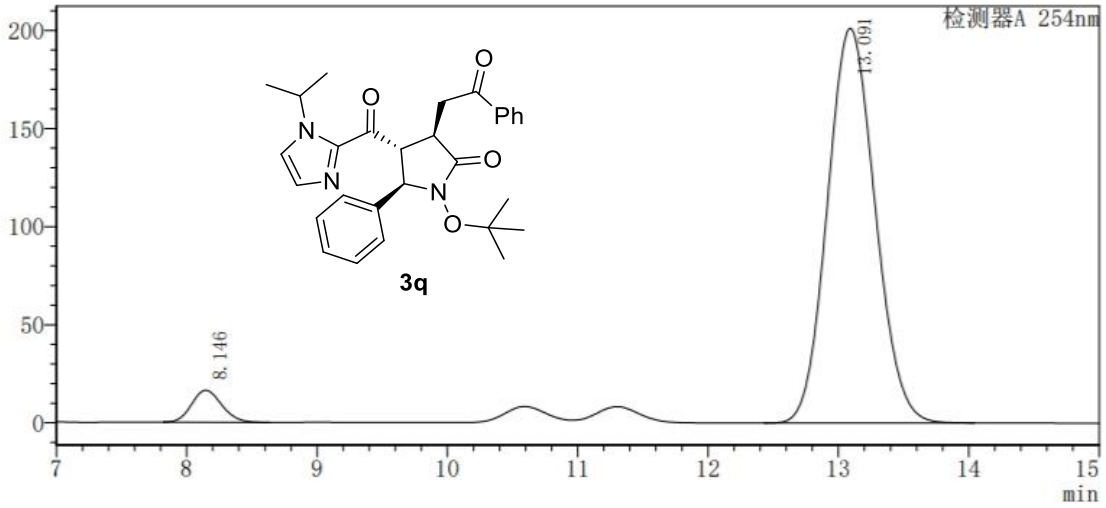
Figure S44. HPLC traces of racemic (reference) and chiral **3p**. Area integration =96.7: 3.3 (93% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	8.080	8104440	498145	49.958
2	12.990	8118215	319272	50.042
总计		16222655	817416	100.000



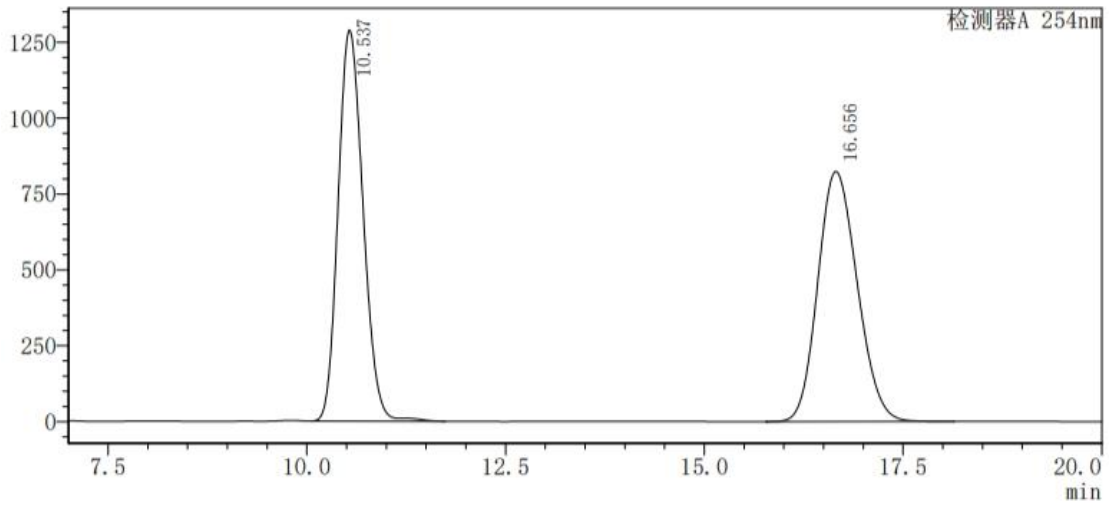
3q

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	8.146	262026	16320	4.872
2	13.091	5116534	201184	95.128
总计		5378560	217504	100.000

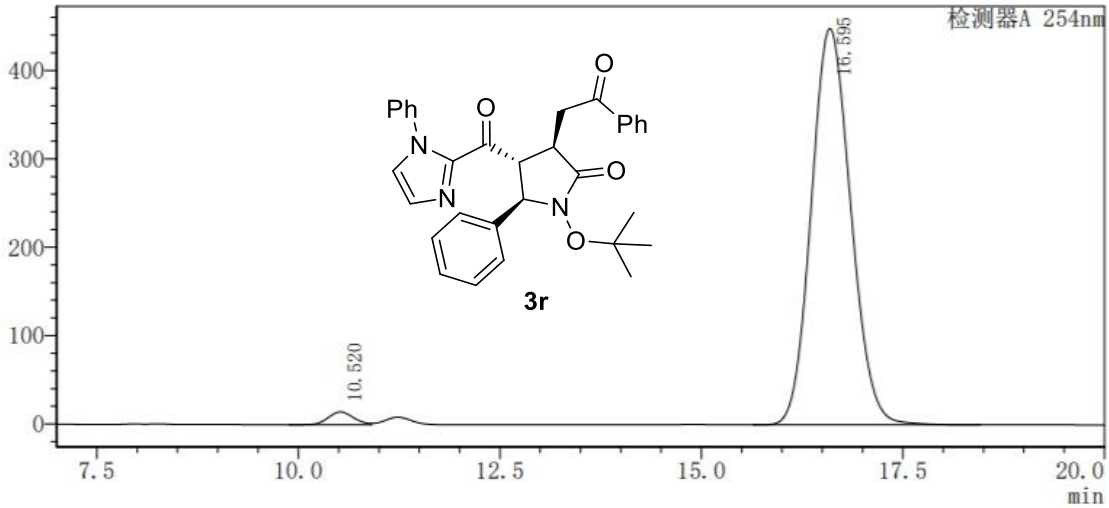
Figure S45. HPLC traces of racemic (reference) and chiral **3q**. Area integration = 95.1:4.9 (90% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.537	28171217	1288945	49.736
2	16.656	28470233	824426	50.264
总计		56641450	2113371	100.000



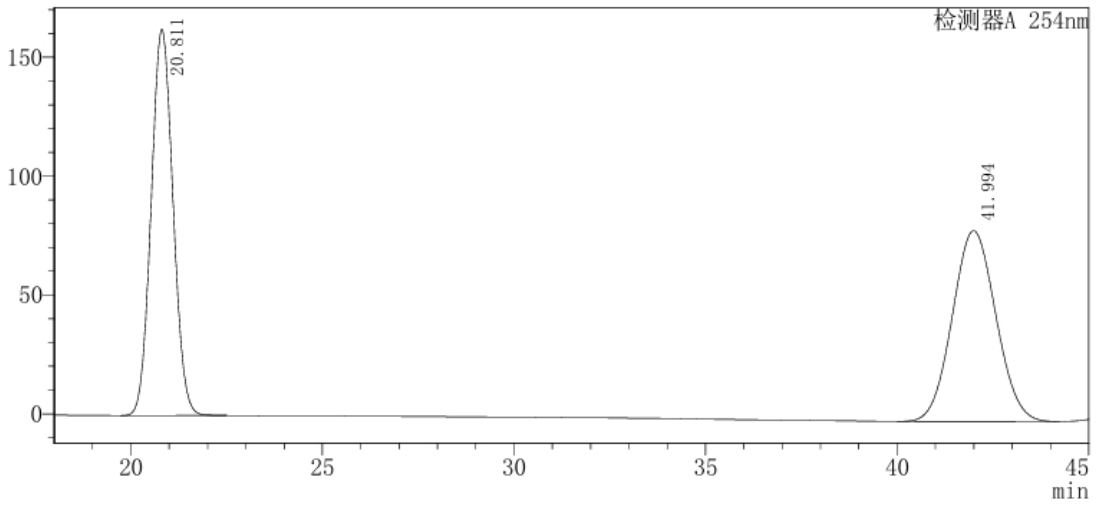
3r

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.520	320702	14551	2.054
2	16.595	15295362	448474	97.946
总计		15616064	463024	100.000

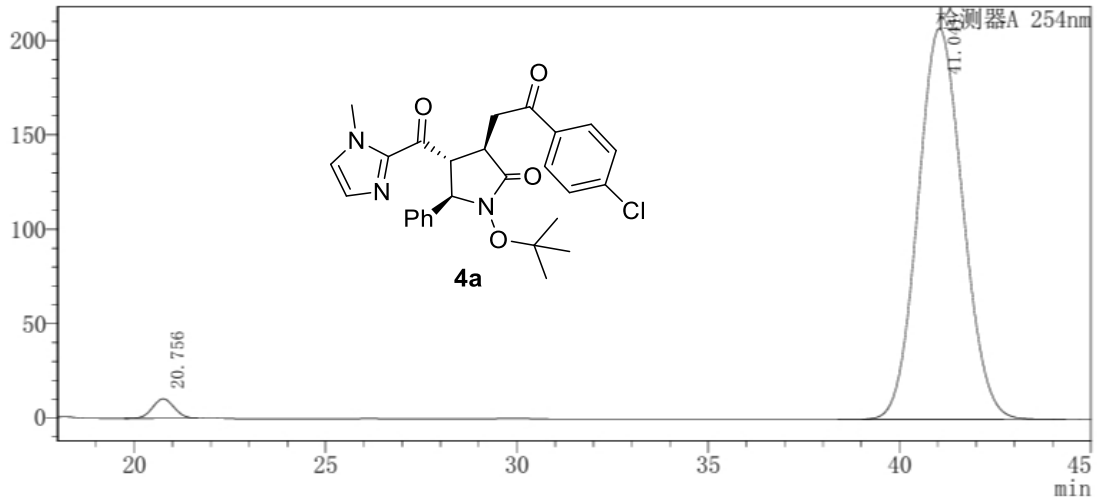
Figure S46. HPLC traces of racemic (reference) and chiral **3r**. Area integration = 97.9:2.1 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	20.811	6439613	162397	50.388
2	41.994	6340559	80255	49.612
总计		12780171	242652	100.000

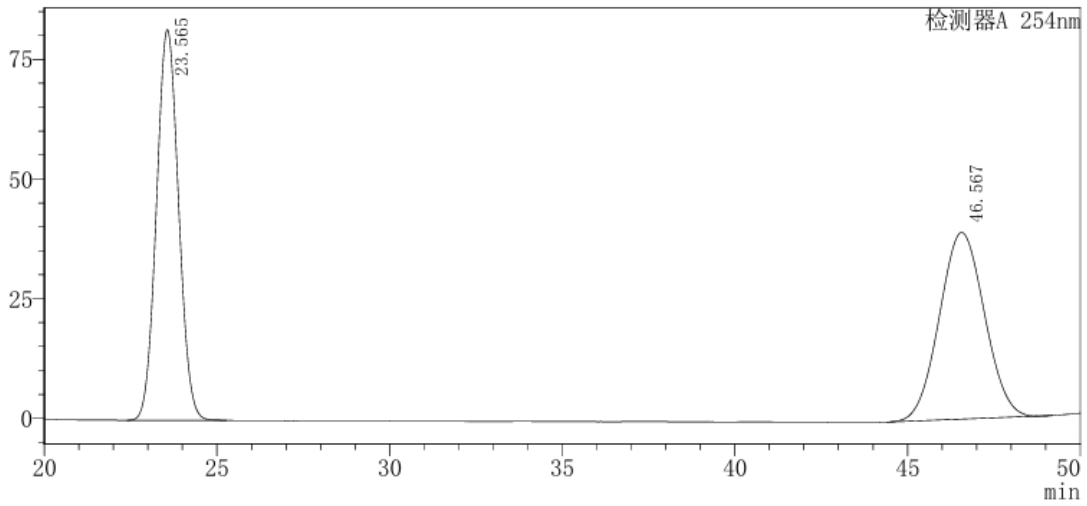


〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	20.756	403937	10328	2.341
2	41.041	16851098	207089	97.659
总计		17255035	217417	100.000

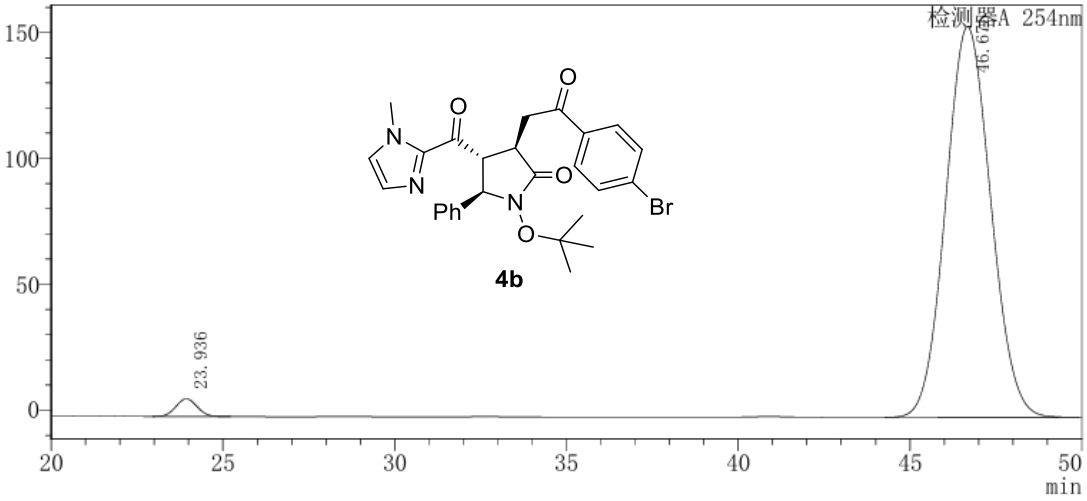
Figure S47. HPLC traces of racemic (reference) and chiral **4a**. Area integration = 2.3:97.7 (95% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	23.565	3646745	81673	50.700
2	46.567	3545979	39025	49.300
总计		7192724	120698	100.000



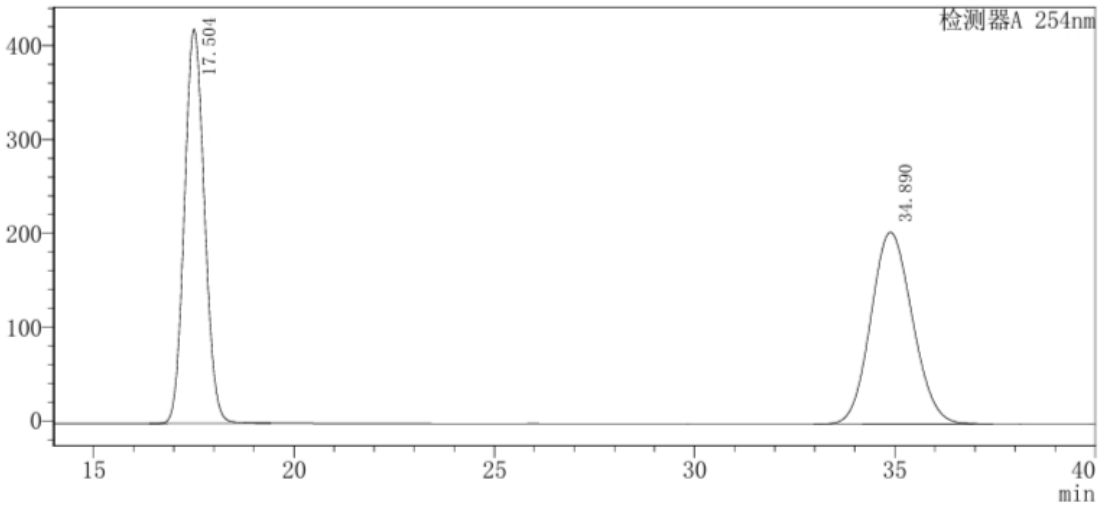
4b

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	23.936	303535	7027	2.097
2	46.675	14168759	155138	97.903
总计		14472295	162166	100.000

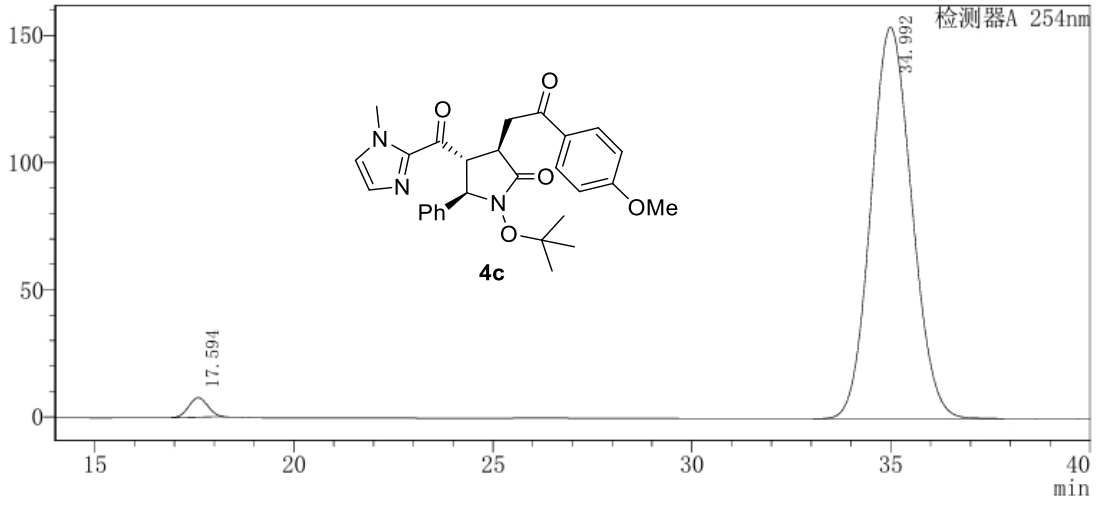
Figure S48. HPLC traces of racemic (reference) and chiral **4b**. Area integration = 97.9: 2.1 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	17.504	14597665	419769	49.824
2	34.890	14701037	204177	50.176
总计		29298702	623946	100.000



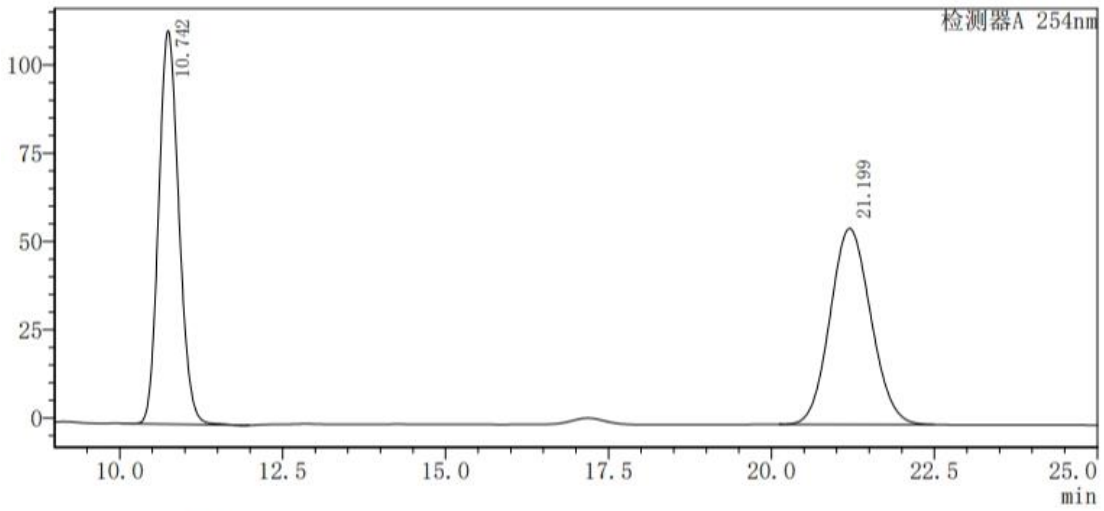
4c

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	17.594	250943	7594	2.234
2	34.992	10981528	153901	97.766
总计		11232471	161495	100.000

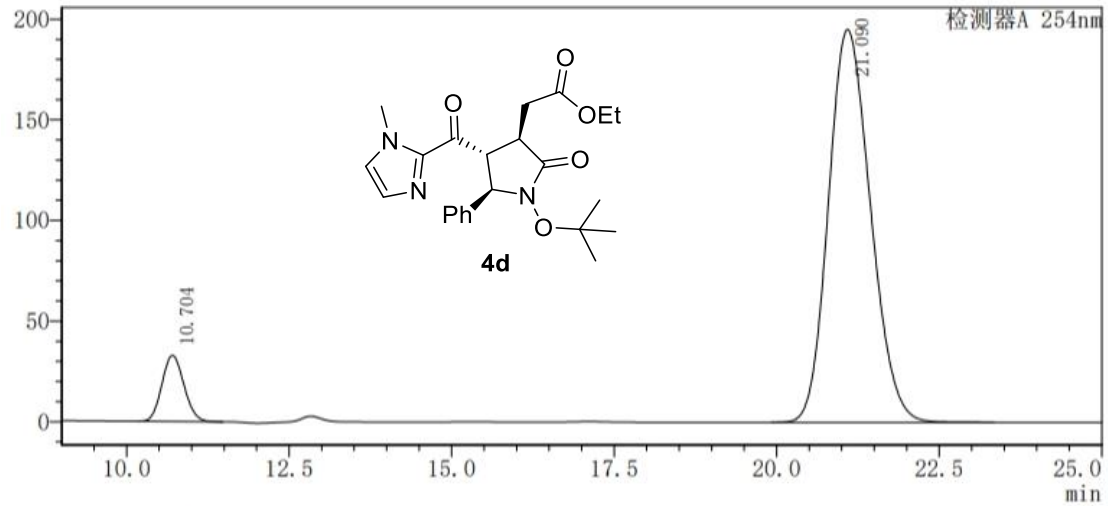
Figure S49. HPLC traces of racemic (reference) and chiral **4c.** Area integration = 97.8:2.2 (96% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.742	2406088	111483	49.876
2	21.199	2418013	55538	50.124
总计		4824102	167021	100.000



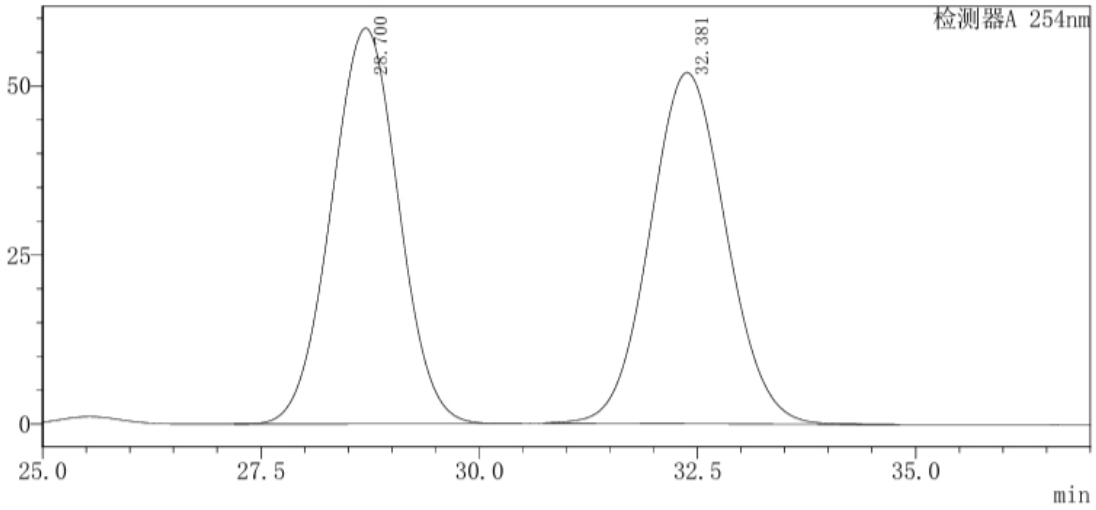
4d

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	10.704	776654	32848	8.124
2	21.090	8783532	195197	91.876
总计		9560186	228045	100.000

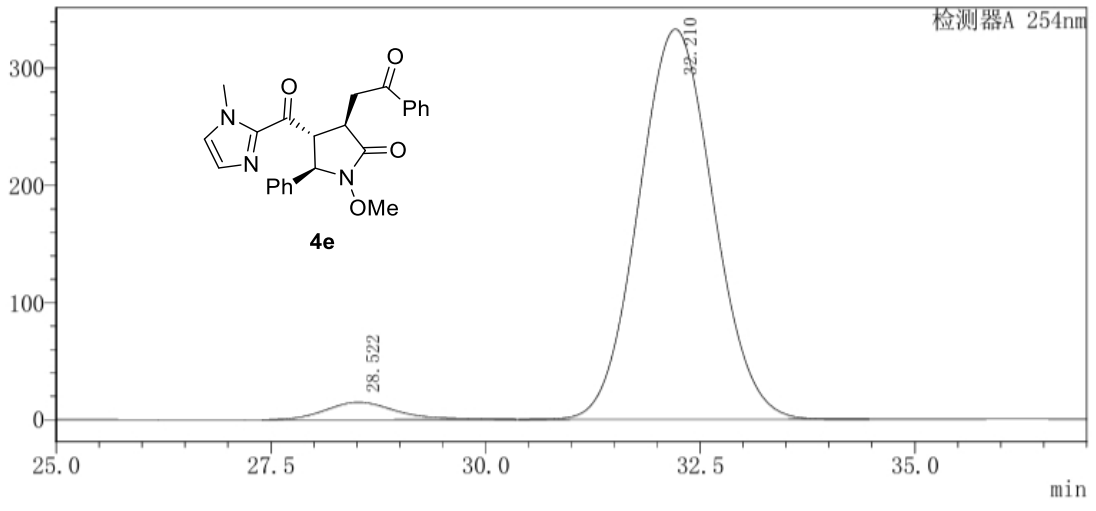
Figure S50. HPLC traces of racemic (reference) and chiral **4d**. Area integration =8.1:91.9 (84% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	28.700	3146508	58557	49.920
2	32.381	3156594	51926	50.080
总计		6303102	110482	100.000

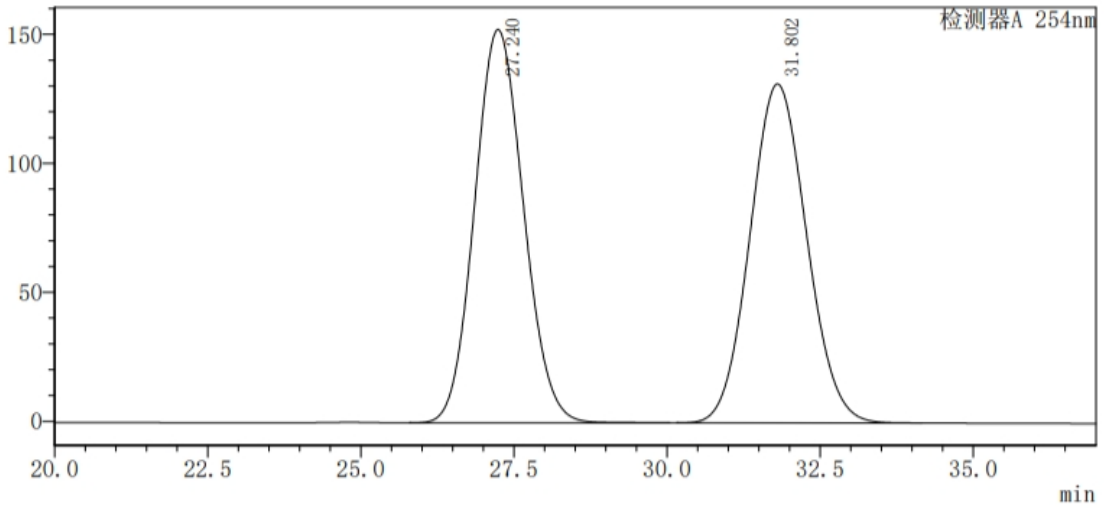


〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	28.522	850127	14786	4.038
2	32.210	20205580	333120	95.962
总计		21055707	347906	100.000

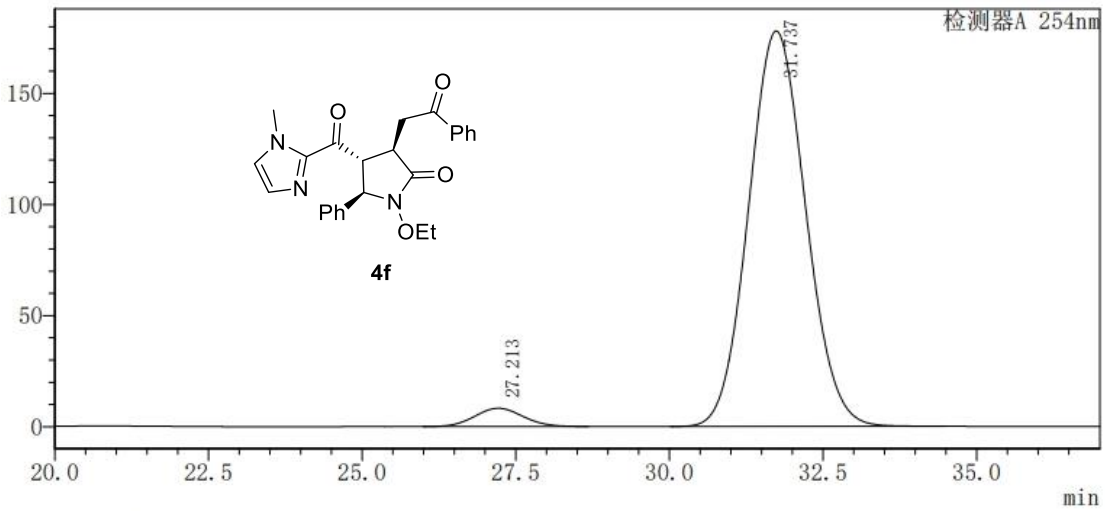
Figure S51. HPLC traces of racemic (reference) and chiral **4e**. Area integration = 95.9:4.1 (92% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	27.240	8485059	152555	50.037
2	31.802	8472520	131452	49.963
总计		16957579	284007	100.000



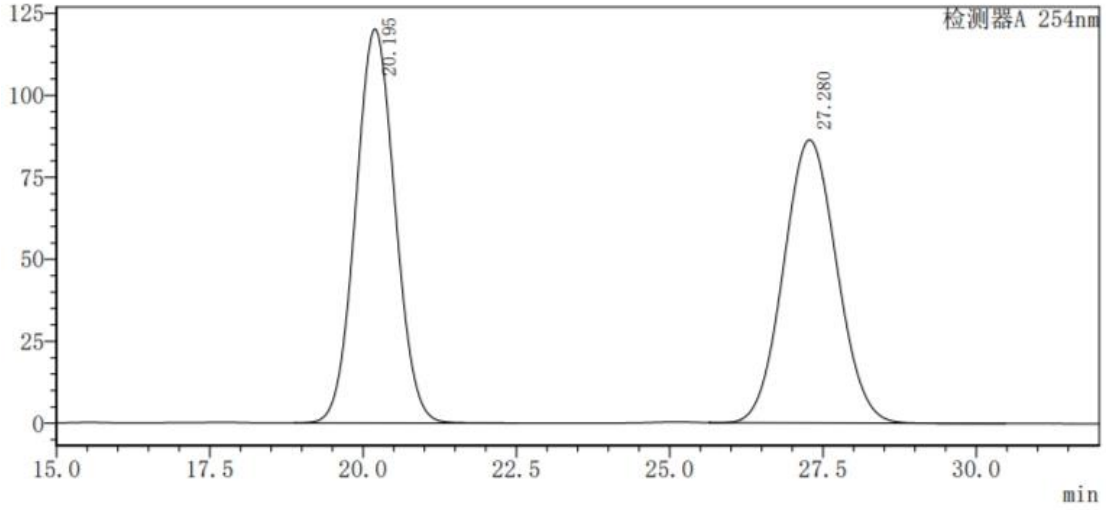
4f

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	27.213	450057	8217	3.770
2	31.737	11489210	177958	96.230
总计		11939267	186175	100.000

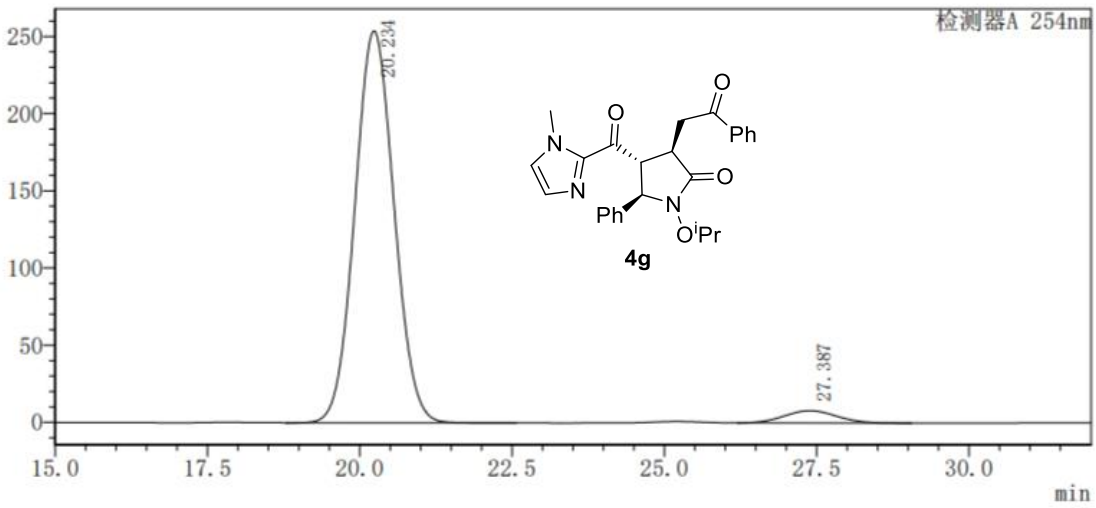
Figure S52. HPLC traces of racemic (reference) and chiral **4f**. Area integration = 96.2:3.8 (92% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	20.195	5373448	120152	50.735
2	27.280	5217744	86355	49.265
总计		10591192	206508	100.000



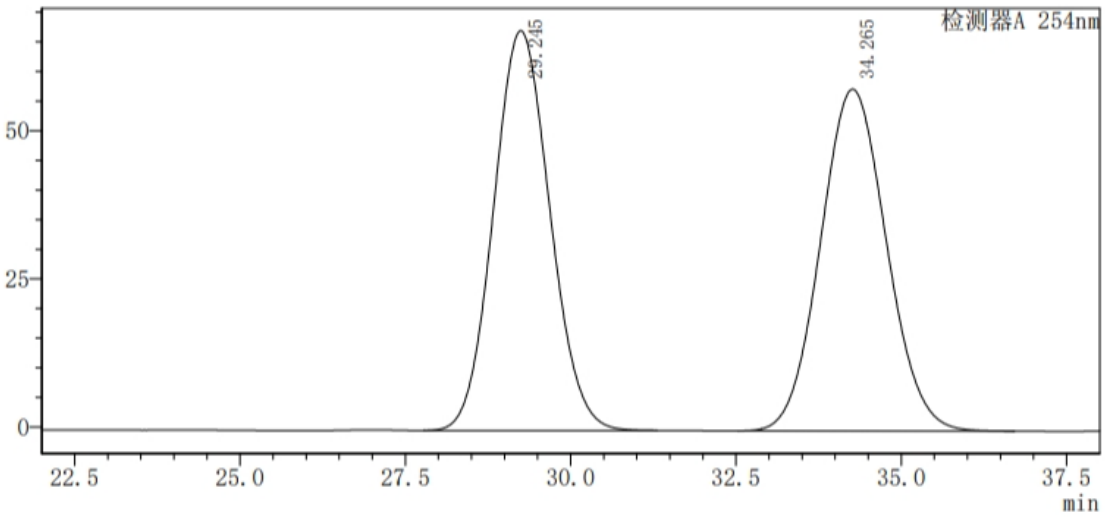
4g

〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	20.234	11371590	253846	96.007
2	27.387	472931	7939	3.993
总计		11844521	261785	100.000

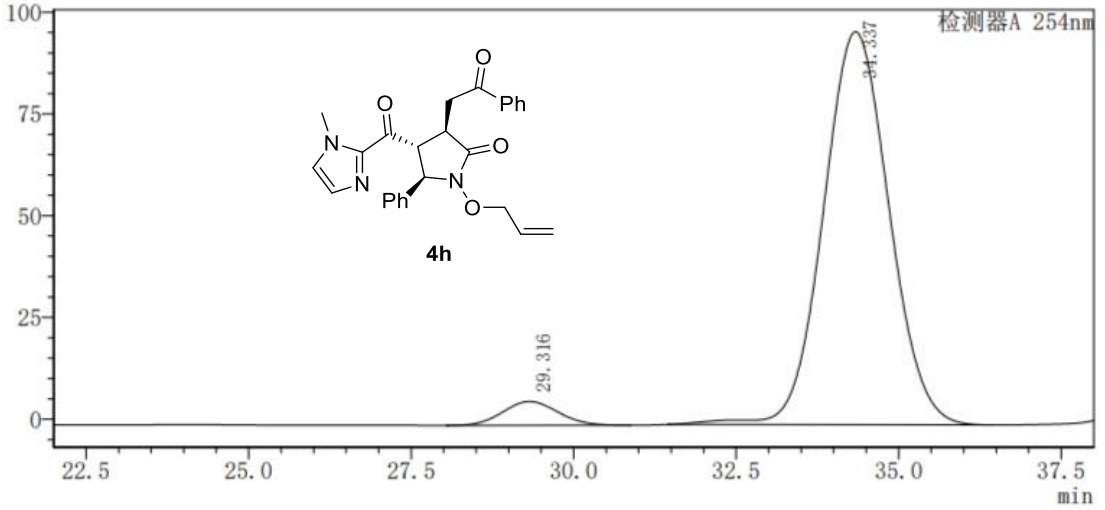
Figure S53. HPLC traces of racemic (reference) and chiral **4g**. Area integration =96.0:4.0 (92% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	29.245	4003530	67464	50.008
2	34.265	4002191	57680	49.992
总计		8005722	125144	100.000

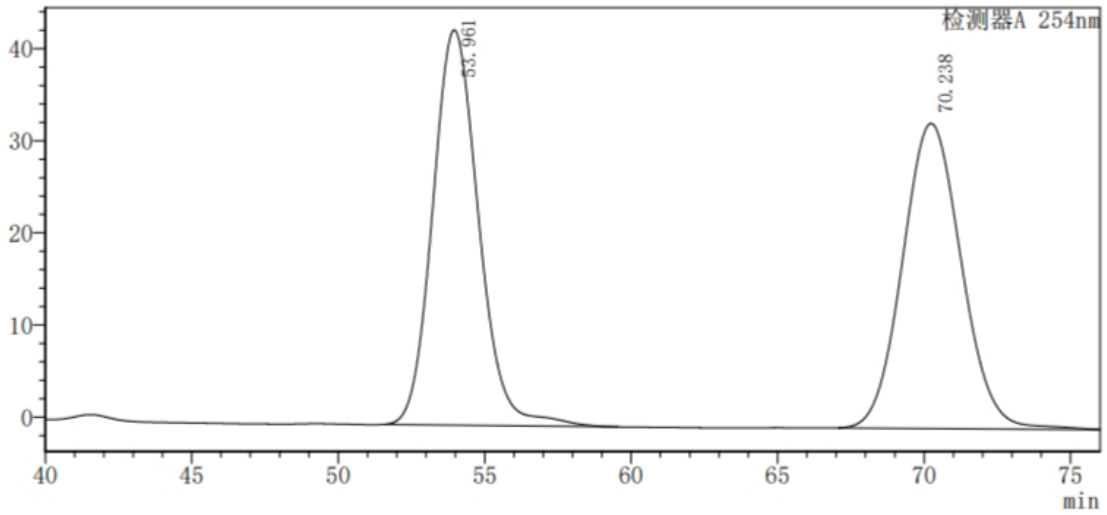


〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	29.316	347372	5861	4.855
2	34.337	6807377	96574	95.145
总计		7154749	102435	100.000

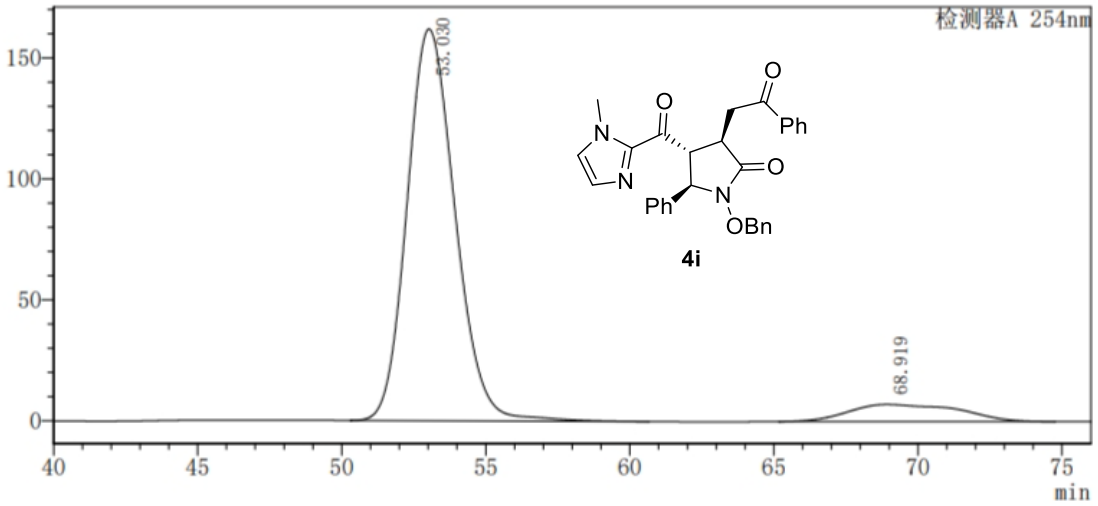
Figure S54. HPLC traces of racemic (reference) and chiral **4h**. Area integration = 95.1:4.9 (90% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	53.961	4675885	42894	50.281
2	70.238	4623536	33118	49.719
总计		9299421	76012	100.000

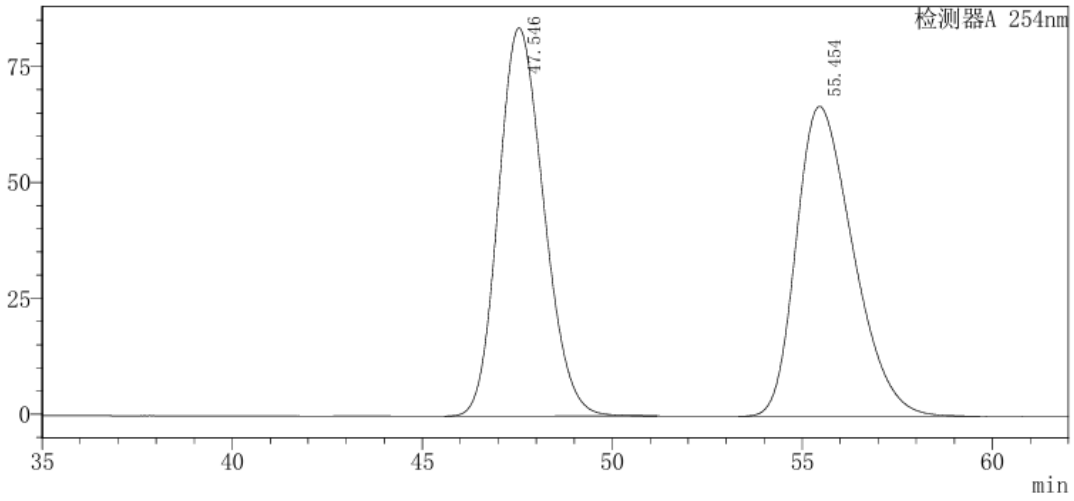


〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	53.030	18768109	161953	90.796
2	68.919	1902431	7085	9.204
总计		20670540	169039	100.000

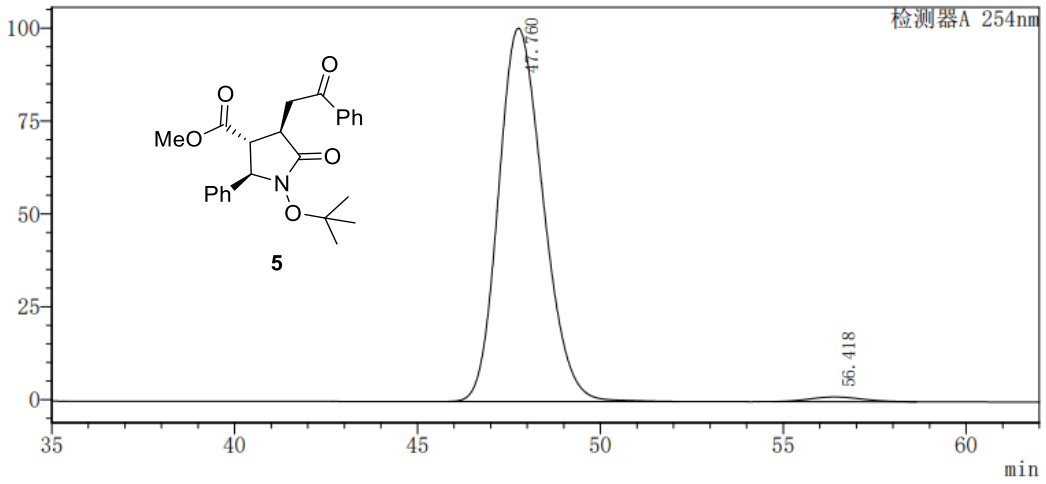
Figure S55. HPLC traces of racemic (reference) and chiral **4i**. Area integration = 90.8:9.2 (82% ee).



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	47.546	6953997	83747	49.979
2	55.454	6959936	66860	50.021
总计		13913932	150608	100.000



〈峰表〉

检测器A 254nm

峰号	保留时间	面积	高度	面积%
1	47.760	8519061	100502	98.537
2	56.418	126451	1267	1.463
总计		8645512	101769	100.000

Figure S56. HPLC traces of racemic (reference) and chiral **5**. Area integration = 98.5:1.5 (97% ee).

8. Single Crystal X-Ray Diffraction Studies

The single crystal for compound **4g** was prepared from a mixture solvent of ethyl acetate and *n*-hexane (v/v = 3:1). Diffraction data were collected on a Bruker APEX-II CCD area detector using graphite-monochromated Cu-Kα radiation (λ = 1.54184 Å) at 293 K. The crystal structures were resolved by direct methods and all calculations were performed on the SHELXL-97 program package. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were added in the riding model and refined with isotropic thermal parameters. The absolute configuration of **4g** was determined as (3*R*, 4*R*, 5*R*) based on its single crystal X-ray analysis. The structure is shown in **Figure S53**. The detailed information is listed in the **Table S1**. Crystallographic data for **4g** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number **CCDC 2407123**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

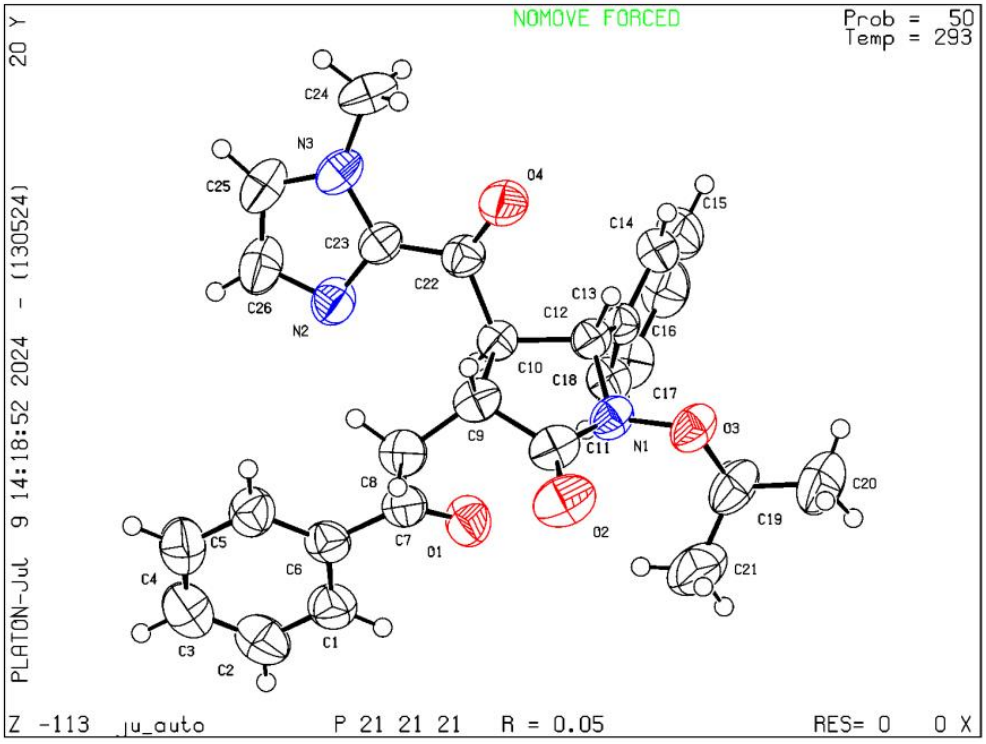


Figure S57. Crystal structure of **4g** to verify absolute configuration.

Table S1. Crystal data and structure refinement for **4g**.

Bond precision	**C-C = 0.0042 Å**	**Z**	**4**
Wavelength	1.54184 Å	**μ (mm^{-1})**	0.701
Cell	a = 10.0143(2) b = 12.5104(2) c = 18.6301(3) α = 90 β = 90 γ = 90	**F000**	944.0
		F000'	946.88
		h, k, l_{max}	12, 15, 22
Temperature	293 K	**N_{ref}**	4211
Volume	2334.03(7)	**T_{min}, T_{max}**	0.959,0.973
Crystal system	orthorhombic	**Data completeness**	0.99
Space group	P 21 21 21	**θ (max)**	68.013
Hall group	P 2ac 2ab	**R(reflections)**	0.0509(3928)
Moiety formula	$C_{26}H_{27}N_3O_4$	**wR2(reflections)**	0.1273(4211)
Sum formula	$C_{26}H_{27}N_3O_4$	**S**	1.040
Mr	445.50	**Npar**	301
Density (g/cm^3)	1.268		

9. References

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