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Supplemental Information

Catalytic Asymmetric Radical Diamination of Alkenes

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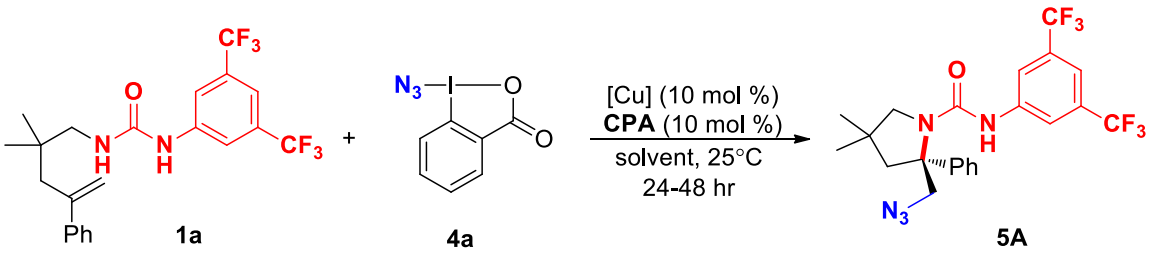
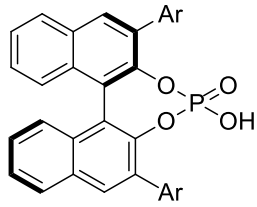
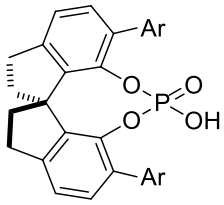
I. Supplemental Tables

Table S1. Screening of Reaction Conditions for Azidyl Radical[a]





(*R*)-**A7**: Ar = 1-Naphthyl
(*R*)-**A8**: Ar = 9-phenanthrenyl
(*R*)-**A9**: Ar = 1-Pyrenyl



(*S*)-**A10**: Ar = Ph
(*S*)-**A4**: Ar = 4-PhC_6H_4
(*S*)-**A5**: Ar = 1-Pyrenyl

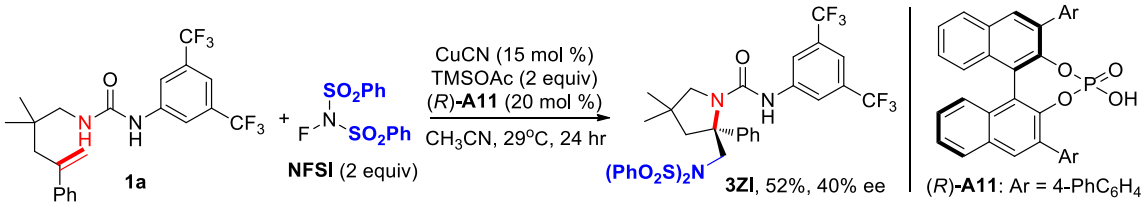
entry	CPA	Additive	solvent	yield (%)[b]	ee (%)[c]
1	(*R*)-**A7**	-	1,4-dioxane	82	7
2	(*R*)-**A8**	-	1,4-dioxane	80	13
3	(*R*)-**A9**	-	1,4-dioxane	85	33
4	(*S*)-**A10**	-	1,4-dioxane	82	13
5	(*S*)-**A4**	-	1,4-dioxane	81	0
6	(*S*)-**A5**	-	1,4-dioxane	86	71
7	(*S*)-**A5**	-	THF	77	55
8	(*S*)-**A5**	-	EA	20	42
9[d]	(*S*)-**A5**	-	1,4-dioxane	42	3
10[e]	(*S*)-**A5**	-	1,4-dioxane	36	23
11[f]	(*S*)-**A5**	-	1,4-dioxane	84	84
12[g]	(*S*)-**A5**	-	1,4-dioxane	83	79
13[f,k]	(*S*)-**A5**	3 Å MS	1,4-dioxane	84	83
14[f,k]	(*S*)-**A5**	4 Å MS	1,4-dioxane	85	88
15[f,k]	(*S*)-**A5**	5 Å MS	1,4-dioxane	62	75
16[f,h,k]	(*S*)-**A5**	4 Å MS	1,4-dioxane	86	89
17[f,i,k]	(*S*)-**A5**	4 Å MS	1,4-dioxane	85	92
18[f,j,k]	(*S*)-**A5**	4 Å MS	1,4-dioxane	84	90

[a]Reaction conditions: **1a** (0.05 mmol), **2** (1.2 equiv), CuI (10 mol %), CPA (10 mol %), solvent (1.0 mL), 25°C, 24 hr under argon.

[b]Yield based on ^{1}H NMR analysis of the crude product using CH_2Br_2 as an internal standard.

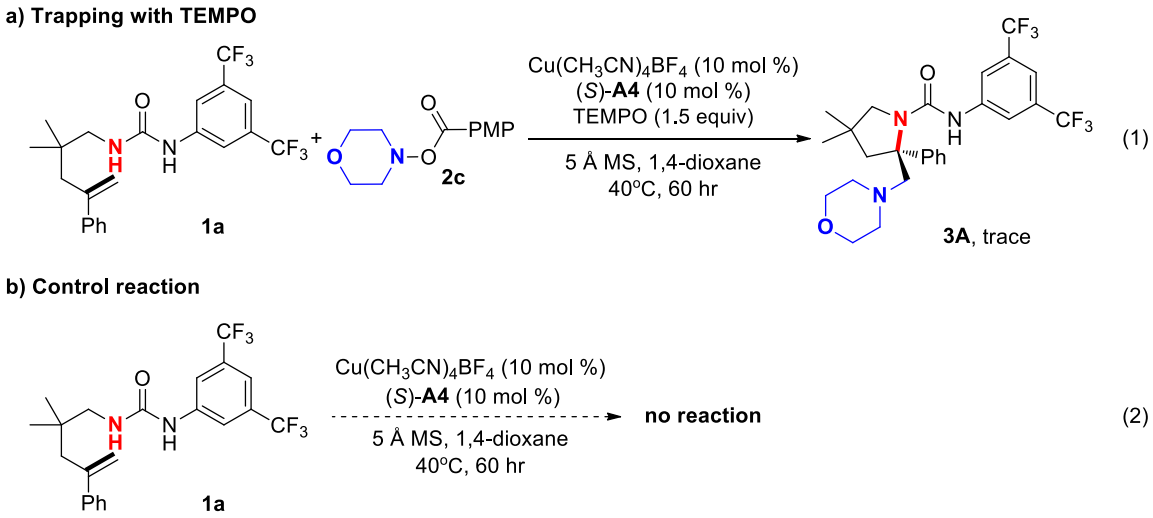
[c]Ee value based on HPLC analysis.
[d]$Cu(CH_3CN)_4BF_4$ (10 mol %) was employed at 25°C for 48 hr.
[e]CuBr (10 mol %) was employed was employed at 25°C for 48 hr.
[f]1,4-Dioxane (2.0 mL) was employed.
[g]1,4-Dioxane (4.0 mL) was employed.
[h]1.2 Equiv of Na_2CO_3 was added.
[i]1.2 Equiv of $NaHCO_3$ was added.
[j]1.2 Equiv of $KHCO_3$ was added.
[k]molecular sieves (50.0 mg) was added.

II. Supplemental Schemes



Scheme S1. Asymmetric Diamination of Alkene with NFSI

Abbreviations: NFSI, *N*-fluorobenzenesulfonimide; TMSOAc, trimethylsilyl acetate.



Scheme S2. Mechanistic Study

III. Supplemental Experimental Procedures

1. General information

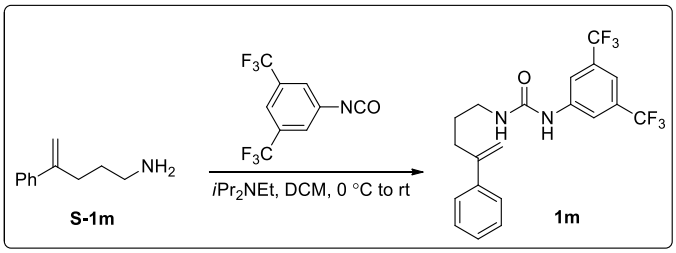
All reactions were carried out under argon atmosphere using Schlenk techniques. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. $Cu(CH_3CN)_4BF_4$ and CuI were purchased from Sigma-Aldrich. Chiral phosphoric acid (**CPA**) was purchased from Daicel Chiral Technologies (China). Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 GF254 plates. Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040-0.063 mm). Visualization on TLC was achieved by use of UV light (254 nm) or iodine. NMR spectra were recorded on Bruker DRX-500 and DPX 400 spectrometer at 400 or 500 MHz for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR and 376 MHz for ^{19}F NMR in $CDCl_3$ and acetone-d_6 with tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in ppm and coupling constants are given in Hz. Data for ^{1}H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; p, pentet, m, multiplet; br, broad), coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). Mass spectrometric data were obtained using Bruker Apex IV RTMS. Enantiomeric excess (ee) was determined using Agilent high-performance liquid chromatography (HPLC) with a Hatachi detector (λ = 320, 254, 230 or 214 nm). Column conditions are reported in the experimental section below. X-ray diffraction was measured on a 'Bruker APEX-II CCD' diffractometer with Cu-Kα radiation.

2. Procedures for synthesis of substrates

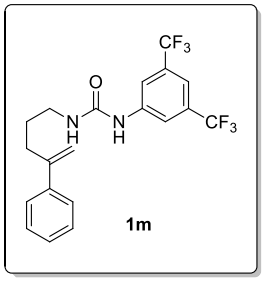
Substrates **1a**–**1l**, **1p**–**1s**, **1u**, and **1v** were prepared according to reported procedures.[1,2]

Synthesis of 1m, 1n and 1o

S-1m was prepared according to reported procedures.[2]



To a stirred solution of **S**-**1m** (2.0 mmol) and *i*Pr_2NEt (2.0 mmol) in anhydrous CH_2Cl_2 (4.0 mL) was slowly added 1-isocyanato-3,5-bis(trifluoromethyl)-benzene (2.0 mmol) at 0 °C. Then the reaction mixture was warmed to room temperature and stirred for an additional 1 h. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography (eluent: petroleum ether/CH_2Cl_2 = 100/1 to 1/2, using petroleum ether (100%) to remove CH_2Cl_2 for sample loading at first) to afford **1m** (1.72 mmol, 86% yield)**.**



1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-phenylpent-4-en-1-yl)urea (1m, 86% yield**)**

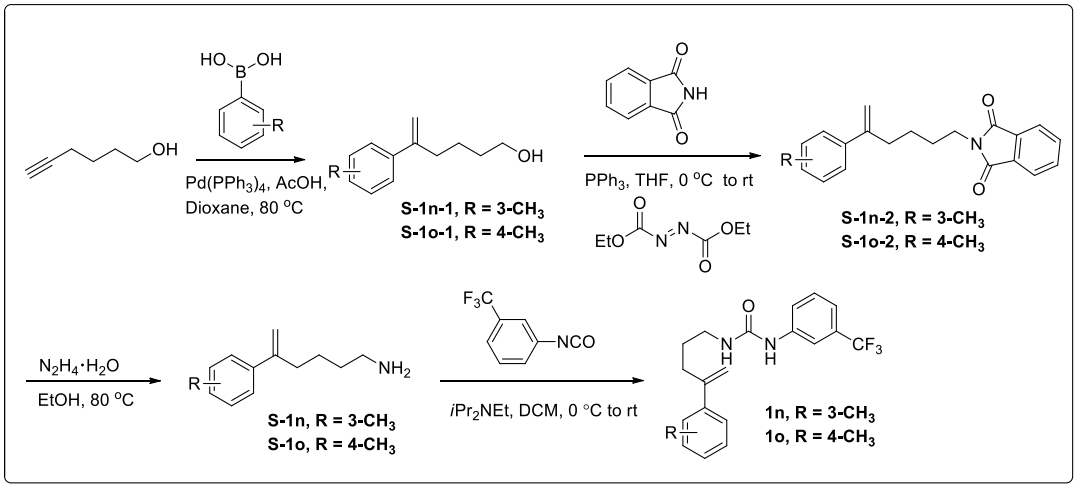
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 3H), 7.41 (s, 1H), 7.34 (dd, *J* = 5.0, 3.5 Hz, 2H), 7.31–7.26 (m, 2H), 7.26–7.20 (m, 1H), 5.49 (s, 1H), 5.25 (d, *J* = 0.5 Hz, 1H), 5.01 (d, *J* = 1.0 Hz, 1H), 3.23 (dd, *J* = 13.0, 7.5 Hz, 2H), 2.51 (t, *J* = 7.5 Hz, 2H), 1.73–1.59 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 147.3, 140.7, 140.5, 132.3 (q, *J* = 33.3 Hz), 128.5, 127.7, 126.1, 123.2 (q, *J* = 272.8 Hz), 118.7 (d, *J* = 3.0 Hz), 116.0 (t, *J* = 3.6 Hz), 113.1, 40.0, 32.6, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{19}F_6N_2O$ $[M + H]^+$ 417.1396, found 417.1392.

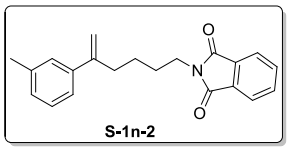
S-1n-1 and **S-1o-1** were prepared according to reported procedures.[3]



To a solution of **S-1n-1** (0.57 g, 3.0 mmol), *O*-Phthalimide (0.44 g, 3.0 mmol), and PPh_3 (0.79 g, 3.0 mmol) in 20.0 mL THF was added diethyl azodicarboxylate (0.5 mL, 3.0 mmol) at 0 °C. The mixture was allowed to warm to room temperature for 18 h, evacuated the solvent and purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 20:1-5:1) to give **S-1n-2** (0.8 g, 83%).

To a solution of **S-1n-2** (0.64 g, 2.0 mmol) in EtOH (15.0 mL) was added hydrazine monohydrate (0.4 mL, 6.0 mmol) at room temperature. The reaction mixture was stirred and heated to reflux for 2 h. After cooling down to room temperature, the mixture was filtered and the filtrate was concentrated *in vacuo* to afford crude amine, which was not purified for the next step.

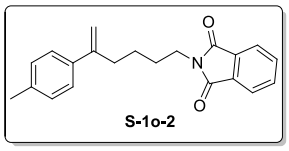
Urea substrates **1n** and **1o** were obtained by the similar procedure for the compound **1m**.



2-(5-(*m*-tolyl)hex-5-en-1-yl)isoindoline-1,3-dione (S-1n-2, 83% yield**)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85–7.80 (m, 2H), 7.72–7.67 (m, 2H), 7.22–7.13 (m, 3H), 7.07 (d, *J* = 5.0 Hz, 1H), 5.26 (s, 1H), 5.08 (s, 1H), 3.73 (t, *J* = 7.5 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.91–1.80 (m, 2H).

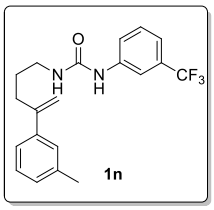
^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 147.3, 140.9, 137.8, 133.8, 132.1, 128.2, 126.8, 123.14, 123.10, 112.6, 37.7, 32.6, 27.0, 21.4.



2-(5-(*p*-tolyl)hex-5-en-1-yl)isoindoline-1,3-dione (S-1o-2, 89% yield**)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.81 (m, 2H), 7.79–7.61 (m, 2H), 7.29 (d, *J* = 5.0 Hz, 2H), 7.14 (d, *J* = 5.0 Hz, 2H), 5.28 (s, 1H), 5.08 (s, 1H), 3.75 (t, *J* = 7.5 Hz, 2H), 2.57 (t, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 1.94–1.82 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 146.9, 137.9, 137.1, 133.8, 132.0, 128.9, 125.9, 123.1, 111.9, 37.7, 32.5, 27.0, 21.0.

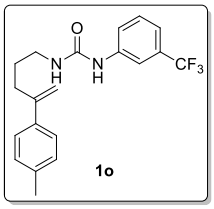


1-(4-(*m*-tolyl)pent-4-en-1-yl)-3-(3-(trifluoromethyl)phenyl)urea (1n, 67% yield**)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.43 (d, *J* = 10.0 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 1H), 7.22–7.10 (m, 5H), 7.06 (d, *J* = 5.0 Hz, 1H), 5.47 (s, 1H), 5.22 (s, 1H), 4.98 (s, 1H), 3.19 (dd, *J* = 10.0, 5.0 Hz, 2H), 2.47 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 1.66–1.55 (m, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.7 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{22}F_3N_2O$ $[M + H]^+$ 363.1679, found 363.1668.



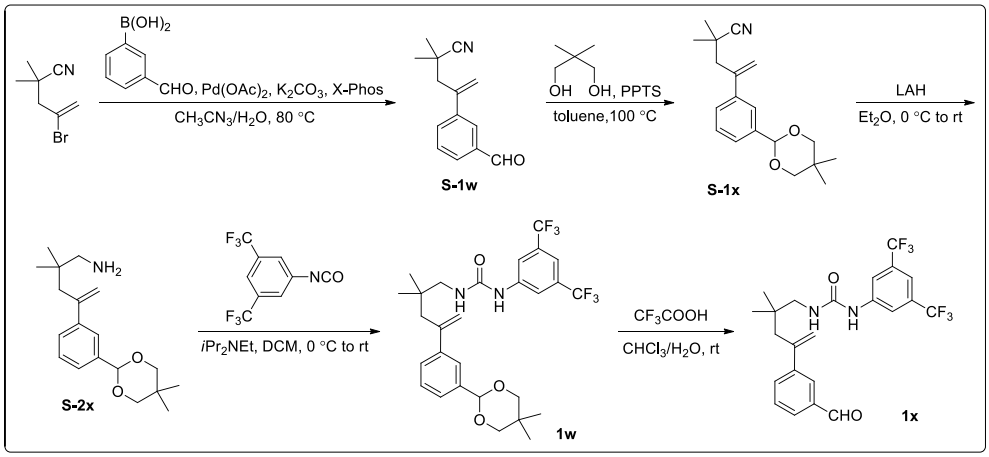
1-(4-(*p*-tolyl)pent-4-en-1-yl)-3-(3-(trifluoromethyl)phenyl)urea (1o, 74% yield**)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.46 (d, *J* = 5.0 Hz, 1H), 7.32–7.20 (m, 5H), 7.10 (d, *J* = 10.0 Hz, 2H), 5.26 (t, *J* = 5.0 Hz, 1H), 5.23 (s, 1H), 4.97 (s, 1H), 3.21 (dd, *J* = 10.0, 5.0 Hz, 2H), 2.49 (t, *J* = 6.9 Hz, 2H), 2.31 (s, 3H), 1.67–1.57 (m, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.6 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{22}F_3N_2O$ $[M + H]^+$ 363.1679, found 363.1668.

Synthesis of 1w and 1x



S-1w was prepared according to reported procedures.[1,2]

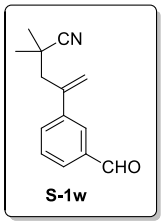
To a solution of **S**-**1w** (12.0 mmol) in toluene (24.0 mL) was added neopentyl glycol (36.0 mmol) and PPTS (1.98 mmol) under argon. Then the reaction was stirred for 18 h at 100 °C. After complete conversion (monitored by TLC), the reaction mixture was extracted with EtOAc. The combined organic layers were concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc = 20/1) to get **S**-**1x** (10.8 mmol, 90% yield).

To a suspension of $LiAlH_4$ (456.0 mg, 12.0 mmol) in Et_2O (36.0 mL) at 0 °C was slowly added a solution of **S**-**1x** (6.0 mmol) in Et_2O (4.0 mL). Then the mixture was warmed to room temperature and stirred for additional 3 h. The reaction mixture was quenched by slow portionwise addition of water (1 mL) in Na_2SO_4 (8.0 g) at 0 °C. The reaction mixture was warmed to room temperature, stirred for additional 30 min, filtered and concentrated *in vacuo* to afford **S**-**2x**, which was directly

used in the next reaction without further purification.

To a stirred solution of **S-2x** (ca. 5.21 mmol) and *i*Pr_2NEt (5.21 mmol) in anhydrous CH_2Cl_2 (13.0 mL) was slowly added 1-isocyanato-3,5-bis(trifluoromethyl)-benzene (5.21 mmol) at 0 °C. Then the reaction mixture was warmed to room temperature and stirred for an additional 1 h. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography (eluent: petroleum ether/CH_2Cl_2 = 100/1 to 1/5, using petroleum ether (100%) to remove CH_2Cl_2 for sample loading at first) to afford **1w** (4.3 mmol, 83% yield)**.**

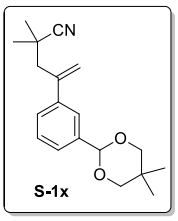
To a solution of **1w** (3.0 mmol) in H_2O (3.0 mL)/$CHCl_3$ (50.0 mL) was added CF_3COOH (6.0 mL). The mixture was stirred for 3 h at room temperature. After complete reaction, the mixture was quenched by $NaHCO_3$ (aq). The organic layer was separated, dried, filtered and concentrated *in vacuo*. The residue thus obtained was purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 20/1 to 5/1) to afford **1x** (2.22 mmol, 74% yield).



4-(3-formylphenyl)-2,2-dimethylpent-4-enenitrile (S-1w)

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90 (s, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 5.52 (s, 1H), 5.38 (s, 1H), 2.80 (s, 2H), 1.28 (s, 6H).

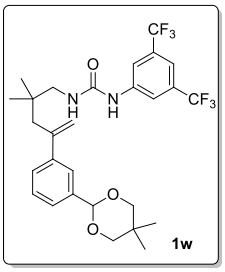
^{13}C NMR (125 MHz, $CDCl_3$) δ 192.2, 142.9, 142.5, 136.6, 132.6, 129.6, 129.3, 127.1, 124.3, 120.1, 45.4, 32.9, 27.1.



4-(3-(5,5-dimethyl-1,3-dioxan-2-yl)phenyl)-2,2-dimethylpent-4-enenitrile (S-1x)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.44 (dt, *J* = 6.5 Hz, *J* = 2.0 Hz, 1H), 7.37–7.32 (m, 2H), 5.47 (s, 1H), 5.40 (s, 1H), 5.31 (s, 1H), 3.77 (d, *J* = 11.0 Hz, 2H), 3.65 (d, *J* = 11.0 Hz, 2H), 2.77 (s, 2H), 1.30 (s, 3H), 1.24 (s, 6H), 0.81 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 141.8, 138.8, 128.5, 126.9, 125.6, 124.2, 118.9, 101.6, 77.7, 45.3, 33.4, 30.3, 27.1, 23.1, 21.9.



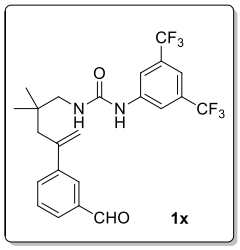
1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(3-(5,5-dimethyl-1,3-dioxan-2-yl) phenyl)-2,2-dimethylpent-4-en-1-yl)urea (1w)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 2H), 7.67 (s, 1H), 7.46–7.44 (m, 3H), 7.42–7.39 (m, 1H), 6.62 (s, 1H), 5.49 (s, 1H), 5.32 (s, 1H), 5.12 (s, 1H), 3.82 (t, *J* = 6.5 Hz, 1H), 3.78 (d, *J* = 11.0 Hz, 2H), 3.72 (d, *J* = 11.0 Hz, 2H), 2.73 (d, *J* = 6.5 Hz, 2H), 2.48 (s, 2H), 1.32 (s, 3H), 0.94 (s, 6H), 0.82 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 145.6, 144.1, 140.9, 138.3, 132.1, 131.9 (q, *J* = 33.0 Hz), 129.5, 128.5, 125.8, 123.2 (q, *J* = 271.1 Hz), 118.9, 117.9, 115.5, 102.2, 77.9, 48.3, 45.2, 35.9, 30.3, 26.1, 22.9, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{28}H_{33}F_6N_2O_3$ $[M + H]^+$ 559.2391, found 559.2390.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(3-formylphenyl)-2,2-dimethylpent-4-en-1-yl)urea (1x)

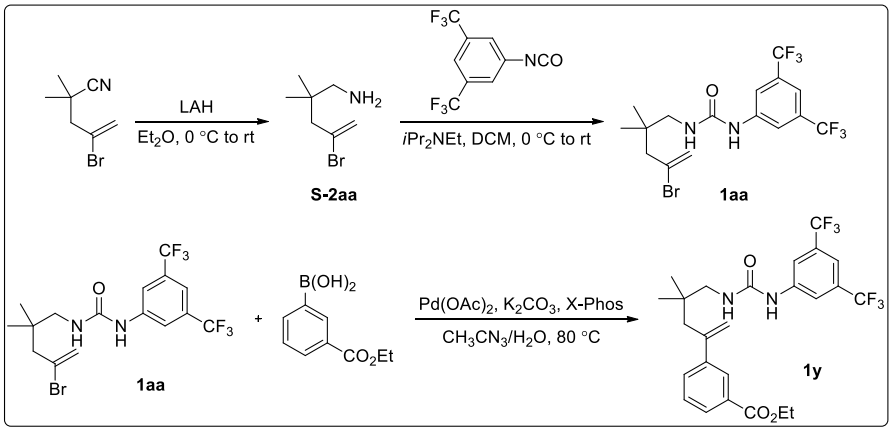
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.89 (s, 1H), 7.81 (s, 2H), 7.73 (d, *J* = 7.2 Hz, 1H), 7.66 (t, *J* = 2.8 Hz, 2H), 7.49 (t, *J* = 3.6 Hz, 1H), 7.43 (s, 1H), 5.35 (s, 1H), 5.28 (t, *J* = 6.0 Hz, 1H), 5.13 (s, 1H), 2.98 (d, *J* = 6.0 Hz, 2H), 2.52 (s, 2H), 0.76 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 193.3, 155.3, 144.7, 144.0, 140.6, 136.3, 132.8, 132.2 (q, *J* = 33.0 Hz), 129.9, 129.4, 125.9, 123.1 (q, *J* = 271.2 Hz), 118.9, 118.4, 115.7, 50.0, 44.5, 35.7, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{23}H_{23}F_6N_2O_2$ $[M + H]^+$ 473.1658, found 473.1660.

Synthesis of 1y

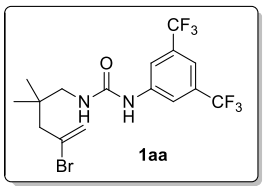


S-2aa was prepared according to reported procedures.[1,2]

To a stirred solution of **S-2aa** (4.0 mmol) and *i*Pr_2NEt (4.0 mmol) in anhydrous CH_2Cl_2 (10.0 mL) was slowly added 1-isocyanato-3,5-bis(trifluoromethyl)-benzene (4.0 mmol) at 0 °C. Then, the reaction mixture was stirred for additional 60 min at 0 °C. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 100/1 to 10/1, using petroleum ether (100%) to remove CH_2Cl_2 for sample loading at first) to afford **1aa** (3.6 mmol, 90% yield).

To a solution of **1aa** (2.0 mmol), 3-ethoxycarbonylphenylboronic acid (3.0 mmol), K_2CO_3 (6.0 mmol) and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos, 0.16 mmol) in CH_3CN/H_2O (6.0 mL/3.0 mL) was added $Pd(OAc)_2$ (0.08 mmol). Then the flask was briefly evacuated and backfilled with argon three times. Upon completion, the flask was sealed and the reaction mixture was stirred at 80 °C for 12 h under argon atmosphere. Next, the reaction mixture was cooled to room temperature and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to afford a crude product, which was further purified by flash chromatography (eluent: petroleum ether/EtOAc = 100/1 to 7/1) to give **1y** (0.4 mmol, 20%

yield).

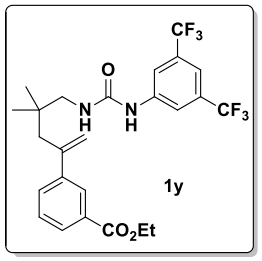


1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-bromo-2,2-dimethylpent-4-en-1-yl)urea (1aa)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 2H), 7.49 (s, 1H), 6.92 (s, 1H), 5.98 (s, 2H), 5.10 (t, *J* = 7.5 Hz, 1H), 3.25 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 2H), 1.01 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 140.4, 132.4 (q, *J* = 33.0 Hz), 128.8, 123.1 (q, *J* = 271.1 Hz), 121.3, 118.7, 116.0, 50.3, 49.2, 35.8, 25.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.2 (s, 6F).



Ethyl3-(5-(3-(3,5-bis(trifluoromethyl)phenyl)ureido)-4,4-dimethylpent-1-en-2-yl)benzoate (1y)

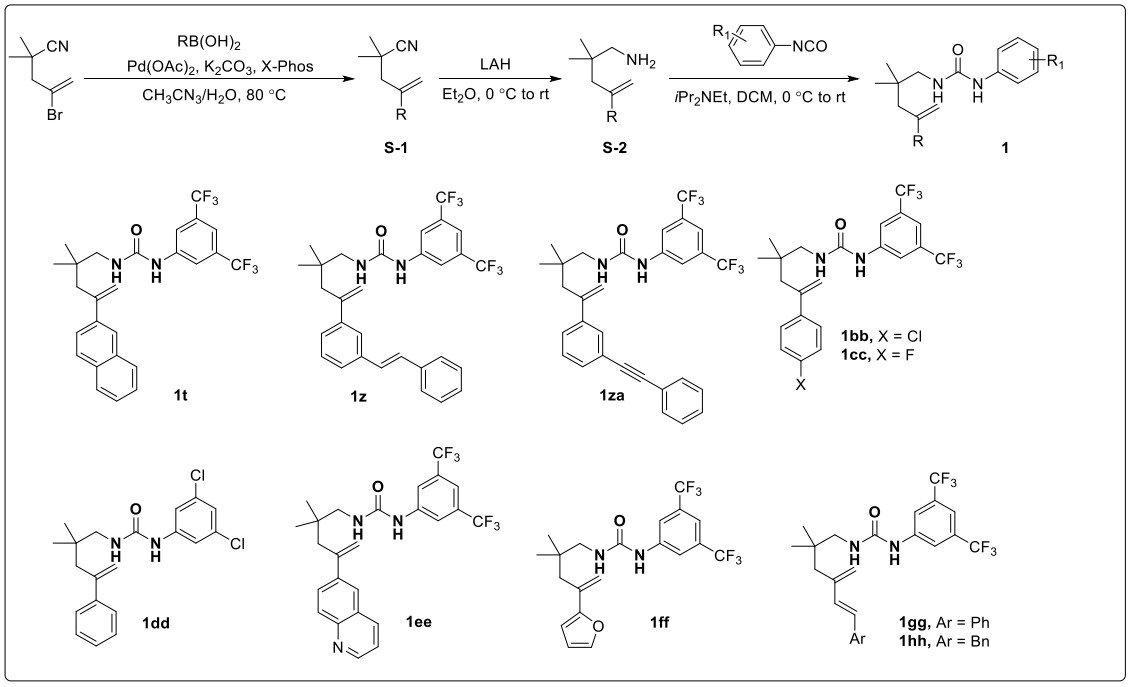
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.94 (s, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.55 (s, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 5.43 (s, 1H), 5.17 (s, 1H), 4.89 (t, *J* = 7.2 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 2.82 (d, *J* = 6.4 Hz, 2H), 2.55 (s, 2H), 1.41 (t, *J* = 7.2 Hz, 3H), 0.87 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 155.0, 144.6, 143.0, 141.2, 132.0 (q, *J* = 33.0 Hz), 131.2, 130.3, 129.2, 128.3, 126.6, 123.3 (q, *J* = 271.0 Hz), 118.4, 117.9, 115.2, 61.8, 48.9, 44.0, 35.8, 25.9, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

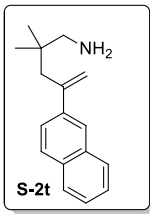
HRMS (ESI) *m/z* calcd. for $C_{25}H_{27}F_6N_2O_3$ $[M + H]^+$ 517.1920, found 517.1921.

Synthesis of 1t, 1z, 1za, 1bb-1hh



S-1 and **S-2** were prepared according to reported procedures.[1,2]

To a stirred solution of **S-2** (2.0 mmol) and *i*Pr_2NEt (2.0 mmol) in anhydrous CH_2Cl_2 (5.0 mL) was slowly added 1-isocyanato-3,5-bis(trifluoromethyl)-benzene (2.0 mmol) at 0 °C. Then, the reaction mixture was warmed to room temperature and stirred for an additional 1 h. After complete conversion (monitored by TLC), the crude mixture was directly purified by silica gel column chromatography (eluent: petroleum ether/CH_2Cl_2 = 100/1 to 1/5, using petroleum ether (100%) to remove CH_2Cl_2 for sample loading at first) to give urea substrates **1t**, **1z**, **1za**, and **1bb-1hh**.

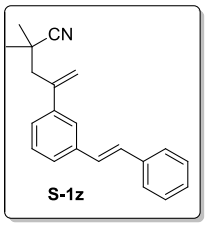


2,2-dimethyl-4-(naphthalen-2-yl)pent-4-en-1-amine (S-2t)

(1.01 g, 76% overall yield in two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19–8.17 (m, 1H), 7.86–7.84 (m, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.51–7.46 (m, 2H), 7.45–7.38 (m, 2H), 5.43 (d, *J* = 2.0 Hz, 1H), 5.26 (d, *J* = 8.0 Hz, 1H), 2.62 (s, 2H), 2.33 (s, 2H), 0.89 (br s, 2H), 0.79 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 142.3, 134.0, 130.9, 128.5, 127.3, 126.0, 125.8, 125.6, 125.2, 119.9, 52.7, 47.6, 36.4, 25.3.

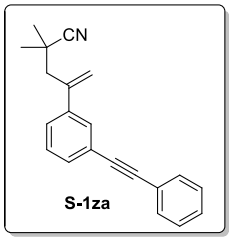


2,2-dimethyl-4-(3-styrylphenyl)pent-4-enenitrile (S-1z)

(740 mg, 81% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 3H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 1.5 Hz, 2H), 5.50 (s, 1H), 5.33 (s, 1H), 2.80 (s, 2H), 1.28 (s, 6H).

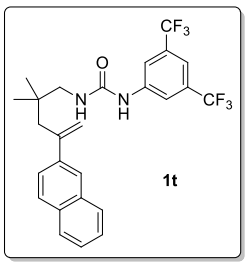
^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 142.2, 137.6, 137.2, 129.1, 128.8, 128.7, 128.4, 127.8, 126.6, 125.8(2), 125.8(1), 124.8, 124.7, 118.9, 45.5, 33.3, 27.1.



4-(3-(5,5-dimethyl-1,3-dioxan-2-yl)phenyl)-2,2-dimethylpent-4-enenitrile (S-1za)

(570 mg, 76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.53 (m, 3H), 7.46 (td, *J* = 1.5 Hz, *J* = 7.0 Hz, 1H), 7.37–7.31 (m, 5H), 5.48 (d, *J* = 1.0 Hz, 1H), 5.34 (d, *J* = 1.0 Hz, 1H), 2.77 (s, 2H), 1.27 (s, 6H).



1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(naphthalen-2-yl)pent-4-en-1-yl)urea (1t)

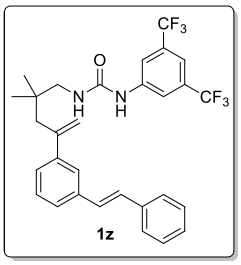
(890 mg, 90% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85–7.49 (m, 4H), 7.62 (s, 2H), 7.54 (dd, *J* = 2.0 Hz, *J* = 8.0 Hz, 1H), 7.50 (dt, *J* = 1.0 Hz, *J* = 6.5 Hz, 1H), 7.47–7.45 (m, 1H), 7.44 (s, 1H), 5.97 (s, 1H), 5.43 (d, *J* = 1.5 Hz, 1H), 5.19 (d, *J* = 1.5 Hz, 1H), 4.31 (t, *J* = 6.0 Hz, 1H), 2.97 (d, *J* = 6.0 Hz, 2H), 2.62 (s, 2H), 0.88 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 146.0, 140.8, 140.4, 133.2, 132.6, 132.1 (q, *J* = 33.1Hz), 128.3, 127.9, 127.7, 126.6, 126.2, 125.1, 125.0, 123.1 (q, *J* = 271.1 Hz), 118.3, 118.2, 115.7, 50.0, 45.3, 35.8, 25.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{26}H_{25}F_6N_2O$ $[M + H]^+$ 495.1866, found 495.1867.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(3-styrylphenyl)pent-4-en-1-yl)urea (1z)

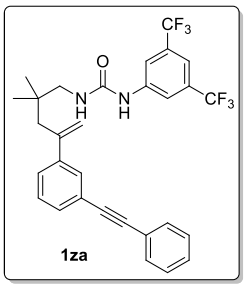
(951 mg, 87% overall yield in two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (s, 2H), 7.54 (s, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 5.5 Hz, 2H), 7.38–7.32 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.15(d, *J* = 16.5 Hz, 1H), 7.11 (d, *J* = 16.5 Hz, 1H), 6.39 (s, 1H), 5.34 (s, 1H), 5.12 (s, 1H), 4.48 (s, 1H), 2.99 (d, *J* = 7.5Hz, 2H), 2.54 (s, 2H), 0.87 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 156.1, 146.0, 143.6, 140.3, 137.4, 137.0, 132.1 (q, *J* = 33.1 Hz), 129.0, 128.7, 128.3, 127.8, 126.5, 125.7, 125.4, 124.7, 123.0 (q, *J* = 271.1 Hz), 118.5, 117.6, 115.8, 50.2, 45.1, 35.7, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{29}F_6N_2O$ $[M + H]^+$ 547.2179, found 547.2177.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(3-(phenylethynyl)phenyl)pent-4-en-1-yl)urea (1za)

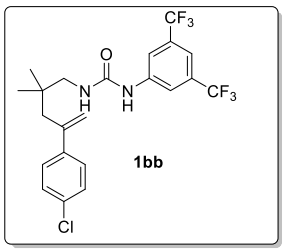
(933 mg, 85% overall yield in two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 2H), 7.57 (s, 1H), 7.53–7.51 (m, 2H), 7.45–7.43 (m, 2H), 7.36–7.31 (m, 4H), 7.26 (s, 1H), 6.66 (s,1H), 5.33 (s, 1H), 5.11 (s, 1H), 4.63 (s, 1H), 2.99 (d, *J* = 6.0 Hz, 2H), 2.51 (s, 2H), 0.84 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 145.3, 143.6, 140.4, 132.2 (q, *J* = 33.3 Hz), 131.6, 130.6, 129.4, 128.7, 128.5, 128.4, 128.6, 123.1 (q, *J* = 270.7 Hz), 123.3, 122.8, 118.5, 118.2, 115.9, 89.8, 89.1, 50.0, 45.0, 35.8, 25.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{27}F_6N_2O$ $[M + H]^+$ 545.2022, found 545.2023.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(4-chlorophenyl)-2,2-dimethylpent-4-en-1-yl)urea (1bb)

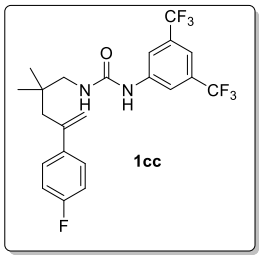
(850 mg, 89% overall yield in two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 2H), 7.44 (s, 1H), 7.37 (s, 1H), 7.25-7.23 (m, 4H), 5.24 (s, 1H), 5.20 (s, 1H), 5.02 (s, 1H), 3.01 (d, *J* = 5.5 Hz, 2H), 2.44 (s, 2H), 0.75 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 145.0, 141.6, 140.3, 133.2, 132.1 (q, *J* = 33.1 Hz), 128.5, 127.6, 123.1 (q, *J* = 271.2 Hz), 118.6, 117.9, 116.0, 50.3, 45.0, 35.7, 25.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.2 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{22}F_6ON_2Cl$ $[M + H]^+$ 479.1319, found 479.1306.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(4-fluorophenyl)-2,2-dimethylpent-4-en-1-yl)urea (1cc)

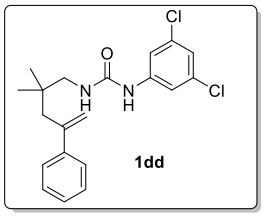
(811 mg, 88% overall yield in two steps).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 2H), 7.60 (s, 1H), 7.43 (s, 1H), 7.28-7.26 (m, 2H), 6.94 (t, *J* = 8.5 Hz, 2H), 5.36 (s, 1H), 5.19 (s, 1H), 4.99 (s, 1H), 3.01 (d, *J* = 6.0 Hz, 2H), 2.43 (s, 2H), 0.74 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 161.2, 155.6, 140.3, 139.1, 132.2 (q, *J* = 33.1 Hz), 127.9 (d, *J* = 7.9 Hz), 123.0 (q, *J* = 271.1 Hz), 118.6, 117.4, 116.0, 115.2, 50.3, 45.2, 35.7, 25.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.2 (s, 6F), −115.0 (s, 1F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{22}F_7ON_2$ $[M + H]^+$ 463.1615, found 463.1600.



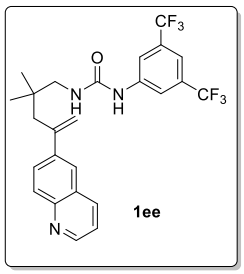
1-(3,5-dichlorophenyl)-3-(2,2-dimethyl-4-phenylpent-4-en-1-yl)urea (1dd)

(682 mg, 90% overall yield in two steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.31-7.29 (m, 2H), 7.28–7.24 (m, 2H), 7.23–7.21 (m, 1H), 7.15 (d, *J* = 2.0 Hz, 2H), 6.94 (t, *J* = 2.0 Hz, 1H), 5.56 (t, *J* = 5.6 Hz, 1H), 5.22 (s, 1H), 5.00 (s, 1H), 2.97 (d, *J* = 2.0 Hz, 2H), 2.44 (s, 2H), 0.74 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 146.2, 143.2, 140.9, 135.2, 128.4, 127.3, 126.4, 122.7, 117.7, 117.3, 50.2, 45.1, 35.7, 25.5.

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{23}ON_2Cl_2$ $[M + H]^+$ 377.1182, found 377.1185.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-(quinolin-6-yl)pent-4-en-1-yl)urea (1ee)

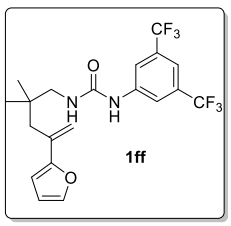
(420 mg, 56% overall yield in two steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.76 (s, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.75 (d, *J* = 9.4 Hz, 3H), 7.63 (d, *J* = 8.6 Hz, 1H), 7.37 (s, 2H), 5.74 (s, 1H), 5.34 (s, 1H), 5.10 (s, 1H), 3.05 (d, *J* = 5.4 Hz, 2H), 2.52 (s, 2H), 0.64 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 149.9, 147.1, 145.2, 141.8, 141.1, 136.9, 132.0 (q, *J* = 33.2 Hz), 129.0, 128.4, 128.3, 124.9, 123.2 (q, *J* = 272.7 Hz), 121.6, 119.0, 118.0, 115.3, 50.3, 44.9, 35.7, 25.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.6 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{24}F_6N_3O$ $[M + H]^+$ 496.1818, found 496.1816.



1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-(furan-2-yl)-2,2-dimethylpent-4-en-1-yl)urea (1ff)

(382 mg, 85% overall yield in two steps)

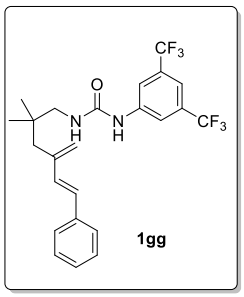
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 2H), 7.48 (s, 1H), 7.34 (s, 1H), 6.76 (s, 1H), 6.37 (s, 1H), 6.34 (s, 1H), 5.63 (s, 1H), 4.96 (s, 1H), 4.88 (s, 1H), 3.13

(d, *J* = 6.2 Hz, 2H), 2.36 (s, 2H), 0.92 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 155.4, 141.7, 140.6, 134.2, 132.1 (q, *J* = 33.5 Hz), 123.1 (q, *J* = 272.8 Hz), 118.5, 115.6, 113.7, 111.3, 106.5, 50.1, 42.5, 35.4, 25.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{21}F_6N_2O_2$ $[M + H]^+$ 435.1502, found 435.1504.



(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-methylene-6-phenylhex-5-en-1-yl)urea (1gg)

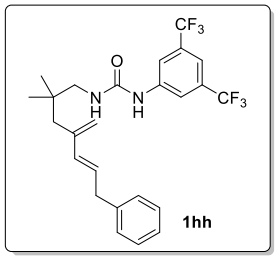
(624 mg, 67% overall yield in two steps)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.69 (s, 2H), 7.47-7.31 (m, 3H), 7.26 (dd, *J* = 8.5, 6.5 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.75 (d, *J* = 16.2 Hz, 1H), 6.54 (d, *J* = 16.3 Hz, 1H), 5.83 (s, 1H), 5.26 (s, 1H), 4.92 (s, 1H), 3.15 (d, *J* = 6.0 Hz, 2H), 2.24 (s, 2H), 0.9 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 144.3, 142.6, 140.4, 137.0, 132.2 (q, *J* = 30.7 Hz), 128.8, 128.6, 127.6, 126.4, 123.1 (q, *J* = 271.1 Hz), 119.5, 118.6, 115.9, 50.4, 41.2, 35.3, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ −61.2 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{25}F_6N_2O$ $[M + H]^+$ 471.1866, found 471.1865.



(*E*)-1-(3,5-bis(trifluoromethyl)phenyl)-3-(2,2-dimethyl-4-methylene-7-phenylhept-5-en-1-yl)urea (1hh)

(710 mg, 73% overall yield in two steps)

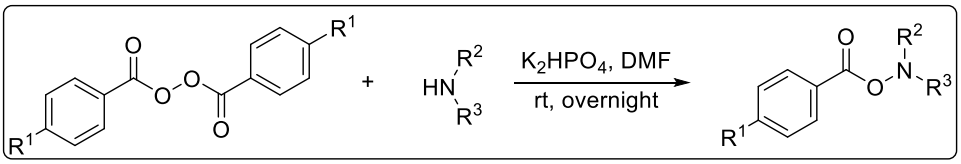
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 2H), 7.43 (s, 1H), 7.28 (dd, *J* = 13.6, 6.3 Hz, 2H), 7.23-7.14 (m, 3H), 6.89 (s, 1H), 6.19 (d, *J* = 15.6 Hz, 1H), 5.92-5.77 (m, 1H), 5.13 (s, 1H), 5.10 (s, 1H), 4.85 (s, 1H), 3.43 (d, *J* = 6.9 Hz, 2H), 3.07 (d, *J* = 6.2 Hz, 2H), 2.13 (s, 2H), 0.87 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 142.4, 140.5, 140.3, 134.9, 132.1 (q, *J* = 33.3 Hz), 128.9, 128.7, 128.6, 126.4, 123.2 (q, *J* = 272.7 Hz), 118.6, 118.0, 115.8, 49.8, 41.0, 39.2, 35.4, 25.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{27}F_6N_2O$ $[M + H]^+$ 485.2022, found 485.2020.

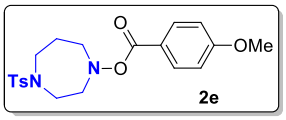
General procedure for preparation of *O*-benzoylhydroxylamines 2a–j



O-Benzoylhydroxylamines **2a**–**j** were synthesized using literature procedures.[4]

An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with aryl peroxyanhydride (1.0 mmol, 1.0 equiv), dipotassium hydrogen phosphate (1.5 mmol, 1.5 equiv), secondary amines (1.1 mmol, 1.1 equiv) and anhydrous *N,N*-dimethylformamide (5 mL), and the

sealed tube was then stirred at room temperature overnight. Upon completion (monitored by TLC), the reaction mixture was quenched with water (5 mL), and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extract was washed with brine (2 × 10 mL), dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by flash chromatography using petroleum ether/EtOAc (6/1) as the eluent to afford the corresponding *O*-benzoylhydroxylamines.



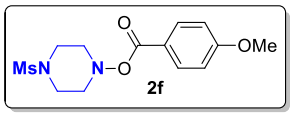
4-tosyl-1,4-diazepan-1-yl 4-methoxybenzoate (2e)

(242 mg, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.51 (d, *J* = 3.0 Hz, 2H), 3.43–3.37 (m, 6H), 2.43 (s, 3H), 2.19–1.94 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 163.7, 143.6, 135.9, 131.6, 130.0, 127.1, 121.4, 113.9, 59.9, 57.0, 55.6, 46.8, 44.2, 23.8, 21.7.

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{25}O_5N_2S$ $[M + H]^+$ 405.1479, found 405.1478.



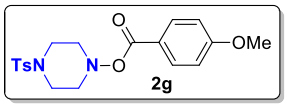
4-(methylsulfonyl)piperazin-1-yl 4-methoxybenzoate (2f)

(239 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.0 Hz, 1H), 7.94 (d, *J* = 2.4 Hz, 1H), 6.92 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.86 (s, 3H), 3.73 (s, 2H), 3.52 (s, 2H), 3.26 (s, 2H), 3.11 (s, 2H), 2.83 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 163.8, 131.7, 121.0, 113.9, 55.6, 55.3, 44.4, 34.9.

HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{19}O_5N_2S$ $[M + H]^+$ 315.1009, found 315.1004.



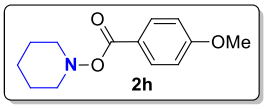
4-tosylpiperazin-1-yl 4-methoxybenzoate (2g)

(238 mg, 61% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96–7.82 (m, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.14–6.79 (m, 2H), 3.85 (s, 3H), 3.68 (s, 2H), 3.44 (s, 2H), 3.07 (s, 2H), 2.84 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 163.8, 144.3, 132.1, 131.7, 129.9, 128.0, 121.1, 113.9, 55.6, 55.2, 44.9, 21.7.

HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{22}O_5N_2NaS$ $[M + Na]^+$ 413.1142, found 413.1140.



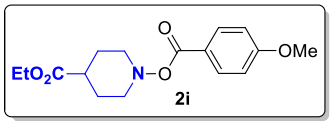
Piperidin-1-yl 4-methoxybenzoate (2h)

(191 mg, 81% yield).

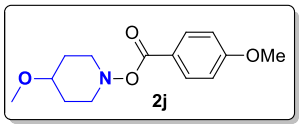
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9.0 Hz, 2H), 6.90 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.48 (s, 2H), 2.74 (s, 2H), 1.82–1.79 (m, 4H), 1.73–1.66 (m, 1H), 1.27 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 163.4, 131.5, 122.1, 113.7, 57.6, 55.6, 25.1, 23.5.

HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{18}O_3N$ $[M + H]^+$ 236.1281, found 236.1280.



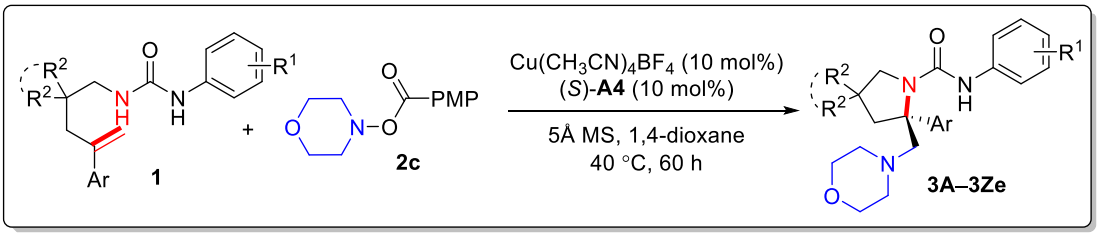
Ethyl-1-((4-methoxybenzoyl)oxy)piperidine-4-carboxylate (2i)
(225 mg, 73% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 4.14 (d, *J* = 6.0 Hz, 2H), 3.85 (s, 3H), 3.59 (s, 1H), 3.25 (s, 1H), 2.75 (s, 1H), 2.66–1.57 (m, 6H), 1.27–1.25 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 164.6, 163.6, 131.6, 121.8, 113.8, 60.7, 56.3, 55.6, 40.6, 27.8, 14.3.
HRMS (ESI) *m*/*z* calcd. for $C_{16}H_{22}O_5N$ $[M + H]^+$ 308.1492, found 308.1491.



4-methoxypiperidin-1-yl 4-methoxybenzoate (2j)
(217 mg, 82% yield).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.85 (s, 3H), 3.53 (s, 1H), 3.35 (s, 3H), 3.22 (s, 2H), 2.84 (s, 1H), 2.26–1.61 (m, 5H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 163.5, 131.6, 121.9, 113.8, 56.1, 55.9, 55.6, 54.3, 52.3.
HRMS (ESI) *m*/*z* calcd. for $C_{14}H_{20}O_4N$ $[M + H]^+$ 266.1387, found 266.1385.

3. General procedures for asymmetric diamination of unactivated alkenes

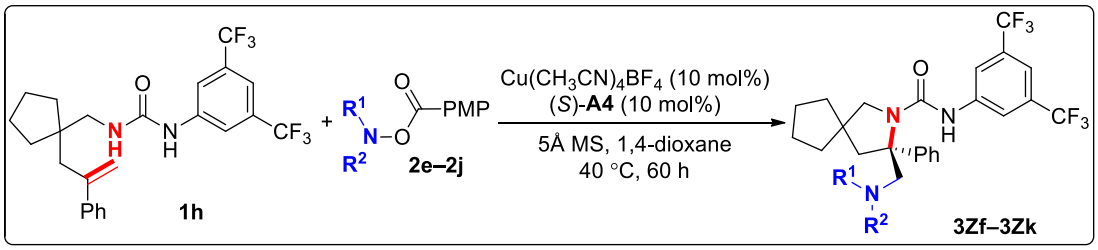
General procedures for asymmetric diamination of substrates 1a–1za, 1bb–1hh with 2c



To an oven-dried resealable Schlenk tube equipped with a magnetic stir bar was added urea substrate **1** (0.1 mmol, 1.0 equiv), $Cu(CH_3CN)_4BF_4$ (3.1 mg, 0.01 mmol, 10 mol%), chiral phosphoric acid (*S*)-**A4** (6.2 mg, 0.01 mmol, 10 mol%), *O*-benzoyl hydroxylmorpholine **2c** (0.15 mmol, 1.5 equiv) and activated 5 Å molecular sieves (100 mg) under argon. Then 2.0 mL of anhydrous 1,4-dioxane was added at room temperature and the sealed tube was stirred at 40 °C. Upon completion (monitored by TLC), the solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (eluent: petroleum ether/EtOAc = 20/1 to 2/1) to afford the desired product **3A–3Ze**.

Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.

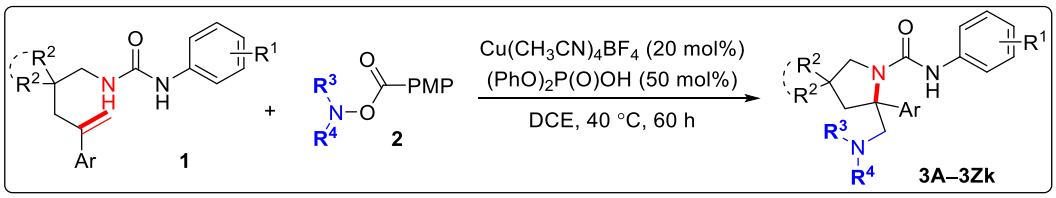
General procedures for asymmetric diamination of substrate 1h with 2e–2j



To an oven-dried resealable Schlenk tube equipped with a magnetic stir bar was added urea substrate **1h** (0.1 mmol, 1.0 equiv), $Cu(CH_3CN)_4BF_4$ (3.1 mg, 0.01 mmol, 10 mol%), chiral phosphoric acid (*S*)-**A4** (6.2 mg, 0.01 mmol, 10 mol%), *O*-benzoylhydroxylamines **2e–2j** (0.15 mmol, 1.5 equiv) and activated 5 Å molecular sieves (100 mg) under argon. Then 2.0 mL of anhydrous 1,4-dioxane was added at room temperature and the sealed tube was stirred at 40 °C. Upon completion (monitored by TLC), the solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (eluent: petroleum ether/EtOAc = 20/1 to 2/1) to afford desired products **3Zf–3Zk**.

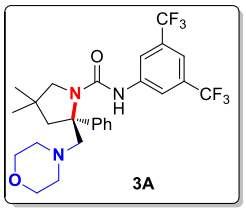
Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.

General procedures for preparation of racemic 3A–3Zk



The racemic products **3A–3Zk** were prepared by following similar procedures as described above using $Cu(CH_3CN)_4BF_4$ (6.2 mg, 0.02 mmol, 20 mol%) and diphenyl phosphate (12.5 mg, 0.05 mmol, 50 mol%) as catalyst at 60 °C in anhydrous DCE (2.0 mL) for 40 h. Upon completion (monitored by TLC), the solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 20/1 to 2/1) to give the racemic products.

Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-phenylpyrrolidine-1-carboxamide (3A)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.3 mL/min, λ = 254 nm), t_R (minor) = 24.78 min, t_R (major) = 27.52 min.

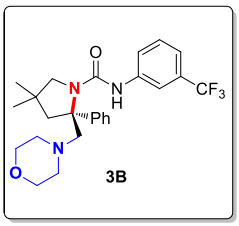
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.04 (s, 1H), 7.64 (s, 2H), 7.39 (s, 1H), 7.31–7.29 (m, 2H), 7.25–7.23 (m, 2H), 7.20–7.17 (m, 1H), 3.75 (d, *J* = 11.0 Hz, 1H), 3.62 (d, *J* = 11.0 Hz, 1H), 3.60–3.46 (m, 4H), 3.41 (d, *J* = 15.0 Hz, 1H), 3.07 (d, *J* = 15.0 Hz, 1H), 2.77 (s, 2H), 2.70–2.68 (m, 2H), 2.18 (d, *J* = 13.5 Hz, 1H), 2.03 (d, *J* = 13.0 Hz, 1H), 1.26 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 144.6, 141.0, 131.9 (q, *J* = 33.1 Hz), 129.0, 127.4, 125.8, 123.4 (q, *J* = 272.7 Hz), 119.0, 115.4, 71.0, 67.1, 66.6, 63.6, 58.8, 56.1, 35.2, 28.9, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{26}H_{30}F_6N_3O_2$ $[M + H]^+$ 530.2237, found 530.2232.

$[\alpha]_D^{27}$ = +19.8 (*c* 1.02, CH_2Cl_2).



(*S*)-4,4-dimethyl-2-(morpholinomethyl)-2-phenyl-*N*-(3-(trifluoromethyl)phenyl)pyrrolidine-1-carboxamide (3B)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 40.19 min, t_R (major) = 45.44 min.

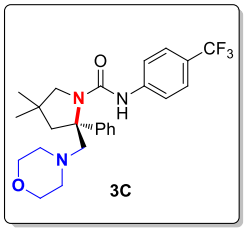
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.64 (s, 1H), 7.52 (s, 1H), 7.32–7.24 (m, 6H), 7.21–7.16 (m, 2H), 3.75 (d, *J* = 11.0 Hz, 1H), 3.63 (d, *J* = 11.0 Hz, 1H), 3.54 (s, 4H), 3.40 (d, *J* = 15.0 Hz, 1H), 3.05 (d, *J* = 15.0 Hz, 1H), 2.73 (s, 2H), 2.68-2.64 (m, 2H), 2.15 (d, *J* = 13.0 Hz, 1H), 2.06 (d, *J* = 15.0 Hz, 1H), 1.25 (s, 3H), 1.00 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 144.7, 131.0 (q, *J* = 32.0 Hz), 139.9, 129.2, 128.8, 127.2, 126.0, 124.1 (q, *J* = 272.4 Hz), 122.8, 118.9 (q, *J* = 3.8 Hz), 116.5 (q, *J* = 3.8 Hz), 70.9, 67.1, 66.6, 63.5, 58.7, 56.0, 35.1, 28.8, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{31}F_3N_3O_2$ $[M + H]^+$ 462.2363, found 462.2361.

$[\alpha]_D^{27}$ = +61.6 (*c* 0.55, CH_2Cl_2).



(*S*)-4,4-dimethyl-2-(morpholinomethyl)-2-phenyl-*N*-(4-(trifluoromethyl) phenyl)pyrrolidine-1-carboxamide (3C)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 18.76 min, t_R (major) = 21.88 min.

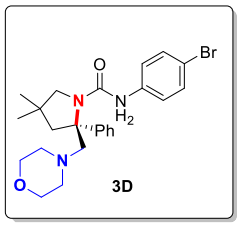
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.51 (s, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.32–7.26 (m, 5H), 7.20–7.18 (m, 1H), 3.76 (d, *J* = 11.0 Hz, 1H), 3.63 (d, *J* = 11.0 Hz, 1H), 3.58–3.55 (m, 4H), 3.40 (d, *J* = 15.0 Hz, 1H), 3.05 (d, *J* = 15.0 Hz, 1H), 2.75 (s, 2H), 2.69–2.67 (m, 2H), 2.14 (d, *J* = 13.0 Hz, 1H), 2.05 (d, *J* = 10.0 Hz, 1H), 1.26 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 144.8, 142.7, 128.9, 127.2, 126.0 (q, *J* = 3.8 Hz), 125.9, 124.5 (q, *J* = 271.2 Hz), 123.9 (q, *J* = 32.6 Hz), 119.0, 71.0, 66.9, 66.7, 63.6, 58.7, 56.1, 35.1, 28.9, 28.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ −61.8 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{31}F_3N_3O_2$ $[M + H]^+$ 462.2363, found 462.2361.

$[\alpha]_D^{27}$ = +28.8 (*c* 0.78, CH_2Cl_2).



(*S*)-*N*-(4-bromophenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-phenylpy rrolidine-1-carboxamide (3D)

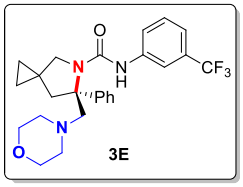
HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.4 mL/min, λ = 254 nm), t_R (minor) = 23.94 min, t_R (major) = 26.18 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.30 (s, 1H), 7.31–7.25 (m, 6H), 7.19 (t, *J* = 7.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 3.73 (d, *J* = 10.5 Hz, 1H), 3.61 (d, *J* = 11.0 Hz, 1H), 3.52 (s, 4H), 3.37 (d, *J* = 15.0 Hz, 1H), 3.02 (d, *J* = 15.0 Hz, 1H), 2.71 (s, 2H), 2.65–2.62 (m, 2H), 2.12 (d, *J* = 13.0 Hz, 1H), 2.06 (s, 1H), 1.24 (s, 3H), 0.99 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 144.9, 138.5, 131.7, 128.8 127.2, 126.1, 121.5, 114.9, 70.9, 67.0, 66.8, 63.6, 58.7, 56.0, 35.1, 28.9, 28.4.

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{31}BrN_3O_2$ $[M + H]^+$ 472.1594, found 472.1598.

$[\alpha]_D^{27}$ = +15.6 (*c* 0.44, CH_2Cl_2).



(*S*)-6-(morpholinomethyl)-6-phenyl-*N*-(3-(trifluoro-methyl)phenyl)-5-az aspiro[2.4]heptane-5-carboxamide (3E)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 19.75 min, t_R (major) = 24.79 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.38 (s, 1H), 7.33–7.28 (m, 4H), 7.23–7.14 (m, 3H), 7.11 (d, *J* = 7.0 Hz, 1H), 4.11 (d, *J* = 10.5 Hz, 1H), 3.67–3.52 (m, 4H), 3.43 (d, *J* = 15.0 Hz, 1H), 3.39 (d, *J* = 11.0 Hz, 1H), 3.14 (d, *J* = 15.0 Hz, 1H), 2.85 (s, 2H), 2.80 (s, 2H), 2.35

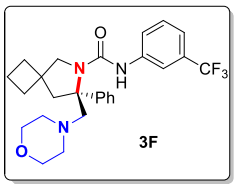
(d, *J* = 13.0 Hz, 1H), 1.74 (d, *J* = 12.0 Hz, 1H), 0.78–0.74 (m, 1H), 0.67–0.60 (m, 2H), 0.51–0.47 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 144.1, 139.9, 131.0 (q, *J* = 32.0 Hz), 129.1, 129.0, 127.5, 125.7, 124.1 (q, *J* = 272.4 Hz), 121.8, 118.6, 115.5, 71.7, 66.9, 64.9, 57.3, 56.4, 52.6, 18.8, 14.3, 6.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.6 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{29}F_3N_3O_2$ $[M + H]^+$ 460.2206, found 460.2204.

$[\alpha]_D^{27}$ = +50.7 (*c* 0.58, CH_2Cl_2).



(*S*)-7-(morpholinomethyl)-7-phenyl-*N*-(3-(trifluoro-methyl)phenyl)-6-azaspiro[3.4]octane-6-carboxamide (3F)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, *λ* = 254 nm), t_R (minor) = 21.15 min, t_R (major) = 28.94 min.

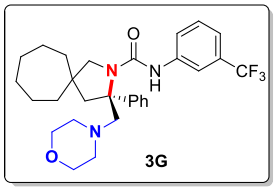
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.26 (s, 1H), 7.42 (s, 1H), 7.31–7.26 (m, 2H), 7.26–7.20 (m, 4H), 7.19–7.07 (m, 2H), 4.08–3.75 (m, 2H), 3.55 (s, 4H), 3.39 (d, *J* = 15.0 Hz, 1H), 2.85 (d, *J* = 15.0 Hz, 1H), 2.78 (s, 2H), 2.72 (s, 2H), 2.23–2.05 (m, 4H), 2.03–1.77 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 144.1, 139.9, 131.0 (q, *J* = 32.0 Hz), 129.2, 128.9, 127.3, 124.1 (q, *J* = 272.8 Hz), 122.2, 118.7 (q, *J* = 3.7 Hz), 115.9 (q, *J* = 3.8 Hz), 70.9, 66.8, 65.7, 61.8, 56.9, 56.2, 42.1, 34.7, 31.2, 17.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{26}H_{31}F_3N_3O_2$ $[M + H]^+$ 474.2363, found 474.2361.

$[\alpha]_D^{27}$ = +38.8 (*c* 0.82, CH_2Cl_2).



(*S*)-3-(morpholinomethyl)-3-phenyl-*N*-(3-(trifluoro-methyl)phenyl)-2-azaspiro[4.6]undecane-2-carboxamide (3G)

HPLC analysis: Chiralcel IA (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.4 mL/min, *λ* = 254 nm), t_R (minor) = 68.49 min, t_R (major) = 72.88 min.

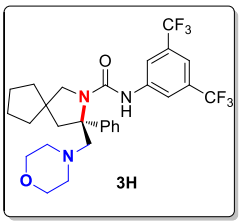
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1H), 7.52 (s, 1H), 7.35–7.24 (m, 6H), 7.21–7.14 (m, 2H),, 3.74 (d, *J* = 11.0 Hz, 1H), 3.64 (d, *J* = 11.0 Hz, 1H), 3.54 (m, 4H), 3.40 (d, *J* = 15.0 Hz, 1H), 3.01 (d, *J* = 15.0 Hz, 1H), 2.73 (s, 2H), 2.67–2.65 (m, 2H), 2.28–2.05 (m, 2H), 1.96–1.82 (m, 1H), 1.70–1.32 (m, 10H), 1.30–1.04 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 144.8, 140.0, 131.0 (q, *J* = 32.0 Hz), 129.2, 128.8, 127.1, 126.0, 124.2 (q, *J* = 272.4 Hz), 122.7, 118.9 (q, *J* = 3.7 Hz), 116.4 (q, *J* = 3.8 Hz), 70.8, 67.1, 66.7, 63.2, 58.1, 56.1, 42.1, 40.8, 40.4, 29.4, 29.3, 24.2, 23.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.7 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{37}F_3N_3O_2$ $[M + H]^+$ 516.2832, found 516.2833.

$[\alpha]_D^{27}$ = +22.1 (*c* 1.17, CH_2Cl_2).



(*S*)-N-(3,5-bis(trifluoromethyl)phenyl)-3-(morpholino-methyl)-3-phenyl-2-azaspiro[4.4]nonane-2-carboxamide (3H)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.3 mL/min, λ = 254 nm), t_R (minor) = 30.97 min, t_R (major) = 36.12 min.

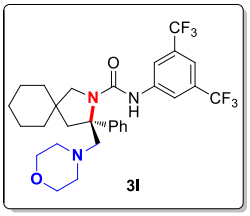
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.92 (s, 1H), 7.60 (s, 2H), 7.37 (s, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.0 Hz, 1H), 3.73 (d, *J* = 11.0 Hz, 1H), 3.67 (d, *J* = 11.0 Hz, 1H), 3.55 (s, 4H), 3.42 (d, *J* = 15.0 Hz, 1H), 3.05 (d, *J* = 15.0 Hz, 1H), 2.80 (s, 2H), 2.74 (s, 2H), 2.33 (d, *J* = 13.0 Hz, 1H), 2.06 (d, *J* = 13.0 Hz, 1H), 1.98–1.79 (m, 1H), 1.79–1.44 (m, 7H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 144.5, 141.0, 131.9 (q, *J* = 33.1 Hz), 129.0, 127.5, 125.7, 123.4 (q, *J* = 272.7 Hz), 118.8 (d, *J* = 3.2 Hz), 115.3 (t, *J* = 3.4 Hz), 70.8, 66.7, 66.2, 62.4, 56.9, 56.2, 46.3, 39.3, 38.2, 25.0, 24.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m/z* calcd. for $C_{28}H_{32}F_6N_3O_2$ $[M + H]^+$ 556.2393, found 556.2392.

$[\alpha]_D^{27}$ = +23.2 (*c* 0.94, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-(morpholino-methyl)-3-phenyl-2-azaspiro[4.5]decane-2-carboxamide (3I)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.3 mL/min, λ = 254 nm), t_R (minor) = 32.81 min, t_R (major) = 41.85 min.

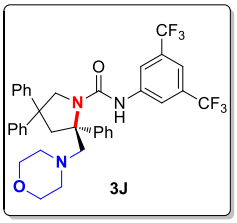
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.00 (s, 1H), 7.64 (s, 2H), 7.39 (s, 1H), 7.32–7.27 (m, 2H), 7.25–7.21 (m, 2H), 7.21–7.16 (m, 1H), 3.78–3.72 (m, 2H), 3.54 (s, 4H), 3.40 (d, *J* = 15.0 Hz, 1H), 3.00 (d, *J* = 15.0 Hz, 1H), 2.72 (s, 2H), 2.67–2.65 (m, 2H), 2.16 (d, *J* = 13.5 Hz, 1H), 2.11–1.93 (m, 1H), 1.74–1.63 (m, 1H), 1.57–1.42 (m, 4H), 1.41–1.28 (m, 4H), 1.28–1.16 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 144.6, 141.1, 131.9 (q, *J* = 33.1 Hz), 129.1, 127.4, 125.8, 123.4 (q, *J* = 272.7 Hz), 119.0 (d, *J* = 3.2 Hz), 115.4 (t, *J* = 3.4 Hz), 70.3, 67.5, 66.6, 61.1, 57.0, 56.1, 38.9, 37.9, 37.9, 25.9, 23.6, 23.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) m/z calcd. for $C_{29}H_{34}F_6N_3O_2$ $[M + H]^+$ 570.2550, found 570.2553.

$[\alpha]_D^{27}$ = +14.7 (*c* 0.74, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(morpholinomethyl)-2,4,4-triphenylpyrrolidine-1-carboxamide (3J)

HPLC analysis: Chiralcel ID (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 15.23 min, t_R (major) = 18.95 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.07 (s, 1H), 7.55 (s, 2H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.38 (s, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.29–7.23 (m, 5H), 7.20–7.14 (m, 6H), 5.10 (d, *J* = 10.5 Hz, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 3.71–3.19 (m, 4H), 3.10 (d, *J* = 15.0 Hz, 1H), 3.04 (d, *J* = 13.0 Hz, 1H), 2.87 (dd, *J* = 13.0, 1.5 Hz, 1H), 2.79–2.22 (m, 5H).

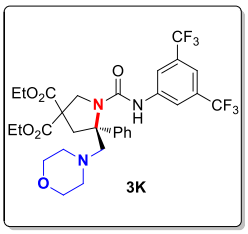
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 146.0, 145.3, 144.7, 140.7, 131.9 (q, *J* = 33.1 Hz), 129.3,

129.0, 128.8, 127.6, 127.0, 126.8, 126.4, 126.1, 125.3, 123.3 (q, *J* = 272.7 Hz), 118.9 (d, *J* = 3.2 Hz), 115.5 (p, *J* = 3.8 Hz), 70.9, 66.5, 63.8, 58.6, 56.3, 55.9, 50.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{36}H_{34}F_6N_3O_2$ $[M + H]^+$ 654.2546, found 654.2550.

$[\alpha]_D^{27}$ = -114.7 (*c* 1.05, CH_2Cl_2).



(*S*)-diethyl-1-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-5-(morpholinomethyl)-5-phenylpyrrolidine-3,3-dicarboxylate (3K)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, *λ* = 254 nm), t_R (minor) = 29.30 min, t_R (major) = 37.98 min.

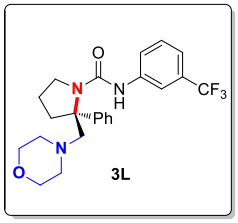
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (s, 2H), 7.40 (s, 1H), 7.36–7.29 (m, 2H), 7.25–7.19 (m, 3H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.34 (d, *J* = 12.0 Hz, 1H), 4.32–4.23 (m, 2H), 4.13–3.91 (m, 2H), 3.55 (s, 4H), 3.41 (d, *J* = 15.0 Hz, 1H), 2.92 (d, *J* = 14.0 Hz, 1H), 2.86–2.78 (m, 2H), 2.74 (s, 2H), 2.67 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H), 1.15 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 169.1, 154.9, 142.5, 140.6, 132.0 (q, *J* = 33.2 Hz), 129.2, 128.1, 125.9, 123.3 (q, *J* = 272.7 Hz), 119.0 (d, *J* = 2.8 Hz), 115.8 (t, *J* = 3.4 Hz), 70.1, 66.7, 65.7, 62.6, 62.5, 56.3, 56.0, 55.1, 49.7, 14.2, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{34}F_6N_3O_6$ $[M + H]^+$ 646.2346, found 646.2346.

$[\alpha]_D^{27}$ = +13.2 (*c* 1.38, CH_2Cl_2).



(*S*)-2-(morpholinomethyl)-2-phenyl-*N*-(3-(trifluoro-methyl)phenyl)pyrrolidine-1-carboxamide (3L)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, *λ* = 254 nm), t_R (minor) = 24.59 min, t_R (major) = 26.94 min.

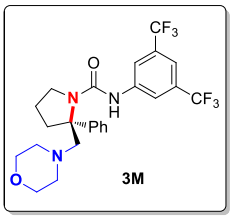
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.42 (s, 1H), 7.33–7.26 (m, 4H), 7.24–7.17 (m, 3H), 7.14–7.10 (m, 1H), 4.04–3.89 (m, 1H), 3.81–3.74 (m, 1H), 3.65–3.53 (m, 4H), 3.46 (d, *J* = 15.0 Hz, 1H), 2.87–2.67 (m, 5H), 2.17–2.05 (m, 2H), 1.98–1.83 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 144.0, 140.0, 131.0 (q, *J* = 32.0 Hz), 129.1, 129.0, 127.5, 125.8, 124.1 (q, *J* = 272.8 Hz), 122.0, 118.7 (q, *J* = 3.7 Hz), 115.7 (q, *J* = 3.9 Hz), 70.1, 66.9, 65.6, 56.2, 50.1, 45.0, 22.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{23}H_{27}F_3N_3O_2$ $[M + H]^+$ 434.2050, found 434.2050.

$[\alpha]_D^{27}$ = +42.6 (*c* 0.63, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(morpholinomethyl)-2-phenylpyrrolidine-1-carboxamide (3M)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 18.42 min, t_R (minor) = 23.66 min.

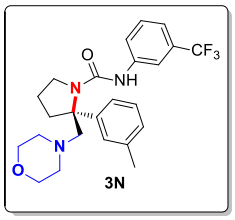
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 7.54 (s, 2H), 7.35 (s, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 3.94 (dd, *J* = 17.6, 9.6 Hz, 1H), 3.80–3.75 (m, 1H), 3.58 (s, 4H), 3.48 (d, *J* = 14.8 Hz, 1H), 2.82–2.78 (m, 5H), 2.28–2.02 (m, 2H), 2.01–1.92 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 143.8, 141.0, 131.9 (q, *J* = 32.8 Hz), 129.2, 127.6, 125.6, 123.4 (q, *J* = 272.2 Hz), 118.3, 115.2, 70.3, 66.9, 65.6, 56.3, 50.1, 45.0, 22.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{26}F_6N_3O_2$ $[M + H]^+$ 502.1924, found 502.1921.

$[\alpha]_D^{27}$ = +28.9 (*c* 0.54, CH_2Cl_2).



(*S*)-2-(morpholinomethyl)-2-(*m*-tolyl)-*N*-(3-(trifluoromethyl)phenyl)pyrrolidine-1-carboxamide (3N)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm), t_R (minor) = 16.38 min, t_R (major) = 19.22 min.

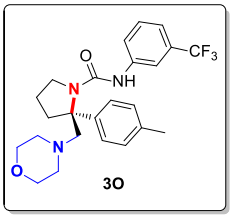
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.36 (s, 1H), 7.22 (d, *J* = 4.5 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 5.0 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 7.5 Hz, 1H), 3.93 (dd, *J* = 18.5, 8.5 Hz, 1H), 3.78–3.74 (m, 1H), 3.58 (s, 4H), 3.43 (d, *J* = 14.5 Hz, 1H), 2.86–2.66 (m, 5H), 2.25 (s, 3H), 2.17–2.02 (m, 2H), 2.01–1.85 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 143.9, 140.1, 138.7, 131.0 (q, *J* = 32.5 Hz), 129.1, 128.8, 128.2, 126.5, 124.1 (q, *J* = 272.2 Hz), 122.8, 122.0, 118.6 (q, *J* = 3.8 Hz), 115.67 (q, *J* = 3.8 Hz), 70.0, 66.9, 65.6, 56.2, 50.0, 44.8, 22.1, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{29}F_3N_3O_2$ $[M + H]^+$ 448.2206, found 448.2205.

$[\alpha]_D^{27}$ = +22.5 (*c* 1.09, CH_2Cl_2).



(*S*)-2-(morpholinomethyl)-2-(*p*-tolyl)-*N*-(3-(trifluoromethyl)phenyl)pyrrolidine-1-carboxamide (3O)

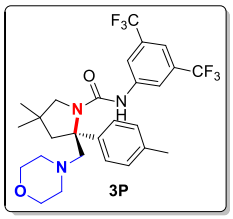
HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm), t_R (major) = 19.80 min, t_R (minor) = 27.46 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.34 (s, 1H), 7.29-7.26 (m, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.16–7.07 (m, 5H), 3.92 (dd, *J* = 18.5, 8.0 Hz, 1H), 3.79–3.71 (m, 1H), 3.57 (s, 4H), 3.42 (d, *J* = 14.5 Hz, 1H), 2.82–2.63 (m, 5H), 2.26 (s, 3H), 2.13–2.04 (m, 2H), 1.99–1.83 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 140.8, 140.0, 137.2, 131.0 (q, *J* = 32.5 Hz), 129.7, 129.2, 125.7, 124.2 (q, *J* = 272.2 Hz), 122.3, 118.7 (q, *J* = 3.8 Hz), 115.9 (q, *J* = 3.8 Hz), 69.9, 66.9, 65.7, 56.2, 50.1, 45.0, 22.0, 20.9.

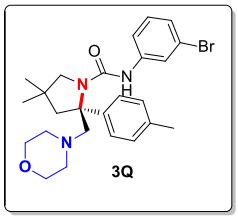
^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{29}F_3N_3O_2$ [M + H]$^+$ 448.2206, found 448.2205.
$[\alpha]_D^{27}$ = +18.1 (*c* 0.66, CH_2Cl_2).



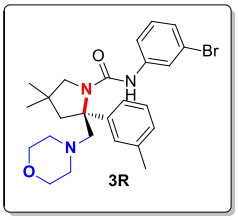
(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(*p*-tolyl)pyrrolidine-1-carboxamide (3P)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.35 mL/min, λ = 254 nm), t_R (minor) = 19.93 min, t_R (major) = 21.16 min.
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.98 (s, 1H) 7.63 (s, 2H), 7.39 (s, 1H), 7.14–7.07 (m, 4H), 3.74 (d, *J* = 11.0 Hz, 1H), 3.60 (d, *J* = 11.0 Hz, 1H), 3.54 (s, 4H), 3.37 (d, *J* = 15.0 Hz, 1H), 3.05 (d, *J* = 15.0 Hz, 1H), 2.75 (s, 2H), 2.69 (s, 2H), 2.26 (s, 3H), 2.15 (d, *J* = 13.5 Hz, 1H), 2.00 (d, *J* = 12.5 Hz, 1H), 1.25 (s, 3H), 1.01 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 141.5, 141.1, 137.2, 131.9 (q, *J* = 33.1 Hz), 129.7, 125.8, 123.4 (q, *J* = 273.3 Hz), 119.1 (d, *J* = 3.0 Hz), 115.4 (t, *J* = 3.8 Hz), 70.9, 67.2, 66.7, 63.5, 58.8, 56.1, 35.1, 28.9, 28.4, 20.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).
HRMS (ESI) m/z calcd. for $C_{27}H_{32}F_6N_3O_2$ [M + H]$^+$ 544.2393, found 544.2395.
$[\alpha]_D^{27}$ = +11.9 (*c* 1.08, CH_2Cl_2).



(*S*)-*N*-(3-bromophenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(*p*-tolyl)pyrrolidine-1-carboxamide (3Q)

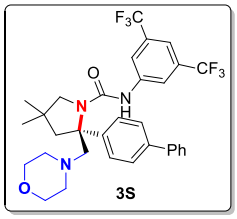
HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 22.98 min, t_R (major) = 27.64 min.
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.33 (s, 1H), 7.47 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.04–7.00 (m, 3H), 3.71 (d, *J* = 10.5 Hz, 1H), 3.62–3.47 (m, 5H), 3.33 (d, *J* = 15.0 Hz, 1H), 2.99 (d, *J* = 15.0 Hz, 1H), 2.68 (s, 2H), 2.64–2.61 (m, 2H), 2.29 (s, 3H), 2.10 (d, *J* = 12.5 Hz, 1H), 2.04 (s, 1H), 1.22 (s, 3H), 0.97 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 141.6, 140.9, 136.9, 130.0, 129.5, 126.0, 125.3, 122.9, 122.5, 118.4, 70.6, 67.3, 66.7, 63.5, 58.8, 56.0, 35.0, 28.9, 28.4, 21.0.
HRMS (ESI) m/z calcd. for $C_{25}H_{33}BrN_3O_2$ [M + H]$^+$ 486.1751, found 486.1754.
$[\alpha]_D^{27}$ = +20.3 (*c* 0.60, CH_2Cl_2).



(*S*)-*N*-(3-bromophenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(*m*-tolyl)pyrrolidine-1-carboxamide (3R)

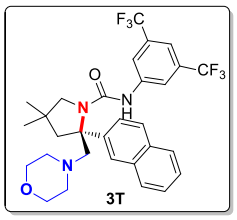
HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 19.02 min, t_R (major) = 25.10 min.
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.46 (s, 1H), 7.22–7.15 (m, 1H), 7.08–6.98 (m, 6H), 3.72 (d, *J* = 11.0 Hz, 1H), 3.60 (d, *J* = 11.0 Hz, 1H), 3.55 (s, 4H), 3.35 (d, *J* = 15.0 Hz, 1H), 3.00 (d, *J* = 15.0 Hz, 1H), 2.69 (s, 2H), 2.65–2.58 (m, 2H), 2.29 (s, 3H), 2.12 (d, *J* = 13.0 Hz, 1H), 2.06 (s, 1H), 1.23 (s, 3H), 0.99 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 144.6, 140.9, 138.5, 130.0, 128.7, 127.9, 126.8, 125.3, 123.2, 122.8, 122.5, 118.3, 70.7, 67.3, 66.8, 63.5, 58.6, 56.0, 35.1, 28.9, 28.4, 21.8.

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{33}BrN_3O_2$ [M + H]$^+$ 486.1751, found 486.1754.
$[\alpha]_D^{27}$ = +28.0 (*c* 0.54, CH_2Cl_2).



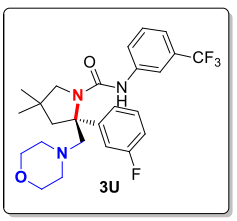
(*S*)-2-([1,1'-biphenyl]-4-yl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)pyrrolidine-1-carboxamide (3S)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.3 mL/min, λ = 254 nm), t_R (major) = 37.58 min, t_R (minor) = 42.29 min.
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.15 (s, 1H), 7.70 (s, 2H), 7.55–7.50 (m, 4H), 7.43–7.39 (m, 3H), 7.35–7.31 (m, 3H), 3.79 (d, *J* = 10.5 Hz, 1H), 3.65 (d, *J* = 11.0 Hz, 1H), 3.57 (s, 4H), 3.45 (d, *J* = 15.0 Hz, 1H), 3.11 (d, *J* = 15.0 Hz, 1H), 2.79 (s, 2H), 2.74 (s, 2H), 2.21 (d, *J* = 13.0 Hz, 1H), 2.07 (s, 1H), 1.28 (s, 3H), 1.05 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 143.6, 141.0, 140.3, 140.0, 132.0 (q, *J* = 33.1 Hz), 128.9, 127.7, 127.6, 127.0, 126.3, 123.4 (q, *J* = 272.7 Hz), 119.0 (d, *J* = 3.2 Hz), 115.5, 70.9, 67.3, 66.6, 63.6, 58.9, 56.1, 35.3, 28.9, 28.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ –63.0 (s, 6F).
HRMS (ESI) *m*/*z* calcd. for $C_{32}H_{34}F_6N_3O_2$ [M + H]$^+$ 606.2250, found 606.2253.
$[\alpha]_D^{27}$ = +9.2 (*c* 1.25, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(naphthalen-2-yl)pyrrolidine-1-carboxamide (3T)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 13.12 min, t_R (major) = 14.75 min.
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.22 (s, 1H), 7.79–7.71 (m, 4H), 7.61 (s, 2H), 7.50–7.44 (m, 2H), 7.33–7.29 (m, 2H), 3.83 (d, *J* = 11.0 Hz, 1H), 3.68 (d, *J* = 11.0 Hz, 1H), 3.54 (d, *J* = 15.0 Hz, 5H), 3.17 (d, *J* = 15.0 Hz, 1H), 2.78 (s, 2H), 2.72 (s, 2H), 2.28 (d, *J* = 13.5 Hz, 1H), 2.10 (d, *J* = 12.0 Hz, 1H), 1.29 (s, 3H), 1.01 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 141.5, 141.0, 133.0, 132.3, 131.9 (q, *J* = 33.1 Hz), 129.3, 128.0, 127.6, 127.0, 126.6, 124.5, 124.1, 123.3 (q, *J* = 272.8 Hz), 119.1 (d, *J* = 2.9 Hz), 115.4, 71.1, 67.6, 66.6, 63.6, 58.6, 56.1, 35.2, 29.0, 28.3.
^{19}F NMR (376 MHz, $CDCl_3$) –63.1 (s, 6F).
HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{32}F_6N_3O_2$ [M + H]$^+$ 580.2393, found 580.2397.
$[\alpha]_D^{27}$ = +38.8 (*c* 1.02, CH_2Cl_2).



(*S*)-2-(3-fluorophenyl)-4,4-dimethyl-2-(morpholinomethyl)-*N*-(3-(trifluoromethyl)phenyl)pyrrolidine-1-carboxamide (3U)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.6 mL/min, λ = 254 nm), t_R (minor) = 18.60 min, t_R (major) = 20.03 min.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.39–7.23 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 7.00 (dt, *J* = 10.8, 2.0 Hz, 1H), 6.90 (td, *J* = 8.0, 2.0 Hz, 1H), 3.72 (d, *J* = 10.8 Hz, 1H), 3.62 (d, *J* = 10.8 Hz, 1H), 3,57 (s, 4H), 3.37 (d, *J* = 14.8 Hz, 1H), 3.04 (d, *J* = 14.8 Hz, 1H), 2.74 (s, 2H), 2.69–2.64 (m, 2H), 2.10 (s, 2H), 1.25 (s, 3H),

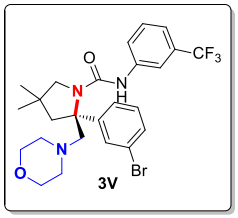
1.01 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1 (d, *J* = 246.6 Hz), 155.7, 148.0, 147.9, 139.9, 131.2 (q, *J* = 32.1 Hz), 130.5 (d, *J* = 5.4 Hz), 129.3, 124.1 (q, *J* = 272.4 Hz), 122.7, 119.2 (d, *J* = 3.4 Hz), 116.4 (q, *J* = 3.9 Hz), 114.1 (d, *J* = 20.9 Hz), 113.4 (d, *J* = 22.9 Hz), 70.8, 66.7, 63.5, 58.6, 56.1, 35.3, 28.8, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) –62.6 (s, 3F), –111.4 (s, 1F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{30}F_4N_3O_2$ $[M + H]^+$ 480.2269, found 480.2269.

$[\alpha]_D^{27}$ = +10.2 (*c* 0.82, CH_2Cl_2).



(*S*)-2-(3-bromophenyl)-4,4-dimethyl-2-(morpholinomethyl)-*N*-(3-(trifluoromethyl)phenyl)pyrrolidine-1-carboxamide (3V)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, *λ* = 254 nm), t_R (major) = 25.26 min, t_R (minor) = 28.18 min.

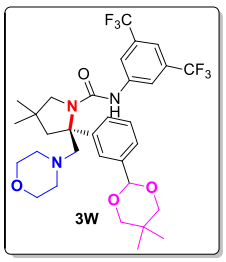
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.63 (s, 1H), 7.56 (s, 1H), 7.44 (t, *J* = 1.7 Hz, 1H), 7.40–7.27 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 8.0 Hz, 1H), 3.72 (d, *J* = 9.5 Hz, 1H), 3.65–3.45 (m, 5H), 3.37 (d, *J* = 15.0 Hz, 1H), 3.03 (d, *J* = 14.5 Hz, 1H), 2.73 (s, 2H), 2.67–2.63 (m, 2H), 2.10 (s, 2H), 1.24 (s, 3H), 1.01 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 147.4, 139.8, 131.2 (q, *J* = 32.1 Hz), 130.5, 130.2, 129.3, 126.1, 124.8, 124.1 (q, *J* = 272.4 Hz), 122.8, 119.2 (d, *J* = 3.4 Hz), 119.0, 116.5 (q, *J* = 3.8 Hz), 70.7, 66.8, 63.4, 58.4, 56.1, 35.4, 28.7, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) –62.7 (s, 3F).

HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{30}BrF_3N_3O_2$ $[M + H]^+$ 540.1468, found 540.1473.

$[\alpha]_D^{27}$ = +11.7 (*c* 0.85, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(3-(5,5-dimethyl-1,3-dioxan-2-yl)phenyl)-4,4-dimethyl-2-(morpholino-methyl)pyrrolidine-1-carboxamide (3W)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, *λ* = 254 nm), t_R (minor) = 13.17 min, t_R (major) = 14.88 min.

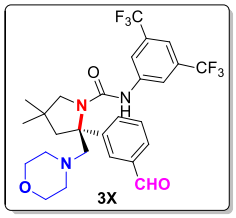
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.82 (s, 1H), 7.65 (s, 2H), 7.57 (s, 1H), 7.36 (s, 1H), 7.29–7.17 (m, 3H), 5.29 (s, 1H), 3.78–3.68 (m, 3H), 3.63–3.50 (m, 7H), 3.42 (d, *J* = 15.2 Hz, 1H), 3.08 (d, *J* = 14.8 Hz, 1H), 2.79 (s, 4H), 2.24 (d, *J* = 13.6 Hz, 1H), 2.02 (d, *J* = 13.6 Hz, 1H), 1.29 (s, 3H), 1.22 (s, 3H), 1.08 (s, 3H), 0.79 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 145.3, 140.9, 139.0, 131.8 (q, *J* = 33.0 Hz), 129.4, 126.6, 125.7, 123.5, 123.4 (q, *J* = 272.7 Hz), 118.8 (q, *J* = 3.0 Hz), 115.2, 101.7, 77.8, 70.8, 66.7, 63.7, 58.3, 56.1, 35.3, 30.3, 29.0, 28.4, 23.0, 21.9.

^{19}F NMR (376 MHz, $CDCl_3$) –63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{32}H_{40}F_6N_3O_4$ $[M + H]^+$ 644.2918, found 644.2900.

$[\alpha]_D^{27}$ = +43.8 (*c* 1.03, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(3-formylphenyl)-4,4-dimethyl-2-(morpholinomethyl)pyrrolidine-1-carboxamide (3X)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 15.72 min, t_R (minor) = 21.77 min.

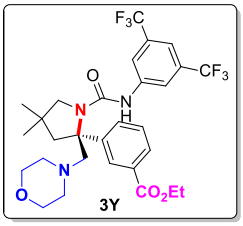
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.12 (s, 1H), 9.97 (s, 1H), 7.84 (s, 1H), 7.69 (d, *J* = 7.0 Hz, 1H), 7.61 (s, 2H), 7.51–7.46 (m, 2H), 7.43–7.37 (m, 1H), 3.75 (s, 1H), 3.71–3.45 (m, 6H), 3.12 (d, *J* = 12.8 Hz, 1H), 2.82 (s, 2H), 2.74 (s, 2H), 2.17–2.04 (m, 2H), 1.29 (s, 3H), 1.04 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 155.6, 146.5, 140.8, 136.6, 132.1 (q, *J* = 33.3 Hz), 132.0(5), 130.1, 127.2, 125.3, 123.3 (q, *J* = 272.7 Hz), 118.7, 115.7, 70.9, 66.7, 63.6, 58.6, 56.2, 44.4, 35.6, 28.8, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{27}H_{30}F_6N_3O_3$ $[M + H]^+$ 558.2186, found 558.2189.

$[\alpha]_D^{27}$ = +45.6 (*c* 0.97, CH_2Cl_2).



(*S*)-Ethyl3-(1-((3,5-bis(trifluoromethyl)phenyl)carbamoyl)-4,4-dimethyl-2-(morpholinomethyl)pyrrolidin-2-yl)benzoate (3Y)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (minor) = 14.59 min, t_R (major) = 15.96 min.

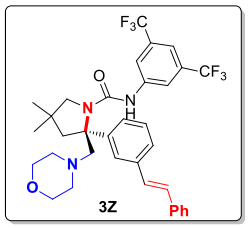
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (s, 1H), 8.03 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.61 (s, 2H), 7.44–7.30 (m, 3H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.76 (d, *J* = 10.8 Hz, 1H), 3.62–3.45 (m, 6H), 3.11 (d, *J* = 15.1 Hz, 1H), 2.83 (s, 2H), 2.77 (s, 2H), 2.18 (d, *J* = 13.6 Hz, 1H), 2.06 (s, 1H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.29 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 155.8, 145.6, 140.9, 132.0 (q, *J* = 33.1 Hz), 130.7, 130.5, 129.7, 128.5, 126.7, 123.3 (q, *J* = 272.7 Hz), 118.6, 115.4, 70.9, 66.7, 63.6, 61.4, 58.5, 56.1, 35.5, 28.9, 28.4, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{34}F_6N_3O_4$ $[M + H]^+$ 602.2448, found 602.2449.

$[\alpha]_D^{27}$ = +19.6 (*c* 0.53, CH_2Cl_2).



(*S,E*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinoethyl)-2-(3-styrylphenyl)pyrrolidine-1-carboxamide (3Z)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 320 nm), t_R (minor) = 15.45 min, t_R (major) = 19.34 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.16 (s, 1H), 7.70 (s, 2H), 7.44 (d, *J* = 7.5 Hz, 2H), 7.40–7.23 (m, 7H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.04–6.92 (m, 2H), 3.79 (d, *J* = 11.0 Hz, 1H), 3.64 (d, *J* = 11.0 Hz, 1H), 3.56 (s, 4H), 3.44 (d, *J* = 15.0 Hz, 1H), 3.10 (d, *J* = 15.0 Hz, 1H), 2.77 (s, 2H), 2.74–2.65 (m, 2H), 2.22 (d, *J* = 13.5 Hz, 1H), 2.08 (s, 1H), 1.27 (s, 3H), 1.03 (s, 3H).

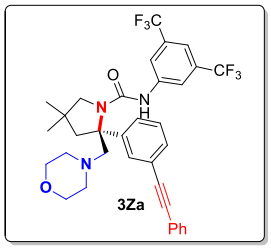
^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 145.0, 141.1, 138.2, 136.9, 132.0 (q, *J* = 33.1 Hz), 129.8, 129.3, 128.8, 128.0, 126.7, 125.2, 125.0, 124.3, 123.4 (q, *J* = 272.7 Hz), 119.1 (d, *J* = 3.1 Hz),

115.5, 71.0, 67.7, 66.6, 63.5, 58.8, 56.1, 35.2, 28.9, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) –63.0 (s, 6F).

HRMS (ESI) m/z calcd. for $C_{34}H_{36}F_6N_3O_2$ $[M + H]^+$ 632.2706, found 632.2707.

$[\alpha]_D^{27}$ = +7.6 (*c* 0.85, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(3-(phenylethynyl)phenyl)pyro-lidine-1-carboxamide (3Za)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 12.87 min, t_R (major) = 14.39 min.

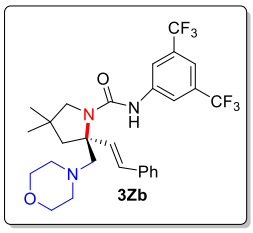
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.18 (s, 1H), 7.73 (s, 2H), 7.51–7.49 (m, 2H), 7.43 (d, *J* = 6.8 Hz, 2H), 7.40–7.32 (m, 4H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 3.76 (d, *J* = 11.2 Hz, 1H), 3.63 (d, *J* = 11.2 Hz, 1H), 3.57 (s, 4H), 3.42 (d, *J* = 15.2 Hz, 1H), 3.08 (d, *J* = 14.8 Hz, 1H), 2.75 (s, 2H), 2.70–2.66 (m, 2H), 2.20 (d, *J* = 13.2 Hz, 1H), 2.11–2.01 (m, 1H), 1.26 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 144.9, 141.0, 132.1 (q, *J* = 33.1 Hz), 131.8, 130.6, 129.1(1), 129.0(7), 128.7, 128.5, 125.9, 124.1, 123.4 (q, *J* = 272.8 Hz), 122.9, 119.2 (q, *J* = 3.2 Hz), 115.6, 90.1, 88.7, 70.7, 67.6, 66.6, 63.5, 58.8, 56.1, 35.2, 28.8, 28.3.

^{19}F NMR (376 MHz, $CDCl_3$) –63.0 (s, 6F).

HRMS (ESI) *m/z* calcd. for $C_{34}H_{34}F_6N_3O_2$ [[M + H]$^+$ 630.2550, found 630.2549.

$[\alpha]_D^{27}$ = +39.5 (*c* 0.65, CH_2Cl_2).



(*S*,*E*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-styrylpyrrolidine-1-carboxamide (3Zb)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 98/2, flow rate 0.4 mL/min, λ = 254 nm), t_R (minor) = 19.88 min, t_R (major) = 22.89 min.

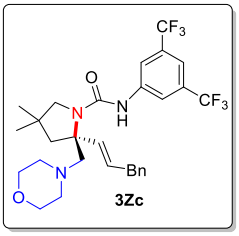
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.08 (s, 1H), 7.93 (s, 2H), 7.44 (s, 1H), 7.31-7.27 (m, 2H), 7.25 (d, *J* = 9.1 Hz, 3H), 6.47 (d, *J* = 16.4 Hz, 1H), 6.32 (d, *J* = 15.6 Hz, 1H), 3.81 (d, *J* = 10.1 Hz, 1H), 3.69-3.56 (m, 4H), 3.37 (d, *J* = 11.1 Hz, 1H), 3.03 (d, *J* = 14.5 Hz, 1H), 2.90 (d, *J* = 14.6 Hz, 1H), 2.80 (s, 2H), 2.75 (s, 2H), 2.05 (d, *J* = 13.1 Hz, 1H), 1.89 (d, *J* = 11.8 Hz, 1H), 1.19 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.2, 141.2, 136.0, 133.4, 132.1 (q, *J* = 33.2 Hz), 129.3, 128.9, 128.1, 126.2, 123.3 (q, *J* = 270.8 Hz), 119.0, 115.4, 68.5, 68.2, 66.6, 61.5, 56.0, 55.6, 35.3, 28.0, 27.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m/z* calcd. for $C_{28}H_{32}F_6N_3O_2$ $[M + H]^+$ 556.2393, found 556.2391.

$[\alpha]_D^{27}$ = +10.2 (*c* 0.52, CH_2Cl_2).



(*S*,*E*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(3-phenylprop-1-en-1-yl)pyrrolidine-1-carboxamide (3Zc)

HPLC analysis: Chiralcel ASH (*n*-hexane/*i*-PrOH = 92/8, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 9.50 min, t_R (minor) = 12.38 min.

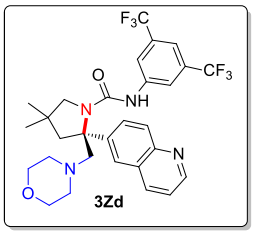
^{1}H NMR (500 MHz, $CDCl_3$) δ 10.88 (s, 1H), 7.93 (s, 2H), 7.46 (s, 1H), 7.21-7.12 (m, 3H), 7.03 (d, *J* = 7.0 Hz, 2H), 5.81-5.70 (m, 1H), 5.66 (d, *J* = 15.8 Hz, 1H), 3.73 (d, *J* = 10.9 Hz, 1H), 3.65-3.47 (m, 4H), 3.34 (d, *J* = 5.8 Hz, 2H), 3.31 (d, *J* = 11.1 Hz, 1H), 2.82 (d, *J* = 14.3 Hz, 1H), 2.75 (d, *J* = 14.6 Hz, 1H), 2.63 (s, 4H), 1.95 (d, *J* = 13.0 Hz, 1H), 1.78 (d, *J* = 12.8 Hz, 1H), 1.15 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 141.4, 139.4, 134.8, 132.0 (q, *J* = 33.2 Hz), 129.5, 128.6, 128.2, 126.5, 123.4 (q, *J* = 272.8 Hz), 118.5, 115.1, 68.4, 67.9, 66.4, 61.5, 56.0, 55.7, 38.8, 35.0, 28.0, 27.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{34}F_6N_3O_2$ $[M + H]^+$ 570.2550, found 570.2546.

$[\alpha]_D^{27}$ = +48.9 (*c* 0.50, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-(morpholinomethyl)-2-(quinolin-6-yl)pyrrolidine-1-carboxamide (3zd)

HPLC analysis: Chiralcel IC (*n*-hexane/*i*-PrOH = 85/15, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 21.71 min, t_R (minor) = 24.45 min.

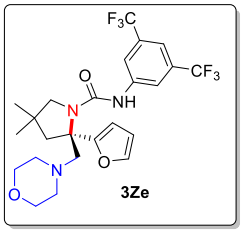
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.39 (s, 1H), 8.89 (s, 1H), 8.06 (t, *J* = 8.4 Hz, 2H), 7.69 (s, 1H), 7.65 (s, 2H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.41 (dd, *J* = 8.2, 4.1 Hz, 1H), 7.37 (s, 1H), 3.82 (d, *J* = 7.7 Hz, 1H), 3.69 (d, *J* = 11.0 Hz, 1H), 3.56 (s, 1H), 3.53 (s, 4H), 3.18 (d, *J* = 14.9 Hz, 1H), 2.76 (s, 2H), 2.68 (dd, *J* = 10.1, 5.2 Hz, 2H), 2.27 (d, *J* = 13.1 Hz, 1H), 2.15 (d, *J* = 20.6 Hz, 1H), 1.27 (s, 3H), 0.98 (s, 3H)..

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 151.0, 147.1, 142.3, 140.8, 136.0, 131.9 (q, *J* = 33.2 Hz), 130.4, 127.9, 127.8, 126.4, 124.4, 123.1 (q, *J* = 272.8 Hz), 119.0, 115.6, 70.7, 67.9, 66.4, 63.4, 58.6, 55.9, 35.1, 28.8, 28.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{31}F_6N_4O_2$ $[M + H]^+$ 581.2346, found 581.2341.

$[\alpha]_D^{27}$ = +8.7 (*c* 1.00, CH_2Cl_2).



(*R*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(furan-2-yl)-4,4-dimethyl-2-(morpholinomethyl)pyrrolidine-1-carboxamide (3ze)

HPLC analysis: Chiralcel IC (*n*-hexane/*i*-PrOH = 98/2, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 22.55 min, t_R (minor) = 24.40 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.15 (s, 1H), 7.82 (s, 2H), 7.42 (s, 1H), 7.29 (d, *J* = 1.1 Hz, 1H), 6.31-6.25 (m, 1H), 6.20 (d, *J* = 3.3 Hz, 1H), 3.74 (d, *J* = 10.9 Hz, 1H), 3.61 (dd, *J* = 6.0, 2.9 Hz, 4H), 3.44 (d, *J* = 10.9 Hz, 1H), 3.16

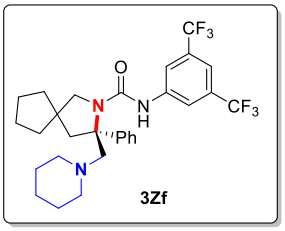
(d, *J* = 14.6 Hz, 1H), 2.97 (d, *J* = 14.6 Hz, 1H), 2.76 (s, 2H), 2.63-2.51 (m, 2H), 2.27 (d, *J* = 13.2 Hz, 1H), 1.84 (d, *J* = 13.2 Hz, 1H), 1.22 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 141.9, 141.1, 131.9 (q, *J* = 33.1 Hz), 123.3 (q, *J* = 272.7 Hz), 118.81, 118.79, 115.3, 110.7, 106.9, 66.9, 66.5, 66.3, 62.3, 55.5, 54.3, 34.9, 28.2, 27.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{28}F_6N_3O_3$ $[M + H]^+$ 520.2029, found 520.2027.

$[\alpha]_D^{27}$ = +8.9 (*c* 1.00, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-phenyl-3-(piperidin-1-ylmethyl)-2-azaspiro[4.4]nonane-2-carboxamide (3Zf)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.3 mL/min, *λ* = 254 nm), t_R (minor) = 12.29 min, t_R (major) = 13.24 min.

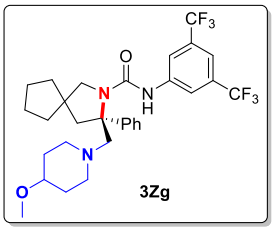
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.60 (s, 1H) 7.66 (s, 2H), 7.33 (s, 1H), 7.30–7.22 (m, 4H), 7.18–7.13 (m, 1H), 3.72 (d, *J* = 11.0 Hz, 1H), 3.68 (d, *J* = 11.5 Hz, 1H), 3.38 (d, *J* = 15.0 Hz, 1H), 2.99 (d, *J* = 15.0 Hz, 1H), 2.71 (s, 3H), 2.30 (d, *J* = 13.5 Hz, 1H), 2.01 (d, *J* = 13.0 Hz, 1H), 1.96–1.88 (m, 1H), 1.79–1.33 (m, 14H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 145.1, 141.5, 131.7 (q, *J* = 32.9 Hz), 128.9, 127.2, 125.7, 123.5 (q, *J* = 272.6 Hz), 118.6 (d, *J* = 3.2 Hz), 114.8, 70.9, 66.2, 62.4, 57.3, 57.0, 46.3, 39.3, 38.1, 25.7, 25.1, 24.3, 23.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{34}ON_3F_6$ $[M + H]^+$ 554.2601, found 554.2601.

$[\alpha]_D^{27}$ = +12.8 (*c* 0.72, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-((4-methoxy-piperidin-1-yl)methyl)-3-phenyl-2-azaspiro[4.4]nonane-2-carboxamide (3Zg)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.3 mL/min, *λ* = 254 nm), t_R (minor) = 21.39 min, t_R (major) = 24.24 min.

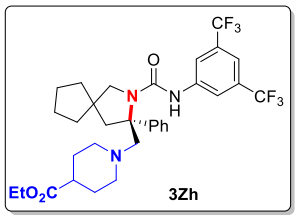
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H) 7.60 (s, 2H), 7.35 (s, 1H), 7.32–7.25 (m, 4H), 7.18 (t, *J* = 7.2 Hz, 1H), 3.74 (d, *J* = 10.8 Hz, 1H), 3.70 (d, *J* = 10.8 Hz, 1H), 3.43 (d, *J* = 15.2 Hz, 1H), 3.28 (s, 3H), 3.25 (s, 1H), 3.04 (d, *J* = 15.2 Hz, 1H). 2.96 (s, 2H), 2.64 (d, *J* = 27.2 Hz, 2H), 2.32 (d, *J* = 13.2 Hz, 1H), 2.09–2.00 (m, 1H), 1.96–1.90 (m, 1H), 1.74–1.71 (m, 4H), 1.65–1.51 (m, 6H), 1.47–1.41 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 144.9, 141.4, 131.8 (q, *J* = 33.1 Hz), 129.0, 127.2, 125.7, 123.4 (q, *J* = 273.2 Hz), 118.5, 114.9, 74.0, 71.0, 65.0, 62.4, 57.0, 55.6, 53.0, 46.3, 39.3, 38.0, 30.2, 25.1, 24.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{36}O_2N_3F_6$ $[M + H]^+$ 584.2706, found 584.2705.

$[\alpha]_D^{27}$ = +11.2 (*c* 0.64, CH_2Cl_2).



(*S*)-Ethyl-1-((2-((3,5-bis(trifluoromethyl)phenyl)car-bamoyl)-3-phenyl-2-azaspiro[4.4]nonan-3-yl)methyl)piperidine-4-carboxylate (3Zh)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.3 mL/min, λ = 254 nm), t_R (minor) = 15.36 min, t_R (major) = 16.96 min.

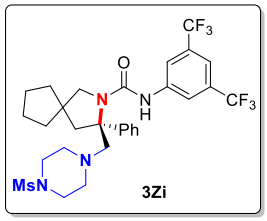
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.25 (s, 1H) 7.62 (s, 2H), 7.34 (s, 1H), 7.31–7.22 (m, 4H), 7.17 (t, *J* = 7.0 Hz, 1H), 4.13–3.98 (m, 2H), 3.73 (d, *J* = 11.5 Hz, 1H), 3.68 (d, *J* = 11.0 Hz, 1H), 3.41 (d, *J* = 15.0 Hz, 1H), 3.08 (s, 2H), 3.02 (d, *J* = 15.0 Hz, 1H), 2.46 (d, *J* = 32.0 Hz, 2H), 2.31 (d, *J* = 13.5 Hz, 1H), 2.03 (d, *J* = 13.0 Hz, 1H), 1.91–1.89 (m, 2H), 1.82–1.47 (m, 10H), 1.42–1.39 (m, 1H), 1.16 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 156.1, 144.7, 141.3, 131.8 (q, *J* = 33.0 Hz), 128.9, 127.3, 125.7, 123.4 (q, *J* = 273.2 Hz), 118.4, 114.9, 70.9, 65.4, 62.4, 60.6, 57.0, 55.3, 46.3, 40.1, 39.3, 38.1, 27.5, 25.0, 24.3, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{32}H_{38}O_3N_3F_6$ $[M + H]^+$ 626.2812, found 626.2813.

$[\alpha]_D^{27}$ = +15.8 (*c* 0.80, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-((4-(methyl-sulfonyl)piperazin-1-yl)methyl)-3-phenyl-2-azaspiro[4.4]nonane-2-carboxamide (3Zi)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm), t_R (minor) = 17.92 min, t_R (major) = 26.09 min.

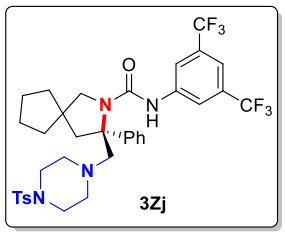
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51 (s, 1H) 7.62 (s, 2H), 7.38 (s, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 6.4 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 3.75 (d, *J* = 10.8 Hz, 1H), 3.68 (d, *J* = 10.8 Hz, 1H), 3.48 (d, *J* = 14.8 Hz, 1H), 3.12–2.87 (m, 9H), 2.57 (s, 3H), 2.34 (d, *J* = 13.2 Hz, 1H), 2.11 (d, *J* = 10.0 Hz, 1H), 1.88 (s, 1H), 1.74–1.53 (m, 6H), 1.39 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 144.0, 141.0, 132.0 (q, *J* = 33.1 Hz), 129.1, 127.6, 125.7, 123.3 (q, *J* = 273.2 Hz), 118.3, 115.3, 70.7, 65.3, 62.4, 56.9, 55.1, 46.2, 45.6, 39.2, 38.1, 33.7, 24.9, 24.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{35}O_3N_4F_6S$ $[M + H]^+$ 633.2329, found 633.2327**.**

$[\alpha]_D^{27}$ = +14.4 (*c* 1.00, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-phenyl-3-((4-tosylpiperazin-1-yl)methyl)-2-azaspiro[4.4]nonane-2-carboxamide (3Zj)

HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 34.39 min, t_R (major) = 39.35 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.23 (s, 1H) 7.37 (d, *J* = 7.5 Hz, 2H), 7.27–7.23 (m, 3H), 7.20–6.93 (m, 7H), 3.67 (d, *J* = 11.0 Hz, 1H), 3.63 (d, *J* = 10.5 Hz, 1H), 3.44 (d, *J* = 15.0 Hz, 1H), 3.05–2.88 (m, 8H), 2.29 (s, 1H), 2.25 (s, 3H), 1.95 (d, *J*

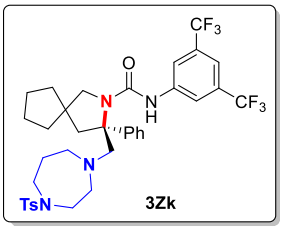
= 54.5 Hz, 2H), 1.84–1.65 (m, 3H), 1.64–1.45 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 144.8, 143.9, 140.2, 131.5, 131.6 (q, *J* = 33.0 Hz), 129.6, 129.2, 127.4, 125.3, 123.1 (q, *J* = 273.2 Hz), 118.8, 115.0, 71.2, 63.6, 62.4, 56.4, 54.8, 46.6, 46.0, 39.4, 38.2, 25.1, 24.2, 21.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{35}H_{39}O_3N_4F_6S$ $[M + H]^+$ 709.2642, found 709.2637.

$[\alpha]_D^{27}$ = +32.5 (*c* 1.22, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-phenyl-3-((4-tosyl-1,4-diazepan-1-yl)methyl)-2-azaspiro[4.4]nonane-2-carboxamide (3Zk)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, *λ* = 254 nm), t_R (major) = 15.46 min, t_R (minor) = 17.37 min.

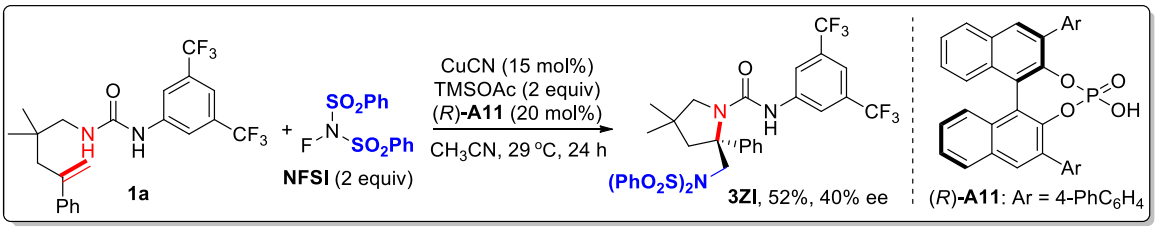
^{1}H NMR (500 MHz, $CDCl_3$) δ 11.39 (s, 1H) 7.78–7.43 (m, 4H), 7.39–7.24 (m, 7H), 7.20 (t, *J* = 7.0 Hz, 1H), 3.86–3.59 (m, 3H), 3.55–3.27 (m, 2H), 3.18–3.15 (m, 3H), 3.00–2.73 (m, 4H), 2.41 (s, 3H), 2.27 (d, *J* = 13.5 Hz, 1H), 2.17 (s, 1H), 1.87–1.79 (m, 3H), 1.76–1.49 (m, 6H), 1.49–1.46 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 143.9, 143.7, 141.6, 135.6, 131.9 (q, *J* = 33.0 Hz), 129.9, 128.9, 127.4, 126.9, 125.8, 123.4 (q, *J* = 273.2 Hz), 118.1, 114.9, 71.1, 62.3, 60.8, 57.1, 56.5, 55.7, 46.8, 45.9, 38.9, 38.0, 27.4, 24.8, 24.5, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ –63.1 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{36}H_{41}O_3N_4F_6S$ $[M + H]^+$ 723.2798, found 723.2797.

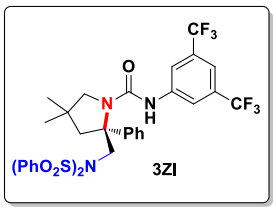
$[\alpha]_D^{27}$ = +6.2 (*c* 0.56, CH_2Cl_2).



Synthesis of 3Zl

An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was added urea substrate **1a** (0.1 mmol, 1.0 equiv), CuCN (1.3 mg, 0.015 mmol, 15 mol%), chiral phosphoric acid (*R*)-**A11** (13.0 mg, 0.02 mmol, 20 mol%) and *N*-fluorobenzenesulfonimide (NFSI, 63 mg, 0.20 mmol, 2 equiv) under argon. Then 2.0 mL of anhydrous CH_3CN was added at room temperature and followed by trimethylsilyl acetate (26.5 mg, 0.20 mmol, 2 equiv). The sealed tube was stirred at 29 °C for 24 h. Upon completion, the solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (eluent: petroleum ether/CH_2Cl_2 = 6/1 to 2/1) to give **3Zl**

(38.4 mg, 52% yield).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-phenyl-2-((*N*-(phenylsulfonyl)phenylsulfonamido)methyl)pyrrolidine-1-carboxamide (3ZI)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 95/05, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 13.66 min, t_R (minor) = 20.95 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 2H), 7.85–7.46 (m, 9H), 7.47–7.28 (m, 6H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.71 (s, 1H), 5.51 (d, *J* = 17.2 Hz, 1H), 4.27 (d, *J* = 17.2 Hz, 1H), 3.57 (d, *J* = 7.6 Hz, 1H), 3.43 (d, *J* = 7.8 Hz, 1H), 2.87 (d, *J* = 13.0 Hz, 1H), 2.25 (d, *J* = 13.0 Hz, 1H), 1.16 (s, 3H), 0.82 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 154.3, 144.5, 141.1, 134.2, 132.2 (q, *J* = 33.2 Hz), 129.1, 128.2, 127.3, 127.1, 123.4 (q, *J* = 272.6 Hz), 119.3 (d, *J* = 3.0 Hz), 116.2 (t, *J* = 3.8 Hz), 73.3, 61.4, 54.1, 52.7, 37.0, 28.4, 27.6.

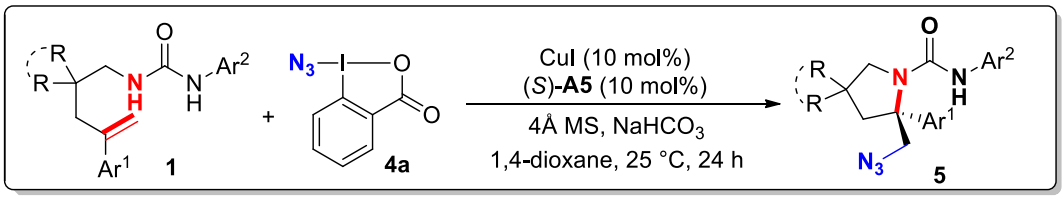
^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) *m/z* calcd. for $C_{34}H_{32}O_5N_3F_6S_2$ $[M + H]^+$ 740.1682, found 740.1663.

$[\alpha]_D^{27}$ = -12.2 (*c* 0.60, CH_2Cl_2).

4. General procedures for asymmetric azidoamination of unactivated alkenes

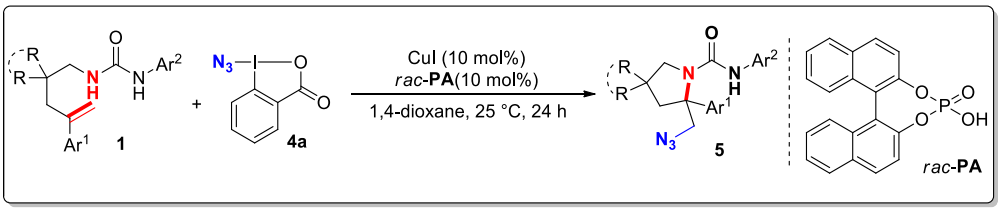
General procedures for asymmetric azidoamination of substrates 1a, 1bb, 1cc, 1dd and 1h with 4a



To an oven-dried resealable Schlenk tube equipped with a magnetic stir bar was added urea substrate **1** (0.1 mmol, 1.0 equiv), CuI (1.9 mg, 0.01 mmol, 10 mol%), chiral phosphoric acid (*S*)-**A5** (7.2 mg, 0.01 mmol, 10 mol%), 1-azido-1λ^3-benzo[d][1,2]iodaoxol-3(1H)-one **4a** (34.7 mg, 0.12 mmol, 1.2 equiv), $NaHCO_3$ (10.1 mg, 0.12 mmol, 1.2 equiv) and activated 4 Å molecular sieves (100 mg) under argon. Then 4.0 mL of anhydrous 1,4-dioxane was added at room temperature and the sealed tube was stirred at 25 °C. Upon completion (monitored by TLC), the solvent was removed *in vacuo* and the residue was purified by silica gel chromatography (eluent: petroleum ether/EtOAc = 50/1 to 20/1) to afford the desired product **5A–5E**.

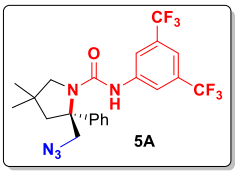
Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.

General procedures for preparation of racemic 5A–5E



The racemic products **5A–5E** were prepared by following similar procedures as described above using CuI (1.9 mg, 0.01 mmol, 10 mol%) and 4-hydroxydinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepine 4-oxide (34.8 mg, 0.01 mmol, 10 mol%) as catalyst at 25 °C in anhydrous 1,4-dioxane (2.0 mL) for 24 h. Upon completion (monitored by TLC), the solvent was removed *in vacuo* and the residue was purified by silica gel column chromatography (eluent: petroleum ether/EtOAc = 50/1 to 20/1) to give the racemic products.

Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.



(*S*)-2-(azidomethyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide (5A)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.8 mL/min, λ = 254 nm), t_R (minor) = 10.18 min, t_R (major) = 11.70 min.

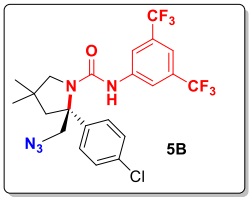
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.49 (s, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 3H), 6.89 (s, 1H), 4.57 (s, 1H), 3.62 (s, 1H), 3.53 (s, 2H), 2.47 (d, *J* = 8.0 Hz, 1H), 2.10 (d, *J* = 8.0 Hz, 1H), 1.18 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 142.8, 140.3, 132.0 (q, *J* = 33.0 Hz), 128.5, 127.3, 125.8, 123.2 (q, *J* = 271.0 Hz), 119.6, 116.3, 71.5, 62.2, 56.9, 52.2, 36.3, 28.0, 27.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{22}F_6N_5O$ $[M + H]^+$ 486.1723, found 486.1718.

$[\alpha]_D^{27}$ = +37.6 (*c* 1.00, CH_2Cl_2).



(*S*)-2-(azidomethyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(4-chlorophenyl)-4,4-dimethylpyrrolidine-1-carboxamide (5B)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 99/1, flow rate 0.4 mL/min, λ = 254 nm), t_R (minor) = 23.42 min, t_R (major) = 24.89 min.

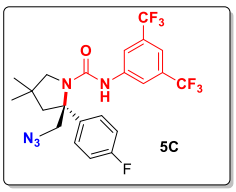
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 2H), 7.52 (s, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 6.82 (s, 1H), 4.57 (d, *J* = 12.5 Hz, 1H), 3.56 (d, *J* = 12.5 Hz, 1H), 3.51 (t, *J* = 12.5 Hz, 2H), 2.48 (d, *J* = 12.5 Hz, 1H), 2.04 (d, *J* = 12.5Hz, 1H), 1.18 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 141.5, 140.2, 133.0, 132.1 (q, *J* = 33.1 Hz), 128.6, 127.3, 123.2 (q, *J* = 271.1 Hz), 119.6, 116.5, 71.4, 62.1, 56.6, 52.1, 36.5, 27.9, 27.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{21}F_6N_5OCl$ $[M + H]^+$ 520.1333, found 520.1333.

$[\alpha]_D^{27}$ = +44.6 (*c* 1.00, CH_2Cl_2).



(*S*)-2-(azidomethyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-(4-fluorophenyl)-4,4-dimethylpyrrolidine-1-carboxamide (5C)

HPLC analysis: Chiralcel ASH (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 10.86 min, t_R (major) = 16.28 min.

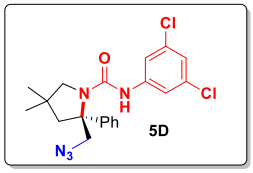
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 2H), 7.53 (s, 1H), 7.26-7.23 (m, 2H), 7.02 (t, *J* = 9.0 Hz, 2H), 6.80 (s, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 3.56 (d, *J* = 12.0 Hz, 1H), 3.52 (t, *J* = 12.0 Hz, 2H), 2.48 (d, *J* = 12.5 Hz, 1H), 2.05 (d, *J* = 12.5Hz, 1H), 1.19 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7 (d, *J* = 245.0 Hz), 153.3, 140.2, 138.7, 132.1 (q, *J* = 33.2 Hz), 127.5 (d, *J* = 7.9 Hz), 123.2 (q, *J* = 271.0 Hz), 119.6, 116.5, 115.3 (d, *J* = 21.3 Hz), 71.4, 62.1, 56.8, 52.4, 36.5, 27.9, 27.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ −63.0 (s, 6F), −115.7 (s, 1F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{21}F_7N_5O$ $[M + H]^+$ 504.1629, found 504.1624.

$[\alpha]_D^{27}$ = +30.7 (*c* 1.00, CH_2Cl_2).



(*S*)-2-(azidomethyl)-*N*-(3,5-dichlorophenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide (5D)

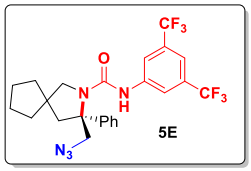
HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm), t_R (minor) = 9.77 min, t_R (major) = 12.72 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 5.6 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 2H), 7.27-7.23 (m, 3H), 7.01 (t, *J* = 5.6 Hz, 1H), 6.55 (s, 1H), 4.56 (d, *J* = 11.6 Hz, 1H), 3.60 (d, *J* = 11.6 Hz, 1H), 3.49 (s, 2H), 2.45 (d, *J* = 12.8 Hz, 1H), 2.08 (d, *J* = 12.8Hz, 1H), 1.18 (s, 3H), 0.90 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 143.5, 141.3, 135.6, 129.0, 127.7, 126.4, 123.6, 118.6, 72.0, 62.6, 57.5, 53.1, 36.9, 28.6, 28.5.

HRMS (ESI) *m*/*z* calcd. for $C_{20}H_{22}N_5OCl_2$ $[M + H]^+$ 418.1196, found 418.1198.

$[\alpha]_D^{27}$ = +35.1 (*c* 1.00, CH_2Cl_2).



(*S*)-3-(azidomethyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-3-phenyl-2-azaspiro[4.4]nonane-2-carboxamide (5E)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.8 mL/min, λ = 254 nm), t_R (minor) = 9.35 min, t_R (major) = 11.68 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (s, 2H), 7.50 (s, 1H), 7.34 (t, *J* = 7.0 Hz, 2H), 7.27 (d, *J* = 7.0 Hz, 3H), 6.81 (s, 1H), 4.58 (s, 1H), 3.69 (s, 1H), 3.60 (s, 2H), 2.60 (d, *J* = 9.0 Hz, 1H), 2.16 (d, *J* = 9.0Hz, 1H), 1.72-1.63 (m, 2H), 1.59 (s, 4H), 1.44-1.42 (m, 1H), 1.05 (s, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 153.1, 142.3, 140.3, 132.1 (q, *J* = 33.0 Hz), 128.5, 127.4, 125.8, 123.2 (q, *J* = 271.0 Hz), 119.4, 116.3, 70.9, 62.0, 56.5, 50.7, 46.9, 38.7, 38.0, 25.0, 24.3.

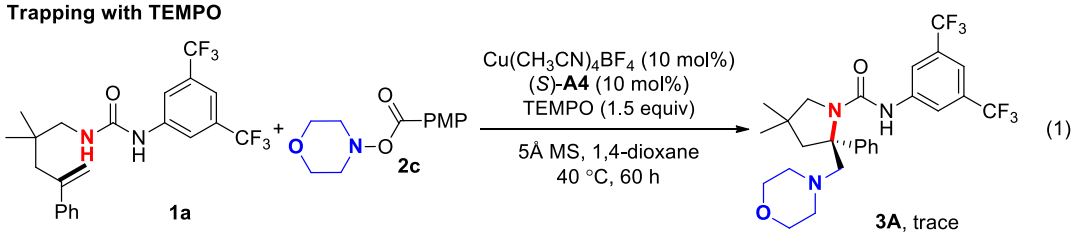
^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{24}H_{24}F_6N_5O$ $[M + H]^+$ 512.1880, found 512.1878.

$[\alpha]_D^{27}$ = +33.0 (*c* 0.90, CH_2Cl_2).

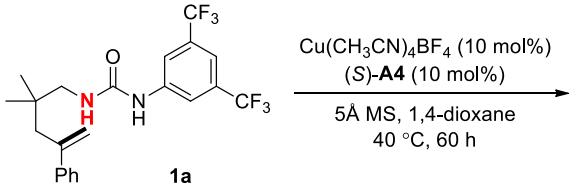
5. Mechanistic study

a) Trapping with TEMPO



(1)

b) Control reaction



(2)

Trapping with TEMPO

To an oven-dried resealable Schlenk tube equipped with a magnetic stir bar was added urea substrate **1a** (0.05 mmol, 1.0 equiv), $Cu(CH_3CN)_4BF_4$ (1.6 mg, 0.005 mmol, 10 mol%), chiral phosphoric acid (*S*)-**A4** (3.1 mg, 0.005 mmol, 10 mol%), 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 11.7 mg, 0.075 mmol, 1.5 equiv), *O*-benzoyl hydroxylmorpholine **2c** (0.075 mmol, 1.5 equiv) and activated 5 Å molecular sieves (50 mg) under argon. Then 1.0 mL of anhydrous 1,4-dioxane was added at room temperature and the sealed tube was stirred at 40 °C for 60 h. Upon completion, $PhOCF_3$ (internal standard, 0.1 mmol, 2.0 equiv) was added to the reaction mixture for direct NMR charaterization. Yield was based on ^{19}F NMR analysis of the crude product.

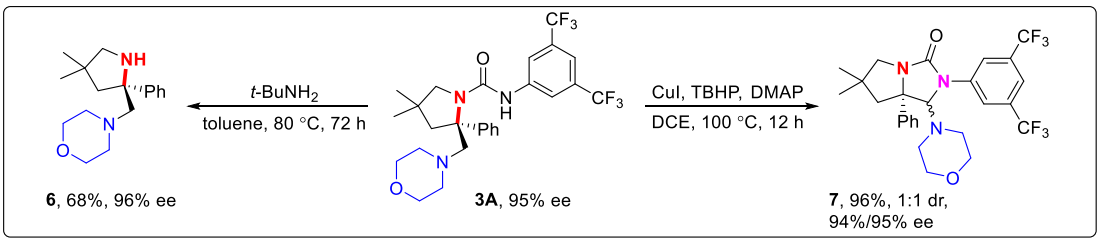
Note: Since the reaction is sensitive to water and air, Schlenk tubes and the reagents must be dried prior to use.

Control reactions

Control reactions were conducted by following the same procedures as described above without addition of TEMPO together with special modifications, as listed below.

For eq. 2, no **2c** was added.

6. Transformations

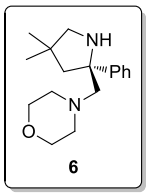


Synthesis of 6

Compound **6** was prepared by following literature procedures.[5] An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with **3A** (158.7 mg, 0.3 mmol), *tert*-butylamine (0.064 mL, 0.6 mmol) and toluene (5.0 mL). The sealed tube was then stirred at 80 °C for 72 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. Then the crude product was concentrated *in vacuo* and purified by flash chromatography using dichloromethane/methanol (10/1) as the eluent to give **6** (56.1 mg, 68% yield).

Synthesis of 7

Compound **7** was prepared by following literature procedures.[6] An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with **3A** (52.9 mg, 0.1 mmol), CuI (1.9 mg, 0.010 mmol), DMAP (3.7 mg, 0.030 mmol), (*t*-BuO)$_2$ (29.2 mg, 0.20 mmol) and DCE (0.5 mL). The flask was then sealed and the mixture was stirred at 100 °C for 12 h. Upon completion, the reaction mixture was cooled down to room temperature and quenched by water (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL) and the organic layer was washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue was purified by flash chromatography using petroleum ether/EtOAc (8/1) as the eluent to give **7-*syn*** (25.3 mg, 48% yield) and **7-*anti*** (25.4 mg, 48% yield).



(*S*)-4-((4,4-dimethyl-2-phenylpyrrolidin-2-yl)methyl)morpholine (6)

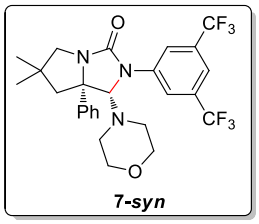
HPLC analysis: Chiralcel AD3 (*n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 8.64 min, t_R (major) = 9.29 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.30 (m, 2H), 7.19 (m, 1H), 3.57 (t, *J* = 4.4 Hz, 4H), 2.82 (d, *J* = 10.4 Hz, 1H), 2.72 (d, 10.4 Hz, 1H), 2.63 (d, *J* = 13.6 Hz, 1H), 2.55 (d, *J* = 13.6 Hz, 1H), 2.35–2.29 (m, 2H), 2.28–2.21 (m, 2H), 1.94 (d, *J* = 12.8 Hz, 1H), 1.87 (d, *J* = 12.8 Hz, 1H) 1.15 (s, 3H), 0.94 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 128.0, 126.1(3), 126.0(7), 69.2, 68.7, 67.3, 59.6, 55.7, 52.6, 40.1, 29.2, 29.1.

HRMS (ESI) *m*/*z* calcd. for $C_{17}H_{27}ON_2$ $[M + H]^+$ 275.2118, found 275.2118.

$[\alpha]_D^{27}$ = -11.7 (*c* 0.86, CH_2Cl_2).



(1*S*,7a*S*)-2-(3,5-bis(trifluoromethyl)phenyl)-6,6-dimethyl-1-morpholino-7a-phenyltetrahydro-1H-pyrrolo[1,2-c]imidazol-3(2H)-one (7-*syn*)

HPLC analysis: Chiralcel ASH (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 9.27 min, t_R (minor) = 12.66 min.

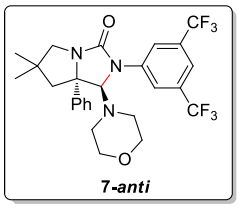
^{1}H NMR (500 MHz, Acetone-d_6) δ 8.38 (s, 2H), 7.75 (s, 1H), 7.57–7.24 (m, 5H), 5.92 (s, 1H), 3.87 (d, *J* = 12.5 Hz, 1H), 3.24 (br s, 1H), 3.02 (d, *J* = 12.5 Hz, 1H), 2.97–2.92 (m, 2H), 2.82 (d, *J* = 17.0 Hz, 1H) 2.68 (br s, 1H), 2.50–2.10 (m, 5H), 1.06 (s, 3H), 0.67 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6) δ 161.5, 142.9, 141.4, 132.4 (q, *J* = 33.1 Hz), 130.1, 129.0, 128.6, 128.0, 126.5, 124.5 (q, *J* = 272.7 Hz), 122.5, 117.3 (p, *J* = 3.8 Hz), 82.4, 75.5, 67.8, 66.9, 60.7, 55.7, 53.7, 44.8, 40.1, 31.7, 29.1.

^{19}F NMR (376 MHz, Acetone-d_6) δ −63.4 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{26}H_{28}O_2N_3F_6$ $[M + H]^+$ 528.2080, found 528.2075.

$[\alpha]_D^{27}$ = -7.3 (*c* 0.97, CH_2Cl_2).



(1*R*,7a*S*)-2-(3,5-bis(trifluoromethyl)phenyl)-6,6-dimethyl-1-morpholino-7a-phenyltetrahydro-1H-pyrrolo[1,2-c]imidazol-3(2H)-one(7-*anti*)

HPLC analysis: Chiralcel OD3 (*n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (minor) = 10.27 min, t_R (major) = 11.15 min.

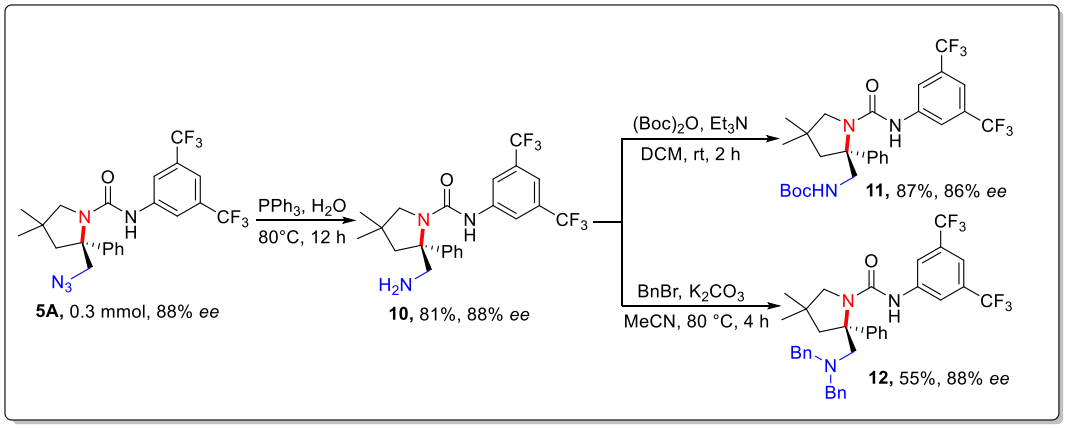
^{1}H NMR (500 MHz, Acetone-d_6) δ 8.39 (s, 2H), 7.62 (s, 1H), 7.49–7.47 (m, 2H), 7.44–7.38 (m, 2H), 7.31–7.28 (m, 1H), 5.17 (s, 1H), 3.61–3.57 (m, 2H), 3.53 (d, *J* = 11.0 Hz, 1H), 3.51–3.48 (m, 1H), 3.16 (d, *J* = 10.5 Hz, 1H), 3.03–3.00 (m, 2H), 2.97–2.88 (m, 2H), 2.84 (s, 1H), 2.67 (d, *J* = 13.0 Hz, 1H), 2.29 (d, *J* = 13.5 Hz, 1H), 1.26 (s, 3H), 0.78 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6) δ 158.1, 147.3, 143.0, 132.2 (q, *J* = 33.0 Hz), 129.8, 128.2, 126.1, 124.6 (q, *J* = 272.7 Hz), 120.3, 116.3 (p, *J* = 3.8 Hz), 86.3, 74.7, 67.9, 58.0, 48.6, 47.7, 42.8, 30.1, 29.3.

^{19}F NMR (376 MHz, Acetone-d_6) δ −63.5 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{26}H_{28}O_2N_3F_6$ $[M + H]^+$ 528.2080, found 528.2081.

$[\alpha]_D^{27}$ = -17.5 (*c* 0.95, CH_2Cl_2).



Synthesis of 10

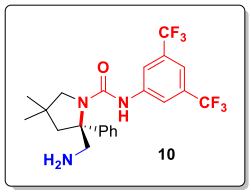
An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with **5A** (145.5 mg, 0.3 mmol), triphenylphosphane (118.0 mg, 0.45 mmol), 0.1mL H_2O and tetrahydrofuran (3.0 mL). The sealed tube was then stirred at 80 °C for 12 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. Then the crude product was concentrated *in vacuo* and purified by flash chromatography using dichloromethane/methanol (10/1) as the eluent to give **10** (111 mg, 81% yield).

Synthesis of 11

An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with **10** (66.0 mg, 0.14 mmol), di-*tert*-butyl dicarbonate (49.0 μL, 0.21 mmol) and 2.0 mL dichloromethane, then added triethylamine (39.0 μL, 0.28 mmol) at 0 °C. The solution was stirred at room temperature for 2 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. Then the crude product was concentrated *in vacuo* and purified by flash chromatography using petroleum ether/EtOAc (8/1) as the eluent to give **11** (70 mg, 87% yield).

Synthesis of 12

An oven-dried resealable Schlenk tube equipped with a magnetic stir bar was charged with **10** (66.0 mg, 0.14 mmol), (bromomethyl)benzene (42 μL, 0.35 mmol), K_2CO_3 (97.0 mg, 0.7 mmol) and 2.0 mL acetonitrile. The solution was stirred at 80 °C for 12 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. The solid was filtered, and the liquid was concentrated *in vacuo* and purified by flash chromatography using petroleum ether/EtOAc (6/1) as the eluent to give **12** (49 mg, 55% yield).



(*S*)-2-(aminomethyl)-*N*-(3,5-bis(trifluoromethyl)phenyl)-4,4-dimethyl-2-phenylpyrrolidine-1-carboxamide (10)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.8 mL/min, λ = 254 nm), t_R (minor) = 15.81 min, t_R (major) = 25.43 min.

^{1}H NMR (500 MHz, $CDCl_3$) δ 12.60 (s, 1H), 7.90 (s, 2H), 7.38 (t, *J* = 7.5 Hz, 3H), 7.27 (s, 1H), 7.24 (d, *J* = 7.5 Hz, 2H), 3.81 (d, *J* = 13.5 Hz, 1H), 3.81 (dd, *J* = 11.2 Hz, 15 Hz,

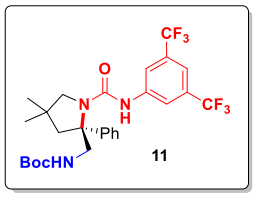
2H), 3.33 (d, *J* = 13.5 Hz, 1H), 2.23 (d, *J* = 13.0 Hz, 1H), 2.13 (d, *J* = 13.0 Hz, 1H), 1.76 (br s, 2H), 1.15 (s, 3H), 0.83 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 142.5, 142.4, 131.6 (q, *J* = 32.7 Hz), 129.2, 127.1, 125.8, 124.4 (q, *J* = 271.0 Hz), 118.2, 114.5, 70.4, 63.1, 59.0, 51.1, 34.2, 28.9, 27.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{22}H_{24}F_6N_3O$ $[M + H]^+$ 460.1818, found 460.1817.

$[\alpha]_D^{27}$ = -9.5 (*c* 1.00, CH_2Cl_2).



(*S*)-*tert*-butyl (1-((3,5-bis(trifluoromethyl)phenyl)carbamoyl) -4,4-dimethyl-2-phenylpyrrolidin-2-yl)methyl)carbamate (11)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.4 mL/min, *λ* = 254 nm), t_R (minor) = 14.67 min, t_R (major) = 18.02 min.

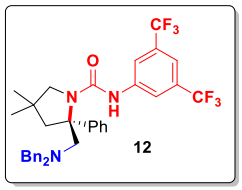
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 2H), 7.50 (s, 1H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.0 Hz, 3H), 6.95 (s, 1H), 5.50 (s, 1H), 4.01 (d, *J* = 7.5 Hz, 1H), 3.74 (d, *J* = 7.5 Hz, 1H), 3.51 (s, 2H), 2.31 (d, *J* = 13.0 Hz, 1H), 2.16 (d, *J* = 13.0 Hz, 1H), 1.39 (s, 9H), 1.14 (s, 3H), 0.84 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 153.7, 142.9, 140.5, 133.9 (q, *J* = 33.1 Hz), 128.5, 126.9, 125.7, 124.1 (q, *J* = 271.1 Hz), 119.4, 116.3, 79.4, 73.3, 62.2, 53.8, 48.5, 36.0, 29.0, 28.3, 28.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F).

HRMS (ESI) *m*/*z* calcd. for $C_{27}H_{31}F_6N_3O_3Na$ $[M + Na]^+$ 582.2162, found 582.2156.

$[\alpha]_D^{27}$ = +25.1 (*c* 0.60, CH_2Cl_2).



(*S*)-*N*-(3,5-bis(trifluoromethyl)phenyl)-2-((dibenzylamino)methyl)-4,4-di methyl-2-phenylpyrrolidine-1-carboxamide(12)

HPLC analysis: Chiralcel ODH (*n*-hexane/*i*-PrOH = 98/2, flow rate 0.4 mL/min, *λ* = 254 nm), t_R (minor) = 15.34 min, t_R (major) = 17.20 min.

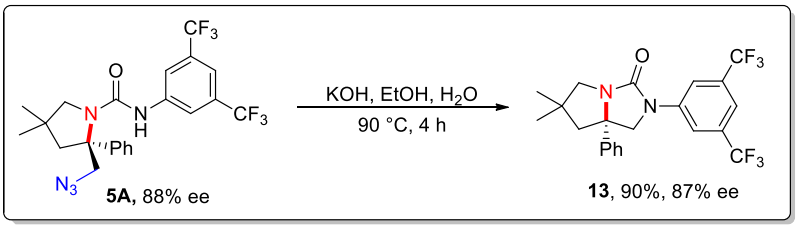
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.78 (s, 1H), 8.25 (s, 2H), 7.52 (s, 1H), 7.35-7.30 (m, 8H), 7.25-7.19 (m, 6H), 7.15 (t, *J* = 7.2 Hz, 1H), 3.98 (d, *J* = 14.4 Hz, 1H), 3.87 (d, *J* = 14.4 Hz, 2H), 3.66 (d, *J* = 10.0 Hz, 2H), 3.62 (s, 1H), 3.52 (d, *J* = 9.6 Hz, 1H), 3.02 (d, *J* = 14.4 Hz, 1H), 2.73 (d, *J* = 12.8 Hz, 1H), 1.60 (d, *J* = 12.8 Hz, 1H), 1.10 (s, 3H), 0.74 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 154.0, 145.9, 143.1, 139.6, 130.8 (q, *J* = 32.4 Hz), 129.2, 128.6, 127.9, 127.3, 127.0, 126.2, 123.9 (q, *J* = 270.8 Hz), 119.7, 114.5, 73.9, 62.2, 59.1, 51.5, 36.1, 28.6, 28.2.

^{19}F NMR (376 MHz, DMSO-d_6) δ −61.7 (s, 6F).

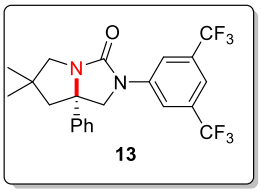
HRMS (ESI) *m*/*z* calcd. for $C_{36}H_{36}F_6N_3O$ $[M + H]^+$ 640.2757, found 640.2754.

$[\alpha]_D^{27}$ = +17.5 (*c* 0.60, CH_2Cl_2).



Synthesis of 13

An resealable Schlenk tube equipped with a magnetic stir bar was charged with **5A** (48.5 mg, 0.1 mmol), KOH (16.5 mg, 0.3 mmol), EtOH (1.0 mL) and water (1.0 mL). The solution was stirred at 90 °C for 4 h. Upon completion (monitored by TLC), the reaction mixture was cooled down to temperature. The solution was extracted with EA (5.0 mL) three times and dried with Na_2SO_4, then the solution was concentrated *in vacuo* and purified by flash chromatography using petroleum ether/EtOAc (50/1) as the eluent to give **5l** (39.8 mg, 90% yield).



(*S*)-2-(3,5-bis(trifluoromethyl)phenyl)-6,6-dimethyl-7a-phenylhexahydro-3H-pyrrolo[1,2-c]imidazol-3-one (13)

HPLC analysis: Chiralcel ASH (*n*-hexane/*i*-PrOH = 97/3, flow rate 0.4 mL/min, λ = 254 nm), t_R (minor) = 12.26 min, t_R (major) = 15.81 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 2H), 7.51 (s, 1H), 7.47–7.38 (m, 4H), 7.35-7.29 (m, 1H), 4.19 (d, *J* = 9.1 Hz, 1H), 3.82 (d, *J* = 12.0 Hz, 1H), 3.76 (d, *J* = 9.1 Hz, 1H), 2.99 (d, *J* = 12.0 Hz, 1H), 2.45 (d, *J* = 12.9 Hz, 1H), 2.12 (d, *J* = 12.9 Hz, 1H), 1.16 (s, 3H), 0.87 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 144.7, 141.3, 132.1 (q, *J* = 33.4 Hz), 129.2, 127.7, 124.5, 123.3 (q, *J* = 271.4 Hz), 116.9, 115.7, 67.8, 59.0, 58.0, 53.8, 41.1, 30.1, 28.1.

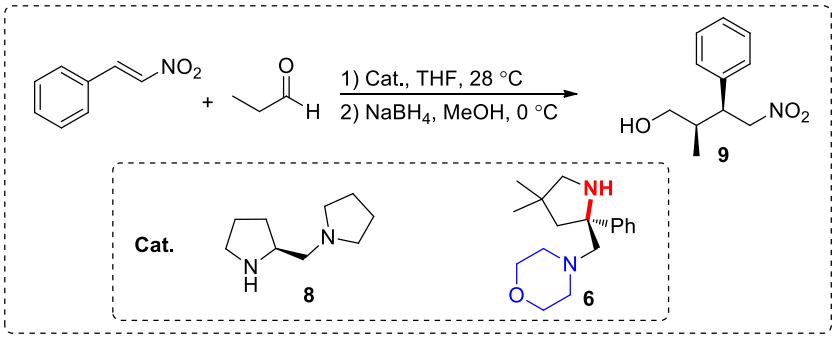
^{19}F NMR (376 MHz, $CDCl_3$) δ −62.9 (s, 6F)

HRMS (ESI) *m/z* calcd. for $C_{22}H_{21}F_6N_2O$ $[M + H]^+$ 443.1553, found 443.1540.

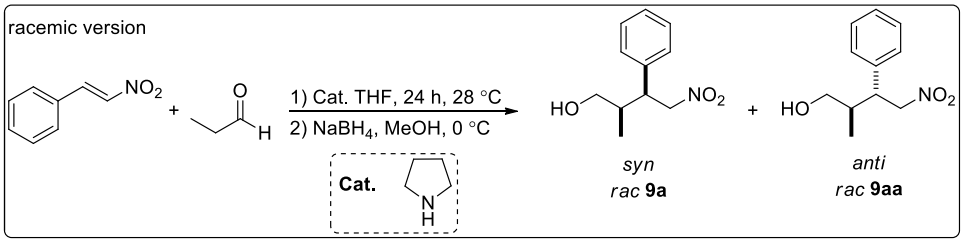
$[\alpha]_D^{27}$ = -49.9 (*c* 1.00, CH_2Cl_2).

7. Application

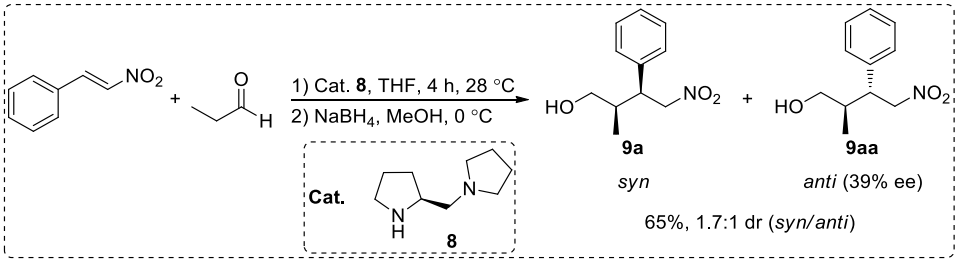
Asymmetric Michael addition

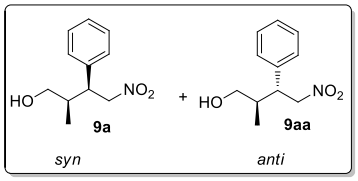


The reaction was conducted by following literature procedures.[7] To a solution of *β*-nitrostyrene (0.05 mmol) in THF (0.2 mL) was added propionaldehyde (0.15 mmol) and pyrrolidine-derived diamine catalyst **6** or **8** (0.015 mmol, 30 mol%). The reaction was stirred at 28 °C for the appropriate time (for **6**: 60 h; for **8**: 4 h). The solution was then diluted with MeOH (1 mL) and $NaBH_4$ (0.25 mmol) was added at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. Upon workup, the solvent was removed *in vacuo*. The residue was treated with saturated NH_4Cl solution (2 mL) and extracted thoroughly with EtOAc (3 × 2 mL). The combined organic phases were dried (Na_2SO_4), concentrated and purified by silica gel chromatography (eluent: petroleum ether/EtOAc = 8/1) to give the desired product **9**.



The racemic products **9a** and **9aa** were prepared by following the same procedures as described above with pyrrolidine as the catalyst.





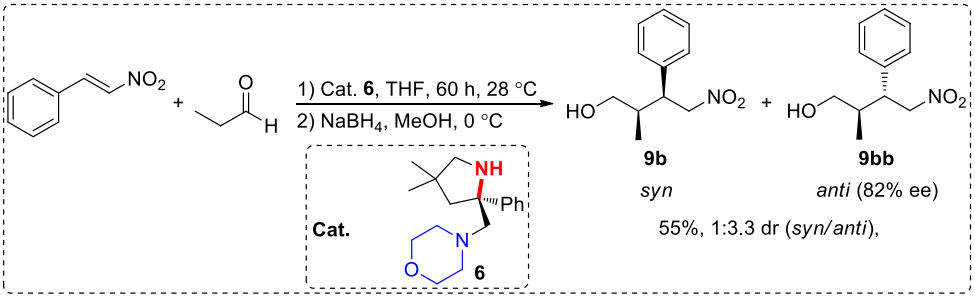
(2*R*,3*S*)-2-methyl-4-nitro-3-phenylbutan-1-ol (9a),
(2*R*,3*R*)-2-methyl-4-nitro-3-phenylbutan-1-ol (9aa)

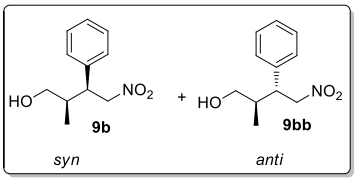
HPLC analysis: Chiralcel IC (*n*-hexane/*i*-PrOH = 96/4, flow rate 1.2 mL/min, λ = 214 nm), t_R (major) = 26.36 min, t_R (minor) = 31.04 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.10 (m, 5H, –C_6H_5), 4.90 (*syn*) and 4.86 (*anti*) (dd, *J* = 12.8, 6.4 and 12.8, 5.6 Hz, 1H, –CH*H*NO_2), 4.78 (*anti*) and 4.76 (*syn*) (dd, *J* = 12.8, 10.0 and 14.4, 9.6 Hz, 1H, –C*H*HNO_2), 3.69–3.63 (*syn*) and 3.56–3.52 (*anti*) (m, 1H, –C*H*–Ph), 3.61 (*syn*) and 3.43 (*anti*) (dd, *J* = 10.8, 4.4 and 10.8, 6.0 Hz, 1H, –CH*H*OH), 3.49 (*syn*) and 3.37 (*anti*) (dd, *J* = 10.8, 6.8 and 10.8, 5.2 Hz, 1H, –C*H*HOH), 2.16–1.94 (m, 1H, –*CH*–CH_3), 1.04 (*anti*) and 0.82 (*syn*) (d, *J* = 6.8 and 6.8 Hz, 3H, –CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) (*anti*) δ 138.1, 128.9, 128.3, 127.8, 79.1, 65.5, 47.3, 38.7, 15.2; (*syn*) δ 137.8, 128.8, 128.5, 127.7, 78.9, 65.8, 46.3, 38.5, 14.2.

$[\alpha]_D^{27}$ = -9.6 (*c* 0.82, CH_2Cl_2).





(2*R*,3*S*)-2-methyl-4-nitro-3-phenylbutan-1-ol (9b),
(2*R*,3*R*)-2-methyl-4-nitro-3-phenylbutan-1-ol (9bb)

HPLC analysis: Chiralcel IC (*n*-hexane/*i*-PrOH = 96/4, flow rate 1.2 mL/min, λ = 214 nm), t_R (major) = 27.12 min, t_R (minor) = 31.97 min.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.10 (m, 5H, –C_6H_5), 4.90 (*syn*) and 4.86 (*anti*) (dd, *J* = 12.4, 6.0 and 12.8, 5.6 Hz, 1H, –C*H*HNO_2), 4.78 (*anti*) and 4.76 (*syn*) (dd, *J* = 12.4, 10.0 and 12.8, 9.6 Hz, 1H, –CH*H*NO_2), 3.69–3.63 (*syn*) and 3.56–3.52 (*anti*) (m, 1H, –C*H*–Ph), 3.61 (*syn*) and 3.43 (*anti*) (dd, *J* = 11.2, 4.8 and 10.8, 6.0 Hz, 1H, –C*H*HOH), 3.49 (*syn*) and 3.37 (*anti*) (dd, *J* = 10.8, 6.8 and 10.8, 5.2 Hz, 1H, –CH*H*OH), 2.16–1.94 (m, 1H, –*CH*–CH_3) , 1.04 (*anti*) and 0.82 (*syn*) (d, *J* = 7.2 and 7.2 Hz, 3H, –CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) (*anti*) δ 138.1, 129.0, 128.3, 127.8, 79.2, 65.5, 47.3, 38.7, 15.2; (*syn*) δ 137.8, 128.8, 128.5, 127.7, 78.9, 65.8, 46.4, 38.5, 14.2.

$[\alpha]_D^{27}$ = -32.0 (*c* 0.68, CH_2Cl_2).

IV. Supplemental Figures

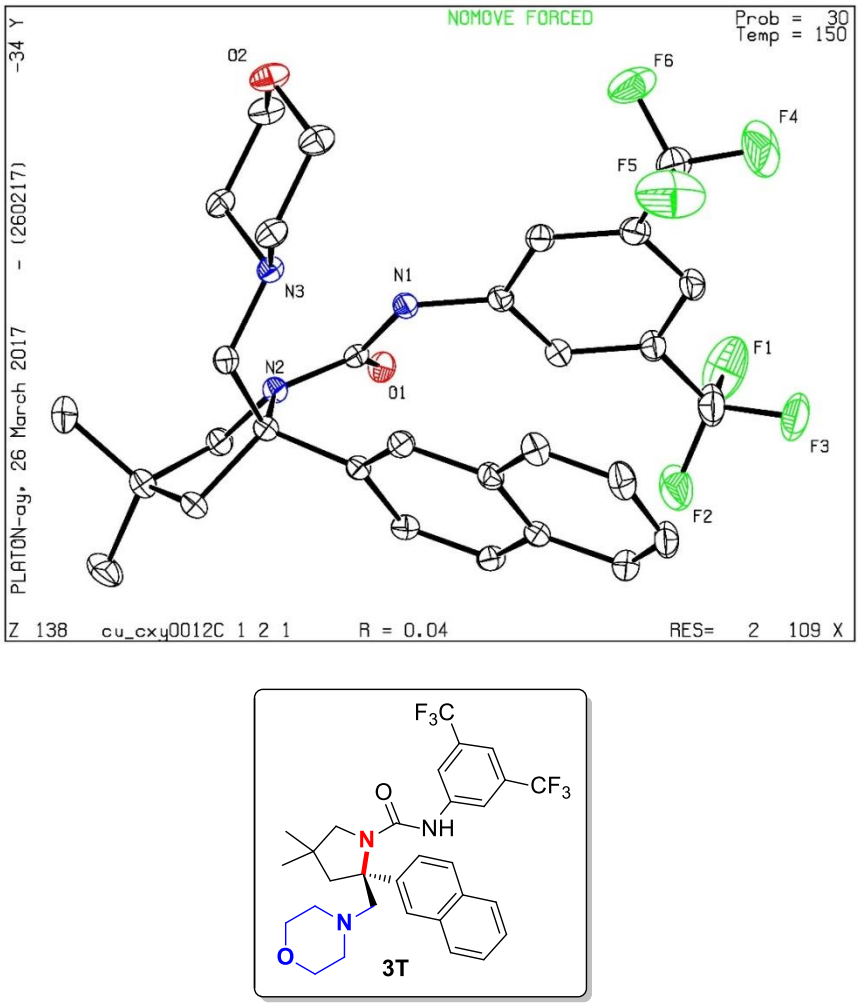
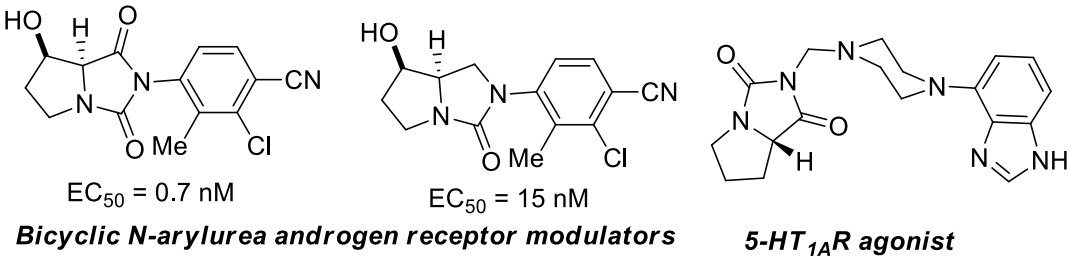


Figure S1. X-ray structure of chiral compound **3T**



Bicyclic N-arylurea androgen receptor modulators ***5-HT$_{1A}$R agonist***

Figure S2. Representative biologically active molecules bearing a pyrrolo[1,2-c]imidazol-3(2H)-one motif

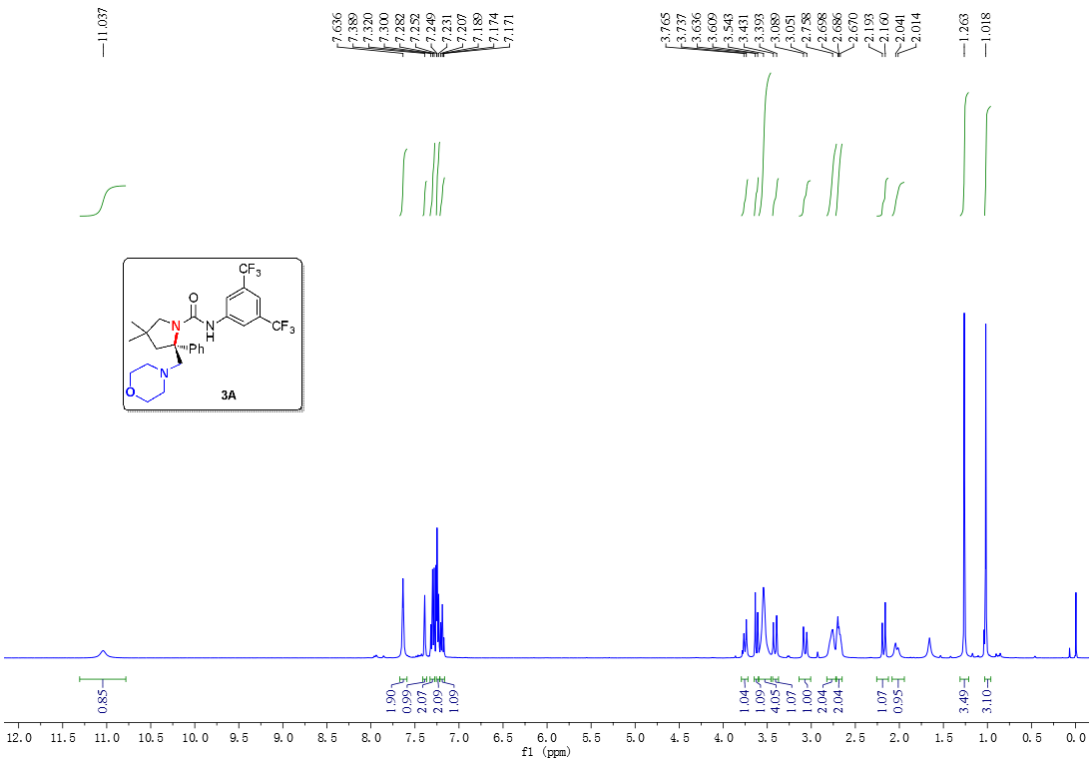


Figure S3. ^{1}H NMR spectrum of **3A**

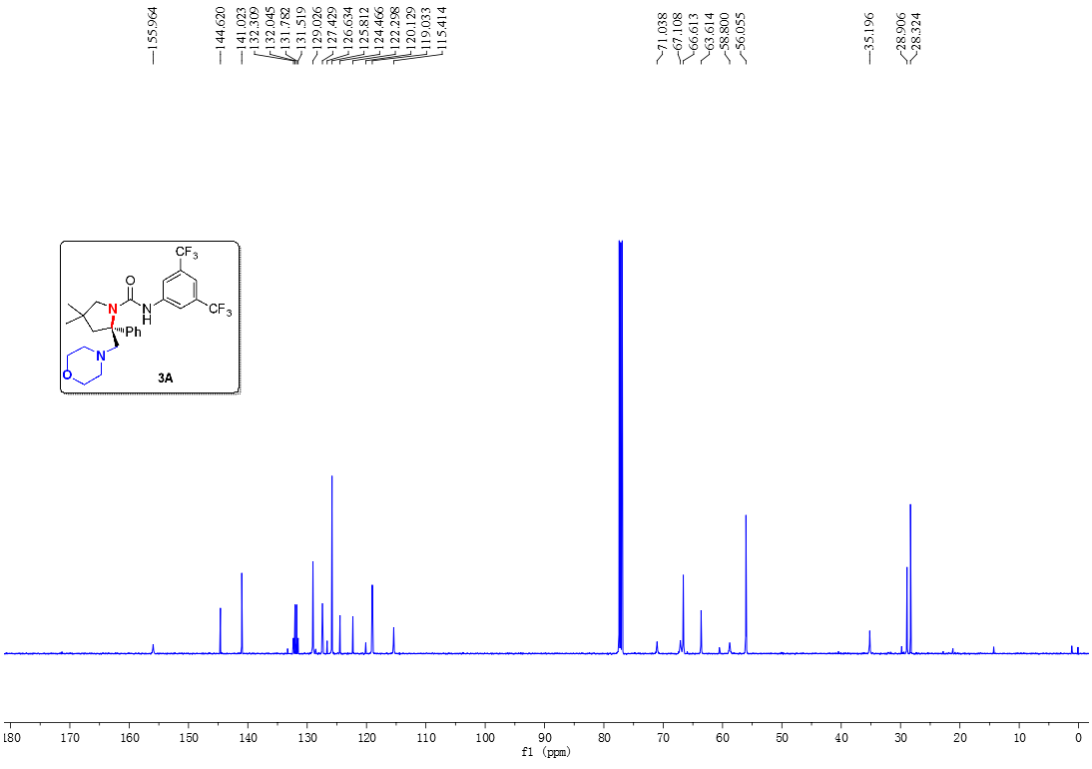


Figure S4. ^{13}C NMR spectrum of **3A**

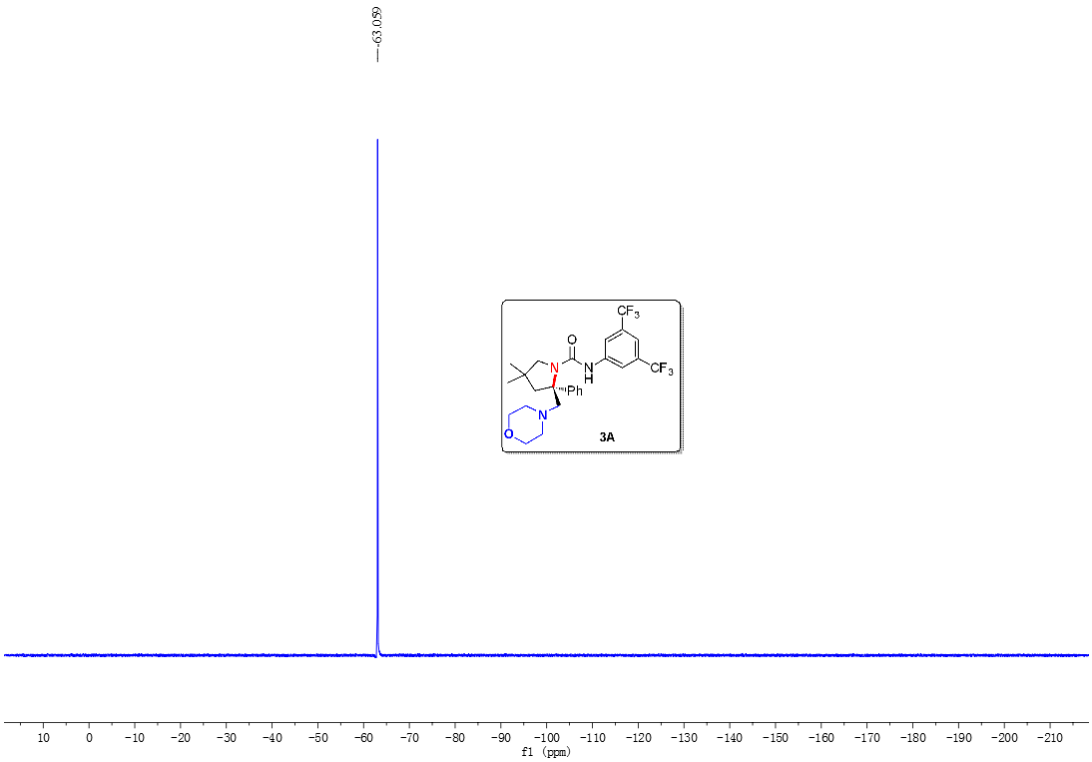


Figure S5. ^{19}F NMR spectrum of **3A**

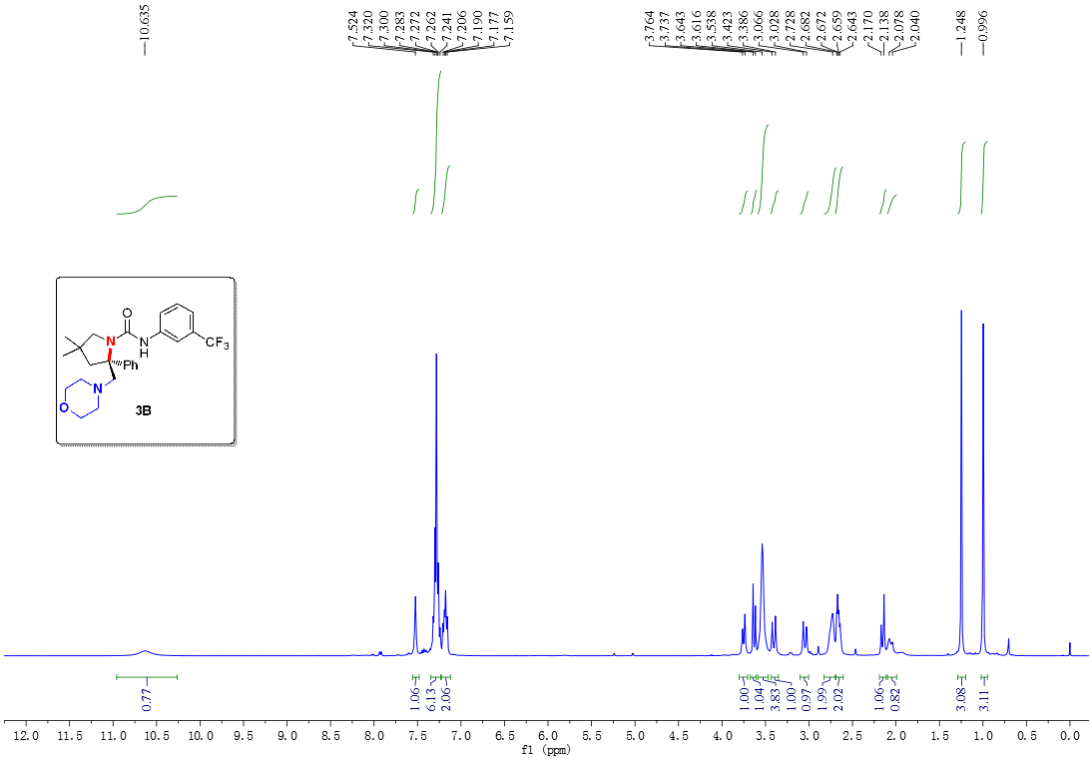


Figure S6. ^{1}H NMR spectrum of **3B**

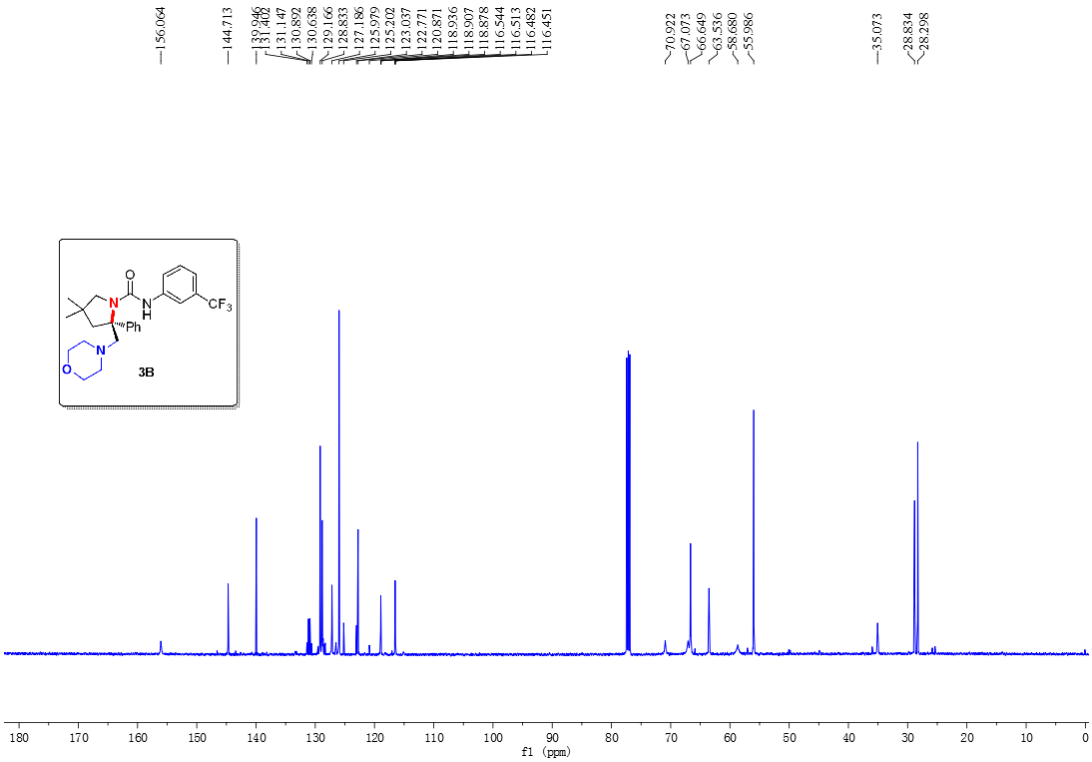


Figure S7. ^{13}C NMR spectrum of **3B**

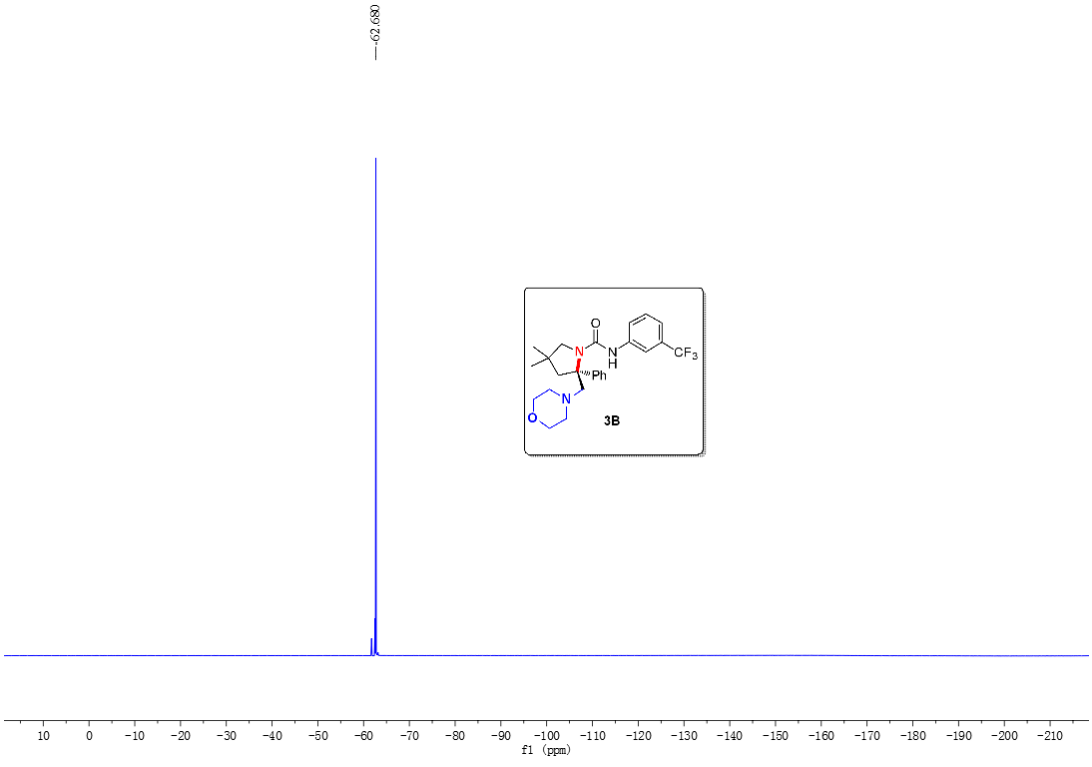


Figure S8. ^{19}F NMR spectrum of **3B**

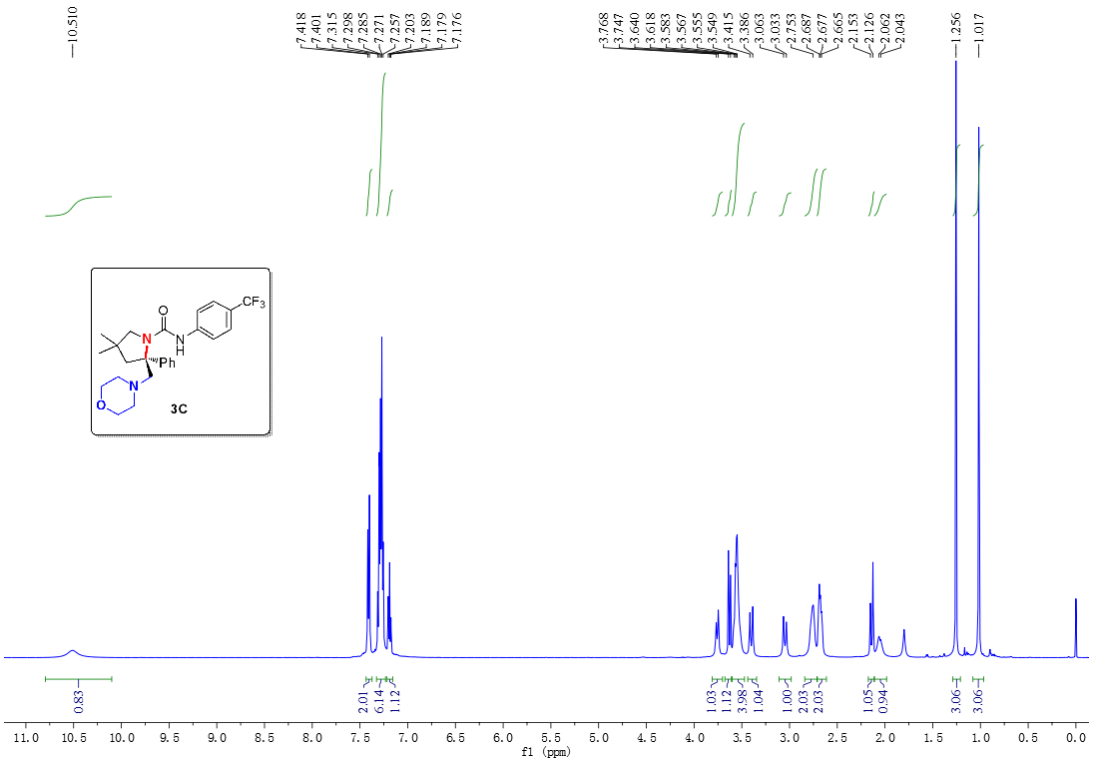


Figure S9. ^{1}H NMR spectrum of **3C**

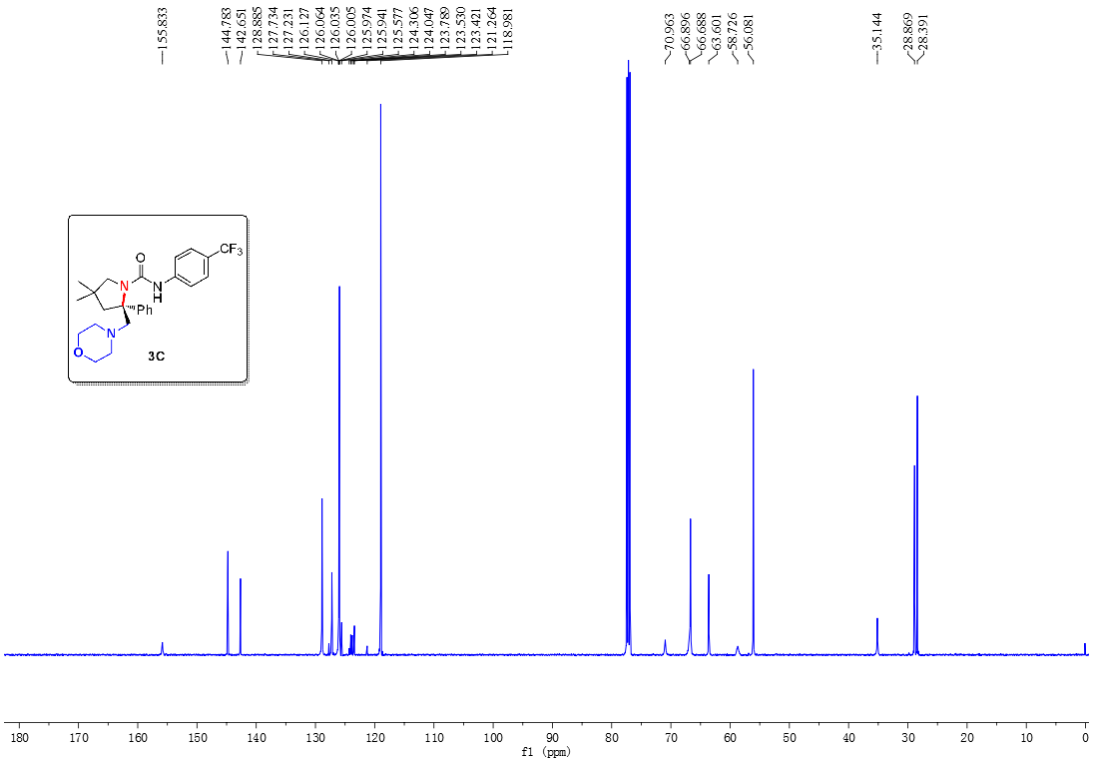


Figure S10. ^{13}C NMR spectrum of **3C**

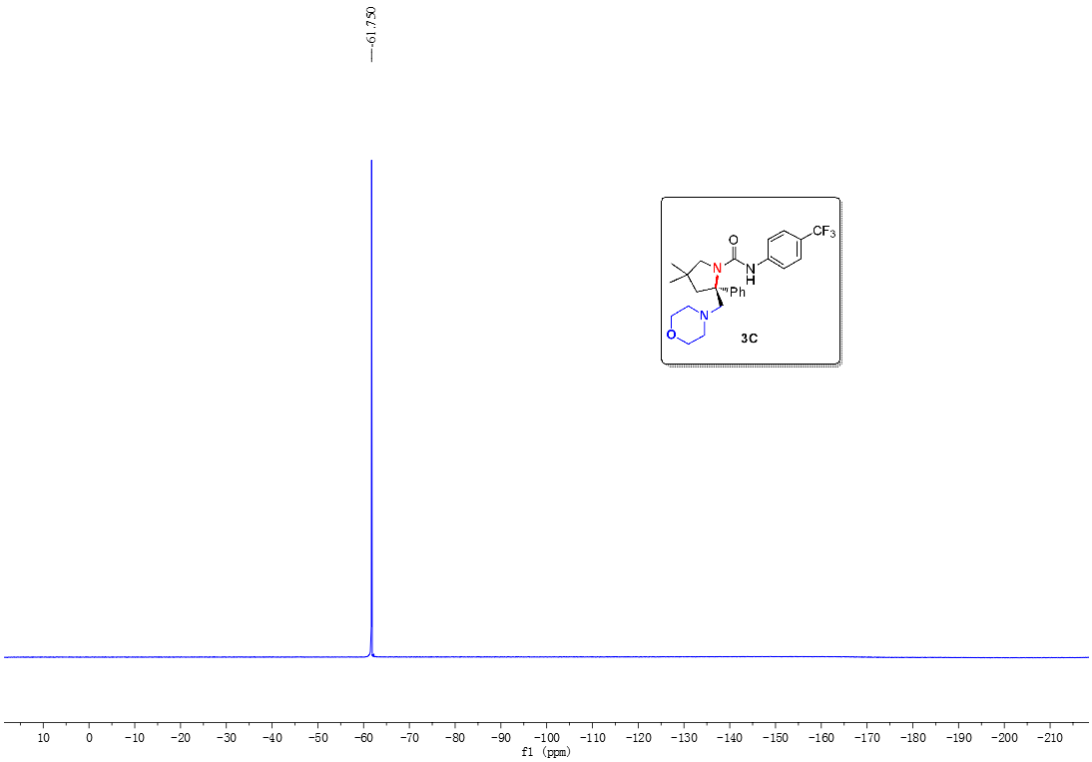


Figure S11. ^{19}F NMR spectrum of **3C**

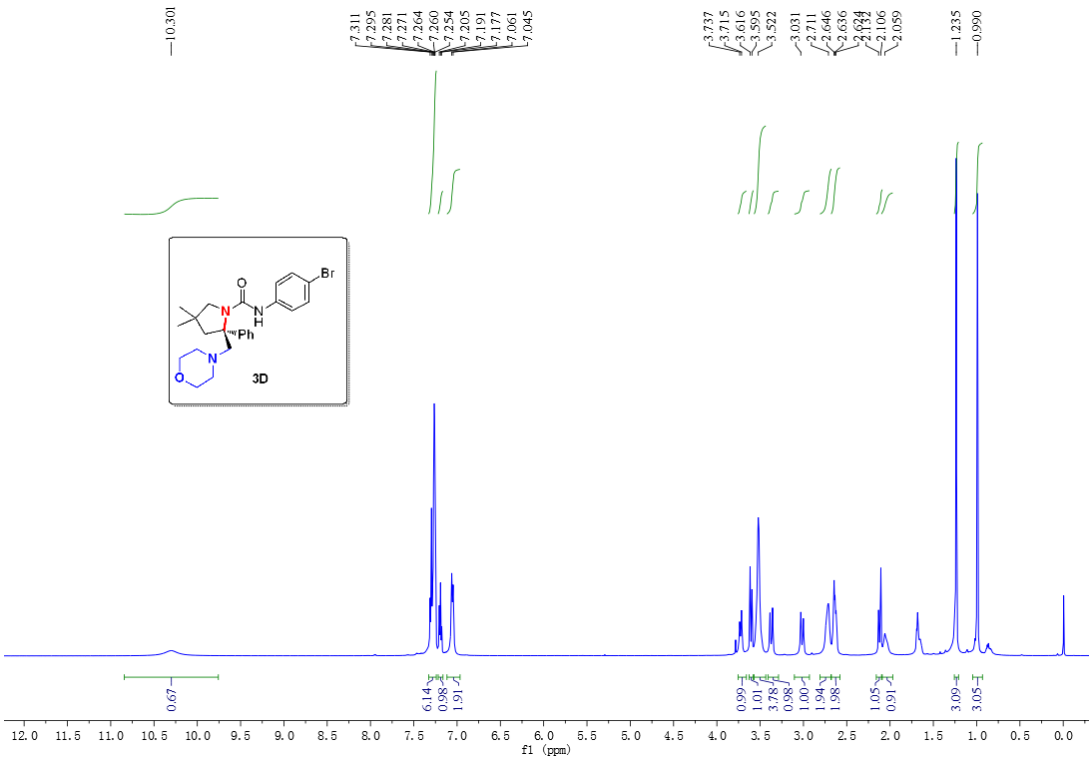


Figure S12. ^{1}H NMR spectrum of **3D**

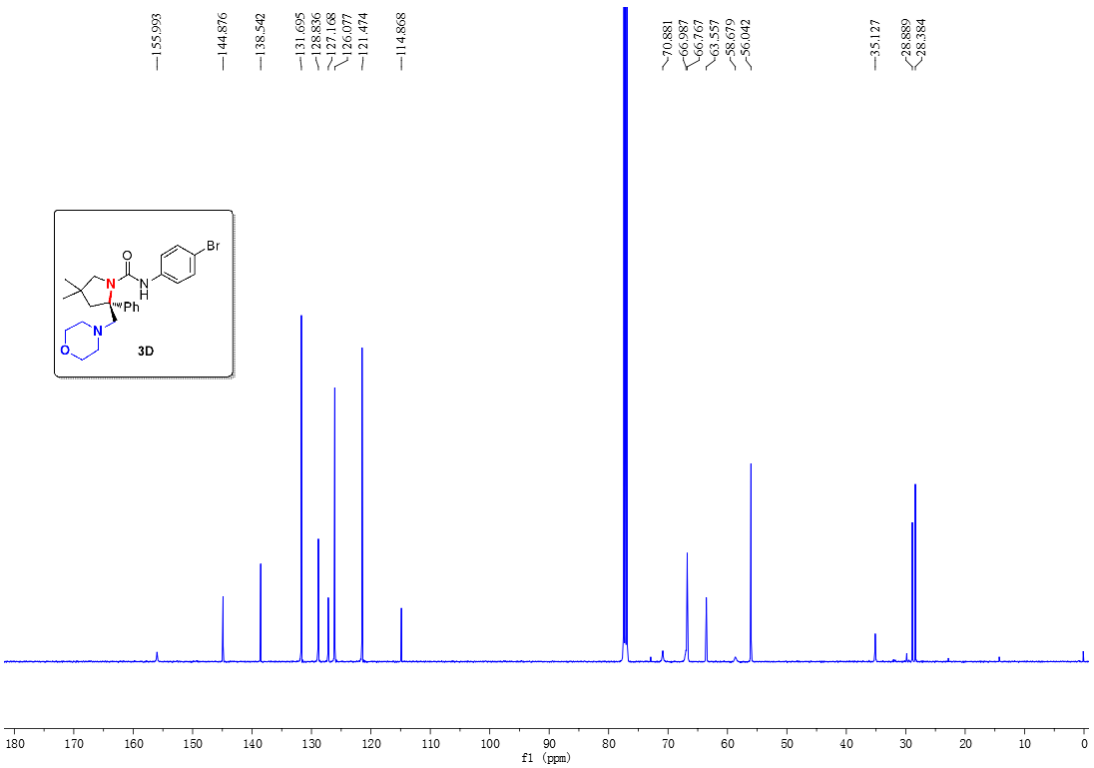


Figure S13. ^{13}C NMR spectrum of **3D**

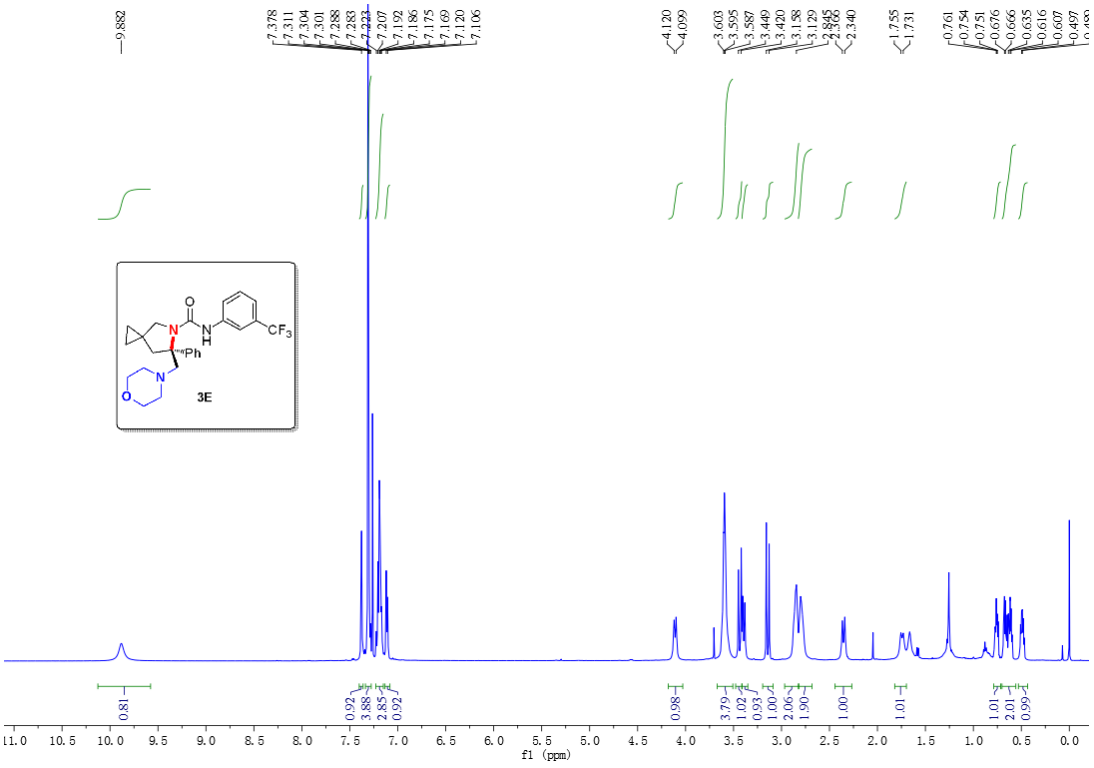


Figure S14. ^{1}H NMR spectrum of 3E

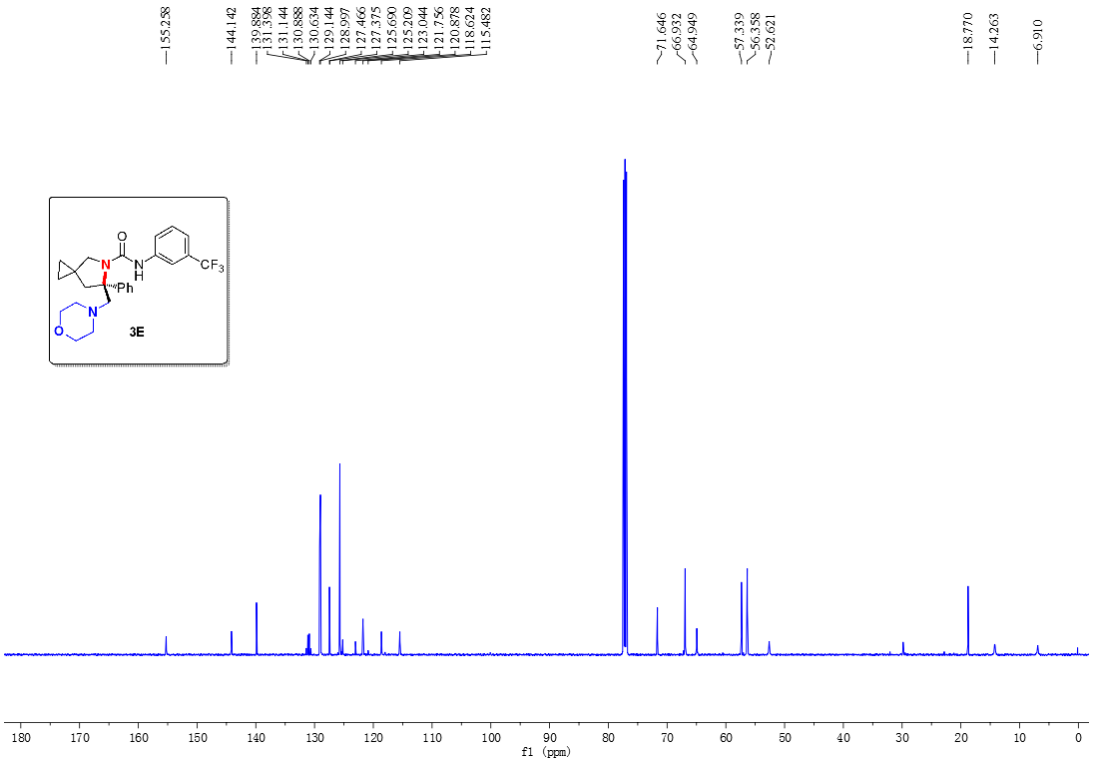


Figure S15. ^{13}C NMR spectrum of **3E**

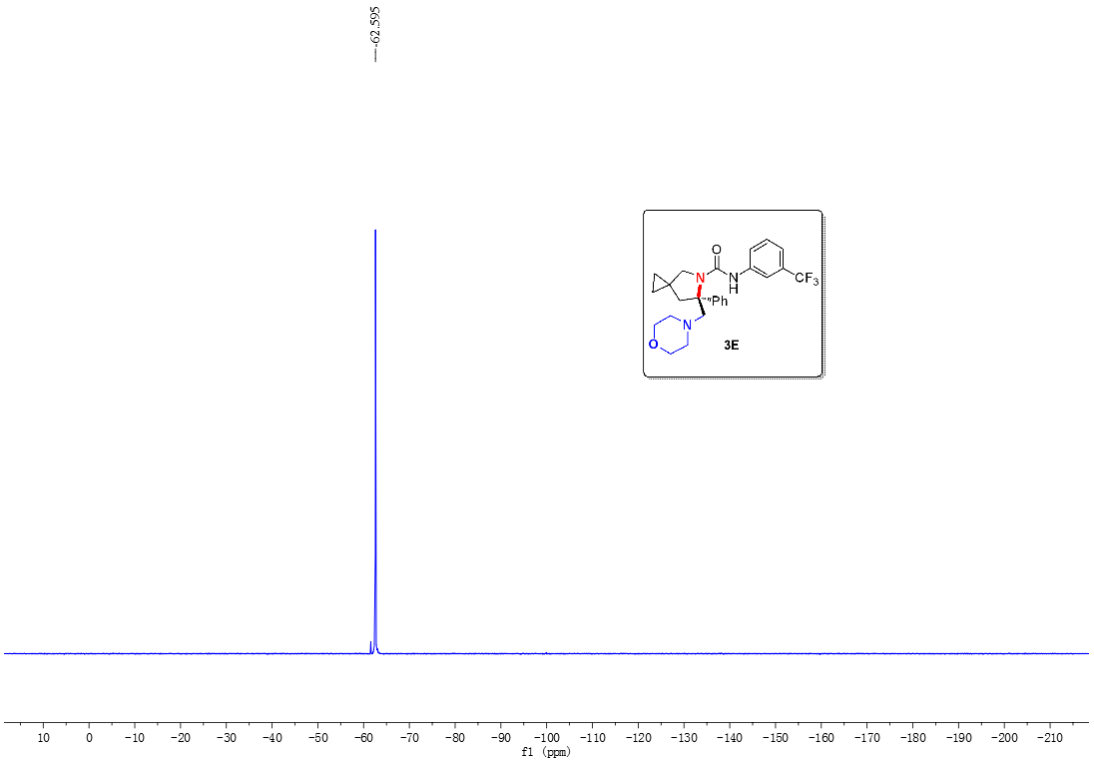


Figure S16. ^{19}F NMR spectrum of **3E**

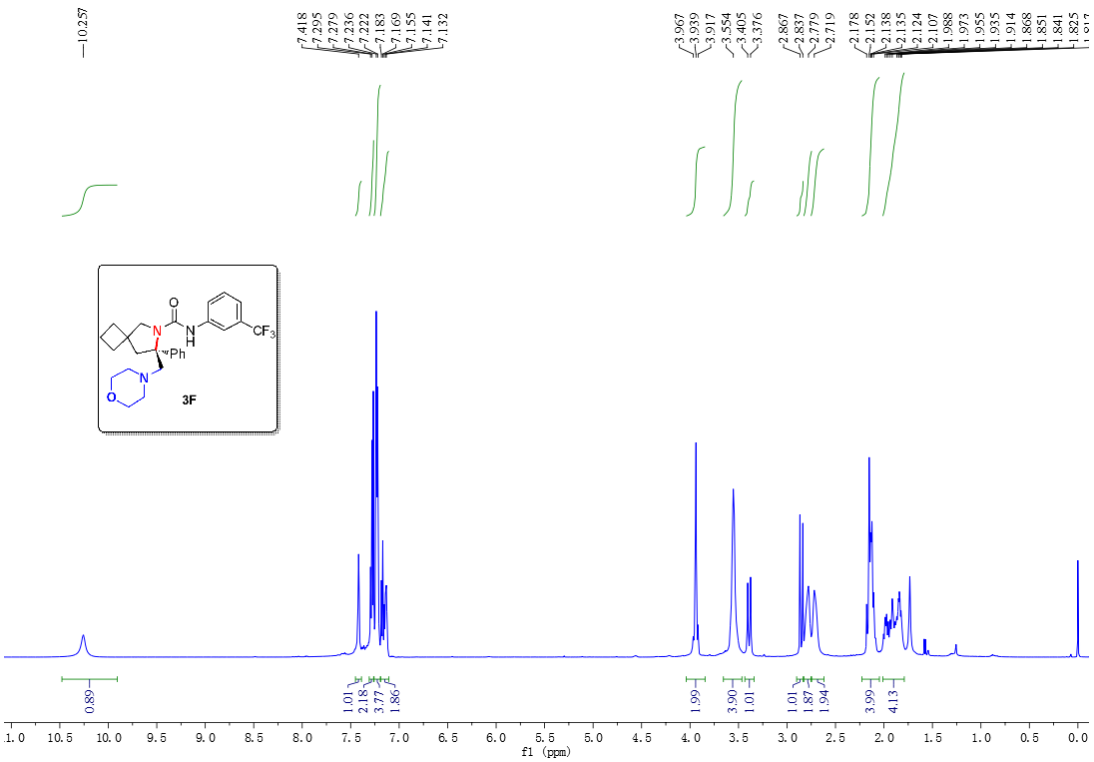


Figure S17. ^{1}H NMR spectrum of **3F**

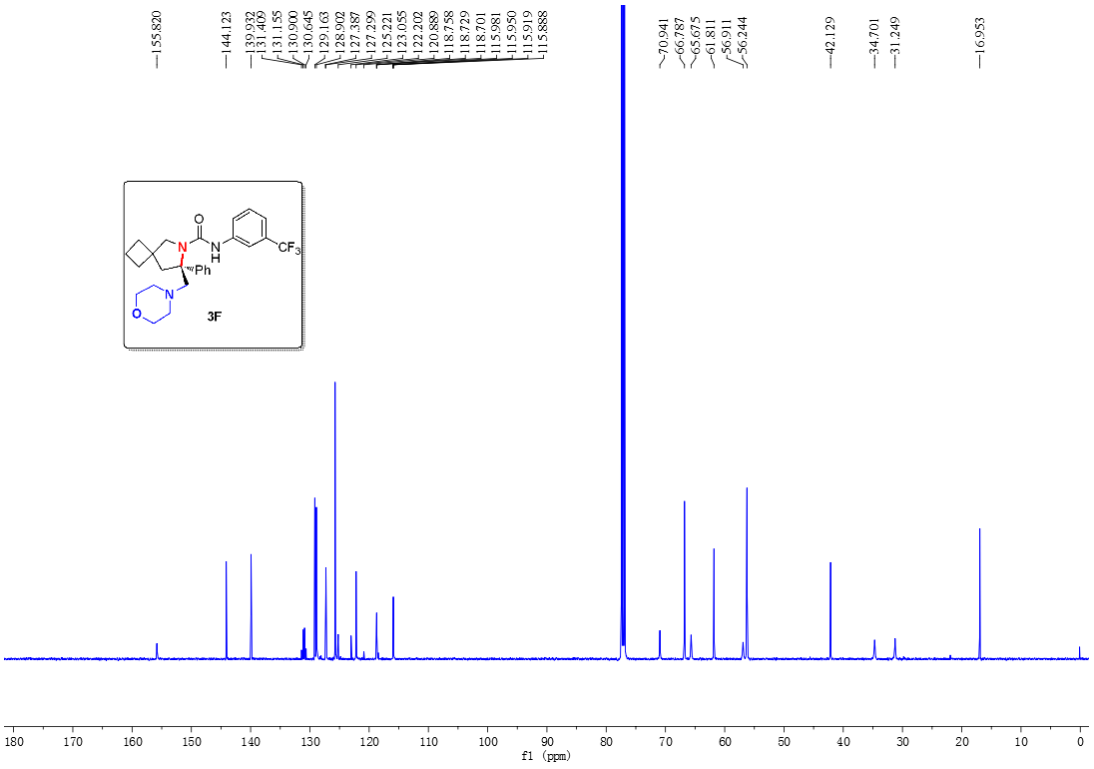


Figure S18. ^{13}C NMR spectrum of **3F**

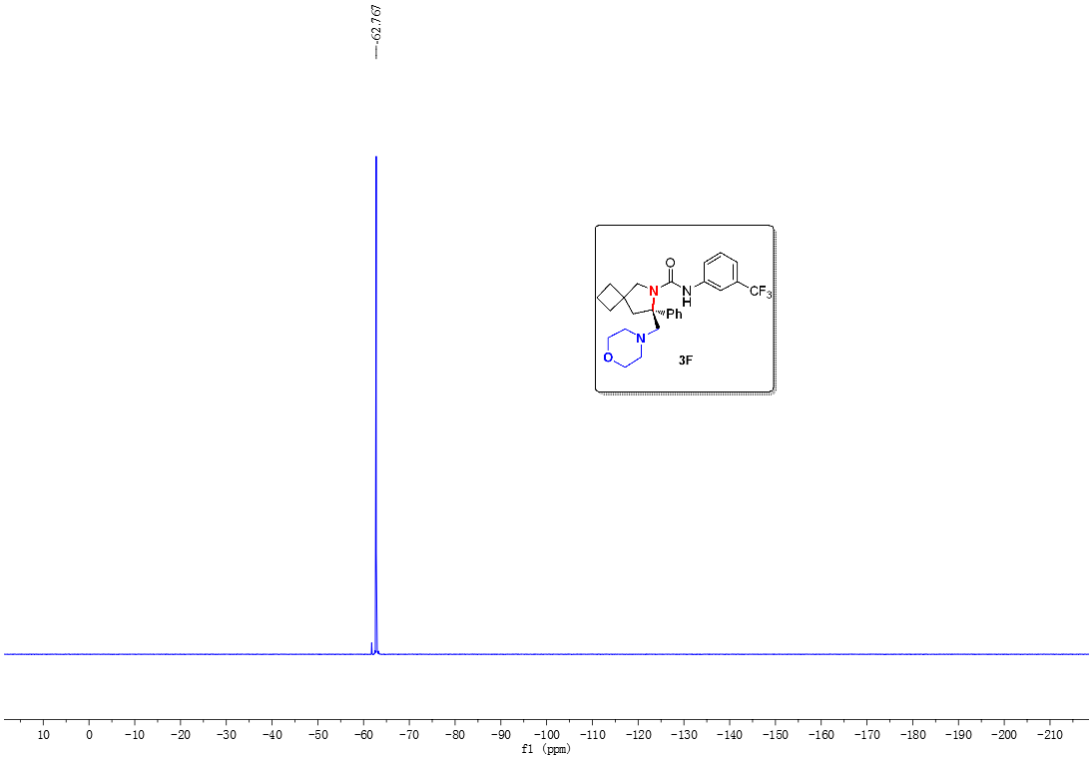


Figure S19. ^{19}F NMR spectrum of **3F**

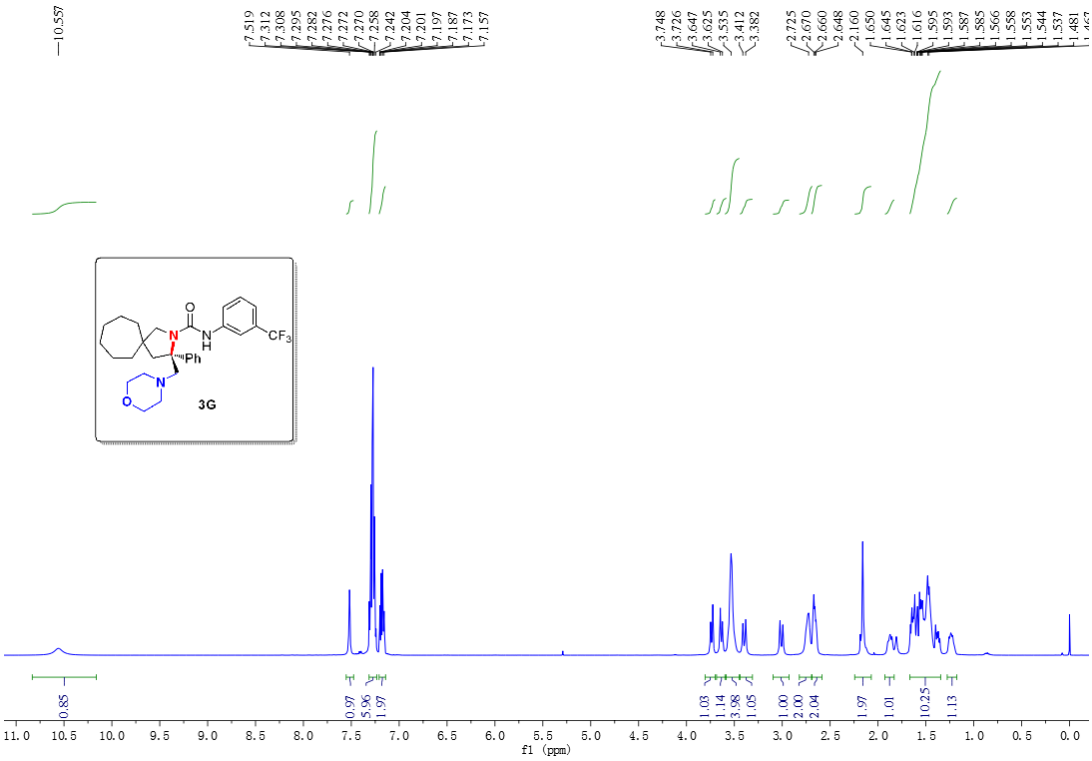


Figure S20. ^{1}H NMR spectrum of **3G**

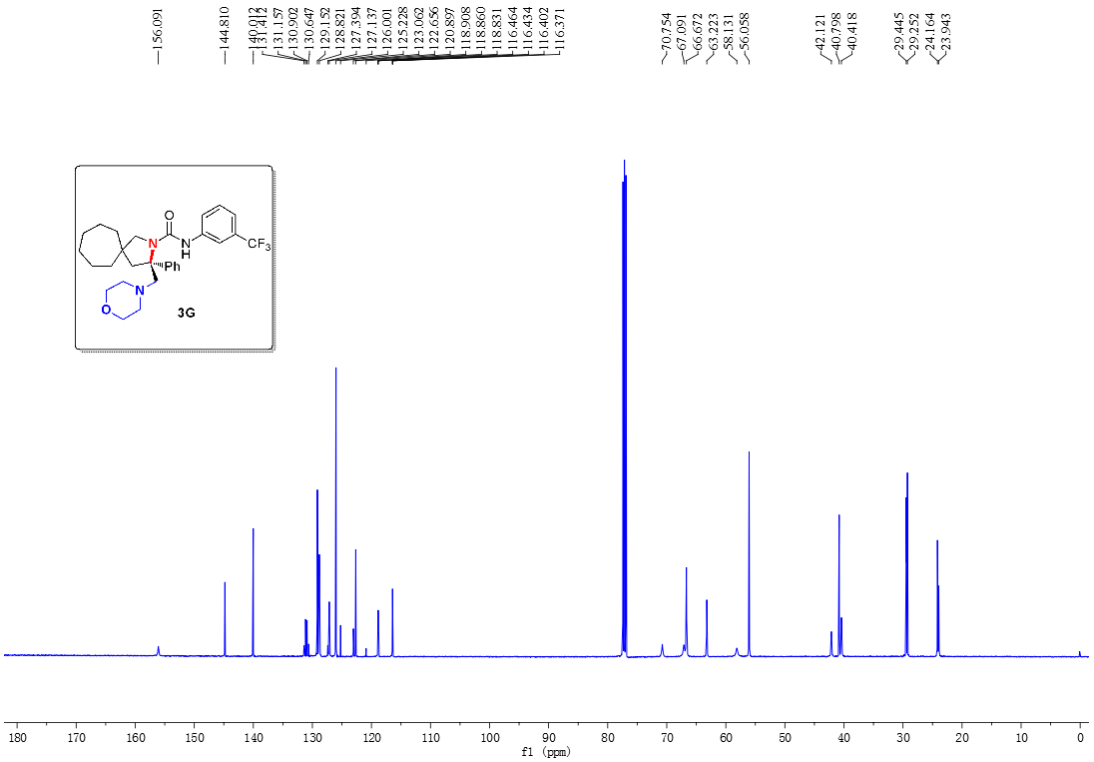


Figure S21. ^{13}C NMR spectrum of **3G**

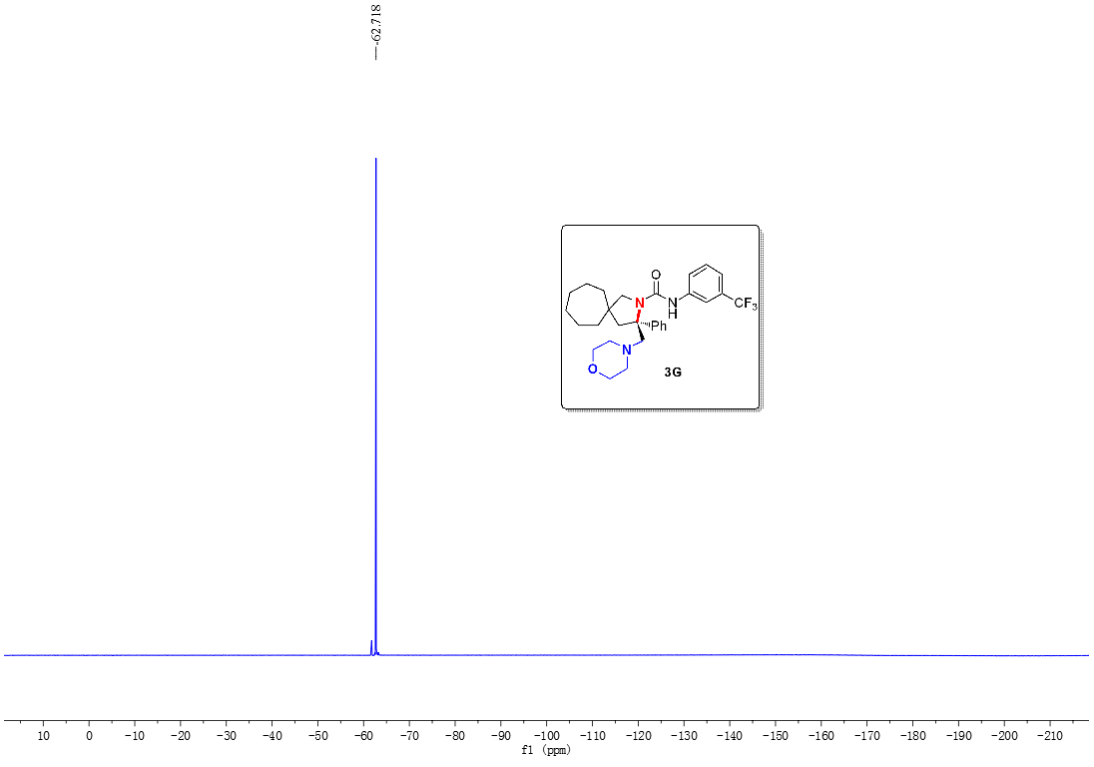


Figure S22. ^{19}F NMR spectrum of **3G**

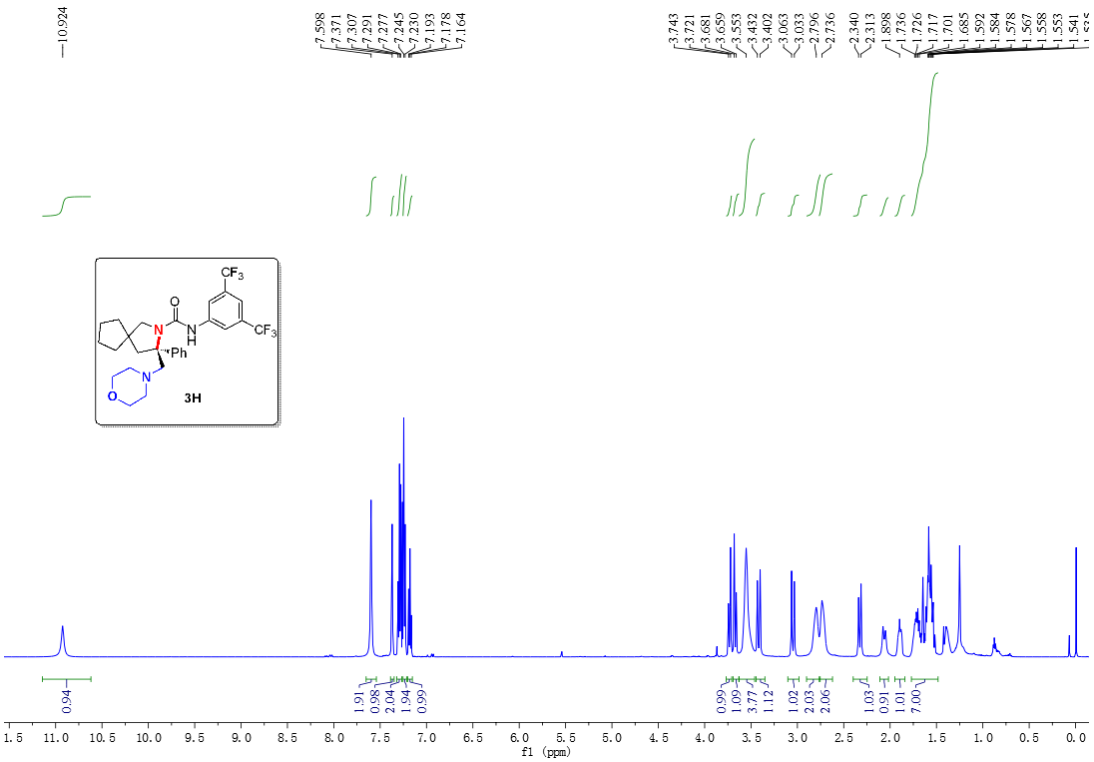


Figure S23. ^{1}H NMR spectrum of **3H**

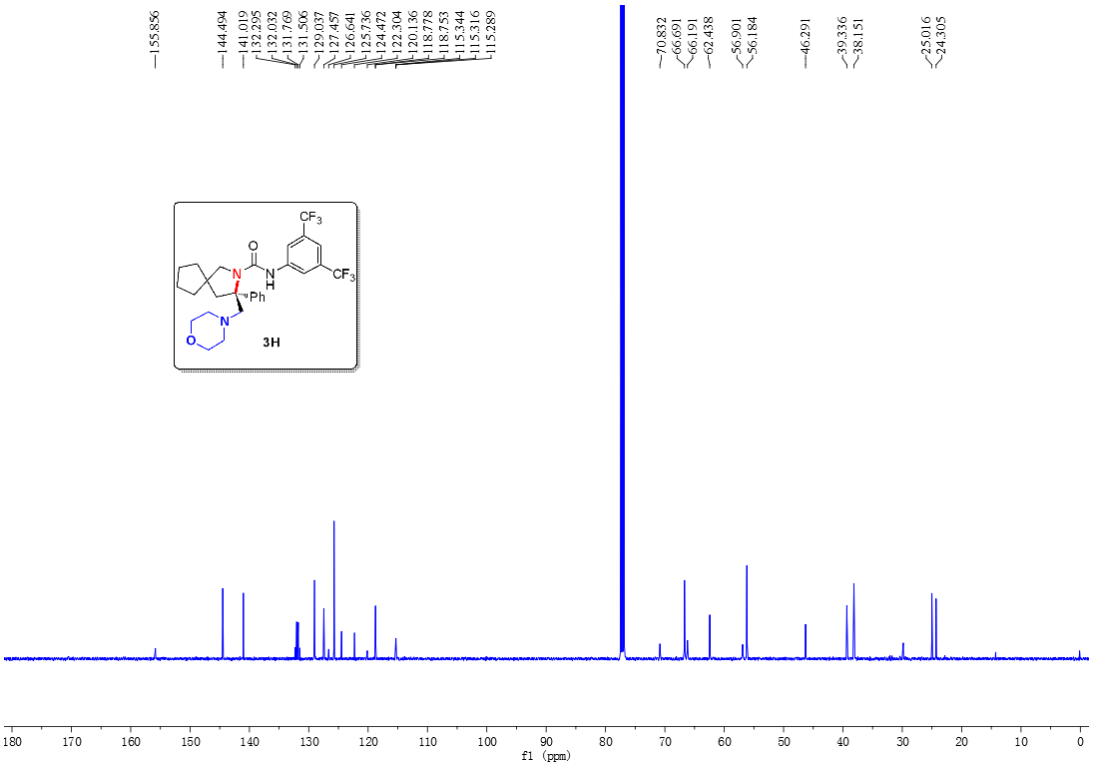


Figure S24. ^{13}C NMR spectrum of **3H**

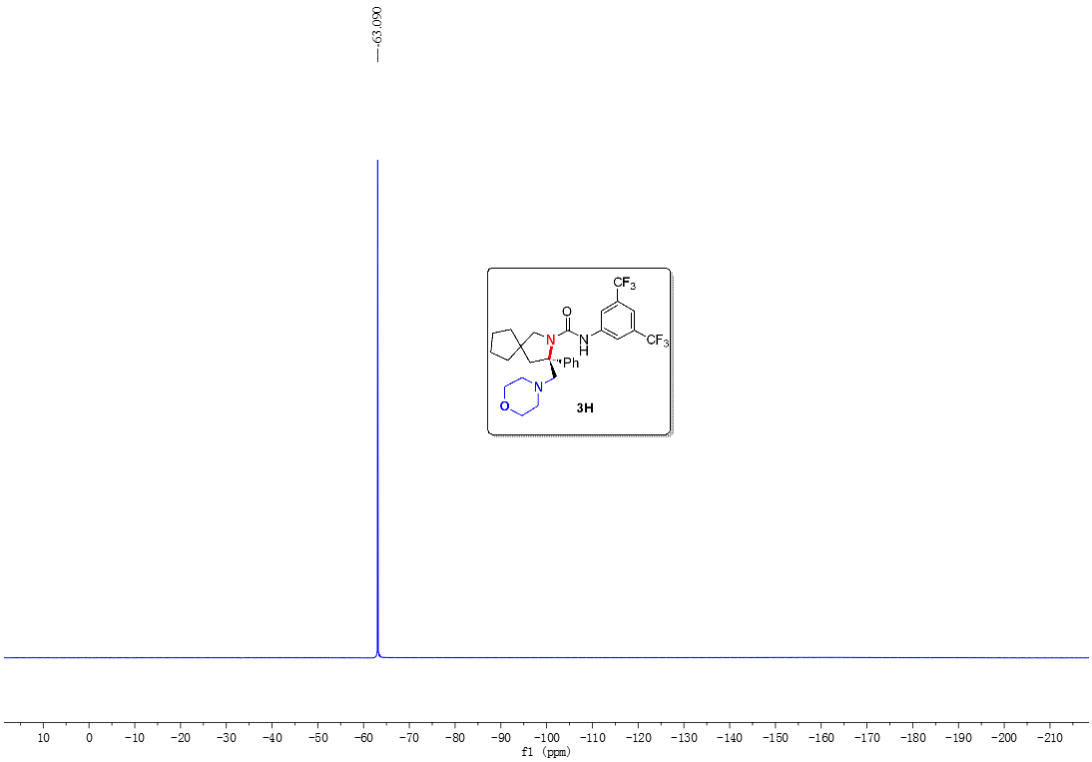


Figure S25. ^{19}F NMR spectrum of **3H**

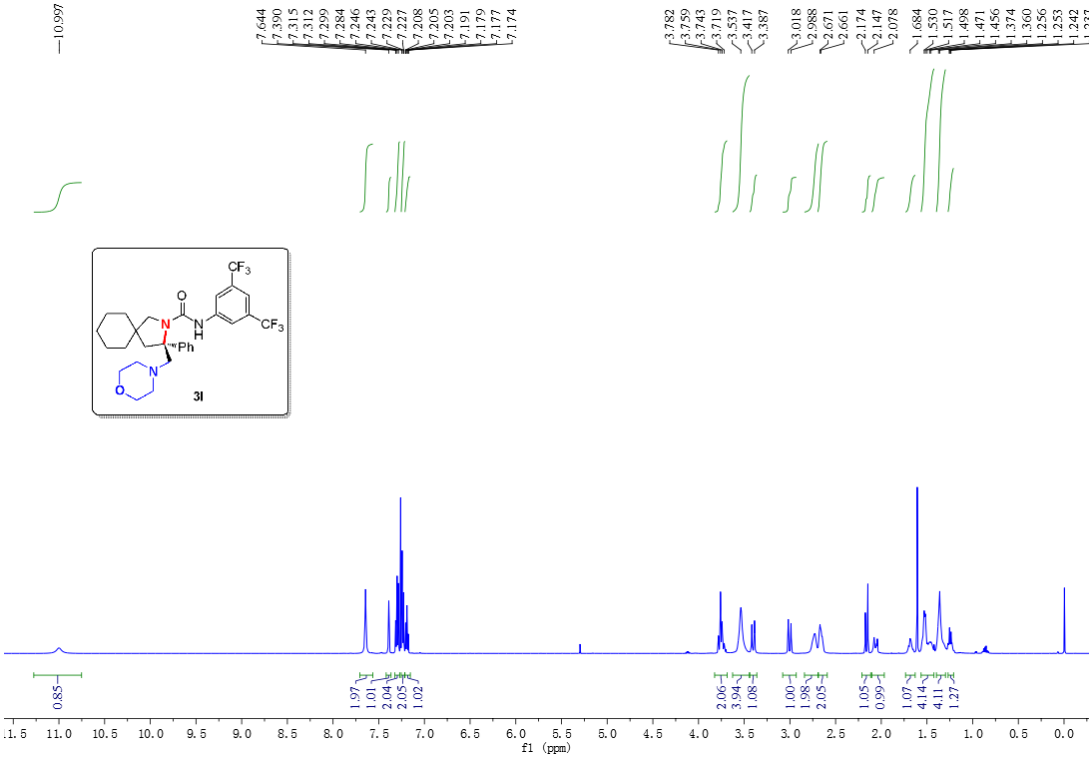


Figure S26. ^{1}H NMR spectrum of **3I**

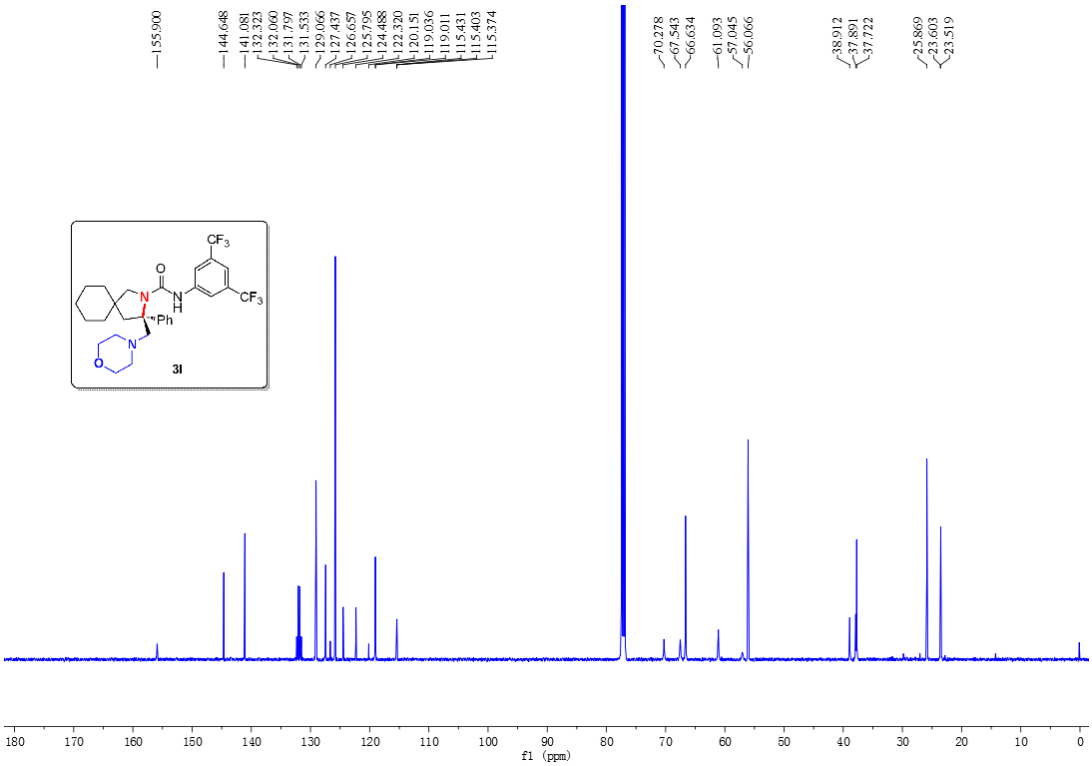


Figure S27. ^{13}C NMR spectrum of **3l**

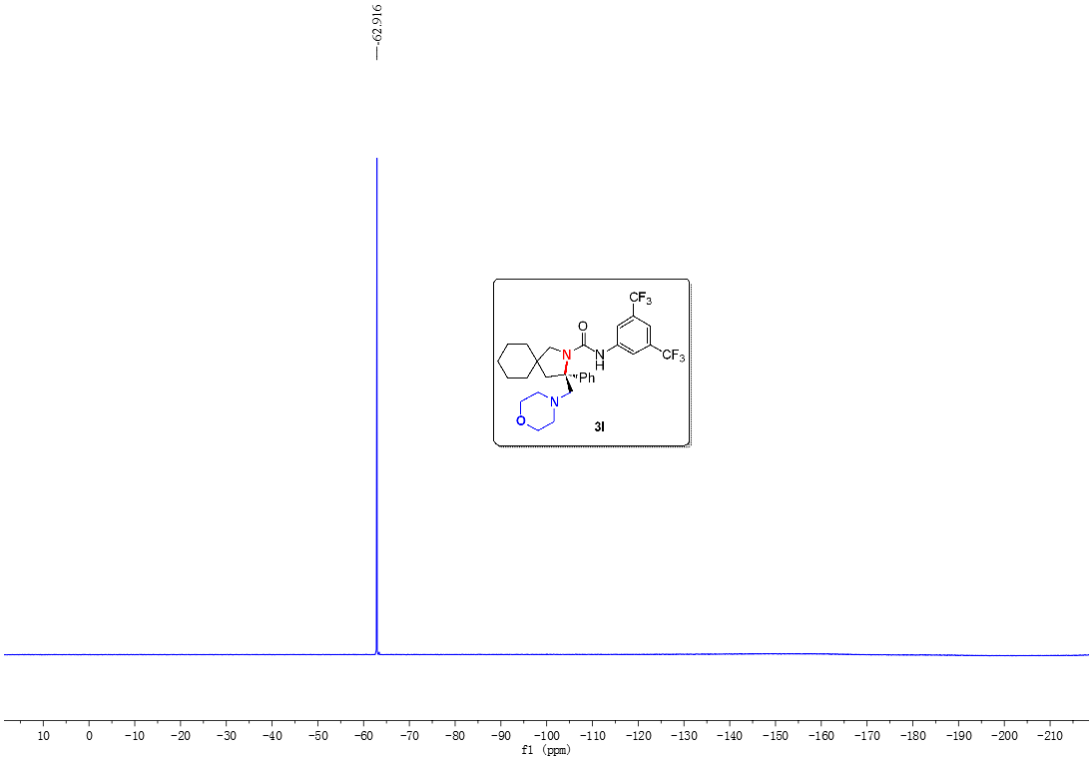


Figure S28. ^{19}F NMR spectrum of **3l**

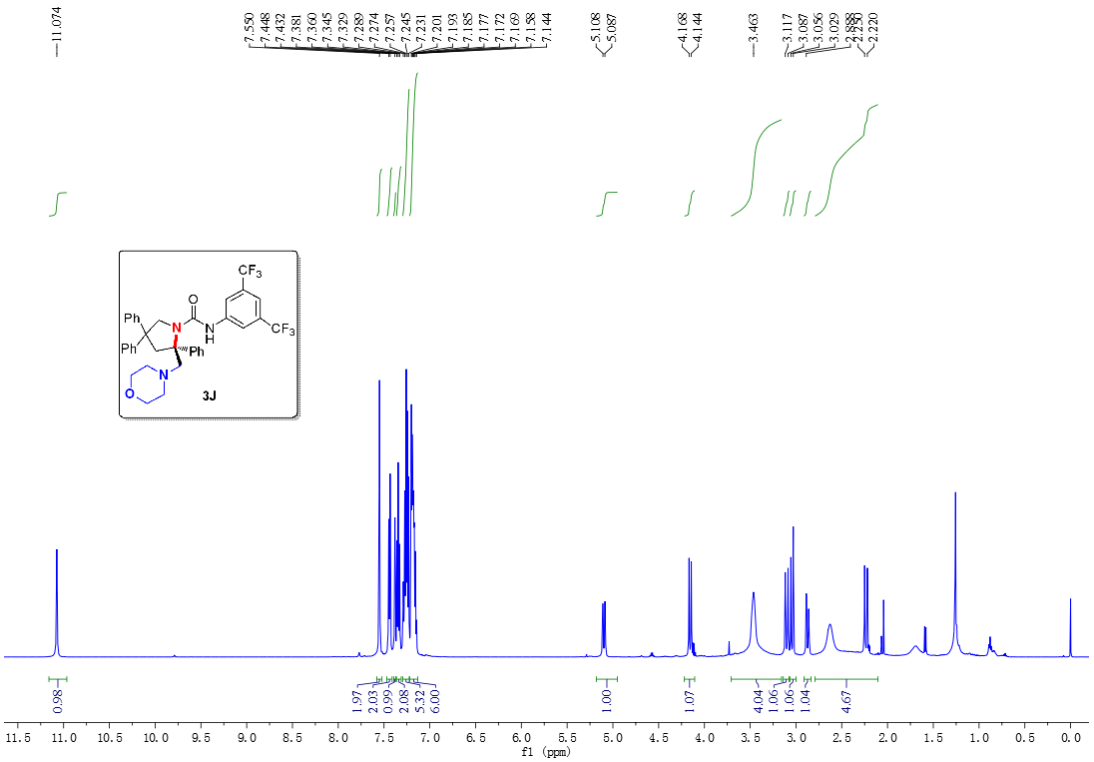


Figure S29. ^{1}H NMR spectrum of **3J**

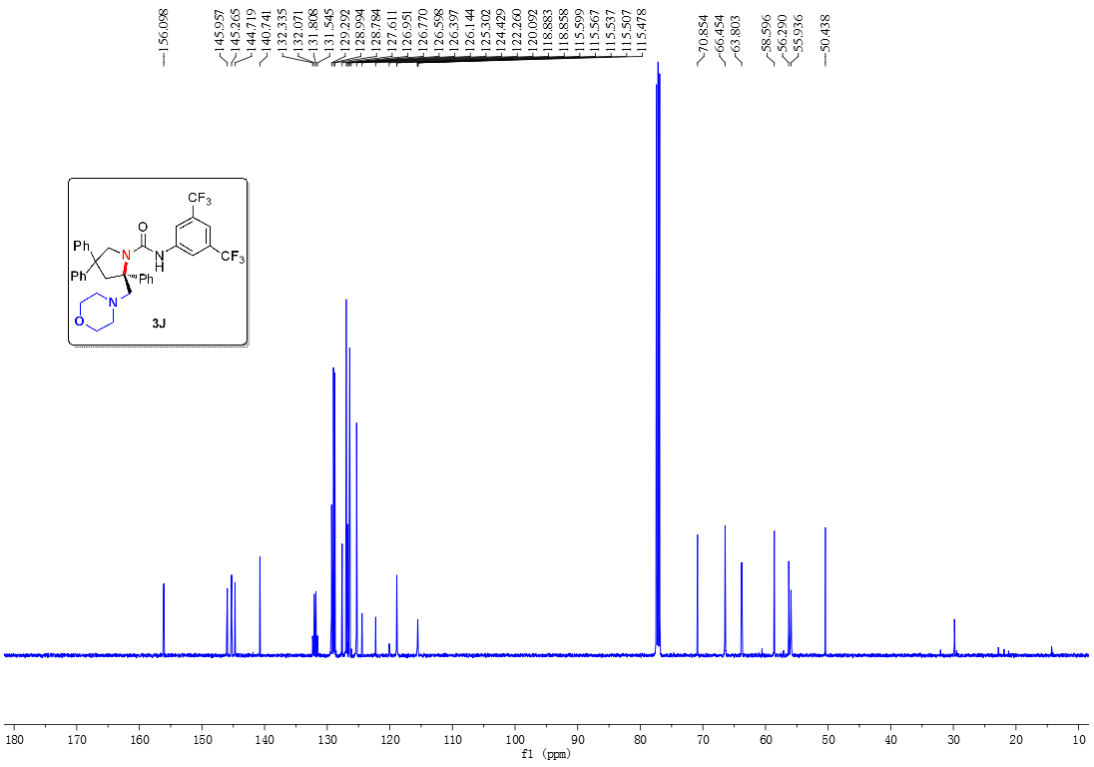


Figure S30. ^{13}C NMR spectrum of **3J**

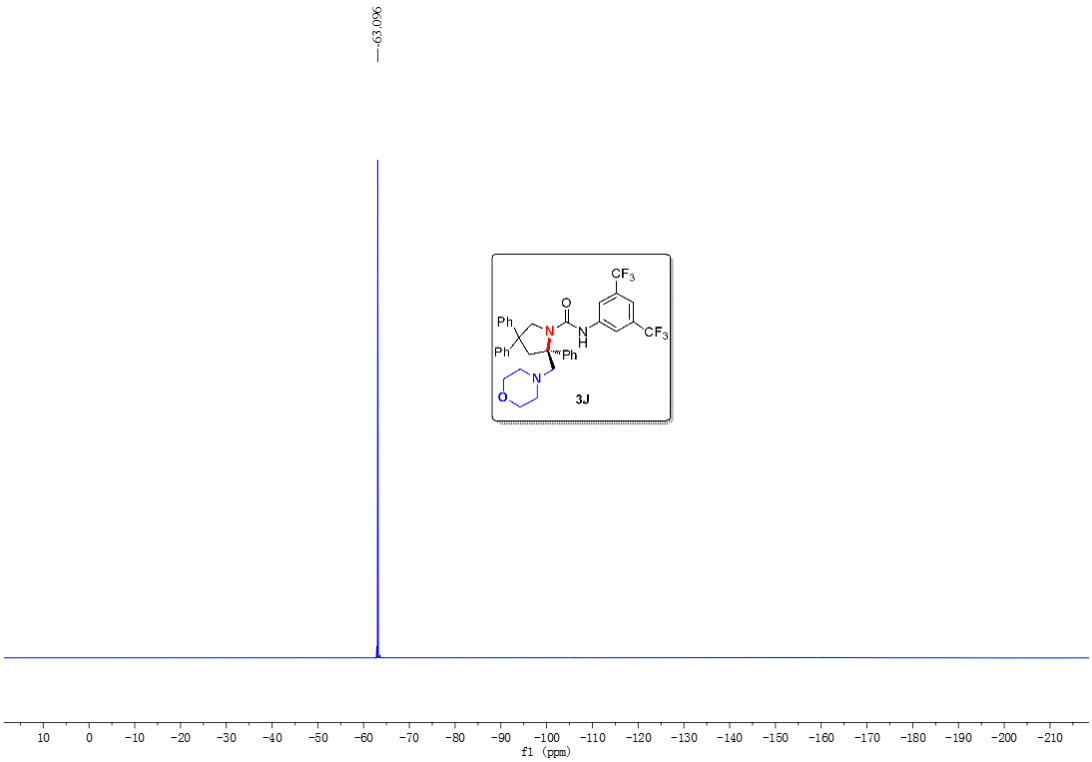


Figure S31. ^{19}F NMR spectrum of **3J**

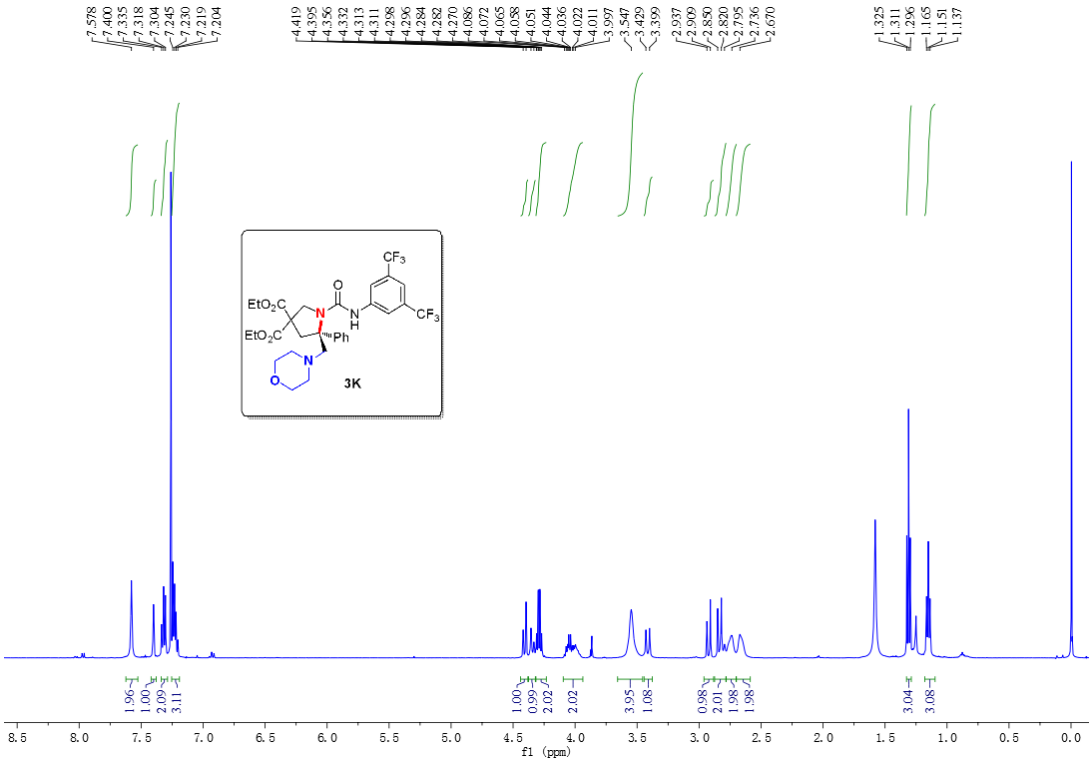


Figure S32. ^{1}H NMR spectrum of **3K**

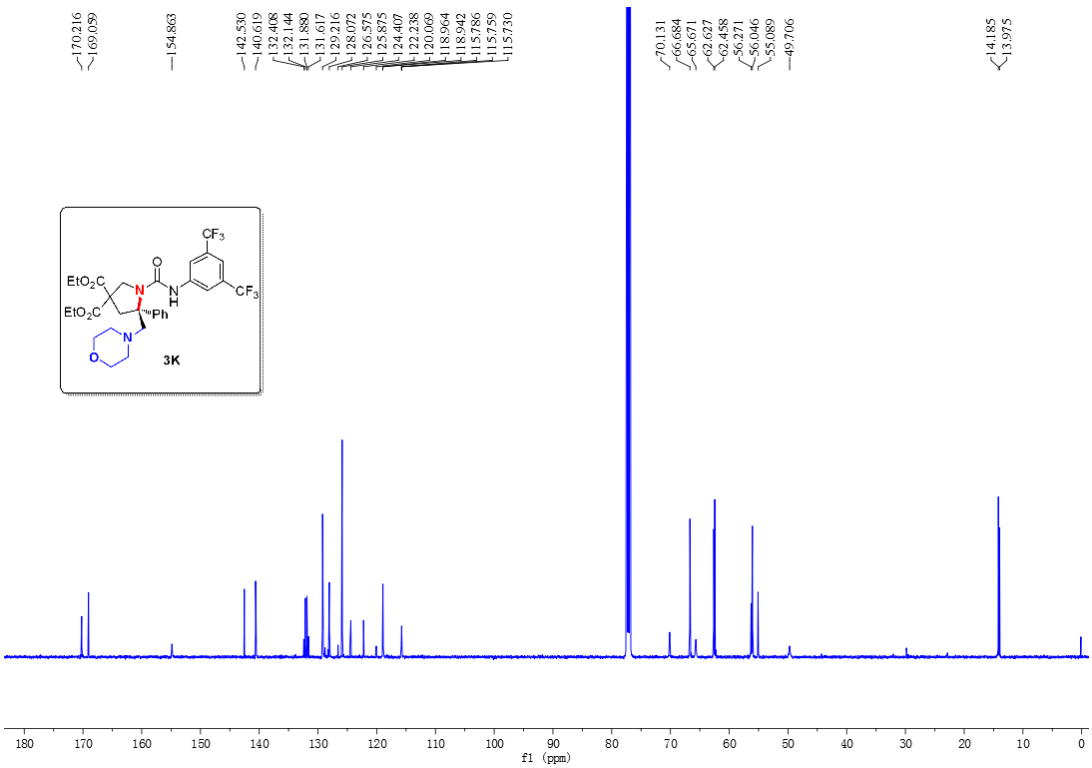


Figure S33. ^{13}C NMR spectrum of **3K**

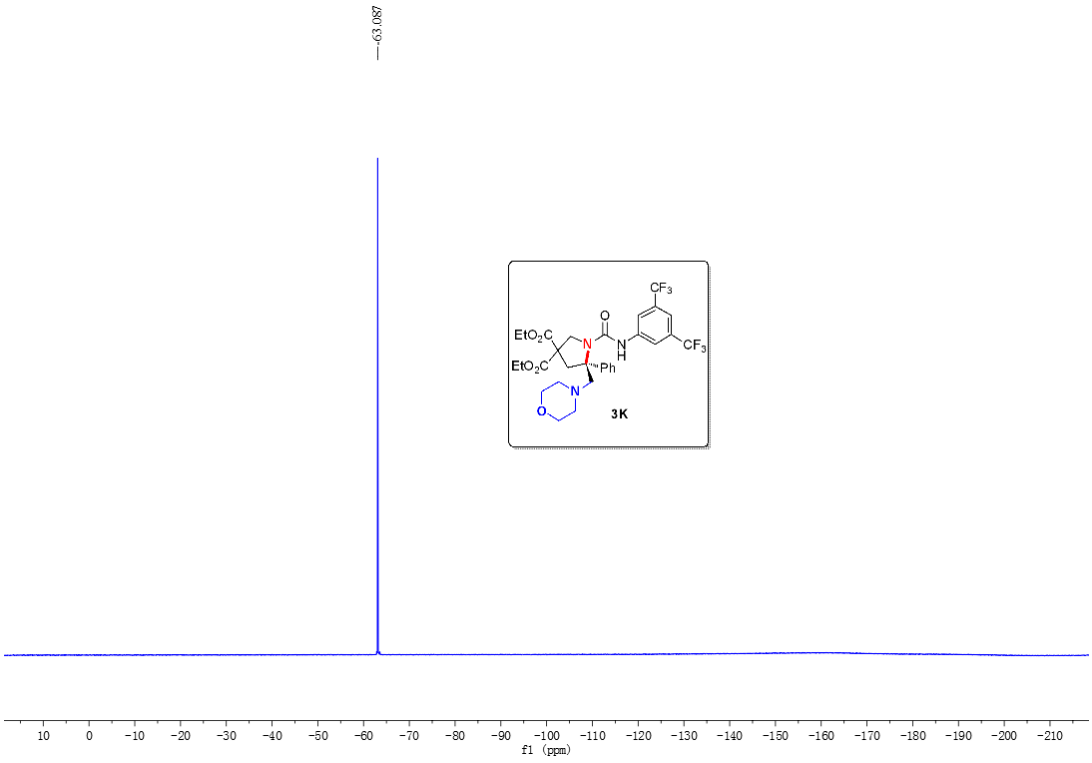


Figure S34. ^{19}F NMR spectrum of **3K**

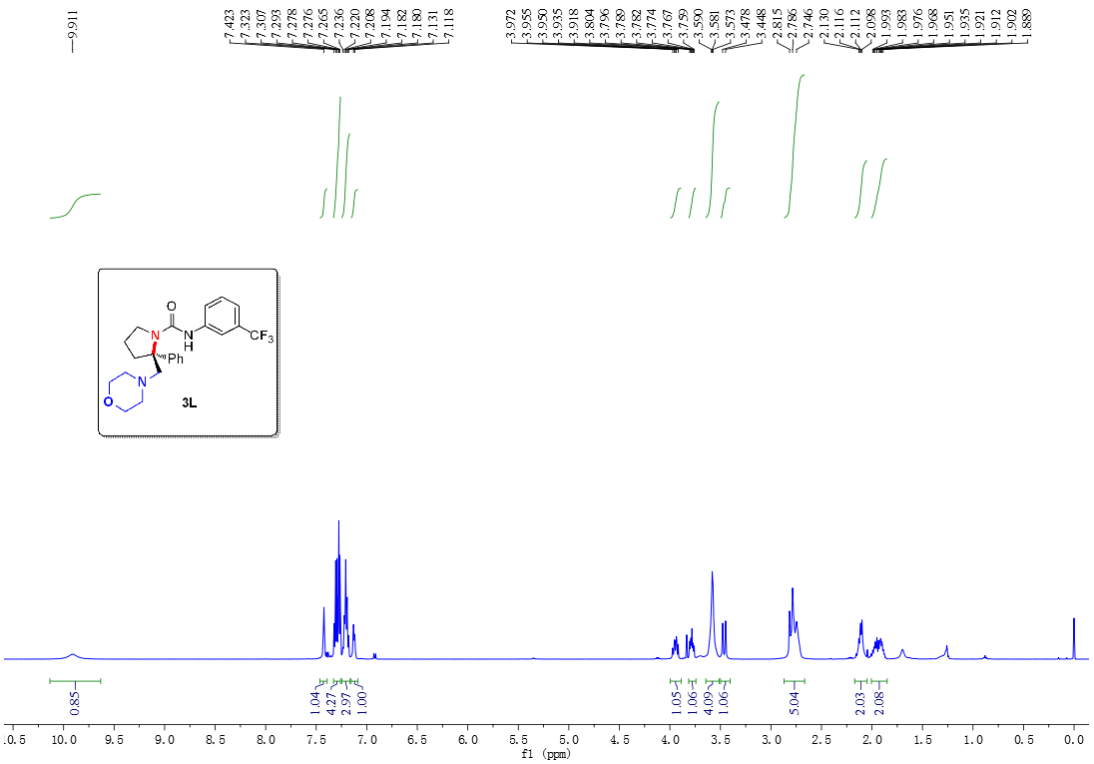


Figure S35. ^{1}H NMR spectrum of **3L**

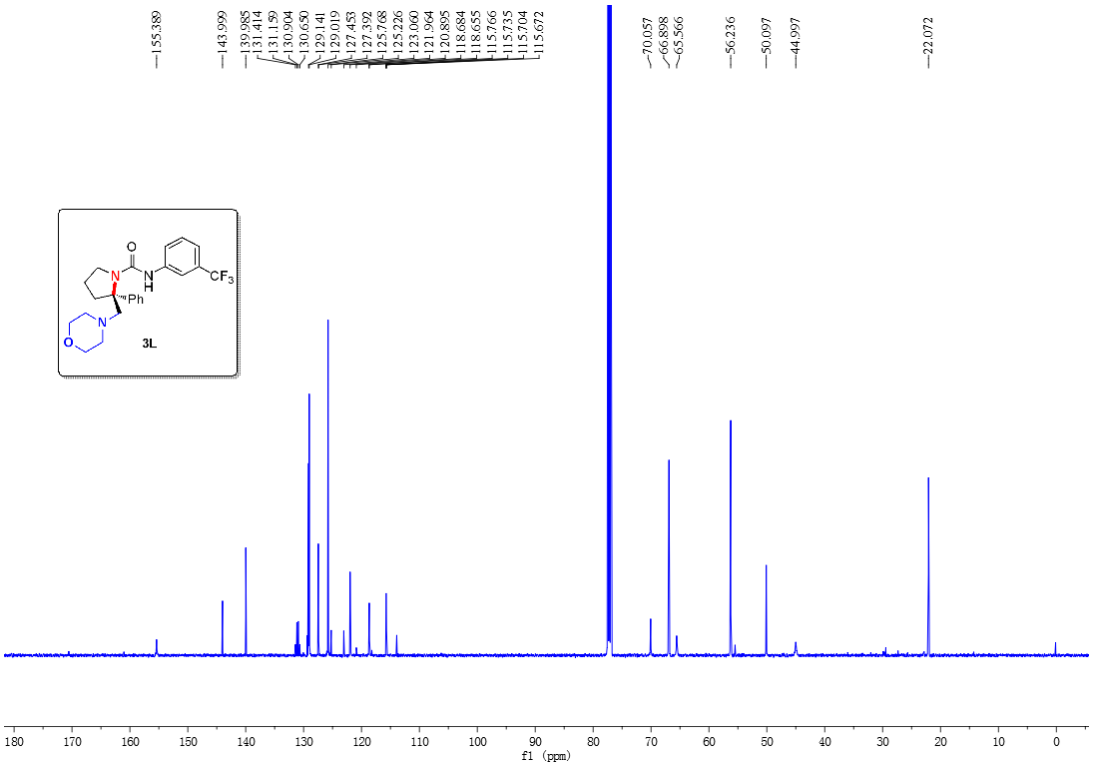


Figure S36. ^{13}C NMR spectrum of **3L**

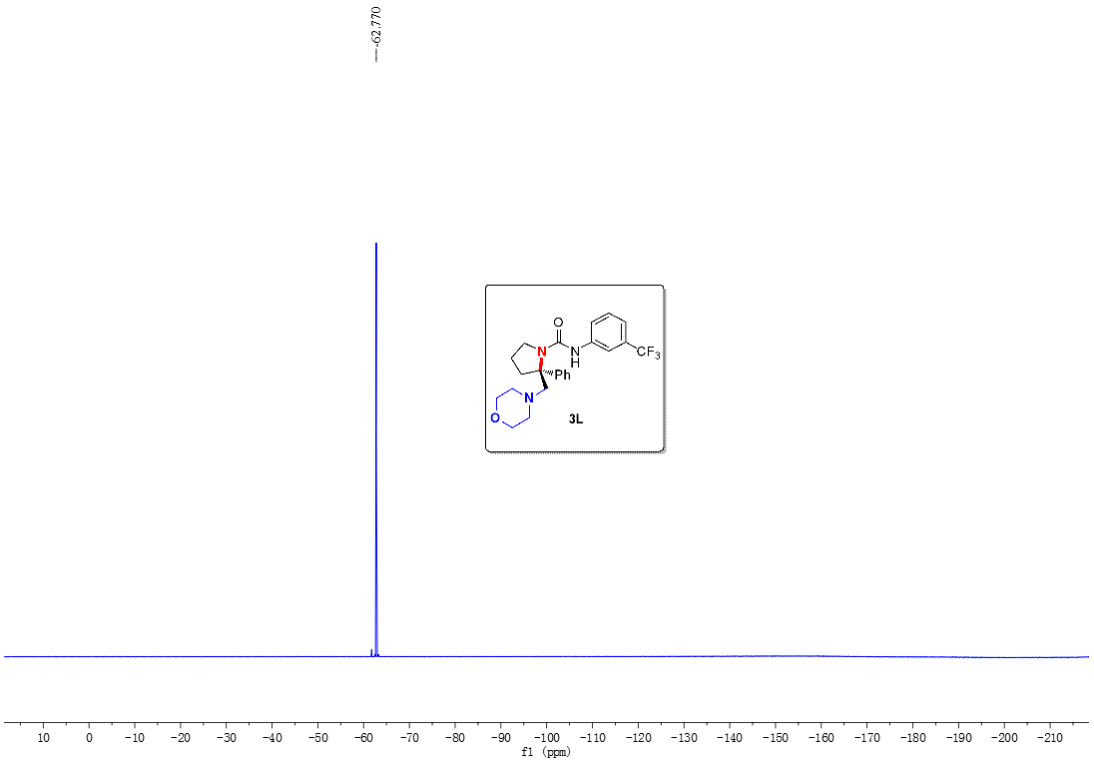


Figure S37. ^{19}F NMR spectrum of **3L**

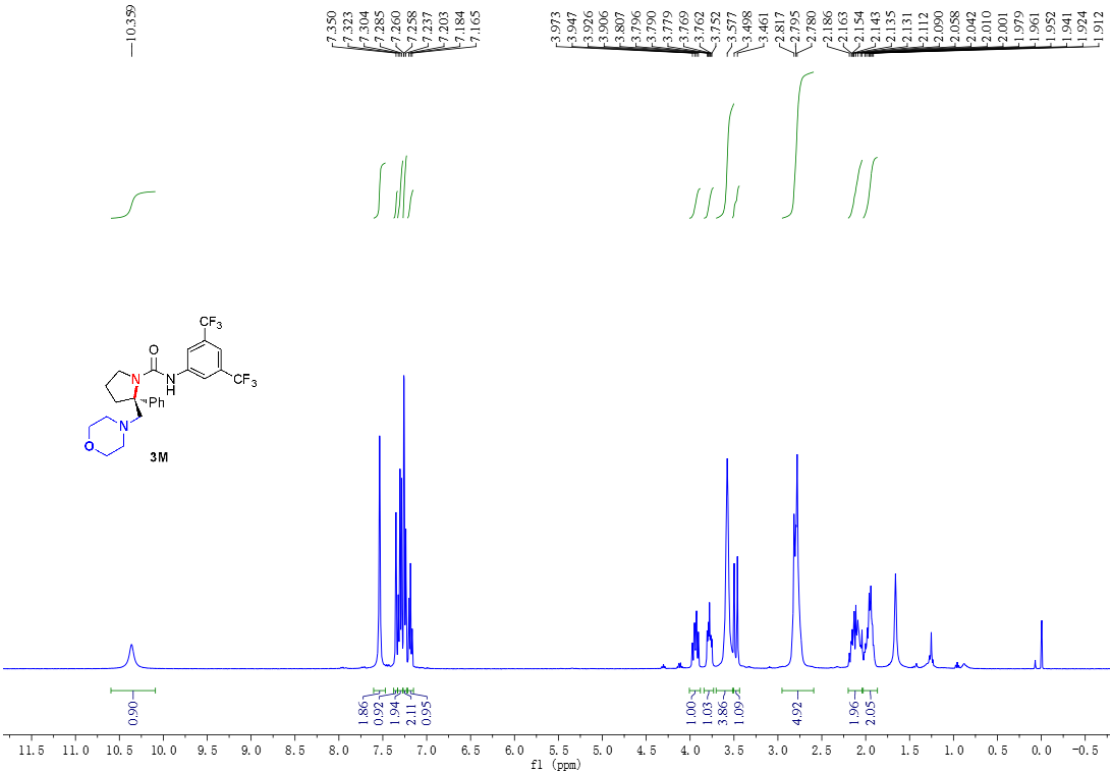


Figure S38. ^{1}H NMR spectrum of **3M**

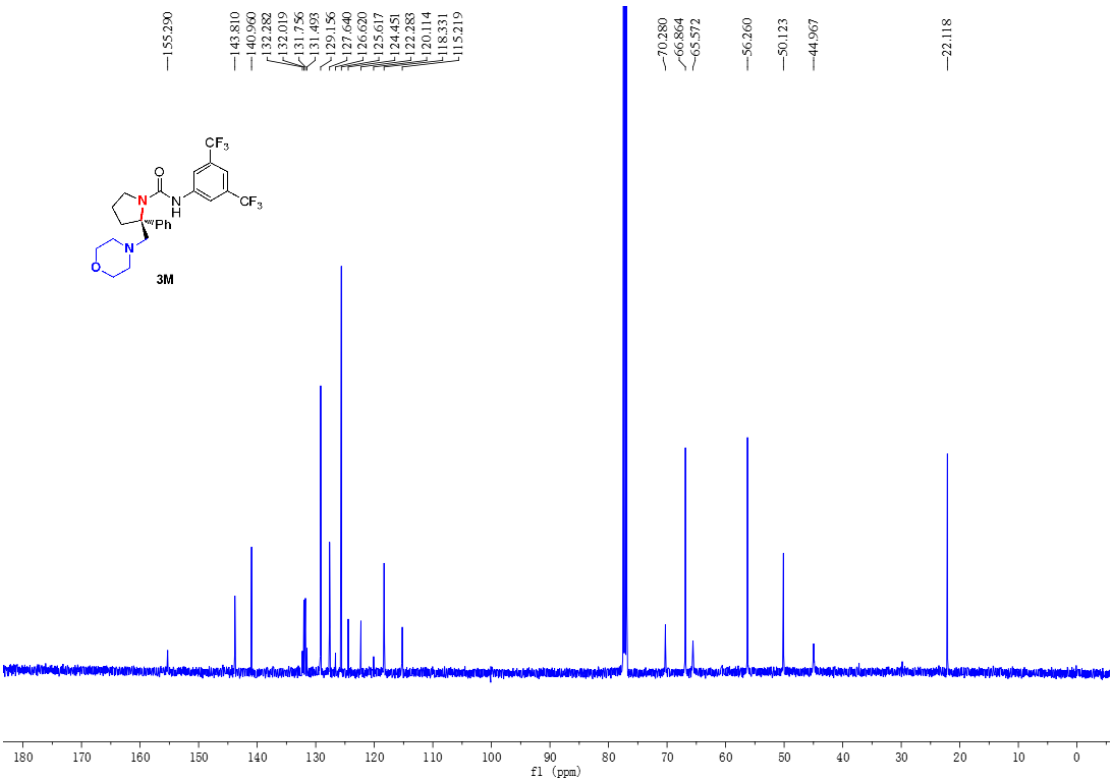


Figure S39. ^{13}C NMR spectrum of **3M**

Figure S40. ^{19}F NMR spectrum of **3M**

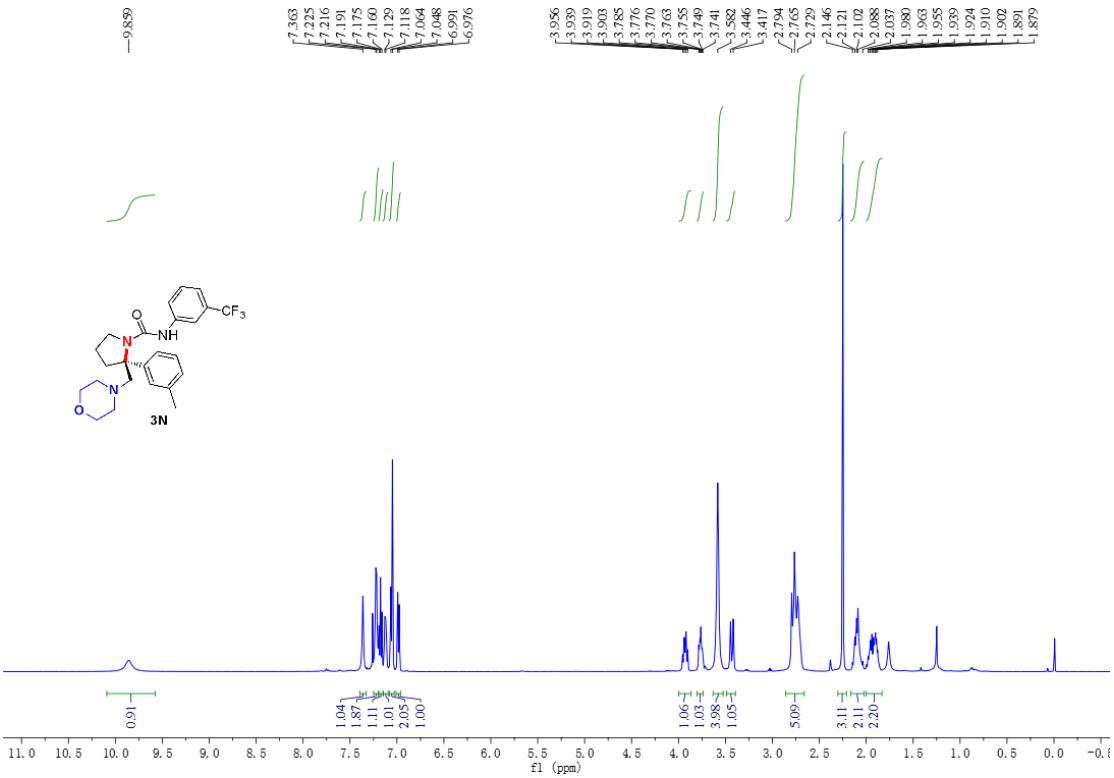


Figure S41. ^{1}H NMR spectrum of **3N**

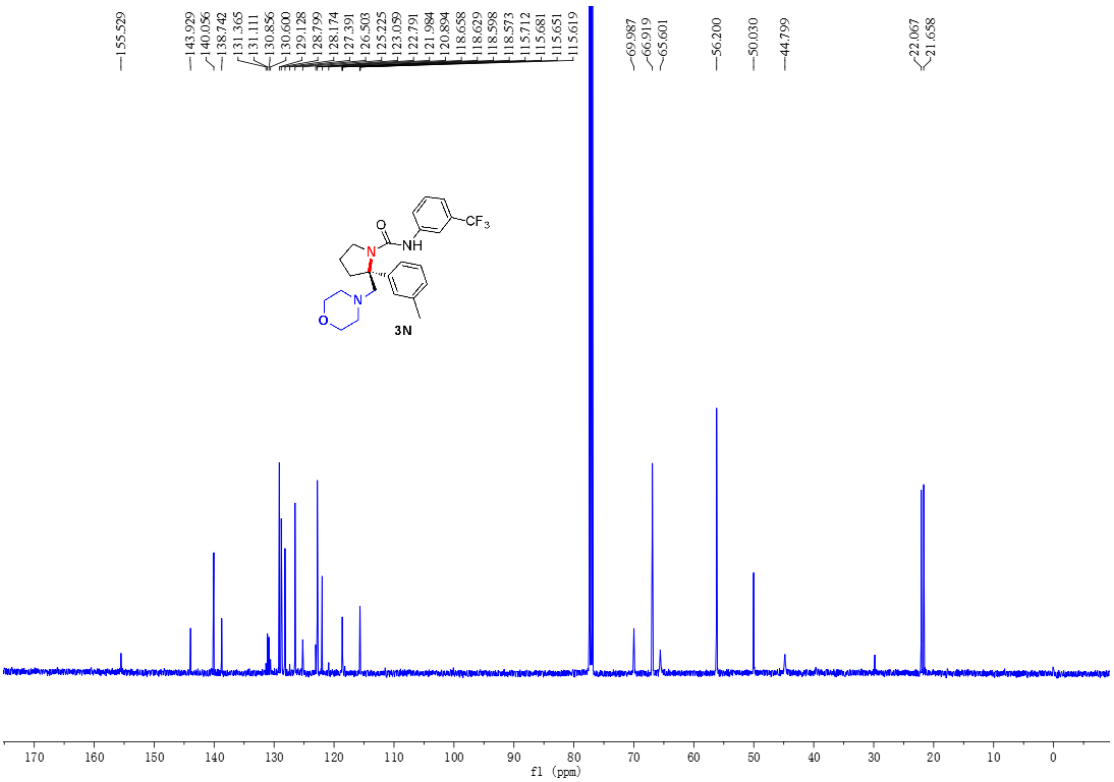


Figure S42. ^{13}C NMR spectrum of **3N**

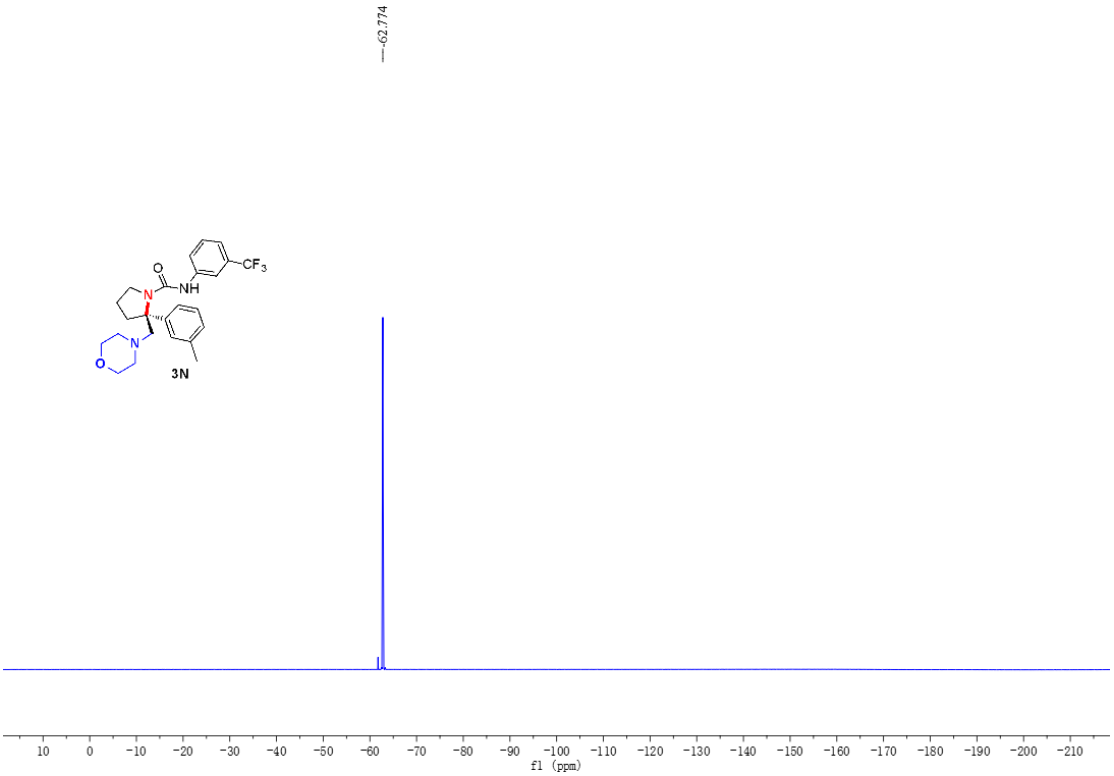


Figure S43. ^{19}F NMR spectrum of **3N**

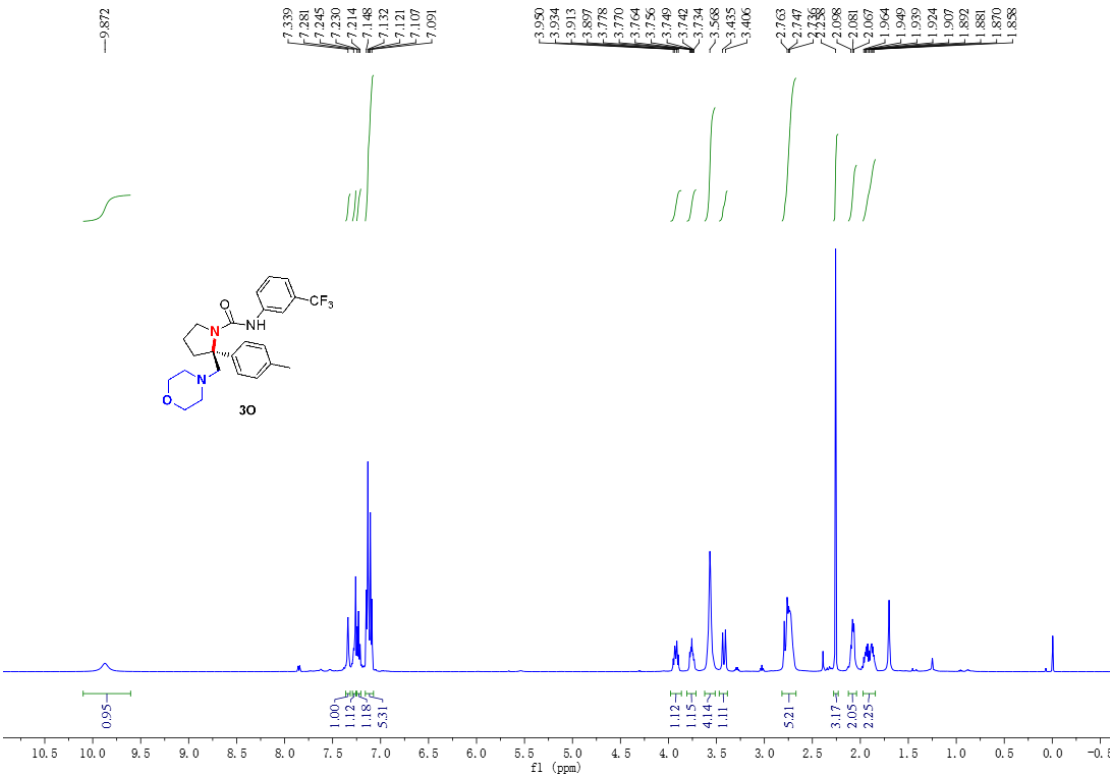


Figure S44. ^{1}H NMR spectrum of **3O**

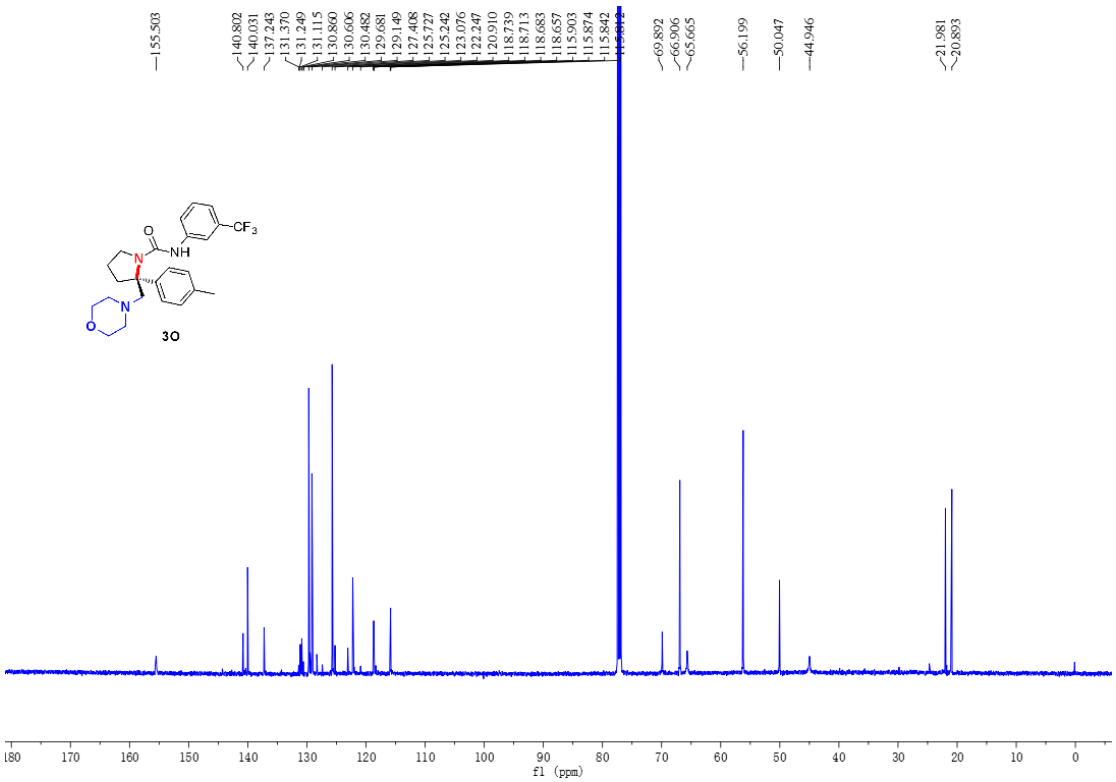


Figure S45. ^{13}C NMR spectrum of **3O**

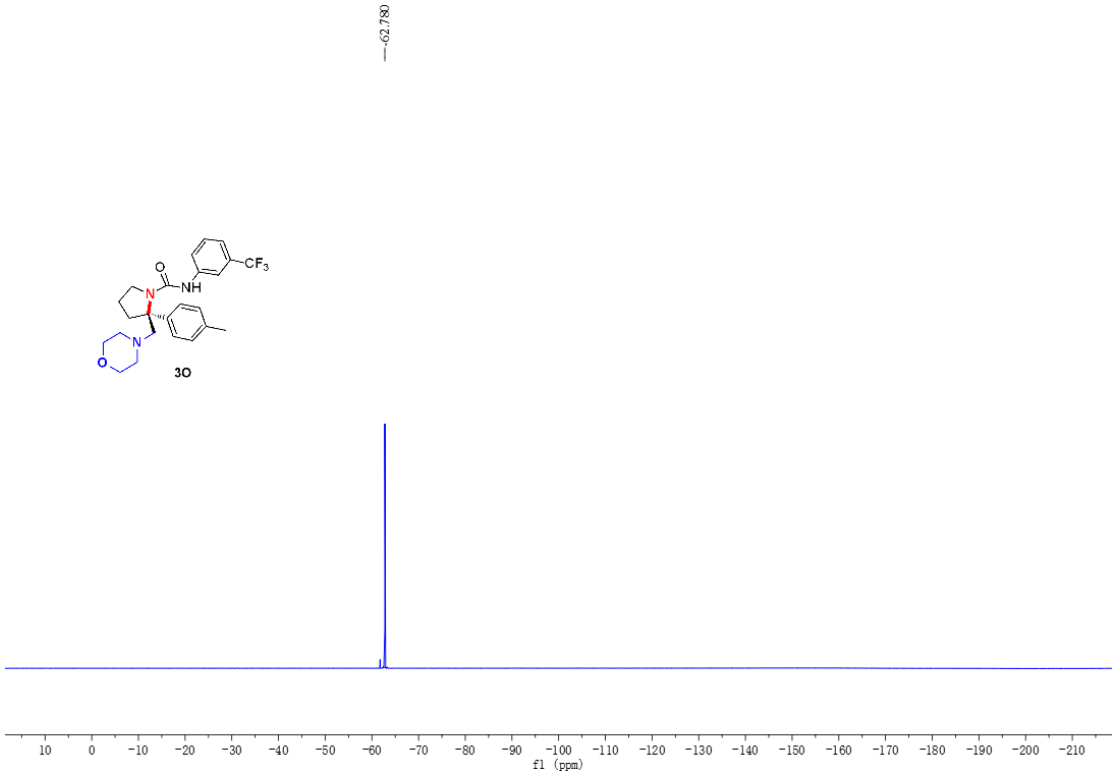


Figure S46. ^{19}F NMR spectrum of **3O**

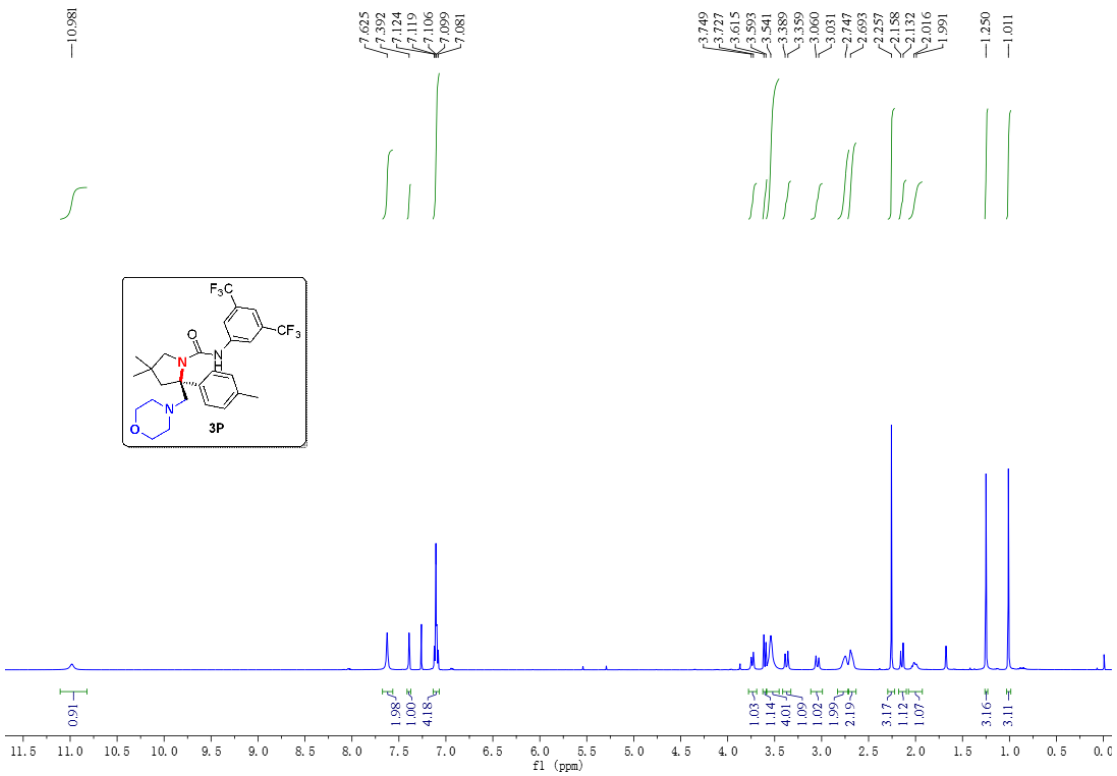


Figure S47. ^{1}H NMR spectrum of **3P**

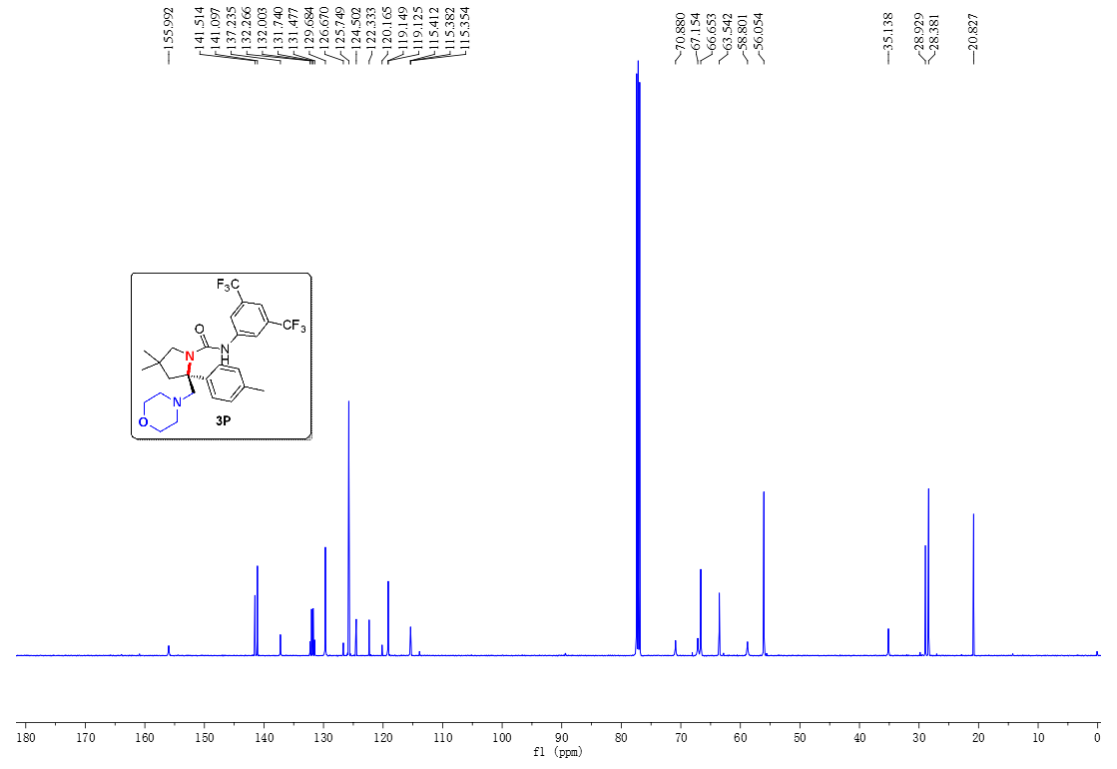


Figure S48. ^{13}C NMR spectrum of **3P**

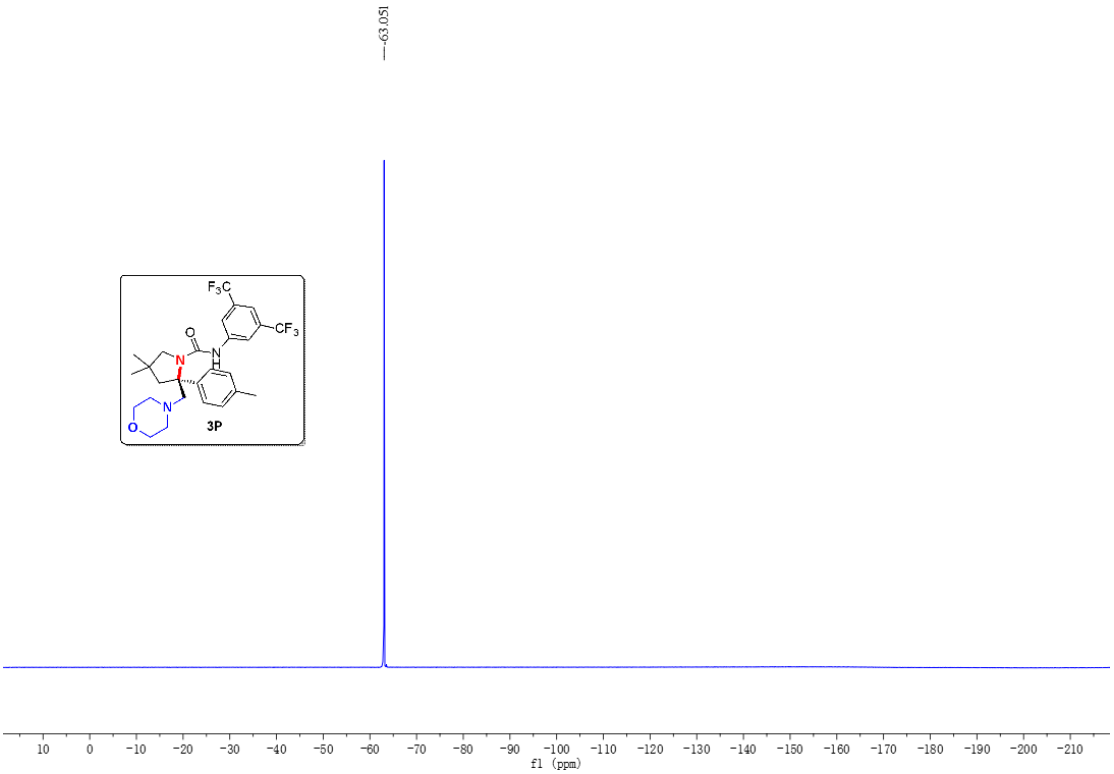


Figure S49. ^{19}F NMR spectrum of **3P**

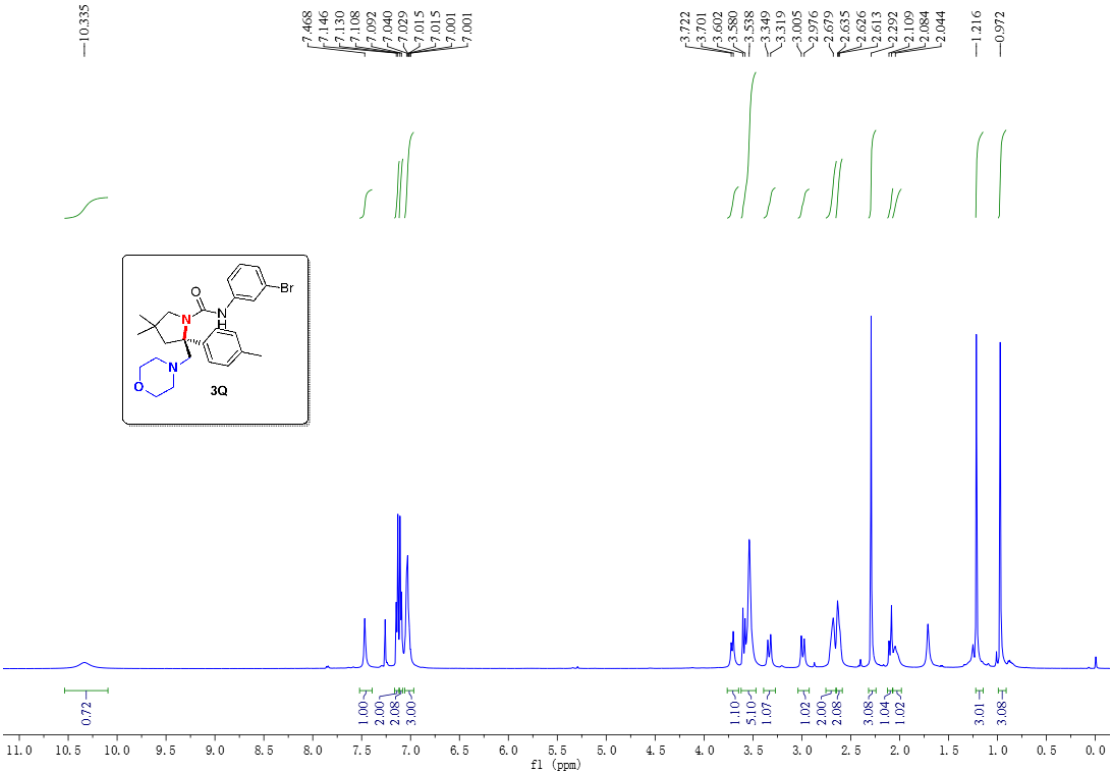


Figure S50. ^{1}H NMR spectrum of **3Q**

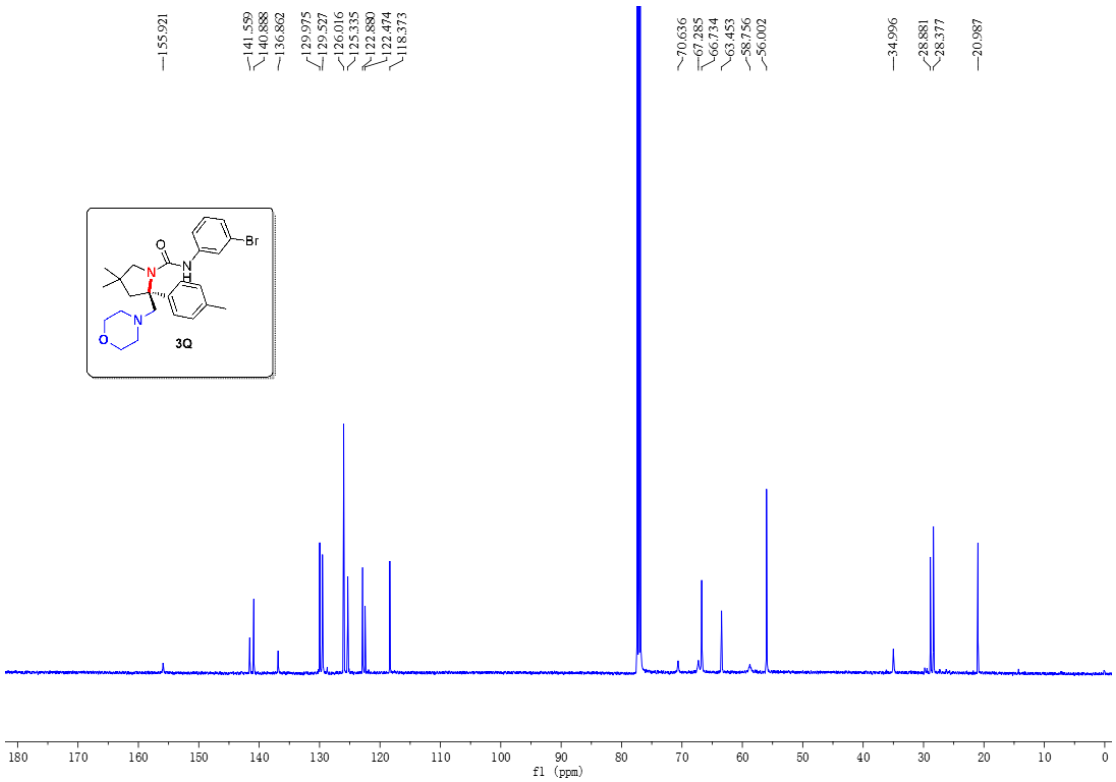


Figure S51. ^{13}C NMR spectrum of **3Q**

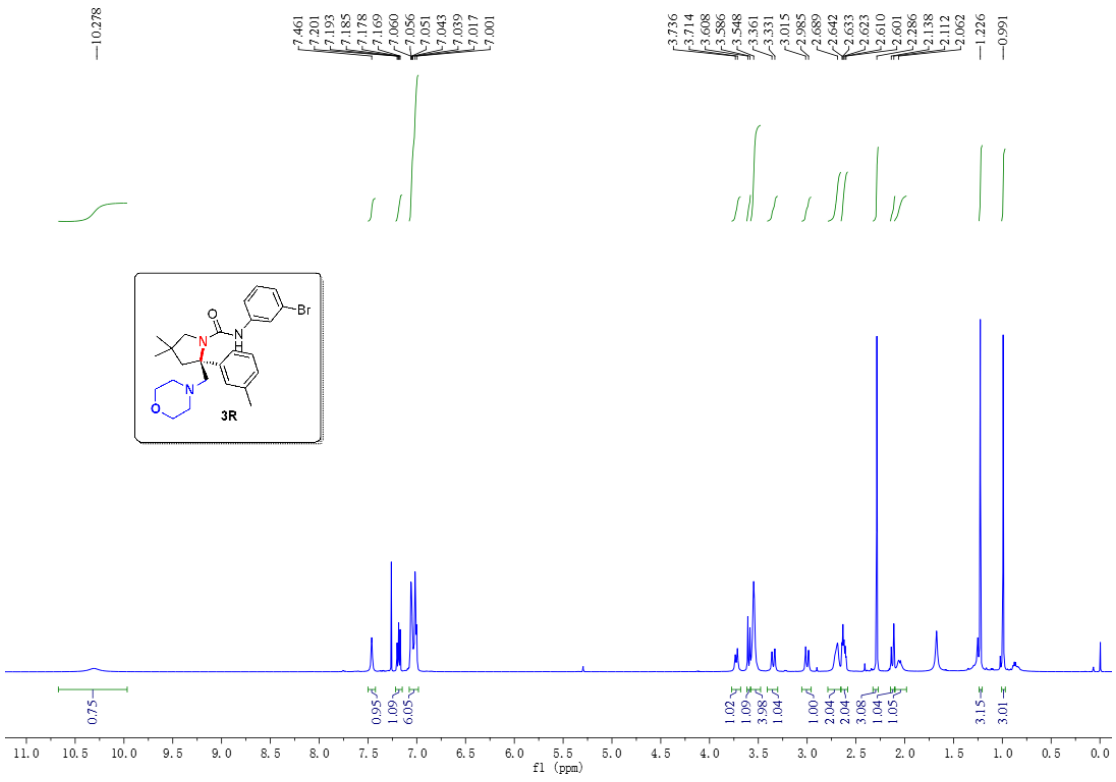


Figure S52. ^{1}H NMR spectrum of **3R**

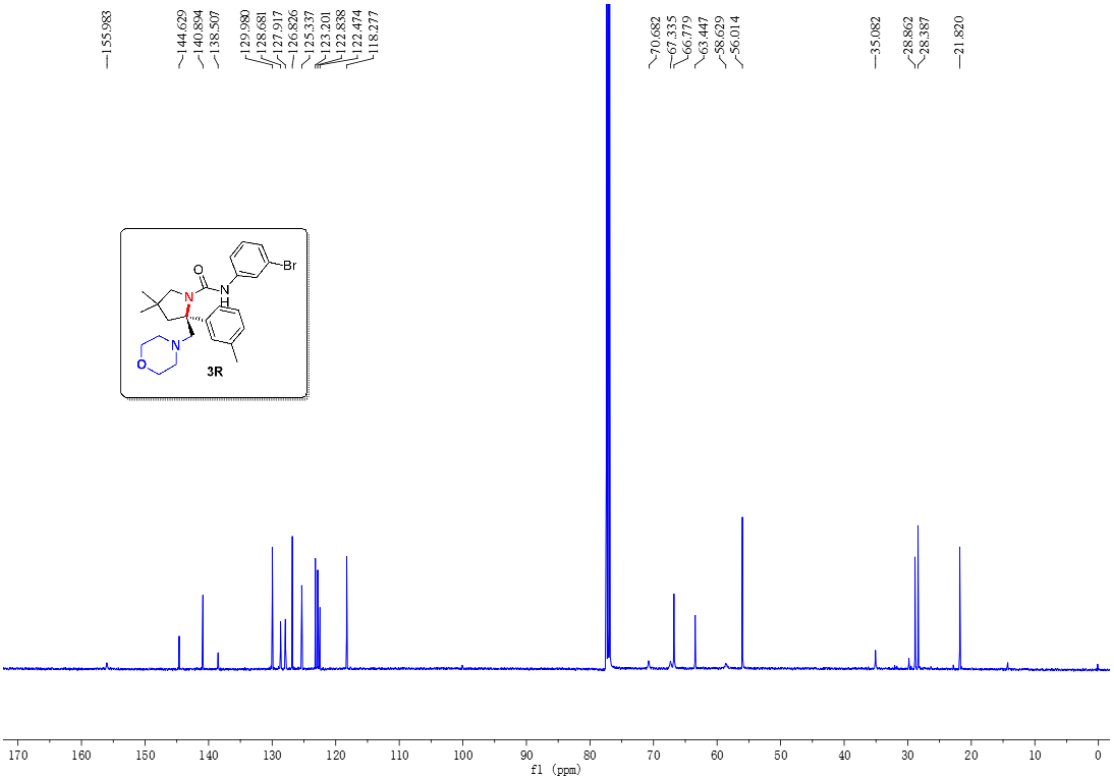


Figure S53. ^{13}C NMR spectrum of **3R**

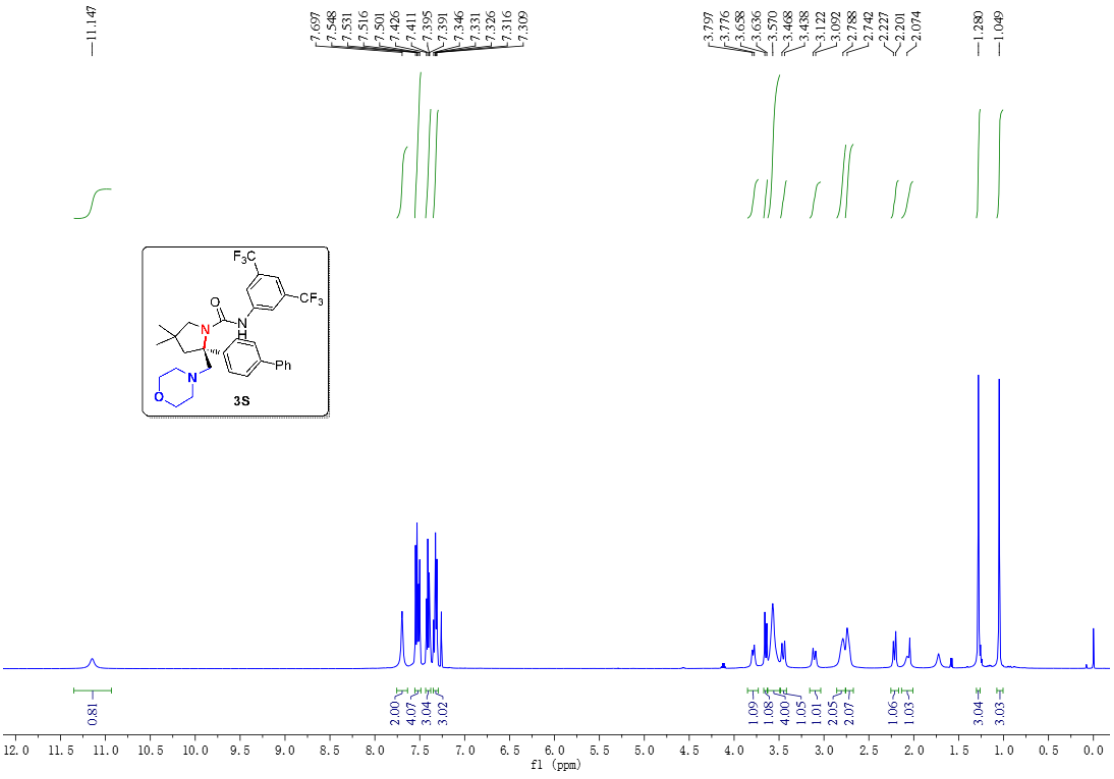


Figure S54. ^{1}H NMR spectrum of **3S**

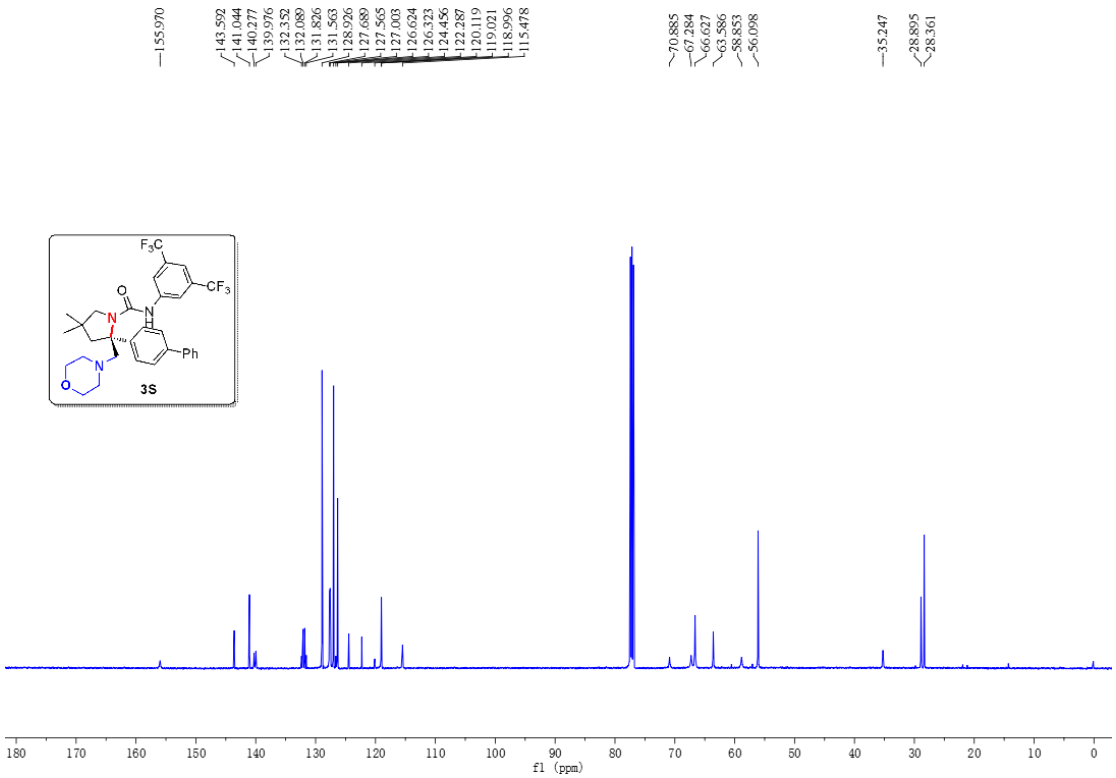


Figure S55. ^{13}C NMR spectrum of **3S**

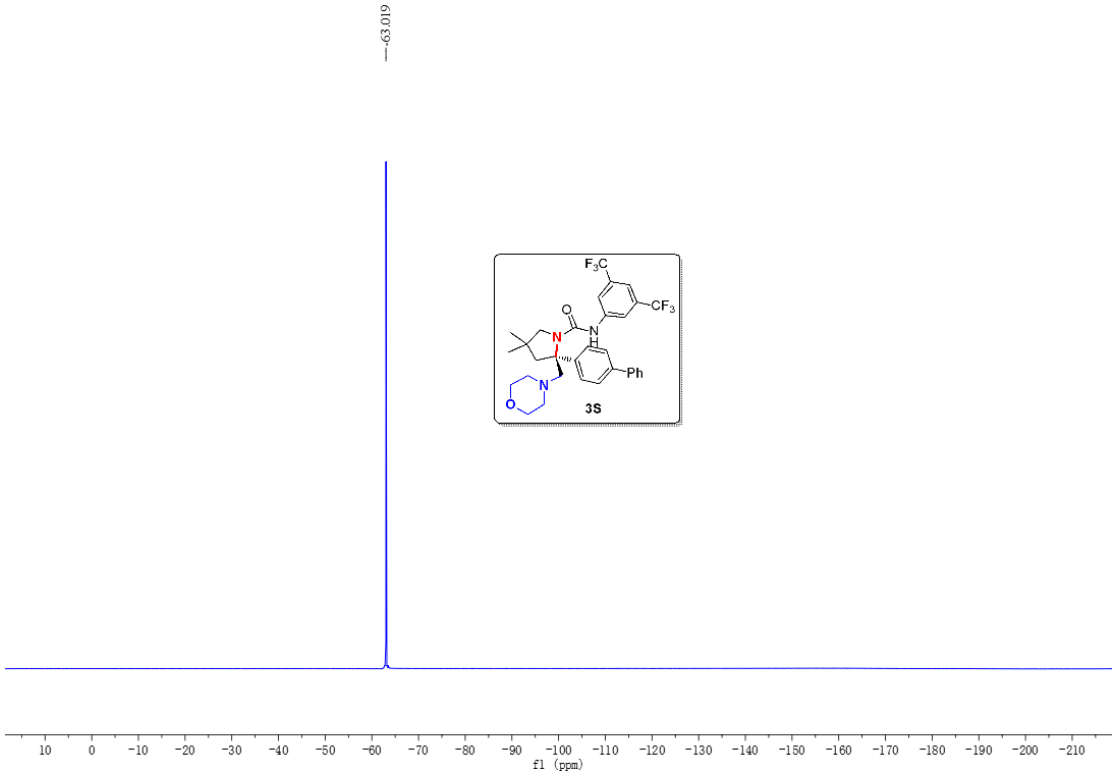


Figure S56. ^{19}F NMR spectrum of **3S**

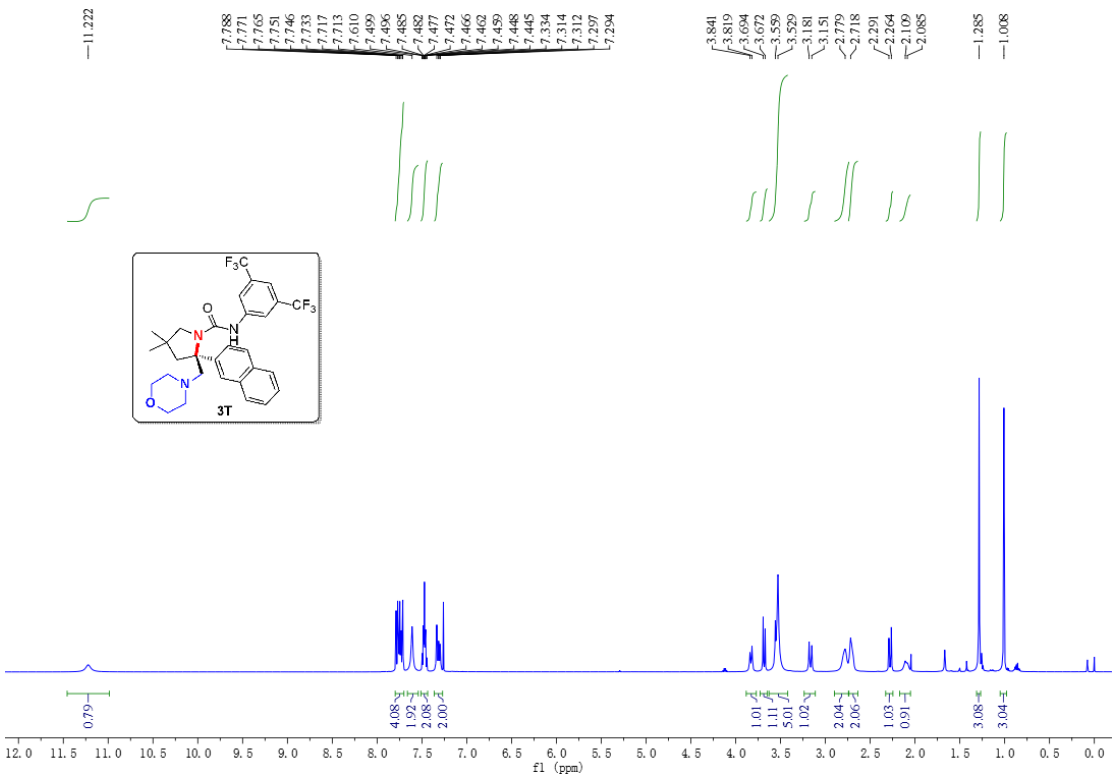


Figure S57. ^{1}H NMR spectrum of **3T**

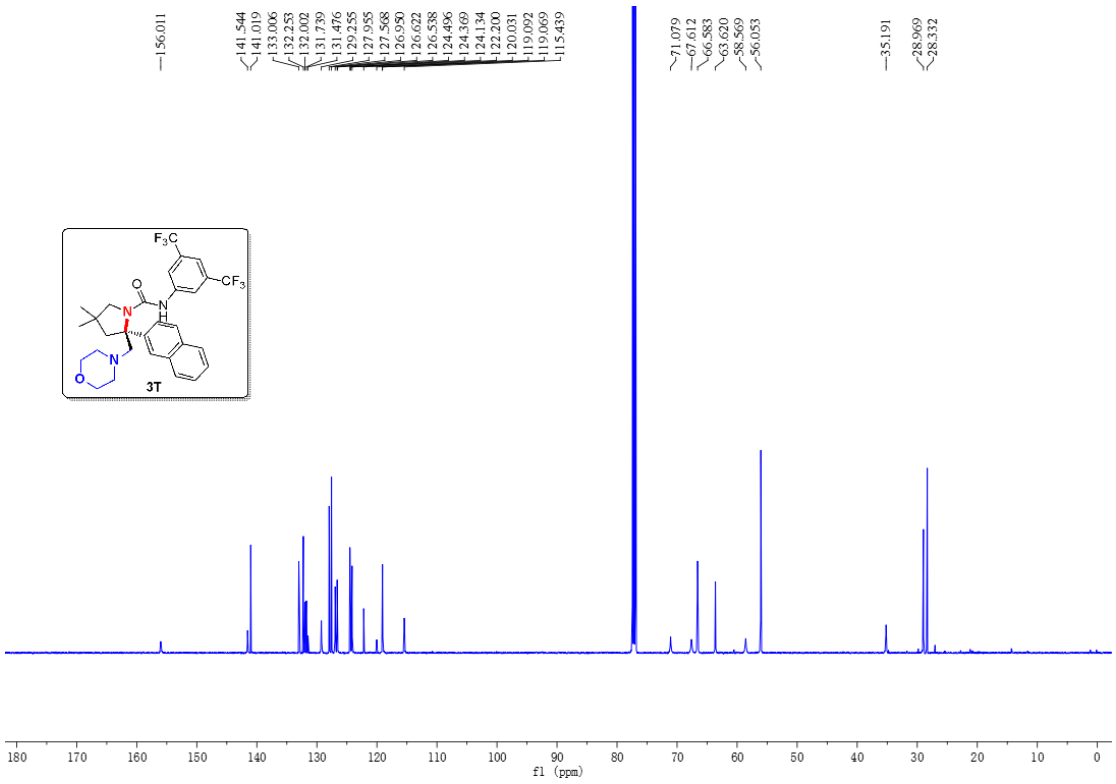


Figure S58. ^{13}C NMR spectrum of **3T**

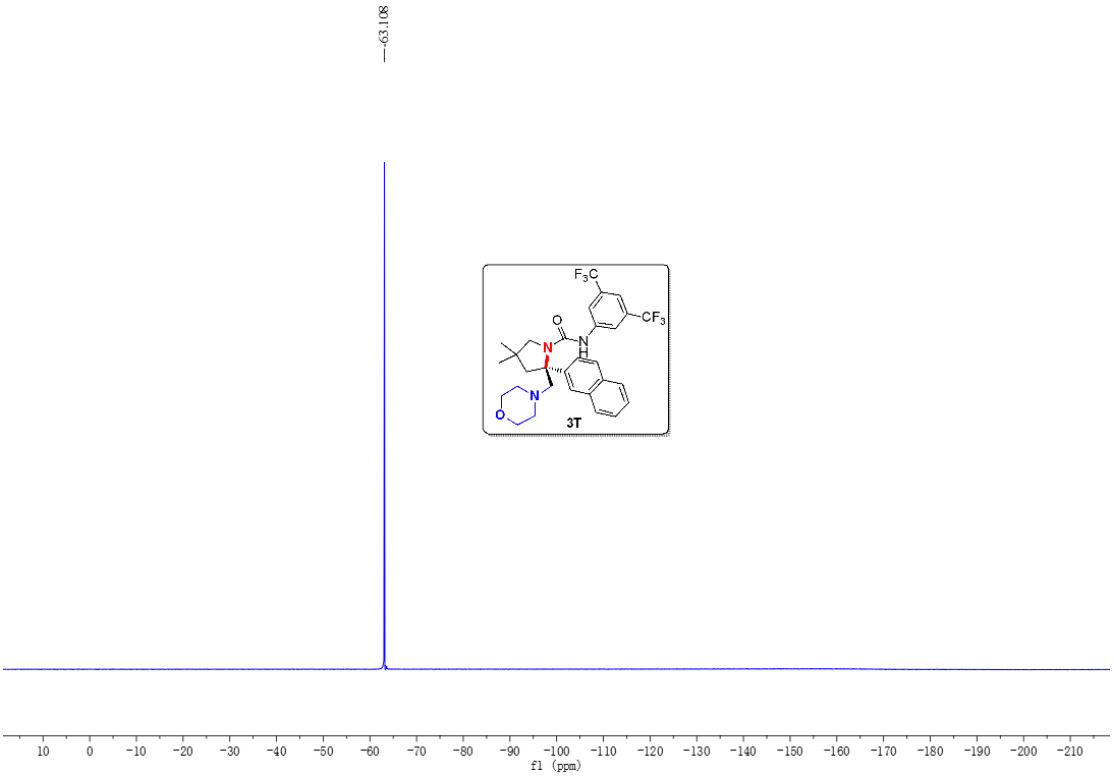


Figure S59. ^{19}F NMR spectrum of **3T**

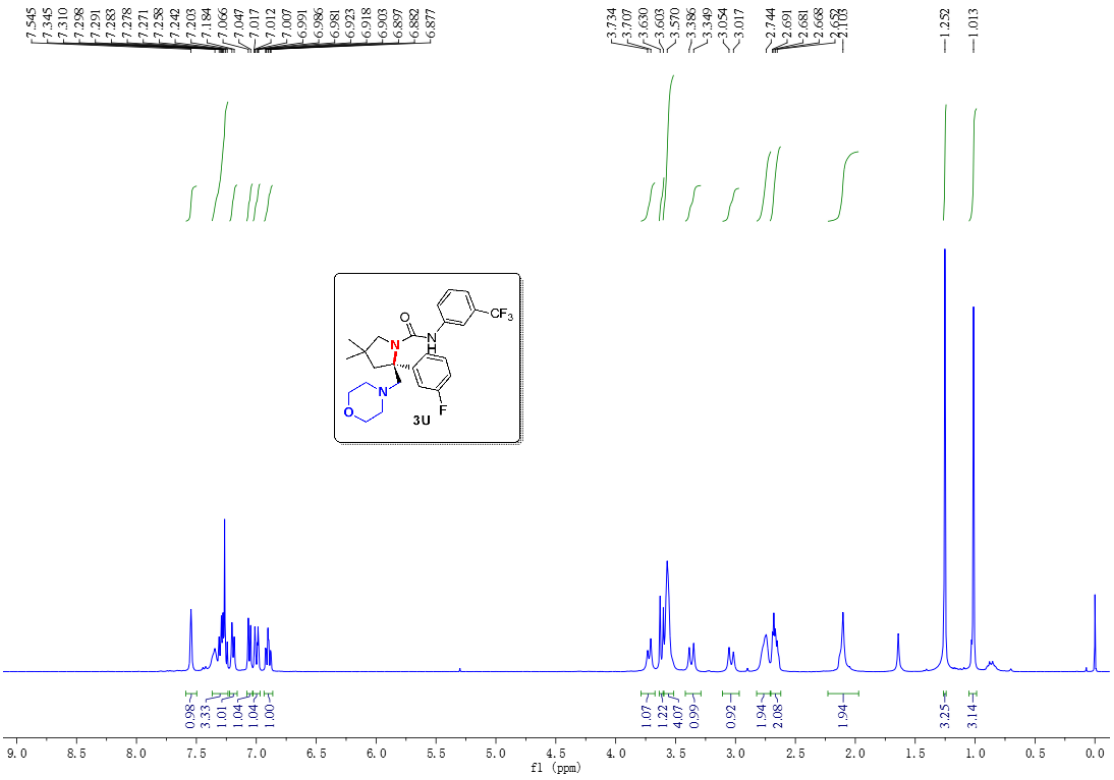


Figure S60. ^{1}H NMR spectrum of **3U**

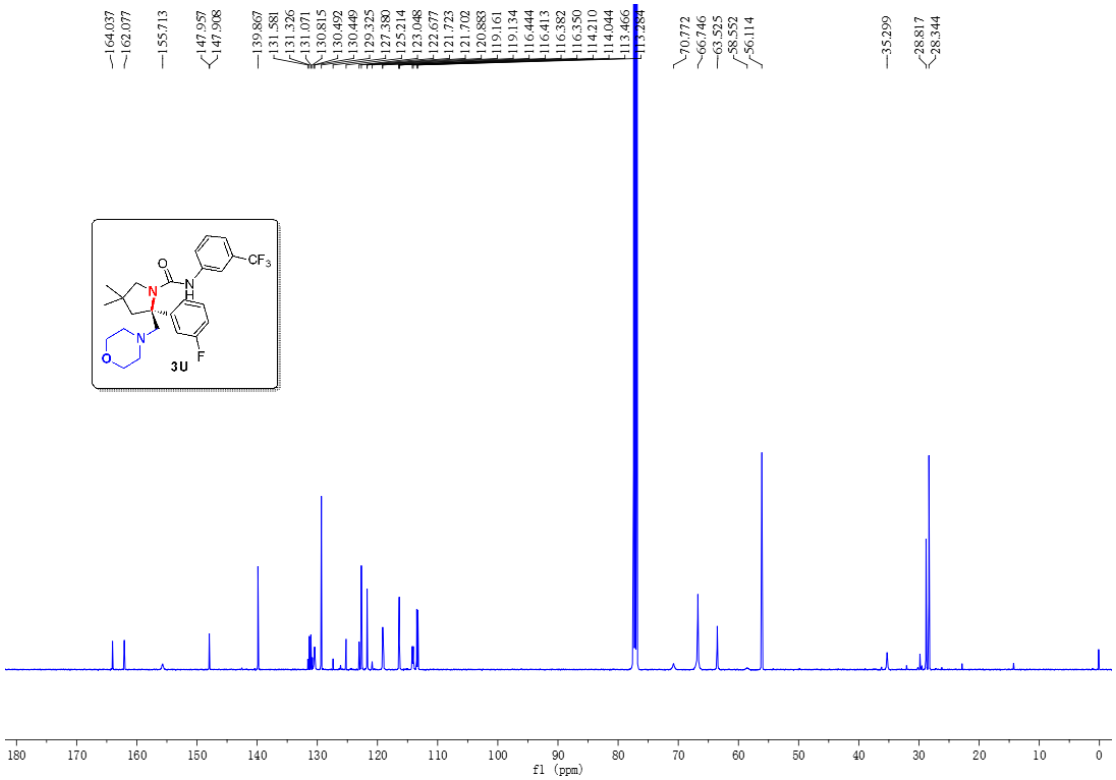


Figure S61. ^{13}C NMR spectrum of **3U**

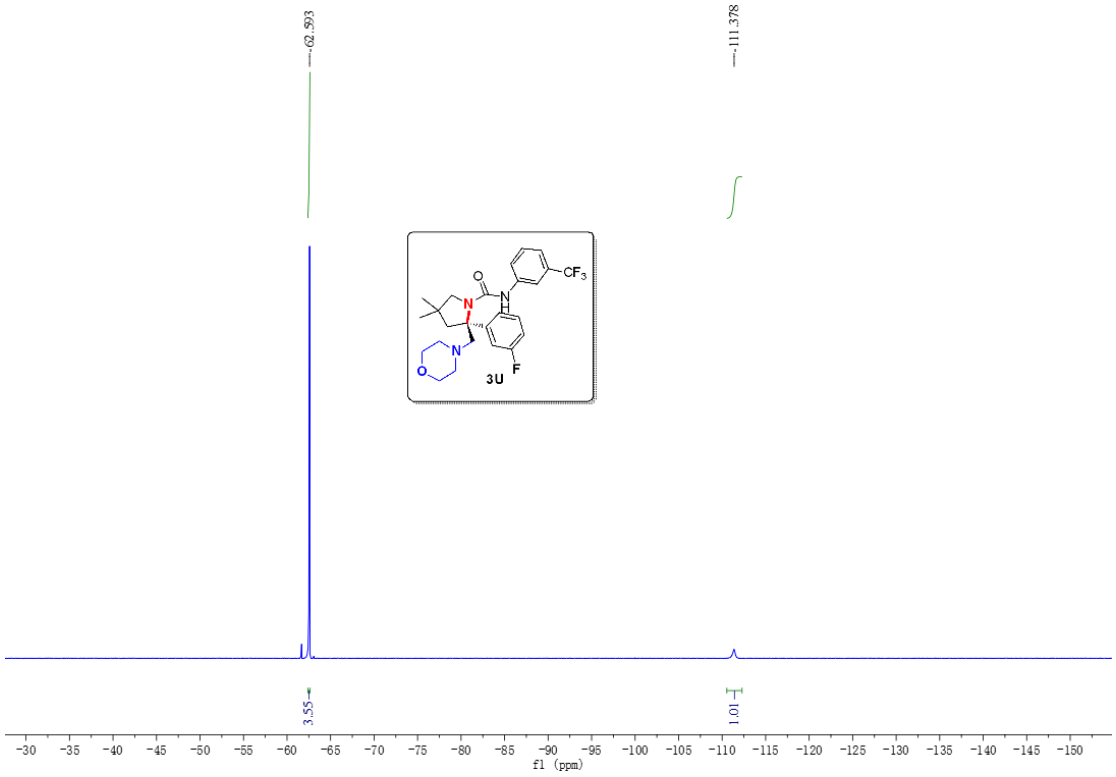


Figure S62. ^{19}F NMR spectrum of **3U**

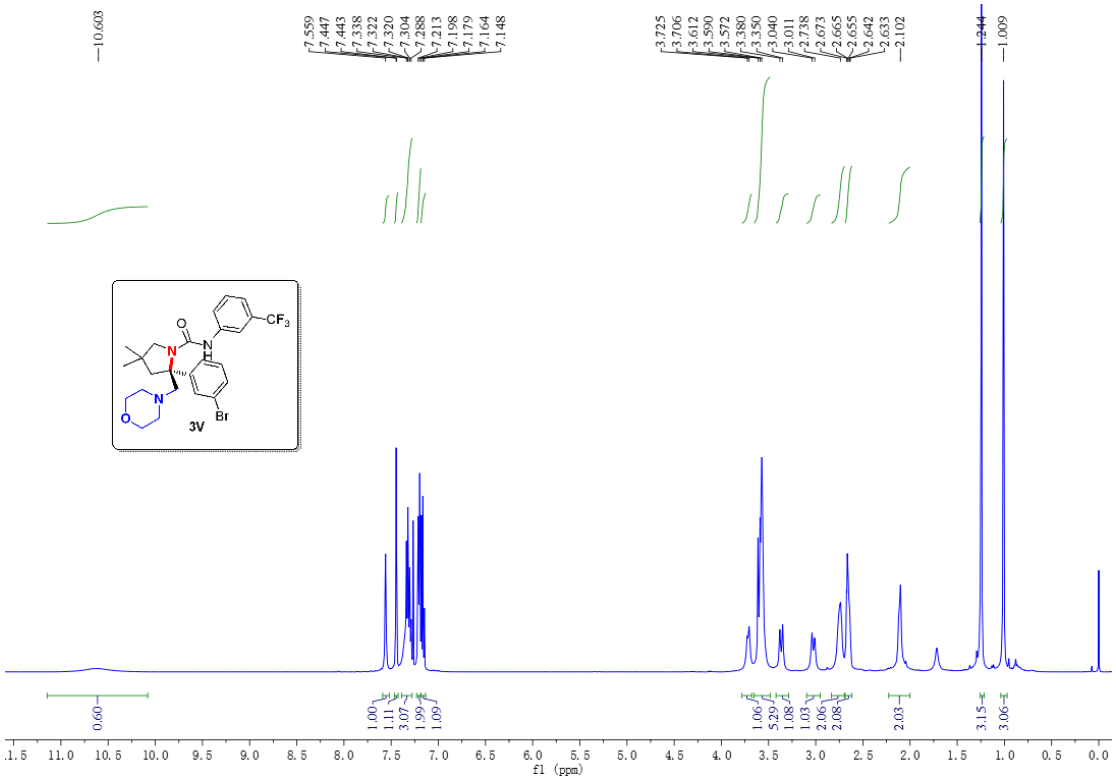


Figure S63. ^{1}H NMR spectrum of **3V**

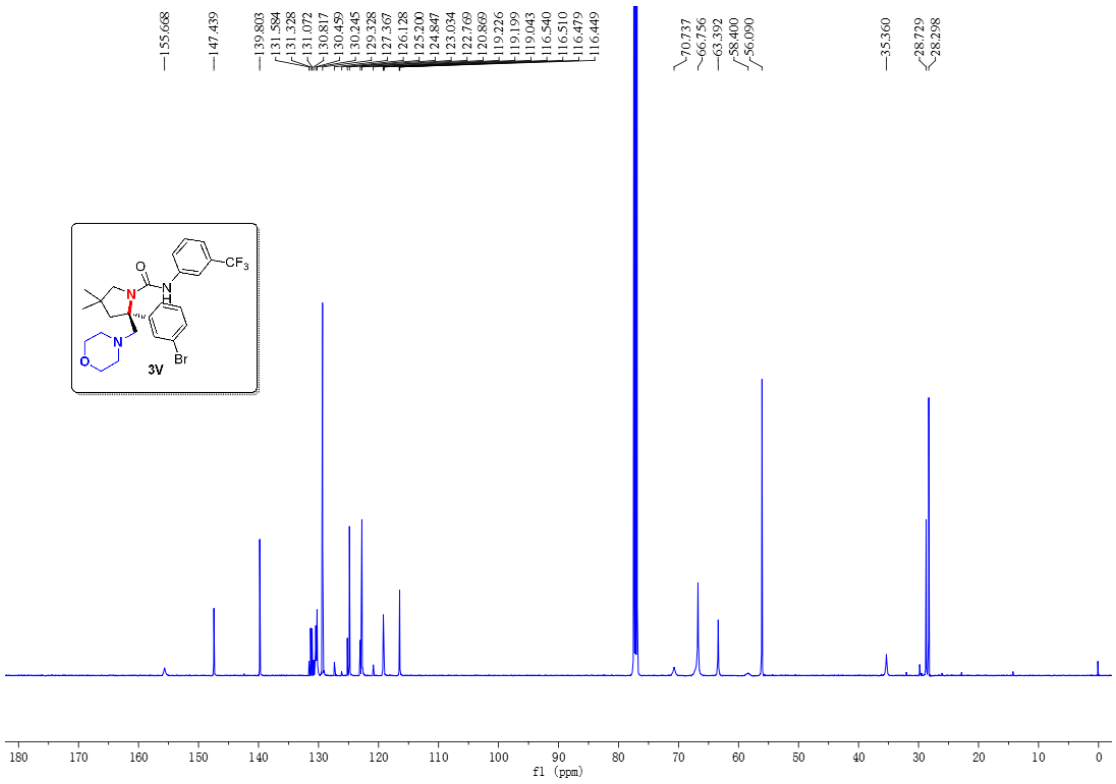


Figure S64. ^{13}C NMR spectrum of **3V**

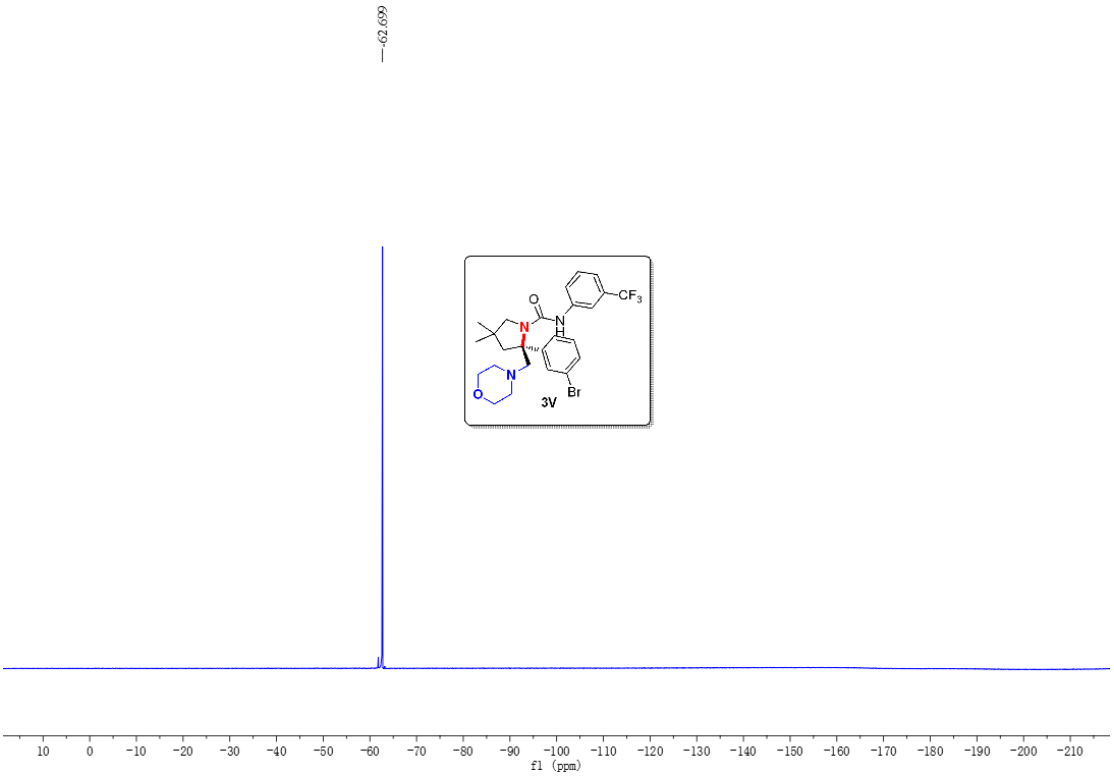


Figure S65. ^{19}F NMR spectrum of **3V**

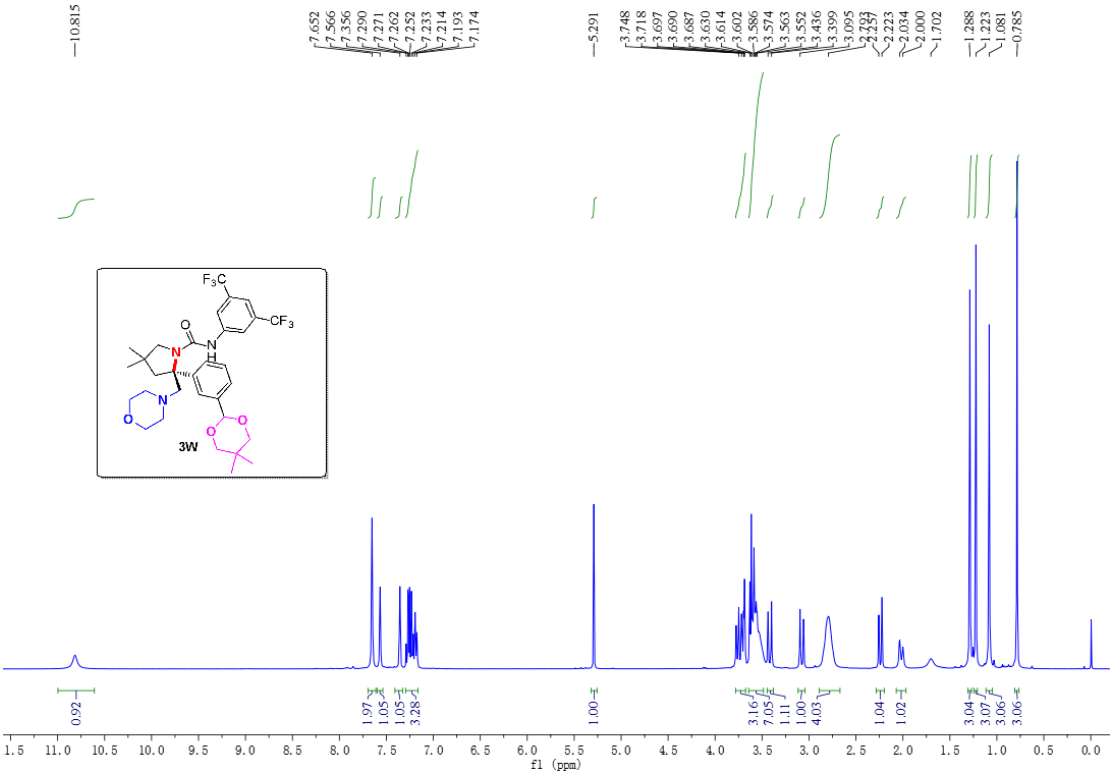


Figure S66. ^{1}H NMR spectrum of **3W**

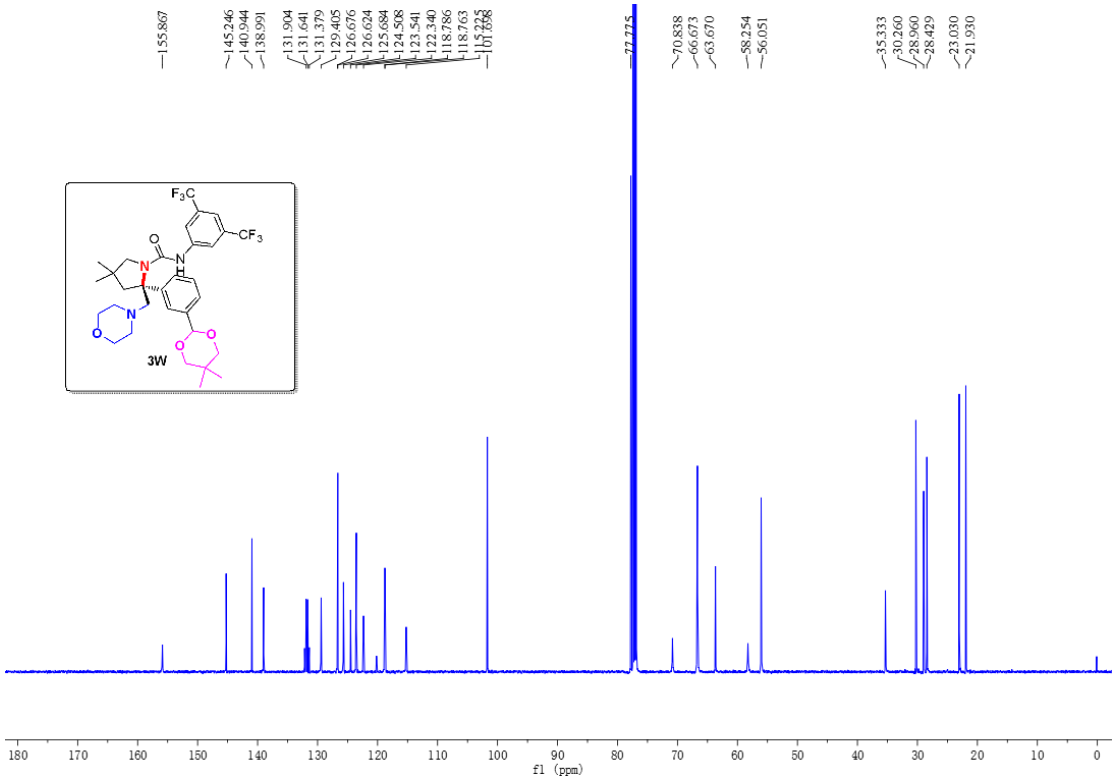


Figure S67. ^{13}C NMR spectrum of **3W**

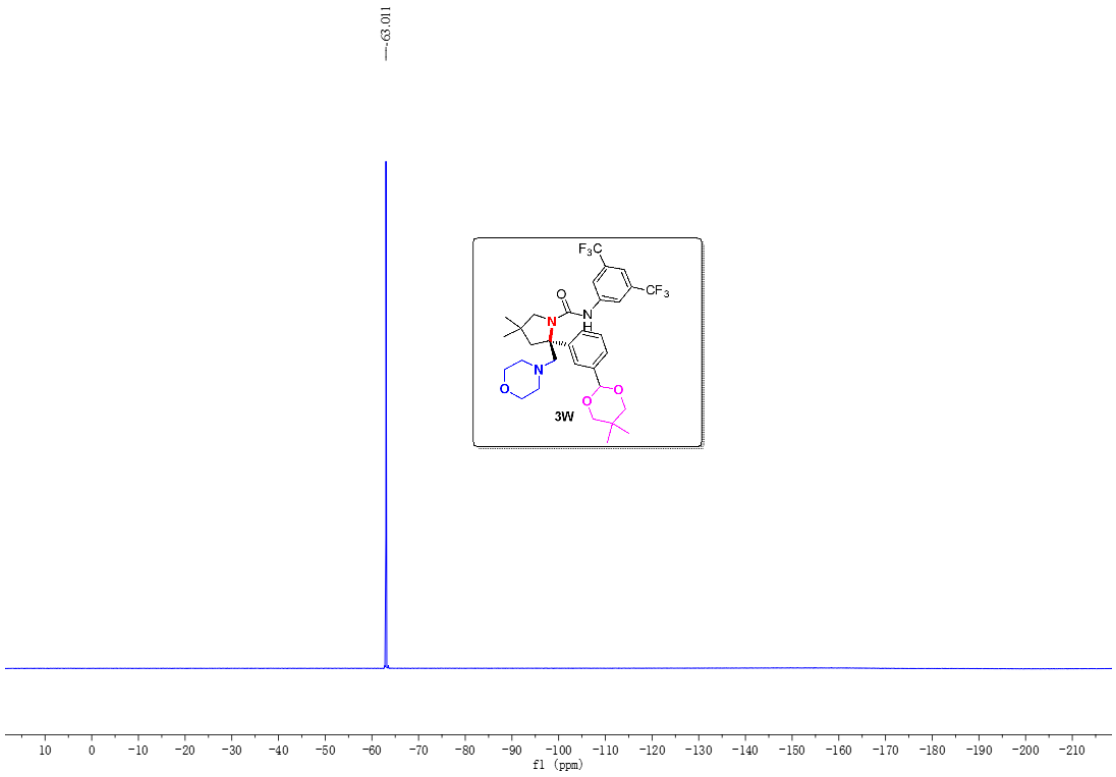


Figure S68. ^{19}F NMR spectrum of **3W**

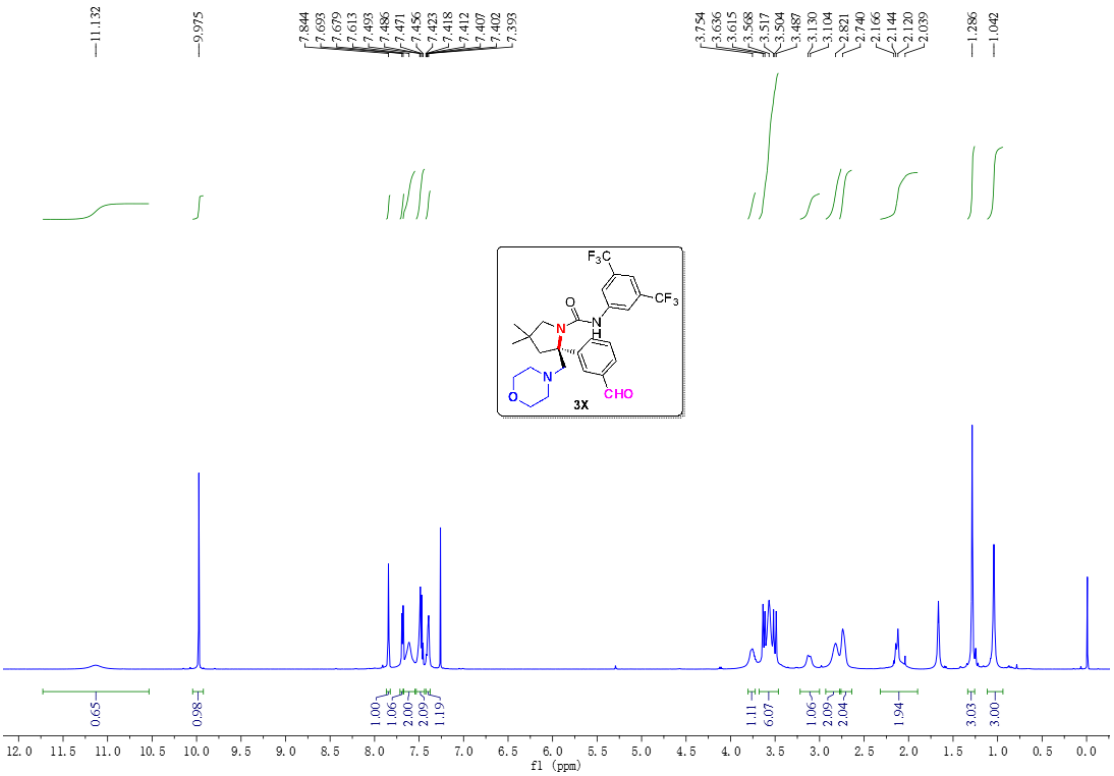


Figure S69. ^{1}H NMR spectrum of **3X**

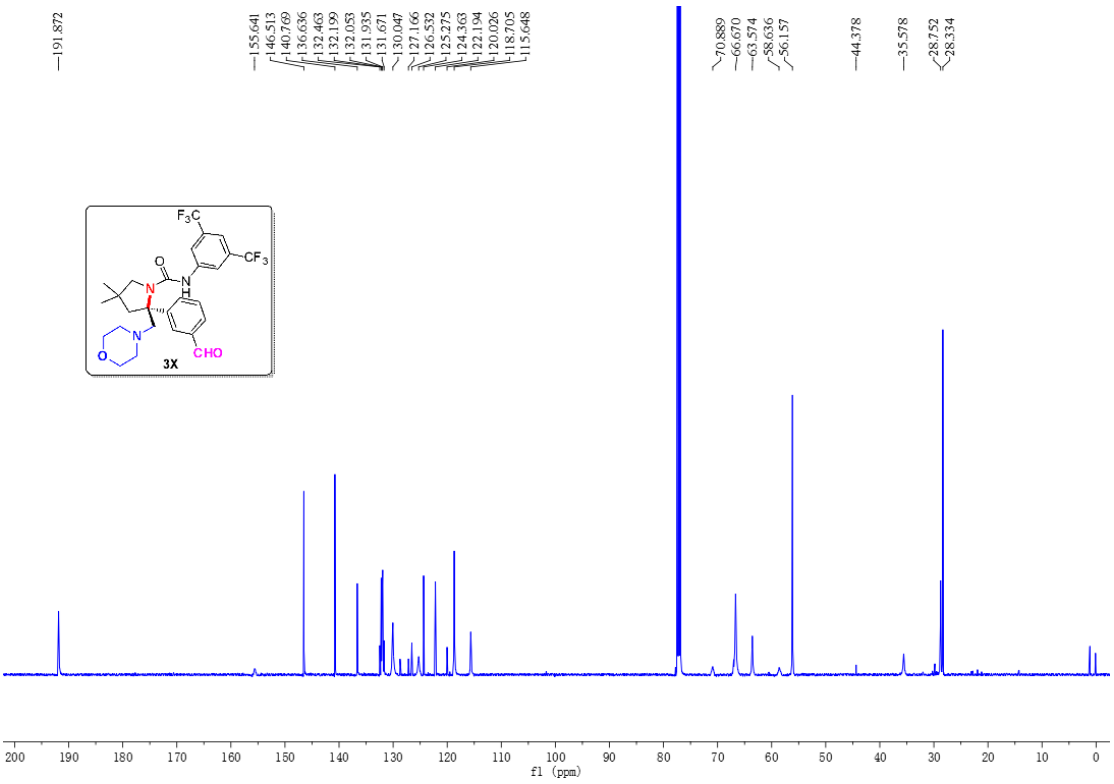


Figure S70. ^{13}C NMR spectrum of **3X**

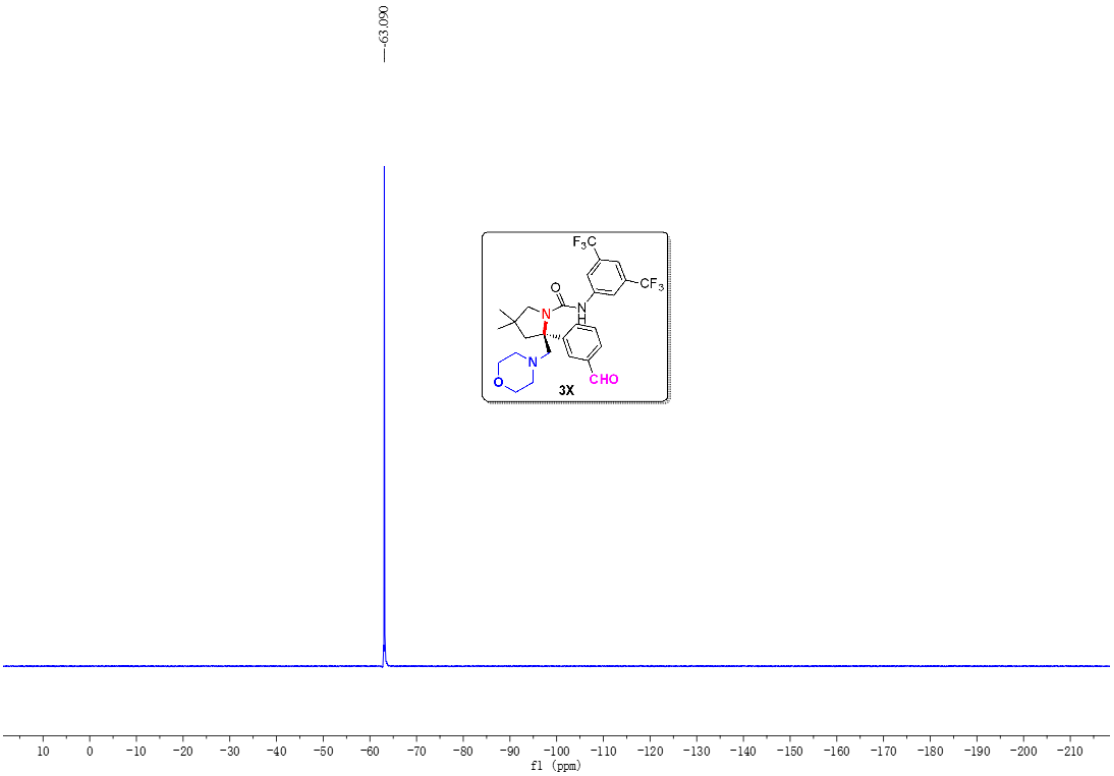


Figure S71. ^{19}F NMR spectrum of **3X**

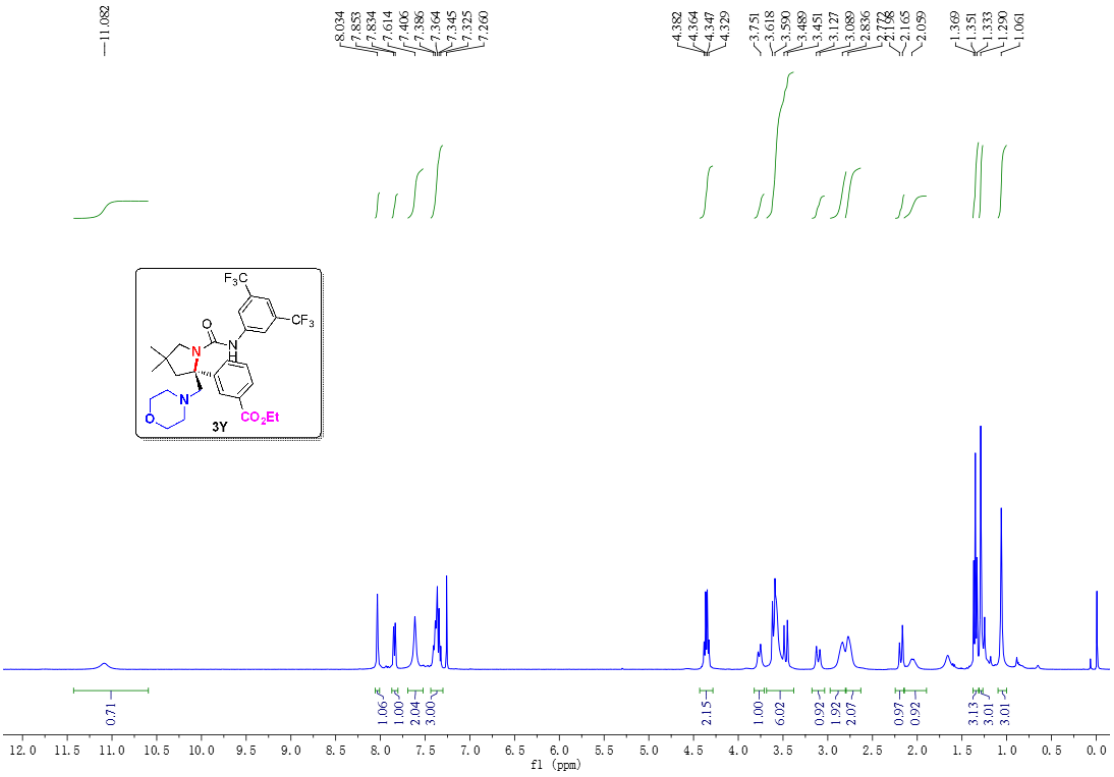


Figure S72. ^{1}H NMR spectrum of **3Y**

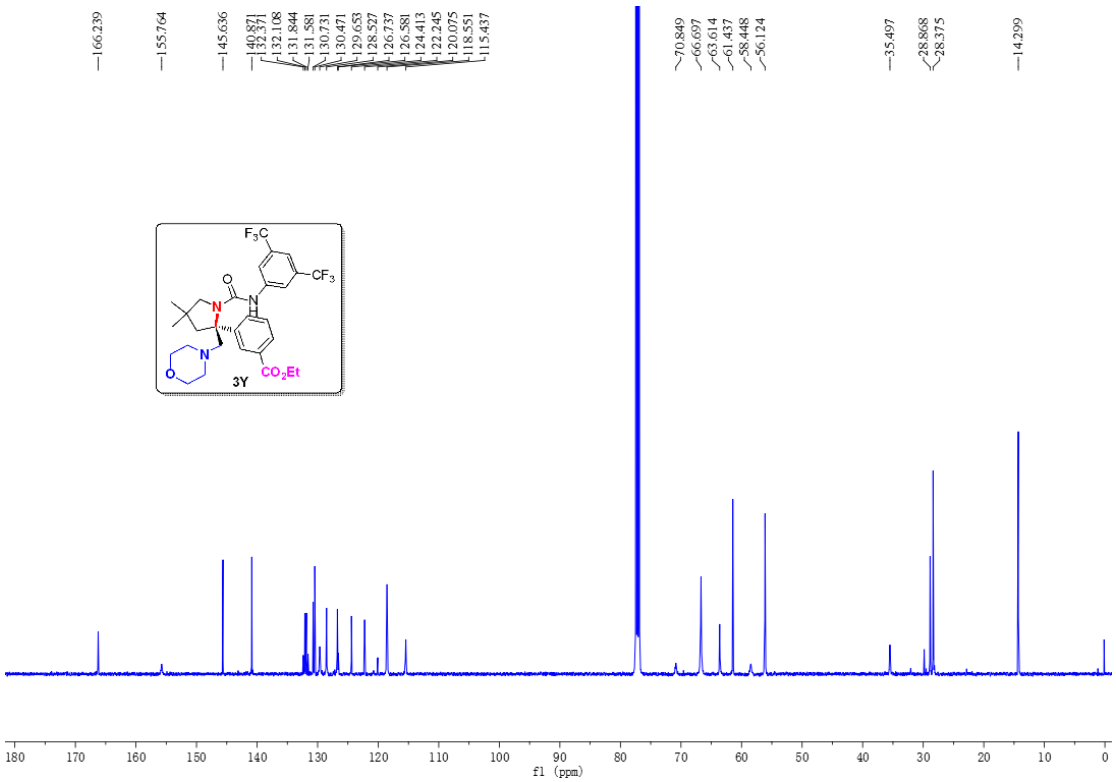


Figure S73. ^{13}C NMR spectrum of **3Y**

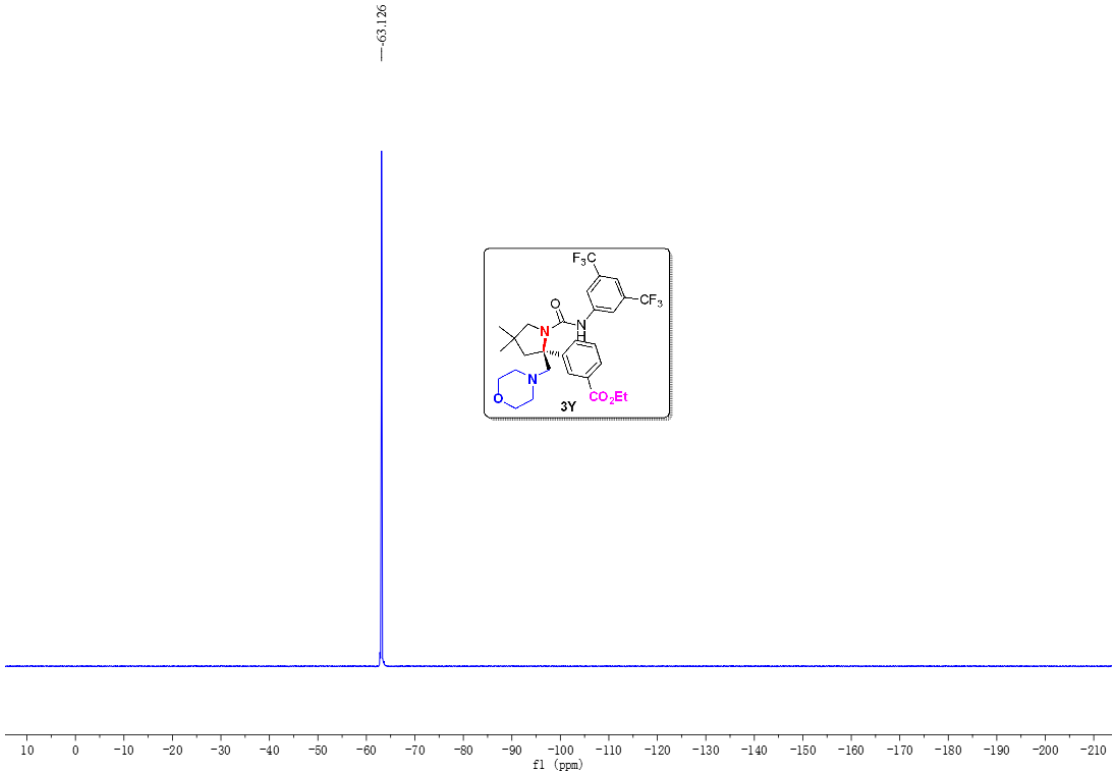


Figure S74. ^{19}F NMR spectrum of **3Y**

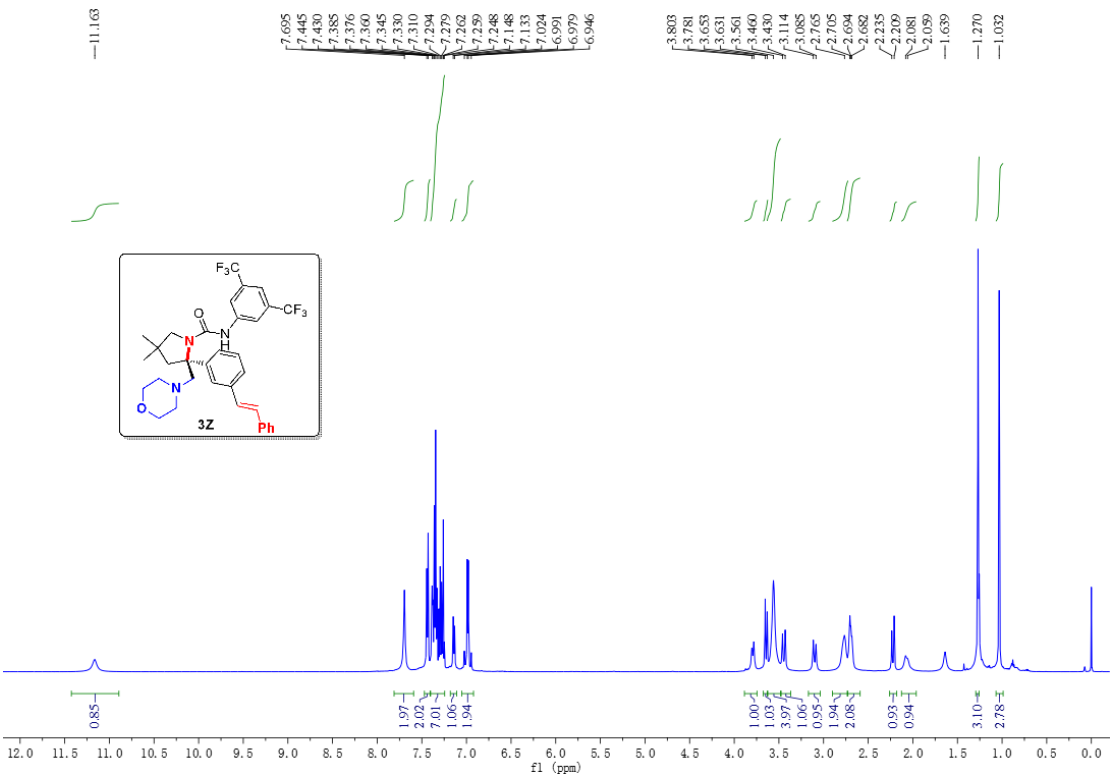


Figure S75. ^{1}H NMR spectrum of **3Z**

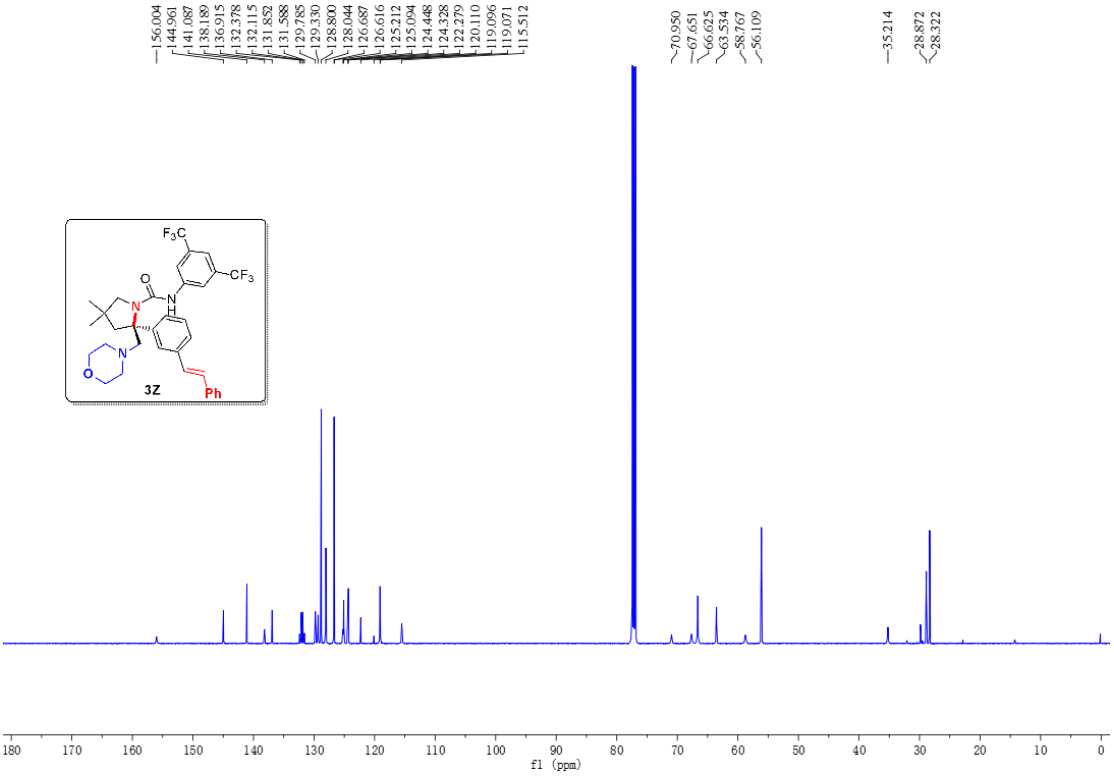


Figure S76. ^{13}C NMR spectrum of **3Z**

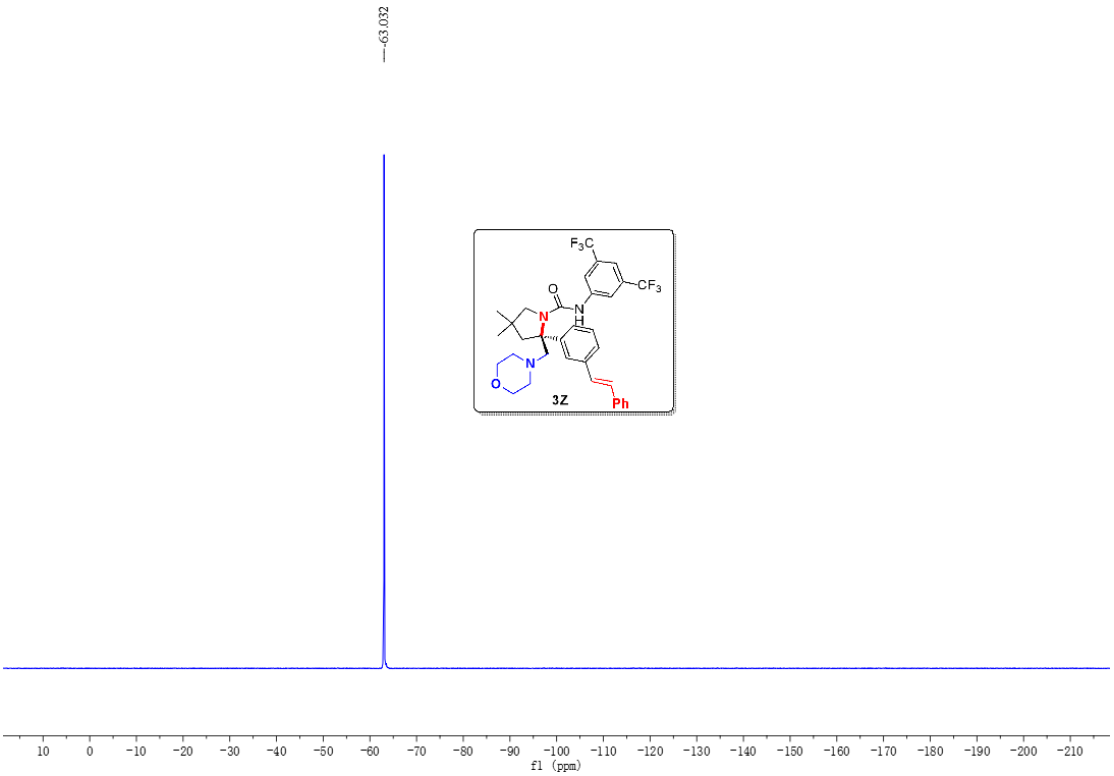


Figure S77. ^{19}F NMR spectrum of **3Z**

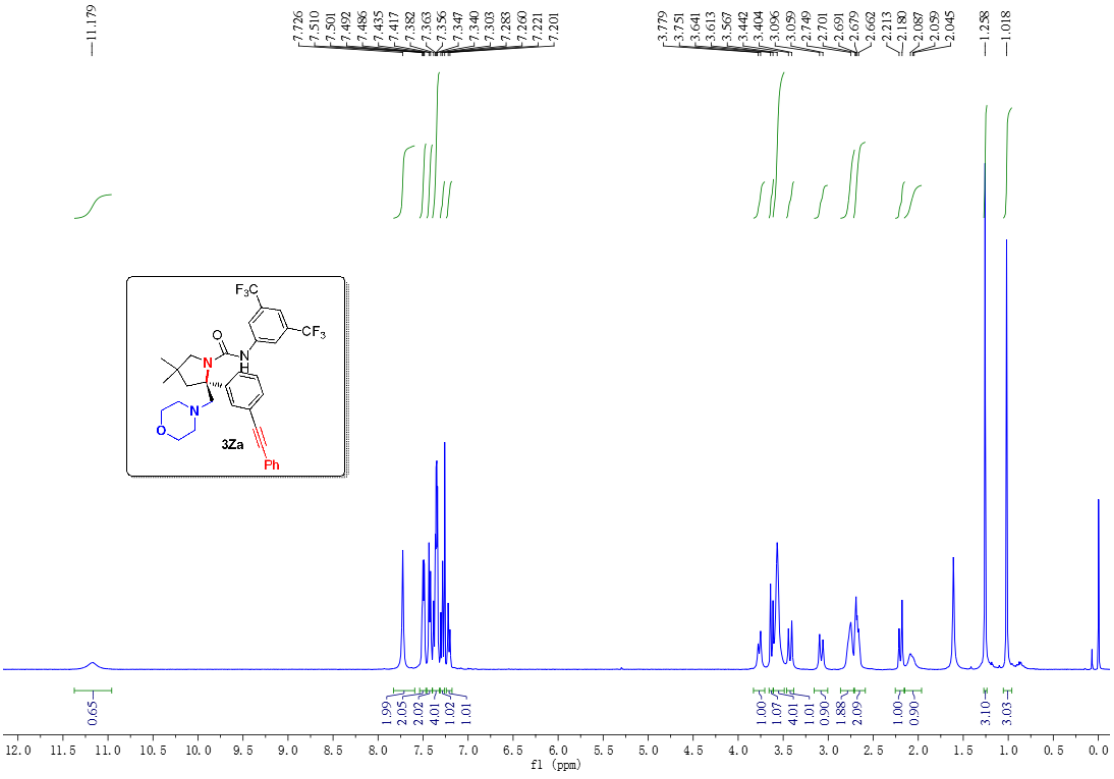


Figure S78. ^{1}H NMR spectrum of **3Za**

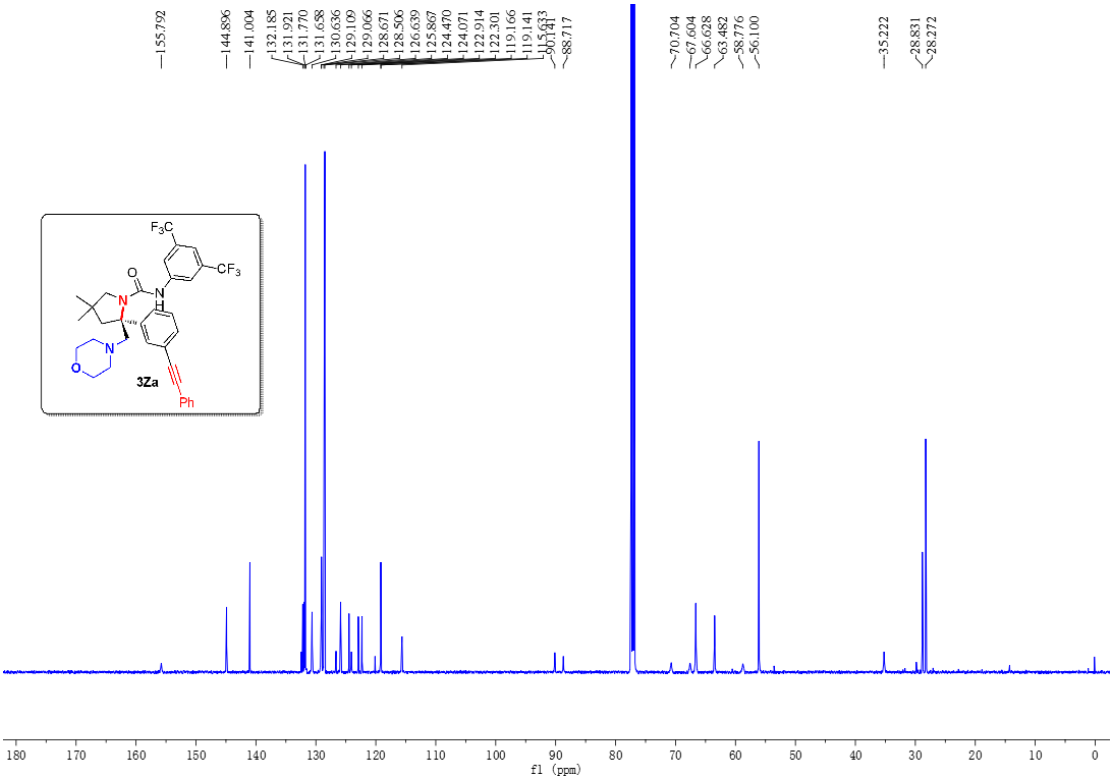


Figure S79. ^{13}C NMR spectrum of **3Za**

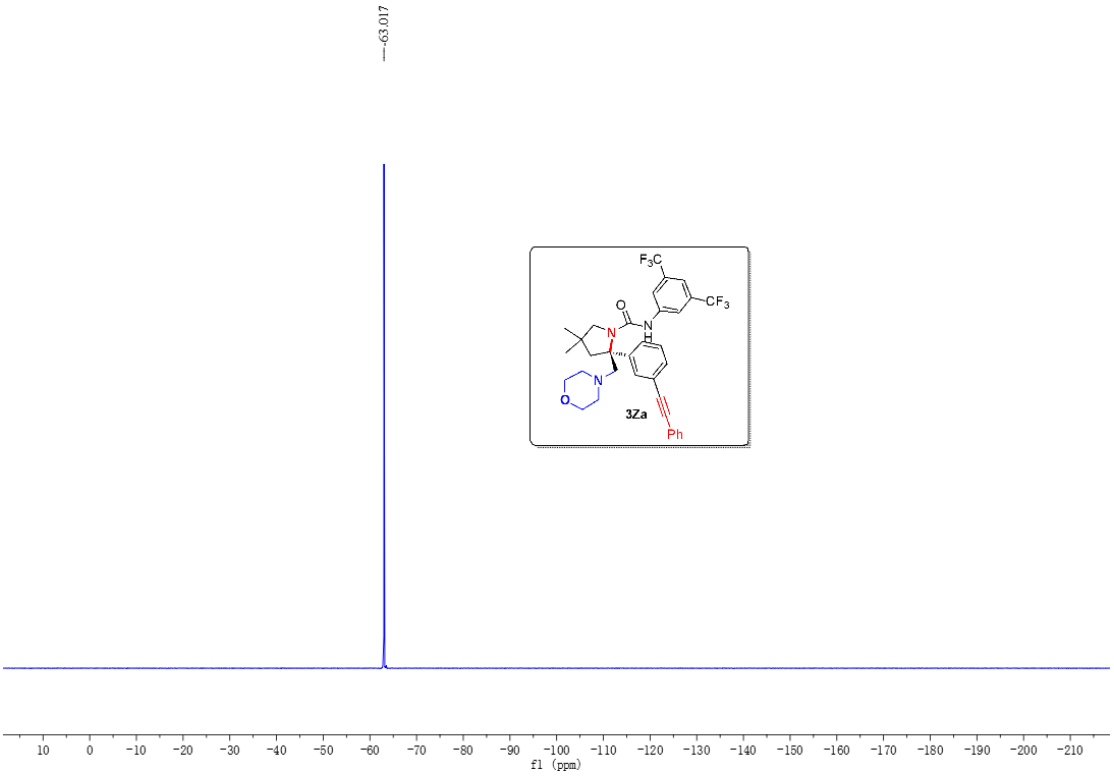


Figure S80. ^{19}F NMR spectrum of **3Za**

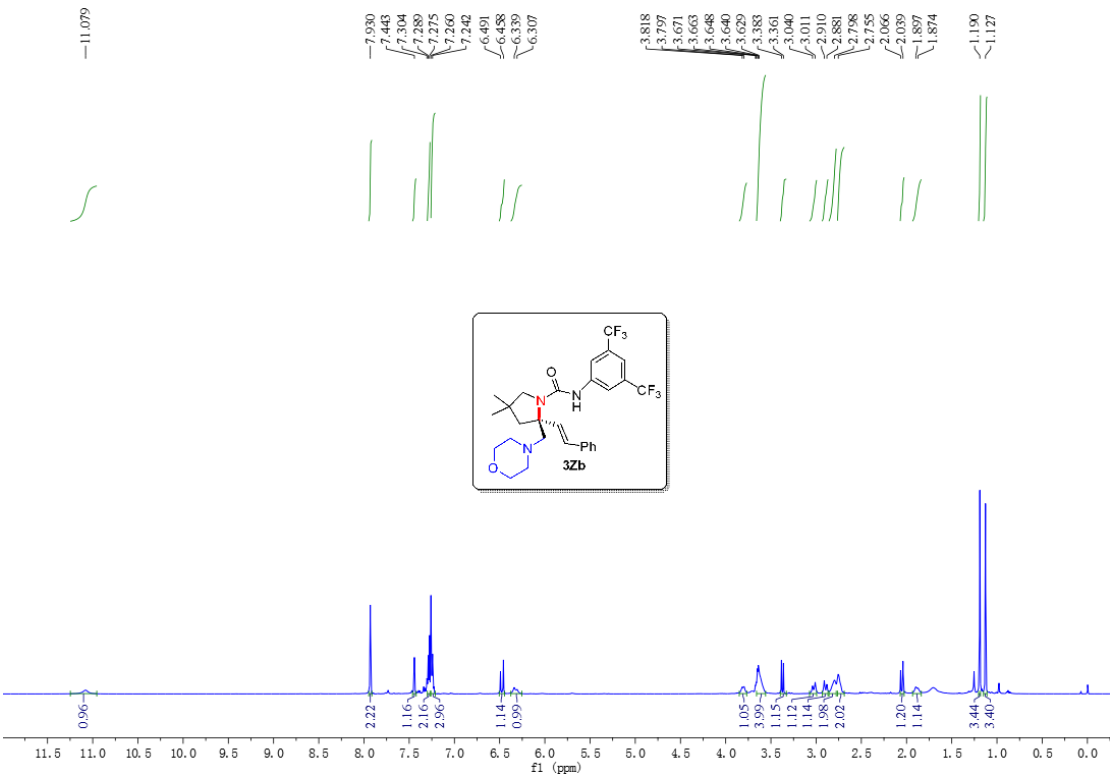


Figure S81. ^{1}H NMR spectrum of **3Zb**

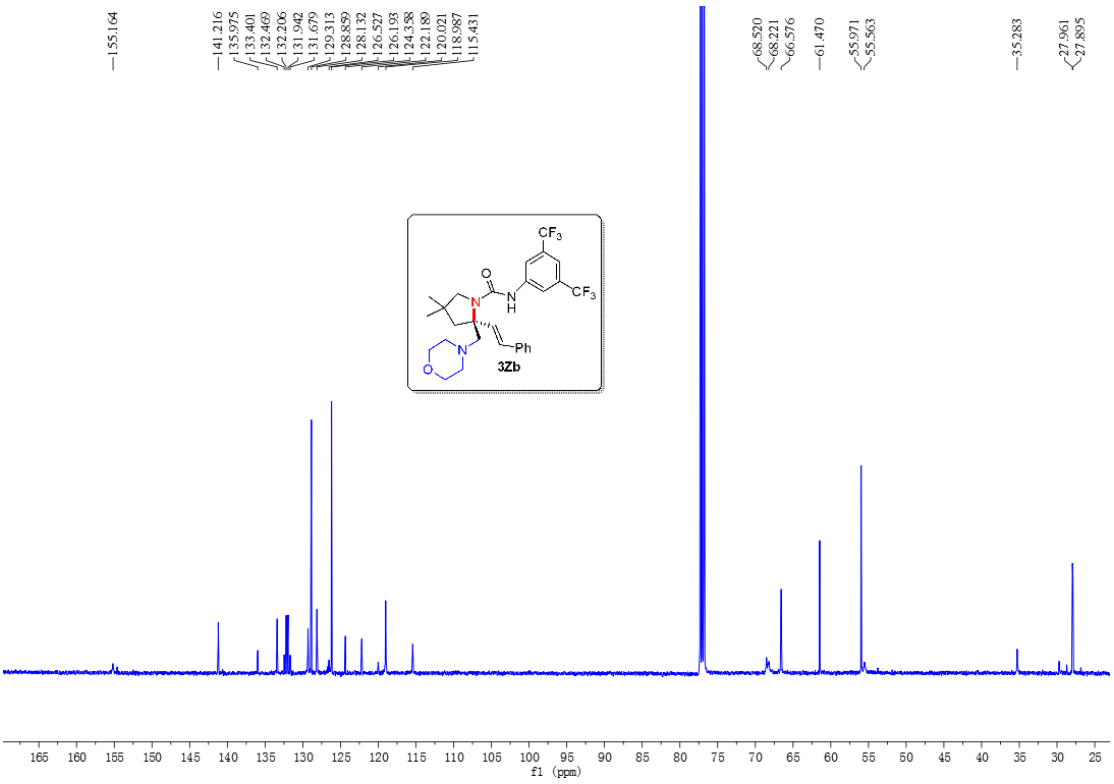


Figure S82. ^{13}C NMR spectrum of **3Zb**

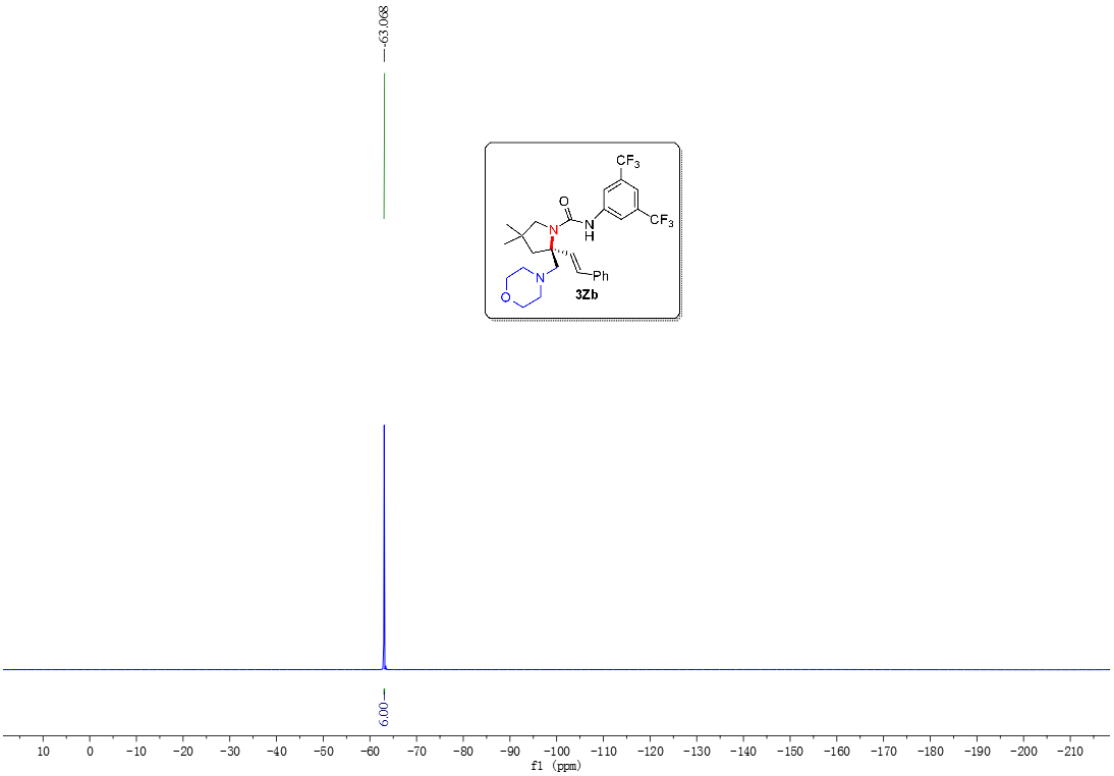


Figure S83. ^{19}F NMR spectrum of **3Zb**

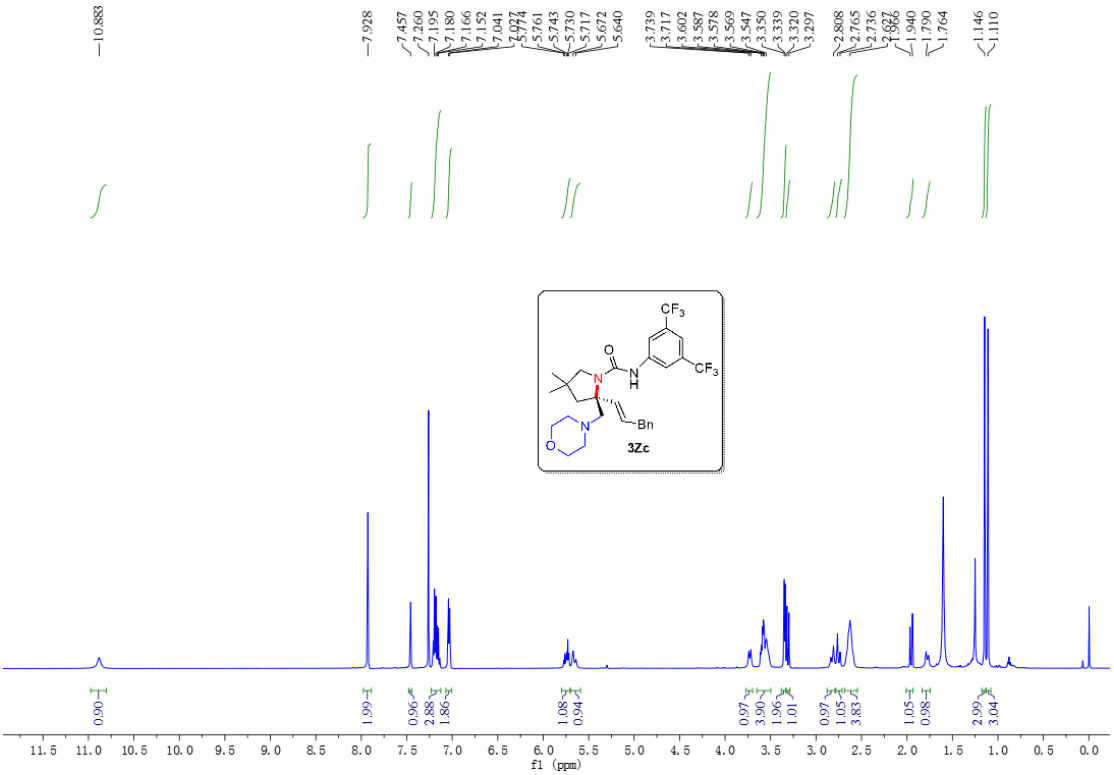


Figure S84. ^{1}H NMR spectrum of **3Zc**

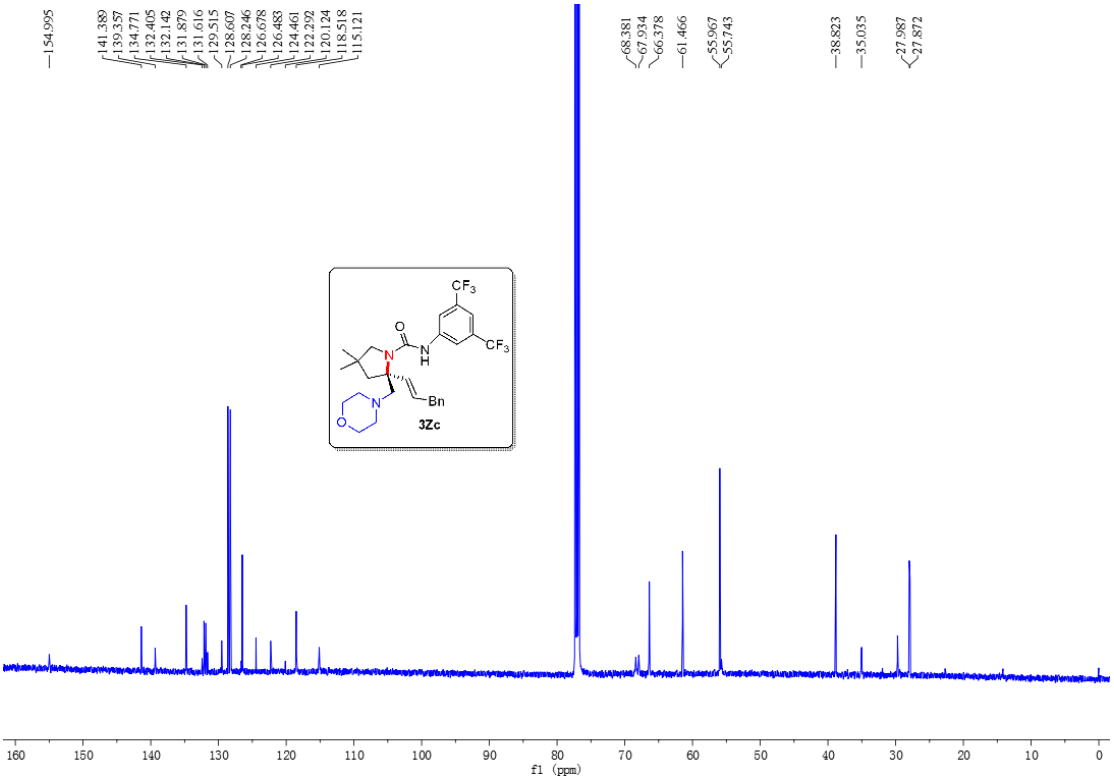


Figure S85. ^{13}C NMR spectrum of **3Zc**

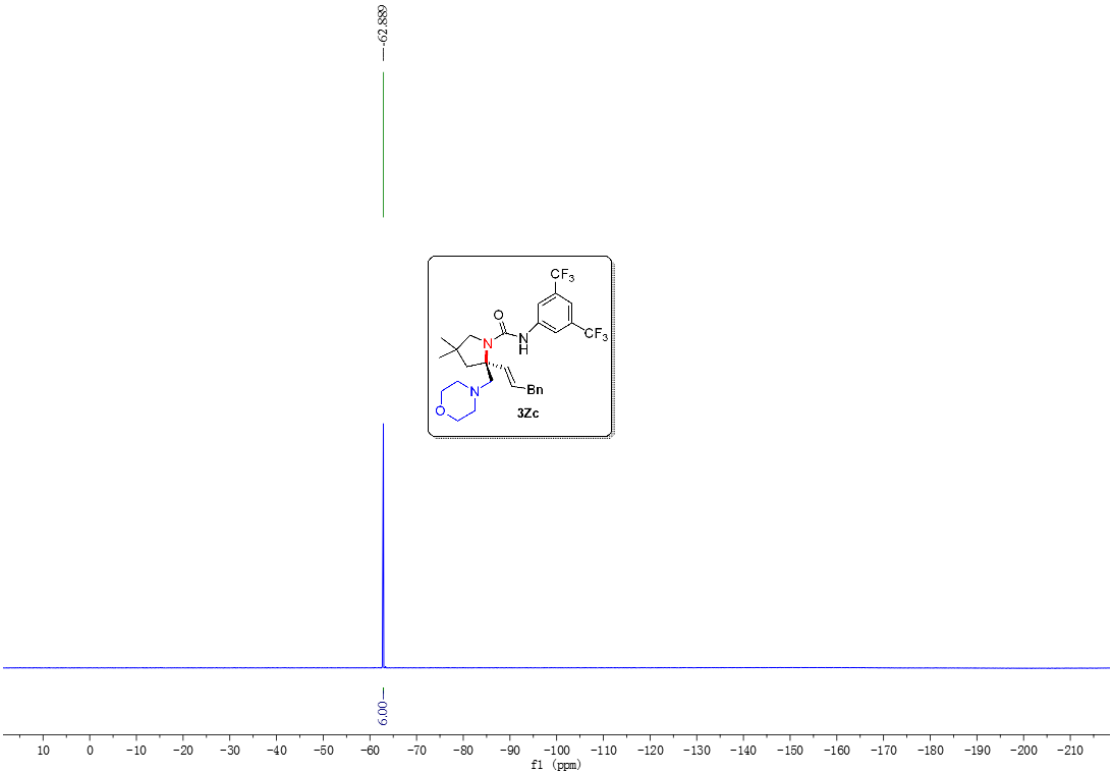


Figure S86. ^{19}F NMR spectrum of **3Zc**

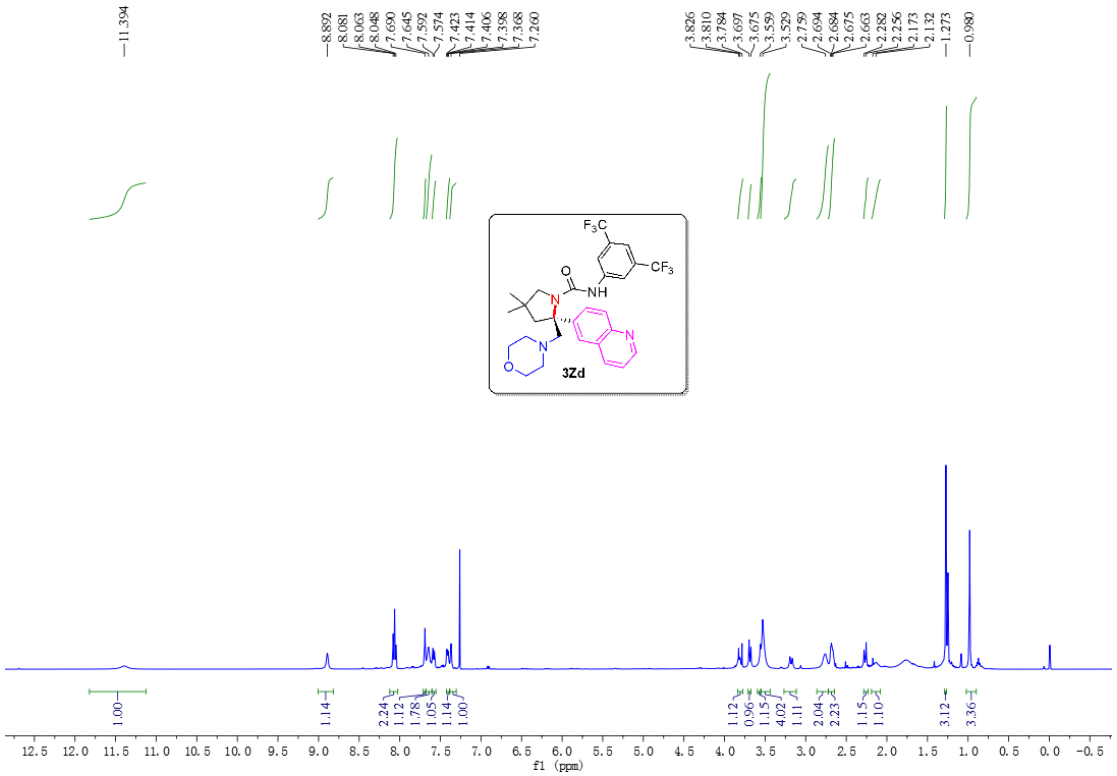


Figure S87. ^{1}H NMR spectrum of **3Zd**

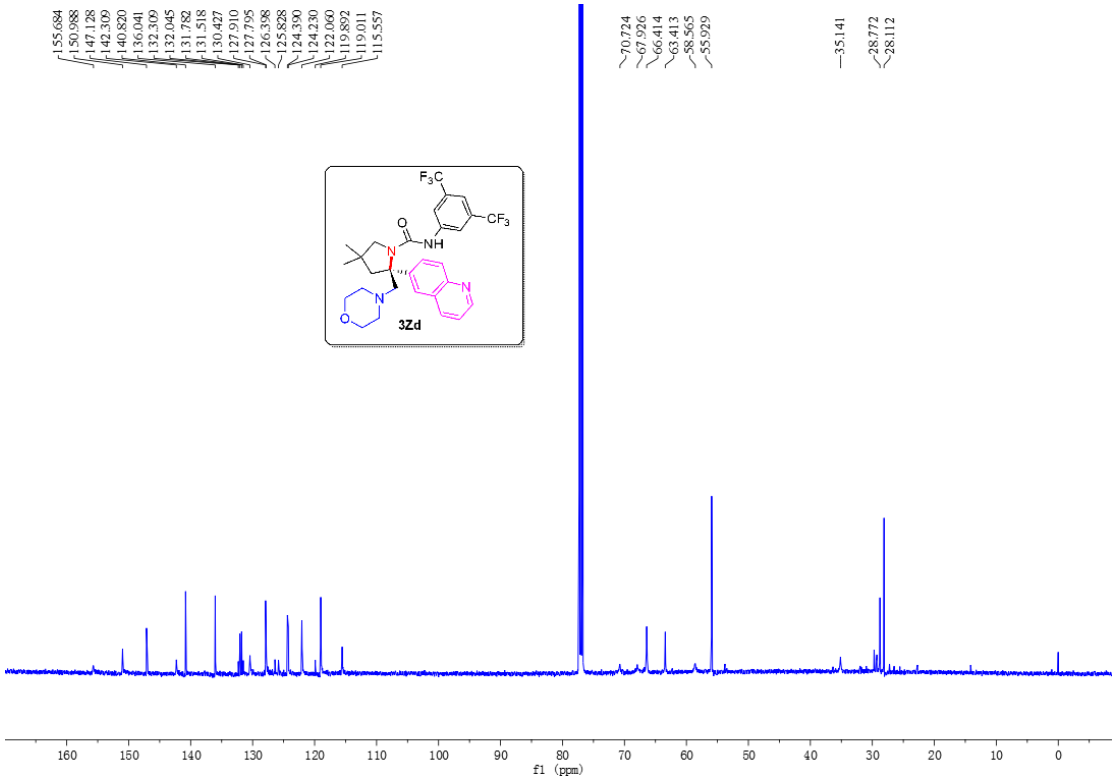


Figure S88. ^{13}C NMR spectrum of **3Zd**

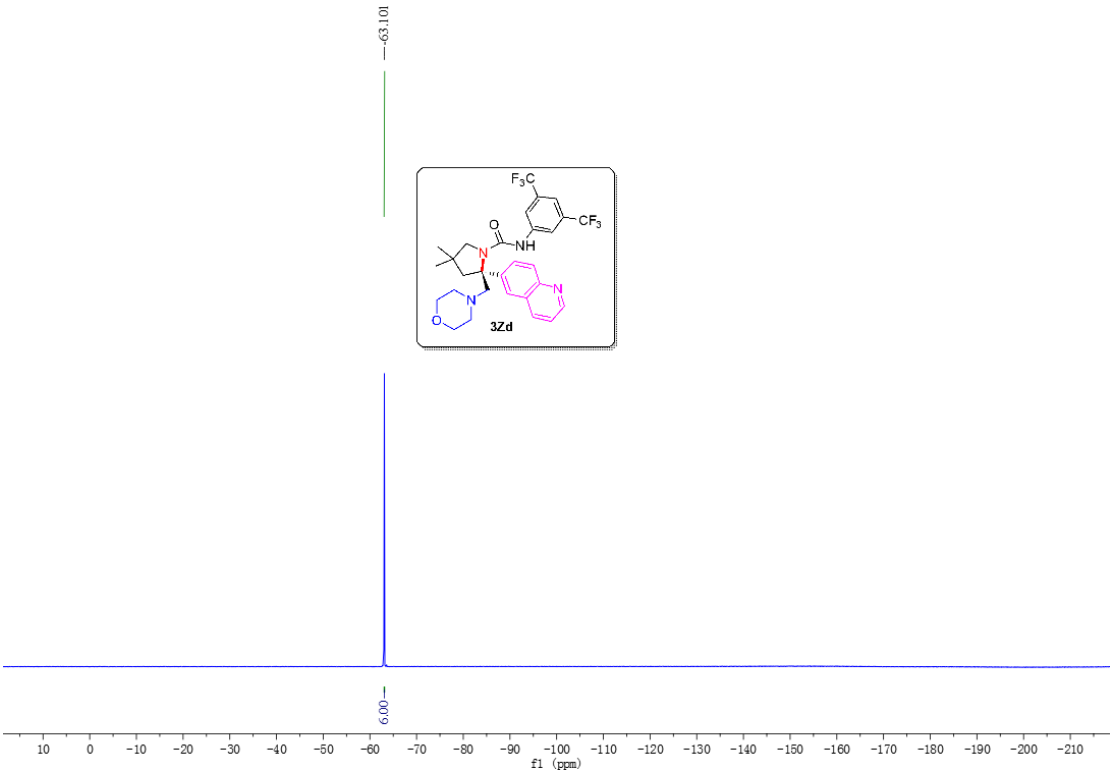


Figure S89. ^{19}F NMR spectrum of **3Zd**

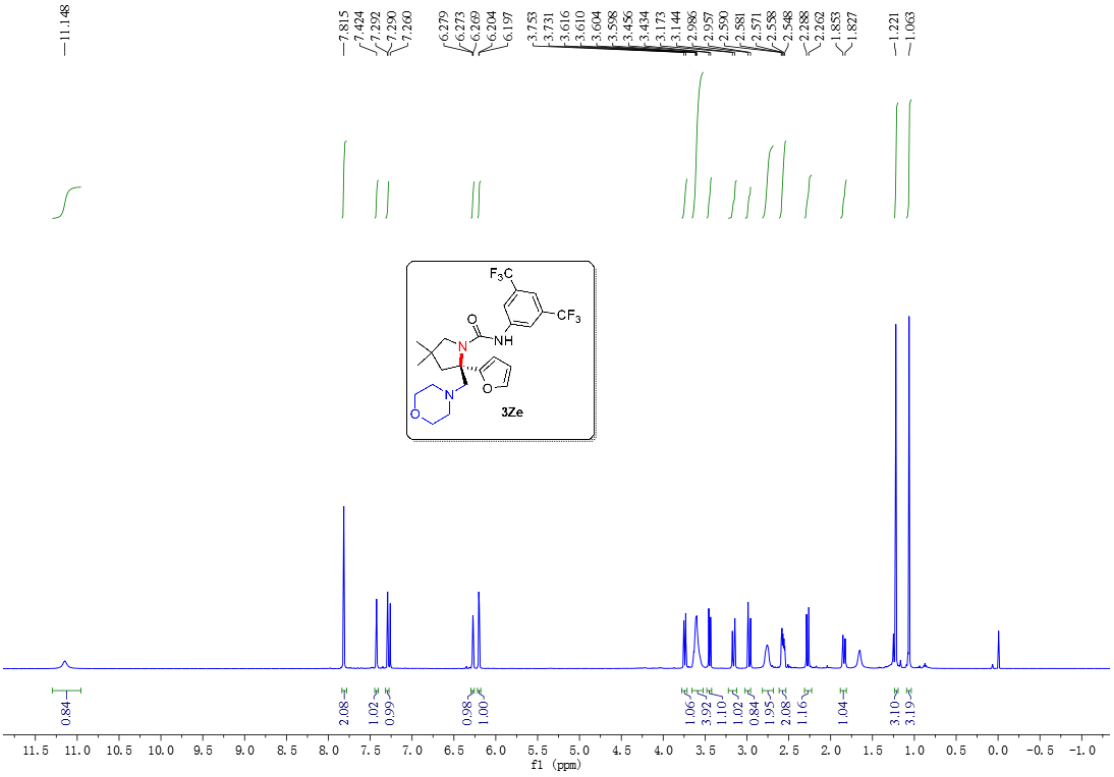


Figure S90. ^{1}H NMR spectrum of **3Ze**

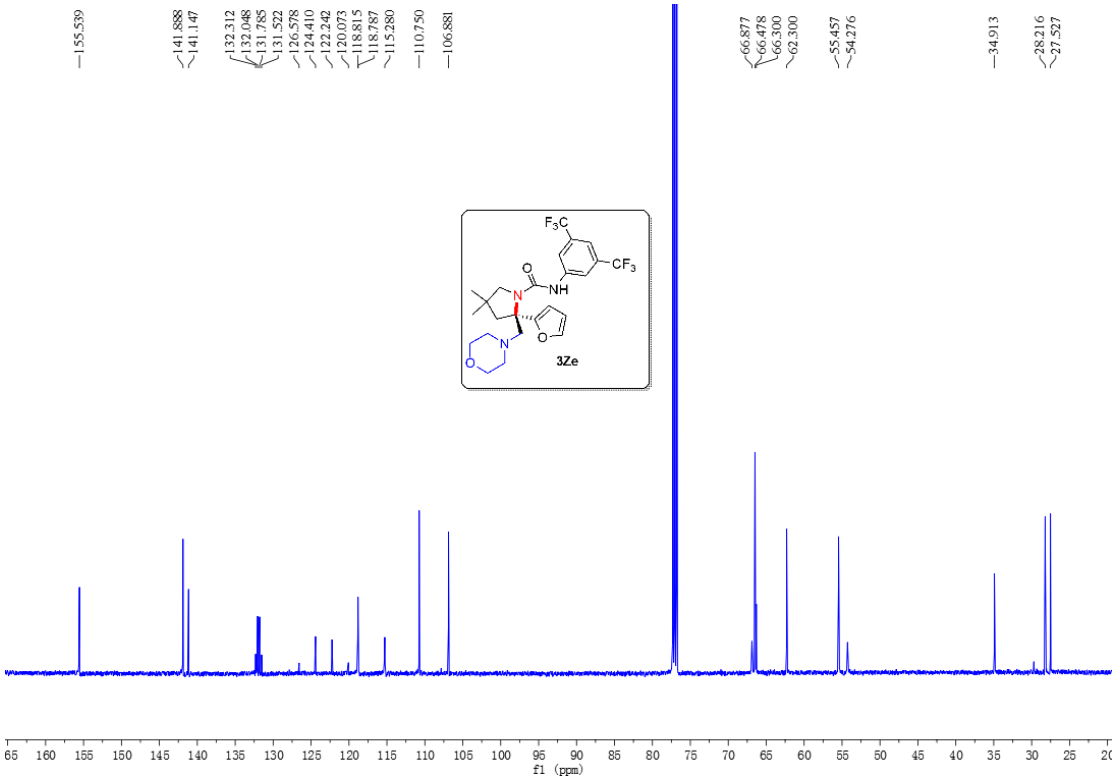


Figure S91. ^{13}C NMR spectrum of **3Ze**

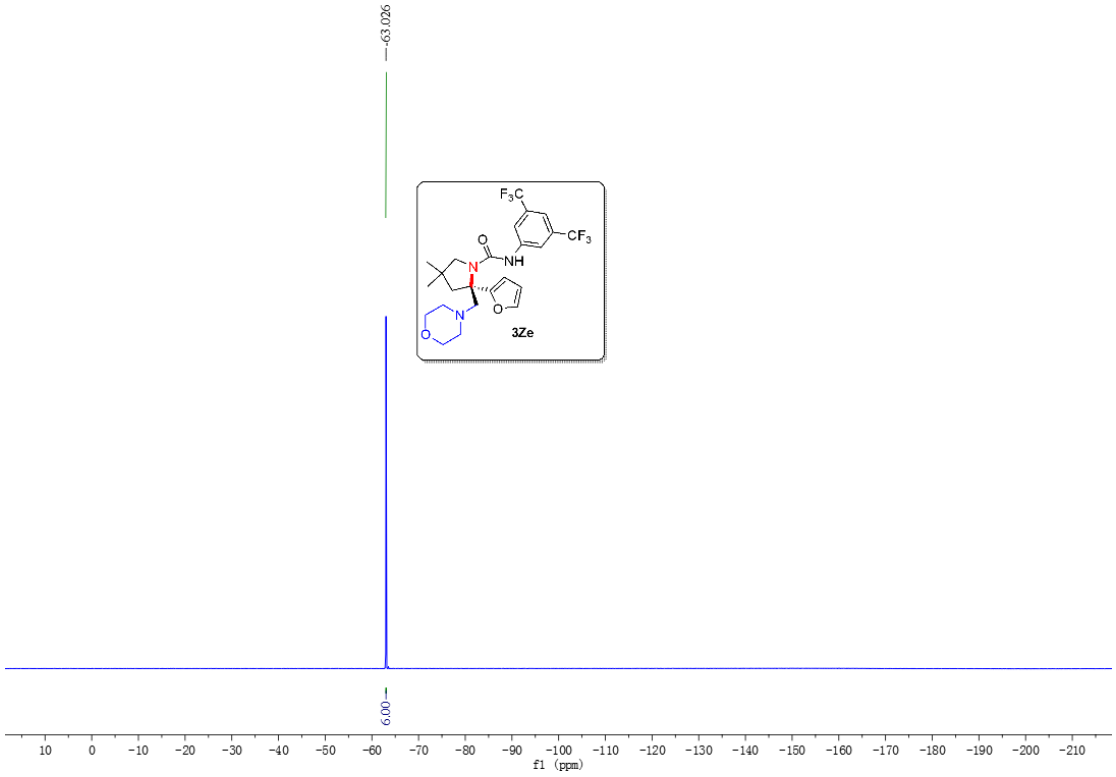


Figure S92. ^{19}F NMR spectrum of **3Ze**

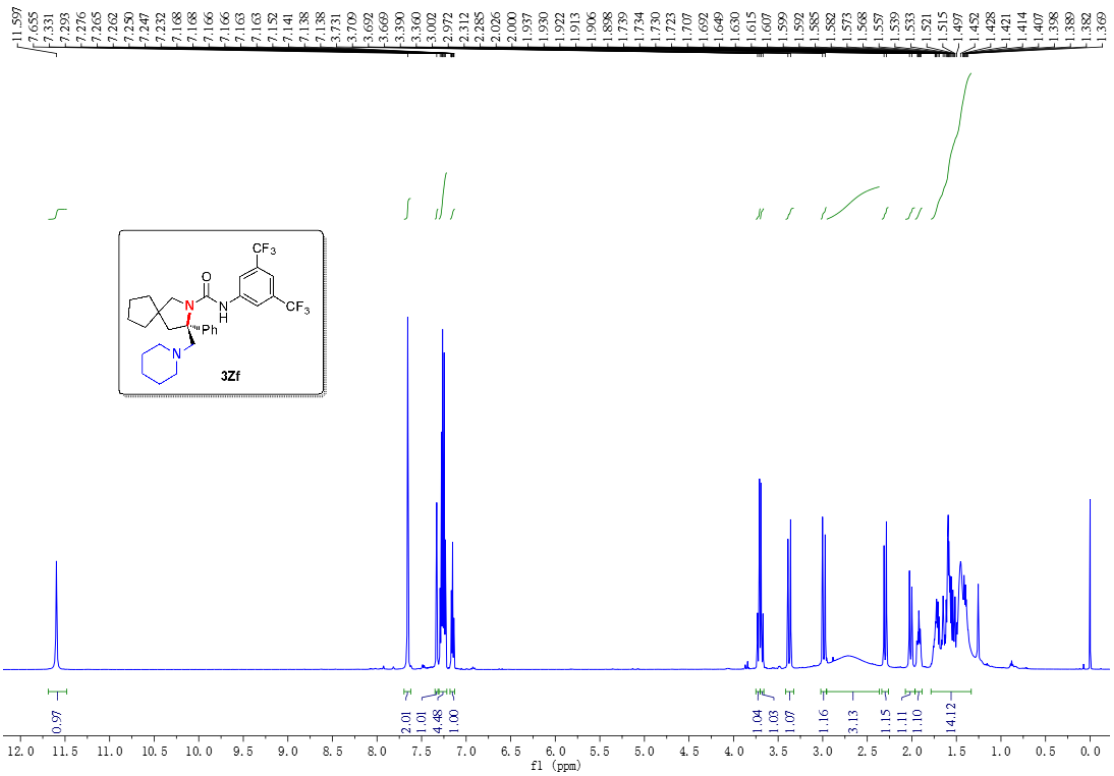


Figure S93. ^{1}H NMR spectrum of **3Zf**

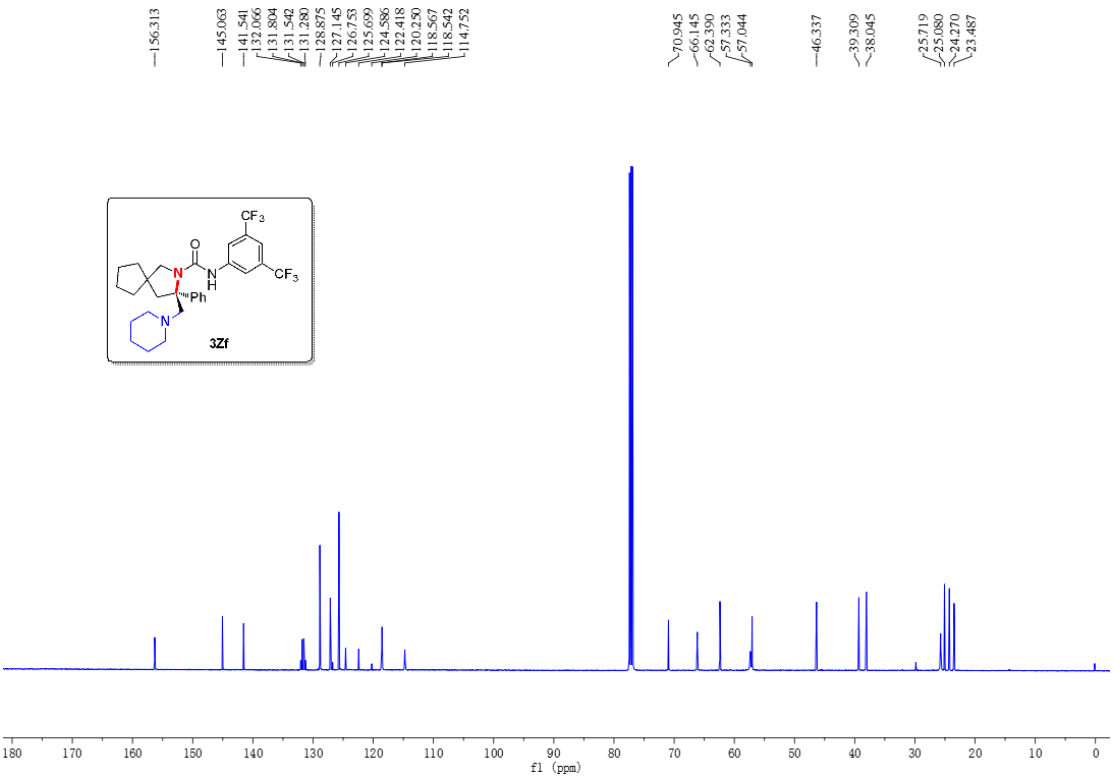


Figure S94. ^{13}C NMR spectrum of **3Zf**

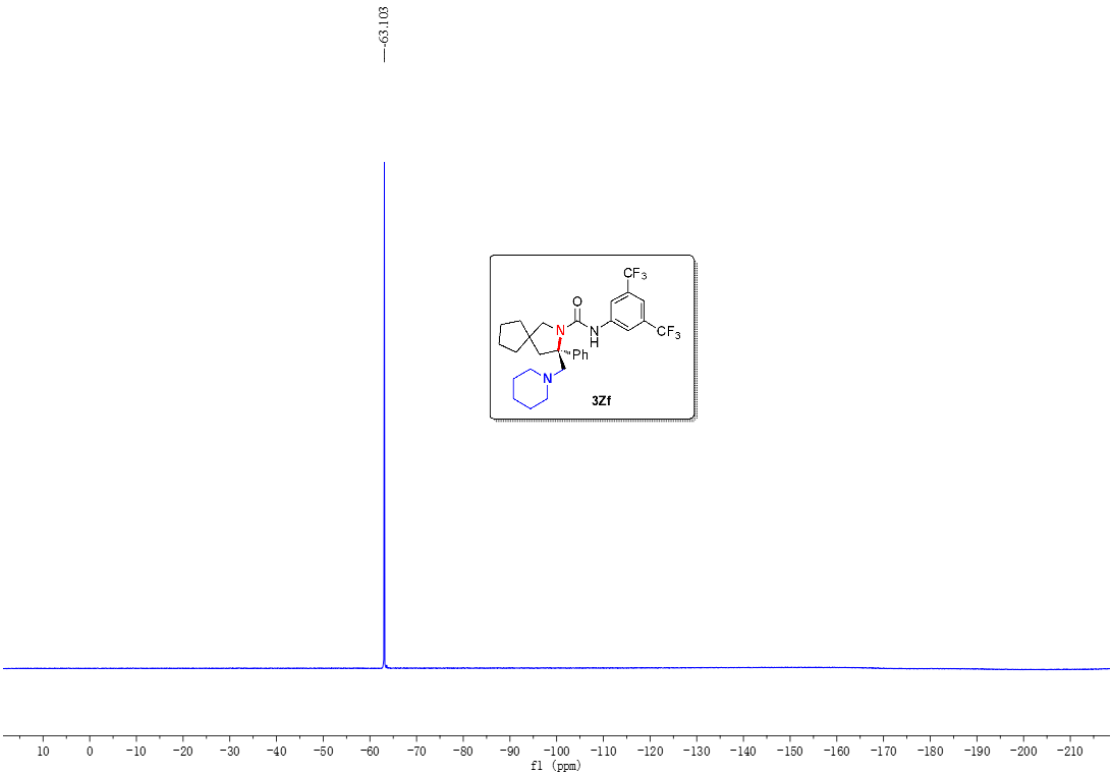


Figure S95. ^{19}F NMR spectrum of **3Zf**

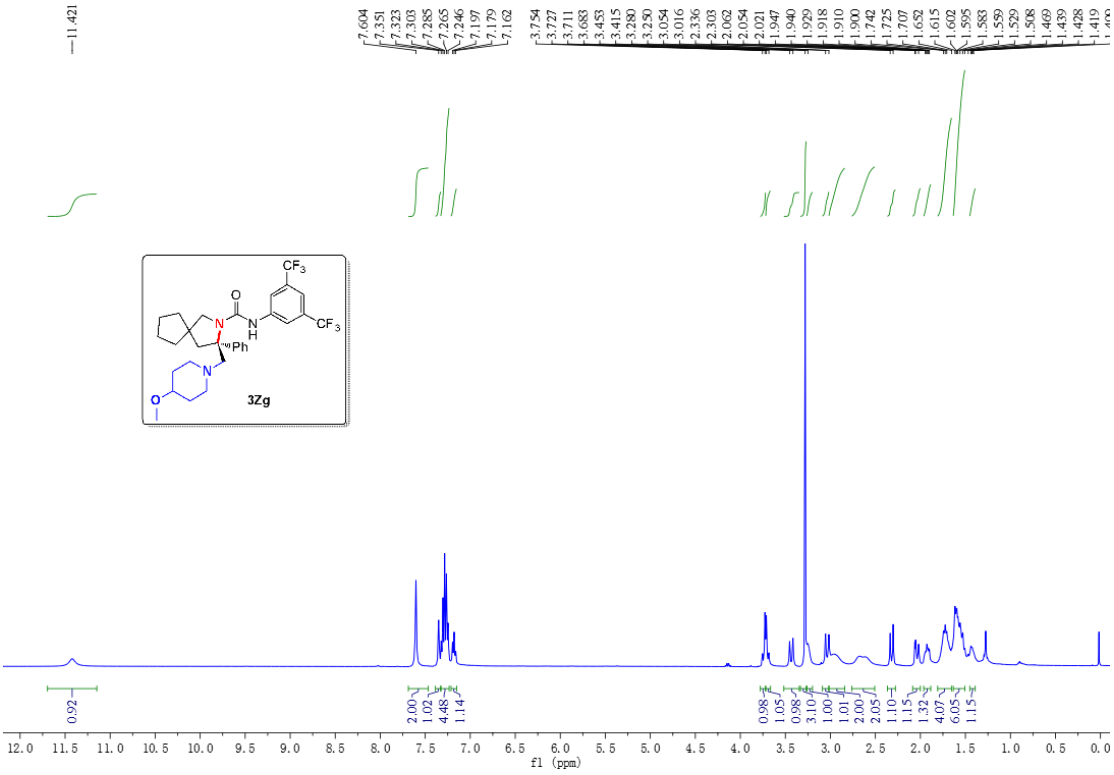


Figure S96. ^{1}H NMR spectrum of **3Zg**

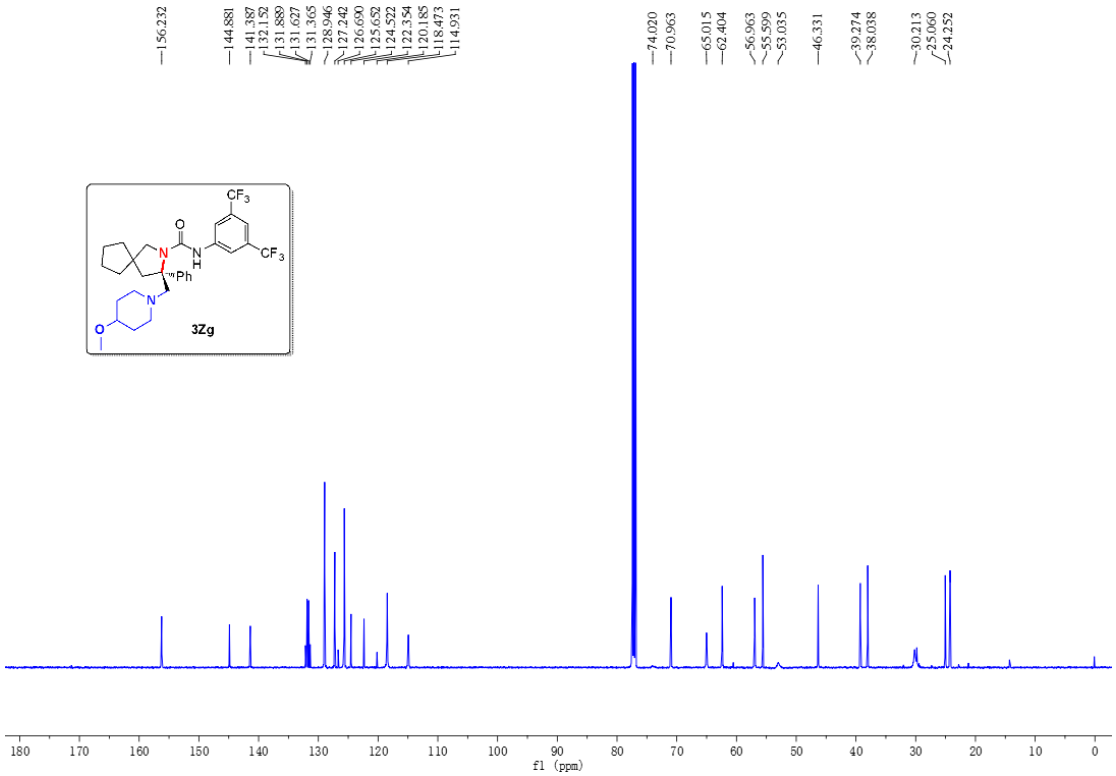


Figure S97. ^{13}C NMR spectrum of **3Zg**

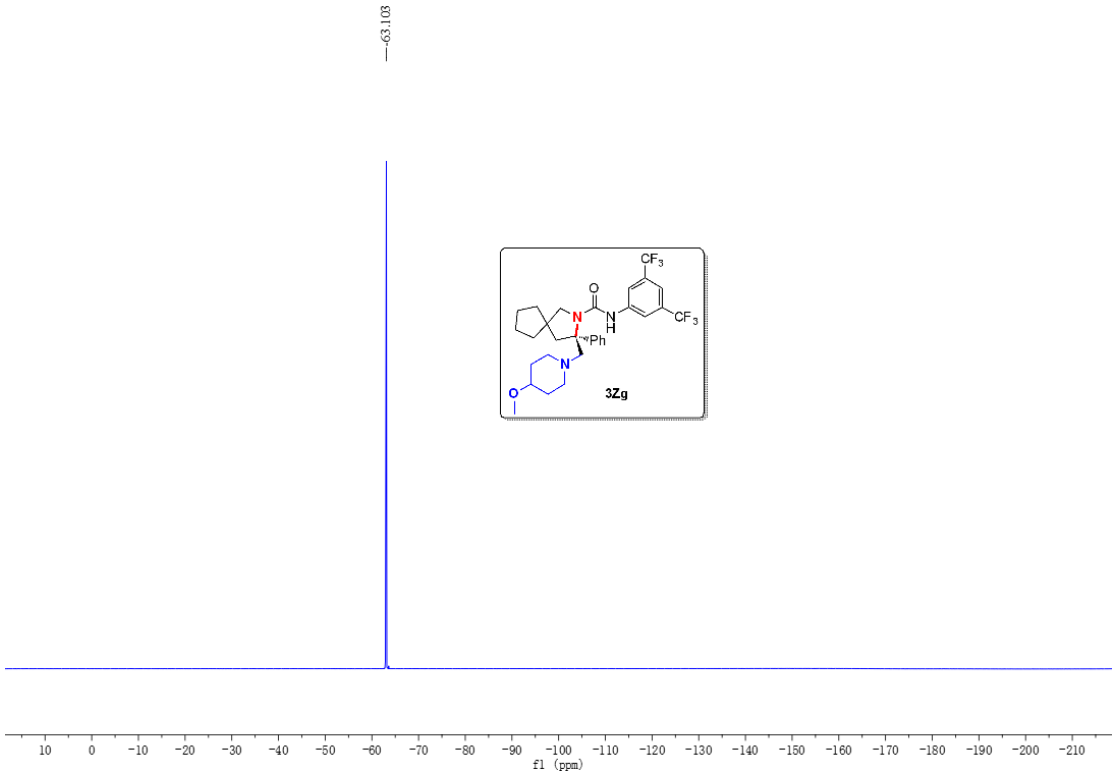


Figure S98. ^{19}F NMR spectrum of **3Zg**

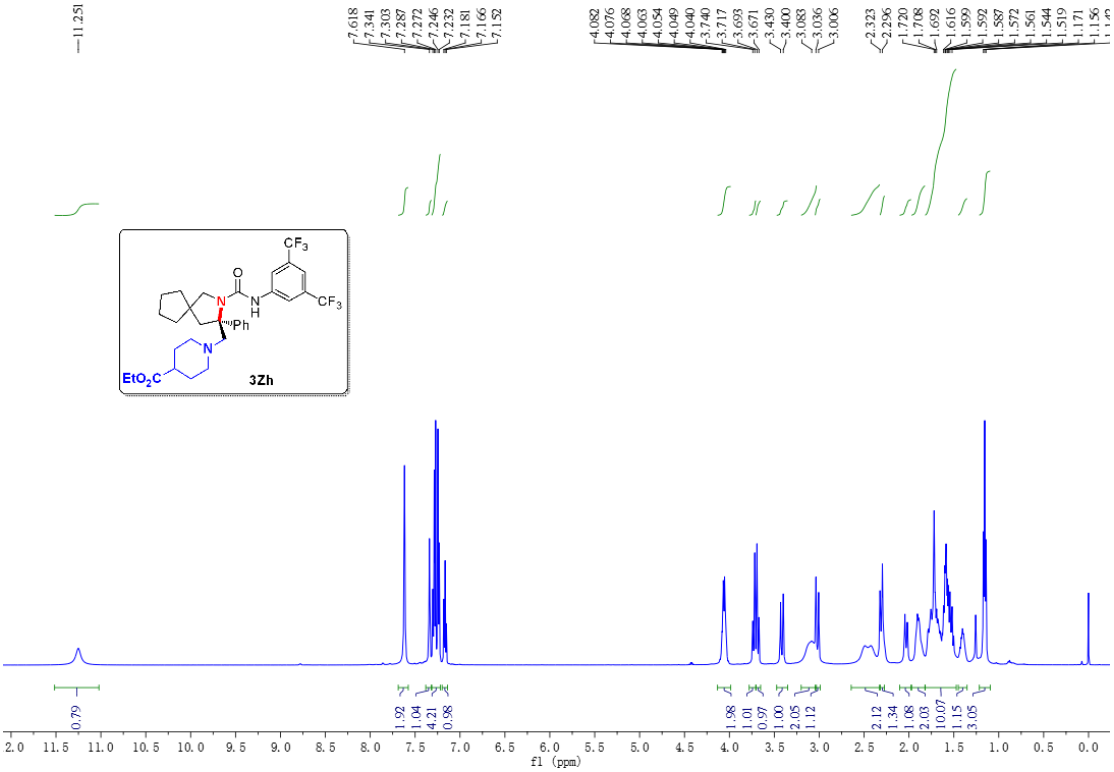


Figure S99. ^{1}H NMR spectrum of **3Zh**

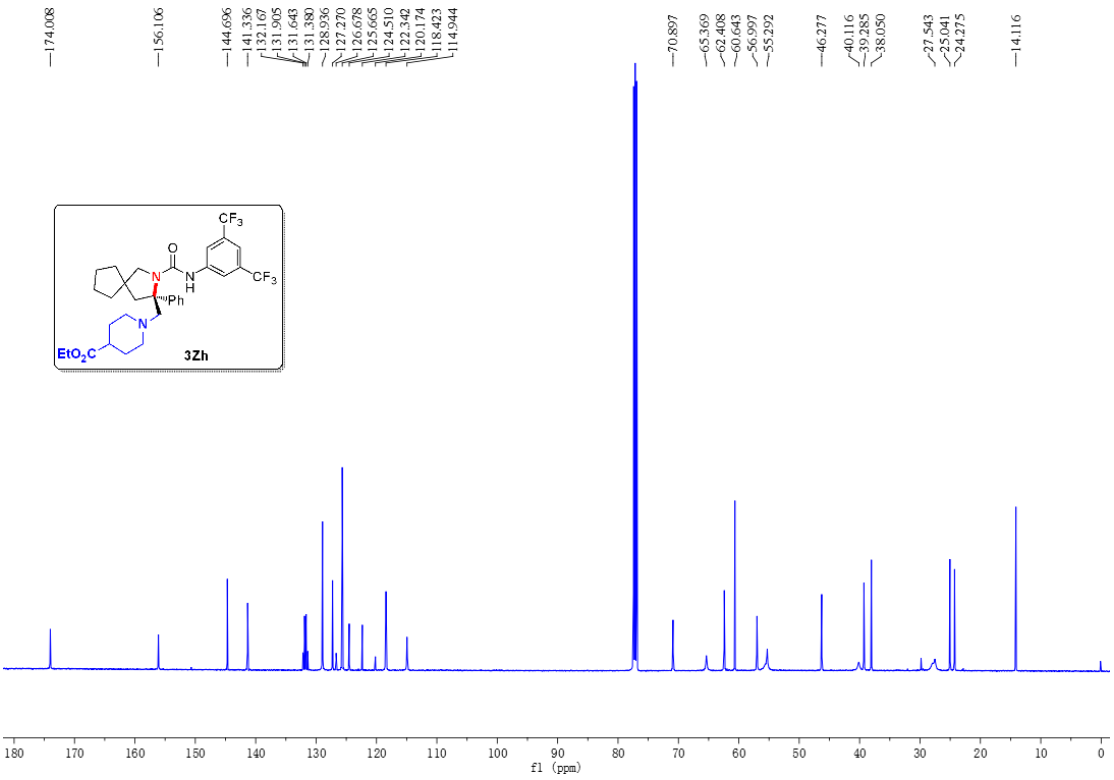


Figure S100. ^{13}C NMR spectrum of **3Zh**

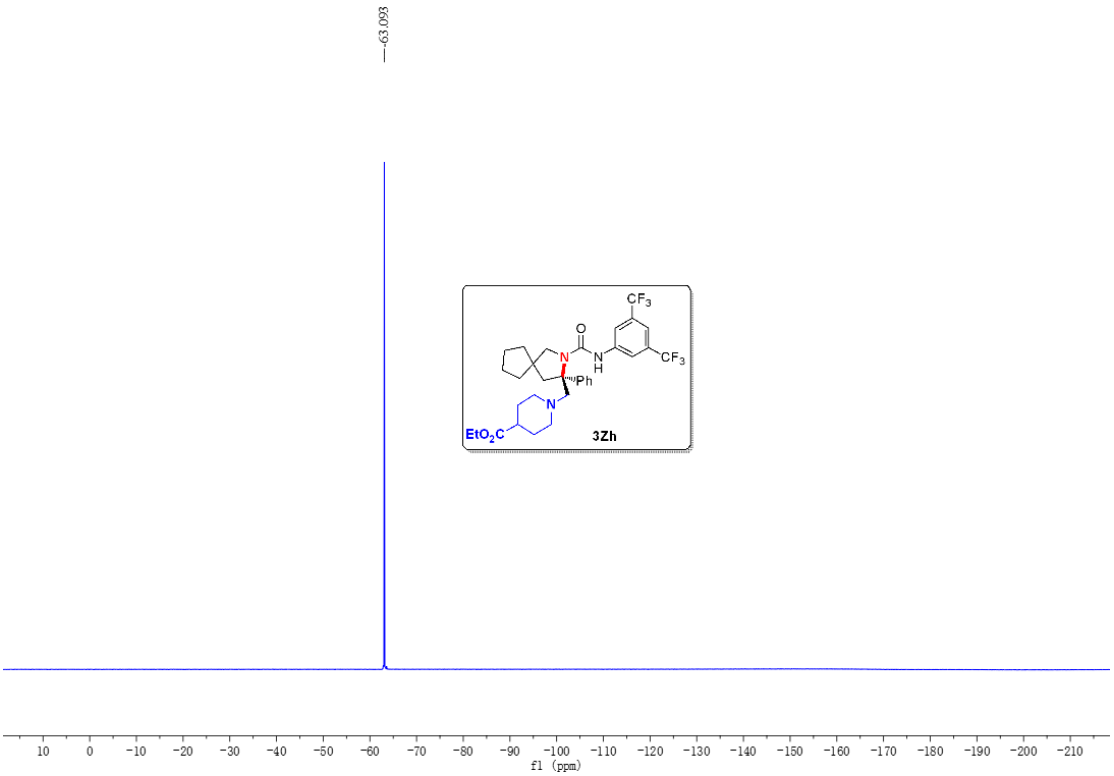


Figure S101. ^{19}F NMR spectrum of **3Zh**

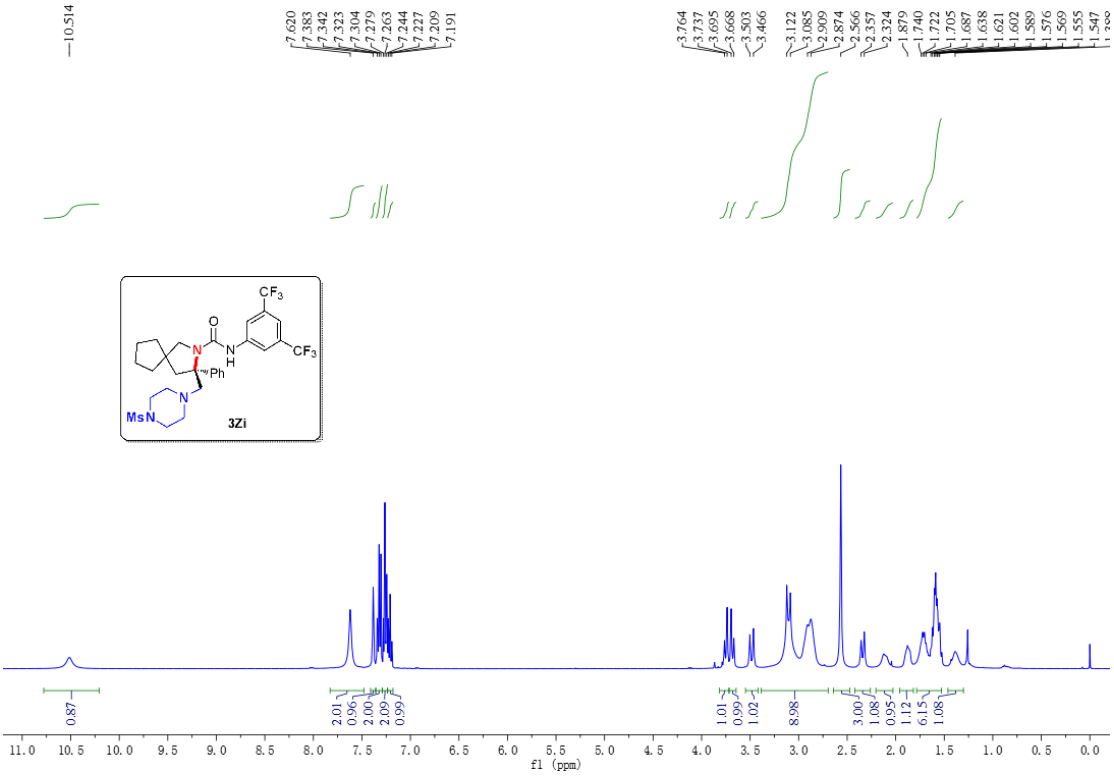


Figure S102. ^{1}H NMR spectrum of **3Zi**

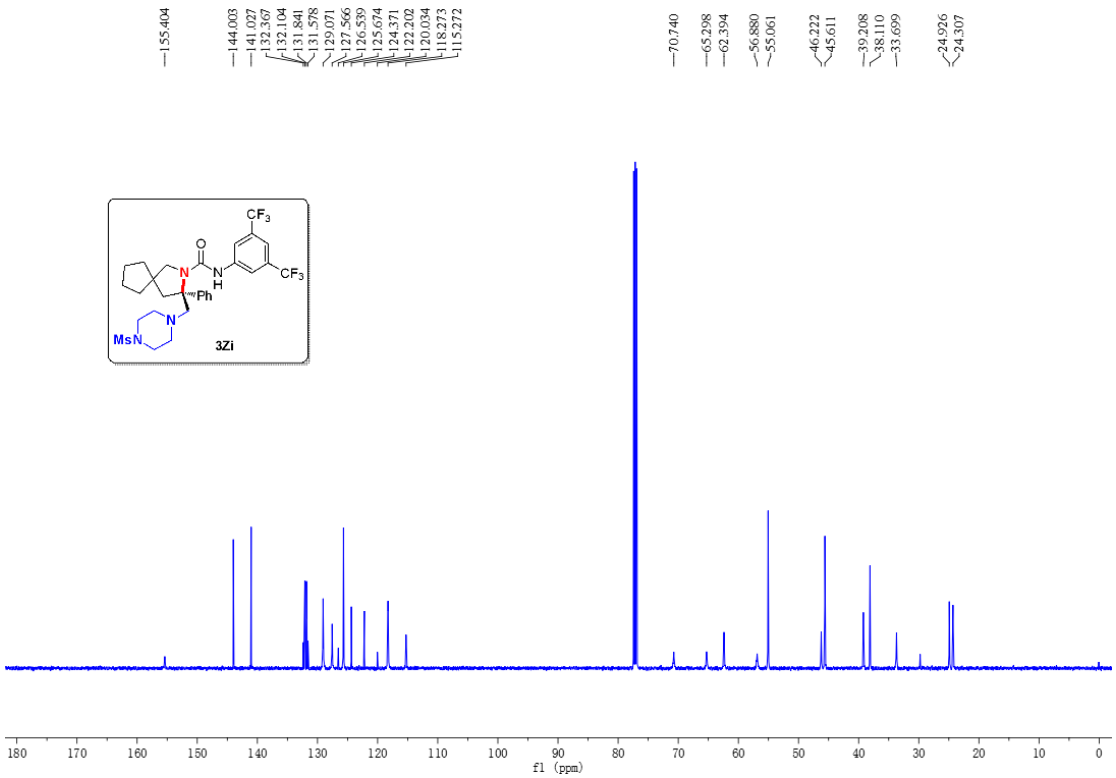


Figure S103. ^{13}C NMR spectrum of **3Zi**

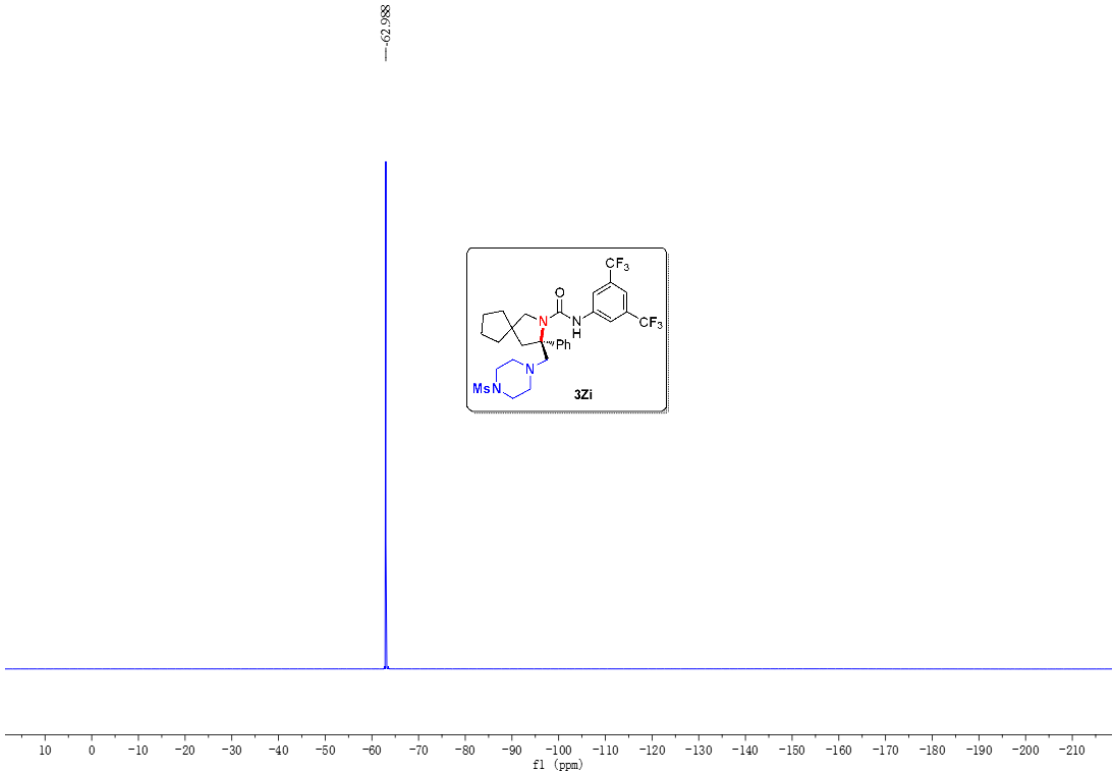


Figure S104. ^{19}F NMR spectrum of **3Zi**

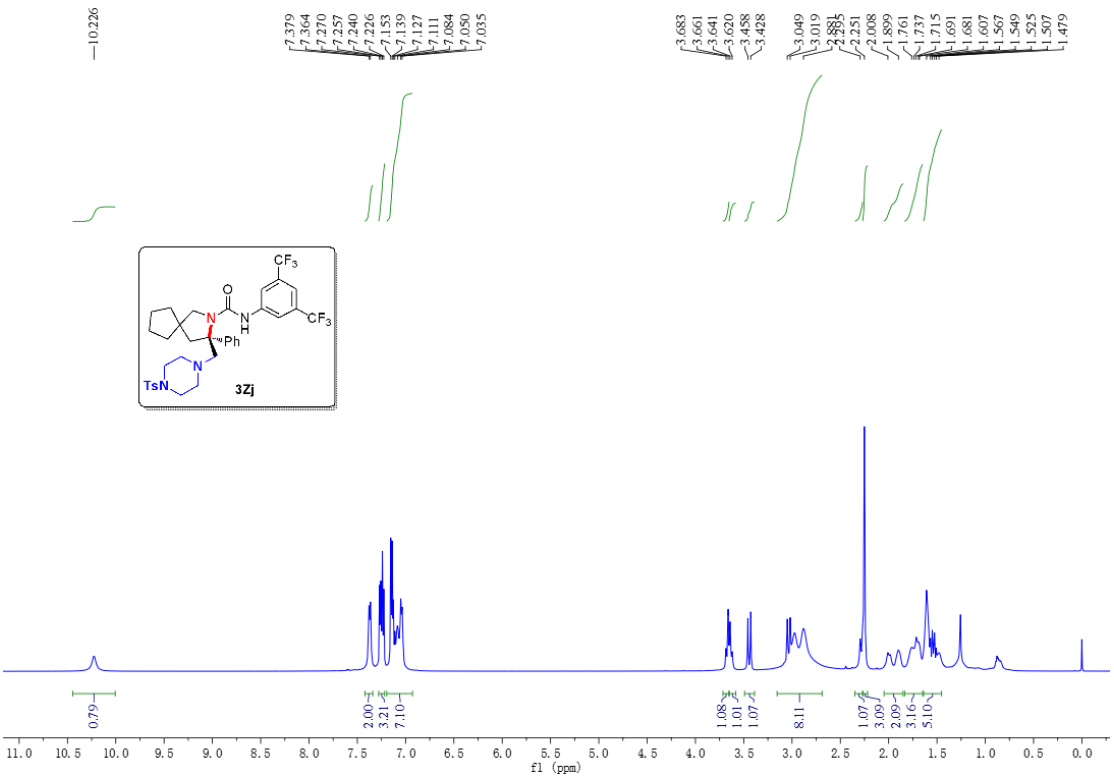


Figure S105. ^{1}H NMR spectrum of **3Zj**

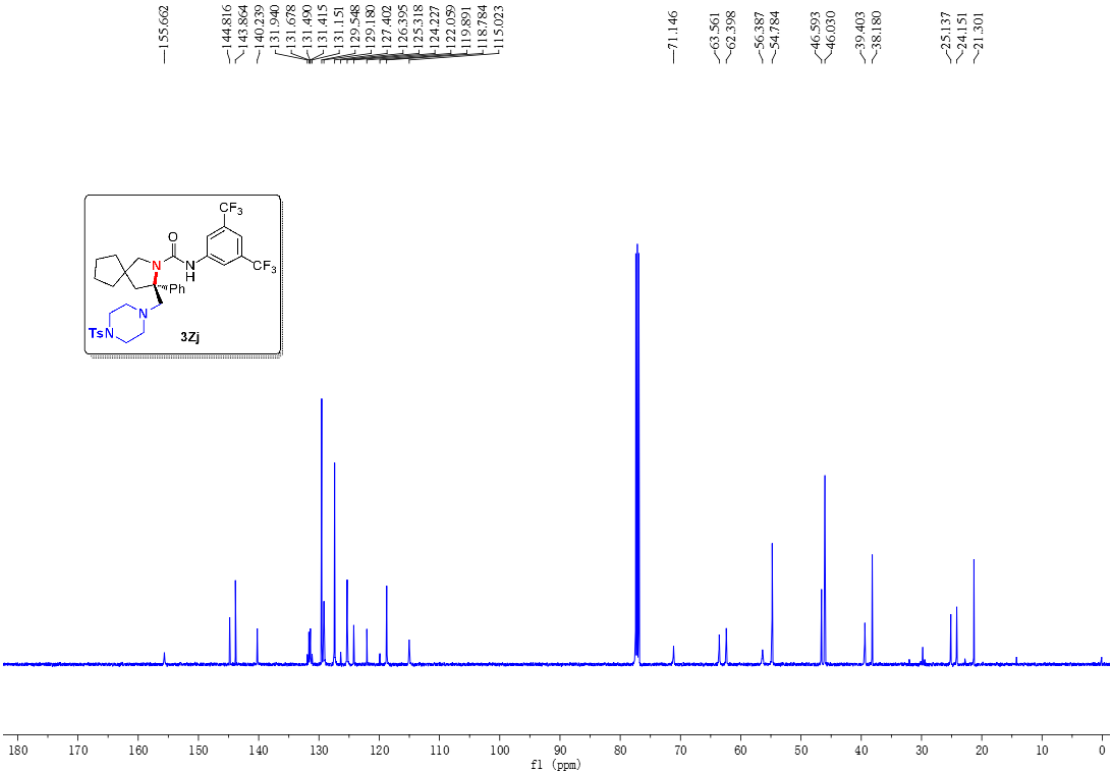


Figure S106. ^{13}C NMR spectrum of **3Zj**

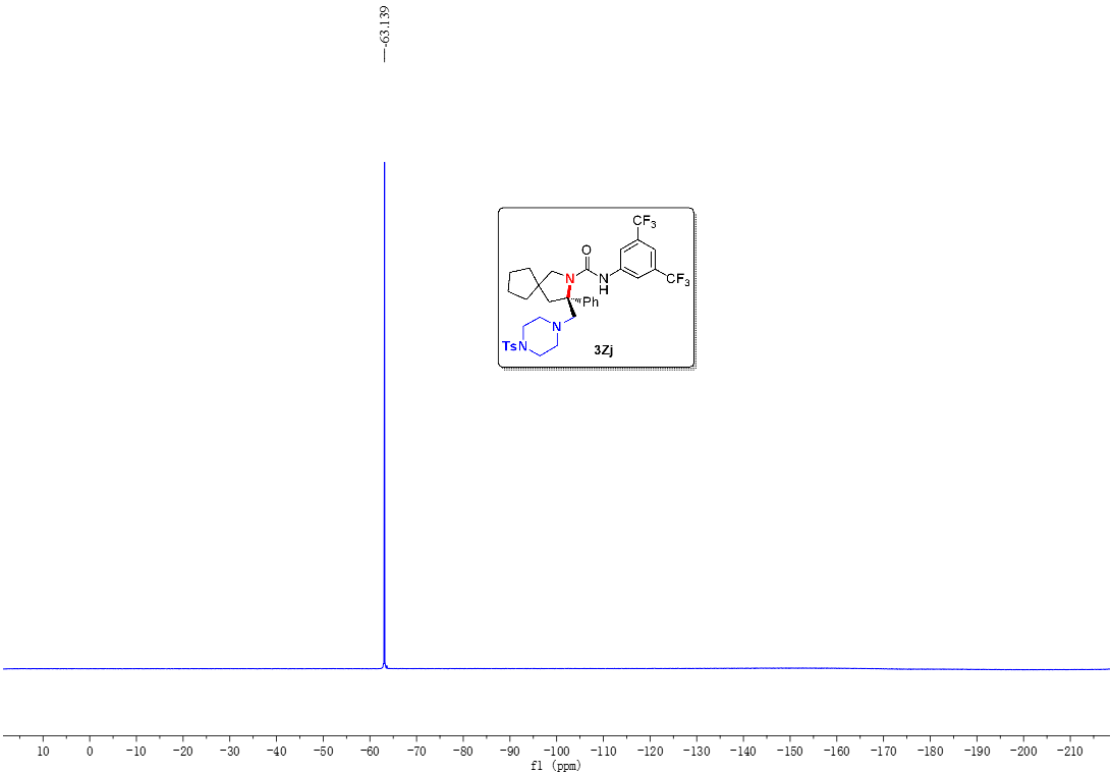


Figure S107. ^{19}F NMR spectrum of **3Zj**

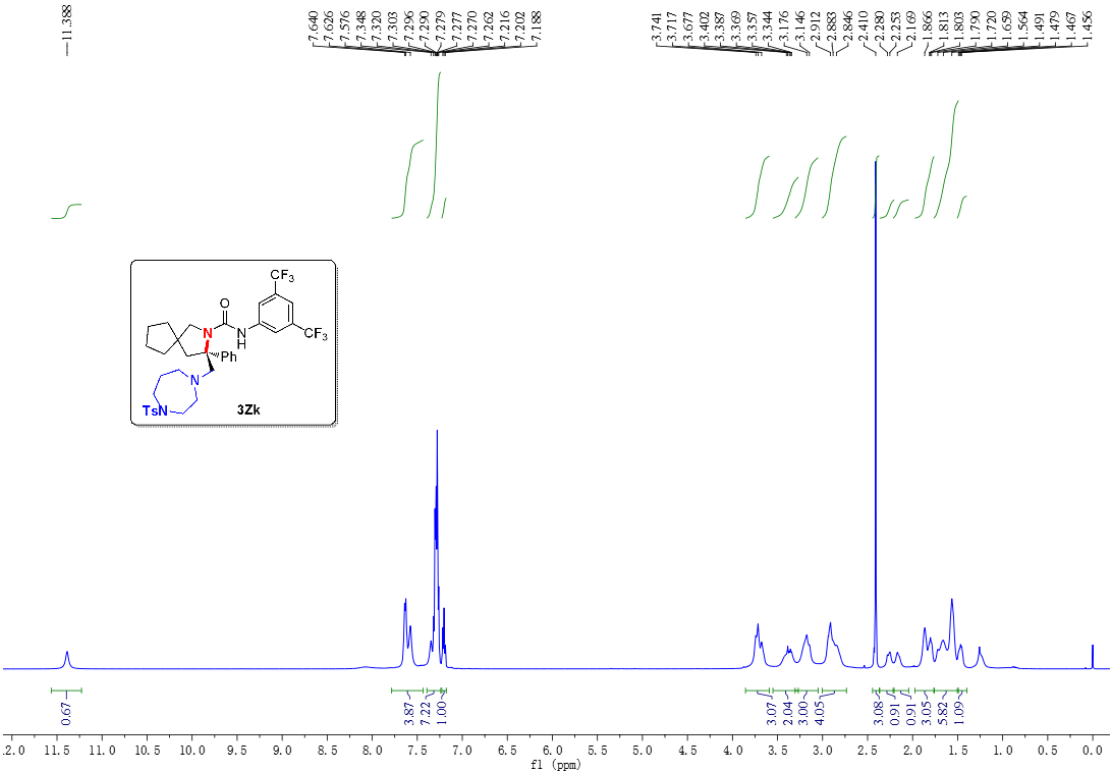


Figure S108. ^{1}H NMR spectrum of **3Zk**

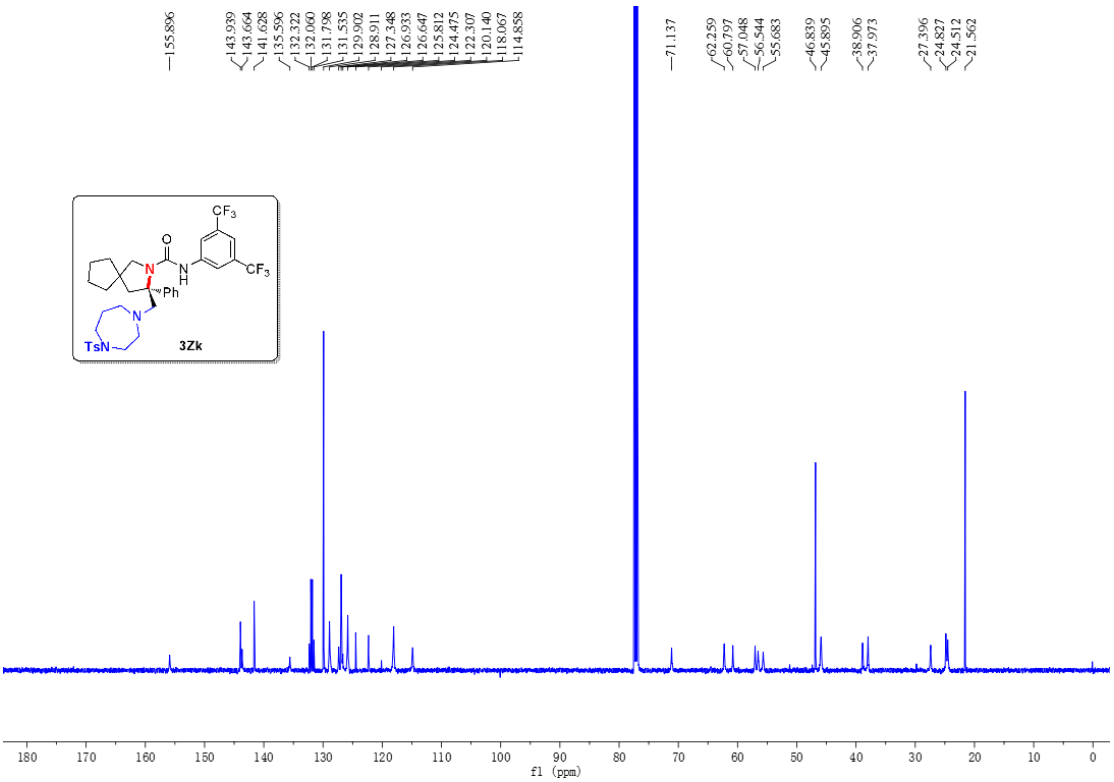


Figure S109. ^{13}C NMR spectrum of **3Zk**

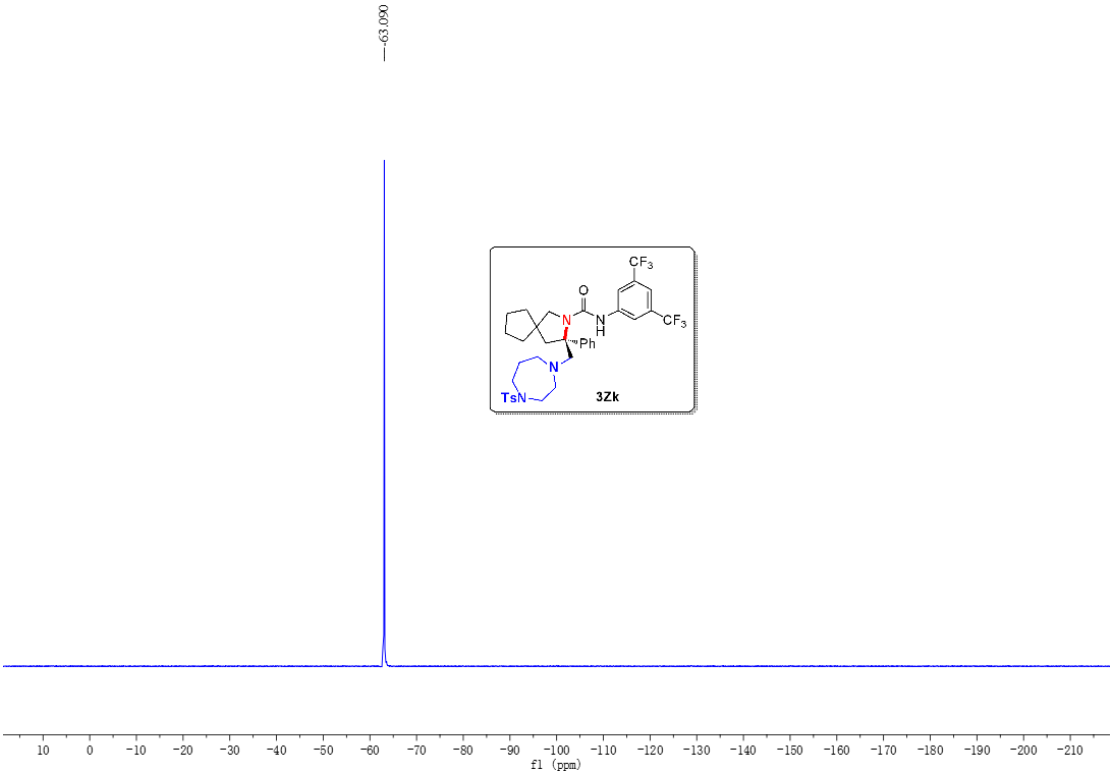


Figure S110. ^{19}F NMR spectrum of **3Zk**

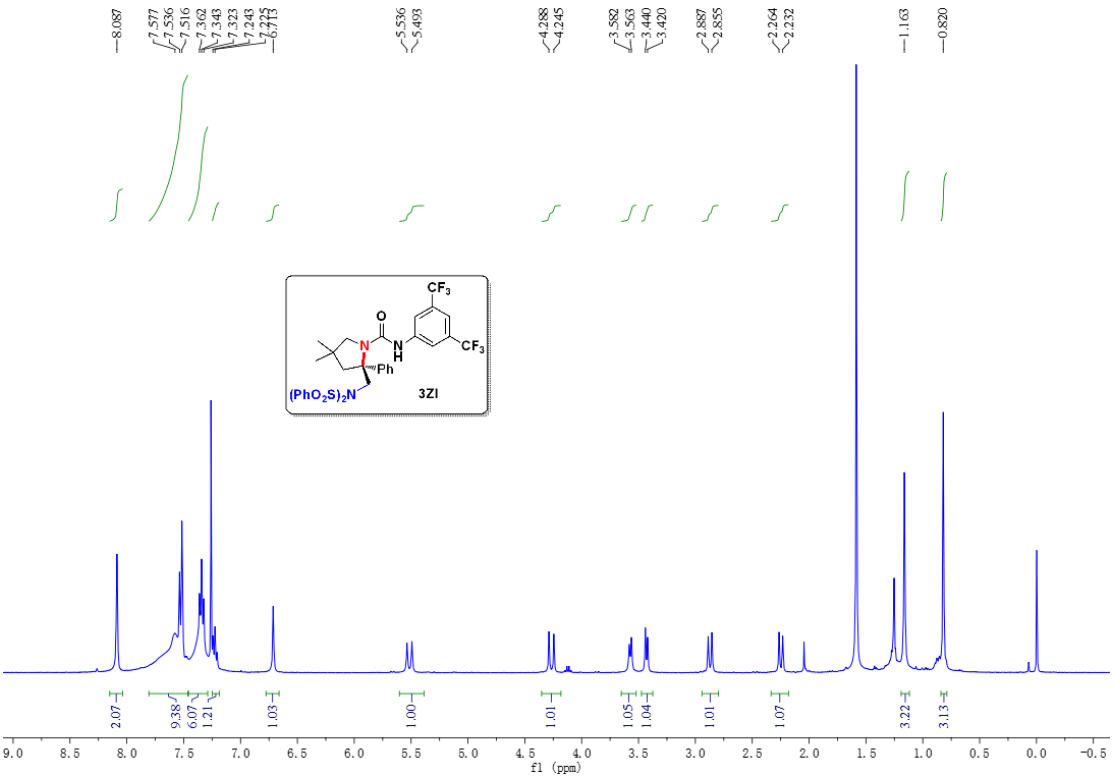


Figure S111. ^{1}H NMR spectrum of **3ZI**

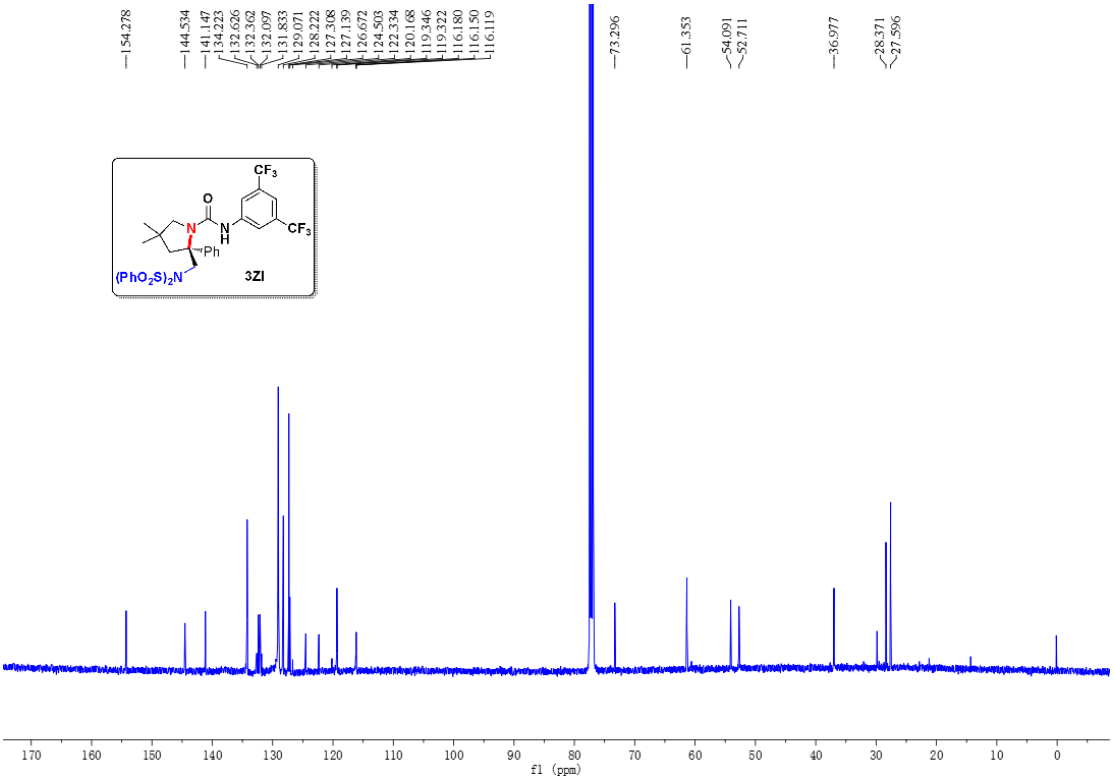


Figure S112. ^{13}C NMR spectrum of **3ZI**

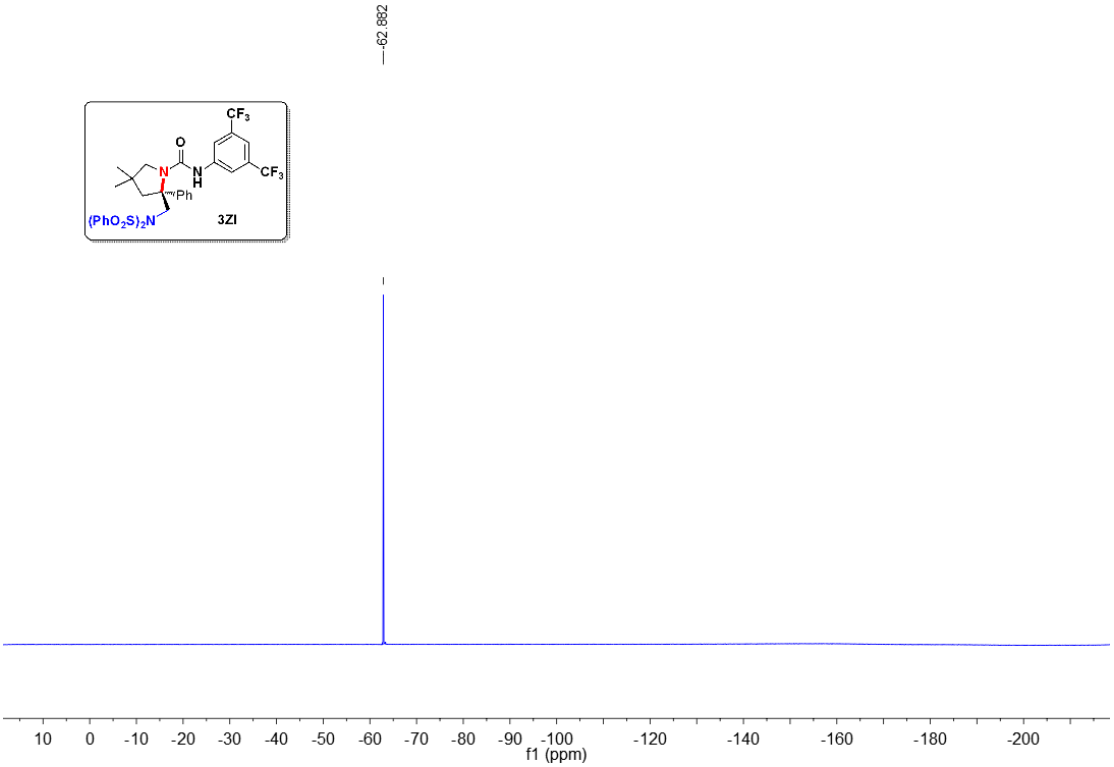


Figure S113. ^{19}F NMR spectrum of **3ZI**

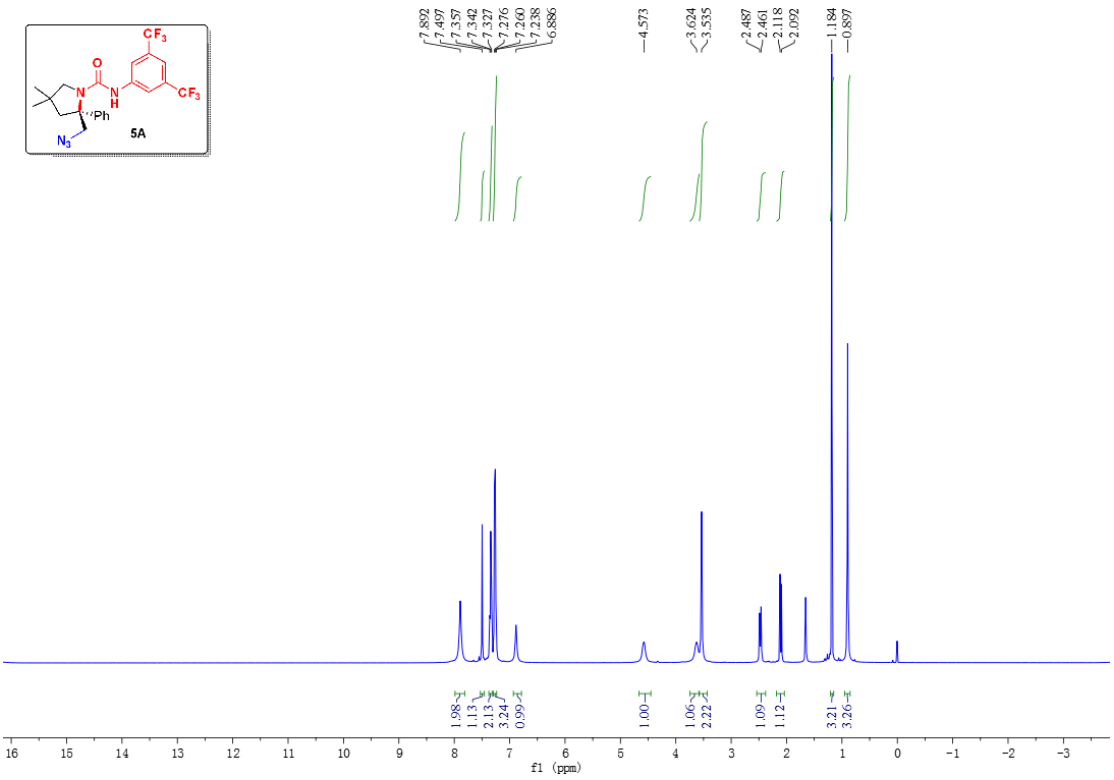


Figure S114. ^{1}H NMR spectrum of **5A**

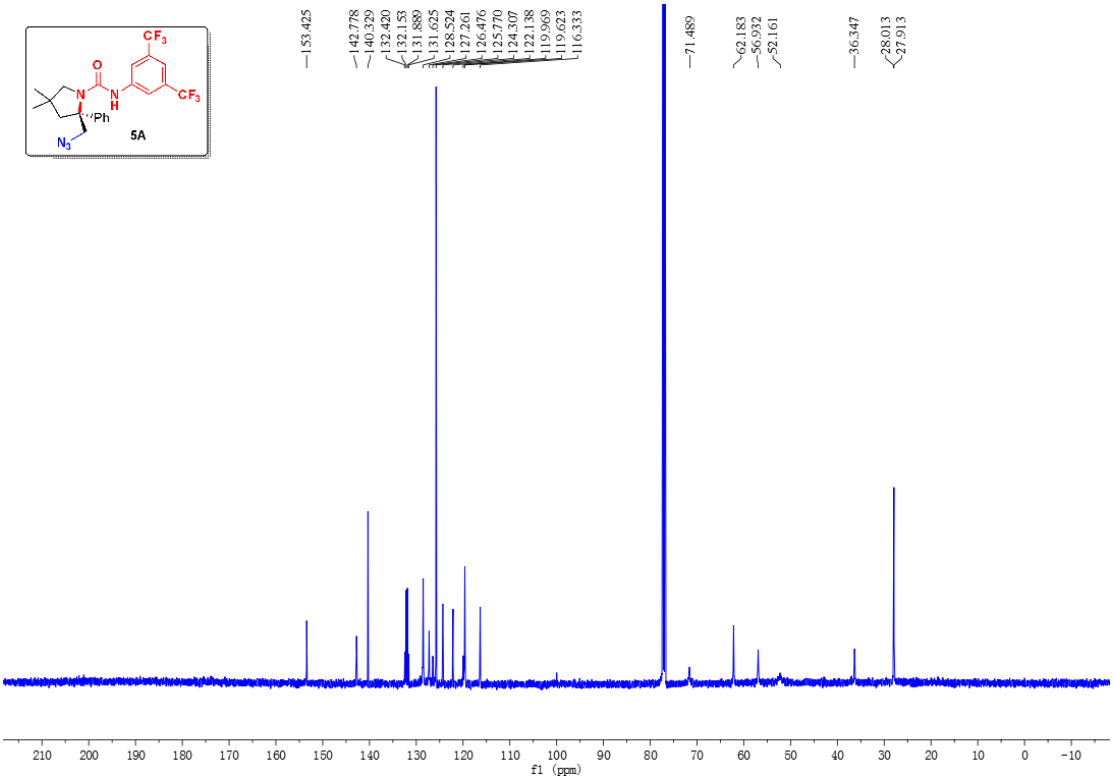


Figure S115. ^{13}C NMR spectrum of **5A**

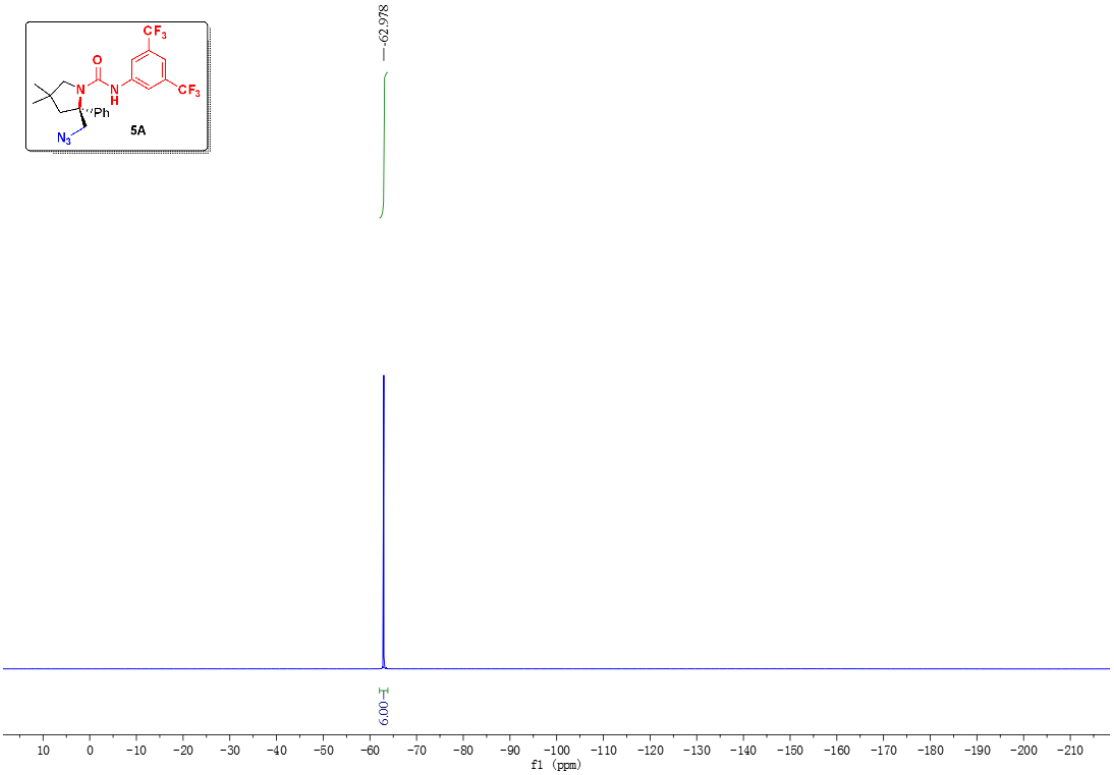


Figure S116. ^{19}F NMR spectrum of **5A**

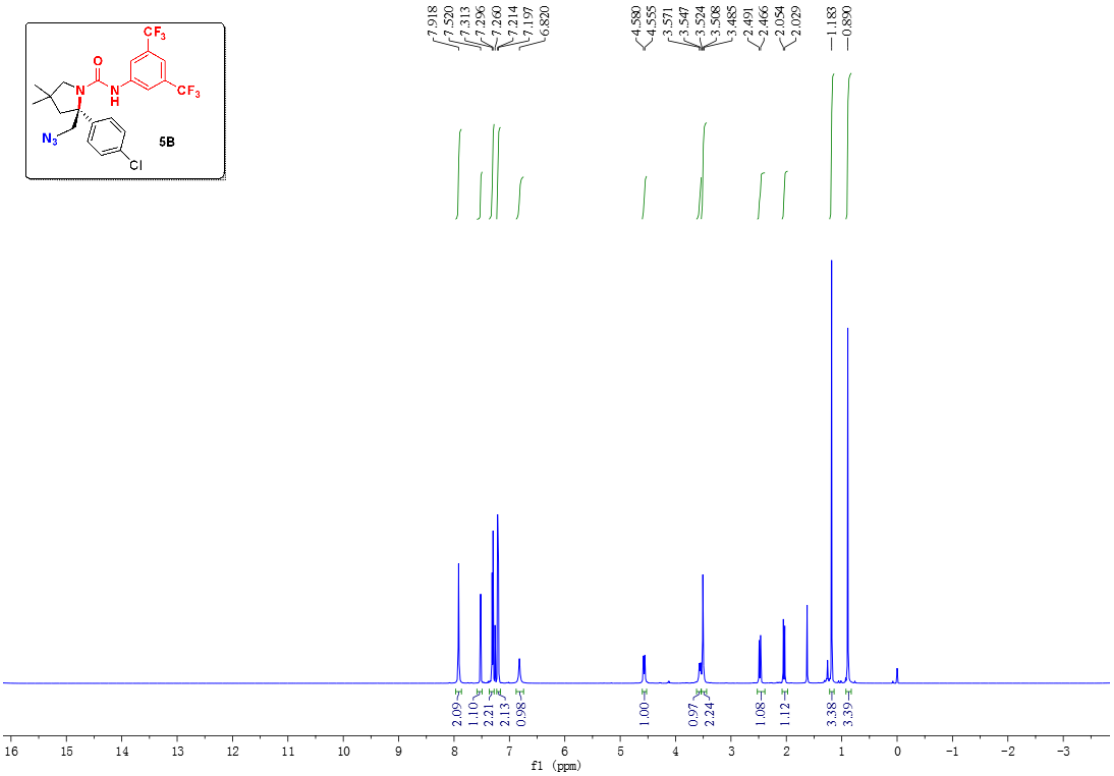


Figure S117. ^{1}H NMR spectrum of **5B**

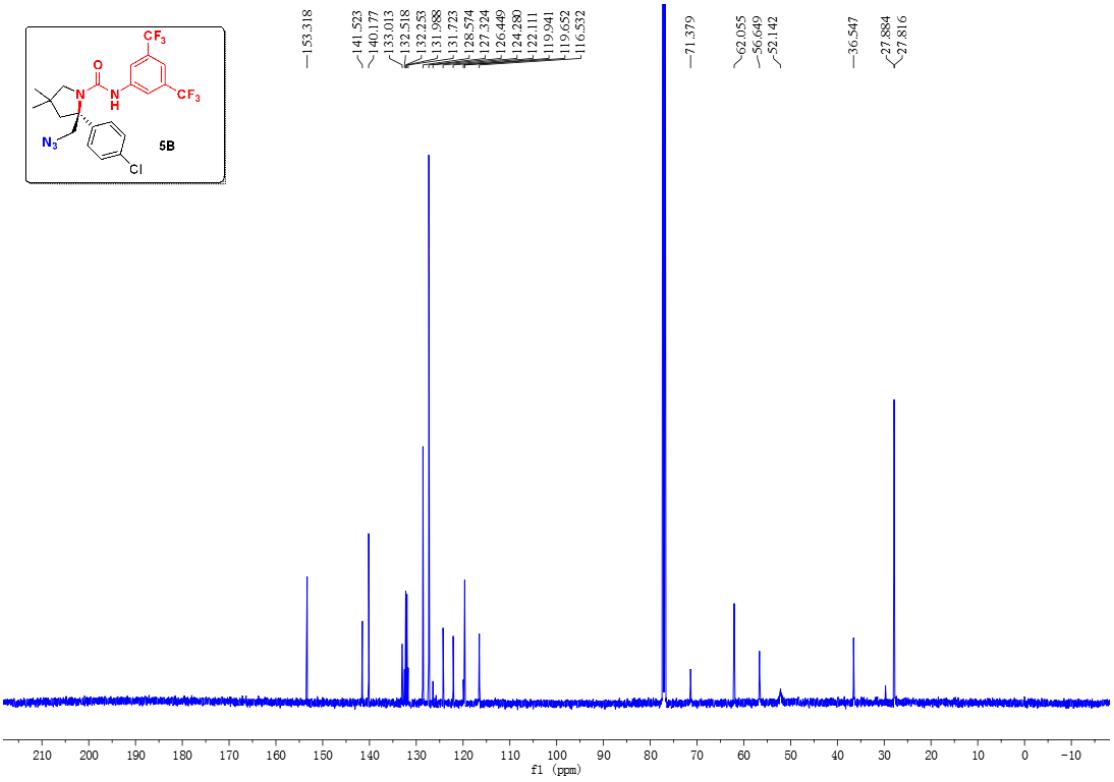


Figure S118. ^{13}C NMR spectrum of **5B**

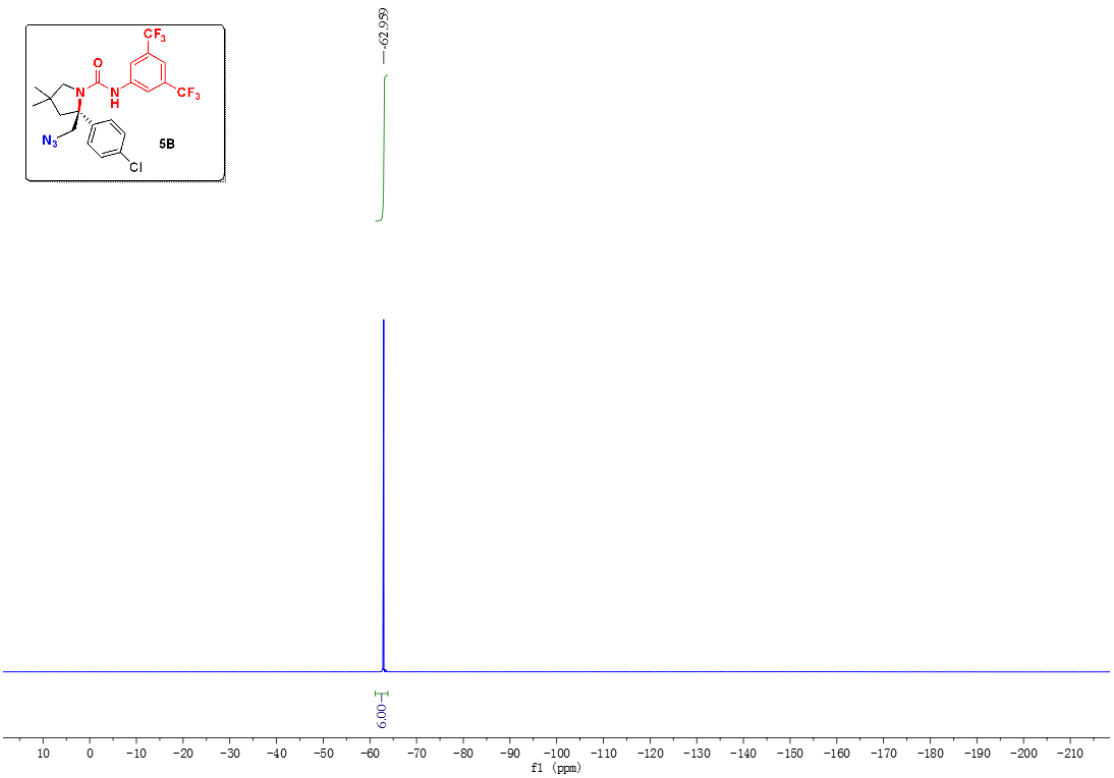


Figure S119. ^{19}F NMR spectrum of **5B**

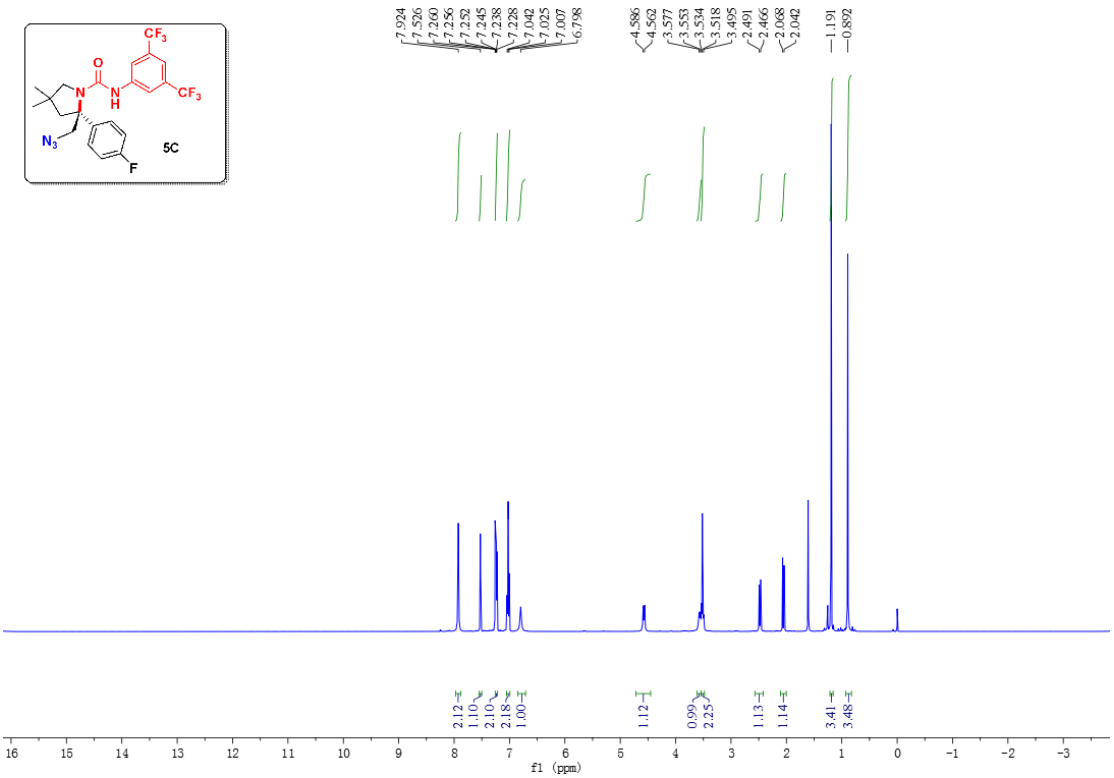


Figure S120. ^{1}H NMR spectrum of **5C**

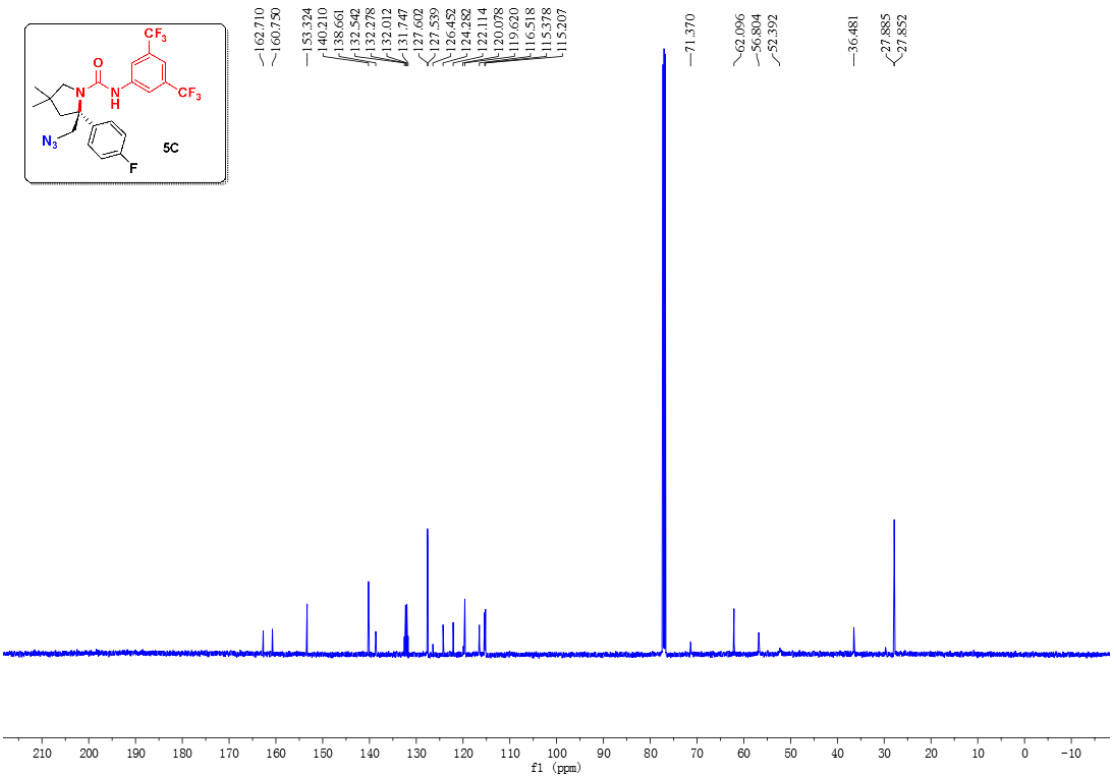


Figure S121. ^{13}C NMR spectrum of **5C**

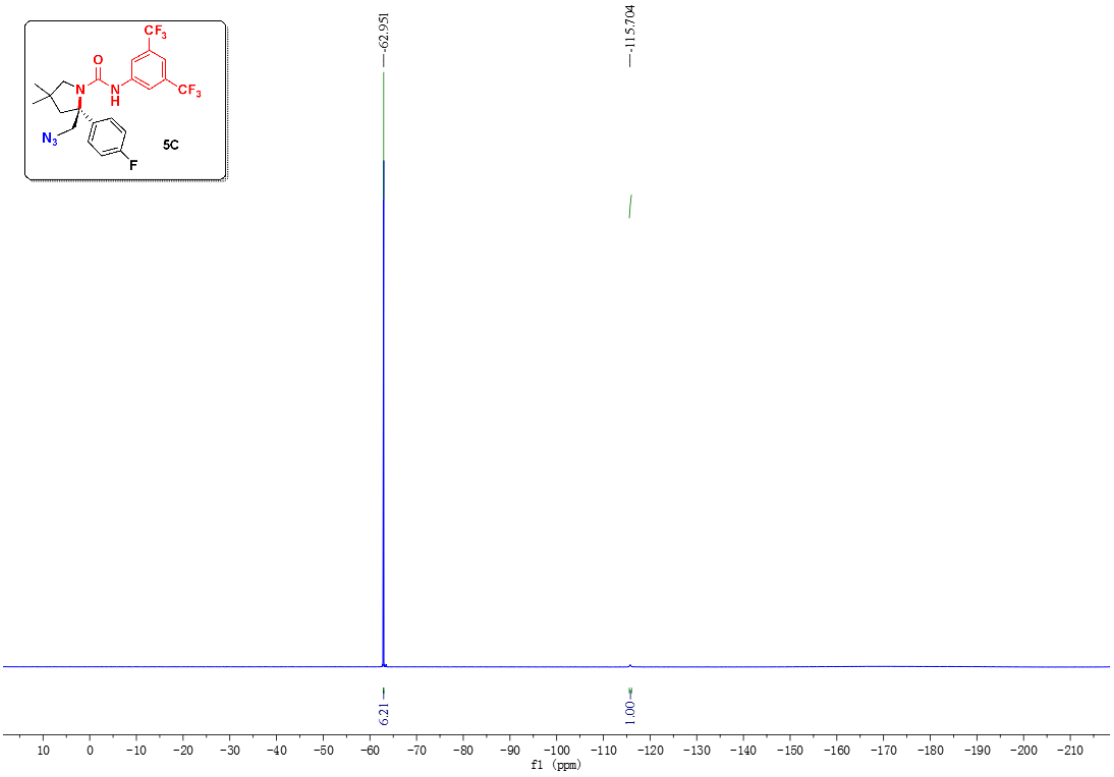


Figure S122. ^{19}F NMR spectrum of **5C**

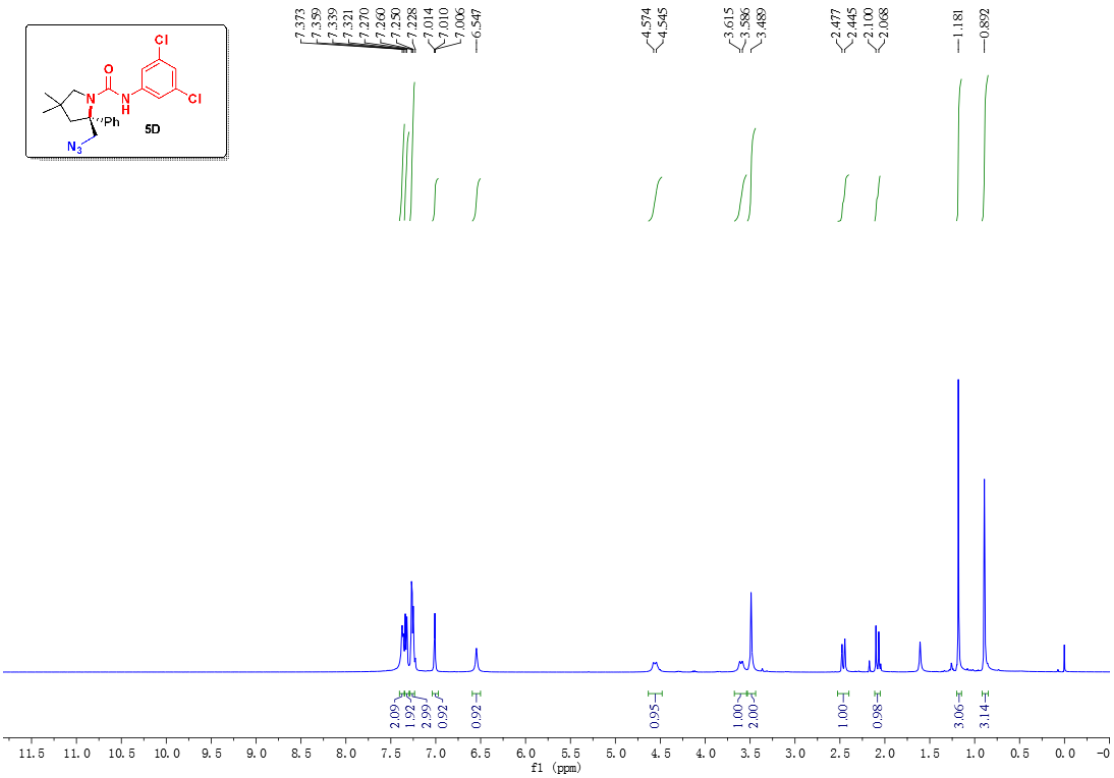


Figure S123. ^{1}H NMR spectrum of **5D**

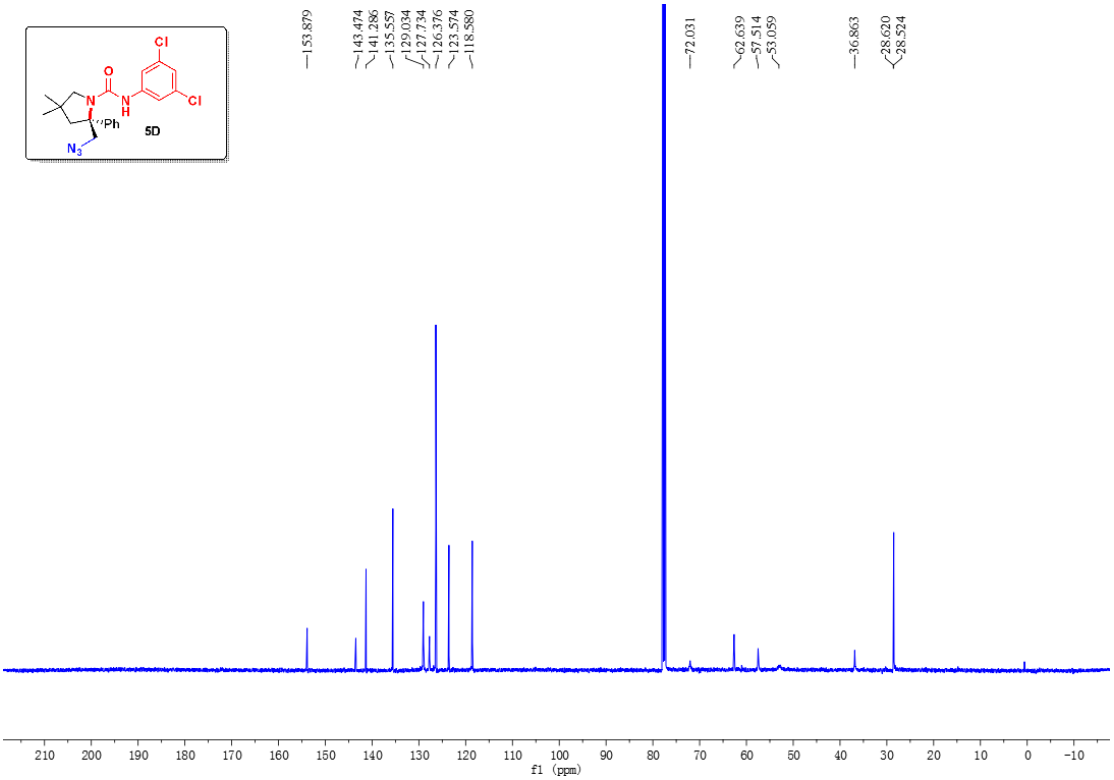


Figure S124. ^{13}C NMR spectrum of **5D**

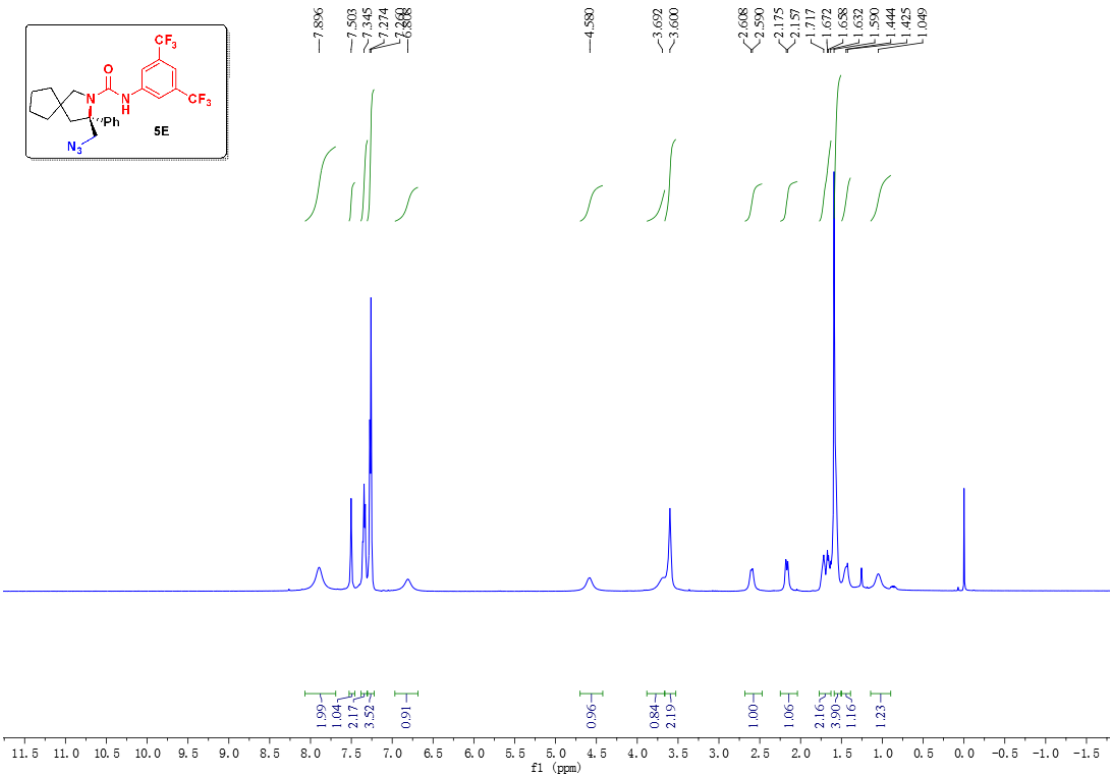


Figure S125. ^{1}H NMR spectrum of **5E**

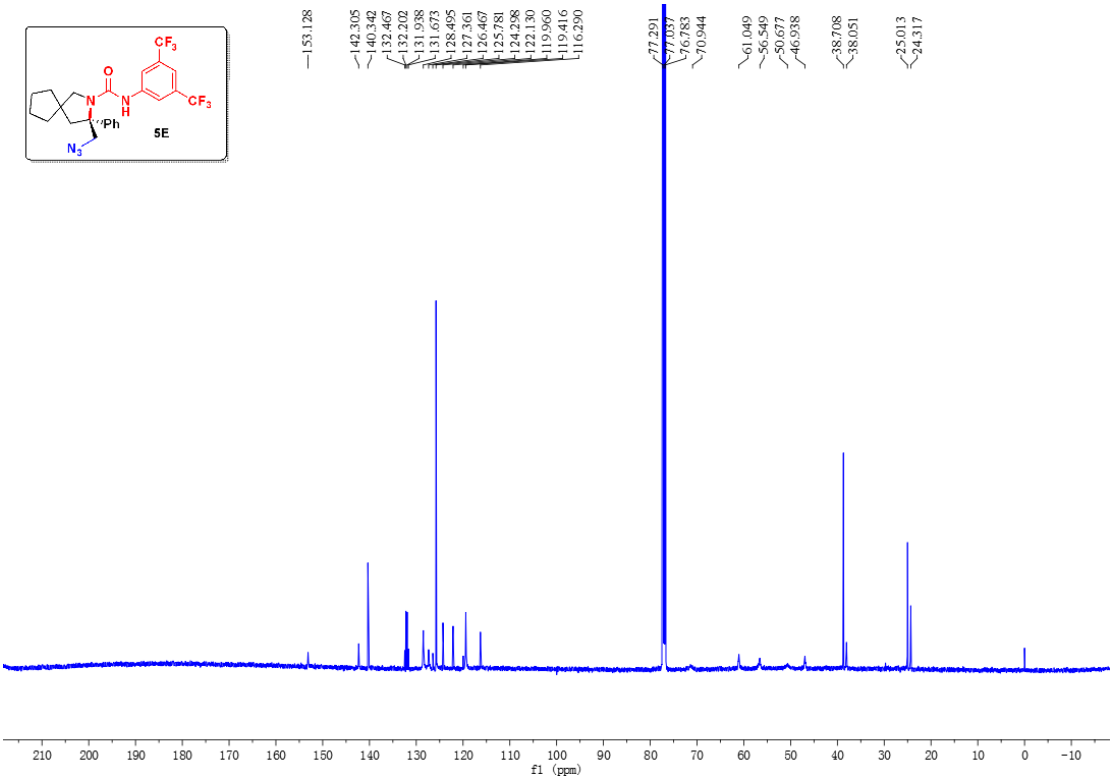


Figure S126. ^{13}C NMR spectrum of **5E**

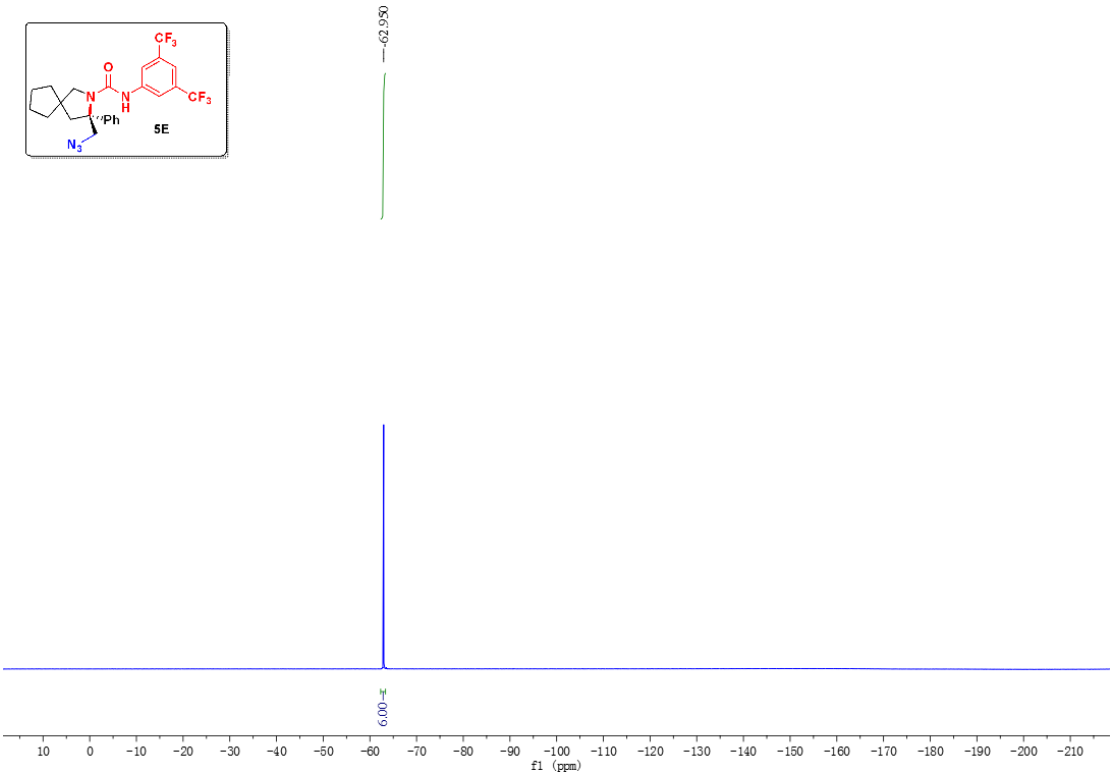


Figure S127. ^{19}F NMR spectrum of **5E**

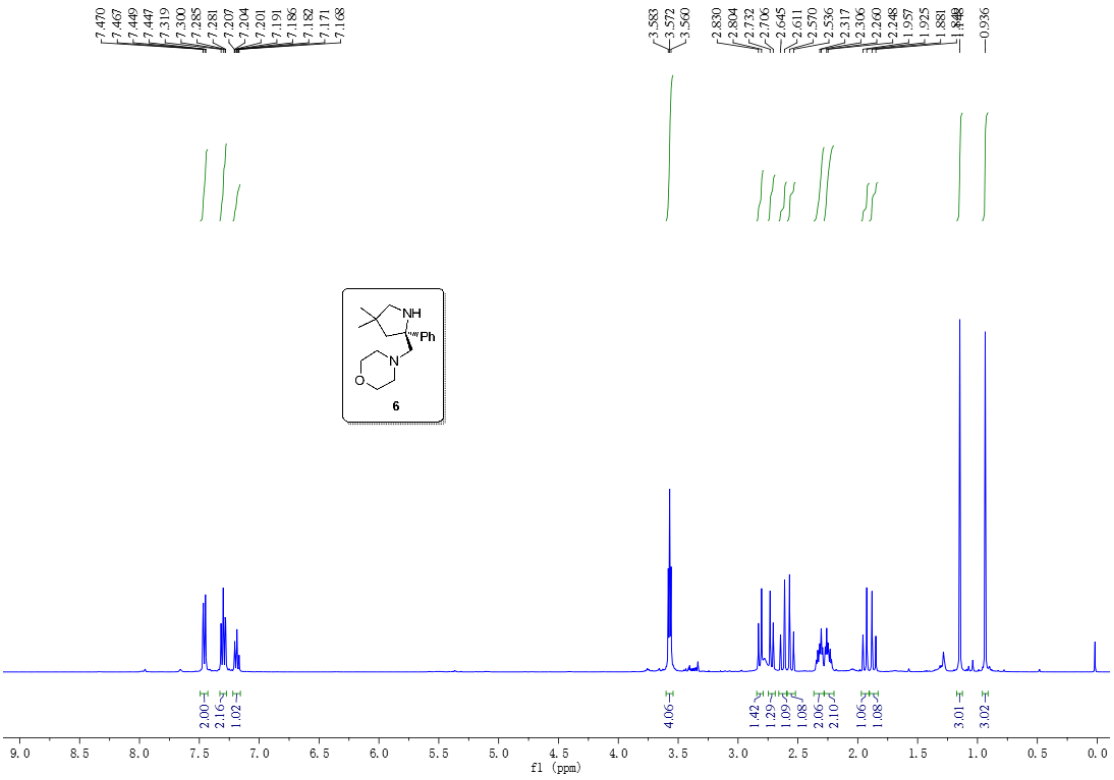


Figure S128. ^{1}H NMR spectrum of **6**

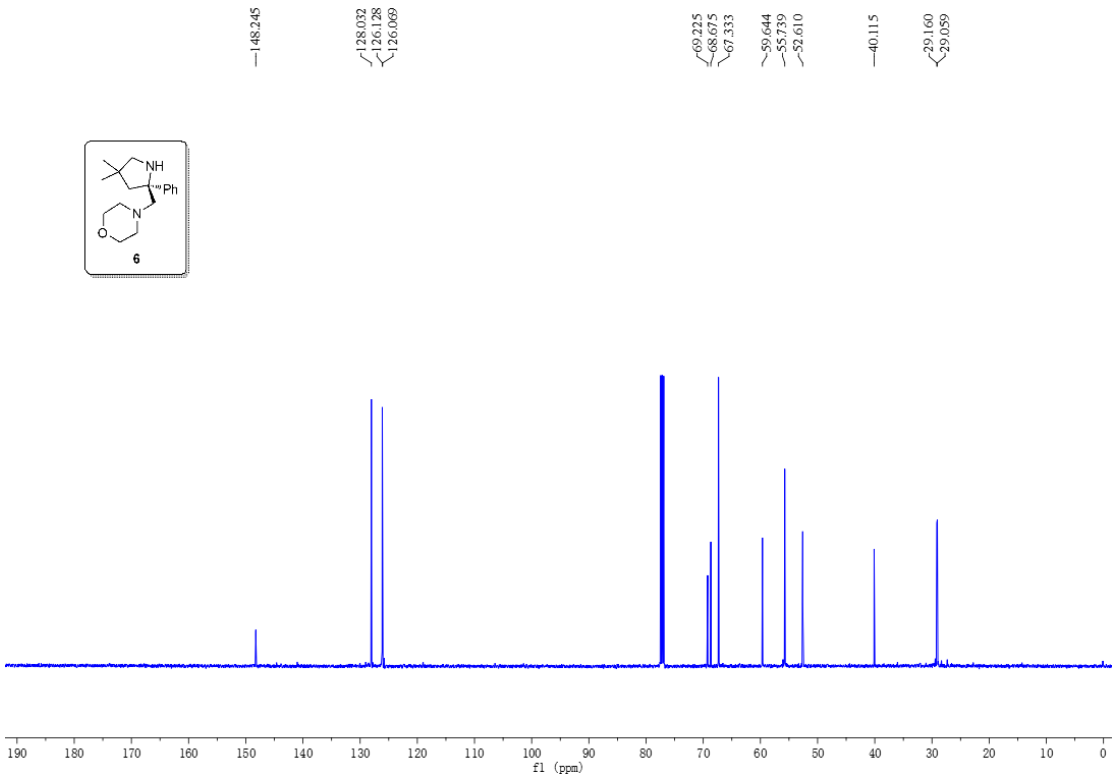


Figure S129. ^{13}C NMR spectrum of **6**

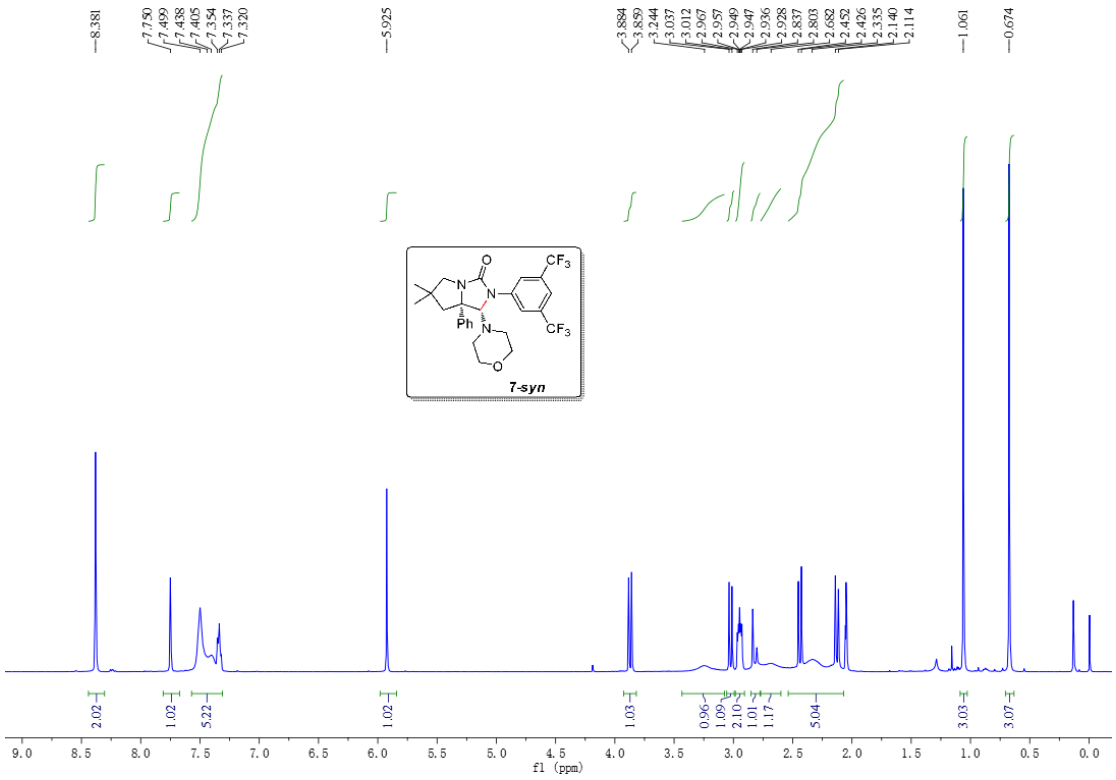


Figure S130. ^{1}H NMR spectrum of ***7-syn***

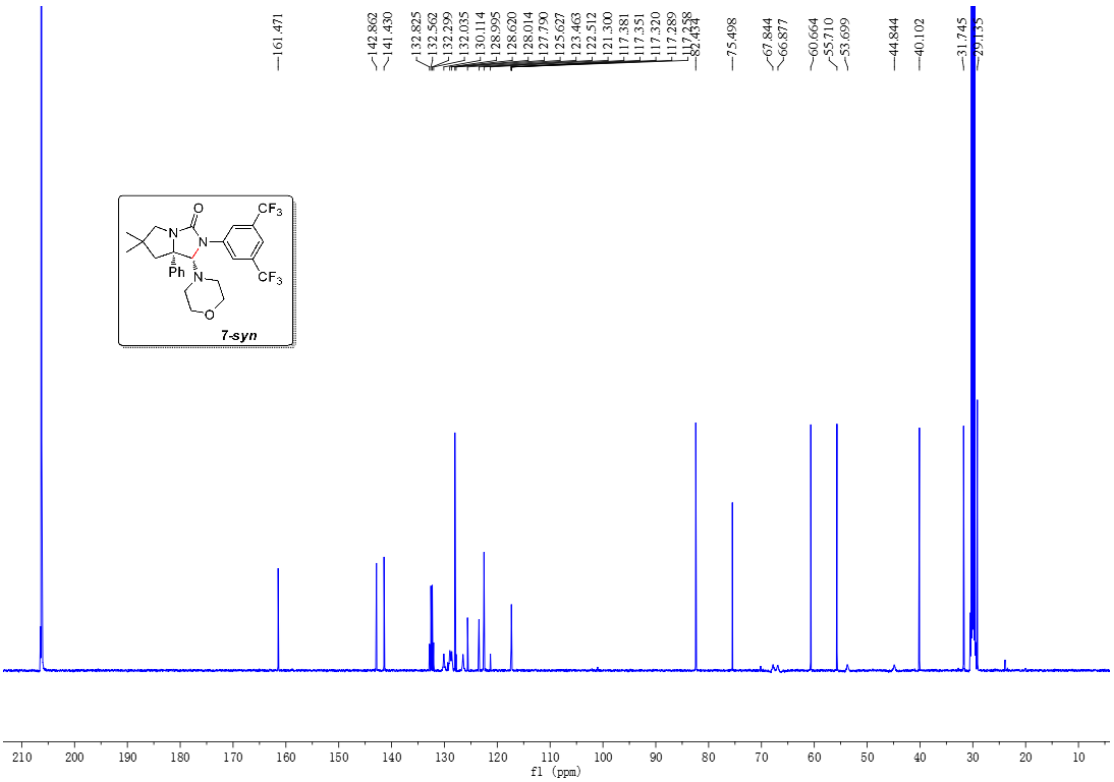


Figure S131. ^{13}C NMR spectrum of **7-*syn***

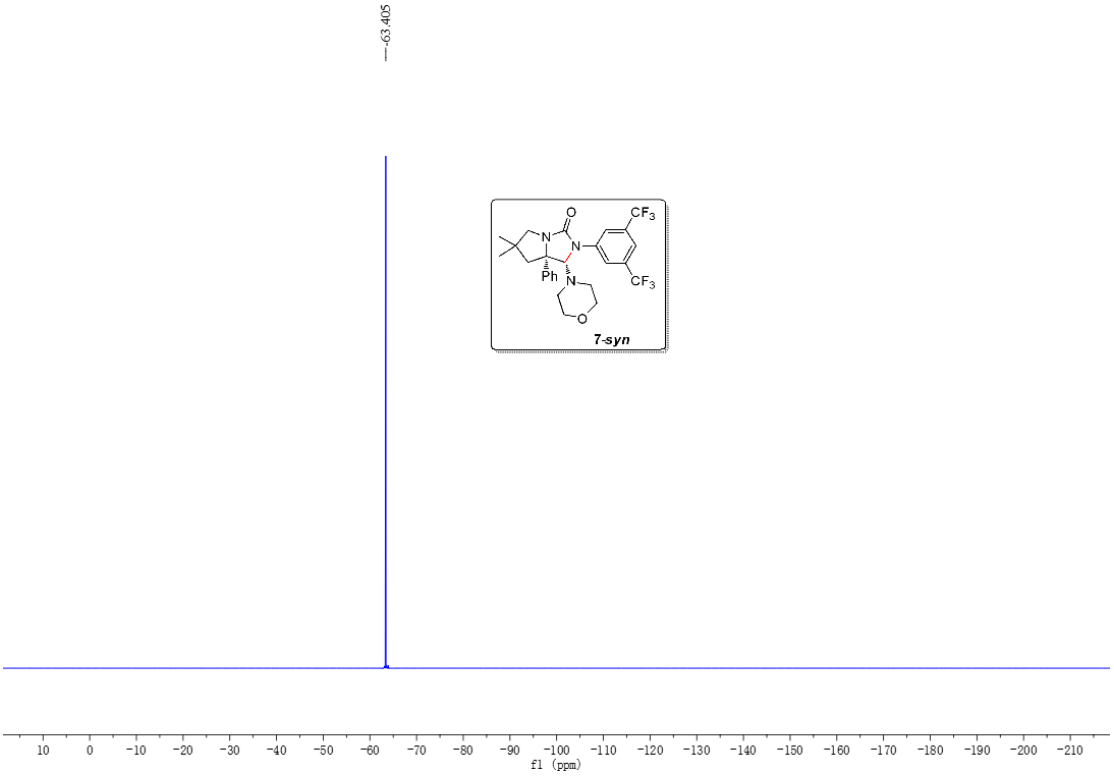


Figure S132. ^{19}F NMR spectrum of **7-*syn***

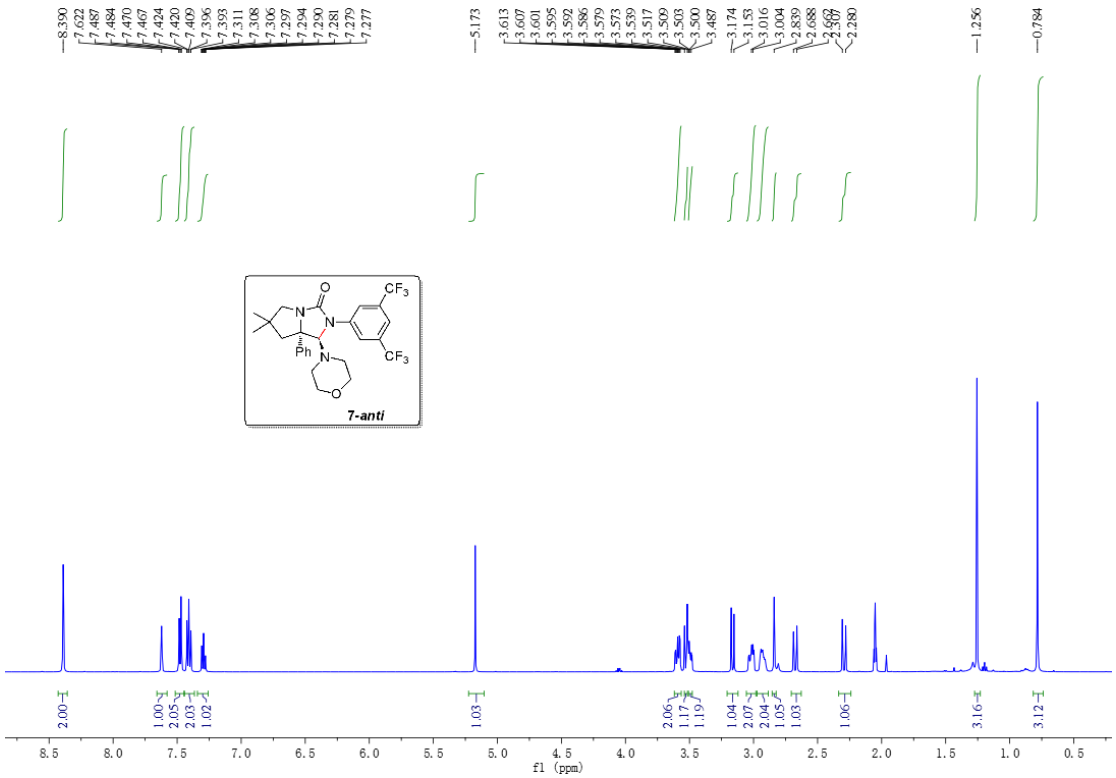


Figure S133. ^{1}H NMR spectrum of ***7-anti***

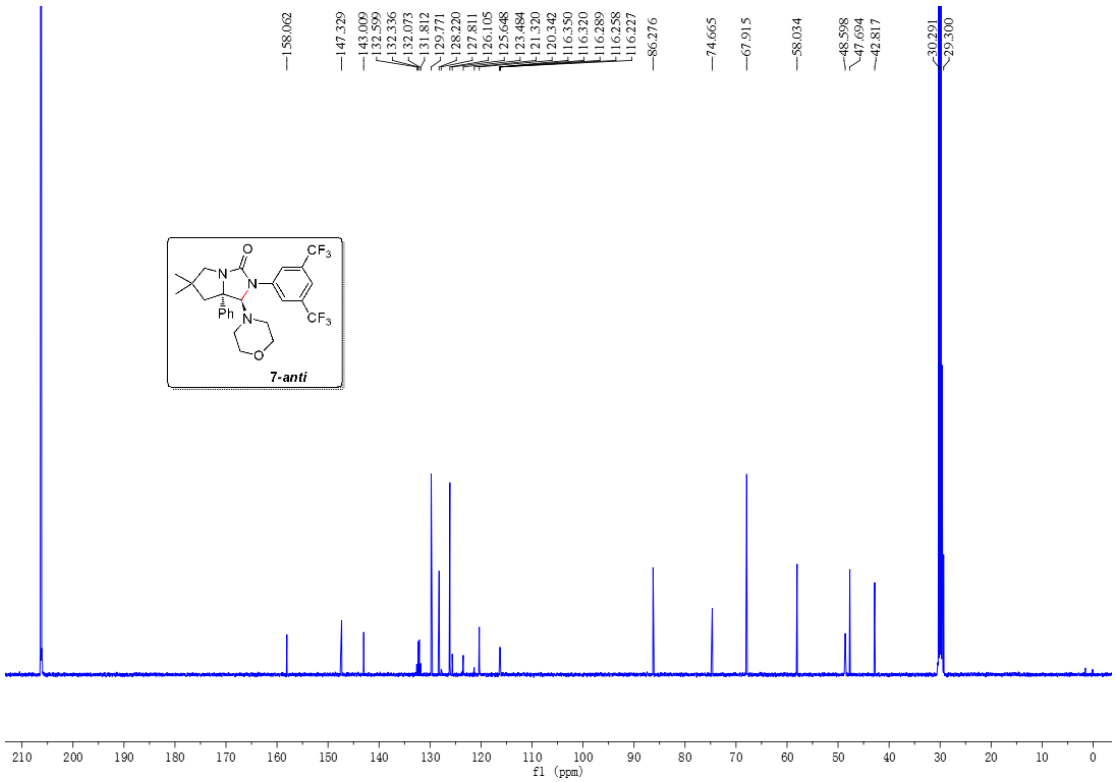


Figure S134. ^{13}C NMR spectrum of ***7-anti***

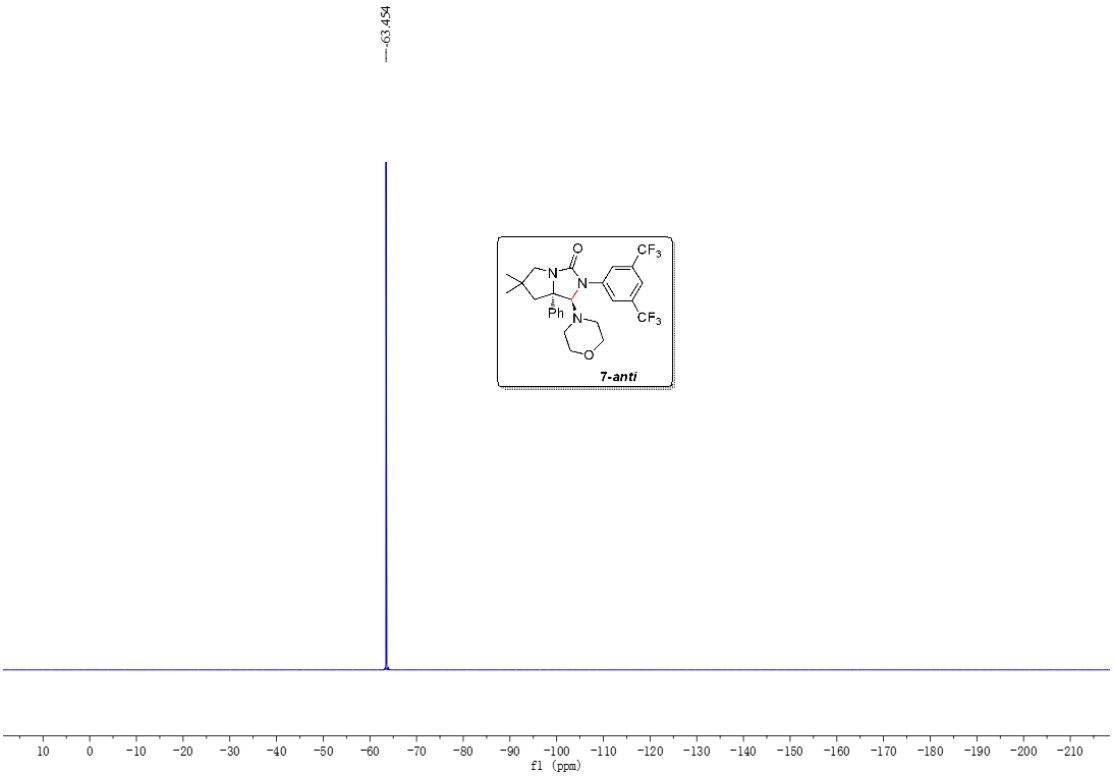


Figure S135. ^{19}F NMR spectrum of **7-*anti***

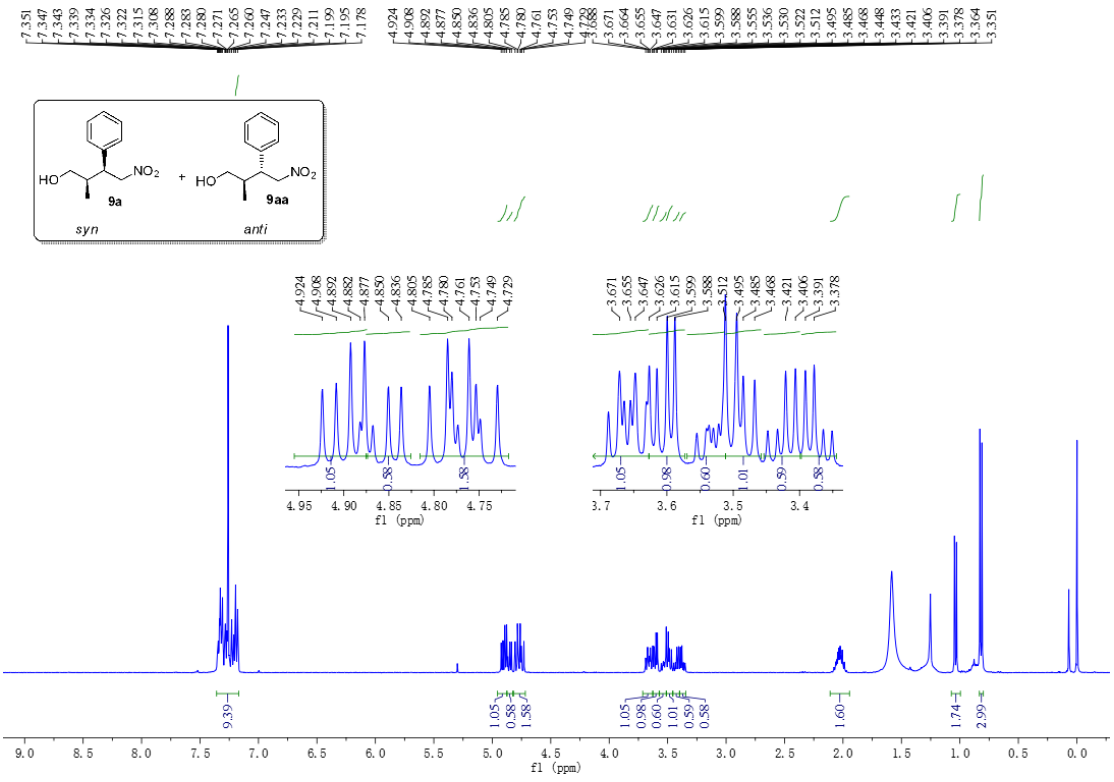


Figure S136. ^{1}H NMR spectrum of **9a** & **9aa**

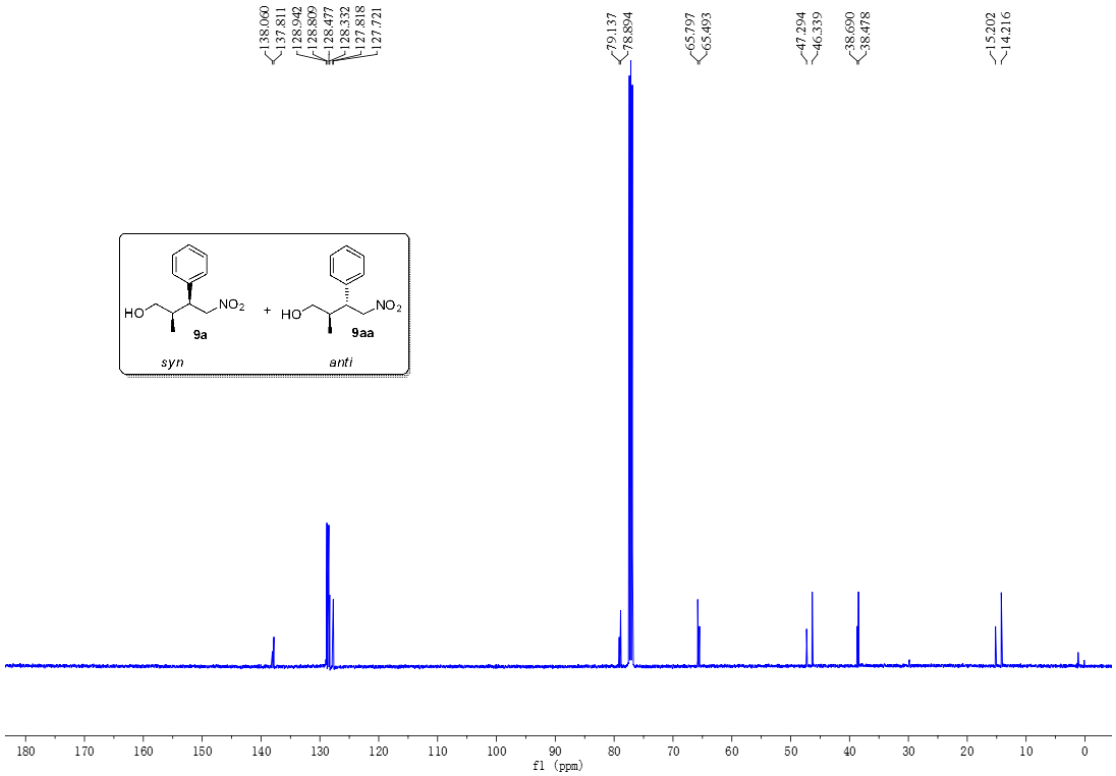


Figure S137. ^{13}C NMR spectrum of **9a** & **9aa**

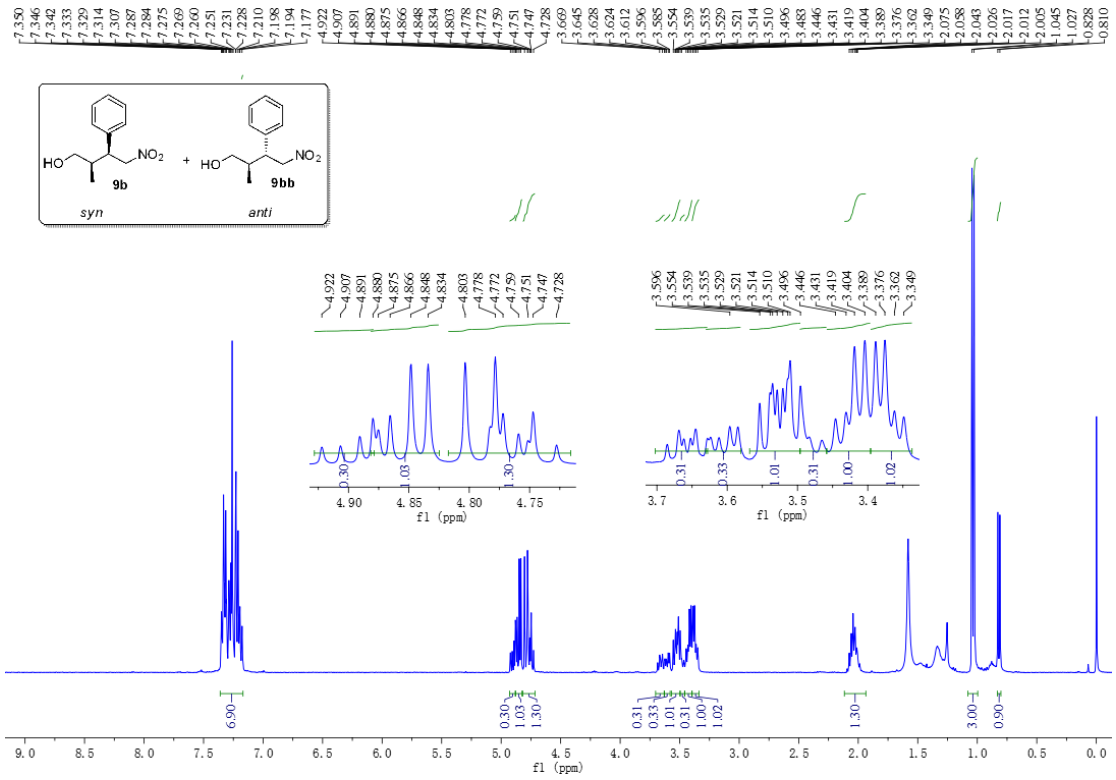


Figure S138. ^{1}H NMR spectrum of **9b** & **9bb**

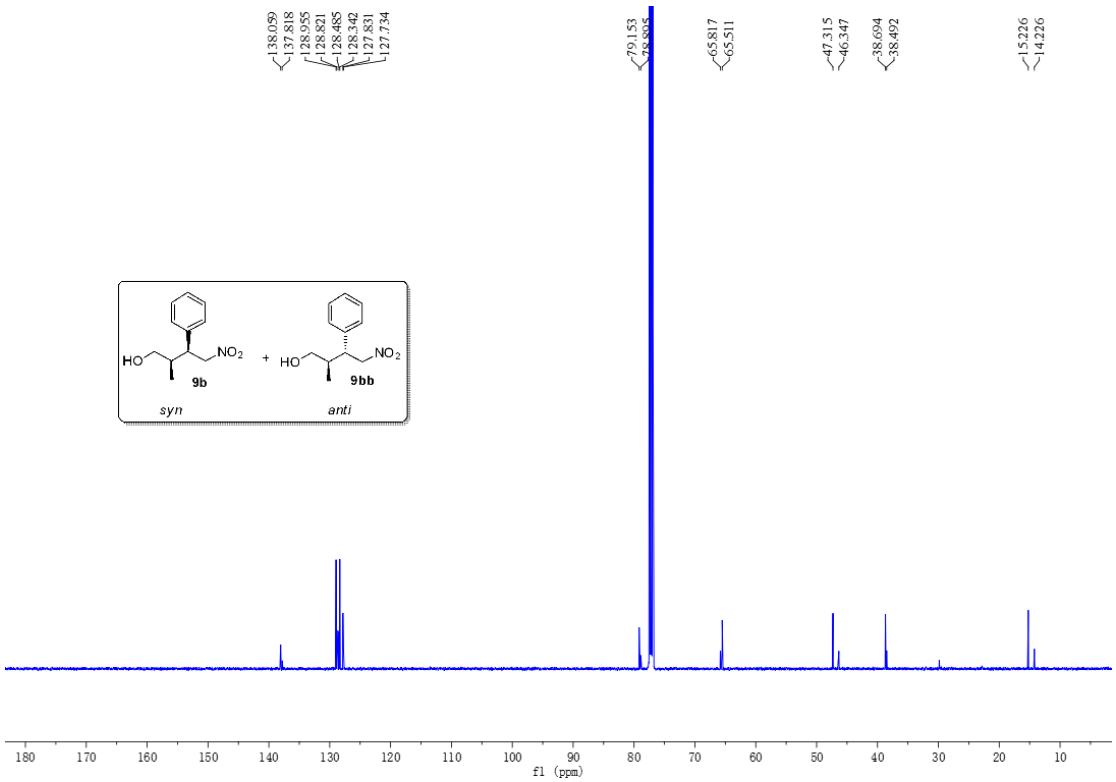


Figure S139. ^{13}C NMR spectrum of **9b** & **9bb**

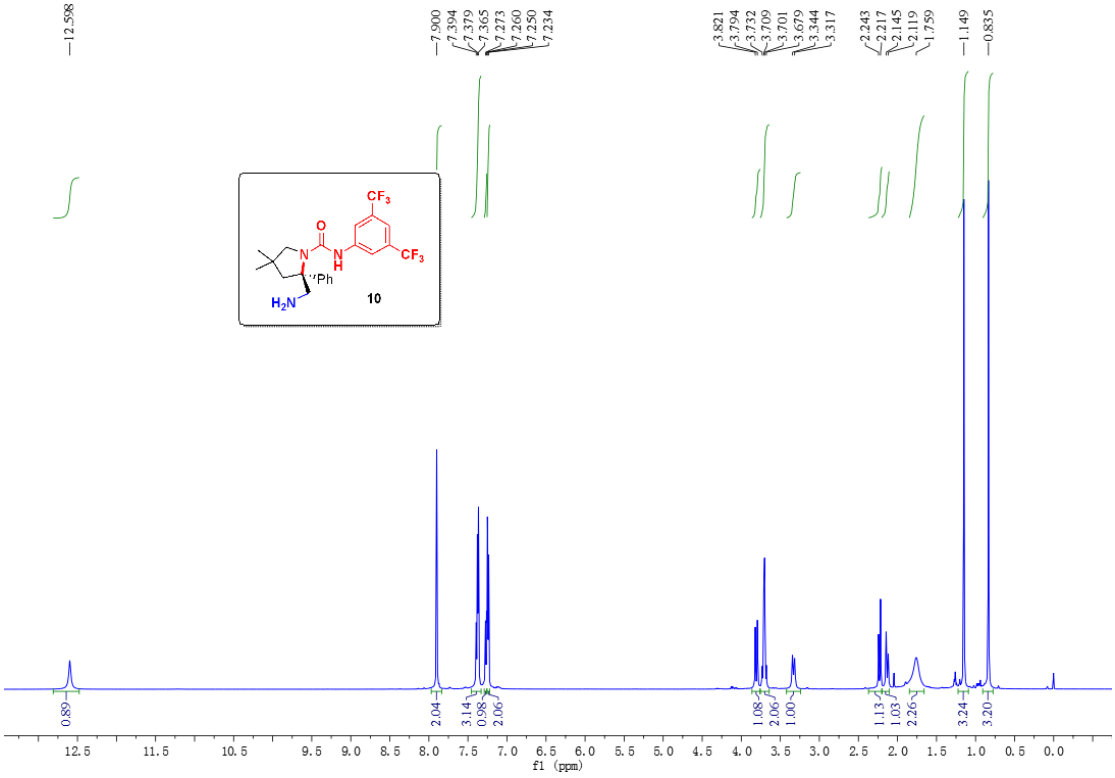


Figure S140. ^{1}H NMR spectrum of **10**

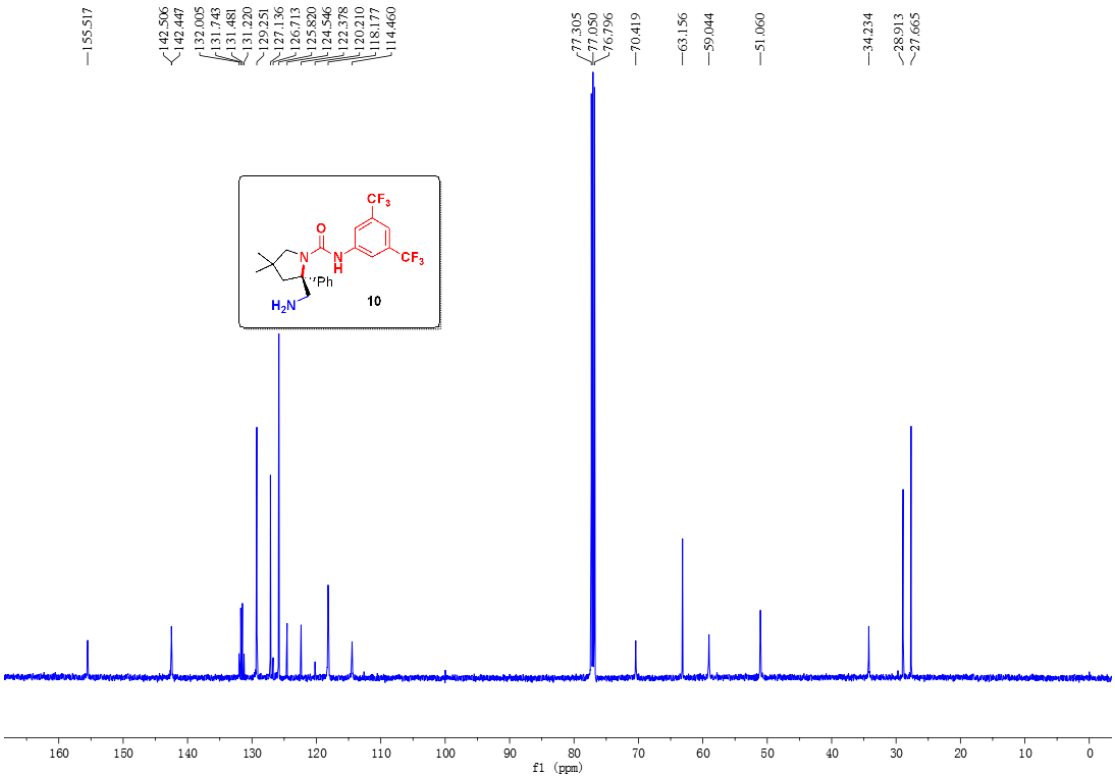


Figure S141. ^{13}C NMR spectrum of **10**

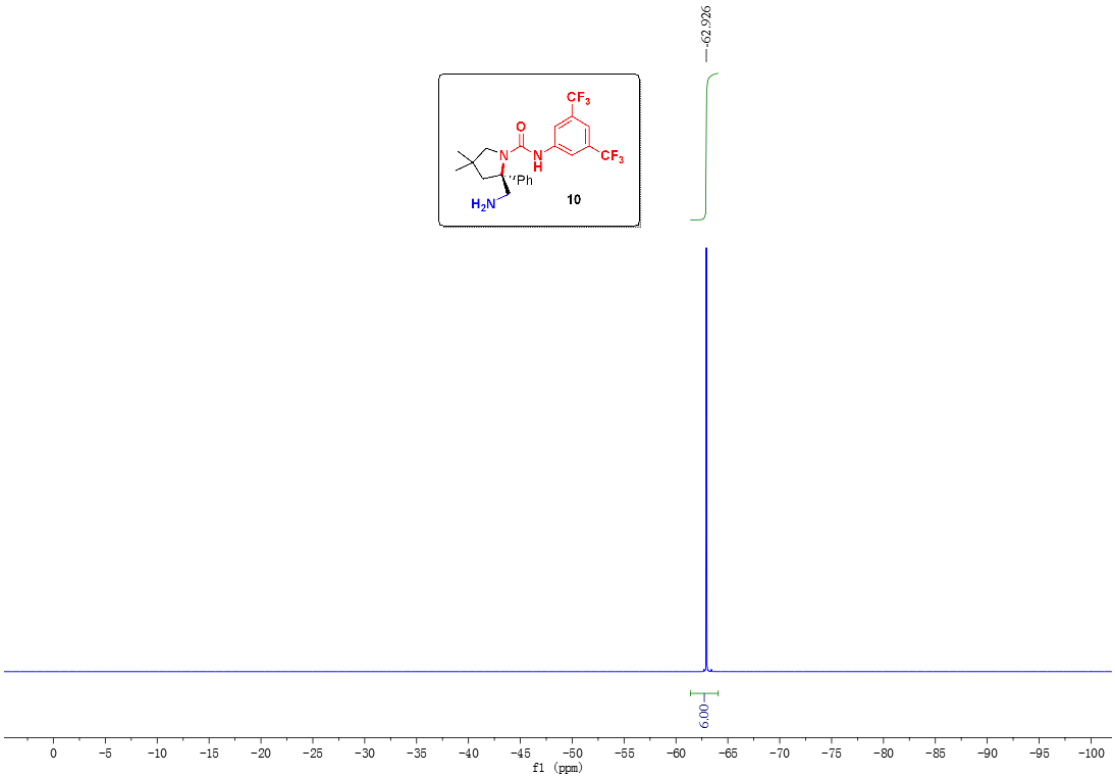


Figure S142. ^{19}F NMR spectrum of **10**

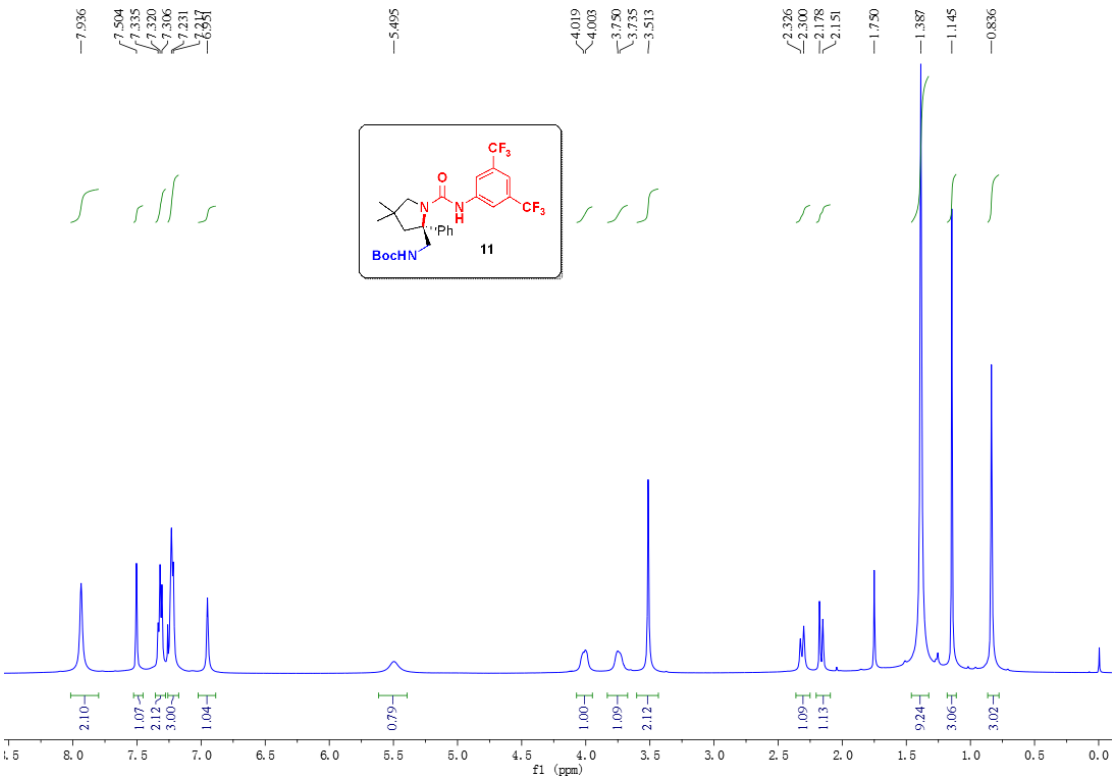


Figure S143. ^{1}H NMR spectrum of **11**

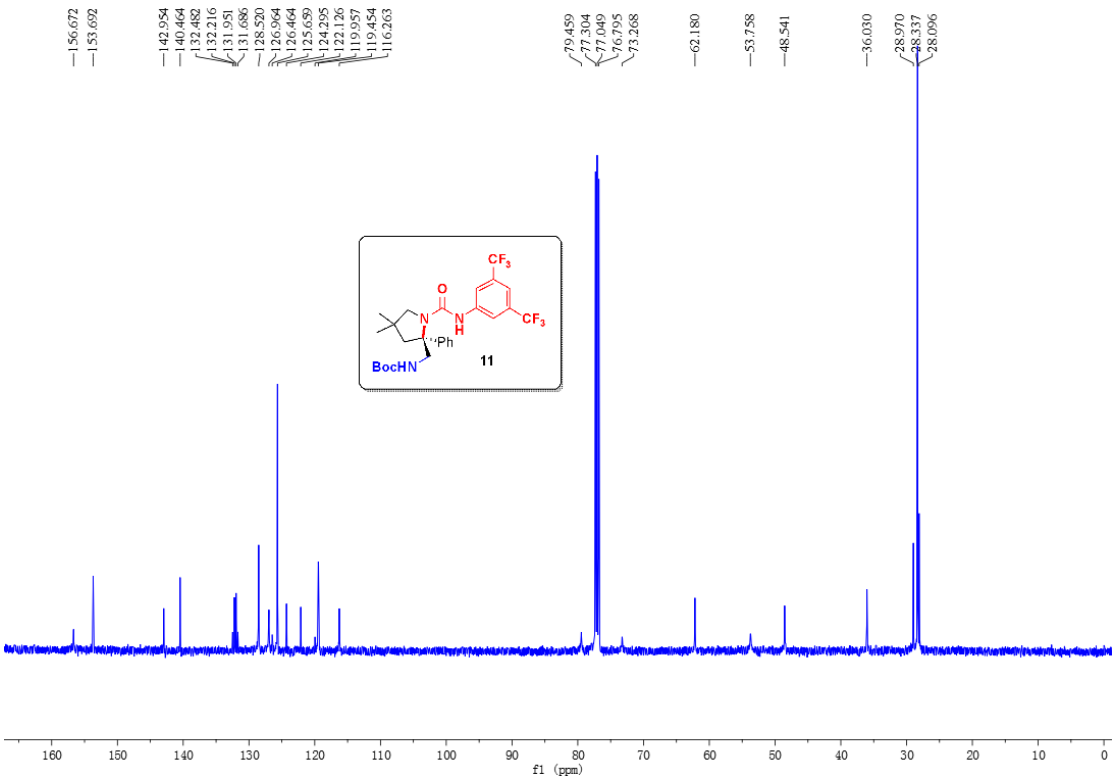


Figure S144. ^{13}C NMR spectrum of **11**

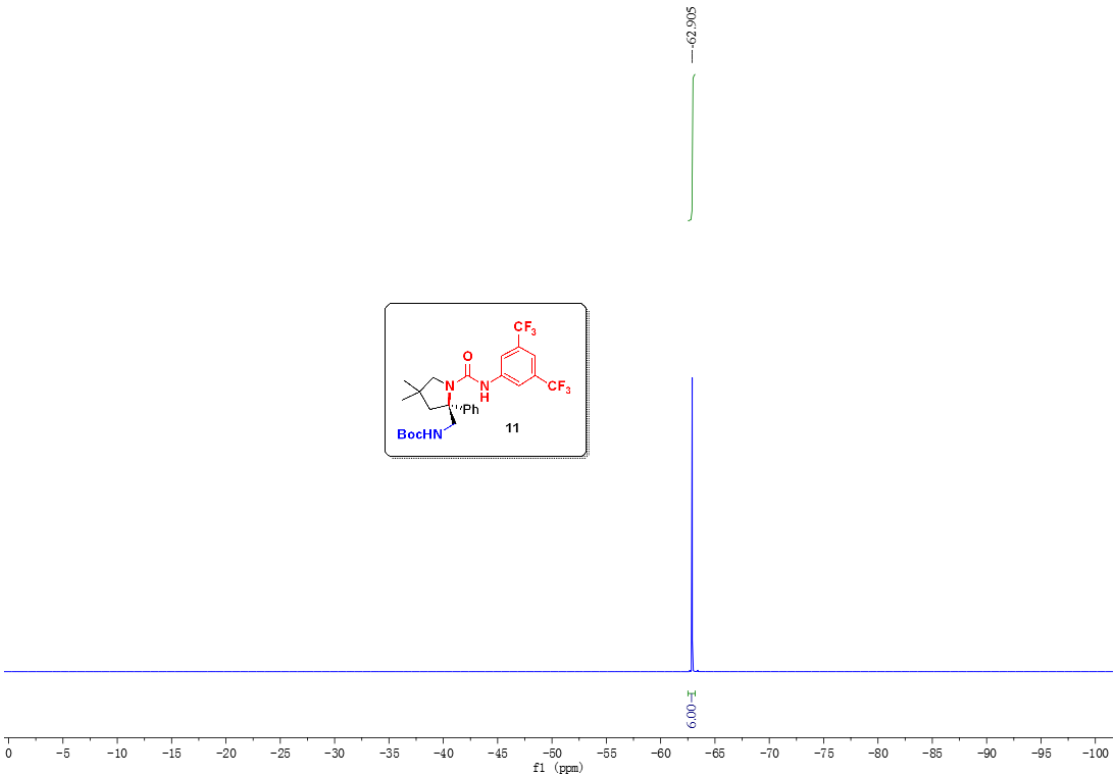


Figure S145. ^{19}F NMR spectrum of **11**

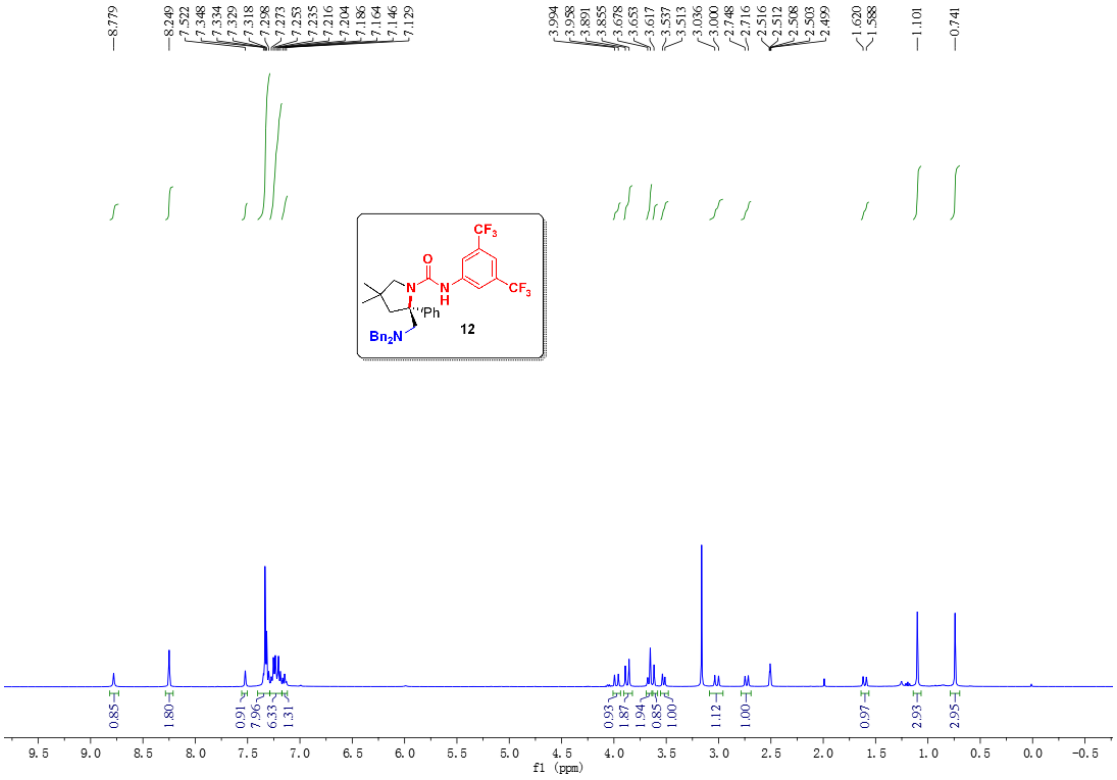


Figure S146. ^{1}H NMR spectrum of **12**

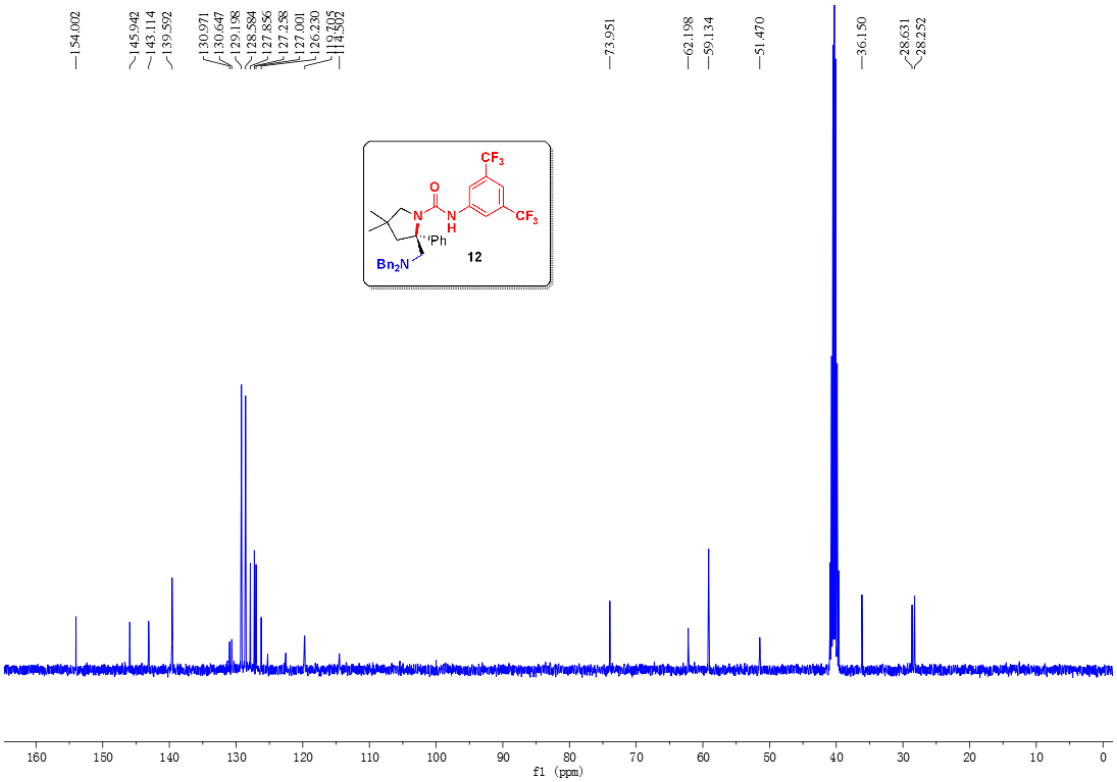


Figure S147. ^{13}C NMR spectrum of **12**

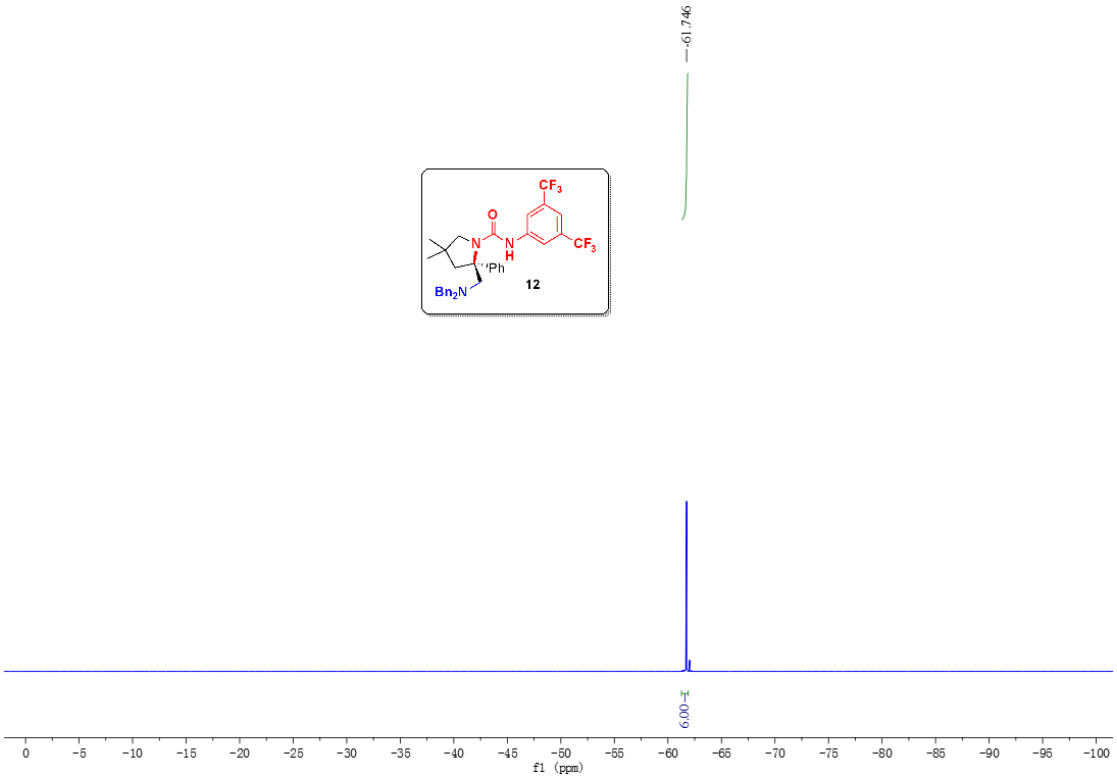


Figure S148. ^{19}F NMR spectrum of **12**

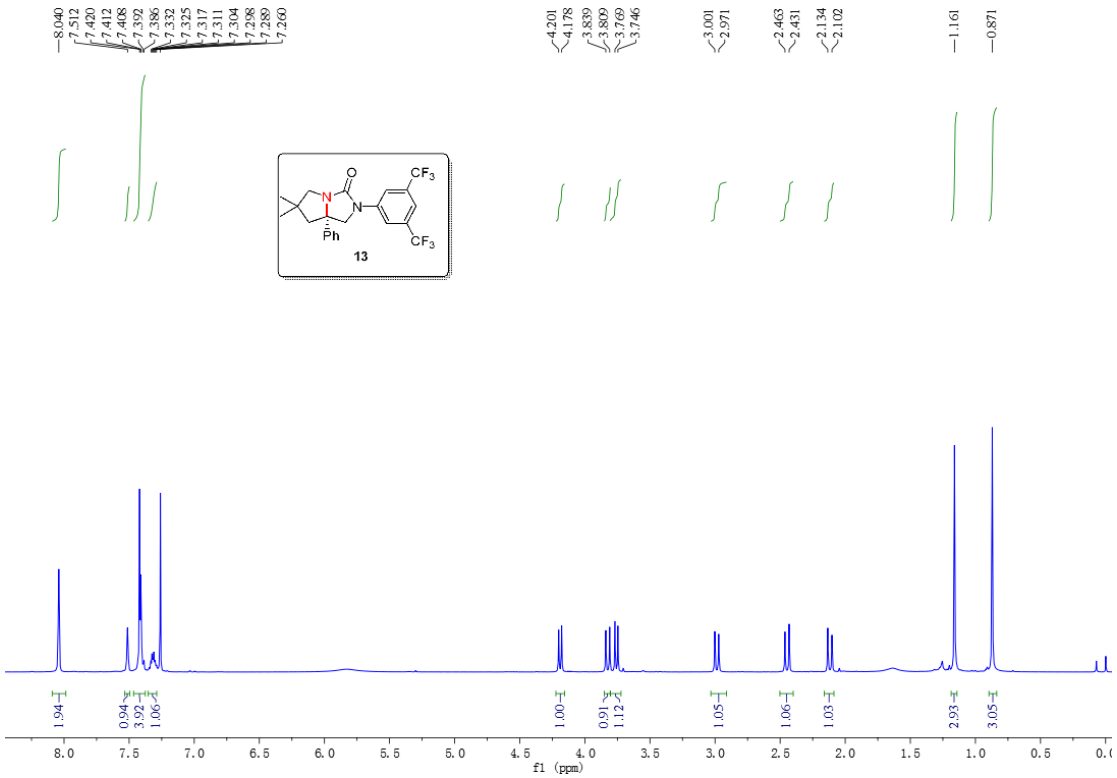


Figure S149. ^{1}H NMR spectrum of **13**

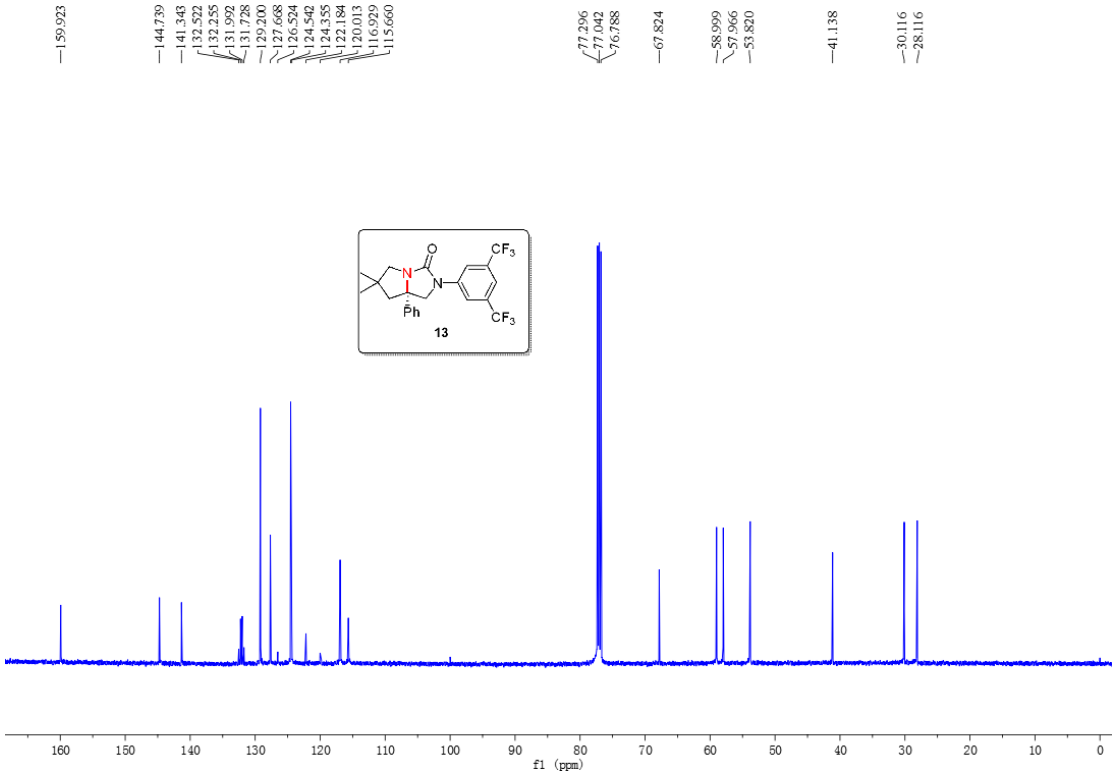


Figure S150. ^{13}C NMR spectrum of **13**

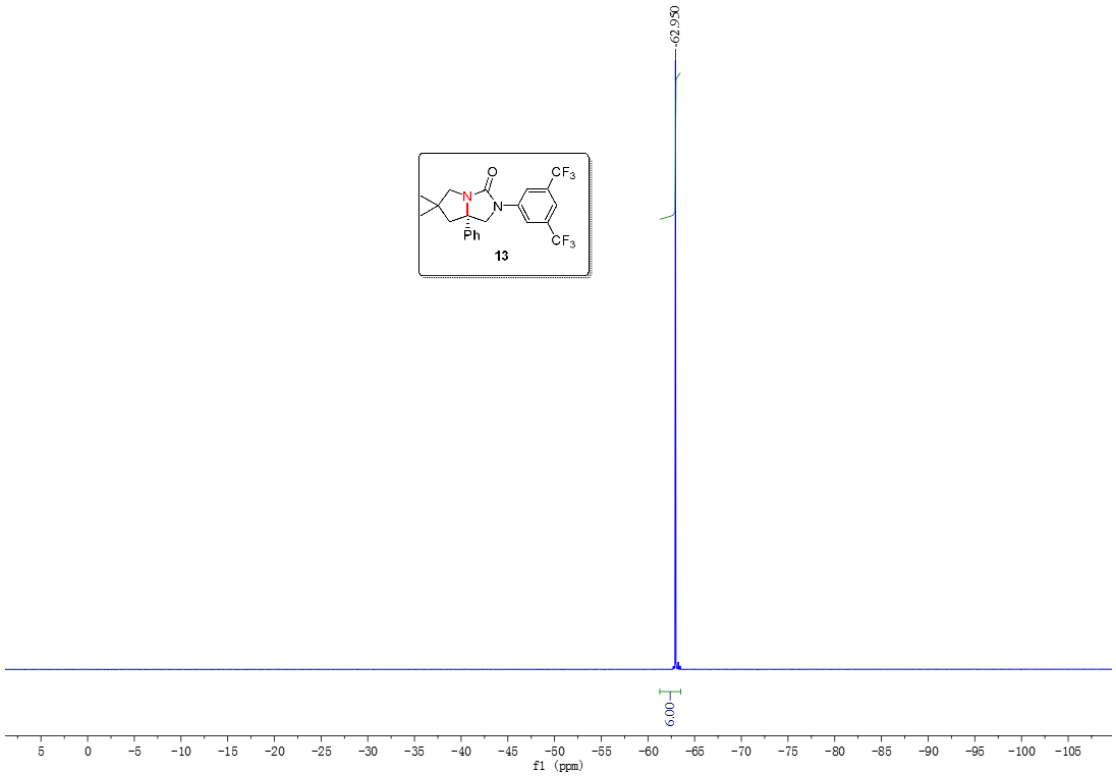
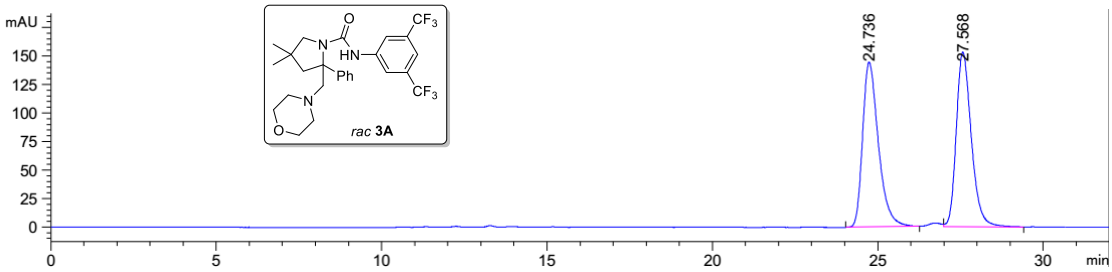


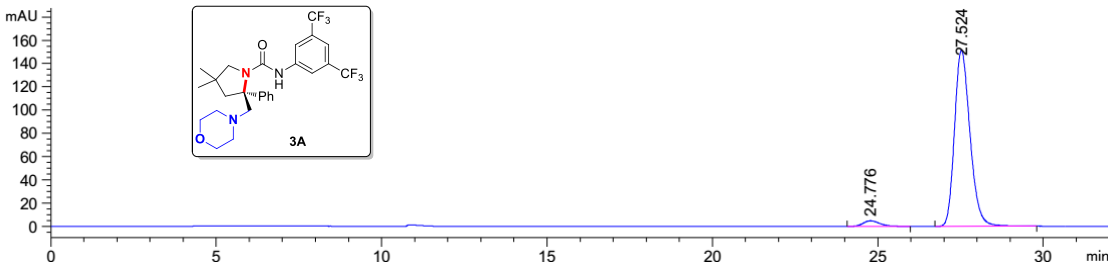
Figure S151. ^{19}F NMR spectrum of **13**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.736	BB	0.5048	4790.56738	144.49049	49.8099
2	27.568	VB	0.4800	4827.14160	153.01495	50.1901
Totals :				9617.70898	297.50545	

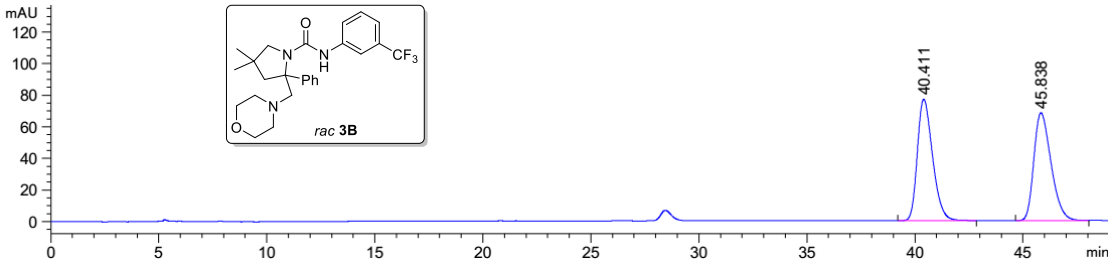
Figure S152. HPLC spectrum of *rac* **3A**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.776	MF R	0.5748	165.31071	4.79366	3.2442
2	27.524	BB	0.5019	4930.24609	151.41750	96.7558
Totals :				5095.55681	156.21116	

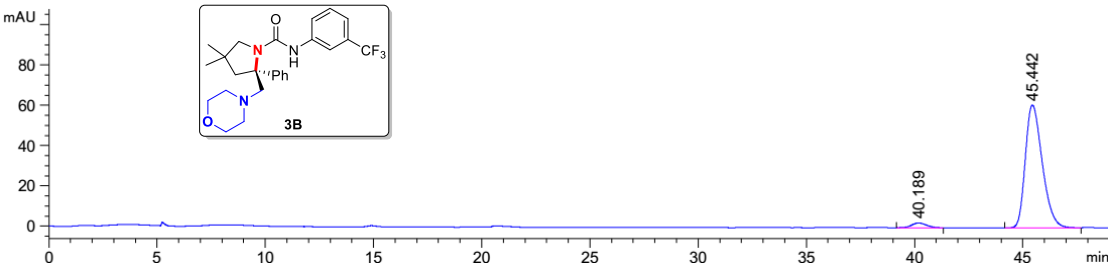
Figure S153. HPLC spectrum of **3A**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.411	BB	0.7527	3763.00610	76.93058	49.9689
2	45.838	BB	0.8547	3767.68530	68.18395	50.0311
Totals :				7530.69141	145.11453	

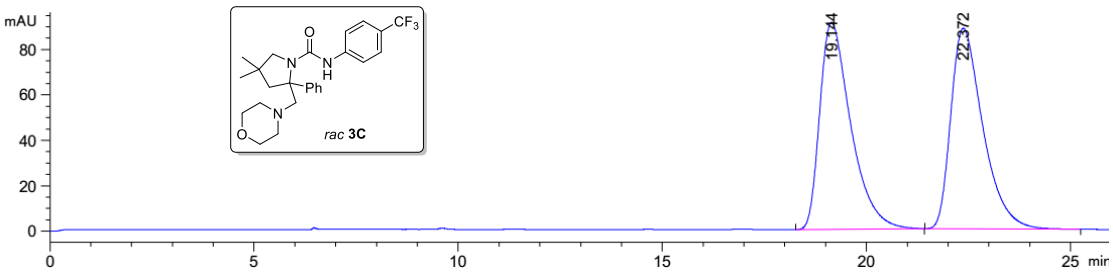
Figure S154. HPLC spectrum of *rac* **3B**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.189	FM R	0.8400	122.07211	2.42202	3.5485
2	45.442	MF R	0.9065	3318.05151	61.00392	96.4515
Totals :				3440.12363	63.42594	

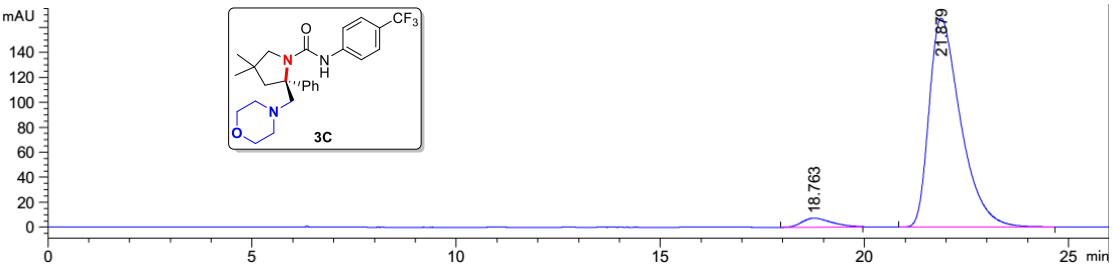
Figure S155. HPLC spectrum of **3B**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.144	BB	0.7934	4804.37646	91.07858	49.9359
2	22.372	BB	0.8303	4816.71191	88.31194	50.0641
Totals :				9621.08838	179.39051	

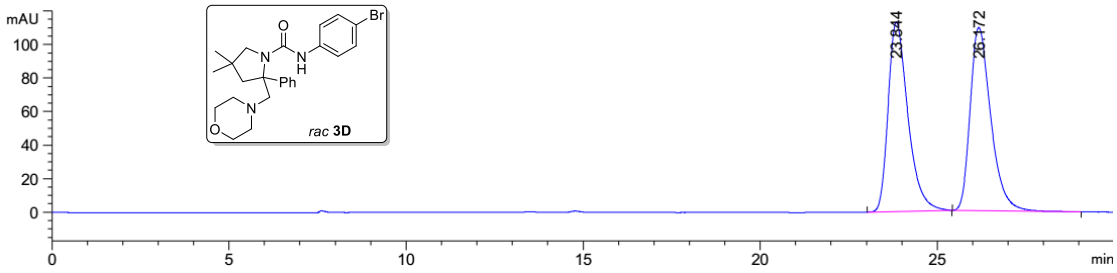
Figure S156. HPLC spectrum of *rac* **3C**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.763	MF R	0.8606	374.21683	7.24756	3.9956
2	21.879	MF R	0.8961	8991.44434	167.23654	96.0044
Totals :				9365.66116	174.48410	

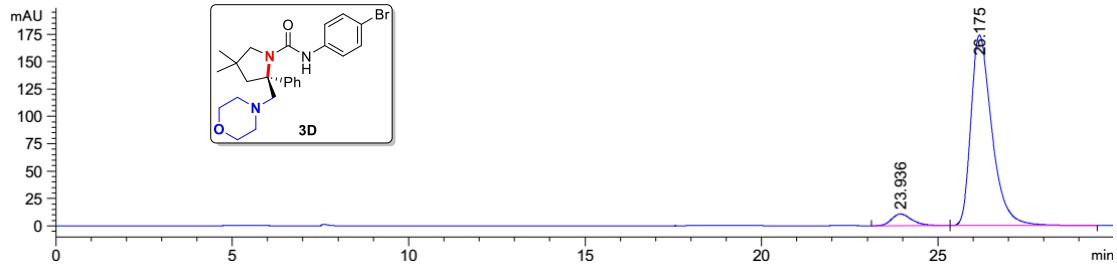
Figure S157. HPLC spectrum of **3C**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.844	BB	0.5928	4381.47510	112.89796	49.7673
2	26.172	BB	0.6182	4422.43994	109.25891	50.2327
Totals :				8803.91504	222.15688	

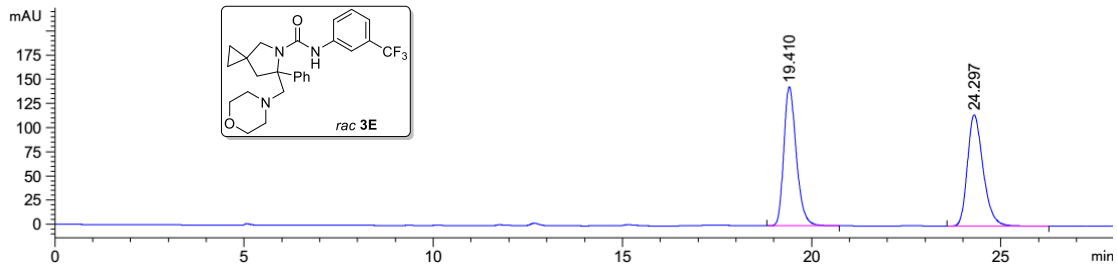
Figure S158. HPLC spectrum of *rac* **3D**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.936	BB	0.6016	426.54874	10.68732	5.5943
2	26.175	BB	0.6289	7198.16211	173.91461	94.4057
Totals :				7624.71085	184.60193	

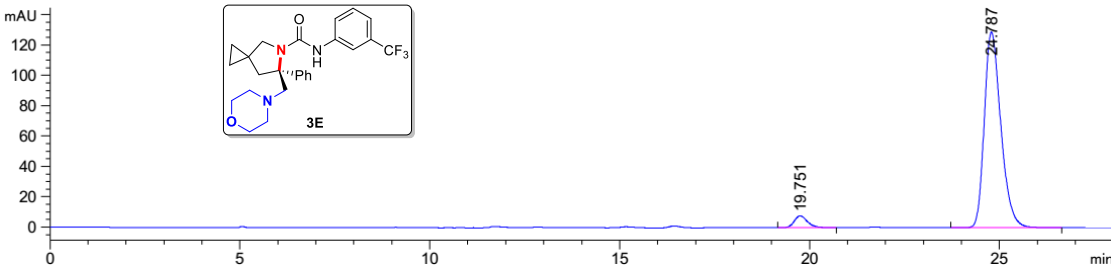
Figure S159. HPLC spectrum of **3D**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.410	BB	0.3517	3301.01831	143.88568	49.7914
2	24.297	BB	0.4418	3328.67798	114.95467	50.2086
Totals :				6629.69629	258.84035	

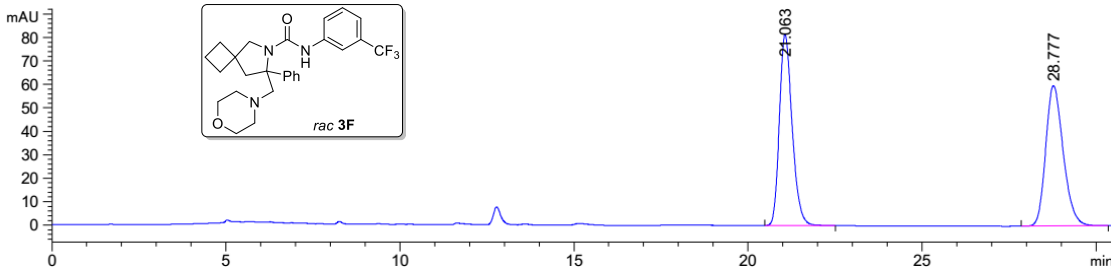
Figure S160. HPLC spectrum of *rac* **3E**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.751	BB	0.3630	188.34413	7.81977	4.5977
2	24.787	BB	0.4653	3908.17188	129.06880	95.4023
Totals :				4096.51601	136.88857	

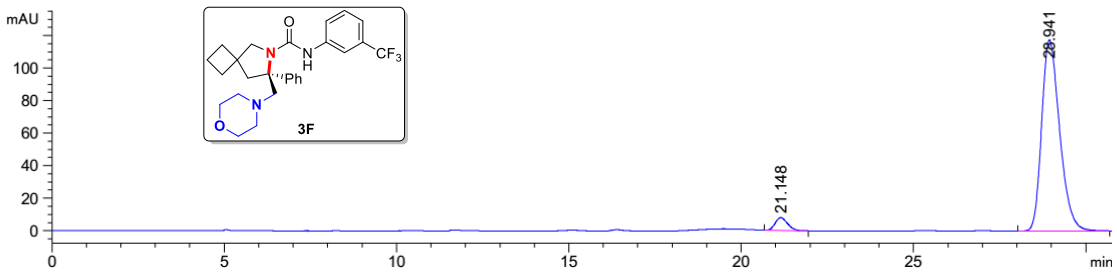
Figure S161. HPLC spectrum of **3E**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.063	BB	0.3890	2078.53271	81.64613	49.8635
2	28.777	BB	0.5379	2089.91211	59.77718	50.1365
Totals :				4168.44482	141.42332	

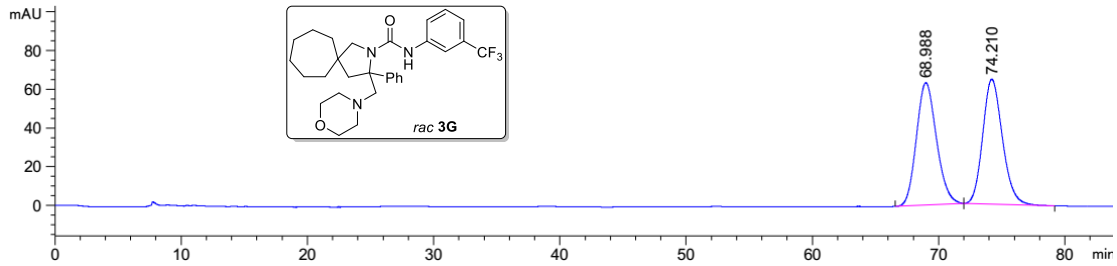
Figure S162. HPLC spectrum of *rac* **3F**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.148	BB	0.3837	197.59810	7.90199	4.4149
2	28.941	MF R	0.6067	4278.06787	117.52602	95.5851
Totals :				4475.66597	125.42801	

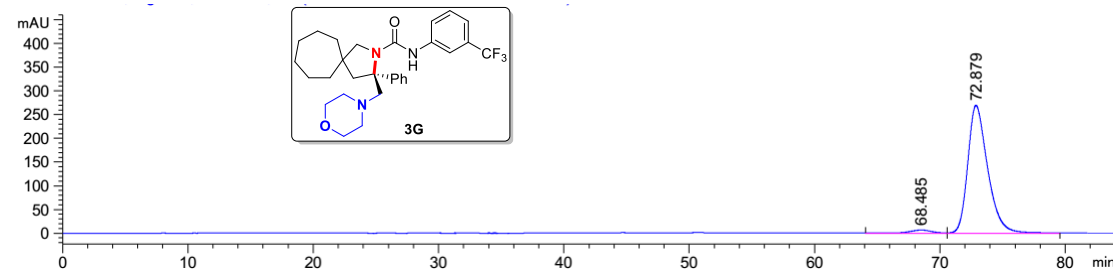
Figure S163. HPLC spectrum of **3F**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	68.988	BB	1.6376	6978.09863	63.22553	49.8611
2	74.210	BB	1.6189	7016.98389	64.51661	50.1389
Totals :				1.39951e4	127.74214	

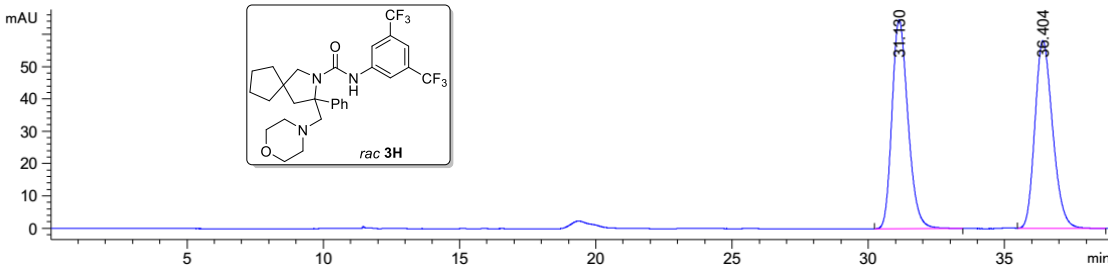
Figure S164. HPLC spectrum of *rac* **3G**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	68.485	MF R	2.3264	964.66327	6.91110	3.1336
2	72.879	FM R	1.8438	2.98202e4	269.54892	96.8664
Totals :				3.07849e4	276.46002	

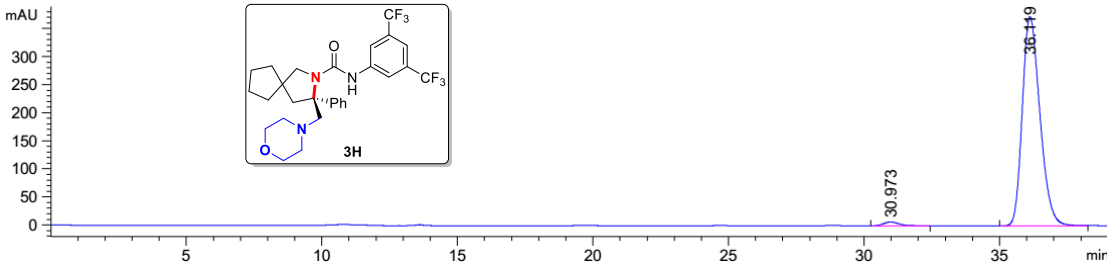
Figure S165. HPLC spectrum of **3G**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.130	BB	0.6279	2638.28882	64.67258	50.0943
2	36.404	BB	0.6957	2628.36108	58.10598	49.9057
Totals :				5266.64990	122.77856	

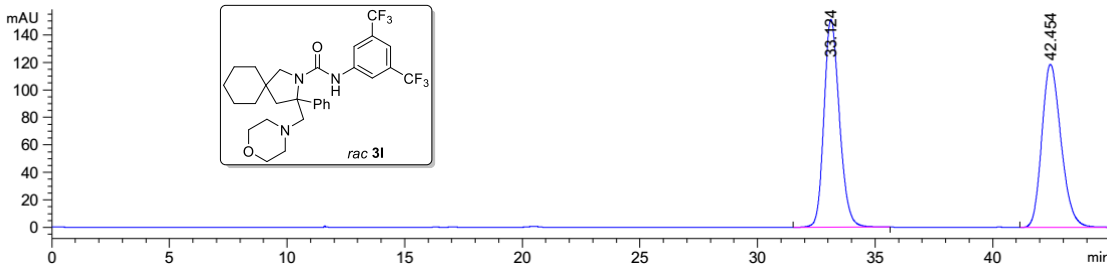
Figure S166. HPLC spectrum of *rac* **3H**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.973	BB	0.5807	269.49310	6.76644	1.5795
2	36.119	MF R	0.7514	1.67925e4	372.46353	98.4205
Totals :				1.70620e4	379.22997	

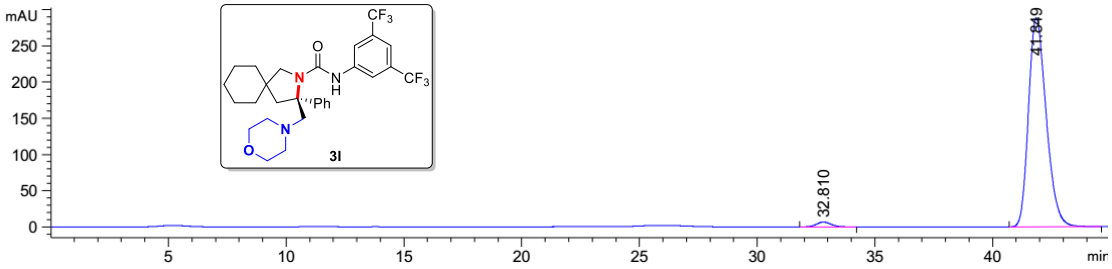
Figure S167. HPLC spectrum of **3H**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.124	BB	0.7037	6915.35498	151.16452	50.6598
2	42.454	BB	0.8705	6735.21533	118.61073	49.3402
Totals :				1.36506e4	269.77525	

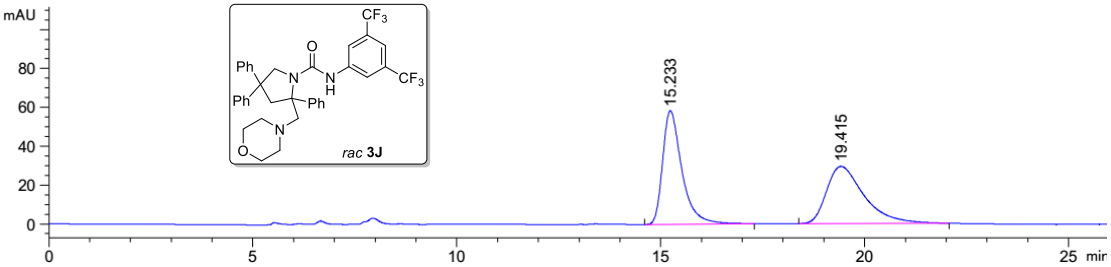
Figure S168. HPLC spectrum of *rac* **3l**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.810	BB	0.6438	296.76727	6.73819	1.9288
2	41.849	BB	0.8058	1.50893e4	288.69400	98.0712
Totals :				1.53861e4	295.43219	

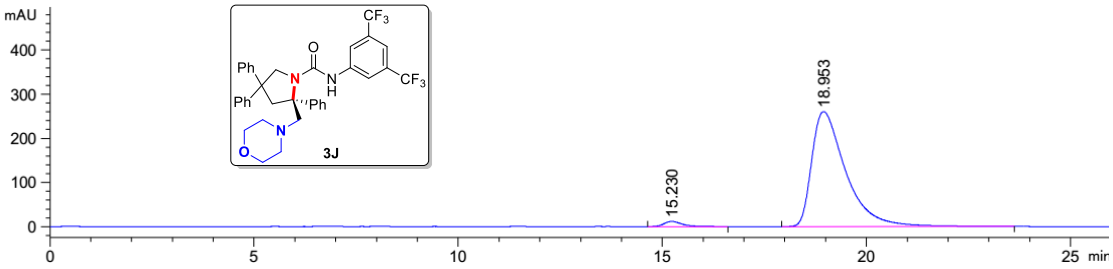
Figure S169. HPLC spectrum of **3l**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.233	BB	0.4950	1922.13098	58.54722	50.6085
2	19.415	BB	0.9348	1875.91089	29.38416	49.3915
Totals :				3798.04187	87.93137	

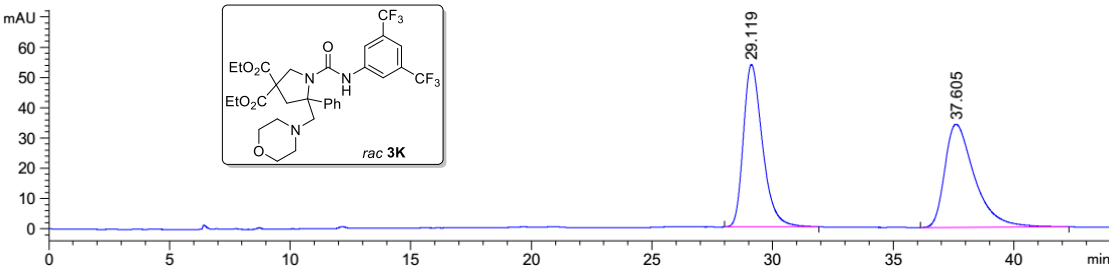
Figure S170. HPLC spectrum of *rac* **3J**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.230	BB	0.4714	362.30716	11.63114	2.3415
2	18.953	BB	0.8725	1.51107e4	260.58212	97.6585
Totals :				1.54730e4	272.21326	

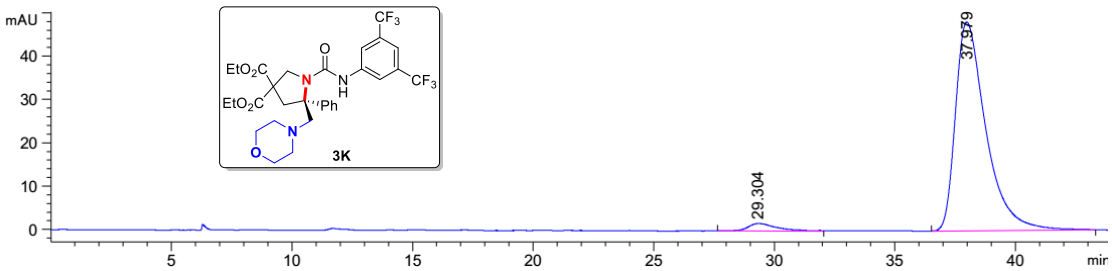
Figure S171. HPLC spectrum of **3J**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.119	BB	0.8388	2954.38940	53.62289	50.1699
2	37.605	BB	1.2876	2934.37598	34.11155	49.8301
Totals :				5888.76538	87.73444	

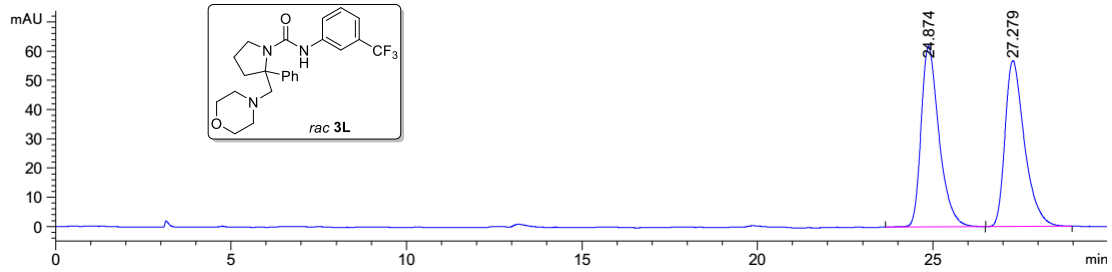
Figure S172. HPLC spectrum of *rac* **3K**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.304	MM R	1.4003	140.62079	1.67366	3.2135
2	37.979	BB	1.2962	4235.35352	48.15170	96.7865
Totals :				4375.97430	49.82536	

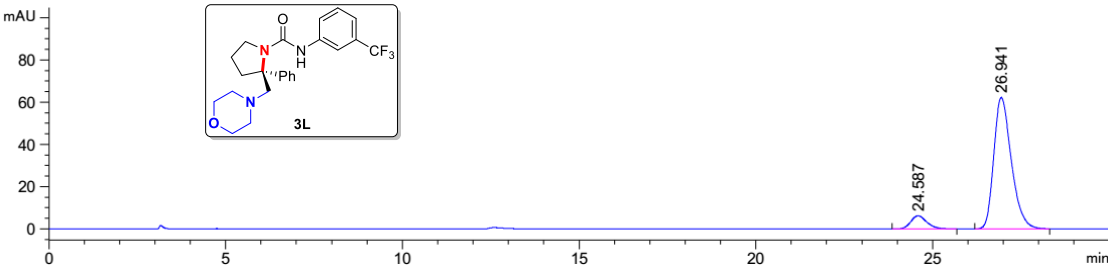
Figure S173. HPLC spectrum of **3K**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.874	BB	0.5389	2202.49512	61.93527	50.1673
2	27.279	BB	0.5830	2187.80420	56.84158	49.8327
Totals :				4390.29932	118.77685	

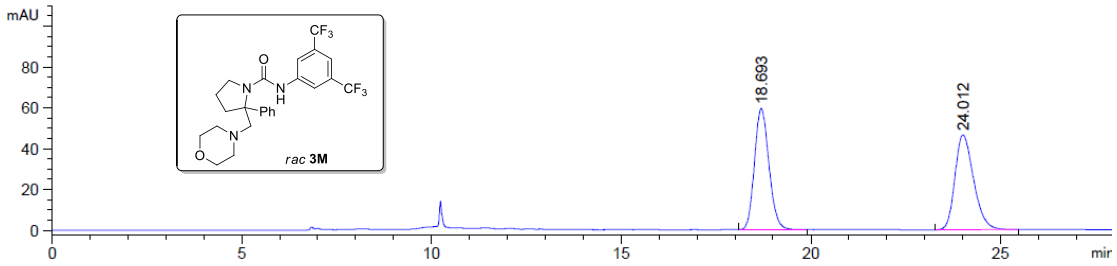
Figure S174. HPLC spectrum of *rac* **3L**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.587	BB	0.4768	196.72939	6.22365	8.3985
2	26.941	BB	0.5307	2145.69507	62.17069	91.6015
Totals :				2342.42445	68.39434	

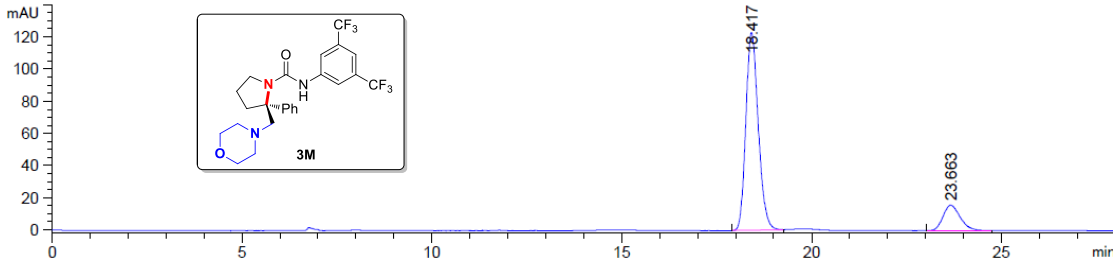
Figure S175. HPLC spectrum of **3L**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.693	BB	0.4120	1577.10803	59.35810	49.8514
2	24.012	BB	0.5243	1586.51184	46.47520	50.1486
Totals :				3163.61987	105.83329	

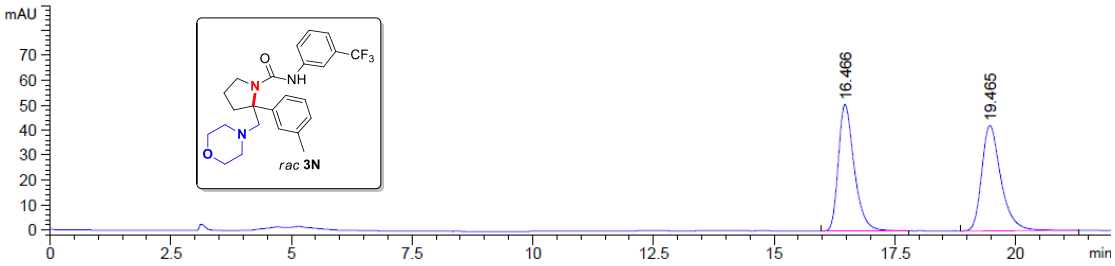
Figure S176. HPLC spectrum of *rac* **3M**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.417	BB	0.3511	2794.65381	122.98658	85.1048
2	23.663	BB	0.4791	489.12607	15.71780	14.8952
Totals :				3283.77988	138.70438	

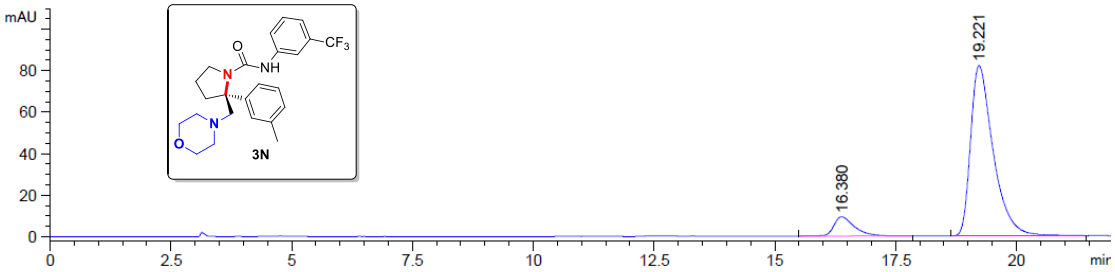
Figure S177. HPLC spectrum of **3M**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.466	BB	0.3468	1162.52002	50.82913	49.7113
2	19.465	BB	0.4209	1176.02075	42.23394	50.2887
Totals :				2338.54077	93.06307	

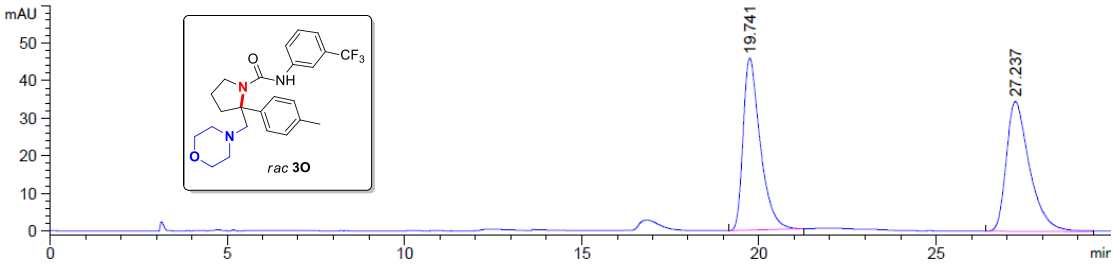
Figure S178. HPLC spectrum of *rac* **3N**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.380	BB	0.4376	276.18210	9.32360	9.3516
2	19.221	BB	0.4886	2677.14429	82.06542	90.6484
Totals :				2953.32639	91.38902	

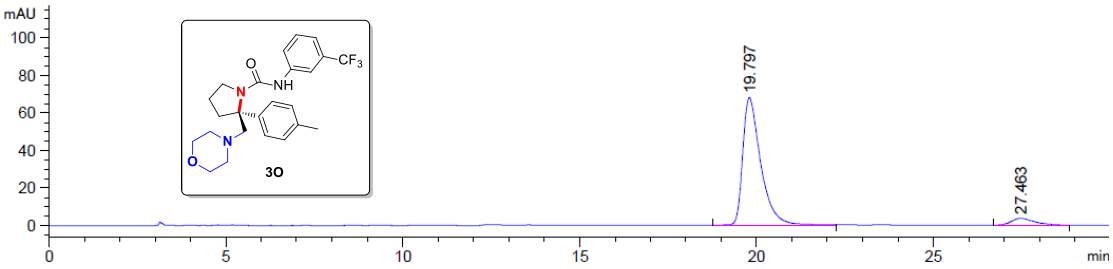
Figure S179. HPLC spectrum of **3N**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

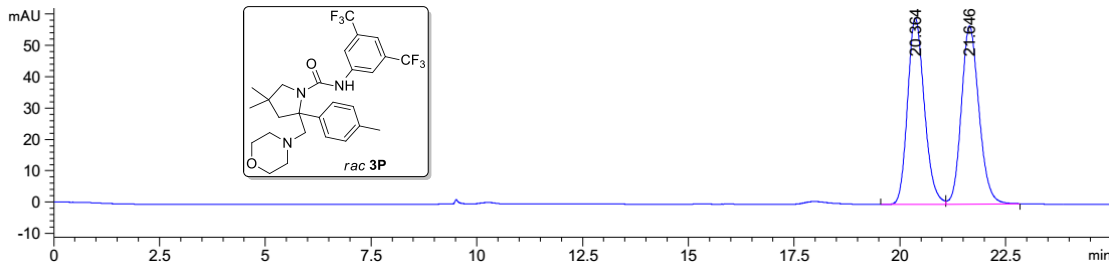
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.741	BB	0.5000	1537.44739	45.76218	49.4671
2	27.237	MF R	0.7593	1570.57251	34.47292	50.5329
Totals :				3108.01990	80.23510	

Figure S180. HPLC spectrum of *rac* **3O**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.797	FM R	0.5882	2399.15894	67.97815	93.7401
2	27.463	BB	0.6461	160.21506	3.58012	6.2599
Totals :				2559.37399	71.55827	

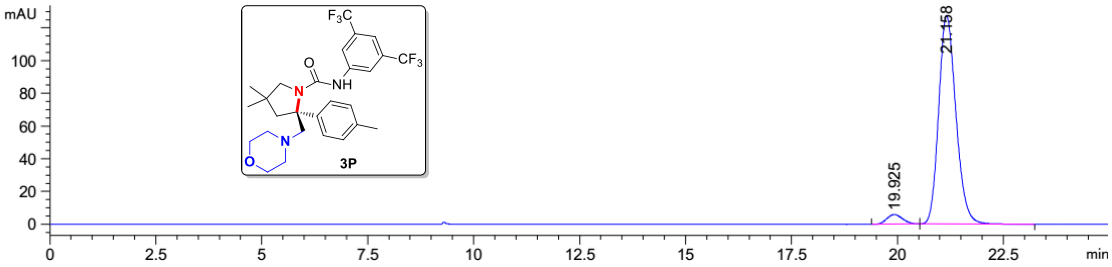
Figure S181. HPLC spectrum of **3O**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.364	MF R	0.4594	1635.63232	59.34458	49.8645
2	21.646	FM R	0.4825	1644.52307	56.80907	50.1355
Totals :				3280.15540	116.15365	

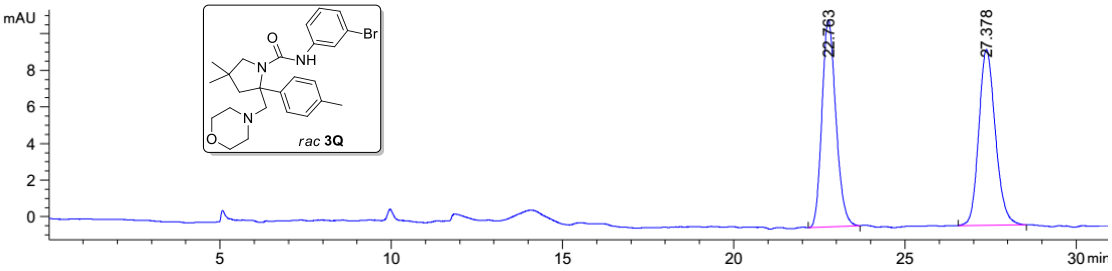
Figure S182. HPLC spectrum of *rac* **3P**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.925	BB	0.3968	154.85654	5.92803	4.1116
2	21.158	BB	0.4346	3611.49512	127.45593	95.8884
Totals :				3766.35165	133.38397	

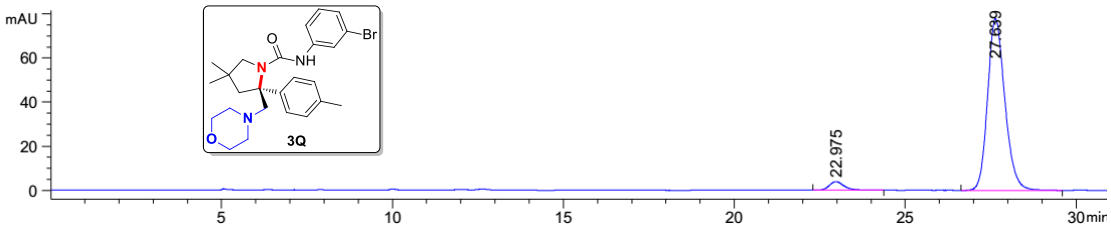
Figure S183. HPLC spectrum of **3P**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.763	BB	0.4366	320.62585	11.31552	49.7969
2	27.378	BB	0.5169	323.24149	9.59807	50.2031
Totals :				643.86734	20.91359	

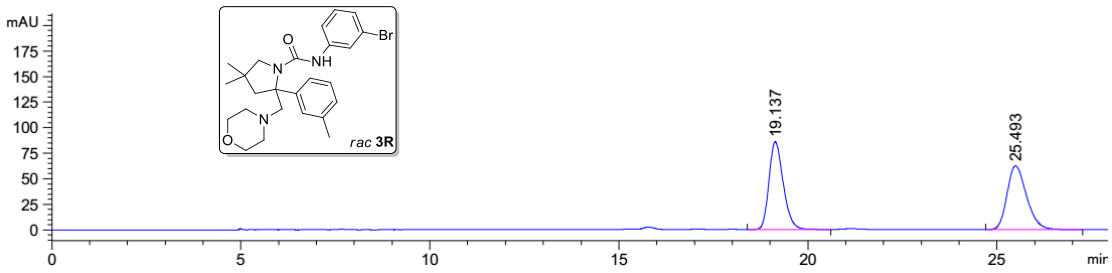
Figure S184. HPLC spectrum of *rac* **3Q**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.975	BB	0.4591	117.31335	3.89827	4.1125
2	27.639	BB	0.5361	2735.29614	77.81753	95.8875
Totals :				2852.60950	81.71580	

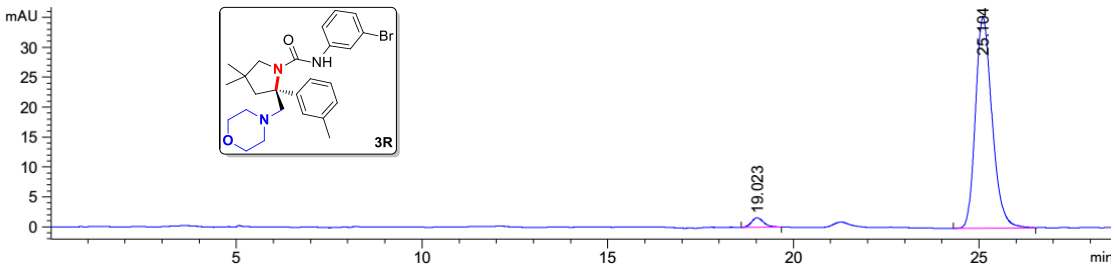
Figure S185. HPLC spectrum of **3Q**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.137	BB	0.4031	2258.91724	85.82243	50.4513
2	25.493	BB	0.5494	2218.50806	62.30365	49.5487
Totals :				4477.42529	148.12608	

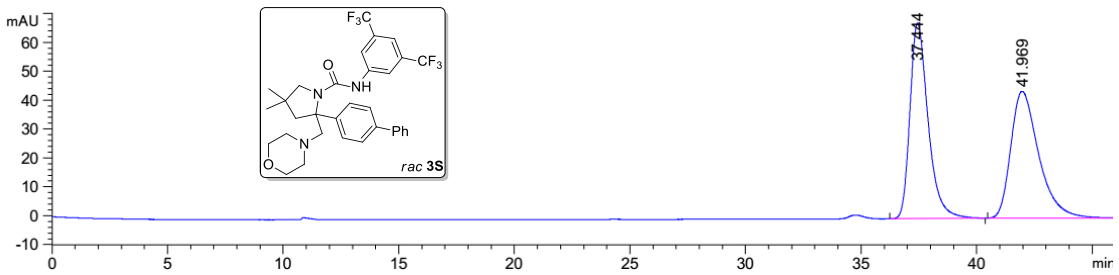
Figure S186. HPLC spectrum of *rac* **3R**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.023	BB	0.3493	36.32740	1.58582	3.2076
2	25.104	BB	0.4755	1096.23083	35.18245	96.7924
Totals :				1132.55823	36.76826	

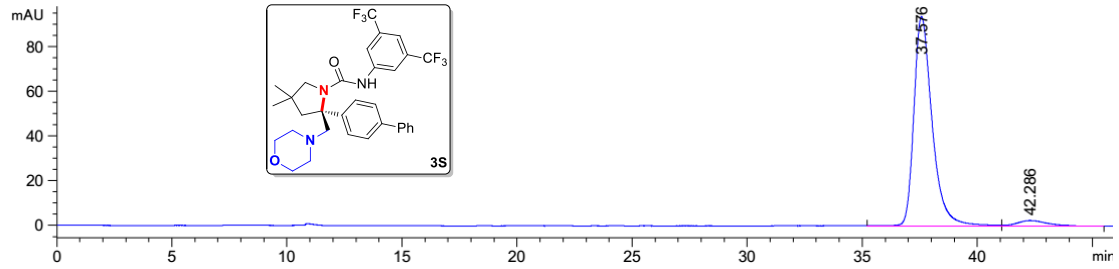
Figure S187. HPLC spectrum of **3R**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.444	BB	0.8255	3695.63770	67.63789	50.0288
2	41.969	BB	1.2657	3691.38354	43.86870	49.9712
Totals :				7387.02124	111.50659	

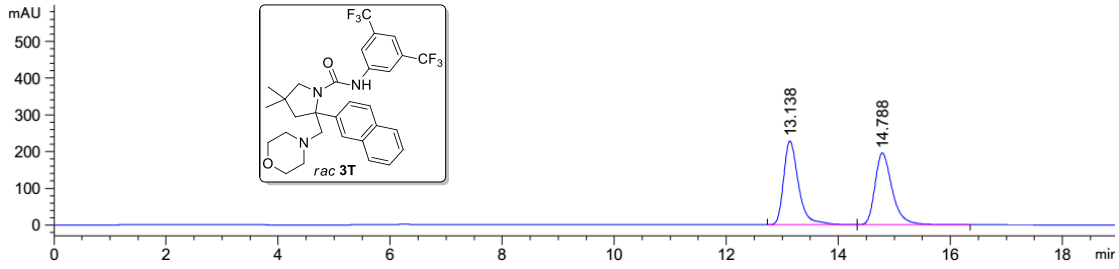
Figure S188. HPLC spectrum of *rac* **3S**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.576	MF R	0.9204	5168.27051	93.58924	95.7693
2	42.286	FM R	1.5582	228.31354	2.44207	4.2307
Totals :				5396.58405	96.03131	

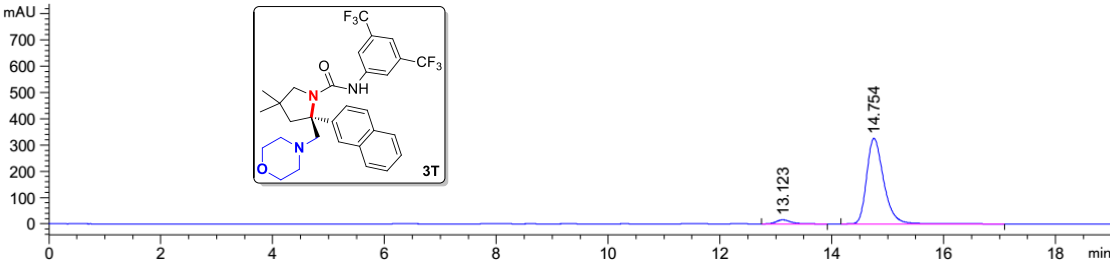
Figure S189. HPLC spectrum of **3S**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.138	BB	0.2794	4204.17139	227.74783	50.3677
2	14.788	BB	0.3241	4142.79541	194.84015	49.6323
Totals :				8346.96680	422.58798	

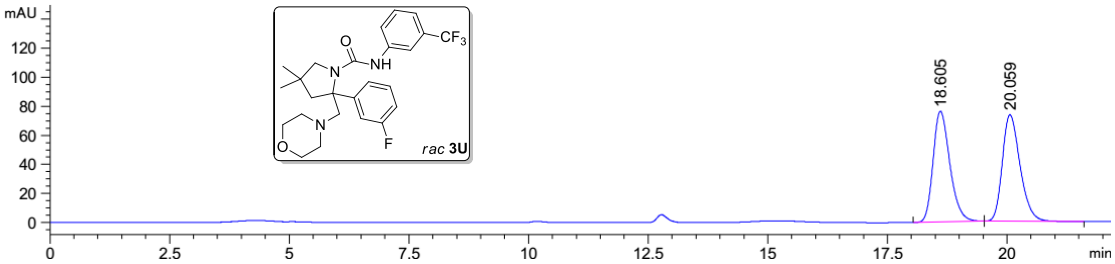
Figure S190. HPLC spectrum of *rac* **3T**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.123	BB	0.2755	274.81369	15.30453	3.8489
2	14.754	BB	0.3218	6865.26611	325.86563	96.1511
Totals :				7140.07980	341.17016	

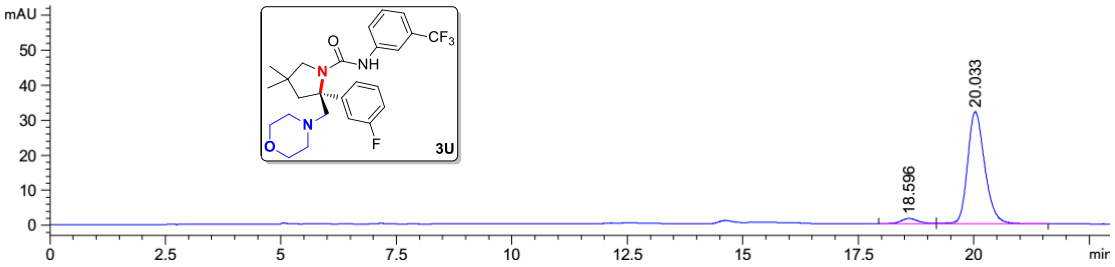
Figure S191. HPLC spectrum of **3T**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.605	BB	0.3746	1862.74451	76.35648	49.6566
2	20.059	BB	0.3967	1888.51160	73.28069	50.3434
Totals :				3751.25610	149.63717	

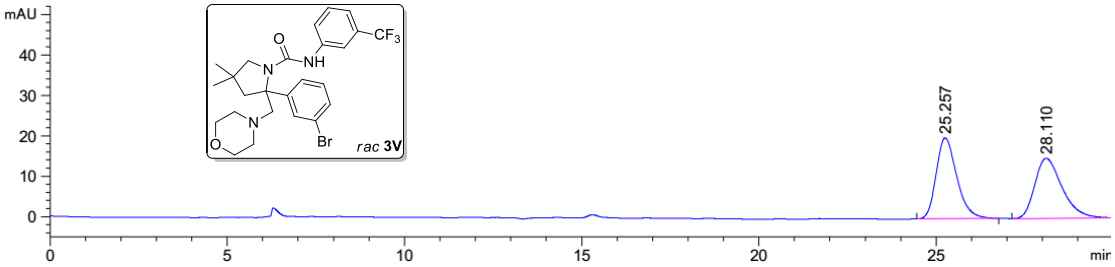
Figure S192. HPLC spectrum of *rac* **3U**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.596	MF R	0.4314	38.81119	1.49954	4.5025
2	20.033	FM R	0.4293	823.18591	31.95993	95.4975
Totals :				861.99710	33.45947	

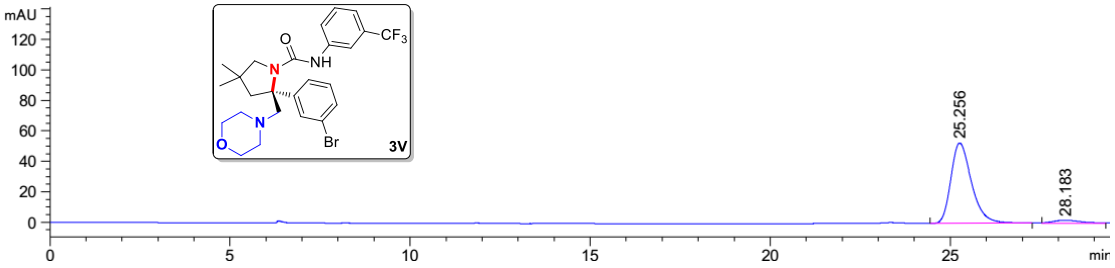
Figure S193. HPLC spectrum of **3U**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.257	BB	0.6207	808.39301	19.95095	50.5543
2	28.110	BB	0.8078	790.66730	14.83519	49.4457
Totals :				1599.06030	34.78614	

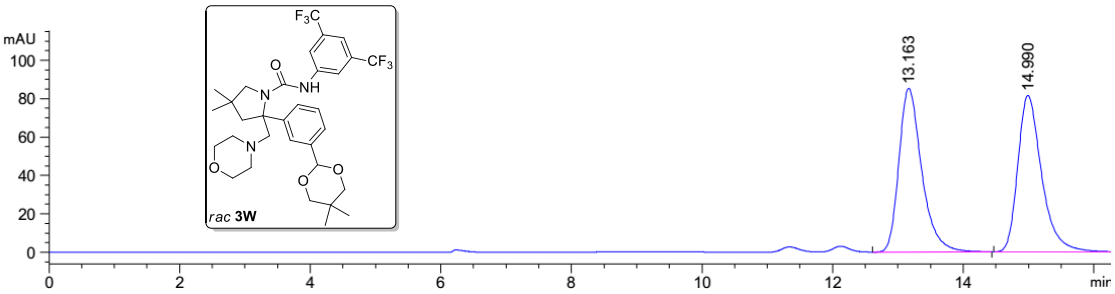
Figure S194. HPLC spectrum of *rac* **3V**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.256	BB	0.6084	2089.17847	52.71655	95.3296
2	28.183	MM R	0.8928	102.35230	1.91074	4.6704
Totals :				2191.53077	54.62728	

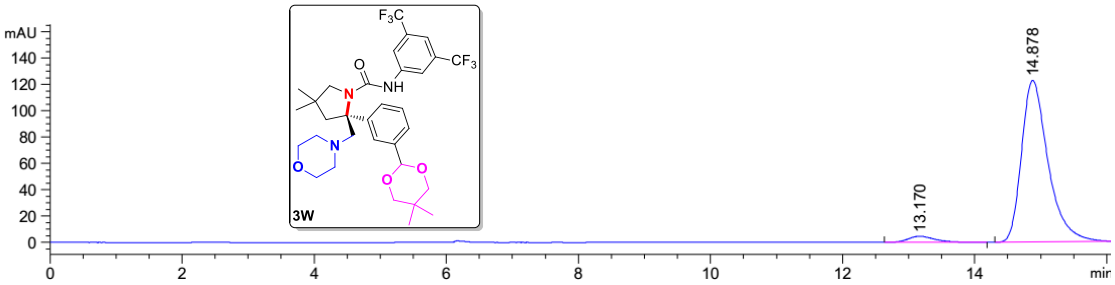
Figure S195. HPLC spectrum of **3V**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.163	BB	0.3693	2070.14136	85.24554	49.9567
2	14.990	BB	0.3870	2073.73315	81.45714	50.0433
Totals :				4143.87451	166.70267	

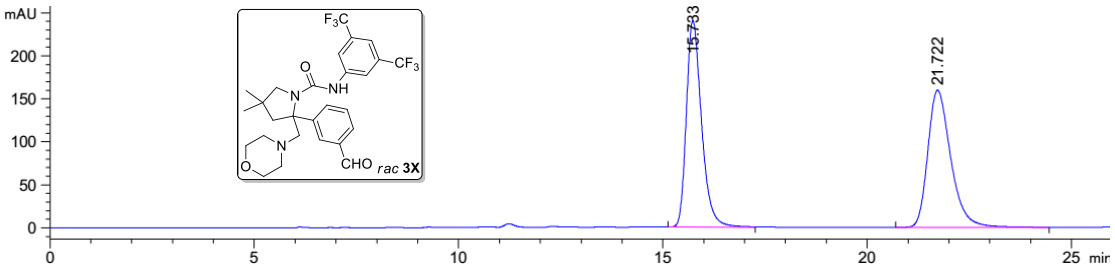
Figure S196. HPLC spectrum of *rac* **3W**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.170	BB	0.4236	130.63898	4.59614	3.6632
2	14.878	BB	0.4242	3435.58960	122.86185	96.3368
Totals :				3566.22858	127.45800	

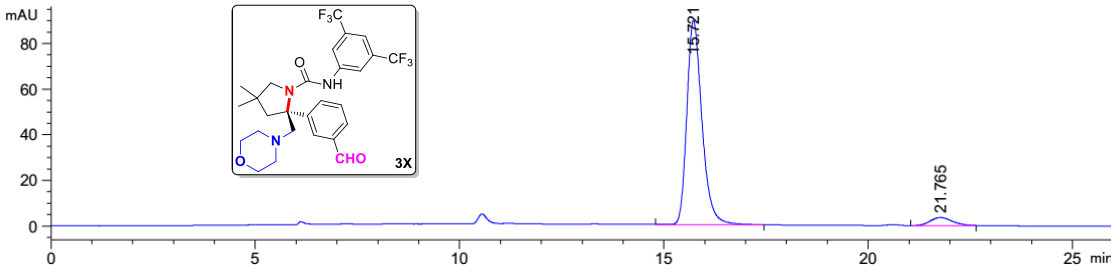
Figure S197. HPLC spectrum of **3W**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.733	MF R	0.4307	6204.83984	240.09406	49.9752
2	21.722	BB	0.5965	6210.99268	159.44231	50.0248
Totals :				1.24158e4	399.53636	

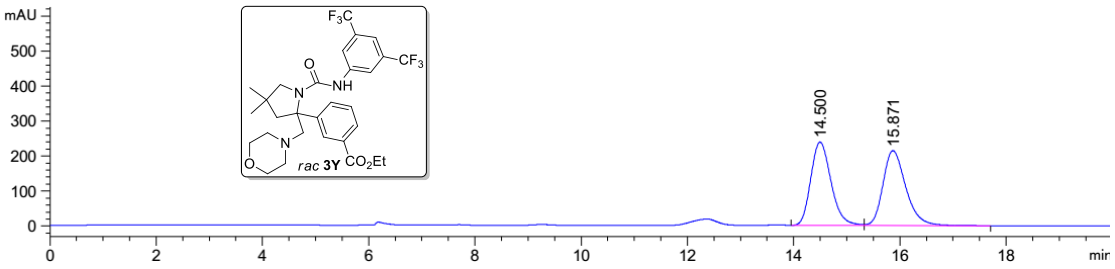
Figure S198. HPLC spectrum of *rac* **3X**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.721	MM R	0.4289	2302.99927	89.48372	94.3331
2	21.765	MF R	0.6442	138.34914	3.57942	5.6669
Totals :				2441.34840	93.06314	

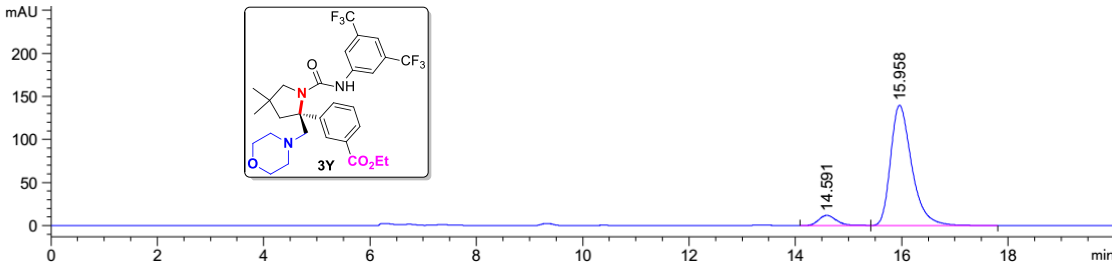
Figure S199. HPLC spectrum of **3X**



Signal 4: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.500	VV	0.4140	6330.66504	238.21480	49.7168
2	15.871	VB	0.4569	6402.78174	214.12115	50.2832
Totals :				1.27334e4	452.33595	

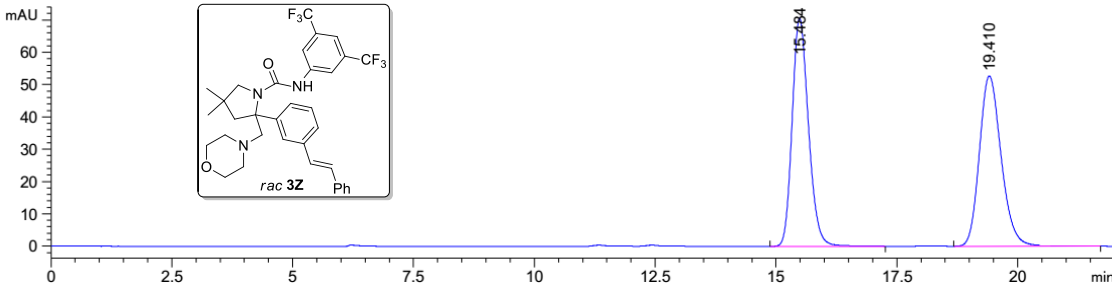
Figure S200. HPLC spectrum of *rac* **3Y**



Signal 3: DAD1 D, Sig=230,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.591	BV	0.3680	286.40286	11.93184	6.8802
2	15.958	VB	0.4234	3876.30249	139.82715	93.1198
Totals :				4162.70535	151.75899	

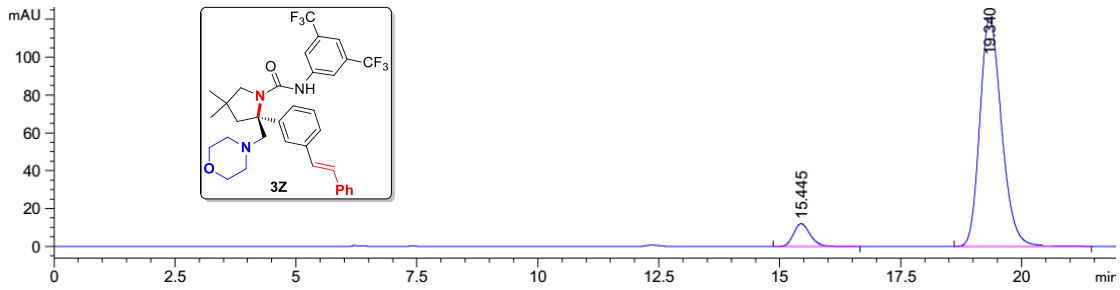
Figure S201. HPLC spectrum of **3Y**



Signal 5: DAD1 F, Sig=320,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.484	BB	0.3593	1654.66467	70.62823	50.0260
2	19.410	BB	0.4836	1652.94751	52.74035	49.9740
Totals :				3307.61218	123.36858	

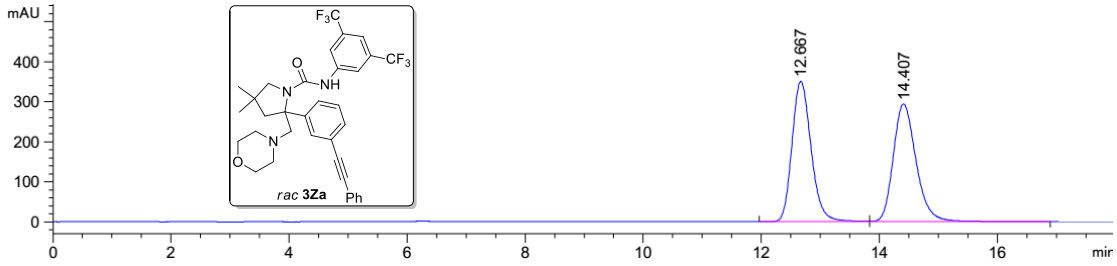
Figure S202. HPLC spectrum of *rac* **3Z**



Signal 5: DAD1 F, Sig=320,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.445	BB	0.3681	286.52859	12.01893	7.0704
2	19.340	BB	0.4803	3765.96680	120.61398	92.9296
Totals :				4052.49539	132.63291	

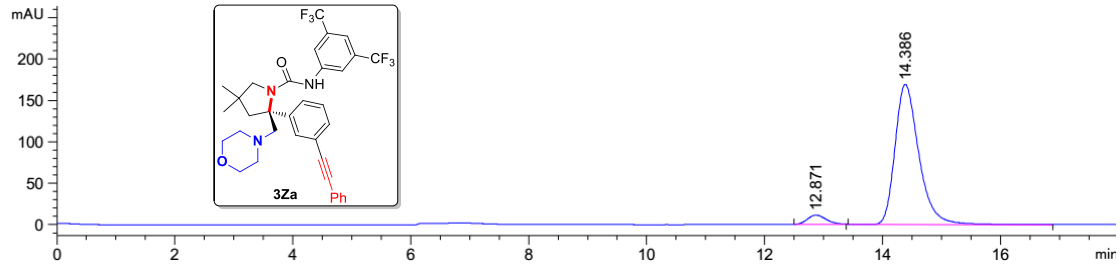
Figure S203. HPLC spectrum of **3Z**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.667	BV	0.3508	7890.59912	350.30600	50.0358
2	14.407	VB	0.4127	7879.30762	294.00195	49.9642
Totals :				1.57699e4	644.30795	

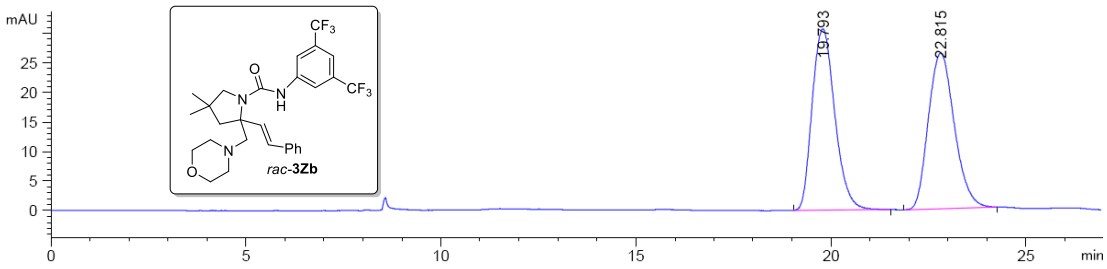
Figure S204. HPLC spectrum of *rac* **3Za**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.871	MM R	0.3693	249.86975	11.27717	4.9290
2	14.386	MM R	0.4741	4819.46777	169.42479	95.0710
Totals :				5069.33752	180.70196	

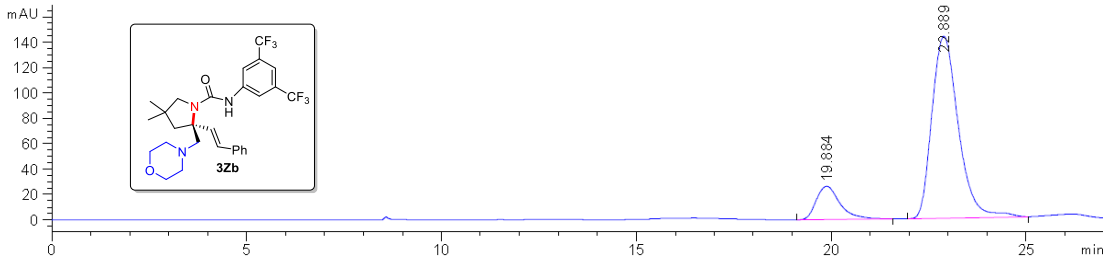
Figure S205. HPLC spectrum of **3Za**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.793	BB	0.6306	1242.68701	30.67630	50.3983
2	22.815	BB	0.7190	1223.04529	26.37282	49.6017
Totals :				2465.73230	57.04913	

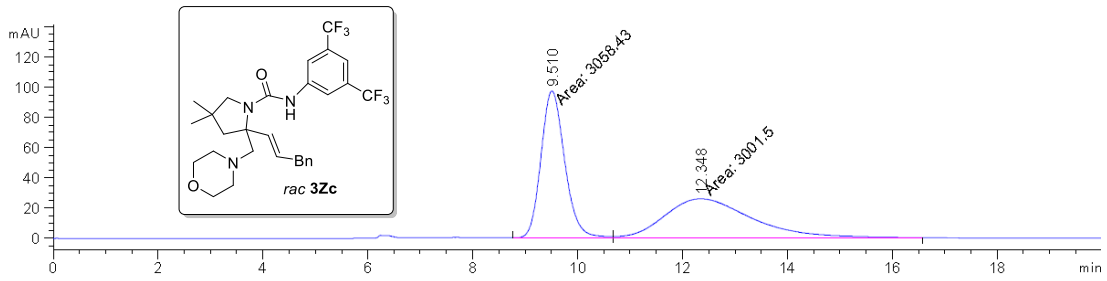
Figure S206. HPLC spectrum of *rac* **3Zb**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.884	BB	0.6450	1098.37927	26.09822	13.9685
2	22.889	BB	0.7326	6764.88721	143.35353	86.0315
Totals :				7863.26648	169.45175	

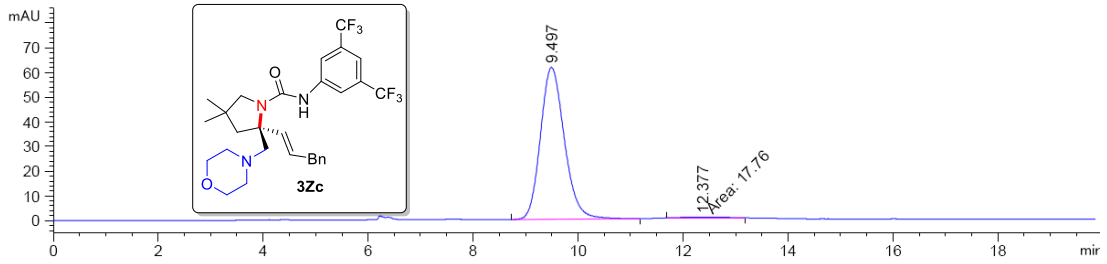
Figure S207. HPLC spectrum of **3Zb**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.510	FM	0.5239	3058.43359	97.29820	50.4698
2	12.348	FM	1.9333	3001.49878	25.87553	49.5302
Totals :				6059.93237	123.17374	

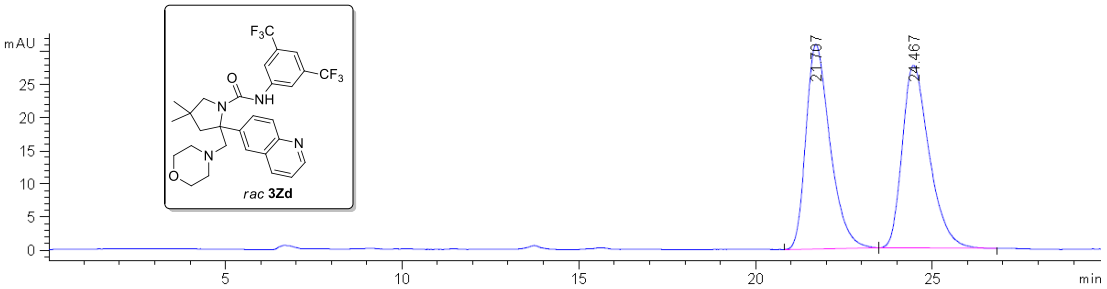
Figure S208. HPLC spectrum of *rac* **3Zc**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.497	BB	0.4874	1943.18103	61.37086	99.0943
2	12.377	MM	0.9371	17.75998	3.15873e-1	0.9057
Totals :				1960.94101	61.68673	

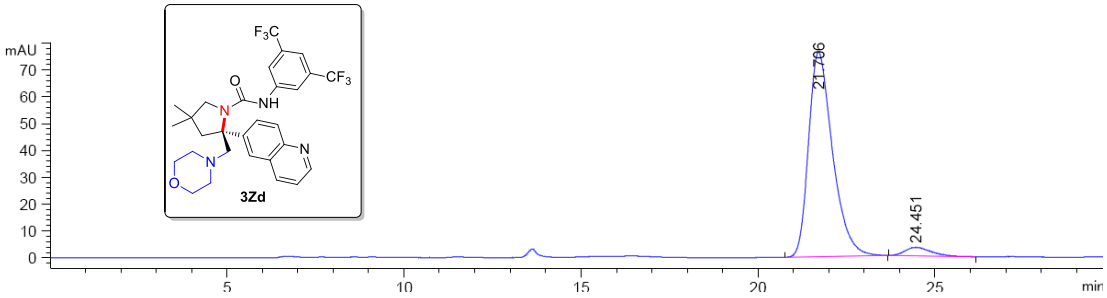
Figure S209. HPLC spectrum of **3Zc**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.707	BB	0.6952	1466.37354	30.92336	50.0579
2	24.467	BB	0.7824	1462.98083	27.60225	49.9421
Totals :				2929.35437	58.52561	

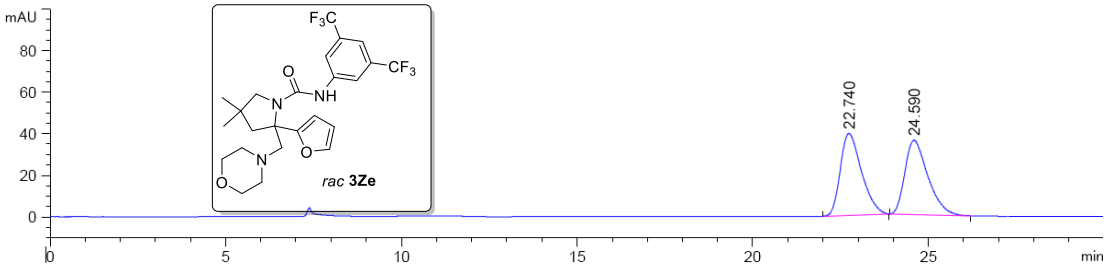
Figure S210. HPLC spectrum of *rac* **3Zd**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.706	BB	0.7068	3590.05713	76.31993	95.7342
2	24.451	BB	0.6059	159.96895	3.14229	4.2658
Totals :				3750.02608	79.46222	

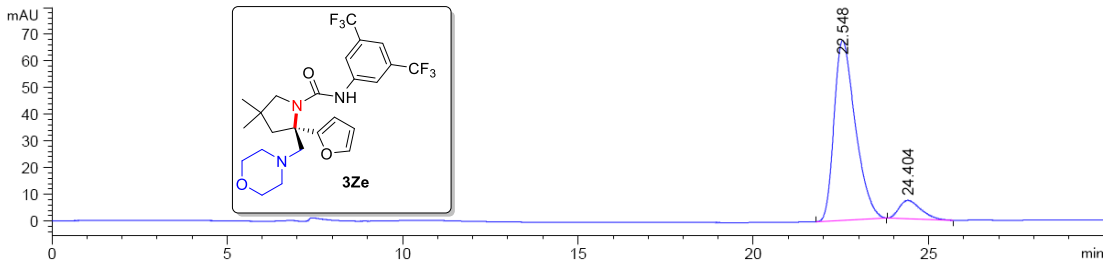
Figure S211. HPLC spectrum of **3Zd**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.740	BB	0.6304	1654.28625	39.51438	50.4460
2	24.590	BB	0.6887	1625.03467	35.72115	49.5540
Totals :				3279.32092	75.23553	

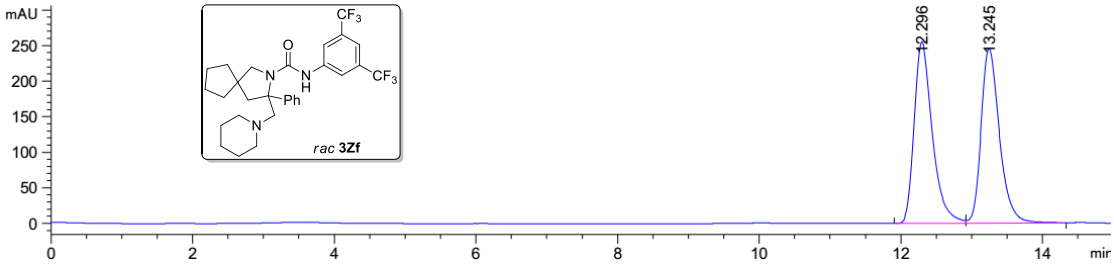
Figure S212. HPLC spectrum of *rac* **3Ze**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.548	BB	0.6356	2845.85571	67.53309	90.5108
2	24.404	BB	0.6144	298.36270	6.92820	9.4892
Totals :				3144.21841	74.46129	

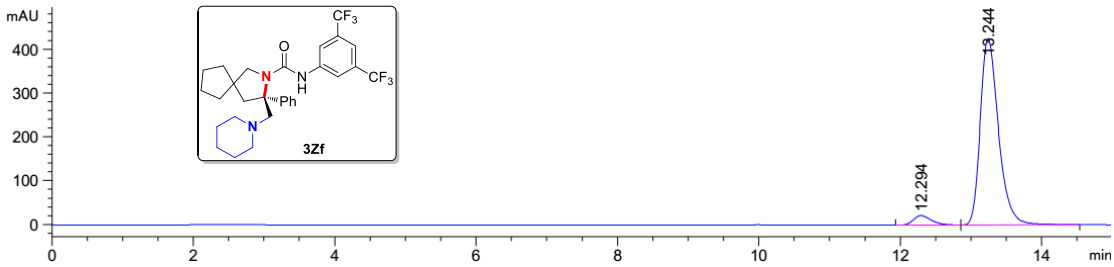
Figure S213. HPLC spectrum of **3Ze**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.296	BV	0.2698	4547.05908	255.35013	50.7645
2	13.245	VB	0.2736	4410.11084	245.48888	49.2355
Totals :				8957.16992	500.83900	

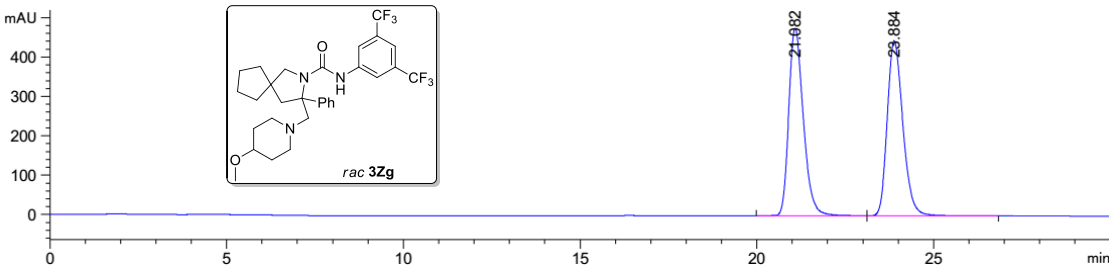
Figure S214. HPLC spectrum of *rac* **3Zf**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.294	FM R	0.2906	379.39581	21.75953	4.7500
2	13.244	BB	0.2728	7607.89404	425.17526	95.2500
Totals :				7987.28986	446.93480	

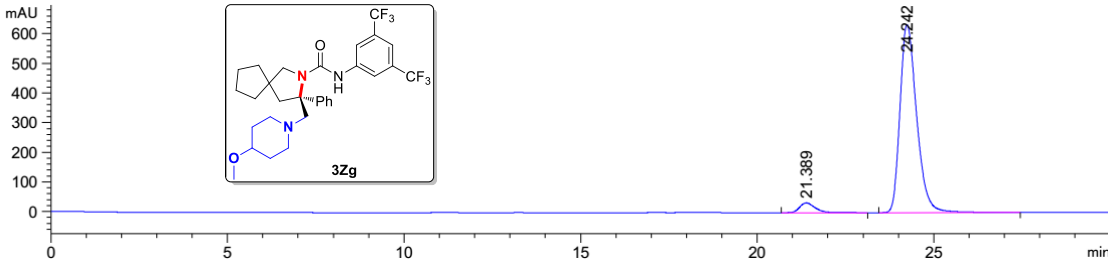
Figure S215. HPLC spectrum of **3Zf**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.082	BB	0.4385	1.36589e4	476.45868	49.9963
2	23.884	BB	0.4765	1.36610e4	444.51266	50.0037
Totals :				2.73199e4	920.97134	

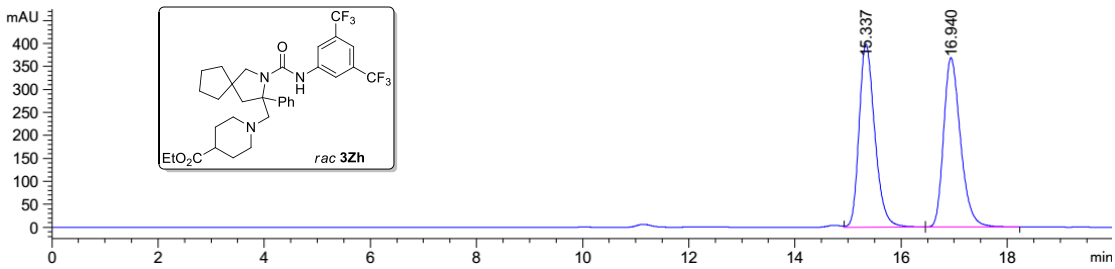
Figure S216. HPLC spectrum of *rac* **3Zg**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.389	BB	0.4663	998.09399	32.86185	4.5788
2	24.242	BB	0.5067	2.08002e4	634.13647	95.4212
Totals :				2.17983e4	666.99833	

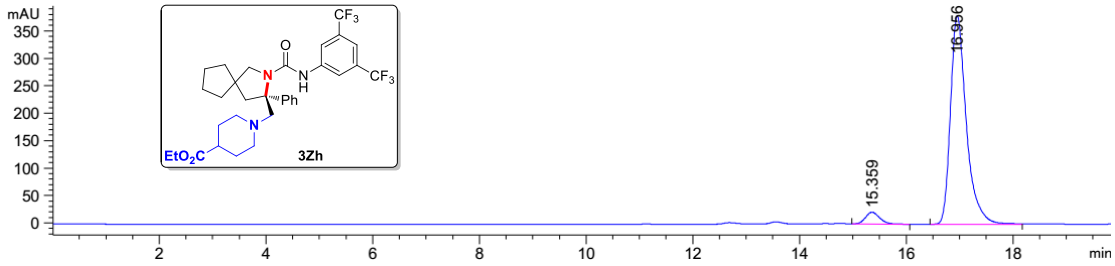
Figure S217. HPLC spectrum of **3Zg**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.337	VB	0.3130	8165.54346	398.67529	50.0491
2	16.940	BB	0.3401	8149.52881	368.37296	49.9509
Totals :				1.63151e4	767.04825	

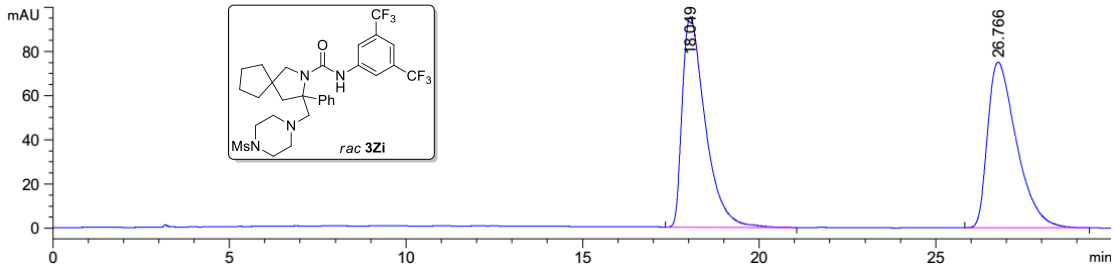
Figure S218. HPLC spectrum of *rac* **3Zh**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.359	BB	0.2826	396.07535	21.53539	4.8002
2	16.956	MF R	0.3451	7855.11768	379.35577	95.1998
Totals :				8251.19302	400.89117	

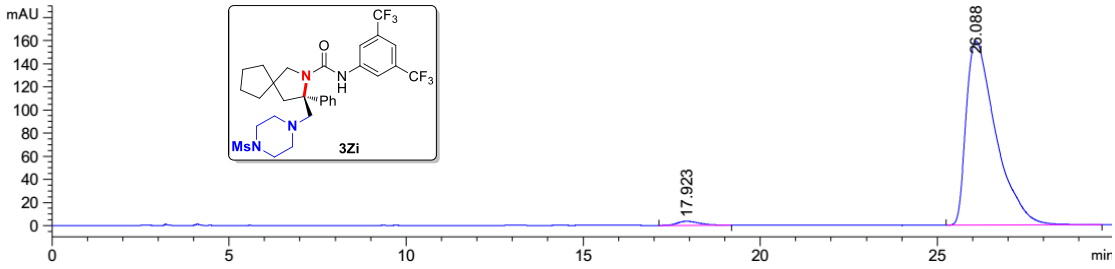
Figure S219. HPLC spectrum of **3Zh**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.049	BB	0.6877	4314.40234	95.02789	50.2925
2	26.766	BB	0.8672	4264.22412	75.01464	49.7075
Totals :				8578.62646	170.04253	

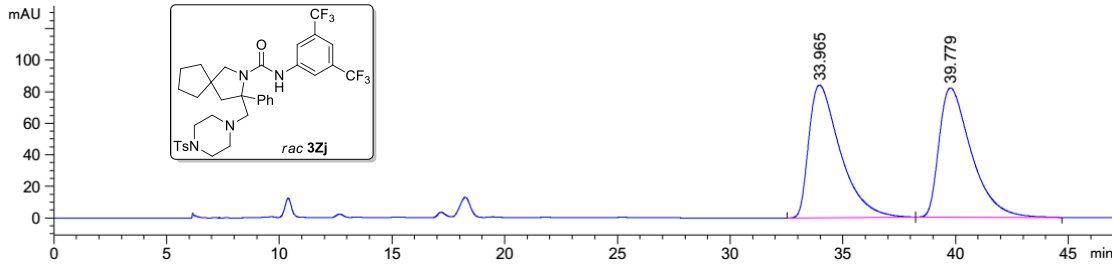
Figure S220. HPLC spectrum of *rac* **3Zi**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.923	BB	0.6323	152.67346	3.49064	1.6201
2	26.088	BB	0.8759	9271.22949	159.08766	98.3799
Totals :				9423.90295	162.57830	

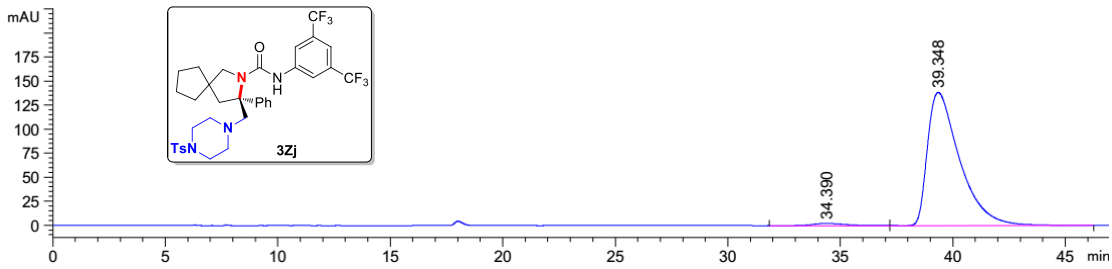
Figure S221. HPLC spectrum of **3Zi**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.965	BB	1.4228	8175.24268	84.19587	50.0854
2	39.779	BB	1.4683	8147.34814	81.92345	49.9146
Totals :				1.63226e4	166.11932	

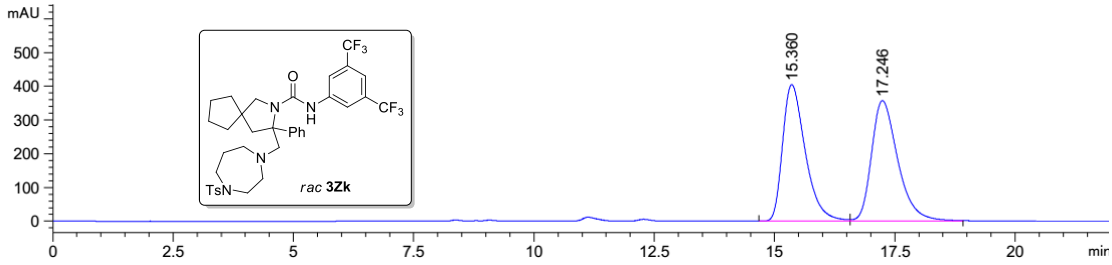
Figure S222. HPLC spectrum of *rac* **3Zj**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.390	MF R	1.6517	231.24765	2.33342	1.6422
2	39.348	FM R	1.6652	1.38504e4	138.62665	98.3578
Totals :				1.40816e4	140.96006	

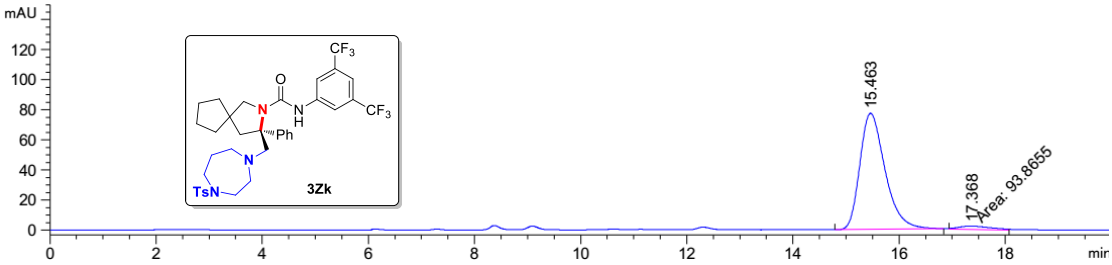
Figure S223. HPLC spectrum of **3Zj**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.360	BV	0.5027	1.32896e4	405.16992	49.3223
2	17.246	MF R	0.6369	1.36548e4	357.31592	50.6777
Totals :				2.69444e4	762.48584	

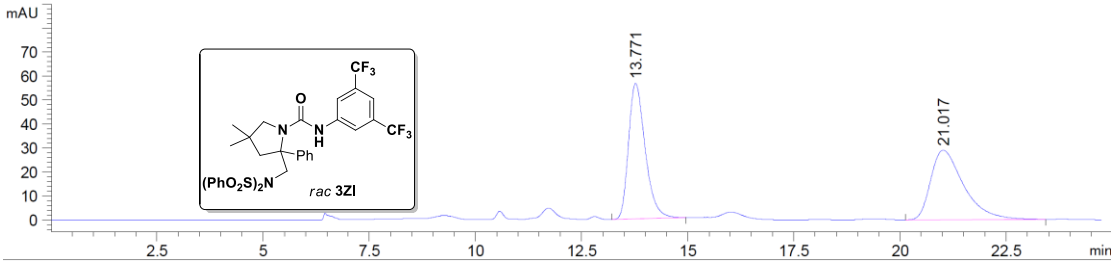
Figure S224. HPLC spectrum of *rac* **3Zk**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.463	BB	0.5044	2544.39844	77.22488	96.4422
2	17.368	MM	0.7009	93.86546	2.23197	3.5578
Totals :				2638.26389	79.45685	

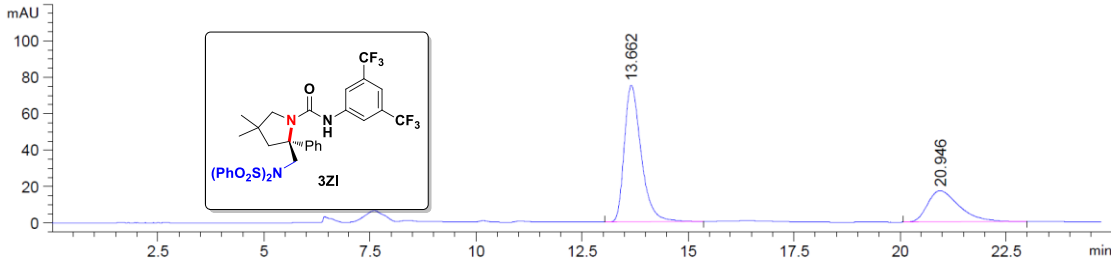
Figure S225. HPLC spectrum of **3Zk**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.771	BB	0.4180	1543.01685	56.61387	49.6825
2	21.017	BB	0.8003	1562.73950	29.01892	50.3175
Totals :				3105.75635	85.63279	

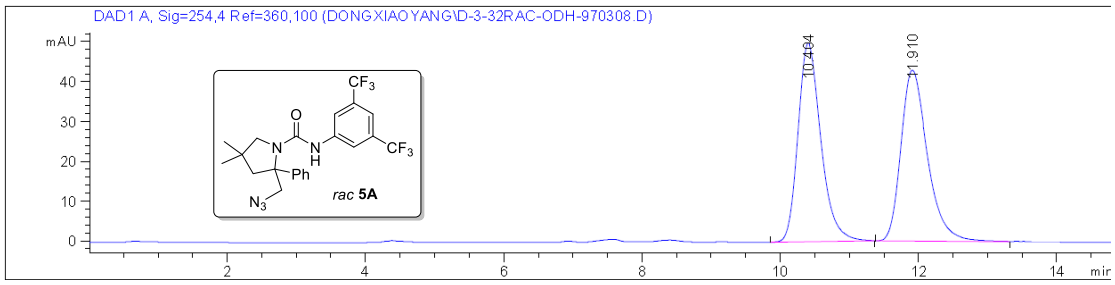
Figure S226. HPLC spectrum of *rac* **3ZI**



Signal 2: DAD1 B, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.662	BB	0.4229	2075.46289	74.99577	69.7658
2	20.946	BB	0.7586	899.43610	17.18536	30.2342
Totals :				2974.89899	92.18113	

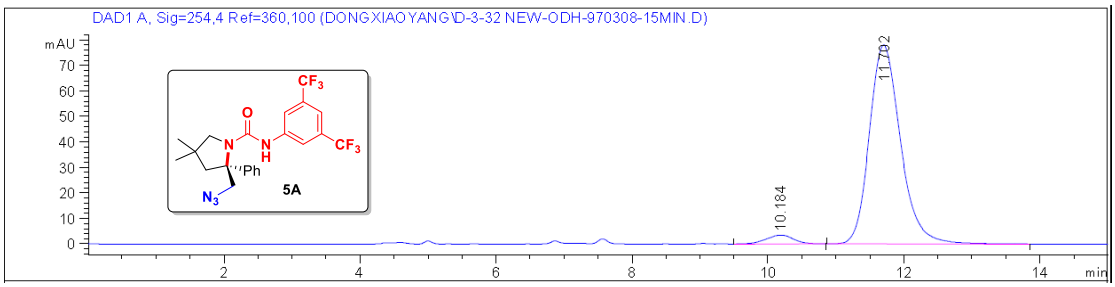
Figure S227. HPLC spectrum of **3ZI**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.404	BB	0.3549	1150.64478	49.91942	50.2689
2	11.910	BB	0.4055	1138.33252	42.91208	49.7311
Totals :				2288.97729	92.83150	

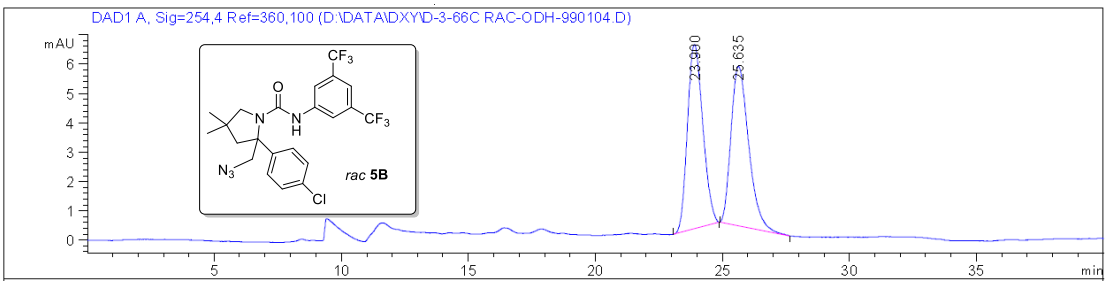
Figure S228. HPLC spectrum of *rac* **5A**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.184	BB	0.3870	99.26238	3.47816	3.8321
2	11.702	BB	0.4900	2491.01221	78.12312	96.1679
Totals :				2590.27459	81.60128	

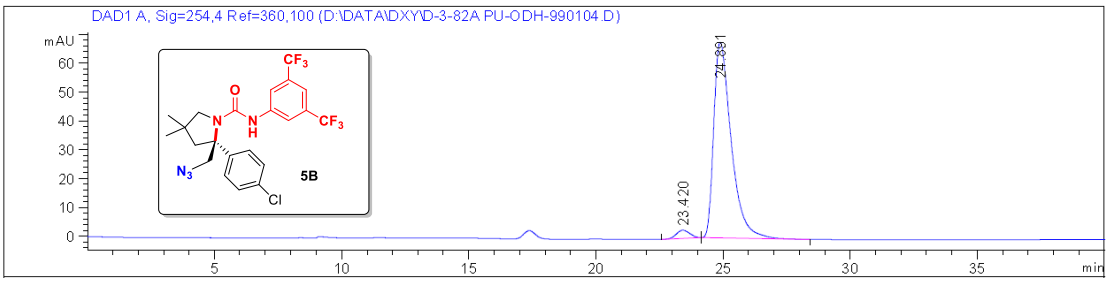
Figure S229. HPLC spectrum of **5A**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.900	BB	0.6348	264.19931	6.28031	50.0801
2	25.635	BB	0.7215	263.35376	5.43275	49.9199
Totals :				527.55307	11.71306	

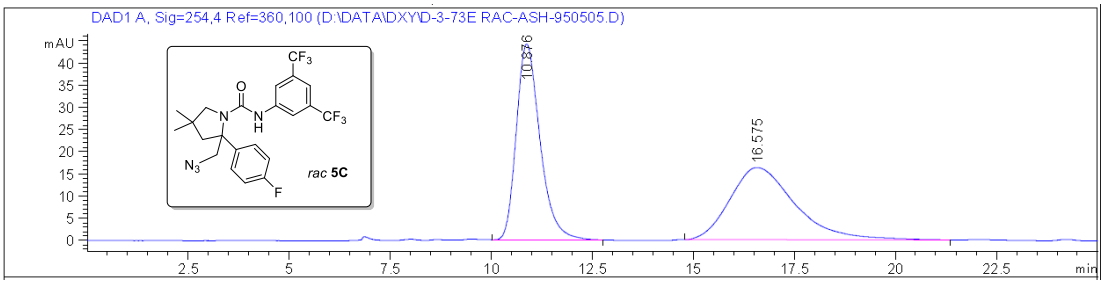
Figure S230. HPLC spectrum of *rac* **5B**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.420	BB	0.5752	107.56152	2.89666	3.2085
2	24.891	BB	0.7114	3244.80518	67.91323	96.7915
Totals :				3352.36669	70.80989	

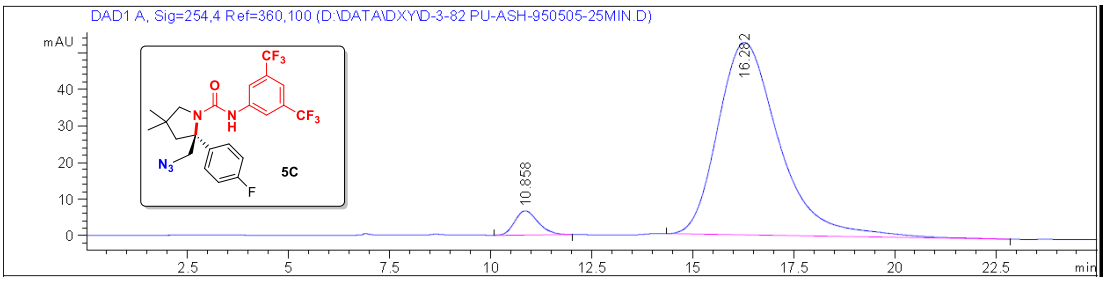
Figure S231. HPLC spectrum of **5B**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.876	BB	0.6237	1797.20117	44.07240	49.7510
2	16.575	BB	1.5793	1815.19019	16.27353	50.2490
Totals :				3612.39136	60.34594	

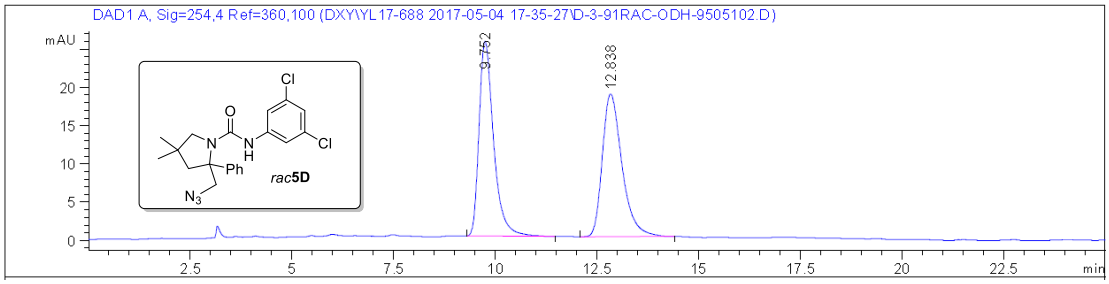
Figure S232. HPLC spectrum of *rac* **5C**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.858	BB	0.6264	265.60690	6.61492	4.5749
2	16.282	BB	1.5965	5540.12012	52.61150	95.4251
Totals :				5805.72702	59.22642	

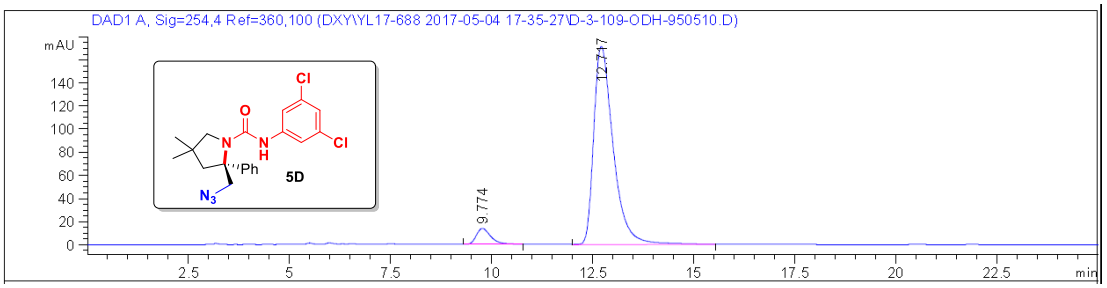
Figure S233. HPLC spectrum of **5C**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.752	BB	0.3767	634.27411	25.45434	50.3053
2	12.838	BB	0.5139	626.57532	18.65434	49.6947
Totals :				1260.84943	44.10868	

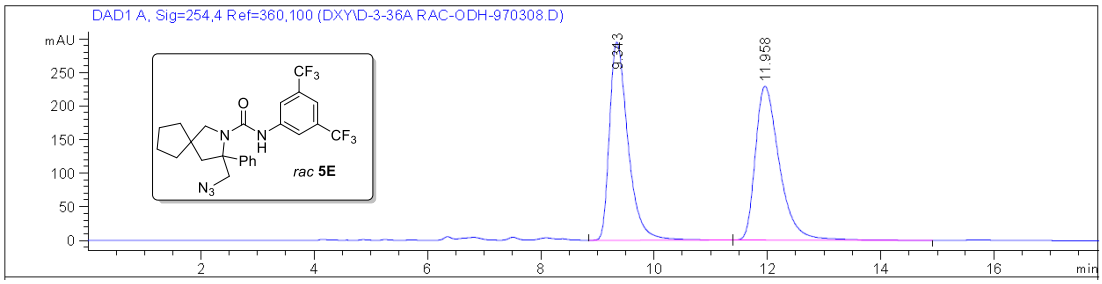
Figure S234. HPLC spectrum of *rac* **5D**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.774	BB	0.3778	344.37418	13.86341	5.6698
2	12.717	BB	0.5080	5729.47949	171.40201	94.3302
Totals :				6073.85367	185.26542	

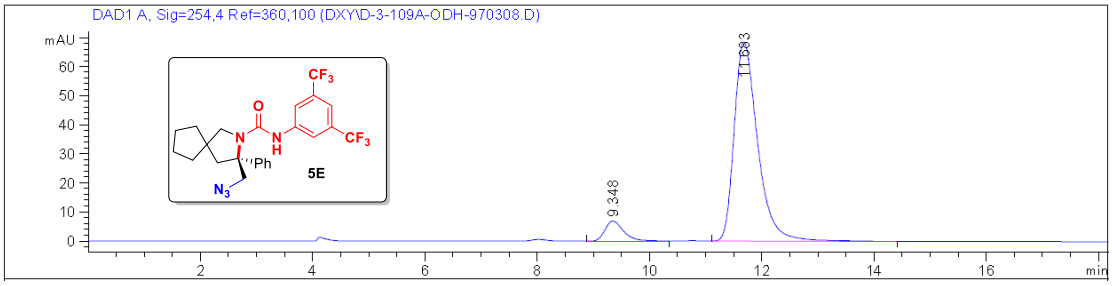
Figure S235. HPLC spectrum of **5D**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.343	BB	0.3467	6693.34180	294.97217	49.8633
2	11.958	BB	0.4508	6730.04443	229.07372	50.1367

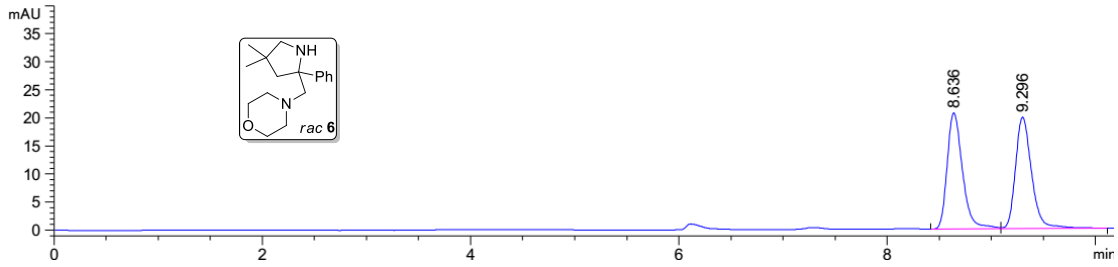
Figure S236. HPLC spectrum of *rac* **5E**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.348	BB	0.3527	159.22681	6.91258	7.4091
2	11.683	BB	0.4425	1989.83850	68.57190	92.5909

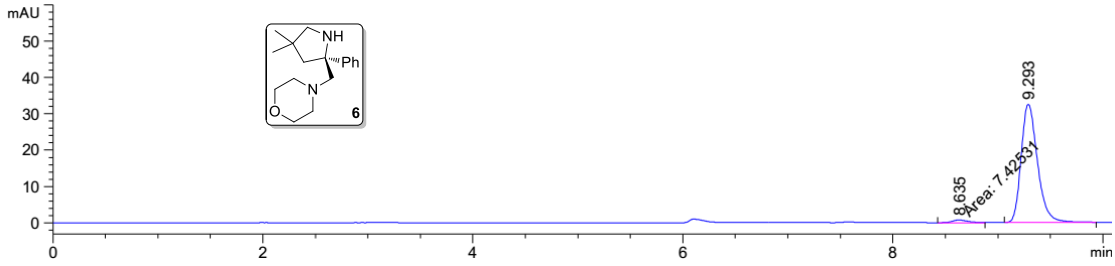
Figure S237. HPLC spectrum of **5E**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.636	BV	0.1577	212.87021	20.74136	49.7097
2	9.296	VB	0.1662	215.35629	19.90606	50.2903
Totals :				428.22650	40.64742	

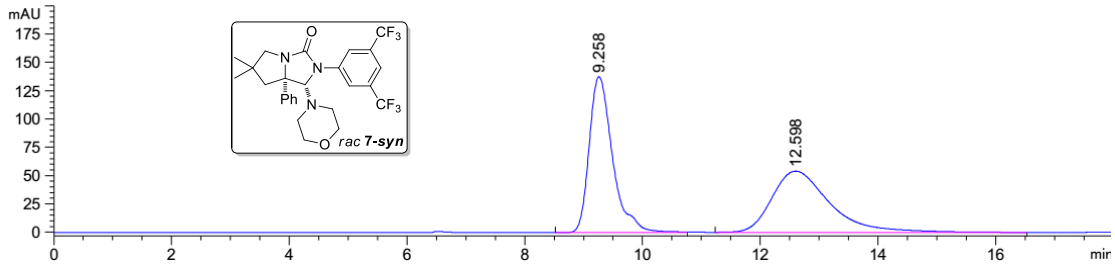
Figure S238. HPLC spectrum of *rac* **6**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.635	MM	0.1702	7.42531	7.26904e-1	2.0667
2	9.293	MF R	0.1801	351.85229	32.55236	97.9333
Totals :				359.27760	33.27927	

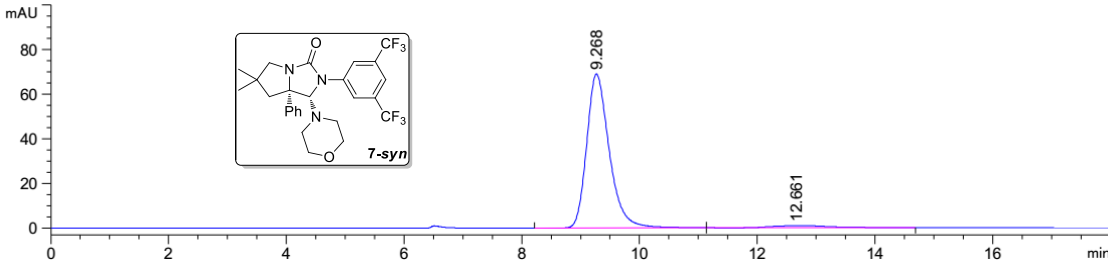
Figure S239. HPLC spectrum of **6**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.258	MF R	0.4592	3787.45117	137.47520	50.7088
2	12.598	BB	1.0270	3681.56348	54.03018	49.2912
Totals :				7469.01465	191.50538	

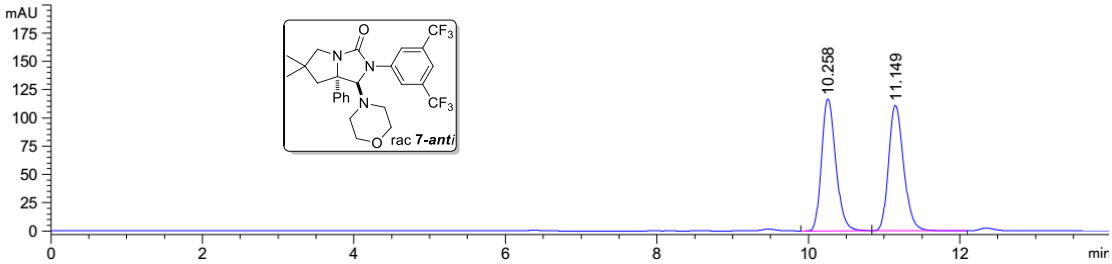
Figure S240. HPLC spectrum of *rac* **7-*syn***



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.268	MF R	0.4432	1834.99292	68.99944	96.8496
2	12.661	FM R	1.0958	59.69089	9.07881e-1	3.1504
Totals :				1894.68381	69.90732	

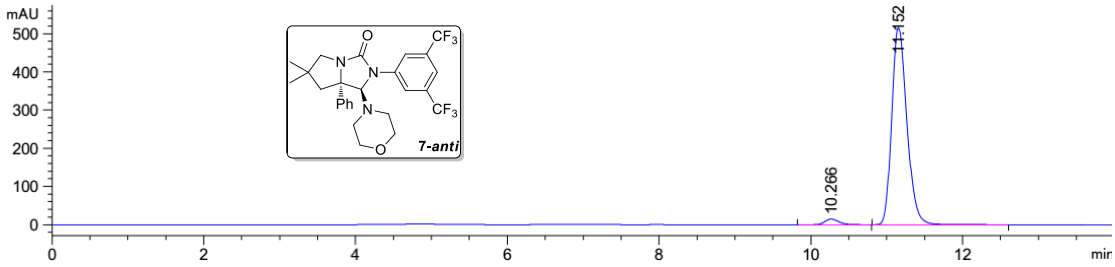
Figure S241. HPLC spectrum of **7-*syn***



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.258	BV	0.2006	1525.02637	116.58412	49.7561
2	11.149	VB	0.2140	1539.97607	110.87405	50.2439
Totals :				3065.00244	227.45817	

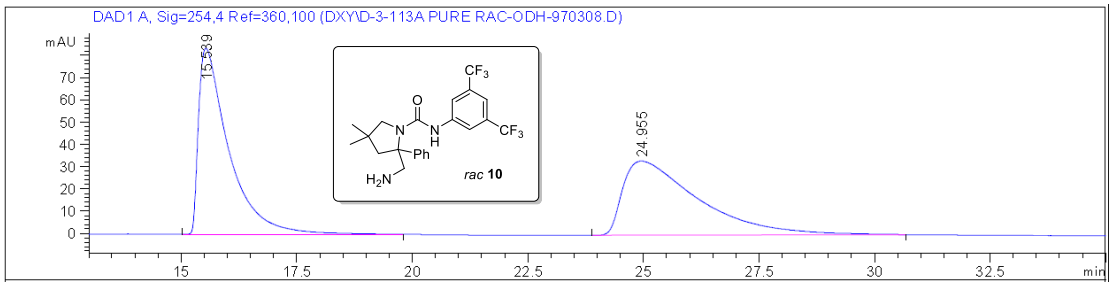
Figure S242. HPLC spectrum of *rac* **7-*anti***



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.266	BB	0.2002	188.51770	14.45210	2.5698
2	11.152	BB	0.2138	7147.48633	515.31958	97.4302
Totals :				7336.00403	529.77168	

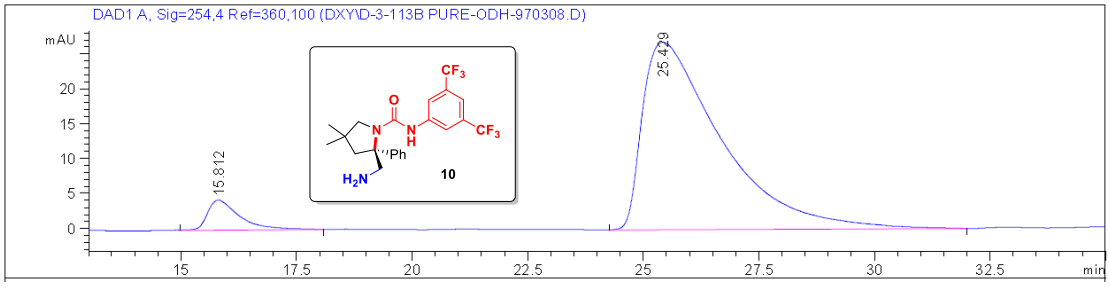
Figure S243. HPLC spectrum of ***7-anti***



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.539	BB	0.6606	3814.62500	83.56472	50.2567
2	24.955	BB	1.5539	3775.65723	33.32157	49.7433
Totals :				7590.28223	116.88629	

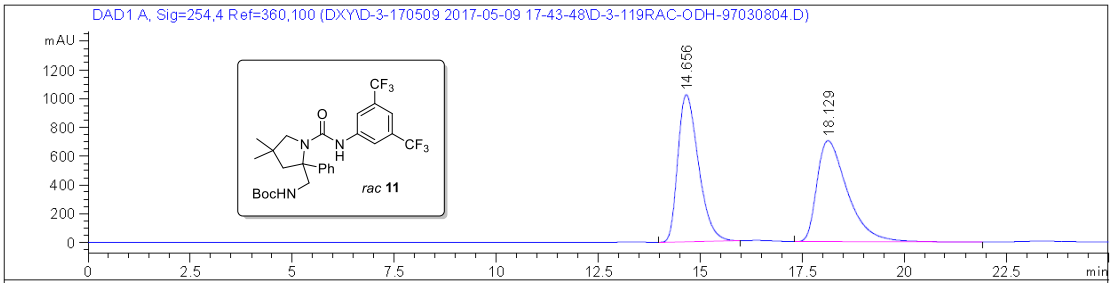
Figure S244. HPLC spectrum of *rac* **10**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.812	BB	0.6843	206.53178	4.27023	6.0728
2	25.429	BB	1.6489	3194.38745	26.87149	93.9272
Totals :				3400.91924	31.14172	

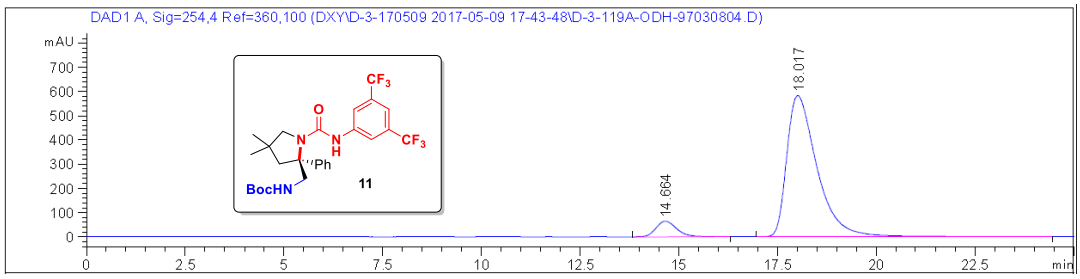
Figure S245. HPLC spectrum of **10**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.656	BB	0.5426	3.59867e4	1022.58588	49.5784
2	18.129	BB	0.7976	3.65987e4	702.79205	50.4216
Totals :				7.25854e4	1725.37793	

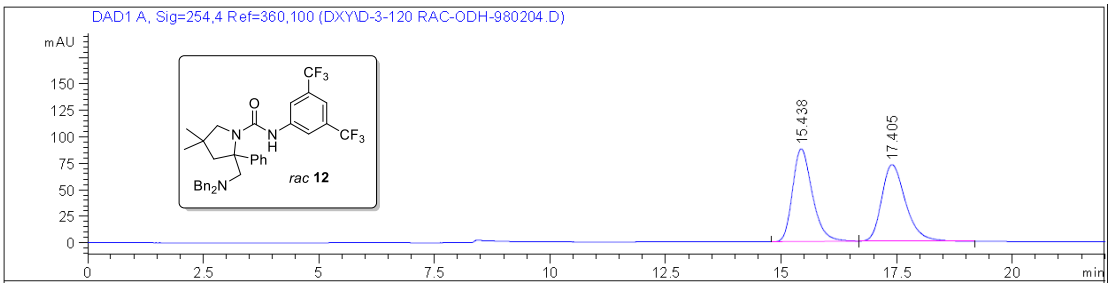
Figure S246. HPLC spectrum of *rac* **11**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.664	BB	0.5573	2353.77808	64.57205	7.0277
2	18.017	BB	0.8011	3.11390e4	583.01276	92.9723
Totals :				3.34928e4	647.58481	

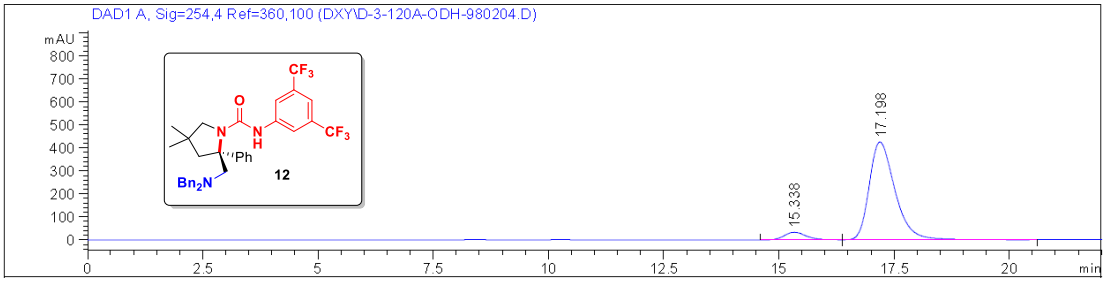
Figure S247. HPLC spectrum of **11**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.438	BB	0.4519	2596.16919	87.57681	50.1735
2	17.405	BB	0.5447	2578.21265	72.19179	49.8265
Totals :				5174.38184	159.76859	

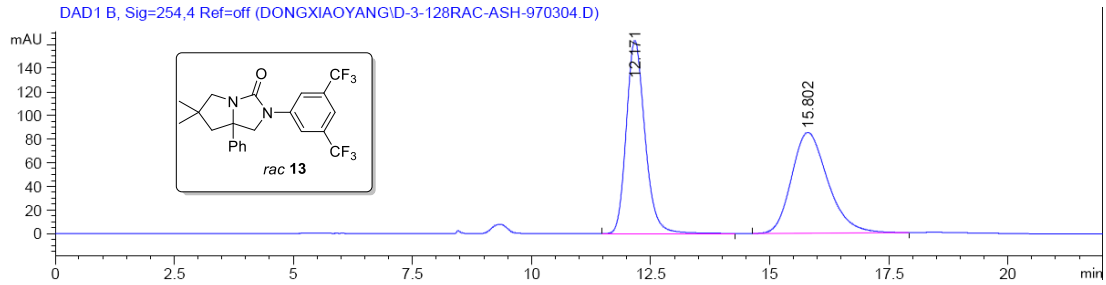
Figure S248. HPLC spectrum of *rac* **12**



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.338	BB	0.4988	1049.80200	32.50508	5.9872
2	17.198	BB	0.5963	1.64842e4	425.23407	94.0128
Totals :				1.75340e4	457.73915	

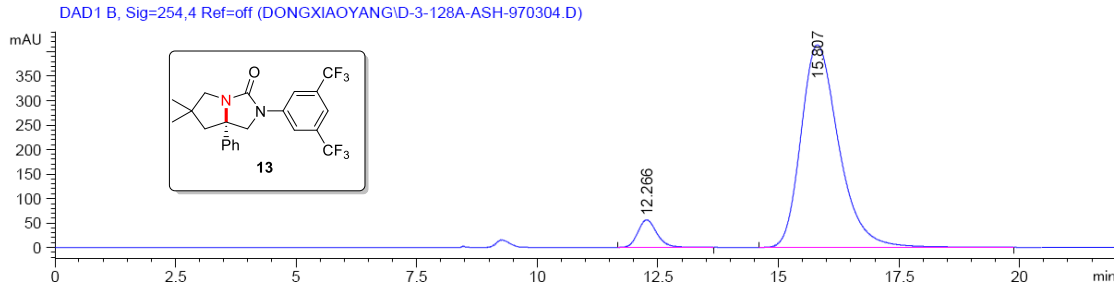
Figure S249. HPLC spectrum of **12**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.171	BB	0.4196	4469.82227	163.16736	49.8002
2	15.802	BB	0.8068	4505.68945	85.22007	50.1998
Totals :				8975.51172	248.38743	

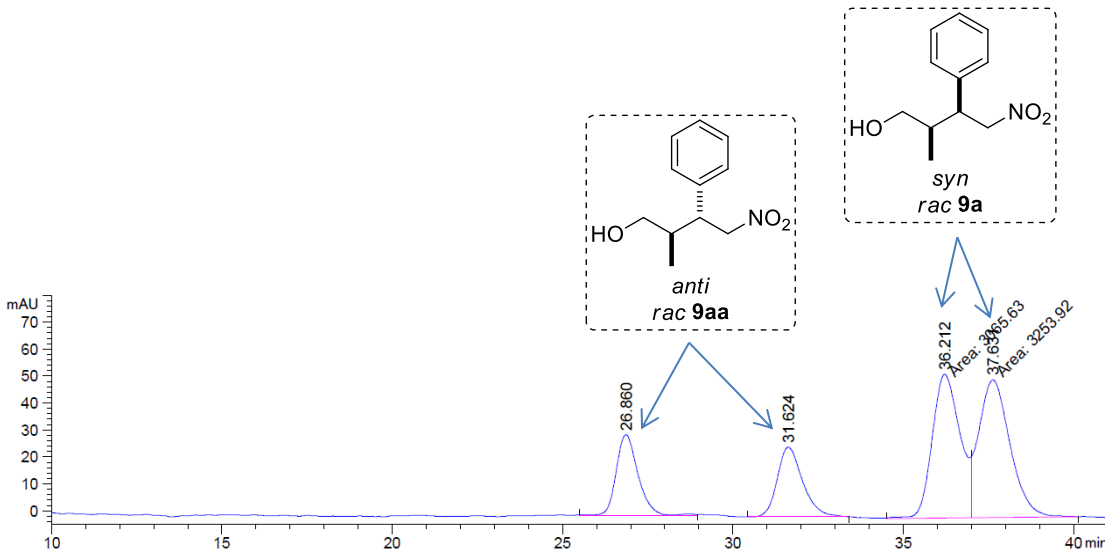
Figure S250. HPLC spectrum of *rac* **13**



Signal 2: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.266	BB	0.4253	1544.19055	56.07375	6.4119
2	15.807	BB	0.8317	2.25391e4	413.62094	93.5881
Totals :				2.40833e4	469.69469	

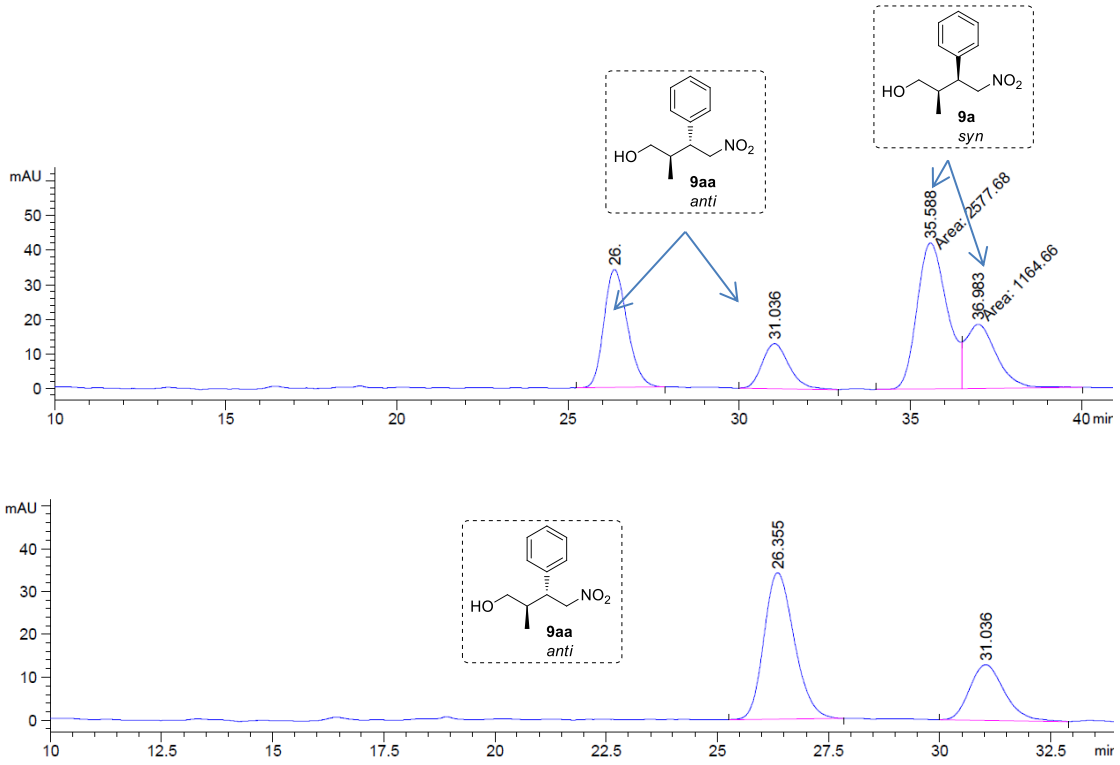
Figure S251. HPLC spectrum of **13**



Signal 2: DAD1 B, Sig=214,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.860	MM R	0.7401	1327.02100	29.88384	14.7732
2	31.624	MM R	0.8611	1336.03625	25.85786	14.8736
3	36.212	MF	0.9559	3065.63306	53.45036	34.1286
4	37.631	FM	1.0610	3253.91504	51.11221	36.2246
Totals :				8982.60535	160.30427	

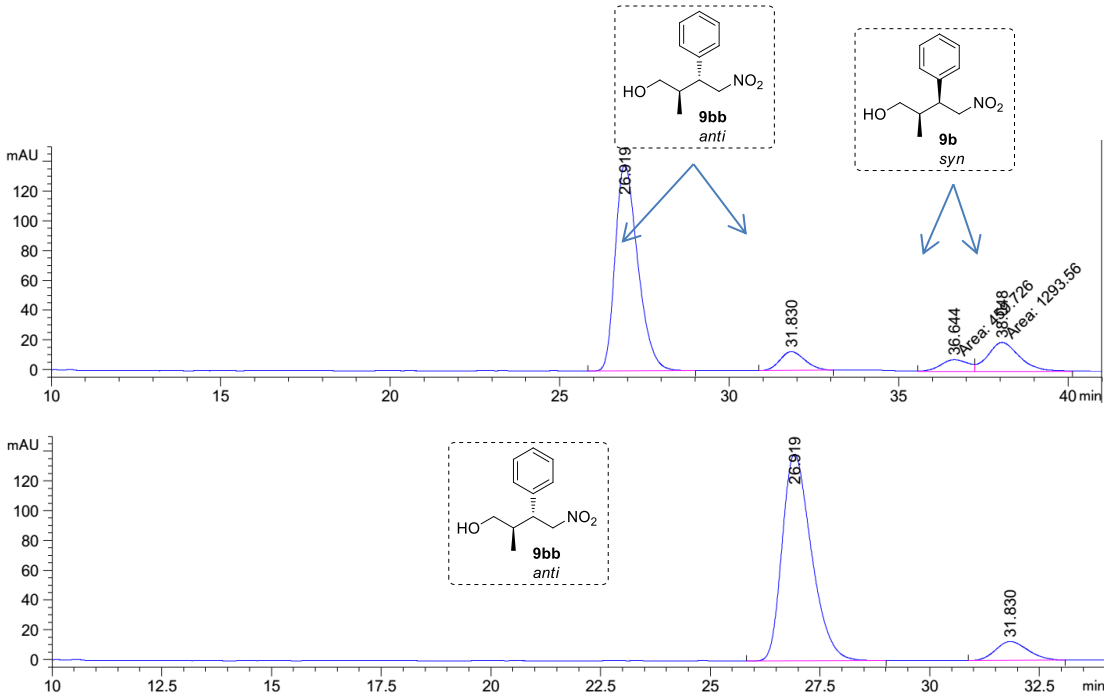
Figure S252. HPLC spectrum of *rac* **9a** & **9aa**



Signal 3: DAD1 C, Sig=214,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.355	BB	0.7379	1618.33655	34.08936	69.5808
2	31.036	BB	0.7855	707.50024	12.98777	30.4192
Totals :				2325.83679	47.07713	

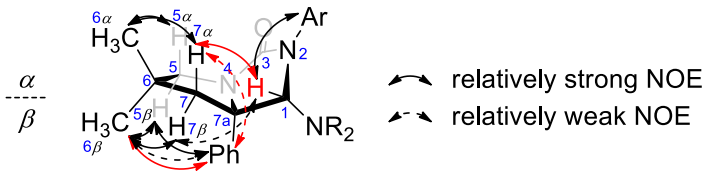
Figure S253. HPLC spectrum of **9a** & **9aa**



Signal 3: DAD1 C, Sig=214,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.919	BB	0.7170	6440.48730	138.90175	90.8909
2	31.830	BB	0.7531	645.46643	12.61194	9.1091
Totals :				7085.95374	151.51369	

Figure S254. HPLC spectrum of **9b** & **9bb**



7-*syn*

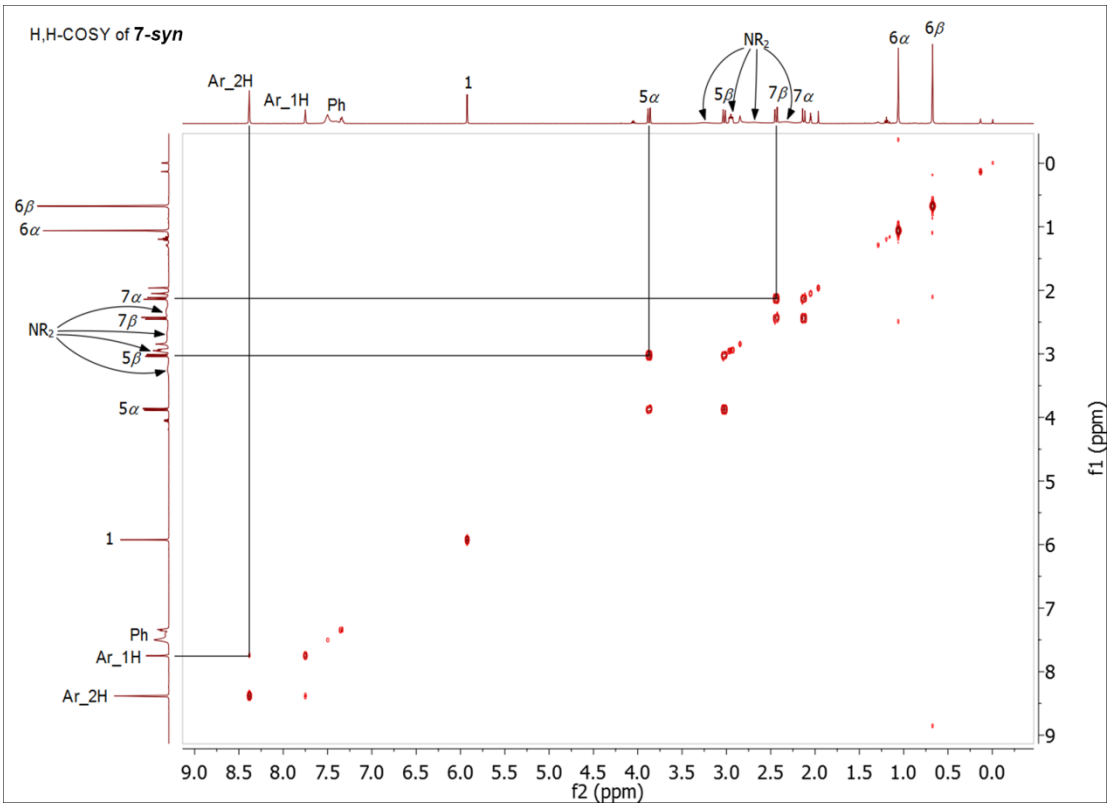


Figure S255. H,H-COSY NMR spectrum of ***7-syn***

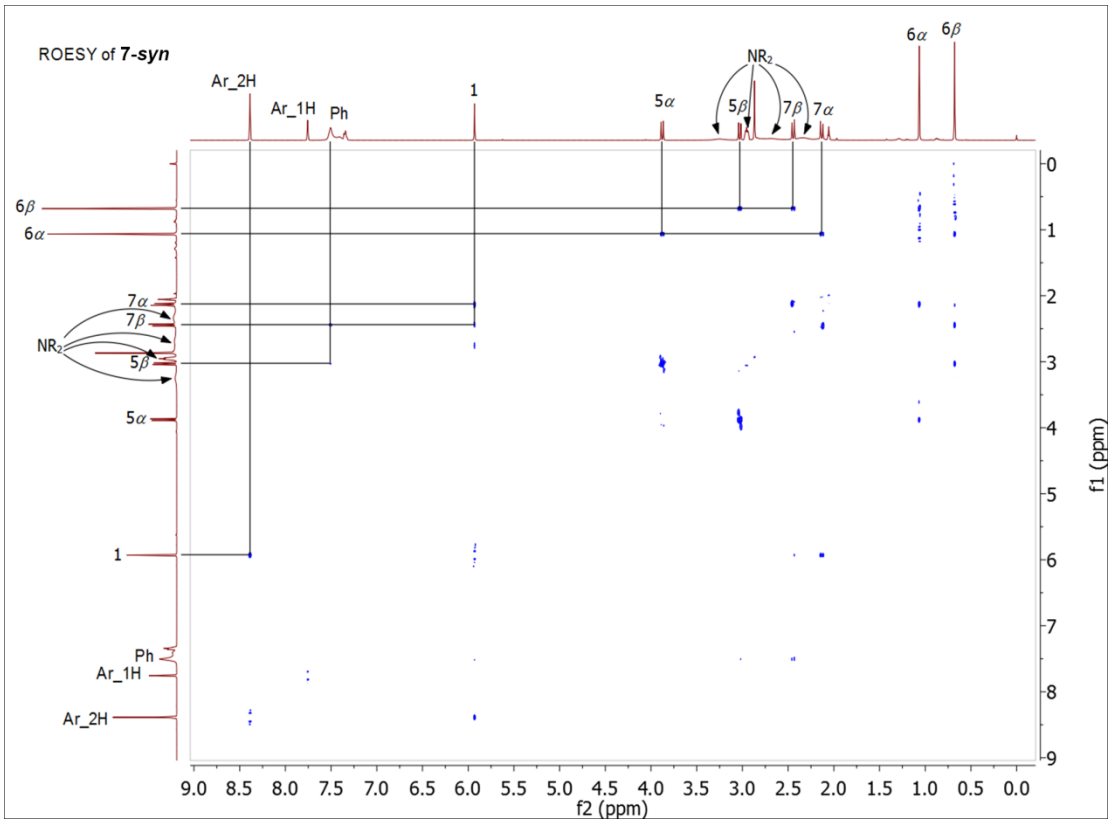
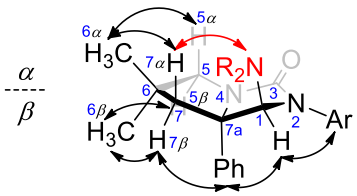


Figure S256. ROESY NMR spectrum of **7-*syn***



7-anti

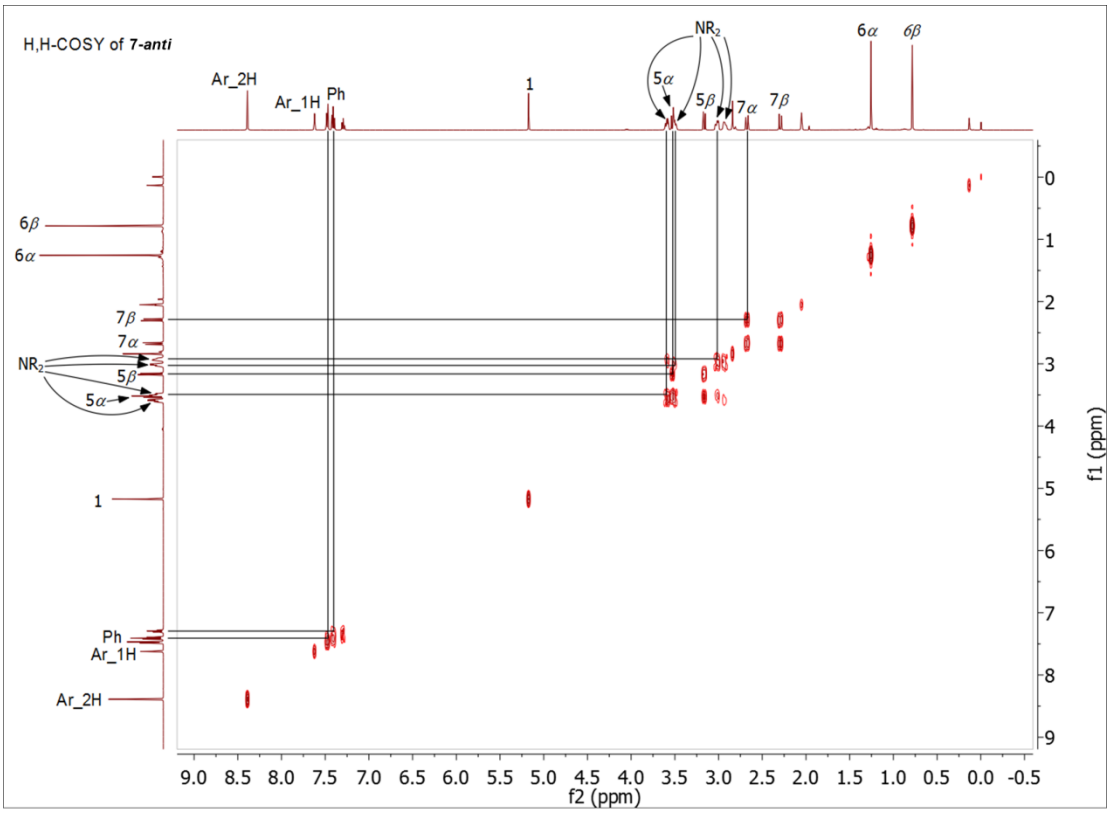


Figure S257. H,H-COSY NMR spectrum of ***7-anti***

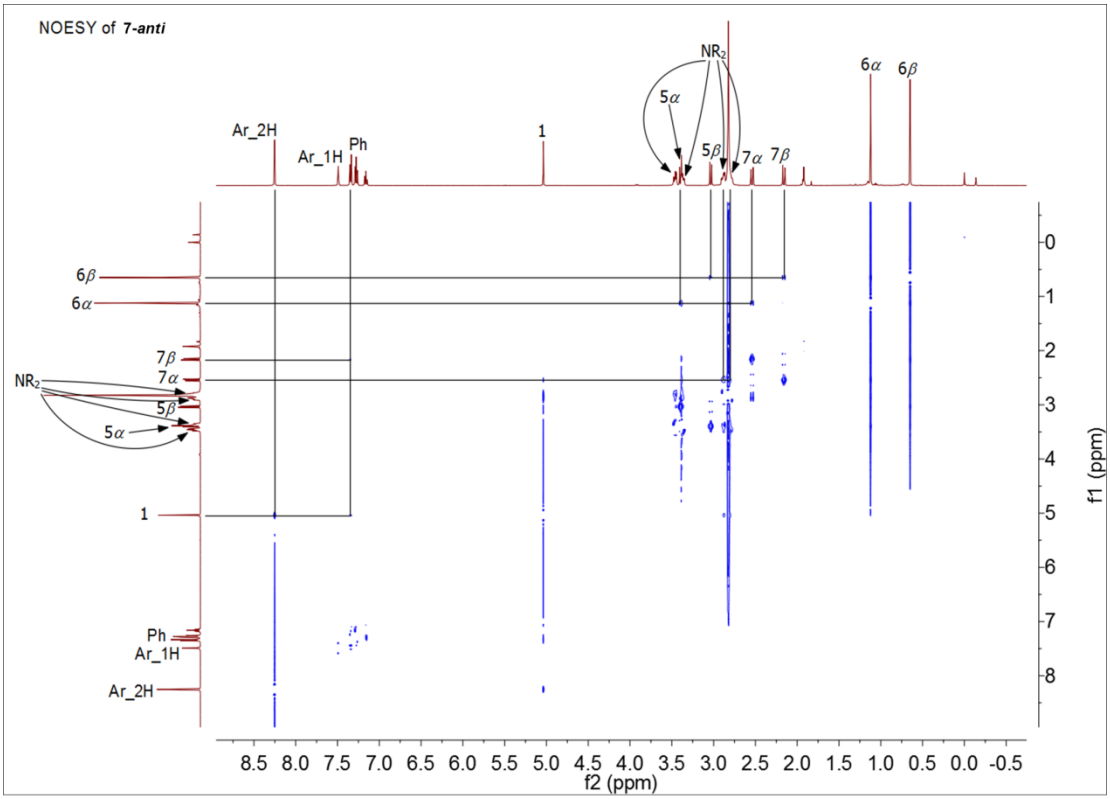


Figure S258. NOESY NMR spectrum of **7-*anti***

V. X-ray Crystallographic Data

A colorless single crystal of **3T** was obtained by recrystallization from EtOAc:Hexane = 1:5. Crystallographic data for **3T** have been deposited in the Cambridge Crystallographic Data Centre (CCDC: 1542541).

Empirical formula	$C_{31}H_{33}F_6N_3O_{2.5}$
Formula weight	601.60
Temperature/K	150.0
Crystal system	monoclinic
Space group	C2
a/Å	28.5401(7)
b/Å	13.2816(3)
c/Å	21.1191(5)
α/°	90
β/°	132.150(2)
γ/°	90
Volume/Å^3	5935.1(3)

Z	8
ρ_{calc}g/cm^3	1.347
μ/mm^{-1}	0.954
F(000)	2512.0
Crystal size/mm^3	0.4 × 0.2 × 0.17
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	5.644 to 149.194
Index ranges	-35 ≤ h ≤ 35, -16 ≤ k ≤ 16, -26 ≤ l ≤ 26
Reflections collected	114376
Independent reflections	12000 [R_{int} = 0.0418, R_{sigma} = 0.0195]
Data/restraints/parameters	12000/83/804
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0397, wR_2 = 0.1014
Final R indexes [all data]	R_1 = 0.0429, wR_2 = 0.1046
Largest diff. peak/hole / e Å^{-3}	0.53/-0.40
Flack parameter	0.02(3)

VI. Supplemental References

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