Supporting Information for

Construction of an α-chiral pyrrolidine library with a rapid and scalable continuous flow protocol

Chao Shan,[a] Liming Cao,[a] Jiasheng Yang,[a] Ruihua Cheng,[b] Xiantong Yao,[b] Chaoming Liang,[b] Maolin Sun*[b] and Jinxing Ye*[a,b]

[a] Engineering Research Center of Pharmaceutical Process Chemistry, Ministry of Education, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China
E-mail: yejx@ecust.edu.cn

[b] School of Biomedical and Pharmaceutical Sciences, Guangdong University of Technology, Guangzhou 510006, China
E-mail: maolinsun@gdut.edu.cn; jinxingye@gdut.edu.cn

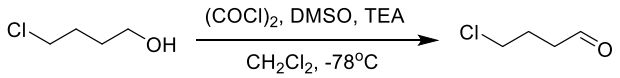
Table of Contents

1. General information

All common reagents and solvents were commercially available and used without further purification. CH_2Cl_2 and THF are dried over 3 Å molecular sieve before being used. Commercially available 3 Å molecular sieves were pre-dried at 300 °C for 24 h immediately before use. All reactions were carried out under a nitrogen atmosphere, and all reaction vessels were pre-dried. ^1H, ^{13}C NMR and ^{19}F-NMR spectral data were recorded using a Bruker AVANCE III 400 or Bruker Ascend 600 spectrometer. Where isomeric compounds are present in materials, the ratios have been determined by ^1H NMR analysis. In most cases the ^1H and ^{13}C NMR data is reported for only the major isomer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane or referenced to residual solvent. NMR data are reported as follows: chemical shift, integration, multiplicity (s: singlet, d: doublet, t: triplet, q: quadruplet, br: broad, m: multiplet), coupling constants (*J* in Hz). High resolution mass spectrometry (ESI) was carried out using a Waters Quatro Macro triple quadrupole mass spectrometer. The syringe pump (TYD01-01) with flow rate 0.184 nL/min ~ 83.318 mL/min was purchased from Baoding Refu Fluid Technology Co. Ltd., and the HPLC pump (2PB-0240) with flow rate 0.01 ~ 20 mL/min was purchased from Bejing Xingda Science & Technology Development Co. Ltd. The precooling tube was made of PFA (1/16" O.D.). The T-mixer (PEEK, 1/16" I.D.) was used to mix two separate feed streams, and the mixture was channeled into the coil reactor (PFA, 1/16" O.D).

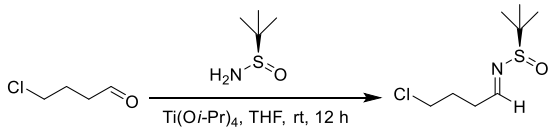
2. General procedures

General procedure 1: Synthesis of 4-chlorobutyraldehyde[1].



To a solution of oxalyl chloride (6.3 mL, 75 mmol, 1.5 equiv.) in dry CH_2Cl_2 (200 mL) was added a solution of DMSO (7.1 mL, 100 mmol, 2 equiv.) in dry CH_2Cl_2 (40 mL) dropwise at -78 °C under nitrogen atmosphere. The resulting solution was stirred at -78 ºC for 30 minutes, then a solution of 4-chloro-1-butanol (5.43 g, 50 mmol, 1 equiv.) in dry CH_2Cl_2 (80 mL) was added dropwise. The mixture was stirred at -78 °C for 30 min, and then TEA (34.7 mL, 250 mmol, 5 equiv.) was added dropwise. The reaction was allowed to warm up to rt, and after stirring for 30 min, the mixture was quenched with H_2O and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and filtered. After removing the solvent in vacuo, column chromatographical purification (hexane: ethyl acetate = 8:1) obtained the pure product (4.28 g, 80%) as a pale yellow oil.

General procedure 2: Synthesis of γ-chloro *N*-(*tert*-butanesulfinyl)imine[2].



4-chlorobutyraldehyde (4.26 g, 40 mmol, 1 equiv.) was dissolved in 80 mL THF under nitrogen atmosphere, *tert*-butyl sulfinamide (4.85 g, 40 mmol, 1 equiv.) and Ti(O*i*-Pr)$_4$ (14.2 mL, 48 mmol, 1.2 equiv.) were added, and the mixture was stirred at room temperature for 12 h. After the reaction was completed, sat. aq. NaCl solution and ethyl acetate were added to the reaction solution, The resulting suspension was filtered through a plug of Celite, and the filter cake was washed with ethyl acetate. After evaporating the solvent, the resulting residue was purified by column chromatography

(hexane: ethyl acetate = 8:1) to afford pure γ-chloro *N*-(*tert*-butanesulfinyl)imine (7.74 g, 92%) as a colorless oil.

General procedure 3: Synthesis of aryl Grignard reagents.

The alkyl Grignard reagents used in this work were purchased commercially, and apart from PhMgBr, the aryl Grignard reagents used in this work were synthesized by general methods.

The preparation of 4-methylphenylmagnesium bromide (1 M in THF) was taken as an example. A three-neck flask equipped with a reflux condenser tube was charged with magnesium turnings (264 mg, 11 mmol, 1.1 equiv.), a little iodine, and dry THF (5 mL) under nitrogen atmosphere. A 5 mL solution was prepared by adding THF to 4-bromomethylbenzene (1710 mg, 10 mmol, 1 equiv.). Half of the solution was introduced slowly with stirring at room temperature, and the reaction mixture was heated until the initiation of the reaction. After initiation, the remaining solution was added dropwise, and the mixture was stirred at 50 ºC for an additional 1 h. After cooling, the Grignard solution was used immediately in a continuous flow reaction.

General procedure 4: Synthesis of α-chiral pyrrolidines in continuous flow.

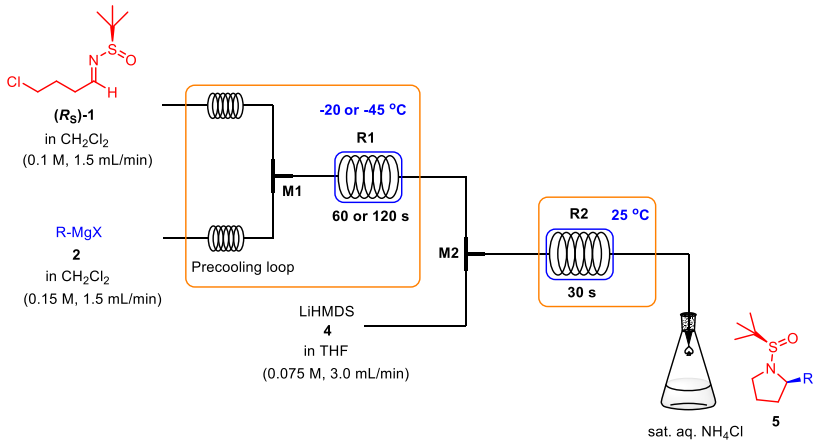


Fig. S1 The flow system for the synthesis of α-chiral pyrrolidines.

As shown in Fig. S1, the flow system consisted of two pre-cooling loops (PFA, 1/16" O.D.), two T-mixers **M1**, **M2** (PEEK, 1/16" I.D.) and two coil reactors **R1**, **R2** (PFA, 1/16" O.D.). The first half of the flow system (pre-cooling loops, **M1** and **R1**) was dipped in a cooling bath (-20 ºC). The latter half (**R2**) was dipped in a water bath (25 ºC). A flask containing a stirred sat. NH_4Cl aqueous solution was placed at the end of the flow system. The reaction solution was quenched as it dropped into this flask.

A solution of **2** (0.15 M in CH_2Cl_2) was obtained by diluting its 1 M THF solution with CH_2Cl_2, and a solution of **(*R*S)-1** (0.1 M in CH_2Cl_2) were prepared. The solutions delivered by syringe pumps passed through the pre-cooling loop (V = 2 mL) at the same flowrate (1.5 mL/min) and were subsequently mixed at **M1**. The resulting mixture passed **R1** (V = 3 mL) with a residence time of 60 s. A solution of **4** (0.075 M in THF) pumped at a rate twice that of **(*R*S)-1** was mixed with the reaction solution at **M2**. The combined stream passed through **R2** (V = 3 mL) with a residence time of 30 s. After a steady state was reached, the product solution was collected for 200 s (0.5 mmol). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2, the combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The diastereomeric ratio was determined by the ^1H NMR of the crude mixture, and the desired diastereomer **5** was isolated by column chromatography (hexane/ethyl acetate = 10:1 ~ 5:1).

General procedure 5: The deprotection procedure to provide free pyrrolidines.

A round-bottom flask was charged with **5a** (503 mg, 2 mmol, 1 equiv.) and HCl solution (2 M in MeOH, 4 mL). After the reaction mixture was stirred for 30 min at room temperature, the solvent was removed under reduced pressure, and the residue was dissolved in water. The aqueous phase was washed with ethyl acetate, and the pH of the solution was adjusted to 12 with 20 wt% NaOH aqueous solution. The aqueous phase was extracted with ethyl acetate and washed with brine. The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure to provide enantioenriched pyrrolidine **6a** in nearly quantitative yield.

3. Effects of temperature and residence time on the yield of (R_S,*R*)-δ-chloro sulfinamide.

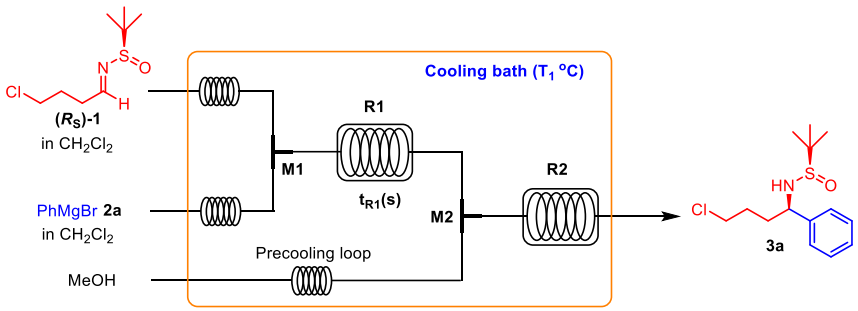


Fig. S2 The flow system for the addition of PhMgBr to γ-chloro *N*-(*tert*-butanesulfinyl)imine.

As shown in Fig. S2, the flow system consisted of two pre-cooling loops (PFA, 1/16" O.D.), two T-mixers **M1**, **M2** (PEEK, 1/16" I.D.) and two coil reactors **R1**, **R2** (PFA, 1/16" O.D.). The whole flow system was located in a cooling bath (T_1 = -40 ~ 25 °C).

A solution of **2a** (0.2 M in CH_2Cl_2) obtained by diluting its 1 M THF solution with CH_2Cl_2, and a solution of **(R_S)-1** (0.1 M in CH_2Cl_2) were prepared. The solutions delivered by syringe pumps passed through the pre-cooling loop (V = 2 mL) at the same flowrate (1.0 ~ 3.0 mL/min) and were subsequently mixed at **M1**. The resulting mixture passed **R1** (V = 3 mL) with a residence time of 30 ~ 90 s. MeOH pumped at a rate twice that of **(R_S)-1** was mixed with the reaction solution at **M2**, and the combined stream subsequently passed through **R2** (V = 2 mL). After a steady state was reached, the effluent was collected for a period of time according to the flow rate (0.5 mmol). The collected solution was concentrated, H_2O and CH_2Cl_2 were added to the residue. The aqueous phase was extracted with CH_2Cl_2. The combined organic phase was dried over Na_2SO_4 and filtered. After removal of the solvent in vacuo, the major diastereomer **3a** was isolated by column chromatography (hexane/ethyl acetate = 3:1). The results are summarized in Table S1.

Table S1. Effects of temperature and residence time on the yield of **3a**

Entry	Flow rate (mL/min)	t_{R1} (s)	T_1(°C)	Yield (%)[a]
1	1.0	90	-40	84
2	1.5	60	-40	75
3	2.0	45	-40	67
4	3.0	30	-40	60
5	1.0	90	-20	86
6	1.5	60	-20	87
7	2.0	45	-20	84
8	3.0	30	-20	78
9	1.0	90	0	83
10	1.5	60	0	84
11	2.0	45	0	83
12	3.0	30	0	81
13	1.0	90	25	78
14	1.5	60	25	80
15	2.0	45	25	80
16	3.0	30	25	79

[a]Isolated yield of the major diastereomer based on the starting **(*R*S)-1**.

4. Effects of temperature on the diastereoselectivity of pyrrolidine.

To determine the influence of temperature on the diastereoselectivity, we conducted the addition reaction at -40 ~ 25 °C with a residence time of 60 s, followed by in-line cyclization to provide pyrrolidine **5a**. As profiled in Fig. S3, performing the reaction at -40 °C, a good diastereocontrol was achieved with 94: 6 dr. Increasing the temperature to -20 °C led to a similar diastereomeric ratio (93: 7). When the reaction was carried out at 0 and 25 °C, the corresponding product **5a** was obtained with lower diastereoselectivity (90: 10 and 88: 12 dr).

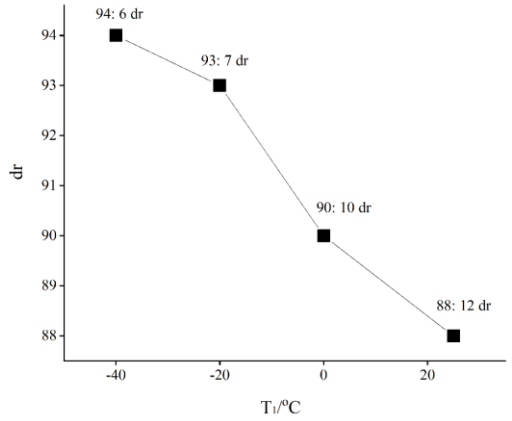


Fig. S3 Effects of temperature on the diastereoselectivity of pyrrolidine.

5. Synthesis of Aticaprant key intermediate on a gram scale.

A solution of **2j** (0.3 M in CH_2Cl_2) obtained by diluting its 1 M THF solution with CH_2Cl_2, a solution of **(*S*S)-1** (0.2 M in CH_2Cl_2), and a solution of **4** (0.15 M in THF) were prepared. The syringe pumps were removed and the reactant solution was introduced into the flow system by HPLC pumps.

Employing these three solution, the preparation of **(S_S,*S*)-5j** was performed by flow reaction method described in the general procedure 4 with a processing time of 30 min. The diastereomeric ratio was 91: 9 determined by the ^{1}H-NMR of the crude product, and 2.02 g of **(S_S,*S*)-5j** was isolated with 80% yield.

The obtained **(S_S,*S*)-5j** (2.02 g, 7.2 mmol) was treated with HCl (14.4 ml, 2 M in MeOH, 4 equiv.) followed by alkalization using NaOH, affording the Aticaprant key intermediate **(*S*)-6j** on a 1.23 g scale (97%).

6. Scale-up preparation of 5a with a self-deigned microfluidic reactor.

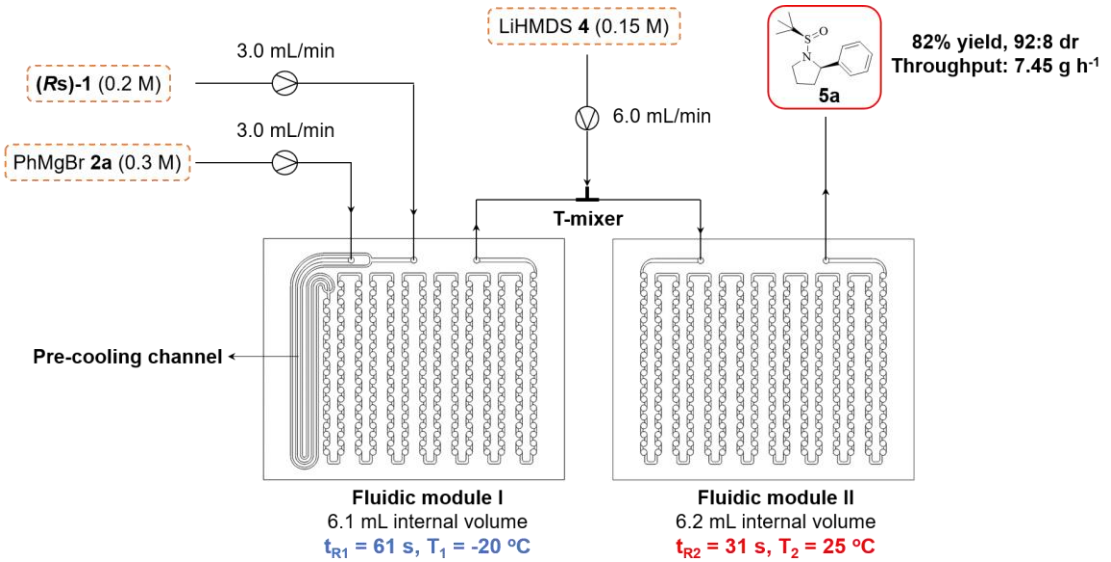


Fig. S4 Schematic representation of scale-up preparation of **5a** with a self-designed microfluidic reactor.

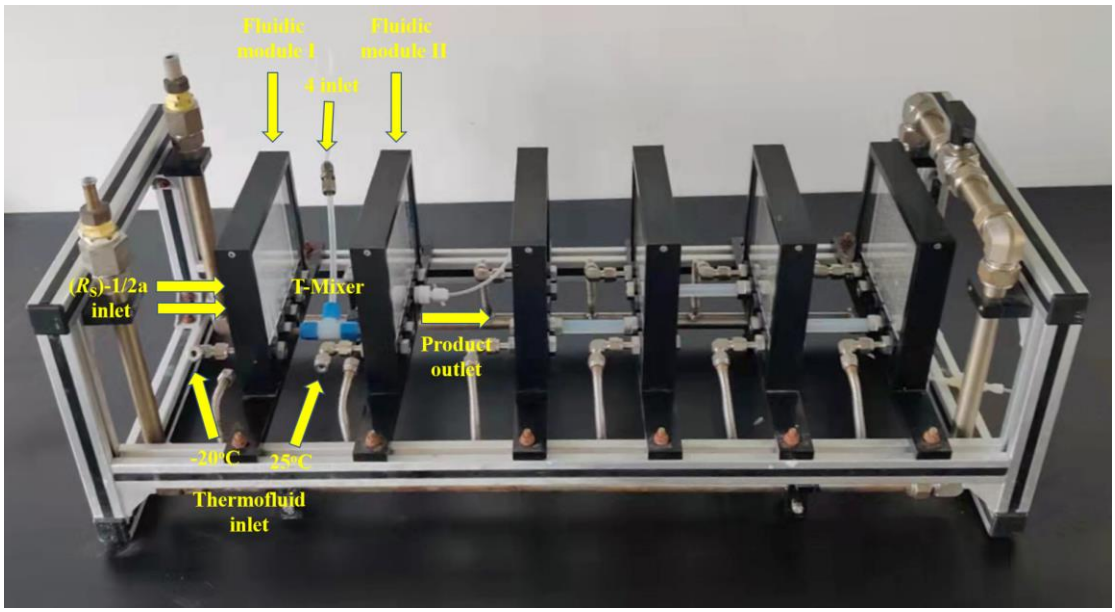


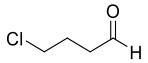
Fig. S5 Photograph of the self-designed microfluidic reactor for the scale-up preparation of **5a**.

A scale-up preparation of **5a** was performed with a self-designed microfluidic glass reactor, and two fluidic modules (I and II, *ca.* 6 mL internal volume each) was used (Fig. S4, S5). The modules were integrated with heat exchangers and connected with two thermostats, ensuring the internal

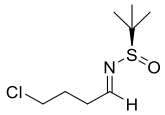
temperature of module I and module II to -20 and 25 °C, respectively.

A solution of **(*R*s)-1** (0.2 M in CH_2Cl_2, 3.0 mL/min) and a solution of **2a** (0.3 M in CH_2Cl_2, 3.0 mL/min) were directly introduced into the micro-reactor by two HPLC pumps. In Fluidic module I, they were passed through pre-cooling channel and mixed at -20 °C, subsequently passed the residence unit. The effluent was then mixed with a solution of **4** (0.15 M in THF, 6.0 mL/min) delivered by another HPLC pump via a T-mixer (PEEK, 1/4" I.D.). The combined stream passed through Fluidic module II at 25 °C and dropped into a flask containing a stirred sat. aq. NH_4Cl solution for quenching. After a steady state was reached, the flow system was running for 1.5 h. The usual workup was performed to provide crude product. The diastereomeric ratio was 92: 8 determined by the ^{1}H-NMR of the crude product, and 11.18 g of **5a** was isolated with 82% yield (7.45 g h^{-1}).

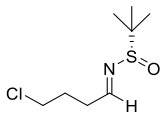
7. Synthesis of compounds



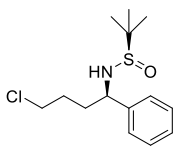
4-Chlorobutanal: The 4-chlorobutanal was synthesized by general procedure 1 using 4-chloro-1-butanol. 80% yield. Pale yellow oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.79 (s, 1H), 3.57 (t, *J* = 6.4 Hz, 2H), 2.65 (t, *J* = 6.8 Hz, 2H), 2.08 (p, *J* = 6.8 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 201.04, 44.20, 41.00, 24.94. The NMR spectral data are in accordance with the reported data[1].



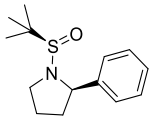
(*R*,*E*)-*N*-(4-Chlorobutylidene)-2-methylpropane-2-sulfinamide (R_S)-1: The compound **(R_S)-1** was synthesized by general procedure 2 using 4-chlorobutanal and (*R*)-*tert*-butyl sulfinamide. 92% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +197.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (t, *J* = 4.0 Hz, 1H), 3.60-3.50 (m, 2H), 2.68-2.59 (m, 2H), 2.11-2.01 (m, 2H), 1.11 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.86, 56.60, 43.98, 33.09, 27.94, 22.29. The NMR spectral data are in accordance with the reported data[2].



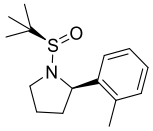
(*S*,*E*)-*N*-(4-Chlorobutylidene)-2-methylpropane-2-sulfinamide (S_S)-1: The compound **(S_S)-1** was synthesized by general procedure 2 using 4-chlorobutanal and (*S*)-*tert*-butyl sulfinamide. 90% yield. Colorless oil. $[\alpha]^{25}_{D}$ = -196.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (t, *J* = 4.0 Hz, 1H), 3.55-3.44 (m, 2H), 2.62-2.54 (m, 2H), 1.96-2.05 (m, 2H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.73, 56.44, 43.85, 32.95, 27.81, 22.15. The NMR spectral data are in accordance with the reported data[2].



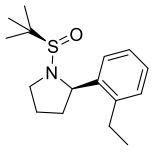
(*R*)-*N*-[(*R*)-4-Chloro-1-phenylbutyl]-2-methylpropane-2-sulfinamide (3a): The product **3a** was synthesized from **(R_S)-1** and phenylmagnesium bromide and isolated as the single diastereomer. 87% yield. White solid, mp 63-65 °C. $[\alpha]^{25}_{D}$ = -53.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39-7.26 (m, 5H), 4.43-4.31 (m, 1H), 3.47 (t, *J* = 6.4 Hz, 3H), 2.21-2.11 (m, 1H), 1.96-1.85 (m, 1H), 1.81-1.68 (m, 1H), 1.66-1.53 (m, 1H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.91, 128.87, 128.11, 127.13, 58.49, 55.83, 44.72, 33.87, 28.81, 22.68. HRMS (ESI) m/z calcd for $C_{14}H_{22}ClNOS$ $[M+H]^+$: 287.1111, found: 287.1116.



(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-phenyl-pyrrolidine (5a): Following general procedure 4, using **(R_S)-1** and phenylmagnesium bromide, the product **5a** was isolated as the single diastereomer. 86% yield. White solid, mp 84-86 °C. $[\alpha]^{25}_{D}$ = +65.8° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34-7.17 (m, 5H), 5.07 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.71-3.63 (m, 1H), 3.61-3.52 (m, 1H), 2.21-2.11 (m, 1H), 1.92-1.71 (m, 3H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.55, 128.31, 126.52, 126.44, 57.44, 57.39, 54.85, 36.59, 24.14, 23.05. HRMS (ESI) m/z calcd for $C_{14}H_{21}NOS$ $[M+H]^+$: 251.1344, found: 251.1346.

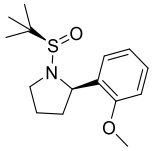


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2-methylphenyl)-pyrrolidine (5b): Following general procedure 4, using **(R_S)-1** and 2-methylphenylmagnesium bromide, the product **5b** was isolated as the single diastereomer. 74% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +47.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 6.8 Hz, 1H), 7.21-7.09 (m, 3H), 5.23 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.74-3.58 (m, 2H), 2.33 (s, 3H), 2.23-2.10 (m, 1H), 1.93-1.79 (m, 2H), 1.68-1.59 (m, 1H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 142.79, 134.47, 130.44, 126.60, 126.33, 125.89, 57.50, 56.08, 53.81, 34.86, 24.34, 23.00, 19.58. HRMS (ESI) m/z calcd for $C_{15}H_{23}NOS$ $[M+H]^+$: 265.1500, found: 265.1504.

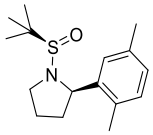


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2-ethylphenyl)-pyrrolidine (5c): Following general procedure 4, using **(R_S)-1** and 2-ethylphenylmagnesium bromide, the product **5c** was isolated as the single diastereomer. 72% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +94.8° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26-7.21 (m, 1H), 7.18-7.09 (m, 3H), 5.28 (dd, *J* = 8.4, 3.2 Hz, 1H), 3.70-3.53 (m, 2H), 2.77-2.58 (m, 2H), 2.22-2.11 (m, 1H), 1.91-1.73 (m, 2H), 1.67-1.57 (m, 1H), 1.21 (t, *J* = 7.6, 3H), 0.98 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 142.05, 140.22, 128.32, 126.68, 126.33,

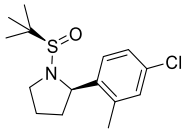
125.61, 57.34, 55.94, 53.21, 35.73, 25.02, 24.37, 22.91, 14.74. HRMS (ESI) m/z calcd for $C_{16}H_{25}NOS$ $[M+H]^+$: 279.1657, found: 279.1655.



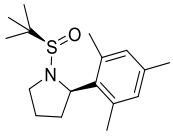
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2-methoxyphenyl)-pyrrolidine (5d): Following general procedure 4, using **(R_S)-1** and 2-methoxyphenylmagnesium bromide, the product **5d** was isolated as the single diastereomer. 56% yield. Colorless oil. $[\alpha]^{25}_D$ = +54.1° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25-7.14 (m, 2H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 5.35 (d, *J* = 7.6 Hz, 1H), 3.79 (s, 3H), 3.69-3.60 (m, 1H), 3.58-3.49 (m, 1H), 2.11-2.02 (m, 1H), 1.90-1.78 (m, 1H), 1.78-1.62 (m, 2H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 156.17, 132.59, 127.71, 127.27, 120.04, 110.17, 57.48, 55.24, 54.95, 52.79, 34.84, 24.05, 23.14. HRMS (ESI) m/z calcd for $C_{15}H_{23}NO_2S$ $[M+H]^+$: 281.1449, found: 281.1446.



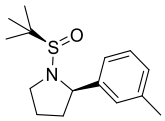
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2,5-dimethylphenyl)-pyrrolidine (5e): Following general procedure 4, using **(R_S)-1** and 2,5-dimethylphenylmagnesium bromide, the product **5e** was isolated as the single diastereomer. 75% yield. Colorless oil. $[\alpha]^{25}_D$ = +91.1° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 7.6 Hz, 1H), 7.00-6.89 (m, 2H), 5.18 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.71-3.54 (m, 2H), 2.27 (d, *J* = 1.2 Hz, 6H), 2.17-2.06 (m, 1H), 1.90-1.75 (m, 2H), 1.64-1.54 (m, 1H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 139.66, 135.94, 134.14, 131.18, 126.44, 126.27, 57.37, 55.76, 53.70, 34.89, 24.19, 22.96, 20.93, 19.40. HRMS (ESI) m/z calcd for $C_{16}H_{25}NOS$ $[M+H]^+$: 279.1657, found: 279.1652.



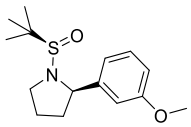
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-chloro-2-methylphenyl)-pyrrolidine (5f): Following general procedure 4, using **(R_S)-1** and 4-chloro-2-methylphenylmagnesium bromide, the product **5f** was isolated as the single diastereomer. 78% yield. White solid, mp 103-106 °C. $[\alpha]^{25}_D$ = +92.5° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 9.2 Hz, 2H), 5.14 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.67-3.52 (m, 2H), 2.27 (s, 3H), 2.17-2.05 (m, 1H), 1.91-1.80 (m, 1H), 1.80-1.68 (m, 1H), 1.60-1.49 (m, 1H), 0.97 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.38, 136.31, 131.93, 130.18, 127.69, 125.86, 57.40, 55.97, 53.22, 34.71, 24.25, 22.87, 19.32. HRMS (ESI) m/z calcd for $C_{15}H_{22}ClNOS$ $[M+H]^+$: 299.1111, found: 299.1114.



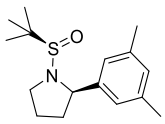
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2,4,6-trimethylphenyl)-pyrrolidine (5g): Following general procedure 4, using **(R_S)-1** and 2,4,6-trimethylphenylmagnesium bromide, the product **5g** was isolated as the single diastereomer. 82% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +48.8° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.78 (d, *J* = 11.6 Hz, 2H), 5.29 (t, *J* = 8.6 Hz, 1H), 3.72-3.56 (m, 2H), 2.41 (d, *J* = 12.4 Hz, 6H), 2.28-2.17 (m, 4H), 1.97-1.88 (m, 1H), 1.87-1.71 (m, 2H), 0.87 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 136.78, 136.44, 135.99, 135.78, 131.14, 129.23, 57.37, 57.29, 52.15, 32.87, 27.49, 22.69, 20.87, 20.74, 20.65. HRMS (ESI) m/z calcd for $C_{17}H_{27}NOS$ $[M+H]^+$: 293.1813, found: 293.1820.



(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(3-methylphenyl)-pyrrolidine (5h): Following general procedure 4, using **(R_S)-1** and 3-methylphenylmagnesium bromide, the product **5h** was isolated as the single diastereomer. 85% yield. White solid, mp 101-102 °C. $[\alpha]^{25}_{D}$ = +82.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19-7.10 (m, 1H), 7.06-6.92 (m, 3H), 4.99 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.68-3.58 (m, 1H), 3.56-3.45 (m, 1H), 2.29 (s, 3H), 2.16-2.05 (m, 1H), 1.88-1.66 (m, 3H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.49, 137.83, 128.18, 127.27, 127.15, 123.51, 57.52, 57.40, 54.71, 36.59, 24.15, 23.08, 21.52. HRMS (ESI) m/z calcd for $C_{15}H_{23}NOS$ $[M+H]^+$: 265.1500, found: 265.1506.

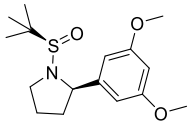


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(3-methoxyphenyl)-pyrrolidine (5i): Following general procedure 4, using **(R_S)-1** and 3-methoxyphenylmagnesium bromide, the product **5i** was isolated as the single diastereomer. 87% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +70.2° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.20 (t, *J* = 8.0 Hz, 1H), 6.84-6.75 (m, 2H), 6.72 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.01 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.76 (s, 3H), 3.67-3.57 (m, 1H), 3.56-3.48 (m, 1H), 2.18-2.06 (m, 1H), 1.90-1.69 (m, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 159.65, 146.43, 129.46, 118.93, 112.44, 111.61, 57.52, 57.41, 55.19, 55.02, 36.65, 24.25, 23.15. HRMS (ESI) m/z calcd for $C_{15}H_{23}NO_2S$ $[M+H]^+$: 281.1449, found: 281.1453.

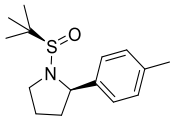


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(3,5-dimethylphenyl)-pyrrolidine (5j): Following general procedure 4, using **(R_S)-1** and 3,5-dimethylphenylmagnesium bromide, the product **5j** was isolated

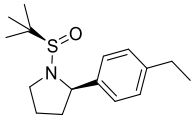
as the single diastereomer. 83% yield. White solid, mp 118-121 °C. $[\alpha]^{25}_{D}$ = +73.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 (s, 3H), 4.96 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.69-3.60 (m, 1H), 3.56-3.47 (m, 1H), 2.28 (s, 6H), 2.17-2.06 (m, 1H), 1.90-1.77 (m, 2H), 1.76-1.67 (m, 1H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.55, 137.75, 128.20, 124.32, 57.65, 57.46, 54.63, 36.64, 24.22, 23.17, 21.45. HRMS (ESI) m/z calcd for $C_{16}H_{25}NOS$ $[M+H]^+$: 279.1657, found: 251.1651.



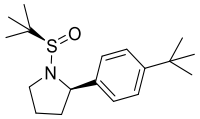
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(3,5-dimethoxyphenyl)-pyrrolidine (5k): Following general procedure 4, using **(*R*$_S$)-1** and 3,5-dimethoxyphenylmagnesium bromide, the product **5k** was isolated as the single diastereomer. 84% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +75.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.38 (d, *J* = 2.0 Hz, 2H), 6.28 (t, *J* = 2.4 Hz, 1H), 4.97 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.75 (s, 6H), 3.64-3.56 (m, 1H), 3.55-3.47 (m, 1H), 2.13-2.05 (m, 1H), 1.88-1.69 (m, 3H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.83, 147.35, 104.68, 98.18, 57.52, 55.30, 55.04, 36.60, 24.32, 23.14. HRMS (ESI) m/z calcd for $C_{16}H_{25}NO_3S$ $[M+H]^+$: 311.1555, found: 311.1560.



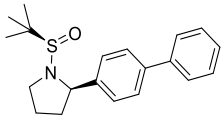
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-methylphenyl)-pyrrolidine (5l): Following general procedure 4, using **(*R*$_S$)-1** and 4-methylphenylmagnesium bromide, the product **5l** was isolated as the single diastereomer. 83% yield. White solid, mp 104-105 °C. $[\alpha]^{25}_{D}$ = +79.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17-7.05 (m, 4H), 5.01 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.69-3.59 (m, 1H), 3.57-3.46 (m, 1H), 2.30 (s, 3H), 2.17-2.06 (m, 1H), 1.88-1.68 (m, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 141.59, 136.10, 129.07, 126.46, 57.47, 54.67, 36.71, 24.16, 23.18, 21.08. HRMS (ESI) m/z calcd for $C_{15}H_{23}NOS$ $[M+H]^+$: 265.1500, found: 265.1508.



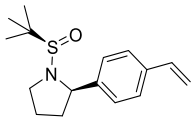
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-ethylphenyl)-pyrrolidine (5m): Following general procedure 4, using **(*R*$_S$)-1** and 4-ethylphenylmagnesium bromide, the product **5m** was isolated as the single diastereomer. 85% yield. White solid, mp 112-114 °C. $[\alpha]^{25}_{D}$ = +91.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17-7.05 (m, 4H), 5.00 (dd, *J* = 8.0, 2.6 Hz, 1H), 3.69-3.58 (m, 1H), 3.55-3.44 (m, 1H), 2.59 (q, *J* = 7.6 Hz, 2H), 2.16-2.04 (m, 1H), 1.89-1.66 (m, 3H), 1.19 (t, *J* = 7.6 Hz, 3H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 142.38, 141.68, 127.77, 126.44, 57.61, 57.43, 54.45, 36.61, 28.39, 24.12, 23.15, 15.43. HRMS (ESI) m/z calcd for $C_{16}H_{25}NOS$ $[M+H]^+$: 279.1657, found: 279.1664.



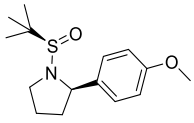
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-*tert*-butylphenyl)-pyrrolidine (5n): Following general procedure 4, using **(R_S)-1** and 4-*tert*-butylphenylmagnesium bromide, the product **5n** was isolated as the single diastereomer. 85% yield. White solid, mp 62-64 °C. $[\alpha]^{25}_{D}$ = +80.9° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 5.03 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.72-3.62 (m, 1H), 3.58-3.46 (m, 1H), 2.20-2.06 (m, 1H), 1.90-1.72 (m, 3H), 1.30 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 149.29, 141.24, 126.14, 125.17, 57.85, 57.47, 54.12, 36.51, 34.40, 31.42, 24.12, 23.19. HRMS (ESI) m/z calcd for $C_{18}H_{29}NOS$ $[M+H]^+$: 307.1970, found: 307.1973.



(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-phenylphenyl)-pyrrolidine (5o): Following general procedure 4, using **(R_S)-1** and 4-phenylphenylmagnesium bromide, the product **5o** was isolated as the single diastereomer. 86% yield. White solid, mp 139-141 °C. $[\alpha]^{25}_{D}$ = +108.9° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.36-7.29 (m, 3H), 5.12 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.74-3.65 (m, 1H), 3.61-3.52 (m, 1H), 2.22 -2.14 (m, 1H), 1.93-1.75 (m, 3H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.70, 140.75, 139.46, 128.77, 127.22, 127.09, 126.99, 57.54, 57.47, 54.74, 36.67, 24.25, 23.20. HRMS (ESI) m/z calcd for $C_{20}H_{25}NOS$ $[M+H]^+$: 327.1657, found: 327.1654.

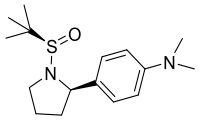


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-vinylphenyl)-pyrrolidine (5p): Following general procedure 4, using **(R_S)-1** and 4-vinylphenylmagnesium bromide, the product **5p** was isolated as the single diastereomer. 81% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +102.1° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.66 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.69 (d, *J* = 17.6 Hz, 1H), 5.18 (d, *J* = 10.8 Hz, 1H), 5.03 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.68-3.58 (m, 1H), 3.57-3.47 (m, 1H), 2.18-2.05 (m, 1H), 1.89-1.66 (m, 3H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.31, 136.43, 135.95, 126.69, 126.26, 113.49, 57.45, 57.26, 54.90, 36.61, 24.20, 23.11. HRMS (ESI) m/z calcd for $C_{16}H_{23}NOS$ $[M+H]^+$: 277.1500, found: 277.1502.

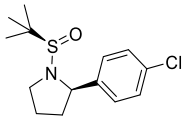


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-methoxyphenyl)-pyrrolidine (5q): Following general procedure 4, using **(R_S)-1** and 4-methoxyphenylmagnesium bromide, the product **5q** was isolated as the single diastereomer. 84% yield. White solid, mp 87-89 °C. $[\alpha]^{25}_{D}$ = +61.5° (c 0.82, CH_2Cl_2).

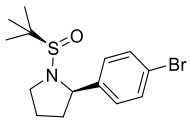
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 4.97 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.76 (s, 3H), 3.68-3.59 (m, 1H), 3.55-3.44 (m, 1H), 2.15 2.05 (m 1H), 1.90-1.75 (m, 2H), 1.75-1.65 (m, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 158.34, 136.73, 127.72, 113.79, 57.53, 57.46, 55.29, 54.39, 36.74, 24.23, 23.26. HRMS (ESI) m/z calcd for $C_{15}H_{23}NO_2S$ $[M+H]^+$: 281.1449, found: 281.1445.



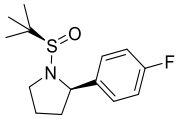
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-*N*,*N*-dimethylphenyl)-pyrrolidine (5r): Following general procedure 4, using **(*R*$_S$)-1** and 4-*N*,*N*-dimethylphenylmagnesium bromide, the product **5r** was isolated as the single diastereomer. 83% yield. Colorless oil. $[\alpha]^{25}_D$ = +102.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 (d, *J* = 8.8 Hz, 2H), 6.67 (d, *J* = 8.8 Hz, 2H), 4.94 (dd, *J* = 7.6, 2.4 Hz, 1H), 3.69-3.60 (m, 1H), 3.52-3.42 (m, 1H), 2.91 (s, 6H), 2.13-2.01 (m, 1H), 1.89-1.76 (m, 2H), 1.76-1.67 (m, 1H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 149.33, 132.23, 127.39, 112.43, 57.76, 57.41, 53.93, 40.65, 36.64, 24.14, 23.26. HRMS (ESI) m/z calcd for $C_{16}H_{26}N_2OS$ $[M+H]^+$: 294.1766, found: 294.1770.



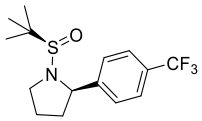
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-chlorophenyl)-pyrrolidine (5s): Following general procedure 4, using **(*R*$_S$)-1** and 4-chlorophenylmagnesium bromide, the product **5s** was isolated as the single diastereomer. 83% yield. White solid, mp 105-108 °C. $[\alpha]^{25}_D$ = +83.8° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32-7.25 (m, 2H), 7.22-7.16 (m, 2H), 5.04 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.69-3.61 (m, 1H), 3.60-3.51 (m, 1H), 2.21-2.10 (m, 1H), 1.94-1.84 (m, 1H), 1.84-1.75 (m, 1H), 1.75-1.67 (m, 1H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.28, 132.31, 128.57, 127.94, 57.52, 56.94, 54.92, 36.60, 24.22, 23.11. HRMS (ESI) m/z calcd for $C_{14}H_{20}ClNOS$ $[M+H]^+$: 285.0954, found: 285.0960.



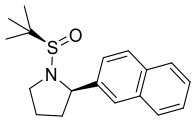
(*R*$_S$,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-bromophenyl)-pyrrolidine (5t): Following general procedure 4, using **(*R*$_S$)-1** and 4-bromophenylmagnesium bromide, the product **5t** was isolated as the single diastereomer. 82% yield. White solid, mp 112-114 °C. $[\alpha]^{25}_D$ = +65.1° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 5.01 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.67-3.58 (m, 1H), 3.58-3.48 (m, 1H), 2.19-2.09 (m, 1H), 1.92-1.82 (m, 1H), 1.82-1.74 (m, 1H), 1.74-1.66 (m, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.90, 131.61, 128.40, 120.48, 57.63, 57.04, 55.07, 36.64, 24.29, 23.20. HRMS (ESI) m/z calcd for $C_{14}H_{20}BrNOS$ $[M+H]^+$: 329.0449, found: 329.0446.



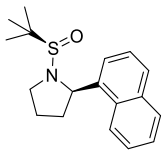
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-fluorophenyl)-pyrrolidine (5u): Following general procedure 4, using **(R_S)-1** and 4-fluorophenylmagnesium bromide, the product **5u** was isolated as the single diastereomer. 84% yield. White solid, mp 84-85 °C. $[\alpha]^{25}_{D}$ = +58.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21-7.12 (m, 2H), 7.00-6.89 (m, 2H), 4.99 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.64-3.56 (m, 1H), 3.53-3.44 (m, 1H), 2.16-2.03 (m, 1H), 1.88-1.71 (m, 2H), 1.71-1.62 (m, 1H), 0.99 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 161.55 (d, *J* = 243.1 Hz), 140.37 (d, *J* = 3.1 Hz), 128.04 (d, *J* = 7.8 Hz), 115.18 (d, *J* = 21.1 Hz), 57.46, 57.06, 54.60, 36.62, 24.16, 23.08. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -116.27 - -116.53 (m, 1F). HRMS (ESI) m/z calcd for $C_{14}H_{20}FNOS$ $[M+H]^+$: 269.1250, found: 269.1256.



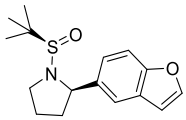
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(4-(trifluoromethyl)phenyl)-pyrrolidine (5v): Following general procedure 4, using **(R_S)-1** and 4-(trifluoromethyl)phenylmagnesium bromide, the product **5v** was isolated as the single diastereomer. 53% yield. White solid, mp 107-109 °C. $[\alpha]^{25}_{D}$ = +71.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.09 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.67-3.59 (m, 1H), 3.58-3.50 (m, 1H), 2.22-2.11 (m, 1H), 1.91-1.82 (m, 1H), 1.81-1.65 (m, 2H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 148.89, 128.96 (q, *J* = 32.2 Hz), 126.85, 125.46 (q, *J* = 3.8 Hz), 124.23 (q, *J* = 270.2 Hz), 57.59, 57.14, 55.12, 36.54, 24.23, 23.05. ^{19}F NMR (565 MHz, Chloroform-*d*) δ -62.40 (s, 3F). HRMS (ESI) m/z calcd for $C_{15}H_{20}F_3NOS$ $[M+H]^+$: 319.1218, found:319.1216.



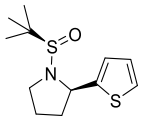
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2-naphthyl)-pyrrolidine (5w): Following general procedure 4, using **(R_S)-1** and 2-naphthylmagnesium bromide, the product **5w** was isolated as the single diastereomer. 81% yield. White solid, mp 120-122 °C. $[\alpha]^{25}_{D}$ = +114.9° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85-7.75 (m, 3H), 7.69 (s, 1H), 7.49-7.40 (m, 2H), 7.36 (dd, *J* = 8.4, 1.6 Hz, 1H), 5.24 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.80-3.69 (m, 1H), 3.66-3.55 (m, 1H), 2.28-2.14 (m, 1H), 1.94-1.75 (m, 3H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 142.00, 133.18, 132.31, 128.24, 127.73, 127.58, 126.08, 125.54, 124.99, 124.83, 57.52, 57.42, 55.02, 36.45, 24.23, 23.05. HRMS (ESI) m/z calcd for $C_{18}H_{23}NOS$ $[M+H]^+$: 301.1500, found: 301.1504.



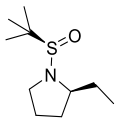
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(1-naphthyl)-pyrrolidine (5x): Following general procedure 4, using **(R_S)-1** and 1-naphthylmagnesium bromide, the product **5x** was isolated as the single diastereomer. 71% yield. Pale yellow solid, mp 123-125 °C. $[\alpha]^{25}_{D}$ = +77.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.6, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.55-7.39 (m, 4H), 5.90-5.81 (m, 1H), 3.82-3.72 (m, 1H), 3.72-3.63 (m, 1H), 2.36-2.21 (m, 1H), 1.98-1.86 (m, 1H), 1.86-1.69 (m, 2H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 139.59, 133.86, 130.32, 128.82, 127.31, 126.09, 125.62, 125.13, 123.59, 123.46, 57.50, 55.65, 54.06, 35.44, 24.31, 22.98. HRMS (ESI) m/z calcd for $C_{18}H_{23}NOS$ $[M+H]^+$: 301.1500, found: 301.1506.



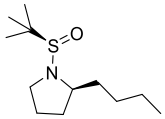
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(5-benzofuranyl)-pyrrolidine (5y): Following general procedure 4, using **(R_S)-1** and 5-benzofuranylmagnesium bromide, the product **5y** was isolated as the single diastereomer. 52% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +73.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (s, 1H), 7.51-7.39 (m, 2H), 7.17 (d, *J* = 8.8 Hz, 1H), 6.73 (s, 1H), 5.15 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.80-3.65 (m, 1H), 3.63-3.48 (m, 1H), 2.26-2.10 (m, 1H), 1.92-1.71 (m, 3H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.94, 145.44, 139.36, 127.46, 123.14, 118.96, 111.27, 106.71, 57.86, 57.57, 54.74, 37.10, 24.23, 23.26. HRMS (ESI) m/z calcd for $C_{16}H_{21}NO_2S$ $[M+H]^+$: 291.1293, found: 291.1290.



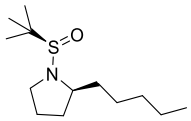
(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-(2-thiophenyl)-pyrrolidine (5z): Following general procedure 4, using **(R_S)-1** and 2-thiophenylmagnesium bromide, the product **5z** was isolated as the single diastereomer. 40% yield. White solid, mp 123-126 °C. $[\alpha]^{25}_{D}$ = +40.5° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (d, *J*=4.8 Hz), 6.95-6.89 (m, 1H), 6.86 (d, *J* = 2.8 Hz, 1H), 5.31-5.19 (m, 1H), 3.67-3.58 (m, 1H), 3.51-3.40 (m, 1H), 2.15-2.04 (m, 1H), 1.96-1.85 (m, 3H), 1.11 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 148.90, 126.82, 123.91, 123.73, 57.67, 54.23, 53.93, 36.78, 24.32, 23.00. HRMS (ESI) m/z calcd for $C_{12}H_{19}NOS_2$ $[M+H]^+$: 257.0908, found: 257.0903.



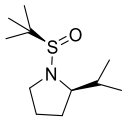
(R_S,*S*)-*N*-(*tert*-Butylsulfinyl)-2-ethyl-pyrrolidine (5aa): Following general procedure 4, using **(R_S)-1** and ethylmagnesium bromide, the product **5aa** was isolated as an 80:20 mixture of diastereomers. 78% yield. Colorless oil. $[\alpha]^{25}_{D}$ = -15.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.59-3.47 (m, 1H), 3.46-3.38 (m, 1H), 3.16-3.02 (m, 1H), 1.84-1.64 (m, 4H), 1.62 -1.48 (m, 1H), 1.44-1.33 (m, 1H), 1.15 (s, 9H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 60.40, 57.35, 48.25, 30.24, 27.28, 24.29, 23.63, 11.09. HRMS (ESI) m/z calcd for $C_{10}H_{21}NOS$ $[M+H]^+$: 203.1344, found: 203.1349.



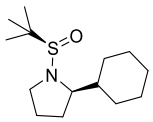
(R_S,*S*)-*N*-(*tert*-Butylsulfinyl)-2-butyl-pyrrolidine (5ab): Following general procedure 4, using **(R_S)-1** and butylmagnesium chloride, the product **5ab** was isolated as an 85:15 mixture of diastereomers. 81% yield. Colorless oil. $[\alpha]_D^{25}$ = -3.3° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.56-3.46 (m, 1H), 3.42-3.32 (m, 1H), 3.07-2.96 (m, 1H), 1.76-1.56 (m, 4H), 1.53 -1.42 (m, 1H), 1.36-1.14 (m, 5H), 1.09 (s, 9H), 0.79 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 59.05, 57.23, 47.90, 34.03, 30.68, 28.99, 24.19, 23.55, 22.69, 14.05. HRMS (ESI) m/z calcd for $C_{12}H_{25}NOS$ $[M+H]^+$: 231.1657, found: 231.1662.



(R_S,*S*)-*N*-(*tert*-Butylsulfinyl)-2-pentyl-pyrrolidine (5ac): Following general procedure 4, using **(R_S)-1** and pentylmagnesium bromide, the product **5ac** was isolated as an 85:15 mixture of diastereomers. 77% yield. Colorless oil. $[\alpha]_D^{25}$ = +1.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.63-3.53 (m, 1H), 3.48-3.38 (m, 1H), 3.16-3.01 (m, 1H), 1.84-1.71 (m, 3H), 1.71 -1.61 (m, 1H), 1.60-1.48 (m, 1H), 1.42-1.19 (m, 7H), 1.15 (s, 9H), 0.84 (t, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 59.18, 57.36, 48.04, 34.37, 31.89, 30.79, 26.58, 24.31, 23.67, 22.69, 14.08. HRMS (ESI) m/z calcd for $C_{13}H_{27}NOS$ $[M+H]^+$: 245.1813, found: 257.1816.

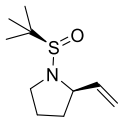


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-isopropyl-pyrrolidine (5ad): Following general procedure 4, using **(R_S)-1** and isopropylmagnesium chloride, the product **5ad** was isolated as an 90:10 mixture of diastereomers. 83% yield. Colorless oil. $[\alpha]_D^{25}$ = +1.7° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.68-3.51 (m, 1H), 3.43-3.29 (m, 1H), 3.28-3.09 (m, 1H), 2.18-2.02 (m, 1H), 1.80 -1.56 (m, 4H), 1.19 (s, 9H), 0.88 (dd, *J* = 12.0, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 62.99, 57.75, 50.58, 31.16, 26.23, 25.51, 23.60, 20.27, 16.78. HRMS (ESI) m/z calcd for $C_{11}H_{23}NOS$ $[M+H]^+$: 217.1500, found: 217.1507.

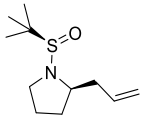


(R_S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-cyclohexyl-pyrrolidine (5ae): Following general procedure 4, using **(R_S)-1** and cyclohexylmagnesium bromide, the product **5ae** was isolated as an 91:9 mixture of diastereomers. 82% yield. Colorless oil. $[\alpha]_D^{25}$ = +20.1° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.54-3.45 (m, 1H), 3.35-3.23 (m, 1H), 3.19-3.06 (m, 1H), 1.76-1.55 (m, 10H), 1.24 -1.11 (m, 11H), 1.11-1.02 (m, 1H), 0.98-0.82 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 62.74,

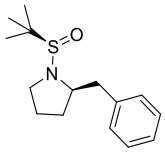
57.52, 49.90, 41.48, 30.65, 27.38, 27.19, 26.54, 26.49, 26.23, 25.19, 23.44. HRMS (ESI) m/z calcd for $C_{14}H_{27}NOS$ $[M+H]^+$: 257.1813, found: 257.1815.



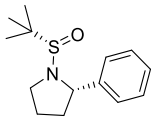
(*R*S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-vinyl-pyrrolidine (5af): Following general procedure 4, using **(*R*S)-1** and vinylmagnesium bromide, the product **5af** was isolated as the single diastereomer. 67% yield. Colorless oil. $[\alpha]_D^{25}$ = -51.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.70-5.54 (m, 1H), 5.12 (d, *J* =16.8 Hz, 1H), 5.02 (d, *J* = 10.4 Hz, 1H), 3.98 (q, *J* = 7.2 Hz, 1H), 3.79-3.64 (m, 1H), 2.82-2.67 (m, 1H), 2.02-1.93 (m, 1H), 1.89-1.80 (m, 1H), 1.77-1.65 (m, 1H), 1.61-1.49 (m, 1H), 1.14 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 140.26, 115.91, 68.05, 57.14, 41.41, 32.73, 25.93, 23.90. HRMS (ESI) m/z calcd for $C_{10}H_{19}NOS$ $[M+H]^+$: 201.1187, found: 201.1184.



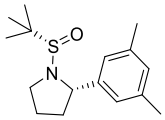
(*R*S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-allyl-pyrrolidine (5ag): Following general procedure 4, using **(*R*S)-1** and allylmagnesium chloride, the product **5ag** was isolated as the single diastereomer. 72% yield. Colorless oil. $[\alpha]_D^{25}$ = -4.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.83-5.60 (m, 1H), 5.12-4.95 (m, 2H), 3.79-3.66 (m, 1H), 3.52-3.40 (m, 1H), 3.18-3.04 (m, 1H), 2.52-2.40 (m, 1H), 2.21-2.10 (m, 1H), 1.85-1.71 (m, 3H), 1.69-1.58 (m, 1H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 135.20, 117.30, 58.15, 57.50, 48.46, 38.93, 30.32, 24.09, 23.64. HRMS (ESI) m/z calcd for $C_{11}H_{21}NOS$ $[M+H]^+$: 215.1344, found: 215.1350.



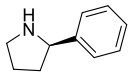
(*R*S,*R*)-*N*-(*tert*-Butylsulfinyl)-2-benzyl-pyrrolidine (5ah): Following general procedure 4, using **(*R*S)-1** and benzylmagnesium chloride, the product **5ah** was isolated as the single diastereomer. 75% yield. Colorless oil. $[\alpha]_D^{25}$ = -37.6° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31-7.24 (m, 2H), 7.23-7.15 (m, 3H), 3.89-3.70 (m, 2H), 3.01 (dd, *J* = 13.2, 5.2 Hz, 1H), 2.87-2.75 (m, 1H), 2.52 (dd, *J* = 12.8, 9.6 Hz, 1H), 1.89-1.74 (m, 2H), 1.74-1.65 (m, 1H), 1.55-1.45 (m, 1H), 1.17 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 138.73, 129.19, 128.44, 126.35, 67.24, 57.14, 43.42, 41.60, 31.24, 25.85, 23.91. HRMS (ESI) m/z calcd for $C_{15}H_{23}NOS$ $[M+H]^+$: 265.1500, found: 265.1504.



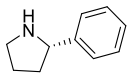
(S_S,*S*)-*N*-(*tert*-Butylsulfinyl)-2-phenyl-pyrrolidine (S_S,*S*)-5a: Following general procedure 4, using **(S_S)-1** and phenylmagnesium bromide, the product **(S_S,*S*)-5a** was isolated as the single diastereomer. 85% yield. White solid, mp 85-86 °C. $[\alpha]^{25}_{D}$ = -64.4° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36-7.17 (m, 5H), 5.07 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.71-3.63 (m, 1H), 3.61-3.52 (m, 1H), 2.19-2.09 (m, 1H), 1.93-1.72 (m, 3H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.68, 128.42, 126.62, 126.56, 57.52, 55.00, 36.71, 24.25, 23.17. HRMS (ESI) m/z calcd for $C_{14}H_{21}NOS$ $[M+H]^+$: 251.1344, found: 251.1348.



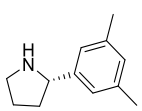
(S_S,*S*)-*N*-(*tert*-Butylsulfinyl)-2-(3,5-dimethylphenyl)-pyrrolidine (*Ss*,*S*)-5j: Following general procedure 4, using **(S_S)-1** and 3,5-dimethylphenylmagnesium bromide, the product **(*Ss*,*S*)-5j** was isolated as the single diastereomer. 82% yield. White solid, mp 117-119 °C. $[\alpha]^{25}_{D}$ = -71.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.81 (s, 3H), 4.95 (dd, *J* = 8.0, 2.4 Hz, 1H), 3.67-3.58 (m, 1H), 3.54-3.45 (m, 1H), 2.26 (s, 6H), 2.15-2.04 (m, 1H), 1.87-1.75 (m, 2H), 1.74-1.66 (m, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.45, 137.64, 128.13, 124.25, 57.67, 57.37, 54.45, 36.53, 24.17, 23.08, 21.34. HRMS (ESI) m/z calcd for $C_{16}H_{25}NOS$ $[M+H]^+$: 279.1657, found: 279.1662.



(*R*)-2-Phenyl-pyrrolidine (6a): The compound **6a** was synthesized by the General Procedure 7 using **5a** and HCl (2 M in MeOH). 98% yield. Colorless oil. $[\alpha]^{25}_{D}$ = +14.0° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31-7.19 (m, 4H), 7.18-7.11 (m, 1H), 4.02 (t, *J* = 8.0 Hz, 1H), 3.24-3.16 (m, 1H), 3.06-2.96 (m, 1H), 2.49 (br, s, 1H) 2.16-2.05 (m, 1H), 1.90-1.71 (m, 2H), 1.65-1.54 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.62, 128.41, 126.87, 126.60, 62.64, 46.98, 34.33, 25.62. HRMS (ESI) m/z calcd for $C_{10}H_{13}N$ $[M+H]^+$: 147.1048, found: 147.1044.

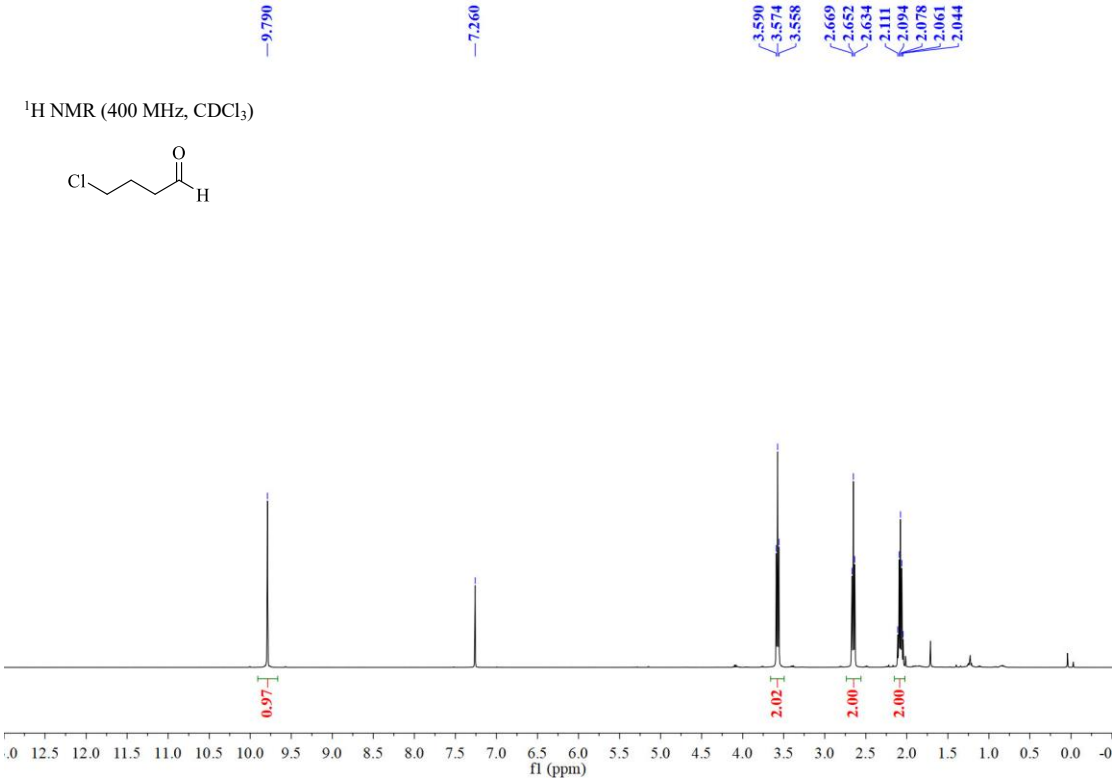


(*S*)-2-Phenyl-pyrrolidine (*S*)-6a: The compound **(*S*)-6a** was synthesized by the General Procedure 5 using **(S_S,*S*)-5a** and HCl (2 M in MeOH). 97% yield. Colorless oil. $[\alpha]^{25}_{D}$ = -15.8° (c 1.00, CH_2Cl_2). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40-7.28 (m, 4H), 7.26-7.20 (m, 1H), 4.12 (t, *J* = 8.0 Hz, 1H), 3.24-3.16 (m, 1H), 3.06-2.97 (m, 1H), 2.51 (br, s, 1H), 2.24-2.15 (m, 1H), 1.98-1.82 (m, 2H), 1.75-1.64 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 143.92, 128.53, 127.12, 126.73, 62.73, 46.87, 34.18, 25.56. HRMS (ESI) m/z calcd for $C_{10}H_{13}N$ $[M+H]^+$: 147.1048, found: 147.1042.

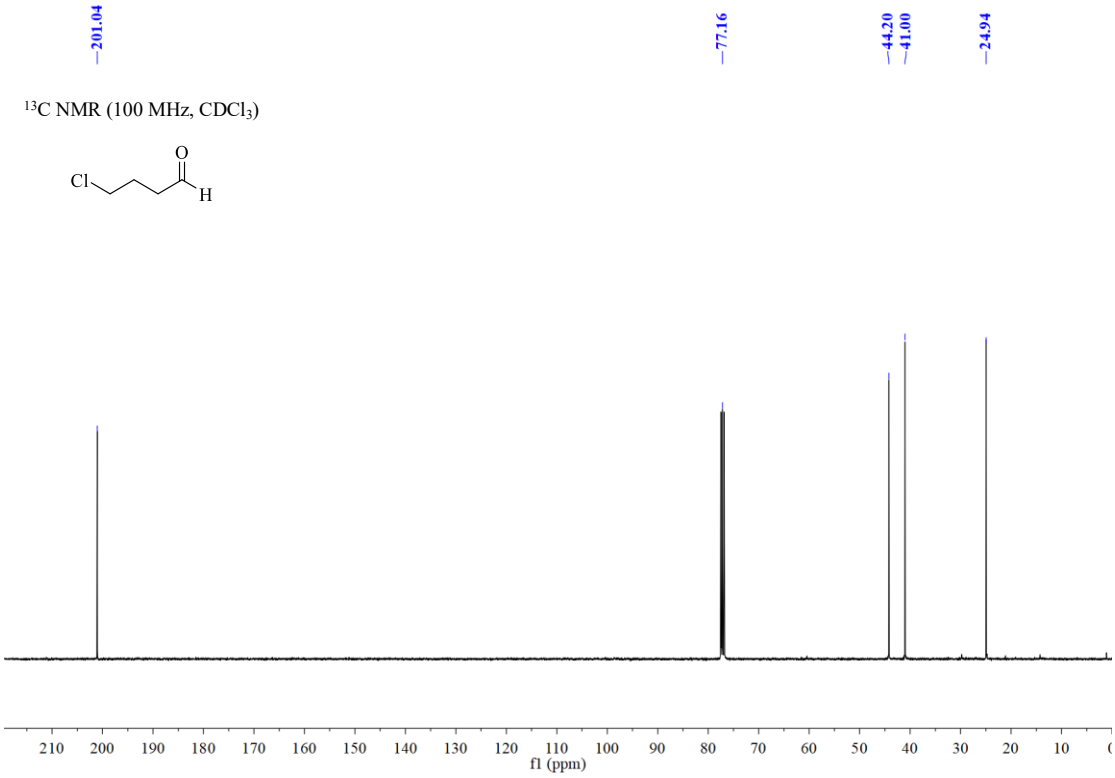


(*S*)-2-(3,5-Dimethylphenyl)-pyrrolidine (*S*)-6j: The compound **(*S*)-6j** was synthesized by the General Procedure 5 using **(*S*$_S$,*S*)-5j** and HCl (2 M in MeOH). 97% yield. $[\alpha]^{25}_{D}$ = -39.6° (c 1.00, CH_2Cl_2). Colorless oil. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.00 (s, 2H), 6.88 (s, 1H), 4.02 (t, *J* = 8.0 Hz, 1H), 3.22-3.14 (m, 1H), 3.02-2.94 (m, 1H), 2.71 (br, s, 1H), 2.32 (s, 6H), 2.20-2.10 (m, 1H), 1.98-1.77 (m, 2H), 1.72-1.61 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.2, 137.4, 128.2, 124.1, 62.3, 46.6, 34.0, 25.2, 21.0. HRMS (ESI) m/z calcd for $C_{12}H_{17}N$ $[M+H]^+$: 175.1361, found: 175.1364.

8. ^{1}H-NMR, ^{19}F-NMR and ^{13}C-NMR Spectra of Compounds

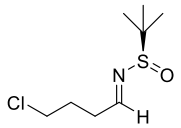


^{1}H NMR (400 MHz, $CDCl_3$)



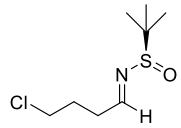
^{13}C NMR (100 MHz, $CDCl_3$)

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



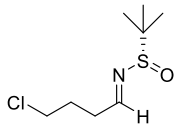
(R_S)-1

^{13}C NMR (100 MHz, $CDCl_3$)



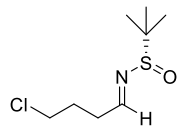
(R_S)-1

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



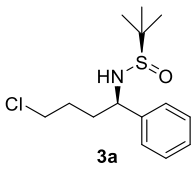
(S_S)-1

^{13}C NMR (100 MHz, $CDCl_3$)



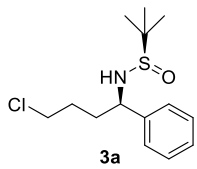
(S_S)-1

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



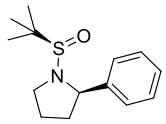
3a

^{13}C NMR (100 MHz, $CDCl_3$)



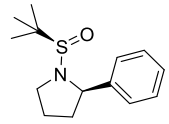
3a

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



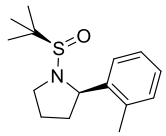
5a

^{13}C NMR (100 MHz, $CDCl_3$)



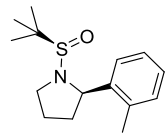
5a

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



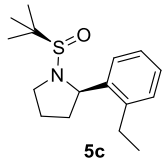
5b

^{13}C NMR (100 MHz, $CDCl_3$)



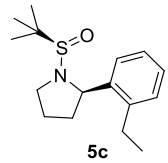
5b

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



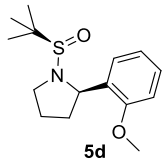
5c

^{13}C NMR (100 MHz, $CDCl_3$)



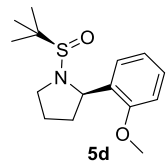
5c

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



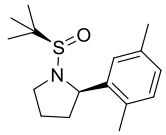
5d

^{13}C NMR (100 MHz, $CDCl_3$)



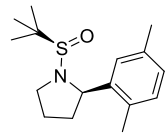
5d

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



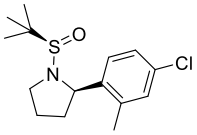
5e

^{13}C NMR (100 MHz, $CDCl_3$)



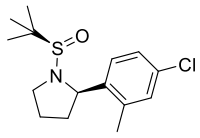
5e

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



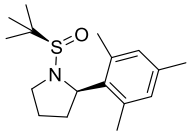
5f

^{13}C NMR (100 MHz, $CDCl_3$)



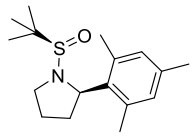
5f

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



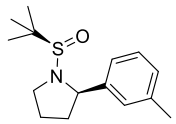
5g

^{13}C NMR (100 MHz, $CDCl_3$)



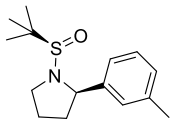
5g

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



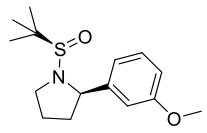
5h

^{13}C NMR (100 MHz, $CDCl_3$)



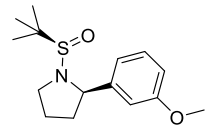
5h

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



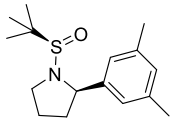
5i

^{13}C NMR (100 MHz, $CDCl_3$)



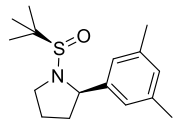
5i

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



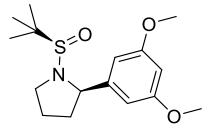
5j

^{13}C NMR (100 MHz, $CDCl_3$)



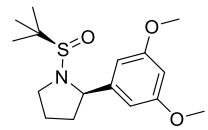
5j

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



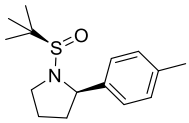
5k

^{13}C NMR (100 MHz, $CDCl_3$)



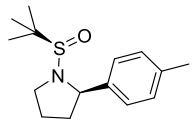
5k

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



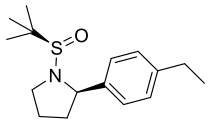
5l

^{13}C NMR (100 MHz, $CDCl_3$)



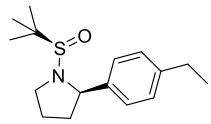
5l

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



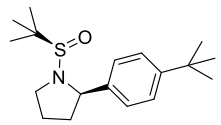
5m

^{13}C NMR (100 MHz, $CDCl_3$)



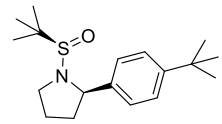
5m

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



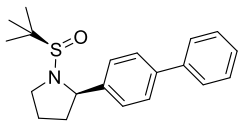
5n

^{13}C NMR (100 MHz, $CDCl_3$)



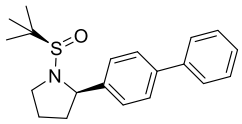
5n

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

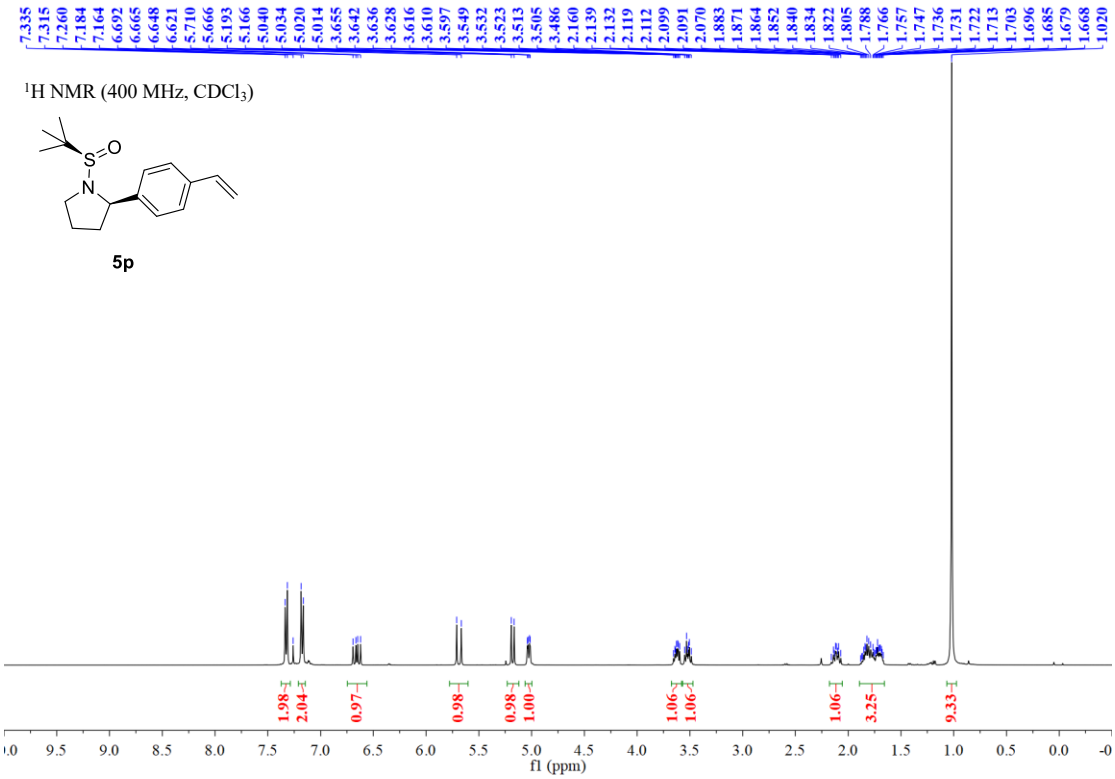


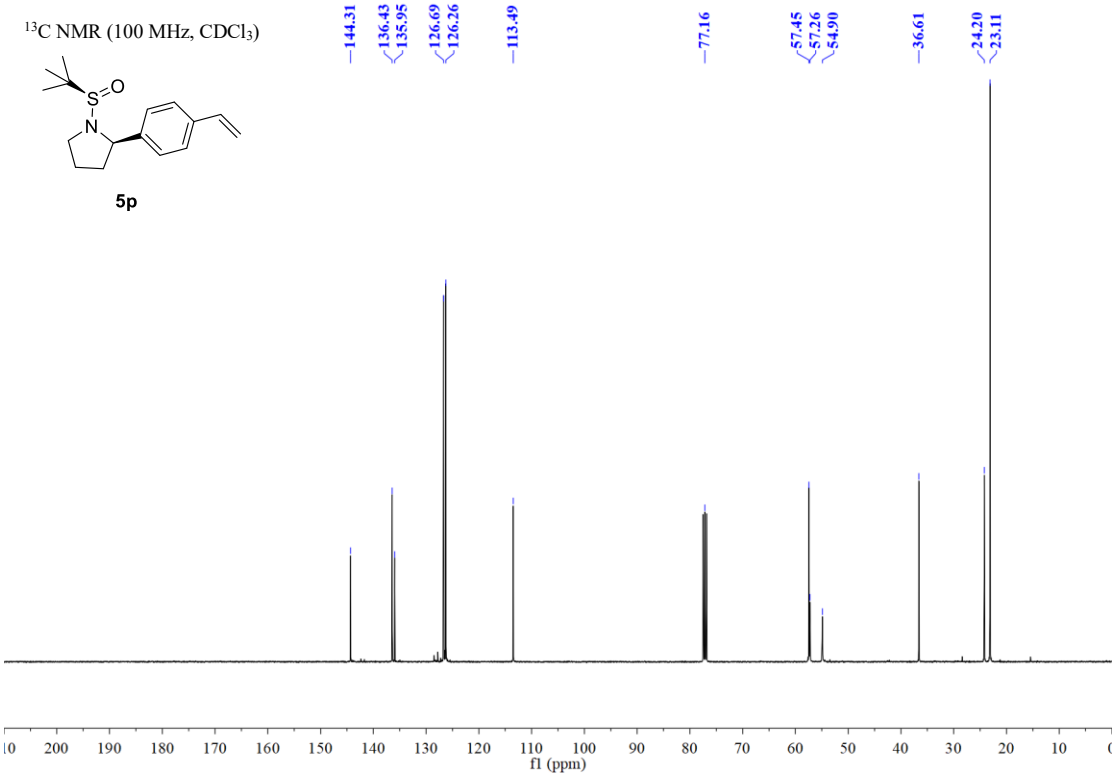
5o

^{13}C NMR (100 MHz, $CDCl_3$)

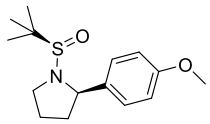


5o


7.335
7.315
7.260
7.184
7.164
6.692
6.665
6.648
6.621
5.710
5.666
5.193
5.166
5.040
5.034
5.020
5.014
3.655
3.642
3.636
3.628
3.616
3.610
3.597
3.549
3.532
3.523
3.513
3.505
3.486
2.160
2.139
2.132
2.119
2.112
2.099
2.091
2.070
1.883
1.871
1.864
1.852
1.840
1.834
1.822
1.805
1.788
1.766
1.757
1.747
1.736
1.731
1.722
1.713
1.703
1.696
1.685
1.679
1.668
1.020
1H NMR (400 MHz, CDCl3)
S
O
N
5p
1.98
2.04
0.97
0.98
0.98
1.00
1.06
1.06
1.06
3.25
9.33
f1 (ppm)

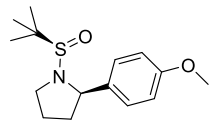

144.31
136.43
135.95
126.69
126.26
113.49
77.16
57.45
57.26
54.90
36.61
24.20
23.11
13C NMR (100 MHz, CDCl3)
S
O
N
5p
f1 (ppm)

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



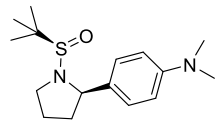
5q

^{13}C NMR (100 MHz, $CDCl_3$)



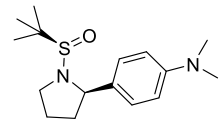
5q

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



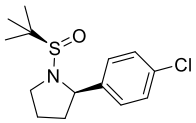
5r

^{13}C NMR (100 MHz, $CDCl_3$)



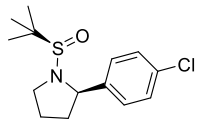
5r

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



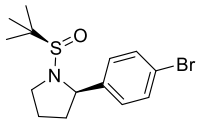
5s

^{13}C NMR (100 MHz, $CDCl_3$)



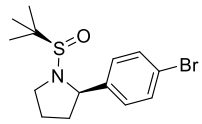
5s

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

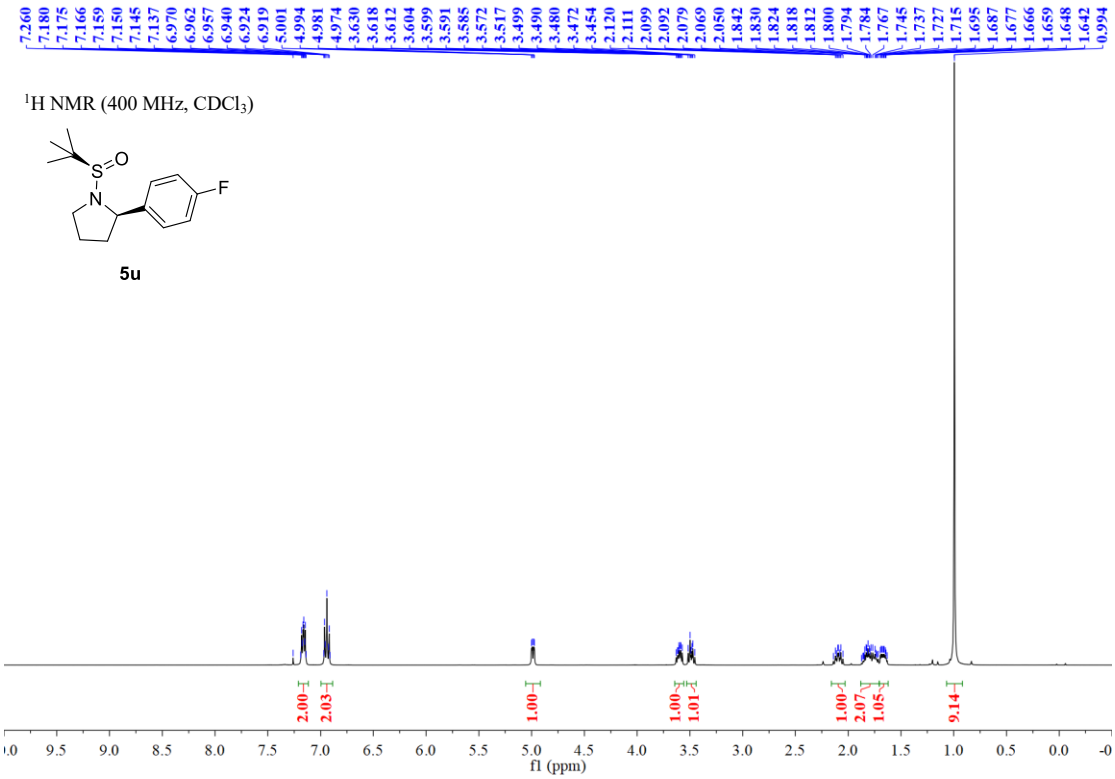


5t

^{13}C NMR (100 MHz, $CDCl_3$)

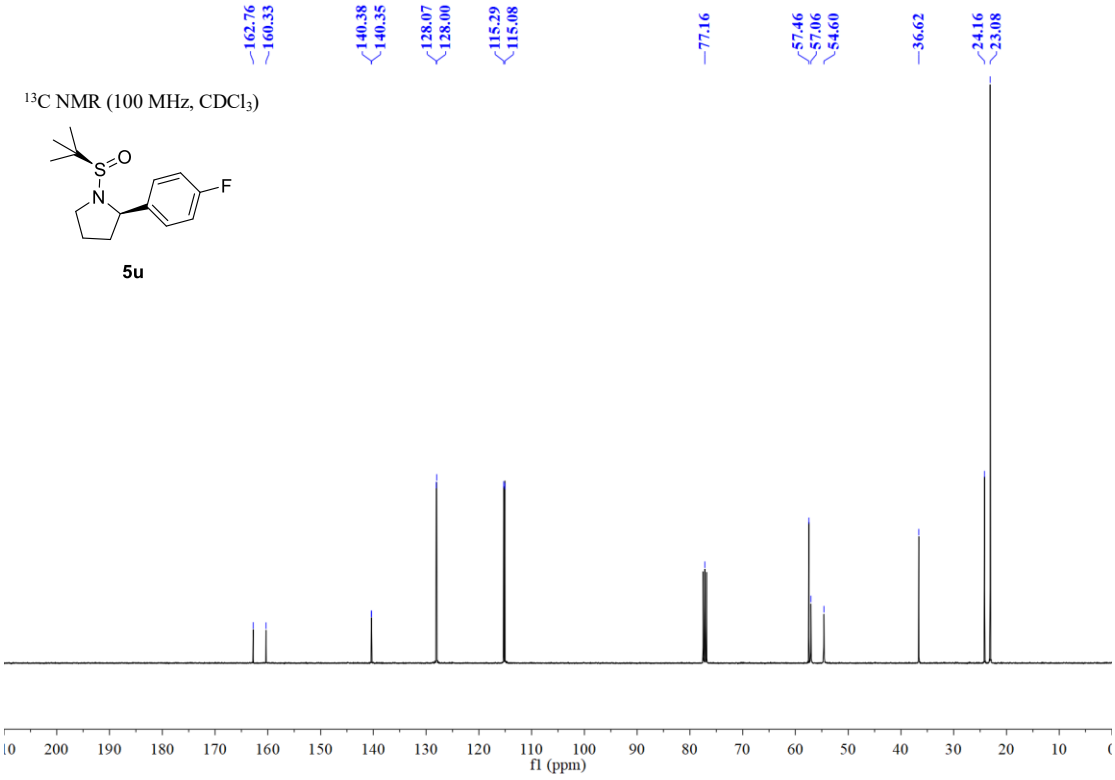


5t



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

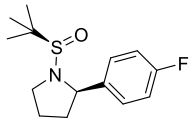
5u



^{13}C NMR (100 MHz, $CDCl_3$)

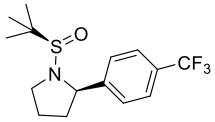
5u

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



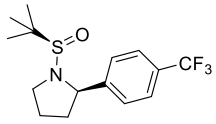
5u

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



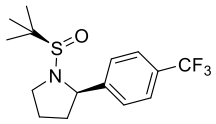
5v

^{13}C NMR (100 MHz, $CDCl_3$)



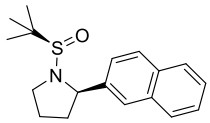
5v

^{19}F NMR (565 MHz, $CDCl_3$)



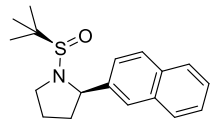
5v

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

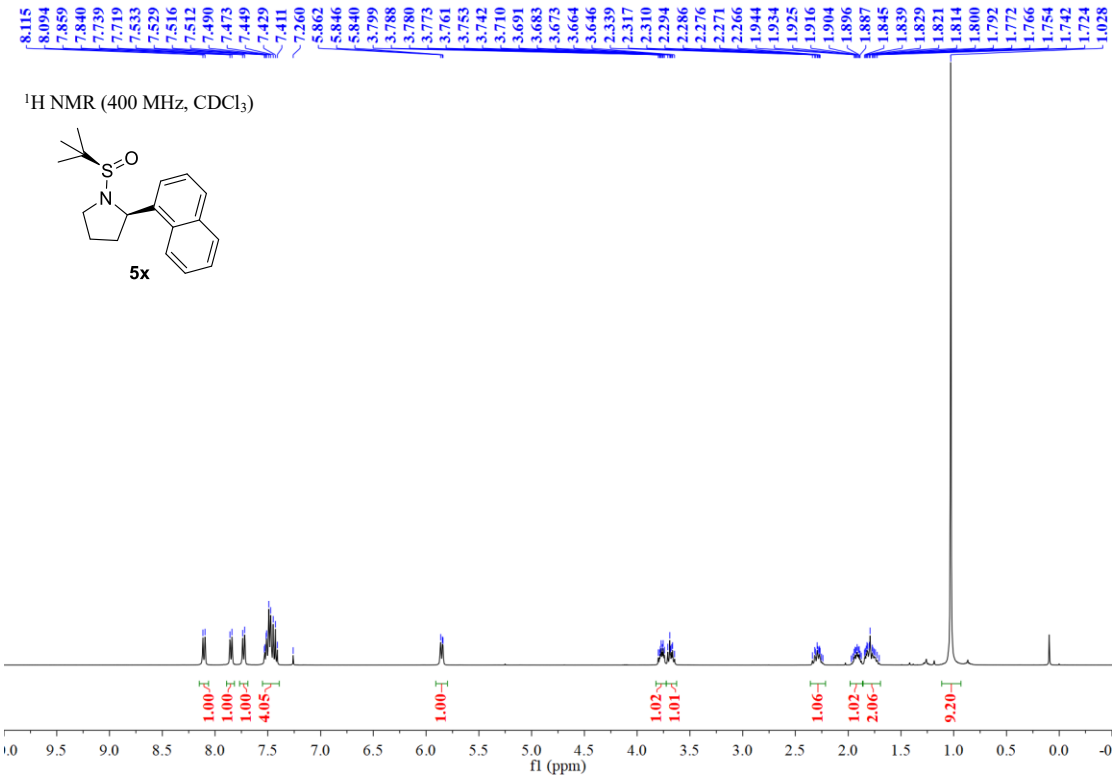


5w

^{13}C NMR (100 MHz, $CDCl_3$)

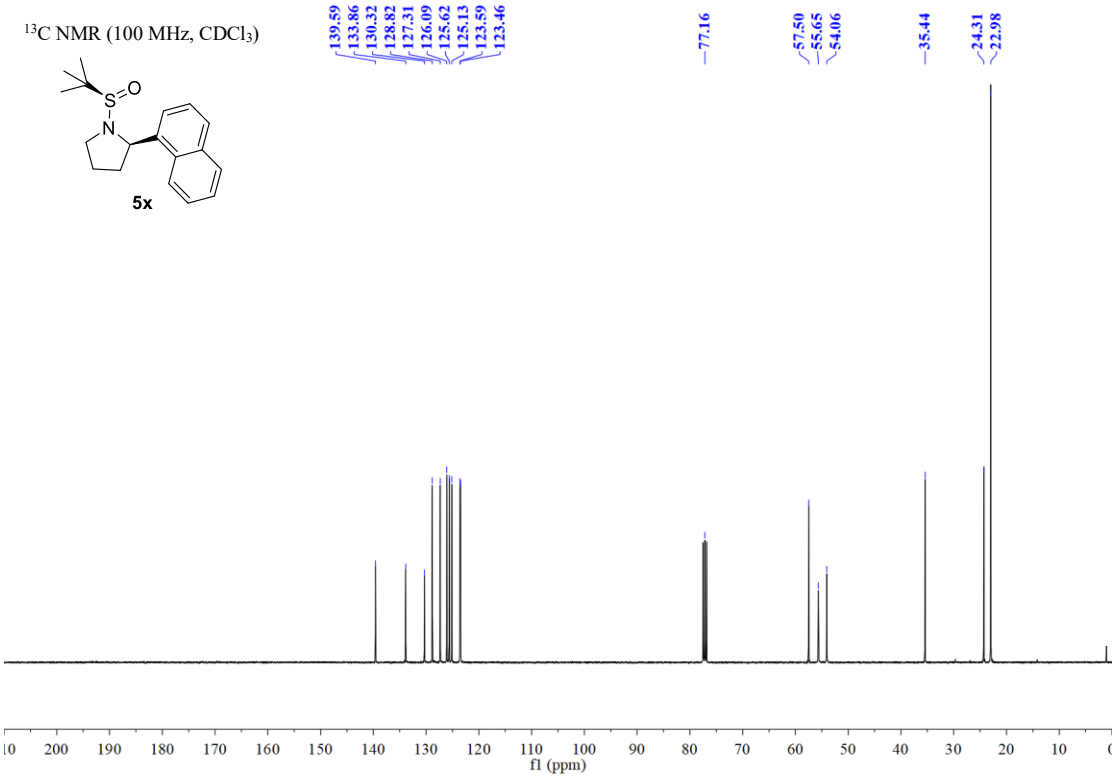


5w



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

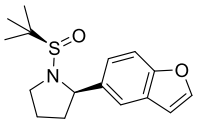
5x



^{13}C NMR (100 MHz, $CDCl_3$)

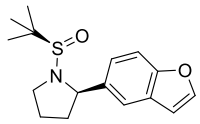
5x

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



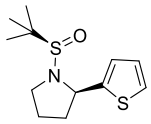
5y

^{13}C NMR (100 MHz, $CDCl_3$)



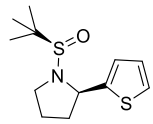
5y

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



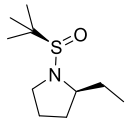
5z

^{13}C NMR (100 MHz, $CDCl_3$)



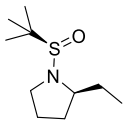
5z

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



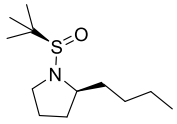
5aa

^{13}C NMR (100 MHz, $CDCl_3$)



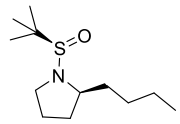
5aa

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



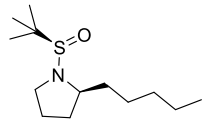
5ab

^{13}C NMR (100 MHz, $CDCl_3$)



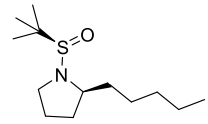
5ab

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



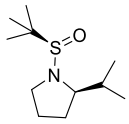
5ac

^{13}C NMR (100 MHz, $CDCl_3$)



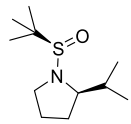
5ac

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

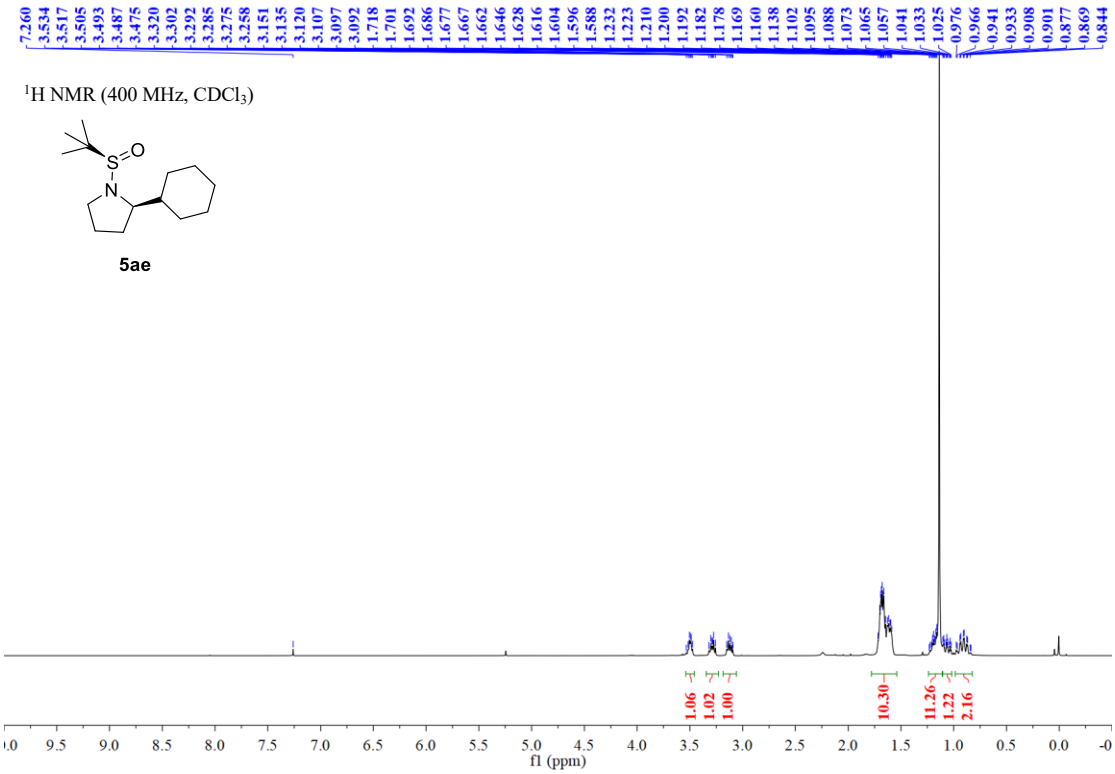


5ad

^{13}C NMR (100 MHz, $CDCl_3$)

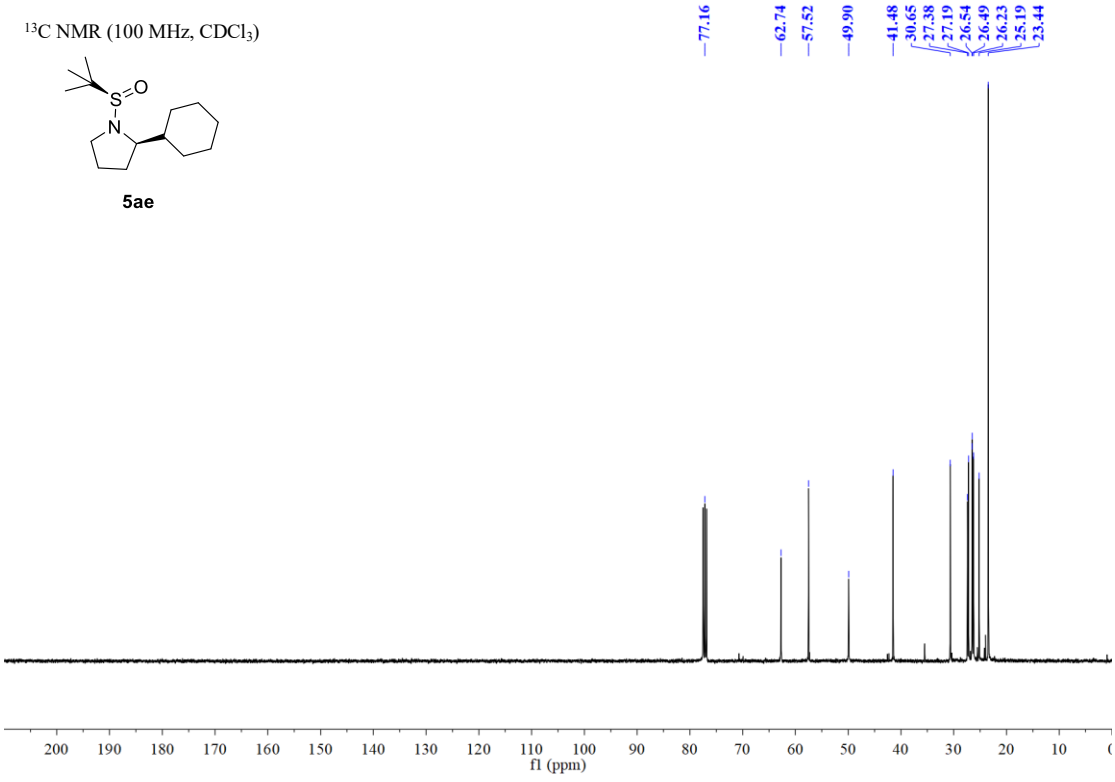


5ad



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

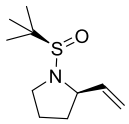
5ae



^{13}C NMR (100 MHz, $CDCl_3$)

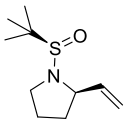
5ae

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



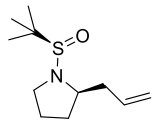
5af

^{13}C NMR (100 MHz, $CDCl_3$)



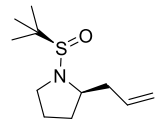
5af

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



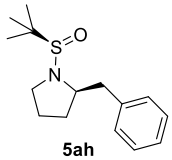
5ag

^{13}C NMR (100 MHz, $CDCl_3$)



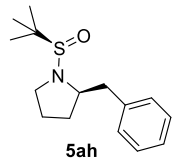
5ag

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



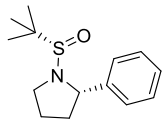
5ah

^{13}C NMR (100 MHz, $CDCl_3$)



5ah

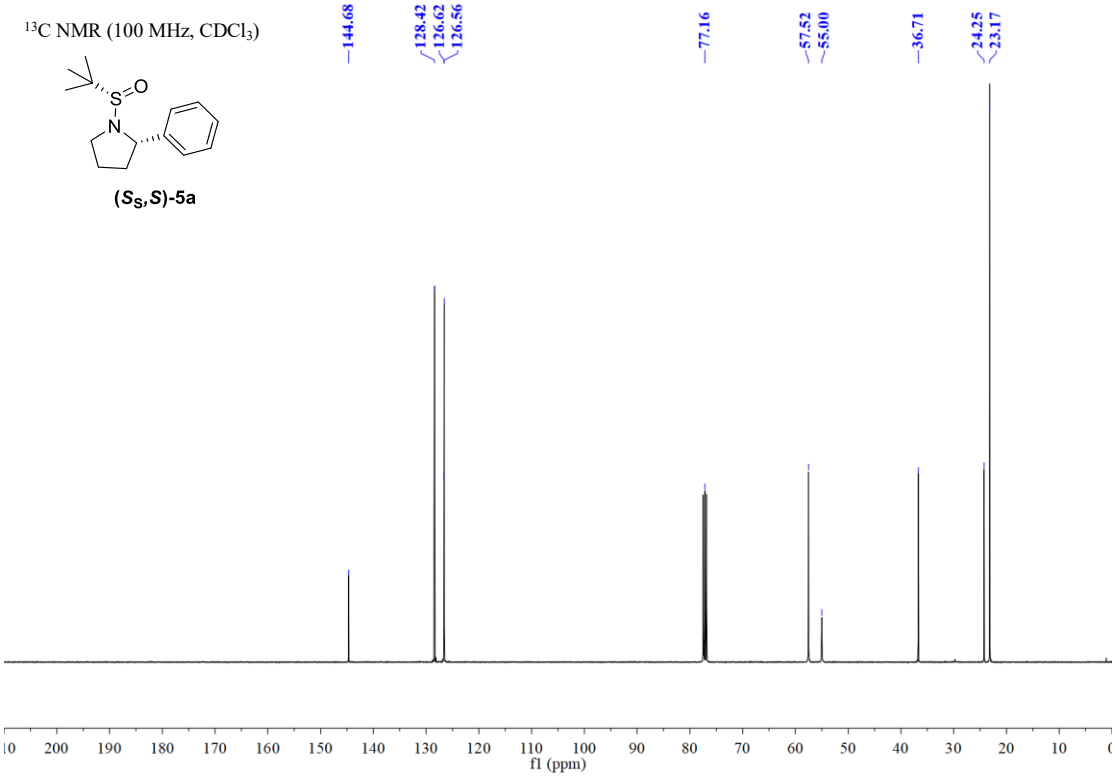
^{1}H NMR (400 MHz, $CDCl_3$)



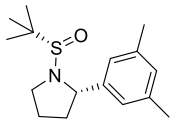
(S_S,*S*)-5a

^{13}C NMR (100 MHz, $CDCl_3$)

(S_S,*S*)-5a

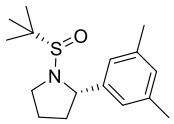


^{1}H NMR (400 MHz, $CDCl_3$)



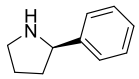
(S_S,*S*)-5j

^{13}C NMR (100 MHz, $CDCl_3$)

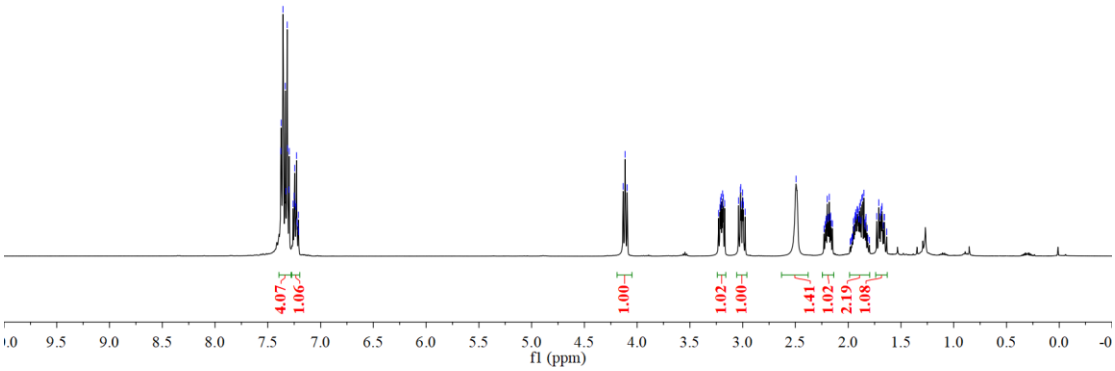


(S_S,*S*)-5j

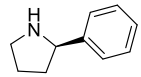
^{1}H NMR (400 MHz, $CDCl_3$)



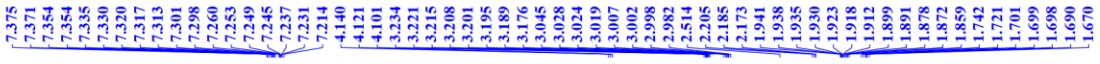
6a



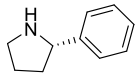
^{13}C NMR (100 MHz, $CDCl_3$)



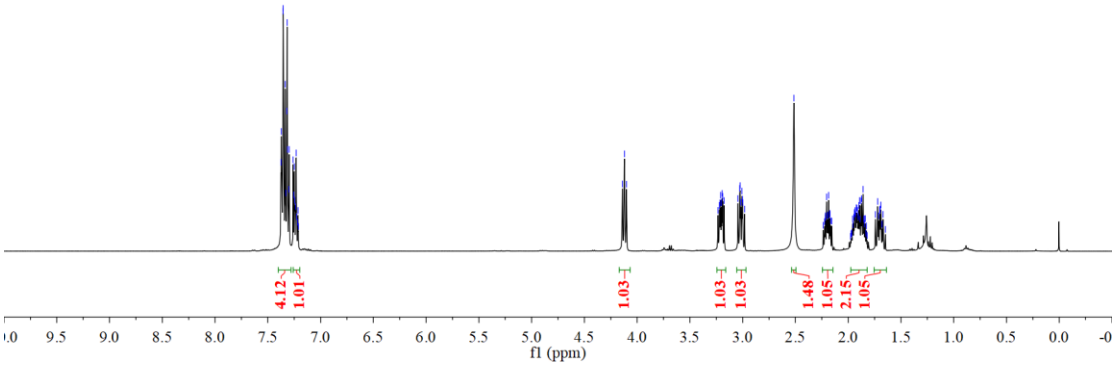
6a



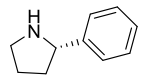
^{1}H NMR (400 MHz, $CDCl_3$)



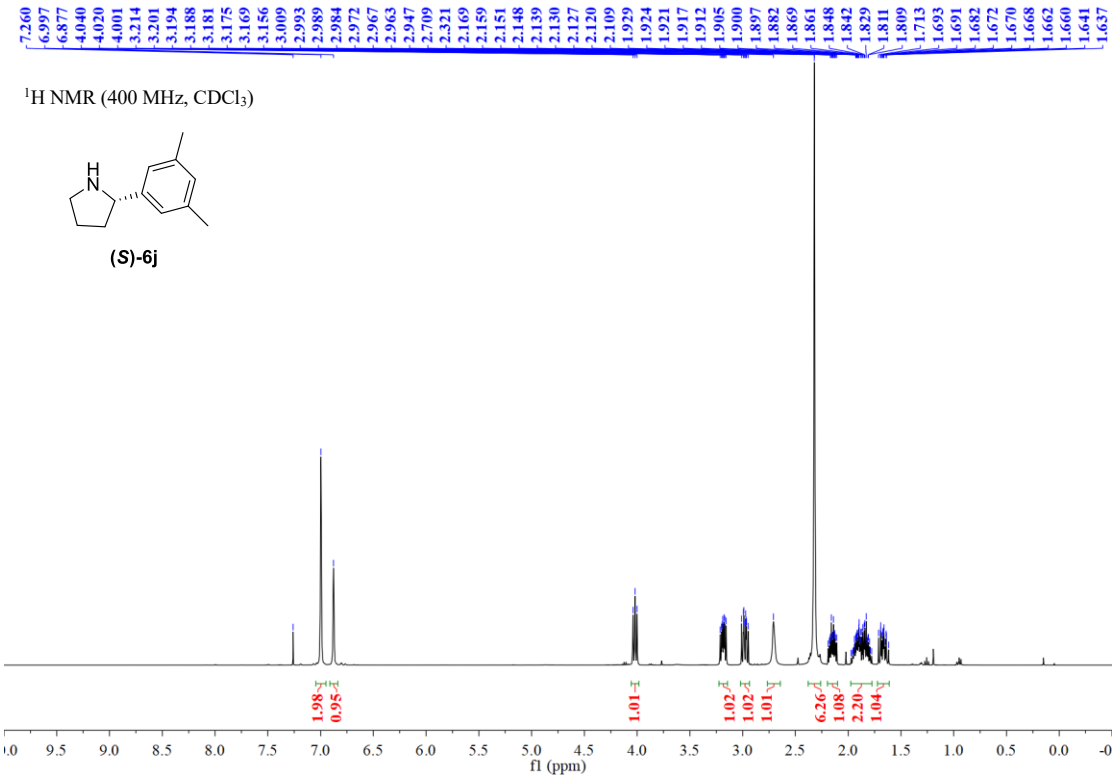
(*S*)-6a

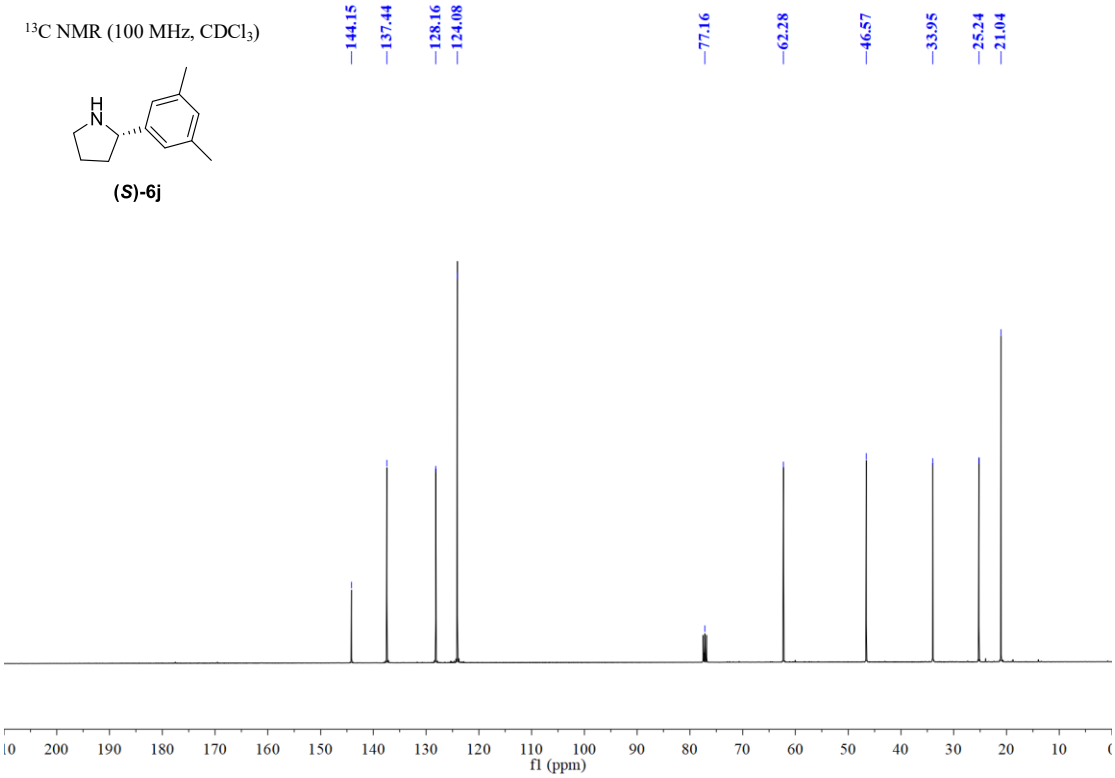


^{13}C NMR (100 MHz, $CDCl_3$)



(*S*)-6a





9. References

[1] X. Han and P. E. Floreancig, *Angew. Chem., Int. Ed.*, 2014, **53**, 11075-11078.

[2] L. R. Reddy and M. Prashad, *Chem. Commun.*, 2010, **46**, 222-224.