Supporting Information

Ir/XuPhos-Catalyzed Direct Asymmetric Reductive Amination of Ketones with Secondary Amines

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1. General Information:

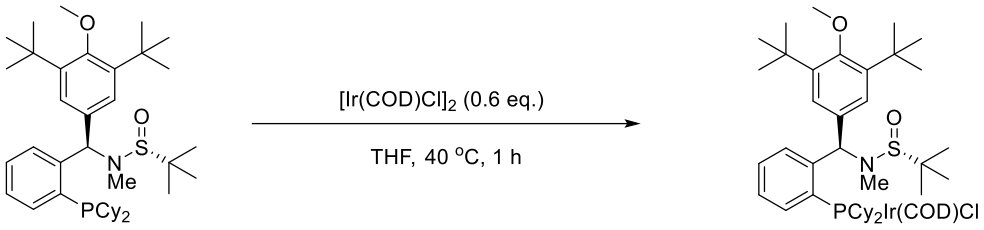
Unless otherwise noted, Materials obtained from commercial suppliers were used directly without further purification. ^{1}H NMR spectra were recorded on a BRUKER 500 (or 600) MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with tetramethylsilane (TMS: 0 ppm) with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on a BRUKER 500 (125 MHz) or 600 (150 MHz) spectrometer in $CDCl_3$ with complete proton decoupling. Chemical shifts are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (δ 7.26 or 77.0 ppm) as the internal standard. All products were further characterized by HRMS (high resolution mass spectra). The enantionmeric excesses of the products were determined by chiral stationary phase HPLC using a Chiralpak OJ-H, OD-H, AD-H, AS-H, or determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent..

Anhydrous tetrahydrofuran (THF), toluene, 1,4-Dioxane and diethyl ether (Et_2O) were distilled from sodium and benzophenone to use; Anhydrous dichloromethane (DCM) and 1,2-dichloroethane (DCE) were distilled from CaH_2. Unless otherwise noted, analytical grade solvents and commercially available reagents were used directly.

Reactions were monitored by thin layer chromatography (TLC) using silicycle pre-coated silica gel plates. Flash column chromatography was performed on silica gel 60 (particle size 200-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate.

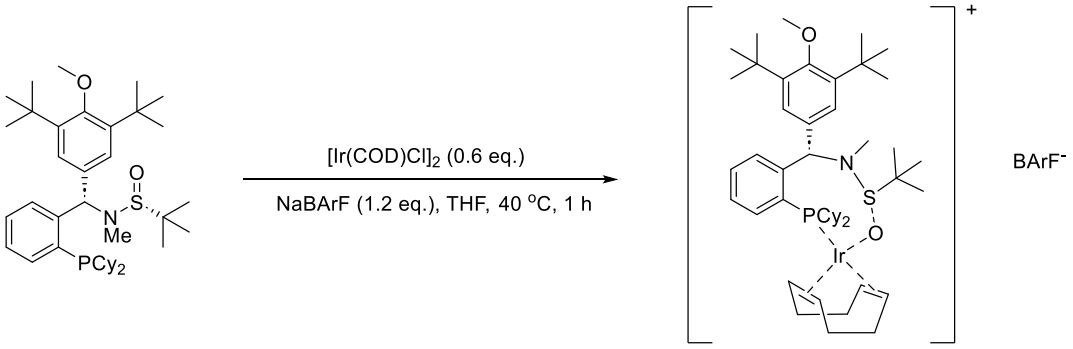
2. Experimental Procedure and Characterization Data

2.1 Typical procedure for the synthesis of Ir catalyst.



NMe-Xu1 **NMe-Xu1-Ir**

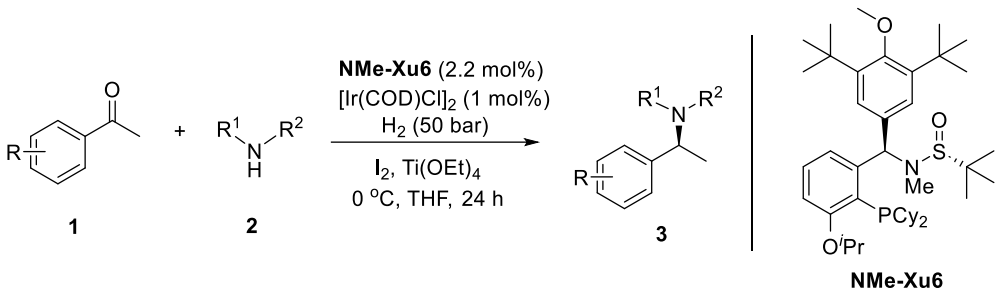
To an oven-dried Schlenk tube was added **NMe-XuPhos**[1] (1 mmol) and $[Ir(COD)Cl]_2$ (0.6 mmol). After vacuuming and refilled with nitrogen for three times, anhydrous THF (5 mL) was added under nitrogen atmosphere. The Schlenk tube was transferred to a heating pot and heated at 40 °C for 1 hour. Upon completion of the reaction, the solution was concentrated under reduced pressure. The crude mixture was then purified by column chromatography on silica gel with PE : EA = 5:1 as eluent to afford the **NMe-Xu1-Ir** as a yellow solid.



NMe-Xu3 **NMe-Xu3-Ir**

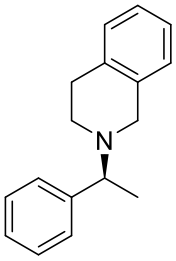
To an oven-dried Schlenk tube was added **NMe-XuPhos**[1] (1 mmol), NaBArF(1.2 mmol) and $[Ir(COD)Cl]_2$ (0.6 mmol). After vacuuming and refilled with nitrogen for three times, anhydrous THF (5 mL) was added under nitrogen atmosphere. The Schlenk tube was transferred to a heating pot and heated at 40 °C for 1 hour. Upon completion of the reaction, the solution was concentrated under reduced pressure. The crude mixture was then purified by column chromatography on silica gel with PE: DCM = 1:1 as eluent to afford the **NMe-Xu3-Ir** as a light yellow solid.

2.2 General procedure for the preparation of the chiral products.



To a vial containing a magnetic stirring bar was added **1** (0.2 mmol), **2** (0.22 mmol), I_2 (2 mol%), $Ti(OEt)_4$ (0.4 mmol), $[Ir(COD)(Cl)]_2$ (1 mol %), and **N-Me-Xu6** (2.2 mol %) under nitrogen atmosphere, anhydrous THF (2 mL) was added and stirred for 30 minutes. Then the vial was transferred in Parr steel autoclave, which was purged three times with hydrogen and finally pressurized to 50 atm. The reaction mixture was stirred at 0 °C for 24 h. The hydrogen gas was released slowly and the solution was quenched with $Na_2SO_4 \cdot 10H_2O$ and filtered. The organic phase was concentrated and purified by column chromotography and then analyzed by chiral HPLC or using ^1H NMR with chemical shift reagent to determine the enantiomicric excesses.

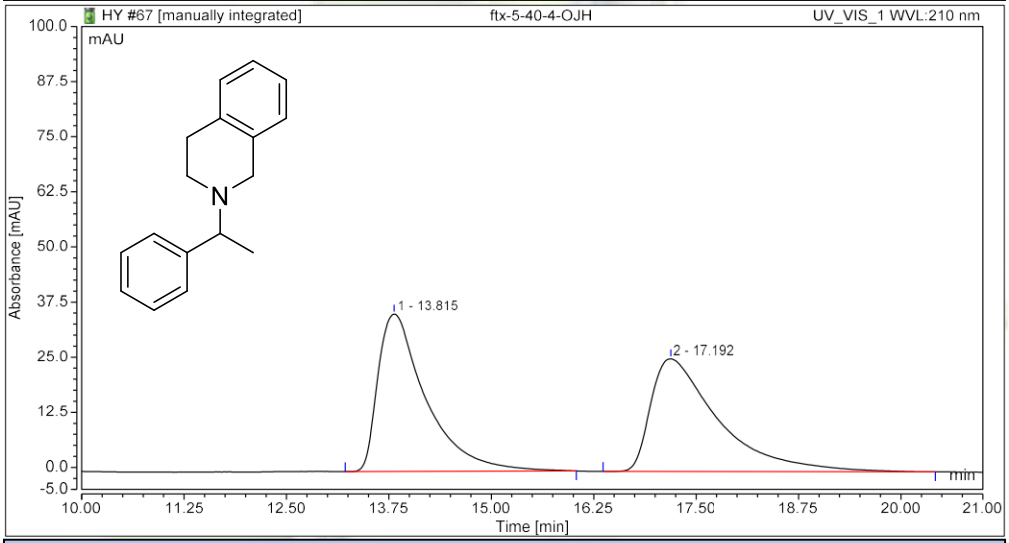
(*S*)-2-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (3a). [2]



PE:EA = 20:1; Yellow oil, 43.6 mg (92% yield), 94% *ee*; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, 2H), 7.10 – 7.05 (m, 3H), 7.01 – 6.96 (m, 1H), 6.88 (d, *J* = 8.5 Hz, 2H), 3.57 – 3.52 (m, 2H), 2.92 – 2.72 (m, 3H), 2.62 – 2.55 (m, 1H), 1.41 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 158.58, 135.15, 134.26, 130.68, 128.65, 128.32, 126.11, 125.32, 125.11, 113.68, 73.60, 58.20, 53.38, 28.21, 20.09. HPLC：Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 9.8 min (major), t_R = 13.6 min (minor). $[\alpha]^{20}_D$ = +3.3 (c 0.7, $CHCl_3$). The absolute

configuration was determined by comparation of the optical rotation value with the data in reference [3] ($[\alpha]^{20}_D$ = +9.2 (c 0.5, $CHCl_3$)). The absolute configuration of other hydrogenation products was assigned by analogy to that of **3a**.

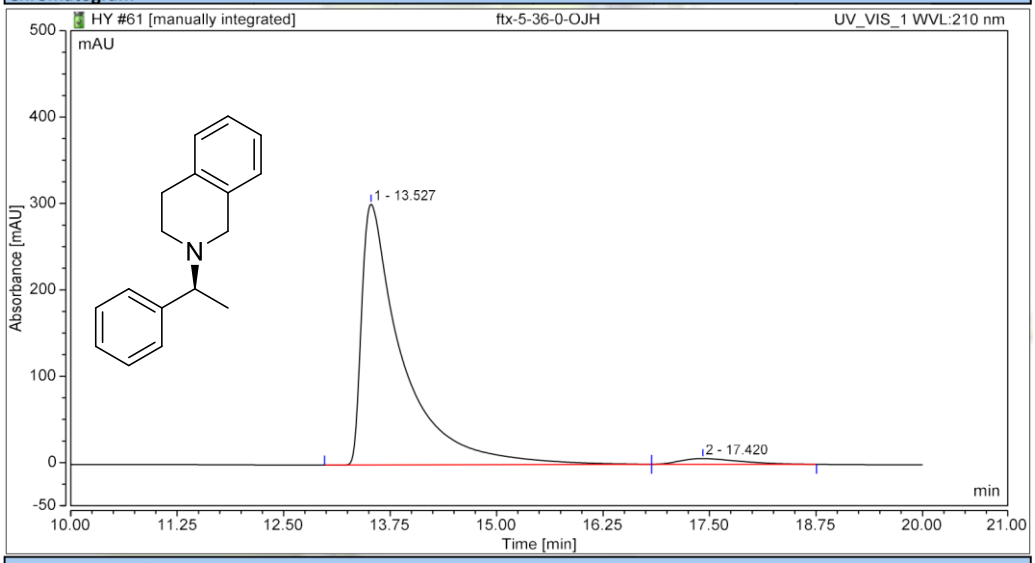
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.815	24.258	35.714	49.87	58.27	n.a.
2		17.192	24.381	25.572	50.13	41.73	n.a.
Total:			**48.639**	**61.286**	**100.00**	**100.00**	

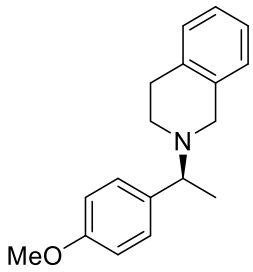
Chromatogram



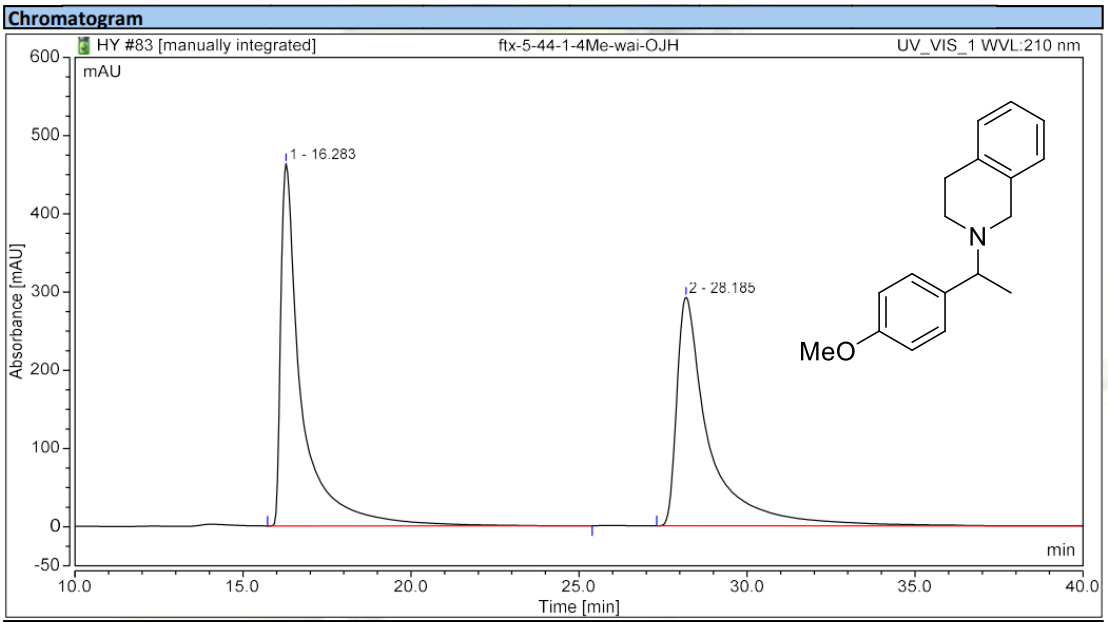
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.527	166.831	302.005	96.88	97.86	n.a.
2		17.420	5.371	6.618	3.12	2.14	n.a.
Total:			**172.202**	**308.624**	**100.00**	**100.00**	

(*S*)-2-(1-(4-methoxyphenyl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3b). [4]

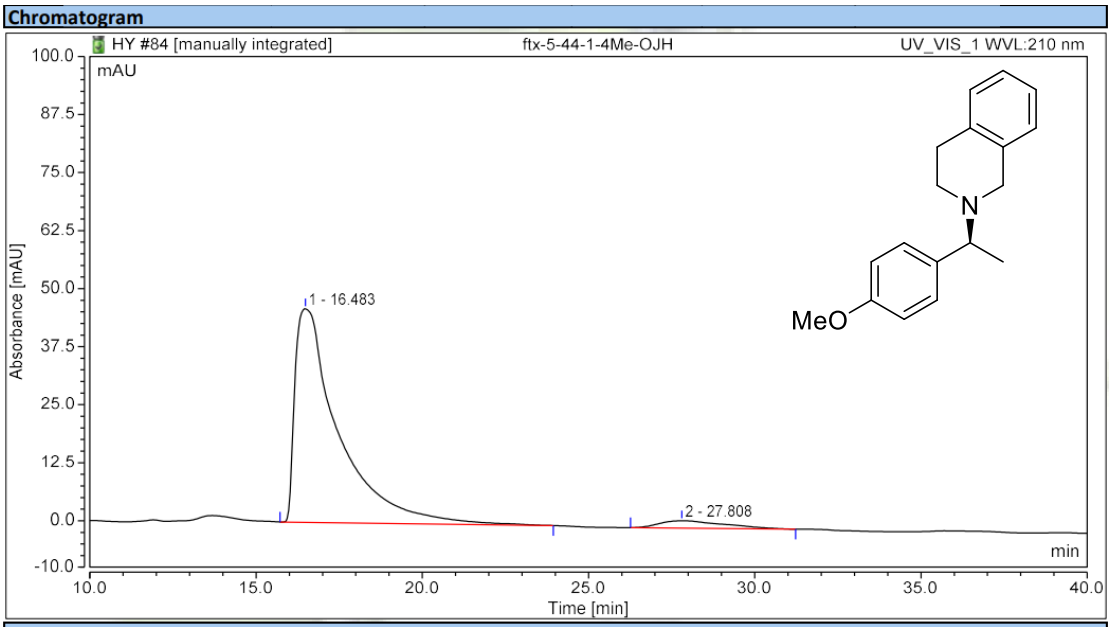


PE:EA = 5:1; Yellow oil, 50.8 mg (95% yield), 91% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.16 – 7.07 (m, 3H), 7.04 – 7.00 (m, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 3.62 – 3.52 (m, 2H), 2.94 – 2.77 (m, 3H), 2.66 – 2.60 (m, 1H), 1.48 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 158.50, 135.18, 134.59, 130.58, 128.59, 128.57, 126.77, 125.94, 125.47, 113.57, 63.62, 55.22, 53.49, 47.85, 29.29, 20.03. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 7.5 min (major), t_R = 9.8 min (minor).



Integration Results

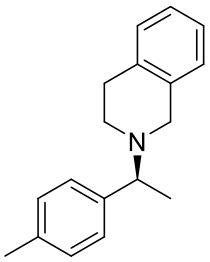
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.283	331.368	463.390	49.99	61.31	n.a.
2		28.185	331.565	292.402	50.01	38.69	n.a.
Total:			**662.934**	**755.792**	**100.00**	**100.00**	



Integration Results

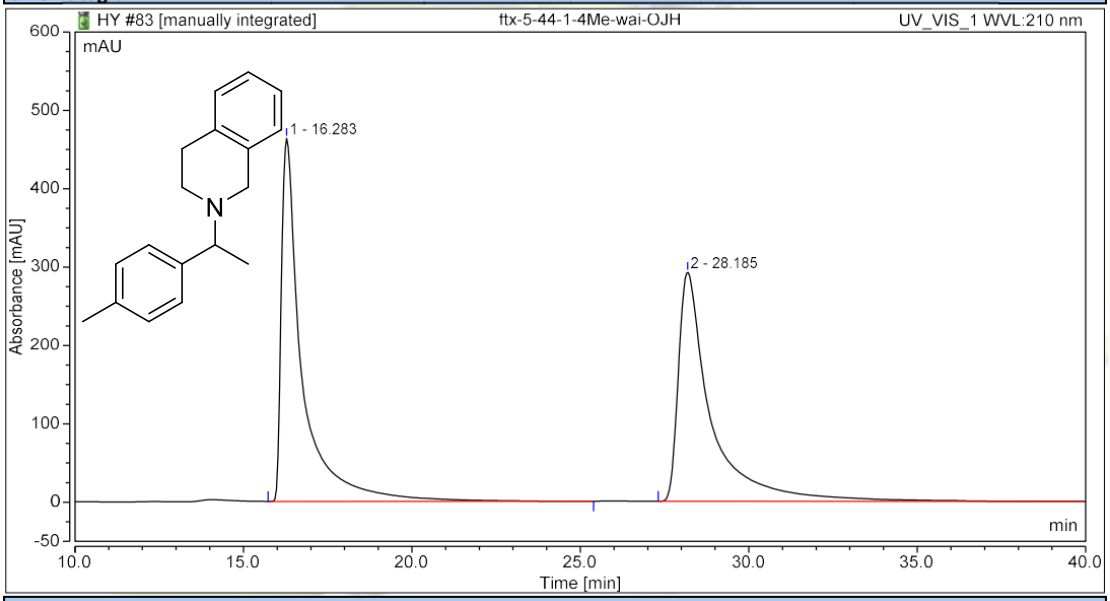
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.483	69.910	46.002	95.09	96.63	n.a.
2		27.808	3.613	1.606	4.91	3.37	n.a.
Total:			**73.523**	**47.608**	**100.00**	**100.00**	

(*S*)-2-(1-(*p*-tolyl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3c).



PE:EA = 30:1; Yellow oil, 46.7 mg (93% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.31 (m, 2H), 7.16 – 7.08 (m, 3H), 7.02 – 6.98 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 3.79 (s, 3H), 3.59 – 3.51 (m, 2H), 2.90 – 2.69 (m, 3H), 2.65 – 2.58 (m, 1H), 1.40 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 158.51, 135.20, 134.49, 130.50, 128.57, 128.51, 126.75, 125.89, 125.40, 113.57, 63.60, 55.20, 53.38, 47.71, 29.21, 20.09. HPLC: Chiralpak OJ-H, hexane : isopropanol = 99:1, 0.5 mL/min, 210 nm, t_R = 16.5 min (major), t_R = 27.8 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{18}H_{21}NNa$: 274.1572, found 274.1568.

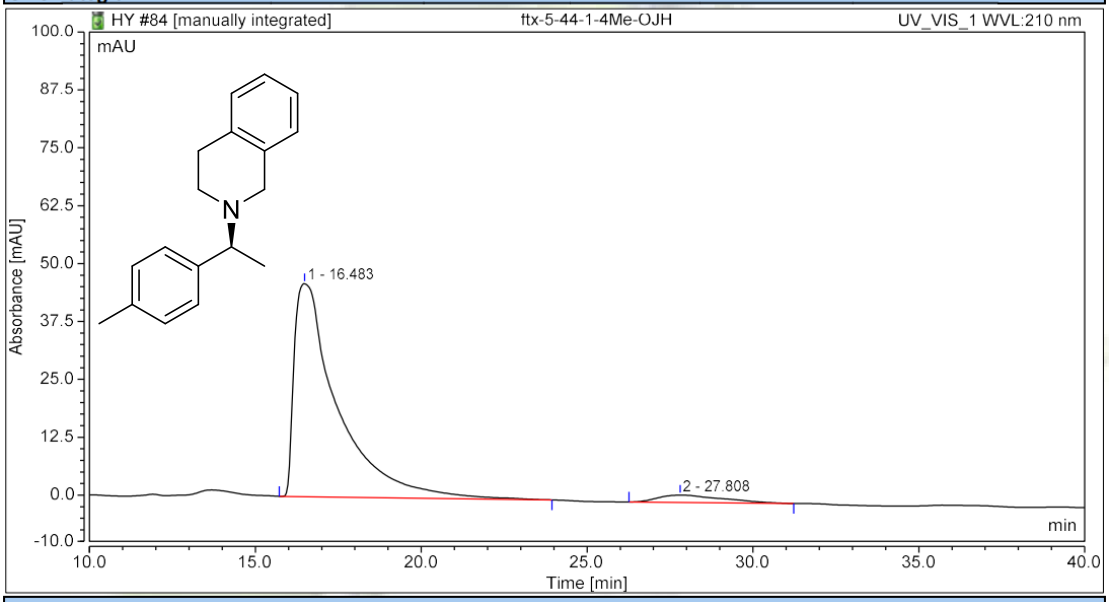
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.283	331.368	463.390	49.99	61.31	n.a.
2		28.185	331.565	292.402	50.01	38.69	n.a.
Total:			**662.934**	**755.792**	**100.00**	**100.00**	

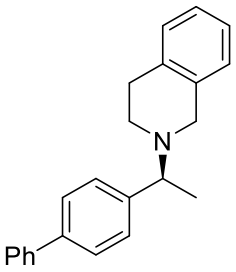
Chromatogram



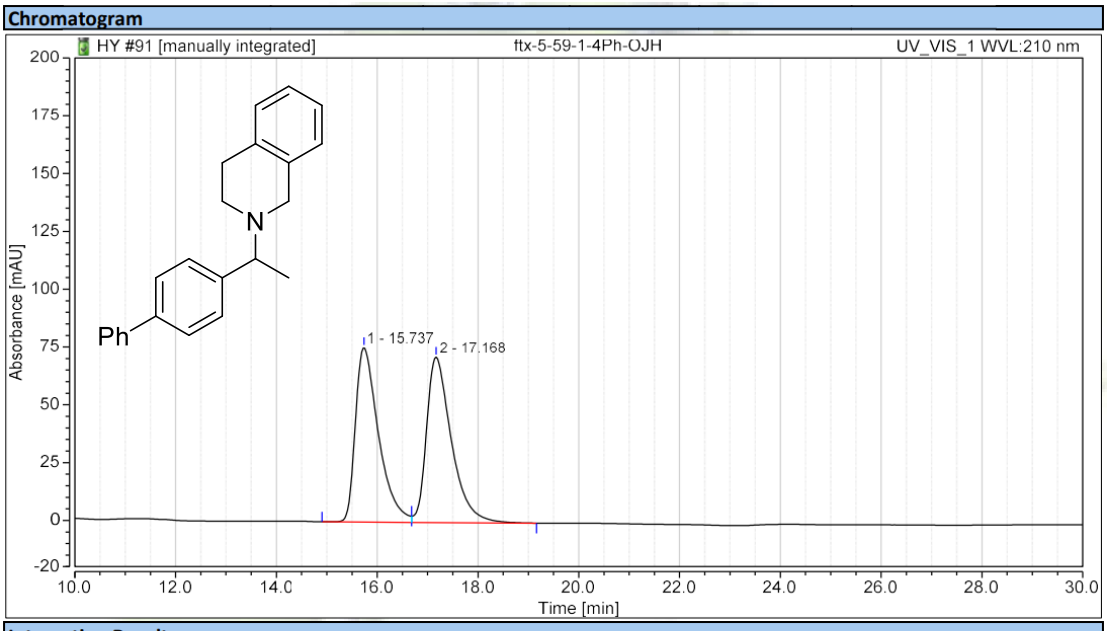
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.483	69.910	46.002	95.09	96.63	n.a.
2		27.808	3.613	1.606	4.91	3.37	n.a.
Total:			**73.523**	**47.608**	**100.00**	**100.00**	

(*S*)-2-(1-([1,1'-biphenyl]-4-yl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3d).

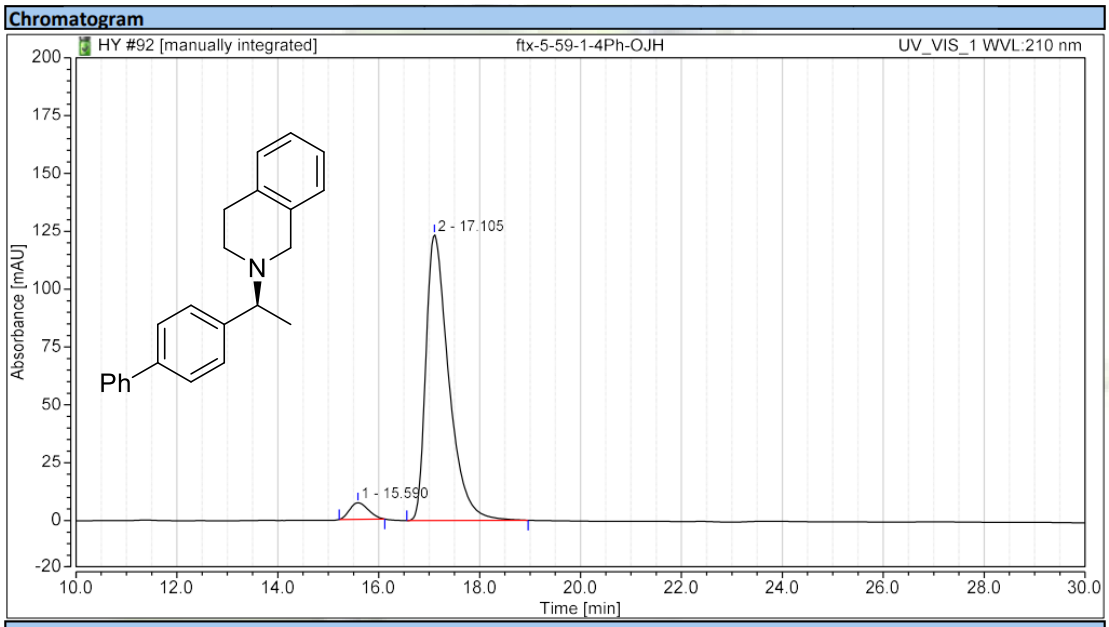


PE:EA = 20:1; Yellow oil, 50.8 mg (90% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 – 7.60 (m, 4H), 7.59 – 7.45 (m, 4H), 7.45 – 7.37 (m, 1H), 7.23 – 7.13 (m, 3H), 7.13 – 7.05 (m, 1H), 3.94 (d, *J* = 14.8 Hz, 1H), 3.76 – 3.64 (m, 2H), 3.09 – 2.86 (m, 3H), 2.79 – 2.68 (m, 1H), 1.59 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.33, 140.87, 139.73, 135.11, 134.54, 128.67, 128.56, 127.91, 127.06, 126.96, 126.73, 125.94, 125.47, 64.00, 53.52, 47.97, 29.30, 20.01. HPLC: Chiralpak OJ-H, hexane: isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 10.3 min (major), t_R = 15.7 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{23}H_{23}NNa$: 336.1728, found 336.1725.



Integration Results

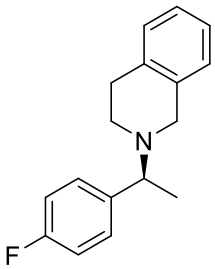
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.737	40.011	75.485	49.42	51.34	n.a.
2		17.168	40.954	71.545	50.58	48.66	n.a.
Total:			**80.965**	**147.030**	**100.00**	**100.00**	



Integration Results

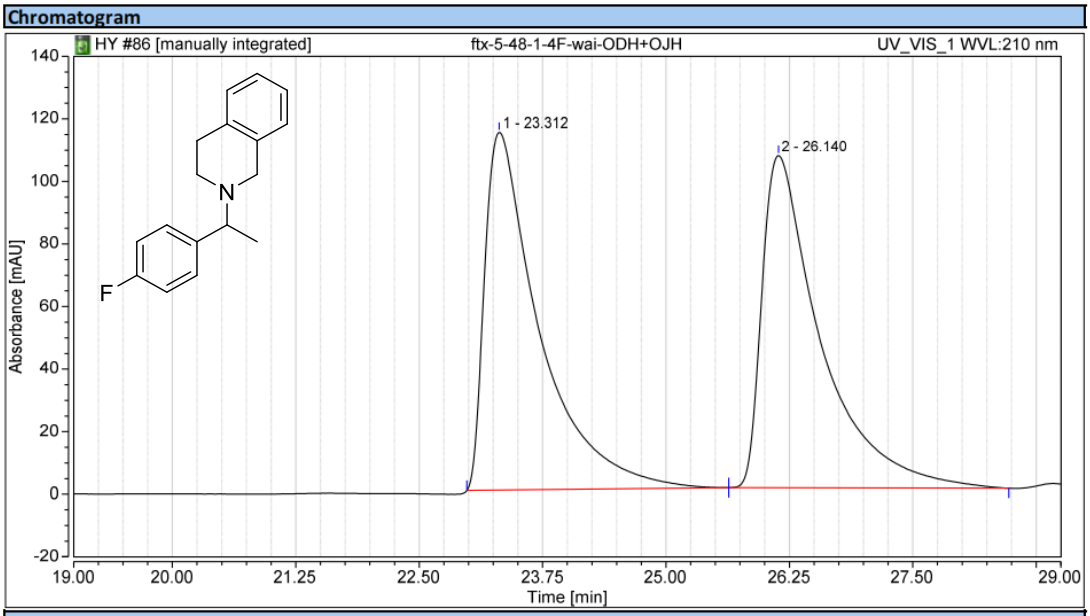
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.590	3.077	7.171	4.53	5.49	n.a.
2		17.105	64.791	123.502	95.47	94.51	n.a.
Total:			**67.868**	**130.673**	**100.00**	**100.00**	

(*S*)-2-(1-(4-fluorophenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3e).



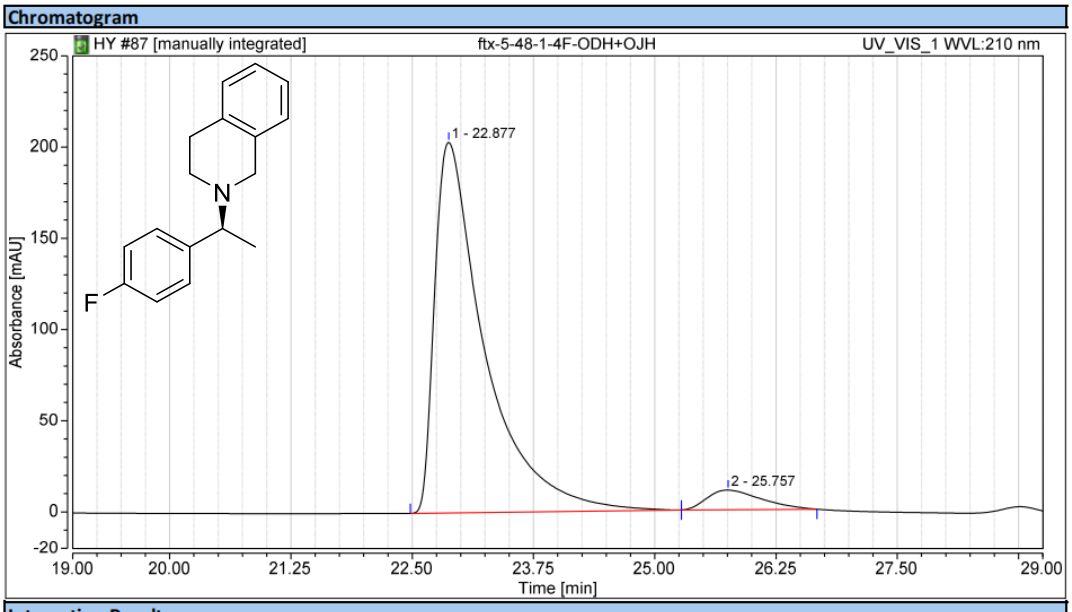
PE:EA = 20:1; Yellow oil, 48.5 mg (95% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.16 – 7.07 (m, 3H), 7.04 – 7.00 (m, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 3.62 – 3.52 (m, 2H), 2.94 – 2.77 (m, 3H), 2.66 – 2.60 (m, 1H), 1.48 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 158.50, 135.18, 134.59, 130.58, 128.59, 128.57, 126.77, 125.94, 125.47, 113.57, 63.62, 55.22, 53.49, 47.85, 29.29, 20.03. HPLC: Chiralpak ODH+OJ-H column, hexane: isopropanol = 98:2,

flow rate = 0.5 mL/min, UV detection at λ = 210 nm, t_R = 22.9 min (major), t_R = 25.7 min (minor). HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{19}FN$: 256.1502, found 336.156.1494.



Integration Results

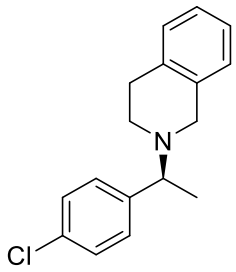
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		23.312	73.189	114.416	50.14	51.86	n.a.
2		26.140	72.776	106.223	49.86	48.14	n.a.
Total:			**145.965**	**220.638**	**100.00**	**100.00**	



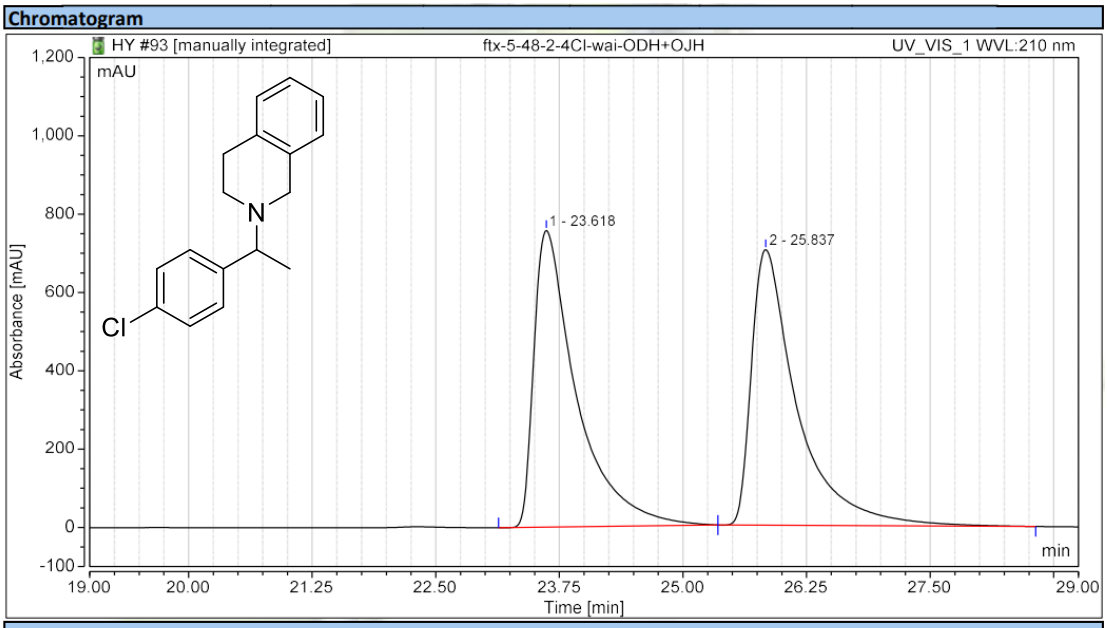
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		22.877	121.175	203.221	94.58	94.96	n.a.
2		25.757	6.943	10.781	5.42	5.04	n.a.
Total:			**128.118**	**214.002**	**100.00**	**100.00**	

(*S*)-2-(1-(4-chlorophenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3f).

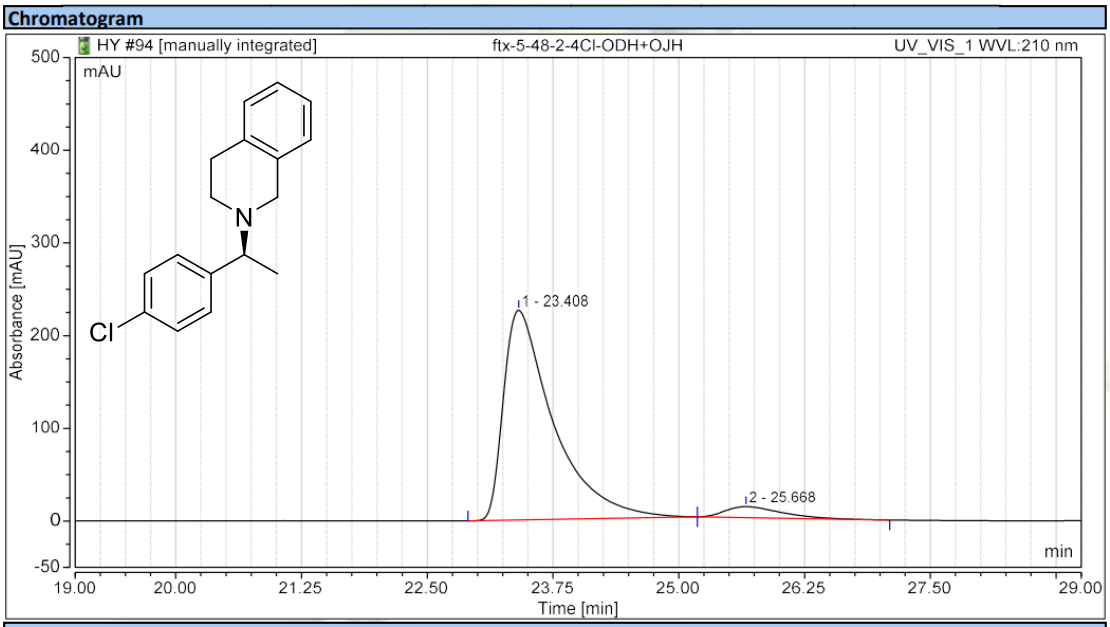


PE:EA = 20:1; Yellow oil, 50.5 mg (95% yield), 91% *ee*;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 4H), 7.15 – 7.06 (m, 3H), 7.02 – 6.96 (m, 1H), 3.80 (d, *J* = 14.7 Hz, 1H), 3.61 – 3.49 (m, 2H), 2.94 – 2.71 (m, 3H), 2.67 – 2.58 (m, 1H), 1.44 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.00, 134.92, 134.47, 132.45, 128.82, 128.61, 128.45, 126.73, 126.05, 125.56, 63.68, 53.48, 47.95, 29.22, 20.01. HPLC: Chiralpak ODH + OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 23.4 min (major), t_R = 25.7 min (minor). HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{17}H_{19}NCl$: 272.1206, found 272.1199.



Integration Results

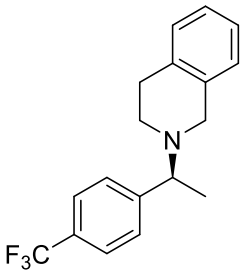
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		23.618	376.432	757.659	50.05	51.84	n.a.
2		25.837	375.690	703.886	49.95	48.16	n.a.
Total:			**752.122**	**1461.545**	**100.00**	**100.00**	



Integration Results

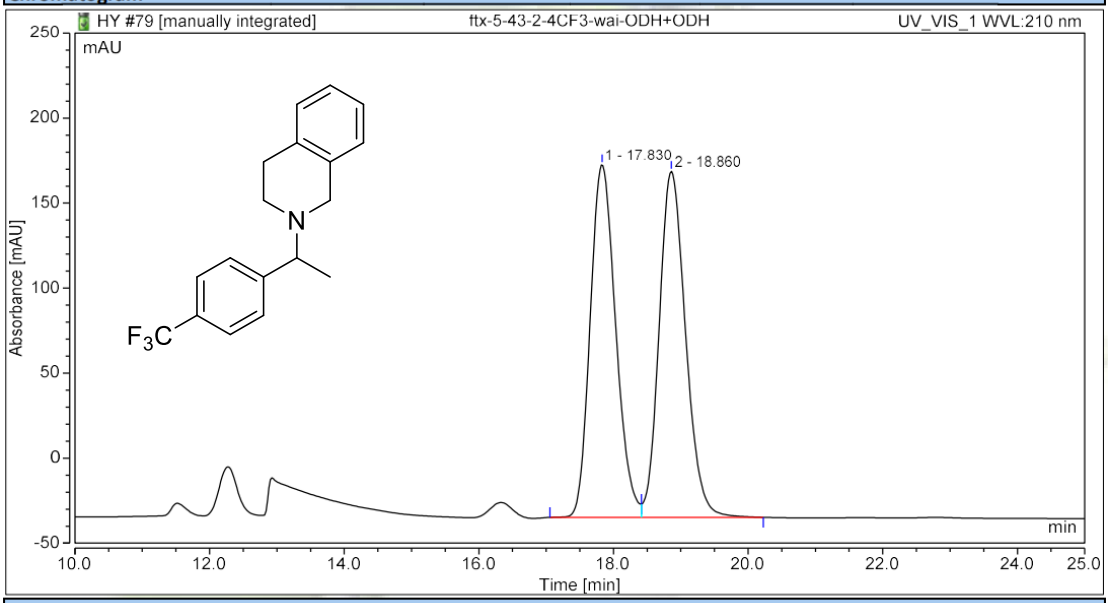
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		23.408	129.887	226.226	94.37	94.99	n.a.
2		25.668	7.743	11.931	5.63	5.01	n.a.
Total:			**137.630**	**238.157**	**100.00**	**100.00**	

(*S*)-2-(1-(4-(trifluoromethyl)phenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3g).



PE:EA = 20:1; Yellow oil, 55.6 mg (91% yield), 90% *ee*;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 2H), 7.20 – 7.11 (m, 3H), 7.06 – 6.99 (m, 1H), 3.86 (d, *J* = 14.7 Hz, 1H), 3.70 – 3.56 (m, 2H), 3.00 – 2.74 (m, 3H), 1.49 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.63, 127.74, 126.74, 126.14, 125.63, 125.35, 125.32, 64.03, 53.50, 48.08, 29.17, 20.06. HPLC: Chiralpak ODH+ODH, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 17.6 min (major), t_R = 18.8 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{18}H_{18}F_3NNa$: 328.3340, found 328.3334.

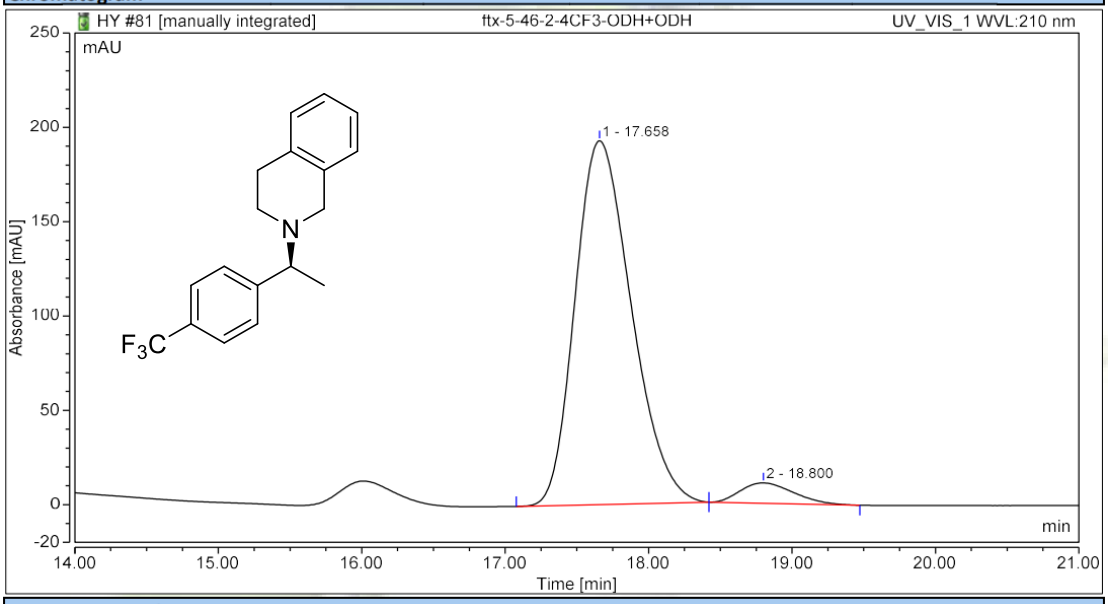
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.830	91.047	207.487	49.58	50.47	n.a.
2		18.860	92.607	203.613	50.42	49.53	n.a.
Total:			**183.654**	**411.101**	**100.00**	**100.00**	

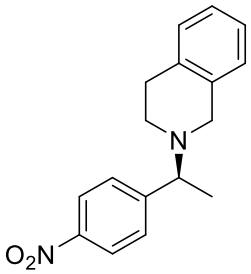
Chromatogram



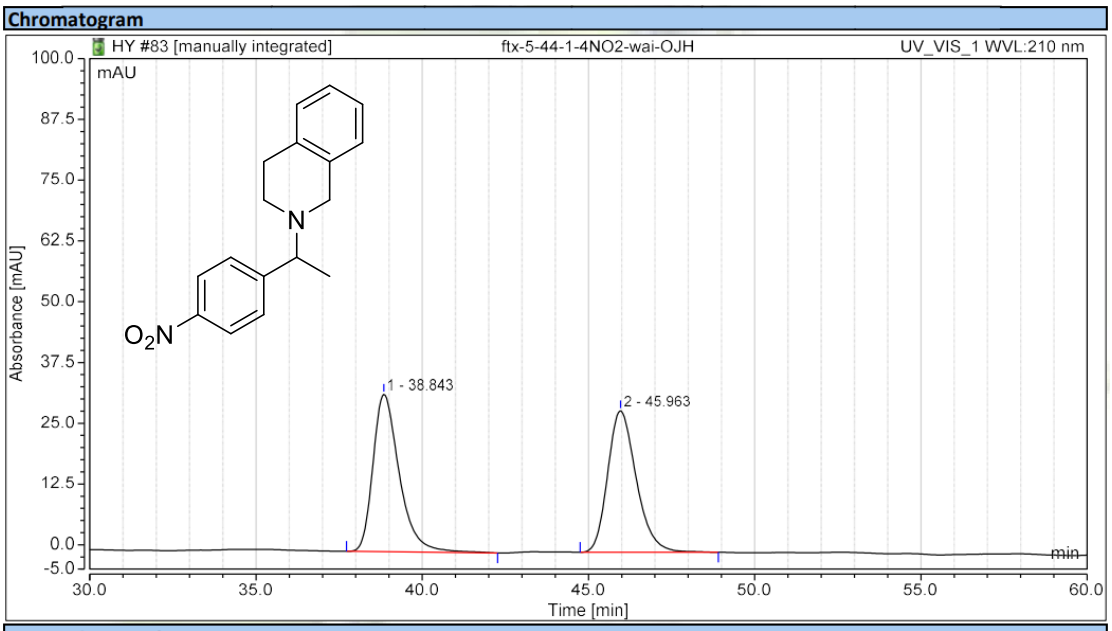
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.658	87.504	192.838	95.00	94.72	n.a.
2		18.800	4.608	10.751	5.00	5.28	n.a.
Total:			**92.112**	**203.589**	**100.00**	**100.00**	

(*S*)-2-(1-(4-nitrophenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3h).

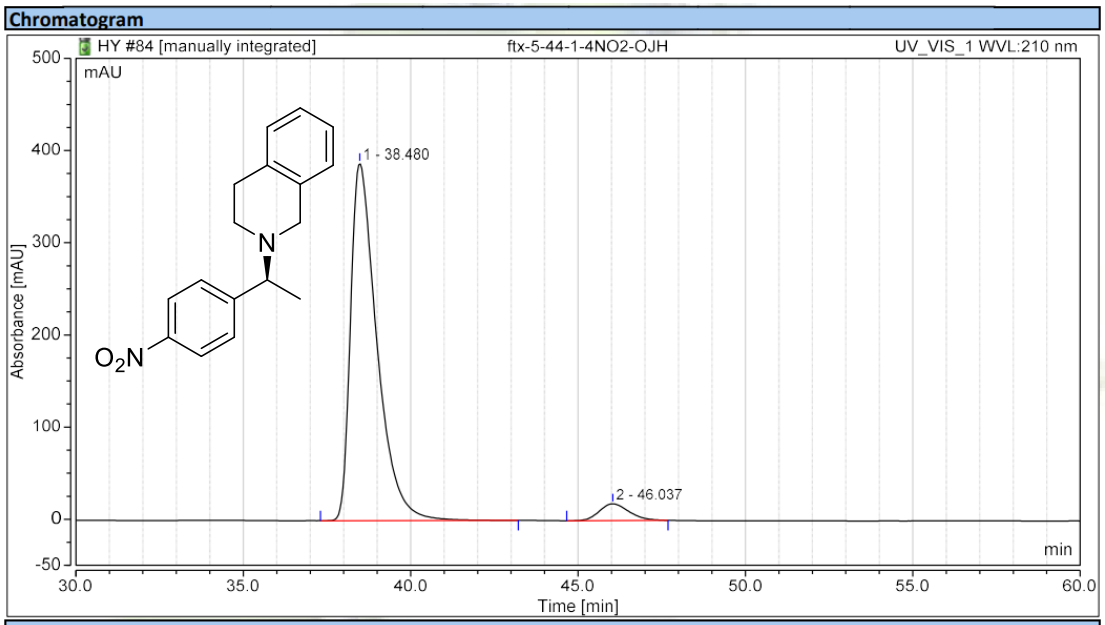


PE:EA = 20:1; Yellow oil, 50.8 mg (90% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 – 8.17 (m, 2H), 7.62 (d, *J* = 8.3 Hz, 2H), 7.22 – 7.11 (m, 3H), 7.06 – 6.98 (m, 1H), 3.86 (d, *J* = 14.6 Hz, 1H), 3.77 – 3.55 (m, 2H), 2.99 – 2.60 (m, 4H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.41, 128.63, 127.74, 126.74, 126.14, 125.63, 125.35, 125.32, 123.17, 64.03, 53.50, 48.08, 29.17, 20.06. HPLC: Chiralpak OJ-H, hexane : isopropanol = 97:3, 0.5 mL/min, 210 nm, t_R = 38.5 min (major), t_R = 46.0 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{17}H_{18}N_2O_2Na$: 305.1266, found 305.1269.



Integration Results

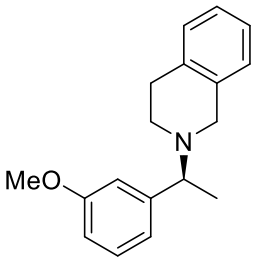
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		38.843	29.872	32.398	50.68	52.67	n.a.
2		45.963	29.072	29.111	49.32	47.33	n.a.
Total:			**58.944**	**61.509**	**100.00**	**100.00**	



Integration Results

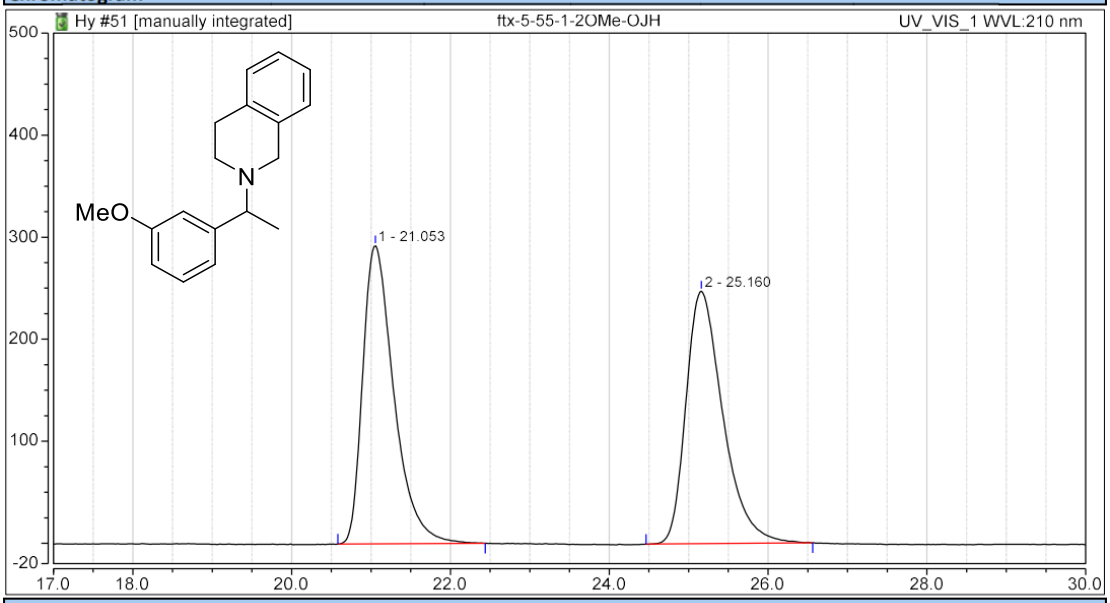
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		38.480	353.136	387.415	95.02	95.54	n.a.
2		46.037	18.505	18.087	4.98	4.46	n.a.
Total:			**371.641**	**405.503**	**100.00**	**100.00**	

(*S*)-2-(1-(3-methoxyphenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3i).



PE:EA = 20:1; Yellow oil, 50.3 mg (94% yield), 91% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.1 Hz, 1H), 7.17 – 7.09 (m, 3H), 7.05 – 6.96 (m, 3H), 6.89 – 6.76 (m, 1H), 3.87 (d, *J* = 14.9 Hz, 1H), 3.84 (s, 3H), 3.65 – 3.48 (m, 2H), 2.97 – 2.76 (m, 3H), 2.69 – 2.56 (m, 1H), 1.49 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.67, 146.19, 135.17, 134.62, 129.23, 128.59, 126.78, 125.97, 125.50, 119.97, 112.95, 112.28, 64.49, 55.21, 53.61, 48.09, 29.32, 20.26. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 9.9 min (major), t_R = 14.1 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{18}H_{21}NONa$: 290.1521, found 290.1510.

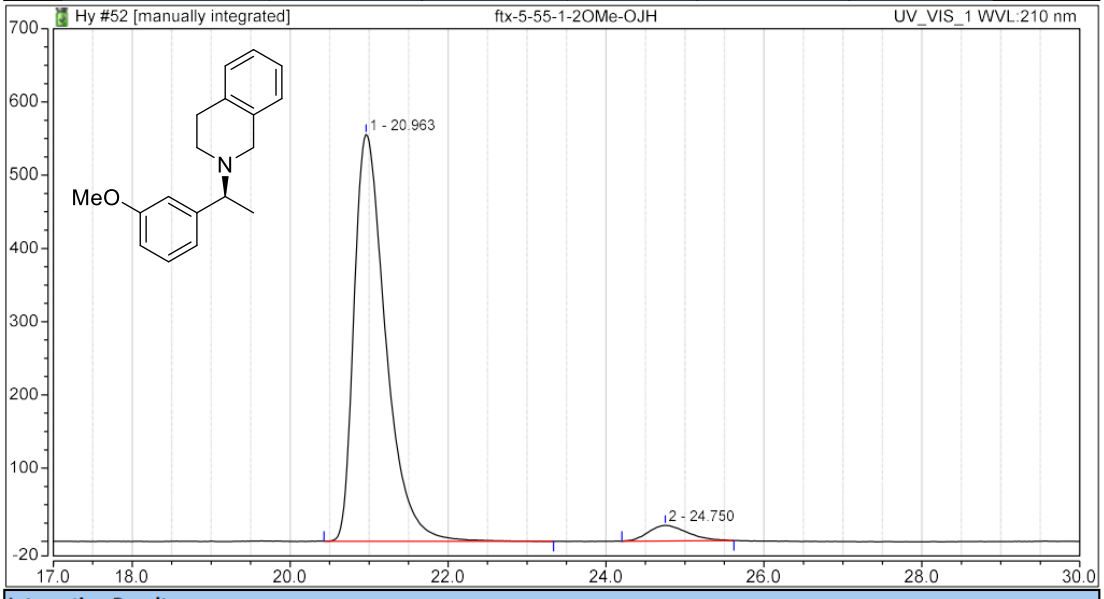
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.053	132.830	292.189	49.93	54.14	n.a.
2		25.160	133.203	247.463	50.07	45.86	n.a.
Total:			**266.033**	**539.653**	**100.00**	**100.00**	

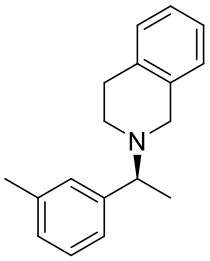
Chromatogram



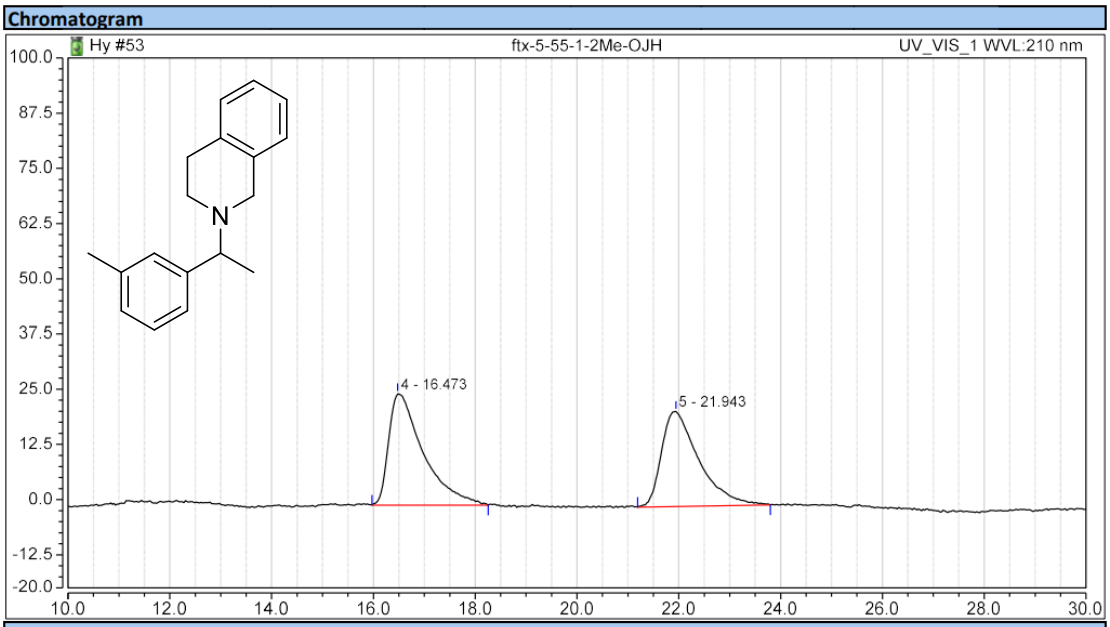
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		20.963	257.254	555.449	95.54	96.34	n.a.
2		24.750	12.019	21.125	4.46	3.66	n.a.
Total:			**269.273**	**576.574**	**100.00**	**100.00**	

(*S*)-2-(1-(*m*-tolyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3j).

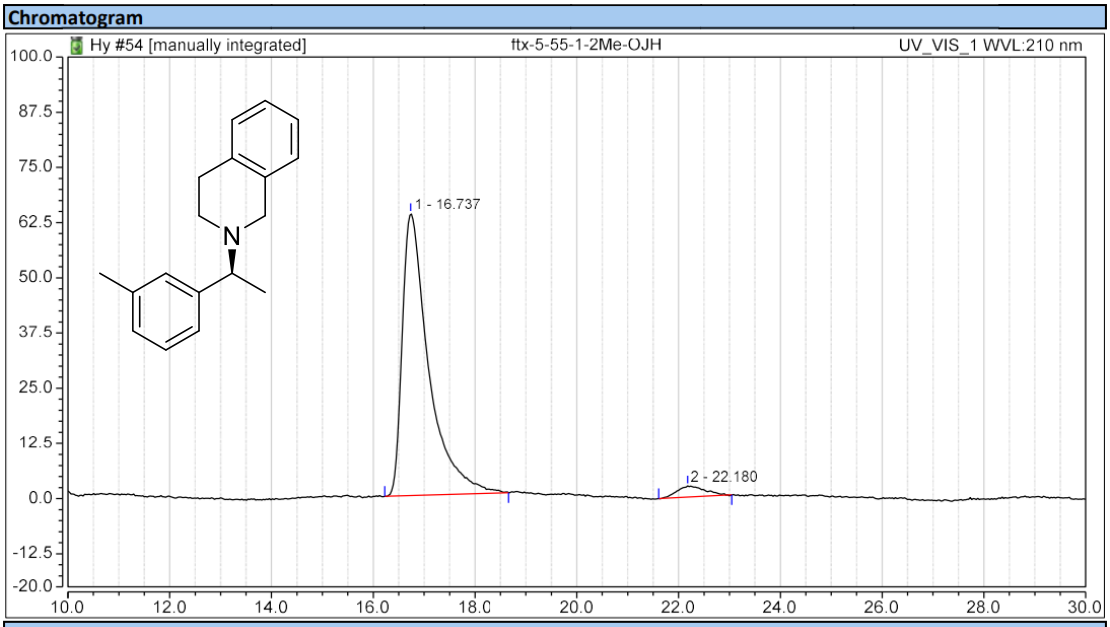


PE:EA = 20:1; Yellow oil, 47.7 mg (95% yield), 92% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.17 (m, 3H), 7.15 – 7.06 (m, 4H), 7.06 – 6.98 (m, 1H), 3.85 (d, *J* = 14.8 Hz, 1H), 3.66 – 3.47 (m, 2H), 2.98 – 2.76 (m, 3H), 2.71 – 2.57 (m, 1H), 2.38 (s, 3H), 1.49 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.29, 137.92, 134.63, 128.63, 128.22, 128.19, 127.71, 126.83, 126.00, 125.53, 124.69, 77.29, 64.51, 53.69, 48.12, 29.30, 21.52, 20.31. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 14.2 min (major), t_R = 17.5 min (minor). HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{22}N$: 252.1752, found 252.1759.



Integration Results

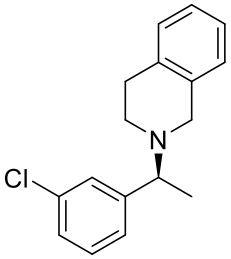
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.220	1.151	12.544	0.99	5.72	n.a.
2		6.387	2.679	31.097	2.31	14.18	n.a.
3		6.477	73.944	128.825	63.81	58.75	n.a.
4		16.473	19.808	25.257	17.09	11.52	n.a.
5		21.943	18.290	21.565	15.79	9.83	n.a.
Total:			**115.872**	**219.288**	**100.00**	**100.00**	



Integration Results

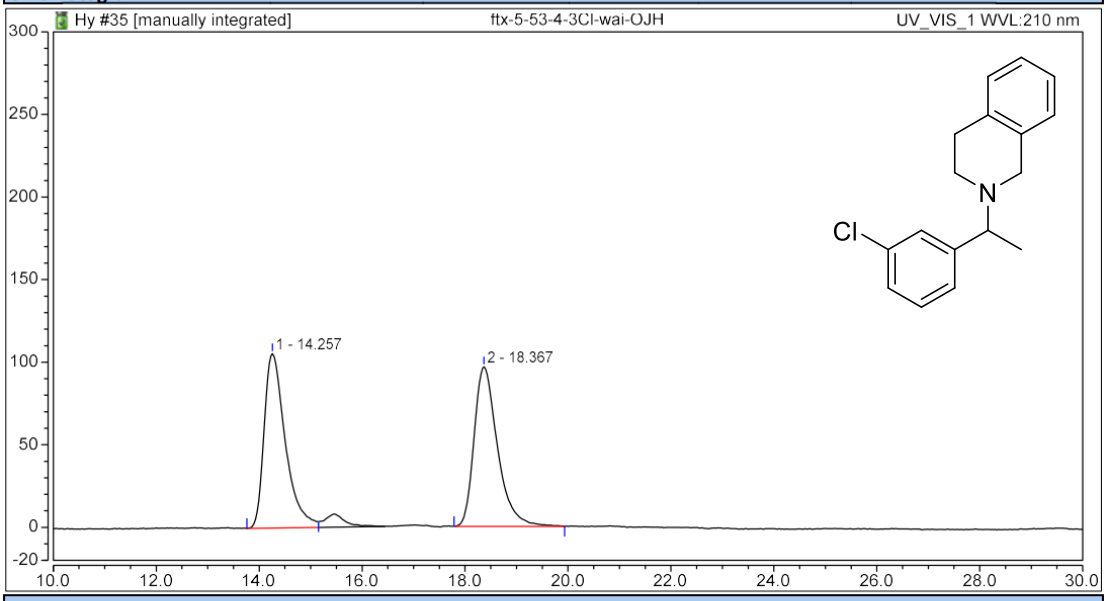
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.737	38.464	63.847	96.16	96.21	n.a.
2		22.180	1.536	2.517	3.84	3.79	n.a.
Total:			**40.000**	**66.364**	**100.00**	**100.00**	

(*S*)-2-(1-(3-chlorophenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3k).



PE:EA = 20:1; Yellow oil, 49.4 mg (91% yield), 92% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 1H), 7.32 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 7.16 – 7.06 (m, 3H), 7.04 – 6.97 (m, 1H), 3.81 (d, *J* = 14.7 Hz, 1H), 3.63 – 3.47 (m, 2H), 2.95 – 2.72 (m, 3H), 2.69 – 2.60 (m, 1H), 1.45 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.74, 134.92, 134.49, 134.21, 129.60, 128.61, 127.54, 127.09, 126.74, 126.05, 125.68, 125.56, 63.96, 53.47, 47.97, 29.25, 19.96. HPLC：Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 14.1 min (major), t_R = 18.3 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{17}H_{18}ClNNa$: 294.1025, found 294.1012.

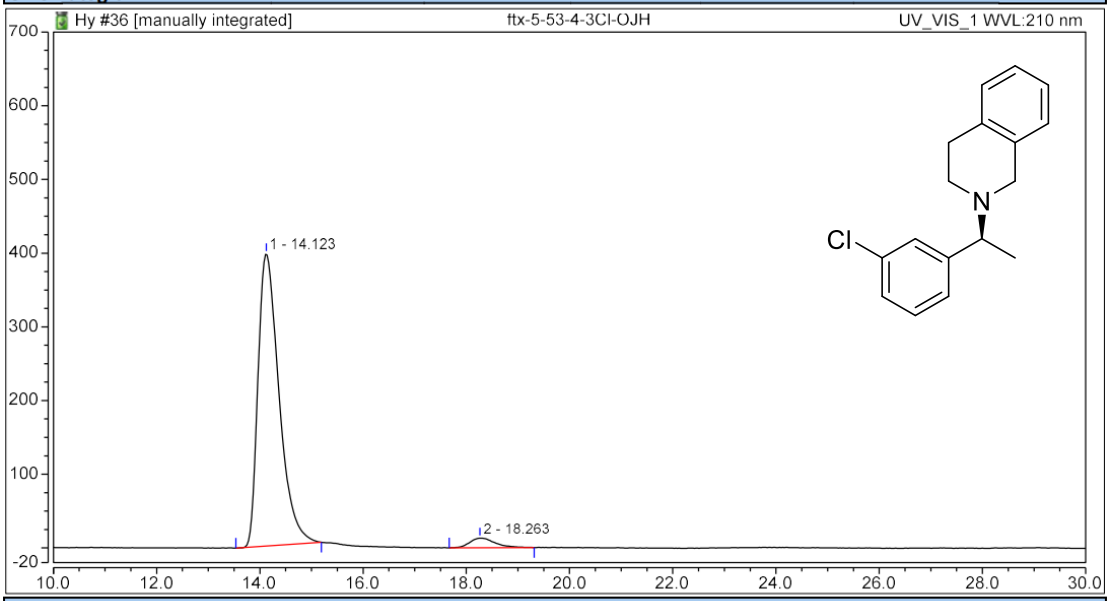
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		14.257	50.355	105.642	49.73	52.21	n.a.
2		18.367	50.910	96.692	50.27	47.79	n.a.
Total:			**101.265**	**202.334**	**100.00**	**100.00**	

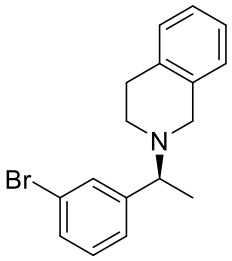
Chromatogram



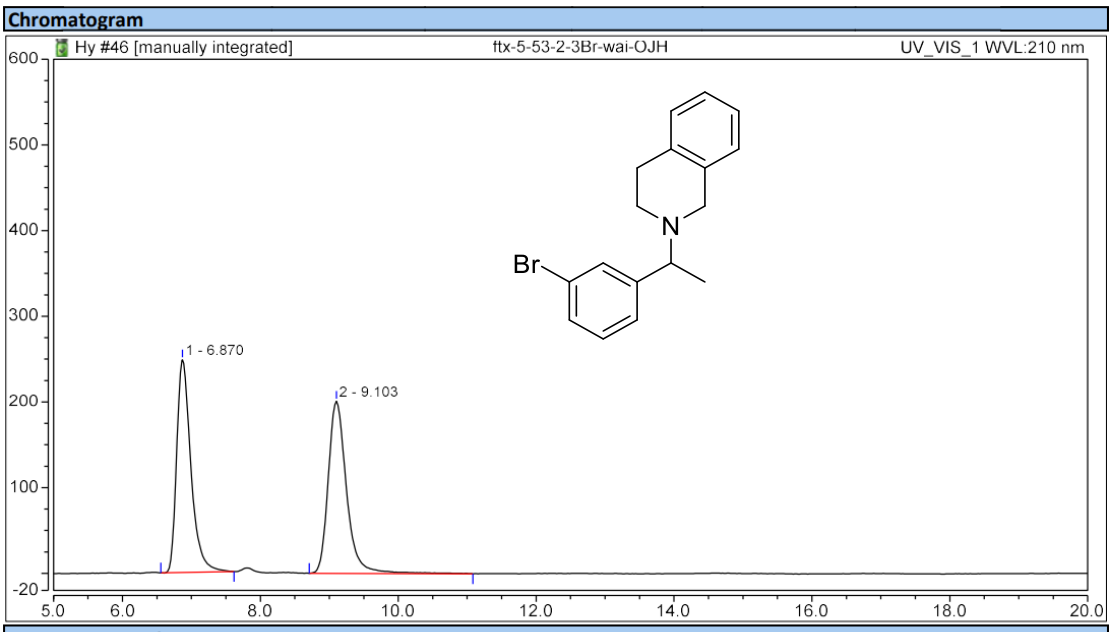
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		14.123	187.032	396.893	96.12	96.79	n.a.
2		18.263	7.548	13.182	3.88	3.21	n.a.
Total:			**194.580**	**410.075**	**100.00**	**100.00**	

(*S*)-2-(1-(3-bromophenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3l).

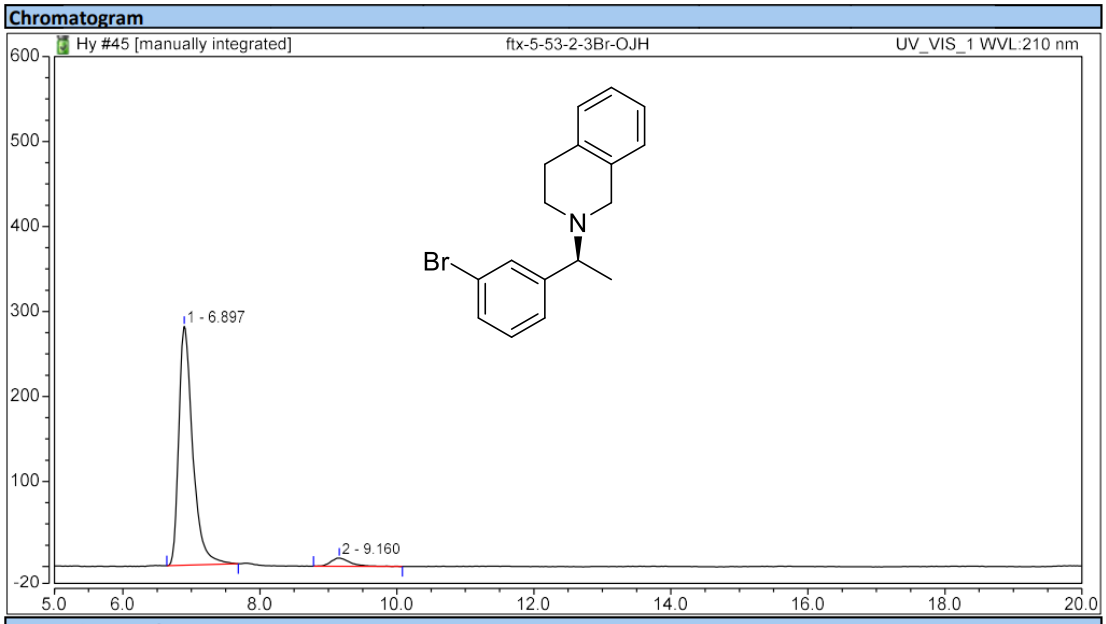


PE:EA = 20:1; Yellow oil, 60.0 mg (95% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (t, *J* = 1.8 Hz, 1H), 7.47 – 7.40 (m, 1H), 7.39 – 7.34 (m, 1H), 7.24 (t, *J* = 7.8 Hz, 1H), 7.21 – 7.11 (m, 3H), 7.09 – 7.01 (m, 1H), 3.85 (d, *J* = 14.7 Hz, 1H), 3.70 – 3.48 (m, 2H), 3.01 – 2.76 (m, 3H), 2.73 – 2.63 (m, 1H), 1.49 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.02, 134.88, 134.45, 130.43, 130.01, 129.92, 128.59, 126.72, 126.12, 126.04, 125.55, 122.52, 63.91, 53.44, 47.95, 29.23, 19.97. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 6.9 min (major), t_R = 9.2 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{17}H_{18}BrNNa$: 338.0520, found 338.0504.



Integration Results

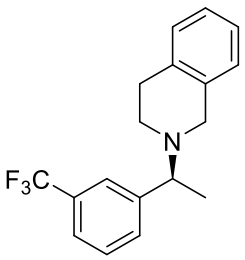
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.870	59.626	248.271	49.07	55.28	n.a.
2		9.103	61.898	200.850	50.93	44.72	n.a.
Total:			**121.523**	**449.121**	**100.00**	**100.00**	



Integration Results

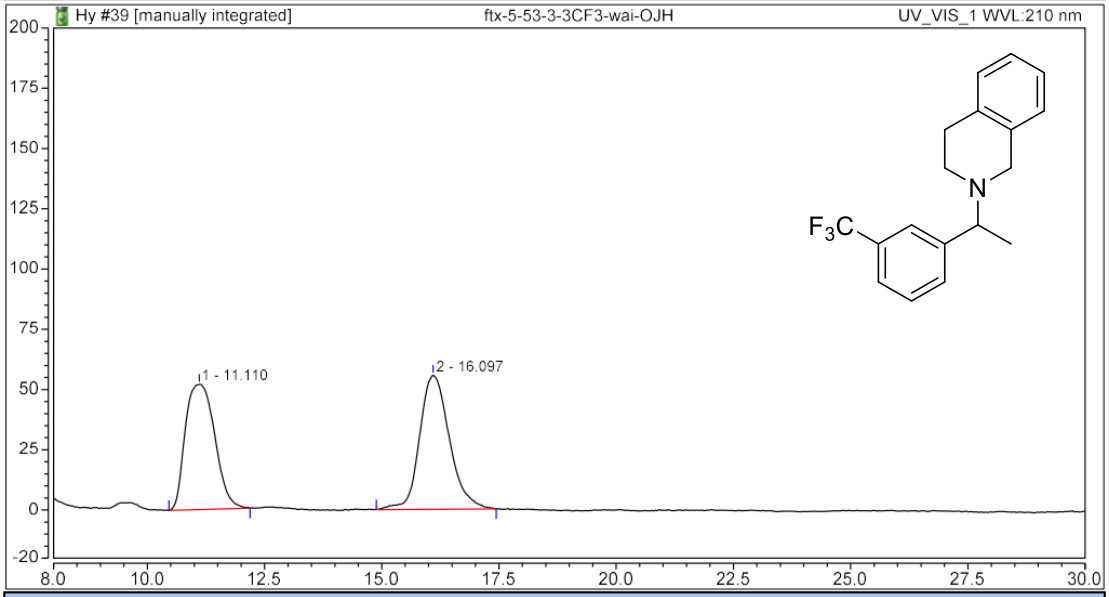
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		6.897	66.557	281.030	95.29	96.67	n.a.
2		9.160	3.290	9.687	4.71	3.33	n.a.
Total:			**69.847**	**290.718**	**100.00**	**100.00**	

(*S*)-2-(1-(3-(trifluoromethyl)phenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3m).



PE:EA = 20:1; Yellow oil, 58.0 mg (95% yield), 91% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.64 – 7.60 (m, 1H), 7.58 – 7.53 (m, 1H), 7.50 – 7.42 (m, 1H), 7.23 – 7.08 (m, 3H), 7.07 – 6.99 (m, 1H), 3.87 (d, *J* = 14.7 Hz, 1H), 3.72 – 3.55 (m, 2H), 2.98 – 2.74 (m, 3H), 2.73 – 2.57 (m, 1H), 1.50 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.72, 134.84, 134.47, 130.85, 128.80, 128.64, 126.75, 126.11, 125.61, 124.17, 124.14, 123.84, 63.98, 53.45, 47.99, 29.21, 19.97. ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.38. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 11.2 min (major), t_R = 16.2 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{18}H_{18}NF3Na$: 328.3340, found 328.3331.

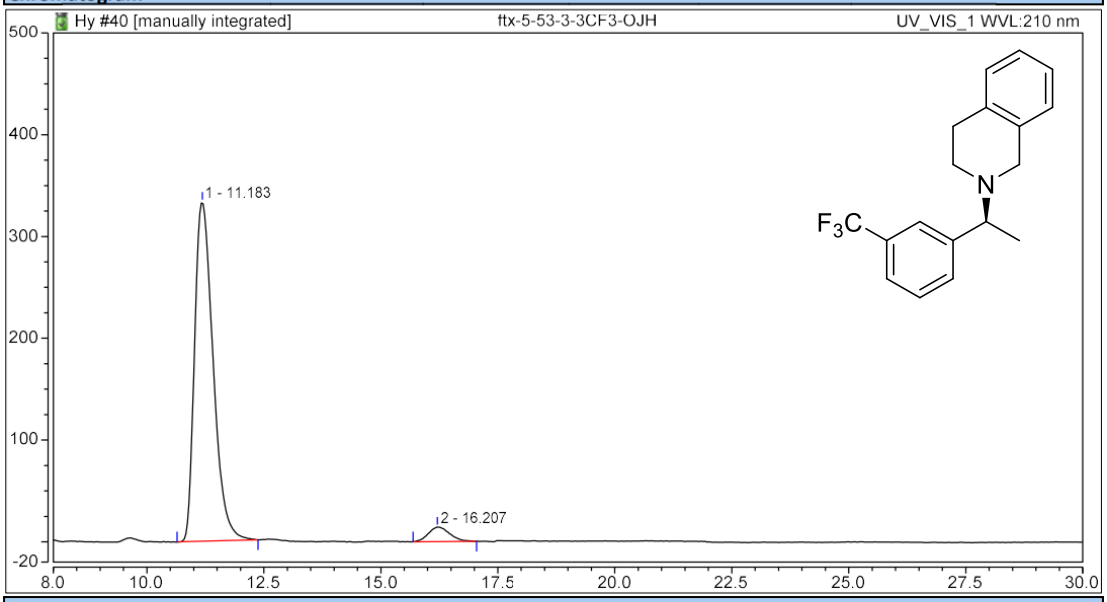
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.110	37.968	51.992	48.00	48.31	n.a.
2		16.097	41.134	55.626	52.00	51.69	n.a.
Total:			**79.102**	**107.618**	**100.00**	**100.00**	

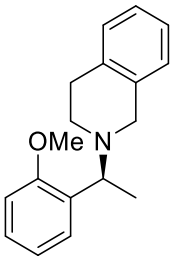
Chromatogram



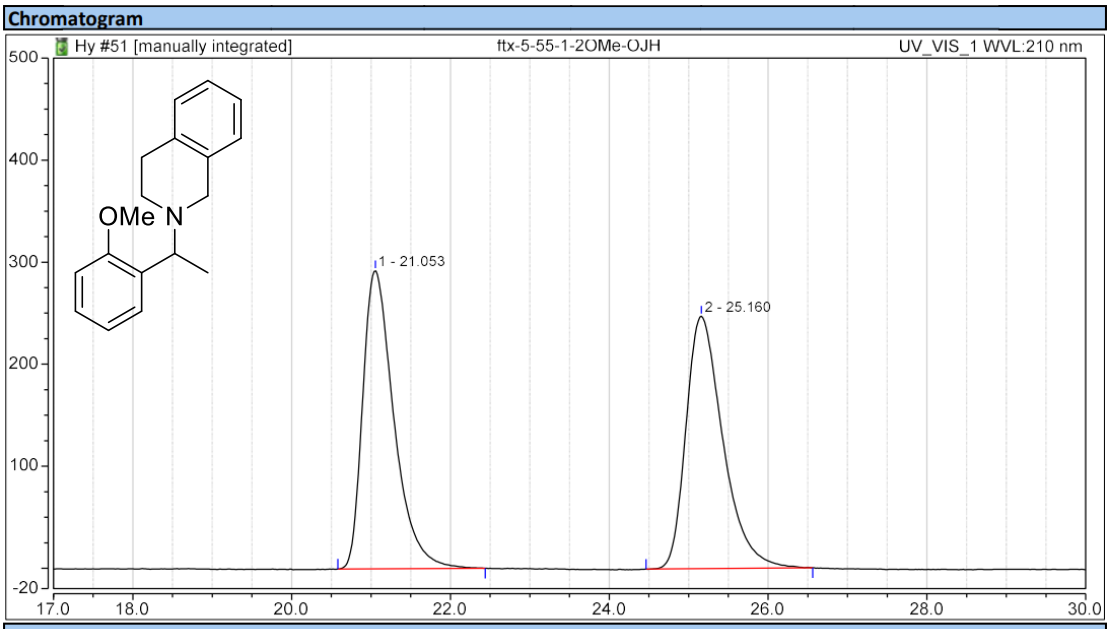
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.183	152.652	333.292	95.37	95.93	n.a.
2		16.207	7.416	14.123	4.63	4.07	n.a.
Total:			**160.068**	**347.415**	**100.00**	**100.00**	

(*S*)-2-(1-(2-methoxyphenyl)ethyl)-1,2,3,4-tetrahydroisoquinoline (3n).

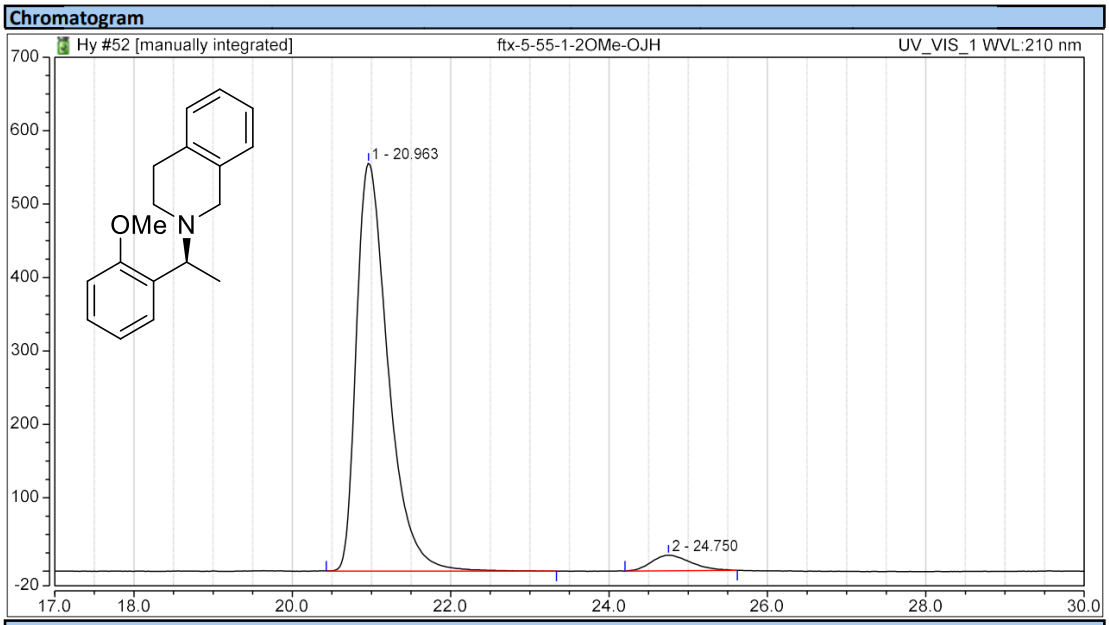


PE:EA = 20:1; Yellow oil, 51.3 mg (96% yield), 91% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.53 (m, 1H), 7.28 – 7.22 (m, 1H), 7.17 – 7.08 (m, 3H), 7.07 – 7.02 (m, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 4.13 (q, *J* = 6.7 Hz, 1H), 3.91 (d, *J* = 14.8 Hz, 1H), 3.87 (s, 3H), 3.60 (d, *J* = 14.8 Hz, 1H), 2.97 – 2.77 (m, 3H), 2.67 – 2.56 (m, 1H), 1.44 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.95, 135.42, 134.74, 132.61, 128.56, 127.62, 127.43, 126.79, 125.89, 125.41, 120.68, 110.50, 55.88, 55.43, 53.74, 48.25, 20.15. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 20.9 min (major), t_R = 24.8 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{18}H_{21}NONa$: 290.1521, found 290.1516.



Integration Results

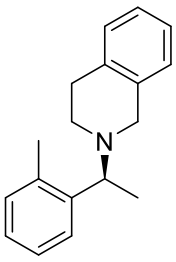
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		21.053	132.830	292.189	49.93	54.14	n.a.
2		25.160	133.203	247.463	50.07	45.86	n.a.
Total:			**266.033**	**539.653**	**100.00**	**100.00**	



Integration Results

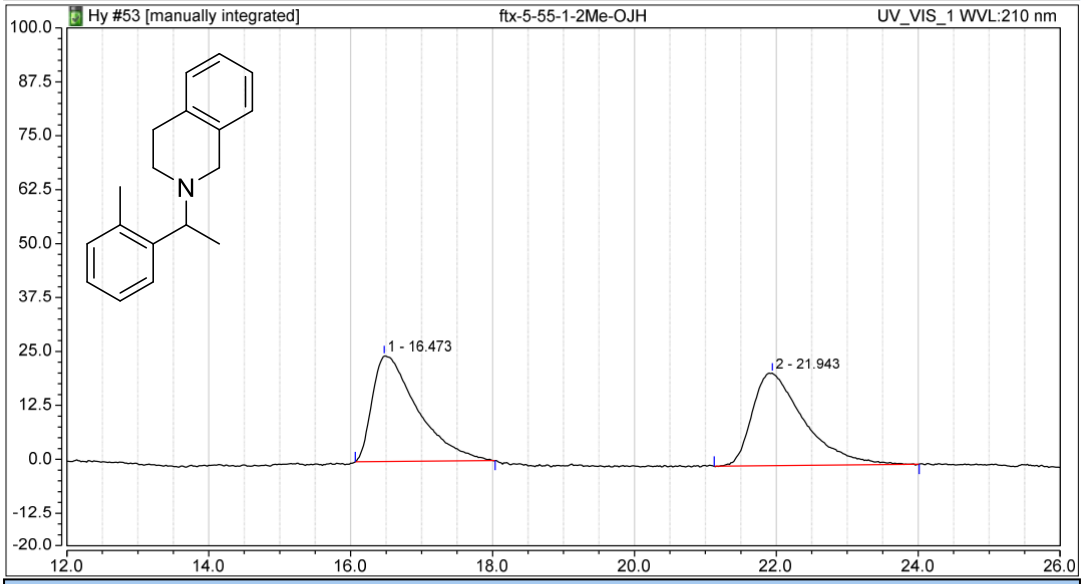
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		20.963	257.254	555.449	95.54	96.34	n.a.
2		24.750	12.019	21.125	4.46	3.66	n.a.
Total:			**269.273**	**576.574**	**100.00**	**100.00**	

(*S*)-2-(1-(*o*-tolyl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3o).



PE:EA = 20:1; Yellow oil, 47.2 mg (94% yield), 92% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 1H), 7.27 – 7.10 (m, 6H), 7.08 – 7.02 (m, 1H), 3.91 (d, *J* = 14.8 Hz, 1H), 3.78 (q, *J* = 6.6 Hz, 1H), 3.61 (d, *J* = 14.7 Hz, 1H), 3.00 – 2.89 (m, 1H), 2.88 – 2.74 (m, 2H), 2.71 – 2.61 (m, 1H), 2.42 (s, 3H), 1.44 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.24, 135.66, 135.29, 134.76, 130.33, 128.57, 126.78, 126.60, 126.32, 126.13, 125.93, 125.46, 60.09, 53.67, 48.22, 29.38, 19.54, 19.16. HPLC: Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 16.7 min (major), t_R = 22.2 min (minor). HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{18}H_{22}N$: 252.1752, found 252.1749.

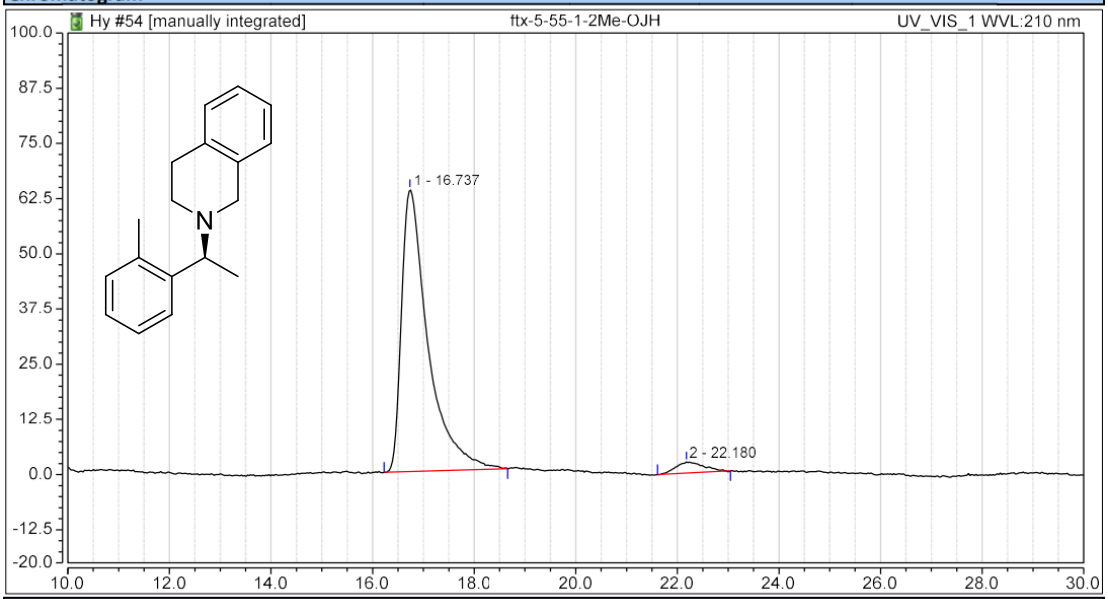
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.473	18.030	24.517	49.92	53.30	n.a.
2		21.943	18.088	21.480	50.08	46.70	n.a.
Total:			**36.118**	**45.997**	**100.00**	**100.00**	

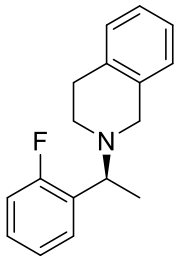
Chromatogram



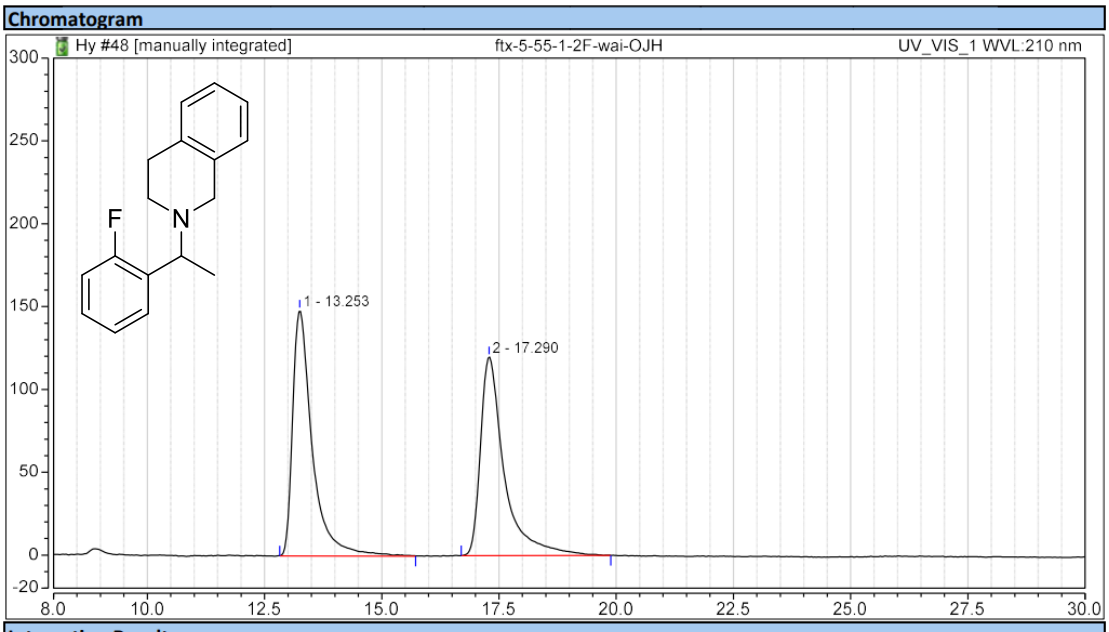
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.737	38.464	63.847	96.16	96.21	n.a.
2		22.180	1.536	2.517	3.84	3.79	n.a.
Total:			**40.000**	**66.364**	**100.00**	**100.00**	

(*S*)-2-(1-(2-fluorophenyl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3p).

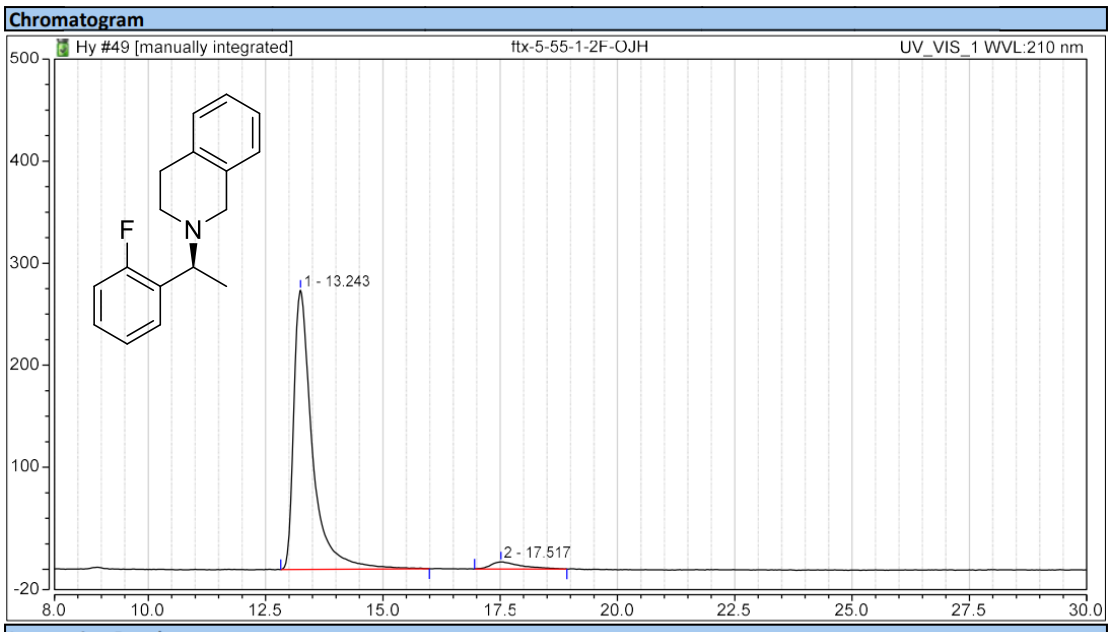


PE: EA = 20:1; Yellow oil, 48.0 mg (94% yield), 92% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 1H), 7.32 – 7.22 (m, 1H), 7.22 – 6.99 (m, 6H), 4.08 (q, *J* = 6.8 Hz, 1H), 3.88 (d, *J* = 14.7 Hz, 1H), 3.63 (d, *J* = 14.7 Hz, 1H), 3.01 – 2.77 (m, 3H), 2.72 – 2.60 (m, 1H), 1.53 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.72, 159.77, 135.09, 134.55, 130.49, 130.39, 128.74, 128.71, 128.64, 128.27, 128.20, 126.81, 126.06, 125.57, 124.13, 124.10, 115.45, 115.26, 56.17, 53.49, 47.98, 29.43, 19.74. ^{19}F NMR (471 MHz, $CDCl_3$) δ -118.60. HPLC：Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 13.2 min (major), t_R = 17.5 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{17}H_{18}FNNa$: 278.1321, found 278.1312.



Integration Results

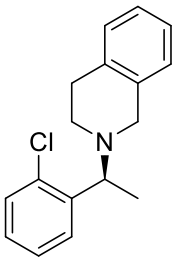
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.253	71.933	148.338	50.44	55.27	n.a.
2		17.290	70.670	120.026	49.56	44.73	n.a.
Total:			**142.603**	**268.364**	**100.00**	**100.00**	



Integration Results

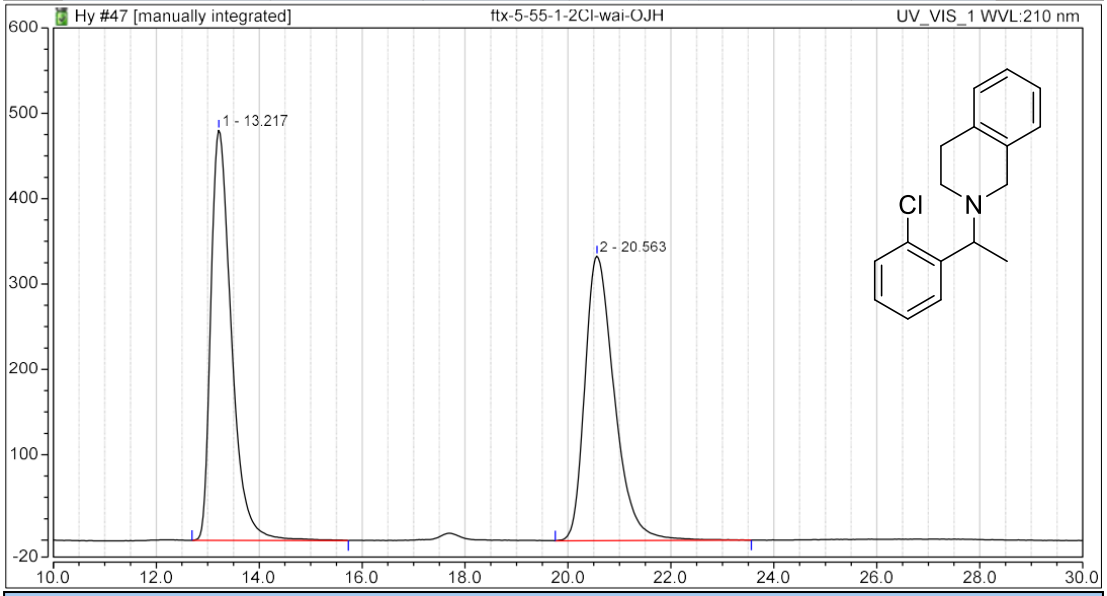
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.243	125.646	273.548	95.98	97.50	n.a.
2		17.517	5.260	7.014	4.02	2.50	n.a.
Total:			**130.906**	**280.562**	**100.00**	**100.00**	

(*S*)-2-(1-(2-chlorophenyl) ethyl)-1,2,3,4-tetrahydroisoquinoline (3q).



PE:EA = 20:1; Yellow oil, 51.1 mg (94% yield), 90% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.60 (m, 1H), 7.45 – 7.38 (m, 1H), 7.34 – 7.27 (m, 1H), 7.26 – 7.12 (m, 4H), 7.11 – 7.04 (m, 1H), 4.12 (q, *J* = 6.6 Hz, 1H), 3.97 (d, *J* = 14.7 Hz, 1H), 3.64 (d, *J* = 14.7 Hz, 1H), 3.02 – 2.90 (m, 1H), 2.89 – 2.77 (m, 2H), 2.76 – 2.65 (m, 1H), 1.47 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.50, 135.02, 134.58, 133.38, 129.40, 128.56, 128.32, 127.69, 127.05, 126.76, 126.01, 125.52, 59.96, 53.75, 48.39, 29.33, 20.12. HPLC：Chiralpak OJ-H, hexane : isopropanol = 98:2, 0.5 mL/min, 210 nm, t_R = 13.4 min (major), t_R = 21.2 min (minor). HRMS (ESI) m/z: $[M+Na]^+$ calculated for $C_{17}H_{18}ClNNa$: 294.1025, found 294.1031.

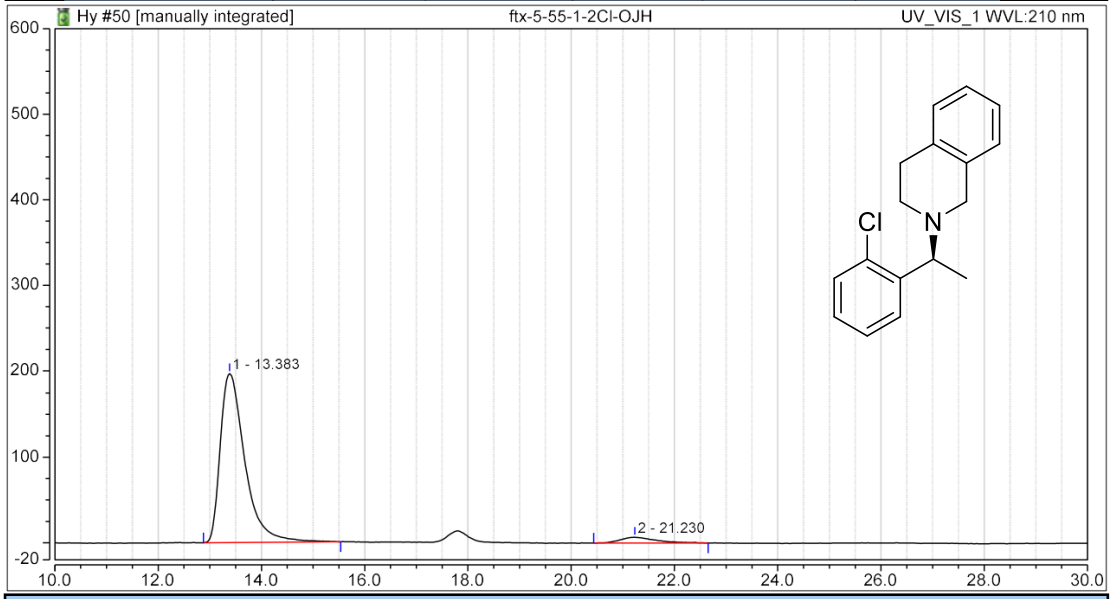
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.217	222.553	480.717	50.10	59.04	n.a.
2		20.563	221.686	333.448	49.90	40.96	n.a.
Total:			**444.240**	**814.164**	**100.00**	**100.00**	

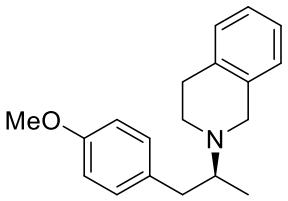
Chromatogram



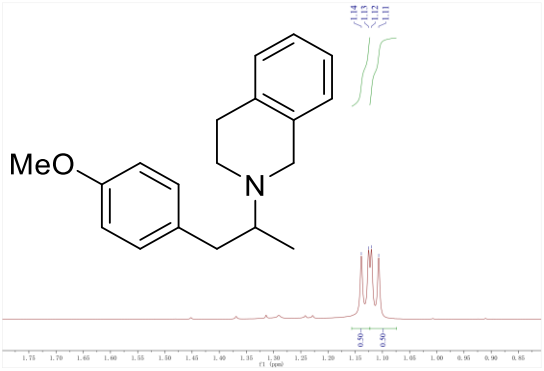
Integration Results

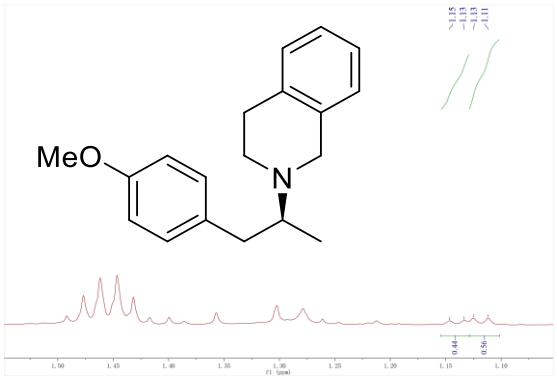
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		13.383	108.972	196.630	95.15	96.60	n.a.
2		21.230	5.558	6.930	4.85	3.40	n.a.
Total:			**114.530**	**203.560**	**100.00**	**100.00**	

(*S*)-2-(1-(4-methoxyphenyl)propan-2-yl)-1,2,3,4-tetrahydroisoquinoline (3r).[2]

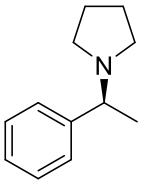


PE:EA = 20:1; Yellow oil, 52.9 mg (94% yield), 14% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.12 (m, 5H), 7.12 – 7.05 (m, 1H), 6.91 – 6.84 (m, 2H), 3.87 (s, 2H), 3.83 (s, 3H), 3.11 – 3.00 (m, 2H), 2.99 – 2.94 (m, 2H), 2.93 – 2.87 (m, 2H), 2.58 – 2.46 (m, 1H), 1.08 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.75, 135.44, 134.64, 132.54, 130.10, 128.73, 126.67, 125.87, 125.43, 113.63, 61.26, 55.17, 51.50, 46.09, 38.49, 29.89, 13.99. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent. HRMS (ESI) m/z: $[M+H]^+$ calculated for $C_{20}H_{26}NO$: 296.2014, found 296.2026.



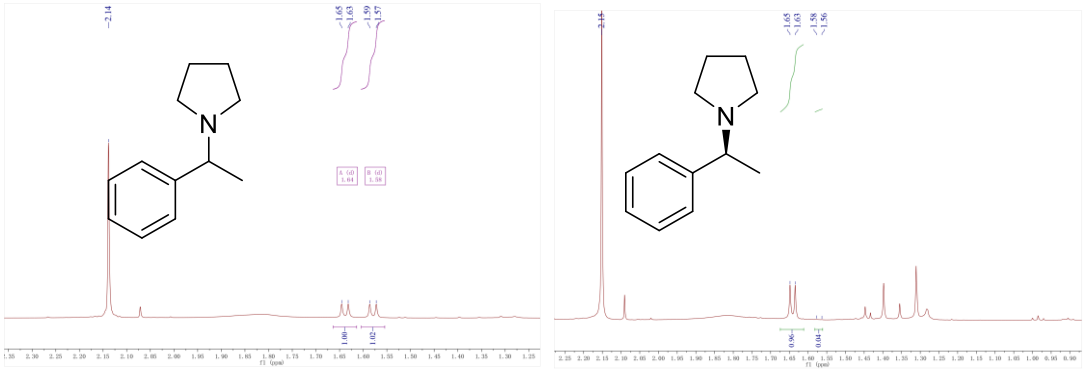


(*S*)-1-(1-phenylethyl)pyrrolidine (3s).[2]

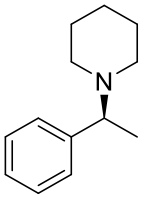


PE:EA = 2:1; Yellow oil, 32.2 mg (92% yield), 94% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 4H), 7.27 – 7.22 (m, 1H), 3.20 (q, *J* = 6.6 Hz, 1H), 2.63 – 2.49 (m, 2H), 2.45 – 2.33 (m, 2H), 1.82 – 1.75 (m, 4H), 1.43 (dd, *J* = 6.6, 1.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.73, 128.22, 127.20, 126.78, 66.00, 52.98, 23.39, 23.18. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as

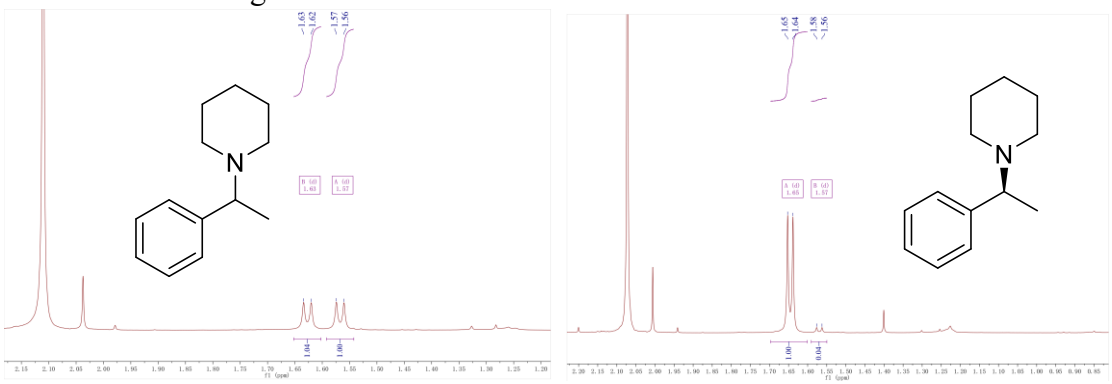
chemical shift reagent.



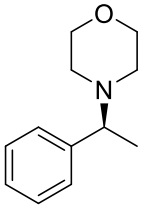
(*S*)-1-(1-phenylethyl)piperidine (3t).[2]



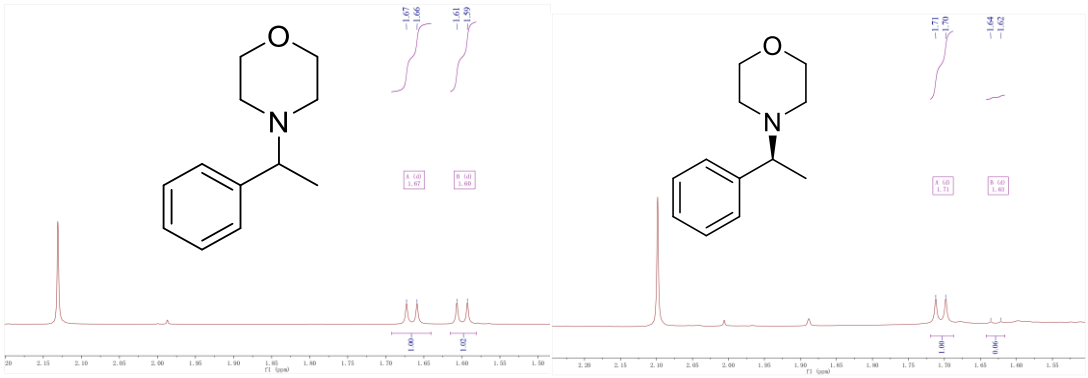
PE:EA = 5:1; Yellow oil, 34.1 mg (90% yield), 92 % *ee*, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 3H), 7.28 – 7.19 (m, 2H), 3.38 (q, *J* = 6.8 Hz, 1H), 2.38 – 2.29 (m, 4H), 1.65 – 1.43 (m, 6H), 1.36 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.91, 127.98, 126.63, 125.37, 65.18, 51.49, 26.26, 24.60, 19.40. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent.



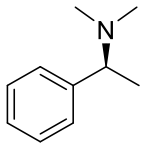
(*S*)-4-(1-phenylethyl)morpholine (3u).[2]



PE:EA = 5:1; Yellow oil, 34.4 mg (90% yield), 89% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 4.4 Hz, 4H), 7.29 – 7.24 (m, 1H), 3.75 – 3.68 (m, 4H), 3.32 (q, J = 6.6 Hz, 1H), 2.57 – 2.46 (m, 2H), 2.44 – 2.34 (m, 2H), 1.38 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.92, 128.26, 127.60, 126.94, 67.21, 65.37, 51.29, 19.81. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent.

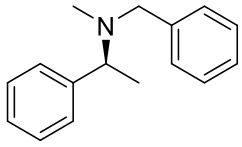


(*S*)-*N*,*N*-dimethyl-1-phenylethan-1-amine(3v)[2]

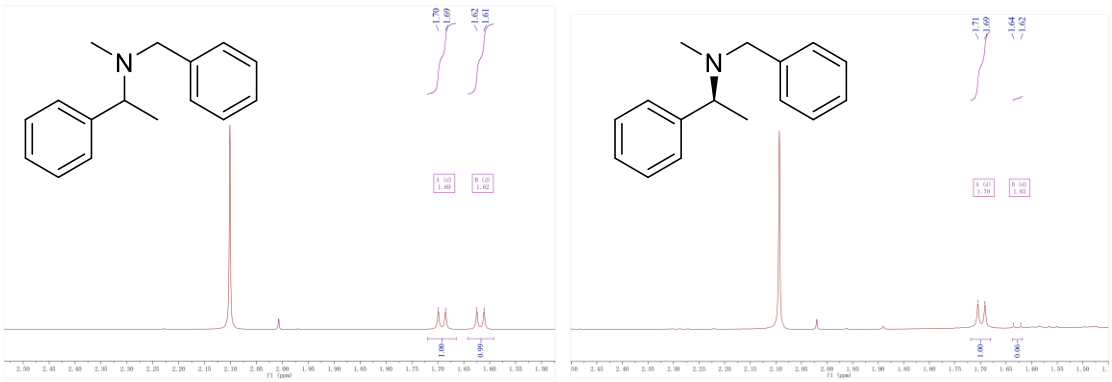


DCM:MeOH = 5:1; Yellow oil, 27.1 mg (91% yield), 91% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 3H), 7.29 – 7.24 (m, 2H), 3.27 (d, *J* = 6.7 Hz, 1H), 2.22 (s, 6H), 1.40 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.08, 128.18, 127.51, 126.86, 65.98, 43.25, 20.24. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent.

(*S*)-*N*-benzyl-N-methyl-1-phenylethan-1-amine(3w)[2]

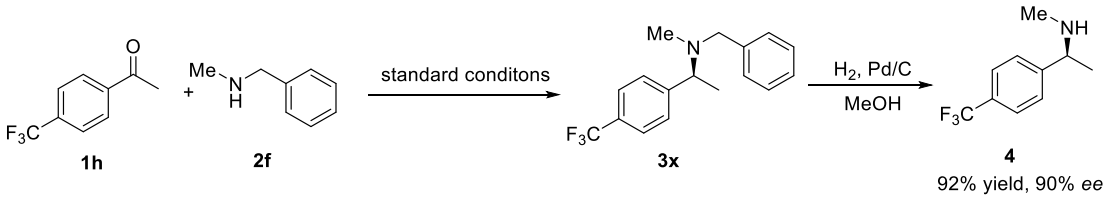


PE:EA = 5:1; Yellow oil, 42.3 mg (94% yield), 89% *ee*; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.42 (m, 2H), 7.40 – 7.29 (m, 6H), 7.30 – 7.23 (m, 2H), 3.73 – 3.55 (m, 2H), 3.35 (d, *J* = 13.3 Hz, 1H), 2.18 (s, 3H), 1.47 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.17, 140.10, 128.72, 128.15, 128.13, 127.67, 126.76, 126.69, 63.21, 58.86, 38.34, 18.37. Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent.



2.3 General procedure for the preparation of 4 and 5.

2.3.1 General procedure for the preparation of 4[2]



Step1:

To a vial containing a magnetic stirring bar was added **1h** (0.2 mmol), **2f** (0.22 mmol), I_2 (2 mol%), $Ti(OEt)_4$ (0.4 mmol), $[Ir(COD)(Cl)]_2$ (1 mol %), and **N-Me-Xu6** (2.2 mol %) under nitrogen atmosphere, anhydrous THF (2 mL) was added and stirred

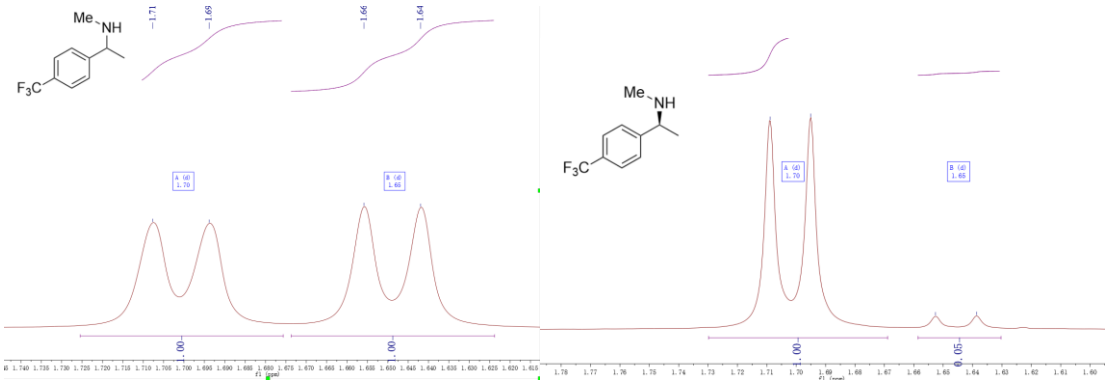
for 30 minutes. Then the vial was transferred in Parr steel autoclave, which was purged three times with hydrogen and finally pressurized to 50 atm. The reaction mixture was stirred at 0 °C for 24 h. The hydrogen gas was released slowly and the solution was quenched with $Na_2SO_4 \cdot 10H_2O$ and filtered. The organic phase was concentrated to give the crude products **3x**, which were used in next step without purification.

Step2:

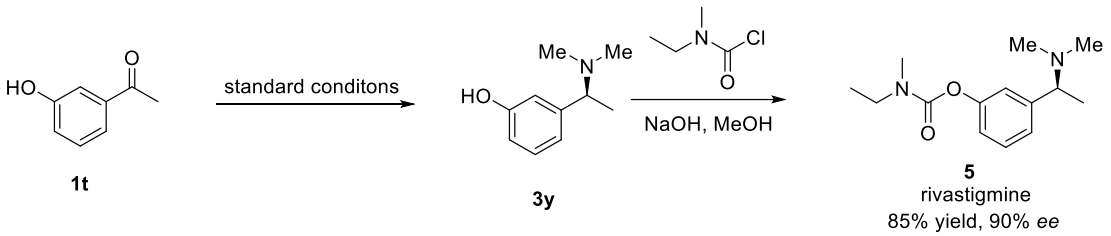
$Pd(OH)_2$ on carbon (10%, 4.5 mg) was added to the solution of **3x** (58.6 mg, 0.2 mmol) and acetic acid (1 drop) in MeOH (2 mL). The resulting mixture was transferred to an autoclave, which was charged with 20 atm of H_2, and stirred at r.t. for 10 h. The hydrogen gas was released slowly and the solution was filter and quenched with aqueous sodium bicarbonate solution. The organic phase was concentrated and purified with column chromotography to afford **4**

(*S*)-*N*-methyl-1-(4-(trifluoromethyl)phenyl)ethan-1-amine(4)[5]

PE:EA=5:1, Yellow oil, 7.3 mg, 92% yield, 90% *ee*. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 3.89 (q, J = 6.7 Hz, 1H), 2.35 (s, 3H), 1.49 (d, J = 6.7 Hz, 3H). Enantiomeric excess was determined by ^{1}H NMR using D-(-)-Mandelic acid as chemical shift reagent.



2.3.2 General procedure for the preparation of rivastigmine. [2]



Step1:

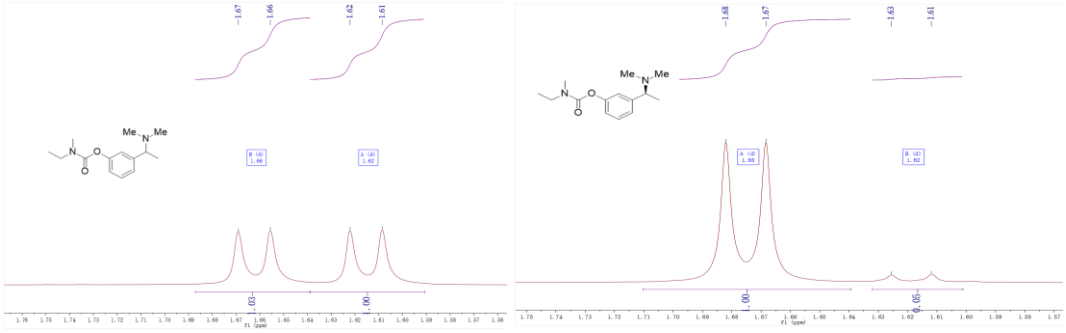
To a vial containing a magnetic stirring bar was added **1t** (0.2 mmol), dimethylamine (0.22 mmol), I_2 (2 mol%), $Ti(OEt)_4$ (0.4 mmol), $[Ir(COD)(Cl)]_2$ (1 mol %), and **N-Me-Xu6** (2.2 mol %) under nitrogen atmosphere, anhydrous THF (2 mL) was added and stirred for 30 minutes. Then the vial was transferred in Parr steel autoclave, which was purged three times with hydrogen and finally pressurized to 50 atm. The reaction mixture was stirred at 0 ^oC for 24 h. The hydrogen gas was released slowly and the solution was quenched with $Na_2SO_4 \cdot 10H_2O$ and filtered. The organic phase was concentrated to give the crude products **3y**, which were used in next step without purification.

Step2:

NaOH (0.25 mmol) was added to the solution of **3y** in CH_3CN (1.5 mL). The the above solution was stirred for 1 h at room temperature, then ethyl(methyl)carbamic chloride (0.22 mmol) was added. The reaction mixture was stirred for 12 h, quenched by aq. NH4Cl solution. CH_3CN was removed under vaccumn and the solution was extracted by EtOAc (5 mL*3). The organic phase was dried over anhydrous Na_2SO_4, concentrated and purified with column chromatograpgy (EtOAc/PE) to give rivastigmine.

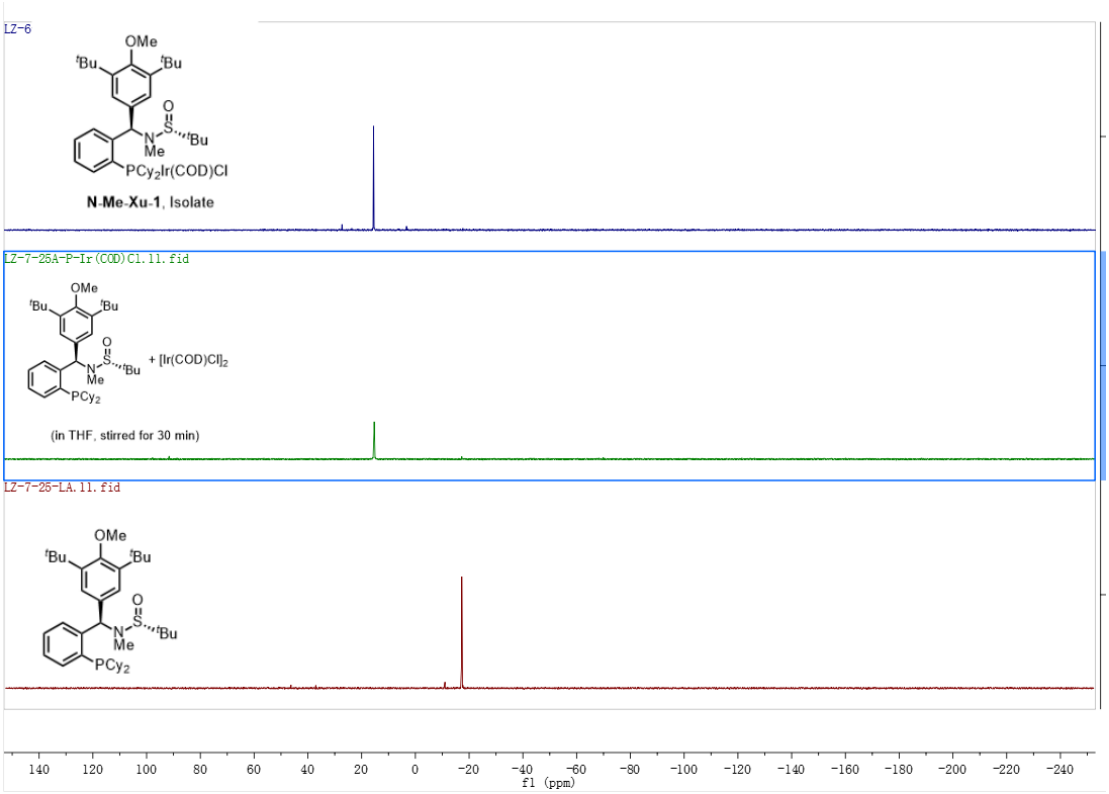
(*S*)-3-[1-(Dimethylamino)ethyl]phenyl Ethyl-(methyl)carbamate(rivastigmine):

PE:EA=20:1, 42.5 mg (85% yield for 2 steps), 90% *ee*, ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 1H), 7.15 – 7.01 (m, 3H), 3.52 – 3.39 (m, 2H), 3.29 (q, J = 6.7 Hz, 1H), 3.04 (d, J = 37.5 Hz, 3H), 2.23 (s, 6H), 1.39 (d, J = 6.7 Hz, 3H), 1.28 – 1.19 (m, 3H). Enantiomeric excess was determined by ^1H NMR using D-(-)-Mandelic acid as chemical shift reagent.

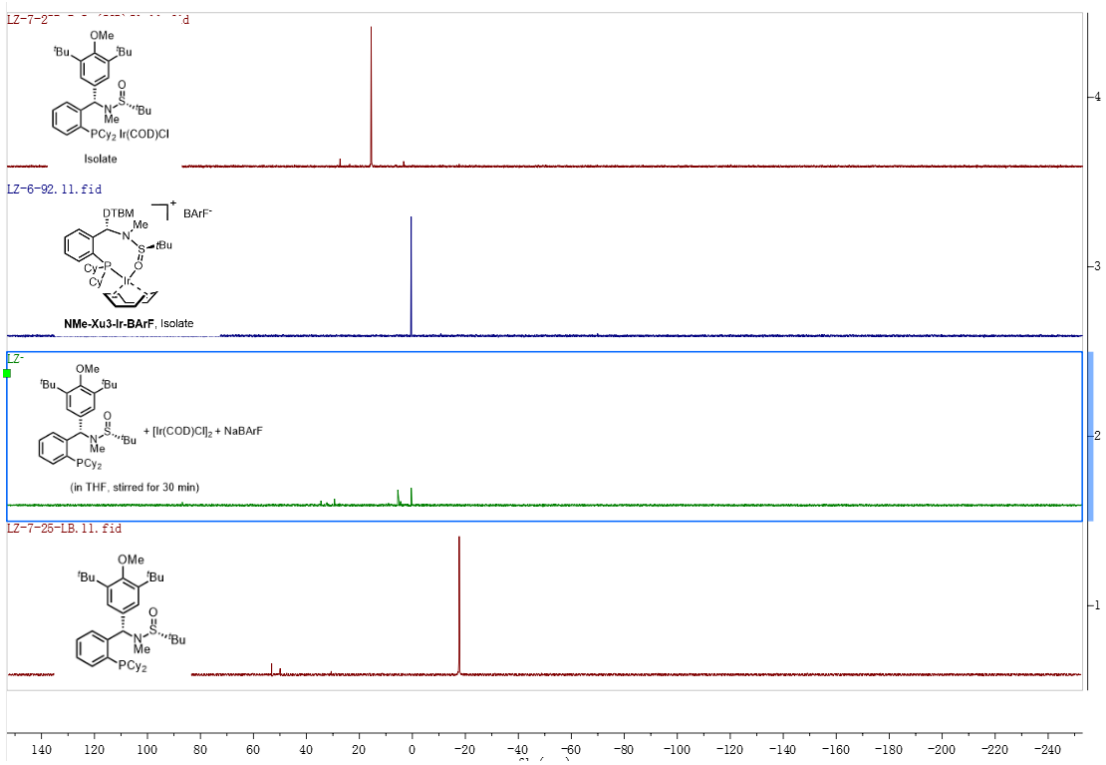


2.3.3 ^{31}P NMR spectra of ligands and Ir catalysts.

^{31}P NMR spectra for N-Me-Xu1 and Ir complexes



^{31}P NMR spectra for N-Me-Xu3 and Ir complexes



3. X-Ray Crystal Data

Crystal Structure Information of NMe-Xu1-Ir

0.1 mL of DCM was added to a 10 mL oven-dried glass sample bottle with 10 mg pure **NMe-Xu1-Ir** to dissolve the sample, then 8 mL n-hexane was slowly added to the solution, sealed with perforated paper, and then the solvent was slowly dried at room temperature to obtain crystals. Single crystal X-ray diffraction data were collected on Bruker Smart Apex II CCD diffractometer. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC)：2371593

Formula: $C_{47}H_{74}IrNO_2PS$

Flack parameter 0.066(7)

Bond precision: C-C = 0.0115 A Wavelength=1.54178

Cell: a=44.8783(13) b=11.8093(3) c=21.0380(6)
alpha=90 beta=115.469(1) gamma=90

Temperature: 187 K

	Calculated	Reported
Volume	10066.2(5)	10066.2(5)
Space group	C 2	C 2
Hall group	C 2y	C 2y
Moiety formula	C47 H74 Cl Ir N O2 P S [+ solvent]	C47 H74 Cl Ir N O2 P S [+ solvent]
Sum formula	C47 H74 Cl Ir N O2 P S [+ solvent]	C47 H74 Cl Ir N O2 P S
Mr	975.77	975.75
Dx,g cm-3	1.288	1.288
Z	8	8
Mu (mm-1)	6.560	6.560
F000	4032.0	4032.0
F000'	4009.46	
h,k,lmax	54,14,25	54,14,25
Nref	18554[9765]	18311
Tmin,Tmax	0.403,0.455	0.525,0.753
Tmin'	0.304	

Correction method= # Reported T Limits: Tmin=0.525 Tmax=0.753
AbsCorr = MULTI-SCAN

Data completeness= 1.88/0.99 Theta(max)= 68.562

Crystal Structure Information of NMe-Xu3-Ir-BArF

0.1 mL of DCM was added to a 10 mL oven-dried glass sample bottle with 10 mg pure **NMe-Xu3-Ir-BArF** to dissolve the sample, then 8 mL n-hexane was slowly added to the solution, sealed with perforated paper, and then the solvent was slowly dried at room temperature to obtain crystals. Single crystal X-ray diffraction data were collected on Bruker Smart Apex II CCD diffractometer. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC)：2328618

Formula: $C_{79}H_{86}BF_{24}IrNO_2PS$

Flack parameter -0.012(3)

Bond precision: C-C = 0.0105 A Wavelength=1.54184

Cell: a=14.1597(1) b=14.8103(1) c=41.8365(4)
alpha=90 beta=90 gamma=90

Temperature: 170 K

	Calculated	Reported
Volume	8773.51(12)	8773.51(12)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C32 H12 B F24, C47 H74 Ir N O2 P S [+ solvent]	C47 H74 Ir N O2 P S, C32 H12 B F24
Sum formula	C79 H86 B F24 Ir N O2 P S [+ solvent]	C79 H86 B F24 Ir N O2 P S
Mr	1803.55	1803.52
Dx, g cm-3	1.365	1.365
Z	4	4
Mu (mm-1)	4.157	4.157
F000	3648.0	3648.0
F000'	3644.32	
h, k, lmax	16, 17, 49	16, 17, 49
Nref	15652[8599]	15626
Tmin, Tmax	0.218, 0.633	0.198, 1.000
Tmin'	0.140	

Correction method= # Reported T Limits: Tmin=0.198 Tmax=1.000 AbsCorr = MULTI-SCAN

Data completeness= 1.82/1.00 Theta(max)= 67.078

R(reflections)= 0.0373(15445) wR2(reflections)= 0.0982(15626)

S = 1.022 Npar= 1002

4. References

[1] Wang, Y.; Wang, L. Chen, M.; Tu, Y.; Liu, Y.; Zhang, J. Palladium/Xu-Phos-catalyzed asymmetric carboamination towards isoxazolidines and pyrrolidines. *Chem. Sci.*, **2021**,*12*, 8241 - 8245.

[2] Wu, Z.; Du, S.; Gao, G.; Yang, W.; Yang, X.; Huang, H.; Chang, M. Secondary Amines as Coupling Partners in Direct Catalytic Asymmetric Reductive Amination, *Chem. Sci*., **2019**, *10*, 4509 - 4514.

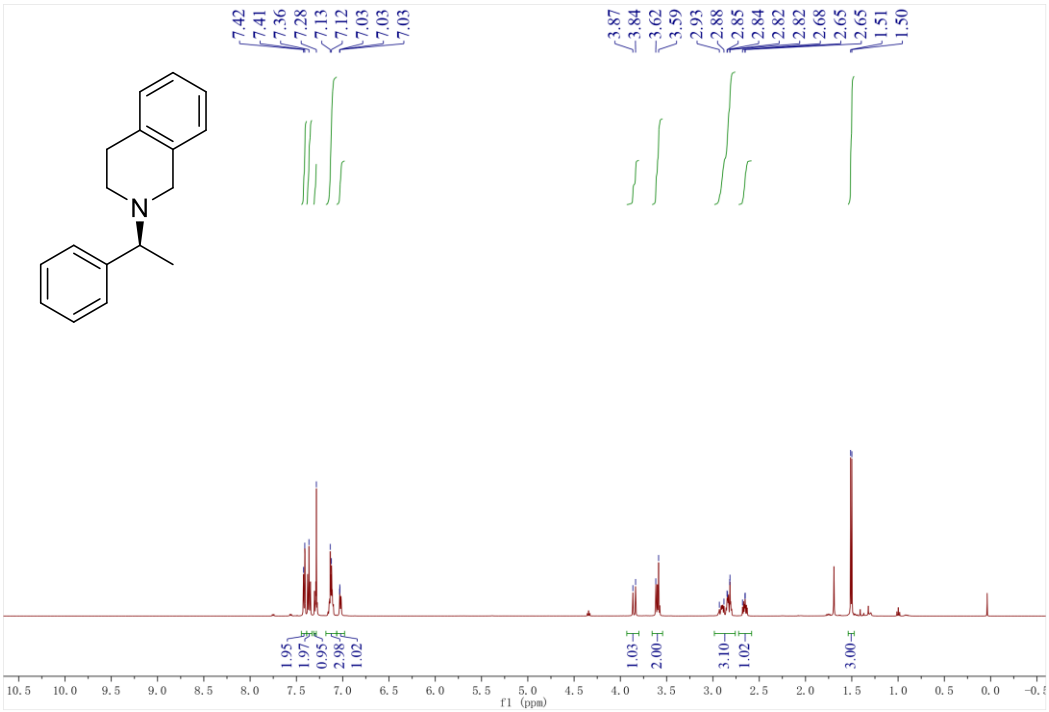
[3] Benmekhbi, L.; Louafi, F.; Roisnel, T.; Hurvois, J.-P. Synthesis of Tetrahydroisoquinoline Alkaloids and Related Compounds through the Alkylation of Anodically Prepared α-Amino Nitriles. *J. Org. Chem*., **2016**, *81*, 6721 - 6739.

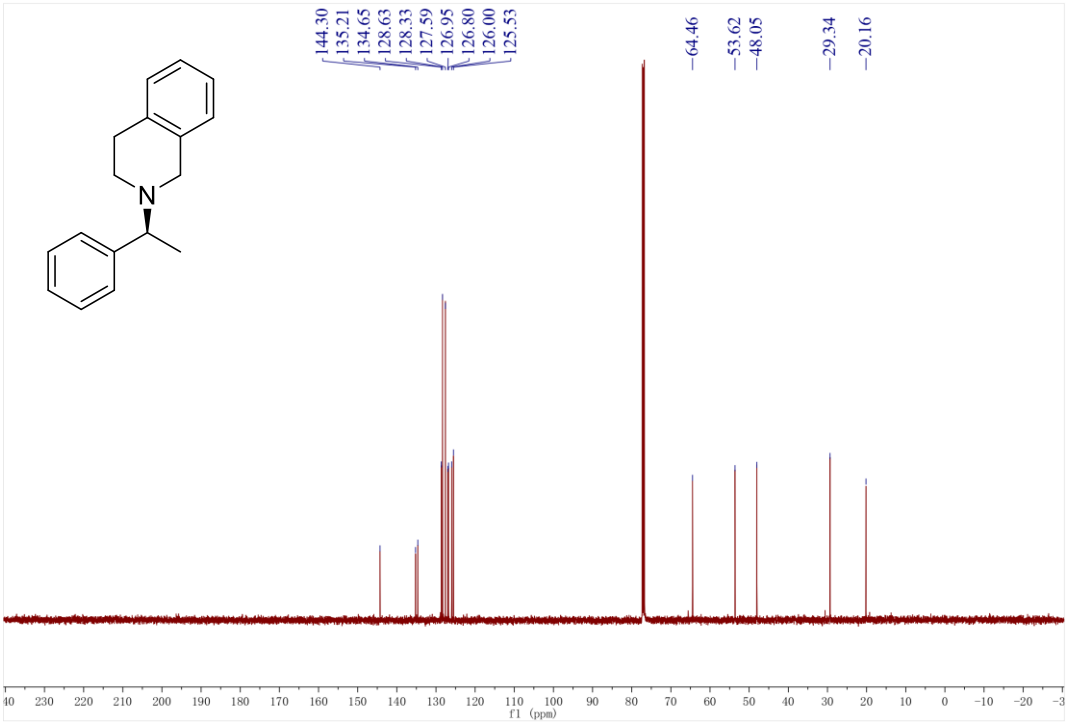
[4] Kumpaty, H. J.; Bhattacharyya, S. Efficient synthesis of N-alkyl tetrahydroisoquinolines by reductive amination, *Synthesis*, **2005**, *13*, 2205 - 2209.

[5] Wen, Y.; Fernández-Sabaté, M.; Lledós, A.; Sciortino, G.; Eills, J.; Marco-Rius, I.; Riera, A.; Verdaguer, X. Cyclometallated Imides as Templates for the H-Bond Directed Iridium-Catalyzed Asymmetric Hydrogenation of N-Methyl, N-Alkyl and N-Aryl Imines. *Angew. Chem. Int. Ed*., **2024**, *63*, e202404955.

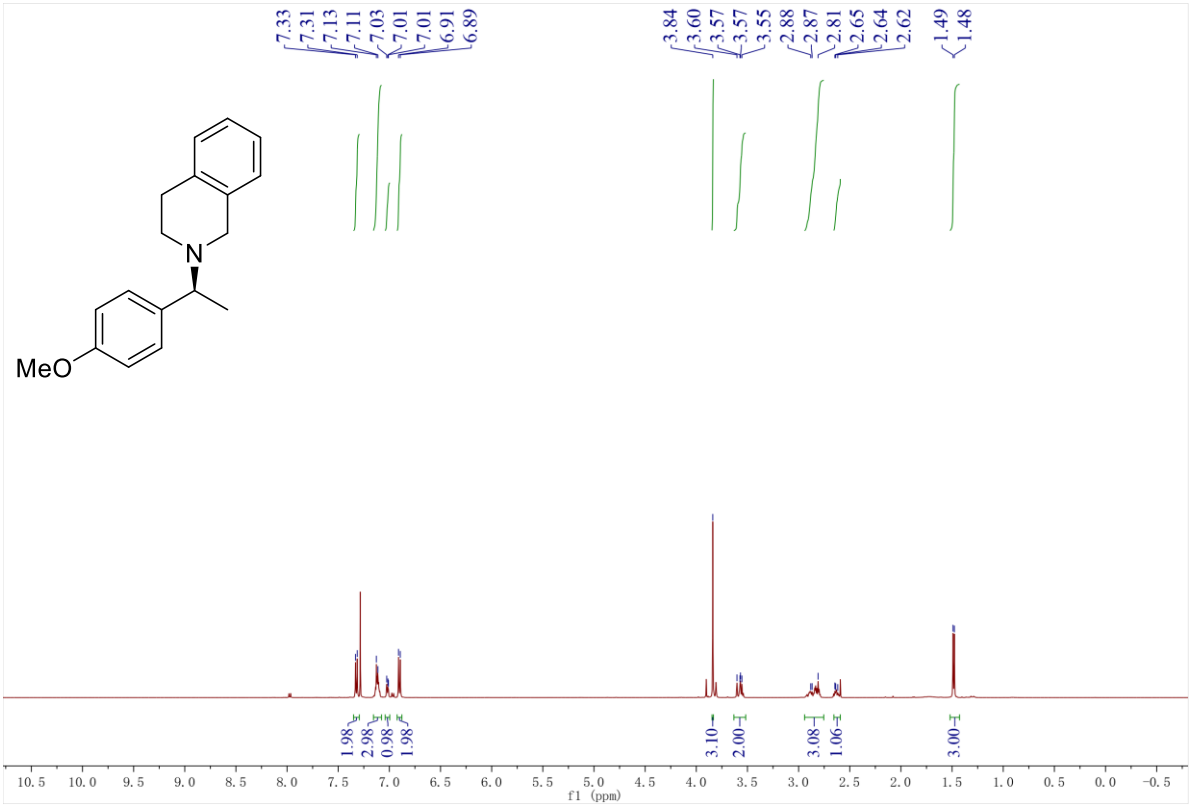
5. NMR Spectra of Hydrogenation Products

(*S*)- 3a





(*S*)-3b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7.31
7.13
7.11
7.03
7.01
7.01
6.91
6.89
3.84
3.60
3.57
3.57
3.55
2.88
2.87
2.81
2.65
2.64
2.62
1.49
1.48
MeO
N
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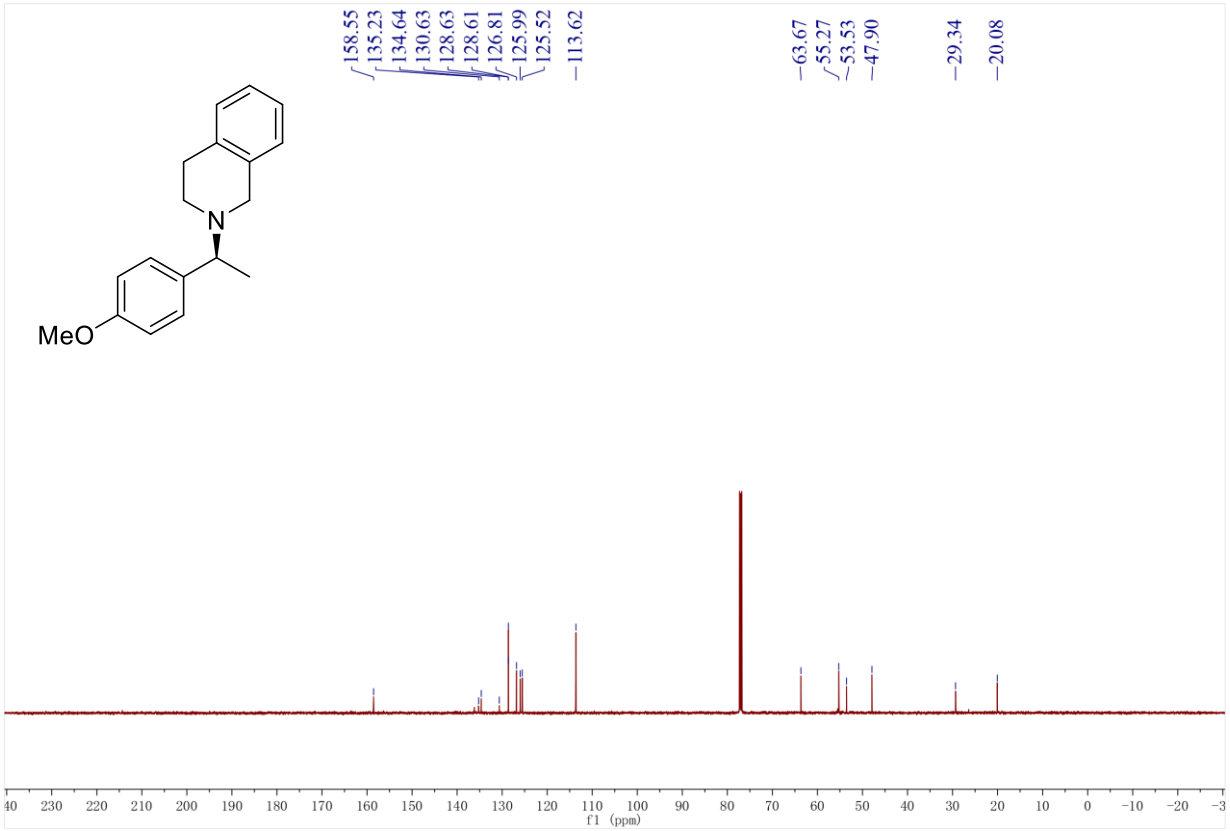
2.98
0.98
1.98
3.10
2.00
3.08
1.06
3.00
f1 (ppm)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128.61
126.81
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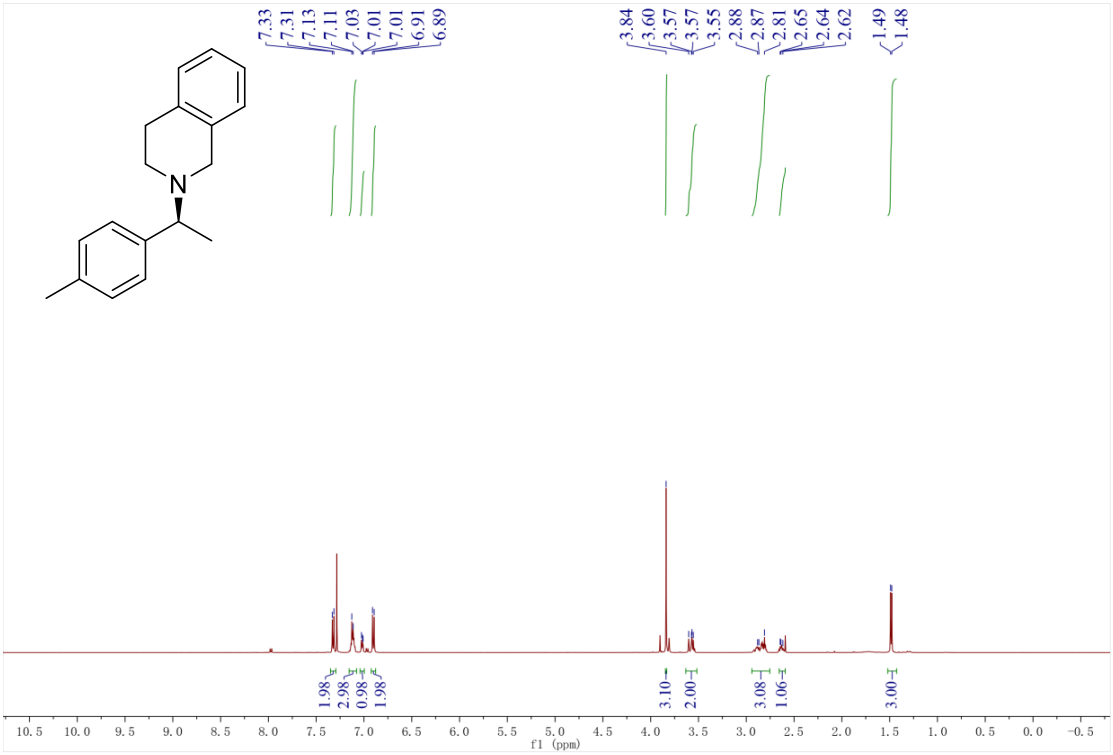
53.53
47.90
29.34
20.08
MeO
N
f1 (ppm)

(*S*)-3c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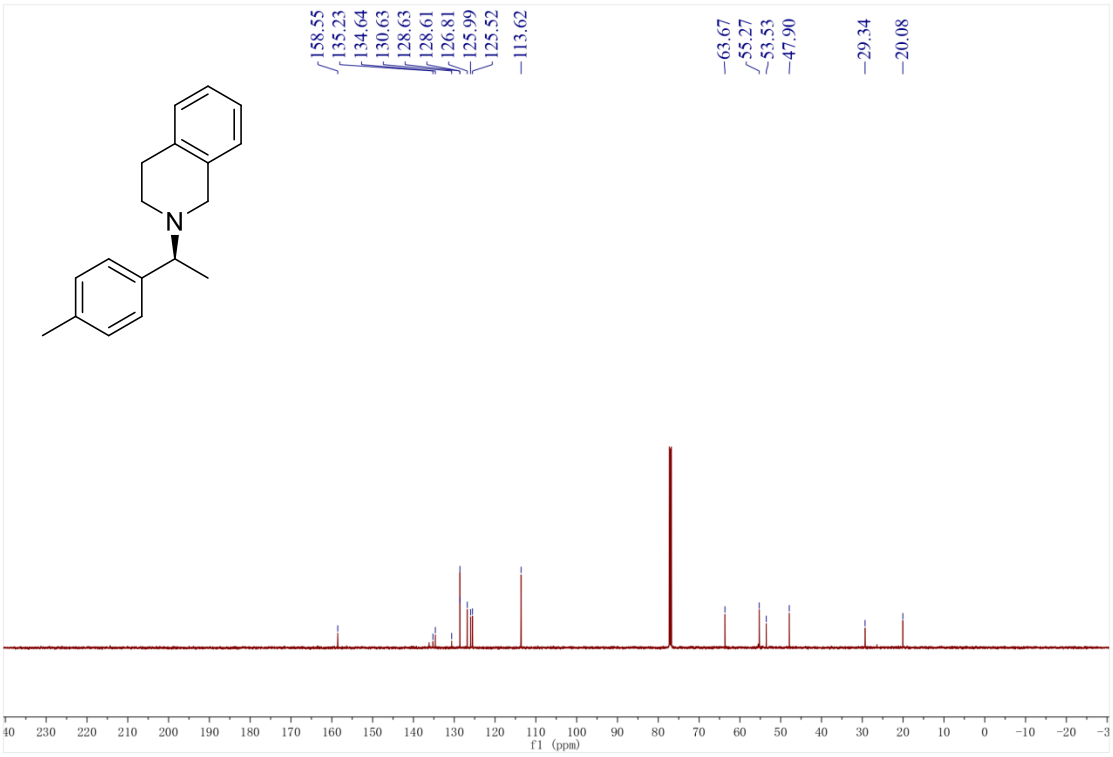
7.31
7.13
7.11
7.03
7.01
7.01
6.91
6.89
3.84
3.60
3.57
3.57
3.55
2.88
2.87
2.81
2.65
2.64
2.62
1.49
1.48
1.98
2.98
0.98
1.98
3.10
2.00
3.08
1.06
3.00
f1 (ppm)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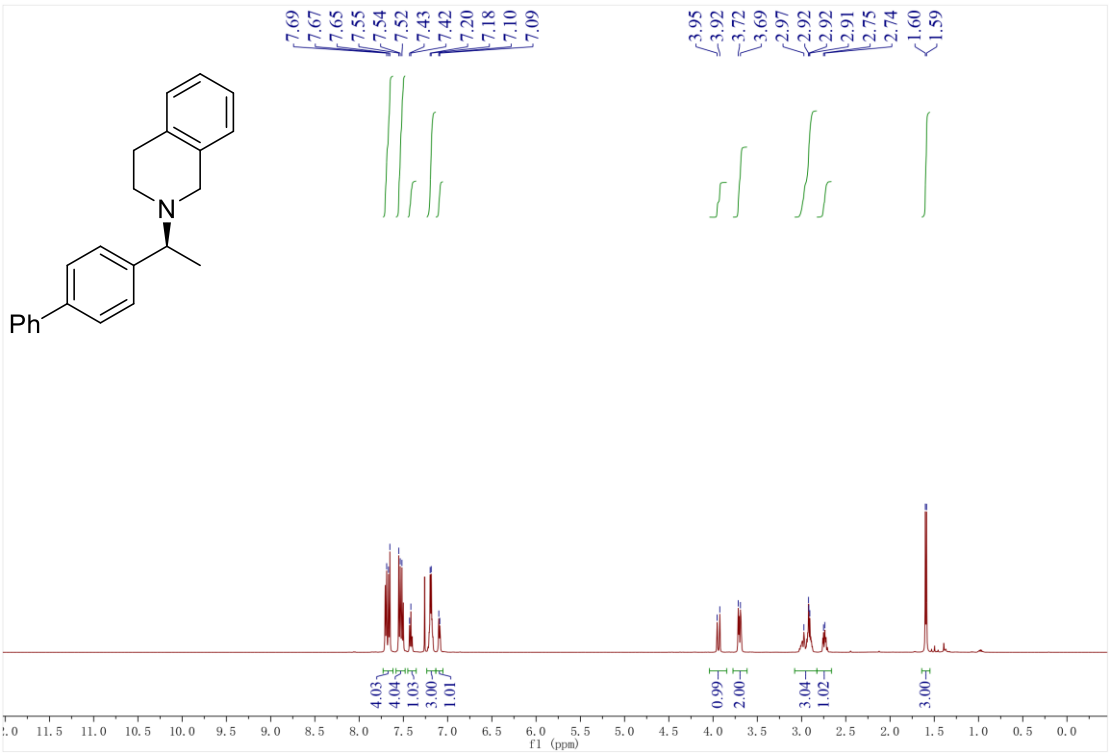
135.23
134.64
130.63
128.63
128.61
126.81
125.99
125.52
113.62
63.67
55.27
53.53
47.90
29.34
20.08
f1 (ppm)

(*S*)-3d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7.67
7.65
7.55
7.54
7.52
7.43
7.42
7.20
7.18
7.10
7.09
3.95
3.92
3.72
3.69
2.97
2.92
2.92
2.91
2.75
2.74
1.60
1.59
N
Ph
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4.04
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1.01
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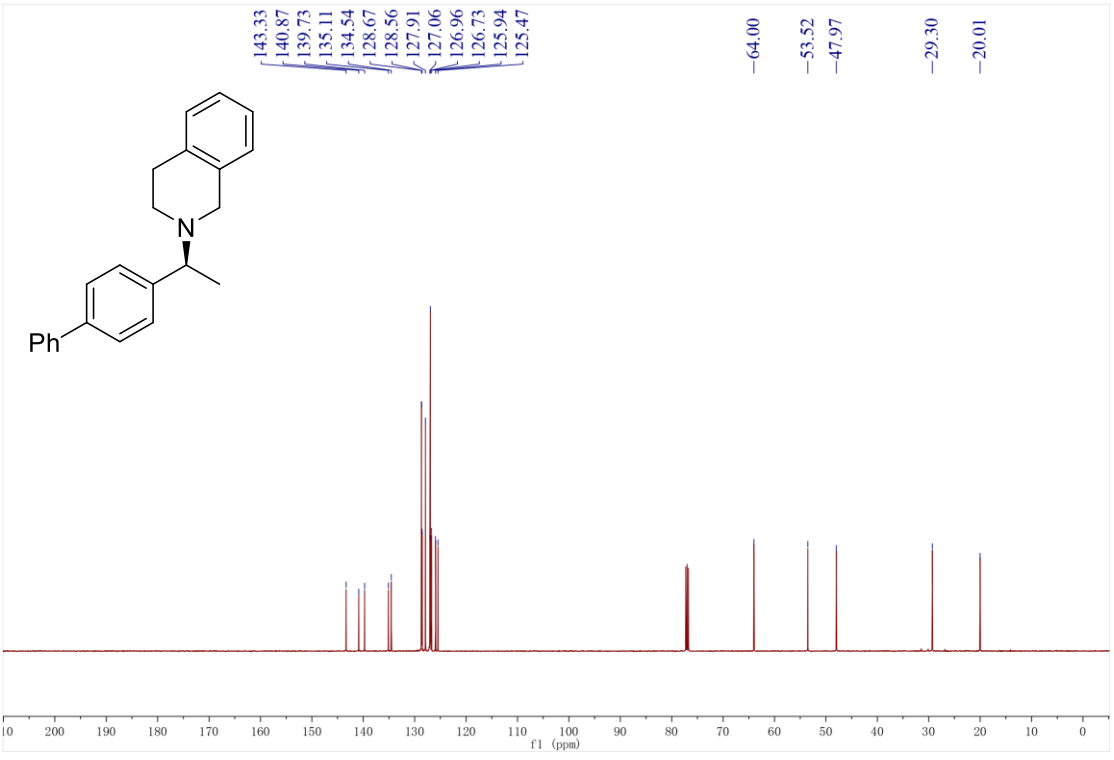
3.04
1.02
3.00
f1 (ppm)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128.56
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126.73
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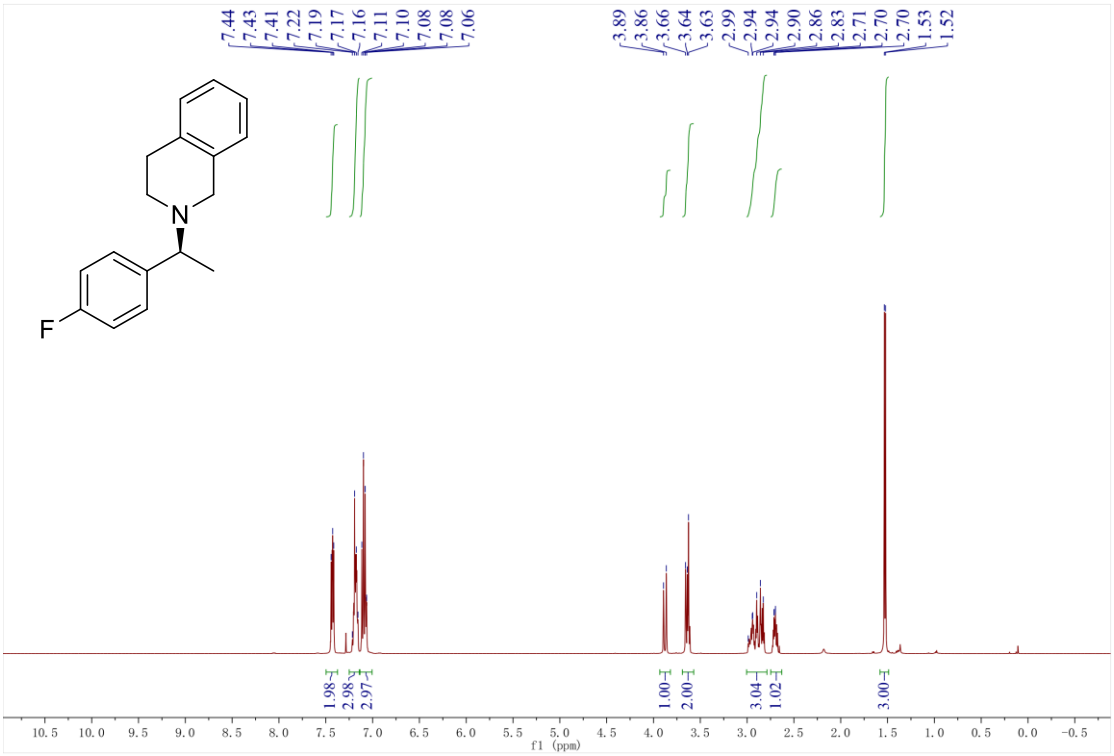
64.00
53.52
47.97
29.30
20.01
N
Ph
f1 (ppm)

(*S*)-3e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7.08
7.08
7.06
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3.86
3.66
3.64
3.63
2.99
2.94
2.94
2.90
2.86
2.83
2.71
2.70
2.70
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1.52
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F
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2.98
2.97
1.00
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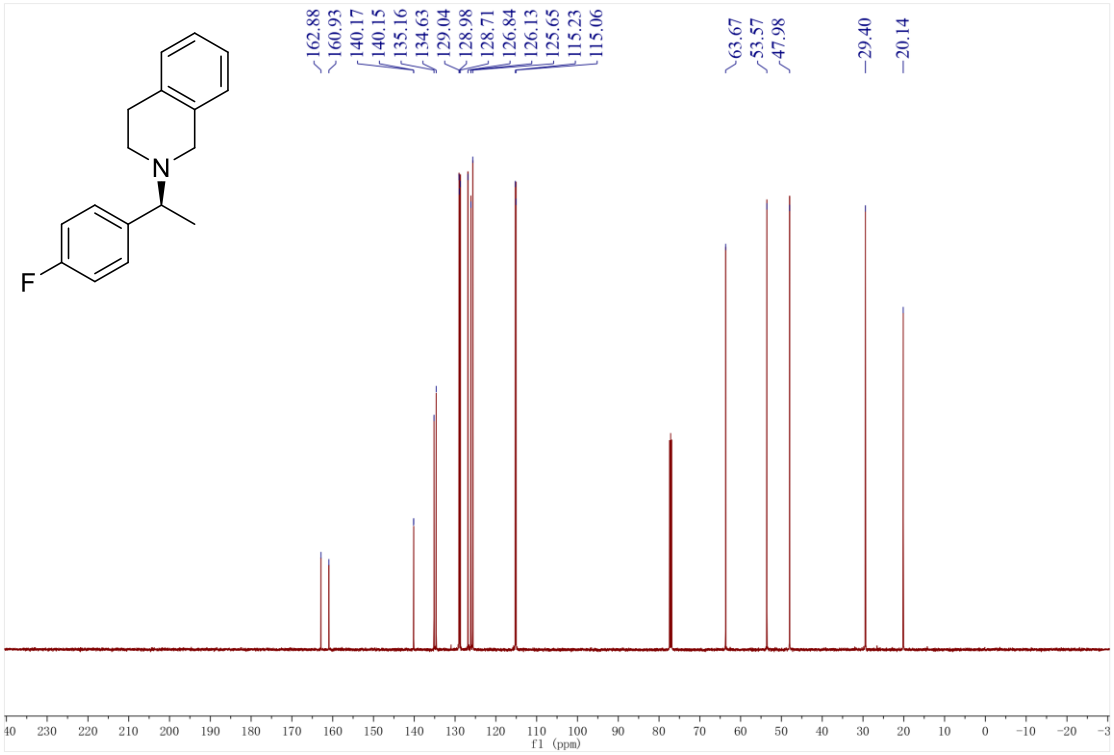
3.04
1.02
3.00
f1 (ppm)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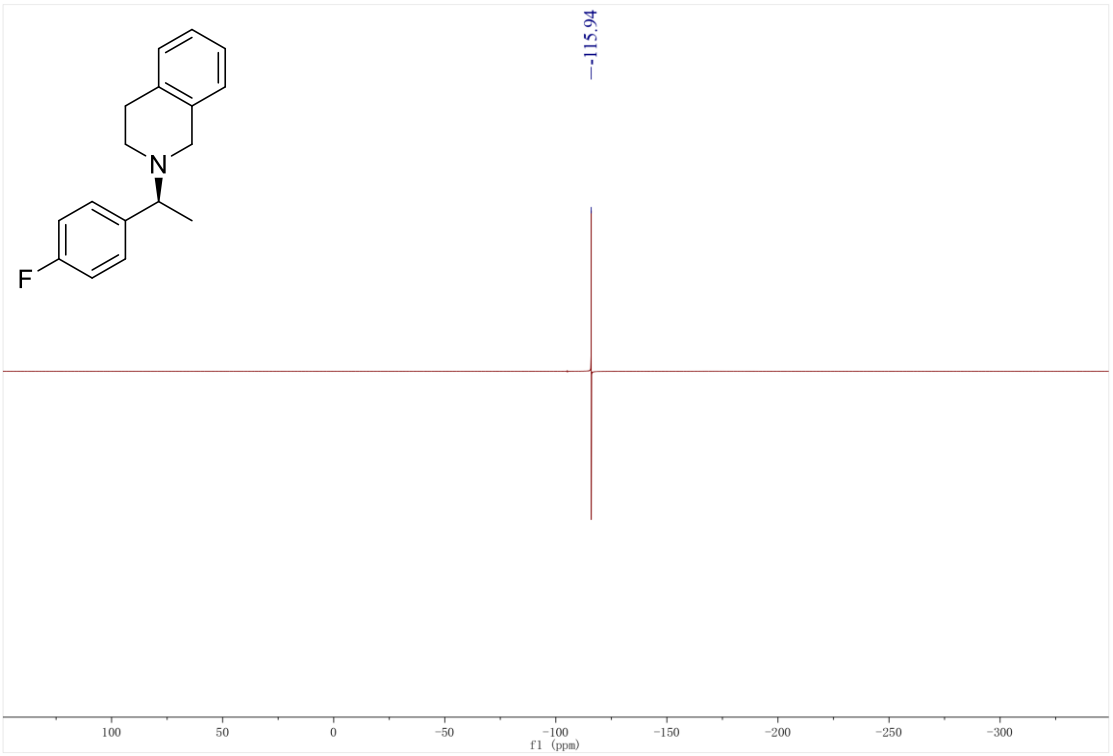
29.40
20.14
N
F
f1 (ppm)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F
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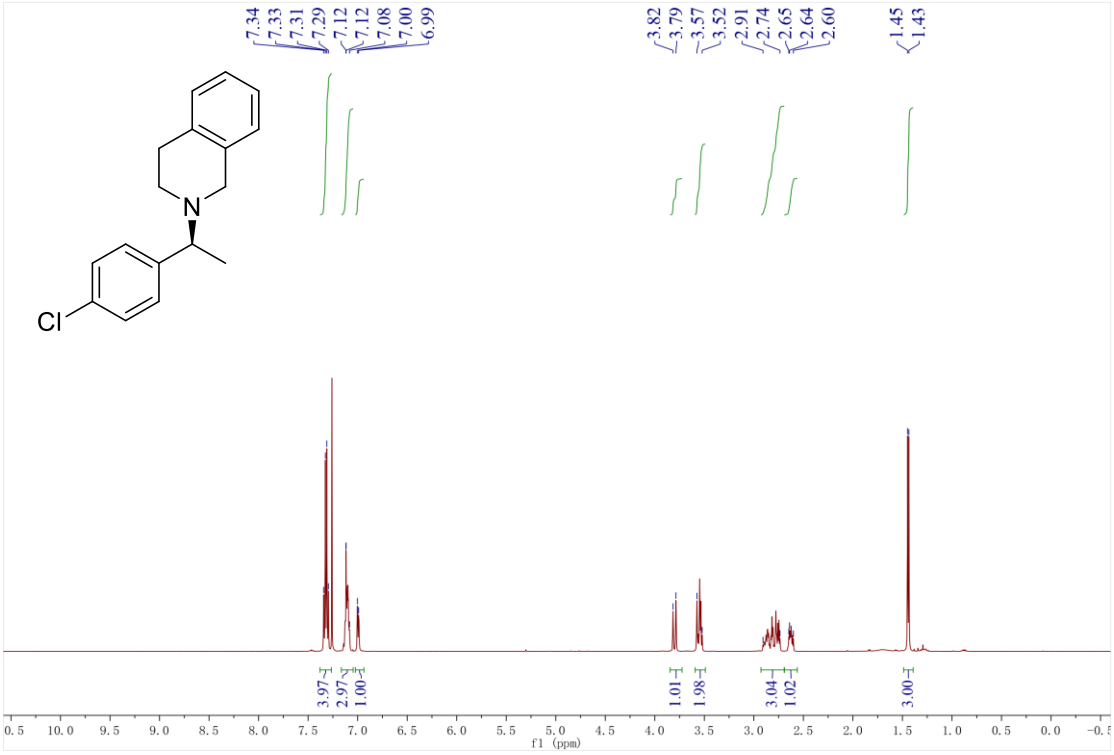
50
0
-50
-100
-150
-200
-250
-300
f1 (ppm)

(*S*)-3f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3.52
2.91
2.74
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2.64
2.60
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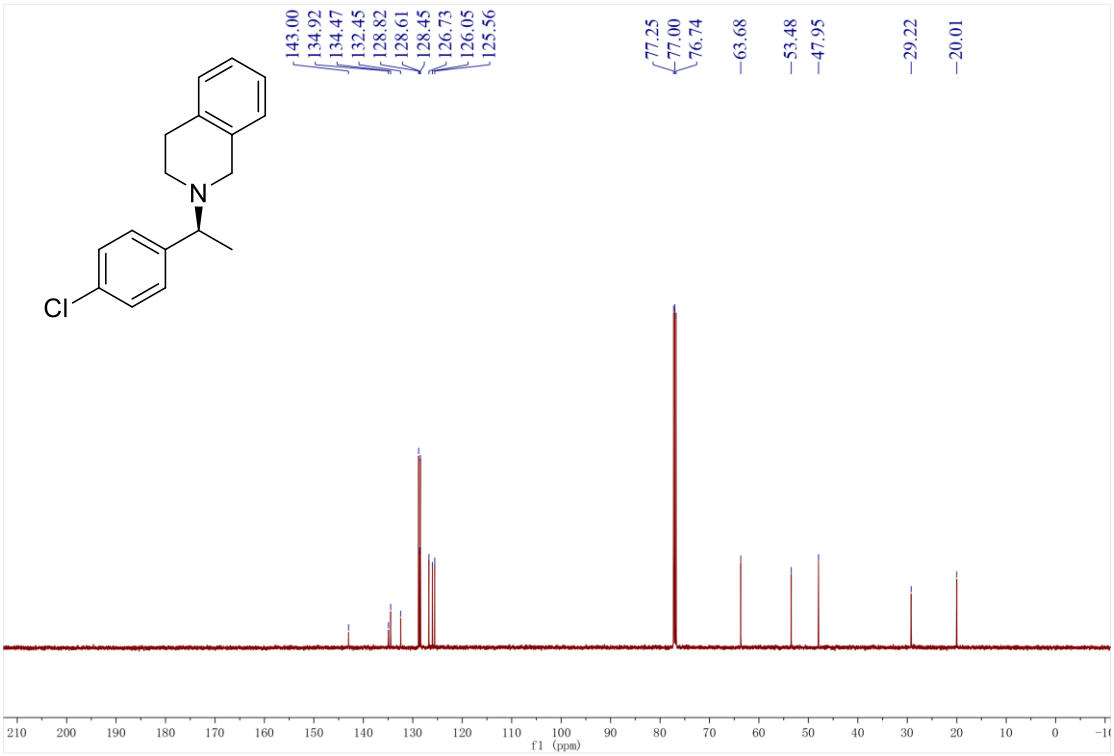
3.00
f1 (ppm)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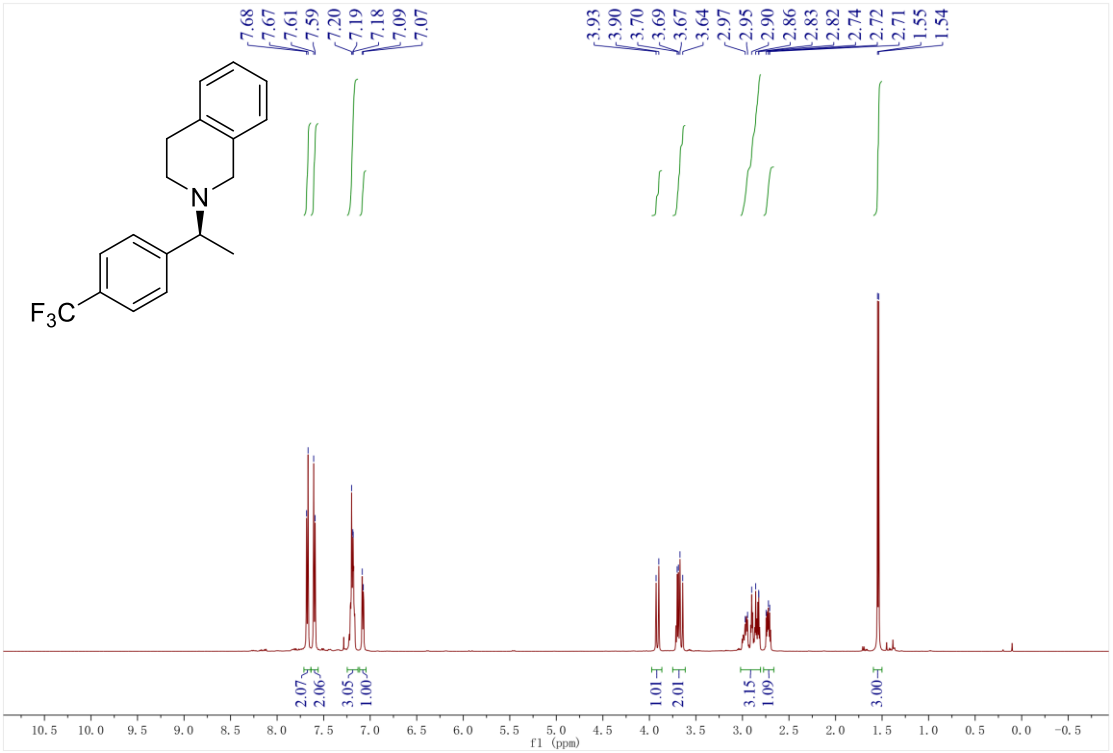
20.01
Cl
N
f1 (ppm)

(*S*)-3g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3.67
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2.97
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2.83
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2.71
1.55
1.54
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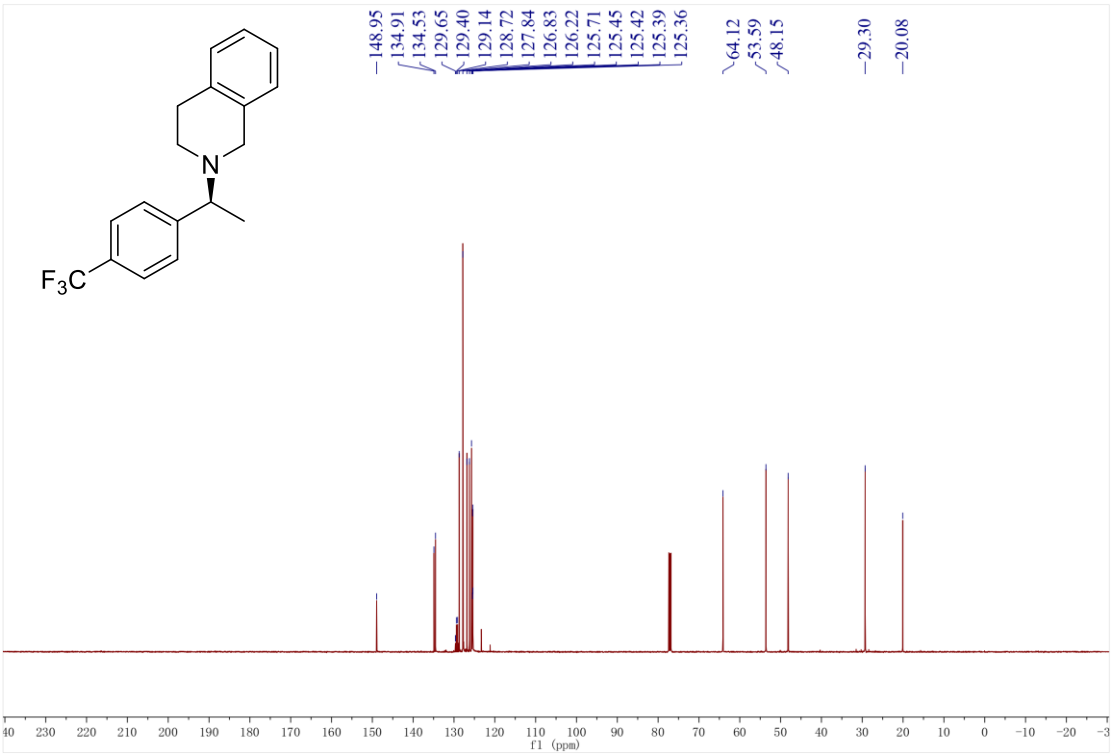
1.09
3.00
F3C
N
f1 (ppm)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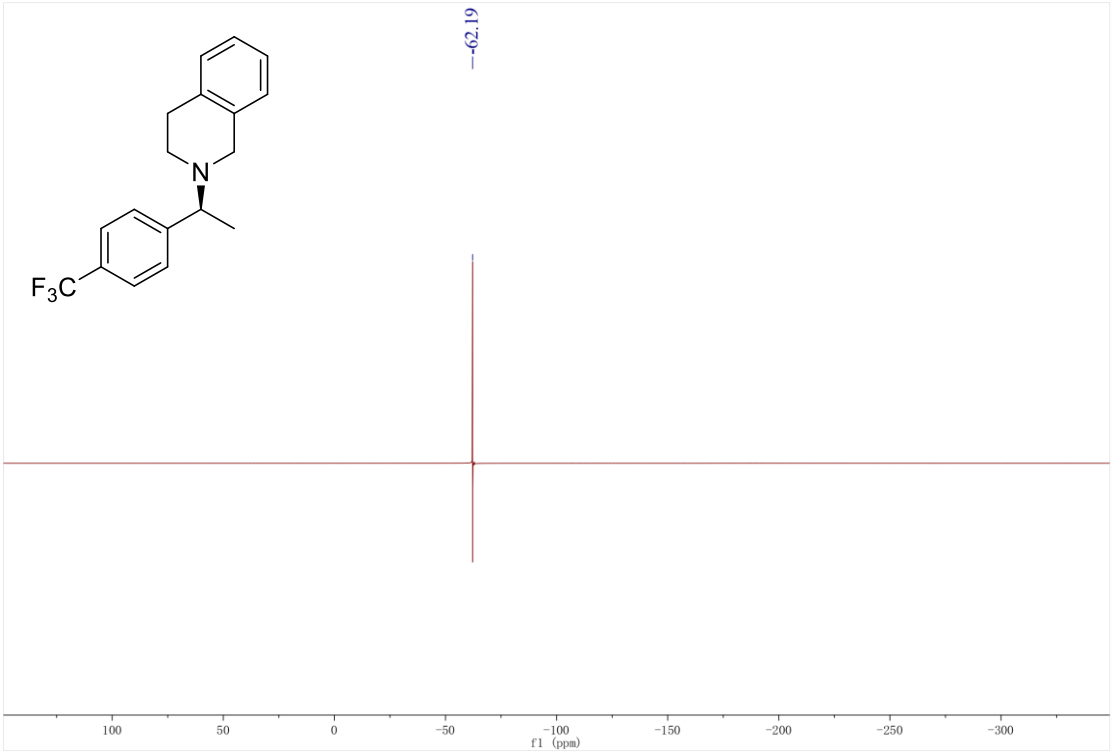
F3C
f1 (ppm)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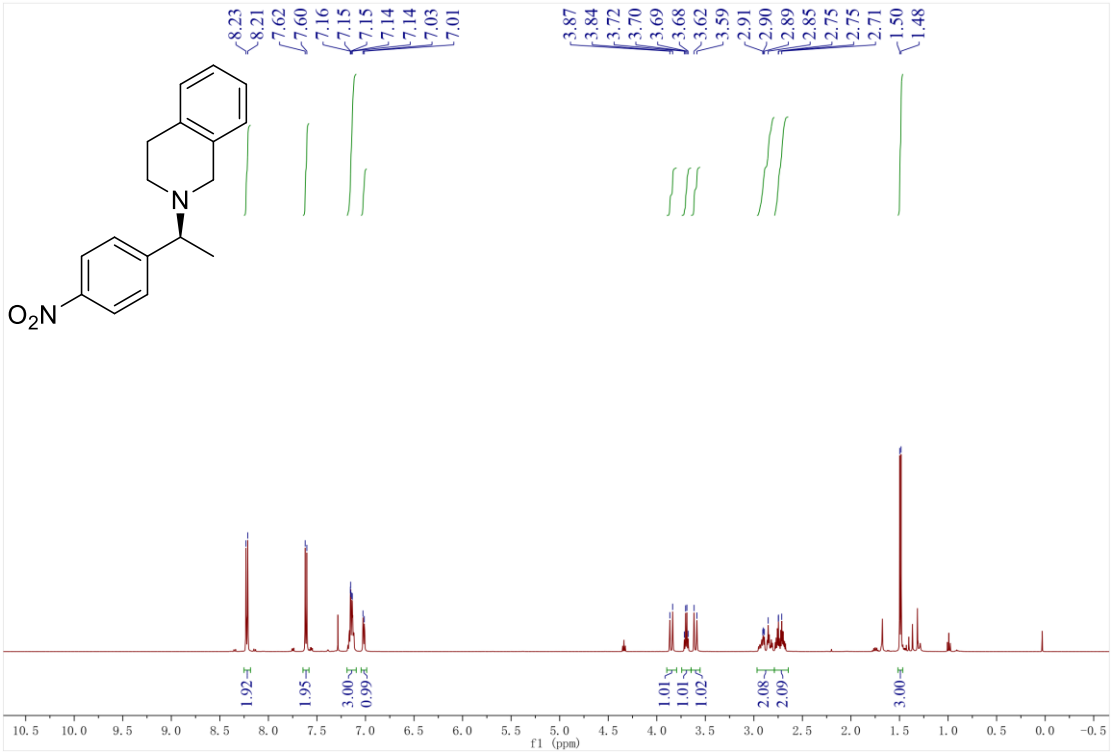
(*S*)-3h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2.71
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N
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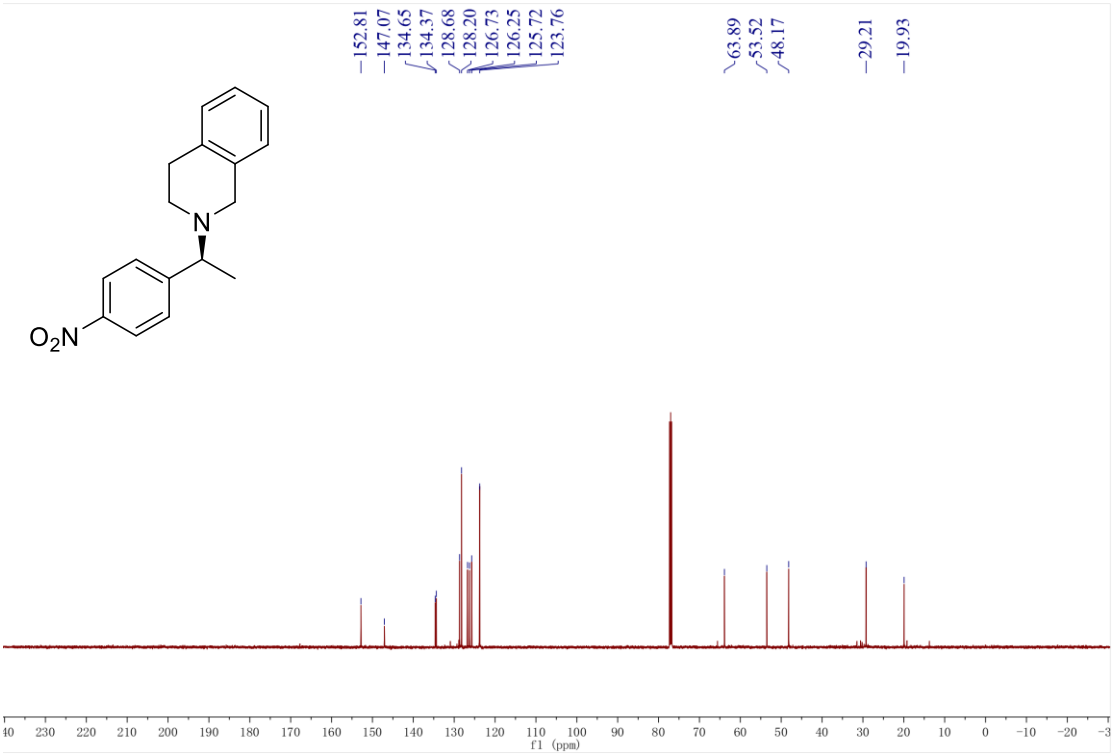
3.00
f1 (ppm)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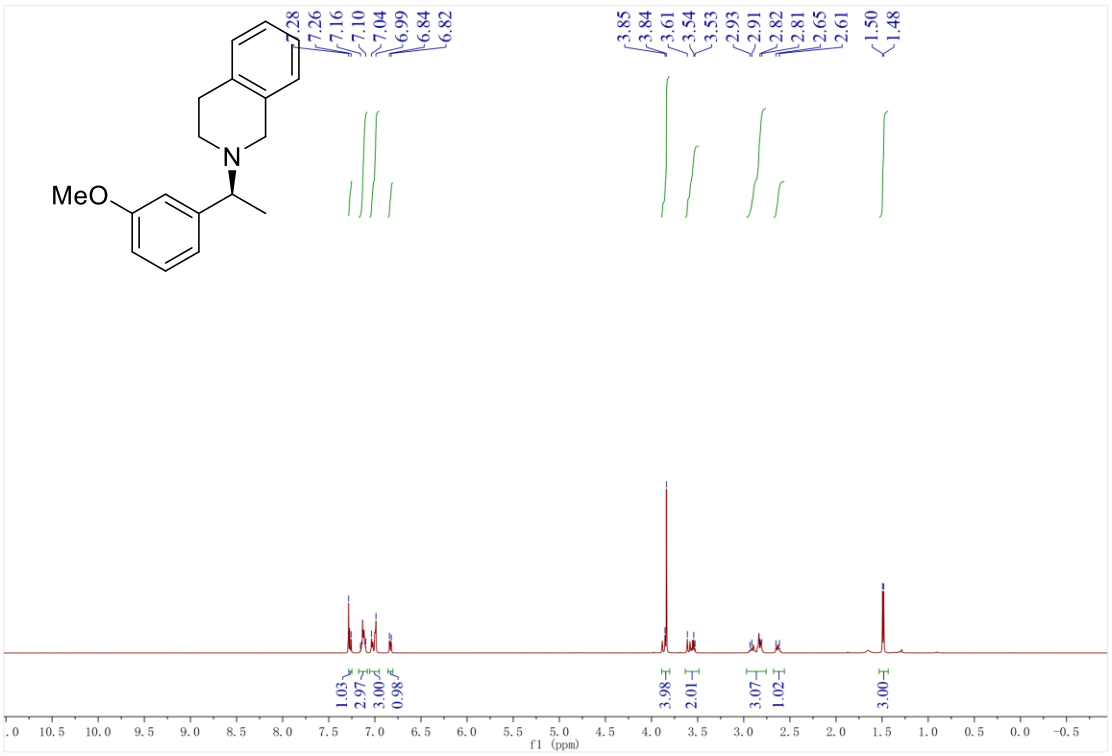
19.93
N
O2N
f1 (ppm)

(*S*)-3i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2.81
2.65
2.61
1.50
1.48
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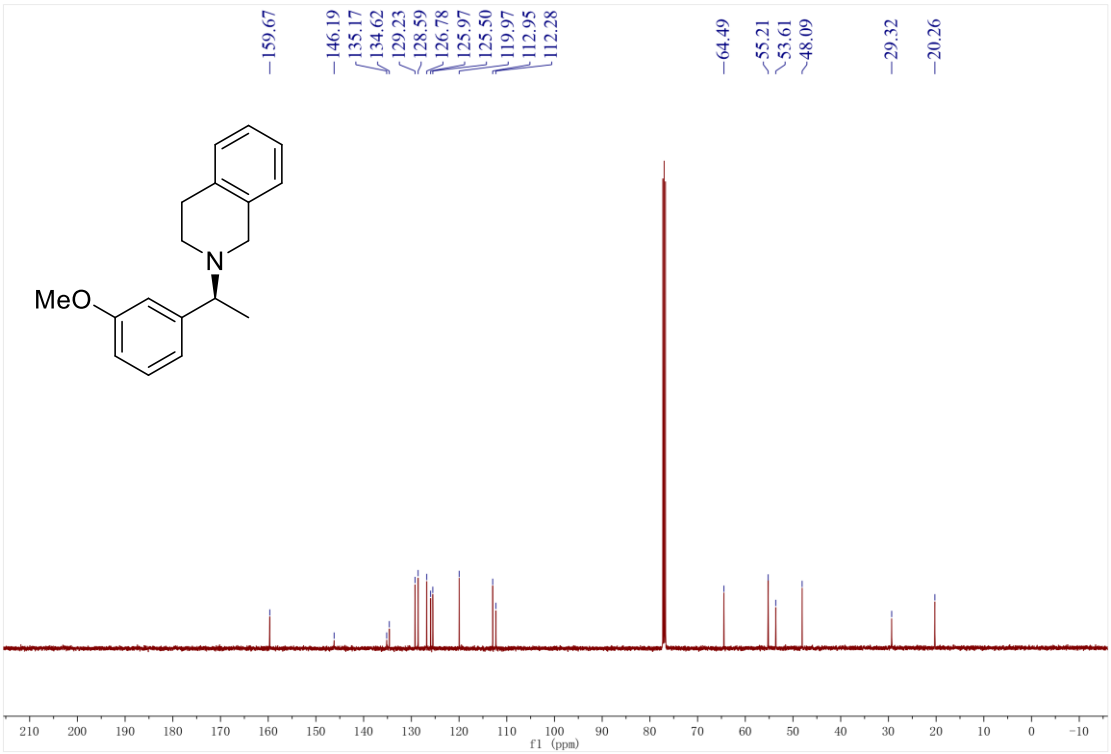
3.00
f1 (ppm)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128.59
126.78
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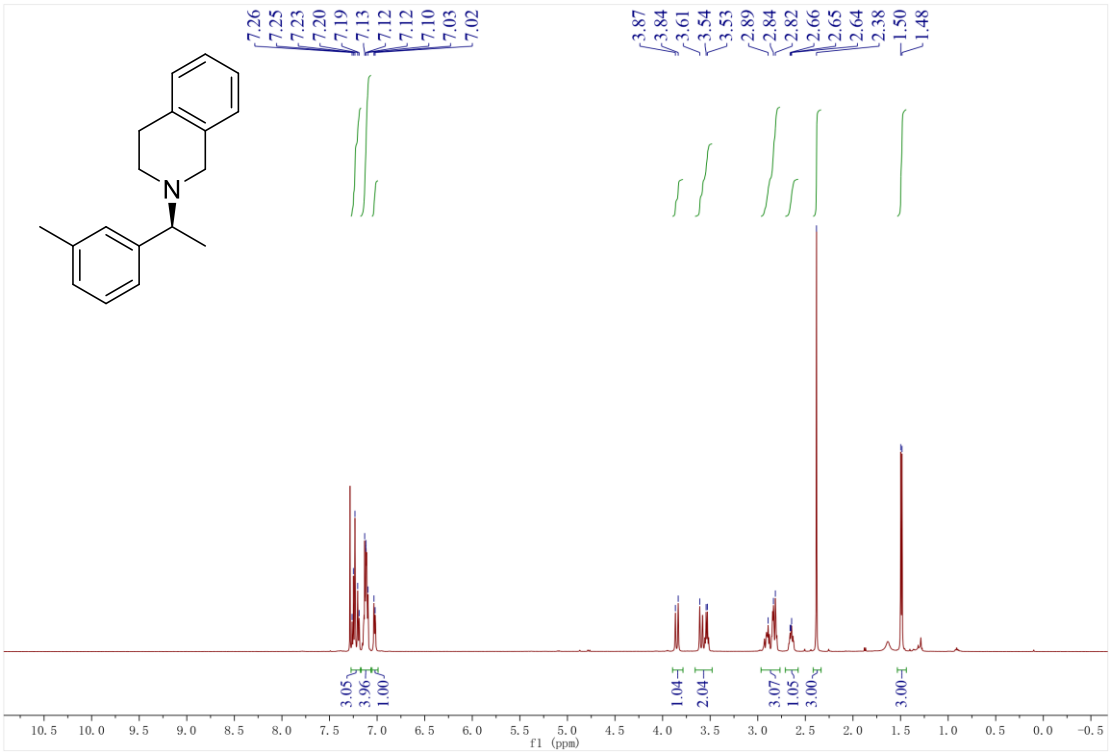
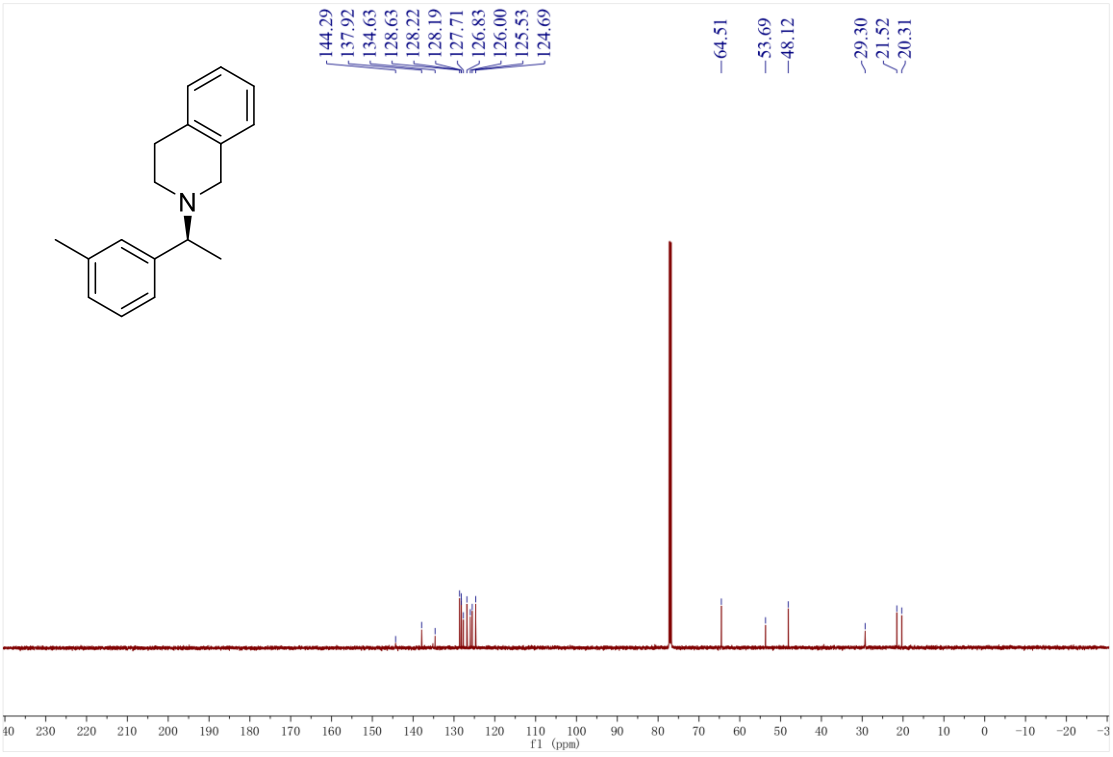
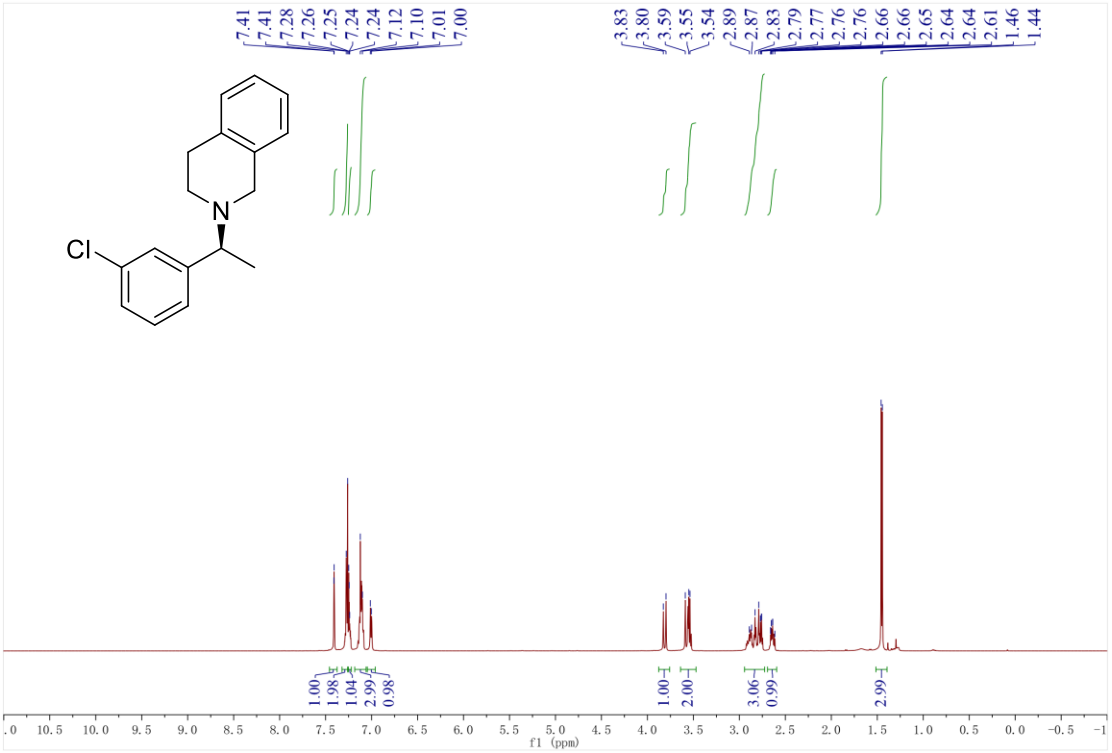
125.50
119.97
112.95
112.28
64.49
55.21
53.61
48.09
29.32
20.26
MeO
N
f1 (ppm)

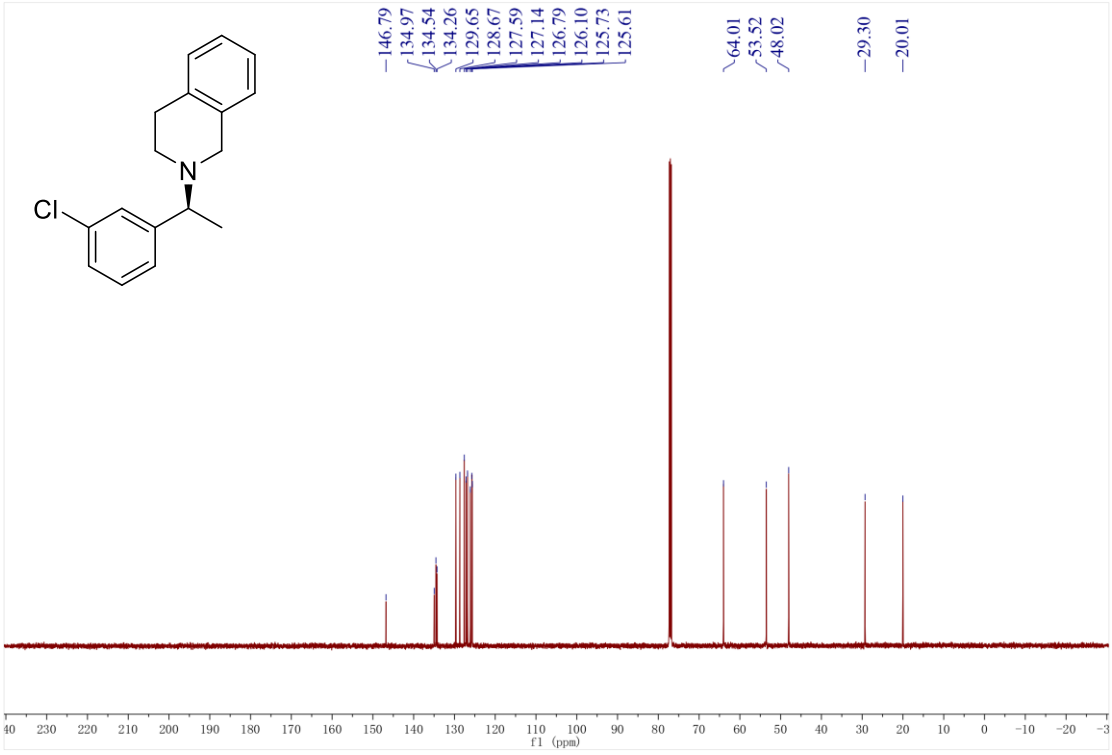
(*S*)-3j


7.26
7.25
7.23
7.20
7.19
7.13
7.12
7.12
7.10
7.03
7.02
3.87
3.84
3.61
3.54
3.53
2.89
2.84
2.82
2.66
2.65
2.64
2.38
1.50
1.48
3.05
3.96
1.00
1.04
2.04
3.07
1.05
3.00
3.00
f1 (ppm)

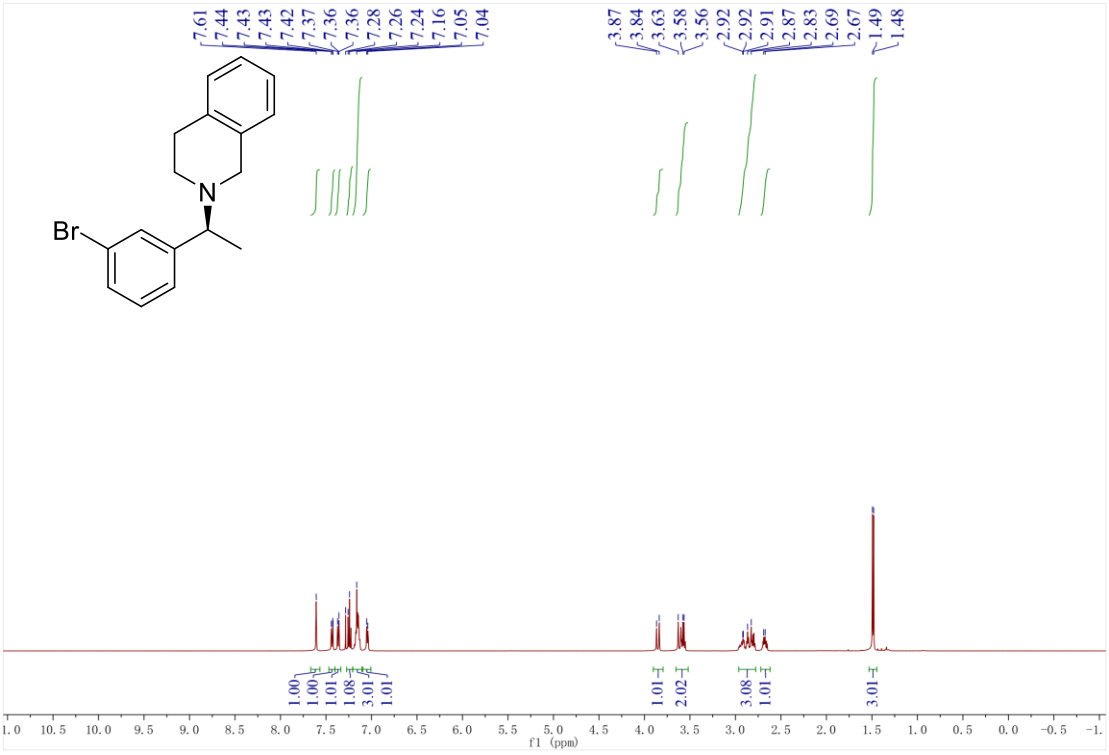

144.29
137.92
134.63
128.63
128.22
128.19
127.71
126.83
126.00
125.53
124.69
64.51
53.69
48.12
29.30
21.52
20.31
f1 (ppm)

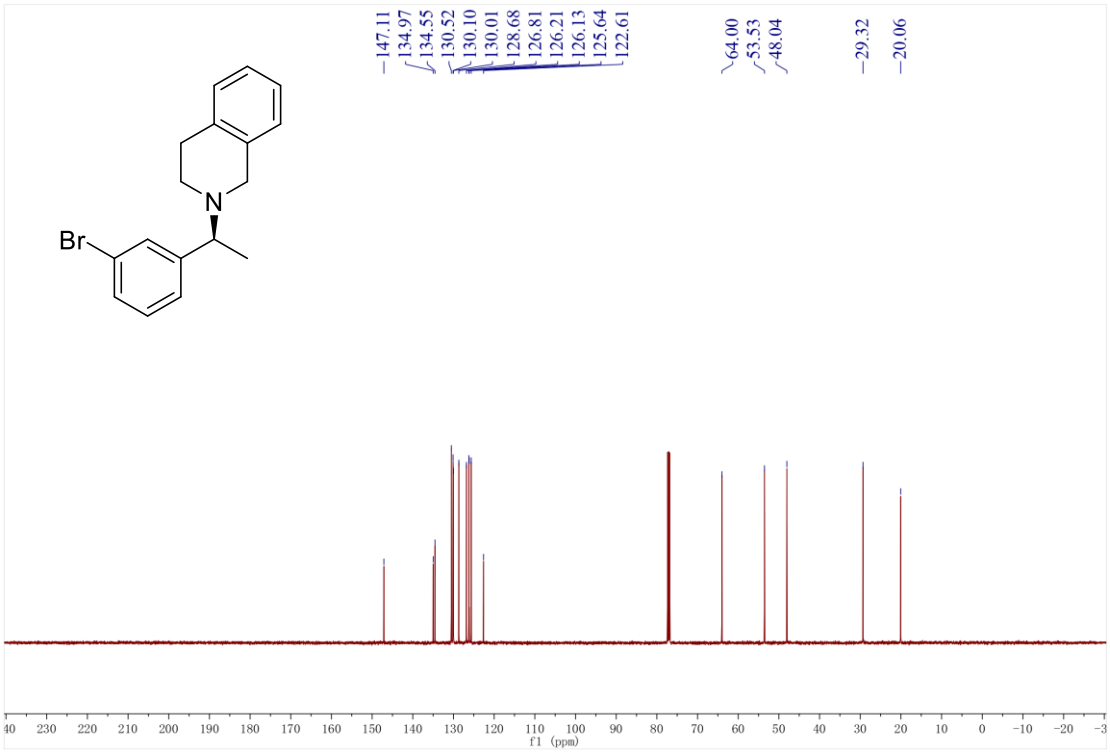
(*S*)-3k


7.41
7.41
7.28
7.26
7.25
7.24
7.24
7.12
7.10
7.01
7.00
3.83
3.80
3.59
3.55
3.54
2.89
2.87
2.83
2.79
2.77
2.76
2.76
2.66
2.66
2.65
2.64
2.64
2.61
1.46
1.44
Cl
N
1.00
1.98
1.04
2.99
0.98
1.00
2.00
3.06
0.99
2.99
f1 (ppm)

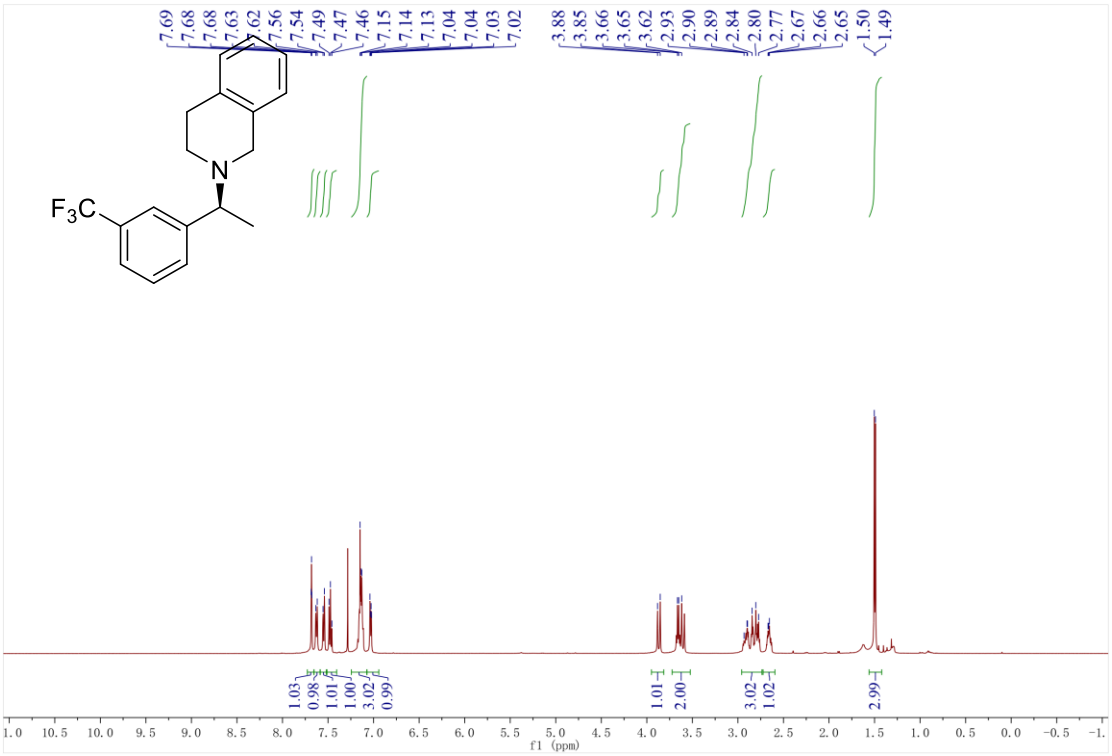

146.79
134.97
134.54
134.26
129.65
128.67
127.59
127.14
126.79
126.10
125.73
125.61
64.01
53.52
48.02
29.30
20.01
Cl
N
f1 (ppm)

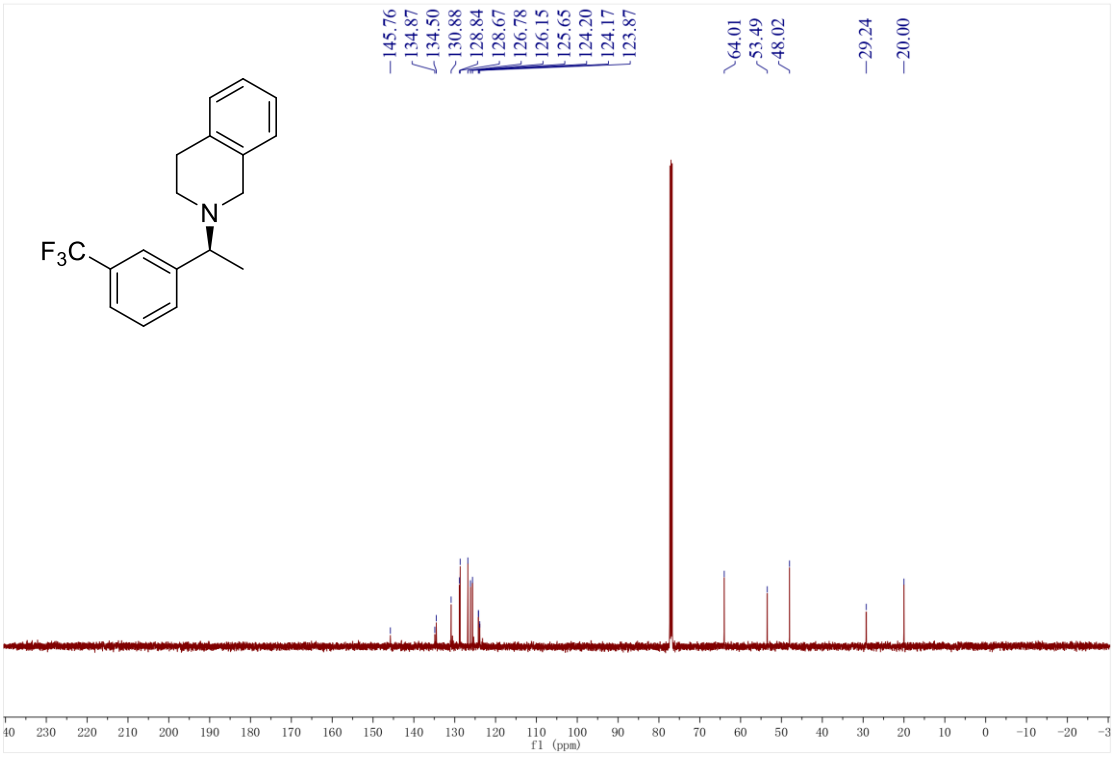
(*S*)-3l

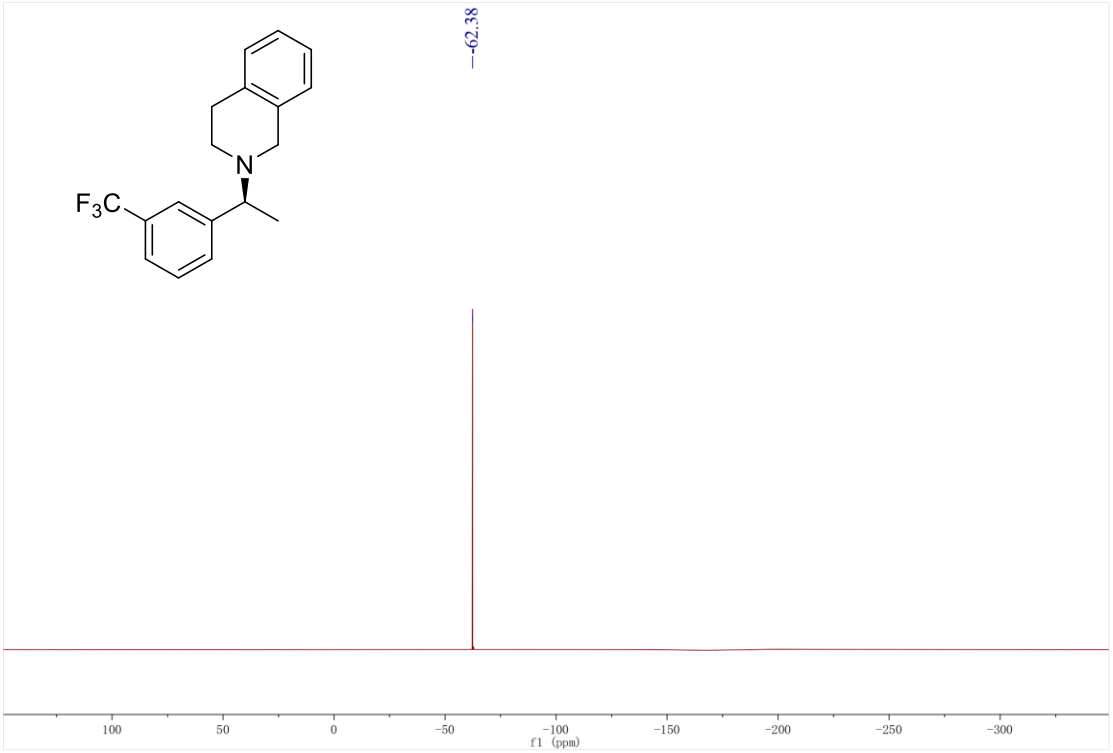

7.61
7.44
7.43
7.43
7.42
7.37
7.36
7.36
7.28
7.26
7.24
7.16
7.05
7.04
3.87
3.84
3.63
3.58
3.56
2.92
2.92
2.91
2.87
2.83
2.69
2.67
1.49
1.48
Br
N
f1 (ppm)


147.11
134.97
134.55
130.52
130.10
130.01
128.68
126.81
126.21
126.13
125.64
122.61
64.00
53.53
48.04
29.32
20.06
Br
N
f1 (ppm)

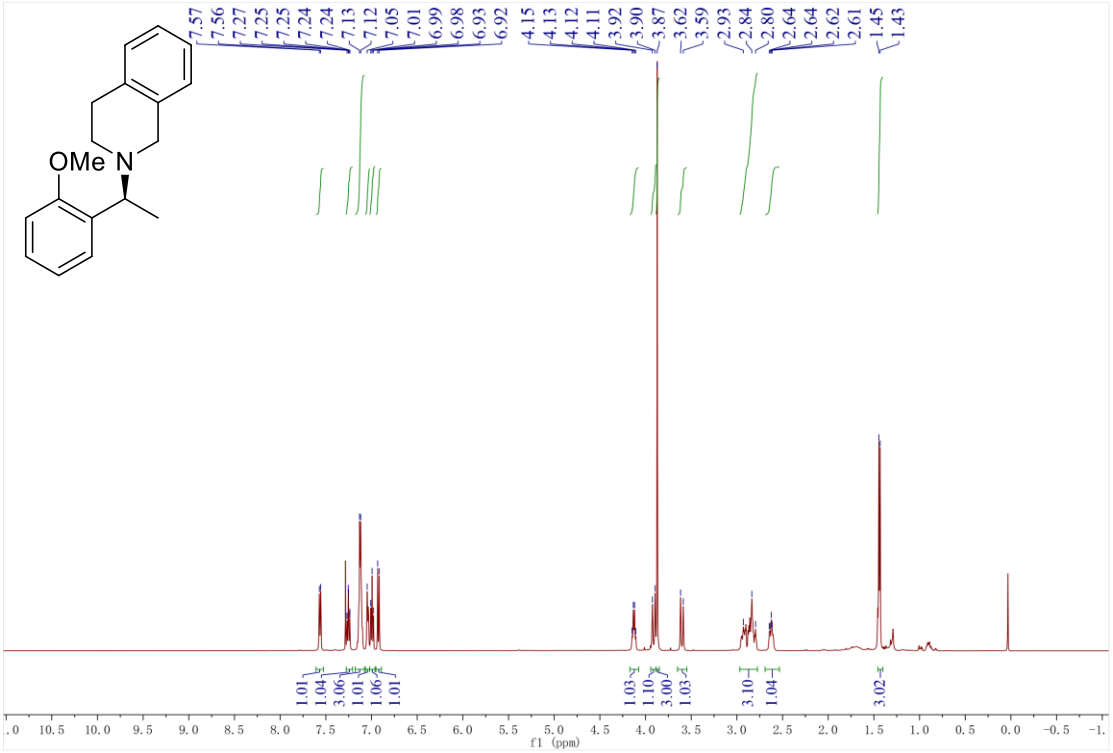
(*S*)-3m

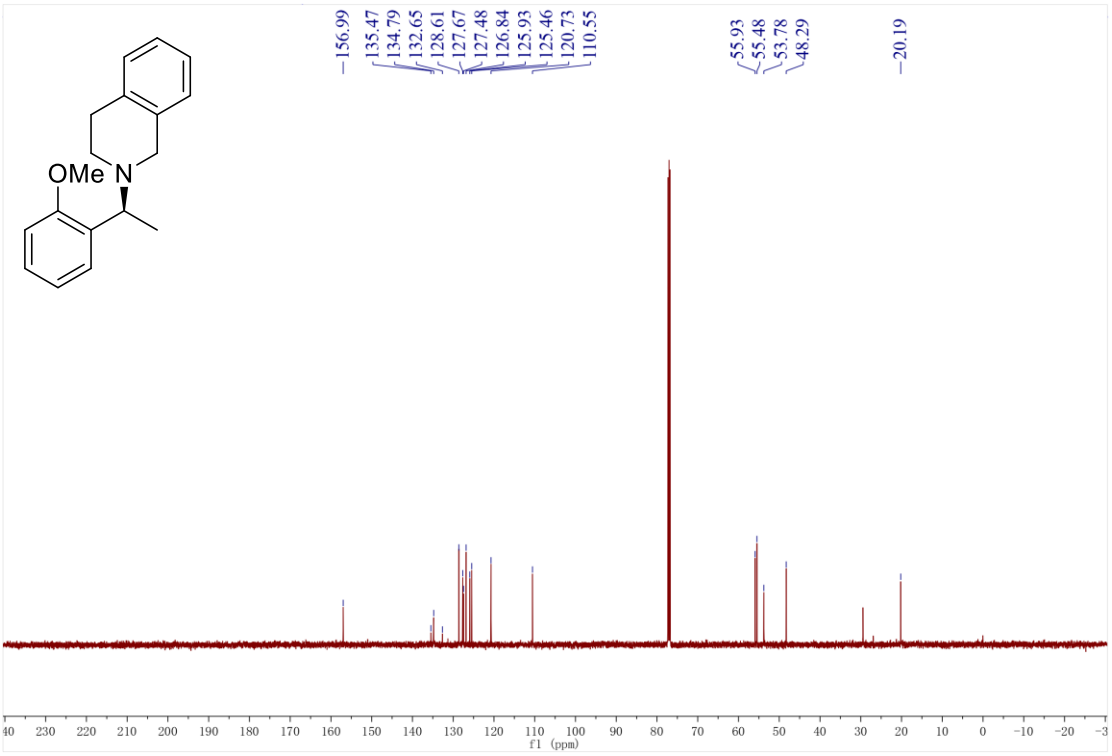

7.69
7.68
7.68
7.63
7.62
7.56
7.54
7.49
7.47
7.46
7.15
7.14
7.13
7.04
7.04
7.03
7.02
3.88
3.85
3.66
3.65
3.62
2.93
2.90
2.89
2.84
2.80
2.77
2.67
2.66
2.65
1.50
1.49
F3C
N
1.03
0.98
1.01
1.00
3.02
0.99
1.01
2.00
3.02
1.02
2.99
f1 (ppm)


145.76
134.87
134.50
130.88
128.84
128.67
126.78
126.15
125.65
124.20
124.17
123.87
64.01
53.49
48.02
29.24
20.00
F3C
N
f1 (ppm)

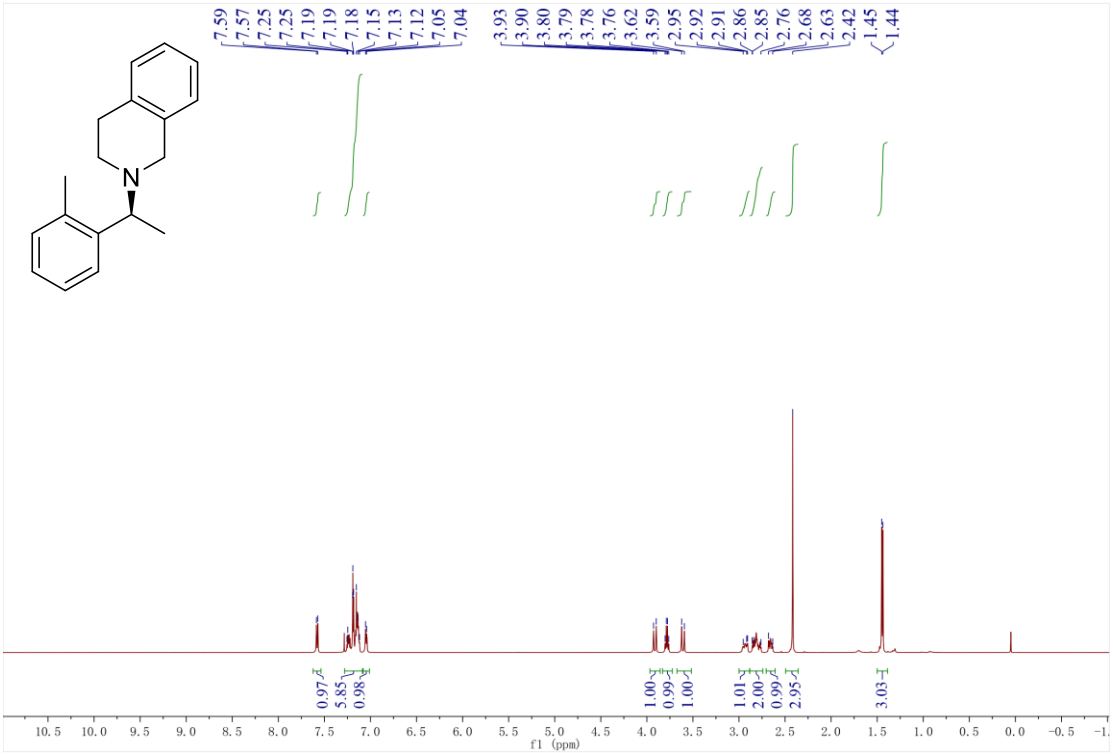

-62.38
N
F3C
100
50
0
-50
-100
-150
-200
-250
-300
f1 (ppm)

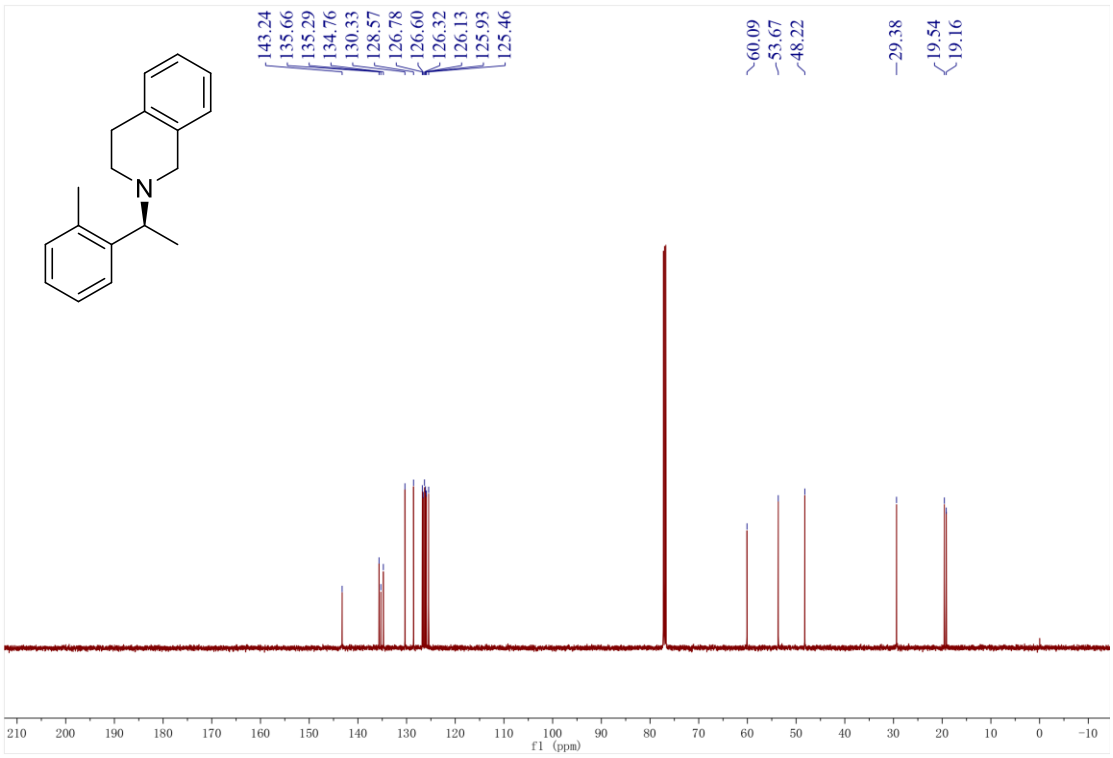
(*S*)-3n


7.57
7.56
7.27
7.25
7.25
7.25
7.24
7.24
7.13
7.12
7.05
7.01
6.99
6.98
6.93
6.92
4.15
4.13
4.12
4.11
3.92
3.90
3.87
3.62
3.59
2.93
2.84
2.80
2.64
2.64
2.62
2.61
1.45
1.43
OMe
N
1.01
1.04
3.06
1.01
1.06
1.01
1.03
1.10
3.00
1.03
3.10
1.04
3.02
f1 (ppm)

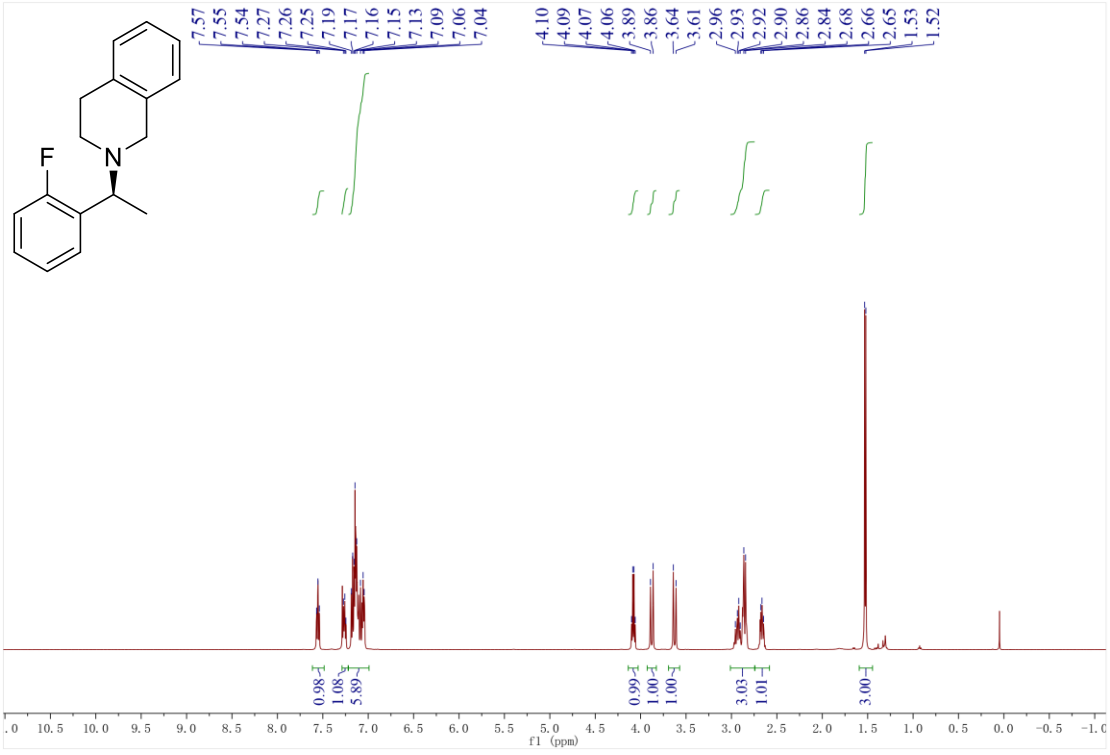

OMe N
156.99
135.47
134.79
132.65
128.61
127.67
127.48
126.84
125.93
125.46
120.73
110.55
55.93
55.48
53.78
48.29
20.19
f1 (ppm)

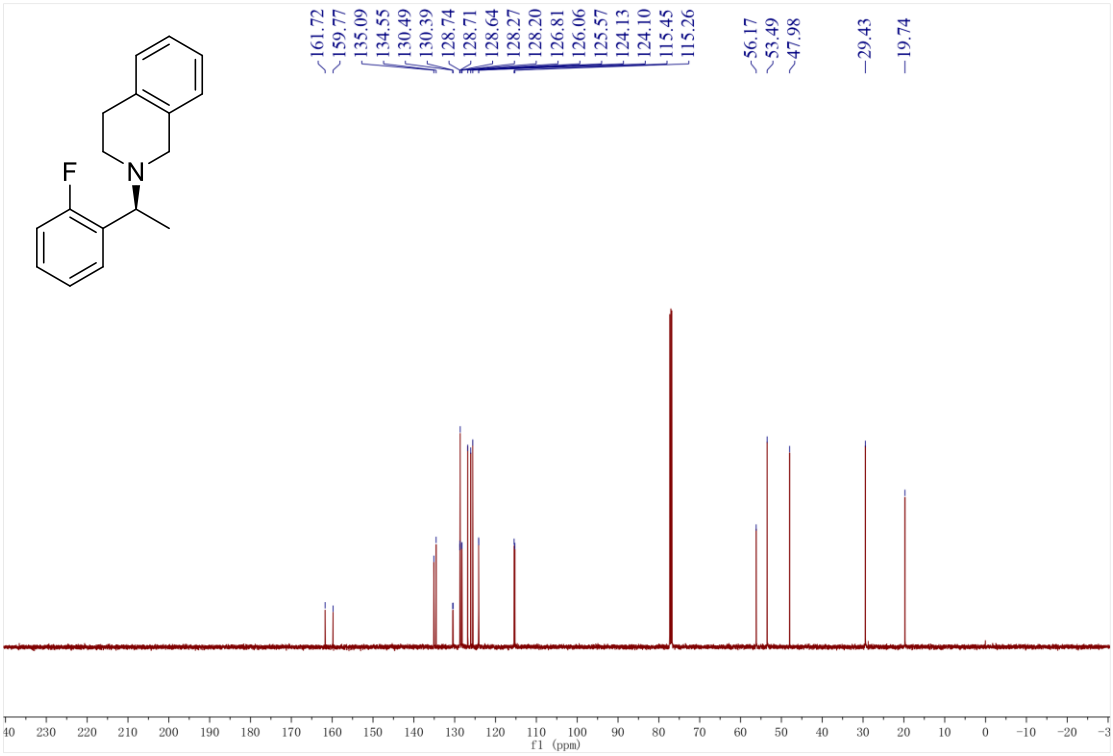
(*S*)-3o

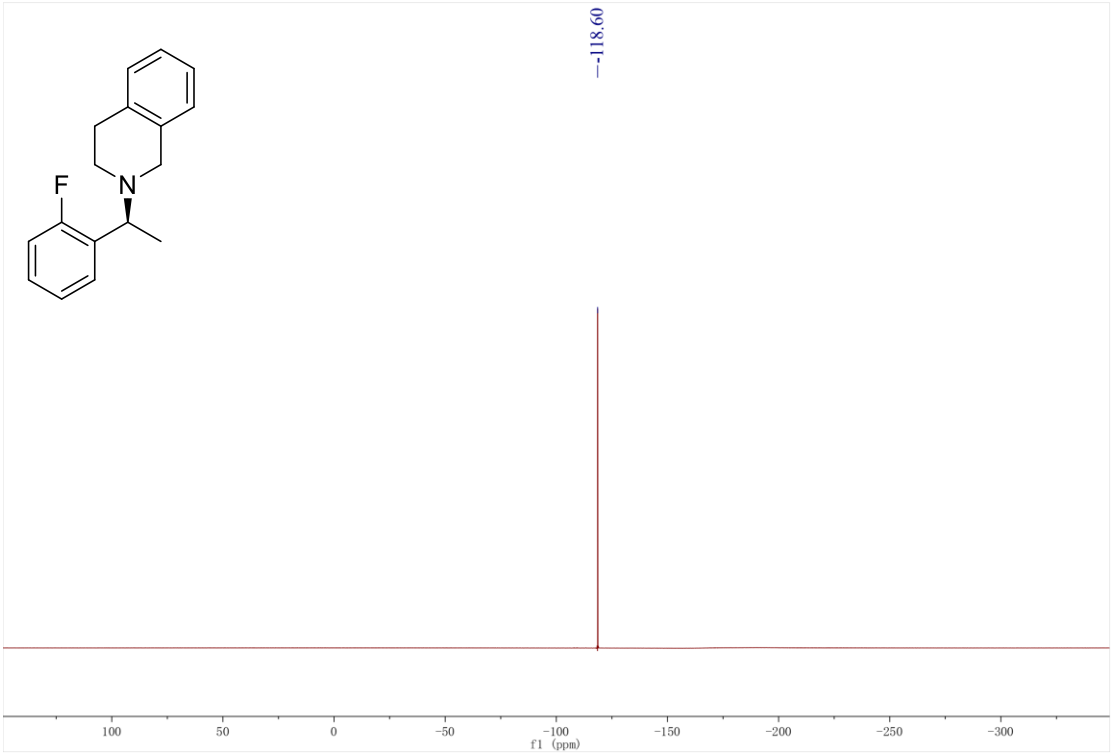

N
7.59
7.57
7.25
7.25
7.19
7.19
7.18
7.15
7.13
7.12
7.05
7.04
3.93
3.90
3.80
3.79
3.78
3.76
3.62
3.59
2.95
2.92
2.91
2.86
2.85
2.76
2.68
2.63
2.42
1.45
1.44
0.97
5.85
0.98
1.00
0.99
1.00
1.01
2.00
0.99
2.95
3.03
f1 (ppm)


143.24
135.66
135.29
134.76
130.33
128.57
126.78
126.60
126.32
126.13
125.93
125.46
60.09
53.67
48.22
29.38
19.54
19.16
f1 (ppm)

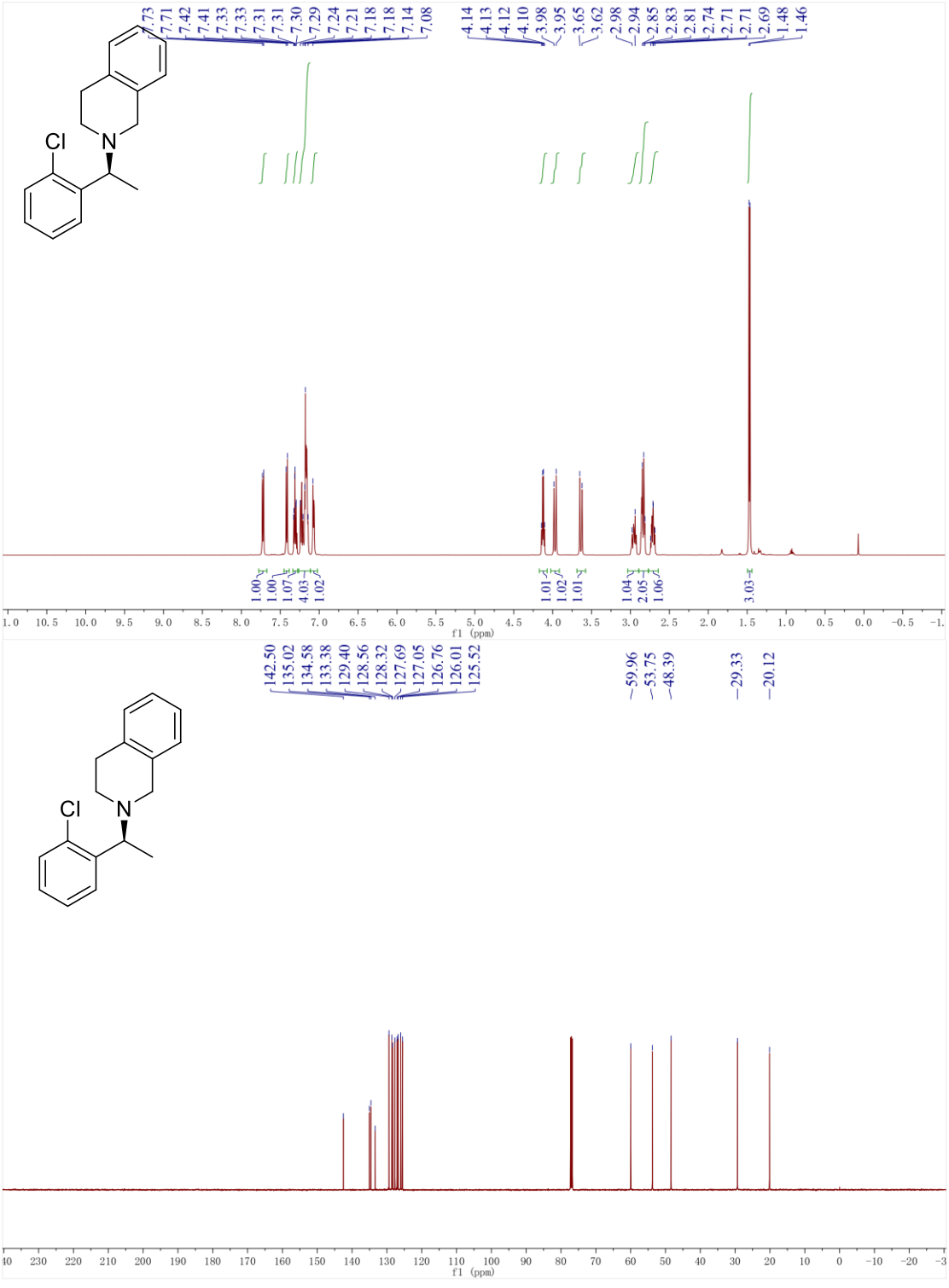
(*S*)-3p


7.57
7.55
7.54
7.27
7.26
7.25
7.19
7.17
7.16
7.15
7.13
7.09
7.06
7.04
4.10
4.09
4.07
4.06
3.89
3.86
3.64
3.61
2.96
2.93
2.92
2.90
2.86
2.84
2.68
2.66
2.65
1.53
1.52
0.98
1.08
5.89
0.99
1.00
1.00
3.03
1.01
3.00
f1 (ppm)

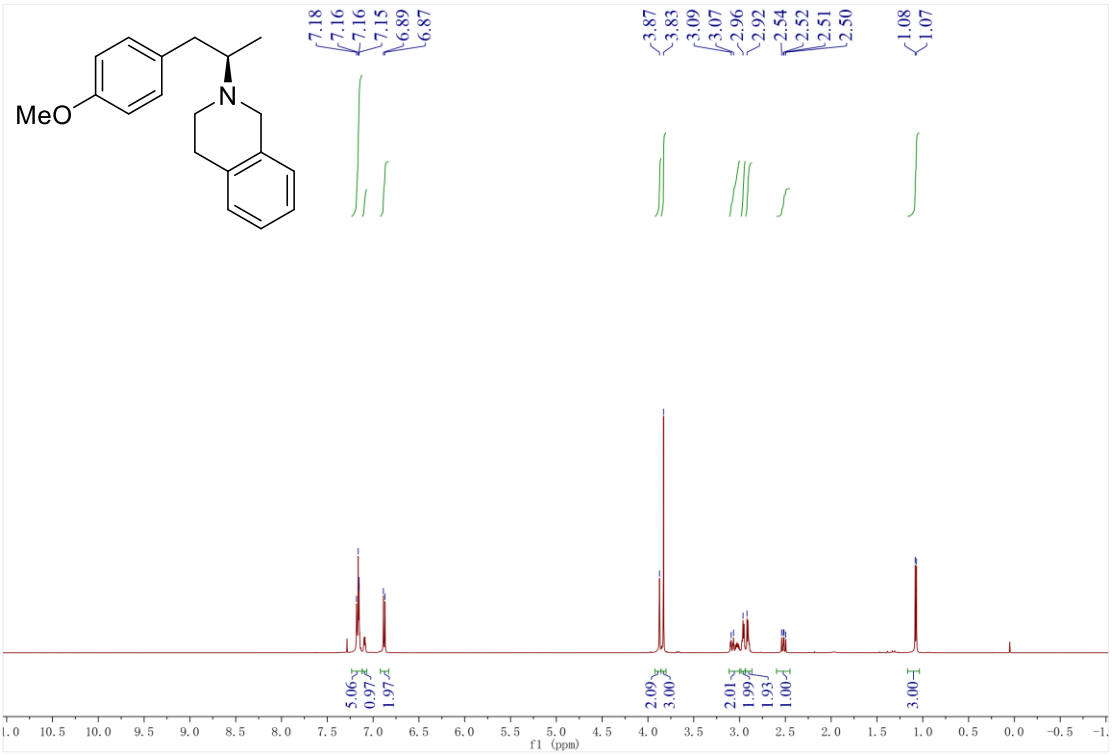

161.72
159.77
135.09
134.55
130.49
130.39
128.74
128.71
128.64
128.27
128.20
126.81
126.06
125.57
124.13
124.10
115.45
115.26
56.17
53.49
47.98
29.43
19.74
F
N
f1 (ppm)

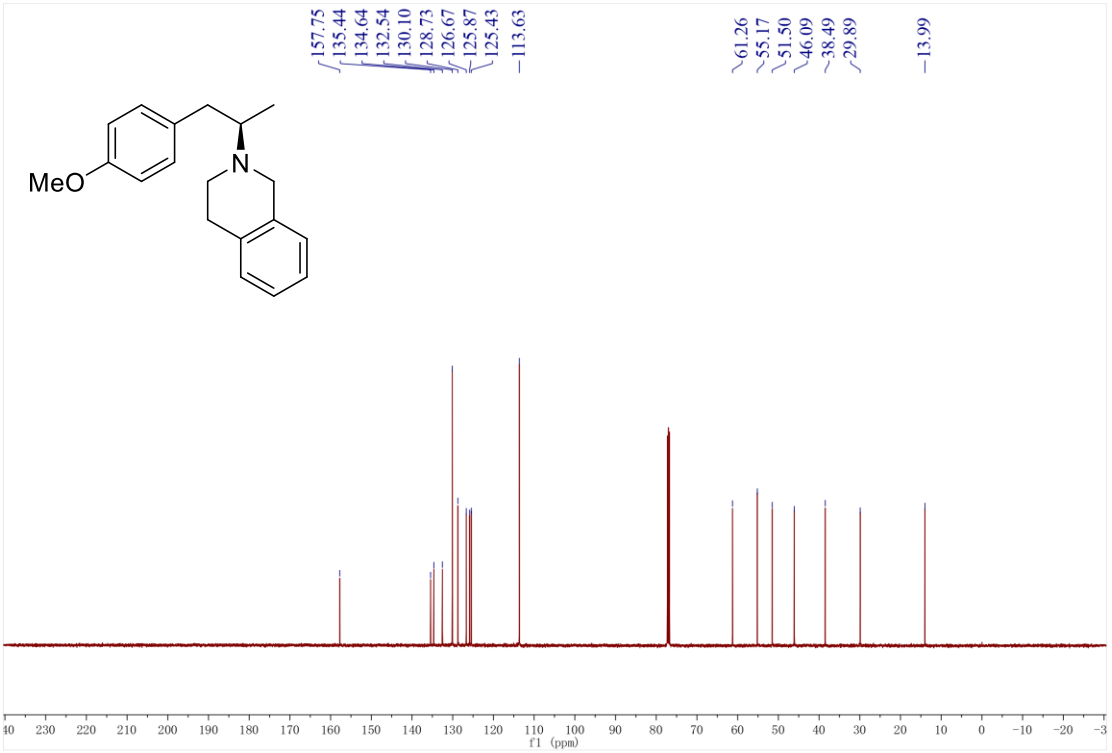

-118.60
F
N
f1 (ppm)

(*S*)-3q

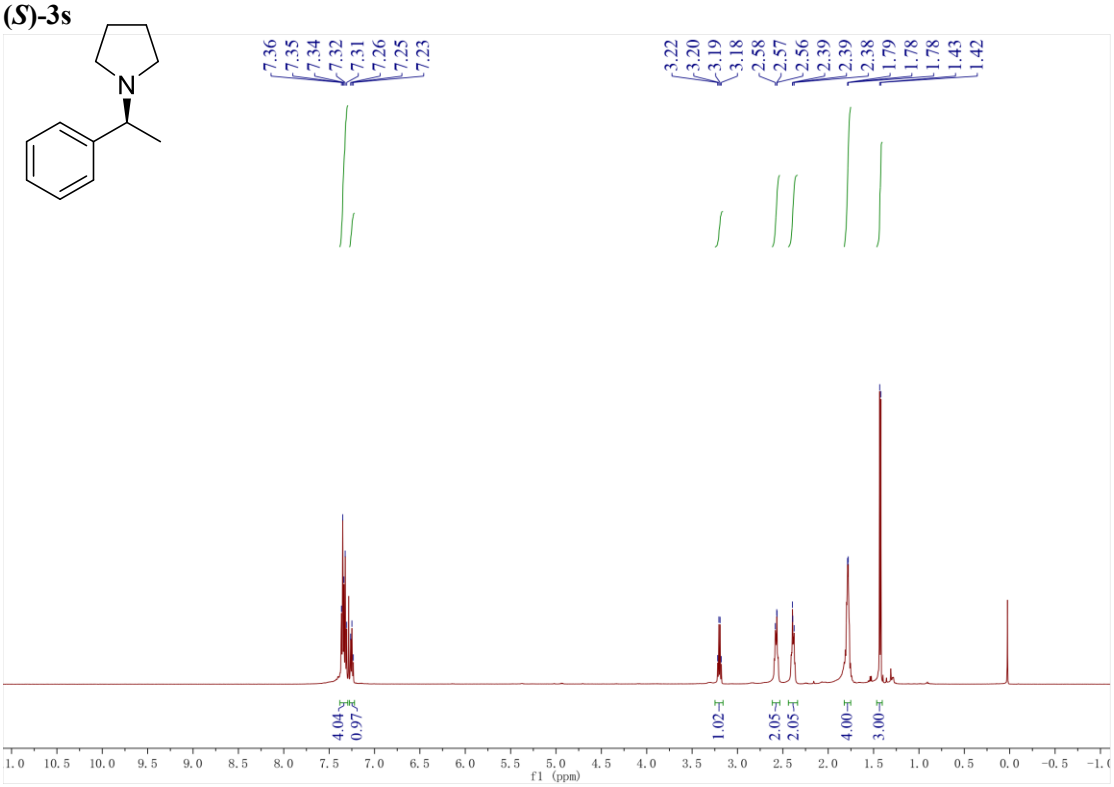

7.73
7.71
7.42
7.41
7.33
7.33
7.31
7.31
7.30
7.29
7.24
7.21
7.18
7.18
7.14
7.08
4.14
4.13
4.12
4.10
3.98
3.95
3.65
3.62
2.98
2.94
2.85
2.83
2.81
2.74
2.71
2.71
2.69
1.48
1.46
Cl
N
1.00
1.00
1.07
4.03
1.02
1.01
1.02
1.01
1.04
2.05
1.06
3.03
f1 (ppm)
142.50
135.02
134.58
133.38
129.40
128.56
128.32
127.69
127.05
126.76
126.01
125.52
59.96
53.75
48.39
29.33
20.12
Cl
N
f1 (ppm)

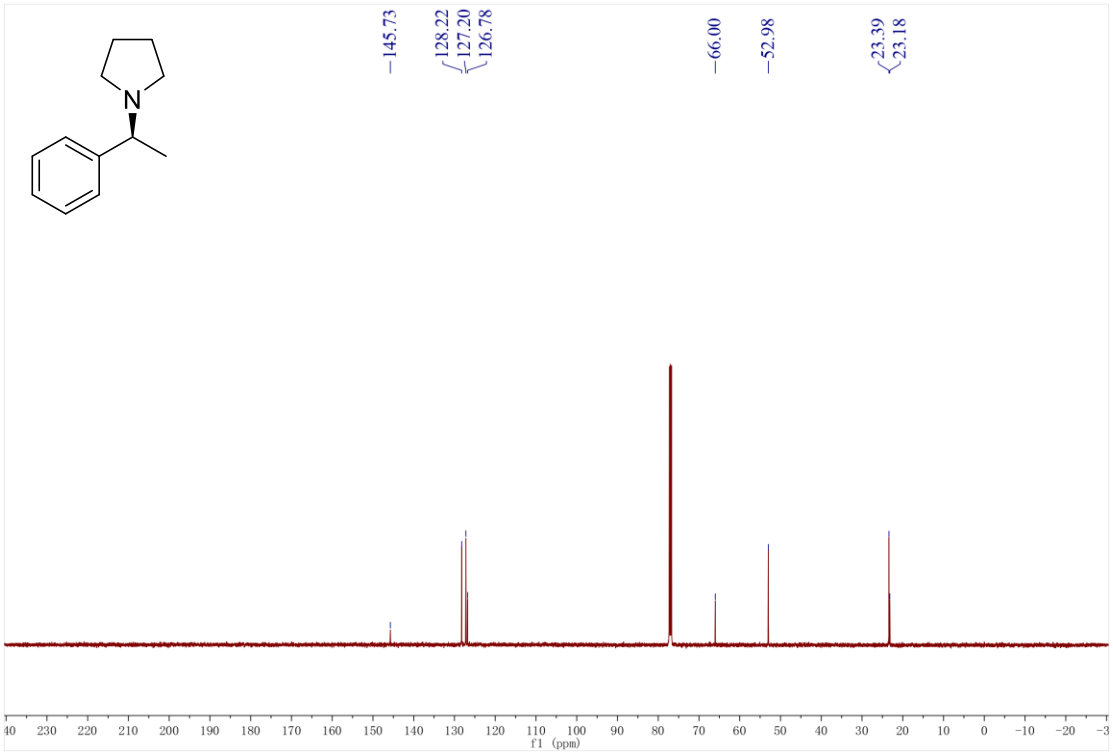
(*S*)-3r


MeO
N
7.18
7.16
7.16
7.15
6.89
6.87
3.87
3.83
3.09
3.07
2.96
2.92
2.54
2.52
2.51
2.50
1.08
1.07
5.06
0.97
1.97
2.09
3.00
2.01
1.99
1.93
1.00
3.00
f1 (ppm)

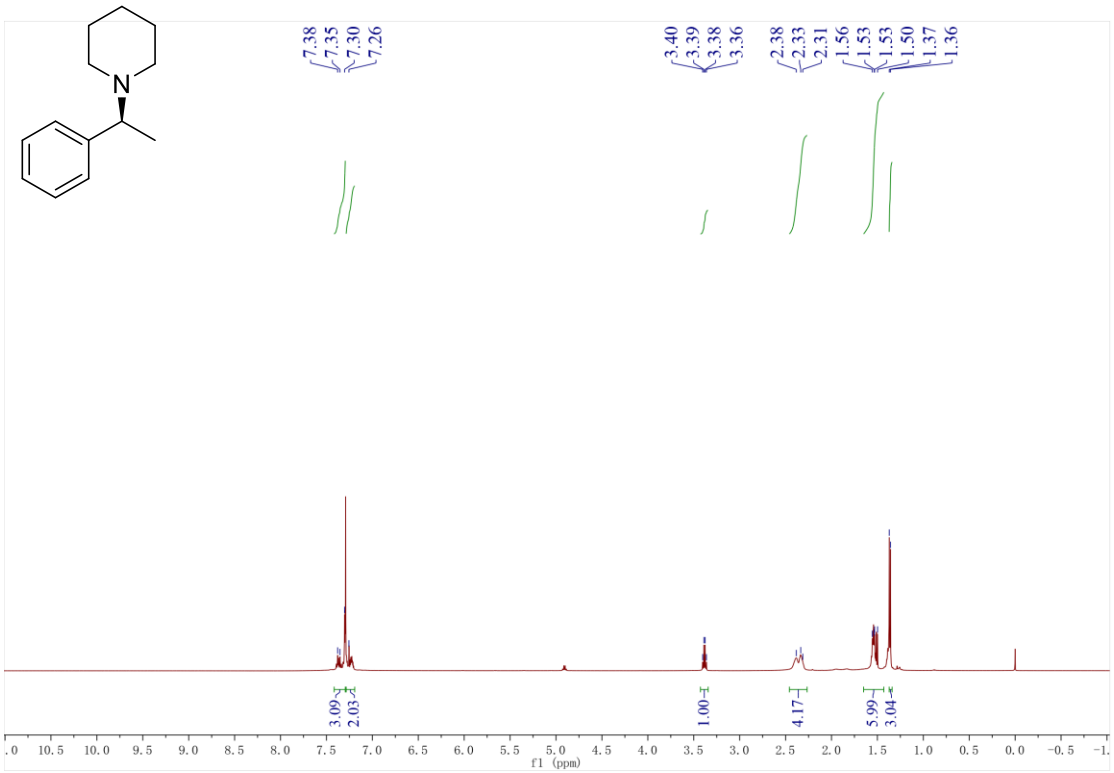

MeO
N
157.75
135.44
134.64
132.54
130.10
128.73
126.67
125.87
125.43
113.63
61.26
55.17
51.50
46.09
38.49
29.89
13.99
f1 (ppm)

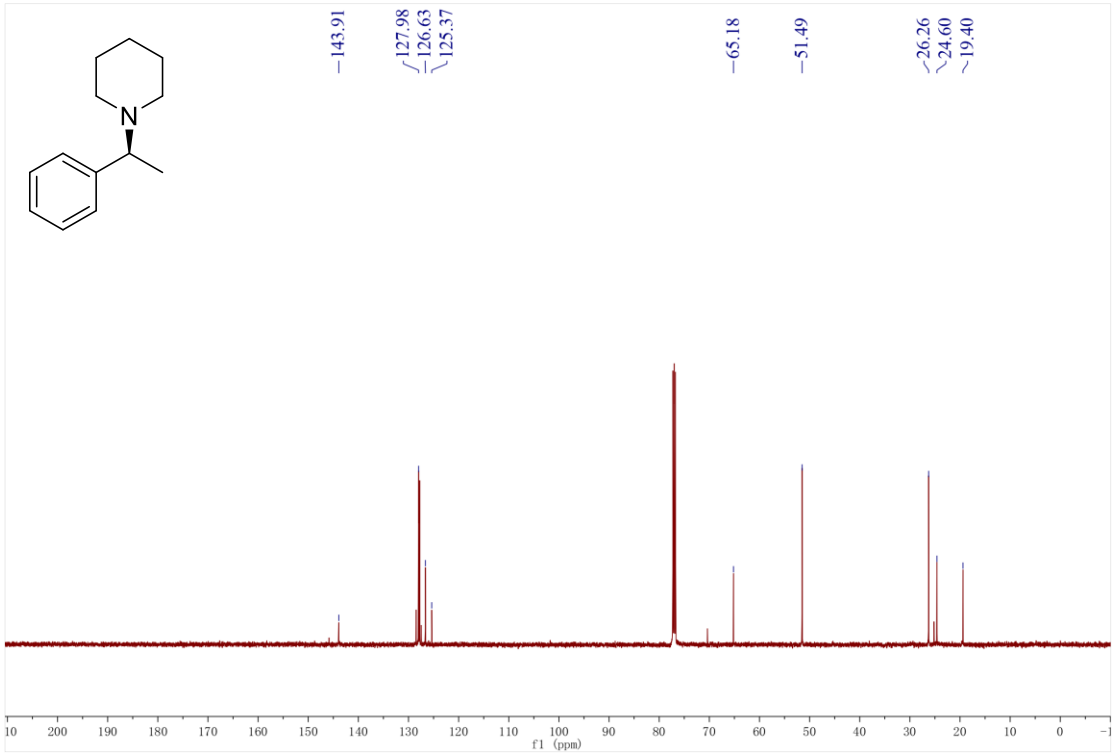
(*S*)-3s


7.36
7.35
7.34
7.32
7.31
7.26
7.25
7.23
3.22
3.20
3.19
3.18
2.58
2.57
2.56
2.39
2.39
2.38
1.79
1.78
1.78
1.43
1.42
4.04
0.97
1.02
2.05
2.05
4.00
3.00
f1 (ppm)

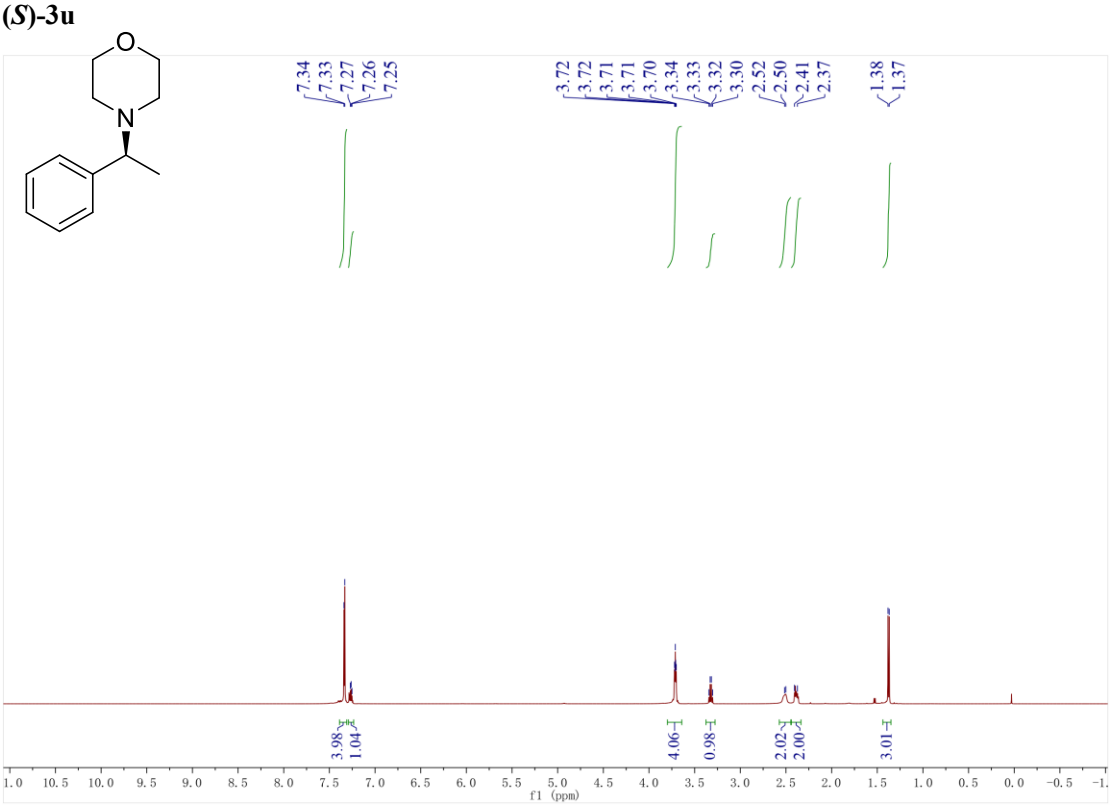

145.73
128.22
127.20
126.78
66.00
52.98
23.39
23.18
f1 (ppm)

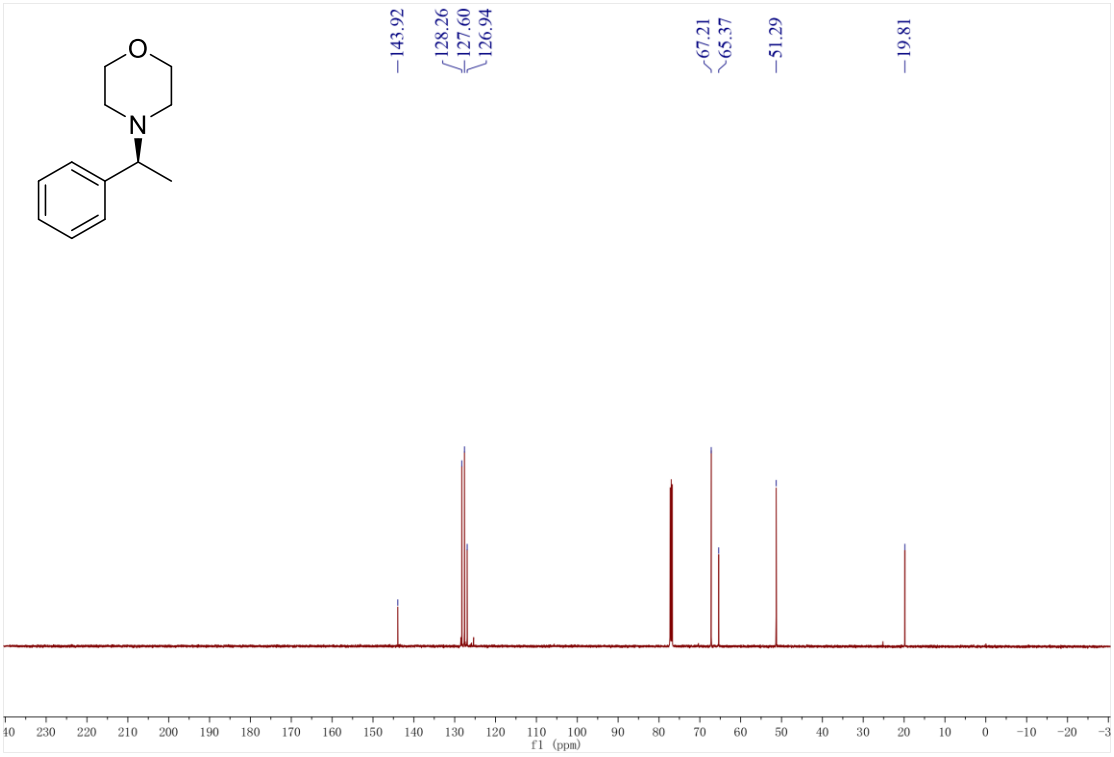
(*S*)-3t


7.38
7.35
7.30
7.26
3.40
3.39
3.38
3.36
2.38
2.33
2.31
1.56
1.53
1.53
1.50
1.37
1.36
3.09
2.03
1.00
4.17
5.99
3.04
f1 (ppm)

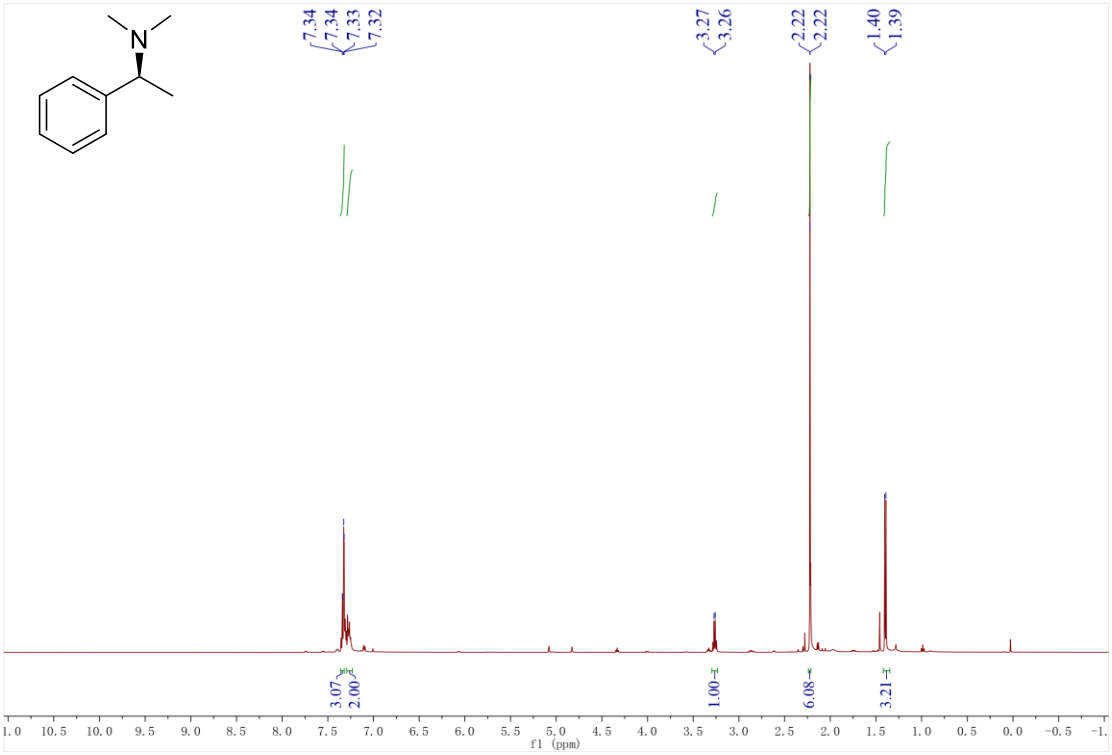

143.91
127.98
126.63
125.37
65.18
51.49
26.26
24.60
19.40
f1 (ppm)

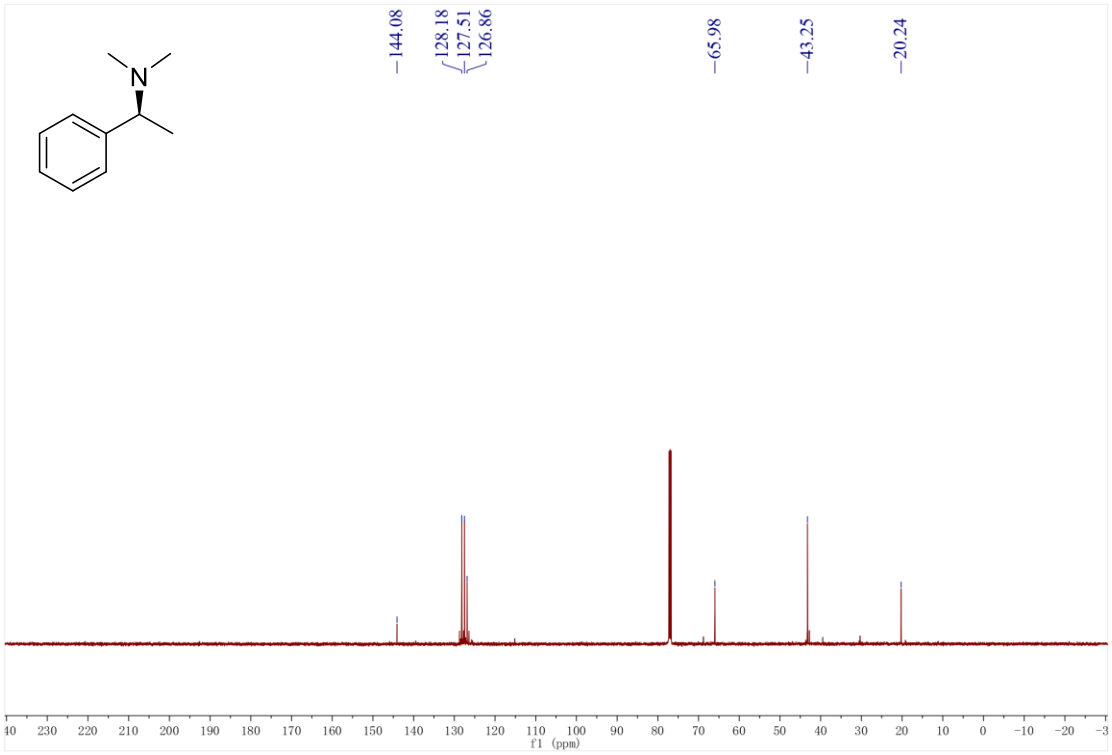
(*S*)-3u


7.34
7.33
7.27
7.26
7.25
3.72
3.72
3.71
3.71
3.70
3.34
3.33
3.32
3.30
2.52
2.50
2.41
2.37
1.38
1.37
3.98
1.04
4.06
0.98
2.02
2.00
3.01
f1 (ppm)

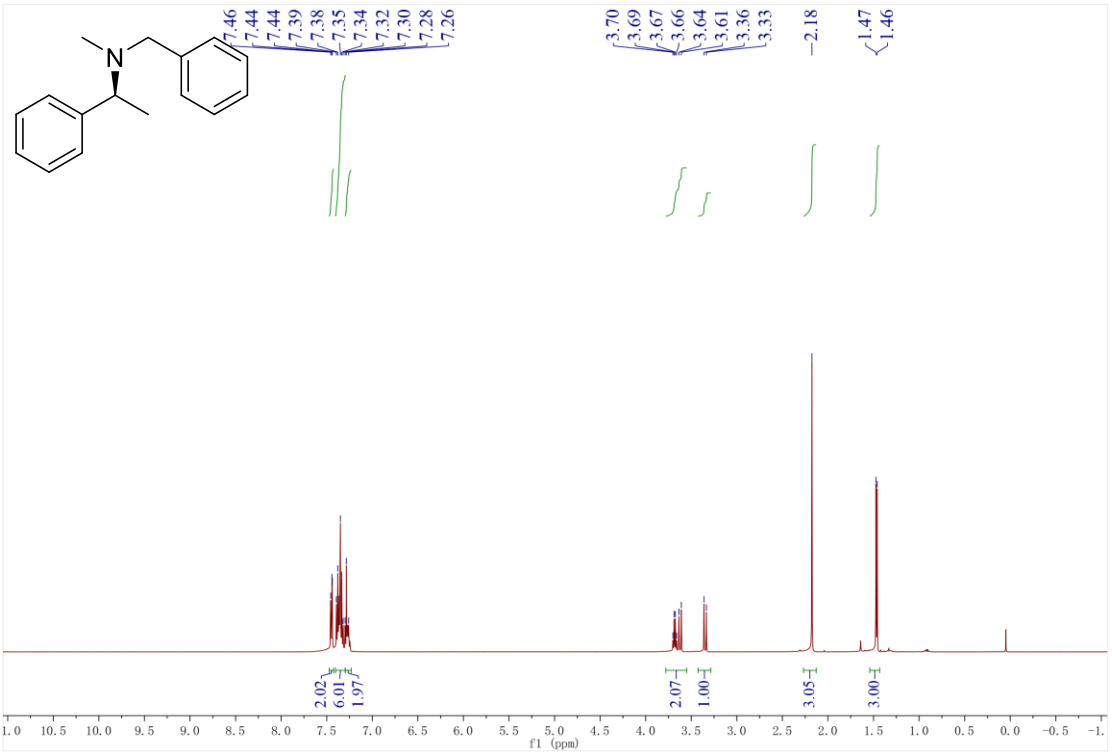

143.92
128.26
127.60
126.94
67.21
65.37
51.29
19.81
f1 (ppm)

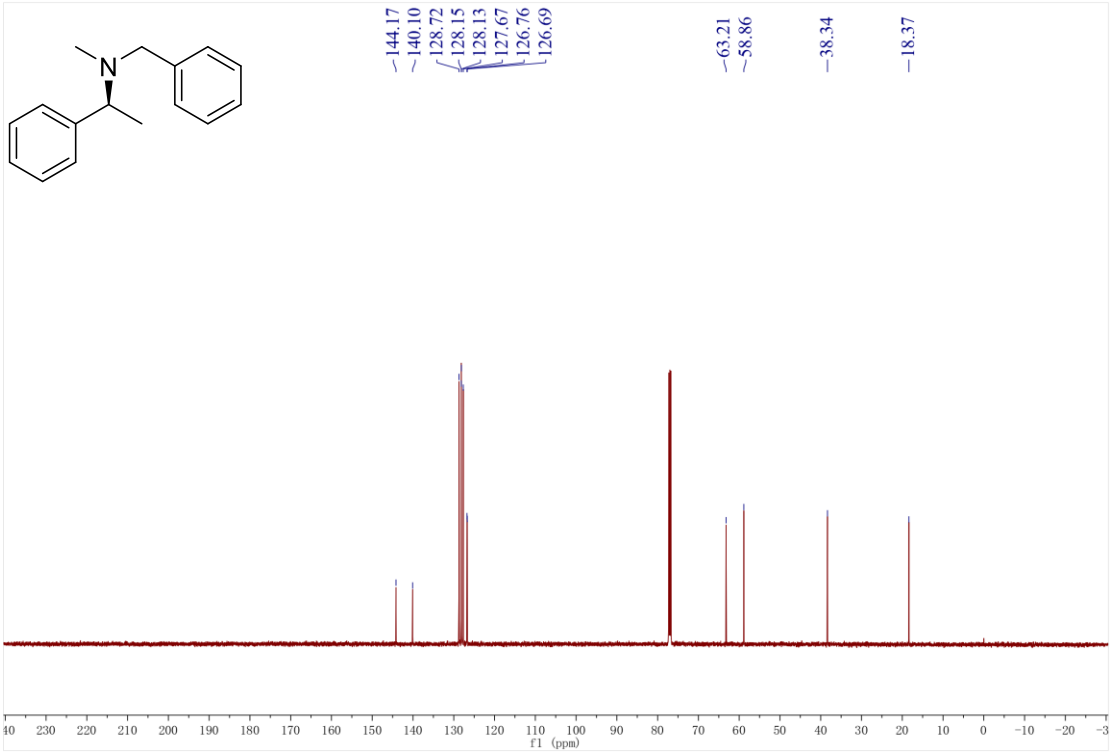
(*S*)-3v


7.34
7.34
7.33
7.32
3.27
3.26
2.22
2.22
1.40
1.39
3.07
2.00
1.00
6.08
3.21
f1 (ppm)

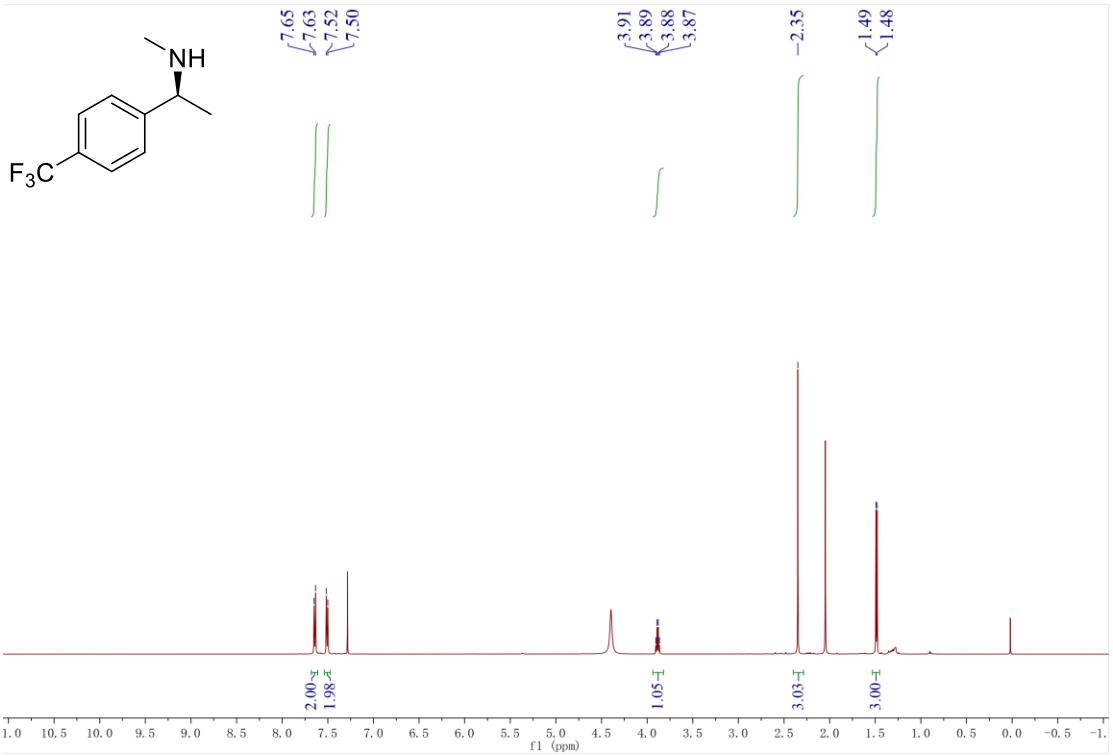

144.08
128.18
127.51
126.86
65.98
43.25
20.24
f1 (ppm)

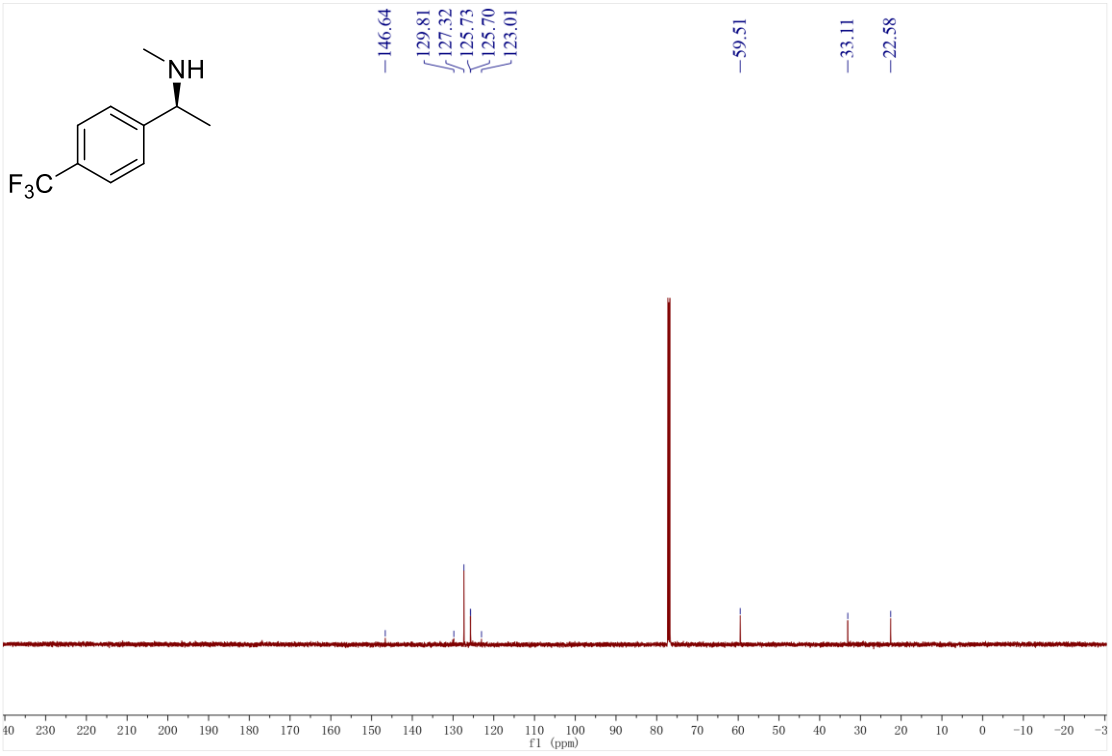
(*S*)-3w

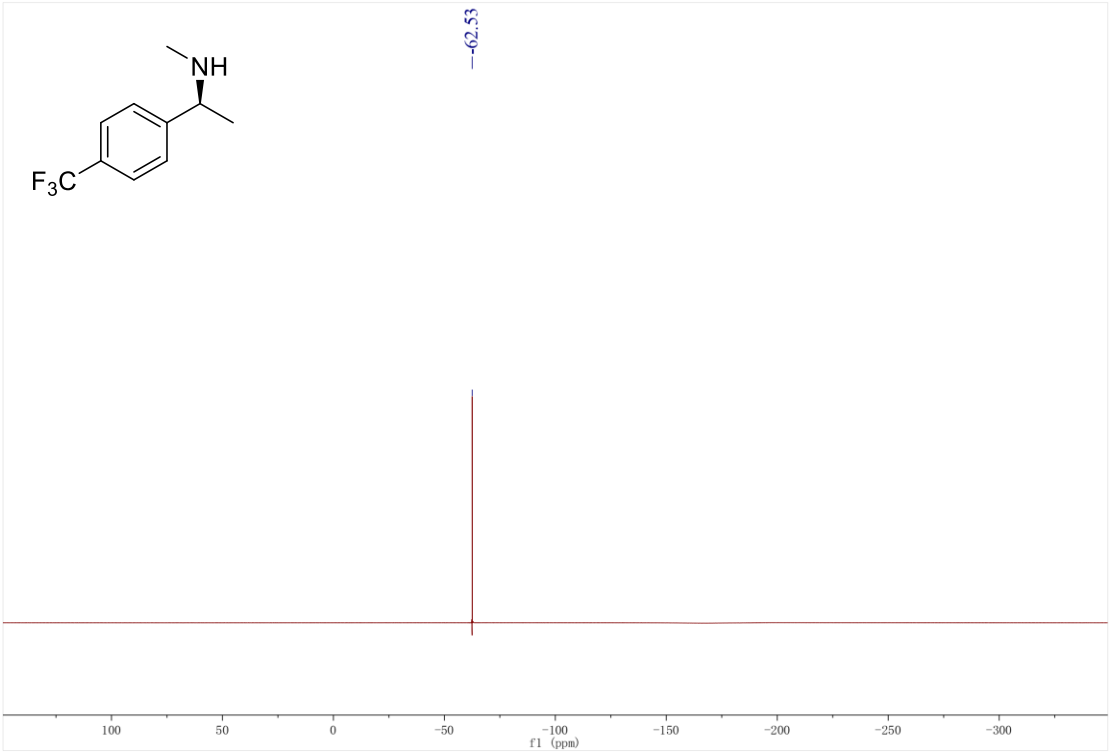

7.46
7.44
7.44
7.39
7.38
7.35
7.34
7.32
7.30
7.28
7.26
3.70
3.69
3.67
3.66
3.64
3.61
3.36
3.33
2.18
1.47
1.46
2.02
6.01
1.97
2.07
1.00
3.05
3.00
f1 (ppm)


144.17
140.10
128.72
128.15
128.13
127.67
126.76
126.69
63.21
58.86
38.34
18.37
f1 (ppm)

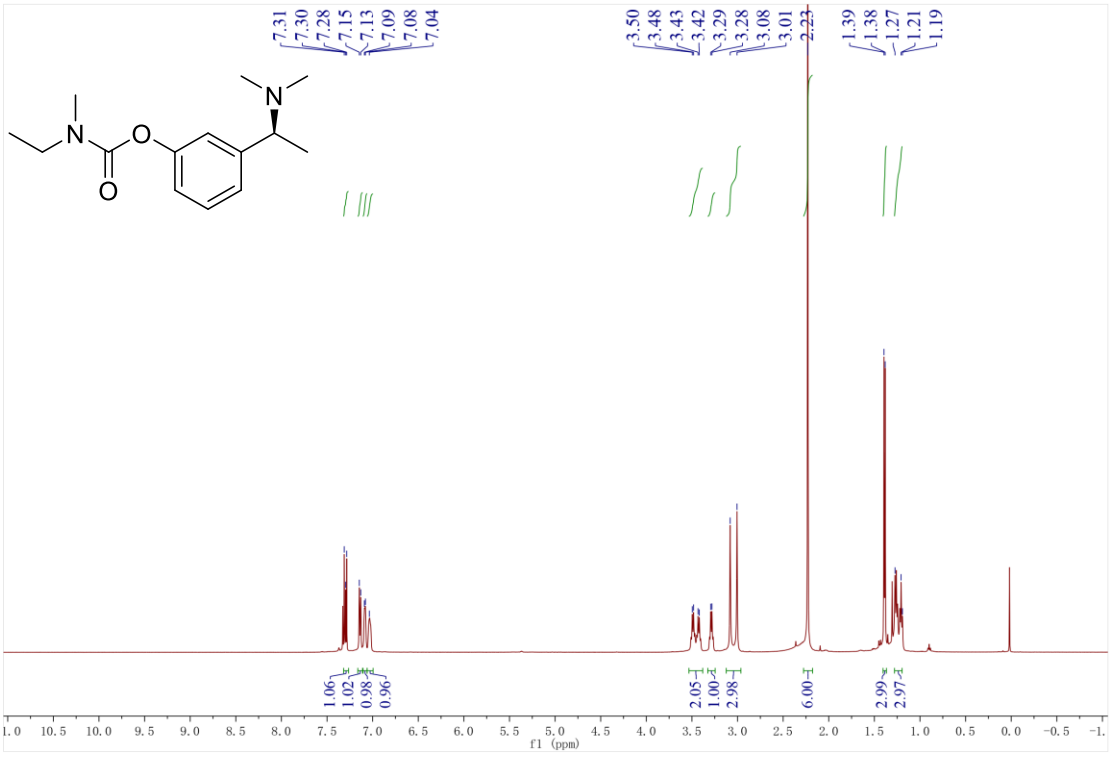
(*S*)-4

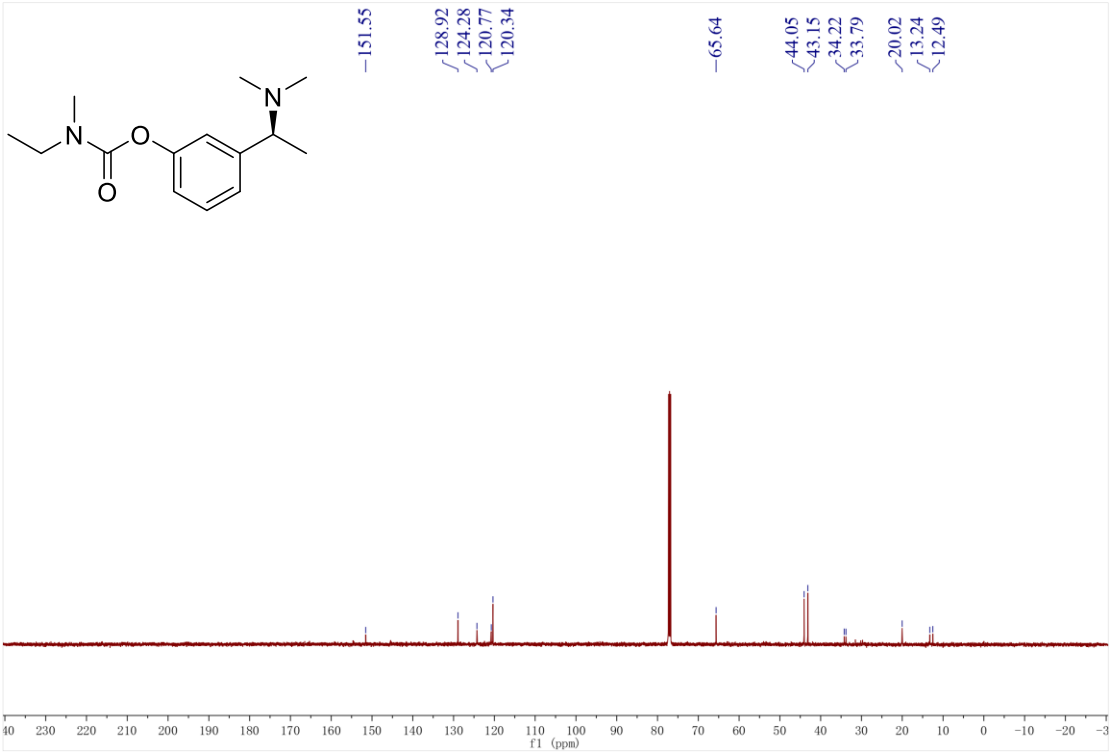

NH
F3C
7.65
7.63
7.52
7.50
3.91
3.89
3.88
3.87
2.35
1.49
1.48
2.00
1.98
1.05
3.03
3.00
f1 (ppm)


NH
F3C
146.64
129.81
127.32
125.73
125.70
123.01
59.51
33.11
22.58
f1 (ppm)


NH
F3C
-62.53
100
50
0
-50
-100
-150
-200
-250
-300
f1 (ppm)

(*S*)-5


7.31
7.30
7.28
7.15
7.13
7.09
7.08
7.04
3.50
3.48
3.43
3.42
3.29
3.28
3.08
3.01
2.23
1.39
1.38
1.27
1.21
1.19
N
N
O
O
1.06
1.02
0.98
0.96
2.05
1.00
2.98
6.00
2.99
2.97
f1 (ppm)


151.55
128.92
124.28
120.77
120.34
65.64
44.05
43.15
34.22
33.79
20.02
13.24
12.49
N
O
O
N
f1 (ppm)