

Supporting Information

Highly Active Nickel Catalysts for Enantioselective Reductive Alkenylation of *N*-Sulfonyl Aldimines

Mengxin Zhao,[†] Lantian Sun,[†] Bo Xiao,^{‡§} and Jianrong Steve Zhou^{†*}

[†]State Key Laboratory of Chemical Oncogenomics, Shenzhen Key Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University Shenzhen Graduate School, 2199 Lishui Road, Nanshan District, Shenzhen 518055, China.

[‡]Lab of Computational Chemistry and Drug Design, State Key Laboratory of Chemical Oncogenomics, Shenzhen Key Laboratory of Chemical Genomics, Peking University Shenzhen Graduate School, Shenzhen 518055, China.

[§]Hoffmann Institute of Advanced Materials, School of Food and Drug, Shenzhen Polytechnic University, Shenzhen 518055, China.

E-mail: jrzhou@pku.edu.cn

Experimental procedures and characterizations

Table of Contents

I. General information
II. Condition optimization of reductive alkenylation of <i>N</i> -sulfonyl aldimines
III. Asymmetric reductive alkenylation of <i>N</i> -sulfonyl aldimines
IV. Product derivatization
V X-ray measurement and a thermal ellipsoid plot of a crystal structure
VI. Reference

I. General Information

All NMR spectra were acquired on Bruker Advance 400 MHz, 300 MHz or 500 MHz NMR spectrometers. ^1H NMR chemical shifts were recorded relative to residual protiated solvents (CDCl_3 : δ 7.26 ppm). Multiplicities were given as: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The number of protons (n) for a given resonance was indicated by nH. Coupling constants were reported as a J value in Hz. ^{13}C NMR chemical shifts were recorded relative to solvent resonance (CDCl_3 : δ 77.16 = ppm). ^{19}F NMR spectra were recorded at 376.6 MHz on 400 MHz NMR spectrometers without any external standard. ^{11}B NMR spectra were recorded at 128 MHz on 400 MHz NMR spectrometers without any external standard. Proof of purity of new compounds was demonstrated with copies of ^1H , ^{13}C , and ^{19}F NMR spectra.

Glassware was dried at 120 °C for at least 3 h before use. Dry dimethyl sulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) were purchased from Aldrich or J&K Scientific and dried and stored over activated 3 Å molecular sieve beads in an argon-filled glove box. Zinc powder were purchased from Aladdin (product number A91216, Lot H2006145, ~600 mesh; 99.99% purity). Manganese powder were purchased from Alfa Aesar (product number 10238, ~325 mesh; 99.3% purity). Unless noted otherwise, commercially available chemicals were used as received without purification. All anhydrous solvents were stored in Schlenk tubes in the glove box. The GC internal standard *n*- $\text{C}_{12}\text{H}_{26}$ was degassed with argon and dried over activated 4 Å molecular sieve beads before use. Flash column chromatography was performed using Qingdao Haiyang Chemical HG/T2354-92 silica gel (200-300 mesh) with the indicated solvent system according to standard techniques.

Gas chromatography (GC) analysis was performed on a Shimadzu GC-2030 instrument with Shimadzu GC column DB-5MS-UI. Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiralcel columns at 35 °C and a mixture of HPLC-grade hexanes and isopropanol as eluent. Optical rotation was measured using a Rudolph AutoPol-I polarimeter equipped with a sodium vapor lamp at 589 nm and the concentration of samples was denoted as *c*.

GC/MS analysis was conducted on Agilent GC-MS 6890N-5975 instrument using a quadrupole mass analyzer and Agilent J & W GC column DB-5MS-UI. LC/MS analysis was conducted on a Shimadzu LCMS-2020 instrument using a single quadrupole mass analyzer. High resolution ESI mass spectra were recorded with an QSTAR Elite (ABI) using a quadrupole-time-of-flight (Q-TOF) mass analyzer or Q Exactive Focus (ThermoFisher) mass spectrometer using an Orbitrap mass analyzer combined with a quadrupole (Q) for precursor ion selection.

II. Condition optimization of reductive alkenylation of *N*-sulfonyl aldimines

A typical procedure: In an argon-filled glove box, NiBr₂(DME) (1.5 mg, 0.005 mmol, 5 mol%), (4*R*,4'*R*)-2,2'-(propane-2,2-diyl)bis(4-phenyl-4,5-dihydrooxazole) **L7** (2.0 mg, 0.006 mmol, 6 mol%), pure *N*-sulfonyl imine **1a** (0.1 mmol) and dry 1,4-dioxane (0.3 mL) were added to a dry 10-mL Schlenk tube. After stirring for 20 min at room temperature, Mn powder (16.5 mg, 0.3 mmol, Alfa Aesar), dry HFIP (33.6 mg, 0.2 mmol), Ti(O*i*-Pr)₄ (56.8 mg, 0.2 mmol), 1-bromocyclohexene (32 mg, 0.2 mmol) and GC standard *n*-C₁₂H₂₆ (20 μL) were added in sequence. The mixture was vigorously stirred at rt for 12 hours. At the end, the reaction mixture was diluted by 5 mL of 4:1 petroleum ether/EtOAc and an aliquot was filtered through a plug of silica gel with washings of 4:1 petroleum ether/EtOAc for GC analysis to determine conversions and calibrated yields. Chiral HPLC analysis (AZ-H *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min) was performed with purified samples to determine the enantioselectivity. The racemic samples were prepared with a similar procedure using bipy.

Figure S1. Effect of chiral ligands on model reductive alkenylation of imine **1a**

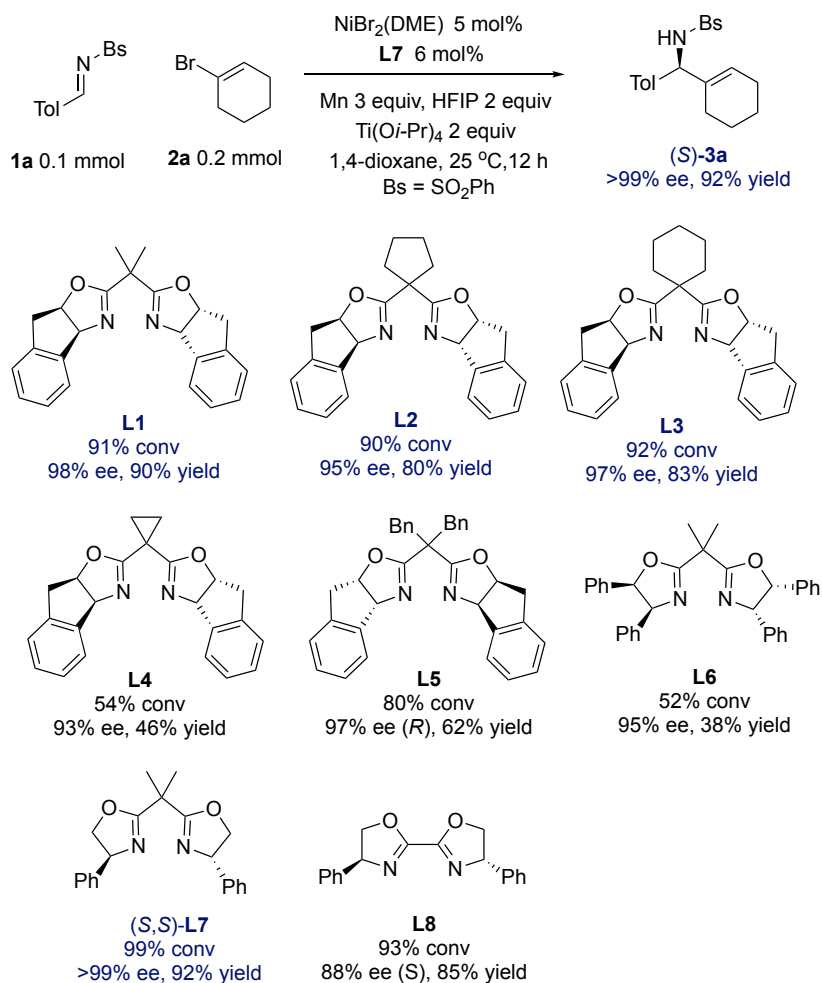


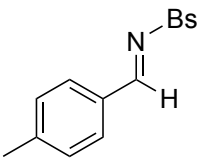
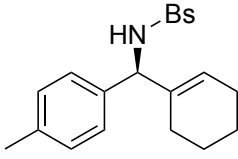
Table S1. Effect of solvents on model reductive alkenylation of imine **1a**

Entry	Solvent	Conv of 1a (%)	Yield (%)	Ee (%)
1	THF	90	88	95
2	2-MeTHF	91	86	93
3	1,4-dioxane	99	92	>99
4	DMSO	40	0	-
5	DMF	38	0	-
6	DME	84	60	93
7	DCM	80	71	90

Table S2. Effect of alcohols and water (2 equiv) on the model reductive alkenylation of aldimine **1a**

Entry	Proton source	Conv of 1a (%)	Yield (%)	Ee (%)
1	none	0	0	-
2	H ₂ O	2	0	-
3	HFIP (3 equiv)	100	92	93
4	HFIP (2 equiv)	99	92	>99
5	HFIP (1 equiv)	61	0	96
6	CF ₃ CH ₂ OH (TFE)	3	0	-
10	<i>t</i> -BuOH	2	0	-

Table S3. Effect of additives on the model reductive alkenylation of aldimine **1a**

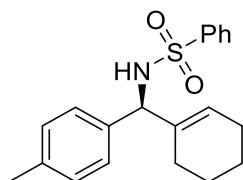
<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;">  <p>1a 0.1 mmol</p> </div> <div style="text-align: center;"> <p>cyclohexenyl bromide 0.2 mmol</p> </div> <div style="text-align: center;"> <p>standard condition</p> <p>NiBr₂(DME) 5 mol% L7 6 mol%</p> <p>Mn 3 equiv, HFIP 2 equiv Ti(Oi-Pr)₄ 2 equiv 1,4-dioxane, 25 °C, 12 h Bs = SO₂Ph</p> </div> <div style="text-align: center;">  <p>3a 92% yield, >99% ee</p> </div> </div>				
Entry	additive	Conv of 1a (%)	Yield (%)	Ee (%)
1	No Ti(Oi-Pr) ₄	32	0	-
2	TiCl ₄	26	0	-
3	LaCl ₃	20	0	-
4	Mg(OTf) ₂	15	0	-
5	LiI	18	0	-
6	NaBr	23	0	-
7	Ti(Oi-Pr) ₄	99	92	>99

III. Asymmetric reductive alkenylation of *N*-sulfonyl aldimines

A typical procedure: In an argon-filled glove box, NiBr₂(DME) (1.5 mg, 0.005 mmol, 5 mol%), (4*R*,4'*R*)-2,2'-(propane-2,2-diyl)bis(4-phenyl-4,5-dihydrooxazole) **L7** (2.0 mg, 0.006 mmol, 6 mol%), pure *N*-sulfonyl imine **1a** (0.1 mmol) and dry 1,4-dioxane (0.3 mL) were added to a dry 10-mL Schlenk tube. After stirring for 20 min at room temperature, Mn powder (16.5 mg, 0.3 mmol, Alfa Aesar), dry HFIP (33.6 mg, 0.2 mmol), Ti(Oi-Pr)₄ (56.8 mg, 0.2 mmol), 1-bromocyclohexene (32 mg, 0.2 mmol) and GC standard *n*-C₁₂H₂₆ (20 μL) were added in sequence. The mixture was vigorously stirred at rt for 12 hours. At the end, the reaction mixture was diluted by 5 mL of 4:1 petroleum ether/EtOAc and filtered through a pad of silica gel with washings of 10-20 mL of 4:1 petroleum ether/EtOAc. The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel to provide products. Chiral HPLC analysis (AZ-H *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min) was performed to determine the enantioselectivity. The racemic samples were prepared with a similar procedure using bipy ligand.

Synthesis of Bs-imines on 0.1 mmol scale: under argon, aromatic aldehyde (0.1 mmol), Bs-amine (0.1 mmol), dry MgSO₄ (80 mg) and dry toluene (0.4 mL) were added to a 10-mL dry Schlenk tube. The mixture was stirred in an oil bath at 140 °C for 30 hours until (almost) full conversion. The crude product was cooled

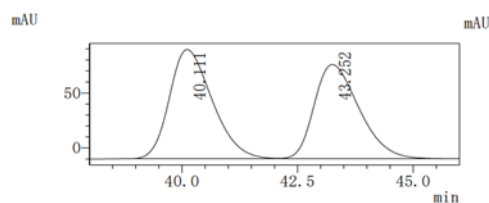
down and filtered through a plug of Celite in a glove box with washings of dry toluene. The filtrate was collected in a 10-mL dry Schlenk tube. Toluene was completely removed under reduced pressure with care. It is important to keep the imine sample from contact with air or moisture, for good reproducibility in the subsequent reactions. The crude imine was used directly in the next step.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3a)

Alkenyl triflate was used. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as yellow oil. 31.4 mg, 92% yield. >99% ee (the other enantiomer was not detected on chiral HPLC). $[\alpha]_D^{28} = -12.1^\circ$ ($c = 0.5$, CHCl_3). The crystals suitable for X-ray diffraction were obtained via vapor diffusion of petroleum ether into a concentrated sample in EtOAc at rt.

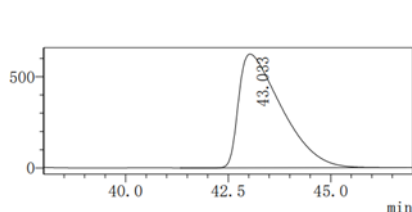
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 40.1$ min (minor), 43.0 min (major).



Peak Table

PDA Ch2 220nm

Peak#	Ret. Time	Area	Area%
1	40.111	6383269	52.584
2	43.252	5755996	47.416
Total		12139265	100.000



Peak Table

PDA Ch2 220nm

Peak#	Ret. Time	Area	Area%
1	43.033	45274669	100.000
Total		45274669	100.000

^1H NMR (400 MHz, CDCl_3): δ 7.78-7.75 (m, 2H), 7.53-7.48 (m, 1H), 7.43-7.39 (m, 2H), 7.03-6.99 (m, 4H), 5.56-5.54 (m, 1H), 4.93 (d, $J = 7.9$ Hz, 1H), 4.82 (d, $J = 7.8$ Hz, 1H), 2.28 (s, 3H), 1.91-1.85 (m, 2H), 1.71-1.65 (m, 1H), 1.63-1.54 (m, 1H), 1.48-1.29 (m, 4H).

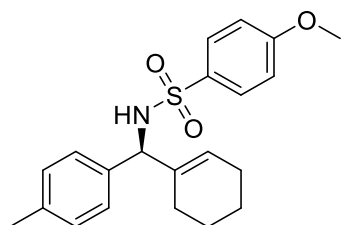
^{13}C NMR (100 MHz, CDCl_3): δ 141.0, 137.3, 136.5, 135.7, 132.4, 129.2, 128.9, 127.5, 127.0, 125.8, 63.2, 25.1, 25.1, 22.4, 22.2, 21.1.

HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$: 342.1522; found: 342.1523.

A reaction procedure on 1 mmol scale: In an argon-filled glove box, $\text{NiBr}_2(\text{DME})$ (0.8 mg, 0.002 mmol, 0.2 mol%), (4*S*,4'*S*)-**L8** (0.8 mg, 0.003 mmol, 0.3 mol%), *N*-sulfonyl imine **1a** (260 mg, 1 mmol) and dry THF (2 mL) were added to a dry 10-mL Schlenk tube. After stirring for 20 min at rt, Mn powder (165 mg, 3 mmol, Alfa Aesar), *t*-BuOH (125 μL , 2 mmol), 1-bromocyclohexene (160 mg, 1.5 mmol) and GC standard *n*- $\text{C}_{12}\text{H}_{26}$ (200

μL) were added in sequence. The mixture was vigorously stirred at rt for 12 hours. At the end, the reaction mixture was diluted by 5 mL of 4:1 petroleum ether/EtOAc and filtered through a pad of silica gel with washings of 10-20 mL of 4:1 petroleum ether/EtOAc. The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel to provide the product. 245 mg, 72% yield and 91% ee.

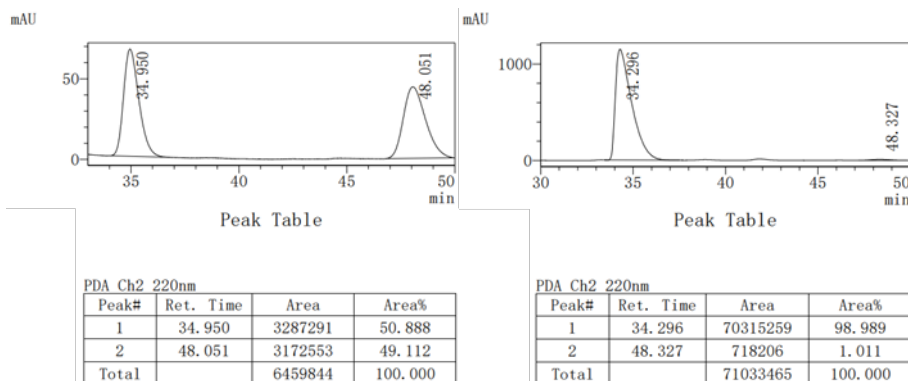
Synthesis of Bs-imines on 1 mmol scale: under argon, aromatic aldehyde (1 mmol), Bs-amine (1 mmol), dry MgSO_4 (800 mg) and dry toluene (2 mL) were added to a 10-mL dry Schlenk tube. The mixture was stirred in an oil bath at 140 °C for 48 hours until (almost) full conversion. The crude product was cooled down and filtered through a plug of Celite in a glove box with washings of dry toluene. Toluene was *completely* removed under reduced pressure with care. It is important to keep the imine sample from contact with air or moisture, for good reproducibility in the subsequent reactions. The crude imine was used directly in the next step.



(S)-N-4-Methoxybenzenesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3b)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 31.5 mg, 85% yield. 98% ee. $[\alpha]_D^{24} = -23.8^\circ$ ($c = 0.5$, CHCl_3).

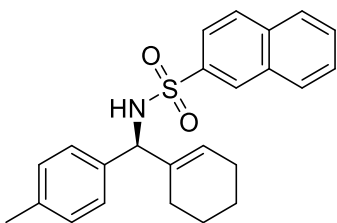
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 34.3$ min (major), 48.3 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.74 (d, $J = 8.9$ Hz, 2H), 7.13-7.05 (m, 4H), 6.92 (d, $J = 9.0$ Hz, 2H), 5.62 (s, 1H), 5.00 (d, $J = 7.7$ Hz, 1H), 4.83 (d, $J = 7.7$ Hz, 1H), 3.90 (s, 3H), 2.34 (s, 3H), 2.02-1.90 (m, 2H), 1.79-1.65 (m, 2H), 1.56-1.38 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 162.8, 137.2, 136.7, 135.9, 132.7, 129.6, 129.2, 127.0, 125.6, 113.9, 63.2, 55.7, 25.2, 25.1, 22.5, 22.2, 21.1.

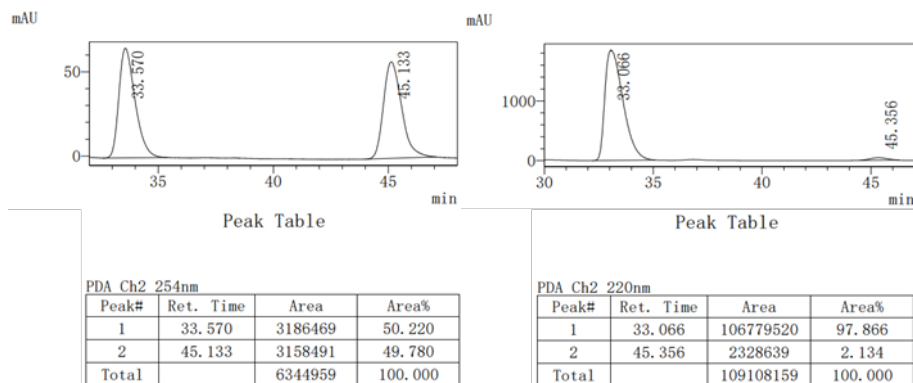
HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{26}\text{NO}_3\text{S}^+$ $[\text{M}+\text{H}]^+$: 372.1628; found: 372.1630.



(S)-N-2-Naphthalenesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3c)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 31.3 mg, 80% yield. 96% ee. $[\alpha]_D^{28} = -17.2^\circ$ ($c = 0.5$, CHCl_3).

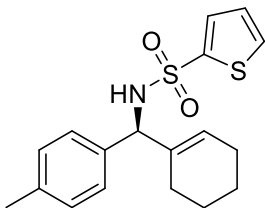
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 33.1$ min (major), 45.4 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.74 (d, $J = 8.9$ Hz, 2H), 7.13-7.05 (m, 4H), 6.92 (d, $J = 9.0$ Hz, 2H), 5.62 (s, 1H), 5.00 (d, $J = 7.7$ Hz, 1H), 4.83 (d, $J = 7.7$ Hz, 1H), 3.90 (s, 3H), 2.34 (s, 3H), 2.02-1.90 (m, 2H), 1.79-1.65 (m, 2H), 1.56-1.38 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 162.8, 137.2, 136.7, 135.9, 132.7, 129.6, 129.2, 127.0, 125.6, 113.9, 63.2, 55.7, 25.2, 25.1, 22.5, 22.2, 21.1.

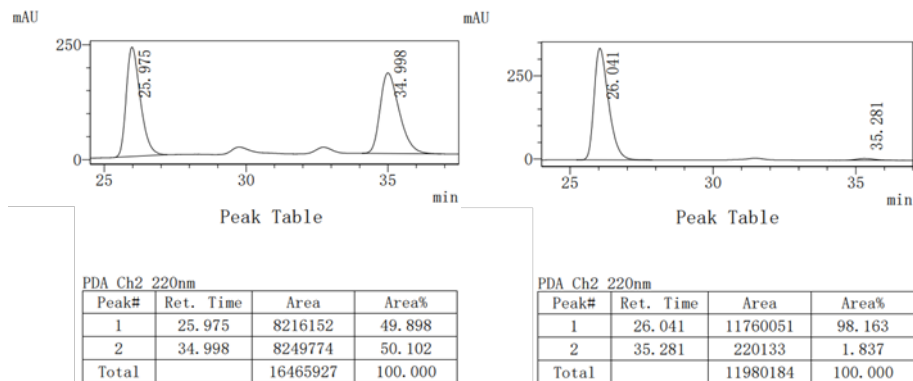
HRMS (ESI): Calcd for $\text{C}_{24}\text{H}_{26}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 392.1679; found: 392.1675.



(S)-N-2-Thiophenesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3d)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as colorless oil. 27.1 mg, 78% yield. 97% ee. $[\alpha]_D^{26} = -11.3^\circ$ ($c = 0.5$, CHCl_3).

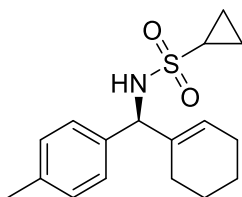
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 26.0$ min (major), 35.3 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.51-7.47 (m, 2H), 7.13-7.01 (m, 4H), 6.99-6.97 (m, 1H), 5.62-5.60 (m, 1H), 5.10 (d, $J = 7.9$ Hz, 1H), 4.87 (d, $J = 8.0$ Hz, 1H), 2.30 (s, 3H), 2.00-1.94 (m, 2H), 1.78-1.67 (m, 2H), 1.55-1.40 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 142.1, 137.3, 136.5, 135.8, 132.5, 131.7, 129.3, 129.0, 127.1, 126.9, 125.6, 63.4, 25.3, 25.2, 22.5, 22.2, 21.2.

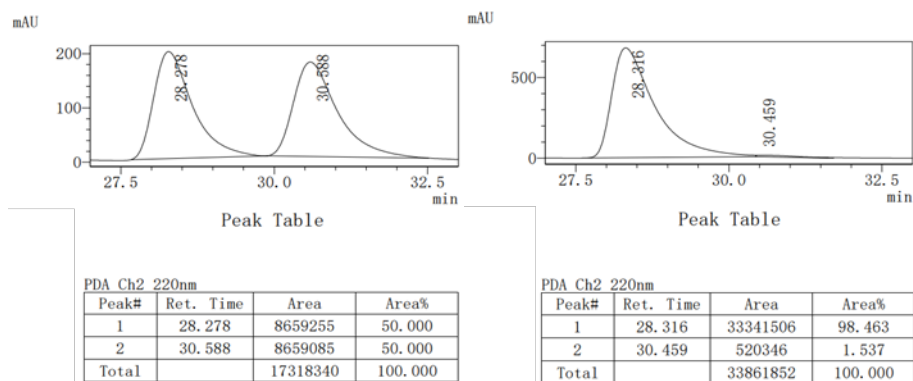
HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2\text{S}_2^+$ $[\text{M}+\text{H}]^+$: 348.1086; found: 348.1087.



(S)-N-Cyclopropanesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3e)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.3 mg, 86% yield. 97% ee. $[\alpha]_D^{24} = -2.1^\circ$ ($c = 0.5$, CHCl_3).

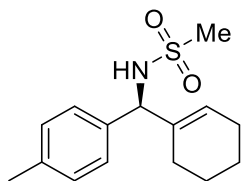
HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 28.3$ min (major), 30.5 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.20 (d, J = 8.2 Hz, 2H), 7.15-7.12 (m, 2H), 5.75-5.73 (m, 1H), 4.92 (d, J = 8.0 Hz, 1H), 4.61 (d, J = 8.0 Hz, 1H), 2.34 (s, 3H), 2.22-2.15 (m, 1H), 2.08-2.05 (m, 2H), 1.96-1.85 (m, 2H), 1.62-1.53 (m, 4H), 1.14-1.02 (m, 2H), 0.88-0.73 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 137.4, 137.3, 129.4, 128.9, 127.2, 125.1, 63.0, 31.6, 25.8, 25.3, 22.7, 22.4, 21.2, 6.0, 5.9.

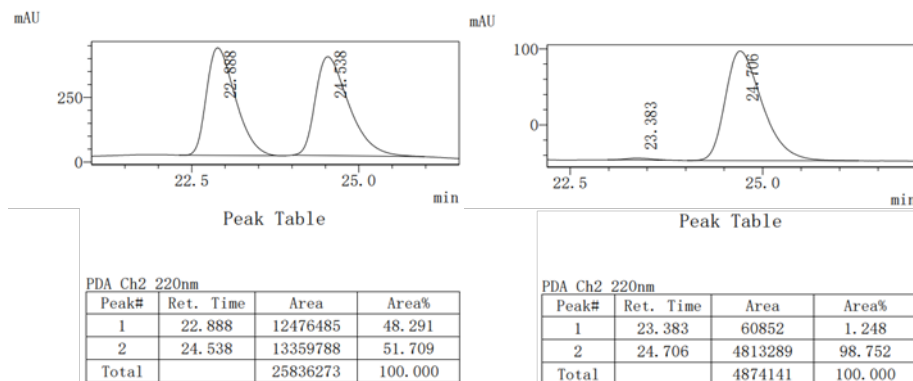
HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 306.1522; found: 306.1525.



(S)-N-Methanesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3f)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 20.9 mg, 75% yield. 98% ee. $[\alpha]_D^{27} = -29.6^\circ$ (c = 0.5, CHCl_3).

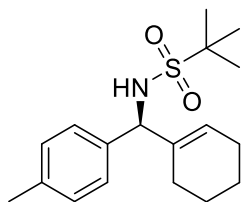
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 220 nm, t_R = 23.4 min (minor), 24.7 min (major).



^1H NMR (400 MHz, CDCl_3): δ 7.19-7.13 (m, 4H), 5.76-5.74 (m, 1H), 5.05 (d, J = 8.1 Hz, 1H), 4.91 (d, J = 8.0 Hz, 1H), 2.74 (s, 3H), 2.33 (s, 3H), 2.09-2.05 (m, 2H), 1.94-1.80 (m, 2H), 1.63-1.52 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 137.6, 136.9, 136.8, 129.5, 127.1, 125.1, 62.9, 41.9, 25.7, 25.2, 22.7, 22.3, 21.2.

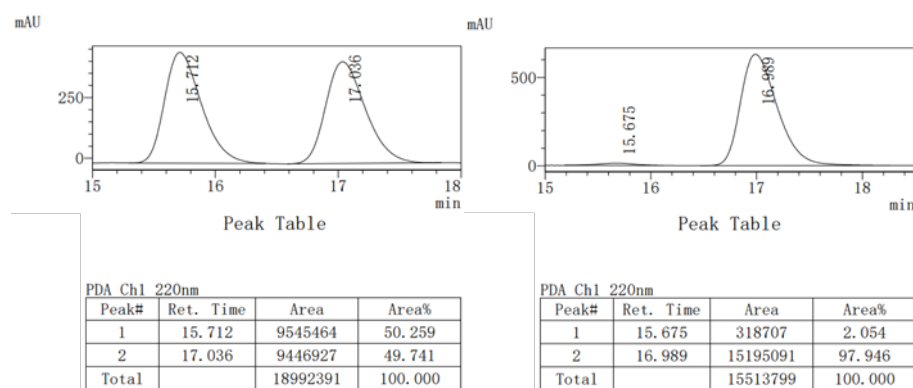
HRMS (ESI): Calcd for $C_{15}H_{22}NO_2S^+$ $[M+H]^+$: 280.1366; found: 280.1365.



(S)-N-tert-Butanesulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3g)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.4 mg, 82% yield. 96% ee. $[\alpha]^{24}_D = -6.6^\circ$ ($c = 0.5$, $CHCl_3$).

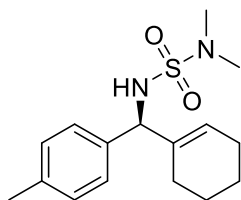
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 98/2, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 15.7$ min (minor), 17.0 min (major).



1H NMR (400 MHz, $CDCl_3$): δ 7.18-7.13 (m, 4H), 5.70 (brs, 1H), 4.90 (d, $J = 9.5$ Hz, 1H), 4.20 (d, $J = 9.5$ Hz, 1H), 2.34 (s, 3H), 2.07 (s, 2H), 1.94-1.80 (m, 2H), 1.60-1.57 (m, 4H), 1.33 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 137.8, 137.3, 129.4, 127.1, 124.8, 63.5, 60.0, 26.2, 25.3, 24.4, 22.8, 22.4, 21.2.

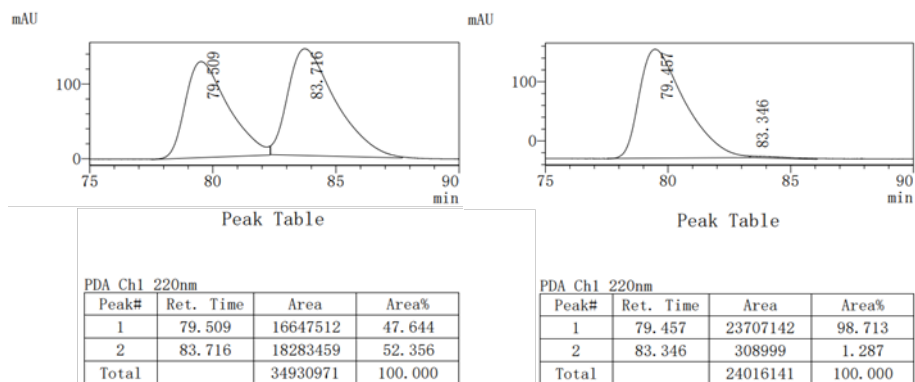
HRMS (ESI): Calcd for $C_{18}H_{28}NO_2S^+$ $[M+H]^+$: 322.1835; found: 322.1835.



(S)-N,N-Dimethylaminosulfonyl-1-(1-cyclohexenyl)-4-methylbenzylamine (3h)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:3) as white solid. 25.3 mg, 82% yield. 98% ee. $[\alpha]^{22}_D = -27.5^\circ$ ($c = 0.5$, $CHCl_3$).

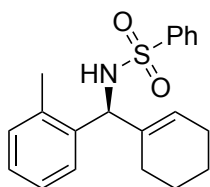
HPLC: Daicel Chiralcel IC-3, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 79.5$ min (major), 83.3 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.18 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 5.74-5.72 (m, 1H), 4.78 (d, J = 7.4 Hz, 1H), 4.69-4.66 (m, 1H), 2.63 (s, 6H), 2.33 (s, 3H), 2.09-2.04 (m, 2H), 1.93-1.83 (m, 2H), 1.61-1.53 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 137.7, 137.3, 137.3, 129.3, 127.2, 124.6, 63.2, 37.9, 25.9, 25.2, 22.7, 22.4, 21.2.

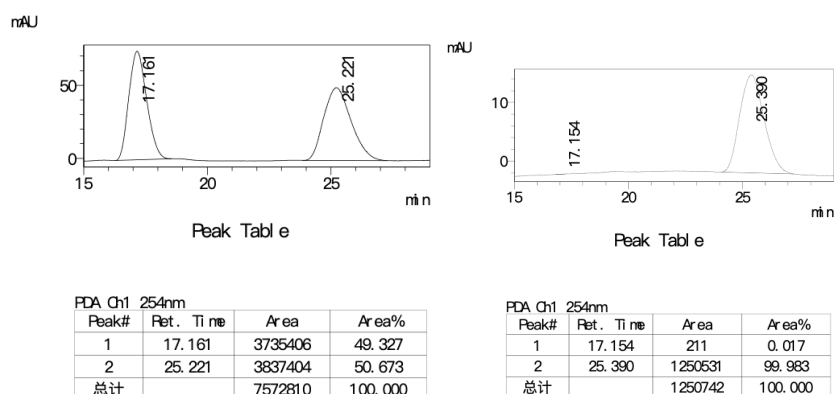
HRMS (ESI): Calcd for $\text{C}_{16}\text{H}_{25}\text{N}_2\text{O}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 309.1631; found: 309.1630.



(*S*)-*N*-Benzenesulfonyl-1-(1-cyclohexenyl)-2-methylbenzylamine (3i)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 31.8 mg, 93% yield. >99% ee. $[\alpha]_D^{20} = -3.6^\circ$ ($c = 2.2$, CHCl_3).

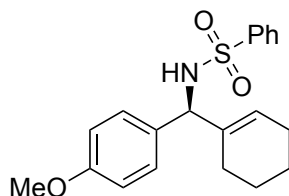
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 17.1$ min (minor), 25.4 min (major).



^1H NMR (400 MHz, CDCl_3): δ 7.76 – 7.67 (m, 2H), 7.49 – 7.41 (m, 1H), 7.41 – 7.29 (m, 2H), 7.12 – 6.91 (m, 4H), 5.40-5.38 (m, 1H), 5.17 (d, J = 7.7 Hz, 1H), 5.04 (d, J = 8.1 Hz, 1H), 2.21 (s, 3H), 1.95 – 1.77 (m, 3H), 1.77 – 1.66 (m, 1H), 1.58 – 1.35 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3): δ 140.6, 137.1, 135.5, 135.1, 132.0, 130.2, 128.4, 127.0, 126.9, 126.3, 125.7, 125.3, 59.3, 25.8, 24.8, 22.2, 21.8, 19.0.

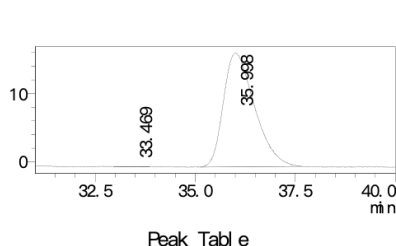
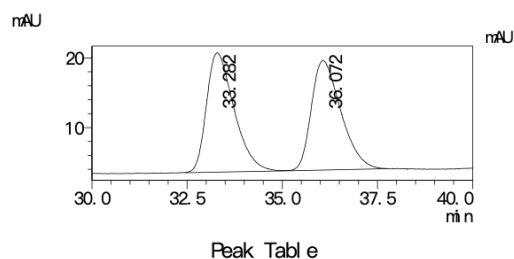
HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 342.1522; found: 342.1523.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-4-methoxybenzylamine (3j)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 31.5 mg, 88% yield. >99% ee. $[\alpha]_D^{20} = -28.9^\circ$ ($c = 1.8$, CHCl_3).

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 33.5$ min (minor), 36.0 min (major).



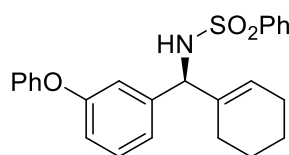
PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	
1	33.282	863002	50.462	
2	36.072	847203	49.538	
总计		1710205	100.000	

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Area%	
1	33.469	625	0.069	
2	35.998	899846	99.931	
总计		900471	100.000	

^1H NMR (400 MHz, CDCl_3): δ 7.84 – 7.72 (m, 2H), 7.59 – 7.46 (m, 1H), 7.46 – 7.35 (m, 2H), 7.10 – 6.96 (m, 2H), 6.80 – 6.68 (m, 2H), 5.55–5.53 (m, 1H), 5.04 (d, $J = 7.9$ Hz, 1H), 4.81 (d, $J = 7.8$ Hz, 1H), 3.75 (s, 3H), 1.97 – 1.79 (m, 2H), 1.77 – 1.55 (m, 2H), 1.51 – 1.29 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3): δ 159.0, 141.0, 135.7, 132.4, 131.6, 128.8, 128.2, 127.4, 125.6, 113.9, 62.9, 55.4, 25.1, 25.1, 22.4, 22.2.

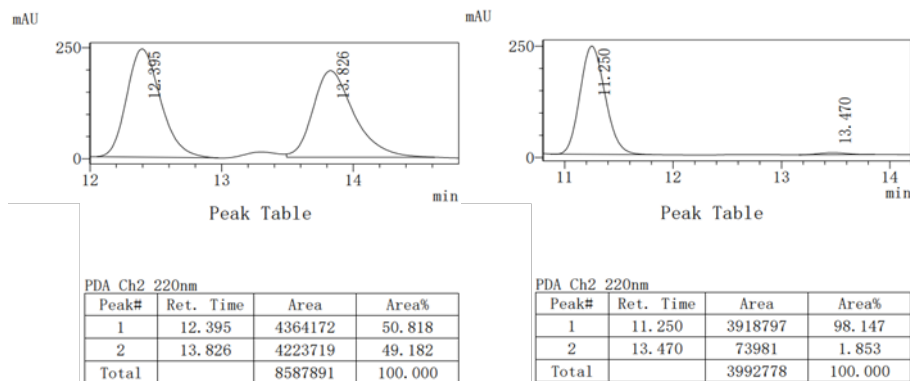
HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{24}\text{NO}_3\text{S}^+ [\text{M}+\text{H}]^+$: 358.1471; found: 358.1474.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-3-phenoxybenzylamine (3k)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:3) as white solid. 30.5 mg, 78% yield. 97% ee. $[\alpha]_D^{26} = -10.7^\circ$ ($c = 0.5$, CHCl_3).

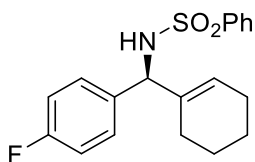
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 11.3$ min (major), 13.5 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 8.26 (d, $J = 1.9$ Hz, 1H), 7.88-7.84 (m, 3H), 7.73 (dd, $J = 8.7, 1.9$ Hz, 1H), 7.64-7.56 (m, 2H), 6.98 (d, $J = 8.1$ Hz, 2H), 6.92 (d, $J = 7.9$ Hz, 2H), 5.56-5.53 (m, 1H), 4.96 (d, $J = 7.8$ Hz, 1H), 4.87 (d, $J = 7.7$ Hz, 1H), 2.18 (s, 3H), 1.74-1.68 (m, 2H), 1.62-1.57 (m, 2H), 1.32-1.19 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 137.7, 137.3, 136.3, 135.7, 134.8, 132.2, 129.3, 129.1, 129.1, 128.9, 128.7, 127.9, 127.4, 127.0, 125.7, 122.7, 63.3, 25.2, 25.1, 22.4, 22.1, 21.0.

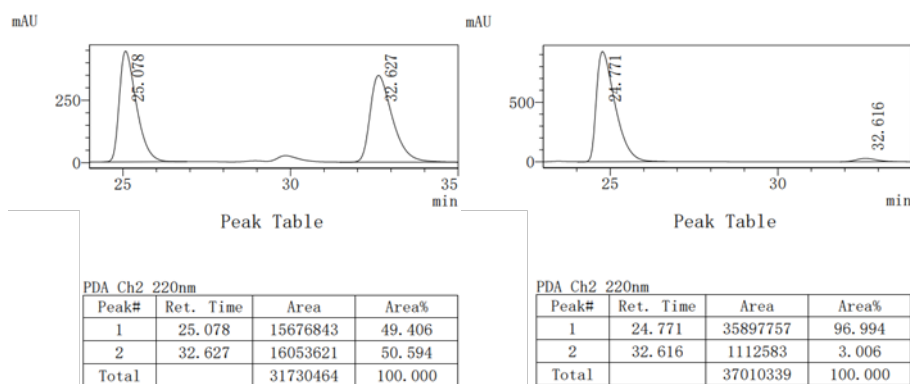
HRMS (ESI): Calcd for $\text{C}_{25}\text{H}_{26}\text{NO}_3\text{S}^+ [\text{M}+\text{H}]^+$: 420.1628; found: 420.1629.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-4-fluorobenzylamine (3l)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 25.5 mg, 74% yield. 94% ee. $[\alpha]_D^{28} = -1.3^\circ$ ($c = 0.5$, CHCl_3).

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 24.8$ min (major), 32.5 min (minor).

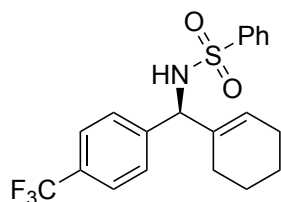


^1H NMR (400 MHz, CDCl_3): δ 7.77-7.74 (m, 2H), 7.53-7.48 (m, 1H), 7.40 (t, $J = 7.7$ Hz, 2H), 7.11-7.07 (m, 2H), 6.87 (t, $J = 8.6$ Hz, 2H), 5.51 (s, 1H), 5.33-5.26 (m, 1H), 4.84 (d, $J = 8.1$ Hz, 1H), 1.95-1.78 (m, 2H), 1.73-1.56 (m, 2H), 1.49-1.30 (m, 4H).

^{19}F NMR (376.6 MHz, CDCl_3): δ -115.21.

^{13}C NMR (100 MHz, CDCl_3): δ 162.2 (d, $J_{\text{C-F}} = 247.5$ Hz), 140.8, 135.4 (d, $J_{\text{C-F}} = 26.8$ Hz), 132.5 (d, $J_{\text{C-F}} = 3.0$ Hz), 128.84, 128.75 (d, $J_{\text{C-F}} = 8.1$ Hz), 127.37, 126.16, 115.40, 115.19, 62.79, 25.10, 25.08, 22.38, 22.07.

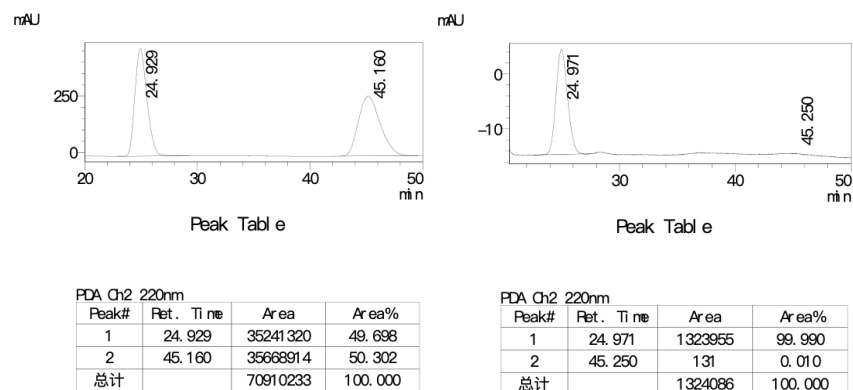
HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{21}\text{FNO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 346.1272; found: 346.1271.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-4-trifluoromethylbenzylamine (3m)

The reaction was conducted at 50 °C. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 35.2 mg, 89% yield. >99% ee. $[\alpha]_{\text{D}}^{20} = -3.3^\circ$ ($c = 1.2$, CHCl_3).

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 25.0$ min (major), 45.3 min (minor).

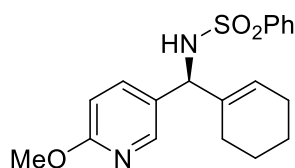


^1H NMR (400 MHz, CDCl_3): δ 7.83 – 7.68 (m, 2H), 7.58 – 7.47 (m, 1H), 7.47 – 7.34 (m, 4H), 7.26 (Ψd, J = 8.1 Hz, 2H), 5.65 – 5.45 (m, 2H), 4.92 (d, J = 8.2 Hz, 1H), 1.99 – 1.75 (m, 2H), 1.75 – 1.55 (m, 2H), 1.52 – 1.28 (m, 4H).

^{19}F NMR (376.6 MHz, CDCl_3): δ -62.59.

^{13}C NMR (101 MHz, CDCl_3): δ 143.5, 140.7, 135.2, 132.6, 129.7 (q, $J_{\text{C-F}}$ = 32.5 Hz), 128.9, 127.5, 127.3, 126.9, 125.4 (q, $J_{\text{C-F}}$ = 3.9 Hz), 124.2 (q, $J_{\text{C-F}}$ = 271.9 Hz), 63.2, 25.1, 25.0, 22.3, 22.0.

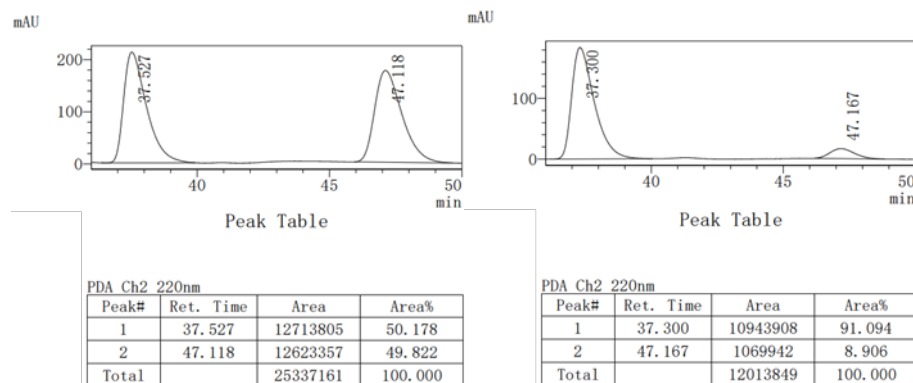
HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{21}\text{F}_3\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 396.1240; found: 396.1241.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-1-(4-methoxy-3-pyridyl)methylamine (3n)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 25.1 mg, 70% yield. 83% ee. $[\alpha]_D^{25} = -1.0^\circ$ (c = 0.5, CHCl_3).

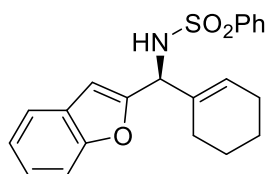
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 220 nm, t_R = 37.3 min (major), 47.2 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.88 (d, J = 2.5 Hz, 1H), 7.77-7.74 (m, 2H), 7.54-7.49 (m, 1H), 7.44-7.40 (m, 2H), 7.36 (dd, J = 8.6, 2.5 Hz, 1H), 6.58 (d, J = 8.6 Hz, 1H), 5.55-5.53 (m, 1H), 4.96 (d, J = 7.7 Hz, 1H), 4.81 (d, J = 7.7 Hz, 1H), 3.88 (s, 3H), 1.95-1.83 (m, 2H), 1.78-1.66 (m, 1H), 1.67-1.58 (m, 1H), 1.52-1.32 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 163.8, 145.7, 140.7, 137.7, 135.2, 132.6, 128.9, 127.7, 127.4, 126.3, 110.9, 60.9, 53.6, 25.3, 25.1, 22.4, 22.1.

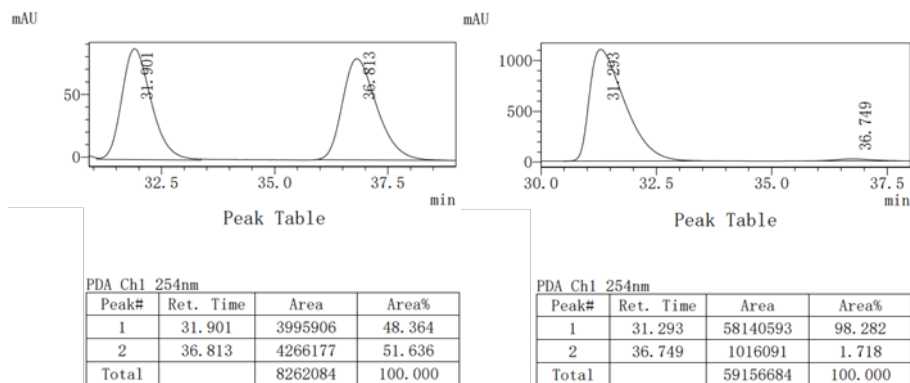
HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3\text{S}^+$ $[\text{M}+\text{H}]^+$: 359.1424; found: 359.1425.



(S)-N-Benzenesulfonyl-1-(2-benzofuryl)-1-(1-cyclohexenyl)-methanimine (3o)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as yellow solid. 30.8 mg, 84% yield. 97% ee. $[\alpha]^{25}_D = -9.2^\circ$ ($c = 0.5$, CHCl_3).

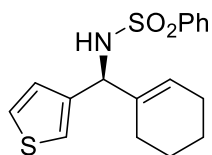
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 31.3$ min (major), 36.7 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.78-7.75 (m, 2H), 7.42-7.35 (m, 2H), 7.32-7.28 (m, 3H), 7.23-7.14 (m, 2H), 6.39 (s, 1H), 5.64-5.63 (m, 1H), 5.22 (d, $J = 8.5$ Hz, 1H), 5.06 (d, $J = 8.5$ Hz, 1H), 1.96-1.87 (m, 3H), 1.82-1.77 (m, 1H), 1.55-1.38 (m, 4H).

^{13}C NMR (100 MHz, CDCl_3): δ 154.8, 154.7, 140.6, 134.0, 132.5, 128.7, 128.0, 127.3, 127.0, 124.3, 123.0, 121.0, 111.2, 104.6, 58.0, 25.3, 25.2, 22.4, 22.0.

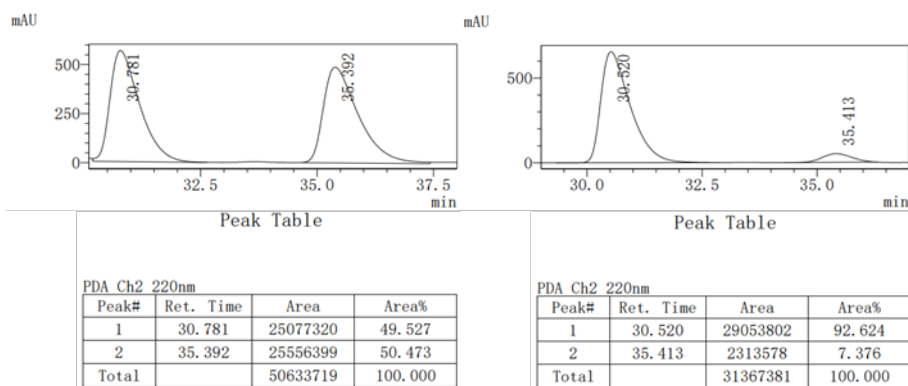
HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_3\text{S}^+$ $[\text{M}+\text{H}]^+$: 368.1315; found: 368.1314.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-1-(2-thienyl)methanimine (3p)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.7 mg, 80% yield. 85% ee. $[\alpha]^{22}_D = -0.9^\circ$ ($c = 0.5$, CHCl_3).

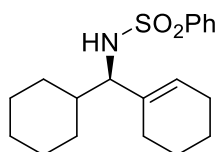
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 30.5$ min (major), 35.4 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.80-7.77 (m, 2H), 7.55-7.51 (m, 1H), 7.46-7.42 (m, 2H), 7.19-7.17 (m, 1H), 6.97-6.96 (m, 1H), 6.81-6.79 (m, 1H), 5.56-5.55 (m, 1H), 4.96 (d, $J = 8.2$ Hz, 1H), 4.86 (d, $J = 8.2$ Hz, 1H), 1.95-1.85 (m, 2H), 1.74-1.58 (m, 2H), 1.50-1.38 (m, 2H), 1.37-1.28 (m, 2H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.0, 135.5, 132.5, 128.8, 127.4, 126.6, 126.2, 126.1, 122.0, 60.0, 25.1, 24.7, 22.4, 22.1.

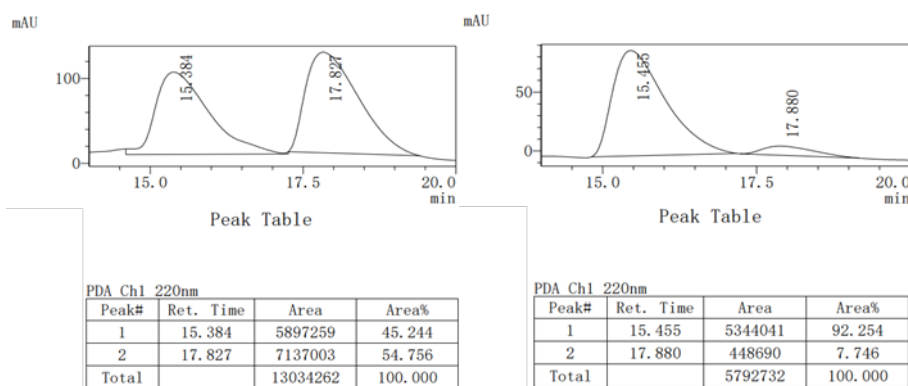
HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_2\text{S}_2^+ [\text{M}+\text{H}]^+$: 334.0930; found: 334.0931.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-1-cyclohexylmethanamine (3q)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.6 mg, 80% yield. 85% ee. $[\alpha]_D^{28} = -0.5^\circ$ ($c = 0.5$, CHCl_3).

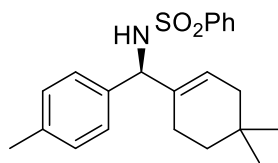
HPLC: Daicel Chiralcel AS-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 15.4$ min (major), 17.9 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.80 (d, $J = 7.7$ Hz, 2H), 7.53-7.49 (m, 1H), 7.46-7.42 (m, 2H), 5.23 (brs, 1H), 4.77 (d, $J = 9.0$ Hz, 1H), 3.40 (t, $J = 9.3$ Hz, 1H), 2.01 (d, $J = 13.3$ Hz, 1H), 1.80-1.74 (d, $J = 8.5$ Hz, 2H), 1.69-1.61 (m, 4H), 1.44-1.24 (m, 5H), 1.18-0.92 (m, 6H), 0.85-0.76 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.6, 133.9, 132.2, 128.7, 127.5, 126.5, 66.1, 39.7, 30.2, 30.0, 26.4, 26.2, 26.0, 24.9, 23.4, 22.2.

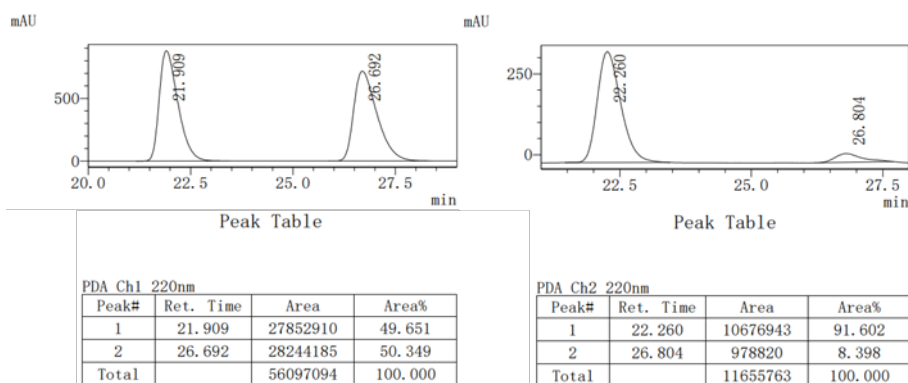
HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 334.1835; found: 334.1837.



(S)-N-Benzenesulfonyl-1-(4,4-dimethyl-1-cyclohexenyl)-4-methylbenzylamine (3r)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 32.2 mg, 87% yield. 83% ee. $[\alpha]_D^{28} = -11.3^\circ$ ($c = 0.5$, CHCl_3).

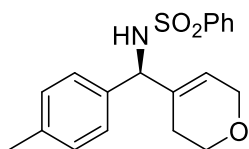
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 22.3$ min (major), 26.8 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.79-7.76 (m, 2H), 7.51-7.47 (m, 1H), 7.41-7.37 (m, 2H), 7.02-6.98 (m, 4H), 5.52-5.49 (m, 1H), 5.18 (d, $J = 7.9$ Hz, 1H), 4.84 (d, $J = 7.9$ Hz, 1H), 2.28 (s, 3H), 1.74-1.61 (m, 4H), 1.24-1.17 (m, 1H), 1.11-1.03 (m, 1H), 0.76 (d, $J = 9.0$ Hz, 6H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.0, 137.2, 136.6, 134.4, 132.3, 129.2, 128.8, 127.4, 126.8, 124.5, 62.8, 39.1, 35.2, 28.6, 28.5, 28.0, 23.0, 21.1.

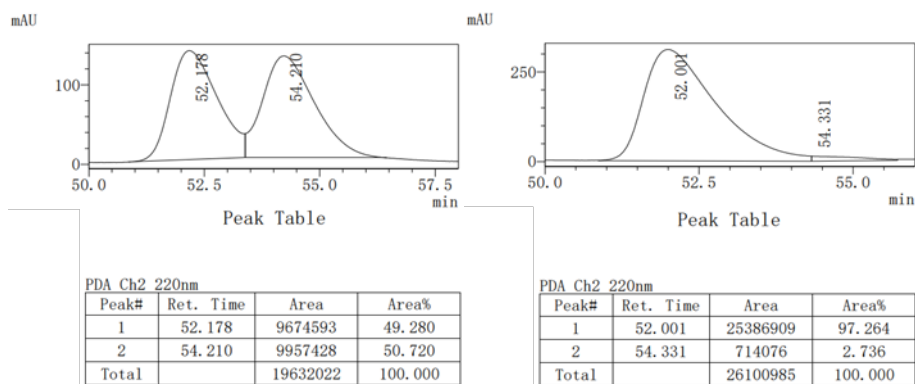
HRMS (ESI): Calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 370.1835; found: 370.1836.



(S)-N-Benzenesulfonyl-1-(3,6-dihydropyran-4-yl)-4-methylbenzylamine (3s)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:3) as colorless oil. 24.8 mg, 72% yield. 95% ee. $[\alpha]_D^{23} = -3.0^\circ$ ($c = 0.5$, CHCl_3).

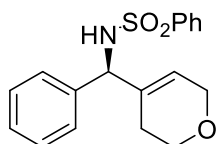
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.3 mL/min, $\lambda = 220$ nm, $t_R = 52.0$ min (major), 54.3 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.77-7.74 (m, 2H), 7.54-7.50 (m, 1H), 7.43-7.40 (m, 2H), 7.01 (d, $J = 7.9$ Hz, 2H), 6.94 (d, $J = 8.1$ Hz, 2H), 5.61 (s, 1H), 4.94 (d, $J = 7.5$ Hz, 1H), 4.83 (d, $J = 7.5$ Hz, 1H), 4.03 (s, 2H), 3.68-3.62 (m, 1H), 3.51-3.46 (m, 1H), 2.28 (s, 3H), 1.93-1.87 (m, 1H), 1.81-1.75 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 140.8, 137.8, 135.5, 134.2, 132.6, 129.5, 129.0, 127.4, 127.1, 123.8, 65.4, 64.0, 62.3, 25.8, 21.2.

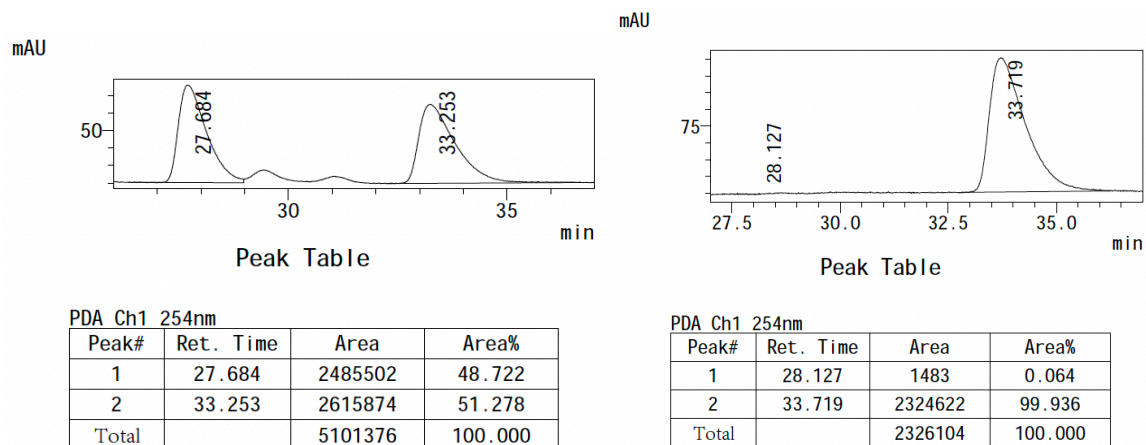
HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{22}\text{NO}_3\text{S}^+ [\text{M}+\text{H}]^+$: 344.1315; found: 344.1316.



(S)-N-Benzenesulfonyl-1-(3,6-dihydropyran-4-yl)-benzylamine (3t)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:3) as white solid. 24.7 mg, 75% yield. 99% ee. $[\alpha]_D^{25} = -24.0^\circ$ ($c = 0.5$, CHCl_3).

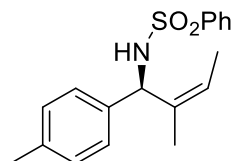
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, $\lambda = 254$ nm, $t_R = 27.8$ min (minor), 33.3 min (major).



^1H NMR (400 MHz, CDCl_3): δ 7.84-7.82 (m, 2H), 7.59-7.55 (m, 1H), 7.48-7.44 (m, 2H), 7.27-7.23 (m, 3H), 7.15-7.13 (m, 2H), 5.73 (d, J = 8.1 Hz, 1H), 5.65-5.63 (m, 1H), 4.96 (d, J = 8.1 Hz, 1H), 4.09-4.06 (m, 2H), 3.73-3.68 (m, 1H), 3.57-3.51 (m, 1H), 2.02-1.95 (m, 1H), 1.90-1.83 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 140.7, 138.4, 134.1, 132.5, 128.9, 128.6, 127.8, 127.2, 127.1, 123.9, 65.2, 63.9, 62.44, 25.6.

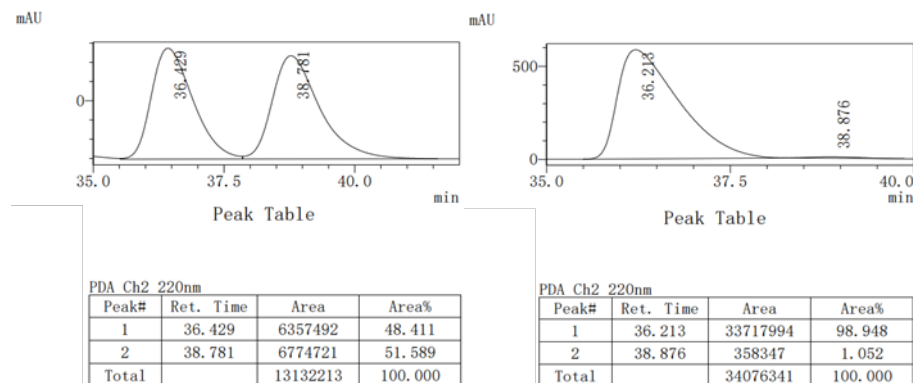
HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{20}\text{NO}_3\text{S}^+$ $[\text{M}+\text{H}]^+$: 330.1158; found: 330.1159.



(*S,Z*)-*N*-Benzenesulfonyl-1-(2-butenyl)-4-methylbenzylamine (3u)

The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.8 mg, 85% yield. 98% ee. $[\alpha]_D^{25} = -2.4^\circ$ (c = 0.5, CHCl_3).

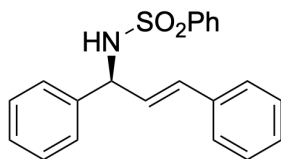
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 220 nm, t_R = 36.2 min (major), 38.9 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.78-7.75 (m, 2H), 7.53-7.49 (m, 1H), 7.44-7.39 (m, 2H), 7.04-6.98 (m, 4H), 5.44-5.39 (m, 1H), 4.91 (d, J = 7.7 Hz, 1H), 4.85 (d, J = 7.5 Hz, 1H), 2.28 (s, 3H), 1.48 (d, J = 6.7 Hz, 3H), 1.33 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 137.4, 136.5, 133.7, 132.4, 129.3, 128.8, 127.4, 126.9, 123.4, 64.3, 21.1, 13.3, 12.9.

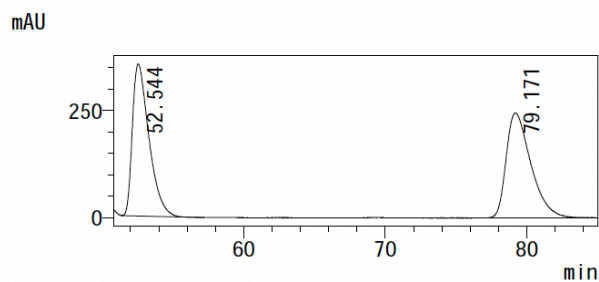
HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 316.1366; found: 316.1365.



(S)-N-Benzenesulfonyl-1-(E)-styrenylbenzylamine (3v) [1616723-52-4]

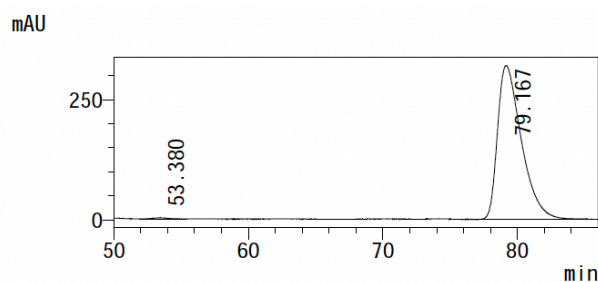
The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:6) as white solid. 31.1 mg, 89% yield. 99% ee. $[\alpha]^{25}_D = +48.0^\circ$ ($c = 0.5$, CHCl_3).

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 254$ nm, $t_R = 52.5$ min (minor), 79.2 min (major).



Peak Table

PDA Ch1 254nm			
Peak#	Ret. Time	Area	Area%
1	52.544	28758094	49.273
2	79.171	29606677	50.727
Total		58364771	100.000



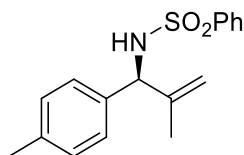
Peak Table

PDA Ch1 254nm			
Peak#	Ret. Time	Area	Area%
1	53.380	162190	0.411
2	79.167	39283904	99.589
Total		39446093	100.000

^1H NMR (400 MHz, CDCl_3): δ 7.78 (d, $J = 7.8$ Hz, 2H), 7.45 (t, $J = 7.5$ Hz, 1H), 7.35 (t, $J = 7.6$ Hz, 2H), 7.28-7.18 (m, 10H), 6.39 (d, $J = 15.8$ Hz, 1H), 6.12 (dd, $J = 15.8, 6.7$ Hz, 1H), 5.34 (d, $J = 7.3$ Hz, 1H), 5.16 (t, $J = 7.0$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3): δ 140.9, 139.7, 136.1, 132.5, 132.3, 128.9, 128.9, 128.6, 128.3, 128.1, 128.0, 127.3, 127.2, 126.7, 59.9.

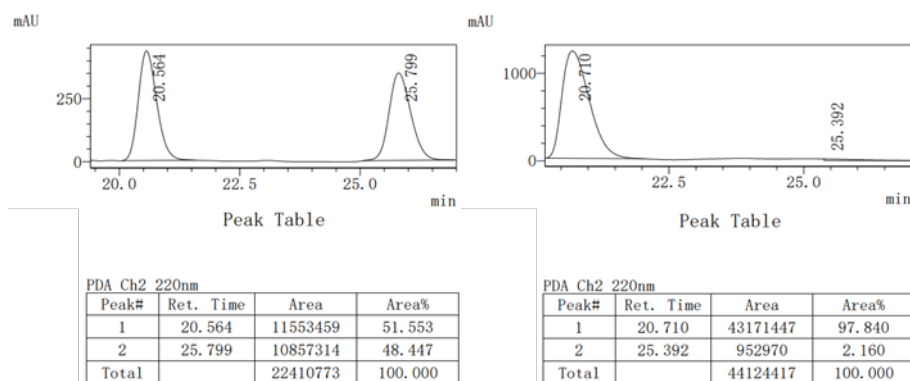
HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 350.1209; found: 350.1208.



(S)-N-Benzenesulfonyl-1-(2-allyl)-4-methylbenzylamine (3w)

The reaction was conducted with a procedure using **L8** in THF and without using $\text{Ti}(\text{O}i\text{-Pr})_4$. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as colorless oil. 24.2 mg, 80% yield. 96% ee. $[\alpha]^{23}_D = -4.2^\circ$ ($c = 0.5$, CHCl_3).

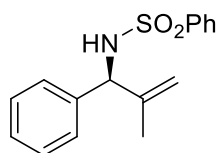
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_R = 20.7$ min (major), 25.4 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.77-7.74 (m, 2H), 7.53-7.49 (m, 1H), 7.43-7.39 (m, 2H), 7.02-6.94 (m, 4H), 4.98 (s, 1H), 4.90 (s, 2H), 4.81 (d, $J = 7.4$ Hz, 1H), 2.28 (s, 3H), 1.54 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 143.6, 140.8, 137.7, 136.0, 132.5, 129.4, 128.9, 127.4, 127.0, 113.4, 62.8, 21.2, 19.7.

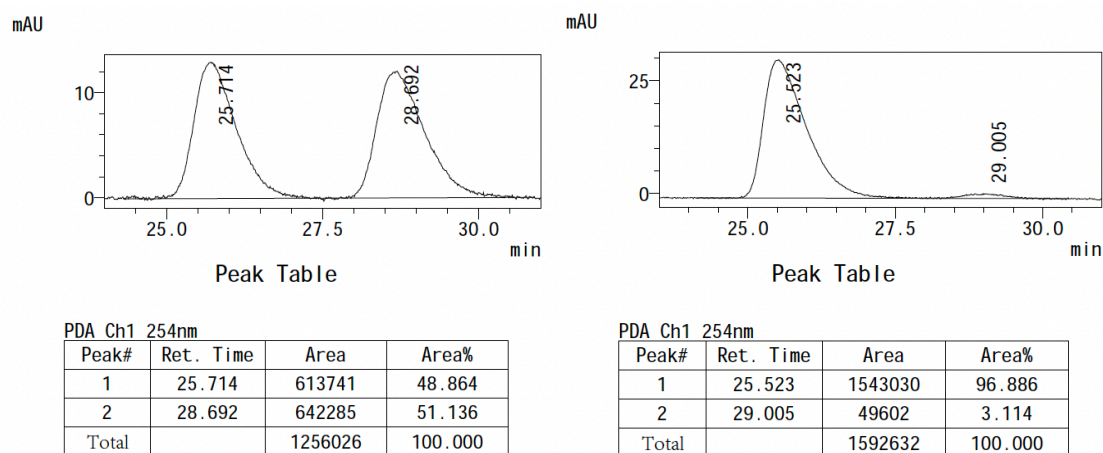
HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 302.1209; found: 302.1210.



(S)-N-Benzenesulfonyl-1-(2-allyl)-benzylamine (3x)

The reaction was conducted with a procedure using **L8** in THF without $\text{Ti}(\text{O}i\text{-Pr})_4$. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 22.7 mg, 79% yield. 94% ee. $[\alpha]_D^{25} = -36.0^\circ$ ($c = 0.5$, CHCl_3).

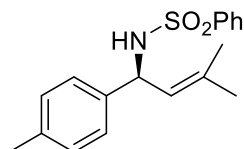
HPLC: Daicel Chiralcel OC-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, $\lambda = 254$ nm, $t_R = 25.7$ min (major), 28.7 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.77-7.74 (m, 2H), 7.50-7.46 (m, 1H), 7.40-7.36 (m, 2H), 7.26-7.16 (m, 3H), 7.09-7.06 (m, 2H), 5.36 (d, J = 7.9 Hz, 1H), 4.95 (s, 1H), 4.89-4.86 (m, 2H), 1.54 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 143.4, 140.7, 138.9, 132.5, 128.7, 128.6, 127.8, 127.3, 127.1, 113.6, 63.0, 19.6.

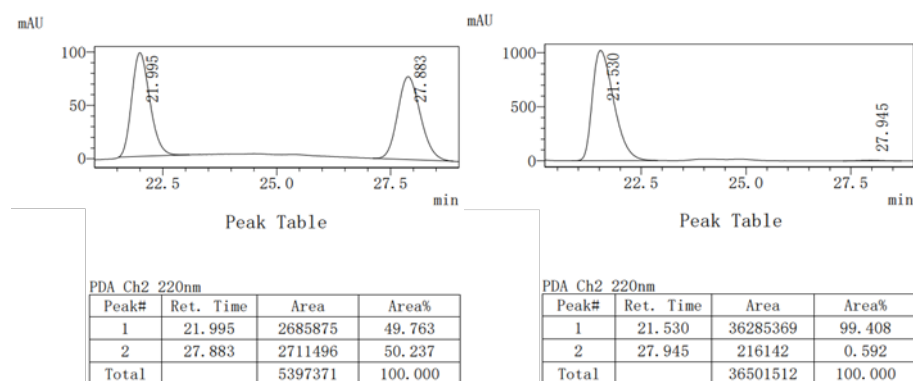
HRMS (ESI): Calcd for $\text{C}_{16}\text{H}_{18}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 288.1053; found: 288.1053.



(S)-N-Benzenesulfonyl-1-(but-2-en-1-yl)-4-methylbenzylamine (3y)

The reaction was conducted with a procedure using **L8** in THF and without using $\text{Ti}(\text{O}i\text{-Pr})_4$. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 26.5 mg, 84% yield. 98% ee. $[\alpha]_D^{28} = +5.9^\circ$ (c = 0.5, CHCl_3).

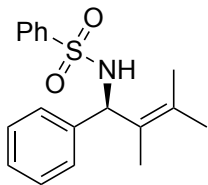
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 220 nm, t_R = 21.5 min (major), 27.9 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.77-7.75 (m, 2H), 7.52-7.48 (m, 1H), 7.42-7.38 (m, 2H), 7.10 (d, J = 7.9 Hz, 2H), 7.03 (d, J = 8.0 Hz, 2H), 5.15-5.04 (m, 3H), 2.28 (s, 3H), 1.54 (s, 6H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.1, 138.0, 137.2, 135.4, 132.3, 129.3, 128.7, 127.3, 126.7, 124.5, 55.7, 25.6, 21.1, 18.1.

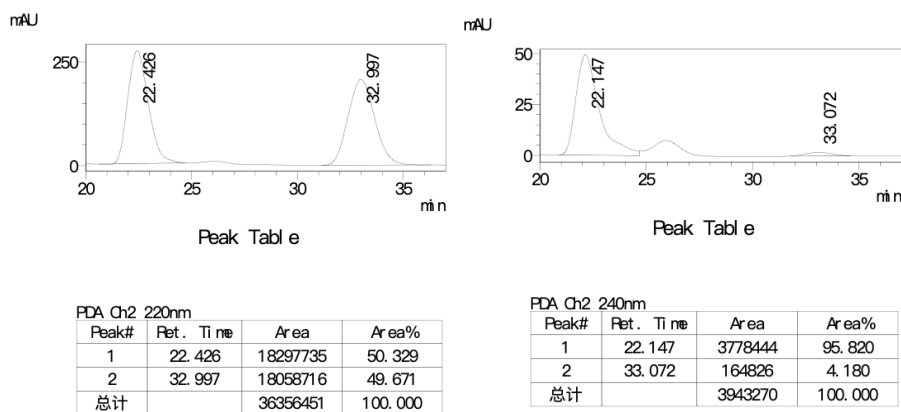
HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 316.1366; found: 316.1360.



(S)-N-Benzenesulfonyl-1-(2,3-dimethylbut-2-en-1-yl)-benzylamine (3z)

The reaction was conducted with a procedure using **L8** in THF without $\text{Ti}(\text{O}i\text{-Pr})_4$ at 50 °C. The product was isolated by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 25.5 mg, 81% yield. 92% ee. $[\alpha]^{20}_{\text{D}} = -2.0^\circ$ ($c = 2.0$, CHCl_3).

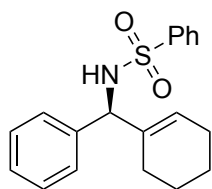
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 22.1$ min (major), 33.1 min (minor).



^1H NMR (400 MHz, CDCl_3): δ 7.90 – 7.80 (m, 2H), 7.60 – 7.51 (m, 1H), 7.49-7.44 (m, 2H), 7.33 – 7.18 (m, 5H), 5.62 (d, $J = 8.3$ Hz, 1H), 5.11 (d, $J = 8.4$ Hz, 1H), 1.66 (d, $J = 1.5$ Hz, 3H), 1.48 (s, 3H), 1.19 (t, $J = 1.3$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3): δ 141.0, 139.7, 132.5, 130.2, 128.7, 128.6, 127.4, 127.3, 126.5, 125.0, 57.9, 20.9, 20.4, 13.2.

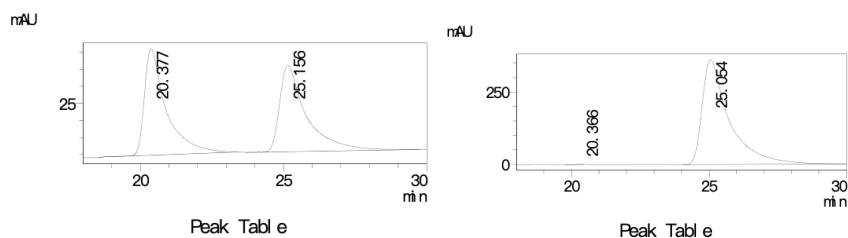
HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2\text{S}^+$ $[\text{M}+\text{H}]^+$: 316.1366; found: 316.1367.



(S)-N-Benzenesulfonyl-1-(1-cyclohexenyl)-benzylamine

The product was isolated from a reaction on 0.1 mmol scale by flash chromatography (ethyl acetate/petroleum ether 1:5) as white solid. 92% yield. >99% ee. $[\alpha]^{28}_{\text{D}} = -6.7^\circ$ ($c = 1.2$, CHCl_3).

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, $\lambda = 220$ nm, $t_{\text{R}} = 20.4$ min (minor), 25.1 min (major).



FDA Ch2 220nm				
Peak#	Ret. Time	Area	Area%	
1	20.377	1654900	50.153	
2	25.156	1644823	49.847	
总计		3299723	100.000	

FDA Ch2 220nm				
Peak#	Ret. Time	Area	Area%	
1	20.366	1295	0.005	
2	25.054	24872430	99.995	
总计		24873725	100.000	

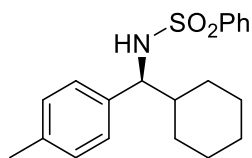
^1H NMR (400 MHz, CDCl_3): δ 7.89 – 7.69 (m, 2H), 7.60 – 7.46 (m, 1H), 7.40 (m, 2H), 7.20 (m, 3H), 7.15 – 7.09 (m, 2H), 5.54 (m, 1H), 5.05 (m, 1H), 4.87 (d, J = 8.0 Hz, 1H), 1.98 – 1.78 (m, 2H), 1.78 – 1.66 (m, 1H), 1.64 – 1.60 (m, 1H), 1.51 – 1.28 (m, 4H).

^{13}C NMR (101 MHz, CDCl_3): δ 140.9, 139.4, 135.6, 132.4, 128.8, 128.5, 127.6, 127.4, 127.0, 126.0, 63.4, 25.1, 25.1, 22.4, 22.1.

HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{22}\text{NO}_2\text{S}^+ [\text{M}+\text{H}]^+$: 328.1366; found: 328.1368.

A procedure for a reaction on 4-mmol scale: In an argon-filled glove box, $\text{NiBr}_2(\text{DME})$ (2.4 mg, 0.008 mmol, 0.2 mol%), bis(oxazoline) **L7** (4.0 mg, 0.012 mmol, 0.3 mol%), pure *N*-sulfonyl imine (0.98 g, 4 mmol) and dry 1,4-dioxane (2 mL) were added to a dry 10-mL Schlenk tube. After stirring for 20 min at rt, Mn powder (660 mg, 12 mmol, Alfa Aesar), dry HFIP (1.34 g, 8 mmol), $\text{Ti}(\text{O}i\text{-Pr})_4$ (2.27 g, 8 mmol), 1-bromocyclohexene (0.966 g, 6 mmol) and GC standard *n*- $\text{C}_{12}\text{H}_{26}$ (400 μL) were added in sequence. The mixture was vigorously stirred at 50 $^\circ\text{C}$ for 48 hours. The reaction mixture was diluted by 10 mL of 4:1 petroleum ether/EtOAc and filtered through a pad of silica gel with washings of 40-60 mL of 4:1 petroleum ether/EtOAc. The filtrate was concentrated and the crude product was purified by flash chromatography on silica gel. 576 mg, 44% yield >99% ee. An incomplete conversion of imine was noted and the conditions was *non-optimized*.

IV. Product derivatization



(*S*)-*N*-Benzenesulfonyl-1-cyclohexyl-1-(4-methylbenzyl)amine (**4a**) [321743-17-3 for racemate]¹

A stock solution of Et_3N (0.1 mL) in EA (10 mL) was prepared and 0.4 mL of this solution was added to a solution of **3a** (0.1 mmol) in 3 mL of MeOH/EtOAc (3/1) at 25 $^\circ\text{C}$. The solution was then carefully deoxygenated by argon bubbling for 30 min. 10% wt Pd/C (45 mg, 0.04 mmol Pd) was then added (the amount

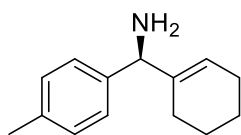
was unoptimized), and H₂ gas from a balloon was bubbled through the solution for 10 min. The suspension was stirred under 1 atm of H₂ atmosphere from a hydrogen balloon at 50 °C for 5 h.² The reaction was completed as monitored by GCMS. The crude mixture was directly filtered through a plug of silica gel (petroleum ether/ethyl acetate 20/1) to give the clean product as white solid (31.5 mg, 92% yield, >99% ee). [α]_D²⁵ = -12.1° (c = 0.5, CHCl₃).

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 254 nm, t_R = 29.3 min (major).

¹H NMR (400 MHz, CDCl₃): δ 7.55 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.23-7.19 (m, 2H), 6.85 (d, J = 7.8 Hz, 2H), 6.75 (d, J = 7.8 Hz, 2H), 5.00 (d, J = 8.4 Hz, 1H), 3.98 (t, J = 8.1 Hz, 1H), 2.19 (s, 3H), 1.91 (d, J = 13.0 Hz, 1H), 1.71-1.67 (m, 1H), 1.59-1.46 (m, 3H), 1.30-1.22 (m, 2H), 1.17-1.01 (m, 3H), 0.94-0.75 (m, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 140.9, 137.0, 136.8, 132.0, 128.9, 128.6, 127.1, 127.0, 63.4, 43.9, 29.9, 29.6, 26.3, 26.1, 21.1.

HRMS (ESI): Calcd for C₂₀H₂₆ONO₂S⁺ [M+H]⁺: 344.1679; found: 344.1680.



(S)-N-1-(Cyclohexen-1-yl)-1-(4-methylbenzyl)amine (4b) [1249910-11-9 for racemate]

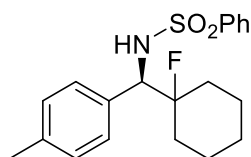
Under argon, to a solution of SmI₂ (0.1 M in 5 mL, 0.5 mmol) in THF was added *N*-Bs-benzylamine (0.05 mmol), H₂O (1.56 mmol) and Et₃N (1 mmol) at room temperature. The reaction mixture immediately turned white upon addition of the amine.³ The reaction mixture was diluted with diethyl ether (4 mL) and treated with an aqueous solution of potassium carbonate (10% w/v). The aqueous phase was extracted with two portions of diethyl ether. The organic extracts were dried and purified through a short column of silica gel (petroleum ether/ethyl acetate 20/1) to give pure product as colorless oil (16.3 mg, 80% yield, >99% ee). [α]_D²⁴ = -2.7° (c = 0.5, CHCl₃).

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 254 nm, t_R = 22.9 min (major).

¹H NMR (400 MHz, CDCl₃): δ 7.21 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 5.81-5.79 (m, 1H), 4.35 (s, 1H), 2.33 (s, 3H), 2.15-2.13 (m, 2H), 2.09-2.05 (br s, NH₂), 1.89-1.71 (m, 2H), 1.58-1.52 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): δ 141.1, 140.5, 136.6, 129.2, 127.0, 121.9, 61.3, 25.5, 25.3, 22.9, 22.7, 21.2.

HRMS (ESI): Calcd for C₁₄H₂₀N⁺ [M+H]⁺: 202.1590; found: 202.1588.



(*R*)-*N*-Benzenesulfonyl-1-(1-fluorocyclohexyl)-1-(4-methylbenzyl)amine (4c)

Under argon, ferric nitrate nonahydrate (80.8 mg, 0.20 mmol) was stirred in degassed H₂O (2 mL). The clear yellow solution was then treated with Selectfluor (35.5 mg, 0.10 mmol) and degassed MeCN (1 mL). A solution of **7a** (17.1 mg, 0.05 mmol) in degassed MeCN (1 mL) at rt was added followed by NaBH₄ (6 mg, 0.16 mmol). After 5 min, to the reaction mixture was added with a second portion of NaBH₄ (6 mg).⁴ The resulting mixture was stirred at rt for 30 min before quenched by 28–30% aqueous NH₄OH (1 mL). The mixture was extracted with CH₂Cl₂ and the organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was directly subjected to flash chromatography (petroleum ether/ethyl acetate 20:1) to give the product as white solid (25.9 mg, 72% yield, >99% ee). [α]_D²⁶ = -3.3° (c = 0.5, CHCl₃).

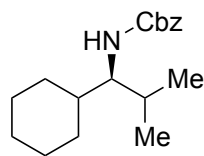
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min, λ = 254 nm, t_R = 14.8 min (major).

¹H NMR (400 MHz, CDCl₃): δ 7.52-7.49 (m, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.19 (t, J = 7.8 Hz, 2H), 6.89-6.83 (m, 4H), 5.25 (d, J = 9.2 Hz, 1H), 4.25 (dd, J = 24.7, 9.2 Hz, 1H), 2.23 (s, 4H), 1.63-1.54 (m, 4H), 1.46-1.39 (m, 2H), 1.36-1.12 (m, 4H).

¹⁹F NMR (376.6 MHz, CDCl₃): δ -170.75.

¹³C NMR (100 MHz, CDCl₃): δ 140.8, 137.5, 133.7, 132.0, 128.9, 128.6, 128.23 (d, J_{C-F} = 2 Hz), 127.1, 97.7 (d, J_{C-F} = 179 Hz), 63.88 (d, J_{C-F} = 18 Hz), 33.3 (d, J_{C-F} = 21 Hz), 33.0 (d, J_{C-F} = 21 Hz), 25.13, 21.93 (d, J_{C-F} = 3 Hz), 21.74 (d, J_{C-F} = 3 Hz), 21.12.

HRMS (ESI): Calcd for C₂₀H₂₅FNO₂S⁺ [M+H]⁺: 362.1585; found: 362.1590.



(*S*)-*N*-CBz-1-(1-isopropyl)-1-(cyclohexyl)methylamine (4d) [2567867-83-6]⁵

i) Under argon, to a solution of SmI₂ (0.1 M in 15 mL, 1.5 mmol) in dry THF was added *N*-benzenesulfonyl benzylamine (43 mg, 0.15 mmol), H₂O (4.5 mmol, 81 mg) and Et₃N (3 mmol, 303 mg) at room temperature. The reaction mixture immediately turned white upon addition of the amine.³ The reaction mixture was stirred for 30 min, then diluted with diethyl ether (20 mL) and treated with an aqueous solution of potassium carbonate

(10% w/v). The aqueous phase was extracted with two portions of diethyl ether. The organic extracts were dried with MgSO_4 to give the unprotected benzylamine.

ii) Under argon, the crude product above was dissolved in 1.8 mL of 25% H_2SO_4 at room temperature and PtO_2 (23 mg, 0.1 mmol) was added. The reaction mixture was hydrogenated under 1 atm of hydrogen pressure (balloon with refilling of H_2) for 24 h.⁶ The reaction mixture was filtered through a short plug of Celite and washed with water. The filtrate was alkalized by 2 M NaOH and extracted with DCM. The organic extracts were dried with MgSO_4 to give the alkylamine.

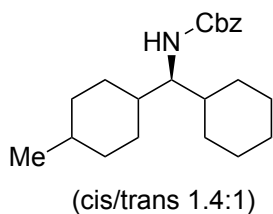
iii) Under argon, the crude alkylamine was dissolved in 1 mL of THF and then DIPEA (58 mg, 0.45 mmol) and CbzCl (51 mg, 0.3 mmol) were added at 0 °C. The reaction mixture was stirred at 70 °C for 24 h.⁷ The reaction was quenched by saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude residue was purified by silica gel column chromatography using hexane/EtOAc (5/1) to give the *N*-Cbz amine (32.6 mg, 75% yield over 3 steps, 94% ee). $[\alpha]^{25}_{\text{D}} = -4.0^\circ$ ($c = 0.5$, CHCl_3).

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min, $\lambda = 214$ nm, $t_{\text{R}} = 11.2$ min (major), 14.9 min (minor).

^1H NMR (400 MHz, CDCl_3): δ 7.39 (d, $J = 7.5$ Hz, 2H), 7.34-7.30 (m, 2H), 7.27-7.24 (m, 1H), 3.88-3.80 (m, 2H), 2.09-2.06 (m, 1H), 1.88-1.83 (m, 2H), 1.77-1.72 (m, 2H), 1.68-1.61 (m, 2H), 1.45-1.42 (m, 1H), 1.23-1.02 (m, 5H), 0.94 (d, $J = 6.7$ Hz, 3H), 0.92 (d, $J = 6.7$ Hz, 3H).

^{13}C NMR (100 MHz, CDCl_3): δ 141.3, 128.6, 128.5, 127.1, 68.3, 55.9, 41.4, 31.3, 30.2, 29.2, 26.9, 26.9, 26.8, 21.0, 18.1.

HRMS (ESI): Calcd for $\text{C}_{18}\text{H}_{28}\text{NO}_2^+$ $[\text{M}+\text{H}]^+$: 290.2115; found: 290.2118.



(S)-N-CBz-1-(1-cyclohexyl)-1-(4-methylcyclohexyl)methylamine (4e) (cis- and trans-isomers)

i) Under argon, to a solution of SmI_2 (0.1 M in 15 mL, 1.5 mmol) in dry THF was added *N*-benzenesulfonyl alkylamine (51 mg, 0.15 mmol), H_2O (4.5 mmol, 81 mg) and Et_3N (3 mmol, 303 mg) at room temperature. The reaction mixture immediately turned white upon addition of the amine.³ The reaction mixture was stirred for 30 min and then diluted with diethyl ether (20 mL) and treated with an aqueous potassium carbonate (10% w/v). The aqueous phase was extracted with two portions of diethyl ether. The organic extracts were dried with MgSO_4 to give the unprotected benzylamine.

ii) Under argon, the crude benzylamine was dissolved in 1.8 mL of 25% H₂SO₄ at room temperature and PtO₂ (23 mg, 0.1 mmol) was added. The reaction mixture was hydrogenated under 1 atm of hydrogen pressure (balloon with refilling of H₂) for 24 h.⁶ The reaction mixture was filtered through a short plug of Celite and washed with water. The filtrate was alkalized by 2 M NaOH and extracted with DCM. The organic extracts were dried with Na₂SO₄ to give the alkylamine.

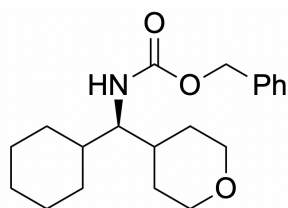
iii) Under argon, the crude alkylamine was dissolved in 1 mL of THF and then DIPEA (58 mg, 0.45 mmol) and CbzCl (51 mg, 0.3 mmol) was added at 0 °C. The reaction mixture was stirred at 70 °C for 24 h.⁷ The reaction was quenched by saturated aqueous NH₄Cl and extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and concentrated under vacuum. The crude residue was purified by silica gel column chromatography using hexane/EtOAc (5/1) to give the desired *N*-Cbz-amine (37.6 mg, 73% yield over 3 steps, >99% ee). [α]_D²⁵ = -14.0° (*c* = 0.5, CHCl₃).

HPLC: Daicel Chiralcel OC-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, λ = 254 nm, *t*_R = 6.4 min (major), 7.5 min (minor).

¹H NMR of 2 isomers (400 MHz, CDCl₃): δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.26-7.22 (m, 1H), 3.84-3.82 (m, 2H), 2.23 (s, 0.6H), 2.08 (s, 0.4H), 1.83-1.49 (m, 11H), 1.43-1.0 (m, 10H), 0.95 (d, *J* = 7.0 Hz, 1.8H), 0.87 (d, *J* = 7.0 Hz, 1.2H).

¹³C NMR of 2 isomers (100 MHz, CDCl₃): δ 141.4, 128.5, 128.4, 127.1, 67.7, 65.7, 56.1, 41.0, 40.7, 40.5, 39.9, 35.7, 35.5, 33.0, 31.8, 31.7, 31.6, 31.3, 31.2, 29.9, 29.0, 28.9, 28.6, 27.9, 27.1, 27.0, 26.91, 26.9, 26.8, 26.8, 26.1, 24.2, 22.8, 19.2.

HRMS (ESI): Calcd for C₂₂H₃₄NO₂⁺ [*M*+H]⁺: 344.2584; found: 344.2586.



(*R*)-*N*-CBz-1-(tetrahydropyran-4-yl)-1-(cyclohexyl)methylamine (4f)

i) Under argon, to a solution of SmI₂ (0.1 M in 15 mL, 1.5 mmol) in THF was added *N*-Bz-amine (49 mg, 0.15 mmol), H₂O (81 mg, 4.5 mmol) and Et₃N (305 mg, 3 mmol) at room temperature. The reaction mixture immediately turned white upon addition of the amine.³ The reaction mixture was stirred for 30 min and then diluted with diethyl ether (20 mL) and treated with aqueous potassium carbonate (10% w/v). The aqueous phase was extracted with two portions of diethyl ether. The organic extracts were dried with MgSO₄ to give the unprotected benzylamine.

ii) Under argon, the crude unprotected benzylamine was dissolved in 1.8 mL of 25% H₂SO₄ at room temperature and PtO₂ (23 mg, 0.1 mmol) was added. The reaction mixture was hydrogenated under 1 atm of hydrogen pressure (balloon with refilling of H₂) for 24 h.⁶ The reaction mixture was filtered through a short plug of Celite and washed with water. The filtrate was alkalized by 2 M NaOH and extracted with DCM. The organic extracts were dried with Na₂SO₄ to give alkylamine.

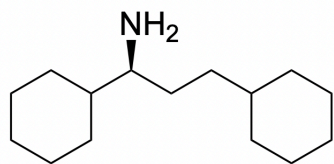
iii) Under argon, the crude alkylamine was dissolved in 1 mL of THF and then DIPEA (58 mg, 0.45 mmol) and CbzCl (51 mg, 0.3 mmol) were added at 0 °C. The reaction mixture was stirred at 70 °C for 24 h.⁷ The reaction was quenched by saturated aqueous NH₄Cl solution and extracted with ethyl acetate. The combined organic layers were dried over MgSO₄ and concentrated under vacuum. The crude residue was purified by silica gel column chromatography using hexane/EtOAc (5/1) to give the desired *N*-Cbz-amine (38.8 mg, 78% yield over 3 steps, 99% ee). [α]_D²⁵ = +2.0° (*c* = 0.5, CHCl₃).

HPLC: Daicel Chiralcel OC-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, λ = 254 nm, *t*_R = 7.5 min (major), 7.8 min (minor).

¹H NMR (400 MHz, CDCl₃): δ 7.37-7.35 (m, 2H), 7.33-7.30 (m, 2H), 7.26-7.22 (m, 1H), 4.02-3.96 (m, 2H), 3.80 (ψq, *J* = 12.5 Hz, 2H), 3.37 (td, *J* = 11.6, 2.3 Hz, 2H), 2.09 (t, *J* = 5.6 Hz, 1H), 1.79-1.40 (m, 10H), 1.30-1.05 (m, 6H).

¹³C NMR (100 MHz, CDCl₃): δ 141.3, 128.5, 128.4, 127.1, 68.6, 68.4, 67.3, 56.2, 40.6, 38.6, 31.4, 31.1, 29.5, 28.2, 26.9, 26.8, 26.7.

HRMS (ESI): Calcd for C₂₀H₃₀NO₃⁺ [*M*+H]⁺: 332.2220; found: 332.2223.



(*S*)-1,3-Dicyclohexylpropan-1-amine (4g) [5080-18-2 for (*S*)-HCl salt]⁸

i) Under argon, to a solution of SmI₂ (0.1 M in 15 mL, 1.5 mmol) in dry THF was added *N*-Bs-benzylamine (52 mg, 0.15 mmol), H₂O (4.5 mmol, 81 mg) and Et₃N (3 mmol, 303 mg) at room temperature. The reaction mixture immediately turned white upon addition of the amine.³ The reaction mixture was stirred for 30 min and then diluted with diethyl ether (20 mL) and treated with aqueous potassium carbonate (10% w/v). The aqueous phase was extracted with two portions of diethyl ether. The organic extracts were dried with MgSO₄ and purified by silica gel column chromatography using hexane/EtOAc (1/1) to give the unprotected benzylamine.

ii) Under argon, the crude benzylamine above was dissolved in 1.8 mL of 25% H₂SO₄ at room temperature and PtO₂ (23.0 mg, 0.1 mmol) was added. The reaction mixture was hydrogenated under 1 atm of hydrogen pressure

(balloon with refilling of H₂) for 24 h.⁶ The reaction mixture was filtered through a short plug of Celite and washed with water. The filtrate was alkalized by 2 M NaOH and extracted with DCM. The organic extracts were dried with Na₂SO₄ to give the alkylamine as white solid (23.8 mg, 71% yield over 2 steps). [α]_D²⁵ = -14.0° (*c* = 0.5, CHCl₃).

¹H NMR (400 MHz, CDCl₃): δ 2.46-2.42 (m, 1H), 1.77-1.60 (m, 11H), 1.49-1.41 (m, 1H), 1.31-1.07 (m, 12H), 1.05-0.95 (m, 2H), 0.93-0.82 (m, 2H).

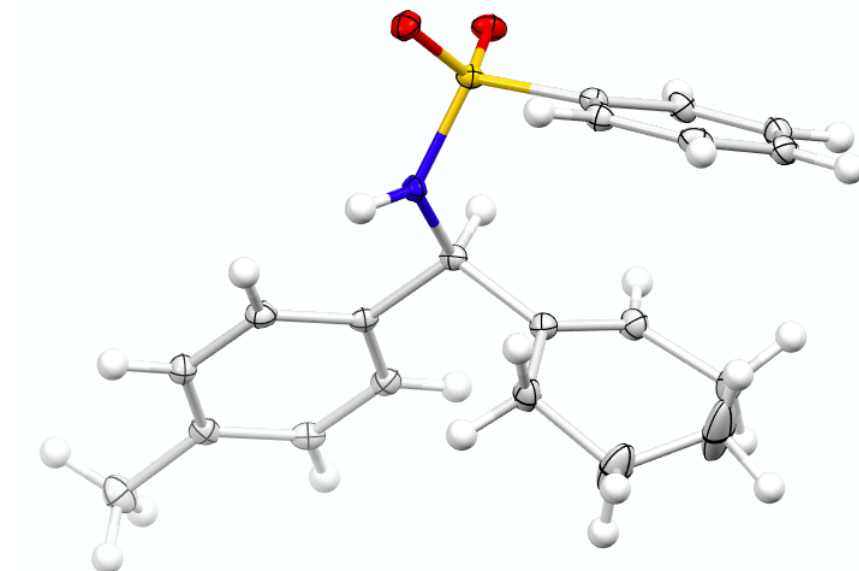
¹³C NMR (100 MHz, CDCl₃): δ 56.5, 43.8, 38.1, 34.4, 33.8, 33.4, 32.0, 29.9, 28.0, 26.9, 26.8, 26.8, 26.6, 26.6, 26.5.

HRMS (ESI): Calcd for C₁₅H₃₀N⁺ [M+H]⁺: 224.2373; found: 224.2372.

V. X-ray measurement and a thermal ellipsoid plot of a crystal structure

Intensity data were collected at 198(2) K using an Rigaku XtaLAB Synergy-R,DW system, Hypix diffractometer microfocus Cu source. The structure was solved by the ShelXT 2018/2 (Sheldrick, 2018) structure solution program using Intrinsic Phasing and refined by Least Squares using version 2018/3 of ShelXL-2018/3 (Sheldrick, 2018). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Hydrogen atom positions were calculated geometrically and refined using the riding model.

Figure S2. Thermal ellipsoid plot for crystal structure of compound **3a** (ellipsoid contour at 40% probability)



VI. Reference

- (1) Patel, N. R.; Kelly, C. B.; Siegenfeld, A. P.; Molander, G. A. Mild, Redox-Neutral Alkylation of Imines Enabled by an Organic Photocatalyst. *ACS Catal.* **2017**, *7* (3), 1766-1770. DOI: 10.1021/acscatal.6b03665.
- (2) Snyder, S. A.; Brill, Z. G. Structural Revision and Total Synthesis of Caraphenol B and C. *Org. Lett.* **2011**, *13* (20), 5524-5527. DOI: 10.1021/ol2022406.
- (3) Ankner, T.; Hilmersson, G. Instantaneous Deprotection of Tosylamides and Esters with SmI₂/Amine/Water. *Org. Lett.* **2009**, *11* (3), 503-506. DOI: 10.1021/ol802243d.
- (4) Zhao, M.; Zhang, L.; Zhou, J. S. Enantioselective Reductive Conjugate Alkenylation of α,β -Unsaturated Ketones and Amides via Nickel Catalysis. *ACS Catal.* **2024**, *14* (8), 6228-6235. DOI: 10.1021/acscatal.4c01263.
- Leggans, E. K.; Barker, T. J.; Duncan, K. K.; Boger, D. L. Iron(III)/NaBH₄-Mediated Additions to Unactivated Alkenes: Synthesis of Novel 20'-Vinblastine Analogues. *Org. Lett.* **2012**, *14* (6), 1428-1431. DOI: 10.1021/ol300173v.
- (5) Qian, D.; Bera, S.; Hu, X. Chiral Alkyl Amine Synthesis via Catalytic Enantioselective Hydroalkylation of Enecarbamates. *J. Am. Chem. Soc.* **2021**, *143* (4), 1959-1967. DOI: 10.1021/jacs.0c11630.
- (6) Hilgraf, R.; Pfaltz, A. Chiral Bis(N-sulfonylamino)phosphine- and TADDOL-Phosphite-Oxazoline Ligands: Synthesis and Application in Asymmetric Catalysis. *Adv. Synth. Catal.* **2005**, *347* (1), 61-77. DOI: <https://doi.org/10.1002/adsc.200404168> (accessed 2025/08/21).
- (7) Chen, F.; He, D.; Chen, L.; Chang, X.; Wang, D. Z.; Xu, C.; Xing, X. Chirality-Economy Catalysis: Asymmetric Transfer Hydrogenation of Ketones by Ru-Catalysts of Minimal Stereogenicity. *ACS Catal.* **2019**, *9* (6), 5562-5566. DOI: 10.1021/acscatal.9b01535.
- (8) Ghislandi, V. Preparation of optically active 1,3-diphenyl-1-aminopropane and 1,3-dicyclohexyl-1-aminopropane. *Farmaco, Edizione Scientifica* **1965**, *20* (12), 860-865.