Catalytic Enantioselective Alkenylation-Heteroarylation of Olefins: Stereoselective Syntheses of 5-7 Membered Azacycles and Oxacycles

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Supporting Information

Experimental procedures and characterization

I. General

All NMR spectra were acquired on Bruker AV 500 MHz or 400 MHz NMR spectrometers. ^{1}H NMR chemical shifts were recorded relative to $SiMe_4$ (δ 0.00) or residual protiated solvents ($CDCl_3$: δ 7.26). 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).

Glassware was dried at 120 ^{o}C for at least 3 h before use. DCM were stored over activated 4 Å molecular sieve beads in an argon-filled glove box. Unless noted otherwise, commercially available chemicals were used as received without purification. The GC internal standard, *n*-$C_{16}H_{34}$ was degassed with argon and dried over activated 4 Å molecular sieve beads before use.

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*-$C_{16}H_{34}$ was degassed with argon and dried over activated 4Å 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.

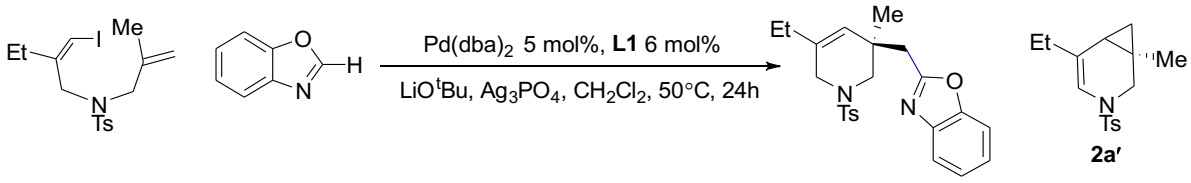
Gas chromatography (GC) analysis was performed on a Shimadzu GC-2030 instrument with Shimadzu GC column DB-5MS-UI. Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiralcel columns at 35 °C and a mixture of HPLC-grade hexanes and isopropanol as eluent. Optical rotation 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 an Agilent GC-MS 6890N-5975 instrument with Agilent J & W GC column DB-5MS-UI. LC/MS analysis was conducted on a Shimadzu LCMS-2020 instrument.

The substrates were prepared using reported procedures[1-4] with modification of the step of CuI-catalyzed Grignard addition to propynol. 3 equiv of Grignard reagents RMgX (R = benzyl, phenyl, isopropyl and isopropenyl) in THF were added to the rest in a THF solution at 0 ^{o}C and then stirred for rt for 24 h before addition of an excess of iodine (1.5 equiv) solution in dry THF at -78 ^{o}C. The crude mixture was warmed to RT and then quenched with Sat.NH_4Cl, and extracted three times with ethyl acetate, dried over anhydrous Na_2SO_4, purified by column chromatography.

II. Optimization of reaction conditions

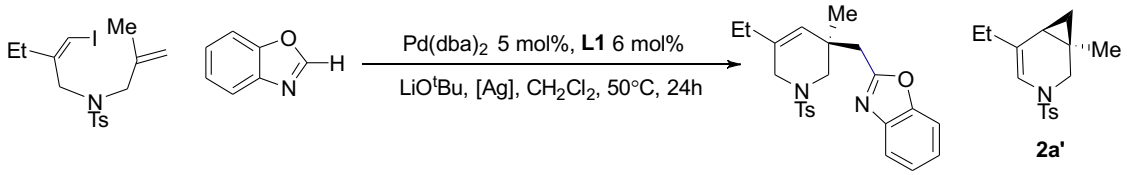
A general procedure: in an argon-filled glove box, $Pd(dba)_2$ (1.4 mg, 0.0025 mmol, 5 mol%), Josiphos **L1** (2.6 mg, 0.003 mmol, 6 mol%) and dry CH_2Cl_2 (0.3 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 15 min at RT, LiO*t*-Bu (8.0 mg, 0.10 mmol, 2 equiv), Ag_3PO_4 (21 mg, 0.05 mmol, 1 equiv), iododiene (0.05 mmol, 1 equiv) and heteroarene (0.10 mmol, 2 equiv) were added. The mixture was capped and vigorously stirred in an oil bath maintained at 50 ^oC for 24 hours. After the mixture was cooled down to RT, GC standard *n*-$C_{16}H_{34}$ (10 μL) was added to determine the conversion and calibrated GC yields of the product and side products. Chiral HPLC analysis was performed on the crude mixture or samples purified by prep-TLC to determine its enantioselectivity.

Table S1. The effect of solvents in place of CH_2Cl_2



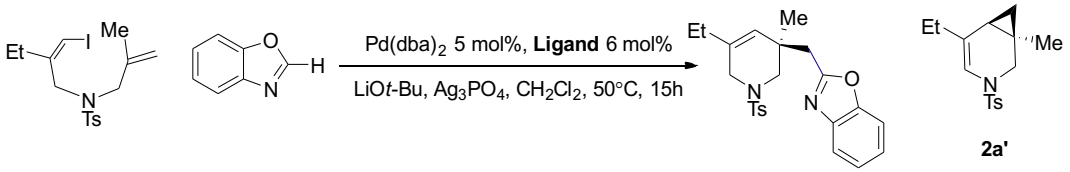
Entry	Solvent	Conv (%)	**3a** (%)	Ee (%)	2a' (%)
1	$PhCF_3$	100	74	87	9
2	MeCN	24	13	80	6
3	*i*-PrOH	29	20	69	0
4	THF	10	3	--	0
5	1,4-Dioxane	16	4	--	0
6	DCE	**100**	**67**	**92**	**22**
7	DCM	**100**	**88**	**92**	**9**

Table S2. The effect of Ag_2CO_3 and other silver salts



Entry	Silver salt	Conv (%)	**3a** (%)	Ee (%)	2a' (%)
1	None	100	48	81	<5
2	Ag_3PO_4	**100**	**88**	**92**	**9**
3	Ag_2CO_3	**100**	**75**	**92**	**12**
4	AgOAc	100	59	94	12
5	$Ag(OCOCF_3)$	**100**	**87**	**89**	**7**
6	AgOTf	**100**	**84**	**89**	**8**

Table S3. The effect of Josiphos ligands and other phosphines



2a'

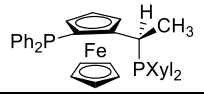
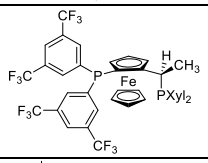
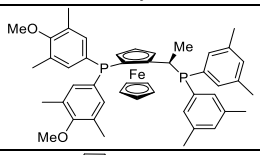
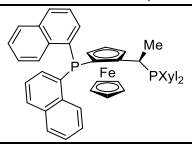
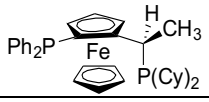
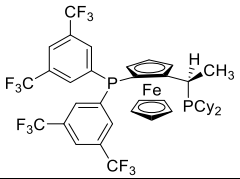
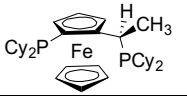
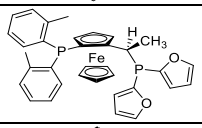
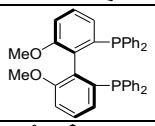
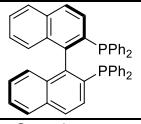
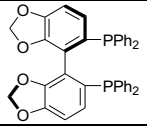
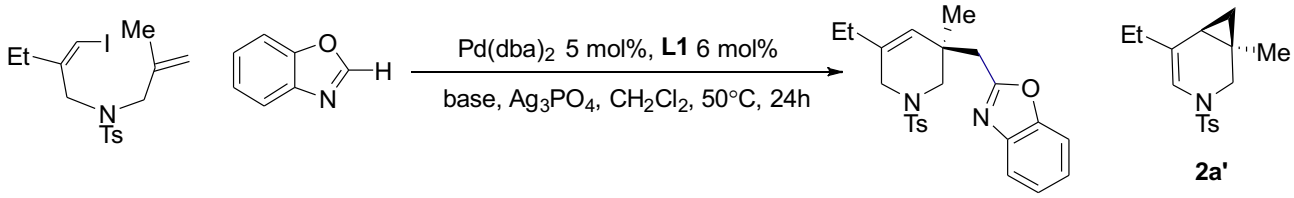
Entry	Josiphos	Conv (%)	Yield (%)	Ee (%)	Bp (%)
1		100	89	40	7
2		100	78	44	12
3		100	84	58	13
4		100	85	70	12
5		89	77	84	10
6		**100**	**88**	**92**	**9**
7		31	16	45	12
8		100	82	45	11
9		100	94	81	3
10		100	89	58	5
11		100	83	80	9

Table S4. The effect of alkoxides in combination with Ag_3PO_4

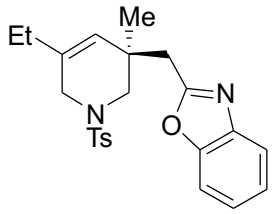


Entry	Base	Conv (%)	**3a** (%)	Ee (%)	Bp (%)
1	K_2CO_3	30	6	69	8
2	Cs_2CO_3	40	18	88	0
3	K_3PO_4	69	12	87	0
4	LiOMe	100	63	58	12
5	LiO*t*-Bu	**100**	**88**	**92**	**9**
6	NaOMe	**100**	**89**	**90**	**0**
7	NaOEt	100	61	86	3
8	NaO*t*-Bu	33	12	86	6
9	KOMe	**100**	**73**	**92**	**0**
10	KO*t*-Bu	92	26	85	5
11	none	16	0	--	0

III. Asymmetric synthesis of piperidine derivatives and other heterocycles

(a) A general procedure for synthesis of substituted 4,5-didehydropiperidines: in an argon-filled glove box, $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 5 mol%), Josiphos **L1** (5.2 mg, 0.006 mmol, 6 mol%) and dry CH_2Cl_2 (0.5 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 20 min at RT, LiO*t*-Bu (16.0 mg, 0.2 mmol), Ag_3PO_4 (42 mg, 0.1 mmol), dienyl iodide (0.1 mmol) and heteroarene (0.2 mmol, 2 equiv) were added. The resulting mixture was capped and vigorously stirred in an oil bath maintained at 50 ^oC for 24 hours until almost full conversion (unless stated otherwise). After the mixture was cooled down to RT, the reaction mixture was passed through a pad of silica gel with washings of 1:1 hexanes/ethyl acetate. After the filtrate was concentrated in

vacuo, the crude product was subjected to flash chromatography using ethyl acetate/hexanes (1:5) as eluent. The enantioselectivity of the purified product was determined by chiral HPLC analysis using Daicel Chiralcel and Chiralpak columns. Similar results were obtained using Schlenk tubes and a vacuum manifold.



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(benzoxazol-2-ylmethyl)-4,5-didehydropiperidine 2a

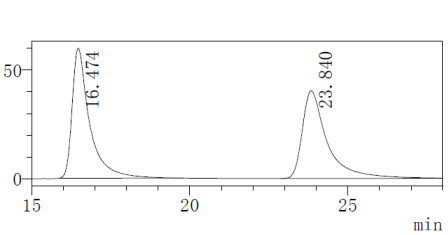
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 37.1 mg, 88% yield. 92% ee. $[\alpha]^{26}_{D}$ = -53.8^{o} (*c* = 2.71, $CHCl_3$).

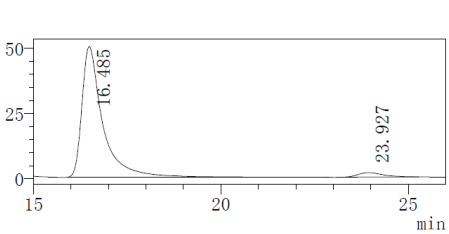
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.63 (m, 3H), 7.54-7.45 (m, 1H), 7.36-7.24 (m, 4H), 5.30 (t, *J* = 1.7 Hz, 1H), 3.56 -3.47 (m, 1H), 3.36-3.25 (m, 2H), 3.09 (d, *J* = 14.2 Hz, 1H), 2.96 (d, *J* = 14.2 Hz, 1H), 2.77 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.94 (q, *J* = 7.5 Hz, 2H), 1.15 (s, 3H), 0.96 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4, 150.9, 143.7, 141.4, 135.1, 133.4, 129.8, 127.8, 126.4, 124.7, 124.2, 119.8, 110.5, 53.5, 47.4, 38.7, 36.7, 27.2, 24.6, 21.6, 12.2.

ESI-MS: Calcd for $C_{23}H_{26}N_2O_3S$ $[M+Na]^+$: 433.2; Found: 432.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min



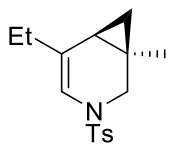


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.474	2302408	50.854
2	23.840	2225079	49.146
Total		4527486	100.000

PDA Ch1 254nm

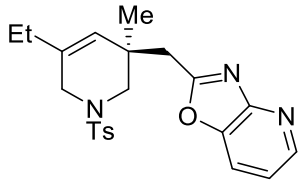
Peak#	Ret. Time	Area	Area%
1	16.485	1929630	95.974
2	23.927	80944	4.026
Total		2010574	100.000



(1*R*,6*S*)-*N*-Tosyl-5-ethyl-1-methyl-3-azabicyclo[4.1.0]hept-4-ene 2a' (2306465-46-1)

Get 41% GC yields. HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 98/2, flow rate = 1.0 mL/min. l = 254 nm, t_R = 8.9 min (major), 10.3 min (minor). enantioselectivity was performed on the samples purified by prep-TLC get 87% in model reaction condition.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 6.07 (t, *J* = 1.2 Hz, 1H), 3.81 (d, *J* = 11.5 Hz, 1H), 2.67 (dd, *J* = 11.5, 1.2 Hz, 1H), 2.42 (s, 3H), 2.09 (q, *J* = 7.4 Hz, 2H), 1.11 (s, 3H), 1.03 (t, *J* = 7.4 Hz, 4H), 0.83 (dd, *J* = 8.3, 4.4 Hz, 1H), 0.59 (dd, *J* = 8.2, 4.4 Hz, 1H), 0.48 (t, *J* = 4.4 Hz, 1H).



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(4-azabenzoxazol-2-ylmethyl)-4,5-didehydropiperidine 2b

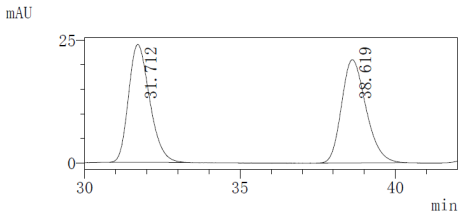
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 30.7mg, 75% yield. 80% *ee*. $[\alpha]^{26}_D$ = +11.1° (*c* = 2.8, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.80 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.72-7.65 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.30-7.23 (m, 1H), 5.34 (t, *J* = 1.8 Hz, 1H), 3.56 (dd, *J* = 15.3, 1.9 Hz, 1H), 3.40 (d, *J* = 11.4 Hz, 1H), 3.29-3.21 (m, 1H), 3.16 (d, *J* = 14.6 Hz, 1H), 3.04 (d, *J* = 14.6 Hz, 1H), 2.68 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.93 (q, *J* = 7.5 Hz, 2H), 1.19 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.8, 155.9, 146.3, 143.8, 143.0, 135.4, 133.2, 129.9, 127.8, 126.1, 119.9, 118.2, 53.5, 47.4, 38.9, 36.8, 27.2, 24.6, 21.7, 12.2.

ESI-MS: Calcd for $C_{22}H_{35}N_3O_3S$ $[M+H]^+$: 412.2. Found: 411.9.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 70/30 flow rate = 0.5 mL/min.



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
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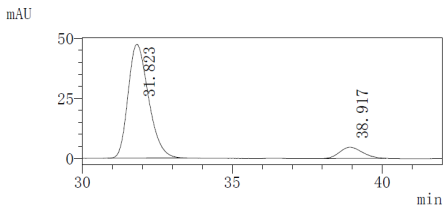
2	38.619	1153585	50.308
Total		2293032	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
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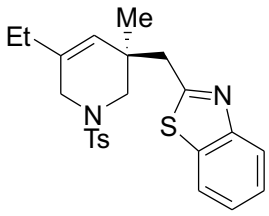
2	38.917	245309	9.839
Total		2493184	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(benzothiazol-2-ylmethyl)-4,5-didehydropiperidine 2c

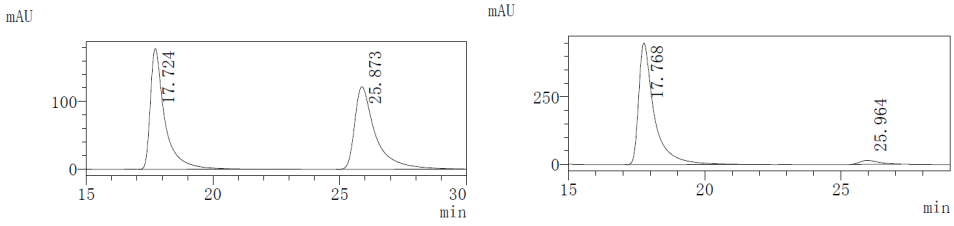
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 39.2 mg, 92% yield. 92% ee**.** $[\alpha]^{24}_{D}$ = -83.2° (*c* = 1.7, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 8.1Hz, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.72-7.66 (m, 2H), 7.45 (dd, *J* = 8.3, 7.2, 1H), 7.40-7.34 (m, 1H), 7.34-7.29 (m, 2H), 5.30 (t, *J* = 1.7 Hz, 1H), 3.61-3.52 (m, 1H), 3.35-3.24 (m, 3H), 3.16 (d, *J* = 13.9 Hz, 1H), 2.69 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.95 (q, *J* = 7.5 Hz, 2H), 1.14 (s, 3H), 1.00 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.6, 153.3, 143.7, 135.8, 135.2, 133.3, 129.9, 127.8, 126.7, 126.0, 124.9, 122.8, 121.5, 53.6, 47.5, 44.2, 36.9, 27.3, 24.6, 21.6, 12.1.

ESI-MS: Calcd for $C_{23}H_{26}N_2O_2S_2$ $[M+H]^+$: 427.1; Found: 427.0.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95.0/5.0, flow rate = 1.0 mL/min.

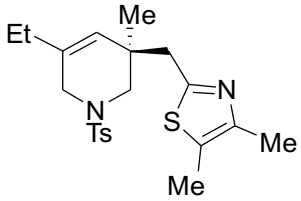


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.724	7027628	50.267
2	25.873	6953049	49.733
Total		13980677	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.768	17825325	96.468
2	25.964	652557	3.532
Total		18477883	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 2d

The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 37.6 mg, 93% yield. 92% ee. $[\alpha]^{24}_{D}$ = -25.8° (*c* = 3.4, $CHCl_3$).

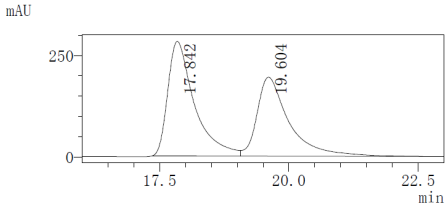
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.34-7.24 (m, 2H), 5.21 (s, 1H), 3.44 (d, *J*

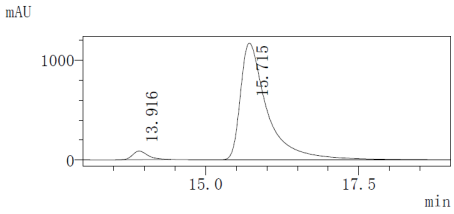
= 15.6 Hz, 1H), 3.29 (d, *J* = 15.6 Hz, 1H), 3.09 (d, *J* = 11.3 Hz, 1H), 3.02 (d, *J* = 14.1 Hz, 1H), 2.89 (d, *J* = 14.1 Hz, 1H), 2.69 (d, *J* = 11.3 Hz, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 2.26 (s, 3H), 1.92 (q, *J* = 7.4 Hz, 2H), 1.04 (s, 3H), 0.97 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 147.5, 143.6, 134.5, 133.2, 129.8, 127.8, 126.9, 126.1, 53.3, 47.4, 43.1, 36.5, 27.2, 24.4, 21.6, 14.7, 12.1, 11.3.

ESI-MS: Calcd for $C_{21}H_{28}N_2O_2S_2$ $[M+H]^+$: 405.2. Found: 405.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



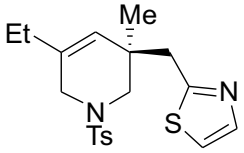


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.842	10154555	54.612
2	19.604	8439475	45.388
Total		18594030	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	13.916	1503091	4.047
2	15.715	35635643	95.953
Total		37138734	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(thiazol-2-ylmethyl)-4,5-didehydropiperidine 2e

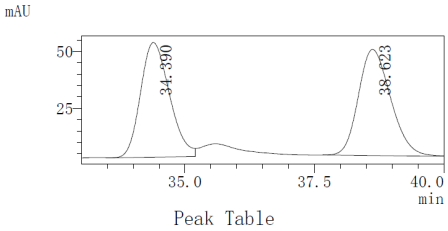
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 31.2mg, 83% yield. 89% *ee*. $[\alpha]^{26}_D$ = -24.3° (*c* = 1.8, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.65 (m, 3H), 7.36-7.30 (m, 2H), 7.21 (d, *J* = 3.4 Hz, 1H), 5.21 (t, *J* = 1.8 Hz, 1H), 3.52 (d, *J* = 15.6 Hz, 1H), 3.31-3.25 (m, 1H), 3.25-3.16 (m, 2H), 3.07 (d, *J* = 14.1 Hz, 1H), 2.66 (d, *J* = 11.4 Hz, 1H), 1.94 (q, *J* = 7.5, 2H), 1.07 (s, 3H), 0.98 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.5, 143.7, 142.4, 134.9, 133.3, 129.8, 127.8, 126.8, 119.0, 53.4, 47.5, 43.0, 36.8, 27.2, 24.4, 21.7, 12.1.

ESI-MS: Calcd for $C_{19}H_{24}N_2O_2S_2$ $[M+Na]^+$:399.1. Found: 398.9.

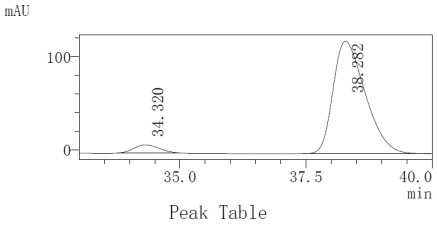
HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

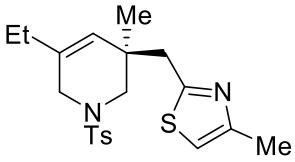
Peak#	Ret. Time	Area	Area%
1	34.390	1964814	49.174
2	38.623	2030803	50.826
Total		3995617	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	34.320	309345	5.484
2	38.282	5331051	94.516
Total		5640397	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(4-methylthiazol-2-ylmethyl)-4,5-didehydropiperidine 2f

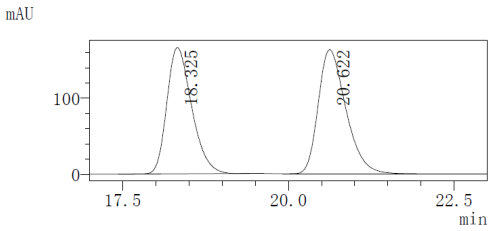
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as colorless oil. 38.5 mg, 84% yield. 92% ee. $[\alpha]^{25}_{D}$ = -29.8° (*c* = 2.9, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.73 (q, *J* = 1.1 Hz, 1H), 5.21 (t, *J* = 1.7 Hz, 1H), 3.51-3.42 (m, 1H), 3.33-3.24 (m, 1H), 3.17-3.09 (m, 2H), 2.99 (d, *J* = 14.0 Hz, 1H), 2.68 (d, *J* = 11.4 Hz, 1H), 2.44 (s, 3H), 2.38 (s, 3H), 1.93 (q, *J* = 7.5 Hz, 2H), 1.07 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 152.3, 143.7, 134.8, 133.2, 129.8, 127.8, 126.8, 113.5, 53.4, 47.5, 43.2, 36.7, 27.2, 24.5, 21.6, 17.2, 12.1.

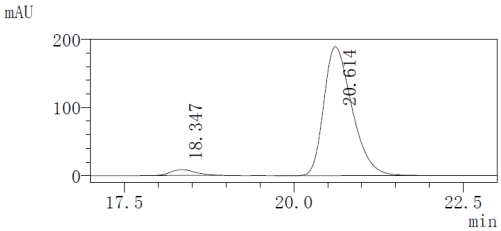
ESI -MS : Calcd for $C_{20}H_{26}N_2O_2S_2$ $[M+H]^+$: 391.1. Found: 390.9.

HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 95.0/5.0 flow rate = 1.0 mL/min



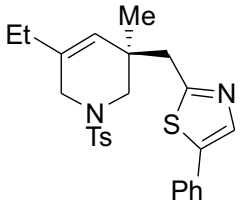
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.325	4314834	47.642
2	20.622	4741915	52.358
Total		9056750	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.347	216272	3.809
2	20.614	5461255	96.191
Total		5677528	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-phenylthiazol-2-ylmethyl)-4,5-didehydropiperidine 2g

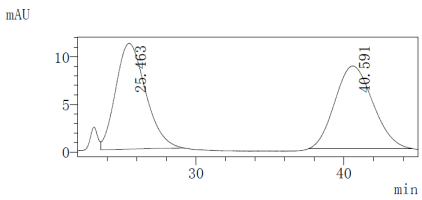
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as colorless oil. 32.1 mg, 71% yield. 92% ee. $[\alpha]^{24}_{D}$ = -49.2° (*c* = 2.7, $CHCl_3$).

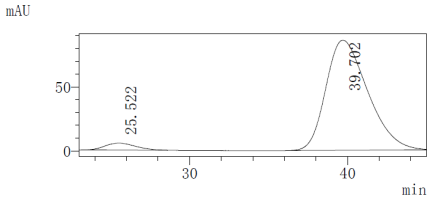
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (s, 1H), 7.73-7.66 (m, 2H), 7.57-7.50 (m, 2H), 7.43-7.35 (m, 2H), 7.35-7.26 (m, 3H), 5.27 (t, *J* = 1.7 Hz, 1H), 3.55 (d, *J* = 15.6 Hz, 1H), 3.33-3.22 (m, 2H), 3.18 (d, *J* = 14.1 Hz, 1H), 3.06 (d, *J* = 14.1 Hz, 1H), 2.69 (d, *J* = 11.3 Hz, 1H), 2.42 (s, 3H), 1.96 (q, *J* = 7.5 Hz, 2H), 1.11 (s, 3H), 1.00 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.9, 143.7, 139.4, 137.8, 135.1, 133.3, 131.6, 129.8, 129.2, 128.2, 127.8, 126.8, 126.7, 53.4, 47.5, 43.4, 36.8, 29.8, 27.3, 24.5, 21.6, 12.2.

ESI-MS: Calcd for $C_{25}H_{28}N_2O_2S_2$ $[M+H]^+$: 453.2. Found:452.9.

HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



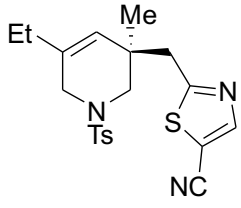


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	25.463	1565977	50.306
2	40.591	1546926	49.694
Total		3112903	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	25.522	725658	4.373
2	39.702	15867059	95.627
Total		16592717	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-cyanothiazol-2-ylmethyl)-4,5-didehydropiperidine 2h

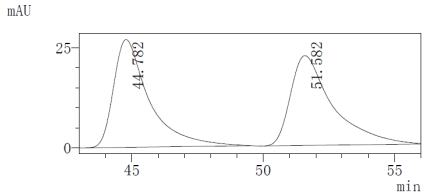
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 32.1 mg, 80% yield. 92% ee. $[\alpha]^{20}_{D}$ = -70.2° (*c* = 2.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (s, 1H), 7.67 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 5.16 (s, 1H), 3.64 (d, *J* = 15.8 Hz, 1H), 3.31 (ψdd, *J* = 18.2, 13.0 Hz, 2H), 3.13 (ψdd, *J* = 15.1, 7.6 Hz, 2H), 2.48 (d, *J* = 11.5 Hz, 1H), 2.43 (s, 3H), 1.96 (q, *J* = 7.4 Hz, 2H), 1.05 (s, 3H), 0.96 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 153.4, 147.2, 144.0, 136.8, 132.8, 130.0, 129.9, 127.8, 127.7, 125.5, 114.1, 53.1, 47.5, 37.5, 37.2, 27.2, 24.3, 21.7, 11.9.

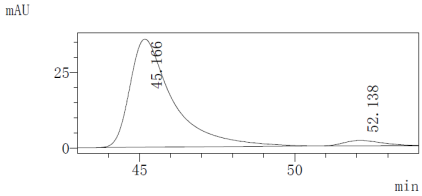
ESI-MS: Calcd for $C_{21}H_{26}N_2O_4S_2$ $[M+H]^+$: 435.1. Found: 434.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



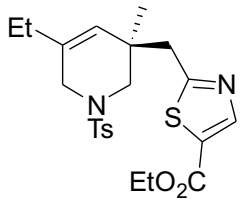
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	44.782	2537746	50.392
2	51.582	2498278	49.608
Total		5036024	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	45.166	3442768	95.719
2	52.138	153986	4.281
Total		3596754	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-ethoxycarbonylthiazol-2-ylmethyl)-4,5-didehydropiperidine 2i

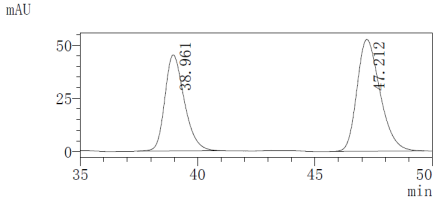
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 32.9 mg, 61% yield. 84% ee. $[\alpha]^{20}_D$ = +71.5° (*c* = 0.6, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.21 (t, *J* = 1.8 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 3.68 (d, *J* = 14.1 Hz, 1H), 3.51-3.42 (m, 1H), 3.35 (d, *J* = 14.2 Hz, 1H), 3.27-3.19 (m, 1H), 3.16 (d, *J* = 11.4 Hz, 1H), 2.64 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.99-1.88 (m, 2H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.00 (s, 3H), 0.97 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.6, 150.7, 144.8, 143.8, 143.5, 135.6, 133.1, 129.8, 127.8, 126.6, 61.4, 53.1, 47.5, 37.5, 36.2, 27.2, 24.5, 21.7, 14.5, 12.0.

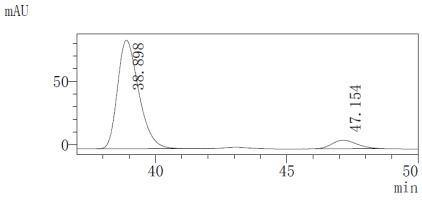
ESI-MS: Calcd for $C_{21}H_{26}N_2O_4S_2$ $[M+H]^+$: 435.1. Found: 434.9.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 80/20 flow rate = 0.5 mL/min.



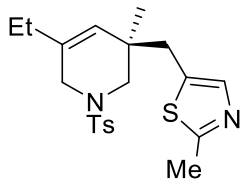
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	38.961	2613372	42.122
2	47.212	3590876	57.878
Total		6204248	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	38.898	4825788	91.762
2	47.154	433267	8.238
Total		5259055	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-methylthiazol-2-ylmethyl)-4,5-didehydropiperidine 2j

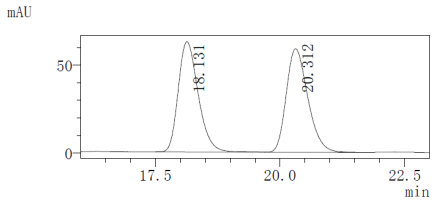
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as white solid. 26.1mg, 67% yield. 86% ee. $[\alpha]^{24}_{D}$ =-4.1° (*c* = 1.5, $CHCl_3$). The C5-selective alkylation of the thiazole next to sulfur atom was established by a proton NMR signal at 7.6 ppm, in comparison with proton NMR data of 2,4-diethylthiazole (C5-H signal at 6.7 ppm) and 2,5-diethylthiazole (C4-H signal at 7.3 ppm).[5]

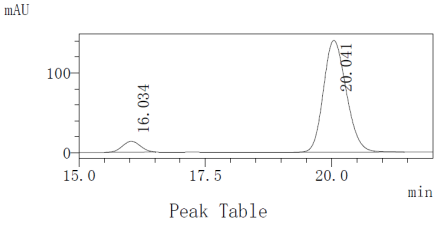
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.61 (s, 1H), 7.35-7.29 (m, 3H), 5.17 (t, *J* = 1.4 Hz, 1H), 3.56 (d, *J* = 15.4 Hz, 1H), 3.25-3.18 (m, 1H), 3.18-3.12 (m, 1H), 2.93-2.80 (m, 2H), 2.70 (s, 5 H), 2.65 (s, 3H), 2.49 (d, *J* = 11.3 Hz, 1H), 2.42 (s, 3H), 1.92 (q, *J* = 7.5 Hz, 2H), 1.02 (s, 3H), 0.94 (t, *J* = 7.5, Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 165.4, 143.7, 141.8, 139.6, 134.9, 133.3, 133.2, 129.8, 128.2, 127.8, 126.8, 53.0, 47.5, 36.9, 36.4, 27.2, 24.3, 21.6, 19.4, 19.3, 12.1.

ESI-MS: Calcd for $C_{20}H_{26}N_2O_2S_2$ $[M+H]^+$: 402.1, Found: 401.9

HPLC: Daicel Chirlcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.





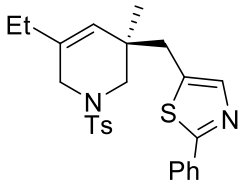
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.131	1747528	49.749
2	20.312	1765175	50.251
Total		3512703	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.034	332736	7.043
2	20.041	4391546	92.957
Total		4724282	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(2-phenylthiazol-5-ylmethyl)-4,5-didehydropiperidine 2k

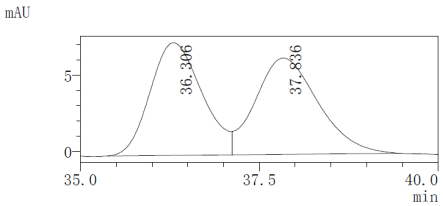
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 4) as colorless oil. 37.0 mg, 82% yield. 85% *ee*. $[\alpha]^{23}_{D} = +88.1^{o}$ (*c* = 2.5, $CHCl_3$).

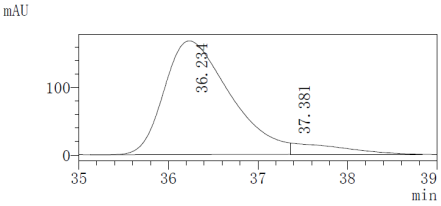
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.88 (m, 2H), 7.71-7.65 (m, 2H), 7.58 (s, 1H), 7.46-7.36 (m, 3H), 7.33 (d, *J* = 8.2 Hz, 2H), 5.22 (t, *J* = 1.8 Hz, 1H), 3.61 (d, *J* = 15.5 Hz, 1H), 3.27-3.17 (m, 2H), 3.01 (d, *J* = 14.6 Hz, 1H), 2.95 (d, *J* = 14.6 Hz, 1H), 2.51 (d, *J* = 11.3 Hz, 1H), 2.42 (s, 3H), 1.91 (q, *J* = 7.5 Hz, 2H), 1.05-0.97 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.5, 143.8, 143.4, 135.2, 134.1, 133.9, 133.1, 129.9, 129.8, 129.0, 127.8, 126.7, 126.4, 53.0, 47.6, 37.1, 36.6, 27.3, 24.4, 21.7, 12.2.

ESI-MS: Calcd for $C_{25}H_{28}N_2O_2S_2$. $[M+H]^+$: 453.2. Found: 452.9.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



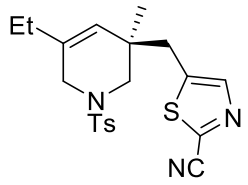


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	36.306	373388	49.244
2	37.836	384847	50.756
Total		758235	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	36.234	8656271	92.879
2	37.381	663675	7.121
Total		9319946	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(2-cyanothiazol-5-ylmethyl)-4,5-didehydropiperidine 2l

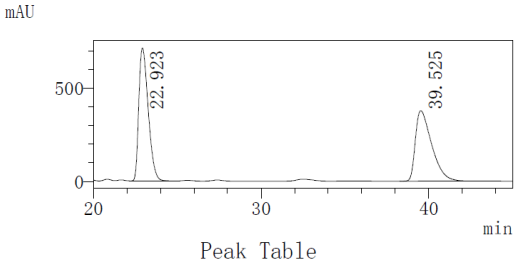
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as colorless oil. 28.5mg, 71% yield. 81% *ee*. $[\alpha]^{23}_{D}$ = +17.8° (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.1 Hz, 1H), 7.72-7.65 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.30-7.23 (m, 1H), 5.34 (t, *J* = 1.8 Hz, 1H), 3.56 (dd, *J* = 15.3, 1.9 Hz, 1H), 3.40 (d, *J* = 11.4 Hz, 1H), 3.29-3.21 (m, 1H), 3.16 (d, *J* = 14.6 Hz, 1H), 3.04 (d, *J* = 14.6 Hz, 1H), 2.68 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.93 (q, *J* = 7.5 Hz, 2H), 1.19 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.1, 144.0, 141.5, 136.6, 135.4, 132.8, 130.0, 127.7, 125.8, 113.1, 52.6, 47.6, 36.7, 36.6, 27.2, 24.2, 21.7, 12.1.

ESI-MS: Calcd for $C_{20}H_{23}N_3O_2S_2$ $[M+H]^+$: 402.1. Found: 401.9.

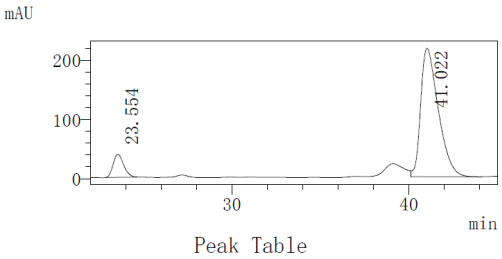
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10 flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

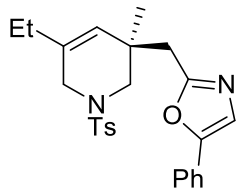
Peak#	Ret. Time	Area	Area%
1	22.923	28106812	52.379
2	39.525	25553566	47.621
Total		53660378	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	23.554	1603072	9.647
2	41.022	15013546	90.353
Total		16616618	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-phenyloxazol-2-ylmethyl)-4,5-didehydropiperidine 2m

The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as white solid. 37.0 mg, 85% yield. 94% ee. $[\alpha]^{26}_{D}$ = -46.5° (*c* = 3.1, $CHCl_3$).

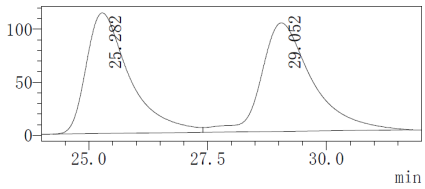
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.66 (m, 2H), 7.66-7.59 (m, 2H), 7.41 (dd, *J* = 8.5, 7.0 Hz,

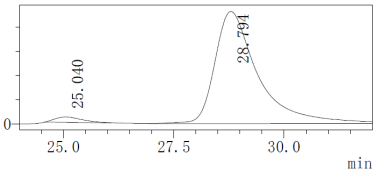
2H), 7.33 (d, J = 3.2 Hz, 1H), 7.32-7.21 (m, 3H), 5.28 (t, J = 1.7 Hz, 1H), 3.55-3.46 (m, 1H), 3.35-3.25 (m, 2H), 2.96 (d, J = 14.4 Hz, 1H), 2.89 (d, J = 14.4 Hz, 1H), 2.72 (d, J = 11.3 Hz, 1H), 1.94 (q, J = 7.5 Hz, 2H), 1.10 (s, 3H), 0.97 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.8, 151.4, 143.7, 134.9, 133.2, 129.8, 129.0, 128.3, 128.2, 127.8, 126.5, 124.1, 121.9, 53.3, 47.5, 38.2, 36.6, 27.2, 24.4, 21.6, 12.1.

ESI-MS: Calcd for $C_{25}H_{28}N_2O_3S$ $[M+H]^+$: 437.2. Found: 437.1

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.





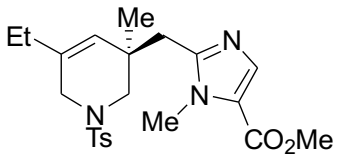
Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	25.282	7217700	48.592
2	29.052	7636088	51.408
Total		14853789	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	25.040	469240	2.834
2	28.794	16086458	97.166
Total		16555698	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-methoxycarbonyl-1-methylimidazol-2-ylmethyl)-4,5-didehydropiperidine 2n

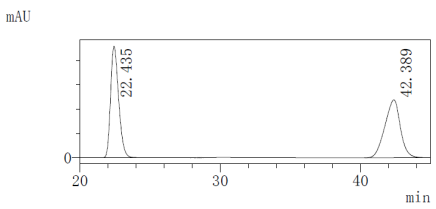
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 28.0 mg, 63% yield. 80% *ee*. $[\alpha]^{23}_D$ = +65.1° (c = 1.0, $CHCl_3$).

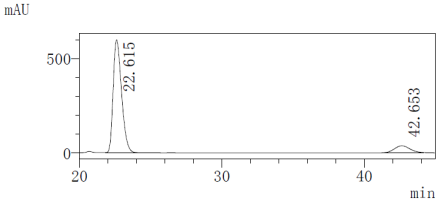
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.65 (m, 3H), 7.34 (d, J = 8.0 Hz, 2H), 5.00 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.71 (d, J = 15.6 Hz, 1H), 3.38 (d, J = 11.4 Hz, 1H), 3.16-3.04 (m, 2H), 2.73 (d, J = 14.4 Hz, 1H), 2.47 (m, 1H), 2.43 (s, 3H), 1.96 (q, J = 7.5 Hz, 2H), 1.14 (s, 3H), 0.93 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.2, 151.0, 143.9, 136.8, 135.1, 133.1, 129.9, 127.9, 126.5, 122.7, 54.2, 51.4, 47.6, 37.4, 36.3, 32.9, 27.2, 24.7, 21.7, 12.1.

ESI-MS: Calcd for $C_{23}H_{31}N_3O_4S$ $[M+H]^+$: 446.2. Found: 445.8.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 70/30 flow rate = 1.0 mL/min.



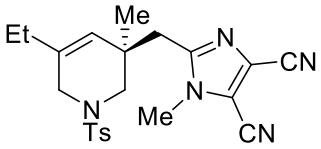


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.435	9159163	50.039
2	42.389	9144745	49.961
Total		18303908	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.615	24723329	90.112
2	42.653	2712880	9.888
Total		27436209	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(4,5-dicyano-1-methylimidazol-2-ylmethyl)-4,5-didehydropiperidine 2o

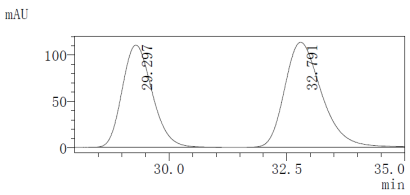
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 21.0 mg, 51% yield, 85% *ee*. $[\alpha]^{20}_{D} = +132.6^{o}$ (*c* = 0.6, $CHCl_3$).

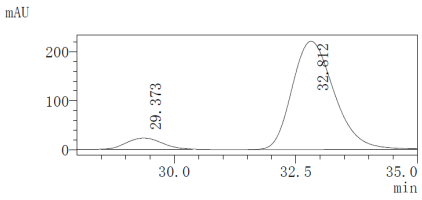
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.39-7.32 (m, 2H), 5.07 (d, *J* = 1.5 Hz, 1H), 3.82 (d, *J* = 15.8 Hz, 1H), 3.75 (s, 3H), 3.45 (d, *J* = 11.6 Hz, 1H), 3.06-2.94 (m, 2H), 2.82 (d, *J* = 14.8 Hz, 1H), 2.44 (s, 3H), 2.21 (d, *J* = 11.6 Hz, 1H), 1.97 (q, *J* = 7.6 Hz, 2H), 1.19 (s, 3H), 0.96 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 151.7, 144.2, 136.2, 132.5, 130.0, 127.8, 126.1, 121.5, 113.0, 112.1, 108.6, 53.5, 47.6, 37.3, 36.0, 33.6, 27.2, 24.6, 21.7, 12.2.

ESI-MS: Calcd for $C_{22}H_{25}N_5O_2S$ $[M+Na]^+$: 446.2. Found: 445.8.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 80/20 flow rate = 1.0 mL/min.



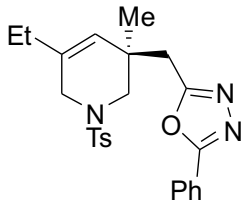


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	29.297	4863938	44.109
2	32.791	6163188	55.891
Total		11027126	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	29.373	1121402	7.749
2	32.812	13350822	92.251
Total		14472224	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-phenyl-1,3,4-oxadiazol-2-ylmethyl)-4,5-didehydropiperidine 2p

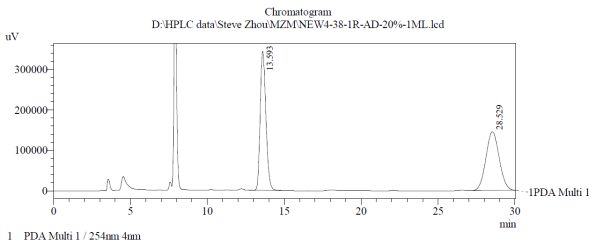
The product was isolated by flash chromatography (ethyl acetate/hexane 1:2) as colorless oil. 38.9 mg, 89% yield. 90% ee. $[\alpha]^{25}_{D}$ = -55.3° (*c* = 3.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): 8.10-8.03 (m, 2H), 7.72-7.65 (m, 2H), 7.55-7.47 (m, 3H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.28 (t, *J* = 1.8 Hz, 1H), 3.64-3.55 (m, 1H), 3.39 (d, *J* = 11.4 Hz, 1H), 3.27-3.18 (m, 1H), 3.11 (d, *J* = 14.7 Hz, 1H), 3.02 (d, *J* = 14.6 Hz, 1H), 2.58 (d, *J* = 11.3 Hz, 1H), 2.42 (s, 3H), 1.94 (q, *J* = 7.4 Hz, 2H), 1.14 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 164.5, 143.8, 135.8, 133.1, 131.7, 129.9, 129.2, 127.8, 127.0, 125.9, 124.1, 53.1, 47.5, 36.4, 35.3, 27.2, 24.5, 21.6, 12.1.

ESI-MS: Calcd for $C_{24}H_{27}N_3O_3S$ $[M+H]^+$: 438.2. Found: 437.9.

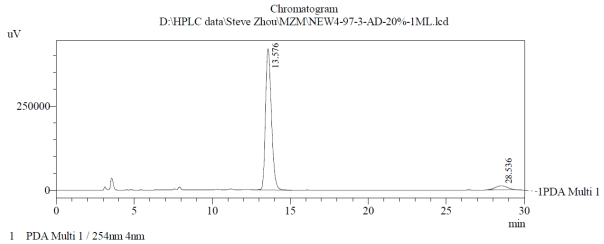
HPLC: Daicel Chiralcel AD-H, *n*-hexane/ethanol 80/20, flow rate = 1.0 mL/min.



PeakTable

Ch1 254nm 4nm

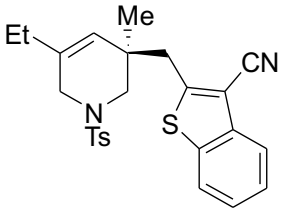
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.593	8906069	344317	50.462	70.336
2	28.529	8742865	145216	49.538	29.664
Total		17648934	489532	100.000	100.000



PeakTable

Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.576	10985577	419856	94.653	97.301
2	28.536	620534	11648	5.347	2.699
Total		11606111	431503	100.000	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(3-cyanobenzothien-2-ylmethyl)-4,5-didehydropiperidine 2q

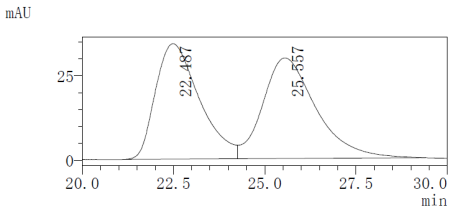
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 36.9 mg, 82% yield. 92% ee. $[\alpha]^{21}_{D}$ = -84.6° (*c* = 2.3, $CHCl_3$).

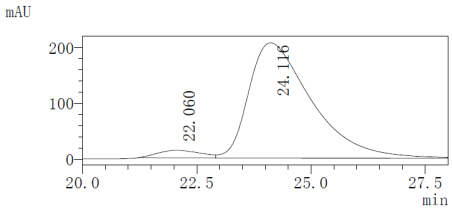
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.85-7.78 (m, 1H), 7.74-7.67 (m, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 8.3, 7.2 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.27 (s, 1H), 3.68-3.60 (m, 1H), 3.41-3.32 (m, 2H), 3.28-3.15 (m, 2H), 2.62 (d, *J* = 11.4 Hz, 1H), 2.43 (s, 3H), 1.97 (q, *J* = 7.5 Hz, 2H), 1.10 (s, 3H), 1.02 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 154.4, 143.9, 138.3, 137.6, 136.0, 133.1, 129.9, 127.8, 126.1, 125.9, 125.9, 122.4, 122.2, 114.7, 107.2, 53.5, 47.6, 40.6, 37.8, 27.2, 24.3, 21.7, 12.0.

ESI-MS: Calcd for $C_{25}H_{26}N_2O_2S_2$ $[M+Na]^+$: 473.1. Found: 473.1

HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min.



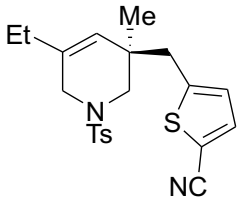


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.487	2849489	48.622
2	25.557	3011029	51.378
Total		5860518	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.060	861824	4.184
2	24.116	19736434	95.816
Total		20598259	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-cyanothien-2-ylmethyl)-4,5-didehydropiperidine 2r

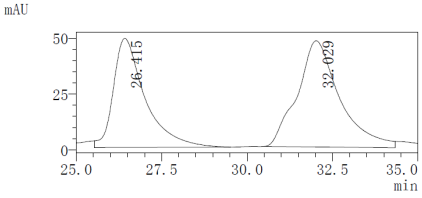
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 34.4 mg, 86% yield. 91% ee. $[\alpha]^{20}_D$ = +98.7° (*c* = 0.8, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.9 Hz, 2H), 7.49 (d, *J* = 3.7 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 2H), 6.96 (d, *J* = 3.7 Hz, 1H), 5.16 (s, 1H), 3.70 (d, *J* = 15.7 Hz, 1H), 3.34 (d, *J* = 11.4 Hz, 1H), 3.13-2.99 (m, 2H), 2.93 (d, *J* = 14.4 Hz, 1H), 2.43 (s, 3H), 2.31 (d, *J* = 11.4 Hz, 1H), 1.95 (q, *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.5 Hz, 3H), 0.94 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 148.4, 143.9, 137.7, 135.6, 132.9, 129.9, 128.4, 127.8, 126.5, 114.7, 108.1, 52.6, 47.6, 39.8, 36.8, 27.2, 24.2, 21.7, 12.1.

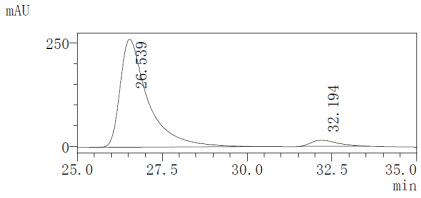
ESI-MS: Calcd for $C_{21}H_{24}N_2O_2S_2$ $[M+Na]^+$: 423.1. Found: 422.8.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



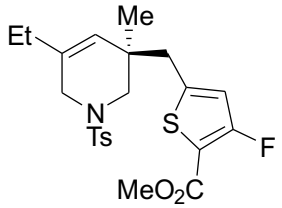
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	26.415	3154617	43.423
2	32.029	4110313	56.577
Total		7264929	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	26.539	14878609	94.951
2	32.194	791218	5.049
Total		15669827	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(4-fluoro-5-methoxycarbonylthien-2-ylmethyl)-4,5-didehydropiperidine 2s

The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 32.9 mg, 73% yield. 85% ee. $[\alpha]^{20}_{D} = +71.8^{o}$ (c = 1.1, $CHCl_3$).

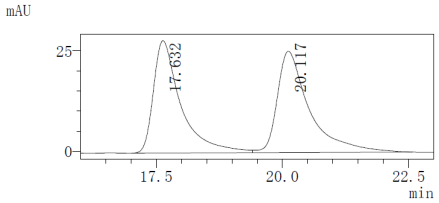
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 6.72 (s, 1H), 5.17 (t, J = 1.9 Hz, 1H), 3.86 (s, 3H), 3.68 (dd, J = 15.6, 1.7 Hz, 1H), 3.30 (d, J = 11.4 Hz, 1H), 3.17-3.08 (m, 1H), 2.91 (d, J = 14.3 Hz, 1H), 2.81 (d, J = 14.3 Hz, 1H), 2.43 (s, 3H), 2.36 (d, J = 11.4 Hz, 1H), 1.95 (q, J = 7.5 Hz, 2H), 0.99 (s, 3H), 0.93 (t, J = 7.5 Hz, 3H).

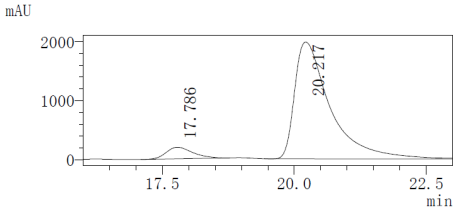
^{13}C NMR (101 MHz, $CDCl_3$): δ 161.1 (d, $J_{C\text{-}F}$ = 3.6 Hz) , 160.7 158.0, 145.7 (d, $J_{C\text{-}F}$ = 9.0 Hz) , 143.9, 135.4, 133.0, 129.9, 127.8, 126.5, 119.0 (d, $J_{C\text{-}F}$ = 14.6 Hz) , 110.9 (d, $J_{C\text{-}F}$ = 9.6 Hz) , 52.7, 52.1, 47.6, 40.8, 36.8, 27.2, 24.2, 21.7, 12.2.

^{19}F NMR (377 MHz, $CDCl_3$): δ -112.8.

ESI-MS: Calcd for: $C_{22}H_{26}FNO_4S_2$ $[M+Na]^+$: 474.1. Found: 473.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



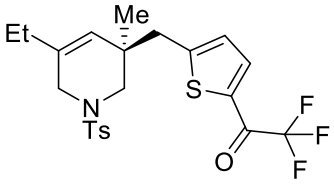


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.632	1060595	48.645
2	20.117	1119676	51.355
Total		2180272	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.786	6862109	6.815
2	20.217	93833036	93.185
Total		100695145	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-trifluoroacetylthien-2-ylmethyl)-4,5-didehydropiperidine 2t

The product was isolated by flash chromatography (ethyl acetate/hexane 1: 8) as light yellow oil. 40.9 mg, 87% yield. 87% *ee*. $[\alpha]^{21}_{D}$ = +98.3° (*c* = 3.0, $CHCl_3$).

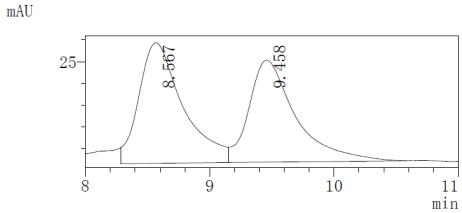
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, *J* = 3.9 Hz, 1H), 7.70-7.64 (m, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 4.0 Hz, 1H), 5.21-5.16 (m, 1H), 3.72 (d, *J* = 15.8 Hz, 1H), 3.36 (d, *J* = 11.4 Hz, 1H), 3.15-3.04 (m, 2H), 3.00 (d, *J* = 14.1 Hz, 1H), 2.43 (s, 3H), 2.34 (d, *J* = 11.4 Hz, 1H), 1.96 (q, *J* = 7.5 Hz, 2H), 1.04 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H).

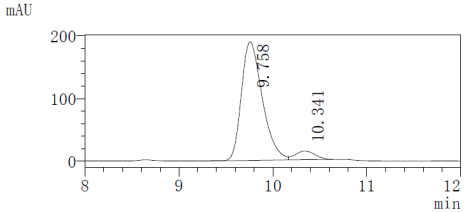
^{13}C NMR (101 MHz, $CDCl_3$): δ 173.5 (q, $J_{C\text{-}F}$ = 36.6 Hz), 155.2, 143.9, 137.0 (q, $J_{C\text{-}F}$ = 3.2 Hz), 135.6, 135.0, 132.9, 130.4, 129.9, 129.1 (q, $J_{C\text{-}F}$ = 57.9 Hz), 127.8, 126.5, 118.1 (q, $J_{C\text{-}F}$ = 290.6 Hz), 52.7, 47.6, 40.5, 37.0, 27.2, 24.3, 21.7, 12.1.

^{19}F NMR (377 MHz, $CDCl_3$): δ -72.0.

ESI-MS: Calcd for $C_{22}H_{24}F_3NO_3S_2$ $[M+H]^+$: 494.1. Found: 493.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



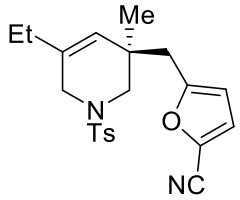


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	8.567	682394	52.729
2	9.458	611755	47.271
Total		1294150	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	9.758	2934673	93.406
2	10.341	207178	6.594
Total		3141852	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(5-cyanofuran-2-ylmethyl)-4,5-didehydropiperidine 2u

The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 16.1mg, 42% yield. 84% ee. $[\alpha]^{20}_{D}$ = +43.3° (*c* = 1.0, $CHCl_3$).

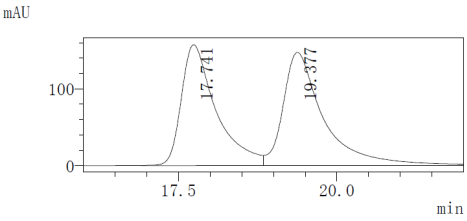
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.

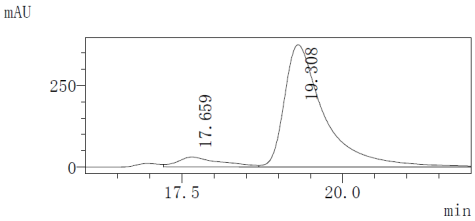
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-8.03 (m, 2H), 7.72-7.65 (m, 2H), 7.55-7.45 (m, 3H), 7.33 (d, *J* = 8.0 Hz, 2H), 5.28 (t, *J* = 1.8 Hz, 1H), 3.64-3.55 (m, 1H), 3.39 (d, *J* = 11.4 Hz, 1H), 3.27-3.18 (m, 1H), 3.11 (d, *J* = 14.7 Hz, 1H), 3.02 (d, *J* = 14.6 Hz, 1H), 2.61 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.94 (q, *J* = 7.4 Hz, 2H), 1.14 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 164.5, 143.8, 135.8, 133.1, 131.7, 129.9, 129.2, 127.8, 127.0, 125.9, 124.1, 53.1, 47.5, 36.4, 35.3, 27.2, 24.5, 21.6, 12.1.

ESI-MS: Calcd for $C_{21}H_{24}N_2O_3S$ $[M+Na]^+$: 407.2. Found: 406.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



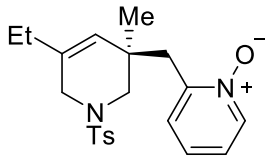


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.741	5994893	47.537
2	19.377	6616105	52.463
Total		12610998	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.659	1380451	7.836
2	19.308	16235270	92.164
Total		17615720	100.000

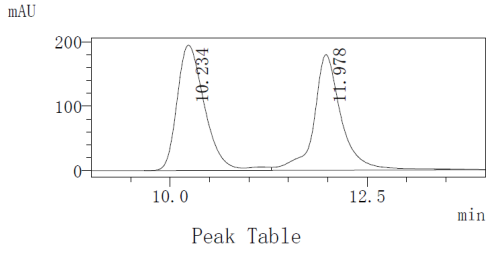


(*R*)-*N*-Tosyl-5-ethyl-3-methyl-3-(pyridin-2-yl)-4,5-didehydropiperidine *N*-oxide 2v

The reaction was conducted using AgOTf (0.05 mmol) at 0.05 mmol scale. The product was isolated by flash chromatography (methanol /dichloromethane 1:50) as colorless oil. 16.0 mg, 83% yield. 91% *ee*. $[\alpha]^{21}_{D}$ = +47.6° (*c* = 0.5, $CHCl_3$). When Ag_3PO_4 was used instead, 78% ee resulted. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 6.5 Hz, 1H), 7.71-7.64 (m, 2H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.38-7.31 (m, 2H), 7.28-7.19 (m, 1H), 7.14 (ψtd, *J* = 7.6, 2.1 Hz, 1H), 5.39-5.34 (s, 1H), 3.65 (d, *J* = 15.5 Hz, 1H), 3.48 (d, *J* = 11.5 Hz, 1H), 3.34 (d, *J* = 13.1 Hz, 1H), 3.09-3.00 (m, 2H), 2.43 (s, 3H), 2.27 (d, *J* = 11.5 Hz, 1H), 1.93 (q, *J* = 7.6 Hz, 2H), 1.02 (s, 3H), 0.96 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.6, 143.9, 139.9, 134.2, 132.8, 129.9, 129.1, 127.9, 127.8, 125.5, 124.0, 52.9, 47.6, 38.6, 37.5, 27.1, 23.9, 21.7, 12.2.

ESI-MS: Calcd for $C_{21}H_{26}N_2O_3S$ $[M+Na]^+$: 409.2. Found: 408.9.

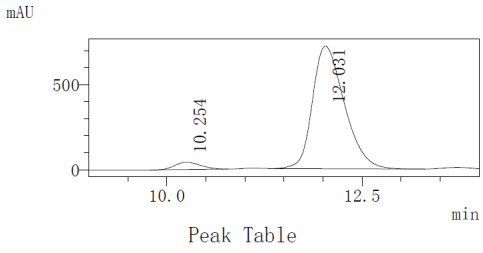
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 80/20 flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

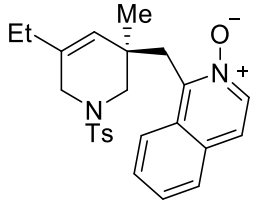
Peak#	Ret. Time	Area	Area%
1	10.234	4735521	51.830
2	11.978	4401060	48.170
Total		9136580	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	10.254	974491	4.543
2	12.031	20474940	95.457
Total		21449432	100.000



(*R*)-2-*N*-Tosyl-5-ethyl-3-methyl-3-(isoquinolin-2-yl)-4,5-didehydropiperidine *N*-oxide 2w

The reaction was conducted using AgOTf (0.1 mmol) at 0.1 mmol scale. The product was isolated by flash chromatography (methanol /dichloromethane 1:50) as colorless oil. 27.5 mg, 63% yield.

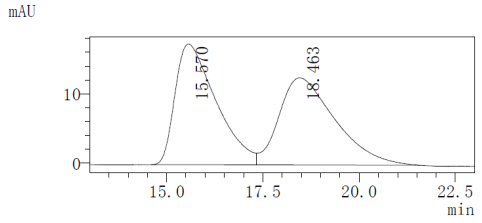
96% *ee*. $[\alpha]^{23}_D$ = +46.2° (*c* = 0.8, $CHCl_3$). When Ag_3PO_4 was used instead, 37.0 mg, 87% yield, 63% ee.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 7.1 Hz, 1H), 8.07-8.01 (m, 1H), 7.76-7.67 (m, 3H), 7.62-7.50 (m, 3H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.10 (s, 1H), 3.76 (d, *J* = 13.3 Hz, 1H), 3.69-3.59 (m, 2H), 3.59 (d, *J* = 2.9 Hz, 1H), 3.10 (d, *J* = 15.5 Hz, 1H), 2.50 (d, *J* = 11.4 Hz, 1H), 2.43 (s, 3H), 1.82-1.70 (m, 2H), 1.28-1.21 (m, 5H), 0.74 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 146.5, 143.8, 137.0, 133.9, 132.9, 129.93, 129.86, 128.8, 128.7, 128.2, 128.01, 127.96, 127.1, 125.8, 122.5, 55.3, 47.5, 39.4, 35.0, 27.1, 25.9, 21.7, 11.8.

ESI-MS: Calcd for $C_{25}H_{28}N_2O_3S$ $[M+Na]^+$: 459.2. Found: 458.8.

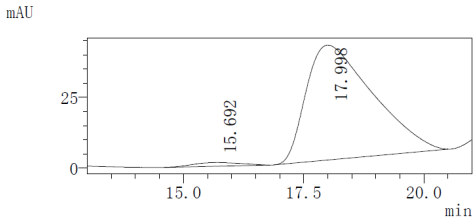
HPLC: Daicel Chiralcel AS-H, *n*-hexane/isopropanol 80/20 flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

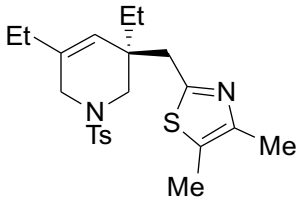
Peak#	Ret. Time	Area	Area%
1	15.570	1288890	50.296
2	18.463	1273741	49.704
Total		2562631	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	15.692	88993	2.229
2	17.998	3904111	97.771
Total		3993104	100.000



(*R*)-2-*N*-Tosyl-3,5-diethyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3a

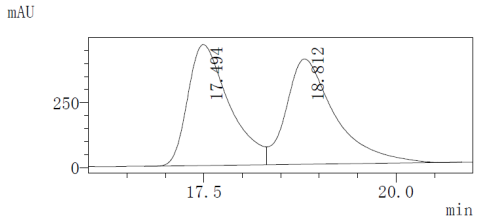
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as colorless oil. 35.3 mg, 85% yield. 96% ee. $[\alpha]^{26}_D$ = -25.6° (*c* = 2.9, $CHCl_3$).

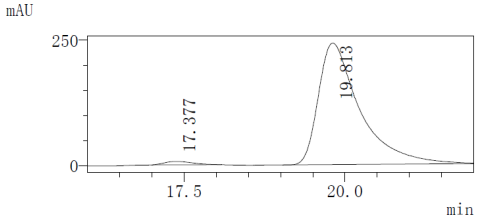
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 5.24 (t, *J* = 1.7 Hz, 1H), 3.38-3.33 (m, 2H), 3.04 (d, *J* = 14.2 Hz, 1H), 2.96-2.88 (m, 3H), 2.41 (s, 3H), 2.29 (s, 3H), 2.23 (s, 3H), 1.94 (q, *J* = 7.4 Hz, 2H), 1.49 (t, *J* = 7.5 Hz, 2H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.85 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 147.3, 143.6, 135.4, 133.3, 129.7, 127.8, 126.0, 125.8, 51.0, 47.4, 40.8, 39.4, 29.9, 27.3, 21.6, 14.7, 12.2, 11.3, 8.3.

ESI-MS: Calcd for $C_{22}H_{30}N_2O_2S_2$ $[M+H]^+$: 419.2. Found: 418.8.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



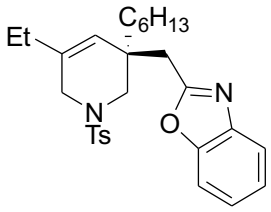


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.494	17496868	49.563
2	18.812	17805180	50.437
Total		35302048	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.377	204484	1.840
2	19.813	10907801	98.160
Total		11112285	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-hexyl-3-(benzoxazol-2-ylmethyl)-4,5-didehydropiperidine 3b

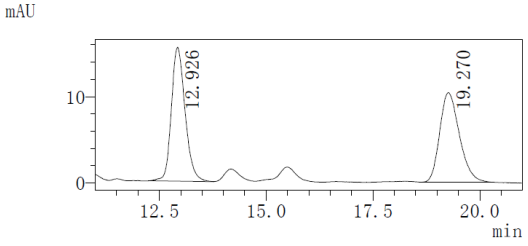
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as colorless oil. 20.9 mg, 77% yield. 94% ee. $[\alpha]^{26}_D$ = +37.8^o (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.64 (m, 3H), 7.48 (d, *J* = 6.0 Hz, 1H), 7.36-7.24 (m, 4H), 5.32 (d, *J* = 1.8 Hz, 1H), 5.32 (t, *J* = 1.7 Hz, 1H), 3.46 (d, *J* = 15.5 Hz, 1H), 3.34 (d, *J* = 15.6 Hz, 1H), 3.20 (d, *J* = 11.4 Hz, 1H), 3.09 (d, *J* = 14.3 Hz, 1H), 2.98 (d, *J* = 14.4 Hz, 1H), 2.92 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 1.94 (q, *J* = 7.5 Hz, 2H), 1.56-1.39 (m, 2H), 1.35-1.23 (m, 9H), 0.96 (t, *J* = 7.5 Hz, 3H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5, 150.9, 143.7, 141.5, 135.5, 133.5, 129.8, 127.9, 125.6, 124.7, 124.2, 119.8, 110.5, 51.6, 47.4, 39.6, 37.5, 36.6, 31.9, 30.3, 29.3, 27.4, 23.8, 22.8, 21.7, 14.2, 12.3.

ESI-MS: Calcd for $C_{28}H_{36}N_2O_3S$ $[M+H]^+$: 481.2. Found: 480.9.

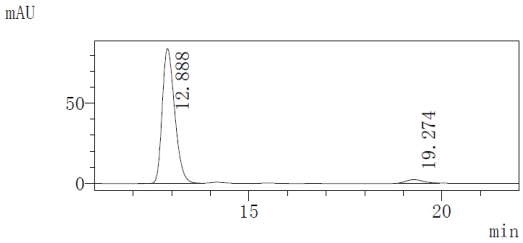
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

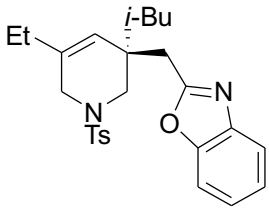
Peak#	Ret. Time	Area	Area%
1	12.926	346356	51.022
2	19.270	332478	48.978
Total		678834	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	12.888	1901315	96.825
2	19.274	62347	3.175
Total		1963662	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-isobutyl-3-(benzoxazol-2-ylmethyl)-4,5-didehydropiperidine 3c

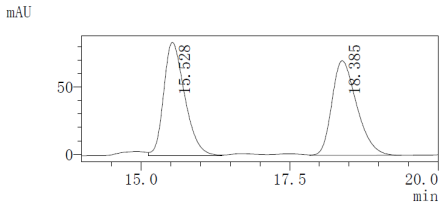
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as colorless oil. 15.8 mg, 70% yield. 91% ee. $[\alpha]^{27}_{D} = 30.9^{o}$ (c = 1.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.64 (m, 3H), 7.53-7.45 (m, 1H), 7.36-7.24 (m, 4H), 5.34 (t, J = 1.7 Hz, 1H), 3.49-3.40 (m, 1H), 3.38-3.29 (m, 1H), 3.22 (d, J = 11.4 Hz, 1H), 3.15 (d, J = 14.4 Hz, 1H), 3.01-2.91 (m, 2H), 2.42 (s, 3H), 1.93 (q, J = 7.5 Hz, 2H), 1.79-1.70 (m, 1H), 1.55 (dd, J = 14.4, 5.4 Hz, 1H), 1.43 (dd, J = 14.4, 6.1 Hz, 1H), 0.96 (t, J = 7.5 Hz, 3H), 0.89 (d, J = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5, 150.9, 143.7, 141.4, 135.2, 133.4, 129.8, 127.9, 125.9, 124.7, 124.2, 119.8, 110.5, 52.2, 47.4, 46.5, 40.1, 37.8, 27.3, 25.4, 24.9, 24.4, 21.7, 12.2.

ESI-MS: Calcd for $C_{26}H_{32}N_2O_2S$ $[M+H]^+$: 453.2. Found: 453.1.

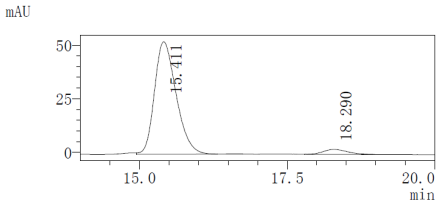
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

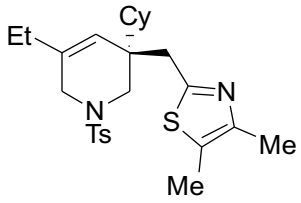
Peak#	Ret. Time	Area	Area%
1	15.528	2078250	50.403
2	18.385	2045021	49.597
Total		4123271	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	15.411	1339388	95.335
2	18.290	65534	4.665
Total		1404922	100.000



(*S*)-*N*-Tosyl-5-ethyl-3-cyclohexyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3d

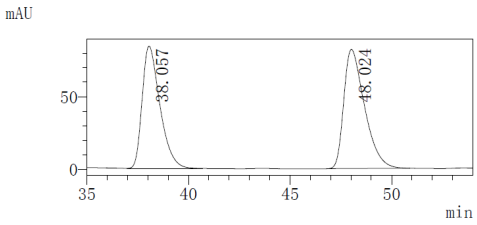
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as yellow oil. 36.1 mg, 78% yield. 94% ee. $[\alpha]^{25}_{D}$ = -41.4 ^{o} (*c* = 2.8, $CHCl_3$).

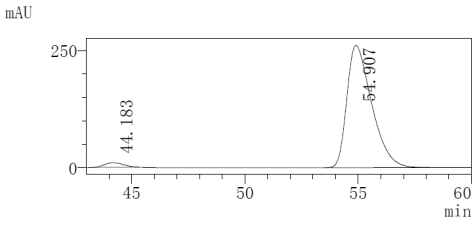
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 5.29 (t, *J* = 1.7 Hz, 1H), 3.35-3.30 (m, 2H), 3.12-2.96 (m, 3H), 2.88 (d, *J* = 11.6 Hz, 1H), 2.42 (s, 3H), 2.26 (s, 3H), 2.24 (s, 3H), 2.00 -1.89 (m, 3H), 1.80-1.61 (m, 4H), 1.55-1.45 (m, 1H), 1.24-0.95 (m, 10H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1, 147.2, 143.5, 135.1, 133.5, 129.8, 127.9, 126.0, 125.9, 48.5, 47.4, 43.6, 41.9, 39.3, 27.7, 27.4, 27.3, 27.1, 27.0, 26.7, 21.7, 14.7, 12.2, 11.3.

ESI-MS: Calcd for $C_{26}H_{36}N_2O_2S_2$ $[M+Na]^+$: 486.1. Found: 485.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



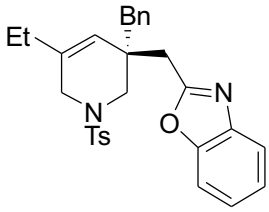


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	38.057	5115374	46.721
2	48.024	5833433	53.279
Total		10948807	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	44.183	574042	2.810
2	54.907	19854777	97.190
Total		20428819	100.000



(*R*)-*N*-Tosyl-5-ethyl-3-benzyl-3-(benzoxazol-2-ylmethyl)-4,5-didehydropiperidine 3e

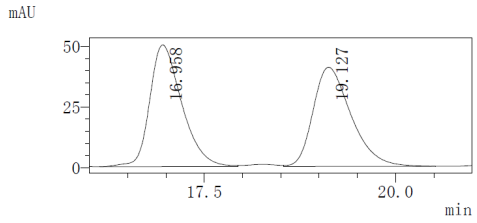
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as colorless oil. 20.9 mg, 86% yield. 93% ee. $[\alpha]^{26}_{D}$ = 10.9^{o} (*c* = 1.5, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.63 (m, 3H), 7.51-7.45 (m, 1H), 7.36-7.22 (m, 9H), 5.28 (t, *J* = 1.7 Hz, 1H), 3.48 (d, *J* = 15.7 Hz, 1H), 3.29 (d, *J* = 15.7 Hz, 1H), 3.20 (d, *J* = 11.5 Hz, 1H), 3.05 (d, *J* = 13.5 Hz, 1H), 3.01-2.86 (m, 4H), 2.42 (s, 3H), 1.91 (q, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.3, 150.8, 143.8, 141.4, 136.9, 135.7, 133.2, 131.0, 129.8, 128.3, 127.9, 126.7, 125.3, 124.8, 124.3, 119.9, 110.5, 51.6, 47.6, 43.3, 40.3, 35.7, 27.3, 21.7, 12.2.

ESI-MS: Calcd for $C_{29}H_{30}N_2O_3S$ $[M+H]^+$: 487.2. Found: 486.9.

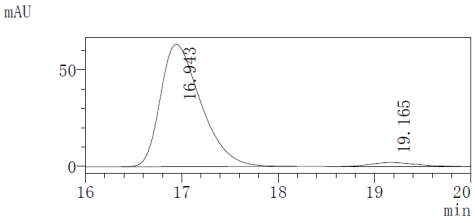
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

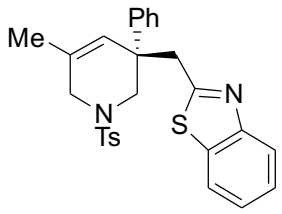
Peak#	Ret. Time	Area	Area%
1	16.958	1465655	50.972
2	19.127	1409767	49.028
Total		2875422	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.943	1847130	96.537
2	19.165	66252	3.463
Total		1913381	100.000



(*R*)-*N*-Tosyl-5-methyl-3-phenyl-3-(benzothiazol-2-ylmethyl)-4,5-didehydropiperidine 3f

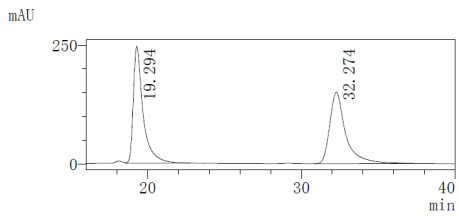
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as light yellow oil. 39.6 mg, 84% yield. 89% ee. $[\alpha]^{26}_D$ = -34.4° (*c* = 3.8, $CHCl_3$).

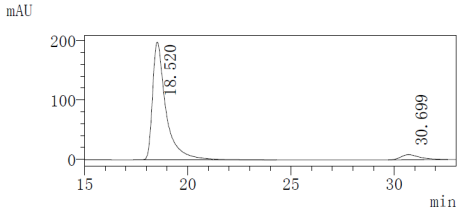
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.61-7.55 (m, 2H), 7.44-7.23 (m, 9H), 5.77 (t, *J* = 1.7 Hz, 1H), 3.83 (d, *J* = 14.5 Hz, 1H), 3.72 (d, *J* = 14.5 Hz, 1H), 3.62 (d, *J* = 16.0 Hz, 1H), 3.46 (d, *J* = 11.7 Hz, 1H), 3.29 (d, *J* = 16.0 Hz,, 1H), 3.16 (d, *J* = 11.7 Hz, 1H), 2.40 (s, 3H), 1.77 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.3, 152.5, 143.7, 142.9, 135.7, 133.4, 131.8, 129.8, 128.8, 127.8, 127.3, 127.2, 125.8, 125.7, 124.9, 122.8, 121.4, 54.3, 48.5, 44.6, 44.3, 21.6, 20.9.

ESI-MS: Calcd for $C_{27}H_{26}N_2O_2S_2$ $[M+H]^+$: 475.1. Found: 474.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



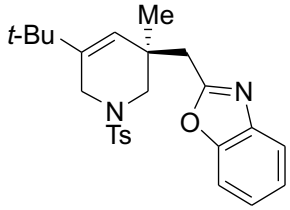


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	19.294	10844394	50.005
2	32.274	10842320	49.995
Total		21686714	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.520	8985496	94.287
2	30.699	544443	5.713
Total		9529938	100.000



(*R*)-*N*-Tosyl-5-*t*-butyl-3-methyl-3-(benzoxazol-2-ylmethyl)-4,5-didehydropiperidine 3g

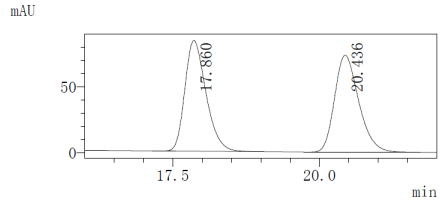
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as white solid. 39.8mg, 91% yield. 80% *ee*. $[\alpha]^{21}_{D} = +49.5^{o}$ (*c* = 3.8, $CHCl_3$).

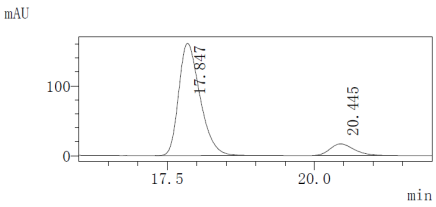
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.64 (m, 3H), 7.47 (d, *J* = 6.0 Hz, 1H), 7.36-7.26 (m, 4H), 5.33 (s, 1H), 3.59 (d, *J* = 15.4 Hz, 1H), 3.42 (d, *J* = 15.4 Hz, 1H), 3.25 (d, *J* = 11.4 Hz, 1H), 3.07 (d, *J* = 14.2 Hz, 1H), 2.95 (d, *J* = 14.2 Hz, 1H), 2.75 (d, *J* = 11.3 Hz, 1H), 2.42 (s, 3H), 1.16 (s, 3H), 0.99 (s, 9H)

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.4, 150.9, 143.7, 141.4, 141.3, 133.4, 129.8, 127.8, 125.0, 124.7, 124.2, 119.8, 110.4, 53.1, 44.5, 38.9, 36.6, 34.7, 29.2, 24.8, 21.6.

ESI-MS: Calcd for $C_{25}H_{30}N_2O_3S$ $[M+H]^+$: 439.2 Found: 438.9.

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



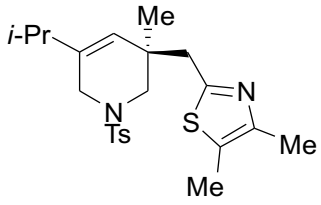


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.860	2105804	50.008
2	20.436	2105099	49.992
Total		4210903	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.847	4037554	89.812
2	20.445	458013	10.188
Total		4495567	100.000



(*R*)-*N*-Tosyl-5-*i*-propyl-3-methyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3h

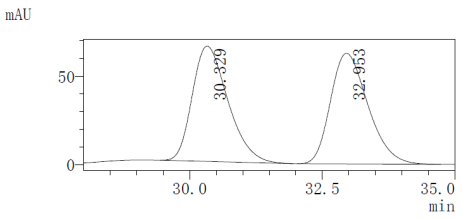
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 37.6mg, 90% yield. 88% ee. $[\alpha]^{26}_{D}$ = -30.0° (*c* = 3.7, $CHCl_3$).

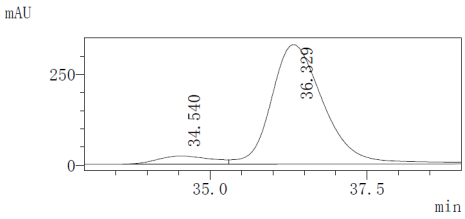
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.22 (t, *J* = 1.4 Hz, 1H), 3.47 (d, *J* = 15.5, Hz, 1H), 3.33 (d, *J* = 15.5, 1H), 3.07 (d, *J* = 11.3 Hz, 1H), 3.02 (d, *J* = 14.0 Hz, 1H), 2.88 (d, *J* = 14.0 Hz, 1H), 2.68 (d, *J* = 11.3 Hz, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 2.26 (s, 3H), 2.17-2.07 (m, 1H), 1.04 (s, 3H), 0.94 (d, *J* = 11.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.5, 147.5, 143.6, 138.8, 133.3, 129.8, 127.8, 126.1, 126.0, 53.4, 46.1, 43.2, 36.4, 32.7, 24.5, 21.6, 21.6, 21.5, 14.7, 11.3.

ESI-MS: Calcd for $C_{22}H_{30}N_2O_2S_2$ $[M+H]^+$: 419.2, Found: 418.9.

HPLC: Daicel Chirlcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



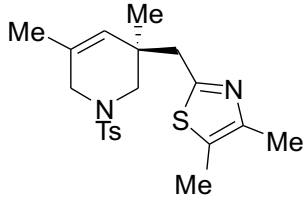


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	30.329	3043458	49.838
2	32.953	3063290	50.162
Total		6106748	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	34.540	1292342	6.232
2	36.329	19444379	93.768
Total		20736721	100.000



(*R*)-*N*-Tosyl-3,5-dimethyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3i

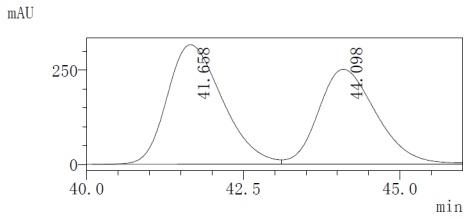
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 32.6 mg, 83% yield. 89% ee. $[\alpha]^{24}_{D}$ = -27.1° (*c* = 2.6, $CHCl_3$).

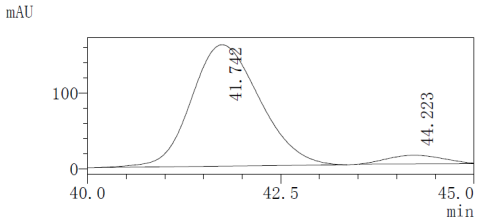
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.24 (t, *J* = 1.8 Hz, 1H), 3.41 (d, *J* = 15.7 Hz, 1H), 3.28 (d, *J* = 15.7 Hz, 1H), 3.09 (d, *J* = 11.4 Hz, 1H), 3.01 (d, *J* = 14.1 Hz, 1H), 2.89 (d, *J* = 14.1 Hz, 1H), 2.70 (d, *J* = 11.4 Hz, 1H), 2.42 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.5, 147.5, 143.6, 133.3, 129.8, 129.0, 128.8, 127.8, 126.1, 53.2, 48.5, 43.0, 36.8, 24.3, 21.6, 20.5, 14.7, 11.3.

ESI-MS: Calcd for $C_{20}H_{26}N_2O_2S_2$ $[M+H]^+$: 391.1. Found: 391.3

HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



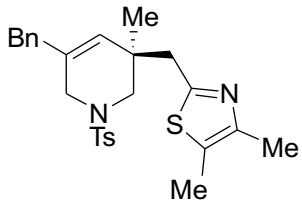


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	41.658	19432751	54.503
2	44.098	16221901	45.497
Total		35654652	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	41.742	9883826	94.540
2	44.223	570799	5.460
Total		10454626	100.000



(*R*)-*N*-Tosyl-5-benzyl-3-methyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3j

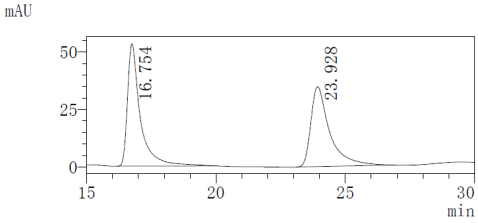
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 37.7 mg, 81% yield, 87% *ee* $[\alpha]^{24}_D$ = -39.1° (*c* = 3.7, $CHCl_3$).

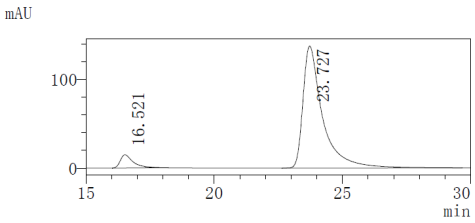
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.59 (m, 2H), 7.32-7.15 (m, 5H), 7.12-7.04 (m, 2H), 5.29 (t, *J* = 1.7 Hz, 1H), 3.42 (d, *J* = 15.7 Hz, 1H), 3.32 (d, *J* = 15.6 Hz, 1H), 3.28-3.18 (m, 2H), 3.10 (d, *J* = 11.5 Hz, 1H), 3.05 (d, *J* = 14.1 Hz, 1H), 2.91 (d, *J* = 14.0 Hz, 1H), 2.76 (d, *J* = 11.4 Hz, 1H), 2.41 (s, 3H), 2.32 (s, 3H), 2.25 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.3, 147.6, 143.6, 138.2, 133.4, 132.5, 130.4, 129.8, 128.9, 128.6, 127.8, 126.5, 126.1, 53.2, 47.2, 43.0, 41.3, 36.9, 24.5, 21.6, 14.7, 11.3.

ESI-MS: Calcd for $C_{26}H_{30}N_2O_2S_2$ $[M+Na]^+$: 489.2. Found: 488.9

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



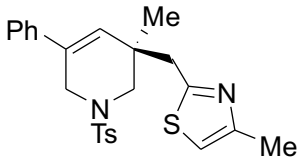


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.754	1840298	51.081
2	23.928	1762420	48.919
Total		3602718	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.521	512821	6.517
2	23.727	7355557	93.483
Total		7868377	100.000



(*R*)-*N*-Tosyl-5-phenyl-3-methyl-3-(4-methylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3k

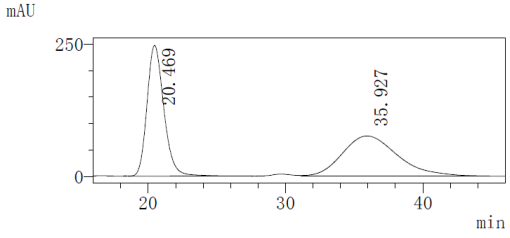
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as colorless oil. 37.6 mg, 86% yield. 94% ee. $[\alpha]^{22}_{D}$ = -41.7° (*c* = 1.0, $CHCl_3$).

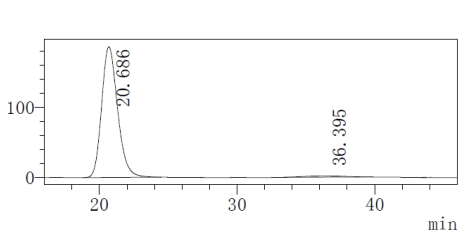
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 6.1 Hz, 2H), 7.37-7.24 (m, 7H), 6.75 (d, *J* = 1.2 Hz, 1H), 5.86 (t, *J* = 2.0 Hz, 1H), 3.91 (d, *J* = 15.7 Hz, 1H), 3.81 (d, *J* = 15.6 Hz, 1H), 3.30-3.21 (m, 2H), 3.11 (d, *J* = 14.1 Hz, 1H), 2.84 (d, *J* = 11.4 Hz, 1H), 2.45 (s, 3H), 2.43 (s, 3H), 1.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.4, 152.5, 143.8, 138.4, 133.2, 132.6, 130.9, 129.9, 128.7, 128.1, 127.9, 125.6, 113.6, 53.1, 46.7, 43.1, 37.4, 24.5, 21.7, 17.2.

ESI-MS: Calcd for $C_{24}H_{26}N_2O_2S_2$ $[M+H]^+$: 439.1. Found: 438.9.

HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



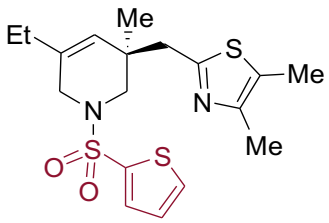


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.469	20992126	49.910
2	35.927	21068024	50.090
Total		42060151	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.686	14944611	97.209
2	36.395	429110	2.791
Total		15373721	100.000



(*R*)-*N*-(2-Thienyl)sulfonyl-5-ethyl-3-methyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3l

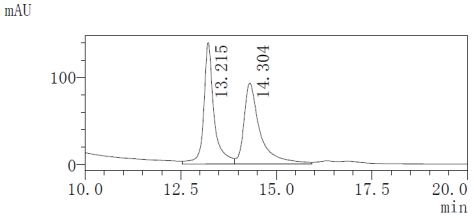
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 5) as white solid. 25.0 mg, 63% yield. 92% ee. $[\alpha]^{26}_{D}$ = -38.0 ° (*c* = 1.2, $CHCl_3$).

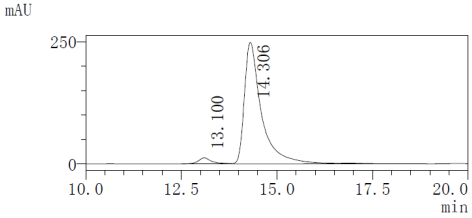
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64-7.54 (m, 2H), 7.14 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.26 (t, *J* = 1.7 Hz, 1H), 3.51 (d, *J* = 15.7 Hz, 1H), 3.42 (d, *J* = 15.6 Hz, 1H), 3.13 (d, *J* = 11.4 Hz, 1H), 3.04 (d, *J* = 14.1 Hz, 1H), 2.92 (d, *J* = 14.1 Hz, 1H), 2.78 (d, *J* = 11.3 Hz, 1H), 2.33 (s, 3H), 2.29 (s, 3H), 1.96 (q, *J* = 7.5 Hz, 2H), 1.09 (s, 3H), 1.00 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.4, 147.6, 136.7, 134.4, 132.5, 132.0, 127.7, 127.1, 126.2, 53.5, 47.5, 43.2, 36.7, 27.3, 24.4, 14.7, 12.2, 11.4.

ESI-MS: Calcd for $C_{18}H_{24}N_2O_2S_3$ $[M+H]^+$: 397.1. Found: 396.8

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



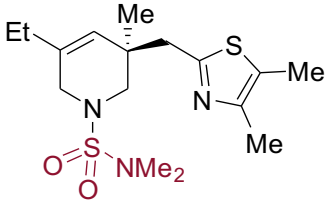


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	13.215	2609800	48.993
2	14.304	2717043	51.007
Total		5326842	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	13.100	304665	3.762
2	14.306	7793000	96.238
Total		8097665	100.000



(*R*)-*N*-(Dimethylamino)sulfonyl-5-ethyl-3-methyl-3-(4,5-dimethylthiazol-2-ylmethyl)-4,5-didehydropiperidine 3m

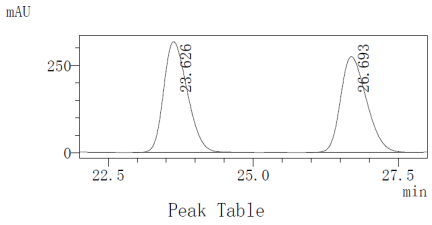
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) with as white solid. 24.3 mg, 68% yield. 89% ee. $[\alpha]^{25}_{D}$ =-28.2^{o} (*c* = 1.6, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.29 (t, *J* = 1.7 Hz, 1H), 3.57 (t, *J* = 2.2 Hz, 2H), 3.25 (d, *J* = 11.9 Hz, 1H), 3.00-2.87 (m, 3H), 2.85 (s, 6H), 2.31 (s, 6H), 2.25(s, 6H), 1.99 (q, *J* = 7.4 Hz, 2H), 1.06-0.98 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 147.6, 135.2, 126.9, 126.0, 53.5, 47.9, 43.1, 38.3, 36.6, 27.4, 24.6, 14.7, 12.2, 11.3.

ESI-MS: Calcd for $C_{16}H_{27}N_3O_2S_2$ [M+H^{+}]: 358.2. Found: 357.9.

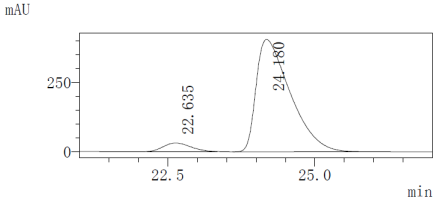
HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

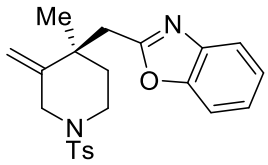
Peak#	Ret. Time	Area	Area%
1	23.626	8985412	51.358
2	26.693	8510269	48.642
Total		17495681	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.635	987938	5.726
2	24.180	16265713	94.274
Total		17253651	100.000

(b) A general procedure for synthesis of substituted 3-methylenepiperidines, a didehydroazepane and a dihydropyran derivative: in an argon-filled glove box, $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 5 mol%), Josiphos **L4** (0.006 mmol, 4.44 mg, 6 mol%) and dry CH_2Cl_2 (0.5 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 15 min at RT, LiO*t*-Bu (16.0 mg, 0.2 mmol), Ag_3PO_4 (42 mg, 0.1 mmol), dienyl iodide (0.1 mmol) and heteroarene (0.2 mmol, 2 equiv) were added. The resulting mixture was capped and vigorously stirred in an oil bath maintained at 80 ^{o}C for 24 hours. After the mixture was cooled down to RT, the reaction mixture was passed through a pad of silica gel with washings of 1:1 hexanes/ethyl acetate. After the filtrate was concentrated in vacuo, the reaction mixture was subjected to flash chromatography using ethyl acetate/hexanes (1:3) as eluent. The enantioselectivity of the purified product was determined by chiral HPLC analysis using Daicel Chiralcel and Chiralpak columns. Similar results were obtained with Schlenk tubes and a vacuum manifold.



(*R*)-*N*-Tosyl-4-(benzoxazol-2-ylmethyl)-4-methyl-3-methylenepiperidine 3n

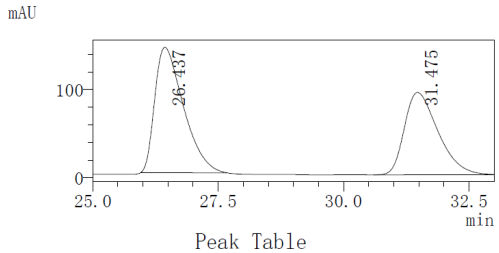
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 13.9 mg (0.05 mmol), 70% yield. 90% ee. $[\alpha]^{25}_{D}$ = -27.0° (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.67 (m, 2H), 7.65 (dd, *J* = 5.9, 3.2 Hz, 1H), 7.46 (dd, *J* = 6.2, 3.0 Hz, 1H), 7.38-7.24 (m, 4H), 5.03 (s, 1H), 4.90 (s, 1H), 3.90 (d, *J* = 12.4 Hz, 1H), 3.56-3.41 (m, 2H), 3.10-2.96 (m, 2H), 2.91 (d, *J* = 14.1 Hz, 1H), 2.45 (s, 3H), 1.80 (ddd, *J* = 13.8, 5.3, 3.4 Hz, 1H), 1.67 (ddd, *J* = 13.8, 5.3, 3.4 Hz, 1H), 1.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.1, 150.8, 145.9, 143.8, 141.2, 133.5, 129.9, 128.0, 124.9, 124.4, 119.8, 112.7, 110.5, 50.0, 42.6, 38.2, 36.8, 36.7, 24.9, 21.7.

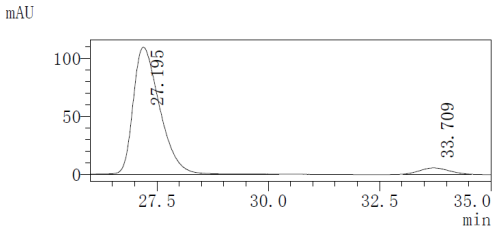
ESI-MS: Calcd for $C_{22}H_{24}N_2O_3S$ $[M+Na]^+$: 419.2. Found: 418.8.

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



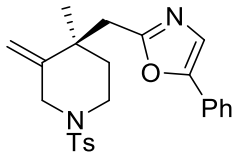
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	26.437	5664640	56.538
2	31.475	4354603	43.462
Total		10019243	100.000



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	27.195	4517481	95.045
2	33.709	235535	4.955
Total		4753016	100.000



(*R*)-*N*-Tosyl-4-methyl-3-methylene-4-(5-phenyloxazol-2-ylmethyl)piperidine 3o

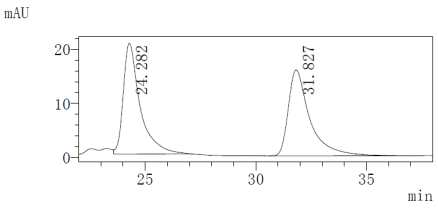
The product was isolated by flash chromatography (ethyl acetate/hexane 1:3) as colorless oil. 24.1mg, 57% yield. 88% ee. $[\alpha]^{26}_{D}$ = -15.0° (*c* = 1.0, $CHCl_3$).

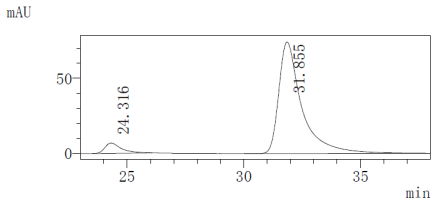
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.66 (m, 2H), 7.58-7.51 (m, 2H), 7.41 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.37-7.30 (m, 3H), 7.18 (s, 1H), 5.04 (s, 1H), 4.90 (s, 1H), 3.92 (dd, *J* = 13.0, 1.5 Hz, 1H), 3.54-3.41 (m, 2H), 3.06-2.97 (m, 1H), 2.91 (d, *J* = 14.3 Hz, 1H), 2.80 (d, *J* = 14.3 Hz, 1H), 2.44 (s, 3H), 1.78-1.68 (m, 1H), 1.66-1.60 (m, 1H), 1.18 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.4, 151.4, 146.1, 143.8, 133.5, 129.9, 129.1, 128.5, 128.1, 128.0, 124.1, 121.9, 112.5, 50.0, 42.6, 38.1, 36.7, 36.4, 24.9, 21.7.

ESI-MS: Calcd for $C_{22}H_{24}N_2O_3S$ $[M+H]^+$: 423.1. Found: 422.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



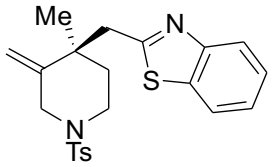


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	24.282	1083025	50.052
2	31.827	1080765	49.948
Total		2163790	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	24.316	331025	6.087
2	31.855	5107079	93.913
Total		5438104	100.000



(*R*)-*N*-Tosyl-4-(benzothiazol-2-ylmethyl)-4-methyl-3-methylenepiperidine 3p

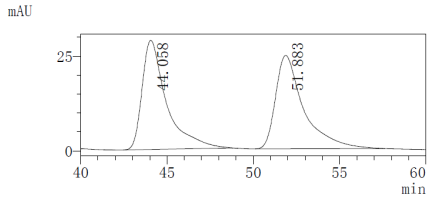
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 13.9 mg (0.05 mmol), 70% yield. 90% ee. $[\alpha]^{26}_D$ = -24.4^o (*c* = 1.6, $CHCl_3$).

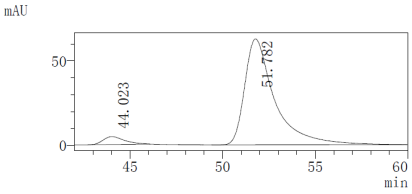
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98-7.91 (m, 1H), 7.85-7.78 (m, 1H), 7.73-7.66 (m, 2H), 7.44 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.37-7.33 (m, 3H), 5.08 (s, 1H), 4.91 (s, 1H), 3.95 (d, *J* = 13.9 Hz, 1H), 3.56-3.41 (m, 2H), 3.16 (d, *J* = 14.1 Hz, 1H), 3.13-3.00 (m, 2H), 2.44 (s, 3H), 1.80 (ddd, *J* = 13.8, 5.2, 3.4 Hz, 1H), 1.66 (ddd, *J* = 13.8, 5.2, 3.4 Hz, 1H), 1.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 167.0, 153.1, 145.9, 143.8, 135.5, 133.5, 129.9, 127.9, 126.1, 125.1, 122.8, 121.4, 113.3, 50.0, 42.6, 41.9, 38.4, 36.9, 25.0, 21.7.

ESI-MS: Calcd for $C_{22}H_{24}N_2O_3S$ $[M+H]^+$: 425.1. Found: 424.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



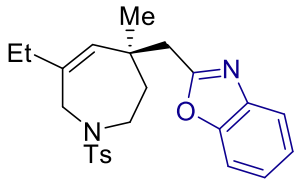


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	44.058	2837398	50.343
2	51.883	2798776	49.657
Total		5636174	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	44.023	366833	4.916
2	51.782	7094508	95.084
Total		7461341	100.000



(*R*)-*N*-Tosyl-6-ethyl-4-methyl-4-(benzoxazol-2-ylmethyl)-5,6-didehydroazepane 3q

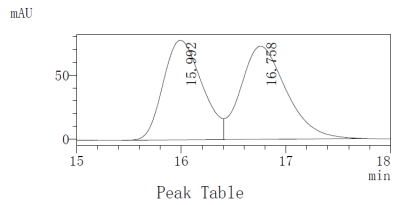
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 30.0 mg, 70% yield. 84% *ee*. $[\alpha]^{24}_{D}$ = -36.88 ^{o} (*c* = 2.37, $CHCl_3$).

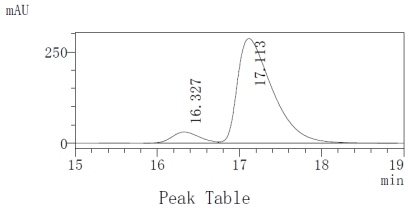
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71-7.63 (m, 3H), 7.47 (d, *J* = 6.0 Hz, 1H), 7.33-7.24 (m, 4H), 5.28 (s, 1H), 3.70 (s, 2H), 3.56-3.50 (m, 1H), 3.39-3.33 (m, 1H), 3.07 (d, *J* = 14.2 Hz, 1H), 2.94 (d, *J* = 14.2 Hz, 1H), 2.08-1.91 (m, 3H), 1.83 (dd, *J* = 14.8, 7.6 Hz, 1H), 1.16 (s, 3H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.7, 150.9, 143.3, 141.4, 138.8, 135.6, 133.1, 129.8, 127.3, 124.7, 124.2, 119.8, 110.5, 47.3, 44.8, 40.5, 39.5, 35.6, 31.3, 27.3, 21.6, 12.9.

ESI-MS: Calcd for $C_{24}H_{28}N_2O_3S$ $[M+H]^+$: 425.2. Found: 425.1.

HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



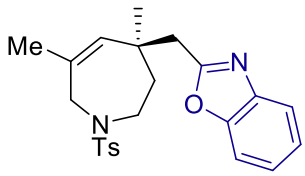


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	15.992	2009683	47.818
2	16.758	2193066	52.182
Total		4202748	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.327	712379	7.750
2	17.113	8479078	92.250
Total		9191457	100.000



(*R*)-*N*-Tosyl-4,6-dimethyl-4-(benzoxazol-2-ylmethyl)-5,6-didehydroazepane 3r

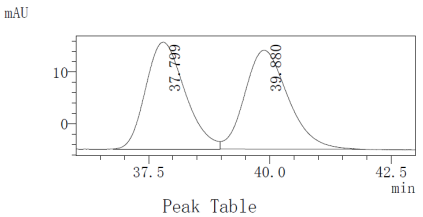
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 17.4 mg, 85% yield. 80% *ee*. $[\alpha]^{24}_{D}$ = 33.8 ^{o} (*c* = 1.42, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.64 (m, 3H), 7.48 (dd, *J* = 6.1, 3.2 Hz, 1H), 7.33-7.24 (m, 4H), 5.31 (d, *J* = 2.2 Hz, 1H), 3.72 (d, *J* = 16.5 Hz, 1H), 3.66 (d, *J* = 16.6 Hz, 1H), 3.57 (ddd, *J* = 12.8, 7.8, 5.2 Hz, 1H), 3.35 (ddd, *J* = 12.3, 7.3, 5.2 Hz, 1H), 3.07 (d, *J* = 14.3 Hz, 1H), 2.93 (d, *J* = 14.2 Hz, 1H), 2.41 (s, 3H), 1.97 (ddd, *J* = 14.8, 7.3, 5.2 Hz, 1H), 1.84 (ddd, *J* = 14.7, 7.8, 5.2 Hz, 1H), 1.74 (m, 1H), 1.72 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 150.9, 143.3, 141.4, 135.6, 134.6, 133.2, 129.8, 127.3, 124.7, 124.2, 119.8, 110.5, 48.3, 44.8, 40.2, 39.5, 35.9, 27.3, 24.5, 21.6.

ESI-MS: Calcd for $C_{23}H_{26}N_2O_3S$ $[M+H]^+$: 411.2. Found: 411.1.

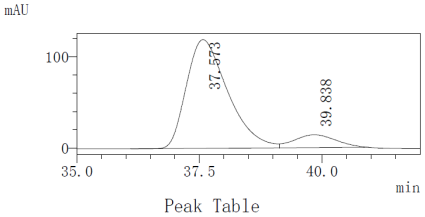
HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

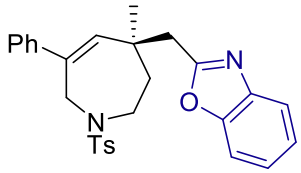
Peak#	Ret. Time	Area	Area%
1	37.799	1163451	49.569
2	39.880	1183677	50.431
Total		2347127	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	37.573	7010901	89.229
2	39.838	846333	10.771
Total		7857234	100.000



(*R*)-*N*-Tosyl-4-methyl-6-phenyl-4-(benzoxazol-2-ylmethyl)-5,6-didehydroazepane 3s

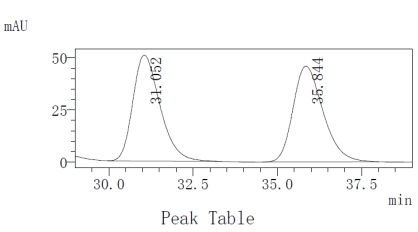
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 30.0 mg, 60% yield. 84% *ee*. $[\alpha]^{24}_{D}$ = -6.0 ^{o} (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.65 (m, 3H), 7.50 (dd, *J* = 6.0, 3.1 Hz, 1H), 7.43-7.23 (m, 10H), 5.71 (s, 1H), 4.25 (d, *J* = 16.9 Hz, 1H), 4.14 (d, *J* = 16.7 Hz, 1H), 3.62-3.44 (m, 2H), 3.16 (d, *J* = 14.2 Hz, 1H), 3.02 (d, *J* = 14.2 Hz, 1H), 2.40 (s, 3H), 2.09 (m, 1H), 1.94 (m, 1H), 1.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 150.9, 143.5, 142.6, 141.4, 138.4, 138.2, 135.5, 129.8, 128.6, 127.6, 127.4, 127.1, 124.8, 124.3, 119.9, 110.5, 47.6, 44.7, 40.7, 40.4, 35.2, 27.0, 21.6.

ESI-MS: Calcd for $C_{28}H_{28}N_2O_3S$ $[M+H]^+$: 473.2. Found: 473.1.

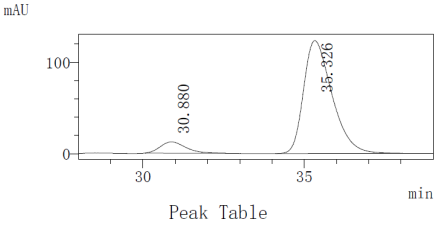
HPLC: Daicel Chiralcel OZ-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

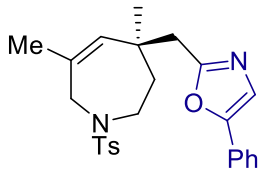
Peak#	Ret. Time	Area	Area%
1	31.052	2854291	50.165
2	35.844	2835474	49.835
Total		5689765	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	30.880	664319	8.105
2	35.326	7531918	91.895
Total		8196238	100.000



(*R*)-*N*-Tosyl-4,6-dimethyl-4-(5-phenyloxazole-2-ylmethyl)-5,6-didehydroazepane 3u

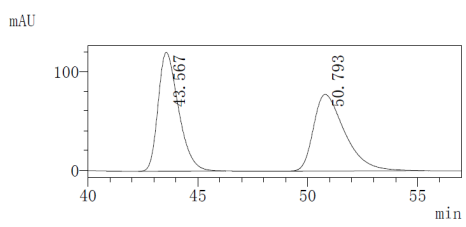
The product was isolated by flash chromatography (ethyl acetate/hexane 1:3) as colorless oil. 15.9 mg, 73% yield. 85% *ee*. $[\alpha]^{24}_D$ = 35.7 ° (*c* = 1.22, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.68-7.62 (m, 2H), 7.48 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.31-7.24 (m, 4H), 5.29 (s, 1H), 3.71 (d, *J* = 16.6 Hz, 1H), 3.63 (d, *J* = 16.7 Hz, 1H), 3.44 (ddd, *J* = 13.3, 8.5, 5.2 Hz, 1H), 3.39-3.25 (m, 2H), 3.12 (d, *J* = 14.2 Hz, 1H), 2.40 (s, 3H), 1.92-1.71 (m, 5H), 1.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.1, 143.5, 138.3, 137.4, 135.5, 134.6, 134.0, 129.8, 127.3, 125.9, 125.9, 122.3, 122.2, 114.8, 107.0, 48.4, 44.5, 43.6, 40.7, 36.0, 27.2, 24.6, 21.6.

ESI-MS: Calcd for $C_{25}H_{28}N_2O_3S$ $[M+H]^+$: 437.2. Found: 437.1.

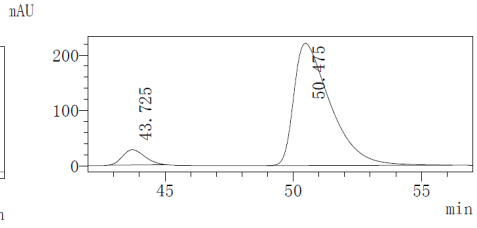
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 85/15, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

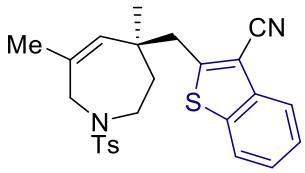
Peak#	Ret. Time	Area	Area%
1	43.567	7790820	50.397
2	50.793	7668025	49.603
Total		15458844	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	43.725	1652747	7.038
2	50.475	21831471	92.962
Total		23484218	100.000



(*R*)-*N*-Tosyl-4,6-dimethyl-4-(benzo[b]thiophene-3-carbonitrile -2-ylmethyl)-5,6-didehydroazepane 3v

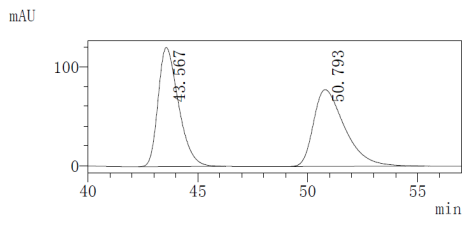
The product was isolated by flash chromatography (ethyl acetate/hexane 1:8) as colorless oil. 17.1 mg, 76% yield. 77% *ee*. $[\alpha]^{24}_{D}$ = 32.9 º (*c* = 0.99, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.67 (m, 2H), 7.62 (dd, *J* = 7.2, 1.7 Hz, 2H), 7.49-7.40 (m, 2H), 7.39-7.23 (m, 5H), 5.34 (s, 1H), 3.73 (s, 2H), 3.62-3.51 (m, 1H), 3.45-3.34 (m, 1H), 3.00 (dd, *J* = 14.4, 1.6 Hz, 1H), 2.86 (dd, *J* = 14.4, 1.6 Hz, 1H), 2.44 (s, 3H), 1.93 (m, 1H), 1.84 (m, 1H) 1.79 (s, 3H), 1.17 (d, *J* = 1.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1, 151.2, 143.3, 135.7, 134.8, 132.9, 129.8, 129.0, 128.3, 128.3, 127.3, 124.1, 122.0, 48.3, 44.7, 40.0, 39.5, 35.8, 27.2, 24.5, 21.6.

ESI-MS: Calcd for $C_{25}H_{26}N_2O_2S_2$ $[M+H]^+$: 451.2. Found: 451.1.

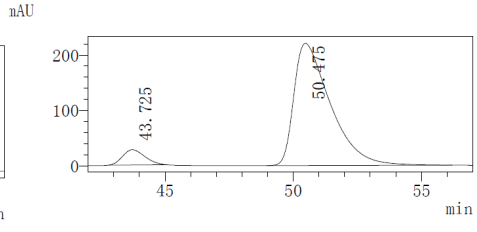
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

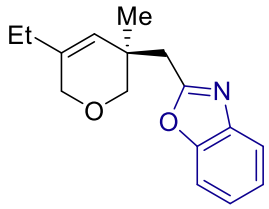
Peak#	Ret. Time	Area	Area%
1	43.567	7790820	50.397
2	50.793	7668025	49.603
Total		15458844	100.000



Peak Table

PDA Ch1 254nm

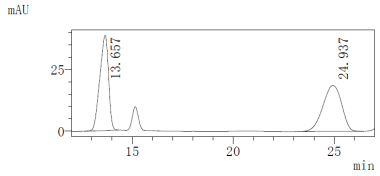
Peak#	Ret. Time	Area	Area%
1	43.725	1652747	7.038
2	50.475	21831471	92.962
Total		23484218	100.000



(*R*)-5-Ethyl-3-methyl-3-(benzoxazol-2-ylmethyl)-3,6-didehydropyran 6a

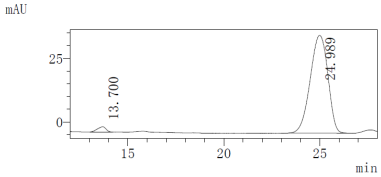
When (*R*)-Xyl-Segphos was used, the product was isolated by flash chromatography (ethyl acetate/hexane 1: 10) as white solid. 25.0 mg, 80% yield. 95% ee. $[\alpha]^{26}_{D} = 37.6^{o}$ (*c* = 2.1, $CHCl_3$)

HPLC: Daicel Chiralcel OJ-H, *n*-hexane/isopropanol 98/2, flow rate = 0.5 mL/min.



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	13.657	1161928	49.206
2	24.937	1199434	50.794
Total		2361361	100.000



Peak Table

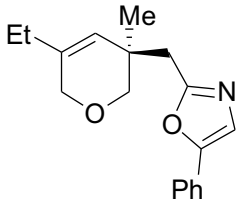
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	13.700	62190	2.465
2	24.989	2461177	97.535
Total		2523367	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 6.1, 3.1 Hz, 1H), 7.49 (dd, *J* = 6.1, 3.1 Hz, 1H), 7.32-7.29 (m, 2H), 5.38 (s, 1H), 4.00 (s, 2H), 3.80 (dd, *J* = 11.1, 2.6 Hz, 1H), 3.39 (dd, *J* = 11.0, 2.5 Hz, 1H), 3.05-2.97 (m, 2H), 1.91 (q, *J* = 7.5 Hz, 2H), 1.07 (s, 3H), 1.00 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 151.0, 141.5, 138.3, 125.5, 124.6, 124.2, 119.8, 110.5, 73.9, 68.2, 38.2, 35.3, 25.6, 23.4, 12.1.

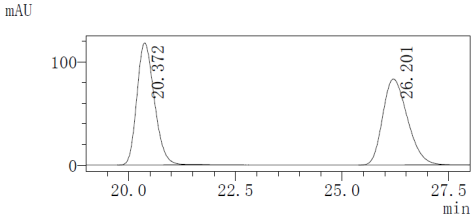
ESI-MS: Calcd for $C_{18}H_{24}N_2O_2S_3$ $[M+H]^+$: 397.1. Found: 396.8



(*R*)-5-Ethyl-3-methyl-3-(5-phenyloxazole-2-ylmethyl)-3,6-didehydropyran 6b

When (*R*)-Xyl-Segphos was used, the product was isolated by flash chromatography (ethyl acetate/hexane 1: 10) as white solid. 25.0 mg, 70% yield. 82% ee. $[\alpha]^{25}_{D} = 35.7^{o}$ (*c* = 1.2, $CHCl_3$).

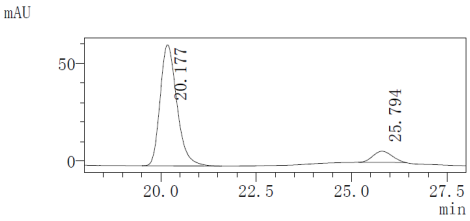
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 95/5, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.372	3387987	50.076
2	26.201	3377638	49.924
Total		6765625	100.000



Peak Table

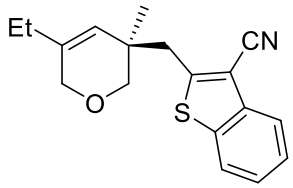
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	20.177	1891397	90.491
2	25.794	198756	9.509
Total		2090153	100.000

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (dd, J = 6.1, 3.1 Hz, 1H), 7.49 (dd, J = 6.1, 3.1 Hz, 1H), 7.32-7.29 (m, 2H), 5.38 (s, 1H), 4.00 (s, 2H), 3.80 (dd, J = 11.1, 2.6 Hz, 1H), 3.39 (dd, J = 11.0, 2.5 Hz, 1H), 3.05-2.97 (m, 2H), 1.91 (q, J = 7.5 Hz, 2H), 1.07 (s, 3H), 1.00 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 151.0, 141.5, 138.3, 125.5, 124.6, 124.2, 119.8, 110.5, 73.9, 68.2, 38.2, 35.3, 25.6, 23.4, 12.1.

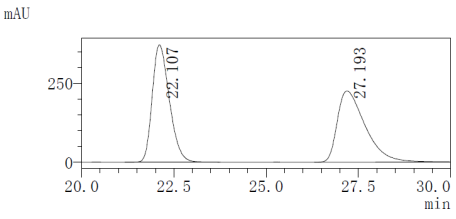
ESI-MS: Calcd for $C_{18}H_{21}NO_2$ $[M+H]^+$: 284.1. Found: 283.9



(*R*)-5-Ethyl-3-methyl-3-(3-cyanobenzothien-2-ylmethyl)-3,6-didehydropyran 6c

When (*R*)-Xyl-Segphos and AgOTf 1 equiv. was used, the product was isolated by flash chromatography (ethyl acetate/hexane 1: 10) as white solid. 22.3 mg, 75% yield. 70% ee. when use Ag_3PO_4 get 80% yield, 50% *ee* $[\alpha]^{24}_D$ = 16.4 ^{o} (*c* = 0.7, $CHCl_3$).

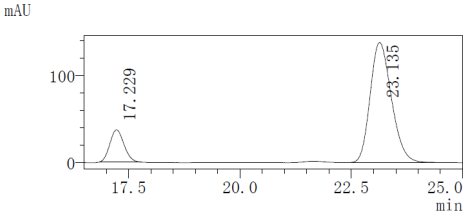
HPLC: Daicel Chiralcel AZ-H, *n*-hexane/isopropanol 98/2, flow rate = 0.5 mL/min.



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	22.107	12011236	50.164
2	27.193	11932559	49.836
Total		23943795	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	17.229	822780	15.159
2	23.135	4604734	84.841
Total		5427515	100.000

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.48 (dd, J = 8.1, 7.2, Hz, 1H), 7.41 (dd, J = 8.3, 7.2 Hz, 1H), 5.34 (h, J = 1.5 Hz, 1H), 4.09-3.94 (m, 2H), 3.74 (d, J =

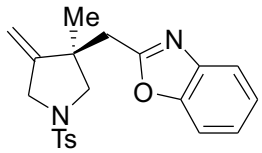
11.0 Hz, 1H), 3.40 (d, J = 11.1 Hz, 1H), 3.34 (d, J = 14.1 Hz, 1H), 3.12 (d, J = 14.1 Hz, 1H), 1.93(q, J = 7.5 Hz, 2H), 1.08 (s, 3H), 1.00 (t, J = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.3, 139.2, 138.2, 137.7, 125.8, 125.8, 124.9, 122.3, 122.2, 114.8, 106.9, 74.2, 68.2, 40.5, 36.5, 25.6, 23.4, 11.9.

ESI-MS: Calcd for $C_{18}H_{19}NOS$ $[M+H]^+$: 298.1. Found: 297.9

IV. Asymmetric synthesis of pyrrolidine derivatives

A general procedure: in an argon-filled glove box, $Pd(dba)_2$ (2.9 mg, 0.005 mmol, 5 mol%), Josiphos **L2** (0.006 mmol, 4.5 mg, 6 mol%) and dry CH_2Cl_2 (0.5 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 15 min at RT, LiO*t*-Bu (16 mg, 0.2 mmol), Ag_3PO_4 (42 mg, 0.1 mmol), dienyl iodide (0.1 mmol) and heteroarene (0.2 mmol, 2 equiv) were added. The resulting mixture was capped and vigorously stirred in an oil bath maintained at 50 or 80 ^oC for 24 hours until almost full conversion (unless stated otherwise). After the mixture was cooled down to RT, the reaction mixture was passed through a pad of silica gel with washings of 1:1 hexanes/ethyl acetate. After the filtrate was concentrated in vacuo, the crude product was subjected to flash chromatography using ethyl acetate/hexanes (1:3) as eluent. The enantioselectivity of the purified product was determined by chiral HPLC analysis using Daicel Chiralcel and Chiralpak columns. Similar results were obtained with Schlenk tubes and a vacuum manifold.



(*R*)-*N*-Tosyl-3-(benzoxazol-2-ylmethyl)-3-methyl-4-methylenepyrrolidine 5a

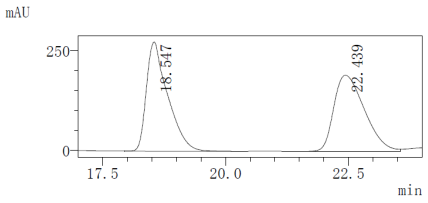
The product was isolated by flash chromatography (ethyl acetate/hexane 1:3) as colorless oil. 32.1 mg, 84% yield. 92% ee. $[\alpha]^{24}_D$ = +36.6 (c = 3.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.67 (m, 2H), 7.67-7.62 (m, 1H), 7.50-7.43 (m, 1H), 7.34-7.24 (m, 4H), 4.94 (s, 1H), 4.87 (s, 1H), 3.93 (ψdt, J = 14.1 2.3 Hz, 1H), 3.88 (ψd, J = 14.1 2.3 Hz, 1H), 3.58 (d, J = 9.5 Hz, 1H), 3.11-3.02 (m, 2H), 2.98 (d, J = 14.6 Hz, 1H), 2.41 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.8, 151.0, 150.8, 143.8, 141.2, 132.6, 129.8, 128.0, 124.9, 124.4, 119.9, 110.5, 107.0, 58.9, 52.0, 45.3, 37.9, 23.8, 21.7.

ESI-MS: Calcd for $C_{21}H_{22}N_2O_3S$ $[M+Na]^+$: 405.1. Found: 404.9

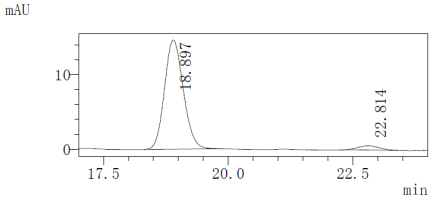
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

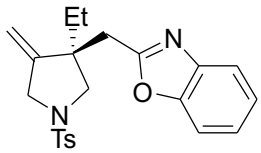
Peak#	Ret. Time	Area	Area%
1	18.547	8274737	50.034
2	22.439	8263556	49.966
Total		16538293	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.897	384379	95.819
2	22.814	16774	4.181
Total		401153	100.000



(*R*)-*N*-Tosyl-3-(benzoxazol-2-ylmethyl)-3-ethyl-4-methylenepyrrolidine 5b

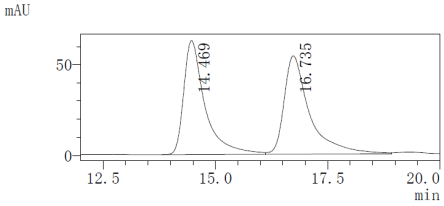
The product was isolated by flash chromatography (ethyl acetate/hexane 1:5) as colorless oil. 33.3 mg, 84% yield. 91% ee. $[\alpha]^{24}_D$ = +36.5° (*c* = 3.1, $CHCl_3$).

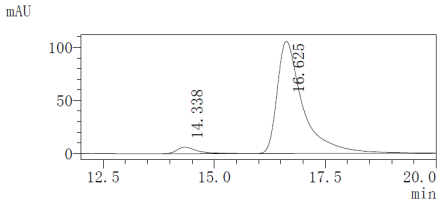
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72-7.66 (m, 2H), 7.63 (m, 1H), 7.44 (m, 1H), 7.33-7.24 (m, 4H), 5.01 (t, *J* = 2.1 Hz, 1H), 4.80 (t, *J* = 2.4 Hz, 1H), 3.92-3.81 (m, 2H), 3.46 (d, *J* = 9.6 Hz, 1H), 3.31 (d, *J* = 9.6 Hz, 1H), 3.14 (d, *J* = 14.8 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.41 (s, 3H), 1.66 (dd, *J* = 14.3, 7.4 Hz, 1H), 1.51 (dd, *J* = 14.3, 7.3 Hz, 1H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.8, 150.7, 148.9, 143.8, 141.2, 132.7, 129.8, 127.9, 124.9, 124.3, 119.9, 110.5, 107.9, 57.6, 52.5, 48.8, 35.3, 29.4, 21.7, 8.7.

ESI-MS: Calcd for $C_{22}H_{24}N_2O_3S$ $[M+Na]^+$: 419.2. Found: 418.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



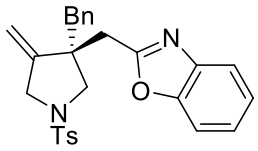


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	14.469	2067493	49.036
2	16.735	2148807	50.964
Total		4216300	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	14.338	196188	4.340
2	16.625	4324778	95.660
Total		4520967	100.000



(*R*)-*N*-Tosyl-3-(benzoxazol-2-ylmethyl)-3-benzyl-4-methylenepyrrolidine 5c

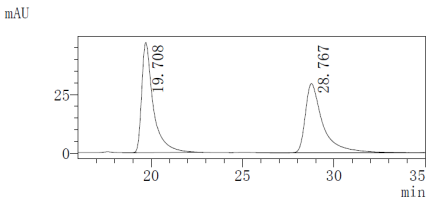
The product was isolated by flash chromatography (ethyl acetate/hexane 1:30) as colorless oil. 43.8 mg, 95% yield. 90% ee. $[\alpha]^{23}_{D}$ = +5.0 ^{o} (*c* = 4.3, $CHCl_3$).

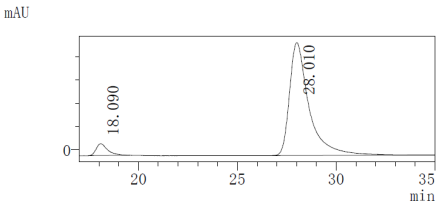
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71-7.64 (m, 3H), 7.49-7.44 (m, 1H), 7.36-7.18 (m, 9H), 4.96 (s, 1H), 4.59 (s, 1H), 3.95 (ψdt, *J* = 14.0, 2.2 Hz, 1H), 3.85 (ψdt, *J* = 14.0, 2.2 Hz, 1H), 3.54 (d, *J* = 9.7 Hz, 1H), 3.33 (d, *J* = 9.6 Hz, 1H), 3.11 (d, *J* = 15.2 Hz, 1H), 3.00-2.88 (m, 3H), 2.42 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.7, 150.6, 148.3, 143.8, 141.2, 136.7, 132.6, 130.8, 129.8, 128.2, 127.9, 126.9, 124.9, 124.3, 119.9, 110.5, 108.7, 57.5, 52.4, 49.3, 42.2, 34.5, 21.7.

ESI-MS : Calcd for $C_{27}H_{26}N_2O_3S$ $[M+Na]^+$: 481.2, Found: 480.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



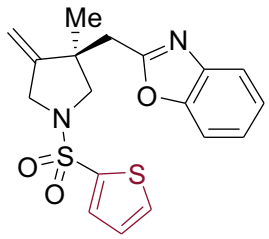


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	19.708	2058943	51.352
2	28.767	1950566	48.648
Total		4009509	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.090	102889	5.732
2	28.010	1692056	94.268
Total		1794944	100.000



(*R*)-*N*-(Thien-2-yl)sulfonyl-3-(benzoxazol-2-ylmethyl)-3-methyl-4-methylenepyrrolidine 5d

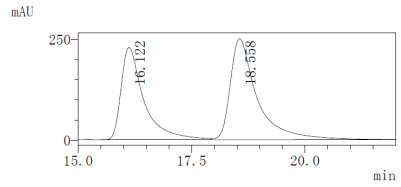
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as white solid. 32.9 mg, 88% yield. 84% *ee*. $[\alpha]^{21}_{D} = +30.1^{o}$ (*c* = 1.7, $CHCl_3$). Crystals suitable for X-Ray diffraction were obtained with vapor diffusion of hexane into a concentrated sample in ethyl acetate.

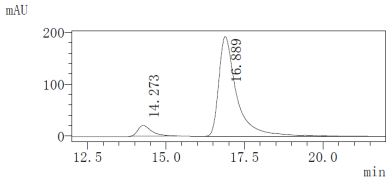
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69-7.63 (m, 1H), 7.62-7.57 (m, 2H), 7.51-7.45 (m, 1H), 7.34-7.28 (m, 2H), 7.13 (dd, *J* = 5.0, 3.8 Hz, 1H), 4.98 (d, *J* = 2.2 Hz, 1H), 4.90 (d, *J* = 2.5 Hz, 1H), 4.04 (dt, *J* = 14.2, 2.4 Hz, 1H), 3.96 (dt, *J* = 14.2, 2.2 Hz, 1H), 3.65 (d, *J* = 9.7 Hz, 1H), 3.15 (d, *J* = 9.7 Hz, 1H), 3.07 (d, *J* = 14.7 Hz, 1H), 3.01 (d, *J* = 14.7 Hz, 1H), 1.24 (s, 3H)

^{13}C NMR (126 MHz, $CDCl_3$): δ 163.7, 150.8, 150.6, 141.2, 135.8, 132.8, 132.2, 127.8, 125.0, 124.4, 119.9, 110.6, 107.3, 59.1, 52.2, 45.4, 37.9, 23.9.

ESI-MS: Calcd for $C_{18}H_{18}N_2O_3S_2$ $[M+Na]^+$: 397.1. Found: 396.8.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



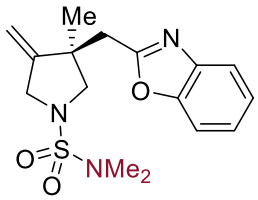


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	16.122	8063961	43.674
2	18.558	10399969	56.326
Total		18463930	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	14.273	627558	7.532
2	16.889	7704422	92.468
Total		8331980	100.000



(*R*)-*N*-(Dimethylamino)sulfonyl-3-(benzoxazol-2-ylmethyl)-3-methyl-4-methylenepyrrolidine 5e

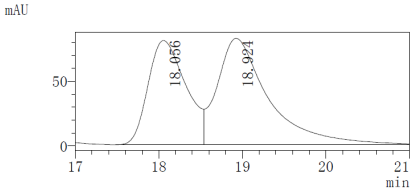
The product was isolated by flash chromatography (ethyl acetate/hexane 1:4) as white solid. 37.3 mg, 91% yield. 90% ee. $[\alpha]^{25}_{D} = +12.7^{o}$ (*c* = 2.5, $CHCl_3$).

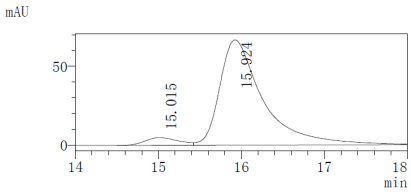
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70-7.65 (m, 1H), 7.52-7.46 (m, 1H), 7.34-7.28 (m, 2H), 5.02 (d, *J* = 2.2 Hz, 1H), 4.95 (d, *J* = 2.5 Hz, 1H), 4.07-4.01 (m, 2H), 3.63 (d, *J* = 9.7 Hz, 1H), 3.21 (d, *J* = 9.7 Hz, 1H), 3.14-3.08 (m, 2H), 2.82 (s, 6H), 1.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 164.0, 151.4, 150.9, 141.3, 124.9, 124.4, 119.9, 110.6, 106.8, 59.3, 52.5, 45.4, 38.2, 38.1, 23.7.

ESI-MS: Calcd for $C_{16}H_{21}N_3O_3S$ $[M+Na]^+$: 358.1, Found: 357.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min.



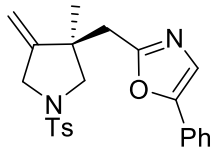


PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	18.056	2541904	41.853
2	18.924	3531556	58.147
Total		6073460	100.000

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	15.015	134527	5.211
2	15.924	2447009	94.789
Total		2581535	100.000



(*R*)-*N*-Tosyl-3-[(5-phenyloxazol-2-yl)methyl]-3-methyl-4-methylenepyrrolidine 5f

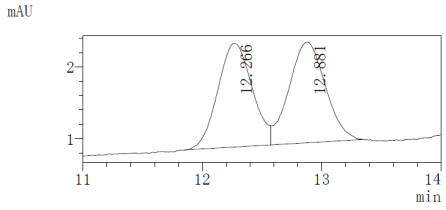
The product was isolated by flash chromatography (ethyl acetate/hexane 1:3) as colorless oil. 31.4 mg, 77% yield, 91% *ee* $[\alpha]^{26}_D$ = +33.4° (*c* = 1.4, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.67 (m, 2H), 7.61-7.54 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.36-7.24 (m, 3H), 7.20 (s, 1H), 4.95 (s, 1H), 4.86 (s, 1H), 3.95 (ψdt, *J* = 14.0, 2.2 Hz, 1H), 3.87 (ψdt, *J* = 14.0, 2.2 Hz, 1H), 3.52 (d, *J* = 9.5 Hz, 1H), 3.04-2.85 (m, 3H), 2.40 (s, 3H), 1.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.2, 151.4, 151.0, 143.8, 132.7, 129.8, 129.0, 128.5, 128.1, 128.0, 124.2, 122.0, 106.9, 58.9, 52.1, 45.4, 37.6, 23.6, 21.7.

ESI-MS: Calcd for $C_{23}H_{24}N_2O_2S$ $[M+H]^+$: 409.2. Found: 408.9

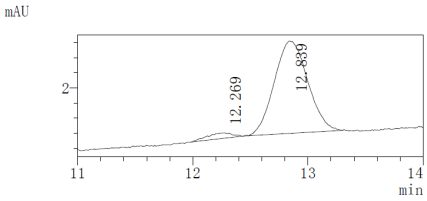
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 90/10, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

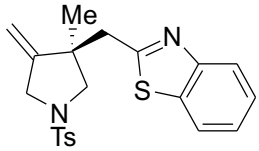
Peak#	Ret. Time	Area	Area%
1	12.266	29040	49.491
2	12.881	29638	50.509
Total		58678	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	12.269	1174	4.541
2	12.839	24681	95.459
Total		25855	100.000



(*R*)-*N*-Tosyl-3-[(benzothiazol-2-yl)methyl]-3-methyl-4-methylenepyrrolidine 5g

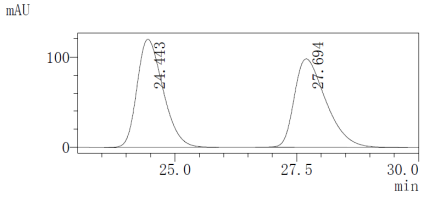
The product was isolated by flash chromatography (ethyl acetate/hexane 1:3) as colorless oil. 27.8 mg, 70% yield. 92% ee. $[\alpha]^{24}_{D}$ = +2.8 (*c* = 2.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.46 (ψt, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 5.00 (s, 1H), 4.91 (s, 1H), 3.90 (d, *J* = 2.4 Hz, 2H), 3.51 (d, *J* = 9.6 Hz, 1H), 3.19 (s, 2H), 3.05 (d, *J* = 9.5 Hz, 1H), 2.38 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.9, 153.2, 151.2, 143.8, 135.5, 132.5, 129.8, 128.0, 126.1, 125.1, 123.0, 121.5, 107.3, 58.7, 52.3, 46.0, 42.9, 24.5, 21.7.

ESI-MS: Calcd for $C_{21}H_{22}N_2O_2S_2$ $[M+Na]^+$: 421.1. Found: 420.8

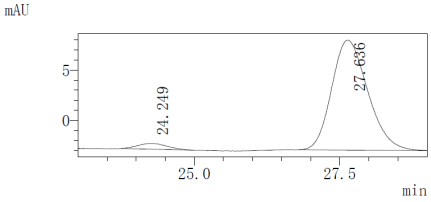
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 95/5, flow rate = 1.0 mL/min.



Peak Table

PDA Ch1 254nm

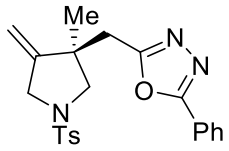
Peak#	Ret. Time	Area	Area%
1	24.443	4433065	50.220
2	27.694	4394303	49.780
Total		8827368	100.000



Peak Table

PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	24.249	20103	4.078
2	27.636	472897	95.922
Total		493000	100.000



(*R*)-*N*-Tosyl-3-[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]-3-methyl-4-methylenepyrrolidine 5h

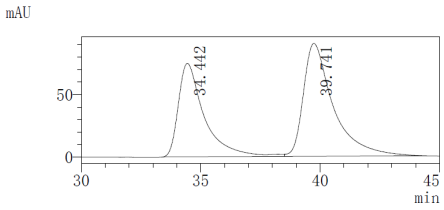
The product was isolated by flash chromatography (ethyl acetate/hexane 1: 2) as colorless oil. 32.7 mg, 80% yield. 86% *ee*. When 80 °C was used instead, 16% yield, 92 *ee*% resulted, $[\alpha]^{22}_{D}$ = -53.5° (*c* = 1.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94-7.87 (m, 2H), 7.63-7.57 (m, 2H), 7.47-7.37 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.88 (s, 1H), 4.77 (s, 1H), 3.91 (ψdt, *J* = 14.1, 2.3 Hz, 1H), 3.72 (ψdt, *J* = 14.2, 2.2 Hz, 1H), 3.42 (d, *J* = 9.6 Hz, 1H), 2.99 (d, *J* = 14.9 Hz, 1H), 2.95-2.85 (m, 2H), 2.30 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.1, 164.0, 150.4, 144.0, 132.6, 131.9, 129.9, 129.2, 128.0, 127.0, 123.9, 107.5, 58.8, 51.9, 45.1, 34.9, 23.3, 21.7.

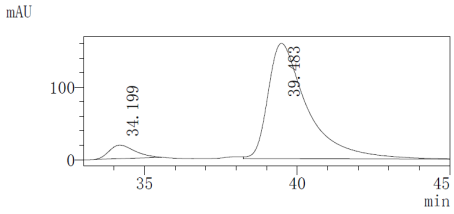
ESI-MS: Calcd for $C_{22}H_{23}N_3O_3S$ $[M+Na]^+$: 432.2. Found: 431.9.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20 flow rate = 0.5 mL/min.



PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	34.442	5620256	41.735
2	39.741	7846379	58.265
Total		13466636	100.000



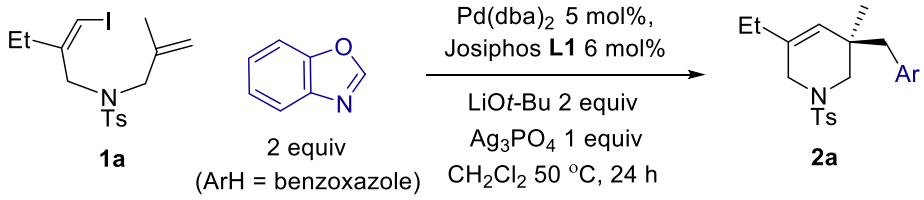
PDA Ch1 254nm

Peak#	Ret. Time	Area	Area%
1	34.199	1073065	6.976
2	39.483	14310196	93.024
Total		15383261	100.000

V. Mechanistic studies

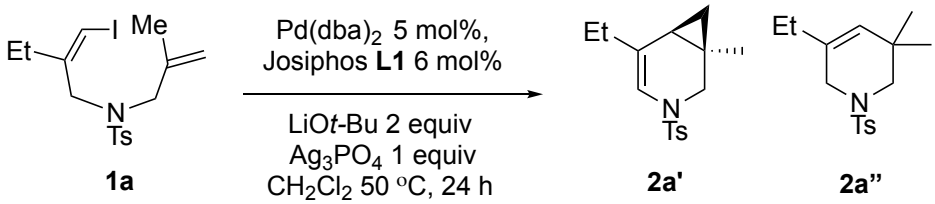
(a) Control reactions of the model domino coupling of benzoxazole

Table S5. Control catalytic domino reaction of **1a**



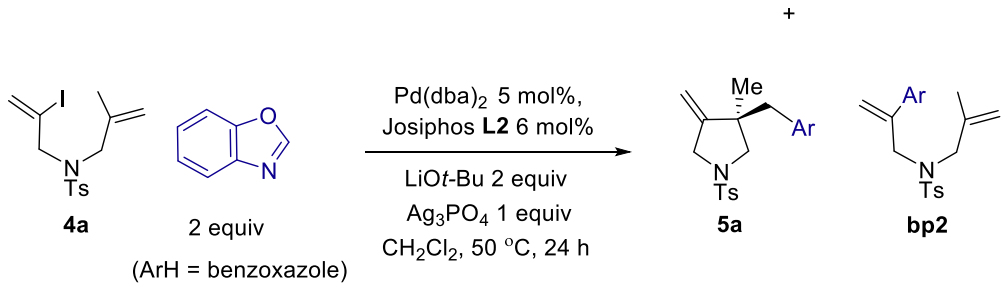
Change to conditions	Conv of **1a** (%)	Yield & ee of **2a** (%)
none	100	82 (92% ee)
no LiO*t*-Bu	16	0
no Ag_3PO_4	100	48 (81% ee)
no LiO*t*-Bu; no Ag_3PO_4	15	0

Table S6. Control catalytic domino reaction of **1a** in the absence of a heteroarene (dibromomethane was added after the reaction as NMR standard to determine NMR yields, due to an overlapping signal of 1,3,5-trimethoxybenzene)



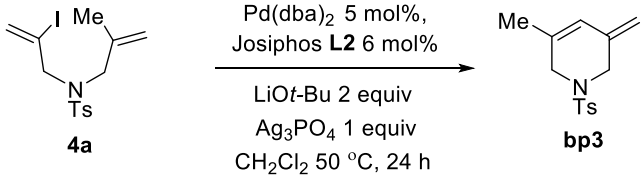
Change to conditions	Conv of **1a** (%)	Yield of **2a**' (%)	Yield of **2a**" (%)
none	100	41 (87% ee)	27
No LiO*t*-Bu	17	<5	<5
No Ag_3PO_4	23	<5	<5
no LiO*t*-Bu; no Ag_3PO_4	15	<5	<5

Table S7. Control catalytic domino reaction of **4a**



Change to conditions	Conv of **4a** (%)	Yield & ee of **2a** (%)	Yield of **bp2** (%)
none	100	93 (92% ee)	0
no LiO*t*-Bu	26	0	0
no Ag_3PO_4	84	31 (71% ee)	26
no LiO*t*-Bu; no Ag_3PO_4	11	0	0

Table S8. Control catalytic domino reaction of **4a** in the absence of a heteroarene



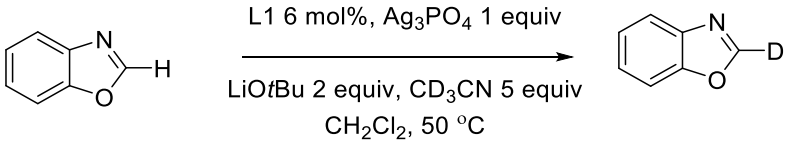
Change to conditions	Conv of **4a** (%)	**2a** (% yield)	**bp3** (%)
only Ag_3PO_4	11	<5	<5
only LiO*t*-Bu	24	<5	15
no LiO*t*-Bu; no Ag_3PO_4	29	<5	

(b) Control deuteration reactions of heteroarenes

A typical procedure for deuteration of heterocycles: in an argon-filled glove box, LiO*t*-Bu (8 mg, 0.1 mmol), Josiphos **L1** (0.006 mmol, 5.2 mg, 6 mol%), Ag_3PO_4 (42 mg, 0.1 mmol) and dry CH_2Cl_2 (0.5 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 15 min at RT, heteroarene (0.1 mmol, 1 equiv) and CD_3CN (26.1 μL, 0.5 mmol) were added. The resulting reaction mixture was capped and vigorously stirred in an oil bath maintained at 50 °C. After 30 min or 2 h, the mixture was cooled down to RT and an aliquot was taken and passed through a plug of

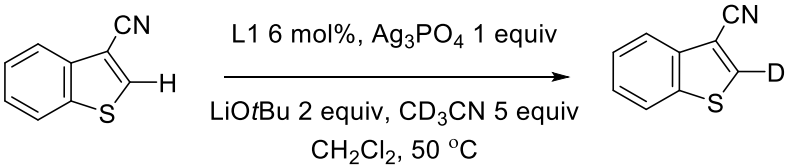
silica gel with washings of 1:1 hexanes/ethyl acetate. After the filtrate was concentrated in vacuo, the crude product was analyzed by crude ^{1}H NMR to determine the ratio of deuteration.

Table S9. Deuteration of benzoxazole



Entry	Conditions	Time (h)	Deuteration (%)
1	Ag_3PO_4, **L1**	0.5	2
		2	2
2	AgOTf, **L1**	0.5	2
		2	2
3	Li*O*t*Bu*	0.5	58
		2	83
4	Ag_3PO_4, **L1**	0.5	**57**
	Li*O*t*Bu*	2	**85**
5	AgOTf, **L1**	0.5	20
	Li*O*t*Bu*	2	34

Table S10. Deuteration of 3-cyanobenzothiophene



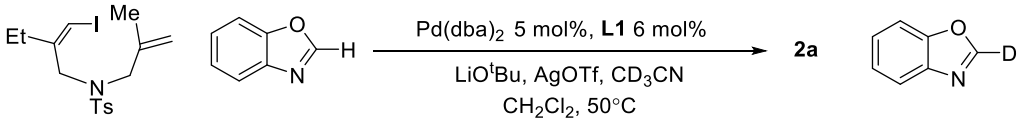
Entry	Conditions	Time (h)	Deuteration (%)
1	Ag_3PO_4, **L1**	0.5	8
		2	11
2	AgOTf, **L1**	0.5	11
		2	14
3	Li*O*t*Bu*	0.5	55
		2	78
4	Ag_3PO_4, **L1**	0.5	29

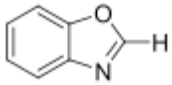
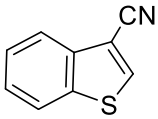
	LiO*t*Bu	2	42
5	AgOTf, **L1** LiO*t*Bu	0.5 2	13 18

(C) Deuteration of heteroarenes in whole catalytic reactions

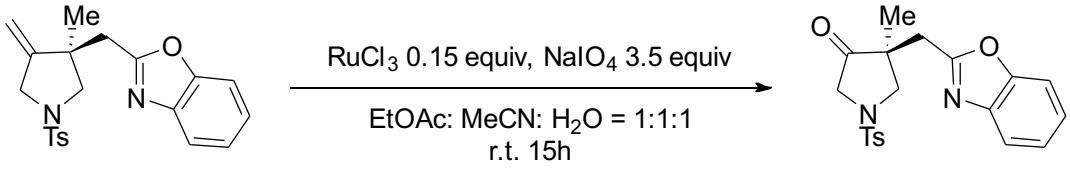
A typical procedure for catalytic domino coupling with CD_3CN: In an argon-filled glove box, $Pd(dba)_2$ (1.5 mg, 0.0025 mmol, 5 mol%), Josiphos **L1** (0.003 mmol, 2.6 mg, 6 mol%) and dry CH_2Cl_2 (0.5 mL) were charged into a dry 10-mL Schlenk tube. After stirring for about 5 min at RT, dienyl iodide **1a** (0.05 mmol) was added to reaction mixture and stirred for 10 min. Then LiO*t*-Bu (8 mg, 0.1 mmol), Ag_3PO_4 (21 mg, 0.05 mmol), heteroarene (0.1 mmol) and CD_3CN (26.1 μL, 0.5 mmol) were added. The resulting mixture was capped and vigorously stirred in an oil bath maintained at 50 ^oC. After 30 min and 2 hours, the mixture was cooled down to RT in the glove box, an aliquot of the reaction mixture was taken and passed through a pad of silica gel with washings of 1:1 hexanes/ethyl acetate to determine GC conversion and product yield NMR yield (NMR standard 1,3,5-Trimethoxybenzene). After reaction, the unreacted heterocycle was recovered and its extent of deuteration was determined by ^1H NMR spectroscopy.

Table S12. Deuterium labelling using 10 equiv CD_3CN (heterocyle: CD_3CN = 5:1) under catalytic domino couplings of three heteroarenes



Entry	Heterocycle	Ag salt	Time (h)	Deuteration of heteroarenes (%)	Conv of **1a** (%)	Yield of **2a** (%)
1		Ag_3PO_4	0.5 2	68 82	42 100	31 87
2		Ag_3PO_4	0.5 2	55 76	33 41	23 32

VI. Product Derivatization



(*S*)-*N*-Tosyl-4-(benzoxazol-2-ylmethyl)-4-methylpyrrolidin-3-one

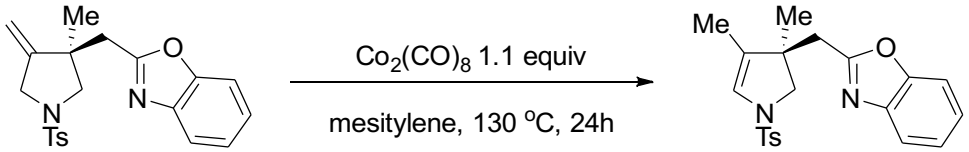
In air, a solution of $NaIO_4$ (41 mg, 0.2 mmol) in water (0.5 mL) was added to a solution of $RuCl_3$ (1.7 mg, 0.008 mmol) in MeCN (0.5 mL) at room temperature. A solution of benzoxazole **5a** (20 mg, 0.052 mmol) in EtOAc (0.5 mL) was then added to this mixture while being stirring at room temperature. After the reaction was completed (as monitored by TLC), the solvent was evaporated and the crude product was extracted with EtOAc (3 mL) three times from the aqueous layer. The combined organic phase was dried over Na_2SO_4 and was then concentrated under reduced pressure. The residue was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give white solid (12.3 mg, 62% yield).

$[\alpha]^{25}_{D}$ = -7.3° (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68-7.66 (m, 2H), 7.41-7.38 (m, 2H), 7.30-7.26 (m, 4H), 3.88 (d, *J* = 17.3 Hz, 1H), 3.62-3.56 (m, 2H), 3.50 (d, *J* = 9.7 Hz, 1H), 3.17 (d, *J* = 16.3 Hz, 1H), 3.06 (d, *J* = 16.3 Hz, 1H), 2.40 (s, 3H), 1.32 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 211.0, 162.6, 150.7, 144.4, 140.8, 131.4, 130.0, 128.1, 125.1, 124.4, 119.9, 110.5, 55.9, 53.6, 48.7, 33.8, 22.4, 21.7.

ESI-MS: Calcd for $C_{20}H_{20}N_2O_4S$ $[M+H]^+$: 385.1; Found: 385.2.



(*R*)-*N*-Tosyl-4-(benzoxazol-2-ylmethyl)-3,4-dimethyl-2,3-didehydropyrrolidine.

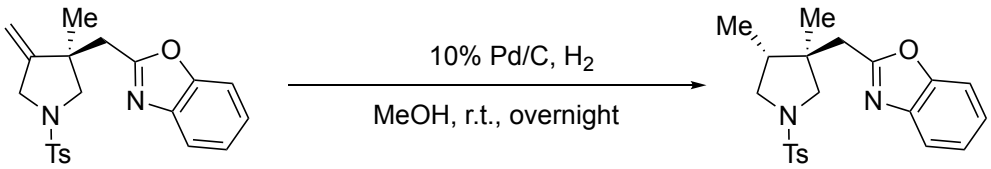
Under argon, to a solution of benzoxazole **5a** (20 mg, 0.052 mmol) in mesitylene (1 mL) in 10 mL Schlenk tube was added $Co_2(CO)_8$ (21 mg, 0.06 mmol). The mixture was then capped tightly and stirred at 130 °C for 24 h. After the reaction was completed after one day (as monitored by TLC),

the mixture was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give colorless oil (18.9 mg, 95% yield). $[\alpha]^{25}_{D}$ = +8.4° (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63-7.59 (m, 3H), 7.45-7.42 (m, 1H), 7.33-7.28 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.07 (q, *J* = 1.6 Hz, 1H), 3.80 (d, *J* = 10.7 Hz, 1H), 3.26 (d, *J* = 10.7 Hz, 1H), 2.88 (d, *J* = 14.6 Hz, 1H), 2.72 (d, *J* = 14.6 Hz, 1H), 2.35 (s, 3H), 1.66 (d, *J* = 1.6 Hz, 3H), 1.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.7, 150.8, 143.8, 141.1, 132.9, 129.6, 127.7, 127.2, 124.9, 124.3, 119.9, 110.5, 58.4, 48.3, 36.6, 24.0, 21.7, 9.4.

ESI-MS: Calcd for $C_{21}H_{22}N_2O_3S$ $[M+H]^+$: 383.1; Found: 383.2.



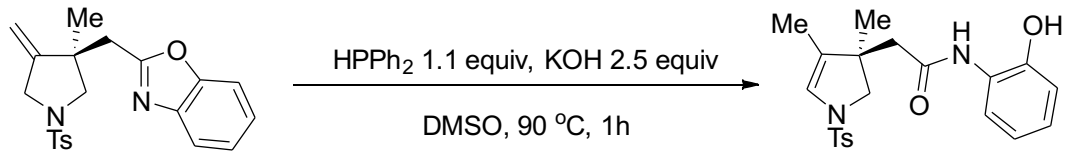
(3*R*,4*S*)-*N*-Tosyl-3-(benzoxazol-2-ylmethyl)-3,4-dimethylpyrrolidine.

To a solution of benzoxazole **5a** (20 mg, 0.052 mmol) in MeOH was added Pd/C (1.0 mg, 10%w/w) and purged with H_2 gas from a balloon for three times at room temperature. After the reaction was completed at rt overnight (as monitored by TLC), the solvent was removed under reduced pressure and the residue was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give white solid (14.0 mg, 70% yield). The dr of 12:1 in the crude product was determined by GC and GCMS. $[\alpha]^{25}_{D}$ = +22.4° (*c* = 1.0, $CHCl_3$). The cis-3,4-dimethyl configuration was determined by NOESY based on a cross-signal between C4-methine and C3-methylene signals and a lack of a cross-signal between C4-methine and C3-methyl signals.

^{1}H NMR of two isomers (400 MHz, $CDCl_3$): δ 7.70-7.65 (m, 3H), 7.51-7.48 (m, 1H), 7.34-7.32 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 3.52 (dd, *J* = 7.9, 2.0 Hz, 1H), 3.40 (d, *J* = 10.1 Hz, 1H), 3.35 (d, *J* = 10.0 Hz, 1H), 2.97-2.91 (m, 2H), 2.74 (d, *J* = 14.5 Hz, 1H), 2.38 (s, 3H), 1.99-1.89 (m, 1H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.79 (s, 3H).

^{13}C NMR of two isomers (101 MHz, $CDCl_3$): δ 164.0, 150.9, 143.5, 141.2, 134.1, 129.7, 127.5, 125.0, 124.5, 119.9, 110.6, 59.4, 53.1, 43.7, 41.1, 37.1, 21.6, 18.3, 11.4.

LC-MS (ESI): Calcd for $C_{21}H_{24}N_2O_3S$ $[M+H]^+$: 385.2; Found: 385.1.



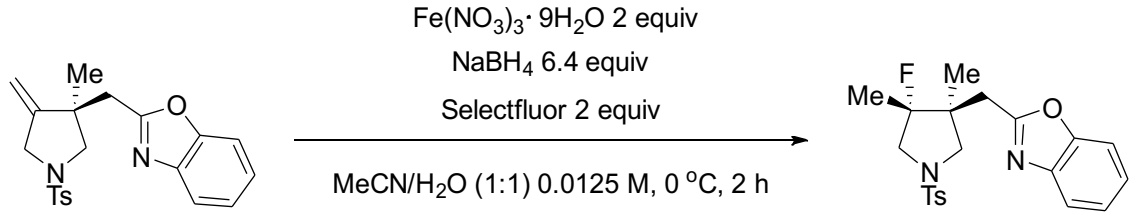
(*R*)-2-*N*-Tosyl-(3,4-dimethyl-1-4,5-didehydropyrrolidinyl)-*N'*-(2-hydroxyphenyl)acetamide

Under argon, to a stirred solution of benzoxazole **5a** (20 mg, 0.052 mmol) in DMSO (1 mL) was added $HPPh_2$ (10.7 mg, 0.057 mmol) and KOH (7.3 mg, 0.13 mmol) at room temperature. After stirring at 90 ^oC for 1 h, the reaction was completed (as monitored by TLC). The mixture was dissolved in 3 mL EtOAc and washed with water. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 mL) three times. The combined organic phase was dried over Na_2SO_4 and then concentrated under reduced pressure. The residue was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give white solid (13.5 mg, 65% yield). $[\alpha]^{25}_D$ = -15.2^o (*c* = 0.3, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (s, OH), 7.66-7.64 (m, 2H), 7.57 (s, NH), 7.28-7.25 (m, 2H), 7.13 (ψtd, *J* = 7.7, 1.6 Hz, 1H), 6.99 (ψtd, *J* = 7.7, 1.4 Hz, 1H), 6.86 (ψtd, *J* = 7.7, 1.4 Hz, 1H), 6.12 (q, *J* = 1.5 Hz, 1H), 3.74 (d, *J* = 10.8 Hz, 1H), 3.23 (d, *J* = 10.8 Hz, 1H), 2.41-2.37 (m, 4H), 2.29 (d, *J* = 14.4 Hz, 1H), 1.62 (d, *J* = 1.5 Hz, 3H), 1.10 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 170.5, 148.8, 144.2, 132.8, 129.8, 127.8, 127.4 (2 signals), 125.5, 125.0, 122.3, 120.7, 120.0, 58.7, 47.4, 44.2, 23.6, 21.7, 9.6.

ESI-MS: Calcd for $C_{21}H_{24}N_2O_4S$ $[M+H]^+$: 400.2; Found: 400.1.



(3*S*,4*R*)-*N*-Tosyl-3-(benzoxazol-2-ylmethyl)-4-fluoro-3,4-dimethylpyrrolidine

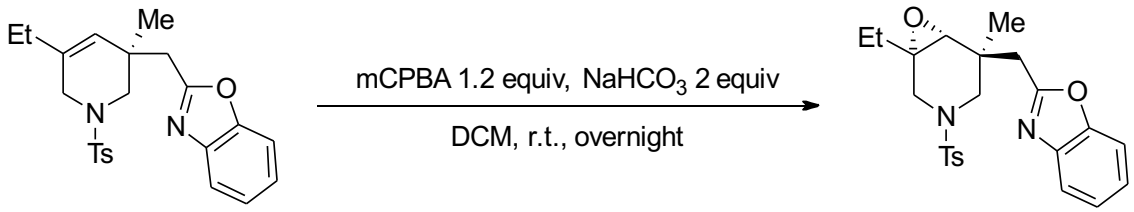
Under argon, ferric nitrate nonahydrate (20.2 mg, 0.05 mmol) was stirred in H_2O (0.5 mL), which was cooled to 0 °C and degassed for 10 min. Selectfluor (17.7 mg, 0.05 mmol) and MeCN (0.5 mL) were added to the reaction mixture. A solution of benzoxazole **5a** (10 mg, 0.025 mmol) in MeCN (0.5 mL) was added to the reaction mixture and then $NaBH_4$ (3.1 mg, 0.08 mmol) was added at 0 °C. After 2 min, another portion of $NaBH_4$ (3.1 mg, 0.08 mmol) was added. The resulting mixture was stirred for 2 h before quench by saturated $NaHCO_3$ and extracted with EtOAc (3 mL x 3). The combined organic phase was dried over Na_2SO_4 and was then concentrated under reduced pressure. The residue was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give a white solid (6.8 mg, 68% yield). The dr 1.5:1 was determined by proton signal integration. $[\alpha]^{25}_D$ = +36.4° (*c* = 0.6, $CHCl_3$).

^{1}H NMR of two isomers (400 MHz, $CDCl_3$): δ 7.75-7.67 (m, 3H), 7.53-7.50 (m, 1H), 7.36-7.32 (m, 2H), 7.27-7.25 (m, 2H), 3.99 (dd, *J* = 9.6, 1.1 Hz, 0.63H), 3.64-3.47 (m, 3H), 3.14-3.08 (m, 1H), 2.93 (d, *J* = 14.8 Hz, 0.48H), 2.81-2.70 (m, 1.28H), 2.43 (s, 1.20H), 2.39 (s, 1.80H), 1.41-1.33 (m, 3H), 1.08 (d, *J* = 1.8 Hz, 1.76H), 0.97 (d, *J* = 14.5 Hz, 1.17H).

^{13}C NMR of two isomers (101 MHz, $CDCl_3$): δ 163.9(163.1), 151.0(150.8), 143.8(143.8), 141.2(141.2), 134.0(134.0), 129.9(129.8), 127.7(127.6), 125.2(125.1), 124.6, 120.0(120.0), 110.7, 103.6 (d, $J_{C\text{-}F}$ = 180.8 Hz), 102.6 (d, $J_{C\text{-}F}$ = 181.5 Hz), 57.9 (d, $J_{C\text{-}F}$ = 24.4 Hz), 57.4 (d, $J_{C\text{-}F}$ = 24.4 Hz), 57.1, 57.0, 55.6, 48.2 (d, $J_{C\text{-}F}$ = 21.0 Hz), 47.5 (d, $J_{C\text{-}F}$ = 18.6 Hz), 34.0 (d, $J_{C\text{-}F}$ = 5.6 Hz), 33.9, 31.4 (d, $J_{C\text{-}F}$ = 9.0 Hz), 29.8, 21.7, 21.7, 21.0 (d, $J_{C\text{-}F}$ = 5.3 Hz), 20.9,16.6, 16.3, 16.1, 15.2 (d, $J_{C\text{-}F}$ = 7.6 Hz).

^{19}F NMR of two isomers (376 MHz, $CDCl_3$): δ -145.4, -147.4 (ratio 1.4:1).

ESI-MS: Calcd for $C_{21}H_{23}FN_2O_3S$ $[M+H]^+$: 402.2; Found: 402.1.



(1*S*,5*S*,6*R*)-*N*-Tosyl-5-(benzoxazol-2-ylmethyl)-3-ethyl-3,4-epoxy-5-methylpiperidine

In air, a stirred solution of benzoxazole **3a** (20 mg, 0.049 mmol) in DCM maintained at 0 °C was added *m*CPBA (11.9 mg, 0.059 mmol) and $NaHCO_3$ (8.2 mg, 0.098 mmol) and then the temperature was raise to room temperature. After the reaction was completed overnight (as monitored by TLC), the crude mixture was washed with saturated $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with DCM (3 mL) three times. The combined organic phase was dried over Na_2SO_4 and was then concentrated under reduced pressure. The residue was directly subjected to silica gel column chromatography (petroleum ether/ethyl acetate 20/1) to give white solid (12.7 mg, 61% yield, dr 1:1). $[\alpha]^{25}_D$ = -23.3° (*c* = 0.9, $CHCl_3$).

^{1}H NMR of two isomers (400 MHz, $CDCl_3$): δ 7.71-7.68 (m, 1H), 7.63-7.61 (m, 2H), 7.53-7.50 (m, 1H), 7.35-7.30 (m, 4H), 3.74-3.68 (m, 1H), 3.35-3.30 (m, 1H), 3.20-2.84 (m, 4H), 2.55 (d, *J* = 11.8 Hz, 0.5H), 2.43 (d, *J* = 6.5 Hz, 3H), 2.37-2.34 (d, *J* = 11.8 Hz, 0.5H), 1.69-1.60 (m, 1H), 1.27 (s, 1.5H), 1.16 (s, 1.5H), 1.00-0.95 (m, 3H).

^{13}C NMR of two isomers (101 MHz, $CDCl_3$): δ 163.9 (163.4), 151.0 (150.9), 144.0 (143.9), 141.4 (141.4), 133.5 (133.2), 130.0 (129.9), 127.7 (127.6), 125.0 (124.9), 124.5 (124.4), 120.0 (119.9), 110.6, 63.3 (63.2), 61.4 (61.3), 49.5 (49.3), 46.2 (46.0), 36.6 (36.5), 36.0 (35.1), 29.1 (28.9).

ESI-MS: Calcd for $C_{23}H_{26}N_2O_4S$ $[M+H]^+$: 426.2; Found: 426.1.

VII. Refeence

[1] R. C. Larock, M. J. Doty, X. Han, *J. Org. Chem.* **1999**, *64*, 8770-8779.
[2] J.-S. Zheng, H.-N. Chang, F.-L. Wang, L. Liu, *J. Anm. Chem. Soc.* **2011**, *133*, 11080-11083.
[3] X. Huang, M. H. Nguyen, M. Pu, L. Zhang, Y. R. Chi, Y.-D. Wu, J. S. Zhou, *Angew Chem Int. Ed.* **2020**, *59*, 10814-10818.
[4] X. Chi, L. Meng, X. Sun, Q. Liu, B. Ai, L. Chen, D. Zhang, P. Zhao, Y. Dong, H. Liu, *Asian J. Org. Chem.* **2019**, *8*, 840-843.
[5] K. M. Aitken, R. A. Aitken, *Tetrahedron* **2008**, *64*, 4384-4386.

VIII. X-ray measurement and thermal ellipsoid plots 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

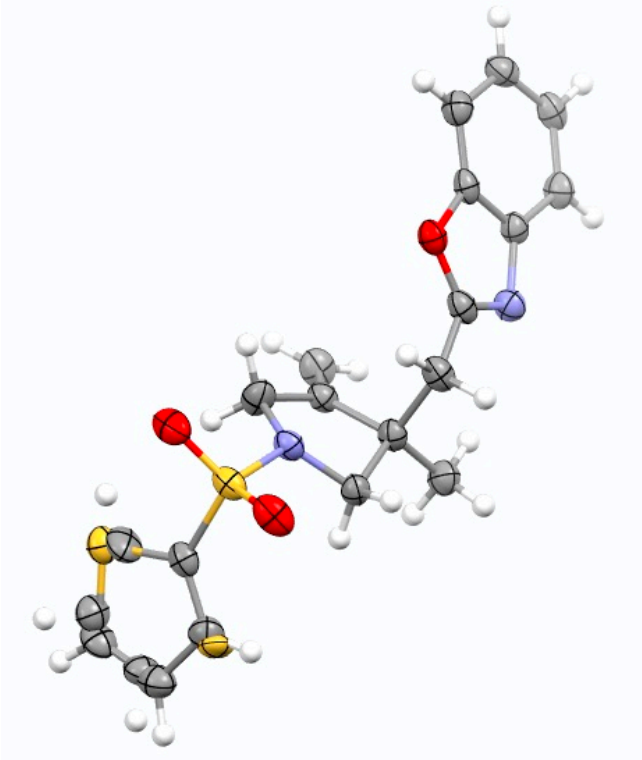


Fig S11. Thermal ellipsoid plot for crystal structure of compound **5d** (ellipsoid contour at 60% probability)