JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b01892 • Publication Date (Web): 10 Sep 2018

ACS Publications

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DBU-Promoted Dynamic Kinetic Resolution in Rh-Catalyzed Asymmetric Transfer Hydrogenation of 5-Alkyl Cyclic Sulfamidate Imines: Stereoselective Synthesis of Functionalized 1,2-Amino Alcohols

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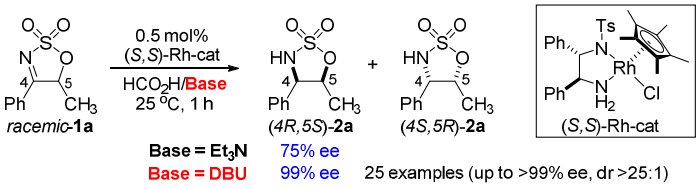
ABSTRACT



Dynamic kinetic resolution (DKR)-driven asymmetric transfer hydrogenation of 5-alkyl cyclic sulfamidate imine produces the corresponding sulfamidate with excellent levels of diastereo- and enantioselectivity by employing a HCO_2H/DBU mixture as the hydrogen source in the presence of the Noyori-type chiral Rh-catalyst at room temperature for 1 h. In this process, DKR was induced by DBU-promoted rapid racemization of the substrate. Stereoselective transformations of the resulting cyclic sulfamidates to functionalized enantiomerically enriched 1,2-amino alcohol and chiral amine substances are also described.

INTRODUCTION

1,2-Amino alcohols are important structural motifs in a wide range of natural products and pharmacologically active compounds.[1] Furthermore, the relative and absolute stereochemistry of the

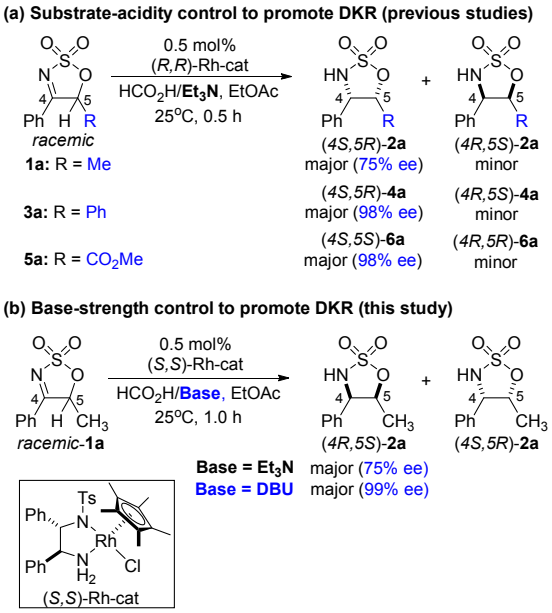
1,2-amino alcohols is an important factor governing their biological activities. Optically active 1,2-amino alcohols have also been used as both chiral auxiliaries and ligands in synthetically important asymmetric transformations. Therefore, the development of methods for stereoselective synthesis of members of this family has received considerable attention.[1]

Dynamic kinetic resolution (DKR), which combines a kinetic resolution process with *in situ* equilibration or racemization of a configurationally labile substrate, has become an important method to generate enantiomerically enriched/pure compounds from racemic substrates in a theoretically quantitative yield.[2]

Asymmetric transfer hydrogenation (ATH) reactions, using hydrogen sources other than molecular hydrogen, have proven to be among the most powerful methods for asymmetric reduction of ketones and imines. These processes, which yield the corresponding chiral alcohols and amines, have advantages associated with operational simplicity, ready availability of hydrogen sources, and use of readily accessible and less sensitive catalysts.[3]

In a recent study in this area, we uncovered a new procedure for DKR-driven ATH reactions of prochiral cyclic sulfamidate imines, which utilizes a mixture of HCO_2H/Et_3N as the hydrogen source and base, along with a well-defined Noyori-type chiral Rh-catalyst (Scheme 1-a).[4]

Scheme 1. ATH of cyclic sulfamate imines accompanied by DKR



In the effort, we showed that ATH reactions of 4,5-disubstituted cyclic sulfamidate imines, possessing configurationally labile stereogenic centers (C5) are accompanied by DKR.[4] We also observed that

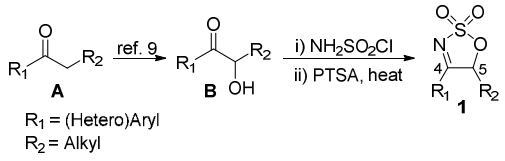
DKR is caused by Et_3N promoted racemization at the acidic C5 stereogenic position under the reaction conditions. As a consequence, a drastic improvement in the stereoselectivity of this process occurs when the sulfamidate imine substrates contain H5 acidity enhancing aryl (**3a**)[4d] or carboxylate groups (**5a**)[4b] instead of a methyl group (**1a**)[4e] at C5 (*eg.,* 98% ee for **4a** and **6a** vs 75% ee for **2a**, Scheme 1-a). However, compare to the excellent stereoselectivities (98% ee) in the ATH of cyclic imine **3a** or **5a**, stereoselectivity in the ATH of 5-methyl cyclic imine **1a** to 5-methyl cyclic sulfamidate **2a** (75% ee) remains to be improved.

While considering other strategies to improve the stereoselectivity of ATH reactions of 5-alkyl substituted cyclic imine **1a**, we envisioned that employing stronger bases than triethylamine[5] could also facilitate rapid racemization of **1a** and, as a result, would lead to higher degrees of stereoselectivity in reaction of 5-alkyl substituted substrate **1a**. In the literature search for strong bases suitable for this study, we found that readily available DBU [p*Ka*(CH_3CN) = 24.34] is much stronger organic base than Et_3N [p*Ka*(CH_3CN) = 18.82] and might serve well in this role.[8] Below, we describe the results of investigation exploring the use of DBU as the base for ATH reactions of 5-alkyl substituted cyclic imines **1** (Scheme 1-b).

RESULTS AND DISCUSSION

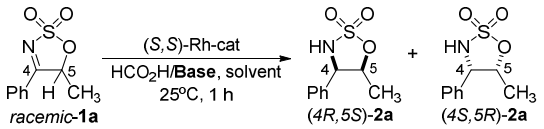
The racemic 5-alkyl cyclic imines **1**, used in this study, were prepared starting with α-hydroxy acetophenone derivatives (**B**)[9] and sulfamoyl chloride by using a previously described procedure (Scheme 2).[4c]

Scheme 2. Synthesis of 5-alkyl cyclic sulfamidate imine **1**



In the first phase of this effort, racemic 4-phenyl-5-methyl cyclic imine **1a** was subjected to ATH reaction conditions employing 2 eqiv of HCO_2H as the hydrogen source and 2 eqiv of Et_3N or DBU in the presence of the Rh-catalyst [(*S,S*)-ClRhCp*(TsDPEN)].[10]

Table 1. Optimization of the ATH-DKR reaction of **1a**[a]



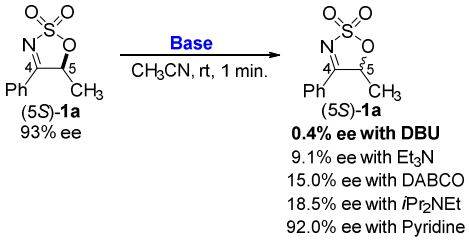
Entry	Cat. amt (mol%)	FA/Base(ratio)	Solvent	Convn (%)[b]	dr[c] (*cis:trans*)	%ee[d]
1	0.5	HCO_2H/Et_3N(5:2)	EtOAc	>99	>25:1	75
2	0.5	HCO_2H/Et_3N(1:1)	EtOAc	>99	>25:1	80
3	0.5	HCO_2H/Et_3N(5:2)	CH_3CN	>99	>25:1	87
4	0.5	HCO_2H/Et_3N(1:1)	CH_3CN	>99	>25:1	98
5	1.0	HCO_2H/**DBU**(1:1)	EtOAc	>99	>25:1	99
6	1.0	HCO_2H/**DBU**(1:1)	CH_3CN	>99	>25:1	>99
7	0.5	HCO_2H/**DBU**(1:1)	CH_3CN	>99	>25:1	>99
8	0.1	HCO_2H/**DBU**(1:1)	CH_3CN	>99	>25:1	>99
9	0.5	HCO_2H/DABCO(1:1)	CH_3CN	>99	>25:1	95
10	0.5	HCO_2H/*i*-Pr_2NEt(1:1)	CH_3CN	>99	>25:1	94
11[e]	0.5	HCO_2H/Pyridine(1:1)	CH_3CN	0	-	-
12	1.0	HCO_2H only	CH_3CN	0	-	-

[a] Reaction conditions: **1a** (0.2 mmol), (*S,S*)-Rh-cat [(*S,S*)-ClRhCp*(TsDPEN)] (0.1-1.0 mol%), HCO_2H/Base (2 eqiv.), solvent (2 mL), rt, 1 h. [b] Determined by ^1H NMR analysis of crude products. [c] Only 4,5-*cis* products were detected by using ^1H NMR analysis of crude product mixtures. [d] Determined by using chiral HPLC. [e] Reaction time: 12 h.

The results, summarized in Table 1, show that replacement of Et_3N by DBU in the reaction of **1a** in EtOAc leads to a dramatic improvement in the degree of enantioselectivity of the ATH reaction, which produces (*4R,5S*)-**2a** with a 99% ee and a dr >25:1 (Table 1, entries 1-2 and 5). The observations also show that solvent has a strong effect on the stereoselectivity of this process (eg., CH_3CN is better solvent than EtOAc, Table 1, entries 2 and 4). In addition, replacement of Et_3N by other bases such as DABCO or *i*-Pr_2NEt in the ATH reaction of **1a** leads to a slight decrease of enantioselectivities of (*4R,5S*)-**2a** (Table 1, entries 9 and 10). Interestingly, when pyridine was employed instead of Et_3N, the ATH reaction was not proceeded at all and **1a** was recovered quantitatively even with longer reaction of 12 h (Table 1, entry 11). The exact role the base plays is not clear yet but the ATH reaction does not proceed in the absence of added base (Table 1, entry 12).

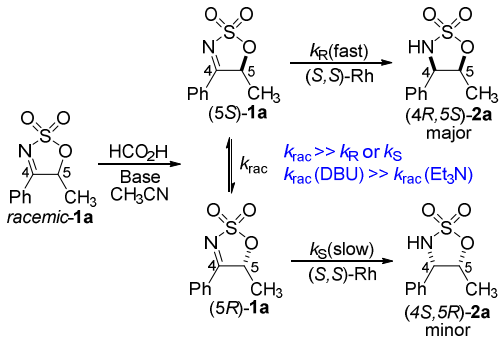
We believe that the high level of stereoselectivity observed in the ATH-DKR reaction of **1a** is a result of rapid racemization of the configurationally labile C5-center promoted by the strong base DBU. To demonstrate this proposal, optically active imine (5*S*)-**1a** (93% ee) was prepared from optically active (*S*)-2-hydroxypropiophenone[4e] and subjected to reaction with DBU in CH_3CN at room temperature for 1 min (Scheme 3).

Scheme 3. Base-mediated racemization of (5*S*)-**1a**



Analysis of the reaction mixture, generated by acid quenching after 1 min, showed that the reduction product **2a** is not formed and that the starting imine (5*S*)-**1a** is recovered in nearly quantitative yield with only a 0.4% ee (see, Scheme 3 and SI). However, when (5*S*)-**1a** (93% ee) was subjected to the reaction with Et_3N for 1 min, (5*S*)-**1a** was recovered with 9.1% ee. These findings show that both DBU and Et_3N promote racemization of (5*S*)-**1a** but that racemization promoted by DBU takes place more rapidly (k_{rac} for DBU >> k_{rac} for Et_3N in Scheme 4) and, consequently, the ATH-DKR reaction using DBU occurs with a higher stereoselectivity (base = DBU: 99% ee for **2a**, base = Et_3N: 75% ee for **2a**). DABCO and *i*-Pr_2NEt also induced racemization of (5*S*)-**1a** but slightly slower than Et_3N or DBU in CH_3CN solvent (after 1 min., base = DABCO: 15% ee for recovered (5S)-**1a**, base = *i*-Pr_2NEt: 18.5% ee for recovered (5S)-**1a**, Scheme 3). Interestingly, when pyridine and (5*S*)-**1a** (93% ee) were allowed to react for 1 min. in CH_3CN, (5*S*)-**1a** was recovered with almost no racemization (92% ee for recovered (5S)-**1a**, Scheme 3).

Scheme 4. Proposed mechanism for DKR in ATH of **1a**

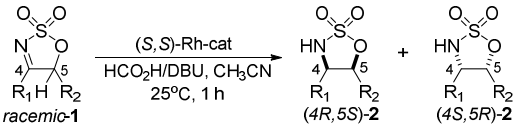


In addition, the results of ^1H NMR spectroscopic analysis show that the 4,5-*trans*-isomer of sulfamidate **2a** is not present in the crude product mixture produced by ATH reaction of **1a**. Thus, as describe previously,[4b,4d] hydrogen addition in the (*S,S*)-ClRhCp*(TsDPEN)-catalyzed reaction of **1a**

occurs exclusively from the less sterically hindered face of the cyclic imine. Moreover, the catalyst loading in this process can be reduced to 0.1 mol% without deterioration of efficiency and stereoselectivity (Table 1, entry 8).

Utilizing the optimal reaction conditions developed in the preliminary studies, we investigated the scope of the ATH-DKR reaction using a variety of 5-alkyl substituted cyclic sulfamidate imines (Table 2).

Table 2. Sulfamidate imine scope of the ATH-DKR reaction[a]



Entry	Substrate **1**, Product **2**	R_1	R_2	Yield (%)[c]	% ee[d]
1	**a**	Ph	Me	90	99.7
2[b]	**a**	Ph	Me	92	-99.2[b]
3	**b**	Ph	Et	96	99.8
4	**c**	Ph	*n*-Pr	97	99.8
5	**d**	Ph	*i*-Pr	94	99.8
6	**e**	Ph	Bn	92	99.3
7	**f**	Ph	*n*-Octyl	96	95.6
8	**g**	Ph	CH_2OMe	91	99.7
9	**h**	Ph	CH_2OBn	97	92.3
10	**i**	Ph	Allyl	96	99.4
11	**j**	4-OMe-Ph	Allyl	91	95.8
12	**k**	4-OMe-Ph	Bn	90	99.7
13	**l**	2-Cl-Ph	Me	92	53.4
14	**m**	3-Cl-Ph	Me	97	99.4
15	**n**	4-Cl-Ph	Me	92	99.6
16	**o**	2-Me-Ph	Me	90	88.1
17	**p**	3-Me-Ph	Me	93	99.6
18	**q**	4-Me-Ph	Me	99	99.5
19	**r**	4-F-Ph	Me	99	99.7
20	**s**	4-OMe-Ph	Me	90	99.6
21	**t**	4-CN-Ph	Me	95	98.2
22	**u**	4-CF_3-Ph	Me	95	99.9
23	**v**	2-Thienyl	Me	94	99.3
24	**w**	2-Naphthyl	Me	93	99.6
25	**y**	*n*-Butyl	Me	91	95.2[f]

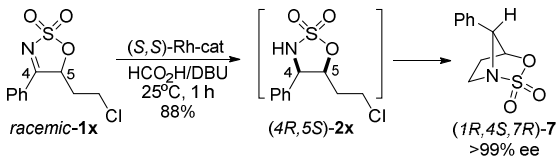
[a] Reaction conditions: **1** (0.2 mmol), (*S,S*)-Rh-cat (0.5 mol%), HCO_2H/DBU (2 eqiv), CH_3CN (2 mL), rt, 1 h. [b]

(*R,R*)-Rh-cat was used and (*4S,5R*)-**2a** was formed [c] Yields of isolated and purified products. [d] Determined by using chiral HPLC. [e] Absolute configuration of **2a** was determined by comparing the sign of the optical rotation and chiral HPLC retention time with those of the known compound (ref. 4e). [f] ee of *N-Cbz* derivative of **2y**.

As the data in Table 2 show, almost all of the substrates undergo complete ATH-DKR reactions within 1 h at room temperature with high efficiencies and stereoselectivities. For example, ATH reactions of cyclic imines bearing ethyl, *n*-propyl, *i*-propyl, allyl and benzyl groups in CH_3CN occur with high efficiencies and excellent levels of stereoselectivity (Table 2, entries 1-6, 8, and 10, >99% ee). Moreover, cyclic imines containing long chain alkyl groups at C5 such as *n*-octyl (**1f**) or benzyoxymethyl (**1h**, CH_2OBn) also react smoothly to produce products in high yields but with slightly decreased levels of enantioselectivity (entries 7 and 9, 92-96% ee). Furthermore, ATH reactions of 4-aryl-5-methyl cyclic imines bearing either electron-withdrawing or electron-donating groups at the *meta*- or *para*-positions of the C-4 phenyl ring lead to production of the corresponding 4-aryl-5-methyl cyclic sulfamidates in high yields and excellent levels of stereoselectivity. However, ATH reactions of 5-methyl cyclic imines possessing C4 *ortho*-substituted phenyl groups (**1l**: 2-Cl-Ph and **1o**: 2-Me-Ph) generate the corresponding sulfamidates in high yields but only moderate levels of enantioselectivity (53-88% ee, entries 13 and 16). The results show that cyclic imines containing 4-thiophene or 4-naphthalene substituents also serve as suitable substrates for the ATH-DKR reaction (entries 23 and 24). ATH reaction of the 4-(*n*-butyl)-5-methyl cyclic imine **1y** also occurs to produce the corresponding sulfamidate **2y** in high yield (91%) but with slightly decreased ee (95% ee, entry 25). Finally, ATH reaction of **1a**, employing the (*R,R*)-Rh-catalyst under the same conditions, produces the enantiomeric sulfamidate (*4S,5R*)-**2a** with the same efficiency and stereoselectivity as those of the reaction using the (*S,S*)-Rh-catalyst (entries 1 and 2).

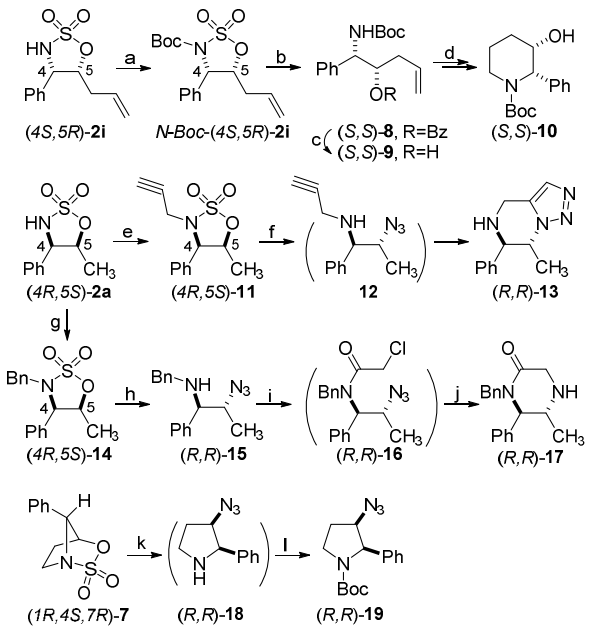
It is interesting to note that under the standard ATH reaction conditions, 5-(2-chloroethyl) substituted cyclic imine **1x** reacts to form the bicyclic sulfamidate **7** in a good yield and an excellent % ee. This product, whose structure and absolute stereochemistry were unambiguously determined by using X-ray crystallography analysis (see SI, CCDC1835266), is likely produced through cyclization of the initially formed 5-(2-chloroethyl) cyclic sulfamidate **2x** under the reaction conditions (Scheme 5).

Scheme 5. ATH of **1x** to bicyclic sulfamidate **7**



Because the highly enantio-enriched cyclic sulfamidates **2** produced in these ATH-DKR reactions contain both a stereogenic carbon bearing an amine moiety and a reactive cyclic sulfamidate group, they are potentially valuable intermediates for the synthesis of chiral 1,2-functionalized amines and 1,2-amino alcohols.[11]

Scheme 6. Stereoselective transformation of sulfamidates[a]



[a]Reaction conditions: (a) $(t\text{-Boc})_2O$, cat. DMAP, CH_3CN, 92%. (b) $PhCO_2H$/CsF, DMF, 60 °C, 3 h, 71%. (c) KCN, MeOH, rt, 3h, 66%. (d) ref. 12. (e) Propagyl bromide, NaH, DMF, rt, 3 h, 82%. (f) i) NaN_3, DMF, 60 °C, 3 h, ii) 1N HCl, Et_2O, 92%. (g) Benzyl bromide, NaH, DMF, rt, 5 h, 89%. (h) i) NaN_3, DMF, rt, 3 h, ii) 1N HCl, Et_2O, 93%. (i) Chloroacetyl chloride, Et_3N, CH_2Cl_2, 0 °C, 91%. (j) PPh_3, MeOH, 80 °C, 5 h, 85%. (k) NaN_3, DMF/CH_3CN, 60 °C, 36 h. (l) $(t\text{-Boc})_2O$, rt, 3 h (66% from **7**).

As part of an effort to demonstrate this potential, (*4S,5R*)-4-phenyl-5-allyl cyclic sulfamidate (**2i**), formed by ATH-DKR reaction of **1i**, was converted to its *N*-Boc derivative, which upon treatment with $PhCO_2H$/CsF undergoes sulfamidate ring opening to form the protected 1,2-amino alcohol (*S,S*)-**8** (Scheme 6). Selective removal of the *O*-benzyl group in this substance using KCN in MeOH produces the *N*-Boc derivative (*S,S*)-**9**, which serves as a precursor to piperidine-3-ol (*S,S*)-**10** that is

reported to be a key intermediate in the synthesis of the nonpeptide neurokinin NK1 receptor agonists, (+)-L-733,060 and (+)-CP-99,994.[12] In addition, NaN_3 treatment of (*4R,5S*)-*N*-propagyl-4-phenyl-5-methyl cyclic sulfamidate (**11**), which is prepared from **2a**, generates the azido-amine **12** that is converted by intramolecular [3+2] cycloaddition reaction[13] under the reaction conditions to the triazolopiperazine **13** in good yield. Moreover, the *N*-benzyl cyclic sulfamidate **14** produced from **2a** undergoes NaN_3 ring opening to form the amino-azide **15**. Treatment of this substance with chloroacety chloride produces amide **16**, which is transformed to (*R,R*)-1-benzyl-5-methyl-6-phenylpiperazin-2-one (**17**) by PPh_3 promoted azide reduction. A final example showing the utility of the enantio-enriched cyclic sulfamidates generated by using the ATH-DKR process is found in the NaN_3 promoted conversion of bicyclic sulfamidate (*1R,4S,7R*)-**7** to the (*R,R*)-*N*-Boc-3-azido-2-phenylpyrrolidine **19** (Scheme 6).

CONCLUSION

In the effort described above, we developed a convenient and highly stereoselective method for the preparation of 4-aryl-5-alkyl cyclic sulfamidates **2**. The process, involving asymmetric transfer hydrogenation (ATH), employs HCO_2H/DBU as the hydrogen source and the Noyori-type chiral Rh catalysts (*S,S*)- or (*R,R*)-Cp*RhCl(TsDPEN). Dynamic kinetic resolution takes place in this process through DBU-promoted rapid racemization of the configurationally labile cyclic imine substrates. In addition, selected stereoselective transformations of the cyclic sulfamidates, generated by the ATH-DKR process, were carried out to demonstrate the use of this method in producing synthetically valuable functionalized chiral amines and 1,2-amino alcohols.

EXPERIMENTAL SECTION

General

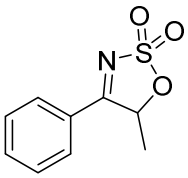
All commercial reagents were used as obtained from commercial sources unless otherwise noted. Reactions were performed with reagent grade solvents except dichloromethane (DCM), ether, THF which were dried and purified using a solvent purification system. The progress of reactions was monitored using thin layer chromatography (TLC) and visualized using UV light and by staining with ethanolic phosphomolybdic acid (PMA) solution or $KMnO_4$ solution followed by heating. Flash column chromatography was carried out on silica gel (38-75 μm). Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates. Preparative thin layer chromatography (PLC) was performed on Merck silica gel 60 F_{254} 2mm plates. Nuclear magnetic

resonance (NMR) spectra were recorded using Bruker 500 MHz NMR instrument (^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz) or Bruker 300 MHz NMR instrument (^{1}H NMR at 300 MHz and ^{13}C NMR at 75 MHz). ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constants (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High performance liquid chromatography (HPLC) was carried out on a Young Lin HPLC system (7725i Injector, SDV 30 Plus Solvent Degassor & Valve Module (Helium Sparging), SP930D Solvent Delivery Pump, UV 730D Absorbance Detector) equipped with a Chiralpak IA, IB, IC, ID or Chiralpak AD-H, Chiralcel OD-H column. Specific rotations were measured on a Rudolph Autopol IV (Automatic polarimeter). High-resolution mass spectra and elemental analysis were obtained from the Korea Research Institute of Chemical Technology. HR-MS were measured with electron impact (EI) or fast atom bombardment (FAB) ionization via double focusing mass analyzer (magnetic and electric fields) or electrospray ionization (ESI) via time of flight (TOF) analyzer. (*R*,*R*)- and (*S*,*S*)-ClRhCp*(TsDPEN) catalysts were prepared according to the literature procedures.[10]

1. General procedure for the synthesis of cyclic imine from α-hydroxy acetophenone derivatives

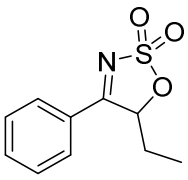
To a solution of 2-hydroxy-1-phenylpropan-1-one (500 mg, 3.33 mmol) in DMA (10 mL) was added sulfamoyl chloride (769 mg, 6.66 mmol) at 0 °C. The reaction mixture was stirred at rt for 2 h, diluted with EtOAc, and washed with saturated NaCl (aq). The organic layer was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was re-dissolved in toluene (10 mL) and catalytic amount of *p*-TSA was added. The mixture was heated for 1 h at 110 °C, cooled to room temperature, diluted with EtOAc (50 mL), and washed with saturated NaCl (aq). The organic layer was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude residue was purified on silica gel column chromatography using EtOAc/hexanes (1:9 to 1:3) as an eluent to afford the title compound as a white solid.

5-Methyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1a)



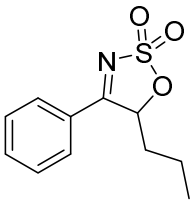
yield: 61% (470 mg as a white solid); mp: 107.0-107.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.80-7.71 (m, 1H), 7.65-7.57 (m, 2H), 5.98 (q, *J* = 7.0 Hz, 1H), 1.79 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4, 135.4, 129.7, 129.6, 127.0, 83.9, 20.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_9NO_3S$ 211.0303; Found 211.0290.

5-Ethyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1b)



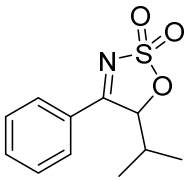
yield: 68% (650 mg as a white solid); mp: 87.0-88.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.90 (m, 2H), 7.77-7.71 (m, 1H), 7.63-7.57 (m, 2H), 5.91 (dd, *J* = 7.3, 3.4 Hz, 1H), 2.26-2.16 (m, 1H), 2.04-1.94 (m, 1H), 1.08 (t, *J* = 7.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 135.3, 129.6, 129.4, 127.4, 89.0, 27.22, 9.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_3S$ 225.0460; Found 225.0446.

4-Phenyl-5-propyl-5H-1,2,3-oxathiazole 2,2-dioxide(1c)



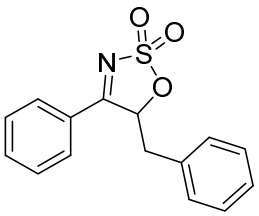
yield: 88% (710 mg as a white solid); mp: 63.8-65.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94-7.90 (m, 2H), 7.77-7.72 (m, 1H), 7.63-7.58 (m, 2H), 5.92 (dd, *J* = 8.6, 3.0 Hz, 1H), 2.11-2.06 (m, 1H), 1.97-1.87 (m, 1H), 1.71-1.60 (m, 1H), 1.58-1.43 (m, 1H), 0.99 (t, *J* = 7.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.9, 135.3, 129.6, 129.5, 127.3, 87.9, 35.8, 18.5, 13.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{13}NO_3S$ 239.0616; Found 239.0614.

5-Isopropyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1d)



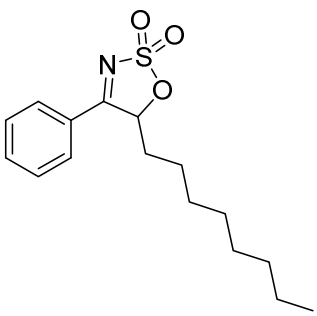
yield: 82% (187 mg as an ivory solid); mp: 107.5-112.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.87 (m, 2H), 7.77-7.70 (m, 1H), 7.64-7.56 (m, 2H), 5.86 (d, *J* = 2.3 Hz, 1H), 2.48-2.35 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 135.1, 129.5, 129.3, 127.7, 92.9, 32.5, 20.1, 14.5.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{13}NO_3S$ 239.0616; Found 239.0613.

5-Benzyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1e)



yield: 38% (500 mg as a white solid); mp: 150.7-153.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 7.99-7.90 (m, 2H), 7.81-7.73 (m, 1H), 7.67-7.59 (m, 2H), 7.39-7.30 (m, 3H), 7.24-7.20 (m, 2H), 6.05 (dd, *J* = 8.7, 3.3 Hz, 1H), 3.37 (dd, *J* = 15.0, 3.3 Hz, 1H), 3.23 (dd, *J* = 15.0, 8.7 Hz, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 135.4, 134.00, 129.7, 129.6, 129.4, 128.9, 127.9, 127.4, 88.0, 40.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{13}NO_3S$ 287.0616; Found 287.0612.

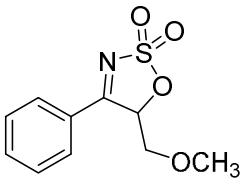
5-Octyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1f)



yield: 70% (495 mg as a colorless oil); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.89 (m, 2H), 7.79-7.70 (m, 1H), 7.65-7.57 (m, 2H), 5.90 (dd, *J* = 8.6, 3.0 Hz, 1H), 2.13-2.03 (m, 1H), 1.98-1.86 (m, 1H), 1.68-1.55 (m,

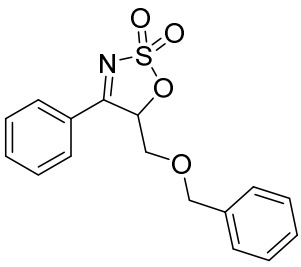
1H), 1.54-1.41 (m, 1H), 1.40-1.20 (m, 10H), 0.89 (t, J = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.9, 135.3, 129.6, 129.5, 127.4, 88.1, 33.9, 31.7, 29.1, 29.0, 28.8, 25.00, 22.6, 14.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{23}NO_3S$ 309.1399; Found 309.1396.

5-(Methoxymethyl)-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1g)



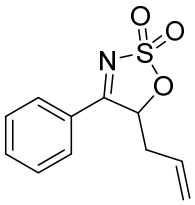
yield: 58% (650 mg as a yellow solid); mp: 149.5-151.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.93 (m, 2H), 7.78-7.71 (m, 1H), 7.65-7.57 (m, 2H), 5.99 (dd, J = 4.0, 2.8 Hz, 1H), 3.99-3.87 (m, 2H), 3.38 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 135.4, 129.5, 129.5, 127.4, 87.4, 71.9, 60.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_4S$ 241.0409; Found 241.0398.

5-((Benzyloxy)methyl)-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1h)



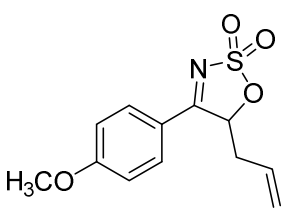
yield: 47% (110 mg as a white solid); mp: 131.5-135.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94-7.86 (m, 2H), 7.77-7.69 (m, 1H), 7.61-7.51 (m, 2H), 7.32-7.23 (m, 3H), 7.21-7.11 (m, 2H), 5.98 (dd, J = 3.9, 2.8 Hz, 1H), 4.65-4.46 (m, 2H), 4.02-3.87 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3, 136.5, 135.3, 129.5, 129.4, 128.5, 128.0, 127.7, 127.4, 87.4, 73.7, 68.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NO_4S$ 317.0722; Found 317.0709.

5-Allyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1i)



yield: 67% (523 mg as an ivory solid); mp: 94.7-95.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96-7.87 (m, 2H), 7.79-7.71 (m, 1H), 7.66-7.56 (m, 2H), 6.00-5.92 (m, 1H), 5.90-5.73 (m, 1H), 5.27-5.18 (m, 1H), 5.15-5.05 (m, 1H), 2.97-2.84 (m, 1H), 2.76-2.62 (m, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 135.4, 129.6, 129.5, 127.3, 120.8, 87.0, 67.1, 37.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{11}NO_3S$ 237.0460; Found 237.0453.

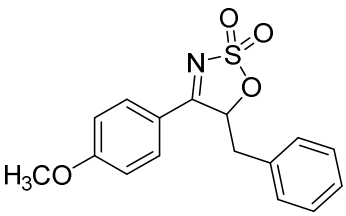
5-Allyl-4-(4-methoxyphenyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1j)



yield: 77% (150 mg as a yellow solid); mp: 133.1-134.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.9 Hz, 2H), 7.07 (d, J = 8.9 Hz, 2H), 5.92-5.88 (m 1H), 5.87-5.78(m 1H), 5.22 (dd, J = 10.2, 1.3 Hz, 1H), 5.12 (dd, J = 17.0, 1.3 Hz, 1H), 3.95 (s, 3H), 2.93-2.85 (m, 1H), 2.73-2.65 (m, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 165.4, 132.00, 129.8, 120.6, 119.4,

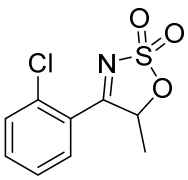
115.1, 86.8, 55.8, 38.3.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{12}H_{13}NO_4S$ 267.0565; Found 267.0561

5-Benzyl-4-(4-methoxyphenyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1k)



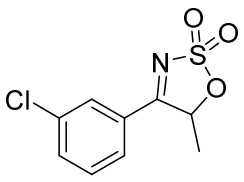
yield: 50% (500 mg as a yellow solid); mp: 130.5-132.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.88 (m, 2H), 7.39-7.31 (m, 3H), 7.28-7.21 (m, 2H), 7.12-7.06 (m, 2H), 5.98 (dd, *J* = 8.9, 3.2 Hz, 1H), 3.97 (s, 3H), 3.35 (dd, *J* = 15.1, 3.2 Hz, 1H), 3.24 (dd, *J* = 15.1, 8.9 Hz, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 165.5, 134.3, 132.1, 129.4, 128.9, 127.8, 119.5, 115.1, 87.8, 55.9, 40.41.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{15}NO_4S$ 317.0722; Found 317.0736.

4-(2-Chlorophenyl)-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide(1l)



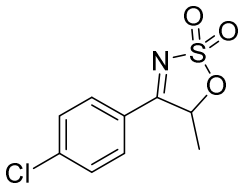
yield: 69% (60 mg as a yellow solid); mp: 88.3-89.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93-7.89 (m, 1H), 7.65-7.61 (m, 1H), 7.60-7.56 (m, 1H), 7.52-7.48 (m, 1H), 6.36 (q, *J* = 7.0 Hz, 1H), 1.64 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.5, 134.8, 133.5, 132.6, 131.5, 127.9, 127.2, 85.9, 18.3.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_8ClNO_3S$ 244.9913; Found 244.9920.

4-(3-Chlorophenyl)-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide(1m)



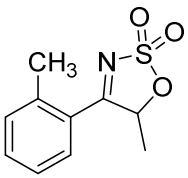
yield: 47% (310 mg as a white solid); mp: 118.8-120.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.93 (m, 1H), 7.82-7.78 (m, 1H), 7.74-7.70 (m, 1H), 7.59-7.54 (m 1H), 5.94 (q, *J* = 7.0 Hz, 1H), 1.79 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 136.0, 135.3, 130.9, 129.5, 128.6, 127.6, 83.8, 20.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_8ClNO_3S$ 244.9913; Found 244.9912.

4-(4-Chlorophenyl)-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide(1n)



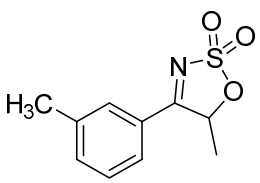
yield: 45% (300 mg as a white solid); mp: 145.7-148.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94-7.85 (m, 2H), 7.65-7.57 (m, 2H), 5.93 (q, *J* = 6.9 Hz, 1H), 1.78 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 142.3, 130.9, 130.1, 125.4, 83.7, 20.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_8ClNO_3S$ 244.9913; Found 244.9914.

5-Methyl-4-(o-tolyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1o)



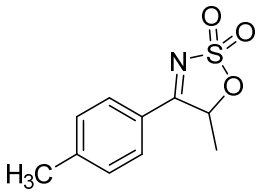
yield: 40% (171 mg as a white solid); mp: 124.3-126.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61-7.53 (m, 1H), 7.49-7.35 (m, 3H), 5.99 (q, *J* = 7.0 Hz, 1H), 2.70 (s, 3H), 1.66 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 141.8, 133.8, 133.1, 129.7, 126.5, 126.1, 85.1, 22.3, 19.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_3S$ 225.0460; Found 225.0446.

5-Methyl-4-(m-tolyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1p)



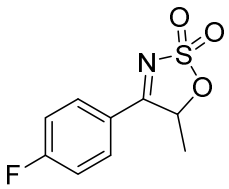
yield: 67% (508 mg as a slightly yellow solid); mp: 72.1-74.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 1H), 5.97 (q, *J* = 7.0 Hz, 1H), 2.48 (s, 3H), 1.77 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.8, 139.8, 136.3, 130.1, 129.4, 126.9, 126.9, 84.0, 21.3, 20.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_3S$ 225.0460; Found 225.0455.

5-Methyl-4-(p-tolyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1q)



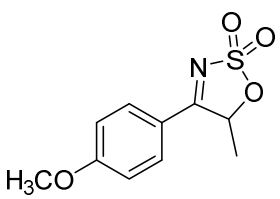
yield: 61% (378 mg as an ivory solid); mp: 120.9-122.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 5.95 (q, *J* = 7.0 Hz, 1H), 2.51 (s, 3H), 1.78 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.3, 147.1, 130.3, 129.8, 124.2, 83.9, 22.0, 20.3.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_3S$ 225.0460; Found 225.0449.

4-(4-Fluorophenyl)-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide(1r)



yield: 74% (503 mg as a white solid); mp: 100.3-101.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05-7.92 (m, 2H), 7.37-7.23 (m, 2H), 5.95 (q, *J* = 7.0 Hz, 1H), 1.78 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 167.0 (d, *J* = 260.0 Hz), 132.4 (d, *J* = 10.9 Hz), 123.3, 117.2 (d, *J* = 22.2 Hz), 83.7, 20.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_8FNO_3S$ 229.0209; Found 229.0209.

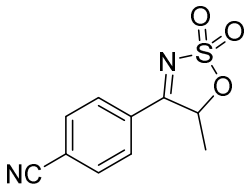
4-(4-Methoxyphenyl)-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide(1s)



yield: 59% (393 mg as a yellow solid); mp: 129.7-130.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.8 Hz, 2H), 7.07 (d, *J* = 8.8 Hz, 2H), 5.92 (q, *J* = 6.9 Hz, 1H), 3.95 (s, 3H), 1.79 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 165.5, 132.1, 119.2, 115.1, 83.6, 55.8, 20.5.;

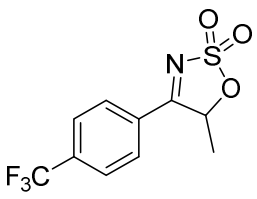
HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_4S$ 241.0409; Found 241.0408.

4-(5-Methyl-2,2-dioxido-5H-1,2,3-oxathiazol-4-yl)benzonitrile(1t)



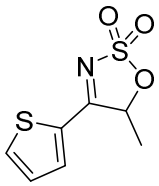
yield: 69% (60 mg as a yellow solid); mp: 160.9-162.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.7 Hz, 2H), 7.91 (d, *J* = 8.7 Hz, 2H), 5.97 (q, *J* = 7.0 Hz, 1H), 1.78 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 133.2, 130.7, 130.0, 118.6, 117.1, 83.7, 19.7.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_8N_2O_3S$ 236.0256; Found 236.0228.

5-Methyl-4-(4-(trifluoromethyl)phenyl)-5H-1,2,3-oxathiazole 2,2-dioxide(1u)



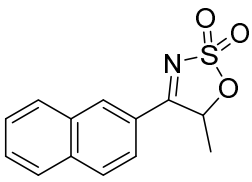
yield: 80% (513 mg as a white solid); mp: 144.7-145.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 2H), 6.01 (q, *J* = 7.0 Hz, 1H), 1.79 (d, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 136.5 (q, *J* = 33.3 Hz), 130.2, 130.0, 126.6 (q, *J* = 3.4 Hz), 123.1 (q, *J* = 273.2 Hz), 83.9, 19.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_8F_3NO_3S$ 279.0177; Found 279.0162.

5-methyl-4-(thiophen-2-yl)-5H-1,2,3-oxathiazole 2,2-dioxide(1v)



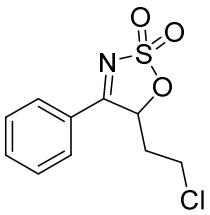
yield: 64% (384 mg as a yellow solid); mp: 94.4-96.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) 7.94 (d, *J* = 5.0 Hz, 1H), 7.78 (d, *J* = 3.9 Hz, 1H), 7.31 (dd, *J* = 5.0, 3.9 Hz, 1H), 5.83 (q, *J* = 6.9 Hz, 1H), 1.88 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 137.4, 135.7, 130.7, 129.4, 83.7, 20.9.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_7H_7NO_3S_2$ 216.9867; Found 216.9857.

5-Methyl-4-(naphthalen-2-yl)-5H-1,2,3-oxathiazole 2,2-dioxide(1w)



yield: 77% (670 mg as a slightly yellow solid); mp: 142.1-143.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39-8.35 (m, 1H), 8.06-7.92 (m, 4H), 7.77-7.62 (m, 2H), 6.12 (q, *J* = 6.9 Hz, 1H), 1.86 (d, *J* = 6.9 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.4, 136.4, 132.4, 132.0, 130.1, 129.7, 129.6, 128.1, 127.8, 124.3, 124.3, 84.0, 20.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for C13H11NO3S 261.0460; Found 261.0460.

5-(2-Chloroethyl)-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide(1x)

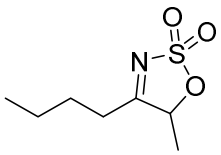


yield: 57% (253.5 mg as a yellow solid); mp: 109.7-110.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.89 (m, 2H), 7.81-7.72 (m, 1H), 7.63 (t, *J* = 7.9 Hz, 2H),

6.20 (dd, J = 10.3, 2.3 Hz, 1H), 3.91-3.79 (m, 2H), 2.52-2.30 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 135.8, 129.8, 129.7, 126.8, 84.1, 40.5, 37.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{10}ClNO_3S$ 259.0070; Found 259.0045

4-Butyl-5-methyl-5H-1,2,3-oxathiazole 2,2-dioxide (1y)

1y was prepared from 2-hydroxy-3-heptanone[14] and sulfamoyl chloride.

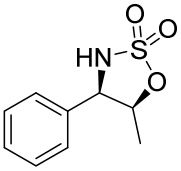


yield: 76% (2.2 g as a colorless oil); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.28 (q, J = 7.0 Hz, 1H), 2.74-2.42 (m, 2H), 1.85-1.71 (m, 2H), 1.66 (d, J = 7.0 Hz, 3H), 1.56-1.37 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.0, 86.1, 30.8, 27.4, 22.5, 18.2, 14.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_7H_{13}NO_3S$ 191.0616; Found 191.0614.

2. General procedure for the asymmetric transfer hydrogenation reaction of 1 to 2

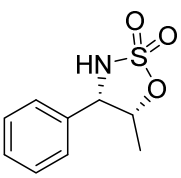
To a solution of 5-methyl-4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide (**1a**, 50 mg, 0.24 mmol), in CH_3CN (2 mL) was added a solution of DBU (72 mg, 0.48 mmol) and HCO_2H (29 mg, 0.48 mmol) in CH_3CN (1 mL) followed by (*S*,*S*)-ClRhCp*(TsDPEN) catalyst (1.5 mg, 0.5 mol%). The reaction mixture was stirred at room temperature for 1 h, diluted with EtOAc (10 mL), and washed with water and saturated NaCl(aq) solution successively. The organic layer was separated, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude residue was purified on silica gel column chromatography using EtOAc/hexanes (1:9 to 1:2) as an eluent to afford the title compound as a white solid.

(*4R,5S*)-5-Methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2a)



Yield: 90% (45 mg as a white solid); mp: 78.2-79.5 ^{o}C; 99.7% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.9 min, t_R(minor) = 14.1 min); $[\alpha]_D^{20}$ = -38.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.37 (m, 5H), 5.26-5.32 (m, 1H), 5.03 (s, 1H), 4.99 (d, J = 6.1 Hz, 1H), 1.15 (d, J = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 129.2, 129.1, 127.3, 82.5, 63.6, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{11}NO_3S$ 213.0460; Found 213.0460.

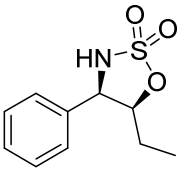
(*4S,5R*)-5-Methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(*ent*-2a)



Yield: 92% (39.2 mg as a white solid); mp: 78.2-79.5 ^{o}C; 99.2% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 8.9 min, t_R(major) = 14.1

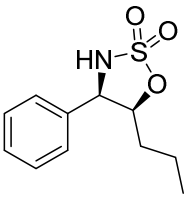
min); $[\alpha]_D^{20}$ = +31.6 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.48-7.37 (m, 5H), 5.26-5.32 (m, 1H), 5.03 (s, 1H), 4.99 (d, *J* = 6.1 Hz, 1H), 1.15 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 129.2, 129.1, 127.3, 82.4, 63.7, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{11}NO_3S$ 213.0454; Found 213.0460.

(*4R,5S*)-5-Ethyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2b)



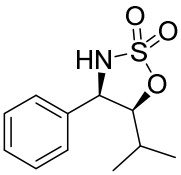
Yield: 96% (48 mg as a white solid); mp: 46.0-46.9 °C; 99.8% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.34min, t_R(minor) = 13.9 min); $[\alpha]_D^{20}$ = -59.5 (*c* 0.5, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) 7.46-7.33 (m, 5H), 5.03-4.97 (m, 1H), 4.95-4.91 (m, 1H), 4.88 (s, 1H), 1.48-1.36 (m, 1H), 1.30-1.21 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 129.2, 129.1, 127.5, 87.5, 63.5, 23.9, 10.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_3S$ 227.0616; Found 227.0609.

(*4R,5S*)-4-Phenyl-5-propyl-1,2,3-oxathiazolidine 2,2-dioxide(2c)



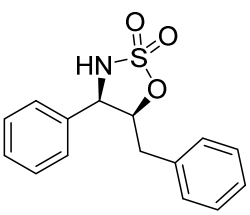
Yield: 97% (48.5 mg as a white solid); mp: 79.3-80.1 °C; 99.8% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 7.7 min, t_R(minor) = 13.3 min); $[\alpha]_D^{20}$ = -40.8 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.49-7.37 (m, 5H), 5.14-5.10 (m, 1H), 4.96-4.93 (m, 1H), 4.85 (s, 1H), 1.57-1.44 (m, 1H), 1.46-1.24 (m, 2H), 1.23-1.14 (m, 1H), 0.87 (t, *J* = 7.2 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.3, 129.2, 129.1, 127.5, 86.0, 63.6, 32.3, 19.0, 13.5.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{15}NO_3S$ 241.0773; Found 241.0765.

(*4R,5S*)-5-Isopropyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2d)



Yield: 94% (45.5 mg as a white solid); mp: 133.3-134.5 °C; 99.8% ee (Chiralcel OD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 7.3 min, t_R(minor) = 16.3 min); $[\alpha]_D^{20}$ = +5.3 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.53-7.34 (m, 5H), 4.92 (s, 1H), 4.82-4.76 (m, 1H), 4.73-4.65 (m, 1H), 1.70-1.51 (m, 1H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.76 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.9, 129.3, 129.1, 128.29, 90.3, 64.0, 28.4, 19.7, 17.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{15}NO_3S$ 241.0773; Found 241.0771.

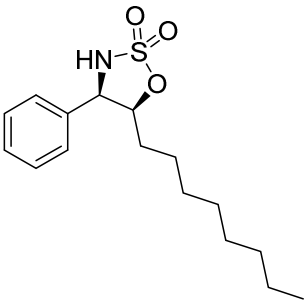
(*4R,5S*)-5-Benzyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2e)



Yield: 92% (53.1 mg as a white solid); mp: 181.5-184.0 °C; 99.3% ee (Chiralpak IC, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 7.8

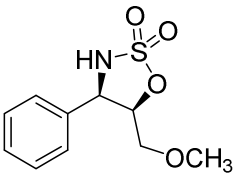
min, t_R(minor) = 9.8 min); $[\alpha]_D^{20}$ = -51.5 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.37 (m, 5H), 7.30-7.21 (m, 3H), 7.07-7.01 (m, 2H), 5.33-5.27 (m, 1H), 5.00 - 4.97 (m, 1H), 4.83 (s, 1H), 2.78 (dd, *J* = 14.9, 9.5 Hz, 1H), 2.48 (dd, *J* = 14.9, 4.3 Hz, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.0, 134.9, 129.5, 129.2, 129.1, 128.7, 127.7, 127.2, 86.0, 63.4, 36.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{15}NO_3S$ 289.0773; Found 289.0775.

(*4R,5S*)-5-Octyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2f)



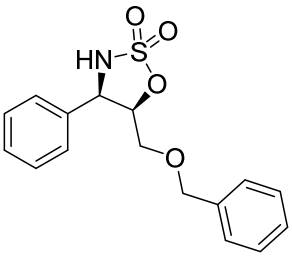
Yield: 96% (59.6 mg as a colorless oil); 95.6% ee (Chiralpak IC, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 6.4 min, t_R(major) = 6.8 min); $[\alpha]_D^{20}$ = -20.2 (*c* 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.37 (m, 5H), 5.15-5.03 (m, 2H), 4.96-4.92 (mz, 1H), 1.49-1.34 (m, 2H), 1.32-1.15 (m, 12H), 0.88 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.3, 129.1, 129.0, 127.5, 86.4, 63.5, 31.7, 30.4, 29.2, 29.0, 29.0, 25.6, 22.6, 14.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{25}NO_3S$ 311.1555; Found 311.1552.

(*4R,5R*)-5-(Methoxymethyl)-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2g)



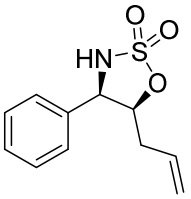
Yield: 91% (44.5 mg as a white solid); mp: 139-141.9 °C; 99.7% ee (Chiralpak AD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 12.8 min, t_R(major) = 14.6 min); $[\alpha]_D^{20}$ = -124.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.40 (m, 3H), 7.38-7.34 (m, 2H), 5.24 (d, *J* = 8.7 Hz, 1H), 5.16 (dd, *J* = 8.7, 6.1 Hz, 1H), 5.12 (ddd, *J* = 6.1, 4.3, 3.2 Hz, 1H), 3.39 (dd, *J* = 11.3, 3.2 Hz, 1H), 3.27 (dd, *J* = 11.3, 4.3 Hz, 1H), 3.20 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.2, 129.1, 129.0, 126.6, 85.0, 70.7, 61.8, 59.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_4S$ 243.0565; Found 243.0567

(*4R,5R*)-5-((Benzyloxy)methyl)-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2h)



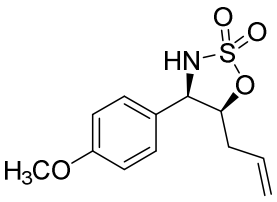
Yield: 97% (31.0 mg as a white solid); mp: 107.1-109.5 °C; 99.5% ee (Chiralpak AD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 12.4 min, t_R(major) = 14.0 min); $[\alpha]_D^{20}$ = -122.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.37 (m, 3H), 7.38-7.26 (m, 6H), 7.22-7.12 (m, 2H), 5.25-5.07 (m, 3H), 4.34 (q, *J* = 11.8 Hz, 2H), 3.51 (dd, *J* = 11.1, 3.2 Hz, 1H), 3.41 (dd, *J* = 11.1, 3.4 Hz, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 133.0, 129.0, 129.0, 128.5, 128.0, 127.7, 126.5, 85.0, 73.8, 68.3, 61.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{17}NO_4S$ 319.0878; Found 319.0873.

(*4R,5S*)-5-Allyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide(2i)



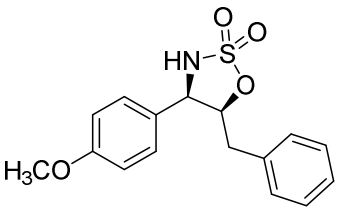
Yield: 96% (45.2 mg as a white solid); mp: 73.7-76.0 °C; 99.4% ee (Chiralpak ID, 20% IPA/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(minor) = 8.1 min, t_R(major) = 8.6 min); $[\alpha]_D^{20}$ = -38.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.37 (m, 5H), 5.75-5.59 (m, 1H), 5.19-5.09 (m, 2H), 5.09-4.90 (m, 3H), 2.31-2.15 (m, 1H), 2.05-1.94 (m, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.9, 131.2, 129.4, 129.1, 127.5, 119.4, 85.0, 63.3, 34.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{11}H_{13}NO_3S$ 239.0616; Found 239.0623.

(*4R,5S*)-5-Allyl-4-(4-methoxyphenyl)-1,2,3-oxathiazolidine 2,2-dioxide(2j)



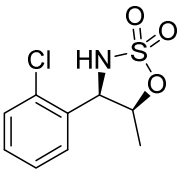
Yield: 91% (49.1 mg as an ivory solid); mp: 116.1-117.5 °C; 95.8% ee (Chiralpak ID, 20% IPA/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(minor) = 10.9 min, t_R(major) = 12.0 min); $[\alpha]_D^{20}$ = -29.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 5.75-5.59 (m, 1H), 5.17-5.00 (m, 3H), 4.95-4.89 (m, 1H), 4.83 (s, 1H), 3.85 (s, 3H), 2.34-2.17 (m, 1H), 2.08-1.93 (m, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 131.3, 128.9, 126.9, 119.3, 114.4, 85.1, 63.0, 55.4, 34.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{12}H_{15}NO_4S$ 269.0722; Found 269.0724.

(*4R,5S*)-5-Benzyl-4-(4-methoxyphenyl)-1,2,3-oxathiazolidine 2,2-dioxide(2k)



Yield: 90% (57.2 mg as a white solid); mp: 188.5-191.2 °C; 99.7% ee (Chiralpak AD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 11.8 min, t_R(major) = 14.8 min); $[\alpha]_D^{20}$ = -22.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.32 (m, 2H), 7.32-7.24 (m, 3H), 7.10-7.05 (m, 2H), 7.01-6.96 (m, 2H), 5.30 (ddd, *J* = 9.4, 5.8, 4.4 Hz, 1H), 4.94 (dd, *J* = 5.8, 3.8 Hz, 1H), 4.79 (d, *J* = 3.8 Hz, 1H), 3.88 (s, 3H), 2.83 (dd, *J* = 14.9, 9.4 Hz, 1H), 2.52 (dd, *J* = 14.9, 4.4 Hz, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 135.1, 129.1, 129.0, 128.6, 127.2, 126.9, 114.5, 86.2, 63.1, 55.4, 36.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{17}NO_4S$ 319.0878; Found 319.0879

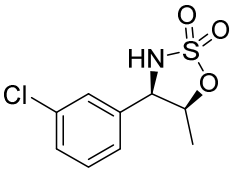
(*4R,5S*)-4-(2-Chlorophenyl)-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide(2l)



Yield: 92% (22.8 mg as a colorless oil); 53.4% ee (Chiralpak AD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 6.3 min, t_R(major) = 7.4 min); $[\alpha]_D^{20}$ = -36.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.72 (m, 1H), 7.46-7.38 (m, 2H), 7.38-7.32 (m, 1H), 5.61 (d, *J* = 6.5 Hz, 1H), 5.43 (p, *J* = 6.5 Hz, 1H), 5.20 (s,

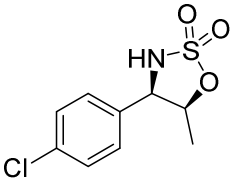
1H), 1.19 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 132.8, 132.6, 130.1, 129.7, 128.7, 127.7, 82.0, 59.6, 15.7.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{10}ClNO_3S$ 247.0070; Found 247.0057.

(*4R,5S*)-4-(3-Chlorophenyl)-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide(2m)



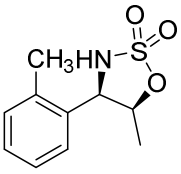
Yield: 97% (48.6 mg as a white solid); mp: 104.1-105.5 °C; 99.4% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.2 min, t_R(minor) = 10.4 min); $[\alpha]_D^{20}$ = -63.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43-7.36 (m, 3H), 7.35-7.30 (m, 1H), 5.32-5.25 (m, 1H), 5.06 (s, 1H), 4.96 (d, *J* = 6.1 Hz, 1H), 1.17 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.0, 135.1, 130.4, 129.4, 127.5, 125.5, 82.1, 63.0, 16.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{10}ClNO_3S$ 247.0070; Found 247.0069.

(*4R,5S*)-4-(4-Chlorophenyl)-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide(2n)



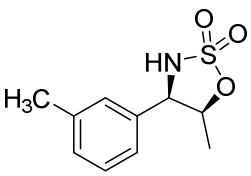
Yield: 92% (46.1 mg as a white solid); mp: 114.5-116.2 °C; 99.6% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 7.6 min, t_R(minor) = 11.1 min); $[\alpha]_D^{20}$ = -40.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 5.33-5.23 (m, 1H), 5.03 (s, 1H), 4.96 (d, *J* = 6.0 Hz, 1H), 1.15 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 133.5, 129.3, 128.8, 82.2, 63.1, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{10}ClNO_3S$ 247.0070; Found 247.0069.

(*4R,5S*)-5-Methyl-4-(*o*-tolyl)-1,2,3-oxathiazolidine 2,2-dioxide(2o)



Yield: 90% (41.0 mg as a white solid); mp: 80.9-82.7 °C; 88.1% ee (Chiralpak AD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 6.7 min, t_R(major) = 7.5 min); $[\alpha]_D^{20}$ = -86.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62-7.51 (m, 1H), 7.37-7.29 (m, 2H), 7.25-7.18 (m, 1H), 5.43-5.37 (m, 1H), 5.36-5.25 (m, 1H), 4.78 (s, 1H), 2.34 (s, 3H), 1.14 (d, *J* = 6.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ ~~δ~~ 135.0, 132.6, 130.9, 128.9, 127.0, 126.4, 81.7, 59.2, 19.5, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_3S$ 227.0616; Found 227.0602.

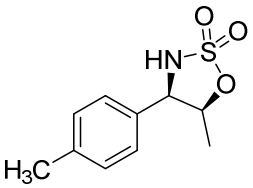
(*4R,5S*)-5-Methyl-4-(*m*-tolyl)-1,2,3-oxathiazolidine 2,2-dioxide(2p)



Yield: 93% (42.5 mg as a colorless oil); 99.6% ee (Chiralpak AD-H, 30% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 5.1 min, t_R(major) = 5.6

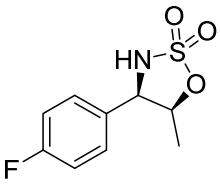
min); $[\alpha]_D^{20}$ = -44.5 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.30 (m, 1H), 7.26-7.20 (m, 1H), 7.21-7.15 (m, 2H), 5.30-5.23 (m, 1H), 4.97-4.93 (m, 1H), 4.88 (s, 1H), 2.41 (s, 3H), 1.16 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 134.7, 130.0, 129.0, 127.8, 124.3, 82.4, 63.6, 21.5, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_3S$ 227.0616; Found 227.0598.

(*4R,5S*)-5-Methyl-4-(*p*-tolyl)-1,2,3-oxathiazolidine 2,2-dioxide(2q)



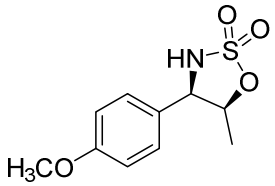
Yield: 99% (45.0 mg as a white solid); mp: 73.9-74.5 °C; 99.5% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.1 min, t_R(minor) = 20.7 min); $[\alpha]_D^{20}$ = -50.2 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.31-7.20 (m, 4H), 5.29-5.22 (m, 1H), 4.97-4.91 (m, 1H), 4.82 (s, 1H), 2.40 (s, 3H), 1.15 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 131.8, 129.8, 127.2, 82.5, 63.5, 21.2, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_3S$ 227.0616; Found 227.0621.

(*4R,5S*)-4-(4-Fluorophenyl)-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide(2r)



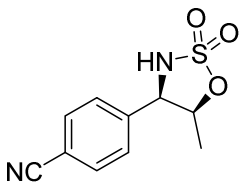
Yield: 99% (45.8 mg as a white solid); mp: 100.5-101.8 °C; 99.7% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 6.6 min, t_R(minor) = 8.8 min); $[\alpha]_D^{20}$ = -28.6 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46-7.32 (m, 2H), 7.23-7.05 (m, 2H), 5.35-5.20 (m, 1H), 5.13 (s, 1H), 5.04-4.87 (m, 1H), 1.14 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1 (d, *J* = 248.2 Hz), 130.8 (d, *J* = 3.5 Hz), 129.2 (d, *J* = 8.3 Hz), 116.1 (d, *J* = 21.4 Hz), 82.4, 63.0, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_9H_{10}FNO_3S$ 231.0365; Found 231.0358.

(*4R,5S*)-4-(4-Methoxyphenyl)-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide(2s)



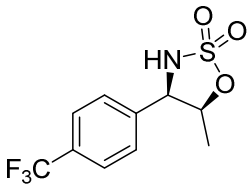
Yield: 90% (44.0 mg as a white solid); mp: 141.5-142.9 °C; 99.6% ee (Chiralcel OD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 10.6 min, t_R(minor) = 14.8 min); $[\alpha]_D^{20}$ = -36.1 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.6 Hz, 2H), 6.96 (d, *J* = 8.6 Hz, 2H), 5.30-5.20 (m, 1H), 4.94-4.89 (m, 1H), 4.83 (s, 1H), 3.85 (s, 3H), 1.16 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 128.6, 126.8, 114.5, 82.5, 63.4, 55.4, 16.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{13}NO_4S$ 243.0565; Found 243.0567.

4-((*4R,5S*)-5-Methyl-2,2-dioxido-1,2,3-oxathiazolidin-4-yl)benzonitrile(2t)



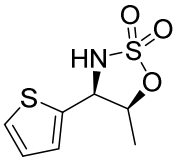
Yield: 95% (22.7 mg as a white solid); mp: 142.2-144.5 °C; 98.2% ee (Chiralpak AD-H, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 12.0 min, t_R(major) = 20.3 min); $[\alpha]_D^{20}$ = -14.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 5.37-5.28 (m, 1H), 5.08-4.96 (m, 2H), 1.15 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 132.8, 128.3, 118.0, 113.3, 81.7, 63.1, 16.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{10}N_2O_3S$ 238.0412; Found 238.0406.

(*4R,5S*)-5-Methyl-4-(4-(trifluoromethyl)phenyl)-1,2,3-oxathiazolidine 2,2-dioxide(2u)



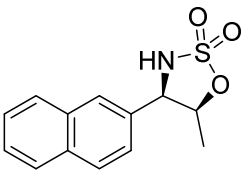
Yield: 95% (53.4 mg as a white solid); mp: 86.1-88.3 °C; 99.9% ee (Chiralpak OD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 9.7 min, t_R(minor) = 11.6 min); $[\alpha]_D^{20}$ = -34.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 2H), 5.37-5.28 (m, 1H), 5.16-4.97 (m, 2H), 1.16 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.00, 131.5 (q, *J* = 32.9 Hz), 127.9, 126.0 (q, *J* = 3.6 Hz), 123.7 (q, *J* = 272.0 Hz), 82.1, 63.1, 16.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{10}F_3NO_3S$ 281.0333; Found 281.0331.

(*4S,5S*)-5-Methyl-4-(thiophen-2-yl)-1,2,3-oxathiazolidine 2,2-dioxide(2v)



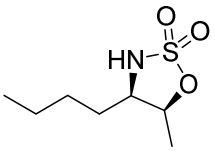
Yield: 94% (41.2 mg as a brown oil); 99.3% ee (Chiralpak AD-H, 40% IPA/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(minor) = 6.5 min, t_R(major) = 7.0 min); $[\alpha]_D^{20}$ = -40.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.18 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.08 (dd, *J* = 5.1, 3.6 Hz, 1H), 5.30-5.18 (m, 2H), 5.16 (s, 1H), 1.29 (d, *J* = 6.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.2, 127.5, 127.3, 126.6, 82.6, 59.9, 15.7.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_7H_9NO_3S_2$ 219.0024; Found 219.0022.

(*4R,5S*)-5-Methyl-4-(naphthalen-2-yl)-1,2,3-oxathiazolidine 2,2-dioxide(2w)



Yield: 93% (49.1 mg as a white solid); mp: 124.1-126.6 °C; 99.6% ee (Chiralpak AD-H, 20% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 8.6 min, t_R(major) = 10.2 min); $[\alpha]_D^{20}$ = -46.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.80 (m, 4H), 7.63-7.51 (m, 2H), 7.55-7.41 (m, 1H), 5.44-5.28 (m, 1H), 5.21-5.08 (m, 1H), 1.17 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.4, 133.1, 132.2, 129.1, 128.1, 127.8, 126.9, 126.8, 124.4, 82.5, 63.8, 16.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{13}H_{13}NO3S$ 263.0616; Found 263.0616.

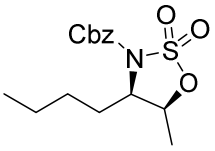
4-Butyl-5-methyl-1,2,3-oxathiazolidine 2,2-dioxide (2y)



Yield: 91% (35.2 mg as a colorless oil); $[\alpha]_D^{20}$ = +16.2 (*c* 0.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.06-4.91 (m, 1H), 4.52 (d, *J* = 8.4 Hz, 1H), 4.01-3.84 (m, 1H), 1.77-1.62 (m, 1H), 1.60-1.47 (m, 2H), 1.45 (d, *J* = 6.6 Hz, 3H), 1.42-1.26 (m, 3H), 0.95 (t, *J* = 7.0 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 84.9, 60.2, 28.7, 28.6, 22.8, 14.9, 14.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_7H_{15}NO_3S$ 193.0773; Found 193.0780.

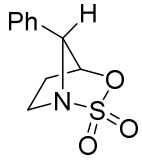
Benzyl 4-butyl-5-methyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide (*N-Cbz*-2y)

To the solution of **2y** (30 mg, 0.16 mmol) in THF (1 mL) was added *t*-BuOK in THF (1 M soln, 0.23 mL, 0.23 mmol). The reaction mixture was stirred for 1 h at rt. Benzyl chloroformate (55 μL, 0.39 mmol) was then added slowly and stirred at rt for 2 h. The reaction mixture was diluted with EtOAc (20 mL), washed with water and saturated NaCl (aq). The organic layer was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:*n*-Hex=1:9 to 1:4) as an eluent to afford the title compound (41 mg, 69%) as a colorless oil.



Yield: 69% (41 mg as a colorless oil); 99.7% ee (Chiralcel OD-H, 5% IPA/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(major) = 21.7 min, t_R(minor) = 24.5 min); $[\alpha]_D^{20}$ = +24.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.31 (m, 5H), 5.43-5.26 (m, 2H), 5.15-5.05 (m, 1H), 4.40-4.28 (m, 1H), 1.78 (p, *J* = 7.5, 6.7 Hz, 2H), 1.53 (d, *J* = 6.5 Hz, 3H), 1.44-1.29 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.6, 135.0, 129.1, 129.0, 128.4, 81.0, 69.8, 62.4, 28.7, 27.7, 23.1, 14.8, 14.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{21}NO_5S$ 327.1140; Found 327.1139.

(*1R,4S,7R*)-7-Phenyl-3-oxa-2-thia-1-azabicyclo[2.2.1]heptane 2,2-dioxide(7)

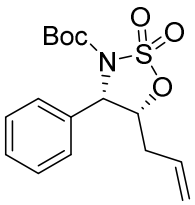


Yield: 82% (18.4 mg as a white solid); mp: 134.9-136.2 °C; 99.9% ee (Chiralpak IC, 10% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(minor) = 22.2 min, t_R(major) = 25.4 min); $[\alpha]_D^{20}$ = +4.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.35 (m, 3H), 7.35-7.25 (m, 2H), 5.62 (s, 1H), 5.49 (s, 1H), 3.87-3.71 (m, 1H), 3.30-3.13 (m, 1H), 2.28-2.11 (m, 1H), 1.87-1.72 (m, 1H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.7, 129.2, 128.8, 125.8, 89.6, 70.9, 45.9, 27.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{10}H_{11}NO_3S$ 225.0460; Found 225.0449.

3. Synthesis of *tert*-butyl (*4S,5R*)-5-allyl-4-phenyl-1,2,3-oxathiazolidine-3-carboxylate

2,2-dioxide (*N-Boc*-2i)

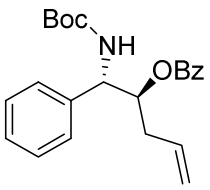
To a solution of (*4S,5R*)-5-allyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide (**2i**, 150 mg, 0.63 mmol) in CH_3CN (5 mL) was added di-*tert*-butyl dicarbonate (273 mg, 1.25 mmol) followed by DMAP(cat.) and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with EtOAc (20 mL), washed with water and saturated NaCl (aq). The organic layer was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:4) as an eluent to afford the title compound (195 mg, 92%) as a white solid.



yield: 92% (195 mg as a white solid); mp: 109.7-111.4 °C; $[\alpha]_D^{20}$ = +6.5 ; ^{1}H NMR (30 MHz, $CDCl_3$) δ 7.51-7.34 (m, 5H), 5.77-5.57 (m, 1H), 5.24-5.11 (m, 3H), 5.14-5.00 (m, 2H), 2.18-1.98 (m, 2H), 1.47 (s, 9H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 134.1, 130.4, 129.2, 128.9, 127.7, 119.8, 85.5, 81.9, 64.7, 34.1, 27.7.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{22}NO_5S$ 340.1218; Found 340.1199.

4. Synthesis of (*1S,2S*)-1-(*t*-Boc-amino)-1-phenylpent-4-en-2-yl benzoate (8)

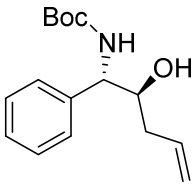
To a solution of (*4S,5R*)-*N-Boc*-**2i** (170 mg, 0.5 mmol) in DMF (5 mL) was added benzoic acid (122 mg, 1.0 mmol) followed by CsF (152 mg, 1.0 mmol) and the mixture was stirred at 60 ℃ for 3 h. The reaction mixture was diluted with EtOAc (20 mL) and the organic layer was washed with water and saturated NaCl (aq). The organic layer was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The crude residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:*n*-Hex=1:9 to 1:3) as an eluent to afford the title compound (134 mg, 71%) as colorless oil.



yield: 71% (134 mg as a colorless oil); $[\alpha]_D^{20}$ = +31.7 ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 2H), 7.64-7.55 (m, 1H), 7.51-7.41 (m, 2H), 7.39-7.29 (m, 5H), 5.94-5.75 (m, 1H), 5.46 (q, *J* = 6.3 Hz, 1H), 5.24 (d, *J* = 9.4 Hz, 1H), 5.18-5.06 (m, 2H), 5.07-4.93 (m, 1Hrlagudf1), 2.44 (t, *J* = 6.5 Hz, 2H), 1.33 (s, 9H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 155.2, 139.4, 133.1, 132.7, 129.9, 129.7, 128.8, 128.4, 127.9, 127.0, 118.8, 79.7, 75.8, 57.0, 36.1, 28.2.; HRMS (FAB, double focusing) m/z: $[M+H]^+$ Calcd for $C_{23}H_{28}NO_4$ 382.2018; Found 382.2034.

5. Synthesis of (*1S,2S*)-*t*-butyl (2-hydroxy-1-phenylpent-4-en-1-yl)carbamate (9)

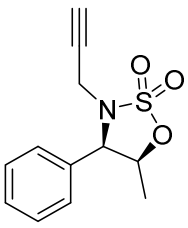
To a solution of (*1S,2S*)-1-((*tert*-butoxycarbonyl)amino)-1-phenylpent-4-en-2-yl benzoate (**8**, 73 mg, 0.19 mmol) in MeOH (5 mL) was added KCN (6.5 mg, 0.1 mmol) and the mixture was stirred at room temperature for 3 h. The solvent was evaporated under reduced pressure, diluted with EtOAc (10 mL), washed with water, and saturated NaCl (aq). The organic layer was separated, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:1) as an eluent to afford title compound (35 mg, 66%) as a white solid.



yield: 66% (35 mg as a white solid); mp: 95.5-96.2 ^{o}C; $[\alpha]_D^{20}$ = +13.1 (*c* 1.0 $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.34 (m, 2H), 7.34-7.29 (m, 3H), 5.97-5.80 (m, 1H), 5.39 (s, 1H), 5.25-5.19 (m, 1H), 5.16 (d, *J* = 3.9 Hz, 1H), 4.71 (s, 1H), 3.91 (s, 1H), 2.44-2.24 (m, 2H), 1.98 (s, 1H), 1.45 (s, 9H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 136.8, 134.0, 128.7, 127.5, 126.58, 118.6, 79.7, 74.3, 58.1 38.7, 28.4.; HRMS (FAB, double focusing) m/z: $[M+H]^+$ Calcd for $C_{16}H_{24}NO_3$ 278.1756; Found 278.1748.

6. Synthesis of (*4R,5S*)-5-methyl-4-phenyl-3-(prop-2-yn-1-yl)-1,2,3-oxathiazolidine 2,2-dioxide (11)

To a solution of 60% NaH (59 mg, 1.46 mmol) in DMF (3 mL) was added (*4R,5S*)-5-methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide (**2a**, 260 mg, 1.22 mmol) at 0 ^{o}C. After stirring for 30 minutes at 0 ^{o}C, propagyl bromide (218 mg, 1.83 mmol) was added to the reaction mixture. The mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with EtOAc (10 mL), washed with water, and saturated NaCl (aq). The organic layer was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:3) as an eluent to afford the title compound (250 mg, 82%) as a colorless oil.

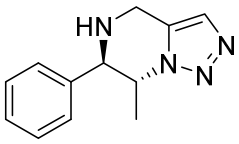


yield: 82% (250 mg as a colorless oil); $[\alpha]_D^{20}$ = -180.5 (*c* 1.0 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.35 (m, 5H), 5.26-5.17 (m, 1H), 4.94 (d, *J* = 6.7 Hz, 1H), 4.13 (d, *J* = 18.0 Hz, 1H), 3.70 (d, *J* = 17.8 Hz, 1H), 2.38 (s, 1H), 1.15 (d, *J* = 6.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 129.5, 129.2, 128.3, 80.3, 75.9, 74.8, 65.7, 34.4, 16.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for

$C_{12}H_{13}NO_3S$ 251.0616; Found 251.0617.

7. Synthesis of (*6R,7R*)-7-methyl-6-phenyl-4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-a]pyrazine (13)

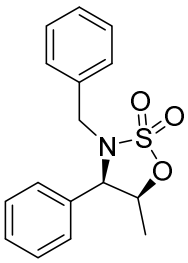
To a solution of (*4R,5S*)-5-methyl-4-phenyl-3-(prop-2-yn-1-yl)-1,2,3-oxathiazolidine 2,2-dioxide (**11**, 100 mg, 0.40 mmol) in DMF (2 mL) was added NaN_3 (52 mg, 0.80 mmol) and the mixture was stirred at 60 °C for 3 h. Upon completion, the reaction mixure was cool to room temperature and contents were diluted with Et_2O (4 mL), treated with 1*N* aqueous HCl (4 mL), and allowed to stir for an additional 12 h at room temperature. Once this operation was completed, the reaction mixture was poured into saturated $NaHCO_3$ solution and extracted EtOAc (10 mL x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography using MeOH/DCM (MeOH:DCM=1:19) as an eluent to afford the title compound (78 mg, 92%) as a white solid.



yield: 92% (78 mg as a white solid); mp: 149.4-151.1 °C; $[\alpha]_D^{20}$ = -103.1 (*c* 1.0 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.48-7.38 (m, 5H), 4.49 (p, *J* = 6.9 Hz, 1H), 4.36 (d, *J* = 15.1 Hz, 1H), 4.22 (d, *J* = 15.2 Hz, 1H), 3.78 (d, *J* = 9.3 Hz, 1H), 2.05 (s, 1H), 1.60 (d, *J* = 6.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.1, 131.8, 129.2, 129.0, 128.0, 66.0, 59.4, 41.6, 16.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{12}H_{14}N_4$ 214.1218; Found 214.1208.

8. Synthesis of (*4R,5S*)-3-benzyl-5-methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide (14)

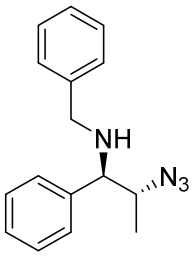
To a solution of 60% NaH (366 mg, 9.1 mmol) in DMF (10 mL) was added (*4R,5S*)-5-methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide (**2a**, 1.3 g, 6.1 mmol) at 0 °C. After stirring for 30 minutes at 0 °C, benzyl bromide (1.6 g, 9.1 mmol) was added to the reaction mixture. The mixture was stirred at room temperature for 5 h. The reaction mixture was diluted with EtOAc (20 mL), washed with water, and saturated NaCl (aq). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:3) as an eluent to afford the title compound (1.65 g, 89%) as a colorless oil.



yield: 89% (1.65 g as a colorless oil); $[\alpha]_D^{20}$ = -102.7 (*c* 0.5 $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) 7.46 – 7.39 (m, 3H), 7.36 – 7.28 (m, 5H), 7.29 – 7.24 (m, 2H), 5.18 (p, *J* = 6.4 Hz, 1H), 4.54 (d, *J* = 14.8 Hz, 1H), 4.45 (d, *J* = 6.2 Hz, 1H), 3.96 (d, *J* = 14.8 Hz, 1H), 1.09 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.4, 133.2, 129.2, 129.0, 128.9, 128.7, 128.4, 128.3, 79.8, 66.2, 48.1, 16.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{17}NO_3S$ 303.0929; Found 303.0927.

9. Synthesis of (*1R,2R*)-2-azido-*N*-benzyl-1-phenylpropan-1-amine (15)

To a solution of (*4R,5S*)-3-benzyl-5-methyl-4-phenyl-1,2,3-oxathiazolidine 2,2-dioxide (**14**, 1.1 g, 3.51 mmol) in DMF (5 mL) was added NaN_3 (456 mg, 7.02 mmol) and the mixture was stirred at 60 ^oC for 3 h. Upon completion, the reaction mixture was cool to room temperature and diluted with Et_2O (8 mL), treated with 1*N* aqueous HCl (8 mL), and allowed to stir for an additional 12 h at room temperature. Once this operation was completed, the reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with EtOAc (15 mL x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:3) as an eluent to afford the title compound (868 mg, 93%) as a colorless oil

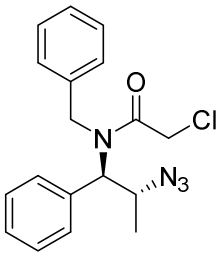


yield: 93% (868 mg as a colorless oil); $[\alpha]_D^{20}$ = -81.1 (*c* 0.5 $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.44 – 7.27 (m, 10H), 3.72 – 3.56 (m, 2H), 3.50 (s, 1H), 3.46 (d, *J* = 4.2 Hz, 1H), 2.26 (br, 1H), 1.09 (d, *J* = 6.5 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 140.1, 128.6, 128.4, 128.2, 128.1, 127.9, 126.9, 67.1, 62.9, 51.2, 16.5.; HRMS (FAB, double focusing) m/z: $[M+H]^+$ Calcd for $C_{16}H_{18}N_4$ 267.1610; Found 267.1613.

10. Synthesis of *N*-((*1R,2R*)-2-azido-1-phenylpropyl)-*N*-benzyl-2-chloroacetamide (16)

To a solution of (*1R,2R*)-2-azido-*N*-benzyl-1-phenylpropan-1-amine (**15**, 266 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added Et_3N (0.28 mL, 2.0 mmol) followed by chloroacetyl chloride (124 mg, 1.1 mmol) at 0 ^oC and the mixture was stirred for 2 h at that temperature. Upon completion, the reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 (10 mL x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure.

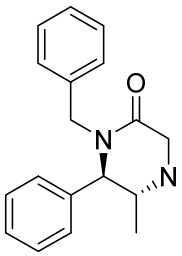
The residue was purified on silica gel column chromatography using EtOAc/hexanes (EA:n-Hex=1:9 to 1:3) as an eluent to afford the title compound (256 mg, 91%) as a colorless oil.



yield: 91% (256 mg as a colorless oil); $[\alpha]_D^{20}$ = -119.5 (*c* 1.0 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.30 (m, 5H), 7.27-7.17 (m, 3H), 7.12 (d, *J* = 7.2 Hz, 0.6H), 7.01 (d, *J* = 6.5 Hz, 1.4H), 5.14 (d, *J* = 10.1 Hz, 0.7H), 4.90 (d, *J* = 17.8 Hz, 0.3H), 4.79 (d, *J* = 10.9 Hz, 0.3H), 4.73 (d, *J* = 10.0 Hz, 0.3H), 4.60 (s, 1.4H), 4.56 – 4.46 (m, 0.7H), 4.32 (d, *J* = 12.0 Hz, 0.3H), 4.07 – 3.86 (m, 2H), 1.23 (d, *J* = 6.3 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 136.7, 136.4, 129.3, 129.0, 129.0, 128.7, 128.5, 127.9, 127.7, 126.5, 65.3, 57.3, 50.0, 42.7, 18.0.; HRMS (FAB, double focusing) m/z: $[M+H]^+$ Calcd for $C_{18}H_{20}ClN_4O$ 343.1326; Found 343.1311.

11. Synthesis of (*5R,6R*)-1-benzyl-5-methyl-6-phenylpiperazin-2-one (17)

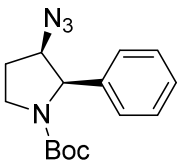
To a solution of *N*-((*1R,2R*)-2-azido-1-phenylpropyl)-*N*-benzyl-2-chloroacetamide (**16**, 100 mg, 0.29 mmol) in MeOH (2 mL) was added PPh_3 (153 mg, 0.58 mmol) and the mixture was stirred at 80 °C for 5 h. Upon completion, the reaction mixture was cooled to room temperature and solvent was removed under reduced pressure. The reaction mixture was dissolved in EtOAc (10 mL) and washed with saturated $NaHCO_3$ solution. The separated saturated $NaHCO_3$ solution was re-extracted with EtOAc (10 mL x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified on silica gel column chromatography using MeOH/CH_2Cl_2 (MeOH: CH_2Cl_2=1:19) as an eluent to afford the title compound (70 mg, 85%) as a white soidd.



yield: 85% (70 mg as a white solid); mp: 102.7-104.2 °C; $[\alpha]_D^{20}$ = -23.7 (*c* 1.0 $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.34 (m, 3H), 7.34-7.25 (m, 4H), 7.17 (d, *J* = 7.3 Hz, 2H), 7.11 (d, *J* = 7.2 Hz, 2H), 5.54 (d, *J* = 14.6 Hz, 1H), 3.98 (d, *J* = 7.2 Hz, 1H), 3.78 (q, *J* = 17.8 Hz, 2H), 3.35 (d, *J* = 14.6 Hz, 1H), 3.09-2.98 (m, 1H), 1.05 (d, *J* = 6.4 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 139.0, 136.8, 129.1, 128.7, 128.4, 127.8, 127.5, 67.1, 55.8, 49.2, 46.7, 18.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{18}H_{20}N_2O$ 280.1576; Found 280.1567.

12. Synthesis of *tert*-butyl (*2R,3R*)-3-azido-2-phenylpyrrolidine-1-carboxylate (19)

NaN_3 (43 mg, 0.67 mmol) was added in a single portion to a solution of (*1R,4S,7R*)-7-phenyl-3-oxa-2-thia-1-azabicyclo[2.2.1]heptane 2,2-dioxide (**7**, 50 mg, 0.22 mmol) in mixture of DMF and CH_3CN (4 mL, 1:1) at room temperature. The resulting mixture was warmed to 60 °C and stirred for 36 h. Upon completion, the reaction mixture was cooled to room temperature and the contents were evaporated under reduced pressure. The crude mixture was dissolved in CH_2Cl_2, treated with 1*N* aqueous HCl (3 mL), and allowed to stir for an additional 30 min at 60 °C. Once this operation was completed, the reaction mixture was poured into saturated $NaHCO_3$ (aq) and extracted with EtOAc (2 x 25 mL). The combined organic layers were then washed with water, dried ($MgSO_4$), and concentrated. The resulting solid was dissolved in CH_2Cl_2 and cooled to 0 °C. (*t*-Boc)$_2$O (58 mg, 0.27 mmol), Et_3N (0.06 mL, 0.44 mmol), and DMAP (cat) were added to this solution. The reaction mixture was stirred at rt for 3 h, quenched with saturated $NaHCO_3$ (aq) and extracted with EtOAc (2 x 25 mL). The combined organic layers were then washed with water, dried ($MgSO_4$), and concentrated and the residue was purified on silica gel column chromatography using EtOAc/hexanes as an eluent to afford **15** (42 mg, 66%) as a white solid.



yield: 66% (42 mg as a white solid); mp: 71.2-72.8 °C; $[\alpha]_D^{23}$ = -23.6 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 7.38-7.25 (m, 5H), 5.04 (br, 1H), 4.41 (br, 1H), 3.70 (br, 1H), 3.64-3.59 (m, 1H), 2.29-2.23 (m, 1H), 2.04-1.98 (m, 1H), 1.43 (s, br, 3H), 1.13 (s, br, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 138.7, 128.2, 127.6, 127.0, 79.9, 64.1, 63.6, 44.5, 28.3, 28.0.; HRMS (FAB, double focusing) m/z: $[M+H]^+$ calcd for $C_{15}H_{20}N_4O_2$ 289.1665, found 289.1653.

13. Base (DBU, Et_3N, DABCO, *i*-Pr_2NEt, and pyridine)-mediated racemization of (*S*)-1a

(5*S*)-**1a** (50 mg, 0.24 mmol, 93% ee) was dissolved in CH_3CN (2 mL) and base (0.48 mmol) was added in one portion. After stirring for 1 min at room temperature, the reaction mixture was quickly quenched with 1N HCl solution (5 mL) and diluted with EtOAc (10 mL). The organic layer was separated and washed with water, saturated $NaHCO_3$ solution, and dried over $MgSO_4$. The solvent was removed under reduced pressure to give crude (5*S*)-**1a** (quantitative recovery). The residue was subjected to chiral HPLC analysis. (Chiralpak AD-H, 5% isopropanol/hexanes, 1.0 mL/min, 215 nm)

Recovered (5*S*)-**1a**: 0.4% ee with DBU, 9.1% ee with Et_3N, 15.0% ee with DABCO, 18.5% ee with *i*-Pr_2NEt, 92% ee with pyridine.

Supporting Information. Copies of ^{1}H-, ^{13}C-NMR, chiral HPLC chromatograms for all new compounds, X-ray crystallographic data in CIF for (*1R,4S,7R*)-**7** (CCDC-1835266).

ACKNOWLEDGMENTS

This research was financially supported by grants from the National Research Foundation of Korea (2017M3A9A5051181) and Korea Research Institute of Chemical Technology (SI1707 & SI1807).

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