Nickel-Catalyzed Asymmetric Hydrogenation of Cyclic Sulfamidate Imines: Efficient Synthesis of Chiral Cyclic Sulfamidates

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HIGHLIGHTS
- Ni-catalyzed asymmetric hydrogenation of cyclic sulfamidate imines
- Efficient preparation of enantioenriched cyclic sulfamidates
- Broad range of substrate scope
- Gram-scale asymmetric hydrogenation with high TON

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Nickel-Catalyzed Asymmetric Hydrogenation of Cyclic Sulfamidate Imines: Efficient Synthesis of Chiral Cyclic Sulfamidates

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SUMMARY
Chiral cyclic sulfamidates are useful building blocks to construct compounds, such as chiral amines, with important applications. Often these compounds can only be generated through expensive precious metal catalysts. Here, Ni(OAc)2/((S, S)-Ph-BPE-catalyzed highly efficient asymmetric hydrogenation of cyclic sulfamidate imines was successfully developed, affording various chiral cyclic sulfamidates with high yields and excellent enantioselectivities (up to 99% yield, >99% enantiomeric excess (ee)). This Ni-catalyzed asymmetric hydrogenation on a gram scale has been achieved with only 0.1 mol% catalyst loading in 99% yield with 93% ee. Other types of N-sulfonyl ketimines were also hydrogenated well to obtain the corresponding products with >99% conversion, 96%–97% yields, and 97%→>99% ee. In addition, this asymmetric methodology could produce other enantioenriched organic molecules, such as chiral β-fluoroamine, amino ether, and phenylglycinol. Moreover, a reasonable catalytic cycle was provided according to the deuterium-labeling studies, which could reveal a possible mechanism for this Ni-catalyzed asymmetric hydrogenation.

INTRODUCTION
Efficient synthesis of chiral cyclic sulfamidates has attracted great attention in the past decades, owing to their versatility working as valuable intermediates for the construction of some important organic compounds and bioactive molecules (Aguilera and Fernandez-Mayoralas, 1996; Williams et al., 2003; Bower et al., 2004, 2007a, 2007b, 2007c, 2010; Jamieson et al., 2009; Lorion et al., 2010; Megia-Fernandez et al., 2011; Boulton et al., 1999; Wei and Lubell, 2000; Espino et al., 2001; Cohen and Halcomb, 2001, 2002; Atfani et al., 2001; Nicolau et al., 2002; Meléndez and Lubell, 2003; Ni et al., 2007; Rönholm et al., 2007; Baig et al., 2010, 2011; Venkateswarlu et al., 2014; Albou et al., 2016; Su et al., 2016; Chen et al., 2014; Kong et al., 2015; Liu et al., 2017; Wu et al., 2018). For example, ring-opening reactions of chiral cyclic sulfamidates can offer convenient and efficient access to chiral amines, amino alcohols, amino acids, and their derivatives (Boulton et al., 1999; Wei and Lubell, 2000; Espino et al., 2001; Cohen and Halcomb, 2001, 2002; Atfani et al., 2001; Nicolau et al., 2002; Meléndez and Lubell, 2003; Ni et al., 2007; Rönholm et al., 2007; Baig et al., 2010, 2011; Venkateswarlu et al., 2014; Albou et al., 2016; Su et al., 2016; Chen et al., 2014; Kong et al., 2015; Liu et al., 2017; Wu et al., 2018). So far the asymmetric catalytic synthetic methods of chiral cyclic sulfamidates were mainly focused on transition metal-catalyzed asymmetric intramolecular amidation of sulfamate esters (Liang et al., 2002; Liang et al., 2004; Fruit and Mueller, 2004; Zhang et al., 2005; Zalatan and Du Bois, 2008; Lin et al., 2008; Ichinose et al., 2011), additions of organoboron reagents to cyclic imines (Chen et al., 2014, 2018; Kong et al., 2015; Liu et al., 2017; Wu et al., 2018; Nishimura et al., 2012, 2013; Luo et al., 2012a, 2012b; Wang et al., 2013; Hepburn et al., 2013; Wang and Xu, 2013; Zhang et al., 2016a), and asymmetric reduction of cyclic ketimines (Wang et al., 2008; Yu et al., 2009; Kang et al., 2010; Lee et al., 2011, 2012; Han et al., 2011; Liu et al., 2019; Itsuno et al., 2014; Seo et al., 2015; Kim et al., 2018).

Asymmetric catalytic hydrogenation of prochiral unsaturated compounds has emerged as a powerful and effective approach for the construction of chiral compounds, which has made tremendous progress (Knowles, 1983; Noyori and Takaya, 1990; Noyori and Ohkuma, 2001; Tang and Zhang, 2003; Blaser et al., 2003; Cui and Burgess, 2005; Minnaard et al., 2007; Zhang et al., 2007, 2016b; Johnson et al., 2007; Zhou, 2007; Roseblade and Pfaltz, 2007; Fleury-Breguet et al., 2010; Xie et al., 2011, 2012; Wang et al., 2012; Chen et al., 2013; Verendel et al., 2014, 2016b). Most of these powerful catalytic systems typically depend on scarce and precious transition metals, such as Ru, Rh, Ir, and Pd, which faced difficulties like limited resource, high cost, and environmental contamination. Therefore, it is important and necessary to devote much effort to developing cheap, earth-abundant, first-row transition metal catalytic systems.

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Recently, the Fe-, Co-, and Ni-catalyzed asymmetric hydrogenation of prochiral unsaturated compounds has received great attention, which shows the great potential of first-row transition metals in catalytic asymmetric (transfer) hydrogenation (Morris, 2009, 2015; Chirik, 2015; Li et al., 2014, 2015, 2017; Bauer and Knöller, 2015; Sui-Seng et al., 2008; Zhou et al., 2011; Monfette et al., 2013, 2016; Lagaditis et al., 2014; Sonnenberg et al., 2014; Lu et al., 2015; Chen et al., 2016; Hamada et al., 2008; Hibino et al., 2009; Dong et al., 2012; Yang et al., 2014, 2016; Guo et al., 2015; Xu et al., 2015; Shevlin et al., 2016; Friedfeld et al., 2013, 2016; Lagaditis et al., 2014; Sonnenberg et al., 2014; Lu et al., 2015; Chen et al., 2016; Hamada et al., 2008; Hibino et al., 2009; Dong et al., 2012; Yang et al., 2014, 2016; Guo et al., 2015; Xu et al., 2015; Shevlin et al., 2016; Gao et al., 2017; Zhao et al., 2019). Among these catalytic methodologies, Ni-catalyzed asymmetric hydrogenation is still in early stage, and there are a few related studies at present (Li et al., 2015, 2017; Hamada et al., 2008; Hibino et al., 2009; Dong et al., 2012; Yang et al., 2014, 2016; Guo et al., 2015; Xu et al., 2015; Shevlin et al., 2016; Gao et al., 2017; Zhao et al., 2019). In 2008 and 2009, Hamada and co-workers reported Ni-catalyzed asymmetric hydrogenation of α-amino-β-ketoester hydrochlorides and substituted aromatic α-amino ketone hydrochlorides through dynamic kinetic resolution (Hamada et al., 2008; Hibino et al., 2009). In 2016, Chirik and co-workers discovered Ni-catalyzed asymmetric hydrogenation of α,β-unsaturated esters (Shevlin et al., 2016). Recently, our group reported Ni-catalyzed asymmetric hydrogenation of functionalized enamides with excellent results (Gao et al., 2017; Li et al., 2017). Despite some progress having been made, it is still quite urgent to explore the wide range of substrate generality, high reactivity, excellent stereoselectivity, and high turnover numbers (TON) for the Ni-catalyzed asymmetric hydrogenation.

Asymmetric hydrogenation of cyclic sulfamidate imines is a direct and effective access to chiral sulfamidates. Zhou and co-workers established highly efficient Pd-catalyzed enantioselective hydrogenation of cyclic sulfamidate imines with excellent results (Wang et al., 2008). To the best of our knowledge, there is no example about cheap transition metal Ni-catalyzed asymmetric hydrogenation of cyclic sulfamidate imines. Herein, we successfully realized the highly efficient Ni-catalyzed asymmetric hydrogenation of cyclic sulfamidate imines to afford chiral cyclic sulfamidates with high yields and excellent enantioselectivities (Scheme 1, up to 99% yield, >99% enantiomeric excess [ee]), and the gram-scale hydrogenation can be easily achieved with only 0.1 mol% catalyst loading (TON = 1,000).

**RESULTS**

**Optimization Reaction Conditions**

We started initial investigation of the Ni(OAc)$_2$-catalyzed asymmetric hydrogenation of model substrate 4-phenyl-1,2,3-oxathiazole 2,2-dioxide 1a to evaluate a variety of important chiral diphosphine ligands (Figure 1) under 60 atm H$_2$ at 80°C in MeOH for 24 h. As shown in Table 1, full conversion and good to excellent enantioselectivities were obtained with (S)-Binapine and (S, S)-Ph-BPE as ligand (>99% conversion, 86%–92% ee, Table 1, entries 1 and 4). Although high catalytic activity was achieved, very poor enantioselective control was afforded in the presence of (Rc, Sp)-DuanPhos and (S, S)-Me-DuPhos (Table 1, entries 2 and 3). In addition, ligands (R, S)-WalPhos, (S)-SegPhos, and (S)-BINAP did not work in this reaction; no reaction was observed (Table 1, entries 5–7). Therefore, (S, S)-Ph-BPE was revealed to be superior with the best enantioselectivity (>99% conversion, 92% ee, Table 1, entry 4). To our delight, the same result can
be achieved when the catalyst loading of Ni(OAc)2/(S, S)-Ph-BPE was decreased from 5.0 mol% to 1.0 mol% (Table 1, entry 8).

Inspired by the promising results, the Ni(OAc)2/(S, S)-Ph-BPE-catalyzed asymmetric hydrogenation of model substrate 4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide 1a was carried out in different solvents. We found that moderate to high conversions and excellent enantioselectivities were obtained in several kinds of alcoholic solvents, such as MeOH, EtOH, iPrOH, CF3CH2OH, and (CF3)2CHOH (62%–99% conversions, 91%–94% ee, Table 2, entries 1–5). Poor conversions and moderate to good enantioselectivities were obtained in nonalcoholic solvents, such as DCM, THF, and toluene. Table 1 shows the screening ligands for Ni-catalyzed asymmetric hydrogenation of 4-phenyl-5H-1,2,3-oxathiazole 2,2-dioxide (1a).

Table 1. Screening Ligands for Ni-Catalyzed Asymmetric Hydrogenation of 4-Phenyl-SH-1,2,3-oxathiazole 2,2-dioxide (1a)

| Entry | Ligand               | Conversion (%) | ee (%) |
|-------|----------------------|----------------|--------|
| 1     | (S)-Binapine         | >99            | 86     |
| 2     | (Rc, Sp)-DuanPhos    | >99            | –2     |
| 3     | (S, S)-Me-DuPhos     | >99            | –13    |
| 4     | (S, S)-Ph-BPE        | >99            | 92     |
| 5     | (R)-WalPhos          | NR             | NA     |
| 6     | (S)-SegPhos          | NR             | NA     |
| 7     | (S)-BINAP            | NR             | NA     |
| 8c    | (S, S)-Ph-BPE        | >99            | 92     |

Table entries are as follows:

- **NR**: no reaction
- **NA**: not available

*Conversion was determined by 1H NMR analysis.

*ee was determined by chiral high-performance liquid chromatography analysis.

*1.0 mol% catalyst loading.
Substrate Scope Study

After establishing the optimized reaction conditions, we sought to examine the substrate scope generality of this Ni-catalyzed asymmetric hydrogenation of cyclic sulfamidate imines. As listed in Table 3, the Ni-catalyzed asymmetric hydrogenation of a variety of aryl-substituted cyclic sulfamidate imines could proceed smoothly, affording the desired hydrogenation products (2a-2l) with full conversions, high yields, and excellent enantioselectivities (>99% conversion, 94%–99% yields, 91%–>99% ee). Diverse aryl-substituted cyclic sulfamidate imines bearing electron-donating (1b-1f) or electron-withdrawing (1g-1l) substituents worked well in this asymmetric hydrogenation. It is worth noting that the hydrogenation product 2i is an important intermediate for the synthesis of the enantiomer of piperazinone acid, which was one of the two main molecular motifs in clinical candidate MK-3207 (McLaughlin et al., 2013). In addition, the position of substituted group on the phenyl ring was also investigated; whether the substituted groups are on the ortho-, meta-, or para-position of the phenyl ring, these asymmetric reductions proceeded efficiently with excellent results. Interestingly, cyclic sulfamidate imines with substituents in ortho-position on the phenyl ring (1b, 1e, 1g) can provide chiral cyclic sulfamidates (2b, 2e, 2g) with higher enantioselectivities. When the phenyl ring was replaced with 2-naphthyl group, the substrate (1m) performed well with 97% yield and 92% ee. Moreover, the heteroaromatic substrate (1n) was hydrogenated with moderate reactivity and excellent enantioselectivity (65% conversion, 55% yield, 95% ee). It is noteworthy that the alkyl substituents (1o-1p) worked smoothly in this asymmetric hydrogenation, providing the desired products (2o-2p) with good to excellent results (>99% conversion, 96%–98% yields, and 83%–92% ee).

Encouraged by these promising reaction results, other types of ketimines were employed in this catalytic system. As shown in Scheme 2, the acetophenone and 2,3-dihydro-1H-inden-1-one-derived N-sulfonyl ketimines 1q and 1r worked efficiently under optimized reaction conditions; the corresponding

Table 2. Screening Solvents for Ni-Catalyzed Asymmetric Hydrogenation of 4-Phenyl-5H-1,2,3-oxathiazole 2,2-dioxide (1a)

| Entry | Solvent  | Conversion (%) | ee (%) |
|-------|----------|---------------|--------|
| 1     | MeOH     | >99           | 92     |
| 2     | EtOH     | 83            | 91     |
| 3     | ‘PrOH    | 62            | 92     |
| 4     | CF3CH2OH | >99           | 94     |
| 5     | (CF3)2CHOH | >99          | 93     |
| 6     | CH2Cl2   | NR            | NA     |
| 7     | THF      | 17            | 87     |
| 8     | Toluene  | 22            | 82     |
| 9     | Ethyl acetate | 12           | 86     |
| 10    | 1,4-dioxane | 7             | 58     |

NR, no reaction; NA, not available.

Unless otherwise noted, all reactions were carried out with a Ni(OAc)2/(S,S)-Ph-BPE/substrate 1a (0.1 mmol) ratio of 1:1:100 in 1.0 mL solvent under 60 atm H2 at 80°C for 24 h; the catalyst was pre-complexed in MeOH (0.1 mL for each reaction vial).

* Conversion was determined by 1H NMR analysis.
** ee was determined by chiral high-performance liquid chromatography analysis.

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hydrogenation products \textbf{2q} and \textbf{2r} were obtained with full conversion, high yields, and excellent enantioselectivities (>99% conversion, 96%–97% yields, 97%–99% ee).

**Synthetic Application**

The synthetic application potentiality of this Ni-catalyzed asymmetric hydrogenation was demonstrated by the gram-scale transformation. The asymmetric reduction of model substrate \textbf{1a} on the 6-mmol scale proceeded well in the presence of just 0.1 mol% catalyst loading (S/C = 1,000), affording product \textbf{2a} in 99% yield with 93% ee, which showed that our catalytic system had excellent catalytic activity (Scheme 3). In addition, >99% ee can be easily achieved in \text{CH}_2\text{Cl}_2/hexane through simple crystallization.

To reveal the great utility of this methodology, some derivatization reactions of hydrogenation product \textbf{2a} were conducted (Scheme 4). The tert-butoxycarbonyl (Boc) group was easily introduced on the nitrogen...
atom of hydrogenation product 2a to prepare compound 3 without loss of enantiomeric purity (Kang et al., 2010). Also, it was treated with tetrabutylammonium fluoride to give enantioenriched β-fluoroamine 4 in 77% yield (Wu et al., 2018; Nishimura et al., 2013). In addition, compound 3 went through nucleophilic attack of 4-methoxyphenol, which led to chiral amino ether 5 in 76% yield (Wu et al., 2018; Nishimura et al., 2013). The hydrogenation product 2a could also be efficiently reduced with LiAlH4 to generate (S)-phenylglycinol 6 in 87% yield and without loss of ee value (>99% ee) (Chen et al., 2014; Liu et al., 2017), which is the key intermediate to construct chiral cyclic carbamate Evans’ auxiliary (Jnoff et al., 2014) and bisoxazoline ligand (S,S)-Ph-Box (Corey et al., 1991; Cornejo et al., 2005; Ouhamou, 2010).

**DISCUSSION**

**Mechanism Study**

To explore the possible reaction mechanism for this Ni-catalyzed asymmetric hydrogenation, a series of isotopic labeling studies were conducted (Scheme 5). The cyclic sulfamidate imine 1a was hydrogenated with 25 atm D2 in CF3CH2OH; the deuterium atom was solely added at the benzylic position and partly at the nitrogen atom of the product. In addition, this reduction was repeated in the presence of H2 and CF3CH2OD, and we found that the deuterium atom was just partly located at the nitrogen atom. Our hydrogenation product 2a was dissolved and stirred in CF3CH2OD, and the deuterium atom was detected to be partly incorporated at the N-H position, which showed that proton exchange should occur in this process. These results suggested that the H atom at the benzylic position of the hydrogenation product was solely from H2.

Based on these observations and previous studies (Shevlin et al., 2016; Gao et al., 2017), the possible catalytic mechanism of this transformation was presented in Scheme 6. The hydrogen was involved in heterolytic cleavage to form [Ni]-H intermediate (II) (Korstanje et al., 2015; Ashby and Halpern, 1991), and it then went through ligand exchange with cyclic sulfamidate imine 1a, followed by enantioselective conjugated addition of [Ni]-H to C=N bond of imine to provide intermediate (TSIII). Subsequent protonation by AcOH released the product 2a. The N-H group of product 2a has the possibility of undergoing H-exchange with CF3CH2OH (or AcOH) to generate compound 2a’. To our delight, the deuterium-labeling experimental observations above are consistent with this possible catalytic cyclic pathway.
Conclusion

In conclusion, the Ni-catalyzed asymmetric hydrogenation of cyclic sulfamidate imines was successfully realized, affording a variety of chiral cyclic sulfamidates with high yields and excellent enantioselectivities (up to 99% yield, >99% ee, and 1,000 TON). Other types of N-sulfonyl ketimines worked well to give the
corresponding hydrogenation products with full conversion, 96%–97% yields, and 97%–>99% ee. In addition, this asymmetric methodology owned great synthetic utility through various product derivations to construct some important enantioenriched organic molecules, such as chiral β-fluoroamine, amino ether, and phenylglycinol. Moreover, a reasonable catalytic cycle was provided to reveal a possible mechanism for this Ni-catalyzed asymmetric hydrogenation based on the deuterium-labeling studies. Further investigations on the detailed mechanisms of Ni-catalyzed asymmetric hydrogenation strategy are in progress in our laboratory.

**Limitations of the Study**
The six-membered cyclic sulfamidate imine was not suitable in this methodology.

**METHODS**
All methods can be found in the accompanying Transparent Methods supplemental file.

**SUPPLEMENTAL INFORMATION**
Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.07.004.
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AUTHOR CONTRIBUTIONS

Y.L. discovered the reported process, designed and carried out almost all the experiments, and composed the manuscript. Z.Y. participated in synthesizing partial substrates. X.T. helped in executing isotopic labeling studies. General guidance, project directing, and manuscript revisions were done by X.-Q.D. and X.Z.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Supplemental Information

Nickel-Catalyzed Asymmetric Hydrogenation of Cyclic Sulfamidate Imines: Efficient Synthesis of Chiral Cyclic Sulfamidates

Yuanhua Liu, Zhiyuan Yi, Xuefeng Tan, Xiu-Qin Dong, and Xumu Zhang
Figure S1. $^1$H NMR spectrum of substrate 1g, related to Table 3.

Figure S2. $^{13}$C NMR spectrum of substrate 1g, related to Table 3.
Figure S3. $^1$H NMR spectrum of substrate 1i, related to Table 3.

Figure S4. $^{13}$C NMR spectrum of substrate 1i, related to Table 3.
Figure S5. $^1$H NMR spectrum of substrate 1p, related to Table 3.

Figure S6. $^{13}$C NMR spectrum of substrate 1p, related to Table 3.
Figure S7. $^1$H NMR spectrum of substrate 1q, related to Scheme 2.

Figure S8. $^{13}$C NMR spectrum of substrate 1q, related to Scheme 2.
Figure S9. $^1$H NMR spectrum of substrate 1r, related to Scheme 2.

Figure S10. $^{13}$C NMR spectrum of substrate 1r, related to Scheme 2.
Figure S11. $^1$H NMR spectrum of 2a, related to Table 3.

Figure S12. $^{13}$C NMR spectrum of 2a, related to Table 3.
Figure S13. $^1$H NMR spectrum of 2b, related to Table 3.

Figure S14. $^{13}$C NMR spectrum of 2b, related to Table 3.
Figure S15. $^1$H NMR spectrum of 2c, related to Table 3.

Figure S16. $^{13}$C NMR spectrum of 2c, related to Table 3.
Figure S17. $^1$H NMR spectrum of 2d, related to Table 3.

Figure S18. $^{13}$C NMR spectrum of 2d, related to Table 3.
Figure S19. $^1$H NMR spectrum of 2e, related to Table 3.

Figure S20. $^{13}$C NMR spectrum of 2e, related to Table 3.
Figure S21. $^1$H NMR spectrum of 2f, related to Table 3.

Figure S22. $^{13}$C NMR spectrum of 2f, related to Table 3.
Figure S23. $^1$H NMR spectrum of 2g, related to Table 3.

Figure S24. $^{13}$C NMR spectrum of 2g, related to Table 3.
Figure S25. $^1$H NMR spectrum of 2h, related to Table 3.

Figure S26. $^{13}$C NMR spectrum of 2h, related to Table 3.
Figure S27. $^1$H NMR spectrum of 2i, related to Table 3.

Figure S28. $^{13}$C NMR spectrum of 2i, related to Table 3.
Figure S29. $^1$H NMR spectrum of 2j, related to Table 3.

Figure S30. $^{13}$C NMR spectrum of 2j, related to Table 3.
Figure S31. $^1$H NMR spectrum of 2k, related to Table 3.

Figure S32. $^{13}$C NMR spectrum of 2k, related to Table 3.
Figure S33. $^1$H NMR spectrum of 2l, related to Table 3.

Figure S34. $^{13}$C NMR spectrum of 2l, related to Table 3.
Figure S35. $^1$H NMR spectrum of 2m, related to Table 3.

Figure S36. $^{13}$C NMR spectrum of 2m, related to Table 3.
Figure S37. $^1$H NMR spectrum of 2n, related to Table 3.

Figure S38. $^{13}$C NMR spectrum of 2n, related to Table 3.
Figure S39. $^1$H NMR spectrum of 2o, related to Table 3.

Figure S40. $^{13}$C NMR spectrum of 2o, related to Table 3.
Figure S41. $^1$H NMR spectrum of 2p, related to Table 3.

Figure S42. $^{13}$C NMR spectrum of 2p, related to Table 3.
Figure S43. $^1$H NMR spectrum of 2q, related to Scheme 2.

Figure S44. $^{13}$C NMR spectrum of 2q, related to Scheme 2.
Figure S45. $^1$H NMR spectrum of 2r, related to Scheme 2.

Figure S46. $^{13}$C NMR spectrum of 2r, related to Scheme 2.
Figure S47. $^1$H NMR spectrum of 3, related to Scheme 4.

Figure S48. $^{13}$C NMR spectrum of 3, related to Scheme 4.
Figure S49. $^1$H NMR spectrum of 4, related to Scheme 4.

Figure S50. $^{13}$C NMR spectrum of 4, related to Scheme 4.
Figure S51. $^1$H NMR spectrum of 5, related to Scheme 4.

Figure S52. $^{13}$C NMR spectrum of 5, related to Scheme 4.
Figure S53. $^1$H NMR spectrum of 6, related to Scheme 4.

Figure S54. $^{13}$C NMR spectrum of 6, related to Scheme 4.
Supplemental Figures for $^1$H spectra of deuterium labeling studies

Figure S55. $^1$H NMR spectrum of 2a-D, related to Scheme 5.

Figure S56. $^1$H NMR spectrum of 2a-D', related to Scheme 5.
Figure S57. $^1$H NMR spectrum of 2a-D'', related to Scheme 5.
Figure S58. HPLC spectrum of racemic-2a, related to Table 3.
Figure S59. HPLC spectrum of 2a, related to Table 3.
Figure S60. HPLC spectrum of racemic-2b, related to Table 3.
Figure S61. HPLC spectrum of 2b, related to Table 3.
Figure S62. HPLC spectrum of racemic-2c, related to Table 3.
Figure S63. HPLC spectrum of 2c, related to Table 3.
Figure S64. HPLC spectrum of racemic-2d, related to Table 3.
Figure S65. HPLC spectrum of 2d, related to Table 3.
Figure S66. HPLC spectrum of racemic-2e, related to Table 3.
**Figure S67.** HPLC spectrum of 2e, related to Table 3.
Figure S68. HPLC spectrum of racemic-2f, related to Table 3.
Figure S69. HPLC spectrum of 2f, related to Table 3.
Figure S70. HPLC spectrum of racemic-2g, related to Table 3.
Figure S71. HPLC spectrum of 2g, related to Table 3.
Figure S72. HPLC spectrum of racemic-2h, related to Table 3.
Figure S73. HPLC spectrum of 2h, related to Table 3.
Figure S74. HPLC spectrum of racemic-2i, related to Table 3.
Figure S75. HPLC spectrum of 2i, related to Table 3.
Figure S76. HPLC spectrum of racemic-2j, related to Table 3.
Figure S77. HPLC spectrum of 2j, related to Table 3.
Figure S78. HPLC spectrum of racemic-2k, related to Table 3.
Figure S79. HPLC spectrum of 2k, related to Table 3.
Figure S80. HPLC spectrum of racemic-21, related to Table 3.
Figure S81. HPLC spectrum of 2l, related to Table 3.
Figure S82. HPLC spectrum of racemic-2m, related to Table 3.
Figure S83. HPLC spectrum of 2m, related to Table 3.
Figure S84. HPLC spectrum of racemic-2n, related to Table 3.
Figure S85. HPLC spectrum of 2n, related to Table 3.
Figure S86. GC spectrum of racemic-2o, related to Table 3.
Figure S87. GC spectrum of 20, related to Table 3.
Figure S88. GC spectrum of racemic-2p, related to Table 3.
Figure S89. GC spectrum of 2p, related to Table 3.
Figure S90. HPLC spectrum of racemic-2q, related to Scheme 2.
Figure S91. HPLC spectrum of 2q, related to Scheme 2.
**Figure S92.** HPLC spectrum of racemic-2r, related to **Scheme 2.**
Figure S93. HPLC spectrum of 2r, related to Scheme 2.
Figure S94. HPLC spectrum of racemic-2a, related to Scheme 3.
Figure S95. HPLC spectrum of 2a, related to Scheme 3.
Figure S96. HPLC spectrum of 2a (Crystallization), related to Scheme 3.
Figure S97. HPLC spectrum of racemic-3, related to Scheme 4.
Figure S98. HPLC spectrum of 3, related to Scheme 4.
Figure S99. HPLC spectrum of racemic-4, related to Scheme 4.
Figure S100. HPLC spectrum of 4, related to Scheme 4.
Figure S101. HPLC spectrum of racemic-5, related to Scheme 4.
Figure S102. HPLC spectrum of 5, related to Scheme 4.
Figure S103. HPLC spectrum of racemic-N-Boc-6, related to Scheme 4.
Figure S104. HPLC spectrum of N-Boc-6, related to Scheme 4.
Transparent Methods

General remarks

All reactions and manipulations that were sensitive to air or moisture were performed in an argon-filled glovebox or using standard Schlenk techniques. Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification. Anhydrous solvents were purchased from J&K Chemicals company, degassed with N₂ and transferred by syringe. Column Chromatography was performed with silica gel (300-400 mesh). Thin layer chromatography (TLC) was performed on EM reagents 0.25 mm silica 60-F plates. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker ADVANCE III (400 MHz) spectrometer with CDCl₃, CD₃OD or DMSO-d₆ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts are reported in parts per million (ppm, δ scale) downfield from TMS at 0.00 ppm and referenced to the CDCl₃ at 7.26 ppm (for ¹H NMR) or 77.0 ppm (for ¹³C NMR). Data are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant in hertz (Hz) and signal area integration in natural numbers. ¹³C NMR analyses were run with decoupling. Enantiomeric excess values were determined by Daicel chiral column on an Agilent 1260 Series HPLC instrument. Optical rotations [α]D²⁵ were measured on a PERKIN ELMER polarimeter 343 instrument.

All the starting aromatic α-hydroxy ketones are the known compounds and were prepared according to the reported literature. [¹-⁴] Aliphatic α-hydroxy ketones were purchased from J&K Chemicals company.

General procedure for the synthesis of substrates

1) Synthesis of cyclic sulfamidate imines:

Method A:

Scheme S1:

Substrates 1a-1d and 1f-1n were synthesized according to the procedure: [⁵] the corresponding α-hydroxy ketone (8.0 mmol, 1.0 equiv.) and sulfamide (12.0 mmol, 1.5 equiv.)
were added in 50 mL of \( p \)-xylene and the solution was refluxed at 150 °C until full consumption of the \( \alpha \)-hydroxy ketone by TLC monitoring. The solution was concentrated to remove \( p \)-xylene under reduced pressure. And the crude was diluted with EtOAc and washed with water and then brine. The organic layer was dried over \( \text{Na}_2\text{SO}_4 \) and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1 to 3:1) and recrystallized with hexane and \( \text{CH}_2\text{Cl}_2 \) to give the corresponding cyclic sulfamidate imines.

**Method B:**

**Scheme S2:**

Substrates 1e, 1o and 1p were synthesized according to the procedure: \(^{[6,7]}\) Formic acid (30 mmol, 1.5 equiv.) was added dropwise to neat chlorosulfonyl isocyanate (30 mmol, 1.5 equiv.) at 0 °C with stirring. Vigorous gas evolution was observed during the addition process. The resulting viscous suspension was stirred at 0 °C until the mixture solidified. 20 mL acetonitrile was added and the solution was stirred for 30 min at room temperature to afford a solution of ClSO\(_2\)NH\(_2\).

The reaction mixture was cooled to 0 °C and a solution of corresponding \( \alpha \)-hydroxy ketone (20 mmol, 1.0 equiv.) and pyridine (30 mmol, 1.5 equiv.) in 10 mL acetonitrile was added dropwise. The reaction was warmed to room temperature and stirred for overnight. The solution was filtered through a short silica column and washed with EtOAc. The solvent was removed in vacuo and then added toluene and \( p \)-toluenesulfonic acid (0.1 equiv.), and the reaction mixture was heated to reflux for 1-2 h. The solvent was evaporated, and the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate to give the desired cyclic sulfamidate imines.

**2) Synthesis of N-sulfonyl imines:**

The N-sulfonyl imine substrates 1q and 1r was prepared according to previously reported method with slight modifications \(^{[8]}\): In a 100 mL round-bottomed flask fitted with a condenser was charged with the ketone (30 mmol, 1.0 equiv.), \( p \)-toluenesulfonamide (33 mmol, 1.1 equiv.)
and Ti(OEt)$_4$ (39 mmol, 1.3 equiv.) in dry toluene (60 mL), and the solution was refluxed at 150 °C until full consumption of the ketone by TLC monitoring. The solution was cooled to room temperature, diluted with EtOAc, quenched with saturated NaHCO$_3$ until no more precipitate was produced, and filtered through a pad of celite. The crude product was purified by flash chromatography on silica gel using mixtures of petroleum ether and EtOAc as the eluent.

The characterization data of compounds 1a, 1b, 1d, 1h, 1o are in accordance with the reported data in the literature. [6] The characterization data of compounds 1f, 1j-1k, 1m-1n are in accordance with the reported data in the literature. [5] The characterization data of compounds 1c, 1e, 1l are in accordance with the reported data in the literature. [7]

4-(2-fluorophenyl)-5H-[1, 2, 3]-oxathiazole 2, 2-dioxide 1g

White solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.31-8.27 (m, 1H), 7.78-7.72 (m, 1H), 7.43-7.39 (m, 1H), 7.30-7.25 (m, 1H), 5.60 (d, $J = 3.4$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.43 (d, $J = 3.0$ Hz), 163.28 (d, $J = 256.0$ Hz), 138.03 (d, $J = 9.0$ Hz), 131.32 (d, $J = 2.0$ Hz), 125.76 (d, $J = 3.0$ Hz), 116.99 (d, $J = 21.0$ Hz), 115.45 (d, $J = 11.0$ Hz), 76.88.

4-(3,5-difluorophenyl)-5H-[1, 2, 3]-oxathiazole 2, 2-dioxide 1i

White solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.48-7.43 (m, 2H), 7.26-7.18 (m, 1H), 5.54 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.36, 164.60 (d, $J = 12.0$ Hz), 162.08 (d, $J = 12.0$ Hz), 129.83, 112.09-110.96 (m), 74.08.

4-ethyl-5H-[1, 2, 3]-oxathiazole 2,2-dioxide 1p
White solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 5.07 (s, 2H), 2.70-2.64 (m, 2H), 1.34 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 185.50, 76.25, 25.35, 8.96.

4-methyl-N-(1-phenylethylidene) benzenesulfonamide 1q

![Chemical Structure](image)

White solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.94 -7.89 (m, 4H), 7.53 (t, $J$ = 7.5 Hz, 1H), 7.41 (t, $J$ = 7.7 Hz, 2H), 7.34 (d, $J$ = 8.0 Hz, 2H), 2.99 (s, 3H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 179.82, 143.49, 138.59, 137.45, 133.13, 129.42, 128.56, 128.22, 127.03, 21.57, 21.14.

N-(2, 3-dihydro-1H-inden-1-ylidene)-4-methylbenzenesulfonamide 1r

![Chemical Structure](image)

Light green solid; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.93 (d, $J$ = 8.0 Hz, 2H), 7.83 (d, $J$ = 7.8 Hz, 1H), 7.56 (t, $J$ = 7.4 Hz, 1H), 7.43 (d, $J$ = 7.7 Hz, 1H), 7.33 (d, $J$ = 8.1 Hz, 3H), 3.43-3.41 (m, 2H), 3.20-3.17 (m, 2H), 2.43 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 188.17, 153.77, 143.55, 137.95, 137.89, 135.06, 129.38, 127.40, 127.21, 125.80, 124.65, 32.92, 29.11, 21.53.

**General procedure for the asymmetric hydrogenation**

A stock solution was made by mixing Ni(OAc)$_2$ with (S, S)-Ph-BPE in a 1:1.1 molar ratio in CF$_3$CH$_2$OH and stirred at room temperature for 4-5 h until forming homogeneous yellow solution in a argon-filled glovebox. An aliquot of the catalyst solution (0.2 mL, 0.001 mmol) was transferred by syringe into the vials with different substrates 1 (0.1 mmol for each) in CF$_3$CH$_2$OH (0.8 mL). The vials were subsequently transferred into an autoclave before closed it, and moved it out from glovebox. The autoclave quickly purged with hydrogen gas for three times, then pressurized to 60 atm H$_2$. The reaction was then stirred at 80 °C for 24 h. After completed, the hydrogen gas was released slowly and carefully. The solution was diluted with EtOAc and passed through a short column of silica gel (eluant: EtOAc) to remove the metal complex, and
concentrated in vacuo. The ee values of all compounds 2 were determined by HPLC analysis or GC analysis on a chiral stationary phase.

The absolute configurations of products 2a-2f, 2h, 2j-2o were determined by comparison of analytical data (optical rotation) with the literature. The absolute configurations of products 2q-2r were determined by comparison of analytical data (optical rotation) with the literature. The absolute configurations of others were assigned by analogy.

(S)-4-phenyl-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2a

White solid; >99% conv., 19.7 mg, 99% yield, 94% ee; [α]D25 = +29.7 (c = 1.0, CHCl3); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; tR = 32.1 min (major), 36.0 min (minor).

1H NMR (400 MHz, CDCl3) δ 7.46-7.38 (m, 5H), 5.10-5.05 (m, 1H), 4.97 (d, J = 6.3 Hz, 1H), 4.83 (dd, J = 8.7, 6.8 Hz, 1H), 4.44 (t, J = 8.6 Hz, 1H); 13C NMR (100 MHz, CDCl3) δ 135.32, 129.51, 129.36, 126.66, 75.05, 59.55.

(S)-4-(o-tolyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2b

Pale yellow solid; >99% conv., 20.5 mg, 96% yield, 96% ee; [α]D25 = +17.3 (c = 1.0, CHCl3); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; tR = 27.6 min (major), 34.1 min (minor). 1H NMR (400 MHz, CDCl3) δ 7.55-7.53 (m, 1H), 7.30-7.26 (m, 2H), 7.22-7.20 (m, 1H), 5.36-5.30 (m, 1H), 4.86-4.81 (m, 2H), 4.43 (t, J = 8.6 Hz, 1H), 2.38 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 135.75, 133.24, 131.06, 129.14, 127.13, 125.66, 74.30, 56.20, 19.10.

(S)-4-(m-tolyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2c
Pale yellow solid; >99% conv., 21.0 mg, 99% yield, 92% ee; $[\alpha]_D^{25} = +28.4$ (c = 1.0, CHCl₃);

The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 32.4$ min (major), 35.6 min (minor). $^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.31 (t, $J = 7.5$ Hz, 1H), 7.22-7.18 (m, 3H), 5.06-5.00 (m, 1H), 4.89 (d, $J = 5.1$ Hz, 1H), 4.83-4.79 (m, 1H), 4.43 (t, $J = 8.6$ Hz, 1H), 2.38 (s, 3H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 139.32, 135.14, 130.26, 127.24, 75.11, 59.57, 21.34.

(S)-4-(p-tolyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2d

Pale yellow solid; >99% conv., 21.1 mg, 99% yield, 94% ee; $[\alpha]_D^{25} = +22.3$ (c = 1.0, CHCl₃);

The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 24.8$ min (major), 31.4 min (minor). $^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.31-7.29 (m, 2H), 7.23 (d, $J = 7.9$ Hz, 2H), 5.06-5.00 (m, 1H), 4.90 (d, $J = 6.5$ Hz, 1H), 4.81-4.77 (m, 1H), 4.42 (t, $J = 8.7$ Hz, 1H), 2.36 (s, 3H); $^{13}$C NMR (100 MHz, CDCl₃) $\delta$ 139.59, 135.14, 130.26, 129.23, 127.24, 123.72, 75.11, 59.43, 21.14.

(S)-4-(2-methoxyphenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2e

White solid; >99% conv., 22.5 mg, 98% yield, >99% ee; $[\alpha]_D^{25} = +42.2$ (c = 0.7, CHCl₃);

The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 12.4$ min (minor), 26.2 min (major). $^1$H NMR (400 MHz, CDCl₃) $\delta$ 7.42-7.36 (m, 2H), 7.04-7.00 (m, 1H), 7.04-7.00 (m, 1H), 6.95 (dd, $J = 8.3$, 1.1 Hz, 1H), 5.29 (d, $J = 9.2$ Hz, 1H), 5.22-5.16 (m, 1H), 4.82-4.79 (m, 1H), 4.48 (t, $J = 8.3$...
Hz, 1H), 3.89 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 156.82, 130.59, 128.69, 122.13, 121.33, 110.89, 74.68, 57.19, 55.51.

(S)-4-(4-methoxyphenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2f

Pale yellow solid; >99% conv., 21.5 mg, 94% yield, 93% ee; $[^{[\alpha]}D]^25_25 = +17.3$ (c = 0.7, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R$ = 54.1 min (major), 63.4 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34 (d, $J$ = 8.7 Hz, 2H), 6.94 (d, $J$ = 8.7 Hz, 2H), 5.05-4.99 (m, 1H), 4.86 (d, $J$ = 6.9 Hz, 1H), 4.80-4.76 (m, 1H), 4.43 (t, $J$ = 8.7 Hz, 1H), 3.82 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.42, 128.17, 126.88, 114.68, 75.26, 59.27, 55.38.

(S)-4-(2-fluorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2g

Pale yellow solid; >99% conv., 20.7 mg, 97% yield, 97% ee; $[^{[\alpha]}D]^25_25 = +15.6$ (c = 1.0, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R$ = 18.2 min (major), 20.7 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.63-7.59 (m, 1H), 7.40-7.35 (m, 1H), 7.26-7.22 (m, 1H), 7.13-7.08 (m, 1H), 5.40-5.35 (m, 1H), 5.09 (d, $J$ = 7.8 Hz, 1H), 4.95-4.91 (m, 1H), 4.46-4.42 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 160.04 (d, $J$ = 245.0 Hz), 130.88 (d, $J$ = 9.0 Hz), 127.96 (d, $J$ = 4.0 Hz), 125.10 (d, $J$ = 3.0 Hz), 123.14 (d, $J$ = 13.0 Hz), 115.77 (d, $J$ = 21.0 Hz), 74.06 (d, $J$ = 3.0 Hz), 53.89 (d, $J$ = 4.0 Hz).

(S)-4-(4-fluorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2h
Pale yellow solid; >99% conv., 21.0 mg, 99% yield, 94% ee; \([\alpha]_{D}^{25} = +23.9 \text{ (c = 1.0, CHCl}_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 28.0\) min (major), 41.1 min (minor). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.44-7.40\) (m, 2H), 7.15-7.10 (m, 2H), 5.10-5.06 (m, 2H), 4.85-4.81 (m, 1H), 4.43-4.39 (m, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 163.15\) (d, \(J = 248.0\) Hz), 131.32 (d, \(J = 3.0\) Hz), 128.61 (d, \(J = 8.0\) Hz), 116.37 (d, \(J = 22.0\) Hz), 74.91, 58.89.

\((S)\)-4-(3,5-difluorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide \(2i\)

![Chemical Structure of \((S)\)-4-(3,5-difluorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide \(2i\)](image)

White solid; >99% conv., 22.6 mg, 96% yield, 91% ee; \([\alpha]_{D}^{25} = +14.9 \text{ (c = 0.7, CHCl}_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 20.8\) min (major), 26.5 min (minor). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.01-6.98\) (m, 2H), 6.87-6.81 (m, 1H), 5.13 (d, \(J = 7.2\) Hz, 1H), 5.09-5.04 (m, 1H), 4.90-4.86 (m, 1H), 4.39-4.35 (m, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 163.40\) (dd, \(J = 250.0, 13.0\) Hz), 140.06 (t, \(J = 9.0\) Hz), 109.61 (q, \(J = 18.0, 7.0\) Hz), 104.78 (t, \(J = 25.0\) Hz), 74.07, 58.42 (t, \(J = 2.0\) Hz).

\((S)\)-4-(3-chlorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide \(2j\)

Pale yellow solid; >99% conv., 22.9 mg, 98% yield, 91% ee; \([\alpha]_{D}^{25} = +17.3 \text{ (c = 0.7, CHCl}_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 36.8\) min (major), 57.5 min (minor). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.43\) (s, 1H), 7.39-7.37 (m, 2H), 7.35-7.31 (m, 1H), 5.09-5.03 (m, 2H), 4.88-4.84 (m, 1H), 4.44-4.38 (m, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 137.74\), 135.22, 130.65, 129.59, 126.79, 124.70, 74.50, 58.82.
(S)-4-(4-chlorophenyl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2k

Pale yellow solid; >99% conv., 22.5 mg, 96% yield, 94% ee; $[\alpha]_D^{25} = +13.6$ (c = 1.0, CHCl$_3$);
The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; $t_R = 31.1$ min (major), 39.1 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42-7.36 (m, 4H), 5.09-5.00 (m, 2H), 4.86-4.82 (m, 1H), 4.41-4.37 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 135.42, 134.12, 129.53, 128.03, 74.67, 58.86.

(S)-4-[2, 2-dioxido-(1, 2, 3)-oxathiazolidin-4-yl] phenyl acetate 2l

Yellow solid; >99% conv., 24.4 mg, 95% yield, 93% ee; $[\alpha]_D^{25} = +17.3$ (c = 0.8, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_R = 66.6$ min (major), 76.6 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.05 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 5.33 (s, 1H), 5.12 (d, $J = 9.1$ Hz, 1H), 4.89-4.85 (m, 1H), 4.41-4.37 (m, 1H), 3.91 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.35, 140.71, 131.03, 130.47, 126.58, 74.38, 59.02, 52.38.

(S)-4-(naphthalen-2-yl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2m

Yellow solid; >99% conv., 24.2 mg, 97% yield, 92% ee; $[\alpha]_D^{25} = +20.3$ (c = 0.6, MeOH);
The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 80:20; flow rate = 0.8 mL/min; UV detection at 210 nm; $t_R = 11.6$ min (major), 14.7 min (minor). $^1$H NMR (400 MHz, CD$_2$OD) $\delta$ 7.94-7.86 (m, 4H), 7.59 (dd, $J = 8.6, 1.9$ Hz, 1H), 7.52-7.49 (m, 2H), 5.23 (t, $J = 7.5$ Hz, 1H), 4.99-4.95 (m, 1H), 4.45 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR
(100 MHz, CD$_3$OD) δ 134.46, 133.43, 133.25, 128.54, 127.66, 127.35, 126.21, 126.20, 125.77, 123.65, 74.65, 59.17.

(R)-4-(thiophen-2-yl)-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2n

White solid; 65% conv., 11.3 mg, 55% yield, 95% ee; [α]$_D^{25}$ = +4.3 (c = 1.0, CHCl$_3$); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 220 nm; $t_R$ = 37.2 min (minor), 42.0 min (major).

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.40 (dd, $J$ = 5.1, 1.2 Hz, 1H), 7.18-7.17 (m, 1H), 7.05 (dd, $J$ = 5.1, 3.6 Hz, 1H), 5.37-5.31 (m, 1H), 4.87-4.83 (m, 2H), 4.56 (t, $J$ = 8.6 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 137.32, 127.59, 127.16, 127.09, 75.22, 55.41.

(S)-4-methyl-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2o

Colorless oil; >99% conv., 13.4 mg, 98% yield, 83% ee; [α]$_D^{25}$ = +28.3 (c = 0.7, CHCl$_3$); The enantiomeric excess was determined by GC (Supelco β-DEX$^{TM}$325, df = 0.25 μm, 0.25 mm i.d.×30 m, fused silica capillary column); carrier gas, N$_2$ (flow 1.2 mL/min); injection temp, 250 °C; initial column temperature, 70 °C; progress rate, 0.3 °C/min; final column temperature, 160 °C; this temperature is held for 30min; detector temp, 260 °C; $t_R$ = 177.9 min (major), 183.2 min (minor). $^1$H NMR (400 MHz, CDCl$_3$) δ 4.67-4.60 (m, 2H), 4.14-4.05 (m, 2H), 1.41 (t, $J$ = 6.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 76.40, 52.35, 17.47.

(−)-4-ethyl-[1, 2, 3]-oxathiazolidine 2, 2-dioxide 2p

Orange oil; >99% conv., 14.5 mg, 96% yield, 92% ee; [α]$_D^{25}$ = −11.3 (c = 0.6, MeOH); The enantiomeric excess was determined by GC (Supelco β-DEX$^{TM}$325, df = 0.25 μm, 0.25 mm
i.d.×30 m, fused silica capillary column); carrier gas, N₂ (flow 1.2 mL/min); injection temp, 250 °C; initial column temperature, 70 °C; progress rate, 1.0 °C/min; final column temperature, 160 °C; this temperature is held for 30 min; detector temp, 260 °C; t<sub>R</sub> = 85.9 min (major), 89.0 min (minor). ¹H NMR (400 MHz, CDCl₃) δ 4.65-4.58 (m, 2H), 4.17 (t, <i>J</i> = 8.1 Hz, 1H), 3.92-3.86 (m, 1H), 1.82-1.65 (m, 1H), 1.02 (t, <i>J</i> = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 74.77, 57.83, 25.80, 10.09.

<chem>(R)-4-methyl-N-(1-phenylethyl) benzenesulfonamide 2q</chem>

White solid; >99% conv., 26.4 mg, 96% yield, 97% ee; [α]<sub>D</sub><sup>25</sup> = +55.6 (c = 1.1, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; t<sub>R</sub> = 16.4 min (minor), 25.2 min (major).

¹H NMR (400 MHz, CDCl₃) δ 7.63-7.61 (m, 2H), 7.20 -7.16 (m, 5H), 7.12-7.08 (m, 2H), 5.08 (d, <i>J</i> = 7.2 Hz, 1H), 4.49-4.42 (m, 1H), 2.38 (s, 3H), 1.41 (d, <i>J</i> = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.07, 141.99, 137.51, 129.39, 128.46, 127.37, 127.03, 126.60, 53.57, 23.52, 21.46.

<chem>(R)-N-(2, 3-dihydro-1H-inden-1-yl)-4-methylbenzenesulfonamide 2r</chem>

Pale yellow solid; >99% conv., 27.8 mg, 97% yield, >99% ee; [α]<sub>D</sub><sup>25</sup> = +29.7 (c = 0.58, CHCl₃); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 90:10; flow rate = 1.0 mL/min; UV detection at 210 nm; t<sub>R</sub> = 16.4 min (major), 22.8 min (minor). ¹H NMR (400 MHz, CDCl₃) δ 7.84-7.82 (m, 2H), 7.33 (d, <i>J</i> = 8.0 Hz, 2H), 7.20-7.12 (m, 3H), 7.08 (d, <i>J</i> = 7.4 Hz, 1H), 4.88-4.79 (m, 2H), 2.88-2.85 (m, 1H), 2.76-2.70 (m, 1H), 2.45 (s, 3H), 2.32-2.28 (m, 1H), 1.76-1.71 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 143.41, 142.75, 141.94, 138.07, 129.74, 128.21, 127.07, 126.77, 124.74, 124.04, 58.64, 34.61, 29.91, 21.54.

Procedure for asymmetric hydrogenation with gram-scale

Scheme S3:
A stock solution was made by mixing Ni(OAc)$_2$ with (S,S)-Ph-BPE in a 1:1.1 molar ratio in CF$_3$CH$_2$OH and stirred at room temperature for 4-5 h until forming homogeneous yellow solution in an argon-filled glovebox. An aliquot of the catalyst solution (1.2 mL, 0.006 mmol) was transferred by syringe into the vials charged with substrate 1a (6.0 mmol) in 0.8 mL CF$_3$CH$_2$OH. The vial was transferred into an autoclave, which was subsequently charged with hydrogen gas. The reaction was then stirred under 80 atm H$_2$ at 80 °C for 4 days. After completed, the hydrogen gas was released slowly and carefully. The solution was passed through a short column of silica gel (eluant: EtOAc) to afford the 2a (1.19 g, >99% conversion, 99% yield, 93% ee). And >99% ee can be obtained through simple crystallization in CH$_2$Cl$_2$/hexane.

**Synthetic transformation**

**Scheme S4:**

Synthesis of (S)-tert-butyl 4-phenyl-1,2,3-oxathiazolidine-3-carboxylate 2,2-dioxide 3:

To a solution of (S)-2a (199.2 mg, 1.0 mmol, >99% ee) and 4-dimethylaminopyridine (DMAP, 24.4 mg, 0.2 mmol) in 3 mL dry dichloromethane was added di-tert-butyl dicarbonate (327.4 mg, 1.5 mmol) and the mixture was stirred at room temperature for overnight. After solvent
evaporation, the residue was purified by silica gel column chromatography to afford the product 3 as white solid (265.0 mg, 89% yield, 99% ee). The absolute configuration of product 3 was determined by comparison of analytical data (optical rotation) with the literature.\(^{[7]}\) \([\alpha]_{D}^{25} = +44.0\) (c = 0.8, CHCl\(_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OD-H column, hexane: isopropanol = 80:20; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 8.6\) min (minor), 11.3 min (major). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.43 - 7.38 (m, 5H), 5.29 (dd, J = 6.7, 4.2 Hz, 1H), 4.88 (dd, J = 9.3, 4.2 Hz, 1H), 4.41 (dd, J = 9.3, 4.2 Hz, 1H), 1.44 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 148.23, 136.87, 129.24, 129.13, 126.12, 85.58, 71.77, 60.73, 27.79.

**Synthesis of (S)-tert-butyl (2-fluoro-1-phenylethyl) carbamate 4:**

To a solution of 3 (29.9 mg, 0.1 mmol) in 1 mL dry THF was added "Bu\(_4\)NF (0.2 mL, 0.2 mmol, 2 equiv., 1 M in THF) and the reaction was stirred at 60 °C overnight. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to give the desired product 4 as white solid (18.4 mg, 77% yield, >99% ee).\(^{[11]-[12]}\) The absolute configuration of product 4 was determined by comparison of analytical data (optical rotation) with the literature.\(^{[13]}\) \([\alpha]_{D}^{25} = +29.7\) (c = 0.9, CHCl\(_3\)); The enantiomeric excess was determined by HPLC on Chiralcel OJ-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; \(t_R = 14.5\) min (minor), 16.2 min (major). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.38 - 7.28 (m, 5H), 5.19 - 5.18 (m, 1H), 4.98 - 4.91 (m, 1H), 4.73 - 4.49 (m, 2H), 1.44 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 155.14, 138.23, 128.71, 127.91, 126.74, 85.10 (d, J = 174.0 Hz), 80.00, 54.51, 28.29.

**Synthesis of (S)-tert-butyl (2-(4-methoxyphenoxy)-1-phenylethyl) carbamate 5:**

The compound 3 (59.9 mg, 0.2 mmol) and 4-methoxyphenol (49.7 mg, 0.4 mmol, 2 equiv.) were dissolved in 1 mL DMSO, KOH (50 μL, 8 M) was added and the reaction was stirred at room temperature overnight. The reaction was diluted with water and extracted with DCM, washed with brine and dried on anhydrous Na\(_2\)SO\(_4\). The solvent was removed and the residue was purified by silica gel column chromatography to afford the product 5 as colorless oil solid (51.9 mg, 76% yield, >99% ee).\(^{[11]-[12]}\) The absolute configuration of product 5 was assigned by analogy with the literature.\(^{[11]-[12]}\) \([\alpha]_{D}^{25} = +7.9\) (c = 1.0, CHCl\(_3\)); The enantiomeric excess was determined
by HPLC on Chiralpak AD-H column, hexane: isopropanol = 95:5; flow rate = 1.0 mL/min; UV detection at 210 nm; t_R = 25.2 min (minor), 39.3 min (major). ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.33 (m, 4H), 7.30-7.27 (m, 1H), 6.81 (s, 4H), 5.35 (s, 1H), 5.03 (s, 1H), 4.19-4.09 (m, 2H), 3.75 (s, 3H), 1.43 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 155.30, 154.09, 152.46, 139.85, 128.50, 127.53, 126.73, 115.61, 114.58, 79.74, 71.32, 55.67, 53.92, 28.32.

**Synthesis of (S)-Phenylglycinol 6:**

To a suspension of lithium aluminum hydride (46 mg, 1.2 mmol) in anhydrous THF (5 mL), a solution of (S)-2a (79.7 mg, 0.4 mmol) in anhydrous THF (5 mL) was added dropwise under N₂ protected. After refluxed overnight, the mixture was cooled to room temperature and quenched with water (10 mL). The THF was removed under vacuum and the aqueous layer was extracted with DCM three times (20 mL×3), and the combined organic layers were dried over Na₂SO₄ and concentrated to provide the desired product as pale yellow solid (48.0 mg, 87% yield, >99% ee). The ee values of (S)-Phenylglycinol 6 was determined with N-Boc-6 by converting to tert-butyl (2-hydroxy-1-phenylethyl) carbamate according to the reported literature.[14] The enantiomeric excess was determined by HPLC on Chiralpak AD-H column, hexane: isopropanol = 92:8; flow rate = 0.3 mL/min; UV detection at 210 nm; t_R = 39.5 min (major), 41.6 min (minor). [α]D²⁵⁵ = +37.4 (c = 0.9, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.26 (m, 5H), 4.06-4.03 (m, 1H), 3.76-3.72 (m, 1H), 3.56 (dd, J = 10.8, 8.4 Hz, 1H), 2.24 (brs, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 142.53, 128.62, 127.51, 126.41, 128.50, 127.53, 126.73, 115.61, 114.58, 79.74, 71.32, 55.67, 53.92, 28.32.

**Deuterium labeling studies**

**Scheme S5:**

A stock solution was made by mixing Ni(OAc)₂ with (S, S)-Ph-BPE in a 1:1.1 molar ratio in CF₃CH₂OH and stirred at room temperature for 4-5 h until forming homogeneous yellow solution in a argon-filled glovebox. An aliquot of the catalyst solution (0.2 mL, 0.001 mmol) was transferred by syringe into the vial charged with substrate 1a (0.1 mmol) in CF₃CH₂OH (0.8 mL).
The vial was subsequently transferred into an autoclave before closed it, and moved it out from glovebox. The autoclave quickly purged with deuterium gas for three times, then pressurized to 25 atm D₂. The reaction was then stirred at 80 °C for 72 h. After completed, the D₂ gas was released slowly and carefully. The solution was diluted with EtOAc and passed through a short column of silica gel (eluant: EtOAc) to remove the metal complex. The solvent was evaporated under reduced pressure to afford the desired compound and was determined by ¹H NMR analysis. ¹H NMR (400 MHz, CDCl₃) δ 7.46-7.38 (m, 5H), 4.94 (s, 0.78 H), 4.83 (d, J = 8.8 Hz, 1H), 4.44 (d, J = 8.7 Hz, 1H).

Scheme S6:

A stock solution was made by mixing Ni(OAc)₂ with (S, S)-Ph-BPE in a 1:1.1 molar ratio in CF₃CH₂OD and stirred at room temperature for 4-5 h until forming homogeneous yellow solution in a argon-filled glovebox. An aliquot of the catalyst solution (0.2 mL, 0.002 mmol) was transferred by syringe into the vial charged with substrate 1a (0.1 mmol) in CF₃CH₂OD (0.8 mL). The vial was subsequently transferred into an autoclave before closed it, and moved it out from glovebox. The autoclave quickly purged with hydrogen gas for three times, then pressurized to 60 atm H₂. The reaction was then stirred at 80 °C for 24 h. After completed, the H₂ gas was released slowly and carefully. The solution was diluted with EtOAc and passed through a short column of silica gel (eluant: EtOAc) to remove the metal complex. The solvent was evaporated under reduced pressure to afford the desired compound and was determined by ¹H NMR analysis. ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.38 (m, 5H), 5.11-5.05 (m, 1H), 4.84 (dd, J = 8.7, 6.8 Hz, 1H), 4.79 (d, J = 6.5 Hz, 0.73 H), 4.46 (t, J = 8.6 Hz, 1H).

Scheme S7:
Compound 2a (10 mg) was dissolved in 0.5 mL CF₃CH₂OD and stirred at 80 °C for 24 h. After completed, the solvent was evaporated under reduced pressure to afford the desired compound and was determined by ¹H NMR analysis. ¹H NMR (600 MHz, CDCl₃) δ 7.46-7.40 (m, 5H), 5.08 (t, J = 7.6 Hz, 1H), 4.84 (dd, J = 8.8, 6.8 Hz, 1H), 4.81 (brs, 0.71 H), 4.46 (t, J = 8.7 Hz, 1H).

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