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Dipeptide-Based Chiral Tertiary Amine-Catalyzed Asymmetric Conjugate Addition Reactions of 5*H*-Thiazol/Oxazol-4-Ones

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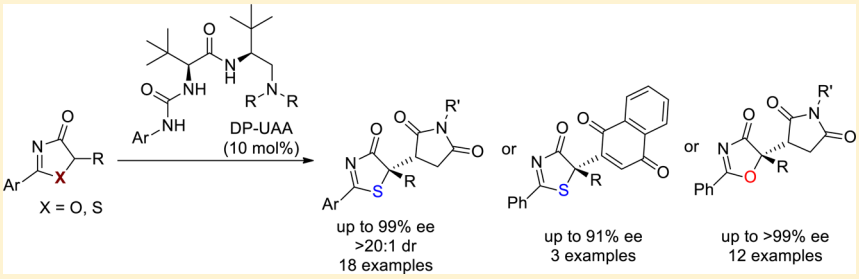
Supporting Information



ABSTRACT: Highly enantio- and chemo-selective 1,4-conjugate addition process of 5*H*-thiazol-4-ones with maleimides or 1,4-naphthoquinones, and 5*H*-oxazol-4-ones with maleimides were performed under a dipeptide-based tertiary amine (DP-UAA) catalyst. A series of valuable *N*,*S*- and *N*,*O*-containing heterocyclic compounds with excellent enantio- and disastereo-selectivities (up to >99% ee, > 20:1 dr) were attained.

INTRODUCTION

Sulfur-functionalized quaternary carbon stereocenters are present in important natural or non-natural products with interesting biological activities.[1] The development of catalytic asymmetric strategies to access these entities has gained interest in recent years,[1,2] and among them, the nucleophilic addition of *S*-containing prochiral carbon centers has been recognized as one of the most direct and efficient methods giving rise to a number of new substrates.[1−3] For instance, in 2013, the Palomo group introduced a highly stereoselective 1,4-conjugate addition reaction of 5*H*-thiazol-4-ones to nitroalkanes.[3a] In this pioneering study, 5*H*-thiazol-4-ones were revealed as a new class of sulfur-containing pronucleophiles to facilitate the synthesis of important chiral α,α-disubstituted α-mercapto carboxylic acids. Nevertheless, only a few examples of 5*H*-thiazol-4-ones as nucleophiles have been reported to date, including Mannich reaction of (arylsulfonyl)acetonitriles,[3b] 1,4-conjugate addition to enones,[3c] allylation,[3d] and γ-addition of allenoates.[3e]

Maleimides have been extensively employed as electrophiles in asymmetric synthesis to provide a straightforward approach for the assembly of chiral succinimide and pyrrolidine motifs in molecules.[4] It is noteworthy that 1,4-conjugate addition reaction between 5*H*-thiazol-4-ones and maleimides can present analogues of biologically important compounds, such as sulfone-based tetrasubstituted carbon-substituted pyrrolidines (calcium channel blockers)[5a] and thiazol-4-one-substituted pyrrolidines (inhibitors of 11-β-hydroxy steroid dehydrogenase type 1).[5b,c] Very recently, we reported that the reactions of 5*H*-thiazol-4-ones with nitroalkenes, 4-oxo-4-arylbutenones, 4-oxo-4-arylbutenoates, and methyleneindolinones experience [4+2] annulation reaction with high chemoselectivity.[3f] These works revealed the good electrophilicity of C2 position of 5*H*-thiazol-4-ones probably due to the poor overlap of the C(2p) and S(3p) orbitals.[6] In this context, the exploration of the reaction between 5*H*-thiazol-4-ones and maleimides to undergo 1,4-conjugate addition process remains highly desirable and challenging. This work just extends our recent research interest in stereoselective construction of chiral sulfur-containing scaffolds.[3f,7]

RESULTS AND DISCUSSION

To explore the reactivity and chemoselectivity, a model reaction between 5*H*-thiazol-4-one **1a** and *N*-phenyl maleimide **2a** was initially evaluated using 10 mol% of Et_3N in toluene at 25 °C (Table 1, entry 1). We were pleased to find that the desired conjugate adduct **3a** could be obtained in 78% yield. The achiral reaction gave excellent chemoselectivity, albeit not fully complete, encouraging us to examine the reaction with chiral organocatalysts (entries 2−5). We first attempted amino acid (*tert*-leucine)-derived thiourea−tertiary amine **I**, a versatile Brønsted base catalyst introduced by the Pedrosa group[8] and extensively applied by our[9] and many other[10] research groups (entry 2). The reaction was slow, but a good enantioselectivity of 80% *ee* of **3a** was obtained. Reactivity was improved with

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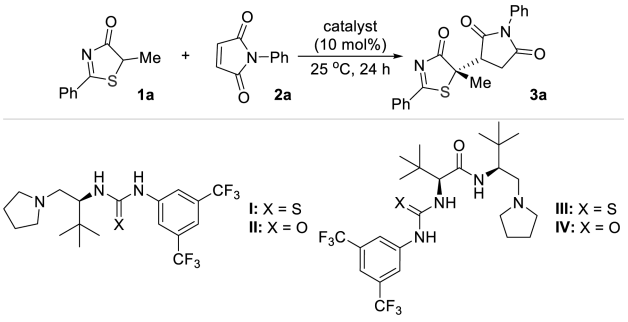
Table 1. Screening Studies[a]



entry	cat.	solvent	yield (%)[b]	*ee* (%)[c]	dr[d]
1	Et_3N	toluene	78	N.A.[e]	8:1
2	**I**	toluene	34	80	12:1
3	**II**	toluene	60	78	11:1
4	**III**	toluene	87	95	12:1
5	**IV**	toluene	96	97	20:1
6	**IV**	Et_2O	87	94	17:1
7	**IV**	CH_2Cl_2	72	72	8:1
8	**IV**	THF	80	77	14:1
9	**IV**	CH_3CN	89	41	3:1

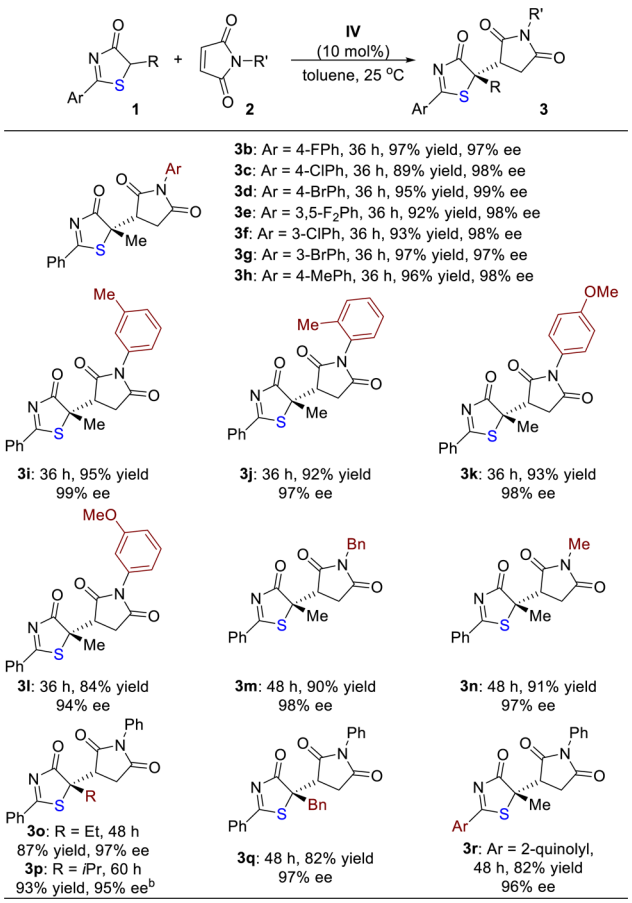
[a]The reaction was carried out with 0.1 mmol of **1a**, 0.2 mmol of **2a**, and 0.01 mmol of catalyst in 2.0 mL solvent. [b]Isolated yield. [c]Determined by HPLC analysis. [d]Determined by crude ^{1}H NMR analysis. [e]N.A. = not available.

similar stereoselectivity when catalyst **II**, having urea instead of thiourea as the H-bonding donor, was used (entry 3).[11] We then assessed dipeptide-based thiourea–amide–tertiary amine (DP-TAA) **III**,[3f] a chiral catalyst that was recently introduced by our group to furnish [4+2] cyclization reaction of 5*H*-thiazol-4-ones with activated alkenes (entry 4). We were delighted that **3a** was obtainable in 87% yield with 95% *ee* and 12:1 dr. Dipeptide-based urea–amide–tertiary amine (DP-UAA) **IV** as the catalyst further accelerated the reaction, affording **3a** in 96% yield with 97% *ee* and 20:1 dr (entry 5). A range of solvents, such as Et_2O, CH_2Cl_2, THF, and CH_3CN, were next screened in succession (entries 6–9), but no optimal ones were found.

With the optimal reaction conditions in hand, the substrate scope with respect to 5*H*-thiazol-4-ones **1** and maleimides **2** was examined (Table 2). We first evaluated the performance of the reactions between 5*H*-thiazol-4-one **1a** and various maleimides **2**. It was observed that a wide range of *N*-aryl (**3a–l**), benzyl (**3m**), and alkyl (**3n**) maleimides worked well with **1a**, affording the corresponding 1,4-conjugate adducts **3a–n** in 84–97% yields with 94–99% *ee* and >20:1 dr within 36–48 h range. The introduction of electron-deficient or electron-rich groups substituents into phenyl group of maleimides, did not affect the chemo- or stereoselective outcomes (**3a–l**). Changing the R group on 5*H*-thiazol-4-one as ethyl (**3o**), isopropyl (**3p**), and benzyl (**3q**) substituents also gave similar reactivity and chemoselectivity with excellent enantio- and diastereoselectivities. By altering the phenyl group of 5*H*-thiazol-4-one to 2-quinolyl, the corresponding adduct **3r** was furnished in 82% yield with 97% ee after 48 h. The absolute configurations of the 1,4-conjugate addition products **3** were assigned on the basis of X-ray crystallographic analysis of a single crystal of **3a**.[12]

In 2007, the Jørgensen group introduced 1,4-naphthoquinones in an asymmetric arylation of β-ketoesters.[13a] Since then,

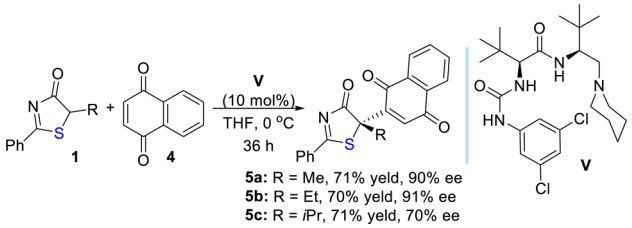
Table 2. Asymmetric 1,4-Conjugate Addition of 5*H*-Thiazol-4-ones 1 to *N*-Maleimides 2[a]



[a]The reaction was carried out with 0.1 mmol of **1**, 0.2 mmol of **2**, 0.01 mmol of **IV** in 2.0 mL toluene at 25 °C. Yields of isolated products are presented. Ee values were determined by HPLC using chiral stationary phase. All drs are >20:1. [b]20 mol% of **IV** was used.

asymmetric reaction of 1,4-naphthoquinones has been robustly applied to introduce an aryl group on the quaternary carbon stereocenters.[13] To demonstrate the versatility of the established 1,4-conjugate addition strategy toward 5*H*-thiazol-4-ones, we therefore shifted our focus to explore asymmetric reaction using 1,4-naphthoquinones as electrophiles, so as to prepare the important chiral α-aryl-α-alkyl α-mercapto carboxylic acid derivatives.[14] As shown in Scheme 1, the reaction between 5*H*-thiazol-4-one **1a** and 1,4-naphthoquinone **4** underwent conjugate addition–aromatization–oxidation sequence, and the corresponding product **5a** was obtained in 71% yield with 90% *ee* when using 10 mol% of DP-UAA **V** catalyst and in THF solvent at 0 °C. The reaction conditions

Scheme 1. Arylation of 5*H*-Thiazol-4-ones 1 to 1,4-Naphthoquinone 4



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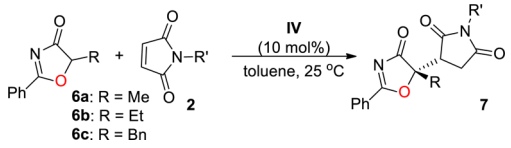
were also effective to 5*H*-thiazol-4-one **1** with ethyl as the R group (**5b**, 70% yield, 91% *ee*). Possibly due to the steric effects of the isopropyl group, moderate enantioselectivity of **5c** was observed.

We[4g] recently reported a highly chemo- and stereoselective [4+2] annulation between 5*H*-oxazol-4-ones[15] and maleimides by using Takemoto's chiral thiourea−tertiary amine catalyst and trace amount of the corresponding 1,4-conjugate addition adducts was detected with poor enantioselectivity in the reactions. Inspired by the success of asymmetric 1,4-conjugate addition reaction of 5*H*-thiazol-4-ones with the DP-UAA catalysts, the reaction between 5*H*-oxazol-4-one **6a** and *N*-phenyl maleimide **2a** was accordingly evaluated under the established reaction conditions (10 mol% of catalyst **IV**, toluene as solvent at 25 °C, Table 3, entry 1). The reaction

Table 3. Asymmetric 1,4-Conjugate Addition of 5*H*-Oxazol-4-ones 6 to *N*-Maleimides 2[a]



entry	7 (R, R′)	*t* (h)	yield (%)[b]	*ee* (%)[c]
1	**7a** (Me, Ph)	12	91	98
2	**7b** (Me, *p*-FPh)	11	98	> 99
3	**7c** (Me, *p*-ClPh)	11	90	> 99
4	**7d** (Me, *p*-BrPh)	22	91	> 99
5	**7e** (Me, *m*-ClPh)	19	92	> 99
6	**7f** (Me, *p*-MePh)	22	93	> 99
7	**7g** (Me, *m*-MePh)	22	96	> 99
8	**7h** (Me, *p*-MeOPh)	20	93	> 99
9	**7i** (Me, *p*-MeOPhCH$_2$)	40	96	> 99
10	**7j** (Me, CH$_3$)	20	93	98
11	**7k** (Et, Ph)	18	97	> 99
12	**7l** (Bn, Ph)	15	98	> 99

[a]The reaction was carried out with 0.1 mmol of **6**, 0.2 mmol of **2**, 0.01 mmol of **IV** in 2.0 mL toluene at 25 °C. [b]Yields of isolated products are presented. [c]ee values were determined by HPLC using chiral stationary phase. All drs are >20:1.

completed in 12 h, and the 1,4-conjugate addition product **7a** was obtained in 91% yield with 98% *ee* and >20:1 dr. This good result prompted us to expand the substrate scope to include maleimides **2** and 5*H*-oxazol-4-ones **6** (entries 2−12). Based on results of the screening, the reactions were completed within 11−40 h, leading to a series of products **7b−l** in 90−98% yields and with more than 98% *ee*. The absolute configurations of 1,4-conjugate adducts **7** could be assigned based on X-ray crystallographic analysis of a single crystal of **7d**.[12]

In the reactions of 5*H*-thiazol-4-ones with maleimides and 1,4-naphthoquinones, the 1,4-conjugate addition adducts were determined as the sole products and without the corresponding [4+2] cyclization adducts were observed whatever using Et$_3$N or chiral catalysts (**IV** and **V**). We proposed that thermodynamical control to access conjugate addition products should be operative, as studied with density functional theory in the previous work.[3f] The absolute configuration of adducts **7** from 5*H*-oxazol-4-ones was determined as the same as products **3**, but notably, it is opposite to the conjugate addition adducts using Takemoto's catalyst.[4g] Therefore, a plausible transition state mode with DP-UAA, different from Takemoto's catalyst, is proposed and depicted in Figure 1. First with the nucleophile (5*H*-oxazol-4-ones and 5*H*-thiazol-4-ones) deprotonated, the

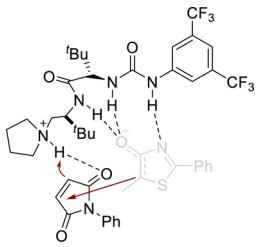
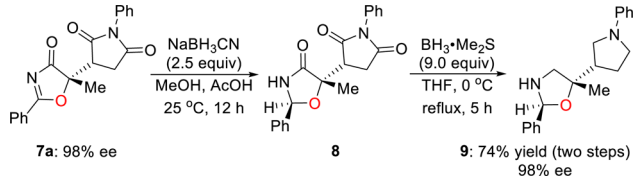


Figure 1. Proposed transition state.

generated enolate would bind to the N−H unit of amide and urea of DP-UAA but not R$_3$NH$^+$ ammonium group of the catalyst. Accordingly, one carbonyl of maleimide will bind to R$_3$NH$^+$ via hydrogen bonding interactions and with this conformation, which is easy for the adduct to subsequent abstract a proton from R$_3$NH$^+$, thus leading to highly chemoselective 1,4-conjugate addition process in the reaction of 5*H*-oxazol-4-ones to maleimides.

In previous works, the chiral adducts derived from 5*H*-thiazol-4-ones have been demonstrated to easily transform to the important α-mercapto carboxylic acid derivatives.[3] To further verify the utility of the method, we attempted to reduce the C−N double bond of **7a** by NaBH$_3$CN at 25 °C (Scheme 2). It was found that the reaction was finished after 12 h, and

Scheme 2. Transformation of Adducts



product **8** could be obtained with excellent diastereoselectivity. By treatment of 9.0 equiv of BH$_3$·Me$_2$S, three amide groups of **8** could be reduced smoothly, affording an interesting *N*-containing heterocycle **9** with the same enantiomeric purity.

CONCLUSION

In summary, the first asymmetric reaction between 5*H*-thiazol-4-ones and maleimides has been developed. By using a DP-UAA catalyst, the reaction could undergo highly chemoselective 1,4-conjugate addition process, affording a variety of valuable sulfur and nitrogen-containing compounds in excellent yields (up to 97%) and stereoselectivities (up to 99% *ee* and >20:1 dr). The strategy was also effective to 1,4-conjugate addition reaction of 5*H*-thiazol-4-ones with 1,4-naphthoquinones, and the corresponding arylated products with biological importance were obtained in up to 91% *ee*. More importantly, this method could modulate the chemoselectivity of 5*H*-oxazol-4-ones with maleimides from [4+2] annulation to 1,4-conjugate addition reaction, probably due to the distinct catalytic mechanisms between DP-UAA and the Takemoto's catalyst. The corresponding 1,4-conjugate addition products were obtained in high yields and with excellent enantio- and diastereoselectivities (up to >99% *ee*, > 20:1 dr).

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EXPERIMENTAL SECTION

General Procedures and Methods. Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reaction mixtures were stirred in 10 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in nonvolatile reagents/compounds was removed in high *vacuo* by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ∼30 mmHg and heated with a water bath at 30−35 °C using rotary evaporator with aspirator. The condenser was cooled with running water at 0 °C.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on precoated plates. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200−300 mesh. Columns were packed as slurry of silica gel in petroleum ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2.0 atm with an air pump.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) and carbon NMR (^{13}C NMR) were recorded in $CDCl_3$ unless otherwise stated. ^{1}H (300 MHz) and ^{13}C (75 MHz) were performed on (300 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as s (singlet), d (doublet), t (triplet), q (quartet), quintet, m (multiplets), dd (doublet of doublets), dt (doublet of triplets), and br (broad). Coupling constants (J) were recorded in Hertz (Hz). The number of proton atoms (n) for a given resonance was indicated by nH. The number of carbon atoms (n) for a given resonance was indicated by nC. HRMS (analyzer: TOF) was reported in units of mass of charge ratio (m/z). Optical rotations were recorded on a polarimeter with a sodium lamp of wavelength 589 nm and reported as follows; $[\alpha]_\lambda^{T\,^\circ C}$ (c = g/100 mL, solvent). Melting points were determined on a microscopic melting point apparatus.

Enantiomeric excesses were determined by chiral high-performance liquid chromatography (HPLC) analysis. UV detection was monitored at 254 nm. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials. All commercial reagents were purchased with the highest purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc), were distilled. Anhydrous DCM and MeCN were freshly distilled from CaH_2 and stored under N_2 atmosphere. THF, Et_2O, and toluene were freshly distilled from sodium/benzophenone before use. Anhydrous methanol was distilled from Mg. All compounds synthesized were stored in a −20 °C freezer and light-sensitive compounds were protected with aluminum foil.

General Procedure for the Synthesis of ***3****.* 5*H*-Thiazol-4-one **1** (0.10 mmol, 1.0 equiv) and catalyst **IV** (0.01 mmol, 0.1 equiv) were dissolved in toluene (2.0 mL) and stirred at 25 °C for 10 min. Then *N*-phenylmaleimide **2** (0.2 mmol, 2 equiv) was added. The reaction mixture was stirred at 25 °C and monitored by TLC. Upon complete consumption of 5*H*-thiazol-4-one **1**, the reaction mixture was loaded onto a short silica gel column, followed by separation with flash chromatography using gradient elution with DCM/MeOH mixtures (400:1 to 200:1). Removing the solvent *in vacuo* afforded product **3**.

General Procedure for the Synthesis of ***5****.* 5*H*-Thiazol-4-one **1** (0.1 mmol, 1.0 equiv) and catalyst **V** (0.01 mmol, 0.1 equiv) were dissolved in THF (1.0 mL) and stirred at 0 °C for 10 min. Then 1,4-naphthaquinone **4** (0.2 mmol, 2 equiv) was added. The reaction mixture was stirred at 0 °C and monitored by TLC. Upon complete consumption of 5*H*-thiazol-4-one **1**, the reaction mixture was loaded onto a short silica gel column, followed by separation with flash chromatography using gradient elution with DCM/MeOH mixtures (400:1 to 100:1). Removing the solvent *in vacuo* afforded product **5**.

General Procedure for the Synthesis of ***7****.* *N*-Phenyl maleimide **2** (0.2 mmol, 2.0 equiv) and catalyst **IV** (0.01 mmol, 0.1 equiv) were dissolved in toluene (2.0 mL) and stirred at 25 °C for 10 min. 5*H*-Oxazol-4-one **6** (0.1 mmol, 1.0 equiv) was added as the second step for slightly unstable. The reaction mixture was stirred at 25 °C and monitored by TLC. Upon complete consumption of **6**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with DCM/MeOH mixtures (500:1 to 300:1). Removing the solvent *in vacuo* afforded product **7**.

General Procedure for the Synthesis of ***9****.* (*S*)-3-((*S*)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-phenylpyrrolidine-2,5-dione **7a** (0.10 mmol, 1.0 equiv) and acetic acid (0.1 mL) were dissolved in a mixed solvent of MeOH (1.0 mL) and DCM (1.0 mL) under nitrogen atmosphere at room temperature. Then sodium cyanoborohydride (2.5 mmol, 2.5 equiv) was added. The reaction was monitored by TLC. Upon complete consumption of **7a**, solvent was removed. The reaction mixture was loaded onto a short silica gel column, followed by separation with flash chromatography using gradient elution with DCM/MeOH mixtures (400:1 to 100:1). Removing the solvent *in vacuo* afforded product **8**. Then borane in THF (1 M, 0.9 mL, 0.9 mmol) was added dropwise to a solution of **8** in THF (2.0 mL). After stirring the reaction mixture for 30 min at 0 °C, the mixture was refluxed for 5 h. The reaction was monitored by TLC. Upon complete consumption of **8**, methanol was added to the mixture at 0 °C, followed by removal of solvent and chromatography on silica gel using gradient elution with DCM/MeOH mixtures (400:1 to 100:1). Removing the solvent *in vacuo* afforded product **9**.

*(R)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**3a**).* White solid, mp 199.0−200.2 °C; 35.0 mg (0.1 mmol), 96% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 91.0 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, J = 7.5 Hz, 2H), 7.73 (t, J = 7.4 Hz, 1H), 7.36−7.60 (m, 5H), 7.28 (d, J = 9.5 Hz, 2H), 3.66 (dd, J = 9.0, 5.5 Hz, 1H), 2.99 (dd, J = 18.4, 9.1 Hz, 1H), 2.18 (dd, J = 18.4, 5.5 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 175.5, 173.5, 136.0, 131.5, 131.3, 129.2, 129.1, 129.0, 126.4, 64.8, 45.8, 32.2, 25.4; HRMS (ESI) m/z 365.0961 (M+H$^+$), calc. for $C_{20}H_{17}N_2O_3S$ 365.0960. The ee was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol =60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.7 min (major), 35.8 min (minor).

*(R)-1-(4-Fluorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3b**).* White solid, mp 166.4−167.7 °C; 37.1 mg (0.1 mmol), 97% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 284.1 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 7.6 Hz, 2H), 7.73 (t, J = 7.4 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.31−7.24 (m, 2H), 7.17 (t, J = 8.5 Hz, 2H), 3.65 (dd, J = 9.0, 5.5 Hz, 1H), 2.98 (dd, J = 18.4, 9.1 Hz, 1H), 2.17 (dd, J = 18.4, 5.5 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.2, 175.4, 173.4, 162.3 (d, $^1J_{C-F}$ = 247.7 Hz), 136.0, 131.4, 129.3, 129.2, 128.2(d, $^3J_{C-F}$ = 8.8 Hz), 127.2(d, $^4J_{C-F}$ = 3.2 Hz), 116.3 (d, $^2J_{C-F}$ = 22.8 Hz), 64.7, 45.8, 32.2, 25.4; HRMS (ESI) m/z 383.0867 (M+H$^+$), calc. for $C_{20}H_{16}FN_2O_3S$ 383.0866. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.6 min (major), 30.1 min (minor).

*(R)-1-(4-Chlorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3c**).* White solid, Mp 191.6−192.5 °C; 35.5 mg (0.1 mmol), 89% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 205.1 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 7.3 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 3.65 (dd, J = 9.1, 5.5 Hz, 1H), 2.98 (dd, J = 18.4, 9.1 Hz, 1H), 2.18 (dd, J = 18.4, 5.5 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.2, 175.2, 173.1, 136.0, 134.8, 131.4, 129.7, 129.4, 129.3, 129.2, 127.6, 64.7, 45.8, 32.2, 25.4; HRMS (ESI) m/z 399.0565 (M+H$^+$), calc. for $C_{20}H_{16}N_2O_3SCl$ 399.0570. The ee was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0

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mL/min; 25 °C; 254 nm; retention time: 19.2 min (major), 48.0 min (minor).

*(R)-1-(4-Bromophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3d**).* White solid, mp 193.0−194.6 °C; 42.1 mg (0.1 mmol), 97% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 360.7 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.3 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.65−7.50 (m, 4H), 7.22−7.14 (m, 2H), 3.65 (dd, *J* = 9.1, 5.5 Hz, 1H), 2.97 (dd, *J* = 18.4, 9.1 Hz, 1H), 2.17 (dd, *J* = 18.4, 5.5 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 193.2, 175.1, 173.0, 136.0, 132.4, 131.4, 130.3, 129.3, 129.2, 127.9, 122.8, 64.6, 45.8, 32.2, 25.4; HRMS (ESI) *m*/*z* 443.0067 (M+H$^+$), calc. for $C_{20}H_{16}BrN_2O_3S$ 443.0065. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.4 min (major), 50.2 min (minor).

*(R)-1-(3,5-Difluorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3e**).* White solid, Mp 72.4−73.1 °C; 36.8 mg (0.1 mmol), 92% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 260.4 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.4 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 6.99−6.92 (m, 2H), 6.91−6.83 (m, 1H), 3.66 (dd, *J* = 9.1, 5.6 Hz, 1H), 2.99 (dd, *J* = 18.4, 9.1 Hz, 1H), 2.19 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 193.1, 174.7, 172.5, 162.8 (dd, $^1J_{C-F}$ = 248.2 Hz, $^3J_{C-F}$ = 13.7 Hz), 136.1, 133.1 (t, $^3J_{C-F}$ = 12.8 Hz), 131.4, 129.3, 129.2, 109.9 (m),, 104.5 (t, $^2J_{C-F}$ = 25.0 Hz),, 64.5, 45.8, 32.1, 25.4; HRMS (ESI) *m*/*z* 401.0781 (M+H$^+$), calc. for $C_{20}H_{15}N_2O_3F_2S$ 401.0771. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 13.3 min (major), 39.0 min (minor).

*(R)-1-(3-Chlorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3f**).* White solid, mp 140.3−140.9 °C; 37.1 mg (0.1 mmol), 93% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 409.5 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.3 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.47−7.36 (m, 2H), 7.34−7.30 (m, 1H), 7.20 (dt, J = 6.8, 2.2 Hz, 1H), 3.66 (dd, *J* = 9.1, 5.5 Hz, 1H), 2.98 (dd, *J* = 18.4, 9.1 Hz, 1H), 2.18 (dd, *J* = 18.4, 5.5 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.26, 175.1, 173.0, 136.0, 134.8, 132.3, 131.4, 130.2, 129.3, 129.2, 129.1, 126.6, 124.6, 64.6, 45.8, 32.2, 25.4; HRMS (ESI) *m*/*z* 399.0573 (M+H$^+$), calc. for $C_{20}H_{16}N_2O_3SCl$ 399.0570. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.7 min (major), 35.0 min (minor).

*(R)-1-(3-Bromophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3g**).* White solid, mp 140.3−141.7 °C; 43.0 mg (0.1 mmol), 97% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 238.2 (*c* 2.0, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.2 Hz, 2H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.60−7.51 (m, 3H), 7.47 (t, *J* = 1.8 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.26−7.22 (m, 1H), 3.65 (dd, *J* = 9.1, 5.6 Hz, 1H), 2.98 (dd, *J* = 18.4, 9.1 Hz, 1H), 2.18 (dd, *J* = 18.4, 5.6 Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 175.1, 173.0, 136.0, 132.4, 132.0, 131.4, 130.4, 129.4, 129.3, 129.2, 125.0, 122.5, 64.6, 45.8, 32.2, 25.4; HRMS (ESI) *m*/*z* 443.0067 (M +H$^+$), calc. for $C_{20}H_{16}N_2O_3SBr$ 443.0065. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 17.4 min (major), 35.1 min (minor).

*(R)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-(p-tolyl)pyrrolidine-2,5-dione (**3h**).* White solid, mp 200.1−201.5 °C; 36.3 mg (0.1 mmol), 96% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 95.0 (*c* 2.0, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.7 Hz, 2H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 3.64 (dd, *J* = 8.9, 5.5 Hz, 1H), 2.97 (dd, *J* = 18.3, 9.0 Hz, 1H), 2.39 (s, 3H), 2.25−2.04 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.4, 175.6, 173.6, 139.1, 136.0, 131.5, 129.9, 129.2, 128.7, 126.2, 64.8, 45.8, 32.2, 25.4, 21.2; HRMS (ESI) *m*/*z* 379.1118 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_3S$ 379.1116. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 30/70; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 29.7 min (major), 65.2 min (minor).

*(R)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-(m-tolyl)pyrrolidine-2,5-dione (**3i**).* White solid, Mp 181.4−182.4 °C; 36.0 mg (0.1 mmol), 95% yield; 99% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 253.5 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.5 Hz, 2H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.10−7.02 (m, 2H), 3.64 (dd, *J* = 9.0, 5.5 Hz, 1H), 2.97 (dd, *J* = 18.3, 9.1 Hz, 1H), 2.40 (s, 3H), 2.22−2.09 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 175.6, 173.5, 139.4, 135.9, 131.5, 131.2, 129.8, 129.3, 129.2, 129.1, 126.9, 123.5, 64.8, 45.8, 32.2, 25.4, 21.3; HRMS (ESI) *m*/*z* 379.1118 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_3S$ 379.1116. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.9 min (major), 34.2 min (minor).

*(R)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-(o-tolyl)pyrrolidine-2,5-dione (**3j**).* White solid, mp 180.2−181.9 °C; 34.8 mg (0.1 mmol), 92% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 205.5 (*c* 2.0, $CHCl_3$) ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (t, *J* = 6.3 Hz, 2H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.41−7.27 (m, 3H), 7.13−7.01(m,, 1H), 3.70 (dd, *J* = 8.1, 6.3 Hz, 1H), 3.01 (dt, *J* = 17.7, 8.7 Hz, 1H), 2.31−2.04 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 195.4, 193.4, 193.3,175.5, 175.4, 173.4, 134.0, 136, 135.5, 131.6, 131.5, 131.3, 130.5, 129.8, 129.4,129.3, 129.2, 129.1, 127.8, 127.1, 127.0, 64.9, 64.7, 46.0, 45.9, 32.4, 32.3, 25.4, 25.3, 18.0, 17.7; HRMS (ESI) *m*/*z* 379.1124 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_3S$ 379.1116. The *ee* was determined by HPLC analysis: CHIRALPAK IE + IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 15/85; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 70.0 min (major), 92.7 min (minor).

*(R)-1-(4-Methoxyphenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3k**).* White solid, mp 190.5−191.0 °C; 36.7 mg (0.1 mmol), 93% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 356.26 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.5 Hz, 2H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.1 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 3.63 (dd, *J* = 9.0, 5.4 Hz, 1H), 2.96 (dd, *J* = 18.3, 9.0 Hz, 1H), 2.22−2.11 (m, 4H): ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 175.7, 173.8, 159.7, 135.9, 131.5, 129.3, 129.2, 127.6, 123.8, 114.5, 64.8, 55.5, 45.7, 32.2, 25.3; HRMS (ESI) *m*/*z* 395.1060 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_4S$ 395.1066. The *ee* was determined by HPLC analysis: CHIRALPAK ID-3 (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 48.5 min (major), 74.6 min (minor).

*(R)-1-(3-Methoxyphenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3l**).* White solid, mp 150.7−151.9 °C; 33.1 mg (0.1 mmol), 84% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 257.7 (*c* 2.0, $CHCl_3$); ^{1}HNMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.4 Hz, 2H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 8.1 Hz, 1H), 6.96 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.80 (t, *J* = 2.1 Hz, 1H), 3.82 (s, 3H) 3.64 (dd, *J* = 9.0, 5.5 Hz, 1H), 2.97 (dd, *J* = 18.3, 9.1 Hz, 1H), 2.17 (dd, *J* = 17.1, 4.2 Hz, 1H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 175.4, 173.4, 160.1, 136.0, 132.3, 131.5, 130.0, 129.3, 129.2, 118.6, 114.6, 112.4, 64.8, 55.4, 45.8, 32.2, 25.4; HRMS (ESI) *m*/*z* 395.1058 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_4S$ 395.1066. The *ee* was determined by HPLC analysis: CHIRALPAK IC with IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 84.2 min (major), 189.6 min (minor).

*(R)-1-Benzyl-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3m**).* White solid, Mp 116.9−118.7 °C; 34.1 mg (0.1 mmol), 90% yield; 98% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 188.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.3 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.40−7.30 (m, 5H), 4.69 (d, *J* = 14.2 Hz, 1H), 4.64 (d, *J* = 14.2 Hz, 1H), 3.46 (dd, *J* = 8.9, 5.3 Hz, 1H), 2.81 (dd, *J* = 18.3, 8.9 Hz, 1H), 2.06 (s, 3H), 1.99 (dd, *J* = 18.3, 5.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.6, 193.3, 176.1, 174.1, 135.9, 135.3, 131.5, 129.2, 129.1, 128.8, 128.7, 128.1, 64.62, 45.6, 42.6, 32.1, 25.3; HRMS (ESI) *m*/*z* 379.1119 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_3S$ 379.1116. The *ee* was determined by HPLC

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analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.0 min (major), 45.8 min (minor).

*(R)-1-Methyl-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)pyrrolidine-2,5-dione (**3n**).* White solid, mp 154.0−155.3 °C; 27.5 mg (0.1 mmol), 91% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 118.6 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.2 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 3.47 (dd, *J* = 8.9, 5.4 Hz, 1H), 3.00 (s, 3H), 2.80 (dd, *J* = 18.2, 8.9 Hz, 1H), 2.08 (s, 3H), 1.98 (dd, *J* = 18.2, 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.7, 193.4, 176.5, 174.5, 135.9, 131.5, 129.2, 64.5, 45.7, 32.0, 25.3, 25.0; HRMS (ESI) *m*/*z* 303.0797 (M+H$^+$), calc. for $C_{15}H_{15}N_2O_3S$ 303.0803. The *ee* was determined by HPLC analysis: CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.8 min (major), 39.7 min (minor).

*(R)-3-((S)-5-Ethyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-phenylpyrrolidine-2,5-dione(**3o**).* White solid, Mp 54.2−55.7 °C; 32.9 mg (0.1 mmol), 87% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 45.4 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.6 Hz, 2H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.60−7.36 (m, 5H), 7.27 (d, *J* = 7.1 Hz, 2H), 3.68 (dd, *J* = 9.0, 5.6 Hz, 1H), 3.05−2.83 (m, 2H), 2.39−2.19 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 193.0, 175.5, 173.6, 136.0, 131.5, 131.4, 129.2, 129.0, 126.4, 70.7, 46.1, 32.2, 30.7, 8.7; HRMS (ESI) *m*/*z* 379.1122 (M+H$^+$), calc. for $C_{21}H_{19}N_2O_3S$ 379.1116. The *ee* was determined by HPLC analysis: CHIRALPAK IC (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.0 min (major), 31.6 min (minor).

*(R)-3-((S)-5-Isopropyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**3p**).* White solid, mp 156.3−157.3 °C; 36.5 mg (0.1 mmol), 93% yield; 95% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 68.971 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ = 8.15 (d, *J* = 7.6 Hz, 2H), 7.71 (t, *J* = 6.9 Hz, 1H), 7.62−7.33 (m,6H), 7.36−7.27 (m, 1H), 4.07−3.95 (m, 1H), 3.03 (dd, *J* = 18.1, 9.1 Hz, 1H), 2.94−2.80 (m, 1H), 2.72 (dd, *J* = 18.1, 5.3 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 3H), 1.08 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.3, 192.7, 175.3, 173.8, 135.8, 131.7, 131.5, 129.3, 129.2, 129.1, 128.9, 126.5, 73.3, 43.4, 34.6, 32.4, 18.6, 16.5; HRMS (ESI) *m*/*z* 393.1270 (M+H$^+$), calc. for $C_{22}H_{21}N_2O_3S$ 393.1273. The *ee* was determined by HPLC analysis: CHIRALPAK IB (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.1 min (major), 22.1 min (minor).

*(R)-3-((S)-5-Benzyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**3q**).* White solid, Mp 81.8−82.7 °C; 36.1 mg (0.1 mmol), 82% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 75.2 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.56−7.40 (m, 5H), 7.35−7.29 (m, 2H), 7.25−7.11 (m, 5H), 4.15 (d, *J* = 13.8 Hz, 1H), 3.83 (dd, *J* = 9.1, 5.7 Hz, 1H), 3.65 (d, *J* = 13.8 Hz, 1H), 3.04 (dd, *J* = 18.3, 9.1 Hz, 1H), 2.27 (dd, *J* = 18.3, 5.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 192.5, 175.8, 173.4, 135.7, 133.8, 131.4, 130.7, 129.3, 129.1, 129.0, 128.1, 127.6, 126.4, 70.9, 45.6, 43.2, 32.4; HRMS (ESI) *m*/*z* 441.1271 (M+H$^+$), calc. for $C_{26}H_{21}N_2O_3S$ 441.1273. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.3 min (major), 36.1 min (minor).

*(R)-3-((S)-5-Methyl-4-oxo-2-(quinolin-2-yl)-4,5-dihydrothiazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**3r**).* White solid, Mp 244.7−245.9 °C; 34.1 mg (0.1 mmol), 82% yield; 97% *ee*; dr =20:1; $[\alpha]_D^{26}$ − 79.8 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.41 (q, *J* = 8.6 Hz, 2H), 8.24 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.56−7.37 (m, 3H), 7.32 (d, *J* = 7.8 Hz, 2H), 3.69 (dd, *J* = 8.3, 6.1 Hz, 1H), 3.00 (dd, *J* = 18.3, 9.0 Hz, 1H), 2.23 (dd, *J* = 18.2, 5.7 Hz, 1H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 194.4, 175.5, 173.5, 148.5, 147.8, 137.6, 131.4, 130.9, 130.5, 129.8, 129.2, 128.9, 127.9, 126.5, 119.7, 63.6, 45.7, 32.3, 25.3; HRMS (ESI) *m*/*z* 416.1061 (M+H$^+$), calc. for $C_{23}H_{18}N_3O_3S$ 416.1069. The *ee* was determined by HPLC analysis: CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 42.8 min (major), 57.2 min (minor).

*(S)-2-(5-Methyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-naphthalene-1,4-dione (**5a**).* Yellow solid, mp 189.5−190.9 °C; 24.7 mg (0.1 mmol), 71% yield; 90% *ee*; $[\alpha]_D^{26}$ − 102.9 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.6 Hz, 2H), 8.06 (t, *J* = 6.3 Hz, 2H), 7.85−7.65 (m, 3H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.14 (s, 1H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 192.7, 184.1, 182.8, 147.8, 136.0, 135.3, 134.4, 134.3, 132.0, 131.8, 131.7, 129.1, 128.9, 127.2, 126.4, 60.4, 24.9; HRMS (ESI) *m*/*z* 348.0697 (M+H$^+$), calc. for $C_{20}H_{14}NO_3S$ 348.0694. The *ee* was determined by HPLC analysis: CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.5 min (minor), 29.2 min (major).

*(S)-2-(5-Ethyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-naphthalene-1,4-dione (**5b**).* Yellow solid, mp 125.7−127.1 °C; 25.3 mg (0.1 mmol), 70% yield; 91% ee; $[\alpha]_D^{26}$ − 394.0 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.7 Hz, 2H), 8.06 (d, *J* = 3.1 Hz, 2H), 7.79−7.63 (m, 3H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.14 (s, 1H), 2.48−2.20 (m, 2H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.5, 192.2, 184.4, 183.5, 147.8, 135.8, 135.4, 134.5, 134.4, 132.1, 131.7, 129.2, 129.1, 127.3, 126.5, 66.4, 30.6, 8.4; HRMS (ESI) *m*/*z* 362.0857 (M+H$^+$), calc. for $C_{21}H_{16}NO_3S$ 362.0851. The *ee* was determined by HPLC analysis: CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.0 min (minor), 57.2 min (major).

*(S)-2-(5-Isopropyl-4-oxo-2-phenyl-4,5-dihydrothiazol-5-yl)-naphthalene-1,4-dione (**5c**).* Yellow solid, mp 130.5−131.8 °C; 24.7 mg (0.1 mmol), 71% yield; 70% *ee*; $[\alpha]_D^{26}$ − 506.2 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20−8.04 (m, 4H), 7.77 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.22 (s, 1H), 2.92 (dt, *J* = 13.6, 6.7 Hz, 1H), 1.13−1.05 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.0, 190.6, 184.3, 184.2, 146.2, 135.9, 135.3, 134.4, 134.1, 131.9, 131.8, 131.6, 129.1, 128.8, 127.1, 126.3, 70.5, 35.2, 18.1, 17.0; HRMS (ESI) *m*/*z* 376.1002 (M+H$^+$), calc. for $C_{22}H_{18}NO_3S$ 376.1007. The *ee* was determined by HPLC analysis: CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 20/80; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 11.2 min (minor), 15.5 min (major).

*(S)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**7a**).* White solid, mp 138.1−139.9 °C; 31.7 mg (0.1 mmol), 91% yield; 98% *ee*; $[\alpha]_D^{26}$ − 160.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.22−8.20 (m, 2H), 7.75−7.71 (m, 1H), 7.56 (t, *J* = 7.8 Hz, 2H), 7.51−7.38 (m, 3H), 7.28−7.27 (m, 1H), 7.25−7.24 (m, 1H), 3.58−3.54 (m, 1H), 3.06−3.96 (m, 1H), 2.59−2.52 (m, 1H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3, 186.3, 173.5, 173.2, 135.9, 131.4, 130.4, 129.3, 129.2, 129.0, 126.4, 125.0, 86.0, 44.0, 30.5, 20.9; HRMS (ESI) *m*/*z* 349.1183 (M+H$^+$), calc. for $C_{20}H_{17}N_2O_4$ 349.1188. The *ee* was determined by HPLC analysis: CHIRALPAK IF (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 9.0 min (minor) and 12.4 min (major).

*(S)-1-(4-Fluorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7b**).* White solid, mp 111.0−112.9 °C; 35.9 mg (0.1 mmol), 98% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 195.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.7 Hz, 2H), 7.74 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.30−7.24 (m, 2H), 7.16−7.13 (m, 2H), 3.57 (dd, *J* = 9.4, 5.1 Hz, 1H), 3.01 (dd, *J* = 18.4, 9.5 Hz, 1H), 2.58 (dd, *J* = 18.4, 5.1 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3, 186.3, 173.4, 173.2, 162.3 (d, $^1J_{C-F}$ = 247.7 Hz), 136.0, 130.3, 129.2, 128.2 (d, $^3J_{C-F}$ = 8.8 Hz), 127.1(d, $^4J_{C-F}$ = 3.3 Hz), 124.9, 116.3 (d, $^2J_{C-F}$ = 22.9 Hz), 85.8, 43.9, 30.4, 20.9; HRMS (ESI) *m*/*z* 389.0902 (M+Na$^+$), calc. for $C_{20}H_{15}N_2O_4FNa$ 389.0914. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.8 min (major) and 32.5 min (minor).

*(S)-1-(4-Chlorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7c**).* White solid, mp 124.8−126.6 °C; 34.4 mg (0.1 mmol), 90% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 318.0 (*c*

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0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 7.2 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.8 Hz, 2H), 3.56 (dd, J = 9.5, 5.2 Hz, 1H), 3.01 (dd, J = 18.4, 9.5 Hz, 1H), 2.58 (dd, J = 18.4, 5.2 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 186.4, 173.2, 172.9, 136.0, 134.8, 130.4, 129.8, 129.5, 129.2, 127.6, 125.0, 85.8, 44.0, 30.4, 20.9; HRMS (ESI) m/z 405.0633 ($M+Na^+$), calc. for $C_{20}H_{15}N_2O_4ClNa$ 405.0618. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.6 min (major) and 32.7 min (minor).

*(S)-1-(4-Bromophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7d**).* White solid, mp 119.9–120.8 °C; 38.9 mg (0.1 mmol), 91% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 220.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 7.2 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.61–7.53 (m, 4H), 7.17 (d, J = 8.7 Hz, 2H), 3.56 (dd, J = 9.5, 5.2 Hz, 1H), 3.01 (dd, J = 18.4, 9.5 Hz, 1H), 2.58 (dd, J = 18.4, 5.2 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 186.3, 173.1, 172.9, 136.0, 132.4, 130.4, 129.2, 127.9, 125.0, 122.8, 85.8, 44.0, 30.4, 20.9; HRMS (ESI) m/z 427.0296 ($M+H^+$), calc. for $C_{20}H_{16}N_2O_4Br$ 427.0293. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.1 min (major) and 42.9 min (minor).

*(S)-1-(3-Chlorophenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7e**).* White solid, mp 140.1–141.5 °C; 35.2 mg (0.1 mmol), 92% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 245.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.2 Hz, 2H), 7.74 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.8 Hz, 2H), 7.40–7.42 (m, 2H), 7.31 (d, J = 1.6 Hz, 1H), 7.19 (m, 1H), 3.56 (dd, J = 9.5, 5.2 Hz, 1H), 3.01 (dd, J = 18.4, 9.5 Hz, 1H), 2.58 (dd, J = 18.4, 5.2 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 186.4, 173.1, 172.8, 136.0, 134.8, 132.4, 130.4, 130.2, 129.2, 129.1, 126.7, 124.9, 124.6, 85.8, 44.0, 30.4, 20.9; HRMS (ESI) m/z 383.0800 ($M+H^+$), calc. for $C_{20}H_{16}N_2O_4Cl$ 383.0799. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.3 min (minor) and 37.7 min (major).

*(S)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-(p-tolyl)pyrrolidine-2,5-dione (**7f**).* White solid, mp 126.1–127.8 °C; 33.7 mg (0.1 mmol), 93% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 360.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.25–8.16 (m, 2H), 7.73 (t, J = 10.6, 4.4 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.3 Hz, 2H), 3.54 (dd, J = 9.5, 5.0 Hz, 1H), 2.99 (dd, J = 18.3, 9.5 Hz, 1H), 2.52 (dd, J = 18.3, 5.0 Hz, 1H), 2.38 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3, 186.3, 173.5, 173.2, 136.0, 131.4, 130.4, 129.3, 129.2, 129.0, 126.4, 125.0, 86.0, 44.0, 30.5, 20.9; HRMS (ESI) m/z 363.1353 ($M+H^+$), calc. for $C_{21}H_{19}N_2O_4$ 363.1345. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 28.7 min (major) and 43.1 min (minor).

*(S)-3-((S)-5-Methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-(m-tolyl)pyrrolidine-2,5-dione (**7g**).* White solid, mp 116.4–117.6 °C; 34.8 mg (0.1 mmol), 96% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 338.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.2 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.40–7.31 (m, 1H), 7.22 (d, J = 7.6 Hz, 1H), 7.03–7.05 (m, 2H), 3.55 (dd, J = 9.5, 5.1 Hz, 1H), 2.99 (dd, J = 18.3, 9.5 Hz, 1H), 2.54 (dd, J = 18.3, 5.1 Hz, 1H), 2.38 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.4, 186.4, 173.6, 173.4, 139.5, 136.0, 131.3, 130.4, 130.0, 129.2, 129.1, 127.0, 125.1, 123.5, 86.0, 44.0, 30.5, 21.4, 20.9; HRMS (ESI) m/z 363.1354 ($M+H^+$), calc. for $C_{21}H_{19}N_2O_4$ 363.1345. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 22.4 min (major) and 32.6 min (minor).

*(S)-1-(4-Methoxyphenyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7h**).* White solid, mp 107.5–109.3 °C; 36.6 mg (0.1 mmol), 94% yield; 98% *ee*; $[\alpha]_D^{26}$ − 195.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.22–8.19 (m, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 7.19–7.14 (m, 2H), 7.00–6.96 (m, 2H), 3.82 (s, 3H), 3.54 (dd, J = 9.5, 5.1 Hz, 1H), 2.94 (dd, J = 18.3, 9.5 Hz, 1H), 2.57 (dd, J = 18.3, 5.1 Hz,1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3, 186.3, 173.7, 173.6, 159.7, 135.9, 130.3, 129.2, 127.6, 125.0, 123.9, 114.6, 86.0, 55.5, 43.9, 30.4, 20.8; HRMS (ESI) m/z 379.1303 ($M+H^+$), calc. for $C_{21}H_{19}N_2O_5$ 379.1294. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 44.8 min (major) and 83.0 min (minor).

*(S)-1-(4-Methoxybenzyl)-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7i**).* White solid, mp 108.3–110.0 °C; 37.7 mg (0.1 mmol), 96% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 240.9 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.69 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 4.61 (dd, J = 13.9 Hz, 2H), 3.81 (s, 3H), 3.34 (dd, J = 9.4, 4.4 Hz, 1H), 2.79 (dd, J = 18.4, 9.4 Hz, 1H), 2.15 (dd, J = 18.4, 4.4 Hz, 1H), 1.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3, 186.1, 174.1, 174.0, 159.3, 135.9, 130.3, 130.2, 129.0, 127.8, 124.7, 114.0, 86.3, 55.2, 43.6, 42.0, 30.3, 20.6; HRMS (ESI) m/z 393.1448 ($M+H^+$), calc. for $C_{22}H_{21}N_2O_5$ 393.1450. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 28.1 min (major) and 98.3 min (minor).

*(S)-1-Methyl-3-((S)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**7j**).* White solid, mp 111.3–113.1 °C; 26.6 mg (0.1 mmol), 93% yield; 98% *ee*; $[\alpha]_D^{26}$ − 247.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, J = 7.2 Hz, 2H), 7.73 (t, J = 7.5 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 3.39 (dd, J = 9.4, 5.3 Hz, 1H), 3.01 (s, 3H), 2.82 (dd, J = 18.2, 9.4 Hz, 1H), 2.34 (dd, J = 18.2, 5.3 Hz, 1H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.4, 186.3, 174.4, 174.3, 135.9, 129.1, 125.0, 85.8, 43.8, 30.1, 25.1, 20.8; HRMS (ESI) m/z 287.1036 ($M+H^+$), calc. for $C_{15}H_{15}N_2O_4$ 287.1032. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 26.8 min (major) and 62.8 min (minor).

*(S)-3-((S)-5-Ethyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**7k**).* White solid, mp 186.2–187.8 °C; 35.2 mg (0.1 mmol), 97% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 394.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, Acetone) δ 8.12 (d, J = 7.7 Hz, 2H), 7.86 (d, J = 16.3 Hz, 1H), 7.69 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 7.36–7.24 (m, 3H), 7.12 (d, J = 7.6 Hz, 2H), 3.73 (dd, J = 9.4, 5.3 Hz, 1H), 3.02 (dd, J = 17.9, 9.5 Hz, 1H), 2.75 (s, 2H), 2.66 (dd, J = 17.9, 5.2 Hz, 1H), 2.47–2.35 (m, 1H), 2.12–2.00 (m, 1H), 1.92 (s, 2H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, d^6-acetone) 191.8, 187.5, 174.9, 174.4, 136.4, 133.4, 130.9, 130.1, 129.7, 129.2, 127.8, 126.5, 90.1, 79.2, 44.3, 7.5; HRMS (ESI) m/z 363.1337 ($M+H^+$), calc. for $C_{21}H_{19}N_2O_4$ 363.1345. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 26.5 min (major) and 56.3 min (minor).

*(S)-3-((S)-5-Benzyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-1-phenylpyrrolidine-2,5-dione (**7l**).* White solid, mp 169.8–171.3 °C; 41.6 mg (0.1 mmol), 98% yield; > 99% *ee*; $[\alpha]_D^{26}$ − 166.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 7.7 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.45–7.31 (m, 5H), 7.19–7.12 (m, 7H), 3.82 (d, J = 14.2 Hz, 1H), 3.57 (dd, J = 9.3, 5.6 Hz, 1H), 3.30 (d, J = 14.3 Hz, 1H), 2.98 (dd, J = 18.3, 9.5 Hz, 1H), 2.68 (dd, J = 18.3, 5.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 186.4, 173.7, 173.3, 135.8, 132.2, 131.3, 130.1, 129.3, 129.1, 129.0, 128.5, 127.8, 126.4, 124.7, 88.7, 43.1, 40.3, 30.5; HRMS (ESI) m/z 425.1496 ($M+H^+$), calc. for $C_{26}H_{21}N_2O_4$ 425.1501. The *ee* was determined by HPLC analysis: CHIRALPAK IE (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 34.2 min (major) and 45.0 min (minor).

*(2S, 5S)-5-Methyl-2-phenyl-5-((R)-1-phenylpyrrolidin-3-yl)-oxazolidine (**9**).* White solid, mp 111.2–112.1 °C; 26.3 mg (0.1 mmol), 70% yield; 98% *ee*; $[\alpha]_D^{26}$ − 438.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.32–7.06 (m, 7H), 6.59 (t, J = 7.2 Hz, 1H), 6.48 (d, J = 8.0 Hz, 2H), 3.77 (s, 1H), 3.37–3.27 (m, 1H), 3.17 (m,

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3H), 2.65−2.50 (m, 2H), 2.42−2.29 (m, 2H), 2.01−1.83 (m, 2H), 1.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.0, 140.1, 129.2, 128.7, 128.2, 127.4, 115.8, 111.8, 71.4, 57.3, 54.8, 48.9, 48.0, 47.1, 25.9, 23.9; HRMS (ESI) m/z 309.1967 ($M+H^+$), calc. for $C_{20}H_{25}N_2O$ 309.1969. The *ee* was determined by HPLC analysis: CHIRALPAK IF (4.6 mm i.d. × 250 mm); hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.1 min (minor) and 32.4 min (major).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02384.

Determination of the absolute configuration by X-ray crystallography, copies of HPLC and NMR spectra (PDF)

X-ray crystallographic data for compound **3a** (CIF)

X-ray crystallographic data for compound **7d** (CIF)

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Notes

The authors declare no competing financial interest.

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