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Highly Enantio- and Diastereoselective [4 + 2] Cycloaddition of 5*H*-oxazol-4-ones with *N*-Maleimides

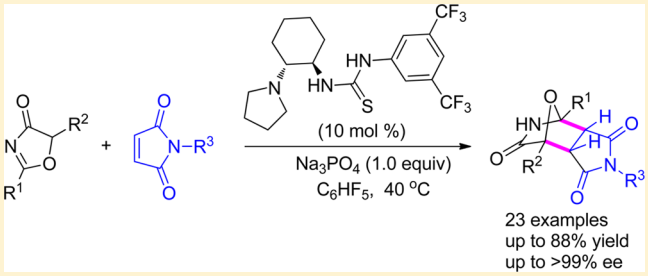
Shuai Qiu,[†,§] Richmond Lee,[‡,§] Bo Zhu,[†] Michelle L. Coote,[‡] Xiaowei Zhao,*[,†] and Zhiyong Jiang*[,†]

[†]Key Laboratory of Natural Medicine and Immuno-Engineering of Henan Province, Henan University, Kaifeng, Henan, P. R. China, 475004

[‡]ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, Australian National University, Canberra, ACT 2601, Australia

Supporting Information

ABSTRACT: An organocatalytic asymmetric reaction between 5*H*-oxazol-4-ones and *N*-substituted maleimides is disclosed. Employing Takemoto's chiral tertiary amine–thiourea as the catalyst, [4 + 2] annulation reactions were performed with high chemoselectivity, leading to a series of biologically important chiral oxo-bridged piperidone-fused succinimides in good to excellent enantioselectivities (up to >99% ee) and >19:1 dr.



A strategic synthon robustly provides comprehensive approaches to access a variety of valuable compounds.[1] In 2004, Trost and co-workers[2] introduced 5*H*-oxazol-4-ones as *α*-alkyl-*α*-hydroxy ester surrogates in a highly enantioselective allylic alkylation. Since then, 5*H*-oxazol-4-ones as an strategic synthon have been demonstrated to afford diverse *α*-alkyl-*α*-hydroxy carboxylic acid derivatives,[3−7] which are structural motifs of numerous chiral molecules with biological importance.[8] For example, Misaki, Sugimura, and co-workers[3] developed a chiral guanidine-catalyzed aldol reaction of 5*H*-oxazole-4-ones, leading to *α*-methyl-*α*,*β*-dihydroxy esters. Asymmetric Mannich reaction of 5*H*-oxazol-4-ones[4] provides an efficient pathway to synthesize chiral *α*-alkylisoserine derivatives. To functionalize the allylic moiety of tertiary alcohols, asymmetric allylic alkylation (AAA) reactions of 5*H*-oxazol-4-ones, including iridium-catalyzed allylic substitutions,[5a] phosphine-catalyzed enantioselective *γ*-addition to allenoates,[5b] and urea-ammonium salt-catalyzed allylation,[5c] have been disclosed by the Hartwig, Lu, and Jiang groups, respectively. A range of highly functionalized *α*-alkyl-*α*-hydroxy carboxylic acid derivatives were attained through developing conjugate addition reactions with various Michael acceptors.[6] In addition, *α*-sulfenylation of 5*H*-oxazol-4-ones was developed to directly embed a heteroquaternary stereogenic center featuring two heteroatoms (O and S) to carbonyl compounds.[7] It is noteworthy that these elegant methods are focused on nucleophilic addition of the C5 atom of 5*H*-oxazol-4-ones.

Very recently, we reported an organocatalytic asymmetric reaction between 5*H*-oxazol-4-ones and itaconimides.[9] Through regulating media and additives, the reaction could undergo either conjugate addition–protonation or [4 + 2] cycloaddition with high chemo-, enantio-, and diastereoselectivities. As a result, two series of chiral adducts, which are the precursors of a kind of *α*-alkyl-*α*-hydroxy carboxylic acid derivatives bearing 1,3-tertiary-heteroquaternary stereocenters (via conjugate addition–protonation) and oxo-bridged piperidones (via [4 + 2] cycloaddition), were successfully obtained. This work proves the feasibility of electrophilic addition to the C2 position of 5*H*-oxazol-4-ones and, thus, further expands their utilities in organic synthesis. Accordingly, the development of novel [4 + 2] annulation of 5*H*-oxazole-4-ones to provide more kinds of important chiral oxo-bridged piperidone derivatives is of current interest.

Succinimides are present in diverse biologically interesting imolecules and are investigated as potential pharmacophores in drug discovery research.[10] In 1982, Freeman and co-workers introduced a mesoionic 1,3-oxazolium-4-olate to react with *N*-maleimides through 1,3-dipolar cycloaddition, leading to a series of oxo-bridged piperidone-fused succinimides.[11] Other efficient 1,3-dipolar annulations that produce this kind of entities were also reported by the Padwa, Kappe, and Schaus groups respectively through devising distinct mesoionic compounds.[12] While these polycyclic succinimides are unusual structural motifs, they still play significant roles in medicinal chemistry, such as the precursors of tricyclic hydroxylpyrrolopyridine-triones (HIV-1 integrases)[13a,b] and the promising candidates[13c] as modulators of nuclear hormone receptor function (molecules **A**–**C**, Figure 1). However, to our knowledge, no asymmetric method has yet been established to synthesize these compounds in a nonracemic form. As an extension of our ongoing investigation toward asymmetric reactions of 5*H*-oxazole-4-ones via organocatalysis,[4b,5c,6b,c,7,9] we were interested in developing an efficient organocatalytic [4

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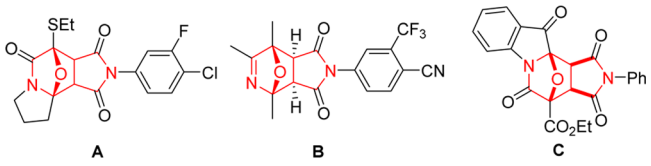
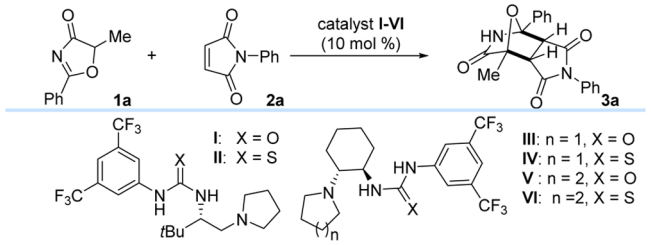


Figure 1. Representative compounds.

+ 2] cycloaddition reaction between 5*H*-oxazol-4-ones and *N*-malemides to facilitate convenient and efficient synthesis of valuable chiral oxo-bridged piperidone-fused succinimides.

Our investigation began with the model reaction between 5*H*-oxazol-4-one **1a** containing a methyl group at the C^5-position and *N*-phenyl maleimide **2a** (Table 1). To probe the

Table 1. Optimization of the Reaction Conditions[a]



entry	cat.	solvent	T (°C)	t (h)	yield (%)[b]	ee (%)[c]
1	Et_3N	DCM	25	36	85	NA
2	**I**	DCM	25	20	35[d]	39
3	**II**	DCM	25	20	31[e]	40
4	**III**	DCM	25	12	51[f]	38
5	**IV**	DCM	25	12	60[g]	66
6	**V**	DCM	25	12	59	30
7	**VI**	DCM	25	12	51	33
8	**IV**	Et_2O	25	12	58	75
9	**IV**	Tol	25	12	68	84
10	**IV**	C_6HF_5	25	12	72	87
11[h]	**IV**	C_6HF_5	25	10	72	91
12[h]	**IV**	C_6HF_5	0	16	68	84
13[h]	**IV**	C_6HF_5	−10	20	60	81
14[h]	**IV**	C_6HF_5	35	10	77	93
15[h]	**IV**	C_6HF_5	40	5	80	95

[a]Reaction conditions: **1a** (0.05 mmol), **2a** (0.075 mmol), catalyst (0.005 mmol), 1.0 mL of solvent. Entry 1, dr of **3a** = 3.3:1. Entries 2−15, dr of **3a** > 19:1. Dr was determined by crude ^{1}H NMR. [b]Yield of isolated product. [c]Determined by HPLC analysis on a chiral stationary phase. [d]Yield of Michael adduct **4a** = 53%, ee = 21%. [e]Yield of **4a** = 57%, ee = 23%. [f]Yield of **4a** = 31%, ee = 13%. [g]Yield of **4a** = 26%, ee = 42%. [h]1.0 equiv of Na_3PO_4 was used as the additive.

feasibility of the reactivity and chemoselectivity, the reaction was first evaluated using 10 mol % of Et_3N as the catalyst in DCM at 25 °C (entry 1). The reaction worked smoothly and afforded the desired [4 + 2] annulation adduct **3a** in 85% yield with 3.3:1 dr after 36 h. This result encouraged us to test the asymmetric version of this reaction. In our previous works,[9,14] amino acid based tertiary amine−(thio)ureas were used as versatile chiral Brønsted bases, accomplishing many challenging reactions with excellent stereoselectivity. Tertiary amine−ureas are especially capable of obtaining highly enantio- and diastereoselective [4 + 2] cyclcoaddition of 5*H*-oxazol-4-ones with *N*-itaconimides. In this context, the reaction was examined by an L-*tert*-leucine-derived tertiary amine−urea **I** as the catalyst (entry 2). We found that the chiral adduct **3a** could be obtained in 35% yield with 39% ee and >19:1 dr after 20 h. The major product was determined as the Michael product **4a** in 53% yield with 21% ee (footnote *d*). The catalyst L-*tert*-leucine-derived tertiary amine−thiourea **II** also did not perform well with enchanced chemo- and enantioselectivity (entry 3). It is highly probable that a different mechanism compared to the reaction between 5*H*-oxazol-4-ones and *N*-itaconimides is operative.

We subsequently attempted Takemoto's chiral tertiary amine−urea **III** and tertiary amine−thiourea **IV** (entries 4−5).[15] Catalyst **IV** improved the ee value of **3a** to 66%, and its yield was increased to 60% (entry 5). When their tertiary amine moiety was changed to pyrrolidine, the corresponding catalysts **V** and **VI** gave poor enantioselectivities. Hence, catalyst **IV** was further selected to study solvent effects (entries 8−10), and pentafluorobenzene (C_6HF_5) was determined as the optimal solvent, giving **3a** in 72% yield with 87% ee and >19:1 dr (entry 10). When 1.0 equiv of Na_3PO_4 was added, the ee value of **3a** increased to 91% (entry 11). Finally, attempts to vary the reaction temperatures demonstrated that the enantioselectivity was improved slightly at higher temperature (entries 12−15); the annulation adduct **3a** was isolated with the best results at 40 °C (80% yield, 95% ee, entry 15).

With the optimal reaction conditions in hand, we investigated the performance of the catalytic asymmetric [4 + 2] annulation reactions between 5*H*-oxazol-4-ones **1** and *N*-substituted maleimides **2** by using 10 mol % of catalyst **IV** (Figure 2 and Table 2). We first evaluated the viability of

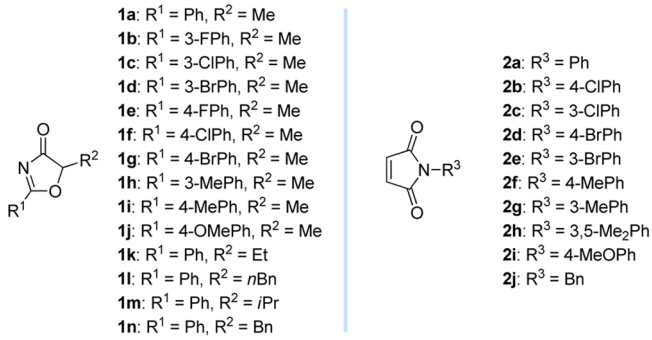


Figure 2. Structures of 5*H*-oxazol-4-ones **1a−m** and *N*-maleimides **2a−j**.

various aryl groups at the C^2-position of 5*H*-oxazol-4-ones with different electronic and steric properties (**1a−j**) using *N*-phenyl maleimide **2a** as the dienophile (entries 1−10). Adducts **3a−j** could be obtained with 70−90% yield, 84−97% ee, and >19:1 dr. Our studies showed that the introduction of diverse substituents onto phenyl groups of 5*H*-oxazol-4-ones hardly affected the enantio- and diastereoselectivities except the chloro group at the *meta*-position (**3c**, entry 3). Other 5*H*-oxazol-4-ones **1k−n** with different substituents at the C^5-position, such as ethyl, *n*-butyl, isopropyl, and benzyl, also presented corresponding [4 + 2] annulation adducts **3k−n** in moderate to good yields with good to excellent enantioselectivities (entries 11−14). A series of *N*-aryl maleimides **2b−i** were found to work well with 5*H*-oxazol-4-one **1a**, affording the corresponding products **3o−v** in 68−85% yield with 88−95% ee (entries 15−22). When the *N*-substituent was changed to be a benzyl group (**2j**), the ee value of adduct **3w** was decreased to 75% ee in 74% yield (entry 23). The absolute configurations of the [4 + 2] cycloaddition products **3** were assigned on the basis

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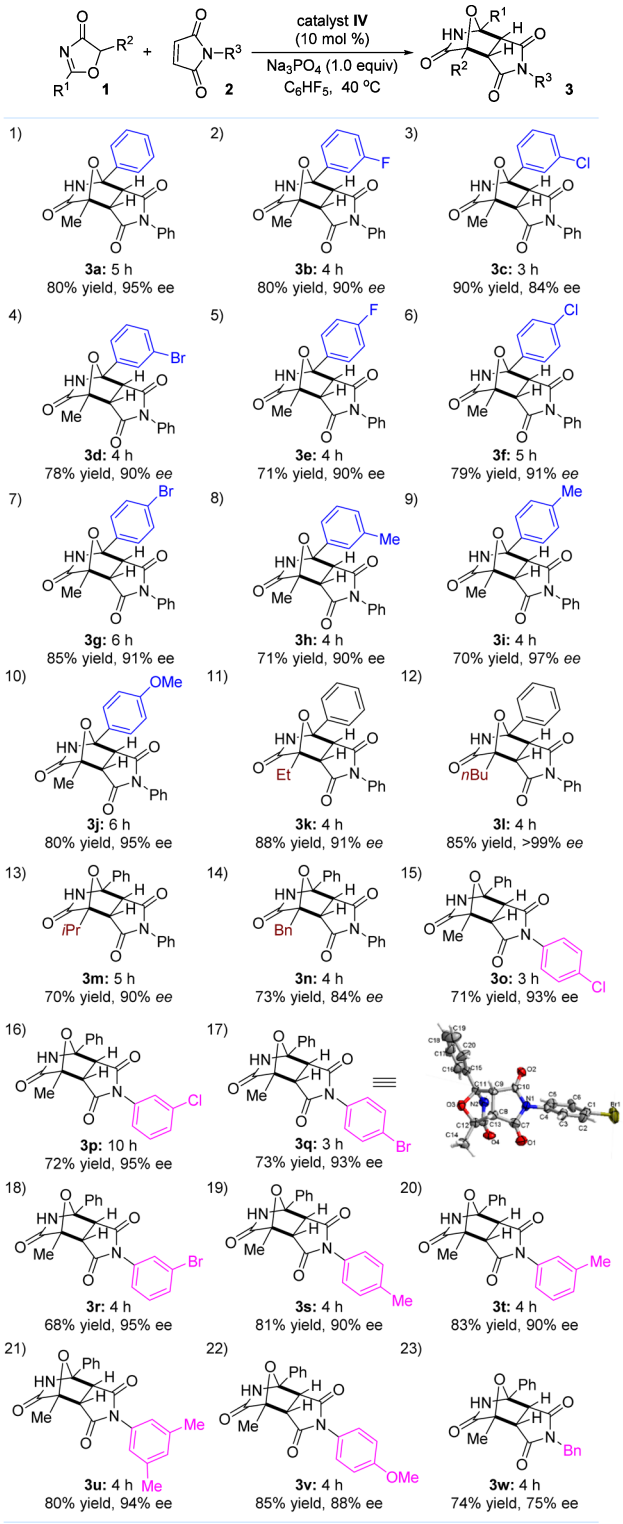
Table 2. [4 + 2] Annulation between 1 and 2[a]



[a]Reaction conditions: **1** (0.1 mmol), **2** (0.15 mmol), catalyst (0.01 mmol), Na_3PO_4 (0.1 mmol), 2.0 mL of C_6HF_5 at 40 °C. In general, when yield was less than 80%, conjugate adduct was observed but in unsatisfactory enantioselectivity.

of X-ray crystallographic analysis of a single crystal of **3q**; other products are tentatively assigned on this basis.[16]

A transition state model has been suggested for the asymmetric [4 + 2] annulation as depicted in Figure 3. The nucleophilic enolate first generated binds to the R_3NH^+ ammonium group of the catalyst via Coulombic attraction, and the thiourea core of the catalyst binds to the electrophile *N*-malemides via hydrogen bonding interactions. The proposed preferred binding mode for the nucleophile to the catalyst is depicted in **INT-A** and **INT-B** for which favorable C_α–H···N noncovalent interaction[17] is present. The bound maleimide however is more flexible and could adopt two conformations which give rise to two sets of diastereomeric products. As structurally resolved by X-ray,[18] the major Michael product **4** originates from **INT-A** and the major [4 + 2] product **3** from **INT-B**. Pathway bifurcation on the basis of thermodynamic and kinetic control has been studied with density functional theory,[9,19] and in this context using $CHCl_3$ as reaction solvent leads to products **3** and **4** (minor) while C_6HF_5 steers preferentially toward **3**. We also propose that the phosphate binds to the catalyst as shown in Figure 3 (far right), in which the role is to enhance the reactivity of electrophile and enforce a binding preference for the nucleophile in the correct conformation.

Synthetic utility of this protocol was demonstrated with [4 + 2] annulation adduct **3j** being subjected to reduction by borane in THF (Scheme 1). A biologically important product 4,7-epoxypyrrolo[3,4-*c*]pyridine[20] **5** is afforded in 68% yield and without compromising the ee value.

In summary, we have developed the first catalytic asymmetric reaction of 5*H*-oxazol-4-ones with *N*-substituted maleimides. In the presence of Takemoto's chiral tertiary amine–thiourea as the catalyst, the reactions could undergo [4 + 2] annulation with satisfactory chemoselectivity, leading to a series of biologically important chiral oxo-bridged piperidone-fused succinimides in good to excellent enantioselectivities (up to >99% ee) and >19:1 dr. This work also demonstrates the potential of 5*H*-oxazol-4-ones as a strategic synthon in the synthesis of chiral oxo-bridged piperidone derivatives.

EXPERIMENTAL SECTION

General Information. *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 a hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in 10 mL sample vials 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 a 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, 60 F_{254}. After elution, the plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining with $KMnO_4$, 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 a slurry of *silica gel* in petroleum ether and an equilibrated solution using the appropriate solvent system. The elution was assisted by applying a pressure of about 2 atm with an air pump.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) and carbon NMR (^{13}C NMR) spectra were recorded in $CDCl_3$ unless otherwise stated. ^{1}H (300 MHz) and ^{13}C (75 MHz) were performed on a 300 MHz spectrometer. Chemical shifts are reported in parts per

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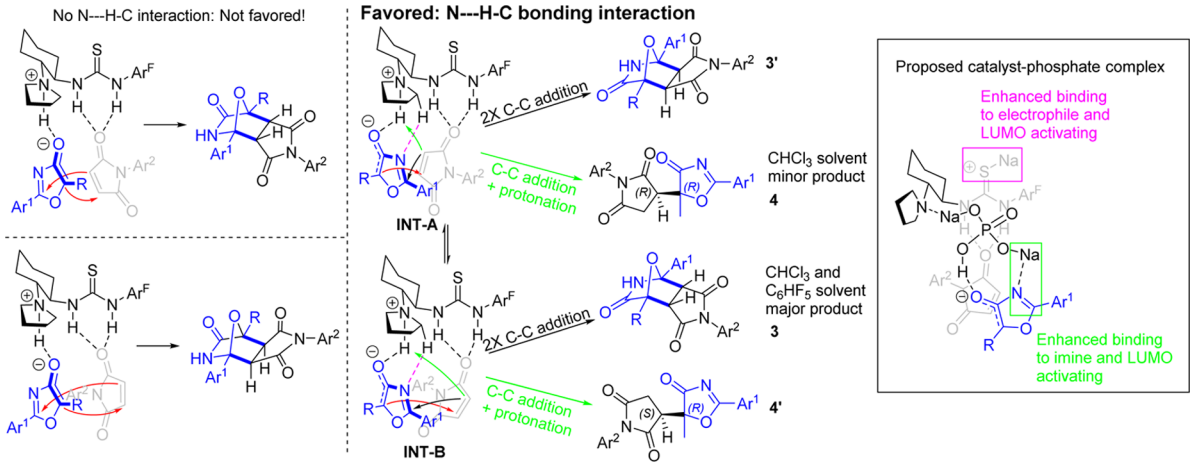
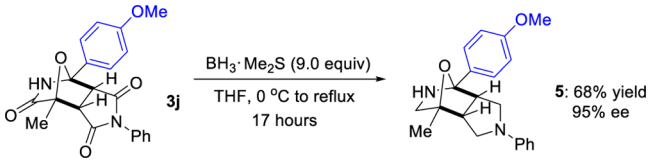


Figure 3. Proposed reaction mechanism.

Scheme 1. Transformation of Adduct



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 was reported in units of mass to charge ratio (m/z). HRMS data (Analyzer: TOF) were reported in units of mass to charge ratio (m/z). Mass samples were dissolved in DCM and MeOH (HPLC grade) unless otherwise stated. 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, 230, and 210 nm at the same time. 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 was freshly distilled from CaH_2 and stored under a N_2 atmosphere. Et_2O, toluene, and C_6HF_5 were freshly distilled from sodium/benzophenone before use. All compounds synthesized were stored in a −20 °C freezer, and light-sensitive compounds were protected with aluminum foil.

*(3aR,4R,7S,7aS)-7-Methyl-2,4-diphenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3a**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3a**. White solid, mp 140.1−141.5 °C; 27.9 mg (0.1 mmol), 80% yield; 95% *ee*; $[\alpha]_D^{26}$ −245.5 (c 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.50−7.36 (m, 6H), 7.21 (d, J = 7.4 Hz, 2H), 6.70 (s, 1H), 4.16 (d, J = 8.5 Hz, 1H), 3.64 (d, J = 8.5 Hz, 1H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 172.3, 171.1, 132.5, 131.2, 130.5, 129.2, 129.1, 128.9, 126.9, 126.5, 94.5, 87.0, 56.6, 51.3, 14.8; HRMS (ESI) m/z 349.1189 (M + H^+), calcd 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).

*(3aR,4R,7S,7aS)-4-(3-Fluorophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3b**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv) and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1b** (19.3 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1b**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo*, afforded product **3b**. White solid, mp 111.3−113.1 °C; 29.3 mg (0.1 mmol), 80% yield; 90% *ee*; $[\alpha]_D^{26}$ −247.5 (c 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 7.5 Hz, 1H), 7.50 (d, J = 9.3 Hz, 1H), 7.35 (m, 4H), 7.12 (d, J = 7.2 Hz, 3H), 6.80 (s, 1H), 4.02 (d, J = 8.5 Hz, 1H), 3.57 (d, J = 8.5 Hz, 1H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 170.9, 162.7 (d, $^1J_{C-F}$ = 246.5 Hz), 134.8, 134.7, 131.0, 130.8, 130.7, 129.3, 129.1, 126.4, 122.6 (two peaks), 117.7, 117.4, 114.4, 114.1, 93.7, 87.1, 56.8, 51.2, 14.7; HRMS (ESI) m/z 367.1097 (M + H^+), calcd for $C_{20}H_{16}N_2O_4F$ 367.1094. 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: 6.8 min (minor) and 10.5 min (major).

*(3aR,4R,7S,7aS)-4-(3-Chlorophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3c**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv) and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1c** (20.9 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1c**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo*, afforded product **3c**. White solid, mp 116.4−117.6 °C; 34.4 mg (0.1 mmol), 90% yield; 84% *ee*; $[\alpha]_D^{26}$ −338.0 (c 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.77 (d, J = 7.1 Hz, 1H), 7.44−7.39 (m, 5H), 7.20 (d, J = 7.1 Hz, 2H), 6.72 (s, 1H), 4.09 (d, J = 8.5 Hz, 1H), 3.63 (d, J = 8.5 Hz, 1H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 170.9, 134.9 134.3, 130.9, 130.6, 130.3, 129.3, 129.1, 127.1, 126.4, 125.1, 93.6, 87.1, 56.8, 51.2, 14.7; HRMS (ESI) m/z 383.0809 (M + H^+), calcd for $C_{20}H_{16}N_2O_4Cl$ 383.0799. The *ee* was determined by HPLC analysis.

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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: 26.0 min (minor) and 34.2 min (major).

*(3aR,4R,7S,7aS)-4-(3-Bromophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3d**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1d** (25.3 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1d**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3d**. White solid, mp 119.9−120.8 °C; 33.3 mg (0.1 mmol), 78% yield; 90% ee; $[\alpha]_D^{26}$ −220.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.42−7.31 (m, 4H), 7.18 (d, *J* = 7.2 Hz, 2H), 6.88 (s, 1H), 4.07 (d, *J* = 8.5 Hz, 1H), 3.62 (d, *J* = 8.5 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 170.9, 134.6, 133.6, 131.0, 130.5, 129.9, 129.2, 129.1, 126.5, 125.5, 122.9, 93.5, 87.1, 56.8, 51.3, 14.7; HRMS (ESI) *m*/*z* 427.0301 (M + H^+), calcd 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 1.5 mL/min; 25 °C; 254 nm; retention time: 4.5 min (minor) and 6.5 min (major).

*(3aR,4R,7S,7aS)-4-(4-Fluorophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3e**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1e** (19.3 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1e**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3e**. White solid, mp 124.8−125.6 °C; 26.0 mg (0.1 mmol), 71% yield; 90% *ee*; $[\alpha]_D^{26}$ −318.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.84 (m, 2H), 7.46−7.36 (m, 3H), 7.21−7.13 (m, 4H), 6.70 (s, 1H), 4.11 (d, *J* = 8.5 Hz, 1H), 3.63 (d, *J* = 8.5 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.3, 171.0, 163.8 (d, $^1J_{C-F}$ = 249.2 Hz), 131.0, 129.3 (two peaks), 129.2, 129.1, 128.5, 128.4, 126.5, 116.1, 115.9, 94.0, 87.1, 56.6, 51.3, 14.7; HRMS (ESI) *m*/*z* 389.0902 (M + Na^+), calcd 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: 8.2 min (major) and 10.0 min (minor).

*(3aR,4R,7S,7aS)-4-(4-Chlorophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3f**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1f** (20.9 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1f**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3f**. White solid, mp 111.0−111.9 °C; 30.2 mg (0.1 mmol), 79% yield; 91% *ee*; $[\alpha]_D^{26}$ −195.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.46−7.35 (m, 5H), 7.20 (d, *J* = 7.5 Hz, 2H), 6.67 (s, 1H), 4.09 (d, *J* = 8.5 Hz, 1H), 3.63 (d, *J* = 8.5 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.3, 171.0, 136.6, 130.9 (two peaks), 129.2, 129.1, 128.4, 126.4, 93.9, 87.1, 56.7, 51.3, 14.73; HRMS (ESI) *m*/*z* 383.0808 (M + H^+), calcd 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 = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.8 min (major) and 16.0 min (minor).

*(3aR,4R,7S,7aS)-4-(4-Bromophenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3g**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1g** (25.3 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1g**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3g**. White solid, mp 126.1−127.8 °C; 36.2 mg (0.1 mmol), 85% yield; 91% *ee*; $[\alpha]_D^{26}$ −360.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.43−7.35 (m, 3H), 7.18 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.06 (s, 1H), 4.05 (d, *J* = 8.5 Hz, 1H), 3.61 (d, *J* = 8.5 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.3, 170.9, 132.1, 131.5, 131.0, 129.3, 129.2, 128.6, 126.5, 125.0, 94.0, 87.1, 56.7, 51.3, 14.7; HRMS (ESI) *m*/*z* 427.0300 (M + H^+), calcd for $C_{20}H_{16}N_2O_4Br$ 427.0293. 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: 9.5 min (minor) and 15.6 min (major).

*(3aR,4R,7S,7aS)-7-Methyl-2-phenyl-4-(m-tolyl)tetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3h**).* *N*-Phenylmaleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1h** (18.9 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1h**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3h**. White solid, mp 107.5−109.3 °C; 25.7 mg (0.1 mmol), 71% yield; 91% *ee*; $[\alpha]_D^{26}$ −195.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.8 Hz, 2H), 7.45−7.30 (m, 5H), 7.22 (d, *J* = 7.5 Hz, 2H), 6.62 (s, 1H), 4.14 (d, *J* = 8.5 Hz, 1H), 3.62 (d, *J* = 8.5 Hz, 1H), 2.41 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 172.3, 171.2, 138.8, 132.3, 131.2, 131.1, 129.2, 129.1, 128.8, 127.4, 126.5, 123.9, 94.5, 87.0, 56.6, 51.3, 21.4, 14.7; HRMS (ESI) *m*/*z* 363.1350 (M + H^+), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 7.0 min (minor) and 9.7 min (major).

*(3aR,4R,7S,7aS)-7-Methyl-2-phenyl-4-(p-tolyl)tetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3i**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1i** (18.9 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1i**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3i**. White solid, mp 138.1−138.9 °C; 25.4 mg (0.1 mmol), 70% yield; 93% *ee*; $[\alpha]_D^{26}$ −160.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 2H), 7.47−7.39 (m, 3H), 7.29 (s, 2H), 7.21 (d, *J* = 7.2 Hz, 2H), 6.61 (s, 1H), 4.16 (d, *J* = 8.5 Hz, 1H), 3.63 (d, *J* = 8.5 Hz, 1H), 2.40 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 172.3, 171.2, 140.7, 131.1, 129.5, 129.4, 129.2, 129.1, 126.9, 126.5, 94.5, 87.0, 56.5, 51.3, 21.3, 14.8; HRMS (ESI) *m*/*z* 363.1353 (M + H^+), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 9.8 min (minor) and 12.1 min (major).

*(3aR,4R,7S,7aS)-4-(4-Methoxyphenyl)-7-methyl-2-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3j**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol,

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0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1j** (20.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1j**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3j**. White solid, mp 108.3−110.0 °C; 30.3 mg (0.1 mmol), 80% yield; 97% *ee*; $[\alpha]_D^{26}$ −240.9 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.48−7.37 (m, 3H), 7.21 (d, *J* = 7.3 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.55 (s, 1H), 4.18 (d, *J* = 8.5 Hz, 1H), 3.85 (s,3H), 3.63 (d, *J* = 8.8 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.4, 171.2, 161.2, 131.2, 129.2, 129.1, 128.7, 126.5, 124.4, 114.2, 94.5, 87.0, 56.4, 55.4, 51.4, 14.8; HRMS (ESI) *m*/*z* 379.1300 (M + H^+), calcd 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: 14.8 min (minor) and 21.3 min (major).

*(3aR,4R,7S,7aS)-7-Ethyl-2,4-diphenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3k**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1k** (18.9 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1k**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3k**. White solid, mp 186.2−187.8 °C; 31.9 mg (0.1 mmol), 88% yield; 91% *ee*; $[\alpha]_D^{26}$ −394.5 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.86−7.81 (m, 2H), 7.49−7.44 (m, 3H), 7.42−7.33 (m, 3H), 7.21−7.18 (m, 2H), 7.02 (s, 1H), 4.11 (d, *J* = 8.5 Hz, 1H), 3.68 (d, *J* = 8.5 Hz, 1H), 2.44 (dq, *J* = 14.9, 7.5 Hz, 1H), 2.21 (dq, *J* = 14.9, 7.4 Hz, 1H), 1.21 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 171.2, 132.5, 131.1, 130.5, 129.2, 129.0, 128.7, 126.9, 126.5, 94.2, 90.3, 56.6, 49.2, 21.8, 7.9; HRMS (ESI) *m*/*z* 363.1337 (M + H^+), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 31.5 min (minor) and 47.3 min (major).

*(3aR,4R,7S,7aS)-7-Butyl-2,4-diphenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3l**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1l** (21.7 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1l**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3l**. White solid, mp 169.8−171.3 °C; 33.2 mg (0.1 mmol), 85% yield; >99% *ee*; $[\alpha]_D^{26}$ −166.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.47−7.34 (m, 6H), 7.20 (d, *J* = 7.2 Hz, 2H), 6.97 (s, 1H), 4.11 (d, *J* = 8.5 Hz, 1H), 3.68 (d, *J* = 8.5 Hz, 1H), 2.46−2.36 (m, 1H), 2.21−2.11 (m, 1H), 1.68−1.58 (m, 2H), 1.52−1.43 (m, 2H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.3, 171.2, 132.5, 131.1, 130.5, 129.0, 126.9, 126.5, 94.3, 90.0, 56.5, 49.7, 28.4, 25.6, 22.8, 13.9; HRMS (ESI) *m*/*z* 391.1664 (M + H^+), calcd for $C_{23}H_{23}N_2O_4$ 391.1658. The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. × 250 mm); Hexane/2-propanol = 70/30; flow rate 1.5 mL/min; 25 °C; 254 nm; retention time: 6.0 min (minor) and 10.2 min (major).

*(3aR,4R,7S,7aS)-7-Isopropyl-2,4-diphenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3m**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1m** (20.3 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1m**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3m**. White solid, mp 111.2−112.1 °C; 26.3 mg (0.1 mmol), 70% yield; 90% ee; $[\alpha]_D^{26}$ −438.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.83−7.81 (m, 2H), 7.46−7.35 (m, 6H), 7.19 (d, *J* = 7.4 Hz, 2H), 6.94 (s, 1H), 4.09 (d, *J* = 8.5 Hz, 1H), 3.83 (d, *J* = 8.5 Hz, 1H), 2.90−2.61 (m, 1H), 1.29−1.26 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 171.2, 132.6, 131.2, 130.4, 129.2, 129.0, 128.8, 127.0, 126.5, 93.8, 92.7, 56.8, 47.4, 27.1, 17.5, 16.7; HRMS (ESI) *m*/*z* 377.1512 (M + H^+), calcd for $C_{22}H_{21}N_2O_4$ 377.1501. 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).

*(3aR,4R,7S,7aS)-7-Benzyl-2,4-diphenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3n**).* *N*-Phenyl maleimide **2a** (26.0 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1n** (25.1 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1n**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3n**. White solid, mp 111.0−112.2 °C; 31.0 mg (0.1 mmol), 73% yield; 84% *ee*; $[\alpha]_D^{26}$ −385.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (s, 2H), 7.46−7.30 (m, 11H), 7.19 (d, *J* = 7.0 Hz, 2H), 7.03 (s, 1H), 3.94 (d, *J* = 8.5 Hz, 1H), 3.58−3.54 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 172.2, 171.3, 134.0, 132.4, 130.1, 130.8, 130.5, 129.2, 129.1, 128.9, 128.6, 127.3, 127.0, 126.5, 94.3, 89.4, 56.3, 47.4, 33.7; HRMS (ESI) *m*/*z* 425.1504 (M + H^+), calcd for $C_{26}H_{21}N_2O_4$ 425.1501. 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: 31.5 min (minor) and 47.3 min (major).

*(3aR,4R,7S,7aS)-2-(4-Chlorophenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3o**).* *N*-Aryl maleimide **2b** (31.1 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a** the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3o**. White solid, mp 122.5−124.3 °C; 27.2 mg (0.1 mmol), 71% yield; 93% *ee*; $[\alpha]_D^{26}$ −380.0 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 2H), 7.49 (s, 3H), 7.33 (d, *J* = 8.4 Hz, 3H), 7.09 (d, *J* = 7.7 Hz, 2H), 4.10 (d, *J* = 8.5 Hz, 1H), 3.61 (d, *J* = 8.5 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 171.9, 170.8, 134.9, 132.3, 130.5, 129.5, 129.4, 129.0, 127.7, 126.8, 94.5, 87.0, 56.7, 51.4, 14.7; HRMS (ESI) *m*/*z* 383.0793 (M + H^+), calcd for $C_{20}H_{16}N_2O_4Cl$ 383.0799. 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: 8.2 min (minor) and 14.8 min (major).

*(3aR,4R,7S,7aS)-2-(3-Chlorophenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3p**).* *N*-Aryl maleimide **2c** (31.1 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of 5*H*-oxazol-4-one **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3p**. White solid, mp 100.1−102.1 °C; 27.5 mg (0.1 mmol), 72% yield; 95% *ee*; $[\alpha]_D^{26}$ −285.4 (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ

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7.83−7.80 (m, 2H), 7.48 (s, 3H), 7.34 (d, J = 4.2 Hz, 2H), 7.24 (s, 1H), 7.11−7.08 (m, 1H), 6.89 (s, 1H), 4.14 (d, J = 8.5 Hz, 1H), 3.63 (d, J = 8.5 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 171.9, 170.7, 134.8, 132.3, 132.1, 130.6, 130.2, 129.3, 129.0, 126.9, 126.7, 124.8, 94.5, 87.1, 56.7, 51.3, 14.7; HRMS (ESI) m/z 383.0809 (M + H$^+$), calcd for $C_{20}H_{16}N_2O_4Cl$ 383.0799. 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: 7.8 min (minor) and 10.4 min (major).

*(3aR,4R,7S,7aS)-2-(4-Bromophenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3q**).* *N*-Aryl maleimide **2d** (37.7 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3q**. White solid, mp 128.6−130.3 °C; 31.1 mg (0.1 mmol), 73% yield; 93% *ee*; $[\alpha]_D^{26}$ −345.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (s, 2H), 7.47 (s, 5H), 7.38 (s, 1H), 7.02 (d, J = 8.3 Hz, 2H), 4.09 (d, J = 8.5 Hz, 1H), 3.61 (d, J = 8.5 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 171.8, 170.8, 132.5, 132.3, 130.5, 129.9, 129.0, 128.0, 126.8, 123.0, 94.5, 87.0, 56.7, 51.4, 14.7; HRMS (ESI) m/z 427.0302 (M + H$^+$), calcd 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: 10.1 min (minor) and 10.8 min (major).

*(3aR,4R,7S,7aS)-2-(3-Bromophenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3r**).* *N*-Aryl maleimide **2e** (37.7 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3r**. White solid, mp 122.4−123.9 °C; 29.0 mg (0.1 mmol), 68% yield; 95% ee; $[\alpha]_D^{26}$ −235.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 3.1 Hz, 2H), 7.48 (s, 4H), 7.40 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 4.13 (d, J = 8.5 Hz, 1H), 3.62 (d, J = 8.5 Hz, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 171.8, 170.7, 132.2, 130.6, 130.5, 129.5, 129.0, 126.9, 125.2, 122.5, 94.5, 87.0, 56.7, 51.3, 14.7; HRMS (ESI) m/z 427.0305 (M + H$^+$), calcd for $C_{20}H_{16}N_2O_4Br$ 427.0293. The *ee* was determined by HPLC analysis. CHIRALPAK IF (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.5 mL/min; 25 °C; 254 nm; retention time: 4.5 min (minor) and 6.5 min (major).

*(3aR,4R,7S,7aS)-7-Methyl-4-phenyl-2-(p-tolyl)tetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3s**).* *N*-Aryl maleimide **2f** (28.1 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3s**. White solid, mp 114.2−115.3 °C; 29.3 mg (0.1 mmol), 81% yield; 90% *ee*; $[\alpha]_D^{26}$ −235.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85−7.83 (m, 2H), 7.48 (s, 3H), 7.23 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 6.75 (s, 1H), 4.13 (d, J = 8.5 Hz, 1H), 3.62 (d, J = 8.5 Hz, 1H), 2.35 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 172.4, 171.3, 139.1, 132.5, 130.4, 129.8, 128.9, 128.4, 126.7, 126.2, 94.4, 87.0, 56.6, 51.3, 21.2, 14.7; HRMS (ESI) m/z 363.1337 (M + H$^+$), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 9.9 min (minor) and 16.9 min (major).

*(3aR,4R,7S,7aS)-7-Methyl-4-phenyl-2-(m-tolyl)tetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3t**).* *N*-Aryl maleimide **2g** (28.1 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3t**. White solid, mp 142.5−143.7 °C; 30.0 mg (0.1 mmol), 83% yield; 90% *ee*; $[\alpha]_D^{26}$ −188.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.49 (s, 3H), 7.33 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.5 Hz, 1H), 7.01 (s, 2H), 6.62 (s, 1H), 4.15 (d, J = 8.5 Hz, 1H), 3.63 (d, J = 8.5 Hz, 1H), 2.36 (s, 3H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.4, 171.2 139.4, 132.4 131.0, 130.5, 130.0, 129.1, 128.9, 127.0, 126.9, 123.5, 94.4, 87.0, 56.6, 51.3, 21.2, 14.8; HRMS (ESI) m/z 363.1346 (M + H$^+$), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 12.0 min (minor) and 9.4 min (major).

*(3aR,4R,7S,7aS)-2-(3,5-Dimethylphenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3u**).* *N*-Aryl maleimide **2h** (30.2 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3u**. White solid, mp 108.9−110.4 °C; 30.1 mg (0.1 mmol), 80% yield; 94% *ee*; $[\alpha]_D^{26}$ −187.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (s, 2H), 7.49 (s, 3H), 7.03 (s, 1H), 6.80 (s, 2H), 6.57 (s, 1H), 4.15 (d, J = 8.5 Hz, 1H), 3.63 (d, J = 8.5 Hz, 1H), 2.32 (s, 6H), 1.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 172.4, 171.2, 139.2, 132.5, 131.0, 130.9, 130.5, 128.9, 126.9, 124.1, 94.4, 87.0, 56.7, 51.3, 21.2, 14.8; HRMS (ESI) m/z 377.1506 (M + H$^+$), calcd for $C_{22}H_{21}N_2O_4$ 377.1501. 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: 8.8 min (major) and 11.8 min (minor).

*(3aR,4R,7S,7aS)-2-(4-Methoxyphenyl)-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3v**).* *N*-Aryl maleimide **2i** (30.5 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3v**. White solid, mp 127.1−128.9 °C; 32.1 mg (0.1 mmol), 85% yield; 88% *ee*; $[\alpha]_D^{26}$ −295.0 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (s, 2H), 7.47 (s, 3H), 7.14 (s, 1H), 7.07 (d, J = 8.2 Hz, 2H), 6.88 (d, J = 8.3 Hz, 2H), 4.08 (d, J = 8.5 Hz, 1H), 3.77 (s, 3H), 3.59 (d, J = 8.4 Hz, 1H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 172.5, 171.4, 159.7, 132.5, 130.4, 128.9, 127.7, 126.9, 123.6, 114.5, 94.4, 87.0, 56.5, 55.4, 51.3, 14.7; HRMS (ESI) m/z 379.1293 (M + H$^+$), calcd for $C_{21}H_{19}N_2O_5$ 379.1294. 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: 14.6 min (minor) and 21.8 min (major).

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*(3aR,4R,7S,7aS)-2-Benzyl-7-methyl-4-phenyltetrahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine-1,3,6(2H,3aH)-trione (**3w**).* *N*-Benzyl maleimide **2j** (28.1 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−300/1 ratio). Removing the solvent *in vacuo* afforded product **3w**. White solid, mp 112.4−113.9 °C; 26.8 mg (0.1 mmol), 74% yield; 64% *ee*; $[\alpha]_D^{26}$ −440.6 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (s, 2H), 7.47 (s, 3H), 7.33−7.28 (m, 5H), 6.39 (s, 1H), 4.70−4.63 (m, 1H), 4.55−4.48 (m, 1H), 3.99 (d, *J* = 8.5 Hz, 1H), 3.51 (d, *J* = 8.5 Hz, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 171.0, 170.7, 134.0, 131.5, 129.5, 127.9, 127.8, 127.7, 127.2, 126.1, 93.1, 85.5, 55.0, 50.7, 41.9, 13.8; HRMS (ESI) *m*/*z* 363.1342 (M + H^+), calcd for $C_{21}H_{19}N_2O_4$ 363.1345. 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: 17.351 min (major) and 26.344 min (minor).

*(3aS,4R,7S,7aR)-4-(4-Methoxyphenyl)-7-methyl-2-phenyl-octahydro-1H-4,7-epoxypyrrolo[3,4-c]pyridine (**5**).* Adduct **3j** (0.1 mmol) was dissolved in dry THF (1.4 mL), and the solvent was cooled at 0 °C by an ice bath. $BH_3{\cdot}Me_2S$ (0.9 mmol, 0.45 mL, 2 M in THF) was then added dropwise over 10 min, and after removal of the cooling bath, the mixture refluxed for 17 h. The reaction mixture was then cooled at 0 °C, and the excess BH_3 was eliminated by dropwise addition of MeOH (0.5 mL). The solvent was then evaporated at reduced pressure. The mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (100:1−20:1 ratio). Removing the solvent *in vacuo* afforded product **5**. White solid, mp 166.3−167.5 °C; 22.9 mg (0.1 mmol), 68% yield; 95% *ee*; $[\alpha]_D^{26}$ −670.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.2 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 2H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.42 (d, *J* = 8.0 Hz, 2H), 4.13 (s, 1H), 3.83 (s, 2H), 3.67 (s, 1H), 3.54 (d, *J* = 9.9 Hz, 1H), 3.38−3.33 (m, 1H), 3.16 (t, *J* = 9.8 Hz, 1H), 3.01 (d, *J* = 11.0 Hz, 1H), 2.77 (d, *J* = 11.0 Hz, 1H), 2.63−2.57 (m, 1H), 2.37 (d, *J* = 5.8 Hz, 1H), 1.24 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 147.0, 134.6, 129.0, 127.0, 115.2, 113.8, 111.0, 70.3, 60.0, 59.9, 55.3, 49.1, 48.4, 46.7, 44.2, 23.7; HRMS (ESI) *m*/*z* 337.1912 (M + H^+), calcd for $C_{21}H_{25}N_2O_2$ 337.1911. 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: 5.6 min (minor) and 10.7 min (major).

*(R)-1-(4-Bromophenyl)-3-((R)-5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)pyrrolidine-2,5-dione (**3q-M**).* *N*-Aryl maleimide **2d** (37.7 mg, 0.15 mmol, 1.5 equiv), Na_3PO_4 (16.4 mg, 0.1 mmol, 1.0 equiv), and catalyst **IV** (4.4 mg, 0.01 mmol, 0.1 equiv) were dissolved in pentafluorobenzene (2.0 mL) and stirred at 40 °C for 10 min. Then 5*H*-oxazol-4-one **1a** (17.5 mg, 0.1 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 40 °C and monitored by TLC. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short *silica gel* column, followed by gradient elution with a DCM/MeOH mixture (500/1−200/1 ratio). Removing the solvent *in vacuo* afforded product **3q-M** (M = Michael) as a side product. White solid, mp 119.9−121.3 °C; 9.0 mg (0.1 mmol), 21% yield; 39% *ee* (after a single recrystallization, *ee* = 73%); $[\alpha]_D^{26}$ 187.5 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.62−7.53 (m, 4H), 7.17 (d, *J* = 8.1 Hz, 2H), 3.56 (dd, *J* = 9.3, 5.0 Hz, 1H), 3.01 (dd, *J* = 18.4, 9.3 Hz, 1H), 2.58 (dd, *J* = 18.4, 5.0 Hz, 1H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 186.4, 173.1, 172.9, 136.0, 132.5, 130.4, 130.3, 129.2, 127.8, 124.9, 122.8, 85.8, 44.0, 30.4, 20.9; HRMS (ESI) *m*/*z* 449.0112 (M + Na^+), calcd for $C_{20}H_{15}BrN_2NaO_4$ 449.0113. 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: 24.2 min (minor) and 41.9 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.6b01451.

General information, copies of HPLC spectra, X-ray crystallographic data, and copies of NMR spectra (PDF)
Crystallographic data (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: chmjzy@henu.edu.cn.
*E-mail: rosamary0530@sina.com.

Author Contributions

§S.Q. and R.L. contributed equally.

Notes

The authors declare no competing financial interest.

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