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Rhodium-catalyzed asymmetric addition of arylboronic acids to cyclic N-sulfonyl ketimines towards the synthesis of α,α-diaryl-α-amino acid derivatives

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Rhodium/chiral diene complex-catalyzed asymmetric addition of arylboronic acids to cyclic ketimines having an ester group proceeded to give the corresponding α-amino acid derivatives in high yields with high enantioselectivity. The cyclic amino acid derivative was transformed into a linear α,α-diaryl-substituted α-N-methylamino acid ester.

Introduction

Transition metal-catalyzed addition reaction of organometallic reagents to imines is one of the most powerful methods for the selective formation of a carbon-carbon bond, which provides an easy access to chirally-activated amines. Although many successful reports on the asymmetric alkylation or arylation to aldimines have been reported, the addition to ketimines giving chiral α-tert-aminos is still a challenging objective in organic chemistry. Pioneering studies of the transition metal-catalyzed asymmetric addition of organometallic reagents to ketimines have been attained by Kanai and Shibasaki (allylboronates, Cu), Charette (dialkylzinc, Cu), and Snapper and Hoveyda (dialkylzinc, Zr). The rhodium-catalyzed asymmetric addition of arylboron reagents to N-sulfonyl ketimines reported by Hayashi and co-workers is an another approach leading to chiral α-tert-amines. On the other hand, cyclic N-sulfonyl and N-acyl ketimines are good substrates for the asymmetric addition to give chiral α-tert-aminos with high enantioselectivity, because the geometry (E or Z) of the imine is fixed, and thus the enantioface of the C= N bond is selectively differentiated without an influence of the isomerization. For example, the rhodium-catalyzed asymmetric arylation of diaryl-substituted cyclic ketimines has been reported by us in 2012 and Xu in 2013. Asymmetric alkenylation and alkylation were also reported by Lam and co-workers. Recently, Pd-catalyzed asymmetric addition of arylboronic acids to the same types of cyclic N-sulfonyl ketimines was reported.

α,α-Disubstituted α-amino acids have been focused on as non-proteinogenic amino acids in medicinal chemistry, and the stereoselective synthesis giving α,α-dialkyl and α,α-alkylaryl substituted α-amino acid derivatives has been developed. We were interested in the development of general synthetic methods for chiral α,α-diaryl-substituted amino acid derivatives in an enantioselective manner. Although it was reported that rhodium can catalyze the asymmetric addition of arylboronic acids to five-membered cyclic N-sulfonyl ketimines substituted with an ester group to give α,α-diaryl-substituted amino acid derivatives, the transformation of the cyclic structure to the linear α-amino acid derivatives has not been achieved probably due to the difficulty of cleavage of the cyclic structure. Our approach leading to chiral α,α-diaryl-α-amino acid derivatives is the asymmetric arylation of cyclic ketimines giving benzosulfilamidates and the subsequent breaking of the cyclic structure (Scheme 1). Here we report that the rhodium/chiral diene complex can catalyze the asymmetric addition of arylboronic acids to cyclic aromatic ketimines having an ester group to give the corresponding α-amino acid derivatives in high yields with high enantioselectivity.

The cyclic amino acid derivative was successfully transformed into a liner α,α-dialkyl-α-N-methylamino acid ester by reductive cleavage of a carbon-oxygen bond constituting the cyclic structure.

Results and discussion
Our initial studies were focused on the addition of phenylboronic acid to cyclic ketimine 1a in the presence of rhodium complexes for the catalytic synthesis of sulfamidates 3aa substituted with an ester group (Table 1). Treatment of 1a with phenylboronic acid (2a, 3 equiv.) in the presence of [Rh(OH)(COD)]2 (5 mol% of Rh) in 1,4-dioxane (0.4 mL) at 60 °C for 12 h gave 3aa in 99% yield (entry 1). The use of [RhCl(cod)]2 as a catalyst in the presence of K2PO4 was found to decrease the yield of 3aa (67% yield, entry 2). We have recently developed chiral diene ligands based on a tetrafluorobenzenoborazarene (tfb) framework, which display high coordination ability to Rh(I) giving stable hydrosoloxorhodium complexes. A ferrocenyl-substituted tfb-ligand (Fc-tfb**) displayed high enantioselectivity (93% ee), but the yield of 3aa was low (34% yield, entry 3). Higher catalytic activity was observed with phenyl-substituted tfb (Ph-tfb**) and benzyl-substituted tfb (Bn-tfb**) giving 3aa in 73% and 99% yield, respectively (entries 4 and 5), with high enantioselectivity (96% ee). The use of ligand L1, which is effective in catalyzing the asymmetric addition of arylboronic acids to aldimeines, gave 3aa in 20% yield with 96% ee (entry 6). A hydrosoloxorhodium complex coordinated with binap [Rh(OH)(S,S-binap)]15 sufficiently catalyzed the present reaction to give a 92% yield of 3aa, but the enantioselectivity was modest (61% ee; entry 7). The reaction in the presence of [Rh(OH)((S,S)-Bn-tfb**)2] using 2 equiv. of phenylboronic acid (2a) proceeded as well to give 3aa in 99% yield with 96% ee within 3 h (entry 8).

The addition of p-tolylboronic acid (2b) to ketimine 1 having ethyl (1a), benzyl (1b), and tert-butyl ester (1c) proceeded to give the corresponding sulfamidates 3ab-3cb in high yields with high enantioselectivity (92–94% ee, eqn. (1)). In the reaction of tert-butyl ester 1c, the use of K2PO4 improved the yield of 3cb to avoid the formation of a small amount of an arylated carboxylic acid observed in the absence of the base. We selected the tert-butyl esters as suitable substrates, which are tolerant to a basic condition and are readily transformed into carboxylic acids.

The results obtained for the reaction of ketimine 1 having a tert-butyl ester group with a variety of arylboronic acids 2 are summarized in Table 2. Aryl groups having electron-donating and -withdrawing substituents (2a–2j) were successfully introduced into ketimine 1c with 86–96% ee (entries 1–10). The addition of p-tolylboronic acid (2b) to ketimines 1d–1h possessing methyl, methoxy, and methylenedioxy proceeded to give the corresponding sulfamidates 3db-3hh with high enantioselectivity (93–97% ee, entries 11–15). A slight decrease of the enantioselectivity was observed in the addition to ketimines 1i and 1j substituted with electron- withdrawing groups (F, Cl) at the 6-position (entries 16 and 17). The reductive cleavage of the O–S bond of benzozulamidates by LiAlH4 has been reported, where 2-(aminomethyl)phenols are formed.6,9b On the other hand,
nickel-catalyzed cross-coupling of benzosulfamidates with phenylboronic product was reported to give *ortho*-phenylated product involving the cleavage of the C–O bond. A nickel catalysis using alkylmagnesium reagents was also reported by Du Bois and co-workers, but the catalytic systems are not applicable to the benzosulfamidates having tetra-substituted α-carbon of the amino group. After screening and modifying the reported catalytic conditions, a nickel catalyst to cleave a C–O bond of the benzosulfamidate formed in the present arylation, it was found that the reductive cleavage of the C–O bond proceeds using diethylzinc as a reducing reagent to give a linear α,α-diaryl-α-amino acid derivative (eqn. (2)). Thus, introduction of a methyl group on the nitrogen atom of 3e followed by reductive cleavage of the C–O bond by use of diethylzinc in the presence of NiCl₂(dippe) in N,N-dimethylacetamide (DMA) at 100 °C for 24 h gave α,α-diaryl-N,N-methylamino acid ester 4 in 70% yield in two steps without loss of the enantiomeric purity.

**Conclusions**

In summary, we have developed the asymmetric synthesis of α,α-diaryl-α-amino acid derivatives in the enantioselective addition of aryloboronic acids to cyclic aromatic ketimines having an ester group catalyzed by a hydroxorhodium/chiral diene complex. The cyclic amino acid derivative was successfully transformed into a linear α,α-diaryl-α,N-methylamino acid ester by reductive cleavage of a carbon-oxygen bond constituting the cyclic structure.

**Experimental**

**General remarks**

All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen. NMR spectra were recorded on JEOL JNM ECA-600 spectrometer (600 MHz for 1H, 150 MHz for 13C). Chemical shifts are reported in δ (ppm) referenced to the residual peak of CDCl₃ (δ 7.26) for 1H NMR, and CDCl₃ (δ 77.00) for 13C NMR. The following abbreviations are used; s: singlet, d: doublet, t: triplet, m: multiplet. Optical rotations were measured on a JASCO P-2200 polarimeter. High-resolution mass spectra were obtained with a Bruker microOTOF spectrometer. Flash column chromatography was performed with Silica Gel 60 N (spherical, neutral) (Cica-Reactant). Preparative thin-layer chromatography was performed with Silica Gel 60 PF₂₅₄ (Merck). Alumina (activated 200) for column chromatography was purchased from Nacalai Tesque.

1,4-Dioxane was purified by passing through a neutral alumina column under N₂. Rhodium complexes, [RhCl(cod)]₂, [RhOH(cod)]₂, [RhOH][(S)-(S)-binap)]₂, [RhOH][(S,S)-Bn-tfb]⁺, [RhOH][(R,R)-Ph-tfb]⁺, [Rh(OH)((S,S)-Fc-tfb)*]₂, were prepared according to the reported procedures.

A diene ligand L₁ (CAS: 1365284-85-0) were prepared according to the reported procedures. Ketimines were prepared as shown in the ESI. All other chemicals were purchased from commercial suppliers and used as received.

**General procedure for Table 1**

A rhodium catalyst (0.0030 mmol of Rh), 1a (25.5 mg, 0.10 mmol), and PhB(OH)₂ (36.6 mg, 0.30 mmol) were placed in a Schlenk tube under nitrogen. 1,4-Dioxane (0.4 mL) was added and the mixture was stirred at 60 °C for 12 h. The mixture was passed through a short column of silica gel with ethyl acetate as eluent. The solvent was removed on a rotary evaporator and the residue was subjected to preparative TLC on silica gel with hexane/ethyl acetate (3:1) to give 3aa. The ee of 3aa was determined by chiral HPLC (Daicel Chiralpak AD-H).

**General procedure for eqn. 1**

[Rh(OH)((S,S)-Bn-tfb)*]₂ (1.6 mg, 0.0030 mmol of Rh), 1a or b or c (0.10 mmol), and p-tolylboronic acid (24.4 mg, 0.20 mmol) were placed in a Schlenk tube under nitrogen. 1,4-Dioxane (0.4 mL) was added and the mixture was stirred at 60 °C for 3 h. The mixture was passed through a short column of silica gel with ethyl acetate as eluent. The solvent was removed on a rotary evaporator and the residue was subjected to preparative TLC on silica gel with hexane/ethyl acetate (3:1) to give 3. The ee of 3 was determined by chiral HPLC.

**General procedure for Table 2**

[Rh(OH)((S,S)-Bn-tfb)*]₂ (3.2 mg, 0.0060 mmol of Rh), 3e (56.6 mg, 0.20 mmol), and aryloboronic acids (2.04 mmol) were placed in a Schlenk tube under nitrogen. 1,4-Dioxane (0.8 mL) was added and the mixture was stirred at 60 °C for 3 h. The mixture was passed through a short column of silica gel with ethyl acetate as eluent. The solvent was removed on a rotary evaporator and the residue was subjected to preparative TLC on silica gel with hexane/ethyl acetate (3:1) to give 3. The ee of 3b was determined by chiral HPLC.

**General procedure for Table 3**

[Rh(OH)((S,S)-Bn-tfb)*]₂ (3.2 mg, 0.0060 mmol of Rh), 1b (0.20 mmol), and p-tolylboronic acid (2b, 48.8 mg, 0.40 mmol) were placed in a Schlenk tube under nitrogen. 1,4-Dioxane (0.8 mL) was added and the mixture was stirred at 60 °C for 3 h. The mixture was passed through a short column of silica gel with ethyl acetate as eluent. The solvent was removed on a rotary evaporator and the residue was subjected to preparative TLC on silica gel with hexane/ethyl acetate (3:1) to give 3.

**Ethyl 4-phenyl-3,4-dihydropyrazine[1,2,3]oxathiazine-4,5-dioxide (3aa)**

The ee was measured by HPLC (Chiralpak AD-H, hexane/2-propanol = 80:20, flow 0.5 mL/min, 254 nm, t₁ = 14.9 min (R), t₂ = 18.9 min (S)); [α]D – 45 (c 0.82, CHCl₃) for 96% ee (S). 1H NMR (CDCl₃) δ 1.28 (t, J = 7.1 Hz, 3H), 3.42–3.44 (m, 4H, 2H), 4.65 (s, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.21–7.26 (m, 3H), 7.34–7.38 (m, 3H), 7.43 (td, J = 8.1, 1.4 Hz, 1H), 7.51 (dd, J = 8.1, 1.4 Hz, 1H); 13C NMR (CDCl₃) δ 13.8, 64.1, 76.8, 118.9, 119.7, 124.9, 127.5, 128.5, 129.8, 130.5, 130.8, 139.3, 151.1, 170.0. HRMS (EI) calcd for C₁₈H₁₂N₂O₃Na₂SO₄·Na⁺ 356.0563, found 356.0564.

**Ethyl 4-(p-tolylo)-3,4-dihydropyrazine[1,2,3]oxathiazine-4,5-carboxylate (3ab)**

The ee was measured by HPLC (Chiralpak AD-H, hexane/2-propanol = 80:20, flow 0.5 mL/min, 254 nm, t₁ = 16.5 min (R), t₂ = 21.7 min (S)); [α]D – 20.
Benzyl 4-(p-tolyl)-3,4-dihydropyridazin-2-one[1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (3bb).

The ee was measured by HPLC (Chiralpak AD-H, hexane-2-propanol = 80:20, flow 0.5 mL/min, 254 nm, \( t_1 = 11.9 \) min (S)), \( t_2 = 28.6 \) min (R)); \( \alpha^{20}_D = 9 \) (c 0.94, CHCl₃) for 85% ee (S). 

1H NMR (CDCl₃) \( \delta = 1.48 \) (s, 9H), 6.50 (s, 1H), 7.02 (t, \( J = 8.5 \) Hz, 2H), 7.14 (dd, \( J = 8.1, 1.4 \) Hz, 1H), 7.17 (d, \( J = 7.8 \) Hz, 1H), 7.17 (d, \( J = 8.6 \) Hz, 2H), 7.25 (td, \( J = 7.8, 1.4 \) Hz, 1H), 7.31 (d, \( J = 8.6 \) Hz, 2H), 7.45 (dd, \( J = 7.8, 1.4 \) Hz, 1H), 7.54 (dd, \( J = 7.8, 1.4 \) Hz, 1H); 13C NMR (CDCl₃) \( \delta = 27.6, 70.6, 86.2, 105.0, 115.3 \) (d, \( J_{CF} = 21 \) Hz), 118.7, 119.9, 124.8, 129.5 (d, \( J_{CF} = 9 \) Hz), 129.9, 130.9, 135.7, 152.1, 162.5 (d, \( J_{CF} = 247 \) Hz), 168.5. HRMS (ESI) cale for \( \text{C}_{19}H_{19}\text{NNaO}_{2}S \) (M+Na)\(^+\) 474.1193, found 474.1187.

**tert-Butyl**

4-(3,4,5-trimethoxyphenyl)-3,4-dihydropyridazin-2-one[1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (3ce).

The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propanol = 80:20, flow 0.5 mL/min, 254 nm, \( t_1 = 11.9 \) min (S)), \( t_2 = 28.6 \) min (R)); \( \alpha^{20}_D = 9 \) (c 0.94, CHCl₃) for 94% ee (S). 

1H NMR (CDCl₃) \( \delta = 1.48 \) (s, 9H), 6.50 (s, 1H), 7.02 (t, \( J = 8.5 \) Hz, 2H), 7.14 (dd, \( J = 8.1, 1.4 \) Hz, 1H), 7.17 (d, \( J = 7.8 \) Hz, 1H), 7.17 (d, \( J = 8.6 \) Hz, 2H), 7.25 (td, \( J = 7.8, 1.4 \) Hz, 1H), 7.31 (d, \( J = 8.6 \) Hz, 2H), 7.45 (dd, \( J = 7.8, 1.4 \) Hz, 1H), 7.54 (dd, \( J = 7.8, 1.4 \) Hz, 1H); 13C NMR (CDCl₃) \( \delta = 27.6, 70.6, 86.2, 105.0, 115.3 \) (d, \( J_{CF} = 21 \) Hz), 118.7, 119.9, 124.8, 129.5 (d, \( J_{CF} = 9 \) Hz), 129.9, 130.9, 135.7, 152.1, 162.5 (d, \( J_{CF} = 247 \) Hz), 168.5. HRMS (ESI) cale for \( \text{C}_{19}H_{19}\text{NNaO}_{2}S \) (M+Na)\(^+\) 402.0782, found 402.0776.

**tert-Butyl**

4-(4-chlorophenyl)-3,4-dihydropyridazin-2-one[1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (3eg).

The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propanol = 80:20, flow 0.5 mL/min, 254 nm, \( t_1 = 11.9 \) min (S)), \( t_2 = 28.6 \) min (R)); \( \alpha^{20}_D = 9 \) (c 0.94, CHCl₃) for 95% ee (S). 

1H NMR (CDCl₃) \( \delta = 1.48 \) (s, 9H), 6.53 (s, 1H), 7.13 (d, \( J = 7.8 \) Hz, 1H), 7.17 (d, \( J = 8.6 \) Hz, 2H), 7.25 (td, \( J = 7.8, 1.4 \) Hz, 1H), 7.31 (d, \( J = 8.6 \) Hz, 2H), 7.45 (dd, \( J = 7.8, 1.4 \) Hz, 1H), 7.54 (dd, \( J = 7.8, 1.4 \) Hz, 1H); 13C NMR (CDCl₃) \( \delta = 27.6, 70.6, 86.3, 118.3, 119.9, 124.8, 128.5, 128.9, 129.9, 131.0, 133.4, 134.8, 151.2, 168.3. HRMS (ESI) cale for \( \text{C}_{19}H_{19}\text{CINaO}_{2}S \) (M+Na)\(^+\) 418.0486, found 418.0481.

**tert-Butyl**

4-(4-bromophenyl)-3,4-dihydropyridazin-2-one[1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (3eh).

The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propanol = 80:20, flow 0.5 mL/min, 254 nm, \( t_1 = 11.9 \) min (S)), \( t_2 = 28.6 \) min (R)); \( \alpha^{20}_D = 9 \) (c 0.94, CHCl₃) for 95% ee (S). 

1H NMR (CDCl₃) \( \delta = 1.48 \) (s, 9H), 6.53 (s, 1H), 7.13 (d, \( J = 7.8 \) Hz, 1H), 7.17 (d, \( J = 8.6 \) Hz, 2H), 7.25 (td, \( J = 7.8, 1.4 \) Hz, 1H), 7.31 (d, \( J = 8.6 \) Hz, 2H), 7.45 (dd, \( J = 7.8, 1.4 \) Hz, 1H), 7.54 (dd, \( J = 7.8, 1.4 \) Hz, 1H); 13C NMR (CDCl₃) \( \delta = 27.6, 70.7, 86.4, 118.3, 119.9, 122.9, 124.8, 129.2, 131.0, 131.5, 138.9, 151.2, 168.2. HRMS (ESI) cale for \( \text{C}_{19}H_{19}\text{BrNaO}_{2}S \) (M+Na)\(^+\) 461.9981, found 461.9980.

**tert-Butyl**

4-(4-trifluoromethylphenyl)-3,4-dihydropyridazin-2-one[1,2,3]oxathiazine-4-carboxylate 2,2-dioxide (3ei).

The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propanol = 80:20, flow 0.5 mL/min, 254 nm, \( t_1 = 9.8 \) min (S)), \( t_2 = 11.4 \) min (R)); \( \alpha^{20}_D = 60 \) (c 0.65, CHCl₃) for 94% ee (S). 

1H NMR (CDCl₃) \( \delta = 1.48 \) (s, 9H), 6.58 (s, 1H), 7.16 (dd, \( J = 8.2, 1.4 \) Hz, 1H), 7.28 (td, \( J = 8.2, 1.4 \) Hz, 1H), 7.36 (d, \( J = 8.1 \) Hz, 2H), 7.48 (td, \( J = 8.1, 1.4 \) Hz, 1H), 7.56 (dd, \( J = 8.1, 1.4 \) Hz, 1H); 13C NMR (CDCl₃) \( \delta = 27.6, 70.7, 86.7, 117.9, 120.1, 123.8 \) (q, \( J_{CF} = 273 \) Hz), 124.9, 125.3.
(q, J_F-C = 3 Hz), 128.0, 129.7, 130.7 (q, J_F-C = 31 Hz), 131.2, 143.6, 151.4, 168.0. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 452.0750, found 452.0744.

terr-Butyl 4-(naphthalen-2-yl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylic acid 2,2-dioxide (3ej). The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propano = 80:20, flow 0.5 mL/min, 254 nm, t_1 = 16.4 min (S), t_2 = 22.6 min (R)); [α]_D\textsuperscript{20} = 26 (c 1.05, CHCl\textsubscript{3}) for 95% ee (S).\textsuperscript{1} H NMR (CDCl\textsubscript{3}) δ 1.47 (s, 9H), 6.54 (s, 1H), 7.18 (dd, J = 8.2, 1.4 Hz, 1H), 7.26 (dd, J = 7.8, 1.4 Hz, 1H), 7.38 (dd, J = 8.9, 2.0 Hz, 1H), 7.44–7.54 (m, 3H), 7.59 (dd, J = 8.1, 1.4 Hz, 1H), 7.63 (d, J = 1.4 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.84 (t, J = 8.9 Hz, 2H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 27.6, 71.4, 86.0, 118.9, 119.8, 124.7, 124.8, 126.5, 126.9, 127.1, 127.6, 128.5, 130.3, 132.6, 133.0, 133.7, 151.2, 168.7. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 434.1033, found 434.1025.

7-ethyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylic acid 2,2-dioxide (3dh). The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propano = 80:20, flow 0.5 mL/min, 254 nm, t_1 = 12.5 min (S), t_2 = 20.2 min (R)); [α]_D\textsuperscript{20} = 12 (c 0.57, CHCl\textsubscript{3}) for 96% ee (S).\textsuperscript{1} H NMR (CDCl\textsubscript{3}) δ 1.46 (s, 9H), 2.31 (s, 3H), 2.34 (s, 3H), 6.39 (s, 1H), 7.09 (d, J = 8.1 Hz, 1H), 7.12 (d, J = 8.9 Hz, 2H), 7.14 (d, J = 8.9 Hz, 2H), 2.62 (d, J = 8.1 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 15.8, 21.1, 27.6, 71.2, 85.5, 115.9, 123.9, 127.5, 127.9, 128.8, 129.0, 131.9, 137.1, 138.4, 149.5, 168.9. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 412.1189, found 412.1186.

terr-Butyl 6-methyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylic acid 2,2-dioxide (3dh). The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propano = 80:20, flow 0.5 mL/min, 254 nm, t_1 = 13.7 min (S), t_2 = 20.4 min (R)); [α]_D\textsuperscript{20} = 15 (c 0.70, CHCl\textsubscript{3}) for 96% ee (S).\textsuperscript{1} H NMR (CDCl\textsubscript{3}) δ 1.46 (s, 9H), 2.34 (s, 3H), 2.38 (s, 3H), 6.39 (s, 1H), 6.92 (s, 1H), 7.01 (d, J = 8.2 Hz, 1H), 7.11 (d, J = 8.9 Hz, 2H), 7.13 (d, J = 8.9 Hz, 2H), 7.36 (d, J = 8.2 Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 21.0, 21.1, 27.6, 70.9, 85.5, 116.3, 119.7, 125.6, 129.1, 130.2, 137.2, 138.4, 141.3, 150.9, 168.9. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 412.1182, found 412.1182.

6-methyl-4-(p-tolyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylic acid 2,2-dioxide (3fh). The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propano = 80:20, flow 0.5 mL/min, 254 nm, t_1 = 18.5 min (S), t_2 = 20.5 min (R)); [α]_D\textsuperscript{20} = 20 (c 1.03, CHCl\textsubscript{3}) for 93% ee (S).\textsuperscript{1} H NMR (CDCl\textsubscript{3}) δ 1.47 (s, 9H), 2.32 (s, 3H), 2.35 (s, 3H), 6.39 (s, 1H), 7.00 (d, J = 8.9 Hz, 1H), 7.13 (d, J = 8.5 Hz, 2H), 7.16 (d, J = 8.5 Hz, 2H), 2.70 (dd, J = 8.9, 1.4 Hz, 1H), 7.28 (d, J = 1.4 Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 20.9, 21.1, 27.6, 71.1, 85.5, 119.0, 119.1, 127.4, 129.1, 130.7, 131.2, 133.4, 137.0, 138.5, 148.9, 168.8. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 412.1189, found 412.1185.

terr-Butyl 6-methoxy-4-(p-tolyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine-4-carboxylic acid 2,2-dioxide (3fh). The ee was measured by HPLC (Chiralpak AS-H, hexane-2-propano = 80:20, flow 0.5 mL/min, 254 nm, t_1 = 10.7 min (R)); [α]_D\textsuperscript{20} = 67 (c 1.01, CHCl\textsubscript{3}) for 94% ee (S).\textsuperscript{1} H NMR (CDCl\textsubscript{3}) δ 1.56 (s, 9H), 2.36 (s, 3H), 2.91 (s, 3H), 6.93 (dd, J = 8.1, 1.4 Hz, 1H), 7.02 (dd, J = 8.1, 1.4 Hz, 1H), 7.03 (td, J = 8.1, 1.4 Hz, 1H), 7.15 (d, J = 8.9 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 7.27 (td, J = 8.1, 1.4 Hz, 1H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) δ 21.1, 27.7, 55.7, 71.1, 85.6, 115.0, 116.3, 120.1, 120.3, 127.4, 129.1, 136.9, 138.5, 144.9, 155.9, 168.7. HRMS (ESI) calcd for C_{16}H_{18}F_{2}NNaO_{5}S (M+Na)\textsuperscript{+} 428.1138, found 428.1135.
NiCl$_2$(dppe)$^{23}$ in N$_2$N-dimethylecetamide (DMA) was added to Et$_2$Zn (1.0 M in toluene solution, 0.20 mL, 0.20 mmol) at room temperature, and the mixture was stirred at 100 °C for 24 h. Saturated NH$_4$Cl (aq., ca. 0.1 mL) and 0.5 M HCl (aq., ca. 0.5 mL) at room temperature was added to the mixture and it was stirred at room temperature for 10 min. The mixture was extracted with ethyl acetate. To the aqueous layer was added with H$_2$O, saturated NH$_4$Cl (aq.), dried over Na$_2$SO$_4$, filtered, and concentrated on a rotary evaporator. The residue was subjected to preparative TLC on silica gel with hexane/ethyl acetate (10:1) to give 4 (21.8 mg, 0.070 mmol, 70% yield).


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Notes and references
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16 The absolute configuration of 3ch produced by use of (S,S)-Bn-tfb* was determined to be S by X-ray crystallographic analysis.