Highly Enantioselective and Regioselective Organocatalytic Direct Mannich Reaction of Methyl Alkyl Ketones with Cyclic Imines Benzo[e][1,2,3]oxathiazine 2,2-dioxides

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1. General methods.

General: 1H NMR, and 13C NMR spectra were recorded on Bruker DRX-400 spectrometers. The chemical shifts for 1H NMR were recorded in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl3, δ 7.26 ppm). The chemical shifts for 13C NMR were recorded in ppm downfield using the central peak of deuterochloroform (77.0 ppm) as the internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). TLC analysis was performed using glass-backed plates coated with 0.2 mm silica. After elution, plate was visualized under at 254 nm UV illumination. All commercially available compounds were used as provided without further purification. The solvents were distilled from appropriate drying agents prior to use, unless otherwise noted. Cyclic imines 1 were prepared according to the procedures reported in the literature.[1]

2. More results on the condition optimization of asymmetric Mannich reaction

<table>
<thead>
<tr>
<th>Entry†</th>
<th>Acid</th>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TFA</td>
<td>THF</td>
<td>10</td>
<td>22</td>
<td>51</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>(+)-CSA</td>
<td>THF</td>
<td>10</td>
<td>72</td>
<td>35</td>
<td>96</td>
</tr>
</tbody>
</table>


S1
<p>| | | | |</p>
<table>
<thead>
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<th></th>
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<tbody>
<tr>
<td>3</td>
<td>TsOH</td>
<td>THF</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>AcOH</td>
<td>THF</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>TFA</td>
<td>Toluene</td>
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<tr>
<td>6</td>
<td>(+)-CSA</td>
<td>Toluene</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>(-)-CSA</td>
<td>Toluene</td>
<td>10</td>
</tr>
</tbody>
</table>

8 | TFA | Toluene | 0 | 24 | 99 | 91 |

The effects of acid were investigated in THF (entries 1-4). In spite of the best ee, the reaction was slower with (+)-CSA than TFA (entries 1 vs 2). However, in optimized solvent (Toluene) TFA afforded the better reactivities and enantioselectivities than CSA (entries 5-7). While temperature was decreased to 0°C, a slightly lower ee values was obtained (entry 8).

3. **Procedure and data of asymmetric Mannich reaction**

**Typical procedure:** To the mixture of quinine-NH₂ C-4 (0.015 mmol, 10 mol%) and cyclic imine 1 (0.15 mmol) in toluene (1.45 mL) was added the solution of TFA (0.03 mmol, 20 mol%) in toluene (0.05 mL). After the reaction mixture was cooled to 10°C, acetone (0.75 mmol) was added. This reaction mixture was stirred in showed reaction time. Direct purification reaction mixture by column chromatography on a silica gel (petroleum ether/DCM) gave the desired Mannich products. The enantiomeric excess was determined by HPLC. Racemic Mannich products were obtained with the combination of 10 mol% benzyl amine and 20 mol% TFA.

**2a:** Known compound²; \( R_f = 0.18 \) (CH₂Cl₂); 96% ee, [α]° = -21.3 (c 0.97, CHCl₃); 

¹H NMR (400 MHz, CDCl₃): \( δ 7.31 \) (t, \( J = 7.6 \) Hz, 1H), 7.17 (t, \( J = 7.5 \) Hz, 1H), 7.11-7.10 (m, 1H), 7.02 (d, \( J = 8.2 \) Hz, 1H), 5.82 (s, 1H), 5.17 (dd, \( J = 7.2, 3.8 \) Hz, 1H), 3.62 (dd, \( J = 18.1, 7.5 \) Hz, 1H), 2.97 (dd, \( J = 18.1, 3.8 \) Hz, 1H), 2.24 (s, 3H); 

¹³C NMR (100 MHz, CDCl₃): \( δ 206.7, 151.1, 129.6, 125.8, 125.4, 121.3, 119.1, 53.3, 46.4, 31.0; \)

HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): \( t_1 = 10.1 \) min (major, \( S \)), \( t_2 = 15.0 \) min.

**2b:** White solid; mp 114.4-115.3°C; \( R_f = 0.30 \) (CH₂Cl₂); 96% ee, [α]° = -18.4 (c 1.03, CHCl₃); 

¹H NMR (400 MHz, CDCl₃): \( δ 7.03-6.96 \) (m, 2H), 6.84-6.81 (m, 1H), 5.89 (s, 1H), 5.14 (dd, \( J = 6.7, 3.9 \) Hz, 1H), 3.57 (dd, \( J = 18.3, 7.4 \) Hz, 1H), 2.98 (dd, \( J = 18.3, 4.1 \) Hz, 1H), 2.24 (s, 3H); 

¹³C NMR (100 MHz, CDCl₃): \( δ 206.6, 159.3 \) (d, \( J_{F,C} = 244.3 \) Hz), 147.0 (d, \( J_{F,C} = 2.7 \) Hz), 123.1 (d, \( J_{F,C} = 7.1 \) Hz), 120.6 (d, \( J_{F,C} = 8.3 \) Hz), 116.6 (d, \( J_{F,C} = 23.5 \) Hz), 112.7 (d, \( J_{F,C} = 24.8 \) Hz), 53.0, 46.4, 30.8; HRMS (ESI): m/z calculated for \( C_{13}H_{19}FNNaO₄S \) [M+Na]+ 282.0207, found: 282.0210; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): \( t_1 = 8.5 \) min (major, \( S \)), \( t_2 = 10.7 \) min.

**2c:** White solid; mp 123.2-124.1°C; \( R_f = 0.34 \) (CH₂Cl₂); 97% ee, [α]° = -52.3 (c 1.17, CHCl₃); 

¹H NMR (400 MHz, CDCl₃): \( δ 7.28 \) (ddd, \( J = 8.8, 2.4, 0.5 \) Hz, 1H), 7.10 - 7.09 (m, 1H), 6.98 (d, \( J = 8.8 \) Hz, 1H), 5.78 (d, \( J = 5.2 \) Hz, 1H), 5.14 (d, \( J = 3.6 \) Hz, 1H), 3.61 (dd, \( J = 18.4, 7.2 \) Hz, 1H), 2.99 (dd, \( J = 18.4, 4.0 \) Hz, 1H), 2.26 (s, 3H); 

¹³C NMR (100 MHz, CDCl₃): \( δ 206.3, 149.7, 130.7, 129.7, 125.7, 122.9, 120.5, 53.1, 46.1, 30.9; \) HRMS (ESI): m/z calculated for \( C_{13}H_{19}CINaO₄S \) [M+Na]+ 297.9911, found: 297.9914; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): \( t_1 = 7.2 \) min.

2d: White solid; mp 125.3-126.6°C; $R_f$ = 0.34 (CH$_2$Cl$_2$); 91% ee, $[\alpha]^{10}_D$ = -42.3 (c 0.93, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.42 (d, $J$ = 8.2 Hz, 1H), 7.25 (s, 1H), 6.92 (d, $J$ = 8.6 Hz, 1H), 5.82 (s, 1H), 5.15 (s, 1H), 3.61 (dd, $J$ = 18.3, 7.0 Hz, 1H), 2.98 (dd, $J$ = 167.6, 1.2 Hz, 1H), 2.26 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.4, 150.1, 132.6, 128.7, 123.3, 120.8, 118.1, 52.9, 46.3, 30.9; HRMS (ESI): m/z calculated for C$_{10}$H$_{18}$BrNNaO$_3$S $[\text{M}^+\text{Na}]^+$ 341.9406, found: 341.9408; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): $t_1$ = 7.4 min (major, S), $t_2$ = 8.7 min.

2e: White solid; mp 111.9-112.6°C; $R_f$ = 0.29 (CH$_2$Cl$_2$); 95% ee, $[\alpha]^{10}_D$ = -46.8 (c 1.06, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.08 (d, $J$ = 8.4 Hz, 1H), $\delta$ 6.89-6.88 (m, 2H), 5.78 (s, 1H), 5.12 (s, 1H), 3.59 (dd, $J$ = 18.1, 7.9 Hz, 1H), 2.94 (dd, $J$ = 18.1, 3.8 Hz, 1H), 2.30 (s, 3H), 2.23 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.7, 149.00, 135.2, 130.2, 126.1, 120.9, 118.8, 53.3, 46.6, 31.0, 20.8; HRMS (ESI): m/z calculated for C$_{11}$H$_{14}$NNaO$_5$S $[\text{M}^+\text{Na}]^+$ 278.0458, found: 278.0464; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): $t_1$ = 10.1 min (major, S), $t_2$ = 12.1 min.

2f: White solid; mp 89.3-89.7°C; $R_f$ = 0.27 (CH$_2$Cl$_2$); 95% ee, $[\alpha]^{10}_D$ = -35.1 (c 1.30, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.94 (d, $J$ = 9.0 Hz, 1H), 6.82 (dd, $J$ = 9.0, 2.8 Hz, 1H), 6.60 (d, $J$ = 2.8 Hz, 1H), 5.76 (d, $J$ = 7.5 Hz, 1H), 5.12 (d, $J$ = 3.8 Hz, 1H), 3.76 (s, 3H), 3.58 (dd, $J$ = 18.1, 7.7 Hz, 1H), 2.95 (dd, $J$ = 18.1, 3.9 Hz, 1H), 2.23 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.9, 160.3, 151.8, 126.4, 113.0, 112.4, 103.8, 55.6, 53.0, 46.3, 31.1; HRMS (ESI): m/z calculated for C$_{11}$H$_{13}$NNaO$_5$S $[\text{M}^+\text{Na}]^+$ 294.0407, found: 294.0409; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): $t_1$ = 10.3 min (major, S), $t_2$ = 12.3 min.

2g: Colorless oil; $R_f$ = 0.23 (CH$_2$Cl$_2$); 96% ee, $[\alpha]^{10}_D$ = -27.3 (c 1.17, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.94 (d, $J$ = 8.6 Hz, 1H), 6.66 (dd, $J$ = 8.6, 2.1 Hz, 1H), 6.45 (s, 1H), 5.06 (dd, $J$ = 7.7, 3.8 Hz, 1H), 4.83 (s, 1H), 3.75 (s, 3H), 3.47 (dd, $J$ = 17.7, 8.0 Hz, 1H), 2.88 (dd, $J$ = 17.8, 3.7 Hz, 1H), 2.19 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.9, 160.3, 151.8, 126.4, 113.0, 112.4, 103.8, 55.6, 53.0, 46.3, 31.1; HRMS (ESI): m/z calculated for C$_{11}$H$_{12}$NNaO$_5$S $[\text{M}^+\text{Na}]^+$ 294.0407, found: 294.0410; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): $t_1$ = 15.2 min (major, S), $t_2$ = 21.7 min.

2h: White solid; mp 116.2-117.0°C; $R_f$ = 0.21 (CH$_2$Cl$_2$); 95% ee, $[\alpha]^{10}_D$ = -24.3 (c 1.44, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.08 (t, $J$ = 8.1 Hz, 1H), 6.87 (d, $J$ = 7.9 Hz, 1H), 6.66 (d, $J$ = 7.9 Hz, 1H), 5.84 (s, 1H), 5.16 (s, 1H), 3.84 (s, 3H), 3.59 (dd, $J$ = 18.1, 7.6 Hz, 1H), 2.94 (dd, $J$ = 18.1, 3.9 Hz, 1H), 2.22 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.7, 156.7, 144.8, 122.2, 119.9, 114.5, 111.1, 55.7, 53.4, 46.5, 31.0; HRMS (ESI): m/z calculated for C$_{10}$H$_{11}$NNaO$_3$S $[\text{M}^+\text{Na}]^+$ 294.0407, found: 294.0411; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): $t_1$ = 15.0 min (major, S), $t_2$ = 26.6 min.

2i: White solid; mp 133.9-135.1°C; $R_f$ = 0.28 (CH$_2$Cl$_2$); 97% ee, $[\alpha]^{10}_D$ = -12.6 (c 1.00, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.69-7.67 (m, 1H), 7.19 (s, 1H), 5.98 (s, 1H), 5.15 (s, 1H), 3.64-3.56 (m, 1H), 2.99 (d, $J$ = 18.4 Hz, 1H), 2.26-2.25 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 206.2, 147.3, 135.8, 127.7, 124.8, 117.9,
113.9, 53.1, 46.2, 30.9; HRMS (ESI): m/z calculated for C_{10}H_{9}Br_{2}NNaO_{4}S [M+Na]^+ 419.8511, found: 419.8514; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 6.3 min (major, S), t₂ = 7.9 min.

2j: White solid; mp 121.7-122.2°C; Rf = 0.26 (CH₂Cl₂); 96% ee, [α]^{21}_{D} = -6.1 (c 1.12, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.54 (d, J = 2.1 Hz, 1H), 7.05 (d, J = 1.8 Hz, 1H), 5.95 (s, 1H), 5.15 (dd, J = 18.4, 7.2 Hz, 1H), 3.60 (dd, J = 18.4, 4.0 Hz, 1H), 2.26 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃): δ 206.2, 146.8, 133.1, 130.8, 124.9, 124.4, 113.5, 53.1, 46.3, 30.8; HRMS (ESI): m/z calculated for C_{10}H_{9}BrClINaO_{4}S [M+Na]^+ 375.9016, found: 375.9015; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 6.1 min (major, S), t₂ = 7.8 min.

2k: White solid; mp 143.3-144.5°C; Rf = 0.29 (CH₂Cl₂); 93% ee, [α]^{31}_{D} = -37.3 (c 1.00, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.33 (d, J = 2.2 Hz, 1H), 6.94 (d, J = 2.0 Hz, 1H), 5.74 (s, 1H), 5.15 (dd, J = 8.4, 3.8 Hz, 1H), 3.61 (dd, J = 17.9, 8.5 Hz, 1H), 2.92 (dd, J = 17.9, 3.9 Hz, 1H), 2.24 (s, 3H), 1.40 (s, 9H), 1.28 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl₃): δ 206.8, 148.0, 147.6, 139.4, 124.3, 121.8, 120.7, 53.6, 47.4, 35.1, 34.6, 31.3, 30.9, 30.0; HRMS (ESI): m/z calculated for C_{10}H_{9}BrClINaO_{4}S [M+Na]^+ 376.1557, found: 376.1557; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 5.8 min (major, S), t₂ = 6.4 min.

4a: Known compound\(^2\); Rf = 0.34 (CH₂Cl₂); 96% ee, [α]^{31}_{D} = -26.7 (c 0.97, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.33-7.29 (m, 1H), 7.17 (td, J = 7.6, 1.0 Hz, 1H), 7.11-7.09 (m, 1H), 7.03 (dd, J = 8.2, 0.8 Hz, 1H), 5.78 (d, J = 4.3 Hz, 1H), 5.19 (d, J = 3.4 Hz, 1H), 3.61 (dd, J = 17.9, 7.5 Hz, 1H), 2.93 (dd, J = 17.9, 3.9 Hz, 1H), 2.58-2.46 (m, 2H), 1.06 (t, J = 7.3 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃): δ 209.5, 151.2, 129.6, 125.7, 125.4, 121.4, 119.2, 53.6, 45.0, 37.2, 7.4; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 9.5 min (major, S), t₂ = 15.9 min.

4b: Known compound\(^2\); Rf = 0.18 (CH₂Cl₂); 95% ee, [α]^{31}_{D} = -21.3 (c 0.97, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.32-7.27 (m, 1H), 7.16 (td, J = 7.5, 0.8 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 5.93 (d, J = 8.0 Hz, 1H), 5.18 (d, J = 7.8, 3.9 Hz, 1H), 3.58 (dd, J = 17.9, 7.7 Hz, 1H), 2.91 (dd, J = 17.9, 3.9 Hz, 1H), 2.48-2.43 (m, 2H), 1.59 (dd, J = 14.7, 7.4 Hz, 2H), 0.89 (t, J = 7.4 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃): δ 209.3, 151.1, 129.5, 125.8, 125.4, 121.4, 119.0, 53.4, 45.7, 45.5, 16.8, 13.5; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 8.3 min (major, S), t₂ = 13.3 min.

4c: White solid; mp 43.1-44.3°C; Rf = 0.56 (CH₂Cl₂); 97% ee, [α]^{31}_{D} = -31.4 (c 0.92, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.32-7.29 (m, 1H), 7.16 (t, J = 7.1 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 5.90 (s, 1H), 5.18 (s, 1H), 3.59 (dd, J = 17.9, 7.6 Hz, 1H), 2.91 (dd, J = 17.9, 3.9 Hz, 1H), 2.54-2.41 (m, 2H), 1.58-1.50 (m, 2H), 1.33-1.24 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl₃): δ 209.4, 151.1, 129.5, 125.8, 125.4, 121.4, 119.0, 53.4, 45.5, 43.6, 25.4, 22.1, 13.7; HRMS (ESI): m/z calculated for C_{10}H_{9}F_{2}NNaO_{4}S [M+Na]^+ 306.0771, found: 306.0773; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 7.3 min (major, S), t₂ = 12.4 min.

4d: Yellow solid; mp 36.3-37.5°C; Rf = 0.47 (CH₂Cl₂); 96% ee, [α]^{12}_{D} = -31.4 (c
0.97, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.29 (t, J = 7.7 Hz, 1H), 7.18-7.14 (m, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 5.96 (s, 1H), 5.18 (td, J = 7.8, 4.0 Hz, 1H), 3.58 (dd, J = 18.0, 7.6 Hz, 1H), 2.88 (dd, J = 18.0, 3.9 Hz, 1H), 2.35 (d, J = 7.0 Hz, 2H), 2.17-2.07 (m, 1H), 0.89 (dd, J = 6.6, 2.5 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 209.1, 151.1, 129.5, 1265.9, 125.3, 121.5, 119.0, 53.3, 52.7, 46.0, 24.4, 22.4, 22.3; HRMS (ESI): m/z calculated for C₁₇H₁₇N₃NaO₃S [M+Na]⁺ 306.0771, found: 306.0774; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 6.4 min (major, S), t₂ = 8.8 min.

4e: White solid; mp 76.5-77.8°C; Rᶠ = 0.32 (PE/EtOAc, 5:1); 87% ee, [α]²⁰D = -38.1 (c 1.25, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 67.33-7.28 (m, 1H), 7.16 (td, J = 7.5, 1.0 Hz, 1H), 7.10-7.08 (m, 1H), 7.02 (dd, J = 8.3 Hz, 1.0 Hz, 1H), 5.87 (d, J = 8.0 Hz, 1H), 5.20-5.15 (m, 1H), 3.59 (dd, J = 18.0, 7.3 Hz, 1H), 2.89 (dd, J = 18.0, 3.9 Hz, 1H), 2.34 (d, J = 6.9 Hz, 2H), 1.87-1.76 (m, 1H), 1.68-1.60 (m, 4H), 1.30-1.06 (m, 4H), 0.96-0.82 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 209.1, 151.2, 129.6, 125.8, 125.3, 121.4, 119.2, 53.5, 51.6, 45.8, 33.8, 33.2, 33.1, 26.1, 26.02, 25.98; HRMS (ESI): m/z calculated for C₁₆H₂₃N₃NaO₃S [M+Na]⁺ 346.1089, found: 346.1088; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 7.2 min (major, S), t₂ = 9.3 min.

4f: White solid; mp 121.7-122.2°C; Rᶠ = 0.29 (PE/EtOAc, 3:1); 92% ee, [α]²⁰D = -13.8 (c 1.73, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.32-7.28 (m, 1H), 7.15-7.11 (m, 2H), 7.09-7.07 (m, 1H), 7.06-7.00 (m, 3H), 6.90 (d, J = 8.0 Hz, 7.7H), 5.66 (d, J = 8.1 Hz, 1H), 5.14 (td, J = 7.8, 3.9 Hz, 1H), 3.74 (s, 2H), 3.66 (dd, J = 18.0, 7.5 Hz, 1H), 2.92 (dd, J = 18.0, 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 206.1, 162.2 (d, Jᶠ-C = 245.0 Hz), 151.1, 131.1 (d, Jᶠ-C = 8.0 Hz), 129.7, 128.38 (d, Jᶠ-C = 3.3 Hz), 125.6, 125.4, 121.0, 119.1, 151.5, 53.5, 50.0, 44.6; HRMS (ESI): m/z calculated for C₁₀H₁₄FNNaO₃S [M+Na]⁺ 358.0525, found: 358.0510; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 8.8 min (major, S), t₂ = 12.0 min.

4g: White solid; mp 121.7-122.2°C; Rᶠ = 0.29 (PE/EtOAc, 3:1); 94% ee, [β]¹⁰⁰D = -6.8 (c 1.66, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.28 (m, 3H), 7.12-7.08 (m, 3H), 7.01-6.99 (m, 1H), 6.91 (d, J = 7.7 Hz, 1H), 5.69 (s, 1H), 5.14 (d, J = 3.5 Hz, 1H), 3.73 (s, 2H), 3.66 (dd, J = 18.0, 7.7 Hz, 1H), 2.92 (dd, J = 18.0, 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 205.9, 151.1, 133.5, 131.1, 130.8, 129.7, 129.1, 125.7, 125.4, 121.0, 119.1, 53.5, 50.1, 44.9; HRMS (ESI): m/z calculated for C₁₈H₁₄ClNNaO₃S [M+Na]⁺ 374.0230, found: 374.0198; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 9.3 min (major, S), t₂ = 12.3 min.

4h: White solid; mp 121.7-122.2°C; Yellow solid; mp 102.7-103.8°C; Rᶠ = 0.43 (CH₂Cl₂); 94% ee, [α]¹⁰⁰D = 6.1 (c 1.73, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.30-7.25 (m, 1H), 7.09-7.04 (m, 3H), 6.99 (d, J = 8.3 Hz, 1H), 6.88-6.84 (m, 3H), 5.79 (s, 1H), 5.10 (d, J = 3.4 Hz, 1H), 3.80 (s, 3H), 3.68 (s, 2H), 3.63 (dd, J = 18.1, 7.2 Hz, 1H), 2.90 (dd, J = 18.1, 3.9 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 207.0, 158.9, 151.1, 130.5, 129.5, 125.7, 125.3, 124.7, 121.1, 118.9, 55.2, 53.4, 50.0, 44.1; HRMS (ESI): m/z calculated for C₁₇H₁₇N₃NaO₃S [M+Na]⁺ 370.0720, found: 370.0719; HPLC (Chiralcel IC column, hexane/iPrOH = 70/30, 0.8 mL/min, 220 nm): t₁ = 16.3 min (major, S), t₂ = 37.5 min.

4i: White solid; mp 36.3-37.5°C; Rᶠ = 0.57 (CH₂Cl₂); 96% ee, [α]¹⁰⁰D = -23.4 (c 0.98, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.25 (m, 3H), 7.19 (t, J = 7.3
4. X-ray structure for compound 2c

The needle-like crystals of the compound 2c were grown from its solution in dichloromethane and hexane, and one of them is suitable for X-ray diffraction analysis. The correctness of the X-ray data and the structure had been checked by using the CheckCIF utility on the submission Web site: http://checkcif.iucr.org.
Copy of NMR

2a

2a
HPLC for racemic and pure enantioenriched sample 2a

HPLC for racemic and pure enantioenriched sample 2b
HPLC for racemic and pure enantioenriched sample 2c

HPLC for racemic and pure enantioenriched sample 2d

Peak areas: 2069.26

Peak areas: 957.2666
HPLC for racemic and pure enantioenriched sample 2e

Signal: 2e
Peak time | Retention time | Absorbance | Enantiomer
--- | --- | --- | ---
10.316 min | 352.559579 | 234.40344 | 59.2459
12.322 min | 352.559579 | 188.14048 | 48.7541

HPLC for racemic and pure enantioenriched sample 2f

Signal: 2f
Peak time | Retention time | Absorbance | Enantiomer
--- | --- | --- | ---
10.132 min | 352.559579 | 78.64223 | 59.3752
12.144 min | 352.559579 | 6.20.6853 | 49.7548

Signal: 2f
Peak time | Retention time | Absorbance | Enantiomer
--- | --- | --- | ---
10.824 min | 352.559579 | 78.64223 | 59.3752
12.331 min | 352.559579 | 6.20.6853 | 49.7548

Signal: 2f
Peak time | Retention time | Absorbance | Enantiomer
--- | --- | --- | ---
20.283 min | 352.559579 | 20.64035 | 97.3084
12.302 min | 352.559579 | 5.68506 | 29.6466
HPLC for racemic and pure enantioenriched sample 2g

HPLC for racemic and pure enantioenriched sample 2h
HPLC for racemic and pure enantioenriched sample 2i

HPLC for racemic and pure enantioenriched sample 2j
HPLC for racemic and pure enantioenriched sample 2k

HPLC for racemic and pure enantioenriched sample 4a

Signal 2: DAD 1 C, Slp=220.8 Ref=560.100

Peak area: 4905.58 9.360

Signal 2: DAD 1 C, Slp=220.8 Ref=560.100

Peak area: 95.0218 15.934

Signal 2: DAD 1 C, Slp=220.8 Ref=560.100

Peak area: 3323.13768 369.00975

Signal 2: DAD 1 C, Slp=220.8 Ref=560.100

Peak area: 5272.01109 372.09416
HPLC for racemic and pure enantioenriched sample 4b

HPLC for racemic and pure enantioenriched sample 4c
HPLC for racemic and pure enantioenriched sample 4d

HPLC for racemic and pure enantioenriched sample 4e
HPLC for racemic and pure enantioenriched sample 4f

HPLC for racemic and pure enantioenriched sample 4g
HPLC for racemic and pure enantioenriched sample 4h

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HPLC for racemic and pure enantioenriched sample 4i

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S39
HPLC for racemic and pure enantioenriched sample 4j

HPLC for racemic and pure enantioenriched sample 4k

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**HPLC for racemic and pure enantioenriched sample 4j**

**HPLC for racemic and pure enantioenriched sample 4k**
HPLC for racemic and pure enantioenriched sample 41

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