Asymmetric [4+2] Annulation of 5H-Thiazol-4-Ones with a Chiral Dipeptide-Based Brønsted Base Catalyst

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1. 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 hypodermic syringe cooled to ambient temperature in a desiccator. Reactions mixtures were stirred in 4 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile 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 30–40 °C using rotary evaporator with aspirator. The condenser was cooled with running water at 0 °C.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated plates, 60 F 254. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining KMnO₄, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate. Columns for flash chromatography (FC) contained silica gel 200–300 mesh. Columns were packed as slurry of silica gel in petroleum ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentations

Proton nuclear magnetic resonance (¹H NMR), carbon NMR (¹³C NMR), and fluorous (¹⁹F NMR) spectra were recorded in CDCl₃ otherwise stated. ¹H (300 MHz) and ¹³C (75 MHz) were performed on a 300MHz spectrometer. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: CDCl₃ (¹H NMR: δ 7.26, singlet; ¹³C 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 of 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; [α]₂⁰°C (c = g/100 mL, solvent). Melting points were determined on a melting point apparatus.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis. UV detection was monitored at 254 nm, 230 nm 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 CH$_2$Cl$_2$, CHCl$_3$ and DCE were freshly distilled from CaH$_2$ and stored under N$_2$ atmosphere. THF, Et$_2$O and toluene 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 aluminium foil.
2. Synthesis of dipeptide-based III

**Step 1:** To a solution of crude Boc-protected amino acid A (2.31 g, 10 mmol) in THF (15 mL), Et$_3$N (2.78 mL, 20 mmol) and BOP (5.41 g, 12 mmol) was added at 0 °C. Pyridine (1.16 mL, 13 mmol) was injected after the mixture was stirred for 0.5 hour at 0 °C. Then the reaction mixture was stirred at room temperature for another 8 hours (monitored by TLC). Solvent was removed under reduced pressure and B was obtained by flash chromatography (silica gel, Hexane/ethyl acetate 10:1–3:1), as a white solid, 2.32 g, 81.6% yield.

**Step 2:** AcCl (4.6 mL, 65.6 mmol) was added to a solution of B (2.32 g, 8.2 mmol) in MeOH (20 mL) 0 °C. The reaction mixture was stirred at room temperature for 8 hours (monitored by TLC). Solvent was removed under reduced pressure and solid C (1.51 g, 100%) was obtained for the next step without any purification.

**Step 3:** LiAlH$_4$ (1.25 g, 32.8 mmol) was added into a solution of C (1.51 g, 8.2 mmol) in THF (20 mL) slowly. The mixture was stirred at 0 °C for about 5.0 minutes then warmed to room temperature and stirred overnight. Subsequently, the reaction was carefully quenched by NaOH aqueous solution (4.0 N, 2 mL). The solids were filtered off and washed by THF, and the filtrate was dried over Na$_2$SO$_4$. Solvent was removed under reduced pressure and D was obtained as yellow oil in 86.5% yield (1.2 g).

**Step 4:** To a solution of diamine D (0.75 g 4.4 mmol) in THF (25 mL) were added TEA (1.84 ml, 13.2 mmol), Boc-protected amino acid A (1.2 g, 5.3 mmol) and HOBT (0.89 g, 6.6 mmol) at −10 °C for 15 min. Then EDCI (1.3 g, 6.6 mmol) was added the mixture, and the mixture was stirred overnight at room temperature. The reaction mixture was poured into water and extracted with AcOEt. The AcOEt layer was washed with water and brine and dried over Na$_2$SO$_4$. Filtration and concentration in vacuo and purification by silica gel flash column chromatography (AcOEt/n-hexane = 1/5) gave 1.28 g (76%) of E as a white solid.

**Step 5** AcCl (1.89 mL, 26.7mmol) was added to a solution of E (1.28 g, 3.34 mmol) in MeOH (20 mL) 0 °C. The reaction mixture was stirred at room temperature for 8 hours (monitored by TLC). Solvent was removed under reduced pressure and solid F (0.95 g, 100%) was obtained for the next step without any purification.
Step 6 (Final step): To a solution of \( \text{F} \) (308.6 mg, 1.09 mmol) in DCM (5 mL) was added 3,5-di(trifluoromethyl)phenyl isothiocyanate (295.2 mg, 1.09 mmol). The resulting solution was stirred for 5 min at 0 \(^\circ\)C. The reaction was concentrated \textit{in vacuo} and the residue was purified by \textit{silica gel} chromatography (\textit{silica gel}, DCM/MeOH 100:1–30:1) to afford product \text{III} as a white solid in 85% yield (513.1 mg).
3. Optimization of reaction conditions for nitroalkene 2a as acceptor

Table 1 Asymmetric [4+2] cyclization catalyzed by amino acid-derived tertiary amine–(thio)ureas

| Entry | Catalyst | Solvent | $T$ (°C) | $t$ (h) | 3a:4 | Yield (%)$^b$ | e.e. (%)$^c$ | d.r.$^d$ | Yield (%)$^b$ | e.e. (%)$^c$ | d.r.$^d$ |
|-------|----------|---------|----------|--------|-------|--------------|-------------|--------|--------------|-------------|--------|
| 1     | Et$_3$N  | CH$_2$Cl$_2$ | 25       | 18     | trace | trace        | n.a.        | n.a.   | n.a.         | n.a.        | n.a.   |
| 2     | I        | CH$_2$Cl$_2$ | 25       | 12     | 1:1   | 42           | 0           | 15:1   | 45           | 64          | 1:1    |
| 3     | II       | CH$_2$Cl$_2$ | 25       | 12     | 3:1   | 62           | 7           | 9:1    | 20           | 3           | 19:1   |
| 4     | III      | CH$_2$Cl$_2$ | 25       | 12     | 4:1   | 73           | 86          | 19:1   | 13           | 88          | 12:1   |
| 5     | IV       | CH$_2$Cl$_2$ | 25       | 12     | 4:1   | 68           | 87          | 8:1    | 18           | 87          | 9:1    |
| 6     | III      | THF      | 25       | 16     | trace | trace        | n.a.        | n.a.   | trace        | n.a.        | n.a.   |
| 7     | III      | toluene  | 25       | 16     | 5:1   | 84           | 94          | >19:1  | 8            | 88          | 12:1   |
| 8     | III      | Et$_2$O  | 25       | 16     | 4:1   | 70           | 92          | >19:1  | 11           | 96          | >19:1  |
| 9     | III      | CHCl$_3$ | 25       | 16     | 4:1   | 72           | 83          | >19:1  | 9            | 85          | >19:1  |
| 10    | III      | toluene  | 25       | 16     | 4:1   | 56           | 95          | >19:1  | 10           | 31          | 3:1    |
| 11    | III      | toluene  | 30       | 18     | 4.5:1 | 78           | 92          | 19:1   | 12           | 75          | 19:1   |
| 12$^e$| III      | toluene  | 25       | 18     | 5:1   | 83           | 95          | >19:1  | 11           | 88          | 12:1   |
| 13$^e$| V        | toluene  | 25       | 18     | 2.5:1 | 68           | −75         | >19:1  | 17           | 13          | >19:1  |

$^a$The reaction was performed using 1a (0.05 mmol) and 2a (0.075 mmol) in 1.0 mL of solvent.

$^b$Isolated yield based on 1a after column chromatography.

$^c$Enantiomeric ratio of product 3a was determined via chiral phase HPLC analysis.

$^d$Determined by crude $^1$H NMR analysis.

$^e$The reaction was performed using 1a (0.2 mmol) and 2a (0.4 mmol) in 4.0 mL of solvent.
4. Optimization of reaction conditions for 4-oxo-4-phenylbutenone 5a as acceptor

Table 2 Condition optimization

| Entry | Catalyst | Solvent  | $T$ (°C) | $t$ (h) | 6a Yield (%) | 6a e.e. (%) | 6a-M Yield (%) | 6a-M e.e. (%) | d.r. |
|-------|----------|----------|----------|--------|--------------|-------------|----------------|---------------|------|
| 1     | Et$_3$N  | CH$_2$Cl$_2$ | 25       | 96     | 11           | n.a.        | 72             | n.a.          | 10:1 |
| 2     | I        | CH$_2$Cl$_2$ | 25       | 3      | 27           | 62          | 57             | 62            | >19:1|
| 3     | II       | CH$_2$Cl$_2$ | 25       | 3      | 44           | 54          | 46             | 37            | >19:1|
| 4     | III      | CH$_2$Cl$_2$ | 25       | 2.5    | 85           | 87          | 12             | 32            | >19:1|
| 5     | IV       | CH$_2$Cl$_2$ | 25       | 3      | 78           | 68          | 18             | 58            | 19:1 |
| 6     | III      | toluene    | 25       | 7      | 54           | 78          | 20             | 73            | >19:1|
| 7     | III      | Et$_2$O    | 25       | 7      | 13           | 71          | 5              | 72            | >19:1|
| 8     | III      | CHCl$_3$   | 25       | 3.5    | 82           | 91          | 10             | 50            | 13:1 |
| 9     | III      | DCE        | 25       | 5      | 80           | 88          | 13             | 26/69         | 11:1 |
| 10    | III      | CHCl$_3$   | 0        | 18     | 80           | 96          | 17             | 60/62         | 13:1 |
| 11    | III      | CHCl$_3$   | -10      | 24     | 86           | 98          | 9              | 69/53         | 19:1 |

*Reaction conditions: 1a (0.05 mmol), 5a (0.075 mmol), solvent (1.0 mL). For product 6a, all d.r.s are >20:1 determined by crude $^1$H NMR.

*Yield of isolated product.

*Ee was determined via chiral phase HPLC analysis.

*Determined by $^1$H NMR analysis.
5. Optimization of reaction conditions for methyleneindolinones 9 as acceptor

Table 3 Condition optimization

| Entry | Solvent | R<sup>1</sup> | R<sup>2</sup> | T (°C) | t (h) | Yield (%)<sup>b</sup> | ee (%)<sup>c</sup> |
|-------|---------|--------------|--------------|--------|------|----------------------|------------------|
| 1     | DCE     | Me           | Et           | 25     | 5    | 85                   | 73               |
| 2     | CHCl<sub>3</sub> | Me           | Et           | 25     | 5    | 91                   | 75               |
| 3     | CHCl<sub>3</sub> | Me           | Et           | -10    | 10   | 86                   | 85               |
| 4     | CHCl<sub>3</sub> | Me           | tBu          | -10    | 12   | 84                   | 80               |
| 5     | CHCl<sub>3</sub> | Boc          | Et           | -10    | 12   | trace                | n.a.             |
| 6     | CHCl<sub>3</sub> | Bn           | Et           | -30    | 24   | 90                   | 94               |
| 7     | CHCl<sub>3</sub> | Bn           | Et           | -30    | 24   | 96                   | 95               |

*aReaction conditions: 1a (0.05 mmol), 9 (0.075 mmol), solvent (1.0 mL). For product 10, all drs are >20:1 determined by crude ¹H NMR.

<sup>b</sup>Yield of isolated product.

<sup>c</sup>ee was determined via chiral phase HPLC analysis.
6. General experimental procedure for the [4+2] annulation of 5H-thiazol-4-ones 1 with nitroalkenes 2

\[
\begin{align*}
\text{Ar} & \quad \text{7} \\
\text{O} & \quad \text{8} \\
\text{N} & \quad \text{9} \\
\text{S} & \quad \text{10} \\
\end{align*}
\]

Nitroalkene 2 (0.4 mmol, 2.0 equiv) and catalyst III (11.5 mg, 0.02 mmol, 0.1 equiv) were dissolved in toluene (4.0 mL) and stirred at 25 °C for 15 min. Then 5H-thiazol-4-one 1 (0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 25 °C and monitored by TLC. Upon complete consumption of 5H-thiazol-4-one 1, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with CH₂Cl₂/MeOH (800/1–300/1). Removing the solvent in vacuo, afforded products 3a-n.
7. General experimental procedure for [4+2] annulation of 5H-thiazol-4-ones 1 with 4-oxo-4-arylbutenones 5

4-Oxo-4-arylbutenone 5 (0.3 mmol, 1.5 equiv) and catalyst III (11.5 mg, 0.02 mmol, 0.1 equiv) were dissolved in CHCl₃ (4.0 mL) and stirred at −10 °C for 15 min. Then 5H-thiazol-4-one 1 (0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred at −10 °C and monitored by TLC. Upon complete consumption of 5H-thiazol-4-one 1, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with CH₂Cl₂/MeOH (800/1–200/1). Removing the solvent in vacuo, afforded products 6a-s.
8. General experimental procedure for [4+2] annulation of 5H-thiazol-4-ones 1 with 4-oxo-4-arylbutenoates 7

(R = Me): 4-Oxo-4-arylbutenoate 7 (0.3 mmol, 1.5 equiv) and catalyst III (11.5 mg, 0.02 mmol, 0.1 equiv) were dissolved in CHCl₃ (4.0 mL) and stirred at −30 °C for 15 min. Then 5H-thiazol-4-one 1 (0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred at −30 °C and monitored by TLC. Upon complete consumption of 5H-thiazol-4-one 1, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with CH₂Cl₂/MeOH (800/1–200/1). Removing the solvent in vacuo, afforded products 8a-f and 8h.

(R = Ph): 4-Oxo-4-arylbutenoate 7 (0.3 mmol, 1.5 equiv), Li₃PO₄ (0.2 mmol, 1.0 equiv) and catalyst III (22.2 mg, 0.04 mmol, 0.2 equiv) were dissolved in CHCl₃ (4.0 mL) and stirred at 30 °C for 15 min. Then 5H-thiazol-4-one 1 (0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred at 30 °C and monitored by TLC. Upon complete consumption of 5H-thiazol-4-one 1, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with CH₂Cl₂/MeOH (800/1–200/1). Removing the solvent in vacuo, afforded products 8g.
9. General experimental procedure for [4+2] annulation of 5\textit{H}-thiazol-4-ones 1 with methyleneindolinones 9

Methyleneindolinones 9 (0.3 mmol, 1.5 equiv) and catalyst III (11.5 mg, 0.02 mmol, 0.1 equiv) were dissolved in CHCl\textsubscript{3} (4.0 mL) and stirred at −30 °C for 15 min. Then 5\textit{H}-thiazol-4-one 1 (0.2 mmol, 1.0 equiv) was added. The reaction mixture was stirred at −30 °C and monitored by TLC. Upon complete consumption of 5\textit{H}-thiazol-4-one 1, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with CH\textsubscript{2}Cl\textsubscript{2}/MeOH (800/1–200/1). Removing the solvent in vacuo, afforded products 10a-n.
10. Chemoselective results

**Table 4** Reactions between 1 and 2 to afford 3 and 4

![Chemoselective reaction diagram](image)

| Entry | Ar            | R¹   | R²       | t (h) | 3a (%) | 4 (%) |
|-------|---------------|------|----------|-------|--------|-------|
| 1     | 2-quinolyl    | Me   | Ph       | 15    | 83     | 11    |
| 2     | 2-quinolyl    | Me   | 4-FPh    | 12    | 78     | 16    |
| 3     | 2-quinolyl    | Me   | 4-ClPh   | 14    | 89     | 6     |
| 4     | 2-quinolyl    | Me   | 4-BrPh   | 13    | 84     | 8     |
| 5     | 2-quinolyl    | Me   | 3-ClPh   | 15    | 85     | 9     |
| 6     | 2-quinolyl    | Me   | 2-ClPh   | 18    | 82     | 12    |
| 7     | 2-quinolyl    | Me   | 4-MePh   | 10    | 72     | 20    |
| 8     | 2-quinolyl    | Me   | 3-MePh   | 13    | 76     | 18    |
| 9     | 2-quinolyl    | Me   | 2-MePh   | 13    | 82     | 16    |
| 10    | 2-quinolyl    | Me   | 2-naphthyl | 16    | 88     | 8     |
| 11    | 2-quinolyl    | Me   | 2-furyl  | 16    | 76     | 18    |
| 12    | 2-quinolyl    | Me   | cyclohexyl | 72    | 41     | 51    |
| 13    | 2-quinolyl    | Et   | Ph       | 14    | 55     | 35    |
| 14    | 4-BrPh        | Me   | Ph       | 14    | 45     | 52    |
| 15    | 3-pyridyl     | Me   | Ph       | 10    | 76     | 19    |

*0.2 mmol scale. *Isolated yields.
Table 5 Reactions between 1 and 5 to afford 6 and 6-M

![Chemical reaction diagram]

| entry | Ar¹ | R¹ | Ar² | R² | t (h) | 6¹ yield (%) | 6-M yield (%) |
|-------|-----|----|-----|----|------|--------------|---------------|
| 1     | 2-quinolyl | Me | Ph  | Me | 24   | 86           | 8             |
| 2     | 2-quinolyl | Me | 4-CF₃Ph | Me | 10   | 90           | trace         |
| 3     | 2-quinolyl | Me | 4-ClPh | Me | 8    | 80           | 11            |
| 4     | 2-quinolyl | Me | 4-BrPh | Me | 24   | 91           | trace         |
| 5     | 2-quinolyl | Me | 3,4-Cl₂Ph | Me | 16   | 95           | trace         |
| 6     | 2-quinolyl | Me | 4-MeOPh | Me | 48   | 87           | 6             |
| 7     | 2-quinolyl | Me | 3-MeOPh | Me | 24   | 82           | 9             |
| 8     | 2-quinolyl | Me | 2-MeOPh | Me | 66   | 64           | 25            |
| 9     | 2-quinolyl | Me | 2-BrPh | Me | 40   | 60           | 28            |
| 10    | 2-quinolyl | Me | 2-thienyl | Me | 12   | 98           | 0             |
| 11    | 2-quinolyl | Me | 2-furyl | Me | 18   | 92           | trace         |
| 12    | 2-quinolyl | Me | Ph  | Et | 36   | 90           | 5             |
| 13    | 2-pyridyl  | Et | Ph  | Me | 24   | 87           | 7             |
| 14    | 3-pyridyl  | Me | Ph  | Me | 24   | 86           | 10            |
| 15    | 2-thienyl  | Me | Ph  | Me | 36   | 70           | 15            |
| 16    | 2-furyl    | Me | Ph  | Me | 16   | 75           | 13            |
| 17    | 4-BrPh     | Me | Ph  | Me | 24   | 54           | 42            |
| 18    | 2-quinolyl | Et | Ph  | Me | 18   | 72           | 10            |
| 19    | 2-quinolyl | Bn | Ph  | Me | 18   | 90           | trace         |

¹0.2 mmol scale. ²Isolated yields.
11. Exploration towards reactions between 5H-oxazol-4-ones and alkenes

The results indicated that the reactions of 5H-oxazol-4-one with a series of activated alkenes under the established reaction conditions only presented conjugate addition adducts, and the corresponding annihilation adducts were not observed yet. The moderate yields for 4-oxo-4-arylbutenone and methyleneindolinone as the substrates are produced by the instability of 5H-oxazol-4-one in the reactions.
12. Experimental procedure for 5a to 11

The [4+2] annulation adduct 5a (41.6 mg, 0.1 mmol, 1.0 equiv) was dissolved in MeOH (1.0 mL) and stirred at 0 °C. Then HCl (12 N, 0.834 mL, 10.0 mmol, 100.0 equiv) was added. The reaction mixture was stirred at room temperature until the reaction completed (3.0 hours). Evaporation of methanol followed by drying under high vacuo and neutralized by NaHCO₃ (aq.) until pH > 7. The mixture was then extracted with EtOAc (3.0 mL x 3), washed with brine, and dried over Na₂SO₄. Concentration was loaded onto a short silica gel column, followed by gradient elution with PE/EA (20/1–2/1). Removing the solvent in vacuo, afforded products gave the 11 (32.7 mg, 73%).
13. Characterization of adducts

White solid, Mp 165.3–166.5 °C; 83% yield; 95% ee; [α]_D^25 = −143.0 (c 1.00, CHCl₃);

^1^H NMR (300 MHz, CDCl₃) δ 8.34 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H),
7.90–7.87 (m, 2H), 7.81–7.73 (m, 2H), 7.68–7.60 (m, 3H), 7.50–7.44 (m, 3H), 6.27
(d, J = 4.8 Hz, 1H), 4.04 (d, J = 4.8 Hz, 1H), 1.29 (s, 3H); ^1^C NMR (75 MHz,
CDCl₃) δ 176.8, 150.1, 147.0, 138.3, 136.0, 130.6, 129.6, 129.1, 129.0, 128.6,
128.0, 127.9, 127.6, 117.4, 98.6, 76.7, 67.1, 54.8, 13.8; HRMS (ESI) m/z 392.1074 (M+H⁺), calc. for
C₂₁H₁₈N₂O₃S 392.1069.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm);
Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.7 min (minor) and
11.3 min (major).

White solid, Mp 163.0–165.0 °C; 78% yield; 97% ee; [α]_D^25 = −296.6 (c 1.00, CHCl₃);

^1^H NMR (300 MHz, CDCl₃) δ 8.34 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H),
7.90–7.87 (m, 2H), 7.81–7.72 (m, 2H), 7.68–7.61 (m, 3H), 7.16 (t, J = 8.6 Hz, 2H),
6.23 (d, J = 4.8 Hz, 1H), 4.01 (d, J = 4.8 Hz, 1H), 1.28 (s, 3H); ^1^C NMR (75 MHz,
CDCl₃) δ 176.7, 150.0, 147.1, 138.3, 131.9, 130.6, 130.3, 130.2, 129.6, 128.6,
127.7, 117.4, 116.2, 115.9, 98.6, 76.7, 66.9, 54.3, 13.8; HRMS (ESI) m/z 410.0972 (M+H⁺), calc. for
C₂₁H₁₈F₂N₂O₃S 410.0975.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm);
Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.9 min (minor) and
11.9 min (major).
White solid, Mp 97.5–98.6 °C; 89% yield; 94% ee; [α]_D^{29} = –298.7 (c 1.00, CHCl₃);

$^1$H NMR (300 MHz, CDCl₃) δ 8.34 (d, $J = 8.5$ Hz, 1H), 8.07 (d, $J = 8.5$ Hz, 1H), 7.90–7.85 (m, 2H), 7.81–7.72 (m, 2H), 7.66–7.61 (m, 3H), 7.44 (d, $J = 8.5$ Hz, 2H), 7.26 (s, 2H), 6.22 (d, $J = 4.8$ Hz, 1H), 4.00 (d, $J = 4.8$ Hz, 1H), 1.29 (s, 4H); $^{13}$C NMR (75 MHz, CDCl₃) δ 176.7, 150.0, 147.1, 138.3, 135.0, 134.6, 130.6, 129.8, 129.6, 129.3, 128.0, 127.9, 127.7, 117.4, 98.3, 76.8, 66.8, 54.4, 13.8; HRMS (ESI) m/z 426.0683 (M+H⁺), calc. for C₂₁H₁₇ClN₃O₃S 426.0679.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.0 min (minor) and 12.4 min (major).

White solid, Mp 95.4–97.1 °C; 84% yield; 96% ee; [α]_D^{21} = –254.6 (c 1.00, CHCl₃);

$^1$H NMR (300 MHz, CDCl₃) δ 8.34 (d, $J = 8.4$ Hz, 1H), 8.07 (d, $J = 8.4$ Hz, 1H), 7.88 (d, $J = 7.1$ Hz, 2H), 7.81–7.72 (m, 2H), 7.66–7.54 (m, 5H), 6.22 (d, $J = 4.8$ Hz, 1H), 3.98 (d, $J = 4.8$ Hz, 1H), 1.29 (s, 3H); $^{13}$C NMR (75 MHz, CDCl₃) δ 176.8, 150.0, 147.1, 138.3, 135.1, 132.2, 130.6, 129.6, 128.0, 127.9, 127.6, 123.1, 117.4, 98.1, 76.8, 66.7, 54.5, 13.8; HRMS (ESI) m/z 470.0175 (M+H⁺), calc. for C₂₁H₁₇BrN₃O₃S 470.0174.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.2 min (minor) and 12.9 min (major).
White solid, Mp 163.2–165.8 °C; 85% yield; 92% ee; \([\alpha]_D^{20} = -464.2\) (c 1.00, CHCl₃);

\(^1\)H NMR (300 MHz, CDCl₃) \(\delta\) 8.34 (d, \(J = 8.4\) Hz, 1H), 8.08 (d, \(J = 8.4\) Hz, 1H), 7.89 (d, \(J = 7.0\) Hz, 2H), 7.81–7.73 (m, 3H), 7.66–7.61 (m, 1H), 7.53–7.51 (m, 1H), 7.45–7.37 (m, 2H), 6.23 (d, \(J = 4.8\) Hz, 1H), 4.00 (d, \(J = 4.8\) Hz, 1H), 1.31 (s, 3H);

\(^{13}\)C NMR (75 MHz, CDCl₃) \(\delta\) 176.5, 150.0, 147.1, 138.3, 138.2, 135.0, 130.6, 130.3, 129.6, 129.2, 128.2, 128.0, 127.9, 127.7, 127.2, 117.4, 98.3, 76.8, 66.8, 54.6, 13.8; HRMS (ESI) m/z 426.0684 (M⁺H⁺), calc. for C₁₂H₁₁ClN₃O₃S 426.0679.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.0 min (minor) and 11.6 min (major).

White solid, Mp 184.0–185.6 °C; 82% yield; 95% ee; \([\alpha]_D^{20} = -306.2\) (c 1.00, CHCl₃);

\(^1\)H NMR (300 MHz, CDCl₃) \(\delta\) 8.34 (d, \(J = 8.2\) Hz, 1H), 8.10 (dd, \(J = 16.6, 8.2\) Hz, 2H), 7.88 (d, \(J = 8.2\) Hz, 1H), 7.77 (dd, \(J = 16.6, 7.6\) Hz, 3H), 7.68–7.59 (m, 1H), 7.52 (d, \(J = 7.6\) Hz, 1H), 7.41 (dt, \(J = 16.6, 7.6\) Hz, 2H), 6.28 (d, \(J = 4.8\) Hz, 1H), 4.89 (d, \(J = 4.8\) Hz, 1H), 1.35 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl₃) \(\delta\) 176.3, 150.1, 147.2, 138.3, 135.9, 133.9, 130.7, 130.2, 130.0, 129.7, 128.1, 128.0, 127.8, 127.7, 127.6, 117.4, 77.0, 98.1, 67.5, 49.7, 12.9; HRMS (ESI) m/z 426.0675 (M⁺H⁺), calc. for C₁₂H₁₁ClN₃O₃S 426.0679.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.8 min (minor) and 15.7 min (major).
White solid, Mp 160.7–161.9 °C; 72% yield; 95% ee; [α]_D^26 –120.4 (c 1.00, CHCl₃);

1H NMR (300 MHz, CDCl₃) δ 8.33 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.89–7.77 (m, 2H), 7.74 (d, J = 8.4 Hz, 1H), 7.65–7.60 (m, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.27 (s, 1H), 7.25 (s, 1H), 6.24 (d, J = 4.8 Hz, 1H), 4.00 (d, J = 4.8 Hz, 1H), 2.40 (s, 3H), 1.29 (s, 3H); 13C NMR (75 MHz, CDCl₃) δ 176.8, 150.2, 147.1, 138.8, 138.2, 133.0, 130.6, 129.7, 129.6, 128.4, 128.0, 127.9, 127.7, 117.4, 98.8, 76.7, 67.1, 54.6, 21.2, 13.8; HRMS (ESI) m/z 406.1222 (M+H⁺), calc. for C₂₂H₂₀N₃O₃S 406.1225.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.8 min (minor) and 14.2 min (major).

White solid, Mp 169.6–170.8 °C; 76% yield; 96% ee; [α]_D^26 –218.1 (c 1.00, CHCl₃);

1H NMR (300 MHz, CDCl₃) δ 8.34 (d, J = 8.5 Hz, 1H), 8.07 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.77 (dd, J = 16.3, 7.8 Hz, 3H), 7.63 (t, J = 7.5 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.43 (s, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.23 (s, 1H), 6.24 (d, J = 4.8 Hz, 1H), 3.99 (d, J = 4.8 Hz, 1H), 2.43 (s, 3H), 1.30 (s, 3H); 13C NMR (75 MHz, CDCl₃) δ 176.8, 150.2, 147.1, 138.8, 138.2, 135.9, 130.6, 129.7, 129.6, 129.4, 129.0, 128.0, 127.9, 127.6, 125.5, 117.5, 98.8, 76.7, 67.1, 54.9, 21.6, 13.8; HRMS (ESI) m/z 406.1223 (M+H⁺), calc. for C₂₂H₂₀N₃O₃S 406.1225.
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.9 min (minor) and 12.9 min (major).

White solid, Mp 182.2–183.5 °C; 82% yield; 93% ee; [α]D 34.6 (c 1.00, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.33 (d, J = 8.3 Hz, 1H), 8.11–8.06 (m, 2H), 7.96 (s, 1H), 7.88 (d, J = 8.3 Hz, 1H), 7.80–7.73 (m, 2H), 7.65–7.60 (m, 1H), 7.38–7.29 (m, 3H), 6.24 (d, J = 4.9 Hz, 1H), 4.49 (d, J = 4.9 Hz, 1H), 2.40 (s, 3H), 1.29 (s, 3H);

13C NMR (75 MHz, CDCl3) δ 176.9, 150.2, 147.1, 138.2, 137.8, 134.6, 131.0, 130.6, 129.6, 128.5, 128.0, 127.8, 127.6, 126.9, 125.9, 117.4, 99.6, 76.8, 67.4, 48.9, 20.4, 13.0; HRMS (ESI) m/z 406.1229 (M+H+), calc. for C22H20N3O3S 406.1225.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.3 min (minor) and 9.5 min (major).

White solid, Mp 181.4–183.0 °C; 88% yield; 95% ee; [α]D 384.7 (c 1.00, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.36 (d, J = 9.1 Hz, 1H), 8.09 (d, J = 9.7 Hz, 2H), 7.97–7.85 (m, 6H), 7.79 (t, J = 7.6 Hz, 2H), 7.63 (t, J = 7.6 Hz, 1H), 7.61–7.54 (m, 2H), 6.40 (d, J = 4.7 Hz, 1H), 4.20 (d, J = 4.7 Hz, 1H), 1.32 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 176.8, 150.2, 147.1, 138.3, 133.4, 133.3, 130.6, 129.6, 129.0, 128.4,
128.1, 127.9, 127.7, 126.7, 125.5, 117.5, 98.5, 76.8, 67.1, 55.2, 13.9; HRMS (ESI) m/z 442.1231 (M+H+), calc. for C_{28}H_{20}N_3O_5S 442.1225.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.0 min (minor) and 16.9 min (major).

White solid, Mp 156.2–157.9 °C; 76% yield; 94% ee; [\alpha]_{D}^{25} = -251.7 (c 1.00, CHCl3);

\(^1\)H NMR (300 MHz, CDCl3) \(\delta\) 8.33 (d, \(J = 8.4\) Hz, 1H), 8.07 (d, \(J = 8.4\) Hz, 1H), 7.88 (d, \(J = 8.4\) Hz, 1H), 7.83 (s, 1H), 7.78 (t, \(J = 7.6\) Hz, 1H), 7.72 (d, \(J = 8.4\) Hz, 1H), 7.63 (t, \(J = 7.6\) Hz, 1H), 7.53 (d, \(J = 2.1\) Hz, 1H), 6.56 (d, \(J = 2.1\) Hz, 1H), 6.51 – 6.44 (m, 1H), 6.27 (d, \(J = 4.6\) Hz, 1H), 4.27 (d, \(J = 4.6\) Hz, 1H), 1.41 (s, 3H);

\(^{13}\)C NMR (75 MHz, CDCl3) \(\delta\) 176.1, 149.9, 149.2, 147.0, 143.4, 138.3, 130.6, 129.6, 128.0, 127.9, 127.6, 117.3, 110.8, 109.9, 96.8, 76.8, 66.4, 49.3, 13.4; HRMS (ESI) m/z 382.0864 (M+H+), calc. for C_{19}H_{16}N_3O_5S 382.0862.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.9 min (minor) and 14.7 min (major).
White solid, Mp 94.0–95.6 °C; 41% yield; 82% ee; [α]_D^{26} = −136.7 (c 1.00, CHCl₃); \(^1\)H NMR (300 MHz, CDCl₃) δ 8.30 (d, \(J = 8.6\) Hz, 1H), 8.05 (d, \(J = 8.6\) Hz, 1H), 7.86 (d, \(J = 7.6\) Hz, 1H), 7.77 (d, \(J = 7.6\) Hz, 2H), 7.61 (d, \(J = 7.6\) Hz, 2H), 5.85 (d, \(J = 4.3\) Hz, 1H), 2.97 (s, 1H), 2.09–1.78 (m, 5H), 1.70 (s, 3H), 1.37–1.19 (m, 6H); \(^1\)C NMR (75 MHz, CDCl₃) δ 177.1, 149.9, 147.0, 138.2, 130.6, 129.6, 128.0, 127.8, 127.6, 117.3, 95.0, 64.5, 52.9, 37.8, 32.0, 28.5, 26.2, 26.0, 13.3; HRMS (ESI) m/z 398.1536 (M+H⁺), calc. for C₂₁H₂₆N₂O₃S 398.1538.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.8 min (minor) and 16.5 min (major).

Green solid, Mp 131.8–132.9 °C; 55% yield; 98% ee; [α]_D^{26} = −201.9 (c 1.98, CHCl₃); \(^1\)H NMR (300 MHz, CDCl₃) δ 8.33 (d, \(J = 8.4\) Hz, 1H), 8.06 (d, \(J = 8.4\) Hz, 1H), 7.90–7.86 (m, 2H), 7.78–7.74 (m, 2H), 7.67–7.59 (m, 3H), 7.45–7.43 (m, 3H), 6.30 (d, \(J = 4.8\) Hz, 1H), 4.03 (d, \(J = 4.8\) Hz, 1H), 2.08–1.96 (m, 1H), 1.33–1.21 (m, 1H), 0.95 (t, \(J = 7.3\) Hz, 3H); \(^1\)C NMR (75 MHz, CDCl₃) δ 176.2, 150.5, 147.1, 138.2, 136.3, 130.5, 129.6, 129.0, 128.8, 128.0, 127.8, 127.6, 117.6, 98.6, 76.0, 73.6, 55.2, 21.4, 10.9; HRMS (ESI) m/z 406.1228 (M+H⁺), calc. for C₂₂H₂₄N₂O₃S 406.1225.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.7 min (minor) and 11.6 min (major).
White solid, Mp 165.3–171.9 °C; 45% yield; 90% ee; [α]D 181.8 (c 1.48, CHCl3); 1H NMR (300 MHz, CDCl3) δ 8.22 (s, 1H), 7.64–7.57 (m, 4H), 7.50–7.49 (m, 2H), 7.43–7.41 (m, 3H), 5.98 (d, J = 4.7 Hz, 1H), 3.90 (d, J = 4.7 Hz, 1H), 1.23 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 178.2, 135.6, 132.6, 130.3, 129.1, 128.5, 127.4, 124.3, 98.5, 76.3, 66.1, 56.1, 13.4; HRMS (ESI) m/z 419.0064 (M+H+), calc. for C18H16BrN2O3 419.0065.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.9 min (minor) and 14.2 min (major).

White solid, Mp 136.9–138.1 °C; 76% yield; 95% ee; [α]D 569.3 (c 1.00, CHCl3); 1H NMR (300 MHz, CDCl3) δ 8.62–8.61 (m, 1H), 7.89–7.83 (m, 2H), 7.70 (d, J = 7.9 Hz, 1H), 7.64–7.61 (m, 2H), 7.45–7.35 (m, 4H), 6.21 (d, J = 4.8 Hz, 1H), 3.91 (d, J = 4.8 Hz, 1H), 1.24 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 177.4), 150.8, 149.6, 137.7, 136.0, 129.0, 128.9, 128.6, 124.5, 120.8, 98.2, 76.6, 66.6, 55.3, 13.7; HRMS (ESI) m/z 342.0911 (M+H+), calc. for C17H16N3O3S 342.0912.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.3 min (minor) and 13.0 min (major).
White solid, Mp 164.9–165.8 °C; 86% yield; 98% ee; [α]D24 +169.6 (c 2.37, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.14 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H),
7.68–7.63 (m, 3H), 7.61–7.56 (m, 2H), 7.48 (dd, J = 7.8, 7.2 Hz, 1H), 7.34 (t, J =
7.2 Hz, 1H), 7.22 (t, J = 7.8 Hz, 2H), 5.70 (d, J = 5.4 Hz, 1H), 3.56 (d, J = 5.4 Hz,
1H), 2.28 (s, 3H), 1.77 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 204.9, 198.2, 176.5,
152.2, 146.7, 137.6, 136.9, 133.1, 129.9, 129.2, 128.4, 128.0, 127.5, 127.3, 127.2, 118.2, 79.6, 66.6,
62.0, 58.4, 32.8, 14.4; HRMS (ESI) m/z 417.1277 (M+H+), calc. for C24H21N2O3S 417.1273.
The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm);
Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.2 min (minor)
and 41.6 min (major).

White solid, Mp 181.7–183.6 °C; 90% yield; 98% ee; [α]D25 −144.8 (c 4.22, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.13 (d, J = 8.4 Hz, 1H), 7.71–7.67 (m, 4H), 7.60–7.53
(m, 3H), 7.51–7.46 (m, 1H), 7.38 (d, J = 8.4 Hz, 2H), 5.65 (d, J = 5.2 Hz, 1H),
3.67 (d, J = 5.2 Hz, 1H), 2.32 (s, 3H), 1.79 (s, 3H); 13C NMR (75 MHz, CDCl3) δ
204.6, 197.2, 176.2, 151.7, 146.5, 139.8, 137.8, 134.2, 133.8, 130.2, 128.8, 128.2,
127.5, 127.4, 125.2, 125.1, 125.0, 121.3, 118.2, 79.7, 66.7, 62.4, 58.2, 32.6, 14.5; HRMS (ESI) m/z
485.1149 (M+H+), calc. for C23H20F3N2O3S 485.1147.
The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm);
Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time: 15.7 min (minor)
24.9 min (major).
Pale yellow solid, Mp 143.2–145.0 °C; 80% yield; 97% ee; [α]$_D^{26}$ = −172.8 (c 2.92, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) δ 8.16 (d, $J = 8.7$ Hz, 1H), 7.73 (t, $J = 8.7$ Hz, 2H), 7.66–7.58 (m, 4H), 7.52–7.48 (m, 2H), 7.18 (d, $J = 8.7$ Hz, 2H), 5.64 (d, $J = 5.3$ Hz, 1H), 3.56 (d, $J = 5.3$ Hz, 1H), 2.30 (s, 3H), 1.78 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.7, 197.0, 176.4, 152.0, 146.7, 139.7, 137.7, 135.3, 130.1, 129.4, 129.1, 128.6, 127.6, 127.4, 118.3, 79.8, 66.7, 61.6, 58.5, 32.7, 14.5; HRMS (ESI) m/z 451.0881 (M+H$^+$), calc. for C$_{24}$H$_{20}$ClN$_2$O$_3$S 451.0883.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.5 min (minor) and 32.7 min (major).

White solid, Mp 175.2–176.5 °C; 91% yield; 99% ee; [α]$_D^{26}$ = −167.5 (c 1.26, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) δ 8.18 (d, $J = 8.4$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 1H), 7.71 (d, $J = 8.4$ Hz, 1H), 7.67–7.60 (m, 2H), 7.54–7.49 (m, 3H), 7.42 (s, 1H), 7.35 (d, $J = 8.4$ Hz, 2H), 5.62 (d, $J = 5.3$ Hz, 1H), 3.57 (d, $J = 5.3$ Hz, 1H), 2.31 (s, 3H), 1.79 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.7, 197.2, 176.4, 151.9, 146.7, 137.8, 135.7, 131.7, 130.2, 129.5, 129.1, 128.4, 127.6, 127.5, 127.4, 118.2, 79.7, 66.7, 61.7, 58.4, 32.8, 14.5; HRMS (ESI) m/z 495.0381 (M+H$^+$), calc. for C$_{24}$H$_{20}$BrN$_2$O$_3$S 495.0378.
The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.8 min (minor) and 32.0 min (major).

White solid, Mp 176.8–178.7 °C; 95% yield; 94% ee; [α]D 191.5 (c 4.46, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.20 (d, J = 8.4 Hz, 1H), 7.76–7.68 (m, 3H), 7.62–7.58 (m, 3H), 7.53–7.48 (m, 1H), 7.44 (dd, J = 8.4, 1.9 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 5.52 (d, J = 5.2 Hz, 1H), 3.69 (d, J = 5.2 Hz, 1H), 2.34 (s, 3H), 1.79 (s, 3H);

13C NMR (75 MHz, CDCl3) δ 204.6, 195.6, 176.2, 151.7, 146.5, 137.8, 137.5, 136.4, 132.8, 130.3, 130.2, 129.8, 128.9, 127.6, 127.5, 127.4, 127.0, 118.2, 79.7, 66.7, 62.2, 58.1, 32.6, 14.5; HRMS (ESI) m/z 485.0493 (M+H’), calc. for C33H19Cl2N2O3S 485.0493.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.9 min (minor) and 30.3 min (major).

White solid, Mp 148.5–150.0 °C; 87% yield; 97% ee; [α]D 190.5 (c 3.78, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.14 (d, J = 8.7 Hz, 1H), 7.73 (dd, J = 8.7, 5.3 Hz, 3H), 7.65 (t, J = 5.3 Hz, 2H), 7.67–7.55 (m, 2H), 7.51–7.46 (m, 1H), 6.69 (d, J = 8.7 Hz, 2H), 5.64 (d, J = 5.4 Hz, 1H), 3.72 (s, 3H), 3.54 (d, J = 5.4 Hz, 1H), 2.29 (s,
3H), 1.76 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 205.1, 196.3, 176.6, 163.6, 152.4, 146.8, 137.5, 130.4, 129.9, 129.8, 129.4, 127.6, 127.3, 127.2, 118.2, 113.6, 79.7, 66.6, 61.5, 58.7, 55.4, 32.8, 14.4; HRMS (ESI) m/z 447.1377 (M+H$^+$), calc. for C$_{25}$H$_{23}$N$_2$O$_4$S 447.1379.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 34.1 min (minor) and 48.8 min (major).

![HPLC graph]

White solid, Mp 149.1–150.8 °C; 82% yield; 96% ee; $[\alpha]_D^{24}$ –192.4 (c 1.47, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.17 (d, $J$ = 8.3 Hz, 1H), 7.73 (t, $J$ = 8.3 Hz, 3H), 7.62 (dd, $J$ = 11.2, 4.6 Hz, 1H), 7.53–7.47 (m, 2H), 7.22 (d, $J$ = 7.7 Hz, 1H), 7.14 (dt, $J$ = 11.2, 4.6 Hz, 2H), 6.89–6.86 (m, 1H), 5.65 (d, $J$ = 5.4 Hz, 1H), 3.72 (s, 3H), 3.55 (d, $J$ = 5.4 Hz, 1H), 2.30 (s, 3H), 1.78 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.9, 197.9, 176.4, 159.5, 152.1, 146.8, 138.2, 137.6, 130.0, 129.4, 129.3, 127.6, 127.4, 127.3, 120.6, 119.9, 118.2, 112.0, 79.5, 66.6, 62.5, 58.4, 55.34, 32.9, 14.4; HRMS (ESI) m/z 447.1381 (M+H$^+$), calc. for C$_{25}$H$_{23}$N$_2$O$_4$S 447.1379.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 23.1 min (minor) and 42.7 min (major).

![HPLC graph]
Weak yellow solid, Mp 132.1–133.8 °C; 64% yield; 94% ee; [α]_D^26 –198.8 (c 2.28, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.00 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 8.5 Hz, 1H), 7.70–7.62 (m, 3H), 7.56 (d, J = 8.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.03–6.97 (m, 2H), 6.54–6.46 (m, 2H), 5.52 (d, J = 5.2 Hz, 1H), 3.80 (d, J = 5.2 Hz, 1H), 3.72 (s, 3H), 2.32 (s, 3H), 1.74 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 205.0, 199.3, 176.2, 156.8, 151.9, 146.6, 137.0, 132.8, 129.9, 129.7, 129.3, 128.5, 127.4, 127.3, 127.2, 120.3, 117.6, 110.4, 78.8, 68.5, 66.4, 57.1, 55.0, 32.3, 14.0; HRMS (ESI) m/z 447.1383 (M+H⁺), calc. for C₂₅H₂₃N₂O₄S 447.1379.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 25.0 min (minor) and 31.4 min (major).

White solid, Mp 151.5–153.0 °C; 60% yield; 99% ee; [α]_D^3 –170.0 (c 0.725, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.94 (d, J = 8.6 Hz, 1H), 7.85 (d, J = 8.6 Hz, 1H), 7.72 (s, 1H), 7.67–7.62 (m, 2H), 7.54–7.45 (m, 2H), 7.11 (dd, J = 7.6, 1.6 Hz, 1H), 6.83 (dd, J = 7.6, 1.6 Hz, 1H), 6.76–6.65 (m, 2H), 5.44 (d, J = 5.1 Hz, 1H), 3.90 (d, J = 5.1 Hz, 1H), 2.29 (s, 3H), 1.71 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 204.6, 198.8, 175.9, 151.4, 146.5, 140.2, 137.5, 132.9, 131.2, 130.2, 129.3, 128.7, 127.5, 127.4, 126.6, 118.6, 117.6, 78.2, 68.2, 66.5, 56.6, 32.6, 14.3; HRMS (ESI) m/z 495.0375 (M+H⁺), calc. for C₂₅H₂₅BrN₂O₄S 495.0378.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.7 min (major) and 23.0 min (minor).
White solid, Mp 179.1–181.0 °C; 98% yield; 99% ee; [α]$_D^{26}$ $-147.2$ (c 4.06, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.19 (d, $J = 8.2$ Hz, 1H), 7.76–7.73 (m, 3H), 7.65 (s, 1H), 7.63–7.58 (m, 1H), 7.51 (d, $J = 8.2$ Hz, 1H), 7.46–7.44 (m, 2H), 6.89–6.86 (m, 1H), 5.52 (d, $J = 5.4$ Hz, 1H), 3.65 (d, $J = 5.4$ Hz, 1H), 2.35 (s, 3H), 1.78 (s, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.8, 190.2, 176.6, 152.1, 146.8, 144.2, 137.6, 134.7, 132.5, 130.9, 129.3, 128.0, 127.6, 127.4, 127.3, 118.3, 79.8, 66.7, 62.5, 59.0, 32.8, 14.4;

HRMS (ESI) m/z 423.0833 (M+H$^+$), calc. for C$_{22}$H$_{19}$N$_2$O$_2$S $423.0837$

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 34.4 min (minor) and 68.6 min (major).

White solid, Mp 165.0–166.2 °C; 92% yield; 99% ee; $[\alpha]_D^{26}$ $-192.1$ (c 1.36, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.20 (d, $J = 8.0$ Hz, 1H), 7.83–7.73 (m, 3H), 7.64 (t, $J = 8.0$ Hz, 1H), 7.55–7.50 (m, 2H), 7.27 (s, 1H), 7.03 (d, $J = 3.6$ Hz, 1H), 6.36–6.31 (m, 1H), 5.39 (d, $J = 5.3$ Hz, 1H), 3.64 (d, $J = 5.3$ Hz, 1H), 2.39 (s, 3H), 1.77 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.5, 185.3, 176.3, 152.3, 152.2, 146.9, 146.6, 137.5, 130.0, 129.4, 127.6, 127.4, 127.3, 118.2, 118.1, 112.5, 79.2, 66.3, 62.9, 58.3, 32.2, 14.3;

HRMS (ESI) m/z 407.1069 (M+H$^+$), calc. for C$_{22}$H$_{19}$N$_2$O$_2$S $407.1066$

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time: 24.4 min (minor) and 38.8 min (major).
White solid, Mp 158.2–160.0 °C; 90% yield; 97% ee; [α]_D^20 –199.8 (c 2.65, CHCl₃);

1H NMR (300 MHz, CDCl₃) δ 8.15 (d, J = 8.5 Hz, 1H), 7.74–7.70 (m, 3H), 7.64–7.56 (m, 3H), 7.54–7.46 (m, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 5.69 (d, J = 5.5 Hz, 1H), 3.50 (d, J = 5.5 Hz, 1H), 2.71–2.60 (m, 1H), 2.35–2.22 (m, 1H), 1.71 (s, 3H), 1.04 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl₃) δ 207.9, 198.3, 176.6, 152.2, 146.8, 137.6, 136.9, 133.2, 129.9, 129.3, 128.4, 128.0, 127.6, 127.3, 127.2, 118.2, 79.5, 66.8, 62.3, 57.4, 39.2, 14.2, 7.6; HRMS (ESI) m/z 431.1430 (M+H⁺), calc. for C_{25}H_{33}N_{2}O_{3}S 431.1429.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.0 min (minor) and 22.4 min (major).

White solid, Mp 138.6–139.1 °C; 87% yield; 98% ee; [α]_D^20 –104.5 (c 1.71, CHCl₃);

1H NMR (300 MHz, CDCl₃) δ 8.81 (d, J = 1.8 Hz, 1H), 8.54 (dd, J = 4.8, 1.8 Hz, 1H), 7.87 – 7.83 (m, 1H), 7.64 – 7.62 (m, 3H), 7.55 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.29 – 7.27 (m, 1H), 5.44 (d, J = 5.4 Hz, 1H), 3.35 (d, J = 5.4 Hz, 1H), 2.24 (s, 3H), 1.71 (s, 3H); 13C NMR (75 MHz, CDCl₃) δ 204.5, 198.3, 177.1, 150.2, 147.3, 136.0, 134.2, 133.9, 130.2, 129.0, 128.0, 123.5, 76.4, 65.6, 61.6, 59.1, 33.0, 14.2; HRMS (ESI) m/z 367.1119 (M+H⁺), calc. for C_{20}H_{19}N_{2}O_{3}S 367.1116.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.9 min (major) and 23.6 min (minor).
White solid, Mp 120.2–122.1 °C; 86% yield; [α]D 112.9 (c 1.81, CHCl3);

1H NMR (300 MHz, CDCl3) δ 8.28–8.27 (m, 1H), 7.67–7.61 (m, 1H), 7.59–7.55 (m, 3H), 7.44–7.38 (m, 1H), 7.28 – 7.23 (m, 3H), 7.10–7.06 (m, 1H), 5.50 (d, J = 5.4 Hz, 1H), 3.40 (d, J = 5.4 Hz, 1H), 2.19 (s, 3H), 1.67 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 204.8, 198.0, 176.6, 152.6, 149.1, 137.1, 136.6, 133.5, 128.6, 128.1, 123.7, 121.0, 78.9, 66.2, 62.4, 58.6, 32.8, 14.4; HRMS (ESI) m/z 367.1112 (M+H+), calc. for C20H19N2O3S 367.1116.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.9 min (major) and 33.6 min (minor).

White solid, Mp 134.4–135.6 °C; 70% yield; 99% ee; [α]D 99.7 (c 0.48, CHCl3);

1H NMR (300 MHz, CDCl3) δ 7.74 (d, J = 7.5 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.28 (dd, J = 5.1, 2.4 Hz, 1H), 7.11–7.10 (m, 1H), 6.98 (s, 1H), 6.90 (dd, J = 5.1, 2.4 Hz, 1H), 5.43 (d, J = 5.5 Hz, 1H), 3.26 (d, J = 5.5 Hz, 1H), 2.21 (s, 3H), 1.70 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 204.2, 198.6, 176.7, 136.9, 136.3, 134.2, 129.1, 128.2, 127.2, 126.6, 126.3, 75.3, 66.2, 61.8, 59.8, 32.9, 14.3; HRMS (ESI) m/z 372.0733 (M+H+), calc. for C19H16NO3S2 372.0728.
The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.4 min (minor) and 25.9 min (major).

White solid, Mp 155.2–156.7 °C; 75% yield; 99% ee; $[\alpha]_D^{20} = -94.3$ (c 0.74, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.72 (d, $J = 7.6$ Hz, 2H), 7.56 (t, $J = 7.6$ Hz, 1H), 7.42 (t, $J = 7.6$ Hz, 2H), 7.29 (s, 1H), 6.91 (s, 1H), 6.45 (d, $J = 3.3$ Hz, 1H), 6.32–6.30 (m, 1H), 5.42 (d, $J = 5.5$ Hz, 1H), 3.32 (d, $J = 5.5$ Hz, 1H), 2.22 (s, 3H), 1.70 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 204.4, 198.1, 176.4, 146.5, 143.0, 136.2, 134.0, 128.9, 128.2, 111.1, 109.0, 72.9, 65.6, 60.8, 58.7, 32.8, 14.3; HRMS (ESI) m/z 356.0958 (M+H$^+$), calc. for C$_{10}$H$_{15}$NO$_3$S 356.0957.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 50.3 min (major) and 54.5 min (minor).

White solid, Mp 140.0–141.8 °C; 54% yield; 99% ee; $[\alpha]_D^{20} = -111.6$ (c 1.61, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.68–7.63 (m, 2H), 7.59–7.54 (m, 1H), 7.48–7.45 (m, 2H), 7.41–7.38 (m, 4H), 7.29 (s, 1H), 5.40 (d, $J = 5.4$ Hz, 1H), 3.31 (d, $J = 5.4$ Hz, 1H), 2.23 (s, 3H), 1.69 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 204.6, 198.4, 177.2, 136.2, 134.2, 133.0, 132.1, 129.0, 128., 127.6, 123.2, 77.7, 65.7, 61.6, 59.4, 33.04, 14.3; HRMS (ESI) m/z 444.0273 (M+H$^+$), calc. for C$_{21}$H$_{16}$BrNO$_3$S 444.0269.
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.7 min (minor) and 9.6 min (major).

![HPLC Chromatogram](image)

Weak yellow solid, Mp 128.1–129.6 °C; 72% yield; 97% ee; [α]_{D}^{26} = -102.5 (c 1.06, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.16 (d, J = 8.5 Hz, 1H), 7.77–7.66 (m, 5H), 7.62–7.56 (m, 1H), 7.52–7.46 (m, 1H), 7.43 (s, 1H), 7.40–7.35 (m, 1H), 7.28–7.23 (m, 1H), 5.70 (d, J = 5.5 Hz, 1H), 3.51 (d, J = 5.5 Hz, 1H), 2.55–2.42 (m, 1H), 2.27 (s, 3H), 1.92–1.80 (m, 1H), 1.15 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 205.3, 198.5, 175.8, 152.4, 146.8, 137.6, 137.0, 133.2, 130.0, 129.3, 128.4, 128.1, 127.6, 127.4, 127.3, 118.3, 79.0, 74.0, 61.9, 58.6, 33.2, 22.1, 12.1; HRMS (ESI) m/z 431.1431 (M+H⁺), calc. for C₂₂H₃₁N₂O₃S 431.1429.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 25.8 min (minor) and 46.4 min (major).

![HPLC Chromatogram](image)

Weak yellow solid, Mp 137.3–138.8 °C; 90% yield; 98% ee; [α]_{D}^{26} = -83.3 (c 4.68, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.06 (d, J = 8.5 Hz, 1H), 7.69–7.62 (m, 6H), 7.58–7.53 (m, 1H), 7.48–7.42 (m, 1H), 7.39–7.34 (m, 3H), 7.30–7.22 (m, 5H), 5.66 (d, J = 5.6 Hz, 1H), 3.87 (d, J = 13.5 Hz, 1H), 3.67 (d, J = 5.6 Hz, 1H), 3.02 (d, J = 13.5 Hz, 1H), 2.29 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 205.6, 198.1, 175.6,
152.1, 146.6, 137.4, 137.2, 136.9, 133.2, 129.8, 129.1, 128.4, 128.3, 128.0, 127.5, 127.3, 127.2, 118.3, 79.1, 74.1, 62.5, 58.2, 33.8, 33.3; HRMS (ESI) m/z 493.1583 (M+H^+), calc. for C_{30}H_{28}N_{2}O_{3}S 493.1586.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.4 min (minor) and 31.8 min (major).

White solid, Mp 141.8–143.2 °C; 87% yield; 95% ee; [α]_D^{28} = –138.4 (c 1.95, CHCl_3);

1H NMR (300 MHz, CDCl_3) δ 8.15 (d, J = 8.5 Hz, 1H), 7.74–7.66 (m, 5H), 7.62 – 7.56 (m, 1H), 7.52–7.44 (m, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 5.76 (d, J = 5.4 Hz, 1H), 4.36–4.22 (m, 2H), 3.34 (d, J = 5.4 Hz, 1H), 1.76 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); 13C NMR (75 MHz, CDCl_3) δ 198.0, 176.6, 170.6, 152.2, 146.8, 137.6, 137.1, 133.1, 129.9, 129.3, 128.3, 128.1, 127.6, 127.4, 127.3, 118.3, 79.9, 66.5, 62.0, 61.8, 53.3, 14.3, 14.2; HRMS (ESI) m/z 447.1383 (M+H^+), calc. for C_{25}H_{23}N_{2}O_{3}S 447.1379.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time: 14.9 min (minor) and 18.1 min (major).
White solid, Mp 157.3–159.0 °C; 97% yield; 97% ee; \([\alpha]_D^{20} = -170.7\) (c 4.98, CHCl₃);

²H NMR (300 MHz, CDCl₃) δ 8.16 (d, \(J = 8.4\) Hz, 1H), 7.73 (t, \(J = 8.4\) Hz, 2H), 7.65–7.57 (m, 5H), 7.53–7.47 (m, 1H), 7.35 (d, \(J = 8.4\) Hz, 2H), 5.69 (d, \(J = 5.4\) Hz, 1H), 4.36–4.19 (m, 2H), 3.35 (d, \(J = 5.4\) Hz, 1H), 1.75 (s, 3H), 1.29 (t, \(J = 7.1\) Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 197.1, 176.61, 170.51, 152.1, 146.7, 137.7, 135.8, 131.5, 130.1, 129.6, 129.1, 128.4, 127.6, 127.4, 118.4, 80.1, 66.6, 61.8, 61.7, 53.2, 14.3, 14.2; HRMS (ESI) m/z 525.0486 (M+H⁺), calc. for C₂₃H₂₂BrN₂O₄S 525.0484.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.2 mL/min; 25 °C; 254 nm; retention time: 39.0 min (major) and 42.1 min (minor).

White solid, Mp 155.4–156.5 °C; 96% yield; 98% ee; \([\alpha]_D^{20} = -124.7\) (c 2.76, CHCl₃);

²H NMR (300 MHz, CDCl₃) δ 8.20 (s, 1H), 7.78–7.74 (m, 1H), 7.72–7.70 (m, 1H), 7.63 (d, \(J = 3.6\) Hz, 2H), 7.58–7.49 (m, 3H), 7.27–7.24 (m, 1H), 5.59 (d, \(J = 5.2\) Hz, 1H), 4.30 (qq, \(J = 10.8, 7.1\) Hz, 2H), 3.43 (d, \(J = 5.2\) Hz, 1H), 1.77 (s, 3H), 1.32 (t, \(J = 7.1\) Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 195.6, 176.5, 170.4, 151.8, 146.6, 137.8, 137.6, 136.6, 132.9, 130.3, 130.2, 130.0, 129.0, 127.6, 127.5, 127.1, 118.3, 80.0, 66.6, 62.4, 62.0, 52.9, 14.3, 14.2; HRMS (ESI) m/z 515.0602 (M+H⁺), calc. for C₂₅H₂₁Cl₂N₂O₄S 515.0599.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.1 min (major) and 14.4 min (minor).
Weak yellow solid, Mp 122.2–124.0 °C; 90% yield; 98% ee; [α]26^D = −173.9 (c 4.61, CHCl₃); 

^{1}H NMR (300 MHz, CDCl₃) δ 8.16 (d, J = 8.7 Hz, 1H), 7.75–7.71 (m, 5H), 7.62–7.57 (m, 1H), 7.2–7.46 (m, 2H), 6.70 (d, J = 8.7 Hz, 2H), 5.71 (d, J = 5.4 Hz, 1H), 4.37–4.20 (m, 2H), 3.74 (s, 3H), 3.32 (d, J = 5.4 Hz, 1H), 1.75 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl₃) δ 196.2, 176.7, 170.7, 163.5, 152.4, 146.8, 137.5, 130.6, 130.0, 129.9, 129.4, 127.6, 127.3, 127.2, 118.3, 113.5, 80.0, 66.5, 61.7, 61.5, 55.4, 53.5, 14.3, 14.2; HRMS (ESI) m/z 477.1481 (M+H^+), calc. for C_{26}H_{23}N_{2}O_{3}S 477.1484.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 20.3 min (minor) and 23.7 min (major).

White solid, Mp 137.5–138.7 °C; 97% yield; 99% ee; [α]26^D = −132.0 (c 4.67, CHCl₃); 

^{1}H NMR (300 MHz, CDCl₃) δ 8.18 (d, J = 8.5 Hz, 1H), 7.74–7.71 (m, 3H), 7.62–7.55 (m, 3H), 7.51–7.46 (m, 2H), 6.90–6.87 (m, 1H), 5.57 (d, J = 5.3 Hz, 1H), 4.37–4.20 (m, 2H), 3.41 (d, J = 5.3 Hz, 1H), 1.76 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl₃) δ 190.0, 176.6, 170.5, 152.1, 146.8, 144.3, 137.6, 134.7, 132.6, 129.9, 129.3, 127.9, 127.6, 127.4, 127.3, 118.2, 80.0, 66.5, 62.7, 61.8, 53.6, 14.2,(two peaks); HRMS (ESI) m/z 453.0943 (M+H^+), calc. for C_{26}H_{21}N_{2}O_{3}S_{2} 453.0943.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 23.2 min (major) and 26.4 min (minor).
White solid, Mp 141.8–143.1 °C; 96% yield; 98% ee; [α]$_D^{185}$ = 186.1 (c 4.29, CHCl$_3$);  

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.19 (d, $J$ = 8.5 Hz, 1H), 7.79–7.73 (m, 3H), 7.65–7.60 (m, 1H), 7.54–7.49 (m, 2H), 7.25 (s, 1H), 7.06 (d, $J$ = 3.6 Hz, 1H), 6.29 (dd, $J$ = 3.6, 1.7 Hz, 1H), 5.45 (d, $J$ = 5.2 Hz, 1H), 4.38–4.22 (m, 2H), 3.46 (d, $J$ = 5.2 Hz, 1H), 1.76 (s, 3H), 1.32 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 185.0, 176.3, 170.5, 152.3, 152.2, 146.8, 146.6, 137.4, 130.0, 129.4, 127.6, 128.4, 127.3, 118.2, 112.3, 79.5, 66.3, 63.1, 61.7, 53.0, 14.2; HRMS (ESI) m/z 437.1175 (M+H$^+$), calc. for C$_{23}$H$_{21}$N$_2$O$_5$S 437.1171.

The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.7 min (minor) and 35.7 min (major).

Pale yellow solid, Mp 158.4–160.1 °C; 67% yield; 90% ee; [α]$_D^{185}$ = 205.7 (c 1.50, CHCl$_3$);  

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.21 (d, $J$ = 8.5 Hz, 1H), 7.83 (d, $J$ = 8.5 Hz, 1H), 7.78–7.70 (m, 4H), 7.64–7.49 (m, 5H), 7.43–7.35 (m, 4H), 7.28 (s, 1H), 7.23 (s, 1H), 5.86 (d, $J$ = 5.4 Hz, 1H), 3.80 (d, $J$ = 5.4 Hz, 1H), 3.82–3.62 (m, 2H), 0.74 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 197.7, 174.5, 170.1, 152.1,
146.8, 137.7, 137.0, 133.2, 131.4, 130.0, 129.3, 128.7, 128.6, 128.4, 128.2, 128.0, 127.6, 127.4, 118.3, 78.4, 74.3, 62.5, 61.3, 54.7, 13.4; HRMS (ESI) m/z 509.1538 (M+H'), calc. for C_{30}H_{28}N_{2}O_{4}S 509.1535.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 60/40; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.3 min (minor) and 50.0 min (major).

White solid, Mp 125.5–126.8 °C; 95% yield; 97% ee; [α]_{D}^{26} = –134.7 (c 3.72, CHCl3);

^1H NMR (300 MHz, CDCl3) δ 8.80 (d, J = 2.0 Hz, 1H), 8.54–8.52 (m, 1H), 7.95 (s, 1H), 7.88–7.84 (m, 1H), 7.68 (d, J = 7.4 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.35–7.24 (m, 3H), 7.24 (s, 0H), 5.43 (d, J = 5.4 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 3.22 (d, J = 5.4 Hz, 1H), 1.68 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H); ^13C NMR (75 MHz, CDCl3) δ 197.7, 177.3, 170.5, 150.1, 147.2, 136.1, 134.0, 133.9, 130.2, 128.8, 128.2, 123.5, 76.7, 65.4, 62.0, 54.0, 14.2; HRMS (ESI) m/z 397.1221 (M+H'), calc. for C_{21}H_{23}N_{2}O_{4}S 397.1222.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.8 min (major) and 24.5 min (minor).
Pale yellow solid, Mp 102.2–103.8 °C; 96% yield; 95% ee; [α]_D^20 = –348.8 (c 0.05, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.95–7.91 (m, 3H), 7.79 (d, J = 8.5 Hz, 1H), 7.74–7.68 (m, 2H), 7.58–7.52 (m, 1H), 7.05–6.88 (m, 4H), 6.84–6.75 (m, 4H), 6.25–6.23 (m, 1H), 4.74 (s, 2H), 3.76 (s, 1H), 3.74–3.51 (m, 2H), 1.98 (s, 3H), 0.53 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.2, 174.2, 167.9, 150.4, 146.6, 143.1, 136.2, 135.0, 130.2, 129.6, 129.4, 128.4, 127.5, 127.4, 127.3, 126.5, 126.4, 126.0, 122.0, 118.9, 108.7, 82.7, 67.8, 63.0, 60.6, 60.2, 44.0, 13.3, 13.1; HRMS (ESI) m/z 550.1803 (M+H⁺), calc. for C$_{32}$H$_{26}$FN$_3$O$_4$S 550.1801.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 36.8 min (minor) and 42.1 min (major).

Pale yellow solid, Mp 130.4–132.2 °C; 98% yield; 94% ee; [α]_D^20 = –138.0 (c 0.05, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.89 (t, J = 9.0 Hz, 3H), 7.77–7.69 (m, 3H), 7.59–7.54 (m, 1H), 7.06 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 8.6 Hz, 1H), 6.88–6.78 (m, 4H), 6.69 (td, J = 8.6, 3.5 Hz, 1H), 6.16 (dd, J = 8.6, 3.5 Hz, 1H), 4.82 (d, J = 15.8 Hz, 1H), 4.69 (d, J = 15.8 Hz, 1H), 3.78–3.60 (m, 3H), 1.97 (s, 3H), 0.59 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.1, 174.1, 167.6, 160.0, 156.8, 150.2, 146.6, 139.1, 139.0, 136.6, 134.7, 130.3, 129.5, 128.4, 127.8, 127.7, 127.6, 127.5, 127.4, 126.5, 118.7, 115.7, 115.4, 114.7, 114.3, 109.2, 109.0, 82.8, 67.8, 62.9, 60.8, 60.2, 44.2, 13.2, 13.1; HRMS (ESI) m/z 590.1529 (M+Na⁺), calc. for C$_{32}$H$_{26}$FN$_3$O$_4$SNa 590.1526.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 51.7 min (major) and 60.1 min (minor).
Pale yellow solid, Mp 155.0–156.3 °C; 97% yield; 92% ee; [α]$_D$ = –140.5 (c 0.05, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.91–7.85 (m, 4H), 7.72 (t, $J = 7.4$ Hz, 2H), 7.59–7.54 (m, 1H), 7.06 (t, $J = 7.4$ Hz, 1H), 7.00–6.94 (m, 2H), 6.88–6.78 (m, 4H), 6.17 (d, $J = 8.3$ Hz, 1H), 4.82 (d, $J = 15.8$ Hz, 1H), 4.69 (d, $J = 15.8$ Hz, 1H), 3.82 – 3.59 (m, 3H), 1.97 (s, 3H), 0.61 (t, $J = 7.1$ Hz, 3H); $^1$C NMR (75 MHz, CDCl$_3$) $\delta$ 176.1, 173.9, 167.6, 150.2, 146.6, 141.6, 136.7, 134.6, 130.4, 129.5, 129.2, 128.5, 127.9, 127.6, 127.5, 126.5, 118.8, 109.6, 82.8, 67.6, 63.0, 60.9, 60.3, 44.1, 13.3, 13.1; HRMS (ESI) m/z 584.1415 (M+H$^+$), calc. for C$_{32}$H$_{27}$ClN$_3$O$_4$S 584.1411.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 54.0 min (major) and 66.0 min (minor).

Pale yellow solid, Mp 145.3–146.3 °C; 98% yield; 90% ee; [α]$_D$ = –86.1 (c 0.05, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J = 2.6$ Hz, 1H), 7.91 (d, $J = 2.6$ Hz, 1H), 7.88 (s, 2H), 7.71 (t, $J = 7.4$ Hz, 2H), 7.56 (t, $J = 7.4$ Hz, 1H), 7.12–7.03 (m, 2H), 6.98 (d, $J = 8.4$ Hz, 1H), 6.85 (t, $J = 7.6$ Hz, 2H), 6.78 (d, $J = 7.6$ Hz, 2H), 6.13 (d, $J = 8.4$ Hz, 1H), 4.81 (d, $J = 15.9$ Hz, 1H), 4.68 (d, $J = 15.9$ Hz, 1H), 3.76–3.66 (m, 3H), 1.97 (s, 3H), 0.60 (t, $J = 7.1$ Hz, 3H); $^1$C NMR (75 MHz, CDCl$_3$) $\delta$ 176.1, 173.8, 167.5, 150.1, 146.6, 142.1, 136.7, 134.5, 132.1, 130.3, 129.4, 129.2, 128.4, 128.2, 127.5, 127.4, 126.5, 118.8, 114.7, 110.0,
67.5, 62.9, 60.9, 60.2, 44.1, 13.3, 13.1; HRMS (ESI) m/z 650.0720 (M+Na\(^+\)), calc. for C\(_{32}\)H\(_{26}\)BrN\(_3\)O\(_4\)SNa 650.0725.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 50.7 min (minor) and 61.3 min (major).

Pale yellow solid, Mp 137.5–138.5 °C; 95% yield; >99% ee; [\(\alpha\)]\(_D\)\(^{24}\) = 431.3 (c 0.05, CHCl\(_3\)); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.99 (s, 1H), 7.93 (d, \(J = 8.4\) Hz, 1H), 7.81 (d, \(J = 8.4\) Hz, 1H), 7.73–7.68 (m, 3H), 7.57–7.52 (m, 1H), 7.01 (t, \(J = 7.8\) Hz, 1H), 6.89 (d, \(J = 7.8\) Hz, 1H), 6.80–6.71 (m, 5H), 6.12 (d, \(J = 7.8\) Hz, 1H), 4.75 (d, \(J = 16.0\) Hz, 1H), 4.69 (d, \(J = 16.0\) Hz, 1H), 3.75 (s, 1H), 3.73–3.54 (m, 2H), 2.29 (s, 3H), 1.98 (s, 3H), 0.53 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 176.3, 174.2, 168.0, 150.5, 146.6, 140.7, 136.2, 135.1, 131.5, 130.2, 129.6, 128.3, 127.5, 127.4, 127.2, 127.1, 126.5, 126.0, 118.9, 108.5, 82.7, 67.9, 62.9, 60.7, 60.1, 44.0, 21.2, 13.2; HRMS (ESI) m/z 586.1780 (M+Na\(^+\)), calc. for C\(_{33}\)H\(_{36}\)N\(_3\)O\(_4\)SNa 586.1776.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 75.3 min (major) and 98.9 min (minor).
Pale yellow solid, Mp 141.1–142.3 °C; 98% yield; 98% ee; [α]D24 –303.4 (c 0.05, CHCl3); 1H NMR (300 MHz, CDCl3) δ 7.90 (s, 1H), 7.86 (d, J = 8.7 Hz, 1H), 7.76 (d, J = 8.7 Hz, 1H), 7.66–7.62 (m, 2H), 7.52–7.46 (m, 2H), 6.95 (t, J = 7.2 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H), 6.75–6.66 (m, 4H), 6.45 (dd, J = 8.5, 2.6 Hz, 1H), 6.06 (d, J = 8.5 Hz, 1H), 4.65 (s, 2H), 3.72–3.50 (m, 6H), 1.90 (s, 3H), 0.50 (t, J = 7.1 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 176.2, 173.9, 167.8, 155.2, 150.3, 146.6, 136.5, 136.3, 135.0, 130.2, 129.5, 128.3, 127.5, 127.4, 127.2, 127.1, 126.5, 118.7, 114.2, 113.5, 109.0, 82.7, 68.0, 62.9, 60.6, 60.0, 55.9, 44.0, 13.3, 13.1; HRMS (ESI) m/z 602.1724 (M+Na+), calc. for C33H29N3O5Na 602.1726.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 93.3 min (major) and 136.3 min (minor).

Pale yellow solid, Mp 96.4–96.9 °C; 97% yield; >99% ee; [α]D24 –133.7 (c 0.05, CHCl3); 1H NMR (300 MHz, CDCl3) δ 7.85–7.75 (m, 4H), 7.64 (t, J = 7.4 Hz, 2H), 7.52–7.46 (m, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.88–6.71 (m, 6H), 6.19 (s, 1H), 4.73 (d, J = 15.9 Hz, 1H), 4.61 (d, J = 15.9 Hz, 1H), 3.70–3.41 (m, 3H), 1.88 (s, 3H), 0.53 (t, J = 7.1 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 176.1, 174.2, 167.6, 150.2, 146.6, 144.2, 136.6, 135.2, 134.4, 130.3, 129.4, 128.5, 127.6, 127.5, 127.4, 127.3, 126.4, 124.4, 121.8, 118.7, 109.1, 82.7, 67.2, 62.8, 60.8, 60.3, 44.1, 13.3, 13.0; HRMS (ESI) m/z 584.1414 (M+H+), calc. for C32H27ClN3O5S 584.1411.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 44.4 min (minor) and 48.8 min (major).
2.3 Hz, 0.54 (t, \(J=136.3\), 1, \(J=62.8\), 6) C33H29N was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 101.9 min (minor) and 110.0 min (major).

Pale yellow solid, Mp 123.0–124.8 °C; 94% yield; >99% ee; \([\alpha]_D^{24} = -269.5\) (c 0.05, CHCl₃); \(^1^H\) NMR (300 MHz, CDCl₃) \(\delta\) 7.92–7.86 (m, 2H), 7.75 (dd, \(J=8.5, 1.6\) Hz, 2H), 7.67–7.62 (m, 2H), 7.52–7.46 (m, 1H), 6.94 (t, \(J=7.1\) Hz, 1H), 6.84 (d, \(J=8.5\) Hz, 1H), 6.73–6.63 (m, 4H), 6.38 (dd, \(J=8.5, 2.3\) Hz, 1H), 5.75 (d, \(J=2.3\) Hz, 1H), 4.68 (d, \(J=15.9\) Hz, 1H), 4.59 (d, \(J=15.9\) Hz, 1H), 3.70–3.48 (m, 6H), 1.89 (s, 3H), 0.54 (t, \(J=7.2\) Hz, 3H); \(^1^C\) NMR (75 MHz, CDCl₃) \(\delta\) 176.2, 174.6, 168.0, 160.7, 150.5, 146.6, 144.3, 136.3, 134.9, 130.2, 129.6, 128.3, 127.5, 127.4, 127.2, 126.5, 118.9, 117.7, 105.4, 96.7, 82.6, 67.5, 62.8, 60.6, 60.1, 55.2, 44.0, 13.4, 13.1; HRMS (ESI) m/z 602.1730 (M+Na\(^+\)), calc. for C_{33}H_{31}N_{2}O_{5}S_{2}Na 602.1726.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 101.9 min (minor) and 110.0 min (major).

Pale yellow solid, Mp 70.4–72.1 °C; 96% yield; 93% ee; \([\alpha]_D^{24} = -240.4\) (c 0.05, CHCl₃); \(^1^H\) NMR (300 MHz, CDCl₃) \(\delta\) 7.88–7.83 (m, 3H), 7.75–7.68 (m, 3H), 7.57–7.52 (m, 1H), 7.11–7.05 (m, 1H), 7.00–6.75 (m, 7H), 5.06 (d, \(J=15.5\) Hz, 1H), 4.78 (d, \(J=15.5\) Hz, 1H), 3.75 (s, 1H), 3.72–3.51 (m, 2H), 1.96 (s, 3H), 0.55 (t, \(J=7.2\) Hz, 3H); \(^1^C\) NMR (75 MHz, CDCl₃) \(\delta\) 176.2, 174.2, 167.6, 150.1, 146.6, 136.5, 136.4, 130.3, 129.5, 128.2, 127.5, 127.4, 127.2, 126.7, 122.5, 122.4, 122.3, 122.2, 118.7, 117.6, 117.3, 82.9, 67.6, 62.8, 60.7, 60.6, 45.5, 13.2, 13.1; HRMS (ESI) m/z 606.1233 (M+Na\(^+\)), calc. for C_{32}H_{28}ClN_{3}O_{4}S_{2}Na 606.1230.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 39.2 min (major) and 65.5 min (minor).
Pale yellow solid, Mp 87.0–88.6 °C; 97% yield; 96% ee; [α]_D^24 -281.9 (c 0.05, CHCl₃); \(^1\)H NMR (300 MHz, CDCl₃) δ 7.90–7.87 (m, 2H), 7.82–7.75 (m, 2H), 7.67–7.63 (m, 2H), 7.52–7.46 (m, 1H), 6.98 (t, J = 7.4 Hz, 1H), 6.86–6.77 (m, 4H), 6.71 (d, J = 7.4 Hz, 1H), 6.62 (d, J = 7.4 Hz, 2H), 5.04 (d, J = 17.0 Hz, 1H), 4.84 (d, J = 17.0 Hz, 1H), 3.74–3.52 (m, 3H), 1.91 (s, 3H), 1.79 (s, 3H), 0.59 (t, J = 7.2 Hz, 3H); \(^1\)C NMR (75 MHz, CDCl₃) δ 176.3, 126.6, 125.2, 129.7, 128.3, 127.8, 127.3, 127.1, 126.6, 126.0, 122.4, 119.1, 119.0, 83.0, 67.2, 63.0, 60.7, 60.6, 45.3, 18.6, 13.5, 13.2; HRMS (ESI) m/z 586.1778 (M+Na^+), calc. for C\(_{33}\)H\(_{29}\)N\(_3\)O\(_4\)SNa 586.1776.

The ee was determined by HPLC analysis. CHIRALPAK ID-3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 79.9 min (major) and 139.8 min (minor).

Pale yellow solid, Mp 87.8–89.8 °C; 94% yield; 90% ee; [α]_D^24 -72.5 (c 0.05, CHCl₃); \(^1\)H NMR (300 MHz, CDCl₃) δ 7.82 (d, J = 7.3 Hz, 1H), 7.61 (s, 1H), 7.28–7.25 (m, 3H), 7.08–7.04 (m, 3H), 6.99–6.88 (m, 5H), 6.46 (d, J = 7.3 Hz, 1H), 5.03 (d, J = 15.7 Hz, 1H), 4.67 (d, J = 15.7 Hz, 1H), 3.68–3.45 (m, 3H), 1.92 (s, 3H), 0.47 (t, J = 7.2 Hz, 3H); \(^1\)C NMR (75 MHz, CDCl₃) δ 177.7, 174.8, 167.6, 142.5, 135.0, 134.9, 129.7, 129.4, 128.7, 128.3, 127.8, 127.3, 127.1, 126.6, 126.0, 122.4, 108.8, 82.6, 68.0, 61.3, 60.7, 60.4, 44.0, 13.2, 12.9; HRMS (ESI) m/z 555.1123 (M+Na^+), calc. for C\(_{29}\)H\(_{23}\)ClN\(_2\)O\(_4\)SNa 555.1121.
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.4 min (major) and 22.5 min (minor).

Pale yellow solid, Mp 101.3–102.6 °C; 96% yield; 95% ee; [α]D 41 –62.0 (c 0.05, CHCl3); 1H NMR (300 MHz, CDCl3) δ 8.25 (d, J = 4.2 Hz, 1H), 7.81–7.78 (m, 1H), 7.59 (s, 1H), 7.33 (td, J = 7.7, 1.7 Hz, 1H), 7.26–7.22 (m, 3H), 7.12–6.98 (m, 4H), 6.92–6.82 (m, 2H), 6.39 (d, J = 7.7 Hz, 1H), 4.89 (d, J = 15.7 Hz, 1H), 4.72 (d, J = 15.7 Hz, 1H), 3.71–3.49 (m, 3H), 1.94 (s, 3H), 0.50 (t, J = 7.2 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 176.6, 174.4, 167.8, 150.4, 148.5, 142.9, 136.0, 135.3, 129.2, 128.5, 127.5, 127.2, 126.1, 126.0, 123.6, 122.0, 121.6, 108.4, 82.8, 67.3, 62.4, 60.6, 60.3, 44.0, 13.2, 13.1; HRMS (ESI) m/z 522.1466 (M+Na+), calc. for C28H23N3O6SNa 522.1463.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 21.1 min (major) and 31.4 min (minor).
Pale yellow solid, Mp 92.3–94.1 °C; 87% yield; >99% ee; [\alpha]_D^{24} –67.8 (c 0.05, CHCl_3); \textsuperscript{1}H NMR (300 MHz, CDCl_3) \delta 7.93–7.91 (m, 3H), 7.80 (d, J = 7.8 Hz, 1H), 7.79–7.68 (m, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.06–7.04 (m, 1H), 6.98–6.91 (m, 3H), 6.86–6.78 (m, 4H), 6.25–6.22 (m, 1H), 4.79 (d, J = 15.8 Hz, 1H), 4.71 (d, J = 15.8 Hz, 1H), 3.79 (s, 1H), 3.72–3.49 (m, 2H), 2.60 (dq, J = 14.5, 7.2 Hz, 1H), 2.40 (dq, J = 14.5, 7.2 Hz, 1H), 1.27 (t, J = 7.2 Hz, 3H), 0.52 (t, J = 7.2 Hz, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl_3) \delta 175.5, 174.3, 167.9, 150.6, 146.6, 143.0, 136.2, 135.0, 130.2, 129.5, 129.3, 128.4, 127.5, 127.4, 127.3, 126.6, 125.9, 121.9, 118.9, 108.6, 81.9, 69.4, 67.5, 60.6, 59.4, 44.0, 20.4, 13.2, 12.0; HRMS (ESI) m/z 586.1775 (M+Na\(^{+}\)), calc. for C\textsubscript{33}H\textsubscript{29}N\textsubscript{3}O\textsubscript{4}SNa 586.1776.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 28.5 min (minor) and 3401 min (major).

Pale yellow solid, Mp 108.2–109.9 °C; 84% yield; 97% ee; [\alpha]_D^{24} –101.0 (c 0.05, CHCl_3); \textsuperscript{1}H NMR (300 MHz, CDCl_3) \delta 7.98–7.89 (m, 3H), 7.73–7.64 (m, 3H), 7.58–7.48 (m, 3H), 7.37–7.30 (m, 3H), 7.24–7.22 (m, 1H), 7.06–6.92 (m, 3H), 6.86–6.78 (m, 5H), 6.24–6.21 (m, 1H), 4.79 (d, J = 15.9 Hz, 1H), 4.72 (d, J = 15.9 Hz, 1H), 3.85 (s, 1H), 3.81 (s, 1H), 3.76–3.53 (m, 2H), 0.54 (t, J = 7.2 Hz, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl_3) \delta 175.1, 174.1, 168.1, 150.4, 146.5, 143.0, 139.1, 136.0, 135.0, 130.1, 130.0, 129.5, 129.4, 128.4, 128.3, 127.5, 127.3, 126.9, 126.6, 125.8, 122.0, 118.9, 108.7, 81.6, 70.7, 68.1, 60.7, 59.5, 44.0, 31.9, 13.3; HRMS (ESI) m/z 648.1932 (M+Na\(^{+}\)), calc. for C\textsubscript{38}H\textsubscript{31}N\textsubscript{3}O\textsubscript{4}SNa 648.1933.

The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 24.8 min (minor) and 44.5 min (major).
White solid, Mp 128.6–129.8 °C; 91% yield; 97% ee; [α]D 26 +183.4 (c 3.44, CHCl3);
1H NMR (300 MHz, CDCl3) δ 8.13 (d, J = 8.5 Hz, 1H), 7.73–7.69 (m, 3H), 7.65–7.56 (m, 4H), 7.48 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.3 Hz, 1H), 7.22 (d, J = 7.3 Hz, 1H), 5.70 (d, J = 5.5 Hz, 1H), 3.50 (d, J = 5.5 Hz, 1H), 2.66 (dq, J = 18.2, 7.2 Hz, 1H), 2.29 (dq, J = 18.2, 7.2 Hz, 1H), 1.72 (s, 3H), 1.04 (t, J = 7.2 Hz, 3H);
13C NMR (75 MHz, CDCl3) δ 207.9, 198.3, 176.6, 152.2, 146.8, 137.5, 137.0, 133.1, 129.9, 129.3, 128.4, 128.0, 127.6, 127.3, 127.2, 118.2, 79.6, 66.8, 62.3, 57.4, 39.1, 14.2, 7.6; HRMS (ESI) m/z 431.1430 (M+H+), calc. for C23H23N2O4S 431.1429.
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 19.7 min (major) and 22.8 min (minor).

Green solid, Mp 121.9–123.0 °C; 73% yield; 98% ee; [α]D 26 +161.4 (c 0.94, CHCl3); 1H NMR (300 MHz, CDCl3) δ 8.06 (d, J = 8.7 Hz, 1H), 7.92 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.58 (ddd, J = 8.4, 6.3, 1.4 Hz, 1H), 7.46 (ddd, J = 8.4, 6.3, 1.4 Hz, 3H), 6.99 (d, J = 7.5 Hz, 1H), 6.86 (t, J = 7.5 Hz, 2H), 5.42 (d, J = 12.5 Hz, 1H), 5.25 (d, J = 12.5 Hz, 1H), 3.91 (s, 3H), 2.28 (s, 3H), 1.75 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 205.5, 198.3, 174.0, 158.5, 146.1, 137.5, 136.6, 131.9, 129.5, 129.2, 128.1, 127.4, 127.0, 126.8, 119.3, 77.3, 62.7, 61.9, 55.0, 53.5, 30.9, 23.7; HRMS (ESI) m/z 449.1539 (M+H+), calc. for C25H25N2O4S 449.1535.
The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.5 min (major) and 37.9 min (minor).
White solid, $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.98 (s, 2H), 7.30 (s, 1H), 4.22 (s, 2H), 2.73 (s, 6H), 1.89 (s, 4H), 1.17 (s, 9H), 1.00 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 182.0, 172.7, 140.2, 131.6, 131.2, 130.9, 130.7, 130.3, 128.8, 128.4, 124.8, 123.9, 121.2, 117.8, 67.0, 65.6, 55.7, 54.0, 34.7, 33.8, 27.3, 26.6, 23.4; HRMS (ESI) m/z 555.2593 (M+H$^+$), calc. for C$_{25}$H$_{37}$F$_6$N$_4$OS 555.2592.
14. Determination of the absolute configuration
(1) Absolute configurations of the [4+2] annulation adducts 3a-n are determined by X-ray structure analysis of the product 3a (CCDC 1419583)

(2) Absolute configurations of the [4+2] annulation adducts 6a-s and 9a-h are determined by X-ray structure analysis of the product 6b (CCDC 1419574)

(3) Absolute configurations of the [4+2] annulation adducts 11a-n are determined by X-ray structure analysis of the product 11d (CCDC 1463891)
15. Computational methods

All quantum chemical calculations were carried out with Gaussian 09. All $\Delta G$ values are reported relative to the individual free starting materials 1, 2 and catalyst III. Optimization of minimum and transition state (TS) structures were first carried out with Becke’s three parameter and Lee-Yang-Parr’s B3LYP density functional using Pople’s 6-31G(d,p) basis set under the SMD polarizable continuum solvent model (toluene parameters). It is important to note that Simón and Goodman showed that B3LYP/6-31G(d) is adequate to model a variety of organocatalytic reactions. Subsequently, Houk et al. applied the dispersion-corrected meta-hybrid M06-2X(D3) approach towards modelling stereoselective intramolecular Aldol reaction and thiourea-amine catalyzed Nazarov cyclization with excellent qualitative agreement to experiment.

The B3LYP/6-31G(d,p) thermal and vibrational corrections from frequency calculations were combined to higher level single-point energies of the optimized geometries. The single-point energies were evaluated with Peverati and Truhlar’s screened-exchange density functional MN12-SX under same polarizable continuum solvent model toluene parameters, herein termed MN12-SX/SMD. The newer meta-hybrid non separable gradient MN12-SX functional was assessed to perform better in chemical energetics and thus preferred over M06-2X. In conjunction with the MN12-SX/SMD, the Wiegend and Aldrich’s def2-TZVPP triple zeta quality basis set was used. Second order derivative or Hessian of the completed calculations were checked to verify transition state structures having only one negative eigenvalue and none for minimum.

Gibbs free energies in solution were calculated from the geometries, frequencies and improved energies using a thermocycle in which the gas-phase was treated using the standard textbook formulae for an ideal gas under the harmonic oscillator / rigid rotor approximation, and the Gibbs free energies of solvation (in toluene) were then calculated using the SMD continuum solvation model. Corrections were included to consider passage of 1 atm gas into 1M in solution, $\Delta G^{1\text{atm} \rightarrow 1\text{M}}$ as follows:

$$\Delta G^{1\text{atm} \rightarrow 1\text{M}} = dN*R*T*\ln(R/T/P)$$

where $dN$ is the number of moles of gas change from reactant to product and $\ln(R/T/P)$ equals to 1.89 at 298 K. We have recently shown that this approach provides an excellent quantitative description of the temperature dependent behavior of solution-phase Diels-Alder reactions.

Electron density topological analyses based on the reduced density gradient was carried out with NCIplot to qualify regions of non-covalent interactions especially hydrogen bonding.
(H-bonding) or regions of repulsive interactions. Regions which are attractive have sign of the second density Hessian eigenvalue, $\text{sign}(\lambda_2)$, as positive and repulsive as negative. The electron density $\rho(r)$ is set at an isovalue of 0.4 au in the $\text{sign}(\lambda_2)\rho(r)$ range of -0.4 to 0.4, which corresponds to blue-green-red color scale (see Figure S1). The 3-D molecular graphics for NCIplot were rendered with VMD\textsuperscript{14} and graphics inset corresponding to the NCIplot showing key H-bond interactions in figure 3 of the manuscript were rendered with Cylview\textsuperscript{15}.

![Figure S1. Non-covalent interaction isosurfaces of optimized TS structures of Mannich process (TS2A-SS and TS2A-RR) and the protonation process (TS2A’-SS and TS2A’-RR). Blue-green-red color scale from -0.4 < $\text{sign}(\lambda_2)\rho(r)$ > 0.4 au, where blue (positive) is favorable and red (negative) is unfavorable interaction. Two images for each TS are flipped horizontally to allow viewing from the front and back sides.](image)

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| Molecule | MN12SX E   | B3LYP E   | $G_{\text{correction}}$ | $H_{\text{correction}}$ | ZPE (298K) | $G_{\text{sol}}$ (MN12SX) |
|---------|------------|------------|------------------------|------------------------|------------|--------------------------|
| III     | -2265.238831 | -2265.933466 | 0.526197               | 0.640233               | 0.60057    | -2264.703614            |
| 1       | -930.478833  | -930.724803  | 0.119136               | 0.169065               | 0.157119   | -930.359697             |
| 2       | -513.963184  | -514.176050  | 0.101575               | 0.146955               | 0.136956   | -513.861609             |
| TS1A-R,R| -3709.692433 | -3710.841985 | 0.796699               | 0.960728               | 0.899259   | -3708.892727            |
| TS1A-S,S| -3709.695202 | -3710.844099 | 0.796696               | 0.961218               | 0.899614   | -3708.895499            |
| TS1B-R,R| -3709.69039  | -3710.83715  | 0.797744               | 0.961166               | 0.899645   | -3708.889639            |
| TS1B-S,S| -3709.688422 | -3710.838464 | 0.797171               | 0.961137               | 0.899743   | -3708.888244            |
| int1A-R,R| -3709.705159 | -3710.854112 | 0.799168               | 0.96316                | 0.90194    | -3708.902984            |
| int1A-S,S| -3709.714753 | -3710.863604 | 0.800902               | 0.963818               | 0.902572   | -3708.910844            |
| int1B-R,R| -3709.714366 | -3710.860514 | 0.796381               | 0.961835               | 0.899977   | -3708.914978            |
| int1B-S,S| -3709.713598 | -3710.861334 | 0.798688               | 0.962503               | 0.901149   | -3708.911903            |
| TS2A-R,R| -3709.699503 | -3710.843566 | 0.804677               | 0.962433               | 0.902263   | -3708.891819            |
| TS2A-S,S| -3709.698245 | -3710.843839 | 0.799844               | 0.962093               | 0.901234   | -3708.895394            |
| int2A-R,R| -3709.710927 | -3710.853914 | 0.802751               | 0.964022               | 0.903051   | -3708.905169            |
| int2A-S,S| -3709.714747 | -3710.857422 | 0.800695               | 0.963549               | 0.902543   | -3708.911038            |
| TS2′A-R,R| -3709.690718 | -3710.836448 | 0.795499               | 0.957718               | 0.896357   | -3708.892212            |
| TS2′A-S,S| -3709.693888 | -3710.837503 | 0.798308               | 0.957859               | 0.897082   | -3708.892573            |
| int2′A-R,R| -3709.712573 | -3710.860005 | 0.792608               | 0.962243               | 0.899753   | -3708.916958            |
| int2′A-S,S| -3709.712922 | -3710.861514 | 0.795597               | 0.962489               | 0.900231   | -3708.914318            |

*All energy values in hatrees.*
Nueleophile 1

\[ \text{[Br3LyP]} 6-31G(d,p) \text{C25H36F6N4O1S1 \text{ROOT\# 09-Dec-2015\#}} \]
\[ \text{freq=noraman rb3lyp/6-31g** opt=maucyc=200 scf=maucyc=200 scrf=\{smd, solvent=toluene\} Cataly...} \]

Gaussian Archive Files

Electrophile 2

\[ \text{\textit{\textbf{S57}}} \]
S58

TS1 A, R

\[
\text{TS1} A \rightarrow R \]

\[
\begin{align*}
\text{C} & , 1.6929735081, -1.56133087, 1.8353043108 \\
\text{N} & , 2.226825342, 1.3263483198, 1.4110303967 \\
\text{O} & , 0.8454359323, 1.2357349183, -0.5083276519 \\
\text{H} & , 3.856273734, -0.956120605, -0.0214520731 \\
\text{H} & , -5.0891603691, 1.157603494, -0.5076458795 \\
\end{align*}
\]
| N  | C  | H  | O  | S  |
|----|----|----|----|----|
| 2137909 | 2.0793403848 | 0.91425141 | C | 0.930165457 | 4.2052566432 | 1.554847777 |
| 9/1/C | 0.8842622772 | 50.67868656 | 2.928511635 | 0.7699736788 | 3.5291247928 |
| 6.343467222 | C | 0.637961038 | 5.8120604108 | 3.3696767079 | H | 0.9854979534 |
| 78 | 5.7292659 | 7.67833189 | 6.5367381889 | 8.461737622 | 2.4455 |
| 621581 | H | 0.6391494463 | 6.0205816989 | 4.3437024241 | H | 0.4466767066 |
| 7.36307 | H | 0.72780 | 0.3584327115 | H | 0.3538435451 | 7.8427727911 |
| 2.7645189417 | C | 0.5713894184 | 0.8461737622 | 2.4455 |
| 0.062158 | H | 0.3619449463 | 6.0205816989 | 4.3437024241 | H | 0.4466767066 |
| F=5.596e-07 | Dipole=6.5299074 | 0.8359522 | 0.103642 | Quadrupole=9.0444 |
| 6.35 | 15.603478 | 24.5017925 | 26.1317886 | 2.768767767 | 3.974612 |
| PG=C01 | C | 0.51436233014 | 0.8490448966 | E3 | 2.0418645287 | 2.9518852856 |
| 24.603478 | 24.5017925 | 26.1317886 | 2.768767767 | 3.974612 |

**TS1-R, R**

| NC-R | FT5 | R3BLYP | 6-31G(d,p) | C42H51F6N7O4S2 | ROOT | 14- Dec- 2015 | 0 |
|-------|-----|--------|------------|--------------|--------|-----------------|---|
| \# f-neg=oran n mb3lyp | 6-31G**=** opt= (tscalc fcc, noeigen, maxcyc=200) scf=makecg=200 | smd, solvent=toluene | iop(1/8=1) | TS for 1st C add |
| conf | R elec, R nuc | conf | cal i | 0.1 | 0.1255 | 0.1965 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |

**TS 1-B, R, R**

| NC-R | FT5 | R3BLYP | 6-31G(d,p) | C42H51F6N7O4S2 | ROOT | 14- Dec- 2015 | 0 |
|-------|-----|--------|------------|--------------|--------|-----------------|---|
| \# f-neg=oran n mb3lyp | 6-31G**=** opt= (tscalc fcc, noeigen, maxcyc=200) scf=makecg=200 | smd, solvent=toluene | iop(1/8=1) | TS for 1st C add |
| conf | R elec, R nuc | conf | cal i | 0.1 | 0.1255 | 0.1965 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |

**TS 2-B, R, R**

| NC-R | FT5 | R3BLYP | 6-31G(d,p) | C42H51F6N7O4S2 | ROOT | 14- Dec- 2015 | 0 |
|-------|-----|--------|------------|--------------|--------|-----------------|---|
| \# f-neg=oran n mb3lyp | 6-31G**=** opt= (tscalc fcc, noeigen, maxcyc=200) scf=makecg=200 | smd, solvent=toluene | iop(1/8=1) | TS for 1st C add |
| conf | R elec, R nuc | conf | cal i | 0.1 | 0.1255 | 0.1965 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |

**TS 3-B, R, R**

| NC-R | FT5 | R3BLYP | 6-31G(d,p) | C42H51F6N7O4S2 | ROOT | 14- Dec- 2015 | 0 |
|-------|-----|--------|------------|--------------|--------|-----------------|---|
| \# f-neg=oran n mb3lyp | 6-31G**=** opt= (tscalc fcc, noeigen, maxcyc=200) scf=makecg=200 | smd, solvent=toluene | iop(1/8=1) | TS for 1st C add |
| conf | R elec, R nuc | conf | cal i | 0.1 | 0.1255 | 0.1965 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |
| 3.951 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 | 0.54542 |
TS1b-$S$

1) [G/NC: R2649/FT5/R3L1YP] 6-31G(d,p) \{C4H25S1/F6N7O4S2\} ROOT: 09- Dec -2015
T5 freq=norman_r3b3/6-31G** opt={ts,calc,frc,noise,gen,maxcyc=200} scf=

\[
\text{Dipole}=-7.0887648,1.0666892,-0.4357827\]
\[
\text{Quadrupole}=-3.4679904,6.016927221,0.0595603102,-0.8331697299,2.7873675858,4.558474073\]
\[
\text{V(E=544.9,Go=0.9,State=1,Al/HF=30.71,3071012222,RSMS=5.153,9999,RSMSf=2.4232922728,Di}ole=-7.0887648,1.0666892,-0.4357827 Qu}d\text{ruple=-3.4679904,6.016927221,0.0595603102,-0.8331697299,2.7873675858,4.558474073.}
16. Copies of NMR Spectra

- NMR Spectra for compound 3ac (Ar = Ph)
- Detailed resonances and chemical shifts are provided in the figure.
3j: Ar = 2-naphthyl
\[ f_1 (\text{ppm}) \]

- \[ 0 \]
- \[ 0.5 \]
- \[ 1.0 \]
- \[ 1.5 \]
- \[ 2.0 \]
- \[ 2.5 \]
- \[ 3.0 \]
- \[ 3.5 \]
- \[ 4.0 \]
- \[ 4.5 \]
- \[ 5.0 \]
- \[ 5.5 \]
- \[ 6.0 \]
- \[ 6.5 \]
- \[ 7.0 \]
- \[ 7.5 \]
- \[ 8.0 \]
- \[ 8.5 \]

\[ 0 \]
- \[ 50 \]
- \[ 100 \]
- \[ 150 \]
- \[ 200 \]
- \[ 250 \]
- \[ 300 \]
- \[ 350 \]
- \[ 400 \]
- \[ 450 \]
- \[ 500 \]

\[ 13.6974 \]
- \[ 55.2778 \]
- \[ 66.5528 \]
- \[ 76.5769 \]
- \[ 76.6215 \]
- \[ 77.0002 \]
- \[ 77.4241 \]
- \[ 98.2455 \]
- \[ 120.8335 \]
- \[ 124.5147 \]
- \[ 128.5922 \]
- \[ 128.8656 \]
- \[ 128.9769 \]
- \[ 135.9792 \]
- \[ 137.6688 \]
- \[ 149.6238 \]
- \[ 150.7896 \]
- \[ 177.3728 \]
$f_1$ (ppm)

$-200$ $0$ $200$ $400$ $600$ $800$ $1000$ $1200$ $1400$ $1600$ $1800$ $2000$ $2200$ $2400$ $2600$ $2800$ $3000$ $3200$

$-50$ $0$ $50$ $100$ $150$ $200$ $250$ $300$ $350$ $400$ $450$ $500$ $550$

14.4785 32.6416 58.1465 62.2557 66.7047 76.5764 77.0000 77.4235 79.6621 118.1911 126.9658 127.5116 128.8957 130.2162 132.8306 136.4561 137.5421 137.8179 146.5218 151.7051 176.2506 195.5803 204.6083

$6e$: $Ar^2 = 3,4$-Cl$_2$Ph

$HN$ $SO$ $Me$ $N$ $COAr^2$ $COMe$ $6e$: $Ar^2 = 3,4$-Cl$_2$Ph
HN
S
O
Me
N
COAr²
6g: Ar² = 3-MeOPh

HN
S
O
Me
N
COAr²
6g: Ar² = 3-MeOPh
$6h: \text{Ar}^2 = 2\text{-MeOPh}$
6k: Ar² = 2-furyl
8a: \( \text{Ar}^2 = \text{Ph} \)
8e: Ar² = 2-thienyl
10b: R = 5-F

10b: R = 5-F
10c: $R = 5$-Cl

$OEt$
10d: R = 5-Br

10d: R = 5-Br
10e: R = 5-Me

HN
S
O
O
10e: R = 5-Me

HN
S
O
O
10e: R = 5-Me

10e: R = 5-Me

10e: R = 5-Me
10h: $R = 6$-OMe
HN
SO
Me
ON
Bn
O
10i: R = 7-Cl

HN
SO
Me
ON
Bn
O
10i: R = 7-Cl

HN
SO
Me
ON
Bn
O
10i: R = 7-Cl
