Enantioselective construction of dispirotetriheterocycles featuring a 4-aminopyrazolone motif through a cascade Michael/cyclization process

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General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Column chromatography was performed on silica gel (200–300 mesh). Enantiomeric excesses (ee) were determined by HPLC using corresponding commercial chiral columns as stated at 30 °C with UV detector at 254 nm. Optical rotations were reported as follows: [α]D (c g/100 mL, solvent). All 1H NMR and 19F NMR spectra were recorded on a Bruker Avance II 400 MHz and Bruker Avance III 471 MHz respectively. 13C NMR spectra were recorded on a Bruker Avance II 101 MHz or Bruker Avance III 126 MHz with chemical shifts reported as ppm (in CDCl3, TMS as internal standard). Data for 1H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad singlet, dd = double doublet, coupling constants in Hz, integration). HRMS (ESI) was obtained with a HRMS/MS instrument (LTQ Orbitrap XL TM). The absolute configuration of 5 was assigned by the X-ray analysis.

4-Isothiocyanato pyrazolones1 and 3-ylideneoxindoles2 were prepared according to the literature procedures. The racemic products were synthesized using quinine/quinidine = 1:1 as catalyst.

Experimental procedures and characterization of products 3aa-3ag and 4-7

General procedure: synthesis of compound 3aa-3ag

\[
\begin{align*}
\text{Ph} \quad \text{N} \quad \text{N} \quad \text{C} \quad \text{R} & \quad \text{Et} \quad \text{OOC} \quad \text{N} \quad \text{Ph} \\
1 & \quad + \quad 2 & \quad \xrightarrow{\text{C3 (5 mol %)}} & \quad 3 \\
\text{Ph} \quad \text{N} \quad \text{N} \quad \text{S} & \quad \text{COOEt} \quad \text{R} \quad \text{R}^1
\end{align*}
\]

To a Schlenk tube equipped with a magnetic stir bar was charged with compound 1 (0.2 mmol) and C3 (5 mmol %), followed with DCM (2 mL). Compound 2 (0.24 mmol) was then added in one portion. The reaction mixture was stirred at room temperature. When compound 1 was consumed as checked by TLC, the reaction was stopped and purified by column chromatography on silica gel directly to give the product 3.

Prepared according to the general procedure within 7 h as white solid (104.4 mg, 89% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]D = 97.7 (c 0.79, CH2Cl2); Mp 150.1-153 °C; 1H NMR (400 MHz, Chloroform-d) δ 9.13 (s, 1H), 8.06 (d, J = 7.9 Hz, 2H), 7.82 (d, J = 6.9 Hz, 2H), 7.63-7.54 (m, 3H), 7.44 (t, J = 7.9 Hz, 2H), 7.41-7.36 (m, 2H), 7.30-7.24 (m, 4H), 7.05 (t, J = 7.7 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.47 (t, J = 7.6 Hz, 1H), 5.22 (d, J = 7.6 Hz, 1H), 5.05 (s, 1H), 4.99 (d, J = 16.0 Hz, 1H), 4.92 (d, J = 16.0 Hz, 1H), 3.75-3.67 (m, 1H), 3.57-3.49 (m, 1H),
0.38 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 202.0, 174.6, 168.9, 165.1, 143.8, 137.5, 135.2, 131.3, 130.5, 129.9, 129.3, 129.20, 129.1, 128.6, 127.7, 127.6, 127.5, 125.9, 123.7, 122.7, 119.2, 109.5, 73.9, 68.2, 61.4, 58.4, 44.7, 12.9; HRMS (ESI) m/z Calcd for C$_{35}$H$_{29}$N$_{4}$O$_{4}$S$^+$ ([M+H]$^+$) 601.1904, Found 601.1901; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, $t_{\text{major}}$ = 8.4 min, $t_{\text{minor}}$ = 37.5 min).

Prepared according to the general procedure within 7 h as white solid (105.6 mg, 86% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [$\alpha$]$_{D}^{25}$ = 92.6 (c 0.43, CH$_2$Cl$_2$); Mp 160.1-162.9 °C; $^1$H NMR (400 MHz, Chloroform-$d$) δ 8.81 (s, 1H), 8.04 (dd, $J = 8.7$, 1.2 Hz, 2H), 7.55 (d, $J = 7.7$ Hz, 1H), 7.50-7.45 (m, 4H), 7.40 (d, $J = 6.7$ Hz, 2H), 7.30-7.25 (m, 5H), 7.04 (td, $J = 7.8$, 1.1 Hz, 1H), 6.65 (d, $J = 7.9$ Hz, 1H), 6.43 (td, $J = 7.6$, 1.0 Hz, 1H), 5.12 (s, 1H), 5.07 (dd, $J = 7.7$, 1.1 Hz, 1H), 4.99 (d, $J = 8.0$ Hz, 1H), 4.96 (d, $J = 12.0$ Hz, 1H), 3.86-3.78 (m, 1H), 3.60-3.47 (m, 1H), 2.67 (s, 3H), 0.43 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 201.9, 168.3, 143.8, 139.2, 137.5, 135.2, 132.1, 130.7, 130.4, 129.1, 128.6, 127.7, 127.6, 127.5, 126.5, 125.9, 123.6, 122.7, 119.1, 109.4, 67.6, 61.4, 58.4, 44.7, 20.5, 13.0; HRMS (ESI) m/z Calcd. for C$_{36}$H$_{31}$N$_{4}$O$_{4}$S$^+$ ([M+H]$^+$) 615.2061, Found 615.2060; Enantiomeric excess was determined to be 98%
(determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C,
0.8 mL/min, t_major = 9.0 min, t_minor = 40.8 min)

Prepared according to the general procedure within 7 h as white solid
(110.5 mg, 90% yield) after silica gel chromatography (EtOAc/petroleum
ether = 1/6). [α]_D^20_° = 70.2 (c 0.64, CH_2Cl_2); CH_2Cl_2); Mp 146.5-148.0 °C;
^1H NMR (400 MHz, Chloroform-d) δ 8.85 (s, 1H), 8.06 (d, J = 8.1 Hz,
2H), 7.61 (d, J = 7.2 Hz, 2H), 7.46-7.38 (m 6H), 7.46-7.38 (m, 4H), 7.06
t, J = 7.7 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.48 (t, J = 7.6 Hz, 1H),
5.29 (d, J = 7.6 Hz, 1H), 5.05 (s, 1H), 4.96 (s, 2H), 3.77-3.65 (m, 1H),
3.57-3.49 (m, 1H), 2.41 (s, 3H), 0.39 (t, J = 7.1 Hz, 3H); ^13C NMR (101
MHz, Chloroform-d) δ 202.1, 168.9, 165.1, 158.0, 143.9, 139.0, 137.6,
135.2, 131.2, 131.1, 130.3, 129.2, 129.2, 129.1, 128.6, 127.6, 127.5, 126.9, 125.9, 123.7, 122.6,
119.1, 109.5, 61.4, 58.3, 44.7, 21.5, 13.0; HRMS (ESI) m/z Calcd. for C_{36}H_{31}N_4O_4S_4 ([M+H]^+)
615.2061, Found 615.2061; Enantiomeric excess was determined to be 99% (determined by
HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, 
t_{major} = 9.4 min, t_{minor} = 35.8 min

Prepared according to the general procedure within 7 h as white solid
(106.8 mg, 87% yield) after silica gel chromatography (EtOAc/petroleum 
ether = 1/6). [\alpha]_D^{25} = 70.2 (c 0.64, CH$_2$Cl$_2$); Mp 146.5-148.0 °C; 1H NMR
(400 MHz, Chloroform-d) δ 8.90 (s, 1H), 8.06 (d, $J = 8.0$ Hz, 2H), 7.69 (d, 
$J = 8.1$ Hz, 2H), 7.47-7.35 (m, 6H), 7.29-7.23 (m, 4H), 7.06 (td, $J = 7.8,
1.2$ Hz, 1H), 6.66 (d, $J = 7.8$ Hz, 1H), 6.47 (td, $J = 7.6, 1.0$ Hz, 1H), 5.23
(dd, $J = 7.8, 1.1$ Hz, 1H), 5.05 (s, 1H), 5.00 (d, $J = 16.0$ Hz, 1H), 4.94 (d, $J
= 16.0$ Hz, 1H), 3.75-3.65 (m, 1H), 3.57-3.49 (m, 1H), 2.48 (s, 3H), 0.38 (t, 
$J = 7.1$ Hz, 3H); 13C NMR (101 MHz, Chloroform-d) δ 202.0, 168.9, 165.1, 143.9, 140.9, 137.6, 135.2, 129.9, 129.8, 129.2, 129.0, 128.6, 128.3, 127.6, 127.5, 125.8, 123.8, 122.5, 119.1, 109.5, 73.8, 68.1, 61.3, 58.3, 44.7, 21.5, 13.0; HRMS (ESI) m/z Calcd. for 
C$_{36}$H$_{27}$N$_4$O$_4$S$^+$ ([M+H]$^+$) 615.2061, Found 615.2059; Enantiomeric excess was determined to be
99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_major = 10.8 min, t_minor = 34.5 min).

Prepared according to the general procedure within 5 h as white solid (107.5 mg, 87% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). \( [\alpha]_D^{19} = 73.4 \) (c 1.36, CH\(_2\)Cl\(_2\)); Mp 150.1-153.7 °C;\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \( \delta \) 9.36 (s, 1H), 8.00 (d, \( J = 7.8 \) Hz, 2H), 7.87-7.80 (m, 2H), 7.44-7.35 (m, 4H), 7.30-7.22 (m, 6H), 7.09 (td, \( J = 7.8, 1.2 \) Hz, 1H), 6.68 (d, \( J = 7.8 \) Hz, 1H), 6.56 (d, \( J = 7.6 \) Hz, 1H), 5.35 (dd, \( J = 7.8, 1.1 \) Hz, 1H), 5.05 (s, 1H), 4.98 (d, \( J = 16.0 \) Hz, 1H), 4.91 (d, \( J = 16.0 \) Hz, 1H) 3.72-3.64 (, 1H), 3.55-3.47 (m, 1H), 0.36 (t, \( J = 7.2 \) Hz, 3H);
\(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) \( \delta \) -109.09 (m).\(^{19}\)F NMR (470 MHz, Chloroform-\(d\)) \( \delta \) -201.8, 169.1, 165.2, 164.1 (d, \( J = 253.5 \) Hz), 157.2, 143.9, 135.1, 132.2 (d, \( J = 9.0 \) Hz), 129.4, 129.0, 128.6, 127.8, 127.7, 127.5, 125.9, 123.4, 122.7, 119.2, 116.3 (d, \( J = 21.2 \) Hz).
Hz), 109.7, 73.8, 68.3, 61.4, 58.4, 44.7, 13.0; HRMS (ESI) m/z Calcd. for C_{35}H_{28}FN_{4}O_{4}S^{+} ([M+H]^{+}) 619.1810, Found 619.1810; Enantiomeric excess was determined to be 96% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_{major} = 15.3 min, t_{minor} = 66.9 min)

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repared according to the general procedure within 18 h as white solid (110.5 mg, 85% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]_{D}^{25} = 50.6 (c 0.36, CH_{2}Cl_{2}); Mp 163.5-164.7 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.97 (s, 1H), 8.61 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.63-7.50 (m, 3H), 7.44 (t, J = 7.8 Hz, 2H), 7.34 (d, J = 7.0 Hz, 2H), 7.28-7.20 (m, 4H), 6.92 (t, J = 7.7 Hz, 1H), 6.56 (d, J = 7.8 Hz, 1H), 6.19 (t, J = 7.7 Hz, 1H), 5.14 (s, 1H), 4.92 (s, 2H), 4.81 (d, J = 7.7 Hz, 1H), 3.69-3.61 (m, 1H), 3.51-3.40 (m, 1H), 0.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, Chloroform-d) δ 202.2, 168.5, 165.1, 143.7, 137.5, 135.1,
134.2, 131.6, 131.1, 129.1, 128.9, 128.6, 128.3, 127.8, 127.7, 127.6, 127.4, 127.3, 126.9, 126.6, 126.0, 125.2, 123.5, 122.4, 119.2, 109.4, 67.6, 61.4, 58.5, 44.7, 12.9; HRMS (ESI) m/z Calcd. for C\textsubscript{39}H\textsubscript{31}N\textsubscript{4}O\textsubscript{4}S\textsuperscript{+} ([M+H]\textsuperscript{+}) 651.2061, Found 651.2060; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \( \lambda = 254 \text{ nm}, 30^\circ \text{C}, 0.8 \text{ mL/min}, t_{\text{major}} = 9.9 \text{ min}, t_{\text{minor}} = 69.9 \text{ min})

Prepared according to the general procedure within 7 h as white solid (113.1 mg, 87% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). \([\alpha]_{D}^{\text{20}} = 61.0 \text{ (c 0.73, CH\textsubscript{2}Cl\textsubscript{2})}; \text{Mp 150.1-153.1}^\circ \text{C}; ^{1}\text{H NMR (400 MHz, Chloroform-\text{d}) \delta 8.98 (s, 1H), 8.26 (s, 1H), 8.12 (d, J = 8.1 Hz, 2H), 8.01 (q, J = 8.6 Hz, 2H), 7.90 (dd, J = 20.0, 8.2 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.50-7.44 (m, 3H), 7.41-7.33 (m, 2H), 7.28-7.21 (m, 4H), 6.91 (t, J = 7.7 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 5.98 (t, J = 7.6 Hz, 1H), 5.35 (d, J = 7.7 Hz, 1H), 5.10 (s, 1H), 4.94 (s, 2H), 3.69-3.58 (m, 1H), 3.57-3.45 (m, 1H), 0.34 (t, J = 7.1 Hz, 3H); ^{13}\text{C NMR (101 MHz, Chloroform-\text{d}) \delta 202.1, 174.7, 169.0, 165.2, 157.6, 143.8, 137.6, 135.1, 133.9, 129.4, 129.1, 129.0, 128.7, 128.6, 127.7, 127.6, 127.6, 127.5, 127.0, 126.2, 125.9, 123.7, 122.4, 119.2, 109.5, 73.8, 68.3, 61.3, 58.5, 44.7, 12.9; HRMS (ESI)
m/z Calcd. for C_{39}H_{31}N_{4}O_{4}S^{+} ([M+H]^{+}) 651.2061, Found 651.2058; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_{major} = 11.4 min, t_{minor} = 72.7 min)

Prepared according to the general procedure within 15 h as white solid (93.2 mg, 77% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]_{D}^{20} = 68.8 (c 0.32, CH_{2}Cl_{2}); Mp 146.1-148.7 °C; \(^1\)H NMR (400 MHz, Chloroform-\(d\)) δ 8.74 (s, 1H), 8.03 (d, \(J = 8.0\) Hz, 2H), 7.62 (d, \(J = 5.1\) Hz, 1H), 7.55 (d, \(J = 3.7\) Hz, 1H), 7.46-7.39 (m, 4H), 7.31-7.24 (m, 4H), 7.20 (t, \(J = 4.4\) Hz, 1H), 7.11 (t, \(J = 7.8\) Hz, 1H), 6.79-6.57 (m, 2H), 5.80 (d, \(J = 7.6\) Hz, 1H), 5.02 (d, \(J = 12.0\) Hz, 1H), 4.99 (s, 1H), 4.95 (d, \(J = 12.0\) Hz, 1H), 3.73-3.48 (m, 2H), 0.40 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-\(d\)) δ 202.1, 165.0, 153.4, 144.0, 137.4, 135.1, 130.5, 129.5, 129.0, 128.6, 127.89, 127.9, 127.5, 125.9, 124.0, 122.7, 119.1, 109.7, 73.5, 68.3, 61.5, 58.8, 44.7, 13.0; HRMS (ESI) m/z Calcd. for C_{33}H_{27}N_{4}O_{4}S^{+} ([M+H]^{+}) 607.1468, Found 607.1464; Enantiomeric excess was determined to be 79% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_{major} = 11.7 min, t_{minor} = 64.4 min)
Prepared according to the general procedure within 2 h as white solid (97.9 mg, 91% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). \([\alpha]_D^{29} = 85.3\) (c 0.91, CH2Cl2); Mp 230.1-233.7 oC; 1H NMR (400 MHz, Chloroform-d) δ 8.79 (s, 1H), 7.95 (d, \(J = 7.8\) Hz, 2H), 7.46-7.37 (m, 4H), 7.36-7.20 (m, 6H), 7.09-7.00 (m, 1H), 6.80 (d, \(J = 7.8\) Hz, 1H), 5.08 (d, \(J = 16.0\) Hz, 1H), 4.99 (s, 1H), 4.95 (d, \(J = 16.0\) Hz, 1H), 3.79-3.71 (m, 1H), 3.65-3.52 (m, 1H), 2.55 (s, 3H), 0.45 (t, \(J = 7.1\) Hz, 3H); 13C NMR (101 MHz, Chloroform-d) δ 201.6, 174.2, 169.0, 165.6, 157.6, 144.1, 137.4, 135.1, 129.8, 129.0, 128.7, 128.5, 127.8, 127.6, 125.7, 123.2, 123.1, 118.9, 110.0, 73.3, 68.4, 61.6, 57.6, 44.7, 16.9, 13.0. HRMS (ESI) m/z Calcd. for C30H27N2O4S4 ([M+H]⁺) 539.1748, Found 539.1747; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_major = 15.1 min, t_minor = 32.5 min)
Prepared according to the general procedure within 2 h as white solid (100.5 mg, 91% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). \([\alpha]_D^{19} = 85.5\) (c 0.91, CH2Cl2); Mp 180.1-182.0°C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.98 (s, 1H), 8.00 (d, \(J = 8.2\) Hz, 2H), 7.47-7.18 (m, 11H), 7.07 (t, \(J = 7.6\) Hz, 1H), 6.81 (d, \(J = 7.9\) Hz, 1H), 5.07 (d, \(J = 16.0\) Hz, 2H), 5.01 (s, 1H), 4.95 (d, \(J = 16.0\) Hz, 1H), 3.79-3.71 (m, 1H), 3.62-3.54 (m, 1H), 2.88 (q, \(J = 7.2\) Hz, 2H), 1.48 (t, \(J = 7.1\) Hz, 3H), 0.47 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 201.5, 165.7, 161.4, 144.1, 137.6, 135.1, 129.8, 128.9, 128.7, 127.7, 127.6, 125.6, 123.4, 123.2, 119.0, 110.0, 73.6, 68.6, 61.6, 57.7, 44.7, 24.0, 13.1, 9.40; HRMS (ESI) m/z Calcd. for C\(_{31}\)H\(_{30}\)N\(_4\)O\(_4\)S\(_4\) ([M+H]\(^+\)) 553.1904, Found 553.1904; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \(\lambda = 254\) nm, 30 °C, 0.8 mL/min, \(t_{major} = 11.5\) min, \(t_{minor} = 35.3\) min)
Prepared according to the general procedure within 3 h as white solid (101.9 mg, 90% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). \([\alpha]_D^{19} = 96.1 \text{ (c 1.06, CH}_2\text{Cl}_2)\]; Mp 125.1-130.7°C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.63 (s, 1H), 8.00 (d, \(J = 8.1\) Hz, 2H), 7.49-7.37 (m, 4H), 7.35-7.23 (m, 6H), 7.07 (t, \(J = 7.6\) Hz, 1H), 6.81 (d, \(J = 7.9\) Hz, 1H), 5.10 (d, \(J = 6.6\) Hz, 1H), 5.01 (s, 1H), 4.95 (d, \(J = 16.0\) Hz, 1H), 3.80-3.72 (m, 1H), 3.62-3.54 (m, 1H), 3.16-3.10 (m, 1H), 1.55 (d, \(J = 6.6\) Hz, 3H), 1.47 (d, \(J = 7.0\) Hz, 3H), 0.48 (t, \(J = 7.1\) Hz, 3H); \(^1^3\)C NMR (101 MHz, Chloroform-d) \(\delta\) 201.2, 174.2, 168.8, 165.6, 164.4, 144.2, 137.6, 135.1, 129.8, 128.9, 128.7, 127.7, 127.6, 125.6, 123.1, 123.1, 118.8, 110.0, 73.6, 68.4, 61.54, 57.9, 44.7, 30.4, 22.6, 19.7, 13.0; HRMS (ESI) m/z Calcd. for C\(_{32}\)H\(_{31}\)N\(_4\)O\(_4\)S\(^+\) ([M+H]\(^+\)) 567.2061, Found 567.2057; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \(\lambda = 254\) nm, 30 °C, 0.8 mL/min, \(t_{\text{major}} = 10.2\) min, \(t_{\text{minor}} = 72.0\) min)
Prepared according to the general procedure within 2 h as white solid (106.0 mg, 94% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). $[\alpha]_{D}^{19} = 64.2$ (c 0.45, CH$_2$Cl$_2$); Mp 147.1-150.9°C; $^1$H NMR (400 MHz, Chloroform-d) δ 8.52 (s, 1H), 7.94 (d, $J = 8.0$ Hz), 7.47-7.38 (m, 5H), 7.34-7.19 (m, 5H), 7.02 (t, $J = 7.6$ Hz, 1H), 6.81 (d, $J = 7.9$ Hz, 1H), 5.10 (d, $J = 16.0$ Hz, 1H), 5.02 (s, 1H), 4.98 (d, $J = 16.0$ Hz, 1H), 3.82-3.76 (m, 1H), 3.64-3.56 (m, 1H), 1.99-1.92 (m, 1H), 1.49-1.38 (m, 1H), 1.34-1.26 (m, 1H), 1.24-1.10 (m, 2H), 0.49 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 174.3, 169.0, 165.5, 161.8, 144.2, 135.2, 129.7, 128.9, 128.7, 127.7, 127.6, 125.6, 123.3, 122.9, 118.8, 110.0, 73.7, 68.2, 61.5, 57.7, 44.7, 13.1, 11.0, 9.3, 9.2; HRMS (ESI) m/z Calcd. for C$_{32}$H$_{29}$N$_4$O$_4$S$^+$ ([M+H]$^+$) 565.1904, Found 565.1906; Enantiomeric excess was determined to be 98% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{major} = 12.1$ min, $t_{minor} = 47.1$ min)
Prepared according to the general procedure within 2 h as white solid (106.0 mg, 94% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]_{D}^{25} = 38.3 (c: 0.68, CH₂Cl₂); Mp 156.1-157.9 °C; \(^1\)H NMR (400 MHz, Chloroform-d) δ 8.47 (s, 1H), 7.84 (d, \(J = 8.1\) Hz, 2H), 7.46 (t, \(J = 6.9\) Hz, 3H), 7.41 (d, \(J = 7.3\) Hz, 2H), 7.36 (t, \(J = 7.5\) Hz, 2H), 7.33-7.23 (m, 7H), 7.14 (t, \(J = 7.4\) Hz, 1H), 7.07 (t, \(J = 7.6\) Hz, 1H), 6.81 (d, \(J = 7.9\) Hz, 1H), 5.06 (d, \(J = 15.8\) Hz, 2H), 4.91 (d, \(J = 15.7\) Hz, 1H), 4.33 (d, \(J = 16.4\) Hz, 1H), 4.14 (d, \(J = 16.4\) Hz, 1H), 3.84-3.70 (m, 1H), 3.67-3.53 (m, 1H), 0.47 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-d) δ 201.2, 174.4, 169.2, 166.0, 159.9, 144.3, 137.5, 135.1, 134.5, 129.9, 129.9, 128.9, 128.7, 128.7, 127.7, 127.6, 127.2, 125.5, 123.4, 123.2, 118.8, 110.1, 73.6, 68.5, 61.7, 58.3, 44.8, 36.8, 13.1; HRMS (ESI) m/z Calcd. for C_{36}H_{31}N_{4}O_{4}S^{+} ([M+H]^{+}) 615.2061, Found 615.2058; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \(\lambda = 254\) nm, 30 °C, 0.8 mL/min, t_{major} = 14.2 min, t_{minor} = 27.2 min)
Prepared according to the general procedure within 8 h as white solid (89.08 mg, 85% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). $\left[\alpha\right]_{19}^{D} = 105.1 \, (c = 0.87, \text{CH}_2\text{Cl}_2)$; Mp 241.3-243.4 °C; $^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.93 (s, 1H), 8.02 (dd, $J = 8.7, 1.2$ Hz, 2H), 7.77 (dt, $J = 6.9, 1.6$ Hz, 2H), 7.63-7.53 (m, 3H), 7.43 (t, $J = 8.0$ Hz, 2H), 7.29-7.22 (m, 1H), 7.17 (td, $J = 7.8, 1.2$ Hz, 1H), 6.78 (d, $J = 7.8$ Hz, 1H), 6.48 (td, $J = 7.6, 1.1$ Hz, 1H), 5.17 (d, $J = 7.6$ Hz, 1H), 4.92 (s, 1H), 3.72-3.66 (m, 1H), 3.62-3.54 (m, 1H), 3.23 (s, 3H), 0.52 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 202.1, 174.3, 165.0, 157.9, 144.7, 131.2, 130.5, 129.9, 129.4, 129.2, 129.0, 127.6, 125.9, 123.6, 122.6, 119.1, 108.3, 73.7, 68.1, 61.3, 58.2, 27.3, 13.1; HRMS (ESI) m/z Calcd. for C$_{29}$H$_{25}$N$_4$O$_4$S$^+ \, ([M+H]$^+$) 525.1591, Found 525.1587; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{major}} = 10.0$ min, $t_{\text{minor}} = 16.4$ min).
Prepared according to the general procedure within 6 h as white solid (104.4 mg, 85% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). $[\alpha]_D^{19} = 91.5$ (c 1.03, CH$_2$Cl$_2$); Mp 152.5-154.2 °C; $^1$H NMR (400 MHz, Chloroform-d) δ 9.03 (s, 1H), 8.00 (d, $J = 7.8$ Hz, 2H), 7.81-7.75 (m, 2H), 7.57-7.49 (m, 3H), 7.38 (dd, $J = 8.6$, 7.4 Hz, 2H), 7.35-7.30 (m, 2H), 7.25-7.14 (m, 4H), 6.80 (d, $J = 7.9$ Hz, 1H), 6.48 (d, $J = 8.0$ Hz, 1H), 5.07 (d, $J = 1.6$ Hz, 1H), 5.00 (s, 1H), 4.90 (d, $J = 16.0$ Hz, 1H), 4.85 (d, $J = 16.0$ Hz, 1H), 3.72-3.64 (m, 2H), 3.50-3.42 (m, 1H), 1.75 (s, 3H), 0.31 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 202.3, 174.6, 169.0, 165.1, 141.4, 137.6, 135.3, 132.1, 130.7, 130.1, 129.5, 129.1, 128.6, 127.7, 127.5, 125.9, 124.6, 119.2, 109.3, 73.8, 68.3, 61.3, 58.4, 44.7, 20.9, 12.9. HRMS (ESI) m/z Calcd. for C$_{36}$H$_{31}$N$_4$O$_4$S$^+$ ([M+H$^+$]) 615.2061, Found 615.2053; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{major}} = 11.9$ min, $t_{\text{minor}} = 28.1$ min)
Prepared according to the general procedure within 6 h as white solid (107.1 mg, 87% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]$_D^{29}$ = 77.8 (c 1.09, CH$_2$Cl$_2$); Mp 156.7-157.8 °C. $^1$H NMR (400 MHz, Chloroform-d) δ 9.06 (s, 1H), 7.86 (dd, $J$ = 6.5, 2.7 Hz, 2H), 7.59-7.49 (m, 3H), 7.41 (t, $J$ = 7.9 Hz, 2H), 7.36 (d, $J$ = 6.7 Hz, 2H), 7.29-7.21 (m, 4H), 6.60 (dd, $J$ = 8.6, 2.4 Hz, 1H), 6.54 (d, $J$ = 8.5 Hz, 1H), 5.31 (d, $J$ = 2.4 Hz, 1H), 5.07 (s, 1H), 4.95 (d, $J$ = 16.0 Hz, 1H), 4.87 (d, $J$ = 16.0 Hz, 1H) 3.69-3.63 (m, 1H), 3.58-3.50 (m, 1H), 3.31 (s, 3H), 0.41 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 201.9, 174.4, 169.2, 165.1, 157.9, 155.9, 137.3, 135.2, 131.6, 130.8, 129.4, 129.2, 129.0, 128.6, 127.6, 127.5, 125.8, 119.1, 114.3, 111.7, 109.9, 73.7, 68.7, 61.4, 58.6, 56.0, 44.8, 13.0; HRMS (ESI) m/z Calcd. for C$_{36}$H$_{31}$N$_4$O$_5$S$^+$ ([M+H$^+$]) 631.2010, Found 631.2003; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, $t_{\text{major}}$ = 12.6 min, $t_{\text{minor}}$ = 51.5 min)
Prepared according to the general procedure within 30 min as white solid (101.1 mg, 82% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). 

$[\alpha]_{D}^{19} = 88.8 \ (c \ 1.09, \ \text{CH}_2\text{Cl}_2); \ Mp \ 151.9-152.2^\circ \text{C}; \ {^1}H \text{ NMR (400 MHz, Chloroform-}d) \ \delta \ 8.98 \ (s, \ 1H), \ 8.03-7.97 \ (m, \ 2H), \ 7.79-7.71 \ (m, \ 2H), \ 7.61 \ (t, \ J = 7.4 \ Hz, \ 1H), \ 7.53 \ (t, \ J = 7.4 \ Hz, \ 2H), \ 7.39 \ (t, \ J = 8.0 \ Hz, \ 2H), \ 7.35-7.29 \ (m, \ 2H), \ 7.26-7.20 \ (m, \ 4H), \ 6.72 \ (td, \ J = 8.6, \ 2.6 \ Hz, \ 1H), \ 6.52 \ (dd, \ J = 8.6, \ 4.2 \ Hz, \ 1H), \ 5.03 \ (s, \ 1H), \ 4.92 \ (d, \ J = 16.0, \ 1H), \ 4.87 \ (d, \ J = 16.0, \ 1H), \ 4.79 \ (dd, \ J = 8.7, \ 2.6 \ Hz, \ 1H), \ 3.80-3.71 \ (m, \ 1H), \ 3.59-3.51 \ (dq, \ J = 10.7, \ 7.1 \ Hz, \ 1H), \ 0.43 \ (t, \ J = 7.1 \ Hz, \ 3H). \ {^{19}}F \text{ NMR (470 MHz, Chloroform-}d) \ \delta \ -119.19 \ (m) \ ; \ {^{13}}C \text{ NMR (101 MHz, Chloroform-}d) \ \delta \ 154.7 \ (d, \ J = 23.5 \ Hz), \ 112.10 \ (d, \ J = 26.9 \ Hz), \ 109.99 \ (d, \ J = 7.9 \ Hz). \ {^{13}}C \text{ NMR (101 MHz, Chloroform-}d) \ \delta \ 201.2, \ 174.4, \ 168.7, \ 164.8, \ 159.9, \ 157.80, \ 157.5, \ 139.8, \ 137.5, \ 134.8, \ 131.1, \ 130.8, \ 129.9, \ 129.4, \ 129.1, \ 128.7, \ 127.8, \ 127.5, \ 125.9, \ 119.1, \ \delta \ 115.5 \ (d, \ J = 23.5 \ Hz), \ 112.1 \ (d, \ J = 27.3 \ Hz), \ 110.0 \ (d, \ J = 8.1 \ Hz), \ 73.9, \ 68.2, \ 61.56, \ 58.0, \ 44.8, \ 13.1; \ \text{HRMS (ESI)} \ m/z \ \text{Calcd. for C}_{35}\text{H}_{28}\text{FN}_{4}\text{O}_{4}\text{S}^+$
([M+H]+) 619.1810, Found 619.1807; Enantiomeric excess was determined to be 99%
(determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_major = 10.9 min, t_minor = 31.0 min)

Prepared according to the general procedure within 15 min as white solid (101.4 mg, 80% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]_D^20 = 92.0 (c 1.09, CH₂Cl₂); Mp 156.7-157.8 °C; ¹H NMR (400 MHz, Chloroform-d) δ 9.00 (s, 1H), 7.99 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 7.4 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 7.9 Hz, 2H), 7.32-7.28 (m, 2H), 7.26-7.16 (m, 5H), 6.99 (dd, J = 8.4, 2.0 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 5.10 (d, J = 2.0 Hz, 1H), 5.01 (s, 1H), 4.91 (d, J = 16.0 Hz, 1H), 4.85 (d, J = 16.0 Hz, 1H), 3.80-3.72 (m, 1H), 3.56-3.48 (m, 1H), 0.40 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, Chloroform-d) δ 201.0, 174.3, 168.7, 164.8, 157.8, 142.4, 134.7, 131.6, 130.6, 129.8, 129.3, 129.3, 129.1, 128.7, 128.0, 127.8, 127.5, 125.9, 124.3, 119.1, 110.5,
73.8, 67.9, 61.6, 58.0, 44.8, 13.1; HRMS (ESI) m/z Calcd. for C_{35}H_{28}ClN_{4}O_{4}S^{+} ([M+H]^{+}) 635.1514, Found 635.1514; Enantiomeric excess was determined to be 94% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 30 °C, 0.8 mL/min, t_{major} = 11.8 min, t_{minor} = 27.3 min)

Prepared according to the general procedure within 15 min as white solid (108.5 mg, 79% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/6). [α]_{D}^{20} = 86.9 (c 1.27, CH_{2}Cl_{2}); Mp 154.1-155.9°C; ^1H NMR (400 MHz, Chloroform-d) δ 9.06 (s, 1H), 8.04 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 7.6 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 7.6 Hz, 2H), 7.42 (t, J = 7.8 Hz, 2H), 7.35 (d, J = 6.5 Hz, 2H), 7.30-7.22 (m, 4H), 7.19 (dd, J = 8.3, 1.8 Hz, 1H), 6.53 (d, J = 8.3 Hz, 1H), 5.38 (d, J = 1.9 Hz, 1H), 5.05 (s, 1H), 4.95 (d, J = 16.0 Hz, 1H), 4.80 (d, J = 16.0 Hz, 1H), 3.85-3.77 (m, 1H), 3.64-3.51 (m, 1H), 0.45 (t, J = 7.1 Hz, 3H); ^13C NMR (101 MHz,
Chloroform-\textsuperscript{d}) $\delta$ 174.2, 168.7, 164.7, 142.9, 137.5, 134.7, 132.3, 131.8, 130.6, 129.7, 129.6, 129.3, 129.1, 128.7, 127.8, 127.5, 126.9, 125.9, 119.1, 115.3, 111.1, 73.8, 67.9, 61.6, 58.1, 44.8, 13.1; HRMS (ESI) m/z Calcd. for C_{35}H_{28}BrN_{4}O_{4}S^{+} ([M+H]^+) 679.1009. Found 679.1014; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, $\lambda = 254$ nm, 30 °C, 0.8 mL/min, $t_{\text{major}} = 12.5$ min, $t_{\text{minor}} = 26.5$ min)

**Synthesis of compound d**

\[
\begin{align*}
\text{Br} & \quad \text{S} \\
\text{N} & \quad \text{N}
\end{align*}
\]

99\% ee, >20:1 dr

\[
\begin{align*}
\text{Br} & \quad \text{COOEt} \\
\text{N} & \quad \text{N}
\end{align*}
\]

62\% yield, 96\% ee, >20:1 dr
To a Schlenk tube equipped with a magnetic stir bar was charged with compound 3ag (0.1 mmol, 64.3 mg) and DCM (2 mL) at 0 °C, mCPBA (0.3 mmol, 54 mg) was added in one portion, then the reaction was stirred at room temperature for 1 h as white solid (93.2 mg, 77% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/3). \([\alpha]^2_{D} = 60.9 \ (c 0.32, \text{CH}_2\text{Cl}_2);\) Mp 140.1-142.7 °C; \(^1\text{H} \text{NMR} (400 \text{ MHz}, \text{Chloroform}-d) \delta 8.00 \ (d, J = 7.5 \text{ Hz}, 2\text{H}), 7.79-7.62 \ (m, 4\text{H}), 7.54 \ (t, J = 7.9 \text{ Hz}, 2\text{H}), 7.42 \ (t, J = 7.9 \text{ Hz}, 2\text{H}), 7.26-7.14 \ (m, 6\text{H}), 6.47 \ (d, J = 8.2 \text{ Hz}, 1\text{H}), 5.32 \ (s, 1\text{H}), 5.02 \ (d, J = 15.8 \text{ Hz}, 1\text{H}), 4.88 \ (s, 1\text{H}), 4.77 \ (d, J = 15.9 \text{ Hz}, 1\text{H}), 3.86-3.80 \ (m, 1\text{H}), 3.60-3.56 \ (m, 1\text{H}), 0.44 \ (t, J = 6.9 \text{ Hz}, 3\text{H}); \(^{13}\text{C} \text{NMR} (101 \text{ MHz, Chloroform}-d) \delta 173.4, 171.3, 164.8, 158.4, 142.8, 137.6, 134.5, 133.5, 132.3, 131.8, 129.4, 129.3, 129.0, 128.7, 127.8, 127.2, 126.9, 125.8, 119.0, 111.0, 67.3, 61.6, 59.0, 55.4, 44.6, 13.1; \) HRMS (ESI) m/z Calcd. for C_{35}H_{28}BrN_{4}O_{5}S^{+} ([M+H]^{+}) 663.1251, Found 663.1238; Enantiomeric excess was determined to be 96% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \(\lambda = 254 \text{ nm, 30 °C, 0.8 mL/min, } t_{\text{major}} = 37.2 \text{ min, } t_{\text{minor}} = 68.7 \text{min})

![Graph](attachment://Graph.png)

| Peak RetTime Type Width Area Height Area % |
|---|---|---|---|---|---|
| 1 | 36.835 BB | 1.3262 | 1.58980e4 | 183.5981 | 50.1103 |
| 2 | 67.138 BB | 2.2213 | 1.58280e4 | 92.45415 | 49.8897 |

![Graph](attachment://Graph2.png)

| Peak RetTime Type Width Area Height Area % |
|---|---|---|---|---|---|
| 1 | 37.236 BB | 1.3729 | 2.40418e4 | 270.50290 | 98.0676 |
| 2 | 68.695 MM | 2.4755 | 473.72968 | 3.18944 | 1.9324 |
Synthesis of compound 5

To a Schlenk tube equipped with a magnetic stir bar was charged with compound 3ag (0.2 mmol, 136.6 mg) and K$_2$CO$_3$ (0.44 mmol, 60.7 mg), followed with acetone (5 mL) at 0 °C. MeI (0.44 mmol, 62.5 mg) was dropwise added into reaction mixture. Then the reaction was stirred at room temperature overnight as white solid (96.9 mg, 70% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/3). $[\alpha]_{D}^{25} = 36.1$ (c 0.13, CH$_2$Cl$_2$); Mp 266.0-270.4 °C; $^1$H NMR (400 MHz, Chloroform-d) δ 8.17 (d, $J$ = 8.0 Hz, 2H), 7.89-7.82 (m, 2H), 7.66-7.57 (m, 3H), 7.48-7.44 (m, 4H), 7.40-7.29 (m, 4H), 7.24 (d, $J$ = 7.4 Hz, 1H), 7.15 (d, $J$ = 1.9 Hz, 1H), 6.60 (d, $J$ = 8.4 Hz, 1H), 5.20 (d, $J$ = 15.7 Hz, 1H), 4.78 (d, $J$ = 15.7 Hz, 1H), 4.12 (s, 1H), 4.06-3.87 (m, 2H), 2.57 (s, 3H), 0.93 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 170.2, 168.5, 166.2, 138.3, 135.2, 132.7, 131.1, 130.0, 129.2, 128.8, 128.8, 127.8, 127.6, 126.5, 126.5, 125.0, 118.6, 115.2, 111.1, 84.5, 68.2, 62.2, 60.9, 44.6, 14.3, 13.6; HRMS (ESI) m/z Calcd. for C$_{36}$H$_{30}$BrN$_4$O$_4$S$^+$ ([M+H$^+$]$^+$) 693.1166, Found 693.1160; Enantiomeric excess was determined to be 99% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, $\lambda$ = 254 nm, 25°C, 0.8 mL/min, $t_{\text{major}}$ = 7.8 min, $t_{\text{minor}}$ = 12.0 min).
Synthesis of compound 6

To a Schlenk tube equipped with a magnetic stir bar was charged with compound 5 (0.05 mmol, 34.6 mg) and chloroform (1 mL) at 0 °C, mCPBA (0.05 mmol, 8.6 mg) was added in one portion. Then the reaction was stirred at room temperature for 1 h as white solid (33.7 mg, 95% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/3).

\[
\alpha_{19}^D = 199.1 \text{ (c 0.22, CH}_2\text{Cl}_2); \]

\[^1H\text{ NMR (400 MHz, Chloroform-}d\text{)} \delta 8.11 (d, J = 7.7 \text{ Hz, 2H}), 7.77-7.81 \text{ (m, 2H), 7.66 (q, J = 3.6 \text{ Hz, 3H}), 7.51-7.42 \text{ (m, 4H), 7.41-7.31 \text{ (m, 3H), 7.31-7.24 \text{ (m, 2H), 7.19 (d, J = 1.9 \text{ Hz, 1H), 6.63 (d, J = 8.3 \text{ Hz, 1H), 5.04 (d, J = 16.0 Hz, 1H), 4.96 (d, J = 16.0 Hz, 1H), 4.13 (s, 1H), 4.08-3.90 (m, 2H), 2.93 (s, 3H), 1.29 (s, 1H), 0.94 (t, J = 7.2 \text{ Hz, 3H};} \]

\[^13C\text{ NMR (101 MHz, Chloroform-}d\text{)} \delta 169.0, 165.4, 155.2, 142.8, 137.8, 134.9, 133.2, 131.5, 130.1, 129.7, 129.4, 129.1, 128.9, 128.8, 127.9, 127.7, 127.5, 126.4, 125.5, 118.7, 115.3, 111.4, 85.0, 67.1, 62.6, 61.1, 45.1, 40.5, 13.6; HRMS (ESI) m/z Calcd. for C_{36}H_{30}BrN_4O_5S_5^+ ([M+H]^+) 709.1115, Found 709.1132; Enantiomeric excess was determined to be 98% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, \(\lambda = 254 \text{ nm, 25 °C, 0.7 mL/min, } t_{\text{major}} = 28.8 \text{min, } t_{\text{minor}} = 33.5 \text{min.} \)
To a Schlenk tube equipped with a magnetic stir bar was charged with compound 6 (0.05 mmol, 34.6 mg) and chloroform (1 mL) at 0 °C. mCPBA (0.1 mmol, 17.2 mg) was added in one portion. Then the reaction was stirred at room temperature for 1 h as white solid (33.7 mg, 95% yield) after silica gel chromatography (EtOAc/petroleum ether = 1/3). \([\alpha]_{D}^{20} = 108.5\) (c 0.54, 95% ee, >20:1 dr).
CH₂Cl₂); ¹H NMR (400 MHz, Chloroform-d) δ 8.11 – 8.06 (m, 2H), 7.76 (dd, J = 6.7, 2.9 Hz, 2H), 7.66 – 7.63 (m, 2H), 7.51 – 7.40 (m, 5H), 7.26 (s, 5H), 7.18 (d, J = 1.9 Hz, 1H), 6.54 (d, J = 8.4 Hz, 1H), 5.03 (d, J = 16.0 Hz, 1H), 4.94 (d, J = 16.0 Hz, 1H), 4.09 (s, 1H), 4.06-3.98 (m, 1H), 3.95-3.87 (m, 1H), 3.28 (s, 3H), 1.26 (s, 1H), 0.91 (t, J = 7.2 Hz, 3H); ¹³C NMR (101 MHz, Chloroform-d) δ 169.0, 165.4, 155.2, 142.8, 137.78, 134.9, 133.2, 131.5, 130.1, 129.78, 129.4, 129.1, 128.9, 127.9, 127.7, 127.5, 126.4, 125.5, 118.7, 115.3, 111.4, 85.1, 67.10, 62.7, 61.1, 45.2, 40.5, 13.6. Enantiomeric excess was determined to be 98% (determined by HPLC using chiral AD-H column, hexane/2-propanol = 70/30, λ = 254 nm, 25 °C, 0.6 mL/min, t_major = 16.0min, t_minor = 22.5min.

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Gram scale synthesis of compound 3ag
To a Schlenk tube equipped with a magnetic stir bar was charged with compound 1a (2 mmol, 594 mg) and C3 (1% mmol, 6.3 mg), followed with DCM (10 ml). Compound 2g (2.4 mmol, 926 mg) was added in one portion. The reaction was checked by TLC. When the compound 1a was consumed up, the reaction was stopped and purified by column chromatography on silica gel directly to give the product 3ag.
References


NMR spectra for compounds