Supporting Information

for

Bioinspired tetraamino-bisthioureia chiral macrocycles in catalyzing decarboxylative Mannich reactions

Hao Guo, Yu-Fei Ao, De-Xian Wang and Qi-Qiang Wang

*Beilstein J. Org. Chem.* **2022**, *18*, 486–496. doi:10.3762/bjoc.18.51

Experimental procedures, characterization data, copies of $^1$H and $^{13}$C NMR spectra
# Table of contents

1. General information .......................................................... S2
2. Synthesis .............................................................................. S3
   2.1 Synthesis of dinitro compounds 3 ................................... S3
   2.2 Synthesis of diamine compounds 4 ............................... S7
   2.3 Synthesis of diisothiocyanate compounds 5 ..................... S10
   2.4 Synthesis of macrocycles M ............................................. S13
   2.5 Synthesis of acyclic control compound 9 ......................... S19
3. Catalysis studies ................................................................. S21
   3.1 Typical procedure for the decarboxylative Mannich reactions ........................................... S21
   3.2 Characterization data for products 8 ............................... S22
4. Copies of $^1$H and $^{13}$C NMR spectra ................................. S39
5. HPLC analysis of products ................................................... S93
6. References ............................................................................ S126
1. General information

All chemicals were obtained from commercial sources and used without further purification unless stated otherwise. Anhydrous solvents such as THF, CH$_2$Cl$_2$, CHCl$_3$, CH$_3$CN, Et$_2$O, 1,4-dioxane, methyl tert-butyl ether (TBME), 1,2-dimethoxyethane (DME), ethyl vinyl ether (EVE), and cyclopentyl methyl ether (CPME) were obtained by conventional methods through distilling with suitable drying agents (Na for THF, Et$_2$O, 1,4-dioxane, MTBE, and toluene; CaH$_2$ for CH$_2$Cl$_2$, CHCl$_3$, CH$_3$CN, and CPME; 4 Å molecular sieves for EVE and DME). NMR spectra were recorded on Bruker 300, 400 or 500 MHz NMR spectrometers. Chemical shifts are reported in ppm and referenced to tetramethylsilane or the residual solvent resonance. Mass spectra were obtained on a Thermo Fisher Exactive Mass Spectrometer. Infrared spectra were recorded on Nicolet-6700 FT-IR spectrometer. Elemental analysis was recorded on Carlo Erba 1106. Optical rotations were performed on Rudolph Autopl VI. High performance liquid chromatography (HPLC) was performed on Shimadzu SCL-20AVP. Melting points are uncorrected.
2. Synthesis

Compounds 3a, 3e, 4a, 4e, 5a, 5e, M1, M5, M7, and M8 were synthesized according to our previous reported method.[1]

2.1 Synthesis of dinitro compounds 3

**General procedure:** To a solution of chiral 1,2-diamine 1 (1.0 equiv) and 1-(bromomethyl)-3-nitro-5-(trifluoromethyl)benzene (2, 2.2 equiv) in acetonitrile, K$_2$CO$_3$ (4 equiv) and KI (if applicable) were added. The resulting mixture was heated at reflux for a given period. After work-up by removal of the solvent under reduced pressure, extraction (if applicable), the crude product was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate as eluent) to give the corresponding dinitro compound 3.
(1S,2S)-\(N^1,N^2\)-Bis(3-nitro-5-(trifluoromethyl)benzyl)-\(N^1,N^2\)-dipropylcyclohexane-1,2-diamine (3b)

Dinitro compound 3b was synthesized according to the general procedure by heating the mixture of (1S,2S)-\(N^1,N^2\)-dipropylcyclohexane-1,2-diamine (1b\(^2\), 3.97 g, 20 mmol), 1-(bromomethyl)-3-nitro-5-(trifluoromethyl)benzene (2, 12.50 g, 44 mmol) and \(K_2\)CO\(_3\) (11.06 g, 80 mmol) in acetonitrile (300 mL) at reflux for 10 h. After work-up by removal of solvent, addition of water (100 mL) and extraction with ethyl acetate (100 mL \(\times\) 3), column chromatography (petroleum ether/ethyl acetate 10:1) gave 3b as a yellow oil (6.08 g, yield: 50%). \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 8.48 (s, 2H), 8.31 (s, 2H), 7.96 (s, 2H), 3.86 (d, \(J = 14.4\) Hz, 1H), 3.53 (d, \(J = 14.4\) Hz, 1H), 2.81-2.64 (m, 2H), 2.48 (t, \(J = 7.6\) Hz, 4H), 2.22-1.98 (m, 2H), 1.91-1.68 (m, 2H), 1.65-1.51 (m, 2H), 1.51-1.37 (m, 2H), 1.30-1.08 (m, 4H), 0.81 (t, \(J = 7.3\) Hz, 6H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 148.4, 145.7, 131.9 (q, \(J = 33.8\) Hz, C-CF\(_3\)), 131.3 (q, \(J = 3.3\) Hz, C-C-CF\(_3\)), 127.0, 123.1 (q, \(J = 271.3\) Hz, CF\(_3\)), 119.3 (q, \(J = 3.8\) Hz, C-C-CF\(_3\)), 60.9, 53.8, 52.9, 26.0, 25.6, 22.0, 12.0; IR (KBr) \(\nu\) 3098, 2934, 2858, 1542, 1471, 1323, 1174, 1136, 1107 cm\(^{-1}\); HRMS (APCI\(^+\)) calc. for [M+H]\(^+\) (C\(_{28}\)H\(_{35}\)F\(_6\)N\(_4\)O\(_4\)+), 605.2557, found 605.2546; [\(\alpha\)]\(_D\)\(^{25}\) = +41.4 (c = 0.50, CHCl\(_3\)).

(1S,2S)-\(N^1,N^2\)-Diisopropyl-\(N^1,N^2\)-bis(3-nitro-(trifluoromethyl)benzyl)cyclohexane-1,2-diamine (3c)

Dinitro compound 3c was synthesized according to the general procedure by heating the mixture of (1S,2S)-\(N^1,N^2\)-diisopropylcyclohexane-1,2-diamine (1c\(^{[3]}\), 5.95 g, 30 mmol), 1-(bromomethyl)-3-nitro-5-(trifluoromethyl)benzene (2, 18.69 g, 66 mmol), \(K_2\)CO\(_3\) (16.60 g, 120 mmol) and KI (300 mg, 1.8 mmol) in acetonitrile (360 mL) at reflux for 40 h. After work-up by removal of solvent, column chromatography (petroleum ether/ethyl acetate 20:1) gave 3c as a yellow solid (15.40 g, yield: 85%). Mp 98-99 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm)
8.47 (s, 2H), 8.32 (s, 2H), 7.95 (s, 2H), 3.77 (d, J = 14.4 Hz, 2H), 3.65 (d, J = 14.4 Hz, 2H), 3.03-2.80 (m, 2H), 2.73-2.54 (m, 2H), 2.24-2.07 (m, 2H), 1.85-1.68 (m, 2H), 1.17 (d, J = 6.6 Hz, 6H), 1.14-1.01 (m, 4H), 0.97 (d, J = 6.5 Hz, 6H); 13C NMR (CDCl3, 100 MHz) δ (ppm) 148.4, 146.0, 131.9 (q, J = 33.7 Hz, C-CF3), 131.5 (q, J = 3.4 Hz, C-C-CF3), 127.2, 123.1 (q, J = 271.2 Hz, CF3), 119.3 (q, J = 3.1 Hz, C-C-CF3), 60.1, 48.5, 48.4, 28.5, 26.4, 23.2, 20.3; IR (KBr) ν 3098, 2936, 2859, 1542, 1352, 1322, 1134, 1108 cm⁻¹; HRMS (APCI⁺) calc. for [M+H]⁺ (C28H35F6N4O4⁺), 605.2557, found 605.2547; [α]D²⁵ = +24.6 (c = 0.50, CHCl3).

(1S,2S)-N¹,N²-Bis(3-nitro-5-(trifluoromethyl)benzyl)-N¹,N²-di(pentan-3-yl)cyclohexane-1,2-diamine (3d)

Dinitro compound 3d was synthesized according to the general procedure by heating the mixture of (1S,2S)-N¹,N²-di(pentan-3-yl)cyclohexane-1,2-diamine (1d[6], 4.58 g, 18 mmol), 1-(bromomethyl)-3-nitro-5-(trifluoromethyl)benzene (2, 15.34 g, 54 mmol) and K₂CO₃ (9.95 g, 72 mmol), KI (180 mg, 1.1 mmol) in acetonitrile (200 mL) at reflux for 72 h. After work-up by removal of solvent, column chromatography (petroleum ether/ethyl acetate 20:1) gave 3d as a yellow oil (4.37 g, yield: 37%). ¹H NMR (CDCl3, 300 MHz) δ (ppm) 8.37 (s, 2H), 8.29 (s, 2H), 7.88 (s, 2H), 3.82-3.62 (m, 4H), 2.78-2.63 (m, 2H), 2.61-2.46 (m, 2H), 2.17-1.99 (m, 2H), 1.77-1.66 (m, 2H), 1.64-1.43 (m, 6H), 1.36-1.11 (m, 6H), 0.94 (t, J = 7.4 Hz, 6H), 0.85 (t, J = 7.4 Hz, 6H); 13C NMR (CDCl3, 125 MHz) δ (ppm) 148.3, 146.4, 131.9 (q, J = 33.7 Hz, C-CF3), 131.0 (q, J = 3.3 Hz, C-C-CF3), 126.6, 123.0 (q, J = 272.9 Hz, CF3), 119.1(q, J = 3.7 Hz, C-C-CF3), 61.8, 60.8, 49.9, 28.5, 27.2, 25.3, 24.5, 12.7, 11.9; IR (KBr) ν 3098, 2935, 2876, 1543, 1323, 1174, 1136 cm⁻¹; HRMS (APCI⁺) calc. for [M+H]⁺ (C32H₄₃F₆N₄O₄⁺), 661.3183, found 661.3178; [α]D²⁵ = +6.4 (c = 0.45, CHCl3).
(1S,2S)-N<sup>1</sup>,N<sup>2</sup>-Bis(3-nitro-5-(trifluoromethyl)benzyl)-1,2-diphenyl-N<sup>1</sup>,N<sup>2</sup>-dipropylethane-1,2-diamine (3f)

Dinitro compound 3f was synthesized according to the general procedure by heating the mixture of (1S,2S)-1,2-diphenyl-N<sup>1</sup>,N<sup>2</sup>-dipropylethane-1,2-diamine 1f<sup>[5]</sup> (3.55 g, 12 mmol), 1-(bromomethyl)-3-nitro-5-(trifluoromethyl)benzene (2, 7.50 g, 26.4 mmol), K<sub>2</sub>CO<sub>3</sub> (6.63 g, 48 mmol) and KI (120 mg, 0.7 mmol) in acetonitrile (180 mL) at reflux for 18 h. After work-up by removal of solvent, column chromatography (petroleum ether/ethyl acetate 10:1) gave 3f as a yellow solid (6.42 g, yield: 76%). Mp 128-129 °C; 1<sup>H</sup>NMR (CDCl<sub>3</sub>, 500 MHz) δ (ppm) 8.50 (s, 2H), 8.37 (s, 2H), 7.98 (s, 2H), 7.20-7.08 (m, 6H), 6.97 (d, J = 7.2 Hz, 4H), 4.50 (s, 2H), 4.03 (d, J = 14.3 Hz, 2H), 3.23 (d, J = 14.3 Hz, 2H), 2.72-2.60 (m, 2H), 2.37-2.22 (m, 2H), 1.81-1.60 (m, 4H), 0.92 (t, J = 7.3 Hz, 6H); 13<sup>C</sup>NMR (CDCl<sub>3</sub>, 100 MHz) δ (ppm) 148.6, 144.9, 135.5, 132.2 (q, J = 33.6 Hz, C-CF<sub>3</sub>), 131.3, 129.5, 128.1, 127.5, 126.9, 123.0 (q, J = 271.4 Hz, CF<sub>3</sub>), 119.6 (q, J = 3.8 Hz, C-C-CF<sub>3</sub>), 64.4, 53.8, 52.6, 21.7, 12.1; IR (KBr) ν 2962, 2875, 1541, 1351, 1174, 1134 cm<sup>−1</sup>; HRMS (ESI<sup>+</sup>) calc. for [M+H]<sup>+</sup> (C<sub>36</sub>H<sub>37</sub>F<sub>6</sub>N<sub>4</sub>O<sub>4</sub>)<sup>+</sup>, 703.2714, found 703.2705; [α]<sub>D</sub><sup>25</sup> = +89.6 (c = 0.50, CHCl<sub>3</sub>).
2.2 Synthesis of diamine compounds 4

General procedure: To a solution of 3 (1.0 equiv) in THF was added a solution of SnCl₂·2H₂O (6.4 equiv) in a given volume of conc. hydrochloric acid. The resulting mixture was stirred at room temperature for a given period. Afterwards, the mixture was treated with a solution of 40% aq. NaOH to adjust pH > 10. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄, and then evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (dichloromethane/methanol as eluent) to give the corresponding diamine compound 4.
Diamine compound 4b was synthesized according to the general procedure by reaction of 3b (6.04 g, 10 mmol) with SnCl₂·2H₂O (11.03 g, 64 mmol), conc. hydrochloric acid (25 mL) in THF (500 mL) for 4 h. After work-up, column chromatography (dichloromethane/methanol 10:1) gave 4b as a yellow oil (4.53 g, yield: 83%). ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.03 (s, 2H), 6.94 (s, 2H), 6.73 (s, 2H), 3.92-3.47 (m, 6H), 3.30 (d, J = 14.1 Hz, 2H), 2.70-2.56 (m, 2H), 2.45 (s, 2H), 2.39-2.27 (m, 2H), 2.09-1.93 (m, 2H), 1.79-1.64 (m, 2H), 1.63-1.36 (m, 4H), 1.17-0.98 (m, 4H), 0.85 (t, J = 7.1 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 146.7, 144.3, 131.1 (q, J = 31.6 Hz, C-CF₃), 124.5 (q, J = 272.4 Hz, CF₃), 118.6, 115.6, 109.7, 60.1, 53.9, 52.1, 26.2, 25.2, 22.0, 12.0; IR (KBr) ν 3385, 3321, 2933, 2858, 2808, 1625, 1464, 1356, 1257, 1161, 1122 cm⁻¹; HRMS (ESI⁻) calc. for [M-H]⁻ (C₂₈H₃₉F₆N₄), 545.3073, found 545.3072; [α]₀²⁵ = +74.6 (c = 0.70, CHCl₃).

Diamine compound 4c was synthesized according to the general procedure by reaction of 3c (15.11 g, 25 mmol) with SnCl₂·2H₂O (27.57 g, 160 mmol), conc. hydrochloric acid (62.5 mL) in THF (1250 mL) for 10 h. After work-up, column chromatography (dichloromethane/methanol 10:1) gave 4c as a yellow oil (11.30 g, yield: 83%). Mp 167-168 °C; ¹H NMR (DMSO-d₆, 400 MHz) δ (ppm) 6.81 (s, 2H), 6.71 (s, 2H), 6.68 (s, 2H), 5.39 (s, br, 4H), 3.56 (d, J = 13.4 Hz, 2H), 3.31 (d, J = 13.0 Hz, 2H), 2.82-2.69 (m, 2H), 2.46-2.36 (m, 2H), 2.15-2.03 (m, 2H), 1.71-1.55 (m, 2H), 1.12 (d, J = 6.4 Hz, 6H), 0.99-0.84 (m, 4H), 0.81 (d, J = 6.4 Hz, 6H); ¹³C NMR (DMSO-d₆, 100 MHz) δ (ppm) 148.9, 142.8, 129.3 (q, J = 30.6 Hz, C-CF₃), 124.7 (q, J = 272.2 Hz, CF₃), 118.11, 112.5 (q, J = 3.9 Hz, C-C-CF₃), 107.7 (q, J = 3.7 Hz, C-C-CF₃), 59.2, 47.2, 45.5, 27.4, 26.1, 23.2, 19.6; IR (KBr) ν 3474, 3392, 2986, 2922, 2849,
1460, 1352, 1322, 1171, 1134, 1107 cm\(^{-1}\); HRMS (ESI\(^{+}\)) calc. for [M+H]\(^{+}\) (C\(_{28}\)H\(_{39}\)F\(_6\)N\(_4\))\(^{+}\), 545.3073, found 545.3068; [\(\alpha\)]\(_D\)\(^{25}\) = +54.4 (c = 0.50, CHCl\(_3\)).

\((15,2S)-N^1,N^2\)-Bis(3-amino-5-((trifluoromethyl)benzyl)\()-N^1,N^2\)-di(pentan-3-yl)cyclohexane-1,2-diamine (4d)

\begin{center}
\includegraphics[width=0.5\textwidth]{structure_4d.png}
\end{center}

Diamine compound 4d was synthesized according to the general procedure by reaction of 3d (1.65 g, 2.5 mmol) with SnCl\(_2\)-2H\(_2\)O (2.76 g, 16 mmol), conc. hydrochloric acid (6.25 mL) in THF (125 mL) for 10 h. After work-up, column chromatography (dichloromethane/methanol 10:1) gave 4d as a yellow oil (1.34 g, yield: 89%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 6.98 (s, 2H), 6.81 (s, 2H), 6.69 (s, 2H), 3.88-3.30 (m, 8H), 2.65 (s, 2H), 2.51 (s, 2H), 2.15-1.97 (m, 2H), 2.13-1.97 (m, 9H), 1.36-1.20 (m, 3H), 1.21-1.03 (m, 4H), 0.94 (t, \(J = 7.1\) Hz, 7H), 0.83 (t, \(J = 7.1\) Hz, 7H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 146.5, 144.9, 131.0 (q, \(J = 31.4\) Hz, C-CF\(_3\)), 124.5 (q, \(J = 270.3\) Hz, CF\(_3\)), 118.6, 115.8 (q, \(J = 3.7\) Hz, C-C-CF\(_3\)), 109.6 (q, \(J = 3.0\) Hz, C-C-CF\(_3\)), 60.8, 60.4, 49.9, 28.3, 27.4, 25.8, 24.4, 12.8, 12.0; IR (KBr) \(\nu\) 3388, 3213, 2933, 2874, 1624, 1464, 1366, 1258, 1161, 1122 cm\(^{-1}\); HRMS (ESI\(^{+}\)) calc. for [M+H]\(^{+}\) (C\(_{32}\)H\(_{47}\)F\(_6\)N\(_4\))\(^{+}\), 601.3699, found 601.3701; [\(\alpha\)]\(_D\)\(^{25}\) = +27.8 (c = 0.50, CHCl\(_3\)).

\((15,2S)-N^1,N^2\)-Bis(3-amino-5-((trifluoromethyl)benzyl)-1,2-diphenyl\()-N^1,N^2\)-di(propylethane)-1,2-diamine (4f)

\begin{center}
\includegraphics[width=0.5\textwidth]{structure_4f.png}
\end{center}

Diamine compound 4f was synthesized according to the general procedure by reaction of 3f (1.40 g, 2.0 mmol) with SnCl\(_2\)-2H\(_2\)O (2.21 g, 12.8 mmol), conc. hydrochloric acid (5 mL) in THF (100 mL) for 3 h. After work-up, column chromatography (dichloromethane/methanol 10:1) gave 4f as a brown solid (1.26 g, yield: 98%). Mp 48-49 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.16-7.09 (m, 4H), 7.09-7.02 (m, 4H), 7.01-6.90 (m, 6H), 6.77 (s, 2H), 4.45 (s, 2H), 3.87 (d, \(J = 14.1\) Hz, 2H), 3.56 (s, br, 4H), 2.96 (d, \(J = 14.1\) Hz, 2H), 2.74-2.62 (m, 2H), 2.16-2.08 (m, 2H), 1.78-1.65 (m, 4H), 0.94 (t, \(J = 7.4\) Hz, 6H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 146.8, 143.7, 136.1,
131.4 (q, J = 31.6 Hz, C-CF₃), 129.8, 127.7, 126.9, 124.5 (q, J = 270.8 Hz, CF₃), 118.4, 115.7 (q, J = 3.7 Hz, C-C-CF₃), 110.0 (q, J = 3.8 Hz, C-C-CF₃), 63.6, 53.8, 51.8, 21.7, 12.2; IR (KBr) ν 3465, 3390, 2961, 2932, 2873, 1625, 1465, 1375, 1356, 1261, 1121 cm⁻¹; HRMS (ESI⁺) calc. for [M+H]+ (C₃₆H₄₁F₆N₄)+, 643.3230, found 643.3203; [α]D₂⁵ = +107.4 (c = 0.50, CHCl₃).

Enantiomers ent-4a, ent-4b and ent-4c were synthesized according to the same methods as described for 4a, 4b and 4c starting from (1R,2R)-Ν¹,Ν²-disubstituted cyclohexane-1,2-diamines, respectively. The characterization data were consistent.

2.3 Synthesis of diisothiocyanate compounds 5

General procedure: To a solution of 4 (1.0 equiv) in CH₂Cl₂ was added 1,1'-thiocarbonyldiimidazole (4.0 equiv). The mixture was stirred at room temperature for a given period. The solvent was evaporated under reduced pressure and the residue was subjected to column chromatography on silica gel to give compounds 5.
(1S,2S)-N¹,N²-Bis(3-isothiocyanato-5-(trifluoromethyl)benzyl)-N¹,N²-dipropyl-cyclohexane-1,2-diamine (5b)

Diisothiocyanate compound 5b was synthesized according to the general procedure by reaction of 4b (2.72 g, 5.0 mmol) with 1,1'-thiocarbonylidiimidazole (3.56 g, 20 mmol) in DCM (200 mL) for 12 h. After work-up, column chromatography (petroleum ether/ethyl acetate 5:1) gave 5b as a brown oil (2.70 g, yield: 86%). ¹H NMR (CDCl₃, 500 MHz) δ (ppm) 7.53 (s, 2H), 7.43 (s, 2H), 7.30 (s, 2H), 3.71 (d, J = 14.3 Hz, 2H), 3.36 (d, J = 14.3 Hz, 2H), 2.68-2.57 (m, 2H), 2.54-2.34 (m, 4H), 2.08-1.96 (m, 2H), 1.83-1.70 (m, 2H), 1.56-1.35 (m, 4H), 1.20-1.06 (m, 4H), 0.82 (t, J = 7.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ (ppm) 145.2, 137.6, 132.1, 131.9 (q, J = 32.8 Hz, C-CF₃), 129.4, 124.2 (q, J = 3.4 Hz, C-CF₃), 123.5 (q, J = 271.2 Hz, CF₃), 121.0 (q, J = 3.6 Hz, C-CF₃), 60.7, 53.8, 52.7, 26.1, 25.5, 22.1, 12.1; IR (KBr) ν 2933, 2857, 2062, 1603, 1456, 1347, 1241, 1169, 1130 cm⁻¹; HRMS (APCI⁺) calc. for [M+H]⁺ (C₃₀H₃₅F₆N₄S₂)+, 629.2202, found 629.2191; [α]D²⁵ = +20.8 (c = 0.50, CHCl₃).

(1S,2S)-N¹,N²-Diisopropyl-N¹,N²-bis(3-isothiocyanato-5-(trifluoromethyl)benzyl)cyclohexane-1,2-diamine (5c)

Diisothiocyanate compound 5c was synthesized according to the general procedure by reaction of 4c (272 mg, 0.5 mmol) with 1,1'-thiocarbonylidiimidazole (356 mg, 2 mmol) in DCM (20 mL) for 4 h. After work-up, column chromatography (petroleum ether/ethyl acetate 5:1) gave 5c as a brown oil (282 mg, yield: 89%). ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.52 (s, 2H), 7.40 (s, 2H), 7.31 (s, 2H), 3.64 (d, J = 14.2 Hz, 2H), 3.48 (d, J = 14.2 Hz, 2H), 2.92-2.75 (m, 2H), 2.61-2.40 (m, 2H), 2.20-2.04 (m, 2H), 1.81-1.63 (m, 2H), 1.17 (d, J = 6.6 Hz, 6H), 1.13-0.99 (m, 4H), 0.93 (d, J = 6.5 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 145.3, 137.5, 132.0, 131.9 (q, J = 32.7 Hz, C-CF₃), 129.5, 124.5 (q, J = 3.4 Hz, C-C-CF₃), 123.5 (q, J = 271.0 Hz, CF₃), 121.1 (q, J = 3.8 Hz, C-C-CF₃), 60.1, 48.2, 47.6, 28.3, 26.5, 23.5, 20.2; IR (KBr) ν 2966, 2934, 2857, 2074, 1602, 1452, 1344, 1241, 1169, 1130 cm⁻¹; HRMS
(APCI$^+$) calc. for [M+H]$^+$ (C$_{30}$H$_{35}$F$_6$N$_4$S$_2^+$), 629.2201, found 629.2193; [$\alpha$]$_D^{25}$ = +26.8 (c = 0.50, CHCl$_3$).

(1S,2S)-N$^1,N^2$-Bis(3-isothiocyanato-5-(trifluoromethyl)benzyl)-N$^1,N^2$-di(pentan-3-yl)cyclohexane-1,2-diamine (5d)

Diisothiocyanate compound 5d was synthesized according to the general procedure by reaction of 4d (1.80 g, 3.0 mmol) with 1,1'-thiocarbonyldiimidazole (2.14 g, 12 mmol) in DCM (120 mL) for 12 h. After work-up, column chromatography (petroleum ether/ethyl acetate 10:1) gave 5d as a brown oil (1.40 g, yield: 68%). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ (ppm) 7.46 (s, 2H), 7.31 (s, 2H), 3.60 (d, $J$ = 14.8 Hz, 2H), 3.52 (d, $J$ = 14.8 Hz, 2H), 2.71-2.56 (m, 2H), 2.53-2.40 (m, 2H), 2.13-1.98 (m, 2H), 3.60-1.46 (m, 6H), 1.31-1.20 (m, 3H), 1.60-1.09 (m, 3H), 0.94 (t, $J$ = 7.4 Hz, 6H), 0.84 (t, $J$ = 7.4 Hz, 6H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ (ppm) 145.7, 137.5, 131.8 ($q$, $J$ = 32.7 Hz, C-CF$_3$), 129.0, 124.2 ($q$, $J$ = 3.8 Hz, C-C-CF$_3$), 123.4 ($q$, $J$ = 271.2 Hz, CF$_3$), 121.0 ($q$, $J$ = 3.8 Hz, C-C-CF$_3$), 61.3, 60.6, 49.7, 28.3, 27.4, 25.5, 24.5, 12.7, 11.9; IR (KBr) $\nu$ 2962, 2933, 2875, 2070, 1602, 1460, 1345, 1241, 1171 cm$^{-1}$; HRMS (APCI$^+$) calc. for [M+H]$^+$ (C$_{34}$H$_{43}$F$_6$N$_4$S$_2^+$), 685.2828, found 685.2833; [$\alpha$]$_D^{25}$ = +0.6 (c = 0.50, CHCl$_3$).

(1S,2S)-N$^1,N^2$-Bis(3-isothiocyanato-5-(trifluoromethyl)benzyl)-1,2-diphenyl-N$^1,N^2$-dipropylethane-1,2-diamine (5f)

Diisothiocyanate compound 5f was synthesized according to the general procedure by reaction of 4f (3.85 g, 6.0 mmol) with 1,1'-thiocarbonyldiimidazole (4.28 g, 24 mmol) in DCM (240 mL) for 10 h. After work-up, column chromatography (petroleum ether/ethyl acetate 5:1) gave 5f as a white solid (2.86 g, yield: 66%). Mp 119-120 $^\circ$C; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ (ppm) 7.60 (s, 2H), 7.46 (s, 2H), 7.37 (s, 2H), 7.20-7.13 (m, 4H), 7.12-7.06 (m, 2H), 6.96 (d, $J$ = 7.2 Hz, 4H), 4.44 (s, 2H), 3.91 (d, $J$ = 14.2 Hz, 2H), 3.09 (d, $J$ = 14.2 Hz, 2H), 2.71-2.59 (m, 2H), 2.29-2.15 (m, 2H),...
1.79-1.60 (m, 4H), 0.94 (t, J = 7.3 Hz, 6H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ (ppm) 144.4, 137.8, 135.7, 132.4, 132.1 (q, J = 32.9 Hz, C-CF$_3$), 129.6, 129.3, 128.0, 127.3, 124.3 (q, J = 3.4 Hz, C-C-CF$_3$), 123.4 (q, J = 271.2 Hz, CF$_3$), 121.4 (q, J = 3.7 Hz, C-C-CF$_3$), 64.2, 53.7, 52.3, 21.4, 12.1; IR (KBr) ν 3028, 2962, 2932, 2848, 2104, 1602, 1454, 1345, 1241, 1172, 1131 cm$^{-1}$; HRMS (APCI) calc. for [M+H]$^+$ (C$_{38}$H$_{37}$F$_6$NaS$_2$), 727.2358, found 727.2347; [α]$_D$$^{25}$ = +109.6 (c = 0.50, CHCl$_3$).

2.4 Synthesis of macrocycles M

![Chemical structures of macrocycles M](image-url)
**General procedure:** To a solution of 4 (1.0 equiv) in corresponding solvent (THF, acetone or pyridine) was added 5 (1.0 equiv) and corresponding base (DMAP or Et₃N). The mixture was stirred at room temperature or heated at reflux for a given period. The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel. The crude product was washed with ethyl acetate and n-hexane to give the corresponding macrocycle M.

**Macrocycle M2**

Macrocycle M2 was synthesized according to the general procedure by reaction of 4b (1.36 g, 2.5 mmol), 5b (1.57 g, 2.5 mmol) and Et₃N (875 μL, 6.3 mmol) in THF (50 mL) at room temperature for 96 h. Column chromatography eluent: dichloromethane/methanol 10:1. Macrocycle M2 was obtained as a light yellow solid (1.54 g, yield: 52%). Mp 141-142 °C; ¹H NMR (DMSO-d₆, 400 MHz) δ (ppm) 9.75 (s, 4H), 7.81-7.31 (m, 12H), 3.63 (d, J = 13.4 Hz, 4H), 3.41 (d, J = 13.4 Hz, 4H), 2.75-2.57 (m, 4H), 2.43-2.28 (m, 4H), 2.00-1.84 (m, 4H), 1.73-1.58 (m, 4H), 1.58-1.30 (m, 8H), 1.18-0.94 (s, 8H), 0.78 (t, J = 7.1 Hz, 12H); ¹³C NMR( DMSO-d₆, 125 MHz, 343 K) δ (ppm) 179.3, 143.1, 139.3, 128.5 (q, J = 31.3 Hz, C-CF₃), 126.9, 123.2 (q, J = 270.6 Hz, CF₃), 120.6, 117.6, 59.9, 53.2, 52.0, 26.1, 25.2, 21.1, 11.3; IR (KBr) ν 2933, 2858, 1546, 1464, 1346, 1319, 1224, 1169, 1127 cm⁻¹; HRMS (ESI) calc. for [M-H]⁻ (C₅₈H₇₁F₁₂N₈S₂⁻), 1171.5057, found 1171.5058; Anal. Calcd. for C₅₈H₇₂F₁₂N₈S₂: C, 59.37; H, 6.19; N, 9.55. Found: C, 59.41; H, 6.18; N, 9.50; [α]D²⁵ = + 73.6 (c = 0.50, CHCl₃).
Macrocycle M3

Macrocycle M3 was synthesized according to the following procedure: 4c (3.26 g, 6 mmol) and 5c (3.77 g, 6 mmol) were dissolved in acetone (150 mL), and then Et3N (1.9 mL, 15 mmol) was added. The mixture was heated at reflux for 6 days. The resulting mixture was cooled to room temperature and stood for 2 h. The precipitate was collected by filtration and redissolved in ethyl ether (40 mL), then saturated NaHCO3 aq. (40 mL) was added and the resulting mixture was stirred at room temperature for 8 h. The organic layer was separated and the aqueous layer was extracted with ethyl ether (100 mL × 3). The combined organic layers were dried over Na2SO4, then concentrated to 4 mL under reduced pressure, and n-hexane (40 mL) was added. The precipitate was collected by filtration to give macrocycle M3 as a yellow solid (2.44 g, yield: 35%). Mp 149-150 °C; 1H NMR (DMSO-d6, 500 MHz, 328 K) δ (ppm) 9.67 (s, 4H), 7.62 (s, 4H), 7.51 (s, 4H), 7.48 (s, 4H), 3.61 (d, J = 14.2 Hz, 4H), 3.51 (d, J = 14.2 Hz, 4H), 3.02-2.84 (m, 4H), 2.67-2.53 (m, 4H), 2.11-1.95 (m, 4H), 1.70-1.57 (m, 4H), 1.12-0.97 (m, 21H), 0.92 (d, J = 5.3 Hz, 12H); 13C NMR (DMSO-d6, 125 MHz, 328 K) δ (ppm) 179.9, 143.6, 139.4, 128.4 (q, J = 31.8 Hz, C-CF3), 123.9 (q, J = 270.1 Hz, CF3), 121.4, 118.2, 59.9, 47.6, 46.8, 28.4, 25.7, 22.9, 19.9; IR (KBr) ν 2928, 2855, 1659, 1608, 1462, 1343, 1225, 1167, 1126 cm⁻¹; HRMS (ESI-) calc. for [M-H]⁻ (C58H71F12N8S2⁻), 1171.5057, found 1171.5062; Anal. Caled. for C58H72F12N8S2: C, 59.37; H, 6.19; N, 9.55. Found: C, 59.38; H, 6.15; N, 9.53; [α]D²⁵ = + 60.8 (c = 0.50, CH3OH).

Macrocycle M4

Macrocycle M4 was synthesized according to the general procedure by reaction of 4d (601 mg, 1 mmol) and 5d (685 mg, 0.5 mmol) in pyridine (400 mL) at room temperature for 96 h. Column chromatography eluent: petroleum ether/ethyl acetate 2:1. Macrocycle M4 was obtained as a yellow solid (561 mg, yield: 42%). Mp
141.4-141.9 °C; \(^1\)H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) (ppm) 9.85 (s, 4H), 7.62 (s, 4H), 7.54 (s, 4H), 7.37 (s, 4H), 3.50 (s, 8H), 2.76-2.57 (m, 4H), 2.09-1.91 (m, 4H), 1.66-1.36 (m, 18H), 1.28-1.00 (m, 14H), 0.88 (t, \(J = 7.2\) Hz, 12H), 0.80 (t, \(J = 7.2\) Hz, 12H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz, 328K) \(\delta\) (ppm) 179.3, 144.0, 139.4, 128.4 (q, \(J = 31.3\) Hz, C-\(CF_3\)), 126.8, 123.9 (q, \(J = 270.6\) Hz, \(CF_3\)), 120.7, 117.1, 60.5, 59.9, 49.0, 28.0, 26.2, 24.4, 23.8, 12.0, 11.1; IR (KBr) \(\nu\) 3231, 2961, 2934, 2875, 1559, 1544, 1464, 1344, 1169, 1127 cm\(^{-1}\); HRMS (ESI) calc. for [M-H]\(^-\) (C\(_{66}\)H\(_{87}\)F\(_{12}\)N\(_{8}\)S\(_{2}\)) , 1283.6309, found 1283.6300; Anal Calcd. for C\(_{66}\)H\(_{88}\)F\(_{12}\)N\(_{8}\)S\(_{2}\): C, 61.66; H, 6.90; N, 8.72. Found: C, 61.56; H, 6.93; N, 8.47; \([\alpha]_D^{25} = +6.0\) (c = 0.50, CHCl\(_3\)).

**Macrocyle M6**

Macrocyle M6 was synthesized according to the general procedure by reaction of 4f (1.61 g, 2.5 mmol), 5f (1.81 g, 2.5 mmol) and DMAP (764 mg, 6.25 mmol) in THF (50 mL) at room temperature for 72 h. Column chromatography eluent: petroleum ether/ethyl acetate 5:1.

Macrocyle M6 was obtained as a white solid (1.51 g, yield: 44%). Mp 146-147 °C; \(^1\)H NMR (DMSO-\(d_6\), 500 MHz, 343 K) \(\delta\) (ppm) 9.45 (s, 4H), 7.67 (s, 8H), 7.52 (s, 4H), 7.21-6.92 (m, 20H), 4.59 (s, 4H), 4.06 (d, \(J = 14.4\) Hz, 4H), 3.16 (d, \(J = 14.4\) Hz, 4H), 2.84-2.61 (m, 4H), 2.29-2.09 (m, 4H), 1.77-1.52 (m, 8H), 0.87 (t, \(J = 6.4\) Hz, 12H); \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz, 343 K) \(\delta\) (ppm) 179.4, 142.4, 139.3, 136.1, 129.1, 128.6 (q, \(J = 31.6\) Hz, C-\(CF_3\)), 127.6, 127.0, 126.2, 123.8 (q, \(J = 271.0\) Hz, C-\(CF_3\)), 121.1, 118.2, 63.30, 53.4, 51.8, 20.5, 11.4; IR (KBr) \(\nu\) 3220, 3029, 2961, 2932, 2874, 1534, 1463, 1344, 1225, 1171, 1128 cm\(^{-1}\); HRMS (ESI) calc. for [M-H]\(^-\) (C\(_{74}\)H\(_{75}\)F\(_{12}\)N\(_{8}\)S\(_{2}\)) , 1367.5370, found 1367.5366; Anal. Calcd. for C\(_{74}\)H\(_{76}\)F\(_{12}\)N\(_{8}\)S\(_{2}\): C, 64.60; H, 5.59; N, 8.18. Found: C, 64.76; H, 5.68; N, 8.05; \([\alpha]_D^{25} = +89.4\) (c = 0.50, CHCl\(_3\)).
Macrocycle M9

Macrocycle M9 was synthesized according to the general procedure by reaction of ent-4a (244 mg, 0.5 mmol), 5f (363 mg, 0.5 mmol) and DMAP (153 mg, 1.25 mmol) in THF (10 mL) at room temperature for 48 h. Column chromatography eluent: dichloromethane/methanol 20:1.

Macrocycle M9 was obtained as a white solid (180 mg, yield: 30%). Mp 143-144 °C; 1H NMR (DMSO-d6, 300 MHz) δ (ppm) 9.78 (d, 4H), 8.00-7.28 (m, 12H), 7.23-6.86 (m, 10H), 4.58 (s, 2H), 3.91 (d, J = 14.3 Hz, 2H), 3.82-3.51 (m, 4H), 3.13 (d, J = 14.4 Hz, 2H), 2.75-2.54 (m, 8H), 1.97-1.82 (m, 2H), 1.78-1.49 (m, 6H), 1.37-1.03 (m, 5H), 0.82 (t, J = 7.3 Hz, 6H); 13C NMR (DMSO-d6, 125 MHz) δ (ppm) 179.4, 142.7, 139.7, 139.6, 136.3, 129.4, 128.7 (q, J = 253.8 Hz, CF3), 127.8, 127.3, 126.6, 125.22, 125.17, 123.1, 123.0, 121.3, 120.8, 120.7, 118.5, 118.0, 63.3, 62.0, 53.4, 51.0, 31.0, 25.3, 22.1, 20.8, 14.0, 11.8; IR (KBr) ν 3214, 2931, 1534, 1461, 1344, 1225, 1169, 1127 cm⁻¹; HRMS (ESI⁺) calc. for [M+H]+ (C62H66F12N8S2+), 1215.4733, found 1215.4717; Anal. Calcd. for C62H66F12N8S2: C, 61.27; H, 5.47; N, 9.22. Found: C, 61.20; H, 5.46; N, 9.10; [α]D25 = +44.8 (c = 0.50, CHCl3).

Macrocycle M10

Macrocycle M10 was synthesized according to the general procedure by reaction of ent-4b (272 mg, 0.5 mmol), 5e (353 mg, 0.5 mmol) and DMAP (153 mg, 1.25 mmol) in THF (10 mL) at room temperature for 48 h. Column chromatography eluent: dichloromethane/methanol 20:1.

Macrocycle M10 was obtained as a white solid (182 mg, yield: 30%). Mp 145 °C; 1H NMR (DMSO-d6, 400 MHz, 333 K) δ (ppm) 9.66 (s, 4H), 7.82 (s, 2H), 7.74 (s, 2H), 7.63 (s, 2H), 7.53 (s, 2H), 7.49 (s, 2H), 7.29 (s, 2H), 7.24 (d, J = 7.6 Hz, 4H), 7.19 (t, 4H), 7.08 (d, J = 7.2 Hz, 2H), 4.63 (s, 2H), 3.74-3.58 (m, 4H), 3.51 (d, J = 13.7 Hz, 2H), 3.41 (d, J = 14.4 Hz, 2H), 3.17 (s, 3H), 2.67-2.58 (m, 2H), 1.96 (s, 1H), 1.78 (d, J = 12.3 Hz, 1H).
2.57-2.50 (m, 2H), 2.43-2.31 (m, 2H), 2.20 (s, 6H), 2.02-1.90 (m, 2H), 1.77-1.63 (m, 2H), 1.55-1.34 (m, 4H), 1.09 (s, 4H), 0.79 (t, 6H); $^{13}$C NMR (DMSO-$d_6$, 125 MHz, 328K) δ (ppm) 178.9, 143.1, 141.8, 139.5, 139.3, 135.8, 129.1, 128.4 (q, $J = 253.8$ Hz, CF$_3$), 127.2, 125.0 124.9, 122.87, 122.7, 120.8, 117.8, 117.6, 66.6, 59.7, 56.9, 53.0, 51.8, 36.4, 25.5, 25.3, 21.2, 11.5; IR (KBr) ν 3030, 2932, 2853, 1544, 1463, 1344, 1224, 1127 cm$^{-1}$; HRMS (ESI$^+$) calc. for [M+H]$^+$ (C$_{62}$H$_{67}$F$_{12}$N$_8$S$_2$ $^+$), 1215.4733, found 1215.4718. Anal. Calcd. for C$_{62}$H$_{66}$F$_{12}$N$_8$S$_2$: C, 61.27; H, 5.47; N, 9.22. Found: C, 60.91; H, 5.53; N, 9.25; [α]$_D^{25}$ = -22.4 (c = 0.50, CHCl$_3$).

**Macrocycle M11**

Macrocycle M11 was synthesized according to the general procedure by reaction of ent-4b (272 mg, 0.5 mmol), 5f (363 mg, 0.5 mmol) and DMAP (153 mg, 1.25 mmol) in THF (10 mL) at room temperature for 96 h. Column chromatography eluent: dichloromethane/methanol 20:1. Macrocycle M11 was obtained as a white solid (203 mg, yield: 32%). Mp 136-137 °C; $^{1}$H NMR (DMSO-$d_6$, 400 MHz, 333 K) δ (ppm) 9.62 (d, $J = 22.7$ Hz, 4H), 7.77 (s, 2H), 7.72 (s, 2H), 7.63 (s, 2H), 7.50 (s, 4H), 7.43 (s, 2H), 7.16-7.07 (m, 8H), 7.07-7.01 (m, 2H), 4.58 (s, 2H), 3.98 (d, $J = 14.6$ Hz, 2H), 3.65 (d, $J = 14.3$ Hz, 2H), 3.41 (d, $J = 14.3$ Hz, 2H), 3.23-3.17 (m, 2H), 2.76-2.60 (m, 4H), 2.45-2.30 (m, 2H), 2.22-2.09 (m, 2H), 2.02-1.91 (m, 2H), 1.72-1.55 (m, 6H), 1.52-1.37 (m, 4H), 1.19-0.99 (m, 4H), 0.95-0.60 (m, 14H); $^{13}$C NMR (DMSO-$d_6$, 125 MHz, 328K) δ (ppm) 179.2, 143.1, 142.5, 139.5, 139.2, 136.3, 129.2, 128.5, 128.4, 127.2, 126.3, 125.1, 125.0, 122.8, 121.0, 120.9, 118.3, 117.7, 63.3, 59.7, 53.5, 53.0, 51.8, 51.7, 25.3, 21.2, 20.6, 11.53, 11.51; IR (KBr) ν 3214, 2960, 2933, 1539, 1463, 1345, 1225, 1170, 1127 cm$^{-1}$; HRMS (ESI$^+$) calc. for [M+H]$^+$ (C$_{66}$H$_{75}$F$_{12}$N$_8$S$_2$ $^+$), 1271.5359, found 1271.5348; Anal. Calcd. for C$_{66}$H$_{74}$F$_{12}$N$_8$S$_2$: C, 62.35; H, 5.87; N, 8.81. Found: C, 61.95; H, 5.78; N, 8.93; [α]$_D^{25}$ = +22.6 (c = 0.50, CHCl$_3$).
Macrocycle M12 was synthesized according to the general procedure by reaction of ent-4c (272 mg, 0.5 mmol), 5f (363 mg, 0.5 mmol) and DMAP (153 mg, 1.25 mmol) in THF (10 mL) at room temperature for 48 h. Column chromatography eluent: dichloromethane/methanol 20:1. Macrocycle M12 was obtained as a white solid (300 mg, yield: 47%). Mp 144-145 °C; 1H NMR (DMSO-d6, 400 MHz, 328 K) δ (ppm) 9.54 (s, 4H), 7.75-7.42 (m, 12 H), 7.15-7.05 (m, 10 H), 4.59 (s, 2H), 3.99-3.97 (m, 2H), 3.51-3.48 (m, 4H), 3.20-3.07 (m, 4H), 2.78-2.65 (m, 4H), 2.15-2.03 (m, 4H), 1.64-1.62 (m, 6H), 1.14-1.07 (m, 8H), 0.97-0.96 (m, 6H), 0.85-0.82 (m, 8H); 13C NMR (DMSO-d6, 125 MHz, 328K) δ (ppm) 179.0, 143.7, 142.5, 141.7, 139.5, 138.2, 136.3, 129.3, 129.2, 128.5, 128.2, 127.2, 126.3, 125.1, 125.0, 122.9, 122.8, 121.3, 121.0, 63.3, 59.2, 53.5, 53.1, 51.8, 47.6, 28.6, 25.7, 22.5, 20.7, 19.9, 11.5; IR (KBr) ν 3202, 2962, 2873, 1549, 1464, 1344, 1318, 1224, 1169, 1127 cm⁻¹; HRMS (ESI⁺) calc. for [M+H]⁺ (C₆₆H₇₅F₁₂N₈S₂⁺), 1271.5359, found 1271.5349; Anal. Calcd. for C₆₆H₇₄F₁₂N₈S₂: C, 62.35; H, 5.87; N, 8.81. Found: C, 62.27; H, 5.75; N, 8.76. [α]D²⁵ = +8.8 (c = 0.50, CH₃OH).

2.5 Synthesis of acyclic control compound 9
N,N-Dimethyl-1-(3-nitro-5-(trifluoromethyl)phenyl)methanamine (10): To a solution of 2 (5.66 g, 20 mmol) in EtOH (30 mL) was added 30 wt % dimethylamine aqueous solution (13.60 g, 100 mmol). The mixture was stirred at room temperature for 40 min. The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate 1:1) to give 10[6] as a yellow oil (4.75 g, yield: 95%). 1H NMR (CDCl3, 400 MHz) δ (ppm) 8.39 (s, 1H), 8.37 (s, 1H), 7.95 (s, 1H), 3.58 (s, 2H), 2.28 (s, 6H).

3-((Dimethylamino)methyl)-5-(trifluoromethyl)aniline (11): To a solution of 10 (9.18 g, 37 mmol) in THF (500 mL) was added a solution of SnCl2·2H2O (26.71 g, 118 mmol) in conc. hydrochloric acid (44 mL). The mixture was stirred at room temperature for 12 h, and then was treated with a solution of 40% aq. NaOH to adjust pH > 10. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (100 mL × 3). The combined organic layers were dried over Na2SO4, and then evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel (dichloromethane/methanol 5:1) to give 11[6] as a yellow solid (8.08 g, yield: 98%). 1H NMR (CDCl3, 400 MHz) δ (ppm) 6.91 (s, 1H), 6.80 (s, 1H), 6.77 (s, 1H), 3.81 (s, br, 2H), 3.34 (s, 2H), 2.23 (s, 6H).

Acyclic control compound 9: To a solution of 5c (628 mg, 1 mmol) in pyridine (10 mL) was added 11 (436 mg, 2 mmol). The mixture was stirred at room temperature for 48 h. The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel (dichloromethane/methanol 5:1) to give 9 as a white solid (680 mg, yield: 64%). Mp 104-105 °C; 1H NMR (DMSO-d6, 400 MHz) δ (ppm) 10.25 (s, 4H), 7.83 (s, 2H), 7.76-7.60 (m, 6H), 7.40 (d, J = 11.4 Hz, 4H), 3.63 (d, J = 13.0 Hz, 2H), 3.51 (s, 4H), 3.45 (d, J = 14.1 Hz, 2H), 2.77-2.62 (m, 2H), 2.20 (s, 12H), 2.12-2.02 (m, 2H), 1.66-1.47 (m, 2H), 1.18-0.68 (m, 18H); 10.15 (s, 4H), 7.82 (s, 2H), 7.70 (s, 2H), 7.68 (s, 2H), 7.64 (s, 2H), 7.54 (s, 2H), 7.36 (s, 2H), 7.25-7.19 (m, 4H), 7.16 (t, J = 7.5 Hz, 4H), 7.08 (t, J = 7.2 Hz, 2H), 4.62 (s, 2H), 3.62 (d, J = 13.7 Hz, 2H), 3.57-3.41 (m, 6H), 2.30-2.10 (m, 18H); 13C NMR (DMSO-d6, 125 MHz) δ
(ppm) 180.0, 149.4, 140.2, 139.6, 129.1, 128.9, 128.4, 127.3, 124.1 (q, \( J = 270.8 \) Hz, CF<sub>3</sub>), 124.0 (q, \( J = 270.8 \) Hz, CF<sub>3</sub>), 124.5, 120.8, 118.5, 117.9, 82.2, 59.3, 47.0, 44.7, 27.6, 26.0, 23.3, 19.8; HRMS (ESI<sup>+</sup>) calc. for [M-H]<sup>-</sup> (C<sub>50</sub>H<sub>50</sub>F<sub>12</sub>N<sub>8</sub>S<sub>2</sub>), 1063.4118, found 1063.4126; IR (KBr) \( \nu = 2940, 2860, 2780, 1545, 1465, 1344, 1170 \) cm<sup>-1</sup>; \([\alpha]_D^{25} = +14.6 \) (c = 0.50, CHCl<sub>3</sub>).

3. Catalysis studies

All the ketimines 6<sup>[7]</sup> and malonic acid half thioesters (MAHTs) 7<sup>[8-9]</sup> are known compounds and were prepared according to literature procedures.

3.1 Typical procedure for the decarboxylative Mannich reactions

![Mannich Reaction Diagram]

**Typical procedure:** The ketimine 6a (52.1 mg, 0.2 mmol) and the macrocycle catalyst M3 (11.8 mg, 0.01 mmol) was added into a 10 mL Schlenk flask equipped with a stirring bar, then dried cyclopentyl methyl ether (CPME, 2.0 mL) and malonic acid half thioester 7a (67.9 mg, 0.3 mmol) were added. The resulting reaction mixture was stirred at room temperature until full consumption of the starting ketimine 6a as indicated by TLC. The reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography on silica gel (petroleum ether/ethyl acetate 3:1) to give the desired product 8a as a white solid.
3.2 Characterization data for products 8

\( \text{S-(4-Methoxyphenyl)} \quad (R)-2-(3-\text{((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl}) \text{ethanethioate (8a)}^{[9]} \)

![Chemical structure of 8a](image)

88% yield; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.37-7.31 (m, 1H), 7.30-7.22 (m, 3H), 7.07 (t, \(J = 7.5\) Hz, 1H), 6.95 (d, \(J = 8.9\) Hz, 2H), 6.87 (d, \(J = 7.6\) Hz, 1H), 6.31 (s, 1H), 3.83 (s, 3H), 3.27 (s, 3H), 3.19 (d, \(J = 15.0\) Hz, 1H), 2.72 (d, \(J = 15.1\) Hz, 1H), 1.24 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 196.8, 175.2, 161.2, 153.8, 143.3, 136.1, 129.5, 129.0, 123.7, 122.8, 117.5, 115.2, 108.6, 80.4, 60.3, 55.6, 47.6, 28.2, 26.9; \([\alpha]D^{25} = +99.6\) (c = 0.50, CHCl\(_3\)); ee: 72%; HPLC analysis CHIRALPAK OD-H, \(n\)-hexane:\(^4\)PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 9.7\) min (major), \(t_2 = 12.1\) min (minor).

\( \text{S-(4-Methoxyphenyl)} \quad (R)-2-(3-\text{((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl}) \text{ethanethioate (8b)} \)

![Chemical structure of 8b](image)

Yellow solid, 48% yield; Mp 158-159 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.77 (s, 1H), 7.28-7.23 (m, 4H), 7.05 (t, \(J = 7.5\) Hz, 1H), 6.95 (d, \(J = 8.7\) Hz, 2H), 6.87 (d, \(J = 7.7\) Hz, 1H), 6.42 (s, 1H), 3.84 (s, 3H), 3.16 (d, \(J = 15.0\) Hz, 1H), 2.84 (d, \(J = 15.2\) Hz, 1H), 1.28 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 176.5, 161.3, 154.0, 140.3, 136.2, 129.5, 124.0, 122.9, 117.5, 115.2, 110.5, 80.7, 60.5, 55.6, 47.4, 28.2; IR (KBr) ν 3278, 2976, 2929, 1690, 1623, 1593, 1497, 1253, 1161, 1026, 827, 751 cm\(^{-1}\); HRMS (ESI\(^+\)) calcd. for [M+Na]\(^+\) (C\(_{22}\)H\(_{24}\)N\(_2\)O\(_5\)SNa\(^+\)), 451.1298, found 451.1294; \([\alpha]D^{25} = +47.2\) (c = 0.50, CHCl\(_3\)); ee: 40%; HPLC analysis CHIRALPAK AD-H, \(n\)-hexane:\(^4\)PrOH = 9:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 10.8\) min (major), \(t_2 = 13.3\) min (minor).
S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1-ethyl-2-oxoindolin-3-yl)ethanethioate (8c)

Yellow solid, 73% yield; Mp 164-165 °C; 1H NMR (CDCl3, 300 MHz) δ (ppm) 7.35-7.22 (m, 4H), 7.06 (t, J = 7.4 Hz, 1H), 6.95-6.87 (m, 3H), 6.24 (s, 1H), 3.94-3.59 (m, 5H), 3.18 (d, J = 15.1 Hz, 1H), 2.76 (d, J = 15.0 Hz, 1H), 1.33-1.25 (m, 12H); 13C NMR (CDCl3, 75 MHz) δ (ppm) 196.6, 174.8, 161.2, 153.8, 142.4, 136.1, 129.4, 129.3, 124.0, 122.6, 117.7, 115.2, 108.7, 80.3, 60.3, 55.5, 47.7, 35.3, 28.2, 12.7; IR (KBr) ν 3251, 2977, 2931, 1727, 1615, 1592, 1496, 1368, 1251, 1160, 1024, 751 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]+ (C24H28N2O5S Na⁺), 479.1611, found 479.1610; [α]D25 = +58.8 (c = 0.50, CHCl3); ee: 64%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 8.7 min (major), t₂ = 17.8 min (minor).

S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1-isopropyl-2-oxoindolin-3-yl)ethanethioate (8d)

Yellow solid, 43% yield; Mp 129-130 °C; 1H NMR (CDCl3, 300 MHz) δ (ppm) 7.33-7.20 (m, 4H), 7.03 (t, J = 8.3 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 6.19 (s, 1H), 4.60 (m, 1H), 3.82 (s, 3H), 3.17 (d, J = 15.0 Hz, 1H), 2.76 (d, J = 14.9 Hz, 1H), 1.51 (d, J = 7.0 Hz, 6H), 1.27 (s, 9H); 13C NMR (CDCl3, 75 MHz) δ (ppm) 196.4, 174.9, 161.2, 153.8, 142.2, 136.1, 129.5, 129.1, 124.1, 122.2, 117.8, 115.2, 110.2, 80.2, 60.1, 55.5, 47.8, 44.6, 28.3, 19.6, 19.3; IR (KBr) ν 3262, 2978, 2931, 1718, 1611, 1591, 1496, 1367, 1250, 1161, 1025, 827, 753 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]+ (C25H30N2O5S Na⁺), 493.1768, found 493.1763; [α]D25 = +37.9 (c = 0.48, CHCl3); ee: 53%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 8.1 min (major), t₂ = 17.7 min (minor).
\( \text{S-(4-Methoxyphenyl) (R)-2-((1-benzyl-3-((\text{tert-butoxycarbonyl})amino)-2-oxoindolin-3-yl)ethanethioate (8e)} \)

![image of molecule]

White solid, 46% yield; Mp 142-143 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \( \delta \) (ppm) 7.38 (d, \( J = 7.3 \) Hz, 2H), 7.34-7.24 (m, 6H), 7.20 (t, \( J = 7.1 \) Hz, 1H), 7.03 (t, \( J = 7.5 \) Hz, 1H), 6.96-6.93 (m, 2H), 6.72 (d, \( J = 7.8 \) Hz, 1H), 5.10-4.83 (m, 2H), 3.83 (s, 3H), 3.21 (d, \( J = 14.8 \) Hz, 1H), 2.82 (d, \( J = 15.0 \) Hz, 1H), 1.28 (d, \( J = 12.8 \) Hz, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \( \delta \) (ppm) 196.7, 175.3, 161.2, 153.8, 142.4, 136.2, 135.9, 129.4, 128.9, 127.7, 127.5, 123.7, 122.9, 117.6, 115.2, 109.6, 80.5, 60.4, 55.6, 47.7, 44.4, 28.3; IR (KBr) \( \nu \) 3330, 2976, 2928, 1711, 1614, 1593, 1497, 1366, 1251, 1172, 1024, 828, 734 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{29}\)H\(_{30}\)N\(_2\)O\(_5\)SNa\(^+\)), 541.1768, found 541.1765; \([\alpha]_D^{25} = +24.2 \) (c = 0.50, CHCl\(_3\)); ee: 37%; HPLC analysis CHIRALPAK OD-H, \( n \)-hexane/PrOH = 7:3, 25 °C, 1 mL/min flow rate, detection at 254 nm, \( t_1 = 8.9 \) min (minor), \( t_2 = 10.5 \) min (major).

\( \text{S-(4-Methoxyphenyl) (R)-2-((3-((\text{tert-butoxycarbonyl})amino)-1-(methoxymethyl)-2-oxoindolin-3-yl)ethanethioate (8f)} \)

![image of molecule]

Yellow solid, 40% yield; Mp 114-115 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) (ppm) 7.35-7.27 (m, 2H), 7.24 (s, 1H), 7.08 (t, \( J = 7.5 \) Hz, 2H), 6.95 (d, \( J = 8.6 \) Hz, 2H), 6.37 (s, 1H), 5.21 (d, \( J = 11.0 \) Hz, 1H), 5.14 (d, \( J = 11.3 \) Hz, 1H), 3.83 (d, \( J = 1.1 \) Hz, 3H), 3.41 (s, 3H), 3.15 (d, \( J = 15.0 \) Hz, 1H), 2.81 (d, \( J = 15.0 \) Hz, 1H), 1.26 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \) (ppm) 196.6, 175.8, 161.3, 153.8, 141.6, 136.1, 129.6, 128.6, 123.7, 123.3, 117.6, 115.2, 110.0, 80.5, 72.1, 60.6, 56.7, 55.5, 47.8, 28.2; IR (KBr) \( \nu \) 3251, 2977, 2931, 1727, 1615, 1592, 1496, 1368, 1251, 1160, 1024, 834, 751 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{24}\)H\(_{28}\)N\(_2\)O\(_6\)SNa\(^+\)), 495.1560, found 495.1559; \([\alpha]_D^{25} = +33.8 \) (c = 0.50, CHCl\(_3\)); ee: 45%; HPLC analysis CHIRALPAK IA, \( n \)-hexane/PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \( t_1 = 8.1 \) min (major), \( t_2 = 17.7 \) min (minor).
\[ S-(4\text{-Methoxyphenyl}) \quad (R)\text{-2-((1-acetyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)ethanethioate (8g)}} \]

Yellow solid, 35% yield; Mp 157-158 °C; \(^1\text{H NMR (CDCl\textsubscript{3}, 400 MHz) }\delta (\text{ppm}) 8.27 (d, J = 8.1 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 7.30-7.28 (m, 1H), 7.24-7.20 (m, 3H), 6.94 (d, J = 8.9 Hz, 2H), 6.35 (s, 1H), 3.83 (s, 3H), 3.13 (d, J = 14.9 Hz, 1H), 2.92 (d, J = 14.8 Hz, 1H), 2.71 (s, 3H), 1.23 (s, 9H); \(^{13}\text{C NMR (CDCl\textsubscript{3}, 100 MHz) }\delta (\text{ppm}) 195.8, 175.8, 170.9, 161.3, 153.8, 139.8, 136.1, 129.9, 128.3, 125.4, 123.0, 117.2, 116.9, 115.3, 81.2, 60.7, 55.5, 48.3, 28.1, 26.8; \text{IR (KBr)} \nu 3377, 2960, 2929, 1751, 1715, 1592, 1497, 1375, 1250, 1018, 771 \text{ cm}^{-1}; \text{HRMS (ESI}^+) \text{ calc. for [M+Na}^+) (C_{24}H_{26}N_{2}O_{6}SNa^+), 493.1404, \text{found 493.1399; } [\alpha]D^{25} = -1.2 (c = 0.42, \text{CHCl}_3); \text{ee: } 16\%; \text{HPLC analysis CHIRALPAK IA, } n\text{-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, } t_1 = 22.1 \text{ min (major), } t_2 = 29.5 \text{ min (minor).}

\[ S-(4\text{-Methoxyphenyl}) \quad (R)\text{-2-((benzyloxy)carbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8h)}} \]

White solid, 73% yield; Mp 56-57 °C; \(^1\text{H NMR (CDCl\textsubscript{3}, 500 MHz) }\delta (\text{ppm}) 7.35 (t, J = 7.7 Hz, 1H), 7.30-7.23 (m, 8H), 7.08 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.87 (s, 1H), 6.66 (s, 1H), 4.92 (s, 2H), 3.82 (s, 3H), 3.24 (d, J = 15.1 Hz, 4H), 2.82 (d, J = 15.4 Hz, 1H); \(^{13}\text{C NMR (CDCl\textsubscript{3}, 125 MHz) }\delta (\text{ppm}) 196.9, 174.7, 161.2, 154.5, 143.4, 136.1, 135.8, 129.8, 128.5, 128.2, 128.3, 128.1, 123.9, 123.0, 117.3, 115.2, 108.7, 67.2, 60.3, 55.5, 47.3, 26.8; \text{IR (KBr)} \nu 3263, 3029, 2958, 2938, 1729, 1697, 1615, 1591, 1252, 1024, 829, 751 \text{ cm}^{-1}; \text{HRMS (ESI}^+) \text{ calc. for [M+Na}^+) (C_{26}H_{24}N_{2}O_{5}SNa^+), 499.1298, \text{found 499.1293; } [\alpha]D^{25} = +30.0 (c = 0.46, \text{CHCl}_3); \text{ee: } 26\%; \text{HPLC analysis CHIRALPAK OD-H, } n\text{-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, } t_1 = 20.9 \text{ min (major), } t_2 = 28.0 \text{ min (minor).}
**S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1,5-dimethyl-2-oxoindolin-3-yl)ethanethioate (8i)**

White solid, 76% yield; Mp 165-166 °C; \(^1^H\) NMR (CDCl\(_3, 300\) MHz) \(\delta\) (ppm) 7.27-7.22 (m, 2H), 7.14-7.09 (m, 2H), 6.98-6.93 (m, 2H), 6.75 (d, \(J = 7.8\) Hz, 1H), 3.83 (s, 3H), 3.24 (s, 3H), 3.16 (d, \(J = 14.9\) Hz, 1H), 2.75 (d, \(J = 14.9\) Hz, 1H), 2.34 (s, 3H), 1.24 (s, 9H); \(^1^C\) NMR (CDCl\(_3, 750\) MHz) \(\delta\) (ppm) 196.8, 175.0, 161.2, 153.7, 140.9, 136.1, 132.3, 129.7, 128.9, 124.4, 117.6, 115.2, 108.3, 80.3, 60.3, 55.5, 47.6, 28.2, 26.8, 21.3; IR (KBr) \(\nu\) 3276, 2977, 2932, 1706, 1625, 1592, 1496, 1369, 1250, 1173, 1029, 832, 754 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na\(^+\)] (C\(_{24}\)H\(_{28}\)N\(_2\)O\(_5\)SNa\(^+\)), 479.1611, found 479.1606; \([\alpha]_D^{25}\) = +102.0 (\(c = 0.50\), CHCl\(_3\)); ee: 74%; HPLC analysis CHIRALPAK OD-H, n-hexane:PrOH = 9:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 18.7\) min (major), \(t_2 = 21.9\) min (minor).

**S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-5-methoxy-1-methyl-2-oxoindolin-3-yl)ethanethioate (8k)**

White solid, 82% yield; Mp 143-144 °C; \(^1^H\) NMR (CDCl\(_3, 400\) MHz) \(\delta\) (ppm) 7.27-7.25 (m, 2H), 6.97-6.91 (m, 3H), 6.87-6.84 (m, 1H), 6.77 (d, \(J = 8.4\) Hz, 1H), 6.30 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.24 (s, 3H), 3.18 (d, \(J = 15.3\) Hz, 1H), 2.77 (d, \(J = 15.2\) Hz, 1H), 1.26 (s, 9H); \(^1^C\) NMR (CDCl\(_3, 100\) MHz) \(\delta\) (ppm) 196.7, 174.8, 161.2, 156.2, 153.7, 136.7, 136.1, 130.2, 117.5, 115.2, 113.9, 111.1, 108.9, 80.4, 56.1, 55.5, 47.6, 28.2, 26.9; IR (KBr) \(\nu\) 3324, 2975, 2935, 2837, 1720, 1593, 1497, 1367, 1251, 1173, 1030, 828 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na\(^+\)] (C\(_{24}\)H\(_{28}\)N\(_2\)O\(_6\)SNa\(^+\)), 495.1560, found 495.1556; \([\alpha]_D^{25}\) = +101.8 (\(c = 0.50\), CHCl\(_3\)); ee: 72%; HPLC analysis CHIRALPAK OD-H, n-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 11.4\) min (major), \(t_2 = 14.0\) min (minor).
S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-6-fluoro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8l)

White solid, 88% yield; Mp 198-199 °C; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.26-7.22 (m, 3H), 6.95 (d, J = 8.5 Hz, 2H), 6.74 (t, J = 8.6 Hz, 1H), 6.60 (d, J = 7.5 Hz, 1H), 6.24 (s, 1H), 3.83 (s, 3H), 3.24-3.19 (m, 4H), 2.78 (d, J = 15.3 Hz, 1H), 1.26 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 196.4, 175.4, 163.9 (d, J = 246.5 Hz, C-F), 161.3, 153.7, 145.1 (d, J = 11.7 Hz, C-C-C-F), 136.1, 124.3, 125.0 (d, J = 9.9 Hz, C-C-C-F), 117.4, 115.2, 108.8 (d, J = 22.4 Hz, C-C-F), 97.5 (d, J = 27.5 Hz, C-C-F), 80.6, 59.8, 55.5, 47.7, 28.2, 27.0; IR (KBr) ν 3327, 2977, 2914, 1729, 1616, 1497, 1383, 1250, 1173, 1086, 830 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]+ (C₂₃H₂₅FN₂O₅SNa⁺), 483.1360, found 483.1355; [α]D²⁵ = +105.6 (c = 0.50, CHCl₃); ee: 70%; HPLC analysis CHIRALPAK OD-H, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 9.2 min (major), t₂ = 12.6 min (minor).

S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-7-fluoro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8m)

White solid, 85% yield; Mp 177-178 °C; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.25 (d, J = 9.7 Hz, 2H), 7.08-6.98 (m, 3H), 6.95 (d, J = 8.9 Hz, 2H), 6.33 (s, 1H), 3.83 (s, 3H), 3.47 (d, J = 2.8 Hz, 3H), 3.17 (d, J = 15.2 Hz, 1H), 2.78 (d, J = 15.2 Hz, 1H), 1.26 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 196.5, 174.9, 161.3, 153.7, 148.0 (d, J = 244.3 Hz, C-F), 136.1, 131.9, 130.0 (d, J = 8.4 Hz, C-C-C-F), 123.3 (d, J = 6.2 Hz, C-C-C-F), 119.4 (d, J = 3.3 Hz, C-C-C-C-F), 117.5 (d, J = 19.4 Hz, C-C-F), 117.3, 115.2, 80.6, 60.3, 55.5, 47.5, 29.4, 29.4, 28.2; IR (KBr) ν 3334, 2976, 2940, 1728, 1632, 1593, 1496, 1249, 1026, 828 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]+ (C₂₃H₂₅FN₂O₅SNa⁺), 483.1860, found 483.1355; [α]D²⁵ = +102.4 (c = 0.50, CHCl₃); ee: 74%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 8.8 min (major), t₂ = 17.0 min (minor).
**S-(4-Methoxyphenyl) \((R)-2-(3-((tert-butoxycarbonyl)amino)-5,6-difluoro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8n)**

White solid, 99% yield; Mp 149-150 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.28-7.25 (m, 2H), 7.19-7.15 (m, 1H), 6.98-6.95 (m, 2H), 6.72-6.68 (m, 1H), 6.19 (s, 1H), 3.84 (s, 3H), 3.25-3.31 (m, 4H), 2.78 (d, \(J = 15.4\) Hz, 1H), 1.28 (s, 9H); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 196.4, 175.0, 161.3, 153.7, 151.2 (dd, \(J = 247.1, 13.9\) Hz, C-F), 146.7 (dd, \(J = 241.6, 13.1\) Hz, C-F), 139.8 (d, \(J = 10.1\) Hz, C-C-F), 136.2, 124.2, 117.1, 115.3, 113.9 (d, \(J = 20.1\) Hz, C-C-F), 98.9 (d, \(J = 23.0\) Hz, C-C-F), 80.8, 59.9, 55.6, 47.5, 28.2, 27.1; IR (KBr) \(\nu\) 3337, 2978, 2935, 1718, 1626, 1593, 1510, 1396, 1252, 1173, 1029, 829, 783 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{23}\)H\(_{24}\)F\(_2\)N\(_2\)O\(_5\)SNa\(^+\)), 501.1266, found 501.1263; \([\alpha]_D^{25}\) = +99.6 (c = 0.50, CHCl\(_3\)); ee: 67%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 8.4\) min (major), \(t_2 = 10.6\) min (minor).

**S-(4-Methoxyphenyl) \((R)-2-(3-((tert-butoxycarbonyl)amino)-5-chloro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8p)**

White solid, 97% yield; Mp 181-182 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.33-7.25 (m, 4H), 6.97 (d, \(J = 9.0\) Hz, 2H), 6.80 (d, \(J = 8.2\) Hz, 1H), 6.29 (s, 1H), 3.84 (s, 3H), 3.25 (s, 3H), 3.17 (d, \(J = 15.2\) Hz, 1H), 2.75 (d, \(J = 15.0\) Hz, 1H), 1.27 (s, 9H); \(^1^3\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 196.6, 174.7, 161.3, 153.7, 141.9, 136.2, 130.4, 129.4, 128.2, 124.2, 117.2, 115.3, 109.6, 80.7, 60.1, 55.5, 47.3, 28.2, 27.0; IR (KBr) \(\nu\) 3281, 2978, 2938, 1709, 1611, 1592, 1495, 1392, 1250, 1172, 1028, 831 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{23}\)H\(_{25}\)ClN\(_2\)O\(_2\)SNa\(^+\)), 499.1065, found 499.1061; \([\alpha]_D^{25}\) = +97.6 (c = 0.50, CHCl\(_3\)); ee: 72%; HPLC analysis CHIRALPAK OD-H, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 9.5\) min (major), \(t_2 = 11.9\) min (minor).
S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-6-chloro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8q)

White solid, 94% yield; Mp 196-197 °C; ¹H NMR (CDCl₃, 500 MHz) δ (ppm) 7.26-7.24 (m, 2H), 7.20 (d, J = 7.9 Hz, 1H), 7.05-7.03 (m, 1H), 6.97-6.94 (m, 2H), 6.88-6.84 (m, 1H), 6.26 (s, 1H), 3.83 (s, 3H), 3.25 (s, 3H), 3.20 (d, J = 15.3 Hz, 1H), 2.77 (d, J = 15.3 Hz, 1H), 1.26 (s, 9H); ¹³C NMR (CDCl₃, 125 MHz) δ (ppm) 196.5, 175.1, 161.3, 153.7, 144.6, 136.1, 135.3, 127.3, 124.7, 122.6, 117.2, 115.2, 109.4, 80.6, 59.8, 55.5, 47.5, 28.2, 27.0; IR (KBr) ν 3324, 2977, 2838, 1729, 1610, 1593, 1496, 1466, 1367, 1251, 1173, 1112, 1028, 828, 734 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]⁺ (C₂₃H₂₅ClN₂O₅SNa⁺), 499.1065, found 499.1061; [α]D²⁵ = +115.0 (c = 0.50, CHCl₃); ee: 73%; HPLC analysis CHIRALPAK OD-H, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 9.0 min (major), t₂ = 12.7 min (minor).

S-(4-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-7-chloro-1-methyl-2-oxoindolin-3-yl)ethanethioate (8r)

White solid, 87% yield; Mp 169-170 °C; ¹H NMR (CDCl₃, 400 MHz) δ (ppm) 7.26-7.23 (m, 3H), 7.16 (d, J = 7.3 Hz, 1H), 7.00-6.94 (m, 3H), 6.34 (s, 1H), 3.83 (s, 3H), 3.63 (s, 3H), 3.14 (d, J = 15.3 Hz, 1H), 2.76 (d, J = 15.2 Hz, 1H), 1.26 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 196.6, 175.5, 161.3, 153.7, 139.2, 136.1, 131.9, 131.8, 123.5, 122.0, 117.3, 116.1, 115.2, 80.7, 59.9, 55.5, 47.5, 30.3, 28.2; IR (KBr) ν 3322, 2977, 2838, 1729, 1610, 1593, 1496, 1466, 1367, 1251, 1173, 1112, 1028, 828, 734 cm⁻¹; HRMS (ESI⁺) calc. for [M+Na]⁺ (C₂₃H₂₅ClN₂O₅SNa⁺), 499.1065, found 499.1060; [α]D²⁵ = +104.0 (c = 0.50, CHCl₃); ee: 70%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t₁ = 9.3 min (major), t₂ = 19.4 min (minor).
**S-(4-Methoxyphenyl) (R)-2-(5-bromo-3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8t)**

White solid, 99% yield; Mp 187-188 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.48-7.45 (m, 1H), 7.42-7.35 (m, 1H), 7.30 (d, \(J = 8.9\) Hz, 2H), 6.98 (d, \(J = 8.9\) Hz, 2H), 6.76 (d, \(J = 8.3\) Hz, 1H), 6.30 (s, 1H), 3.84 (s, 3H), 3.25 (s, 3H), 3.16 (d, \(J = 14.8\) Hz, 1H), 2.73 (d, \(J = 15.0\) Hz, 1H), 1.27 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 196.7, 174.6, 161.3, 153.7, 142.4, 136.3, 132.3, 130.8, 126.9, 117.2, 115.5, 115.3, 110.1, 80.7, 60.1, 55.6, 47.3, 28.2, 27.0; IR (KBr) \(\nu\) 3280, 2977, 2937, 1709, 1609, 1592, 1494, 1391, 1250, 1172, 1028, 832 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{23}\)H\(_{25}\)BrN\(_2\)O\(_5\)SNa\(^+\)), 543.0560, found 543.0554; \([\alpha]_D^{25}\) = +106.0 (c = 0.50, CHCl\(_3\)); ee: 75%; HPLC analysis CHIRALPAK OD-H, n-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 10.5\) min (major), \(t_2 = 12.6\) min (minor).

**S-(4-Methoxyphenyl) (R)-2-(6-bromo-3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8u)**

White solid, 98% yield; Mp 186-187 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.26-7.20 (m, 3H), 7.14 (d, \(J = 7.9\) Hz, 1H), 7.03-7.00 (m, 1H), 6.97-6.94 (m, 2H), 6.27 (s, 1H), 3.83 (s, 3H), 3.24 (s, 3H), 3.19 (d, \(J = 15.7\) Hz, 1H), 2.77 (d, \(J = 15.3\) Hz, 1H), 1.27 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 196.5, 175.0, 161.3, 153.7, 144.7, 136.1, 127.9, 125.6, 125.0, 123.2, 117.2, 115.2, 112.2, 80.7, 59.9, 55.5, 47.4, 28.2, 27.0; IR (KBr) \(\nu\) 3326, 2976, 2931, 1728, 1608, 1592, 1495, 1368, 1250, 1173, 1050, 829 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{23}\)H\(_{25}\)BrN\(_2\)O\(_5\)SNa\(^+\)), 543.0560, found 543.0554; \([\alpha]_D^{25}\) = +105.6 (c = 0.50, CHCl\(_3\)); ee: 71%; HPLC analysis CHIRALPAK OD-H, n-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 9.3\) min (major), \(t_2 = 13.2\) min (minor).
S-(4-Methoxyphenyl) (R)-2-(7-bromo-3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8v)

White solid, 85% yield; Mp 156-157 °C; $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 7.44 (d, $J = 8.1$ Hz, 1H), 7.26-7.18 (m, 3H), 6.96-6.89 (m, 3H), 3.83 (s, 3H), 3.64 (s, 3H), 3.13 (d, $J = 15.0$ Hz, 1H), 2.76 (d, $J = 15.0$ Hz, 1H), 1.26 (s, 9H); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 196.8, 175.7, 161.3, 153.7, 140.6, 136.1, 135.1, 132.3, 123.9, 122.5, 117.3, 115.2, 103.0, 80.7, 59.9, 55.6, 47.5, 30.5, 28.2; IR (KBr) ν 3325, 2977, 2933, 1729, 1609, 1592, 1496, 1463, 1367, 1250, 1173, 1029, 828, 734 cm$^{-1}$; HRMS (ESI$^+$) calc. for [M+Na]$^+$ (C$_{23}$H$_{25}$BrN$_2$O$_5$SNa$^+$), 543.0560, found 543.0557; [α]$_{D}^{25}$ = +84.8 ($c = 0.50$, CHCl$_3$); ee: 66%; HPLC analysis CHIRALPAK IA, n-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, $t_1 = 8.4$ min (major), $t_2 = 10.6$ min (minor).

S-(4-Methoxyphenyl) (R)-2-(7-bromo-3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxo-7-(trifluoromethyl)indolin-3-yl)ethanethioate (8w)

White solid, 74% yield; Mp 151-152 °C; $^1$H NMR (CDCl$_3$, 500 MHz) δ (ppm) δ 7.63 (d, $J = 8.0$ Hz, 1H), 7.46 (d, $J = 7.3$ Hz, 1H), 7.22 (d, $J = 8.7$ Hz, 2H), 7.15 (t, $J = 7.7$ Hz, 1H), 6.95 (d, $J = 8.9$ Hz, 2H), 6.33 (s, 1H), 3.83 (s, 3H), 3.46 (d, $J = 2.4$ Hz, 3H), 3.15 (d, $J = 15.1$ Hz, 1H), 2.77 (d, $J = 15.1$ Hz, 1H), 1.23 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz) δ (ppm) 196.4, 176.1, 161.3, 153.5, 141.2, 136.1, 131.8, 127.4 (q, $J = 6.3$ Hz, C-C-CF$_3$), 126.9, 123.6 (q, $J = 269.9$ Hz, CF$_3$), 117.2, 115.2, 112.9 (q, $J = 32.5$ Hz, C-C-CF$_3$), 80.8, 58.8, 55.5, 47.5, 29.6, 28.1; IR (KBr) ν 3333, 2982, 2840, 1733, 1706, 1599, 1497, 1464, 1250, 1176, 1122, 828, 751 cm$^{-1}$; HRMS (ESI$^+$) calc. for [M+Na]$^+$ (C$_{24}$H$_{25}$F$_3$N$_2$O$_5$SNa$^+$), 533.1329, found 533.1324; [α]$_{D}^{25}$ = +60.6 ($c = 0.50$, CHCl$_3$); ee: 60%; HPLC analysis CHIRALPAK IA, n-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, $t_1 = 7.5$ min (major), $t_2 = 16.2$ min (minor).
S-(2-Methoxyphenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ab)

Yellow solid, 51% yield; Mp 186-187 °C; 1H NMR (CDCl$_3$, 500 MHz) δ (ppm) 7.47-7.43 (m, 1H), 7.35-7.30 (m, 3H), 7.07 (t, $J$ = 7.5 Hz, 1H), 7.00 (t, $J$ = 7.6 Hz, 2H), 6.87 (d, $J$ = 7.8 Hz, 1H), 6.40 (s, 1H), 3.86 (s, 3H), 3.27 (s, 3H), 3.22 (d, $J$ = 15.0 Hz, 1H), 2.76 (d, $J$ = 15.1 Hz, 1H), 1.24 (s, 9H); 13C NMR (CDCl$_3$, 125 MHz) δ (ppm) 195.0, 175.2, 159.3, 153.7, 143.3, 136.6, 132.4, 129.4, 120.9, 128.4, 118.7, 115.1, 111.8, 108.3, 80.3, 60.2, 56.1, 47.7, 28.2, 26.8; IR (KBr) v 3329, 2975, 2933, 1709, 1614, 1503, 1495, 1366, 1276, 1164, 1023, 753 cm$^{-1}$; HRMS (ESI$^+$) calc. for [M+Na]$^+$ (C$_{23}$H$_{26}$N$_2$O$_5$SNa$^+$), 465.1455, found 465.1454; [α]$_D^{25}$ = +80.0 (c = 0.46, CHCl$_3$); ee: 63%; HPLC analysis CHIRALPAK IA, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t$_1$ = 10.3 min (major), t$_2$ = 18.4 min (minor).

S-Phenyl (R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ac)$^9$

64% yield; 1H NMR (CDCl$_3$, 300 MHz) δ (ppm) 7.46-7.39 (m, 3H), 7.37-7.29 (m, 4H), 7.08 (t, $J$ = 7.3 Hz, 1H), 6.87 (d, $J$ = 7.8 Hz, 1H), 3.27-3.20 (m, 4H), 2.81 (d, $J$ = 15.0 Hz, 1H), 1.24 (s, 9H); 13C NMR (CDCl$_3$, 100 MHz) δ (ppm) 195.5, 175.1, 153.8, 143.3, 134.5, 130.1, 129.5, 129.5, 129.0, 126.8, 123.7, 122.9, 108.6, 80.4, 60.3, 47.9, 28.2, 26.8; [α]$_D^{25}$ = +93.4 (c = 0.50, CHCl$_3$); ee: 69%; HPLC analysis CHIRALPAK OD-H, n-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, t$_1$ = 7.5 min (major), t$_2$ = 8.6 min (minor).
**S-(p-Tolyl)** *(R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ad)*

79% yield; \(^1^H\) NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.37-7.31 (m, 1H), 7.31-7.19 (m, 5H), 7.07 (t, \(J = 7.6\) Hz, 1H), 6.87 (d, \(J = 7.8\) Hz, 1H), 6.31 (s, 1H), 3.26 (s, 3H), 3.21 (d, \(J = 15.1\) Hz, 1H), 2.78 (d, \(J = 15.1\) Hz, 1H), 2.38 (s, 3H), 1.24 (s, 9H); \(^1^C\) NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 196.2, 175.1, 153.6, 143.3, 140.6, 134.5, 130.4, 129.5, 128.9, 123.7, 123.3, 122.8, 108.6, 80.4, 60.3, 47.8, 28.2, 26.8, 21.5; \([\alpha]_D^{25}\) = +99.4 (\(c = 0.50, \text{CHCl}_3\)); ee: 74%; HPLC analysis CHIRALPAK IA, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 8.3\) min (major), \(t_2 = 13.8\) min (minor).

**S-(4-Isopropylphenyl)** *(R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ae)*

Yellow solid, 86% yield; Mp 126-127 °C; \(^1^H\) NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.36-7.24 (m, 6H), 7.08 (t, \(J = 7.6\) Hz, 1H), 6.87 (d, \(J = 7.8\) Hz, 1H), 6.32 (s, 1H), 3.27 (s, 3H), 3.21 (d, \(J = 14.8\) Hz, 1H), 2.97-2.90 (m, 1H), 2.78 (d, \(J = 15.0\) Hz, 1H), 1.27-1.23 (m, 15H); \(^1^C\) NMR (CDCl\(_3\), 125 MHz) \(\delta\) 196.2, 175.2, 153.8, 151.3, 143.3, 134.5, 129.5, 128.9, 127.79, 123.7, 123.6, 122.8, 108.6, 80.4, 60.3, 47.8, 34.1, 28.2, 26.9, 23.9; IR (KBr) \(\nu\) 3337, 2963, 2931, 1722, 1614, 1495, 1472, 1367, 1291, 1163, 826, 751 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{25}\)H\(_{30}\)N\(_2\)O\(_4\)SNa\(^+\)), 477.1819, found 477.1818; \([\alpha]_D^{25}\) = +101.8 (\(c = 0.50, \text{CHCl}_3\)); ee: 76%; HPLC analysis CHIRALPAK IA, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 190 nm, \(t_1 = 7.6\) min (major), \(t_2 = 12.6\) min (minor).
\(S\)-(4-Fluorophenyl) \((R)\)-2-(3-\((\text{tert-butoxycarbonyl})\text{amino})\)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8af)

Yellow solid, 76% yield; Mp 187-188 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.36-7.29 (m, 4H), 7.14-7.06 (m, 3H), 6.87 (d, \(J = 7.8\) Hz, 1H), 6.18 (s, 1H), 3.27 (s, 3H), 3.23 (d, \(J = 14.3\) Hz, 1H), 2.83 (d, \(J = 15.1\) Hz, 1H), 1.25 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 195.4, 175.1, 163.9 (d, \(J = 8.6\) Hz, C-C-C-F), 129.6, 128.9, 123.7, 122.9, 122.2 (d, \(J = 3.2\) Hz, C-C-C-C-F), 116.9 (d, \(J = 22.3\) Hz, C-C-F). 108.6, 80.5, 60.2, 47.9, 28.2, 26.8; IR (KBr) \(\nu\) 3312, 2979, 2931, 1722, 1615, 1492, 1366, 1159, 833, 752 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{22}\)H\(_{23}\)FN\(_2\)O\(_4\)SNa\(^+\)), 453.1255, found 453.1254; \([\alpha]_D^{25} = +80.9\) (c = 0.45, CHCl\(_3\)); ee: 77%; HPLC analysis CHIRALPAK OD-H, \(n\)-hexane:PrOH = 9:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 7.1\) min (major), \(t_2 = 8.3\) min (minor).

\(S\)-(2-Fluorophenyl) \((R)\)-2-(3-\((\text{tert-butoxycarbonyl})\text{amino})\)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ag)

Yellow solid, 47% yield; Mp 186-187 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.50-7.45 (m, 1H), 7.36-7.32 (m, 3H), 7.22-7.18 (m, 2H), 7.08 (t, \(J = 7.5\) Hz, 1H), 6.87 (d, \(J = 7.4\) Hz, 1H), 6.23 (s, 1H), 3.27-3.25 (m, 4H), 2.83 (d, \(J = 15.1\) Hz, 1H), 1.25 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 193.6, 175.0, 162.1 (d, \(J = 250.7\) Hz, C-F), 153.7, 143.2, 136.5, 132.9 (d, \(J = 8.2\) Hz, C-C-C-F), 129.6, 128.7, 125.0 (d, \(J = 3.6\) Hz, C-C-C-F), 123.8, 122.9, 116.5 (d, \(J = 22.3\) Hz, C-C-F), 114.2 (d, \(J = 18.6\) Hz), 108.6, 80.5, 60.2, 47.9, 28.2, 26.8; IR (KBr) \(\nu\) 3326, 2974, 2910, 1724, 1702, 1615, 1478, 1358, 1125, 754 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{22}\)H\(_{23}\)FN\(_2\)O\(_4\)SNa\(^+\)), 453.1255, found 453.1254; \([\alpha]_D^{25} = +11.2\) (c = 0.50, CHCl\(_3\)); ee: 12%; HPLC analysis CHIRALPAK OD-H, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 7.9\) min (major), \(t_2 = 8.9\) min (minor).
S-(4-Chlorophenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ah)\(^9\)

\[
\begin{align*}
\text{80\% yield; } & \text{ }^1\text{H NMR (CDCl}_3, \text{500 MHz) } \delta \text{ (ppm) 7.41-7.38 (m, 2H), 7.36-7.30 (m, 2H), 7.27-7.25 (m, 2H), 7.07 (t, } J = 7.4 \text{ Hz, 1H), 6.87 (d, } J = 7.6 \text{ Hz, 1H), 6.15 (s, 1H), 3.26 (s, 3H), 3.24 (d, } J = 10.5 \text{ Hz, 1H), 2.85 (d, } J = 15.1 \text{ Hz, 1H), 1.25 (s, 9H); } \text{ }^{13}\text{C NMR (CDCl}_3, \text{125 MHz) } \delta \text{ (ppm) 194.8, 175.0, 153.8, 143.3, 136.6, 135.7, 129.8, 129.6, 128.8, 125.2, 123.7, 122.9, 108.6, 80.5, 60.2, 48.0, 28.2, 26.8; } \text{[α]}_D^{25} = +93.0 \text{ (c = 0.46, CHCl}_3); \text{ ee: 80\%; HPLC analysis CHIRALPAK OD-H, } n\text{-hexane:PrOH = 4:1, 25 }^\circ\text{C, 1 mL/min flow rate, detection at 254 nm, } t_1 = 7.4 \text{ min (major), } t_2 = 8.8 \text{ min (minor).}
\end{align*}
\]

S-(3-Chlorophenyl) (R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8ai)

\[
\begin{align*}
\text{White solid, 49\% yield; Mp 170-171 }^\circ\text{C; } & \text{ }^1\text{H NMR (CDCl}_3, \text{400 MHz) } \delta \text{ (ppm) 7.42-7.31 (m, 5H), 7.23 (d, } J = 7.6 \text{ Hz, 1H), 7.09 (t, } J = 7.5 \text{ Hz, 1H), 6.87 (d, } J = 7.8 \text{ Hz, 1H), 6.15 (s, 1H), 3.27-3.24 (m, 4H), 2.85 (d, } J = 15.2 \text{ Hz, 1H), 1.25 (s, 9H); } \text{ }^{13}\text{C NMR (CDCl}_3, \text{100 MHz) } \delta \text{ (ppm) 194.4, 175.0, 153.8, 143.3, 135.1, 134.1, 132.6, 130.5, 130.3, 129.6, 128.8, 128.5, 123.8, 122.9, 108.6, 80.6, 77.5, 77.2, 76.8, 60.2, 48.1, 28.2, 26.8; } \text{IR (KBr) } v \text{ 3291, 2981, 2928, 1706, 1612, 1532, 1464, 1166, 763 } \text{cm}^{-1}; \text{ HRMS (ESI\textsuperscript{+} calc. for } [\text{M+Na}]^+ \text{ (C}_{22}\text{H}_{23}\text{ClN}_2\text{O}_4\text{SNa}), 469.0959, \text{ found 469.0957; } [\alpha]_D^{25} = +76.8 \text{ (c = 0.50, CHCl}_3); \text{ ee: 79\%; HPLC analysis CHIRALPAK IA, } n\text{-hexane:PrOH = 4:1, 25 }^\circ\text{C, 1 mL/min flow rate, detection at 254 nm, } t_1 = 9.1 \text{ min (major), } t_2 = 20.4 \text{ min (minor).}
\end{align*}
\]
\(S\)-(4-Bromophenyl) \(\text{(R)}\)-2-(3-((\text{tert}-\text{butoxycarbonyl})\text{amino})-1\text{-methyl-2-oxoindolin-3-yl})\text{ethanethioate (8aj)}\)

Yellow solid, 84\% yield; Mp 179-180 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.55 (d, \(J = 8.5\) Hz, 2H), 7.36-7.26 (m, 2H), 7.19 (d, \(J = 8.5\) Hz, 2H), 7.07 (t, \(J = 7.5\) Hz, 1H), 6.87 (d, \(J = 7.7\) Hz, 1H), 6.15 (s, 1H), 3.26 (s, 4H), 2.85 (d, \(J = 15.2\) Hz, 1H), 1.25 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 194.6, 175.0, 153.8, 143.3, 135.9, 132.7, 129.6, 128.8, 125.9, 124.9, 123.7, 122.9, 108.6, 80.5, 60.2, 48.1, 28.2, 26.8; IR (KBr) v 3319, 2977, 2930, 1722, 1614, 1495, 1367, 1252, 1165, 814, 751 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for \([\text{M+Na}]^+\) (C\(_{22}\)H\(_{23}\)BrN\(_2\)O\(_4\)SNa\(^+\)), 513.0454, found 513.0455; [\(\alpha\)\]D\(_{25}\) = +86.8 (c = 0.50, CHCl\(_3\)); ee: 77\%; HPLC analysis CHIRALPAK IA, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 10.4\) min (major), \(t_2 = 18.0\) min (minor).

\(S\)-(3-Bromophenyl) \(\text{(R)}\)-2-(3-((\text{tert}-\text{butoxycarbonyl})\text{amino})-1\text{-methyl-2-oxoindolin-3-yl})\text{ethanethioate (8ak)}\)

White solid, 73\% yield; Mp 171-172 °C; \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 7.58-7.47 (m, 1H), 7.47 (s, 1H), 7.37-7.26 (m, 4H), 7.09 (t, \(J = 7.5\) Hz, 1H), 6.88 (d, \(J = 7.8\) Hz, 1H), 6.14 (s, 1H), 3.27-3.24 (m, 4H), 2.85 (d, \(J = 15.2\) Hz, 1H), 1.25 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 194.4, 175.0, 153.8, 143.3, 136.9, 133.2, 133.1, 130.8, 129.6, 128.8, 123.8, 123.0, 122.9, 108.7, 80.6, 60.2, 48.1, 28.2, 26.8; IR (KBr) v 3294, 2979, 2927, 1707, 1611, 1532, 1332, 1166, 762 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for \([\text{M+Na}]^+\) (C\(_{22}\)H\(_{23}\)BrN\(_2\)O\(_4\)SNa\(^+\)), 513.0454, found 513.0454; [\(\alpha\)\]D\(_{25}\) = +82.0 (c = 0.50, CHCl\(_3\)); ee: 78\%; HPLC analysis CHIRALPAK IA, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 9.4\) min (major), \(t_2 = 22.8\) min (minor).
$S$-(Naphthalen-2-yl) $(R)$-2-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8al)$^{[9]}$

65% yield; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ (ppm) $\delta$ 7.89-7.82 (m, 4H), 7.57-7.51 (m, 2H), 7.38-7.34 (m, 3H), 7.11 (t, $J = 2.0$ Hz, 1H), 6.88 (d, $J = 7.8$ Hz, 1H), 6.27 (s, 1H), 3.23-3.21 (m, 4H), 2.87 (d, $J = 15.1$ Hz, 1H), 1.25 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ (ppm) $\delta$ 195.7, 175.1, 153.8, 143.3, 134.6, 133.7, 133.6, 130.6, 129.5, 129.2, 128.9, 128.2, 128.0, 127.6, 126.9, 124.1, 123.8, 122.9, 108.6, 80.5, 60.3, 48.0, 28.2, 26.8; $[\alpha]_D^{25} = +107.4$ ($c = 0.5$, CHCl$_3$); ee: 68%; HPLC analysis CHIRALPAK OD-H, $n$-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, $t_1 = 9.6$ min (major), $t_2 = 13.7$ min (minor).

$S$-Benzyl $(R)$-2-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8am)$^{[9]}$

48% yield; $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ (ppm) 7.31-7.20 (m, 6H), 7.11 (d, $J = 8.3$ Hz, 1H), 6.94 (t, $J = 7.6$ Hz, 1H), 6.82 (d, $J = 7.8$ Hz, 1H), 6.27 (s, 1H), 4.14 (d, $J = 14.2$ Hz, 1H), 4.07 (d, $J = 13.5$ Hz, 1H), 3.23 (s, 3H), 3.12 (s, 1H), 2.70 (d, $J = 14.9$ Hz, 1H), 1.25 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ (ppm) 195.9, 175.2, 153.7, 143.2, 136.8, 129.4, 129.0, 128.8, 127.6, 123.7, 122.8, 108.4, 80.5, 60.2, 48.3, 33.9, 28.2, 26.8; $[\alpha]_D^{25} = -7.6$ ($c = 0.5$, CHCl$_3$); ee: 9%; HPLC analysis CHIRALPAK IA, $n$-hexane:iPrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, $t_1 = 9.5$ min (major), $t_2 = 15.7$ min (minor).
S'-Ethyl (R)-2-(3-((tert-butoxycarbonyl)amino)-1-methyl-2-oxoindolin-3-yl)ethanethioate (8an)

Yellow solid, 34% yield; Mp 90-91 °C; \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta\) (ppm) 7.33-7.23 (m, 2H), 7.03 (t, \(J=7.5\) Hz, 1H), 6.85 (d, \(J=7.6\) Hz, 1H), 6.33 (s, 1H), 3.25 (s, 3H), 3.11 (d, \(J=14.4\) Hz, 1H), 2.92-2.84 (m, 2H), 2.68 (d, \(J=14.9\) Hz, 1H), 1.34-1.21 (m, 12H); \(^{13}\)C (CDCl\(_3\), 125 MHz) \(\delta\) (ppm) 196.8, 175.3, 153.8, 143.2, 129.4, 129.0, 123.6, 122.8, 108.5, 80.5, 48.4, 28.3, 28.2, 26.8, 24.1, 14.5; IR (KBr) \(\nu\) 3268, 2974, 2932, 1706, 1613, 1537, 1493, 1363, 1173, 759 cm\(^{-1}\); HRMS (ESI\(^+\)) calc. for [M+Na]\(^+\) (C\(_{18}\)H\(_{24}\)N\(_2\)O\(_4\)SNa\(^+\)), 387.1349, found 387.1348; \([\alpha]\)\(_D\)\(^{25}\) = +2.9 (\(c = 0.35\), CHCl\(_3\)); ee: 9%; HPLC analysis CHIRALPAK OD-H, \(n\)-hexane:PrOH = 4:1, 25 °C, 1 mL/min flow rate, detection at 254 nm, \(t_1 = 5.6\) min (major), \(t_2 = 6.9\) min (minor).
4. Copies of $^1$H and $^{13}$C NMR spectra

$^1$H and $^{13}$C NMR of 3b in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 3c in CDCl$_3$. 

S40
$^1\text{H}$ and $^{13}\text{C}$ NMR of 3d in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 3f in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 4b in CDCl$_3$. 
\(^1H\) and \(^13C\) NMR of 4c in DMSO-\(d_6\).
$^1$H and $^{13}$C NMR of 4d in CDCl$_3$. 
$^{1}\text{H}$ and $^{13}\text{C}$ NMR of 4f in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 5b in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 5c in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 5d in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 5f in CDCl$_3$. 
$^1$H and $^{13}$C NMR of M2 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of M3 in DMSO-$d_6$. 

**Current Data Parameters**
- **NAME**: M3
- **EXPNO**: 2
- **SAMPNO**: 1

**F3 - Acquisition Parameters**
- **Time**: 18.15 s
- **D1**: 0.00 s
- **D2**: 0.00 s
- **D3**: 0.00 s
- **D4**: 0.00 s
- **T1**: 0.00 s
- **T2**: 0.00 s
- **T3**: 0.00 s
- **T4**: 0.00 s

**F2 - Processing parameters**
- **DS**: 1024
- **DG**: 0
- **DS**: 0
- **DG**: 0
- **DS**: 0
- **DG**: 0

**F1 - Data Processing**
- **F1**: 125.743543 MHz
- **F2**: 10.00 MHz

**F1 - Scaling**
- **F1**: 125.743543 MHz
- **F2**: 10.00 MHz
- **F3**: 1024
- **F4**: 0
- **F5**: 0

**F2 - Decimation**
- **F1**: 125.743543 MHz
- **F2**: 10.00 MHz
- **F3**: 1024
- **F4**: 0
- **F5**: 0

**F3 - Decimation**
- **F1**: 125.743543 MHz
- **F2**: 10.00 MHz
- **F3**: 1024
- **F4**: 0
- **F5**: 0
$^1$H and $^{13}$C NMR of M4 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of M6 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of M9 in DMSO-$d_6$. 

---

S55
$^1$H and $^{13}$C NMR of M10 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of M11 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of M12 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of 9 in DMSO-$d_6$. 
$^1$H and $^{13}$C NMR of 8a in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8b in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8c in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8d in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8e in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8f in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8g in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8h in CDCl$_3$. 
$^{1}H$ and $^{13}C$ NMR of 8i in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8k in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8I in CDCl$_3$. 

![NMR Spectra of 8I in CDCl$_3$]
$^{1}$H and $^{13}$C NMR of 8m in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8n in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8p in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8q in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8r in CDCl$_3$. 
$^{1}H$ and $^{13}C$ NMR of 8t in CDCl$_3$. 
\textsuperscript{1}H and \textsuperscript{13}C NMR of 8u in CDCl\textsubscript{3}.
$^1$H and $^{13}$C NMR of 8v in CDCl$_3$. 

S78
$^1$H and $^{13}$C NMR of 8w in CDCl$_3$. 

S79
$^1$H and $^{13}$C NMR of 8ab in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8ac in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8ad in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8ae in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8af in CDCl$_3$. 
$^1$H and $^{13}$C NMR of 8ag in CDCl$_3$. 
\(^1\)H and \(^{13}\)C NMR of 8ah in CDCl\(_3\).
$^1$H and $^{13}$C NMR of 8ai in CDCl$_3$. 
\(^1\)H and \(^{13}\)C NMR of 8aj in CDCl\(_3\).
$^1$H and $^{13}$C NMR of $8\text{ak}$ in CDCl$_3$. 
\(^1\)H and \(^{13}\)C NMR of 8al in CDCl\(_3\).
\(^1\)H and \(^{13}\)C NMR of 8am in CDCl\(_3\).
$^1$H and $^{13}$C NMR of 8an in CDCl$_3$. 

---

S92
5. HPLC analysis of products

![HPLC analysis diagram]

| Peak | Retention Time | Area   | Height | Concentration | Area % |
|------|----------------|--------|--------|---------------|--------|
| 1    | 9.70          | 7033891| 197836 | 0.00          | 85.919 |
| 2    | 12.123        | 1192719| 37471  | 0.00          | 14.081 |
| Total|                | 818610 | 225907 |               | 100.000|

![HPLC analysis diagram]

| Peak | Retention Time | Area   | Height | Concentration | Area % |
|------|----------------|--------|--------|---------------|--------|
| 1    | 9.70           | 1940007| 54835  | 0.00          | 56.112 |
| 2    | 12.111         | 1937238| 46099  | 0.00          | 49.888 |
| Total|                | 3883305| 100954 |               | 100.000|

S93
### 峰表

| 峰号 | 保留时间 | 面积    | 高度   | 浓度 | 面积%  |
|------|----------|---------|--------|------|--------|
| 1    | 7.559    | 2395184 | 193877 | 0.000| 50.115 |
| 2    | 16.529   | 2384220 | 87147  | 0.000| 49.885 |
| 总计 |          | 4779404 | 281024 |      | 100.000|

### 峰表

| 峰号 | 保留时间 | 面积    | 高度   | 浓度 | 面积%  |
|------|----------|---------|--------|------|--------|
| 1    | 7.491    | 8248820 | 652474 | 0.000| 76.469 |
| 2    | 16.466   | 2538278 | 94229  | 0.000| 23.531 |
| 总计 |          | 10787098| 746703 |      | 100.000|
### 峰表

| 峰号 | 保留时间 | 面积   | 高度   | 浓度 | 面积% |
|------|----------|--------|--------|------|-------|
| 1    | 8.940    | 129256 | 38580  | 0.000| 50.691|
| 2    | 10.663   | 115719 | 22240  | 0.000| 49.309|
| 总计 | 242975   | 60820  |        |      | 100.000|

### 峰表

| 峰号 | 保留时间 | 面积   | 高度   | 浓度 | 面积% |
|------|----------|--------|--------|------|-------|
| 1    | 9.930    | 344245 | 10870  | 0.000| 31.667|
| 2    | 10.527   | 745384 | 116375 | 0.000| 68.333|
| 总计 | 10998091 | 254746 |        |      | 100.000|
### 峰表

| 编号 | 保留时间 | 面积   | 高度   | 浓度 | 血积% |
|------|----------|--------|--------|------|-------|
| 1    | 8.117    | 833185 | 238547 | 0.000 |       |
| 2    | 17.728   | 3372364| 110580 | 0.000 |       |
| 总计 |          | 6565749| 349132 |      |       |

### 峰表

| 编号 | 保留时间 | 面积   | 高度   | 浓度 | 血积% |
|------|----------|--------|--------|------|-------|
| 1    | 8.135    | 13149577| 964587 | 0.000 | 72.704|
| 2    | 17.708   | 4969998 | 174493 | 0.000 | 27.296|
| 总计 |          | 1805555 | 1139030|      | 100.000|
### 峰表

| 峰号 | 保留时间 | 面积   | 高度   | 浓度  | 面积% |
|------|-----------|--------|--------|------|-------|
| 1    | 8.379     | 6919557| 461871 | 0.000| 83.538|
| 2    | 10.559    | 1369417| 75794  | 0.000| 16.462|
| 总计 |           | 9319061| 537661 |      | 100.000|
### 峰表

| 峰号 | 保留时间 | 面积   | 高度  | 浓度 | 面积% |
|------|-----------|--------|-------|------|-------|
| 1    | 9.518     | 1559211| 43572 | 0.000| 49.957|
| 2    | 11.564    | 1591961| 36964 | 0.000| 50.043|
| 总计 |           | 3151225| 80537 |      | 100.000|

### 峰表

| 峰号 | 保留时间 | 面积   | 高度  | 浓度 | 面积% |
|------|-----------|--------|-------|------|-------|
| 1    | 9.496     | 3482044| 97590 | 0.000| 55.659|
| 2    | 11.915    | 573511 | 13909 | 0.000| 14.141|
| 总计 |           | 4055335| 111899|      | 100.000|
### 峰表

| 峰号 | 保留时间 | 面积     | 高度     | 浓度 | 面积% |
|------|----------|----------|----------|------|-------|
| 1    | 10.664   | 250574   | 5538     | 0.000| 49.631|
| 2    | 12.660   | 351301   | 5538     | 0.000| 50.369|
| 总计 |          | 591875   | 11396    |      | 100.000|

### 峰表

| 峰号 | 保留时间 | 面积     | 高度     | 浓度 | 面积% |
|------|----------|----------|----------|------|-------|
| 1    | 10.509   | 6291145  | 154391   | 0.000| 87.494|
| 2    | 12.645   | 599188   | 20973    | 0.000| 12.506|
| 总计 |          | 7190333  | 175361   |      | 100.000|
### 峰表

|  | 保持时间 | 峰面积 | 高度 | 浓度 | 血量% |
|---|---------|--------|------|------|-------|
| 1 | 7.623   | 1475176| 63458| 0.000| 49.851|
| 2 | 8.588   | 1483966| 63103| 0.000| 50.149|
| 总计 | 2959143| 126561 | 100.000 |

### 峰表

|  | 保持时间 | 峰面积 | 高度 | 浓度 | 血量% |
|---|---------|--------|------|------|-------|
| 1 | 7.496   | 3071329| 129263| 0.000| 84.568|
| 2 | 8.503   | 360155 | 26325 | 0.000| 15.432|
| 总计 | 3601784| 153788 | 100.000 |

![图示](image)
<峰表>

| 峰号 | 保留时间 | 面积   | 高度 | 浓度 | 面积% |
|------|----------|--------|------|------|-------|
| 1    | 7.925    | 1874520| 73821| 0.000| 49.386|
| 2    | 8.933    | 1920699| 77255| 0.000| 50.614|
| 总计 |          | 3795299| 151077| 100.000|
6. References

[1]. Guo, H.; Zhang, L. W.; Zhou, H.; Meng, W.; Ao, Y. F.; Wang, D. X.; Wang, Q. Q. Angew. Chem., Int. Ed. 2020, 59, 2623.

[2]. Davies, S.; Mortlock, A. Tetrahedron 1993, 49, 4419.

[3]. Owsianik, K.; Wieczorek, W.; Baliń ska, A.; Mikolajczyk, M. Heteroatom Chem. 2014, 25, 690.

[4]. Chunhong, Z.; Liu, F.; Gou, S. Tetrahedron: Asymmetry 2014, 25, 278.

[5]. Mita, T.; Sugawara, M.; Saito, K. Org. Lett. 2014, 16, 3028.

[6]. Gould, A. E.; Adams, R.; Adhikari, S.; Aertgeerts, K.; Afroze, R.; Blackburn, C.; Calderwood, E. F.; Chau, R.; Choutar J.; Duffey, M. O.; England, D. B.; Farrer, C.; Forsyth, N.; Garcia, K.; Gaulin, J.; Greenspan, P. D.; Guo, R.; Harrison, S. J.; Huang, S.-C.; Iartchouk, N.; Janowick, D.; Kim, M.-S.; Kulkarni, B.; Langton, S. P.; Liu, J. X.; Ma, L.-T.; Menon, S.; Mizutani, H.; Paske, E.; Renou, C. C.; Rezaei, M.; Rowland, R. S.; Sintchak, M. D.; Smith, M. D.; Stroud, S. G.; Tregay, M.; Tian, Y.; Veiby, O. P.; Vos, T. J.; Vyskocil, S.; Williams, J.; Xu, T.; Yang, J. J.; Yano, J.; Zeng, H.; Zhang, D. M.; Zhang, Q.; Galvin, K. M. J. Med. Chem. 2011, 54, 1836.

[7]. a) Urban, M.; Franc, M.; Hofmanová, M.; Cisařová, M.; Veselý, M. Org. Biomol. Chem. 2017, 15, 9071. b) Marques, C. S.; Burke, A. J. Eur. J. Org. Chem. 2016, 806. c) Holmquist, M.; Blay, G.; Pedro, J. R. Chem. Commun. 2014, 50, 9309. d) Yan, W. J. W.; D. Feng, J. C.; Li, P.; Zhao, D. P.; Wang, R. Org. Lett. 2012, 14, 2512.

[8]. Hara, N.; Nakamura, S.; Funahashi, Y.; Shibata, N. Adv. Synth. Catal. 2011, 353, 2976.

[9]. Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. Chem. Eur. J. 2012, 18, 9276.