Supporting Information

A Disulfonimide Catalyst for Highly Enantioselective Mukaiyama-Mannich Reaction

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1. Instrumentation and Materials

NMR spectra were recorded on an ECS-400 spectrometer (400 MHz for \(^1\)H NMR, 100 MHz for \(^{13}\)C NMR). Chemical shifts (\(\delta\)) are given in relative to CDCl\(_3\) (\(\delta = 7.26\) ppm for \(^1\)H NMR), acetone-\(d_6\) (\(\delta = 2.05\) ppm for \(^1\)H NMR), dimethyl sulfoxide-\(d_6\) (\(\delta = 2.5\) ppm for \(^1\)H NMR). Multiplicities are indicated as: br (broad), s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Coupling constants (\(J\)) are reported in Hertz (Hz). For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 F254 0.25 mm) were used. Visualization was accomplished by UV light (254 nm), anisaldehyde, KMnO\(_4\), and phosphomolybdic acid. Optical rotations were measured on an ATAGO AP-300 polarimeter with a path length of 100 mm at 589 nm. Anhydrous THF, CHCl\(_3\), toluene, hexane and ether were dried with Glass Contour solvent purification system. Other simple chemicals were analytical-grade and obtained commercially. Enantiomeric ratios were determined by an Agilent 1220 Infinity LC with DAICEL CHIRALPAK (AD-H, OJ-H, IC-H, IF, IE, AY-H, AS-H). ESI mass spectra were measured on a Bruker Daltonics micro TOF.

2. Preparation of catalyst 4b-d

\[
\begin{align*}
\text{Ar} &= 3,5-(\text{NO}_2)_2\text{-4-MeC}_6\text{H}_2 \\
\text{Me}_2\text{NCl} &\quad \text{NMP, K}_2\text{CO}_3 \\
\text{Me}_2\text{NCl} &\quad 260-270^\circ\text{C} \\
\text{K}_2\text{CO}_3 &\quad \text{CH}_3\text{CN, 60 }^\circ\text{C} \\
\text{Ar} &= 3,5-(\text{NO}_2)_2\text{-4-MeC}_6\text{H}_2
\end{align*}
\]

To a solution of 14a (3.300 g, 5 mmol, 1.0 eq.) in NMP (10 mL) was added K\(_2\)CO\(_3\) (1.380 g, 10.0 mmol, 2.0 eq.) and \(N, N\)-dimethylcarbamothioic chloride (740 mg, 6.0 mmol, 1.2 eq.). The reaction mixture was refluxed at 60 °C till the consumption of the starting material (24 h). The reaction mixture

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was cooled down to room temperature and added 1 N HCl (10 mL) and extracted with DCM (10 mL). The organic layer was combined, dried with Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was heated to 270 °C for 1 h under sand bath and cooled to room temperature. The residue was purified by column chromatography silica gel (hexane/EtOAc = 7:1) to give the product 13a (1.512 g, 40% for two steps) as a yellow solids.

(S)-2'-methoxy-3,3'-bis(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-yl dimethylcarbamothioate (13a)

Yellow solids; 1.512g, 40% yield; $[\alpha]^{26}_{D}$ 34.37 ($c$ 1.20, CHCl$_3$), IR (peaks listed in decreasing cm$^{-1}$) 1664.2658, 1530.3888, 1488.5152, 1344.8855 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.41 (s, 2H), 8.27 (s, 2H), 8.04 (s, 2H), 7.98 (d, $J$ = 8.4 Hz, 1H), 7.93 (d, $J$ = 8.0 Hz, 1H), 7.56-7.60 (m, 1H), 7.44-7.47 (m, 1H), 7.37-7.41 (m, 1H), 7.14 (d, $J$ = 8.4 Hz, 1H), 3.11 (s, 3H), 2.62 (s, 3H), 2.61 (s, 3H), 2.53 (s, 6H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 164.8, 152.7, 151.8, 150.8, 141.9, 141.9, 141.7, 139.9, 138.8, 134.0, 133.6, 133.3, 131.0, 130.5, 130.4, 129.8, 129.1, 128.9, 128.6, 128.2, 128.1, 128.0, 127.9, 127.8, 127.1, 127.0, 126.4, 126.2, 125.7, 125.1, 61.0, 37.1, 14.8, 14.7 ppm. HRMS (ESI), m/z calcd. for C$_{38}$H$_{28}$N$_2$O$_{10}$S$^-$, [M-H]$^-$, 746.1562; found: 746.1546.

(S)-2'-methoxy-3,3'-bis(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-sulfonyl chloride (12a)

(S)-2'-methoxy-3,3'-bis(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-yl-dimethylcarbamothioate 13a (960mg, 1.29 eq.) was dissolved in 2 HCl (aq.)/MeCN (1:5, 100 mL). After cooling to 0 °C, N-chlorosuccinimide (843 g, 6.9 mmol) was added in small portions for 5 mins and the mixture became slightly green-yellow. The mixture was warmed to 10-20 °C and kept at this temperature for 30 min. During this the suspension became a solution and later a colorless solid separated. The mixture was extracted with Et$_2$O (2 x15 mL), and the organic phase was washed with brine (5 mL).
After evaporating the solvent the residue was purified by column chromatography silica gel (hexane/EtOAc = 8:1) to afford products 12a in (845 mg, 89% yield).

Yellow solids; 845 mg, 89% yield; [α]25D -18.87 (c 1.06, CHCl3). IR (peaks listed in decreasing cm⁻¹) 1529.3842, 1487.7164, 1340.9406, 1219.1553, 1177.8893, 1157.1090 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δH 8.42 (s, 2H), 8.30 (s, 2H), 8.11 (s, 1H), 8.00-8.05 (m, 3H), 7.81 (t, J = 7.6 Hz, 1H), 7.51-7.55 (m, 2H), 7.39-7.44 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H), 3.14 (s, 3H), 2.70 (s, 3H), 2.64 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δC 152.6, 151.9, 150.8, 140.0, 139.7, 138.4, 134.5, 134.1, 133.6, 132.8, 132.5, 132.2, 131.5, 130.5, 129.7, 129.5, 129.2, 128.8, 128.6, 128.5, 128.3, 127.6, 127.2, 126.4, 126.0, 125.9, 125.3, 61.1, 15.1, 14.8 ppm. HRMS (ESI): m/z calcd. for C₃₅H₂₂N₄O₁₁SCl⁻ [M-H]⁻ 741.0700; found: 741.0690.

(S)-2'-methoxy-3,3'-bis(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-sulfonamide (11a)

To a solution of sulfonyl chloride 12a (586 mg, 0.79 mmol, 1.0 eq.) dissolved in dry 1,4-dioxane (10 mL) under an argon atmosphere was added a solution of 0.7 N NH₃ in 1,4-dioxane (3 mL). The solution was stirred for 12 h at room temperature. After evaporating the solvent, the residue was purified by column chromatography on silica gel to give the coupling product as a yellow solids (513 mg, 90%).

Yellow solids; 513 mg, 90% yield; [α]26D -8.93 (c 1.12, CHCl₃). IR (peaks listed in decreasing cm⁻¹) 1526.5523, 1458.7459, 1337.6596, 1279.0742, 1219.0900, 1173.2460, 1155.9021 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δH 8.30 (d, J = 1.6 Hz, 2H), 8.13 (s, 2H), 7.98 (s, 1H), 7.89 (d, J = 8.0 Hz, 2H), 7.87 (s, 1H), 7.61 (t, J = 7.2 Hz, 1H), 7.34-7.43 (m, 2 H), 7.28 (t, J = 7.6 Hz, 1 H), 7.18 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 4.65 (brs, 2H), 3.03 (s, 3H), 2.55 (s, 3H), 2.50 (s, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δC 151.7, 150.7, 141.4, 138.3, 137.6, 135.6, 134.0, 133.6, 133.1, 133.0, 131.6, 130.4, 129.8, 129.8, 128.9, 128.7, 128.5, 128.3, 127.8, 126.5, 126.3, 125.9, 125.4,
(S)-2\(^\prime\)-methoxy-N-((S)-2\(^\prime\)-methoxy-3,3\(^\prime\)-bis(4-methyl-3,5-dinitrophenyl)-1,1\(^\prime\)-binaphthyl-2-ylsulfonyl)-3,3\(^\prime\)-bis(4-methyl-3,5-dinitrophenyl)-1,1\(^\prime\)-binaphthyl-2-sulfonamide (4c)

To a solution of sulfonyl chloride 12a (320 mg, 0.43 mmol, 1.0 eq.) and sulfonyl amide 11a (310 mg, 0.43 mmol, 1.0 eq.) dissolved in dry CH\(_3\)CN (10 mL) under an argon atmosphere was added K\(_2\)CO\(_3\) (560 mg, 4.1 mmol, 9.5 eq.). The solution was stirred for 12 h at 60 °C. After evaporating the solvent, the residue was purified by column chromatography on silica gel to give the coupling product as yellow solids. The product was dissolved in Et\(_2\)O (10 mL) and added 6 N HCl (1 mL), extracted with Et\(_2\)O (2 x10 mL). The organic layer was combined and concentrated under reduced pressure and removed the trace amount of water by azeotropic distillation with toluene to afford catalyst 4c (547 mg, 89%). Yellow solids; 547 mg, 89% yield; [\(\alpha\)]\(^{25}\) \(\text{D}\) 49.30 (c 1.42, CHCl\(_3\)). Yellow solids; IR (peaks listed in decreasing cm\(^{-1}\)) 1530.7942, 1459.1710, 1385.2663, 1341.4619, 1216.3209 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\)H 8.25 (s, 4H), 7.97-8.01 (m, 4H), 7.88-7.93 (m, 4H), 7.82 (s, 2H), 7.76 (d, \(J = 8.4\) Hz, 2H), 7.63 (t, \(J = 8.0\) Hz, 2H), 7.33-7.38 (m, 4H), 7.20 (t, \(J = 8.0\) Hz, 2H), 7.07 (d, \(J = 8.4\) Hz, 2H), 6.89 (d, \(J = 8.8\) Hz, 2H), 2.81 (s, 6H), 2.66 (s, 6H), 2.60 (s, 6H) ppm; \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\)C 153.4, 151.8, 141.0, 137.4, 137.3, 136.1, 133.9, 133.1, 132.7, 132.7, 132.0, 130.2, 129.9, 129.3, 128.9, 128.8, 128.6, 128.1, 127.7, 127.6, 126.7, 126.7, 126.0, 125.9, 125.0, 60.8, 14.9, 14.8 ppm. HRMS (ESI): \(m/z\) calcd. for C\(_{70}\)H\(_{46}\)N\(_3\)O\(_{22}\)S\(_2\)^-, [M-H]^−, 1428.2199; found: 1428.2218.

(S)-2\(^\prime\)-hydroxy-N-((S)-2\(^\prime\)-hydroxy-3,3\(^\prime\)-bis(4-methyl-3,5-dinitrophenyl)-1,1\(^\prime\)-binaphthyl-2-ylsulfonyl)-3,3\(^\prime\)-bis(4-methyl-3,5-dinitrophenyl)-1,1\(^\prime\)-binaphthyl-2-sulfonamide (4b)

To a solution of catalyst 4c (185 mg, 0.13 mmol, 1.0 eq.) dissolved in dry CH\(_2\)Cl\(_2\) (50 mL) under an argon atmosphere was added a solution of 1 N BBr\(_3\) in CH\(_2\)Cl\(_2\) (2.0 mL, 2.0 mmol, 15.0 eq.) at -78 °C. The solution was stirred over night at room temperature. The reaction was quenched by ice water...
(10 mL) and extracted with Et₂O (3 x10mL). After evaporating the solvent, the residue was purified by column chromatography on silica gel to give the coupling product as yellow solids. The product was dissolved in Et₂O (10 mL) and added 6 N HCl (1 mL), extracted with Et₂O (2 x10 mL). The organic layer was combined and concentrated under reduced pressure and removed the trace amount of water by azeotropic distillation with toluene to afford catalyst 4b (168 mg, 93%).

Yellow solids; 168 mg, 93% yield; [α]_{D}^{26} -41.38 (c 1.16, CHCl₃); IR (peaks listed in decreasing cm⁻¹) 1528.3725, 1486.9798, 1342.5323, 1270.0368, 1145.7784 cm⁻¹;¹H NMR (400 MHz, DMSO-d₆) δH 8.43 (s, 4H), 8.01-8.03 (m, 4H), 7.79 (d, J = 8.4 Hz, 2H), 7.69 (s, 2H), 7.59 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 8.0 Hz, 2H), 7.04 (t, J = 7.6 Hz, 2H), 6.82 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 6.42-6.43 (m, 2H), 2.50 (s, 6H), 2.37 (s, 6H), ppm;¹³C NMR (100 MHz, DMSO-d₆) δC 151.2, 149.6, 149.2, 143.2, 142.6, 139.4, 134.5, 133.9, 133.4, 132.9, 132.2, 130.3, 129.5, 128.8, 128.7, 128.4, 128.2, 128.1, 127.0, 126.8, 126.4, 125.2, 124.5, 124.1, 123.4, 121.5, 14.8 ppm; HRMS (ESI): m/z calcd. for C_{68}H_{42}N_{9}O_{22}S-, [M-H]⁻, 1400.1886; found: 1400.1912.

(S)-2'-(benzyloxy)-N-((S)-2'-(benzyloxy)-3,3'-(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-ylsulfonyl)-3,3'-bis(4-methyl-3,5-dinitrophenyl)-1,1'-binaphthyl-2-sulfonamide (4d)

To a solution of sulfonyl chloride 12b (128 mg, 0.16 mmol, 1.0 eq.) and sulfonyl amide 11b (124 mg, 0.16 mmol, 1.0 eq.) dissolved in dry CH₃CN (10 mL) under an argon atmosphere was added K₂CO₃ (100 mg, 0.72 mmol, 4.5 eq.). The solution was stirred for 12 h at 60 °C. After evaporating the
solvent, the residue was purified by column chromatography on silica gel to give the coupling product as yellow solids. The product was dissolved in Et₂O (10 mL) and added 6 N HCl (1 mL), extracted with Et₂O (2 x 10 mL). The organic layer was combined and concentrated under reduced pressure and removed the trace amount of water by azeotropic distillation with toluene to afford catalyst. The product was dissolved in Et₂O (10 mL) and added 6 N HCl (1 mL), extracted with Et₂O (2 x 10 mL). The organic layer was combined and concentrated under reduced pressure and removed the trace amount of water by azeotropic distillation with toluene to afford catalyst 4d (172 mg, 90%).

Yellow solids; 172 mg, 90% yield; [α]²⁵ D 258.28 (c 1.10, CHCl₃); yellow solids; IR (peaks listed in decreasing cm⁻¹) 1529.1186, 1495.9508, 1342.6505, 1272.7746, 1149.1507 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ_H 8.44 (s, 4H), 8.29 (s, 2H), 8.05 (d, J = 8.4 Hz, 2H), 7.92-7.96 (m, 4H), 7.65-7.69 (m, 4H), 7.39-7.43 (m, 2H), 7.28 (t, J = 8.0 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 6.89-7.02 (m, 10H), 6.39 (d, J = 2.8 Hz, 4H), 4.27 (brs, 2H), 3.87 (brs, 2H), 2.61 (s, 6H), 2.60 (s, 6H) ppm. ¹³C NMR (100 MHz, CDCl₃) δ_C 151.4, 150.7, 149.6, 149.5, 142.6, 140.9, 139.2, 136.9, 134.4, 133.6, 133.1, 133.0, 132.7, 132.6, 131.1, 130.5, 130.4, 130.0, 128.8, 128.6, 128.4, 128.1, 127.2, 126.5, 125.4, 125.1, 123.0, 74.1, 15.0, 14.4 ppm; HRMS (ESI): m/z calcd. for C₆₂H₅₄N₇O₂₂S₂⁺, [M-H]⁺, 1580.2825; found: 1580.2748.

3. General procedure for synthesis of silyl ketene acetal

A solution of n-butyllithium (1.6 M in hexane, 21.3 mL, 33 mmol) was added dropwise to a solution of diisopropylamine (4.97 mL, 33 mmol) in THF (50 mL) at 0 °C. After being stirred 30 min at room temperature, the reaction mixture was cooled to -78 °C, and then appropriate ester (30 mmol) was added dropwise over 5 minutes. The reaction mixture was stirred at -78 °C for 1 h, and then trimethylsilyl chloride (4.5 mL, 36 mmol) was added dropwise over 5 minutes. The reaction mixture was allowed to warm to room temperature and stirred for 6 h. The solvent was evaporated, and cold hexane (50 mL) was added. The resulting suspension was filtered through a short pad of celite. The filtrate was concentrated under reduced pressure. The silyl ketene acetal 2, 5 were purified by distillation to give a silyl ketene acetal. The spectroscopic data of 5 (E/Z = 91:9) are identical to that
reported in the literature\cite{1}.

\((E)-(1,2\text{-dimethoxyprop-1-enyloxy})\text{trimethylsilane (5)}\)[\cite{1}][CAS NO. 92818-02-5]

\[
\begin{align*}
\text{MeO} & \quad \text{OTMS} \\
\text{MeO} & \quad \text{O}
\end{align*}
\]

Colorless oil; 4.172 g, 73\% yield; bp. 58-60 °C /55 mBar; Mixture of E/Z isomers (isomer ratio = 91:9). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta_H \) 3.43 (s, 3H), 3.38 (s, 3H), 1.72 (s, 3H), 0.18 (s, 9H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta_C \) 146.1, 121.4, 56.7, 56.2, 12.5, 0.1 ppm.

4. General procedure for the enantioselective Mannich-type reaction

To a solution of aldimine \(2a\) (19.7 mg, 0.1 mmol) and catalyst \(4c\) (7.2 mg, 0.005 mmol, 5 mol \%) in dry toluene (1 mL) at -78 °C was added dropwise a solution of a ketene silyl acetal \(2\) (51 \(\mu\)L, 0.3 mmol) for 3 min under N\(_2\) gas. After being stirred at the temperature for 24 h, the reaction mixture was quenched by addition of sat. NaHCO\(_3\) (0.2 mL) at -78 °C. The mixture was extracted with DCM (2 x 5 mL). The combined organic layers were successively washed with brine, dried over anhydrous Na\(_2\)SO\(_4\), and concentrated to afford crude product. The crude product was purified by flash column chromatography (SiO\(_2\), hexane: ethyl acetate = 20:1 to give a \(\beta\)-amino ester \(3a\) (29.3 mg, 0.155 mmol) in 98\% yield. The enantiomeric excess was determined by Daicel Chiralpak column.

\((R)\)-methyl 2,2-dimethyl-3-phenyl-3-(phenylamino)propanoate (3a)[\cite{2}][CAS NO.745033-32-3]

\[
\begin{align*}
\text{HN} & \quad \text{CO}_2\text{Me} \\
\text{C} & \quad \text{H}
\end{align*}
\]

(29.3 mg, 94\% yield, 96\% ee), white solid; \([\alpha]^{21}_D\) -3.7 (c 1.13, CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta_H \) 7.23-7.30 (m, 5H), 7.04-7.08 (m, 2H), 6.61 (t, \(J = 7.6 \text{ Hz, 1H}\)), 6.51 (dd, \(J = 8.8 \text{ 0.8 Hz, 1H}\)), 4.82 (brs, 1H), 4.51 (brs, 1H), 3.67 (s, 3H), 1.29 (s, 3H), 1.18 (s, 3H) ppm. \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta_C \) 177.1, 147.0, 139.3, 129.1, 128.4, 128.1, 127.5, 117.4, 113.5, 64.5, 52.2, 47.1, 24.6, 20.8 ppm; HPLC: Daicel Chiralpak AS-H, Hexane/i-ProOH = 99:1, Flow rate 0.5 mL/min, \(\lambda = 250 \text{ nm, } t_R = 14.220 \text{ min (minor isomer), } t_R = 16.767 \text{ min (major isomer)}. \) The absolute configuration of \(3a\) was determined by comparison of the retention times of both enantiomers with literature data\cite{3} (Ref: A. Hasegawa, Y. Naganawa, M. Fushimi, K. Ishihara, H. Yamamoto, Org. Lett.
2006, 8, 3175-3178; see HPLC data) and those of others 3a-3k were proposed to be R by analogy.

(R)-methyl 3-(4-bromophenyl)-2,2-dimethyl-3-(phenylamino)propanoate (3b) [CAS NO. 328047-11-6]

(32.8 mg, 91% yield, 97% ee), white solid; [α]$_D^{25}$ = 37.6 (c 1.01, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ$_H$ 7.41 (d, $J = 8.4$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 7.04-7.08 (m, 2H), 6.62 (t, $J = 7.6$ Hz, 1H), 6.47 (d, $J = 7.6$ Hz, 2H), 4.79 (brs, 1H), 4.44 (brs, 1H), 3.66 (s, 3H), 1.28 (s, 3H), 1.16 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ$_C$ 176.8, 146.7, 138.6, 131.3, 130.1, 129.2, 121.5, 117.7, 113.5, 64.1, 52.3, 46.9, 24.6, 20.9 ppm; SFC: Daicel Chiralpak IF-H, CO$_2$/i-PrOH = 95:5, Flow rate 3.0 mL/min, λ = 250 nm, t$_R$ = 5.438 min (major isomer), t$_R$ = 5.865 min (minor isomer).

(R)-methyl 3-(4-chlorophenyl)-2,2-dimethyl-3-(phenylamino)propanoate [2] (3c) [CAS NO. 745033-32-3]

(29.1 mg, 92% yield, 95% ee), white solid; [α]$_D^{25}$ = -15.63 (c 1.28, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ$_H$ 7.22-7.28 (m, 4H), 7.06 (t, $J = 8.4$ Hz, 2H), 6.63 (t, $J = 7.6$ Hz, 1H), 6.47 (d, $J = 8.8$ Hz, 2H), 4.80 (d, $J = 6.0$ Hz, 2H), 4.46 (d, $J = 6.0$ Hz, 2H), 3.67 (s, 3H), 1.29 (s, 3H), 1.17 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δ$_C$ 176.9, 146.7, 138.0, 133.3, 129.7, 129.2, 128.4, 117.6, 113.5, 64.0, 52.3, 47.0, 24.6, 20.9 ppm; SFC: Daicel Chiralpak IE-H, CO$_2$/i-PrOH = 95:5, Flow rate 2.0 mL/min, λ = 250 nm, t$_R$ = 5.563 min (major isomer), t$_R$ = 6.647 min (minor isomer).

(R)-methyl 2,2-dimethyl-3-(phenylamino)-3-(4-(trifluoromethyl)phenyl)propanoate (3d) [CAS NO. 835651-88-2]

(33.5 mg, 96% yield, 98% ee), white solid; [α]$_D^{25}$ = -9.9 (c 1.01, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ$_H$ 7.57 (d, $J = 8.0$ Hz, 2H),
7.44 (d, J = 8.0 Hz, 2H), 7.06-7.10 (m, 2H), 6.63-6.67 (m, 1H), 6.49 (d, J = 7.6 Hz, 2H), 4.88 (d, J = 6.0 Hz, 1H), 4.56 (d, J = 6.0 Hz, 1H), 3.68 (s, 3H), 1.32 (s, 3H), 1.19 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δC 176.7, 146.6, 143.8, 129.8 (q, $J_{C-F}$ = 32.4 Hz), 129.2, 128.7, 125.2 (q, $J_{C-F}$ = 2.9 Hz), 124.2 ($J_{C-F}$ = 229.2 Hz), 117.8, 113.4, 64.3, 52.3, 47.0, 24.6, 21.0 ppm; SFC: Daicel Chiralpak IE-H, CO$_2$/i-PrOH = 98:2, Flow rate 3.0 mL/min, λ = 250 nm, $t_R$ = 2.778 min (major isomer), $t_R$ = 3.348 min (minor isomer).

(R)-methyl 3-(4-methoxyphenyl)-2,2-dimethyl-3-(phenylamino)propanoate (3e) $^{[5]}$ [CAS NO. 745033-30-1]

(R)-methyl 3-(3-bromo-4-methoxyphenyl)-2,2-dimethyl-3-(phenylamino)propanoate (3f) (28.6 mg, 92% yield, 91% ee), white solid; [α]$^{28}_{D}$ = 0.6 (c 1.01, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δH 7.18 (d, J = 8.8 Hz, 2H), 7.03 (t, J = 8.0 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.59 (t, J = 7.2 Hz, 1H), 6.48 (d, J = 8.0 Hz, 2H), 4.77 (brs, 1H), 4.44 (brs, 1H), 3.76 (s, 3H), 3.64 (s, 3H), 1.25 (s, 3H), 1.15 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δC 177.2, 158.9, 147.0, 131.2, 129.3, 129.0, 117.3, 113.5, 113.5, 63.9, 55.2, 52.1, 47.2, 24.6, 20.8 ppm; HPLC: Daicel Chiralpak AY-H, Hexane/i-PrOH = 98.9:0.9, Flow rate 0.5 mL/min, λ = 220 nm, $t_R = 19.647$ min (major isomer), $t_R = 24.667$ min (minor isomer).

(R)-methyl 3-(3-bromo-4-methoxyphenyl)-2,2-dimethyl-3-(phenylamino)propanoate (3f) (36.7 mg, 94% yield, 96% ee), white solid; [α]$^{26}_{D}$ = 15.8 (c 1.14, CHCl$_3$); yellow solids; m.p. 155-157 °C; IR (peaks listed in decreasing cm$^{-1}$) 2947.8054, 1724.6353, 1601.3880, 1495.8846, 1285.6884, 1253.7928 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δH 7.46 (d, J = 2.0 Hz, 1H), 7.19 (dd, J = 8.8 2.0 Hz, 1H), 7.07 (t, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.49 (d, J = 8.0 Hz, 2H), 4.76 (brs, 1H), 4.40 (brs, 1H), 3.86 (s, 3H), 3.67 (s, 3H), 1.28 (s, 3H), 1.17 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) δC 176.9, 155.2, 146.8, 133.1, 133.0, 129.2, 128.3, 117.6, 113.5, 111.5, 111.4, 63.6,
56.3, 52.2, 47.2, 24.5, 21.0 ppm; HRMS (ESI): m/z calcd. for C_{19}H_{22}BrNaO_{3}, [M+H]^+: 414.0675; found: 414.0656; HPLC: Daicel Chiralpak AY-H, Hexane/i-PrOH = 97:3, Flow rate 0.5 mL/min, λ = 250 nm, t_R = 17.967 min (major isomer), t_R = 25.513 min (minor isomer).

(R)-methyl 2,2-dimethyl-3-(phenylamino)-3-p-tolylpropanoate (3g) [CAS NO. 801219-11-4]

(27.8 mg, 93% yield, 94% ee), white solid, [α]_{D}^{20} -6.00 (c 1.00, CHCl_{3}); ^1H NMR (400 MHz, CDCl_{3}) δ: 7.16 (d, J = 8.4 Hz, 2H), 7.03-7.09 (m, 4H), 6.60 (t, J = 7.2 Hz, 1H), 6.50 (d, J = 7.6 Hz, 2H), 4.78 (brs, 1H), 4.47 (brs, 1H), 3.66 (s, 3H), 2.30 (s, 3H), 1.27 (s, 3H), 1.17 (s, 3H) ppm. ^13C NMR (100 MHz, CDCl_{3}) δ: 177.2, 147.1, 137.1, 136.2, 129.1, 128.8, 128.2, 117.3, 113.5, 64.2, 52.2, 47.1, 24.6, 21.2, 20.8 ppm; HPLC: Daicel Chiralpak IC-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ = 250 nm, t_R = 14.447 min (major isomer), t_R = 25.980 min (minor isomer).

(R)-methyl 2,2-dimethyl-3-(naphthalen-1-yl)-3-(phenylamino)propanoate (3h) [CAS NO. 835651-91-7]

(32.7 mg, 98% yield, 94% ee), [α]_{D}^{24} +169.86 (c 1.46, CHCl_{3}); ^1H NMR (400 MHz, CDCl_{3}) δ: 8.42 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.51-7.55 (m, 2H), 7.41 (t, J = 8.0 Hz, 1H), 6.96-7.00 (m, 2H), 6.57 (t, J = 7.6 Hz, 1H), 6.47 (d, J = 8.0 Hz, 2H), 5.55 (brs, 1H), 5.07 (brs, 1H), 3.69 (s, 3H), 1.28 (s, 3H), 1.22 (s, 3H) ppm. ^13C NMR (100 MHz, CDCl_{3}) δ: 177.3, 147.0, 135.8, 133.7, 129.3, 129.1, 128.2, 126.1, 125.4, 125.3, 125.3, 123.2, 117.4, 113.5, 57.9, 52.3, 48.3, 25.4, 20.7 ppm; HPLC: Daicel Chiralpak AS-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ = 250 nm, t_R = 18.567 min (minor isomer), t_R = 27.173 min (major isomer).

Methyl 2,2-dimethyl-3-(phenylamino)-3-(thiophen-3-yl)propanoate (3i)

s11
(26.5 mg, 91% yield, 89% ee) [α]$_{28}^{D}$ = -30.77 (c 1.43, CHCl$_3$); yellow solids; IR (peaks listed in decreasing cm$^{-1}$) 1724.5819, 1601.1443, 1504.8501, 1317.0274, 1253.0234, 1134.5633 cm$^{-1}$; (91% yield, 88% ee), white solid; [α]$_{28}^{D}$ = -30.77 (c = 1.43, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.14 (d, $J$ = 6.4 Hz, 1H), 7.09 (t, $J$ = 7.6 Hz, 2H), 6.90-6.93 (m, 2H), 6.66 (t, $J$ = 7.2 Hz, 1H), 6.61 (d, $J$ = 7.6 Hz, 2H), 4.82 (brs, 1H), 4.64 (brs, 1H), 3.67 (s, 3H), 1.33 (s, 3H), 1.27 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 176.9, 146.9, 144.3, 129.2, 126.5, 124.5, 118.0, 113.7, 60.8, 52.2, 47.5, 24.0, 21.5 ppm; HRMS (ESI): m/z calcd. for C$_{16}$H$_{19}$NNaO$_2$S$^+$, [M+H]$^+$, 312.1029; found: 312.1014.

Methyl 2,2-dimethyl-3-(phenylamino)-3-(thiophen-2-yl)propanoate (3j$^{[8]}$) [CAS NO. 79388-24-2]

(28.4 mg, 98% yield, 91% ee), white solid; [α]$_{28}^{D}$ = -17.93 (c 1.45, CHCl$_3$);

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.21-7.23 (m, 2H), 7.06-7.11 (m, 3H), 6.69 (t, $J$ = 7.2 Hz, 1H), 6.63 (d, $J$ = 7.6 Hz, 1H), 6.53 (dd, $J$ = 8.8 1.2 Hz, 2H), 4.65 (brs, 1H), 3.66 (s, 3H), 1.29 (s, 3H), 1.21 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 177.2, 147.2, 141.1, 129.1, 127.4, 125.3, 122.8, 117.6, 113.5, 60.6, 52.2, 47.2, 24.2, 21.3 ppm; HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 95:5, Flow rate 0.5 mL/min, $\lambda$ = 250 nm, $t_R = 31.060$ min (minor isomer), $t_R = 45.413$ min (major isomer).

Methyl 3-(furan-2-yl)-2,2-dimethyl-3-(phenylamino)propanoate (3k$^{[5]}$) [CAS NO. 79388-23-1]

(25.3 mg, 93% yield, 70% ee), white solid; [α]$_{28}^{D}$ = -73.08 (c 1.04, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$H 7.30-7.31 (m, 1H), 7.10-7.14 (m, 2H), 6.69 (t, $J$ = 7.2 Hz, 1H), 6.63 (d, $J$ = 7.6 Hz, 2H), 6.25-6.27 (m, 1H), 6.15 (d, $J$ = 3.2 Hz, 1H), 4.71 (brs, 1H), 3.68 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 176.9, 153.5, 147.2, 141.8, 129.2, 118.2, 113.9, 110.2, 108.0, 58.6, 52.2, 47.3, 23.6, 21.3 ppm; HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, $\lambda$ = 250 nm, $t_R = 22.027$ min (minor isomer), $t_R = 24.280$ min (major isomer).
Methyl 2-methoxy-2-methyl-3-phenyl-3-(phenylamino)propanoate (6a)

(27.5 mg, 92% yield, 93% ee), yellow solids; $[\alpha]_{D}^{26} = -76.47$ (c 1.02, CHCl$_3$); yellow solids; IR (peaks listed in decreasing cm$^{-1}$) 3408.8905, 1744.2246, 1602.8180, 1504.2767, 1457.1664, 1103.4164, 1056.6279 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\text{syn/anti} = 97.3$; $\delta_H$ 7.36-7.37 (m, 2H), 7.22-7.30 (m, 3H), 7.01-7.05 (m, 2H), 6.58 (t, $J = 7.6$ Hz, 1H), 6.51 (d, $J = 7.6$ Hz, 2H), 5.01 (d, $J = 8.0$ Hz, 1H, syn), 4.82 (d, $J = 6.4$ Hz, 1H, anti), 4.64 (d, $J = 8.4$ Hz, 1H, syn), 4.59 (d, $J = 7.2$ Hz, 1H, anti), 3.72 (s, 3H, syn), 3.57 (s, 3H, anti), 3.36 (s, 3H, syn), 1.54 (s, 3H, anti), 1.26 (s, 3H, syn) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta_C$ 174.1, 146.8, 138.3, 129.2, 129.0, 128.0, 127.6, 117.4, 113.8, 82.2, 64.2, 52.5, 52.4, 18.8 ppm. HRMS (ESI): m/z calcd. for C$_{18}$H$_{23}$NNaO$_3^+$, [M+Na]$^+$, 322.1414; found: 322.1401; HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, $\lambda = 250$ nm, $t_R = 19.200$ min (major isomer), $t_R = 56.013$ min (minor isomer).

Methyl 3-(4-fluorophenyl)-2-methoxy-2-methyl-3-(phenylamino)propanoate (6b)

(30.2 mg, 96% yield, 93% ee), yellow solids; $[\alpha]_{D}^{27} = -53.57$ (c 1.12, CHCl$_3$); yellow solids; IR (peaks listed in decreasing cm$^{-1}$) 1744.1669, 1602.8505, 1505.9665, 1250.6484, 1223.0144 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\text{syn/anti} = 96.4$; $\delta_H$ 7.32-7.35 (m, 2H), 7.02-7.07 (m, 2H), 6.95-6.99 (m, 2H), 6.60 (t, $J = 7.6$ Hz, 1H), 6.48-6.50 (m, 2H), 4.97 (d, $J = 8.0$ Hz, 1H, syn), 4.76 (d, $J = 6.4$ Hz, 1H, anti), 4.63 (d, $J = 8.4$ Hz, 1H, syn), 4.58 (d, $J = 7.6$ Hz, 1H, anti), 3.72 (s, 3H), 3.57 (s, 3H, anti), 3.37 (s, 3H, syn), 1.55 (s, 3H, anti), 1.25 (s, 3H, syn) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta_C$ 173.9, 162.4 (d, $J_{CF} = 245.1$ Hz), 146.5, 134.0, 130.7 (d, $J_{CF} = 8.6$ Hz), 129.0, 117.6, 114.9 (d, $J_{CF} = 21.9$ Hz), 113.8, 82.0, 63.5, 52.5, 52.4, 18.8 ppm; HRMS (ESI): m/z calcd. for C$_{16}$H$_{20}$FNNaO$_3^+$, [M+Na]$^+$, 340.1319; found: 340.1309; HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, $\lambda = 250$ nm, $t_R = 16.113$ min (major isomer), $t_R = 29.740$ min (minor isomer).
Methyl 3-(4-chlorophenyl)-2-methoxy-2-methyl-3-(phenylamino)propanoate (6c)

(29.6 mg, 89% yield, 91% ee), yellow oil; \([\alpha]^{25}_D = -93.07 (c 1.01, \text{CHCl}_3)\); yellow solids; IR (peaks listed in decreasing cm\(^{-1}\)) 2949.8072, 1744.5923, 1602.9032, 1504.6259, 1490.4390, 1250.2075 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) syn\(/\text{anti} = 95:5\), \(\delta_H\) 7.24-7.32 (m, 4H), 7.01-7.07 (m, 2H), 6.59-6.63 (m, 1H), 6.48-6.52 (m, 2H), 4.98 (d, \(J = 8.0\) Hz, 1H, syn), 4.75 (d, \(J = 8.8\) Hz, 1H, anti), 4.62 (d, \(J = 8.4\) Hz, 1H, syn), 4.58 (d, \(J = 6.8\) Hz, 1H, anti), 3.72 (s, 3H, syn), 3.59 (s, 3H, anti), 3.37 (s, 3H), 1.55 (s, 3H, anti), 1.26 (s, 3H, syn). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta_C\) 173.8, 146.4, 136.9, 133.4, 130.5, 129.1, 128.2, 117.7, 113.8, 81.9, 63.6, 52.6, 52.5, 18.8 ppm; HRMS (ESI): \(m/z\) calcd. for C\(_{18}\)H\(_{20}\)ClNaO\(_3\)^+, [M+Na]^+, 356.1024; found: 356.1019. HPLC: Daicel Chiralpak AD-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, \(\lambda = 250\) nm, \(t_R = 21.627\) min (major isomer), \(t_R = 25.593\) min (minor isomer).

Methyl 2-methoxy-3-(4-methoxyphenyl)-2-methyl-3-(phenylamino)propanoate (6d)

(29.5 mg, 90% yield, 86% ee), yellow oil; \([\alpha]^{28}_D = -47.24 (c 1.24, \text{CHCl}_3)\); yellow solids; IR (peaks listed in decreasing cm\(^{-1}\)) 2950.3685, 1741.8658, 1602.1037, 1504.2433, 1242.6937, 1108.5156 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) syn\(/\text{anti} = 92:8\), \(\delta_H\) 7.27 (d, \(J = 8.8\) Hz, 2H), 7.01-7.05 (m, 2H), 6.81 (d, \(J = 8.8\) Hz, 2H), 6.58 (t, \(J = 8.8\) Hz, 1H), 6.51 (d, \(J = 7.6\) Hz, 2H), 4.96 (brs, 1H), 4.60 (brs, 1H, syn), 4.55 (brs, 1H, anti), 3.77 (s, 3H, syn), 3.75 (s, 3H, anti), 3.71 (s, 3H, syn), 3.58 (s, 3H, anti), 3.36 (s, 3H), 1.53 (s, 3H, anti), 1.25 (s, 3H, syn). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta_C\) 174.2, 159.0, 146.8, 130.2, 129.0, 117.4, 113.9, 113.4, 82.3, 63.6, 55.2, 52.5, 52.4, 18.7 ppm; HRMS (ESI): \(m/z\) calcd. for C\(_{19}\)H\(_{23}\)NaO\(_4\)^+, [M+Na]^+, 352.1519; found: 352.1527. HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, \(\lambda = 250\) nm, \(t_R = 23.667\) min (major isomer), \(t_R = 35.227\) min (minor isomer).
Methyl 3-(3-bromo-4-methoxyphenyl)-2-methoxy-2-methyl-3-(phenylamino)propanoate (6e)

(38.1 mg, 97% yield, 93% ee), yellow solids; [α]$_{D}^{25}$ -47.24 (c 1.27, CHCl$_3$); yellow solids; IR (peaks listed in decreasing cm$^{-1}$) 2947.90, 1743.36, 1601.98, 1497.11, 1253.66, 1053.80 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) syn/anti = 95:5 (major) $\delta$H 7.54 (d, $J$ = 2.4 Hz, 1H), 7.24-7.26 (m, 1H), 7.01-7.05 (m, 2H), 6.78-6.80 (m, 1H), 6.57-6.61 (m, 1H), 6.48 (d, $J$ = 7.6 Hz, 2H), 4.93 (brs, 1H), 4.55 (brs, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.35 (s, 3H), 1.24 (s, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 173.8, 155.3, 146.5, 144.5, 133.8, 132.0, 129.2, 129.1, 117.6, 113.8, 111.4, 111.3, 82.1 63.2, 56.2, 52.6, 52.4, 18.8 ppm; HRMS (ESI): m/z calcd. for C$_{19}$H$_{22}$BrNNaO$_4$+$^+$, [M+Na]$^+$, 430.0624; found: 430.0622. HPLC: Daicel Chiralpak AY-H, Hexane/i-PrOH = 95:5, Flow rate 0.5 mL/min, $\lambda$ = 250 nm, $t_R$ = 16.807 min (major isomer), $t_R$ = 25.227 min (minor isomer).

Methyl 2-methoxy-2-methyl-3-(naphthalen-1-yl)-3-(phenylamino)propanoate (6f)

(31.7 mg, 91% yield, 95% ee), yellow solids; [α]$_{D}^{25}$ 140.43 (c 1.41, CHCl$_3$); yellow solids; IR (peaks listed in decreasing cm$^{-1}$) 2949.7226, 1744.5961, 1601.7540, 1504.0286, 1247.8739, 1183.0820, 1107.7731 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) syn/anti = 96:4, $\delta$H 8.39 (d, $J$ = 8.4 Hz, 1H), 7.89 (d, $J$ = 8.0 Hz, 1H), 7.76 (d, $J$ = 8.0 Hz, 1H), 7.68 (d, $J$ = 8.0 Hz, 1H), 7.63 (t, $J$ = 8.0 Hz, 1H), 7.51 (t, $J$ = 8.0 Hz, 1H), 7.43 (t, $J$ = 8.0 Hz, 1H), 6.95 (t, $J$ = 8.0 Hz, 2H), 6.53 (t, $J$ = 7.6 Hz, 1H), 6.47 (d, $J$ = 8.4 Hz, 2H), 5.70 (brs, 1H, syn), 5.55 (brs, 1H, anti), 5.30 (brs, 1H, syn), 5.09 (brs, 1H, anti), 3.77 (s, 3H, syn), 3.38 (s, 3H, syn), 3.33 (s, 3H, anti), 1.60 (s, 3H, anti), 1.20 (s, 3H, syn) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$C 174.4, 146.7, 134.5, 133.5, 133.1, 129.3, 129.0, 128.1, 126.9, 126.3, 125.6, 125.2, 122.8, 117.3, 113.5, 82.5, 57.6, 52.5, 52.5, 18.5 ppm; HRMS (ESI), HRMS (ESI): m/z calcd. for [C$_{22}$H$_{23}$NNaO$_3$]$^+$, [M+Na]$^+$, 372.1570; found: 372.1564. HPLC: Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, $\lambda$ = 250 nm, $t_R$ = 15.787 min (major isomer), $t_R$ = 23.513 min (minor isomer).
5. Determination of Absolute Configurations

White crystals of 6e suitable for X-ray crystallographic analysis were obtained by recrystallization from EtOAc at room temperature. The structure of 6e is shown in Figure S1. CCDC 1491015 contains the supplementary crystallographic data. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Figure S1. The structure of 6e

A. Crystal Data

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<th>Empirical Formula</th>
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Formula Weight                           408.29  
Crystal Color, Habit                        colorless, prism  
Crystal Dimensions                        0.200 X 0.200 X 0.200 mm  
Crystal System                           orthorhombic  
Lattice Type                              Primitive  
Lattice Parameters                      
\[ a = 8.5367(9) \, \text{Å} \]  
\[ b = 15.034(2) \, \text{Å} \]  
\[ c = 14.726(2) \, \text{Å} \]  
\[ V = 1889.9(4) \, \text{Å}^3 \]  
Space Group                             P\(2_1\)\(2_1\)\(2_1\) (#19)  
Z value                                4  
\(D_{\text{calc}}\)                         1.435 \, \text{g/cm}^3  
F(000)                                 840.00  
m(MoKa)                                22.036 \, \text{cm}^{-1}  

B. Intensity Measurements

Diffractometer                      XtaLAB mini  
Radiation                            MoKa (\(l = 0.71075 \, \text{Å}\))  
graphite monochromated
Voltage, Current 50kV, 12mA

Temperature 20.0 °C

Detector Aperture 75 mm (diameter)

Data Images 540 exposures

w oscillation Range -60.0 - 120.0°

Exposure Rate 10.0 sec./°

Detector Swing Angle 30.00°

w oscillation Range -60.0 - 120.0°

Exposure Rate 10.0 sec./°

Detector Swing Angle 30.00°

w oscillation Range -60.0 - 120.0°

Exposure Rate 10.0 sec./°

Detector Swing Angle 30.00°

Detector Position 50.00 mm

Pixel Size 0.146 mm

2dmax 54.9°

No. of Reflections Measured Total: 20009
Unique: 4319 (Rint = 0.0595) Friedel pairs: 1855

Corrections Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution Direct Methods
Refinement

Full-matrix least-squares on F^2

Function Minimized

S w (Fo^2 - Fc^2)^2

Least Squares Weights

w = 1/ [ s^2(Fo^2) + (0.0397 - P)^2 + 0.4811 · P ]

where P = (Max(Fo^2,0) + 2Fc^2)/3

2q_{\text{max}} cutoff

54.9°

Anomalous Dispersion

All non-hydrogen atoms

No. Observations (All reflections)

4319

No. Variables

227

Reflection/Parameter Ratio

19.03

Residuals: R1 (I>2.00s(I))

0.0371

Residuals: R (All reflections)

0.0494

Residuals: wR2 (All reflections)

0.0877

Goodness of Fit Indicator

1.019

Flack Parameter

0.986(9)

Max Shift/Error in Final Cycle

0.000

Maximum peak in Final Diff. Map

0.41 e^-/Å^3

Minimum peak in Final Diff. Map

-0.48 e^-/Å^3

6. References


7. NMR Data
8. HPLC Data

**Conditions:** HPLC, Daicel Chiralpak AS-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ = 250 nm

**Racemic:**

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**DAD:** 250 nm/Band 4 nm Reference 360 nm/Band 100 nm

**Chiral:**

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**DAD:** 250 nm/Band 4 nm Reference 360 nm/Band 100 nm

**Total:**

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>100.000</td>
</tr>
</tbody>
</table>

544
**Conditions:** SFC, Daicel Chiralpak IF, CO$_2$/i-PrOH = 95:5, Flow rate 3.0 mL/min, $\lambda$ = 250 nm

Racemic:
クロマトグラム

ユーザ名 | user
時間 | 2018/05/25 13:25:37
コントロール | SFD スリーブリングシステム
測定 | 2018/05/25 10:19:08
注入量 | 5.00 [μL]
サンプル | 2
プロダクト | Sukalyn
採取時間 | 15.0 [mm]
分析シーケンス | Zhou_J95
コントロールメソッド | zhou_J95_5
ピーク検出テーブル
追加情報

データ取り込み間隔 | 100 [mm/s]
波形処理メソッド | (マニュアル)

<table>
<thead>
<tr>
<th>ピーク</th>
<th>CH</th>
<th>OR (mm)</th>
<th>製品 (μg/mm)</th>
<th>吸収 (AU)</th>
<th>ノイズ</th>
<th>NTP</th>
<th>分離</th>
<th>ピークID</th>
<th>分析時間</th>
<th>質量</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.0</td>
<td>5.43</td>
<td>470.176</td>
<td>255.95</td>
<td>0.40</td>
<td>54.47</td>
<td>N/A</td>
<td>1.068</td>
<td>1.282</td>
<td>5.01</td>
</tr>
<tr>
<td>2</td>
<td>5.0</td>
<td>5.86</td>
<td>250.48</td>
<td>251.11</td>
<td>1.52</td>
<td>1.22</td>
<td>N/A</td>
<td>1.000</td>
<td>1.202</td>
<td>5.01</td>
</tr>
</tbody>
</table>
**Conditions:** SFC, Daicel Chiralpak IE, CO$_2$/i-PrOH = 95:5, Flow rate 2.0 mL/min, $\lambda$= 250 nm

Racemic:
Chiral:
Conditions: SFC, Daicel Chiralpak IE, CO$_2$/i-PrOH = 98:2, Flow rate 3.0 mL/min, λ = 250 nm

Racemic:

IE: $\text{He/CO}_2 = 98:2$

flow rate = 3.0 mL/min
クロマトグラム

チャンネル情報+ビーグ情報

数値計算式

Chiral:
Conditions: HPLC, Daicel Chiralpak AY-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ= 220 nm

Racemic:

Chiral:
Conditions: HPLC, Daicel Chiralpak AY-H, Hexane/i-PrOH = 97:3, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

Chiral:
**Conditions:** HPLC, Daicel Chiralpak IC-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ = 250 nm

**Racemic:**

![Racemic chromatogram](image1)

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.14</td>
<td>53.073</td>
<td>26.18</td>
<td>40.927</td>
</tr>
</tbody>
</table>

**Chiral:**

![Chiral chromatogram](image2)

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.44</td>
<td>96.993</td>
<td>25.980</td>
<td>3.005</td>
</tr>
</tbody>
</table>

Total:

<table>
<thead>
<tr>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.000</td>
</tr>
</tbody>
</table>
**Conditions:** HPLC, Daicel Chiralpak AS-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ = 250 nm

**Racemic:**

![Racemic chromatogram image]

**Chiral:**

![Chiral chromatogram image]
**Conditions:** HPLC, Daicel Chiralpak AY-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ= 250 nm

**Racemic:**

![Racemic HPLC Chromatogram](image1)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.060</td>
<td></td>
<td>56.082</td>
</tr>
<tr>
<td>27.747</td>
<td></td>
<td>43.918</td>
</tr>
<tr>
<td><strong>合計</strong></td>
<td></td>
<td><strong>100.000</strong></td>
</tr>
</tbody>
</table>

**Chiral:**

![Chiral HPLC Chromatogram](image2)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.393</td>
<td></td>
<td>94.394</td>
</tr>
<tr>
<td>28.527</td>
<td></td>
<td>5.606</td>
</tr>
<tr>
<td><strong>合計</strong></td>
<td></td>
<td><strong>100.000</strong></td>
</tr>
</tbody>
</table>

Ss55
**Conditions:** HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 95:5, Flow rate 0.5 mL/min, λ= 250 nm

**Racemic:**

![Racemic chromatogram]

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Height (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30.560</td>
<td>400</td>
</tr>
<tr>
<td>44.620</td>
<td>400</td>
</tr>
</tbody>
</table>

**Chiral:**

![Chiral chromatogram]

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Height (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31.060</td>
<td>400</td>
</tr>
<tr>
<td>45.413</td>
<td>400</td>
</tr>
</tbody>
</table>

**Summary:**

<table>
<thead>
<tr>
<th></th>
<th><strong>49.701</strong></th>
<th><strong>50.299</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>100.000</td>
<td>100.000</td>
</tr>
</tbody>
</table>
Conditions: HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.840</td>
<td>50.123</td>
</tr>
<tr>
<td>25.373</td>
<td>49.877</td>
</tr>
<tr>
<td>合計</td>
<td>100.000</td>
</tr>
</tbody>
</table>

Chiral:

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.027</td>
<td>15.087</td>
</tr>
<tr>
<td>24.280</td>
<td>84.903</td>
</tr>
<tr>
<td>合計</td>
<td>100.000</td>
</tr>
</tbody>
</table>
**Conditions:** HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, λ = 250 nm

**Racemic:**

**Chiral:**

<table>
<thead>
<tr>
<th>retention time</th>
<th>area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.033</td>
<td>49.443</td>
</tr>
<tr>
<td>53.553</td>
<td>50.567</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>retention time</th>
<th>area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>19.200</td>
<td>96.740</td>
</tr>
<tr>
<td>56.013</td>
<td>3.270</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>total area</th>
<th>100.000</th>
</tr>
</thead>
</table>
Conditions: HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

![Graph of racemic compound](image)

<table>
<thead>
<tr>
<th>保留时间</th>
<th>保留面积</th>
<th>面积%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.247</td>
<td>50.427</td>
<td></td>
</tr>
<tr>
<td>29.380</td>
<td>49.573</td>
<td></td>
</tr>
<tr>
<td>合計</td>
<td></td>
<td>100.000</td>
</tr>
</tbody>
</table>

Chiral:

![Graph of chiral compound](image)

<table>
<thead>
<tr>
<th>保留时间</th>
<th>保留面积</th>
<th>面积%</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.113</td>
<td>96.345</td>
<td></td>
</tr>
<tr>
<td>29.740</td>
<td>3.655</td>
<td></td>
</tr>
<tr>
<td>合計</td>
<td></td>
<td>100.000</td>
</tr>
</tbody>
</table>
**Conditions:** HPLC, Daicel Chiralpak AD-H, Hexane/i-PrOH = 99:1, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

![Racemic Graph](image)

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.307</td>
<td>60.721</td>
</tr>
<tr>
<td>28.500</td>
<td>49.279</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.000</strong></td>
</tr>
</tbody>
</table>

Chiral:

![Chiral Graph](image)

<table>
<thead>
<tr>
<th>Retention Time</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>21.627</td>
<td>95.380</td>
</tr>
<tr>
<td>25.593</td>
<td>4.610</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.000</strong></td>
</tr>
</tbody>
</table>
Conditions: HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

Chiral:
**Conditions:** HPLC, Daicel Chiralpak AY-H, Hexane/i-PrOH = 95:5, Flow rate 0.5 mL/min, λ = 250 nm

**Racemic:**

![Racemic chromatogram](image)

<table>
<thead>
<tr>
<th>Retention Time (min)</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.953</td>
<td>7.864</td>
</tr>
<tr>
<td>15.407</td>
<td>42.07C</td>
</tr>
<tr>
<td>25.273</td>
<td>6.97C</td>
</tr>
<tr>
<td>27.987</td>
<td>42.49C</td>
</tr>
</tbody>
</table>

**Chiral:**

![Chiral chromatogram](image)

<table>
<thead>
<tr>
<th>Retention Time (min)</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.807</td>
<td>96.581</td>
</tr>
<tr>
<td>25.227</td>
<td>3.419</td>
</tr>
</tbody>
</table>

**Total Area:** 100.000
Conditions: HPLC, Daicel Chiralpak OJ-H, Hexane/i-PrOH = 90:10, Flow rate 0.5 mL/min, λ= 250 nm

Racemic:

![Racemic Chromatogram]

DAD: シグナル A, 250 nm/バンド幅4 nm リファレンス 360 nm/バンド幅100 nm 結果

<table>
<thead>
<tr>
<th>リテンションタイム</th>
<th>面積%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.947</td>
<td>50.170</td>
</tr>
<tr>
<td>23.360</td>
<td>49.830</td>
</tr>
</tbody>
</table>

合計：100.000

Chiral:

![Chiral Chromatogram]

DAD: シグナル A, 250 nm/バンド幅4 nm リファレンス 360 nm/バンド幅100 nm 結果

<table>
<thead>
<tr>
<th>リテンションタイム</th>
<th>面積%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.787</td>
<td>97.728</td>
</tr>
<tr>
<td>23.513</td>
<td>2.272</td>
</tr>
</tbody>
</table>

合計：100.000