Supplementary Information

Molecular Recognition of Ketomalonates by Asymmetric Aldol Reaction of Aldehydes with Secondary-Amine Organocatalysts

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General Information: Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. 1H NMR spectra were measured on a JEOL JNM-FX400 (400MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane (in the case of CDCl3) as an internal standard. Data were reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quintet, m = multiplet, br = broad, and app = apparent), and coupling constants (Hz). 13C NMR spectra were recorded on a JEOL JNM-FX400 (100MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments using Daicel CHIRALPAK AD-H 4.6 mm × 25 cm column. The high-resolution mass spectra (HRMS) were performed on Applied Biosystems Mariner 8295 API-TOF and Bruker microTOF. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck 1.09386.9025, 230-400 mesh). Dichloromethane, acetonitrile and toluene were purchased from Wako Pure Chemistry Co. Inc. Dichloromethane and acetonitrile were stored over 4 Å molecular sieves. Toluene was further purified by passing through neutral alumina under nitrogen atmosphere. Commercially available aldehydes were distilled and stored under argon atmosphere at −17 °C. (S)-5-(2-Pyrrolidinyl)-1H-tetrazole ((S)-2) was purchased from Aldrich. Amino sulfonamide (S)-31 was synthesized according to the literature procedure and used after purification by column chromatography. Other simple chemicals were purchased and used as such.
Synthesis of hydrated 1-(2,6-di-tert-butylphenyl) 3-ethyl 2-oxomalonate (1c)

\[ \text{HOOC} \rightarrow \text{OEt} + \text{tBu-} \text{OH} \xrightarrow{\text{POCl}_3, \text{CHCl}_3} \text{tBu-} \text{OOC} \rightarrow \text{OEt} \xrightarrow{\text{SeO}_2, \text{dioxane}} \text{tBu-} \text{OOC} \rightarrow \text{OEt} \]

To a solution of 2,6-di-tert-butylphenol (1.24 g, 6.0 mmol) and ethyl hydrogen malonate (660 µL, 5.0 mmol) in chloroform (12.5 mL) was added POCl₃ (2.3 mL, 15.0 mmol) dropwise at room temperature. After 8 h of reflux, the mixture was cooled to 0 °C. The reaction mixture was added NaHCO₃ at 0 °C and extracted with CH₂Cl₂. The organic layer was concentrated under vacuum and purified by flash column chromatography on silica gel (hexane/ethyl acetate = 20/1) to afford 2,6-di-tert-butylphenyl ethyl malonate (1.33 g, 4.2 mmol, 83% yield). To a solution of the obtained malonate in dioxane (20 mL) was added SeO₂ (702 mg, 6.2 mmol) at room temperature. After 12 h of reflux, the reaction mixture was cooled to room temperature, concentrated and filtered with ethyl acetate. The filtrate was concentrated under vacuum and purified by flash column chromatography on silica gel (hexane/ethyl acetate = 5/1) to afford hydrated oxomalonate 1c (383 mg, 1.1 mmol, 26% yield); \(^1\)H NMR (400 MHz, CDCl₃) δ 7.41 (1H, d, J = 2.4 Hz, Ar-H), 7.24 (1H, dd, J = 8.4, 2.4 Hz, Ar-H), 6.93 (1H, d, J = 8.4 Hz, Ar-H), 5.02 (2H, s, OH), 4.40 (2H, q, J = 7.2 Hz, OCH₂CH₃), 1.36 (3H, t, J = 7.2 Hz, OCH₂CH₃), 1.33 (9H, s, CCH₃), 1.32 (9H, s, CCH₃); \(^{13}\)C NMR (100 MHz, CDCl₃) δ 168.2, 167.4, 149.1, 146.8, 140.1, 124.3, 124.0, 121.7, 90.3, 63.8, 34.7, 34.6, 31.4, 29.9, 13.9; IR (neat) 3447, 2961, 2909, 2870, 1748, 1493, 1219, 1157, 1084 cm\(^{-1}\); HRMS (ESI-TOF) Calcd. for C₁₀H₁₃NaO₆: 375.1778 ([M + Na]⁺), Found: 375.1783 ([M + Na]⁺).

1-(2,6-Dimethylphenyl) 3-ethyl 2-oxomalonate in hydrated form (1a)

\(^1\)H NMR (400 MHz, CDCl₃) δ 7.11-7.05 (3H, m, Ar-H), 4.91 (2H, s, OH), 4.43 (2H, q, J = 7.2 Hz, OCH₂CH₃), 2.16 (6H, s, Ar-CH₃), 1.39 (3H, t, J = 7.2 Hz, OCH₂CH₃); \(^{13}\)C NMR (100 MHz, CDCl₃) δ 168.2, 166.6, 147.4, 129.9, 128.8, 126.7, 90.2, 64.0, 15.9, 13.9; IR (neat) 3366, 2965, 1775, 1213, 1155, 1088, 789 cm\(^{-1}\); HRMS (ESI-TOF) Calcd. for C₁₃H₁₆NaO₆: 291.0839 ([M + Na]⁺), Found: 291.0840 ([M + Na]⁺).

1-(2,6-Di-isopropylphenyl) 3-ethyl 2-oxomalonate in hydrated form (1b)

\(^1\)H NMR (400 MHz, CDCl₃) δ 7.28-7.24 (1H, m, Ar-H), 7.19 (1H, app s, Ar-H), 7.17 (1H, d, J = 1.2 Hz, Ar-H), 4.90 (2H, s, OH), 4.43 (2H, q, J = 7.2 Hz, OCH₂CH₃), 2.97 (2H, m, CH₂CH₃), 1.42 (3H, t, J = 7.2 Hz, OCH₂CH₃), 1.18 (12H, d, J = 6.8 Hz CH₂CH₃); \(^{13}\)C NMR (100 MHz, CDCl₃) δ 168.3, 167.5, 144.8, 140.2, 127.4, 124.2, 90.2, 64.1, 26.9, 23.5 (br), 23.0 (br), 13.8; IR (neat) 3447, 2984, 2361, 1746, 1474, 1219, 1157, 1134, 1094, 773 cm\(^{-1}\); HRMS (ESI-TOF) Calcd. for C₁₅H₂₄NaO₆: 347.1465 ([M + Na]⁺), Found: 347.1460 ([M + Na]⁺).
**Table S1** *anti*-Selective aldol reactions between 3-phenylpropanal and 1c catalyzed by (S)-2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>anti/syn</th>
<th>ee (%)</th>
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<td>3.0/1</td>
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<td>4.1/1</td>
<td>98</td>
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<td>96</td>
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<tr>
<td>4</td>
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<td>5</td>
<td>DMF</td>
<td>57</td>
<td>2.6/1</td>
<td>97</td>
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</table>

* a The reaction of 3-phenylpropanal (0.125 mmol) with 1c (0.1 mmol) was performed in the presence of (S)-2 (0.01 mmol) in a solvent (100 μL) at room temperature for 2 h. b Isolated yield. c Determined by 1H-NMR. d The ee of *anti*-4c was determined by HPLC using chiral column after conversion to the corresponding γ-lactone.

**Table S2** *syn*-Selective aldol reactions between 3-phenylpropanal and 1c catalyzed by (S)-3

<table>
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<th>anti/syn</th>
<th>ee (%)</th>
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<td>MeCN</td>
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<td>DMF</td>
<td>82</td>
<td>1/2.8</td>
<td>92</td>
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</table>

* a The reaction of 3-phenylpropanal (0.125 mmol) with 1c (0.1 mmol) was performed in the presence of (S)-3 (0.005 mmol) in a solvent (100 μL) at room temperature for 2 h. b Isolated yield. c Determined by 1H-NMR. d The ee of *syn*-4c was determined by HPLC using chiral column after conversion to the corresponding γ-lactone.

**General procedure for the *anti*-selective aldol reaction of aldehydes with 1c catalyzed by (S)-2**

To a stirred solution of hydrated 1-(2,6-di-tert-butylphenyl) 3-ethyl 2-oxomalonate 1c (35 mg, 0.1 mmol) and (S)-2 (1.4 mg, 0.01 mmol) in toluene (100 μL) was added a donor aldehyde (0.125 mmol) at room temperature. After stirring for the time indicated in Table 4, the reaction mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. The residue was purified by flash column chromatography on silica gel to afford the...
corresponding aldol adduct. To a solution of the aldol adduct in dichloromethane (1.0 mL) was added 0.64M solution of L-selectride in THF (0.2 mL, 0.13 mmol) dropwise at \(-78^\circ C\). After stirring for 1h, the reaction mixture was treated with 1M solution of HCl in diethyl ether (0.15 mL, 0.15 mmol) and stirred for further 1h. The reaction mixture was then quenched with water and extracted with dichloromethane. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$ and concentrated. The residue was purified by flash column chromatography on silica gel to afford the corresponding \(\gamma\)-lactone.

(3S,4R)-Ethyl 4-methyl-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 1)

[\(\alpha\)]$_D^{+}$ = -16.2 (c 0.2, CHCl$_3$; 95% ee); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.54 (1H, dd, $J$ = 8.8, 7.2 Hz, OCH$_2$), 4.35 (2H, app qd, $J$ = 7.2, 2.0 Hz, OCH$_3$), 4.05 (1H, dd, $J$ = 8.8, 7.2 Hz, OCHH), 3.72 (1H, s, OH), 2.99-2.90 (1H, m, CH), 1.33 (3H, $\beta$, $J$ = 7.2 Hz, OCH$_2$CH$_3$), 1.11 (3H, d, $J$ = 7.2 Hz, CHCH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.2, 167.7, 74.7, 72.7, 63.6, 38.7, 14.0, 10.4; IR (neat) 3480, 2963, 2359, 1786, 1746, 1267, 1165, 1017, 772 cm$^{-1}$; HRMS (ESI-TOF) Calcd. C$_8$H$_{12}$NaO$_3$: 211.0577 ([M + Na]$^+$), Found: 211.0575 ([M + Na]$^+$); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, $\lambda$ = 230 nm, retention time: 23.6 min (minor) and 25.6 min (major).

(3S,4R)-Ethyl 4-ethyl-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 2)

[\(\alpha\)]$_D^{+}$ = -10.1 (c 0.5, CHCl$_3$; 97% ee); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.51 (1H, dd, $J$ = 8.8, 7.6 Hz, OCH$_2$), 4.36 (2H, q, $J$ = 7.2 Hz, OCH$_2$CH$_3$), 4.10 (1H, app t, 8.8 Hz, OCHH), 3.79 (1H, s, OH), 2.87-2.79 (1H, m, CH), 1.76-1.65 (1H, m, CHHCH$_3$), 1.53-1.42 (1H, m, CHHCH$_3$), 1.34 (3H, $\beta$, $J$ = 7.2 Hz, OCH$_2$CH$_3$), 0.91 (3H, $\beta$, $J$ = 7.6 Hz, CH$_2$CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.2, 170.7, 76.8, 71.3, 63.6, 45.4, 18.5, 14.0, 11.2; IR (neat) 3466, 2970, 2918, 1786, 1738, 1466, 1368, 1256, 1155, 1045, 1007 cm$^{-1}$; HRMS (ESI-TOF) Calcd. C$_9$H$_4$NaO$_3$: 225.0733 ([M + Na]$^+$), Found: 225.0720 ([M + Na]$^+$); Daicel Chiralpak AD-H, hexane/2-propanol = 20/1, flow rate 0.5 mL/min, $\lambda$ = 210 nm, retention time: 37.9 min (minor) and 41.7 min (major).

(3S,4R)-Ethyl 4-benzyl-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 3)

[\(\alpha\)]$_D^{+}$ = 13.0 (c 0.7, CHCl$_3$; 98% ee); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.30-7.26 (2H, m, Ar-H), 7.24-7.16 (3H, m, Ar-H), 4.46 (1H, dd, $J$ = 8.8, 7.6 Hz, OCHH), 4.19 (1H, app t, $J$ = 8.8 Hz, OCHH), 4.11 (1H, dq, $J$ = 10.8, 7.2 Hz, OCHHCH$_3$), 4.02 (1H, dq, $J$ = 10.8, 7.2 Hz, OCHHCH$_3$), 3.88 (1H, s, OH), 3.26-3.17 (1H, m, CH), 2.99 (1H, dd, $J$ = 14.0, 8.4 Hz, CHHPh), 2.70 (1H, dd, $J$ = 14.0, 7.2 Hz, CHHPh), 1.14 (3H, $\beta$, $J$ = 7.2 Hz, OCH$_2$CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.8, 169.8, 137.5, 129.0, 128.6, 126.9, 76.6, 70.9, 63.4, 45.7, 31.0, 13.8; IR (neat) 3462, 2970, 2361, 1740, 1368, 1229, 1020, 746, 702 cm$^{-1}$; HRMS (ESI-TOF) Calcd. for C$_{14}$H$_{20}$NaO$_5$: 287.0890 ([M + Na]$^+$), Found: 287.0886 ([M + Na]$^+$); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, $\lambda$ = 210 nm, retention time: 25.8 min (major) and 29.5 min (minor).

(3S,4R)-Ethyl 4-(cyclohexylmethyl)-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 4)
The residue was purified by flash column chromatography on silica gel to afford the corresponding aldol adduct. To a solution of the aldol adduct in dichloromethane (2.0 mL) was added 0.64M solution of L-selectride in THF (0.2 mL, 0.13 mmol) dropwise at −78 °C. After stirring for 1h, the reaction mixture was quenched with water and extracted with dichloromethane. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. The residue was purified by flash column chromatography on silica gel to afforded the corresponding γ-lactone.
Hz, CHCH₃); ¹³C NMR (100 MHz, CDCl₃) δ 173.4 168.8, 79.3, 70.7, 63.5, 41.4, 14.2, 11.3; IR (neat) 2969, 2361, 2340, 1788, 1746, 1262, 1219, 1020, 768 cm⁻¹; HRMS (ESI-TOF) Calcd. C₆H₁₂NaO₅: 211.0577 ([M + Na⁺]); Found: 211.0579 ([M + Na⁺]); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 230 nm, retention time: 32.6 min (minor) and 34.5 min (major).

(3S,4S)-Ethyl 4-ethyl-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 7)

[α]D³ = -67.6 (c 0.2, CHCl₃; 95% ee); ¹H NMR (400 MHz, CDCl₃) δ 4.50 (1H, dd, J = 8.8, 8.4 Hz, OCHH), 4.39 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.33 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.09 (1H, dd, 11.2, 8.8 Hz, OCHH), 3.78 (1H, s, OH), 2.73-2.64 (1H, m, CH), 1.69-1.58 (1H, m, CHHCH₃), 1.45-1.36 (1H, m, CHHCH₃), 1.35 (3H, t, J = 7.2 Hz, OCH₂CH₃), 0.98 (3H, t, J = 7.6 Hz, CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 173.6, 168.9, 79.2, 70.0, 63.4, 48.0, 20.1, 14.1, 11.6; IR (neat) 3478, 2969, 2938, 2359, 1786, 1748, 1117, 1017, 912, 744 cm⁻¹; HRMS (ESI-TOF) Calcd. C₆H₁₁NaO₅: 225.0733 ([M + Na⁺]); Found: 225.0730 ([M + Na⁺]); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 235 nm, retention time: 29.4 min (minor) and 34.6 min (major).

(3S,4S)-Ethyl 4-benzyl-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 8)

[α]D³ = -157.6 (c 0.1, CHCl₃; 95% ee); ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.23 (3H, m, Ar-H), 7.15-7.13 (2H, m, Ar-H), 4.47 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.39 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.26 (1H, app t, J = 8.4 Hz, OCHH), 4.22 (1H, dd, J = 9.6, 9.2 Hz, OCHH), 3.84 (1H, s, OH), 3.09-3.03 (1H, m, CH), 3.03 (1H, dd, J = 14.8, 4.8 Hz, CH₂PH₂), 2.54 (1H, dd, J = 14.8, 11.6 Hz, CH₂PH₂), 1.41 (3H, t, J = 7.2 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 168.7, 136.9, 128.9, 128.4, 127.1, 78.8, 69.8, 63.7, 48.0, 33.0, 14.2; IR (neat) 3462, 2980, 2918, 2359, 1786, 1746, 1140, 1018, 747, 702 cm⁻¹; HRMS (ESI-TOF) Calcd. for C₁₃H₁₆NaO₅: 287.0890 ([M + Na⁺]); Found: 287.0886 ([M + Na⁺]); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 210 nm, retention time: 30.1 min (minor) and 32.9 min (major).

(3S,4S)-Ethyl 4-(cyclohexylmethyl)-3-hydroxy-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 9)

[α]D³ = -55.0 (c 0.2, CHCl₃; 95% ee); ¹H NMR (400 MHz, CDCl₃) δ 4.47 (1H, app t, J = 8.8 Hz, OCHH), 4.39 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.33 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.09 (1H, dd, J = 11.2, 8.8 Hz, OCHH), 3.77 (1H, s, OH), 2.91-2.82 (1H, m, CH), 1.71-1.66 (5H, m, CH₂Cy), 1.49-1.43 (1H, m, CHHcy), 1.34 (3H, t, J = 7.2 Hz, OCH₂CH₃), 1.28-1.12 (5H, m, CH₂Cy, CHHcy), 0.92-0.85 (2H, m, CH₂Cy); ¹³C NMR (100 MHz, CDCl₃) δ 173.9, 169.0, 79.2, 70.3, 63.4, 43.9, 35.2, 34.6, 33.6, 33.1, 26.3, 26.0 (two peaks overlap), 14.1; IR (neat) 3466, 2924, 2851, 2361, 1786, 1749, 1449, 1136, 1016, 772 cm⁻¹; HRMS (ESI-TOF) Calcd. for C₁₄H₁₄NaO₅: 293.1359 ([M + Na⁺]); Found: 293.1360 ([M + Na⁺]); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 240 nm, retention time: 29.0 min (major) and 31.8 min (minor).

(3S,4S)-Ethyl 3-hydroxy-4-isopropyl-2-oxotetrahydrofuran-3-carboxylate (Table 4, entry 10)
[α]_D^25 −76.3 (c 0.3, CHCl₃; 96% ee); ¹H NMR (400 MHz, CDCl₃) δ 4.47 (1H, dd, J = 8.8, 8.4 Hz, OCHH), 4.38 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.34 (1H, dq, J = 10.8, 7.2 Hz, OCHHCH₃), 4.14 (1H, dd, J = 10.8, 8.8 Hz, OCHH), 3.75 (1H, s, OH), 2.47-2.40 (1H, m, CH), 1.77-1.68 (1H, m, CH(CH₃)₂), 1.34 (3H, t, J = 7.2 Hz, OCH₂CH₃), 1.01 (3H, d, J = 6.8 Hz, CH(CH₃)(CH₃)), 0.91 (3H, d, J = 6.8 Hz, CH(CH₃)(CH₃)); ¹³C NMR (100 MHz, CDCl₃) δ 174.0, 169.1, 79.1, 69.7, 63.4, 53.0, 28.1, 20.8, 20.6, 14.1; IR (neat) 3476, 2967, 2878, 2359, 2340, 1786, 1749, 1123, 1018, 912, 744 cm⁻¹; HRMS (ESI-TOF) Calcd. for C₁₀H₁₆NaO₅: 239.0890 ([M + Na]⁺), Found: 239.0893 ([M + Na]⁺); Daicel Chiralpak AD-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 220 nm, retention time: 23.5 min (major) and 25.0 min (minor).

Synthesis of ethyl (3R,4R)-3-amino-4-benzyl-2-oxotetrahydrofuran-3-carboxylate (syn-7)

To a solution of γ-lactone anti-5 (14 mg, 0.05 mmol) and triethylamine (15 μL, 0.115 mmol) in dichloromethane (80 μL) was added MeSO₂Cl (4.6 μL, 0.06 mmol) dropwise at 0 °C argon atmosphere. After stirring at 0 °C for 12 h, the reaction mixture was added NH₄Cl and extracted with CH₂Cl₂. The organic layer was concentrated under vacuum and purified by flash column chromatography on silica gel (hexane/ethyl acetate = 5/1) to afford the mesylated γ-lactone anti-6 (10.6 mg, 0.031 mmol, 62% yield).

To a solution of obtained anti-6 (1.8mg, 0.005 mmol) in anhydrous DMF (25 μL) was added NaN₃ (1.0 mg, 0.015 mmol) at room temperature. After stirring for 24 h, the reaction mixture was added NH₄Cl to quench excess azide and extracted with EtOAc. The organic layer was concentrated under vacuum and roughly purified by flash column chromatography on silica gel (hexane/ethyl acetate = 5/1) to afford the corresponding α-azido-γ-lactone. To a solution of the obtained α-azido-γ-lactone and 10% Pd/C (0.2 mg) in EtOH (0.1 mL) was stirred at room temperature under hydrogen atmosphere for 24 h. After filtration through celite, the filtrate was concentrated under vacuum and purified by flash column chromatography on silica gel (hexane/ethyl acetate = 3/1) to afford amino lactone (1.3 mg, 0.005 mmol, 99% yield for two steps). ¹H NMR, ¹³C NMR and IR match those reported in the literature.⁴ [α]_D²⁰ = −9.6 (c = 0.1, CHCl₃; 95% ee); HPLC analysis: Daicel Chiralpak AS-H, hexane/2-propanol = 10/1, flow rate 0.5 mL/min, λ = 210 nm, retention time: 56.1 min (minor) and 71.4 min (major).

Determination of the absolute stereochemistry of syn-5 and anti-5

The relative and absolute configuration of anti-5 was determined to be (3S,4S) by converting to syn-7 as described above and by comparison of the sign of the optical rotation with the reported value.⁴ Based on this information, the absolute configuration of syn-5 obtained in the reaction catalyzed by (S)-2 was determined to be (3S,4R) by converting to anti-5 using NaOEt and by comparison of the HPLC retention times.
References


