The Importance of Iminium Geometry Control in Enamine Catalysis. Identification of a New Catalyst Architecture for Aldehyde-Aldehyde Couplings.

Ian K. Mangion, Alan B. Northrup and David W. C. MacMillan*

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125

General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego. Dioxane and diethyl ether were obtained from EM Science and used as supplied. Non-aqueous reagents were transferred under nitrogen via syringe or cannula. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an ice-water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still. Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F plates. Visualization of the developed chromatogram was performed by fluorescence quenching or by anisaldehyde stain.

$^1$H and $^{13}$C NMR spectra were recorded on a Varian Mercury 300 (300 MHz and 75 MHz) Spectrometer as noted, and are internally referenced to residual protio solvent signals. Data for $^1$H NMR are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant (Hz) and assignment. Data for $^{13}$C NMR are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm$^{-1}$). Mass spectra were obtained from the California Institute of Technology Mass Spectral Facility. Gas liquid chromatography (GLC) was performed on Hewlett-Packard 6850 and 6890 Series gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using a Bodman [β]-DM (30 m x 0.25 mm) column or an ASTEC Chiraldex [β]-BP (30 m x 0.25 mm) or [β]-PH (30 m x 0.25 mm) column as noted. High
performance liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using a Chiralcel AD column (1.6 x 25 cm) and AD guard (1.6 x 5 cm), a Chiralcel OJ column (1.6 x 25 cm) and OJ guard (5 cm), or a Chiralcel ODH column (1.6 x 25 cm) and ODH guard (1.6 x 5 cm), as noted. For experiments wherein more than one isomer is possible, only characterization data for the major isomer is provided.

**(2R, 3R)-1,1-Dimethoxy-2-methyl-pentan-3-ol (Table 2, entry 1).** Freshly distilled propionaldehyde (621 µL, 8.61 mmol) was added to a stirring 4 °C solution of (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (70.7 mg, 0.287 mmol) and trichloroacetic acid (46.9 mg, 0.287 mmol) in dioxane (8.6 mL). After 36 h methanol (14.4 mL) and Amberlyst-15 (359 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (1 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (85:15 pentane:Et₂O) afforded the title compound as a clear, colorless oil in 86% yield (400 mg, 2.46 mmol), 94% ee and 4:1 anti:syn. IR (film) 3457, 2966, 2934, 2868, 1463, 1432, 1382, 1099, 1069, 977.5, 945.6 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.28 (d, 1H, J = 6.3 Hz, CH(OCH₃)₂); 3.50 (m, 1H, CHOH); 3.42 (s, 3H, OCH₃); 3.35 (s, 3H, OCH₃); 1.84 (m, 1H, CHCH₃); 1.59 (m, 1H, CH₂CH₃); 1.37 (m, 1H, CH₂CH₃); 0.95 (t, 3H, J = 7.2 Hz, CH₂CH₃); 0.86 (d, 3H, J = 6.6 Hz, CHCH₃); ¹³C NMR (75 MHz, CDCl₃) δ 109.0, 74.1, 55.9, 53.5, 40.6, 27.4, 12.0, 9.7; HRMS (CI) exact mass calculated for [M + H]⁺ (C₄H₁₀O₃) requires m/z 163.1334, found m/z 163.1340. [a]D = 34.06 (c = 1.0, CHCl₃). The product ratios were determined by GLC analysis of the tert-butyl carbonate derived from the product alcohol by the method of Hassner³ using a Bodman Chiraldex □-PH (30 m x 0.25 mm) column (80 °C isotherm, 14 psi); (2R, 3R) anti isomer tᵣ = 85.8 min, (2S, 3S) anti isomer tᵣ = 90.8 min, (2R, 3S) and (2S, 3R) syn isomers tᵣ = 82.9, 104.5 min.

**(2R, 3R)-1,1-Dimethoxy-2,4-dimethyl-pentan-3-ol (Table 2, entry 2).** A 4 °C solution of freshly distilled propionaldehyde (76.8 µL, 1.06 mmol) in 0.88 mL Et₂O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (976 µL, 10.6 mmol), (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (52.4 mg, 0.213 mmol) and trifluoroacetic acid (16.4 µL, 0.213 mmol) in Et₂O (1.2 mL) at 4 °C. After 37 h methanol (5.32
mL) and Amberlyst-15 (133 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (4 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (4:1 pentane: Et₂O) afforded the title compound as a clear, colorless oil in 90% yield (181 mg, 0.961 mmol), 95% ee and 5:1 anti:syn. IR (film) 3504, 2961, 2923, 2871, 1457, 1387, 1105, 1073, 996.3 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.30 (d, 1H, J = 5.7 Hz, CH(CH₃)₂); 3.49 (d, 1H, J = 2.1 Hz, CHOH); 3.42 (s, 3H, OCH₃); 3.36 (m, 4H, CHOH, OCH₃); 1.88 (m, 1H, CHCH₃); 1.76 (m, 1H, CH(CH₃)₂); 0.98 (d, 3H, J = 6.6 Hz, CH₃); 0.85 (d, 6H, J = 7.8 Hz, CH(CH₃)₂); ¹³C NMR (75 MHz, CDCl₃) δ 109.3, 77.2, 56.2, 53.6, 38.8, 30.2, 20.6, 14.9, 11.9; HRMS (CI) exact mass calculated for [M + H]⁺ (C₉H₁₉O₃) requires m/z 177.1492, found m/z 177.1487. [α]D = 20.4 (c = 1.0, CHCl₃). The product ratios were determined by GLC analysis using a Bodman Chiraldex [α]-DM (30 m x 0.25 mm) column (70 °C isotherm, 12 psi); (2R, 3R) anti isomer t₁ = 62.0 min, (2S, 3S) anti isomer t₁ = 59.0 min, (2R, 3S) and (2S, 3R) syn isomers t₁ = 65.0 min.

(1R, 2R)-1-Cyclohexyl-3,3-dimethoxy-2-methyl-propan-1-ol (Table 2, entry 3). A 4 °C solution of freshly distilled propionaldehyde (76.6 µL, 1.06 mmol) in 0.92 mL Et₂O was added slowly over the course of 36 h to a stirring suspension of cyclohexanecarboxaldehyde (1.28 mL, 10.6 mmol), (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (52.2 mg, 0.212 mmol) and trifluoroacetic acid (16.3 µL, 0.212 mmol) in Et₂O (1.00 mL) at 4 °C. After 44 h methanol (5.30 mL) and Amberlyst-15 (130 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (6 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (97:3 pentane: Et₂O) afforded the title compound as a clear, colorless oil in 81% yield (186 mg, 0.860 mmol), 97% ee and 5:1 anti:syn. ¹H NMR, ¹³C NMR, and IR data are consistent with those already reported.⁵ [α]D = 14.0 (c = 1.0, MeOH); lit: [α]D = 0.5 (c = 1.12, MeOH); 19% ee. The product ratios were determined by GLC analysis of the acetate derived from the product alcohol by the method of Khorana⁴ using a Bodman Chiraldex [α]-DM (30 m x 0.25 mm) column (105 °C isotherm, 12 psi); (1R, 2R) anti isomer t₁ = 103.8 min, (1S, 2S) anti isomer t₁ = 103.4 min, (1R, 2S) and (1S, 2R) syn isomers t₁ = 106.0 min.
(1R, 2R)-3,3-Dimethoxy-2-methyl-1-phenyl-propan-1-ol (Table 2, entry 4). A 4 °C solution of freshly distilled propionaldehyde (66.7 µL, 0.925 mmol) in 0.83 mL Et₂O was added slowly over the course of 36 h to a stirring suspension of benzaldehyde (940 µL, 9.25 mmol), (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (45.6 mg, 0.185 mmol) and trichloroacetic acid (30.2 mg, 0.185 mmol) in Et₂O (0.95 mL) at 4 °C. After 48 h methanol (4.60 mL) and PPTS (46.5 mg, 0.185 mmol) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (15 h), at which point the solution was concentrated in vacuo. Flash chromatography (4:1 pentane: Et₂O) afforded the title compound as a clear, colorless oil in 61% yield (115 mg, 0.545 mmol), 93% ee and 4:1 anti:syn. ¹H NMR, ¹³C NMR, and IR data are consistent with those already reported.⁵ [Δ]₀ = -13.06 (c = 1.0, MeOH); lit: [Δ]₀ = -16.20 (c = 1.06, MeOH). The product ratios were determined by GLC analysis using a Bodman Chiraldex [D]-DM (30 m x 0.25 mm) column (120 °C isotherm, 12 psi); (1R, 2R) anti isomer tᵣ = 75.6 min, (1S, 2S) anti isomer tᵣ = 80.6 min, (2R, 3S) and (2S, 3R) syn isomers tᵣ = 86.1 min.

(3R, 4R)-4-Dimethoxymethyl-2-methyl-octan-3-ol (Table 2, entry 5). A 4 °C solution of freshly distilled hexanal (165 µL, 1.37 mmol) in 0.80 mL Et₂O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (1.18 mL, 13.7 mmol), (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (67.5 mg, 0.274 mmol) and trifluoroacetic acid (21.1 µL, 0.274 mmol) in Et₂O (1.0 mL) at 4 °C. After 40 h methanol (6.9 mL) and Amberlyst-15 (171 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (4 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (5:1 pentane: Et₂O) afforded the title compound as a clear, colorless oil in 72% yield (202 mg, 0.801 mmol), 91% ee and 6:1 anti:syn. IR (film) 3520, 2956, 2932, 2872, 1467, 1379, 1365, 1200, 1188, 1101, 1074, 996.5 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.42 (d, 1H, J = 3.9 Hz, CH(OCH₃)₂); 3.42 (s, 3H, OCH₃); 3.40 (s, 3H, OCH₃); 3.34 (m, 2H, CHOH, CHOH); 1.76 (m, 2H, CHCH(OCH₃)₂, CH(CH₃)₂); 1.48-1.18 (m, 6H, CH(CH₂)₂CH₃); 0.94-0.85 (m, 9H, CH(CH₃)₂, (CH₂)₃CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 108.2, 76.2, 56.5, 55.0, 42.3, 31.3, 29.6, 25.9, 23.5, 20.2, 17.6, 14.4; HRMS (CI) exact mass calculated for [M – H]⁺ (C₁₂H₂₅O₃) requires m/z 217.1804, found m/z 217.1805. [Δ]₀ = 6.40 (c = 1.0, CHCl₃). The diastereomeric ratio was determined by ¹H NMR
integration of the crude product (300 MHz, CDCl₃):  4.42 (d, 1H, major), 4.39 (d, 1H, minor). The enantiomeric purity was determined by conversion to the (R)-MTPA ester derivative and ¹H NMR integration (300 MHz, CDCl₃):  4.07 (d, 1H, major), 4.10 (d, 1H, minor).

**(2R, 3R)-2-Benzyl-1,1-dimethoxy-4-methyl-pentan-3-ol (Table 2, entry 6).** A 4 °C solution of freshly distilled hydrocinnamaldehyde (132 µL, 1.00 mmol) in 0.86 mL Et₂O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (908 µL, 10.0 mmol), (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (49.3 mg, 0.200 mmol) and trifluoroacetic acid (15.4 µL, 0.200 mmol) in Et₂O (1.0 mL) at 4 °C. After 40 h methanol (5.0 mL) and Amberlyst-15 (188 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (4 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (4:1 pentane: Et₂O) afforded the title compound as a clear, colorless oil in 80% yield (202 mg, 0.801 mmol), 91% ee and 5:1 anti:syn. IR (film) 3517, 2958, 2873, 2834, 1495, 1453, 1366, 1207, 1111, 1068, 1032, 964.4, 747.5, 700.6 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) J 7.31-7.16 (m, 5H, C₆H₅); 4.30 (d, 1H, J = 3.3 Hz, CH(OCH₃)₂); 3.45 (s, 3H, OCH₃); 3.29 (m, 2H, CH₂O, CHO); 2.77 (d, 2H, J = 7.8 Hz, CH₂C₆H₅); 2.16 (m, 1H, CHCH(OCH₃)₂); 1.78 (m, 1H, CH(CH₃)₂); 0.94 (d, 3H, J = 6.9 Hz, CH(CH₃)₂); 0.86 (d, 3H, J = 6.9 Hz, CH(CH₃)₂); ¹³C NMR (75 MHz, CDCl₃) J 129.3, 128.6, 128.5, 126.1, 107.9, 75.8, 57.0, 56.1, 44.6, 32.2, 31.7, 19.9, 18.0; HRMS (CI) exact mass calculated for [M⁺]⁺ (C₉H₁₆O₂) requires m/z 252.1726, found m/z 252.1724. [Δ]₀ = -10.78 (c = 1.0, CHCl₃). The diastereomeric ratio was determined by ¹H NMR integration of the crude product (300 MHz, CDCl₃):  4.30 (d, 1H, major), 4.08 (d, 1H, minor). The enantiomeric purity was determined by conversion to the (R)-MTPA ester derivative and ¹H NMR integration (300 MHz, CDCl₃):  4.05 (d, 1H, major), 4.10 (d, 1H, minor).

**2,2-Dimethyl-propionic acid (2S, 3R)-2-hydroxy-4,4-dimethoxy-3-methyl-butyl ester (Table 2, entry 7).** A 4 °C solution of freshly distilled propionaldehyde (290 µL, 4.02 mmol) and 2,2-dimethyl-propionic acetoxyacetaldehyde (116 mg, 0.805 mmol) in 0.60 mL Et₂O was added slowly over the course of 36 h to a stirring solution of (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (40.0 mg, 0.161 mmol) and trifluoroacetic acid (12.4 µL, 0.161
mmol) in Et₂O (0.60 mL). After 36 h methanol (4.0 mL) and Amberlyst-15 (200 mg) was added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (8 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (95:5 hexanes:acetone) afforded the title compound as a clear, colorless oil in 58% yield (116 mg, 0.467 mmol), 90% ee and 4:1 anti:syn. IR (film) 3469, 2961, 2929, 1729, 1482, 1462, 1393, 1367, 1286, 1163, 1107, 1071, 945.4 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 4.35 (d, 1H, J = 5.7 Hz, CH(OCH₃)₂); 4.22 (dd, 1H, J = 11.4, 3.3 Hz, CH₂OC(O)C(CH₃)₃); 4.09 (dd, 1H, J = 11.4, 5.4 Hz, CH₂OC(O)C(CH₃)₃); 3.81 (m, 1H, CHO); 3.44 (s, 3H, OCH₃); 3.40 (s, 3H, OCH₃); 2.01 (m, 1H, CHCH₃); 1.21 (s, 9H, C(CH₃)₃); 0.93 (d, 3H, J = 7.2 Hz, CH₂CH₃); ¹³C NMR (75 MHz, CDCl₃) δ 108.4, 71.8, 67.1, 56.3, 54.5, 39.1, 38.8, 27.6, 11.7; HRMS (CI) exact mass calculated for [M + H]⁺ (C₁₂H₂₅O₃) requires m/z 249.1702, found m/z 249.1690. [α]D = 4.20 (c = 1.0, CHCl₃). The product ratios were determined by GLC analysis of the product using a Bodman Chiraldex α-PH (30 m x 0.25 mm) column (120 °C isotherm, 14 psi); (2R, 3S) anti isomer tᵣ = 107.8 min, (2S, 3R) anti isomer tᵣ = 114.7 min, (2R, 3S) and (2S, 3R) syn isomers tᵣ = 127.3, 142.4 min.

(2R, 3R)-1,3-Bis-benzylkoxy-4,4-dimethoxy-butan-2-ol (Table 2, entry 8). Freshly distilled benzylkoxyacetaldelye (621 μL, 8.61 mmol) was added to a −20 °C stirring solution of (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (81.8 mg, 0.332 mmol) and trichloroacetic acid (54.2 mg, 0.332 mmol) in Et₂O (0.35 mL). After 72 h methanol (2.8 mL) and Amberlyst-15 (138 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (2 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (3:2-2:3 pentane:Et₂O, linear gradient) afforded the title compound as a clear, colorless oil in 64% yield (134 mg, 0.387 mmol), 92% ee and 4:1 anti:syn. IR (film) 3468, 2927, 2862, 1454, 1365, 1325, 1202, 1075, 736.6, 698.2 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.22 (m, 10H, C₆H₃); 4.82-4.43 (m, 5H, CH(OCH₃)₂, CH₂C₆H₅); 4.00 (s, 1H, CHO); 3.65-3.41 (m, 10H, OCH₃, CHO, CH₂OBN, CHOBN); ¹³C NMR (75 MHz, CDCl₃) δ 128.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 106.2, 78.9, 78.3, 74.6, 73.6, 71.2, 69.7, 56.6, 56.2; HRMS (CI) exact mass calculated for [M − H]⁺ (C₂₀H₂₅O₅) requires m/z 345.1702, found m/z 345.1691. [α]D = −2.48 (c = 1.0, CHCl₃). The product ratios were determined by HPLC using a Chiracel OJ and
OJ guard column (6% ethanol/hexanes, 1 mL/min): (2R, 3R) anti isomer tᵣ = 41.7 min, (2S, 3S) anti isomer tᵣ = 31.4 min, (2R, 3S) and (2S, 3R) syn isomers tᵣ = 22.1, 24.8 min.

**Determination of the absolute stereochemistry of (2R, 3R)-1,3-Bis-benzyloxy-4,4-dimethoxy-butan-2-ol.** (2S, 3S)-3-Hydroxy-2,3-bis-(benzyloxy)-propionaldehyde (20 mg, 0.067 mmol) was prepared as reported previously⁶ and dissolved in MeOH (0.33 mL). Amberlyst-15 (8 mg) was added in one portion with stirring. After 6 h, the Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (1:1 pentane: Et₂O) afforded (2S, 3S)-1,3-bis-benzyloxy-4,4-dimethoxy-butan-2-ol as a clear, colorless oil in 64% yield (14 mg, 0.043 mmol); ¹H NMR, ¹³C NMR, and IR data match those reported above, but with an opposite rotation: [α]D = 2.61 (c = 1.0, CHCl₃).

(2R, 3R)-1,3-Bis-benzylsulfanyl-4,4-dimethoxy-butan-2-ol (Table 2, entry 9). Freshly distilled benzylsulfanylacetalddehyde (300 mg, 1.80 mmol) was added to a 4 °C stirring solution of (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (14.8 mg, 0.060 mmol) and trifluoroacetic acid (4.6 µL, 0.060 mmol) in Et₂O (0.60 mL). After 48 h methanol (2.8 mL) and Amberlyst-15 (138 mg) were added in one portion. The solution was stirred until the reaction was judged complete by TLC analysis (2 h). The Amberlyst-15 resin was removed by filtration through a fritted filter, and the filtrate was concentrated in vacuo. Flash chromatography (4:1 pentane:Et₂O) afforded the title compound as a clear, colorless oil in 84% yield (192 mg, 0.504 mmol), 97% ee and 11:1 anti:syn. IR (film) 3464, 3058, 3026, 2918, 2820, 1606, 1582, 1494, 1453, 1117, 1070, 1030, 765.8, 701.8 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) [hex] 7.40-7.18 (m, 10 H, C₄H₅); 4.37 (d, 1H, J = 3.3 Hz, CH(OCH₃)₂); 3.93 (m, 1H, CHOH); 3.78 (s, 2H, CH₂C₆H₅); 3.72 (s, 2H, CH₂C₆H₅); 3.35 (s, 6H, OCH₃); 3.18 (m, 1H, CHCH(OCH₃)₂); 2.87 (dd, 1H, J = 7.2, 4.2 Hz, CH₂SBn); 2.54 (dd, 1H, J = 13.8, 7.2 Hz, CH₂SBn) ¹³C NMR (75 MHz, CDCl₃) [hex] 138.3, 138.2, 129.4, 129.2, 129.1, 128.7, 127.4, 127.2, 107.7, 70.4, 56.5, 56.4, 51.3, 37.5, 36.7; HRMS (CI) exact mass calculated for [M – H]+ (C₂₀H₂₅O₉S₂) requires m/z 377.1245, found m/z 377.1253. [α]D = 15.54 (c = 1.0, CHCl₃). The product ratios were determined by HPLC using a Chiracel AD and AD guard column (4% isopropanol/hexanes, 1 mL/min): (2R, 3R) anti isomer tᵣ = 31.2 min, (2S, 3S) anti isomer tᵣ = 27.1 min, (2R, 3S) and (2S, 3R) syn isomers tᵣ = 43.5 min.
(2S, 3R)-3-Hydroxy-2,3-bis-triisopropylsilanoxo-propionaldehyde (Table 2, entry 10). Freshly prepared triisopropylsilanoxo-acetaldehyde (900 mg, 4.17 mmol) was added to a 4 °C stirring solution of (2S, 5S)-5-benzyl-2-tert-butyl-3-methyl-imidazolidin-4-one (34.2 mg, 0.138 mmol) and trifluoroacetic acid (10.8 µL, 0.138 mmol) in Et₂O (1.38 mL). After 36 h, the reaction was diluted in Et₂O, and then successively washed with saturated aqueous solutions of NH₄Cl, NaHCO₃, and brine. The organic layer was dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (40:1 pentane:Et₂O) was performed on a silica column pre-washed with a solution of diethyl amine (150 mL) in pentane (900 mL), followed by 300 mL of the eluent to remove excess amine. The title compound was obtained from this column as a clear, colorless oil in 84% yield (504 mg, 1.17 mmol), 92% ee, 4:1 syn:anti. IR (film) 3559, 2944, 2867, 1729, 1464, 1384, 1384, 1248, 1119, 1068, 1015, 996.0, 882.3, 785.8, 683.1 cm⁻¹. ¹H NMR and ¹³C NMR data are consistent with those already reported,⁶ [α]D = 0.60 (c = 1.0, CHCl₃).

Determination of the absolute stereochemistry of (2S, 3R)-3-Hydroxy-2,3-bis-triisopropylsilanoxo-propionaldehyde. (2S, 3R)-3-Hydroxy-2,3-bis-triisopropylsilanoxo-propionaldehyde was reduced and converted to the corresponding benzylidene acetal as reported previously for stereochemical proof.⁷ Removal of the silyl groups with TBAF furnished 1,3-(R)-O-benzylidene-D-threitol, whose IR, ¹H NMR and ¹³C NMR data are consistent with those already reported.⁷ [α]D = −3.75 (c = 0.7, MeOH); lit: [α]D = −6 (c = 1.0, MeOH)