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

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General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] 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.[2] 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 (δ 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 γ-BP (30 m x 0.25 mm) or γ-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.

(2*R*, 3*R*)-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 ºC solution of (2*S*, 5*S*)-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:Et_2O) 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, $CDCl_3$) δ 4.28 (d, 1H, *J* = 6.3 Hz, C**H**$(OCH_3)_2$); 3.50 (m, 1H, C**H**OH); 3.42 (s, 3H, OC**H$_3$**); 3.35 (s, 3H, OC**H$_3$**); 1.84 (m, 1H, C**H**CH_3); 1.59 (m, 1H, C**H$_2$**CH_3); 1.37 (m, 1H, C**H$_2$**CH_3); 0.95 (t, 3H, *J* = 7.2 Hz, CH_2C**H$_3$**); 0.86 (d, 3H, *J* = 6.6 Hz, CHC**H$_3$**); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.0, 74.1, 55.9, 53.5, 40.6, 27.4, 12.0, 9.7; HRMS (CI) exact mass calculated for $[M + H]^+$ ($C_8H_{19}O_3$) requires *m*/*z* 163.1334, found *m*/*z* 163.1340. $[\alpha]_D$ = 34.06 (c = 1.0, $CHCl_3$). The product ratios were determined by GLC analysis of the *tert*-butyl carbonate derived from the product alcohol by the method of Hassner[3] using a Bodman Chiraldex Γ-PH (30 m x 0.25 mm) column (80 ºC isotherm, 14 psi); (2*R*, 3*R*) *anti* isomer t_r = 85.8 min, (2*S*, 3*S*) *anti* isomer t_r = 90.8 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 82.9, 104.5 min.

(2*R*, 3*R*)-1,1-Dimethoxy-2,4-dimethyl-pentan-3-ol (Table 2, entry 2). A 4 ºC solution of freshly distilled propionaldehyde (76.8 μL, 1.06 mmol) in 0.88 mL Et_2O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (976 μL, 10.6 mmol), (2*S*, 5*S*)-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 Et_2O (1.2 mL) at 4 ºC. 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: Et_2O) 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, $CDCl_3$) □ 4.30 (d, 1H, *J* = 5.7 Hz, C**H**$(OCH_3)_2$); 3.49 (d, 1H, *J* = 2.1 Hz, CH**OH**); 3.42 (s, 3H, OC**H**$_3$); 3.36 (m, 4H, C**H**OH, OC**H**$_3$); 1.88 (m, 1H, C**H**CH_3); 1.76 (m, 1H, C**H**$(CH_3)_2$); 0.98 (d, 3H, *J* = 6.6 Hz, C**H**$_3$); 0.85 (d, 6H, *J* = 7.8 Hz, CH(C**H**$_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) □ 109.3, 77.2, 56.2, 53.6, 38.8, 30.2, 20.6, 14.9, 11.9; HRMS (CI) exact mass calculated for $[M + H]^+$ ($C_9H_{21}O_3$) requires *m*/*z* 177.1492, found *m*/*z* 177.1487. $[□]_D$ = 20.4 (c = 1.0, $CHCl_3$). The product ratios were determined by GLC analysis using a Bodman Chiraldex □-DM (30 m x 0.25 mm) column (70 ºC isotherm, 12 psi); (2*R*, 3*R*) *anti* isomer t_r = 62.0 min, (2*S*, 3*S*) *anti* isomer t_r = 59.0 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 65.0 min.

(1*R*, 2*R*)-1-Cyclohexyl-3,3-dimethoxy-2-methyl-propan-1-ol (Table 2, entry 3). A 4 ºC solution of freshly distilled propionaldehyde (76.6 *μ*L, 1.06 mmol) in 0.92 mL Et_2O was added slowly over the course of 36 h to a stirring suspension of cyclohexanecarboxaldehyde (1.28 mL, 10.6 mmol), (2*S*, 5*S*)-5-benzyl-2-*tert*-butyl-3-methyl-imidazolidin-4-one (52.2 mg, 0.212 mmol) and trifluoroacetic acid (16.3 *μ*L, 0.212 mmol) in Et_2O (1.00 mL) at 4 ºC. 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: Et_2O) 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, ^{13}C NMR, and IR data are consistent with those already reported.[5] $[□]_D$ = 14.0 (c = 1.0, MeOH); lit: $[□]_D$ = 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 Khorana[4] using a Bodman Chiraldex □-DM (30 m x 0.25 mm) column (105 ºC isotherm, 12 psi); (1*R*, 2*R*) *anti* isomer t_r = 103.8 min, (1*S*, 2*S*) *anti* isomer t_r = 103.4 min, (1*R*, 2*S*) and (1*S*, 2*R*) *syn* isomers t_r = 106.0 min.

(1*R*, 2*R*)-3,3-Dimethoxy-2-methyl-1-phenyl-propan-1-ol (Table 2, entry 4). A 4 ºC solution of freshly distilled propionaldehyde (66.7 μL, 0.925 mmol) in 0.83 mL Et_2O was added slowly over the course of 36 h to a stirring suspension of benzaldehyde (940 μL, 9.25 mmol), (2*S*, 5*S*)-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 Et_2O (0.95 mL) at 4 ºC. 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: Et_2O) afforded the title compound as a clear, colorless oil in 61% yield (115 mg, 0.545 mmol), 93% ee and 4:1 *anti*:*syn*. ^{1}H NMR, ^{13}C NMR, and IR data are consistent with those already reported.[5] $[\alpha]_D$ = –13.06 (c = 1.0, MeOH); lit: $[\alpha]_D$ = –16.20 (c = 1.06, MeOH). The product ratios were determined by GLC analysis using a Bodman Chiraldex β-DM (30 m x 0.25 mm) column (120 ºC isotherm, 12 psi); (1*R*, 2*R*) *anti* isomer t_r = 75.6 min, (1*S*, 2*S*) *anti* isomer t_r = 80.6 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 86.1 min.

(3*R*, 4*R*)-4-Dimethoxymethyl-2-methyl-octan-3-ol (Table 2, entry 5). A 4 ºC solution of freshly distilled hexanal (165 μL, 1.37 mmol) in 0.80 mL Et_2O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (1.18 mL, 13.7 mmol), (2*S*, 5*S*)-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 Et_2O (1.0 mL) at 4 ºC. 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: Et_2O) 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}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.42 (d, 1H, *J* = 3.9 Hz, C**H**$(OCH_3)_2$); 3.42 (s, 3H, OC**H$_3$**); 3.40 (s, 3H, OC**H$_3$**); 3.34 (m, 2H, CH**OH**, C**H**OH); 1.76 (m, 2H, C**H**CH$(OCH_3)_2$, C**H**$(CH_3)_2$); 1.48-1.18 (m, 6H, CH$(CH_2)_3CH_3$); 0.94-0.85 (m, 9H, CH$(CH_3)_2$, $(CH_2)_3CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $[M - H]^+$ ($C_{12}H_{25}O_3$) requires *m*/*z* 217.1804, found *m*/*z* 217.1805. $[\alpha]_D$ = 6.40 (c = 1.0, $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR

integration of the crude product (300 MHz, $CDCl_3$): 4.42 (d, 1H, major), 4.39 (d, 1H, minor). The enantiomeric purity was determined by conversion to the (*R*)-MTPA ester derivative and ^{1}H NMR integration (300 MHz, $CDCl_3$): 4.07 (d, 1H, major), 4.10 (d, 1H, minor).

(2*R*, 3*R*)-2-Benzyl-1,1-dimethoxy-4-methyl-pentan-3-ol (Table 2, entry 6). A 4 ºC solution of freshly distilled hydrocinnamaldehyde (132 μL, 1.00 mmol) in 0.86 mL Et_2O was added slowly over the course of 36 h to a stirring suspension of isobutyraldehyde (908 μL, 10.0 mmol), (2*S*, 5*S*)-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 Et_2O (1.0 mL) at 4 ºC. 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: Et_2O) 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}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.31-7.16 (m, 5H, $C_6\mathbf{H_5}$); 4.30 (d, 1H, J = 3.3 Hz, C**H**$(OCH_3)_2$); 3.45 (s, 3H, OC$\mathbf{H_3}$); 3.39 (s, 3H, OC$\mathbf{H_3}$); 3.28 (m, 2H, CHO**H**, **C H**OH); 2.77 (d, 2H, J = 7.8 Hz, C$\mathbf{H_2}C_6H_5$); 2.16 (m, 1H, C**H**CH$(OCH_3)_2$); 1.78 (m, 1H, C**H**$(CH_3)_2$); 0.94 (d, 3H, J = 6.9 Hz, CH(C$\mathbf{H_3}$)$_2$); 0.86 (d, 3H, J = 6.9 Hz, CH(C$\mathbf{H_3}$)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $[M]^+$ ($C_{15}H_{24}O_3$) requires *m*/*z* 252.1726, found *m*/*z* 252.1724. $[]_D$ = –10.78 (c = 1.0, $CHCl_3$). The diastereomeric ratio was determined by ^{1}H NMR integration of the crude product (300 MHz, $CDCl_3$): 4.30 (d, 1H, major), 4.08 (d, 1H, minor). The enantiomeric purity was determined by conversion to the (*R*)-MTPA ester derivative and ^{1}H NMR integration (300 MHz, $CDCl_3$): 4.05 (d, 1H, major), 4.10 (d, 1H, minor).

2,2-Dimethyl-propionic acid (2*S*, 3*R*)-2-hydroxy-4,4-dimethoxy-3-methyl-butyl ester (Table 2, entry 7). A 4 ºC 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 Et_2O was added slowly over the course of 36 h to a stirring solution of (2*S*, 5*S*)-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 Et_2O (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, $CDCl_3$) □ 4.35 (d, 1H, *J* = 5.7 Hz, C**H**$(OCH_3)_2$); 4.22 (dd, 1H, *J* = 11.4, 3.3 Hz, C**H**$_2$OC(O)C$(CH_3)_3$); 4.09 (dd, 1H, *J* = 11.4, 5.4 Hz, C**H**$_2$OC(O)C$(CH_3)_3$); 3.81 (m, 1H, C**H**OH); 3.44 (s, 3H, OC**H**$_3$); 3.40 (s, 3H, OC**H**$_3$); 2.01 (m, 1H, C**H**CH_3); 1.21 (s, 9H, C(C**H**$_3)_3$); 0.93 (d, 3H, *J* = 7.2 Hz, CH_2C**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) □ 108.4, 71.8, 67.1, 56.3, 54.5, 39.1, 38.8, 27.6, 11.7; HRMS (CI) exact mass calculated for $[M + H]^+$ ($C_{12}H_{25}O_5$) requires *m*/*z* 249.1702, found *m*/*z* 249.1690. $[□]_D$ = 4.20 (c = 1.0, $CHCl_3$). The product ratios were determined by GLC analysis of the product using a Bodman Chiraldex □-PH (30 m x 0.25 mm) column (120 ºC isotherm, 14 psi); (2*R*, 3*S*) *anti* isomer t_r = 107.8 min, (2*S*, 3*R*) *anti* isomer t_r = 114.7 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 127.3, 142.4 min.

(2*R*, 3*R*)-1,3-Bis-benzyloxy-4,4-dimethoxy-butan-2-ol (Table 2, entry 8). Freshly distilled benzyloxyacetaldehyde (621 □L, 8.61 mmol) was added to a –20 ºC stirring solution of (2*S*, 5*S*)-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 Et_2O (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:Et_2O, 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, $CDCl_3$) □ 7.43-7.22 (m, 10H, C_6**H**$_5$); 4.82-4.43 (m, 5H, C**H**$(OCH_3)_2$, C**H**$_2C_6H_5$); 4.00 (s, 1H, CHO**H**); 3.65-3.41 (m, 10H, OC**H**$_3$, C**H**OH, C**H**$_2$OBn, C**H**OBn); ^{13}C NMR (75 MHz, $CDCl_3$) □ 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 $[M – H]^+$ ($C_{20}H_{25}O_5$) requires *m*/*z* 345.1702, found *m*/*z* 345.1691. $[□]_D$ = –2.48 (c = 1.0, $CHCl_3$). The product ratios were determined by HPLC using a Chiracel OJ and

OJ guard column (6% ethanol/hexanes, 1 mL/min): (2*R*, 3*R*) *anti* isomer t_r = 41.7 min, (2*S*, 3*S*) *anti* isomer t_r = 31.4 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 22.1, 24.8 min.

Determination of the absolute stereochemistry of (2*R*, 3*R*)-1,3-Bis-benzyloxy-4,4-dimethoxy-butan-2-ol. (2*S*, 3*S*)-3-Hydroxy-2,3-bis-(benzyloxy)-propionaldehyde (20 mg, 0.067 mmol) was prepared as reported previously[6] 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: Et_2O) afforded (2*S*, 3*S*)-1,3-bis-benzyloxy-4,4-dimethoxy-butan-2-ol as a clear, colorless oil in 64% yield (14 mg, 0.043 mmol); ^{1}H NMR, ^{13}C NMR, and IR data match those reported above, but with an opposite rotation: $[\alpha]_D$ = 2.61 (c = 1.0, $CHCl_3$).

(2*R*, 3*R*)-1,3-Bis-benzylsulfanyl-4,4-dimethoxy-butan-2-ol (Table 2, entry 9). Freshly distilled benzylsulfanylacetaldehyde (300 mg, 1.80 mmol) was added to a 4 ºC stirring solution of (2*S*, 5*S*)-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 Et_2O (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:Et_2O) 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}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.18 (m, 10 H, $C_6\mathbf{H_5}$); 4.37 (d, 1H, *J* = 3.3 Hz, C**H**$(OCH_3)_2$); 3.93 (m, 1H, C**H**OH); 3.78 (s, 2H, C$\mathbf{H_2}C_6H_5$); 3.72 (s, 2H, C$\mathbf{H_2}C_6H_5$); 3.35 (s, 6H, OC$\mathbf{H_3}$); 3.18 (m, 1H, C**H**CH$(OCH_3)_2$); 2.87 (dd, 1H, *J* = 7.2, 4.2 Hz, C$\mathbf{H_2}$SBn); 2.54 (dd, 1H, *J* = 13.8, 7.2 Hz, C$\mathbf{H_2}$SBn) ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 $[M - H]^+$ ($C_{20}H_{25}O_3S_2$) requires *m/z* 377.1245, found *m/z* 377.1253. $[\alpha]_D$ = 15.54 (c = 1.0, $CHCl_3$). The product ratios were determined by HPLC using a Chiracel AD and AD guard column (4% isopropanol/hexanes, 1 mL/min): (2*R*, 3*R*) *anti* isomer t_r = 31.2 min, (2*S*, 3*S*) *anti* isomer t_r = 27.1 min, (2*R*, 3*S*) and (2*S*, 3*R*) *syn* isomers t_r = 43.5 min.

(2*S*, 3*R*)-3-Hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde (Table 2, entry 10). Freshly prepared triisopropylsilanoxy-acetaldehyde (900 mg, 4.17 mmol) was added to a 4 ºC stirring solution of (2*S*, 5*S*)-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 Et_2O (1.38 mL). After 36 h, the reaction was diluted in Et_2O, and then successively washed with saturated aqueous solutions of NH_4Cl, $NaHCO_3$, and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography (40:1 pentane: Et_2O) 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, 1248, 1119, 1068, 1015, 996.0, 882.3, 785.8, 683.1 cm^{-1}. ^1H NMR and ^{13}C NMR data are consistent with those already reported,[6] $[\alpha]_D = 0.60$ (c = 1.0, $CHCl_3$).

Determination of the absolute stereochemistry of (2*S*, 3*R*)-3-Hydroxy-2,3-bis-triisopropylsilanoxy-propionaldehyde. (2*S*, 3*R*)-3-Hydroxy-2,3-bis-triisopropylsilanoxy-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-benzylidine-D-threitol, whose IR, ^1H NMR and ^{13}C NMR data are consistent with those already reported.[7] $[\alpha]_D = -3.75$ (c = 0.7, MeOH); lit: $[\alpha]_D = -6$ (c = 1.0, MeOH)

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