

(Diisopinocampheyl)borane-Mediated Reductive Aldol Reactions of Acrylate Esters: Enantioselective Synthesis of *Anti*-Aldols

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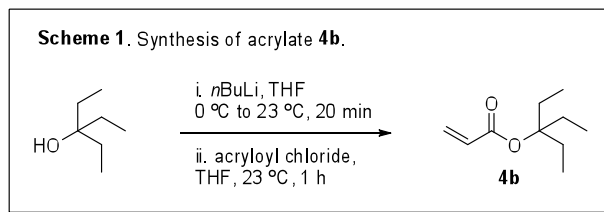
[‡]These authors equally contributed.

SUPPORTING INFORMATION – Experimental Procedures

General Methods: Tetrahydrofuran, dichloromethane, and toluene were purified by passing through a solvent column of activated alumina (A-1). Anhydrous diethyl ether was used directly from the sealed bottle (Sigma-Aldrich, 296082). Commercially available reagents were used without further purification. Commercially available *tert*-butyl acrylate (Acros Organics, 37113) was stored under an inert atmosphere in a $-20\text{ }^{\circ}\text{C}$ freezer and used without further purification. All commercially available aldehydes were purified by distillation under vacuum prior to use. (Diisopinocampheyl)borane was prepared according to the procedure described by Brown.¹ Standard handling techniques for air-sensitive compounds were employed for all the operations. Unless otherwise indicated, all reactions were conducted under an atmosphere of argon using flamed-dried glassware. Removal of solvents was accomplished on a rotary evaporator at reduced pressure. Enantiomeric excess and absolute configurations were determined by using the Mosher² method.

Physical Properties and Spectroscopic Measurements: ^1H NMR spectra were recorded on a Bruker spectrometer at 400 MHz. ^{13}C NMR spectra were recorded on a Bruker spectrometer at 100 MHz. The proton signal for non-deuterated solvent (δ 7.26 ppm for CHCl_3) was used as an internal reference for ^1H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the δ 77.0 ppm resonance of CDCl_3 . Infrared (IR) spectra were recorded neat on a Perkin-Elmer Spectrum One FT-IR Spectrometer equipped with Universal ATR Sampling Accessory. Optical rotations were measured on a Rudolph Autopol IV polarimeter using a quartz cell with 1 mL capacity and a 1 dm path length. High-resolution mass spectra were recorded on a spectrometer at the University of Illinois Mass Spectrometry Laboratory. Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates precoated with a 0.25-mm thickness of silica gel. TLC plates were visualized with UV light and/or by staining with cerium molybdate (5g $\text{Ce}(\text{SO}_4)_2$, 25g $(\text{NH}_4)\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$, 450 mL H_2O , 50 mL H_2SO_4). Preparative thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates precoated with a 0.5-mm thickness of silica gel. Column chromatography was generally performed according to the method of Still³ using Kieselgel 60 (230-400 mesh) silica gel.

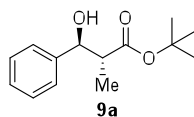
Synthesis of Acrylate **4b**



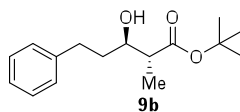
To a 0 °C solution of 3-ethyl-3-pentanol (2.75 mL, 20 mmol) in THF (60 mL) was added *n*-butyllithium (1.6 M in hexanes, 13.75 mL, 22 mmol) and the mixture was allowed to warm up to room temperature for 20 min. A solution of acryloyl chloride (1.86 mL, 22 mmol) in THF (6 mL) was then added dropwise and the mixture was stirred for 1 h. The reaction was then diluted with saturated aqueous NH₄Cl solution. The organic layer was separated, dried over Na₂SO₄ and filtered into a 100-mL round-bottom flask equipped with a distillation set-up. THF was gently evaporated and acrylate **4b** was obtained by distillation (60-62 °C, 13 Torr) as a colorless oil (2.4 g, 70 %): ¹H (400 MHz, CDCl₃) 6.22 (dd, *J* = 1.7, 17.3 Hz, 1H), 5.97 (dd, *J* = 10.4, 17.3 Hz, 1H), 5.64 (dd, *J* = 1.8, 10.3 Hz, 1H), 1.79 (q, *J* = 7.6 Hz, 6H), 0.75 (t, *J* = 7.6 Hz, 9H); ¹³C (100 MHz, CDCl₃) 165.0, 130.0, 128.9, 88.2, 26.6 (3C), 7.4 (3C); IR (neat) 2972, 2945, 2884, 1717, 1636, 1620, 1458, 1402, 1297, 1276, 1198, 1134, 985, 920, 865, 811 cm⁻¹; HRMS (ESI) calcd for C₁₀H₁₉O₂ [M+H]⁺ 171.1380, found 171.1383.

General Procedure for Reductive Aldol Reactions

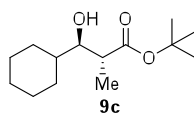
To a 0 °C suspension of (^l or ^dIpc)₂BH [weighed and crushed into a fine powder in a glovebox], 72 mg, 0.25 mmol) in Et₂O (1.0 mL) was added acrylate **4** (0.275 mmol). The solution was stirred 2 h at 0 °C at which time it became homogeneous. The resulting mixture was cooled to -78 °C, aldehyde **7** (0.213 mmol) was added, and the solution was stirred at -78 °C for 12 h. Aqueous pH 7 buffer solution (0.5 mL) in methanol (0.5 mL) followed by an aqueous solution of hydrogen peroxide (35% wt, 0.5 mL) in methanol (0.5 mL) were added to the reaction mixture, and the resulting mixture was then stirred for 6 h at room temperature. The aqueous phase was extracted three times with CH₂Cl₂ (10 mL each). The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. Purification of the crude product by flash chromatography (90:10 hexanes-ethyl acetate) provided the β-hydroxyesters **9** (from **4a**) or **10** (from **4b**). In certain cases a second flash chromatography step is required to completely remove isopinocampheol using (90/10 : toluene/ethyl acetate).



tert-butyl (2*R*,3*S*)-3-hydroxy-2-methyl-3-phenylpropanoate (9a): prepared from **4a** and (*^t*Ipc)₂BH (40mg, 79% yield, dr 18:1, 86% ee *anti*, 51% ee for minor *syn* isomer), clear oil: $[\alpha]_D^{27.1} = -17.7$ ($c = 0.13$, EtOH); ¹H (400 MHz, CDCl₃) δ *anti*: 7.37-7.33 (m, 4H), 7.32-7.29 (m, 1H), 4.71 (dd, $J = 4.9, 8.0$ Hz, 1H), 3.18 (d, $J = 4.9$ Hz, 1H), 2.72 (quint., $J = 7.5$ Hz, 1H), 1.45 (s, 9H), 1.03 (d, $J = 7.2$ Hz, 3H); ¹H (400 MHz, CDCl₃) δ *syn* (**10a**): 5.02 (dd, $J = 3.0, 4.4$ Hz, 1H), 3.12 (d, $J = 3.0$ Hz, 1H), 2.68 (dq, $J = 4.4, 7.2$ Hz, 1H), 1.39 (s, 9H), 1.10 (d, $J = 7.2$ Hz, 3H); ¹³C (100 MHz, CDCl₃) δ *anti*: 175.34, 141.8, 128.3 (2C), 127.8, 126.6 (2C), 81.2, 76.3, 47.7, 28.0 (3C), 14.7; ¹³C (100 MHz, CDCl₃) δ *syn* (**10a**): 175.31, 141.5, 128.1 (2C), 127.4, 126.1 (2C), 81.1, 73.8, 47.0, 27.9 (3C), 11.1; IR (neat) 3452, 2978, 2936, 1727, 1456, 1367, 1148, 1020 cm⁻¹; HRMS (ESI) calcd for C₁₄H₂₀O₃Na [M+Na]⁺ 259.1310, found 259.1315.

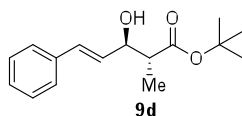


tert-butyl (2*R*,3*R*)-3-hydroxy-2-methyl-5-phenylpentanoate (9b): prepared from **4a** and (*^t*Ipc)₂BH (49 mg, 87% yield, dr 20:1, 64% ee), clear oil: $[\alpha]_D^{28.5} = +4.3$ ($c = 0.14$, CHCl₃); ¹H (400 MHz, CDCl₃) δ 7.32-7.25 (m, 2H), 7.23-7.15 (m, 3H), 3.63 (dddd, $J = 4.0, 6.0, 6.9, 8.8$ Hz, 1H), 2.92 (d, $J = 7.3$ Hz, 1H), 2.87 (ddd, $J = 5.0, 8.9, 13.7$ Hz, 1H), 2.70 (ddd, $J = 7.1, 9.5, 13.7$ Hz, 1H), 2.43 (dq, $J = 5.9, 7.2$ Hz, 1H), 1.83-1.71 (m, 2H), 1.46 (s, 9H), 1.18 (d, $J = 7.2$ Hz, 3H); ¹³C (100 MHz, CDCl₃) δ 175.5, 142.0, 128.5 (2C), 128.4 (2C), 125.8, 81.1, 72.7, 45.8, 36.7, 32.0, 28.1 (3C), 14.4; IR (neat) 3458, 2978, 2935, 1726, 1456, 1367, 1148 cm⁻¹; HRMS (ESI) calcd for C₁₆H₂₄O₃Na [M+Na]⁺ 287.1623, found 287.1621.

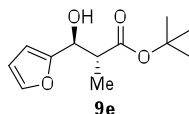


tert-butyl (2*R*,3*R*)-3-cyclohexyl-3-hydroxy-2-methylpropanoate (9c): prepared from **4a** and (*^t*Ipc)₂BH (36 mg, 70% yield, dr 20:1, 59% ee), clear oil: $[\alpha]_D^{28.6} = -3.7$ ($c = 0.43$, CHCl₃); ¹H (400 MHz, CDCl₃) δ 3.29 (dt, $J = 5.4, 6.8$ Hz, 1H), 2.69 (d, $J = 7.9$ Hz, 1H), 2.57 (dq, $J = 5.6, 7.2$ Hz, 1H), 1.90-1.84 (m, 1H), 1.80-1.73 (m, 2H), 1.68-1.62 (m, 2H), 1.46 (s, 9H), 1.24-0.99 (m, 6H), 1.2 (d, $J = 7.2$ Hz, 3H); ¹³C (100 MHz, CDCl₃) δ 176.1, 81.0, 78.0, 42.4, 41.6, 29.9, 28.1 (3C), 27.5,

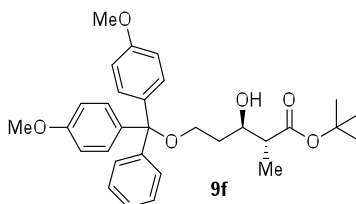
26.41, 26.37, 26.1, 15.0; IR (neat) 3498, 2977, 2925, 2853, 1709, 1451, 1393, 1368, 1256, 1207, 1152, 986, 851 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{26}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 265.1780, found 265.1776.



tert-butyl (2R,3R,4E)-3-hydroxy-2-methyl-5-phenylpent-4-enoate (9d): prepared from **4a** and $(^i\text{Pr})_2\text{BH}$ (39 mg, 69% yield, dr 13:1, 64% ee *anti*, 23% ee for minor *syn* isomer), clear oil: $[\alpha]_{\text{D}}^{28.5} = -6.8$ ($c = 0.19$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 7.40-7.35 (m, 2H), 7.34-7.29 (m, 2H), 7.26-7.22 (m, 1H), 6.64 (d, $J = 16.0$ Hz, 1H), 6.19 (dd, $J = 6.6, 15.9$ Hz, 1H), 4.33 (ddt, $J = 1.3, 5.7, 6.8$ Hz, 1H), 2.90 (d, $J = 5.8$ Hz, 1H), 2.56 (quint., $J = 7.1$ Hz, 1H), 1.46 (s, 9H), 1.21 (d, $J = 7.1$ Hz, 3H); ^{13}C (100 MHz, CDCl_3) δ 174.9, 136.5, 131.7, 129.6, 128.5 (2C), 127.7, 126.5 (2C), 81.2, 74.6, 46.2, 28.1 (3C), 14.2; IR (neat) 3444, 2977, 2936, 1725, 1368, 1151 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{22}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 285.1467, found 285.1472.

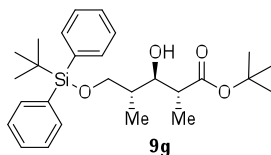


tert-butyl (2R,3S)-3-(2-furyl)-3-hydroxy-2-methylpropanoate (9e): prepared from **4a** and $(^i\text{Pr})_2\text{BH}$ (39 mg, 81% yield, dr 15:1, 73% ee), clear oil: $[\alpha]_{\text{D}}^{28.6} = -22.7$ ($c = 0.18$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 7.36 (dd, $J = 0.7, 1.9$ Hz, 1H), 6.32 (dd, $J = 1.8, 3.2$ Hz, 1H), 6.27 (td, $J = 0.9, 3.2$ Hz, 1H), 4.71 (t, $J = 7.0$ Hz, 1H), 3.31 (d, $J = 6.6$ Hz, 1H), 2.89 (quint., $J = 7.2$ Hz, 1H), 1.44 (s, 9H), 1.10 (d, $J = 7.2$ Hz, 3H); ^{13}C (100 MHz, CDCl_3) δ 174.9, 154.6, 142.1, 110.1, 107.2, 81.3, 69.9, 45.1, 28.0 (3C), 14.3; IR (neat) 3437, 2978, 2935, 1725, 1368, 1148, 1009 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 249.1103, found 249.1108.

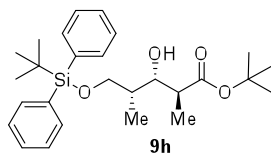


tert-butyl 5-O-[bis(4-methoxyphenyl)(phenyl)methyl]-2,4-dideoxy-2-methyl-D-erythro-pentionate (9f): prepared from **4a** and $(^i\text{Pr})_2\text{BH}$ (40 mg, 77% yield, dr 20:1, 54% ee), clear oil: $[\alpha]_{\text{D}}^{28.6} = -10.0$ ($c = 0.22$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 7.44-7.39 (m, 2H), 7.33-7.27 (m, 6H), 7.24-7.17 (m, 1H), 6.85-6.80 (m, 4H), 3.90-3.83 (m, 1H), 3.79 (s, 6H), 3.34 (td, $J = 6.0, 9.3$ Hz, 1H), 3.23 (ddd, $J = 5.6, 6.9, 9.3$ Hz, 1H), 3.13 (d, $J = 5.2$ Hz, 1H), 2.41 (quint., $J = 6.8$ Hz, 1H),

1.81-1.67 (m, 2H), 1.44 (s, 9H), 1.14 (d, $J = 7.2$ Hz, 3H); ^{13}C (100 MHz, CDCl_3) δ 175.1, 158.4 (2C), 144.9, 136.2, 136.1, 130.0 (4C), 128.1 (2C), 127.8 (2C), 126.7, 113.1 (4C), 86.4, 80.7, 72.2, 61.6, 55.2 (2C), 46.0, 34.3, 28.1 (3C), 13.8; IR (neat) 3511, 2934, 1724, 1608, 1509, 1247, 1175, 1151, 1068, 1032, 910, 827 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{38}\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 529.2566, found 529.2572.

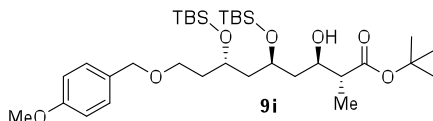


tert-butyl 5-O-[tert-butyl(diphenyl)silyl]-2,4-dideoxy-2,4-dimethyl-D-ribonate (9g): prepared from **7g** and **4a** using $(^1\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture indicated dr 4:1; **9g** isolated after purification: 64 mg, 66% yield, dr 9:1), clear oil: $[\alpha]_{\text{D}}^{28.6} = -14.3$ ($c = 0.53$, CHCl_3); ^1H (400 MHz, CDCl_3) δ *major*: 7.68 (ddd, $J = 1.8, 3.8, 7.7$ Hz, 4H), 7.44-7.36 (m, 6H), 3.75 (dd, $J = 4.9, 10.0$ Hz, 1H), 3.71 (dd, $J = 5.3, 10.0$ Hz, 1H), 3.57 (broad q, $J = 6.0$ Hz, 1H), 3.42 (broad d, $J = 7.1$ Hz, 1H), 2.64 (dq, $J = 5.2, 7.2$ Hz, 1H), 1.85 (tquint., $J = 5.1, 6.9$ Hz, 1H), 1.46 (s, 9H), 1.18 (d, $J = 7.1$ Hz, 3H), 1.05 (s, 9H), 0.99 (d, $J = 7.0$ Hz, 3H); ^1H (400 MHz, CDCl_3) δ *minor*: see **9h**; ^{13}C (100 MHz, CDCl_3) δ *major*: 175.2, 135.6 (4C), 133.24, 133.22, 129.7 (2C), 127.70 (2C), 127.68 (2C), 80.7, 77.2, 66.8, 43.3, 38.4, 28.1 (3C), 26.8 (3C), 19.2, 14.6, 14.4; ^{13}C (100 MHz, CDCl_3) δ *minor*: see **9h**; IR (neat) 3502, 2964, 2932, 2858, 1707, 1590, 1473, 1461, 1428, 1392, 1368, 1257, 1150, 1111, 1075, 823, 740, 700 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{41}\text{O}_4\text{Si}$ $[\text{M}+\text{H}]^+$ 457.2774, found 457.2774.



tert-butyl 5-O-[tert-butyl(diphenyl)silyl]-2,4-dideoxy-2,4-dimethyl-D-lyxonate (9h): prepared from **7g** and **4a** using $(^d\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture indicated the reaction dr = 6:1; **9h** isolated after purification: 58 mg, 60% yield, dr 7:1), clear oil: $[\alpha]_{\text{D}}^{28.6} = -3.3$ ($c = 0.40$, CHCl_3); ^1H (400 MHz, CDCl_3) δ *major*: 7.71-7.66 (m, 4H), 7.46-7.37 (m, 6H), 3.95 (ddd, $J = 3.1, 4.7, 8.3$ Hz, 1H), 3.70 (d, $J = 5.6$ Hz, 2H), 2.82 (d, $J = 4.9$ Hz, 1H), 2.51 (qd, $J = 7.2, 8.4$ Hz, 1H), 1.78 (dtq, $J = 3.4, 5.5, 7.0$ Hz, 1H), 1.47 (s, 9H), 1.10 (d, $J = 7.1$ Hz, 3H), 1.08 (s, 9H), 0.91 (d, $J = 7.0$ Hz, 3H); ^1H (400 MHz, CDCl_3) δ *minor*: see **9g**; ^{13}C (100 MHz, CDCl_3) δ *major*: 175.8, 135.7 (2C), 135.6 (2C), 133.6, 133.4, 129.74, 129.71, 127.7 (4C), 80.7, 74.0, 67.5, 44.1, 37.1, 28.1

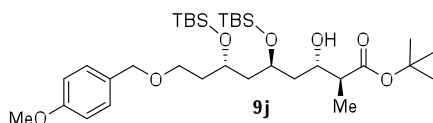
(3C), 26.9 (3C), 19.3, 14.5, 9.8; ^{13}C (100 MHz, CDCl_3) δ *minor*: see **9g**; IR (neat) 3518, 2965, 2932, 2859, 2323, 1710, 1473, 1458, 1428, 1392, 1368, 1257, 1151, 1106, 1082, 1028, 986, 824, 740, 700 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{41}\text{O}_4\text{Si}$ $[\text{M}+\text{H}]^+$ 457.2774, found 457.2767.



tert-butyl

5,7-bis-*O*-[*tert*-butyl(dimethyl)silyl]-2,4,6,8-tetradecoxy-9-*O*-(4-

methoxybenzyl)-2-methyl-*D*-allo-nononate (9i**):** prepared from **7h** and **4a** using $(^l\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 4:1; **9i** isolated after purification: 101 mg, 74% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{28.6} = -6.7$ ($c = 0.64$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 7.26-7.22 (m, 2H), 6.88-6.84 (m, 2H), 4.42 (d, $J = 11.5$ Hz, 1H), 4.38 (d, $J = 11.5$ Hz, 1H), 3.95 (quint., $J = 6.4$ Hz, 1H), 3.90-3.83 (m, 1H), 3.82-3.75 (m, 1H), 3.80 (s, 3H), 3.53-3.45 (m, 2H), 3.21 (d, $J = 4.5$ Hz, 1H), 2.41 (dq, $J = 5.8, 7.2$ Hz, 1H), 1.84-1.53 (m, 6H), 1.44 (s, 9H), 1.14 (d, $J = 7.2$ Hz, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.08 (s, 6H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C (100 MHz, CDCl_3) δ 174.8, 159.0, 130.6, 129.2 (2C), 113.7 (2C), 80.6, 72.6, 71.5, 69.6, 67.3, 66.6, 55.2, 46.5, 46.1, 41.6, 37.5, 28.1 (3C), 25.85 (3C), 25.84 (3C), 18.0, 17.9, 13.6, -4.0, -4.2, -4.3, -4.4; IR (neat) 3506, 2953, 2930, 2857, 1727, 1614, 1514, 1472, 1463, 1368, 1249, 1154, 1094, 1039, 910, 833, 773, 732 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{34}\text{H}_{65}\text{O}_7\text{Si}_2$ $[\text{M}+\text{H}]^+$ 641.4269, found 641.4265.

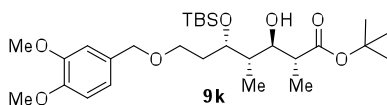


tert-butyl

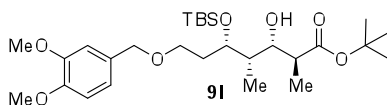
5,7-bis-*O*-[*tert*-butyl(dimethyl)silyl]-2,4,6,8-tetradecoxy-9-*O*-(4-

methoxybenzyl)-2-methyl-*L*-gulo-nononate (9j**):** prepared from **7h** and **4a** using $(^d\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 3:1; **9j** isolated after purification: 68 mg, 50% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{28.6} = -15.9$ ($c = 0.39$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 7.27-7.21 (m, 2H), 6.88-6.83 (m, 2H), 4.42 (d, $J = 11.4$ Hz, 1H), 4.38 (d, $J = 11.4$ Hz, 1H), 4.07-3.93 (m, 2H), 3.84-3.77 (m, 1H), 3.79 (s, 3H), 3.50 (dd, $J = 6.3, 7.2$ Hz, 2H), 3.35 (d, $J = 4.3$ Hz, 1H), 2.38 (quint., $J = 6.9$ Hz, 1H), 1.84-1.62 (m, 4H), 1.59 (dd, $J = 3.6, 10.3$ Hz, 1H), 1.52 (ddd, $J = 2.6, 6.3, 14.0$ Hz, 1H), 1.45 (s, 9H), 1.11 (d, $J = 7.1$ Hz, 3H), 0.87 (s, 9H), 0.86 (s, 9H), 0.08 (s, 3H), 0.07 (s, 6H), 0.04 (s, 3H); ^{13}C (100 MHz, CDCl_3) δ 174.8, 159.1, 130.5, 129.2 (2C), 113.7 (2C), 80.5, 72.6, 70.0, 68.3, 67.2, 66.5, 55.2, 46.6, 45.4, 39.9, 37.1, 28.1 (3C), 25.8 (6C), 18.0, 17.9, 13.7, -4.1, -4.36, -4.44, -4.66; IR (neat) 3507, 2953, 2930, 2857, 1728, 1614, 1514, 1472, 1463, 1368, 1302, 1249, 1212,

1154, 1094, 1039, 939, 911, 833, 773 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{34}\text{H}_{65}\text{O}_7\text{Si}_2$ $[\text{M}+\text{H}]^+$ 641.4269, found 641.4264.

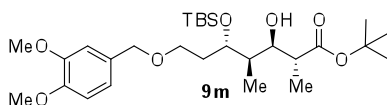


(2R,3R,4S,5S)-tert-butyl 5-((tert-butyldimethylsilyl)oxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (9k): prepared from **7i** and **4a** using $(^t\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 1:2 (**9k**:**9l**); **9k** isolated after purification: 26 mg of **9k**, 23% yield, dr >20:1 and 52 mg of **9l**, 46% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{28.6} = -14.7$ (c = 0.15, CHCl_3); ^1H (400 MHz, CDCl_3) δ *minor*: 6.89-6.812 (m, 3H), 4.44 (d, $J = 11.5$ Hz, 1H), 4.39 (d, $J = 11.5$ Hz, 1H), 4.15 (ddd, $J = 2.2, 5.4, 7.6$ Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.74 (d, $J = 5.9$ Hz, 1H), 3.61 (ddd, $J = 3.3, 5.9, 9.3$ Hz, 1H), 3.48 (dt, $J = 1.9, 6.7$ Hz, 2H), 2.57 (dq, $J = 3.3, 7.1$ Hz, 1H), 1.88-1.75 (m, 3H), 1.43 (s, 9H), 1.21 (d, $J = 7.2$ Hz, 3H), 0.87 (s, 9H), 0.84 (d, $J = 7.0$ Hz, 3H), 0.10 (s, 3H), 0.07 (s, 3H); ^1H (400 MHz, CDCl_3) δ *major*: see **9l**; ^{13}C (100 MHz, CDCl_3) δ 174.5, 148.9, 148.5, 130.9, 120.2, 111.0, 110.8, 80.5, 75.9, 72.9, 71.8, 67.0, 55.9, 55.8, 43.0, 40.9, 33.3, 28.1 (3C), 25.8 (3C), 18.0, 14.1, 11.7, -4.5, -4.6; ^{13}C (100 MHz, CDCl_3) δ *major*: see **9l**; IR (neat) 3480, 2955, 2931, 1728, 1517, 1463, 1367, 1259, 1156, 1078, 1033, 837 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{51}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 527.3404, found 527.3405.

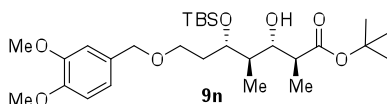


(2S,3S,4S,5S)-tert-butyl 5-((tert-butyldimethylsilyl)oxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (9l): prepared from **7i** and **4a** using $(^d\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 9:1 (**9l**:**9k**); **9l** isolated after purification: 75 mg of **9l**, 67% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{28.5} = +0.4$ (c = 0.82, CHCl_3); ^1H (400 MHz, CDCl_3) δ *major*: 6.88-6.81 (m, 3H), 4.42 (d, $J = 11.6$ Hz, 1H), 4.38 (d, $J = 11.6$ Hz, 1H), 3.92-3.88 (m, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.82 (ddd, $J = 3.0, 5.0, 8.3$ Hz, 1H), 3.46 (t, $J = 6.7$ Hz, 2H), 2.9 (d, $J = 5.1$ Hz, 1H), 2.47 (quint., $J = 7.4$ Hz, 1H), 1.87 (q, $J = 6.5$ Hz, 2H), 1.68-1.60 (m, 1H), 1.44 (s, 9H), 1.07 (d, $J = 7.1$ Hz, 3H), 0.89 (d, $J = 7.0$ Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^1H (400 MHz, CDCl_3) δ *minor*: see **9k**; ^{13}C (100 MHz, CDCl_3) δ *major*: 175.7, 148.9, 148.5, 130.9, 120.2, 110.9, 110.8, 80.7, 74.1, 73.1, 72.9, 66.7, 55.9, 55.8, 44.3, 39.3, 34.2, 28.0 (3C), 25.9 (3C), 18.0, 14.6, 8.1, -4.2, -4.5; ^{13}C (100 MHz, CDCl_3) δ *minor*: see **9k**; IR (neat) 3530, 2952, 2933, 2858, 2323, 1726, 1594,

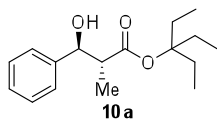
1516, 1464, 1368, 1257, 1154, 1082, 1030, 911, 835, 774, 731 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{51}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 527.3404, found 527.3400.



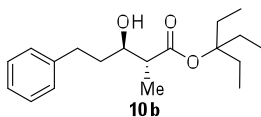
(2R,3R,4R,5S)-tert-butyl 5-((tert-butyldimethylsilyl)oxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (9m): prepared from **7j** and **4a** using $(^t\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 8:1 (**9m**:**9n**); **9m** isolated after purification: 76 mg, 68% yield, dr >20:1), clear oil: $[\alpha]_{\text{D}}^{28.7} = +6.7$ (c = 0.24, CHCl_3); ^1H (400 MHz, CDCl_3) δ 6.87-6.77 (m, 3H), 4.44 (d, $J = 11.6$ Hz, 1H), 4.34 (d, $J = 11.6$ Hz, 1H), 4.06 (td, $J = 2.1, 9.4$ Hz, 1H), 3.94 (ddd, $J = 3.3, 5.9, 7.7$ Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.52-3.37 (m, 2H), 3.39 (d, $J = 2.0$ Hz, 1H), 2.39 (qd, $J = 7.1, 9.4$ Hz, 1H), 2.04-1.85 (m, 2H), 1.58 (ddq, $J = 2.1, 3.3, 7.1$ Hz, 1H), 1.45 (s, 9H), 0.94 (d, $J = 7.0$ Hz, 3H), 0.90 (d, $J = 7.1$ Hz, 3H), 0.86 (s, 9H), 0.068 (s, 3H), 0.065 (s, 3H); ^{13}C (100 MHz, CDCl_3) δ 175.6, 148.9, 148.5, 130.8, 120.2, 110.9, 110.8, 80.4, 75.2, 72.8, 72.1, 66.2, 55.8, 55.7, 44.3, 36.1, 34.6, 28.0 (3C), 25.8 (3C), 17.9, 14.0, 10.4, -4.60, -4.66; IR (neat) 3495, 2955, 2932, 2858, 1728, 1516, 1463, 1367, 1257, 1153, 1088, 1030 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{51}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 527.3404, found 527.3406.



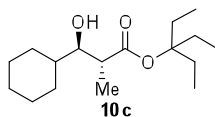
(2S,3S,4R,5S)-tert-butyl 5-((tert-butyldimethylsilyl)oxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (9n): prepared from **7j** and **4a** using $(^d\text{Ipc})_2\text{BH}$. ^1H NMR analysis of crude reaction mixture, dr = 3:1 (**9n**:**9m**); **9n** isolated after purification: 73 mg, 65% yield, dr 2:1), clear oil: $[\alpha]_{\text{D}}^{28.7} = -9.7$ (c = 0.34, CHCl_3); ^1H (400 MHz, CDCl_3) δ *major*: 6.91-6.78 (m, 3H), 4.42 (s, 2H), 4.24 (ddd, $J = 2.4, 3.8, 9.7$ Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.57 (dt, $J = 4.6, 8.8$ Hz, 1H), 3.49 (td, $J = 7.5, 9.0$ Hz, 1H), 3.25-3.16 (m, 2H), 2.59 (dq, $J = 2.1, 7.3$ Hz, 1H), 1.81-1.70 (m, 2H), 1.66-1.54 (m, 1H), 1.45 (s, 9H), 1.27 (d, $J = 7.2$ Hz, 3H), 0.85 (s, 9H), 0.84 (d, $J = 6.9$ Hz, 3H), 0.01 (s, 6H); ^1H (400 MHz, CDCl_3) δ *minor*: see **9m**; ^{13}C (100 MHz, CDCl_3) δ *major*: 176.1, 148.9, 148.4, 131.2, 120.2, 111.1, 110.8, 81.3, 76.1, 72.8, 69.5, 67.9, 55.9, 55.7, 44.4, 41.7, 30.9, 28.0 (3C), 25.8 (3C), 18.0, 15.4, 10.2, -4.5, -4.7; ^{13}C (100 MHz, CDCl_3) δ *minor*: see **9m**; IR (neat) 3488, 2956, 2933, 2857, 1727, 1516, 1463, 1367, 1257, 1151, 1091, 1030 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{28}\text{H}_{51}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 527.3404, found 527.3410.



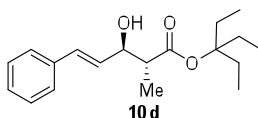
(2R,3S)-3-ethylpentan-3-yl 3-hydroxy-2-methyl-3-phenylpropanoate (10a): prepared from **4b** and (*t*-Ipc)₂BH (48 mg, 81% yield, dr 14:1, 85% ee *anti*, 98% ee for minor *syn* isomer), clear oil: $[\alpha]_D^{26.9} = -27.4$ ($c = 0.35$, CHCl₃); ¹H (400 MHz, CDCl₃) δ *anti*: 7.36-7.33 (m, 4H), 7.32-7.27 (m, 1H), 4.69 (dd, $J = 4.8, 8.0$ Hz, 1H), 3.30 (d, $J = 4.6$ Hz, 1H), 2.74 (qd, $J = 7.2, 7.9$ Hz, 1H), 1.82 (q, $J = 7.6$ Hz, 6H), 1.05 (d, $J = 7.3$ Hz, 3H), 0.79 (t, $J = 7.5$ Hz, 9H); ¹H (400 MHz, CDCl₃) δ *syn*: 5.07 (d, $J = 4.1$ Hz, 1H), 3.13 (broad s, 1H), 2.73 (qd, $J = 7.1, 4.2$ Hz, 1H), 1.81 (q, $J = 7.6$ Hz, 6H), 1.11 (d, $J = 7.2$ Hz, 3H), 0.78 (t, $J = 7.5$ Hz, 9H); ¹³C (100 MHz, CDCl₃) δ *anti*: 175.1, 141.9, 128.3 (2C), 127.8, 126.6 (2C), 89.3, 76.3, 47.9, 26.8 (3C), 15.1, 7.50 (3C); ¹³C (100 MHz, CDCl₃) δ *syn*: 175.1, 141.6, 128.2 (2C), 127.3, 126.1 (2C), 89.2, 73.6, 47.0, 26.8 (3C), 11.0, 7.53 (3C); IR (neat) 3479, 2972, 2942, 2883, 2318, 1707, 1495, 1457, 1379, 1259, 1189, 1135, 1081, 1021, 891, 867, 766, 733, 701 cm⁻¹; HRMS (ESI) calcd for C₁₇H₂₇O₃ [M+H]⁺ 279.1960, found 279.1963.



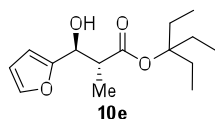
(2R,3R)-3-ethylpentan-3-yl 3-hydroxy-2-methyl-5-phenylpentanoate (10b): prepared from **4b** and (*t*-Ipc)₂BH (49 mg, 75% yield, dr 13:1, 87% ee *anti*), clear oil: $[\alpha]_D^{26.9} = +7.5$ ($c = 0.60$, CHCl₃); ¹H (400 MHz, CDCl₃) δ *anti*: 7.31-7.26 (m, 2H), 7.23-7.16 (m, 3H), 3.63 (broad s, 1H), 2.98 (broad s, 1H), 2.88 (ddd, $J = 5.6, 9.6, 13.7$ Hz, 1H), 2.70 (ddd, $J = 7.0, 9.6, 13.7$ Hz, 1H), 2.46 (dq, $J = 6.4, 7.3$ Hz, 1H), 1.84 (q, $J = 7.5$ Hz, 6H), 1.86-1.74 (m, 2H), 1.21 (d, $J = 7.3$ Hz, 3H), 0.83 (t, $J = 7.5$ Hz, 9H); ¹H (400 MHz, CDCl₃) δ *syn*: 3.91 (ddd, $J = 3.2, 3.6, 9.3$ Hz, 1H), 1.83 (q, $J = 7.5$ Hz, 6H), 1.14 (d, $J = 7.5$ Hz, 3H), 0.82 (t, $J = 7.5$ Hz, 9H); ¹³C (100 MHz, CDCl₃) δ *anti*: 175.3, 142.1, 128.4 (2C), 128.3 (2C), 125.75, 89.3, 72.7, 46.0, 36.6, 32.0, 26.8 (3C), 14.8, 7.6 (3C); ¹³C (100 MHz, CDCl₃) δ *syn*: 175.4, 142.0, 128.6 (2C), 128.2 (2C), 125.79, 89.1, 71.0, 45.1, 35.6, 32.4, 26.8 (3C), 10.9, 7.6 (3C); IR (neat) 3469, 2972, 2942, 2883, 1705, 1604, 1497, 1456, 1380, 1359, 1264, 1192, 1133, 1097, 1079, 1041, 934, 866, 747, 700 cm⁻¹; HRMS (ESI) calcd for C₁₉H₃₁O₃ [M+H]⁺ 307.2273, found 307.2271.



(2R,3R)-3-ethylpentan-3-yl 3-cyclohexyl-3-hydroxy-2-methylpropanoate (10c): prepared from **4b** and (ⁱIpc)₂BH (44 mg, 73% yield, dr >20:1, 83% ee *anti*), clear oil: $[\alpha]_D^{26.8} = -2.6$ (c = 0.43, CHCl₃); ¹H (400 MHz, CDCl₃) δ 3.24 (ddd, *J* = 5.5, 6.5, 8.2 Hz, 1H), 2.79 (d, *J* = 8.2 Hz, 1H), 2.60 (dq, *J* = 5.4, 7.2 Hz, 1H), 1.94-1.87 (m, 1H), 1.85-1.79 (m, 6H), 1.77-1.71 (m, 2H), 1.67-1.60 (m, 2H), 1.38 (tdt, *J* = 3.3, 6.3, 11.4 Hz, 1H), 1.25-1.19 (m, 1H), 1.22 (d, *J* = 7.3 Hz, 3H), 1.18-1.00 (m, 4H), 0.82 (t, *J* = 7.5 Hz, 9H); ¹³C (100 MHz, CDCl₃) δ 175.9, 89.1, 78.0, 42.4, 41.5, 30.0, 27.7, 26.8 (3C), 26.4, 26.3, 26.0, 15.5, 7.5 (3C); IR (neat) 3518, 2972, 2927, 2854, 1705, 1457, 1379, 1259, 1193, 1181, 1132, 1079, 1034, 986, 917, 878, 731 cm⁻¹; HRMS (ESI) calcd for C₁₇H₃₂O₃Na [M+Na]⁺ 307.2249, found 307.2250.

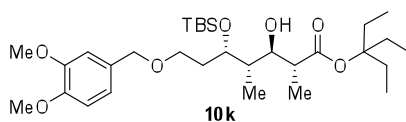


(2R,3R,E)-3-ethylpentan-3-yl 3-hydroxy-2-methyl-5-phenylpent-4-enoate (10d): prepared from **4b** and (ⁱIpc)₂BH (44 mg, 68% yield, dr 13:1, 84% ee *anti*), clear oil: $[\alpha]_D^{26.8} = +3.0$ (c = 0.10, CHCl₃); ¹H (400 MHz, CDCl₃) δ *anti*: 7.39-7.36 (m, 2H), 7.34-7.29 (m, 2H), 7.26-7.21 (m, 1H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 6.8, 15.8 Hz, 1H), 4.33 (ddd, *J* = 4.4, 6.7, 7.1 Hz, 1H), 3.06 (d, *J* = 4.9 Hz, 1H), 2.59 (quint., *J* = 7.2 Hz, 1H), 1.84 (q, *J* = 7.6 Hz, 6H), 1.23 (d, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.5 Hz, 9H); ¹H (400 MHz, CDCl₃) δ *syn*: 6.67 (dd, *J* = 1.3, 15.9 Hz, 1H), 6.21 (dd, *J* = 5.8, 15.8 Hz, 1H), 4.60-4.55 (m, 1H), 3.03 (d, *J* = 4.6 Hz, 1H), 2.67 (dq, *J* = 4.0, 7.2 Hz, 1H), 1.21 (d, *J* = 7.2 Hz, 3H); ¹³C (100 MHz, CDCl₃) δ *anti*: 174.7, 136.5, 131.9, 129.6, 128.50 (2C), 127.7, 126.49 (2C), 89.35, 74.6, 46.5, 26.77 (3C), 14.7, 7.57 (3C); ¹³C (100 MHz, CDCl₃) δ *syn*: 174.6, 136.7, 131.3, 128.8, 128.48 (2C), 127.6, 126.44 (2C), 89.37, 72.9, 45.6, 26.80 (3C), 11.7, 7.60 (3C); IR (neat) 3445, 2972, 2942, 2883, 1705, 1496, 1457, 1379, 1357, 1263, 1188, 1133, 1080, 1030, 967, 923, 892, 866, 749, 693 cm⁻¹; HRMS (ESI) calcd for C₁₉H₂₈O₃Na [M+Na]⁺ 327.1936, found 327.1935.

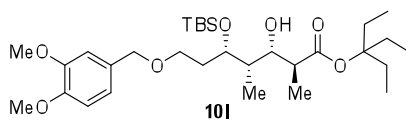


(2R,3S)-3-ethylpentan-3-yl 3-(furan-2-yl)-3-hydroxy-2-methylpropanoate (10e): prepared from **4b** and (ⁱIpc)₂BH (39 mg, 68% yield, dr 10:1, 83% ee *anti*), clear oil: $[\alpha]_D^{26.8} = -16.6$

($c = 0.47$, CHCl_3); ^1H (400 MHz, CDCl_3) δ *anti*: 7.36 (dd, $J = 0.9$, 1.8 Hz, 1H), 6.32 (dd, $J = 1.8$, 3.2 Hz, 1H), 6.29 (d, $J = 3.2$ Hz, 1H), 4.71 (dd, $J = 6.4$, 7.5 Hz, 1H), 3.37 (d, $J = 6.5$ Hz, 1H), 2.95 (quint., $J = 7.4$ Hz, 1H), 1.82 (q, $J = 7.5$ Hz, 6H), 1.13 (d, $J = 7.3$ Hz, 3H), 0.80 (t, $J = 7.5$ Hz, 9H); ^1H (400 MHz, CDCl_3) δ *syn*: 7.34 (dd, $J = 0.8$, 1.7 Hz, 1H), 5.0 (dd, $J = 4.7$, 5.1 Hz, 1H), 3.06 (d, $J = 5.3$ Hz, 1H), 2.91 (dq, $J = 4.9$, 7.2 Hz, 1H), 1.20 (d, $J = 7.2$ Hz, 3H); ^{13}C (100 MHz, CDCl_3) δ *anti*: 174.7, 154.6, 142.1, 110.15, 107.3, 89.5, 69.9, 45.2, 26.76 (3C), 14.8, 7.52 (3C); ^{13}C (100 MHz, CDCl_3) δ *syn*: 174.2, 154.5, 141.7, 110.20, 106.7, 89.4, 68.8, 44.7, 26.77 (3C), 12.1, 7.54 (3C); IR (neat) 3477, 2973, 2944, 2884, 1709, 1505, 1458, 1381, 1263, 1190, 1135, 1010, 922, 881, 811, 736 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{24}\text{O}_4\text{Na}$ $[\text{M}+\text{Na}]^+$ 291.1572, found 291.1573.



(2*R*,3*R*,4*S*,5*S*)-3-ethylpentan-3-yl-5-((*tert*-butyldimethylsilyloxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (10k): prepared from **7i**, **4b** and (^tIpc) $_2\text{BH}$; ^1H NMR analysis of crude reaction mixture, dr = 2:1 (**10k**:**10l**); **10k** isolated after purification: 56 mg, 46% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{27.1} = -7.0$ ($c = 0.39$, CHCl_3); ^1H (400 MHz, CDCl_3) δ 6.89-6.79 (m, 3H), 4.42 (d, $J = 11.4$ Hz, 1H), 4.38 (d, $J = 11.4$ Hz, 1H), 4.21 (ddd, $J = 2.2$, 6.1, 7.3 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.58 (d, $J = 7.1$ Hz, 1H), 3.50 (ddd, $J = 3.9$, 7.5, 9.4 Hz, 1H), 3.45 (t, $J = 6.7$ Hz, 2H), 2.61 (dq, $J = 3.5$, 7.2 Hz, 1H), 1.90-1.67 (m, 9H), 1.24 (d, $J = 7.2$ Hz, 3H), 0.86 (s, 9H), 0.85 (d, $J = 7.5$ Hz, 3H), 0.80 (t, $J = 7.5$ Hz, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^1H (400 MHz, CDCl_3) δ *minor*: see **10l**; ^{13}C (100 MHz, CDCl_3) δ 174.7, 149.0, 148.5, 130.9, 120.1, 111.0, 110.9, 88.8, 75.8, 72.9, 70.7, 67.0, 55.9, 55.8, 42.9, 41.0, 34.0, 26.8 (3C), 25.8 (3C), 18.0, 15.2, 11.1, 7.6 (3C), -4.5, -4.6; ^{13}C (100 MHz, CDCl_3) δ *minor*: see **10l**; IR (neat) 3502, 2934, 2884, 2857, 1703, 1594, 1516, 1459, 1419, 1385, 1360, 1259, 1190, 1157, 1133, 1079, 1032, 937, 868, 835, 802, 775 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{57}\text{O}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 569.3874, found 569.3872.

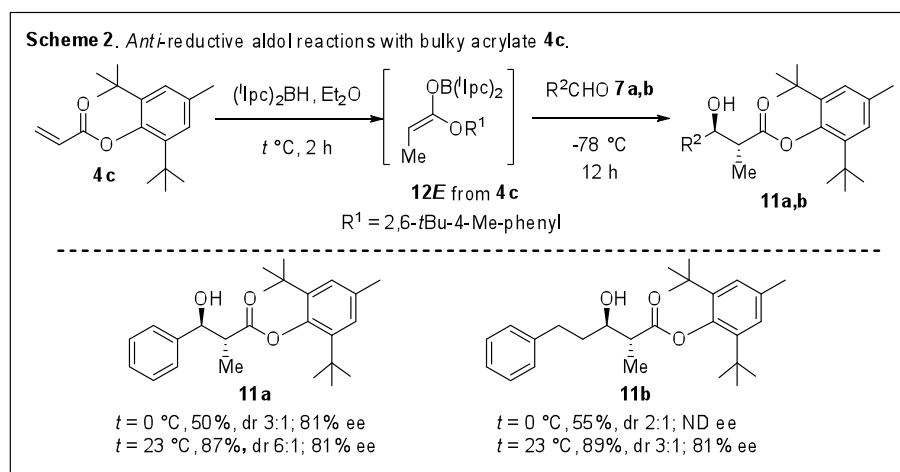


(2*S*,3*S*,4*S*,5*S*)-3-ethylpentan-3-yl-5-((*tert*-butyldimethylsilyloxy)-7-((3,4-dimethoxybenzyl)oxy)-3-hydroxy-2,4-dimethylheptanoate (10l): prepared from **7i**, **4b** and (^dIpc) $_2\text{BH}$; ^1H NMR analysis of crude reaction mixture, dr = 13:1 (**10l**:**10k**); **10l** isolated after purification: 81 mg, 67% yield, dr >20:1, clear oil: $[\alpha]_{\text{D}}^{27.1} = -1.1$ ($c = 0.35$, CHCl_3); ^1H (400 MHz,

CDCl₃) δ 6.88-6.80 (m, 3H), 4.42 (d, J = 11.7 Hz, 1H), 4.38 (d, J = 11.7 Hz, 1H), 3.93-3.89 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.86-3.83 (m, 1H), 3.46 (t, J = 6.7 Hz, 2H), 2.92 (d, J = 4.5 Hz, 1H), 2.48 (qd, J = 7.2, 8.5 Hz, 1H), 1.88 (q, J = 6.4 Hz, 2H), 1.82 (q, J = 7.5 Hz, 6H), 1.65 (ddq, J = 2.5, 4.6, 7.1 Hz, 1H), 1.08 (d, J = 7.2 Hz, 3H), 0.88 (d, J = 7.1 Hz, 3H), 0.86 (s, 9H), 0.81 (t, J = 7.5 Hz, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ¹H (400 MHz, CDCl₃) δ *minor*: see **10k**; ¹³C (100 MHz, CDCl₃) δ 175.2, 149.0, 148.5, 131.0, 120.1, 111.0, 110.9, 88.7, 74.1, 73.4, 72.8, 66.7, 55.9, 55.8, 44.8, 38.7, 34.2, 26.8 (3C), 25.8 (3C), 18.0, 14.8, 7.7, 7.6 (3C), -4.2, -4.5; ¹³C (100 MHz, CDCl₃) δ *minor*: see **10k**; IR (neat) 3536, 2935, 2883, 2857, 1723, 1594, 1516, 1461, 1419, 1379, 1360, 1258, 1188, 1157, 1135, 1082, 1030, 983, 938, 834, 803, 773 cm⁻¹; HRMS (ESI) calcd for C₃₁H₅₇O₇Si [M+H]⁺ 569.3874, found 569.3879.

Reductive aldol reactions using the 2,6-di-tert-butyl-4-methylphenyl acrylate (**4c**)

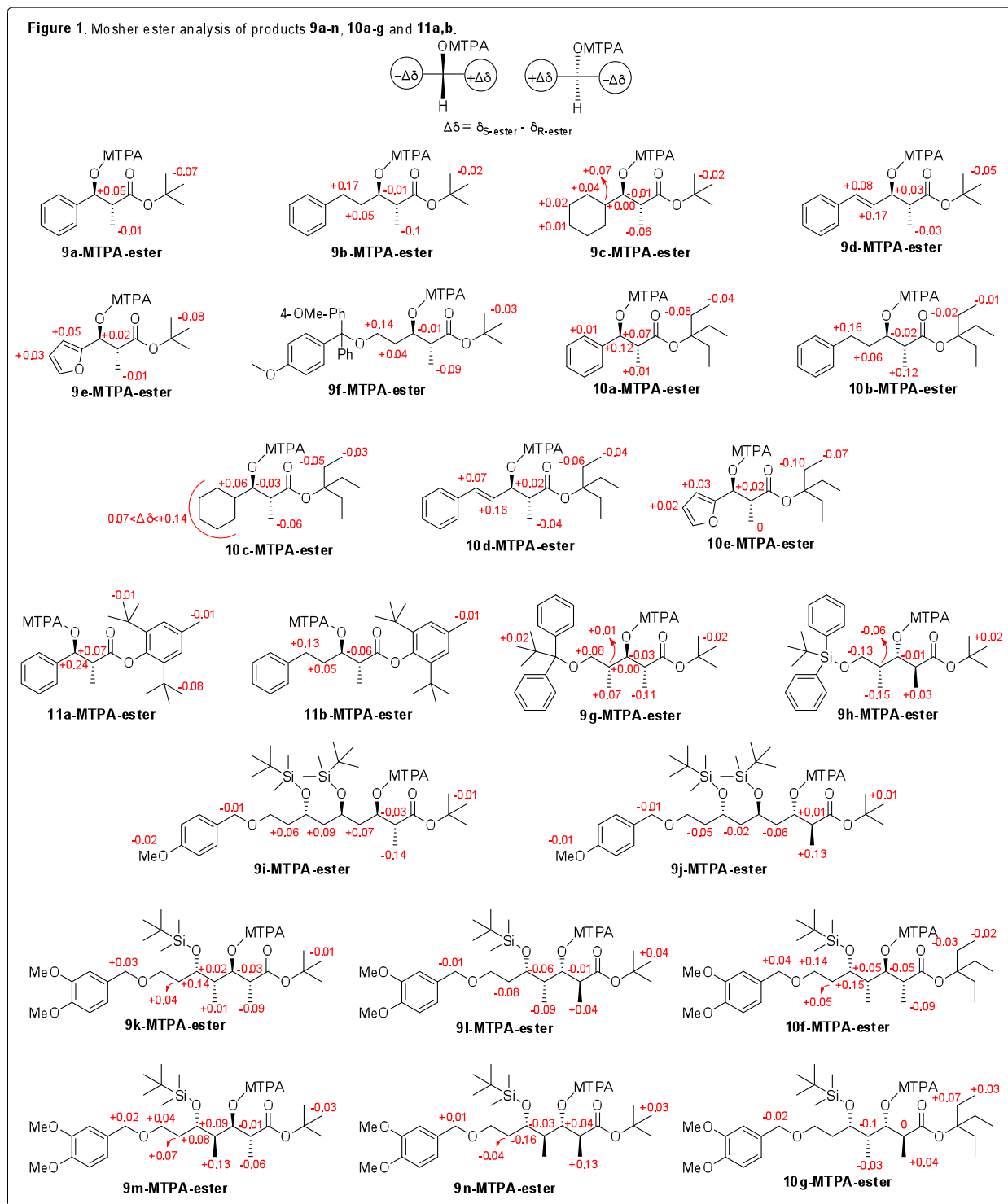
During our efforts to improve enantioselectivity of the *anti*-reductive aldol reaction, we also investigated bulky acrylate **4c** inspired by the work of Heathcock (Scheme 2).⁴ Acrylate **4c** was synthesized according to the procedure described by Merck.⁵ Characterization data obtained for **4b** were in agreement with a literature report.⁶



Anti-aldol adducts **11a** and **11b** were generated in good yield when the hydroboration of **4c** was performed at room temperature, and the *anti*-aldols were obtained with 81% ee from benzaldehyde and dihydrocinnamaldehyde, respectively. However, lower diastereoselectivities were observed in comparison with **4b**, presumably owing to steric hindrance which impacted the 1,3-borotropic shift in the generation of enolborinate **12E** from **4c**.

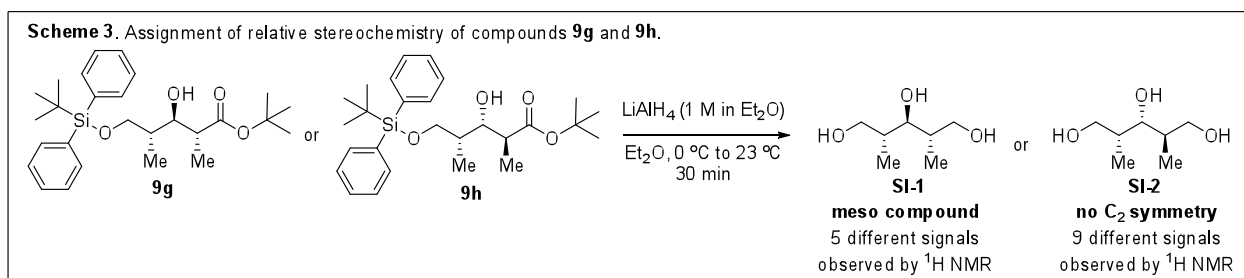
Assignment of hydroxyl group absolute stereochemistry

The absolute stereochemistry of the hydroxyl group of all aldols group were assigned by using the Mosher method. Key differential ^1H chemical shifts (ppm) in the pairs of diastereomeric MTPA esters generated are summarized below (Figure 1).



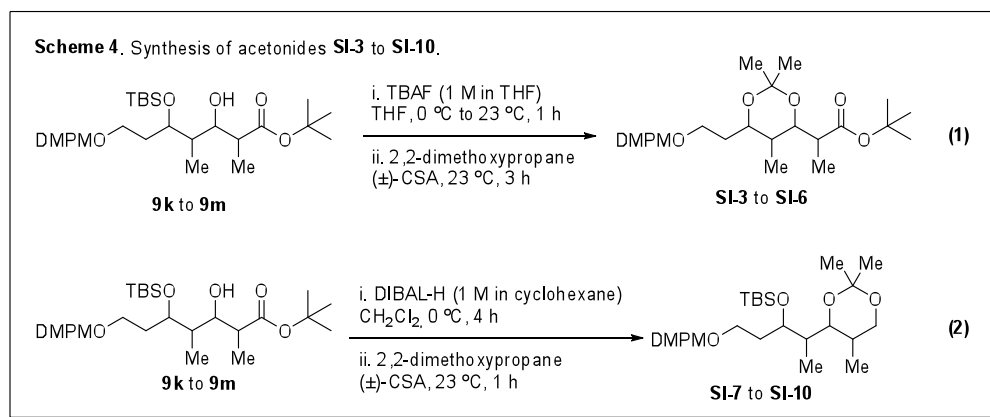
Assignment of relative stereochemistry

The relative stereochemistry of aldols **9a,c,d**⁷ and **9b,e**⁸ (which are known compounds) were assigned by comparison with NMR data in the literature. The relative stereochemistry of aldol adducts **9g** and **9h** was determined by reduction of the *tert*-butyl ester moiety with concomitant TBDPS deprotection to give the corresponding triols **SI-1** and **SI-2** respectively (Scheme 3).



A solution of **9g** (9.1 mg, 0.02 mmol, 1 equiv) in anhydrous Et_2O (200 μL) was added dropwise at 0 °C to a suspension of lithium aluminum hydride (1 M in Et_2O , 40 μL , 0.04 mmol). The mixture was warmed up to room temperature and was allowed to stir for 30 minutes. The reaction was quenched with water (1.5 μL), then a 15% aqueous NaOH solution (2.4 μL) and water again (4.8 μL). The resulting solid was filtered off and water (1 mL) was added to the filtrate. The aqueous layer was extracted three times with dichloromethane (1 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and evaporated under reduce pressure.

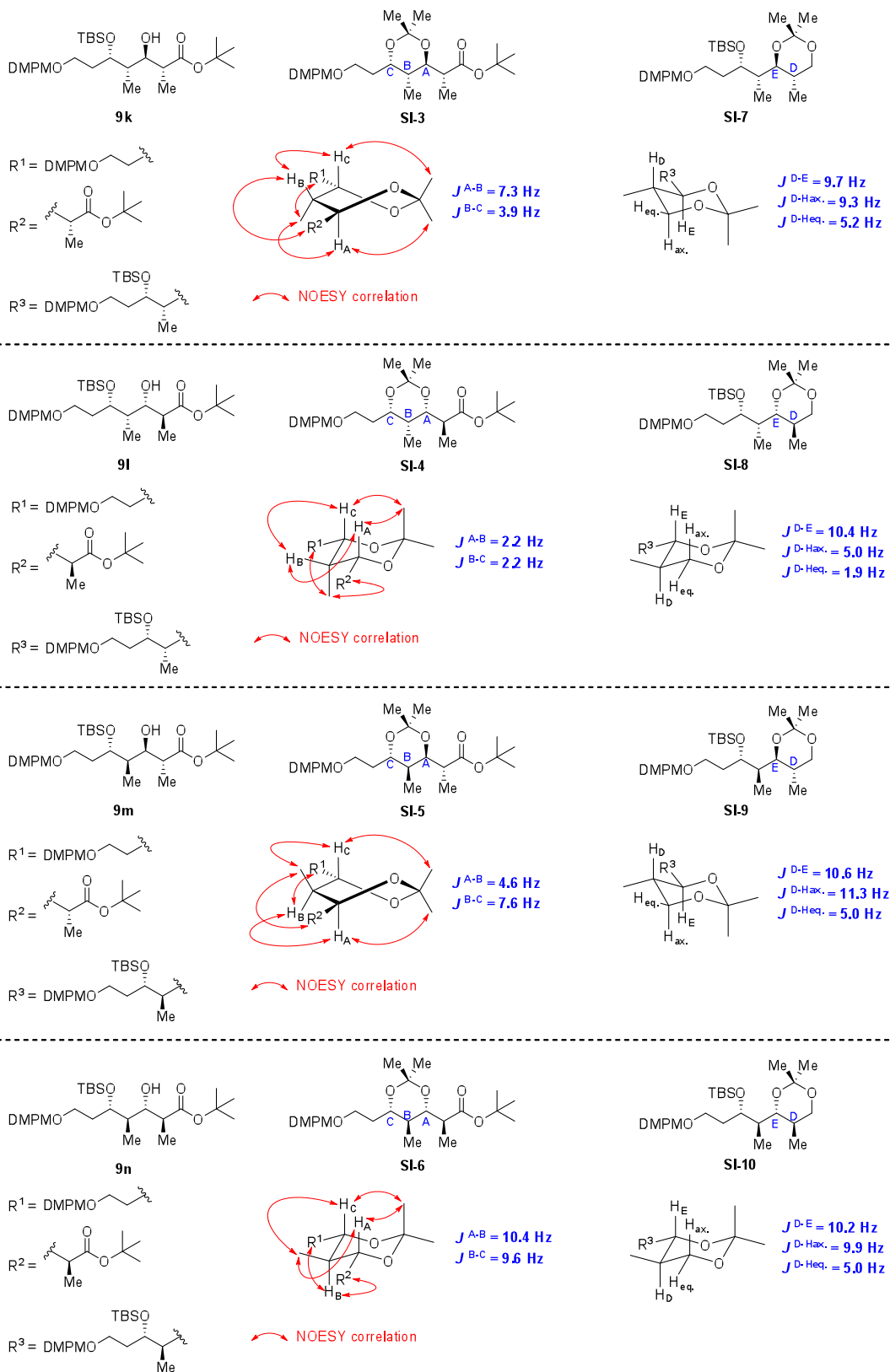
The relative stereochemistry of aldol adducts **9k** to **9n** was determined by synthesis of both internal **SI-3** to **SI-6** and terminal **SI-7** to **SI-10** acetonides (Scheme 4). Study of the coupling constants as well as nOe analyses allowed the unambiguous assignment of these structures (Figure 2).



Synthesis of internal acetonides **SI-3** to **SI-6**, typical procedure given for **SI-3** (eq.1): To a solution of aldol adduct **9k** (10 mg, 0.019 mmol) in THF (100 μ L) was added at 0 $^{\circ}$ C under inert atmosphere a solution of tetrabutylammonium fluoride (1 M in THF, 39 μ L, 0.039 mmol). The mixture was allowed to warm up to room temperature and was stirred for 1 h at this temperature. An aqueous buffer solution (pH= 7.00, 1 mL) was added and the aqueous layer was extracted three times with CH_2Cl_2 (1 mL). The combined organic layers were dried over Na_2SO_4 and solvent was removed under reduce pressure. The crude diol was purified by flash chromatography (80/20 : CH_2Cl_2 /ethyl acetate). Pure diol was solubilized in 2,2-dimethoxypropane (100 μ L). A catalytic amount of racemic camphor sulfonic acid (< 1 mg) was added to the solution at room temperature and the mixture was allowed to stir for 3 h. Freshly distilled triethylamine (25 μ L) was added to the solution and the volatiles were then removed under reduced pressure, providing the desired clean internal acetonide **SI-3** as a colorless oil.

Synthesis of internal acetonides **SI-7** to **SI-10**, typical procedure given for **SI-7** (eq.2): To a solution of aldol adduct **9k** (25 mg, 0.047 mmol) in CH_2Cl_2 (500 μ L) was slowly added at 0 $^{\circ}$ C under inert atmosphere a solution of diisobutyl aluminum hydride (1 M in cyclohexane, 240 μ L, 0.237 mmol) and the reaction mixture was stirred at this temperature for 4 h. A saturated aqueous solution of Rochelle's salt (3 mL) was added followed by CH_2Cl_2 (3 mL) and the mixture was stirred at room temperature until complete separation of layers. The aqueous layer was extracted two times with CH_2Cl_2 (3 mL), the combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduce pressure. Flash chromatography (30/70 : hexanes/ethyl acetate) afforded pure diol which was solubilized in 2,2-dimethoxypropane (300 μ L). A catalytic amount of racemic camphor sulfonic acid (< 1 mg) was added to the solution at room temperature and the mixture was allowed to stir until completion (monitored by TLC), usually within 1 h. Freshly distilled triethylamine (50 μ L) was added to the solution and the volatiles were then removed under reduced pressure, providing the desired clean terminal acetonide **SI-7** as a colorless oil.

Figure 2. Assignment of relative stereochemistry of compounds **9k-l**.



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