1,5-Asymmetric Induction in Boron-Mediated β -Alkoxy Methyl Ketone Aldol Addition Reactions

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Supporting Information

General Information: Melting points are uncorrected. Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a sodium or mercury lamp and reported as follows: $[\alpha]_D$ (*c* g/100mL, solvent). Infrared spectra were recorded on a Perkin Elmer model 1600 FT-IR spectrometer. ^1H NMR spectra were recorded on Bruker AM-500 (500 MHz), AM-400 (400 MHz), or AM-300 (300 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuteriochloroform: δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were recorded on Bruker AM-500 (125 MHz) or AM-400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuteriochloroform: δ 76.9 ppm). Mass spectra were obtained on a JEOL AX-505 or SX-102 high resolution magnetic sector mass spectrometer by the Harvard University Mass Spectrometry Laboratory.

Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Flash chromatography was performed as previously described¹ on EM silica gel 60 (230-240 mesh). Solvents for extraction and chromatography were HPLC grade. High performance liquid chromatography was performed on a Hewlett-Packard 1090 and 1050 Series HPLC with UV detector using either Chiracel-OD or Zorbax normal phase columns (4.6 mm ID X 25 cm).

All experiments were carried out under a nitrogen atmosphere in oven or flame-dried glassware. Dichloromethane (CH_2Cl_2) was distilled from CaH_2 under an inert atmosphere of nitrogen. Diethylether (Et_2O) and tetrahydrofuran (THF) were distilled from potassium/benzophenone ketyl. Hydrocinnamaldehyde, isobutyraldehyde, isovaleraldehyde and benzaldehyde were distilled from anhydrous CaSO_4 . All other commercially obtained reagents were used as received. 9-Borabicyclo[3.3.1]nonyl trifluoromethanesulfonate² (9-BBN triflate), di-*n*-butylboryl trifluoromethanesulfonate,² chlorodicyclohexylborane,³ and freshly prepared samarium(II) iodide⁴ were prepared according to literature procedures.

General procedure for the boron aldol reaction. To a solution of the methyl ketone (1.00 mmol) in 9 mL of Et₂O was added 1.10 mmol of *i*-Pr₂NEt. The solution was cooled to -78 °C and 1.05 mmol of Bu₂BOTf was added dropwise. The resulting white heterogeneous mixture was stirred 30 minutes at -78 °C followed by the slow addition of 1.1 mmol of a 1.0 M solution of aldehyde in Et₂O over a period of 15 minutes. The mixture was stirred 2 h at -78 °C and 7 mL of a pH = 7 buffer/MeOH (1/6, v/v) solution was added. This resulting clear solution was placed at 0 °C followed by the addition of 3 mL of a 30% H₂O₂/MeOH (1/2, v/v) solution. The ice bath was removed and the reaction was stirred 1 h at room temperature. The solution was diluted with Et₂O and water. The aqueous phase was extracted with Et₂O and combined organic layers were washed with saturated aqueous. NaHCO₃, saturated aqueous. NaCl, dried over MgSO₄ and concentrated under reduced pressure. Product alcohols were purified by flash chromatography.

Stereochemical Assignments. Two different procedures were used to define the 1,5-relationship between the newly generated stereocenter and the inducing β -alkoxy substituent. The first approach is specific to aldol adduct **5** (Article Table 1). A 50:50 mixture of isomers was generated by addition of the lithium enolate **4** to dihydrocinnamaldehyde. This mixture was separated by preparative HPLC and after reduction of the ketone and removal of the *p*-methoxybenzyl ether, each triol was analyzed by ¹³C NMR spectroscopy (Scheme 1). The 1,5-anti product exhibited fifteen ¹³C NMR resonances, while the all syn meso product showed only nine ¹³C NMR signals.

In cases where it was not possible to take advantage of molecular symmetry, the relative stereochemistry was determined using a straightforward general procedure (Scheme 2). For example, Tishchenko⁵ anti reduction of the β -hydroxy ketone **8c** followed by DDQ cyclization of

the PMB ether led to the *p*-methoxybenzylidene acetal. NOE studies of this cyclic intermediate confirmed the 1,3-syn relation of the acetal and indirectly the 1,5-anti relationship of the benzoate ester.

4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (4-ketone). To a solution of 18.4 g (51.5 mmol) of amide⁶ in 250 mL of THF at -78 °C was added 20.6 mL (61.8 mmol) of a 3.0 M solution of MeMgCl in THF in one portion. The reaction was warmed to 0 °C over 3 h followed by the addition of 0.1 equivalent of MeMgCl at -10 °C. After 1 h at 0 °C the solution was cooled to -50 °C and diluted with 500 mL of Et₂O and 50 mL of saturated aqueous NH₄Cl. The layers were separated and the aqueous phase was extracted twice with 50 mL of Et₂O. Combined organic layers were washed with saturated aqueous NaHCO₃ and brine, dried over anhydrous MgSO₄ and concentrated *in vacuo*. Purification by flash chromatography (10–20% EtOAc in hexanes) provided 14.5 g (90%) of the title compound as a colorless oil: IR (thin film) ν 3025, 2934, 1714, 1612, 1513, 1454, 1358, 1301, 1248, 1174, 1034, 822, 751, 701 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.28–7.14 (m, 7H, ArH), 6.88–6.85 (m, 2H, ArH), 4.45 (s, 2H, OCH₂Ar), 3.94 (quint, *J* = 6 Hz, 1H, CHOPMB), 3.79 (s, 3H, OCH₃), 2.78 (dd, *J* = 16, 7 Hz, 1H, CH₂COCH₃), 2.74–2.62 (m, 2H, CH₂CH₂Ph), 2.53 (dd, *J* = 16, 5 Hz, 1H, CH₂COCH₃), 2.13 (s, 3H, COCH₃), 1.92–1.79 (m, 2H, CH₂CH₂Ph) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 207.3, 159.1, 141.7, 130.4, 129.3, 128.3, 128.2, 125.7, 113.7, 74.5, 71.1, 55.1, 48.4, 36.0, 31.3, 31.0 ppm. *R*_f 0.30 (20 % EtOAc/hexanes); Exact mass calcd for C₂₀H₂₄O₃: 312.1725. Found: 312.1735 (EI).

(3*R, 7*R**)-1,9-Diphenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-5-nonanone (anti-5).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone **4-ketone** (320.4 mg, 1.03 mmol), Bu₂BOTf (271 μ L, 1.08 mmol), Hunig's base (197 μ L, 1.13 mmol) and hydrocinnamaldehyde solution (1.13 mL, 1.13 mmol). Purification by flash chromatography (25% EtOAc in hexane) provided 382 mg (83%) of the alcohol. HPLC analysis of the unpurified racemic product (Chiracel-OD, 20% ethanol in hexane, 1.0 mL/min, 220 nm, *T*_R (Maj) = 16.5 min and 58.5 min, *T*_R (Min) = 22.1 and 35.1 min) revealed a 94:6 ratio of diastereoisomers anti-5 and syn-5. These two isomers were separated on HPLC using a preparative column (Zorbax, 21.2

mm X 25 cm, 10% EtOAc/30% CH₂Cl₂/60% hexanes, 9 mL/min, 100 μ L injected of a 60 mg/mL solution, T_R (Maj) = 44.8 min and T_R (Min) = 48.4 min): IR (thin film): 3452, 3025, 2932, 1707, 1612, 1513, 1454, 1247, 1064, 1032, 700 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.29-7.15 (m, 12H, ArH), 6.85 (dt, *J* = 9, 3 Hz, 2H, ArH), 4.46 (d, *J* = 11 Hz, 1H, OCH₂Ar), 4.39 (d, *J* = 11 Hz, 1H, OCH₂Ar), 4.06-4.00 (m, 1H, CHOH), 3.96-3.92 (m, 1H, CHOPMB), 3.78 (s, 3H, OCH₃), 3.04 (d, *J* = 4 Hz, 1H, CHOH), 2.80-2.48 (m, 8H, CH₂CH₂Ph, CH₂COCH₂), 1.94-1.74 (m, 3H, CH₂CH₂Ph), 1.68-1.61 (m, 1H, CH₂CH₂Ph) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 210.7, 159.2, 141.7, 141.6, 130.1, 129.4, 128.3, 128.3, 128.2, 125.8, 125.7, 113.7, 74.6, 71.2, 66.7, 55.2, 50.4, 48.2, 37.9, 35.8, 31.6, 31.3 ppm. R_f 0.2 (30 % EtOAc/hexanes); Exact mass calcd for C₂₉H₃₄O₄+NH₄: 464.2801 . Found: 464.2793 (CI, NH₃ atmosphere).

(3R*, 7S*)-1,9-Diphenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-5-nonanone (syn-5). IR (thin film): 3462, 3026, 2932, 2861, 1707, 1612, 1514, 1454, 1248, 1069, 1032, 700 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.30-7.15 (m, 12H, ArH), 6.85 (dt, *J* = 9, 3 Hz, 2H, ArH), 4.45 (d, *J* = 11 Hz, 1H, OCH₂Ar), 4.40 (d, *J* = 11 Hz, 1H, OCH₂Ar), 4.03-3.97 (m, 1H, CHOH), 3.96-3.91 (m, 1H, CHOPMB), 3.78 (s, 3H, OCH₃), 3.10 (dd, *J* = 4, 1 Hz, 1H, CHOH), 2.81-2.50 (m, 8H, CH₂CH₂Ph, CH₂COCH₂), 1.93-1.75 (m, 3H, CH₂CH₂Ph), 1.68-1.61 (m, 1H, CH₂CH₂Ph) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 210.8, 159.2, 141.8, 141.6, 130.1, 129.5, 128.4, 128.3, 128.2, 125.8, 125.7, 113.8, 74.6, 71.2, 66.9, 55.2, 50.4, 48.3, 38.0, 35.8, 31.6, 31.3 ppm. R_f 0.2 (30 % EtOAc/hexanes); Exact mass calcd for C₂₉H₃₄O₄Na: 469.2355. Found: 469.2372 (FAB, MNBA, added NaI).

Stereochemical proof of (5): The stereochemistry of anti-5 and syn-5 was assigned by analysis of the derived triol.

(3R*, 7R*)-1,9-Diphenyl-3,5,7-trihydroxy-nonane. To a solution of 1,9-diphenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-5-nonanone (anti-5) (94.4 mg, 0.211 mmol) in 1.5 mL of toluene at -78 °C was added 634 μ L (0.634 mmol) of a 1.0 M solution of DIBAL-H in hexane. The resulting clear solution was stirred 30 min at -78 °C and the reaction was diluted with Et₂O followed by the addition of 500 μ L of saturated aqueous Rochelle's salt. The resulting mixture was warmed to room temperature and stirred for 1 hour. Layers were separated and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by flash chromatography (40% EtOAc in hexane) to afford 94 mg (100%) of the diol as a 1:1 mixture of isomers. This colorless oil was dissolved in methanol followed by the addition of 10 mg of the Pearlman's catalyst (20% Pd(OH)₂). The resulting mixture was purged with H₂ and then stirred at room temperature under a 1 atmosphere pressure of H₂. After 1 hour the reaction was filtered through a short pad of Celite and rinsed with 25 mL of MeOH. The volatiles were removed under reduced pressure

and the residue was purified by flash chromatography (60-70% EtOAc in hexanes) to afford 62.9 mg (91%) of the triol as a white solid. ^1H NMR and ^{13}C NMR analysis clearly indicate that this product was unsymmetrical as expected for a 1,5-anti relationship: mp 61-62 °C; IR (CHCl_3): 3541, 3296, 3025, 2926, 2902, 2850, 1602, 1455, 1117, 1092, 1050, 1018, 751, 700 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.28-7.14 (m, 10 H, ArH), 4.36 (s(br), 1H, CHOH), 4.17 (m (br), 1H, CHOH), 3.95 (m (br), 1H, CHOH), 3.88-3.85 (m, 1H, CHOH), 3.74 (s(br), 1H, CHOH), 3.39 (s(br), 1H, CHOH), 2.80-2.61 (m, 4H, $\text{CH}_2\text{CH}_2\text{Ph}$), 1.87-1.49 (m, 8H, $\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 141.8, 141.7, 128.3, 128.2, 125.7, 125.7, 72.1, 70.2, 68.3, 42.8, 42.6, 39.6, 39.0, 32.0, 31.5 ppm. R_f 0.3 (60 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{21}\text{H}_{29}\text{O}_3$: 329.2117. Found: 329.2125 (CI, NH_3 atmosphere).

(3R*, 7S*)-1,9-Diphenyl-3,5,7-trihydroxy-nonane. To a solution of 38.9 mg (0.087 mmol) of hydroxy ketone *syn*-5 in 1.4 mL of THF and 350 μL of MeOH at 0 °C was added 261 μL of a 1.0 M solution of Et_2BOMe in THF. After 15 min of stirring, NaBH_4 (33 mg) was added in one portion. The reaction was warmed to room temperature and after 6 h, MeOH (2 mL) was added at 0 °C followed by 500 μL of 6 N NaOH and 500 μL of H_2O_2 (30%). The ice bath was removed and the solution was stirred for 45 min at room temperature. The solution was diluted with 40 mL of EtOAc/ Et_2O and 10 mL of water. The layers were separated and the aqueous phase was extracted with EtOAc (2 X 10 mL). The combined organic layers were washed with saturated aqueous NaHCO_3 and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (40 % EtOAc in hexane) to produce 36 mg (92%) of the diol as 10:1 mixture of isomers. This mixture was dissolved in 1 mL of MeOH followed by the addition of 10 mg of the Pearlman's catalyst (20% $\text{Pd}(\text{OH})_2$). The resulting mixture was purged with H_2 and then stirred at room temperature under a 1 atmosphere pressure of H_2 . After 1 hour the reaction was filtered through a short pad of Celite and rinsed with 25 mL of MeOH. The volatiles were removed under reduced pressure and the residue was purified by flash chromatography (40% EtOAc in CH_2Cl_2) to afford 18 mg (85 %) of the triol as a white solid. ^1H NMR and ^{13}C NMR showed signals for a symmetric triol indicating a 1,5-syn relationship: mp 87.6-88.3 °C; IR (CHCl_3): 3464, 3010, 2928, 2856, 1602, 1496, 1454, 1118, 790, 701 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.30-7.17 (m, 10H), 4.32 (s(br), 1H), 4.13-4.08 (m, 1H), 3.91 (m (br), 2H), 3.09 (s(br), 2H), 2.79-2.64 (m, 4H), 1.86-1.52 (m, 8H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 141.7, 128.4, 128.3, 125.8, 73.6, 72.1, 43.5, 39.6, 31.6 ppm. R_f 0.3 (60% EtOAc/hexanes); Exact mass calcd for $\text{C}_{21}\text{H}_{28}\text{O}_3\text{Na}$: 351.1936. Found: 351.1931 (FAB, MNBA, added NaI).

3-[4-(Methoxybenzyl)oxy]-4-methyl-N-methoxy-N-methyl-pentanamide.

Lithium

diisopropylamide (LDA) was generated by addition of 15.6 mL (39 mmol) of *n*-butyllithium (2.5M solution in hexanes) to a solution of 5.4 mL (39 mmol) of diisopropylamine in 50 mL of THF at -78°C . After 10 min, a solution of 4.0 g (39 mmol) of the Weinreb amide in 10 mL of THF was added dropwise (1 mL THF rinse) and the resulting solution was stirred at -78°C for 30 min. Isobutyraldehyde 3.9 mL (42.9 mmol) was added dropwise and the solution was stirred at -78°C for 50 min. The reaction was quenched at -78°C by the addition of saturated aqueous NH_4Cl , and the mixture was warmed to ambient temperature. The mixture was diluted with Et_2O and washed once with saturated aqueous NH_4Cl . The aqueous washings were extracted twice with Et_2O . The combined organic layers were washed with saturated aqueous NaHCO_3 and brine, dried over anhydrous MgSO_4 , and concentrated *in vacuo*. Purification by flash chromatography (60% EtOAc in hexanes) provided 5.73 g (84%) of the 3-hydroxy-4-methyl-N-methoxy-N-methyl-pentanamide. To a solution of 5.7 g (32.5 mmol) of this alcohol and 10.4 g (36.8 mmol) of the 4-methoxybenzyloxy acetimidate in 100 mL of Et_2O at room temperature was added 86 μL of trifluoromethanesulfonic acid. After 30 min, the reaction was diluted with 10 mL of saturated aqueous NaHCO_3 and 100 mL of Et_2O . The layers were separated and the organic extract was washed with brine, dried over anhydrous MgSO_4 and concentrated *in vacuo*. The residue was dissolved in 15 mL of CH_2Cl_2 and was stirred 10 min at -78°C . The heterogeneous cold solution was quickly filtered and rinsed two times with 5 mL of cold CH_2Cl_2 . Solvent was removed *in vacuo* and the residue was purified by flash chromatography (3-7% EtOAc in CH_2Cl_2) to provide 5.8 g (60%) of the desired benzyl ether as a colorless oil: IR (thin film): 3462, 2960, 2937, 2804, 1661, 1612, 1513, 1465, 1385, 1248, 1174, 1071, 1036, 822 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.24 (d, $J = 9$ Hz, 2H, ArH), 6.85-6.82 (m, 2H, ArH), 4.50 (d, $J = 11$ Hz, 1H, OCH_2Ar), 4.46 (d, $J = 11$ Hz, 1H, OCH_2Ar), 3.84 (quint, $J = 4$ Hz, 1H, CHOPMB), 3.75 (s, 3H, OCH_3), 3.62 (s, 3H, NOCH_3), 3.18 (s, 3H, NCH_3), 2.78 (dd, $J = 15, 8$ Hz, 1H, $\text{CH}_2\text{CON}(\text{OMe})\text{Me}$), 2.41 (dd, $J = 15, 3$ Hz, 1H, $\text{CH}_2\text{CON}(\text{OMe})\text{Me}$), 1.95-1.87 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 0.94 (d, $J = 7$ Hz, 6H, $\text{CH}(\text{CH}_3)_2$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 172.7, 158.6, 130.8, 128.9, 113.2, 80.3, 71.9, 60.8, 54.8, 33.7, 31.7, 31.4, 17.7, 17.6 ppm. R_f 0.2 (30 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{16}\text{H}_{25}\text{NO}_4$: 295.1784. Found: 295.1783 (EI).

3-[4-(Methoxybenzyl)oxy]-5-methyl-2-hexanone (6a).

To a solution of 4.19 g (14.2 mmol) of amide in 70 mL of THF at -78°C was added 5.67 mL (17.0 mmol) of a 3.0 M solution of MeMgBr

in THF in one portion. The reaction was warmed to 0 °C over 3 h followed by the addition of 0.1 equivalent of MeMgBr at -10 °C. After 1 h at 0 °C the solution was cooled to -50 °C and diluted with 100 mL of Et₂O and 10 mL of saturated aqueous NH₄Cl. The layers were separated and the aqueous phase was extracted twice with 20 mL of Et₂O. Combined organic layers were washed with saturated aqueous NaHCO₃ and brine, dried over anhydrous MgSO₄ and concentrated *in vacuo*. Purification by flash chromatography (15% EtOAc in hexane) provided 1.7 g (50%) of the title compound as a colorless oil: IR (thin film): 2960, 2874, 1716, 1613, 1586, 1514, 1465, 1355, 1248, 1076, 822 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.22 (dt, *J* = 9, 2 Hz, 2H, ArH), 6.85 (dt, *J* = 9, 2 Hz, 2H, ArH), 4.46 (d, *J* = 11 Hz, 1H, OCH₂Ar), 4.41 (d, *J* = 11 Hz, 1H, OCH₂Ar), 3.78-3.75 (m, 1H, CHOPMB), 3.77 (s, 3H, OCH₃), 2.67 (dd, *J* = 16, 9 Hz, 1H, CH₂COCH₃), 2.43 (dd, *J* = 16, 4 Hz, 1H, CH₂COCH₃), 2.15 (s, 3H, CH₂COCH₃), 1.96-1.89 (m, 1H, CH(CH₃)₂), 0.91 (d, *J* = 7 Hz, 6H, CH(CH₃)₂); ¹³C NMR (100 MHz, CDCl₃) δ 208.0, 158.9, 130.6, 129.1, 113.5, 79.8, 71.6, 55.0, 44.8, 31.0, 30.8, 18.0, 17.3. R_f 0.3 (20% EtOAc/hexanes); Exact mass calcd for C₁₅H₂₂O₃: 250.1569. Found: 250.1558 (EI).

3-*tert*-Butyldimethylsilyloxy-5-phenyl-*N*-methoxy-*N*-methyl-pentanamide. To a solution of 803 mg (3.38 mmol) of the alcohol⁵ and 512 μL (4.40 mmol) of 2,6-lutidine in 11 mL of CH₂Cl₂ at 0 °C was added 933 μL (4.06 mmol) of *tert*-butyldimethylsilyl trifluoromethanesulfonate. After 30 min, 25 mL of H₂O was added to quench and the mixture was extracted with two 25 mL portions of CH₂Cl₂. The combined organic extracts were washed with 25 mL of H₂O and 25 mL of brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Purification by MPLC (Michel-Miller column size C, 25% EtOAc in hexanes) afforded 1.15 g (96%) of the title compound as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.25 (m, 3 H, ArH), 7.21-7.16 (m, 2 H, ArH), 4.32 (m, 1 H, CHOTBS), 3.68 (s, 3 H, OCH₃), 3.17 (s, 1 H, NCH₃), 2.83-2.61 (m, 3 H, CH₂Ph and CH₂C=O), 2.47 (m, 1 H, CH₂), 1.92-1.75 (m, 2 H, CH₂CH₂Ph), 0.90 (s, 9 H, SiC(CH₃)₃), 0.10 (s, 3 H, SiCH₃), 0.05 (s, 3 H, SiCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 172.2, 142.3, 128.4, 128.2, 125.6, 69.0, 61.2, 39.6, 39.5, 31.8, 31.4, 25.8, 25.7, 18.0, -4.7, -4.8 ppm.

4-*tert*-Butyldimethylsilyloxy-6-phenyl-2-hexanone (6b). To a solution of 575 mg (1.64 mmol) of amide in 8 mL of THF at -78 °C was added 709 μL (2.13 mmol) of a 3.0 M solution of MeMgCl in THF in one portion. The reaction was warmed to 0 °C over 3 h followed by the

addition of 0.1 equivalent of MeMgCl at $-10\text{ }^{\circ}\text{C}$. After 1 h at $0\text{ }^{\circ}\text{C}$ the solution was cooled to $-50\text{ }^{\circ}\text{C}$ and diluted with 20 mL of Et₂O and 5 mL of saturated aqueous NH₄Cl. The layers were separated and the aqueous phase was extracted twice with 5 mL of Et₂O. Combined organic layers were washed with saturated aqueous NaHCO₃ and brine, dried over anhydrous MgSO₄ and concentrated *in vacuo*. Purification by flash chromatography (5 % EtOAc in hexanes) provided 393 mg (78 %) of the title compound as a colorless oil: IR (thin film) ν 2954, 2929, 2857, 1718, 1603, 1496, 1471, 1360, 1255, 1093, 836, 776, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.32-7.19 (m, 5H, ArH), 4.27 (quint, $J = 6\text{ Hz}$, 1H, CHOTBS), 2.74-2.64 (m, 3H, CH₂CH₂Ph, CH₂COCH₃), 2.56 (dd, $J = 15, 5\text{ Hz}$, 1H, CH₂COCH₃), 2.18 (s, 3H, COCH₃), 1.89-1.76 (m, 2H, CH₂CH₂Ph), 0.94 (s, 9H, SiC(CH₃)₃), 0.12 (s, 3H, SiCH₃), 0.08 (s, 3H, SiCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 207.3, 141.9, 128.2, 128.1, 125.6, 68.4, 50.6, 39.2, 31.4, 31.2, 25.7, 17.8, -4.8, -4.9 ppm. *R*_f 0.3 (5 % EtOAc/hexanes); Exact mass calcd for C₁₈H₃₁SiO₂: 307.2094. Found: 307.2097 (CI, NH₃ atmosphere).

(3*R, 7*S**)-1-Phenyl-3-hydroxy-7-[4-(methoxybenzyl)oxy]-8-methyl-5-nonanone (*anti*-7a).**

The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-5-methyl-2-hexanone (252.5 mg, 1.01 mmol), Bu₂BOTf (266 μ L, 1.06 mmol), Hunig's base (193 μ L, 1.11 mmol) and hydrocinnamaldehyde solution (1.11 mL, 1.11 mmol). Purification by flash chromatography (25% EtOAc in hexanes) provided 346 mg (89%) of the alcohol contaminated with < 5% of the syn isomer. ¹³C NMR analysis (100 MHz, CDCl₃, Maj = 66.6, 44.2 and 37.7 ppm, Min = 66.8, 44.3 and 37.8 ppm) of the unpurified product revealed a 95:5 ratio of diastereoisomers *anti*-7a and *syn*-7a. IR (thin film) ν 3463, 3026, 2958, 2933, 2873, 1709, 1612, 1514, 1248, 1071, 1035, 822, 750, 701 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.28-7.15 (m, 7H, ArH), 6.82 (dt, $J = 9, 3\text{ Hz}$, 2H, ArH), 4.47 (d, $J = 11\text{ Hz}$, 1H, OCH₂Ar), 4.35 (d, $J = 11\text{ Hz}$, 1H, OCH₂Ar), 4.05-4.00 (m, 1H, CHOH), 3.78-3.75 (m, 1H, CHOPMB), 3.75 (s, 3H, OCH₃), 3.18 (d, $J = 3\text{ Hz}$, 1H, CHOH), 2.79-2.73 (m, 1H, CH₂CH₂Ph), 2.68-2.58 (m, 3H, CH₂CH₂Ph, CH₂COCH₂), 2.51 (dd, $J = 18, 9\text{ Hz}$, 1H, CH₂COCH₂), 2.37 (dd, $J = 16, 3\text{ Hz}$, 1H, CH₂COCH₂), 1.98-1.92 (m, 1H, CH(CH₃)₂), 1.80-1.73 (m, 1H, CH₂CH₂Ph), 1.66-1.59 (m, 1H, CH₂CH₂Ph), 0.90 (d, $J = 7\text{ Hz}$, 6H, CH(CH₃)₂) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 211.4, 159.0, 141.7, 130.3, 129.2, 128.2, 128.2, 125.6, 113.6, 80.0, 71.6, 66.6, 55.0, 50.6, 44.4, 37.8, 31.5, 30.5, 18.1, 17.0 ppm. *R*_f 0.2 (20 % EtOAc/hexanes); Exact mass calcd for C₂₄H₃₂O₄+NH₄: 402.2645. Found: 402.2665 (CI, NH₃ atmosphere).

Stereochemical proof of (7a): The stereochemistry of *anti*-7a was assigned by analysis of the derived diol.

(3R*, 7S*)-1-Phenyl-3,7-dihydroxy-8-methyl-5-nonanone. To a solution of 92.2 mg of 1-phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone *anti*-**7a** in 2 mL of MeOH was added 10 mg of Pearlman's catalyst (20% Pd(OH)₂). The resulting mixture was purged with H₂ and then stirred at room temperature under a 1 atmosphere pressure of H₂. After 4 hour the reaction was filtered through a short pad of Celite and rinsed with 25 mL of MeOH. The volatiles were removed under reduced pressure and the residue was purified by flash chromatography (40% EtOAc in hexanes) to afford 62 mg (98%) of the diol as a white solid. Following the same procedure, 1-phenyl-3-hydroxy-7-[4-(Methoxybenzyl)oxy]-8-methyl-5-nonanone *anti*-**8c** was found to produce the same diol in 98% yield as shown by TLC, ¹H NMR and ¹³C NMR: mp 52-53 °C; IR *v* (CHCl₃) 3473, 3024, 3013, 2963, 2933, 2877, 1701, 1603, 1454, 1386, 1058, 701 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.16 (m, 5H, ArH), 4.11-4.07 (m, 1H, CHOH), 3.87-3.82 (m, 1H, CHOH), 3.34 (d, *J* = 3 Hz, 1H, CHOH), 3.06 (d, *J* = 4 Hz, 1H, CHOH), 2.83-2.76 (m, 1H, CH₂CH₂Ph), 2.70-2.49 (m, 5H, CH₂CH₂Ph, CH₂COCH₂), 1.86-1.77 (m, 1H, CH₂CH₂Ph), 1.74-1.62 (m, 2H, CH₂CH₂Ph, CH(CH₃)₂), 0.92 (d, *J* = 7 Hz, 3H, CH(CH₃)₂), 0.90 (d, *J* = 7 Hz, 3H, CH(CH₃)₂) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 212.5, 141.6, 128.2, 125.7, 72.1, 66.6, 50.1, 46.9, 38.0, 33.1, 31.6, 18.1, 17.5 ppm. R_f 0.3 (40% EtOAc/hexanes); Exact mass calcd for C₁₆H₂₄O₃+NH₄: 282.2069. Found: 282.2083 (CI, NH₃ atmosphere).

1,9-Diphenyl-3-tert-butyltrimethylsilyloxy-7-hydroxy-5-nonanone (*syn*-7b**).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-tert-Butyltrimethylsilyloxy-6-phenyl-2-hexanone (**6b**) (54.2 mg, 0.177 mmol), Bu₂BOTf (46.6 μL, 0.185 mmol), Hunig's base (34 μL, 0.195 mmol) and hydrocinnamaldehyde (25.6 μL, 0.195 mmol). ¹H NMR analysis (400 MHz, CDCl₃, Maj: 0.92, 0.11 and 0.06 ppm, Min: 0.90, 0.10 and 0.03 ppm) revealed a 40:60 ratio of diastereoisomers *anti*-**7b** and *syn*-**7b**. IR (thin film) *v* 3464, 3027, 2929, 2857, 1707, 1603, 1454, 1255, 1090, 836, 777, 735, 699 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.18 (m, 10H, ArH), 4.28-4.24 (m, 1H, CHOTBS), 4.09-4.05 (m, 1H, CHOH), 3.20 (d, *J* = 3 Hz, 1H, CHOH (Maj.)), 3.17 (d, *J* = 3 Hz, 1H, CHOH (Min.)), 2.87-2.50 (m, 8H, CH₂CH₂Ph, CH₂COCH₂), 1.89-1.66 (m, 4H, CH₂CH₂Ph), 0.92 (s, 9H, SiC(CH₃)₃ (Maj.)), 0.90 (s, 9H, SiC(CH₃)₃ (Min.)), 0.11 (s, 3H, SiCH₃ (Maj.)), 0.10 (s, 3H, SiCH₃ (Min.)), 0.06 (s,

3H, SiCH₃ (Maj.)), 0.03 (s, 3H, SiCH₃ (Min.)) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 210.9, 210.8, 141.8, 141.7, 141.7, 128.3, 128.3, 128.1, 125.7, 68.5, 68.3, 66.6, 66.5, 50.9, 50.7, 50.5, 50.4, 39.2, 39.1, 37.9, 37.8, 31.6, 31.6, 31.2, 31.2, 25.7, 25.7, 17.9, 17.8, -4.7, -4.8, -4.8 ppm. R_f 0.3 (15 % EtOAc/hexanes); Exact mass calcd for C₂₇H₄₁SiO₃: 441.2825. Found: 441.2807 (CI, NH₃ atmosphere).

Stereochemical proof of (7b): The stereochemistry of *anti*-7b and *syn*-7b was assigned by comparison with authentic *anti*-7b prepared from *anti*-5 (TBSCl, Imidazole; Pearlman's catalyst, H₂).

(3R*,7R*)1-Phenyl-3-hydroxy-7,9-bis-[4-(methoxybenzyl)oxy]-5-nonanone (*anti*-7c). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone (6c) (0.213 g, 0.612 mmol), Bu₂BOTf (160 μL, 0.642 mmol), Hunig's base (116 μL, 0.685 mmol), and hydrocinnamaldehyde solution (0.685 mL, 0.685 mmol). Purification by flash chromatography (30% EtOAc in hexanes) provided 0.227 g (77%) of the product as a mixture of diastereomers. HPLC analysis of the unpurified product (Zorbax silica, 30 % EtOAc in hexanes, 1.0 mL/min, Tr (min)=28.3 min, Tr(maj)=30.3 min) indicated a 88:12 mixture of isomers. IR (thin film): 3472, 3030, 2930, 2859, 1704, 1604, 1512, 1455, 1362, 1298, 1248, 1177, 1091, 1034, 820 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.23 (m, 8H, ArH), 6.97-6.91 (m, 5H, ArH), 4.49-4.47 (m, 4H, OCH₂Ar), 4.20-4.11 (m, 2H, CHOPMB and CHOH), 3.87 (s, 3H, OCH₃), 3.62-3.56 (m, 2H, CH₂OPMB), 3.21 (br s, 1H, CHOH), 2.89-2.54 (m, 6H, CH₂C=O and CH₂Ph), 1.98-1.67 (m, 4H, CH₂CH₂Ph, and CH₂CHOPMB) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 210.7, 159.2, 141.8, 130.3, 129.4, 129.3, 128.4, 128.3, 125.8, 113.7, 72.9, 72.6, 71.4, 66.8, 66.0, 55.2, 50.4, 48.6, 37.9, 34.3, 31.7 ppm; R_f 0.20 (20% EtOAc in hexanes); Exact mass calcd for C₃₁H₃₈O₆Na: 529.2566. Found 529.2568 (FAB, MNBA, added NaI).

Stereochemical proof of *anti*-7c: The stereochemistry of *anti*-7c was assigned by analysis of the derived benzylidene acetal.

(3R*,5R*,7R*)-1-Phenyl-3-acetoxy-5-hydroxy-7,9-bis-[4-(methoxybenzyl)oxy]-nonane. To a cooled solution of ketone 7c (0.126 gm, 0.261 mmol) in THF (3.0 mL) at -10 °C was added acetaldehyde (0.296 mL, 5.22 mmol). A solution of samarium iodide (2.61 mL of a 0.1 M soln in THF) was added by syringe. After stirring for 15 min, saturated aqueous NaHCO₃ solution was added and the mixture warmed to room temperature. The mixture was extracted with Et₂O (2 x 15 mL). The combined organic solutions were washed with brine, dried over MgSO₄, filtered, and

concentrated. The residue was purified by flash chromatography (25% EtOAc in hexanes) to afford 88 mg (64%) of the desired alcohol. IR (thin film): 3484, 2934, 1732, 1612, 1513, 1454, 1373, 1302, 1248, 1174, 1034, 820, 701 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.24 (m, 9H, ArH), 6.98-6.93 (m, 4H, ArH), 5.25-5.18 (m, 1H, CHOAc), 4.53 (ABq, $J_{\text{AB}}=11.0$ Hz, $\Delta V_{\text{AB}}=12.4$ Hz, 2H, PMPCH₂OCH), 4.51 (s, 2H, PMPCH₂O), 3.89 (s, 3H, ArOCH₃), 3.88 (s, 3H, ArOCH₃), 3.77 (m, 1H, CHOR), 3.67-3.59 (m, 3H, CHOR), 2.78-2.66 (m, 2H, ArCH₂CH₂), 2.13 (s, 3H, CH₃C=O), 2.10-1.64 (m, 8 H, CH₂CHOR) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 171.6, 159.2, 141.1, 130.3, 129.4, 129.3, 128.4, 128.3, 125.9, 113.8, 72.2, 71.6, 71.3, 70.4, 66.3, 66.0, 55.2, 42.8, 41.4, 36.5, 34.1, 31.8, 21.0 ppm; R_f 0.45 (2 x 40% EtOAc in hexanes); Exact mass calcd for $\text{C}_{33}\text{H}_{42}\text{O}_7\text{Na}$: 573.2828. Found 573.2846 (FAB, MNBA, added NaI).

(3R*,5R*,7R*)-4-[2-(4-Methoxyphenyl)-4-(methoxyphenyl)oxyethyl-1,3-dioxan-6-yl]-3-acetoxy-1-phenyl-butane. To a solution of the alcohol (33 mg, 0.063 mmol) in dichloromethane (3 mL) was added 3 Å molecular sieves (ca. 50 mg). After stirring for 20 min., the mixture was treated with DDQ (0.016 g, 0.070 mmol). After stirring for 30 min., the mixture was diluted with Et₂O and washed with saturated aqueous NaHCO₃ (3 x 20 mL) and brine. The organic solution was dried over MgSO₄, filtered and concentrated. The residue was purified by flash chromatography (20% EtOAc in hexanes) to give 8 mg (27%) of the product as a colorless oil. The illustrated NOE measurements established the 1,3-syn relationship of the disubstituted acetal and thereby confirmed the 1,5-anti relationship of the parent aldol compound **7c**. IR (thin film): 3026, 3001, 2919, 2858, 1734, 1613, 1586, 1514, 1248, 1102, 1033, 829, 701 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.29-7.36 (d, $J=8.4$ Hz, 2H, ArH), 7.27-7.24 (m, 5H, ArH), 7.20-7.14 (m, 3H, ArH), 6.88-6.85 (m, 3H, ArH), 5.42 (s, 1H, ArCH(OR)₂), 5.30-5.24 (m, 1H, CHOAc), 4.49-4.41 (ABq, $J_{\text{AB}}=11.6$ Hz, $\Delta V_{\text{AB}}=7.88$ Hz, 2H, CH₂OPMB), 4.00-3.96 (m, 1H, CHOR), 3.86-3.74 (m, 1H, CHOR), 3.80 (s, 3H, ArOCH₃), 3.78 (s, 3H, ArOCH₃), 3.69-3.64 (m, 1H, CH₂OPMB), 3.60-3.53 (m, 1H, CH₂OPMB), 2.68-2.60 (m, 2H, CH₂Ar), 2.04 (s, 3H, CH₃CO₂R), 1.91-1.72 (m, 4H, CH₂CH₂OPMB and CH₂CH(OAc)CH₂), 1.62-1.55 (m, 2H, PhCH₂CH₂), 1.55-1.51 (dd, $J=2.2, 10.7$ Hz, 1H, CH₂CHOR), 1.46-1.37 (q, $J=10.7$ Hz, 1H, CH₂CHOR) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 171.0, 130.5, 129.2, 128.3, 128.2, 127.2, 125.8, 113.7, 113.4, 100.0, 73.4, 73.3, 72.6, 70.7, 65.6, 55.2, 40.6, 37.2, 36.5, 36.0, 31.5, 21.2 ppm; R_f 0.39 (20% EtOAc in hexanes); Exact mass calcd for $\text{C}_{33}\text{H}_{40}\text{O}_7\text{Na}$: 571.2672. Found 571.2690 (FAB, MNBA, added NaI).

(3R*)-1-Phenyl-3-hydroxy-6-[2-(4-methoxyphenyl)-1,3-dioxan-6(R)-yl]-5-hexanone (*anti*-7d). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **6e** (0.097 g, 0.388 mmol), Bu₂BOTf (106 μ L, 0.427 mmol), Hunig's base (79 μ L, 0.466 mmol), and hydrocinnamaldehyde solution (0.466 mL, 0.466 mmol). Purification by flash chromatography (50% EtOAc in hexanes) provided 0.078 g (52%) of the product as a mixture of diastereomers. HPLC analysis of the unpurified product (Zorbax silica, 50% EtOAc in hexanes, 0.5 mL/min, Tr (min)=19.4 min, Tr(maj)=20.5 min) indicated a 93:07 mixture of isomers. IR (thin film) ν 3481, 2926, 2852, 1717, 1665, 1558, 1495, 1455, 1365, 1249, 1173, 1098, 1032, 829, 750 cm^{-1} ; ¹H NMR (400 MHz, CDCl₃) δ 7.47-7.45 (m, 2H, ArH), 7.40-7.36 (m, 3H, ArH), 7.30-7.26 (m, 3H, ArH), 6.98-6.95 (m, 2H, ArH), 4.47-4.41 (m, 1H, CHOR), 4.36-4.33 (dd, J =4.0, 11.0 Hz, 1H, CHOR), 4.20-4.13 (heptet, J =4.1 Hz, 1H, CHOH), 4.11-4.04 (dt, J =2.5, 12.0 Hz, 1H, CHOR), 3.88 (s, 3H, ArOCH₃), 2.99-2.93 (dd, J =7.7, 15.8 Hz, 1H, CH₂C=O), 2.90-2.60 (m, 5H, CH₂C=O and ArCH₂), 1.97-1.85 (m, 2H, ArCH₂CH₂), 1.81-1.73 (m, 1H, ROCH₂CH), 1.70-1.67 (dd, J =13.2, 1.3 Hz, ROCH₂CH) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 209.6, 159.9, 141.7, 130.8, 12.4, 128.3, 127.2, 125.8, 113.6, 101.1, 73.3, 66.8, 66.7, 55.2, 50.7, 49.3, 37.9, 31.7, 31.0 ppm; R_f 0.14 (50% EtOAc in hexanes); Exact mass calcd for C₂₃H₂₈O₅: 384.1937. Found 384.1956 (EI).

4S-[(Triphenylmethyloxy)-methyl]-6(R)-[1-phenyl-3R-hydroxy-5-hexanone]-2-phenyl-1,3-dioxane (*anti*-7e). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **7f** (0.030 g, 0.061 mmol), Bu₂BOTf (0.019 μ L, 0.076 mmol), Hunig's base (16 μ L, 0.092 mmol), and hydrocinnamaldehyde solution (0.092 mL, 0.092 mmol). Purification by flash chromatography (25% EtOAc in hexanes) provided 0.040 g (70%) of the product as a single isomer by ¹H NMR and ¹³C NMR (> 95:5 *anti*). IR (thin film): 3500, 3057, 3025, 2922, 2871, 1706, 1591, 1489, 1450, 1335, 1258, 1079, 1021, 900, 740 cm^{-1} ; ¹H NMR (400 MHz, CDCl₃) δ 7.71-7.68 (d, J =7.7 Hz, 6H, ArH), 7.24-7.07 (m, 14H, ArH), 5.84 (s, 1H, ArCH(OR)₂), 4.19-4.16 (m, 1H, CHOR), 3.99-3.95 (m, 1H, CHOR), 3.88-3.85 (m, 1H, CHOR), 3.35 (dd, J =5.5, 9.5 Hz, 1H, one of TrOCH₂), 3.24-3.21 (dd, J =4.4 Hz, 9.5 Hz, 1H, one of TrOCH₂), 2.93 (br s, 1H, CHOH), 2.82-2.75 (m, 1H, PhCH₂), 2.67-2.59 (m, 1H, PhCH₂), 2.47-2.41 (dd, J =7.7, 16.0 Hz, 1H, CH₂C=O), 2.00-1.95 (dd, J =4.4, 15.7 Hz, 1H, CH₂C=O), 1.74-1.65 (m, 1H, PhCH₂CH₂), 1.52-1.43 (m, 1H, PhCH₂CH₂), 1.39-1.31 (q, J =12.0 Hz, 1

H, dioxane CH₂-axial *H*), 1.27-1.23 (d, *J*=12.8 Hz, 1H, dioxane-CH₂-equatorial *H*) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 208.5, 44.5, 142.4, 139.2, 129.2, 128.8, 128.6, 128.1, 127.2, 126.6, 126.0, 100.9, 86.9, 75.9, 72.9, 67.1, 66.7, 50.7 ppm; *R*_f 0.26 (30% EtOAc in hexanes); Exact mass calcd for C₄₂H₄₂O₅Na: 649.2930. Found 649.2947 (FAB, MNBA, added NaI).

Adduct (7f) : The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **6d** (10 mg, 0.031 mmol), Bu₂BOTf (8.2 μL, 0.033 mmol), Hunig's base (6 μL, 0.034 mmol), and hydrocinnamaldehyde (4.5 μL, 0.034 mmol). Purification by flash chromatography (40 % EtOAc in hexanes) provided 7 mg (70%) of the product as a 89 : 11 mixture of isomers (HPLC : Zorbax, 20% EtOAc/CH₂Cl₂). *Anti*-**7f** was found to be the major isomer and the relative stereochemistry was proved by X-ray crystallography. mp 60-61 °C; IR (thin film) ν 4368, 3087, 3056, 3026, 2927, 2882, 1708, 1495, 1453, 1410, 1360, 1180, 1146, 1095, 1069, 1031, 947, 738, 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.35-7.16 (m, 10H, Ar*H*), 4.56 (d, *J*=12.2 Hz, 1H, PhCH₂O), 4.51 (d, *J*=12.2 Hz, 1H, PhCH₂O), 4.48 (m, 1H, CHOR), 4.12-4.04 (m, 2H, CHOR, CHOH), 3.92 (m, 4H, O(CH₂)₂O), 3.64 (dd, *J*=10.2, 7.2 Hz, 1H, CH₂OBn), 3.45 (dd, *J*=10.2, 4.4 Hz, 1H, CH₂OBn), 3.20 (d, *J*=3.6 Hz, 1H, OH), 2.96 (dd, *J*=15.5, 8.3 Hz, 1H, ROCHCH₂C=O), 2.79 (ddd, *J*=13.7, 9.9, 5.3 Hz, 1H, PhCH₂CH₂), 2.68-2.58 (m, 3H, C=OCH₂CHOH, PhCH₂CH₂), 2.62 (dd, *J*=15.5, 9.3 Hz, 1H, ROCHCH₂C=O), 1.88 (dd, *J*=13.4, 4.8 Hz, 1H, CH₂CH(OR)CH₂C=O), 1.82-1.74 (m, 1H, PhCH₂CH₂), 1.76 (dd, *J*=13.3, 4.2 Hz, 1H, CH₂CH(OR)CH₂OBn), 1.69-1.61 (m, 1H, PhCH₂CH₂), 1.63 (dd, *J*=13.3, 7.3 Hz, 1H, CH₂CH(OR)CH₂OBn), 1.59 (dd, *J*=13.4, 5.7 Hz, 1H, CH₂CH(OR)CH₂C=O) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 210.4, 142.0, 128.5, 128.4, 127.8, 127.7, 125.9, 106.4, 77.3, 73.4, 71.4, 70.2, 68.0, 66.9, 64.5, 50.5, 47.1, 38.6, 38.2, 36.2, 31.9 ppm; *R*_f 0.35 (50% EtOAc in hexanes); Exact mass calcd for C₂₇H₃₄O₆Na: 477.2253. Found 477.2258 (FAB, MNBA, added NaI).

(3*R, 7*R**)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-9-methyl-5-decanone (8a).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction: 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (319.4 mg, 1.02 mmol), Bu₂BOTf (270 μL, 1.07 mmol), Hunig's base (196 μL, 1.12 mmol) and isovaleraldehyde solution (1.12 mL, 1.12 mmol). Purification by flash chromatography (20% EtOAc in hexanes) provided 358 mg (88%) of the alcohol contaminated with <10% of the syn isomer. HPLC analysis

of the unpurified product (Zorbax Silica, 12 % EtOAc in hexane, 1.0 mL/min, T_R (Maj) = 49 min, T_R (Min) = 54.5 min) revealed a 90:10 ratio of anti and syn diastereoisomers respectively. IR (thin film) ν 3462, 3026, 2954, 2932, 2868, 1708, 1613, 1514, 1455, 1249, 1069, 1035, 822, 700 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.29-7.15 (m, 7H, ArH), 6.86 (dt, J = 9, 3 Hz, 2H, ArH), 4.46 (d, J = 11 Hz, 1H, OCH_2Ar), 4.41 (d, J = 11 Hz, 1H, OCH_2Ar), 4.13-4.07 (m, 1H, CHOH), 3.98-3.93 (m, 1H, CHOPMB), 3.79 (s, 3H, OCH_3), 2.94 (d, J = 3 Hz, 1H, CHOH), 2.78 (dd, J = 16, 8 Hz, 1H, CH_2COCH_2), 2.74-2.62 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 2.58-2.43 (m, 3H, CH_2COCH_2), 1.94-1.71 (m, 3H, $\text{CH}_2\text{CH}_2\text{Ph}$, $\text{CH}(\text{CH}_3)_3$), 1.46-1.40 (m, 1H, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 1.12-1.06 (m, 1H, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 0.91 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 0.90 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 210.6, 159.2, 141.6, 130.2, 129.3, 128.3, 128.2, 125.8, 113.7, 74.6, 71.2, 65.5, 55.1, 50.9, 48.2, 45.4, 35.8, 31.2, 24.2, 23.1, 21.9 ppm. R_f 0.4 (30 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4$: 398.2457. Found: 398.2474 (EI).

Stereochemical proof of anti-diastereomer. The stereochemistry of the anti diastereomer was assigned by analysis of the derived benzylidene acetal.

(3R*, 5R*, 7R*)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-5-hydroxy-7-benzoyl-9-methyl-decane.

To a solution of 140 mg (0.351 mmol) of 1-phenyl-3-[4-(Methoxybenzyl)oxy]-7-hydroxy-9-methyl-5-decanone anti diastereomer in 1 mL of THF was added 142 μL (1.4 mmol) of benzaldehyde and the solution was cooled to -10°C . To this resulting clear solution was added 1.0 mL of a 0.1 M solution of SmI_2 in THF. The reaction was monitored by TLC and an additional portion of the SmI_2 solution (2.0 mL) was added after 1 h. The reaction was warmed to room temperature and was diluted with Et_2O and saturated aqueous NaHCO_3 . Layers were separated and the aqueous phase was extracted with Et_2O . The combined organic layers were washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (15% EtOAc in hexanes) to afford 107 mg (60%) of the desired alcohol: IR (thin film) ν 3500, 3062, 3026, 3000, 2954, 2869, 1714, 1612, 1514, 1452, 1276, 1249, 1112, 1070, 1028, 821, 713, 700 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.08-8.05 (m, 2H, ArH), 7.58 (tt, J = 7, 1 Hz, 1H, ArH), 7.47-7.44 (m, 2H, ArH), 7.25-7.09 (m, 7H, ArH), 6.77 (dt, J = 9, 3 Hz, 2H, ArH), 5.48-5.41 (m, 1H, CHOBz), 4.47 (d, J = 11 Hz, 1H, OCH_2Ar), 4.36 (d, J = 11 Hz, 1H, OCH_2Ar), 3.78-3.72 (m, 1H, CHO), 3.76 (s, 3H, OCH_3), 3.74 (s, 1H, CHOH), 3.67-3.61 (m, 1H, CHO), 2.64-2.60 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 1.91-1.58 (m, 8H, $\text{CH}_2\text{CH}(\text{OPMB})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{OBz})\text{CH}_2\text{CH}$), 1.45-1.38 (m, 1H, $\text{CH}_2\text{CH}(\text{CH}_3)_2$), 0.94 (d, J = 6 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 0.93 (d, J = 6 Hz, 3H, $\text{CH}(\text{CH}_3)_2$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 167.2, 159.0, 142.0, 132.9, 130.2, 130.1, 129.6, 129.3, 128.3, 128.2, 125.6, 113.7, 76.7, 70.7, 70.0, 65.8, 55.1, 44.1, 43.5, 40.9, 35.3, 31.0, 24.7, 23.1, 22.0 ppm. R_f 0.3 (15 %

EtOAc/hexanes); Exact mass calcd for $C_{32}H_{40}O_5Na$: 527.2773. Found: 527.2759 (FAB, MNBA, added NaI).

(4*R)-5-[2-(4-Methoxyphenyl)-4-(*R**)-(2-phenyleth-1-yl)-1,3-dioxan-6-(*R**)-yl]-4-benzoyl-2-methyl-pentane.** To a suspension of 50 mg of molecular sieves (3 Å) and 24 mg (0.104 mmol) of DDQ in 500 μ L of CH_2Cl_2 was added 44 mg (0.087 mmol) of the alcohol as a solution in 400 μ L of THF (200 μ L rinse). This mixture was stirred 1 h at room temperature and then was diluted with Et_2O and saturated aqueous $NaHCO_3$. Layers were separated and the aqueous phase was extracted with Et_2O . The combined organic layers were washed four times with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (7% EtOAc in hexane) to produce 35.5 mg (83%) of benzylidene acetal. The illustrated NOE measurements established the 1,3-syn relationship between the benzylidene oxygen and confirmed the 1,5-anti relationship of the parent compound, 1-phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-9-methyl-5-decanone *anti*-**9a**: IR (thin film): 3062, 3028, 2953, 2867, 1715, 1615, 1517, 1452, 1272, 1111, 1027, 828, 713 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.05-8.03 (m, 2H, ArH), 7.56-7.53 (m, 1H, ArH), 7.49-7.41 (m, 4H, ArH), 7.28-7.23 (m, 2H, ArH), 7.18-7.15 (m, 3H, ArH), 6.89 (dt, J = 9, 3 Hz, 2H, ArH), 5.59-5.54 (m, 1H, $CHOBz$), 5.41 (s, 1H, $CHPMP$), 3.91-3.86 (m, 1H, $CHOCHPMP$), 3.80 (s, 3H, OCH_3), 3.76-3.70 (m, 1H, $CHOCHPMP$), 2.84-2.70 (m, 2H, CH_2CH_2Ph), 2.02-1.43 (m, 9H, $CH_2CH(O)CH_2CH(O)CH_2CH(OBz)CH_2CH$), 0.94 (t, J = 6 Hz, 6H, $CH(CH_3)_2$) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 159.5, 141.8, 132.6, 131.3, 130.6, 129.4, 128.4, 128.2, 127.1, 125.7, 113.4, 99.9, 75.2, 73.3, 70.2, 55.2, 44.2, 41.3, 37.3, 37.2, 31.1, 24.6, 23.0, 22.3 ppm. R_f 0.2 (5 % EtOAc/hexanes); Exact mass calcd for $C_{32}H_{38}O_5Na$: 525.2617. Found: 525.2618 (FAB, MNBA, added NaI).

(3*R, 7*S**)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone (8c).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (321.3 mg, 1.03 mmol), Bu_2BOTf (271 μ L, 1.08 mmol), Hunig's base (197 μ L, 1.13 mmol) and isobutyraldehyde solution (1.13 mL, 1.13 mmol). Purification by flash chromatography (20 % EtOAc in hexanes) provided 332 mg (84%) of the alcohol contaminated with < 6% of the syn

isomer. HPLC analysis of the unpurified product (Zorbax Silica, 10 % EtOAc in hexane, 1.0 mL/min, T_R (Maj) = 59.6 min, T_R (Min) = 65.3 min) and ^{13}C NMR (125 MHz, CDCl_3 , Maj = 210.79 ppm, Min = 210.98 ppm) revealed a 94:6 ratio of anti and syn diastereoisomers respectively. IR (thin film) ν 3472, 3026, 2959, 2934, 2872, 1709, 1613, 1514, 1455, 1249, 1076, 1035, 822, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.29-7.15 (m, 7H, ArH), 6.86 (dt, J = 9, 3 Hz, 2H, ArH), 4.46 (d, J = 11 Hz, 1H, OCH_2Ar), 4.41 (d, J = 11 Hz, 1H, OCH_2Ar), 3.98-3.93 (m, 1H, CHOPMB), 3.81-3.76 (m, 1H, CHOH), 3.79 (s, 3H, OCH_3), 2.92 (d, J = 4 Hz, 1H, CHOH), 2.80 (dd, J = 16, 8 Hz, 1H, CH_2COCH_2), 2.74 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 2.58-2.51 (m, 2H, CH_2COCH_2), 2.47 (dd, J = 17, 10 Hz, 1H, CH_2COCH_2), 1.94-1.80 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 1.67-1.60 (m, 1H, $\text{CH}(\text{CH}_3)_2$), 0.90 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 0.87 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 210.9, 159.1, 141.6, 130.2, 129.3, 128.3, 128.2, 125.7, 113.7, 74.5, 72.0, 71.2, 55.1, 48.3, 47.4, 35.8, 32.8, 31.2, 18.1, 17.6 ppm. R_f 0.3 (30 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{24}\text{H}_{32}\text{O}_4$: 384.2301. Found: 384.2300 (EI).

Stereochemical proof of anti diastereomer. The stereochemistry of the anti-diastereomer was assigned by analysis of the derived benzylidene acetal.

(3*R, 5*R**, 7*S**)-1-Phenyl-3-[4-(Methoxybenzyl)oxy]-5-hydroxy-7-benzoyl-8-methyl-nonane.**

To a solution of 125 mg (0.325 mmol) of 1-phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone in 1 mL of THF was added 132 μL (1.3 mmol) of benzaldehyde and the solution was cooled to -10°C . To this resulting clear solution was added 975 μL of a 0.1 M solution of SmI_2 in THF. The reaction was monitored by TLC and after 1 h the solution was warmed to room temperature. The solution was stirred 30 min and then diluted with Et_2O and saturated aqueous NaHCO_3 . Layers were separated and the aqueous phase was extracted with Et_2O . The combined organic layers were washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (20% EtOAc in hexane) to afford 149 mg (94%) of the desired alcohol: IR (thin film) ν 3500, 3062, 3027, 2961, 2874, 2836, 1714, 1612, 1514, 1452, 1277, 1249, 1111, 1070, 1028, 822, 713, 701 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.09-8.07 (m, 2H, ArH), 7.60-7.56 (m, 1H, ArH), 7.48-7.44 (m, 2H, ArH), 7.24-7.08 (m, 7H, ArH), 6.77 (dt, J = 9, 3 Hz, 2H, ArH), 5.25-5.21 (m, 1H, CHOBz), 4.46 (d, J = 11 Hz, 1H, OCH_2Ar), 4.35 (d, J = 11 Hz, 1H, OCH_2Ar), 3.79-3.71 (m, 1H, CHO), 3.76 (s, 3H, OCH_3), 3.70 (d, J = 2 Hz, 1H, CHOH), 3.67-3.61 (m, 1H, CHO), 2.60 (dd, J = 10, 6 Hz, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 2.00-1.59 (m, 7H, $\text{CH}_2\text{CH}(\text{OPMB})\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{CH}(\text{OBz})\text{CH}$), 1.01 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$), 0.98 (d, J = 7 Hz, 3H, $\text{CH}(\text{CH}_3)_2$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 167.1, 159.0, 142.0, 132.9, 130.2, 130.1, 129.6, 129.3, 128.3, 128.2, 128.1, 125.6, 113.7, 76.8, 76.1, 70.0, 66.0, 55.1, 41.0, 39.7, 35.2, 32.2, 30.9, 18.6, 17.5

ppm. R_f 0.3 (20 % EtOAc/hexanes); Exact mass calcd for $C_{31}H_{38}O_5Na$: 513.2617. Found: 513.2623 (FAB, MNBA, added NaI).

(3*S)-4-[2-(4-methoxyphenyl)-4-(*R**)-(2-phenyleth-1-yl)-1,3-dioxan-6-(*R**)-yl]-3-benzoyl-2-methyl-butane.** To a suspension of 50 mg of molecular sieves (3 Å) and 31.1 mg (0.137 mmol) of DDQ in 500 μ L of CH_2Cl_2 was added 56.1 mg (0.114 mmol) of the alcohol as a solution in 400 μ L of THF (200 μ L rinse). This mixture was stirred 1 h at room temperature and then was diluted with Et_2O and saturated aqueous $NaHCO_3$. Layers were separated and the aqueous phase was extracted with Et_2O . The combined organic layers were washed four times with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (10% EtOAc in hexanes) to produce 42.4 mg (76%) of benzylidene acetal. The illustrated NOE measurements established the 1,3-syn relationship of the disubstituted benzylidene acetal and confirmed the 1,5-anti relationship of the parent compound, 1-phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone: IR (thin film) ν 3062, 3026, 2961, 2858, 1715, 1615, 1517, 1452, 1272, 1110, 1027, 825, 713 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H, ArH), 7.58-7.42 (m, 5H, ArH), 7.28-7.15 (m, 5H, ArH), 6.91-6.89 (m, 2H, ArH), 5.44-5.40 (m, 1H, $CHOBz$), 5.40 (s, 1H, $CHPMP$), 3.86-3.80 (m, 1H, $CHOCHPMP$), 3.80 (s, 3H, OCH_3), 3.75-3.68 (m, 1H, $CHOCHPMP$), 2.84-2.68 (m, 2H, CH_2CH_2Ph), 2.04-1.42 (m, 7H, $CH_2CH(O)CH_2CH(O)CH_2CH(OBz)CH$), 1.00 (d, $J = 7$ Hz, 3H, $CH(CH_3)_2$), 0.97 (d, $J = 7$ Hz, 3H, $CH(CH_3)_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 159.5, 141.7, 132.7, 131.3, 130.5, 129.5, 128.4, 128.2, 128.2, 127.1, 125.7, 113.3, 99.9, 75.2, 75.1, 73.3, 55.2, 37.7, 37.3, 37.2, 32.1, 31.0, 18.3, 17.3 ppm. R_f 0.3 (10 % EtOAc/hexanes); Exact mass calcd for $C_{31}H_{36}O_5Na$: 511.2461. Found: 511.2453 (FAB, MNBA, added NaI).

(3*R, 7*S**)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8,8-dimethyl-5-nonanone (8d).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (322.6 mg, 1.03 mmol), Bu_2BOTf (272 μ L, 1.08 mmol), Hunig's base (198 μ L, 1.14 mmol) and pivalaldehyde solution (1.14 mL, 1.14 mmol). Purification by flash chromatography (15% EtOAc in hexanes) provided 336.6 mg (82%) of the alcohol contaminated with < 5% of the syn isomer. HPLC analysis of the unpurified product (Zorbax Silica, 8 % EtOAc in hexanes, 1.0

mL/min, T_R (Maj) = 52.5 min, T_R (Min) = 59.2 min) and ^{13}C NMR (125 MHz, CDCl_3 , Maj = 211.00 and 33.96 ppm, Min = 211.28 and 34.02 ppm) revealed a 95:5 ratio of anti and syn diastereoisomers respectively. IR (thin film): 3499, 3026, 2954, 2868, 1709, 1613, 1514, 1248, 1082, 1035, 822, 701 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.29-7.15 (m, 7H, ArH), 6.86 (dt, J = 9, 3 Hz, 2H, ArH), 4.47 (d, J = 11 Hz, 1H, OCH_2Ar), 4.41 (d, J = 11 Hz, 1H, OCH_2Ar), 3.99-3.93 (m, 1H, CHOPMB), 3.79 (s, 3H, OCH_3), 3.70 (d, J = 10 Hz, 1H, CHOH), 2.88 (s(br), 1H, CHOH), 2.81 (dd, J = 16, 8 Hz, 1H, CH_2COCH_2), 2.77-2.62 (m, 4H, $\text{CH}_2\text{CH}_2\text{Ph}$), 2.60-2.52 (m, 2H, CH_2COCH_2), 2.44 (dd, J = 17, 10 Hz, 1H, CH_2COCH_2), 1.94-1.80 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$), 0.87 (s, 9H, $\text{C}(\text{CH}_3)_3$) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 210.8, 159.0, 141.5, 130.2, 129.2, 128.2, 128.1, 125.6, 113.6, 74.5, 74.5, 71.0, 54.9, 48.3, 45.4, 35.7, 33.9, 31.1, 25.4 ppm. R_f 0.4 (20 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4$: 398.2457. Found: 398.2450 (EI).

(1S*, 5R*)-1,7-Diphenyl-5-[4-(methoxybenzyl)oxy]-1-hydroxy-3-heptanone (8e). The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (321.8 mg, 1.03 mmol), Bu_2BOTf (272 μL , 1.08 mmol), Hunig's base (197 μL , 1.13 mmol) and benzaldehyde solution (1.13 mL, 1.13 mmol). Purification by flash chromatography (20 % EtOAc in hexanes) provided 379.6 mg (88%) of the alcohol contaminated with < 4% of the syn isomer. HPLC analysis of the unpurified product (Zorbax Silica, 13 % EtOAc in hexane, 1.0 mL/min, T_R (Maj) = 43.5 min, T_R (Min) = 48.2 min) revealed a 96:4 ratio of anti and syn diastereoisomers respectively. IR (thin film) ν 3448, 3027, 2933, 2863, 1710, 1612, 1514, 1454, 1248, 1065, 1033, 822, 753, 701 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.14 (m, 12H, ArH), 6.85 (dt, J = 9, 3 Hz, 2H, ArH), 5.09 (dt, J = 9, 3 Hz, 1H, CHOH), 4.44 (d, J = 11 Hz, 1H, OCH_2Ar), 4.38 (d, J = 11 Hz, 1H, OCH_2Ar), 3.97-3.91 (m, 1H, CHOPMB), 3.76 (s, 3H, OCH_3), 3.39 (d, J = 3 Hz, 1H, CHOH), 2.84-2.59 (m, 5H, $\text{CH}_2\text{CH}_2\text{Ph}$, CH_2COCH_2), 2.51 (dd, J = 16, 5 Hz, 1H, CH_2COCH_2), 1.93-1.83 (m, 2H, $\text{CH}_2\text{CH}_2\text{Ph}$); ^{13}C NMR (100 MHz, CDCl_3) δ 209.7, 159.1, 142.6, 141.5, 130.1, 129.3, 128.3, 128.3, 128.1, 127.4, 125.7, 125.4, 113.6, 74.4, 71.1, 69.6, 55.0, 52.3, 48.2, 35.8, 31.1 ppm. R_f 0.3 (30 % EtOAc/hexanes); Exact mass calcd for $\text{C}_{27}\text{H}_{30}\text{O}_4\text{Na}$: 441.2042. Found: 441.2034 (FAB, MNBA, added NaI).

(3*R*,5*S*)-3-*tert*-Butyldimethylsilyloxy-5-hydroxy-8-[2-phenyl-4-(*R*)-(triphenylmethyloxy)-methyl-1,3-dioxan-6(*S*)-yl]-octan-7-on-1-oic acid-2-(*R*)-naphthylethanol ester (13). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): ketone **1** (0.100 g, 0.203 mmol), Bu₂BOTf (53 μ L, 0.213 mmol), Hunig's base (41 μ L, 0.244 mmol), and aldehyde (*R*)-**11**⁷ (0.098 g, 0.244 mmol). Purification by flash chromatography (20% EtOAc in hexanes) provided 0.154 g (85%) of the product as a mixture of diastereomers. HPLC analysis of the unpurified product (Zorbax silica, 20% EtOAc in hexanes, 1.0 mL/min, Tr (min)=14.9 min, Tr(maj)=15.8 min) indicated a 91 : 09 mixture of isomers. IR (thin film) ν 3600, 3057, 2928, 1733, 1490, 1449, 1265, 1080, 1019, 838, 739, 701, 632 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.80-7.58 (m, 10H, ArH), 7.44-7.41 (dd, *J*=1.5, 8.5 Hz, 1H, ArH), 7.29-7.01 (m, 16H, ArH); 6.18-6.14 (q, *J*=6.5 Hz, 1H, ArCH(Me)OR), 5.43 (s, 1H, ArCH(OR)₂), 4.53-4.48 (m, 1H, CHOTBS), 4.19 (m, 1H, CHOH), 4.16-4.09 (m, 1H, CHOR), 3.84-3.82 (m, 1H, CHOR), 3.44-3.41 (dd, *J*=5.6, 9.5 Hz, 1H, TrOCH₂), 3.18-3.15 (dd, *J*=4.5, 9.5 Hz, 1H, TrOCH₂), 3.08 (s, 1H, CHOH), 2.65-2.55 (m, 2H, CH₂CO₂R), 2.44-2.38 (dd, *J*=7.6, 16.1 Hz, 1H, CH₂C=O), 2.21-2.09 (m, 2H, CH₂C=O), 1.99-1.93 (dd, *J*=4.7, 16.1 Hz, CH₂C=O), 1.81-1.74 (m, 1H, CHCHOR), 1.60-1.54 (m, 1H, CHCHOR), 1.51-1.49 (d, *J*=6.5 Hz, 3H, ArCHCH₃), 1.34-1.19 (m, 2H, CH₂CHOR), 0.881 (s, 9H, (CH₃)₃CSi), 0.07 (s, 3H, CH₃Si), 0.03 (3, 3H, CH₃Si) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 208.0, 170.5, 144.6, 139.3, 133.5, 129.2, 128.7, 128.6, 128.2, 128.1, 127.8, 127.2, 126.6, 126.3, 125.7, 124.5, 100.9, 86.9, 76.0, 72.8, 72.5, 67.8, 67.2, 65.1, 51.0, 49.2, 44.0, 42.6, 33.6, 25.9, 22.2, 18.0, -4.5, -4.6 ppm; R_f 0.17 (20% EtOAc in hexanes); Exact mass calcd for C₅₆H₆₄O₈Na: 915.4268. Found 529.4222 (FAB, MNBA, added NaI).

(3*S*,5*S*)-3-*tert*-Butyldimethylsilyloxy-5-hydroxy-8-[2-phenyl-4-(*R*)-triphenylmethyloxy)-methyl-1,3-dioxan-6(*S*)-yl]-octan-7-on-1-oic acid-2-(*S*)-naphthylethanol ester (14). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **1** (0.100 g, 0.203 mmol), Bu₂BOTf (61 μ L, 0.223 mmol), Hunig's base (42 μ L, 0.250 mmol), and aldehyde (0.089 g, 0.223 mmol). Enolization was conducted at -78 °C. The solution was cooled to -115°C and the aldehyde (*S*)-**11** added as a solution in Et₂O. Purification by flash chromatography (15% EtOAc in hexanes) provided 0.144 g (80%) of the product as a mixture of diastereomers. HPLC analysis of the unpurified product (Zorbax silica, 20% EtOAc in hexanes, 1.0 mL/min, Tr (maj)=16.2 min, Tr(min)=19.2 min) indicated a 96 : 04 mixture of isomers. [α]_D²³₅₈₉ -3.30° (*c* = 1.47, CHCl₃); IR (thin film) ν 3507, 3046,

3015, 2851, 1728, 1594, 1492, 1446, 1379, 1251, 1215, 754 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.71-7.61 (m, 11H, ArH), 7.45 (d, $J=8.5$ Hz, 1H, ArH), 7.29-7.01 (m, 15H, ArH); 6.17 (q, $J=6.5$ Hz, 1H, ArCH(Me)OR), 5.44 (s, 1H, ArCH(OR) $_2$), 4.61 (m, 1H, CHOTBS), 4.41-4.33 (m, 1H, CHOH), 4.18-4.08 (m, 1H, CHOR), 3.90-3.78 (m, 1H, CHOR), 3.46-3.43 (dd, $J=5.6, 9.6$ Hz, 1H, TrOCH $_2$), 3.22 (br s, CHOH), 3.21-3.17 (dd, $J=5.6, 9.6$ Hz, 1H, TrOCH $_2$), 2.64-2.54 (m, 2H, CH $_2$ CO $_2$ R), 2.45-2.41 (dd, $J=7.4, 16.0$ Hz, 1H, CH $_2$ C=O), 2.18-2.06 (m, 2H, CH $_2$ C=O), 2.00-1.96 (dd, $J=4.8, 16.0$ Hz, CH $_2$ C=O), 1.62-1.46 (m, 2H, CHCHOR), 1.51-1.49 (d, $J=6.5$ Hz, 3H, ArCHCH $_3$), 1.39-1.23 (m, 2H, CH $_2$ CHOR), 0.928 (s, 9H, (CH $_3$) $_3$ CSi), 0.17 (s, 3H, CH $_3$ Si), 0.08 (3, 3H, CH $_3$ Si) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 208.0, 169.9, 144.6, 139.5, 139.4, 133.8, 133.7, 129.2, 128.7, 128.6, 128.4, 128.2, 128.1, 127.2, 126.6, 126.3, 126.1, 125.5, 124.6, 100.9, 87.0, 77.5, 76.0, 72.9, 72.5, 67.2, 64.4, 51.2, 49.1, 43.6, 43.4, 33.6, 29.9, 26.0, 22.3, 18.2, -4.66 ppm; R_f 0.21 (20% EtOAc in hexanes); Exact mass calcd for $\text{C}_{56}\text{H}_{64}\text{O}_8\text{Na}$: 915.4268. Found 529.4271 (FAB, MNBA, added NaI).

Stereochemical Proof for 14. Methylation of the aldol adduct (Me_3OBF_4 , di-*tert*-butylmethylpyridine, CH_2Cl_2) and spiroketalization (CSA, MeOH) afforded the spiroketal. The illustrated coupling constants and NOE measurements established the 1,5-*anti* relationship of the parent aldol compound 14.

(3*S*,5*S*)-1-[(Phenyl)methoxy]-3-[4-(methoxybenzyl)oxy]-5-hydroxy-8-[2-phenyl-4-(*R*)-(triphenylmethoxy)methyl-1,3-dioxan-6-(*S*)-yl]-octa-7-one (15). The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **1** (0.065 g, 0.132 mmol), Bu_2BOTf (343 μL , 0.125 mmol), Hunig's base (23 μL , 0.132 mmol), and aldehyde **12** (0.032 g, 0.100 mmol). Purification by flash chromatography (35% EtOAc in hexanes) provided 0.067 g (81%) of the product as a mixture of diastereomers. HPLC analysis of the unpurified product (Zorbax silica, 25% EtOAc in hexanes, 1.0 mL/min, Tr (min)=32.5 min, Tr(maj)=37.2 min) indicated a 96:04 mixture of isomers: 1,5 *anti*-**15** and 1,5 *syn*-**15**. $[\alpha]^{23}_{589} +21.43^\circ$ ($c = 0.695$, CHCl_3); IR (thin film): 3476, 3059, 3033, 2922, 2868, 1713, 1612, 1586, 1513, 1248, 1175, 900, 822, 700 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.51-7.47 (m, 8H, ArH), 7.37-7.18 (d, $J=8.0$ Hz, 2H, ArH), 5.52 (s, 1H, ArCH(OR) $_2$), 4.49-4.44 (m, ArCH $_2$ OCH $_2$, 2H), 4.38-4.34 (d, $J=12.0$ Hz, 2H, ArCH $_2$ OCH $_2$), 4.23-4.20 (m, 1H, CHOR), 4.12-4.10 (m, 1H, CHOR), 3.82-3.73 (m, 1H, CHOR), 3.76 (s, 3H, ArOCH $_3$), 3.58-3.50 (m, 3H, one of CHOR and

CH₂OBn), 3.36-3.32 (dd, $J=5.8, 9.6$ Hz, 1H, TrOCH₂), 3.09-3.06 (dd, $J=4.8, 9.6$ Hz, 1H, TrOCH₂), 2.88-2.82 (dd, $J=7.2, 16.3$, 1H CH₂C=O), 2.61-2.48 (m, 3H, CH₂C=O), 1.94-1.82 (m, 2H, CH₂CHOPMB), 1.73-1.67 (m, 1H, BnOCH₂CH₂), 1.61-1.56 (m, 2H, TrOCH(OR)CH₂ and BnOCH₂CH₂), 1.52-1.43 (q, $J=11.5$ Hz, 1H, CHOR) ppm; ¹³C NMR (101 MHz, CDCl₃) δ 208.2, 159.2, 143.9, 138.3, 138.2, 130.0, 129.5, 128.7, 128.3, 128.1, 127.7, 126.9, 126.0, 113.8, 110.5, 86.4, 77.2, 75.8, 75.5, 73.0, 72.7, 70.5, 66.6, 66.5, 66.4, 55.2, 50.9, 49.4, 40.7, 33.9, 33.6, 29.6 ppm; R_f 0.16 (30% EtOAc in hexanes). Exact mass calcd for C₅₃H₅₆O₈Na: 843.3873. Found 843.3837 (FAB, MNBA, added NaI).

Stereochemical proof of 15. The stereochemistry of **15** was assigned by analysis of the derived benzylidene acetal.

1-[4S--(Phenylmethoxy)ethyl-2-(4-methoxyphenyl)-1,3-dioxan-6-(S)-yl]-3-[4-(2-phenyl-4-(R)-triphenylmethyloxymethyl-1,3-dioxan-6-(S)-yl]-2-propanone. To a solution of alcohol **15** (20 mg, 0.024 mmol) in dichloromethane (3 mL) was added 3 Å molecular sieves (ca. 50 mg). After stirring for 20 min, the mixture was treated with DDQ (0.007 g, 0.029 mmol). After stirring for 30 min, the mixture was diluted with Et₂O and washed with saturated aqueous NaHCO₃ (3 x 20 mL) and brine. The organic solution was dried over MgSO₄, filtered and concentrated. The residue was purified by flash chromatography (20% EtOAc in hexanes) to give 10 mg (50%) of the product as a colorless oil. The illustrated NOE measurements established the 1,3-syn relationship of the disubstituted acetal and thereby confirmed the 1,5 anti relationship to the parent aldol compound. [α]_D²³₅₈₉ +6.47° (c = 0.35, CHCl₃); IR (thin film) ν 3055, 2924, 2856, 1717, 1615, 1517, 1490, 1449, 1265, 1249, 1126, 1028, 738, 701 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.48-7.46 (m, 8H, ArH), 7.34-7.21 (m, 19H, ArH), 6.82-6.80 (d, $J=8.6$ Hz, 2H, ArH), 5.58 (s, ArCH(OR)₂), 5.46 (s, ArCH(OR)₂), 4.53-4.46 (ABq, $J_{AB}=12.0$ Hz, $\Delta V_{AB}=5.4$ Hz, 2H, PhCH₂O), 4.41-4.30 (m, 2H, CHOR), 4.12-4.07 (m, 1H, CHOR), 4.04-4.01 (m, 1H, CHOR), 3.74 (s, ArOCH₃), 3.68-3.62 (m, 1H, BnOCH₂), 3.58-3.53 (m, 1H, BnOCH₂), 3.35-3.32 (dd, $J=5.7, 9.6$ Hz, TrOCH₂), 3.08-3.04 (dd, $J=4.9, 9.6$ Hz, 1H, TrOCH₂), 2.92-2.83 (dt, $J=7.6, 16.2$ Hz, 2H, CH₂C=O), 2.61-2.55 (m, 2H, CH₂C=O), 1.91-1.77 (m, 2H, BnOCH₂CH₂), 1.73-1.70 (d, $J=13.1$ Hz, 1H, dioxane CH₂, equatorial H), 1.67-1.64 (d, $J=13.0$ Hz, dioxane CH₂, equatorial H), 1.51-1.32 (two overlapping quartets, $J=13.0$ Hz, dioxane CH₂, axial H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ 206.0, 143.9, 138.0, 128.7, 128.3, 128.1, 127.7, 127.6, 127.5, 127.2, 126.9, 126.0, 113.4, 100.5, 100.4, 75.8, 73.5, 72.9, 72.7, 66.5, 65.9, 55.2, 49.8, 43.3, 36.7, 36.0, 33.6 ppm; R_f 0.37 (40% EtOAc in hexanes) Exact mass calcd for C₅₃H₅₄O₈Na: 841.3716. Found 841.3700 (FAB, MNBA, added NaI).

(3*S*,5*R*)-1-[(Phenyl)methoxy]-3-[4-(methoxybenzyl)oxy]-5-hydroxy-8-[2-phenyl-4-(*R*)-(tri-phenylmethoxy)methyl-1,3-dioxan-6-(*S*)-yl]-octa-7-one (16). A solution of the silyl enol ether **10** (0.075 g, 0.104 mmol) in dichloromethane (2 mL) was treated with a solution of the aldehyde **12** (0.034 g, 0.106 mmol) in dichloromethane (1 mL). The solution was cooled to -78°C . A solution of $\text{BF}_3 \cdot \text{OEt}_2$ (0.111 mL of a 1M soln in CH_2Cl_2) was added. The solution was stirred for 90 min at -78°C . Triethylamine (0.5 mL) and saturated aqueous NaHCO_3 (1mL) were added and the mixture warmed to ambient temperature. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic solutions were washed with saturated aq. NaHCO_3 (20 mL), satd. aq. NH_4Cl (20 mL), and brine (20 mL). The solution was dried over MgSO_4 , filtered, and concentrated. The residue was redissolved in THF (2 mL) and treated with 25 μL $\text{HF} \cdot \text{pyridine}$ (to cleave the silylated aldol adduct). After stirring for 30 min, the solution was quenched with saturated aq. NaHCO_3 and worked up as before. The residue was purified by flash chromatography (35% EtOAc in hexanes) to give 57 mg (66%) of the product **12**. HPLC analysis of the unpurified product (Zorbax silica, 25% EtOAc in hexanes, 1.0 mL/min, Tr (maj)=31.6 min, Tr(min)=36.7 min) indicated a 82:18 mixture of isomers. The major product diastereomer corresponded to the previously observed 1,5-syn aldol adduct (**1**→**15**; minor isomer) **16**. $[\alpha]_{\text{D}}^{23} +9.91^{\circ}$ ($c = 0.585$, CHCl_3) IR (thin film) ν 3479, 3059, 2922, 2868, 1711, 1612, 1586, 1514, 1491, 1449, 1412, 1344, 1302, 1248, 1079, 901 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.51-7.47 (m, 8H, ArH), 7.35-7.19 (m, 19H, ArH), 6.85-6.83 (d, $J=8.7$ Hz, 2H, ArH), 5.60 (s, 1H, ArCH(OR)₂), 4.46-4.44 (m, 4H, ArCH₂OCH₂), 4.40-4.31 (m, 2H, CHOR), 4.13-4.10 (m, 1H, CHOR), 3.90-3.84 (m, 1H, CHOR), 3.77 (s, 3H, ArOCH₃), 3.59-3.49 (m, 2H, BnOCH₂CH₂), 3.37-3.31 (m, 2H, one of TrOCH₂ and CHOH), 3.10-3.06 (dd, $J=9.6, 4.8$ Hz, 1H, one of TrOCH₂), 2.89-2.83 (dd, $J=7.3, 16.3$ Hz, 1H, CH₂C=O), 2.65-2.51 (m, 3H, CH₂C=O), 1.97-1.78 (m, 2H, BnOCH₂CH₂), 1.74-1.66 (m, 2H, CH₂CHOR), 1.55-1.44 (m, 2H, CH₂CHOR) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 208.7, 159.2, 143.9, 138.3, 130.3, 129.6, 128.7, 128.3, 128.1, 127.7, 127.6, 127.5, 126.9, 126.0, 113.8, 100.4, 86.4, 75.8, 73.4, 72.9, 72.7, 71.4, 66.6, 66.5, 64.7, 55.2, 50.9, 49.2, 40.5, 34.2, 33.6, 28.8 ppm; R_f 0.35 (50% EtOAc in hexanes); Exact mass calcd for $\text{C}_{53}\text{H}_{56}\text{O}_8\text{Na}$: 843.3873. Found 843.3864 (FAB, MNBA, added NaI).

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