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# 1,5-Asymmetric Induction in Methyl Ketone Aldol Addition Reactions. Diastereoselective Double Stereodifferentiating Aldol Fragment Coupling Processes.

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## Supplementary Material

**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:  $[\alpha]_D^{25}$  (c g/100 mL solvent). Infrared spectra were recorded on a Perkin Elmer model 1600 FT-IR spectrometer.  $^1\text{H}$  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:  $\delta$  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.  $^{13}\text{C}$  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:  $\delta$  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 described<sup>1</sup> 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 ( $\text{CH}_2\text{Cl}_2$ ) was distilled from  $\text{CaH}_2$  under an inert atmosphere of nitrogen. Diethylether ( $\text{Et}_2\text{O}$ ) and tetrahydrofuran (THF) were distilled from potassium/benzophenone ketyl. Hydrocinnamaldehyde, isobutyraldehyde, isovaleraldehyde and benzaldehyde were distilled from anhydrous  $\text{CaSO}_4$ . All other commercially obtained reagents were used as received. 9-Borabicyclo[3.3.1]nonyl trifluoromethanesulfonate<sup>2</sup> (9-BBN triflate), di-*n*-butylboryl trifluoromethanesulfonate,<sup>2</sup> chlorodicyclohexylborane,<sup>3</sup> and freshly prepared samarium(II) iodide<sup>4</sup> were prepared according to literature procedures.



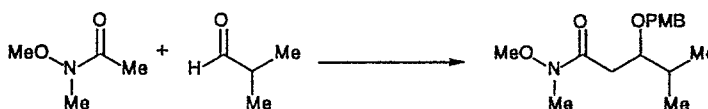
**4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (1-ketone).** To a solution of 18.4 g (51.5 mmol) of amide<sup>5</sup> in 250 mL of THF at  $-78^\circ\text{C}$  was added 20.6 mL (61.8 mmol) of a 3.0 M solution of  $\text{MeMgCl}$  in THF in one portion. The reaction was warmed to  $0^\circ\text{C}$  over 3 h followed by the addition of 0.1 equivalent of  $\text{MeMgCl}$  at  $-10^\circ\text{C}$ . After 1 h at  $0^\circ\text{C}$  the solution was cooled to  $-50^\circ\text{C}$  and diluted with 500 mL of  $\text{Et}_2\text{O}$  and 50 mL of saturated aqueous  $\text{NH}_4\text{Cl}$ . The layers were separated and the aqueous phase was extracted twice with 50 mL of  $\text{Et}_2\text{O}$ . Combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over anhydrous  $\text{MgSO}_4$  and concentrated *in vacuo*. Purification by flash chromatography (10–20%  $\text{EtOAc}$  in hexanes) provided 14.5 g (90%) of the title compound as a colorless oil: IR (thin film)  $\nu$  3025, 2934, 1714, 1612, 1513, 1454, 1358, 1301, 1248, 1174, 1034, 822, 751, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28–7.14 (m, 7H, ArH), 6.88–6.85 (m, 2H, ArH), 4.45 (s, 2H,  $\text{OCH}_2\text{Ar}$ ), 3.94 (quint,  $J = 6$  Hz, 1H,  $\text{CHOPMB}$ ), 3.79 (s, 3H,  $\text{OCH}_3$ ), 2.78 (dd,  $J = 16$ , 7 Hz, 1H,  $\text{CH}_2\text{COCH}_3$ ), 2.74–2.62 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.53 (dd,  $J = 16$ , 5 Hz, 1H,  $\text{CH}_2\text{COCH}_3$ ), 2.13 (s, 3H,  $\text{COCH}_3$ ), 1.92–1.79 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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 %  $\text{EtOAc}$ /hexanes); Exact mass calcd for  $\text{C}_{20}\text{H}_{24}\text{O}_3$ : 312.1725. Found: 312.1735 (EI).



**3-*tert*-Butyldimethylsilyloxy-5-phenyl-*N*-methoxy-*N*-methyl-pentanamide.** To a solution of 803 mg (3.38 mmol) of the alcohol<sup>5</sup> and 512  $\mu$ L (4.40 mmol) of 2,6-lutidine in 11 mL of  $\text{CH}_2\text{Cl}_2$  at 0 °C was added 933  $\mu$ L (4.06 mmol) of *tert*-butyldimethylsilyl trifluoromethanesulfonate. After 30 min, 25 mL of  $\text{H}_2\text{O}$  was added to quench and the mixture was extracted with two 25 mL portions of  $\text{CH}_2\text{Cl}_2$ . The combined organic extracts were washed with 25 mL of  $\text{H}_2\text{O}$  and 25 mL of brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , 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:  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{OCH}_3$ ), 3.17 (s, 1 H,  $\text{NCH}_3$ ), 2.83-2.61 (m, 3 H,  $\text{CH}_2\text{Ph}$  and  $\text{CH}_2\text{C=O}$ ), 2.47 (m, 1 H,  $\text{CH}_2$ ), 1.92-1.75 (m, 2 H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 0.90 (s, 9 H,  $\text{Si}(\text{CH}_3)_3$ ), 0.10 (s, 3 H,  $\text{SiCH}_3$ ), 0.05 (s, 3 H,  $\text{SiCH}_3$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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 (3b).** To a solution of 575 mg (1.64 mmol) of amide in 8 mL of THF at -78 °C was added 709  $\mu$ L (2.13 mmol) of a 3.0 M solution of  $\text{MeMgCl}$  in THF in one portion. The reaction was warmed to 0 °C over 3 h followed by the addition of 0.1 equivalent of  $\text{MeMgCl}$  at -10 °C. After 1 h at 0 °C the solution was cooled to -50 °C and diluted with 20 mL of  $\text{Et}_2\text{O}$  and 5 mL of saturated aqueous  $\text{NH}_4\text{Cl}$ . The layers were separated and the aqueous phase was extracted twice with 5 mL of  $\text{Et}_2\text{O}$ . Combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over anhydrous  $\text{MgSO}_4$  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)  $\nu$  2954, 2929, 2857, 1718, 1603, 1496, 1471, 1360, 1255, 1093, 836, 776, 699  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32-7.19 (m, 5H, ArH), 4.27 (quint,  $J = 6$  Hz, 1H, CHOTBS), 2.74-2.64 (m, 3H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ,  $\text{CH}_2\text{COCH}_3$ ), 2.56 (dd,  $J = 15$ , 5 Hz, 1H,  $\text{CH}_2\text{COCH}_3$ ), 2.18 (s, 3H,  $\text{COCH}_3$ ), 1.89-1.76 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 0.94 (s, 9H,  $\text{Si}(\text{CH}_3)_3$ ), 0.12 (s, 3H,  $\text{SiCH}_3$ ), 0.08 (s, 3H,  $\text{SiCH}_3$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{18}\text{H}_{31}\text{SiO}_2$ : 307.2094. Found: 307.2097 (CI,  $\text{NH}_3$  atmosphere).



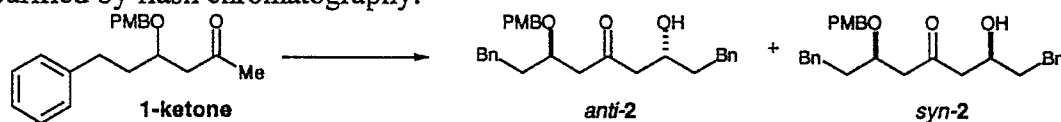
**3-[4-(Methoxybenzyloxy)-4-methyl-*N*-methoxy-*N*-methyl-pentanamide.** Lithium diisopropylamide (LDA) was generated by addition of 15.6 mL (39 mmol) of *n*-butyllithium (2.5M solution in hexanes) to a solution of 5.4 mL (39 mmol) of diisopropylamine in 50 mL of THF at -78 °C. After 10 min, a solution 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  $\text{NH}_4\text{Cl}$ , and the mixture was warmed to ambient temperature. The mixture was diluted with  $\text{Et}_2\text{O}$  and washed once with saturated aqueous  $\text{NH}_4\text{Cl}$ . The aqueous washings were extracted twice with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over anhydrous  $\text{MgSO}_4$ , 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  $\text{Et}_2\text{O}$  at room temperature was added 86  $\mu$ L of trifluoromethanesulfonic acid. After 30 min, the reaction was diluted with 10 mL of saturated aqueous  $\text{NaHCO}_3$  and 100 mL of  $\text{Et}_2\text{O}$ . The layers were separated and the organic extract was washed with brine, dried over anhydrous  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was dissolved in 15 mL of  $\text{CH}_2\text{Cl}_2$  and was stirred 10 min at -78 °C. The heterogeneous cold solution was quickly filtered and rinsed two times with 5 mL of

cold  $\text{CH}_2\text{Cl}_2$ . Solvent was removed *in vacuo* and the residue was purified by flash chromatography (3-7 % EtOAc in  $\text{CH}_2\text{Cl}_2$ ) to provide 5.8 g (60%) of the desired benzyl ether as a colorless oil: IR (thin film)  $\nu$  3462, 2960, 2937, 2804, 1661, 1612, 1513, 1465, 1385, 1248, 1174, 1071, 1036, 822  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.24 (d,  $J$  = 9 Hz, 2H, ArH), 6.85-6.82 (m, 2H, ArH), 4.50 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.46 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.84 (quint,  $J$  = 4 Hz, 1H,  $\text{CHOPMB}$ ), 3.75 (s, 3H,  $\text{OCH}_3$ ), 3.62 (s, 3H,  $\text{NOCH}_3$ ), 3.18 (s, 3H,  $\text{NCH}_3$ ), 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;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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-(Methoxybenzyloxy)-5-methyl-2-hexanone (3a).** To a solution of 4.19 g (14.2 mmol) of amide in 70 mL of THF at  $-78^\circ\text{C}$  was added 5.67 mL (17.0 mmol) of a 3.0 M solution of  $\text{MeMgBr}$  in THF in one portion. The reaction was warmed to  $0^\circ\text{C}$  over 3 h followed by the addition of 0.1 equivalent of  $\text{MeMgBr}$  at  $-10^\circ\text{C}$ . After 1 h at  $0^\circ\text{C}$  the solution was cooled to  $-50^\circ\text{C}$  and diluted with 100 mL of  $\text{Et}_2\text{O}$  and 10 mL of saturated aqueous  $\text{NH}_4\text{Cl}$ . The layers were separated and the aqueous phase was extracted twice with 20 mL of  $\text{Et}_2\text{O}$ . Combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over anhydrous  $\text{MgSO}_4$  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  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{OCH}_2\text{Ar}$ ), 4.41 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.78-3.75 (m, 1H,  $\text{CHOPMB}$ ), 3.77 (s, 3H,  $\text{OCH}_3$ ), 2.67 (dd,  $J$  = 16, 9 Hz, 1H,  $\text{CH}_2\text{COCH}_3$ ), 2.43 (dd,  $J$  = 16, 4 Hz, 1H,  $\text{CH}_2\text{COCH}_3$ ), 2.15 (s, 3H,  $\text{CH}_2\text{COCH}_3$ ), 1.96-1.89 (m, 1H,  $\text{CH}(\text{CH}_3)_2$ ), 0.91 (d,  $J$  = 7 Hz, 6H,  $\text{CH}(\text{CH}_3)_2$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{15}\text{H}_{22}\text{O}_3$ : 250.1569. Found: 250.1558 (EI).

**General procedure for the boron aldol reaction.** To a solution of the methyl ketone (1.00 mmol) in 9 mL of  $\text{Et}_2\text{O}$  was added 1.10 mmol of  $i\text{-Pr}_2\text{NEt}$ . The solution was cooled to  $-78^\circ\text{C}$  and 1.05 mmol of  $\text{Bu}_2\text{BOTf}$  was added dropwise. The resulting white heterogeneous mixture was stirred 30 minutes at  $-78^\circ\text{C}$  followed by the slow addition of 1.1 mmol of a 1.0 M solution of aldehyde in  $\text{Et}_2\text{O}$  over a period of 15 minutes. The mixture was stirred 2 h at  $-78^\circ\text{C}$  and 7 mL of a pH = 7 buffer/MeOH (1/6, v/v) solution was added. This resulting clear solution was placed at  $0^\circ\text{C}$  followed by the addition of 3 mL of a 30%  $\text{H}_2\text{O}_2$ /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  $\text{Et}_2\text{O}$  and water. The aqueous phase was extracted with  $\text{Et}_2\text{O}$  and combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$ , saturated aqueous  $\text{NaCl}$ , dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Product alcohols were purified by flash chromatography.

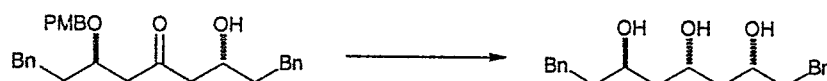


**(3R\*, 7R\*)-1,9-Diphenyl-3-[4-(methoxybenzyloxy)-7-hydroxy-5-nonanone (anti-2).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyloxy)-6-phenyl-2-hexanone 1-ketone (320.4 mg, 1.03 mmol),  $\text{Bu}_2\text{BOTf}$  (271  $\mu\text{L}$ , 1.08 mmol), Hunig's base (197  $\mu\text{L}$ , 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-2* and *syn-2*. These two isomers were separated on HPLC using a preparative column (Zorbax, 21.2 mm X 25 cm, 10 % EtOAc/30 %  $\text{CH}_2\text{Cl}_2$ /60 % hexanes, 9 mL/min, 100  $\mu\text{L}$  injected of a 60 mg/mL solution,  $T_R$  (Maj) = 44.8 min and  $T_R$  (Min) = 48.4 min): IR (thin film)  $\nu$  3452, 3025, 2932, 1707, 1612, 1513, 1454, 1247, 1064, 1032, 700  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29-7.15 (m, 12H, ArH), 6.85 (dt,

$J = 9, 3$  Hz, 2H, ArH), 4.46 (d,  $J = 11$  Hz, 1H, OCH<sub>2</sub>Ar), 4.39 (d,  $J = 11$  Hz, 1H, OCH<sub>2</sub>Ar), 4.06-4.00 (m, 1H, CHOH), 3.96-3.92 (m, 1H, CHOPMB), 3.78 (s, 3H, OCH<sub>3</sub>), 3.04 (d,  $J = 4$  Hz, 1H, CHOH), 2.80-2.48 (m, 8H, CH<sub>2</sub>CH<sub>2</sub>Ph, CH<sub>2</sub>COCH<sub>2</sub>), 1.94-1.74 (m, 3H, CH<sub>2</sub>CH<sub>2</sub>Ph), 1.68-1.61 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>Ph) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  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 C<sub>29</sub>H<sub>34</sub>O<sub>4</sub>+NH<sub>4</sub>: 464.2801. Found: 464.2793 (CI, NH<sub>3</sub> atmosphere).

**(3R\*, 7S\*)-1,9-Diphenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-5-nonanone (syn-2).** IR (thin film)  $\nu$  3462, 3026, 2932, 2861, 1707, 1612, 1514, 1454, 1248, 1069, 1032, 700 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.30-7.15 (m, 12H, ArH), 6.85 (dt,  $J = 9, 3$  Hz, 2H, ArH), 4.45 (d,  $J = 11$  Hz, 1H, OCH<sub>2</sub>Ar), 4.40 (d,  $J = 11$  Hz, 1H, OCH<sub>2</sub>Ar), 4.03-3.97 (m, 1H, CHOH), 3.96-3.91 (m, 1H, CHOPMB), 3.78 (s, 3H, OCH<sub>3</sub>), 3.10 (dd,  $J = 4, 1$  Hz, 1H, CHOH), 2.81-2.50 (m, 8H, CH<sub>2</sub>CH<sub>2</sub>Ph, CH<sub>2</sub>COCH<sub>2</sub>), 1.93-1.75 (m, 3H, CH<sub>2</sub>CH<sub>2</sub>Ph), 1.68-1.61 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>Ph) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  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 C<sub>29</sub>H<sub>34</sub>O<sub>4</sub>Na: 469.2355. Found: 469.2372 (FAB, MNBA, added NaI).

**Stereochemical proof of (2):** The stereochemistry of *anti*-2 and *syn*-2 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*-2) (94.4 mg, 0.211 mmol) in 1.5 mL of toluene at -78 °C was added 634  $\mu$ 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 Et<sub>2</sub>O followed by the addition of 500  $\mu$ 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 Na<sub>2</sub>SO<sub>4</sub> 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)<sub>2</sub>). The resulting mixture was purged with H<sub>2</sub> and then stirred at room temperature under a 1 atmosphere pressure of H<sub>2</sub>. 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. <sup>1</sup>H NMR and <sup>13</sup>C NMR analysis clearly indicate that this product was unsymmetrical as expected for a 1,5-*anti* relationship: mp 61-62 °C; IR (CHCl<sub>3</sub>)  $\nu$  3541, 3296, 3025, 2926, 2902, 2850, 1602, 1455, 1117, 1092, 1050, 1018, 751, 700 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  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, CH<sub>2</sub>CH<sub>2</sub>Ph), 1.87-1.49 (m, 8H, CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  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 C<sub>21</sub>H<sub>29</sub>O<sub>3</sub>: 329.2117. Found: 329.2125 (CI, NH<sub>3</sub> 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*-2 in 1.4 mL of THF and 350  $\mu$ L of MeOH at 0 °C was added 261  $\mu$ L of a 1.0 M solution of Et<sub>2</sub>BOMe in THF. After 15 min of stirring, NaBH<sub>4</sub> (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  $\mu$ L of 6 N NaOH and 500  $\mu$ L of H<sub>2</sub>O<sub>2</sub> (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<sub>2</sub>O 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<sub>3</sub> and brine, dried over Na<sub>2</sub>SO<sub>4</sub> 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 % Pd(OH)<sub>2</sub>). The resulting mixture was purged with H<sub>2</sub> and then stirred at room temperature under a 1 atmosphere pressure of H<sub>2</sub>. 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<sub>2</sub>Cl<sub>2</sub>) to afford 18 mg (85 %) of the triol as a white solid. <sup>1</sup>H NMR and <sup>13</sup>C NMR showed signals for a symmetric triol indicating a 1,5-*syn* relationship: mp 87.6-88.3 °C; IR (CHCl<sub>3</sub>)  $\nu$  3464, 3010, 2928, 2856, 1602, 1496, 1454, 1118, 790, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.30-7.17 (m, 10H, ArH), 4.32 (s(br), 1H, CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)), 4.13-4.08 (m, 1H, CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)), 3.91 (m (br), 2H, CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)), 3.09 (s(br), 2H, CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)), 2.79-2.64 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>Ph), 1.86-1.52 (m, 8H, CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>CH(OH)CH<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  141.7, 128.4, 128.3, 125.8, 73.6, 72.1, 43.5, 39.6, 31.6 ppm. R<sub>f</sub> 0.3 (60 % EtOAc/hexanes); Exact mass calcd for C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>Na: 351.1936. Found: 351.1931 (FAB, MNBA, added NaI).



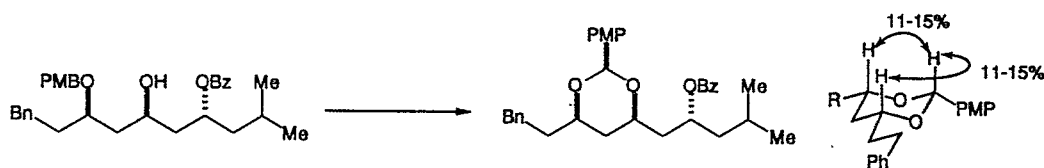
**(3R\*, 7R\*)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-9-methyl-5-decanone.** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction: 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (319.4 mg, 1.02 mmol), Bu<sub>2</sub>BOTf (270  $\mu$ L, 1.07 mmol), Hunig's base (196  $\mu$ L, 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<sub>R</sub> (Maj) = 49 min, T<sub>R</sub> (Min) = 54.5 min) revealed a 90:10 ratio of *anti* and *syn* diastereoisomers respectively. IR (thin film)  $\nu$  3462, 3026, 2954, 2932, 2868, 1708, 1613, 1514, 1455, 1249, 1069, 1035, 822, 700 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.29-7.15 (m, 7H, ArH), 6.86 (dt, *J* = 9, 3 Hz, 2H, ArH), 4.46 (d, *J* = 11 Hz, 1H, OCH<sub>2</sub>Ar), 4.41 (d, *J* = 11 Hz, 1H, OCH<sub>2</sub>Ar), 4.13-4.07 (m, 1H, CHOH), 3.98-3.93 (m, 1H, CHOPMB), 3.79 (s, 3H, OCH<sub>3</sub>), 2.94 (d, *J* = 3 Hz, 1H, CHOH), 2.78 (dd, *J* = 16, 8 Hz, 1H, CH<sub>2</sub>COCH<sub>2</sub>), 2.74-2.62 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>Ph), 2.58-2.43 (m, 3H, CH<sub>2</sub>COCH<sub>2</sub>), 1.94-1.71 (m, 3H, CH<sub>2</sub>CH<sub>2</sub>Ph, CH(CH<sub>3</sub>)<sub>3</sub>), 1.46-1.40 (m, 1H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 1.12-1.06 (m, 1H, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>), 0.91 (d, *J* = 7 Hz, 3H, CH(CH<sub>3</sub>)<sub>2</sub>), 0.90 (d, *J* = 7 Hz, 3H, CH(CH<sub>3</sub>)<sub>2</sub>) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>f</sub> 0.4 (30 % EtOAc/hexanes); Exact mass calcd for C<sub>25</sub>H<sub>34</sub>O<sub>4</sub>: 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-decanone.** 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  $\mu$ L (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<sub>2</sub> in THF. The reaction was monitored by TLC and an additional portion of the SmI<sub>2</sub> solution (2.0 mL) was added after 1 h. The reaction was warmed to room temperature and was diluted with Et<sub>2</sub>O and saturated aqueous NaHCO<sub>3</sub>. Layers were separated and the aqueous phase was extracted with Et<sub>2</sub>O. The combined organic layers were washed with saturated aqueous NaHCO<sub>3</sub> and brine, dried over MgSO<sub>4</sub> 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)  $\nu$  3500, 3062, 3026, 3000, 2954, 2869, 1714, 1612, 1514, 1452, 1276, 1249, 1112, 1070, 1028, 821, 713, 700 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>2</sub>Ar), 4.36 (d, *J* = 11 Hz, 1H, OCH<sub>2</sub>Ar), 3.78-3.72 (m, 1H, CHO), 3.76 (s, 3H, OCH<sub>3</sub>), 3.74 (s, 1H, CHOH), 3.67-3.61 (m, 1H, CHO), 2.64-2.60 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>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;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  167.2, 159.0, 142.0, 132.9, 130.2, 130.1, 129.6, 129.3, 128.3, 128.2, 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  $\text{C}_{32}\text{H}_{40}\text{O}_5\text{Na}$ : 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  $\mu$ L of  $\text{CH}_2\text{Cl}_2$  was added 44 mg (0.087 mmol) of the alcohol as a solution in 400  $\mu$ L of THF (200  $\mu$ L rinse). This mixture was stirred 1 h at room temperature and then was diluted with  $\text{Et}_2\text{O}$  and saturated aqueous  $\text{NaHCO}_3$ . Layers were separated and the aqueous phase was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed four times with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was purified by flash chromatography (7 %  $\text{EtOAc}$  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*-11): IR (thin film)  $\nu$  3062, 3028, 2953, 2867, 1715, 1615, 1517, 1452, 1272, 1111, 1027, 828, 713  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{CHOBz}$ ), 5.41 (s, 1H,  $\text{CHPMP}$ ), 3.91-3.86 (m, 1H,  $\text{CHOCHPMP}$ ), 3.80 (s, 3H,  $\text{OCH}_3$ ), 3.76-3.70 (m, 1H,  $\text{CHOCHPMP}$ ), 2.84-2.70 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.02-1.43 (m, 9H,  $\text{CH}_2\text{CH}(\text{O})\text{CH}_2\text{CH}(\text{O})\text{CH}_2\text{CH}(\text{OBz})\text{CH}_2\text{CH}$ ), 0.94 (t,  $J$  = 6 Hz, 6H,  $\text{CH}(\text{CH}_3)_2$ ) ppm;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  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 %  $\text{EtOAc}$ /hexanes); Exact mass calcd for  $\text{C}_{32}\text{H}_{38}\text{O}_5\text{Na}$ : 525.2617. Found: 525.2618 (FAB, MNBA, added NaI).



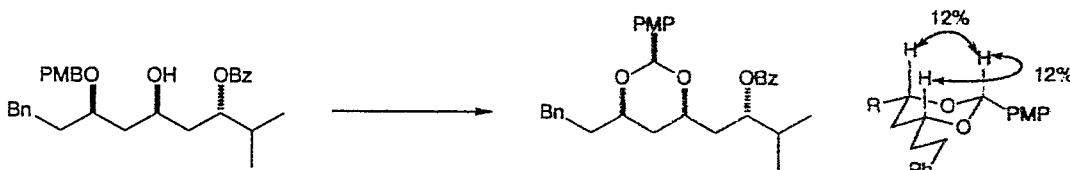
**(3*R*\*, 7*S*\*)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone.** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (321.3 mg, 1.03 mmol),  $\text{Bu}_2\text{BOTf}$  (271  $\mu$ L, 1.08 mmol), Hunig's base (197  $\mu$ L, 1.13 mmol) and isobutyraldehyde solution (1.13 mL, 1.13 mmol). Purification by flash chromatography (20 %  $\text{EtOAc}$  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 %  $\text{EtOAc}$  in hexane, 1.0 mL/min,  $T_R$  (Maj) = 59.6 min,  $T_R$  (Min) = 65.3 min) and  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , Maj = 210.79 ppm, Min = 210.98 ppm) revealed a 94:6 ratio of *anti* and *syn* diastereoisomers respectively. IR (thin film)  $\nu$  3472, 3026, 2959, 2934, 2872, 1709, 1613, 1514, 1455, 1249, 1076, 1035, 822, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29-7.15 (m, 7H, ArH), 6.86 (dt,  $J$  = 9, 3 Hz, 2H, ArH), 4.46 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.41 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.98-3.93 (m, 1H,  $\text{CHOPMB}$ ), 3.81-3.76 (m, 1H,  $\text{CHOH}$ ), 3.79 (s, 3H,  $\text{OCH}_3$ ), 2.92 (d,  $J$  = 4 Hz, 1H,  $\text{CHOH}$ ), 2.80 (dd,  $J$  = 16, 8 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 2.74 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.58-2.51 (m, 2H,  $\text{CH}_2\text{COCH}_2$ ), 2.47 (dd,  $J$  = 17, 10 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 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;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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 %  $\text{EtOAc}$ /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.





**(3R\*, 5R\*, 7S\*)-1-Phenyl-3-[4-(Methoxybenzyl)oxy]-5-hydroxy-7-benzoyl-8-methylnonanone.** 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  $\mu$ L (1.3 mmol) of benzaldehyde and the solution was cooled to  $-10^{\circ}\text{C}$ . To this resulting clear solution was added 975  $\mu$ L of a 0.1 M solution of  $\text{SmI}_2$  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  $\text{Et}_2\text{O}$  and saturated aqueous  $\text{NaHCO}_3$ . Layers were separated and the aqueous phase was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over  $\text{MgSO}_4$  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)  $\nu$  3500, 3062, 3027, 2961, 2874, 2836, 1714, 1612, 1514, 1452, 1277, 1249, 1111, 1070, 1028, 822, 713, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{CHOBz}$ ), 4.46 (d,  $J = 11$  Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.35 (d,  $J = 11$  Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.79-3.71 (m, 1H,  $\text{CHO}$ ), 3.76 (s, 3H,  $\text{OCH}_3$ ), 3.70 (d,  $J = 2$  Hz, 1H,  $\text{CHOH}$ ), 3.67-3.61 (m, 1H,  $\text{CH}_2\text{O}$ ), 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;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{31}\text{H}_{38}\text{O}_5\text{Na}$ : 513.2617. Found: 513.2623 (FAB, MNBA, added NaI).

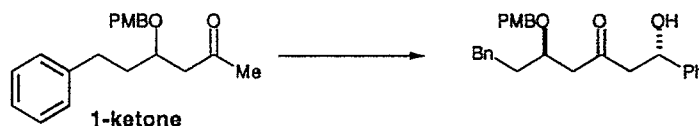


**(3S\*)-4-[2-(4-methoxyphenyl)-4-(R\*)-(2-phenyleth-1-yl)-1,3-dioxan-6-(R\*)-yl]-3-benzoyl-2-methyl-butane.** To a suspension of 50 mg of molecular sieves (3 Å) and 31.1 mg (0.137 mmol) of DDQ in 500  $\mu$ L of  $\text{CH}_2\text{Cl}_2$  was added 56.1 mg (0.114 mmol) of the alcohol as a solution in 400  $\mu$ L of THF (200  $\mu$ L rinse). This mixture was stirred 1 h at room temperature and then was diluted with  $\text{Et}_2\text{O}$  and saturated aqueous  $\text{NaHCO}_3$ . Layers were separated and the aqueous phase was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed four times with saturated aqueous  $\text{NaHCO}_3$  and brine, dried over  $\text{MgSO}_4$  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)  $\nu$  3062, 3026, 2961, 2858, 1715, 1615, 1517, 1452, 1272, 1110, 1027, 825, 713  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{CHOBz}$ ), 5.40 (s, 1H,  $\text{CHPMP}$ ), 3.86-3.80 (m, 1H,  $\text{CHOCHPMP}$ ), 3.80 (s, 3H,  $\text{OCH}_3$ ), 3.75-3.68 (m, 1H,  $\text{CHOCHPMP}$ ), 2.84-2.68 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.04-1.42 (m, 7H,  $\text{CH}_2\text{CH}(\text{O})\text{CH}_2\text{CH}(\text{O})\text{CH}_2\text{CH}(\text{OBz})\text{CH}$ ), 1.00 (d,  $J = 7$  Hz, 3H,  $\text{CH}(\text{CH}_3)_2$ ), 0.97 (d,  $J = 7$  Hz, 3H,  $\text{CH}(\text{CH}_3)_2$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{31}\text{H}_{36}\text{O}_5\text{Na}$ : 511.2461. Found: 511.2453 (FAB, MNBA, added NaI).

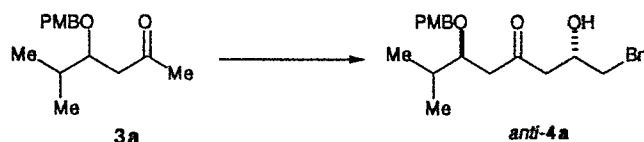


**(3R\*, 7S\*)-1-Phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8,8-dimethyl-5-nonanone.** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (322.6 mg, 1.03 mmol),  $\text{Bu}_2\text{BOTf}$  (272  $\mu$ L, 1.08 mmol), Hunig's base (198  $\mu$ 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  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ , 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)  $\nu$  3499, 3026, 2954, 2868, 1709, 1613, 1514, 1248, 1082, 1035, 822, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.29–7.15 (m, 7H, ArH), 6.86 (dt,  $J$  = 9, 3 Hz, 2H, ArH), 4.47 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.41 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.99–3.93 (m, 1H,  $\text{CHOPMB}$ ), 3.79 (s, 3H,  $\text{OCH}_3$ ), 3.70 (d,  $J$  = 10 Hz, 1H,  $\text{CHOH}$ ), 2.88 (s(br), 1H,  $\text{CHOH}$ ), 2.81 (dd,  $J$  = 16, 8 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 2.77–2.62 (m, 4H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.60–2.52 (m, 2H,  $\text{CH}_2\text{COCH}_2$ ), 2.44 (dd,  $J$  = 17, 10 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 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;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  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).

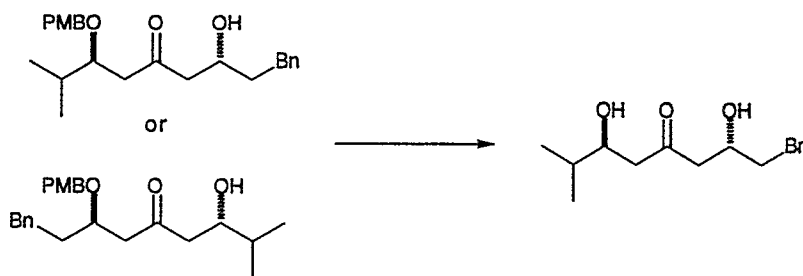


**(1S\*, 5R\*)-1,7-Diphenyl-5-[4-(methoxybenzyl)oxy]-1-hydroxy-3-heptanone.** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-6-phenyl-2-hexanone (321.8 mg, 1.03 mmol),  $\text{Bu}_2\text{BOTf}$  (272  $\mu\text{L}$ , 1.08 mmol), Hunig's base (197  $\mu\text{L}$ , 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)  $\nu$  3448, 3027, 2933, 2863, 1710, 1612, 1514, 1454, 1248, 1065, 1033, 822, 753, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33–7.14 (m, 12H, ArH), 6.85 (dt,  $J$  = 9, 3 Hz, 2H, ArH), 5.09 (dt,  $J$  = 9, 3 Hz, 1H,  $\text{CHOH}$ ), 4.44 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.38 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 3.97–3.91 (m, 1H,  $\text{CHOPMB}$ ), 3.76 (s, 3H,  $\text{OCH}_3$ ), 3.39 (d,  $J$  = 3 Hz, 1H,  $\text{CHOH}$ ), 2.84–2.59 (m, 5H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ,  $\text{CH}_2\text{COCH}_2$ ), 2.51 (dd,  $J$  = 16, 5 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 1.93–1.83 (m, 2H,  $\text{CH}_2\text{CH}_2\text{Ph}$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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).

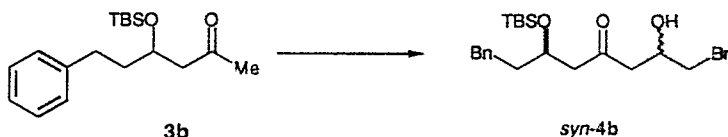


**(3R\*, 7S\*)-1-Phenyl-3-hydroxy-7-[4-(methoxybenzyl)oxy]-8-methyl-5-nonanone (*anti*-4a).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-[4-(Methoxybenzyl)oxy]-5-methyl-2-hexanone (252.5 mg, 1.01 mmol),  $\text{Bu}_2\text{BOTf}$  (266  $\mu\text{L}$ , 1.06 mmol), Hunig's base (193  $\mu\text{L}$ , 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.  $^{13}\text{C}$  NMR analysis (100 MHz,  $\text{CDCl}_3$ , 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*-4a and *syn*-4a. IR (thin film)  $\nu$  3463, 3026, 2958, 2933, 2873, 1709, 1612, 1514, 1248, 1071, 1035, 822, 750, 701  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28–7.15 (m, 7H, ArH), 6.82 (dt,  $J$  = 9, 3 Hz, 2H, ArH), 4.47 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.35 (d,  $J$  = 11 Hz, 1H,  $\text{OCH}_2\text{Ar}$ ), 4.05–4.00 (m, 1H,  $\text{CHOH}$ ), 3.78–3.75 (m, 1H,  $\text{CHOPMB}$ ), 3.75 (s, 3H,  $\text{OCH}_3$ ), 3.18 (d,  $J$  = 3 Hz, 1H,  $\text{CHOH}$ ), 2.79–2.73 (m, 1H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 2.68–2.58 (m, 3H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ,  $\text{CH}_2\text{COCH}_2$ ), 2.51 (dd,  $J$  = 18, 9 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 2.37 (dd,  $J$  = 16, 3 Hz, 1H,  $\text{CH}_2\text{COCH}_2$ ), 1.98–1.92 (m, 1H,  $\text{CH}(\text{CH}_3)_2$ ), 1.80–1.73 (m, 1H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 1.66–1.59 (m, 1H,  $\text{CH}_2\text{CH}_2\text{Ph}$ ), 0.90 (d,  $J$  = 7 Hz, 6H,  $\text{CH}(\text{CH}_3)_2$ ) ppm;  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{24}\text{H}_{32}\text{O}_4 + \text{NH}_4$ : 402.2645. Found: 402.2665 (CI,  $\text{NH}_3$  atmosphere).

**Stereochemical proof of (4a):** The stereochemistry of *anti*-4a was assigned by analysis of the derived diol.

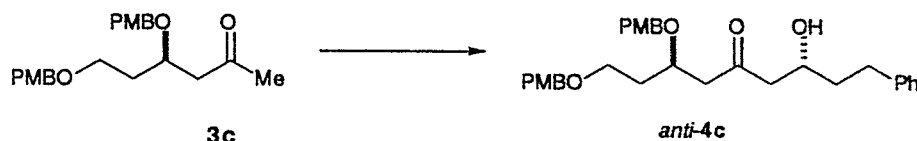


**(3*R*\*, 7*S*\*)-1-Phenyl-3,7-dihydroxy-8-methyl-5-nonanone.** To a solution of 92.2 mg of 1-phenyl-3-[4-(methoxybenzyl)oxy]-7-hydroxy-8-methyl-5-nonanone *anti*-4a in 2 mL of MeOH was added 10 mg of Pearlman's catalyst (20 % Pd(OH)<sub>2</sub>). The resulting mixture was purged with H<sub>2</sub> and then stirred at room temperature under a 1 atmosphere pressure of H<sub>2</sub>. 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*-12 was found to produce the same diol in 98 % yield as shown by TLC, <sup>1</sup>H NMR and <sup>13</sup>C NMR: mp 52-53 °C; IR ν (CHCl<sub>3</sub>) 3473, 3024, 3013, 2963, 2933, 2877, 1701, 1603, 1454, 1386, 1058, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 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, CH<sub>2</sub>CH<sub>2</sub>Ph), 2.70-2.49 (m, 5H, CH<sub>2</sub>CH<sub>2</sub>Ph, CH<sub>2</sub>COCH<sub>2</sub>), 1.86-1.77 (m, 1H, CH<sub>2</sub>CH<sub>2</sub>Ph), 1.74-1.62 (m, 2H, CH<sub>2</sub>CH<sub>2</sub>Ph, CH(CH<sub>3</sub>)<sub>2</sub>), 0.92 (d, *J* = 7 Hz, 3H, CH(CH<sub>3</sub>)<sub>2</sub>), 0.90 (d, *J* = 7 Hz, 3H, CH(CH<sub>3</sub>)<sub>2</sub>) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 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<sub>f</sub> 0.3 (40 % EtOAc/hexanes); Exact mass calcd for C<sub>16</sub>H<sub>24</sub>O<sub>3</sub>+NH<sub>4</sub>: 282.2069. Found: 282.2083 (CI, NH<sub>3</sub> atmosphere).



**1,9-Diphenyl-3-*tert*-butyldimethylsilyloxy-7-hydroxy-5-nonanone (*syn*-4b).** The following reagents were combined in the amount indicated according to the General Procedure for the boron aldol reaction (*vide supra*): 4-*tert*-Butyldimethylsilyloxy-6-phenyl-2-hexanone (3b) (54.2 mg, 0.177 mmol), Bu<sub>2</sub>BOTf (46.6 μL, 0.185 mmol), Hunig's base (34 μL, 0.195 mmol) and hydrocinnamaldehyde (25.6 μL, 0.195 mmol). <sup>1</sup>H NMR analysis (400 MHz, CDCl<sub>3</sub>, 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*)-4b and (*syn*)-4b. IR (thin film) ν 3464, 3027, 2929, 2857, 1707, 1603, 1454, 1255, 1090, 836, 777, 735, 699 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) 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, CH<sub>2</sub>CH<sub>2</sub>Ph, CH<sub>2</sub>COCH<sub>2</sub>), 1.89-1.66 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>Ph), 0.92 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub> (Maj.)), 0.90 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub> (Min.)), 0.11 (s, 3H, SiCH<sub>3</sub> (Maj.)), 0.10 (s, 3H, SiCH<sub>3</sub> (Min.)), 0.06 (s, 3H, SiCH<sub>3</sub> (Maj.)), 0.03 (s, 3H, SiCH<sub>3</sub> (Min.)) ppm; <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) 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<sub>f</sub> 0.3 (15 % EtOAc/hexanes); Exact mass calcd for C<sub>27</sub>H<sub>41</sub>SiO<sub>3</sub>: 441.2825. Found: 441.2807 (CI, NH<sub>3</sub> atmosphere).

**Stereochemical proof of (4b):** The stereochemistry of *anti*-4b and *syn*-4b was assigned by comparison with authentic *anti*-4b prepared from *anti*-2 (TBSCl, Imidazol; Pearlman's catalyst, H<sub>2</sub>).



**(3*R*\*, 7*R*\*)-1-Phenyl-3-hydroxy-7,9-bis-[4-(methoxybenzyl)oxy]-5-nonanone (*anti*-4c).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron

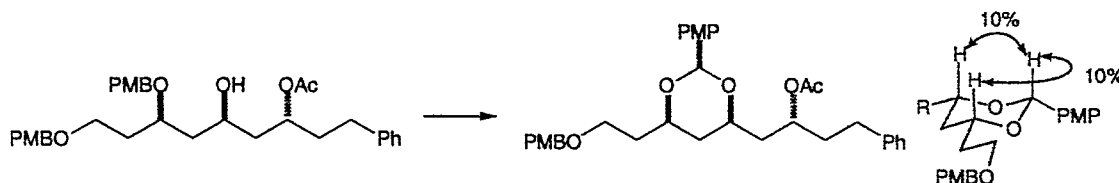
aldol reaction (*vide supra*): methyl ketone (**3c**) (0.213 g, 0.612 mmol), Bu<sub>2</sub>BOTf (160  $\mu$ L, 0.642 mmol), Hunig's base (116  $\mu$ L, 0.685 mmol), and hydrocinnamaldehyde solution (0.685 mL, 0.685 mmol). Purification by flash chromatography (30 % EtOAc in hexanes) provided 0.227 g (77 %) 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)  $\nu$  3472, 3030, 2930, 2859, 1704, 1604, 1512, 1455, 1362, 1298, 1248, 1177, 1091, 1034, 820  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.38-7.23 (m, 8H, ArH), 6.97-6.91 (m, 5H, ArH), 4.49-4.47 (m, 4H, OCH<sub>2</sub>Ar), 4.20-4.11 (m, 2H, CHOPMB and CHOH), 3.87 (s, 3H, OCH<sub>3</sub>), 3.62-3.56 (m, 2H, CH<sub>2</sub>OPMB), 3.21 (br s, 1H, CHOH), 2.89-2.54 (m, 6H, CH<sub>2</sub>C=O and CH<sub>2</sub>Ph), 1.98-1.67 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>Ph, and CH<sub>2</sub>CHOPMB) ppm; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>f</sub> 0.20 (20% EtOAc in hexanes); Exact mass calcd for C<sub>31</sub>H<sub>38</sub>O<sub>6</sub>Na: 529.2566. Found 529.2568 (FAB, MNBA, added NaI).

**Stereochemical proof of *anti*-4c:** The stereochemistry of *anti*-4c was assigned by analysis of the derived benzylidene acetal.



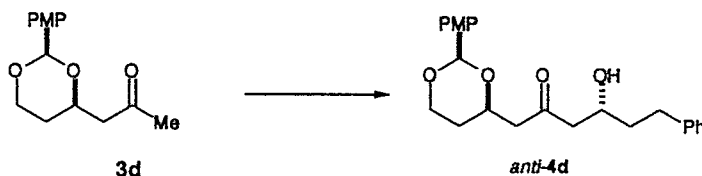
**(3R\*,5R\*,7R\*)-1-Phenyl-3-acetoxy-5-hydroxy-7,9-bis-[4-(methoxybenzyl)oxy]-nonane.**

To a cooled solution of ketone **4c** (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 NaHCO<sub>3</sub> solution was added and the mixture warmed to room temperature. The mixture was extracted with Et<sub>2</sub>O (2 x 15 mL). The combined organic solutions were washed with brine, dried over MgSO<sub>4</sub>, 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)  $\nu$  3484, 2934, 1732, 1612, 1513, 1454, 1373, 1302, 1248, 1174, 1034, 820, 701  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>AB</sub>=11.0 Hz,  $\Delta$ V<sub>AB</sub>=12.4 Hz, 2H, PMPCH<sub>2</sub>OCH), 4.51 (s, 2H, PMPCH<sub>2</sub>O), 3.89 (s, 3H, ArOCH<sub>3</sub>), 3.88 (s, 3H, ArOCH<sub>3</sub>), 3.77 (m, 1H, CHOR), 3.67-3.59 (m, 3H, CHOR), 2.78-2.66 (m, 2H, ArCH<sub>2</sub>CH<sub>2</sub>), 2.13 (s, 3H, CH<sub>3</sub>C=O), 2.10-1.64 (m, 8 H, CH<sub>2</sub>CHOR) ppm; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>f</sub> 0.45 (2 x 40% EtOAc in hexanes); Exact mass calcd for C<sub>33</sub>H<sub>42</sub>O<sub>7</sub>Na: 573.2828. Found 573.2846 (FAB, MNBA, added NaI).

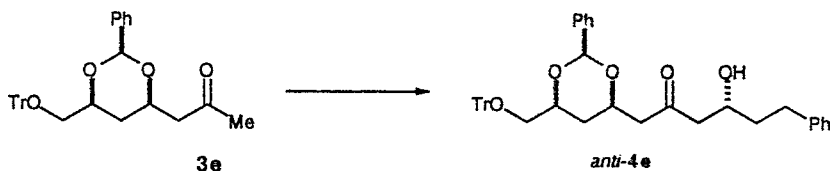


**(3R\*,5R\*,7R\*)-4-[2-(4-Methoxyphenyl)-4-(methoxyphenyl)oxyethyl-1,3-dioxan-6-yl]-3-acetoxy-1-phenyl-butane.** To a solution of the alcohol (33 mg, 0.063 mmol) in dichloromethane (3 mL) was added 3 Å molecular sieves (ca. 50 mg). After stirring for 20 min., the mixture was treated with DDQ (0.016 g, 0.070 mmol). After stirring for 30 min., the mixture was diluted with Et<sub>2</sub>O and washed with saturated aqueous NaHCO<sub>3</sub> (3 x 20 mL) and brine. The organic solution was dried over MgSO<sub>4</sub>, 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 **4c**. IR (thin film)  $\nu$  3026, 3001, 2919, 2858, 1734, 1613, 1586, 1514, 1248, 1102, 1033, 829, 701  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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)<sub>2</sub>), 5.30-5.24 (m, 1H, CHOAc), 4.49-4.41 (ABq, J<sub>AB</sub>=11.6 Hz,  $\Delta$ V<sub>AB</sub>=7.88 Hz, 2H, CH<sub>2</sub>OPMB), 4.00-3.96 (m, 1H, CHOR), 3.86-3.74 (m, 1H, CHOR), 3.80 (s, 3H, ArOCH<sub>3</sub>), 3.78 (s, 3H, ArOCH<sub>3</sub>), 3.69-3.64 (m, 1H, CH<sub>2</sub>OPMB), 3.60-3.53 (m, 1H, CH<sub>2</sub>OPMB), 2.68-2.60 (m, 2H, CH<sub>2</sub>Ar), 2.04 (s, 3H, CH<sub>3</sub>CO<sub>2</sub>R), 1.91-1.72 (m, 4H, CH<sub>2</sub>CH<sub>2</sub>OPMB and CH<sub>2</sub>CH(OAc)CH<sub>2</sub>), 1.62-1.55 (m, 2H, PhCH<sub>2</sub>CH<sub>2</sub>), 1.55-1.51 (dd, J=2.2, 10.7 Hz, 1H, CH<sub>2</sub>CHOR), 1.46-1.37 (q, J=10.7 Hz, 1H, CH<sub>2</sub>CHOR)

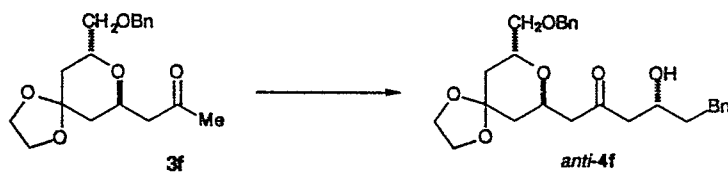
ppm;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.0, 130.5, 129.2, 128.3, 128.2, 127.2, 125.8, 113.7, 113.4, 100.0, 73.4, 73.3, 72.6, 70.7, 65.6, 55.2, 40.6, 37.2, 36.5, 36.0, 31.5, 21.2 ppm;  $R_f$  0.39 (20% EtOAc in hexanes); Exact mass calcd for  $\text{C}_{33}\text{H}_{40}\text{O}_7\text{Na}$ : 571.2672. Found 571.2690 (FAB, MNBA, added NaI).



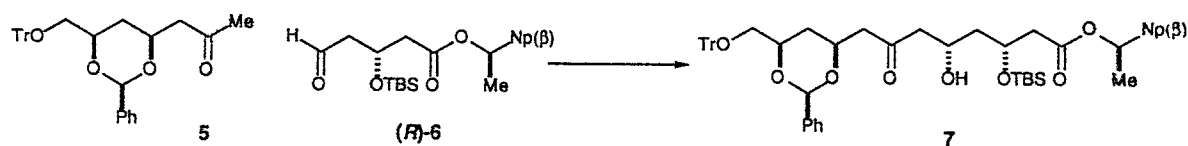
**(3R\*)-1-Phenyl-3-hydroxy-6-[2-(4-methoxyphenyl)-1,3-dioxan-6(R)-yl]-5-hexanone (anti-4d).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **3d** (0.097 g, 0.388 mmol),  $\text{Bu}_2\text{BOTf}$  (106  $\mu\text{L}$ , 0.427 mmol), Hunig's base (79  $\mu\text{L}$ , 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)  $\nu$  3481, 2926, 2852, 1717, 1665, 1558, 1495, 1455, 1365, 1249, 1173, 1098, 1032, 829, 750  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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,  $\text{ArOCH}_3$ ), 2.99-2.93 (dd,  $J=7.7, 15.8$  Hz, 1H,  $\text{CH}_2\text{C}=\text{O}$ ), 2.90-2.60 (m, 5H,  $\text{CH}_2\text{C}=\text{O}$  and  $\text{ArCH}_2$ ), 1.97-1.85 (m, 2H,  $\text{ArCH}_2\text{CH}_2$ ), 1.81-1.73 (m, 1H,  $\text{ROCH}_2\text{CH}$ ), 1.70-1.67 (dd,  $J=13.2, 1.3$  Hz,  $\text{ROCH}_2\text{CH}$ ) ppm;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{23}\text{H}_{28}\text{O}_5$ : 384.1937. Found 384.1956 (ED).



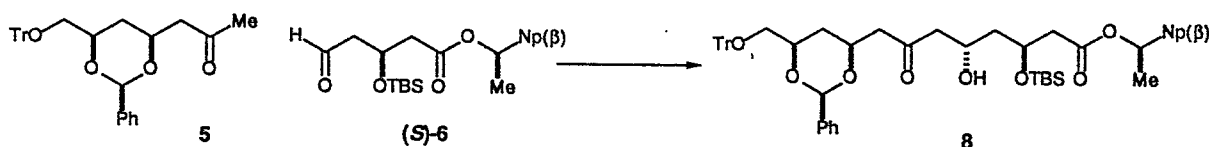
**4S-[(Triphenylmethoxy)-methyl]-6(R)-[1-phenyl-3R-hydroxy-5-hexanone]-2-phenyl-1,3-dioxane (anti-4e).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **3e** (0.030 g, 0.061 mmol),  $\text{Bu}_2\text{BOTf}$  (0.019  $\mu\text{L}$ , 0.076 mmol), Hunig's base (16  $\mu\text{L}$ , 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  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR (> 95 : 5 *anti*). IR (thin film)  $\nu$  3500, 3057, 3025, 2922, 2871, 1706, 1591, 1489, 1450, 1335, 1258, 1079, 1021, 900, 740  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71-7.68 (d,  $J=7.7$  Hz, 6H, ArH), 7.24-7.07 (m, 14H, ArH), 5.84 (s, 1H,  $\text{ArCH}(\text{OR})_2$ ), 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  $\text{TrOCH}_2$ ), 3.24-3.21 (dd,  $J=4.4$  Hz, 9.5 Hz, 1H, one of  $\text{TrOCH}_2$ ), 2.93 (br s, 1H, CHOH), 2.82-2.75 (m, 1H,  $\text{PhCH}_2$ ), 2.67-2.59 (m, 1H,  $\text{PhCH}_2$ ), 2.47-2.41 (dd,  $J=7.7, 16.0$  Hz, 1H,  $\text{CH}_2\text{C}=\text{O}$ ), 2.00-1.95 (dd,  $J=4.4, 15.7$  Hz, 1H,  $\text{CH}_2\text{C}=\text{O}$ ), 1.74-1.65 (m, 1H,  $\text{PhCH}_2\text{CH}_2$ ), 1.52-1.43 (m, 1H,  $\text{PhCH}_2\text{CH}_2$ ), 1.39-1.31 (q,  $J=12.0$  Hz, 1 H, dioxane  $\text{CH}_2$ -axial H), 1.27-1.23 (d,  $J=12.8$  Hz, 1H, dioxane- $\text{CH}_2$ -equatorial H) ppm;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{42}\text{H}_{42}\text{O}_5\text{Na}$ : 649.2930. Found 649.2947 (FAB, MNBA, added NaI).



**Ketone (4f) :** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **3f** (10mg, 0.031 mmol), Bu<sub>2</sub>BOTf ( 8.2  $\mu$ L, 0.033 mmol), Hunig's base (6  $\mu$ L, 0.034 mmol), and hydrocinnamaldehyde (4.5  $\mu$ L, 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/CH<sub>2</sub>Cl<sub>2</sub>). **Anti-4f** was found to be the major isomer and the relative stereochemistry was proved by X-ray cristallography.. mp 60-61°C; IR (thin film)  $\nu$  4368, 3087, 3056, 3026, 2927, 2882, 1708, 1495, 1453, 1410, 1360, 1180, 1146, 1095, 1069, 1031, 947, 738, 699 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.35-7.16 (m, 10H, ArH), 4.56 (d, *J*=12.2 Hz, 1H, PhCH<sub>2</sub>O), 4.51 (d, *J*=12.2 Hz, 1H, PhCH<sub>2</sub>O), 4.48 (m, 1H, CHOR), 4.12-4.04 (m, 2H, CHOR, CHOH), 3.92 (m, 4H, O(CH<sub>2</sub>)<sub>2</sub>O), 3.64 (dd, *J*=10.2, 7.2 Hz, 1H, CH<sub>2</sub>OBn), 3.45 (dd, *J*=10.2, 4.4 Hz, 1H, CH<sub>2</sub>OBn), 3.20 (d, *J*=3.6 Hz, 1H, OH), 2.96 (dd, *J*=15.5, 8.3 Hz, 1H, ROCHCH<sub>2</sub>C=O), 2.79 (ddd, *J*=13.7, 9.9, 5.3 Hz, 1H, PhCH<sub>2</sub>CH<sub>2</sub>), 2.68-2.58 (m, 3H, C=OCH<sub>2</sub>CHOH, PhCH<sub>2</sub>CH<sub>2</sub>), 2.62 (dd, *J*=15.5, 9.3 Hz, 1H, ROCHCH<sub>2</sub>C=O), 1.88 (dd, *J*=13.4, 4.8 Hz, 1H, CH<sub>2</sub>CH(OR)CH<sub>2</sub>C=O), 1.82-1.74 (m, 1H, PhCH<sub>2</sub>CH<sub>2</sub>), 1.76 (dd, *J*=13.3, 4.2 Hz, 1H, CH<sub>2</sub>CH(OR)CH<sub>2</sub>OBn), 1.69-1.61 (m, 1H, PhCH<sub>2</sub>CH<sub>2</sub>), 1.63 (dd, *J*=13.3, 7.3 Hz, 1H, CH<sub>2</sub>CH(OR)CH<sub>2</sub>OBn), 1.59 (dd, *J*=13.4, 5.7 Hz, 1H, CH<sub>2</sub>CH(OR)CH<sub>2</sub>C=O) ppm; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>f</sub> 0.35 (50% EtOAc in hexanes); Exact mass calcd for C<sub>27</sub>H<sub>34</sub>O<sub>6</sub>Na: 477.2253. Found 477.2258 (FAB, MNBA, added NaI).

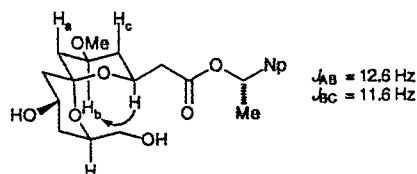


**(3R,5S)-3-tert-Butyldimethylsilyloxy-5-hydroxy-8-[2-phenyl-4-(R)-(triphenylmethyloxy)-methyl-1,3-dioxan-6(S)-yl]-octan-7-on-1-oic acid-2-(R)-naphthylethanol ester (7).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): ketone **5** (0.100 g, 0.203 mmol), Bu<sub>2</sub>BOTf ( 53  $\mu$ L, 0.213 mmol), Hunig's base (41  $\mu$ L, 0.244 mmol), and aldehyde **(R)-6** (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)  $\nu$  3600, 3057, 2928, 1733, 1490, 1449, 1265, 1080, 1019, 838, 739, 701, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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)<sub>2</sub>), 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, TrOCH<sub>2</sub>), 3.18-3.15 (dd, *J*=4.5, 9.5 Hz, 1H, TrOCH<sub>2</sub>), 3.08 (s, 1H, CHOH), 2.65-2.55 (m, 2H, CH<sub>2</sub>CO<sub>2</sub>R), 2.44-2.38 (dd, *J*=7.6, 16.1 Hz, 1H, CH<sub>2</sub>C=O), 2.21-2.09 (m, 2H, CH<sub>2</sub>C=O), 1.99-1.93 (dd, *J*=4.7, 16.1 Hz, CH<sub>2</sub>C=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, ArCHCH<sub>3</sub>), 1.34-1.19 (m, 2H, CH<sub>2</sub>CHOR), 0.881 (s, 9H, (CH<sub>3</sub>)<sub>3</sub>CSi), 0.07 (s, 3H, CH<sub>3</sub>Si), 0.03 (3, 3H, CH<sub>3</sub>Si) ppm; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  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<sub>f</sub> 0.17 (20% EtOAc in hexanes); Exact mass calcd for C<sub>56</sub>H<sub>64</sub>O<sub>8</sub>Na: 915.4268. Found 529.4222 (FAB, MNBA, added NaI).

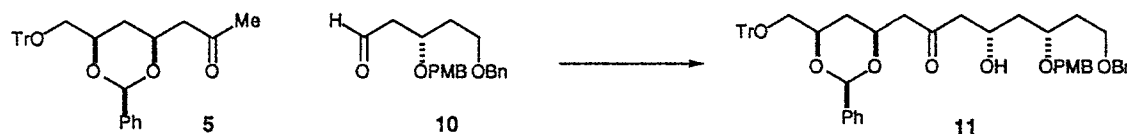


**(3S,5S)-3-tert-Butyldimethylsilyloxy-5-hydroxy-8-[2-phenyl-4-(R)-triphenylmethyloxy)-methyl-1,3-dioxan-6(S)-yl]-octan-7-on-1-oic acid-2-(S)-naphthylethanol ester (8).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone **5** (0.100 g, 0.203 mmol), Bu<sub>2</sub>BOTf ( 61  $\mu$ L, 0.223 mmol), Hunig's base (42  $\mu$ 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)-6** added as a solution in Et<sub>2</sub>O 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.  $[\alpha]_D^{25} -3.30^\circ$  ( $c = 1.47$ ,  $\text{CHCl}_3$ ); IR (thin film)  $\nu$  3507, 3046, 3015, 2851, 1728, 1594, 1492, 1446, 1379, 1251, 1215, 754  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  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;  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  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).



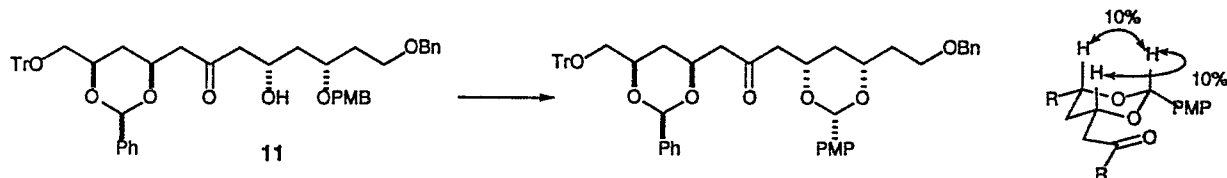
**Stereochemical Proof for 8.** Methylation of the aldol adduct ( $\text{Me}_3\text{OBF}_4$ , di-*tert*-butylmethylpyridine,  $\text{CH}_2\text{Cl}_2$ ) and spiroketalization (CSA, MeOH) afforded the spiroketal. The illustrated coupling constants and NOE measurements established the 1,5 *anti* relationship of the parent aldol compound 8.



**(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 (11).** The following reagents were combined in the amounts indicated according to the General Procedure for the boron aldol reaction (*vide supra*): methyl ketone 5 (0.065 g, 0.132 mmol),  $\text{Bu}_2\text{BOTf}$  (343  $\mu\text{L}$ , 0.125 mmol), Hunig's base (23  $\mu\text{L}$ , 0.132 mmol), and aldehyde 10 (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* 11 and 1,5 *syn* 11.  $[\alpha]_D^{25} +21.43^\circ$  ( $c = 0.695$ ,  $\text{CHCl}_3$ ); IR (thin film)  $\nu$  3476, 3059, 3033, 2922, 2868, 1713, 1612, 1586, 1513, 1248, 1175, 900, 822, 700  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  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 CH $_2$ OBN), 3.36-3.32 (dd,  $J=5.8, 9.6$  Hz, 1H, TrOCH $_2$ ), 3.09-3.06 (dd,  $J=4.8, 9.6$  Hz, 1H, TrOCH $_2$ ), 2.88-2.82 (dd,  $J=7.2, 16.3$ , 1H CH $_2$ C=O), 2.61-2.48 (m, 3H, CH $_2$ C=O), 1.94-1.82 (m, 2H, CH $_2$ CHOPMB), 1.73-1.67 (m, 1H, BnOCH $_2$ CH $_2$ ), 1.61-1.56 (m, 2H, TrOCH(OR)CH $_2$  and BnOCH $_2$ CH $_2$ ), 1.52-1.43 (q,  $J=11.5$  Hz, 1H, CHOR) ppm;  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{C}_{53}\text{H}_{56}\text{O}_8\text{Na}$ : 843.3873. Found 843.3837 (FAB, MNBA, added NaI).

**Stereochemical proof of 11.** The stereochemistry of 11 was assigned by analysis of the derived benzylidene acetal.





**(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 **11** (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 Et<sub>2</sub>O and washed with saturated aqueous NaHCO<sub>3</sub> (3 x 20 mL) and brine. The organic solution was dried over MgSO<sub>4</sub>, 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 of the parent aldol compound **9**. [ $\alpha$ ]<sub>D</sub><sup>23</sup><sub>589</sub> +6.47° (c = 0.35, CHCl<sub>3</sub>); IR (thin film)  $\nu$  3055, 2924, 2856, 1717, 1615, 1517, 1490, 1449, 1265, 1249, 1126, 1028, 738, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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)<sub>2</sub>), 5.46 (s, ArCH(OR)<sub>2</sub>), 4.53-4.46 (ABq, *J*<sub>AB</sub>=12.0 Hz,  $\Delta$ *V*<sub>AB</sub>=5.4 Hz, 2H, PhCH<sub>2</sub>O), 4.41-4.30 (m, 2H, CHOR), 4.12-4.07 (m, 1H, CHOR), 4.04-4.01 (m, 1H, CHOR), 3.74 (s, ArOCH<sub>3</sub>), 3.68-3.62 (m, 1H, BnOCH<sub>2</sub>), 3.58-3.53 (m, 1H, BnOCH<sub>2</sub>), 3.35-3.32 (dd, *J*=5.7, 9.6 Hz, TrOCH<sub>2</sub>), 3.08-3.04 (dd, *J*=4.9, 9.6 Hz, 1H, TrOCH<sub>2</sub>), 2.92-2.83 (dt, *J*=7.6, 16.2 Hz, 2H, CH<sub>2</sub>C=O), 2.61-2.55 (m, 2H, CH<sub>2</sub>C=O), 1.91-1.77 (m, 2H, BnOCH<sub>2</sub>CH<sub>2</sub>), 1.73-1.70 (d, *J*=13.1 Hz, 1H, dioxane CH<sub>2</sub>, equatorial *H*), 1.67-1.64 (d, *J*=13.0 Hz, dioxane CH<sub>2</sub>, equatorial *H*), 1.51-1.32 (two overlapping quartets, *J*=13.0 Hz, dioxane CH<sub>2</sub>, axial *H*) ppm; <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  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*<sub>f</sub> 0.37 (40% EtOAc in hexanes) Exact mass calcd for C<sub>53</sub>H<sub>54</sub>O<sub>8</sub>Na: 841.3716. Found 841.3700 (FAB, MNBA, added NaI).



**(3S,5R)-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 (12).** A solution of the silyl enol ether **9** (0.075 g, 0.104 mmol) in dichloromethane (2 mL) was treated with a solution of the aldehyde **10** (0.034 g, 0.106 mmol) in dichloromethane (1 mL). The solution was cooled to -78 °C. A solution of BF<sub>3</sub>·OEt<sub>2</sub> (0.111 mL of a 1M soln in CH<sub>2</sub>Cl<sub>2</sub>) was added. The solution was stirred for 90 min at -78 °C. Triethylamine (0.5 mL) and saturated aqueous NaHCO<sub>3</sub> (1 mL) 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<sub>3</sub> (20 mL), satd. aq. NH<sub>4</sub>Cl (20 mL), and brine (20 mL). The solution was dried over MgSO<sub>4</sub>, filtered, and concentrated. The residue was redissolved in THF (2 mL) and treated with 25  $\mu$ L HF-pyridine (to cleave the silylated aldol adduct). After stirring for 30 min, the solution was quenched with saturated aq. NaHCO<sub>3</sub> 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 (**5**→**11**; minor isomer) **12**. [ $\alpha$ ]<sub>D</sub><sup>23</sup><sub>589</sub> +9.91° (c = 0.585, CHCl<sub>3</sub>) IR (thin film)  $\nu$  3479, 3059, 2922, 2868, 1711, 1612, 1586, 1514, 1491, 1449, 1412, 1344, 1302, 1248, 1079, 901 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  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)<sub>2</sub>), 4.46-4.44 (m, 4H, ArCH<sub>2</sub>OCH<sub>2</sub>), 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, ArOCH<sub>3</sub>), 3.59-3.49 (m, 2H, BnOCH<sub>2</sub>CH<sub>2</sub>), 3.37-3.31 (m, 2H, one of TrOCH<sub>2</sub> and CHOH), 3.10-3.06 (dd, *J*=9.6, 4.8 Hz, 1H, one of TrOCH<sub>2</sub>), 2.89-2.83 (dd, *J*=7.3, 16.3 Hz, 1H, CH<sub>2</sub>C=O), 2.65-2.51 (m, 3H, CH<sub>2</sub>C=O), 1.97-1.78 (m, 2H, BnOCH<sub>2</sub>CH<sub>2</sub>), 1.74-1.66 (m, 2H, CH<sub>2</sub>CHOR), 1.55-1.44 (m, 2H, CH<sub>2</sub>CHOR) ppm; <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  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  $C_{53}H_{56}O_8Na$ : 843.3873. Found 843.3864 (FAB, MNBA, added NaI).

### References and Notes

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