Supporting Information

Combinatorial Synthesis of Polyketide Libraries: Asymmetric Aldol Reactions with α-Chiral Aldehydes on Solid Support

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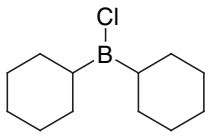
General Comments

^{1}H NMR spectra were recorded on the following instruments: Bruker DRX500 (500 MHz), AM400 or DRX400 (400 MHz), DPX250 (250 MHz). ^{13}C NMR spectra were recorded on Bruker DPX250 and DRX400 spectrometers and all chemical shift values are reported in ppm on the δ scale relative to the deuterated solvent. The ^{13}C NMR resin samples were prepared allowing the resin to swell in CD_2Cl_2 or $CDCl_3$ and the samples were degassed. Gel phase ^{13}C NMR spectra were acquired by changing some acquisition values: 1) acquisition (Aq) 0.12 sec; 2) time domain (Td) 6026; 3) delayed 1 (D1) 0.88. Infrared spectra were recorded on a Perkin-Elmer 1620 Series (FT-IR) spectrophotometer, using 5 mm sodium chloride plates or 0.1 mm sodium chloride solution cells. Wavelengths of maximum absorbance (ν_{max}) are quoted in wavenumbers (cm^{-1}) calibrated relative to polystyrene. Resin IR spectra were recorded by single-bead IR analysis using a Perkin Elmer Spectrum 1000 IR spectrometer in conjunction with a Perkin Elmer Autoimage IR/visible microscope. Beads were flattened in a Specac diamond compression cell. Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium D-line (589 nm) and are reported as follows: [α]\s(20, D) concentration (*c* in g /100 mL) and solvent. Analytical thin layer chromatography (t.l.c) was carried out on Merck Kieselgel 60 F254 plates with visualisation by ultraviolet irradiation and/or anisaldehyde, potassium permanganate, phosphomolybdic acid or phosphomolybdic acid / $Ce_2(SO_4)_3$ dips. Flash chromatography was carried out on Merck Kieselgel 60 (230-400 mesh).

Reagents and solvents were purified by standard means. Dichloromethane (DCM) and methanol were distilled from calcium hydride and stored under an argon atmosphere; tetrahydrofuran (THF) and diethyl ether were distilled from sodium wire/benzophenone under an argon atmosphere. Triethylamine, diisopropylethylamine were distilled from and stored over calcium hydride. 2,2-Dimethoxypropane was distilled from calcium hydride. All experiments were performed under anhydrous conditions in an atmosphere of Ar, except where stated, using oven-dried apparatus and employing standard techniques for handling air-sensitive materials.

Dicyclohexylboron chloride[1]



To a stirred solution of cyclohexene (10.6 mL, 8.60 g, 105 mmol, distilled over CaH_2) in dry ether (45 mL) under an argon atmosphere at -5 °C was added dropwise, *via* syringe, monochloroborane-dimethylsulfide complex (5.8 mL, 6.14 g, 50 mmol). The exothermic reaction was allowed to warm to room temperature for 2.5 h to give a clear solution. The solvent was removed by distillation and further distillation under reduced pressure afforded the title compound as a colourless oil (6.4 g, 60%); **bp** 90-91 °C / 0.43 mm Hg 104-105 °C / 0.5 mmHg. This reagent could be stored in the freezer at -27 °C without degradation for a period of several months : **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 36.3, 27.7, 27.2, 26.6.

Samarium diiodide[2]

SmI_2 (0.1M in THF)

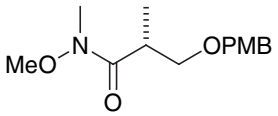
Samarium metal (0.93 g, 6.08 mmol) and iodine (1.14 g, 4.50 mmol) in THF (45 mL) were heated to reflux for 2 h (oxygen was rigorously excluded). The resultant deep blue solution (approx. 0.1 M in THF) was allowed to cool and used immediately.

Zinc Borohydride

$Zn(BH_4)_2$ (0.21M in Et_2O)

A solution of $ZnCl_2$ (anhydrous, 2.17 g, 14.7 mmol) in dry Et_2O (30 mL) was stirred for 1 h at 50°C until almost complete dissolution, the solution was then cannulated to a solution of $NaBH_4$ in dry Et_2O (40 mL) then the mixture stirred at RT for 16 h. The solution was decanted, cannulated and stored into a dry flask under Ar.

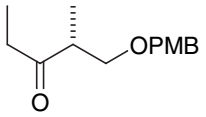
(*R*)-3-(*p*-Methoxybenzyloxy)-*N*,2-dimethyl-*N*-methoxypropionamide: (*R*)-32.



To a stirred solution of methyl (*R*)-(-)-3-hydroxy-2-methylpropionate (3.10 g, 29.9 mmol) and 4-methoxybenzyl-2,2,2-trichloroacetimidate (9.40 g, 33.3 mmol) in Et_2O (240 mL) at 0 °C was cautiously added triflic acid (0.15 M in Et_2O; 0.50 mL, 76.4 mmol, 0.29 mol%). The resulting yellow solution was allowed to warm to room temperature and then stirred for a further 1 h. The reaction was then quenched by the careful addition of sat. aq. $NaHCO_3$ (100 mL). The organic layer was separated and washed with brine (100 mL). The aqueous layers were sequentially re-extracted with Et_2O (100 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give a mixture of white crystals and a supernatant yellow oil. This mixture was triturated with hexane (50 mL) and filtered through a

plug of glass wool, with hexane rinses (150 mL). Removal of the solvent *in vacuo* and purification by flash chromatography (EtOAc/Hexane, 1/6) afforded the PMB ether as a colourless oil (4.64 g, 19.5 mmol, 74%). This material was used in the following reaction. To a stirred slurry of this ester (2.0 g, 8.39 mmol) and *N,O*-dimethylhydroxylamine hydrochloride (1.20 g, 12.3 mmol) in THF (24.0 mL) at -20 °C was added dropwise over 15 min ^{i}PrMgCl (2 M in THF; 12.6 mL, 25.2 mmol). The rate of addition was controlled to maintain the reaction temperature below -15 °C. The reaction mixture was stirred for 30 min at -20 °C before being quenched with Aqueous NH4Cl (50 mL). After dilution with EtOAc (100 mL), the organic layer was separated and washed with brine (50 mL). The aqueous layers were extracted with EtOAc (2x 100 mL) and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash chromatography (EtOAc/Hexane, 1/1) afforded the Weinreb amide **(*R*)-32** as a colourless oil (2.14 g, 8.01 mmol, 96%). $[\alpha]_D^{20}$ -3.9 (*c* 1.33, $CHCl_3$); **IR** 1659, 1612, 1513, 1464 cm^{-1}; ^{1}**H NMR** δ ($CDCl_3$, 400 MHz) 7.22 (2H, d, *J* = 8.6 Hz, ArH), 6.85 (2H, d, *J* = 8.6 Hz, ArH), 4.43 (1H, ABq, *J* = 11.6 Hz, OC<u>H</u>$_2$Ar), 3.78 (3H, s, ArO<u>Me</u>), 3.63-3.69 (5H, m, N-OMe+OC<u>H</u>$_2$CHMe), 3.35-3.40 (1H, m, C<u>H</u>Me), 3.19 (3H, s, NMe), 1.09 (3H, d, *J* = 6.9 Hz, CH<u>Me</u>); ^{13}**C NMR** δ ($CDCl_3$, 100.6 MHz) 14.2, 35.8, 55.2, 61.5, 72.3, 72.9, 113.7, 129.1, 130.4, 159.1; **m/z** (FAB) 268 (100%), 241 (30); **HRMS** (FAB) calcd for $C_{14}H_{22}NO_4$ ($M+H^+$) 268.1549. Found 268.1550.

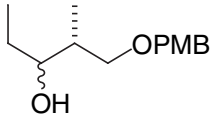
(*R*)-1-(*p*-Methoxybenzyloxy)-2-methylpentan-3-one: (*R*)-4. *



To a stirred solution of Weinreb amide (13.8 g, 51.0 mmol) in THF (250 mL) at -20 °C under argon was added dropwise EtMgBr (3 M in Et_2O, 33.83 mL, 100 mmol). The reaction mixture was stirred for 1 h and was then partitioned between sat. aq. NH_4Cl (600 mL) and Et_2O (400 mL). The aqueous layer was extracted with Et_2O (3x 600 mL) and the organic phases were washed with brine (300 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash chromatography (EtOAc:hexane, 1:9) afforded the ketone (*R*)-**4** as a pale yellow oil (10.95 g, 91%); $[\alpha]_D^{20}$ -22.5 (c 1.12, $CHCl_3$); **IR** (Thin film) 2936, 1713, 1613, 1513, 1248, 1093 cm^{-1}; ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.16 (2H, d, *J* = 8.7 Hz, Ar<u>H</u>), 6.82 (2H, d, *J* = 8.7 Hz, Ar<u>H</u>), 4.36 (2H, ABq, *J* = 11.7 Hz, OC<u>H</u>$_2$Ar), 3.73 (3H, s, OC<u>H</u>$_3$), 3.55 (1H, dd, *J* = 9.0, 7.8 Hz, H1), 3.39 (1H, dd, *J* = 9.0, 5.5 Hz, H1'), 2.84-2.79 (1H, m, H2), 2.45 (2H, q, *J* = 7.3 Hz, C<u>H</u>$_2$CH$_3$), 1.03-0.99 (3H, m, C<u>H</u>$_3$CH$_2$), 0.99 (3H, d, *J* = 7.3 Hz, C<u>H</u>$_3$CH); ^{13}**C NMR** δ (100.6 MHz; $CDCl_3$) 213.4, 159.2, 130.2, 129.1, 113.7, 72.8, 72.0, 55.1, 46.1, 35.1, 13.5, 7.5; **m/z** (ES^+) 459 (40%), 260 (18), 259 (100), 243 (25), 186 (30); **HRMS** (ES^+) calcd for $C_{14}H_{20}O_3Na$ (M+Na) 259.1312. Found 259.1352.

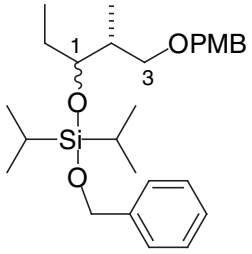
* The enantiomeric ketone (*S*)-**4** was prepared in an identical fashion by starting out with methyl (*S*)-(-)-3-hydroxy-2-methylpropionate**.**

(2*R*, 3*RS*)-1-(4-Methoxy-benzyloxy)-2-methyl-pentan-3-ol: 9.



To a stirred solution of ketone (*R*)-**4** (611 mg, 2.59 mmol) in dry Et_2O was added $LiAlH_4$ (1 M in THF, 5.17 mmol) at 0°C under Ar. After stirring for 1 h at 0°C, the mixture was quenched slowly by a solution of Rochelle's salt (aq, sat) at 0°C and the mixture was stirred for another 1 h at RT. The solution was filtered and then extracted with EtOAc, the combined organic phases were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, Hexane/EtOAc 4:1) afforded **9** as a colourless oil (550 mg, 89%), as a 1.4 :1 mixture of diastereomers in favour of the *syn* isomer. **IR** ($CHCl_3$) 3484, 3007, 2964, 2876, 1612, 1586, 1518, 1454, 1302, 1248, 1109, 1082, 1035, 974, 827, 804 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (4H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 6.86 (4H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 4.43 (4H, s, C$\underline{H}_2$Ar), 3.97 (6H, s, ArOC$\underline{H}_3$), 3.63 (2H, m, H3), 3.56 (1H, dd, J_1 = 4.2, J_2 = 9.2 Hz, H1), 3.48 (2H, d, *J* = 5.4 Hz, H1), 3.43 (1H, dd, J_1 = 7.4, J_2 = 9.2 Hz, H1'), 3.30 (1H, s, OH), 2.58 (1H, s, OH), 1.85 (1H, m, H3), 1.57 (1H, m, H3), 1.41 (4H, m, C$\underline{H}_2$CH$_3$), 0.95 (3H, t, *J* = 7.2 Hz, CH$_2$C$\underline{H}_3$), 0.94 (3H, t, *J* = 7.4 Hz, CH$_2$C$\underline{H}_3$), 0.90 (3H, d, *J* = 7.1 Hz, CHC$\underline{H}_3$), 0.87 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.3, 159.2, 130.3, 130.0, 129.2, 129.1, 128.2, 113.9, 113.8, 76.9, 75.1, 74.6, 74.3, 73.0, 72.9, 55.1, 37.9, 37.5, 27.4, 26.9, 13.9, 10.7, 10.6, 9.6; **m/z** (CI^+, NH_3) 256 (MH^+, 25%), 237 (100), 154 (75); **HRMS** (ES^+) Calcd for $C_{14}H_{26}NO_3$ ($M+NH_4^+$) 256.1913 Found 256.1908.

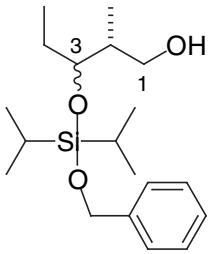
(1*RS*, 2*R*)-Benzyloxy-[1-ethyl-3-(4-methoxy-benzyloxy)-2-methyl-propoxyl-diisopropyl-silane: <u>solution model 33</u>.



To a stirred solution of alcohols **9** (855 mg, 3.59 mmol) in DCM (5 mL) was added imidazole (1.22 g, 17.9 mmol) then diisopropylsilyldichloride (644 µl, 3.59 mmol). After stirring for 1 h at RT, benzyl alcohol (371 µl, 3.59 mmol) was added and stirring was continued for 16 h, before addition of aqueous NH4Cl (sat.). After extraction with dichloromethane (4 x), the combined organic phases were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (short pad of silica gel, PE/Et_2O 120:1) afforded the silyl ether **33** as a colourless oil (1.39 g, 85%,). **IR** ($CHCl_3$) 2963, 2867, 1612, 1513, 1462, 1248, 1097, 1066, 1036 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (8H, m, Ar$\underline{H}_{Ph}$), 7.25 (2H, m, Ar$\underline{H}_{Ph}$), 6.86 (4H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 6.85 (4H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 4.86 (4H, m, C$\underline{H}_2$Ph), 4.37 (4H, m, C$\underline{H}_2$Ar$_{PMB}$), 3.96 (1H, td, J_1 = 2.4, J_2 = 6.7 Hz, H1), 3.88 (1H, q, *J* = 5.3 Hz, H1), 3.79 (6H, s, ArOC$\underline{H}_3$), 3.49 (2H, m, H3), 3.27 (2H, m, H3'), 2.04 (1H, m, H2), 1.93 (1H, m, H2), 1.59-1.46 (4H, m, C$\underline{H}_2$CH$_3$), 1.06 (28H,

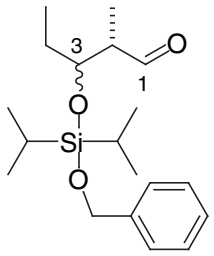
s, Si(^{i}Pr)$_2$), 0.93 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$), 0.89 (3H, t, J = 7.6 Hz, CH$_2$C$\underline{H}_3$), 0.88 (3H,d, J = 6.8 Hz, CHC$\underline{H}_3$), 0.83 (3H, t, J = 7.5 Hz, CH$_2$C$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.1, 141.4, 131.0, 130.9, 129.2, 129.1, 128.2, 126.8, 126.1, 125.9, 125.8, 113.7, 75.4, 74.4, 73.1, 72.7, 72.6, 72.4, 64.7, 64.6, 64.5, 55.2, 38.3, 37.1, 27.4, 25.9, 17.8, 17.7 (x2), 17.5, 12.8, 12.7, 12.6, 12.3, 10.6, 10.3; **m/z** (CI$^+$, NH_3) 476 (50%), 459 (48, MH$^+$), 248 (40), 231 (100), 204 (29); **HRMS** (ES$^+$) Calcd for $C_{27}H_{43}O_4Si$ (MH$^+$) 459.2930 Found 459.2935.

(2*R*, 3*RS*)-3-(Benzyloxy-diisopropyl-silanyloxy)-2-methyl-pentan-1-ol: <u>solution model 34</u>.



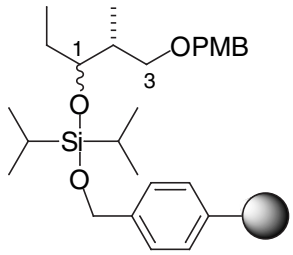
To a stirred solution of PMB ether **33** (632 mg, 1.38 mmol) in DCM/pH 7 buffer (20/1) at 0°C was added recrystallised DDQ (376 mg, 1.65 mmol). After stirring for 90 min at RT, $NaHCO_3$ (sat. aq) was added. Following extraction with dichloromethane, the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (short pad of silica gel, PE/EtOAc 120:1) afforded alcohol **34** as a colourless oil (364 g, 78%). **IR** (Thin Film) 3406, 2869, 2867, 1463, 1378, 1251, 1207, 1098, 1065, 1027, 884, 730 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ; 7.33 (8H, m, Ar$\underline{H}$), 7.27 (2H, m, Ar$\underline{H}$), 4.89 (2H, s, C$\underline{H}_2$Ph), 4.88 (2H, s, C$\underline{H}_2$Ph), 4.01 (1H, td, J_1 = 2.5, J_2 = 7.1 Hz, H3), 3.90 (1H, q, J = 5.5 Hz, H3), 3.79 (1H, dt, J_1 = 4.4, J_2 = 9.0 Hz, H1), 3.65 (1H, ddd, J_1 = 5.0, J_2 = 8.7, J_3 = 13.7 Hz, H1), 3.54 (1H, ddd, J_1 = 5.0, J_2 = 6.7, J_3 = 11.4 Hz, H1), 3.48 (1H, ddd, J_1 = 5.4, J_2 = 6.9, J_3 = 10.9 Hz, H1), 2.63 (1H, dd, J_1 = 5.1, J_2 = 7.0 Hz, OH), 2.56 (1H, dd, J_1 = 5.1, J_2 = 6.6 Hz, OH), 1.88 (1H, m, H2), 1.80 (1H, m, H2), 1.69-1.55 (4H, m, H4 x2), 1.09 (28H, m, Si(^{i}Pr)$_2$, 0.99 (3H, d, J = 7.0 Hz, CHC$\underline{H}_3$), 0.88 (3H, t, J = 7.4 Hz, C$\underline{H}$CH$_3$), 0.87 (3H, t, J = 7.5 Hz, CH$_2$C$\underline{H}_3$), 0.80 (3H, d, J = 6.9 Hz, C$\underline{H}$CH$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 140.7, 140.5, 129.1, 128.3, 128.2, 127.2, 127.0, 126.2, 125.9, 74.9, 65.4, 65.1, 64.9, 64.8, 64.6, 38.5, 37.9, 27.1, 26.6, 17.5, 17.4, 14.2, 12.6, 12.4, 12.3, 10.3, 9.9, 8.7; **m/z** (CI$^+$, NH_3) 356 (32%), 339 (40, MH$^+$), 312 (100), 248 (51), 231 (100), 204 (23); **HRMS** (ES$^+$) Calcd for $C_{19}H_{35}O_3Si$ (MH$^+$) 339.2364 Found 339.2346.

(2*S*, 3*RS*)-3-(Benzyloxy-diisopropyl-silanyloxy)-2-methyl-pentanal: <u>solution model 12</u>.



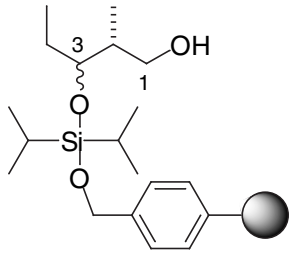
To a stirred solution of alcohol **34** (273 mg, 0.80 mmol) in DCM (5 mL) was added Dess-Martin Periodinane (685 mg, 1.60 mmol). After stirring for 0.5 h at RT, hexanes was added until a precipitate was formed; the mixture was then adsorbed on silica gel and purified by flash chromatography (long pad of silica gel, Hex/EtOAc 50:1) to afford aldehyde **12** as a colourless oil (236 mg, 88%,). **IR** (Thin film) 2963, 2866, 1726, 1463, 1378, 1254, 1098, 1067, 1027, 884 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.79 (1H, s, C<u>H</u>O), 9.75 (1H, d, *J* = 2.2 Hz, C<u>H</u>O), 7.34 (8H, m, Ar<u>H</u>), 7.26 (2H, m, Ar<u>H</u>), 4.87 (2H, m, C<u>H$_2$</u>Ph), 4.85 (2H, m, C<u>H$_2$</u>Ph), 4.31 (1H, td, J_1 = 3.3, J_2 = 6.7 Hz, H3), 4.14 (1H, q, *J* = 5.6 Hz, H3), 2.57 (1H, m, H2), 2.49 (1H, qd, J_1 = 3.3, J_2 = 7.1Hz, H2), 1.63 (4H, m, C<u>H$_2$</u>CH$_3$), 1.07 (31H, m, Si(<u>^{i}Pr</u>)$_2$+CHC<u>H$_3$</u>), 0.89 (9H, m, CH$_2$C<u>H$_3$</u>(x2)+ CHC<u>H$_3$</u>); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 205.1, 204.7, 128.2, 126.9, 125.8 (x2), 74.7, 73.5, 64.6, 50.7, 50.4, 27.5, 27.3, 17.5, 17.4, 12.6, 12.5, 12.4 (x2), 10.2, 10.0, 9.1, 7.0; **m/z** (CI^+, NH_3) 354 (18, M+NH_4), 248 (52) 246 (48), 231 (67), 229 (100); **HRMS** (ES^+) Calcd for $C_{19}H_{36}NO_3Si$ (M+NH_4) 354.2464 Found 354.2458.

(1*RS*, 2*R*)-[1-Ethyl-3-(4-methoxy-benzyloxy)-2-methyl-propoxy]-diisopropyl-silanyloxy-methoxypolystyrene: <u>resin 11</u>.



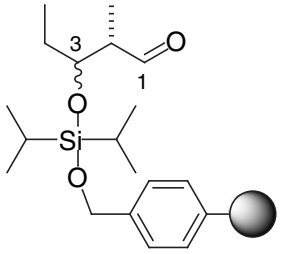
To a stirred solution of alcohols **9** (1.47 g, 6.17 mmol) in dry DMF (5 mL) was added imidazole (2.5 g, 37.0 mmol) then diisopropylsilyldichloride (1.1 mL, 6.17 mmol). After stirring for 1h at RT, the mixture was transferred *via* cannula to pre-swollen hydroxymethyl polystyrene resin (1.18 g, 1.02 mmol, loading 0.87 mmol/g) in DMF. After shaking for 36 h, the resin was filtered off, washed in turn with DMF, H_2O, THF/H_2O, THF, DCM and MeOH, then dried under high vacuum at 60°C for 4 h. A second cycle of reaction was then repeated for another 36 h. After washing and drying, 1.56 g of resin **11** was obtained (the loading, 0.75mmol/g, was determined by cleavage with TBAF). **IR** (Single Bead) 3028, 2928, 2867, 1604, 1514, 1494, 1454, 1374, 1249, 1090, 1019, 887, 819, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, CD_2Cl_2) δ 159.0, 131.0, 113.5, 75.3, 74.3, 73.0, 72.5, 72.3, 64.3, 55.1, 38.3, 37.1, 27.3, 25.9, 17.5, 13.0, 12.6, 10.4, 10.0, 9.4.

(2*R*, 3*RS*)-3-(Diisopropyl-silanyloxy-methoxypolystyrene)-2-methyl-pentan-1-ol: <u>resin 35</u>.



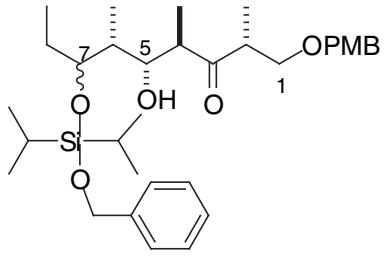
To resin **11** (318 mg, 0.254 mmol) swollen in DCM, was added at 0˚C recrystallised DDQ (115 mg, 0.51 mmol). After shaking for 3 h at RT, the solution was filtered off, the resin was washed in turn with DCM, THF/H_2O, THF, DCM and MeOH, then dried under high vacuum at 60°C for 4 h. This gave pale yellowish resin **35** (330 mg). **IR** (Single Bead) 3580, 3494, 3029, 2925, 2869, 1703, 1605, 1494, 1454, 1095, 1055, 1030, 844, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, CD_2Cl_2), δ 77.2, 74.9, 65.2, 64.9, 38.7, 38.4, 26.9, 26.7, 17.3, 15.1, 13.9, 12.6, 12.5, 10.2, 9.9, 8.7.

(2*S, 3RS*)-3-(Diisopropyl-silanyloxy-methoxypolystyrene)-2-methyl-pentanal: <u>resin 3</u>.



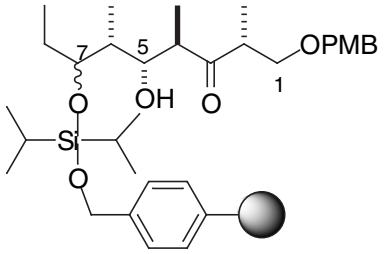
To resin **35** (326 mg, 0.283 mmol), swollen in DCM, was added pyridine (114 µl, 1.42 mmol) followed by Dess-Martin periodinane[3] (242 mg, 0.56 mmol). After shaking for 6 h at RT, the solution was filtered off and the resin was washed in turn with DCM, THF/H_2O, THF, DCM and MeOH, then dried under high vacuum at 60°C for 4 h. This afforded the pale yellow resin **3** (330 mg). **IR** (Single Bead) 3028, 2924, 2867, 2723, 1725, 1703, 1605, 1584, 1494, 1454, 1376, 1267, 1067, 886, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, CD_2Cl_2), δ 204.6, 204.2, 74.7, 73.5, 64.5, 50.6, 50.4, 27.4, 17.3, 17.3, 15.0, 12.6, 12.4, 10.1, 9, 8.9, 6.8.

5-hydroxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-3-one: <u>solution model 14</u>.



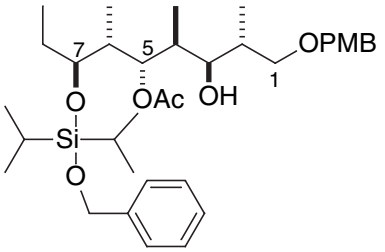
To a solution of dicyclohexylboron chloride (554 μL, 2.83 mmol) in diethyl ether (1 mL) was added triethylamine (497 μL, 3.54 mmol) at 0˚C. After stirring for 15 min, a solution of ketone (*R*)-**4** (668 mg, 2.83 mmol) in diethyl ether (0.5 mL + 0.5 mL rinse) was added *via* cannula. The resulting mixture was stirred for 2 h at 0°C. After cooling to -78˚C, the enolate solution was transfered *via* cannula to a solution of aldehyde (214 mg, 0.63 mmol) in diethyl ether (0.5 mL) and stirring was continued at -78˚C for 1h, before storing the mixture in the freezer at -27°C for 16 h. After addition of pH 7 buffer, the aqueous phase was extracted with diethyl ether, and the combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was redissolved in a mixture of methanol (0.5 mL) and pH 7 buffer (0.5 mL) at 0°C, and H_2O_2 (30% aq, 0.5 mL) was then added. The mixture was warmed up to RT and stirred for 2 h. The layers were separated and the aqueous phase was extracted with dichloromethane. The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash chromatography (silica gel, PE/Et_2O 8:1 then 6:1) gave aldol adduct **14** as a colourless oil (350 mg, 95%, 97% ds). **IR** (Thin Film) 3492, 2964, 2937, 2866, 1711, 1612, 1513, 1462, 1376, 1302, 1248, 1100, 1088, 1035, 821 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (8H, m, Ar<u>H</u>$_{Ph}$), 7.27 (2H, m, Ar<u>H</u>$_{Ph}$), 7.17 (4H, d, *J* = 8.5 Hz, Ar<u>H</u>$_{PMB}$), 6.86 (4H, d, *J* = 8.5 Hz, Ar<u>H</u>$_{PMB}$), 4.87 (4H, s, C<u>H</u>$_2$Ph), 4.40 (4H, m, C<u>H</u>$_2$Ar$_{PMB}$), 4.20 (1H, br d, *J* = 9.8 Hz, H5), 3.88 (1H, dt, J_1 = 2.7, J_2 = 8.6 Hz, H5), 3.79 (6H, s, ArOC<u>H</u>$_3$), 3.62 (2H, t, *J* = 8.5 Hz, H1), 3.45 (2H, m+dd, J_1 = 5.1, J_2 = 8.9 Hz, H1'), 3.38 (1H, d, *J* = 1.9 Hz, OH), 3.20 (1H, d, *J* = 3.2 Hz OH), 3.05 (2H, m, H2), 2.89 (2H, m, H4), 1.83-1.57 (6H, m, H6+CH$_2$C<u>H</u>$_3$x2), 1.07 (28H, s, Si(<u>^{i}Pr</u>)$_2$), 1.05 (3H, d, *J* = 7.0 Hz, CHC<u>H</u>$_3$), 1.04 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.98 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.97 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.92 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.89 (3H, t, *J* = 7.6 Hz, CH$_2$C<u>H</u>$_3$), 0.83 (3H, t, *J* = 7.5 Hz, CH$_2$C<u>H</u>$_3$), 0.81 (3H, t, *J* = 7.5 Hz, CH$_2$C<u>H</u>$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 217.7, 217.3, 159.2, 140.7, 140.4, 130.3, 130.1, 129.2, 128.3, 128.2, 127.0, 126.9, 126.0, 125.9, 113.7 (x2), 78.9, 78.3, 72.9, 72.4, 64.8, 64.7, 55.2, 49.2, 48.8, 47.3, 46.6, 36.3, 35.0, 27.6, 27.3, 17.5, 17.4, 13.3, 13.1, 13.0, 12.8, 12.6, 12.5, 12.2, 10.1, 9.7, 9.0, 5.8; **m/z** (CI^+, NH_3) 590 (72%), 573 (100, MH^+), 482 (61), 465 (100), 391 (49), 374 (70), 229 (33); **HRMS** (ES^+) Calcd for $C_{33}H_{53}O_6Si$ (MH^+) 573.3611 Found 573.3616.

(2*R*, 4*R*, 5*R*, 6*R*, 7*RS*)-7-(Diisopropyl-silanyloxy-methoxypolystyrene)-5-hydroxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-3-one: <u>resin 13</u>.



To a solution of dicyclohexylboron chloride (437 µl, 2.23 mmol) in diethyl ether (1 mL) was added triethylamine (365 µl, 2.60 mmol) at 0˚C. After stirring for 15 min, a solution of ketone (*R*)-**4** (527 mg, 2.23 mmol) in diethyl ether (0.5 mL + 0.5 mL rinse) was added *via* cannula. The resulting mixture was stirred for 3 h at 0°C. After cooling to -78˚C, the enolate solution was transfered *via* cannula to the aldehyde resin **3** (428 mg, 0.37 mmol), swollen in diethyl ether (1.5 mL), and shaking was continued at -78˚C for 1 h, before storing in the freezer at -27°C for 16 h. The solution was filtered off and the resin was washed with diethyl ether and dried under high vacuum for 3 h at 60°C. A second cycle of aldol reaction with the same conditions and amounts of reagents was carried out on this resin sample swollen in diethyl ether. After 16 h in the freezer, the solution was filtered off and the resin was washed in turn with Et_2O, pH 7 buffer, Et_2O and MeOH. The resin was then swollen in a mixture of MeOH (1 mL), DMF (2 mL), pH 7 buffer (1 mL) at 0°C and 3 mL of H_2O_2 were added. Shaking was continued for 2 h at 0°C before storing in the freezer at -27°C for 16 h. The solution was filtered off, and the resin was washed in turn with H_2O, THF/H_2O, THF, DCM and MeOH, then dried under high vacuum for 4 h at 60°C. This afforded resin **13** (478 mg). **IR** (Single Bead) 3503, 3062, 3028, 2928, 1713, 1603, 1585, 1514, 1494, 1453, 1375, 1249, 1090, 1031, 822, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, CD_2Cl_2) δ 216.9, 216.6, 159.2, 130.3, 129.1, 113.6, 79.2, 77.1, 72.8, 72.3, 64.6, 55.1, 49.1, 48.6, 47.3, 46.7, 36.2, 34.9, 27.5, 17.3, 15.0, 13.0, 12.8, 12.2, 10.0, 9.5, 8.9, 5.5.

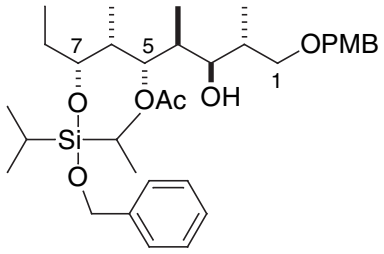
(2*R*, 3*R*, 4*S*, 5*S*, 6*S*, 7*S*)-7-(benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl, 5-acetoyl-nonan-3-ol: <u>solution model 15a</u>.



To a solution of acetaldehyde (800 µl, excess, freshly distilled) in THF was added SmI_2 (freshly prepared; 0.1 M in THF, 3.8 mL, 0.38 mmol) at -20˚C under argon. After stirring for 5 min, aldol adduct **14** (362 mg, 0.632 mmol) in THF was added *via* cannula to the premixed yellow solution. After complete addition, the mixture was allowed to warm-up to 0˚C for 3 h, then left in the freezer for 16 h before addition of $NaHCO_3$ (sat. aq). Following extraction with

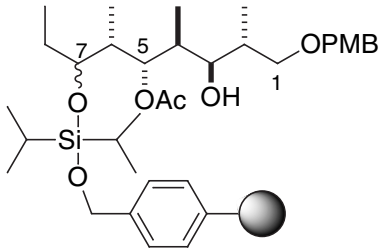
EtOAc, the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, PE/Ether 6:1 to 4:1, gradient) afforded isomer **15a** as a colourless oil (140 mg, 36%); $[\alpha]_D^{20}$ -2.0 (*c* 0.48, $CHCl_3$); **IR** (Thin Film) 3509, 2975, 2943, 2866, 1714, 1610, 1513, 1458, 1370, 1302, 1251, 1093, 1065, 1027, 885, 815, 733 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ 7.33 (4H, m, Ar$\underline{H}_{Ph}$), 7.24 (3H, m, Ar$\underline{H}_{Ph}$), 6.86 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 5.15 (1H, dd, J_1 = 2.2, J_2 = 9.6 Hz, H5), 4.87 (2H, s, C$\underline{H}_2$Ph), 4.43 (2H, ABq, *J* = 13.8 Hz, C$\underline{H}_2$Ar$_{PMB}$), 3.82 (4H, m, ArOC$\underline{H}_3$+H7), 3.61 (1H, dd, J_1 = 4.3, J_2 = 8.9 Hz, H1), 3.44 (1H, dd, J_1 = 6.1, J_2 = 8.9 Hz, H1'), 3.28 (1H, ddd, J_1 = 1.6, J_2 = 3.5, J_3 = 9.8 Hz, H3), 3.15 (1H, d, *J* = 3.5 Hz, OH), 2.03 (3H, s, C$\underline{H}_3$CO), 2.00 (1H, qdd, J_1 = 2.2, J_2 = 6.8, J_3 = 13.2 Hz, H6), 1.87 (1H, m, H2), 1.79 (1H, ddq, J_1 = 1.3, J_2 = 6.9, J_3 = 9.6 Hz, H4), 1.61 (1H, qdd, J_1 = 4.8, J_2 = 7.3, J_3 = 14.4 Hz, C$\underline{H}_2$CH$_3$), 1.55 (1H, qdd, J_1 = 5.4, J_2 = 7.3, J_3 = 14.4 Hz, C$\underline{H}_2$CH$_3$), 1.07 (14H, s, Si($^i\underline{Pr}$)$_2$), 0.91 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.88 (3H, t, *J* = 7.3 Hz, CH$_2$C$\underline{H}_3$), 0.86 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$), 0.82 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 172.1, 159.0, 141.2, 130.9, 129.0, 128.1, 126.8, 125.7, 113.7, 75.5, 75.4, 73.7, 72.8, 71.1, 64.4, 55.2, 37.9, 36.4, 36.3, 26.2, 21.1, 17.7, 17.6, 17.5, 13.9, 12.6, 12.5, 9.1, 8.7; **m/z** (CI^+, NH_3) 635 (38%), 634 (80), 617 (40), 527 (46), 526 (100), 509 (52), 389 (36), 374 (50); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH^+) 617.3873 Found 617.3880.

(2*R*, 3*R*, 4*S*, 5*S*, 6*S*, 7*R*)-7-(Benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-acetoyl-nonane-3-ol: <u>solution model 15b</u>.



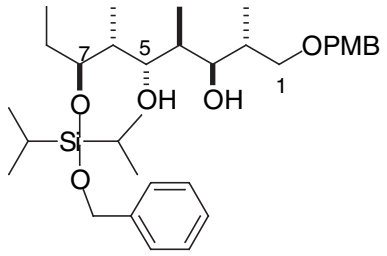
Diastereoisomer **15b** was obtained by chromatography as a colourless oil from the previous procedure (201 mg, 51%). $[\alpha]_D^{20}$ –10.0° (*c* 1.2, $CHCl_3$); **IR** (Thin Film) 3509, 2975, 2855, 1714, 1613, 1513, 1462, 1374, 1302, 1248, 1097, 1027, 956, 884 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (4H, m, Ar$\underline{H}_{Ph}$), 7.24 (3H, m+d, *J* = 8.7 Hz, Ar$\underline{H}_{Ph}$), 6.86 (2H, d, *J* = 8.7 Hz, Ar$\underline{H}_{PMB}$), 5.07 (1H, dd, J_1 = 3.4, J_2 = 8.9 Hz, H5), 4.88 (2H, s, C$\underline{H}_2$Ph), 4.43 (2H, ABq, *J* = 11.6 Hz, C$\underline{H}_2$Ar$_{PMB}$), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.75 (1H, dt, J_1 = 4.6, J_2 = 6.8 Hz, H7), 3.59 (1H, dd, J_1 = 4.6, J_2 = 8.9 Hz, H1), 3.46 (1H, dd, J_1 = 5.8, J_2 = 8.9 Hz, H1'), 3.32 (1H, ddd, J_1 = 1.3, J_2 = 3.2, J_3 = 9.7 Hz, H3), 3.12 (1H, d, *J* = 3.2 Hz, OH), 2.03 (3H, s, CH_3CO), 2.01 (1H, m, H6), 1.86 (2H, m, H2+H4), 1.65 (1H, qdd, J_1 = 4.6, J_2 = 7.4, J_3 = 14.4 Hz, C$\underline{H}_2$CH$_3$), 1.60 (1H, qdd, J_1 = 4.7, J_2 = 7.4, J_3 = 14.4 Hz, C$\underline{H}_2$CH$_3$), 1.08 (14H, m, Si($^i\underline{Pr}$)$_2$), 0.97 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$), 0.87 (3H, t, *J* = 7.4 Hz, CH$_2$C$\underline{H}_3$), 0.85 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$), 0.84 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 171.8, 159.0, 141.1, 130.7, 129.0, 128.1, 126.8, 125.7, 113.7, 75.9, 74.9, 73.8, 72.8, 71.4, 64.5, 55.2, 37.4, 36.3, 36.1, 26.5, 21.0, 17.7, 17.6, 17.5, 13.9, 12.7, 12.5, 9.5, 8.6, 8.7; **m/z** (CI^+, NH_3) 635 (25%), 634 (49), 527 (49), 526 (100), 509 (33), 389 (49); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH^+) 617.3873 Found 617.3879.

(2*R*, 3*R*, 4*S*, 5*S*, 6*S*, 7*RS*)-7-(Diisopropyl-silanyloxy-methoxypolystyrene)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-acetoyl-nonane-3-ol: resin 16.



To resin **13** (411 mg, 0.357 mmol), swollen in THF (3 mL), was added a premixed solution of acetaldehyde (200 μl, excess) and SmI_2 (freshly prepared; 0.1M in THF, 3.57 mL, 0.357 mmol) in THF *via* cannula at -20˚C. After shaking for 2 h at 0˚C, the mixture was transferred into the fridge (0˚C, no shaking) for 16 h. The solution was filtered off and the resin was washed in turn with THF, $NaHCO_3$ solution (sat. aq), H_2O, THF/H_2O, methanol, THF and dichloromethane, then dried under reduced pressure at 50˚C for 3 h. A second cycle was carried out to enable the reaction to go to completion. This gave a pale **or**ange resin **16** (410 mg). IR (Single Bead) 3506, 3062, 3029, 2922, 1736, 1604, 1586, 1514, 1494, 1454, 1372, 1250, 1094, 1031, 821, 758 cm-1; 13C NMR (100.6 MHz, CD2Cl2), δ 171.6, 159.1, 130.8, 129.0, 113.5, 75.5, 74.9, 73.9, 72.7, 71.3, 69.6, 64.3, 55.1, 44.0, 42.7, 40.4, 37.5, 36.3, 26.4, 20.9, 17.5, 13.6, 12.6, 9.4, 9.1, 8.5.

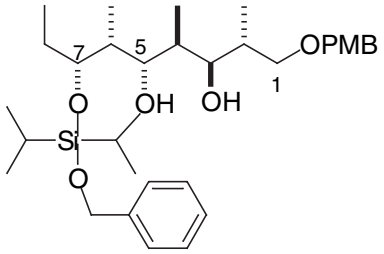
(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*S*)-7-(Benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol: solution model 20a.



To a solution of acetate **15a** (100 mg, 0.162 mmol) in dry THF was added a solution of $LiBH_4$ (freshly prepared, 2 M in THF, 1.6 mL, 3.24 mmol). The reaction mixture was stirred for 16 h at RT before the addition of aqueous NH4Cl (sat. aq) at 0°C. Following extraction with EtOAc, the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, PE/EtOAc 9:1, then 6:1, gradient) afforded diol **20a** as a colourless oil (44 mg, 47%); $[\alpha]_D^{20}$ –12.0 (*c* 0.34, $CHCl_3$); **IR** ($CHCl_3$) 3467, 3018, 2967, 2869, 1612, 1513, 1463, 1249, 1083, 1013 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (4H, m, Ar$\underline{H}_{Ph}$), 7.24 (3H, m+d, J = 8.6 Hz, Ar$\underline{H}_{Ph}$), 6.86 (2H, d, J = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.88 (2H, s, C$\underline{H}_2$Ph), 4.45 (2H, ABq, J = 11.3 Hz, C$\underline{H}_2$Ar$_{PMB}$), 4.02 (1H, br d, J = 9.3 Hz, H5), 3.95 (1H, ddd, J_1 = 3.3, J_2 = 5.1, J_3 = 13.1 Hz, H7), 3.93 (1H, br d, J = 9.6 Hz, H3), 3.79 (3H, s, ArOC$\underline{H}_3$), 3.65 (2H, m, 2 x OH), 3.55 (1H, dd, J_1 = 5.0, J_2 = 8.9 Hz, H1), 3.53 (1H, dd, J_1 = 8.9, J_2 = 16.9 Hz, H1'), 1.97 (1H, m, H2),

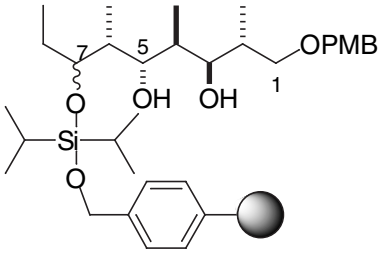
1.84-1.73 (3H, m, H4+H8), 1.67 (1H, m, H6), 1.09-1.06 (14H, m, Si(^{i}Pr)$_2$), 1.03 (3H, d, J = 7.1 Hz, CHC$\underline{H}_3$), 0.81 (3H, t, J = 7.5 Hz, $CH_2C\underline{H}_3$), 0.79 (3H, d, J = 7.1 Hz, CHC$\underline{H}_3$), 0.77 (3H, d, J = 7.0 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.2, 140.7, 129.9, 129.3, 128.2, 126.9, 125.9, 113.8, 79.9, 74.7, 73.1, 70.6, 64.7, 55.2, 37.3, 36.1, 35.2, 27.3, 17.6, 17.5, 13.1, 12.6, 10.7, 9.8, 8.8; **m/z** (CI^+, NH_3) 576 (42%, MH^+), 575 (100), 485 (40); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH^+) 575.3768 Found 575.3766.

(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*R*)-7-(Benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol: <u>solution model 20b</u>.



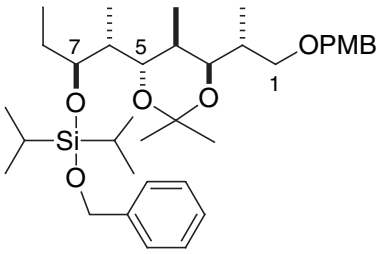
To a solution of acetate **15b** (97 mg, 0.157 mmol) in dry THF was added a solution of $LiBH_4$ (freshly prepared, 2 M in THF, 1.6 mL, 3.15 mmol) and the reaction mixture was stirred for 16 h at RT. Aqueous NH_4Cl (sat. aq) was added at 0°C, then the mixture was extracted with EtOAc and the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, PE/EtOAc 9:1, then 6:1) afforded diol **20b** as a colourless oil (39 mg, 44%); **$[\alpha]_D^{20}$** –18.0 (*c* 0.25, $CHCl_3$); **IR** (Thin Film) 3449, 2963, 2866, 1613, 1513, 1462, 1248, 1095, 1028, 825 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (4H, m, Ar$\underline{H}_{Ph}$), 7.24 (3H, m+d, J = 8.7 Hz, Ar$\underline{H}_{Ph}$), 6.86 (2H, d, J = 8.7 Hz, Ar$\underline{H}_{PMB}$), 4.87 (2H, s, C$\underline{H}_2$Ph), 4.45 (2H, ABq, J = 11.5 Hz, C$\underline{H}_2$Ar$_{PMB}$), 3.98 (1H, ddd, J_1 = 2.5, J_2 = 4.8, J_3 = 9.5 Hz, H7), 3.88 (1H, dt, J_1 = 1.7, J_2 = 7.8 Hz, H3), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.76 (1H, brs, OH), 3.75 (1H, m, H5), 3.54 (1H, dd, J_1 = 5.1, J_2 = 9.1 Hz, H1), 3.53 (1H, dd, J_1 = 9.1, J_2 = 16.8 Hz, H1'), 3.41 (1H, d, J = 3.8 Hz, OH), 1.97 (1H, m, H2), 1.77 (2H, m, H4+H6), 1.72-1.61 (1H, m, H8), 1.07 (14H, m, Si(^{i}Pr)$_2$), 0.95 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$), 0.87 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$), 0.80 (3H, t, J = 7.5 Hz, $CH_2C\underline{H}_3$), 0.77 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.2, 140.8, 129.9, 129.3, 128.2, 126.9, 125.9, 113.8, 78.9, 76.3, 75.3, 73.1, 64.6, 55.2, 36.9, 36.8, 35.9, 27.7, 17.6, 17.5, 17.4, 13.2, 12.9, 12.6, 10.0, 9.6, 5.9; **m/z** (CI^+, NH_3) 576 (42%, MH^+), 575 (100), 467 (32); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH^+) 575.3768 Found 575.3765.

(*2R, 3R, 4S, 5S, 6R, 7RS*)-7-(Diisopropyl-silanyloxy-methoxypolystyrene)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol : <u>resin 18</u>.



To resin **16** (306 mg, approx. 0.21 mmol), swollen in THF (3 mL), was added *via* cannula $LiBH_4$ solution (2.1 mL, 2M in THF, 4.2 mmol, 20 equiv) at -78˚C. The mixture was allowed to warm up to RT and shaken for 20 h. The solution was filtered off and the resin was washed with H_2O/THF (1:1 v/v) ; after shaking for 1 h with this mixture, the resin was washed in turn with H_2O, THF, DCM and MeOH and dried under reduced pressure at 60˚C. This gave pale yellow resin **18 (**320 mg). ^{13}C NMR spectroscopy indicated complete removal of the acetate. **IR** (Single Bead) 3487, 3028, 2922, 1603, 1586, 1514, 1494, 1453, 1249, 1090, 821, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, CD_2Cl_2), δ 159.4, 129.2, 127.9, 113.7, 79.3, 78.3, 76.1, 75.0, 74.3, 72.9, 71.3, 64.5, 55.1, 37.9, 37.3, 36.0, 27.4, 17.3, 12.6, 10.5, 9.6, 8.7.

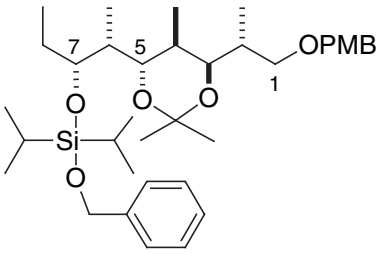
(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*S*)-3,5-Isopropylidendioxy-7-(benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>solution model 22a</u>.



To a stirred solution of *anti* diol **20a** (24 mg, 0.0418 mmol) in dichloromethane (1.5 mL) at 0˚C was added 2,2-dimethoxypropane (155 µl, 1.25 mmol) followed by PPTS (2 mg, cat). The solution was allowed to warm up to RT and stirred for 16 h. After termination of the reaction by addition of solid $NaHCO_3$, the mixture was absorbed on silica gel and purified by flash chromatography (silica gel, PE/Et_2O 20:1) to give acetonide **22a** as a colourless oil (21 mg, 82%); $[\alpha]_D^{20}$ +0.7 (*c* 0.29, $CHCl_3$); **IR** ($CHCl_3$) 2939, 2871, 2359, 1612, 1513, 1463, 1381, 1249, 1094, 1067, 1017 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33 (4H, m, Ar<u>H</u>$_{Ph}$), 7.25 (3H, m, Ar<u>H</u>$_{Ph}$), 6.87 (2H, d, *J* = 8.7 Hz, Ar<u>H</u>$_{PMB}$), 4.85 (2H, s, C<u>H</u>$_2$Ph), 4.40 (2H, s, C<u>H</u>$_2$Ar$_{PMB}$), 3.86 (1H, td, J_1 = 3.2, J_2 = 6.4 Hz, H7), 3.80 (3H, s, ArOC<u>H</u>$_3$), 3.53 (2H, m, H1+H3 or H5 interchangeable), 3.36 (2H, m, H1+H3 or H5 interchangeable), 1.80 (1H, qdd, J_1 = 3.0, J_2 = 6.6, J_3 = 13.2 Hz, H2), 1.77 (2H, m, H4+H6), 1.71-1.59 (3H, m, H4, H6, H8), 1.48 (1H, m, H8'), 1.28 (3H, s, CC<u>H</u>$_3$), 1.23 (3H, s, CC<u>H</u>$_3$), 1.09 (14H, m, Si(ⁱ<u>Pr</u>)$_2$), 0.91 (3H, t, *J* = 7.4 Hz, CH$_2$C<u>H</u>$_3$), 0.90 (3H, d, *J* = 6.7 Hz, CHC<u>H</u>$_3$), 0.87 (3H, d, *J* = 7.0 Hz, CHC<u>H</u>$_3$), 0.81 (3H, d, *J* = 7.0 Hz,

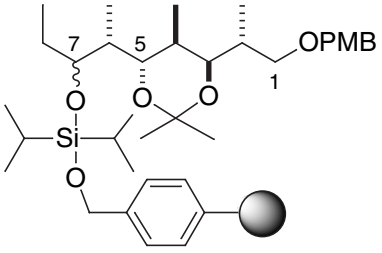
$CHC\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.0, 141.3, 131.0, 129.1, 128.1, 126.7, 125.7, 113.6, 100.2, 76.0, 74.8, 72.8, 72.3, 70.2, 64.3, 55.2, 42.5, 36.1, 33.8, 25.9, 25.0, 23.7, 17.8, 17.7, 17.6, 13.3, 12.7, 12.6, 11.7, 9.1, 8.4; **m/z** (CI^+, NH_3) 632 (38%), 615 (71), 557 (43), 377 (47), 329 (48); **HRMS** (ES^+) Calcd for $C_{36}H_{59}O_6Si$ (MH^+) 615.4081 Found 615.4091.

(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*R*)-3,5-Isopropylidendioxy-7-(benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>solution model 22b</u>.



To a stirred solution of *anti* diol **20b** (41 mg, 0.071 mmol) in dichloromethane (1.5 mL) at 0˚C was added 2,2-dimethoxypropane (222 µl, 1.79 mmol) followed by PPTS (2 mg, cat). The solution was allowed to warm up to RT and stirred for 16 h. After termination of the reaction by addition of solid $NaHCO_3$, the mixture was absorbed onto silica gel and purified by flash chromatography (PE/Et_2O 20:1) to give acetonide **22b** as a colourless oil (33 mg, 84%); **$[\alpha]_D^{20}$** +5.5 (*c* 0.73, $CHCl_3$); **IR** ($CHCl_3$) 2965, 2855, 2359, 1613, 1513, 1462, 1378, 1247, 1225, 1096, 1016, 884, 808 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37-7.31 (4H, m, $Ar\underline{H}_{Ph}$), 7.26 (3H, m+d, *J* = 8.7 Hz, $Ar\underline{H}_{Ph}$), 6.86 (2H, d, *J* = 8.7 Hz, $Ar\underline{H}_{PMB}$), 4.90 (2H, s, $C\underline{H}_2Ph$), 4.41 (2H, s, $C\underline{H}_2Ar_{PMB}$), 3.83 (1H, q, J_1 = 5.5 Hz, H7), 3.81 (3H, s, $ArOC\underline{H}_3$), 3.57 (1H, dd, J_1 = 4.5, J_2 = 6.3 Hz, H1), 3.54 (1H, m, H3), 3.44 (1H, dd, J_1 = 2.6, J_2 = 7.3 Hz, H5), 3.38 (1H, dd, J_1 = 6.3, J_2 = 8.7 Hz, H1'), 1.87-1.75 (2H, m, H2+H4), 1.72-1.61 (2H, m, H6+H8), 1.59-1.49 (1H, m, H8'), 1.30 (3H, s, $CC\underline{H}_3$), 1.24 (3H, s, $CC\underline{H}_3$), 1.09 (14H, m, $Si(^i\underline{Pr})_2$), 0.96 (3H, d, *J* = 7.0 Hz, $CHC\underline{H}_3$), 0.94 (3H, d, *J* = 6.7 Hz, $CHC\underline{H}_3$), 0.89 (3H, t, *J* = 7.4 Hz, $CH_2C\underline{H}_3$), 0.86 (3H, d, *J* = 6.6 Hz, $CHC\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.0, 141.2, 131.0, 129.1, 128.1, 126.7, 125.8, 113.6, 100.2, 76.0, 73.7, 72.8, 72.3, 70.2, 64.5, 55.2, 41.4, 35.7, 33.8, 26.4, 25.0, 23.5, 17.7, 17.6, 13.4, 12.8, 12.7, 11.8, 10.4, 9.7; **m/z** (CI^+, NH_3) 632 (30%), 616 (50), 615 (100), 557 (70); **HRMS** (ES^+) Calcd for $C_{36}H_{59}O_6Si$ (MH^+) 615.4081 Found 615.4081.

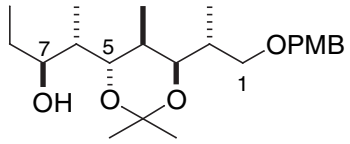
(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*RS*)-3,5-Isopropylidendioxy-7-(diisopropyl-silanyloxy-methoxy-polystyrene)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>resin 21</u>.



To resin **18** (194 mg, 0.168 mmol), swollen in dichloromethane (3 mL), was added 2,2-dimethoxypropane (2 mL) and camphorsulfonic acid (10 mg) at RT. After shaking for 2 days,

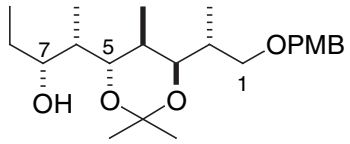
the solution was filtered off. The resin was washed with dichloromethane, methanol, THF and dichloromethane and dried under reduced pressure at 50˚C for 3 h. This gave pale yellow resin **21** (247 mg); **IR** (Single Bead) 2924, 1604, 1586, 1514, 1495, 1454, 1379, 1248, 1225, 1091, 1032, 886, 757 cm^{-1}; **^{13}C NMR** (100.6 MHz, $CDCl_3$), δ 159.0, 135.6, 131.0, 129.1, 127.9, 113.7, 100.2, 74.6, 73.7, 72.3, 70.2, 67.9, 55.2, 42.3, 41.4, 35.8, 33.8, 26.5, 26.1, 25.6, 25.1, 23.9, 17.8, 13.5, 12.7, 11.9, 10.5, 9.8, 8.8.

(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*S*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-ol: solution model 23a.



To a solution of silyl ether **22a** (19 mg, 0.031 mmol) in acetonitrile (1 mL) in a polypropylene bottle was added a solution of HF/pyridine in pyridine (0.5 mL, 8.3 M in pyridine) at 0˚C. After stirring for 3 h at RT, $NaHCO_3$ (aq sat) was added and the mixture was extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, gradient PE/Et_2O 3:1) gave alcohol **23a** as a colourless oil (10 mg, 82%); **$[\alpha]_D^{20}$** +1.3 (*c* 0.45, $CHCl_3$); **IR** ($CHCl_3$) 3489, 2936, 2877, 1612, 1513, 1463, 1383, 1247, 1093, 1017 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 6.88 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.40 (2H, s, C$\underline{H}_2$Ar$_{PMB}$), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.65 (1H, dd, J_1 = 2.0, J_2 = 7.3 Hz, H5), 3.59 (1H, dd, J_1 = 4.1, J_2 = 10.8 Hz, H3), 3.52 (1H, dd, J_1 = 2.9, J_2 = 8.7 Hz, H1), 3.47 (1H, m, H7), 3.38 (1H, dd, J_1 = 6.2, J_2 = 8.7 Hz, H1'), 2.97 (1H, d, *J* = 6.3 Hz, OH), 1.91 (1H, qdd, J_1 = 4.1, J_2 = 6.9, J_3 = 7.3 Hz, H4), 1.85-1.79 (1H, m, H2), 1.65 (1H, m, H6), 1.52 (2H, m, H8), 1.34 (3H, s, CC$\underline{H}_3$), 1.26 (3H, s, CC$\underline{H}_3$), 1.02 (3H, d, *J* = 7.1 Hz, CHC$\underline{H}_3$), 0.96 (3H, t, *J* = 7.5 Hz, $CH_2C\underline{H}_3$), 0.95 (3H, d, *J* = 6.8 Hz, CHC$\underline{H}_3$), 0.86 (3H, d, *J* = 6.7 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.0, 130.9, 129.1, 113.7, 100.7, 76.4, 75.3, 72.8, 72.0, 70.3, 55.2, 39.2, 34.2, 33.7, 28.5, 24.9, 23.7, 13.3, 12.1, 11.7, 10.2; **m/z** (CI^+, NH_3) 395 (83%, MH^+), 377 (100), 337 (30), 319 (29), 275 (35), 257 (40); **HRMS** (ES^+) Calcd for $C_{23}H_{39}O_5$ (MH^+) 395.2797 Found 395.2791.

(2*R*, 3*R*, 4*S*, 5*S*, 6*R*, 7*R*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-ol: solution model 23b.



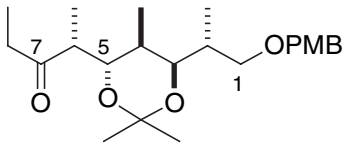
To a solution of silyl ether **22b** (35 mg, 0.057 mmol) in acetonitrile (1 mL) in a polypropylene bottle was added a solution of HF/pyridine in pyridine (0.8 mL, 8.3 M in pyridine) at 0˚C. After stirring for 3 h at RT, $NaHCO_3$ (aq sat) was added and the mixture was extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and evaporated *in*

vacuo. Flash chromatography (silica gel, gradient PE/Et_2O 2:1) gave alcohol **23b** as a colourless oil (18.5 mg, 82%); $[\alpha]_D^{20}$ +4.0° (*c* 0.63, $CHCl_3$); **IR** ($CHCl_3$) 3492, 2987, 2936, 2878, 1612, 1513, 1463, 1382, 1248, 1161, 1074, 1035, 1017 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 6.87 (2H, d, *J* = 8.5 Hz, Ar$\underline{H}_{PMB}$), 4.40 (2H, s, C$\underline{H}_2Ar_{PMB}$), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.67 (1H, m, H7), 3.59 (1H, dd, J_1 = 4.2, J_2 = 10.7 Hz, H3), 3.51 (1H, dd, J_1 = 2.9, J_2 = 8.7 Hz, H1), 3.47 (1H, dd, J_1 = 1.9, J_2 = 7.5 Hz, H5), 3.39 (1H, dd, J_1 = 6.0, J_2 = 8.7 Hz, H1'), 3.22 (1H, s, OH), 1.91 (1H, m, H4), 1.85-1.79 (1H, m, H2), 1.61-1.55 (2H, m, H6+H8), 1.39 (1H, m, H8'), 1.36 (3H, s, CC$\underline{H}_3$), 1.27 (3H, s, CC$\underline{H}_3$), 0.94 (6H, d, *J* = 7.0 Hz, 2 x CHC$\underline{H}_3$), 0.93 (3H, t, *J* = 7.5 Hz, $CH_2C\underline{H}_3$), 0.86 (3H, d, *J* = 6.7 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (62.5 MHz, $CDCl_3$) δ 159.1, 131.0, 129.2, 113.7, 100.8, 80.9, 78.5, 72.9, 72.0, 70.2, 55.3, 38.7, 34.9, 33.8, 27.6, 24.8, 23.8, 13.4, 11.9, 10.5, 5.5; **m/z** (CI^+, NH_3) 395 (100%), 377 (60), 337 (32), 319 (30), 275 (65); **HRMS** (ES^+) Calcd for $C_{23}H_{39}O_5$ (MH^+) 395.2797 Found 395.2798.

Cleavage of alcohols 23a and 23b from resin 21

To resin **21** (67 mg, 0.058 mmol, maximum loading 0.54 mmol) swollen in dry THF was added a 1 M solution of TBAF in THF (290 µl, 0.29 mmol) at RT under Ar. After stirring overnight at RT, the solution was filtered off and quenched by aqueous NH4Cl (aq, sat) and stirring was continued for 30 min. The resin was washed in turn with DCM, H_2O, THF/H_2O, DCM then dried under reduced pressure at 50°C, leading to 59 mg of resin. Evaporation of the filtrate gave the released epimeric alcohols, which were separated by flash chromatography to give **23a** (3.4 mg) and **23b** (4.8 mg). This corresponds to 43% overall yield for 7 steps performed on the resin (calculated loading 0.32 mmol/g). Compounds **23a** and **23b** had identical physical and spectroscopic data to that listed above using the solution model.

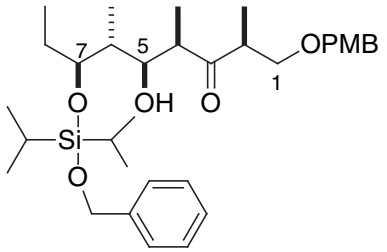
(2*R*, 3*R*, 4*S*, 5*S*, 6*R*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-one: 5.



To a solution of alcohol **23a** or **23b** (6.4 mg, 0.015 mmol) in dichloromethane (1 mL) was added pyridine (7.2 µl, 0.09 mmol) then Dess-Martin periodinan[3] (19.5 mg, 0.045 mmol) at RT. After stirring for 90 min, hexane was added and the mixture was absorbed on silica gel and purified by flash chromatography (Hexane/EtOAc 9:1) to give ketone **5** as a colourless oil (5.6 mg, 88%); $[\alpha]_D^{20}$ -17.6 (*c* 0.54, $CHCl_3$); **IR** ($CHCl_3$), 2986, 2937, 1708, 1611, 1513, 1460, 1380, 1247, 1086, 1034, 1021 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 (2H, d, *J* = 8.7 Hz, Ar$\underline{H}_{PMB}$), 6.87 (2H, d, *J* = 8.7 Hz, Ar$\underline{H}_{PMB}$), 4.40 (2H, s, C$\underline{H}_2Ar_{PMB}$), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.58 (1H, dd, J_1 = 4.3, J_2 = 10.9 Hz, H5), 3.56 (1H, dd, J_1 = 4.0, J_2 = 10.5 Hz, H3), 3.52 (1H, dd, J_1 = 2.9, J_2 = 8.7 Hz, H1), 3.38 (1H, dd, J_1 = 6.2, J_2 = 8.7 Hz, H1'), 2.61 (1H, qd, J_1 = 4.3, J_2 = 6.9 Hz, H6), 2.50 (2H, q (x2), *J* = 7.3 Hz, H8), 1.86 (1H, m, H4), 1.81 (1H, m, H2), 1.29 (3H, s, CC$\underline{H}_3$), 1.24 (3H, s, CC$\underline{H}_3$), 1.13 (3H, d, *J* = 7.0 Hz, CHC$\underline{H}_3$), 1.03 (3H, t, *J* = 7.2 Hz, $CH_2C\underline{H}_3$), 0.92 (3H, d, *J* = 6.7 Hz, CHC$\underline{H}_3$), 0.88 (3H, d, *J* = 6.7 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 213.3, 159.0, 130.9, 129.1, 113.6, 100.6, 75.5, 72.8, 72.1, 70.0, 55.2, 49.7, 34.8, 33.7, 24.9, 23.6, 13.3,

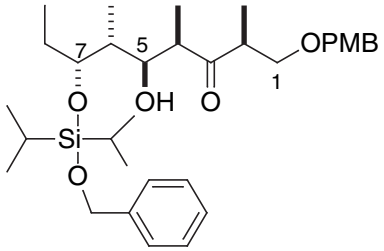
12.1, 11.1, 7.7; **m/z** (CI^+, NH_3) 410 (30%), 393 (100, MH^+), 335 (60), 317 (28), 273 (50); **HRMS** (ES^+) Calcd for $C_{23}H_{37}O_5$ (MH^+) 393.2641 Found 393.2638.

(2*S*, 4*R*, 5*S*, 6*R*, 7*S*)-7-(Benzyloxy-diisopropyl-silanyloxy)-5-hydroxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-3-one: <u>solution model 24a</u>.



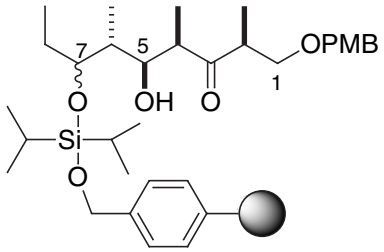
To a solution of $Ti(O^iPr)_4$ (210 µl, 0.709 mmol) in dry DCM (0.5 mL) was added $TiCl_4$ (1M in DCM freshly prepared, 0.709 mmol) at 0°C. After stirring for 5 min at 0°C under Ar, the mixture was cannulated into a solution of ketone (*S*)-**4** (161.5 mg, 0.684 mmol) in dry DCM (0.7 mL) at -78°C. After stirring for 5 min, $^iPr_2NEt$ was added and the resulting orange mixture was left stirring at -78°C for 1 h for enolization. A solution of aldehyde **12** (89 mg, 0.273 mg) in dry DCM (1 mL) was then added to the mixture *via* cannula. After stirring for 20 min, Aqueous NH4Cl (sat. aq) was added to the reaction mixture. The mixture was extracted with DCM, and the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (short pad of silica gel, PE/EtOAc 80:1 to 60:1) gave recovered ketone (*S*)-**4** followed (40 :1) by the separated aldol adduct **24a** as a colourless oil (59 mg, 39%) and its epimer **24b** (77 mg, 51%). **24a** had $[\alpha]_D^{20}$ +1.5 (*c* 0.82, $CHCl_3$); **IR** (Thin Film) 3509, 2938, 2864, 1712, 1613, 1513, 1460, 1376, 1302, 1248, 1097, 1066, 821, 731 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (4H, m, Ar<u>H</u>$_{Ph}$), 7.22 (1H, m, Ar<u>H</u>$_{Ph}$), 7.18 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>$_{PMB}$), 6.85 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>$_{PMB}$), 4.90 (2H, s, C<u>H</u>$_2$Ph), 4.36 (2H, ABq, *J* = 11.2 Hz, C<u>H</u>$_2$Ar$_{PMB}$), 4.22 (1H, dt, J_1 = 3.2, J_2 = 9.0 Hz, H7), 3.82 (1H, m, H5), 3.78 (3H, s, ArOC<u>H</u>$_3$), 3.60 (1H, t, *J* = 9.0 Hz, H1), 3.43 (1H, dd, J_1 = 4.8, J_2 = 8.5 Hz, H1'), 3.17-3.08 (1H, m, H2), 2.92 (1H, d, *J* = 3.0 Hz, OH), 2.70 (1H, qd, J_1 = 1.7, J_2 = 7.0 Hz, H4), 1.90 (1H, m, H6), 1.47-1.26 (2H, m, H8), 1.09 (14H, s, Si(<u>^{i}Pr</u>)$_2$), 1.00 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.95 (3H, t, *J* = 7.3 Hz, CH$_2$C<u>H</u>$_3$), 0.94 (3H, d, *J* = 7.0 Hz, CHC<u>H</u>$_3$), 0.74 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 218.1, 159.3, 141.4, 129.6, 129.3, 128.1, 126.7, 125.7, 113.8, 74.1, 73.2, 73.1, 71.1, 64.3, 55.2, 48.5, 44.2, 40.9, 23.7, 17.6 (x3), 17.5, 13.7, 12.6, 12.3, 11.1, 9.9, 7.0; **m/z** (CI^+, NH_3) 573 (100%, MH^+), 294 (55), 256 (100), 246 (80); **HRMS** (ES^+) Calcd for $C_{33}H_{47}O_6Si$ (MH^+) 573.3611 Found 573.3607.

(2*S*, 4*R*, 5*S*, 6*R*, 7*R*)-7-(Benzyloxy-diisopropyl-silanyloxy)-5-hydroxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-3-one: <u>solution model 24b</u>.



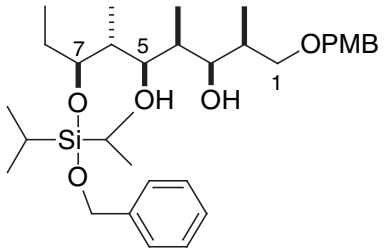
Diastereoisomer **24b** was obtained as a colourless oil from the previous procedure (77 mg, 51%); $[\alpha]_D^{20}$ -12.0 (*c* 0.54, $CHCl_3$); **IR** (Thin Film) 3491, 2939, 2865, 1712, 1613, 1513, 1462, 1376, 1302, 1248, 1098, 828, 732 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32 (4H, m, Ar$\underline{H}_{Ph}$), 7.23 (1H, m, Ar$\underline{H}_{Ph}$), 7.18 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 6.84 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.87 (2H, s, C$\underline{H}_2$Ph), 4.35 (2H, ABq, *J* = 11.7 Hz, C$\underline{H}_2$Ar$_{PMB}$), 4.26 (1H, t, *J* = 6.9 Hz, H7), 4.17 (1H, m, H5), 3.78 (3H, s, ArOC$\underline{H}_3$), 3.57 (1H, t, *J* = 8.7 Hz, H1), 3.39 (1H, d, *J* = 2.9 Hz, OH), 3.31 (1H, dd, J_1 = 5.3, J_2 = 8.6 Hz, H1'), 3.11 (1H, m, H2), 2.72 (1H, m, H4), 1.66 (2H, m, H6+H8), 1.60-1.53 (1H, m, H8), 1.07 (17H, s, CH_3+Si($^i\underline{Pr}$)$_2$), 0.97 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$), 0.84 (3H, t, *J* = 7.4 Hz, $CH_2C\underline{H}_3$), 0.78 (3H, d, *J* = 7.0 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 217.0, 159.2, 141.1, 129.7, 129.2, 128.2, 126.8, 125.9, 125.7, 113.8, 73.7, 73.0, 72.5, 70.8, 64.5, 55.2, 48.5, 43.6, 38.3, 27.5, 17.6 (x2), 14.0, 12.6, 12.5, 10.4, 9.2, 7.4; **m/z** (CI^+, NH_3) 573 (100%, MH^+), 293 (55), 256 (100); **HRMS** (ES^+) Calcd for $C_{33}H_{47}O_6Si$ (MH^+) 573.3611 Found 573.3607.

(2*S*, 4*R*, 5*S*, 6*R*, 7*RS*)-7-(Diisopropyl-silanyloxy-methoxypolystyrene)-5-hydroxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-3-one: <u>resin 25.</u>



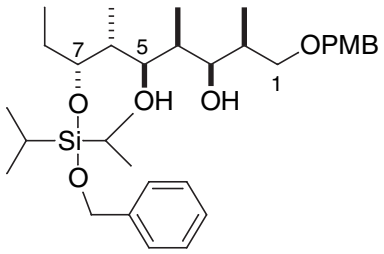
To a solution of Ti(O^iPr)$_4$ (294 µl, 0.994 mmol) in dry DCM (2 mL) was added $TiCl_4$ (1M in DCM freshly prepared, 0.994 mmol) at 0°C. After stirring for 5 min at 0°C under Ar, the mixture was added *via* cannula to a solution of ketone (*S*)-**4** (228 mg, 0.966 mmol) in dry DCM (0.7 mL) at -78°C. After stirring for 5 min, $^iPr_2NEt$ was added and the resulting orange mixture was left stirring at -78°C for 1 h for complete enolization. The enolate solution was then transferred *via* cannula to the swollen resin **3** in dry DCM (2 mL) at -78°C and the mixture was shaken for 5 h at the same temperature for complete conversion. The enolate solution was filtered off and the resin was washed in turn with DCM (3x), THF/H_2O, THF, MeOH, DCM, then dried under reduced pressure for 3 h at 60°C. This gave the pale yellow resin **25** (230 mg); **IR** (Single Bead) 3463, 3028, 2924, 2867, 1703, 1604, 1586, 1514, 1494, 1454, 1375, 1303, 1249, 1225, 1093, 1032, 821, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, $CDCl_3$), δ 218.0, 217.0, 159.2, 129.2, 125.8, 113.8, 74.1, 73.2, 72.6, 71.2, 70.9, 64.3, 55.2, 48.5, 44.2, 43.6, 38.4, 27.4, 23.8, 17.7, 15.2, 14.1, 13.8, 13.4, 12.5, 11.2, 10.5, 10.0, 9.3, 7.5, 7.2.

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*S*)-7-(Benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol: <u>solution model 26a</u>.



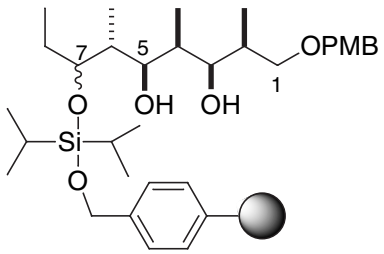
To a stirred solution of β-hydroxy ketone **24a** (12 mg, 0.019 mmol) in dry DCM was added a freshly prepared solution of $Zn(BH_4)_2$ (274 µl, 0.057 mmol, 0.21 M in Et_2O) at –78°C. The mixture was then allowed to warm up to –30°C and stirred for 2 h under argon before adding a mixture of MeOH/pH 7 buffer (1:1, v:v) at –30°C. After warming-up to RT, the solution was extracted with DCM, and the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Preparative TLC (silica gel plates, hexane/EA 3:1) afforded diol **26a** as a colourless oil (10 mg, 91%). Sometimes a small amount of diol was still complexed with Zn salts; stirring with silica gel in EtOAc for 5 h led to to decomplexation and recovery of further material; $[\alpha]_D^{20}$ +2.5 (*c* 0.27, $CHCl_3$); **IR** ($CHCl_3$) 3458, 3016, 2967, 2868, 1612, 1513, 1463, 1383, 1248, 1066, 829 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (4H, m, Ar<u>H</u>$_{Ph}$), 7.26-7.21 (3H, m+d, *J* = 8.6 Hz, Ar<u>H</u>$_{Ph}$), 6.86 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>$_{PMB}$), 4.90 (2H, s, C<u>H</u>$_2$Ph), 4.40 (2H, ABq, *J* = 11.7 Hz, C<u>H</u>$_2$Ar$_{PMB}$), 4.03 (1H, m, H7), 3.80 (3H, s, ArOC<u>H</u>$_3$), 3.68 (1H, dd, J_1 = 3.1, J_2 = 6.5 Hz, H3), 3.62 (2H, m, H5+OH), 3.47 (1H, s, OH), 3.37 (2H, d, *J* = 4.9 Hz, H1), 1.92 (1H, m, H2), 1.84 (1H, m, H6), 1.73 (1H, m, H4), 1.63 (1H, m, H8); 1.53 (1H, m, H8'); 1.10 (14H, m, Si(<u>^{i}Pr</u>)$_2$), 1.04 (3H, d, *J* = 6.8 Hz, CHC<u>H</u>$_3$), 0.94 (3H, t, *J* = 7.3 Hz, CH$_2$C<u>H</u>$_3$), 0.87 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$), 0.72 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.1, 140.8, 130.4, 129.0, 128.2, 126.9, 125.7, 113.7, 79.1, 79.0, 77.7, 73.4, 72.8, 64.6, 55.2, 40.1, 36.5, 36.1, 26.4, 17.5 (x2), 17.4, 13.4, 12.6, 12.5, 12.4, 9.1, 5.4; **m/z** (CI^+, NH_3) 575 (20%), 467 (100); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH+) 575.3768 Found 575.3778.

(2S, 3R, 4S, 5R, 6R, 7R)-7-(Benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol: solution model 26b.



To a stirred solution of β-hydroxy ketone **24b** (10.8 mg, 0.018 mmol) in dry DCM was added a freshly prepared solution of $Zn(BH_4)_2$ (270 µl, 0.056 mmol, 0.21 M in Et_2O) at –78°C. The mixture was then allowed to warm-up to –30°C and stirred for 2h under argon before addition of a mixture of MeOH/pH 7 buffer (1:1, v:v) at –30°C. After warming to RT, the solution was extracted with DCM, and the combined organic layers were dried (Na_2SO_4) and evaporatied in vacuo. Flash chromatgraphy (silica gel, PE/diethyl ether 6:1) afforded diol **26b** as a colourless oil (8.7 mg, 88%); $[\alpha]_D^{20}$ +10.5 (c 0.17, CHCl3); **IR** (CHCl3) 3439, 2987, 2867, 1612, 1513, 1463, 1381, 1248, 1090, 1046, 826 cm-1; **^{1}H NMR** (400 MHz, CDCl3) d 7.34 (4H, m, ArHPh), 7.27-7.21 (3H, m+d, J = 8.6 Hz, ArHPh), 6.86 (2H, d, J = 8.6 Hz, ArHPMB), 4.87 (2H, s, CH2Ph), 4.41 (2H, ABq, J = 11.6 Hz, C$\underline{H}_2$Ar$_{PMB}$), 4.35 (1H, brs, OH), 4.04 (1H, td, J_1 = 2.1, J_2 = 6.7 Hz, H7), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.76-3.70 (2H, m, H5+OH); 3.66 (1H, dd, J_1 = 3.0, J_2 = 6.5 Hz, H3), 3.37 (2H, d, J = 4.9 Hz, H1), 1.92 (1H, m, H2), 1.82 (1H, m, H6), 1.72 (1H, m, H4), 1.61 (2H, m, H8); 1.09 (14H, m, Si($^i\underline{Pr}$)$_2$), 1.05 (3H, d, J = 6.8 Hz, CHC$\underline{H}_3$), 0.91 (3H, t, J = 7.5 Hz, CH$_2$C$\underline{H}_3$), 0.87 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$), 0.67 (3H, d, J = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.0, 139.9, 130.5, 129.0, 128.4, 127.4, 126.3, 113.7, 78.8, 74.0, 72.9, 65.2, 55.2, 39.0, 36.3, 35.9, 25.8, 17.3 (x3), 13.4, 12.3 (x3), 10.9, 10.8, 5.7; **m/z** (CI^+, NH_3) 575 (15), 485 (10), 467 (100); **HRMS** (ES^+) Calcd for $C_{35}H_{57}O_7Si$ (MH^+) 575.3768 Found 575.3763.

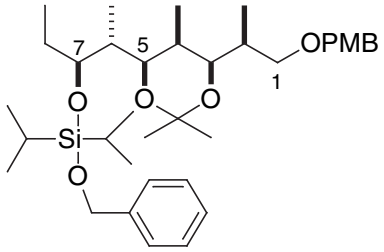
(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*RS*)-7-(Diisopropyl-silanyloxy-methoxypolystyrene)-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonane-3,5-diol : <u>resin 27</u>.



To resin **24** (232 mg, 0162 mmol), swollen in dry DCM (1 mL), was added a freshly prepared solution of $Zn(BH_4)_2$ (3.8 mL, 0.812 mmol, 0.21 M in Et_2O) at –78°C. After shaking for 1 h and 3 h at –30°C, the solution was filtered off and the resin was treated carefully with a solution of Rochelle's salt. Shaking was continued with a mixture of Rochelle's salt and DMF

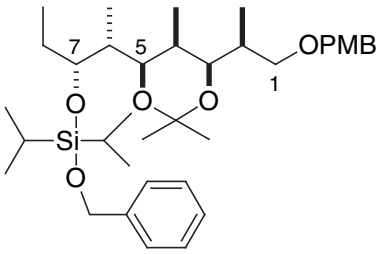
(1:1, 2 mL) overnight. The solution was then filtered off, and the resin was washed in turn with H_2O, THF/H_2O, THF, MeOH and DCM; then dried under high vacuum for 3 h at 60°C. This gave resin **27** (240 mg). **IR** (Single Bead) 3433, 3028, 2925, 1604, 1514, 1494, 1454, 1390, 1249, 1119, 820, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, $CDCl_3$), δ 159.2, 129.1, 113.8, 79.1, 78.7, 73.9, 72.9, 65.1, 55.2, 36.2, 26.5, 25.6, 17.5, 13.5, 12.5, 11.4, 11.0, 9.1, 5.8.

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*S*)-3,5-Isopropylidendioxy-7-(benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>solution model 31a</u>.



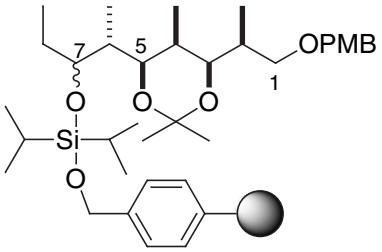
To a stirred solution of diol **27a** (23 mg, 0.040 mmol) in dry DMF (1 mL) at 0°C was added 2-methoxypropene (freshly distilled, 192 µl, 2.00 mmol) followed by CSA (1 mg, cat). The solution was stirred for 90 min at 0°C under Ar. After termination of the reaction by addition of solid Na_2CO_3, the mixture was evaporated 3 times with toluene then absorbed onto silica gel and purified by flash chromatography (PE/Et_2O 20/1) to give acetonide **31a** as a colourless oil (19.6 mg, 80%). **$[\alpha]_D^{20}$** -8.0 (*c* 0.20, $CHCl_3$); **IR** ($CHCl_3$) 2938, 2866, 2359, 1611, 1513, 1466, 1380, 1248, 1172, 1091, 1062, 1010 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (4H, m, Ar<u>H</u>$_{Ph}$), 7.23 (3H, m+d, *J* = 8.7 Hz, Ar<u>H</u>$_{Ph}$), 6.87 (2H, d, *J* = 8.7 Hz, Ar<u>H</u>$_{PMB}$), 4.90 (2H, s, C<u>H</u>$_2$Ph), 4.40 (2H, ABq, *J* = 11.8 Hz, C<u>H</u>$_2$Ar$_{PMB}$), 4.17 (1H, dt, J_1 = 3.1, J_2 = 8.9 Hz, H7), 3.80 (3H, s, ArOC<u>H</u>$_3$), 3.57 (1H, dd, J_1 = 1.8, J_2 = 9.5 Hz, H3), 3.50 (1H, dd, J_1 = 1.9, J_2 = 10.3 Hz, H5), 3.29 (2H, m, H1), 1.95 (1H, m, H2), 1.83 (1H, m, H4), 1.45-1.29 (3H, m, H6+H8), 1.31 (6H, s, CC<u>H</u>$_3$), 1.09 (14H, m, Si(^{i}<u>Pr</u>)$_2$), 1.02 (3H, d, *J* = 6.6 Hz, CHC<u>H</u>$_3$), 0.95 (3H, t, *J* = 7.3 Hz, CH$_2$C<u>H</u>$_3$), 0.73 (3H, d, *J* = 7.0 Hz, CHC<u>H</u>$_3$), 0.73 (3H, d, *J* = 6.7 Hz, CHC<u>H</u>$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 59.1, 141.5, 130.6, 129.1, 128.0, 126.6, 125.7, 113.7, 98.5, 76.3, 74.6, 73.5, 72.8, 71.2, 64.3, 55.2, 40.3, 35.0, 31.0, 29.8, 23.7, 19.4, 17.6, 17.5 (x3), 14.8, 12.6, 12.5, 11.5, 8.4, 4.8; **m/z** (CI^+, NH_3) 632 (10%), 615 (52), 366 (50), 319 (100); HRMS (ES^+) Calcd for $C_{36}H_{59}O_6Si$ (MH^+) 615.4081 Found 615.4091.

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*R*)-3,5-Isopropylidendioxy-7-(benzyloxy-diisopropyl-silanyloxy)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>solution model 31b</u>.



To a stirred solution of diol **27b** (24 mg, 0.0418 mmol) in dichloromethane (1.5 mL) at 0˚C was added 2,2-dimethoxypropane (155 µl, 1.25 mmol) followed by PPTS (2 mg, cat.). The solution was allowed to warm to RT and stirred for 17 h. After termination of the reaction by addition of solid $NaHCO_3$, the mixture was absorbed on to silica gel and purified by flash chromatography (PE/Et_2O 20/1) to give the acetonide **31b** as a colourless oil (21 mg, 82%); $[\alpha]_D^{20}$ -5.6˚ (*c* 0.32, $CHCl_3$); **IR** ($CHCl_3$) 2941, 2867, 2359, 1513, 1463, 1379, 1248, 1088, 1066, 1033, 883 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$), δ 7.32 (4H, m, Ar<u>H</u>$_{Ph}$), 7.23 (3H, m+d, *J* = 8.6 Hz, Ar<u>H</u>$_{Ph}$), 6.87 (2H, d, *J* = 8.6 Hz, Ar<u>H</u>$_{PMB}$), 4.86 (2H, s, C<u>H</u>$_2$Ph), 4.41 (2H, ABq, *J* = 11.7 Hz, C<u>H</u>$_2$Ar$_{PMB}$), 4.16 (1H, dd, J_1 = 5.2, J_2 = 8.3 Hz, H7), 3.80 (3H, s, OC<u>H</u>$_3$), 3.73 (1H, dd, J_1 = 1.9, J_2 = 9.8 Hz, H5), 3.50 (1H, dd, J_1 = 1.7, J_2 = 9.5 Hz, H3), 3.32 (1H, dd, J_1 = 4.2, J_2 = 9.3 Hz, H1), 3.28 (1H, dd, J_1 = 5.5, J_2 = 9.3 Hz, H1'), 1.84 (1H, m, H2), 1.66 (1H, m, H8), 1.59-1.51 (2H, m, H6+H8), 1.43 (1H, m, H4), 1.33 (3H, s, CC<u>H</u>$_3$), 1.32 (3H, s, CC<u>H</u>$_3$), 1.08 (14H, m, Si(<u>i</u>Pr)$_2$), 1.01 (3H, d, *J* = 6.6 Hz, CHC<u>H</u>$_3$), 0.80 (6H, m, CHC<u>H</u>$_3$+CH$_2$C<u>H</u>$_3$), 0.72 (3H, d, *J* = 6.9 Hz, CHC<u>H</u>$_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.1, 141.3, 130.6, 129.0, 128.1, 126.7, 125.8, 113.7, 98.8, 76.2, 73.4, 72.7, 72.3, 71.2, 64.3, 55.2, 37.3, 34.9, 31.1, 30.1, 28.3, 20.1, 17.9, 17.8 (x2), 17.7, 14.8, 12.9, 12.8, 10.2, 6.9, 4.9; **m/z** (CI^+, NH_3) 615 (100%, MH^+), 557 (35), 539 (38), 419 (38); **HRMS** (ES^+) Calcd for $C_{36}H_{59}O_6Si$ (MH^+) 615.4081 Found 615.4074.

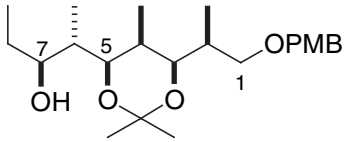
(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*RS*)-3,5-Isopropylidendioxy-7-(diisopropyl-silanyloxy-methoxypolystyrene)-1-(4-methoxy-benzyloxy)-2,4,6-trimethylnonane: <u>resin 29</u>.



To resin **27** (177 mg, 0.106 mmol), swollen in dry DMF, were added 2-methoxypropene (610 µl, 457 mmol) and CSA (2 mg) at 0°C. After shaking at room temperature for 40 h, the solution was filtered off and the resin was washed in turn with DCM, THF, MeOH and DCM, then dried under high vacuum for 3 h at 60°C. This afforded resin **29** (180 mg); **IR** (Single Bead) 3031, 2928, 1605, 1514, 1494, 1456, 1380, 1249, 1076, 1031, 821, 758 cm^{-1}; **^{13}C NMR** (100.6 MHz, $CDCl_3$), δ 159.1, 129.1, 113.8, 98.6, 76.3, 74.7, 73.8, 73.5, 72.8, 71.3, 68.0, 55.2,

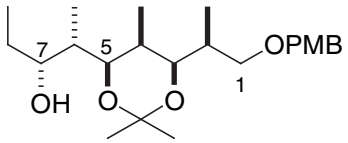
37.3, 35.1, 31.1, 30.0, 28.3, 23.9, 20.1, 19.6, 17.8, 14.9, 13.0, 12.7, 10.4, 8.6, 7.0, 5.0.

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*S*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-ol: solution model 30a.



To a solution of silyl ether **31a** (17 mg, 0.027 mmol) in THF (1 mL) was added a solution of TBAF (68 µl, 1M in THF). After stirring for 1 h at RT, aqueous NH4Cl (aq sat) was added and the solution was extracted with EtOAc. The combined organic layers were dried (Na_2SO_4), and evaporated *in vacuo*. Flash chromatography (silica gel, gradient PE/Et_2O 3:1) gave the alcohol **30a** as a colourless oil (10 mg, 82%). $\mathbf{[\alpha]_D^{20}}$ -1.8 (*c* 0.16, $CHCl_3$); **IR** ($CHCl_3$) 3541, 2936, 1612, 1513, 1463, 1382, 1248, 1178, 1035, 1011, 976 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.22 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 6.87 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.40 (2H, ABq, *J* = 11.8 Hz, C$\underline{H}_2Ar_{PMB}$), 4.25 (1H, s, OH), 3.80 (3H, s, OC$\underline{H}_3$), 3.74 (1H, dd, J_1 = 1.8, J_2 = 9.6 Hz, H5), 3.64 (1H, dd, J_1 = 1.8, J_2 = 9.4 Hz, H3), 3.51 (1H, m, H7), 3.31 (2H, m, H1), 1.85 (1H, m, H2), 1.69 (2H, m, H4+H8), 1.44 (3H, s, CC$\underline{H}_3$), 1.39 (3H, s, CC$\underline{H}_3$), 1.42-1.33 (1H, m, H8), 1.03 (3H, d, *J* = 6.6 Hz, CHC$\underline{H}_3$), 0.97 (3H, t, *J* = 7.3 Hz, $CH_2C\underline{H}_3$), 0.84 (3H, d, *J* = 7.4 Hz, CHC$\underline{H}_3$), 0.69 (3H, d, *J* = 6.9 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.1, 130.5, 129.1, 113.7, 99.1, 80.0, 76.1, 72.8, 71.1, 55.2, 38.9, 35.0, 31.2, 29.9, 26.9, 19.7, 14.7, 11.1, 9.2, 5.1; **m/z** (CI^+, NH_3) 395 (100%, MH^+), 358 (25), 337 (70), 319 (20), 257 (38), 154 (50), 138 (48), 121 (100); **HRMS** (ES^+) Calcd for $C_{23}H_{39}O_5$ (MH^+) 395.2797 Found 395.2786.

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*, 7*R*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-ol: solution model 30b.



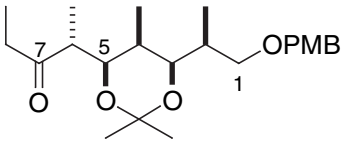
To a solution of silyl ether **31b** (19 mg, 0.031 mmol) in acetonitrile (1 mL) in a polypropylene bottle was added a solution of HF/pyridine in pyridine (0.5 mL, 8.3M in pyridine) at 0˚C. The solution was allowed to reach RT. After stirring for 3 h, $NaHCO_3$ solution (aq sat) was added. Following extraction with EtOAc, the combined organic layers were dried (Na_2SO_4) and evaporated *in vacuo*. Flash chromatography (silica gel, gradient PE/Et_2O 3:1) gave alcohol **30b** as a colourless oil (10 mg, 82%). $\mathbf{[\alpha]_D^{20}}$ +15.1 (*c* 0.22, $CHCl_3$); **IR** ($CHCl_3$) 3496, 2937, 2876, 1611, 1513, 1463, 1381, 1248, 1173, 1108, 1011, 977 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.23 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 6.87 (2H, d, *J* = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.40 (2H, ABq, *J* = 11.8 Hz, C$\underline{H}_2Ar_{PMB}$), 3.83 (1H, dd, dd, J_1 = 1.8, J_2 = 10.2 Hz, H5), 3.81 (3H, s, ArOC$\underline{H}_3$), 3.64 (1H,

dd, J_1 = 1.7, J_2 = 9.5 Hz, H3), 3.48 (1H, m, H7); 3.31 (2H, d, J = 4.6 Hz, H1), 2.61 (1H, d, J = 8.6 Hz, OH), 1.92 (1H, m, H6), 1.85 (1H, m, H2), 1.49-1.34 (3H, m, H4+H8), 1.42 (3H, s, CC$\underline{H}_3$), 1.38 (3H, s, CC$\underline{H}_3$), 1.02 (3H, d, J = 6.7 Hz, CHC$\underline{H}_3$), 1.01 (3H, t, J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.84 (3H, d, J = 6.7 Hz, CHC$\underline{H}_3$), 0.72 (3H, d, J = 7.1 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 159.1, 130.5, 129.1, 113.7, 107.0, 98.9, 80.0, 76.3, 76.2, 75.6, 72.8, 71.1, 55.2, 38.6, 35.0, 31.1, 29.9, 25.6, 19.6, 14.7, 11.4, 11.0, 5.0; **m/z** (CI^+, NH_3) 395 (100%, MH^+), 337 (30), 275 (38), 257 (48), 178 (50), 154 (48); **HRMS** (ES^+) Calcd for $C_{23}H_{39}O_5$ (MH^+) 395.2797 Found 395.2792.

Cleavage of 30a and 30b from resin 29

To resin **30** (133 mg, 0.08 mmol, maximum loading 0.6 mmol) swollen in dry THF was added a 1 M solution of TBAF in THF (400µl, 0.4 mmol) at RT under Ar. After stirring overnight at RT, the solution was filtered off and quenched by aqueous NH_4Cl (aq, sat), and stirring was continued for 30 min. The resin was washed with DCM, H_2O, THF/H_2O, DCM then dried under reduced pressure at 50°C. This gave 100 mg of resin and 9.7 mg of an inseparable mixture of epimeric alcohols **30a** and **30b**, which were oxidized together to prduce ketone **6** following the Dess-Martin procedure in order to determine the overall diastereoselectivity (24% overall yield for 6 steps on solid support, loading 0.25 mmol/g, 90% ds by NMR).

(2*S*, 3*R*, 4*S*, 5*R*, 6*R*)-3,5-Isopropylidendioxy-1-(4-methoxy-benzyloxy)-2,4,6-trimethyl-nonan-7-one, 6.



To a solution of alcohols **30** (10 mg, 0.025 mmol) in dichloromethane (1 mL) was added pyridine (12 µl, 0.15 mmol) then Dess-Martin periodinane (32 mg, 0.076 mmol) at RT. After stirring for 90 min, hexane was added and the mixture was absorbed on to silica gel and purified by flash chromatography (silica gel, hexane/EtOAc 9:1) to give ketone **6** as a colourless oil (9.5 mg, 94%); **$[\alpha]_D^{20}$** -21.0 (*c* 0.4, $CHCl_3$); **IR** (Thin film), 2969, 2878, 1715, 1613, 1513, 1456, 1378, 1248, 1201, 1183, 1092, 1037, 1012, 981 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ 7.22 (2H, d, J = 8.6 Hz, Ar$\underline{H}_{PMB}$), 6.86 (2H, d, J = 8.6 Hz, Ar$\underline{H}_{PMB}$), 4.39 (2H, ABq, J = 11.8 Hz, $C\underline{H}_2Ar_{PMB}$), 3.92 (1H, dd, J_1 = 2.0, J_2 = 10.0 Hz, H5), 3.80 (3H, s, ArOC$\underline{H}_3$), 3.63 (1H, dd, J_1 = 1.8, J_2 = 9.5 Hz, H3), 3.30 (2H, d, J = 4.6 Hz, H1), 2.71 (1H, dq, J_1 = 7.0, J_2 = 10.0 Hz, H6), 2.51 (2H, dq, J_1 = 7.2, J_2 = 17.9 Hz, H8), 2.43 (2H, dq, J_1 = 7.2, J_2 = 17.9 Hz, H8'), 1.84 (1H, m, H2), 1.46 (1H, m, H4), 1.30 (3H, s, CC$\underline{H}_3$), 1.29 (3H, s, CC$\underline{H}_3$), 1.02 (3H, t, J = 7.2 Hz, $CH_2C\underline{H}_3$), 1.01 (3H, d, J = 6.6 Hz, CHC$\underline{H}_3$), 0.86 (3H, d, J = 7.0 Hz, CHC$\underline{H}_3$), 0.82 (3H, d, J = 6.7 Hz, CHC$\underline{H}_3$); **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 214.9, 159.1, 130.5, 129.1, 113.7, 98.8, 75.9, 75.8, 72.8, 71.1, 55.2, 46.9, 36.9, 35.0, 30.4, 29.7, 19.3, 14.7, 11.8, 7.4, 5.0; **m/z** (CI^+, NH_3) 410 (10%), 393 (100, MH^+), 335 (100), 317 (23), 273 (20), 248 (20), 215 (23); **HRMS** (ES^+) Calcd for $C_{23}H_{37}O_5$ (MH^+) 393.2641 Found 393.2638.

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2. Imamoto, T. ; Ono, M. *Chem. Lett.* **1987**, 501.
3. (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Dess, J. B. ; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.