Supplementary Material (ESI) for Chemical Communications

Supporting Information

Towards the Combinatorial Synthesis of Spongistatin Fragment Libraries by Asymmetric Aldol Reactions on Solid Support

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General Experimental

^{1}H nuclear magnetic resonance (^{1}H NMR) spectra were recorded using an internal deuterium lock for the indicated reference at ambient temperatures on the following instruments: Bruker DRX 500 Fourier Transform instrument (500 MHz), Bruker DRX 400 Fourier Transform instrument (400 MHz) and Bruker DPX 400 Fourier Transform instrument (400 MHz). Data are presented as follows: chemical shift (in ppm on the δ scale relative to δ_{TMS} = 0), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, spt = septet, m = multiplet, br = broad), coupling constant and assignment. Assignments were made either on the basis of unambiguous chemical shift or coupling pattern, COSY experiments or by comparison to fully interpreted spectra for enantiomeric, identical or related compounds. ^{13}C NMR spectra were recorded at 125.08 MHz on Bruker DRX 500 or 100.6 MHz on Bruker AM 400 using internal deuterium lock for the indicated reference at ambient probe temperatures on the above instruments, and are reported in ppm on the δ scale. The solvent peak was used as an internal reference δ_H =7.26 ppm and δ_C 77.0 was used for $CDCl_3$.

Infrared (IR) spectra were recorded on a Perkin-Elmer 1620 (FT-IR) spectrophotometer calibrated relative to polystyrene using 5 mm sodium chloride plates or a sodium chloride solution cell. Wavelengths of maximum absorbance (ν_{max}) are quoted in cm^{-1}.

High and low resolution mass spectra were acquired using positive chemical ionisation using NH_4^+ (+CI, NH_3) by the EPSRC National Mass Spectrometry Service Centre, Swansea, UK and the Departmental Mass Spectrometry Service, University Chemical Laboratory, Cambridge, using electron impact (EI), electrospray (+ESI), chemical ionisation (+CI) or fast atom bombardment (+FAB) ionisation techniques. The parent ion $[M]^+$ or $[M + H]^+$ or $[M + NH_4]^+$ or $[M + Na]^+$ is quoted.

Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium D line (589 nm) and are reported as follows: $[\alpha]_D$ concentration (*c* in g/100 ml) and solvent (all the rotations were measured at a temperature of 20 ˚C).

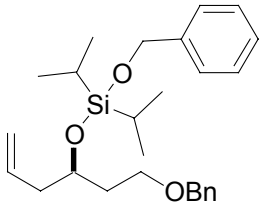
Analytical thin layer chromatography (t.l.c) was carried out on Merck Kieselgel 60 F_{254} plates with visualisation by ultraviolet, anisaldehyde, potassium permanganate and/or phosphomolybdic acid dips. Flash column chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) under a positive pressure by means of hand bellows or by means of compressed air line (the use of the term in this work also implies removal of the solvent *in vacuo* afterwards).

Reagents and solvents were purified by standard means. Dichloromethane, hexane, acetonitrile, toluene and methanol were distilled from calcium hydride and stored under an argon atmosphere; tetrahydrofuran and diethyl ether were distilled from sodium wire/benzophenone and subsequently stored under an argon atmosphere. Triethylamine, diisopropylethylamine, and 2,6-lutidine were distilled from and stored over calcium hydride. Triphenylphosphine and imidazole were recrystallised from distilled ethanol and subsequently stored under argon atmosphere. All other chemicals were used as received, except where otherwise quoted in the experimental text. Solvents used for extractions in work-up and flash column chromatography were distilled.

All experiments were performed under anhydrous conditions in an atmosphere of argon, except where stated, using oven-dried apparatus and employing standard techniques for handling air-sensitive materials.

Except stated otherwise all reactions on solid support were run in a fritted polypropylene syringe. The resin was washed three times with the dry reaction solvent before use. For mixing the resin commercial magnetic stir bars were used.

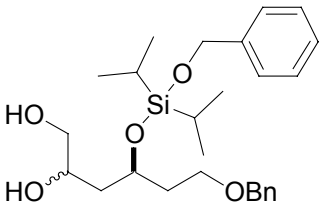
(1*R*)-BENZYLOXY-[1-(2-BENZYLOXY-ETHYL)-BUT-3-ENYLOXY]-DIISOPROPYL-SILANE (11B)



To a stirred solution of imidazole (4.94 g, 72.56 mmol, 5 equiv.) in dry DCM (20.0 mL) was added diisopropylsilyldichloride (2.62 mL, 14.52 mmol, 1 equiv.) and stirred for 5 min. A white solid was precipitating. Homoallylic alcohol **9**[1] (3.0 g, 14.54 mmol, 1 equiv.) in dry DCM (12.0 mL) was added to the solution and stirred 2 h at rt. Benzylalcohol (1.5 mL, 14.54 mmol, 1 equiv.) was added and the emulsion was stirred over night at rt. The reaction was quench with aqueous, sat. NH_4Cl (100 mL) and the aqueous phase was extracted with DCM (4 x 100 mL). The organic layers were combined and dried with Na_2SO_4. Purification by flash column chromatography (hexane) afforded the desired product **11b** (6.08 g, 5.79 mmol, 98%) as a colourless oil.

R_f 0.66 (20% EtOAc/hexane); **$[\alpha]_D$** -7.8 (*c* 1.11, $CHCl_3$); **IR** (thin film) 2944, 2866, 1641, 1496, 1463, 1454, 1376, 1306, 1250, 1207, 1095, 1067, 1028, 999, 914, 884, 809, 730, 695 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.21-7.36 (10H, m, ArH), 5.76-5.89 (1H, m, 5-CH), 5.02-5.06 (1H, m, -CH=C$\underline{H}_a$H$_b$), 4.98-5.02 (1H, m, -CH=CH$_a\underline{H}_b$), 4.87 (2H, s, -OCH$_2$Ph), 4.47, 4.42 (2H, AB$_q$, *J*= 11.8 Hz, -OCH$_2$Ph), 4.09-4.18 (1H, m, 3-CH), 3.51-3.61 (2H, m, 1-C$\underline{H}_a$H$_b$ and 1-CH$_a\underline{H}_b$), 2.27-2.33 (2H, m, 4-C$\underline{H}_a$H$_b$ and 4-CH$_a\underline{H}_b$), 1.73-1.90 (2H, m, 2-C$\underline{H}_a$H$_b$ and 2-CH$_a\underline{H}_b$), 1.06-1.08 (14H, m, iPr); **^{13}C NMR** δ (100 MHz, $CDCl_3$) 141.2, 138.6, 134.7, 128.3, 128.2, 127.6, 127.4, 126.8, 125.8, 117.1, 72.9, 69.3, 66.9, 64.4, 42.0, 36.5, 17.5, 17.5, 12.5, 12.5; **HRMS** (ES+) calcd. for $C_{26}H_{42}O_3SiN$ $[M+NH_4]^+$ 444.2934, found 444.2930.

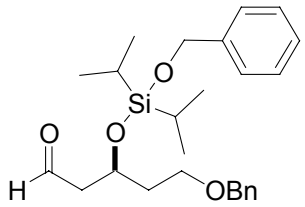
(2*RS*,4*S*)-6-BENZYLOXY-4-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-HEXANE-1,2-DIOL



Alkene **11b** (6.07 g, 14.23 mmol) in a 3:1 mixture of acetone (120 mL) and H_2O (40 mL) was treated with NMO (2.10 g, 17.93 mmol, 1.26 equiv.) followed by OsO_4 (2.5 wt. % in 2-methyl-2-propanol, 1.48 mL, 0.118 mmol, 0.8 mol%). The resultant mixture was left stirring at rt for 2 days. The reaction was quenched by the addition of 10% $Na_2S_2O_3$ (100 mL) and stirred for 30 mins. EtOAc (100 mL) was added, the layers were separated and the aqueous phase was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (gradient 10% to 60% EtOAc/petrol ether 40-60) to provide the title compound (5.02 g, 77%) as a viscous, colourless oil, consisting of both diastereomers in an approx. 1:1 ratio. The compound was used without further characterisation

[1] The synthesis of alcohol **9** has been described: Paterson, I.; Oballa, R. M.; Norcross, R. D. *Tetrahedron Lett.* **1996**, *37*, 8581.

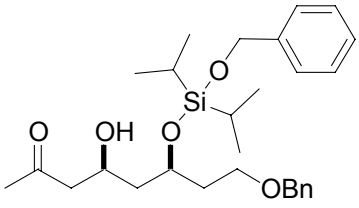
(3*S*)-5-BENZYLOXY-3-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-PENTANAL (8B)



To a cold (0°C) solution of diol (4.93 g, 10.69 mmol) in dry DCM (100 mL) Na_2CO_3 (2.63 g, 18.25 mmol, 2.3 equiv.) and $Pb(OAc)_4$ (5.75 g, 12.97 mmol, 1.2 equiv.) were added and stirred for 20 min until TLC showed complete conversion. The suspension was filtered through Celite® and toluene (100 mL) was added. The reaction was concentrated *in vacuo* and the residue was flash chromatographed (5% EtOAc/petrol ether 40-60) to yield the aldehyde **8b** (3.11 g, 65 %), as colourless oil.

R_f 0.47 (20% EtOAc/hexane); **$[\alpha]_D$** –2.5 (*c* 1.20, $CHCl_3$); **IR** (liquid film) 2945, 2893, 2866, 1725, 1496, 1463, 1454, 1377, 1251, 1207, 1094, 1066, 1027, 1013, 919, 884, 810, 731, 695 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 9.77-9.78 (1H, m, 5-C<u>H</u>O), 7.21-7.37 (10H, m, ArH), 4.87 (2H, s, -OCH_2Ph), 4.63 (1H, qn, *J*= 5.8 Hz, 3-CH), 4.47, 4.42 (2H, AB_q, *J*= 11.8 Hz, -OCH_2Ph), 3.51-3.60 (2H, m, 1-C<u>H$_a$</u>H$_b$ and 1-CH$_a$<u>H$_b$</u>), 2.54-2.68 (2H, m, 4-CH_2), 1.84-2.01 (2H, m, 2-C<u>H$_a$</u>H$_b$ and 2-CH$_a$<u>H$_b$</u>), 1.06-1.08 (14H, m, iPr); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 201.8, 140.8, 138.3, 128.3, 128.2, 127.6, 127.5, 127.0, 125.9, 72.9, 66.3, 65.9, 64.6, 50.9, 37.5, 17.4, 17.3, 12.4, 12.3; **HRMS** (ES+) calcd. for $C_{25}H_{40}O_4SiN$ $[M+NH_4]^+$ 446.2727, found 446.2730.

(4*S*,6*S*)-8-BENZYLOXY-6-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-4-HYDROXY-OCTAN-2-ONE (12B)

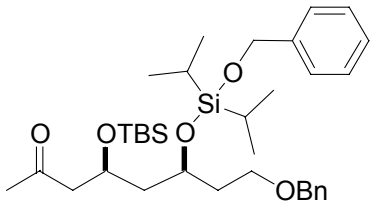


A round bottomed flask containing commercial (–)-Ipc_2BCl (1.12 g, 3.499 mmol, 1.5 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (33 mL) and the solution was cooled to 0 °C. Dry Et_3N (585 µL, 2.095 mmol, 1.8 equiv.) was added followed by dry acetone (377 µL, 5.134 mmol, 2.2 equiv., freshly distilled from $CaSO_4$). The resultant white suspension was stirred at 0 °C for 45 min and then cooled to -78 °C. A solution of the aldehyde **8b** (1.0 g, 2.333 mmol, 1.0 equiv.) in dry Et_2O (1 mL + 2 x 1 mL for washings) was added *via* cannula, and the suspension was stirred at -78 °C for 5 h and then -20 °C for 16 h. To the cold suspension was added pH 7 buffer (15 mL) and after warming to room temperature, the layers were separated. The aqueous phase was extracted with Et_2O (3 x 50 mL) and the combined organic extracts were concentrated *in vacuo*. The resultant residue was taken up in MeOH (18 mL) and pH 7 buffer (9 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (6 mL) was added and the mixture was warmed to rt and stirred for 2 h. Et_2O (50 mL) and H_2O (25 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (2 x 75 mL) and EtOAc (2 x 75 mL). The combined organic extracts were washed with brine (2 x 75 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil was flash chromatographed (gradient 10% to 30% EtOAc in hexane) to yield the 1,3-*syn* aldol adduct **12b** (954 mg, 84%).

R_f 0.10 (20% EtOAc in hexane); **$[\alpha]_D$** +8.4 (*c* 3.25 $CHCl_3$); **IR** (liquid film) 3467, 2866, 1710, 1496, 1454, 1377, 1361, 1094, 1067, 1027, 884, 810, 732, 696 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.21-7.36 (10H, m, ArH), 4.87 (2H,

s, -OC$\underline{H}_2$Ph), 4.48, 4.40 (2H, AB_q *J*= 11.8 Hz, -OC$\underline{H}_2$Ph), 4.32 (1H, qn, *J*= 5.9 Hz, 3-CH), 4.17-4.25 (1H, m, 5-CH), 3.55 (2H, t, *J*= 6.4 Hz, 1-CH_2), 3.27 (1H, d, *J*= 2.8 Hz, -OH), 2.48 (2H, d, *J*= 6.1 Hz, 6-CH_2), 2.08 (3H, s, 8-CH_3), 1.85-1.98 (2H, m, 2-CH_2), 1.54-1.76 (2H, m, 4-CH_2), 1.07 (14H, d, J= 2.1 Hz, iPr); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.2, 140.9, 138.4, 128. 3, 128.2, 127.6, 127.5, 126.9, 125.9, 73.0, 68.9, 66.7, 65.6, 64.6, 50.5, 43.2, 37.0, 30.6, 17.5, 17.4, 12.4, 12.4; **HRMS** (ES+) calcd. for $C_{28}H_{46}NO_5Si$ [M+NH_4^+] 504.3140, found 504.3145.

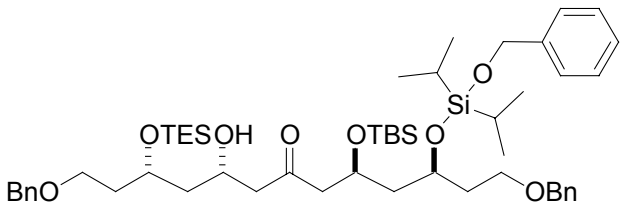
(4*S*,6*S*)-8-BENZYLOXY-6-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-4-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-OCTAN-2-ONE (6B)



To a cold (-78 °C), stirred solution of alcohol **12b** (0.4839 g, 0.994 mmol, 1.0 equiv.) in dry THF (10 mL) was added 2,6-lutidine (0.347 mL, 2.983 mmol, 3.0 equiv.) followed by TBSOTf (0.342 mL, 1.491 mmol, 1.5 equiv.). The resultant solution was stirred at -78 °C for 2 h and then EtOH (1 mL) was added to quench the excess TBSOTf. The reaction was allowed to warm to rt and then concentrated *in vacuo*. The residue was dissolved in Et_2O (20 mL) and saturated aqueous $NaHCO_3$ (10 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (4 x 20 mL). The combined organic extracts were washed with pH 7 buffer (2 x 15 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil (dr > 97 : 3) was flash chromatographed (10% Et_2O in hexane) to yield the 1,3-*syn* TBS-ether **6b** (0.5308 g, 89%), as colourless oils.

R$_f$ 0.42 (10% EE in hexane); **[α]$_D$** –0.3 (*c* 2.34, $CHCl_3$); **IR** (liquid film) 2929, 2864, 1718, 1463, 1455, 1360, 1253, 1095, 1066, 1027, 1004, 884, 834, 807, 776, 730, 695 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.20-7.35 (10H, m, ArH), 4.85 (2H, s, -OC$\underline{H}_2$Ph), 4.46, 4.43 (2H, AB_q, *J*= 12.1 Hz), 4.27 (1H, qn, *J*= 6.3 Hz, 5-CH), 4.20 (1H, qn, *J*= 6.3 Hz, 3-CH), 3.57 (2H, t, *J*= 6.5 Hz, 1-C$\underline{H}_a$H$_b$ and 1-CH$_a\underline{H}_b$), 2.51 (2H, dd, *J*= 6.0, 2.0 Hz, 6-C$\underline{H}_a$H$_b$ and 6-CH$_a\underline{H}_b$), 2.06 (3H, s, 8-CH_3), 1.58-1.95 (4H, m, 2-C$\underline{H}_a$H$_b$, 2-CH$_a\underline{H}_b$, 4-C$\underline{H}_a$H$_b$ and 4-CH$_a\underline{H}_b$), 1.07 (14H, m, iPr), 0.84 (9H, s, -OSiMe$_2$$^t\underline{Bu}$), 0.01, -0.04 (6H, s, s, -OSi$\underline{Me}_2$^{t}Bu); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 207.4, 141.1, 138.6, 128.2, 128.1, 127.6, 127.4, 126.8, 125.9, 72.9, 67.3, 66.7, 66.3, 64.5, 51.2, 45.1, 36.9, 31.4, 25.8, 17.9, 17.6, 17.5, 17.5, 17.5, 12.5, 12.5, -4.5, -4.6; **HRMS** (ES+) calcd. for $C_{34}H_{60}O_5Si_2N$ [M+NH_4^+] 618.40100, found 618.401035.

(3*S*,5*S*,9*S*,11S)-1,13-BIS-BENZYLOXY-3-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-5-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-9-HYDROXY-11-TRIETHYLSILANYLOXY-TRIDECAN-7-ONE (4B)

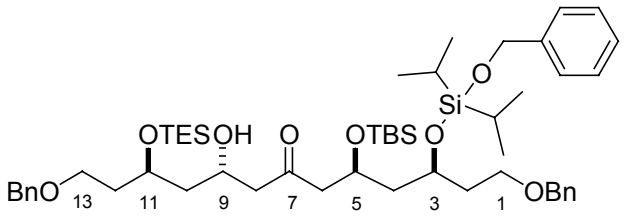


A round bottomed flask containing commercial (–)-Ipc$_2$BCl (398.6 mg, 1.24 mmol, 1.5 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (8 mL) and the solution was cooled

to 0 °C. Dry Et_3N (196 µL, 1.41 mmol, 1.7 equiv.) was added followed by a solution of the ketone **6b** (500 mg, 0.83 mmol, 1.0 equiv.) in dry Et_2O (2 mL + 2 x 1 mL for washings). The resultant white suspension was stirred at 0 °C for 1 h and then cooled to -78 °C. A solution of the aldehyde **7**[2] (414 mg, 1.29 mmol, 1.5 equiv.) in dry Et_2O (2 mL + 2 x 1 mL for washings) was added, *via* cannula, and the suspension was stirred at -78 °C for 6 h and over night at – 20 °C. The reaction was quenched by the addition of pH 7 buffer (6.3 mL) and stirred at room temperature for 10 min. Et_2O (21 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined organic extracts were concentrated *in vacuo*. The resultant residue was taken up in MeOH (12.7 mL) and pH 7 buffer (6.3 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (3.38 mL) was added and the mixture was warmed to rt and stirred for 2 h. Et_2O (21 mL) and H_2O (21 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 21 mL) and EtOAc (2 x 21 mL). The combined organic extracts were washed with $NaHCO_3$ (8.4 mL) and brine (8.4 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil was flash chromatographed (10% Et_2O in hexane) to yield 1,5-*anti*-aldol adducts **4b** (685 mg, 89%, dr > 97:3).

R_f 0.43 (20% EtOAc in hexane); **$[\alpha]_D$** +5.8 (*c* 0.90 $CHCl_3$); I**R (**liquid film) 3448, 2951, 2929, 2867, 1711, 1496, 1455, 1411, 1378, 1362, 1252, 1206, 1098, 1028, 1006, 885, 836, 808, 777, 733, 697 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.20-7.38 (15H, m, ArH), 4.85 (2H, s, -OCH_2Ph), 4.50, 4.42 (2H, AB_q, *J*= 11.8 Hz, -OCH_2Ph), 4.50, 4.42 (2H, AB_q, *J*= 13.8 Hz, -$OC\underline{H}_2$Ph), 4.29 (1H, qn, *J*= 5.9 Hz, 5-CH), 4.19 (1H, qn, *J*= 5.8 Hz, 3-CH), 4.06-4.22 (2H, m, 9-CH and 11-CH), 3.56, 3.53 (4H, t, *J*= 6.6 Hz, 1-CH_aH_b and 13-CH_aH_b), 3.37 (1H, d, *J*= 2.3 Hz, -OH), 2.52 (2H, m, 6-CH_2), 2.43-2.49 (2H, m, 8-CH_3), 1.70-1.96 (5H, m, 2-CH_aH_b, 4-$CH_a\underline{H}_b$, 12-CH_aH_b) 1.50-1.66 (3H, m, 4-$C\underline{H}_aH_b$, 10-CH_aH_b), 1.06 (14H, m, iPr), 0.95 (9H, t, *J*= 8.0 Hz, -$OSi(CH_2C\underline{H}_3)_3$), 0.83 (9H, s, -$OSiMe_2{}^t\underline{Bu}$), 0.61 (6H, q, *J*= 7.7 Hz, -$OSi(C\underline{H}_2CH_3)_3$), 0.04, 0.00 (6H, s, s, -$OSi\underline{Me}_2{}^tBu$); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209. 6, 141.1, 138.6, 138.5, 128.3, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 126.8, 125.9, 73.0, 72.9, 68.8, 67.3, 66.7, 66.7, 66.1, 65.8, 64.5, 51.5, 51.1, 45.2, 43.4, 37.2, 25.8, 17.9, 17.6, 17.6, 17.5, 17.5, 12.5, 12.5, 6.8, 5.0, -4.5, -4.6; **HRMS** (ES+) calcd. for $C_{52}H_{90}NO_8Si_3$ $[M+NH_4^+]$ 940.5969, found 940.5961.

(3*S*,5*S*,9*S*,11S)-1,13-BIS-BENZYLOXY-3-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-5-(TERT-BUTYL-DIMETHYL-SILANYLOXY)-9-HYDROXY-11-TRIETHYLSILANYLOXY-TRIDECAN-7-ONE (15B)

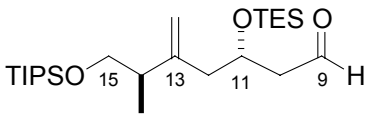


A round bottomed flask containing commercial (–)-Ipc_2BCl (79.7 mg, 0.25 mmol, 1.6 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (1.6 mL) and the solution was cooled to -78 °C. Dry Et_3N (54 µL, 0.39 mmol, 2.4 equiv.) was added followed by a solution of the ketone **12a** (97.3 mg, 0.16 mmol, 1.0 equiv.) in dry Et_2O (0.4 mL + 2 x 0.2 mL for washings). The resultant white suspension was stirred at 0 °C for 1 h and then cooled to -78 °C. A solution of the aldehyde *ent*-**7**[3] (82.8 mg, 0.40 mmol, 2.5 equiv.) in dry Et_2O (0.5 mL + 2 x 0.2 mL for washings) was added, *via* cannula, and the suspension was stirred at -78 °C for 6 h and over night at – 20 °C. The reaction was quenched by the addition of pH 7 buffer (1.5 mL) and stirred at room temperature for 10 min. Et_2O (10 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined organic extracts were concentrated *in vacuo*. The resultant residue was taken up in MeOH (2.5 mL) and pH 7 buffer (1.5 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (0.7 mL) was added and the mixture was warmed to rt and stirred for 2 h. Et_2O (10 mL) and H_2O (10 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 10 mL) and EtOAc (2 x 10 mL). The combined organic extracts were washed with $NaHCO_3$ (5 mL) and brine (5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil (dr 92:8) was flash chromatographed (10% EtOAc in hexane) to give the aldol adduct **15b** (85 mg, 66 %) as a colourless oil.

[2] Aldehyde **7** has been described earlier: Paterson, I.; Oballa, R. M.; Norcross, R. D. *Tetrahedron Lett.* **1996**, *37*, 8581.
[3] Aldehyde *ent*-**7** was obtained from alcohol **9** by Mitsunobu inversion, TES-protection and subsequent ozonolysis.

Rf 0.25 (10% EtOAc in hexane); **[α]D** +2.0 (*c* 2.85 CH_2Cl_2); I**R (**liquid film) 3452, 2967, 2969, 1734, 1534, 1289, 1156, 898 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.18-7.35 (15H, m, ArH), 4.86 (2H, s, -OCH_2Ph), 4.45 (4H, AB_q, *J*= 12.0 Hz, -OCH_2Ph, -OCH_2Ph), 4.10-4.32 (4H, m, 3-CH, 5-CH, 9-CH, 11-CH), 3.45-3.60 (4H, 1-CH_aH_b, 13-CH_aH_b), 2.35-2.55 (4H, m, 6-CH_2, 8-CH_2), 1.50-1.92 (8H, m, 2-CH_2, 4-CH_2, 10-CH_2,12-CH_2), 1.06 (14H, m, iPr), 0.96 (9H, t, *J*= 8.1 Hz, -OSi(CH_2C$\underline{H}_3$)$_3$), 0.80 (9H, s, -OSiMe$_2$$^t\underline{Bu}$), 0.58 (6H, q, *J*= 8.1 Hz, -OSi(C$\underline{H}_2$$CH_3$)$_3$), 0.04, -0.02 (6H, s, s, -OSi$\underline{Me}_2$^{t}Bu); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.6, 141.1, 138.6, 138.5, 128.4, 128.3, 128.2, 127.7, 127.6, 127.5, 127.4, 126.9, 125.9, 73.0, 73.0, 68.8, 67.7, 67.3, 66.8, 66.2, 65.9, 64.3, 51.6, 51.2, 45.2, 43.4, 37.2, 25.8, 17.9, 17.6, 17.6, 17.5, 17.5, 12.5, 12.5, 6.9, 5.0, -4.5, -4.6; **HRMS** (ES+) calcd. for $C_{52}H_{86}O_8Si_3Na$ [M+Na] 945.5528, found 945.5538.

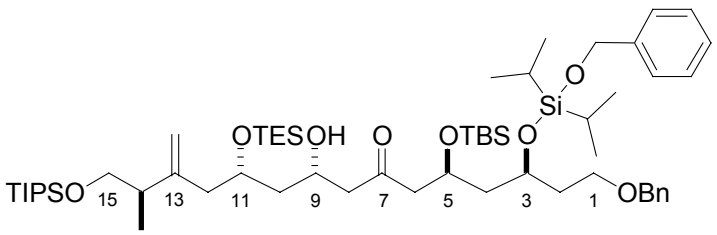
(3*S*)-5-[1-(TRIISOPROPYLSILOXY)-PROP-2-(*R*)-YL]-3-(TRIETHYLSILOXY)-HEX-5-ENAL (14)



To a suspension of Dess-Martin periodinane (99.7 mg, 0.235 mmol, 2 equiv.) in CH_2Cl_2 (560 µL) was added dry pyridine (95 µL, 1.17 mmol, 10 equiv.) at rt. The resultant mixture was stirred at rt for further 15 min before a solution of the corresponding alcohol[4] (52.3 mg, 0.118 mmol) in CH_2Cl_2 (186 µL + 2 x 186 µL washings) was added. The reaction was stirred at rt for further 30 min and purified by flash chromatography (gradient elution, 5:95 → 10:90 Et_2O/light petroleum) to afford aldehyde **14** (44 mg, 85%) as a colourless oil:

R_f 0.50 (10:90 Et_2O/hexane); **[α]D** +17.4 (*c* 2.14, $CHCl_3$); IR (liquid film) 1727, 1640, 1461 cm^{-1}; ^{1}H NMR δ (500 MHz, $CDCl_3$) 9.80 (1H, m, 9-C$\underline{H}$O), 4.88 (1H, s, C=C$\underline{H}_a\underline{H}_b$), 4.82 (1H, s, C=C$H_a\underline{H}_b$), 4.35-4.40 (1H, m, 11-C$\underline{H}$), 3.69 (1H, dd, *J* = 9.4, 5.9 Hz, 15-C$\underline{H}_a\underline{H}_b$), 3.50 (1H, dd, *J* = 9.4, 7.3 Hz, 15-C$H_a\underline{H}_b$), 2.60 (1H, ddd, *J* = 15.9, 4.0, 1.5 Hz, 10-C$\underline{H}_a\underline{H}_b$), 2.49 (1H, dd, *J* = 15.9, 6.9, 2.8 Hz, 10-C$H_a\underline{H}_b$), 2.40 (1H, dd, *J* = 14.0, 4.9 Hz, 12-C$\underline{H}_a\underline{H}_b$), 2.21-2.30 (2H, m, 12-C$H_a\underline{H}_b$ + 14-C$\underline{H}$), 1.04-1.12 (24H, m, 14-CHC$\underline{H}_3$ + Si(C$\underline{H}$(CH_3)$_2$)$_3$), 0.95 (9H, t, *J* = 7.9 Hz, Si(CH_2C$\underline{H}_3$)$_3$), 0.62 (6H, q, *J* = 7.9 Hz, Si(C$\underline{H}_2$$CH_3$)$_3$); ^{13}C NMR δ (62.5 MHz, $CDCl_3$) 202.0, 148.1, 112.2, 67.6, 67.3, 50.4, 44.2, 42.4, 18.0, 16.7, 12.0, 6.8, 4.9; HRMS (+FAB) calcd. for $C_{24}H_{49}O_3Si_2$ [M-H^+] 441.3220, found: 441.3216.

(*3S*,*5S*,*9S*,*11S*)-1-BENZYLOXY-3-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-5-(*TERT*-BUTYLDIMETHYLSILOXY)-9-HYDROXY-13-[1-(TRIISOPROPYLSILOXY)-PROP-2-(*R*)-YL]-11-(TRIETHYLSILOXY)-TETRADEC-13-EN-7-ONE (3B)



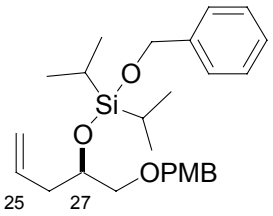
A round bottomed flask containing (-)-Ipc_2BCl (48.2 mg, 0.150 mmol, 1.5 equiv.) was placed under vacuum for 1 h to remove any traces of HCl. The flask was charged with argon and Et_2O (1.4 mL) was added. The solution was cooled to 0 ˚C and Et_3N (15.8 µL, 0.114 mmol, 1.7 equiv.) was added, followed by a solution of ketone **6b** (40.1 mg, 0.067

[4] The corresponding alcohol has been described by Paterson I.; Oballa R.M. *Tetrahedron Lett.* **1997**, 38, 8241.

mmol, 1 equiv.) in Et_2O (100 µL + 2 x 100 µL washings) *via* cannula. The reaction mixture was stirred for further 40 min at 0 ˚C then cooled to -78 ˚C before a solution of aldehyde **14** (44.4 g, 0.100 mmol, 1.5 equiv.) in Et_2O (100 µL + 2 x 100 µL washings) was added *via* cannula. The reaction was stirred at -78 ˚C for further 6 h then at -20 ˚C for 16 h. The reaction was quenched by the addition of pH7 buffer (1.6 mL) at 0 ˚C and allowed to warm to room temperature. H_2O (5 mL) was added, the layers were separated and the aqueous phase was extracted with Et_2O (3 x 5 mL). The combined organics were concentrated *in vacuo* and the resultant residue was taken up in MeOH (3.1 mL), pH7 buffer (1.6 mL) and cooled to 0 ˚C. A 30% solution of H_2O_2 (0.7 mL) was added and the mixture was warmed to rt and stirred for 2 h. Et_2O (10 mL) and H_2O (10 mL) were added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 10 mL) and EtOAc (2 x 10 mL). The combined organics were washed with brine (2 x 1 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (gradient elution, 0:% to 10% Et_2O/hexane) of the crude product (dr > 97:3) afforded the aldol product **3b** (59.1 mg, 85%) as a colourless oils:

R_f 0.60 (20:80 EtOAc/hexanes); $[\alpha]_D$ +10.1 (*c* 1.21, $CHCl_3$); IR (liquid film) 3514, 2943, 2866, 1710, 1463, 1412, 1382, 1363, 1252, 1207, 1095, 1068, 1028, 1012, 884, 836, 808, 777, 732, 696 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.20-7.35 (10H, m, ArH), 4.85 (2H, s, -OCH_2Ar), 4.85 (1H, s, C=CH_aH_b), 4.80 (1H, s, C=CH_aH_b), 4.46, 4.42 (2H, AB_q, *J* = 12.3 Hz, -OCH_2Ar), 4.29 (1H, qn, *J* = 5.9 Hz, 5-CH), 4.12-4.24 (2H, m, 3-CH and 11-CH), 4.03-4.12 (1H, m, 11-CH), 3.70 (1H, dd, *J* = 9.6, 5.4 Hz, 15-CH_aH_b), 3.57 (2H, t, *J*= 6.7 Hz, 1-CH_aH_b), 3.51 (1H, br. s, -OH), 3.47 (1H, dd, *J*= 9.5, 7.6 Hz, 15-CH_aH_b), 2.38-2.60 (4H, m, 6-CH_2 and 8-CH_2), 2.15-2.38 (3H, m, 12-CH_2 and 14-CH), 1.47-1.96 (6H, m, 2-CH_2, 4-CH_2 and 10-CH_2), 1.04-1.10 (38H, m, iPr and 14-C-Me and Si(CH(CH_3)$_2$)$_3$), 0.97 (9H, t, *J*=7.8 Hz, Si(CH_2CH_3)$_3$), 0.83 (9H, s, SiC(CH_3)$_3$), 0.59-0.68 (6H, m, Si(CH_2CH_3)$_3$), 0.04 (3H, s, OSiMe_2^{t}Bu), 0.00 (3H, s, OSiMe_2^{t}Bu); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.1, 148.3, 141.1, 138.6, 128.3, 128.2, 127.6, 127.4, 126.8, 125.9, 111.7, 72.9, 71.3, 67.7, 67.3 , 66.8, 66.5, 66.0, 64.5, 51.5, 51.3, 45.2, 44.2, 42.8, 42.5, 36.9, 25.8, 18.0, 17.9, 17. 6, 17.6, 17.5, 17.5, 16.7, 12.5, 12.5, 12.0, 6.8, 5.2, -4.6, -4.6; HRMS (ES+) calcd. for $C_{58}H_{110}NO_8Si_4$ [M+NH_4^+] 1060.7303, found: 1060.7311.

(4*R*)-5-(*P*-METHOXYBENZYLOXY)-4-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-1-PENTENE

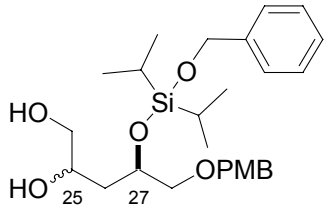


To a stirred solution of imidazole (3.82 g, 56.1 mmol, 5.0 equiv.) in dry CH_2Cl_2 (16.0 mL) was added diisopropylsilyldichloride (2.02 mL, 11.2 mmol, 1.0 equiv.) and stirred for 5 min. A white solid was precipitating. Homoallylic alcohol **16**[5] (2.5 g, 11.2 mmol, 1.0 equiv.) in dry DCM (6.0 mL) was added to the solution and stirred 2 h at rt. Benzylalcohol (1.2 mL, 11.2 mmol, 1 equiv.) was added and the emulsion was stirred for 36 h at rt. The reaction was quenched with aqueous, sat. NH_4Cl (80 mL) and the aqueous phase was extracted with DCM (4 x 50 mL). The organic layers were combined and dried with Na_2SO_4. Purification by flash column chromatography (gradient 0% to 5% EtOAc/hexane) afforded the desired product (4.66 g, 10.5 mmol, 94%) as a colourless oil.

R_f 0.60 (20% EtOAc/hexane); $[\alpha]_D$ +0.3 (*c* 1.56, $CHCl_3$); **IR** (thin film) 2943, 2865, 1641, 1612, 1587, 1513, 1497, 1463, 1365, 1302, 1247, 1207, 1172, 1097, 1066, 1038, 999, 916, 884, 820, 759, 731, 695 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.20-7.36 (5H, m, ArH), 7.22 (2H, d, *J*= 8.8 Hz, ArH), 6.85 (2H, d, *J*= 8.5 Hz, ArH), 5.78-5.91 (1H, m, 25-CH), 5.00-5.10 (2H, m, -CH=CH_aH_b and -CH=CH_aH_b), 4.86 (2H, s, -OCH_2Ph), 4.41 (2H, s, -OCH_2Ph), 4.12 (1H, qn, *J*= 5.5 Hz, 27-CH), 3.80 (3H, s, -OCH_3), 3.41 (2H, ddd, J= 16.0, 9.6, 5.6 Hz, 28-CH_2), 2.26-2.44 (2H, m, 26-CH_2), 1.08 (7H, m, iPr), 1.06 (7H, m, iPr); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 159.1, 141.3, 134.6, 130.5, 129.2, 128.1, 126.8, 125.8, 117.1, 113.7, 73.5, 72.9, 71.0, 64.4, 55.2, 39.2, 17.5, 17.5, 17.4, 17.4, 12.4, 12.4; **HRMS** (ES+) calc. for $C_{26}H_{42}NO_4Si$ [M+NH_4]$^+$ 460.2878, found 460.2874.

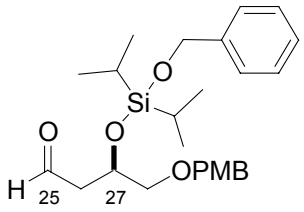
[5] Alcohol **16** has been described earlier by Paterson I.; Wallace D.J.; Gibson K.R. *Tetrahedron Lett.* **1997**, 38, 8911.

(2RS,4R)-5-(P-METHOXYBENZYLOXY)-4-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-PENTANE-1,2-DIOL



A solution of the above prepared alkene (9.42 g, 28.0 mmol) in 3:1 acetone (38 mL) and H_2O (13 mL) was treated with NMO (636 mg, 5.43 mmol, 1.2 equiv.) and OsO_4 (2.5 wt % in 2-methyl-propanol, 450 µL, 0.036 mmol, 0.85 mol%) and the resultant mixture was stirred over night at rt. The remaining oxidant was quenched by the addition of 10% $Na_2S_2O_3$ (50 mL) and the mixture stirred for 1 h before the addition of Et_2O (12.5 mL) and separation of the layers. The aqueous phase was extracted with EtOAc (3 x 12.5 mL), the combined organic extracts were washed with brine (12.5 mL) and the brine was back-extracted with EtOAc (5 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash chromatography (60:40 EtOAc/hexanes) afforded the title compound (1.76 g, 82%), as a colourless oil. The product was used without further characterization.

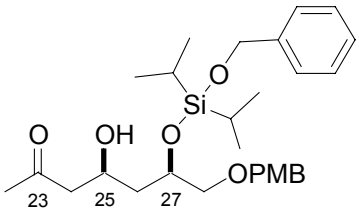
(3*R*)-4-(*P*-METHOXYBENZYLOXY)-3-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-BUTANAL)



To a solution of this diol (1.01 g, 2.123 mmol, 1equiv.) in MeOH (16 mL) and pH 7 buffer (6 mL) was added H_2O (0.8 mL) until all the solid had dissolved. The resultant solution was cooled to 0 ºC, $NaIO_4$ (546 mg, 2.55 mmol, 1.2 equiv.) added and the resultant mixture allowed to warm to rt overnight. The mixture was concentrated *in vacuo* and H_2O (23 mL) was added to dissolve the precipitate. The solution was extracted with Et_2O (3 x 8 mL), the combined organic extracts were washed with brine (5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash chromatography (gradient 0% to 5% EtOAc/petrol ether 40-60) afforded the desired aldehyde (922 mg, 97%) as a colourless oil:

R_f 0.41 (20% EtOAc/hexanes); **$[\alpha]_D$** +8.9 (*c* 1.21 $CHCl_3$); **IR** (liquid film) 2946, 2867, 1725, 1613, 1586, 1514, 1497, 1464, 1455, 1378, 1366, 1303, 1248, 1208, 1174, 1096, 1067, 1028, 920, 884, 820, 732, 696 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 9.77 (1H, t, *J* = 2.4 Hz, 25-C<u>H</u>O), 7.22-7.36 (5H, m, ArH), 7.19 (2H, d, *J*= 8.8 Hz, ArH), 6.85 (2H, d, *J*= 8.8 Hz, ArH), 4.84 (2H, s, -OCH_2Ph), 4.55 (1H, qn, *J* = 4.8 Hz, 27-CH), 4.39 (2H, s, OCH_2Ph), 3.80 (3H, s, -OCH_3), 3.53 (1H, dd, *J* = 9.5, 4.8 Hz, 28-C<u>H</u>$_a$H$_b$), 3.40 (1H, dd, *J* = 9.4, 6.4 Hz, 28-CH$_a$<u>H</u>$_b$), 2.63 (2H, dddd, *J*= 38.1, 16.0, 5.7, 2.3 Hz, 26-CH_2), 0.99-1.11 (14H, m, iPr); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 201.4, 159.2, 140.5, 129.9, 129.3, 128.2, 127.0, 125.8, 113.7, 73.4, 73.0, 67.2, 64.6, 55.2, 48.9, 17.4, 17.3, 12.3, 12.2 HRMS (ES+) calcd. for $C_{25}H_{40}NO_5Si$ $[M+NH_4]^+$ 462.2676, found 462.2670.

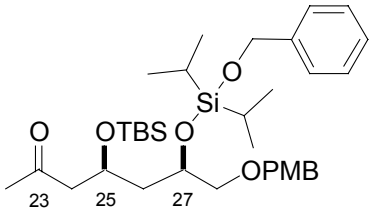
(4*S*,6*R*)-6-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-4-HYDROXY-7-(4-METHOXY-BENZYLOXY)-HEPTAN-2-ONE



A round bottomed flask containing commercial (–)-Ipc_2BCl (162 mg, 0.506 mmol, 1.5 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (5 mL) and the solution was cooled to 0 °C. Dry Et_3N (84.6 µL, 0.607 mmol, 1.8 equiv.) was added followed by dry acetone (54.5 µL, 0.742 mmol, 2.2 equiv., freshly distilled off of $CaSO_4$). The resultant white suspension was stirred at 0 °C for 1 h and then cooled to -78 °C. A solution of the above prepared aldehyde (154 mg, 0.345 mmol, 1.0 equiv.) in dry Et_2O (300 µL + 2 x 200 µL for washings) was added, *via* cannula, and the suspension was stirred at -78 °C for 6 h and then -20 °C for 16 h. To the cold suspension was added pH 7 buffer (900 µL), warmed to rt and then MeOH (900 µL) was added. After cooling to 0 °C a 30% aqueous solution of H_2O_2 (900 µL) was added and the mixture was warmed to rt and stirred for 2 h. H_2O (4 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (4 x 75 mL) and the combined organic extracts were washed with brine (1 x 3 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil (dr > 96:4) was flash chromatographed (gradient 10% to 40% EtOA/petrol ether 40-60) to yield the 1,3-*syn* aldol adduct (153 mg, 88%).

R_f 0.32 (40% EtOAc in hexane); **$[\alpha]_D$** +8.7 (*c* 1.31, $CHCl_3$); **IR** (liquid film) 3440, 2927, 2866, 1709, 1613, 1587, 1514, 1497, 1464, 1420, 1363, 1302, 1248, 1216, 1173, 1095, 1067, 1037, 1010, 931, 885, 820, 758, 733, 696; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.23-7.37 (5H, m, ArH), 7.20 (2H, d, *J*= 8.4, ArH), 6.85 (2H, d, *J*= 8.5 Hz, ArH), 4.84 (2H, s, -OCH_2Ar), 4.42, 4.38 (2H, ABq, *J*= 11.5 Hz, -OCH_2Ar), 4.20-4.30 (2H, m, 25-CH and 27-CH), 3.79 (3H, s, -OCH_3), 3.52 (1H, dd, J= 9.7, 4.6 Hz, 28-C$\underline{H_a}H_b$), 3.44 (1H, dd, *J*= 9.6, 5.4 Hz, 28-C$H_a\underline{H_b}$), 3.39 (1H, d, *J*= 2.4 Hz, -OH), 2.44-2.61 (2H, m, 24-CH_2), 2.11 (3H, s, 22-CH_3), 1.69-1.79 (2H, m, 26-CH_2), 1.00-1.12 (14H, m, iPr); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 208.9, 159.2, 140.9, 130.1, 129.4, 128.2, 126.9, 125.9, 113.7, 73.8, 73.0, 70.0, 65.3, 64.6, 55.2, 50.5, 41.4, 30.7, 17.4, 17.4, 12.4, 12.3; **HRMS** (ES+) calcd. for $C_{28}H_{46}NO_6Si$ [$M+NH_4^+$] 520.3089, found 520.3088.

(4*S*,6*R*)-6-(BENZYLOXY-DIISOPROPYL-SILANYLOXY)-4-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-7-(4-METHOXY-BENZYLOXY)-HEPTAN-2-ONE

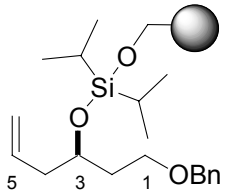


To a cold (-78 °C), stirred solution of this alcohol (152.6 mg, 0.304 mmol, 1.0 equiv.) in dry DCM (5 mL) was added 2,6-lutidine (106.0 µL, 0.908 mmol, 3.0 equiv.) followed by TBSOTf (139 µL, 0.616 mmol, 2.0 equiv.). The resultant solution was stirred at -78 °C for 2 h and then sat. $NaHCO_3$ (0.8 mL) was added to quench the excess TBSOTf. The reaction was allowed to warm to rt and H_2O (5 mL) was added. The layers were separated and the aqueous phase was extracted with Et_2O (4 x 5 mL). The combined organic extracts were washed with brine (1 x 2 mL), dried (Na_2SO_4)

and concentrated *in vacuo*. The crude oil was flash chromatographed to yield the 1,3-*syn* TBS-ether (55 mg, 29%), as colourless oils.

R_f 0.44 (20% EE in hexane); **$[\alpha]_D$** +10.2 (*c* 0.77, $CHCl_3$); **IR** (liquid film) 2928, 2858, 1718, 1613, 1587, 1514, 1497, 1464, 1361, 1302, 1249, 1207, 1172, 1099, 1067, 1038, 1006, 885, 835, 810, 777, 732, 696; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.24-7.35 (5H, m, ArH), 7.21 (2H, d, *J*= 8.5 Hz, ArH), 6.84 (2H, d, *J*= 8.5 Hz, ArH), 4.87, 4.83 (2H, ABq, *J*= 13.2 Hz, -OCH_2Ar), 4.41, 4.39 (2H, ABq, *J*= 11.5 Hz, -OCH_2Ar), 4.34 (1H, qn, *J*= 5.9 Hz, 25-CH), 4.15 (1H, qn, *J*= 5.8 Hz, 27-CH), 3.79 (3H, s, -OCH_3), 3.42 (2H, ddd., *J*= 15.6, 9.7, 5.2 Hz, 28-C$\underline{H_a}H_b$ and 28-$CH_a\underline{H_b}$), 2.49-2.61 (2H, m, 24-CH_2), 2.08 (3H, s, 22-CH_3), 1.74 (2H, t, *J*= 6.3 Hz, 26-CH_2), 1.01-1.11 (14H, m, iPr), 0.84 (9H, s, -$OSiMe_2{}^t\underline{Bu}$), 0.03, 0.00 (6H, s, -$OSi\underline{Me}_2{}^t$Bu); **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 207.6, 159.1, 141.2, 130.4, 129.3, 128.1, 126.8, 125.9, 113.7, 74.1, 72.9, 68.8, 66.4, 64.5, 55.2, 51.0, 42.7, 31.5, 25.8, 17.9, 17.6, 17.5, 17.5, 17.5, 12.5, 12.4, -4.5, -4.8; **HRMS** (ES+) calcd. for $C_{34}H_{60}NO_6Si_2N$ [$M+NH_4^+$] 634.3965, found 634.3960.

(1*R*)-METHOXYPOLYSTYRENE-[1-(2-BENZYLOXY-ETHYL)-BUT-3-ENYLOXY]-DIISOPROPYL-SILANE (11A)



A. Loading

To a stirred solution of imidazole (5.29 g, 77.68 mmol, 10 equiv.) in dry DMF (20 mL) was added diisopropylsilyldichloride (2.34 mL, 12.95 mmol, 3 equiv.) and stirred for 5 min. Homoallylic alcohol **9** (2.67 g, 12.95 mmol, 3 equiv.) in dry DMF (5 mL + 2 x 1 mL for washing) was added to the solution and stirred for 2 h at rt. The mixture was transfered *via* cannula to the swollen hydroxymethylpolystyrene resin (4.96 g, loading 0.87 mmol/g, 4.31 mmol, 1 equiv.), which was washed with dry DMF (3 x) before. After stirring for 24 h at rt the solution was filtered off, the resin was washed with DMF and DCM and dried under high vaccum at 40 °C for 4 h. A second cycle of reaction was then repeated for another 24 h. After the same washing and drying treatment 6.26 g of resin **11a** were obtained (calculated loading before/after capping approx. 0.65/0.61).

IR (single beads) 3059, 3025, 2920, 1601, 1498, 1452, 1366, 1089, 1029, 909, 884, 817, 754, 696 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 138.5, 134.7, 117.1, 72.9, 69.3, 66.9, 64.4, 42.1, 36.6, 17.6, 12.5.

B. Capping

A stirred solution of imidazole (5.29 g, 77.68 mmol, 10 equiv.) in dry DMF (20 mL) was added diisopropylsilyldichloride (2.34 mL, 12.95 mmol, 3 equiv.) and stirred for 5 min. The mixture was transfered *via* cannula to the loaded hydroxymethylpolystyrene resin (6.26 g), which was washed with dry DMF (3 x) before. After stirring for 2 h at rt MeOH (2.66 mL) was added and the suspension was stirred o/n at rt. Afterwards the solution was filtered off, the resin was washed with DCM, DCM/MeOH, MeOH and DCM and dried under high vaccum at 40 °C for 4 h to yield a pale yellow resin (6.64 g, calculated loading after capping approx.0.61).

C. Deterimation of the loading by cleavage from the resin with TBAF/THF

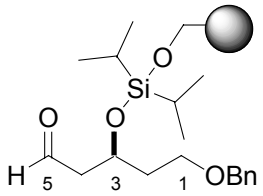
To resin **11a** (0.0975 g) swollen in dry THF was added a solution of 1M TBAF/THF (0.58 mL, 0.58 mmol, ~ 10 equiv.) in dry THF (2 mL) at rt under argon. After stirring for 48 h at rt, the solution was filtered off and quenched by sat. NH_4Cl, and stirring was continued for 30 min. The resin was washed with THF, DCM, MeOH and DCM. The

organic layer was dried with Na_2SO_4 and concentrated to dryness und reduced pressure. The residue was purified by flash chromatography (20% EtOAc/petrol ether 40-60) to give the homoallylic alcohol as colorless oil (14.7 mg, calculated loading approx. 0.73 mmol/g)

D. Recycling of the homoallylic alcohol 9

The reaction mixture from A. were collected and the solvent was removed under vacuo. The residue was dissolved in THF (220 mL) and 1M TBAF/THF (28 mL) was added. The solution was stirred for 20 min at rt and another 3 mL of 1M TBAF/THF were added. After stirring for 5 min at rt the reaction mixture was quenched with sat. NH_4Cl (150 mL). The aqueous phase was extracted with EtOAc (4 x). The combined organic layers were washed with brine and dried with Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (gradient 0% to 10% EtOAc/petrol ether 40-60) to yield homoallylic alcohol **9** as colorless oil.

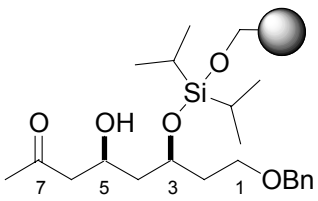
(3*S*)-5-BENZYLOXY-3-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-PENTANAL (8A)



In a round-bottomed flask a spatula tip of $NaHCO_3$ was added to a stirred suspension of the resin-bound homoallylic alcohol **11a** (3.8254 g, approx. loading 0.61 mmol/g, 2.33 mmol, 1.0 equiv.) in dry CH_2Cl_2 (100 mL) to help to suppress hydrolysis. Afterwards the reaction mixture was cooled to –78 °C. A stream of O_3 was then bubbled through this mixture until the solution became slightly blue in colour (*circa* 1 min), indicating an excess of O_3. The O_3 generator was turned off and O_2 was bubbled through the mixture until the blue colour dissipated. Triphenylphosphine (3.6 g, 13.725 mmol, 5.9 equiv.) was added and the mixture was warmed to rt and sonicated for 9 h. The suspension was stirred over night at rt and the resin was filtered off through a fritted syringe. The resin was washed with DCM, MeOH and DCM and dried under reduced pressure for 6 h at 40 °C. This gave 3.8306 g of a pale yellow resin (**8a**).

IR (single beads) 3060, 3026, 2923, 2866, 1725, 1601, 1493, 1452, 1370, 1090, 1029, 906, 885, 821, 755, 696, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 201.6, 138.2, 72.9, 66.3, 65.9, 64.5, 50.9, 37.5, 17.4, 12.3.

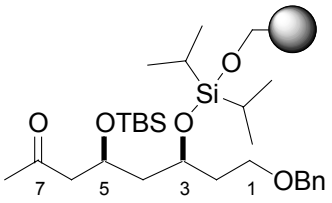
(4*S*,6*S*)-8-BENZYLOXY-6-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-4-HYDROXY-OCTAN-2-ONE (12A)



Commercial (–)-Ipc$_2$BCl (780.1 mg, 2.43 mmol, 5.4 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (3.7 mL) and the solution was cooled to 0 °C. Dry Et_3N (407 µL, 2.92 mmol, 6.5 equiv.) was added followed by dry acetone (262 µL, 3.57 mmol, 7.9 equiv., freshly distilled off of $CaSO_4$). The resultant white suspension was stirred at 0 °C for 1 h and then cooled to -78 °C. The enolate solution was transfered *via* cannula (1 x 500 µl washing) to a cooled (- 78 °C) round bottom flask, containing the resin bound aldehyde **8a** (738 mg resin, approx. loading 0.61 mmolg^{-1}, 0.450 mmol, 1.0 equiv.), which was swollen in dry Et_2O (3 mL). The suspension was stirred at -78 °C for 5 h. The reaction was quenched with pH7 buffer (3.7 mL) and the reaction mixture was allowed to warm to rt. The resin was filtered off and washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH and DCM. After drying the resin o/n under HV a second cycle of aldol reaction was carried out under the same conditions as mentioned above. After quenching, washing and drying, the resin was swollen in a mixture of MeOH (12.5 mL), pH 7 buffer (6.3 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (4 mL) was added and the mixture was warmed to rt. After stirring for 2 h the solution was filtered off, the resin was washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH, DCM and dried under HV for 3 h at 40 °C to yield a pale yellow resin (**12a**, 690 mg).

IR (single beads) 3025, 2920, 2866, 1708, 1601, 1493, 1452, 1366, 1090, 884, 821, 754, 696, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.0, 138.4, 73.0, 68.9, 66.7, 65.7, 64.5, 50.5, 43.2, 36.9, 30.7, 17.5, 12.4.

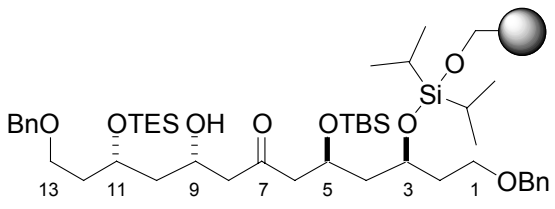
(4*S*,6*S*)-8-BENZYLOXY-6-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-4-(TERT-BUTYL-DIMETHYLSILANYLOXY)-OCTAN-2-ONE (6A)



The resin-bound alcohol **12a** (517 mg, approx. loading 0.61 mmolg^{-1}, 0.315 mmol, 1 equiv.) was washed with dry DMF (3 x 5 mL) and cooled to 0 °C. A solution of imidazole (52.8 mg, 0.776 mmol, 2.5 equiv.), TBSCl (117 mg, 0.776 mmol, 2.5 equiv.) in DMF (1 mL + 2 x 1 mL washing) was added via cannula and the suspension was stirred at rt for 16 h. The reaction was quenched by the addition of MeOH (0.5 mL) and the solution was filtered off. After washing the resin with DMF, MeOH and DCM, the resin was dried under reduced pressure for 3 h at 40 °C. A second cycle of reaction was then repeated for another 16 h. This gave a pale yellow resin (**6a**, 560 mg).

IR (single beads) 3060, 3026, 2925, 2864, 1717, 1601, 1493, 1453, 1362, 1265, 1181, 1155, 1094, 1029, 941, 906, 884, 835, 757, 737, 696, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 207.3, 138.5, 72.9, 67.2, 66.7, 66.4, 64.4, 51.2, 45.1, 37.0, 31.5, 25.8, 17.9, 17.5, 12.5, -4.5, -4.6.

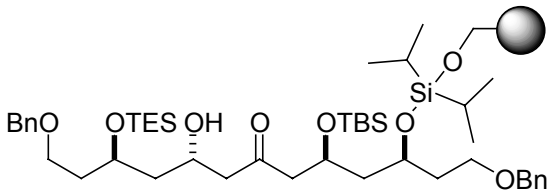
(3*S*,5*S*,9*S*,11*S*)-1,13-BIS-BENZYLOXY-3-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-5-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-9-HYDROXY-11-TRIETHYLSILANYLOXY-TRIDECAN-7-ONE (4A)



A round bottomed flask containing commercial (–)-Ipc$_2$BCl (49.0 mg, 0.153 mmol, 3.0 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (200 µL) and the solution was cooled to 0 °C. Dry Et_3N (26.4 µL, 0.189 mmol, 3.7 equiv.) was added. The solution was cooled to -78 °C and transfered *via* cannula (2 x 300 µl washings) to the cooled (-78 °C) resin-bound ketone **6a** (101.3 mg, approx. loading 0.5 mmolg^{-1}, 0.051 mmol, 1 equiv.), which was washed with dry Et_2O (3 x 2.5 mL) beforehand. After stirring this suspension for 4 h at 0 °C, the temperature was lowered to - 78°C and a solution of the aldehyde **7** (98 mg, 0.304 mmol, 6.0 equiv.) in dry Et_2O (150 µL + 2 x 150 µL washings) was added *via* cannula. The reaction mixture was stirred 4 h at -78 °C and 16 h at -20 °C. The reaction was quenched with pH7 buffer (2.5 mL) and the reaction mixture was allowed to warm to rt. The resin was filtered off and washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH and DCM. After drying the resin o/n under HV a second cycle of aldol reaction was carried out under the same conditions as mentioned above. After quenching, washing and drying, the resin was swollen in a mixture of MeOH (2.5 mL), pH 7 buffer (1.3 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (0.8 mL) was added and the mixture was warmed to rt. After stirring at rt for 2 h the solution was filtered off, the resin was washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH, DCM and dried under HV for 3 h at 40 °C to yield a pale yellow resin (**4a**, 128 mg).

IR (single beads) 3060, 3026, 2923, 2867, 1716, 1601, 1493, 1453, 1376, 1250, 1094, 1029, 906, 885, 836, 737, 696, 664 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.7, 138.5, 73.0, 73.0, 68.8, 67.3, 66.8, 66.7, 66.3, 65.9, 64.4, 51.5, 51.2, 45.2, 43.4, 37.2, 25.9, 17.9, 17.6, 12.5, 6.9, 5.1, -4.5, -4.6.

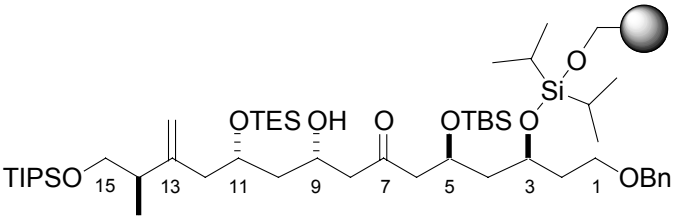
(3*S*,5*S*,9*S*,11*R*)-1,13-BIS-BENZYLOXY-3-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-5-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-9-HYDROXY-11-TRIETHYLSILANYLOXY-TRIDECAN-7-ONE (15A)



A round bottomed flask containing commercial (–)-Ipc$_2$BCl (49.0 mg, 0.153 mmol, 3.0 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (200 µL) and the solution was cooled to 0 °C. Dry Et_3N (26.4 µL, 0.189 mmol, 3.7 equiv.) was added. The solution was cooled to -78 °C and transfered *via* cannula (2 x 300 µl washings) to the cooled (-78 °C) resin-bound ketone **6a** (101.3 mg, approx. loading 0.5 mmolg^{-1}, 0.051 mmol, 1 equiv.), which was washed with dry Et_2O (3 x 2.5 mL) beforehand. After stirring this suspension for 4 h at 0 °C, the temperature was lowered to - 78°C and a solution of the aldehyde *ent*-**7** (98 mg, 0.304 mmol, 6.0 equiv.) in dry Et_2O (150 µL + 2 x 150 µL washings) was added *via* cannula. The reaction mixture was stirred 4 h at -78 °C and 16 h at -20 °C. The reaction was quenched with pH7 buffer (2.5 mL) and the reaction mixture was allowed to warm to rt. The resin was filtered off and washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH and DCM. After drying the resin o/n under HV a second cycle of aldol reaction was carried out under the same conditions as mentioned above. After quenching, washing and drying, the resin was swollen in a mixture of MeOH (2.5 mL), pH 7 buffer (1.3 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (0.8 mL) was added and the mixture was warmed to rt. After stirring at rt for 2 h the solution was filtered off, the resin was washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH, DCM and dried under HV for 3 h at 40 °C to yield a pale yellow resin (**15a**, 124 mg).

IR (single beads) 3060, 3026, 2925, 2865, 1716, 1601, 1493, 1453, 1366, 1250, 1094, 1029, 906, 884, 835, 747, 696, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 209.6, 138.5, 73.0, 68.8, 67.7, 67.3, 66.7, 66.2, 65.9, 64.3, 51.6, 51.2, 45.2, 43.4, 37.2, 25.8, 17.9, 17.5, 12.4, 6.9, 5.0, -4.5.

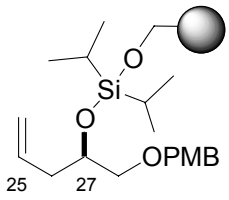
(3*S*,5*S*,9*S*,11*S*)-1-BENZYLOXY-3-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-5-(*TERT*-BUTYLDIMETHYLSILOXY)-9-HYDROXY-13-[1-(TRIISOPROPYLSILOXY)-PROP-2-(*R*)-YL]-11-(TRIETHYLSILOXY)-TETRADEC-13-EN-7-ONE (3A)



A round bottomed flask containing commercial (–)-Ipc$_2$BCl (47.9 mg, 0.148 mmol, 3.2 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (110 µL) and the solution was cooled to 0 °C. Dry Et_3N (24.0 µL, 0.172 mmol, 3.7 equiv.) was added. The solution was cooled to -78 °C and transfered *via* cannula (2 x 150 µl washings) to the cooled (-78 °C) resin-bound ketone **6a** (92.7 mg, approx. loading 0.5 mmolg^{-1}, 0.046 mmol, 1 equiv.), which was washed with dry CH_2Cl_2 (3 x 2.5 mL) beforehand. After stirring this suspension for 3 h at 0 °C, the temperature was lowered to - 78°C and a solution of the aldehyde **14** (122 mg, 0.276 mmol, 6.0 equiv.) in dry Et_2O (70 µL + 2 x 70 µL washings) was added *via* cannula. The reaction mixture was stirred 4 h at -78 °C and 16 h at -20 °C. The reaction was quenched with pH7 buffer (2.5 mL) and the reaction mixture was allowed to warm to rt. The resin was filtered off and washed with pH7 buffer, pH7 buffer'/MeOH and MeOH. The resin was swollen in MeOH (1 mL), DMF (2.5 mL) and pH7 buffer (2.5 mL) and cooled to 0 °C. 30% aqueous H_2O_2 was added and stirred 2.5 h at rt. The resin was washed with MeOH, DMF, CH_2Cl_2. After drying under HV for 3 h at 40 °C a pale yellow resin (104 mg) was yielded.

IR (single beads) 3514, 2943, 2866, 1710, 1463, 1412, 1382, 1363, 1252, 1207, 1095, 1068, 1028, 1012, 884, 836, 808, 777, 732, 696 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 148.2, 138.5, 111.7, 72.9, 71.3, 67.7, 67.5, 67.2, 66.7, 66.5, 66.1, 64.5, 51.5, 51.4, 48.1, 44.2, 42.7, 42.5, 36.9, 25.8, 18.0, 17.9, 17.5, 16.7, 12.4, 12.0, 6.9, 5.1, -4.6.

(*R*)-5-(*p*-METHOXYBENZYLOXY)-4-(METHOXYPOLYSTYRENE-DIISOPROPYLSILOXY)-1-PENTENE (17)



A. Loading

To a stirred solution of imidazole (3.94 g, 57.87 mmol, 18 equiv.) in dry DMF (18 mL) was added diisopropylsilyldichloride (1.76 mL, 9.74 mmol, 3 equiv.) and stirred for 5 min. Homoallylic alcohol **16** (2.14 g, 9.65 mmol, 3 equiv.) in dry DMF (6 mL + 2 x 1 mL for washing) was added to the solution and stirred for 2 h at rt. The mixture was transfered *via* cannula to the swollen hydroxymethylpolystyrene resin (3.70 g, loading 0.87 mmol/g, 3.22 mmol, 1 equiv.), which was washed with dry DMF (3 x) before. After stirring for 24 h at rt the solution was filtered off, the resin was washed with DMF and DCM and dried under high vaccum at 40 °C for 4 h. A second cycle of reaction was then repeated for another 24 h. After the same washing and drying treatment 4.41 g of resin **17** were obtained (calculated loading before and after capping approx. 0.48 mmol/g).

IR (single beads) 3059, 3026, 2923, 2865, 1602, 1513, 1493, 1452, 1366, 1246, 1093, 1030, 907, 885, 821, 756, 696, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 159.1, 134.6, 130.5, 129.2, 117.1, 113.7, 73.5, 72.9, 71.0, 64.4, 55.2, 39.2, 17.5, 17.4, 12.4;

B. Capping

A stirred solution of imidazole (3.94 g, 57.87 mmol, 18 equiv.) in dry DMF (18 mL) was added diisopropylsilyldichloride (1.76 mL, 9.74 mmol, 3 equiv.) and stirred for 5 min. The mixture was transfered *via* cannula to the loaded hydroxymethylpolystyrene resin (4.41 g), which was washed with dry DMF (3 x) before. After stirring for 2 h at rt MeOH (2.00 mL) was added and the suspension was stirred for 24 h at rt. Afterwards the solution was filtered off, the resin was washed with DCM, DCM/MeOH, MeOH and DCM and dried under high vaccum at 40 °C for 4 h to yield a pale yellow resin (4.41 g, calculated loading after capping approx. 0.48 mmol/g).

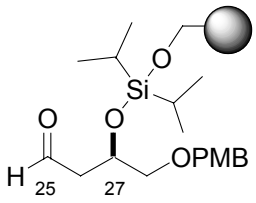
C. Deterimation of the loading by cleavage from the resin with TBAF/THF

To resin **17** (0.1159 g) swollen in dry THF was added a solution of 1M TBAF/THF (0.58 mL, 0.58 mmol, ~ 10 equiv.) in dry THF (2 mL) at rt under argon. After stirring for 48 h at rt, the solution was filtered off and quenched by sat. NH_4Cl, and stirring was continued for 30 min. The resin was washed with THF, DCM, MeOH and DCM. The organic layer was dried with Na_2SO_4 and concentrated to dryness und reduced pressure. The residue was purified by flash chromatography (20% EtOAc/petrol ether 40-60) to give the homoallylic alcohol as colorless oil (13.1 mg, calculated loading approx. 0.51 mmol/g)

D. Recycling of the homoallylic alcohol 16

The reaction mixture from A. were collected and the solvent was removed under vacuo. The residue was dissolved in THF (220 mL) and 1M TBAF/THF (28 mL) was added. The solution was stirred for 20 min at rt and another 3 mL of 1M TBAF/THF were added. After stirring for 5 min at rt the reaction mixture was quenched with sat. NH_4Cl (150 mL). The aqueous phase was extracted with EtOAc (4 x). The combined organic layers were washed with brine and dried with Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (gradient 0% to 10% EtOAc/petrol ether 40-60) to yield homoallylic alcohol **16** as colorless oil.

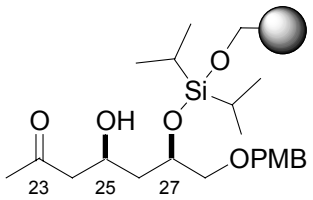
(3*R*)-4-(*p*-METHOXYBENZYLOXY)-3-(METHOXYPOLYSTYRENE-DIISOPROPYLSILOXY)-BUTANAL



In a round-bottomed flask a spatula tip $NaHCO_3$ was added to a stirred suspension of the resin-bound homoallylic alcohol **17** (3.11 g, approx. loading 0.5 mmol/g, 1.56 mmol, 1.0 equiv.) in dry CH_2Cl_2 (200 mL) to help to suppress hydrolysis. Afterwards the reaction mixture was cooled to –78 °C. A stream of O_3 was then bubbled through this mixture until the solution became slightly blue in colour (*circa* 1 min), indicating an excess of O_3. The O_3 generator was turned off and O_2 was bubbled through the mixture until the blue colour dissipated. Triphenylphosphine (2.6 g, 9.91 mmol, 6.4 equiv.) was added and the mixture was warmed to rt and sonicated for 9 h. The suspension was stirred over night at rt and the resin was filtered off through a fritted syringe. The resin was washed with DCM, MeOH and DCM and dried under reduced pressure for 6 h at 40 °C. This gave 3.01 g of a pale yellow resin.

IR (single beads) 3060, 3026, 2923, 2865, 1725, 1602, 1513, 1493, 1452, 1366, 1302, 1247, 1179, 1090, 1029, 906, 884, 821, 756, 696, 665 cm^{-1}; **^{13}C NMR** δ (100 MHz, $CDCl_3$) 201.2, 159.2, 113.8, 73.5, 73.0, 67.3, 64.5, 55.2, 48.9, 17.4, 12.2.

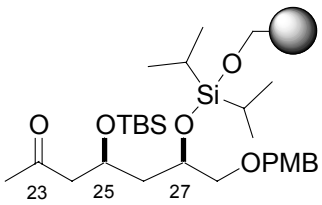
(4*S*,6*R*)-6-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-4-HYDROXY-7-(4-METHOXY-BENZYLOXY)-HEPTAN-2-ONE



Commercial (–)-Ipc_2BCl (780 mg, 2.43 mmol, 4.8 equiv.) was placed under high vacuum for 1 h to remove any traces of HCl. To this flask was added dry Et_2O (3.7 mL) and the solution was cooled to 0 °C. Dry Et_3N (407 µL, 2.91 mmol, 5.8 equiv.) was added followed by dry acetone (262 µL, 3.57 mmol, 7.0 equiv., freshly distilled off of $CaSO_4$). The resultant white suspension was stirred at 0 °C for 45 min and then cooled to -78 °C. The enolate solution was transfered via cannula (1 x 500 µl washing) to a cooled (- 78 °C) round bottom flask, containing the above prepared resin bound aldehyde (1.01 g resin, approx. loading 0.5 mmol/g, 0.505 mmol, 1.0 equiv.), which was swollen in dry Et_2O (3 mL). The suspension was stirred at -78 °C for 5.5 h. The reaction was quenched with pH7 buffer (3.7 mL) and the reaction mixture was allowed to warm to rt. The resin was filtered off and washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH and DCM. After drying the resin o/n under HV a second cycle of aldol reaction was carried out under the same conditions as mentioned above. After quenching, washing and drying, the resin was swollen in a mixture of MeOH (12.5 mL), pH 7 buffer (6.3 mL) and cooled to 0 °C. A 30% aqueous solution of H_2O_2 (4 mL) was added and the mixture was warmed to rt. After stirring for 2 h the solution was filtered off, the resin was washed with pH7 buffer, H_2O,H_2O/MeOH, MeOH, DCM and dried under HV for 3 h at 40 °C to yield a pale yellow resin (1.06 g).

IR (single beads) 3059, 3025, 2922, 2865, 1708, 1602, 1512, 1493, 1452, 1365, 1247, 1179, 1090, 1030, 906, 884, 818, 757, 695, 665 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 208.8, 159.2, 113.7, 73.8, 73.0, 70.0, 65.3, 64.4, 55.2, 50.5, 41.4, 30.7, 17.4, 12.4.

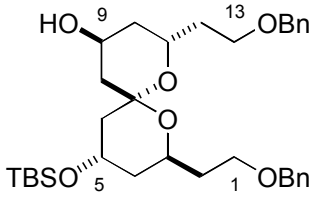
(4*S*,6*R*)-6-(METHOXYPOLYSTYRENE-DIISOPROPYL-SILANYLOXY)-4-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-7-(4-METHOXY-BENZYLOXY)-HEPTAN-2-ONE (18)



The above prepared resin-bound alcohol (520 mg, loading approx. 0.5 mmol/g, 0.26 mmol, 1 equiv.) was washed with dry DMF (3 x 5 mL) and cooled to 0 °C. A solution of imidazole (42.6 mg, 0.626 mmol, 2.4 equiv.), TBSCl (94.4 mg, 0.626 mmol, 2.4 equiv.) in DMF (1 mL + 2 x 1 mL washing) was added via cannula and the suspension was stirred at rt for 16 h. The reaction was quenched by the addition of MeOH (0.5 mL) and the solution was filtered off. After washing the resin with DMF, MeOH and DCM, the resin was dried under reduced pressure for 3 h at 40 °C. A second cycle of reaction was then repeated for another 16 h. This gave a pale yellow resin (**18**, 545 mg).

IR (single beads) 3026, 2923, 2865, 1717, 1602, 1512, 1493, 1452, 1365, 1248, 1093, 1030, 885, 833, 756, 696, 664 cm^{-1}; **^{13}C NMR** δ (100.6 MHz, $CDCl_3$) 207.5, 159.1, 113.7, 74.1, 72.9, 68.8, 66.4, 64.4, 55.2, 51.1, 42.7, 31.6, 25.9, 18.0, 17.5, 12.5, 12.4, -4.5, -4.7.

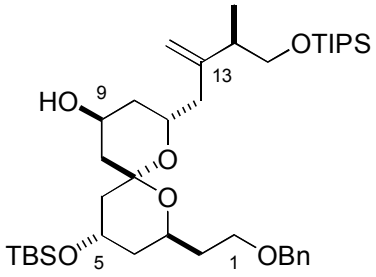
(2*S*,4*S*,6*R*,8*S*,10*S*)-2,8-BIS-(2-BENZYLOXY-ETHYL)-10-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-1,7-DIOXA-SPIRO[5.5]UNDECAN-4-OL (5)



To a suspension of 94.2 mg solid bound aldol product **4a** in THF (2 mL) was added under argon 300 µl HF*pyr in pyridine (1/1 vol-%) at once at room temperature and stirred for 1 h. The mixture was dropped into a sat. aq. solution of $NaHCO_3$ (3 mL) and EtOAc (10 mL) was added. After phase separation, the aqueous phase was thoroughly extracted with EtOAc. The combined organic phases were dried (Na_2SO_4) and the solvent evaporated. The crude product contained a mixture of **5** as one of the products together with its C7-isomer and partially cyclised hemiacetals (ratio ~ 1:2:2). This was dissolved in DCM (1 mL) and MeOH (1mL) and treated with catalytic amounts of pyridinium *p*-toluenesulfonate (PPTS) at room temperature. After 4 hours, NEt_3 (500 µl) was added the solvent evaporated. Flash chromatography (0% to 30 %EtOAc/hexane) afforded spiroacetal **5** (12.2 mg, 21.4 µmol) and 7-*epi*-**5** and partially cyclised hemiacetal (3.2 mg combined yield). The last two compounds were submitted to the same reaction conditions to give after workup and flash chromatography another 1.8 mg (3.1 µmol) of **5**. Combined yield: 14.0 mg (24.5 µmol, 17% over 7 steps on solid support).

R_f 0.46 (40% EtOAc in hexane); **$[\alpha]_D$** –52 (*c* 1.10, $CHCl_3$); **IR** (liquid film) 3445.9, 2928.2, 1097.5 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.21-7.39 (10H, m, ArH), 4.40 (2H, dd, *J*= 43.5, 12.0 Hz, -OCH_aH_bAr), 4.42 (2H, s, -OCH_2Ar), 4.27 (1H, d, *J*= 10.4 Hz, -OH), 4.16-4.22 (1H, m, 3-CH or 5-CH or 11-CH), 4.06-4.13 (2H, m, 3-CH and/or 5-CH and/or 11-CH), 4.03 (1H, dt, *J*= 10.1, 3.2 Hz, 9-CH), 3.59-3.70 (2H, m, 1-CH_aH_b or 13-CH_aH_b), 3.42-3.53 (2H, m, 1-CH_aH_b or 13-CH_aH_b), 1.41-1.83 (12H, m, 2-CH_aH_b, 4-CH_aH_b, 6-CH_aH_b, 8-CH_aH_b, 10-CH_aH_b, 12-CH_aH_b), 0.91 (9H, s, -$OSiMe_2{}^tBu$), 0.05 (6H, s, $OSiMe_2{}^tBu$), **^{13}C NMR** δ (62.5 MHz, $CDCl_3$) 138.8, 138.3, 128.3, 127.9, 127.6, 127.5, 127.4, 98.3, 73.1, 72.9, 67.8, 67.3, 65.2, 64.4, 63.2, 61.1, 41.4, 40.8, 38.7, 38.1, 35.9, 35.9, 25.9, 18.2, -4.7, -4.9; **HRMS** (+FAB) calcd. for $C_{33}H_{51}O_6Si$ (MH^+) 571.3455, found 571.3487.

(2*S*,*4S*,*6R*,*8S*,*10S*)-8-(2-BENZYLOXY-ETHYL)-10-(*TERT*-BUTYL-DIMETHYL-SILANYLOXY)-2-[1-(TRIISOPROPYLSILOXY)-PROP-2-(*R*)-YL]-1,7-DIOXA-SPIRO[5.5]UNDECAN-4-OL (2)



To a suspension of 52.0 mg solid bound aldol product **3a** in THF (1 mL) was added under argon 200 µl HF*pyr in pyridine (1/1 vol-%) at once at room temperature and stirred for 30 min. The mixture was dropped into a sat. aq. solution of $NaHCO_3$ (3 mL) and EtOAc (8 mL) was added. After phase separation, the aqueous phase was thoroughly extracted with EtOAc. The combined organic phases were dried (Na_2SO_4) and the solvent evaporated. The crude product was dissolved in DCM (0.4 mL) and MeOH (0.4 mL) and treated with catalytic amounts of pyridinium *p*-

toluenesulfonate (PPTS) at room temperature. After 1 hour, NEt_3 (500 µl) was added the solvent evaporated. Flash chromatography (0% to 20 %EtOAc/hexane) afforded spiroacetal **2** (2.2 mg, 3.18 µmol) and unwanted isomers, which were which submitted again to the same reaction conditions to give after workup and flash chromatography a combined yield of 2.8 mg (4.1 µmol, 5.3% yield over 7 steps on solid support).

R_f 0.52 (20% EtOAc in hexane); **$[\alpha]_D$** –37 (*c* 1.00, $CHCl_3$); **IR** (liquid film) 2925.4, 1461,8, 1096,1 cm^{-1}; **^{1}H NMR** δ (400 MHz, $CDCl_3$) 7.28-7.35 (5H, m, ArH), 4.82 (1H, s, -C=CH*H*), 4.78 (1H, s, -C=C*H*H), 4.50 (1H, d, *J*= 11.8 Hz, OCH_2Ph), 4.43 (1H, d, *J*= 11.8 Hz, OCH_2Ph), 4.28 (1H, m, 3-CH), 4.01-4.18 (3H, m, 5-H, 9-H, 11-H), 3.65 (1H, dd, *J*= 9.8, 9.3 Hz, 15-H), 3.57 (2H, t, *J*= 6.6, 1-H), 3.45 (1H, dd, *J*= 9.8, 9.3 Hz, 15-H), 2.42 (1H, dd, *J*= 14.3, 5.4 Hz, 12-H), 2.25 (1H, m, 14-H), 2.04 (1H, dd, *J*= 14.3, 8.2 Hz, 12-H), 1.68-1.93 (5H, m, 2-H, 2-H, 4-H, 4-H, 10-H), 1.46-1.63 (4H, m, 6-H, 6-H, 8-H, 8-H), 1.36 (t, *J*= 12.7 Hz, 10-H), 1.00-1.15 (24H, m, C_{14}-Me, -OSi(C*H*(CH_3)$_2$)$_3$), 0.92 (9H, s, -$OSiMe_2$-^{t}*Bu*), 0.02, -0.02 (6H, s, s, -OSi*Me*$_2$^{t}Bu). **^{13}C NMR** δ (62.5 MHz, $CDCl_3$) 147.8, 138.1, 128.2, 127.6, 127.3, 111.3, 98.6, 73.1, 67.6, 65.2, 64.2, 63.5, 63.4, 42.9, 41.8, 41.3, 40.8, 38.9, 37.4, 35.9, 25.9, 18.3, 16.2, 12.0, -4.6, -5.0; **HRMS** (+FAB) calcd. for $C_{39}H_{70}O_6Si_2$ (M^+) 690.4711, found 690.4752.