Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# Synthetic studies toward the brasilinolides: controlled assembly of a protected C1–C38 polyol based on fragment union by complex aldol reactions

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***Supporting Information Available:***

## 1. General Experimental Procedures

$^{1}H$ and proton-decoupled $^{13}C$ nuclear magnetic resonance (NMR) spectra were recorded using an internal deuterium lock at ambient probe temperature on the following machines: Bruker DRX500 Fourier transform instrument (500 MHz), Bruker Advance BB (500 MHz), and Bruker DPX400 Fourier transform instrument (400 MHz). Internal references of $\delta_H$ = 7.26 ppm and $\delta_C$ = 77.0 ppm were used for residual protons and carbons in $CDCl_3$ respectively; $\delta_H$ = 7.16 ppm and $\delta_C$ = 128.1 ppm for residual protons in $C_6D_6$. All $^{1}H$ NMR data is represented as: chemical shift (in ppm on the $\delta$ scale relative to $\delta_{TMS}$ = 0 ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sex = sextet, m = multiplet, br. = broad, app. = apparent, obs. = obscured), coupling constant (*J* in Hz) and assignment. Coupling constants were taken directly from spectra and uncorrected. Assignments were determined either on the basis of unambiguous chemical shift or coupling pattern, $^{1}H$–$^{1}H$ COSY experiments, or by analogy to fully interpreted data for related compounds.

Infra-red spectra were recorded on the Perkin Elmer Spectrum One FT-IR machine. Absorbance frequencies (v) are quoted in wavenumbers ($cm^{-1}$). The abbreviations s, m, w, and br indicate respectively sharp, medium, weak and broad absorbances where appropriate.

High resolution mass spectra (HRMS) were recorded by either the departmental Mass Spectrometry Service (University Chemical Laboratories, Cambridge) or at the EPSRC Mass Spectrometry Service (Swansea, UK) using electrospray ($ES^+$) or electron ionisation (EI). The parent ion (M+) is quoted with the indicated cation.

Optical rotations were measured on a Perkin Elmer 241 polarimeter at the sodium d-line (589 nm) and are reported as an $[\alpha]_D^{20}$ value together with concentration of solution (c in $g.dL^{-1}$) and solvent. All rotations were measured at a temperature of 20 ºC.

Analytical thin layer chromatography (TLC) was carried out on Merck Kieselgel 60 $F_{254}$ plates with visualisation by phosphomolybdic acid/$Ce_2(SO_4)_3$ dip, potassium permanganate dip or ultra-violet light. Flash column chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) silica under a positive pressure by means of compressed air, unless otherwise stated. Chiral analytical High Performance Liquid Chromatography (HPLC) was carried out using a Dacial Chemical Industries Ltd. Chiracel OD column equipped with a Gilson UV detector (Model 111B) at a wavelength of 254 nm). A flow rate of 1 $mL.min^{-1}$ was used unless otherwise stated.

Reagents were purified by standard means under an argon atmosphere. Dichloromethane, 1,2-dichloroethane, methanol, *tert*-butylmethylether (MTBE), acetonitrile, triethylamine, di-*iso*-propylamine, 2,6-lutidine, pyridine, benzene and toluene were distilled from calcium hydride. *n*-Butyronitrile and *iso*-butyraldehyde were distilled from $CaCl_2$. Tetrahydrofuran and diethylether

were distilled from potassium/benzophenone and sodium wire/benzophenone respectively. Acetic acid was purified by heating with $CrO_3$ and subsequent distillation. Di-*iso*-propylethylamine was first distilled from ninhydrin and then from KOH. DDQ was recrystallised from a saturated solution of refluxing chloroform ($CHCl_3$). All other chemicals were used as received, except where explicitly stated otherwise. Solvents used for all extractions in work-up were distilled. Aqueous solutions of sodium bicarbonate ($NaHCO_3$), sodium carbonate ($Na_2CO_3$), sodium chloride (brine), sodium sulfite ($Na_2SO_3$), sodium thiosulfate ($Na_2S_2O_3$), ammonium chloride ($NH_4Cl$), Rochelle salt ($Na^+/K^+$ tartrate), copper(II) sulfate ($CuSO_4$) and pH 7 buffer were saturated. Molecular sieves were activated by heating under vacuum and/or in a microwave.

Ozone was generated using a Peak Scientific Ozone Generator connected to a dioxygen supply. Quenching of excess $O_3$ was affected by purging with an $O_2$ stream.

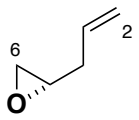
All experiments were performed under anhydrous conditions (barring those where water is a solvent or is liberated through the course of the reaction), using oven-dried apparatus, an argon atmosphere and standard techniques for handling air-sensitive materials. Unless otherwise stated, reactions were performed at room temperature (rt).

## 2) Experimental Data for the C1-C19 Fragments

### 2.1 Synthesis of the C1-C8 Methyl Ketone 9

#### 2.1.1 Route A

**EPOXIDE 13**



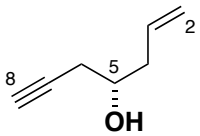

Copper(I) bromide (717 mg, 5.00 mmol) was suspended in $Et_2O$ (100 mL) and cooled to –78 ºC. Vinyl magnesium bromide (50.0 mL, 50.0 mmol, 1 M solution in THF) was added, followed by (*S*)-(+)-epichlorohydrin **12** (3.91 mL, 50.0 mmol). The reaction was warmed to –78 ºC and stirred for 6 h. The mixture was poured on to water (200 mL), extracted with $Et_2O$ (3 × 100 mL) and dried ($Na_2SO_4$). $Et_2O$ was removed under reduced pressure (30 ºC, 300 mmHg). Distillation sequentially removed THF and collected the purified product. The intermediate chlorohydrin **98** (4.43 g, 36.7 mmol, 73%) was afforded as a colourless oil (68 ºC, 20 mmHg). Chlorohydrin **98** (2.63 g, 21.8 mmol) was added to freshly ground potassium hydroxide pellets (4.37 g, 36.2 mmol) and distilled at atmospheric pressure. The product was further dried ($Na_2SO_4$) and decanted. Epoxide **13** (2.28 g, 27.1 mmol, 75%) was collected as a colourless oil (80 ºC, 1 atm).

**98**: **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 5.82 (1H, ddt, *J* = 17.3, 10.3, 7.1 Hz, C5H), 5.17 (1H, ddd, *J* = 17.3, 3.3, 1.5 Hz, C6$H_aH_b$), 5.16 (1H, ddd, *J* = 10.3, 2.0, 1.1 Hz, C6$H_aH_b$), 3.88 (1H, m, C3H), 3.63 (1H, dd, *J* = 11.1, 3.8 Hz, C4$H_aH_b$), 3.51 (1H, dd, *J* = 11.1, 6.6 Hz, C4$H_aH_b$), 2.35 (2H, m, C2$H_2$), 2.22 (1H, d, *J* = 4.8 Hz, C3(H)OH). **$[\alpha]_D^{20}$** +4.9 (*c* = 1.0, $CHCl_3$).

**13**: **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 5.83 (1H, ddt, *J* = 17.1, 10.3, 6.7 Hz, C5H), 5.17 (1H, ddt, *J* = 17.1, 1.6, 1.6 Hz, C6$H_aH_b$), 5.11 (1H, ddt, *J* = 10.3, 1.8, 1.2 Hz, C6$H_aH_b$), 3.00 (1H, ddt, *J* = 5.4, 3.9, 2.7 Hz, C3H), 2.77 (1H, dd, *J* = 5.0, 3.9 Hz, C2$H_aH_b$), 2.51 (1H, dd, *J* = 5.0, 2.7 Hz, C2$H_aH_b$), 2.38-2.27 (2H, m, C4$H_2$). **$[\alpha]_D^{20}$** –0.8 (*c* = 1.0, $CHCl_3$).

This data is in agreement with that reported by Gupta *et al.*[1]

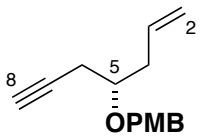
**ALCOHOL 99**




Lithium acetylene•ethylene diamine complex (205 mg, 2.00 mmol) was dissolved in DMSO (1.5 mL) and the mixture was stirred for 30 minutes at rt. Epoxide **13** (187 mg, 1.00 mmol) was added and the reaction was stirred for 24 h at rt. After addition of water (20 mL), the mixture was extracted with $Et_2O$ (3 × 20 mL) and the combined organic phases were washed with brine (2 × 20 mL), dried ($Na_2SO_4$) and filtered. Careful evaporation of the solvent (40 °C, 500 Torr) gave the alcohol **99** as a colourless oil in an $Et_2O$ solution (99.0 mg, 90%).

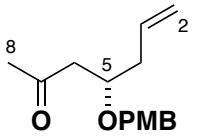
**$R_f$** 0.38 (3:1 PE/EtOAc). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta_H$ 5.83 (1H, ddt, *J* = 17.5, 10.3, 7.1 Hz, C3H), 5.20-5.13 (2H, m, C2H), 3.88-3.79 (1H, m, C5H), 2.47-2.25 (4H, m, C4$H_aH_b$, C4$H_aH_b$, C6$H_aH_b$, C6$H_aH_b$), 2.06 (1H, t, *J* = 2.7 Hz, C8H), 2.00 ppm (1 H, d, 3J = 3.8 Hz, C5(H)OH).
This data is in agreement with that reported by Maddess *et al.*[2]

**PMB ETHER 14**




Alcohol **99** (469 mg, 4.26 mmol) was dissolved in THF (15 mL), cooled to 0 °C and sodium hydride (241 mg, 6.02 mmol, 60% dispersion in mineral oil) was added. After stirring for 30 minutes at 0 °C, 4-methoxybenzyl bromide (0.87 mL, 6.02 mmol) was added dropwise and the reaction was warmed to rt overnight. The reaction mixture still contained some starting material. Additional sodium hydride (37.0 mg, 926 µmol, 60% dispersion in mineral oil) and 4-methoxybenzyl bromide (130 µL, 926 µmol) was added and the reaction was stirred for 3 h at rt. Thereafter, triethylamine (2 mL) and MeOH (3 mL) were added and the mixture was stirred for 30 min at rt to react the excess 4-methoxybenzyl bromide. The reaction mixture was diluted with $Et_2O$ (50 mL) and filtered through $SiO_2$, eluting with $Et_2O$, and the solvents were evaporated under reduced pressure. The crude product was purified by column chromatography (6:1 → 4:1 PE/EtOAc) yielded the PMB ether **14** as a colourless oil (761 mg, 1.17 mmol, 78%).
**$R_f$** 0.44 (3:1 PE/EtOAc). **$^1$H NMR** (400 MHz, $CDCl_3$) $\delta_H$ 7.28 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}$H), 6.87 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}$H), 5.83 (1 H, ddt, *J* = 17.2, 10.2, 7.1 Hz, C3H), 5.17-5.06 (2H, m, C2H), 4.57 (1H, d, *J* = 11.4 Hz, C5(H)OC$H_aH_bAr_{PMB}$), 4.50 (1H, d, *J* = 11.4 Hz, C5(H)OC$H_aH_bAr_{PMB}$), 3.80 (3H, s, $Ar_{PMB}$OMe), 3.60 (1H, qn, *J* = 5.9 Hz, C5H), 2.50-2.35 (4H, m, C4$H_aH_b$, C4$H_aH_b$, C6$H_aH_b$, C6$H_aH_b$), 2.01 (1H, t, *J* = 2.7 Hz, C8H). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.4, 134.3, 130.6, 129.4, 117.7, 113.9, 81.3, 76.5, 71.1, 70.2, 55.4, 38.1, 23.6. **IR** (thin film) 3293, 2910, 2836, 2119, 1613, 1514, 1464, 1440, 1347, 1302, 1248, 1173, 1091, 1037, 996, 916, 822, 734 $cm^{-1}$. **$[\alpha]_D^{20}$** +10.7 (*c* = 1.0, $CHCl_3$). **HRMS** ($ES^+$) Calculated for $C_{15}H_{22}O_2N$ $[M + NH_4]^+$ 248.1645, found 248.1645.

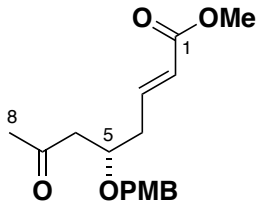
**METHYL KETONE 15**




Alkyne **14** (731 mg, 3.17 mmol) was dissolved in acetone (25 mL) and water (110 µL, 6.34 mmol) and PPTS (1.19 g, 4.76 mmol) and $Hg(OAc)_2$ (303 mg, 950 µmol) were added. After stirring for 16 h at rt, the mixture was diluted with $Et_2O$ (20 mL) and filtered through $SiO_2$, eluting with $Et_2O$, and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (3:1 → 2:1 PE/EtOAc) to yield the product methyl ketone **15** as a colourless oil (649 mg, 2.61 mmol, 82%).
**$R_f$** 0.28 (3:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.23 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 6.86 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 5.81 (1H, ddt, *J* = 17.4, 10.4, 7.1 Hz, C3H), 5.13-5.07 (2H, m, C2H), 4.52 (1H, d, *J* = 10.9 Hz,

C5(H)OC$\underline{H_a}H_bAr_{PMB}$), 4.42 (1H, d, *J* = 10.9 Hz, C5(H)OC$H_a\underline{H_b}Ar_{PMB}$), 4.03-3.96 (1H, m, C5$\underline{H}$), 3.79 (3 H, s, $Ar_{PMB}O\underline{Me}$), 2.71 (1H, dd, *J* = 16.2, 7.8 Hz, C6$\underline{H_a}H_b$), 2.52 (1H, dd, *J* = 16.2, 4.6 Hz, C6$H_a\underline{H_b}$), 2.40-2.28 (2H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$,), 2.14 ppm (3H, s, C8$\underline{H_3}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 207.6, 159.4, 134.2, 130.6, 129.5, 117.9, 113.9, 74.7, 71.4, 55.4, 48.3, 38.5, 31.3. **$[\alpha]_D^{20}$** +40.7 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 2912, 2251, 1713, 1612, 1514, 1302, 1247, 1173, 1073, 1035, 909, 731 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{15}H_{24}O_3N$ [M + $NH_4$]$^+$ 266.1751, found 266.1752.

**METHYL KETONE 9**

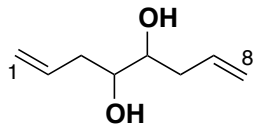



Grubbs II catalyst (21.7 mg, 25.6 µmol, 1 mol%) was dissolved in $CH_2Cl_2$ (7.5 mL) and methyl ketone **15** (636 mg, 2.56 mmol) and methyl acrylate (460 µL, 5.12 mmol) were added sequentially. The mixture was stirred at rt for 6 d. After diluting the reaction mixture with PE/EtOAc (20 mL, 2:1), the solution was filtered through $SiO_2$, eluting with PE/EtOAc (2:1), and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (10:1 PE/EtOAc) to yield the ketone **9** as colourless oil (635 mg, 2.07 mmol, 81%). Resubmission of the residual starting material together with the homodimer of ketone **15** under the above condition yielded more of the desired product **9** (85.2 mg, 278 µmol, 11%).

**$R_f$** 0.39 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.23-7.19 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.93 (1H, dt, *J* = 15.6, 7.6 Hz, C3$\underline{H}$), 6.87-6.83 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.86 (1H, dt, *J* = 15.6, 1.5 Hz, C2$\underline{H}$), 4.47 (2H, d, *J* = 11.1Hz, C5(H)OC$\underline{H_a}H_bAr_{PMB}$), 4.43 (2H, d, J = 11.1Hz, C5(H)OC$H_a\underline{H_b}Ar_{PMB}$), 4.05 (1H, dddd, *J* = 16.4, 7.6, 7.4, 5.5 Hz, C5$\underline{H}$(OR)), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.73 (3H, s, C1$O_2\underline{Me}$), 2.74 (1H, dd, *J* = 16.5, 7.4 Hz, C6$\underline{H_a}H_b$), 2.50-2.39 (3H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$, C6$H_a\underline{H_b}$), 2.13 (3H, s, C8$\underline{H_3}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 206.7, 166.5, 159.3, 144.5, 130.0, 129.4, 123.7, 113.8, 73.6, 71.5, 55.2, 51.4, 48.0, 36.7, 31.0. **IR** (thin film) 3018.9, 2951.3, 1715.2, 1658.3, 1612.6, 1586.5, 1513.7 $cm^{-1}$. **$[\alpha]_D^{20}$** +25.5 (*c* = 1.0, $CHCl_3$). **HRMS** ($ES^+$) Calculated for $C_{17}H_{22}O_5$ [M + $NH_4$]$^+$ 324.1805, found at 324.1802.

### 2.1.2 Route B

**DIOL 100**



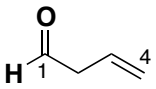

Potassium iodide (20.0 g, 120 mmol) and $SnCl_2 \cdot 2H_2O$ (13.5 g, 60.0 mmol) were dissolved in water (100 mL) and warmed to 35 ºC. To the orange suspension was added allyl bromide (5.20 mL, 60.0 mmol) and glyoxal (2.30 mL, 20.0 mmol, 40% solution in $H_2O$) was added dropwise *via* dropping funnel over 10 min at 30 ºC. The reaction was stirred for 30 min at this temperature and then extracted with $CH_2Cl_2$ (2 × 150 mL). The organic extracts were washed with sodium thiosulfate solution (200 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The product was purified by column chromatography (1:1 PE/EtOAc). Diol **100** (2.30 g, 16.2 mmol, 81%) was collected as colourless crystals as a mixture of diastereoisomers (2.3:1).

**$R_f$** 0.35 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 5.86 (2H, tdd, *J* = 10.9, 6.7, 2.8 Hz, C2H, C7H), 5.21-5.12 (4H, m, C1$H_2$ , C8$H_2$), 3.67* (2H, ddt, *J* = 6.2, 3.7, 3.3 Hz, C4H, C5H), 3.55 (2H, ddt, *J* = 5.0, 4.6, 4.5 Hz, C4H, C5H), 2.39* (2H, ddt, *J* = 4.6, 2.5, 1.5 Hz, C3$H_aH_b$, C6$H_aH_b$), 2.35 (2H, ddt, J = 4.6, 2.5, 1.5 Hz, C3$H_aH_b$, C6$H_aH_b$), 2.31-2.22 (2H, m, C3$H_aH_b$, C6$H_aH_b$), 2.09 (1H, d, *J* = 4.5 Hz, OH), 1.99* (1H, d, *J* = 3.3 Hz, OH).

(* indicates distinguishable peaks from the minor diastereomer)

This data is in agreement with that reported by Samoshin *et al.*[3]

**BUT-3-ENAL 18**

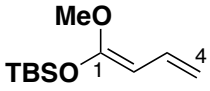



A solution of diol **100** (1.02 g, 7.17 mmol), pH 4 buffer (1.5 mL) and $CH_2Cl_2$ (2.5 mL) was prepared at rt. Sodium metaperiodate (3.00 g, 14.0 mmol) was added and the reaction stirred until complete by TLC (45 min). The organic phase was separated and washed with sodium thiosulfate solution (5 mL) and brine (5 mL). After drying ($Na_2SO_4$) and filtering, aldehyde **18** in $CH_2Cl_2$ was used in further experiments immediately.

**$R_f$** 0.50 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 9.70 (1H, t, *J* = 1.8 Hz, C1HO), 5.92 (1H, ddt, *J* = 17.3, 10.4, 6.8 Hz, C3H), 5.29 (1H, obs dd, *J* = 10.4, 1.8 Hz, C4$H_aH_b$), 5.22 (1H, dd, *J* = 17.3, 1.3 Hz, C4$H_aH_b$), 3.20 (2H, dd, *J* = 6.9, 1.8 Hz, C2$H_2$).

This data is in agreement with that reported by Crimmins *et al.*[4]

**SILYL KETENE ACETAL 17**

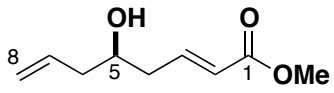



To a solution of di-*iso*-propylamine (23.4 mL, 166 mmol) in THF (250 mL) at 0 ºC was added *n*-butyllithium (100 mL, 160 mmol, 1.60 M solution in hexanes). The mixture was stirred at 0 ºC for 15 min and cooled to –78 ºC. DMPU (25.3 mL, 210 mmol) was added and the resulting white suspension stirred for 15 min. Methyl crotonate (13.4 mL, 126 mmol) was added and the resulting yellow solution stirred for 15 min. *tert*-Butyldimethylsilyl chloride (24.6 g, 163 mmol) in THF (25 mL) was added slowly *via* cannula over 10 min and the reaction stirred for a further 45 min at –78 ºC before warming to rt for 3 h. The reaction was quenched on the addition of $NaHCO_3$ solution (125 mL) and extracted with PE (2 × 500 mL). The combined organic extracts were washed with $NaHCO_3$ solution (5 × 250 mL) and brine (250 mL). The solution was further dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. Silyl ketene acetal **17** (22.0 g, 103 mmol, 62%) was obtained after distillation (55 ºC, 0.3 mmHg) as a colourless liquid.

**$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 6.53 (1H, dt, *J* = 17.2, 10.4 Hz, C3H), 4.85 (1H, dd, *J* = 17.2, 2.1 Hz, C4$H_aH_b$), 4.60 (1H, dd, *J* = 17.3, 2.2 Hz, C4$H_aH_b$), 4.48 (1H, d, *J* = 10.4 Hz, C2H), 3.57 (3H, s, C1OMe), 0.95 (9H, s, C1OSi$^t$BuMe$_2$), 0.18 (6H, s, C1OSi$^t$BuMe$_2$).

This data is in agreement with that reported by Simsek *et al*.[5]

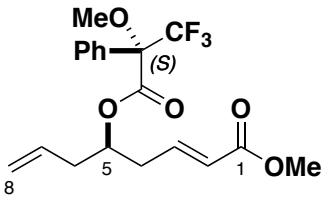
**ALCOHOL 19**




*N*-Tosyl-D-tryptophan (10.2 g, 28.4 mmol) was suspended in $CH_2Cl_2$ (250 mL). Phenylboron dichloride (3.13 mL, 30.6 mmol) was slowly added and the brown solution stirred at rt for 1 h. The $CH_2Cl_2$ was removed under reduced pressure and replaced with *n*-butyronitrile (100 mL) before cooling to –78 ºC. A solution of silyl ketene acetal **17** (7.65 g, 35.7 mmol), aldehyde **18** (1.34 g, 19.1 mmol) and *iso*-propanol (2.5 mL) in *n*-butyronitrile (25 mL) was added slowly *via* cannula over 20 min. The reaction was stirred at –78 ºC for 3 h before quenching with $NaHCO_3$ solution (500 mL). The mixture was extracted with $Et_2O$ (3 × 250 mL), washed with brine (250 mL) and dried ($Na_2SO_4$). The crude product was filtered, concentrated *in vacuo* and purified by column chromatography (6:1 PE/EtOAc followed separately by 10:1 PE/EtOAc (long column of $SiO_2$)). Alcohol **19** (1.83 g, 10.8 mmol, 57%) was collected as a yellow oil.

**$R_f$** 0.54 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 6.99 (1H, dt, *J* = 15.8, 7.6 Hz, C3H), 5.92 (1H, dt, *J* = 15.8, 1.5 Hz, C2H), 5.86-5.77 (1H, m, C7H), 5.19-5.18 (1H, m, C8$H_aH_b$), 5.17-5.14 (1H, m, C8$H_aH_b$), 3.85-3.78 (1H, m, C5H), 3.73 (3H, s, C1O$_2$Me), 2.46-2.29 (3H, m, C4$H_2$, C6$H_aH_b$), 2.23-2.16 (1H, m, C6$H_aH_b$), 1.71 (1H, d, *J* = 3.5 Hz, C5(H)OH). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 166.7, 145.2, 134.0, 123.5, 118.7, 69.3, 51.4, 41.5, 39.4. **$[\alpha]_D^{20}$** –8.1 (*c* = 1.4, $CHCl_3$). **IR** (thin film) 3438.3 (br), 3017.4, 2951.1, 1709.4, 1658.4, 1642.9 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_9H_{14}O_3$ $[M + NH_4]^+$ 188.1281, found 188.1283.

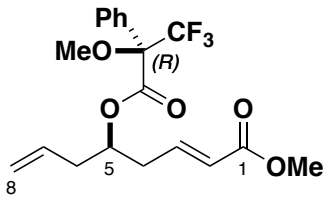
**MOSHER ESTER 19S**




(*S*)-MTPA (10 mg, 42 µmol) was dissolved in $CH_2Cl_2$ (0.2 mL) and DMAP (1 crystal) added. DCC (0.2 mL, 1.0 M in $CH_2Cl_2$) was added to the stirring solution, followed by the secondary alcohol **19** (5.0 mg, 29 µmol). When the reaction was complete by TLC, the solvent was evaporated and the crude product purified by column chromatography (10:1 PE/EtOAc, transferred in PE). Mosher ester **19S** (8.8 mg, 23 µmol, 79%) was prepared as a colourless oil.

**$R_f$** 0.72 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.53-7.49 (2H, m, $Ar_{Ph}\underline{H}$), 7.43-7.34 (3H, m, $Ar_{Ph}\underline{H}$), 6.75 (1H, dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 5.78 (1H, dt, *J* = 15.7, 1.4 Hz, C2$\underline{H}$), 5.74 (1H, ddt, *J* = 16.2, 11.1, 7.1 Hz, C7$\underline{H}$), 5.27 (1H, tt, *J* = 6.2, 6.1 Hz, C5$\underline{H}$), 5.14 (1H, dt, *J* =11.1, 1.5 Hz, C8$\underline{H_a}H_b$), 5.13 (1H, dt, *J* = 16.2, 1.1 Hz, C8$H_a\underline{H_b}$), 3.71 (3H, s, C1$O_2\underline{Me}$), 3.53 (3H, s, C(Ph)($CF_3$)(O$\underline{Me}$)), 2.50 (2H, ddd, *J* = 7.4, 6.1, 1.4 Hz, C4$\underline{H_2}$), 2.44 (2H, dddd, *J* = 7.1, 6.2, 1.5, 1.1 Hz, C6$\underline{H_2}$).

**MOSHER ESTER 19R**

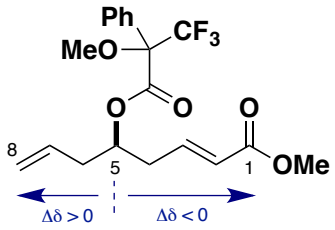



(*R*)-MTPA (10 mg, 42 µmol) was dissolved in $CH_2Cl_2$ (0.2 mL) and DMAP (1 crystal) added. DCC (0.2 mL, 1.0 M in $CH_2Cl_2$) was added to the stirring solution, followed by the secondary alcohol **19** (5.0 mg, 29 µmol). When the reaction was complete by TLC, the solvent was evaporated and the crude product purified by column chromatography (10:1 PE/EtOAc, transferred in PE). Mosher ester **19R** (7.5 mg, 19 µmol, 66%) was prepared as a colourless oil.

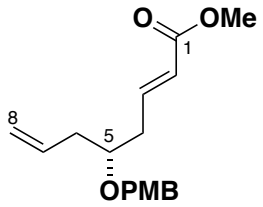
**$R_f$** 0.72 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.52-7.48 (2H, m, $Ar_{Ph}\underline{H}$), 7.41-7.35 (3H, m, $Ar_{Ph}\underline{H}$), 6.87 (1H, dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 5.88 (1H, dt, *J* = 15.7, 1.4 Hz, C2$\underline{H}$), 5.62 (1H, ddt, *J* = 16.2, 11.1, 7.1 Hz, C7$\underline{H}$), 5.25 (1H, tt, *J* = 6.2, 6.1 Hz, C5$\underline{H}$), 5.06 (1H, dt, *J* = 11.1, 1.5 Hz, C8$\underline{H_a}H_b$), 5.05 (1H, dt, *J* = 16.2, 1.1 Hz, C8$H_a\underline{H_b}$), 3.73 (3H, s, C1$O_2\underline{Me}$), 3.51 (3H, s, C(Ph)($CF_3$)(O$\underline{Me}$)), 2.56 (2H, ddd, *J* = 7.4, 6.1, 1.4 Hz, C4$\underline{H_2}$), 2.38 (2H, dddd, *J* = 7.1, 6.2, 1.5, 1.1 Hz, C6$\underline{H_2}$).

**MOSHER ESTER ANALYSIS OF 19S AND 19R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C1$O_2$Me | 3.71 | 3.73 | –0.02 |
| C2H | 5.78 | 5.88 | –0.10 |
| C3H | 6.75 | 6.87 | –0.12 |
| C4$H_2$ | 2.50 | 2.56 | –0.06 |
| C5H | 5.27 | 5.25 | +0.02 |
| C6$H_2$ | 2.44 | 2.38 | +0.06 |
| C7H | 5.74 | 5.62 | +0.12 |
| C8$H_aH_b$ | 5.14 | 5.06 | +0.08 |
| C8$H_aH_b$ | 5.13 | 5.05 | +0.08 |



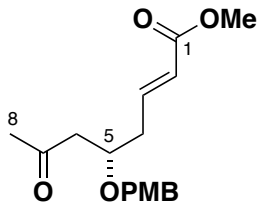
**PMB ETHER 20**




Alcohol **19** (187 mg, 1.10 mmol) and 4-methoxybenzyl-2,2,2-trichloroacetimidate (466 mg, 1.65 mmol) were concentrated from benzene (5.0 mL) and dissolved in THF (10 mL). The solution was cooled to 0 ºC and triphenylcarbenium tetrafluoroborate (18.2 mg, 55.0 µmol) added. The mixture was warmed to rt and stirred for 24 h. The reaction was quenched with MeOH (1.0 mL) and after stirring for 30 min was diluted with EtOAc (10 mL) and $NaHCO_3$ solution (10 mL). The organic phase was separated and the aqueous phase extracted with EtOAc (3 × 15 mL). The combined extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (20:1 → 10:1 PE/EtOAc). Methyl enoate **20** (203 mg, 699 µmol, 64%) was collected as a colourless oil.

**$R_f$** 0.33 (10:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.26 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.97 (1H, dt, *J* = 15.6, 7.4 Hz, C3$\underline{H}$), 6.88 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.87 (1H, dt, *J* = 15.6, 1.5 Hz, C2$\underline{H}$), 5.81 (1H, m, C7$\underline{H}$), 5.13-5.09 (1H, m, C8$\underline{H_a}H_b$), 5.08-5.06 (1H, m, C8$H_a\underline{H_b}$), 4.50 (1H, d, *J* = 11.3 Hz, C5(H)OC$\underline{H_a}H_bAr_{PMB}$), 4.45 (1H, d, *J* = 11.3 Hz, C5(H)OC$H_a\underline{H_b}Ar_{PMB}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.73 (3H, s, C1$O_2\underline{Me}$), 3.56 (1H, tt, *J* = 5.9, 5.9 Hz, C5$\underline{H}$), 2.45-2.40 (2H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$), 2.39-2.25 (2H, m, C6$\underline{H_a}H_b$, C6$H_a\underline{H_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 166.8, 159.2, 145.6, 134.2, 130.4, 129.3, 123.1, 117.6, 113.8, 71.4, 70.8, 55.3, 51.4, 38.3, 36.6. **$[\alpha]_D^{20}$** –6.6 (*c* = 1.3, $CHCl_3$). **IR** (thin film) 2935.7, 2837.8, 1721.2, 1657.3, 1612.6, 1586.1, 1513.2 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{17}H_{22}O_4$ $[M + NH_4]^+$ 308.1856, found 308.1857.

**METHYL KETONE 9**

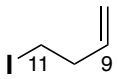



A suspension of $PdCl_2$ (38.0 mg, 0.321 mmol) and CuCl (321 mg, 3.21 mmol) in 7:1 DMF/$H_2O$ (20 mL) was prepared and stirred under an $O_2$ atmosphere for 30 min at 0 ºC. Olefin **20** (931 mg, 3.21 mmol) in 10 mL DMF–$H_2O$ (7:1) was added and the reaction stirred at 0 ºC for 24 h. The reaction was warmed to rt and stirred for a further 12 h. The resulting green suspension was diluted with pH 7 buffer (40 mL) and $CH_2Cl_2$ (100 mL) and the organic phase separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 100 mL) and the organic extracts washed with saturated aqueous $CuSO_4$ solution (100 mL) and brine (2 × 200 mL). The solution was dried ($Na_2SO_4$), filtered, concentrated *in vacuo* and purified by column chromatography (10:1 PE/EtOAc). Methyl ketone **9** (641 mg, 2.08 mmol, 63%) was isolated as a pale yellow oil. Also separated was the isomeric aldehyde (31.0 mg, 101 µmol, 5%) and recovered alkene **20** (70.0 mg, 241 µmol, 8%). All spectroscopic data for **9** matched the material generated from Route A

**$R_f$** 0.39 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.23-7.19 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.93 (1H, dt, *J* = 15.6, 7.6 Hz, C3$\underline{H}$), 6.87-6.83 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.86 (1H, dt, *J* = 15.6, 1.5 Hz, C2$\underline{H}$), 4.47 (2H, d, *J* = 11.1Hz, C5(H)OC$\underline{H_a}H_bAr_{PMB}$), 4.43 (2H, d, J = 11.1Hz, C5(H)OC$H_a\underline{H_b}Ar_{PMB}$), 4.05 (1H, dddd, *J* = 16.4, 7.6, 7.4, 5.5 Hz, C5$\underline{H}$(OR)), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.73 (3H, s, $C1O_2\underline{Me}$), 2.74 (1H, dd, *J* = 16.5, 7.4 Hz, C6$\underline{H_a}H_b$), 2.50-2.39 (3H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$, C6$H_a\underline{H_b}$), 2.13 (3H, s, C8$\underline{H_3}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 206.7, 166.5, 159.3, 144.5, 130.0, 129.4, 123.7, 113.8, 73.6, 71.5, 55.2, 51.4, 48.0, 36.7, 31.0. **IR** (thin film) 3018.9, 2951.3, 1715.2, 1658.3, 1612.6, 1586.5, 1513.7 $cm^{-1}$. **$[\alpha]_D^{20}$** +25.5 (*c* = 1.0, $CHCl_3$). **HRMS** ($ES^+$) Calculated for $C_{17}H_{22}O_5$ $[M + NH_4]^+$ 324.1805, found at 324.1802.

## 2.2. Synthesis of the C9-C13 Fragment 8

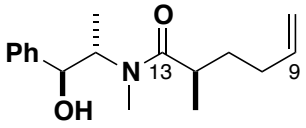
**4-IODOBUT-1-ENE**




Triphenylphosphine (11.0 g, 42.0 mmol) and imidazole (2.86 g, 42.0 mmol) were dissolved in $CH_2Cl_2$ (100 mL) and the solution cooled to 0 ºC. Iodine (10.7 g, 42.0 mmol) was added slowly (exothermic) and the reaction stirred for 15 min. 3-Buten-1-ol (3.48 mL, 40.0 mmol) was added slowly at 0 ºC (exothermic) and the mixture warmed to rt for 3 h. The solvent was removed *in vacuo* (30 ºC, 500 mmHg) and replaced with pentane (200 mL). The suspension was filtered through Celite® and the filtrate was decanted away from any further recrystallised $PPh_3$. The solution was concentrated *in vacuo* (30 ºC, 500 mmHg) and distilled (33 ºC, 23 mmHg) to afford 4-iodo-but-1-ene (18.9 g, 28.5 mmol, 68%) as a colourless liquid to be used as soon as possible.

**$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 5.75 (1H, ddt, *J* = 18.2, 11.3, 6.7 Hz, C9$\underline{H}$), 5.12 (1H obs dt, C9(H)C$\underline{H_a}H_b$), 5.11 (1H, obs dt, C9(H)C$H_a\underline{H_b}$), 3.18 (2H, t, *J* = 7.3 Hz, C11$\underline{H_2}$), 2.62 (2H, dtt, *J* = 7.3, 6.7, 1.3 Hz, C10$\underline{H_2}$).
This data is in agreement with that reported by Ren *et al.*[7]

**AMIDE 22**

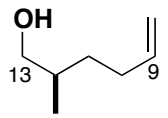



A suspension of lithium chloride (1.75 g, 45.6 mmol, dried in an oven (200 ºC) for 1 d *in vacuo*) in THF (15 mL) was cooled to 0 ºC. After sequential addition of di-*iso*-propylamine (2.40 mL, 17.1 mmol) and *n*-butyllithium (9.86 mL, 15.8 mmol, 1.6 M solution in hexanes), the reaction was stirred for 15 min before warming to rt for a further 20 min. The mixture was cooled to –78 ºC and a solution of amide **21**[8] (1.69 g, 7.60 mmol) in THF (30 mL) was added *via* cannula and stirred for 45 min. The reaction was warmed to 0 ºC for 15 min and to rt for a further 15 min. After cooling to –78 ºC, 4-iodobut-1-ene (2.76 g, 15.2 mmol) was added dropwise and the mixture stirred for 1 h before warming to 0 ºC for 1 h. When complete by TLC ($KMnO_4$ stain), the reaction was quenched with $NH_4Cl$ solution (25 mL) and $Na_2S_2O_3$ solution (1 mL). The phases were separated and the aqueous layer extracted with EtOAc (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (2:1 → 1:1 PE/EtOAc) to afford amide **22** (1.98 g, 7.14 mmol, 94%) as a yellow oil.

**$R_f$** 0.42 (1:4 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39-7.30 (4H, m, Ar$_{Ph}\underline{H}$), 7.28-7.25 (1H, m, Ar$_{Ph}\underline{H}$), 5.78 (1H, m, C9$\underline{H}$), 4.95 (1H, br s, C9(H)$\underline{H_a}H_b$), 4.93-4.91 (1H, br m, C9(H)$\underline{H_a}H_b$), 4.61 (1H, d, *J* = 7.6 Hz, PhC$\underline{H}$(OH)R), 4.44 (1H, br s, PhCH(O$\underline{H}$)R), 2.84 (3H, s, C(O)N$\underline{Me}$R), 2.63 (1H, dq, *J* = 7.6, 6.8 Hz, C(O)N(Me)C$\underline{H}$(Me)R), 2.09-2.04 (1H, m, C12$\underline{H}$), 2.04-1.89 (2H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$), 1.82-1.71 (1H, m, C11$\underline{H_a}H_b$), 1.45-1.35 (1H, m, C11$H_a\underline{H_b}$), 1.13 (3H, d, *J* = 7.0 Hz, C12(H)$\underline{Me}$), 1.09 (3H, d, *J* = 6.8 Hz,

C(O)N(Me)CH(Me)R), [data corresponds to that of the major rotamer where appropriate]. **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 178.9, 142.6, 138.3, 128.3, 127.6, 126.3, 115.0, 77.3, 77.1, 76.5, 35.7, 33.0, 31.5, 17.4, 14.5. **$[\alpha]_D^{20}$** –61.6 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 3401, 2942, 2866, 1621, 1463, 1105, 701, 680, 658 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{17}H_{25}NO_2$ $[M + H]^+$ 276.1958, found 276.1960.

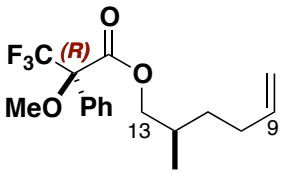
**ALCOHOL 23**




*n*-Butyllithium (71.6 mL, 115 mmol, 1.6 M solution in hexanes) was added slowly to a solution of di-*iso*-propylamine (16.9 mL, 120 mmol) in THF (45 mL) at 0 ºC and stirred for 1 h. $NH_3 \cdot BH_3$ (3.71 g, 120 mmol) was added and the suspension stirred at 0 ºC for a further 1 h. A solution of amide **22** (7.89 g, 28.7 mmol) in THF (30 mL) was added *via* cannula and the mixture allowed to warm to rt for 4 h. The reaction was quenched at 0 ºC on the addition of HCl solution (120 mL, 2 M), extracted with $Et_2O$ (3 × 100 mL) and the combined organic phases were with a 1:1 solution of aqueous HCl (1.5 M) and brine (2 × 100 mL). The organic phase was dried ($Na_2SO_4$) and carefully concentrated *in vacuo* (30-35 ºC, 300 mmHg) to give the crude alcohol in a solution of $Et_2O$/THF. The crude product was purified by column chromatography (9:1 $PE_{30\text{-}40}/Et_2O$) and carefully concentrated *in vacuo* (35-40 ºC, 250 mmHg) to afford alcohol **23** (3.14 g containing *ca.* 8%wt $Et_2O$, 25.6 mmol, 88%) as a colourless, volatile oil.

**$R_f$** 0.61 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 5.74 (1H, ddt, *J* = 17.2, 10.3, 6.6 Hz, C9H), 4.95 (1H, dt, *J* = 17.2, 2.0 Hz, C9(H)C$H_aH_b$), 4.86 (1H, dt, *J* = 10.3, 2.1 Hz, C9(H)C$H_aH_b$), 3.45 (1H, dd, *J* = 10.5, 5.8 Hz, C13$H_aH_b$), 3.36 (1H, dd, *J* = 10.5, 6.4 Hz, C13$H_aH_b$), 2.08-1.95 (2H, m, C10$H_2$), 1.63-1.54 (1H, m, C12H), 1.50 (1H, m, C11$H_aH_b$), 1.26 (1H, br s, C13$H_2$OH), 1.20-1.10 (1H, m, C11$H_aH_b$), 0.86 (3H, d, *J* = 6.7 Hz, C12(H)Me). **$[\alpha]_D^{20}$** +10.2 (*c* = 1.1, $CHCl_3$). **IR** (thin film) 3414, 2961, 2932, 2877, 2248, 1458, 1426, 1385, 1090, 1041, 991, 756 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_7H_{14}O$ $[M + NH_4]^+$ 114.1039, found 114.1037.

**MOSHER ESTER 23R**

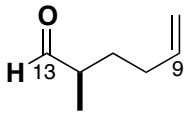



Alcohol **23** (10 mg, 88 µmol) was dissolved in $CH_2Cl_2$ (0.3 mL) and DMAP (1 crystal) and (*R*)-MTPA (82 mg, 175 *µ*mol) were added. DCC (0.3 mL, 1.0 M in $CH_2Cl_2$) was added to the stirring solution and the reaction stirred at rt for 16 h. When the reaction was complete by TLC, the solvent was evaporated and the crude product (single compound by $^1$H NMR spectroscopy) purified by column chromatography (50:1 PE/EtOAc, transferred in PE) to give ester **23R** (14.5 mg, 44 µmol, 50%, >95:5 dr) as a colourless oil.

**$R_f$** 0.53 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.53-7.50 (2H, m, $Ar_{Ph}H$), 7.42-7.38 (3H, m, $Ar_{Ph}H$), 5.75 (1H, ddt, *J* = 16.9, 10.2, 6.7 Hz, C9H), 5.00 (1H, ddd, *J* = 16.9, 3.4, 1.6 Hz, C9(H)C$H_aH_b$), 4.95 (1H, br

d, *J* = 10.2 Hz, C9(H)$CH_aH_b$), 4.24 (1H, dd, *J* = 10.7, 5.7 Hz, C13$H_aH_b$), 4.10 (1H, dd, *J* = 10.7, 6.5 Hz, C13$H_aH_b$), 3.55 (3H, s, $O_2C(CF_3)(Ph)(OMe)$), 2.15-1.98 (2H, m, C10$H_2$), 1.94-1.84 (1H, m, C12H), 1.50-1.42 (1H, m, C11$H_aH_b$), 1.33-1.22 (1H, m, C11$H_aH_b$), 0.93 (3H, d, *J* = 6.8, C12(H)Me). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 166.7, 138.2, 132.4, 129.6, 128.4, 127.4, 124.5, 122.2, 114.8, 71.0, 55.4, 32.2, 31.8, 30.8, 16.6. **$[\alpha]_D^{20}$** +37.9 (*c* = 0.39, $CHCl_3$). **IR** (thin film) 2926, 2853, 1748, 1451, 1261, 1169, 1122, 1082, 1021, 913 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{17}H_{25}F_3NO_3$ $[M + NH_4]^+$ 348.1787, found 348.1789.

**ALDEHYDE 8**

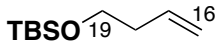



To a cooled solution of DMSO (233 µL, 1.65 mmol) in $CH_2Cl_2$ (2 mL) was added oxalyl chloride (142 µL, 1.24 mmol) and the mixture stirred for 5 min. A solution of alcohol **13** (94 µL, 825 µmol) in $CH_2Cl_2$ (1 mL) was added and the reaction stirred for a further 15 min at –78 ºC. Triethylamine (902 µL, 2.48 mmol) was added dropwise and the reaction stirred at –78 ºC for 15 min before warming to rt for 15 min. When complete by TLC, the reaction was quenched by the addition of $NH_4Cl$ solution (1 mL) and the aqueous phase extracted with $CH_2Cl_2$ (3 × 3 mL). The combined organic phases were washed with brine (5 mL), dried ($Na_2SO_4$) and carefully decanted to give a solution of volatile aldehyde **8** (89.9 mg, 800 µmol, 97%) in $CH_2Cl_2$, the concentration of which was determined by $^1$H NMR immediately prior to use in further reactions.

**$R_f$** 0.48 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.57 (1H, d, *J* = 1.8 Hz, C13HO), 5.72 (1H, ddt, *J* = 16.9, 10.3, 6.6 Hz, C9H), 5.00-4.91 (2H, m, C9(H)C$H_aH_b$, C9(H)$CH_aH_b$), 2.32 (1H, qdd, *J* = 7.0, 6.9, 1.8 Hz, C12H), 2.08-2.01 (2H, m, C10(H)C$H_aH_b$, C10(H)$CH_aH_b$), 1.77 (1H, ddt, *J* = 13.8, 9.0, 6.5 Hz, C11$H_aH_b$), 1.38 (1H, ddt, *J* = 13.8, 8.6, 6.8 Hz, C11$H_aH_b$), 1.04 (3H, d, *J* = 7.0 Hz, C12(H)Me). **$[\alpha]_D^{20}$** –13.1 (*c* =1.2, $CHCl_3$). This data is in agreement with that reported by Boeckman.[9]

## 2.3. Synthesis of the C14-C19 Fragment 7

### TBS ETHER 24

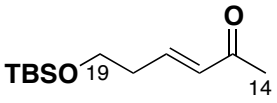



But-3-en-1-ol (4.28 mL, 50.0 mmol) and imidazole (4.08 g, 60.0 mmol) were dissolved in $CH_2Cl_2$ (40 mL) at 0 ºC. *tert*-Butyldimethylsilyl chloride (8.29 g, 55.0 mmol) was added and the reaction stirred for 15 min at 0 ºC and then 4 h at rt. The white suspension was diluted with PE/EtOAc (1:1, 50 mL) and filtered through a pad of silica eluting with PE/EtOAc (1:1). The solution was concentrated *in vacuo* to yield silyl ether **24** (8.31 g, 44.6 mmol, 89%).

**$R_f$** 0.76 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 5.82 (1H, ddt, *J* = 17.0, 10.2, 6.9 Hz, C17H), 5.07 (1H, dt, *J* = 17.2, 1.9 Hz, C16$H_a$), 5.02(1H, dt, *J* = 10.3, 1.9 Hz, C16$H_b$), 3.67 (2H, t, *J* = 6.8 Hz, C19$H_2$), 2.28 (2H, dt, *J* = 6.9, 6.8 Hz, C18$H_2$), 0.89 (9H, s, C19OSi$^t$BuMe$_2$), 0.05 (6H, s, C19OSi$^t$BuMe$_2$).

This data is in agreement with that reported by Ferrié *et al.*[10]

### ENONE 25

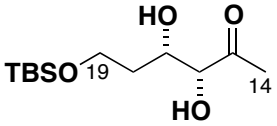



Silyl ether **24** (4.00 g, 21.5 mmol) was dissolved in $CH_2Cl_2$ and cooled to –78 ºC. Ozone was bubbled through the solution until a blue colour persisted. The solution was purged with a stream of dioxygen until the blue colour faded. 1-Triphenylphosphoranylidene-2-propanone (10.2 g, 32.2 mmol) was added and the reaction stirred for 30 min at –78 ºC. The white suspension was warmed to rt and stirred overnight to yield an orange solution. The solution was filtered through a pad of silica, eluting with $Et_2O$ and concentrated *in vacuo*. The crude product was purified by column chromatography (3:1 $PE_{30\text{-}40}$/$Et_2O$). Enone **25** (3.35 g, 14.7 mmol, 69%) was obtained as a yellow oil.

**$R_f$** 0.73 (2:1 $PE_{30\text{-}40}$/$Et_2O$). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.82 (1H, dt, *J* = 16.1, 7.1 Hz, C17H), 6.11 (1H, dt, *J* = 16.1, 1.6 Hz, C16H), 3.75 (2H, t, *J* = 6.3 Hz, C19$H_2$), 2.44 (2H, ddt, *J* = 7.1, 6.3, 1.6 Hz, C18$H_2$), 2.25 (3H, s, C14$H_3$), 0.89 (9H, s, C19OSi$^t$BuMe$_2$), 0.06 (6H, s, C19OSi$^t$BuMe$_2$).

This data is in agreement with that reported by Mortensen *et al.*[11]

### DIOL 26

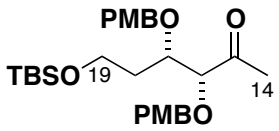



Potassium osmate dihydrate (186 mg, 506 µmol), $(DHQ)_2AQN$ (1.08 g, 1.23 mmol) and methylsulfonamide (4.81 g, 50.6 mmol) were dissolved in a mixture of *tert*-butanol (100 mL) and water (500 mL) and stirred for 30 min at rt. Potassium carbonate (21.7 g, 157 mmol), potassium ferricyanide (51.7 g, 157 mmol) and

sodium hydrogencarbonate (12.8 g, 152 mmol) were added and the mixture stirred for a further 30 min. The reaction was cooled to 0 ºC and enone **25** (11.6 g, 50.6 mmol) was added. The yellow suspension was stirred until complete by TLC (16 h) and quenched with the addition of sodium thiosulfate solution (400 mL). After stirring for 1 h, the reaction mixture was extracted with EtOAc (5 × 500 mL) and the combined extracts washed with brine (500 mL) and dried ($Na_2SO_4$). The extracts were concentrated *in vacuo* and purified by column chromatography (4:1 PE/EtOAc). Diol **26** (12.1 g, 46.1 mmol, 91%) was isolated as a yellow oil. The determination of enantiomeric purity (97% *ee*) was achieved by chiral HPLC of the *bis*-PMB ether derivative **7**.

**$R_f$** 0.36 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 4.30-4.25 (1H, m, C17H), 4.08 (1H, dd, *J* = 5.2, 2.3 Hz, C16H), 3.92 (1H, ddd, *J* = 10.3, 4.8, 4.8 Hz, C19$H_aH_b$), 3.85 (1H, ddd, *J* = 10.3, 9.2, 3.4 Hz, C19$H_aH_b$), 3.68 (1H, d, *J* = 5.2 Hz, OH), 3.16 (1H, d, *J* = 5.2 Hz, OH), 2.31 (3H, s, C14$H_3$), 1.93-1.84 (1H, m, C18$H_aH_b$), 1.79-1.73 (1H, m, C18$H_aH_b$), 0.90 (9H, s, C19OSi$^t$BuMe$_2$), 0.09 (6H, s, C19OSi$^t$BuMe$_2$). **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta_C$ 208.8, 79.8, 71.9, 62.0, 35.3, 26.1, 26.0, 18.3, –5.4. **$[\alpha]_D^{20}$** +20.7 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 3438, 2954, 2928, 2857, 1716, 1471, 1360, 1253, 1087, 1005, 940, 835, 777, 737, 667 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{12}H_{27}O_4Si$ $[M + H]^+$ 263.1673, found 263.1674.

**C14-19 METHYL KETONE 7**

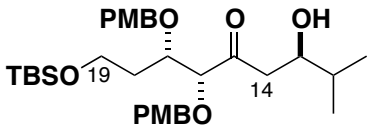



Diol **26** (2.27 g, 8.66 mmol) and 4-methoxybenzyl-2,2,2-trichloroacetimidate (9.78 g, 34.6 mmol) were concentrated from benzene (20 mL) and subsequently dissolved in THF (100 mL) at 0 ºC. Triphenylcarbenium tetrafluoroborate (13.2 mg, 40.0 $\mu$mol) was added at 0 ºC, the reaction warmed to rt and stirred for 20 h. When complete by TLC, MeOH (3 mL) was added and the quenched reaction stirred for 30 min. The mixture was filtered through a pad of silica and purified by extensive column chromatography (2:1 PE/$Et_2O$, then 3:1 → 5:1 PE/EtOAc, to remove PMBOH and $PMB_2O$). The *bis*-PMB ether **7** (3.35 g, 12.8 mmol, 77%) was collected as a colourless oil.

**$R_f$** 0.44 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 7.18 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 6.87 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 6.83 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}$H), 4.62 (1H, d, *J* = 11.6 Hz, OC$H_aH_bAr_{PMB}$), 4.49 (1H, d, *J* = 11.1 Hz, OC$H_aH_bAr_{PMB}$), 4.44 (1H, d, *J* = 11.1 Hz, OC$H_aH_bAr'_{PMB}$), 4.36 (1H, d, J = 11.6 Hz, OC$H_aH_bAr'_{PMB}$), 3.92 (1H, ddd, *J* = 7.0, 5.9, 4.2 Hz, C17H), 3.80 (3H, s, $Ar_{PMB}$OMe), 3.79 (3H, s, $Ar'_{PMB}$OMe), 3.78 (1H, d, *J* = 4.2 Hz, C16H), 3.62-3.56 (1H, m, C19$H_aH_b$), 3.45 (1H, dt, *J* = 10.3, 5.7 Hz, C19$H_aH_b$), 3.14 (3H, s, C14$H_3$), 1.76-1.70 (2H, m, C18$H_aH_b$ , C18$H_aH_b$), 0.87 (9H, s, C19 OSi$^t$BuMe$_2$), 0.01 (3H, s, C19OSi$^t$BuMe$_a$Me$_b$), 0.00 (3H, s, C19OSi$^t$BuMe$_a$Me$_b$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 211.0, 159.7, 159.4, 130.5, 130.1, 129.9, 129.5, 114.0, 113.9, 86.7, 76.7, 73.0, 72.7, 59.2, 55.4 (2C), 33.7, 27.7, 26.1, 18.4, –5.2. **$[\alpha]_D^{20}$** +20.7 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 2930, 2857, 1713, 1612, 1586, 1513, 1464, 1352, 1302, 1247, 1173, 1084, 1034, 939, 832, 776 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{28}H_{46}NO_6Si$ $[M + NH_4]^+$ 520.3089, found 520.3087. **HPLC** (Chiracel OD) $R_t$ = 8.47 (minor), 9.38 (major) min (flow rate 1.0 mL.min$^{-1}$, 5% *iso*-propanol in hexane) indicated 97% *ee*.

### 2.4. Fragment coupling to C1-C19 fully protected southern fragment 5 and model studies

**ALDOL PRODUCT 29 -** *Investigating the substrate induction of ketone 7*




*Conditions A:* Dicyclohexylboron chloride (35.7 µL, 163 *µ*mol) was dissolved in $Et_2O$ (1.0 mL) at –78 ºC and triethylamine (26.0 µL, 189 µmol) was added dropwise *via* syringe. A solution of methyl ketone **7** (63.0 mg, 125 µmol) in $Et_2O$ (1.0 mL, stirred over $CaH_2$ for 30 min) was added dropwise at –78 ºC and the reaction warmed to 0 ºC for 1 h. The mixture was cooled to –78 ºC and *iso*-butyraldehyde (23.4 µL, 250 µmol, distilled from $CaCl_2$) added dropwise. The reaction was stirred for a further 3 h at –78 ºC and kept at –23 ºC (freezer) for 16 h. The reaction was quenched by the sequential addition of MeOH (0.5 mL), pH 7 buffer solution (2.0 mL) and hydrogen peroxide solution (2.0 mL, 30% aq.) and the solution stirred for 1 h at rt. The solution was extracted with $Et_2O$ (3 × 10 mL) and the combined organic extracts washed with brine (30 mL) and dried ($Na_2SO_4$). The solvents were removed *in vacuo* and the residue was purified by column chromatography (5:1 PE/EtOAc → 3:1 PE/$Et_2O$). Alcohol **29** (61.0 mg, 106 µmol, 85%, dr 84:16) was isolated as a colourless oil.

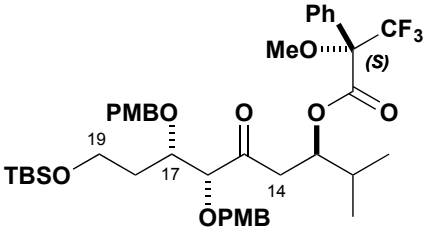
*Conditions B*: (–)-DIP chloride (94.0 µL, 293 µmol, dried *in vacuo* for 1 h) was dissolved in $Et_2O$ (1.0 mL) at –78 ºC and triethylamine (47.0 µL, 342 *µ*µmol) was added dropwise *via* syringe. A solution of methyl ketone **7** (113 mg, 224 µmol) in $Et_2O$ (1.0 mL, stirred over $CaH_2$ for 30 min) was added dropwise at –78 ºC and the reaction warmed to 0 ºC for 1 h. The mixture was cooled to –78 ºC and *iso*-butyraldehyde (106 µL, 1.13 mmol, distilled from $CaCl_2$) added dropwise. The reaction was stirred for a further 3 h at –78 ºC and kept at –23 ºC (freezer) for 16 h. The reaction was quenched by the sequential addition of MeOH (0.5 mL), pH 7 buffer solution (2.0 mL) and hydrogen peroxide solution (2.0 mL, 30% aq.) and the solution stirred for 1 h at rt. The solution was extracted with $Et_2O$ (3 × 10 mL) and the combined organic extracts washed with brine (30 mL) and dried ($Na_2SO_4$). The solvents were removed *in vacuo* and the residue purified by column chromatography (5:1 PE/EtOAc → 3:1 PE/$Et_2O$). Alcohol **29** (85.0 mg, 145 µmol, 65%, dr 94:6) was isolated as a colourless oil.

*Conditions C:* Dibutylboron triflate (254 µL, 1.01 mmol) was dissolved in $Et_2O$ (5.0 mL) at –78 ºC and di-*iso*-propylethylamine (234 µL, 1.34 mmol) was added dropwise *via* syringe. A solution of methyl ketone **7** (422 mg, 839 µmol, dried azeotropically from PhH) in $Et_2O$ (5.0 mL, stirred over $CaH_2$ for 30 min) was added dropwise at –78 ºC and the reaction stirred for 30 min. The mixture was cooled to –98 ºC and *iso*-butyraldehyde (315 µL, 3.36 µmol, distilled from $CaCl_2$) added dropwise. The reaction was stirred for a further 2 h at –98 ºC and –78 ºC for 4 h. The reaction was quenched by the sequential addition of MeOH (1.0 mL), pH 7 buffer solution (4.0 mL) and hydrogen peroxide solution (3.0 mL, 30% aq.) and the solution stirred for 30 min at rt. The solution was extracted with $Et_2O$ (3 × 40 mL) and the combined organic extracts washed with brine (100 mL) and dried ($Na_2SO_4$). The solvents were removed *in vacuo* and the residue purified by column chromatography (5:1 → 3:1 PE/EtOAc). Alcohol **29** (280 mg, 487 µmol, 58% (unoptimised), dr >95:5) was isolated as a colourless oil.

The absolute stereochemistry of the newly-formed hydroxyl stereocentre was determined by formation of the Mosher ester derivatives **29S** and **29R**.

**$R_f$** 0.47 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 7.16 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.83 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 4.65 (1H, d, *J* = 11.6 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.49 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.36 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.35 (1H, d, *J* = 11.6 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 3.94 (1H, ddd, *J* = 7.0, 5.9, 4.2 Hz, C17$\underline{H}$), 3.81 (1H, d, *J* = 3.9 Hz, C16$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.75 (1H, m, C14C$\underline{H}$(OH)CHMe$_2$), 3.57 (1H, ddd, *J* = 10.5, 7.0, 5.3 Hz, C19$\underline{H_a}H_b$), 3.39 (1H, ddd, *J* = 10.5, 5.6, 5.6 Hz, C19$H_a\underline{H_b}$), 2.94 (1H, d, *J* = 3.2 Hz, C14CH(O$\underline{H}$)CHMe$_2$), 2.71 (1H, dd, *J* = 18.0, 2.0 Hz, C14$\underline{H_a}H_b$), 2.52 (1H, dd, *J* = 18.0, 10.1 Hz, C14$H_a\underline{H_b}$), 1.83-1.69 (3H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C14CH(OH)C$\underline{H}$Me$_2$), 0.87 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.86 (3H, d, *J* = 6.8 Hz, C14CH(OH)CH$\underline{Me_a}Me_b$), 0.84 (3H, d, *J* = 6.8 Hz, C14CH(OH)CH$Me_a\underline{Me_b}$), 0.01 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.00 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 219.4, 164.2, 163.3, 136.3, 134.7, 134.3, 133.6, 118.4, 118.3, 90.2, 81.9, 81.6, 81.5, 81.2, 63.5, 59.8, 48.2, 37.7, 37.6, 30.4, 22.8, 22.2, –0.89 [NMR signals from major diastereomer]. **$[\alpha]_D^{20}$** *A*: +28.8 (dr 84:16, *c* = 0.8, $CHCl_3$). *B*: +41.5 (dr 94:6, *c* = 0.8, $CHCl_3$). **IR** (thin film) 3505.5, 2955.5, 2929.0, 2857.0, 1708.9, 1612.2, 1586.4, 1513.6 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{32}H_{50}O_7Si$ $[M + NH_4]^+$ 592.3664, found 592.3666.

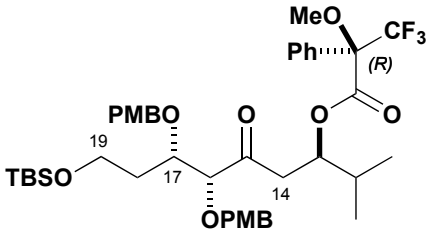
**MOSHER ESTER 29S**




Alcohol **29** (10.0 mg, 17.4 µmol) was dissolved in $CH_2Cl_2$ (300 µL) and DMAP (4.3 mg, 32.8 µmol), (*S*)-MTPA (16.3 mg, 69.6 µmol) and DCC (69.6 µL, 69.6 µmol, 1 M solution in $CH_2Cl_2$) were added. The mixture was stirred at rt for 16 h. The solvents were removed under reduced pressure and the crude mixture was purified by column chromatography (4:1 → 2:1 PE/EtOAc) yielded the Mosher ester **29S** (5.4 mg, 6.83 µmol, 39%) as a colourless oil.

**$R_f$** 0.37 (3:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.55-7.50 (2H, m, $Ar_{Ph}\underline{H}$), 7.40-7.36 (3H, m, $Ar_{Ph}\underline{H}$), 7.14 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 7.12 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.811 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.806 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 5.43 (1H, td, *J* = 9.3, 3.3 Hz, C14C$\underline{H}$(OR)CHMe$_2$), 4.48 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.47 (1H, d, *J* = 11.5 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.32 (1 H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.19 (1H, d, *J* = 11.5 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 3.94-3.88 (1H, m, C17$\underline{H}$), 3.778 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.777 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.75 (1H, d, *J* = 3.6 Hz, C16$\underline{H}$), 3.58-3.51 (1H, m, C19$\underline{H_a}H_b$), 3.50 (3H, s, C(Ph)($CF_3$)(O$\underline{Me}$)), 3.39-3.33 (1H, m, C19$H_a\underline{H_b}$), 3.04 (1H, dd, *J* = 18.8, 9.4 Hz, C14$\underline{H_a}H_b$), 2.55 (1 H, dd, *J* = 18.8, 3.0 Hz, C14$H_a\underline{H_b}$), 1.99-1.91 (1 H, m, C14CH(OR)C$\underline{H}$Me$_2$), 1.82-1.66 (2H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 0.87 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.76 (3H, d, *J* = 6.9 Hz, C14CH(OR)CH$\underline{Me_a}Me_b$), 0.75 (3H, d, *J* = 6.8 Hz, C14CH(OR)CH$Me_a\underline{Me_b}$), 0.002 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.000 ppm (6H, s, Si$^t$Bu$Me_a\underline{Me_b}$).

**MOSHER ESTER 29R**

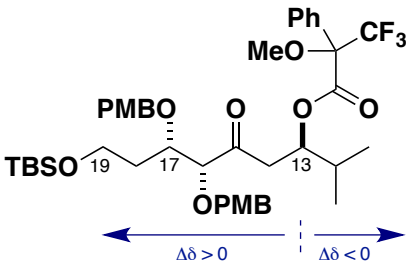



Alcohol **29** (10.0 mg, 17.4 µmol) was dissolved in $CH_2Cl_2$ (300 µL), and DMAP (4.3 mg, 32.8 µmol), (*R*)-MTPA (16.3 mg, 69.6 *µ*mol) and DCC (69.6 µL, 69.6 µmol, 1 M solution in $CH_2Cl_2$) were added. The mixture was stirred at rt for 16 h. EtOAc (5 mL) was added and the mixture was washed with water (5 mL) and brine (5 mL), dried ($Na_2SO_4$), filtered and the solvents were removed under reduced pressure. The residue was purified by column chromatography (4:1 → 2:1 PE/EtOAc) to yield Mosher ester **29R** (4.4 mg, 5.56 µmol, 32%) as colourless oil.

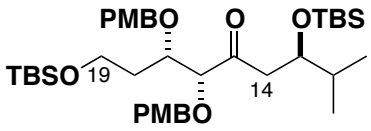
**$R_f$** 0.41 (3:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.55-7.50 (2H, m, $Ar_{Ph}\underline{H}$), 7.40-7.35 (3H, m, $Ar_{Ph}\underline{H}$), 7.15 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.13 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.84 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.82 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.49 (1H, td, *J* = 9.3, 3.2 Hz, C14C$\underline{H}$(OR)CHMe$_2$), 4.47 (1H, d, *J* = 11.0 Hz, OC$\underline{H_a}H_b$Ar$_{PMB}$), 4.36 (1H, d, *J* = 11.6 Hz, OC$\underline{H_a}H_b$Ar$_{PMB}$), 4.31 (1H, d, *J* = 11.0 Hz, OCH$_a\underline{H_b}$Ar$_{PMB}$), 4.08 (1H, d, *J* = 11.6 Hz, OCH$_a\underline{H_b}$Ar$_{PMB}$), 3.92-3.85 (1 H, m, C17$\underline{H}$), 3.80 (3H, s, Ar$_{PMB}$O$\underline{Me}$), 3.78 (3H, s, Ar$_{PMB}$O$\underline{Me}$), 3.63 (1H, d, $\underline{J}$ = 3.7 Hz, C16$\underline{H}$), 3.55 (3H, s, C(Ph)(CF$_3$)(O$\underline{Me}$)), 3.55-3.48 (1 H, m, C19$\underline{H_a}H_b$), 3.35 (1 H, dt, *J* = 10.6, 5.7 Hz, C19H$_a\underline{H_b}$), 3.08 (1H, dd, *J* = 18.8, 9.4 Hz, C14$\underline{H_a}H_b$), 2.49 (1H, dd, *J* = 18.8, 3.0 Hz, C14H$_a\underline{H_b}$), 1.99-1.91 (1H, m, C14CH(OR)C$\underline{H}$Me$_2$), 1.80-1.66 (2H, m, C18$\underline{H_a}H_b$, C18H$_a\underline{H_b}$), 0.88 (3H, d, *J* = 6.9 Hz, C14CH(OR)CH$\underline{Me_a}$Me$_b$), 0.87 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.81 (3H, d, *J* = 6.9 Hz, C14CH(OR)CHMe$_a\underline{Me_b}$), 0.00 ppm (6H, s, Si$^t$Bu$\underline{Me_2}$).

**MOSHER ESTER ANALYSIS OF 29S AND 29R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C14CH(OR)CH$\underline{Me_a}Me_b$ | 0.76 | 0.88 | –0.12 |
| C14CH(OR)CH$Me_a\underline{Me_b}$ | 0.75 | 0.81 | –0.06 |
| C14CH(OR)C$\underline{H}Me_2$ | 1.95 | 1.95 | 0.00 |
| C14C$\underline{H}$(OR)CH$Me_2$ | 5.43 | 5.49 | –0.06 |
| C14$\underline{H_a}H_b$ | 3.04 | 3.08 | –0.04 |
| C14$H_a\underline{H_b}$ | 2.55 | 2.49 | +0.06 |
| C16$\underline{H}$ | 3.75 | 3.63 | +0.12 |
| C17$\underline{H}$ | 3.91 | 3.89 | +0.02 |
| C18$\underline{H_a}H_b$ | 1.75 | 1.74 | +0.01 |
| C18$H_a\underline{H_b}$ | 1.70 | 1.70 | 0.00 |
| C19$\underline{H_a}H_b$ | 3.54 | 3.51 | +0.03 |
| C19$H_a\underline{H_b}$ | 3.36 | 3.35 | +0.01 |



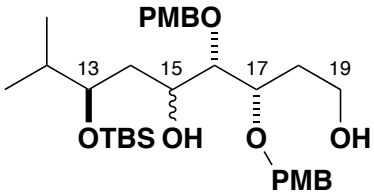
**TBS ETHER 101**




Alcohol **29** (75.0 mg, 130 µmol) and 2,6-lutidine (40.0 µL, 373 µmol) were dissolved in $CH_2Cl_2$ (1.0 mL) and cooled to –78 ºC. TBSOTf (30.5 µL, 116 µmol) was added dropwise *via* syringe over 5 min and the reaction stirred at –78 ºC for 30 min. MeOH (3 mL) was added and the mixture warmed to rt. The solution was diluted with PE/EtOAc (5 mL, 1:1) and filtered through a pad of silica. The solvents were removed *in vacuo* and the crude product purified by column chromatography (10:1 PE/EtOAc). TBS ether **101** (85.3 mg, 124 µmol, 95%) was collected as a pale yellow oil.

**$R_f$** 0.71 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.26 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 7.16 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.81 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 4.68 (1H, d, *J* = 11.3 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.46 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.41 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.31 (1H, d, *J* = 11.3 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.18 (1H, m, C14C$\underline{H}$(OTBS)C$HMe_2$), 3.91 (1H, ddd, *J* = 7.0, 6.1, 4.1 Hz, C17$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.81 (1H, d, *J* = 4.1 Hz, C16$\underline{H}$), 3.57 (1H, ddd, *J* = 10.3, 7.3, 5.5 Hz, C19$\underline{H_a}H_b$), 3.39 (1H, ddd, *J* = 10.3, 5.7, 5.7 Hz, C19$H_a\underline{H_b}$), 2.71 (1H, dd, *J* = 18.0, 8.1 Hz, C14$\underline{H_a}H_b$), 2.52 (1H, dd, *J* = 18.0, 3.8 Hz, C14$H_a\underline{H_b}$), 1.78-1.67 (3H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C14CH(OTBS)C$\underline{H}Me_2$), 0.88 (3H, d, *J* = 6.9 Hz, C14CH(OTBS)CH$\underline{Me_a}Me_b$), 0.87 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.86 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.84 (3H, d, *J* = 6.9 Hz, C14CH(OTBS)CH$Me_a\underline{Me_b}$), 0.09 (3H, s, C14C(H)OSi$^t$Bu$\underline{Me_a}Me_b$), 0.03 (3H, s, C14C(H)OSi$^t$Bu$Me_a\underline{Me_b}$), 0.01 (3H, s, C19OSi$^t$Bu$\underline{Me_a}$Me), 0.00 (3H, s, C19OSi$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 212.3, 159.5, 159.2, 130.4, 130.1, 129.7, 129.4, 113.8, 113.7, 86.4, 72.8, 71.6, 60.4, 59.1, 55.2, 42.6, 33.6, 26.0, 25.7, 21.0, 18.2, 17.5, 17.2, 14.2, –2.9, –4.3, –4.8, –5.4. **$[\alpha]_D^{20}$** +26.3 (*c* = 0.96, $CHCl_3$, dr 94:6). **IR** (thin film) 2956.5, 2857.3, 1714.2, 1614.7, 1513.9, 1463.5 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{38}H_{64}O_7Si_2$ $[M + NH_4]^+$ 706.4529, found 706.4535.

**DIOL 102**

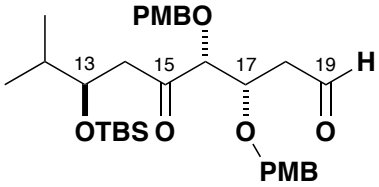



To a stirred solution of ketone **101** (118 mg, 171 µmol) in MeOH (6 mL) at 0 ºC was added $NaBH_4$ (39 mg, 1.0 mmol). The reaction mixture was warmed to RT and stirred for 2 h. $CH_2Cl_2$ (20 mL) and pH 7 buffer solution (20 mL) were then added and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 20 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was redissolved in MeOH (3 mL) and $CH_2Cl_2$ (3 mL) and PPTS (3 crystals) was added. After 5 h, $NaHCO_3$ solution (20 mL) and $CH_2Cl_2$ (20 mL) were added and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 20 mL) and the combined organic layers were dried

($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography to afford diol **102** (81.0 mg, 140 µmol, 82%) as an inseparable mixture of diastereomers.

*Major diastereomer:* **$R_f$** 0.07 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.24 (4H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.90-6.84 (4H, m, $Ar_{PMB}\underline{H}$), 4.74 (1H, d, *J* = 11.1 Hz, $OC\underline{H}_aH_bAr_{PMB}$), 4.64 (1H, d, *J* = 11.1 Hz, $OC\underline{H}_aH_bAr_{PMB}$), 4.53 (1H, d, *J* = 11.1 Hz, $OCH_a\underline{H}_bAr_{PMB}$), 4.51 (1H, d, *J* = 11.1 Hz, $OCH_a\underline{H}_bAr_{PMB}$), 3.89-3.80 (2H, m, C15$\underline{H}$, C17$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (1H, ddd, *J* = 6.8, 4.4, 2.3 Hz, C13$\underline{H}$), 3.74-3.68 (2H, m, C19$\underline{H}_aH_b$, C19$H_a\underline{H}_b$), 3.68-3.61 (1H, m, C16$\underline{H}$), 3.57 (1H, br. d, *J* = 1.5 Hz, O$\underline{H}$), 2.28 (1H, br. d, *J* = 5.5 Hz, O$\underline{H}$), 1.97-1.73 (4H, m, C14$\underline{H}_aH_b$, C14$H_a\underline{H}_b$, C18$\underline{H}_aH_b$, C18$H_a\underline{H}_b$), 1.50-1.36 (1H, m, C13H(OTBS)C$\underline{H}Me_aMe_b$), 0.88 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.82 (3H, d, *J* = 6.9 Hz, C13H(OTBS)CH$\underline{Me}_aMe_b$), 0.81 (3H, d, *J* = 6.9 Hz, C13H(OTBS)CH$Me_a\underline{Me}_b$), 0.06 (3H, s, OSi$^t$Bu$\underline{Me}_aMe_b$), 0.04 (3H, s, OSi$^t$Bu$Me_a\underline{Me}_b$).

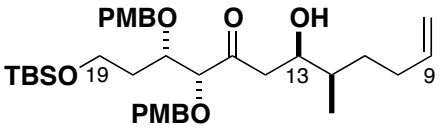
**KETOALDEHYDE 64**




To a stirred solution of oxalyl chloride (57 µL, 670 µmol) in $CH_2Cl_2$ (3 mL) at –78 ºC was added DMSO (94 µL, 1.3 mmol). After 20 min, diol **102** (127 mg, 220 µmol) in $CH_2Cl_2$ (2 mL) were added *via* cannula. After a further 20 min, $Et_3N$ (365 µL, 2.64 mmol) was added and the reaction mixture was stirred for 30 min before being warmed to 0 ºC and stirred for 30 min. The reaction was quenched with $NH_4Cl$ solution (10 mL) and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (4:1 PE/EtOAc) to afford ketoaldehyde **64** (120 mg, 209 µmol, 95%) as a colourless oil.

**$R_f$** 0.58 (3:1 PE/EtOAc. **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 9.64 (1H, dd, *J* = 2.3, 1.0 Hz, C19$\underline{H}$O), 7.24 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 7.14 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.83 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 4.65 (1H, d, *J* = 11.2 Hz, $OC\underline{H}_aH_bAr_{PMB}$), 4.45 (1H, d, *J* = 11.1 Hz, $OC\underline{H}_aH_bAr_{PMB}$), 4.39 (1H, s, *J* = 11.1, $OCH_a\underline{H}_bAr_{PMB}$r), 4.28 (1H, d, *J* = 11.2 Hz, $OCH_a\underline{H}_bAr_{PMB}$), 4.24 (1H, dt, *J* = 5.8, 4.0 Hz, C17$\underline{H}$), 4.17 (1H, dt, *J* = 8.2, 3.6, Hz, C13$\underline{H}$), 3.83 (1H, d, *J* = 3.9 Hz, C16$\underline{H}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 2.97 (1H, dd, *J* = 17.9, 8.2 Hz, C14$\underline{H}_aH_b$), 2.70 (1H, ddd, *J* = 17.3, 5.9, 1.0 Hz, C18$\underline{H}_aH_b$), 2.56 (1H, ddd, *J* = 17.3, 5.9, 1.0 Hz, C18$H_a\underline{H}_b$), 2.34 (1H, dd, *J* = 17.8, 3.7 Hz, C14$H_a\underline{H}_b$), 1.75-1.68 (1H, m, C13H(OTBS)C$\underline{H}Me_aMe_b$), 0.86 (3H, d, *J* = 6.8 Hz, C13H(OTBS)CH$Me_a\underline{Me}_b$), 0.86 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.09 (3H, s, OSi$^t$Bu$\underline{Me}_aMe_b$), 0.01 (3H, s, OSi$^t$Bu$Me_a\underline{Me}_b$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 211.7, 200.2, 159.6, 159.4, 130.3, 129.8, 128.8, 113.9, 113.8, 85.5, 75.3, 73.1, 72.7, 71.8, 55.3 (2C), 44.8, 42.9, 33.6, 26.0, 18.1, 17.6, 17.1, –4.3, –4.8. **$[\alpha]_D^{20}$** +29.6 (*c* = 0.46, $CHCl_3$). **IR** (thin film) 2929, 1721, 1616, 1515, 1465 $cm^{-1}$.

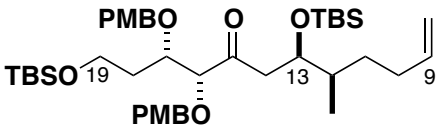
**ALDOL PRODUCT 28**




A solution of dibutylboron triflate (1.35 mL, 5.36 mmol) in $Et_2O$ (16 mL) was cooled to –78 ºC and di-*iso*-propylethylamine (1.32 mL, 7.60 mmol) added dropwise. After stirring for 10 min, a solution of ketone **7** (2.25 g, 4.48 mmol, dried azeotropically from PhH) in $Et_2O$ (16 mL + 2 mL wash, stirred over $CaH_2$ for 30 min) was added *via* cannula to give a bright yellow suspension. After enolising for 30 min, the mixture was cooled to –98 ºC and a solution of aldehyde **8** (1.00 g, 8.96 mmol, dried azeotropically from PhH) in $Et_2O$ (16 mL + 2 mL wash, stirred over $CaH_2$ for 30 min) added slowly down the side of the flask. The suspension was stirred for 2 h at –98 ºC before warming to –78 ºC for a further 4 h. The reaction was quenched by the careful addition of MeOH (15 mL) and, on warming to rt, diluted with pH 7 buffer solution (20 mL) and $H_2O_2$ (20 mL, 30% aq.). After stirring for 30 min, the layers were separated and the aqueous phase extracted with $Et_2O$ (3 × 50 mL). The combined organic phases were washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (9:1 PE/EtOAc) to afford aldol product **28** (2.70 g, 4.39 mmol, 98%, >95:5 dr) as a yellow oil.

**$R_f$** 0.48 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 7.16 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.82 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 5.78 (1H, ddt, *J* = 17.0, 10.4, 6.6 Hz, C9$\underline{H}$), 5.00 (1H, br d, *J* = 17.0 Hz, C(H)C$\underline{H_a}H_b$), 4.94 (1H, br d, *J* = 10.4 Hz, C(H)C$H_a\underline{H_b}$), 4.64 (1H, d, *J* = 11.5 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.49 (1H, d, *J* = 11.0 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.36 (1H, d, *J* = 11.5 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.35 (1H, d, *J* = 11.0 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.94 (1H, dt, *J* = 6.6, 3.9 Hz, C17$\underline{H}$), 3.90-3.85 (1H, m, C13$\underline{H}$), 3.82 (1H, d, *J* = 3.8 Hz, C16$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.60-3.55 (1H, m, C19$\underline{H_a}H_b$), 3.39 (1H, app dt, *J* = 10.7, 5.5 Hz, C19$H_a\underline{H_b}$), 2.87 (1H, d, *J* = 2.9 Hz, C13(H)O$\underline{H}$), 2.67 (1H, dd, *J* = 18.0, 1.8 Hz, C14$\underline{H_a}H_b$), 2.55 (1H, *J* = 18.0, 10.0 Hz, C14$H_a\underline{H_b}$), 2.15-2.05 (1H, m, C10$\underline{H_a}H_b$), 2.04-1.96 (1H, m, C10$H_a\underline{H_b}$), 1.81-1.70 (2H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.55-1.48 (1H, obs m, C12$\underline{H}$), 1.46-1.39 (1H, m, C11$\underline{H_a}H_b$), 1.19-1.11 (1H, m, C11$H_a\underline{H_b}$), 0.87 (9H, s, Si$^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.006 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), –0.001 (3H, s, Si$^t$BuMe$_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 215.0, 159.3 (2C), 138.9, 130.2, 130.1, 129.8, 129.1, 114.4, 114.0, 113.8, 85.4, 73.2, 72.5, 70.3, 59.5, 55.3, 55.2, 44.0, 37.5, 33.2, 31.9, 31.5, 26.0, 18.2, 14.1, –5.4, –5.3. **$[\alpha]_D^{20}$** +38.8 (*c* = 0.98, $CHCl_3$). **IR** (thin film) 3488, 2953, 2928, 2856, 1710, 1612, 1514, 1463, 1302, 1247, 1174, 1087, 1035, 832, 776 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{35}H_{54}O_7NSi$ $[M + NH_4]^+$ 632.3977, found 632.3975.

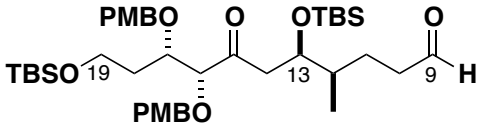
**TBS ETHER 30**




To a solution of alcohol **28** (322 mg, 524 µmol, dried azeotropically from PhH) and 2,6-lutidine (92 µL, 786 µmol) in $CH_2Cl_2$ (5 mL) at –78 °C was added TBSOTf (144 µL, 629 *µ*mol) dropwise. The mixture was stirred at –78 °C for 30 min and, when complete by TLC, was quenched with MeOH (1 mL), warmed to rt and diluted with $NaHCO_3$ solution (10 mL). The organic layer was separated and the aqueous phase extracted with $CH_2Cl_2$ (3 × 30 mL). The combined organic phases were dried ($Na_2SO_4$), concentrated *in vacuo* and purified by column chromatography (20:1 PE/EtOAc) to give TBS ether **30** as colourless oil (408 mg, 514 µmol, 98%).

**$R_f$** 0.65 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.28 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.18 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.88 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.84 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 5.83 (1H, dddd, *J* = 17.0, 10.3, 6.9, 3.8 Hz, C9$\underline{H}$), 5.04 (1H, dq, *J* = 17.0, 1.9, C9(H)C$\underline{H_a}H_b$), 4.95 (1 H, dq, *J* = 10.3, 2.0 Hz, C9(H)C$\underline{H_a}H_b$), 4.69 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.48 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.43 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.33 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.26 (1H, dt, *J* = 7.5, 3.7 Hz, C13$\underline{H}$), 3.92 (1H, ddd, *J* = 10.3, 6.1, 3.6 Hz, C17$\underline{H}$), 3.82 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (1H, d, *J* = 4.1 Hz, C16$\underline{H}$), 3.60 (1H, ddd, *J* = 10.3, 7.2, 5.6 Hz, C19$\underline{H_a}H_b$), 3.44 (1H, dt, *J* = 10.3, 5.7 Hz, C19$H_a\underline{H_b}$), 3.03 (1H, dd, *J* = 18.1, 7.5 Hz, C14$\underline{H_a}H_b$), 2.37 (1H, dd, *J* = 18.1, 3.7 Hz, C14$H_a\underline{H_b}$), 2.19-2.11 (1H, m, C10$\underline{H_a}H_b$), 2.04-1.96 (1H, m, C10$H_a\underline{H_b}$), 1.79-1.71 (2H, m, C18$\underline{H_a}H_b$, C12$\underline{H}$), 1.70-1.64 (1H, m, C18$H_a\underline{H_b}$), 1.57-1.53 (1H, m, C11$\underline{H_a}H_b$), 1.17-1.10 (1H, m, C11$H_a\underline{H_b}$), 0.90-0.87 (18H, 2 overlapping s, Si$^t\underline{Bu}Me_2$), 0.77 (3H, d, *J* = 6.9 Hz, C12(H)$\underline{Me}$), 0.11 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.03 (3H, s, Si$^t$BuMe$_a\underline{Me_b}$), 0.02 (3H, s, Si$^t$BuMe$_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 212.1, 159.5, 159.2, 139.1, 130.4, 130.1, 129.7, 129.4, 114.2, 113.9, 113.7, 86.3, 72.8, 72.7, 70.9, 59.1, 55.3, 43.1, 38.3, 33.6, 31.9, 31.0, 26.0, 25.9, 18.3, 18.1, 14.6, – 4.2, –4.7, –5.4, –5.3. **$[\alpha]_D^{20}$** +28.9 (*c* = 1.06, $CHCl_3$). **IR** (thin film) 2955, 2928, 2856, 1717, 1613, 1514, 1463, 1302, 1248, 1086, 1037, 833, 775 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{41}H_{68}O_7NSi_2$ $[M + NH_4]^+$ 747.4842, found 746.4839.

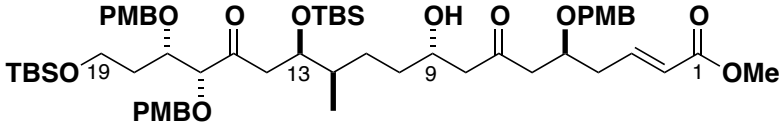
**C9-C19 ALDEHYDE 31**




To a solution of olefin **30** (99.0 mg, 136 µmol) in $CH_2Cl_2$ (5 mL) and MeOH (5 mL) was added $NaHCO_3$ powder (125 mg, 1.49 mmol) and Sudan Red 7B indicator (spatula tip). The purple solution was cooled to –78 ºC and subjected to a stream of ozone *via* pipette until a colour change to orange resulted (<20 s). The reaction flask was purged with argon (2 min) and triphenylphosphine was added (37.4 mg, 143 µmol). The reaction was warmed to rt and stirred for 2 h. The mixture was diluted with 1:1 PE/EtOAc and filtered through a pad of silica. The solution was concentrated *in vacuo* and purified by column chromatography (12:1 PE/EtOAc). Aldehyde **31** (98 mg, 135 µmol, 99%) was obtained as a colourless oil.

**$R_f$** 0.52 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.74 (1H, t, *J* = 1.7 Hz, C9$\underline{H}$O), 7.25 (2H, d, *J* = 8.5 Hz, Ar$_{PMB}\underline{H}$), 7.15 (2H, d, *J* = 8.3 Hz, Ar$_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.5 Hz, Ar$_{PMB}\underline{H}$), 6.82 (2H, d, *J* = 8.3 Hz, Ar$_{PMB}\underline{H}$), 4.66 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_b$Ar$_{PMB}$), 4.47 (1H, d, *J* = 11.0 Hz, OC$\underline{H_a}H_b$Ar$_{PMB}$), 4.38 (1H, d, *J* = 11.0, OC$H_a\underline{H_b}$Ar$_{PMB}$), 4.32 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}$Ar$_{PMB}$),4.22 (1H, ddd, *J* = 7.4, 3.9, 3.0 Hz, C13$\underline{H}$), 3.90 (1H, app dt, *J* = 6.0, 4.1 Hz, C17$\underline{H}$), 3.80 (3H, s, Ar$_{PMB}$O$\underline{Me}$), 3.78 (3H, s, Ar$_{PMB}$O$\underline{Me}$), 3.77 (1H, d, *J* = 4.1 Hz, C16$\underline{H}$), 3.56 (1H, app dt, *J* = 10.4, 5.5 Hz, C19$\underline{H_a}H_b$), 3.42 (1H, app dt, *J* = 10.4, 5.5 Hz, C19$H_a\underline{H_b}$), 2.98 (1H, dd, *J* = 18.2, 7.8 Hz, C14$\underline{H_a}H_b$), 2.46 (1H, ddd, *J* = 9.5, 5.7, 1.7 Hz, C10$\underline{H_a}H_b$), 2.41 (2H, m, C10$H_a\underline{H_b}$, C14$H_a\underline{H_b}$), 1.87 (1H, m, C11$\underline{H_a}H_b$), 1.78-1.67 (2H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.55-1.48 (1H, obs m, C12$\underline{H}$), 1.39-1.29 (1H, m, C11$H_a\underline{H_b}$), 0.87 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.85 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.74 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}$Me$_b$), 0.02 (3H, s, Si$^t$Bu$\underline{Me_a}$Me$_b$), 0.002 (3H, s, Si$^t$BuMe$_a\underline{Me_b}$), –0.001 (3H, s, Si$^t$BuMe$_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 212.0, 202.6, 159.7, 159.4, 130.5, 130.2, 129.8, 129.4, 114.0, 113.8, 86.3, 77.3, 73.1, 72.8, 70.7, 59.3, 55.4*, 43.3, 42.4, 38.6, 33.6, 26.1*, 24.4, 18.4, 18.2, 14.7, –4.2, –4.6, –5.2 (2C). **$[\alpha]_D^{20}$** +30.9 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 2956, 2931, 2856, 1725, 1613, 1515, 1388, 1303, 1250, 1174, 1092, 1037, 835, 776 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{40}H_{66}O_8NaSi_2$ $[M + Na]^+$ 753.4188, found 753.4219.

**ALDOL PRODUCT 33**



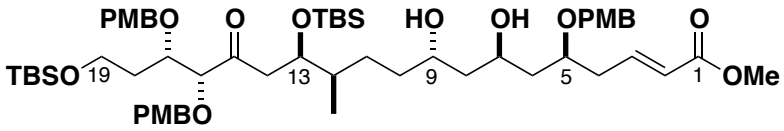

Dicyclohexylboron chloride (1.25 g, 5.72 mmol) was dissolved in $Et_2O$ (25 mL) at –78 ºC and triethylamine (1.00 mL, 7.15 mmol) was added dropwise *via* syringe. A solution of methyl ketone **9** (1.75 g, 5.72 mmol, dried azeotropically from PhH) in $Et_2O$ (25 mL, stirred over $CaH_2$ for 30 min) was added dropwise at –78 ºC and the reaction warmed to 0 ºC for 1 h. The mixture was cooled to –78 ºC and a solution of aldehyde **31** (2.09 g, 2.86 mmol, dried azeotropically from PhH) in $Et_2O$ (25 mL, stirred over $CaH_2$ for 30 min) added dropwise. The reaction was stirred for a further 3 h at –78 ºC and kept at –23 ºC (freezer) for 16 h. The reaction was quenched by the careful addition of MeOH (15 mL) and, on warming to rt, diluted with pH 7

buffer solution (20 mL) and $H_2O_2$ (20 mL, 30% aq.). After stirring for 30 min, the layers were separated and the aqueous phase extracted with $Et_2O$ (3 × 100 mL). The combined organic phases were dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (6:1 → 4:1 → 3:1 PE/EtOAc) to afford aldol product **33** (2.89 g, 2.72 mmol, 95%) as a colourless oil.

**$R_f$** 0.22 (2:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 7.21 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.15 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.94 (1H, dt, *J* = 15.2, 7.4 Hz, C3$\underline{H}$), 6.86 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.82 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.88 (H, d, *J* = 15.7 Hz, C2$\underline{H}$), 4.67 (1H, d, *J* = 11.4 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.50-4.36 (4H, m, $OC\underline{H_a}H_bAr_{PMB}$, $OC\underline{H_a}H_bAr_{PMB}$ $OCH_a\underline{H_b}Ar_{PMB}$, $OCH_a\underline{H_b}Ar_{PMB}$), 4.31 (1H, d, *J* = 11.4 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.24-4.19 (1H, m, C13$\underline{H}$), 4.11-4.05 (1H, m, C5$\underline{H}$), 4.02-3.95 (1H, m, C9$\underline{H}$), 3.94-3.88 (1H, m, C17$\underline{H}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.75 (1H, m, *J* = 4.0 Hz, C16$\underline{H}$), 3.73 (3H, s, $C1O_2\underline{Me}$), 3.59-3.53 (1H, m, C19$\underline{H_a}H_b$), 3.45-3.37 (1H, m, C19$H_a\underline{H_b}$), 2.98 (1H, dd, *J* = 18.1, 8.0 Hz, C14$\underline{H_a}H_b$), 2.85 (1H, br s, C9(H)O$\underline{H}$), 2.76 (1H, dd, *J* = 16.4, 7.6 Hz, C6$\underline{H_a}H_b$), 2.57 (1H, dd, *J* = 17.3, 2.5 Hz, C8$\underline{H_a}H_b$), 2.53-2.42 (4H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$, C6$H_a\underline{H_b}$, C8$H_a\underline{H_b}$), 2.34 (1H, dd, *J* = 18.1, 3.9 Hz, C14$H_a\underline{H_b}$), 1.78-1.64 (3H, m, C10$\underline{H_a}H_b$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.51-1.36 (3H, m, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$), 1.01-0.91 (1H, m, C11$H_a\underline{H_b}$), 0.86 (9H, s, Si$^t\underline{Bu}Me_2$), 0.85 (9H, s, Si$^t\underline{Bu}Me_2$), 0.74 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.02 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.00 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), –0.01 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 212.3, 210.1, 166.7, 159.6, 159.5, 159.3, 144.5, 130.5, 130.2, 130.0, 129.8, 129.6, 129.4, 123.9, 114.0 (2C), 113.8, 86.3, 77.3, 73.7, 72.9, 72.8, 71.7, 71.0, 68.1, 59.2, 55.4 (2C), 51.6, 50.5, 48.2, 43.2, 39.1, 36.9, 34.9, 33.6, 27.6, 26.1 (2C), 18.4, 18.2, 14.9, –4.1, –4.6, –5.3 (2C). **$[\alpha]_D^{20}$** +39.9 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 3014, 2954, 2931, 2858, 1714, 1613, 1514, 1464, 1249, 1216, 1035, 834, 752, 667 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{57}H_{88}O_{13}NaSi_2$ $[M + Na]^+$ 1059.5656, found 1059.5656.

The relative stereochemistry was assigned by correlation with intermediates to those previously prepared during synthesis optimisation.[12]

**DIOL 34**



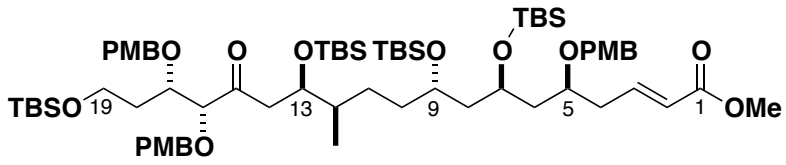

To a slurry of $Me_4NBH(OAc)_3$ (1.74 g, 6.63 mmol) in MeCN (5 mL) was added AcOH (5 mL) and the mixture stirred for 30 min at rt. The mixture was carefully cooled to –30 ºC and a solution of aldol product **33** (688 mg, 663 µmol, dried azeotropically from PhH) in MeCN (10 mL + 5 mL wash) was added. After stirring at –30 ºC for 2 d, the reaction was poured on to a solution of Na/K tartrate and $NaHCO_3$ (200 mL, 1:1) at 0 ºC and stirred rapidly for 1 h at rt. The layers were separated and the aqueous phase extracted with EtOAc (4 × 100 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (3:1 → 2:1 PE/EtOAc) to afford diol **34** (657 mg, 632 µmol, 95%) as a colourless oil.

**$R_f$** 0.59 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 8.9 Hz, $Ar_{PMB}\underline{H}$), 7.24 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 7.15 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.95 (1H, dt, *J* = 15.4, 7.5 Hz, C3$\underline{H}$), 6.88 (2H, d, *J* = 8.9 Hz,

$Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.81 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 5.91 (1H, d, *J* = 15.4 Hz, C2$\underline{H}$), 4.67 (1H, d, *J* = 11.4 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.62 (1H, d, *J* = 10.8 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.45 (1H, d, *J* = 11.0 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.41 (1H, d, *J* = 10.8 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.39 (1H, d, *J* = 11.0 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.30 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.25-4.19 (1H, m, C13$\underline{H}$), 4.12-4.06 (1H, m, C7$\underline{H}$), 3.93-3.87 (1H, m, C17$\underline{H}$), 3.87-3.80 (2H, m, C5$\underline{H}$, C9$\underline{H}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.75 (1H, d, *J* = 4.1 Hz, C16$\underline{H}$), 3.74 (3H, s, C1$O_2\underline{Me}$), 3.59-3.52 (1H, m, C19$\underline{H_a}H_b$), 3.44-3.38 (1H, m, C19$H_a\underline{H_b}$), 2.98 (1H, dd, *J* = 18.1, 8.0 Hz, C14$\underline{H_a}H_b$), 2.57-2.46 (2H, m, C4$\underline{H_a}H_b$, C4$H_a\underline{H_b}$), 2.34 (1H, dd, *J* = 18.1, 3.9 Hz, C14$H_a\underline{H_b}$), 1.81 (1H, dt, *J* = 14.6, 9.9 Hz, C6$\underline{H_a}H_b$), 1.76-1.62 (3H, m, C10$\underline{H_a}H_b$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.58-1.37 (6H, m, C6$H_a\underline{H_b}$, C8$\underline{H_a}H_b$, C8$H_a\underline{H_b}$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$), 1.01-0.91 (1H, m, C11$H_a\underline{H_b}$), 0.86 (9H, s, Si$^t\underline{Bu}Me_2$), 0.84 (9H, s, Si$^t\underline{Bu}Me_2$), 0.75 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.01 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.00 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), –0.01 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 212.3, 166.6, 159.7, 159.6, 159.3, 144.3, 130.5, 130.2, 129.8, 129.7, 129.5, 129.4, 124.0, 114.2, 114.0, 113.8, 86.3, 86.3, 78.4, 77.3, 72.9, 72.8, 71.1, 71.0, 69.5, 69.4, 59.3, 55.41, 55.38, 51.7, 43.3, 42.8, 41.1, 39.3, 36.6, 36.0, 33.6, 27.9, 26.10, 26.08, 18.4, 18.3, 14.9, –4.1, –4.6, –5.2, –5.3. **$[\alpha]_D^{20}$** +45.1 (*c* = 0.94, $CHCl_3$). **IR** (thin film) 3474, 2928, 2856, 1719, 1658, 1612, 1586, 1514, 1463, 1437, 1359.9, 1324, 1302, 1248, 1173, 1080, 1035 937, 834, 776, 756, 665 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{57}H_{94}O_{13}NSi_2$ [M + $NH_4$]$^+$ 1056.6258, found 1056.6267.

The relative stereochemistry was assigned by correlation with intermediates to those previously prepared during synthesis optimisation.[12]

**C1-C19 FRAGMENT 5**

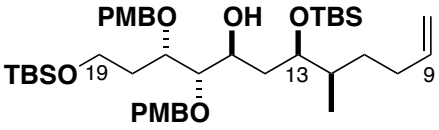



Diol **34** (1.05 g, 1.01 mmol, dried azeotropically from PhH) was dissolved in $CH_2Cl_2$ (15 mL) and 2,6-lutidine (468 *μ*L, 4.04 mmol) added. The solution was cooled to –78 ºC and TBSOTf (580 μL, 2.53 mmol) was added dropwise. After 1 h, the reaction was quenched by the addition of MeOH (5 mL) at –78 ºC before dilution with $NaHCO_3$ solution (25 mL). The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (5 × 40 mL). The combined organic phases were washed with brine (100 mL), dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (12:1 PE/EtOAc) to give *bis*-TBS ether **5** (1.19 g, 988 μmol, 97%) as a colourless oil.

**$R_f$** 0.64 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.26-7.22 (4H, m, $Ar_{PMB}\underline{H}$), 7.15 (2H, br d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.98 (1H, app dt, *J* = 15.8, 7.3 Hz, C3$\underline{H}$), 6.88-6.84 (4H, m, $Ar_{PMB}\underline{H}$), 6.81 (2H, br d, *J* = 8.7 Hz), 5.86 (1H, dt, *J* = 15.8, 1.2 Hz, C2$\underline{H}$), 4.69 (1H, d, *J* = 11.6 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.49-4.39 (4H, m, OC$\underline{H_a}H_bAr_{PMB}$, OC$\underline{H_a}H_bAr_{PMB}$, OC$H_a\underline{H_b}Ar_{PMB}$, OC$H_a\underline{H_b}Ar_{PMB}$), 4.28 (2H, d, *J* = 11.5 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.25-4.22 (1H, m, C13$\underline{H}$), 3.95 (2H, m, C7$\underline{H}$, C17$\underline{H}$), 3.81-3.73 (2H, obs m, C9$\underline{H}$, C16$\underline{H}$), 3.79 (6H, 2 overlapping s, $Ar_{PMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.72 (3H, s, C1$O_2\underline{Me}$), 3.68-3.62 (1H, m, C5$\underline{H}$), 3.53 (1H, ddd, *J* = 10.3, 7.2, 5.6 Hz, C19$\underline{H_a}H_b$), 3.36 (1H, app dt, 10.3, 5.8 Hz, C19$H_a\underline{H_b}$), 2.99 (1H, dd, *J* = 18.2, 8.1

Hz, C14$\underline{H_a}H_b$), 2.52-2.45 (1H, m, C4$\underline{H_a}H_b$), 2.39-2.31 (2H, m, C4$H_a\underline{H_b}$, C14$H_a\underline{H_b}$), 1.87 (1H, app dt, *J* = 12.8, 6.3 Hz, C6$\underline{H_a}H_b$), 1.74-1.65 (2H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.65-1.56 (4H, m, C6$H_a\underline{H_b}$, C8$\underline{H_a}H_b$, C8$H_a\underline{H_b}$, C11$\underline{H_a}H_b$), 1.55-1.28 (3H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C12$\underline{H}$), 1.01-0.96 (1H, m, C11$H_a\underline{H_b}$), 0.89-0.83 (36H, 4 overlapping s, Si$^t\underline{Bu}Me_2$), 0.75 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.09 (3H, Si$^t$Bu$\underline{Me_a}Me_b$), 0.06 (3H, Si$^t$Bu$\underline{Me_a}Me_b$), 0.05 (6H, 2 overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (3H, Si$^t$Bu$Me_a\underline{Me_b}$), 0.02 (3H, Si$^t$Bu$Me_a\underline{Me_b}$), –0.009 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), –0.01 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 212.3, 166.7, 159.5, 159.24, 159.22, 145.8, 130.6, 130.1, 129.8, 129.7, 129.3, 123.1, 113.9, 113.8, 113.7, 86.0, 81.6, 77.2, 75.9, 75.6, 74.7, 74.6, 73.2, 72.8, 72.6, 71.2, 70.8, 70.5, 70.4, 70.3, 67.5, 59.5, 59.0, 55.3, 55.24, 55.22, 51.4, 45.81, 45.77, 43.0, 42.9, 39.5, 38.1, 37.1, 36.7, 36.6, 36.1, 33.7, 33.5, 29.7, 27.5, 27.1, 26.00, 25.97, 25.95, 18.3, 18.2, 18.12, 18.05, 18.04, 14.8, 14.2, 1.0, –3.7, –3.8, –3.9, –4.2, –4.26, –4.28, –4.6, –5.30, –5.33, –5.4. **$[\alpha]_D^{20}$** +11.3 (*c* = 2.5, $CHCl_3$). **IR** (thin film) 2953.2, 2929.4, 2857.2, 1726.6 (br), 1613.7, 1514.6, 1463.5, 1249.2, 1082.2, 1038.5, 835.0, 774.7 cm$^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{69}H_{118}O_{13}Si_4Na$ $[M + Na]^+$ 1289.7542, found 1289.7575.

**ALCOHOL 103** - *model studies*

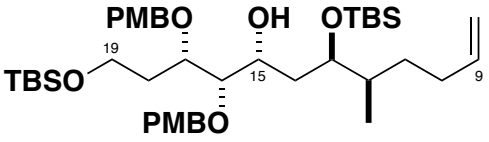



A solution of ketone **30** (49.2 mg, 67.5 µmol) in $Et_2O$ (0.5 mL) was prepared and cooled to –50 ºC. A solution of $Zn(BH_4)_2$ (6.75 mL, 1.01 mmol, 0.15 M in $Et_2O$) was added slowly and the reaction stirred for 1 h. The reaction was warmed to –30 ºC for a further 2 h before carefully quenching with $Na^+/K^+$ tartrate solution (2 mL) and stirring rapidly for 30 min. The layers were separated and the aqueous phase extracted with EtOAc (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The product was purified by column chromatography (10:1 PE/EtOAc) to afford alcohol **103** (48.2 mg, 66.2 µmol, 98%) as a colourless oil and single diastereomer by $^1$H NMR spectroscopy. The relative stereochemistry was assumed on the basis of similar 1,2-*anti* selective reductions using $Zn(BH_4)_2$. The C15 epimer **104** was also synthesised by 1,3-*anti* selective reduction that was less diastereoselective (*vide infra*).

**$R_f$** 0.39 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.24 (4H, br d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.85 (4H, br d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 5.79 (1H, ddt, *J* = 16.7, 10.2, 6.6 Hz, C9$\underline{H}$), 5.00 (1H, br d, *J* = 17.1 Hz, C9(H)C$\underline{H_a}H_b$), 4.93 (1H, br d, *J* = 10.0 Hz, C9(H)C$H_a\underline{H_b}$), 4.59 (2H, overlapping d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.56 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.55 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.52 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.49 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.90-3.85 (2H, m, C19$\underline{H_a}H_b$, C19$H_a\underline{H_b}$), 3.83-3.78 (1H, obs m, C17$\underline{H}$), 3.80 (6H, overlapping s, $Ar_{PMB}O\underline{Me}$), 3.68-3.59 (2H, m, C13H, C15H), 3.41 (C15(H)O$\underline{H}$), 3.35-3.32 (1H, d, *J* = 6.0, 4.3 Hz, C16$\underline{H}$), 2.16-2.08 (1H, m, C10$\underline{H_a}H_b$), 2.02-1.93 (1H, m, C10$H_a\underline{H_b}$), 1.88-1.74 (3H, m, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$, C18$\underline{H_a}H_b$), 1.64-1.55 (2H, m, C12$\underline{H}$, C18$H_a\underline{H_b}$), 1.48 (1H, ddd, *J* = 14.4, 9.6, 7.6 Hz, C11$\underline{H_a}H_b$), 1.19 (1H, ddd, *J* = 14.4, 10.7, 5.4 Hz, C11$H_a\underline{H_b}$), 0.90 (9H, s, Si$^t\underline{Bu}Me_2$), 0.89 (9H, s, Si$^t\underline{Bu}Me_2$), 0.79 (3H, d, *J* = 6.6 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.038 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), 0.033 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$) [Spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.23, 159.21, 139.2, 130.53, 130.51, 129.75, 129.72, 114.1, 113.74, 113.72,

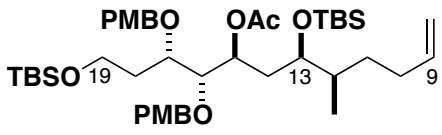
81.5, 75.8, 74.9, 73.2, 72.6, 70.3, 59.5, 55.2 (2C), 36.9, 36.2, 33.7, 31.9, 31.3, 29.7, 25.94, 25.90, 18.2, 18.0, 14.0, –4.3, –5.3, –5.4. **[α]$_D^{20}$** –6.1 (*c* = 0.88, $CHCl_3$). **IR** (thin film) 3464.3 (br), 2957.0, 2928.6, 2855.7, 1612.3, 1514.5, 1463.7, 1250.3, 1091.5, 1036.8, 834.5, 775.1 $cm^{-1}$.

**ALCOHOL 104** - *MODEL STUDIES*




To a solution of ketone **30** (100 mg, 137 µmol) in MTBE at –98 ºC was added DIBAL (548 µL, 1.64 mmol, 1 M solution in hexane) dropwise. The reaction was stirred for 1 h and, when complete by TLC, was quenched by the addition of MeOH (2 mL) and $Na^+/K^+$ tartrate solution (2 mL) and diluted with EtOAc (5 mL). On warming to rt and stirring for 1 h, the layers were separated and the aqueous phase extracted with EtOAc (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The product was purified by column chromatography (10:1 PE/EtOAc) to afford alcohol 1**04** (92 mg, 126 µmol, 92%) as a colourless oil. The $^1H$ NMR spectrum of the crude product indicated that it was formed in 8:1 dr.
**$R_f$** 0.41 (4:1 PE/EtOAc). **$^1H$ NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.24 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 5.80 (1H, ddt, *J* = 16.7, 10.2, 6.6 Hz, C9$\underline{H}$), 5.00 (1H, br d, *J* = 17.1 Hz, C9(H)C$\underline{H_a}H_b$), 4.93 (1H, br d, *J* = 10.0 Hz, C9(H)C$H_a\underline{H_b}$), 4.72 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.58 (2H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.56 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.55 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.51 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.48 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.90-3.79 (3H, m, C13$\underline{H}$, C15$\underline{H}$, C17$\underline{H}$), 3.81 (6H, overlapping s, $Ar_{PMB}O\underline{Me}$), 3.70 (2H, m, C19$\underline{H_a}H_b$, C19$H_a\underline{H_b}$), 3.29 (1H, dd, *J* = 5.6, 4.3 Hz, C16$\underline{H}$), 2.26 (1H, d, J = 5.8 Hz, C15(H)O$\underline{H}$), 2.18-2.09 (1H, m, C10$\underline{H_a}H_b$), 2.00-1.92 (1H, m, C10$H_a\underline{H_b}$), 1.91-1.82 (1H, m, C18$\underline{H_a}H_b$), 1.74-1.55 (3H, m, C11$\underline{H_a}H_b$, C12$\underline{H}$, C18$H_a\underline{H_b}$), 1.43-1.40 (2H, m, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.03-0.95 (1H, m, C11$H_a\underline{H_b}$), 0.91 (9H, s, Si$^t\underline{Bu}Me_2$), 0.88 (9H, s, Si$^t\underline{Bu}Me_2$), 0.81 (3H, d, *J* = 6.6 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.05 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), 0.04 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$) [Spin system broken across C12-C13 by restricted rotation]. **$^{13}C$ NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.4, 159.1, 139.3, 131.0, 130.5, 129.9, 129.4, 114.1, 113.84, 113.77, 83.1, 76.2, 73.8, 72.7, 72.6, 67.4, 59.5, 55.3 (2C), 38.7, 37.0, 34.1, 32.1, 30.1, 26.00, 25.99 18.3, 18.1, 15.4, –4.3, –4.5, –5.27, –5.32. **[α]$_D^{20}$** –0.048 (*c* = 2.0, $CHCl_3$). I**R** (thin film) 3513.9 (br), 2954.7, 2929.5, 2857.1, 1613.1, 1514.3, 1463.3, 1249.4, 1081.7, 1038.2, 835.2, 775.0 $cm^{-1}$.

**ACETATE ESTER 105** - *MODEL STUDIES*

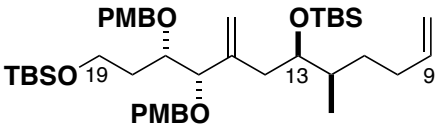



Alcohol **103** (15.0 mg, 20.5 µmol) was dissolved in $CH_2Cl_2$ (0.5 mL) and cooled to 0 ºC. Triethylamine (40 µL, 288 µmol) was added, followed by acetic anhydride (20 µL, 212 µmol) and DMAP (1 crystal). The reaction was complete after 30 min and the yellow solution was quenched with $NaHCO_3$ solution (1 mL). The mixture

was extracted with $CH_2Cl_2$ (3 × 5 mL) and the combined organic extracts washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 PE/EtOAc) to give ester **105** (14.5 mg, 18.8 µmol, 90%) as a colourless oil.

**$R_f$** 0.21 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.26 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 7.22 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.84 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 5.79 (1H, ddt, *J* = 17.3, 10.2, 6.5 Hz, C9$\underline{H}$), 5.00-4.98 (1H, m, C15$\underline{H}$), 4.99 (1H, br dd, *J* = 17.3, 1.6 Hz, C9(H)C$\underline{H_a}H_b$), 4.93 (1H, br d, *J* = 10.2 Hz, C9(H)C$H_a\underline{H_b}$), 4.64 (1H, d, *J* = 10.8 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.40 (2H, app s, OC$\underline{H_a}H_bAr_{PMB}$, OC$H_a\underline{H_b}Ar_{PMB}$), 4.44 (1H, d, *J* = 10.7 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.74-3.68 (1H, m, C19$\underline{H_a}H_b$), 3.68-3.62 (3H, m, C13$\underline{H}$, C17$\underline{H}$, C19$H_a\underline{H_b}$), 3.59 (1H, dd, *J* = 6.8, 2.7 Hz, C16$\underline{H}$), 2.06-1.96 (3H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C14$\underline{H_a}H_b$), 1.96 (3H, s, C15(H)O$\underline{Ac}$), 1.85 (1H, ddd, *J* = 14.7, 9.8, 2.1 Hz, C14$H_a\underline{H_b}$), 1.81-1.75 (1H, m, C18$\underline{H_a}H_b$), 1.65 (1H, ddd, *J* = 13.8, 9.3, 4.5 Hz, C18$H_a\underline{H_b}$), 1.52-1.46 (1H, m, C12$\underline{H}$), 1.46-1.40 (1H, m, C11$\underline{H_a}H_b$), 1.31-1.23 (1H, m, C11$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}Me_2$), 0.88 (9H, s, Si$^t\underline{Bu}Me_2$), 0.80 (3H, d, *J* = 6.6 Hz, C12(H)$\underline{Me}$), 0.09 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.034 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.032 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), 0.028 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$) [Spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.3, 159.12, 159.07, 139.1, 131.0, 130.8, 129.5, 129.4, 114.1, 113.68, 113.65, 82.5, 76.1, 73.9, 73.4, 72.3, 71.3, 59.1, 55.27, 55.25, 35.6, 34.6, 34.0, 33.3, 31.7, 25.93 (2C), 25.89, 21.1, 18.2, 18.1, 12.7, –4.1, –4.7, –5.4 (2C). **$[\alpha]_D^{20}$** –27.8 (*c* = 0.42, $CHCl_3$). **IR** (thin film) 2957.0, 2928.6, 2856.7, 1738.5, 1612.9, 1585.4 (w), 1514.0, 1463.4, 1361.1, 1246.6, 1173.1, 1079.5, 835.7, 774.9 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{43}H_{76}NO_8Si_2$ $[M + NH_4]^+$ 790.5109, found 790.5108.

**OLEFIN 74** - *MODEL STUDIES*



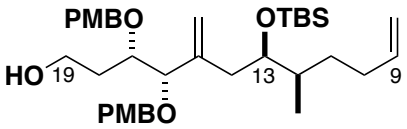

*Conditions A:* To a stirred suspension of Nysted Reagent (7.90 mL, 4.11 mmol, 20%wt slurry in THF) in THF (2 mL) at 0 ºC was added dropwise $TiCl_4$ (0.34 mL, 3.1 mmol). After 10 min, ketone **30** (160 mg, 219 µmol) in THF (3 mL) was added *via* cannula and the reaction mixture was warmed to rt and stirred for 1 h. The reaction was quenched by slowly cannulating into a cold (0 ºC) mixture of $NaHCO_3$ solution (10 mL) and $Na^+$/$K^+$ tartrate solution (10 mL). After stirring for 1 h, the layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (40 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The crude residue was purified by column chromatography (9:1 PE/EtOAc) to give alkene **74** (149 mg, 205 µmol, 94%) as a colourless oil.

*Conditions B:* To a slurry of zinc dust (6.00 g, 91.7 mmol) in THF (42 mL) was added lead(II) iodide (395 mg, 39.1 mmol ). A small portion of diiodomethane (500 µL, 6.21 mmol) was added and the mixture sonicated until reaction initiated. After a further 5 min of sonication, the mixture was cooled to 0 ºC and the remaining diiodomethane (2.65 mL, 32.9 mmol) added dropwise to give a green solution. Titanium tetrachloride (2.17 mL, 19.8 mmol) was carefully added at 0 ºC *via* syringe close to the reaction mixture surface [yellow fumes observed]. After stirring at rt for 45 min, ketone **30** (255 mg, 716 µmol, dried azeotropically from PhH (3 × 5 mL) in THF (1 mL + 1 mL wash) was added to the resulting black slurry and the reaction was stirred at rt for

12 h. The mixture was quenched by transferring *via* pipette to a 1:1 solution of $NaHCO_3$ and $Na^+/K^+$ tartrate (300 mL) at 0 °C and stirred vigorously for 6 h to afford a white/grey suspension. The liquid was decanted and the layers separated. The aqueous phase was extracted with EtOAc (3 × 200 mL) and the combined organics washed with brine (200 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Olefin **74** (385 mg, 530 µmol, 74%) was afforded as a colourless oil.

**$R_f$** 0.38 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.26 (1H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 7.23 (1H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.84 (1H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.83 (1H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 5.78 (1H, ddt, *J* = 17.2, 10.4, 6.5 Hz, C9$\underline{H}$), 5.14 (1H, br s, C15C$\underline{H_a}H_b$), 5.05 (1H, br s, C15C$H_a\underline{H_b}$), 4.98 (1H, ddd, *J* = 17.2, 3.4, 1.6 Hz, C9(H)C$\underline{H_a}H_b$), 4.92 (1H, br d, *J* = 10.4 Hz, C9(H)C$H_a\underline{H_b}$), 4.76 (1H, d, *J* = 10.7 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.51 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.48 (1H, d, *J* = 10.7 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.28 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.89 (1H, dt, *J* = 6.9, 1.7 Hz, C16$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77-3.70 (2H, obs m, C16$\underline{H}$, C17$\underline{H}$), 3.69-3.63 (1H, m, C19$\underline{H_a}H_b$), 3.62-3.55 (1H, m, C19$H_a\underline{H_b}$), 2.18-1.90 (4H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.71-1.43 (4H, m, C11$\underline{H_a}H_b$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.28-1.21 (1H, m, C11$H_a\underline{H_b}$), 0.89 (18H, 2 overlapping s, Si$^t\underline{Bu}Me_aMe_b$), 0.83 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$),0.02 (6H, 2 overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), 0.01 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.1 (2C), 143.4, 139.2, 131.4, 130.9, 129.6, 129.2, 115.8, 114.1. 113.7, 87.5, 73.8, 70.4, 59.4, 55.3, 36.2, 35.9, 34.9, 32.7, 31.9, 26.0, 18.3, 18.1, 13.2, –4.0, –4.5, –5.3. **$[\alpha]_D^{20}$** –0.7 (*c* = 3.4, $CHCl_3$). **IR** (thin film) 2929.5, 2857.2, 1513.9, 1463.0, 1249.1, 1084.2, 835.9, 774.0 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{42}H_{76}O_6NSi_2$ $[M + NH_4]^+$ 744.5049, found 744.5051.

**ALCOHOL 75** - *MODEL STUDIES*

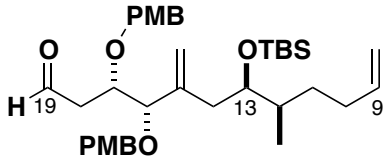



A stock solution of HF · pyridine (600 µL, 6.65 µmol) in pyridine (1.2 mL) and THF (4.2 mL) was prepared. To a solution of TBS ether **74** (213 mg, 293 µmol) in THF (2.5 mL) was added the HF · pyridine stock solution (2.5 mL). The reaction stirred for 4 h at rt and quenched by the addition of $NaHCO_3$ solution (5 mL). The layers were separated and the aqueous phase extracted with EtOAc (4 × 20 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (8:1 PE/EtOAc) to afford alcohol **75** (172 mg, 6.38 µmol, 96%) as a colourless oil.

**$R_f$** 0.33 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.26 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 7.23 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 5.78 (1H, dddd, *J* = 17.1, 13.1, 10.1, 6.5 Hz, C9$\underline{H}$), 5.18 (1H, s, C15C$\underline{H_a}H_b$), 5.09 (1H, s, C15C$H_a\underline{H_b}$), 4.99 (1H, d, *J* = 17.1 Hz, C9(H)C$\underline{H_a}H_b$), 4.93 (1H, d, *J* = 10.1 Hz, C9(H)C$H_a\underline{H_b}$), 4.81 (1H, d, *J* = 10.9 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.54 (1H, d, *J* = 10.9 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.53 (1H, d, *J* = 11.5 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.29 (1H, d, *J* = 11.5 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.91-3.88 (1H, m, C13$\underline{H}$), 3.84 (1H, d, *J* = 7.1 Hz, C16$\underline{H}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77-3.73 (1H, m, C17$\underline{H}$), 3.68-3.62 (2H, m, C19$\underline{H_a}H_b$ C19$H_a\underline{H_b}$), 2.16 (2H, obs m, C14$\underline{H_a}H_b$ C14$H_a\underline{H_b}$), 2.13-2.05 (2H, m, C10$\underline{H_a}H_b$, C19$H_aH_bO\underline{H}$), 2.00-1.94 (1H, m, C10$H_a\underline{H_b}$), 1.67-1.53 (3H, m, C12$\underline{H}$,

C18$\underline{H_a}H_b$ C18$H_a\underline{H_b}$), 1.52-1.45 (1H, m, C11$\underline{H_a}H_b$), 1.28-1.21 (1H, m, C11$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}Me_aMe_b$), 0.84 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.3, 159.1, 142.9, 139.1, 130.6, 130.5, 129.9, 129.3, 116.4, 114.2, 113.8, 113.7, 86.9, 79.0, 73.9, 73.8, 70.4, 60.5, 55.3 (2C), 36.1, 33.8, 32.6, 31.8, 25.9, 18.1, 13.2, –4.0, –4.4. **IR** (thin film) 3463.0, 2931.0, 2857.0, 1613.0, 1514.0, 1248.0, 1037.0, 836.0 cm$^{-1}$. **$[\alpha]_D^{20}$** –4.4 (*c* = 2.4, $CHCl_3$). **HRMS** (ES$^+$) Calculated for $C_{36}H_{60}O_6NSi$ $[M + NH_4]^+$ 630.4184, found 630.4181.

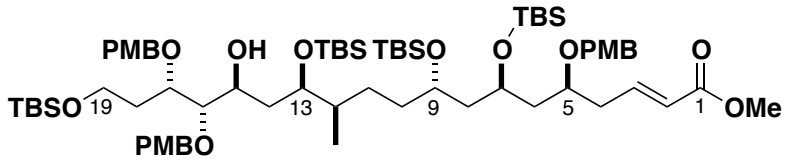
**ALDEHYDE 76** - *MODEL STUDIES*




To a solution of alcohol **75** (173 mg, 284 µmol) in $CH_2Cl_2$ (5 mL) was added sequentially $NaHCO_3$ (60 mg, 712 *µ*mol) and Dess–Martin periodinane (161 mg, 426 µmol). The reaction was stirred at rt for 1 h and quenched by the addition of $Na_2S_2O_3$ solution (5 mL). The mixture was stirred for 30 min and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (5 × 20 mL) and the combined organic extracts dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 PE/EtOAc) to give aldehyde **76** (164 mg, 270 µmol, 95%) as a colourless oil.

**$R_f$** 0.48 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.64 (1H, br s, C19$\underline{H}$O), 7.24 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 7.19 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.86 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.84 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 5.79 (1H, dddd, *J* = 17.0, 13.2, 10.2, 6.6 Hz, C9$\underline{H}$), 5.22 (1H, s, C15C$\underline{H_a}H_b$), 5.12 (1H, s, C15C$H_a\underline{H_b}$), 4.99 (1H, dd, *J* = 17.1, 1.4 Hz, C9(H)C$\underline{H_a}H_b$), 4.93 (1H, d, *J* = 10.2 Hz, C9(H)C$H_a\underline{H_b}$), 4.68 (1H, d, *J* = 11.0 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.53 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.52 (1H, d, *J* = 11.0 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.26 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.10-4.06 (1H, m, C17$\underline{H}$), 3.86-3.83 (2H, m, C13$\underline{H}$, C16$\underline{H}$), 3.81 (3H, s, $Ar_{PMB}$O$\underline{Me}$), 3.80 (3H, s, $Ar_{PMB}$O$\underline{Me}$), 2.52-2.50 (2H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 2.19-2.06 (3H, m, C10$\underline{H_a}H_b$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 2.00-1.94 (1H, m, C10$H_a\underline{H_b}$), 1.66-1.60 (1H, m, C12$\underline{H}$), 1.55-1.48 (1H, m, C11$\underline{H_a}H_b$), 1.27-1.19 (1H, m, C11$H_a\underline{H_b}$), 0.88 (9H, s, Si$^t\underline{Bu}Me_aMe_b$), 0.82 (3H, d, *J* = 6.8 Hz, C12(H)$\underline{Me}$), 0.05 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 201.0, 159.3, 159.2, 142.6, 139.1, 130.3, 130.2, 129.7, 129.4, 116.1, 114.3, 113.8, 84.5, 75.1, 74.2, 73.2, 70.6, 55.3 (2C), 45.8, 36.4, 36.3, 32.4, 31.8, 25.9, 18.1, 13.5, –4.0, –4.4. **IR** (thin film) 2933.0, 1726.0, 1613.0, 1514.0, 1249.0, 1077.0, 1037.0, 836.0 cm$^{-1}$. **$[\alpha]_D^{20}$** +3.7 (*c* = 1.7, $CHCl_3$). **HRMS** (ES$^+$) Calculated for $C_{36}H_{58}O_6NSi$ $[M + NH_4]^+$ 628.4028, found 628.4026.

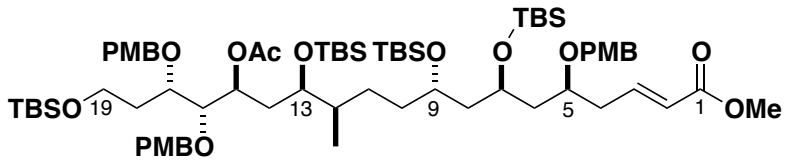
**ALCOHOL 82**




Ketone **5** (473 mg, 373 µmol) was dissolved in $Et_2O$ (50 mL) and the solution cooled to –30 ºC. Zinc borohydride (100 ml, 15.0 mmol, 0.15 M solution in $Et_2O$) was added *via* syringe and the reaction stirred for 1 h at –30 ºC, 1 h at –20 ºC, 1 h at –10 ºC and 1 h at 0 ºC [there is no $R_f$ change in this reaction]. The reaction was quenched by the addition of $Na^+/K^+$ tartrate solution (200 mL) and stirring vigorously for 2 h. The layers were separated and the aqueous phase extracted with EtOAc (5 × 300 mL). The combined organic phases were washed with brine (300 mL) and concentrated *in vacuo*. Alcohol **82** (474 mg, 373 µmol, quant.) was afforded as a colourless oil without any further purification.

**$R_f$** 0.42 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.28-7.21 (6H, m, $Ar_{PMB}\underline{H}$), 6.99 (1H, dt, *J* = 15.5, 7.3 Hz, C3$\underline{H}$), 6.88-6.84 (6H, m, $Ar_{PMB}\underline{H}$), 5.87 (1H, d, *J* = 15.5 Hz, C2$\underline{H}$), 4.58 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.57 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.55 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.51-4.47 (2H, overlapping d, OC$H_a\underline{H_b}Ar_{PMB}$), 4.42 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.95-3.91 (1H, m, C9$\underline{H}$), 3.91-3.85 (2H, m, C7$\underline{H}$, C13$\underline{H}$), 3.85-3.73 (2H, obs m, C15$\underline{H}$, C17$\underline{H}$), 3.81-3.80 (9H, overlapping s, $Ar_{PMB}O\underline{Me}$), 3.73 (3H, s, C1$O_2\underline{Me}$), 3.70-3.59 (3H, m, C5$\underline{H}$, C19$\underline{H_a}H_b$, C19$H_a\underline{H_b}$), 3.47 (1H, br s, C15(H)O$\underline{H}$), 3.37 (1H, m, C16$\underline{H}$), 2.53-2.45 (1H, m, C4$\underline{H_a}H_b$), 2.40-2.32 (1H, m, C4$H_a\underline{H_b}$), 1.90-1.80 (3H, m, C14$\underline{H_a}H_b$, C6$\underline{H_a}H_b$, C8$\underline{H_a}H_b$), 1.80-1.73 (1H, m, C14$H_a\underline{H_b}$), 1.66-1.59 (3H, m, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.59-1.44 (5H, m, C6$H_a\underline{H_b}$, C8$H_a\underline{H_b}$, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C12$\underline{H}$), 1.39-1.30 (1H, m, C11$\underline{H_a}H_b$), 1.13-1.04 (1H, m, C11$H_a\underline{H_b}$), 0.91 (9H, s, Si$^t\underline{Bu}Me_2$), 0.90 (9H, s, Si$^t\underline{Bu}Me_2$), 0.88 (18H, overlapping s, Si$^t\underline{Bu}Me_2$), 0.79 (3H, d, *J* = 6.4 Hz, C12(H)$\underline{Me}$), 0.089 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.081 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.069 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.060 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), 0.054 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), 0.047 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), 0.040 (6H, overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), [spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 166.7, 159.22, 159.20, 159.1, 145.7, 130.5, 129.7, 129.7, 129.2, 123.0, 113.72 (3C), 113.71 (2C), 81.5, 75.9, 75.5, 74.6, 73.2, 72.6, 70.8, 70.4, 70.3, 67.5, 60.3, 59.5, 55.23, 55.21, 51.4, 45.8, 42.9, 38.1, 37.1, 36.5, 36.1, 33.7, 27.4, 25.96 (2C), 25.93 (3C), 18.2, 18.05, 18.02, 18.01, 14.2, –3.80, –3.88, –3.89, –4.20, –4.22, –4.31, –5.33, –5.36. **$[\alpha]_D^{20}$** +2.7 (*c* = 4.0, $CHCl_3$). **IR** (thin film) 3483.5 (br), 2951.9, 2931.8, 2886.1, 2858.0, 17.28.1, 1614.0, 1514.5, 1471.6, 1463.8, 1249.8, 1082.3, 1038.7, 835.2, 774.1.6 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{69}H_{120}O_{13}Si_4Na$ $[M + Na]^+$ 1291.7698, found 1291.7666.

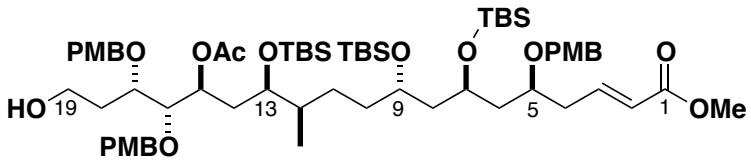
**ACETATE ESTER 83**




Alcohol **82** (474 mg, 373 µmol) was dissolved in $CH_2Cl_2$ (15 mL) and cooled to 0 ºC. Triethylamine (259 µL, 1.87 mmol), acetic anhydride (146 µL, 1.49 mmol) and DMAP (1 crystal) were added sequentially and the reaction warmed to rt for 12 h [there is no $R_f$ change for this reaction]. The reaction was quenched by the addition of $NaHCO_3$ solution (20 mL). The layers were separated and the aqueous phase extracted with EtOAc (4 × 50 mL). The combined organic phases were washed with brine (100 mL) and concentrated *in vacuo*. The crude product was purified by column chromatography (10:1 → 5:1 PE/EtOAc) to give ester **83** (479 mg, 363 µmol, 97%) as a colourless oil.

**$R_f$** 0.42 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.28 (6H, m, $Ar_{PMB}\underline{H}$), 6.99 (1H, dt, *J* = 15.5, 7.3 Hz, C3$\underline{H}$), 6.89-6.81 (6H, m, $Ar_{PMB}\underline{H}$), 5.88 (1H, d, *J* = 15.5 Hz, C2$\underline{H}$), 5.01-4.96 (1H, m, C15$\underline{H}$), 4.64 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.60 (2H, app s, OC$\underline{H_a}H_bAr_{PMB}$), 4.48 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.44 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.41 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 3.93 (1H, m, C9$\underline{H}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.80 (6H, overlapping s, $Ar_{PMB}O\underline{Me}$), 3.76-3.58 (7H, obs m, C5$\underline{H}$, C7$\underline{H}$, C13$\underline{H}$, C16$\underline{H}$, C17$\underline{H}$, C19$\underline{H_a}H_b$, C19$H_a\underline{H_b}$), 3.72 (3H, s, C1$O_2\underline{Me}$), 2.53-2.46 (1H, m, C4$\underline{H_a}H_b$), 2.39-2.32 (1H, m, C4$H_a\underline{H_b}$), 2.02-1.92 (1H, obs m, C14$\underline{H_a}H_b$), 1.94 (3H, s, C15(H)O$\underline{Ac}$), 1.89-1.75 (3H, m, C6$\underline{H_a}H_b$, C8$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.69-1.52 (4H, m, C8$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.45-1.32 (4H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$), 1.23-1.16 (1H, m, C11$H_a\underline{H_b}$), 0.890 (9H, s, Si$^t\underline{Bu}Me_2$), 0.886 (9H, s, Si$^t\underline{Bu}Me_2$), 0.87 (18H, br s, Si$^t\underline{Bu}Me_2$), 0.80 (3H, d, *J* = 6.4 Hz, C12(H)$\underline{Me}$), 0.09 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.07 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.06-0.02 (18H, overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), [spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.2, 166.7, 159.12, 159.11, 159.07, 145.7, 131.0, 130.8, 130.5, 129.5, 129.4, 129.2, 123.1, 113.73, 113.66, 113.64, 82.3, 76.1, 74.6, 73.8, 73.3, 72.1, 71.9, 70.8, 70.3, 67.5, 59.1, 55.2 (3C), 51.4, 45.8, 42.8, 37.1, 36.7, 36.2, 34.6, 34.1, 29.7, 25.92, 25.91 (2C), 21.1, 18.2, 18.1, 18.04, 18.00, 12.6, –3.86 (2C), –3.92, –4.0, –4.1, –5.4 (2C). **$[\alpha]_D^{20}$** –13.0 (*c* = 8.6, $CHCl_3$). **IR** (thin film) 2951.9, 2929.5, 2857.4, 1732.0, 1730.8, 1613.4, 1514.5, 1463.3, 1249.0, 1083.9, 1038.9, 835.5, 774.6 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{71}H_{126}NO_{14}Si_4$ $[M + NH_4]^+$ 1328.8255, found 1328.8252.

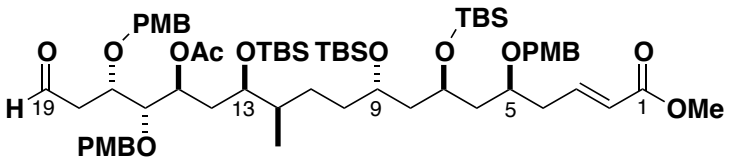
**ALCOHOL 84**




To a solution of TBS ether **83** (479 mg, 365 µmol) in THF (25 mL) was added acetic acid (105 µL, 1.83 mmol) and TBAF (730 µL, 730 µmol, 1.0 M solution in THF). The reaction was stirred at rt for 36 h and quenched with $NaHCO_3$ solution (20 mL) at the first sight of multiply deprotected species by TLC. The layers were separated and the aqueous phase extracted with EtOAc (5 × 20 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (5:1 → 3:1 PE/EtOAc) to give sequentially recovered TBS ether **83** (76 mg, 57.9 µmol, 16%) and alcohol **84** (323 mg, 270 µmol, 74%) as colourless oils.

**$R_f$** 0.30 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.28-7.21 (6H, m, $Ar_{PMB}\underline{H}$), 6.98 (1H, dt, *J* = 15.5, 7.3 Hz, C3$\underline{H}$), 6.89-6.83 (6H, m, $Ar_{PMB}\underline{H}$), 5.87 (1H, d, *J* = 15.5 Hz, C2$\underline{H}$), 5.02-4.95 (1H, m, C15$\underline{H}$), 4.67 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.63 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.59 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.49-4.39 (3H, m, OC$H_a\underline{H_b}Ar_{PMB}$), 3.92 (1H, m, C9$\underline{H}$), 3.81 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.80 (6H, br s, $Ar_{PMB}O\underline{Me}$), 3.74-3.60 (7H, obs m, C5$\underline{H}$, C7$\underline{H}$, C13$\underline{H}$, C16$\underline{H}$, C17$\underline{H}$, C19$\underline{H_a}H_b$, C19$H_a\underline{H_b}$), 3.72 (3H, s, C1$O_2\underline{Me}$), 2.54-2.46 (1H, m, C4$\underline{H_a}H_b$), 2.40-2.32 (1H, m, C4$H_a\underline{H_b}$), 2.02-1.92 (1H, obs, m, C14$\underline{H_a}H_b$), 1.96 (3H, s, C15(H)O$\underline{Ac}$), 1.91-1.80 (3H, m, C6$\underline{H_a}H_b$, C8$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.76-1.67 (1H, m, C6$H_a\underline{H_b}$), 1.65-1.50 (4H, m, C8$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$), 1.45-1.30 (4H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$), 1.21-1.11 (1H, m, C11$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}Me_2$), 0.86 (18H, br s, Si$^t\underline{Bu}Me_2$), 0.79 (3H, d, *J* = 6.4 Hz, C12(H)$\underline{Me}$), 0.08 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.07 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (12H, 4 overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), [spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.3, 166.7, 159.3, 159.2, 159.1, 145.7, 130.50, 130.47, 130.3, 129.7, 129.5, 129.2, 123.1, 113.8, 113.73, 113.69, 81.7, 78.0, 77.2, 74.5, 73.9, 73.0, 71.92, 71.89, 70.7, 70.2, 67.4, 60.2, 55.2 (2C), 51,4, 45. 8, 42.6, 36.8, 36.7, 36.0, 34.1, 33.7, 29.5, 25.92, 25.90, 21.1, 18.1, 18.03, 17.99, 12.8, –3.9 (3C), –4.0, –4.2, –4.6. **$[\alpha]_D^{20}$** –12.5 (*c* = 1.4, $CHCl_3$). **IR** (thin film) 3443.0 (br), 2928.7, 2857.9, 1729.3, 1612.9, 1514.3, 1463.1, 1246.6, 1172.7, 1062.1, 1038.6, 835.4, 774.1 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{65}H_{108}O_{14}Si_3Na$ $[M + Na]^+$ 1219.6939, found 1219.6963.

**C1-C19 SOUTHERN FRAGMENT 81**

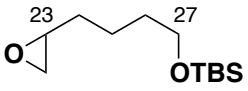



To a solution of alcohol **84** (300 mg, 250 *μ*mol) in $CH_2Cl_2$ (10 mL) was added sodium hydrogen carbonate (42 mg, 501 μmol) and Dess–Martin periodinane (159 mg, 376 μmol). After stirring for 30 min at rt, the reaction was quenched by the addition of $Na_2S_2O_3$ solution (10 mL) and stirred for a further 30 min. The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (5 × 10 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (10:1 → 3:1 PE/EtOAc) to afford aldehyde **81** (294 mg, 244 μmol, 98%) as a colourless oil. **$R_f$** 0.33 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.66 (1H, br s, C19HO), 7.27-7.16 (6H, m, $Ar_{PMB}H$), 6.98 (1H, dt, *J* = 15.5, 7.3 Hz, C3H), 6.88-6.82 (6H, m, $Ar_{PMB}H$), 5.88 (1H, d, *J* = 15.5 Hz, C2H), 5.06-5.01 (1H, m, C15H), 4.58 (1H, d, *J* = 11.2 Hz, $OCH_aH_bAr_{PMB}$), 4.54 (1H, d, *J* = 11.2 Hz, $OCH_aH_bAr_{PMB}$), 4.49-4.40 (4H, m, $OCH_aH_bAr_{PMB}$, $OCH_aH_bAr_{PMB}$), 4.08-4.03 (1H, m, C17H), 3.93 (1H, m, C9H), 3.79 (3H, s, $Ar_{PMB}OMe$), 3.78-3.77 (7H, m, $Ar_{PMB}OMe$, $Ar_{PMB}OMe$, C7H), 3.75-3.69 (4H, m, $C1O_2Me$, C9H), 3.68 (1H, m, C5H), 3.63-3.59 (2H, m, C16H, C13H), 2.70 (1H, br dd, *J* = 17.0, 4.2 Hz, $C18H_aH_b$), 2.64 (1H, br dd, *J* = 17.0, 7.4 Hz, $C18H_aH_b$), 2.50 (1H, ddd, *J* = 14.4, 7.3, 5.4 Hz, $C4H_aH_b$), 2.36 (1H, ddd, *J* = 14.4, 7.3, 7.0 Hz, $C4H_aH_b$), 1.96-1.92 (1H, obs m, $C6H_aH_b$), 1.95 (3H, s, C15(H)OC(O)Me), 1.89-1.81 (2H, m, $C14H_aH_b$, $C6H_aH_b$), 1.63-1.58 (1H, m, $C8H_aH_b$), 1.58-1.51 (2H, m, $C14H_aH_b$, $C8H_aH_b$), 1.45-1.40 (2H, m, $C10H_aH_b$, C12H), 1.40-1.31 (2H, m, $C11H_aH_b$, $C11H_aH_b$), 1.21-1.11 (1H, m, $C11H_aH_b$), 0.88 (9H, $Si^tBuMe_2$), 0.86 (18H, br s, $Si^tBuMe_2$), 0.77 (3H, d, *J* = 6.1 Hz, C12(H)Me), 0.068 (3H, s, $Si^tBuMe_aMe_b$), 0.064 (3H, s, $Si^tBuMe_aMe_b$), 0.049-0.036 (9H, 3 overlapping s, $Si^tBuMe_aMe_b$, $Si^tBuMe_aMe_b$), 0.032 (3H, s, $Si^tBuMe_aMe_b$), [spin system broken across C12-C13 by restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 200.6, 171.1, 170.1, 166.7, 159.34, 159.28, 159.1, 145.7, 130.5, 129.9, 129.8, 129.7, 129.6, 129.2, 123.0, 113.73, 113.69, 79.9, 74.5, 74.0, 73.2, 72.5, 72.0, 71.4, 70.7, 70.2, 67.4, 60.3, 55.2 (2C), 51.3, 36.9, 36.8, 36.1, 34.8, 29.3, 25.89 (2C), 25.86 (2C), 21.04, 20.97, 18.02, 18.00, 17.95, 14.1, 12.9, –3.9, –4.0, –4.1, –4.2, –4.6. **$[\alpha]_D^{20}$** –4.5 (*c* = 6.0, $CHCl_3$). **IR** (thin film) 2951.9, 2933.8, 2896.2, 2857.8, 1730.3, 1658.7 (w), 1613.8, 1514.7, 1463.6, 1249.3, 1072.2, 1038.4, 835.6, 774.4 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{65}H_{110}NO_{14}Si_3$ $[M + NH_4]^+$ 1212.7234, found 1212.7243.

## 3) Experimental Data for the C20-C38 Fragments

### 3.1. Towards C20-C28 β-ketophosphonate (*S*)-10

**EPOXIDE (±)-38**

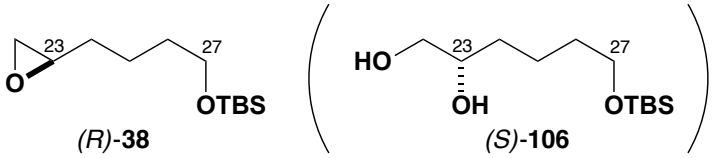



5-Hexen-1-ol (7.00 g, 69.9 mmol) was dissolved in $CH_2Cl_2$ (120 mL) and imidazole (5.71 g, 83.9 mmol) was added. TBSCl (11.6 g, 76.9 mmol) was added at rt and the white suspension stirred for 3 h. The reaction was quenched on the addition of $NaHCO_3$ solution (100 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 250 mL) and the combined organics were washed with brine (300 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was dissolved in $CH_2Cl_2$ (250 mL) and the solution cooled to 0 ºC. *meta*-Chloroperbenzoic acid (40.1 g, 140 mmol, 60% purity) was added in 6 portions and the reaction warmed to rt and stirred for 16 h. The mixture was filtered through Celite® into a 1:1 mixture $NaHCO_3$ and $Na_2S_2O_3$ solutions (300 mL). The layers were separated and the aqueous phase extracted with $Et_2O$ (3 × 250 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with $CH_2Cl_2$ to remove the majority of *meta*-chlorobenzoic acid by-product by filtration. The crude product was purified by column chromatography (15:1 PE/EtOAc) to afford epoxide **(±)-38** (14.3 g, 62.2 mmol, 90%) as a yellow oil.

**$R_f$** 0.66 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 3.62 (2H, t, *J* = 6.2 Hz, C19$H_2$), 2.93-2.89 (1H, m, C23H), 2.75 (1H, dd, *J* = 5.0, 4.0 Hz, C13(H)(O)C$H_a$C$H_b$), 2.47 (1H, dd, *J* = 5.0, 2.7 Hz, C13(H)(O)C$H_a$C$H_b$), 1.61-1.46 (6H, m, C24$H_a$$H_b$, C24$H_a$$H_b$, C25$H_a$$H_b$, C25$H_a$$H_b$, C26$H_a$$H_b$, C26$H_a$$H_b$), 0.89 (9H, s, Si$^t$BuMe$_2$), 0.48 (6H, s, Si$^t$BuMe$_2$).

This data is in agreement with that reported by Myers *et al.*[13]

**EPOXIDE (*R*)-38**



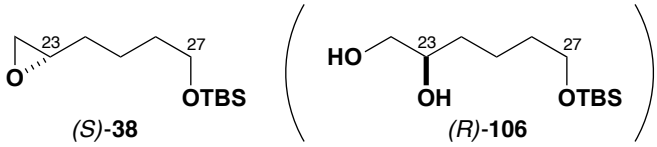

To (*R,R*)-(–)-N,N'-*bis*-(3,5-di-*tert*-butyl-salicyclidene)-1,2-cyclohexanediamine cobalt(II) (237 mg, 393 µmmol) was added AcOH (90.0 µL, 1.37 mmol). The flask was flushed with air and the catalyst was stirred for 10 min. Epoxide (±)-**38** (18.1 g, 78.6 mmol) and THF (1.00 mL) were then added. The mixture was cooled to 0 ºC and $H_2O$ (779 µL, 43.2 mmol) was added dropwise. The reaction was warmed to rt and stirred for 24 h, then purified directly by flash column chromatography (4:1 → 1:1 PE/EtOAc) to give epoxide (*R*)-**38** (7.35 g, 31.9 mmol, 41%) as a brown oil and alcohol (*S*)-**106** (9.95 g, 40.1 mmol, 51%) as an oil. The enantiomeric

excess (>90% by $^1$H NMR, likely to by >98% from literature precedent) and absolute stereochemistry of epoxide (*R*)-**38** was determined by elaboration to Mosher esters (23*R*)-**39S** and (23*R*)-**39R** (*vide infra*).

**$R_f$** 0.66 (4:1 PE/EtOAc). $^1$H NMR (500 MHz, $CHCl_3$) $\delta_H$ 3.62 (2H, app. t, *J* = 6.1 Hz, C27$\underline{H_2}$), 2.93-2.89 (1H, m, C23$\underline{H}$), 2.75 (1H, dd, *J* = 5.1, 4.1 Hz, C23(H)(O)C$\underline{H_a}$CH$_b$), 2.47 (1H, dd, *J* = 5.1, 2.7 Hz, C23(H)(O)CH$_a$C$\underline{H_b}$), 1.61-1.45 (6H, m, C24$\underline{H_a}$H$_b$, C24H$_a$$\underline{H_b}$, C25$\underline{H_a}$H$_b$, C25H$_a$$\underline{H_b}$, C26$\underline{H_a}$H$_b$, C26H$_a$$\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.05 (6H, s, Si$^t$Bu$\underline{Me_2}$). **[α]$_D^{20}$** –0.6 (*c* = 2.4, $CHCl_3$). **IR** (thin film) 2930, 2859, 2359, 1472, 1256, 1099 cm$^{-1}$.

This data is in agreement with that reported by Myers *et al.*[13]

**EPOXIDE (*S*)-38**



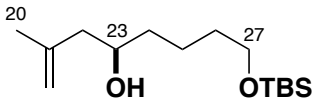

*(S)*-**38** *(R)*-**106**

Acetic acid (36.0 µL, 632 µmol) was added to stirring (*S,S*)-(+)-*N,N'-bis*-(3,5-di-*tert*-butylsalicyidene)-1,2-cyclohexane diaminocobalt(II) (95.4 µL, 158 µmol) and the reaction vessel flushed with air for 10 min. Racemic epoxide (±)-**38** (7.29 g, 31.6 mmol) was added in THF (0.5 mL) and the mixture cooled to 0 ºC. To the dark red solution, $H_2O$ (313 µL, 17.4 mmol) was added dropwise and the reaction warmed to rt for 16 h. The reaction mixture was purified directly by column chromatography (3:1 PE/EtOAc) to afford epoxide (*S*)-**38** (3.29 g, 14.3 mmol, 45%) as an oil. Further elution (1:1 PE/EtOAc) isolated diol (*R*)-**106** (3.62g, 14.6 mmol, 46%). The enantiomeric excess (>90% by $^1$H NMR, likely to by >98% from literature precedent) and absolute stereochemistry of epoxide (*S*)-**38** was determined by elaboration to Mosher esters (*23S*)-**39S** and (*23S*)-**39R** (*vide infra*).

**$R_f$** 0.66 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 3.62 (2H, t, *J* = 6.2 Hz, C27$\underline{H_2}$), 2.93-2.89 (1H, m, C23$\underline{H}$), 2.75 (1H, dd, *J* = 5.0, 4.0 Hz, C23(H)(O)C$\underline{H_a}$CH$_b$), 2.47 (1H, dd, *J* = 5.0, 2.7 Hz, C13(H)(O)CH$_a$C$\underline{H_b}$), 1.61-1.46 (6H, m, C24$\underline{H_a}$H$_b$, C24H$_a$$\underline{H_b}$, C25$\underline{H_a}$H$_b$, C25H$_a$$\underline{H_b}$, C26$\underline{H_a}$H$_b$, C26H$_a$$\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}$Me$_2$), 0.48 (6H, s, Si$^t$Bu$\underline{Me_2}$).

This data is in agreement with that reported by Myers *et al.*[13]

**ALCOHOL (*R*)-39**

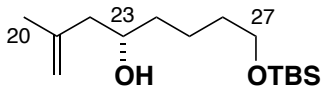



(*R*)-**39**

To anhydrous CuI (83.0 mg, 0.434 mmol) was added a solution of epoxide (*R*)-**38** (1.00 g, 4.34 mmol) in THF (8 mL). The slurry was cooled to –78 ºC whereupon *iso*-propenyl magnesium bromide (17.3 mL, 8.68 mmol, 0.5 M solution in THF) was added. The reaction was stirred for 1 h and then quenched with $NH_4Cl$ solution (10 mL). The layers were separated and the aqueous phase was extracted with $Et_2O$ (3 × 10 mL). The combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (4:1 PE/EtOAc) gave alcohol (*R*)-**39** (1.11 g, 4.29 mmol, 99%) as an oil.

**$R_f$** 0.37 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 4.88 (1H, s, C21C$\underline{H_a}H_b$), 4.80 (1H, s, C21C$H_a\underline{H_b}$), 3.76-3.70 (1H, m, C23$\underline{H}$), 3.62 (2H, t, *J* = 6.3 Hz, C27$\underline{H_2}$), 2.21 (1H, dd, *J* = 13.6, 3.4 Hz, C22$\underline{H_a}H_b$), 2.09 (1H, dd, *J* = 12.6, 9.3 Hz, C22$H_a\underline{H_b}$), 1.76 (3H, s, C20$\underline{H_3}$), 1.70 (1H, d, *J* = 2.8 Hz, C23(H)O$\underline{H}$), 1.58-1.38 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t$$\underline{Bu}$Me$_2$), 0.05 (6H, s, Si$^t$Bu$\underline{Me_2}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 143.3, 113.8, 69.0, 63.5, 46.6, 37.2, 33.2, 26.4, 22.8, 22.4, 18.8, -4.9. **$[\alpha]_D^{20}$** +3.9 (*c* = 2.1, $CHCl_3$). **IR** (thin film) 3422, 2930, 2858, 1647, 1472, 1463, 1254, 1100, 835, 775 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{15}H_{33}O_2Si$ 273.2244 $[M + H]^+$ found 273.2248.

**ALCOHOL (*S*)-39**

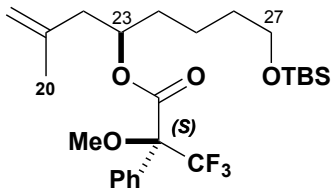



A solution of epoxide (*S*)-**38** (3.16 g, 15.5 mmol) in THF (25 mL) was added *via* cannula to copper(I) iodide (296 mg, 1.55 mmol, dried *in vacuo* 1 h). The solution was cooled to –78 °C and *iso*-propenylmagnesium bromide (62.0 mL, 31.0 mmol, 0.5 M solution in THF) was added slowly. The reaction was complete after 2.5 h and quenched by the careful addition of $NH_4Cl$ solution (30 mL) followed by warming to at rt for 15 min. The layers were separated and the aqueous phase extracted with $Et_2O$ (3 × 100 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (9:1 PE/EtOAc) to give alcohol (*S*)-**39** (3.67 g, 13.4 mmol, 87%) as an oil.

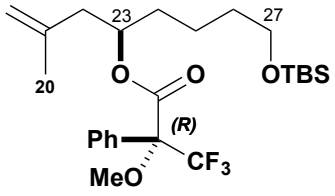
**$R_f$** 0.38 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 4.88 (1H, br s, C21C$\underline{H_a}H_b$), 4.80 (1H, br s, C21C$H_a\underline{H_b}$), 3.76-3.70 (1H, m, C23$\underline{H}$), 3.62 (2H, t, *J* = 6.3 Hz, C27$\underline{H_2}$), 2.21 (1H, dd, *J* = 13.6, 3.3 Hz, C22$\underline{H_a}H_b$), 2.09 (1H, dd, *J* = 13.6, 9.4 Hz, C22$H_a\underline{H_b}$), 1.76 (3H, s, C20$\underline{H_3}$), 1.58-1.38 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t$$\underline{Bu}$Me$_2$), 0.89 (9H, s, Si$^t$$\underline{Bu}$Me$_2$), 0.05 (6H, s, Si$^t$Bu$\underline{Me_2}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 143.3, 113.8, 69.0, 63.5, 46.6, 37.2, 33.2, 26.4, 22.8, 22.4, 18.8, –4.9.

This data is in agreement with that reported for the enantiomer (*vide supra*).

**MOSHER ESTERS (*23R*)-39S AND (*23R*)-39R**




*(23R)*-**39S**




*(23R)*-**39R**

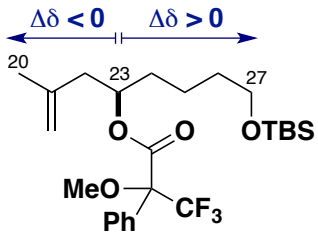
To a stirred solution of alcohol (*R*)-**39** (10 mg, 34 µmmol) in $CH_2Cl_2$ (0.5 mL) was added (*S*)-MTPA (17 mg, 73 µmol), DCC (1 M solution in $CH_2Cl_2$, 73 µL, 73 µmol) and DMAP (1 crystal). After 1 h, $NaHCO_3$ solution (5 mL) and $CH_2Cl_2$ (5 mL) were added and the layers separated. The organic layer was dried ($MgSO_4$), concentrated under reduced pressure and purified by column chromatography (97:3 PE/EtOAc) to give ester (*23R*)-**39S** (12 mg, 25 µmol, 73%) as a colourless oil. The other diastereomer (*23R*)-**39R** was prepared by the same procedure using (*R*)-MTPA.

(*23R*)-**39S**: **$R_f$** 0.51 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.54-7.52 (2H, m, Ar<u>H</u>), 7.41-7.36 (3H, m, Ar<u>H</u>), 5.30-5.23 (1H, m, C23<u>H</u>), 4.72 (1H, s, C21C<u>H$_a$</u>H$_b$), 4.65 (1H, br. s, C21CH$_a$<u>H$_b$</u>), 3.58 (2H, app. t, *J* = 6.2 Hz, C27<u>H$_2$</u>), 3.54 (3H, s, C(O<u>Me</u>)(Ph)($CF_3$)), 2.35 (1H, dd, *J* = 14.1, 7.6, C22<u>H$_a$</u>H$_b$), 2.21 (1H, dd, *J* = 14.1, 5.6 Hz, C22H$_a$<u>H$_b$</u>), 1.69 (3H, s, C20<u>H$_3$</u>) 1.67-1.63 (2H, m, C24<u>H$_a$</u>H$_b$, C24H$_a$<u>H$_b$</u>) 1.53-1.48 (2H, m, C26<u>H$_a$</u>H$_b$, C26H$_a$<u>H$_b$</u>), 1.45-1.33 (2H, m, C25<u>H$_a$</u>H$_b$, C25H$_a$<u>H$_b$</u>), 0.88 (9H, s, Si<u>$^t$Bu</u>Me$_2$), 0.04 (6H, s, Si$^t$Bu<u>Me$_2$</u>).

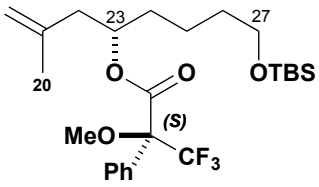
(*23R*)-**39R**: **$R_f$** 0.51 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.56-7.54 (2H, m, Ar<u>H</u>), 7.43-7.35 (3H, m, Ar<u>H</u>), 5.31-5.26 (1H, m, C23<u>H</u>), 4.82 (1H, br. s, C21C<u>H$_a$</u>H$_b$), 4.76 (1H, s, C21CH$_a$<u>H$_b$</u>), 3.55 (3H, s, C(O<u>Me</u>)(Ph)($CF_3$)), 3.52 (2H, app. t, *J* = 6.3 Hz, C27<u>H$_2$</u>), 2.43 (1H, dd, *J* = 14.2, 7.8 Hz, C22<u>H$_a$</u>H$_b$), 2.27 (1H, dd, *J* = 14.1, 5.6 Hz, C22H$_a$<u>H$_b$</u>), 1.76 (3H, s, C20<u>H$_3$</u>), 1.62 - 1.56 (2H, m, C24<u>H$_a$</u>H$_b$, C24H$_a$<u>H$_b$</u>), 1.50-1.40 (2H, m, C26<u>H$_a$</u>H$_b$, C26H$_a$<u>H$_b$</u>), 1.34-1.19 (2H, C25<u>H$_a$</u>H$_b$, C25H$_a$<u>H$_b$</u>), 0.88 (9H, s, Si<u>$^t$Bu</u>Me$_2$), 0.03 (6H, s, Si$^t$Bu<u>Me$_2$</u>).

**MOSHER ESTER ANALYSIS OF (*23R*)-39S AND (*23R*)-39R[6]**

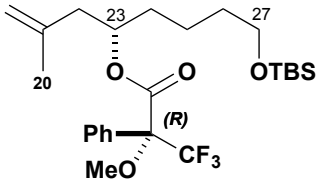
| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C20$H_3$ | 1.69 | 1.76 | –0.06 |
| C21C$H_aH_b$ | 4.72 | 4.82 | –0.10 |
| C21C$H_aH_b$ | 4.65 | 4.76 | –0.11 |
| C22$H_aH_b$ | 2.35 | 2.43 | –0.08 |
| C22$H_aH_b$ | 2.21 | 2.27 | –0.03 |
| C23H | 5.26 | 5.29 | –0.03 |
| C24$H_aH_b$, C24$H_aH_b$ | obs. | obs. | - |
| C25$H_aH_b$, C25$H_aH_b$ | obs. | obs. | - |
| C26$H_aH_b$, C26$H_aH_b$ | obs. | obs. | - |
| C27$H_2$ | 3.58 | 3.52 | +0.06 |
| Si$^t$Bu$Me_2$ | 0.88 | 0.88 | 0.00 |
| Si$^t$Bu$Me_2$ | 0.04 | 0.03 | +0.01 |



**MOSHER ESTERS (*23S*)-39*S* AND (*23S*)-39R**




*(23S)*-**39S**




*(23S)*-**39R**

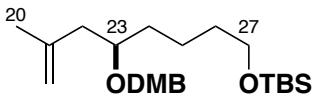
Alcohol (*S*)-**39** (15 mg, 55 µmol) was dissolved in $CH_2Cl_2$ (0.2 mL) and triethylamine (5 drops) added. (*S*)-MTPA (20 mg, 85 µmol) was added, followed by DMAP (1 crystal) and EDC (2 drops). After 2 h, the reaction was diluted with $CH_2Cl_2$ (1 mL) and HCl (1 mL, 1 M aq.) and the aqueous phase extracted with $CH_2Cl_2$ (3 × 5 mL). The organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (50:1 PE/EtOAc) to give ester (*23S*)-**39S** (9.0 mg, 17 µmol, 31%) as a colourless oil. The other diastereomer (*23S*)-**39R** was prepared by the same procedure using (*R*)-MTPA.

(*23S,S*)-**106**: **$R_f$** 0.50 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.56-7.54 (2H, m, Ar<u>H</u>), 7.43-7.35 (3H, m, Ar<u>H</u>), 5.31-5.26 (1H, m, C23<u>H</u>), 4.82 (1H, br. s, C21C<u>H$_a$</u>H$_b$), 4.76 (1H, br s, C21CH$_a$<u>H$_b$</u>), 3.55 (3H, s, C(O<u>Me</u>)(Ph)($CF_3$)), 3.52 (2H, app. t, *J* = 6.3 Hz, C27<u>$H_2$</u>), 2.43 (1H, dd, *J* = 14.2, 7.8 Hz, C22<u>H$_a$</u>H$_b$), 2.27 (1H, dd, *J* = 14.1, 5.6 Hz, C22H$_a$<u>H$_b$</u>), 1.76 (3H, s, C20<u>$H_3$</u>), 1.62-1.56 (2H, m, C24<u>H$_a$</u>H$_b$, C24H$_a$<u>H$_b$</u>), 1.50-1.40 (2H, m, C26<u>H$_a$</u>H$_b$, C26H$_a$<u>H$_b$</u>), 1.34-1.19 (2H, m, C25<u>H$_a$</u>H$_b$, C25H$_a$<u>H$_b$</u>), 0.88 (9H, s, Si<u>$^t$Bu</u>$Me_2$), 0.03 (6H, s, Si$^t$Bu<u>$Me_2$</u>).

(*23S,R*)-**105**: **$R_f$** 0.50 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.54-7.52 (2H, m, Ar<u>H</u>), 7.41-7.36 (3H, m, Ar<u>H</u>), 5.30-5.23 (1H, m, C23<u>H</u>), 4.72 (1H, br. s, C21C<u>H$_a$</u>H$_b$), 4.65 (1H, br s, C21CH$_a$<u>H$_b$</u>), 3.58 (2H, t, *J* = 6.3 Hz, C27<u>$H_2$</u>), 3.54 (3H, s, C(O<u>Me</u>)(Ph)($CF_3$)), 2.35 (1H, dd, *J* = 14.0, 7.6 Hz, C22<u>H$_a$</u>H$_b$), 2.21 (1H, dd, *J* = 14.0, 5.4 Hz, C22H$_a$<u>H$_b$</u>), 1.69 (3H, s, C20<u>$H_3$</u>), 1.67-1.63 (2H, m, C24<u>H$_a$</u>H$_b$, C24H$_a$<u>H$_b$</u>), 1.53-1.48 (2H, m, C26<u>H$_a$</u>H$_b$, C26H$_a$<u>H$_b$</u>), 1.45-1.32 (2H, m, C25<u>H$_a$</u>H$_b$, C25H$_a$<u>H$_b$</u>), 0.88 (9H, s, Si<u>$^t$Bu</u>$Me_2$), 0.03 (6H, s, Si$^t$Bu<u>$Me_2$</u>).

This data is in agreement with that reported for the enantiomeric compounds (*vide supra*).

**DMB ETHER (*R*)-40**

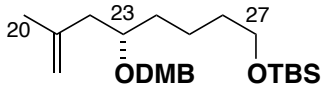



To a stirred solution of alcohol (*R*)-**39** (2.00 g, 7.34 mmol) at 0 ºC in DMF (20 mL) was added NaH (363 mg, 9.08 mmol, 60% in mineral oil). After stirring for 30 min, DMBCl (1.69 g, 9.08 mmol) was added and the reaction mixture was allowed to warm to rt and then stirred for a further 16 h. Upon re-cooling to 0 ºC, $NH_4Cl$ solution (50 mL) was carefully added, followed by EtOAc (50 mL). The phases were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by column chromatography (4:1 PE/EtOAc) to afford DMB ether (*R*)-**40** (2.54 g, 6.00 mmol, 82%) as a colourless oil.

**$R_f$** 0.34 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.91 (1H, d, *J* = 1.8 Hz, Ar$_{DMB}$<u>H</u>), 6.86 (1H, dd, *J* = 8.1, 1.8 Hz, Ar$_{DMB}$<u>H</u>), 6.81 (1H, d, *J* = 8.1 Hz, Ar$_{DMB}$<u>H</u>), 4.79 (1H, br. s, C21C<u>H$_a$</u>H$_b$), 4.76 (1H, br. s,

C21C$H_aH_b$), 4.48 (1H, d, J = 11.2 Hz, OC$H_aH_b$Ar$_{DMB}$), 4.44 (1H, d, J = 11.2 Hz, OC$H_aH_b$Ar$_{DMB}$), 3.87 (3H, s, Ar$_{DMB}$OMe), 3.86 (3H, s, Ar$_{DMB}$OMe), 3.60 (3H, t, *J* = 6.3 Hz, C27$H_2$), 3.53 (1H, app. qn *J* = 6.0 Hz, C23H), 2.35 (1H, dd, *J* = 13.9, 6.4 Hz, C22$H_aH_b$), 2.17 (1H, dd, J = 13.9, 6.1 Hz, C22$H_aH_b$), 1.74 (3H, s, C20$H_3$), 1.57-1.33 (6H, m, C24$H_aH_b$, C24$H_aH_b$, C25$H_aH_b$, C25$H_aH_b$, C26$H_aH_b$, C26$H_aH_b$), 0.89 (9H, s, Si$^t$BuMe$_2$), 0.04 (6H, s, Si$^t$BuMe$_2$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 149.0, 148.5, 143.0, 131.6, 120.1, 112.6, 111.2, 110.9, 77.2, 70.8, 63.1, 55.9, 55.7, 42.7, 33.8, 33.0, 26.0, 22.9, 21.7, 18.4, –5.3. **[α]$_D^{20}$** +11.1 (*c* = 1.7 $CHCl_3$). **IR** (thin film) 2932, 2857, 1594, 1517, 1464, 1528, 1098, 836, 775 cm$^{-1}$. **HRMS** (EI$^+$) Calculated for $C_{24}H_{46}O_4NSi$ $[M + NH_4]^+$ 440.3191, found 440.3194.

**DMB ETHER (*S*)-40**

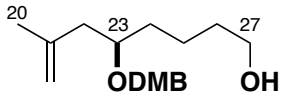



A solution of alcohol (*S*)-**39** (3.38 g, 12.3 mmol) in DMF (30 mL) was cooled to 0 ºC and sodium hydride (1.42 g, 35.6 mmol, 60%wt dispersion in mineral oil) was added. After 30 min, DMBCl (6.64 g, 35.6 mmol) was added and the mixture was warmed to rt for 16 h. The solution was cooled to 0 ºC and quenched with $NH_4Cl$ solution (20 mL). The mixture was diluted with EtOAc (50 mL) and the layers separated. The aqueous phase was extracted with EtOAc (3 × 100 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (9:1 PE/EtOAc) to give alcohol (*S*)-**40** (4.48 g, 10.6 mmol, 86%) as an oil. [NB: There is no $R_f$ change in this reaction]

**$R_f$** 0.38 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.91 (1H, d, *J* = 1.5 Hz, Ar$_{DMB}$H), 6.86 (1H, dd, *J* = 8.1, 1.5 Hz, Ar$_{DMB}$H), 6.81 (1H, d, *J* = 8.1 Hz, Ar$_{DMB}$H), 4.79 (1H, br. s, C21C$H_aH_b$), 4.76 (1H, br. s, C21C$H_aH_b$), 4.48 (1H, d, *J* = 11.2 Hz, OC$H_aH_b$Ar$_{DMB}$), 4.44 (1H, d, *J* = 11.2 Hz, OC$H_aH_b$Ar$_{DMB}$), 3.87 (3H, s, Ar$_{DMB}$OMe), 3.86 (3H, s, Ar$_{DMB}$OMe), 3.60 (2H, t, *J* = 6.3 Hz, C27$H_2$), 3.56-3.49 (1H, m, C23H), 2.35 (1H, dd, *J* = 13.9, 6.4 Hz, C22$H_aH_b$), 2.16 (1H, dd, = 13.9, 6.1 Hz, C22$H_aH_b$), 1.74 (3H, s, C20$H_3$), 1.57-1.33 (6H, m, C24$H_aH_b$, C24$H_aH_b$, C25$H_aH_b$, C25$H_aH_b$, C26$H_aH_b$, C26$H_aH_b$), 0.89 (9H, s, Si$^t$BuMe$_2$), 0.04 (6H, s, Si$^t$BuMe$_2$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 149.0, 148.5, 143.0, 131.6, 120.1, 112.6, 111.2, 110.9, 77.2, 70.8, 63.1, 55.9, 55.7, 42.7, 33.8, 33.0, 26.0, 22.9, 21.7, 18.4, –5.3.

This data is in agreement with that reported for the enantiomer (*vide supra*).

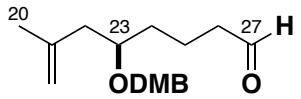
**DMB ETHER (*R*)-41**




To a stirred solution of TBS ether (*R*)-**40** (1.16 g, 2.75 mmol) in MeOH (10 mL) was added PPTS (69.0 mg, 275 μmol). After stirring for 6 h, $NaHCO_3$ solution (40 mL) and EtOAc (50 mL) were added. The layers were separated and the aqueous phase was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The crude alcohol (*R*)-**41** (841 mg, 2.73 mmol, 99%) was used without further purification.

**$R_f$** 0.23 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.92 (1H, d, *J* = 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.86 (1H, dd, *J* = 8.1, 1.9 Hz, $Ar_{DMB}\underline{H}$), 6.82 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 4.80 (1H, s, C21C$\underline{H_a}H_b$), 4.77 (1H, s, C21C$H_a\underline{H_b}$), 4.50 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.62 (2H, app. t, *J* = 6.3 Hz, C27$\underline{H_2}$), 3.57-3.52 (1H, m, C23$\underline{H}$), 2.38 (1H, dd, *J* = 13.8, 6.3 Hz, C22$\underline{H_a}H_b$), 2.17 (1H, dd, *J* = 13.7, 6.1 Hz, C22$H_a\underline{H_b}$), 1.75 (3H, s, C20$\underline{H_3}$), 1.63 (1H, br. s, C27$H_2O\underline{H}$), 1.58-1.49 (5H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 1.44-1.37 (1H, m, C25$H_a\underline{H_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 149.0, 148.5, 143.0, 131.5, 120.2, 112.7, 111.3, 110.9, 77.0, 70.8, 62.8, 56.0, 55.8, 42.7, 33.7, 32.8, 22.9, 21.6. **$[\alpha]_D^{20}$** +19.6 (*c* = 0.26, $CHCl_3$). **IR** (thin film) 3398, 2936, 2862, 1646, 1609, 1594, 1516, 1464, 1263, 1237, 1157, 1138, 1029 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{18}H_{29}O_4$ $[M + H]^+$ 309.2060, found 309.2058.

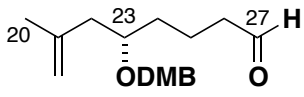
#### ALDEHYDE (*R*)-42




To a solution of alcohol (*R*)-**41** (667 mg, 2.16 mmol) in $CH_2Cl_2$ (10 mL) was added Dess–Martin periodinane (1.50 g, 3.54 mmol). After stirring for 1 h, $NaHCO_3$ solution (10 mL) and $Na_2S_2O_3$ solution (10 mL) were added. After a further 30 min, $H_2O$ (10 mL) and $CH_2Cl_2$ (40 mL) were added and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 50 mL) and the combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The crude residue was purified by column chromatography (4:1 PE/EtOAc) to give aldehyde (*R*)-**42** (563 mg, 1.84 mmol, 85%) as a pale yellow oil.

**$R_f$** 0.24 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.74 (1H, t, *J* = 1.7 Hz, C27$\underline{H}$O),6.90 (1H, d, *J* = 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.86 (1H, dd, *J* = 8.1, 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.81 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 4.80 (1H, br. s, C21C$\underline{H_a}H_b$), 4.75 (1H, br. s, C21C$H_a\underline{H_b}$), 4.50 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.42 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.54 (1H, app. dq, *J* = 4.5, 6.6 Hz, C23$\underline{H}$), 2.43-2.37 (3H, m, C26$\underline{H_2}$, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 13.9, 6.6 Hz, C22$H_a\underline{H_b}$), 1.84-1.75 (1H, m, C25$\underline{H_a}H_b$), 1.74 (3H, s, C20$\underline{H_3}$), 1.70-1.64 (1H, m, C25$H_a\underline{H_b}$), 1.59-1.47 (2H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 202.4, 149.0, 148.6, 142.7, 131.3, 120.2, 112.9, 111.2, 110.9, 76.6, 70.8, 55.9, 55.8, 43.9, 42.5, 33.3, 22.9, 18.1. **$[\alpha]_D^{20}$** +22.7 (*c* = 0.4 $CHCl_3$). **IR** (thin film) 2937, 1722, 1645, 1593, 1516, 1264, 1237, 1029 $cm^{-1}$. **HRMS** (ESI) Calculated for $C_{18}H_{30}O_4N$ $[M + NH_4]^+$ 324.2169, found 324.2166.

#### ALDEHYDE (*S*)-42



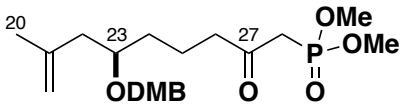

TBS ether (*S*)-**40** (4.48 g, 10.6 mmol) was dissolved in methanol (40 mL) at rt and pyridinium *para*-toluenesulfonate (366 mg, 1.45 mmol) was added. The reaction was stirred for 16 h and, on completion by TLC, was diluted with EtOAc (100 mL) and $NaHCO_3$ solution (100 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic phases were dried ($MgSO_4$)

and concentrated *in vacuo*. The crude residue (*S*)-**41** was dissolved in $CH_2Cl_2$ (50 mL) and Dess–Martin periodinane added (7.12 g, 16.8 mmol). After 1 h, $Na_2S_2O_3$ solution (50 mL) was added and the mixture stirred for 30 min. The mixture was diluted with $CH_2Cl_2$ (50 mL) and $H_2O$ (50 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 100 mL) and the combined organic phases dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (50:1 → 4:1 PE/EtOAc) to give aldehyde (*S*)-**42** (4.48 g, 10.6 mmol, 86%) as an oil.

**$R_f$** 0.24 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.74 (1H, t, *J* = 1.7 Hz, C27HO), 6.91 (1H, d, *J* = 1.8 Hz, $Ar_{DMB}$H), 6.86 (1H, dd, *J* = 8.1, 1.8 Hz, $Ar_{DMB}$H), 6.82 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}$H), 4.80 (1H, br. s, C21C$H_aH_b$), 4.75 (1H, br. s, C21C$H_aH_b$), 4.50 (1H, d, *J* = 11.3 Hz, OC$H_aH_b$$Ar_{DMB}$), 4.42 (1H, d, *J* = 11.3 Hz, OC$H_aH_b$$Ar_{DMB}$), 3.88 (3H, s, $Ar_{DMB}$OMe), 3.86 (3H, s, $Ar_{DMB}$OMe), 3.54 (1H, app. ddd, *J* = 8.5, 6.4, 4.5 Hz, C23H), 2.42 (2H, dt, *J* = 7.1, 1.7 Hz, C26$H_2$), 2.39 (1H, dd, *J* = 13.8, 6.0 Hz, C22$H_aH_b$), 2.16 (1H, dd, *J* = 13.9, 6.6 Hz, C22$H_aH_b$), 1.85-1.75 (1H, m, C25$H_aH_b$), 1.74 (3H, s, C20$H_3$), 1.70-1.64 (1H, m, C25$H_aH_b$), 1.60-1.46 (2H, m, C24$H_aH_b$, C24$H_aH_b$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 202.4, 149.0, 148.6, 142.7, 131.3, 120.2, 112.9, 111.2, 110.9, 76.6, 70.8, 55.9, 55.8, 43.9, 42.5, 33.3, 22.9, 18.1.

This data is in agreement with that reported for the enantiomer (*vide supra*).

**C20-C28 β-KETOPHOSPHONATE (*R*)-10**

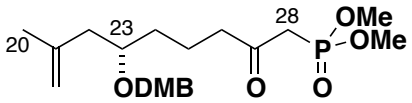



To a stirred solution of methyl methylphosphonate (482 µL, 4.45 mmol) in THF (3 mL) at –78 ºC was added *n*-butyllithium (2.76 mL, 4.45 mmol, 1.6 M solution in hexanes). After 30 min, a solution of aldehyde (*R*)-**42** (341 mg, 1.11 mmol) in THF (3 mL) was added *via* cannula. The reaction mixture was stirred for a further 10 min before quenching with $NH_4Cl$ solution (10 mL). The layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were dried ($Na_2SO_4$) and the solvents were evaporated under reduced pressure. To the crude yellow oil was added $CH_2Cl_2$ (5 mL) and Dess–Martin periodinane (950 mg, 2.22 mmol). After stirring for 30 min, $Na_2S_2O_3$ solution (5 mL) was added and the mixture stirred for a further 30 min. $H_2O$ (10 mL) and $CH_2Cl_2$ (10 mL) were then added and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 15 mL) and the combined organics were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (EtOAc) gave phosphonate (*R*)-**10** (347 mg, 810 µmol, 73%) as a pale yellow oil.

**$R_f$** 0.10 (EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.89 (1H, d, *J* = 1.8 Hz, $Ar_{DMB}$H), 6.83 (1H, dd, *J* = 8.1, 1.8 Hz, $Ar_{DMB}$H), 6.79 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}$H), 4.77 (1H, br. s, C21C$H_aH_b$), 4.73 (1H, br. s, C21C$H_aH_b$), 4.47 (1H, d, *J* = 11.2 Hz, OC$H_aH_b$$Ar_{DMB}$), 4.40 (1H, d, J = 11.2 Hz, OC$H_aH_b$$Ar_{DMB}$), 3.85 (3H, s, $Ar_{DMB}$OMe), 3.84 (3H, s, $Ar_{DMB}$OMe), 3.75 (6H, d, $^3J_{H\text{-}P}$ = 11.1 Hz, P(O)(OMe)$_2$), 3.54-3.50 (1H, m, C23H), 3.02 (2H, d, $^2J_{H\text{-}P}$ = 22.7 Hz, C(O)C28$H_2$P(O)(OMe)$_2$), 2.59-2.56 (2H, m, C26$H_2$), 2.34 (1H, dd, *J* = 13.8, 6.2 Hz, C22$H_aH_b$), 2.13 (1H, dd, *J* = 13.8, 6.2 Hz, C22$H_aH_b$), 1.77-1.68 (1H, m, C25$H_aH_b$), 1.72 (3H, s, C20$H_3$), 1.65-1.56 (1H, m, C25$H_aH_b$), 1.54-1.42 (2H, m, C24$H_aH_b$, C24$H_aH_b$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 201.7 (d, $J_{C\text{-}P}$ = 6.2 Hz), 149.0, 148.5, 142.8, 131.4, 120.2, 112.8, 111.2, 110.9, 76.8, 70.8, 55.9, 55.8, 53.0, 53.0, 44.1, 42.6, 41.3 (d,

$J_{C\text{-}P}$ = 127 Hz), 33.1, 22.9, 19.4. **[α]$_D^{20}$** +11.5 (*c* = 2.3, $CHCl_3$). **IR** (thin film) 3486, 2953, 2855, 1714, 1516, 1262, 1239, 1028, 809 $cm^{-1}$. **HRMS** ($ES^+$) Calcualted for $C^{21}H^{33}O^7NaP$ $[M + Na]^+$ 451.1862, found 451.1866.

**C20-C28 β-KETOPHOSPHONATE (*S*)-10**

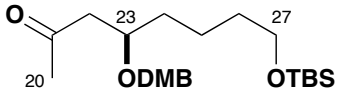



A solution of dimethyl-methylphosphonate (1.09 mL, 10.1 mmol) in THF (6 mL) was prepared and cooled to –78 ºC. *n*-Butyllithium (6.23 mL, 3.89 mmol, 1.6 M solution in hexanes) was added dropwise and the mixture stirred for 30 min. A solution of aldehyde (*S*)-**42** (770 mg, 2.51 mmol) in THF (6 mL) was added *via* cannula and the reaction maintained at –78 ºC for 10 min. The reaction was quenched by the dropwise addition of $NH_4Cl$ solution (10 mL) and the layers separated. The aqueous phase was diluted with $H_2O$ (20 mL) and $CH_2Cl_2$ (20 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 100 mL) and the combined organic phases washed with brine (100 mL), dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (1:1 PE/EtOAc → EtOAc) to give phosphonate (*S*)-**10** (850 mg, 1.98 mmol, 79%) as a yellow oil.

**$R_f$** 0.11 (EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 6.89 (1H, br. s, $Ar_{DMB}\underline{H}$), 6.83 (1H, br. d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 6.79 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 4.77 (1H, br. s, C21C$\underline{H_a}H_b$), 4.73 (1H, br. s, C21C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.40 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.84 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.75 (6H, d, $^3J_{H\text{-}P}$ = 11.1 Hz, P(O)(O$\underline{Me}$)$_2$), 3.54-3.50 (1H, m, C23$\underline{H}$), 3.05 (2H, d, $^2J_{H\text{-}P}$ = 22.7 Hz, C(O)C$\underline{H_2}$P(O)(OMe)$_2$), 2.58 (2H, app. t, *J* = 7.1 Hz, C26$\underline{H_2}$), 2.34 (1H, dd, *J* = 13.8, 6.2 Hz, C22$\underline{H_a}H_b$), 2.13 (1H, dd, *J* = 13.8, 6.2 Hz, C22$H_a\underline{H_b}$), 1.72 (3H, s, C20$\underline{H_3}$), 1.66-1.42 (4H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 201.7 (d, $J_{C\text{-}P}$ = 6.2 Hz), 149.0, 148.5, 142.8, 131.4, 120.2, 112.8, 111.2, 110.9, 76.8, 70.8, 55.9, 55.8, 53.0, 53.0, 44.1, 42.6, 41.3 (d, $J_{C\text{-}P}$ = 127 Hz), 33.1, 22.9, 19.4.

This data is in agreement with that reported for the enantiomer (*vide supra*).

**MODEL KETONE (*R*)-63**

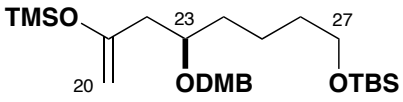



To a stirred solution of alkene (*R*)-**39** (1.40 g, 3.32 mmol) in THF (6 mL) and $H_2O$ (5 mL) was added $OsO_4$ (208 µL, 16.6 µmol, 2.5%wt solution in *t*-BuOH) and NMO (945 µL, 4.56 mmol, 50%wt solution in $H_2O$). After 3 h, $Na_2S_2O_3$ solution (5 mL) and $NaHCO_3$ solution (5 mL) were added and the mixture was stirred for a further 30 min. The mixture was diluted with EtOAc (20 mL) and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), dried ($Na_2SO_4$) and concentrated under reduced pressure. The residue was redissolved in $CH_2Cl_2$ (8 mL) and $NaIO_4$–$SiO_2$ (3 spatula tips) was added. After stirring for 3 h, the solids were filtered off and the filtrate was concentrated under reduced pressure. The residue was

purified by column chromatography (3:1 PE/EtOAc) to afford ketone (*R*)-**63** (1.30 g, 3.07 mmol, 92%) as a colourless oil.

**$R_f$** 0.22 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 6.85-6.80 (3H, m, $Ar_{DMB}\underline{H}$), 4.47 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{DMB}$), 4.42 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{DMB}$), 3.94-3.89 (1H, m, C23$\underline{H}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.60 (2H, t, *J* = 6.4 Hz, C27$\underline{H_2}$), 2.74 (1H, dd, *J* = 15.9, 7.7 Hz, C22$\underline{H_a}H_b$), 2.50 (1H, dd, *J* = 15.9, 4.8 Hz, C22$H_a\underline{H_b}$), 2.15 (3H, s, C20$\underline{H_3}$), 1.64-1.35 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.04 (6H, s, OSi$^t$Bu$\underline{Me_2}$). **$^{13}$C NMR** (125 Hz, $CDCl_3$) $\delta_C$ 207.7, 149.0, 148.6, 131.1, 120.3, 111.2, 110.9, 75.4, 71.5, 63.0, 55.9, 55.8, 48.6, 34.2, 32.9, 31.2, 26.0, 21.6, 18.4, –5.3. **$[\alpha]_D^{20}$** –2.7 (*c* = 2.2, $CHCl_3$). **IR** (thin film) 2932, 2857, 1718, 1517, 1465, 1261, 1097, 835, 776 $cm^{-1}$. **HRMS** (EI) Calculated for $C_{23}H_{44}O_5NSi$ $[M + NH_4]^+$ 442.2983, found 442.2983.

**SILYL ENOL ETHER (*R*)-65**

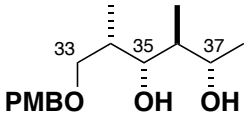



A mixture of TMSCl (0.5 mL) and $Et_3N$ (0.5 mL) was centrifuged for 5 min at 60 rpm. 40 µL of the supernatant was added to a solution of ketone (*R*)-**63** (20 mg, 36 µmol) in THF (1 mL) at –78 ºC and then LiHMDS (100 µL, 100 µmol, 1 M solution in THF) was added dropwise. After 10 min, the reaction was quenched with pH 7 buffer solution (5 mL), extracted with PE (2 × 5 mL) and dried ($MgSO_4$). Evaporation of the solvents under reduced pressure gave the crude silyl enol ether (*R*)-**65** (19 mg, 31 µmol, 85%), which was used immediately without further purification.

**$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 6.91 (1H, d, *J* = 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.86 (1H, dd, *J* = 8.2, 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.2 Hz, $Ar_{DMB}\underline{H}$), 4.51 (1H, d, *J* = 11.2 Hz, $OC\underline{H_a}H_bAr_{DMB}$), 4.41 (1H, d, *J* = 11.2 Hz, $OCH_a\underline{H_b}Ar_{DMB}$), 4.12 (1H, s, C20$\underline{H_a}H_b$), 4.09 (1H, s, C20$H_a\underline{H_b}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.61-3.57 (3H, m, C23$\underline{H}$, C27$\underline{H_2}$), 2.38 (1H, dd, *J* = 13.9, 6.3 Hz, C22$\underline{H_a}H_b$), 2.12 (1H, dd, *J* = 13.9, 6.5 Hz, C22$H_a\underline{H_b}$), 1.57 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.88 (9H, s, OSi$^t\underline{Bu}Me_2$), 0.20 (9H, s, OSi$(C\underline{H_3})_3$), 0.03 (6H, s, OSi$^t$Bu$\underline{Me_2}$).

### 3.2. Synthesis of the C20-C28 Fragment 11

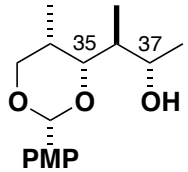
**DIOL 45**




To a stirred solution of dicyclohexylboron chloride (14.9 mL, 67.8 mmol) and triethylamine (10.6 mL, 76.3 mmol) in $Et_2O$ (120 mL) at 0 ºC was added ethyl ketone **36** (10.0 g, 42.4 mmol) in $Et_2O$ (40 mL) *via* cannula and the reaction mixture was stirred for 1.5 h, forming enolate **43**. Upon cooling to –78 ºC, acetaldehyde (freshly distilled from $CaCl_2$, 7.13 mL, 127 mmol) was added and the reaction mixture was stirred for 1.5 h before transferring to a freezer (–20 ºC) for 16 hr. The reaction mixture (containing complex **44**) was then re-cooled to –78 ºC and $LiBH_4$ (3.20 g, 170 mmol) in THF (60 mL) was added *via* cannula. The reaction mixture was stirred for 2.5 h and then cannulated into $NH_4Cl$ solution (200 mL). The layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 150 mL). The combined organic layers were concentrated under reduced pressure and the residue was redissolved in MeOH (150 mL) and NaOH (100 mL, 10% aq.) and cooled to 0 ºC before the dropwise addition of $H_2O_2$ (50 mL, 30% aq.). The reaction mixture was allowed to warm to rt and stirred for 3 h before dilution with $H_2O$ (200 mL) and $CH_2Cl_2$ (350 mL). The layers were separated and the aqueous layer extracted with $CH_2Cl_2$ (3 ×300 mL). The combined organic layers were washed with brine (1 L), dried ($Na_2SO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (15:85 → 35:65 PE/EtOAc) and the cyclohexanol contaminant removed at 0.5 mmHg over 10 h to afford diol **45** (10.5 g, 37.3 mmol, 88%) as a colourless crystalline solid.

**$R_f$** 0.13 (3:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 6.9 Hz, $Ar_{PMB}\underline{H}$), 6.89 (2H, d, *J* = 6.9 Hz, $Ar_{PMB}\underline{H}$), 4.47 (1H, d, *J* = 11.9 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.44 (1H, d, *J* = 11.9 Hz, $OCH_a\underline{H_b}Ar_{DMB}$), 4.40 (1H, br. s, O<u>H</u>), 3.93 (1H, br. s, O<u>H</u>), 3.84-3.80 (5H, m, $Ar_{PMB}O\underline{Me}$, C37<u>H</u>), 3.77 (1H, br. d, *J* = 9.9 Hz, C35<u>H</u>), 3.58 (1H, dd, *J* = 9.0, 4.1 Hz, $C33\underline{H_a}H_b$), 3.54 (1H, dd, *J* = 9.0, 4.8 Hz, $C33H_a\underline{H_b}$) 1.96-1.89 (1H, m, C34<u>H</u>), 1.61-1.53 (1H, m, C36<u>H</u>), 1.18 (3H, d, *J* = 6.2 Hz, $C38\underline{H_3}$), 0.98 (3H, d, *J* = 7.1 Hz, C34(H)<u>Me</u>), 0.74 (3H, d, *J* = 6.9 Hz, C36(H)<u>Me</u>). **$^{13}$C NMR** (125 MHz, $CDCl_3$) δC 159.3, 130.0, 129.2, 113.9, 79.7, 75.4, 73.2, 72.6, 55.2, 42.4, 35.0, 21.2, 12.8, 9.3. **$[\alpha]_D^{20}$** +3.1 (*c* = 2.0, $CHCl_3$). **m.p.** 38-42 ºC. **IR** (thin film) 3363, 2971, 1613, 1514, 1458, 1302, 1248, 1091, 1036, 820 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{16}H_{27}O_4$ $[M + H]^+$ 283.1904, found 283.1901.

**PMP ACETAL 46**

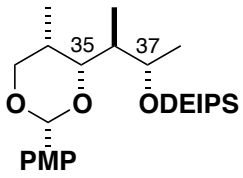



A slurry of PMB ether **45** (7.00 g, 24.8 mmol) and 4 Å molecular sieves (*ca.* 8 g) in $CH_2Cl_2$ (300 mL) was prepared and cooled to –10 ºC. A solution of DDQ (7.88 g, 34.7 mmol) in $CH_2Cl_2$ (500 mL) was added *via* cannula and the reaction stirred for 1 h. When complete by TLC, the mixture was filtered through Celite® on

to $NaHCO_3$ solution (300 mL). The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (2 × 300 mL). The combined organic phases were wash ed with brine (2 × 200 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 PE/EtOAc) to give PMP acetal **46** (6.69 g, 23.7 mmol, 92%) as a colourless crystalline solid.

**$R_f$** 0.38 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 6.9 Hz, $Ar_{PMB}\underline{H}$), 6.89 (2H, d, *J* = 6.9 Hz, $Ar_{PMB}\underline{H}$), 4.47 (1H, d, *J* = 11.9 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.44 (1H, d, *J* = 11.9 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.40 (1H, br s, C(H)O$\underline{H}$), 3.93 (1H, br s, C(H)O$\underline{H}$), 3.84-3.80 (5H, m, $Ar_{PMB}O\underline{Me}$, C37$\underline{H}$), 3.77 (1H, br d, *J* = 9.9 Hz, C35$\underline{H}$), 3.58 (1H, dd, *J* = 9.0, 4.1 Hz, C33$\underline{H_a}H_b$), 3.54 (1H, dd, *J* = 9.0, 4.8 Hz, C33$H_a\underline{H_b}$) 1.96-1.89 (1H, m, C34$\underline{H}$), 1.61-1.53 (1H, m, C36$\underline{H}$), 1.18 (3H, d, *J* = 6.2 Hz, C37(H)$\underline{Me}$), 0.98 (3H, d, *J* = 7.1 Hz, C34(H)$\underline{Me}$), 0.74 (3H, d, *J* = 6.9 Hz, C36(H)$\underline{Me}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 160.1, 130.8, 128.2, 113.7, 101.8, 85.8, 74.0, 71.7, 55.3, 41.1, 30.1, 20.3, 10.9, 10.8. **m.p.** 47-52 ºC. **$[\alpha]_D^{20}$** –12.6 (*c* = 2.0, $CHCl_3$). **IR** (thin film) 3442, 2969, 2841, 1615, 1518, 1249, 1168, 1111, 1033, 829 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{16}H_{25}O_4$ $[M + H]^+$ 281.1747, found 281.1747.

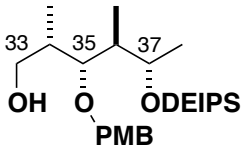
**DEIPS ETHER 47**




A solution of alcohol **46** (6.00 g, 21.4 mmol, dried azeotropicalley from PhH) and imidazole (4.32 g, 32.1 mmol) in $CH_2Cl_2$ (100 mL) was prepared. Chlorodiethyl-*iso*-propylsilane (5.31 g, 32.1 mmol) was added and the reaction stirred for 30 min at rt. The reaction was quenched by the careful addition of $NaHCO_3$ solution (100 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 100 mL) and the combined organic phases washed with brine (200 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography to give DEIPS ether **47** (8.47 g, 20.8 mmol, 97%) as a colourless oil.

**$R_f$** 0.59 (5:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39 (2H, d, *J* = 8.8 Hz, $Ar_{PMP}\underline{H}$), 6.88 (2H, d, *J* = 8.8 Hz, $Ar_{PMP}\underline{H}$), 5.39 (1H, s, $OC\underline{H}Ar_{PMP}$), 4.31 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.06 (1H, dd, *J* = 11.2, 2.3 Hz, C33$\underline{H_a}H_b$), 4.01 (1H, dd, *J* = 11.2, 1.1 Hz, C33$H_a\underline{H_b}$), 3.81 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.54 (1H, dd, *J* = 10.7, 2.1 Hz, C35$\underline{H}$), 2.01-1.93 (1H, m, C36$\underline{H}$), 1.63-1.57 (1H, m, C34$\underline{H}$), 1.16 (3H, d, *J* = 6.9 Hz, C34(H)$\underline{Me}$), 1.03 (3H, d, *J* = 6.4 Hz, C38$\underline{H_3}$), 1.00-0.95 (12H, overlapping 2 dd & d, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$), 0.94-0.84 (1H, m, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.81 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.63-0.57 (4H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$). **$^{13}$C NMR** (500 MHz, $CDCl_3$) 159.8, 131.7, 127.2, 113.5, 101.2, 81.5, 74.1, 66.7, 55.3, 40.9, 29.9, 17.4, 16.9, 13.1, 10.9, 7.5, 7.1, 7.1, 3.8, 3.8. **$[\alpha]_D^{20}$** –6.1 (*c* = 0.19, $CHCl_3$). **IR** (thin film) 2957, 2877, 1616, 1518, 1249, 1166, 1113, 1050, 829, 726 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{23}H_{41}O_4Si$ $[M + H]^+$ 409.2769, found 409.2773.

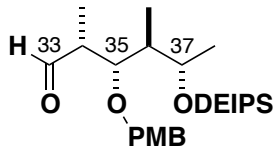
**ALCOHOL 48**




A solution of PMP acetal **47** (2.50 g, 6.13 mmol) in $CH_2Cl_2$ (50 mL) was cooled to –78 ºC and DIBAL (12.2 mL, 12.2 mmol, 1 M solution in $CH_2Cl_2$) was added dropwise. The reaction was warmed to 0 ºC and stirred for 2 h. $Na^+/K^+$ tartrate solution (50 mL) was added carefully at 0 ºC and the mixture stirred vigorously for 1.5 h. The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (3 × 100 mL). The combined organic phases were washed with brine (200 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (5:1 PE/EtOAc) to yield alcohol **48** (2.32 g, 5.64 mmol, 93%) as a colourless oil.

**$R_f$** 0.25 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 6.87 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 4.49 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.45 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.18 (dq, *J* = 6.3, 3.8 Hz, C37$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.61 (2H, dd, *J* = 6.7, 5.5 Hz, C33$\underline{H_2}$), 3.42 (1H, dd, *J* = 9.5, 2.2 Hz, C35$\underline{H}$), 1.99-1.90 (2H, m, C34$\underline{H}$, C36$\underline{H}$), 1.68 (1H, t, *J* = 5.5 Hz, C33(H)O$\underline{H}$), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 0.99-0.96 (12H, overlapping 2 dd & d, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$), 0.90 (3H, d, *J* = 7.0 Hz, C34(H)$\underline{Me}$), 0.90-0.85 (obs septet, *J* = 6.3Hz, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.83 (3H, d, *J* = 7.1 Hz, C36(H)$\underline{Me}$), 0.62-0.55 (4H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.1, 131.1, 129.1, 113.7, 81.2, 73.6, 68.1, 66.5, 55.3, 42.9, 37.7, 18.2, 17.4, 13.1, 10.3, 10.0, 7.1, 3.8. **$[\alpha]_D^{20}$** +2.9 (*c* = 2.0, $CHCl_3$). **IR** (thin film) 3407, 2957, 2877, 1614, 1515, 1464, 1249, 1037, 725 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{23}H_{43}O_4Si$ $[M + H]^+$ 411.2925, found 411.2922.

**ALDEHYDE 49**

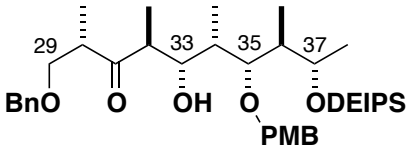



To a solution of alcohol **48** (198 mg, 481 µmol) in $CH_2Cl_2$ (6 mL) was sequentially added $NaHCO_3$ powder (81 mg, 962 µmol) and Dess–Martin periodinane (306 mg, 722 µmol). After stirring for 30 min at rt, the reaction was quenched by the addition of $Na_2S_2O_3$ solution (5 mL) and the mixture stirred vigorously for 30 min. The mixture was diluted with $H_2O$ (10 mL) and $CH_2Cl_2$ (10 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 20 mL) and the combined organics dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (50:1 → 6:1 PE/EtOAc) to afford aldehyde **49** (184 mg, 447 µmol, 93%) as a colourless oil to be used immediately.

**$R_f$** 0.38 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.82 (1H, br s, C33$\underline{H}$O), 7.17 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 6.85 (2H, d, *J* = 8.4 Hz, $Ar_{PMB}\underline{H}$), 4.31 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.23 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.18 (1H, dq, *J* = 6.2, 4.1 Hz, C37$\underline{H}$), 3.82 (1H, dd, *J* = 9.3, 1.8 Hz, C35$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 2.54 (1H, dq, *J* = 7.1, 1.4 Hz, C34$\underline{H}$), 1.96 (1H, ddq, *J* = 9.3, 7.1, 4.1 C36$\underline{H}$), 1.18 (3H, d, *J* = 7.1

Hz, C34(H)Me), 0.99-0.93 (12H, overlapping 2dd & d, Si($CH_2$Me)$_2$(CHMe$_2$), Si($CH_2$Me)$_2$(CHMe$_2$)), 0.91-0.84 (obs septet, *J* = 6.3Hz, Si($CH_2$Me)$_2$(CHMe$_2$)), 0.86 (3H, d, *J* = 7.1Hz, C36(H)Me), 0.62-0.54 (4H, m, Si($CH_2$Me)$_2$(CHMe$_2$)).**$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 204.9, 159.2, 130.4, 129.1, 113.7, 79.1, 72.5, 68.0, 55.3, 49.2, 42.9, 18.1, 17.3, 13.2, 10.2, 7.3, 7.0, 4.0, 3.9. **[α]$_D^{20}$** –21.3 (*c* = 2.0, $CHCl_3$); **IR** (thin film) 2955, 1736, 1614, 1515, 1464, 1383, 1303, 1249, 1037, 964, 724 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{23}H_{41}O_4Si$ [M + H]$^+$ 409.2769, found 409.2773.

**ALDOL PRODUCT 51**

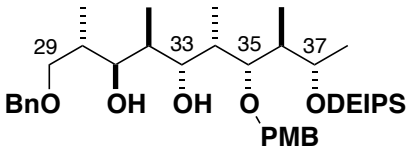



Ethyl ketone **35** and aldehyde **49** were dried azeotropically (3 × 10 mL PhH) prior to use. A solution of dicyclohexylboron chloride (6.28 mL, 28.6 mmol) was prepared in $Et_2O$ (30 mL) at 0 ºC. Triethylamine (4.98 mL, 35.8 mmol) was added dropwise and the mixture stirred for 30 min. A solution of ethyl ketone **35** (6.57g, 31.4 mmol) in $Et_2O$ (5 mL, stirred over $CaH_2$ for 30 min) was added *via* syringe forming a bright yellow suspension immediately. The suspension was stirred at –78 ºC for 1 h then at 0 ºC for a further 1 h to form enolate **50**. The mixture was cooled to –78 ºC and a solution of aldehyde **49** (5.53g, 13.5 mmol) in $Et_2O$ (30 mL, stirred over $CaH_2$ for 30 min) was added slowly *via* cannula. The reaction was stirred at –78 ºC for 1.5 h and held at –23 ºC (freezer) for 16 h. On complete consumption of aldehyde, the reaction was quenched at 0 ºC by the sequential addition of MeOH (20 mL), pH 7 buffer solution (20 mL) and $H_2O_2$ (15 mL, 30% aq.) dropwise. The solution was stirred for 30 min at rt over which time the yellow colour faded. The organic phase was separated and the aqueous phase extracted with $Et_2O$ (3 × 150 mL). The combined organic phases were washed with brine, dried ($Na_2SO_4$) and concentrated *in vacuo*. The cyclohexanol by-product was removed by co-evaporation with xylenes (3 × 10 mL) and the residue purified by column chromatography (20:1 PE/EtOAc [any higher polarity will not separate recovered ethyl ketone **35** from product]). Aldol product **51** (7.99 g, 13.0 mmol, 96%) was isolated as a colourless oil.

**R$_f$** 0.47 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.35 (5H, m, Ar$_{Bn}$H), 7.21 (2H, d, *J* = 8.4 Hz, Ar$_{PMB}$H), 6.85 (2H, d, *J* = 8.4 Hz, Ar$_{PMB}$H), 4.51 (1H, d, *J* = 12.0 Hz, OH$_a$H$_b$Ar$_{Bn}$), 4.473 (1H, d, *J* = 12.0 Hz, OH$_a$H$_b$Ar$_{Bn}$), 4.470 (1H, d, *J* = 10.8 Hz, OH$_a$H$_b$Ar$_{PMB}$), 4.43 (1H, d, *J* = 10.8 Hz, OH$_a$H$_b$Ar$_{PMB}$), 4.14-4.09 (1H, m, C37H), 3.90 (1H, br app dt, *J* = 9.0, 1.9 Hz, C33H), 3.79 (3H, s, Ar$_{PMB}$OMe), 3.65 (1H, dd, *J* = 8.3, 8.2 Hz, C35H), 3.52-3.47 (2H, m, C29H$_a$H$_b$, C29H$_a$H$_b$), 3.27 (1H, d, *J* = 2.0 Hz, C33(H)OH), 3.11-3.04 (1H, m, C30H), 2.90 (1H, dq, *J* = 8.8, 7.0 Hz, C32H), 2.04 -1.97 (1H, m, C36H), 1.92-1.87 (1H, m, C34H), 1.15 (3H, s, *J* = 6.2 Hz, C38H$_3$), 1.06 (3H, d, *J* = 6.9 Hz, C32(H)Me), 1.00-0.92 (18H, m, C30(H)Me, C34(H)Me, Si($CH_2$Me)$_2$(CHMe$_2$), Si($CH_2$Me)$_2$(CHMe$_2$)), 0.90-0.86 (1H, obs, m, Si($CH_2$Me)$_2$(CHMe$_2$)), 0.88 (3H, s, *J* = 7.1 Hz, C36(H)Me), 0.62-0.57 (4H, m, Si($CH_2$Me)$_2$(CHMe$_2$)). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 217.4, 159.2, 138.1, 130.3, 129.2, 128.3, 127.6 (3C), 113.8, 85.7, 78.3, 73.3, 72.9, 72.7, 68.5, 55.3, 49.1, 47.0, 43.2, 35.6, 19.3, 17.4, 13.2, 13.1, 10.6, 7.2, 7.1, 6.7, 4.0, 4.0. **[α]$_D^{20}$** +37.1 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 3514, 2938, 1712,

1614, 1514, 1456, 1249,1093, 1032, 728 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{36}H_{62}O_6NSi$ [M + $NH_4$]$^+$ 632.4341, found 632.4345.

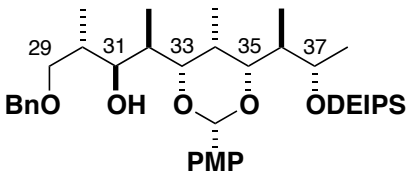
**DIOL 52**




To a slurry of $Me_4NBH(OAc)_3$ (236 mg, 5.63 mmol) in MeCN (2.5 mL) at rt was added AcOH (2.5 mL) and the mixture stirred at rt for 20 min. After careful cooling to –30 ºC, a solution of ketone **51** (236 mg, 384 µmol) in MeCN (5 mL) was added and the reaction stirred for 36 h. The reaction was quenched by transferring *via* cannula to a rapidly stirring solution of Na/K tartrate and $NaHCO_3$ (50 mL) at 0 ºC. The solution was stirred for a further 1 h and diluted with $Et_2O$ (50 mL). The layers were separated and the aqueous phase extracted with $Et_2O$ (3 × 50 mL). The combined organic phases were washed with brine (50 mL) dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 PE/EtOAc) to afford diol **52** (214 mg, 349 µmol, 91%) as a colourless oil.

**$R_f$** 0.26 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36-7.27 (5H, m, $Ar_{Bn}\underline{H}$), 7.23 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 6.85 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}\underline{H}$), 4.55 (1H, d, *J* = 11.8 Hz, $O\underline{H_a}H_bAr_{Bn}$), 4.50 (1H, d, *J* = 11.8 Hz, $OH_a\underline{H_b}Ar_{Bn}$), 4.49 (1H, d, *J* = 10.8 Hz, $O\underline{H_a}H_bAr_{PMB}$), 4.46 (1H, d, *J* = 10.8 Hz, $OH_a\underline{H_b}Ar_{PMB}$), 4.18-4.13 (1H, m, C37$\underline{H}$), 3.91 (1H, br app dt, *J* = 9.4, 1.9 Hz, C33$\underline{H}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77 (1H, br dd, *J* = 7.6, 3.0, C31$\underline{H}$), 3.71 (1H, br s, O$\underline{H}$), 3.60-3.52 (2H, m, C29$\underline{H_a}H_b$, C29$H_a\underline{H_b}$), 3.47 (1H, d, *J* = 2.1 Hz, O$\underline{H}$), 3.45 (1H, dd, *J* = 8.8, 2.1 Hz, C35$\underline{H}$), 2.04-1.95 (3H, m, C30$\underline{H}$, C34$\underline{H}$, C36$\underline{H}$), 1.76 (1H, app dqn, *J* = 7.0, 1.6 Hz, C32$\underline{H}$), 1.12 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.93 (15H, m, C30(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$), 0.92-0.85 (1H, obs m, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.89-0.86 (6H, 2 overlapping d, C32(H)$\underline{Me}$, C36(H)$\underline{Me}$), 0.80 (3H, d, *J* =6.9 Hz, C34(H)$\underline{Me}$), 0.62-0.56 (4H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.2, 137.8, 130.5, 129.1, 128.4, 127.7, 127.7, 113.8, 85.7, 77.6, 76.6, 75.1, 73.5, 73.0, 68.2, 55.3, 43.3, 37.1, 36.5, 36.1, 18.8, 17.4, 13.3, 13.2, 10.4, 9.6, 7.2, 7.2, 7.1, 4.0, 3.9. **$[\alpha]_D^{20}$** +9.1 (*c* = 1.3, $CHCl_3$); **IR** (thin film) 3448, 2939, 2876, 1613, 1515, 1456, 1249, 1095, 1031, 964, 730 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{36}H_{61}O_6Si$ [M + H]$^+$ 617.4232, found 617.4232.

**PMP ACETAL 53**

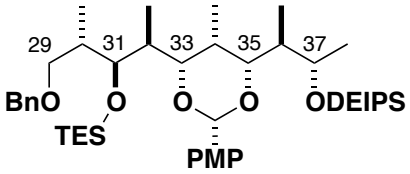



A slurry of PMB ether **52** (198 mg, 321 µmol) and 4 Å molecular sieves (*ca.* 500 mg) in $CH_2Cl_2$ (5 mL) was cooled to 0 ºC. A solution of DDQ (101 mg, 451 µmol) in $CH_2Cl_2$ (20 mL) was added slowly *via* cannula and the mixture stirred for a further 1.5 h at 0 ºC. The reaction was quenched by filtering through Celite® on to

$NaHCO_3$ (50 mL). The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic phases were washed with $NaHCO_3$ solution (100 mL) and brine (100 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified immediately by column chromatography (15:1 → 10:1 PE/EtOAc) to give PMP acetal **53** (168 mg, 273 µmol, 85%) as a colourless oil. [On scales >500 mg, it was found to be preferable to perform this reaction with 0.9 equivalents of DDQ and termination of the reaction at the first sight of any over-oxidation orthoester by-product by TLC]

**$R_f$** 0.74 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.40 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.36-7.28 (5H, m, $Ar_{Bn}\underline{H}$), 6.88 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 5.46 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.57 (1H, d, *J* = 11.8 Hz, $O\underline{H_a}H_bAr_{Bn}$), 4.52 (1H, d, *J* = 11.8 Hz, $OH_a\underline{H_b}Ar_{Bn}$), 4.34 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 3.93 (1H, app dt, *J* = 9.3, 2.0 Hz, C31$\underline{H}$), 3.88 (1H, dd, *J* = 9.9, 1.7 Hz, C33$\underline{H}$), 3.62 (1H, obs d, *J* = 2.0 Hz, C31(H)O$\underline{H}$), 3.60 (1H, dd, *J* = 9.0, 4.2 Hz, C29$\underline{H_a}H_b$), 3.53 (1H, app t, *J* = 9.0 Hz, C29$H_a\underline{H_b}$), 3.49 (1H, dd, *J* = 10.6, 1.8 Hz, C35$\underline{H}$), 2.04-1.97 (2H, m, C30$\underline{H}$, C36$\underline{H}$), 1.87-1.78 (1H, m, C32$\underline{H}$), 1.64-1.57 (1H, m, C34$\underline{H}$), 1.03 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.94 (12H, m, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$), 0.94-0.88 (1H, obs m, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.91 (3H, d, *J* = 6.8 Hz, C34(H)$\underline{Me}$), 0.83-0.80 (6H, 2 overlapping d, C32(H)$\underline{Me}$, C36(H)$\underline{Me}$), 0.78 (3H, d, *J* = 7.0 Hz, C30(H)$\underline{Me}$), 0.65-0.57 (4H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 137.8, 132.1, 128.5, 127.8*, 127.7, 127.2, 113.3, 100.6, 82.9, 81.0, 76.9, 74.4, 73.5, 67.1, 55.3, 40.8, 36.5, 36.1, 30.5, 17.4, 17.0, 13.4, 13.1, 7.6, 7.1, 7.1, 7.1, 5.4, 3.9, 3.8. **$[\alpha]_D^{20}$** +20.5 (*c* = 3.2, $CHCl_3$). **IR** (thin film) 3497, 2966, 1617, 1518, 1455, 1249, 1168, 1102, 1032, 970, 729 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{36}H_{59}O_6Si$ $[M + H]^+$ 615.4075, found 615.4073.

**TES ETHER 54**

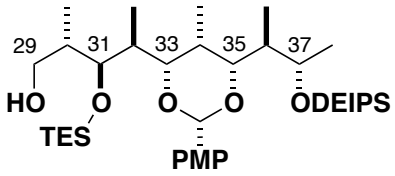



A solution of alcohol **53** (410 mg, 666 µmol) in $CH_2Cl_2$ (4 mL) was cooled to –78 ºC and 2,6-lutidine (232 µL, 2.00 mmol) was added. TBSOTf was added dropwise (226 µL, 1.00 mmol) and the reaction stirred for 30 min. The reaction was quenched by the addition of MeOH (2 mL) and $NaHCO_3$ (10 mL). The aqueous phase was extracted with EtOAc (5 × 25 mL) and the combined organic phases dried ($Na_2SO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (15:1 PE/EtOAc) to afford TES ether **54** (480 mg, 658 µmol, 99%) as a colourless oil.

**$R_f$** 0.59 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.37 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.33-7.31 (5H, m, $Ar_{Bn}\underline{H}$), 6.83 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 5.38 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.49 (1H, d, *J* = 12.1 Hz, $O\underline{H_a}H_bAr_{Bn}$), 4.46 (1H, d, *J* = 12.1 Hz, $OH_a\underline{H_b}Ar_{Bn}$), 4.33 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.08 (1H, br d, *J* = 7.8 Hz, C31$\underline{H}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.58-3.53 (2H, m, C29$\underline{H_a}H_b$, C33$\underline{H}$), 3.40 (1H, br d, *J* = 10.4 Hz, C35$\underline{H}$), 3.25 (1H, app t, *J* = 8.4 Hz, C29$H_a\underline{H_b}$), 2.04-1.98 (1H, m, C36$\underline{H}$), 1.98-1.92 (1H, m, C30$\underline{H}$), 1.81 (1H, app dq, *J* = 9.8, 7.1 C32$\underline{H}$), 1.61-1.52 (1H, m, C34$\underline{H}$), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.89 (28H, m, C30(H)$\underline{Me}$, C34(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.78 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.64-0.56 (10H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$, $Si(C\underline{H_2}Me)_3$), [spin system

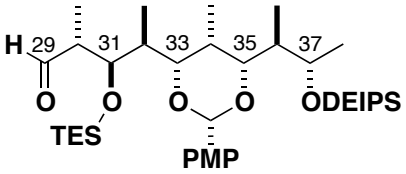
interrupted across C32-C33 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.5, 138.9, 131.9, 128.2, 127.4, 127.3, 127.1, 113.3, 100.5, 83.0, 81.5, 73.7, 73.0, 72.0, 67.2, 55.3, 40.7, 39.0, 36.7, 30.6, 17.4, 17.2, 14.4, 13.1, 7.9, 7.8, 7.1, 5.7, 5.5, 3.9. 3.8. **$[\alpha]_D^{20}$** +8.1 (*c* = 0.6, $CHCl_3$). **IR** (thin film) 2956, 2877, 1617, 1517, 1458, 388, 1249, 1103, 1032, 731 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{42}H_{72}O_6Si_2$ $[M]^+$ 728.4862, found 728.4855.

**ALCOHOL 55**




Raney–Nickel (4 spatula loads (*ca.* 1 g)) was added to a solution of benzyl ether **54** (650 mg, 891 µmol) in EtOH (8 mL) and the mixture stirred rapidly at rt. The atmosphere was replaced with hydrogen (balloon) and the reaction stirred overnight. The mixture was filtered through Celite® eluting with EtOH (100 mL) and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (9:1 PE/EtOAc) to afford alcohol **55** (523 mg, 818 µmol, 92%) as a colourless oil. [It was found to be important to age freshly prepared Raney–Nickel for at least 2 d under EtOH to minimise the formation of unidentified by-products].
**$R_f$** 0.20 (9/1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.89 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.31 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.15 (1H, app d, *J* = 6.7 Hz, C31$\underline{H}$), 3.81 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.55 (1H, dd, *J* = 10.4, 1.7 Hz, C33$\underline{H}$), 3.53-3.44 (2H, m, C29$\underline{H_a}H_b$, C29$H_a\underline{H_b}$), 3.41 (1H, dd, *J* = 10.7, 1.9 Hz, C35$\underline{H}$), 2.47 (1H, dd, *J* = 8.7, 4.2 Hz, C29$H_aH_bO\underline{H}$), 2.06-2.00 (1H, m, C36$\underline{H}$), 1.91-1.83 (1H, m, C30$\underline{H}$), 1.77 (1H, app dq, *J* = 10.1, 6.3 Hz, C32$\underline{H}$), 1.64-1.52 (1H, m, C34$\underline{H}$), 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.02-0.91 (25H, m, C34(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2(CHMe_2)$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$), 0.85-0.81 (9H, 3 overlapping d, C30(H)$\underline{Me}$, C32(H)$\underline{Me}$, C36(H)$\underline{Me}$), 0.70-0.57 (10H, m, $Si(C\underline{H_2}Me)_2(CHMe_2)$, $Si(C\underline{H_2}Me)_3$), [spin system interrupted across C32-C33 due to restricted rotation]. **$^{13}$C NMR** (100 MHz, $CDCl_3$) $\delta_C$ 159.7, 131.4, 127.0, 113.5, 100.9, 83.0, 82.5, 73.5, 67.1, 66.3, 55.2, 40.9, 40.7, 36.6, 30.6, 17.4, 17.2, 13.3, 13.1, 8.8, 7.8, 7.1, 7.1, 7.0, 5.4, 5.3, 3.8, 3.8. **$[\alpha]_D^{20}$** +10.5 (*c* = 1.7, $CHCl_3$). **IR** (thin film) 3670, 2959, 2877, 1617, 1518, 1462, 1383, 1250, 1037, 725 cm$^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{35}H_{67}O_6Si_2$ $[M + H]^+$ 639.4471, found 639.4472.

**C29-C38 ALDEHYDE 11**



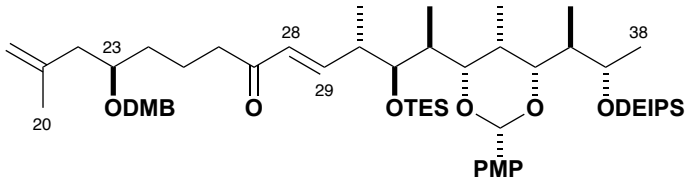

To a solution of alcohol **55** (400 mg, 626 µmol) in $CH_2Cl_2$ (15 mL) was sequentially added $NaHCO_3$ powder (158 mg, 1.88 mmol) and Dess–Martin periodinane (398 mg, 939 µmol). After stirring for 30 min at rt, the reaction was quenched by the addition of $Na_2S_2O_3$ solution (15 mL) and the mixture stirred vigorously for 30

min. The mixture was diluted with $H_2O$ (30 mL) and $CH_2Cl_2$ (30 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 40 mL) and the combined organics dried ($Na_2SO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography (50:1 → 9:1 PE/EtOAc) to afford aldehyde **11** (365 mg, 582 μmol, 92%) as a colourless oil to be used immediately.

**$R_f$** 0.57 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.70 (1H, d, *J* = 2.9 Hz, C29HO), 7.37 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}$H), 6.89 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}$H), 5.38 (1H, s, $O_2$CHAr$_{PMP}$), 4.40 (1H, app d, *J* = 7.5 Hz, C13H), 4.30 (1H, dq, *J* = 6.3, 3.4 Hz, C37H), 3.82 (3H, s, $Ar_{PMP}$OMe), 3.59 (1H, dd, J = 10.1, 1.3 Hz, C33H), 3.42 (1H, dd, *J* = 10.3, 1.0 Hz, C35H), 2.55 (1H, dq, *J* = 7.0, 4.5 Hz, C30H), 2.05-1.98 (1H, m, C36H), 1.81-1.75 (1H, m, C32H), 1.62-1.57 (1H, m, C34H), 1.06 (3H, d, *J* = 6.3 Hz, C38H$_3$), 1.02-0.93 (25H, m, C30(H)Me, Si(CH$_2$Me)$_2$(CHMe$_2$), Si(CH$_2$Me)$_2$(CHMe$_2$), Si(CH$_2$Me)$_3$), 0.92 (3H, d, *J* = 6.7 Hz, C34(H)Me), 0.84-0.82 (6H, 2 overlapping d, C32(H)Me, C36(H)Me), 0.65-0.58 (10H, m, Si(CH$_2$Me)$_2$(CHMe$_2$), Si(CH$_2$Me)$_3$), [spin system interrupted across C32-C33 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 205.0, 159.7, 131.6, 127.2, 113.4, 100.8, 82.9, 80.9, 72.1, 67.2, 55.3, 51.4, 40.7, 37.8, 30.6, 17.4, 17.3, 13.1, 11.4, 8.0, 7.9, 7.1, 7.1, 7.0, 5.6, 5.4, 3.9, 3.8. **$[\alpha]_D^{20}$** +19.3 (*c* = 0.49, $CHCl_3$). **IR** (thin film) 2954, 2877, 1729, 1617, 1518, 1459, 1249, 1032, 969, 725 cm$^{-1}$. **HRMS** (EI) Calculated for $C_{35}H_{65}O_6Si_2$ $[M + H]^+$ 637.4314, found 637.4316.

### 3.3. Coupling of 10 and 11 to the C20-C38 Fragment 6 and model studies

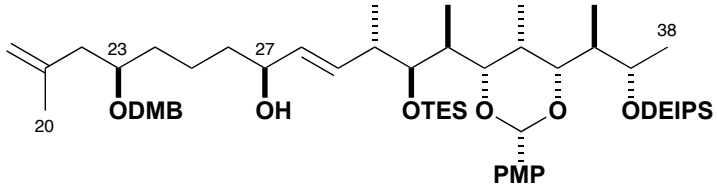
**ENONE 56**




To a slurry of anyhydrous $Ba(OH)_2$ (30 mg, 180 µmol) in THF (1 mL) was added phosphonate (*R*)-**10** (65 mg, 150 µmol) and the mixture stirred at RT for 45 min. A solution of aldehyde **11** (65 mg, 99 µmol) in THF (1 mL) and $H_2O$ (25 µL) was then added *via* cannula and the reaction mixture was stirred for a further 16 h. The reaction was quenched with $NH_4Cl$ solution (2 mL), extracted with $Et_2O$ (3 × 3 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (4:1 PE/EtOAc) to afford enone **56** (90 mg, 93 µmol, 91%) as a colourless oil. Further elution of the column with EtOAc provided excess phosphonate (*R*)-**10** (17 mg, 40 µmol) as a colourless oil.

**$R_f$** 0.22 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.26 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.92 (1H, d, *J* = 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.88 (2H, d, *J* = 8.8 Hz, $Ar_{PMP}\underline{H}$), 6.87-6.80 (3H, m, $Ar_{DMB}\underline{H}$, C29$\underline{H}$), 6.08 (1H, d, *J* = 16.0 Hz, C28$\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.80 (1H, s, C21C$\underline{H_a}H_b$), 4.76 (1H, s, C21C$H_a\underline{H_b}$), 4.48 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.32 (1H, dq, *J* = 3.5, 6.4 Hz, C37$\underline{H}$), 4.10 (1H, d, *J* = 7.0 Hz, C31$\underline{H}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.81 (3H, s, $Ar_{PMP}\underline{OMe}$), 3.57-3.52 (2H, m, C23$\underline{H}$, C33$\underline{H}$), 3.41 (1H, dd, *J* = 10.6, 1.7 Hz, C35$\underline{H}$), 2.54-2.42 (3H, m, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 2.36 (1H, dd, *J* = 13.9, 6.5 Hz, C22$\underline{H_a}H_b$), 2.17 (1H, dd, *J* = 13.9, 6.2 Hz, C22$H_a\underline{H_b}$), 2.05-1.98 (1H, m, C36$\underline{H}$), 1.82-1.74 (2H, m, C25$\underline{H_a}H_b$, C32$\underline{H}$), 1.74 (3H, s, C20$\underline{H_3}$), 1.70-1.62 (1H, m, C25$H_a\underline{H_b}$), 1.59 (1H, dt, *J* = 6.7, 1.7 Hz, C34$\underline{H}$), 1.55-1.46 (2H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$), 1.06 (3H, d, *J* = 6.4 Hz, C38$\underline{H_3}$), 1.01-0.94 (25H, m, C30(H)$\underline{Me}$, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2$Me)$_2$(CH$\underline{Me_2}$), Si($CH_2\underline{Me}$)$_3$, Si($CH_2$Me)$_2$(C$\underline{H}$Me$_2$)), 0.90 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.84 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.78 (3H, d, *J* = 6.9 Hz, C(32(H)$\underline{Me}$), 0.63-0.58 (10H, m, Si(C$\underline{H_2}$Me)$_3$, Si(C$\underline{H_2}$Me)$_2$$^i$Pr). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 200.2, 159.6, 150.8, 149.0, 148.5, 142.9, 131.7, 131.5, 129.7, 127.1, 120.2, 113.4, 112.7, 111.2, 110.9, 100.7, 82.9, 81.5, 77.0, 74.0, 70.8, 67.2, 55.9, 55.8, 55.3, 42.7, 42.6, 40.8, 40.0, 37.6, 33.6, 30.5, 22.9, 20.0, 17.4, 17.3, 16.7, 13.1, 8.0, 7.9, 7.1, 7.1, 5.7, 5.4, 3.9, 3.8. **$[\alpha]_D^{20}$** +2.7 (*c* = 8.0, $CHCl_3$). **IR** (thin film) 2954, 2876, 1697, 1674, 1618, 1592, 1517, 1463, 1249, 1031, 726 cm$^{-1}$. **HRMS** (ESI) Calculated for $C_{54}H_{94}O_9NSi_2$ $[M + NH_4]^+$ 956.6462, found 956.6463.

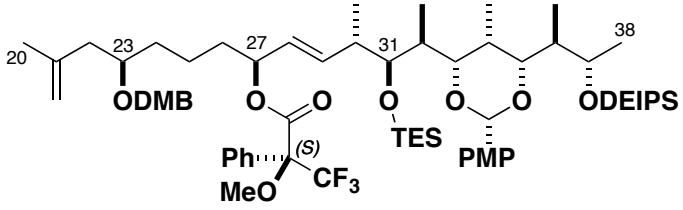
**ALLYLIC ALCOHOL 57**




To a stirred solution of enone **56** (90 mg, 93 µmol) in THF (2 mL) at –78 °C was added (*R*)-Me-CBS catalyst (20 µL, 20 µmol, 1 M solution in toluene) and $BH_3$•$SMe_2$ (19 µL, 200 µmol) and the solution was allowed to warm to –50 °C over 30 min. The reaction was carefully quenched at –78 °C by the dropwise addition of MeOH (3 mL) before warming to rt. The solvents were then removed under reduced pressure. The addition of further MeOH (3 mL) and evaporation was repeated three more times. The residue was purified by column chromatography (4:1 PE/EtOAc) to give alcohol **57** (79 mg, 81 µmol, 88%, >95:5 d.r.) as a colourless oil.

**$R_f$** 0.27 (7:3 PE/EtOA). **$^1$H NMR** (500 MHz, $CDCl_3$) δH 7.37 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.90 (1H, d, *J* = 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.88 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.84 (1H, dd, *J* = 8.0, 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.0 Hz, $Ar_{DMB}\underline{H}$) 5.65 (1H, dd, *J* = 15.6, 7.5 Hz, C29H), 5.43 (1H, dd, *J* = 15.5, 7.0 Hz, C28H), 5.38 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, s, C21C$\underline{H_a}H_b$), 4.76 (1H, s, C21C$H_a\underline{H_b}$), 4.48 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.32 (1H, dq, *J* = 6.4, 3.4 Hz, C37H), 4.04-3.99 (2H, m, C31H, C27H), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.55-3.50 (2H, m, C23H, C33H), 3.40 (1H, dd, *J* = 10.6, 1.6 Hz, C35H), 2.36-2.28 (2H, m, C22$\underline{H_a}H_b$, C30H), 2.16 (1H, dd, *J* = 13.9, 6.0 Hz, C22$H_a\underline{H_b}$), 2.05-1.98 (1H, m, C36H), 1.821.75 (1H, m, C32H), 1.73 (3H, s, C20$\underline{H_3}$), 1.61-1.41 (5H, m, C24$\underline{H_a}H_b$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C27(H)OH, C34H), 1.39-1.33 (3H, m, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$), 1.06 (3H, d, *J* = 6.4 Hz, C38$\underline{H_3}$), 1.00-0.95 (25H, m, C30(H)Me, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.90 (3H, d, *J* = 6.7 Hz, C34(H)Me), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)Me), 0.78 (3H, d, *J* = 6.9 Hz, C32(H)Me), 0.66-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.6, 148.9, 148.5, 143.0, 135.8, 132.3, 131.9, 131.5, 127.1, 120.1, 113.3, 112.6, 111.2, 110.8, 100.7, 83.0, 81.9, 77.1, 74.0, 73.2, 70.8, 67.2, 55.9, 55.8, 55.3, 42.7, 42.3, 40.7, 37.3, 37.1, 33.9, 30.4, 22.9, 21.4, 17.4, 17.2, 17.1, 13.1, 8.4, 7.8, 7.2, 7.1, 5.8, 5.4, 3.8, 3.8. **$[\alpha]_D^{20}$** +3.3 (*c* = 2.1, $CHCl_3$). **IR** (thin film) 3471, 2937, 2876, 1615, 1592, 1517, 1463, 1249, 1032, 970, 726 $cm^{-1}$. **HRMS** (ESI) Calculated for $C_{54}H_{96}O_9NSi_2$ $[M + NH_4]^+$ 958.6618, found 958.6611.

**MOSHER ESTER 57S**

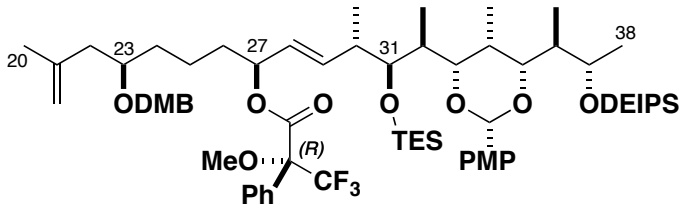



To a stirred solution of alcohol **57** (5.0 mg, 5.3 µmol) in $CH_2Cl_2$ (0.5 mL) was added (*S*)-MTPA (5.0 mg, 21 µmol), DCC (21 µL, 21 µmol, 1 M solution in $CH_2Cl_2$) and DMAP (1 crystal). After 2 h, direct purification by

column chromatography (19:1 PE/EtOAc) gave Mosher ester **57S** (3.4 mg, 2.9 µmol, 55%) as a colourless oil.

**$R_f$** 0.44 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.45-7.40 (2H, m, $Ar_{Ph}\underline{H}$), 7.38-7.32 (5H, m, $Ar_{Ph}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.88 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.86 (1H, d, *J* = 1.6 Hz, $Ar_{DMB}\underline{H}$), 6.82 (1H, dd, *J* = 8.1, 1.6 Hz, $Ar_{DMB}\underline{H}$), 6.79 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.93 (1H, dd, *J* = 14.8, 7.3 Hz, C29$\underline{H}$), 5.47-5.40 (2H, m, C27$\underline{H}$, C28$\underline{H}$), 5.37 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, s, C21C$\underline{H_a}H_b$) 4.72 (1H, s, C21C$H_a\underline{H_b}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.41 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, qd, *J* = 6.2, 3.3 Hz, C37$\underline{H}$), 4.06 (1H, d, *J* = 5.4 Hz, C31$\underline{H}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.54 (1H, dd, *J* = 14.0, 1.3 Hz, C33$\underline{H}$), 3.51 (3H, s, C($CF_3$)(Ph)O$\underline{Me}$), 3.46-3.40 (1H, m, C23$\underline{H}$), 3.39 (1H, dd, *J* = 11.1, 1.9 Hz, C35$\underline{H}$), 2.34-2.26 (1H, m, C22$\underline{H_a}H_b$, C30$\underline{H}$), 2.08 (1H, dd, *J* = 14.1, 6.0 Hz, C22$H_a\underline{H_b}$), 2.03-1.98 (1H, m, C36$\underline{H}$), 1.82-1.63 (3H, m, C32$\underline{H}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 1.71 (3H, s, C20$\underline{H_3}$), 1.61-1.50 (3H, m, C34$\underline{H}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$), 1.32-1.18 (3H, m, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$), 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.94 (25H, m, C30(H)$\underline{Me}$, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$($CH\underline{Me_2}$), Si($CH_2\underline{Me}$)$_3$, Si($CH_2Me$)$_2$($C\underline{H}Me_2$)), 0.89 (3H, d, *J* = 7.0 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, J = 7.2 Hz, C36(H)$\underline{Me}$), 0.74 (3H, d, *J* = 6.8 Hz, C32(H)$\underline{Me}$), 0.64-0.58 (10H, m, Si($C\underline{H_2}Me$)$_3$, Si($C\underline{H_2}Me$)$_2$$^i$Pr).

**MOSHER ESTER 57R**

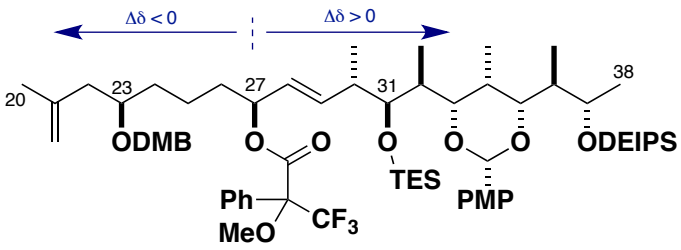



To a stirred solution of alcohol **57** (5.0 mg, 5.3 µmol) in $CH_2Cl_2$ (0.5 mL) was added (*R*)-MTPA (5.0 mg, 21 µmol), DCC (21 µL, 21 µmol, (1 M solution in $CH_2Cl_2$) and DMAP (1 crystal). After 2 h, direct purification by column chromatography (19:1 PE/EtOAc) gave Mosher ester **57R** (3.8 mg, 3.3 µmol, 62%) as a colourless oil.

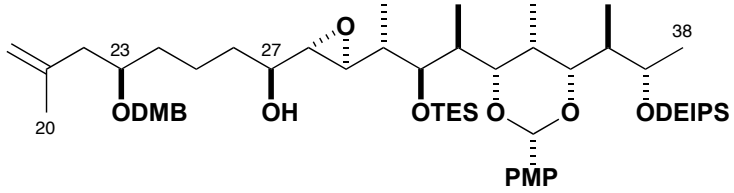
**$R_f$** 0.44 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.51-7.48 (2H, m, $Ar_{Ph}\underline{H}$), 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$) 7.35-7.32 (3H, m, $Ar_{Ph}\underline{H}$), 6.88 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.86 (1H, d, *J* = 1.9 Hz, $Ar_{DMB}\underline{H}$), 6.82 (1H, dd, *J* = 8.0, 1.9 Hz, $Ar_{DMB}\underline{H}$), 6.79 (1H, d, *J* = 8.0 Hz, $Ar_{DMB}\underline{H}$), 5.83 (1H, dd, *J* = 15.5, 7.3 Hz, C29$\underline{H}$), 5.42-5.37 (1H, m, C27$\underline{H}$), 5.37 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 5.33 (1H, dd, *J* = 7.2, 15.5 Hz, C28$\underline{H}$), 4.79 (1H, s, C21C$\underline{H_a}H_b$) 4.74 (1H, s, C21C$H_a\underline{H_b}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.40 (1H, d, *J* = 11.3, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 6.4, 3.6 Hz, C37$\underline{H}$), 4.02 (1H, d, *J* = 5.5 Hz, C31$\underline{H}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.52-3.47 (2H, m, C23$\underline{H}$, C33$\underline{H}$), 3.51 (3H, s, C($CF_3$)(Ph)O$\underline{Me}$), 3.39 (1H, dd, *J* = 10.6, 1.6 Hz, C35$\underline{H}$), 2.33 (1H, dd, *J* = 13.9, 6.3 Hz, C22$\underline{H_a}H_b$), 2.32-2.27 (1H, m, C30$\underline{H}$), 2.12 (1H, dd, J = 13.9, 6.3 Hz, C22$H_a\underline{H_b}$), 2.03-1.97 (1H, m, C36$\underline{H}$), 1.74-1.67 (2H, m, C32$\underline{H}$, C26$\underline{H_a}H_b$), 1.72 (3H, s, C20$\underline{H_3}$), 1.62-1.45 (4H, m, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$H_a\underline{H_b}$, C34$\underline{H}$), 1.37-1.21 (2H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$), 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.94 (22H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$($CH\underline{Me_2}$), Si($CH_2\underline{Me}$)$_3$, Si($CH_2Me$)$_2$($C\underline{H}Me_2$)), 0.92 (3H, d, *J* = 7.0 Hz, C30(H)$\underline{Me}$), 0.86 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.82 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.73 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.63-0.57 (10H, m, Si($C\underline{H_2}Me$)$_3$, Si($C\underline{H_2}Me$)$_2$$^i$Pr).

**MOSHER ESTER ANALYSIS OF 57S AND 57R[6]**

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C20$H_3$ | 1.71 | 1.72 | –0.01 |
| C21C$H_aH_b$ | 4.79 | 4.79 | 0.00 |
| C21C$H_aH_b$ | 4.72 | 4.74 | –0.02 |
| C22$H_aH_b$ | 2.29 | 2.33 | –0.04 |
| C22$H_aH_b$ | 2.08 | 2.12 | –0.04 |
| C23H | 3.43 | obs. | - |
| OC$H_aH_bAr_{DMB}$ | 4.44 | 4.44 | 0.00 |
| OC$H_aH_bAr_{DMB}$ | 4.41 | 4.40 | +0.01 |
| C24$H_aH_b$, C24$H_aH_b$ | obs. | obs. | - |
| C25$H_aH_b$, C25$H_aH_b$ | obs. | obs. | - |
| C26$H_aH_b$, C26$H_aH_b$ | obs. | obs. | - |
| C27H | obs. | 5.39 | - |
| C28H | obs. | 5.33 | - |
| C29H | 5.93 | 5.83 | +0.10 |
| C30H | 2.32 | 2.30 | +0.02 |
| C30(H)Me | obs. | 0.92 | - |
| C31H | 4.06 | 4.02 | +0.04 |
| C32H | obs. | obs. | - |
| C32(H)Me | 0.74 | 0.73 | +0.01 |
| C33H | 3.54 | obs. | - |
| C34H | obs. | obs. | - |
| C34(H)Me | 0.89 | 0.86 | +0.03 |



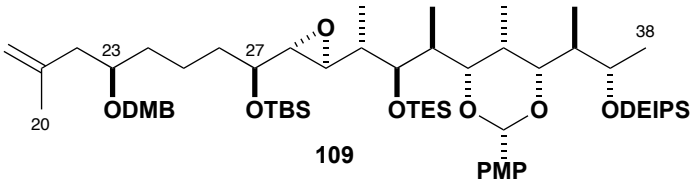
**EPOXIDE 58**




To a stirred slurry of allylic alcohol **57** (20 mg, 21 μmol) and activated 4 Å powdered molecular sieves (15 mg) in $CH_2Cl_2$ (1.0 mL) at –25 ºC was added (+)-DIPT (9.5 μL, 32 μmol) and $Ti(O\textit{i}\text{-}Pr)_4$ (5.9 μL, 21 μmol). The reaction was stirred for 20 min before the addition of dry *tert*-butylhydrogen peroxide (12 μL, 64 μmol, 5.5 M solution in decane). The reaction was transferred to the freezer (–20 ºC) overnight, before being poured into $CH_2Cl_2$ (10 mL) and NaOH solution (10 mL, 10% aq.) and the mixture was vigorously stirred for 2 h. The layers were then separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (88:12 PE/EtOAc) to afford epoxide **58** (12 mg, 13 μmol, 59%) as a colourless oil. $^1$H NMR analysis of the crude reaction mixture indicated 7:1 dr.

**$R_f$** 0.26 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.8 Hz, $Ar_{PMP}\underline{H}$), 6.91 (1H, d, *J* = 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.88 (2H, d, J = 8.8 Hz, $Ar_{PMP}\underline{H}$), 6.85 (1H, dd, *J* = 8.2, 1.8 Hz, $Ar_{DMB}\underline{H}$), 6.81 (1H, d, *J* = 8.2 Hz, $Ar_{DMB}\underline{H}$), 5.35 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.80 (1H, s, C21C$\underline{H_a}H_b$), 4.76 (1H, s, C21C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.4 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 3.4, 6.3 Hz, C37$\underline{H}$), 4.17 (1H, d, *J* = 6.2 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.2, 1.6 Hz, C33$\underline{H}$), 3.54-3.45 (2H, m, C23$\underline{H}$, C27$\underline{H}$), 3.40 (1H, dd, *J* = 10.7, 1.7 Hz, C35$\underline{H}$), 2.96 (1H, dd, *J* = 5.2, 2.4 Hz, C29$\underline{H}$), 2.75 (1H, dd, *J* = 4.4, 2.4 Hz, C28$\underline{H}$), 2.34 (1H, dd, *J* = 14.0, 6.6 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 14.0, 6.0 Hz, C22$H_a\underline{H_b}$), 2.06-1.99 (1H, m, C36$\underline{H}$), 1.85-1.79 (1H, m, C30$\underline{H}$), 1.78 (1H, d, *J* = 3.8 Hz, C27(H)O$\underline{H}$), 1.78-1.71 (1H, m, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.62-1.57 (1H, m, C34$\underline{H}$), 1.57-1.47 (2H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$), 1.43-1.27 (3H, m, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$) 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (25H, m, C30(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2{}^i$Pr, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.91 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 6.9 Hz, C36(H)$\underline{Me}$), 0.82 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.68-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^i$Pr). $^{13}$C NMR (125 MHz, CDCl3) $\delta_C$ 159.7, 149.0, 148.4, 143.0, 131.5, 131.5, 127.2, 120.1, 113.4, 112.7, 111.2, 110.8, 100.9, 83.0, 82.2, 77.1, 72.0, 71.8, 70.8, 70.0, 67.1, 59.5, 57.4, 55.9, 55.8, 55.3, 42.7, 40.7, 40.3, 37.5, 33.9, 33.9, 30.4, 22.9, 21.4, 17.4, 17.2, 13.1, 12.3, 8.8, 7.8, 7.1, 5.4, 3.8, 3.8. **$[\alpha]_D^{20}$** +6.0 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 2924, 1519, 1465, 1250, 1029, 727 cm$^{-1}$. **HRMS** (ESI) Calculated for $C_{54}H_{93}O_{10}Si_2Na$ $[M + Na]^+$ 979.6098, found 979.6121.

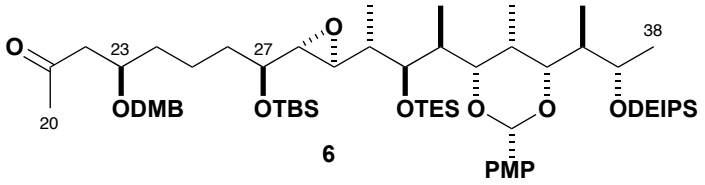
**TBS ETHER 109**




To a stirred solution of alcohol **58** (18 mg, 19 µmol) in $CH_2Cl_2$ (0.3 mL) at –78 ºC was added 2,6-lutidine (8.8 µL, 75 µmol) and TBSOTf (8.6 µL, 38 µmol). After 30 min, $NaHCO_3$ solution (10 mL) and $CH_2Cl_2$ (10 mL) were added and the layers were separated. The aqueous layer was extracted with $CH_2Cl_2$ (3 × 10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (9:1 PE/EtOAc) afforded TBS ether **109** (19 mg, 18 µmol, 95%) as a colourless oil.

**$R_f$** 0.41 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.90 (1H, d, *J* = 1.7, $Ar_{DMB}\underline{H}$), 6.87-6.84 (3H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.2 Hz, $Ar_{DMB}\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, s, C21C$\underline{H_a}H_b$), 4.76 (1H, s, C21C$H_a\underline{H_b}$), 4.46 (1H, d, *J* = 12.1 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 12.1 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.32 (1H, dq, *J* = 3.2, 6.4 Hz, C37$\underline{H}$), 4.15 (1H, dd, *J* = 6.8, 0.8 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.2, 1.7 Hz, C33$\underline{H}$), 3.45-3.42 (2H, m, C23$\underline{H}$, C27$\underline{H}$), 3.41 (1H, dd, *J* = 10.6, 1.6 Hz, C35$\underline{H}$), 2.98 (1H, dd, *J* = 3.2, 2.3 Hz, C29$\underline{H}$), 2.74 (1H, dd, *J* = 5.3, 2.3 Hz, C28$\underline{H}$), 2.34 (1H, dd, *J* = 14.1, 6.6 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 14.0, 6.0 Hz, C22$H_a\underline{H_b}$), 2.04-1.99 (1H, m, C36$\underline{H}$), 1.95-1.92 (1H, m, C30$\underline{H}$), 1.88-1.84 (1H, m, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.61-1.46 (5H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C34$\underline{H}$), 1.32-1.22 (2H, m, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (22H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.91-0.86 (15H, m, C34(H)$\underline{Me}$, C36(H)$\underline{Me}$, $Si{}^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 7.1 Hz, C32(H)$\underline{Me}$), 0.81 (3H, d, *J* = 6.7 Hz, C30(H)$\underline{Me}$), 0.69-0.56 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$), 0.02 (6H, s, $Si{}^tBu\underline{Me_2}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 159.5, 148.9, 148.4, 143.0, 131.8, 131.5, 127.1, 120.1, 113.3, 112.6, 111.1, 110.9, 100.7, 82.9, 81.8, 77.1, 72.6, 72.1, 70.9, 67.2, 58.7, 58.1, 55.9, 55.8, 55.3, 42.8, 40.7, 38.7, 37.6, 35.2, 34.1, 34.1, 30.5, 25.9, 25.9, 22.9, 22.6, 22.4, 21.1, 20.4, 18.1, 17.4, 17.2, 14.1, 13.1, 10.8, 8.6, 7.8, 7.2, 7.2, 7.1, 7.1, 5.5, 3.8, 3.8, –4.2, –4.8. **$[\alpha]_D^{20}$** +1.3 (*c* = 0.3, $CHCl_3$). **IR** (thin film) 2955, 1616, 1518, 1463, 1430, 1034, 970, 832, 726 cm$^{-1}$. **HRMS** (ESI) Calculated for $C_{60}H_{110}O_{10}NSi_3$ $[M + NH_4]^+$ 1088.7432, found 1088.7429.

**METHYL KETONE 6**

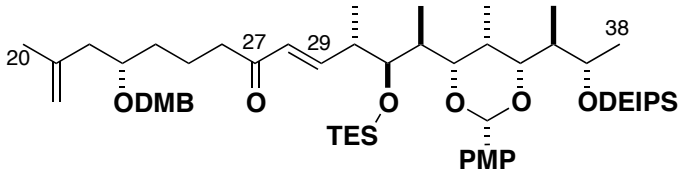



**6**

To a stirred solution of alkene **109** (3.0 mg, 2.8 μmol) in THF (0.2 mL) and $H_2O$ (0.3 mL) was added NMO (50% wt. in water, 5 drops) and $OsO_4$ (1 drop, 2.5 wt. % in *t*-BuOH). After 4 h, $Na_2S_2O_3$ solution (2 mL) was added and the mixture was stirred for 30 min. The layers were then separated and the aqueous layer was extracted with EtOAc (3 × 5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (19:1 PE/EtOAc) to give ketone **6** (2.7 mg, 2.5 μmol, 90%) as a colourless oil.

**$R_f$** 0.23 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CDCl_3$) $\delta_H$ 7.36 (1H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.87-6.79 (5H, m, $Ar_{DMB}\underline{H}$, $Ar_{PMP}\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.47 (1H, d, *J* = 11.0 Hz, $OC\underline{H_a}H_bAr_{DMB}$), 4.40 (1H, d, *J* = 11.0 Hz, $OCH_a\underline{H_b}Ar_{DMB}$), 4.32 (1H, dq, *J* = 6.2, 3.4 Hz, C37$\underline{H}$), 4.15 (d, *J* = 6.7 Hz, C31$\underline{H}$), 3.94-3.89 (1H, m, C23$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.3, 1.4 Hz, C33$\underline{H}$), 3.43-3.40 (2H, m, C35$\underline{H}$, C27$\underline{H}$), 2.97 (1H, app. t, *J* = 2.6 Hz, C29$\underline{H}$), 2.75-2.70 (2H, m, C28$\underline{H}$, $C22\underline{H_a}H_b$), 2.49 (1H, dd, *J* = 15.9, 4.6 Hz, $C22H_a\underline{H_b}$), 2.14 (3H, s, $C20\underline{H_3}$), 2.05-1.99 (1H, m, C36$\underline{H}$), 1.95 (1H, app. qn d, *J* = 6.8, 3.2 Hz, C30$\underline{H}$), 1.89-1.82 (1H, m, C32$\underline{H}$), 1.61-1.48 (5H, m, $C24\underline{H_a}H_b$, $C24H_a\underline{H_b}$, $C26\underline{H_a}H_b$, $C26H_a\underline{H_b}$, C34$\underline{H}$), 1.39-1.21 (2H, m, $C25\underline{H_a}H_b$, $C25H_a\underline{H_b}$), 1.06 (3H, d, *J* = 6.3 Hz, $C38\underline{H_3}$), 1.00-0.95 (22H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.91 (3H, d, *J* = 6.8 Hz, C34(H)$\underline{Me}$), 0.87 (9H, s, $Si{}^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 7.1 Hz, C36(H)$\underline{Me}$), 0.81 (3H, d, *J* = 6.7 Hz, C32(H)$\underline{Me}$), 0.80 (3H, d, *J* = 6.7 Hz, C30(H)$\underline{Me}$), 0.67-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$), 0.02 (6H, s, $Si{}^t\underline{Bu}Me_2$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 207.6, 159.5, 148.9, 148.6, 131.8, 131.1, 127.1, 120.3, 113.3, 111.2, 110.9, 100.7, 82.9, 81.8, 75.4, 72.5, 72.2, 71.6, 67.2, 58.5, 58.2, 55.9, 55.8, 55.3, 48.6, 40.7, 38.7, 37.6, 35.2, 34.4, 31.2, 30.5, 29.7, 25.9, 20.8, 18.2, 17.4, 17.2, 13.1, 10.7, 8.5, 7.8, 7.2, 7.1, 5.6, 5.5, 5.4, 3.8, 3.8, –4.2, –4.8. **$[\alpha]_D^{20}$** –4.5 (*c* = 0.4, $CHCl_3$). **IR** (thin film) 2954, 1718, 1616, 1518, 1464, 1250, 1033, 835, 723 $cm^{-1}$. **HRMS** (ESI) Calculated for $C_{59}H_{108}O_{11}NSi_3$ $[M + NH^4]^+$ 1090.7225, found 1090.7217.

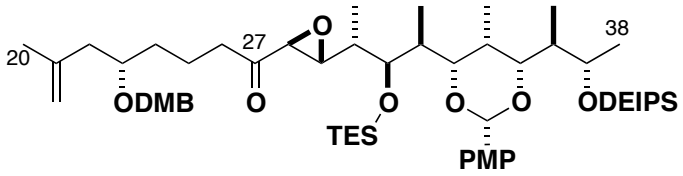
**ENONE 85**




A slurry of phosphonate (*S*)-**10** (258 mg, 603 µmol) and barium hydroxide (101 mg, 603 µmol) was prepared in THF (2 mL) and stirred at rt for 45 min. A solution of aldehyde **11** (96 mg, 151 µmol) in THF/$H_2O$ (1 mL, 40:1) was added *via* cannula, washing with THF–$H_2O$ (1 mL, 40:1). The reaction was stirred at rt for 12 h and quenched by the addition of $NH_4Cl$ (5 mL). The mixture was diluted with EtOAc (10 mL) and the layers separated. The aqueous phase was extracted with EtOAc (4 × 25 mL) and the combined organic phases washed with brine (100 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (9:1 PE/EtOAc) and enone **85** (135 mg, 145 µmol, 96%) was collected as a colourless oil. Further elution (EtOAc) recovered the excess phosphonate (*S*)-**10**.

**$R_f$** 0.16 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.93-6.79 (6H, m, C29$\underline{H}$, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.07 (1H, dd, *J* = 15.9, 0.9 Hz, C28$\underline{H}$), 5.38 (1H, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21=C$\underline{H_a}H_b$), 4.76 (1H, br s, C21=C$H_a\underline{H_b}$), 4.48 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.10 (1H, br d, *J* = 6.7 Hz, C31$\underline{H}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.81 (3H, s, $Ar_{PMP}\underline{OMe}$), 3.58-3.51 (2H, m, C23$\underline{H}$, C33$\underline{H}$),3.40 (1H, dd, *J* = 10.3, 1.6 Hz, C35$\underline{H}$), 2.51-2.43 (3H, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 2.36 (1H, dd, *J* = 14.1, 6.2 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 14.1, 6.1 Hz, C22$H_a\underline{H_b}$), 2.04-1.97 (1H, m, C36$\underline{H}$), 1.81-1.71 (2H, obs m, C25$\underline{H_a}H_b$, C32$\underline{H}$), 1.74 (3H, s, C20$\underline{H_3}$), 1.69-1.48 (5H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$H_a\underline{H_b}$, C30$\underline{H}$, C34$\underline{H}$), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.02-0.92 (24H, m, C30(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$), 0.92-0.88 (1H, obs, m, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.90 (3H, d, *J* = 6.8 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 7.0 Hz, C32(H)$\underline{Me}$), 0.78 (3H, d, *J* = 6.9 Hz, C36(H)$\underline{Me}$), 0.64-0.56 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 200.3, 159.6, 150.8, 149.0, 148.5, 142.9, 131.7, 131.5, 129.7, 127.1, 120.2, 113.4, 112.7, 111.2, 110.9, 100.7, 82.9, 81.4, 74.0, 70.8, 67.2, 55.9, 55.8, 55.3, 42.7, 40.7, 40.0, 37.6, 33.6, 30.5, 22.9, 20.0, 17.4, 17.3, 16.7, 13.1, 8.0, 7.8, 7.14, 7.13, 5.7, 5.4, 3.9, 3.8. **$[\alpha]_D^{20}$** –0.9 (*c* = 1.3, $CHCl_3$). **IR** (thin film) 2937.5, 2878.9, 1696.6, 1671.3, 1617.7, 1593.0, 1517.4, 1460.3, 1378.1, 1249.8, 1100.0, 1031.7, 971.1, 727.4 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{54}H_{90}NaO_9Si_2$ $[M + Na]^+$ 961.6016, found 961.6036.

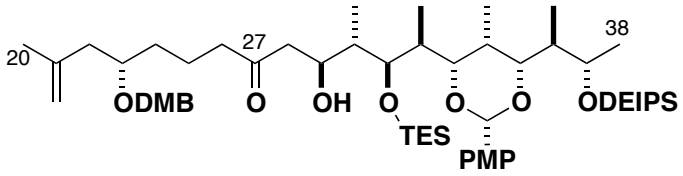
**EPOXYKETONE 86**




To a mixture of THF (1.4 mL) and $CaH_2$ (2 big pieces) at 0 ºC was added *tert*-butylhydrogen peroxide solution (0.55 mL, 2.18 mmol, 4 M solution in PhMe) and the solution stirred for 5 min. *n*-Butyllithium (1.09 mL, 1.74 mmol, 1.6 M solution in hexanes) was added and the mixture stirred for 20 min at 0 ºC and a further 20 min at rt. The mixture was cooled to –78 ºC and a solution of enone **85** (102 mg, 109 µmol, dried azeotropically from PhH) in THF (1.4 mL + 1.4 mL wash, dried briefly over $CaH_2$) was added dropwise and the reaction stirred for 10 min. The mixture was warmed to –23 ºC (freezer) for 16 h. The reaction was quenched by quickly transferring on to pH 7 buffer solution (10 mL) *via* pipette washing with EtOAc, and the layers separated. The aqueous phase was extracted with EtOAc (5 × 25 mL) and the combined organics washed with brine (50 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 → 6:1 PE/EtOAc) to afford epoxyketone **86** (94.5 mg, 98.8 µmol, 91%) as a colourless oil. The relative stereochemistry of the product was determined by reductive ring opening to hydroxyketone **107** and subsequent Mosher ester analysis[6] of the derivatives **107S** and **107R**.

**$R_f$** 0.16 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.37 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}\underline{H}$), 6.92-6.83 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.40 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21=C$\underline{H_a}H_b$), 4.75 (1H, br s, C21=C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.42 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.18 (1H, br d, *J* = 5.9 Hz, C31$\underline{H}$), 3.88 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.3, 1.5 Hz, C33$\underline{H}$), 3.55 (1H, obs m, C23$\underline{H}$), 3.41 (1H, dd, *J* = 10.5, 1.3 Hz, C35$\underline{H}$), 3.16 (1H, d, *J* = 2.0 Hz, C28$\underline{H}$), 3.08 (1H, dd, *J* = 6.6, 2.0 Hz, C29$\underline{H}$), 2.44-2.32 (2H, m, C22$\underline{H_a}H_b$, C26$\underline{H_a}H_b$), 2.21-2.10 (2H, m, C22$H_a\underline{H_b}$, C26$H_a\underline{H_b}$), 2.06-1.98 (1H, m, C36$\underline{H}$), 1.84-1.39 (m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C30$\underline{H}$, C32$\underline{H}$, C34$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.06 (1H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (22H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2{}^i\underline{Pr}$, $Si(CH_2\underline{Me})_3$), 0.92-0.87 (6H, 2 overlapping d, C30(H)$\underline{Me}$, C34(H)$\underline{Me}$), 0.85-0.82 (6H, 2 overlapping d, C32(H)$\underline{Me}$, C36(H)$\underline{Me}$), 0.68-0.58 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 208.0, 159.6, 149.0, 148.5, 142.8, 131.7, 131.4, 127.1 (2C), 120.2, 113.4, 112.8, 111.2, 110.8, 100.7, 83.0, 81.9, 73.1, 70.8, 67.2, 60.2, 57.9, 55.9, 55.8, 55.3, 42.6, 41.7, 40.8, 37.9, 36.7, 33.4, 30.5, 22.9, 19.1, 17.4 (2C), 17.2, 13.10, 13.07, 8.4, 7.8, 7.17, 7.14, 7.12, 5.7 (2C, 5.4, 3.9, 3.8. **$[\alpha]_D^{20}$** –8.4 (*c* = 1.0, $CHCl_3$). **IR** (thin film) 2956.1, 2975.9, 1711.8, 1613.2, 1590.4, 1517.5, 1463.8, 1380.6, 1249.4, 1097.5, 1034.3, 971.1, 725.4 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{51}H_{88}O_{10}Si_2N$ $[M + NH_4]^+$ 930.5941, found 930.5931.

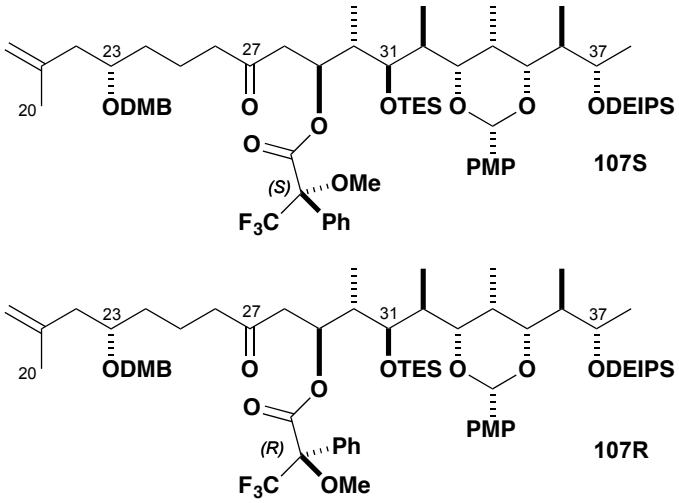
**HYDROXYKETONE 107**




Epoxyketone **27** (18.0 mg, 18.9 μmol) was dissolved in THF (0.6 mL) and MeOH (0.06 mL) and cooled to –30 ºC. Samarium diiodide (0.75 mL, 75.5 μmol, 0.1 M solution in THF) was added dropwise and the deep blue colour faded to yellow over 5 min. Brine (0.5 mL) was added dropwise at –30 ºC and the reaction was warmed to rt. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic phase dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography to give β-hydroxyketone **107** (15.1 mg, 15.9 μmol, 84%) as a colourless oil.

**$R_f$** 0.33 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.34 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}\underline{H}$), 6.92 (1H, d, *J* = 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.87 (1H, d, *J* = 8.6 Hz, $Ar_{PMP}\underline{H}$), 6.85 (1H, obs dd, *J* = 8.1, 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.37 (1H, s, C$\underline{H}$PMP), 4.79 (1H, br s, C21=C$\underline{H_a}H_b$), 4.75 (1H, br s, C21=C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.2 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.2 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.30 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.21 (1H, br d, *J* = 6.2 Hz, C31$\underline{H}$), 3.96-3.91 (1H, m, C29$\underline{H}$), 3.88 (3H, s, $Ar_{DMB}OC\underline{H_3}$), 3.86 (3H, s, $Ar_{DMB}OC\underline{H_3}$), 3.78 (3H, s, $Ar_{PMP}OC\underline{H_3}$), 3.54-3.50 (1H, obs dt, C23$\underline{H}$), 3.53 (1H, dd, *J* =10.6, 1.7 Hz, C33$\underline{H}$), 3.40 (1H, dd, *J* =10.5, 1.5 Hz, C35$\underline{H}$), 3.30 (1H, br s, C29(H)O$\underline{H}$), 2.45-2.43 (2H, overlapping obs d, C28$\underline{H_a}H_b$, C28$H_a\underline{H_b}$), 2.39 (2H, t, *J* = 7.3 Hz, C26$\underline{H_2}$), 2.35 (1H, dd, *J* = 14.1, 6.6 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 14.1, 6.3 Hz, C22$H_a\underline{H_b}$), 2.02 (1H, ddq, *J* = 7.0, 3.6, 3.4 Hz, C36$\underline{H}$), 1.82-1.77 (1H, m, C32$\underline{H}$), 1.76-1.65 (2H, obs m, C30$\underline{H}$, C25$\underline{H_a}H_b$), 1.74 (3H, s, C20$\underline{H_3}$), 1.63-1.55 (2H, m, C25$H_a\underline{H_b}$, C34$\underline{H}$), 1.50-1.45 (2H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$), 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (22H, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$$^i\underline{Pr}$, Si($CH_2\underline{Me}$)$_3$), 0.93 (3H, d, *J* = 7.0 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.81 (3H, d, *J* = 7.0 Hz, C32(H)$\underline{Me}$), 0.79 (3H, d, *J* = 7.1 Hz, C30(H)$\underline{Me}$), 0.67-0.57 (10H, m, Si($C\underline{H_2}Me$)$_3$, Si($C\underline{H_2}Me$)$_2$$^i$Pr), [spin system interrupted across C31-C32 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 210.7, 159.7, 148.9, 148.4, 142.9, 131.4, 131.3, 127.1, 120.1, 113.4, 112.7, 111.2, 110.8, 101.2, 83.0, 82.6, 76.9, 72.1, 70.7, 70.2, 67.0, 55.9, 55.8, 55.2, 47.1, 45.2, 43.8, 42.6, 40.7, 36.5, 33.4, 30.5, 22.9, 19.4, 17.3, 17.2, 13.0, 12.2, 8.9, 7.8, 7.08, 7.06, 7.03, 5.3, 3.8, 3.7. **$[\alpha]_D^{20}$** –5.9 (*c* = 1.1, $CHCl_3$). **IR** (thin film) 3511.7 (br), 2938.2, 2877.0, 1711.4, 1615.9, 1592.5, 1517.1, 1462.9, 1378.1, 1249.1, 1158.5, 1052.2, 968.8, 829.3, 725.4 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{53}H_{98}O_{11}Si_2N$ $[M + NH_4]^+$ 976.6365, found 976.6605.

**MOSHER ESTERS 107S AND 107R**




To a solution of alcohol **107** (5.0 mg, 5.2 μmol) in $CH_2Cl_2$ (0.5 mL) and pyridine (0.5 mL) was added, separately, either (*R*)-α-methoxy-α-(trifluromethyl)phenylacetic acid chloride (0.2 mL, *ca.* 26 μmol, *ca.* 0.13 M solution in $CH_2Cl_2$) or (*S*)-α-methoxy-α-(trifluromethyl)phenylacetic acid chloride (0.2 mL, *ca.* 26 μmol, *ca.* 0.13 M solution in $CH_2Cl_2$) and the reactions stirred for 1 h. When reaction was complete by TLC, $NaHCO_3$ solution (1 mL) was added and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (3 × 5 mL) and the combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude products were purified by column chromatography (9:1 PE/EtOAc). From the reaction using (*S*)-MTPA-Cl was obtained ester **113S** (4.7 mg, 4.3 μmol, 83%) as a colourless oil. From the reaction using (*R*)-MTPA-Cl was obtained ester **113R** (4.1 mg, 3.7 μmol, 71%) as a colourless oil.

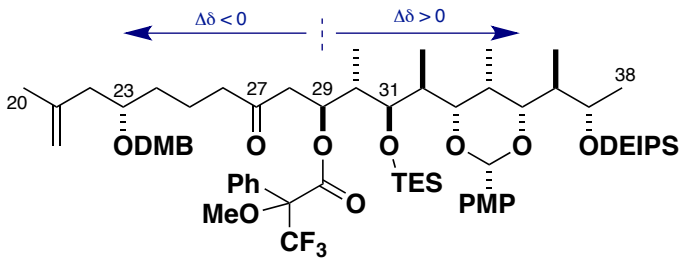
**107S: $R_f$** 0.53 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.49-7.46 (2H, m, $Ar_{Ph}\underline{H}$), 7.38-7.31 (5H, m, $Ar_{Ph}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.92-6.78 (5H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.86-5.82 (1H, m, C29$\underline{H}$), 5.35 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.80 (1H, br s, C21=C$\underline{H_a}H_b$), 4.75 (1H, br s, C21=C$H_a\underline{H_b}$), 4.45 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.42 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.26 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.01 (1H, br d, *J* = 6.6 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.54 (1H, br d, *J* = 10.1 Hz, C33$\underline{H}$), 3.50-3.45 (1H, obs m, C23$\underline{H}$), 3.48 (3H, s, C29(H)$O_2$C(O$\underline{Me}$)(Ph)($CF_3$)), 3.38 (1H, br d, *J* = 10.4 Hz, C35$\underline{H}$), 2.67 (1H, dd, *J* = 17.3, 10.0 Hz, C28$\underline{H_a}H_b$), 2.51 (1H, dd, *J* = 17.7, 3.0 Hz, C28$H_a\underline{H_b}$), 2.33 (2H, app dd, *J* = 13.9, 6.6 Hz, C26$\underline{H_2}$), 2.17-2.09 (3H, m, C22$\underline{H_a}H_b$, C22$H_a\underline{H_b}$, C30$\underline{H}$), 2.08-1.83 (3H, m, C32$\underline{H}$, C34$\underline{H}$, C36$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.63-1.22 (4H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$), 1.04 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.02-0.93 (22H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2$Me)$_2$$^i\underline{Pr}$, Si($CH_2\underline{Me}$)$_3$), 0.93 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.77 (3H, d, *J* = 6.9 Hz, C30(H)$\underline{Me}$), 0.69-0.56 (13H, m, C32(H)$\underline{Me}$, Si($C\underline{H_2}$Me)$_3$, Si($C\underline{H_2}$Me)$_2$$^i$Pr). **[α]$_D^{20}$** –18.3 (*c* = 0.06, $CHCl_3$). **IR** (thin film) 2924.6, 2855.7, 1747.2, 1711.8, 1610.7, 1517.1, 1461.5, 1244.1, 1050.4 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{64}H_{103}F_3O_{12}Si_2N$ $[M + NH_4]^+$ 1190.6965, found 1190.6934.

**107R: $R_f$** 0.53 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.49-7.46 (2H, m, $Ar_{Ph}\underline{H}$), 7.36-7.33 (3H, m, $Ar_{Ph}\underline{H}$), 7.27-7.26 (2H, obs d, $Ar_{PMP}\underline{H}$), 6.91-6.83 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.79 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.81-5.77 (1H, m, C29$\underline{H}$), 5.36 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21C$\underline{H_a}H_b$), 4.74 (1H, br s, C21C$H_a\underline{H_b}$), 4.46 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.42 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.26 (1H,

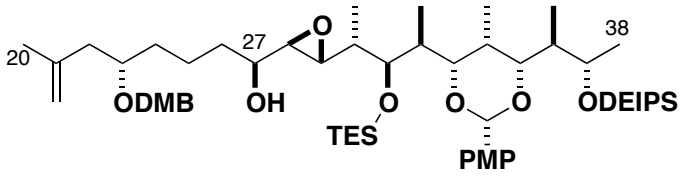
dq, *J* = 6.4, 3.4 Hz, C37H), 3.99 (1H, br d, *J* = 6.6 Hz, C31H), 3.86 (3H, s, $Ar_{DMB}$OMe), 3.85 (3H, s, $Ar_{DMB}$OMe), 3.79 (3H, s, $Ar_{PMP}$OMe), 3.53 (1H, br d, *J* = 10.1 Hz, C33H), 3.50-3.45 (1H, obs m, C23H), 3.46 (3H, s, C29(H)$O_2$C(OMe)(Ph)($CF_3$)), 3.38 (1H, br d, *J* = 10.4 Hz, C35H), 2.70 (1H, dd, *J* = 17.7, 9.9 Hz, C28$H_aH_b$), 2.60 (1H, dd, *J* = 17.7, 2.8 Hz, C28$H_aH_b$), 2.36 (2H, app dd, *J* = 13.9, 6.6 Hz, C26$H_2$), 2.18-2.07 (4H, m, C22$H_aH_b$, C22$H_aH_b$, C30H, C36H), 2.04-1.97 (2H, m, C32H, C34H), 1.91-1.82 (1H, m, C25$H_aH_b$), 1.73 (3H, s, C20$H_3$), 1.62-1.43 (3H, m, C24$H_aH_b$, C24$H_aH_b$, C25$H_aH_b$,), 1.04 (3H, d, *J* = 6.3 Hz, C38$H_3$), 1.00-0.85 (22H, m, Si($CH_2$Me)$_2$$^i$Pr, Si($CH_2$Me)$_2$$^i$Pr, Si($CH_2$Me)$_3$), 0.91 (3H, d, *J* = 6.7 Hz, C34(H)Me), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)Me), 0.71-0.68 (6H, 2 overlapping d, C30(H)Me, C32(H)Me), 0.66-0.56 (10H, m, Si($CH_2$Me)$_3$, Si($CH_2$Me)$_2$$^i$Pr). **[α]$_D^{20}$** +3.7 (*c* = 0.08, $CHCl_3$). **IR** (thin film) 2925.9, 1747.2, 1612.4, 1514.6, 1456.5, 1250.1, 10.82.4 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{64}H_{103}F_3O_{12}Si_2N$ $[M + NH_4]^+$ 1190.6965, found 1190.6926.

**MOSHER ESTER ANALYSIS FOR 107S AND 107R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C20$\underline{H_3}$ | 1.73 | 1.73 | 0.00 |
| C21=C$\underline{H_a}H_b$ | 4.80 | 4.79 | +0.01 |
| C21=C$H_a\underline{H_b}$ | 4.75 | 4.74 | +0.01 |
| C22$\underline{H_a}H_b$, C22$H_a\underline{H_b}$ | obs. | obs. | - |
| C23$\underline{H}$ | 3.48 | 3.48 | - |
| OC$\underline{H_a}H_bAr_{DMB}$ | 4.45 | 4.46 | –0.01 |
| OC$H_a\underline{H_b}Ar_{DMB}$ | 4.42 | 4.42 | 0.00 |
| C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$ | obs. | obs. | - |
| C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$ | obs. | obs. | - |
| C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$ | 2.33 | 2.36 | –0.03 |
| C28$\underline{H_a}H_b$ | 2.67 | 2.70 | –0.03 |
| C28$H_a\underline{H_b}$ | 2.51 | 2.60 | –0.09 |
| C29$\underline{H}$ | 5.84 | 5.79 | +0.05 |
| C30$\underline{H}$ | obs. | obs. | - |
| C30(H)$\underline{Me}$ | 0.77 | obs. | - |
| C31$\underline{H}$ | 4.01 | 3.99 | +0.02 |
| C32$\underline{H}$ | obs. | obs. | - |
| C32(H)$\underline{Me}$ | obs. | obs. | - |
| C33$\underline{H}$ | 3.54 | 3.53 | +0.01 |
| C34$\underline{H}$ | obs. | obs. | - |
| C34(H)$\underline{Me}$ | 0.93 | 0.91 | 0.02 |



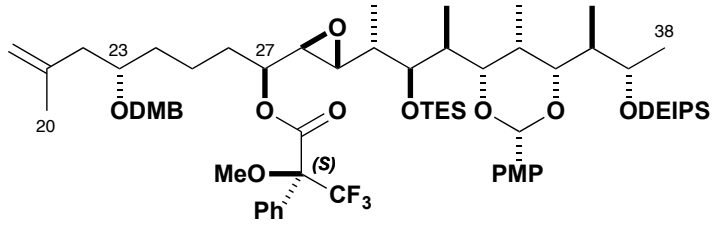
**EPOXY ALCOHOL 87**




Epoxyketone **86** (147 mg, 154 μmol) was dried azeotropically (3 × 5 mL PhH) and dissolved in MTBE (25 mL). The solution was cooled to –98 °C and DIBAL (308 μL, 308 μmol, 1 M solution in $CH_2Cl_2$) was added very slowly down the side of the flask [dr severely eroded if added too quickly]. Reaction was complete after 5 min and was quenched at –98 °C by the addition of MeOH (2 mL). The mixture was warmed to rt, at which point $Na^+/K^+$ tartrate solution (20 mL) was added and the solution stirred vigourously for 1 h. The phases were separated and the aqueous phase extracted with EtOAc (5 × 30 mL). The combined organic phases were washed with brine (30 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue (crude dr 10:1) was purified by careful column chromatography (8:1 → 7:1 → 6.5:1 → 6:1 PE/EtOAc) to separate the naturally C27 configured diastereomer **87** (122 mg, 128 μmol, 83% isolated yield). The minor diastereomer (9%) was recycled *via* Dess–Martin oxidation to epoxyketone **86** (98% yield).

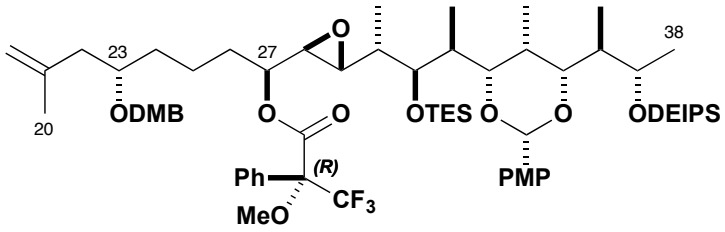
**$R_f$** 0.15 (major), 0.19 (minor) (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.38 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}\underline{H}$), 6.92-6.83 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.2 Hz, $Ar_{DMB}\underline{H}$), 5.40 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br. s, C21=C$\underline{H_a}H_b$), 4.75 (1H, br. s, C21=C$H_a\underline{H_b}$), 4.48 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.33 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.21 (1H, br. d, *J* = 5.0 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.55 (1H, dd, *J* = 10.1, 1.6 Hz, C33$\underline{H}$), 3.55-3.51 (1H, obs. m, C23$\underline{H}$), 3.44-3.38 (1H, obs. m, C27$\underline{H}$), 3.41 (1H, dd, *J* = 10.3, 1.4 Hz, C35$\underline{H}$), 2.92 (1H, dd, *J* = 7.1, 2.3 Hz, C29$\underline{H}$), 2.70 (1H, dd, *J* = 5.0, 2.3 Hz, C28$\underline{H}$), 2.36 (1H, dd, *J* = 13.8, 6.4 Hz, C22$\underline{H_a}H_b$), 2.15 (1H, dd, *J* = 13.8, 6.2 Hz, C22$H_a\underline{H_b}$), 2.07-1.98 (1H, m, C36$\underline{H}$), 1.85-1.74 (1H, m, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.65-1.46 (8H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$, C34$\underline{H}$), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (21H, m, Si$(CH_2\underline{Me})_2{}^iPr$, Si$(CH_2Me)_2CH\underline{Me_2}$, Si$(CH_2\underline{Me})_3$), 0.93-0.87 (1H, obs m, Si$(CH_2Me)_2C\underline{H}Me_2$), 0.91 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.90 (3H, d, *J* = 7.1 Hz, C30(H)$\underline{Me}$), 0.85 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.84 (3H, d, *J* = 6.9 Hz, C36(H)$\underline{Me}$), 0.70-0.57 (10H, m, Si$(C\underline{H_2}Me)_3$, Si$(C\underline{H_2}Me)_2{}^iPr$).

**MOSHER ESTER 87S**




**$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.55-7.59 (2H, m, $Ar_{Ph}\underline{H}$), 7.40-7.34 (5H, m, $Ar_{Ph}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.89-6.79 (5H, m, $Ar_{DMB}\underline{H}$, $Ar_{PMP}\underline{H}$), 5.40 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.86-4.79 (1H, m, C27(<u>H</u>)OR), 4.79 (1H, br. s, C21=C$\underline{H_a}H_b$), 4.72 (1H, br. s, C21=C$H_a\underline{H_b}$), 4.43 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.39 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.36-4.30 (1H, m, C37<u>H</u>), 4.21 (1H, br. d, *J* = 5.0 Hz, C31<u>H</u>), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.58 (3H, s, C27(H)$O_2$C(O<u>Me</u>)(Ph)($CF_3$)), 3.58-3.51 (1H, obs. m, C33<u>H</u>), 3.45-3.39 (1H, m, C23<u>H</u>, C35<u>H</u>), 2.89 (1H, dd, *J* = 7.4, 2.0 Hz, C29<u>H</u>), 2.83 (1H, dd, *J* = 7.5, 2.0 Hz, C28<u>H</u>), 2.30 (1H, dd, *J* = 13.8, 6.4 Hz, C22$\underline{H_a}H_b$), 2.07 (1H, d, *J* = 13.8, 6.2 Hz, C22$H_a\underline{H_b}$), 2.04-1.99 (1H, m, C36<u>H</u>), 1.84-1.74 (1H, m, C32<u>H</u>), 1.71 (3H, s, C20$\underline{H_3}$), 1.65-1.46 (8H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30<u>H</u> (1.50 ppm by COSY), C34<u>H</u>), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (21H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2CH\underline{Me_2}$, $Si(CH_2\underline{Me})_3$), 0.93-0.82 (13H, m, C30(H)<u>Me</u>, C32(H)<u>Me</u>, C34(H)<u>Me</u>, C36(H)<u>Me</u>, $Si(CH_2Me)_2C\underline{H}Me_2$), 0.68-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$).

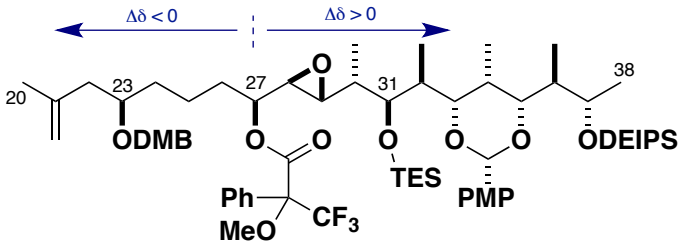
**MOSHER ESTER 87R**



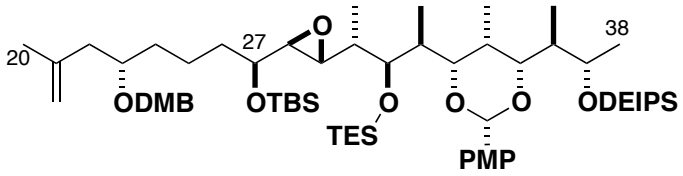

**$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.55-7.59 (2H, m, $Ar_{Ph}\underline{H}$), 7.38 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}\underline{H}$), 7.37-7.34 (3H, m, $Ar_{Ph}\underline{H}$), 6.90-6.81 (4H, m, $Ar_{DMB}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.79 (1H, d, *J* = 8.2 Hz, $Ar_{DMB}\underline{H}$), 5.40 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.92-4.86 (1H, m, C27(<u>H</u>)OR), 4.80 (1H, br. s, C21=C$\underline{H_a}H_b$), 4.74 (1H, br. s, C21=C$H_a\underline{H_b}$), 4.45 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.40 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.36-4.30 (1H, m, C37<u>H</u>), 4.18 (1H, br. d, *J* = 5.0 Hz, C31<u>H</u>), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.84 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.57-3.54 (1H, obs. m, C33<u>H</u>), 3.55-3.51 (1H, obs. m, C23<u>H</u>), 3.51 (3H, s, C27(H)$O_2$C(O<u>Me</u>)(Ph)($CF_3$)), 3.40 (1H, dd, *J* = 10.3, 1.4 Hz, C35<u>H</u>), 2.81 (1H, dd, *J* = 7.4, 2.0 Hz, C29<u>H</u>), 2.78 (1H, dd, *J* = 6.7, 2.0 Hz, C28<u>H</u>), 2.34 (1H, dd, *J* = 13.8, 6.4 Hz, C22$\underline{H_a}H_b$), 2.11 (1H, d, *J* = 13.8, 6.2 Hz, C22$H_a\underline{H_b}$), 2.06-1.99 (1H, m, C36<u>H</u>), 1.81-1.72 (1H, m C32<u>H</u>), 1.72 (3H, s, C20$\underline{H_3}$), 1.66-1.24 (9H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30<u>H</u> (1.46 ppm by COSY), C32<u>H</u>, C34<u>H</u>), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (21H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2CH\underline{Me_2}$, $Si(CH_2\underline{Me})_3$), 0.93-0.82 (13H, m, C30(H)<u>Me</u>, C34(H)<u>Me</u>, C36(H)<u>Me</u>, $Si(CH_2Me)_2C\underline{H}Me_2$), 0.81 (3H, d, *J* = 6.9 Hz, C32(H)<u>Me</u>), 0.68-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$).

**MOSHER ESTER ANALYSIS FOR 87S AND 87R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C20$H_3$ | 1.71 | 1.72 | –0.01 |
| C21=C$H_aH_b$ | 4.79 | 4.80 | –0.01 |
| C21=C$H_aH_b$ | 4.72 | 4.74 | –0.02 |
| C22$H_aH_b$ | 2.30 | 2.34 | –0.04 |
| C22$H_aH_b$ | 2.07 | 2.11 | –0.04 |
| C23H | obs. | obs. | - |
| OC$H_aH_bAr_{DMB}$ | 4.43 | 4.45 | –0.02 |
| OC$H_aH_bAr_{DMB}$ | 4.39 | 4.40 | –0.01 |
| C24$H_aH_b$, C24$H_aH_b$ | obs. | obs. | - |
| C25$H_aH_b$, C25$H_aH_b$ | obs. | obs. | - |
| C26$H_aH_b$, C26$H_aH_b$ | obs. | obs. | - |
| C28H | 2.83 | 2.78 | +0.05 |
| C29H | 2.89 | 2.81 | +0.09 |
| C30H | 1.50 | 1.46 | +0.04 |
| C30(H)Me | obs. | obs. | - |
| C31H | 4.21 | 4.18 | +0.03 |
| C32H | 1.79 | 1.76 | +0.03 |
| C32(H)Me | obs. | 0.81 | - |
| C33H | 3.55 | 3.55 | 0.00 |



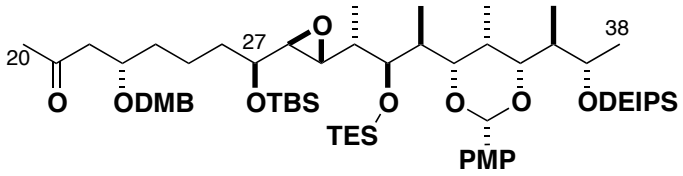
**TBS ETHER 88**




Alcohol **87** (104 mg, 109 µmol) was dried azeotropically (3 × 5 mL PhH) and dissolved in $CH_2Cl_2$ (10 mL). The solution was cooled to –78 ºC and 2,6-lutidine (37 µL, 326 µmol) added, followed by TBSOTf (37 µL, 163 µmol). After 45 min, the reaction was quenched at –78 ºC by the addition of MeOH (0.5 mL). The solution was warmed to rt and diluted with $NaHCO_3$ solution (5 mL) and $CH_2Cl_2$ (5 mL). The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (4 × 10 mL). The combined organic phases were washed with brine (20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (15:1 PE/EtOAc) to give TBS ether **88** (106 mg, 99.2 µmol, 91%) as a colourless oil.

**$R_f$** 0.68 (4/1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.40 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.89-6.85 (1H, obs dd, $Ar_{DMB}\underline{H}$), 6.88 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.84 (1H, dd, *J* = 8.1, 1.7 Hz, $Ar_{DMB}\underline{H}$), 6.79 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.41 (1H, s, $Ar_{PMP}\underline{H}$), 4.79 (1H, br s, C20C$\underline{H_a}H_b$), 4.75 (1H, br s, C20C$\underline{H_a}H_b$), 4.44 (2H, app s, OC$\underline{H_a}H_bAr_{DMB}$, OC$H_a\underline{H_b}Ar_{DMB}$), 4.34 (1H, dq, *J* = 6.2, 3.4 Hz, C37$\underline{H}$), 4.20 (1H, br d, *J* = 5.5 Hz, C31$\underline{H}$), 3.89 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.2, 1.3 Hz, C33$\underline{H}$), 3.53-3.47 (1H, m, C23$\underline{H}$), 3.41 (1H, dd, *J* = 10.5, 1.4 Hz, C35$\underline{H}$), 3.24-3.19 (1H, m, C27$\underline{H}$), 2.69 (1H, dd, *J* = 7.3, 2.1 Hz, C29$\underline{H}$), 2.63 (1H, dd, *J* = 6.3, 2.1 Hz, C28$\underline{H}$), 2.34 (1H, dd, *J* = 14.0, 6.6 Hz, C22$\underline{H_a}H_b$), 2.14 (1H, *J* = 14.0, 6.0 Hz, C22$H_a\underline{H_b}$), 2.02 (1H, ddq, *J* = 6.8, 3.6, 3.4 Hz, C36$\underline{H}$), 1.80 (1H, dq, *J* = 10.2, 7.0 Hz, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.64-1.58 (1H, m, C34$\underline{H}$), 1.53-1.41 (7H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00 (22H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$$^i\underline{Pr}$, Si($CH_2\underline{Me}$)$_3$), 0.91-0.88 (6H, obs m, C30(H)$\underline{Me}$, C34(H)$\underline{Me}$), 0.89 (9H, s, Si$^t\underline{Bu}Me_2$), 0.833 (3H, s, *J* = 7.0 Hz, C32(H)$\underline{Me}$), 0.827 (3H, s, *J* = 6.8 Hz, C36(H)$\underline{Me}$), 0.69-0.58 (10H, m, Si($C\underline{H_2}Me$)$_3$, Si($C\underline{H_2}Me$)$_2$$^i$Pr), 0.11 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$), [spin system interrupted across C31-C32 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.6, 149.0, 148.5, 143.0, 131.9, 131.5, 127.1, 120.1, 113.3, 112.6, 111.2, 110.9, 100.6, 83.0, 82.0, 77.1, 74.4, 73.0, 70.8, 67.2, 60.4, 58.4, 55.9, 55.8, 55.2, 42.7, 42.3, 40.8, 37.7, 34.8, 34.1, 30.5, 25.9 (2C), 22.9, 21.5, 18.2, 17.4, 17.2, 13.9, 13.1, 8.5, 7.8, 7.18, 7.12, 7.11, 5.6, 5.5, 3.9, 3.8, –4.2, –5.0. **$[\alpha]_D^{20}$** +1.8 (*c* = 1.1, $CHCl_3$). **IR** (thin film) 2952.8, 2870.9, 1616.3, 1590.4, 1517.3, 1463.0, 1386.4, 1340.2, 1249.2, 1158.9, 1103.4, 969.5, 831.4, 776.8, 727.2 cm$^{-1}$**.** **HRMS** (ES$^+$) Calculated for $C_{60}H_{106}O_{10}Si_3$ $[M + NH_4]^+$ 1088.7438, found 1088.7439.

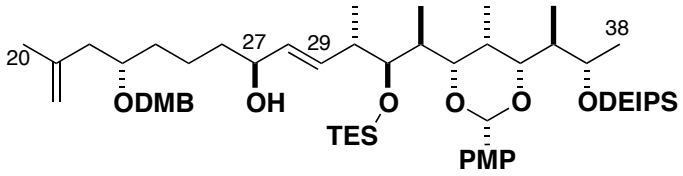
**NORTHERN FRAGMENT 89**




Olefin **88** (102 mg, 97.0 μmol) was dissolved in THF (1 mL) and $H_2O$ (1.5 mL) at rt. NMO (80 μL, 389 μmol, 50%wt solution in $H_2O$) and $OsO_4$ (5 μL, 388 nmol, 2.5%wt in $^tBuOH$) were added and the solution turned brown. Reaction was complete after 4 h and quenched by the addition of $Na_2S_2O_3$ solution (5 mL) and EtOAc (5 mL). After stirring for 30 min, the layers were separated and the aqueous phase extracted with EtOAc (5 × 10 mL). The combined organic phases were washed with brine (10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The crude residue was dissolved in $CH_2Cl_2$ (10 mL) and $NaIO_4$–$SiO_2$ (3 spatulas) was added. When the reaction was complete by TLC (15 min), the reaction mixture was filtered, washing with $CH_2Cl_2$ (200 mL). The solvent was removed *in vacuo* and the crude product purified by column chromatography (10:1 → 6:1 PE/EtOAc) to afford methyl ketone **89** (90.0 mg, 85.4 μmol, 88%) as a colourless oil.

**$R_f$** 0.31 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.87 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.84-6.78 (3H, m, $Ar_{DMB}\underline{H}$), 5.41 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.46 (1H, d, *J* = 11.2 Hz, $OC\underline{H_a}H_bAr_{DMB}$), 4.39 (1H, d, *J* = 11.2 Hz, $OCH_a\underline{H_b}Ar_{DMB}$), 4.34 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.22 (1H, br d, *J* = 5.4 Hz, C31$\underline{H}$), 3.93-3.86 (1H, m, C23$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, br d, *J* = 10.1 Hz, C33$\underline{H}$), 3.42 (1H, br d, *J* = 10.4 Hz, C35$\underline{H}$), 3.25-3.20 (1H, m, C27$\underline{H}$), 2.72 (1H, dd, *J* = 15.8, 7.8 Hz, C22$\underline{H_a}H_b$), 2.70 (1H, obs m, C29$\underline{H}$), 2.63 (1H, dd, *J* = 6.6, 2.0 Hz, C28$\underline{H}$), 2.46 (1H, dd, *J* = 15.8, 4.5 Hz, C22$H_a\underline{H_b}$), 2.14 (3H, s, C20$\underline{H_3}$), 2.02 (1H, ddq, *J* = 10.4, 7.1, 3.4 Hz, C36$\underline{H}$), 1.81 (1H, app dq, *J* = 9.9, 6.9 Hz, C32$\underline{H}$), 1.64-1.42 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$, C34$\underline{H}$), 1.42-1.33 (2H, m, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$,), 1.07 (3H, d, *J* = 6.4 Hz, C38$\underline{H_3}$), 1.01-0.95 (24H, m, C30(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2{}^i\underline{Pr}$, $Si(CH_2\underline{Me})_3$), 0.93-0.83 (16H, m, C32(H)$\underline{Me}$, C36(H)$\underline{Me}$, $Si{}^t\underline{Bu}Me_aMe_b$), 0.84 (3H, d, *J* = 6.9 Hz, C34(H)$\underline{Me}$), 0.69-0.58 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$), 0.12 (3H, s, $Si{}^t\underline{Bu}\underline{Me_a}Me_b$), 0.04 (3H, s, $^tBuSiMe_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 207.6, 159.5, 148.9, 148.6, 131.8, 131.1, 128.3, 127.1, 120.3, 113.3, 111.2, 110.9, 100.6, 82.9, 82.0, 75.3, 74.3, 73.0, 71.6, 67.2, 60.4, 58.4, 55.9, 55.8, 55.2, 48.6, 42.3, 40.8, 37.7, 34.7, 34.4, 31.2, 30.4, 25.9, 21.2, 18.4, 17.4, 17.2, 13.9, 13.1, 8.6, 7.8, 7.2, 7.15, 7.13, 5.6, 5.5, 3.9, 3.8, -4.2, -5.0. **$[\alpha]_D^{20}$** +6.8 (*c* = 1.55, $CHCl_3$). **IR** (thin film) 2958, 2877, 1717, 1616, 1594, 1512, 1464, 1418, 1382, 1351, 1249, 1159 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{59}H_{108}O_{11}Si_3N$ $[M + NH_4]^+$ 1090.7225, found 1090.7221.

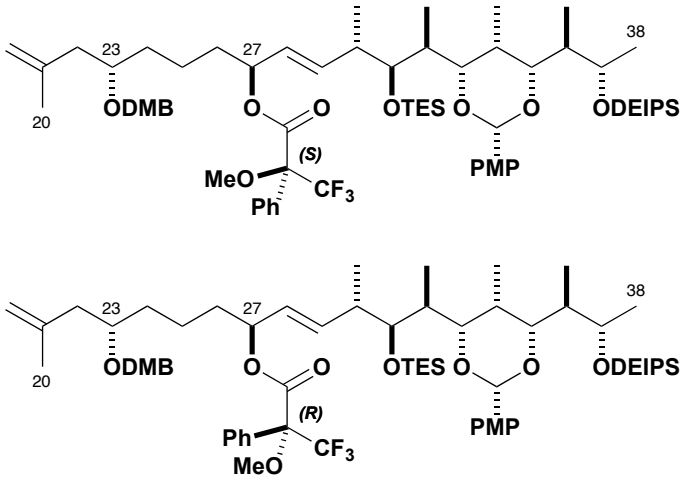
**ALLYLIC ALCOHOL 94**




Enone **85** (72.6 mg, 77.3 μmol, dried azeotropically from PhH) was dissolved in THF (2 mL) and the solution cooled to –78 ºC. (*R*)-Methyl-CBS catalyst (0.1 mL, 100 μmol, 1 M solution in PhMe) and borane · dimethylsulfide complex (0.1 mL, 164 μmol) were added sequentially and the reaction warmed to –50 ºC. When reaction was complete by TLC, the solution was cooled to –78 ºC and quenched by the dropwise addition of MeOH (3 mL) with rapid stirring for 30 min. The reaction mixture was warmed to rt and concentrated *in vacuo*. The residue was azeotroped with MeOH (3 × 2 mL) and purified by column chromatography (6:1 PE/EtOAc). Allylic alcohol **94** (64.0 mg, 86.5 μmol, 88%) was collected as a colourless oil.

**$R_f$** 0.16 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.37 (2H, d, *J* = 8.5 Hz, $Ar_{PMP}\underline{H}$), 6.92-6.83 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.0 Hz, $Ar_{PMP}\underline{H}$), 5.65 (1H, dd, *J* = 15.6, 7.5 Hz, C29$\underline{H}$), 5.43 (1H, dd, *J* = 15.6, 7.0 Hz, C28$\underline{H}$), 5.38 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21C$\underline{H_a}H_b$), 4.75 (1H, br s, C21C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.32 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.03 (1H, br d, *J* = 6.3 Hz, C31$\underline{H}$), 4.02-3.98 (1H, obs m, C27$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.54 (1H, br d, *J* = 10.3 Hz, C33$\underline{H}$), 3.54-3.50 (1H, obs m, C23$\underline{H}$), 3.40 (1H, br d, *J* = 10.5 Hz, C35$\underline{H}$), 2.37-2.28 (2H, m, C22$\underline{H_a}H_b$, C30$\underline{H}$), 2.15 (1H, dd, *J* = 13.1, 5.3 Hz, C22$H_a\underline{H_b}$), 2.04-1.97 (1H, m, C36$\underline{H}$), 1.81-1.74 (1H, m, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.60-1.39 (7H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C34$\underline{H}$), 1.36 (1H, d, *J* = 3.4 Hz, C27(H)O$\underline{H}$), 1.06 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.93 (24H, m, C30(H)$\underline{Me}$, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2(CH\underline{Me_2})$, $Si(CH_2\underline{Me})_3$), 0.93-0.84 (1H, obs m, $Si(CH_2Me)_2(C\underline{H}Me_2)$), 0.89 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.76 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.65-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$). **$^{13}$C NMR** (125 MHz, $d_6$-PhH) $\delta_C$ 160.2, 150.0, 149.4, 143.2, 134.7, 133.4, 132.02, 131.96, 120.0, 113.6, 112.8, 111.9, 111.5, 101.8, 83.2, 82.1, 76.9, 74.3, 72.9, 70.7, 67.4, 55.33, 55.29, 54.5, 42.7, 42.4, 41.3, 37.9, 37.2, 34.1, 30.8, 30.1, 23.0, 21.8, 17.5, 17.4, 16.9, 13.3, 8.4, 7.8, 7.4, 7.32, 7.29, 6.0, 5.6, 4.04, 4.01. **$[\alpha]_D^{20}$** –0.5 (*c* = 0.2, $CHCl_3$). **IR** (thin film) 3438.0, 2938.1, 2876.1, 1615.4, 1590.4, 1517.4, 1463.4, 1379.9, 1249.4, 1101.8, 1029.2, 970.4, 727.2 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{54}H_{96}NO_9Si_2$ $[M + NH_4]^+$ 958.6618, found 958.6659.

**MOSHER ESTERS 94S AND 94R**

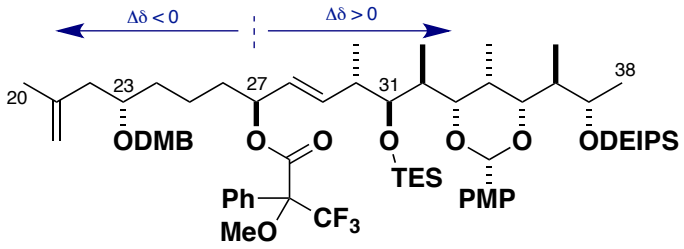



**94S:** $\mathbf{R_f}$ 0.44 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.52-7.48 (2H, m, $Ar_{Ph}\underline{H}$), 7.38-7.32 (5H, m, $Ar_{Ph}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.90-6.74 (5H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.97-5.90 (1H, m, C27$\underline{H}$), 5.46-5.39 (2H, m, C28$\underline{H}$, C29$\underline{H}$), 5.37 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.78 (1H, br s, C21C$\underline{H_a}H_b$), 4.71 (1H, br s, C21C$H_a\underline{H_b}$), 4.42 (1H, d, *J* = 11.3, O$\underline{H_a}H_bAr_{DMB}$), 4.39 (1H, d, *J* = 11.3, O$H_a\underline{H_b}Ar_{DMB}$), 4.30 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.03 (1H, br d, *J* = 5.4 Hz, C31$\underline{H}$), 3.863 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.860 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.51 (3H, s, C27(H)$O_2$C(O$\underline{Me}$)(Ph)($CF_3$)), 3.50 (1H, obs dd, C33$\underline{H}$), 3.46-3.39 (1H, m, C23$\underline{H}$), 3.37 (1H, dd, *J* = 10.5, 1.3 Hz, C35$\underline{H}$), 2.43-2.38 (1H, m, C30$\underline{H}$), 2.36-2.25 (2H, m, C22$\underline{H_a}H_b$, C22$\underline{H_a}H_b$), 2.02-1.97 (1H, m, C36$\underline{H}$), 1.97-1.91 (1H, m, C32$\underline{H}$), 1.79-1.18 (7H, obs m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C34$\underline{H}$), 1.70 (3H, s, C20$\underline{H_3}$), 1.04 (3H, d. *J* = 6.3 Hz, C38$\underline{H_3}$), 0.99-0.93 (21H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$($CH\underline{Me_2}$), Si($CH_2\underline{Me}$)$_3$), 0.93-0.86 (1H, obs m, Si($CH_2Me$)$_2$(C$\underline{H}$$Me_2$)), 0.88 (3H, d, *J* = 6.8 Hz, C30(H)$\underline{Me}$), 0.85 (3H, d, *J* = 6.9 Hz, C34(H)$\underline{Me}$), 0.81 (3H, d, *J* =6.9 Hz, C32(H)$\underline{Me}$), 0.73 (3H, d, *J* = 6.8 Hz, C36(H)$\underline{Me}$), 0.63-0.57 (10H, m, Si(C$\underline{H_2}$Me)$_3$, Si(C$\underline{H_2}$Me)$_2$$^i$Pr). **$[\alpha]_D^{20}$** –4.5 (*c* = 0.20, $CHCl_3$). **IR** (thin film) 2924.1, 2853.2, 1744.9, 1658.7, 1618.3, 1517.3, 1463.1, 1260.3, 1168.7, 1168.7, 1103.1, 1030.9 $cm^{-1}$.

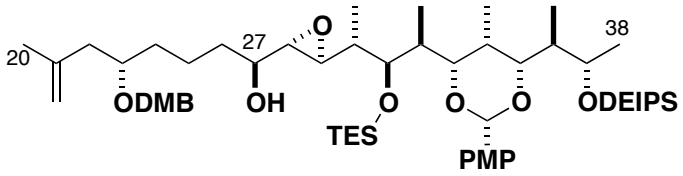
**94R:** $\mathbf{R_f}$ 0.44 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.56-7.50 (2H, m, $Ar_{Ph}\underline{H}$), 7.43-7.32 (5H, m, $Ar_{Ph}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.91-6.74 (5H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.89-5.81 (1H, m, C27$\underline{H}$), 5.42-5.29 (2H, obs m, C28$\underline{H}$, C29$\underline{H}$), 5.37 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21C$\underline{H_a}H_b$), 4.74 (1H, br s, C21C$H_a\underline{H_b}$), 4.44 (1H, d, *J* = 11.3, O$\underline{H_a}H_bAr_{DMB}$), 4.41 (1H, d, *J* = 11.3, O$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$),4.05 (1H, br d, *J* = 5.3 Hz, C31$\underline{H}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.84 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.50 (1H, obs dd, C33$\underline{H}$), 3.44-3.33 (2H, m, C23$\underline{H}$, C35$\underline{H}$), 3.41 (3H, s, C27(H)$O_2$C(O$\underline{Me}$)(Ph)($CF_3$)), 2.40-2.37 (1H, m, C30$\underline{H}$), 2.35-2.27 (2H, m, C22$\underline{H_a}H_b$, C22$\underline{H_a}H_b$), 2.02-1.97 (1H, m, C36$\underline{H}$), 1.97-1.87 (1H, obs m, C32$\underline{H}$), 1.79-1.18 (7H, obs m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C34$\underline{H}$), 1.70 (3H, s, C20$\underline{H_3}$), 1.04 (3H, d. *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.92 (21H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$($CH\underline{Me_2}$), Si($CH_2\underline{Me}$)$_3$), 0.92-0.86 (4H, obs m, C30(H)$\underline{Me}$), Si($CH_2Me$)$_2$(C$\underline{H}$$Me_2$)), 0.85 (3H, d, *J* = 6.9 Hz, C34(H)$\underline{Me}$), 0.82 (3H, d, *J* =6.9 Hz, C32(H)$\underline{Me}$), 0.73 (3H, d, *J* = 6.8 Hz, C36(H)$\underline{Me}$), 0.63-0.57 (10H, m, Si(C$\underline{H_2}$Me)$_3$, Si(C$\underline{H_2}$Me)$_2$$^i$Pr). **$[\alpha]_D^{20}$** +1.2 (*c* = 0.25, $CHCl_3$). **IR** (thin film) 2927.4, 2854.8, 1743.9, 1676.1, 1613,2m 1517.6, 1452.1, 1250.7, 1164.4, 1101.8, 1018.9 $cm^{-1}$.

**MOSHER ESTER ANALYSIS FOR 94S AND 94R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C20$\underline{H_3}$ | 1.70 | 1.70 | 0.00 |
| C21C$\underline{H_a}H_b$ | 4.78 | 4.79 | –0.01 |
| C21C$H_a\underline{H_b}$ | 4.71 | 4.74 | –0.03 |
| C22$\underline{H_a}H_b$, C22$H_a\underline{H_b}$ | obs. | obs. | - |
| C23$\underline{H}$ | 3.43 | 3.39 | –0.04 |
| OC$\underline{H_a}H_bAr_{DMB}$ | 4.42 | 4.44 | –0.02 |
| OC$H_a\underline{H_b}Ar_{DMB}$ | 4.39 | 4.41 | –0.02 |
| C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$ | obs. | obs. | - |
| C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$ | obs. | obs. | - |
| C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$ | obs. | obs. | - |
| C27$\underline{H}$ | 5.94 | 5.85 | +0.09 |
| C28$\underline{H}$, C29$\underline{H}$ | 5.46-5.39 | 5.42-5.29 | +ve |
| C30$\underline{H}$ | 2.41 | 2.39 | +0.02 |
| C30(H)$\underline{Me}$ | 0.88 | obs. | - |
| C31$\underline{H}$ | 4.03 | 4.05 | –0.02 |
| C32$\underline{H}$ | 1.94 | obs. | - |
| C32(H)$\underline{Me}$ | 0.81 | 0.82 | –0.01 |
| C33$\underline{H}$ | 3.50 | obs. | - |



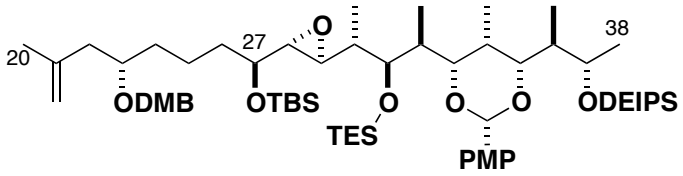
**EPOXIDE 95**




A stock solution of Ti(O*i*-Pr)$_4$ (161 µL, 532 µmol) and (+)-DET (137 µL, 798 µmol) in $CH_2Cl_2$ (9.7 mL) was prepared and stirred over 4 Å molecular sieves (*ca* 1 g) for 20 min at rt. Allylic alcohol **94** (50 mg, 53 µmol) was dissolved in $CH_2Cl_2$ (1 mL) over 4 Å molecular sieves (*ca* 50 mg) and cooled to –25 ºC. The stock solution (0.1 mL = Ti(O$^i$Pr)$_4$ (1.61 µL, 5.32 µmol, 10 mol%), (+)-DET (1.37 µL, 7.98 µmol, 15 mol%)) was added *via* syringe and the the mixture stirred for 20 min. *t*-BuOOH (45 µL, 213 µmol, 4.7 M solution in PhMe) was added and the reaction stirred for 12 h at –25 ºC. The reaction was quenched by the addition of $Na^+/K^+$ tartrate solution (2 mL), diluting with $CH_2Cl_2$ (3 mL) and stirring at rt for 1.5 h. The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (4 × 5 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude residue (2:1 dr by $^1$H NMR analysis) was purified by column chromatography (7:1 → 6:1 PE/EtOAc) to afford the desired epoxide **95** (28 mg, 29 µmol, 59%) and undesired epoxide **87** (13 mg, 14 µmol, 27%) as colourless oils.

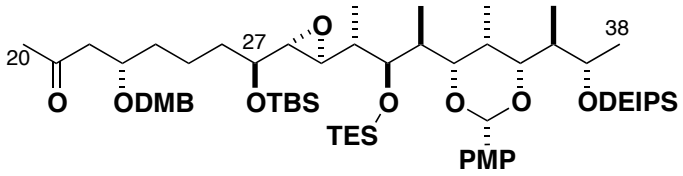
**$R_f$** 0.19 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.92-6.84 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.81 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.38 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.80 (1H, br s, C21C$\underline{H_a}H_b$), 4.76 (1H, br s, C21C$H_a\underline{H_b}$), 4.47 (1H, d, *J* = 11.3 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 11.3 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.31 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.17 (1H, br d, *J* = 6.3 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.79 3.87 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.1, 1.4 Hz, C33$\underline{H}$), 3.54-3.50 (1H, m, C23$\underline{H}$), 3.50-3.45 (1H, m, C27$\underline{H}$), 3.40 (1H, dd, *J* = 10.4, 1.6 Hz), 2.95 (1H, dd, *J* = 5.2, 2.4 Hz, C29$\underline{H}$),2.76 (1H, dd, *J* = 4.4, 2.4 Hz, C28$\underline{H}$), 2.35 (1H, dd, *J* = 13.9, 6.4 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 13.9, 6.1 Hz, C22$H_a\underline{H_b}$), 2.05-1.99 (1H, m, C36$\underline{H}$), 1.81-1.76 (1H, obs m, C32$\underline{H}$), 1.66-1.28 (8H, obs m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C27(H)O$\underline{H}$, C30$\underline{H}$, C34$\underline{H}$), 1.73 (3H, br s, C20$\underline{H_3}$), 1.05 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.93 (24H, m, C30(H)$\underline{Me}$, Si(C$H_2\underline{Me})_2$$^i$Pr, Si(C$H_2$Me)$_2$(C$\underline{H}$Me$_2$), Si(C$H_2\underline{Me})_3$), 0.92-0.87 (1H, obs m, Si(C$H_2$Me)$_2$(C$\underline{H}$Me$_2$)), 0.91 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.83 (3H, d, *J* = 6.9 Hz, C32(H)$\underline{Me}$), 0.82 (3H, d, *J* = 6.8 Hz, C36(H)$\underline{Me}$), 0.68-0.57 (10H, m, Si(C$\underline{H_2}$Me)$_3$, Si(C$\underline{H_2}$Me)$_2$$^i$Pr). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.7, 149.0, 148.5, 143.0, 131.5, 128.3, 127.2, 120.2, 113.4, 112.7, 111.2, 110.9, 100.9, 83.0, 82.2, 77.2, 71.8, 70.9, 70.1, 67.1, 59.5, 57.4, 55.9, 55.8, 55.3, 42.8, 40.8, 40.3, 37.5, 34.0, 33.9, 30.4, 22.9, 21.5, 17.4 (2C), 17.2, 13.1, 12.7, 8.8, 7.8, 7.14, 7.11, 5.5, 5.4, 3.84, 3.78. **$[\alpha]_D^{20}$** –3.1 (*c* = 1.2, $CHCl_3$). **IR** (thin film) 3460.6, 2937.2, 2871.4, 1615.8, 1587.9, 1516.6, 1459.2, 1379.1, 1340.9, 1248.2, 1158.1, 1083.2, 1011.5, 969.1, 762.7 cm$^{-1}$. **HRMS** (ES$^+$) Calculated for $C_{54}H_{92}NaO_{10}Si_2$ $[M + Na]^+$ 979.6121, found 979.6074.

**TBS ETHER 96**




Alcohol **95** (21 mg, 22 μmol, dried azeotropically from PhH) was dissolved in $CH_2Cl_2$ (1.5 mL) and cooled to –78 ºC. 2,6-Lutidine (9.4 μL, 41 μmol) and TBSOTf (9.5 μL, 82 μmol) were added sequentially and the mixture stirred for 15 min. When complete by TLC, the reaction was quenched by the addition of MeOH (0.1 mL) at –78 ºC followed by dilution with $NaHCO_3$ solution (2 mL) and $CH_2Cl_2$ (2 mL). The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (5 × 5 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude residue was purified by column chromatography (9:1 → 6:1 PE/EtOAc) to afford TBS ether **96** (20.3 mg, 19.0 μmol, 86%) as a colourless oil. **$R_f$** 0.52 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.90 (1H, d, *J* = 1.6 Hz, $Ar_{DMB}\underline{H}$), 6.87-6.84 (3H, m, $Ar_{DMB}\underline{H}$, $Ar_{PMP}\underline{H}$), 6.80 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.79 (1H, br s, C21C$\underline{H_a}H_b$), 4.76 (1H, br s, C21C$H_a\underline{H_b}$), 4.45 (2H, br s, OC$\underline{H_a}H_bAr_{DMB}$, OC$H_a\underline{H_b}Ar_{DMB}$), 4.33 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.15 (1H, br d, *J* = 4.1 Hz, C31$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.57 (1H, dd, *J* = 10.1, 1.4 Hz, C33$\underline{H}$), 3.55-3.49 (1H, m, C23$\underline{H}$), 3.46-3.41 (1H, obs m, C27$\underline{H}$), 3.41 (1H, dd, *J* = 10.4, 1.0 Hz, C35$\underline{H}$), 2.98 (1H, dd, *J* = 2.7, 2.2 Hz, C29$\underline{H}$), 2.75 (1H, dd, *J* = 5.3, 2.2 Hz, C28$\underline{H}$), 2.34 (1H, dd, *J* = 14.0, 6.6 Hz, C22$\underline{H_a}H_b$), 2.16 (1H, dd, *J* = 14.0, 6.0 Hz, C22$H_a\underline{H_b}$), 2.06-1.98 (1H, m, C36$\underline{H}$), 1.98-1.91 (1H, app br tq, *J* = 6.9, 3.2 Hz, C30$\underline{H}$), 1.86 (1H, app br dq, *J* = 10.1, 6.9 Hz, C32$\underline{H}$), 1.73 (3H, s, C20$\underline{H_3}$), 1.63-1.56 (1H, m, C34$\underline{H}$), 1.55-1.45 (6H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (21H, m, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$CH$\underline{Me_2}$, Si($CH_2\underline{Me}$)$_3$), 0.94-0.89 (1H, obs m, Si($CH_2Me$)$_2$C$\underline{H}Me_2$), 0.91 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.87 (9H, s, Si$^t$$\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.81 (3H, d, *J* = 6.8 Hz, C32(H)$\underline{Me}$), 0.80 (3H, d, *J* = 6.9 Hz, C30(H)$\underline{Me}$), 0.68-0.57 (10H, m, Si(C$\underline{H_2}$Me)$_3$, Si(C$\underline{H_2}$Me)$_2$$^i$Pr), 0.02 (6H, s, Si$^t$Bu$\underline{Me_2}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 159.5, 149.0, 148.5, 143.0, 131.9, 131.6, 127.1, 120.2, 113.3, 112.6, 111.2, 110.9, 100.7, 83.0, 81.8, 72.6, 72.3, 70.9, 67.2, 58.6, 58.2, 55.9, 55.8, 55.3, 42.8, 40.8, 38.7, 37.6, 35.1, 34.2, 30.8, 25.9, 22.9, 21.2, 18.2, 17.4, 17.2, 13.1, 10.7, 8.5, 7.8, 7.2, 7.13, 7.11, 5.5, 5.4, 3.9, 3.8, –4.2, –4.8. **$[\alpha]_D^{20}$** –5.2 (*c* = 1.7, $CHCl_3$). **IR** (thin film) 2949.8, 2876.8, 1617.9, 1584.4, 1517.5, 1463.3, 1249.6, 1102.8, 1031.7, 832.3, 725.6 cm$^{-1}$. **MS** (ES$^+$) Calculated for $C_{60}H_{106}NaO_{10}Si_3$ $[M + Na]^+$ 1093.6992, found 1093.7034.

**C20-C38 Northern fragment 97**



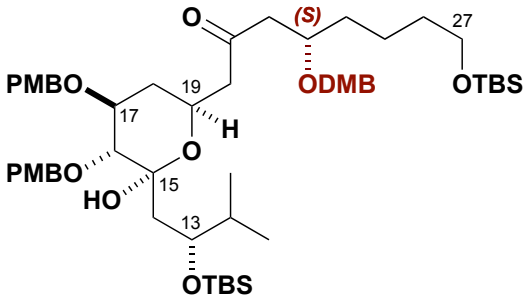

To a solution of alkene **96** (17 mg, 16 µmol) in THF (0.2 mL) and $H_2O$ (0.3 mL) was added NMO (4 drops, 50 %wt solution in $H_2O$) and $OsO_4$ (4 drops, 2 %wt in *t*-BuOH). The brown solution was stirred for 30 min until reaction was complete by TLC. The reaction was quenched by the addition of $Na_2S_2O_3$ (2 mL), diluted with EtOAc (2 mL) and stirred for 30 min. The organic layer was separated and the aqueous phase extracted with EtOAc (5 × 5mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was dissolved in $CH_2Cl_2$ (1 mL) and $NaIO_4$–$SiO_2$ (1 spatula) was added. The reaction was complete by TLC after 10 min and the mixture filtered, eluting with $CH_2Cl_2$ (40 mL). The solvent was removed under reduced pressure and the crude product purified by column chromatography (5:1 PE/EtOAc). Methyl ketone **97** (14.5 mg, 13.5 µmol, 85%) was collected as a colourless oil.

**$R_f$** 0.23 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.36 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 6.87-6.82 (4H, m, $Ar_{PMP}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.80 (1H, d, *J* = 8.6 Hz, $Ar_{DMB}\underline{H}$), 5.39 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.47 (1H, d, *J* = 11.1 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.40 (d, *J* = 11.1 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.32 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.15 (1H, br d, *J* = 6.8 Hz, C31$\underline{H}$), 3.94-3.88 (1H, m, C23$\underline{H}$), 3.87 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.56 (1H, dd, *J* = 10.2, 1.5 Hz, C33$\underline{H}$), 3.44-3.39 (2H, m, C27$\underline{H}$, C35$\underline{H}$), 2.97 (1H, app t, *J* = 2.6 Hz, C29$\underline{H}$), 2.76-2.70 (2H, m, C22$\underline{H_a}H_b$, C28$\underline{H}$), 2.48 (1H, dd, *J* = 15.9, 4.5 Hz, C22$H_a\underline{H_b}$), 2.15 (3H, s, C20$\underline{H_3}$), 2.05-1.99 (1H, m, C36$\underline{H}$), 1.95 (1H, app br tq, *J* = 6.9, 3.2 Hz, C30$\underline{H}$), 1.86 (1H, app br dq, *J* = 10.1, 6.9 Hz, C32$\underline{H}$), 1.63-1.37 (7H, m, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C34H), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (21H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2CH\underline{Me_2}$, $Si(CH_2\underline{Me})_3$), 0.94-0.89 (1H, obs m, $Si(CH_2Me)_2C\underline{H}Me_2$), 0.90 (3H, d, *J* = 6.7 Hz, C34(H)$\underline{Me}$), 0.87 (9H, s, $Si{}^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 7.0 Hz, C36(H)$\underline{Me}$), 0.81 (3H, d, *J* = 6.8 Hz, C32(H)$\underline{Me}$), 0.80 (3H, d, *J* = 6.9 Hz, C30(H)$\underline{Me}$), 0.68-0.57 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$), 0.02 (6H, s, $Si{}^tBu\underline{Me_2}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 207.6, 159.5, 148.9, 148.6, 131.8, 131.1, 127.1, 120.3, 113.3, 111.2, 110.9, 100.7, 83.0, 81.8, 75.4, 72.6, 72.2, 71.6, 67.2, 58.5, 58.3, 55.9, 55.8, 55.3, 48.7, 40.7, 38.6, 37.6, 35.1, 34.5, 31.2, 30.5, 29.7, 25.9 (2C), 20.9, 18.2, 17.4, 17.2, 13.1, 10.7, 8.5, 7.8, 7.2, 7.13, 7.12, 5.5, 5.4, 3.9, 3.8, –4.2, –4.8. **$[\alpha]_D^{20}$** +0.5 (*c* = 1.3, $CHCl_3$). **IR** (thin film) 2933.4, 2875.9, 1716.9, 1614.1, 1593.0, 1517.0, 1463.0, 1249.6, 1087.0, 1031.7, 834.5, 775.5, 726.5 $cm^{-1}$. **HRMS** ($ES^+$) Calculated for $C_{59}H_{104}NaO_{11}Si_3$ $[M + Na]^+$ 1095.6779, found 1095.6741.

## 4. Experimental Data for C1-C38 Coupled Intermediates

### 4.1 Model Studies for C19–C20 Bond Construction

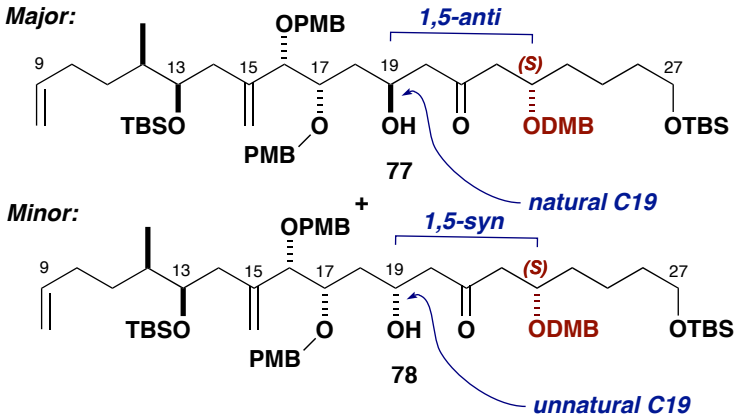
#### HEMIACETAL 73




To a stirred solution of ketone (*S*)-**63** (46 mg, 84 µmol) in $Et_2O$ (0.7 mL) at 0 ºC was added (*c*-Hex)$_2$BCl•$NEt_3$ (133 µL of a stock solution composed of dicyclohexylboron chloride (184 µL, 838 µmol), $Et_3N$ (146 µL, 1.05 mmol) and $Et_2O$ (1.0 mL)). After 1 h, the reaction mixture was cooled to –78 ºC and aldehyde **73** (30 mg, 52 µmol) in $Et_2O$ (0.7 mL) was added *via* cannula. The reaction was stirred for 1.5 h then transferred to a freezer (–23 ºC) overnight. The reaction was quenched with pH 7 buffer solution (5 mL) and extracted with $Et_2O$ (3 × 5 mL). To the combined organic extracts was added silica gel (*ca* 1 g) and the slurry was stirred for 1.5 h. The solution was then filtered and concentrated under reduced pressure. The residue was purified by column chromatography (17:3 PE/EtOAc) to afford hemiacetal **73** (14 mg, 14 µmol, 27%), recovered ketone (*S*)-**63** (14 mg, 26 µmol) and an inseparable, uncharacterisable mixture of two product-related isomers (10 mg).

**$R_f$** 0.52 (1:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $C_6D_6$) $\delta_H$ 7.38 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.27 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.00-6.90 (2H, m, $Ar_{DMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.86 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.81 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.66 (1H, d, *J* = 7.9 Hz, $Ar_{DMB}\underline{H}$), 5.20 (1H, br. s, C15O$\underline{H}$), 5.14 (1H, d, *J* = 11.0 Hz, O$C\underline{H_a}H_bAr_{PMB}$), 4.76-4.71 (1H, m, C19$\underline{H}$), 4.67 (1H, d, *J* = 10.9 Hz, O$CH_a\underline{H_b}Ar_{PMB}$), 4.64 (1H, d, *J* = 12.6 Hz, O$C\underline{H_a}H_bAr_{DMB}$), 4.62 (1H, d, *J* = 12.6 Hz, O$CH_a\underline{H_b}Ar_{DMB}$), 4.61 (1H, d, *J* = 11.0 Hz, O$C\underline{H_a}H_bAr_{PMB}$), 4.54 (1H, d, *J* = 11.1 Hz, O$CH_a\underline{H_b}Ar_{PMB}$), 4.28 (1H, ddd, *J* = 4.9, 9.1, 10.2 Hz, C17$\underline{H}$), 4.20-4.15 (1H, m, C23$\underline{H}$), 3.86-3.83 (1H, m, C13$\underline{H}$), 3.70-3.67 (2H, m, C27$\underline{H_2}$), 3.69 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.53 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.43 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.41 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.40 (1H, d, *J* = 7.0 Hz, C16$\underline{H}$), 2.80 (1H, dd, *J* = 16.1, 7.2 Hz, C22$\underline{H_a}H_b$), 2.69 (1H, dd, *J* = 16.1, 7.4 Hz, C20$\underline{H_a}H_b$), 2.42-2.25 (4H, m, C13H(OTBS)C$\underline{H}Me_aMe_b$, C14$\underline{H_a}H_b$, C20$H_a\underline{H_b}$, C22$H_a\underline{H_b}$), 2.16 (1H, ddd, *J* = 12.4, 4.9, 2.0 Hz, C18$\underline{H_a}H_b$), 1.87 (1H, dd, *J* = 14.5, 3.9 Hz, C14$H_a\underline{H_b}$), 1.64-1.48 (7H, m, C18$H_a\underline{H_b}$,C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 1.01-1.00 (15H, m, C13H(OTBS)CH$\underline{Me_a}Me_b$, C13H(OTBS)CH$Me_a\underline{Me_b}$, OSi$^t$$\underline{Bu}Me_2$), 0.96 (9H, s, OSi$^t$$\underline{Bu}Me_2$), 0.25 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.19 (6H, s, Si$^t$Bu$\underline{Me_2}$), 0.14 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $C_6D_6$) $\delta_C$ 205.7, 159.5, 159.4, 150.0, 149.6, 131.8, 131.5, 131.5, 129.7, 129.2, 120.2, 113.8, 113.8, 112.3, 111.9, 100.1, 84.1, 77.7, 77.2, 75.4, 75.0, 71.6, 71.2, 64.1, 63.0, 55.5, 55.4, 54.5*, 49.9, 48.0, 38.0, 37.4, 34.5, 33.1, 26.0, 26.0, 21.8, 19.9, 19.1, 18.3, 18.0, -4.2, -4.8, -5.3. **$[\alpha]_D^{20}$** +15.8 (*c* = 1.2, $CHCl_3$). **IR** (thin film) 3425, 2935, 2857, 1716, 1613, 1515, 1464, 1249, 1093, 1035, 835, 777 cm$^{-1}$. **HRMS** (ESI) calculated for $C_{55}H_{92}O_{12}Si_2N$ [M + $NH_4$]$^+$ 1014.6153, found 1014.6154.

**ALDOL PRODUCTS 77 AND 78**




*Conditions A ((c-Hex)$_2$BCl aldol):* A stock solution of dicyclohexylboron chloride (270 µL, 409 µmol) and $Et_3N$ (210 µL, 1.51 mmol) in $Et_2O$ (1.00 mL) was prepared. The stock solution (148 µL) was added to a solution of ketone (*S*)-**63** (101 mg, 184 µmol) in $Et_2O$ (1.5 mL) at 0 ºC. After stirring for 1 h, the reaction mixture was cooled to –78 ºC whereupon a solution of aldehyde **76** (25 mg, 41 µmol) in $Et_2O$ (1.5 mL) that was pre-dried for 15 min with $CaH_2$ was added *via* cannula. The reaction mixture was stirred for 2 h at –78 ºC before transferring to a freezer (–20 ºC) for 16 h. The reaction was quenched with pH 7 buffer solution (3 mL) and extracted with $Et_2O$ (3 × 5 mL). To the combined organic layers was added silica gel (*ca* 1 g) and the slurry stirred for 1 h before filtration and concentration under reduced pressure. The crude residue was purified by column chromatography (4:1 PE/EtOAc) to give aldol adducts **77** (14 mg, 12 µmol, 30%) and **78** (5.1 mg, 4.9 µmol, 10%) and recovered methyl ketone (*S*)-**63** (60 mg, 0.11 mmol) as colourless oils. $^1$H NMR analysis of the crude reaction mixture indicated 3:1 dr **77**:**78**.

*Conditions B (Bu$_2$BOTf aldol):* A stock solution of $Bu_2BOTf$ (154 µL, 638 µmol) and *i*-$Pr_2NEt$ (114 µL, 695 µmol) in $Et_2O$ (1.00 mL) was prepared. The stock solution (127 µL) was added to a solution of ketone (*S*)-**63** (35 mg, 64 µmol) in $Et_2O$ (0.7 mL) at –78 ºC. After 30 min, aldehyde **76** (25 mg, 41 µmol) in $Et_2O$ (0.7 mL) was added *via* cannula. After stirring for a further 4 h, the reaction was quenched with MeOH (2 mL) and pH 7 buffer solution (5 mL). The layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 5 mL). To the combined organic layers was added silica gel (*ca* 1 g) and the slurry was stirred for 1 h before filtration and concentration under reduced pressure. The crude residue was purified by column chromatography (4:1 PE/EtOAc) to give aldol adducts **77** (24 mg, 23 µmol, 55%) and **78** (5 mg, 5 µmol 12%) and recovered methyl ketone (*S*)-**63** (10 mg, 31 µmol) as colourless oils. $^1$H NMR analysis of the crude reaction mixture indicated 3.5:1 dr **77**:**78**.

*Conditions C (9-BBNCl aldol):* To a stirred solution of 9-BBNCl•$SMe_2$ (30 mg, 137 µmol) and *i*-$Pr_2NEt$ (31 µL, 189 µmol) in $Et_2O$ (1 mL) at –95 ºC was added ketone (*S*)-**63** (58 mg, 106 µmol, dried over $CaH_2$ for 30 min) in $Et_2O$ (0.8 mL) *via* cannula. After stirring for 30 min, aldehyde **76** (15 mg, 25 µmol) in $Et_2O$ (0.8 mL) was added *via* cannula. After a further 2 h, the reaction was quenched with MeOH (2 mL) and then pH 7 buffer solution (5 mL). The layers were separated and the aqueous layer was extracted with $Et_2O$ (3 × 5 mL). To the combined organic layers was added silica gel (*ca* 1 g) and the slurry was stirred for 1 h. The solution was then filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (4:1 PE/EtOAc) to give aldol adducts **77** (13.6 mg, 12 µmol, 48%) and **78** (2.6 mg, 2.5 µmol,

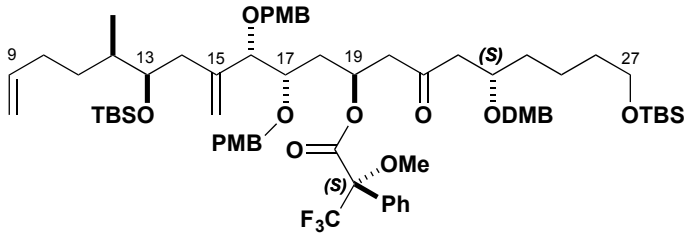
10%) and recovered methyl ketone (*S*)-**63** as colourless oils. $^1$H NMR analysis of the crude reaction mixture indicated 4.8:1 dr **77**:**78**.

*The remaining conditions in **Table 1** were screened by substituting Lewis acids and bases into the above procedures.*

**77**: **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.25 (2H, d, *J* = 8.7, $Ar_{PMB}\underline{H}$), 7.23 (2H, d, *J* = 8.7, $Ar_{PMB}\underline{H}$), 6.87-6.80 (6H, m, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.78 (1H, d, *J* = 7.9 Hz, $Ar_{DMB}\underline{H}$), 5.77 (1H, ddt, *J* = 17.1, 10.3, 6.7 Hz, C9$\underline{H}$), 5.13 (1H, br. s, C15=C$\underline{H_a}H_b$), 5.06 (1H br. s, C15=C$H_a\underline{H_b}$), 4.98 (1H, dd, *J* = 17.1, 1.4 Hz, C9(H)=C$\underline{H_a}H_b$), 4.96 (1H, dd, *J* = 10.0, 1.4 Hz, C9(H)=C$H_a\underline{H_b}$), 4.80 (1H, d, *J* = 10.8 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.52 (1H, d, *J* = 10.8 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.51 (1H, d, *J* = 11.4 Hz, OCC$\underline{H_a}H_bAr_{PMB}$), 4.43 (1H, d, *J* = 11.1 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.40 (1H, d, *J* = 11.1 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 4.29 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.26-4.21 (1H, m, C19$\underline{H}$), 3.94-3.85 (3H, m, C13$\underline{H}$, C16$\underline{H}$, C23$\underline{H}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.84 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.80-3.76 (1H, obs. m, C17$\underline{H}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.59 (2H, t, *J* = 6.3 Hz, C27$\underline{H_2}$), 3.00 (1H, br. s, C19(H)O$\underline{H}$), 2.70 (1H, dd, *J* = 16.0, 7.8 Hz, C22$\underline{H_a}H_b$), 2.50-2.47 (2H, m, C20$\underline{H_a}H_b$, C20$H_a\underline{H_b}$), 2.44 (1H, dd, *J* = 16.0, 4.7 Hz, C22$H_a\underline{H_b}$), 2.17 (2H, br. d, *J* = 6.5 Hz, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 2.12-2.05 (1H, m, C10$\underline{H_a}H_b$), 2.00-1.91 (1H, m, C10$H_a\underline{H_b}$), 1.66-1.22 (11H, m, C11$\underline{H_a}H_b$, C11$H_a\underline{H_b}$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (9H, s, Si$^t\underline{Bu}Me_2$), 0.88 (9H, s, Si$^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (6H, s, Si$^t$Bu$\underline{Me_2}$), 0.03 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 210.3, 159.2, 159.0, 149.0, 148.6, 143.1, 139.2, 131.0 130.9, 130.7, 129.9, 129.2, 120.3, 116.4, 114.1, 113.8, 113.7, 111.3, 111.0, 87.1, 75.2, 74.2, 73.9, 71.6, 70.4, 64.3, 63.0, 55.9, 55.8, 55.3, 51.1, 48.3, 38.3, 36.14, 36.11, 34.1, 32.8, 32.7, 31.9, 29.7, 28.2, 25.97, 25.96, 21.5, 18.4, 18.1, 13.1, –4.0, –4.5, –5.3 (2C). **$[\alpha]_D^{20}$** +0.098 (*c* = 1.6, $CHCl_3$). **IR** (thin film) 3447, 2928, 2857, 1708, 1613, 1514, 1463, 1249, 1093, 1033, 836, 775 cm$^{-1}$. **HRMS** (ESI) calculated for $C_{59}H_{98}O_{11}Si_2N$ $[M + NH_4]^+$ 1052.6673, found 1052.6678.

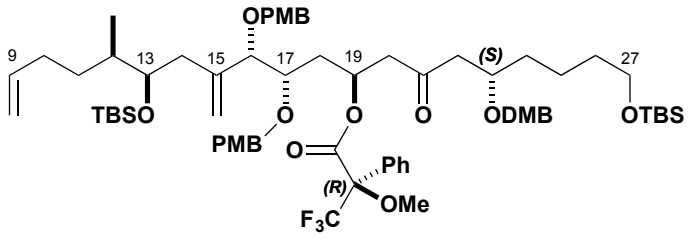
**78**: **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.7, $Ar_{PMB}\underline{H}$), 7.19 (2H, d, *J* = 8.3, $Ar_{PMB}\underline{H}$), 6.88-6.77 (7H, m, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.78 (1H, ddt, *J* = 17.1, 10.3, 6.7 Hz, C9$\underline{H}$), 5.18 (1H, br. s, C15=C$\underline{H_a}H_b$), 5.08 (1H br. s, C15=C$H_a\underline{H_b}$), 4.99 (1H, br. d, *J* = 17.1 Hz, C9(H)=C$\underline{H_a}H_b$), 4.93 (1H, br. d, *J* = 10.0 Hz, C9(H)=C$H_a\underline{H_b}$), 4.76 (1H, d, *J* = 10.8 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.53 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.49 (1H, d, *J* = 10.8 Hz, OCC$\underline{H_a}H_bAr_{PMB}$), 4.40 (2H, br. s, OC$\underline{H_a}H_bAr_{DMB}$, OC$H_a\underline{H_b}Ar_{DMB}$), 4.24 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.07-4.01 (1H, m, C19$\underline{H}$), 3.93-3.83 (2H, obs. m, C16$\underline{H}$, C23$\underline{H}$), 3.85 (6H, br. s, $Ar_{DMB}O\underline{Me}$), 3.82-3.76 (1H, obs. m, C13$\underline{H}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.76-3.70 (1H, m, C17$\underline{H}$), 3.60 (2H, t, *J* = 6.3 Hz, C27$\underline{H_2}$), 3.52 (1H, br. s, C19(H)O$\underline{H}$), 2.70 (1H, dd, *J* = 16.0, 7.8 Hz,C22$\underline{H_a}H_b$), 2.51 (1H, dd, *J* = 16.6, 8.6 Hz, C20$\underline{H_a}H_b$), 2.43 (1H, dd, *J* = 16.0, 4.3 Hz, C22$H_a\underline{H_b}$), 2.33 (1H, dd, *J* = 16.6, 3.1 Hz, C20$H_a\underline{H_b}$), 2.18-1.95 (4H, m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.69-1.20 (11H, m, C11$\underline{H_a}H_b$, C11$H_a\underline{H_b}$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (18H, br. s, Si$^t\underline{Bu}Me_2$),0.83 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (9H, s, Si$^t$Bu$\underline{Me_2}$, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CDCl_3$) $\delta_C$ 209.5, 159.3, 159.2, 148.9, 148.6, 142.6, 139.1, 131.0, 130.4, 130.2, 129.9, 129.5, 120.3, 116.0, 114.3, 113.8, 111.3, 110.9, 85.5, 78.7, 75.2, 74.0, 73.2, 71.6, 70.4, 66.4, 63.0, 55.9, 55.8, 55.3, 55.2, 50.8, 48.4, 37.6, 36.2, 36.1, 34.3, 32.9, 32.6, 31.8, 29.7, 26.0, 26.0, 21.6, 18.4, 18.1, 13.3, –4.0, –4.4, –5.3.

**MOSHER ESTER 77S**




To a stirred solution of alcohol **77** (3.0 mg, 2.9 µmol) in $CH_2Cl_2$ (300 µL) and pyridine (50 µL) at –40 ºC was added (*R*)-Mosher acid chloride (2 drops). After 40 min, he crude residue was purified by direct column chromatography (17:3 PE/EtOAc) to afford (*S*)-Mosher ester **77S** (1.3 mg, 1.1 µmol, 40%) as a colourless oil. **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.51 (2H, br. d, *J* = 7.3 Hz, $Ar_{Ph}\underline{H}$), 7.36-7.32 (3H, m, $Ar_{Ph}\underline{H}$), 7.26 (2H, d, *J* = 8.3, $Ar_{PMB}\underline{H}$), 7.24 (2H, d, *J* = 8.3, $Ar_{PMB}\underline{H}$), 6.86-6.78 (6H, m, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.75 (1H, d, *J* = 8.1 Hz, $Ar_{DMB}\underline{H}$), 5.78 (1H, ddt, *J* = 17.0, 10.2, 6.7 Hz, C9$\underline{H}$), 5.72-5.67 (1H, m, C19($\underline{H}$)OR), 5.09 (1H, br. s, C15=C$\underline{H_a}H_b$), 5.04 (1H br. s, C15=C$H_a\underline{H_b}$), 4.99 (1H, br. dq, *J* = 17.0, 1.6 Hz, C9(H)=C$\underline{H_a}H_b$), 4.93 (1H, br. dq, *J* = 10.2, 1.6 Hz, C9(H)=C$H_a\underline{H_b}$), 4.72 (1H, d, *J* = 10.2 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.46 (1H, d, *J* = 11.4 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.38 (2H, br. s, OCC$\underline{H_a}H_bAr_{PMB}$, OCC$H_a\underline{H_b}Ar_{PMB}$), 4.32 (1H, d, *J* = 10.2 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.22 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 3.88-3.81 (2H, m, C13$\underline{H}$, C23$\underline{H}$), 3.83 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.82 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.71 (1H, d, *J* = 6.6 Hz, C16$\underline{H}$), 3.58-3.54 (1H, obs. m, C17$\underline{H}$), 3.56 (2H, t, *J* = 6.5 Hz, C27$\underline{H_2}$), 3.47 (3H, s, C19(H)$O_2$C(O$\underline{Me}$)(Ph)($CF_3$)), 2.80 (1H, dd, *J* = 17.2, 7.9 Hz, C20$\underline{H_a}H_b$), 2.67 (1H, dd, *J* = 17.0, 4.6 Hz, C20$H_a\underline{H_b}$), 2.66 (1H, dd, *J* = 16.2, 7.4 Hz, C22$\underline{H_a}H_b$), 2.38 (1H, dd, *J* = 16.2, 4.9 Hz, C22$H_a\underline{H_b}$), 2.16-1.92 (4H, obs. m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.67 (1H, ddd, *J* = 14.9, 8.4, 2.0, C18$\underline{H_a}H_b$), 1.65-1.60 (1H, obs. m, C12$\underline{H}$), 1.56-1.52 (1H, obs. m, C18$H_a\underline{H_b}$), 1.54-1.17 (8H, m, C11$\underline{H_a}H_b$, C11$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.88 (9H, s, Si$^t$B$\underline{u}Me_2$), 0.87 (9H, s, Si$^t$B$\underline{u}Me_2$), 0.81 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.04 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.03 (6H, s, Si$^t$Bu$\underline{Me_2}$), 0.02 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$).

**MOSHER ESTER 77R**

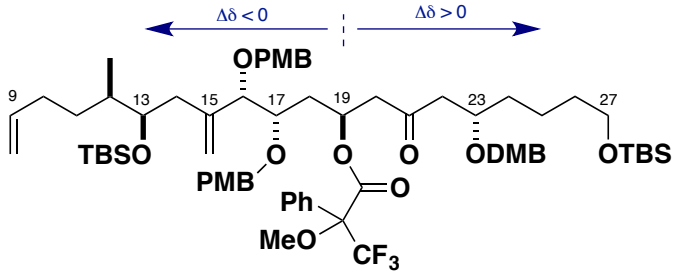



To a stirred solution of alcohol **77** (3.0 mg, 2.9 µmol) in $CH_2Cl_2$ (300 µL) and pyridine (50 µL) at –40 ºC was added (*S*)-Mosher acid chloride (2 drops). After 40 min, the crude residue was purified by direct column chromatography (17:3 PE/EtOAc) to afford (*R*)-Mosher ester **77R** (2.1 mg, 1.8 µmol, 62%) as a colourless oil.

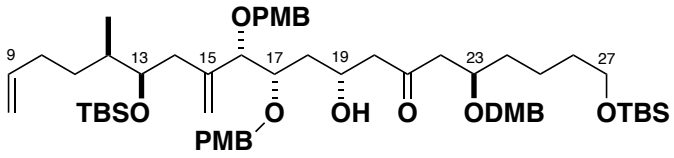
**$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.52 (2H, br. d, *J* = 7.3 Hz, $Ar_{Ph}\underline{H}$), 7.36-7.32 (3H, m, $Ar_{Ph}\underline{H}$), 7.24 (2H, d, *J* = 8.3, $Ar_{PMB}\underline{H}$), 7.22 (2H, d, *J* = 8.3, $Ar_{PMB}\underline{H}$), 6.87-6.74 (7H, m, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.82-5.73 (2H, m, C9$\underline{H}$, C19($\underline{H}$)OR), 5.14 (1H, br. s, C15=C$\underline{H_a}H_b$), 5.05 (1H br. s, C15=C$H_a\underline{H_b}$), 4.99 (1H, br. d, *J* = 17.0 Hz, C9(H)=C$\underline{H_a}H_b$), 4.93 (1H, br. d, *J* = 10.2 Hz, C9(H)=C$H_a\underline{H_b}$), 4.73 (1H, d, *J* = 10.4 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.50 (1H, d, *J* = 10.6 Hz, OC$\underline{H_a}H_bAr_{DMB}$), 4.44 (1H, d, *J* = 10.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.38 (2H, br. s, OC$\underline{H_a}H_bAr_{PMB}$, OC$H_a\underline{H_b}Ar_{PMB}$), 4.26 (1H, d, *J* = 10.6 Hz, OC$H_a\underline{H_b}Ar_{DMB}$), 3.89-3.81 (1H, obs. m, C13$\underline{H}$), 3.83 (6H, br. s, $Ar_{DMB}O\underline{Me}$), 3.81-3.77 (1H, obs. m, C23$\underline{H}$), 3.80 (6H, br. s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.76 (1H, d, *J* = 6.6 Hz, C16$\underline{H}$), 3.62-3.59 (1H, obs. m, C17$\underline{H}$), 3.56 (2H, t, *J* = 6.5 Hz, C27$\underline{H_2}$), 3.45 (3H, s, C19(H)$O_2$C($O\underline{Me}$)(Ph)($CF_3$)), 2.79 (1H, dd, *J* = 17.1, 8.0 Hz, C20$\underline{H_a}H_b$), 2.62-2.54 (2H, m, C20$H_a\underline{H_b}$, C22$\underline{H_a}H_b$), 2.26 (1H, dd, *J* = 16.2, 3.9 Hz, C22$H_a\underline{H_b}$), 2.18-1.92 (4H, obs. m, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 1.74 (1H, br. dd, *J* = 14.6, 8.2, C18$\underline{H_a}H_b$), 1.66-1.20 (9H, obs. m, C11$\underline{H_a}H_b$, C11$H_a\underline{H_b}$, C12$\underline{H}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 1.61-1.57 (1H, obs. m, C18$H_a\underline{H_b}$), 0.88 (9H, s, Si$^t\underline{Bu}Me_2$), 0.87 (9H, s, Si$^t\underline{Bu}Me_2$), 0.81 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.05-0.02 (12H, m, Si$^t$Bu$\underline{Me_2}$).

**MOSHER ESTER ANALYSIS OF 77S AND 77R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C9H | 5.78 | obs. | - |
| C9(H)=C$H_aH_b$ | 4.99 | 4.99 | 0.00 |
| C9(H)=C$H_aH_b$ | 4.93 | 4.93 | 0.00 |
| C10$H_aH_b$, C10$H_aH_b$ | obs. | obs. | - |
| C11$H_aH_b$, C11$H_aH_b$ | obs. | obs. | - |
| C12H | 1.63 | obs. | - |
| C12(H)Me | 0.81 | 0.81 | 0.00 |
| C13H | obs. | 3.85 | - |
| C14$H_aH_b$, C14$H_aH_b$ | obs. | obs. | - |
| C15=C$H_aH_b$ | 5.09 | 5.14 | –0.05 |
| C15=C$H_aH_b$ | 5.04 | 5.05 | –0.01 |
| C16H | 3.71 | 3.76 | –0.05 |
| C17H | 3.56 | 3.61 | –0.05 |
| C18C$H_aH_b$ | 1.67 | 1.74 | –0.07 |
| C18C$H_aH_b$ | 1.54 | 1.59 | –0.05 |
| C19(H)OR | 5.70 | obs. | - |
| C20C$H_aH_b$ | 2.80 | 2.79 | +0.01 |
| C20C$H_aH_b$ | 2.67 | 2.62-2.54 | +ve |
| C22C$H_aH_b$ | 2.66 | 2.62-2.54 | +ve |
| C22C$H_aH_b$ | 2.38 | 2.26 | +0.12 |
| C23H | 3.88-3.81 | 3.81-3.77 | +ve |



**ALDOL PRODUCT 79**

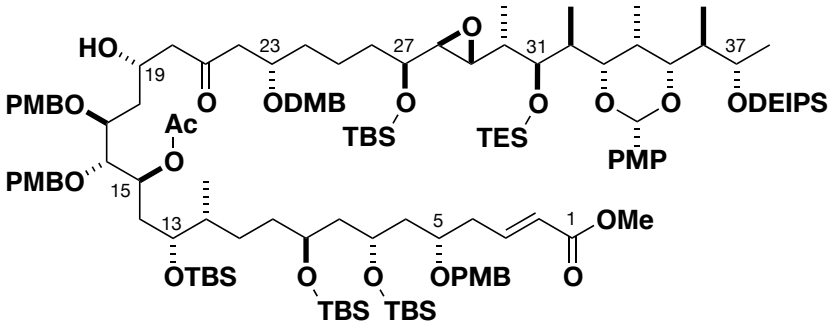



**$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.24 (2H, d, *J* = 8.7, $Ar_{PMB}\underline{H}$), 7.19 (2H, d, *J* = 8.7, $Ar_{PMB}\underline{H}$), 6.87-6.80 (6H, m, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.78 (1H, d, *J* = 7.9 Hz, $Ar_{DMB}\underline{H}$), 5.77 (1H, ddt, *J* = 17.0, 10.3, 6.7 Hz, C9$\underline{H}$), 5.17 (1H, br. s, C15=C$\underline{H_a}H_b$), 5.07 (1H br. s, C15=C$H_a\underline{H_b}$), 4.98 (1H, dd, *J* = 17.0, 1.5 Hz, C9(H)=C$\underline{H_a}H_b$), 4.92 (1H, dd, *J* = 10.0, 1.4 Hz, C9(H)=C$H_a\underline{H_b}$), 4.77 (1H, d, *J* = 10.9 Hz, OC$\underline{H_a}H_bAr_{PMB}$), 4.52 (1H, d, *J* = 11.4 Hz, OCC$\underline{H_a}H_bAr_{PMB}$), 4.49 (1H, d, *J* = 10.9 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.42 (2H, br. s, OC$\underline{H_a}H_bAr_{DMB}$, OC$H_a\underline{H_b}Ar_{DMB}$), 4.24 (1H, d, *J* = 11.4 Hz, OC$H_a\underline{H_b}Ar_{PMB}$), 4.12-4.04 (1H, m, C19$\underline{H}$), 3.90-3.85 (3H, obs. m, C13$\underline{H}$, C16$\underline{H}$, C23$\underline{H}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.81-3.74 (1H, obs. m, C17$\underline{H}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.58 (2H, t, *J* = 6.3 Hz, C27$\underline{H_2}$), 3.54 (1H, br. s, C19(H)O$\underline{H}$), 2.70 (1H, dd, *J* = 16.3, 7.4 Hz, C22$\underline{H_a}H_b$), 2.50 (1H, dd, *J* = 16.6, 8.3 Hz, C20$\underline{H_a}H_b$), 2.46 (1H, dd, *J* = 16.3, 4.9 Hz, C22$H_a\underline{H_b}$), 2.34 (1H, dd, *J* = 16.6, 3.9 Hz, C20$H_a\underline{H_b}$), 2.18-2.04 (3H, m, C10$\underline{H_a}H_b$,C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$), 2.00-1.91 (1H, m, C10$H_a\underline{H_b}$), 1.68-1.21 (11H, m, C11$\underline{H_a}H_b$, C11$H_a\underline{H_b}$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$), 0.89 (18H, br. s, Si$^t\underline{Bu}Me_2$), 0.83 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.06 (3H, s, Si$^t$Bu$\underline{Me_a}Me_b$), 0.04 (6H, s, Si$^t$Bu$\underline{Me_2}$), 0.03 (3H, s, Si$^t$Bu$Me_a\underline{Me_b}$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 209.2, 159.3, 159.2, 148.9, 148.6, 142.6, 139.1, 131.1, 130.4, 130.2, 129.9, 129.4, 120.3, 116.2, 114.3, 113.8, 113.7, 11.2, 110.9, 8.9, 77.3, 75.0, 74.0, 73.2, 71.5, 70.4, 66.5, 63.0, 55.9, 55.8, 55.3, 55.2, 50.7, 48.5, 37.7, 36.2, 34.2, 32.9, 32.6, 31.8, 26.0, 25.9, 21.6, 18.4, 18.1, 13.3, –4.0, –4.4, –5.3 (2C).

By comparison of the 1H NMR chemical shifts at C19 and C20 to compounds **77** and **78**, the C19 stereocentre in aldol product **79** was assigned as (*R*) as drawn. Compound **79** is the the C23 epimer of compound **78**.

### 4.2 C1-C38 Intermediates

#### ALDOL PRODUCT 90

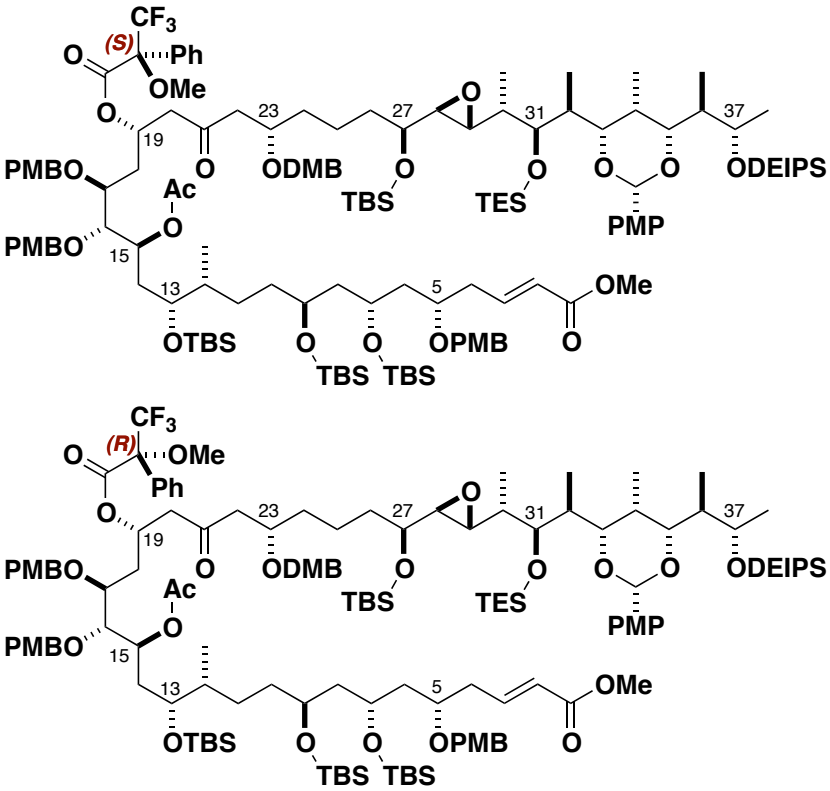



To a solution of dibutylboron triflate (26.4 µl, 105 µmol, freshly distilled) in $Et_2O$ (0.5 mL) at –78 ºC was added di-*iso*-propylethylamine (24.0 µl, 145 µmol). A solution of ketone **81** (86.8 mg, 80.8 µmol, dried azeotropically from PhH and stirred for 30 min over $CaH_2$ immediately prior to use) in $Et_2O$ (0.5 mL + 0.3 mL wash) was added dropwise and the mixture stirred for 45 min at –78 ºC to give a vivid yellow suspension. The mixture was cooled to –98 ºC and a solution of aldehyde **89** (145 mg, 121 µmol, dried azeotropically from PhH and stirred for 30 min over $CaH_2$ immediately prior to use) in $Et_2O$ (0.5 mL + 0.3 mL wash) was added dropwise down the side of the reaction vessel. The reaction was stirred at –98 ºC for 1 h before warming to –78 ºC for a further 4 h. The mixture was quickly transferred on to pH 7 buffer solution (2 mL) *via* pipette and the layers separated. The aqueous phase was extracted with EtOAc (5 × 5 mL) and the combined organic phases stirred over $SiO_2$ for 30 min. The mixture was filtered, concentrated *in vacuo* and purified by column chromatography (7:1 → 6.5:1 (mainly ketone) → 6:1 (mainly aldehyde) → 4:1 → 3:1 PE/EtOAc) to afford the product **90** (88.0 mg, 38.8 µmol, 3.5:1 dr, 48%) as a colourless oil, the diastereomers being separable on repeated chromatography. The reaction proceeded in 95% yield based on recovered ketone.

**$R_f$** 0.10 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.26-7.20 (6H, m, $Ar_{PMB}\underline{H}$), 6.98 (dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 6.89-6.79 (10H, m, $Ar_{PMP}\underline{H}$, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.77 (1H, d, *J* = 8.6 Hz, $Ar_{DMB}\underline{H}$), 5.87 (1H, d, *J* = 15.7 Hz, C2$\underline{H}$), 5.41 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.98 (1H, m, C15$\underline{H}$), 4.65 (1H, d, *J* = 10.7 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.61 (1H, d, *J* = 11.4 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.57 (1H, d, *J* = 11.4 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.49-4.36 (5H, m, $OC\underline{H_a}H_bAr_{PMB}$, $OCH_a\underline{H_b}Ar_{PMB}$, $OC\underline{H_a}H_bAr_{DMB}$, $OCH_a\underline{H_b}Ar_{DMB}$), 4.34 (1H, dq, *J* = 6.4, 3.4 Hz, C37$\underline{H}$), 4.29-4.23 (1H, m, C19$\underline{H}$), 4.21 (1H, br d, *J* = 5.4 Hz, C31$\underline{H}$), 3.93-3.86 (2H, m, C7$\underline{H}$, C23$\underline{H}$), 3.83 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.82 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.80-3.78 (2H, obs m, C9$\underline{H}$, C17$\underline{H}$), 3.79 (6H, 2 overlapping s, $Ar_{PMB}O\underline{Me}$), 3.77 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.71 (3H, s, $C1O_2\underline{Me}$), 3.68-3.60 (2H, m, C5$\underline{H}$, C13$\underline{H}$), 3.59 (1H, dd, *J* = 6.8, 3.3 Hz, C16$\underline{H}$), 3.57 (1H, br d, *J* = 10.4 Hz, C33$\underline{H}$), 3.42 (1H, ddd, *J* = 10.5, 1.4 Hz, C35$\underline{H}$), 3.26-3.21 (1H, m, C27$\underline{H}$), 3.04 (1H, br d, *J* = 2.2 Hz, C19(H)O$\underline{H}$), 2.72 (1H, dd, *J* = 15.6, 7.8 Hz, C22$\underline{H_a}H_b$), 2.71-2.69 (1H, obs m, C29$\underline{H}$), 2.63 (1H, dd, *J* = 6.5, 2.0 Hz, C28$\underline{H}$), 2.56 (1H, dd, *J* = 16.8, 2.5 Hz, C20$\underline{H_a}H_b$), 2.53-2.50 (1H, obs m, C4$\underline{H_a}H_b$), 2.50-2.46 (1H, m, C20$H_a\underline{H_b}$), 2.41 (1H, dd, *J* = 16.0, 4.3 Hz, C22$H_a\underline{H_b}$), 2.36 (1H, ddd, *J* = 7.4, 7.0, 7.0 Hz, C4$H_a\underline{H_b}$), 2.02 (1H, ddq, *J* = 10.4, 7.1, 3.4 Hz, C36$\underline{H}$), 1.95-1.87 (2H, obs m, C6$\underline{H_a}H_b$, C14$\underline{H_a}H_b$), 1.92 (3H, s, C15(H)O$\underline{Ac}$), 1.87-1.77 (3H, m, C6$H_a\underline{H_b}$, C14$H_a\underline{H_b}$, C32$\underline{H}$), 1.67-1.32 (15H, C8$\underline{H_a}H_b$, C8$H_a\underline{H_b}$, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$,

C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 1.23-1.12 (1H, m, C11$H_a\underline{H_b}$), 1.07 (3H, d, $J$ = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (24H, m, C30(H)$\underline{Me}$, Si($CH_2\underline{Me}$)$_2$$^i$Pr, Si($CH_2Me$)$_2$$^i\underline{Pr}$), Si($CH_2\underline{Me}$)$_3$), 0.92-0.85 (45H, m, C32(H)$\underline{Me}$, C34(H)$\underline{Me}$, C36(H)$\underline{Me}$, Si$^t\underline{Bu}Me_aMe_b$), 0.79 (3H, d, $J$ = 6.6 Hz, C12(H)$\underline{Me}$), 0.70-0.58 (10H, m, Si($C\underline{H_2}Me$)$_3$, Si($C\underline{H_2}Me$)$_2$$^i$Pr), 0.12 (3H, s, Si$\underline{Me_a}Me_b$$^t$Bu), 0.08 (3H, s, Si$\underline{Me_a}Me_b$$^t$Bu), 0.06 (3H, s, Si$\underline{Me_a}Me_b$$^t$Bu), 0.05-0.03 (15H, overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), [spin systems interrupted across C12-C13 and C32-C33 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_H$ 210.3, 170.2, 166.7, 159.5, 159.22, 159.19, 159.14, 148.9, 148.6, 145.8, 131.8, 130.9, 130.7, 130.6, 130.5, 129.8, 129.5, 129.3, 129.2, 127.1, 123.1, 120.4, 113.8, 113.7, 113.3, 111.2, 111.0, 100.6, 83.0, 82.0, 81.8, 75.8, 75.1, 74.6, 74.2, 73.7, 73.5, 73.0, 72.0, 71.8, 71.7, 70.8, 70.3, 67.5, 67.2, 64.2, 60.5, 58.3, 55.9, 55.8, 55.27, 55.25, 51.4, 51.4, 51.5, 51.4, 51.1, 42.8, 38.3, 37.7, 37.0, 36.7, 36.2, 36.2, 34.7, 34.5, 34.2, 34.1, 30.5, 29.7, 29.4, 26.0 (2C), 21.2, 21.1, 18.17, 18.11, 18.07, 18.03, 17.4, 17.2, 14.1, 13.1, 12.8, 8.5, 7.8, 7.22, 7.15, 7.13, 5.6, 5.5, 3.9, 3.8, –3.82, –3.86, –3.89, –4.0, –4.1, –4.2, –4.5, –5.0. **$[\alpha]_D^{20}$** +1.2 ($c$ = 0.40, $CHCl_3$). **IR** (thin film) 2955.9, 2855.7, 1733.6, 1729.6, 1716.9, 1613.2, 1515.5, 1461.5, 1249.2, 1034.3, 835.8, 775.0 cm$^{-1}$. **HRMS** (ES$^-$) Calculated for $C_{124}H_{210}O_{25}Si_6Cl$ $[M + Cl]^-$ 2302.3471, found 2302.3425.

**MOSHER ESTERS 90S AND 90R**




To separate solutions of aldol product **90** (6 mg, 2.6 μmol) in $CH_2Cl_2$ (0.5 mL) and pyridine (0.5 mL) was added either (*R*)- or (*S*)-MTPA-Cl (0.2 mL, 260 μmol, 0.13 M solution in $CH_2Cl_2$). When complete by TLC, the yellow solutions were quenched by the addition of $NaHCO_3$ solution (1 mL) and the layers separated. The aqueous phase was extracted with EtOAc (5 × 5 mL) and the combined organic phase dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The products were purified by column chromatography (5:1 PE/EtOAc) to afford Mosher esters **90S** and **90R** as colourless oils.

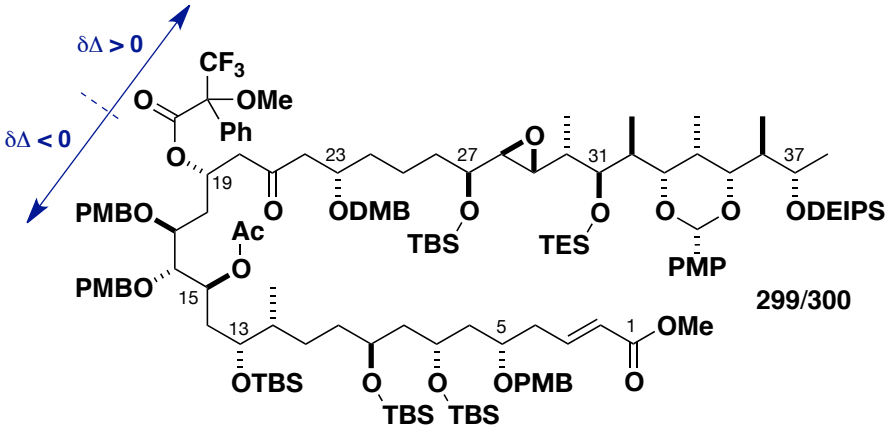
**90S: $^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.52-7.49 (2H, m, $Ar_{Ph}\underline{H}$), 7.39 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.35-7.31 (3H, m, $Ar_{Ph}\underline{H}$), 7.23 (2H, d, *J* = 8.7 Hz, $Ar_{PMB}\underline{H}$), 7.22 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 7.19 (2H, d, *J* = 8.6 Hz, $Ar_{PMB}\underline{H}$), 6.97 (1H, dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 6.88 (10H, m, $Ar_{PMP}\underline{H}$, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 6.75 (1H, d, *J* = 8.6 Hz, $Ar_{DMB}\underline{H}$), 5.86 (1H, d, *J* = 15.8 Hz, C2$\underline{H}$), 5.71-5.65 (1H, m, C19$\underline{H}$), 5.41 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.95-4.90 (1H, m, C15$\underline{H}$), 4.55 (1H, d, *J* = 10.4 Hz, $OC\underline{H_a}H_bAr_{PMB}$), 4.48-4.41 (4H, m, $OC\underline{H_a}H_bAr_{PMB}$, $OCH_a\underline{H_b}Ar_{PMB}$), 4.40-4.38 (2H, app br s, $OC\underline{H_a}H_bAr_{DMB}$, $OCH_a\underline{H_b}Ar_{DMB}$), 4.34 (1H, dq, *J* = 6.3, 3.4 Hz, C37$\underline{H}$), 4.25 (1H, d, *J* = 10.3 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.22 (1H, br d, *J* = 5.5 Hz, C31$\underline{H}$), 3.92-3.86 (1H, m, C7$\underline{H}$), 3.86-3.76 (2H, obs m, C9$\underline{H}$, C23$\underline{H}$), 3.82 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.81 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.79 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.74 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.71 (3H, s, $C1O_2\underline{Me}$), 3.60-3.56 (2H, m, C5$\underline{H}$, C16$\underline{H}$), 3.57 (1H, dd, *J* = 10.4, 1.6 Hz, C33$\underline{H}$), 3.55-3.52 (1H, m, C13$\underline{H}$), 3.52-3.50 (1H, m, C17$\underline{H}$), 3.47 (3H, s, $C19(H)O_2C(Ph)(CF_3)(O\underline{Me})$), 3.42 (1H, dd, *J* = 10.4, 1.6 Hz, C35$\underline{H}$), 3.26-3.20 (1H, m, C27$\underline{H}$), 2.84 (1H, dd, *J* = 17.2, 8.0 Hz, $C20\underline{H_a}H_b$), 2.74-2.65 (3H, m, $C20H_a\underline{H_b}$, $C22\underline{H_a}H_b$, C29$\underline{H}$), 2.60 (1H, dd, *J* = 6.6, 2.2 Hz, C28$\underline{H}$), 2.52-2.45 (1H, m, $C4\underline{H_a}H_b$), 2.41-2.25 (2H, m, $C4H_a\underline{H_b}$, $C22H_a\underline{H_b}$), 2.08-1.90 (3H, m, $C6\underline{H_a}H_b$, $C14\underline{H_a}H_b$, C36$\underline{H}$), 1.88 (3H, s, $C15(H)O\underline{Ac}$), 1.88-1.79 (3H, m, $C6H_a\underline{H_b}$, $C14H_a\underline{H_b}$, C32$\underline{H}$), 1.79-1.17 (16H, m,

C8$H_aH_b$, C8$H_a$$H_b$, C10$H_aH_b$, C10$H_a$$H_b$, C11$H_aH_b$, C11$H_a$$H_b$, C12H, C18$H_aH_b$, C18$H_a$$H_b$, C24$H_aH_b$, C24$H_a$$H_b$, C25$H_aH_b$, C25$H_a$$H_b$, C26$H_aH_b$, C26$H_a$$H_b$, C30H), 1.07 (3H, d, *J* = 6.3 Hz, C38$H_3$), 1.02-0.95 (21H, m, Si($CH_2$Me)$_2$$^i$Pr, Si($CH_2$Me)$_2$$^i$Pr), Si($CH_2$Me)$_3$), 0.93-0.82 (48H, m, C30(H)Me, C32(H)Me, C34(H)Me, C36(H)Me, Si$^t$BuMe$_2$), 0.74 (3H, d, *J* = 6.6 Hz, C12(H)Me), 0.69-0.58 (10H, m, Si($CH_2$Me)$_3$, Si($CH_2$Me)$_2$$^i$Pr), 0.11 (3H, s, Si$^t$BuMe$_a$Me$_b$), 0.07 (3H, s, Si$^t$BuMe$_a$Me$_b$), 0.03-0.01 (18H, m, Si$^t$BuMe$_a$Me$_b$, Si$^t$BuMe$_a$Me$_b$).

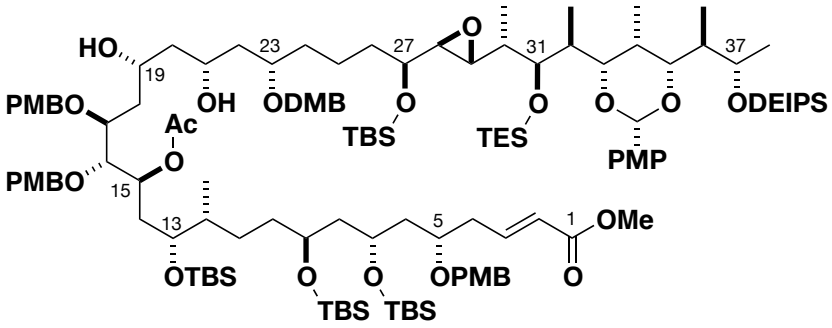
**90R: $^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.53-7.50 (2H, m, $Ar_{Ph}$H), 7.39 (2H, d, *J* = 8.6 Hz, $Ar_{PMP}$H), 7.35-7.31 (3H, m, $Ar_{Ph}$H), 7.25-7.21 (4H, m, $Ar_{PMB}$H), 7.20 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}$H), 6.97 (1H, dt, *J* = 15.5, 7.3 Hz, C3H), 6.89-6.77 (10H, m, $Ar_{PMP}$H, $Ar_{PMB}$H), $Ar_{DMB}$H), 6.75 (1H, d, *J* = 8.6 Hz, $Ar_{DMB}$H), 5.87 (1H, br d, *J* = 15.5 Hz, C2H), 5.77-5.71 (1H, m, C19H), 5.41 (1H, s, $O_2$CH$Ar_{PMP}$), 5.00-4.95 (1H, m, C15H), 4.59 (1H, d, *J* = 10.3 Hz, OC$H_aH_bAr_{PMB}$), 4.50 (2H, app br s, OC$H_aH_bAr_{DMB}$, OC$H_a$$H_b$$Ar_{DMB}$), 4.47 (1H, d, *J* = 11.3 Hz, OC$H_aH_bAr_{PMB}$), 4.41 (1H, d, *J* = 11.2 Hz, OC$H_aH_bAr_{PMB}$), 4.37 (2H, br s, OC$H_aH_bAr_{PMB}$, OC$H_a$$H_b$$Ar_{PMB}$), 4.35-4.31 (2H, m, OC$H_a$$H_b$$Ar_{PMB}$, C37H), 4.21 (1H, br d, *J* = 5.5 Hz, C31H), 3.92-3.86 (1H, m, C7H), 3.85-3.76 (4H, obs m, C9H, C23H), 3.82 (3H, s, $Ar_{DMB}$OMe), 3.81 (3H, s, $Ar_{DMB}$OMe), 3.794 (3H, s, $Ar_{PMP}$OMe), 3.785 (3H, s, $Ar_{PMB}$OMe), 3.784 (3H, s, $Ar_{PMB}$OMe), 3.74 (3H, s, $Ar_{PMB}$OMe), 3.71 (3H, s, C1$O_2$Me), 3.68-3.55 (5H, m, C5H, C13H, C16H, C17H, C33H), 3.43 (3H, s, C19(H)$O_2$C(Ph)($CF_3$)(OMe)), 3.42 (1H, obs dd, C35H), 3.26-3.21 (1H, m, C27H), 2.80 (1H, dd, *J* = 17.2 8.3 Hz, C20$H_aH_b$), 2.69 (1H, dd, *J* = 7.4, 2.1 Hz, C29H), 2.65-2.63 (1H, obs m, C20$H_a$$H_b$), 2.63-2.58 (2H, m, C22$H_aH_b$, C28H), 2.39-2.22 (3H, m, C4$H_aH_b$, C4$H_a$$H_b$, C22$H_a$$H_b$), 2.09-1.95 (3H, m, C6$H_aH_b$, C14$H_aH_b$, C36H), 1.95-1.76 (3H, m, C6$H_a$$H_b$, C14$H_a$$H_b$, C32H), 1.89 (3H, s, C15(H)OAc), 1.69-1.10 (16H, m, C8$H_aH_b$, C8$H_a$$H_b$, C10$H_aH_b$, C10$H_a$$H_b$, C11$H_aH_b$, C11$H_a$$H_b$, C12H, C18$H_aH_b$, C18$H_a$$H_b$, C24$H_aH_b$, C24$H_a$$H_b$, C25$H_aH_b$, C25$H_a$$H_b$, C26$H_aH_b$, C26$H_a$$H_b$, C30H), 1.07 (3H, d, *J* = 6.3 Hz, C38$H_3$), 1.02-0.95 (21H, m, Si($CH_2$Me)$_2$$^i$Pr, Si($CH_2$Me)$_2$$^i$Pr), Si($CH_2$Me)$_3$), 0.94-0.82 (48H, m, C30(H)Me, C32(H)Me, C34(H)Me, C36(H)Me, Si$^t$BuMe$_2$), 0.74 (3H, d, *J* = 6.6 Hz, C12(H)Me), 0.69-0.58 (10H, m, Si($CH_2$Me)$_3$, Si($CH_2$Me)$_2$$^i$Pr), 0.11 (3H, s, Si$^t$BuMe$_a$Me$_b$), 0.07 (3H, s, Si$^t$BuMe$_a$Me$_b$), 0.06-0.02 (18H, m, Si$^t$BuMe$_a$Me$_b$, Si$^t$BuMe$_a$Me$_b$).

**MOSHER ESTER ANALYSIS OF 90S AND 90R**[6]

| Proton | $\delta_S$ | $\delta_R$ | $\Delta\delta = \delta_S - \delta_R$ |
|---|---|---|---|
| C14$\underline{H_2}$ | 1.88, 1.80 | 1.88, 1.80 | 0.00, 0.00 |
| C15$\underline{H}$ | 4.93 | 4.98 | –0.05 |
| C15(H)$\underline{Ac}$ | 1.88 | 1.89 | –0.01 |
| C16$\underline{H}$ | 3.57 | 3.61 | –0.04 |
| C17$\underline{H}$ | 3.50 | 3.60 | –0.10 |
| C18$\underline{H_2}$ | 1.96, 1.75 | 2.02, 1.83 | –0.06, –0.08 |
| C19$\underline{H}$ | 5.68 | 5.74 | –0.06 |
| C20$H_2$ | 2.87, 2.75 | 2.82, 2.65 | +0.05, +0.10 |
| C21 | - | - | - |
| C22$\underline{H_2}$ | obs | obs | - |
| C23$\underline{H}$ | 3.87 | 3.83 | +0.04 |



**DIOL 91**

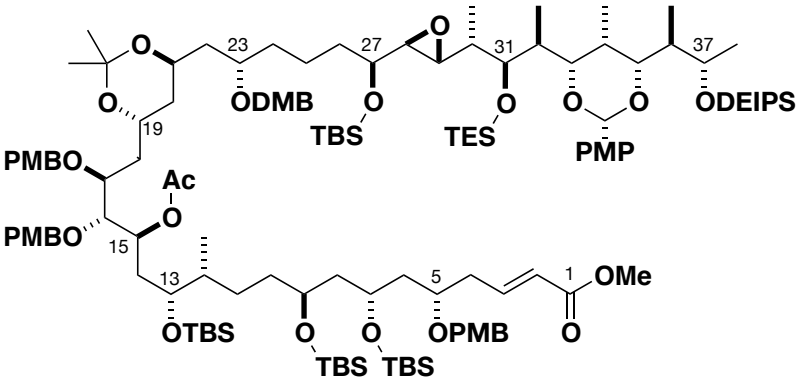



A solution of $Me_4NBH(OAc)_3$ (79.0 mg, 300 μmol) in MeCN (1 mL) and AcOH (1 mL) was prepared and stirred at rt for 30 min. The mixture was carefully cooled to –30 °C and a solution of aldol product **90** (68 mg, 30 μmol, dried azeotropically from PhH) in MeCN (1 mL + 1 mL wash) was added dropwise. The solution was stirred at –30 °C for 2 d and when the reaction was complete by TLC was poured onto a 1:1 mixture of $NaHCO_3$ and $Na^+/K^+$ tartrate solution (10 mL) washing with EtOAc (20 mL). The mixture was stirred rapidly at rt for 1 h and the layers separated. The aqueous phase was extracted with EtOAc (5 × 5 mL) and the combined organic phase dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The product was purified by column chromatography (4:1 → 2:1 → 1:1 PE/EtOAc) to afford the diol **91** (58.0 mg, 25.4 μmol, 85%) as a colourless oil. The relative stereochemistry was proved by preparation of acetonide **108**.

**$R_f$** 0.25 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.26-7.20 (6H, m, $Ar_{PMB}\underline{H}$), 6.98 (1H, dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 6.89-6.79 (11H, m, $Ar_{PMP}\underline{H}$, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.87 (1H, d, *J* = 15.7 Hz, C2$\underline{H}$), 5.41 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.99 (1H, m, C15$\underline{H}$), 4.67-4.58 (3H, m, $OC\underline{H_a}H_bAr_{PMB}$), 4.55 (1H, d, *J* = 11.2 Hz, $OCH_a\underline{H_b}Ar_{PMB}$), 4.45-4.37 (4H, m, $OC\underline{H_a}H_bAr_{PMB}$, $OCH_a\underline{H_b}Ar_{PMB}$, $OC\underline{H_a}H_bAr_{DMB}$, $OCH_a\underline{H_b}Ar_{DMB}$), 4.37-4.30 (1H, m, C37$\underline{H}$), 4.21 (1H, br d, *J* = 5.3 Hz, C31$\underline{H}$), 4.12-4.05 (1H, m, C21$\underline{H}$), 3.99 (1H, br s, O$\underline{H}$), 3.89-3.83 (2H, obs m, C7$\underline{H}$, C23$\underline{H}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.85 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.81-3.76 (2H, obs m, C9$\underline{H}$, C17$\underline{H}$), 3.79 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.78 (6H, 2 overlapping s, $Ar_{PMB}O\underline{Me}$), 3.76 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.71 (3H, s, C1$O_2\underline{Me}$), 3.69-3.60 (4H, m, C5$\underline{H}$, C13$\underline{H}$, C16$\underline{H}$, C19$\underline{H}$), 3.56 (1H, dd, *J* = 10.3, 1.4 Hz, C33$\underline{H}$), 3.42 (1H, dd, *J* = 10.4, 1.4 Hz, C35$\underline{H}$), 3.30 (1H, br d, *J* = 2.9 Hz, O$\underline{H}$), 3.28-2.23 (1H, m, C27$\underline{H}$), 2.71 (1H, dd, *J* = 7.4, 2.1 Hz, C29$\underline{H}$), 2.64 (1H, dd, *J* = 6.5, 2.1 Hz, C28$\underline{H}$), 2.53-2.46 (1H, m, C4$\underline{H_a}H_b$), 2.39-2.31 (1H, m, C4$H_a\underline{H_b}$), 2.02 (1H, ddq, *J* = 10.3, 7.0 3.4 Hz, C36$\underline{H}$), 1.98-1.88 (2H, obs m, C6$\underline{H_a}H_b$, C14$\underline{H_a}H_b$), 1.92 (3H, s, C15(H)O$\underline{Ac}$), 1.88-1.79 (3H, m, C6$H_a\underline{H_b}$, C14$H_a\underline{H_b}$, C32$\underline{H}$), 1.78-1.66 (3H, m, C20$\underline{H_a}H_b$, C22$\underline{H_a}H_b$, C22$H_a\underline{H_b}$), 1.65-1.28 (16H, m, C8$\underline{H_a}H_b$, C8$H_a\underline{H_b}$, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C20$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 1.21-1.13 (1H, C11$H_a\underline{H_b}$), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.01-0.95 (24H, m, C30(H)$\underline{Me}$, Si$(CH_2\underline{Me})_2{}^i$Pr, Si$(CH_2Me)_2{}^i\underline{Pr}$), Si$(CH_2\underline{Me})_3$), 0.93-0.82 (45H, m, C32(H)$\underline{Me}$, C34(H)$\underline{Me}$, C36(H)$\underline{Me}$, Si$^t\underline{Bu}Me_aMe_b$), 0.78 (3H, d, *J* = 6.4 Hz, C12(H)$\underline{Me}$), 0.69-0.57 (10H, m, Si$(C\underline{H_2}Me)_3$, Si$(C\underline{H_2}Me)_2{}^i$Pr), 0.12 (3H, s, Si$\underline{Me_a}Me_b{}^t$Bu), 0.07 (3H, s, Si$\underline{Me_a}Me_b{}^t$Bu), 0.06 (3H, s, Si$\underline{Me_a}Me_b{}^t$Bu), 0.05-0.02 (15H, overlapping s, Si$^t$Bu$\underline{Me_a}Me_b$, Si$^t$Bu$Me_a\underline{Me_b}$), [spin systems interrupted across C12-C13 and C32-C33 due to restricted rotation]. **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.3, 166.7, 159.5, 159.17, 159.13, 149.1, 148.7, 145.8, 131.8, 130.73, 130.67, 130.55, 130.45, 129.7, 129.5, 129.3, 127.1, 123.1, 120.4, 113.8, 113.72, 113.68, 113.3, 111.1, 111.0, 100.6, 83.0, 82.02, 81.98, 80.0, 74.6, 74.1, 73.8, 73.4, 72.9, 72.0, 70.8, 70.6, 70.3, 69.7, 67.5, 67.2, 65.5, 60.5, 58.5, 55.91, 55.86, 55.27, 55.26, 55.23, 51.4,

45.8, 43.7, 42.8, 42.4, 40.83, 40.76, 39.0, 37.7, 37.0, 36.7, 36.2, 34.9, 34.1, 33.6, 33.5, 31.9, 30.4, 29.7, 29.6, 29.5, 29.4, 29.2, 29.1, 26.0 (2C), 24.7, 21.1, 20.7, 18.2, 18.11, 18.07, 18.03, 17.4, 17.2, 14.1, 14.0, 13.1, 12.8, 8.6, 7.8, 7.2, 7.15, 7.14, 5.6, 5.5, 3.9, 3.8, –3.8, –3.9, –4.0, –4.10, –4.15, –4.5, –5.0. **$[\alpha]_D^{20}$** +0.4 (*c* = 1.1, $CHCl_3$). **IR** (thin film) 3443.0, 2929.5, 2856.4, 1730.3 (br), 1613.3, 1587.3, 1514.5, 1462.9, 1246.6, 1033.9, 834.4, 773.3 $cm^{-1}$.**HRMS** ($ES^+$) Calculated for $C_{124}H_{212}O_{25}Si_6Na$ $[M + Na]^+$ 2292.3826, found 2292.3790.

**ACETONIDE 108**

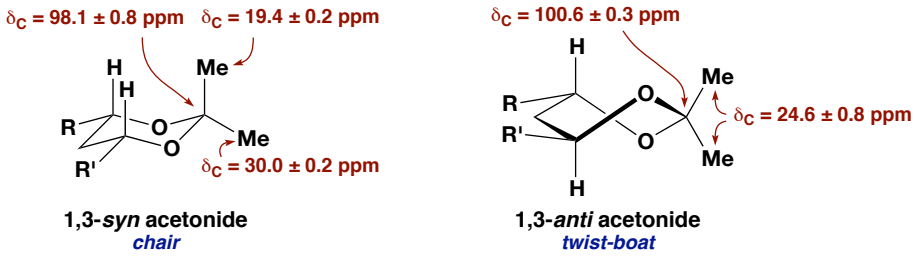



Diol **91** (9.8 mg, 4.3 µmol) was dissolved in $CH_2Cl_2$ (500 µL) and 2,2-dimethoxypropane (100 µL) at rt. Pyridinium *para*-toluenesulfonate (1 crystal) was added and the reaction stirred for 30 min until complete by TLC. The reaction was quenched by the addition of $NaHCO_3$ solution (1 mL) and the layers separated. The aqueous phase was extracted with $CH_2Cl_2$ (4 × 5 mL) and the combined organic phases dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (10:1 → 7:1 → 5:1 PE/EtOAc) to afford acetonide **108** (9.2 mg, 4.0 µmol, 92%) as a colourless oil.

**$R_f$** 0.73 (7:3 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.39 (2H, d, *J* = 8.7 Hz, $Ar_{PMP}\underline{H}$), 7.27-7.19 (6H, m, $Ar_{PMB}\underline{H}$), 6.98 (1H, dt, *J* = 15.7, 7.4 Hz, C3$\underline{H}$), 6.89-6.79 (11H, m, $Ar_{PMP}\underline{H}$, $Ar_{PMB}\underline{H}$, $Ar_{DMB}\underline{H}$), 5.87 (1H, d, *J* = 15.7 Hz, C2$\underline{H}$), 5.40 (1H, s, $O_2C\underline{H}Ar_{PMP}$), 4.98-4.94 (1H, m, C15$\underline{H}$), 4.71-4.53 (3H, m, $OC\underline{H_a}H_bAr_{PMB}$), 4.53-4.30 (6H, m, C37$\underline{H}$, $OCH_a\underline{H_b}Ar_{PMB}$, $OC\underline{H_a}H_bAr_{DMB}$, $OCH_a\underline{H_b}Ar_{DMB}$), 4.20 (1H, br d, *J* = 5.5 Hz, C31$\underline{H}$), 4.03-3.95 (1H, m, C21$\underline{H}$), 3.94-3.67 (3H, obs m, C9$\underline{H}$, C19$\underline{H}$, C23$\underline{H}$), 3.86 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.84 (3H, s, $Ar_{DMB}O\underline{Me}$), 3.80 (3H, s, $Ar_{PMP}O\underline{Me}$), 3.79 (6H, 2 overlapping s, $Ar_{PMB}O\underline{Me}$), 3.78 (3H, s, $Ar_{PMB}O\underline{Me}$), 3.75-3.70 (1H, obs m, C17$\underline{H}$), 3.71 (3H, s, C1$O_2\underline{Me}$), 3.68-3.53 (3H, obs m, C5$\underline{H}$, C13$\underline{H}$, C16$\underline{H}$), 3.56 (1H, dd, *J* = 10.5, 1.7 Hz, C33$\underline{H}$), 3.41 (1H, br d, *J* = 10.6 Hz, C35$\underline{H}$), 3.28-3.21 (1H, m, C27$\underline{H}$), 2.70 (1H, dd, *J* = 7.7, 2.2 Hz, C29$\underline{H}$), 2.61 (1H, dd, *J* = 6.6, 2.2 Hz, C28$\underline{H}$), 2.53-2.44 (1H, m, C4$\underline{H_a}H_b$), 2.39-2.25 (1H, m, C4$H_a\underline{H_b}$), 2.04-1.98 (1H, m, C36$\underline{H}$), 1.98-1.77 (5H, obs m, C6$\underline{H_a}H_b$, C6$H_a\underline{H_b}$, C14$\underline{H_a}H_b$, C14$H_a\underline{H_b}$, C32$\underline{H}$), 1.92 (3H, s, C15(H)O$\underline{Ac}$), 1.76-1.23 (19H, m, C8$\underline{H_a}H_b$, C8$H_a\underline{H_b}$, C10$\underline{H_a}H_b$, C10$H_a\underline{H_b}$, C11$\underline{H_a}H_b$, C12$\underline{H}$, C18$\underline{H_a}H_b$, C18$H_a\underline{H_b}$, C20$\underline{H_a}H_b$, C20$H_a\underline{H_b}$, C24$\underline{H_a}H_b$, C24$H_a\underline{H_b}$, C22$\underline{H_a}H_b$, C22$H_a\underline{H_b}$, C25$\underline{H_a}H_b$, C25$H_a\underline{H_b}$, C26$\underline{H_a}H_b$, C26$H_a\underline{H_b}$, C30$\underline{H}$), 1.28 (6H, br s, $O_2C\underline{Me_a}Me_b$, $O_2CMe_a\underline{Me_b}$), 1.07 (3H, d, *J* = 6.3 Hz, C38$\underline{H_3}$), 1.00-0.95 (21H, m, $Si(CH_2\underline{Me})_2{}^iPr$, $Si(CH_2Me)_2{}^i\underline{Pr}$), $Si(CH_2\underline{Me})_3$), 0.94-0.82 (48H, m, C30(H)$\underline{Me}$, C32(H)$\underline{Me}$, C34(H)$\underline{Me}$, C36(H)$\underline{Me}$, $Si^t\underline{Bu}Me_aMe_b$, 0.79 (3H, d, *J* = 6.7 Hz, C12(H)$\underline{Me}$), 0.69-0.58 (10H, m, $Si(C\underline{H_2}Me)_3$, $Si(C\underline{H_2}Me)_2{}^iPr$), 0.11 (3H, s, $Si^tBu\underline{Me_a}Me_b$), 0.08 (3H, s, $Si^tBuMe_a\underline{Me_b}$), 0.07-0.2 (18H, m, $Si^tBu\underline{Me_a}Me_b$,

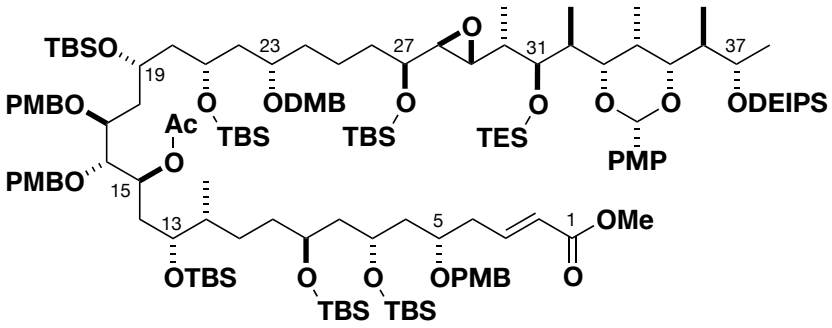
Si$^t$BuMe$_a$Me$_b$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.3, 166.7, 159.5, 159.2, 159.1, 148.9, 148.5, 145.8, 131.8, 131.5, 131.4, 130.8, 130.7, 130.5, 129.8, 129.7, 129.48, 129.46, 129.3, 129.2, 127.1, 123.1, 120.2, 113.8, 113.71, 113.66, 113.3, 111.14, 111.06, 111.0, 100.6, 100.2, 83.0, 82.0, 77.7, 77.6, 76.5, 75.8, 74.6, 74.4, 73.7, 73.1, 72.1, 70.8, 70.5, 70.3, 67.5, 67.2, 63.8, 63.1, 63.8, 63.1, 60.6, 60.4, 58.3, 55.9, 55.8, 55.3, 55.2, 51.4, 45.8, 42.5, 40.7, 40.3, 39.2, 386, 37.8, 37.1, 36.8, 36.2, 35.0, 34.6, 34.2, 30.5, 29.8, 29.3, 26.0 (2C), 24.9, 24.8, 21.4, 21.1, 18.2, 18.10, 18.07, 18.04, 17.4, 17.2, 14.3, 14.2, 13.1, 12.8, 8.5, 7.8, 7.22, 7.15, 7.13, 5.6, 5.5, 3.9, 3.8, –3.8, –3.9, –4.0, –4.1, –4.2, –4.5, –5.0.

The $\delta_C$ = 110.6, 24.9 and 24.8 ppm signals are consistent with an 1,3-*anti* relationship between C19 and C21 (twist-boat conformation of the acetonide).




*Empirical $^{13}$C NMR chemical shifts for acetonides – Rychnovsky method*[14]

**TBS ETHER 92**

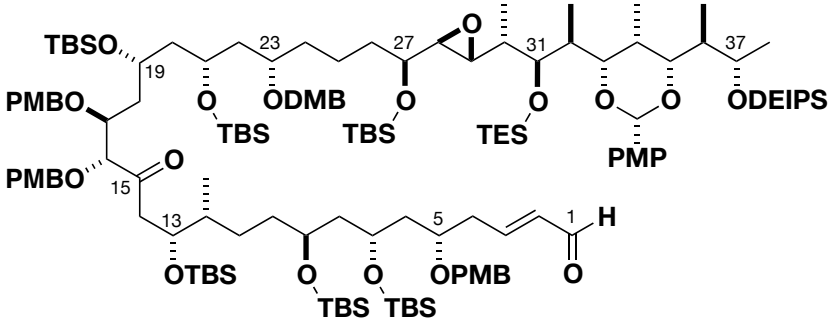



Diol **91** (30.0 mg, 13.2 µmol, dried azeotropically from PhH) was dissolved in $CH_2Cl_2$ (1 mL) and 2,6-lutidine (7.5 µL, 6.60 µmol) was added. The solution was cooled to –78 ºC and TBSOTf (9.1 µL, 39.6 µmol) added slowly. After 30 min, the reaction was quenched by the careful addition of MeOH (0.1 mL) and $NaHCO_3$ solution (3 mL). The layers were separated and the aqueous phase was extracted with $CH_2Cl_2$ (5 × 5 mL). The combined organic phases dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The product was purified by column chromatography (15:1 → 10:1 → 8:1 PE/EtOAc) to give silyl ether **92** (32.1 mg, 12.8 µmol, 98%) as a colourless oil.

**$R_f$** 0.21 (9:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 7.40 (2H, d, *J* = 8.7 Hz, Ar$_{PMP}$H), 7.24 (2H, d, *J* = 8.5 Hz, Ar$_{PMB}$H), 7.23 (2H, d. *J* = 8.5 Hz, Ar$_{PMB}$H), 7.19 (2H, d, *J* = 8.6 Hz, Ar$_{PMB}$H), 6.98 (1H, dt, *J* = 15.5, 7.3 Hz, C3H), 6.89-6.82 (8H, m, Ar$_{PMP}$H, Ar$_{PMB}$H, Ar$_{DMB}$H), 6.80-6.76 (3H, m, Ar$_{PMB}$H, Ar$_{DMB}$H), 5.87 (1H, dt, *J* = 15.5, 1.3 Hz, C2H), 5.41 (1H, s, $O_2$CHAr$_{PMP}$), 5.04-4.99 (1H, m, C15H), 4.64 (1H, d, *J* = 10.7 Hz, OCH$_a$H$_b$Ar$_{PMB}$), 4.55 (2H, app br d, OCH$_a$H$_b$Ar$_{PMB}$), 4.49-4.38 (4H, m, OCH$_a$H$_b$Ar$_{PMB}$, OCH$_a$H$_b$Ar$_{DMB}$,), 4.36-4.31 (2H, m,

$OCH_aH_bAr_{DMB}$, C37H), 4.20 (1H, br d, *J* = 5.6 Hz, C31H), 3.94-3.87 (2H, m, C19H, C21H), 3.86-3.81 (1H, obs m, C7H), 3.84 (3H, s, $Ar_{DMB}OMe$), 3.80 (3H, s, $Ar_{DMB}OMe$), 3.792 (3H, s, $Ar_{PMP}OMe$), 3.787 (3H, s, $Ar_{PMB}OMe$), 3.75-3.70 (2H, obs m, C9H, C17H), 3.72 (6H, 2 overlapping s, $Ar_{PMB}OMe$), 3.70-3.58 (4H, m, $C1O_2Me$, C5H, C13H, C16H), 3.56 (1H, dd, *J* = 10.3, 1.5 Hz, C33H), 3.52-3.46 (1H, m, C23H), 3.41 (1H, dd, *J* = 10.6, 1.6 Hz, C35H), 3.24-3.18 (1H, m, C27H), 2.66 (1H, dd, *J* = 7.9, 2.1 Hz, C29H), 2.58 (1H, dd, *J* = 6.8, 2.1 Hz, C28H), 2.52-2.45 (1H, m, $C4H_aH_b$), 2.38-2.30 (1H, m, $C4H_aH_b$), 2.04-1.98 (1H, m, C36H), 1.95-1.89 (1H, obs m, $C14H_aH_b$), 1.90 (3H, s, C15(H)OAc), 1.89-1.79 (4H, m, $C6H_aH_b$, $C6H_aH_b$, $C14H_aH_b$, C32H), 1.79-1.28 (19H, m, $C8H_aH_b$, $C8H_aH_b$, $C10H_aH_b$, $C10H_aH_b$, $C11H_aH_b$, C12H, $C18H_aH_b$, $C18H_aH_b$, $C20H_aH_b$, $C20H_aH_b$, $C24H_aH_b$, $C24H_aH_b$, $C22H_aH_b$, $C22H_aH_b$, $C25H_aH_b$, $C25H_aH_b$, $C26H_aH_b$, $C26H_aH_b$, C30H), 1.07 (3H, d, *J* = 6.3 Hz, $C38H_3$), 1.01-0.95 (21H, $Si(CH_2Me)_2{}^iPr$, $Si(CH_2Me)_2{}^iPr$), $Si(CH_2Me)_3$), 0.92-0.81 (66H, m, C30(H)Me, C32(H)Me, C34(H)Me, C36(H)Me, $Si^tBuMe_aMe_b$), 0.78 (3H, d, *J* = 6.7 Hz, C12(H)Me), 0.68-0.58 (10H, m, $Si(CH_2Me)_3$, $Si(CH_2Me)_2{}^iPr$), 0.11 (3H, s, $Si^tBuMe_aMe_b$), 0.08-0.05 (9H, 3 overlapping s, $Si^tBuMe_aMe_b$, $Si^tBuMe_aMe_b$), 0.05-0.01 (24H, m, $Si^tBuMe_aMe_b$, $Si^tBuMe_aMe_b$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 170.0, 166.7, 159.5, 159.15, 159.13, 159.0, 148.9, 148.3, 145.8, 131.8, 131.7, 131.0, 130.6, 130.5, 129.4, 129.3, 129.1, 127.1, 123.1, 120.1, 113.8, 113.7, 113.6, 113.3, 111.0, 110.9, 100.6, 83.0, 81.8, 81.5, 76.5, 76.3, 74.6, 73.6, 73.2, 72.6, 71.9, 71.7, 70.83, 70.81, 70.3, 67.8, 67.5, 67.3, 67.2, 60.7, 60.4, 58.5, 55.9, 55.8, 55.3, 55.24, 55.16, 51.4, 47.4, 45.8, 42.9, 42.62, 42.60, 40.7, 39.9, 37.7, 37.1, 36.5, 36.3, 35.1, 34.8, 34.4, 30.5, 29.7, 29.6, 26.03, 25.97, 25.94, 22.0, 21.1, 18.2, 18.08, 18.06, 18.03, 18.01, 17.4, 17.2, 14.5, 14.2, 13.1, 12.6, 8.4, 7.8, 7.2, 7.14, 7.13, 5.6, 5.4, 3.9, 3.8, –3.5, –3.8, –3.89, –3.94, –3.96, –4.1, –4.2, –4.6, –5.0.

**ENAL 93**




Ester **92** (6.5 mg, 2.6 µmol, dried azeotropically from PhH) was dissolved in $CH_2Cl_2$ (1 mL) and cooled to –78 ºC. DIBAL (21 µL, 21 µmol) was added dropwise. When complete by TLC (30 min - *n.b.* the slower saponification at C15 does not change the $R_f$), MeOH (0.5 mL) was added at –78 ºC and the mixture diluted with $Na^+/K^+$ tartrate solution (2 mL). After stirring vigorously for 30 min, the layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (4 × 10 mL). The combined organic phases were dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The crude residue was dissolved in $CH_2Cl_2$ (1 mL) and $NaHCO_3$ powder (2.1 mg, 26 µmol) and Dess–Martin periodinane (4.4 mg, 10.4 µmol) added sequentially. The reaction was complete by TLC after 40 min (*n.b.* change in oxidation level at C15 does not affect $R_f$). The reaction was quenched by the addition of $Na_2S_2O_3$ solution (1 mL) and the mixture stirred for 15 min. The layers were separated and the aqueous phase extracted with $CH_2Cl_2$ (5 × 10 mL). The combined organic phases were

dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (10:1 → 3:1 PE/EtOAc) to afford enal **93** (5.8 mg, 2.3 µmol, 90%) as a colourless oil.

**$R_f$** 0.54 (4:1 PE/EtOAc). **$^1$H NMR** (500 MHz, $CHCl_3$) $\delta_H$ 9.45 (1H, d, *J* = 8.1 Hz, C1HO), 7.39 (1H, d, *J* = 8.6 Hz, $Ar_{PMP}$H), 7.26-7.21 (4H, m, $Ar_{PMB}$H), 7.12 (2H, d, *J* = 8.5 Hz, $Ar_{PMB}$H), 6.88-6.83 (8H, m, $Ar_{PMP}$H, $Ar_{PMB}$H, $Ar_{DMB}$H), 6.83-6.79 (1H, obs m, C3H), 6.79-6.75 (3H, m, $Ar_{DMB}$H, $Ar_{PMB}$H), 6.12 (1H, dd, *J* = 15.6, 8.1 Hz, C2H), 5.41 (1H, s, $O_2$CH$Ar_{PMP}$), 4.63 (1H, d, *J* = 11.3 Hz, OC$H_aH_bAr_{PMB}$), 4.51 (1H, d, *J* = 11.2 Hz, OC$H_aH_bAr_{PMB}$), 4.48-4.28 (8H, m, OC$H_aH_bAr_{PMB}$, OC$H_aH_bAr_{PMB}$, OC$H_aH_bAr_{DMB}$, OC$H_aH_bAr_{DMB}$), 4.27-4.22 (1H, m, C37H), 4.20 (1H, br. d, *J* = 5.4 Hz, C31H), 3.97-3.90 (2H, obs. m, C19H, C21H), 3.90-3.80 (2H, obs m, C7H, C9H, C17H), 3.84 (3H, s, $Ar_{DMB}$OMe), 3.83 (3H, s, $Ar_{DMB}$OMe), 3.80-3.70 (9H, m, C5H, C9H, C16H, $Ar_{PMB}$OMe), 3.79 (6H, 2 overlapping s, $Ar_{PMP}$OMe, $Ar_{PMB}$OMe), 3.77 (3H, s, $Ar_{PMB}$OMe), 3.72 (3H, s, C1$O_2$Me), 3.56 (1H, br d, *J* = 10.3 Hz, C33H), 3.51-3.44 (1H, m, C23H), 3.41 (1H, br d, *J* = 10.5 Hz, C35H), 3.24-3.19 (1H, m, C27H), 3.01 (1H, dd, *J* = 18.1, 7.9 Hz, C14$H_aH_b$), 2.67 (1H, dd, *J* = 7.7, 1.8 Hz, C29H), 2.62 (1H, dd, *J* = 12.0, 5.8 Hz, C4$H_aH_b$), 2.59 (1H, dd, *J* = 6.5, 1.8 Hz, C28H), 2.49-2.40 (1H, m, C4$H_aH_b$), 2.36-2.27 (1H, m, C14$H_aH_b$), 2.07-1.97 (2H, m, C36H), 1.95-1.76 (3H, m, C6$H_aH_b$, C6$H_aH_b$, C32H), 1.73-1.23 (19H, m, C8$H_aH_b$, C8$H_aH_b$, C10$H_aH_b$, C10$H_aH_b$, C11$H_aH_b$, C12H, C18$H_aH_b$, C18$H_aH_b$, C20$H_aH_b$, C20$H_aH_b$, C24$H_aH_b$, C24$H_aH_b$, C22$H_aH_b$, C22$H_aH_b$, C25$H_aH_b$, C25$H_aH_b$, C26$H_aH_b$, C26$H_aH_b$, C30H), 1.07 (3H, d, *J* = 6.3 Hz, C38$H_3$), 1.01-0.94 (21H, m, Si($CH_2$Me)$_2$$^i$Pr, Si($CH_2$Me)$_2$$^i$Pr), Si($CH_2$Me)$_3$), 0.92-0.81 (66H, m, C30(H)Me, C32(H)Me, C34(H)Me, C36(H)Me, Si$^t$BuMe$_a$Me$_b$), 0.73 (3H, d, *J* = 6.5 Hz, C12(H)Me), 0.69-0.57 (10H, m, Si($CH_2$Me)$_3$, Si($CH_2$Me)$_2$$^i$Pr), 0.11 (3H, s, Si$^t$BuMe$_a$Me$_b$), 0.09-0.00 (33H, m, Si$^t$BuMe$_a$Me$_b$, Si$^t$BuMe$_a$Me$_b$). **$^{13}$C NMR** (125 MHz, $CHCl_3$) $\delta_C$ 211.6, 193.8, 159.5, 159.4, 159.3, 159.1, 154.9, 148.8, 148.3, 134.8, 131.9, 131.6, 130.3, 129.9, 129.4, 129.33, 129.27, 128.3, 127.1, 120.1, 113.9, 113.8, 113.7, 113.3, 110.94, 110.92, 100.6, 83.0, 81.9, 77.6, 76.1, 74.6, 74.4, 73.1, 72.9, 72.5, 72.4 71.1, 70.84, 70.80, 70.31, 67.6, 67.5, 67.2, 67.1, 60.7, 58.5, 55.9, 55.8, 55.3, 55.24, 55.21, 55.17, 47.0, 45.7, 43.0, 42.8, 42.7 42.6, 40.7, 39.5, 39.2, 37.7, 37.5, 36.7, 35.1, 34.7, 30.5, 29.7, 27.1, 26.01, 26.00, 25.97, 25.93, 21.8, 18.2, 18.12, 18.08, 18.05, 18.03, 18.00, 17.4, 17.2, 14.6, 14.5, 13.1, 8.5, 7.8, 7.22, 7.15, 7.14, 5.6, 5.4, 3.9, 3.8, –3.5, –3.73, –3.76, –3.84, –3.9, –4.0, –4.17, –4.20, –4.7, –5.0. **$[\alpha]_D^{20}$** +8.5 (*c* = 0.63, $CHCl_3$). **IR** (thin film) 2928.1, 2856.2, 1737.1, 1714.3, 1695.5, 1613.5, 1249.4, 1080.0, 1036.2, 827.0, 774.4 $cm^{-1}$.

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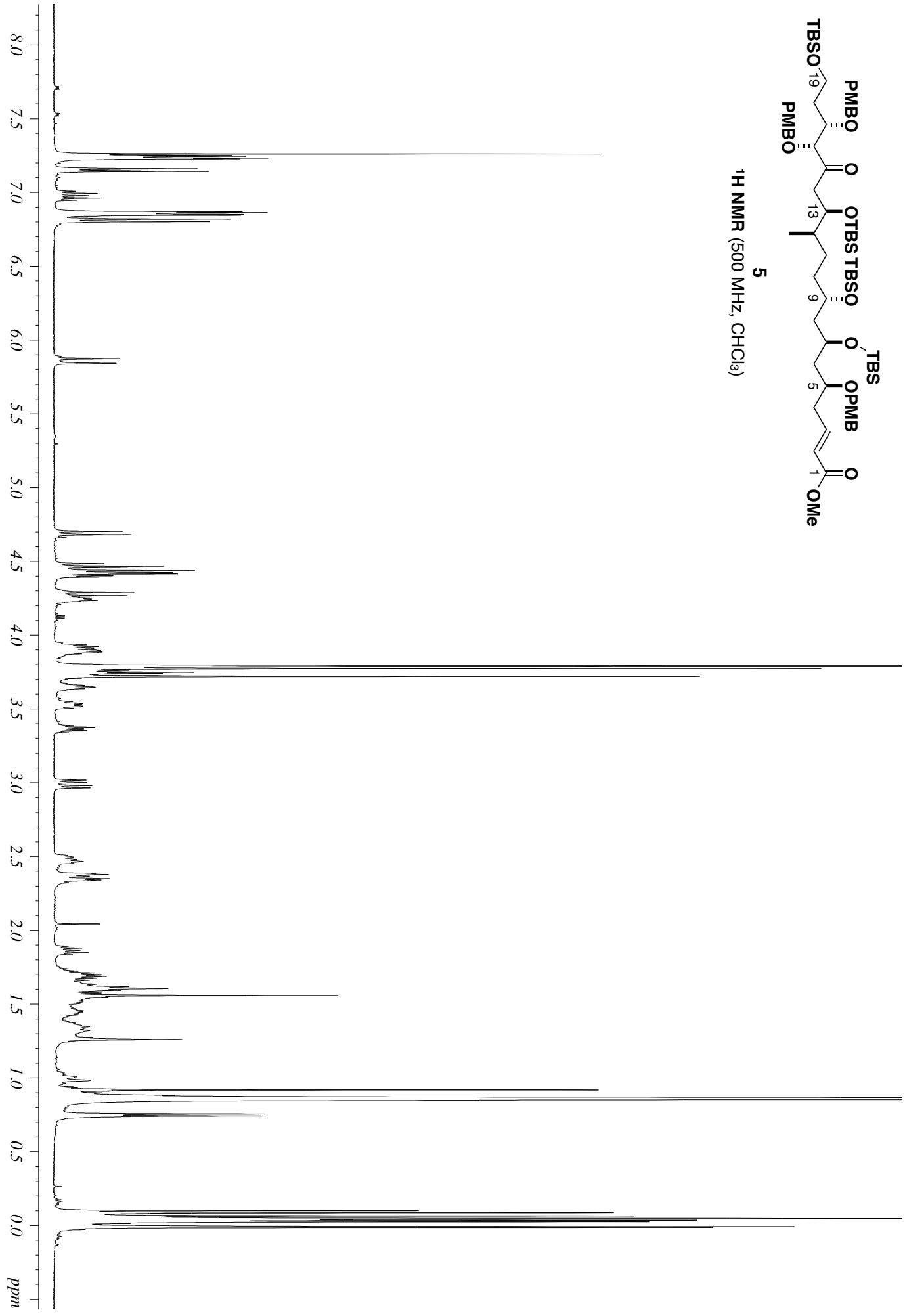
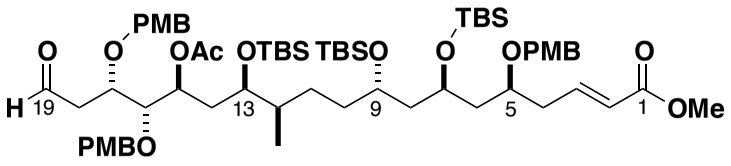
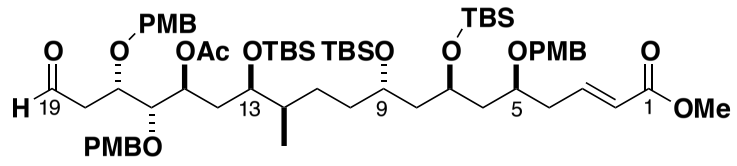
## 6. Selected NMR Spectra





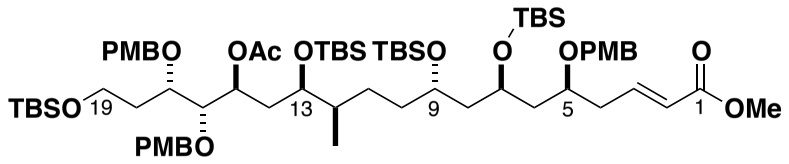

**81**

**$^1$H NMR** (500 MHz, $CHCl_3$)



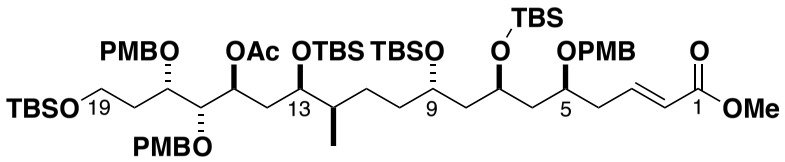

**81**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



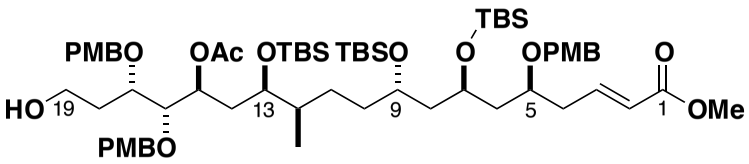

**83**

**$^1$H NMR** (500 MHz, $CHCl_3$)



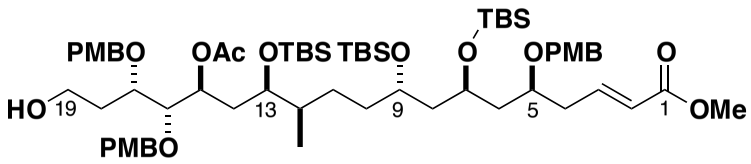

**83**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



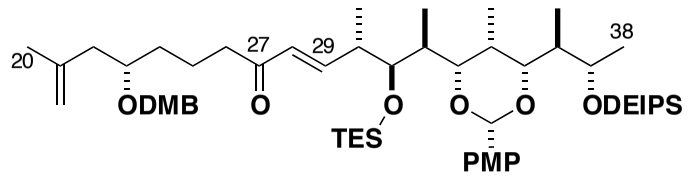

**84**

**$^1$H NMR** (500 MHz, $CHCl_3$)



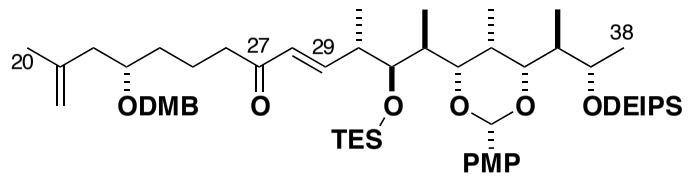

**84**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



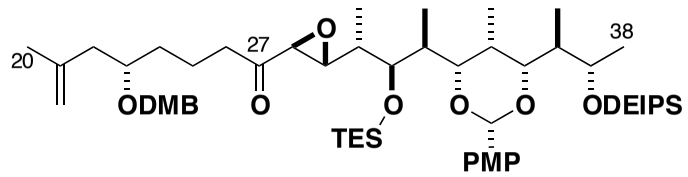

**85**

**$^1$H NMR** (500 MHz, $CHCl_3$)



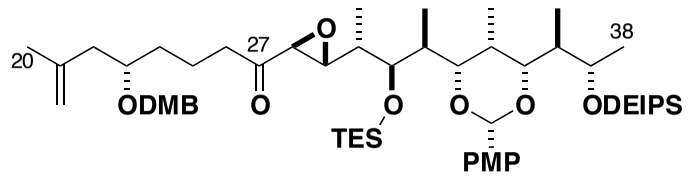

**85**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



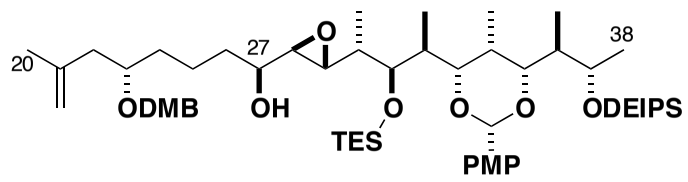

**86**

**$^1$H NMR** (500 MHz, $CHCl_3$)



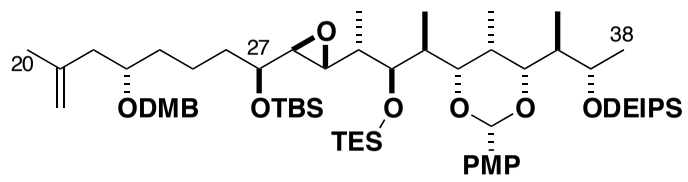

**86**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



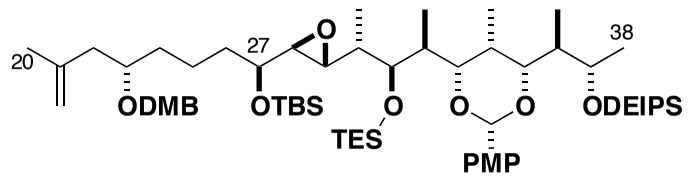

**87**

**$^1$H NMR** (500 MHz, $CHCl_3$)



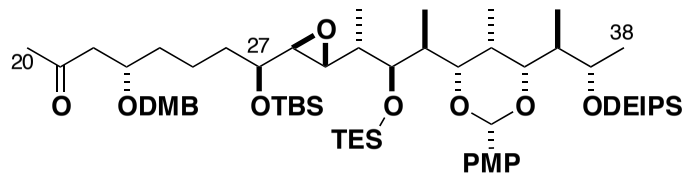

**88**

**$^1$H NMR** (500 MHz, $CHCl_3$)



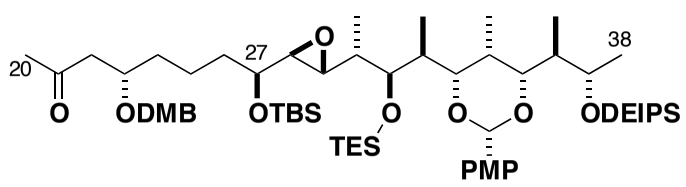

**88**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



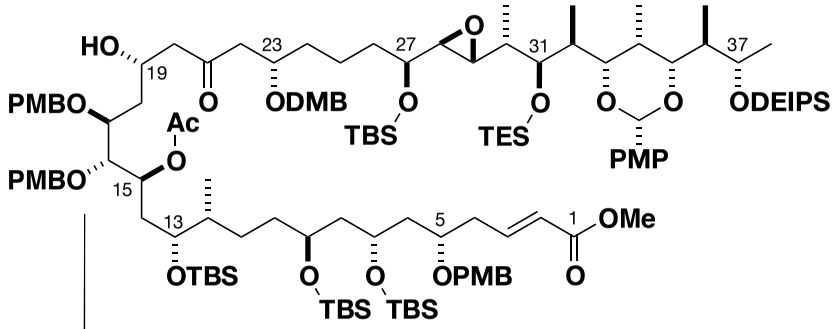

**89**

**$^1$H NMR** (500 MHz, $CHCl_3$)



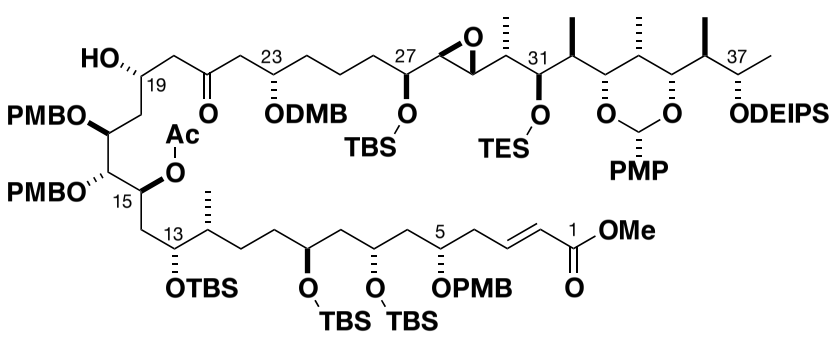

**89**

**$^{1}$C NMR** (125 MHz, $CHCl_3$)



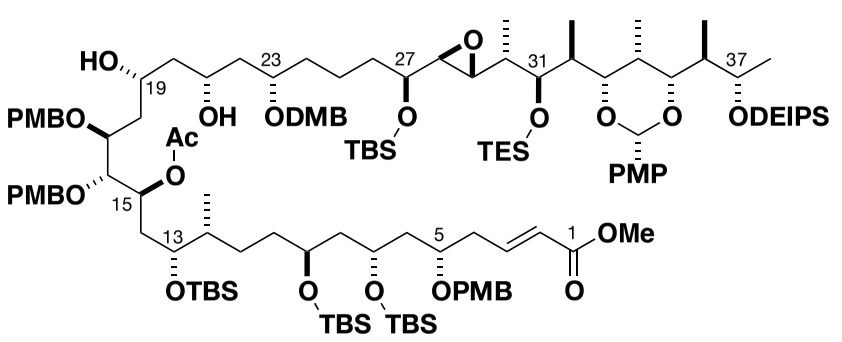

**90**

**$^1$H NMR** (500 MHz, $CHCl_3$)



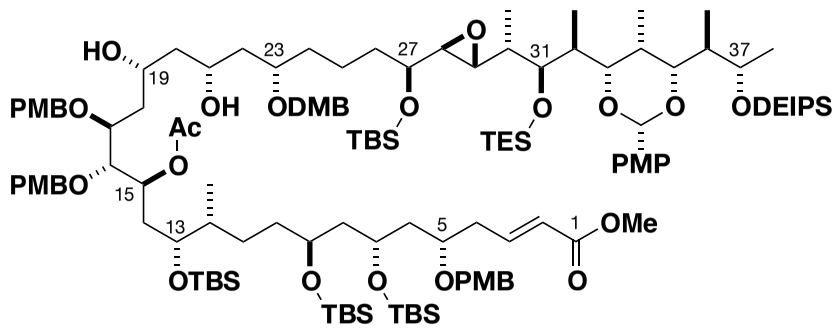

**90**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



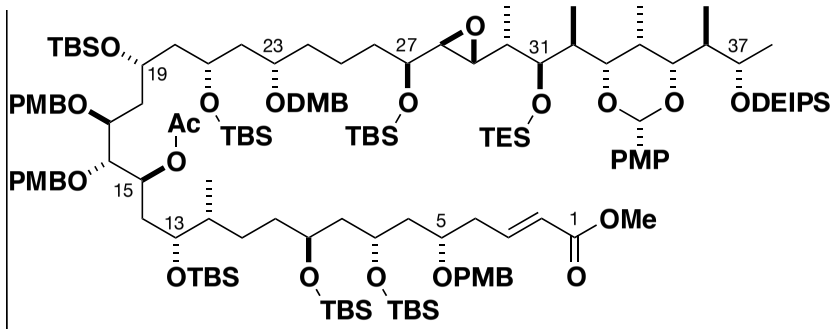

**91**

**$^1$H NMR** (500 MHz, $CHCl_3$)



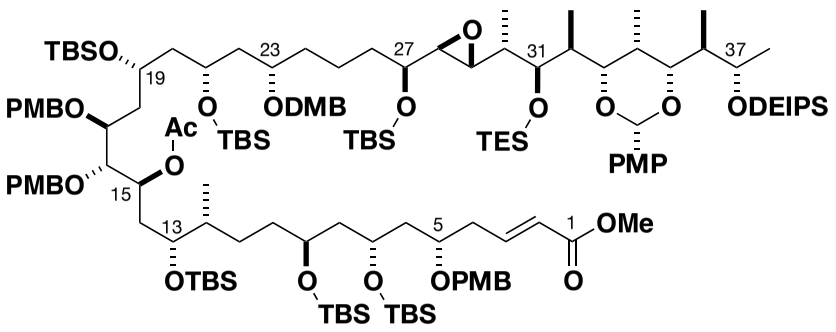

**91**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



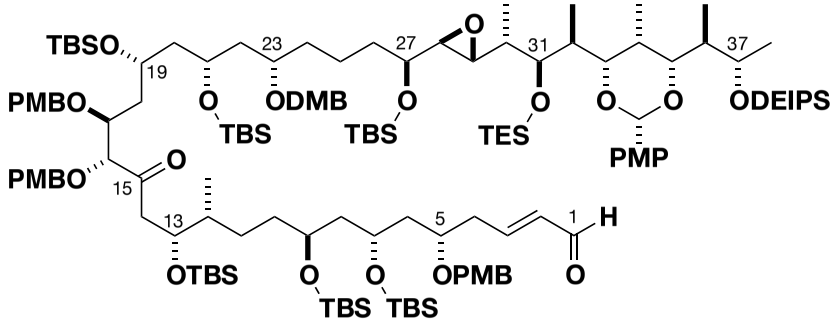

**92**

**$^1$H NMR** (500 MHz, $CHCl_3$)



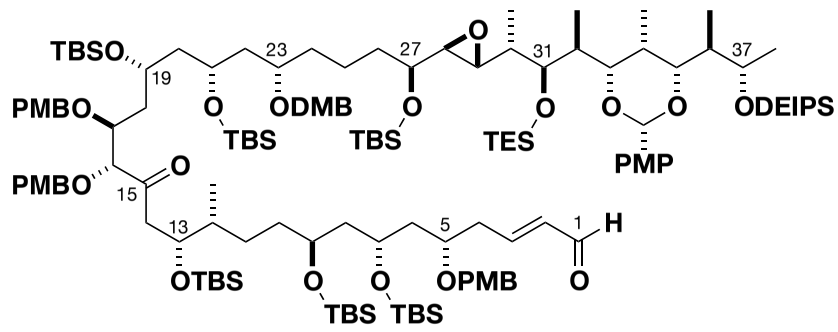

**92**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



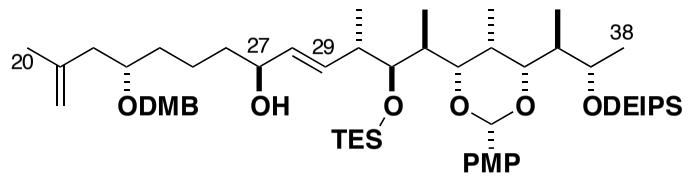

**93**

**$^1$H NMR** (500 MHz, $CHCl_3$)



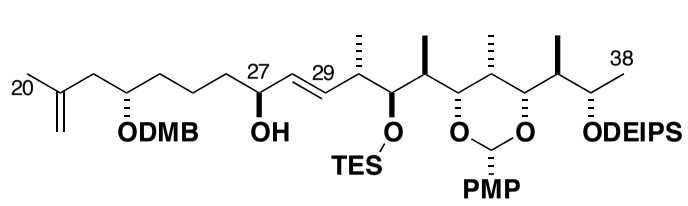

**93**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



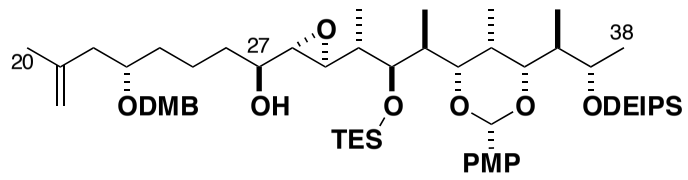

**94**

**$^1$H NMR** (500 MHz, $CHCl_3$)



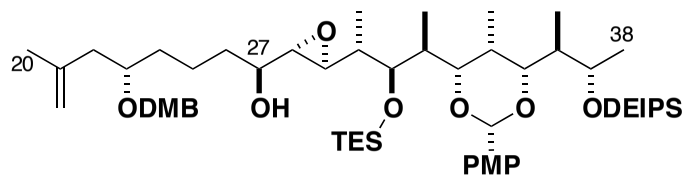

**94**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)




**95**

**$^1$H NMR** (500 MHz, $CHCl_3$)

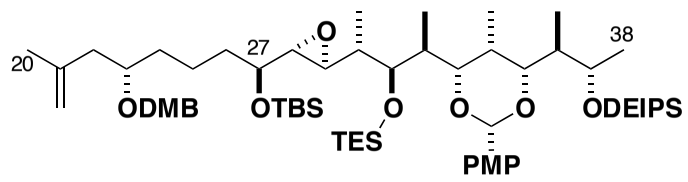



**95**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)

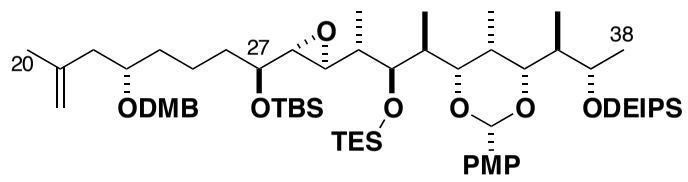
126

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



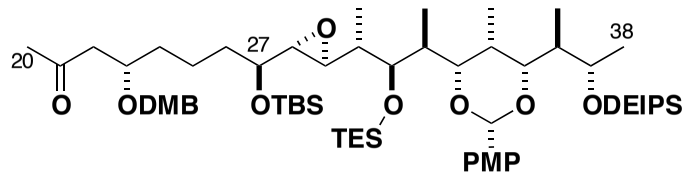

**96**

**$^1$H NMR** (500 MHz, $CHCl_3$)



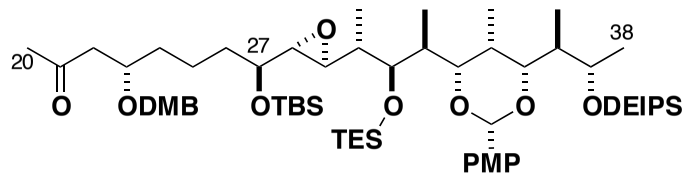

**96**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



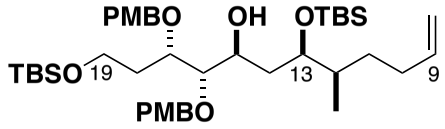

**97**

**$^1$H NMR** (500 MHz, $CHCl_3$)



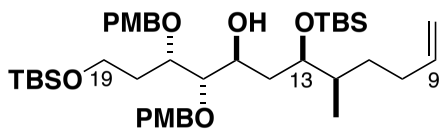

**97**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)



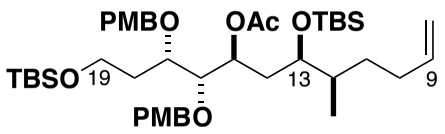

**105**

**$^1$H NMR** (500 MHz, $CHCl_3$)



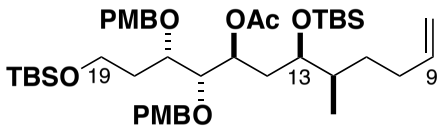

**103**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)




**105**

**$^1$H NMR** (500 MHz, $CHCl_3$)




**105**

**$^{13}$C NMR** (125 MHz, $CHCl_3$)