

Practical and Efficient Synthesis of the C-16-C28 Spiroketal Fragment (CD) of the Spongistatins

Supporting Information

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General Experimental

All non-aqueous reactions were performed in oven dried glassware (150 °C), cooled under an atmosphere of dry argon at temperatures which were those of the external bath. All temperatures were measured in degrees Celsius (°C).

Nuclear magnetic resonance spectra were performed using deuteriochloroform as a solvent unless stated otherwise. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on Bruker AM 400 (400 MHz) or Bruker DRX-600 (600 MHz) spectrometers with residual protic solvent as the internal standard (CHCl_3 , $\delta_{\text{H}} = 7.26$, s). Carbon nuclear magnetic resonance (^{13}C NMR) were recorded on a Bruker AM 400 (100 MHz) or Bruker DRX-600 (150 MHz) spectrometers using central resonance of CDCl_3 as the internal standard ($\delta_{\text{C}} = 77.0$, t) and assignments were made using a range of NMR experiments (DEPT135, COSY, HMQC, HMBC). All chemical shifts are quoted in parts per million (ppm) downfield from tetramethylsilane, measured to the centre of the signal except in the case of multiplets of more than one proton which are quoted as a range. Coupling constants are quoted in Hertz (Hz) and are rounded to the nearest 0.1 Hz,. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (b), apparent (ap.) and combinations of the above. Where relevant, the assignments H_{ax} and H_{eq} define axial and equatorial orientated proton resonances respectively. Data is reported as follows chemical shift δ (ppm), (assignment).

Diagrams of each compound have been included to illustrate the assignment of the NMR spectra. The compounds have been named according to IUPAC nomenclature utilising the ACD/Name computer program.

Infra-red (IR) spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Universal ATR sampling accessory from 4000-600 cm^{-1} . All samples were run as thin films deposited neat or *via* the evaporation of dichloromethane/chloroform solutions to a diamond/ZnSe plate. Absorption maxima are reported in wavenumbers (cm^{-1}) and the following abbreviations are used to define signal strengths: br, broad; s, sharp; m, medium; w, weak.

Mass spectra were obtained on a Micromass Platform HP1050 LC/MS (+ESI), a Waters Alliance HT2795 LC/MS (+ESI), a Kratos MS890MS spectrometer (+EI), a Kratos QTOF spectrometer (+ESI) or a Bruker BIOAPEX 4.7 FTICR (+ESI) spectrometer at the Department of Chemistry,

University of Cambridge.

Optical rotations were measured using a Perkin Elmer Model 343 polarimeter using a sodium lamp (λ 589 nm, D-line); $[\alpha]_D^{25}$ values are reported in $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$, concentration (c) in g per 100 mL.

Chromatography refers to flash column chromatography according to the method of Still¹ and was carried out using BDH F₂₅₄ Kieselgel 60 (230-400 mesh) (33-70 μ m) as the stationary phase and eluted with a positive pressure of compressed air.

Analytical thin layer chromatography was performed using pre-coated Merck glass backed silica gel plates (Silicagel 60 F₂₅₄). Visualisation was by ultra violet light and/or treatment with acidic potassium permanganate (VII), acidic ammonium molybdate (IV) or anisaldehyde stains followed by heating as appropriate.

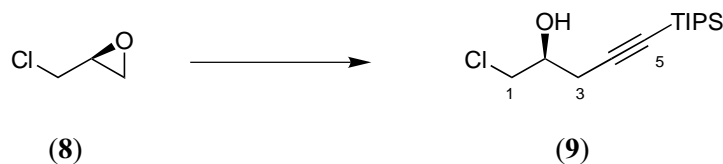
Light petroleum or petrol refers to the fraction of petroleum ether that boils between 40°C and 60°C. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were dried over sodium benzophenone ketyl and distilled under an atmosphere of dry argon. Dichloromethane (CH₂Cl₂), toluene, acetonitrile (MeCN) and methanol (MeOH) were dried over calcium hydride and distilled under an atmosphere of dry argon. All other solvents and commercially available reagents were purified using standard procedure as required.²

Synthetic intermediates were dried *in vacuo* before use in non-aqueous reactions. All aqueous solutions are saturated unless otherwise stated. Butyllithium was titrated against *iso*-propanol using 2,2'-dipyridyl as the indicator. Triethylamine was distilled prior to use.

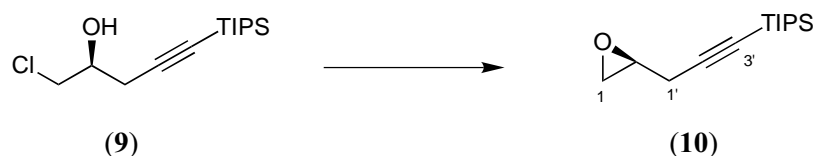
1) W.C.Still, M.Khan, A.Mitra; *J.Org.Chem.*, **1978**, 43, 2923.

2) D.D.Perrin, W.L.F.Armerego; *Purification of laboratory chemicals*, Permagon, Oxford (1997).

Experimental Procedures

(2*S*)-1-Chloro-5-(triisopropylsilyl)pent-4-yn-2-ol (9)

n-Butyllithium (2.46 M solution in hexanes, 23.7 ml, 58.3 mmol) was added to a solution of (triisopropylsilyl)acetylene (11.6 ml, 51.9 mmol) in THF (150 ml) at -78 °C. After 0.5 h boron trifluoride-THF complex (6.4 ml, 58.3 mmol) was added dropwise and the solution stirred for a further 0.5 h at -78 °C. (*S*)-Epichlorohydrin (**8**) (3.00 g, 32.4 mmol) in THF (50 ml) was then added dropwise. The solution was stirred for 2 h and then quenched with aqueous ammonium chloride (50 ml) and allowed to warm to room temperature. The aqueous phase was separated and extracted with Et₂O (3 x 50 ml). The combined organic layers were washed with brine (80 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 19:1 then 9:1 then 4:1) afforded *chlorohydrin* (**9**) (8.33 g, 94%) as a colourless oil; *R*_f(Petrol-Et₂O) 0.12; [α]_D²⁵ +9.3 (*c* 1.50, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3362br w (OH), 2175m (C≡C), 675s (C-Cl); δ_{H} (400 MHz; CDCl₃) 1.06 (12H, s, Si(CH(CH₃)₂)₂), 1.07 (6H, s, SiCH(CH₃)₂), overlapping 1.05-1.07 (3H, m, Si(CH(CH₃)₂)₃), 2.33 (1H, d, *J* 6.1, OH), 2.59 (1H, dd, *J* 6.7, 16.9, 3-H_A), 2.66 (1H, dd, *J* 5.5, 16.9, 3-H_B), 3.66 (1H, dd, *J* 5.9, 11.1, 1-H_A), 3.73 (1H, dd, *J* 4.7, 11.1, 1-H_B) and 3.99 (1H, ap. sextet, *J* 5.9, 2-H); δ_{C} (100 MHz; CDCl₃) 11.2 (Si(CH(CH₃)₂)₃), 18.6 (Si(CH(CH₃)₂)₃), 25.8 (3-C), 48.1 (1-C), 69.8 (2-C), 84.5 (5-C) and 102.7 (4-C); *m/z* (+ESI) 297 ([MNa]⁺, 59%), 158 (100); Found (+ESI): [MNa]⁺, 297.1408. C₁₄H₂₇OSiClNa requires *MNa*, 297.1417.

(2*S*)-2-(3'-Triisopropylsilylprop-2'-yn-1'-yl)oxirane (10)

BEMP on polystyrene (loading *ca.* 2.2 mmol g⁻¹, 13.70 g, 15.1 mmol) was added to a solution of *chlorohydrin* (**9**) (4.14 g, 15.1 mmol) in MeCN (100 ml) at room temperature. The resulting suspension was shaken overnight. The resin was removed by filtration, washed successively with

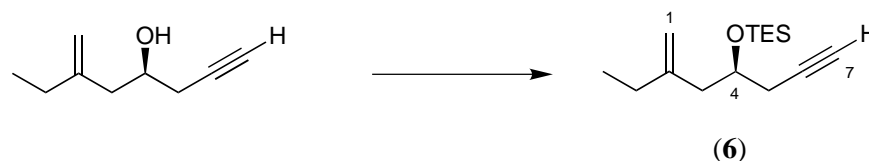
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3- H_A), 2.44 (1H, dd, J 4.5, 13.9, 3- H_B), 2.49 (2H, ap. dd, J 2.5, 6.0, 5- H_A , 5- H_B), 3.84-3.91 (1H, m, 4-H), 4.84 (1H, s, 1- H_A) and 4.89 (1H, d, J 1.5, 1- H_B); δ_C (100 MHz; $CDCl_3$) 11.2 (Si(CH(CH $_3$) $_2$) $_3$), 12.2 (2-CCH $_2$ CH $_3$), 18.6 (Si(CH(CH $_3$) $_2$) $_3$), 28.3 (5-C), 28.7 (2-CCH $_2$ CH $_3$), 43.3 (3-C), 67.9 (4-C), 83.6 (7-C), 104.6 (6-C), 111.3 (1-C) and 147.9 (2-C); m/z (+ESI) 312 ([MNH $_4$] $^+$, 100%), 295 ([MH] $^+$, 10), 172 (11), 121 (10), 105 (30); Found (+ESI): [MNa] $^+$, 317.2289. C $_{18}$ H $_{34}$ OSiNa requires MNa, 317.2277.

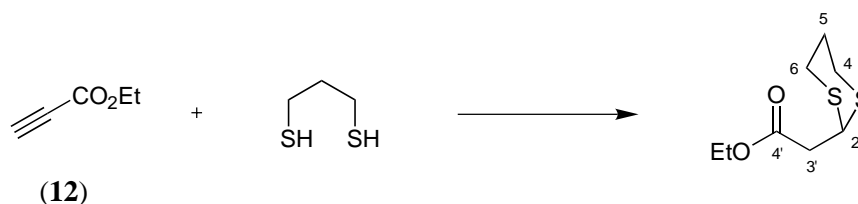
(4S)-2-Ethylhept-1-en-6-yn-4-ol



Tetra *n*-butylammonium fluoride (1 M solution in THF, 23.8 ml, 22.8 mmol) was added to a solution of alcohol (11) (3.50 g, 11.88 mmol) in THF (25 ml) at room temperature. After 2 h the reaction was diluted with Et $_2$ O (50 ml) and quenched with aqueous ammonium chloride (50 ml). The aqueous layer was separated and extracted with Et $_2$ O (4 x 50 ml). The combined organic extracts were washed with brine (80 ml), dried (MgSO $_4$) and concentrated *in vacuo* (\geq 50 mbar). Flash chromatography on silica gel (30-40 Petrol-Et $_2$ O, 9:1 then 4:1) afforded *terminal alkyne* (1.62 g, 99%) as a colourless oil; R_f (Petrol-Et $_2$ O, 2:1) 0.29; $[\alpha]_D^{25}$ -0.4 (c 2.23, $CHCl_3$); ν_{max} (thin film)/cm $^{-1}$ 3383br w (OH), 3307m (alkyne C-H), 3078w (alkene C-H), 2119w (C \equiv C), 1645m (alkene C=C); δ_H (400 MHz; $CDCl_3$) 1.05 (3H, t, J 7.4, 2-CCH $_2$ CH $_3$), 2.02 (1H, d, J 3.7, OH), 2.06 (1H, t, J 2.6, 7-H) overlapping 2.05-2.14 (2H, m, 2-CCH $_2$ CH $_3$), 2.23 (1H, dd, J 8.6, 14.0, 3- H_A), 2.38 (1H, dd, J 4.2, 14.0, 3- H_B), 2.40-2.43 (2H, m, 5- H_A , 5- H_B), 3.87-3.94 (1H, m, 4-H), 4.85 (1H, s, 1- H_A) and 4.90 (1H, d, J 1.4, 1- H_B); δ_C (100 MHz; $CDCl_3$) 12.2 (2-CCH $_2$ CH $_3$), 26.7 (5-C), 28.7 (2-CCH $_2$ CH $_3$), 43.3 (3-C), 67.6 (4-C), 70.8 (7-C), 80.7 (6-C), 111.4 (1-C) and 147.6 (2-C); m/z (+ESI) 123 ([M-Me] $^+$, 27%), 119 (40), 100 (17), 83 (27), 68 (100); Found (+EI): [M-Me] $^+$, 123.0815. C $_8$ H $_{11}$ O requires *M-Me*, 123.0810.

(4S)-2-Ethyl-(4-triethylsilanyloxy)hept-1-en-6-yne (6)

Chlorotriethylsilane (4.86 ml, 22.9 mmol) was added to a solution of alcohol (3.08 g, 22.30 mmol) and imidazole (3.34 g, 49.08 mmol) in THF (25 ml) at room temperature. After 1 h the reaction was portioned between sodium hydrogen carbonate (50 ml) and Et₂O (50 ml). The aqueous layer was separated and extracted with Et₂O (4 x 75 ml). The combined organic extracts were washed with brine (175 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 49:1) afforded *silyl ether* (6) (4.96 g, 88%) as a colourless oil; *R*_f (Petrol-Et₂O, 50:1) 0.39; (α)_D²⁵ +2.4 (*c* 1.38, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3314m (alkyne C-H), 2122w (C≡C), 1645m (alkene C=C); δ_{H} (400 MHz; CDCl₃) 0.61 (6H, q, *J* 8.0, Si(CH₂CH₃)₃), 0.96 (9H, t, *J* 8.0, Si(CH₂CH₃)₃), 1.03 (3H, t, *J* 7.4, 2-CCH₂CH₃), 1.99 (1H, ap. t, *J* 2.6, 7-H), 2.06 (2H, q, *J* 7.4, 2-CCH₂CH₃), 2.25 (1H, dd, *J* 6.3, 13.7, 3-H_A), 2.32 (1H, dd, *J* 2.6, 6.0, 5-H_A), 2.35 (1H, dd, *J* 2.6, 6.0, 5-H_B), 2.38 (1H, dd, *J* 6.1, 13.7, 3-H_B), 3.95 (1H, ap. quint., *J* 6.0, 4-H), 4.80 (1H, s, 1-H_A) and 4.82 (1H, d, *J* 1.5, 1-H_B); δ_{C} (100 MHz; CDCl₃) 4.9 (Si(CH₂CH₃)₃), 6.8 (Si(CH₂CH₃)₃), 12.2 (2-CCH₂CH₃), 27.1 (5-C), 29.2 (2-CCH₂CH₃), 43.8 (3-C), 69.9 (2 lines, 4-C, 7-C), 81.7 (6-C), 111.0 (1-C) and 147.7 (2-C); *m/z* (+ESI) 275 ([MNa]⁺, 100%), 248 (10), 176 (11); Found (+ESI): [MNa]⁺, 275.1792. C₁₅H₂₈OSiNa requires *MNa*, 275.1807.

(1,3)-Dithianyl-2-yl ethanoic acid ethyl ester

NaOEt (10.0 g, 145 mmol) was added in one portion to a stirred solution of ethyl propiolate (10.6 g, 108 mmol) and 1,3 propanedithiol (11.75 g, 108 mmol) in THF:EtOH (1:1) (180 ml) at -10 °C (ice/acetone bath). The resulting solution was stirred for 14 h, allowing the temperature to rise to 0

°C. After this time, the mixture was quenched with aqueous ammonium chloride solution (100 ml). The aqueous layer was separated and extracted with Et₂O (4 x 100 ml). The combined organic extracts were washed with aqueous ammonium chloride solution (100 ml), aqueous sodium hydrogen carbonate (20 ml) and brine (100 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 19:1 then 9:1 then 4:1) afforded *dithiane* (11.55 g, 52%) as a pale yellow oil; *R*_f (Ether:Petrol, 3:7) 0.29; *v*_{max} (thin film)/cm⁻¹ 2981w (C-H stretch), 2901w (C-H stretch), 1731s (C=O), 1422s (C-H deformation); *δ*_H (400 MHz; CDCl₃) 1.27 (3H, t, *J* 7.1, OCH₂CH₃), 1.87-1.94 (1H, m, 5-H_a), 2.05-2.13 (1H, m, 5-H_b), 2.16 (1H, d, *J* 7.4, 3'-H), 2.84-2.93 (4H, m, 4-H_a, 4-H_b, 6-H_a, 6-H_b), 4.18 (2H, q, *J* 7.1, CH₂CH₃), 4.40 (1H, t, *J* 7.4, 2-H); *δ*_C (100 MHz; CDCl₃) 14.1 (OCH₂CH₃), 25.3 (5-C), 29.5 (4-C, 6-C), 40.6 (3'-C), 41.9 (2-C), 61.0 (OCH₂CH₃), 169.7 (4'-C); *m/z* (+EI) 206 ([M]⁺, 44%), 177 (30), 132 (69), 119 (100), 91 (5), 69 (78)); Found (+EI): [M]⁺, 206.0436. C₈H₁₄O₂S₂ requires *M*, 206.0435.

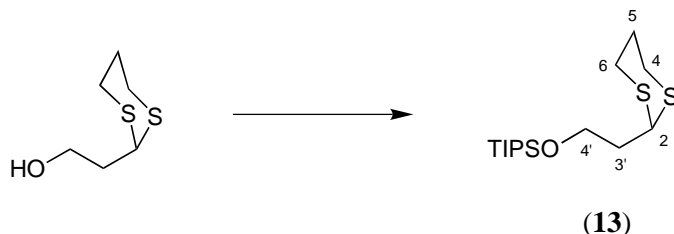
(1,3)-Dithia-2-yl ethanol



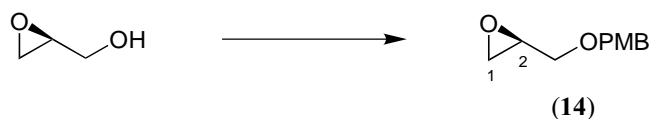
THF (160 ml) was added dropwise to solid LiAlH₄ (2.06 g, 54.4 mmol) cooled at -78 °C (careful : strong exotherm). After stirring of the resulting suspension for 0.2 h a solution of the ester (11.22 g, 54.4 mmol) in THF (50 ml) was added dropwise. The reaction mixture was then stirred at -78°C for 5 h and for a further 18 h at room temperature. The reaction mixture was then quenched by the slow addition of water (8 ml) at 0 °C followed by aqueous Rochelle's salt (200 ml), the mixture was stirred at room temperature for 20 h. The aqueous layer was separated and extracted with Et₂O (2 x 300 ml). The combined organic extracts were washed with distilled water (300 ml) and brine (300 ml), dried (MgSO₄). The solution was then filtered through a small pad of silica gel (Et₂O) and concentrated *in vacuo* afforded *alcohol* (8.66 g, 97%) as a pale yellow oil; *R*_f (Ether:Petrol, 3:7) 0.11; *v*_{max} (thin film)/cm⁻¹ 3392b s (OH), 2932w (C-H stretch), 2899w (C-H stretch), 1422s (C-H deformation); *δ*_H (400 MHz; CDCl₃) 1.73 (1H, t, *J* 5.4, OH), 1.84-1.95 (1H, m, 5-H_a), 2.03 (2H, ap.dd (dt), *J* 6, 7, 3'-H), 2.08-2.16 (1H, m, 5-H_b), 2.81-2.92 (4H, m, 4-H_a, 4-H_b, 6-H_a, 6-H_b), 3.83 (2H, ap.dd (dt), *J*, 6, 11, 4'-H), 4.23 (1H, t, *J* 7, 2-H); *δ*_C (100 MHz; CDCl₃) 25.9 (5-C), 30.3 (4-C, 6-

C), 38.0 (3'-C), 44.4 (2-C), 59.8 (4'-C); m/z (+EI) 164 $[M]^+$, 51%), 131 (80), 84 (19), 69 (100); Found (+EI): $[M]^+$, 164.0330. $C_6H_{12}O_1S_2$ requires M , 164.0335.

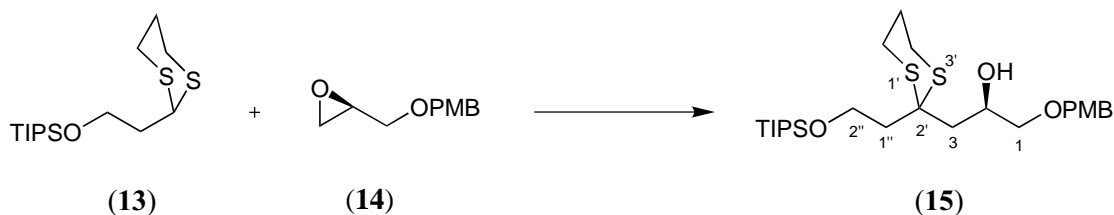
(1,3) Dithian-2-yl-(ethoxy)trisopropylsilane (13)



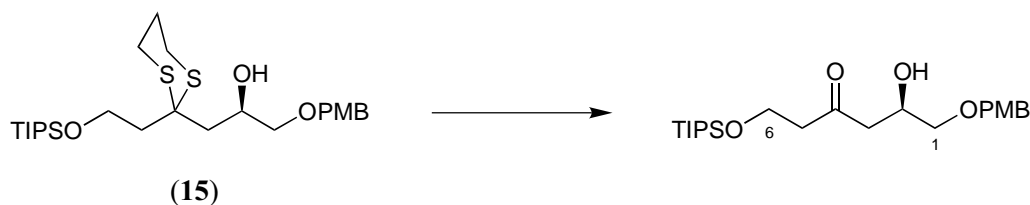
A solution of alcohol in THF (50 ml) was added to a stirred solution of imidazole (7.91 g, 116.15 mmol) and triisopropylsilylchloride (13.24 g, 68.65 mmol) in THF (150 ml) cooled at 0 °C. The resulting solution was allowed to warm to room temperature and stirred for a further 16 h. After this time, water (150 ml) was added and the mixture stirred vigorously for 0.5 h. The aqueous layer was separated and extracted with Et_2O (3 x 200 ml). The combined organic extracts were washed with brine (300 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol- Et_2O , 19:1 then 9:1 then 4:1) afforded *protected alcohol* (13) (16.71 g, 99%) as a pale yellow oil; R_f (Petrol- Et_2O , 9:1) 0.34; ν_{max} (thin film)/ cm^{-1} 2941w (C-H stretch), 2895w (C-H stretch), 2865 (C-H stretch), 1463s (C-H deformation); δ_H (400 MHz; $CDCl_3$) 1.01-1.14, 21H, m, (Si- $CH(CH_3)_2$), 1.83-1.93 (1H, m, 5- H_a), 1.98 (2H, ap.dd (dt), J 1.4, 8.1, (3'-H), 2.08-2.13 (1H, m, 5- H_b), 2.80-2.90 (4H, m, 4- H_a , 4- H_b , 6- H_a , 6- H_b), 3.85 (2H, t, J 6.3, 4'-H), 4.25 (1H, t, J 7, 2-H); δ_C (100 MHz; $CDCl_3$) 12.0 (Si- $CH(CH_3)_2$), 18.0 (Si- $CH(CH_3)_2$), 26.1 (5-C), 30.2 (4-C, 6-C), 38.6 (3'-C), 43.8 (2-C), 59.7 (4'-C); m/z (+EI) 320 ($[M]^+$, 38%), 277 (100), 247 (38), 221 (8), 169 (37), 131 (48), 119 (26), 100 (10), 69 (91); Found (+EI): $[M]^+$, 320.1650. $C_{15}H_{32}O_1S_2$ requires M , 320.1664.

(2R)-2-(*p*-Methoxybenzyloxymethyl)oxirane (14)

(*S*)-Glycidol (5.00 g, 67.6 mmol) in THF (10 ml) was added to a solution of sodium hydride (60% dispersion in mineral oil, 2.43 g, 101.25 mmol) in THF (40 ml) at 0 °C. The mixture was stirred until the effervescence ceased, then *p*-methoxybenzyl chloride (15.85 g, 101.25 mmol) and tetra-*n*-butylammonium iodide (2.5 g, 10 mol%) were added. The solution was allowed to warm to room temperature overnight. The mixture was poured into H₂O (100 ml) and extracted with Et₂O (4 x 100 ml). The combined organic layers were washed with H₂O (2 x 100 ml) and brine (200 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-EtOAc, 5:1) afforded *epoxide* (14) (9.84 g, 75%) as a pale yellow oil; *R*_f(Petrol-EtOAc, 5:1) 0.16; $[\alpha]_{\text{D}}^{25} +3.6$ (*c* 1.24, CHCl₃); ν_{max} (thin film)/cm⁻¹ 1612m (Ar C=C), 1586w (Ar C=C), 1512s (Ar C=C); δ_{H} (400 MHz; CDCl₃) 2.61 (1H, dd, *J* 2.7, 5.0, 1-H_A), 2.79 (1H, dd, *J* 4.4, 5.0, 1-H_B), 3.15-3.19 (1H, m, 2-H), 3.42 (1H, dd, *J* 5.8, 11.4, CH_AH_BOAr), 3.73 (1H, dd, *J* 3.1, 11.4, CH_AH_BOAr), 3.81 (3H, s, ArOCH₃), 4.49 (1H, d, *J* 11.5, OCH_AH_BAr), 4.55 (1H, d, *J* 11.5, OCH_AH_BAr), 6.89 (2H, d, *J* 8.7, Ar-*meta*-H) and 7.28 (2H, d, *J* 8.7, Ar-*ortho*-H); δ_{C} (100 MHz; CDCl₃) 44.3 (1-C), 50.9 (2-C), 55.3 (ArOCH₃), 70.5, 73.0 (OCH₂Ar, CH₂OAr), 113.8 (Ar-*meta*-C), 129.4 (Ar-*ortho*-C), 130.0 (Ar-*ipso*-C) and 159.3 (Ar-*para*-C); *m/z* (+EI) 194 ([M]⁺, 8%), 136 (24), 121 (80), 69 (100); Found (+EI): [M]⁺, 194.0949. C₁₁H₁₄O₃ requires *M*, 194.0943.

(2*R*)-1-(*p*-Methoxybenzyloxy)-3-(2'-(2''-(triisopropylsilanyloxy)ethyl)-(1',3')dithian-2'-yl)propan-2-ol (15)

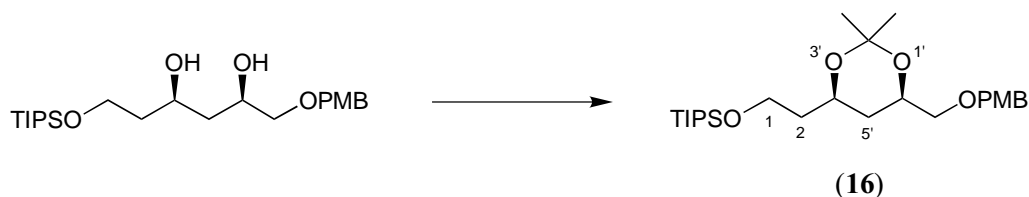
n-Butyllithium (2.69 M in heptane, 7.74 ml, 21.4 mmol) was added dropwise to a solution of dithiane (**13**) (4.00 g, 12.8 mmol) in THF (100 ml) at room temperature. After 15 min the solution was cooled to -10 °C and epoxide (**14**) (2.07 g, 10.7 mmol) in THF (10 ml) added dropwise. After 1 h the reaction was quenched with water (50 ml). The aqueous phase was separated and extracted with Et₂O (3 x 50 ml). The combined organic extracts were washed with brine (100 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 5:1 then 1:1 then 1:3) afforded *alcohol* (**15**) (5.39 g, 98%) as a colourless oil; *R*_f(Petrol-Et₂O, 2:1) 0.12; [α]_D²⁵ +17.8 (*c* 0.5, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3443br w (OH), 1612m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl₃) 1.05 (6H, s, SiCH(CH₃)₂), 1.06 (12H, s, Si(CH(CH₃)₂)₂), overlapping 1.04-1.08 (3H, m, Si(CH(CH₃)₂)₃), 1.89-2.00 (2H, m, 5'-H_A, 5'-H_B), 2.16 (1H, dd, *J* 2.3, 15.3, 3-H_A), 2.22 (1H, dd, *J* 8.2, 15.3, 3-H_B) overlapping 2.21-2.25 (1H, m, 1''-H_A), 2.37 (1H, dt, *J* 14.5, 7.1, 1''-H_B), 2.77 (1H, ddd, *J* 3.5, 7.3, 14.8, 4'-H_A or 6'-H_A), 2.79 (1H, ddd, *J* 3.5, 7.3, 14.8, 4'-H_A or 6'-H_B), 2.84 (1H, ddd, *J* 3.5, 8.6, 14.5, 4'-H_B or 6'-H_B), 2.90 (1H, ddd, *J* 3.5, 8.6, 14.5, 4'-H_B or 6'-H_B), 3.38 (1H, d, *J* 3.2, OH), 3.40 (1H, dd, *J* 9.5, 13.3, 1-H_A), 3.41 (1H, dd, *J* 9.5, 14.1, 1-H_B), 3.80 (3H, s, ArOCH₃), 3.87 (1H, ddd, *J* 5.5, 7.6, 10.2, 2''-H_A), 3.99 (1H, dt, *J* 10.2, 7.1, 2''-H_B), 4.18-4.22 (1H, m, 2-H), 4.48 (1H, d, *J* 11.8, OCH_AH_BAr), 4.50 (1H, d, *J* 11.8, OCH_AH_BAr), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_{C} (100 MHz; CDCl₃) 11.9 (Si(CH(CH₃)₂)₃), 18.0 (Si(CH(CH₃)₂)₃), 25.0 (5'-C), 26.1, 26.3 (4'-C, 6'-C), 41.7 (1''-C), 42.4 (3-C), 50.9 (2'-C), 55.3 (ArOCH₃), 59.7 (2''-C), 67.5 (2-C), 72.9 (OCH₂Ar), 74.2 (1-C), 113.8 (Ar-*meta*-C), 129.3 (Ar-*ortho*-H), 130.3 (Ar-*ipso*-C) and 159.2 (Ar-*para*-C); *m/z* (+ESI) 537 ([MNH₄]⁺, 2%), 269 (100); Found (+ESI): [MNa]⁺, 537.2508. C₂₆H₄₆O₄S₂SiNa requires *MNa*, 537.2505.

(2*R*)-2-Hydroxy-1-(*p*-methoxybenzyloxy)-6-(triisopropylsilanyloxy)hexan-4-one

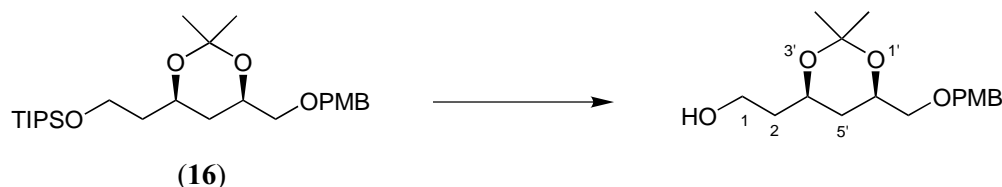
Iodine (3.94 g, 15.54 mmol) was added portionwise to a solution of dithiane (15) (2.00 g, 3.89 mmol) in MeCN (30 ml) and aqueous sodium hydrogen carbonate (10 ml) at 0 °C. After 1 h the reaction was diluted with Et₂O (40 ml) and quenched with a mixture of aqueous sodium thiosulfate (15 ml) and aqueous sodium hydrogen carbonate (15 ml). The aqueous phase was separated and extracted with Et₂O (4 x 50 ml). The combined organic extracts were washed with brine (150 ml), dried (MgSO₄) and concentrated *in vacuo*, affording *hydroxy ketone* (1.58 g, 96%) as a yellow oil, which was used without further purification. For analytical purposes, flash chromatography on silica gel (Petrol-Et₂O, 1:1); *R_f* (Et₂O-Petrol, 2:1) 0.40; [α]_D²⁵ +9.9 (*c* 2.03, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3469br w (OH), 1710s (C=O), 1613m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl₃) 1.03 (6H, s, SiCH(CH₃)₂), 1.04 (12H, s, Si(CH(CH₃)₂)₂), overlapping 1.05-1.11 (3H, m, Si(CH(CH₃)₂)₃), 2.64 (1H, t, *J* 6.2, 5-H_A), 2.65 (1H, t, *J* 6.2, 5-H_B), 2.69 (1H, ap. d, *J* 4.5, 3-H_A), 2.70 (1H, ap. d, *J* 7.2, 3-H_B), 2.98 (1H, d, *J* 3.9, OH), 3.41 (1H, dd, *J* 6.1, 9.6, 1-H_A), 3.46 (1H, dd, *J* 4.6, 9.6, 1-H_B), 3.80 (3H, s, ArOCH₃), 3.97 (2H, 2 x t, *J* 6.2 and 6.2, 6-H_A, 6-H_B), 4.24 (1H, m, 2-H), 4.47 (1H, d, *J* 11.6, OCH_AH_BAr), 4.49 (1H, d, *J* 11.6, OCH_AH_BAr), 6.88 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*ortho*-H); δ_{C} (100 MHz; CDCl₃) 11.9 (Si(CH(CH₃)₂)₃), 17.9 (Si(CH(CH₃)₂)₃), 46.6 (5-C), 46.9 (3-C), 55.3 (ArOCH₃), 59.1 (6-C), 66.8 (2-C), 73.0 (2 lines, 1-C, OCH₂Ar), 113.8 (Ar-*meta*-C), 129.4 (Ar-*ortho*-C), 130.1 (Ar-*ipso*-C), 159.3 (Ar-*para*-C) and 210.0 (4-C); *m/z* (+ESI) 442 ([MNH₄]⁺, 8%), 269 (100), 121 (38); Found (+ESI): [MNa]⁺, 447.2554. C₂₃H₄₀O₅SiNa requires *MNa*, 447.2543.

(2*R*, 4*R*)-1-(*p*-Methoxybenzyloxy)-6-(triisopropylsilanyloxy)hexan-2,4-diol

Diethylmethoxyborane (1 M solution in THF, 5.05 ml, 5.05 mmol) was added dropwise to a solution of ketone (1.58 g, 3.75 mmol) in THF (30 ml) and MeOH (10 ml) at $-78\text{ }^{\circ}\text{C}$. After 1.5 h sodium borohydride (0.245 g, 6.48 mmol) was added and the solution stirred at $-78\text{ }^{\circ}\text{C}$ for 4 h. A further portion of sodium borohydride (0.123 g, 3.25 mmol) was added and the solution stirred overnight at $-78\text{ }^{\circ}\text{C}$. The solution was then quenched with glacial acetic acid (10 ml) and was stirred at room temperature for 0.5 h. The mixture was diluted with Et₂O (30 ml) and H₂O (40 ml). The aqueous phase was separated and extracted with Et₂O (4 x 50 ml). The combined organic extracts were washed with brine (150 ml), dried (MgSO₄) and concentrated *in vacuo*. The residue was then azeotroped using 5% glacial acetic acid in MeOH (5 x 60 ml) followed by toluene (3 x 60 ml). Flash chromatography on silica gel (Petrol 100% then 1:1 Petrol:Ether) afforded *diol* (1.48 g, 94%) as a yellow oil. R_f (Et₂O-Petrol, 2:1) 0.25; $[\alpha]_D^{25}$ -1.6 (c 1.73, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3435br m (OH), 1613m (Ar C=C), 1586w (Ar C=C), 1513m (Ar C=C); δ_H (600 MHz; CDCl₃) 1.06 (6H, s, SiCH(CH₃)₂), 1.07 (12H, s, Si(CH(CH₃)₂)₂), 1.08-1.13 (3H, m, Si(CH(CH₃)₂)₃), 1.63-1.65 (2H, m, 3-H_A, 3-H_B), 1.65-1.68 (1H, m, 5-H_A), 1.75 (1H, dtd, J 17.3, 8.7, 4.5, 5-H_B), 3.41 (1H, dd, J 9.5, 11.1, 1-H_A), 3.42 (1H, dd, J 9.5, 11.9, 1-H_B), 3.53 (1H, d, J 2.0, 2-COH), 3.80 (3H, s, ArOCH₃), 3.90 (1H, ddd, J 3.9, 8.7, 10.1, 6-H_A), 3.97 (1H, dt, J 10.1, 4.5, 6-H_B), 4.07 (1H, d, J 1.9, 4-COH) overlapping 4.04-4.08 (1H, m, 2-H), 4.09-4.14 (1H, m, 4-H), 4.49 (2H, s, OCH₂Ar), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) 11.8 (Si(CH(CH₃)₂)₃), 17.9 (Si(CH(CH₃)₂)₃), 38.9 (5-C), 40.1 (3-C), 55.3 (ArOCH₃), 62.8 (6-C), 70.7 (2-C), 72.2 (4-C), 73.0 (OCH₂Ar), 74.1 (1-C), 113.8 (Ar-*meta*-C), 129.4 (Ar-*ortho*-C), 130.3 (Ar-*ipso*-C) and 159.3 (Ar-*para*-C); m/z (+ESI) 449 ([MNa]⁺, 3%), 427 ([MH]⁺, 8), 121 (100); Found (+ESI): [MNa]⁺, 449.2691. C₂₃H₄₂O₅SiNa requires *MNa*, 449.2699.

(4'*R*, 6'*R*)-2-((6'-(*p*-Methoxybenzyloxymethyl)-2',2'-dimethyl(1',3')dioxan-4'-yl)ethoxy)triisopropylsilane (16)

para-Toluenesulfonic acid monohydrate (80 mg, 12 mol%) was added to a stirred solution of diol (1.48 g, 3.48 mmol) and 2,2-dimethoxypropane (10 ml, 81.24 mmol) in acetone (60 ml) at 0 °C. After 1 h sodium hydrogen carbonate solution (10 ml) was added and the acetone removed *in vacuo* and the residue partitioned between Et₂O (25 ml) and water (15 ml). The aqueous phase was separated and extracted with Et₂O (4 x 30 ml). The combined organic extracts were washed with brine (150 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 5:1) afforded *acetonide* (**16**) (3.58 g, 99%, 89% from dithiane (**15**)) as a colourless oil; *R*_f(Petrol-Et₂O, 5:1) 0.25; [α]_D²⁵ +15.6 (*c* 1.415, CHCl₃); ν_{max} (thin film)/cm⁻¹ 1613m (Ar C=C), 1587w (Ar C=C), 1513s (Ar C=C); δ_H (600 MHz; CDCl₃) 1.05 (18H, 2 x s, SiCH(CH₃)₂), Si(CH(CH₃)₂)₂ overlapping 1.04-1.07 (3H, m, Si(CH(CH₃)₂)₃), 1.22 (1H, ap. q, *J* 12.0, 5'-H_A), 1.40 (3H, s, 2'-CCH₃), 1.45 (3H, s, 2'-CCH₃), 1.55 (1H, dt, *J* 12.0, 2.5, 5'-H_B), 1.62-1.71 (2H, m, 2-H_A, 2-H_B), 3.34 (1H, dd, *J* 4.9, 9.9, CH_AH_BOAr), 3.48 (1H, dd, *J* 5.8, 9.9, CH_AH_BOAr), 3.72 (1H, dt, *J* 10.1, 5.4, 1-H_A), 3.80 (3H, s, ArOCH₃), 3.81 (1H, ddd, *J* 5.1, 8.2, 10.1, 1-H_B), 4.07-4.13 (2H, m, 4'-H, 6'-H), 4.47 (1H, d, *J* 11.8, OCH_AH_BAr), 4.53 (1H, d, *J* 11.8, OCH_AH_BAr), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) 12.0 (Si(CH(CH₃)₂)₃), 18.0 (Si(CH(CH₃)₂)₃), 19.7 (2'-CCH₃), 30.2 (2'-CCH₃), 34.1 (5'-C), 39.7 (2-C), 55.2 (ArOCH₃), 59.0 (1-C), 65.3 (4'-C), 68.6 (6'-C), 73.1 (OCH₂Ar), 73.4 (CH₂OAr), 98.6 (2'-C), 113.8 (Ar-*meta*-C), 129.3 (Ar-*ortho*-C), 130.4 (Ar-*ipso*-C) and 159.2 (Ar-*para*-C); *m/z* (+ESI) 484 ([MNH₄]⁺, 2%), 467 ([MH]⁺, 1), 121 (100); Found (+ESI): [MNa]⁺, 489.3005. C₂₆H₄₆O₅SiNa requires *MNa*, 489.3012.

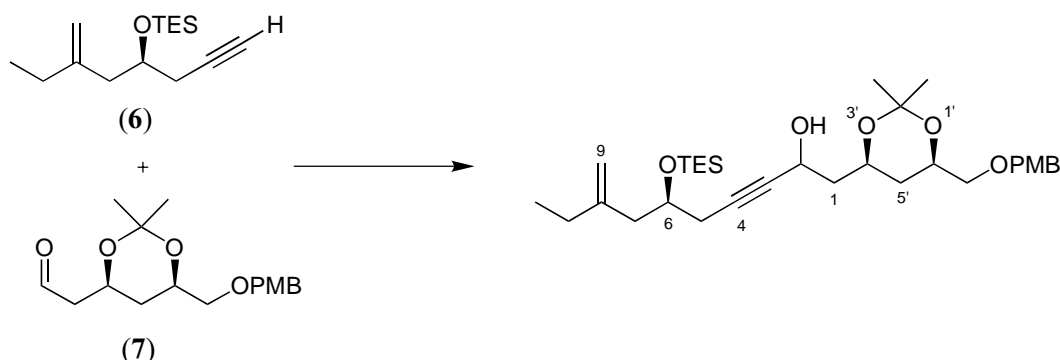
(4'*R*, 6'*R*)-2-(6'-(*p*-Methoxybenzyloxymethyl)-2',2'-dimethyl(1',3')dioxan-4'-yl)ethan-1-ol

Tetra *n*-butylammonium fluoride (1 M solution in THF, 14.2 ml, 14.2 mmol) was added to a solution of acetonide **(16)** (3.30 g, 7.08 mmol) in THF (20 ml) at room temperature. After 2 h the reaction was diluted with Et₂O (50 ml) and quenched with aqueous ammonium chloride (30 ml). The aqueous layer was separated and extracted with Et₂O (3 x 50 ml). The combined organic extracts were washed with brine (80 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Et₂O-Petrol, 3:1 then 5:1 then 1:0) afforded *alcohol* (2.16 g, 98%) as a colourless oil; *R*_f(Et₂O-Petrol, 3:1) 0.16; $[\alpha]_{\text{D}}^{25} +22.32$ (*c* 1.68, CHCl₃); ν_{max} (thin film)/cm⁻¹ 3455br w (OH), 1612m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl₃) 1.33 (1H, td, *J* 12.9, 11.7, 5'-H_A), 1.41 (3H, s, 2'-CCH₃), 1.47 (3H, s, 2'-CCH₃), 1.51 (1H, dt, *J* 12.9, 2.6, 5'-H_B), 1.68-1.77 (2H, m, 2-H_A, 2-H_B), 2.45 (1H, s, OH), 3.34 (1H, dd, *J* 5.0, 10.0, CH_AH_BOAr), 3.48 (1H, dd, *J* 5.7, 10.0, CH_AH_BOAr), 3.73-3.79 (2H, m, 1-H_A, 1-H_B), 3.80 (3H, s, ArOCH₃), 4.07-4.14 (2H, m, 4'-H, 6'-H), 4.47 (1H, d, *J* 11.8, OCH_AH_BAr), 4.52 (1H, d, *J* 11.8, OCH_AH_BAr), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*para*-H); δ_{C} (100 MHz; CDCl₃) 19.8 (2'-CCH₃), 30.1 (2'-CCH₃), 33.6 (5'-C), 38.2 (2-C), 55.3 (ArOCH₃), 60.8 (1-C), 68.5 (6'-C), 69.0 (4'-C), 73.1, 73.2 (CH₂OAr, OCH₂Ar), 98.7 (2'-C), 113.8 (Ar-*meta*-C), 129.4 (Ar-*ortho*-C), 130.2 (Ar-*ipso*-C) and 159.2 (Ar-*para*-C); *m/z* (+ESI) 328 ([MNH₄]⁺, 3%), 311 ([MH]⁺, 1), 121 (100); Found (+ESI): [MNa]⁺, 333.1666. C₁₇H₂₆O₅Na requires *MNa*, 333.1678.

(4*S*, 6*R*)-(6-(*p*-Methoxybenzyloxymethyl)-2,2-dimethyl(1,3)dioxan-4-yl)acetaldehyde (7)

Dimethylsulfoxide (0.69 ml, 10.2 mmol) was added dropwise to a solution of oxalyl chloride (0.84 ml, 10.2 mmol) in CH₂Cl₂ (12 ml) at -78 °C. After 0.5 h alcohol (1.27 g, 4.10 mmol) in CH₂Cl₂ (6 ml) was added dropwise and the solution stirred for a further 2 h at -78 °C. Triethylamine (3.77 ml, 28.7 mmol) was then added dropwise and the solution was allowed to warm to -30 °C over 1 h. The reaction was diluted with Et₂O (50 ml) and quenched with H₂O (30 ml). The aqueous layer was separated and extracted with Et₂O (3 x 50 ml). The combined organic extracts were washed with brine (80 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 2:1 then 1:1) afforded *aldehyde (7)* (1.15 g, 91%) as a yellow oil; *R*_f (Et₂O-Petrol, 5:1) 0.66; [α]_D²⁵ +12.0 (*c* 1.42, CHCl₃); ν_{max} (thin film)/cm⁻¹ 1723s (C=O), 1612m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_{H} (400 MHz; CDCl₃) 1.29 (1H, ap. q, *J* 12.0, 5-H_A), 1.39 (3H, s, 2-CCH₃), 1.48 (3H, s, 2-CCH₃), 1.61 (1H, ap. dt, *J* 12.0, 2.5, 5-H_B), 2.47 (1H, ddd, *J* 1.9, 4.9, 16.5, 4-CCH_ACH_BCHO), 2.61 (1H, ddd, *J* 1.9, 7.3, 16.5, 4-CCH_AH_BCHO), 3.61 (1H, dd, *J* 5.0, 10.0, CH_AH_BOAr), 3.48 (1H, dd, *J* 5.5, 10.0, CH_AH_BOAr), 3.80 (3H, s, ArOCH₃), 4.11 (1H, m, 6-H), 4.38-4.44 (1H, m, 4-H), 4.47 (1H, d, *J* 11.8, OCH_AH_BAr), 4.52 (1H, d, *J* 11.8, OCH_AH_BAr), 6.87 (2H, d, *J* 8.5, Ar-*meta*-H), 7.25 (2H, d, *J* 8.5, Ar-*ortho*-H) and 9.77 (1H, t, *J* 1.9, CHO); δ_{C} (100 MHz; CDCl₃) 19.6 (2-CCH₃), 29.9 (2-CCH₃), 33.6 (5-C), 49.9 (4-CH₂CHO), 55.3 (ArOCH₃), 64.4 (4-C), 68.3 (6-C), 73.0, 73.1 (CH₂OAr, OCH₂Ar), 98.9 (C-2), 113.8 (Ar-*meta*-C), 129.4 (Ar-*ortho*-C), 130.2 (Ar-*ipso*-C), 159.3 (Ar-*para*-C) and 200.8 (CHO); *m/z* (+ESI) 331 ([MNa]⁺, 5%), 326 (55), 308 ((M)⁺, 3), 121 (100); Found (+ESI): [MNa]⁺, 331.1523. C₁₇H₂₄O₅Na requires *MNa*, 331.1521.

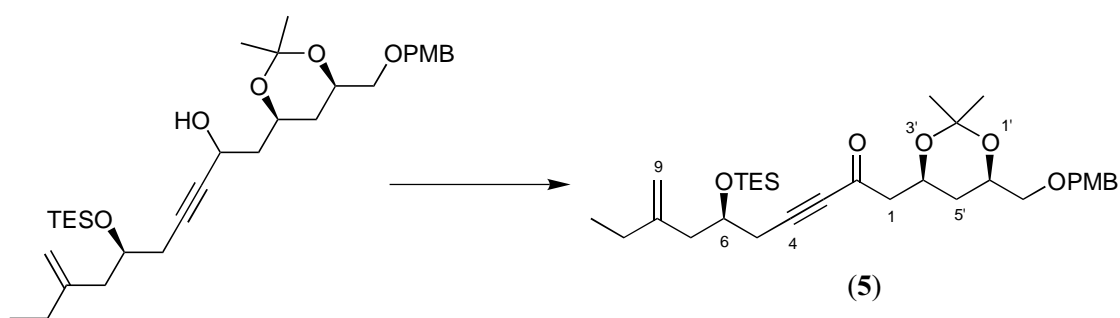
(2*RS*, 4'*R*, 6*R*, 6'*R*)-8-Ethyl-1-(6'-(*p*-methoxybenzyloxymethyl)-2',2'-dimethyl(1',3')dioxan-4'-yl)-6-(triethylsilanyloxy)non-8-en-3-yn-2-ol



Isopropylmagnesium chloride (2 M solution in THF, 3.47 ml, 6.94 mmol) was added to a solution of alkyne (6) (1.75 g, 6.94 mmol) in THF (23 ml) at 0 °C. The solution was then warmed to room temperature and stirred for 1.5 h. The solution was cooled to -10 °C and a solution of aldehyde (7) (1.65 g, 5.35 mmol) in THF (25 ml) was added. After 3 h at -10 °C, the reaction was quenched with aqueous ammonium chloride (30 ml) and warmed to room temperature. The aqueous layer was separated and extracted with Et₂O (3 x 80 ml). The combined organic extracts were washed with brine (150 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 2:1 then 1:1) afforded *alcohol* (2.79 g, 93%) as a colourless oil and as a 1:1 mixture of C(2) diastereoisomers; *R*_f (Et₂O-Petrol, 2:1) 0.53, 0.57; *v*_{max} (thin film)/cm⁻¹ 3430br w (OH), 1645w (alkene C=C), 1613m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); *δ*_H (600 MHz; CDCl₃) 0.60 (6H, q, *J* 7.9, Si(CH₂CH₃)₃), 0.95 (9H, t, *J* 7.9, Si(CH₂CH₃)₃), 1.03 (3H, t, *J* 7.2, 8-CCH₂CH₃), 1.29 (0.5H, ap. q, *J* 12.4, 5'-H_A), 1.33 (0.5H, ap. q, *J* 12.4, 5'-H_A), 1.39, 1.40 (3H, s, 2'-CCH₃), 1.46 (1.5H, s, 2'-CCH₃), 1.48 (0.5H, dt, *J* 13.0, 2.6, 5'-H_B), 1.51 (1.5H, s, 2'-CCH₃), 1.54 (0.5H, dt, *J* 13.0, 2.3, 5'-H_B), 1.73-1.78 (1H, m, 1-H_A), 1.88-1.97 (1H, m, 1-H_B), 2.05 (2H, q, *J* 7.2, 8-CCH₂CH₃), 2.20-2.24 (1H, 2 x dd, *J* 5.7, 13.6 and *J* 5.7, 13.6, 7-H_A), 2.31-2.42 (3H, m, 5-H_A, 5-H_B, 7-H_B), 2.74 (0.5H, s, OH), 3.25 (0.5H, d, *J* 7.8, OH), 3.32-3.36 (1H, 2 x dd, *J* 4.8, 9.8 and *J* 4.8, 9.8, CH_AH_BOAr), 3.45-3.49 (1H, 2 x dd, *J* 5.6, 9.8 and *J* 5.6, 9.8, CH_AH_BOAr), 3.80 (3H, s, ArOCH₃), 3.91 (1H, ap. sextet, *J* 5.7, 6-H), 4.07-4.15 (1.5H, m, 4'-H, 6'-H, 6'-H), 4.47 (1H, 2 x d, *J* 11.8 and *J* 11.8, OCH_AH_BAr) overlapping 4.44-4.49 (0.5H, 4'-H), 4.52 (1H, 2 x d, *J* 11.8 and *J* 11.8, OCH_AH_BAr), 4.57-4.59 (1H, m, 2-H), 4.78 (1H, s, 9-H_A), 4.81 (1H, s, 9-H_B), 6.88 (2H, d, *J* 8.5, Ar-*meta*-H) and 7.25 (2H, d, *J* 8.5, Ar-*ortho*-H); *δ*_C (100 MHz; CDCl₃) 5.0 (Si(CH₂CH₃)₃), 6.9

(Si(CH₂CH₃)₃), 12.2 (8-CCH₂CH₃), 19.8 (2 x 2'-CCH₃), 27.5 (5-C), 29.2 (8-CCH₂CH₃), 30.0, 30.1 (2'-CCH₃), 33.5, 33.8 (5'-C), 42.6 (1_A-C), 43.8, 43.9 (7-C), 44.3 (1_B-C), 55.3 (ArOCH₃), 60.8, 61.4 (2-C), 67.1, 68.1 (4'-C), 68.4, 68.6 (6'-C), 70.1 (2 x 6-C), 73.1 (CH₂OAr, OCH₂Ar), 82.3, 82.4, 82.5, 82.6 (3-C, 4-C), 98.8 (2 x 2'-C), 111.0 (9-C), 113.8 (Ar-*meta*-C), 129.3 (2 x Ar-*ortho*-C), 130.3 (Ar-*ipso*-C), 147.8 (8-C) and 159.2 (Ar-*para*-C); *m/z* (+ESI) 583 ([MNa]⁺, 20%), 578 ([MNH₄]⁺, 100), 561 ([MH]⁺, 31), 543 (43), 503 (40), 485 (20), 411 (21), 373 (33), 353 (41), 241 (40), 156 (32), 120 (100); Found (+ESI): [MNa]⁺, 583.3448. C₃₂H₅₂O₆SiNa requires *MNa*, 583.3431.

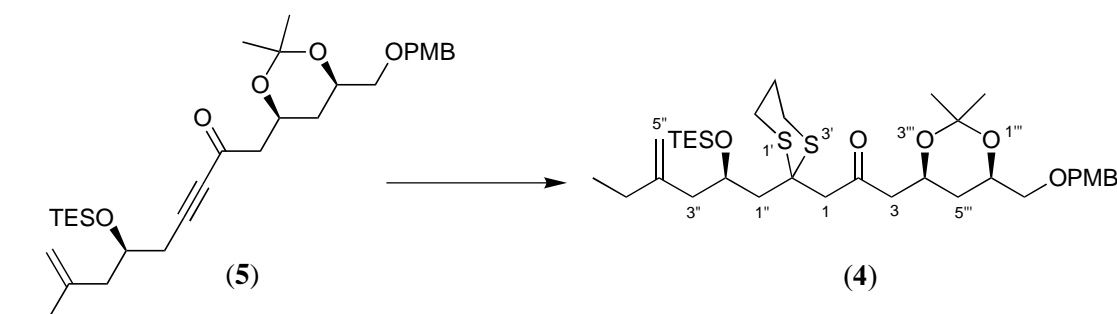
(4'*S*, 6*R*, 6'*R*)-8-Ethyl-1-(6'-(*p*-methoxybenzyloxymethyl)-2',2'-dimethyl(1',3')dioxan-4'-yl)-6-(triethylsilyloxy)non-8-en-3-yn-2-one (5)



Dess-Martin Periodinane (1.14 g, 2.70 mmol) was added to a solution of alcohol (1.01 g, 1.89 mmol) in CH₂Cl₂ (8 ml) at room temperature. After 3.5 h the solution was diluted with Et₂O (15 ml) and quenched with a mixture of aqueous sodium thiosulfate (3 ml) and aqueous sodium hydrogen carbonate (3 ml). The mixture was stirred for 45 min, then aqueous phase was separated and extracted with Et₂O (3 x 50 ml). The combined organic extracts were washed with brine (80 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 3:1) afforded *ynone* (**5**) (0.99 g, 99%) as a colourless oil; *R*_f (Petrol-Et₂O, 2:1) 0.57; [α]_D²⁵ +3.1 (*c* 1.41, CHCl₃); *v*_{max} (thin film)/cm⁻¹ 2214m (C≡C), 1675s (C=O), 1613m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_H (600 MHz; CDCl₃) 0.61 (6H, q, *J* 7.9, Si(CH₂CH₃)₃), 0.96 (9H, t, *J* 7.9, Si(CH₂CH₃)₃), 1.03 (3H, t, *J* 7.4, 8-CCH₂CH₃), 1.23 (1H, ap. q, *J* 11.9, 5'-H_A), 1.38 (3H, s, 2'-CCH₃), 1.47 (3H, s, 2'-CCH₃), 1.60 (1H, dt, *J* 12.8, 2.4, 5'-H_B), 2.04 (2H, q, *J* 7.4, 8-CCH₂CH₃), 2.28 (1H, dd, *J* 6.0, 13.8, 7-H_A), 2.31 (1H, dd, *J* 6.7, 13.8, 7-H_B), 2.46 (1H, dd, *J* 5.7, 17.1, 5-H_A), 2.55 (1H, dd, *J* 5.6, 17.1, 5-H_B), 2.57 (1H, dd, *J* 5.7, 16.1, 1-H_A), 2.78 (1H, dd, *J* 7.1, 16.1, 1-H_B), 3.34 (1H, dd, *J* 4.8, 10.0, CH_AH_BOAr), 3.46 (1H, dd, *J* 5.7, 10.0, CH_AH_BOAr), 3.80 (3H, s, ArOCH₃), 4.00 (1H, ap. quint., *J* 6.0, 6-H), 4.08-4.12 (1H, m, 6'-H), 4.47 (1H, d, *J* 11.8,

OCH_AH_BAr) overlapping 4.45-4.49 (1H, m, 4'-H), 4.52 (1H, d, *J* 11.8, OCH_AH_BAr), 4.79 (1H, s, 9-H_A), 4.83 (1H, d, *J* 1.4, 9-H_B), 6.87 (2H, d, *J* 8.6, Ar-*meta*-H) and 7.25 (2H, d, *J* 8.6, Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) 4.9 (Si(CH₂CH₃)₃), 6.8 (Si(CH₂CH₃)₃), 12.2 (8-CCH₂CH₃), 19.6 (2'-CCH₃), 27.5 (5-C), 29.1 (8-CCH₂CH₃), 30.0 (2'-CCH₃), 33.4 (5'-C), 44.2 (7-C), 51.9 (1-C), 55.3 (ArOCH₃), 65.0 (4'-C), 68.4 (6'-C), 69.3 (6-C), 73.1 (CH₂OAr, OCH₂Ar), 82.4 (3-C), 92.1 (4-C), 98.9 (2'-C), 111.5 (9-C), 113.8 (Ar-*meta*-C), 129.3 (Ar-*ortho*-C), 130.3 (Ar-*ipso*-C), 147.3 (8-C), 159.2 (Ar-*para*-C) and 184.8 (2-C); *m/z* (+ESI) 581 ([MNa]⁺, 9%), 576 ([MNH₄]⁺, 100), 559 ([MH]⁺, 29), 501 (20), 427 (10), 369 (11), 121 (100); Found (+ESI): [MNa]⁺, 581.3289. C₃₂H₅₀O₆SiNa requires *MNa*, 581.3274.

(2''*R*, 4'''*S*, 6'''*R*)-1-(2'-(4''-Ethyl-2''-(triethylsilanyloxy)pent-4''-en-1''-yl)-(1',3')dithian-2'-yl)-3-(6'''-(*p*-methoxybenzyloxymethyl)-2'''',2'''-dimethyl-(1''',3''')dioxan-4'''-yl)propan-2-one (4)



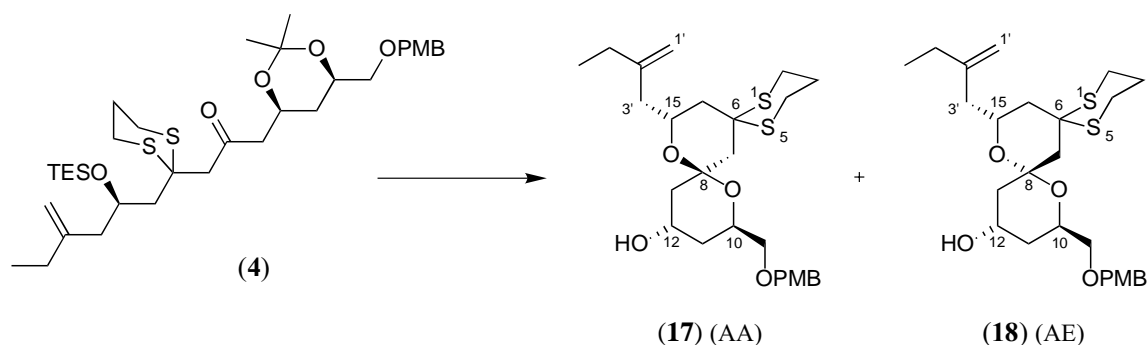
1,3-Propanedithiol (0.23 ml, 2.30 mmol) was added to a solution of ynone (**5**) (1.03 g, 1.84 mmol) and sodium methoxide (135 mg, 2.49 mmol) in MeOH (12 ml) and CH₂Cl₂ (4 ml) at -10 °C. The solution was stirred overnight whilst warming to 5 °C and was then diluted with Et₂O (30 ml) and quenched with aqueous ammonium chloride (30 ml). The aqueous layer was separated and extracted with Et₂O (4 x 30 ml). The combined organic extracts were washed with brine (60 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 5:1 then 2:1) afforded *dithiane* (**4**) (1.20 g, 98%) as a colourless oil; *R_f*(Et₂O-Petrol, 2:1) 0.62; $[\alpha]_D^{25}$ -1.32 (*c* 1.52, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 1708m (C=O), 1613m (Ar C=C), 1514s (Ar C=C); δ_H (600 MHz; CDCl₃) 0.64 (6H, q, *J* 8.0, Si(CH₂CH₃)₃), 0.97 (9H, t, *J* 8.0, Si(CH₂CH₃)₃), 1.05 (3H, t, *J* 7.3, 4''-CCH₂CH₃), 1.20 (1H, ap. q, *J* 11.9, 5'''-H_A), 1.38 (3H, s, 2'''-CCH₃), 1.46 (3H, s, 2'''-CCH₃), 1.61 (1H, dt, *J* 12.8, 2.5, 5'''-H_B), 1.91-1.95 (2H, m, 5'-H), 2.00-2.12 (2H, m, 4''-CCH₂CH₃), 2.20 (1H, dd, *J* 9.6, 13.4, 3''-H_A), 2.25 (1H, dd, *J* 8.2, 15.0, 1''-H_A), 2.32-2.36 (2H, m, 1''-H_B, 3''-H_B), 2.50 (1H, dd, *J* 5.5, 16.0, 3-H_A), 2.75 (1H, dd, *J* 6.7, 16.0, 3-H_B) overlapping 2.70-2.81 (4H, m, 4'-H, 6'-

H), 3.09 (1H, d, J 15.9, 1- H_A), 3.30 (1H, d, J 15.9, 1- H_B), 3.33 (1H, dd, J 4.5, 10.2, CH_AH_BOAr), 3.45 (1H, dd, J 5.9, 10.2, CH_AH_BOAr), 3.80 (3H, s, $ArOCH_3$), 4.09 (1H, dtd, J 11.9, 5.9, 2.5, 6'''-H), 4.27-4.30 (1H, m, 2''-H), 4.35 (1H, dtd, J 11.9, 6.7, 5.5, 4'''-H), 4.47 (1H, d, J 11.8, OCH_AH_BOAr), 4.52 (1H, d, J 11.8, OCH_AH_BOAr), 4.81 (1H, s, 5''- H_A), 4.83 (1H, d, J 1.1, 5''- H_B), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; $CDCl_3$) 5.5 ($Si(CH_2CH_3)_3$), 7.0 ($Si(CH_2CH_3)_3$), 12.2 (4''-CCH₂CH₃), 19.7 (2'''-CCH₃), 24.9 (5'-C), 26.2, 26.5 (4'-C, 6'-C), 29.0 (4''-CCH₂CH₃), 30.0 (2'''-CCH₃), 33.6 (5'''-C), 43.8 (1''-C), 46.2 (3''-C), 49.4 (2''-C), 50.8 (3-C), 51.9 (1-C), 55.2 ($ArOCH_3$), 65.6 (4'''-C), 68.4 (6'''-C), 69.0 (2''-C), 73.0 (OCH_2Ar), 73.2 (CH_2OAr), 98.8 (2'''-C), 111.4 (5''-C), 113.7 (Ar-*meta*-C), 129.3 (Ar-*ortho*-C), 130.3 (Ar-*ipso*-C), 148.0 (4''-C), 159.2 (Ar-*para*-C) and 204.5 (2-C); m/z (+ESI) 689 ($[MNa]^+$, 30%), 684 ($[MNH_4]^+$, 100), 667 ($[MH]^+$, 68), 609 (19), 535 (33), 439 (72), 363 (10), 307 (11), 249 (61), 231 (22), 121 (30); Found (+ESI): $[MNa]^+$, 689.3325. $C_{35}H_{58}O_6S_2SiNa$ requires MNa , 689.3342.

(8*R*, 10*R*, 12*S*, 15*R*)-15-(2'-Ethylprop-1'-en-3'-yl)-10-(*p*-methoxybenzyloxymethyl)-9,14-dioxo-1,5-dithiadispiro(5.1.5.3)hexadecan-12-ol (17) (AA)

and

(8*S*, 10*R*, 12*S*, 15*R*)-15-(2'-Ethylprop-1'-en-3'-yl)-10-(*p*-methoxybenzyloxymethyl)-9,14-dioxo-1,5-dithiadispiro(5.1.5.3)hexadecan-12-ol (18) (AE)



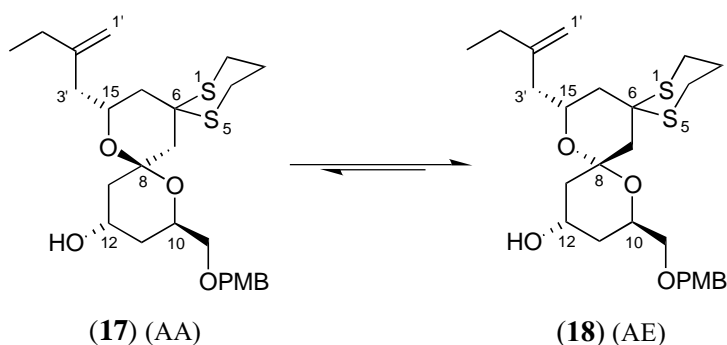
Perchloric acid (10% v/v solution in H_2O , 12.5 ml) was added to a solution of dithiane (4) (1.74 g, 2.61 mmol) in MeCN (30 ml) and CH_2Cl_2 (30 ml) at 0 °C. After 0.5 h the solution was diluted with Et_2O (50 ml) and neutralised using aqueous sodium hydrogen carbonate (50 ml). The aqueous phase was separated and extracted with Et_2O (4 x 50 ml). The combined organic extracts were washed with brine (80 ml), dried ($MgSO_4$) and concentrated *in vacuo*, affording a 4:1 mixture of stereoisomers favouring the undesired axial-axial spiroketal. Flash chromatography on silica (CH_2Cl_2 - Et_2O , 1:0 then 10:1 then 5:1 then 3:1 then 2:1) provided, in order of elution: *axial*-

equatorial spiroketal (18) (AE) (256 mg, 19%) as a colourless oil; R_f (CH₂Cl₂-Et₂O, 5:1) 0.57; $[\alpha]_D^{25}$ -31.6 (*c* 2.77, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3519w (OH), 1646w (alkene C=C), 1612m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_H (600 MHz; CDCl₃) 1.05 (3H, t, *J* 7.4, 2'-CCH₂CH₃), 1.49 (1H, dd, *J* 3.4, 14.5, 13-H_{ax}), 1.57 (1H, td, *J* 13.5, 3.0, 11-H_{ax}), 1.72 (1H, ap. dq, *J* 13.5, 2.2, 11-H_{eq}), 1.94-1.98 (1H, m, 3-H_A), 2.02 (1H, dd, *J* 11.4, 13.8, 16-H_{ax}) overlapping 2.00-2.07 (1H, m, 3-H_B), 2.08 (1H, d, *J* 14.7, 7-H_{ax}), 2.09-2.15 (2H, m, 2'-CCH₂CH₃), 2.20 (1H, dd, *J* 4.6, 13.8, 3'-H_A), 2.27 (1H, dd, *J* 1.3, 14.7, 7-H_{eq}), 2.34 (1H, d, *J* 13.8, 16-H_{eq}), 2.38 (1H, dd, *J* 8.6, 13.8, 3'-H_B), 2.56 (1H, ddd, *J* 2.1, 2.8, 14.5, 13-H_{eq}), 2.74 (1H, ddd, *J* 3.2, 7.2, 14.5, 2-H_A or 4-H_A), 2.84 (1H, ddd, *J* 3.4, 7.2, 14.5, 2-H_A or 4-H_A), 2.88 (1H, ddd, *J* 3.4, 9.3, 14.5, 2-H_B or 4-H_B), 2.97 (1H, ddd, *J* 3.2, 9.3, 14.5, 2-H_B or 4-H_B), 3.49 (2H, d, *J* 4.7, CH₂OAr), 3.65 (1H, d, *J* 11.0, OH), 3.81 (3H, s, ArOCH₃), 4.03 (1H, ap. dq, *J* 11.0, 2.9, 12-H), 4.13 (1H, dddd, *J* 2.1, 4.6, 8.6, 11.4, 15-H), 4.39-4.43 (1H, m, 10-H), 4.53 (1H, d, *J* 12.1, OCH_AH_BAr), 4.55 (1H, d, *J* 12.1, OCH_AH_BAr), 4.88 (1H, d, *J* 0.8, 1'-H_A), 4.90 (1H, dd, *J* 1.6, 2.8, 1'-H_B), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.27 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) 12.2 (2'-CCH₂CH₃), 25.1 (3-C), 26.6, 26.8 (2-C, 4-C), 28.9 (2'-CCH₂CH₃), 34.3 (11-C), 37.5 (13-C), 41.3 (16-C), 43.0 (3'-C), 45.9 (6-C), 47.9 (7-C), 55.3 (ArOCH₃), 64.7 (12-C), 65.0 (10-C), 68.2 (15-C), 72.8 (CH₂OAr), 73.0 (OCH₂Ar), 99.0 (8-C), 111.7 (1'-C), 113.7 (Ar-*meta*-C), 129.1 (Ar-*ortho*-C), 130.6 (Ar-*ipso*-C), 147.2 (2'-C) and 159.1 (Ar-*para*-C); *m/z* (+ESI) 512 ([MNH₄]⁺, 11%), 495 ([MH]⁺, 100), 349 (62), 121 (23); Found (+ESI): [MNa]⁺, 517.2059. C₂₆H₃₈O₅S₂Na requires *MNa*, 517.2058.

axial-axial spiroketal (17) (AA) (1.04 g, 79%) as a colourless oil; R_f (CH₂Cl₂-Et₂O, 5:1) 0.19; $[\alpha]_D^{25}$ +35.3 (*c* 2.92, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3455br w (OH), 1645w (alkene C=C), 1612m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_H (600 MHz; CDCl₃) 1.03 (3H, t, *J* 7.4, 2'-CCH₂CH₃), 1.49 (1H, dd, *J* 11.0, 13.7, 16-H_{ax}), 1.56 (1H, dd, *J* 8.0, 13.2, 13-H_{ax}), 1.60 (1H, ddd, *J* 3.2, 8.3, 13.0, 11-H_{eq}), 1.65 (1H, d, *J* 14.6, 7-H_{ax}), 1.82-1.87 (1H, m, 3-H_A), 1.90 (1H, ddd, *J* 1.2, 4.2, 13.2, 13-H_{eq}), 1.97-2.05 (4H, m, 3-H_B, 11-H_{ax}, 2'-CH₂CH₃), 2.11 (1H, dd, *J* 8.5, 13.9, 3'-H_A), 2.30 (1H, dd, *J* 5.1, 13.9, 3'-H_B), 2.52 (1H, ap. dt, *J* 13.7, 1.8, 16-H_{eq}), 2.59 (1H, dt, *J* 14.2, 3.8, 2-H_A or 4-H_A), 2.61 (1H, dd, *J* 2.1, 14.6, 7-H_{eq}), 2.69 (1H, dt, *J* 14.2, 3.8, 2-H_A or 4-H_A), 2.81 (1H, ddd, *J* 2.9, 11.6, 14.2, 2-H_B or 4-H_B), 3.06 (1H, ddd, *J* 2.9, 11.6, 14.2, 2-H_B or 4-H_B), 3.62 (2H, d, *J* 6.8, CH₂OAr), 3.80 (3H, s, ArOCH₃), 4.20-4.26 (2H, m, 10-H, 12-H), 4.35 (1H, dddd, *J* 1.8, 5.1, 8.5, 11.0, 15-H), 4.47 (1H, d, *J* 11.6, OCH_AH_BAr), 4.51 (1H, d, *J* 11.6, OCH_AH_BAr), 4.78 (1H, s, 1'-H_A), 4.82 (1H, d, *J* 1.4, 1'-H_B), 6.86 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz;

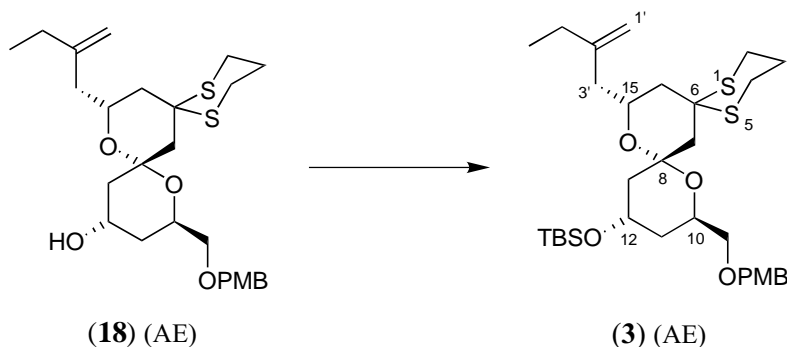
CDCl₃) 12.4 (2'-CCH₂CH₃), 25.3 (3-C), 26.2, 26.3 (2-C, 4-C), 29.2 (2'-CCH₂CH₃), 34.6 (11-C), 41.2 (16-C), 41.9 (3'-C), 44.7 (13-C), 45.7 (7-C), 46.8 (6-C), 55.3 (ArOCH₃), 62.4 (12-C), 66.0 (15-C), 70.2 (10-C), 71.5 (CH₂OAr), 72.8 (OCH₂Ar), 98.6 (8-C), 110.7 (1'-C), 113.7 (Ar-*meta*-C), 129.2 (Ar-*ortho*-C), 130.6 (Ar-*ipso*-C), 147.4 (2'-C) and 159.1 (Ar-*para*-C); *m/z* (+ESI) 517 ([MNa]⁺, 100%), 495 ([MH]⁺, 100), 349 (53), 121 (29); Found (+ESI): [MNa]⁺, 517.2058. C₂₆H₃₈O₅S₂Na requires *MNa*, 517.2058.

Epimerisation of (8*R*, 10*R*, 12*S*, 15*R*)-15-(2'-Ethylprop-1'-en-3'-yl)-10-(*p*-methoxybenzyloxymethyl)-9,14-dioxo-1,5-dithiadispiro(5.1.5.3)hexadecan-12-ol (17) (AA)



Perchloric acid (3.5 wt% in H₂O, 9.7 ml, 3.38 mmol) was added to a vigorously stirred solution of axial-axial spiroketal (17) (AA) (1.04 g, 2.11 mmol) and calcium perchlorate tetrahydrate (3.27 g, 10.5 mmol) in CH₂Cl₂ (65 ml) and MeCN (6.5 ml) at room temperature. Vigorous stirring was continued overnight (16 h), the solution was then diluted with Et₂O (80 ml) and quenched with aqueous sodium hydrogen carbonate (80 ml). The aqueous layer was separated and extracted with Et₂O (4 x 50 ml). The combined organic extracts were washed with brine (100 ml), dried (MgSO₄) and concentrated *in vacuo*, affording a 2.2:1 mixture of C(8) stereoisomers favouring the desired axial-equatorial spiroketal (18) (AE). Flash chromatography on silica gel (CH₂Cl₂-Et₂O, 1:0 then 10:1 then 5:1 then 3:1 then 2:1) provided, in order of elution: *axial-equatorial spiroketal* (18) (AE) (1.73 g, 69%) as a colourless oil; data *vide ante*; and *axial-axial spiroketal* (17) (AA) (0.863 g, 33%) as a colourless oil; data *vide ante*.

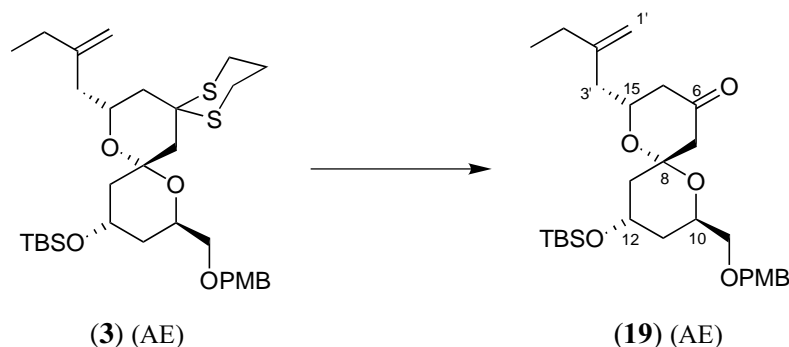
(8*S*, 10*R*, 12*S*, 15*R*)-12-(*tert*-Butyldimethylsilanyloxy)-15-(2'-ethylprop-1'-en-3'-yl)-10-(*p*-methoxybenzyloxymethyl)-9,14-dioxo-1,5-dithiadispiro(5.1.5.3)hexadecane (3) (AE)



tert-Butyldimethylsilyl trifluoromethanesulfonate (1.00 ml, 4.37 mmol) and 2,6-lutidine (0.38 ml, 3.28 mmol) in CH₂Cl₂ (7 ml) were added dropwise over 1 h to a solution of spiroketal alcohol (18) (AE) (1.08 g, 2.19 mmol) and 2,6-lutidine (1.27 ml, 10.93 mmol) in CH₂Cl₂ (35 ml) at -78 °C. After 1 h at -78 °C the solution was diluted with Et₂O (65 ml) and quenched with aqueous sodium hydrogen carbonate (40 ml). The aqueous layer was separated and extracted with Et₂O (3 x 40 ml). The combined organic extracts were washed with brine (80ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 5:1 then 2:1) afforded *silyl spiroketal* (3) (AE) (1.27 g, 95%) as a colourless oil; *R*_f (Petrol-Et₂O, 2:1) 0.33; [α]_D²⁵ -17.5 (*c* 1.76, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 1644w (alkene C=C), 1613m (Ar C=C), 1587w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl₃) 0.04, 0.05 (2 x 3H, 2 x s, Si(CH₃)₂), 0.89 (9H, s, SiC(CH₃)₃), 1.03 (3H, t, *J* 7.4, 2'-CCH₂CH₃), 1.53-1.56 (1H, m, 11-H_{eq}), 1.62 (1H, dd, *J* 3.7, 14.7, 13-H_{ax}), 1.65 (1H, td, *J* 11.4, 3.7, 11-H_{ax}), 1.74 (1H, dd, *J* 11.1, 13.9, 16-H_{ax}), 1.95 (1H, d, *J* 14.4, 7-H_{ax}) overlapping 1.92-2.01 (2H, m, 3-H_A, 3-H_B), 2.03 (2H, q, *J* 7.4, 2'-CCH₂CH₃), 2.20 (1H, dd, *J* 9.3, 14.3, 3'-H_A), 2.29 (1H, dd, *J* 1.3, 14.4, 7-H_{eq}), 2.40 (1H, d, *J* 13.9, 16-H_{eq}), 2.49-2.52 (2H, m, 3'-H_B, 13-H_{eq}), 2.73 (1H, ddd, *J* 3.3, 6.9, 14.4, 2-H_A or 4-H_A), 2.80-2.84 (2H, m, 2-H_A or 4-H_A and 2-H_B or 4-H_B), 2.96 (1H, ddd, *J* 3.3, 9.2, 14.4, 2-H_B or 4-H_B), 3.47 (2H, d, *J* 4.8, CH₂OAr), 3.80 (3H, s, ArOCH₃), 4.04 (1H, dddd, *J* 1.8, 4.4, 9.3, 11.1, 15-H), 4.11 (1H, ap. quint., *J* 3.7, 12-H), 4.52 (2H, s, OCH₂Ar), overlapping 4.52-4.56 (1H, m, 10-H), 4.74 (1H, s, 1'-H_A), 4.81 (1H, s, 1'-H_B), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.27 (2H, AA'BB', Ar-*ortho*-H); δ_{C} (100 Mhz, CDCl₃) -4.9, -4.7 (Si(CH₃)₂), 12.4 (2'-CCH₂CH₃), 18.2 (SiC(CH₃)₃), 25.3 (3-C), 26.0 (SiC(CH₃)₃), 26.4, 26.7 (2-C, 4-C), 29.5 (2'-CCH₂CH₃), 35.0 (11-C), 38.6 (13-C), 40.8 (16-C), 42.2 (3'-C), 47.0 (6-C), 48.4 (7-C), 55.2 (ArOCH₃), 64.5 (12-C), 64.8 (10-C), 67.7 (15-C), 72.9 (CH₂OAr, OCH₂Ar),

97.7 (8-C), 110.2 (1'-C), 113.7 (Ar-*meta*-C), 129.2 (Ar-*ortho*-C), 130.7 (Ar-*ipso*-C), 147.6 (2'-C) and 159.1 (Ar-*para*-C); m/z (+ESI) 631 ($[MNa]^+$, 3%), 609 ($[MH]^+$, 69), 351 (10), 349 (100), 121 (46); Found (+ESI): $[MNa]^+$, 631.2938. $C_{32}H_{52}O_5S_2SiNa$ requires MNa , 631.2923.

(2*R*, 6*S*, 8*R*, 10*S*)-10-(*tert*-Butyldimethylsilanyloxy)-2-(2'-ethylprop-1'-en-3'-yl)-8-(*p*-methoxybenzyloxymethyl)-1,7-dioxaspiro(5.5)undecan-4-one (19) (AE)



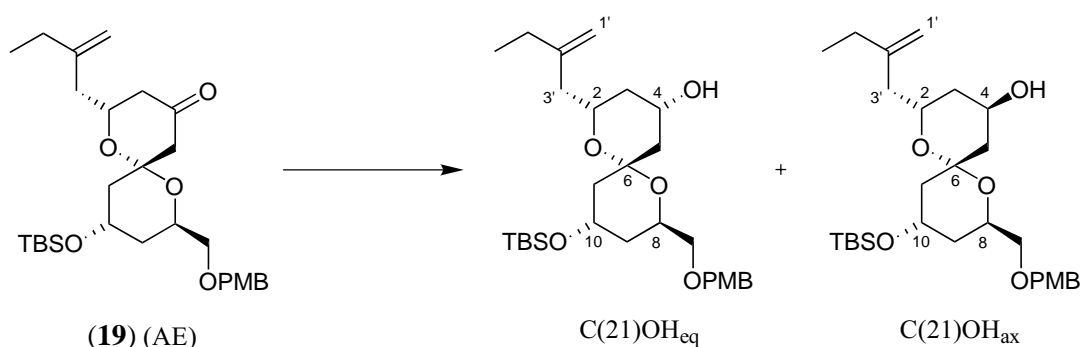
Bis(trifluoroacetoxy)iodobenzene (71 mg, 0.17 mmol) was added to a solution of dithianyl spiroketal (3) (AE) (50 mg, 0.08 mmol) in MeOH (0.5 ml) at 0 °C. After 0.5 h the reaction was diluted with Et₂O (3 ml), quenched with aqueous sodium hydrogen carbonate (2 ml) and stirred vigorously for 20 min. The aqueous phase was separated and extracted with Et₂O (4 x 2 ml). The combined organic extracts were washed with aqueous sodium hydrogen carbonate (4 ml) and brine (4 ml) then concentrated *in vacuo*. The crude material was dissolved in a glacial AcOH-THF-H₂O (4:4:1) mixture (0.75 ml) and stirred at 30 °C for 5 h. [Progress of this reaction was monitored by LC/MS using a reverse gradient. Retention times: 5.45 min (19); 5.62 min (methoxy acetal). Mobile phase: 10 mM NH₄OAc-0.1% HCO₂H (Solvent A); MeCN-H₂O (95:5). Method: 0.00-4.19 min (A:B 1:0); 4.20-8.00 min (A:B, 0:1); flow rate 1.00 ml min⁻¹; analysis wavelengths 215 nm (start) to 390 nm (end); column and sample temperature 20 °C]. The reaction was diluted with Et₂O (2 ml) and quenched with aqueous sodium hydrogen carbonate (2 ml). The aqueous phase was separated and extracted with Et₂O (4 x 2 ml). The combined organic extracts were washed with aqueous sodium hydrogen carbonate (4 ml) and brine (4 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 3:1) afforded *spiroketal ketone* (19) (AE) (35 mg, 82%) as a colourless oil; R_f (Petrol-Et₂O, 2:1) 0.43; $[\alpha]_D^{25}$ -47.9 (c 1.43, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 1728s (C=O), 1646w (alkene C=C), 1613m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_H (800 MHz; CDCl₃) 0.04, 0.05 (2 x 3H, 2 x s, Si(CH₃)₂), 0.90 (9H, s, SiC(CH₃)₃), 1.01 (3H, t, J 7.4, 2'-CCH₂CH₃), 1.54 (1H, dd, J 3.8, 14.2, 11-H_{ax}) overlapping 1.53-1.59 (2H, m, 9-H_{ax}, 9-

H_{eq}), 1.95 (1H, ddd, J 1.3, 3.6, 14.2, 11- H_{eq}), 2.00 (2H, q, J 7.4, 2'- CCH_2CH_3), 2.26 (1H, dd, J 8.6, 13.8, 3- H_{ax}), 2.36 (1H, dd, J 3.3, 15.9, 3'- H_A), 2.51 (1H, d, J 15.5, 5- H_A), 2.53 (1H, d, J 15.5, 5- H_B), 2.55 (1H, dd, J 11.3, 15.9, 3'- H_B), 2.57 (1H, dd, J 4.6, 13.8, 3- H_{eq}), 3.44 (2H, d, J 5.0, CH_2OAr), 3.80 (3H, s, $ArOCH_3$), 4.12-4.15 (2H, m, 2-H, 10-H), 4.48 (1H, d, J 12.0, OCH_AH_BAr), 4.50 (1H, d, J 12.0, OCH_AH_BAr), 4.56-4.59 (1H, m, 8-H), 4.70 (1H, s, 1'- H_A), 4.79 (1H, d, J 1.5, 1'- H_B), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; $CDCl_3$) -4.9, -4.8 ($Si(CH_3)_2$), 12.2 (2'- CCH_2CH_3), 18.1 ($SiC(CH_3)_3$), 25.9 ($SiC(CH_3)_3$), 29.2 (2'- CCH_2CH_3), 34.8 (9-C), 39.5 (11-C), 43.5 (3-C), 44.3 (3'-C), 51.9 (5-C), 55.2 ($ArOCH_3$), 64.2 (10-C), 65.1 (8-C), 70.1 (2-C), 72.8 (CH_2OAr), 72.9 (OCH_2Ar), 99.1 (6-C), 111.1 (1'-C), 113.7 (Ar-*meta*-C), 129.1 (Ar-*ortho*-C), 130.5 (Ar-*ipso*-C), 146.7 (2'-C), 159.1 (Ar-*para*-C) and 207.3 (4-C); m/z (+ESI) 541 ($[MNa]^+$, 5%), 536 ($[MNH_4]^+$, 100), 519 ($[MH]^+$, 11), 387 (19), 121 (71); Found (+ESI): $[MNa]^+$, 541.2954. $C_{29}H_{46}O_6SiNa$ requires MNa , 541.2961.

(2*R*, 4*S*, 6*R*, 8*R*, 10*S*)-10-(*tert*-Butyldimethylsilanyloxy)-2-(2'-ethylprop-1'-en-3'-yl)-8-(*p*-methoxybenzyloxymethyl)-1,7-dioxaspiro(5.5)undecan-4-ol (AE)

and

(2*R*, 4*R*, 6*R*, 8*R*, 10*S*)-10-(*tert*-Butyldimethylsilanyloxy)-2-(2'-ethylprop-1'-en-3'-yl)-8-(*p*-methoxybenzyloxymethyl)-1,7-dioxaspiro(5.5)undecan-4-ol (AE)



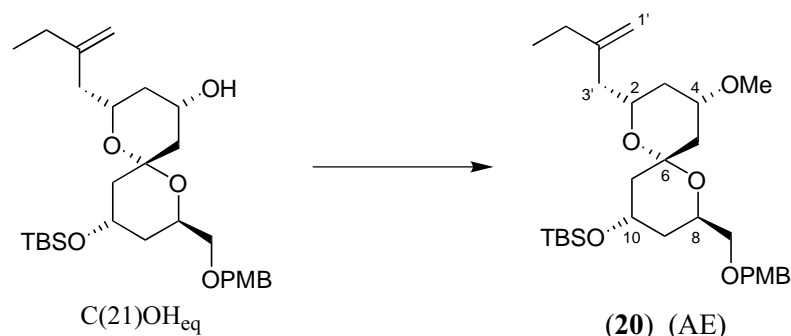
Cerium trichloride heptahydrate (122 mg, 0.33 mmol) was added to a solution of spiroketal ketone **(19) (AE)** (53 mg, 0.100 mmol) in MeOH (0.5 ml) at room temperature. After 0.5 h the solution was cooled to -78 °C and sodium borohydride (8 mg, 0.21 mmol) added in one portion. After a further 0.5 h the reaction was diluted with Et₂O (3 ml) and quenched with aqueous sodium hydrogen carbonate (2 ml). The aqueous layer was separated and extracted with Et₂O (3 x 4 ml). The combined organic extracts were washed with brine (5 ml), dried (MgSO₄) and concentrated *in vacuo*, affording a 13:1 mixture of C(4) diastereoisomers (50 mg, 94%) favouring the required alcohol, which was used without further purification. For analytical purposes, flash chromatography

on silica gel (Petrol-Et₂O, 3:1 then 1:1 then 1:2) afforded, in order of elution: undesired axial (minor) *spiroketal alcohol* (AE) as a colourless oil; R_f (Et₂O-Petrol, 2:1) 0.24; $[\alpha]_D^{25}$ -9.0 (c 0.3, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3430br w (OH), 1645w (alkene C=C), 1613m (Ar C=C), 1587w (Ar C=C), 1513s (Ar C=C); δ_H (600 MHz; CDCl₃) 0.03, 0.05 (2 x 3H, 2 x s, Si(CH₃)₂), 0.90 (9H, s, SiC(CH₃)₃), 1.01 (3H, t, J 7.4, 2'-CCH₂CH₃), 1.53 (1H, dd, J 7.8, 13.0, 5-H_{eq}), 1.53-1.57 (2H, m, 3-H_{eq}, 9-H_{eq}), 1.62 (1H, ddd, J 3.8, 11.0, 13.3, 9-H_{ax}), 1.62 (1H, dd, J 3.8, 14.3, 11-H_{ax}), 1.82 (1H, dddd, J 1.1, 4.0, 5.7, 13.3, 3-H_{ax}), 1.94 (1H, ddd, J 1.1, 4.3, 13.0, 5-H_{ax}), 1.99 (2H, ap. quint., J 7.4, 2'-CCH₂CH₃), 2.06 (1H, ddd, J 1.6, 3.8, 14.3, 11-H_{eq}), 2.39 (1H, dd, J 9.7, 14.2, 3'-H_A), 2.49 (1H, dd, J 4.7, 14.2, 3'-H_B), 3.43 (1H, dd, J 10.3, 11.9, CH_AH_BOAr), 3.44 (1H, dd, J 10.3, 12.3, CH_AH_BOAr), 3.80 (3H, s, ArOCH₃), 4.11 (1H, ap. quint., J 3.8, 10-H), 4.15 (1H, ap. sextet, J 5.0, 2-H), 4.29 (1H, ap. septet, J 4.0, 4-H), 4.43-4.47 (1H, m, 8-H), 4.48 (1H, d, J 11.9, OCH_AH_BAr), 4.51 (1H, d, J 11.9, OCH_AH_BAr), 4.75 (1H, s, 1'-H_A), 4.78 (1H, s, 1'-H_B), 6.86 (2H, AA'BB', Ar-*meta*-H) and 7.25 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) -4.9, -4.7 (Si(CH₃)₂), 12.3 (2'-CCH₂CH₃), 18.1 (SiC(CH₃)₃), 25.9 (SiC(CH₃)₃), 29.0 (2'-CCH₂CH₃), 35.3 (9-C), 36.4 (3-C), 41.2 (11-C), 42.1 (3'-C), 45.0 (5-C), 55.3 (ArOCH₃), 62.9 (4-C), 64.5 (2 lines, 8-C, 10-C), 69.6 (2-C), 72.8, 72.9 (CH₂OAr, OCH₂Ar), 98.6 (6-C), 110.1 (1'-C), 113.7 (Ar-*meta*-C), 129.1 (Ar-*ortho*-C), 130.7 (Ar-*ipso*-C), 148.5 (2'-C) and 159.1 (Ar-*para*-C); m/z (+ESI) 543 ([MNa]⁺, 11%), 503 (47), 389 (21), 371 (100), 285 (11), 251 (19), 165 (10), 120 (44); Found (+ESI): [MNa]⁺, 543.3135. C₂₉H₄₈O₆SiNa requires *MNa*, 543.3118.

Desired equatorial (major) *spiroketal alcohol* (AE) as a colourless oil; R_f (Et₂O-Petrol, 2:1) 0.15; $[\alpha]_D^{25}$ -9.5 (c 0.89, CHCl₃); ν_{\max} (thin film)/cm⁻¹ 3452br w (OH), 1645w (alkene C=C), 1613m (Ar C=C), 1587w (Ar C=C), 1514m (Ar C=C); δ_H (600 MHz; CDCl₃) 0.04, 0.05 (2 x 3H, 2 x s, Si(CH₃)₂), 0.89 (9H, s, SiC(CH₃)₃), 1.02 (3H, t, J 7.4, 2'-CCH₂CH₃), 1.27 (1H, td, J 10.4, 12.8, 3-H_{ax}), 1.50 (1H, dd, J 9.6, 12.6, 5-H_{ax}), 1.54 (1H, dd, J 3.9, 14.2, 11-H_{ax}), 1.57 (1H, dddd, J 1.4, 2.7, 3.9, 13.4, 9-H_{eq}), 1.67 (1H, ddd, J 3.9, 11.3, 13.4, 9-H_{ax}), 1.86 (1H, d, J 6.4, OH), 2.02 (2H, q, J 7.4, 2'-CCH₂CH₃) overlapping 1.97-2.04 (3H, m, 3-H_{eq}, 5-H_{eq}, 11-H_{eq}), 2.22 (1H, dd, J 8.6, 13.9, 3'-H_A), 2.49 (1H, dd, J 4.7, 13.9, 3'-H_B), 3.47 (1H, dd, J 10.5, 11.5, CH_AH_BOAr), 3.48 (1H, dd, J 10.5, 12.1, CH_AH_BOAr), 3.70 (1H, dddd, J 2.8, 4.7, 8.6, 10.4, 2-H), 3.80 (3H, s, ArOCH₃), 3.88-3.92 (1H, m, 4-H), 4.12 (1H, ap. quint., J 3.9, 10-H), 4.49 (1H, d, J 11.8, OCH_AH_BAr), 4.52 (1H, d, J 11.8, OCH_AH_BAr), 4.54-4.58 (1H, m, 8-H), 4.74 (1H, s, 1'-H_A), 4.79 (1H, d, J 1.5, 1'-H_B), 6.87 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) -4.8, -4.7

(Si(CH₃)₂), 12.3 (2'-CCH₂CH₃), 18.2 (SiC(CH₃)₃), 26.0 (SiC(CH₃)₃), 29.5 (2'-CCH₂CH₃), 35.2 (9-C), 37.5 (11-C), 39.3 (3-C), 42.8 (3'-C), 45.4 (5-C), 55.3 (ArOCH₃), 64.4 (10-C), 64.8 (8-C), 65.5 (4-C), 69.2 (2-C), 72.8 (2 lines, CH₂OAr, OCH₂Ar), 98.5 (6-C), 110.4 (1'-C), 113.7 (Ar-*meta*-C), 129.2 (Ar-*ortho*-C), 130.6 (Ar-*ipso*-C), 147.7 (2'-C) and 159.1 (Ar-*para*-C); *m/z* (+ESI) 538 ([MNH₄]⁺, 31%), 389 (32), 371 (68), 247 (12), 247 (12), 127 (43), 121 (100); Found (+ESI): [MNa]⁺, 543.3115. C₂₉H₄₈O₆SiNa requires *MNa*, 543.3118.

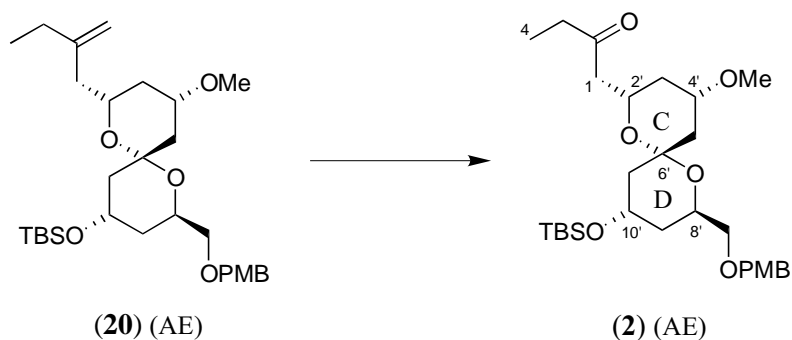
(2*R*, 4*S*, 6*R*, 8*R*, 10*S*)-10-(*tert*-Butyldimethylsilanyloxy)-2-(2'-ethylprop-1'-en-3'-yl)-4-methoxy-8-(*p*-methoxybenzyloxymethyl)-1,7-dioxaspiro(5.5)undecane (20) (AE)



Sodium hydride (60% dispersion in mineral oil, 32 mg, 0.96 mmol) was added to a solution of crude spiroketal alcohol (AE) (50 mg, 0.10 mmol) and methyl iodide (0.12 ml, 1.93 mmol) in THF (1 ml) at 0 °C then allowed to warm to room temperature immediately. After 1.5 h the solution was diluted with Et₂O (3 ml) and quenched with aqueous ammonium chloride (2 ml). The aqueous layer was separated and extracted with Et₂O (3 x 3 ml). The combined organic extracts were washed with brine (5 ml), dried (MgSO₄) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol-Et₂O, 3:1) afforded methoxy spiroketal (20) (AE) (43 mg, 78% from ketone (19)) as a colourless oil; *R*_f (Petrol-Et₂O, 2:1) 0.16; [α]_D²⁵ -7.0 (*c* 1.41, CHCl₃); ν_{max} (thin film)/cm⁻¹ 1645w (alkene C=C), 1613m (Ar C=C), 1587w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl₃) 0.049, 0.053 (2 x 3H, 2 x s, Si(CH₃)₂), 0.90 (9H, s, SiC(CH₃)₃), 1.02 (3H, t, *J* 7.4, 2'-CCH₂CH₃), 1.10 (1H, ap. q, *J* 11.6, 3-H_{ax}), 1.37 (1H, t, *J* 11.6, 5-H_{ax}), 1.54 (1H, dd, *J* 4.0, 14.3, 11-H_{ax}), 1.59 (1H, dddd, *J* 1.3, 2.9, 4.0, 13.5, 9-H_{eq}), 1.72 (1H, ddd, *J* 4.0, 11.2, 13.5, 9-H_{ax}), 2.03 (2H, q, *J* 7.4, 2'-CCH₂CH₃) overlapping 2.02-2.09 (3H, m, 3-H_{eq}, 5-H_{eq}, 11-H_{eq}), 2.20 (1H, dd, *J* 8.5, 13.9, 3'-H_A), 2.48 (1H, dd, *J* 4.7, 13.9, 3'-H_B), 3.32 (3H, s, 4-COCH₃), 3.43 (1H, tt, *J* 11.6, 4.4, 4-H), 3.49 (1H, dd, *J* 10.6, 11.2, CH_AH_BOAr), 3.50 (1H, dd, *J* 10.6, 11.2, CH_AH_BOAr), 3.65 (1H, dddd, *J* 2.2, 4.7, 8.5, 11.6, 2-H), 3.80 (3H, s, ArOCH₃), 4.12 (1H, ap. quint., *J* 4.0, 10-H), 4.51 (1H, d, *J* 11.9, OCH_AH_BAr), 4.53 (1H, d, *J* 11.9, OCH_AH_BAr), 4.54-4.57 (1H, m, 8-H), 4.74 (1H, s, 1'-H_A), 4.80 (1H, d, *J* 1.5, 1'-H_B), 6.86 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_{C} (100 MHz; CDCl₃) -4.8, -4.7 (Si(CH₃)₂), 12.4 (2'-CCH₂CH₃), 18.3 (SiC(CH₃)₃), 26.0 (SiC(CH₃)₃), 29.6 (2'-CCH₂CH₃), 35.4 (9-C), 36.2 (11-C), 36.6 (3-C), 42.8 (3'-C), 43.2 (5-C), 55.3, 55.4 (4-COCH₃, ArOCH₃), 64.6 (10-C), 65.1 (8-C), 69.3 (2-C), 72.7 (CH₂OAr), 72.8 (OCH₂Ar), 74.4 (4-C), 98.4 (6-C), 110.4 (1'-C), 113.7 (Ar-*meta*-C), 129.2 (Ar-*ortho*-C), 130.7 (Ar-*ipso*-C), 147.7 (2'-C) and 159.1 (Ar-*para*-C); *m/z*

(+ESI) 557 ($[\text{MNa}]^+$, 12%), 552 ($[\text{MNH}_4]^+$, 91), 503 (64), 403 (10), 371 (63), 285 (12), 120 (100); Found (+ESI): $[\text{MNa}]^+$, 557.3280. $\text{C}_{30}\text{H}_{50}\text{O}_6\text{SiNa}$ requires MNa , 557.3274.

(2'S, 4'S, 6'R, 8'R, 10'S)-1-(10'-(*tert*-Butyldimethylsilanyloxy)-4'-methoxy-8'-(*p*-methoxybenzyloxymethyl)-1',7'-dioxadispiro(5.5)undec-2'-yl)butan-2-one (2) (AE)



Osmium tetroxide (5 wt% solution in *t*-butanol, 2 drops) was added to a solution of spiroketal alkene **(20)** (AE) (51 mg, 0.10 mmol) and 4-methylmorpholine *N*-oxide (22 mg, 0.19 mmol) in acetone (1.6 ml) and H_2O (0.4 ml) at room temperature. After 7 h aqueous sodium thiosulfate (2 ml) and H_2O (0.5 ml) were added and the mixture stirred for 0.5 h. The acetone was removed *in vacuo* and the residue extracted with EtOAc (4 x 2 ml). The combined organic extracts were washed with brine (5 ml), dried (MgSO_4) and concentrated *in vacuo*. The yellow oil was taken up in a MeOH- H_2O (2:1) mixture (1.5 ml). Sodium periodate (102 mg, 0.48 mmol) was added and the mixture stirred for 1 h at room temperature. The solution was diluted with Et_2O (5 ml) and quenched with H_2O (3 ml). The aqueous phase was separated and extracted with Et_2O (4 x 3 ml). The combined organic extracts were washed with brine (5 ml), dried (MgSO_4) and concentrated *in vacuo*. Flash chromatography on silica gel (Petrol- Et_2O , 1:1) afforded spiroketal ketone **(2)** (AE) (42 mg, 82%) as a colourless oil; R_f (Et_2O -Petrol, 2:1) 0.36; $[\alpha]_D^{25}$ -21.8 (*c* 0.95, CHCl_3); ν_{max} (thin film)/ cm^{-1} 1715s (C=O), 1613m (Ar C=C), 1586w (Ar C=C), 1513s (Ar C=C); δ_{H} (600 MHz; CDCl_3) 0.015, 0.026 (2 x 3H, 2 x s, $\text{Si}(\text{CH}_3)_2$), 0.85 (9H, s, $\text{SiC}(\text{CH}_3)_3$), 1.04 (3H, t, *J* 7.4, 4-H) overlapping 1.02-1.07 (1H, m, 3'- H_{ax}), 1.37 (1H, ap. t, *J* 12.0, 5'- H_{ax}), 1.50 (1H, dd, *J* 3.8, 14.4, 11'- H_{ax}), 1.57 (1H, dddd, *J* 1.3, 2.7, 3.8, 13.5, 9'- H_{eq}), 1.68 (1H, ddd, *J* 3.8, 11.5, 13.5, 9'- H_{ax}), 2.05 (1H, ddd, *J* 1.7, 4.4, 12.0, 5'- H_{eq}), 2.14 (1H, ddd, *J* 1.3, 3.8, 14.4, 11'- H_{eq}), 2.21 (1H, ddt, *J* 12.0, 4.0, 2.2, 3'- H_{eq}), 2.40 (2H, q, *J* 7.4, 3-H), 2.66 (1H, dd, *J* 8.9, 17.1, 1- H_{A}), 2.83 (1H, dd, *J* 3.8, 17.1, 1- H_{B}), 3.32 (3H, s, 4'- COCH_3), 3.46 (1H, dd, *J* 10.6, 11.4, $\text{CH}_\text{A}\text{H}_\text{B}\text{OAr}$) and 3.47 (1H, dd, *J* 10.6, 11.4, $\text{CH}_\text{A}\text{H}_\text{B}\text{OAr}$) overlapping 3.46-3.51 (1H, m, 4'-H), 3.80 (3H, s, ArOCH_3), 3.93 (1H, dddd, *J* 2.2, 3.8, 8.9, 11.3, 2'-

H), 4.11 (1H, ap. quint., J 3.8, 10'-H), 4.51 (2H, s, OCH₂Ar) overlapping 4.49-4.53 (1H, m, 8'-H), 6.86 (2H, AA'BB', Ar-*meta*-H) and 7.26 (2H, AA'BB', Ar-*ortho*-H); δ_C (100 MHz; CDCl₃) -5.0, -4.9 (Si(CH₃)₂), 7.7 (4-C), 18.1 (SiC(CH₃)₃), 25.8 (SiC(CH₃)₃), 35.2 (9'-C), 35.6 (11'-C), 36.9 (3-C), 37.0 (3'-C), 43.2 (5'-C), 48.6 (1-C), 55.3 (ArOCH₃), 55.5 (4'-COCH₃), 64.4 (10'-C), 65.1 (8'-C), 66.6 (2'-C), 72.7 (CH₂OAr), 72.9 (OCH₂Ar), 73.9 (4'-C), 98.4 (6'-C), 113.7 (Ar-*meta*-C), 129.2 (Ar-*ortho*-C), 130.6 (Ar-*ipso*-C), 159.1 (Ar-*para*-C) and 209.3 (2-C); m/z (+ESI) 559 ([MNa]⁺, 5%), 554 ([MNH₄]⁺, 100), 373 (10), 301 (7), 121 (13); Found (+ESI): [MNa]⁺, 559.3077. C₂₉H₄₈O₇SiNa requires *MNa*, 559.3067.