Stereoselective construction of the key intermediate for the synthesis of the tetrahydropyranyl antifungal agents (+)-restricticin and (+)-lanomycin

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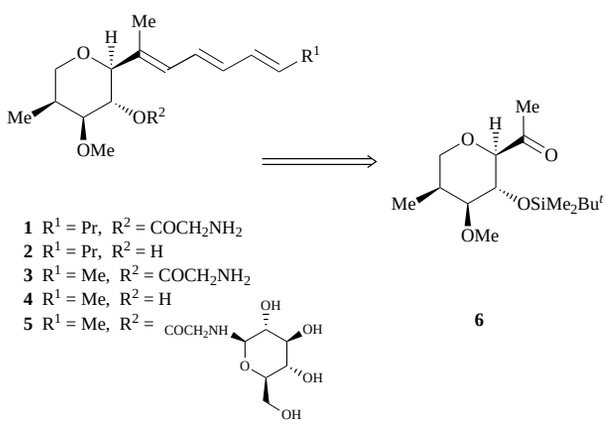
Stereoselective construction of the key intermediate for the synthesis of naturally occurring antifungal agents, such as (+)-restricticin and (+)-lanomycin, has been achieved by employing a chelation-controlled aldol reaction of methyl α-methyltetronate with (*R*)-cyclohexylideneglyceraldehyde as a key step.

Introduction

The novel class of potent antifungal agents having a tetrahydropyran ring, such as (+)-restricticin **1** and restrictinol **2** from *Penicillium restrictum*,[1] and (+)-lanomycin **3**, lanomycinol **4** and glucolanomycin **5** from *Pycnidiophora dispersa*,[2] have recently been isolated and their structures have also been determined spectroscopically as shown in Scheme 1. These



1 R^1 = Pr, R^2 = $COCH_2NH_2$
2 R^1 = Pr, R^2 = H
3 R^1 = Me, R^2 = $COCH_2NH_2$
4 R^1 = Me, R^2 = H
5 R^1 = Me, R^2 =

6

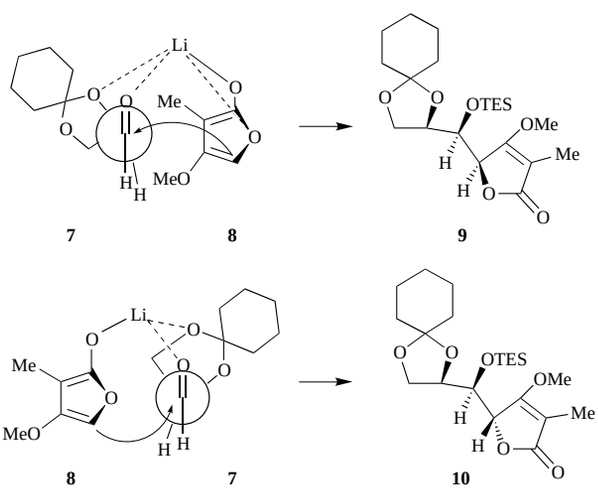
Scheme 1

compounds have been shown to inhibit the cytochrome *P*-450 enzyme lanosterol 14α-demethylase in the steroid-biosynthetic pathway. Owing to their interesting structural feature of bearing four contiguous chiral centres on the tetrahydropyran ring and also their novel mode of action, which has been unknown hitherto for naturally occurring antifungals, many efforts have been devoted to their synthesis. Since it is well established that the 2-acetyltetrahydropyran derivative **6** would be a versatile precursor for the synthesis of these antifungal agents, a number of syntheses of the key precursor **6** in an optically active form have been achieved by employing L-aldohexoses,[3] L-quebrachitol,[4] and D-tartaric acid[5] as the chiral starting material. Very recently, Paterson and Nowak also published[6] an elegant synthesis of (+)-restricticin by application of the anti-selective aldol reaction of the chiral boron enolate with an aldehyde.

We are also interested in the stereoselective construction of the key intermediate **6** for the synthesis of tetrahydropyranyl antifungal agents by using the chelation-controlled aldol reaction[7] of methyl α-methyltetronate **8** with (*R*)-2,3-*O*-cyclohexylideneglyceraldehyde **7** as a key reaction, and report here our own successful results.

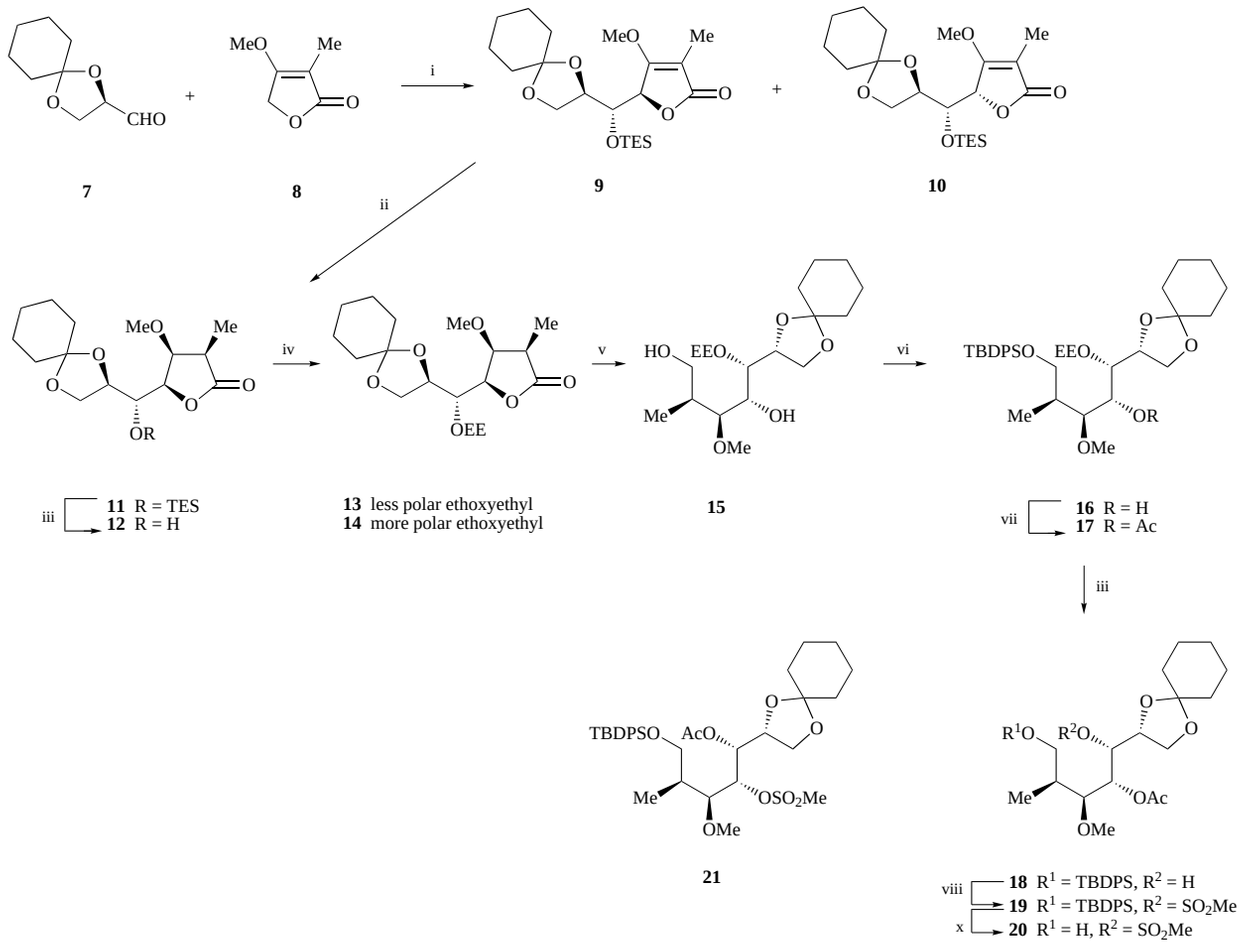
Results and discussion

The reaction of the lithium salt of methyl α-methyltetronate **8** with (*R*)-2,3-*O*-cyclohexylideneglyceraldehyde **7** in tetrahydrofuran (THF) at −78 °C, followed by quenching with triethylsilyl chloride (TESCl), gave the adducts (**9** and **10**) in 66 and 16% yield, respectively. The major isomer would be expected as the chelation-controlled product based on our previous works[7] as depicted in Scheme 2. Catalytic reduction of the major

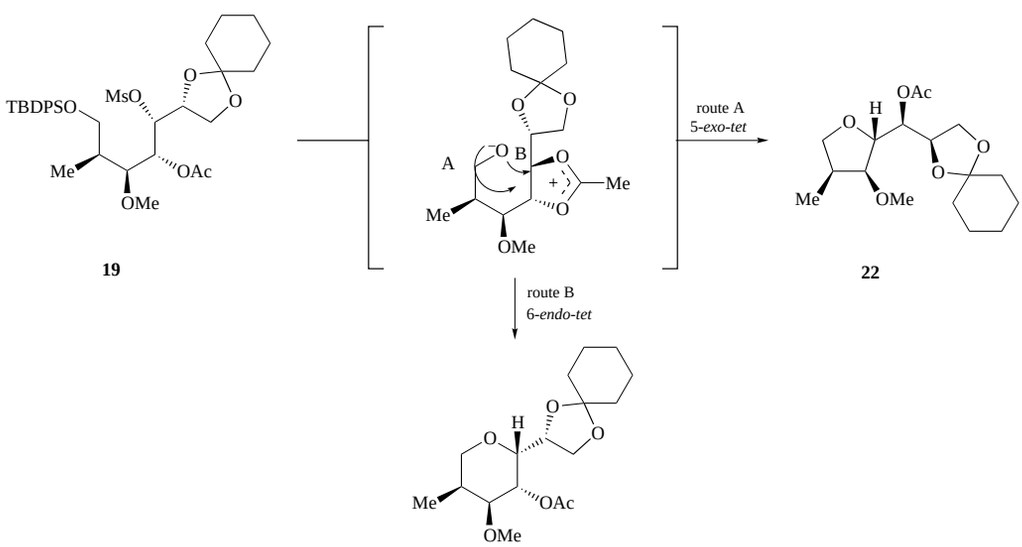


Scheme 2

isomer **9** over rhodium on alumina[8] under 7 atm of hydrogen afforded the γ-lactone **11** stereoselectively as the sole product in quantitative yield (Scheme 3). The silyl ether **11** was then converted into the ethoxyethyl ethers (**13** and **14**) in quantitative yield, in the ratio 1 : 1, by two steps involving desilylation with aq. acetic acid and subsequent treatment of the alcohol **12** with ethyl vinyl ether and pyridinium toluene-*p*-sulfonate (PPTS), since the silyl group was found not to be a suitable protecting group for further conversion. Although the diastereoisomers at the ethoxyethyl group (**13** and **14**) could be separated by column chromatography on silica gel, the stereochemistry of the newly generated stereogenic centre at the ethoxyethyl group could not be determined at this stage. Both compounds, however, could be used for the next step, since this stereogenic centre was removed at a later stage of this synthesis. Reduction of the less polar ethoxyethyl ether **13** with lithium triethylborohydride provided the diol **15**, which on selective silylation with 1 mol equiv. of *tert*-butyldiphenylsilyl chloride (TBDPSCl) gave the silyl ether **16** in 69% yield from compound **13**. This com-



Scheme 3 *Reagents and conditions*: i, LDA, THF, −78 °C; then TESCl; ii, Rh on alumina, H_2, EtOAc, room temp.; iii, aq. AcOH, THF, room temp.; iv, ethyl vinyl ether, PPTS, CH_2Cl_2, room temp.; v, $LiBEt_3H$, THF, −78 °C; vi, TBDPSCl, Et_3N, DMAP, CH_2Cl_2, room temp.; vii, Ac_2O, DMAP, pyridine, room temp.; viii, $MeSO_2Cl$, Et_3N, DMAP, CH_2Cl_2, room temp.; ix, Bu_4NF, THF, room temp.

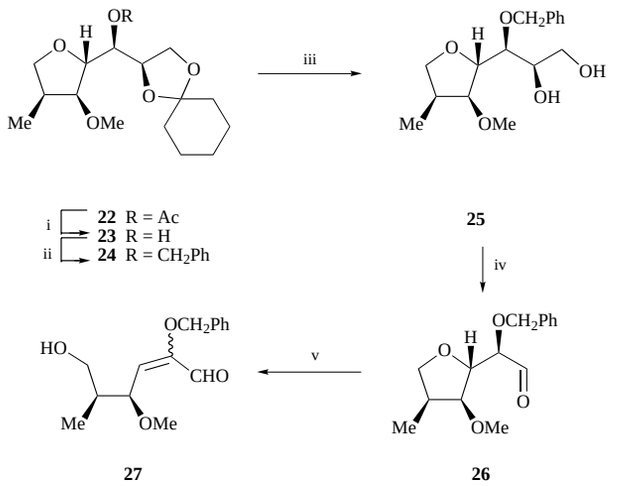


Scheme 4

pound has the contiguous four chiral centres, three of which have the same configuration related to the 3-, 4- and 5-positions of restricticinol. In order to construct the tetrahydropyran ring, we attempted the cyclisation of the corresponding acetate **17** and also of the benzyl ether **28**. Acetylation of the alcohol **16** with acetic anhydride gave the acetate **17**, which on deprotection of the ethoxyethyl group with aq. acetic acid followed by methanesulfonylation of the resulting secondary alcohol **18** with methanesulfonyl chloride afforded the sulfonate **19** in 80% overall yield together with the isomeric acetate **21**, probably derived by rearrangement of the acetyl group during the deprotection, in 16% yield. Desilylation of the major compound **19** with tetrabutylammonium fluoride (TBAF) at room temp. proceeded smoothly to afford the cyclisation product **22** in 60% yield together with the desilylated compound **20** in 32% yield. Although we expected the formation of the tetrahydropyran ring in this cyclisation, cyclisation to both a 6-membered and/or 5-membered ring was plausible, based on consideration of reaction mechanisms as illustrated in Scheme 4.

As a means to determine the structure and hopefully to syn-

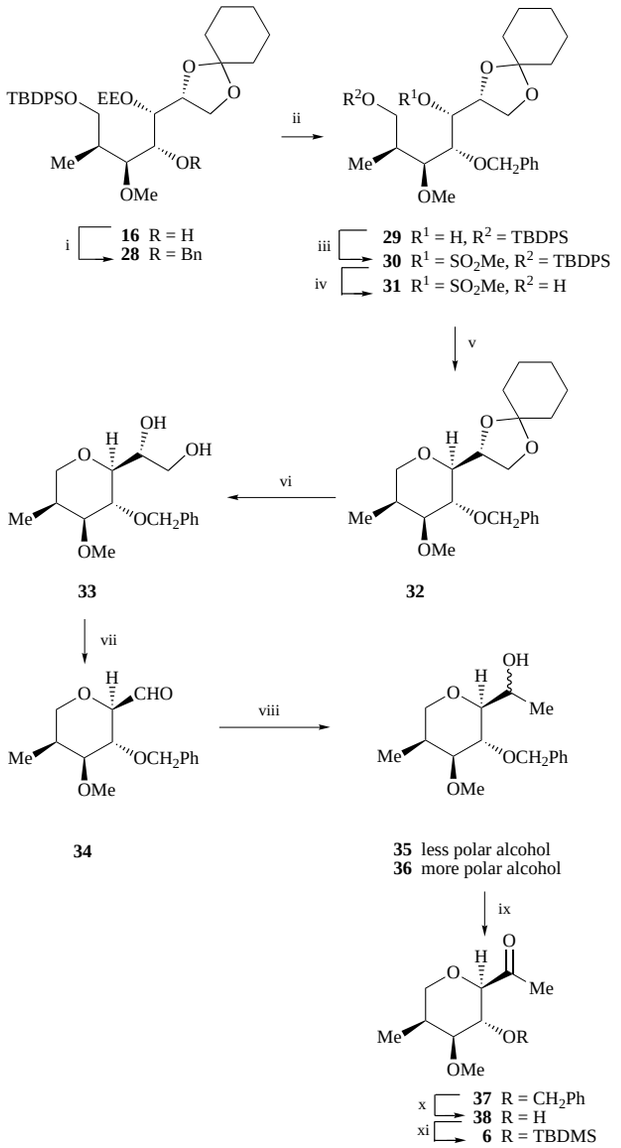
thesise the desired natural product, the cyclisation product **22** was treated with potassium carbonate to give the alcohol **23**, which on benzylation with benzyl bromide in the presence of sodium hydride provided the benzyl ether **24**. Deprotection of the cyclohexylidene group of compound **24** with aq. acetic acid, followed by treatment of the resulting diol **25** with sodium periodate afforded the aldehyde **26**. Finally, base treatment of the aldehyde **26** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) brought about a retro-Michael reaction to yield the α, β-unsaturated aldehyde **27** as a mixture of *E* and *Z* isomers, in the ratio 7 : 1 (Scheme 5). These results clearly suggested that the cyclisation of the methanesulfonate **19** provided the tetrahydrofuran derivatives **22**, *via* route A in Scheme 4, arising from neighbouring-group participation of the acetyl group.



Scheme 5 *Reagents and conditions*: i, K_2CO_3, MeOH, room temp.; ii, BnBr, NaH, DMF, room temp.; iii, aq. AcOH, 60 °C; iv, $NaIO_4$, CH_2Cl_2–water, room temp.; v, DBU, THF, room temp.

Cyclisation of the benzyl ether **31** afforded the desired product as follows. Acid hydrolysis of the ethoxyethyl group of the polyether **28** and subsequent methanesulfonylation of the resulting alcohol **29** with methanesulfonyl chloride gave the sulfonate **30** in 97% yield from substrate **28** (Scheme 6). After desilylation of the methanesulfonate **30** with TBAF, the resulting alcohol **31** was subjected to an intramolecular S_N2 reaction with aq. sodium hydroxide in toluene in the presence of phase-transfer catalyst to furnish the cyclised compound **32** bearing the correct chiral centre at the 2-position in 80% yield. The stereochemistries of the four contiguous chiral centres on the tetrahydropyran ring were assumed to have the same configurations as those of the natural product based on NMR spectroscopy and this was unambiguously confirmed by its further conversion into the known key intermediate **6**.[3,5] Hydrolysis of the cyclohexylidene group of compound **32** with aq. acetic acid, followed by cleavage of the resulting diol **33** with sodium periodate, gave the aldehyde **34**. Introduction of a methyl group into aldehyde **34** with methyllithium gave the diastereoisomers **35** and **36** in 19 and 66% yield, respectively. Oxidation of both alcohols **35** and **36** with pyridinium chlorochromate (PCC) afforded the same ketone **37** in 97 and 97% yield, respectively. Debenzylation of compound **37** under the catalytic reduction conditions and subsequent silylation of the resulting alcohol **38** with *tert*-butyldimethylsilyl chloride (TBDMSCl) furnished the desired compound **6**, whose spectroscopic data, including specific rotation {$[\alpha]_D$ +28.4 (*c* 0.7, MeOH) and $[\alpha]_D$ +23.8 (*c* 0.5, $CHCl_3$); lit.,[4] $[\alpha]_D$ +25 (*c* 0.35, MeOH) and lit.,[5] $[\alpha]_D$ +14.4 (*c* 0.63, $CHCl_3$)}, were identical with those reported. Since this compound has already been converted into (+)-restricticin [3] and (+)-lanomycin [5] by elongation of the side-chains, this synthesis constitutes their formal synthesis.

The more polar diastereoisomer at the ethoxyethyl group of compound **14** was also converted into the alcohol **29** by



Scheme 6 *Reagents and conditions*: i, BnBr, NaH, Bu_4NI, THF, room temp.; ii, aq, AcOH, room temp.; iii, $MeSO_2Cl$, Et_3N, DMAP, CH_2Cl_2, room temp.; iv, Bu_4NF, THF, room temp.; v, NaOH, Bu_4NBr, toluene–water, 90 °C; vi, aq. AcOH, 60 °C; vii, $NaIO_4$, CH_2Cl_2, 0 °C; viii, MeLi, Et_2O, −78 °C; ix, PCC, NaOAc, CH_2Cl_2, room temp.; x, H_2, $Pd(OH)_2$, EtOAc, room temp.; xi, TBDMSCl, imidazole, DMF, room temp.

adopting essentially the same procedure as for the synthesis of compound **29** from compound **13**, in four steps involving reduction with lithium triethylborohydride, silylation with TBDPSCl, benzylation with benzyl bromide, and de-ethoxyethylation with acid treatment, in 95% overall yield.

Thus, we have demonstrated an alternative path to the key intermediate for the synthesis of the tetrahydropyranyl antifungal agents (+)-restricticin and (+)-lanomycin by using the chelation-controlled aldol reaction of the tetronate derivative with the chiral aldehyde as a key reaction. This strategy could be applicable to the stereoselective synthesis of the derivatives of these types of natural products.

Experimental

General methods

Mps were measured with a Yanagimoto MP apparatus and are uncorrected. IR spectra were recorded for thin films on a JASCO FT/IR-200 Fourier transform IR spectrophotometer. ^1H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$ on a JEOL PMX 270 instrument (270 MHz), and chemical shifts are reported in ppm on the δ-scale from internal Me_4Si.

J-Values are given in Hz. Mass spectra were measured with a JEOL JMS D-300 spectrometer. Optical rotations were taken with a JASCO DIP-360 polarimeter, and $[a]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. All new compounds described in the Experimental section were homogeneous on TLC.

(1′*R*,2′*R*,5*S*)-Methyl 5-(2′,3′-cyclohexylidenedioxy-1′-triethylsiloxypropyl)-3-methyltetronate 9 and (1′*R*,2′*R*,5*R*)-methyl 5-(2′,3′-cyclohexylidenedioxy-1′-triethylsiloxypropyl)-3-methyltetronate 10

To a stirred solution of lithium diisopropylamide (LDA), prepared from diisopropylamine (5.41 cm^3, 38.6 mmol) and a 1.63 M solution of *n*-BuLi in hexane (23.7 cm^3, 38.6 mmol), in THF (100 cm^3) was added a solution of methyl α-methyltetronate **8** (3.8 g, 29.7 mmol) in THF (10 cm^3) at −78 °C and this mixture was allowed to warm to −20 °C. After being stirred for 30 min at the same temperature, the solution was again cooled to −78 °C and a solution of (*R*)-2,3-*O*-cyclohexylideneglyceraldehyde **7** (5.0 g, 29.7 mmol) in THF (15 cm^3) was slowly added to the solution over the period of 45 min, and the mixture was stirred at the same temperature for 2 h. TESCl (10 cm^3, 59.4 mmol) was added and the resulting mixture was stirred for a further 1 h. The reaction was quenched by addition of saturated aq. ammonium chloride and the whole mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation off of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (9:1, v/v) afforded the γ-*alkyltetronate* **9** (5.5 g, 66%) as an oil, $[a]_D$ +9.3 (*c* 1.1, $CHCl_3$) (Found: M$^+$, 412.2274; C, 60.95; H, 9.00. $C_{21}H_{36}O_6Si$ requires *M*, 412.2269; C, 61.15; H, 8.80%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1760 and 1680; δ_H 0.47–0.63 (6 H, m, 3 × SiCH_2CH$_3$), 0.92 (9 H, t, *J* 7.9, 3 × SiCH$_2$CH_3), 1.38–1.42 (2 H, br s, cyclohexylidene protons), 1.57–1.61 (8 H, m, cyclohexylidene protons), 1.99 (3 H, s, Me), 3.86 (1 H, dd, *J* 5.5 and 8.5, 7-H), 3.96 (1 H, dd, *J* 1.2 and 7.3, 5-H), 4.07 (1 H, dd, *J* 6.1 and 8.5, 7-H), 4.12 (3 H, s, OMe), 4.20 (1 H, ddd, *J* 5.5, 6.1 and 7.3, 6-H) and 4.82 (1 H, t, *J* 1.2, 4-H); δ_C 5.1, 6.7, 8.5, 23.7, 24.0, 25.1, 34.5, 36.5, 58.5, 66.4, 71.0, 75.6, 77.8, 99.0, 109.7, 170.1 and 174.8.

Further elution with the same solvent system afforded the *diastereoisomer* **10** (1.33 g, 16%) as an oil, $[a]_D$ −24.5 (*c* 0.8, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1760 and 1675; δ_H 0.56–0.65 (6 H, m, 3 × SiCH_2CH$_3$), 0.93 (9 H, t, *J* 7.9, 3 × SiCH$_2$CH_3), 1.35–1.45 (2 H, br s, cyclohexylidene protons), 1.58 (8 H, br d, *J* 12.7, cyclohexylidene protons), 2.00 (3 H, s, Me), 3.86 (1 H, dd, *J* 5.1 and 8.5, 7-H), 3.93–4.04 (2 H, m, 5- and 7-H), 4.11 (3 H, s, OMe), 4.19 (1 H, dd, *J* 5.1 and 7.3, 6-H) and 4.87 (1 H, br s, 4-H); δ_C 4.8, 6.6, 8.6, 23.7, 24.0, 25.0, 34.6, 36.5, 58.8, 66.8, 73.5, 74.3, 79.1, 98.6, 110.0, 171.2 and 174.9 (Found: M$^+$, 412.2279).

(2*R*,3*S*,4*R*,5*R*,6*R*)-6,7-Cyclohexylidenedioxy-3-methoxy-2-methyl-5-triethylsiloxyheptan-4-olide 11

A solution of the tetronate **10** (4.2 g, 10.2 mmol) in ethyl acetate (20 cm^3) was hydrogenated over 5% rhodium on alumina (1.4 g) in the presence of sodium hydrogen carbonate (0.8 g) for 8 h under medium pressure (7.0 atm) of hydrogen. The catalyst was filtered off and the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (9:1, v/v) afforded the γ-*butyrolactone* **11** (4.2 g, 100%) as an oil, $[a]_D$ +14.7 (*c* 3.1, $CHCl_3$) (Found: C, 60.94; H, 9.54. $C_{21}H_{38}O_6Si$ requires C, 60.84; H, 9.24%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1780; δ_H 0.52–0.77 (6 H, m, 3 × SiCH_2CH$_3$), 0.96 (9 H, t, *J* 7.9, 3 × SiCH$_2$CH_3), 1.31 (3 H, d, *J* 7.3, Me), 1.37–1.69 (10 H, m, C_6H_{10}), 2.69 (1 H, dq, *J* 4.3 and 7.3, 2-H), 3.43 (3 H, s, OMe), 3.81–3.91 (1 H, m, 4-H), 3.94 (1 H, dd, *J* 3.1 and 4.3, 3-H), 4.00–4.10 (3 H, m, 5-H and 7-H$_2$) and 4.26 (1 H, dd, *J* 4.9 and 8.5, 6-H); δ_C 5.1, 5.6, 6.9, 23.8, 24.1, 25.2, 34.8, 36.0, 42.8, 60.0, 66.5, 70.6, 76.3, 80.7, 83.9, 110.0 and 177.0.

(2*R*,3*S*,4*S*,5*R*,6*R*)-6,7-Cyclohexylidenedioxy-5-hydroxy-3-methoxy-2-methylheptan-4-olide 12

A solution of the triethylsilyl ether **11** (1.13 g, 2.74 mmol) in acetic acid–water–THF (3:1:1, 30 cm^3) was stirred at room temp. for 5 h. After removal of the solvents, the residue was dissolved in dichloromethane and the organic layer was washed successively with saturated aq. sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation off of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:2, v/v) afforded the *alcohol* **12** (0.80 g, 95%) as needles, mp 120 °C (from hexane–ethyl acetate); $[a]_D$ −12.5 (*c* 0.5, $CHCl_3$) (Found: M$^+$, 300.1577; C, 59.60; H, 8.00. $C_{15}H_{24}O_6$ requires *M*, 300.1572; C, 60.00; H, 8.05%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3500 and 1780; δ_H 1.32 (3 H, d, *J* 7.3, Me), 1.35–1.76 (10 H, m, C_6H_{10}), 2.78 (1 H, dq, *J* 5.5 and 7.3, 2-H), 3.38 (1 H, d, *J* 1.8, OH), 3.58 (3 H, s, OMe), 3.87 (1 H, dt, *J* 1.8 and 7.9, 5-H), 4.02 (1 H, ddd, *J* 3.1, 5.5 and 7.9, 6-H), 4.14 (1 H, dd, *J* 5.5 and 11.0, 7-H), 4.17–4.22 (2 H, m, 3- and 7-H) and 4.63 (1 H, dd, *J* 1.8 and 4.6, 4-H); δ_C 8.6, 23.7, 24.1, 25.1, 34.8, 36.6, 41.3, 60.7, 67.1, 71.6, 74.6, 79.1, 83.3, 110.1 and 177.2.

(2*R*,3*S*,4*R*,5*R*,6*R*)-6,7-Cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptan-4-olides 13 and 14

To a stirred solution of the alcohol **12** (700 mg, 2.33 mmol) and ethyl vinyl ether (4.46 cm^3, 46.6 mmol) in methylene dichloride (10 cm^3) was added portionwise PPTS (117 mg, 0.47 mmol) at 0 °C, and the resulting mixture was stirred for 15 min at ambient temp. under argon. After addition of saturated aq. sodium hydrogen carbonate, the mixture was extracted with methylene dichloride. The extract was washed with brine and dried over Na_2SO_4. Evaporation off of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:1, v/v) afforded the *less polar ethoxyethyl ether* **13** (434 mg, 50%) as needles, mp 57.5–60.5 °C (from hexane–ethyl acetate); $[a]_D$ +71.6 (*c* 0.5, $CHCl_3$) (Found: M$^+$, 372.2144; C, 61.00; H, 8.55. $C_{19}H_{32}O_7$ requires *M*, 372.2146; C, 61.25; H, 8.65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1784; δ_H 1.20 (3 H, d, *J* 6.7, Me), 1.30 (3 H, d, *J* 5.5, Me), 1.32 (3 H, d, *J* 7.3, Me), 1.41–1.75 (10 H, m, C_6H_{10}), 2.71 (1 H, dq, *J* 5.5 and 7.3, 2-H), 3.40–3.67 (2 H, m, 5- and 6-H), 3.46 (3 H, s, OMe), 3.98 (2 H, q, *J* 7.3, CH_2O), 3.94–4.18 (3 H, m, 7-H$_2$ and 3-H), 4.29 (1 H, dd, *J* 3.0 and 9.2, 4-H) and 4.88 (1 H, q, *J* 5.5, OCHO); δ_C 8.6, 15.2, 20.1, 23.6, 23.8, 24.9, 34.4, 35.7, 42.2, 59.7, 61.2, 67.3, 73.8, 75.5, 80.4, 84.1, 101.3, 110.1 and 177.0

Further elution with the same solvent system afforded the *more polar ethoxyethyl ether* **14** (430 mg, 49.5%) as an oil, $[a]_D$ +18.6 (*c* 0.9, $CHCl_3$) (Found: M$^+$, 372.2139; C, 61.10; H, 8.75. $C_{19}H_{32}O_7$ requires C, 61.25; H, 8.65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1780; δ_H 1.21 (3 H, d, *J* 6.7, Me), 1.31 (3 H, d, *J* 5.5, Me), 1.32 (3 H, d, *J* 7.3, Me), 1.36–1.46 (2 H, br s, cyclohexylidene protons), 1.58–1.64 (8 H, m, cyclohexylidene protons), 2.68 (1 H, dq, *J* 5.5 and 7.3, 2-H), 3.44 (3 H, s, OMe), 3.65 (2 H, dq, *J* 6.7 and 9.2, CH_2O), 3.89–3.95 (2 H, m, 3- and 4-H), 4.02 (1 H, dd, *J* 6.1 and 7.8, 5-H), 4.11–4.17 (1 H, m, 6-H), 4.20–4.35 (2 H, m, 7-H$_2$), 4.98 (1 H, q, *J* 5.5, OCHO); δ_C 8.6, 15.1, 20.3, 23.7, 23.9, 25.0, 34.5, 35.9, 42.1, 60.0, 61.2, 65.2, 72.5, 75.2, 80.4, 82.4, 100.9, 109.5 and 176.8.

(2*S*,3*S*,4*R*,5*S*,6*R*)-6,7-Cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptane-1,4-diol with the less polar ethoxyethyl ether 15

To a stirred solution of the less polar ethoxyethyl ether **13** (200 mg, 0.54 mmol) in THF (4 cm^3) was added dropwise a 1 M solution of lithium triethylborohydride in THF (1.35 cm^3, 1.62 mmol) at −78 °C, and the resulting mixture was stirred at room temp. for 1 h under argon. The reaction was quenched by addition of saturated aq. sodium hydrogen carbonate and the mixture was stirred for a further 20 min. The whole mixture was

then extracted with ethyl acetate and the extract was washed with brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:3, v/v) afforded the *alcohol* **15** (201 mg, 99.4%) as an oil, $[\alpha]_D$ +31.8 (*c* 1.6, $CHCl_3$) (Found: C, 60.45; H, 9.75. $C_{19}H_{36}O_7$ requires C, 60.60; H, 9.65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3470; δ_H 1.05 (3 H, d, *J* 7.1, Me), 1.22 (3 H, t, *J* 7.1, Me), 1.32 (3 H, d, *J* 5.3, Me), 1.40 (2 H, br s, cyclohexylidene protons), 1.61 (8 H, br d, *J* 14.2, cyclohexylidene protons), 2.00–2.08 (1 H, m, 2-H), 3.43–3.82 (7 H, m, 1-H_2, 3-, 4- and 5-H and 7-H_2), 3.54 (3 H, s, OMe), 3.98–4.20 (3 H, m, 6-H and OCH_2) and 4.83 (1 H, q, *J* 5.3, OCHO); δ_C 14.8, 15.1, 20.0, 23.6, 23.8, 24.9, 34.5, 36.1, 38.0, 60.0, 61.3, 64.2, 67.0, 72.6, 75.5, 76.6, 82.8, 100.5 and 109.7 [Found: *m*/*z*, 330.2038. $C_{17}H_{30}O_6$ (*M* −EtOH) requires *m*/*z*, 330.2040].

(2*S*,3*S*,4*R*,5*S*,6*R*)-1-(*tert*-Butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptan-4-ol with the less polar ethoxyethyl group 16

To a stirred solution of the diol **15** (950 mg, 2.53 mmol) in methylene dichloride (10 cm^3) were added triethylamine (1.4 cm^3, 10.12 mmol), 4-(dimethylamino)pyridine (DMAP) (62 mg, 0.5 mmol) and TBDPSCl (1.97 cm^3, 7.59 mmol), and the resulting mixture was stirred for 10 h at room temp. under argon. After addition of saturated aq. ammonium chloride, the mixture was extracted with methylene dichloride. The extract was washed with brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (6:1, v/v) afforded the recovered starting material **15** (209 mg, 22%) and the *silyl ether* **16** (1.07 g, 69%) as an oil, $[\alpha]_D$ +19.5 (*c* 1.6, $CHCl_3$) (Found: M^+, 614.3629; C, 68.05; H, 8.95. $C_{35}H_{54}O_7Si$ requires *M*, 614.3639; C, 68.35; H, 8.85%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3520; δ_H 1.02 (3 H, d, *J* 6.7, Me), 1.08 (9 H, s, Bu), 1.21 (3 H, t, *J* 7.1, Me), 1.29 (3 H, d, *J* 5.3, Me), 1.37 (2 H, br s, cyclohexylidene protons), 1.53–1.63 (8 H, m, cyclohexylidene protons), 2.01–2.16 (1 H, m, 2-H), 3.43–3.76 (7 H, m, 1-H_2, 3-, 4- and 5-H and 7-H_2), 3.43 (3 H, s, OMe), 3.97–4.18 (3 H, m, 6-H and OCH_2), 4.84 (1 H, q, *J* 5.3, OCHO), 7.25–7.42 (6 H, m, ArH) and 7.66–7.68 (4 H, m, ArH); δ_C 13.9, 15.3, 19.2, 20.2, 23.7, 23.9, 25.1, 26.9, 34.6, 36.2, 37.3, 59.0, 61.4, 65.4, 67.0, 71.6, 75.8, 77.2, 80.8, 100.7, 109.6, 127.5, 129.5, 133.5, 133.6, 135.5 and 135.6.

(2*S*,3*S*,4*R*,5*R*,6*R*)-4-Acetoxy-1-(*tert*-butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-5-ethoxyethoxy-3-methoxy-2-methylheptane 17

A solution of the alcohol **16** (300 mg, 0.49 mmol), acetic anhydride (1.0 cm^3, 10.59 mmol), DMAP (12 mg, 0.98 mmol) and pyridine (2 cm^3) was stirred at ambient temp. for 1.5 h. The mixture was treated with ethyl acetate and the organic layer was washed successively with saturated aq. potassium hydrogen sulfate, aq. sodium hydrogen carbonate, and brine, and dried over Na_2SO_4. Evaporation off of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (6:1, v/v) afforded the *acetate* **17** (317 mg, 99%) as an oil, $[\alpha]_D$ +14.5 (*c* 1.1, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1746; δ_H 0.83 (3 H, d, *J* 6.9, Me), 1.01 (9 H, s, Bu), 1.14 (3 H, t, *J* 7.1, Me), 1.15 (3 H, d, *J* 5.3, Me), 1.38 (2 H, br s, cyclohexylidene protons), 1.61 (8 H, br d, *J* 15.9, cyclohexylidene protons), 1.75–1.79 (1 H, m, 2-H), 2.01 (3 H, s, Ac), 3.40 (3 H, s, OMe), 3.38–3.61 (4 H, m, 1-H_2, 3- and 5-H), 3.74 (1 H, dd, *J* 4.6 and 11.6, 7-H), 3.78 (1 H, dd, *J* 6.9 and 11.6, 7-H), 3.90–4.13 (3 H, m, OCH_2 and 6-H), 4.68 (1 H, q, *J* 5.3, OCHO), 5.12 (1 H, dd, *J* 2.3 and 7.1, 4-H), 7.26–7.35 (6 H, m, ArH) and 7.56–7.61 (4 H, m, ArH); δ_C 14.0, 15.4, 19.2, 20.2, 21.0, 23.7, 24.0, 25.1, 26.9, 34.5, 36.3, 37.3, 60.5, 61.4, 65.0, 67.3, 74.1, 74.4, 76.4, 80.7, 100.6, 109.8, 127.5, 129.5, 129.6, 133.4, 133.6, 135.6, 135.7 and 170.1 (Found: M^+, 656.3708. $C_{37}H_{56}O_8Si$ requires *M*, 656.3744).

(2*S*,3*S*,4*R*,5*R*,6*R*)-4-Acetoxy-1-(*tert*-butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-3-methoxy-2-methyl-5-methylsulfonyloxyheptane 19 and (1*R*,3*R*,4*R*,5*S*,6*S*)-3-acetoxy-7-(*tert*-butyldiphenylsiloxy)-1,2-cyclohexylidenedioxy-5-methoxy-6-methyl-4-methylsulfonyloxyheptane 21

A solution of the ethoxyethyl ether **17** (100 mg, 0.15 mmol) in THF–acetic acid–water (0.5:1.5:0.5 cm^3) was stirred for 6 h at room temp. After evaporation of the mixture, the residue was taken up with methylene dichloride and the organic layer was washed successively with saturated aq. sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation off of the solvent gave an alcohol **18**, which, without further purification, was dissolved in methylene dichloride. To this solution were added triethylamine (0.64 cm^3, 0.45 mmol), DMAP (3.7 mg, 0.30 mmol) and methanesulfonyl chloride (0.24 cm^3, 0.30 mmol), and the resulting mixture was stirred at room temp. for 1 h. The mixture was diluted with methylene dichloride and the organic layer was washed successively with aq. ammonium chloride and brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:1, v/v) afforded the acetyl-migration product **21** (15 mg, 16%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1751 and 1364; δ_H 1.02 (3 H, d, *J* 6.9, Me), 1.03 (9 H, s, Bu^t), 1.36 (2 H, br s, cyclohexylidene protons), 1.55 (8 H, br s, cyclohexylidene protons), 1.93–2.03 (1 H, m, 6-H), 2.13 (3 H, s, Ac), 3.07 (3 H, s, Me), 3.37 (1 H, t, *J* 6.3, 5-H), 3.44 (3 H, s, Me), 3.65–3.74 (2 H, m, 7-H_2), 3.91 (1 H, dd, *J* 6.4 and 11.8, 1-H), 4.09 (1 H, dd, *J* 6.1 and 6.4, 2-H), 4.26 (1 H, dd, *J* 6.1 and 11.8, 1-H), 5.10 (1 H, dd, *J* 4.1 and 6.3, 4-H), 5.46 (1 H, dd, *J* 4.1 and 6.4, 3-H), 7.35–7.47 (6 H, m, ArH) and 7.65–7.70 (4 H, m, ArH) (Found: M^+, 662.2964. $C_{34}H_{50}O_9Si$ requires *M*, 662.2945).

Further elution with the same solvent system gave the desired sulfonate **19** (77 mg, 80%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1749 and 1352; δ_H 0.96 (3 H, d, *J* 6.9, Me), 1.07 (9 H, s, Bu^t), 1.39 (2 H, br s, cyclohexylidene protons), 1.58 (8 H, br d, *J* 12.9, cyclohexylidene protons), 2.03–2.07 (1 H, m, 2-H), 2.09 (3 H, s, Ac), 3.12 (3 H, s, Me), 3.42 (3 H, s, Me), 3.45 (1 H, t, *J* 5.4, 3-H), 3.62 (1 H, dd, *J* 4.4 and 10.2, 7-H), 3.74 (1 H, dd, *J* 5.7 and 10.2, 7-H), 3.94 (2 H, d, *J* 7.3, 1-H_2), 4.26 (1 H, ddd, *J* 3.3, 4.4 and 5.7, 6-H), 5.22 (1 H, dd, *J* 3.3 and 5.4, 5-H), 5.41 (1 H, t, *J* 5.4, 4-H), 7.35–7.47 (6 H, m, ArH) and 7.65–7.70 (4 H, m, ArH); δ_C 14.3, 19.2, 21.0, 23.6, 23.9, 25.0, 26.9, 34.1, 35.8, 36.7, 39.1, 60.4, 64.1, 64.8, 71.8, 74.6, 78.9, 81.2, 109.7, 127.6, 129.6, 133.3, 133.4, 135.6, 135.7 and 170.0 (Found: M^+, 662.2927).

(2*S*,3*S*,4*S*,1′*S*,2′*R*)-2-(1′-Acetoxy-2′,3′-cyclohexylidenedioxypropyl)-3-methoxy-4-methyltetrahydrofuran 22

To a stirred solution of the methanesulfonate **19** (70 mg, 0.11 mmol) in THF (2 cm^3) was added dropwise 1 M TBAF in THF (0.17 cm^3, 0.17 mmol) at 0 °C, and the resulting solution was stirred for 15 min at ambient temp. The mixture was treated with saturated aq. ammonium chloride and extracted with ethyl acetate. The extract was washed with brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (1:1, v/v) afforded the cyclisation product **22** (22 mg, 60%) as an oil, $[\alpha]_D$ −40.5 (*c* 0.4, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1740; δ_H 1.99 (3 H, d, *J* 7.1, Me), 1.41 (2 H, br s, cyclohexylidene protons), 1.60–1.69 (8 H, m, cyclohexylidene protons), 1.88–1.97 (1 H, m, 4-H), 2.05 (3 H, s, Ac), 2.95 (1 H, br t, *J* 4.3, unassignable proton), 3.12 (1 H, dd, *J* 4.3 and 8.1, unassignable proton), 3.28 (1 H, dd, *J* 5.4 and 8.1, unassignable proton), 3.50 (3 H, s, OMe), 3.84–3.93 (1 H, m, unassignable proton) and 4.00–4.21 (4 H, m, unassignable protons); δ_C 14.3, 20.9, 23.8, 23.9, 25.1, 35.0, 36.0, 36.3, 55.2, 58.7, 59.4, 65.4, 66.4, 73.4, 80.6, 110.9 and 170.9 (Found: M^+, 328.1881. $C_{17}H_{28}O_6$ requires *M*, 328.1885).

Further elution with the same solvent system gave the alcohol **20** (13 mg, 32%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1747, 1352 and

1365; δ_H 1.20 (3 H, d, *J* 6.9, Me), 1.41 (2 H, br s, cyclohexylidene protons), 1.59 (8 H, br d, *J* 12.2, cyclohexylidene protons), 2.02–2.07 (1 H, m, 2-H), 2.15 (3 H, s, Ac), 3.13 (3 H, s, SMe), 3.41 (1 H, t, *J* 5.4, unassignable proton), 3.50 (3 H, s, OMe), 3.69 (2 H, br d, *J* 5.4, unassignable protons), 3.96 (2 H, br d, *J* 6.9, unassignable protons), 4.25–4.32 (1 H, m, unassignable proton), 5.13 (1 H, dd, *J* 4.6 and 5.4, 5-H) and 5.36 (1 H, t, *J* 5.4, 4-H).

(2*R*,3*S*,4*S*,1′*S*,2′*R*)-2-(2′,3′-Cyclohexylidenedioxy-1′-hydroxypropyl)-3-methoxy-4-methyltetrahydrofuran 23

To a stirred solution of the acetate **22** (18 mg, 0.055 mmol) in methanol (2 cm^3) was added portionwise potassium carbonate (23 mg, 0.165 mmol) at 0 °C, and the resulting mixture was stirred at room temp. for 1 h. After evaporation of the mixture, the residue was treated with water and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation off of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:1, v/v) afforded the alcohol **23** (15 mg, 96%) as an oil, $[\alpha]_D$ +14.7 (*c* 0.3, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3460; δ_H 1.03 (3 H, d, *J* 6.5, Me), 1.32–1.42 (2 H, m, cyclohexylidene protons), 1.63 (8 H, br d, *J* 9.9, cyclohexylidene protons), 2.25–2.42 (1 H, m, 4-H), 2.49 (1 H, d, *J* 4.1, OH), 3.37 (3 H, s, OMe), 3.55 (2 H, t, *J* 8.1, unassignable protons), 3.78–3.83 (3 H, m, unassignable protons), 3.97–4.09 (2 H, m, unassignable protons) and 4.22 (1 H, dd, *J* 6.6 and 12.5, 3′-H) (Found: M^+, 286.1780. $C_{15}H_{26}O_5$ requires *M*, 286.1780).

(2*S*,3*S*,4*S*,1′*S*,2′*R*)-2-(1′-Benzyloxy-2′,3′-cyclohexylidenedioxypropyl)-3-methoxy-4-methyltetrahydrofuran 24

To a stirred suspension of sodium hydride (65% in oil; 3.6 mg, 0.098 mmol) in *N*,*N*-dimethylformamide (DMF) (2 cm^3) was added a solution of the alcohol **23** (14 mg, 0.049 mmol) and benzyl bromide (0.015 cm^3, 0.123 mmol) in DMF (1 cm^3) at 0 °C and the mixture was stirred at room temp. for 1.5 h. After addition of saturated aq. ammonium chloride, the mixture was extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (6:1, v/v) afforded the benzyl ether **24** (18 mg, 98%) as an oil, $[\alpha]_D$ +60.0 (*c* 0.3, $CHCl_3$); δ_H 0.97 (3 H, d, *J* 6.9, Me), 1.32–1.48 (2 H, m, cyclohexylidene protons), 1.56–1.72 (8 H, m, cyclohexylidene protons), 2.22–2.33 (1 H, m, 4-H), 3.17 (3 H, s, OMe), 3.42 (1 H, d, *J* 8.1, unassignable proton), 3.48 (1 H, dd, *J* 3.2 and 7.5 Hz, unassignable proton), 3.62 (1 H, dd, *J* 3.2 and 6.3, unassignable proton), 3.67–3.74 (2 H, m, unassignable protons), 3.95 (1 H, dd, *J* 6.3 and 8.1, unassignable proton), 4.05 (1 H, dd, *J* 6.1 and 8.1, unassignable proton), 4.33–4.42 (1 H, m, unassignable proton), 4.74 (1 H, d, *J* 11.9, OC*H*HPh), 4.93 (1 H, d, *J* 11.9, OCH*H*Ph), and 7.35–7.38 (5 H, m, Ph).

(2*S*,3*S*,4*S*,1′*S*,2′*R*)-2-(1′-Benzyloxy-2′,3′-dihydroxypropyl)-3-methoxy-4-methyltetrahydrofuran 25

A solution of the ketal **24** (15 mg, 0.04 mmol) in acetic acid–water (1.5 cm^3; 2:1) was stirred at 60 °C for 2 h. After removal of the solvent, the residue was purified by column chromatography on silica gel with hexane–ethyl acetate (1:2, v/v) as eluent to give the glycol **25** (11.5 mg, 98%) as an oil, $[\alpha]_D$ +28.2 (*c* 0.2, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3330 and 3250; δ_H 0.99 (3 H, d, *J* 7.1, Me), 2.33–2.40 (1 H, m, 4-H), 2.96 (1 H, br s, OH), 2.98 (1 H, br s, OH), 3.24 (3 H, s, OMe), 3.50–3.65 (4 H, m, unassignable protons), 3.78–3.89 (2 H, m, unassignable protons), 3.98–4.08 (2 H, m, unassignable protons), 4.64 (1 H, d, *J* 11.7, OC*H*HPh), 4.70 (1 H, d, *J* 11.7, OCH*H*Ph) and 7.36 (5 H, s, Ph) (Found: M^+, 296.1634. $C_{16}H_{24}O_5$ requires *M*, 296.1624).

(2*R*,2′*S*,3′*S*,4′*S*)-2-Benzyloxy-2-(3′-methoxy-4′-methyltetrahydrofuran-2′-yl)acetaldehyde 26

To a stirred solution of the glycol **25** (11 mg, 0.037 mmol) in methylene dichloride (0.6 cm^3) and water (0.2 cm^3) was added portionwise sodium periodate (12 mg, 0.056 mmol) at 0 °C, and the resulting mixture was stirred at room temp. for a further 1 h. After addition of saturated aq. hydrogen carbonate, the mixture was extracted with methylene dichloride. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:1, v/v) afforded the aldehyde **26** (9.5 mg, 97%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 1725; δ_H 1.00 (3 H, d, *J* 6.9, Me), 2.27–2.37 (1 H, m, 4′-H), 3.23 (3 H, s, OMe), 3.49 (1 H, dd, *J* 7.9 and 8.1, 5′-H), 3.71 (1 H, dd, *J* 4.3 and 5.9, 3′-H), 3.87–3.89 (1 H, m, 2-H), 4.02 (1 H, dd, *J* 6.9 and 8.1, 5′-H), 4.16 (1 H, t, *J* 4.3, 2′-H), 4.56 (1 H, d, *J* 12.0, OC*H*HPh), 4.82 (1 H, d, *J* 12.0, OCH*H*Ph), 7.36 (5 H, s, Ph) and 9.73 (1 H, s, CHO) [Found: *m*/*z*, 235.1355. $C_{14}H_{19}O_3$ (*M* −CHO) requires *m*/*z*, 235.1334].

2-Benzyloxy-6-hydroxy-4-methoxy-5-methylhex-2-enal 27

To a stirred solution of the aldehyde **26** (9 mg, 0.034 mmol) in THF (2 cm^3) was added DBU (0.006 cm^3, 0.004 mmol) at ambient temp. and the mixture was heated at reflux for 2 h under argon. After treatment with saturated aq. ammonium chloride, the mixture was extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:2, v/v) afforded the unsaturated aldehyde **27** (6 mg, 67%) as an oil, $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 and 1695; δ_H 0.75 (0.42 H, d, *J* 6.3, Me), 0.76 (2.58 H, d, *J* 7.1, Me), 1.82–1.97 (1 H, m, 5-H), 3.09 (2.58 H, s, OMe), 3.22 (0.42 H, s, OMe), 3.46–3.56 (2 H, m, 6-H_2), 4.15 (1 H, dd, *J* 7.3 and 8.9, 4-H), 5.14 (1 H, d, *J* 7.5, OC*H*HPh), 5.18 (1 H, d, *J* 7.5, OC*H*HPh), 5.81 (1 H, d, *J* 8.9, 3-H), 7.35 (5 H, s, Ph), 9.35 (0.86 H, s, CHO), 9.76 (0.14 H, s, CHO) (Found: M^+, 264.1356. $C_{15}H_{20}O_4$ requires *M*, 264.1362).

(2*R*,3*S*,4*R*,5*S*,6*R*)-4-Benzyloxy-1-(*tert*-butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptane with the less polar ethoxyethyl group 28

To a stirred suspension of sodium hydride (65% in oil; 217 mg, 5.86 mmol) and tetrabutylammonium iodide (TBAI) (217 mg, 0.59 mmol) in THF (10 cm^3) was added a solution of the less polar ethoxyethyl ether **16** (1.8 g, 2.93 mmol) in THF (20 cm^3) at 0 °C, and then benzyl bromide (0.52 cm^3, 4.40 mmol) was added to this mixture. The resulting solution was stirred at room temp. for 12 h, treated with saturated aq. ammonium chloride, and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (14:1, v/v) afforded the *benzyl ether* **28** (1.94 g, 94%) as an oil, $[\alpha]_D$ +21.5 (*c* 2.1, $CHCl_3$) (Found: C, 71.35; H, 8.60. $C_{42}H_{60}O_7Si$ requires C, 71.55; H, 8.60%); δ_H 0.88 (3 H, d, *J* 6.9, Me), 1.01 (9 H, s, Bu^t), 1.20 (3 H, t, *J* 7.1, Me), 1.25 (3 H, d, *J* 5.3, Me), 1.37 (2 H, br s, cyclohexylidene protons), 1.56 (8 H, s, br s, cyclohexylidene protons), 1.95–1.99 (1 H, m, 2-H), 3.39 (1 H, dd, *J* 5.3 and 7.1, 3-H), 3.43 (3 H, s, OMe), 3.49–3.70 (4 H, m, CH_2O and 1-H_2), 3.77 (1 H, dd, *J* 5.3 and 6.4, 4-H), 3.86 (1 H, t, *J* 6.4, 5-H), 3.98–4.07 (1 H, m, unassignable proton), 4.07–4.14 (1 H, m, unassignable proton), 4.12–4.22 (1 H, m, unassignable proton), 4.57 (1 H, d, *J* 11.3, OC*H*HPh), 4.76 (1 H, d, *J* 11.3, OCH*H*Ph), 4.87 [1 H, q, *J* 5.3, OC*H*(Me)O], 7.22–7.44 (11 H, m, ArH) and 7.64–7.68 (4 H, m, ArH); δ_C 14.6, 15.6, 19.3, 20.4, 23.8, 24.1, 25.2, 27.0, 34.6, 36.3, 37.2, 60.5, 61.2, 65.3, 67.2, 74.6, 80.0, 82.7, 100.8, 109.3, 127.5, 128.2, 129.5, 133.8, 135.6 and 138.5 [Found: *m*/*z*, 631.3484. $C_{38}H_{51}O_6Si$ (*M* −EE) requires *m*/*z*, 631.3454].

(2*R*,3*R*,4*S*,5*S*,6*S*)-4-Benzyloxy-7-(*tert*-butyldiphenylsiloxy)-1,2-cyclohexylidenedioxy-5-methoxy-6-methylheptan-3-ol 29

A solution of the ethoxyethyl ether **28** (1.0 g, 1.42 mmol) in acetic acid–water (3:1; 12 cm^3) was stirred for 3 h at room temp. After concentration of the mixture, the residue was dissolved in ethyl acetate and the organic layer was washed successively with saturated aq. sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane-ethyl acetate (6:1, v/v) afforded the *alcohol* **29** (897 mg, 100%) as an oil, $[a]_D$ −16.6 (*c* 1.3, $CHCl_3$) (Found: C, 71.95; H, 8.25. $C_{38}H_{52}O_6Si$ requires C, 72.10; H, 8.30%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3540 and 3460; δ_H 1.04–1.10 (12 H, m, Me and Bu^t), 1.37 (2 H, br s, cyclohexylidene protons), 1.47–1.57 (8 H, m, cyclohexylidene protons), 2.00–2.10 (1 H, m, 6-H), 2.63 (1 H, d, *J* 7.6, OH), 3.43 (3 H, s, OMe), 3.38–3.47 (1 H, m, 5-H), 3.57 (1 H, br t, *J* 7.4, 3-H), 3.73 (2 H, d, *J* 5.6, 7-H_2), 3.85–4.13 (4 H, m, 1-H_2, 2- and 4-H), 4.65 (1 H, d, *J* 11.2, OC*H*HPh), 4.79 (1 H, d, *J* 11.2, OCH*H*Ph), 7.23–7.47 (11 H, m, ArH) and 7.65–7.73 (4 H, m, ArH); δ_C 14.8, 19.3, 23.8, 24.0, 25.1, 26.9, 34.8, 36.5, 37.6, 60.5, 64.9, 67.1, 73.3, 74.7, 75.6, 84.6, 109.6, 127.6, 127.7, 128.0, 128.3, 129.5, 133.8, 135.6 and 138.3 [Found: *m*/*z*, 632.3558. $C_{38}H_{52}O_6Si$ (*M* requires *m*/*z*, 632.3533].

(2*S*,3*S*,4*R*,5*R*,6*R*)-4-Benzyloxy-1-(*tert*-butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-3-methoxy-2-methyl-5-methylsulfonyloxyheptane 30

To a stirred solution of the alcohol **29** (880 mg, 1.39 mmol) in methylene dichloride (17 cm^3) were successively added triethylamine (0.39 cm^3, 2.78 mmol), DMAP (34 mg, 0.28 mmol) and methanesulfonyl chloride (0.16 cm^3, 2.09 mmol) at 0 °C, and the resulting mixture was stirred for 1 h at ambient temp. under argon. The mixture was treated with saturated aq. ammonium chloride and extracted with methylene dichloride. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (4:1, v/v) afforded the *sulfonate* **30** (961 mg, 97%) as needles, mp 97.5–98 °C (from hexane–diethyl ether); $[a]_D$ +14.6 (*c* 1.0, $CHCl_3$) (Found: M^+, 710.3282; C, 65.60; H, 7.60. $C_{39}H_{54}O_8SSi$ requires *M*, 710.3307; C, 65.90; H, 7.65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1358; δ_H 1.01 (3 H, d, *J* 6.7, Me), 1.07 (9 H, s, Bu^t), 1.37 (2 H, br s, cyclohexylidene protons), 1.50–1.60 (8 H, m, cyclohexylidene protons), 2.05–2.17 (1 H, m, 2-H), 3.06 (3 H, s, SO_2Me), 3.41 (3 H, s, OMe), 3.39–3.46 (1 H, m, 3-H), 3.65 (1 H, dd, *J* 4.8 and 9.9, 1-H), 3.77 (1 H, dd, *J* 5.6 and 9.9, 1-H), 3.89–3.98 (3 H, m, 7-H_2 and 4-H), 4.23 (1 H, m, 6-H), 4.60 (1 H, d, *J* 11.2, OC*H*HPh), 4.77 (1 H, d, *J* 11.2, OCH*H*Ph), 5.06 (1 H, br t, *J* 4.0, 5-H), 7.23-7.48 (11 H, m, ArH) and 7.66–7.74 (4 H, m, ArH); δ_C 14.9, 19.2, 23.6, 23.9, 25.0, 26.9, 34.2, 35.8, 36.9, 39.0, 60.7, 65.0, 65.1, 74.8, 75.0, 78.8, 80.7, 83.3, 109.4, 127.6, 127.8, 128.0, 128.4, 129.6, 133.5, 133.6, 135.6 and 137.7.

(2*S*,3*S*,4*R*,5*R*,6*R*)-4-Benzyloxy-6,7-cyclohexylidenedioxy-3-methoxy-2-methyl-5-methylsulfonyloxyheptan-1-ol 31

To a stirred solution of the silyl ether **30** (920 mg, 1.3 mmol) in THF (10 cm^3) was added a 1 M THF solution of TBAF (1.95 cm^3, 1.95 mmol) at 0 °C, and the resulting mixture was stirred for 2 h at ambient temp. under argon. After addition of saturated aq. ammonium chloride, the mixture was concentrated to leave a residue, which was extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1, v/v) afforded the *primary alcohol* **31** (611 mg, 100%) as an oil, $[a]_D$ +11.7 (*c* 1.1, $CHCl_3$) (Found: C, 58.50; H, 7.70. $C_{23}H_{36}O_8S$ requires C, 58.45; H, 7.70%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3480; δ_H 0.95 (3 H, d, *J* 6.9, Me), 1.26 (2 H, br s, cyclohexylidene protons), 1.40–1.50 (8 H, m, cyclohexylidene protons), 1.80–1.90 (1 H, m, 2-H), 2.53 (1 H, br s, OH), 2.91 (3 H, s, SO_2Me), 3.29 (1 H, dd, *J* 4.0 and 7.3, 3-H), 3.37 (3 H, s, OMe), 3.50 (1 H, dd, *J* 5.6 and 11.0, 1-H), 3.59 (1 H, dd, *J* 3.5 and 11.0, 1-H), 3.81–3.90 (3 H, m, 7-H_2 and 4-H), 4.19 (1 H, m, 6-H), 4.57 (1 H, d, *J* 11.0, OC*H*HPh), 4.68–4.76 (2 H, m, 5-H and OCH*H*Ph) and 7.12–7.23 (5 H, m, Ph); δ_C 14.7, 23.6, 23.9, 25.0, 34.4, 35.8, 36.0, 39.0, 53.2, 61.3, 64.6, 65.5, 74.0, 75.2, 78.9, 80.1, 85.7, 109.8, 127.8, 128.1, 128.4 and 137.7.

(1′*R*,2*S*,3*R*,4*S*,5*S*)-3-Benzyloxy-2-(1′,2′-cyclohexylidenedioxyethyl)-4-methoxy-5-methyltetrahydropyran 32

To a stirred solution of the alcohol **31** (570 mg, 1.21 mmol) in toluene–water (9:1; 20 cm^3) were added tetrabutylammonium bromide (19 mg, 0.06 mmol) and sodium hydroxide (966 mg, 2.42 mmol), and the resulting mixture was stirred for 1.5 h at 90 °C. After addition of saturated aq. ammonium chloride, the mixture was extracted with ethyl acetate and the extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (7:1, v/v) afforded the *cyclisation product* **32** (359 mg, 80%) as needles, mp 72–72.5 °C (from ethanol); $[a]_D$ −7.8 (*c* 1.1, $CHCl_3$) (Found: M^+, 376.2243; C, 70.05; H, 8.55. $C_{22}H_{32}O_5$ requires *M*, 376.2248; C, 70.20; H, 8.55%); δ_H 0.96 (3 H, d, *J* 7.1, Me), 1.40 (2 H, br s, cyclohexylidene protons), 1.52–1.75 (8 H, m, cyclohexylidene protons), 2.13–2.25 (1 H, m, 5-H), 3.07 (1 H, dd, *J* 3.6 and 9.2, 2-H), 3.42 (3 H, s, OMe), 3.37–3.50 (2 H, m, 4- and 6-H), 3.66 (1 H, t, *J* 9.2, 3-H), 3.84 (1 H, br d, *J* 11.5, 6-H), 3.92–4.02 (2 H, m, 2′-H_2), 4.32–4.41 (1 H, m, 1′-H), 4.62 (1 H, d, *J* 10.7, OC*H*HPh), 4.93 (1 H, d, *J* 10.7, OCH*H*Ph) and 7.26–7.36 (5 H, m, Ph); δ_C 10.8, 24.0, 25.2, 32.3, 35.3, 35.5, 56.2, 65.1, 70.8, 74.4, 75.1, 75.7, 79.4, 85.1, 109.3, 127.5, 127.8, 128.3 and 138.7.

(1′*R*,2*S*,3*R*,4*S*,5*S*)-3-Benzyloxy-2-(1′,2′-dihydroxyethyl)-4-methoxy-5-methyltetrahydropyran 33

A solution of the ketal **32** (320 mg, 0.85 mmol) in acetic acid–water (2:1; 4.5 cm^3) was stirred at 60 °C for 2 h. Concentration of the mixture gave a residue, which was dissolved in ethyl acetate. The organic layer was washed successively with saturated aq. sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:3, v/v) afforded the *diol* **33** (223 mg, 89%) as needles, mp 93–94 °C (from hexane–diethyl ether); $[a]_D$ +11.9 (*c* 1.0, $CHCl_3$) (Found: M^+, 296.1625; C, 64.85; H, 8.05. $C_{16}H_{24}O_5$ requires *M*, 296.1621; C, 64.85; H, 8.15%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 and 3300; δ_H 1.04 (3 H, d, *J* 7.3, Me), 2.15–2.26 (1 H, m, 5-H), 2.62 (1 H, br s, OH), 2.65 (1 H, br s, OH), 3.20 (1 H, dd, *J* 1.8 and 9.4, 2-H), 3.38–3.45 (1 H, m, 4-H), 3.41 (3 H, s, OMe), 3.53 (1 H, dd, *J* 2.1 and 11.5, 6-H), 3.63–3.82 (4 H, m, 2′-H_2, 3- and 6-H), 3.84–3.93 (1 H, m, 1′-H), 4.65 (1 H, d, *J* 10.7, OC*H*HPh), 4.92 (1 H, d, *J* 10.7, OC*H*HPh) and 7.23–7.37 (5 H, m, Ph); δ_C 10.8, 32.1, 56.2, 65.3, 69.1, 71.0, 73.9, 75.1, 81.2, 84.8, 127.6, 127.9, 128.3 and 138.5.

(1′*RS*,2*S*,3*R*,4*S*,5*S*)-3-Benzyloxy-2-(1′-hydroxyethyl)-4-methoxy-5-methyltetrahydropyrans 35 and 36

To a stirred solution of the diol **33** (123 mg, 0.42 mmol) in methylene dichloride–water (3:1; 4 cm^3) was added sodium periodate (133 mg, 0.63 mmol) at 0 °C, and the resulting solution was stirred for a further 2 h at the same temp. After treatment with saturated aq. sodium hydrogen carbonate, the mixture was extracted with methylene dichloride and the extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave the aldehyde **34**, which, without further purification, was subjected to the next reaction. The aldehyde **34** obtained above was dissolved in diethyl ether (3 cm^3) and the solution was cooled to −78 °C. To this solution was added a 1.02 M ethereal solution of methyllithium (1.2 cm^3, 1.26 mmol) at the same temperature, and the solution was stirred for a

further 3 h. The mixture was treated with saturated aq. ammonium chloride and extracted with diethyl ether. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (4:3, v/v) afforded the *less polar alcohol* **35** (22 mg, 19%) as an oil, $[\alpha]_D$ +16.0 (*c* 0.4, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3480; δ_H 1.03 (3 H, d, *J* 7.1, Me), 1.26 (3 H, d, *J* 6.6, Me), 1.95 (1 H, br s, OH), 2.15–2.25 (1 H, m, 5-H), 2.97 (1 H, dd, *J* 1.8 and 9.2, 2-H), 3.38–3.45 (1 H, m, 4-H), 3.42 (3 H, s, OMe), 3.53 (1 H, dd, *J* 2.3 and 11.5, 6-H), 3.67 (1 H, t, *J* 9.2, 3-H), 3.79 (1 H, dd, *J* 1.8 and 11.5, 6-H), 3.95–4.07 (1 H, m, 1′-H), 4.64 (1 H, d, *J* 10.9, OC*H*HPh), 4.92 (1 H, d, *J* 10.9, OCH*H*Ph) and 7.24–7.37 (5 H, m, Ph); δ_C 11.0, 20.3, 32.2, 56.2, 65.8, 70.8, 74.6, 75.0, 82.2, 85.2, 127.6, 128.0, 128.4 and 138.7 (Found: M^+, 280.1684. $C_{16}H_{24}O_4$ requires *M*, 280.1675).

Further elution with the same solvent system gave the *more polar diastereomer* **36** (77 mg, 66%) as an oil, $[\alpha]_D$ +8.3 (*c* 1.2, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3470; δ_H 1.01 (3 H, d, *J* 7.3, Me), 1.12 (3 H, d, *J* 6.6, Me), 2.15–2.25 (1 H, m, 5-H), 2.70 (1 H, br s, OH), 3.12–3.21 (1 H, m 2-H), 3.39 (3 H, s, OMe), 3.39–3.44 (2 H, m, 3- and 4-H), 3.50 (1 H, dd, *J* 2.1 and 11.5, 6-H), 3.77 (1 H, dd, *J* 1.5 and 11.5, 6-H), 3.93–4.06 (1 H, m, 1′-H), 4.59 (1 H, d, *J* 11.0, OC*H*HPh), 4.94 (1 H, d, *J* 11.0, OCH*H*Ph) and 7.24–7.63 (5 H, m, Ph); δ_C 11.4, 17.9, 32.6, 56.3, 68.5, 71.3, 75.0, 76.5, 82.7, 85.8, 128.1, 128.4, 128.8 and 138.7 (Found: M^+, 280.1679).

(2*R*,3*R*,4*S*,5*S*)-2-Acetyl-3-benzyloxy-4-methoxy-5-methyltetrahydropyran 37 from the less polar alcohol 35

To a stirred suspension of PCC (208 mg, 0.96 mmol), Celite (250 mg) and sodium acetate (79 mg, 0.96 mmol) in methylene dichloride (5 cm^3) was added a solution of the alcohol **35** (90 mg, 0.32 mmol) in methylene dichloride (2 cm^3) at room temp. and the resulting mixture was stirred for a further 3 h at the same temp. After addition of an excess of diethyl ether, the insoluble material was filtered off and the filtrate was concentrated to leave a residue, which was purified by column chromatography on silica gel, using hexane–ethyl acetate (4:1, v/v) as eluent, to give the *ketone* **37** (86.3 mg, 97%) as an oil, $[\alpha]_D$ +21.8 (*c* 1.5, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1724; δ_H 0.95 (3 H, d, *J* 7.1, Me), 2.20 (3 H, s, Ac), 2.20–2.30 (1 H, m, 5-H), 3.31 (3 H, s, OMe), 3.28–3.34 (1 H, m, 4-H), 3.55 (1 H, dd, *J* 3.6 and 11.4, 6-H), 3.76 (1 H, dd, *J* 4.3 and 11.4, 6-H), 3.85–3.92 (2 H, m, 2- and 3-H), 4.63 (1 H, d, 11.4, OC*H*HPh), 4.71 (1 H, d, *J* 11.4, OCH*H*Ph) and 7.24–7.37 (5 H, m, Ph); δ_C 11.6, 26.8, 30.5, 56.9, 68.2, 73.3, 73.7, 81.6, 81.7, 127.6, 127.9, 128.3, 138.0 and 206.7 (Found: M^+, 278.1514. $C_{16}H_{22}O_4$ requires *M*, 278.1518).

(2*R*,3*R*,4*S*,5*S*)-2-Acetyl-3-benzyloxy-4-methoxy-5-methyltetrahydropyran 37 from the more polar alcohol 36

The more polar alcohol **36** (120 mg, 0.43 mmol) was oxidised with PCC (277 mg, 1.28 mmol) by the same procedure as described above to give the ketone **37** (115 mg, 97%). This compound was identical with the authentic sample obtained above.

(2*R*,3*R*,4*S*,5*S*)-2-Acetyl-3-hydroxy-4-methoxy-5-methyltetrahydropyran 38

A mixture of the benzyl ether **37** (82 mg, 0.29 mmol), 10% palladium(II) hydroxide on carbon (15 mg) and ethyl acetate (3 cm^3) was stirred for 2 h at room temp. under hydrogen. After filtration to remove the catalyst, the filtrate was concentrated to leave a residue, which was purified by column chromatography on silica gel, using hexane–ethyl acetate (1:1, v/v) as eluent, to give the *alcohol* **38** (52 mg, 94%) as an oil; $[\alpha]_D$ +93.1 (*c* 0.7, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3448 and 1722; δ_H 0.96 (3 H, d, *J* 7.1, Me), 2.17–2.27 (1 H, m, 5-H), 2.24 (3 H, s, Ac), 3.25–3.33 (2 H, m, 4-H and OH), 3.36 (3 H, s, OMe), 3.50 (1 H, d, *J* 9.2, 2-H), 3.56 (1 H, dd, *J* 2.3 and 11.7, 6-H), 3.72 (1 H, t, *J* 8.9, 3-H) and 3.83 (1 H, dd, *J* 2.0 and 11.7, 6-H); δ_C 10.7, 26.9, 31.3, 56.4, 67.6, 70.9, 82.9, 83.8 and 209.4 (Found: M^+, 188.1054. $C_9H_{16}O_4$ requires *M*, 188.1049).

(2*R*,3*R*,4*S*,5*S*)-2-Acetyl-3-(*tert*-butyldimethylsiloxy)-4-methoxy-5-methyltetrahydropyran 6

To a stirred solution of the alcohol **38** (50 mg, 0.27 mmol) and imidazole (24 mg, 0.32 mmol) in DMF (2 cm^3) was added TBDMSCl (24 mg, 0.35 mmol) at room temp., and the resulting mixture was stirred for a further 24 h at the same temp. The mixture was treated with saturated aq. ammonium chloride and extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the mixture gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (95:5, v/v) afforded the known ketone **6** (68 mg, 199%) as an oil, $[\alpha]_D$ +28.4 (*c* 0.7, MeOH); +23.8 (*c* 0.8, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1728; δ_H 0.06 (3 H, s, SiMe), 0.09 (3 H, s, SiMe), 0.87 (9 H, s, Bu^t), 0.94 (3 H, d, *J* 7.1, Me), 2.24 (3 H, s, Ac), 2.24–2.32 (1 H, m, 5-H), 3.10 (1 H, dd, *J* 3.8 and 6.1, 4-H), 3.27 (3 H, s, OMe), 3.55 (1 H, dd, *J* 3.6 and 11.4, 6-H), 3.71 (1 H, br d, *J* 6.1, 2-H), 3.75 (1 H, dd, *J* 6.4 and 11.4, 6-H) and 4.11 (1 H, br t, *J* 6.1, 3-H); δ_H −5.1, −4.6, 11.8, 18.1, 25.8, 26.7, 29.8, 56.4, 67.3, 68.3, 82.4, 84.5 and 206.7. These data were identical with those reported.[3]

(2*S*,3*S*,4*R*,5*S*,6*R*)-6,7-Cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptane-1,4-diol, a diastereomer of compound 15, from the more polar ethoxyethyl ether 14

The reduction of the γ-lactone **14** with the more polar ethoxyethyl group (1.8 g, 4.84 mmol) with a 1 M THF solution of lithium triethylborohydride (14.5 cm^3, 14.5 mmol) in THF (50 cm^3) was carried out as for the preparation of the diol **15** with the less polar ethoxyethyl group, to give the *title diol* (1.81 g, 99.5%), a diastereomer of compound **15**, as an oil, $[\alpha]_D$ −15.1 (*c* 1.1, $CHCl_3$) (Found: M^+, 376.2456; C, 60.50; H, 9.50. $C_{19}H_{36}O_7$ requires *M*, 376.2461; C, 60.60; H, 9.65%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3465; δ_H 1.04 (3 H, d, *J* 7.1, Me), 1.22 (3 H, t, *J* 6.9, Me), 1.33 (3 H, d, *J* 5.4, Me), 1.41 (2 H, br s, cyclohexylidene protons), 1.54–1.68 (8 H, m, cyclohexylidene protons), 2.02–2.08 (1 H, m, 2-H), 3.03 (1 H, br s, OH), 3.38–3.70 (7 H, m, 3- and 4-H, OH, OCH_2 and 1-H_2), 3.52 (3 H, s, OMe), 3.89–4.04 (3 H, m, 6-H and 7-H_2), 4.20–4.30 (1 H, m, 5-H) and 4.83 (1 H, q, *J* 5.1, OCHO); δ_C 14.8, 15.3, 20.4, 23.8, 23.9, 25.1, 34.8, 36.0, 37.3, 59.9, 62.4, 64.8, 65.0, 72.2, 76.4, 77.5, 83.3, 102.4 and 109.0.

(2*S*,3*S*,4*R*,5*S*,6*R*)-1-(*tert*-Butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptan-4-ol, a diastereomer of compound 16, with the more polar ethoxyethyl group

The silylation of the above diol, a diastereomer of compound **15** (1.1 g, 2.9 mmol) with TBDPSCl (1.0 cm^3, 3.77 mmol) and imidazole (398 mg, 5.8 mmol) in DMF (30 cm^3) was carried out as for the preparation of the silyl ether **16** with the less polar ethoxyethyl group to give the *title ether* (1.72 g, 96%), a diastereomer of compound **16**, as an oil, $[\alpha]_D$ −9.6 (*c* 1.2, $CHCl_3$) (Found: M^+, 614.3629; C, 68.10; H, 8.80. $C_{35}H_{54}O_7Si$ requires *M*, 614.3639; C, 68.35; H, 8.85%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3482; δ_H 1.03 (3 H, d, *J* 6.9, Me), 1.07 (9 H, s, Bu^t), 1.21 (3 H, t, *J* 7.1, Me), 1.33 (3 H, d, *J* 5.1, Me), 1.40 (2 H, br s, cyclohexylidene protons), 1.56–1.64 (8 H, m, cyclohexylidene protons), 2.08–2.22 (1 H, m, 2-H), 3.33–3.38 (2 H, m, unassignable protons), 3.42 (3 H, s, OMe), 3.50–3.62 (3 H, m, unassignable protons), 3.65–3.70 (2 H, m, unassignable protons), 3.88–4.00 (2 H, m, unassignable protons), 4.00–4.05 (1 H, m, unassignable proton), 4.16–4.24 (1 H, m, unassignable proton), 4.86 (1 H, q, *J* 5.1, OCHO), 7.34–7.45 (6 H, m, Ph) and 7.65–7.69 (4 H, m, Ph); δ_C 14.6, 15.4, 19.2, 20.4, 23.8, 24.0, 25.2, 26.9, 34.9, 36.0, 37.0, 59.3, 62.4, 64.5, 65.4, 71.7, 76.6, 77.4, 81.4, 102.3, 108.7, 127.6, 129.5, 133.7, 133.8, 135.6 and 135.7.

(2*S*,3*S*,4*R*,5*S*,6*R*)-4-Benzyloxy-1-(*tert*-butyldiphenylsiloxy)-6,7-cyclohexylidenedioxy-5-(1-ethoxyethoxy)-3-methoxy-2-methylheptane 28 with the more polar ethoxyethyl group

Benzylation of the above alcohol (1.55 g, 2.52 mmol), a diastereomer of compound **16**, with benzyl bromide (0.45 cm^3, 3.78 mmol), sodium hydride (65% in oil; 186 mg, 5.04 mmol) and TBAI (186 mg, 0.5 mmol) in THF (20 cm^3) was carried out as for the preparation of the benzyl ether **28** with the less polar ethoxyethyl group to give the title compound, a diastereomer of compound **18** (1.75 g, 99%) as an oil, $[\alpha]_D$ −8.2 (*c* 0.9, $CHCl_3$) (Found: C, 71.30; H, 8.60. $C_{42}H_{60}O_7Si$ requires C, 71.55; H, 8.60%); δ_H 0.98 (3 H, d, *J* 6.9, Me), 1.06 (9 H, s, Bu^t), 1.16 (3 H, t, *J* 7.1, Me), 1.31 (3 H, d, *J* 5.3, Me), 1.35 (2 H, br s, cyclohexylidene protons), 1.43–1.62 (8 H, m, cyclohexylidene protons), 2.16–2.30 (1 H, m, 2-H), 3.42 (3 H, s, Me), 3.46–3.60 (4 H, m, CH_2O and 1-H_2), 3.71 (1 H, dd, *J* 3.6 and 7.4, 4-H), 3.78–3.85 (2 H, m, unassignable protons), 3.98 (1 H, t, *J* 7.4, unassignable proton), 4.14 (1 H, dt, *J* 1.8 and 7.4, unassignable proton), 4.26 (1 H, dd, *J* 2.0 and 3.6, unassignable proton), 4.57 (1 H, d, *J* 11.4, OC*H*HPh), 4.76 (1 H, d, *J* 11.4, OCH*H*Ph), 5.04 [1 H, q, *J* 5.3, OC*H*(Me)O], 7.22–7.46 (11 H, m, ArH) and 7.67–7.74 (4 H, m, ArH); δ_C 15.3, 15.4, 19.2, 20.5, 23.7, 24.0, 25.2, 26.9, 33.8, 36.1, 36.8, 60.7, 61.1, 64.7, 65.2, 74.6, 77.5, 80.4, 84.0, 100.7, 107.9, 127.5, 127.6, 128.2, 128.3, 129.6, 133.7, 133.8, 135.6 and 138.5 [Found: *m*/*z*, 631.3455. $C_{38}H_{51}O_6Si$ (M − EE) requires *m*/*z*, 631.3454].

Deprotection of the ethoxyethyl group of a diastereomer of compound 28

A solution of the ethoxyethyl ether above (1.0 g, 1.42 mmol), a diastereomer of compound **28**, in acetic acid–water (3:1, 12 cm^3) was stirred for 3 h at room temp. After concentration of the mixture, the residue was dissolved in ethyl acetate and the organic layer was washed successively with saturated aq. sodium hydrogen carbonate and brine, and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (6:1, v/v) afforded the alcohol **29** (897 mg, 100%) as an oil, which was identical with the authentic sample obtained from the less polar diastereomer **28**.

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