Dispiroketals in synthesis. Part 25.[1] Further reactions of dispiroketal protected glycolate to afford optically active 1,2,3,4-tetraols

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Received (in Cambridge) 3rd February 1999, Accepted 22nd April 1999

Glycolic acid can be converted to optically active 1,2,3,4-tetraols using a dispiroketal unit as a protecting group and chiral auxiliary. Aldol reactions of dispiroketal protected glycolate with aldehydes afford one diastereoisomer preferentially with two newly formed stereogenic centres. To extend the polyol chain, the carbonyl group of the aldol product is converted to a vinyl ether by the Tebbe reagent after protection of the free alcohol. A subsequent hydroboration–oxidation protocol affords the dispiroketal protected tetraol. The final deprotection of the tetraol occurs selectively without epimerisation or migration of the silyloxy protecting groups.

Introduction

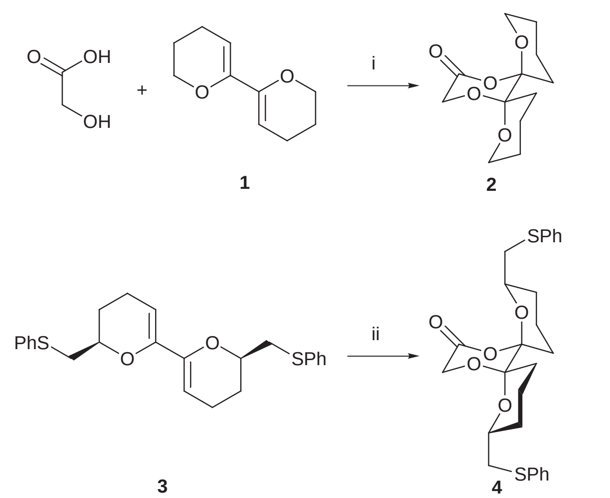
Sequences of 1,2-diols are observed in many natural products of biological significance, ranging from simple monosaccharides[2] to palytoxin.[3] The development of methods for the stereocontrolled preparation of polyols is therefore essential for the synthesis of polyhydroxylated natural products.[4] At present, the selective protection and deprotection protocols of hydroxy groups of polyols are necessary for successful polyol synthesis.

In recent years, our group has developed the use of bi(dihydropyran) derivatives for the regio- and stereoselective protection of 1,2-diols as their corresponding dispiroketals.[5] Chiral bi(dihydropyran)s are versatile and offer the possibility of enantioselectively desymmetrising *meso* polyols, thermodynamically resolving racemic 1,2-diols, and selectively protecting diequatorial vicinal diols in sugars.[6] The dispiroketal protecting group in sugars may also play an important role for the reactivity tuning in glycoside coupling reactions.[7] Dispiroketals are not only used as protecting groups, they may also be synthetically useful as chiral auxiliaries.[8]

Here, we report the enantiodifferentiating preparation of 1,2,3,4-tetraols from a dispiroketal protected glycolate. The dispiroketal unit acts both as a protecting group and a chiral auxiliary to yield a dispiroketal protected tetraol which is then selectively deprotected. Thus, the dual-function of dispiroketals provides an opportunity to assemble valuable protected homochiral polyols in an efficient fashion.

Results and discussion

The dispiroketal protected glycolate **2** was obtained as a racemate in 67% yield by treating bi(dihydropyran) **1** and glycolic acid with a catalytic quantity of $Ph_3P{\cdot}HBr$ in CH_2Cl_2 for 17 h at room temperature (Scheme 1). The dispiroketal **2** was obtained as a single racemic diastereoisomer with maximum anomeric stabilisation. The protected glycolate was then deprotonated by treatment with LDA in THF at −78 °C and reacted in a highly diastereodifferentiating manner with benzaldehyde in the presence of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU) to give only 2 diastereoisomers out of four possible diastereoisomers[9] (Table 1). The structure of the major isomer **5a**, formed as a racemate in 89% yield, which has an equatorial alkyl group and is an *erythro* diol, was determined by X-ray



1 2 3 4

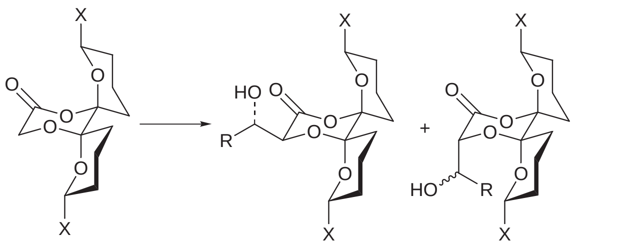
Scheme 1 *Reagents and conditions*: i, $Ph_3P{\cdot}HBr$, CH_2Cl_2, rt, 17 h, 67%; ii, glycolic acid, $Ph_3P{\cdot}HBr$, CH_2Cl_2, rt, 6 h, 94%.

crystallography (Fig. 1).† The minor diastereoisomer **5b** (2% yield), which has an axial alkyl group, was assigned from evidence of a strong NOE between the axial proton on C-2 and the benzyl proton but the configuration of the newly formed hydroxy group remained, however, undetermined. The large preference for one diastereomer could be rationalised by considering the chair-like six-membered transition state[10] whereby the alkyl group of the aldehyde was directed pseudo-equatorially in the transition state (Scheme 2). Extension of the reaction time to 3 h decreased the product yield to only 58%. Interestingly, when the aldol reaction was quenched after warming up to room temperature, dehydration occurred to give the *Z* olefin **9** as the only product in 19% yield (Scheme 3). The stereochemistry of **9** was determined by NOESY ^{1}H NMR. This result clearly indicated that the aldol reaction needed to be worked up at −78 °C to minimise the *syn*-dehydration and potential retro-aldol products.

The aldol product **5a** could be deprotected by treatment with camphorsulfonic acid and ethylene glycol in methanol to give

† CCDC reference number 207/326. See http://www.rsc.org/suppdata/p1/1999/1647 for crystallographic files in .cif format.

Table 1 Stereodifferentiating aldol reaction of dispiroketal protected glycolate



a **b**

2 X = H

4 X = CH_2SPh

5 X = H, R = Ph

6 X = H, R = CH_2=CH

7 X = CH_2SPh, R = Ph

8 X = CH_2SPh, R = CH_2=CH

Dispiroketal	RCHO	Products (Yield, %)
2	R = Ph	**5a** (89), **5b** (2)
2	R = CH_2=CH	**6a** (78)
4	R = Ph	**7a** (84)
4	R = CH_2=CH	**8a** (78), **8b** (3)
4	R = Bu^t	No adduct

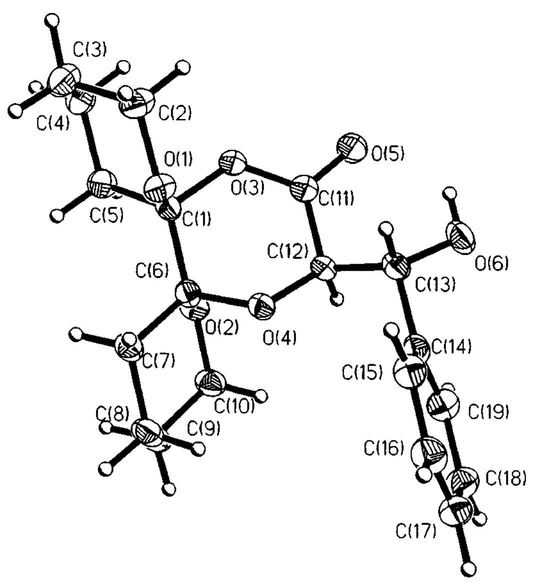
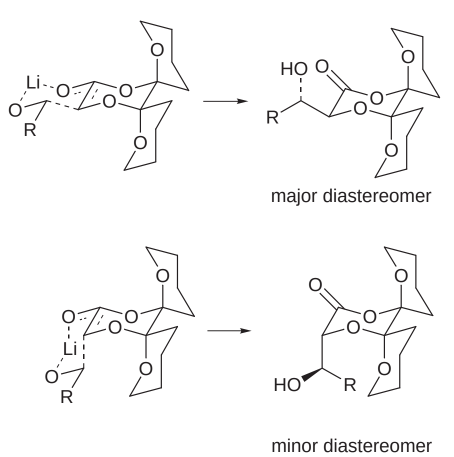


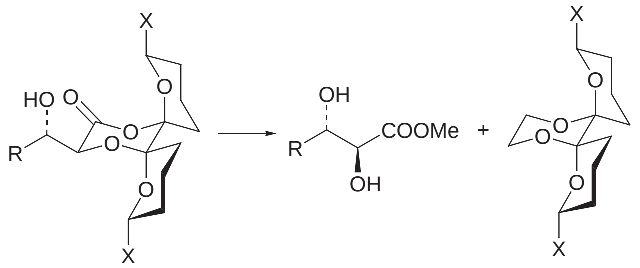
Fig. 1 X-Ray structure of aldol product **5a**.



Scheme 2 Transition states of the aldol reaction.

methyl 2,3-dihydroxy-3-phenylpropionoate **10** and ethylene glycol dispiroketal **12** in high yields (Table 2). The diol **10** was obtained as a single racemic diastereoisomer, whose relative

Table 2 Deprotection of the aldol products



5a X = H, R = Ph

6a X = H, R = CH_2=CH

7a X = CH_2SPh, R = Ph

8a X = CH_2SPh, R = CH_2=CH

10 R = Ph

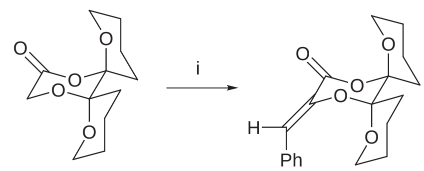
11 R = CH_2=CH

12 X = H

13 X = CH_2SPh

Reactant	Products (yield, %)
5a[a]	**10** (95)[a] **12** (94)
6a[a]	**11** (62)[a] **12** (79)
8a	**10** (99)[b] **13** (98)
8a	**11** (81)[b] **13** (96)

[a] Racemic mixture. [b] Enantiopurity excess is greater than 95%.



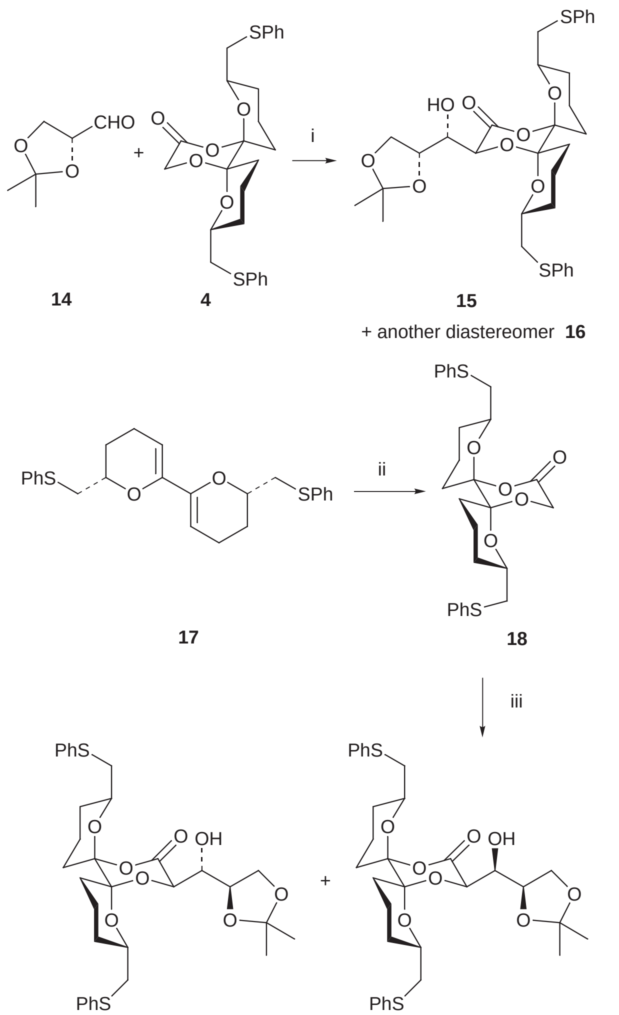
2 **9**

Scheme 3 *Reagents and conditions*: i, Pr^i_2NH, Bu^nLi, THF, DMPU, then PhCHO at −78 °C to rt, overnight, 19%.

stereochemistry was determined to be *erythro* by comparison with the spectroscopic properties to those reported in the literature.[11–13] Importantly, these results indicated that the deprotection step proceeds without epimerisation. When acrolein was used instead of benzaldehyde, the stereoselective aldol product **6a** was also obtained and deprotected readily using similar procedures to give the racemic *anti* diol **11**.

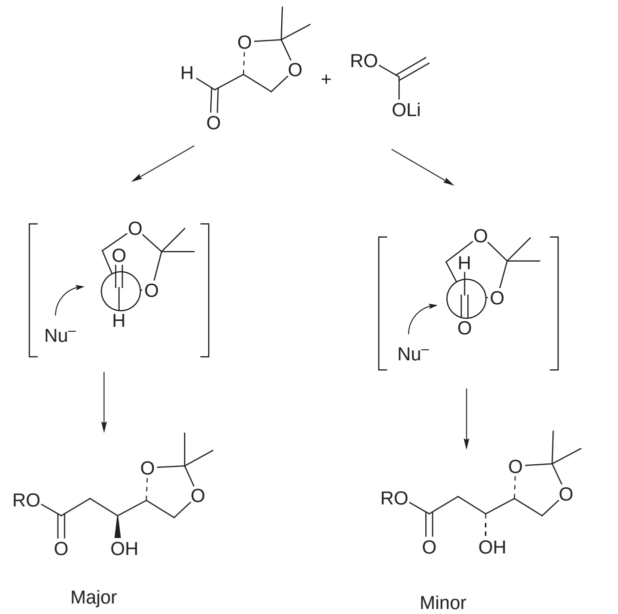
The above results suggested that enantiodifferentiating aldol reactions could be achieved potentially using chiral dispiroketals. Optically active dispiroketal **4** was prepared from enantiomerically pure bi(dihydropyran) **3** (Scheme 1) as a single diastereoisomer with the side chain phenylthiomethyl substituents equatorial, as indicated from the NOE signal observed between 15-H and 2-H. The aldol reaction of the enolate derived from **4** gave preferentially one diastereoisomer using benzaldehyde, acrolein and acetaldehyde, respectively. However, in the case of pivalaldehyde, no adduct was obtained and only the starting material **4** was recovered. It was subsequently found that the reaction occurs when HMPA was used instead of DMPU as a co-solvent.[14] The deprotection of the benzaldehyde reaction product **7a** in methanol in the presence of camphorsulfonic acid (CSA) and ethylene glycol gave methyl (+)-*erythro*-2,3-dihydroxy-3-phenylpropionoate **10**. After comparison of the optical rotation with literature values,[13] the absolute stereochemistry of **10** was assigned as (2*S*,3*S*). The absolute structure of the deprotected diol **10** indicated that the aldol product **7a** had the same relative structure as racemic aldol product **5a**, whose relative stereochemistry was determined by X-ray crystallography. In agreement with the above evidence, the ee of **10** was determined to be greater than 95% (*i.e.* essentially enantiopure) by analysis of the corresponding Mosher ester. Methyl (2*S*,3*S*)-2,3-dihydroxypent-4-enoate **11** was also obtained in enantiomerically pure form (ee >95%) from **8a**.

2,3-*O*-Isopropylidene-D-glyceraldehyde, which is readily accessible from inexpensive D-manitol, has been widely used as an important chiral C_3 building block.[15] By use of this homochiral aldehyde in an aldol reaction with a chiral dispiroketal unit, we allowed the effect of double asymmetric induction[16,17] on the stereoselectivity to be examined. The aldol reaction of the D-glyceraldehyde derivative **14** with the dispiroketal protected glycolate **4** gave products in low yield and poor stereoselectivity, as depicted in Scheme 4. The major stereoisomer **15**,



Scheme 4 *Reagents and conditions*: i, Pr^i_2NH, Bu^nLi, THF, DMPU, then **14** at −78 °C, 30 min, 14% (**15**:**16** 6:4, mixture); ii, glycolic acid, $Ph_3P{\cdot}HBr$, CH_2Cl_2, rt, 8 h, 86%; iii, Pr^i_2NH, Bu^nLi, THF, DMPU, then **14** at −78 °C, 60 min (**19**: 54%, **20**: 9%, the other 2 diastereomers mixture: 4%, recovered **18**: 14%).

expected from a chair-like six-membered transition state, had an unfavourable stereostructure as predicted by Felkin's non-chelation model[18] on nucleophilic additions of D-glyceraldehyde (Scheme 5).[19] The mismatched pair of the chiral enolate and the chiral aldehyde could be avoided by using the (+) form dispiroketal protected glycolate **18** prepared from (*S*,*S*)-2,2′-bis(phenylthiomethyl)bi(dihydropyran) **17**. As expected, the aldol reaction using **18** afforded **19**, which had an equatorial alkyl group as judged from the strong NOE spectrum between 2-H and 15-H, as the major isomer in 54% yield (Scheme 4). Minor isomers, however, were also obtained in significant quantities. The minor isomer **20** also had an equatorial alkyl group as judged from the NOE signal between 2-H and 15-H. The formation of the unpredicted stereoisomer **20** by a chair-like six-membered transition state, suggested the contribution of



Scheme 5 Stereoselectivity of an aldol reaction of 2,3-*O*-isopropylidene-D-glyceraldehyde with an enolate (ref. 18).

another chelation model[20] for the aldol transition state. The co-ordination of a lithium ion to an α- or β-oxygen of glyceraldehyde may threaten the preference of the chair-like six-membered transition state.

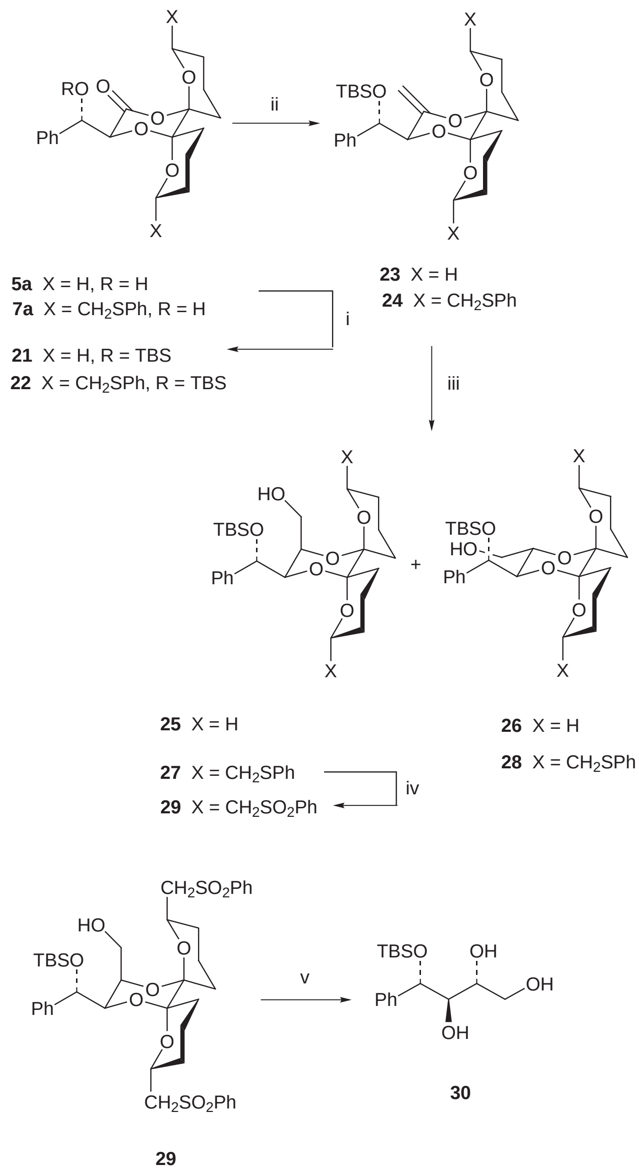
The aldol reactions mentioned above afforded the stereocontrolled diols. Further reactions from these aldol products were performed in order to extend the polyol chain in a stereocontrolled manner. Thus, the carbonyl group of the racemic aldol product **5a** was converted to the vinyl ether **23** by using the Tebbe reagent after protection of the free alcohol *moiety* of **5a**. A subsequent two-step hydroboration–oxidation sequence from **23** afforded the alcohols **25** and **26** as a mixture of isomers in which **25** is the major product (Scheme 6). These compounds were easily separated by chromatography and their stereochemistry was readily determined by ^{1}H NMR spectroscopy. The axial alcohol **25** was formed preferentially by hydroboration from the least hindered olefin face.[21]

Similar procedures were applied to the enantiomerically pure aldol product **7a** to yield **27** as an optically active compound (Scheme 6). Furthermore, oxidation of the phenylthiomethyl groups at the 2- and 9-positions lead to selective deprotection of the dispiroketal *moiety via* base promoted β-elimination of bis-sulfone **29** generated by oxidation.[5c] Deprotection under mild conditions afforded the optically active tertraol **30** without migration of the TBS group.

In summary we have developed a preparative method for the enantiodifferentiating synthesis of 1,2,3,4-tetraols *via* 2,3-dihydroxycarboxylates using the versatile dispiroketal unit as a protecting group and a chiral auxiliary. The dispiroketal protected polyols can be deprotected selectively without epimerisation and migration of silyloxy protecting groups.

Experimental

Proton NMR spectra were recorded on a Bruker DRX-600 (600 MHz) or DPX-200 (200 MHz) spectrometer as solutions in $CDCl_3$ using the residual $CHCl_3$ as an internal reference (7.26 ppm). Coupling constants *J* are quoted in Hz. ^{13}C NMR spectra were recorded on a Bruker DRX-600 (150 MHz), AM-400 (100 MHz) or DPX-200 (50 MHz) spectrometer as solutions in $CDCl_3$. ^{19}F NMR spectra were recorded on a Bruker AC-250 (150 MHz) spectrometer as solutions in $CDCl_3$. Infra-red spectra were recorded as thin films between sodium chloride plates deposited from $CDCl_3$ solution on a Perkin-



Scheme 6 *Reagents and conditions*: i, TBSCl, imidazole, DMF, rt, **21**: 98%, **22**: 67%; ii, Tebbe reagent, THF, pyridine, rt, **23**: 96%, **24**: 88%; iii, 9-BBN, THF, rt, 3 h, then NaOH, H_2O_2, rt, 30 min, from **23** to yield **25** (86%) and **26** (14%), from **24** to yield **27** (60%) and **28** (20%); iv, MCPBA, CH_2Cl_2, rt, 1.5 h, 88%; v, $LiN(TMS)_2$, THF, rt, 30 min, 53%.

Elmer 1600 series FTIR spectrometer. Mass spectra were recorded at the EPSRC mass spectrometry service, Swansea. Microanalyses were performed in the University of Cambridge microanalysis laboratory. X-Ray crystallographic data were obtained by Cambridge University Department of Chemistry crystallographic service. Melting points were determined on a Reicher hot stage apparatus and are uncorrected. Optical rotations were measured using an Optical Activity AA-1000 polarimeter and are quoted in 10^{-1} deg cm^2 g^{-1}. Flash column chromatography was performed on Merck 9385 Kieselgel 60 silica (230–400 mesh) using hexane, 40–60 petroleum ether (petrol), diethyl ether (ether) or ethyl acetate as eluents. The reactions were monitored by thin layer chromatography and the plates were visualised with UV light (254 nm) and acidified ammonium molybdate(IV).

All reactions were carried out under an argon atmosphere with dry freshly distilled solvents, under anhydrous conditions. Tetrahydrofuran (THF), diethyl ether (ether) and pentane were distilled from sodium–benzophenone and dichloromethane (DCM), triethylamine (NEt_3), benzene and toluene were distilled from calcium hydride. Dimethylformamide (DMF) was dried over 4 Å molecular sieves.

Preparation of 2,2′-bis(phenylthiomethyl)-3,3′,4,4′-tetrahydro-6,6′-bi-2*H*-pyran 3 and 17

Chiral 2,2′-bis(phenylthiomethyl)-3,3′,4,4′-tetrahydro-6,6′-bi-2*H*-pyran **3** and **17** were prepared according to literature procedures.[6a] By using 99.99% $Pd(MeCN)_2Cl_2$ (Aldrich) and 99.995% anhydrous $CuCl_2$ (Aldrich), the coupling reaction of 2-triisopropylsilyloxymethyl-3,4-dihydro-2*H*-pyran proceeded in 53% yield. The formed 2,2′-bis(triisopropylsilyloxymethyl)-3,3′,4,4′-tetrahydro-6,6′-bi-2*H*-pyran was enriched in optical purity by recrystallisation from ethanol. The conversion of triisopropylsilyloxymethyl groups to phenylthiomethyl groups was performed using the literature method.[6a]

Preparation of 2,3-*O*-isopropylidene-D-glyceraldehyde 14

The title compound was prepared from C–C bond cleavage of 1,2:5,6-di-*O*-isopropylidene-D-mannitol by $Pb(OAc)_4$ in benzene.[22] The formed aldehyde was unstable due to the tendency for polymerisation. Thus, the aldehyde was used for aldol reactions immediately after distillation under reduced pressure.

(6*R**,7*R**)-1,8,13,16-Tetraoxadispiro[5.0.5.4]hexadecan-14-one 2

To a solution of bi(dihydropyran) **1** (1.0 g, 6.0 mmol) and glycolic acid (0.68 g, 8.9 mmol, 1.5 eq.) in CH_2Cl_2 (50 ml) was added $Ph_3P{\cdot}HBr$ (0.2 g, 0.6 mmol, 0.1 eq.). The mixture was stirred at room temperature for 17 h during which time the mixture became yellow–orange, then the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1:3) gave the title compound **2** (0.98 g, 4.0 mmol, 67%) as a white solid; mp 103 °C (ether–petrol) (Found: C, 59.47; H, 7.48. $C_{12}H_{18}O_5$ requires C, 59.49; H, 7.49%); ν_{max}(film)/cm^{-1} 2954, 1748, 1602, 1522, 1441, 1358, 1295, 1255, 1072, 984; δ_H (200 MHz; $CDCl_3$) 4.33 (1H, d, *J* 17.6, 15-H), 4.25 (1H, d, *J* 17.6, 15-H), 4.06–3.46 (4H, m, 2-H × 2, 9-H × 2), 2.03–1.54 (12H, m); δ_C (50 MHz; $CDCl_3$) 167.3 (C=O), 103.3, 95.0 (6-C, 7-C), 62.9, 62.3 (2-C, 9-C), 59.5 (15-C), 28.4, 27.8, 24.5, 24.3, 17.9, 17.1 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (CI) 260 (MNH_4^+), 243 (MH^+, 11%), 167 (100) [Found (MH^+) 243.1232. $C_{12}H_{19}O_5$ requires *M*H, 243.1232].

General procedure for aldol reactions

A solution of LDA in THF (2.5 ml) was prepared under argon from diisopropylamine (1.1 eq.) and Bu^nLi (1.6 M solution in hexane, 1.1 eq.). After stirring for 20 min and cooling to −78 °C, a solution of the dispiroketal protected glycolate in THF (1.0 ml) was added *via* cannula, the flask being rinsed with THF (2 × 0.75 ml). After stirring for 30 min at −78 °C, a second portion of Bu^nLi solution (1.1 eq.) and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU) (0.5 ml) as a co-solvent were added. The mixture was allowed to stir for 30 min at −78 °C, then the appropriate aldehyde (2.0 eq.) was introduced. The reaction was quenched at −78 °C by the addition of saturated aqueous ammonium chloride after stirring for 30 min. The mixture was then allowed to warm up to room temperature and water added to dissolve the precipitated salts. The phases were separated and the aqueous layer was extracted with ether (×3). The combined organic extracts were dried ($MgSO_4$), evaporated *in vacuo* and the residue purified by flash chromatography (eluent: ether–petrol 1:3→1:1; gradient) to give the desired compound.

(6*R,7*R**,15*S**)-15-[(*S**)-(Hydroxy)phenylmethyl]-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 5a and (6*R**,7*R**,15*R**)-15-[(*R**)-(hydroxy)phenylmethyl]-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 5b.** Following the general procedure with the dispiroketal protected glycolate **2** (120 mg, 0.50 mmol) and benzaldehyde (0.1 ml, 1.0 mmol), a mixture of **5a** and **5b** (158 mg, 0.454 mmol, 91%) was obtained after flash chromatography (eluent: ether–petrol 1:2). The ratio of **5a** and

5b was determined by ^{1}H NMR as 97.5:2.5, which gives a de of 95%. Careful flash chromatography (eluent: ether–petrol 1:3→1:1; gradient) allows the separation of the mixture of **5b** and **5a** (in order of elution).

5a: mp 117–119 °C (ether) (Found: C, 65.56; H, 6.91. $C_{19}H_{24}O_6$ requires C, 65.50; H, 6.94%); ν_{max}(film)/cm^{-1} 3460, 2953, 1744, 1602, 1454, 1356, 1072; δ_H (600 MHz; CDCl$_3$) 7.43 (2H, d, *J* 7.5, Ar), 7.34 (2H, t, *J* 7.5, Ar), 7.28 (1H, t, *J* 7.5, Ar), 5.13 (1H, d, *J* 3.7, PhC*H*), 4.35 (1H, d, *J* 5.1, 15-H), 4.04 (1H, d, *J* 1.9, OH), 3.92–3.87 (1H, m, 9$_{eq}$-H), 3.74–3.70 (2H, m, 9$_{ax}$-H, 2$_{eq}$-H), 3.48 (1H, td, *J* 11.4, 3.2, 2$_{ax}$-H), 1.98–1.46 (12H, m); δ_C (50 MHz; CDCl$_3$) 167.4 (C=O), 138.5, 127.8, 127.8, 126.8 (Ar), 103.5, 95.6 (6-C, 7-C), 74.3, 73.9 (15-C, Ph*C*H), 62.8, 62.4 (2-C, 9-C), 28.4, 27.7, 24.4, 24.2, 17.8, 17.1 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (CI) 366 (MNH$_4^+$, 6%), 349 (MH$^+$, 3), 243 (13), 167 (100) [Found (MH$^+$) 349.1651. $C_{19}H_{25}O_6$ requires *M*H, 349.1651].

5b: ν_{max}(film)/cm^{-1} 3473, 2949, 2360, 1722, 1454, 1440, 1354, 1288, 1240, 1214, 1184, 1108, 1074, 1052, 989, 964, 912, 760, 731, 700, 668; δ_H (600 MHz; CDCl$_3$) 7.48 (2H, d, *J* 7.4, Ar), 7.37 (2H, t, *J* 7.4, Ar), 7.32 (1H, t, *J* 7.3, Ar), 4.93 (1H, d, *J* 8.7, PhC*H*), 4.49 (1H, br, OH), 4.40 (1H, d, *J* 8.7, 15-H), 3.93–3.83 (3H, m, 9-H, 2-H), 3.76–3.73 (1H, m, 9-H or 2-H), 2.03–1.91 (2H, m), 1.75–1.26 (10H, m); δ_C (50 MHz; CDCl$_3$) 172.1 (C=O), 139.3, 128.1, 128.0, 127.4 (Ar), 104.4, 96.2 (6-C, 7-C), 74.2, 72.5 (15-C, Ph*C*H), 63.1, 62.1 (2-C, 9-C), 28.5, 28.4, 24.8, 24.2, 17.7, 17.4 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (CI) 366 (MNH$_4^+$, 2%), 349 (MH$^+$, 6), 243 (12), 167 (100) [Found (MH$^+$) 349.1651. $C_{19}H_{25}O_6$ requires *M*H, 349.1651].

(6*R,7*R**)-(*Z*)-15-Benzylidene-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 9.** The same general procedure for aldol reactions (**2**: 122 mg, 0.5 mmol) was applied except that the reaction was quenched after warming up to room temperature to give the title compound **9** (31.5 mg, 19%); ν_{max}(film)/cm^{-1} 3431, 2951, 1725, 1631, 1376, 1363, 1270, 1182, 1075, 995; δ_H (600 MHz; CDCl$_3$) 7.82 (2H, d, *J* 7.5, Ar), 7.38 (2H, t, *J* 7.5, Ar), 7.31 (1H, t, *J* 7.5, Ar), 7.00 (1H, s, PhC*H*=), 4.02–3.97 (1H, m, 9-H or 2-H), 3.86–3.82 (1H, m, 2-H or 9-H), 3.73–3.70 (1H, m, 9-H or 2-H), 3.62 (1H, td, *J* 11.6, 3.6, 2$_{ax}$-H or 9$_{ax}$-H), 2.14–2.00 (3H, m), 1.89–1.84 (1H, m), 1.77–1.57 (8H, m); δ_C (100 MHz; CDCl$_3$) 160.5 (C=O), 137.0, 133.5, 128.6, 128.5 (Ar), 118.9 (Ph*C*H=), 102.3, 97.5 (6-C, 7-C), 63.0, 62.5 (2-C, 9-C), 28.5, 27.5, 24.5, 24.4, 18.5, 17.3 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (CI) 348 (MNH$_4^+$, 62%), 331 (MH$^+$, 98), 167 (100) [Found (MH$^+$) 331.1545. $C_{19}H_{23}O_5$ requires *M*H, 331.1545].

(1′*S,6*R**,7*R**,15*S**)-15-(1-Hydroxyprop-2-enyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 6a.** By the general procedure using **2** (120 mg, 0.5 mmol) and acrolein (74 ml, 1.0 mmol), the title compound **6a** (115 mg, 78%) was obtained as a white solid after flash chromatography (eluent: ether–petrol 1:3→1:1; gradient); mp 88 °C (ether–petrol) (Found: C, 60.63; H, 7.45. $C_{15}H_{22}O_6$ requires C, 60.39; H, 7.43%); ν_{max}(film)/cm^{-1} 3480, 2952, 2877, 1746, 1641, 1570, 1440, 1375, 1355, 1290, 1251, 1215, 1186, 1107, 1072, 995, 965, 884, 735; δ_H (600 MHz; CDCl$_3$) 6.02 (1H, ddd, *J* 17.2, 10.5, 6.4, 2′-H), 5.40 (1H, d, *J* 17.2, 3′-H), 5.26 (1H, d, *J* 10.5, 3′-H), 4.52 (1H, br, 1′-H), 4.25 (1H, d, *J* 3.8, 15-H), 4.00–3.95 (1H, m, 9$_{eq}$-H), 3.82–3.76 (2H, m, 9$_{ax}$-H, 2$_{eq}$-H), 3.67–3.62 (1H, m, 2$_{ax}$-H), 3.50 (1H, br, OH), 2.00–1.79 (4H, m), 1.72–1.55 (8H, m); δ_C (50 MHz; CDCl$_3$) 166.9 (C=O), 134.8 (2′-C), 117.3 (3′-C), 103.2, 95.6 (6-C, 7-C), 73.9, 73.7 (15-C, 1′-C), 62.9, 62.5 (2-C, 9-C), 28.5, 27.6, 24.5, 24.2, 17.9, 17.0 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (CI) 299 (MH$^+$, 2%), 167 (100) [Found (MH$^+$) 299.1494. $C_{15}H_{23}O_6$ requires *M*H, 299.1495].

Methyl (2*RS*,3*RS*)-2,3-dihydroxy-3-phenylpropionoate 10

To a solution of **5a** (98.3 mg, 0.282 mmol) in anhydrous methanol (5 ml) was added CSA (18.8 mg, 0.081 mmol, 0.3 eq.) and ethylene glycol (36 mg, 0.58 mmol, 2.0 eq.). The mixture was heated under reflux for 4 h and after cooling to room temperature the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1:3→1:0; gradient) gave in order of elution, the ethylene glycol dispiroketal **12** (60.3 mg, 0.267 mmol, 94%), which had identical spectroscopic properties to those reported in literature,[5] and the diol **10** (52.3 mg, 0.260 mmol, 95%). The melting point of **10** (87–90 °C) was in agreement with the one reported for the (2*RS*,3*RS*) form (87 °C), but not with the one of the (2*RS*,3*SR*) form (69 °C).[10] ^{1}H NMR spectral data[11,12] are also in agreement with that of the (2*RS*,3*RS*)-diol. **10**: mp 87–90 °C (ether–petrol) (Found: C, 61.15; H, 6.20. $C_{10}H_{12}O_4$ requires C, 61.22; H, 6.16%); ν_{max}(film)/cm^{-1} 3379, 2930, 1735, 1602, 1454, 1384, 1236, 1106, 1052; δ_H (600 MHz; CDCl$_3$) 7.37–7.30 (5H, m, Ar), 5.02 (1H, t, *J* 5.1, 3-H), 4.51 (1H, t, *J* 5.2, 2-H), 3.70 (3H, s, Me), 2.87 (1H, d, *J* 6.6, OH), 2.84 (1H, d, *J* 6.1, OH); δ_C (50 MHz; CDCl$_3$) 172.3 (C=O), 138.5, 128.3, 128.2, 126.3 (Ar), 75.0 (CH), 74.8 (CH), 52.4 (Me); *m/z* (CI) 214 (MNH$_4^+$, 100%), 196 (M$^+$, 16%), 108 (16) [Found (MNH$_4^+$) 214.1079. $C_{10}H_{16}O_4N$ requires *M*NH$_4$, 214.1079].

Methyl (2*RS*,3*RS*)-2,3-dihydroxypent-4-enoate 11

To a solution of **6a** (69.3 mg, 0.232 mmol) in anhydrous methanol (5 ml) was added CSA (15.6 mg, 0.067 mmol, 0.3 eq.) and ethylene glycol (34 mg, 0.55 mmol, 2.0 eq.). The mixture was heated under reflux for 2 h and after cooling the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1:3→1:0; gradient) gave in order of elution the ethylene glycol dispiroketal **12** (42.0 mg, 79%) and the title compound **11** (21.0 mg, 62%). **11**: ν_{max}(film)/cm^{-1} 3407, 2956, 1739, 1642, 1441, 1223, 1124, 1059, 966, 935, 741; δ_H (200 MHz; CDCl$_3$) 5.85 (1H, ddd, *J* 17.2, 10.4, 5.9, 4-H), 5.34 (1H, dt, *J* 17.2, 1.5, 5-H), 5.25 (1H, dt, *J* 10.4, 1.4, 5-H), 4.47–4.30 (2H, m, 2-H, 3-H), 3.79 (3H, s, Me), 3.19 (1H, br, OH), 2.70 (1H, br, OH); δ_C (50 MHz; CDCl$_3$) 172.5 (C=O), 134.7 (4-C), 117.8 (5-C), 74.0, 73.8 (2-C, 3-C), 52.5 (Me); *m/z* (CI) 164 (MNH$_4^+$, 100%), 132 (18), 118 (31) [Found (MNH$_4^+$) 164.0923. $C_6H_{14}O_4N$ requires *M*NH$_4$, 164.0923].

(2*R*,6*S*,7*R*,9*R*)-2,9-Bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 4

To a solution of bi(dihydropyran) **3** (213 mg, 0.53 mmol) and glycolic acid (76 mg, 1.0 mmol, 1.9 eq.) in CH_2Cl_2 (15 ml) was added Ph$_3$P·HBr (20 mg, 0.06 mmol, 0.1 eq.). The mixture was stirred at room temperature for 6 h during which time the mixture became yellow–orange, then the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1:3) gave the title compound **4** (0.238 mg, 0.49 mmol, 94%) as a colourless oil; $[\alpha]_D^{23}$ −50.3 (*c* 0.35, CHCl$_3$); ν_{max}(film)/cm^{-1} 2931, 1745, 1585, 1480, 1379, 1301, 1209, 1097, 1050; δ_H (600 MHz; CDCl$_3$) 7.33–7.31 (4H, m, Ar), 7.28–7.24 (4H, m, Ar), 7.18–7.15 (2H, m, Ar), 4.27 (1H, d, *J* 17.4, 15-H), 4.18 (1H, d, *J* 17.4, 15-H), 4.16–4.13 (1H, m, 9-H), 3.81–3.77 (1H, m, 2-H), 3.07–2.96 (4H, m, C*H*$_2$SPh), 1.96–1.26 (12H, m); δ_C (100 MHz; CDCl$_3$) 167.0 (C=O), 136.5, 136.5, 129.4, 129.1, 129.0, 128.9, 126.1, 126.0 (Ar), 103.8, 95.8 (6-C, 7-C), 71.6, 71.5 (2-C, 9-C), 59.5 (15-C), 39.5, 39.1 (*C*H$_2$SPh), 29.7, 29.1, 27.9, 27.4, 18.1, 17.2 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m/z* (EI) 486 (M$^+$, 3%), 410 (22), 123 (76), 55 (100) [Found (M$^+$) 486.1535. $C_{26}H_{30}O_5S_2$ requires *M*, 486.1535].

(2*R*,6*S*,7*R*,9*R*,15*S*)-15-[(*S*)-(Hydroxy)phenylmethyl]-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]-hexadecan-14-one 7a

Using the general procedure with **4** (213 mg, 0.44 mmol) and benzaldehyde (0.1 ml, 1.0 mmol), the title compound **7a**

(218 mg, 0.368 mmol, 84%) was obtained as an oil after flash chromatography (eluent: ether–petrol 1 : 3→1 : 1; gradient); $[\alpha]_D^{23}$ −51.9 (*c* 0.37, $CHCl_3$); ν_{max}(film)/cm^{-1} 3484, 2946, 2360, 1751, 1583, 1480, 1438, 1208, 1049, 691; δ_H (600 MHz; $CDCl_3$) 7.38 (2H, d, *J* 7.5, Ar), 7.31–7.26 (11H, m, Ar), 7.19 (2H, t, *J* 7.5, Ar), 5.08 (1H, d, *J* 5.2, PhC*H*), 4.22 (1H, d, *J* 5.5, 15-H), 4.15 (1H, dtd, *J* 11.6, 5.8, 2.1, 9-H), 4.04 (1H, br, OH), 3.58 (1H, dtd, *J* 10.1, 5.8, 2.0, 2-H), 3.03–2.92 (4H, m, CH_2SPh), 1.95–1.21 (12H, m); δ_C (100 MHz; $CDCl_3$) 167.3 (C=O), 138.6, 136.4, 136.2, 129.3, 129.1, 129.0, 129.0, 127.9, 127.8, 126.9, 126.2, 126.0 (Ar), 104.0, 96.4 (6-C, 7-C), 74.1, 73.8 (15-C, Ph*C*H), 71.5, 71.4 (2-C, 9-C), 39.3, 38.7 (*C*H_2SPh), 29.5, 29.1, 28.0, 27.2, 18.0, 17.0 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m*/*z* (CI) 610 (MNH_4^+, 14%), 593 (MH^+, 6), 504 (17), 411 (100), 303 (24) [Found (MH^+) 593.2030. $C_{33}H_{37}O_6S_2$ requires *M*H, 593.2031].

Deprotection of 7a to give methyl (2*S*,3*S*)-2,3-dihydroxy-3-phenylpropionoate 10 and (2′*S*,2″*S*,6′*R*,6″*R*)-1,2-*O*-[6′,6″-bis(phenylthiomethyl)-3′,3″,4′,4″,5′,5″,6′,6″-octahydro-2′,2″-bi(2*H*-pyran-2′,2″-diyl)]ethane-1,2-diol 13

To a solution of **7a** (36.0 mg, 0.061 mmol) in anhydrous methanol (2 ml) was added CSA (6.2 mg, 0.0267 mmol, 0.4 eq.) and ethylene glycol (15 mg, 0.24 mmol, 4.0 eq.). The mixture was heated under reflux for 4 h. After cooling the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1 : 1→neat ether gradient) gave the ethylene glycol dispiroketal **13** (28.2 mg, 0.0596 mmol, 98%) and the diol **10** (11.9 mg, 0.0606 mmol, 99%). The absolute stereochemistry of **10** was determined as (2*S*,3*S*) by comparing the optical rotation with that reported in the literature {ref. $[\alpha]_D^{22}$ −41.3 (*c* 0.48, $CHCl_3$) for the (2*R*,3*R*)-form}.[12] All spectroscopic data of enantiopure **10** were identical to racemic **10** (see above).

10: $[\alpha]_D^{23}$ +36.1 (*c* 0.72, $CHCl_3$).

13: $[\alpha]_D^{24}$ −71.7 (*c* 0.90, $CHCl_3$); ν_{max}(film)/cm^{-1} 2926, 1630, 1584, 1481, 1438, 1287, 1082, 1036, 966, 911, 736, 690; δ_H (600 MHz; $CDCl_3$) 7.37 (4H, d, *J* 7.4, Ar), 7.26 (4H, t, *J* 7.7, Ar), 7.15 (2H, t, *J* 7.4, Ar), 4.01 (2H, d, *J* 7.6, CH_AH_B), 3.89–3.84 (2H, m, 6′-H, 6″-H), 3.38 (2H, d, *J* 7.7, C$H_A$$H_B$), 3.13 (2H, dd, *J* 13.3, 6.2, CH_AH_BSPh), 2.95 (2H, dd, *J* 13.3, 6.0, CH_AH_BSPh), 1.82–1.69 (6H, m), 1.62–1.57 (2H, m), 1.43 (2H, td, *J* 13.4, 4.8), 1.26–1.20 (2H, m); δ_C (50 MHz; $CDCl_3$) 137.2, 128.9, 128.7, 125.7 (Ar), 96.6 (2′-C, 2″-C), 69.4 (6′-C, 6″-C), 58.3 (1-C, 2-C), 39.4 (*C*H_2SPh), 29.9, 28.0, 18.1 (3′-C, 4′-C, 5′-C, 3″-C, 4″-C, 5″-C); *m*/*z* (CI) 490 (MNH_4^+, 46%), 473 (MH^+, 12), 411 (100), 303 (53) [Found (MH^+) 473.1820. $C_{26}H_{33}O_4S_2$ requires *M*H, 473.1820].

Mosher esterification of methyl (2*S*,3*S*)-2,3-dihydroxy-3-phenylpropionoate 10 prepared above

To a stirred solution of methyl (2*S*,3*S*)-2,3-dihydroxy-3-phenylpropionoate **10** (14.4 mg, 0.073 mmol) in CH_2Cl_2 (1 ml), was added Et_3N (0.1 ml), DMAP (5 mg) and (*R*)-(−)-MTPACl (α-methoxy-α-trifluoromethylphenylacetyl chloride, 100 ml) at 0 °C, and the resulting mixture was allowed to warm up to room temperature over 1 h. The mixture was quenched by water and extracted with ether (×3). The combined organic phases were washed with brine, dried (Na_2SO_4) and evaporated *in vacuo* under reduced pressure. The resulting residue was purified by flash chromatography (eluent: ether–petrol 1 : 1) to give the bis(MTPA) ester (62.6 mg, 85%) as an oil; δ_H (200 MHz; $CDCl_3$) 7.50–7.00 (15H, m, Ar), 6.39 (1H, d, *J* 4.5, 2-H or 3-H), 5.70 (1H, d, *J* 4.5, 2-H or 3-H), 3.73 (3H, s, Me), 3.46 (3H, d, *J* 1.2, Me), 3.43 (3H, d, *J* 1.2, Me); δ_F (235 MHz; $CDCl_3$) −72.13 (3F, s, CF_3), −72.36 (3F, s, CF_3).

The other isomer was not detected with ^{1}H and ^{19}F NMR, which implies the optical purity of the initial diol is >95% ee.

Data for the other isomer obtained from the racemic sample; δ_H (200 MHz; $CDCl_3$) 7.50–7.00 (15H, m, Ar), 6.45 (1H, d, *J* 5.4, 2-H or 3-H), 5.62 (1H, d, *J* 5.4, 2-H or 3-H), 3.62 (3H, s, Me), 3.41 (3H, d, *J* 1.2, Me), 3.24 (3H, d, *J* 1.2, Me); δ_F (235 MHz; $CDCl_3$) −71.41 (3F, s, CF_3), −72.41 (3F, s, CF_3).

(1′*S*,2*R*,6*S*,7*R*,9*R*,15*S*)-15-(1-Hydroxyprop-2-enyl)-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 8a and (1′*R*,2*R*,6*S*,7*R*,9*R*,15*R*)-15-(1-hydroxyprop-2-enyl)-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 8b

The general procedure using **4** (76.9 mg, 0.158 mmol) and acrolein (25 ml, 0.374 mmol, 2.0 eq.) gave in order of elution **8b** (2.4 mg, 0.004 mmol, 3%) and **8a** (54.6 mg, 0.10 mmol, 64%) following flash chromatography (eluent: ether–petrol 1 : 3→1 : 1; gradient).

8a: $[\alpha]_D^{21}$ −79.1 (*c* 0.69, $CHCl_3$); ν_{max}(film)/cm^{-1} 3495, 2952, 1748, 1584, 1481, 1439, 1208, 1041; δ_H (600 MHz; $CDCl_3$) 7.36 (2H, d, *J* 7.8, Ar), 7.31 (2H, d, *J* 8.1, Ar), 7.28–7.24 (4H, m, Ar), 7.18–7.15 (2H, m, Ar), 6.00 (1H, ddd, *J* 17.2, 10.5, 6.2, 2′-H), 5.38 (1H, dt, *J* 17.2, 1.2, 3′-H), 5.25 (1H, dt, *J* 10.5, 1.2, 3′-H), 4.51–4.47 (1H, m, 1′-H), 4.16 (1H, dtd, *J* 11.7, 5.7, 2.4, 9-H), 4.14 (1H, d, *J* 3.8, 15-H), 3.76 (1H, dtd, *J* 11.7, 5.9, 1.9, 2-H), 3.39 (1H, d, *J* 2.3, OH), 3.05–2.96 (4H, m, CH_2SPh), 1.97–1.26 (12H, m); δ_C (100 MHz; $CDCl_3$) 166.4 (C=O), 136.3, 136.3, 134.9, 129.4, 129.1, 129.0, 128.9, 126.2, 126.1 (Ar, 2′-C), 117.4 (3′-C), 103.8, 96.4 (6-C, 7-C), 73.9, 73.6 (15-C, 1′-C), 71.5, 71.4 (2-C, 9-C), 39.4, 38.9 (*C*H_2SPh), 29.5, 29.1, 28.2, 27.1, 18.1, 17.0 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m*/*z* (CI) 560 (MNH_4^+, 44%), 543 (MH^+, 17), 504 (24), 411 (100) [Found (MH^+) 543.1875. $C_{29}H_{35}O_6S_2$ requires *M*H, 543.1875].

8b: $[\alpha]_D^{26}$ −55.5 (*c* 0.51, $CHCl_3$); ν_{max}(film)/cm^{-1} 3488, 2920, 1731, 1654, 1584, 1481, 1439, 1206, 1041, 736; δ_H (600 MHz; $CDCl_3$) 7.40–7.14 (10H, m, Ar), 5.94 (1H, ddd, *J* 17.3, 10.6, 5.6, 2′-H), 5.24 (1H, d, *J* 17.3, 3′-H), 5.20 (1H, d, *J* 10.6, 3′-H), 4.30–3.95 (4H, m, 1′-H, 2-H, 9-H, 15-H), 3.81 (1H, d, *J* 3.0, OH), 3.04–2.97 (4H, m, CH_2SPh), 1.95–1.25 (12H, m); δ_C (50 MHz; $CDCl_3$) 171.0 (C=O), 136.4, 136.2, 135.7, 129.3, 128.9, 126.1, 125.9 (Ar, 2′-C), 117.3 (3′-C), 104.4, 96.7 (6-C, 7-C), 72.3, 72.3, 72.2, 70.6 (1′-C, 2-C, 9-C, 15-C), 39.3, 38.9 (*C*H_2SPh), 29.6, 29.3, 28.3, 27.7, 18.0, 17.5 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C); *m*/*z* (CI) 560 (MNH_4^+, 3%), 543 (MH^+, 2), 411 (9), 303 (11), 78 (100) [Found (MH^+) 543.1875. $C_{29}H_{35}O_6S_2$ requires *M*H, 543.1875].

Deprotection of 8a to give methyl (2*S*,3*S*)-2,3-dihydroxypent-4-enoate 11

To a solution of **8a** (54.3 mg, 0.10 mmol) in anhydrous methanol (2.5 ml) was added CSA (8 mg, 0.03 mmol, 0.3 eq.) and ethylene glycol (15 mg, 0.24 mmol, 2.4 eq.). The mixture was heated under reflux for 4 h. After cooling the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1 : 1→neat ether; gradient) gave the ethylene glycol dispiroketal **13** (45.3 mg, 0.096 mmol, 96%) and **11** (11.9 mg, 0.081 mmol, 81%). **11**: $[\alpha]_D^{23}$ +2.7 (*c* 1.19, $CDCl_3$).

Mosher esterification of methyl (2*S*,3*S*)-2,3-dihydroxypent-4-enoate 11 prepared in above

To a stirred solution of methyl (2*S*,3*S*)-2,3-dihydroxypent-4-enoate **11** (11.9 mg, 0.081 mmol), Et_3N (0.1 ml) and DMAP (5 mg) in CH_2Cl_2 (1.0 ml) was added (*R*)-(−)-MTPACl (100 ml) at 0 °C, and the mixture was allowed to warm up to room temperature over 1 h. The mixture was quenched by water and extracted with ether (×3). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated *in vacuo*. The resulting residue was purified by flash chromatography (eluent: ether–petrol 1 : 1) to give the bis(MTPA)ester (22.7 mg, 0.0392 mmol, 48%) as an oil; δ_H (600 MHz; $CDCl_3$) 7.60 (2H, d, *J* 7.8, Ar), 7.44 (2H, d, *J* 7.7, Ar), 7.41–7.32 (6H, m, Ar), 5.90

(1H, dd, *J* 7.5, 2.8, 3-H), 5.73 (1H, ddd, *J* 17.2, 10.5, 7.5, 4-H), 5.60 (1H, d, *J* 3.0, 2-H), 5.35 (1H, d, *J* 19.4, 5-H), 3.44 (1H, d, *J* 10.7, 5-H), 3.78 (3H, s, Me), 3.54 (3H, d, *J* 1.2, Me), 3.44 (3H, d, *J* 1.2, Me); δ_F (235 MHz; $CDCl_3$) −72.19 (3F, s, CF_3), −72.39 (3F, s, CF_3).

The other isomer was not detected by ^{1}H or ^{19}F NMR spectroscopy, which implies that the optical purity of the initial diol is >95% ee.

Data for the other isomer obtained from the racemic sample; δ_H (200 MHz; $CDCl_3$) 7.62–7.28 (10H, m, Ar), 6.03–5.40 (5H, m), 3.71 (3H, s, Me), 3.48 (3H, d, *J* 1.2, Me), 3.43 (3H, d, *J* 1.2, Me); δ_F (235 MHz; $CDCl_3$) −72.15 (3F, s, CF_3), −72.38 (3F, s, CF_3).

(1′*S*,2*R*,2′*R*,6*S*,7*R*,9*R*,15*S*)-15-[(2′,3′-*O*-Isopropylidene-1′,2′,3′-trihydroxy)propyl]-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 15

Using the general procedure with **4** (86.2 mg, 0.177 mmol) and **14** (46 mg, 0.346 mmol, 2.0 eq.), a mixture of **15** and **16** (15.6 mg, 0.0252 mmol, 14%) was obtained after flash chromatography (eluent: ether–petrol 1 : 3→1 : 1; gradient). The ratio of **15** and **16** was determined by ^{1}H NMR spectroscopy as 6 : 4.

15: δ_H (600 MHz; $CDCl_3$) 7.35–7.12 (10H, m, Ar), 4.68 (1H, d, *J* 4.8, 15-H), 4.68 (1H, q, *J* 6.6, 2′-H), 4.29–4.25 (1H, m, 9-H or 2-H), 4.10–3.95 (3H, m, 3′-H × 2, 2-H or 9-H), 3.84–3.80 (1H, m, 1′-H), 3.19 (1H, br, OH), 3.03–2.95 (4H, m, C*H*$_2$SPh), 1.95–1.20 (12H, m), 1.40 (3H, s, Me), 1.35 (3H, s, Me).

16: δ_H (600 MHz; $CDCl_3$) 7.35–7.12 (10H, m, Ar), 4.32 (1H, q, *J* 6.9, 2′-H), 4.19–4.15 (1H, m, 9-H or 2-H), 4.10–3.95 (3H, m, 3′-H × 2, 15-H), 3.80–3.78 (1H, m, 2-H or 9-H), 3.67 (1H, t, *J* 7.8, 1′-H), 3.49 (1H, br, OH), 3.03–2.95 (4H, m, C*H*$_2$SPh), 1.95–1.20 (12H, m), 1.43 (3H, s, Me), 1.39 (3H, s, Me).

(2*S*,6*R*,7*S*,9*S*)-2,9-Bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 18

To a solution of bi(dihydropyran) **17** (0.84 g, 2.05 mmol) and glycolic acid (312 mg, 4.1 mmol) in CH_2Cl_2 (60 ml) was added $Ph_3P{\cdot}HBr$ (68.6 mg, 0.20 mmol). The mixture was stirred at room temperature for 8 h during which time the mixture became yellow–orange, then the solvent was evaporated *in vacuo*. Purification of the residue by flash chromatography (eluent: ether–petrol 1 : 3) gave the title compound **18** (0.86 mg, 1.77 mmol, 86%).

(1′*R*,2*S*,2′*R*,6*R*,7*S*,9*S*,15*R*)-15-[(2′,3′-*O*-Isopropylidene-1′,2′,3′-trihydroxy)propyl]-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 19 and (1′*S*,2*S*,2′*R*,6*R*,7*S*,9*S*,15*R*)-15-[(2′,3′-*O*-isopropylidene-1′,2′,3′-trihydroxy)propyl]-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 20

The general procedure using **18** (103 mg, 0.212 mmol) and **14** (55 mg, 0.424 mmol, 2.0 eq.) gave in order of elution the reactant **18** (14.1 mg, 0.0289 mmol, 14%), the mixture of the two most minor diastereomers (4.7 mg, 0.0076 mmol, 4%), **20** (11.5 mg, 0.086 mmol, 19%), and **19** (70.6 mg, 0.1144 mmol, 54%) after chromatography (eluent: ether–petrol 1 : 3→1 : 1; gradient).

19: $[a]_D^{23}$ +56.0 (*c* 1.41, $CDCl_3$); ν_{max}(film)/cm^{-1} 3481, 2935, 2937, 1748, 1584, 1481, 1439, 1372, 1302, 1254, 1209, 1161, 1106, 1043, 983, 956, 913, 844, 731, 691; δ_H (600 MHz; $CDCl_3$) 7.36–7.14 (10H, m, Ar), 4.46 (1H, d, *J* 1.6, 15-H), 4.38 (1H, q, *J* 6.5, 2′-H), 4.18–4.09 (2H, m, 3′-H, 9-H), 4.04–4.00 (1H, m, 3′-H), 3.95 (1H, d, *J* 8.0, 1′-H), 3.82–3.79 (1H, m, 2-H), 3.27 (1H, d, *J* 2.2, OH), 3.05–2.98 (4H, m, C*H*$_2$SPh), 1.96–1.65 (6H, m), 1.53–1.24 (6H, m), 1.40 (3H, s, Me), 1.38 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 165.9 (C=O), 136.4, 136.1, 129.4, 128.9, 128.9, 128.8, 126.2, 125.8 (Ar), 109.2, 103.4, 96.2 (6-C, 7-C, Me$_2$*C*), 74.3, 74.0, 72.1, 71.4, 71.4 (1′-C, 2-C, 2′-C, 9-C, 15-C), 66.8 (3′-C), 39.6 (*C*H$_2$SPh), 38.8 (*C*H$_2$SPh), 29.3, 29.2, 28.1, 27.2, 18.0, 16.9 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 26.8 (Me), 25.4 (Me); *m*/*z* (CI) 634 (MNH_4^+, 14%), 617 (MH^+, 16), 411 (42), 303 (100), 240 (39) [Found (MH^+) 617.2240. $C_{32}H_{41}O_8S_2$ requires *M*H, 617.2243].

20: $[a]_D^{23}$ +49.9 (*c* 1.15, $CDCl_3$); ν_{max}(film)/cm^{-1} 3493, 2984, 2938, 1749, 1584, 1481, 1439, 1372, 1302, 1256, 1209, 1160, 1144, 1044, 982, 912, 852, 735, 691; δ_H (600 MHz; $CDCl_3$) 7.36–7.13 (10H, m, Ar), 4.23–4.19 (2H, m, 2-H, 2′-H), 4.11 (1H, d, *J* 1.6, 15-H), 4.03–3.99 (1H, m, 1′-H), 3.80 (1H, t, *J* 7.7, 3′-H), 3.69–3.64 (1H, m, 9-H), 3.59 (1H, t, *J* 7.7, 3′-H), 3.15 (1H, d, *J* 10.4, OH), 3.03 (2H, d, *J* 5.6, C*H*$_2$SPh), 3.00 (2H, d, *J* 6.0, C*H*$_2$SPh), 2.00–1.67 (8H, m), 1.60–1.20 (4H, m), 1.40 (3H, s, Me), 1.36 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 167.6 (C=O), 136.4, 136.1, 129.2, 129.0, 128.9, 128.8, 126.1, 126.0 (Ar), 109.7, 103.4, 96.2 (6-C, 7-C, Me$_2$*C*), 76.4, 72.8, 71.6, 71.3, 70.7 (1′-C, 2-C, 2′-C, 9-C, 15-C), 65.7 (3′-C), 39.1 (*C*H$_2$SPh), 38.6 (*C*H$_2$SPh), 29.5, 28.7, 27.7, 27.1, 18.1, 16.8 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 26.4 (Me), 25.6 (Me); *m*/*z* (CI) 634 (MNH_4^+, 34%), 617 (MH^+, 21), 411 (96), 303 (100), 240 (37) [Found (MH^+) 617.2240. $C_{32}H_{41}O_8S_2$ requires *M*H, 617.2243].

(6*R,7*R**,15*S**)-15-[(*S**)-(*tert*-Butyldimethylsilyloxy)phenylmethyl]-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecan-14-one 21**

To a solution of **5a** (163 mg, 0.47 mmol) in DMF (2.5 ml), imidazole (106 mg, 1.56 mmol, 3.3 eq.) and *tert*-butyldimethylsilyl chloride (122 mg, 0.81 mmol, 1.7 eq.) were added and stirred at room temperature for 1 day. Due to incomplete reaction, extra imidazole (122 mg, 1.79 mmol, 3.8 eq.) and *tert*-butyldimethylsilyl chloride (128 mg, 0.85 mmol, 1.8 eq.) were added to the mixture and stirred for another 2 days. The reaction was then quenched with H_2O and the mixture was extracted with ether (×3). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Flash chromatography (eluent: ether–petrol 1 : 7) gave the title compound **21** as a colourless oil (214 mg, 0.46 mmol, 98%); ν_{max}(film)/cm^{-1} 2951, 2856, 1742, 1471, 1356, 1253, 1102, 1074, 1002, 952, 836, 778; δ_H (600 MHz; $CDCl_3$) 7.38 (2H, d, *J* 7.2, Ar), 7.24 (2H, t, *J* 7.3, Ar), 7.20 (1H, t, *J* 7.2, Ar), 5.26 (1H, d, *J* 3.5, PhC*H*), 4.44 (1H, d, *J* 3.6, 15-H), 3.75–3.71 (1H, m), 3.64–3.59 (1H, m), 3.28–3.22 (1H, m), 3.13–3.09 (1H, m), 1.86–1.36 (12H, m), 0.91 (9H, s, Bu^t), 0.10 (3H, s, Me), −0.08 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 167.4 (C=O), 139.9, 127.9, 127.2, 127.1 (Ar), 103.2, 95.2 (6-C, 7-C), 75.1, 74.5 (15-C, Ph*C*H), 62.2, 61.9 (2-C, 9-C), 28.3, 27.8, 24.7, 24.1, 18.1, 17.1 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.7 (Bu^t), 18.1 (Bu^t), −4.9 (Me), −5.1 (Me); *m*/*z* (CI) 463 (MH^+, 3%), 167 (100) [Found (MH^+) 463.2516. $C_{25}H_{39}O_6Si$ requires *M*H, 463.2516].

(6*R,7*R**,14*S**)-14-[(*S**)-(*tert*-Butyldimethylsilyloxy)phenylmethyl]-15-methylene-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane 23**

To a solution of **21** (213.5 mg, 0.46 mmol) in THF (5 ml) and pyridine (1 ml) was added a 0.5 M solution of the Tebbe reagent in toluene (1.4 ml, 0.69 mmol, 1.5 eq.) at −78 °C. After stirring for 10 min, the mixture was warmed up to room temperature and stirred for 1 h. Then, the mixture was quenched with a saturated Na_2CO_3 solution (1 ml) and ether at 0 °C. The solid formed was filtered over Celite and washed with ether. The organic filtrate was dried ($MgSO_4$) and evaporated *in vauco*. The resulting residue was purified by flash chromatography (eluent: ether–petrol 1 : 7) to give the title compound **23** (204 mg, 0.443 mmol, 96%); mp 109–110 °C (ether–petrol) (Found: C, 67.94; H, 8.74. $C_{26}H_{40}O_5Si$ requires C, 67.79; H, 8.75%); ν_{max}(film)/cm^{-1} 2951, 2856, 1742, 1471, 1356, 1253, 1102, 1074, 1002, 952, 836, 778; δ_H (600 MHz; $CDCl_3$) 7.42 (2H, d, *J* 7.3, Ar), 7.28 (2H, t, *J* 7.3, Ar), 7.22 (1H, t, *J* 7.3, Ar), 4.88 (1H, d, *J* 8.2, PhC*H*), 4.79 (1H, s, CH_2=), 4.74 (1H, s, CH_2=), 4.22 (1H, d, *J* 8.2, 14-H), 4.00–3.93 (1H, m), 3.72–3.68 (1H, m), 3.44–3.40 (1H, m), 2.93 (1H, td, *J* 10.8, 1.9), 1.95–1.87 (1H, m), 1.86–1.81 (1H, m), 1.64–1.57 (3H, m), 1.55–1.50 (2H, m), 1.46 (1H, td, *J* 13.5, 4.7), 1.36–1.25 (2H, m), 1.07–1.03 (2H, m), 0.87 (9H, s, Bu^t), 0.09 (3H, s, Me), −0.37 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 153.4 (14-C), 142.4, 127.7, 127.4, 127.3 (Ar), 99.1, 96.6 (6-C, 7-C), 95.4 (CH_2=), 74.5, 70.6 (14-C, Ph*C*H), 61.0, 60.7 (2-C, 9-C), 28.4, 28.3, 24.8, 24.6, 17.9, 17.5 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 29.6 (Bu^t), 17.9 (Bu^t), −4.0 (Me), −5.1 (Me); *m*/*z* (CI) 461 (MH^+, 3%), 329 (63), 167 (100) [Found (MH^+) 461.2723. $C_{26}H_{41}O_5Si$ requires *M*H, 461.2723].

(6*R,7*R**,14*R**,15*R**)-14-[(*S**)-(*tert*-Butyldimethylsilyloxy)-phenylmethyl]-15-hydroxymethyl-1,8,13,16-tetraoxadispiro-[5.0.5.4]hexadecane 25 and (6*R**,7*R**,14*R**,15*S**)-14-[(*S**)-(*tert*-butyldimethylsilyloxy)phenylmethyl]-15-hydroxymethyl-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane 26**

A solution of 9-borabicyclo[3.3.1]nonane (9-BBN) (0.75 ml of 0.5 M in THF, 0.375 mmol, 4.9 eq.) was added to **23** (35.4 mg, 0.077 mmol) and the resulting mixture was stirred at room temperature for 3 h. Then, the solution was cooled to 0 °C and treated with 10% NaOH solution (0.4 ml) and H_2O_2 (30%, 0.4 ml) for 30 min. The reaction mixture was quenched with saturated Na_2CO_3 aqueous solution and the mixture was extracted with ether (×3). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by flash chromatography (eluent: ether–petrol 1 : 3→1 : 1; gradient) to give in order of elution **25** (31.6 mg, 0.066 mmol, 86%) then **26** (5.3 mg, 0.011 mmol, 14%).

25: ν_{max}(film)/cm^{-1} 3469, 2949, 2857, 1465, 1360, 1254, 1209, 1162, 1091, 1035, 854, 838, 770, 733; δ_H (600 MHz; $CDCl_3$) 7.43 (2H, d, *J* 7.5, Ar), 7.29 (2H, t, *J* 7.5, Ar), 7.23 (1H, t, *J* 7.3, Ar), 4.97 (1H, d, *J* 9.2, PhC*H*), 4.19 (1H, d, *J* 10.5, OH), 4.14 (1H, dd, *J* 9.2, 4.1, 14-H), 4.08 (1H, td, *J* 11.9, 3.6, 15-H), 4.05–3.99 (3H, m, C*H*$_2$OH, 2_{ax}-H), 3.77–3.75 (1H, m, 2_{eq}-H), 3.22–3.19 (1H, m, 9_{eq}-H), 2.37 (1H, td, *J* 10.6, 1.9, 9_{ax}-H), 1.85–1.15 (12H, m), 0.87 (9H, s, Bu^t), 0.10 (3H, s, Me), −0.36 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 142.6, 127.6, 127.5, 127.5 (Ar), 96.6, 94.6 (6-C, 7-C), 74.2 (Ph*C*H), 72.4, 71.7 (14-C, 15-C) 63.2, 61.8, 60.1 (CH_2OH, 2-C, 9-C), 29.5, 28.6, 25.0, 24.5, 17.9, 17.6 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.7 (Bu^t), 18.1 (Bu^t), −3.9 (Me), −5.5 (Me); *m*/*z* (CI) 496 (MNH_4^+, 2%), 479 (MH^+, 11), 167 (100), 118 (19) [Found (MH^+) 479.2829. $C_{26}H_{43}O_6Si$ requires *M*H, 479.2829].

26: ν_{max}(film)/cm^{-1} 3474, 2927, 2856, 1454, 1360, 1253, 1210, 1191, 1161, 1072, 999, 837, 776, 733, 700; δ_H (600 MHz; $CDCl_3$) 7.39 (2H, d, *J* 7.4, Ar), 7.29 (2H, t, *J* 7.4, Ar), 7.22 (1H, t, *J* 7.3, Ar), 4.77 (1H, d, *J* 6.0, PhC*H*), 4.01–3.97 (1H, m, 15-H), 3.81 (1H, dd, *J* 9.4, 6.1, 14-H), 3.77–3.73 (1H, m, C*H*$_2$OH), 3.73–3.66 (2H, m, 2-H × 2), 3.54 (1H, dd, *J* 11.7, 7.7, C*H*$_2$OH), 3.47–3.43 (1H, m, 9_{eq}-H), 3.02–2.97 (1H, m, 9_{ax}-H), 2.17 (1H, br, OH), 1.78–1.16 (12H, m), 0.90 (9H, s, Bu^t), 0.08 (3H, s, Me), −0.17 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 142.4, 127.6, 127.2, 126.9 (Ar), 96.0, 95.5 (6-C, 7-C), 75.7 (Ph*C*H), 72.7, 69.9 (14-C, 15-C), 62.7 (*C*H$_2$OH), 60.6, 60.5 (2-C, 9-C), 29.6, 28.2, 24.8, 24.8, 18.3, 17.7 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.9 (Bu^t), 18.1 (Bu^t), −4.6 (Me), −4.8 (Me); *m*/*z* (CI) 496 (MNH_4^+, 17%), 287 (10), 167 (100), 118 (23) [Found (MNH_4^+) 496.3094. $C_{26}H_{46}O_6NSi$ requires *M*NH$_4$, 496.3094].

(2*R*,6*S*,7*R*,9*R*,15*S*)-15-[(*S*)-(*tert*-Butyldimethylsilyloxy)phenyl-methyl]-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro-[5.0.5.4]hexadecan-14-one 22

A solution of **7a** (44.7 mg, 0.075 mmol) in DMF (1 ml) containing imidazole (24.2 mg, 0.36 mmol, 4.8 eq.) and *tert*-butyl-dimethylsilyl chloride (36.1 mg, 0.24 mmol, 3.2 eq.) was stirred at room temperature for 7 h. To complete the reaction, more imidazole (39.5 mg, 0.58 mmol, 7.7 eq.) and *tert*-butyl-dimethylsilyl chloride (54.1 mg, 0.36 mmol, 4.8 eq.) were added to the solution and the mixture was stirred for another 17 h. The reaction was quenched with H_2O and the mixture was extracted with ether (×3). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Flash chromatography (eluent: ether–petrol 1 : 5→1 : 3; gradient) gave the title compound **22** as a colourless oil (35.8 mg, 0.051 mmol, 67%); $[\alpha]_D^{23}$ −31.0 (*c* 1.08, $CHCl_3$); ν_{max}(film)/cm^{-1} 2951, 2855, 2360, 1744, 1585, 1481, 1439, 1257, 1205, 1104, 1051, 992, 957, 910, 837, 778, 736, 701; δ_H (600 MHz; $CDCl_3$) 7.39–7.10 (15H, m, Ar), 5.32 (1H, d, *J* 4.0, PhC*H*), 4.88 (1H, d, *J* 4.0, 15-H), 3.82–3.78 (1H, m, 9-H), 3.69 (1H, dtd, *J* 11.7, 6.0, 2.3, 2-H), 3.04 (1H, dd, *J* 13.8, 7.1, PhSC*H*$_A$H$_B$), 2.96 (1H, dd, *J* 13.8, 5.0, PhSCH$_A$*H*$_B$), 2.52 (2H, d, *J* 5.6, C*H*$_2$SPh), 1.83–1.54 (8H, m), 1.37–1.19 (4H, m), 0.87 (9H, s, Bu^t), 0.05 (3H, s, Me), −0.14 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 166.8 (C=O), 140.1, 136.9, 136.8, 128.8, 128.7, 128.0, 127.3, 125.8, 125.7 (Ar), 103.8, 96.0 (6-C, 7-C), 74.2, 73.9 (15-C, Ph*C*H), 71.9, 70.6 (2-C, 9-C), 39.1 (*C*H$_2$SPh), 38.4 (*C*H$_2$SPh), 29.8, 28.4, 27.9, 27.3, 18.1, 16.9 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.6 (Bu^t), 18.0 (Bu^t), −5.0 (Me), −5.1 (Me); *m*/*z* (CI) 707 (MH^+, 7%), 411 (100), 303 (15) [Found (MH^+) 707.2900. $C_{39}H_{51}O_6SiS_2$ requires *M*H, 707.2896].

(2*R*,6*R*,7*S*,9*R*,14*S*)-14-[(*S*)-(*tert*-Butyldimethylsilyloxy)phenyl-methyl]-15-methylene-2,9-bis(phenylthiomethyl)-1,8,13,16-tetra-oxadispiro[5.0.5.4]hexadecane 24

To a solution of **22** (34.7 mg, 0.049 mmol) in THF (2.5 ml) containing pyridine (0.5 ml) was added 0.5 M solution of the Tebbe reagent in toluene (0.15 ml, 0.075 mmol, 1.5 eq.) at −78 °C. After stirring for 5 min, the mixture was warmed up to room temperature and stirred for 30 min. Then, the mixture was quenched with a saturated Na_2CO_3 solution (0.5 ml) and ether at 0 °C. The formed solid was filtered over Celite and washed with ether. The organic filtrate was dried ($MgSO_4$) and evaporated *in vacuo*. The resulting residue was purified by flash chromatography (eluent: ether–petrol 1 : 7→1 : 5; gradient) to give the title compound **24** (30.3 mg, 0.043 mmol, 88%); $[\alpha]_D^{23}$ −11.1 (*c* 1.57, $CHCl_3$); ν_{max}(film)/cm^{-1} 2949, 2928, 2360, 1662, 1585, 1481, 1439, 1257, 1201, 1167, 1091, 1040, 910, 855, 838, 777, 736, 700; δ_H (600 MHz; $CDCl_3$) 7.37–7.14 (15H, m, Ar), 4.84 (1H, d, *J* 6.8, PhC*H*), 4.64 (1H, s, CH_2=), 4.46 (1H, s, CH_2=), 4.32 (1H, d, *J* 6.8, 14-H), 4.10–4.05 (1H, m, 9-H or 2-H), 3.40–3.35 (1H, m, 2-H or 9-H), 3.12 (1H, dd, *J* 13.5, 4.6, PhSC*H*$_A$-H$_B$), 3.05 (1H, dd, *J* 13.5, 6.3, PhSC*H*′$_A$H′$_B$), 2.86 (1H, dd, *J* 13.5, 5.9, PhSCH′$_A$*H*′$_B$), 2.84 (1H, dd, *J* 13.5, 7.7, PhS-CH$_A$*H*$_B$), 1.90–1.03 (12H, m), 0.90 (9H, s, Bu^t), 0.11 (3H, s, Me), −0.28 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 152.5 (15-C), 142.1, 137.3, 137.0, 128.8, 128.7, 128.5, 128.5, 127.5, 127.4, 127.0, 125.5, 125.5 (Ar), 99.5, 97.2 (6-C, 7-C), 95.4 (CH_2=), 74.8, 70.7, 69.7, 69.0 (2-C, 9-C, 14-C, Ph*C*H), 39.0 (*C*H$_2$SPh), 38.7 (*C*H$_2$SPh), 29.8, 29.4, 27.8, 27.7, 17.9, 17.8 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.8 (Bu^t), 18.1 (Bu^t), −4.3 (Me), −4.8 (Me); *m*/*z* (CI) 705 (MH^+, 1%), 573 (6), 411 (17) , 221 (100) [Found (MH^+) 705.3100. $C_{40}H_{53}O_5SiS_2$ requires *M*H, 705.3103].

(2*R*,6*S*,7*S*,9*R*,14*R*,15*R*)-14-[(*S*)-(*tert*-Butyldimethylsilyloxy)-phenylmethyl]-15-hydroxymethyl-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane 27 and (2*R*,6*S*,7*S*,9*R*,14*R*,15*S*)-14-[(*S*)-(*tert*-butyldimethylsilyloxy)phenyl-methyl]-15-hydroxymethyl-2,9-bis(phenylthiomethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane 28

A solution of 9-BBN (1.0 ml of 0.5 M in THF, 0.50 mmol, 5.7 eq.) was added to **24** (61.6 mg, 0.0873 mmol), and stirred at room temperature for 3 h. Then, the resulting solution was cooled to 0 °C and treated with a 10% NaOH solution (0.5 ml) and H_2O_2 (30%, 0.5 ml) for 30 min. The reaction mixture was quenched with a saturated Na_2CO_3 aqueous solution and the mixture was extracted with ether (×3). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by flash chromatography (eluent: ether–petrol 1 : 5→1 : 2; gradient) to give in order of elution **27** (37.9 mg, 0.0524 mmol, 60%) then **28** (12.8 mg, 0.0177 mmol, 20%).

27: $[\alpha]_D^{23}$ −0.2 (*c* 1.00, $CHCl_3$); ν_{max}(film)/cm^{-1} 3472, 2928, 2855, 1584, 1480, 1438, 1254, 1191, 1090, 1011, 982, 910, 856, 838, 777, 736, 690; δ_H (600 MHz; $CDCl_3$) 7.40–7.14 (15H, m, Ar), 4.89 (1H, d, *J* 8.8, PhC*H*), 4.24 (1H, dd, *J* 8.8, 4.1, 14-H), 4.16–4.12 (1H, m, 2-H), 4.06–4.02 (1H, m, CH_AH_BOH), 3.92–3.89 (2H, m, CH_AH_BOH, 15-H), 3.82 (1H, d, *J* 10.3, OH), 3.22 (1H, dd, *J* 13.3, 3.9, $PhSCH_AH_B$), 2.94 (1H, dd, *J* 13.3, 7.9, $PhSCH_AH_B$), 2.88 (1H, dd, *J* 13.2, 6.8, $PhSCH'_AH'_B$), 2.75 (1H, dd, *J* 13.2, 5.1, $PhSCH'_AH'_B$), 2.66–2.62 (1H, m, 9-H), 1.90–1.00 (12H, m), 0.88 (9H, s, Bu^t), 0.09 (3H, s, Me), −0.32 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 142.1, 137.7, 136.4, 128.8, 128.7, 128.7, 127.6, 127.6, 127.5, 125.8, 125.5 (Ar), 97.6, 95.8 (6-C, 7-C), 74.5, 72.0, 71.6, 70.1, 69.1 (2-C, 9-C, 14-C, 15-C, Ph*C*H), 63.0 (CH_2OH), 39.3 (CH_2SPh), 38.7 (CH_2SPh), 29.5, 29.4, 29.2, 28.1, 17.9, 17.8 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.7 (Bu^t), 17.9 (Bu^t), −4.0 (Me), −5.4 (Me); *m/z* (CI) 740 (MNH_4^+, 10%), 723 (MH^+, 16), 705 (32), 411 (100), 303 (47) [Found (MH^+) 723.3210. $C_{40}H_{55}O_6SiS_2$ requires *M*H, 723.3209].

28: $[\alpha]_D^{23}$ −16.4 (*c* 1.22, $CDCl_3$); ν_{max}(film)/cm^{-1} 3424, 2927, 2855, 1584, 1480, 1438, 1258, 1200, 1104, 1036, 836, 777, 737, 690; δ_H (600 MHz; $CDCl_3$) 7.34–7.14 (15H, m, Ar), 4.67–4.65 (1H, m, PhC*H*), 3.94–3.91 (2H, m, 14-H, 15-H), 3.84–3.80 (1H, m, 2-H), 3.60–3.55 (1H, m, CH_AH_BOH), 3.48–3.42 (1H, m, CH_AH_BOH), 3.37–3.32 (1H, m, 9-H), 3.06 (1H, dd, *J* 13.4, 6.0, $PhSCH_AH_B$), 3.01 (1H, dd, *J* 13.5, 7.2, $PhSCH'_AH'_B$), 2.93 (1H, dd, *J* 13.4, 6.0, $PhSCH_AH_B$), 2.85 (1H, dd, *J* 13.5, 5.0, $PhSCH'_AH'_B$), 1.91 (1H, dd, *J* 7.9, 5.1, OH), 1.75–1.06 (12H, m), 0.90 (9H, s, Bu^t), 0.08 (3H, s, Me), −0.16 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 142.0, 137.6, 137.3, 129.0, 128.7, 128.7, 128.4, 127.6, 127.1, 127.0, 125.7, 125.4 (Ar), 96.6, 96.3 (6-C, 7-C), 75.9, 72.0, 69.8, 69.7, 69.3 (2-C, 9-C, 14-C, 15-C, Ph*C*H), 62.6 (CH_2OH), 39.3 (CH_2SPh), 39.1 (CH_2SPh), 30.1, 29.6, 27.6, 27.6, 18.3, 18.0 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.9 (Bu^t), 18.2 (Bu^t), −4.7 (Me); *m/z* (CI) 740 (MNH_4^+, 12%), 411 (11), 132 (53), 126 (56), 52 (100) [Found (MNH_4^+) 740.3480. $C_{40}H_{58}O_6NSiS_2$ requires MNH_4, 740.3475].

(2*R*,6*S*,7*S*,9*R*,14*R*,15*R*)-14-[(*S*)-(*tert*-Butyldimethylsilyloxy)-phenylmethyl]-15-hydroxymethyl-2,9-bis(phenylsulfonylmethyl)-1,8,13,16-tetraoxadispiro[5.0.5.4]hexadecane 29

To a solution of **27** (37.9 mg, 0.0524 mmol) in CH_2Cl_2 (2 ml), was added MCBPA (50–60% purity, 90 mg, 0.26 mmol) at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 1.5 h. The reaction was quenched with a saturated Na_2SO_3 aqueous solution at 0 °C, and extracted with CH_2Cl_2 (×4). The combined organic phases were dried (Na_2SO_4) and evaporated *in vacuo*. The resulting residue was purified by flash chromatography (eluent: neat ether) to afford the title compound **29** (36.3 mg, 0.0461 mmol, 88%) as a white solid; mp 118 °C (ether); $[\alpha]_D^{23}$ −41.7 (*c* 1.54, $CHCl_3$); ν_{max}(film)/cm^{-1} 3520, 3056, 2933, 1770, 1586, 1447, 1365, 1303, 1261, 1202, 1148, 1087, 1067, 1039, 1006, 970, 909, 860, 838, 780, 735, 688; δ_H (600 MHz; $CDCl_3$) 7.93 (2H, d, *J* 7.6, Ar), 7.89 (2H, d, *J* 7.6, Ar), 7.67 (1H, t, *J* 7.4, Ar), 7.60–7.53 (5H, m, Ar), 7.49 (2H, t, *J* 7.7, Ar), 7.35 (2H, t, *J* 7.6, Ar), 7.26 (1H, t, *J* 7.3, Ar), 4.81 (1H, d, *J* 8.5, PhC*H*), 4.48 (1H, td, *J* 8.5, 2.8, 2-H), 4.25 (1H, dd, *J* 8.5, 3.9, 14-H), 4.02–3.97 (1H, m, CH_AH_BOH), 3.88–3.85 (1H, m, 15-H), 3.72 (1H, dd, *J* 12.1, 2.0, CH_AH_BOH), 3.40 (1H, br, OH), 3.33 (1H, dd, *J* 14.1, 3.3, $PhSO_2CH_AH_B$), 3.29–3.22 (2H, m, $PhSCH'_AH'_B$, 9-H), 3.15 (1H, dd, *J* 14.1, 8.3, $PhSCH_AH_B$), 3.00–2.95 (1H, m, $PhSCH'_AH'_B$), 1.84 (1H, br d, *J* 12.7), 1.64–0.87 (10H, m), 0.92 (9H, s, Bu^t), 0.59 (1H, br d, *J* 13.7), 0.08 (3H, s, Me), −0.25 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 141.4, 141.1, 139.8, 133.7, 132.9, 129.3, 128.9, 127.9, 127.8, 127.7, 127.7, 127.6 (Ar), 97.2, 95.6 (6-C, 7-C), 74.7, 72.0, 71.1, 65.8, 64.9 (2-C, 9-C, 14-C, 15-C, Ph*C*H), 61.9, 61.9, 61.6 (CH_2OH, 2 × CH_2SPh), 30.9, 29.7, 28.6, 27.9, 17.5, 17.0 (3-C, 4-C, 5-C, 10-C, 11-C, 12-C), 25.8 (Bu^t) 18.0 (Bu^t), −4.1 (Me), −5.3 (Me); *m/z* (CI) 804 (MNH_4^+, 45%), 787 (MH^+, 92), 672 (58), 647 (75), 492 (95), 475 (100) [Found (MH^+) 787.3010. $C_{40}H_{55}O_{10}SiS_2$ requires *M*H, 787.3006].

(2*R*,3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-4-phenylbutane-1,2,3-triol 30

To a stirred solution of **29** (35.3 mg, 0.045 mmol) in THF (1.0 ml) under argon was added a solution of lithium bis(trimethylsilyl)amide (1.0 M in THF, 0.12 ml, 0.12 mmol, 2.5 eq.) at 0 °C, and the resulting mixture was stirred for 30 min at room temperature. The reaction mixture was quenched with saturated NH_4Cl aquous solution and then extracted with ether (×3). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (eluent: ether–petrol 1:1→neat ether; gradient) to give the title compound **30** (7.5 mg, 0.024 mmol, 53%) as a colourless oil; $[\alpha]_D^{23}$ +32.0 (*c* 0.75, $CHCl_3$); ν_{max}(film)/cm^{-1} 3415, 2954, 2929, 2857, 1635, 1472, 1389, 1306, 1254, 1085, 910, 838, 779, 734; δ_H (600 MHz; $CDCl_3$) 7.39–7.29 (5H, m, Ar), 4.79 (1H, d, *J* 6.2, 4-H), 3.84–3.78 (3H, m, 2 × H-1, 3-H), 3.60 (1H, td, *J* 6.7, 4.2, 2-H), 2.99 (1H, br, OH), 2.27 (1H, br, OH), 1.60 (1H, br, OH), 0.89 (9H, s, Bu^t), 0.06 (3H, s, Me), −0.19 (3H, s, Me); δ_C (50 MHz; $CDCl_3$) 140.4, 128.3, 128.1, 127.3 (Ar), 77.2, 76.4, 71.9 (2-C, 3-C, 4-C), 63.9 (1-C), 25.7 (Bu^t), 18.0 (Bu^t), −4.6 (Me), −5.2 (Me); *m/z* (CI) 330 (MNH_4^+, 10%), 313 (MH^+, 19%), 198 (100) [Found (MH^+) 313.1835. $C_{16}H_{29}O_4Si$ requires *M*H, 313.1835].

Acknowledgements

We acknowledge financial support from the BP Endowment (to S. V. L.), the Novartis Research Fellowship (to S. V. L. and D. L.), the Japan Society for the Promotion of Science (to M. F.) and Pfizer Limited (to D. L.). We are also grateful to the EPSRC mass spectrometry service at Swansea.

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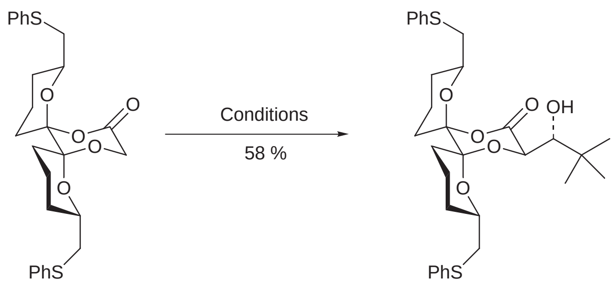

18 **31**

Reagents and conditions: i, Pr^i_2NH, Bu^nLi, THF–HMPA (3 : 1 mixture), –78 °C, 30 min then pivaldehyde at –78 °C, 30 min.

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Paper 9/00951E