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Stereocontrolled Synthesis of Functionalised Cyclohexanes *via* the Lithium Amide-mediated Rearrangement of a *meso* 4,5-Disubstituted Cyclohexene Oxide

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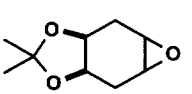
Abstract: Reaction of a 90:10 mixture of diastereomeric *meso* 4,5-disubstituted cyclohexene oxides (prepared *via* a stereoselective epoxidation reaction) with a mixed base system of a lithium amide and potassium *tert*-butoxide produces a 72% yield of an allylic alcohol and a 9.6% yield of recovered epoxide, both as single diastereoisomers. The relative stereochemistry of the epoxides and the allylic alcohol is established by converting the allylic alcohol into a novel bicyclic ether. The allylic alcohol is also used to prepare single diastereosiomers of a range of functionalised cyclohexanes.

Introduction

The conversion of cyclic epoxides into allylic alcohols using lithium amide bases (including chiral bases) is a well studied and useful synthetic transformation.[1,2] Despite this, rearrangment of *meso* 4,5-disubstituted cyclohexene oxides has received very little attention. The first example of such a reaction was reported by Krow[3] in 1977 when lithium diethylamide was used to rearrange what was believed[4] to be a single unidentified diastereoisomer of epoxide **1**. In a similar fashion, during studies aimed at elucidating the stereochemistry of electrophilic additions to 3-norcarenes, Paquette[5] also used lithium diethylamide to rearrange single diastereoisomers of *meso* cyclopropyl epoxides *trans*- and *cis*-**2** [R = H, Me, –$(CH_2)_3$–].



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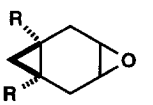

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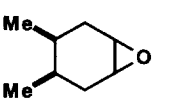

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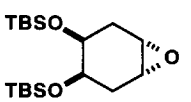
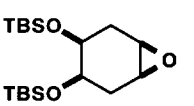
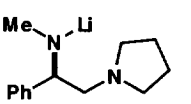


trans-**4**



cis-**4**

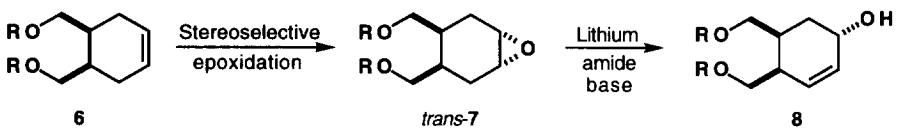


(*R*)-**5**

Nearly twenty years after Krow's initial report, Mori[6] described the *enantioselective* rearrangement of an inseparable 89:11 mixture of epoxides *trans*- and *cis*-**3** using Asami's[7] chiral lithium amide base. Most recently, we[8] used Singh's[9] chiral base (*R*)-**5** to convert the separated epoxides *trans*- and *cis*-**4** into the corresponding allylic alcohols with 76% ee and 92% ee respectively. These two reactions are the first ever enantioselective rearrangements of *single* diastereoisomers of *meso* 4,5-disubstituted cyclohexene oxides.

In order to extend the scope of the lithium amide-induced epoxide rearrangement reaction in synthesis, we decided to investigate the hitherto unknown conversion of *meso* 4,5-disubstituted cyclohexene oxides such

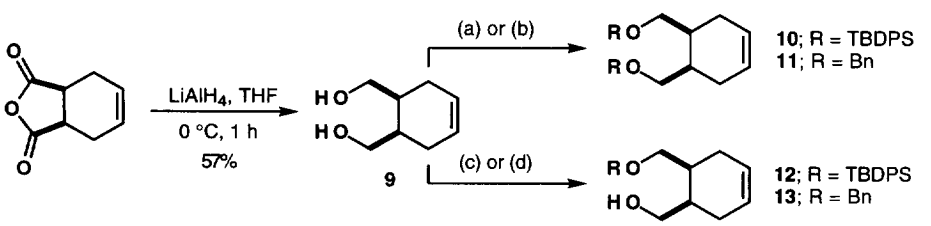
as *trans*-**7** into allylic alcohols **8**. The results of a study on the stereoselectivity of epoxidation of 4,5-disubstituted cyclohexenes **6** and the successful rearrangement of epoxide *trans*-**7** (R = TBDPS) using a mixed base system of a lithium amide (derived from a diamine) and potassium *tert*-butoxide are the subject of this paper. In addition, the use of allylic alcohol **8** (R = TBDPS) in the stereocontrolled synthesis of functionalised cyclohexanes including a novel 2-substituted-6-oxabicyclo[3.2.1]octane system is described.



6 *trans*-**7** **8**

Epoxidation study

It was our initial aim to develop stereocontrolled syntheses of each of the two diastereoisomers of *meso* 4,5-disubstituted cyclohexenes **7**. With this in mind, we decided to prepare some mono- and diprotected alkenes **10-13** and then study their epoxidation using different conditions. The common intermediate in the synthesis of each of alkenes **10-13** is diol **9** which is commercially available[10] or can be readily prepared by lithium aluminium hydride reduction[11] of the cheaper *cis*-1,2,3,6-tetrahydrophthalic anhydride. In our hands, this reduction gave a 57% yield of diol **9** after chromatography; standard silylation and benzylation furnished diprotected alkenes **10** and **11** and monoprotected alkenes **12** and **13** in good yields.



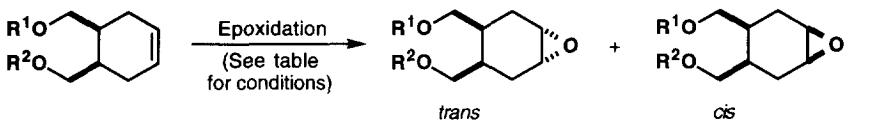
Reagents: (a) 2.5 eq TBDPSCl, 3 eq imidazole, DMF, rt, 20 h (89%); (b) 2.5 eq NaH, 2 eq BnBr, DMF, rt, 1.5 h (48%); (c) 1 eq TBDPSCl, 1.1 eq imidazole, DMF, rt, 18 h (57%); (d) 1.1 eq NaH, 1.1 eq, BnBr, DMF, rt, 1 h (67%)

The yields and stereoselectivities of epoxidising the mono- and diprotected alkenes **10-13** as well as the unprotected alkene **9** using different reaction conditions are summarised in Table 1. Alkenes **9**, **12** and **13** (Table 1, entries 1, 4 and 5) were epoxidised using vanadyl acetoacetonate [$VO(acac)_2$] and *tert*-butyl hydroperoxide in the hope that epoxidation would occur *cis* to the free hydroxyl groups. In each case, ^1H NMR spectroscopy of the crude product mixture indicated that only one epoxide product was present and we initially assigned them as *cis* epoxides based on literature precedent.[12,13] Good isolated yields were obtained after purification by chromatography although isolation of the water-soluble epoxy diol *cis*-**14** was problematic and this compound was never obtained completely pure (90% pure by ^1H NMR spectroscopy).

In contrast to the epoxidations of alkenes with free hydroxyl groups, diprotected alkenes **10** and **11** (Table 1, entries 2 and 3) were epoxidised using standard *m*-CPBA conditions. The stereoselectivities were once again determined by ^1H NMR spectroscopy of the crude product mixtures and, in the case of disilyl epoxides *trans*- and *cis*-**15**, this ratio did not change after purification by chromatography. As can be seen, the sterically demanding *tert*-butyldiphenylsilyl protecting group resulted in a more highly stereoselective epoxidation than the benzyl protecting group (compare Table 1; entries 2 and 3). In both cases, we assigned

the major products as having *trans* relative stereochemistry since Mori[6a] had obtained an 89:11 mixture of epoxides *trans*- and *cis*-**3** when the structurally similar *cis*-4,5-dimethylcyclohexene was epoxidised. The *trans* selectivity of these types of epoxidations can best be explained in terms of preferential attack of the reagent on the face of the alkene opposite to the bulky axial substitutent assuming that the cyclohexene ring adopts the preferred half-chair conformation (see Figure 1).[12,13]

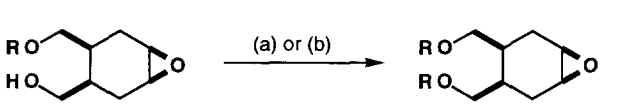
Table 1: Epoxidation of *meso*-4,5-disubstituted cyclohexenes



Entry	Alkene	R^1	R^2	Conditions	Epoxide	*cis* : *trans*[a]	Yield (%)[b]
1	**9**	H	H	$VO(acac)_2$/^{t}BuOOH	**14**	≥97 : 3	45[c]
2	**10**	TBDPS	TBDPS	*m*-CPBA	**15**	10 : 90	95
3	**11**	Bn	Bn	*m*-CPBA	**16**	33 : 67	100[d]
4	**12**	H	TBDPS	$VO(acac)_2$/^{t}BuOOH	**17**	≥97 : 3	76
5	**13**	H	Bn	$VO(acac)_2$/^{t}BuOOH	**18**	≥97 : 3	47

[a] Ratio of epoxides determined by ^{1}H NMR spectroscopy on the crude product mixtures; [b] Yields after purification by chromatography; [c] Product was shown to be 90% pure by ^{1}H NMR spectroscopy; [d] Yield of crude product.

Since we needed diprotected epoxides for our proposed epoxide rearrangement reactions, both monoprotected epoxides *cis*-**17** and *cis*-**18** were protected further (see below). With monosilyl epoxide *cis*-**17**, the yield was not very good; it seems reasonable to suggest that intramolecular hydrogen bonding between the epoxide oxygen lone pairs and the remaining hydroxyl group can account for the low reactivity. As well as providing us with diprotected epoxides *cis*-**15** and *cis*-**16**, it was clear from their ^{1}H NMR spectra that these epoxides were the minor diastereomeric products obtained from epoxidising diprotected alkenes **10** and **11** with *m*-CPBA. As we shall see later, epoxide *trans*-**15** has been converted into bicylic ether **21**. This enabled us to unequivocally establish the relative stereochemistry of epoxide *trans*-**15** and provided compelling evidence in support of all of our other stereochemical assignments in this paper.



cis-**17**; R = TBDPS
cis-**18**; R = Bn

cis-**15**; R = TBDPS
cis-**16**; R = Bn

Reagents: (a) 1 eq TBDPSCl, 2 eq ^{i}Pr$_2$NEt, DMAP, CH_2Cl_2, rt, 90 h; (b) 1.1 eq NaH,1.1 eq, BnBr, DMF, rt, 1 h (65%)

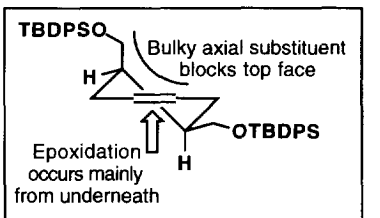


Figure 1

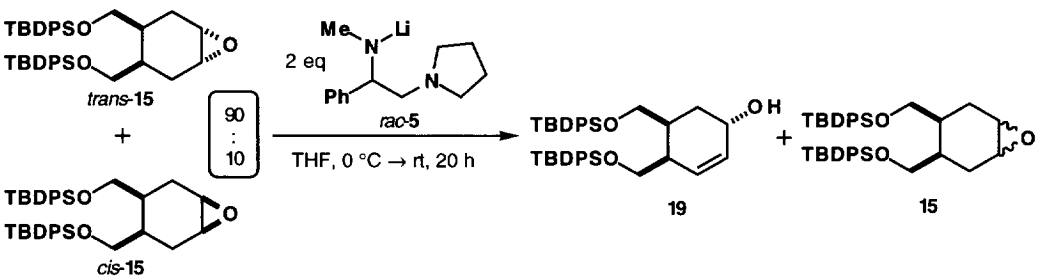
The epoxidation results can be summarised as follows. Starting from diol **9** and using a sequence of monoprotection, $VO(acac)_2$-directed epoxidation and further protection allows epoxides *cis*-**7** to be selectively

prepared. In contrast, diprotection of diol **9** followed by *m*-CPBA epoxidation enables epoxides *trans*-**7** to be prepared albeit with reduced stereoselectivity.

Lithium amide-mediated epoxide rearrangment

Now that we had developed good methods for the selective preparation of each of epoxides *trans*- and *cis*-**7**, we were ready to study their base-induced rearrangement. Since our main interest was in synthesising bicyclic ether **21** (see later), we particularly wanted to study the rearrangement of *trans* diprotected epoxides. Unfortunately, our most suitable candidate, epoxide *trans*-**15**, had only been prepared as a 90:10 mixture of *trans*- and *cis*-**15** and, despite considerable effort, it was not possible to separate the two diastereoisomers using chromatography or crystallisation. Thus, we decided to attempt the rearrangement reaction on the *mixture* of epoxides in the hope that the allylic alcohol products would be readily separable (Table 2).

Table 2: Rearrangement of the *mixture* of epoxides *trans*- and *cis*-15



Entry	Additive	Allylic alcohol **19**	Recovered epoxide **15**	
		Yield (%)	Yield (%)	*cis* : *trans*
1	–	73	15	64 : 36
2	KO^{t}Bu	72	9.6	≥97 : 3

Treatment of the 90:10 mixture of epoxides *trans*- and *cis*-**15** with two equivalents of lithium amide *rac*-**5** (generated from the corresponding racemic diamine which was prepared using chemistry that had been developed in our laboratory[14]) produced allylic alcohol **19** in 73% isolated yield as a single diastereoisomer by ^{1}H and ^{13}C NMR spectroscopy. In addition, from the chromatography, we also recovered a 15% yield of epoxide **15** which was shown to be a 64:36 mixture of *cis*- and *trans*-**15** (Table 2; entry 1).

The composition of the recovered epoxide **15** indicates that most of *trans*-**15** had rearranged to **19** but, significantly, *none* of *cis*-**15** had reacted with the lithium amide base. Fortuitously, the difference in reactivity between the two diastereomeric epoxides *trans*- and *cis*-**15** had enabled us to effect a relatively easy and efficient separation. In reality, we found that it was very difficult to obtain consistently high yields of allylic alcohol **19** using two equivalents of lithium amide *rac*-**5** alone; the reaction was simply not robust enough and, for this reason, attention was switched to trying to find reproducible conditions for the conversion of epoxide *trans*-**15** into allylic alcohol **19**.

It is well documented that lithium amides derived from diamines are more reactive in epoxide rearrangement reactions than lithium dialkylamides such as LDA.[15] In addition, Schlosser has shown that cyclohexene oxide can be rearranged smoothly and efficiently at low temperatures (–20 °C) when LDA is

used in combination with potassium *tert*-butoxide.[16,17] Combining these two known observations, we decided to carry out the rearrangement of the mixture of epoxides **15** using a mixed base system composed of a diamine-derived lithium amide (*rac*-**5**) *and* potassium *tert*-butoxide (Table 2; entry 2). As had been observed with lithium amide *rac*-**5** alone, only epoxide *trans*-**15** rearranged to give a completely reproducible 72% yield of a single diastereoisomer of allylic alcohol **19**. In this case, we also isolated a 9.6% yield of unreacted *crystalline* epoxide which was shown by ^{1}H and ^{13}C NMR spectroscopy to be entirely *cis*-**15**. Thus, the use of a novel mixed base system was not detrimental to the efficient separation of epoxides *trans*- and *cis*-**15** and, more importantly, it did allow us to reproducibly prepare synthetically useful quantities of allylic alcohol **19**.

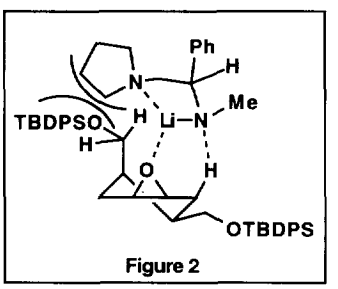


Figure 2

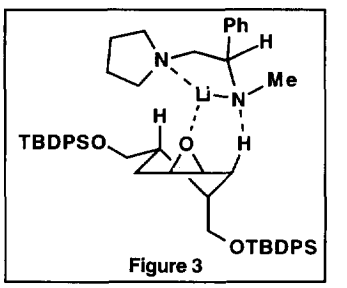
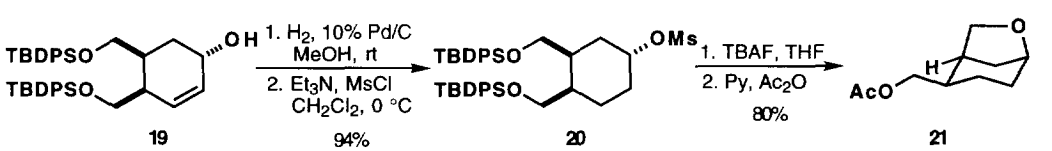


Figure 3

The difference in reactivity observed with epoxides *trans*- and *cis*-**15** was not completely without precedent. For example, we had previously noted that epoxide *trans*-**4** rearranged to the corresponding allylic alcohol far more quickly than its diastereoisomer *cis*-**4**.[8] In order to rationalise the difference in reactivity between *trans*- and *cis*-**15**, we prefer to assume that the reaction proceeds *via syn* elimination of a pseudo-axial β-hydrogen[18] and have constructed the two diastereomeric transition states (Figures 2 and 3). With epoxide *cis*-**15** (Figure 2), it is clear that there are severe steric interactions between the axial substituent and the lithium amide base. Presumably, such interactions are sufficiently significant to prevent reaction. In contrast, in the reaction of epoxide *trans*-**15**, the bulky axial substituent is on the opposite side to the reacting lithium amide base and *syn* elimination can proceed smoothly (Figure 3).

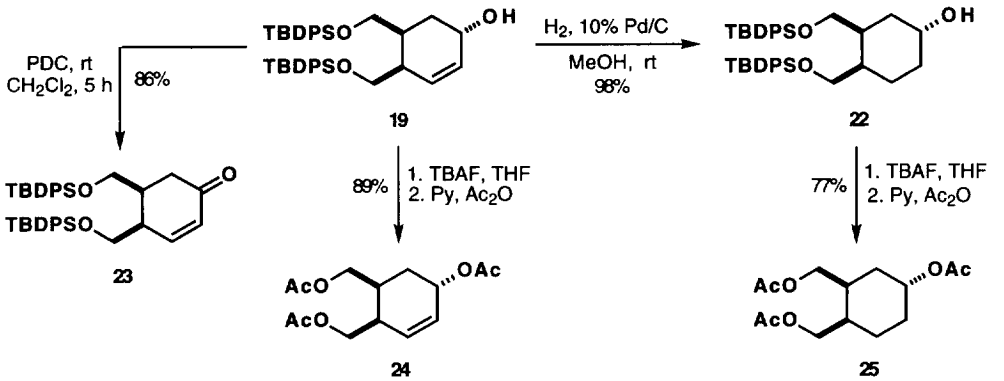
Synthetic applications

Allylic alcohol **19** is a potentially useful synthetic intermediate. In particular, we were interested in using it to prepare a 2-substituted-6-oxabicyclo[3.2.1]octane. Thus, allylic alcohol **19** was hydrogenated and the resulting alcohol was mesylated to give **20**. Then, TBAF deprotection with concomitant cyclisation of the axial hydroxyl group followed by acetylation of the remaining free hydroxyl group produced bicyclic ether **21** in an efficient 75% overall yield from allylic alcohol **19**. Of course, this successful synthesis of bicyclic ether **21** unequivocally established the relative stereochemistry of epoxides **15** since cyclisation to give **21** could only occur if allylic alcohol **19** had both the hydroxylmethyl groups *trans* to the hydroxyl group.



19 94% 20 21

In order to demonstrate the usefulness of allylic alcohol **19**, it has also been converted into a number of other functionalised cyclohexanes. Simple PDC oxidation of **19** afforded enone **23** whilst hydrogenation of **19** gave alcohol **22**, both in high yields. TBAF deprotection of each of alcohols **19** and **22** generated triols which were most easily isolated as their triacetates **24** and **25** respectively.



Summary

We have developed methods for the stereoselective synthesis of each of the diprotected epoxides *trans*- and *cis*-**7**. We have also shown that it is possible to rearrange a mixture of epoxides **15** to the corresponding allylic alcohol **19**. This transformation is noteworthy for a number of reasons. First of all, rearrangement of epoxides like *trans*-**15** have never previously been described. Secondly, nobody has used a lithium amide such as *rac*-**5** (derived from a diamine) in tandem with potassium *tert*-butoxide for epoxide rearrangement reactions. Thirdly, this is only the second time that a difference in reactivity of diastereomeric epoxides to rearrangement has been used to effect their efficient separation.[19] In addition, the product of the rearrangement reaction, allylic alcohol **19**, has been converted into a range of single diastereoisomers of functionalised cyclohexanes thus demonstrating the usefulness of our methods in stereoselective synthesis.

Experimental Section

General

All solvents were distilled before use. THF was freshly distilled form sodium-benzophenone ketyl whereas CH_2Cl_2 was freshly distilled from calcium hydride. Triethylamine was stored over potassium hydroxide pellets. Butyllithium was titrated against diphenylacetic acid before use. All non-aqueous reactions were carried out under oxygen-free nitrogen using oven-dried glassware. Petrol refers to the fraction of petroleum ether boiling in the range 40-60 °C and was distilled in Winchester quantities before use.

Fisher Matrix silica 60 was used for flash column chromatography; thin layer chromatography was carried out on commercially available Merck 5554 aluminium-backed silica plates. Proton and carbon NMR spectra were recorded on a Jeol EX-270 (270 MHz) instrument using an internal deuterium lock. Chemical shifts are quoted in parts per million downfield of tetramethylsilane. Carbon NMR spectra were recorded with broad band proton decoupling and were assigned using DEPT experiments.

Melting points were measured on an Electrothermal IA9100 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis FT-IR spectrometer. Chemical

ionisation and high resolution mass spectra were recorded on a Fisons Analytical (VG) Autospec spectrometer. Microanalysis was carried out at the University of East Anglia.

(4*R,5*S**)-4,5-Di(hydroxymethyl)cyclohexene 9**

A solution of *cis*-1,2,3,6-tetrahydrophthalic anhydride (5.09 g, 33.45 mmol) in THF (130 cm^3) was added over 10 min to a stirred suspension of lithium aluminium hydride (2.54 g, 66.9 mmol) in THF (20 cm^3) at 0 °C under nitrogen. The resulting mixture was stirred at 0 °C under nitrogen for 1 h and then at room temperature for 30 min. After cooling to 0 °C, water (2.5 cm^3), 15% sodium hydroxide solution (2.5 cm^3) and then water again (7.5 cm^3) were carefully added dropwise and the mixture was stirred for a further 30 min. The aluminium salts were removed by filtration and the filtrate was diluted with water (20 cm^3) and Et_2O (50 cm^3). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil (3.56 g, 67%). Purification by flash chromatography on silica with EtOAc as eluent gave diol **9** (3.03 g, 57%) as a colourless oil, R_F(EtOAc) 0.3; ν_{max}(film)/cm^{-1} 3342 (OH), 3022, 2892, 1438, 1032 and 663; δ_H(270 MHz; $CDCl_3$) 5.62 (2 H, t, *J* 1.5, HC=CH), 3.73 (2 H, dd, *J* 6.8 and 10.9, 2 × CH_AH_BOH), 3.59 (2 H, dd, *J* 3.4 and 10.9, 2 × CH_AH_BOH), 3.25 (2 H, br s, 2 × CH_2OH) and 2.18-1.96 (6 H, m, 2 × CH_2 and 2 × CH); δ_C(67.5 MHz; $CDCl_3$) 125.75 (HC=CH), 64.0 (CH_2OH), 38.0 (CH) and 21.1 (CH_2); *m/z* 160 (10%, $M^+ + NH_4$), 143 (100, $M^+ + H$) and 125 (35, M – OH)(Found: $M^+ + H$, 143.1068. $C_8H_{14}O_2$ requires *M* + H, 143.1072).

(4*R,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexene 10**

Imidazole (722 mg, 10.7 mmol) and *tert*-butyldiphenylsilyl chloride (1.8 cm^3, 7.0 mmol) were added successively to a stirred solution of diol **9** (500 mg, 3.51 mmol) in DMF (5 cm^3) at room temperature under nitrogen. After 20 h at room temperature, water (5 cm^3) and EtOAc (15 cm^3) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 10 cm^3). The combined organic extracts were washed with water (10 cm^3), brine (3 × 10 cm^3) and then water (10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (40:1) as eluent gave disilyl alkene **10** (1.94 g, 89%) as white crystalline needles, mp 68-69 °C (from petrol), R_F(40:1 petrol-EtOAc) 0.3; ν_{max}(Nujol)/cm^{-1} 3048, 1445 and 1105 (Si–O); δ_H(270 MHz; $CDCl_3$) 7.62 (8 H, dd, *J* 1.4 and 7.8, *o*-Ph), 7.41-7.27 (12 H, m, *m*- and *p*-Ph), 5.58 (2 H, br s, HC=CH), 3.62 (2 H, dd, *J* 5.5 and 10.1, 2 × CH_AH_BOSi), 3.53 (2 H, dd, *J* 7.6 and 9.8, 2 × CH_AH_BOSi), 2.13-1.95 (6 H, m, 2 × CH_2 and 2 × CH) and 1.00 (18 H, s, 2 × CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.6 (Ph), 133.9 (*ipso*-Ph), 129.4 (Ph), 127.6 (Ph), 125.7 (HC=CH), 64.6 (CH_2OSi), 37.4 (CH), 26.8 (CMe_3), 26.7 (CH_2) and 19.2 (CMe_3); *m/z* 636 (87%, $M^+ + NH_4$), 619 (10, $M^+ + H$), 363 (100, M – TBDPSO) and 274 (43)(Found: $M^+ + NH_4$, 636.3696. $C_{40}H_{50}O_2Si_2$ requires $M + NH_4$, 636.3693).

(4*R,5*S**)-4,5-Di(benzyloxymethyl)cyclohexene 11**

Sodium hydride (195 mg of a 70% dispersion in mineral oil, 4.87 mmol) was added to a stirred solution of diol **9** (268 mg, 1.89 mmol) in DMF (5 cm^3) at room temperature under nitrogen. After 10 min, benzyl bromide (647 mg, 3.78 mmol) was added dropwise and the reaction mixture was stirred for a further 90 min at

room temperature. Then, water (1 cm^3) was carefully added dropwise and the reaction mixture was diluted with water (14 cm^3) and Et_2O (15 cm^3). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 cm^3). The combined organic extracts were washed with water (2 × 15 cm^3) and then brine (3 × 20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by flash chromatography on silica with petrol-Et_2O (10:1) and then petrol-Et_2O (1:1) as eluent gave monobenzyl alkene **13** (193 mg, 44%) as a pale yellow oil and dibenzyl alkene **11** (294 mg, 48%) as a pale yellow oil, R_F(10:1 petrol-Et_2O) 0.15; ν_{max}(film)/cm^{-1} 3025, 1452, 1364 and 1097; δ_H(270 MHz; $CDCl_3$) 7.40-7.21 (5 H, m, 2 × Ph), 5.63 (2 H, br s, HC=CH), 4.49 (4 H, s, 2 × $PhCH_2O$), 3.50 (2 H, dd, *J* 5.8 and 9.2, 2 × CH_AH_BOBn), 3.40 (2 H, dd, *J* 7.5 and 9.2, 2 × CH_AH_BOBn) and 2.32-1.92 (6 H, m, 2 × CH_2 and 2 × CH); δ_C(67.5 MHz; $CDCl_3$) 138.7 (*ipso*-Ph), 128.3 (Ph), 127.5 (Ph), 127.4 (Ph), 125.6 (HC=CH), 73.0 ($PhCH_2O$), 71.3 (CH_2OBn), 34.8 (CH) and 27.0 (CH_2); *m/z* 323 (100%, M^+ + H), 233 (9) and 215 (16, M − BnO)(Found: M^+ + H, 323.2017. $C_{22}H_{26}O_2$ requires *M* + H, 323.2011).

(4*R,5*S**)-5-*Tert*-butyldiphenylsilyloxymethyl-4-hydroxymethylcyclohexene 12**

Imidazole (511 mg, 8 mmol) and *tert*-butyldiphenylsilyl chloride (1.86 cm^3, 7.0 mmol) were added successively to a stirred solution of diol **9** (995 mg, 7 mmol) in DMF (8 cm^3) at room temperature under nitrogen. After 18 h at room temperature, water (10 cm^3) and EtOAc (20 cm^3) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 15 cm^3). The combined organic extracts were washed with water (15 cm^3), brine (3 × 15 cm^3) and then water (15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (5:1) as eluent gave disilyl alkene **10** (520 mg, 12.5%) as a white solid and monosilyl alkene **12** (1.51 g, 57%) as a colourless oil, R_F(5:1 petrol-EtOAc) 0.2; δ_H(270 MHz; $CDCl_3$) 7.70-7.64 (8 H, m, *o*-Ph), 7.47-7.30 (12 H, m, *m*- and *p*-Ph), 5.56 (2 H, br m, HC=CH), 3.73 (1 H, dd, *J* 7.0 and 10.4, CH_AH_BO), 3.66 (3 H, m, CH_AH_BO and CH_2O), 2.73 (1 H, br s, CH_2OH), 2.15-1.88 (6 H, m, 2 × CH_2 and 2 × CH) and 1.06 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.6 (Ph), 135.55 (Ph), 133.1 (*ipso*-Ph), 129.8 (Ph), 129.75 (Ph), 127.7 (Ph), 125.6 (HC=CH), 125.4 (HC=CH), 65.3 (CH_2O), 64.1 (CH_2O), 37.8 (CH), 37.2 (CH), 27.2 (CH_2), 26.8 (CMe_3), 26.5 (CH_2) and 19.1 (CMe_3); *m/z* 381 (100%, M^+ + H) and 363 (11, M − H_2O)(Found: M^+ + H, 381.2257. $C_{24}H_{32}O_2Si$ requires *M* + H, 381.2249).

(4*R,5*S**)-5-Benzyloxymethyl-4-hydroxymethylcyclohexene 13**

Sodium hydride (160 mg of a 70% dispersion in mineral oil, 3.99 mmol) was added to a stirred solution of diol **9** (506 mg, 3.57 mmol) in DMF (8 cm^3) at room temperature under nitrogen. After 10 min, benzyl bromide (612 mg, 3.99 mmol) was added dropwise and the reaction mixture was stirred for a further 1 h at room temperature. Then, water (1 cm^3) was carefully added dropwise and the reaction mixture was diluted with water (10 cm^3) and Et_2O (15 cm^3). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 cm^3). The combined organic extracts were washed with water (15 cm^3) and then brine (3 × 20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by flash chromatography on silica with petrol-Et_2O (1:1) as eluent gave monobenzyl alkene **13** (551 mg, 67%) as a pale yellow oil, R_F(5:1 petrol-Et_2O) 0.3; ν_{max}(film)/cm^{-1} 3390 (OH), 3023, 1450 and 1095; δ_H(270 MHz; $CDCl_3$) 7.39-7.27 (5 H, m, Ph), 5.63 (1 H, dd, *J* 1.9 and 10.4, HC=CH), 5.61 (1 H, dd, *J*

1.9 and 10.0, HC=C*H*), 4.55 (1 H, d, *J* 12.1, PhCH_AH_BO), 4.50 (1 H, d, *J* 11.9, PhCH_AH_BO), 3.67-3.52 (3 H, m, CH_2O and CH_AH_BO), 3.41 (1 H, dd, *J* 4.5 and 9.3, CH_AH_BO), 2.67 (1 H, br s, CH_2OH) and 2.29-1.92 (6 H, m, 2 × CH and 2 × CH_2); δ_C(67.5 MHz; $CDCl_3$) 137.8 (*ipso*-Ph), 128.5 (Ph), 127.8 (Ph), 127.8 (Ph), 125.7 (H*C*=CH), 125.4 (HC=*C*H), 73.4 (PhCH_2O), 71.8 (CH_2OBn), 64.4 (CH_2OH), 38.0 (CH), 34.9 (CH), 27.9 (CH_2) and 26.3 (CH_2); *m/z* 233 (100%, M^+ + H), 143 (5), 123 (6) and 108 (10)(Found: M^+ + H, 233.1544. $C_{15}H_{20}O_2$ requires *M* + H, 233.1542).

(1*R,2*S**,4*R**,5*S**)-4,5-Di(hydroxymethyl)cyclohexene Oxide *cis*-14**

Tert-butyl hydroperoxide (1.2 cm^3 of a 2.5 M solution in toluene, 3.0 mmol) was added dropwise to a stirred solution of diol **9** (211 mg, 1.48 mmol) in CH_2Cl_2 (8 cm^3) at room temperature under nitrogen. Then, vanadyl acetylacetonate (5 mg, 0.02 mmol) was added. After 72 h at room temperature, some of the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica with EtOAc and then CH_2Cl_2-MeOH (5:1) as eluent to give epoxide *cis*-**14** (105 mg, 45%; 90% pure by ^1H NMR spectroscopy) as a pale yellow oil, R_F(EtOAc) 0.2; δ_H(270 MHz; $CDCl_3$) 3.70 (2 H, dd, *J* 6.4 and 11.3, 2 × CH_AH_BOH), 3.61 (2 H, dd, *J* 3.9 and 11.4, 2 × CH_AH_BOH), 3.22 (2 H, dd, *J* 1.2 and 2.2, 2 × CHO) and 2.09-1.95 (6 H, m, 2 × CH_2 and 2 × CH); δ_C(67.5 MHz; $CDCl_3$) 64.3 (CH_2OH), 52.1 (CHO), 36.1 (CH) and 26.6 (CH_2).

(1*S,2*R**,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexene Oxide *trans*-15 and (1*R**,2*S**,4R*,5S*)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexene Oxide *cis*-15**

Sodium hydrogencarbonate (287 mg, 3.42 mmol) and *m*-CPBA (591 mg of 70% pure material, 3.42 mmol) were added successively to a stirred solution of disilyl alkene **10** (1.63 g, 2.63 mmol) in CH_2Cl_2 (20 cm^3) at room temperature under nitrogen. After 20 h at room temperature, 20% sodium sulfite solution (20 cm^3) was added and the mixture was stirred for a further 20 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 30 cm^3). The combined organic extracts were washed with 20% sodium sulfite solution (2 × 40 cm^3) and then saturated sodium hydrogencarbonate solution (2 × 40 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil which contained a 90:10 mixture of epoxides *trans*- and *cis*-**15** (by ^1H NMR spectroscopy). Purification by flash chromatography on silica with petrol-EtOAc (10:1) as eluent gave the same 90:10 mixture of epoxides *trans*- and *cis*-**15** (1.58 g, 95%) as a viscous, nearly crystalline oil, R_F(10:1 petrol-EtOAc) 0.4; ν_{max}(film)/cm^{-1} 3067, 1467, 1429 and 1107 (Si–O); δ_H(270 MHz; $CDCl_3$) 7.66-7.54 (16 H, m, *o*-Ph), 7.44-7.26 (24 H, m, *m*- and *p*-Ph), 3.66 (2 H, dd, *J* 5.6 and 10.2, 2 × C$H_AH_BO^{cis}$), 3.57 (2 H, dd, *J* 7.0 and 10.2, 2 × C$H_AH_BO^{cis}$), 3.56 (2 H, dd, *J* 5.2 and 10.1, 2 × C$H_AH_BOSi^{trans}$), 3.46 (2 H, dd, *J* 6.7 and 10.1, 2 × C$H_AH_BOSi^{trans}$), 3.11 (2 H, br s, 2 × CHO^{cis}), 3.03 (2 H, br s, 2 × CHO^{trans}), 2.02-1.78 (12 H, m, 2 × CH_2 and 2 × CH), 0.99 (18 H, s, 2 × CMe_3^{cis}) and 1.0 (18 H, s, 2 × CMe_3^{trans}); δ_C(67.5 MHz; $CDCl_3$) 135.55 (Ph^{cis}), 135.5 (Ph), 133.9 (*ipso*-Ph^{cis}), 133.6 (*ipso*-Ph^{trans}), 129.6 (Ph)^{trans}, 129.5 (Ph^{cis}), 127.6 (Ph), 127.5 (Ph^{trans}), 65.7 (CH_2O^{cis}), 64.3 (CH_2OSi^{trans}), 51.8 (CHO), 37.2 (CH^{cis}), 34.1 (CH^{trans}), 26.9 (CMe_3^{cis}), 26.8 (CMe_3^{trans}), 25.8 (CH_2^{cis}), 25.3 (CH_2^{trans}), 19.2 (CMe_3^{cis}) and 19.1 (CMe_3^{trans}); *m/z* 635 (100%, M^+ + H), 379 (17, M – TBDPSO) and 123 (7)(Found: M^+ + H, 635.3377. $C_{40}H_{50}O_3Si$ requires *M* + H, 635.3379).

(1*S,2*R**,4*R**,5*S**)-4,5-Di(benzyloxymethyl)cyclohexene Oxide *trans*-16 and (1*R**,2*S**,4*R**,5*S**)-4,5-Di(benzyloxymethyl)cyclohexene Oxide *cis*-16**

Sodium hydrogencarbonate (72 mg, 0.86 mmol) and *m*-CPBA (212 mg of a 70% pure material, 0.86 mmol) were added successively to a stirred solution of dibenzyl alkene **11** (210 mg, 0.67 mmol) in CH_2Cl_2 (4 cm^3) at room temperature under nitrogen. After 15 h at room temperature, 20% sodium sulfite solution (20 cm^3) was added and the mixture was stirred for a further 45 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were washed with 20% sodium sulfite solution (2 × 20 cm^3) and then saturated sodium hydrogencarbonate solution (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product (243 mg, 107%) as a yellow oil which contained a 67:33 mixture of epoxides *trans*- and *cis*-**16** (by ^1H NMR spectroscopy), R_F(1:1 petrol-Et_2O) 0.4; ν_{max}(film)/cm^{-1} 1712, 1452 and 1096; δ_H(270 MHz; $CDCl_3$) 7.38-7.24 (20 H, m, Ph), 4.45 (4 H, br s, 2 × $PhCH_2O^{cis}$), 4.46 (4 H, br s, 2 × $PhCH_2O^{trans}$), 3.54-3.14 (8 H, m, 2 × CH_2O), 3.15 (4 H, br s, 2 × CHO) and 2.11-1.80 (12 H, m, 2 × CH and 2 × CH_2); δ_C(67.5 MHz; $CDCl_3$) 138.5 (*ipso*-Ph), 128.3 (Ph), 127.6 (Ph), 127.5 (Ph), 127.5 (Ph), 127.5 (Ph), 73.0 ($PhCH_2O^{cis}$), 72.9 ($PhCH_2O^{trans}$), 72.4 (CH_2O^{cis}), 71.0 (CH_2O^{trans}), 51.8 (CHO^{cis}), 51.6 (CHO^{trans}), 34.9 (CH^{cis}), 31.7 (CH^{trans}), 29.7 (CH_2^{trans}) and 26.3 (CH_2^{cis}); *m/z* 339 (100%, M^+ + H), 91 (94, Bn), 108 (47, BnO) and 231 (34, M – BnO)(Found: M^+ + H, 339.1963. $C_{22}H_{26}O_3$ requires *M* + H, 339.1960).

(1*R,2*S**,4*R**,5*S**)-5-*Tert*-butyldiphenylsilyloxymethyl-4-hydroxymethylcyclohexene Oxide *cis*-17**

Tert-butyl hydroperoxide (1 cm^3 of a 1.6 M solution in toluene, 1.6 mmol) was added to a stirred solution of monosilyl alkene **12** (330 mg, 0.87 mmol) in CH_2Cl_2 (8 cm^3) at room temperature under nitrogen. Vanadyl acetylacetonate (5 mg, 0.02 mmol) was added and the mixture was stirred for 20 h at room temperature. Then, 20% sodium sulfite solution (15 cm^3) was added and the mixture was stirred for a further 45 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 25 cm^3). The combined organic extracts were washed with 20% sodium sulfite solution (30 cm^3) and then saturated sodium hydrogencarbonate solution (30 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by flash chromatography on silica with petrol-EtOAc (2:1) as eluent gave monosilyl epoxide *cis*-**17** (263 mg, 76%) as a colourless oil, R_F(2:1 petrol-EtOAc) 0.4; δ_H(270 MHz; $CDCl_3$) 7.67-7.62 (4 H, m, *o*-Ph), 7.42-7.35 (6 H, m, *m*- and *p*-Ph), 3.80 (1 H, dd, *J* 7.5 and 10.7, CH_AH_BO), 3.66-3.51 (2 H, m, 2 × CH_AH_BO), 3.39 (1 H, dd, *J* 4.8 and 8.8, CH_AH_BO), 3.18-3.13 (2 H, m, 2 × CHO), 2.07-1.86 (4 H, m, 2 × CH_2) and 1.05 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.5 (Ph), 133.1 (*ipso*-Ph), 133.2 (*ipso*-Ph), 129.6 (Ph), 127.7 (Ph), 65.9 (CH_2O), 64.3 (CH_2O), 52.0 (CHO), 51.7 (CHO), 36.6 (CH), 35.8 (CH), 26.8 (CMe_3), 26.6 (CH_2), 26.5 (CH_2) and 19.2 (CMe_3); *m/z* 397 (79%, M^+ + H) and 141 (100)(Found: M^+ + H, 397.2204. $C_{24}H_{32}O_3Si$ requires *M* + H, 397.2199).

(1*R,2*S**,4*R**,5*S**)-5-Benzyloxymethyl-4-hydroxymethylcyclohexene Oxide *cis*-18**

Tert-butyl hydroperoxide (2 cm^3, 5.1 mmol) was added dropwise to a stirred solution of monobenzyl alkene **13** (330 mg, 0.87 mmol) in CH_2Cl_2 (8 cm^3) at room temperature under nitrogen. Vanadyl acetylacetonate (12 mg, 0.05 mmol) was added and the mixture was stirred for 20 h at room temperature. Then, 20% sodium sulfite solution (25 cm^3) was added and the mixture was stirred for a further 45 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts

were washed with 20% sodium sulfite solution (30 cm^3) and then saturated sodium hydrogencarbonate solution (2 × 20 cm^3), dried ($MgSO_4$) and evaporated under reduced to give the crude product as an oil. Purification by flash chromatography on silica with petrol-Et_2O (1:2) as eluent gave monobenzyl epoxide *cis*-**18** (234 mg, 47%) as an oil, R_F(1:2 petrol-Et_2O) 0.15; δ_H(270 MHz; $CDCl_3$) 7.41-7.25 (5 H, m, Ph), 4.48 (2 H, t, *J* 11.7, $PhCH_2$), 3.70-3.25 (4 H, m, 2 × CH_2O), 3.19-3.15 (2 H, m, 2 × CHO) and 2.17-1.77 (6 H, m, 6 × CH); δ_C(67.5 MHz; $CDCl_3$) 137.7 (*ipso*-Ph), 128.5 (Ph), 127.5 (Ph), 73.3 ($PhCH_2O$), 72.3 ($BnOCH_2$), 64.4 (CH_2OH), 52.0 (CHO), 51.5 (CHO), 36.0 (CH), 33.6 (CH), 27.6 (CH_2) and 25.6 (CH_2); *m/z* 249 (100%, M^+ + H), 141 (31, M – BnO) and 231 (17, M – H_2O)(Found: M^+ + H, 249.1494. $C_{15}H_{20}O_3$ requires *M* + H, 249.1491).

(1*R,2*S**,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexene Oxide *cis*-15**

Diisopropylethylamine (0.1 cm^3, 0.57 mmol), DMAP (3 mg, 0.03 mmol) and *tert*-butyldiphenylsilyl chloride (0.08 cm^3, 0.29 mmol) were added successively to a stirred solution of epoxide *cis*-**17** (98 mg, 0.26 mmol) in CH_2Cl_2 (4 cm^3) at room temperature under nitrogen. After 90 h at room temperature, water (15 cm^3) and EtOAc (40 cm^3) were added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 15 cm^3). The combined organic extracts were washed with water (15 cm^3), brine (3 × 15 cm^3), 2% hydrochloric acid (15 cm^3) and then water (20 cm^3), dried ($MgSO_4$) and evaporated under reduced to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (10:1) as eluent gave disilyl epoxide *cis*-**15** [identified by δ_H(270 MHz; $CDCl_3$) 3.11 (2 H, br s, 2 × CHO) and 0.99 (18 H, s, 2 × CMe_3) which was contaminated with *tert*-butyldiphenylsilanol.

(1*R,2*S**,4*R**,5*S**)-4,5-Di(benzyloxymethyl)cyclohexene Oxide *cis*-16**

Sodium hydride (32 mg of a 70% dispersion in mineral oil, 0.81 mmol) was added to a stirred solution of monobenzyl epoxide *cis*-**18** (176 mg, 0.71 mmol) in DMF (3 cm^3) at room temperature under nitrogen. After 10 min, benzyl bromide (132 mg, 0.8 mmol) was added dropwise and the reaction mixture was stirred for a further 1.5 h at room temperature. Then, water (1 cm^3) was carefully added dropwise and the reaction mixture was diluted with water (9 cm^3) and Et_2O (15 cm^3). The layers were separated and the aqueous layer was extracted with Et_2O (3 × 15 cm^3). The combined organic extracts were washed with water (15 cm^3) and brine (3 × 20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by flash chromatography on silica with petrol-Et_2O (1:1) as eluent gave epoxide *cis*-**16** (149 mg, 65%) as a pale yellow oil, R_F(1:1 petrol-Et_2O) 0.4; δ_H(270 MHz; $CDCl_3$) 7.38-7.24 (10 H, m, 2 × Ph), 4.45 (4 H, br s, 2 × $PhCH_2O$), 3.54-3.48 (2 H, m, 2 × CH_AH_BO), 3.42-3.36 (2 H, m, 2 × CH_AH_BO), 3.15 (2 H, br s, 2 × CHO) and 2.03-1.89 (6 H, m, 2 × CH_2 and 2 × CH); δ_C(67.5 MHz; $CDCl_3$) 138.6 (*ipso*-Ph), 132.8 (Ph), 127.6 (Ph), 127.5 (Ph), 73.0 ($PhCH_2O$), 72.6 (CH_2O), 51.8 (CHO), 34.4 (CH) and 26.3 (CH_2); *m/z* 233 (100%, M^+ + H), 143 (5, M – Bn), 123 (6) and 108 (10)(Found: M^+ + H, 233.1544. $C_{15}H_{20}O_2$ requires *M* + H, 233.1542).

(1*S,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohex-2-enol 19**

Butyllithium (0.79 cm^3 of a 1.5 M solution in hexane, 1.1 mmol) was added dropwise to a stirred solution of racemic *N*-methyl-1-phenyl-2-(1-pyrrolidinyl)ethanamine[14] (224 mg, 1.1 mmol) in THF (2 cm^3) at 0 °C under

nitrogen. After 30 min at 0 °C, a 90:10 mixture of epoxides *trans*- and *cis*-**15** (348 mg, 0.55 mmol) in THF (2 cm^3) was added dropwise by means of a canula. The reaction mixture was allowed to warm to room temperature and, after 16 h at room temperature, saturated ammonium chloride solution (4 cm^3) and Et_2O (10 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 cm^3). The combined organic extracts were washed with 2% hydrochloric acid (10 cm^3), water (10 cm^3) and then brine (10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (4:1) as eluent gave a 36:64 mixture (by ^1H NMR spectroscopy) of epoxides *trans*- and *cis*-**15** (98 mg, 15%) as an oil and allylic alcohol **19** (273 mg, 73%) as a colourless, nearly crystalline oil, R_F(4:1 petrol-EtOAc) 0.3; ν_{max}(film)/cm^{-1} 3341 (OH), 3066, 1467, 1428 and 1109 (Si–O); δ_H(270 MHz; $CDCl_3$) 7.65-7.58 (8 H, m, *o*-Ph), 7.44-7.30 (12 H, m, *m*- and *p*-Ph), 5.94-5.85 (2 H, m, HC=CH), 4.21 (1 H, dd, *J* 4.4 and 7.0, C*H*OH), 3.75 (1 H, dd, *J* 7.3 and 10.2, CH_AH_BOSi), 3.69-3.48 (3 H, m, CH_AH_BOSi and CH_2O), 2.57-2.51 (1 H, m, H^4), 2.37-2.24 (1 H, m, H^5), 1.95 (1 H, ddd, *J* 4.9 and 11.2 and 13.6, H^6),1.65 (1 H, dt, *J* 3.4 and 13.6, $H^{6'}$), 1.58 (1 H, br s, CHO*H*), 1.01 (9 H, s, CMe_3) and 0.98 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.6 (Ph), 135.5 (Ph), 133.8 (*ipso*-Ph), 133.6 (*ipso*-Ph), 133.5 (*ipso*-Ph), 132.45 (Ph), 129.6 (Ph), 127.6 (HC=CH), 64.9 (CH_2O), 64.3 (CHO), 63.7 (CH_2O), 39.1 (CH), 34.6 (CH), 32.0 (CH_2), 26.9 (*CMe*$_3$), 26.8 (*CMe*$_3$), 19.2 (*C*Me$_3$) and 19.1 (*C*Me$_3$); *m/z* 652 (57%, $M^+ + NH_4$), 634 (35, M – H_2O), 379 (95, M – TBDPSO), 361 (100) and 196 (33)(Found: $M^+ + NH_4$, 652.3651. $C_{40}H_{50}O_3Si_2$ requires $M + NH_4$, 652.3642). This experiment was very difficult to reproduce.

(1*S,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohex-2-enol 19**

Butyllithium (2.31 cm^3 of a 1.5 M solution in hexane, 3.2 mmol) was added dropwise to a stirred solution of *N*-methyl-1-phenyl-2-(1-pyrrolidinyl)ethanamine[14] (277 mg, 3.24 mmol) in THF (2 cm^3) at 0 °C under nitrogen. After 30 min at 0 °C, a solution of potassium *tert*-butoxide (363 mg, 3.2 mmol) in THF (5 cm^3) was added dropwise by means of a canula and the mixture was stirred for a further 15 min. Then, a 90:10 mixture of epoxides *trans*- and *cis*-**15** (1.015 g, 1.6 mmol) in THF (4 cm^3) was added dropwise by means of a canula. The reaction mixture was allowed to warm to room temperature and, after 16 h at room temperature, saturated ammonium chloride solution (10 cm^3) and Et_2O (20 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 20 cm^3). The combined organic extracts were washed with 2% hydrochloric acid (15 cm^3), water (15 cm^3) and then brine (15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (4:1) as eluent gave epoxide *cis*-**15** (98 mg, 9.6%) as rectangular plates, mp 111-112 °C (from petrol); (Found: C, 75.4; H, 8.1%. $C_{40}H_{50}O_3Si$ requires C, 75.6; H, 7.9%); δ_H(270 MHz; $CDCl_3$) 7.66-7.54 (8 H, m, *o*-Ph) , 7.44-7.28 (12 H, m, *m*- and *p*-Ph), 3.66 (2 H, dd, *J* 5.6 and 10.2, 2 × CH_AH_BO), 3.57 (2 H, dd, *J* 7.0 and 10.2, 2 × CH_AH_BO), 3.11 (2 H, br s, 2 × CHO), 2.02-1.78 (6 H, m, 2 × CH_2 and 2 × CH) and 0.99 (18 H, s, 2 × CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.55 (Ph), 135.5 (Ph), 133.9 (*ipso*-Ph), 129.5 (Ph), 127.6 (Ph), 65.7 (CH_2O), 51.8 (CHO), 37.2 (CH), 26.9 (*CMe*$_3$), 25.8 (CH_2) and 19.2 (*C*Me$_3$) and allylic alcohol **19** (731 mg, 72%) as a colourless, nearly crystalline oil.

(1*S,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexanol 22**

A suspension of allylic alcohol **19** (107 mg, 0.17 mmol) and 10% palladium on charcoal (10 mg) in MeOH (4 cm^3) was stirred vigorously for 16 h at room temperature under a hydrogen atmosphere. Then, the suspension was filtered through celite to remove the catalyst. After washing several times with MeOH, the filtrate was evaporated under reduced pressure to give crude alcohol **22** (105 mg, 98%) as a colourless oil, R_F(EtOAc) 0.3; ν_{max}(film)/cm^{-1} 3359 (OH), 3060, 1464, 1383 and 1070; δ_H(270 MHz; $CDCl_3$) 7.66-7.58 (8 H, m, *o*-Ph) , 7.45 7.29 (12 H, m, *m*- and *p*-Ph), 3.68 (1 H, dd, *J* 6.1 and 10.2, CH_AH_BOSi), 3.58 (1 H, dd, *J* 6.8 and 10.4, CH_AH_BOSi), 3.74-3.47 (1 H, m, CH_AH_BOSi), 3.74-3.47 (1 H, m, CH_AH_BOSi), 2.29-2.20 (1 H, m, CH), 2.10-2.01 (1 H, m, CH), 1.89-1.79 (2 H, m, 2 × CH), 1.72-1.05 (4 H, m, 4 × CH), 1.01 (9 H, s, CMe_3) and 1.00 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.6 (Ph), 135.5 (Ph), 133.9 (*ipso*-Ph), 133.7 (*ipso*-Ph), 129.6 (Ph), 129.5 (Ph), 127.6 (Ph), 66.8 (CHO), 65.0 (CH_2OSi), 63.1 (CH_2OSi), 40.5 (CH), 37.6 (CH), 35.9 (CH_2), 33.5 (CH_2), 26.9 (CMe_3), 23.0 (CH_2), 19.22 (CMe_3) and 19.16 (CMe_3); *m/z* 654 (17%, $M^+ + NH_4$), 619 (12, M – H_2O), 381 (100, M – TBDPSO) and 363 (27)(Found: $M^+ + NH_4$, 654.3796. $C_{40}H_{52}O_3Si_2$ requires $M + NH_4$, 654.3799).

(1*S,4*R**,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohexan-1-yl Methanesulfonate 20**

Triethylamine (1.05 cm^3 of a 0.7 M solution in CH_2Cl_2, 0.75 mmol) was added dropwise to a stirred solution of alcohol **22** (366 mg, 0.58 mmol) in CH_2Cl_2 (4 cm^3) at 0 °C under nitrogen. Then, methanesulfonyl chloride (0.47 cm^3 of a 1.3 M solution in CH_2Cl_2, 0.6 mmol) was added. After 30 min at 0 °C, water (5 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 cm^3) and the combined organic extracts were washed with dilute hydrochloric acid (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with petrol-EtOAc (4:1) as eluent gave mesylate **20** (395 mg, 96%) as a colourless oil, R_F(4:1 petrol-EtOAc) 0.4; δ_H(270 MHz; $CDCl_3$) 7.63-7.54 (8 H, m, *o*-Ph), 7.44-7.27 (12 H, m, *m*- and *p*-Ph), 4.98-4.89 (1 H, m, CHOMs), 3.64 (1 H, dd, *J* 5.8 and 10.2, CH_AH_BOSi), 3.60-3.46 (3 H, m, CH_AH_BOSi and CH_2OSi), 2.95 (3 H, s, SO_2Me), 2.30-2.21 (1 H, m, CH), 1.96-1.89 (2 H, m, 2 × CH), 1.76-1.5 (3 H, m, 3 × CH), 1.00 (9 H, s, CMe_3) and 0.98 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 135.6 (Ph), 133.9 (*ipso*-Ph), 129.4 (Ph), 127.6 (Ph), 125.7 (Ph), 64.6 (CH_2OSi), 37.4 (CH), 26.8 (CMe_3), 26.7 (CH_2) and 19.2 (CMe_3); *m/z* 732 (30%, $M^+ + NH_4$), 636 (85), 619 (55), 459 (60) and 363 (100)(Found: $M^+ + NH_4$, 732.3568. $C_{41}H_{54}O_5SSi_2$ requires $M + NH_4$, 732.3574).

(1*S,2*R**,5*R**)-2-Acetoxymethyl-6-oxabicyclo[3.2.1]octane 21**

A solution of mesylate **20** (280 mg, 0.39 mmol) and tetrabutylammonium fluoride (2 cm^3 of 1 M solution in THF, 2 mmol) was stirred at room temperature under nitrogen for 15 h. The solution was evaporated under reduced pressure and the residue was dissolved in pyridine (2 cm^3) and acetic anhydride (2 cm^3) and stirred at room temperature for 20 h. Then, water (5 cm^3) and Et_2O (15 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 25 cm^3). The combined organic extracts were washed with water (20 cm^3), dilute hydrochloric acid (2 × 25 cm^3), saturated sodium hydrogencarbonate solution (2 × 25 cm^3) and then water (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product as a pale yellow oil. Purification by flash chromatography on silica with CH_2Cl_2 as eluent gave bicyclic ether **21** (58 mg, 80%) as a pale yellow oil, R_F(10:1 CH_2Cl_2-MeOH) 0.5; ν_{max}(film)/cm^{-1} 1737

(C=O); δ_H(270 MHz; $CDCl_3$) 4.33 (1 H, dd, *J* 5.1 and 5.6, CHO), 3.92 (1 H, d, *J* 8.5, CH_AH_BO), 3.89 (2 H, d, *J* 7.0, CH_2OAc), 3.70 (1 H, dd, *J* 4.4 and 8.5, CH_AH_BO), 2.36 (1 H, t, *J* 4.6, CH), 2.06 (3 H, s, CH_3), 2.06-1.93 (2 H, m, 2 × CH), 1.80-1.73 (1 H, m, CH), 1.60 (2 H, d, *J* 11.4, CH) and 1.44-1.25 (2 H, m, 2 × CH); δ_C(67.5 MHz; $CDCl_3$) 171.3 (C=O), 74.8 (CHO), 68.5 (CH_2OAc), 67.1 (CH_2O), 38.9 (CH), 38 (CH_2), 36.8 (CH), 31.5 (CH_2), 21.9 (CH_2) and 21.0 (CH_3); *m/z* 202 (100%, $M^+ + NH_4$), 185 (20) and 124 (20)(Found: $M^+ + NH_4$, 202.1446. $C_{10}H_{16}O_3$ requires $M + NH_4$, 202.1443).

(4*R,5*S**)-4,5-Di(*tert*-butyldiphenylsilyloxymethyl)cyclohex-2-enone 23**

Pyridinium dichromate (154 mg, 0.41 mmol) was added in one portion to a stirred solution of allylic alcohol **19** (172 mg, 0.27 mmol) in CH_2Cl_2 (4 cm^3) at room temperature under nitrogen. After 5 h at room temperature, some of the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica with petrol-EtOAc (4:1) as eluent to give enone **23** (148 mg, 86%) as a colourless oil, R_F(4:1 petrol-EtOAc) 0.55; ν_{max}(film)/cm^{-1} 3068, 1680 (C=O), 1467, 1426, 1387 and 1108 (Si–O); δ_H(270 MHz; $CDCl_3$) 7.60-7.55 (8 H, m, *o*-Ph), 7.45-7.29 (12 H, m, *m*- and *p*-Ph) 6.94 (1 H, dd, *J* 4.9 and 10.2, H^3), 6.11 (1 H, dd, *J* 1.7 and 10.2, H^2), 3.88 (1 H, dd, *J* 6.3 and 10.4, CH_AH_BOSi), 3.78 (1 H, dd, *J* 5.1 and 10.4, CH_AH_BOSi), 3.71 (1 H, dd, *J* 6.7 and 10.3, CH_AH_BOSi), 3.62 (1 H, dd, *J* 6.3 and 10.3, CH_AH_BOSi), 2.8-2.36 (4 H, m, CH_2 and 2 × CH), 0.982 (9 H, s, CMe_3) and 0.987 (9 H, s, CMe_3); δ_C(67.5 MHz; $CDCl_3$) 199.4 (C=O), 151.2 (C^3), 135.6 (Ph), 135.5 (Ph), 133.2 (*ipso*-Ph), 133.0 (*ipso*-Ph), 132.9 (*ipso*-Ph), 130.4 (Ph), 129.8 (Ph), 129.7 (Ph), 127.7 (C^2), 64.4 (CH_2O), 62.9 (CH_2O), 39.7 (CH), 38.8 (CH_2), 26.8 (CMe_3), 19.14 (CMe_3) and 19.08 (CMe_3); *m/z* 650 (37%, $M^+ + NH_4$), 555 (53), 299 (100), 274 (58), 216 (45) and 196 (75)(Found: $M^+ + NH_4$, 650.3494. $C_{40}H_{48}O_3Si_2$ requires $M + NH_4$, 650.3486).

(1*S,4*R**,5*S**)-4,5-Di(acetoxymethyl)cyclohex-2-en-1-yl Acetate 24**

Tetrabutylammonium fluoride (1.0 cm^3 of 1 M solution in THF, 1 mmol) was added dropwise to a stirred solution of allylic alcohol **19** (168 mg, 0.27 mmol) in THF (1.0 cm^3) at room temperature under nitrogen. The resulting solution was stirred at room temperature for 15 h and then evaporated under reduced pressure to give the crude product. The residue was dissolved in pyridine (1.5 cm^3) and acetic anhydride (1.5 cm^3) and stirred at room temperature for 20 h. Then, water (5 cm^3) and Et_2O (15 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 25 cm^3). The combined organic extracts were washed with water (20 cm^3), dilute hydrochloric acid (2 × 25 cm^3), saturated sodium hydrogencarbonate solution (2 × 25 cm^3) and then water (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with CH_2Cl_2 as eluent gave triacetate **24** (67 mg, 89%) as a pale yellow oil, R_F(10:1 CH_2Cl_2-MeOH) 0.5; ν_{max}(film)/cm^{-1} 1727 (C=O), 1644, 1371, 1262 and 1036; δ_H(270 MHz; $CDCl_3$) 5.94 (1 H, dd, *J* 3.6 and 10.2, *H*C=CH), 5.92-5.87 (1 H, m, HC=C*H*), 5.29-5.25 (1 H, m, CHOAc), 4.15-4.08 (3 H, m, CH_AH_BOAc and CH_2OAc), 4.02 (1 H, dd, *J* 5.8 and 11.4, CH_AH_BOAc), 2.73-2.65 (1 H, m, CH), 2.51-2.38 (1 H, m, CH), 2.07 (3 H, s, CH_3), 2.06 (3 H, s, CH_3), 2.04 (3 H, s, CH_3) and 1.91 1.70 (2 H, m, CH_2); δ_C(67.5 MHz; $CDCl_3$) 170.83 (C=O), 170.71 (C=O), 170.45 (C=O), 132.2 (H*C*=CH), 126.7 (HC=*C*H), 66.1 (CHO), 65.1 (CH_2O), 63.1 (CH_2O), 35.4 (CH), 31.4 (CH), 28.1 (CH_2), 21.2 (CH_3) and 20.9 (2 × CH_3); *m/z* 302 (83%, $M^+ + NH_4$), 225 (100%, M – OAc), 122 (26) and 105 (25)(Found: $M^+ + NH_4$, 302.1606. $C_{14}H_{20}O_6$ requires $M + NH_4$, 302.1604).

(1*S,4*R**,5*S**)-4,5-Di(acetoxymethyl)cyclohexan-1-yl Acetate 25**

Tetrabutylammonium fluoride (2.0 cm^3 of 1 M solution in THF, 2 mmol) was added dropwise to a stirred solution of alcohol **22** (228 mg, 0.36 mmol) in THF (1.5 cm^3) at room temperature under nitrogen. The resulting solution was stirred at room temperature for 15 h and then evaporated under reduced pressure to give the crude product. The residue was dissolved in pyridine (2 cm^3) and acetic anhydride (2 cm^3) and stirred at room temperature for 20 h. Then, water (5 cm^3) and Et_2O (15 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3 × 25 cm^3). The combined organic extracts were washed with water (20 cm^3), dilute hydrochloric acid (2 x 25 cm^3), saturated sodium hydrogencarbonate solution (2 × 25 cm^3) and then water (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product. Purification by flash chromatography on silica with CH_2Cl_2 as eluent gave triacetate **25** (75 mg, 77%) as a pale yellow oil, R_F(10:1 CH_2Cl_2-MeOH) 0.5; ν_{max}(film)/cm^{-1} 1727 (C=O), 1456, 1370, 1261 and 1036; δ_H(270 MHz; $CDCl_3$) 4.99-4.90 (1 H, m, CHOAc), 4.08 (1 H, dd, *J* 7.3 and 16.3, CH_AH_BOAc), 4.04 (1 H, dd, *J* 7.3 and 11.4, CH_AH_BOAc), 4.13-4.00 (2 H, m, CH_2OAc), 2.41-2.30 (1 H, m, CH), 2.13-2.02 (1 H, m, CH), 2.07 (3 H, s, CH_3), 2.06 (3 H, s, CH_3), 2.05 (3 H, s, CH_3) and 1.94-1.27 (6 H, m, 6 × CH); δ_C(67.5 MHz; $CDCl_3$) 170.94 (C=O), 170.88 (C=O), 170.4 (C=O), 68.9 (CHO), 64.4 (CH_2O), 64.3 (CH_2O), 35.8 (CH), 33.7 (CH), 31.4 (CH_2), 28.4 (CH_2), 22.7 (CH_2), 21.3 (CH_3) and 20.9 (2 × CH_3); *m/z* (100%, $M^+ + NH_4$), 227 (10) and 106 (15)(Found: $M^+ + NH_4$, 304.1764. $C_{14}H_{22}O_6$ requires $M + NH_4$, 304.1760).

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