Chiral lithium amide base-mediated rearrangement of bis-protected *meso*-4,5-dihydroxy cyclohexene oxides: enantioselective synthesis of (4*R*,5*S*)- and (4*S*,5*R*)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enone

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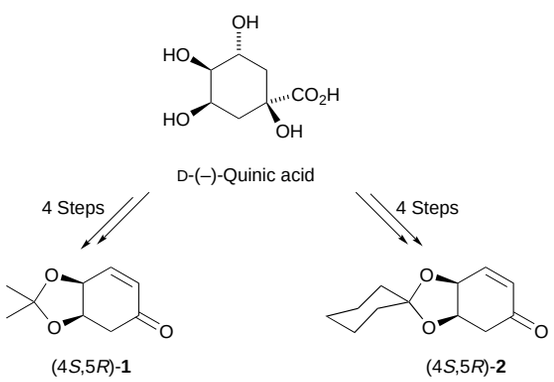
The asymmetric synthesis of (4*R*,5*S*)- and (4*S*,5*R*)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enone are described. Such bis-protected enones are useful intermediates in synthesis, and compounds with (4*S*,5*R*)-stereochemistry have previously been prepared from D-(−)-quinic acid. This paper reports the first synthesis of enones with (4*R*,5*S*)-stereochemistry. The route to the bis-protected enones involves chiral base-mediated rearrangement of *meso*-cyclohexene oxides to allylic alcohols followed by PDC oxidation. Two new chiral base reactions are described: rearrangement of a *trans*-epoxide generates an allylic alcohol of 76% ee (93% yield) whilst that of a *cis*-epoxide produces an allylic alcohol of 92% ee (38% yield); suggestions for the observed differences in yield and enantioselectivities are proposed.

Introduction

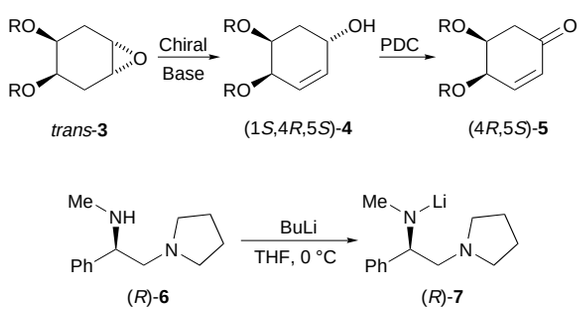
Enantiomerically pure bis-protected 4,5-dihydroxycyclohex-2-enones such as (4*S*,5*R*)-**1** and (4*S*,5*R*)-**2** are useful and versatile intermediates in organic synthesis. Both enones can be readily prepared in multigram quantities from commercially available D-(−)-quinic acid[1–3] (Scheme 1) and have been used in numerous synthetic endeavours.[4–15] Highlights include the preparation of intermediates[4] for the synthesis of the immunosupressant FK-506[5] and for the construction of the tricyclic core of manzamine A;[6] formal syntheses of (+)-aphidoloin[7] and (+)-epibatidine;[8] and total syntheses of the insulin agonist 6-*O*-(2-amino-2-deoxy-α-D-glucopyranosyl)-D-*chiro*-inositol-1-phosphate[9] and (+)-eutypoxide B.[10]



Scheme 1

Despite the usefulness of enones **1** and **2** in synthesis, there have been no reports of the preparation of 'unnatural' enones (4*R*,5*S*)-**1** or (4*R*,5*S*)-**2** and only one report of a synthetic approach to *racemic* **1**.[16] We therefore became interested in developing a route[17] to *enantiomerically enriched* bis-protected enones **5** which would be flexible enough to allow the preparation of a range of enones with protecting groups and stereochemistries different to those present in the known[2,3,16] enones (4*S*,5*R*)-**1** and (4*S*,5*R*)-**2** (Scheme 2).

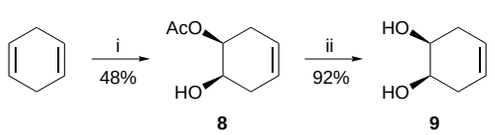
Our proposed route is an extension of Krow's synthesis of racemic **1**[16] and the key step is the chiral lithium amide base-mediated rearrangement of *meso*-cyclohexene oxides such as *trans*-**3** to enantiomerically enriched allylic alcohols **4** (Scheme 2). Such rearrangement reactions[18] are well documented for cyclohexene oxide itself[19,20] and for *meso*-cyclopentene oxides.[20,21] However, prior to our study, there had been only one example of the enantioselective rearrangement of *meso*-cyclohexene oxides.[22] For the conversion of epoxides **3** into allylic alcohols **4**, we intended using Singh's[20] chiral lithium amide bases (*R*)- or (*S*)-**7** [generated from the corresponding diamines (*R*)- or (*S*)-**6** for which we had previously described useful synthetic approaches[23]]. In this way, our synthetic strategy would be suitable for the preparation of enones (4*R*,5*S*)-**5** [and their enantiomers (4*S*,5*R*)-**5**] and we now report in full[17] the success of our approach to enantiomerically enriched bis-protected 4,5-dihydroxycyclohex-2-enones with syntheses of each of enones (4*R*,5*S*)-**5** and (4*S*,5*R*)-**5** (in which R = TBDMS). The syntheses are accomplished *via* two new chiral base-mediated rearrangement reactions of *meso*-cyclohexene oxides.



Scheme 2

Results and discussion

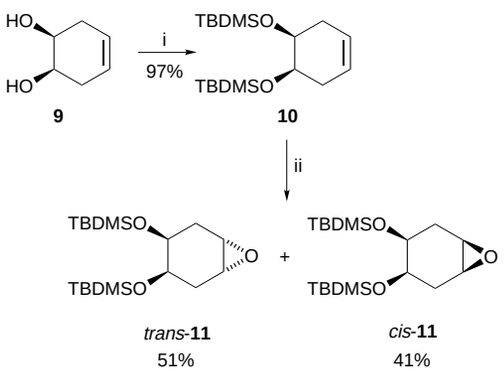
As a starting point, we prepared the known 1,2-diol **9** using a route slightly modified from that reported by Krow[16] (Scheme 3). Woodward hydroxy-acetylation of cyclohexa-1,4-diene



Scheme 3 *Reagents and conditions*: i, (a) KIO_3, I_2, AcOH 60 °C, 3 h; (b) KOAc, reflux, 3 h; (c) water; ii, Amberlite IRA(OH), 2:1 MeOH–THF, rt, 1 h

using iodine and potassium iodate in acetic acid gave a moderate 48% yield of monoacetate **8**. The conversion of monoacetate **8** into 1,2-diol **9** using Krow's method[16] (potassium carbonate in methanol followed by aqueous work-up) was low yielding in our hands due to the water solubility of the product 1,2-diol **9**. Thus, taking our lead from Tschamber,[24] we preferred to use commercially available Amberlite resin in conjunction with methanol to perform the methanolysis. In this way, an excellent and reproducible yield (>90%) of 1,2-diol **9** was obtained.

Our next task was to bis-protect 1,2-diol **9** and then epoxidise the alkene moiety (Scheme 4). Standard bis-silylation using



Scheme 4 *Reagents and conditions*: i, 2.4 equiv. TBDMSCl, 5 equiv. imidazole, CH_2Cl_2, rt, 16 h; ii, *m*-CPBA, CH_2Cl_2, rt, 16 h

TBDMSCl generated the known[25] bis-silyl ether **10** which was epoxidised using *m*-CPBA in CH_2Cl_2 to give a 56:44 mixture of diastereomeric epoxides **11** (as judged by ^{1}H NMR spectroscopy of the crude product mixture†). The low diastereoselectivity of this epoxidation reaction was quite surprising as we had anticipated that epoxidation would occur preferentially *trans* to the bulky axial silylated hydroxy group (Fig. 1).[26] Nonetheless, the two epoxide products **11** were easily separated by chromatography (isolated yields of 51 and 41%) and both were useful substrates for our proposed chiral base rearrangement reactions.

After analysis of each of the diastereomeric epoxides **11** by 500 MHz NOESY experiments, we assigned the major epoxide as *trans*-**11**, the formation of which was rationalised by a slight preference for *m*-CPBA to attack bis-silyl alkene **10** *trans* to the axial substituent (see Fig. 1). Although the assignment of epoxide stereochemistry was also consistent with a predicted and observed difference in the reactivity of *trans*- and *cis*-**11** with chiral base (*R*)-**7** (*vide infra*), we were keen to provide additional evidence to support our assignments. Thus, monosilyl protected alkene **12** (prepared in 80% yield from 1,2-diol **9**) was subjected to a Sharpless transition metal-directed epoxidation (Scheme 5). The single diastereomeric epoxide that was obtained was assigned as *cis*-**13** by literature precedent.[27] The ^{1}H NMR spectrum of epoxide *cis*-**13** was significantly different to that of its diastereomer *trans*-**13** which was obtained as a by-product in the bis-silylation of epoxy diol *trans*-**14**‡ (Scheme 5). In actual fact, we used this difference in the ^{1}H NMR spectra of *cis*- and *trans*-**13** to assign the stereochemistry of epoxy diol *trans*-**14**. This in turn meant that the bis-silyl epoxide obtained from bis-silylation of epoxy diol *trans*-**14** had to be *trans*-**11**,

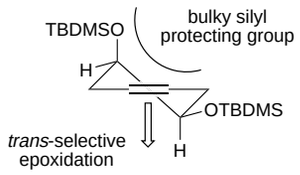
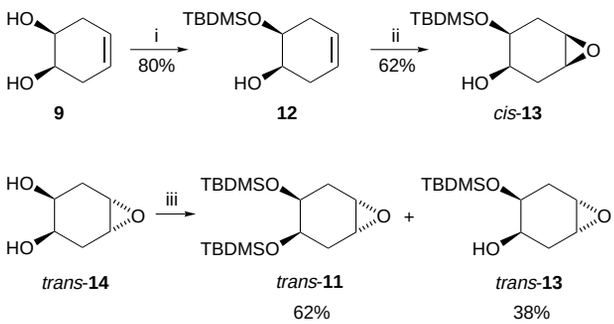


Fig. 1

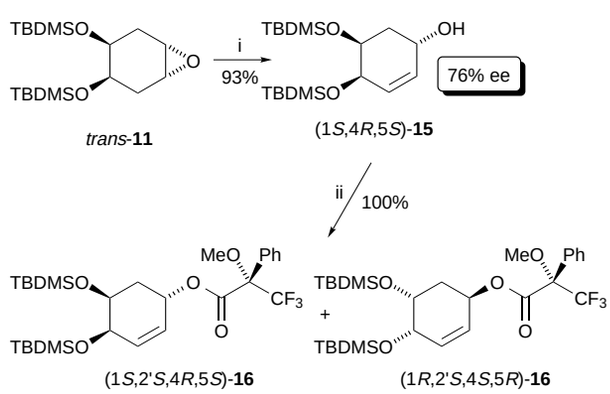


Scheme 5 *Reagents and conditions*: i, 1.2 equiv. TBDMSCl, 2.5 equiv. imidazole, CH_2Cl_2, rt, 22 h; ii, $VO(acac)_2$, 2 equiv. Bu^{t}OOH, CH_2Cl_2–toluene, rt, 24 h; iii, 2 equiv. TBDMSCl, 5 equiv. imidazole, CH_2Cl_2, rt, 72 h

the ^{1}H NMR spectrum of which was identical to the major product of epoxidation of bis-silyl alkene **10** (see Scheme 4). Our assignments of epoxide stereochemistry were therefore established unequivocally.

With epoxides *trans*- and *cis*-**11** separated and in hand, we could now study their chiral base-mediated rearrangement and a direct comparison of the efficiency and enantioselectivity of the two reactions could be assessed. This was especially important because other researchers had found dramatic differences in reactivity and enantioselectivity with diastereomeric *meso*-cyclopentene oxides[20,21] and spiro epoxides.[28]

Chiral diamine (*R*)-**7** was prepared from (*R*)-styrene oxide[23b] and converted into chiral base (*R*)-**7** (see Scheme 2) by treatment with *n*-butyllithium in THF at 0 °C. Then, epoxide *trans*-**11** was added and the resulting solution was allowed to warm slowly to room temperature over 5 hours. After this length of time, the reaction was judged to be complete by TLC and a single allylic alcohol product **15** was isolated in 93% yield (Scheme 6). Preparation of the Mosher's esters **16**[29] in the usual



Scheme 6 *Reagents and conditions*: i, (a) 1.3 equiv. (*R*)-7, THF 0 °C ⟶ rt, 5 h; (b) NH_4Cl (aq.); ii, 1.2 equiv. (*R*)-MTPACl, 2 equiv. Et_3N DMAP, CH_2Cl_2, rt, 16 h

manner indicated that **15** had been generated with an encouraging 76% ee. We initially assigned the allylic alcohol as (1*S*,4*R*,5*S*)-**15** by comparison with the sense of induction obtained by Singh with cyclohexene oxide[20] and by the fact that we knew it had *trans*-relative stereochemistry.

The assignment of the (1*S*,4*R*,5*S*)-stereochemistry was confirmed by NMR analysis of the Mosher's esters **16** using

† The CHO signal for the major epoxide *trans*-**11** appears at δ_H 3.15 ppm whereas that due to the minor epoxide *cis*-**11** appears at δ_H 3.01 ppm; the major epoxide *trans*-**11** is faster running by TLC.

‡ Epoxy diol *trans*-**14** was prepared in the following manner: the diacetate of 1,2-diol **9** was prepared and epoxidised with *m*-CPBA to give a major epoxide product which was isolated pure by chromatography; methanolysis of the diacetate epoxide using Amberlite according to the conditions described in Scheme 2 gave epoxy diol *trans*-**14**. The details of this synthesis will be described elsewhere.

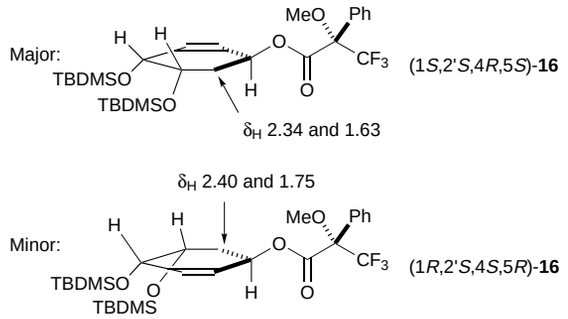
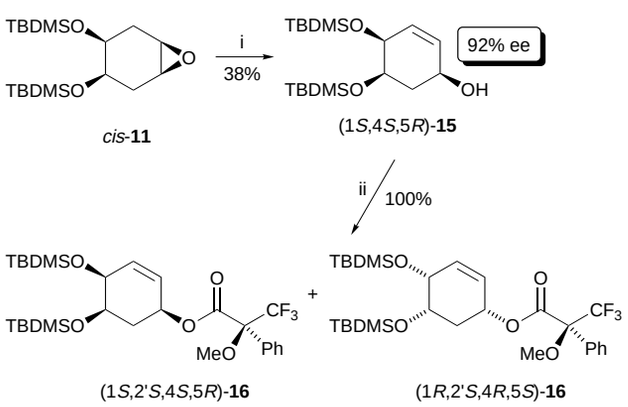


Fig. 2

Kakisawa's method [30] (Scheme 6). The diastereomeric Mosher's esters obtained from allylic alcohol (1*S*,4*R*,5*S*)-**15** of 76% ee are depicted schematically in Fig. 2. The ester moiety prefers to adopt the conformation shown so that the shielding effect of the phenyl ring on the CH_2 adjacent to the stereogenic centre produces predictable effects on the relative chemical shifts of the diastereomeric Mosher's esters. Since the major product had δ_H values for the diastereotopic CH_2 protons which were more upfield than those in the minor product and we knew that the Mosher's ester configuration was (*S*),§ the stereogenic centre of the allylic hydroxy group must also be (*S*).[30a]

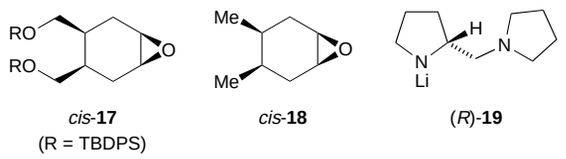
When we reacted the diastereomeric epoxide *cis*-**11** under the same chiral base conditions as for *trans*-**11** [1.3 equiv. of chiral base (*R*)-**7**, THF, 0 °C to room temperature over 5 hours], we found that the reaction was far more sluggish. Even when we left the reaction for 4 hours at 0 °C and then at room temperature for 16 hours, we were only able to isolate a 38% yield of allylic alcohol **15** which was accompanied with a 39% yield of recovered starting material *cis*-**11** (Scheme 7). Although a lower



Scheme 7 *Reagents and conditions*: i, (a) 1.3 equiv. (*R*)-7, THF 0 °C ⟶ rt, 20 h; (b) NH_4Cl (aq.); ii, 1.2 equiv. (*R*)-MTPACl, 2 equiv. Et_3N DMAP, CH_2Cl_2, rt, 16 h

yield of the allylic alcohol was obtained in this case, preparation of the Mosher's esters indicated that the reaction had proceeded with high enantioselectivity (92% ee). The allylic alcohol product was assigned as (1*S*,4*S*,5*R*)-**15** by analogy with Singh's results and by NMR analysis of Mosher's esters **16**.¶

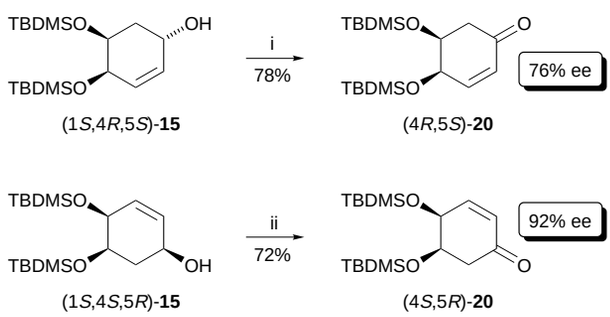
The difference in reactivity and observed enantioselectivities between the rearrangements of epoxides *trans*- and *cis*-**11** using chiral bases is worthy of further comment. Such differences have been observed with diastereomeric spiro epoxides [28] and are not without precedent for *meso*-cyclohexene oxides. For example, we had previously been unable to rearrange epoxide *cis*-**17** using lithium amide *rac*-**7** even though the corresponding



epoxide *trans*-**17** rearranged smoothly.[31] Moreover, Mori and co-workers had found that rearrangement of epoxide *cis*-**18** using Asami's chiral base (*R*)-**19** proceeded with higher enantioselectivity (allylic alcohol of 92% ee) than epoxide *trans*-**18** (allylic alcohol of 69% ee).[22a]

In order to rationalise these observed differences, we prefer to assume that the reaction proceeds *via syn*-elimination of a pseudo-axial β-hydrogen.[32] In *cis* epoxides, there is an axial substituent on the same side as the epoxide and coordinating chiral base: with epoxide *cis*-**17**, steric interactions with this axial substituent are sufficient to prevent reaction; in contrast, with epoxides *cis*-**11** and *cis*-**18**, such steric interactions manifest themselves as improved enantioselectivities when compared to their *trans*-counterparts. Indeed, with *trans*-epoxides, there is a less sterically demanding axial hydrogen on the same side as the epoxide and coordinating chiral base. This is essentially analogous to the situation with cyclohexene oxide and it is comforting to note that the enantioselectivities observed in rearranging cyclohexene oxide with chiral bases (*R*)-**7** (77% enantioselectivity [20]) and (*R*)-**19** (81% enantioselectivity [19c]) are virtually the same as those observed by us for epoxide *trans*-**11** (76% enantioselectivity; see Scheme 6) and by Mori for epoxide *trans*-**18** (69% enantioselectivity [22a]) respectively.

Finally, in order to complete the synthesis of enantiomerically enriched bis-protected 4,5-dihydroxycyclohex-2-enones, allylic alcohols (1*S*,4*R*,5*S*)-**15** and (1*S*,4*S*,5*R*)-**15** were oxidised using PDC to the corresponding cyclohexenones (Scheme 8).



Scheme 8 *Reagents and conditions*: i, 1.3 equiv. PDC, CH_2Cl_2, rt, 3 h; ii, 1.3 equiv. PDC, CH_2Cl_2, rt 4 h

These reactions presented no problems and as expected afforded enantiomeric enones (4*R*,5*S*)-**20** and (4*S*,5*R*)-**20** (confirmed by opposite signs of their optical rotations). Thus, we had developed a route to each enantiomer of cyclohexenones **5** using the same enantiomer of chiral lithium amide base [(*R*)-**7**] to rearrange different diastereomeric epoxides (*trans*- and *cis*-**11**). Alternatively, we could have achieved the same result by combining a single diastereomeric epoxide (*e.g. trans*-**11**) with either enantiomer of chiral base **7**.

In summary, our new route to bis-protected 4,5-dihydroxycyclohex-2-enones **5** is six steps from cyclohexa-1,4-diene. This is only slightly longer than the known four step syntheses from D-(−)-quinic acid.[1–3] Significantly, our method can be used to prepare either enantiomer of a cyclohexenone **5** (R = TBDMS) and we have described the first synthesis of

§ Particular care must be exercised when analysing the Mosher's esters. Because of a change in priority of substituents, (*R*)-Mosher's acid chloride (*R*)-MTPACl has the same absolute stereochemistry as (*S*)-Mosher's acid (*S*)-MTPA and (*S*)-Mosher's esters. Thus, in the example in Scheme 6, (*R*)-MTPACl generates (*S*)-Mosher's esters.

¶ In the case of allylic alcohol (1*S*,4*S*,5*R*)-**15** of 92% ee, it was also necessary to prepare the diastereomeric Mosher's esters from the *racemic* allylic alcohol (generated in 35% yield from reaction of epoxide *cis*-**11** with lithium amide *rac*-**7**) in order to elucidate the signals for the minor diastereomeric Mosher's ester. Full details are described in the Experimental section.

cyclohexenones (4*R*,5*S*)-**5** which have opposite absolute stereochemistry to those enones prepared from D-(−)-quinic acid. Further work is in progress to extend the use of the chiral base-mediated rearrangements of *meso*-cyclohexene oxides in synthesis.

Experimental

General

THF Was dried over sodium–benzophenone and distilled before use. CH_2Cl_2 Was dried over calcium hydride and distilled before use. *n*-Butyllithium was titrated against diphenylacetic acid before use.[33] Amberlite IRA(OH) and *m*-CPBA (approx. 70% pure) were used as supplied by Aldrich Chemical Company Ltd. Light petroleum refers to the fraction boiling in the range 40–60 °C and was redistilled in Winchester quantities before use. All non-aqueous reactions were carried out under oxygen-free nitrogen using oven-dried glassware. Flash column chromatography was carried out using ICN Biomedicals GmbH 33–63 silica (60 Å) according to the method of Still, Kahn and Mitra.[34] Thin layer chromatography was carried out on commercially available Merck 5554 aluminium-backed silica plates.

Proton (270 MHz) and carbon (67.5 MHz) NMR spectra were recorded on a JEOL EX-270 spectrometer using an internal deuterium lock. All samples were recorded as solutions in deuteriated chloroform and chemical shifts are quoted in parts per million downfield of tetramethylsilane. Coupling constant (*J*) values are given in Hz. Carbon NMR spectra were recorded with broad band proton decoupling and were assigned using DEPT experiments. ^1H–^1H and ^1H–^{13}C COSY experiments were recorded on a JEOL EX-270 spectrometer whereas NOESY experiments were carried out on a Bruker AMX-500 spectrometer.

Melting points were measured on an Electrothermal IA 9100 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis FT IR spectrometer as neat films or as solutions in chloroform. Chemical ionisation and high resolution mass spectra were recorded on a Fisons Analytical (VG) Autospec spectrometer. Optical rotations were recorded on a JASCO DIP-370 polarimeter (using the sodium D line; 589 nm) at 20 °C and $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. Microanalyses were carried out at the University of East Anglia.

The synthesis of *rac*- and (*R*)-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine has been described in full elsewhere.[23b]

General methods

Method A: rearrangement of epoxides to allylic alcohols

n-Butyllithium (1.5 M solution in hexane, 1.05 mmol) was added dropwise to a stirred solution of *rac*- or (*R*)-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (1.0 mmol) in THF (2.5 cm^3) at 0 °C under nitrogen. After 30 min at 0 °C, a solution of the epoxide *trans*- or *cis*-**11** (0.8 mmol) in THF (2.5 cm^3) was added dropwise by means of a cannula and the resulting solution was allowed to warm to room temperature over 4 h. After stirring at room temperature for the required length of time (1 or 16 h), saturated aqueous ammonium chloride (3 cm^3) and Et_2O (20 cm^3) were added and the layers were separated. The aqueous layer was diluted with water (10 cm^3) and then 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 (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a pale yellow oil which was purified by flash column chromatography.

Method B: preparation of Mosher's esters

(*R*)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (0.05 mmol; 98% ee) was added dropwise to a stirred solution of the allylic alcohol (0.03 mmol), triethylamine (0.07 mmol) and catalytic DMAP (1 mg) in CH_2Cl_2 (2 cm^3) at room temperature under nitrogen. After 16 h, water (5 cm^3) and Et_2O (10 cm^3) were added. The layers were separated and the aqueous layer was extracted with Et_2O (2 × 10 cm^3). The combined organic extracts were washed with 2% hydrochloric acid (10 cm^3) and then with water (10 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil which was analysed by ^1H NMR spectroscopy.

(4*R**,5*S**)-5-Acetoxy-4-hydroxycyclohexene 8

Cyclohexa-1,4-diene (10.0 g, 0.125 mol) was added to a stirred solution of potassium iodate (5.7 g, 0.031 mol) and iodine (15.8 g, 0.0625 mol) in glacial acetic acid (200 cm^3) and the resulting mixture was stirred at 60 °C for 3 h. After cooling to room temperature, potassium acetate (12.5 g, 0.125 mol) was added and the resulting solution was refluxed for an additional 3 h. After cooling, water (2.0 cm^3) was added and the solvent was evaporated under reduced pressure. Et_2O (125 cm^3) was added and the organic layer was washed with saturated aqueous sodium thiosulfate (2 × 50 cm^3) to remove the residual iodine, dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a brown oil. Purification by flash chromatography on silica with Et_2O–light petroleum (1:3 ⟶ 3:1) as eluent gave known[16] monoacetate **8** (9.35 g, 48%) as a pale yellow oil; R_F(3:1 Et_2O–light petroleum) 0.3; ν_{max}(film)/cm^{-1} 3452 (OH), 3031, 2919, 1734 (C=O), 1654 (C=C), 1374, 1248, 1035 and 671; δ_H(270 MHz; $CDCl_3$) 5.60 (2 H, s, HC=CH), 5.06 [1 H, ddd, *J* 2.0, 6.0 and 7.0 (appearing as a triplet of doublets), C*H*OAc], 4.06 [1 H, ddd, *J* 2.0, 5.0 and 5.0 (appearing as a triplet of doublets), C*H*OH], 2.47–2.28 (4 H, m, 2 × CH_2) and 2.11 (3 H, s, Me); δ_C(67.5 MHz; $CDCl_3$) 171.1 (C=O), 123.6 (H*C*=CH), 123.4 (HC=*C*H), 72.1 (CHOAc), 67.1 (CHOH), 31.45 (CH_2), 27.7 (CH_2) and 21.2 (Me); *m*/*z* (CI, NH_3) 157 [100%, $(M + H)^+$], 139 (15, M − OH) and 96 (M − OAc) [Found: $(M + H)^+$, 157.0866. $C_8H_{12}O_3$ requires *M* + H, 157.0865].

(4*R**,5*S**)-4,5-Dihydroxycyclohexene 9

Amberlite IRA(OH) (12.9 g) was added to a stirred solution of monoacetate **8** (3.45 g, 21.8 mmol) in MeOH (20 cm^3) and THF (8 cm^3) under nitrogen at room temperature. After 1 h, the mixture was filtered and the resin was washed well with hot MeOH (30 cm^3). Then, the filtrate was evaporated under reduced pressure to give the crude product. Purification by flash chromatography using a short plug of silica with EtOAc as eluent gave known[24] diol **9** (2.29 g, 92%) as white crystals, mp 79–80 °C (from EtOAc) (lit.,[24] 79 °C); R_F(EtOAc) 0.2; δ_H(270 MHz; $CDCl_3$) 5.57 (2 H, t, *J* 1.5, =CH), 3.93 (2 H, t, *J* 5.5, C*H*OH), 3.20 (2 H, br s, CHO*H*) and 2.38–2.10 (4 H, m, CH_2); δ_C(67.5 MHz; $CDCl_3$) 123.7 (=CH), 68.9 (CHOH) and 30.9 (CH_2); *m*/*z* (CI, NH_3) 132 [100%, $(M + NH_4)^+$] [Found: $(M + NH_4)^+$, 132.1026. $C_6H_{10}O_2$ requires *M* + NH_4, 132.1024].

(4*R**,5*S**)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohexene 10

Imidazole (6.74 g, 99.0 mmol) and *tert*-butyldimethylsilyl chloride (7.01 g, 46.5 mmol) were added successively in portions to a stirred solution of diol **9** (2.23 g, 19.5 mmol) in CH_2Cl_2 (50 cm^3) at room temperature under nitrogen. After 16 h, water (20 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (30 cm^3). The combined organic extracts were washed with 2% hydrochloric acid (30 cm^3) and then water (30 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with light petroleum–EtOAc (40:1) as eluent gave known[25] bis-silyl alkene **10** (6.47 g, 97%) as a colourless oil; R_F(EtOAc) 0.7; ν_{max}(film)/cm^{-1} 3029, 2956, 2857, 1471, 1251 (SiBu^{t}Me$_2$) and 1122 (SiBu^{t}Me$_2$); δ_H(270 MHz; $CDCl_3$) 5.49 (2 H, t, *J* 1.5, =CH), 3.84 [2 H, ddd, *J* 1.0, 4.0 and 6.0 (appearing as a triplet

of doublets), CHOSi], 2.26–2.08 (4 H, m, CH_2), 0.88 (18 H, s, CMe_3), 0.06 (6 H, s, $SiMe_AMe_B$) and 0.04 (6 H, s, $SiMe_AMe_B$); δ_C(67.5 MHz; $CDCl_3$) 124.1 (=CH), 70.7 (CHOSi), 32.6 (CH_2), 26.0 (CMe_3), 18.2 (CMe_3), −4.4 ($SiMe_AMe_B$) and −4.7 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 343 [100%, $(M + H)^+$], 285 (20, $M - CMe_3$) and 211 (30, $M - OSiBu^tMe_2$) [Found: $(M + H)^+$, 343.2492. $C_{18}H_{38}O_2Si_2$ requires *M* + H, 343.2489].

(1*S**,2*R**,4*R**,5*S**)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohexene oxide *trans*-11 and (1*R**,2*S**,4*R**,5*S**)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohexene oxide *cis*-11

m-CPBA (1.3 g of 70% pure material, 5.3 mmol) Was added in one portion to a stirred solution of bis-silyl alkene **10** (1.5 g, 4.3 mmol) in CH_2Cl_2 (17 cm^3) at room temperature under nitrogen. After 16 h, 20% aqueous sodium sulfite (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 (2 × 40 cm^3). The combined organic extracts were washed with 20% aqueous sodium sulfite (20 cm^3) and then saturated aqueous sodium hydrogen carbonate (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil (1.56 g, 100%) which contained a 56:44 mixture of epoxides *trans*- and *cis*-**11** (by ^1H NMR spectroscopy). Purification by flash chromatography on silica with light petroleum–EtOAc (20:1) as eluent gave epoxide *trans*-**11** (785 mg, 51%) as a colourless oil; R_F(20:1 light petroleum–EtOAc) 0.4; ν_{max}(film)/cm^{-1} 2952, 2927, 2857, 1471, 1371, 1255 ($SiBu^tMe_2$), 1139, 1105, 1078, 836 ($SiBu^tMe_2$) and 777; δ_H(270 MHz; $CDCl_3$) 3.67 [2 H, dd, *J* 5.0 and 5.0 (appearing as a triplet), CHOSi], 3.15 (2 H, d, *J* 1.0, CHO), 2.12–1.95 (4 H, m, CH_2), 0.88 (18 H, s, CMe_3) and 0.04 (12 H, s, $SiMe_2$); δ_C(67.5 MHz; $CDCl_3$) 68.8 (CHOSi), 52.1 (CHO), 31.2 (CH_2), 25.9 (CMe_3), 18.1 (CMe_3), −4.5 ($SiMe_AMe_B$) and −4.8 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 359 [100%, $(M + H)^+$], 301 (25, $M - CMe_3$) and 227 (20, $M - OSiBu^tMe_2$) [Found: $(M + H)^+$, 359.2441. $C_{18}H_{38}O_3Si_2$ requires *M* + H, 359.2438] and epoxide *cis*-**11** (634 mg, 41%) as a colourless oil; R_F(20:1 light petroleum–EtOAc) 0.3; ν_{max}(film)/cm^{-1} 2954, 2929, 2856, 1473, 1253 ($SiBu^tMe_2$), 1108, 1083, 879, 836 ($SiBu^tMe_2$) and 775; δ_H(270 MHz; $CDCl_3$) 3.67 (2 H, ddd, *J* 1.0, 4.0 and 6.5, CHOSi), 3.03–2.99 (2 H, m, CHO), 2.18 (2 H, ddd, *J* 1.0, 6.5 and 15.0, CH_AH_B), 1.89 (2 H, dddd, *J* 1.0, 2.5, 4.0 and 15.0, CH_AH_B), 0.84 (18 H, s, CMe_3) and 0.01 (12 H, s, $SiMe_2$); δ_C(67.5 MHz; $CDCl_3$) 69.7 (CHOSi), 50.1 (CHO), 30.7 (CH_2), 25.9 (CMe_3), 18.2 (CMe_3), −4.5 ($SiMe_AMe_B$) and −4.8 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 359 [100%, $(M + H)^+$] [Found: $(M + H)^+$, 359.2441. $C_{18}H_{38}O_3Si_2$ requires *M* + H, 359.2438].

The assignments of the relative stereochemistry of epoxides *trans*- and *cis*-**11** were made using 500 MHz NOESY experiments. For epoxide *trans*-**11**, there was no detectable NOE between the signals at δ_H 3.67 and 3.15 ppm. In contrast, for epoxide *cis*-**11**, there was a weak NOE between the signals at δ_H 3.67 and 3.01 ppm.

(4*R**,5*S**)-5-*tert*-Butyldimethylsilyloxy-4-hydroxycyclohexene 12

Imidazole (1.50 g, 22.0 mmol) and *tert*-butyldimethylsilyl chloride (1.56 g, 10.4 mmol) were added successively in portions to a stirred solution of diol **9** (1.0 g, 8.8 mmol) in CH_2Cl_2 (20 cm^3) at room temperature under nitrogen. After 22 h, water (10 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were washed with 2% hydrochloric acid (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by flash chromatography on silica with EtOAc as eluent gave monosilyl alkene **12** (1.61 g, 80%) as a pale yellow oil; R_F(40:1 light petroleum–EtOAc) 0.4; ν_{max}(film)/cm^{-1} 3464 (OH), 2951, 1466, 1087 ($SiBu^tMe_2$) and 837 ($SiBu^tMe_2$); δ_H(270 MHz; $CDCl_3$) 5.58–5.50 (2 H, m, =CH), 3.92–3.85 (2 H, m, C*H*OSi and C*H*OH), 2.31–2.18 (4 H, m, CH_2), 0.88 (9 H, s, CMe_3), 0.09 (3 H, s, $SiMe_AMe_B$) and 0.08 (3 H, s, $SiMe_AMe_B$); δ_C(67.5 MHz; $CDCl_3$) 123.8 (=CH), 123.5 (=CH), 69.8 (CHOSi), 69.1 (CHOH), 31.3 (CH_2), 30.5 (CH_2), 25.8 (CMe_3), 18.1 (CMe_3), −4.5 ($SiMe_AMe_B$) and −4.8 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 229 [75%, $(M + H)^+$], 211 (100, $M - OH$) and 171 (25, $M - CMe_3$) [Found: $(M + H)^+$, 229.1616. $C_{12}H_{24}O_2Si$ requires *M* + H, 229.1624].

(1*R**,2*S**,4*R**,5*S**)-5-*tert*-Butyldimethylsilyloxy-4-hydroxycyclohexene oxide *cis*-13

Vanadyl acetylacetonate (2.5 mg, 0.01 mmol) was added to a stirred solution of monosilyl alkene **12** (200 mg, 0.88 mmol) and *tert*-butyl hydroperoxide (0.63 cm^3 of a 2.63 M solution in toluene, 1.6 mmol) in CH_2Cl_2 (5 cm^3) at room temperature under nitrogen. After 24 h, 20% aqueous sodium sulfite (5 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3). The combined organic extracts were washed with 20% sodium sulfite (20 cm^3), saturated aqueous sodium hydrogen carbonate (20 cm^3) and then water (20 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product which contained a >97:3 mixture of epoxides *cis*- and *trans*-**13** (by ^1H NMR spectroscopy). Purification by flash chromatography on silica with light petroleum–EtOAc (2:1) as eluent gave epoxide *cis*-**13** (133 mg, 62%) as a yellow oil; R_F(1:1 light petroleum–EtOAc) 0.5; ν_{max}(film)/cm^{-1} 3499 (OH), 2937 and 1105 ($SiBu^tMe_2$); δ_H(270 MHz; $CDCl_3$) 3.72–3.66 (2 H, m, C*H*OSi and C*H*OH), 3.22–3.19 (2 H, m, CHO), 2.68 (1 H, br d, *J* 7.8, OH), 2.47–1.96 (4 H, m, CH_2), 0.90 (9 H, s, CMe_3) and 0.08 (6 H, s, $SiMe_2$); δ_C(67.5 MHz; $CDCl_3$) 69.7 (CHOSi), 68.9 (CHOH), 52.1 (CHO), 51.5 (CHO), 30.3 (CH_2), 29.0 (CH_2), 25.8 (CMe_3), 18.1 (CMe_3), −4.6 ($SiMe_AMe_B$) and −4.7 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 262 [75%, $(M + NH_4)^+$] and 245 [100%, $(M + H)^+$] [Found: $(M + H)^+$, 245.1566. $C_{12}H_{24}O_3Si$ requires *M* + H, 245.1573].

(1*S**,2*R**,4*R**,5*S**)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohexene oxide *trans*-11 and (1*S**,2*R**,4*R**,5*S**)-5-*tert*-butyldimethylsilyloxy-4-hydroxycyclohexene oxide *trans*-13

Imidazole (132 mg, 1.9 mmol), *tert*-butyldimethylsilyl chloride (139 mg, 0.9 mmol) and catalytic DMAP (2 mg) were added successively in portions to a stirred solution of epoxy diol *trans*-**14** (49 mg, 0.4 mmol) in CH_2Cl_2 (2 cm^3) at room temperature under nitrogen. After 72 h, water (5 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were washed with water (10 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by flash chromatography on silica with light petroleum–EtOAc (10:1 ⟶ 1:1) as eluent gave epoxide *trans*-**11** (83 mg, 62%) as a colourless oil and epoxide *trans*-**13** (36 mg, 38%) as a pale yellow oil; R_F(4:1 light petroleum–EtOAc) 0.2; ν_{max}(film)/cm^{-1} 3577 (OH), 1128 ($SiBu^tMe_2$) and 835 ($SiBu^tMe_2$); δ_H(270 MHz; $CDCl_3$) 3.80 (1 H, ddd, *J* 2.0, 5.0 and 7.5, CHOSi), 3.66 (1 H, br m, C*H*OH), 3.21 (1 H, m, CHO), 3.12 (1 H, m, CHO), 2.18–2.09 (3 H, m, CH_2 and CH_AH_B), 2.00 (1 H, ddd, *J* 2.5, 8.0 and 15.0), 0.88 (9 H, s, CMe_3), 0.06 (3 H, s, $SiMe_AMe_B$) and 0.05 (3 H, s, $SiMe_AMe_B$); δ_C(67.5 MHz; $CDCl_3$) 67.9 (CHO), 67.5 (CHO), 53.0 (CHO), 50.2 (CHO), 30.0 (CH_2), 29.0 (CH_2), 25.7 (CMe_3), 18.0 (CMe_3), −4.7 ($SiMe_AMe_B$) and −4.9 ($SiMe_AMe_B$); *m*/*z* (CI, NH_3) 262 [30%, $(M + NH_4)^+$], 245 [100, $(M + H)^+$] and 227 (20, $M - OH$) [Found: $(M + H)^+$, 245.1574. $C_{12}H_{24}O_3Si$ requires *M* + H, 245.1573].

(1*S*,4*R*,5*S*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enol 15

Using general method A, *n*-butyllithium (0.7 cm^3 of a 1.5 M solution in hexane, 1.05 mmol), (*R*)-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (206 mg, 1.0 mmol) and epoxide

trans-**11** (280 mg, 0.8 mmol) in THF (5 cm^3) gave the crude product after 5 h at 0 °C ⟶ room temperature. Purification by flash chromatography on silica with light petroleum–EtOAc (5:1) as eluent gave allylic alcohol (1*S*,4*R*,5*S*)-**15** (261 mg, 93%, 76% ee) as white crystals, mp 60–62 °C (from light petroleum); R_F(4:1 light petroleum–EtOAc) 0.4; $[\alpha]_D$ −87.1 (*c* 0.6 in $CHCl_3$) [Found: C, 60.5; H, 10.7%; $(M + H)^+$, 359.2447. $C_{18}H_{38}O_3Si_2$ requires C, 60.3; H, 10.7%; *M* + H, 359.2438]; $\nu_{max}(CHCl_3)$/cm^{-1} 3606 (OH), 1601 (C=C) and 835 (SiBu^{t}Me$_2$); δ_H(270 MHz; $CDCl_3$) 5.75 (1 H, m, H^2), 5.65 [1 H, dddd, *J* 1.0, 1.0, 3.0 and 10.0 (appearing as a double double triplet), H^3], 4.45 (1 H, m, H^1), 4.13 [1 H, dddd, *J* 1.0, 1.0, 3.0 and 3.0 (appearing as a triplet of triplets), H^4], 4.07 [1 H, ddd, *J* 2.0, 3.0 and 8.0 (appearing as a doublet of triplets), H^5], 2.25 (1 H, dddd, *J* 0.5, 5.0, 8.0 and 13.0, CH_AH$_B$), 1.55 (1 H, ddd, *J* 2.2, 6.0 and 13.0, CH$_A$$H_B$), 0.90 (9 H, CMe$_3$), 0.89 (9 H, CMe$_3$), 0.08 (3 H, s, SiMe), 0.08 (3 H, s, SiMe), 0.08 (3 H, s, SiMe) and 0.07 (3 H, s, SiMe); δ_C(67.5 MHz; $CDCl_3$) 131.1 (C^3), 130.3 (C^2), 69.7 (C^5), 68.8 (C^4), 65.9 (C^1), 37.5 (C^6), 26.0 (C*Me*$_3$), 25.9 (C*Me*$_3$), 18.35 (*C*Me$_3$), 18.3 (*C*Me$_3$), −4.4 (2 × SiMe) −4.6 (SiMe) and −4.9 (SiMe); *m*/*z* (CI, NH_3) 359 [25%, $(M + H)^+$], 341 (10, M − OH), 301 (10, M − CMe$_3$) and 227 (100, M − OSiBu^{t}Me$_2$).

The ^{1}H and ^{13}C NMR spectra were fully assigned using ^{1}H–^{1}H and ^{1}H–^{13}C COSY experiments.

(1*S,4*R**,5*S**)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enol 15**

Using general method A, *n*-butyllithium (0.95 cm^3 of a 1.5 M solution in hexane, 1.4 mmol), *rac*-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (288 mg, 1.4 mmol) and epoxide *trans*-**11** (460 mg, 1.3 mmol) in THF (12.5 cm^3) gave the crude product after 16 h at 0 °C ⟶ room temperature. Purification by flash chromatography on silica with light petroleum–EtOAc (10:1 ⟶ 5:1) as eluent gave allylic alcohol (1*S**,4*R**,5*S**)-**15** (355 mg, 77%) as white crystals, mp 57–58°C (from light petroleum) [Found: C, 60.5; H, 10.7%; $(M + H)^+$, 359.2440. $C_{18}H_{38}O_3Si_2$ requires C, 60.3; H, 10.7%; *M* + H, 359.2438].

(1*S*,4*S*,5*R*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enol 15

Using general method A, *n*-butyllithium (0.75 cm^3 of a 1.5 M solution in hexane, 1.1 mmol), (*R*)-*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (232 mg, 1.14 mmol) and epoxide *cis*-**11** (319 mg, 0.9 mmol) in THF (6 cm^3) gave the crude product after 20 h at 0 °C ⟶ room temperature. Purification by flash chromatography on silica with light petroleum–EtOAc (6:1) as eluent gave recovered epoxide *cis*-**11** (125 mg, 39%) as a colourless oil and allylic alcohol (1*S*,4*S*,5*R*)-**15** (120 mg, 38%, 92% ee) as white crystals, mp 43–45 °C (from light petroleum); R_F(4:1 light petroleum–EtOAc) 0.5; $[\alpha]_D$ +20.6 (*c* 0.6 in $CHCl_3$) [Found: C, 60.5; H, 10.9%; $(M + H)^+$, 359.2457. $C_{18}H_{38}O_3Si_2$ requires C, 60.3; H, 10.7%; *M* + H, 359.2438]; $\nu_{max}(CHCl_3)$/cm^{-1} 3527 (OH), 1601 (C=C), 1121 (SiBu^{t}Me$_2$) and 836 (SiBu^{t}Me$_2$); δ_H(270 MHz; $CDCl_3$) 5.85 [1 H, dddd, *J* 1.5, 1.5, 3.0 and 10.0 (appearing as a doublet of quintets), H^2], 5.56 [1 H, dddd, *J* 1.0, 1.0, 2.0 and 10.0 (appearing as a doublet of quintets), H^3], 4.12 (1 H, m, H^4), 4.10–4.02 (1 H, m, H^1), 4.00 (1 H, m, H^5), 2.93 (1 H, d, *J* 10.5, CHO*H*), 2.13 (1 H, dddd, *J* 1.0, 3.5, 6.0 and 14.0, CH_AH$_B$), 1.86 (1H, ddd, *J* 1.5, 5.0 and 14.0, CH$_A$$H_B$), 0.92 (9 H, CMe$_3$), 0.89 (9 H, CMe$_3$), 0.12 (3 H, s, SiMe), 0.11 (3 H, s, SiMe) and 0.09 (6 H, s, 2 × SiMe); δ_C(67.5 MHz; $CDCl_3$) 130.2 (C^2), 130.0 (C^3), 70.1 (C^4 or C^5), 70.0 (C^4 or C^5), 64.6 (C^1), 35.7 (C^6), 26.1 (C*Me*$_3$), 25.9 (C*Me*$_3$), 18.4 (*C*Me$_3$), 18.2 (*C*Me$_3$), −4.4 (2 × SiMe), −4.7 (SiMe) and −4.9 (SiMe); *m*/*z* (CI, NH_3) 359 [10%, $(M + H)^+$], 341 (100, M − OH), 301 (10, M − CMe$_3$) and 227 (50, M − OSiBu^{t}Me$_2$).

The ^{1}H and ^{13}C NMR spectra were fully assigned using ^{1}H–^{1}H and ^{1}H–^{13}C COSY experiments.

(1*S,4*S**,5*R**)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enol 15**

Using general method A, *n*-butyllithium (0.45 cm^3 of a 1.5 M solution in hexane, 0.7 mmol), *rac* -*N*-methyl-1-phenyl-2-(pyrrolidin-1-yl)ethanamine (138 mg, 0.7 mmol) and epoxide *cis*-**11** (220 mg, 0.6 mmol) in THF (5 cm^3) gave the crude product after 20 h at 0 °C ⟶ room temperature. Purification by flash chromatography on silica with light petroleum–EtOAc (10:1 ⟶ 5:1) as eluent gave recovered epoxide *cis*-**11** (90 mg, 41%) as a colourless oil and allylic alcohol (1*S**,4*S**,5*R**)-**15** (76 mg, 35%) as white crystals, mp 56–58 °C (from light petroleum) [Found: C, 60.65; H, 10.8%; $(M + H)^+$, 359.2433. $C_{18}H_{38}O_3Si_2$ requires C, 60.3; H, 10.7%; *M* + H, 359.2438].

(1*S*,2′*S*,4*R*,5*S*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate 16

Using general method B, (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (10 μl, 0.05 mmol; 98% ee), allylic alcohol (1*S*,4*R*,5*S*)-**15** (12 mg, 0.03 mmol), triethylamine (10 μl, 0.07 mmol) and catalytic DMAP (1 mg) in CH_2Cl_2 (2 cm^3) gave the crude product as a colourless oil (20 mg, 100%); R_F(10:1 light petroleum–EtOAc) 0.5; δ_H(270 MHz; $CDCl_3$) for Mosher's ester (1*S*,2′*S*,4*R*,5*S*)-**16**: 7.53–7.49 (2 H, m, Ph), 7.42–7.37 (3 H, m, Ph), 5.88 (1 H, dd, *J* 3.5 and 10.0, *H*C=CH), 5.80 (1 H, dd, *J* 3.5 and 10.0, HC=C*H*), 5.67 (1 H, m, H^1), 4.11 [1 H, dd, *J* 3.0 and 3.0 (appearing as a triplet), H^4 or H^5], 4.00 [1 H, ddd, *J* 3.0, 3.0 and 9.0 (appearing as a triplet), H^4 or H^5], 3.55 (3 H, q, *J* 1.0, OMe), 2.34 (1 H, ddd, *J* 5.0, 9.0 and 14.0, CH_AH$_B$), 1.63 (1 H, ddd, *J* 1.5, 4.0 and 14.0, CH$_A$$H_B$), 0.89 (9 H, CMe$_3$), 0.87 (9 H, CMe$_3$), 0.07 (9 H, s, 3 × SiMe) and 0.01 (3 H, s, SiMe); δ_H(270 MHz; $CDCl_3$) for Mosher's ester (1*RS*,2′*S*,4*S*,5*R*)-**16**: 3.52 (3 H, q, *J* 1.0, OMe), 2.40 (1 H, ddd, *J* 5.0, 9.0 and 14.0, CH_AH$_B$) and 1.75 (1 H, ddd, *J* 1.5, 4.0 and 14.0, CH$_A$$H_B$).

(1*S*,2′*S*,4*S*,5*R*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate 16

Using general method B, (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (12 μl, 0.06 mmol; 98% ee), allylic alcohol (1*S*,4*S*,5*R*)-**15** (16 mg, 0.045 mmol), triethylamine (10 μl, 0.07 mmol) and catalytic DMAP (1 mg) in CH_2Cl_2 (2 cm^3) gave the crude product as a colourless oil (26 mg, 100%); R_F(10:1 light petroleum–EtOAc) 0.5; δ_H(270 MHz; $CDCl_3$) for Mosher's ester (1*S*,2′*S*,4*S*,5*R*)-**16**: 7.56–7.51 (2 H, m, Ph), 7.43–7.35 (3 H, m, Ph), 5.91 (1 H, ddd, *J* 1.5, 5.0 and 10.0, *H*C=CH), 5.73 (1 H, ddd, *J* 1.0, 2.5 and 10.0, HC=C*H*), 5.52 (1 H, m, H^1), 4.02 (1 H, m, H^4 or H^5), 3.66 [1 H, ddd, *J* 3.0, 3.0 and 11.5 (appearing as a doublet of triplets), H^4 or H^5], 3.56 (3 H, q, *J* 1.0, OMe), 2.12 [1 H, ddd, *J* 9.0, 11.5 and 11.5 (appearing as a triplet of doublets), CH_AH$_B$], 1.99 (1 H, m, CH$_A$$H_B$), 0.89 (9 H, CMe$_3$), 0.86 (9 H, CMe$_3$), 0.08 (3 H, s, SiMe), 0.06 (3 H, s, 2 × SiMe) and 0.04 (3 H, s, SiMe).

(1*S*,2′*S*,4*S*,5*R*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate 16 and (1*R*,2′*S*,4*R*,5*S*)-4,5-bis(*tert*-butyldimethylsilyloxy)cyclohex-2-en-1-yl 2′-methoxy-2′-trifluoromethyl-2′-phenylacetate 16

Using general method B, (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (10 μl, 0.05 mmol; 98% ee), allylic alcohol (1*S**,4*S**,5*R**)-**15** (13 mg, 0.04 mmol), triethylamine (10 μl, 0.07 mmol) and catalytic DMAP (1 mg) in CH_2Cl_2 (2 cm^3) gave the crude product as a colourless oil (21 mg, 100%); R_F(10:1 light petroleum–EtOAc) 0.5; δ_H(270 MHz; $CDCl_3$) for Mosher's ester (1*R*,2′*S*,4*R*,5*S*)-**16**: 7.56–7.51 (2 H, m, Ph), 7.43–7.35 (3 H, m, Ph), 5.87 (1 H, ddd, *J* 1.5, 5.0 and 10.5, *H*C=CH), 5.59 (1 H, ddd, *J* 1.0, 2.5 and 10.5, HC=C*H*), 5.52 (1 H, m, H^1), 4.02 (1 H, m, H^4 or H^5), 3.67 [1 H, ddd, *J* 3.0, 3.0 and 11.5 (appearing as a doublet of triplets), H^4 or H^5], 3.57 (3 H, q, *J* 1.0, OMe), 2.20 [1 H, ddd, *J* 9.5, 11.5 and 11.5 (appearing as a triplet of doublets), CH_AH$_B$], 2.03 (1 H, m, CH$_A$$H_B$), 0.90 (9 H, CMe$_3$), 0.85 (9 H, CMe$_3$), 0.09 (3 H, s, SiMe), 0.07 (3 H, s, 2 × SiMe) and 0.05 (3 H, s, SiMe).

(4*R*,5*S*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enone 20 Pyridinium dichromate (71 mg, 0.19 mmol) was added in one portion to a stirred solution of allylic alcohol (1*S*,4*R*,5*S*)-**15** (48 mg, 0.13 mmol) in CH_2Cl_2 (2 cm^3) at room temperature under nitrogen. After 3 h, the crude reaction mixture was purified directly by flash chromatography on silica with light petroleum–EtOAc (9:1) as eluent to give enone (4*R*,5*S*)-**20** (37 mg, 78%, 76% ee) as a waxy solid; R_F(4:1 light petroleum–EtOAc) 0.55; $[\alpha]_D$ −93.0 (*c* 0.7 in $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1680 (C=O), 1601 (C=C), 1159 ($SiBu^tMe_2$) and 835 ($SiBu^tMe_2$); δ_H(270 MHz; $CDCl_3$) 6.70 (1 H, ddd, *J* 1.0, 3.0 and 10.0, H^3), 5.96 (1 H, dd, *J* 1.5 and 10.0, H^2), 4.43 [1 H, ddd, *J* 1.5, 3.0 and 3.0 (appearing as a triplet of doublets), H^4], 4.18 (1 H, dddd, *J* 1.0, 3.0, 3.0 and 7.0, H^5), 2.75 (1 H, dd, *J* 7.0 and 16.0, CH_AH_B), 2.47 (1 H, dd, *J* 3.0 and 16.0, CH_AH_B), 0.91 (9 H, CMe_3), 0.85 (9 H, CMe_3), 0.12 (3 H, s, SiMe), 0.12 (3 H, s, SiMe) and 0.05 (6 H, s, 2 × SiMe); δ_C(67.5 MHz; $CDCl_3$) 198.0 (C=O), 149.2 (C^3), 129.3 (C^2), 71.5 (C^4 or C^5), 69.4 (C^4 or C^5), 44.5 (C^6), 25.9 (CMe_3), 25.7 (CMe_3), 18.3 (CMe_3), 18.1 (CMe_3), −4.5 (2 × SiMe), −4.7 (SiMe) and −4.9 (SiMe); *m*/*z* (CI, NH_3) 357 [25%, $(M + H)^+$] and 225 (100, $M - OSiBu^tMe_2$) [Found: $(M + H)^+$, 357.2281. $C_{18}H_{36}O_3Si_2$ requires *M* + H, 357.2281].

(4*S*,5*R*)-4,5-Bis(*tert*-butyldimethylsilyloxy)cyclohex-2-enone 20 Pyridinium dichromate (80 mg, 0.21 mmol) was added in one portion to a stirred solution of allylic alcohol (1*S*,4*S*,5*R*)-**15** (43 mg, 0.12 mmol) in CH_2Cl_2 (2 cm^3) at room temperature under nitrogen. After 4 h, the crude reaction mixture was purified directly by flash chromatography on silica with light petroleum–EtOAc (9:1) as eluent to give enone (4*S*,5*R*)-**20** (31 mg, 72%, 92% ee) as a waxy solid, $[\alpha]_D$ +109.8 (*c* 0.65 in $CHCl_3$) [Found: C, 60.65; H, 10.3%; $(M + H)^+$, 357.2281. $C_{18}H_{36}O_3Si_2$ requires C, 60.6; H, 10.2%; *M* + H, 357.2281].

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