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An investigative study of kinetic resolutions by the Sharpless asymmetric dihydroxylation reaction

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Abstract—The requirements for a highly selective kinetic resolution with the Sharpless asymmetric dihydroxylation (AD) reaction were investigated with a number of alkene substrates. It was found that with 1-phenyl-4-*tert*-butylcyclohexene enantioselectivity is very high, yet diastereoselectivity is poor and kinetic resolution is ineffective. With 5-methyl-2-phenylbicyclo[3.2.0]heptan-2-ene both diastereoselectivity and enantioselectivity are high and kinetic resolution is effective. It was discovered that the transition state for the product-determining step in the Sharpless AD reaction is not product-like, and effective kinetic resolution can occur when one face of a chiral alkene is hindered.

1. Introduction

The Sharpless asymmetric dihydroxylation (AD)[1] and asymmetric epoxidation (AE)[2] reactions have proved to be very effective means whereby asymmetry can be introduced into molecules starting from prochiral alkenes and allylic alcohols, respectively. The AE reaction has also proved useful for effecting kinetic resolution of chiral allylic alcohols. However, the AD reaction has only been successfully applied to effect kinetic resolutions in a limited number of cases and the reasons for this are not well understood.[1]

Investigations by Sharpless and coworkers demonstrated that kinetic resolution of some axially chiral alkenes is possible through application of the asymmetric dihydroxylation technology.[3] Reaction of the alkenes **1** and **2** with the commercially available α and β AD-mixes resulted in kinetic resolution. The k_{rel} values for the enantiomers of **1** with AD mix-β and AD mix-α was 9.7 and 5.0, respectively and those for the enantiomers of **2** were 32.0 and 26.5, respectively. It was reasoned that the kinetic resolution observed in these experiments is the result of dihydroxylation of the faster reacting olefin from the intrinsically disfavoured diastereoface (Fig. 1).

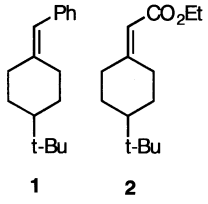
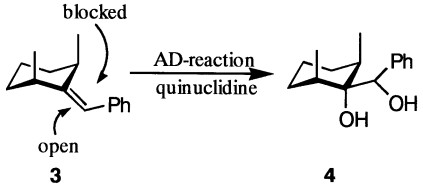


Figure 1.

It has also been discovered recently that the dihydroxylation reaction of the alkene **3** with quinuclidine (an achiral accelerating ligand) gave exclusively the diastereomer **4** which resulted from attack on the face *trans* to the two methyl groups.[4] When the chiral ligand, $(DHQD)_2$-PHAL was used the diol **4** formed in an 86% ee, after a 23% conversion. Its enantiomer was obtained in greater than a 95% ee, after 40% conversion, when the chiral ligand was (DHQ_2)-PHAL[4] (Scheme 1).

In 1996 we explored[5] the kinetic resolution of 1-phenyl-4-*tert*-butylcyclohexene **5** as a method to make chiral auxiliaries and found that it was ineffective. This led us to explore this area in more detail and the results obtained were communicated earlier.[6] Herein we describe the full experimental details for those studies.



Scheme 1.

Keywords: Sharpless asymmetric dihydroxylation; kinetic resolutions; transition state.

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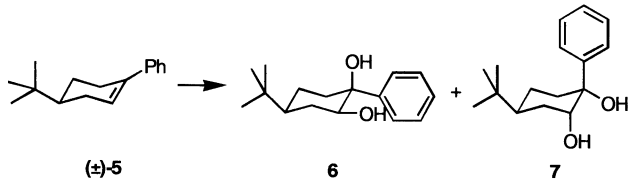
2. Results and discussion

2.1. Kinetic resolution of the alkene 5

The AD reaction of 1-phenylcyclohexene proceeds with high asymmetric induction,[3] 99% ee with AD mix-β and 97% ee with AD mix-α. It was therefore reasoned that reaction of these reagents with 1-phenyl-4-*tert*-butylcyclohexene **5** should also proceed with high asymmetric induction. However, in this case two diastereomeric products would form. For example with AD mix-β the enantio-enriched diastereomers **6** and **7** would be expected (Scheme 2).

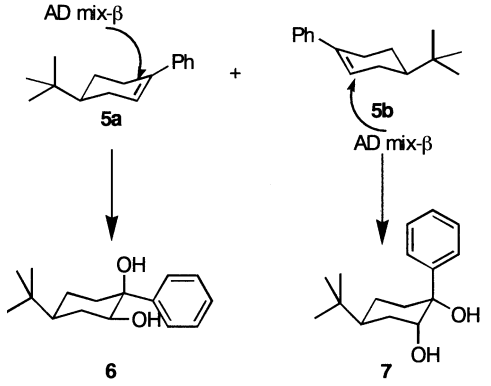


Scheme 2.

If these molecules exist predominately in the expected chair conformations, then due to the ring locking effect of the *tert*-butyl substituent it can be seen that diastereomer **6** has the phenyl group in an equatorial position whereas the phenyl group in the other diastereomer **7** has an axial orientation. Molecular modeling (GAUSSIAN94) revealed that diastereomer **7** was 15.9 kJ mol^{-1} higher in energy than the diastereomer **6**. It was thus reasoned that if the transition state for the product-determining step in the AD reaction is product-like, there would be a considerable difference in the rate of formation of the two diastereomers, and an effective kinetic resolution should be possible.

The required racemic diols[7] were formed by two methods; by reaction of **5** with OsO_4 and NMO, and also by reaction with a modified Sharpless dihydroxylation reaction where quinuclidine was used as an achiral accelerating ligand.[8] Both methods produced a mixture of approximately 4:1 ratio of the diols **6** to **7**.

The AD reaction on the alkene **5** was performed following Sharpless's recommended procedure[9] for tri-substituted alkenes. It is expected, from Sharpless's mnemonic[8] that the AD mix-β will preferentially attack the top face (as drawn) of enantiomer **5a** whereas it will preferentially attack the bottom face of enantiomer **5b** (Scheme 3). It is therefore expected that, if there is very high facial selectivity of the reagent for the alkene and the reaction is allowed to go to completion, that both the diols **6** and **7** would be produced in equal quantities.[10] Under these conditions the ratio of the diols **6** and **7** indicates nothing about the relative rates of attack of the AD mix from the two sides of the alkene **5**. Initially when the reaction was carried to completion at 0°C equal qualities of the diols **6** and **7** were produced, as determined by integration of the ^{1}H NMR resonances of the protons on the carbon bearing the secondary hydroxyl group. The diols **6** and **7** were obtained in an 84% yield after separation by flash column chromatography, with care taken so as to not optically enrich the diols.



Scheme 3. *Conditions*: (a) AD mix-β, $MeSO_2NH_2$, *tert*-BuOH, H_2O, 0°C, 24 h, 84%.

^{1}H NMR chiral shift reagent experiments on the corresponding racemic mono acetates of the separated diols **6** and **7** was not useful. However, similar experiments with the racemic diols themselves gave baseline separation of the *tert*-butyl resonances.[†] This observation was useful for two reasons; each *tert*-butyl resonance is a singlet, and this resonance is the largest peak for each enantiomer in the ^{1}H NMR spectrum. Therefore, with the optically enriched diols the ratio of the enantiomers can be integrated accurately. In this way it was determined that the optical purity of **6** was greater than 99% ee since the *tert*-butyl resonance due to the minor enantiomer was not visible in the spectrum whereas one ^{13}C–H satellite of the *tert*-butyl resonance of the major isomer was. The addition of 1% of the racemic diol in this experiment gave a discernible peak for the minor enantiomer which was of comparable intensity to this ^{13}C–H satellite. The optical purity of diol **7** could only be determined to be greater than 95% ee due to distortion of the baseline. Addition of 5% of the racemate was required before a discernible peak for the *tert*-butyl resonance of the minor enantiomer could be readily observed. By the arguments of Gutté and Horeau,[10] if two diastereomers are formed in equal quantities then the optical purity of each diastereomer must be equal. Within the experimental limits, these chiral shift reagent ^{1}H NMR experiments confirm this expectation.

A kinetic resolution with the AD reaction was then studied under the normal conditions and the relative rates for the enantiomers (E or k_{rel}) were determined following a literature procedure[11] which is related to the relationship derived by Kagan.[12] During the reaction, the percentage conversion of the racemic alkene **5** was determined by NMR spectroscopy. This was done by removing aliquots, which were quenched with a solution of sodium sulfite. The disappearance, in the NMR spectrum, of the vinyl proton of alkene **5** with the appearance of the protons on the carbon bearing the secondary hydroxyl group of the diols **6** and **7** were used to make this determination. The alkene remaining was separated from the diols **6** and **7** and this alkene **5** was converted, by the achiral dihydroxylation reaction, with quinuclidine, into the diols **6** and **7**. The enantiopurity of the major diol **6** from this reaction, and hence that of the

[†] Contrary to our expectation and previous observations that tightly complexed compounds give too much line broadening in high field NMR to be useful.

alkene **5**, was then determined as described earlier. Two separate experiments were conducted at 0°C and the reactions were stopped at 15 conversion and 94% conversion, respectively. For the former reaction the ratio of diasteremores **6** and **7** was ~2:1, for the later, ~52:42. The ee for the remaining alkene **5**, for the former reaction, was determined as ~4% and, for the latter, as ~86%. This computes to an *E* of ~2 in each case. This small *E* difference means that the kinetic resolution is ineffective as a means of obtaining the pure enantiomers.

The small *E* value obtained shows that the energy difference of the products is not reflected in the transition state of the product-determining step. Therefore, this transition state is not product like. Consequently an early (the starting alkenes are energetically identical) rather than a late transition is indicated for the product-determining step.

It can be reasoned that, if the product-determining step in the AD reaction is reactant-like and if the alkene is highly enantiofacially directing, then a kinetic resolution should be effective when there is considerable difference in the ease of approach to the two faces of a chiral alkene. This reasoning can be applied to the example where such an effect has been observed recently[4] for a molecule **3** which displays axial chirality. We therefore proposed to investigate this further, first with the alkene **8** and then, as things turned out, with the alkene **9** (Fig. 2).

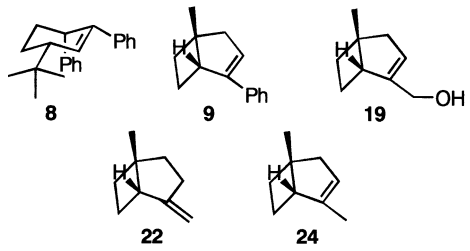
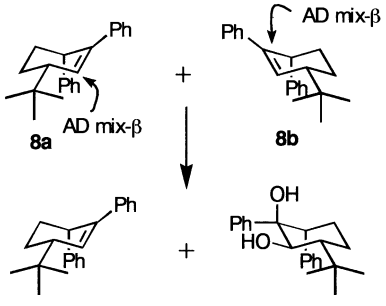


Figure 2.

2.2. Synthesis of the alkene 8

With the diol **6** in hand it was expected that alkene **8** might easily be synthesized. Alkene **8** was expected to be very effectively resolved by the Sharpless AD reaction. The *tert*-butyl group locks one phenyl group in the axial position and an inspection of a molecular model reveals that the alkene **8** is effectively blocked from attack adjacent to the axial phenyl group. Therefore, with AD mix-β the enantiomer **8b** would be expected to react faster and it was expected that a kinetic resolution should be effective (Scheme 4).

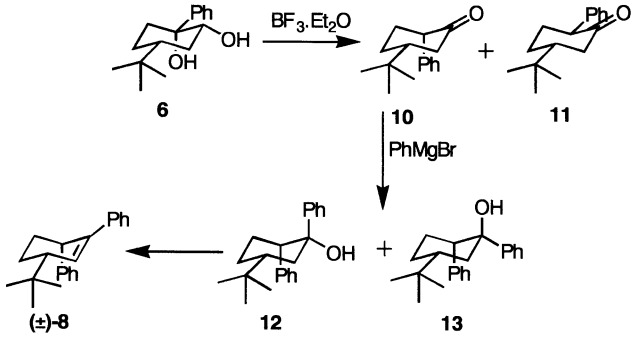


Scheme 4.

It is known[13] that rearrangement of the racemic diol **6** with boron trifluoride etherate gives the ketone **10** as the major product. Treatment of the mixture with acid (HBr, acetic acid) changes the ratio to 1:10 now in favour of the more stable equatorial alkene **11**. We find that pure ketone **10** can be obtained in reasonable quantities directly after rearrangement by purification of the mixture by 'flash' column chromatography. The time that the compound spends on the column must be kept to a minimum to obviate isomerisation to the more stable isomer.

The stereochemistry for each of the two products **10** and **11** was confirmed by comparison of the coupling constants for the benzylic protons in the ^{1}H NMR spectrum. The diastereomer with the axial phenyl group **10** has the resonance due to the benzylic proton at δ 3.71 ppm (t, J=4.5 Hz), the small couplings suggesting an equatorial proton. The isomer **11** has the benzylic resonance at δ 3.54 ppm (dd, J=5 and 8 Hz), the larger coupling being consistent with an axial orientation for that proton.

Reaction of the ketone **10** with phenylmagnesium bromide gave mostly one alcohol product (Scheme 5), which was tentatively assigned the structure **12** by the following reasoning. It was anticipated that the alcohol **12** might form preferentially to the alcohol **13** due to the steric blocking effect of the axial phenyl substituent. The ^{1}H NMR spectrum has a resonance due to the benzylic proton at δ 3.47 ppm (dd, J=4 and 10 Hz). The coupling constant of 10 Hz implies that this proton is axial. The ^{1}H NMR spectrum of the crude reaction mixture showed a small amount of the starting ketone **10** but no sign of the isomeric ketone **11**. This suggested that no isomerisation of the ketone **10** occurred under the Grignard conditions. The presence of axial benzylic proton is best rationalized by assuming a twist boat conformation (Fig. 3) which would allow all



Scheme 5. *Conditions*: (a) $BF_3{\cdot}Et_2O$, benzene, 25°C, 3 h, 54% (b) PhMgBr, Et_2O, 25°C, 40 min, 83% (c) $MgSO_4$, CH_2Cl_2, H_2SO_4, 25°C, 20 min, 80%.

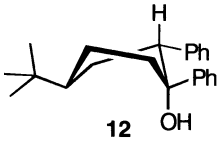
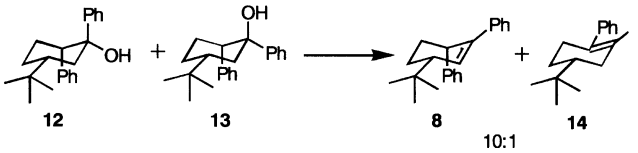


Figure 3.



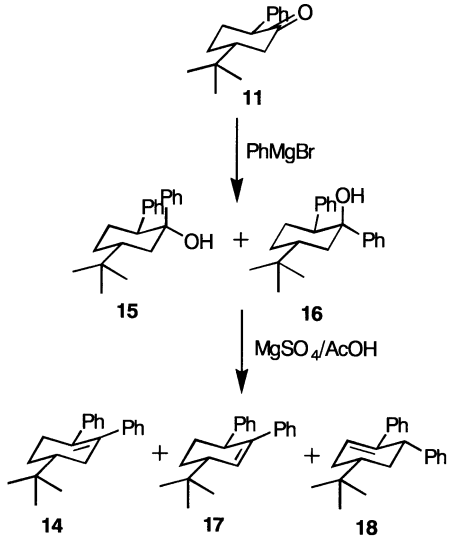
Scheme 6. *Conditions*: (a) $MgSO_4$, CH_2Cl_2, H_2SO_4, 25°C, 20 min, 80%.

three large substituents to occupy equatorial positions. This conformation puts the benzylic proton in a pseudo axial position, which would account for the observed large coupling.

This initial mixture of alcohols **12** and **13** could be purified, with difficulty, by flash chromatography to give pure **12**, however the crude mixture could be used in the next reaction, dehydration, without purification.

Dehydration of the crude tertiary alcohol **12**, under conditions which could favour the kinetic product, was accomplished with concentrated sulfuric acid absorbed in anhydrous magnesium sulfate.[14] In the reaction, two alkenes are formed in a ratio of 10:1. The major product was obtained after purification of the mixture by flash chromatography. The ^{1}H NMR spectrum of the major product has two characteristic resonances, a 1H broad singlet at δ 6.47 ppm assigned to the vinylic proton, and a 1H multiplet at δ 4.00 ppm consistent with the benzylic proton. This benzylic proton resonance has only small couplings, suggesting that it is equatorial and this is consistent with the expected structure **8** (Scheme 6).

The minor product was identified as the stilbene **14** by the lack of benzene or alkene resonances in its ^{1}H NMR spectrum. In order to confirm the identity of the stilbene **14** it was formed by a different route. The ketone **11** was carried through a similar series of reactions used to form the alkene **8**. One major alcohol product formed from the Grignard reaction. The ^{1}H NMR spectrum of this major product is quite different to that of the alcohol **12**. It is clear that the alcohol **12** could not have formed by



Scheme 7. *Conditions*: (a) PhMgBr, Et_2O, 25°C, 1 h, 86% (b) $MgSO_4$, CH_2Cl_2, H_2SO_4, 25°C, 1 h, 35% (**14**).

epimerisation of the ketone **10** to the ketone **11**. The ^{1}H NMR spectrum of the major product has a benzylic resonance at δ 3.03 ppm (dd, J=13 and 4 Hz). The large coupling (13 Hz) suggests that the proton is axial and hence the phenyl group has remained equatorial. The rest of the spectrum does not indicate whether the new phenyl group has entered *cis* (**15**) or *trans* (**16**) (Scheme 7). As the alcohol was only an intermediate, its configuration was not pursued.

Dehydration of this alcohol **15** or **16** gave mainly three alkenes (Scheme 7). The ratio of these alkenes was **14/17/18** (3:1:1) (determined by integration of the *tert*-butyl proton signals in the ^{1}H NMR spectra). The two alkenes **14** and **17** were identified with some certainty, however the structure of **18** was only tentatively assigned. In the spectrum of the crude mixture it was observed that there were two different olefinic signals, a broad singlet at δ 6.23 ppm which was assigned to **17** and a dd at δ 6.46 ppm (J=3 and 5 Hz) which by deductive reasoning was assigned to **18**. The synthesis of the stilbene **14** in a larger amount allowed its full spectral characterisation and confirmed that it was the minor product formed by dehydration of the alcohol **12**.

The ratio of the three alkenes (**14**, **17** and **18**) varied with reaction time. After 40 min (the time required for the dehydration reaction to be complete) the ratio of the alkenes was **14/17/18** (3:1:1); however, after 5 days the ratio of the alkenes had changed and now the alkene **8** had formed. The ratio of the products was now **14/17/18/8** (4.5:1:1.7:1).

The AD reaction on the alkene **8** using Sharpless's recommended procedure,[8] at 0°C, gave no reaction. After several days a large number of low R_f products were observed on TLC.[‡] It appeared that the alkene **8** was not soluble in the reaction mixture, therefore, sufficient dichloromethane was added to ensure that the alkene **8** was dissolved, but still no reaction occurred. Reaction of the alkene **8** under similar conditions with quinuclidine, which has less steric bulk than the AD ligands, gave similar results. This interesting new alkene **8** seems to be largely unreactive under Sharpless's standard dihydroxylation conditions. It is likely that this is due to too much steric hindrance at the double bond.

2.3. Synthesis and kinetic resolution of the alkene 9

Recently we completed[15] an asymmetric synthesis of grandisol in which the key step is the kinetic resolution of the primary allylic alcohol **19** using a Sharpless AE reaction. The key feature, in that resolution, is that the molecule presents both an open convex face and a more-hindered, concave face to reagents. The reaction proceeds to give products of attack on one face only, the convex face. This *cis* 4,5 ring system appeared suitable to pursue the study of the kinetic resolution by the AD reaction. Indeed, the alkene **9** appears ideal for this study (see Fig. 2 for structures). Control of product formation in the Sharpless AD reaction should be determined mainly by the enantiofacial selectivity of the styrene moiety. The concave face of this molecule is

[‡] The pattern was similar to the decomposition of the alkene **8** on standing alone.

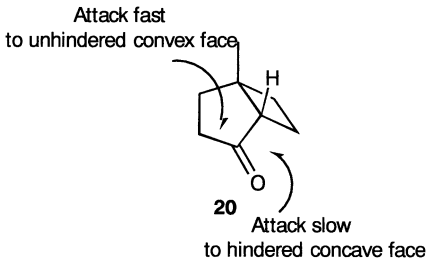


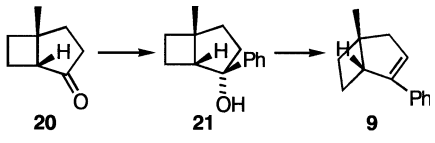
Figure 4.

hindered, so there should be a considerable difference in the rate of reaction of the enantiomers of this molecule and, by our reasoning a kinetic resolution should be effective.

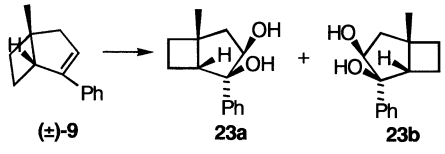
Reaction of the bicyclic ketone **20** with phenylmagnesium bromide gave a single racemic alcohol. However, the structure is presumed to be that of diastereomer **21**, formed by attack from the unhindered top face of the ketone **20**. No resonances corresponding to other diastereomers could be seen in the ^{1}H NMR spectrum. Unfortunately, crystals suitable for X-ray analysis could not be obtained. Inspection of a molecular model reveals that the bicyclic ketone **20** has an open accessible convex face and also a much more hindered concave face (Fig. 4). The observation that attack of a reagent comes preferentially from the top face in this system has been argued previously for attack of dimethylsulfonium methylide ($(CH_3)_3S^+I^-$)) on the bicyclic ketone **20** and for attack of MCPBA on the corresponding methylene compound **22**.[15]

Dehydration of the tertiary alcohol **21** gave the required alkene **9** as an oil (scheme 8). The alkene **9** was somewhat unstable and initially the yield for the elimination reaction was only 50%. However, addition of the radical inhibitor 2,6,-di-*tert*-butyl-*p*-cresol during the work-up process, increased the yield to greater than 80%, presumably by preventing free-radical polymerisation of the alkene.

Dihydroxylation of the alkene **9** with quinuclidine as the ligand, gave only one diastereomer. This was presumed to be the diol **23** formed from attack of the reagent from the unhindered top face (scheme 9). No resonances which could



Scheme 8. *Conditions*: (a) PhMgBr, Et_2O, reflux, 1 h, 88% (b) $MeSO_2Cl$, Et_3N, CH_2Cl_2, 0°C, 4 h, 81%.



Scheme 9. *Conditions*: (a) $K_3Fe(CN)_6$, K_2CO_3, quinuclidine, OsO_4, $MeSO_2NH_2$, *tert*-BuOH, H_2O, 25°C, 24 h, 50%.

be assigned to the other diol were observed in the ^{1}H NMR spectrum of the product.

A kinetic resolution with the AD reaction was then studied under the normal conditions and the relative rates (E) of the reaction for the enantiomers were determined following a similar procedure to that described earlier.[11] The kinetic resolution of this substrate was examined in two separate experiments with 26 and 50% oxidant, respectively. However, because the alkene **9** is somewhat unstable, the percentage conversion could not be determined accurately. Therefore, in each case the ee for both the diol (presumed to be enantiomer **23a**, based on the application of Sharpless's mnemonic) and the recovered alkene **9** were determined, after separation in the following way. The diol **23a** was converted to the mono Mosher ester derivative and the ee was determined by ^{1}H NMR spectral analysis. It was first shown that the ^{1}H NMR spectrum of the diastereomers from the racemic diol gave base-line separation for the methoxy resonances at δ 3.37 and 3.53 ppm. The product from the kinetic resolution showed the peak at δ 3.37 ppm as the major resonance. The alkene from the kinetic resolution was converted to the diol, presumed to be mainly enantiomer **23b**, by the achiral dihydroxylation reaction with quinuclidine as the ligand. This diol was then converted to the mono Mosher ester derivative from which the ee was obtained. The peak at δ 3.53 ppm was now the major peak.

The ee for the diols in the two reactions were 88 and 80% respectively, and for the alkenes they were 52 and 80%, respectively. From these results the enantiomeric ratios for these two reactions calculate to E=26 and 21, respectively.[16] These are the same within experimental error and this result implies an effective kinetic resolution giving >95% ee in the remaining alkene after 60% conversion.

2.4. Kinetic resolution of the methyl alkene 24

The allylic alcohol **19** undergoes very effective kinetic resolution under the conditions of the Sharpless AE reaction.[15] The methyl alkene **24** presents very similar overall steric requirements to those of the allylic alcohol **19**, therefore, it was of interest to compare the effectiveness of this alkene to kinetic resolution in the Sharpless AD reaction. It has been shown earlier[15] that very high diastereoselection occurs in the achiral dihydroxylation of the alkene **24**. Two reactions were conducted at 0°C and stopped at 26 and 24% conversion. The ee of the product was determined by conversion to the corresponding Mosher esters. In the former reaction the enantiomeric excess of the product was 23%, in the latter the enantiomeric excess was 24%. These results translate to a E value of only 1.8. These results show that a kinetic resolution was ineffective. The methyl group is not very enantioselectively enhancing.

The question arises, why the AE reaction is often effective in the kinetic resolution whereas the AD reaction is usually ineffective? The obvious difference between these reactions of allylic alcohols and alkenes in the complexing ability of the hydroxyl group in the alcohols, and the requirement for prior co-ordination of this group with the Ti centre for the AE reaction to proceed.[2] That is, the diastereomeric

transition states which control both the diastereoselection and the enantioselection in the AE reaction are intramolecular. No such strong prior co-ordination occurs with the AD reaction in these cases. In this case, if the reagent can approach closely enough to the double bond, reaction will take place and enantioselectivity will be determined by the substituents on the double bond. That is, when co-ordination to the double bond does occur it is the environment local to the double bond, which dictates the outcome. Diastereoselectivity is however, only controlled by the initial ease of approach to each side of the double bond and is controlled by the gross features of the molecule. In broad terms the situation is somewhat analogous, but more complicated, to the situation pertaining to epoxide formation from the reaction of ketones with sulfur ylids.[17] In those cases the diastereomeric products from the reaction of the reactive ylid are controlled by the initial approach of the reagent, whereas the products from the reaction of the less reactive ylid are controlled by intramolcular interactions.

In conclusion we find with the *tert*-butyl alkene **5** enantioselectivity to the double bond is very high due to the enantioselectivity enhancing phenyl moiety but diastereoselectivity is poor (~2:1), attack can occur reasonably well from either side of the double bond and kinetic resolution is ineffective. With the methyl alkene **24** diastereoselectivity is high, reaction occurs only from one side of the double bond but enantioselectivity is poor, as the methyl group is not very enantioselectivity enhancing, and kinetic resolution is ineffective. However, with the phenyl alkene **9** both diastereoselectivity and enantioselectivity are high and kinetic resolution is effective. These results are consistent with an early, rather than a late transition state for the product determining step in the AD reaction.

3. Experimental

3.1. General Procedure

Melting points were taken on a Kofler hot stage apparatus under a Reichert microscope and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian spectrometer at 200, 300 or 600 MHz, as indicated. Optical rotations were measured with a Perkin–Elmer 141MC Polarimeter. MS were recorded on a VG ZAP 2HF mass spectrometer, GC–MS were measured on a Finnigan MAT GCQ spectrometer operating at an ionization energy of 70 eV. Elemental analyses were carried out at the University of Otago, Dunedin, New Zealand. Flash chromatography was performed with Merck Kieselgel 60 (230–400 mesh ASTM). TLC was performed with Merck DC Alufolien Kieselgel $60f_{254}$ which were visualized either with UV light or by staining with acidic ammonium molybdate solution. Organic solutions were dried over Na_2SO_4 or $MgSO_4$. Other anhydrous solvents and reagents were prepared according to standard laboratory procedures.[18] All calculations were performed with Gaussian 94 (revision C), Gaussian, Inc., Pittsburgh, PA., 1995.

3.1.1. (4*RS*)-1-Phenyl-4-*tert*-butylcyclohexene (5). The method of Garbisch was followed, on a smaller scale.[19] The product was distilled under reduced pressure (100°C/0.4 mmHg) to give mainly the required alkene (83%) and redistilled to give the pure alkene, 54% yield. *m/z*: 214 (M^+, 65%), 57 (100%). δ_H (200 MHz): 0.92 (s, 9H), 1.2–1.6 (complex, 7H), 6.12 (m, 1H), 7.1–7.4 (complex, 5H). δ_C (50 MHz): 25.1, 27.9, 29.6, 31.5, 32.9, 44.5, 125.6, 126.0, 127.2, 128.8, 137.1, 142.9. ν_{max}: 2690, 1395, 1365 cm^{-1}.

3.1.2. 1-Phenyl-4-*tert*-butylcyclohexan-1,2-diols (6) and (7). The general procedure outlined by Sharpless for phenylcyclohexene[20] was used as follows.

A mixture of AD mix-β (1.40 g), *tert*-BuOH (5 mL), H_2O (5 mL), and $MeSO_2NH_2$ (0.095 g) was cooled to 0°C, where upon some of the dissolved salts precipitated. Racemic **5** (139 μL, 1 mmol) was added and the reaction mixture stirred with a mechanical stirrer (500 rpm) for 24 h at 0°C, after which time TLC analysis indicated a lack of starting alkene. Sodium sulfite (1.5 g) was added and the mixture stirred for 1 h while it came to room temperature. EtOAc (10 mL) was added and after separation of the layers, the aqueous layer was re-extracted with more EtOAc (3×5 mL). The combined extracts were washed with 2N KOH (15 mL), dried ($MgSO_4$) and the solvent was removed in vacuo. Separation of the diols from the ligand was effected by flash chromatography (CH_2Cl_2/EtOAc, 90/10 v/v) to give a mixture of the diols (0.209 g, 84% yield).

(1R,2R,4R)-1-tert-Butyl-4-phenylcyclohexan-1,2-diol (**6**): This diol was the first eluted of the two diols from normal phase chromatography. Recrystallized from hexanes/CH_2Cl_2 mp 152–153°C. *m/z*: 248 (M^+, 15%), 133 (100%); 105.(27%). δ_H (200 MHz): 0.93 (s, 9H), 1.0–2.0 (complex, 7H), 1.55 (s, 1H, OH), 2.58 (d, 1H, OH), 4.02 (ddd, 1H, *J*=11, 4 and 3 Hz), 7.2–7.6 (m, 5H). Exchange with D_2O revealed the OH resonances and changed the ddd at 4.02 ppm to a dd (11, 4 Hz). δ_C (50 MHz): 22.1, 27.6, 30.6, 32.4, 38.5, 46.6, 75.3, 75.4, 125.1, 127.0, 128.5, 146.3. ν_{mzx}: 3290 cm^{-1} (OH). $[\alpha]_D$=−3° +/− 0.5° (*c*=5, EtOH). Chiral shift analysis of the diol **6** (8 mg) with $Eu(hfc)_3$ (10 mg) in 15% C_6D_6–CCl_4 gave a 99% ee. Separation of the Bu^t protons' resonance due to the minor enantiomer was not visible by proton NMR, but the ^{13}CH satellite of the Bu^t protons' resonance of the major isomer was. Addition of 1% of the racemate gave a discernible peak for the minor enantiomer.

(1R,2R,4S)-1-tert-Butyl-4-phenylcyclohexan-1,2-diol (**7**): eluted second from normal phase chromatography of the mixture of two diols. Recrystallized from MeOH/H_2O mp 101–102°C. *m/z*: 248 (M^+, 5%); 133 (100%); 105.(38%).; 55.(98%). δ_H (300 MHz): 0.80 (s, 9H), 1.0–2.3 (complex, 2H), 1.55–1.70 (complex, 1H), 1.92 (m, 1H, *J*= 14.1 Hz+smaller coupling), 2.07 (dt, 1H, *J*=4.2, 13.5 Hz), 2.20–2.35 (complex, 2H), 2.77 (t, 1H, OH), 4.37 (br. s, 1H), 7.20–7.60 (complex, 5H). Exchange with D_2O revealed the OH resonances and changed the multiplet at 4.38 ppm demonstrating that a small coupling to OH was present. δ_C (75.5 MHz): 24.5, 27.5, 30.1, 31.9, 32.5, 39.6, 72.8, 74.5, 126.6, 127.8, 128.6, 143.3. ν_{max}: 3290 cm^{-1} (OH). $[\alpha]_D$=−14°+/−1° (*c*=2, EtOH). Chiral shift analysis of the diol **7** (8 mg) with $Eu(tfc)_3$ (6 mg) in 15% C_6D_6–CCl_4

gave >95% ee. Addition of 5% of the racemate was required before a discernible peak for the *tert*-Bu protons' resonance of the minor isomer could be detected.

3.1.3. Racemic diols (1*RS*,2*RS*,4*RS*)-1-*tert*-butyl-4-phenylcyclohexan-1,2-diol (6) and (1*RS*,2*RS*,4*SR*)-1-*tert*-butyl-4-phenylcyclohexan-1,2-diol (7). *Quinuclidine procedure*: The procedure followed was similar to that described earlier except that for 1 mmol of alkene $K_3Fe(CN)_6$ (0.98 g, 3 equiv.), K_2CO_3 (0.41 g, 3 equiv.), quinuclidine (0.001 g, 0.01 equiv.), and OsO_4 (20 μL, 4 wt% solution 0.002 equiv.) replaced the AD mix. A single recrystallisation of the mixture from hexanes/CH_2Cl_2 yields pure diol **6**. Alternatively, separation can be effected using flash chromatography. The ratio of the two diols was **6**:**7** (4.5:1), as determined by the ^{1}H NMR spectrum and mass recovery. δ_H (200 MHz), δ_C (50 MHz) and other spectral properties are identical to the optically active **6** and **7**. Mp **6** 153–153.5°C, **7** 101–102°C, (lit[7] 150–151.5°C **6**, 101–102.5°C **7**).

NMO procedure: With some modifications to the method of Van Rheenen,[21] alkene **5** (0.14 mL, 1.0 mmol) and an aqueous solution of 41 mg/ mL OsO_4 (0.2 mL, 7 mg, 0.03 mmol) were added to NMO (0.206 g, 1.76 mmol) in H_2O (0.5 mL) and acetone (5 mL).and the reaction mixture stirred vigorously until TLC analysis indicated no more starting material (approx. 85 h). A slurry of fluorisil (0.13 g) and sodium hydrosulfite (0.03 g) in water (2 mL) was added and the mixture stirred for 10 min at ambient temperature. The mixture was filtered through a pad of celite which was washed with additional acetone (3×10 mL). Solvent was removed under reduced pressure and the residue was taken up in water (10 mL). This solution was extracted with CH_2Cl_2 (3×10 mL), the combined organic extracts were dried and solvent was removed under reduced pressure to give the diols (0.21 g). Separation of the diols was achieved by flash chromatography (EtOAc/CH_2Cl_2, 10/90 v/v), the ratio of the two diols was **6**:**7** (3.8:1), as determined by ^{1}H NMR spectroscopy and mass recovery. All spectral properties were identical to those listed earlier for the optically enriched isomers.

In general, these reactions were run as detailed earlier for initial formation of **6** and **7** with the AD mix-β, however, the scale and the time of quenching were varied. All reactions were conducted at 0°C. The reaction was monitored by ^{1}H NMR spectroscopy. Aliquots (0.2 mL) were removed at discrete time intervals and quenched with sodium sufite solution (0.5 mL, 1.5 g/5 mL). The sample was extracted with EtOAc (3×5 mL), the combined extracts washed with 2N $KOH_{(aq)}$ (0.5 mL) and dried. Solvent was removed in vacuo and the samples were analysed by ^{1}H NMR spectroscopy.

Once the desired degree of conversion had been reached (determined from the ^{1}H NMR spectrum), the reaction was quenched and worked up as described earlier. The alkene **5** was separated by short column chromatography CH_2Cl_2/petroleum spirit (5:95, v/v), it was converted to the corresponding diols **6** and **7** using the achiral dihydroxylation reaction with quinuclidine as the achiral ligand. After separation the ee of the diol **6** was then measured using the chiral shift analysis experiment described earlier.

For the 15% conversion experiment the ratio of **6** to **7** was ~2:1. The ee for the remaining alkene **5**, was ~4%. The calculated *E* was 1.8. For the 85% conversion the ratio was, ~52:42, the ee for the remaining alkene was ~86%. The calculated *E* was 2.0.

3.1.4. (2*RS*,5*SR*)-5-*tert*-Butyl-2-phenylcyclohexanone (10) and (2*RS*,5*RS*)-5-*tert*-butyl-2-phenylcyclohexanone (11). A mixture composed mostly of these ketones was generated by the method of Barili et al.[22] Integration of the ^{1}H NMR singlet resonances for *tert*-Bu protons and also for the benzylic protons gives an estimated ratio of **10**:**11** (2:1) (variable between trials). After a trial using (1*R*,2*R*,4*R*)-1-*tert*-butyl-4-phenylcyclohexan-1,2-diol **7** (1.42 g), boron trifluoride etherate (1.4 mL) in benzene (140 mL) purification of the crude product (1.28 g) by flash chromatography (EtOAc/hexanes, 7:93 v/v) gave (2*RS*, 5*RS*)-5-*tert*-butyl-2-phenylcyclohexanone (first eluting) **10** as a colourless oil (583 mg, 54%). δ_H (200 MHz): 0.85 (s, 9H), 1.50–2.60 (complex, 7H), 3.71 (t, 1H, *J*=4.2 Hz), 7.20–7.40 (complex, 5H). δ_C (50 MHz): 22.2, 27.0, 28.7, 32.7, 41.2, 48.7, 53.3, 126.8, 127.3, 128.8, 138.1, 189.5.

Second eluting is a mixture of (2*RS*, 5*RS*)-5-*tert*-butyl-2-phenylcyclohexanone (**10**) and (2*RS*, 5*SR*)-5-*tert*-butyl-2-phenylcyclohexanone (**11**) as an oily solid (494 mg, 46%). This mixture was equilibrated following the method of Barili et al.[22] Recrystallisation of the equilibrated mixture from hexanes yields pure (2*RS*, 5*RS*)-5-*tert*-butyl-2-phenylcyclohexanone **11**, mp 96–97.5°C. *m/z*: 230 (M^+ 64%); 173 (29); 91 (100). δ_H (200 MHz): 0.94 (s, 9H), 1.5–2.7 (complex, 7H), 3.54 (dd, 1H, *J*=5.1 and 8.1 Hz), 7.05–7.40 (complex, 5H). δ_C (50 MHz): 27.6, 27.9, 33.5, 35.09, 44.8, 51.02, 57.9, 127.6, 129.0, 129.4, 139.5, 203.4. ν_{max}: 1714 (C=O) cm^{-1}.

3.1.5. (1*RS*,2*RS*,5*RS*)-5-*tert*-Butyl-1,2-diphenylcyclohexan-1-ol (12). To a stirred solution of PhMgBr (1.5 mL, 0.85 M, 1.25 mmol) under an N_2 atmosphere was added (2*RS*,5*RS*)-5-*tert*-butylcyclohexanone **10** (238 mg 1.03 mmol) in Et_2O (4 mL) via syringe over a period of 10 min the mixture was stirred for a further 30 min. Excess sat. $NH_4Cl_{(aq.)}$ was added and the mixture stirred for 5 min. The layers were separated and the ether washed again with NH_4Cl solution. The organic layer was dried over $CaCl_2$ and the solvent removed to yield the crude alcohol product (325 mg) as a colourless oil. Purification by flash chromatography (EtOAc/hexanes, 6/94 v/v) gave the *title compound* as a colourless oil. *m/z*: 308 (M^+). δ_H (300 MHz): 0.89 (s, 9H), 1.60–1.90 (complex, 6H), 2.10–2.30 (complex, 2H), 3.47 (dd, 1H, *J*=3.6 and 9.9 Hz); 7.00–7.50 (complex, 10H). δ_C (75.5 MHz): 23.1, 25.8, 27.2, 32.6, 39.7, 41.6, 48.5, 76.0, 125.2, 126.6, 126.6, 128.0, 128.0, 129.6, 141.1, 148.5. ν_{max} (neat): 3558, 3466 (OH), 1601 cm^{-1}.

3.1.6. (3*RS*,6*RS*)-3-*tert*-Butyl-1,6-diphenylcyclohex-1-ene (8). To a stirred suspension of anhydrous $MgSO_4$ (0.178 g, 4 equiv) in CH_2Cl_2 (1.5 mL) was added conc. H_2SO_4 (1 equiv., 20 μL).[23] The suspension was allowed to stir for

20 min and then crude alcohol **12** (100 mg, 0.325 mmol) was added in CH_2Cl_2 (1 mL). After 2 h the $MgSO_4/H_2SO_4$ was filtered off and the solvent removed under reduced pressure to yield a colourless oil. Integration of the *tert*-Bu region of the ^1H NMR spectrum of the crude product demonstrates a ratio of 90:5 of the peaks at δ 1.01 (*title compound* **8**) and δ 0.94 (stilbene **14**). Purification using flash chromatography (EtOAc/hexanes 0.3/99.7, v/v). First was a white solid (4 mg, 4%) having identical ^1H NMR data to stilbene **14** (see Section 3.1.8). This was followed by the *title compound* as a colourless oil (75 mg 80%). Anal. Calcd for $C_{22}H_{26}$: C, 90.98; H, 9.02. Found: C, 90.10; H, 9.03. *m/z*: 290 (M^+); 233. δ_H (300 MHz): 1.02 (s, 9H), 1.28 (m, 1H), 1.51 (m, 1H), 1.90–2.20 (complex, 3H), 3.99 (m, 1H, width at 1/2 height ~8 Hz), 6.47 (m, 1H, width at 1/2 height ~1.5 Hz), 6.90–7.60 (complex, 10H). δ_C (75.5 MHz): 18.2, 27.5, 32.4, 33.5, 41.9, 47.2, 125.8, 125.9, 126.7, 128.1, 128.2, 128.8, 130.5, 138.2, 142.1, 145.2. ν_{max} (neat): 3058; 2958; 2866; 2815; 1600 cm^{-1}.

3.1.7. (1*RS*,2*SR*,5*RS*)-5-*tert*-Butyl-1,2-diphenylcyclohexan-1-ol (15) and/or (1*SR*,2*SR*,5*RS*)-5-*tert*-butyl-1,2-diphenylcyclohexan-1-ol (16). To a stirred solution of PhMgBr (1.90 mL, 1.05 M, 2 mmol) under an N_2 atmosphere was added **11** (300 mg, 1.30 mmol) dissolved in Et_2O (4 mL). After stirring for a further 1 h, excess aq. $NH_4Cl_{(sat)}$ (20 mL) was added and the mixture stirred for 5 min. The layers were separated and the aqueous layer extracted with Et_2O (10 mL). The combined organic phases were dried over $MgSO_4$ and the solvent removed under reduced pressure to yield the crude alcohol product as a colourless oil. Integration of the *tert*-Bu region of the ^1H NMR spectrum of the crude mixture revealed the peaks at δ 0.94 and δ 0.92 were in the ratio of 1:12. Purification by flash chromatography (EtOAc/hexanes 6/94, v/v) gave the *title compound* as a colourless oil. Recrystallisation by concentration of a hexanes solution gave an analytically pure sample, mp 116–127°C. Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.49; H, 9.18. *m/z*: 308 (M^+). δ_H (300 MHz): 0.91, (s, 9H), 1.20–1.40 (complex, 1H), 1.60–2.10 (complex, 6H), 2.25 (dq, 1H, *J*=3.6 and 12.9 Hz), 3.04 (dd, 1H, *J*=3.9 and 12.9 Hz), 6.90–6.95 (m, 2H), 7.00–7.30 (complex, 8H). δ_C (75 MHz): 27.4, 27.5, 28.7, 32.2, 41.9, 42.9, 52.6, 76.5, 114.8, 126.2, 126.3, 127.7, 127.8, 129.0, 141.4, 148.1. ν_{max} (neat): 3564; 3470 (OH); 2949; 2866; 1603 cm^{-1}.

3.1.8. (4*RS*)-*tert*-Butyl-cyclohexyl-1,2-stilbene (14). To a stirred suspension of anhydrous $MgSO_4$ (0.350 g) in CH_2Cl_2 (1 mL) was added conc. H_2SO_4 (1 equiv, 35 μL).[23] The suspension was allowed to stir for 20 min and then the crude alcohol **15** or **16** (70 mg, 0.228 mmol) was added with the aid of CH_2Cl_2 (1 mL). When the reaction was complete (TLC), $MgSO_4/H_2SO_4$ was filtered off and the solvent removed under reduced pressure to yield a colourless oil (66.5 mg). Integration of the *tert*-Bu region of the ^1H NMR spectrum of the crude product shows a ratio of 1.5:3:1 of the peaks at δ 0.97 (**17**): δ 0.95 (**14**): δ 0.76 (**18**). Resubjecting the crude mixture to the same conditions for 5 days then demonstrates a ^1H NMR spectrum further enriched in stilbene. The appearance of the *tert*-butyl resonance for (3*RS*, 6*RS*)-3-*tert*-butyl-1,6-diphenylcyclohex-1-ene **8** at δ 1.02 ppm was also observed. Purification by flash chromatography (EtOAc/hexanes 0.3/99.7 v/v) gave the *title compound* **14** (eluted first) (23 mg 35%). The compound was further purified by recrystallisation (methanol) mp 108–109°C. Anal. Calcd for $C_{22}H_{26}$: C, 90.98; H, 9.02. Found: C, 91.24; H, 9.31. *m/z*: 290 (100% M^+); 233 ($-Bu^t$); 115; 91; 41. δ_H (300 MHz): 0.95 (s, 9H), 1.20–1.70 (complex, 3H), 1.90–2.65 (complex, 7H), 6.90–7.20 (complex, 10H). δ_C (75 MHz): 24.5, 27.2, 32.3, 33.4, 33.8, 44.7, 125.7, 125.8, 127.6, 127.7, 129.1, 129.1, 134.8, 135.2 143.7, 144.1. ν_{max} (nujol mull): 3074; 1599 cm^{-1}.

As the spectral data of stilbene **14** was known with some certainty the spectra of the other two alkenes could be assigned. The slower eluting fraction contained 2 compounds, GC–MS confirmed that they were isomeric. Careful column separation gave the alkene **17** with minimal contamination.

*(3RS, 6*SR*)-3-tert-butyl-1,6-diphenylcyclohex-1-ene* (**17**): GC MS (E.I.) 290 (M^+), 233 ($-Bu^t$). δ_H (300 MHz): 0.97 (s, 9H), 1.40–1.90 (complex, 4H), 2.10–2.30 (complex, 2H), 3.93 (m, 1H, width at 1/2 height 36 Hz), 6.23 (br. s, 1H), 7.00–7.30 (complex, 10H). δ_C (75 MHz): 23.2, 27.5, 33.5, 34.7, 44.5, 46.6, 125.6, 126.0, 126.5, 127.8, 128.2, 128.2, 130.9, 140.6, 142.8, 146.0.

3.1.9. Attempted kinetic resolution of (3*RS*, 6*RS*)-3-*tert*-butyl-1,6-diphenylcyclohex-1-ene (8). The general procedure of Sharpless outlined previously was followed, all trials were conducted at room temperature. In some trials dichloromethane was added to help solubilize the alkene. Addition of alkene resulted in a bright green colour of the organic layer, which faded after several hours. TLC after various lengths of time indicated that the starting alkene **8** was present in greatest amount with a large number of minor lower R_f products present. No dihydroxylation reaction was apparent.

3.1.10. (1*SR*,5*SR*)-5-Methylbicyclo[3.2.0]heptan-2-one (20). Compound **20** was synthesized following the method of Cargill[24] as reported earlier.[15]

3.1.11. (1*SR*,2*SR*,5*SR*)-5-Methyl-2-phenylbicyclo[3.2.0]heptan-2-ol (21). Bromobenzene (1.4 mL, 13.24 mmol) was added dropwise to Mg (339 mg, 13.95 mmol), activated with I_2, in dry Et_2O (6 mL). The mixture was then refluxed for 1 h. The bicyclic ketone **20** (0.5 mL, 4.03 mmol) in Et_2O (3 mL) was added dropwise. After 2 h, sat. NH_4Cl was added, the organic phase was separated, washed with 10% $NaHCO_3$ and H_2O, dried and solvent removed in vacuo. Flash chromatography (hexane/EtOAc, 70/30, v/v) gave the *title compound* as a colourless liquid, which crystallized in part on standing (719 mg, 88%), mp 56–58°C *m/z*: 200(M^+, 10%), 183(15), 128(47), 115(57), 105(82), 77(100). δ_H (600 MHz):[¶] 1.22 (s, 3H, CH_3), 1.29 (dt, 1H, *J*=6.5, 13.2 Hz, $H4_a$), 1.50 (ddd, 1H, *J*=1.8, 6.0, 13.2 Hz, $H4_b$), 1.90 (m, 2H, H6), 2.0–2.1 (complex, 3H, $H3_a$, H7), 2.43 (dt, 1H, *J*=6.5, 13.2 Hz, $H3_b$), 2.60 (dd, 1H, *J*=5.4, 9.5 Hz, H1), 7.22 (d, 1H, *J*=7.5 Hz, H4′), 7.31 (dd, 2H, *J*=7.5, 8.4 Hz, H3′), 7.42 (d, 2H, *J*=8.4 Hz, H2′). δ_C

[¶] COSY and HETCOR experiments were used to assign the resonances.

(150 MHz): 14.7(CH_2), 26.5(CH_3), 31.3(CH_2), 37.8(CH_2), 40.3(CH_2), 44.4(q), 51.5(CH), 82.9(q), 125.6(CH), 126.8(CH), 128.0(CH), 147.9(q). ν_{max}(neat): 3369(br. s) cm^{-1}.

3.1.12. (1*RS*,5*SR*)-5-Methyl-2-phenylbicyclo[3.2.0]heptan-2-ene (9). To a solution of the alcohol **21** (688 mg, 3.4 mmol) in CH_2Cl_2 (5 mL) was added triethylamine (0.4 mL). To the solution, cooled to 0°C, was added methanesulfonyl chloride (0.4 mL, 6.46 mmol). After the reaction was stirred for 4 h, 2,6-di-*tert*-butyl-*p*-cresol was added, the reaction mixture was washed with 15% $HCl_{(aq)}$ (5 mL), extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were washed with sat. $NaCl_{(aq)}$ (5 mL), dried and solvent removed in vacuo. Flash chromatography (hexanes) gave the *title compound* as a colourless liquid (507 mg, 81%). If the alkene **9** was not being used immediately more 2,6-di-*tert*-butyl-*p*-cresol was added and the alkene **9** was stored at 5°C. *m/z*: 184(M^+, 30%), 156(100), 115(45). δ_H (300 MHz): 1.20 (s, 3H, CH_3), 1.6–2.0 (complex, 3H, ring protons), 2.1–2.4 (complex, 3H, ring protons), 3.05 (br. s, 1H, ring proton), 6.05 (br. s, 1H, olefinic), 7.0–7.3 (m, 5H, aromatic protons). δ_C (75 MHz): 24.0, 25.5, 33.2, 43.6, 48.2, 50.8, 125.4, 125.7, 126.7, 128.1, 135.7, 145.2. ν_{max}(neat): 3000(s), 1594(m), 1494(s), 1446(s), 754(s), 690(s) cm^{-1}.

3.1.13. (1*SR*,2*SR*,3*SR*,5*SR*)-5-Methyl-2-phenylbicyclo-[3.2.0] heptan-2,3-diol (23). The general procedure for achiral dihydroxylation, was repeated with $K_3Fe(CN)_6$ (761 mg, 2.31 mmol), K_2CO_3 (165 mg, 1.19 mmol), quinuclidine (2.9 mg, 0.03 mmol), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), $MeSO_2NH_2$ (67 mg, 0.71 mmol), *tert*-BuOH (3 mL), H_2O (3 mL) and the alkene **9** (164 mg, 1.34 mmol). After stirring at ambient temperature for 24 h sodium sulfite (734 mg, 5.8 mmol) was added. Purification by flash chromatography (EtOAc/hexanes, 30/70 v/v) gave the *title compound* as white crystals (146 mg, 50%), mp 116–118°C. *m/z*: 218(M^+, 25%), 189(55), 180(65), 149(75), 122(100). δ_H (300 MHz): 1.29 (s, 3H), 1.65–1.9 (complex, 5H), 2.0 (m, 1H), 2.45 (m, 1H), 4.95 (dd, 1H, *J*=6.9 and 10.5 Hz), 7.2–7.5 (m, 5H). δ_C (75 MHz): 16.2, 28.0, 29.6, 30.6, 40.1, 46.2, 53.0, 74.9, 83.6, 126.9, 127.3, 128.2, 142.0. ν_{max}(neat): 3490(br. s, OH), 3295(br. s, OH), 2800(s), 1500(w), 1270(m), 1150(m), 1100(s), 750(s), 700(s)cm^{-1}.

3.1.14. (1*R*,2*R*,3*R*,5*R*)-5-Methyl-2-phenylbicyclo[3.2.0]-heptan-2,3-diol (23b). In a similar manner; the optically active alkene **9b** was dihydroxylated with the following reagents. K_2CO_3 (116 mg, 0.84 mmol), $K_3Fe(CN)_6$ (303 mg, 0.92 mmol), $MeSO_2NH_2$ (67 mg, 0.71 mL), quinuclidine (2.9 mg, 0.03 mmol), *tert*-BuOH (3 mL), H_2O (3 mL), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), and the optically active alkene **9b** (52 mg, 0.28 mmol). Upon work-up and purification the *title compound* was obtained as white crystals (45 mg, 74%). The ee was determined as described later.

3.1.15. Formation of the racemic Mosher esters of the phenyl diol: (1*RS*,3*RS*,4*RS*,5*RS*)-4-hydroxy-1-methyl-4-phenylbicyclo[3.2.0]hept-3-yl (2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate. According to the procedure of Hassner,[25] the following reagents were combined; the diol **23** (7 mg, 0.03 mmol), CH_2Cl_2 (0.5 mL), DCC (22 mg, 0.11mmols), DMAP (5 mg, 0.04 mmol) and (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (23 mg, 0.10 mmol). Flash chromatography (hexanes/EtOAC 95/5 v/v) eluant gave the *title compound* as a colourless liquid (9 mg, 63%). From the ^1H NMR spectrum of the products from the racemic and optically active samples it was possible to assign the following data. Diastereomer A: δ_H (300 MHz): 1.33 (s, 3H), 1.3–2.5 (9H, complex), 3.37 (br. s, 3H), 6.26 (dd, 1H), 7.35–7.55 (m, 5H). Diastereomer B: δ_H (300 MHz): 1.35 (s, 3H), 1.3–2.5 (9H, complex), 3.53 (br. s, 3H), 6.28 (dd, 1H), 7.35–7.55 (m, 5H).

3.1.16. Kinetic resolution of (1*RS*,5*SR*)-5-methyl-2-phenylbicyclo[3.2.0]heptan-2-ene (9). *Kinetic resolution A*: a mixture of K_2CO_3 (73 mg, 0.53 mmol), $K_3Fe(CN)_6$ (118 mg, 0.36 mmol), $MeSO_2NH_2$ (37 mg, 0.38 mmol), $(DHQD)_2$-PHAL (2 mg, 0.01 mmol), *tert*-BuOH (3 mL), H_2O (3 mL), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), were combined and cooled to 0°C. The mixture was stirred with the aid of a mechanical stirrer (350 rpm). Once the reaction mixture had reached 0°C, the stirring was stopped and racemic alkene **9** (125 mg, 0.68 mmol) was added. After stirring at 0°C for 3 h the reaction mixture was quenched with sodium sulfite solution (4 mL, 0.5 g/mL). The solution was then worked-up according to the general procedure. The ee of the optically acitve diol **23a** (30 mg recovered) was determined as for the racemic diol (88% ee). The optical purity of the active alkene **9b** (52 mg recovered) was determined by initially converting the alkene **9b** to the optically active diol **23b**, and then to the corresponding Mosher esters (52% ee).

Kinetic resolution B: the above procedure was repeated with K_2CO_3 (84 mg, 0.61 mmol), $K_3Fe(CN)_6$ (189 mg, 0.57 mmol), $MeSO_2NH_2$ (44 mg, 0.46 mmol), $(DHQD)_2$-PHAL (2 mg, 0.01 mmol), *tert*-BuOH (3 mL), H_2O (3 mL), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), and racemic alkene **9** (108 mg, 0.58 mmol). The ee of both products was determined as described earlier and found to be 80% for the diol (68 mg recovered) and 80% for the alkene (32 mg recovered).

3.1.17. Kinetic resolution of (1*SR*,5*RS*)-2,5-dimethylbicyclo[3.2.0]hept-2-ene (24). The required alkene was synthesized according to a method reported earlier.[15]

Kinetic resolution A: a mixture of K_2CO_3 (96 mg, 0.69 mmol), $K_3Fe(CN)_6$ (179 mg, 0.54 mmol), $MeSO_2NH_2$ (41 mg, 0.43 mmol), $(DHQD)_2$-PHAL (2 mg, 0.01 mmol), *tert*-BuOH (4 mL), H_2O (4 mL), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), were combined and cooled to 0°C. The mixture was stirred with the aid of a mechanical stirrer (350 rpm). Once the reaction mixture had reached 0°C, the stirring was stopped and racemic alkene **24** (128 mg, 1.05 mmol) was added. After stirring at 0°C for 3 h the reaction was quenched with sodium sulfite solution (4 mL, 0.5 g mL^{-1}). The solution was then worked-up according to the general procedure. The ee of the optically active diol (21 mg recovered) was determined by conversion to the corresponding Mosher esters (23% ee).

Kinetic resolution B: the above procedure was repeated with K_2CO_3 (96 mg, 0.69 mmol), $K_3Fe(CN)_6$ (187 mg, 0.57 mmol), $MeSO_2NH_2$ (48 mg, 0.50 mmol), $(DHQD)_2$-PHAL (3 mg, 0.01 mmol), *tert*-BuOH (4 mL), H_2O (4 mL), OsO_4 (50 μL, 4 wt% solution, 2.0 mg, 0.01 mmol), and racemic alkene **24** (125 mg, 1.02 mmol). The enantiomeric excess of the optically active diol (22 mg recovered) was determined by conversion to the corresponding Mosher esters (23% ee).

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