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Synthesis of a new C_2-Symmetric Chiral Diol: Application to Asymmetric Allylboration.

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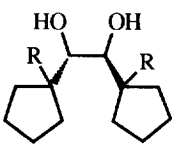
Abstract: New C_2-symmetric chiral diol **1b** was prepared from diol **3a**, by a thionyl chloride mediated double elmination, hydrogenation and deprotection sequence. A comparative study of the asymmetric allylboration of benzaldehyde with the allylboronates **12** and **13** showed 15 and 18 % e.e. respectively in the corresponding homoallylic alcohol **14**. © 1997 Elsevier Science Ltd.

Introduction.

One of the most useful tools to be developed over recent years for asymmetric synthesis has been the use of the asymmetric allylation of aldehydes.[1] Of these methods, allylation using allylboronate derivatives has been particularly useful for the preparation of stereochemically defined molecules.[2]

Following on from recent reports from these laboratories[3] on the use of a new, readily available, hindered C_2-symmetric diol auxiliary **1a** for the controlled asymmetric reduction of remote carbonyl groups,[4] an investigation of the utility of the diol **1a** and its de-methoxylated counterpart **1b** in asymmetric allylation processes was undertaken. In this paper, we report the result of these studies and the process by which **1a** was de-oxygenated to **1b**.



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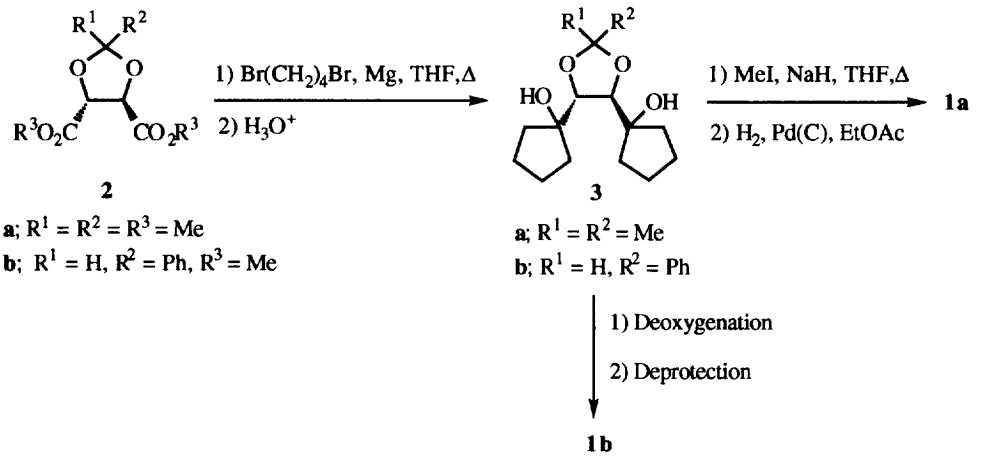
a; R = OMe
b; R = H

Results and Discussion.

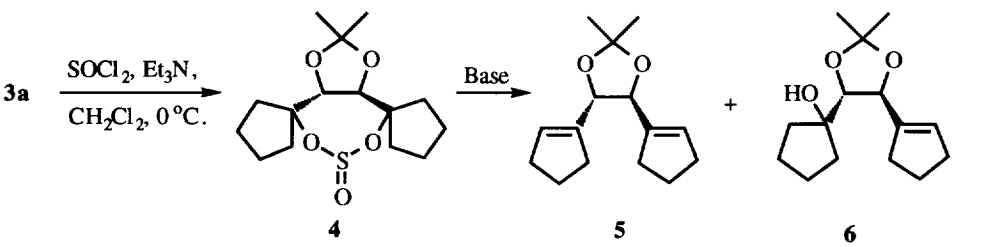
Both antipodes of bis-methoxy ethane diol **1a** are readily available on multi-gram scale from tartrate esters*via* an acetal protection, bis-Grignard and methylation sequence (**Scheme 1**).[3b] Similarly, it was envisaged that diol **1b** would be accessible from intermediate diol **3a**, which is in turn available from isopropylidene tartrate esters by a double deoxygenation and deprotection sequence.

This proved more difficult than originally envisaged due to the lack of reactivity of the hindered tertiary alcohols of **3**. For example, diol **3a** failed to react cleanly with methanesulphonyl chloride/triethylamine[5] or sodium hydride/carbon disulfide/iodomethane.[6] However upon using thionyl chloride, according to the method of Sharpless,[7] it was expected that diol **3a** would afford sulfite **4**, which upon double elimination would provide **5** (**Scheme 2**).

Scheme 1.



Scheme 2.



However, addition of four equivalents of triethylamine to a solution of 1,4-diol **3a** followed by thionyl chloride gave two products, which were identified as mono- and di-eliminated derivatives **6** and **5** in 20 % and 40 % yields respectively after chromatographic separation.

The poor yield and selectivity observed in the formation of bis-alkene **5** prompted optimisation of the reaction by examining alternative reaction conditions. By carrying out the thionyl chloride/triethylamine mediated elimination at -78 °C in dichloromethane it was hoped to promote the formation of alkene **5**. However, under these conditions, only the cyclic sulfite **4** was obtained in 93 % yield. Unfortunately, attempts to directly obtain solely the bis-alkene **5** by varying reaction conditions only resulted in decomposition products. Therefore, alternative methods for the direct elimination of cyclic sulfite **4** to give **5** were examined.

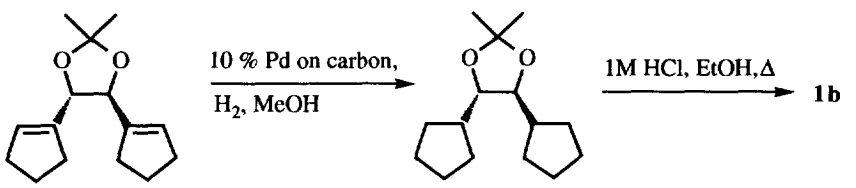
Cyclic sulfite **4** proved unreactive towards 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) mediated elimination. However, reaction of sulfite **4** with triethylamine over extended periods did provide only the alkene **5**, but in a maximum yield of 30 % and product formation was also accompanied by considerable

decomposition. In an attempt to improve the efficiency of the elimination process, the cyclic sulfite **4** was exposed to catalytic ruthenium(VIII) oxide mediated oxidation[8] in order to access the more reactive cyclic sulfate derivative of **4**. However, only complex mixtures of products were produced.

Finally reaction of diol **3a** with thionyl chloride/pyridine was attempted using the procedure of Corey[9] to effect elimination to give **6**. Addition of four equivalents of a 1:1 mixture of thionyl chloride and pyridine to a solution of 1,4-diol **3a** at -78 °C resulted in the formation of sulfite **4**. However, when the reaction was quenched at -10 °C, formation of a 1:1 mixture of mono-eliminated derivative **6** and cyclic sulfite **4** was observed.

Hydrogenation of the alkene derivative **5** using 10 % palladium on carbon in ethyl acetate gave isopropylidene derivative **7** in 98 % yield (**Scheme 3**) and acetal hydrolysis with hydrochloric acid in ethanol gave the C_2-symmetric diol **1b** in 64 % yield. The stability of **1b** under these hydrolysis conditions contrasts with that of **1a**, which readily undergoes pinacol rearrangement.

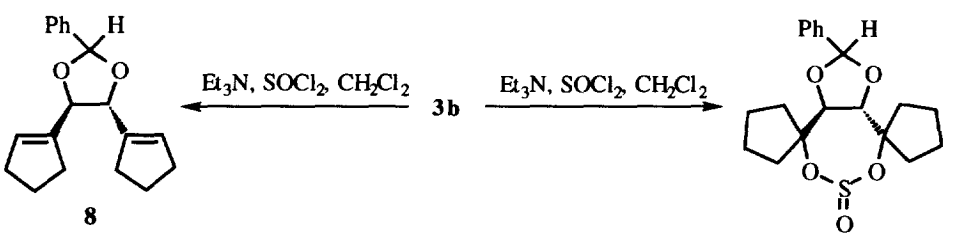
Scheme 3.



5 **7**

1,2-Diol **1a** could also be accessed more readily, especially on larger scales using the benzylidene acetal protection, *i.e.* starting from acetal **2b**. Thus reaction of **2b** with dibromobutane and magnesium, as previously reported,[3] gave **3b**. Elimination of diol **3b** using thionyl chloride/triethylamine was then attempted to effect the formation of the di-eliminated derivative **8** (**Scheme 4**). However, formation of cyclic sulfite **9** ensued in 87% yield and clean elimination of **9** could not be effected under a variety of different basic conditions without causing decomposition.

Scheme 4.



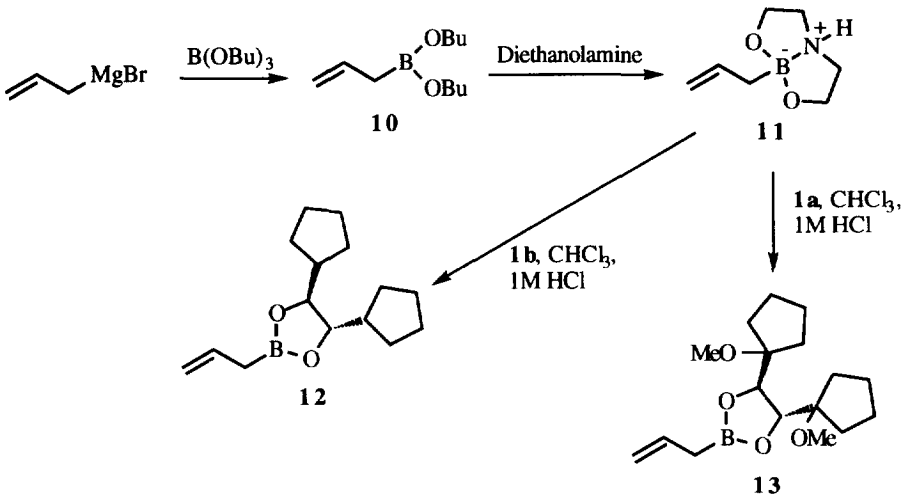
8 **9**

Having obtained diols **1a** and **1b**, it was decided to test the synthetic utility of these chiral diols as boronate esters *via* the preparation of chiral allylboronates **13** and **12** respectively, as shown in the **Scheme 5**. Preparation of dibutyl allylboronate **10** was achieved according to the procedure of Roush[10] and preparation of the diethanolamine ester **11** was carried out using the method of Matteson.[11] The boronate esters **13** and **12**

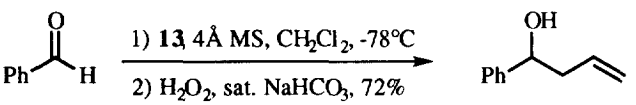
were then readily available by transesterification of **11** with either diols **1a** or **1b** (**Scheme 5**) using standard conditions.[3]

The utility of chiral allylboronate derivative **13** in asymmetric allylation reactions was then attempted with benzaldehyde under exceptionally rigorously dry conditions, in dichloromethane at -78 °C. The allylation was remarkably slow, but after 12 hours the reaction was complete and the homoallylic alcohol **14** in obtained 72 % yield, together with recovered diol **1a** (60 %) after chromatography (**Equation 1**).

Scheme 5.



Equation 1.



Measurement of the optical rotation of the homoallylic alcohol **14** gave an $[\alpha]^{24}_{D}$ of -10.5 ° [*c* 0.25, chloroform], which when compared with a literature[12,13] value of -44.9 ° showed an optical purity of 23 %. The absolute configuration of the major enantiomer of the homoallylic alcohol **14** could be assigned (*S*) on the basis of the negative rotation. A more accurate measurment of the e.e. of homoallylic alcohol **14** produced by **Equation 1** was achieved by preparation of the corresponding Mosher ester, *i.e.* **15**, as shown in **Equation 2**. Examination of the ^{19}F CF_3 signals of **15** showed that its' precursor (*i.e.* **14** from **Equation 1**) had been obtained with an e.e. of only 18 %. This was also confirmed by the intensities of the OMe signals in the ^{1}H nmr spectrum of **15**.

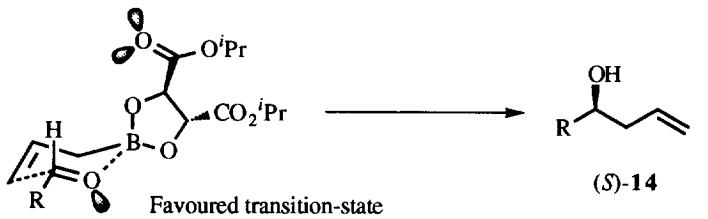
Mechanistic studies of the transition-state involved in the allyl addition of tartrate derived allylboronate to aldehydes has been carried out by Roush[14,15] and showed that (*S*)-**14** (**Scheme 6**) was obtained preferentially from the reaction of (*R,R*)-tartrate derived allylboronates. The stereochemistry induced by the tartrate auxiliary is defined by a tight transition-state **16**, where non-bonding interactions between the lone pair on the aldehydic

oxygen, and the ester carbonyl is minimised. The transition-state **17** is considered to be disfavoured due to the lone pair-lone pair alignment.

Equation 2.

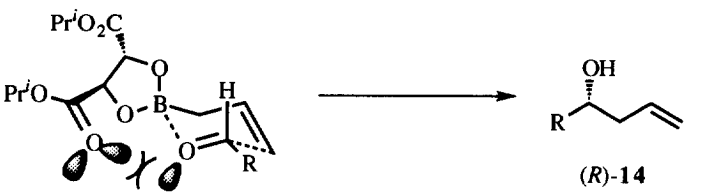
15

Scheme 6.

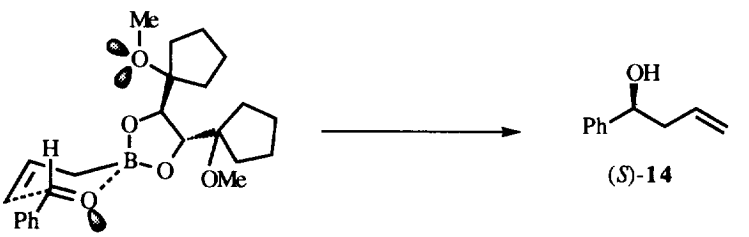


Favoured transition-state

16



17 Disfavoured transition-state



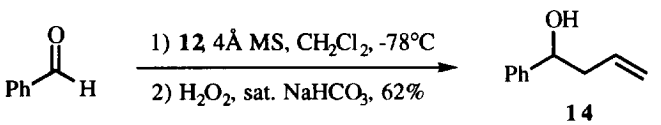
18

The stereochemistry of the asymmetric allyl addition between benzaldehyde and allylboronate **13** therefore can be predicted by a transition-state such as **18** according to Roush's model (**Scheme 6**), thus leading to the (*S*)-homoallylic alcohol **14** as the major product. Although this is indeed the case, the poor asymmetric induction is perhaps indicative of the fact that boronate **13** should be less Lewis-acidic than its

tartrate relatives, therefore it is expected that transition-state **18** is less tight than the corresponding transition-state **16**. This effect certainly seems to be reflected by the low reactivity of **13** and hence the long reaction time (12 hours) required for allylation.

The next question was whether the methoxy groups of allylboronate **13** could be adversely affect the allyation process. Thus, examination of the asymmetric allylation of benzaldehyde with allylboronate derivative (*S,S*)-**12** was attempted. In a similar manner to **13**, the reaction of **12** with benzaldehyde was slow (12 hours to completion) and homoallylic alcohol **14** (**Equation 3**) was obtained in 62 % yield after chromatography. Measurement of optical rotation of **14** (from **Equation 3**) gave an $[\alpha]^{24}_{D}$ of -8.5° (*c* 0.25, chloroform), showing an optical purity of 19 %. Confirmation of the low asymmetric induction was derived by preparation of the corresponding Mosher ester derivative, which showed an e.e. of 15 %.

Equation 3.



14

The fact that equally poor enantiomeric excess is obtained when swapping from allylboronates **13** to **12** is probably indicative of a loose transition-state due to low boron Lewis-acidity (*vide supra*) and that the presence of the methoxy groups in **13**, fails to profoundly affect the stereoelectronic effects operating in the reaction. The fact that the major factor operating on the reactions shown in **Equations 1** and **3** is probably low boron Lewis-acidity is further demonstrated by the discovery that allylboronates **13** and **12** show surprising stability to moisture (compared to tartrate esters). Indeed, this is demontrated by the fact that both boronates **13** and **12** could be readily purified by silica gel chromatography without attendant hydrolysis.

Summary.

Although the asymmetric induction using allylboronates **12** and **13** is low, it is interesting to compare the efficiency of these boronate esters with other chiral diol boronate systems; the most efficient, simple allylboronate derived agents in the allylation of benzaldehyde are: 1) the camphor derived agents of Hoffmann,[12] which provide **14** in 71 % e.e.; and 2) the tartrate derived agents of Roush,[18,15] which provide **14** in 71-85 % e.e. However, simple diols such as 2,3-butanediol and 2,4-pentanediol are ineffective or poor as asymmetric allylating agents when utilised as allylboronate esters;[18] for example providing **14** with 17 and 0 % e.e. respectively. Although C_2-symmetric diols **1** are similarly inefficient when utilised in allylboration reactions, the ease of preparation of diol **1a** in particular, indicates potential utility for future asymmetric applications to augment those already reported.[3]

Experimental.

For thin layer chromatography Merck [silica gel 60 F_{254} (Art. 5735) or Macherey-Nagel [Sil G/UV_{254} (Art.805201)] silica coated plastic sheets were employed. Chromatograms were developed with either iodine vapour or a phosphomolybdic acid (10.0 g in 100 ml of ethanol or methanol) spray and with subsequent heating. For silica gel chromatography Merck Kieselgel H (Type 60) or Acros silica gel (0.035-0.07 mm) was

used. n-Butyllithium was purchased from Aldrich. Toluene and dichloromethane were dried by distillation from calcium hydride, and tetrahydrofuran was distilled from sodium-benzophenone ketyl immediately prior to use, and all distillations carried out under an atmosphere of argon. Light petroleum refers to the fraction boiling in the range 40-60 °C. All anhydrous reactions were carried out in oven dried (140 °C) glassware and cooled under a stream of argon. For rotary evaporation, a Büchi rotary evaporator or a Büchi cold finger rotary evaporator was used followed by evaporation under-high vacuum. Bulb to bulb distillation was achieved using a Büchi GKR-51 Kügelrohr distillation apparatus. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. For optical rotation measurements an Optical Activity AA-1000 polarimeter was used. ^{1}H and ^{13}C NMR were recorded at 300 and 75.6 MHz respectively on a Bruker AC300 NMR spectrometer, using $CDCl_3$ as a internal standard. ^{11}B and ^{19}F NMR spectra were recorded at 64.2 and 188.3 MHz respectively, on a Bruker AC200 NMR spectrometer, relative to $BF_3.OEt_2$ (δ ^{11}B = 0.00) and CF_3CO_2H (δ ^{19}F= 0.00) as external standards. Infrared spectra were recorded on a Perkin-Elmer 783, equipped with a PE600 data station, or a Perkin-Elmer 1600 Series FTIR. UV spectra were recorded on a Perkin-Elmer λ15 spectrometer. Electron impact (EI) (70 e.v) and chemical ionisation (CI) mass spectra were recorded on a Kratos MS25. Fast atom bombardment (FAB) spectra were recorded on a Kratos MS50, using a *meta*-nitrobenzylalcohol or thioglycerol matrix, and accurate mass determinations employed a Kratos Concept IS spectrometer. Microanalyses were performed using a Carlo-Erba 1106 elemental analyser.

(1R,2R)-1,2-Di(1-hydroxycyclopentyl)-1,2-(O-isopropylidene)ethane-1,2-diol ***3a****.*

To a stirred mixture of dry magnesium turnings (7.0 g), tetrahydrofuran (300 ml) and 1,4-dibromobutane (22.0 ml, 67.4 mmol) under argon, was added a few crystals of iodine. Once the exothermic reaction started the temperature was maintained at 30-40 °C using an ice bath. After 30 min., the reaction was heated under reflux for 4 h. Ester **2a**[17] (15.0 g, 68.8 mmol) in dry tetrahydrofuran (100 ml) was added at 0 °C. and the mixture was refluxed for a further 6 h, cooled to room temperature and quenched with saturated ammonium chloride (100 ml). After partitioning between ethyl acetate and saturated ammonium chloride, the organic layer was dried ($MgSO_4$) and evaporated to give a sticky white solid. The solid was recrystallised from hexane to give pure 1,4-diol derivative **3a** (9.45 g, 50 %) as fine colourless needles: M.P. 162-165 °C; $[\alpha]^{20}_D$ = 19° [*c* 1.0, chloroform]; υ_{max} (film) *inter alia* 3250 br (OH) cm^{-1}; δ (^{1}H, $CDCl_3$) 1.39 (6H, s, 2 x CH_3), 1.98-1.43 (16H, m, cyclopentyl CH_2), 3.01 (2H, br s, 2 x OH), and 3.93 (2H, s, 2 x CH) (addition of D_2O caused the signal at δ 3.01 to disappear); δ (^{13}C, $CDCl_3$) 23.9, 24.1, 27.4, 34.5, 38.2, 81.6, 81.8, and 107.5; m/z (CI) 288 $(M+NH_4)^+$, and 271 $(M+H)^+$; Accurate m.s: $C_{15}H_{24}O_4$ $(M+H)^+$ requires m/z 271.1909, peak at m/z 271.1909.

(1R,2R)-1,2-Bis(1,2-cyclopentenyl)-1,2-(O-isopropylidene)ethane-1,2-diol ***5****, and (1R,2R)-1-(1,2-cyclopentenyl)-2-(1-hydroxycyclopentyl)-1,2-(O-isopropylidene)ethane-1,2-diol* ***6****.*

To a solution of isopropylidene 1,4-diol derivative **3a** (1.00 g, 3.70 mmol) in dry dichloromethane (15 ml) under argon at 0 °C, was added freshly distilled thionyl chloride (0.404 ml, 5.55 mol) followed by dry

triethylamine (2.07 ml, 14.80 mmol). The reaction was stirred at 0 °C for 30 min, and the resulting dark brown solution was quenched with water (10 ml). The organic layer was washed with 1M hydrochloric acid (10 ml), and water; the aqueous layer was re-extracted with dichloromethane. The combined organic extracts were dried ($MgSO_4$) and evaporated to give a dark brown oil. Purification by Kugelrohr distillation (125 °C, 0.3 mmHg) gave a crude mixture of mono- and di-eliminated products **5** and **6** respectively. Separation of the mixture by silica gel chromatography (ethyl acetate : hexane, gradient elution) gave pure di-eliminated acetonide derivative **5** (0.400 g, 40 %) as a pale yellow oil: $[\alpha]^{20}_D$ = +16.5° [*c* 0.20, chloroform]; υ_{max} (film) *inter alia* 1575 (C=C) cm^{-1}; δ (^1H, $CDCl_3$) 1.43 (6H, s, 2 x CH_3), 1.85-2.48 (12H, br m, cyclopentyl CH_2), 4.42 (2H, s, 2 x CH), and 5.73 (2H, t, *J* = 3.8 Hz, 2 x C:CH), δ (^{13}C, $CDCl_3$) 23.4, 27.1, 31.4, 31.5, 78.5, 108.3, 129.5, and 140.6; m/z (FAB) *inter alia* 235 (M+H)+; Accurate m.s: $C_{15}H_{23}O_2$ $(M+H)^+$, requires m/z 235.1698, peak at m/z 235.1705; and pure mono-eliminated acetonide derivative **6** (0.190 g, 20 %) as a pale yellow oil: $[\alpha]^{20}_D$ = -41.3° [*c* 0.30, chloroform]; υ_{max} (film) *inter alia* 3400 (OH) cm^{-1}; δ (^1H, $CDCl_3$) 1.42 and 1.47 (each 3H, s, CH_3), 1.50-2.49 (14 H, br m, cyclopentyl CH_2), 3.99 (1H, d, *J* = 7.8 Hz, OC<u>H</u>.CHO), 4.71 (1H, d, *J* = 7.8 Hz, OCH.C<u>H</u>O), and 5.83 (1H, t, *J* = 3.8 Hz, C:CH); δ (^{13}C, $CDCl_3$) 23.3, 23.7, 30.0, 30.9, 39.1, 39.4, 27.0, 27.1, 77.6, 79.9, 83.6, 109.0, 131.5, and 141.5; m/z (FAB) *inter alia* 253 $(M+H)^+$; Accurate m.s: $C_{15}H_{25}O_3$ $(M+H)^+$ requires m/z 253.1804, peak at m/z 253.1795.

Preparation of sulfite ester 4.

To a solution of isopropylidene 1,4-diol derivative **3a** (1.00 g, 3.70 mmol) in dry dichloromethane (15 ml) under argon, at -78 °C was added pyridine (1.19 ml, 14.8 mmol) followed by thionyl chloride (0.540 ml, 7.40 mmol). The reaction mixture was stirred at -78 °C for 5 h, warmed to -10 °C and quenched with water. The organic layer was separated, washed with 2M hydrochloric acid and water and the aqueous layer was re-extracted with dichloromethane. The combined organic extracts were dried ($MgSO_4$), and evaporated to give the sulfite **4** (1.09 g, 93 %) as a pale brown oil: $[\alpha]^{20}_D$ = +24.5° [*c* 0.4, chloroform]; υ_{max} (film) *inter alia* 1452 and 1436 (S:O) cm^{-1}; δ (^1H, $CDCl_3$) 1.42 (6H, s, 2 x CH_3), 1.61-2.40 (16H, br m, cyclopentyl CH_2), 4.32 (1H, d, *J* = 9.2 Hz, C<u>H</u>.CH), and 4.64 (1H, d, *J* = 9.2 Hz, CH.C<u>H</u>); δ (^{13}C, $CDCl_3$) 23.0, 23.3, 23.9, 24.2, 31.9, 38.3, 38.3, 39.5, 26.9, 27.0, 79.0, 80.1, 93.2, 93.7, and 110.3; m/z (CI) *inter alia* 334 $(M+NH_4)^+$; Accurate m.s: $C_{15}H_{28}NO_5S$ $(M+NH_4)^+$ requires m/z 334.1688, peak at m/z 334.1693.

(1S,2S)-1,2-Dicyclopentyl-1,2-(O-isopropylidene)ethane-1,2-diol 7.

To a stirred solution of dicyclopentenenyl isopropylidene derivative **5** (0.300 g, 1.28 mmol) in ethyl acetate was added 10 % palladium on carbon (50 mg). The mixture was degassed *via* a water aspirator and saturated with hydrogen for 3 days. The resulting solution was filtered through Celite and evaporated to furnish pure cyclopentyl isopropylidene derivative **7** (0.300 g, 98 %) as a pale yellow oil: $[\alpha]^{20}_D$ = -31.2° [*c* 0.30, chloroform]; υ_{max} (film) *inter alia* 1350 (C.O.C) cm^{-1}; δ (^1H, $CDCl_3$) 1.24-1.90 (18H, br m, cyclopentyl CH_2

and $CH_2.CH$) 1.38 (6H, s, 2 x CH_3), and 3.66 (2H, d, J = 5.7 Hz, 2 x O.CH); δ (^{13}C, $CDCl_3$) 25.6, 26.1, 27.3, 29.7, 27.1, 42.7, 83.7, and 107.7; m/z (FAB) *inter alia* 239 $(M+H)^+$, 178 $(M-C_3H_6O)^+$; Accurate m.s: $C_{15}H_{27}O_2$ $(M+H)^+$ requires m/z 239.2011, peak at m/z 239.1649.

(1S,2S)-Dicyclopentylethane-1,2-diol ***1b***.

To a solution of cyclopentyl acetonide derivative **7** (0.30 g, 1.26 mmol) in ethanol (10 ml), was added 2M hydrochloric acid (1.00 ml). The mixture was refluxed for 6 h, volatile components were removed by evaporation and the reaction mixture was diluted with ethyl acetate and saturated sodium chloride. The organic phase was separated and washed with saturated sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated to give pure diol **1b** (0.159 g, 64 %) as a colourless solid: M.P. 96 °C; $[\alpha]^{20}_D$ = +19.5° [*c* 0.2, chloroform]; υ_{max} (film) *inter alia* 3400 br (OH) cm^{-1}; δ (^1H, $CDCl_3$) 1.00-2.05 (20H, br m, cyclopentyl CH_2, 2 x CH_2.CH and 2 x OH), 3.23 (2H, d, J = 8.0 Hz, 2 x OCH) (addition of D_2O caused the signal at δ1.00-2.05 to become an 18H, m); δ (^{13}C, $CDCl_3$) 25.2, 25.3, 28.9, 29.1, 42.7 and 77.0 (CH.OH); m/z (FAB) *inter alia* 216 $(M+NH_4)^+$; Accurate m.s: $C_{12}H_{26}NO_2$ $(M+NH_4)^+$ requires m/z 216.1964, peak at m/z 216.1958.

Preparation of benzylidene sulfite ***9***.

To a solution of benzylidine diol derivative (*S,S*)-**3b** (0.500 g, 1.57 mmol) in dry dichloromethane (10 ml) under argon at -78 °C, was added triethylamine (0.220 ml, 6.28 mmol) followed by thionyl chloride (0.229 ml, 3.14 mmol). The reaction mixture was stirred at -78 °C for 5 h, quenched with water at -30 °C and after warming to room temperature the organic layer was washed with 1M hydrochloric acid and water. The aqueous layer was re-extracted with dichloromethane and the combined organic extracts were dried ($MgSO_4$), and evaporated to give sulfite **9** (0.500 g, 87 %) as pale yellow crystals and a 1:1 mixture of diastereoisomers: M.P. 88-94 °C; $[\alpha]^{20}_D$ = +32° [*c* 0.5, chloroform]; υ_{max} (film) *inter alia* 1452 and 1436 (S:O) cm^{-1}; λ_{max} (EtOH) 204.9 (ε 8177) nm; δ (^1H, $CDCl_3$) 1.68-2.30 (32H, br m, cyclopentyl CH_2), 4.50 and 4.55 (each 1H, d, J = 5.0 Hz, 2 x CHO), 4.98 (2H, d, J = 8.9 Hz, CHO), 5.97 (1H, s, PhCH), 5.99 (1H, s, PhCH) and 7.39-7.48 (10H, m, aromatic CH); δ (^{13}C, $CDCl_3$) 23.2, 23.3, 23.5, 23.6, 23.9, 24.0, 24.1, 24.4, 24.6, 32.1, 32.3, 32.7, 32.8, 38.6, 39.61, 36.66, 79.3, 80.5, 81.1, 82.0, 93.0, 93.8, 95.2, 95.8, 105.3, 105.4, 126.7, 126.8, 128.5, and 129.8; m/z (FAB) *inter alia* 363 $(M-H)^+$; Accurate m.s: $C_{19}H_{25}O_5S$ $(M+NH_4)^+$ requires m/z 365.1430, peak at m/z 382.1691.

Diethanolamine allylboronate ***11***.

To a solution of dibutyl allylboronate derivative **10**[16] (4.00 g, 21.3 mmol) in dry ether (40 ml) under Ar, was added diethanolamine (10.11 ml of a 2M solution in isopropanol). The reaction was allowed to stir at room temperature for 8 h, the resulting solid was separated by decanting the solvent and dried under vacuum to give allylboronate derivative **11** (3.05 g, 92 %) as a white solid: υ_{max} (KBr disc) 3400 br (NH) cm^{-1}; δ (^{11}B,

$CDCl_3$) +11.0; δ (^1H, $CDCl_3$) 1.47 (2H, br d, *J* = 8.1 Hz, CH_2B), 2.73-2.85 (2H, m, 2 x C<u>H</u>H.N), 3.13-3.27 (2H, m, 2 x CH<u>H</u>.N), 3.82-4.0 (4H, br m, OCH_2), 4.76-5.01 (2H, m, CH:C<u>H</u>$_2$), 5.30 (1H, br s, NH), and 5.91-6.07 (1H, m, C<u>H</u>:CH_2) (addition of D_2O caused the signal at δ5.30 to disappear); Analysis calc. for $C_7H_{14}O_2BN$: C, 54.1; H, 9.0; N, 9.0; and B, 7.0. found C, 53.9; H, 9.3; N, 9.1; and B, 6.6 %.

(4S,5S)-4,5-Dicyclopentyl-2-allyl-1,3,2-dioxaborolane ***12****.*

To a solution of diethanolamine allylboronate **11** (0.116 g, 0.754 mmol) in chloroform (5.0 ml) was added 1,4-diol **1b** (0.136 g, 0.686 mmol) followed by 2M hydrochloric acid (2 ml). The reaction mixture was stirred at room temperaturefor 12 hours, the aqueous layer was re-extracted with chloroform and the combined organic extracts dried ($MgSO_4$) and evaporated to give allylboronate ester **12** (0.164 g, 96 %) as a pale yellow oil: $[\alpha]^{20}_D$ = -38.0° [*c* 0.5, chloroform]; δ (^{11}B, $CDCl_3$) +22.8; δ (^1H, $CDCl_3$) 1.20-1.96 (18H, br m, cyclopentyl CH_2 and CH), 3.93 (2H, d, *J* = 6.0 Hz, 2 x O.CH), 4.88-5.06 (2H, m, CH=C<u>H</u>$_2$), 5.81-5.95 (1H, m, C<u>H</u>=CH_2); δ (^{13}C, $CDCl_3$) 25.2, 27.5, 28.1, 45.0, 84.2, 114.6, and 134.2; m/z (FAB) *inter alia* 249 $(M+H)^+$, 235 $(M-CH)^+$, and 207 $(M-C_3H_3)^+$; Accurate m.s: $C_{15}H_{26}O_2B$ $(M+H)^+$ requires m/z 249.2026, peak at m/z 249.2017.

(4R,5R)-4,5-Bis(1-methoxycyclopentyl)-2-allyl-1,3,2-dioxaborolane ***13****.*

To a stirred solution of diethanolamine ester **11** (2.00 g, 12.98 m mol) and 1,4-diol (*R,R*)-**1a** (2.68 g, 10.38 mmol) in chloroform (25 ml) was added 2M hydrochloric acid (4 ml). After 14 h, the organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic extracts were dried ($MgSO_4$) and evaporated to give a crude oil. Purification of the oil by silica gel chromatography (ethyl acetate : hexane, 2 : 8 as the eluent) gave pure allylboronate derivative **13** (3.25 g, 81 %) as a colourless oil: $[\alpha]^{20}_D$ = -23° [*c* 0.15, chloroform]; υ_{max} (film) *inter alia* 1575 (C=C), and 1050 (OMe) cm^{-1}; δ (^{11}B, $CDCl_3$) +22.7; δ (^1H, $CDCl_3$) 1.55-1.78 (16H, br m, cyclopentyl CH_2), 3.23 (6H, s, 2 x OMe), 4.31 (2H, s, 2 x O.CH), 4.90-5.02 (2H, m, CH:C<u>H</u>$_2$), and 5.78-5.87 (1H, m, C<u>H</u>:CH_2); δ (^{13}C, $CDCl_3$) 24.5, 31.1, 31.7, 50.4, 80.0, 87.8, 114.8 and 133.9; m/z (EI) *inter alia* 308 $(M)^+$; Analysis calc. for $C_{17}H_{29}O_4$: C, 66.2; H, 9.4; B, 3.5. Found: C, 66.0; H, 9.7; B, 3.2 %.

Racemic 1-phenylbut-3-en-1-ol ***14*** *from allylmagnesium bromide and benzaldehyde.*

To a stirred mixture of freshly distilled benzaldehyde (7.0 g, 66.03 mmol), dry toluene (130 ml) under Ar at 0 °C was allylmagnesium bromide (66.0ml of a 1M solution in diethyl ether). The reaction was stirred for 18 h, quenched with water, extracted with ethyl acetate, dried ($MgSO_4$) and evaporated to give a crude oil. Purification of the oil by silica gel chromatography (ethyl acetate : hexane, gradient elution) gave racemic homoallylic alcohol **14** (8.40 g, 86 %) as a pale yellow oil. All spectroscopic and analytical data were identical to that reported in the literature.[12,13]

1:1 mixture of diastereoisomeric Mosher ester derivatives 15.

Dry pyridine (0.10 ml), (-)-α-methoxy-α–triflurophenylacetyl chloride (0.034 g, 0.136 mmol) and racemic alcohol **14** as prepared from the previous experiment (0.020 g, 0.136 mmol) were mixed at room temperature for 12 hours. The reaction mixture was diluted with dichloromethane, washed with 2M hydrochloric acid, saturated sodium hydrogen carbonate, and saturated sodium chloride. The aqueous layers were re-extracted with dichloromethane and the combined organic extracts were dried ($MgSO_4$), and evaporated to give α–methoxy triflurophenyl acetyl derivative **15** (0.502 g, 101 %) as a pale yellow oil 1:1 mixture of diastereoisomers:[12,13] δ (^{19}F, $CDCl_3$) 6.20 and 6.44 (each CF_3); δ (^1H, $CDCl_3$) 2.52-2.62 and 2.64-2.79 [each 2H, m, CH(OH)C<u>H</u>2], 3.44 and 3.45 (each 3H, s, 2 x OCH_3), 4.95-5.15 (4H, m, CH_2=CH), 5.59-5.80 (2H, m, C<u>H</u>=CH_2), 5.98-6.05 (2H, m, PhC<u>H</u>O), and 7.20-7.43 (10H, m, aromatic CH); m/z (CI) *inter alia* 382 $(M+NH_4)^+$; Accurate m.s: $C_{20}H_{23}NO_3F_3$ $(M+NH_4)^+$ requires m/z 382.1630, peak at m/z 382.1639.

(S)-1-Phenylbut-3-en-1-ol 14 from (4R,5R)-4,5-bis(1-methoxycyclopentyl)-2-allyl-1,3,2-dioxaborolane 13.

To a stirred mixture of allylboronate (dried exhaustively over P_2O_5 under vacuum) (*R,R*)-**13** (0.200 g, 0.649 mmol), dichloromethane (6.0 ml) and activated molecular sieves 4 Å (0.100 g) under Ar at -78 °C, was added freshly distilled benzaldehyde (0.079 ml, 0.779 mmol). The reaction was stirred for 12 h, quenched with hydrogen peroxide (1.0 ml, 0.779 mol) and saturated sodium hydroxide, diluted with dichloromethane and the residue filtered. The aqueous layer was separated and washed with dichloromethane, the combined organic extracts were dried ($MgSO_4$) and evaporated to give a crude oil. Purification of the oil by silica gel chromatography (ethyl acetate : hexane, gradient elution) gave homoallylic alcohol **14** (0.083 g, 72 %) as a pale yellow oil. The analytical and spectral data were identical to those reported: $[\alpha]^{20}_D$ = -10.5° [*c* 0.25, chloroform] [lit. $[\alpha]^{20}_D$ = -44.9° [*c* 7.38, benzene].[12,13]

Preparation of Mosher ester 15 from the above experiment.

Dry pyridine (0.10 ml), (-)-α-methoxy-α–triflurophenylacetyl chloride (0.034 g, 0.136 mmol) and (*S*)-alcohol **14** from the previous experiment (0.020 g, 0.136 mmol) were mixed at room temperature for 12 hours. The reaction mixture was diluted the with dichloromethane, washed with 2M hydrochloric acid, saturated sodium hydrogen carbonate, and saturated sodium chloride. The aqueous layers were re-extracted with dichloromethane and the combined organic extracts were dried ($MgSO_4$), and evaporated to give α–methoxy-α-trifluorophenyl acetyl derivative **15** (0.502 g, 101 %) as a pale yellow oil and a mixture of diastereoisomers (18 % d.e.). All analytical and spectral data were identical to those reported above. The diagnostic difference between the two diastereoisomers were: δ (^{19}F, $CDCl_3$) 6.20 and 6.44 (each CF_3); δ (^1H, $CDCl_3$) 3.44 and 3.45 (each 3H, s, 2 x OCH_3).

(S)-1-Phenylbut-3-en-1-ol 14 from (4S,5S)-4,5-dicyclopentyl-2-allyl-1,3,2-dioxaborolane 12.

To a mixture of allylboronate (rigorously dried over P_2O_5 under vacuum) **12** (0.200 g, 0.806 mmol), dichloromethane (6.0 ml) and activated molecular 4 Å sieves (0.100 g) under Ar at -78 °C, was added freshly

distilled benzaldehyde (0.079 ml, 0.779 mmol). The reaction was stirred at -78 °C for 12 h, quenched with hydrogen peroxide (1.0 ml, 0.779 mol) and saturated sodium hydroxide, diluted with dichloromethane and the residue filtered. The aqueous layer was separated and re-extracted with dichloromethane, the combined organic extracts were dried ($MgSO_4$) and evaporated to give a crude oil. Purification of the oil by silica gel chromatography (ethyl acetate : hexane, gradient elution) gave homoallylic alcohol **14** (0.072 g, 62 %) as a pale yellow oil. The analytical and spectral data are similar to those reported above: $[\alpha]^{20}_D$ = -8.5° [*c* 0.25, chloroform] [lit. $[\alpha]^{20}_D$ = -44.9° (*c* 7.38, benzene).[12,13]

Preparation of Mosher ester 15 from the above experiment.

Dry pyridine (0.10 ml), (-)-α-methoxy-α-trifluromethyl)phenylacetyl chloride (0.034 g, 0.136 mmol), and alcohol **14** from the previous experiment (0.020 g, 0.136 mmol) were mixed and left at room temperature for 12 hours. The mixture was diluted with dichloromethane, washed with 2M hydrochloric acid, saturated sodium hyrdogen carbonate and satured sodium chloride. The aqueous layers were re-extracted with dichloromethane, the combined organic extracts were dried ($MgSO_4$) and evaporated to give a mixture of diastereoisomers of **15** (0.049 g, 99 %) as a pale yellow oil. Analytical and spectral data were identical to that obtained above. The ^{19}F NMR and ^{1}H NMR data showed the d.e. of **15** was 15 %.

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