Synthesis of (*R*)- or (*S*)-diphenylphosphinoyl hydroxy aldehydes and 1,2-diols using Mukaiyama's bicyclic aminal methodology and Sharpless asymmetric dihydroxylation

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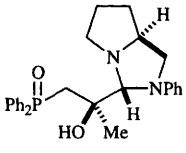
Two different approaches to diphenylphosphinoyl hydroxy aldehydes and 1,2-diols are compared. A lengthy chiral auxiliary approach using proline-derived aminals enables hydroxy aldehydes and 1,2-diols of known absolute stereochemistry and high enantiomeric excess to be synthesised. In contrast, a much shorter asymmetric dihydroxylation route generates 1,2-diols with lower enantiomeric excesses and unexpected (in view of Sharpless's mnemonic) absolute stereochemistry. The dihydroxylation results are thus of both mechanistic and synthetic value.

In the preceding paper,[1] we described the stereoselective synthesis of each one of the four hydroxy aminals *anti*- and *syn*-**1**† and *anti*- and *syn*-**2**. The pivotal point in our synthetic approach was an asymmetric Horner–Wittig addition reaction in which a chiral auxiliary was attached to the electrophile. We imagined these hydroxy aminals to be precursors of optically active hydroxy aldehydes **3** and **4** as well as 1,2-diols **5** and **6**.[2] Additionally, we envisaged that β-hydroxy phosphine oxides such as **3**, **4**, **5** and **6** would be valuable synthetic intermediates for elaboration to a range of optically active allylically functionalised molecules using some of our own established methods.[3]

In this paper, we report the simple conversion of single diastereoisomers of hydroxy aminals **1** and **2** into hydroxy aldehydes **3** and **4** and compare the overall synthetic route with two alternative aminal-based approaches to the same hydroxy aldehydes. Reduction of hydroxy aldehydes **3** and **4** to the corresponding 1,2-diols **5** and **6** is also described. The aminal



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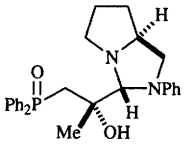
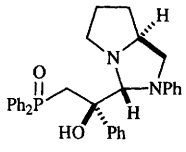


anti-**1**



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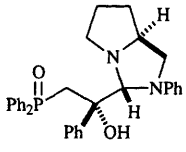
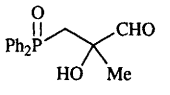


anti-**2**



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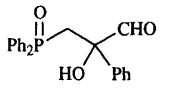

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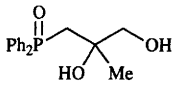

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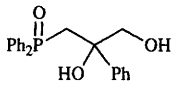

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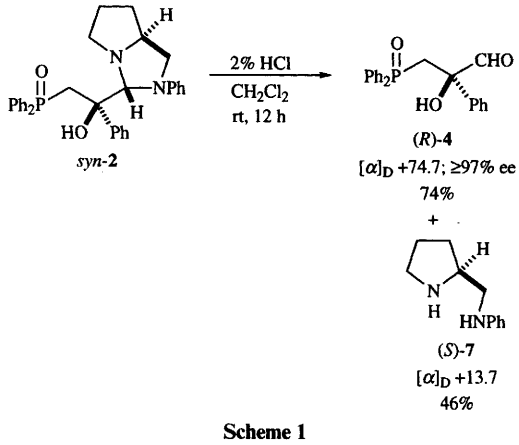
methodology used to synthesise these 1,2-diols is then compared with a completely different and much more direct route: Sharpless asymmetric dihydroxylation[4] of allylic phosphine oxides.[5] As we shall see, our investigation into the asymmetric dihydroxylation of some 1,1-disubstituted allylic phosphine oxides turned out to be of mechanistic as well as synthetic value. Finally, our preliminary results assessing the synthetic potential of these β-hydroxy phosphine oxides are described towards the end of this paper.

† With reference to hydroxy aminals such as **1** and **2**, the terms *syn* and *anti* were defined in the preceding paper.[1]

Conversion of hydroxy aminals into hydroxy aldehydes and 1,2-diols

For the trivial conversion of hydroxy aminals into hydroxy aldehydes, Mukaiyama dissolved his hydroxy aminals in Et_2O and treated them with 2% hydrochloric acid for 12 h at 0 °C.[6] However, since phosphine oxides have limited solubility in Et_2O, we preferred to carry out the aminal hydrolysis reactions in a vigorously stirred 1:1 mixture of CH_2Cl_2 and 2% hydrochloric acid. Our modified reaction conditions worked very well and, as a representative example, hydroxy aminal *syn*-**2** gave hydroxy aldehyde (*R*)-**4** in 74% yield after 12 h at room temperature (Scheme 1). Neutralisation of the acidic aqueous

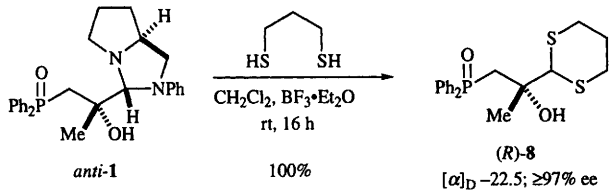


Scheme 1

layer followed by extraction allowed recovery of diamine (*S*)-**7** thus demonstrating the potential of recycling the diamine chiral auxiliary. All of our hydroxy aminals were deprotected in this way and the results are presented in Table 1.

In one case, an alternative way of removing the aminal functionality, namely the direct conversion of the aminal into a dithiane, was attempted. This novel method of deprotection was very successful: treatment of hydroxy aminal *anti*-**1** with propane-1,3-dithiol in the presence of boron trifluoride–diethyl ether afforded a quantitative yield of dithiane (*R*)-**8** (Scheme 2).

As we shall describe later, we also hoped to synthesise optically active 1,2-diols **5** and **6** using the Sharpless asymmetric dihydroxylation reaction. Therefore, hydroxy aldehydes **3** and **4** were reduced to 1,2-diols **5** and **6** using lithium aluminium hydride (Table 2), enabling us to correlate the optical rotations of these 1,2-diols with the same 1,2-diols made using the dihydroxylation reaction.



Scheme 2

Table 1 Conversion of hydroxy aminals **1** and **2** into hydroxy aldehydes **3** and **4**

Hydroxy aminal	Hydroxy aldehyde	Yield (%)	$[\alpha]_D$	Ee (%)
syn-**1**[a]	(*R*)-**3**	96	+5.4	80
anti-**1**	(*S*)-**3**	97	−2.7	≥97
syn-**2**	(*R*)-**4**	74[b]	+74.7	≥97
anti-**2**	(*S*)-**4**	65[c]	−73.5	≥97

[a] 90:10 Ratio of *syn*- and *anti*-**1**. [b] Diamine (*S*)-**7** was recovered in 46% yield. [c] Diamine (*S*)-**7** was recovered in 77% yield.

Table 2 Conversion of hydroxy aldehydes **3** and **4** into 1,2-diols **5** and **6**

Hydroxy aldehyde[a]	1,2-Diol	Yield (%)	$[\alpha]_D$	Ee (%)
(*R*)-**3**	(*R*)-**5**	99	+8.2	80
(*S*)-**3**	(*S*)-**5**	96	−10.1	≥97
(*R*)-**4**	(*R*)-**6**	57	+30.2	≥97
(*S*)-**4**	(*S*)-**6**	61	−30.8	≥97

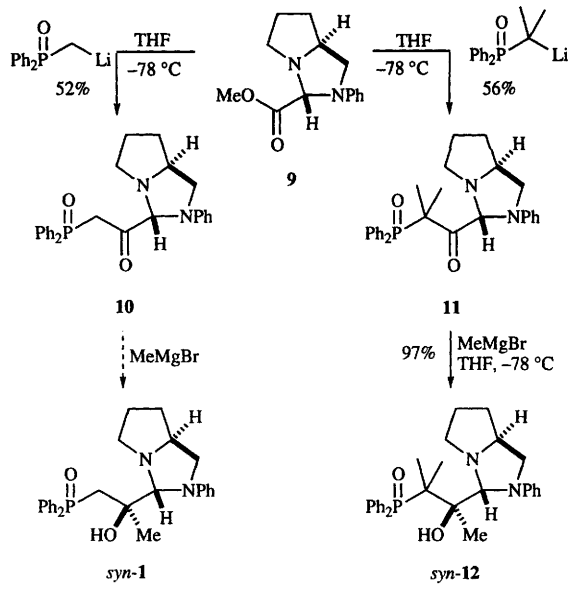
[a] Reaction conditions: lithium aluminium hydride, THF, room temp.

An alternative approach to hydroxy aminal *syn*-1—reversing the order of introduction of the substituents

We have already described a stereoselective synthesis of hydroxy aminal *syn*-**1** using the Felkin[7] non-chelation controlled addition of a lithiated phosphine oxide to a keto aminal.[1] However, a potentially more highly stereoselective route to hydroxy aminals involves adding the two substituents (in this case, diphenylphosphinoylmethyl and methyl) in the opposite order. Thus, we decided to study the addition of methylmagnesium bromide to β-keto phosphine oxide aminal **10** (Scheme 3), a reaction that we believed would proceed under Cram[8] chelation control to give hydroxy aminal *syn*-**1** as the sole product.

β-Keto phosphine oxide **10** was synthesised in a respectable 52% yield using an acylation reaction with the known[1,6] methyl ester **9**. We were particularly pleased with the yield of this reaction because methyl ester **9** is by far the most structurally complex ester that we have used in intermolecular acylation reactions with phosphine oxides.[9] Unfortunately, methylmagnesium bromide [with or without added cerium(III) chloride[10]] and methyllithium failed to add to β-keto phosphine oxide **10**. In all cases, we recovered only the starting phosphine oxide. Presumably, with Grignard reagents and alkyllithiums, enolisation of the rather acidic protons α to phosphorus in β-keto phosphine oxides such as **10** occurs in preference to carbonyl addition. Indeed, Bartoli[11] has recently reported the same observation: Grignard reagents did not add to some simple β-keto phosphine oxides although, in his examples, the use of organocerate reagents[12] (generated by transmetallation of organolithiums) solved this problem.

In order to test our enolisation theory for the failure of Grignard addition to β-keto phosphine oxide **10**, we used another successful acylation reation to synthesise the 'blocked' β-keto phosphine oxide **11** and found that methylmagnesium added smoothly and with essentially complete stereoselectivity (as judged by ^{1}H NMR). Hydroxy aminal *syn*-**12** was obtained



Scheme 3

in essentially quantitative yield (Scheme 3) and the relative stereochemistry was assigned by comparison with Mukaiyama's results[6] assuming that the reaction proceeds under Cram[8] chelation control (see preceding paper[1]).

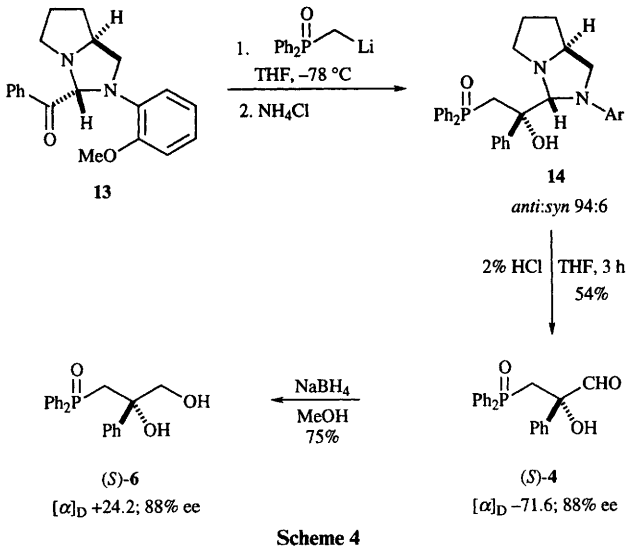
As can be seen from the results, this alternative approach to hydroxy aminals was far from general: we could add Grignard reagents only to 'blocked' β-keto phosphine oxides such as **11**. Unfortunately then, this limitation meant that this new strategy was not going to be a synthetically useful method.

An alternative 'one-pot' approach to hydroxy aldehyde 4—modification of the aminal structure

Mukaiyama has reported highly stereoselective additions of Grignard reagents to keto aminals derived from diamine (*S*)-**7**.[6] In contrast, addition of lithium enolates to these keto aminals was less stereoselective[13] although an improvement in stereoselectivity was observed when the aniline functionality of the aminals was changed from a simple phenyl ring to an *o*-methoxy substituted aromatic ring (*e.g.* **13**). The most successful reactions of keto aminals described in the preceding paper involved the use of lithiated phosphine oxides (reactions of phosphine oxide Grignard reagents were very sluggish)[1] and we wondered whether we could make use of modified keto aminals (*e.g.* **13**) to provide an improved route to our hydroxy aldehyde **4**.

Keto aminal **13** containing the modified aniline group was synthesised starting from (*S*)-*N*-(benzyloxycarbonyl)proline[1,14] using a published route.[13,14] Conversion of phenyl ketone **13** into hydroxy aldehyde (*S*)-**4** was accomplished using an essentially one-pot procedure: phenyl ketone **13** was reacted with lithiated methyldiphenylphosphine oxide to give a mixture of hydroxy aminals **14** and, after quenching with ammonium chloride, the crude reaction mixture was then treated with 2% hydrochloric acid and the mixture stirred vigorously for 3 h to effect the aminal hydrolysis. Subsequent purification by chromatography afforded hydroxy aldehyde (*S*)-**4** in 54% yield over the two steps (Scheme 4). In a separate experiment, the ratio of *anti*- and *syn*-**14** was determined as 96:4 from ^{1}H NMR of the crude addition product. Thus, hydroxy aldehyde (*S*)-**4** had 88% ee.

The product was assigned as hydroxy aldehyde (*S*)-**4** on the basis of $[\alpha]_D^{20}$ −71.6 which correlated with hydroxy aldehyde (*S*)-**4** ($[\alpha]_D^{20}$ −73.5) in Table 1. This is in fact exactly the same sense (and a similar degree) of asymmetric induction that Mukaiyama had obtained when he had added a lithium enolate to the same phenyl ketone.[13] Hydroxy aldehyde (*S*)-**4** (88% ee)

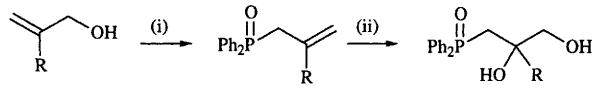


Scheme 4

has also been reduced to 1,2-diol (*S*)-**6**. Despite this encouraging one-pot synthesis of hydroxy aldehyde (*S*)-**4**, the use of keto aminals such as **13** has not been explored any further.

An alternative synthesis of 1,2-diols 5 and 6—Sharpless asymmetric dihydroxylation of allylic phosphine oxides

An alternative synthetic route to 1,2-diols **5** and **6** is dihydroxylation of allylic phosphine oxides **15** and **16** respectively. Furthermore, if we used the Sharpless asymmetric dihydroxylation[4] reaction then we should be able to synthesise optically active 1,2-diols **5** and **6** (Scheme 5) far more quickly



(i) Arbuzov rearrangement
(ii) Sharpless asymmetric dihydroxylation

Scheme 5

than we had done using the aminal methodology. A comparison of these two very different synthetic approaches to diphenylphosphinoyl 1,2-diols is presented at the end of this paper.

For the purpose of studying their asymmetric dihydroxylation, we needed to synthesise allylic phosphine oxides **15** and **16**. Previously, an Arbuzov reaction of an allylic iodide was used to synthesise allylic phosphine oxide **15**.[15] However, we preferred to synthesise both allylic phosphine oxides **15** and **16** using the Arbuzov rearrangement[16] of commercially available 2-methylprop-2-en-1-ol and 2-phenylprop-2-en-1-ol **17** (synthesised using a literature procedure)[17] respectively. The reactions proceed *via* [2,3] sigmatropic rearrangement of the corresponding phosphinites which are generated *in situ* from the allylic alcohol, pyridine and chlorodiphenylphosphine; the yields of allylic phosphine oxides **15** and **16** are recorded in Table 3.

The asymmetric dihydroxylation reactions of allylic phosphine oxides **15** and **16** were carried out using commercially available[18] AD-mix-β in a 1:1 mixture of Bu^{t}OH and water at 0 °C.[19] Optically active 1,2-diols **5** and **6** were isolated in good yields after chromatography (Table 3). The sense of the asymmetric induction in these two reactions was the same and could be assigned by comparison with the optical rotations of the 1,2-diols made using the aminal methodology (see Table 2). The enantiomeric excesses of 1,2-diols (*R*)-**5** and (*R*)-**6** obtained from the asymmetric dihydroxylation reactions were determined by carrying out 400 MHz ^{1}H

Table 3 Synthesis of allylic phosphine oxides **15** and **16** and 1,2-diols **5** and **6**

Arbuzov rearrangement[a]		Sharpless asymmetric dihydroxylation reaction[b]			
Product	Yield (%)	Product	Yield (%)	$[\alpha]_D$	Ee (%)[c]
15	54	(*R*)-**5**	74	+7.9	55
16	77	(*R*)-**6**	75	−28.2	86

[a] Reaction conditions: pyridine, Ph_2PCl, Et_2O, −78 °C then toluene, reflux, 21 h. [b] Reaction conditions: AD-mix-β, Bu^{t}OH–water (1:1), 0 °C, 72 h. [c] Enantiomeric excess determined using Pirkle's chiral shift reagent (see text).

NMR spectroscopy in the presence of Pirkle's chiral solvating agent, (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol.[20] We have found this to be an excellent way of determining the enantiomeric excesses of a wide range of functionalised phosphine oxides;[21] our general method is described in the Experimental section. For comparison, 1,2-diols *rac*-**5** and *rac*-**6** were synthesised using our Sharpless-style racemic dihydroxylation protocol.[22]

As a result of his extensive studies, Sharpless has provided synthetic chemists with a mnemonic[23] (Fig. 1) which predicts the sense of induction in his dihydroxylation reaction—in general, the largest alkene substituent occupies the so-called attractive southwest quadrant. In Fig. 1, we have superimposed allylic phosphine oxide **16** onto the mnemonic in such a way that dihydroxylation on the top face with AD-mix-β generates the observed major enantiomer 1,2-diol (*R*)-**6**. The largest alkene substituent in our example is undoubtedly the diphenylphosphinoylmethyl group and yet this group does not occupy the attractive region. Instead, it is the phenyl ring which orientates itself in this position. At first sight then, it would appear that our results contradict the Sharpless mnemonic. Indeed, Hale *et al.* have also observed this apparently anomalous behaviour in the asymmetric dihydroxylation of other 1,1-disubstituted alkenes.[24]

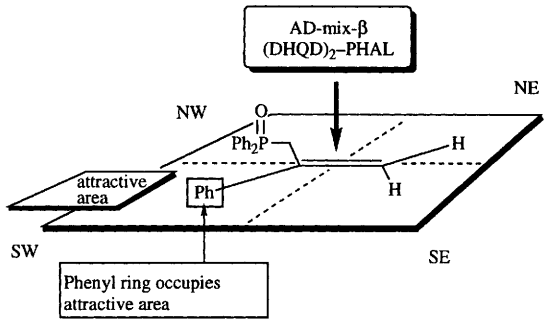


Fig. 1 The Sharpless mnemonic

In order to rationalise our apparently anomalous results, we turned our attention to the most recent mechanistic model that Sharpless has proposed to explain both the sense and degree of asymmetric induction in the dihydroxylation reaction.[4,23,25–26] Sharpless prefers the [2 + 2] cycloaddition pathway (followed by 1,2 migration) rather than the more generally accepted [3 + 2] cycloaddition[27] and his model considers the relative energies of metallaoxetanes, the first intermediates in this proposed pathway. Using Sharpless's mechanistic analysis, we have identified the supposed lowest energy metallaoxetane obtained from dihydroxylating allylic phosphine oxide **16**—it is depicted in Fig. 2. Here, the group which can be best stabilised by solvophobic and π-interactions occupies the pseudoequatorial position directly above the aromatic portion of the ligand. This, of course, corresponds to the attractive southwest quadrant of the mnemonic and it is the phenyl ring which would

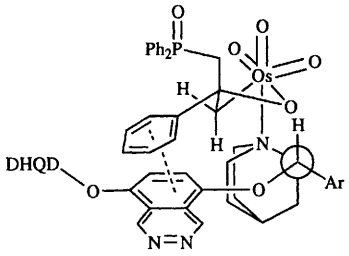


Fig. 2 Favoured metallaoxetane in dihydroxylation

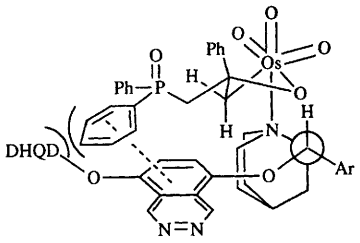


Fig. 3 Disfavoured metallaoxetane in dihydroxylation

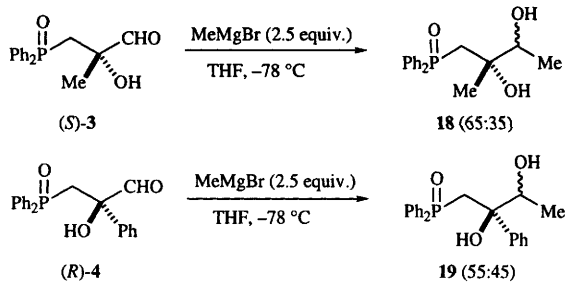
prefer to sit in this position with the diphenylphosphinoylmethyl group pointing out into free space. In contrast, swapping the two alkene substituents around would point the diphenylphosphinoylmethyl group straight into the other half of the dimeric ligand as shown in Fig. 3. We suggest that there is quite simply not enough room for the sterically demanding diphenylphosphinoyl group to be accommodated in the chiral pocket and dihydroxylation occurs preferentially *via* the metallaoxetane depicted in Fig. 2. Thus, our apparently anomalous results are just a feature of the use of the mnemonic and Sharpless has recently suggested[4] the following order for the tendency of a substituent to occupy the attractive southwest quadrant: aryl > alkyl > methyl = $PhCH_2OCH_2-$ = R_3SiOCH_2-. Additionally, then, we suggest that $Ph_2P(O)CH_2-$ (diphenylphosphinoylmethyl) is similar to R_3SiOCH_2-.

We do have one piece of evidence in support of the mechanistic analysis described above: 1,2-diol (*R*)-**5** (methyl substituent) was obtained with 55% ee and 1,2-diol (*R*)-**6** (phenyl substituent) was obtained with 86% ee. On changing the alkene substituent from methyl to phenyl, we would have expected this trend in enantioselectivity since π-interactions are more significant than solvophobic ones. Other results from our laboratories are consistent with this observed trend.[5]

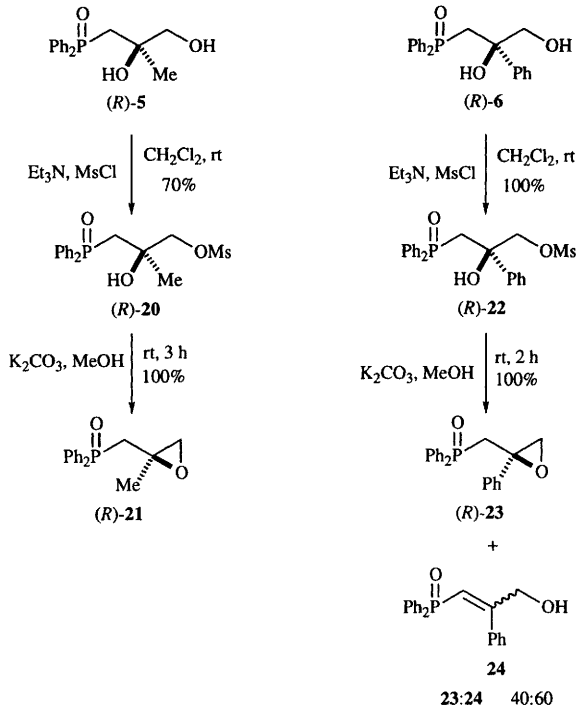
Synthetic transformations of hydroxy aldehydes and 1,2-diols

In this section, we briefly summarise some of our preliminary results in the synthetic use of these hydroxy aldehydes and 1,2-diols. The 1,2-diols (*R*)-**5** and (*R*)-**6** obtained from the dihydroxylation reactions have been converted into the corresponding hydroxy aldehydes (*R*)-**3** and (*R*)-**4** using Swern[28] oxidation.‡ We have attempted only one type of synthetic reaction with our diphenylphosphinoyl hydroxy aldehydes **3** and **4**, namely, the addition of Grignard reagents to the unprotected hydroxy aldehydes.[3,2] Thus, excess methylmagnesium bromide was added to hydroxy aldehyde (*S*)-**3** to give a mixture of 1,2-diols **18** with poor stereoselectivity (Scheme 6). An analogous result was obtained with hydroxy aldehyde (*R*)-**4**.

We had more success with the 1,2-diols. Using a two step synthetic sequence (mesylation followed by potassium carbonate-mediated cyclisation), 1,2-diols **5** and **6** have been converted into the corresponding terminal epoxides **21** and **23**



Scheme 6



Scheme 7

(Scheme 7). Unfortunately, both epoxides **21** and **23** were rather unstable; they decomposed to the corresponding vinyl phosphine oxides on standing in deuteriochloroform over a period of hours. Indeed, in the reaction of the phenyl substituted methanesulfonate **22**, we were not able to isolate a pure sample of epoxide **23**. The sensitivity of β-epoxy phosphine oxides to elimination has been noted before.[21]

Conclusions

Of the two main synthetic approaches to 1,2-diols **5** and **6** described in this paper, the asymmetric dihydroxylation route is considerably shorter and far more direct. However, because we recrystallised hydroxy aminals **1** and **2** to diastereoisomeric purity, the 1,2-diols synthesised by this approach were of higher enantiomeric excess. In addition, without the X-ray crystal structure analysis[1] of hydroxy aminal *anti*-**1**, we would not have been able to assign the absolute stereochemistry of 1,2-diols **5** and **6**. With this unequivocal assignment of stereochemistry, we were able to analyse the asymmetric dihydroxylation reactions more fully. In particular, our results provide further evidence that care must be exercised when using Sharpless's mnemonic to predict the sense of induction in the asymmetric dihydroxylation of 1,1-disubstituted alkenes.

Experimental

General methods have been described previously.[1] The carbon atoms in the bicyclic aminals are referred to by numbers as

‡ In contrast, attempted pyridinium dichromate[29] oxidation gave complete 1,2-diol cleavage and oxidation with Dess–Martin's[30] periodinane reagent was accompanied with around 50% 1,2-diol cleavage.[31]

defined in the preceding paper.[1] Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh) according to the method of Still, Kahn and Mitra.[33] AD-mix-β (1.4 g, equivalent to 1 mmol of alkene) contains $K_3Fe(CN)_6$ (980 mg, 3.0 mmol), K_2CO_3 (410 mg, 3.0 mmol), $(DHQD)_2$-PHAL§ (7.8 mg, 0.01 mmol) and $K_2OsO_2(OH)_4$ (0.74 mg, 0.002 mmol).[18,19] Enantiomeric excesses were determined by measuring the integration of the 400 or 200 MHz ^{1}H NMR spectrum in the presence of (*R*)-Pirkle's chiral shift reagent. (*R*)-Pirkle's reagent is (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)-ethanol.[20]

General method for enantiomeric excess determination

A 400 MHz ^{1}H NMR spectrum of the optically active phosphine oxide in the presence of no additives whatsoever was recorded. Then, a sample containing 1 mg of optically active phosphine oxide and typically 4–6 mg of Pirkle's chiral shift reagent (3–4 equiv.) was prepared in 1.5 cm^3 of $CDCl_3$. The 400 MHz ^{1}H NMR spectrum of this sample was recorded and the peaks due to the two enantiomers of the phosphine oxide were identified. If no splitting was detected, a further 4–6 mg of Pirkle's reagent was added and another 400 MHz ^{1}H NMR spectrum was recorded. Integration of the peaks due to each enantiomer allowed an accurate determination of the enantiomeric excess. In general, we demonstrated that Pirkle's reagent did cause splitting of signals by recording the 400 MHz ^{1}H NMR spectrum of racemic phosphine oxide in the presence of Pirkle's chiral shift reagent. However, in cases where the phosphine oxide had <85% ee, this was not necessary—the peaks arising from the minor enantiomer were obvious from the 400 MHz ^{1}H NMR spectrum of the optically active sample in the presence of Pirkle's reagent.

General method for the hydrolysis of aminals

Hydrochloric acid (2%; 5 cm^3) was added to a stirred solution of the aminal (0.5 mmol) in CH_2Cl_2 (5 cm^3) at room temperature and the resulting two phase mixture was stirred vigorously for 12 h. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. In addition, the acidic aqueous layer was neutralised by careful addition of potassium carbonate and extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give recovered (*S*)-(+)-2-(anilinomethyl)pyrrolidine (*S*)-**7** as a pale yellow oil.

(*R*)-3-Diphenylphosphinoyl-2-hydroxy-2-methylpropanal 3

By the general method described above, a 90:10 ratio of alcohols *syn*- and *anti*-**1** (130 mg, 0.3 mmol) gave *aldehyde* (*R*)-**3** (81 mg, 96%) as a non-crystallisable foam after 24 h at room temperature; R_f(EtOAc) 0.2; $[\alpha]_D^{20}$ +5.4 (*c* 2.9 in $CHCl_3$; 80% ee); $\nu_{max}(CHCl_3)/cm^{-1}$ 3350 (OH), 1733 (C=O), 1438 (P–Ph) and 1121 (P=O); δ_H(200 MHz, $CDCl_3$) 9.62 (1 H, s, CHO), 7.78–7.67 (4 H, m, *o*-Ph_2PO), 7.65–7.38 (6 H, m, *m*- and *p*-Ph_2PO), 5.63 (1 H, br s, OH), 2.86 (1 H, dd, *J* 10.1 and 15.2, PCH_AH_B), 2.69 (1 H, dd, *J* 9.1 and 15.2, PCH_AH_B) and 1.29 (3 H, d, *J* 1.3, Me); δ_C(50 MHz, $CDCl_3$) 203.4$^+$ (d, *J* 4.8, CHO), 133.9–128.5 (Ph_2PO), 77.0$^-$ (COH), 37.1$^-$ (d, *J* 70.2, PCH_2) and 24.8 (d, *J* 9.1, Me); *m*/*z* 288 (5%, M$^+$), 273 (30, M − Me), 259 (80, M − CHO), 201 (100, Ph_2PO), 77 (20, Ph) and 59 (100) (Found: M$^+$, 288.0919. $C_{16}H_{17}O_3P$ requires *M*, 288.0915).

(*S*)-3-Diphenylphosphinoyl-2-hydroxy-2-methylpropanal 3

By the general method described above, alcohol *anti*-**1** (237 mg, 0.5 mmol) gave aldehyde (*S*)-**3** (148 mg, 97%) as a non-crystallisable foam after 24 h at room temperature identical (TLC and ^{1}H NMR) to that obtained previously; R_f(EtOAc) 0.2; $[\alpha]_D^{20}$ −2.7 (*c* 1.3 in $CHCl_3$; ≥97% ee) (Found: M$^+$, 288.0919. $C_{16}H_{17}O_3P$ requires *M*, 288.0915).

(*R*)-3-Diphenylphosphinoyl-2-hydroxy-2-phenylpropanal 4

By the general method described above, alcohol *syn*-**2** (239 mg, 0.47 mmol) gave the crude product as a colourless oil after 12 h at room temperature. Purification by chromatography on silica with EtOAc–hexane (4:1) as eluent gave aldehyde (*R*)-**4** (122 mg, 74%) as a waxy solid. Crystallisation from EtOAc–hexane (1:1) gave *aldehyde* (*R*)-**4** as plates, mp 118–120 °C (from 1:1 EtOAc–hexane); R_f(EtOAc) 0.55; $[\alpha]_D^{20}$ +74.7 (*c* 3.0 in $CHCl_3$; ≥97% ee) (Found: C, 71.6; H, 5.5; P, 8.5%; M$^+$, 350.1060. $C_{21}H_{19}O_3P$ requires C, 72.0; H, 5.5; P, 8.8%; *M*, 350.1072); ν_{max}(Nujol)/cm^{-1} 3350 (OH), 1737 (C=O), 1591 (Ph), 1438 (P–Ph) and 1309 (P=O); δ_H(200 MHz, $CDCl_3$) 9.48 (1 H, d, *J* 1.8, CHO), 7.80–7.63 (2 H, m, *o*-Ph_2PO), 7.61–7.07 (13 H, m, Ph and Ph_2PO), 6.60* (1 H, br s, OH), 3.22 (1 H, dd, *J* 10.6 and 15.1, PCH_AH_B) and 3.07 (1 H, dd, *J* 7.6 and 15.1, PCH_AH_B); δ_C(50 MHz, $CDCl_3$) 199.1$^+$ (d, *J* 7.2, CHO), 133.0–125.9 (Ph and Ph_2PO), 80.6$^-$ (COH) and 37.0$^-$ (d, *J* 69.5, PCH_2); *m*/*z* 350 (20%, M$^+$), 321 (100, M − CHO), 201 (90, Ph_2PO) and 77 (60, Ph).

In addition, (*S*)-(+)-2-(anilinomethyl)pyrrolidine (*S*)-**7** (38 mg, 46%) was recovered as a pale yellow oil identical (TLC and ^{1}H NMR) to that obtained previously; $[\alpha]_D^{20}$ +13.7 (*c* 1.5 in EtOH).

(*S*)-3-Diphenylphosphinoyl-2-hydroxy-2-phenylpropanal 4

By the general method described above, alcohol *anti*-**2** (196 mg, 0.4 mmol) gave the crude product as an oil after 12 h at room temperature. Purification by chromatography on silica with EtOAc–hexane (4:1) as eluent gave aldehyde (*S*)-**4** (88 mg, 65%) as a waxy solid. Crystallisation from EtOAc–hexane (1:1) gave aldehyde (*S*)-**4** as plates identical (TLC and ^{1}H NMR) to that obtained previously, mp 120–122 °C (from 1:1 EtOAc–hexane); R_f(EtOAc) 0.55; $[\alpha]_D^{20}$ −73.5 (*c* 0.4 in $CHCl_3$; ≥97% ee) (Found: C, 71.8; H, 5.5; P, 8.7%; M$^+$, 350.1060. $C_{21}H_{19}O_3P$ requires C, 72.0; H, 5.5; P, 8.8%; *M*, 350.1072).

In addition, (*S*)-(+)-2-(anilinomethyl)pyrrolidine (*S*)-**7** (52 mg, 77%) was recovered as a pale yellow oil identical (TLC and ^{1}H NMR) to that obtained previously; $[\alpha]_D^{20}$ +14.0 (*c* 2.5 in EtOH).

Conversion of hydroxy aminal *anti*-1 into dithiane (*R*)-8

A solution of hydroxy aminal *anti*-**1** (12 mg, 0.03 mmol), boron trifluoride–diethyl ether (7 μl, 0.06 mmol) and propane-1,3-dithiol (4 μl, 0.04 mmol) in CH_2Cl_2 (2 cm^3) was stirred at room temperature for 72 h. Water (2 cm^3) was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organics were washed with 10% aqueous sodium hydroxide, dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave *dithiane* (*R*)-**8** (14 mg, 100%) as an oil, R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ −22.5 (*c* 1.2 in $CHCl_3$; ≥97% ee) (Found: M$^+$, 378.0888. $C_{19}H_{23}O_2PS_2$ requires *M*, 378.0877); ν_{max}(Nujol)/cm^{-1} 3360 (OH), 1592 (Ph), 1438 (P–Ph) and 1168 (P=O); δ_H(200 MHz, $CDCl_3$) 7.82–7.74 (4 H, m, *o*-Ph_2PO), 7.48–7.36 (6 H, m, *m*- and *p*-Ph_2PO), 5.41 (1 H, s, OH), 4.19 (1 H, s, SCHS), 3.00 (1 H, dd, *J* 10.2 and 15.2, PCH_AH_B), 2.88–2.60 (4 H, m, PCH_AH_B and CH_2CH), 2.33 (1 H, dt, *J* 2.4 and 11.9, CH), 1.98–1.90 (1 H, m, CH), 1.79–1.57 (1 H, m, CH) and 1.36 (3 H, s, Me); δ_C(50 MHz, $CDCl_3$) 134.3–128.3 (Ph_2PO), 75.2$^-$ (d, *J* 4.8, COH), 59.8$^+$ (d, *J* 8.8, SCHS), 36.9$^-$ (d, *J* 69.3, PCH_2), 30.4$^-$ (SCH_2), 30.3$^-$ (SCH_2), 27.0$^+$ (d, *J* 6.7, Me) and 25.5$^-$ (CH_2); *m*/*z* 378 (5%, M$^+$), 360 (40, M − H_2O), 259 [90, M − $CHS_2(CH_2)_3$], 201 (80, Ph_2PO), 159 (100) and 77 (10, Ph).

General method for the reduction of hydroxy aldehydes

A solution of the hydroxy aldehyde (0.1 mmol) and lithium

§ $(DHQD)_2PHAL$ is a chiral ligand containing two dihydroquinidine units linked by a phthalazine spacer (see ref. 4).

aluminium hydride (0.3 mmol) in THF (3 cm^3) was stirred under argon at room temperature. After 45 min, water (1 cm^3) was added carefully. The THF was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2–water (1:1; 20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product which was purified by chromatography on silica with EtOAc as eluent.

(*R*)-3-Diphenylphosphinoyl-2-methylpropane-1,2-diol 5

By the general method described above, hydroxy aldehyde (*R*)-**3** (21 mg, 0.07 mmol) gave 1,2-*diol* (*R*)-**5** (20 mg, 99%) as needles, mp 122–125 °C (from EtOAc); R_f(EtOAc) 0.15; $[\alpha]_D^{20}$ +8.2 (*c* 1.0 in $CHCl_3$; 80% ee) (Found: C, 66.4; H, 6.4; P, 10.7%; M^+, 290.1055. $C_{16}H_{19}O_3P$ requires C, 66.2; H, 6.6; P, 10.7%; *M*, 290.1072); ν_{max}(Nujol)/cm^{-1} 3400 (OH), 3262 (OH), 1463 (P–Ph) and 1161 (P=O); δ_H(200 MHz, $CDCl_3$) 7.87–7.66 (4 H, m, *o*-Ph_2PO), 7.59–7.41 (6 H, m, *m*- and *p*-Ph_2PO), 4.24 (1 H, s, COH), 4.01 (1 H, dd, *J* 6.4 and 7.3, CH_2OH), 3.57 (1 H, dd, *J* 6.4 and 11.5, CH_AH_BOH), 3.40 (1 H, ddd, *J* 1.2, 7.5 and 11.4, CH_AH_BOH), 2.70 (1 H, dd, *J* 12.4 and 15.3, PCH_AH_B), 2.60 (1 H, dd, *J* 9.0 and 15.2, PCH_AH_B) and 1.19 (3 H, d, *J* 1.4, Me); δ_C(63 MHz, $CDCl_3$) 134.2–128.6 (Ph_2PO), 72.9$^-$ (d, *J* 5.2, COH), 70.3$^-$ (d, *J* 6.4, CH_2OH), 38.65$^-$ (d, *J* 69.4, PCH_2) and 26.8$^+$ (d, *J* 7.6, Me); *m*/*z* 291 (40%, M^+ + H), 290 (10, M^+), 259 (90, M − CH_2OH), 202 (100, Ph_2POH), 201 (80, Ph_2PO) and 77 (20, Ph).

(*S*)-3-Diphenylphosphinoyl-2-methylpropane-1,2-diol 5

By the general method described above, hydroxy aldehyde (*S*)-**3** (29 mg, 0.1 mmol) gave 1,2-diol (*S*)-**5** (28 mg, 96%) as needles identical (TLC and ^1H NMR) to that obtained previously, mp 117–119 °C (from EtOAc); R_f(EtOAc) 0.15; $[\alpha]_D^{20}$ −10.1 (*c* 1.2 in $CHCl_3$; ⩾97% ee).

(*R*)-3-Diphenylphosphinoyl-2-phenylpropane-1,2-diol 6

By the general method described above, hydroxy aldehyde (*R*)-**4** (45 mg, 0.13 mmol) gave 1,2-*diol* (*R*)-**6** (26 mg, 57%) as fine needles, mp 206–207 °C (from EtOAc); R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ −30.8 (*c* 2.5 in $CHCl_3$; ⩾97% ee) (Found: C, 71.6; H, 6.0; P, 8.85%; M^+, 352.1230. $C_{21}H_{21}O_3P$ requires C, 71.6; H, 6.0; P, 8.8%; *M*, 352.1228); ν_{max}(Nujol)/cm^{-1} 3455 (OH), 1438 (P–Ph) and 1231 (P=O); δ_H(200 MHz, $CDCl_3$) 7.75–7.65 (2 H, m, *o*-Ph_2PO), 7.56–7.19 (10 H, m, Ph and Ph_2PO), 7.15 (3 H, m, Ph), 5.67* (1 H, s, COH), 3.78 (1 H, ddd, *J* 1.3, 7.8 and 9.1, CH_AH_BOH), 3.65* (1 H, dd, *J* 5.0 and 7.9, CH_2OH), 3.51 (1 H, ddd, *J* 2.8, 4.9 and 7.8, CH_AH_BOH), 3.23 (1 H, dd, *J* 13.4 and 15.1, PCH_AH_B) and 2.60 (1 H, dd, *J* 6.7 and 15.1, PCH_AH_B); δ_C(50 MHz, $CDCl_3$) 143.1$^-$ (*ipso*-Ph), 132.0–125.0 (Ph and Ph_2PO), 76.5$^-$ (COH), 71.0$^-$ (d, *J* 9.0, CH_2OH) and 37.7$^-$ (d, *J* 70.1, PCH_2); *m*/*z* 353 (30%, M^+ + H), 352 (5, M^+), 321 (100, M − CH_2OH), 215 (60), 202 (95, Ph_2POH), 201 (100, Ph_2PO) and 77 (70, Ph).

(*S*)-3-Diphenylphosphinoyl-2-phenylpropane-1,2-diol 6

By the general method described above, hydroxy aldehyde (*S*)-**4** (41 mg, 0.12 mmol) gave 1,2-diol (*S*)-**6** (25 mg, 61%) as fine needles identical (TLC and ^1H NMR) to that obtained previously, mp 202–204 °C (from EtOAc); R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ +30.2 (*c* 2.3 in $CHCl_3$; ⩾97% ee).

2-(2′-Diphenylphosphinoyl-1′-oxoethyl)-3-phenyl-1,3-diazabicyclo[3.3.0]octane 10

Butyllithium (0.55 cm^3 of a 1.5 M solution in hexane, 0.8 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (175 mg, 0.8 mmol) in THF (5 cm^3) under argon at −78 °C to give an orange coloured solution. After 30 min at −78 °C, a solution of methyl ester **9** [1,6] (196 mg, 0.8 mmol) in THF (2.5 cm^3) was added dropwise and the resulting solution was stirred at −78 °C for 1 h. Saturated aqueous ammonium chloride (1 cm^3) was added and the mixture allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2–water (1:1; 20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc as eluent gave recovered methyl ester **9** (20 mg, 10%) and *ketone* **10** (177 mg, 52%) as a non-crystallisable foam, R_f(EtOAc) 0.35; $[\alpha]_D^{20}$ +60.3 (*c* 1.3 in $CHCl_3$) (Found: M^+, 430.1814. $C_{26}H_{27}N_2O_2P$ requires *M*, 430.1810); ν_{max}(Nujol)/cm^{-1} 1721 (C=O), 1598 (Ph), 1573 (Ph), 1505 (Ph), 1438 (P–Ph) and 1190 (P=O); δ_H(400 MHz, $CDCl_3$) 7.79–7.74 (4 H, m, *o*-Ph_2PO), 7.53–7.42 (6 H, m, *m*- and *p*-Ph_2PO), 7.12 (2 H, dd, *J* 7.5 and 8.4, *m*-NPh), 6.67 (1 H, t, *J* 7.3, *p*-NPh), 6.49 (2 H, d, *J* 7.9, *o*-NPh), 4.97 (1 H, s, H^2), 4.15 (1 H, dd, *J* 13.9 and 17.0, PCH_AH_B), 3.69–3.63 (1 H, m, H^5), 3.61 (1 H, t, *J* 7.9, $H^{4'}$), 3.49 (1 H, dd, *J* 12.1 and 13.9, PCH_AH_B), 3.18 (1 H, ddd, *J* 4.5, 7.0 and 9.8, $H^{8'}$), 3.08 (1 H, dd, *J* 6.4 and 7.8, H^4), 2.73 (1 H, td, *J* 7.6 and 9.7, H^8), 2.06–2.02 (1 H, m, $H^{6'}$), 1.91–1.86 (1 H, m, H^7), 1.82–1.75 (1 H, m, $H^{7'}$) and 1.72–1.67 (1 H, m, H^6); δ_C(100 MHz, $CDCl_3$) 199.9$^-$ (d, *J* 5.2, C=O), 145.8$^-$ (*ipso*-NPh), 133.6–128.5 (*m*-NPh and Ph_2PO), 117.3$^+$ (*p*-NPh), 112.8$^+$ (*o*-NPh), 86.0$^+$ (C^2), 62.1$^+$ (C^5), 54.7$^-$ (C^4 or C^8), 53.2$^-$ (C^4 or C^8), 41.9$^-$ (d, *J* 60.0, PCH_2), 30.5$^-$ (C^6 or C^7) and 25.0$^-$ (C^6 or C^7); *m*/*z* 430 (10%, M^+), 414 (90), 244 (40), 243 (30), 201 (40, Ph_2PO), 187 [100, M − $Ph_2P(O)CH_2CO$], 107 (50), 77 (60, Ph) and 70 (95).

Full assignment of the ^1H NMR spectrum was made possible with 500 MHz COSY and NOESY analyses of β-keto phosphine oxide **10**.

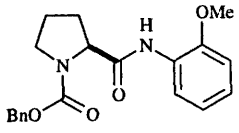
2-(2′-Diphenylphosphinoyl-2′-methyl-1′-oxopropyl)-3-phenyl-1,3-diazabicyclo[3.3.0]octane 11

In the same way, butyllithium (2.3 cm^3 of a 1.5 M solution in hexane, 3.45 mmol), isopropylphosphine oxide [34] (844 mg, 3.5 mmol) in THF (10 cm^3) and a solution of methyl ester **9** (500 mg, 2.0 mmol) in THF (2 cm^3) gave the crude product as a yellow oil. Purification by chromatography on silica with EtOAc as eluent gave *ketone* **11** (523 mg, 56%) as a non-crystallisable foam, R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ +36.2 (*c* 1.0 in $CHCl_3$) (Found: M^+, 458.2145. $C_{28}H_{31}N_2O_2P$ requires *M*, 458.2163); ν_{max}($CHCl_3$)/cm^{-1} 1706 (C=O), 1599 (Ph), 1573 (Ph), 1506 (Ph), 1437 (P–Ph) and 1218 (P=O); δ_H(400 MHz, $CDCl_3$) 7.91–7.86 (2 H, m, *o*-Ph_2PO), 7.83–7.78 (2 H, m, *o*-Ph_2PO), 7.51–7.34 (6 H, m, *m*- and *p*-Ph_2PO), 7.08 (2 H, dd, *J* 7.6 and 8.4, *m*-NPh), 6.61 (1 H, t, *J* 7.3, *p*-NPh), 6.53 (2 H, d, *J* 7.9, *o*-NPh), 5.53 (1 H, s, H^2), 3.60 (1 H, t, *J* 8.0, $H^{4'}$), 3.50–3.45 (1 H, m, H^5), 3.42–3.36 (1 H, m, $H^{8'}$), 3.05 (1 H, t, *J* 7.7, H^4), 2.65 (1 H, q, *J* 8.6, H^8), 2.04–1.55 (4 H, m, $H^{6'}$, H^7, $H^{7'}$ and H^6), 1.66 (3 H, d, *J* 5.2, Me_A) and 1.62 (3 H, d, *J* 5.3, Me_B); δ_C(50 MHz, $CDCl_3$) 205.6$^-$ (C=O), 145.4$^-$ (*ipso*-NPh), 132.7–127.8 (*m*-NPh and Ph_2PO), 116.4$^+$ (*p*-NPh), 112.5$^+$ (*o*-NPh), 82.0$^+$ (C^2), 60.5$^+$ (C^5), 53.8$^-$ (C^4 or C^8), 53.4$^-$ (C^4 or C^8), 51.2$^-$ (d, *J* 59.8, PC), 30.2$^-$ (C^6 or C^7) and 24.6$^-$ (C^6 or C^7), 22.3$^+$ (Me) and 21.5$^+$ (Me); *m*/*z* 458 (5%, M^+), 430 (50, M − CO), 242 (50) and 187 [100, M − $Ph_2P(O)CMe_2CO$].

Addition of methylmagnesium bromide to ketone 11. 2-[(1′*R*)-2′-Diphenylphosphinoyl-1′-hydroxy-1′,2′-dimethylpropyl]-3-phenyl-1,3-diazabicyclo[3.3.0]octane *syn*-12

In the same way, methylmagnesium bromide (0.1 cm^3 of a 3 M solution in Et_2O, 0.3 mmol) and ketone **11** (92 mg, 0.2 mmol) in THF (4 cm^3) gave the crude product as a non-crystallisable foam (92 mg, 97%) which contained a ⩾97:3 ratio of *alcohols* *syn*-**12** and *anti*-**12** (by ^1H NMR), R_f(EtOAc) 0.4 (Found: M^+, 474.2448. $C_{29}H_{35}N_2O_2P$ requires *M*, 474.2436); ν_{max}(Nujol)/cm^{-1} 3300 (OH), 1598 (Ph), 1504 (Ph), 1438 (P–Ph) and 1208 (P=O); δ_H(200 MHz, $CDCl_3$) 8.18–8.04 (4 H, m, *o*-Ph_2PO),

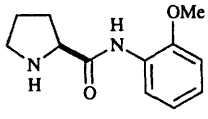
7.52–7.40 (6 H, m, *m*- and *p*-Ph_2PO), 7.20 (2 H, dd, *J* 7.2 and 8.8, *m*-NPh), 6.98 (2 H, d, *J* 7.9, *o*-NPh), 6.68 (1 H, t, *J* 7.2, *p*-NPh), 5.40 (1 H, s, OH), 4.62 (1 H, s, H^2), 3.89–3.72 (1 H, m, H^5), 3.69 (1 H, q, *J* 7.75, $H^{4'}$), 2.90 (1 H, t, *J* 8.4, H^4), 2.46–2.36 (1 H, m, $H_{8'}$), 2.07–1.98 (2 H, m, H^8 and $H^{6'}$), 1.74–1.42 (3 H, m, H^7, $H^{7'}$ and H^6), 1.66 (3 H, d, *J* 22.8, Me_A), 1.42 (3 H, d, *J* 18.1, Me_B) and 1.25 (3 H, s, *Me*COH); δ_C(100 MHz, $CDCl_3$) 149.9$^-$ (*ipso*-NPh), 134.9–128.2 (*m*-NPh and Ph_2PO), 116.5$^+$ (*p*-NPh), 113.7$^+$ (*o*-NPh), 85.8$^+$ (d, *J* 5.9, C^2), 83.0$^-$ (COH), 62.1$^+$ (C^5), 57.0$^-$ (C^4 or C^8), 53.7$^-$ (C^4 or C^8), 45.7$^-$ (d, *J* 65.3, PC), 31.0$^-$ (C^6 or C^7), 23.9$^-$ (C^6 or C^7), 22.2$^+$ (Me), 21.4$^+$ (Me) and 19.8$^+$ (d, *J* 5.2, *Me*COH); *m*/*z* 474 (10%, M^+), 431 (50), 368 (50), 254 (50), 201 (90, Ph_2PO), 187 [100, M – $Ph_2P(O)CMe_2C(Me)OH$] and 77 (40, Ph).



25

(*S*)-*N*-(benzyloxycarbonyl)prolin-*o*-anisidide 25

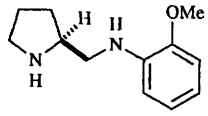
Using Mukaiyama's method,[14] (*S*)-*N*-(benzyloxycarbonyl)-prolin-*o*-anisidide **25** was prepared in 96% yield as plates, mp 69–71 °C (from acetone); R_f(EtOAc) 0.6; $[\alpha]_D^{20}$ −70.0 (*c* 1.2 in EtOH) (Found: C, 67.7; H, 6.3; N, 7.8%; M^+, 354.1600. $C_{20}H_{22}N_2O_4$ requires C, 67.8; H, 6.3; N, 7.9%; M, 354.1580); ν_{max}(Nujol)/cm^{-1} 3284 (NH), 1710 (C=O, amide I), 1688 (C=O, NCO_2Bn), 1605 (Ph and NAr) and 1546 (NH bend, amide II); the ^{1}H NMR is very broad due to carbamate rotamer interconversion: δ_H(400 MHz, $CDCl_3$) 8.9 and 8.3 (1 H, 2 × br s, NH), 8.34 (2 H, d, *J* 7.7, *o*-NC_6H_4OMe), 7.4–7.0 (7 H, br m, Ph and C_6H_4OMe), 6.84 (1 H, d, *J* 8.0, *o*-C_6H_4OMe), 5.3–5.1 (2 H, br m, $PhCH_2O$), 4.6–4.4 (1 H, br m, NC*H*CONH), 3.9–3.4 (2 H, br m, NCH_2), 3.79 (3 H, br s, OMe) and 2.5–1.8 (4 H, br m, CH_2CH_2); two rotamers are observed for some signals in the ^{13}C NMR: δ_C(100 MHz, $CDCl_3$) 169.8$^-$ (C=O), 148.2 (*ipso*-C_6H_4OMe), 136.4 (*ipso*-NC_6H_4OMe), 128.4$^+$, 128.0$^+$, 127.8$^+$, 123.9$^+$, 121.0$^+$, 119.9$^+$, 110.0$^+$, 67.3$^-$ ($PhCH_2O$), 61.7$^+$ (NCHCONH), 55.8$^+$ (OMe), 47.0$^-$ (NCH_2), 31.1 (CH_2CH_2), 28.6 (CH_2CH_2), 24.6 (CH_2CH_2) and 23.8 (CH_2CH_2); *m*/*z* 354 (40%, M^+), 204 (40, M – CONH-C_6H_4OMe), 160 (70), 91 (100, $PhCH_2$) and 77 (40, Ph).



26

(*S*)-prolin-*o*-anisidide 26

Using Mukaiyama's method and our modified procedure,[1,14] (*S*)-prolin-*o*-anisidide **26** was prepared in 87% yield as cubes, mp 68–70 °C (from cyclohexane); R_f(EtOAc) 0.15; $[\alpha]_D^{20}$ −42.2 (*c* 1.2 in EtOH) (Found: C, 65.3; H, 7.4; N, 12.6%; M^+, 220.1209. $C_{12}H_{16}N_2O_2$ requires C, 65.4; H, 7.3; N, 12.7%; *M*, 220.1212); ν_{max}(Nujol)/cm^{-1} 3324 (NH), 3212 (NH), 1668 (C=O, amide I), 1600 (Ph) and 1532 (NH bend, amide II); δ_H(400 MHz, $CDCl_3$) 10.06 (1 H, br s, amide NH), 8.41 (1 H, dd, *J* 1.6 and 7.9, *o*-NC_6H_4OMe), 7.02 (1 H, dt, *J* 1.6 and 7.6, *m*-C_6H_4OMe), 6.94 (1 H, dt, *J* 1.3 and 7.7, *p*-C_6H_4OMe), 6.86 (1 H, dd, *J* 1.3 and 8.1, *o*-C_6H_4OMe), 3.87 (3 H, s, OMe), 3.91–3.85 (1 H, m, 3.06 NC*H*CONH), 3.07 (1 H, td, *J* 6.8 and 10.2, NCH_AH_B), 2.99 (1 H, td, *J* 6.4 and 10.3, NCH_AH_B), 2.49 (1 H, br s, NH), 2.18 (1 H, tdd, *J* 7.5, 9.0 and 13.0, $NCHCH_AH_B$), 2.05 (1 H, dtd, *J* 5.9, 6.6 and 12.8, $NCHCH_AH_B$) and 1.82–1.66 (2 H, m, CH_2); δ_C(63 MHz, $CDCl_3$) 173.6$^-$ (C=O), 148.7$^-$ (*ipso*-C_6H_4OMe), 127.7$^-$ (*ipso*-NC_6H_4OMe), 123.7$^+$, 122.8$^+$, 119.6$^+$, 110.2$^+$ (*o*-C_6H_4OMe), 61.6$^+$ (NCHCONH), 55.9$^+$ (OMe), 47.5$^-$ (NCH_2), 31.0$^-$ (CH_2CH_2) and 26.4$^-$ (CH_2CH_2); *m*/*z* 220 (40%, M^+), 195 (70), 123 (70), 108 (70) and 70 (100, M – $CONHC_6H_4OMe$).



27

(*S*)-(+)-2-(*o*-anisidinomethyl)pyrrolidine 27

Using Mukaiyama's method,[14] (*S*)-(+)-2-(*o*-anisidinomethyl)pyrrolidine **27** was prepared in 39% yield as a pale yellow oil, bp 192–193 °C/0.2 mmHg (lit.,[14] 150 °C/0.6 mmHg); $[\alpha]_D^{20}$ + 13.7 (*c* 1.0 in EtOH) {lit.,[14] $[\alpha]_D^{24}$ +25.2 (*c* 1.08 in EtOH)} (Found: M^+, 206.1420. $C_{12}H_{18}N_2O$ requires *M*, 206.1419); δ_C(63 MHz, $CDCl_3$) 147.0$^-$ (*ipso*-C_6H_4OMe), 138.5$^-$ (*ipso*-NC_6H_4OMe), 121.2$^+$, 116.4$^+$, 110.0$^+$, 109.4$^+$, 57.8$^+$ (NCHCONH), 55.4$^+$ (OMe), 48.8$^-$ (NCH_2), 46.6$^-$ (NCH_2), 29.7$^-$ (CH_2CH_2) and 25.7$^-$ (CH_2CH_2). The ^{1}H NMR was in agreement with that described by Mukaiyama.[14]

2-Benzoyl-3-(*o*-methoxyphenyl)-1,3-diazabicyclo[3.3.0]octane 13

Using Mukaiyama's method,[13] crude **13** was obtained as a yellow oil. Purification by chromatography on silica with Et_2O–hexane (3:2) as eluent gave phenyl ketone **13** (945 mg, 95%) as a yellow foam, R_f(EtOAc) 0.65 (Found: M^+, 322.1674. $C_{20}H_{22}N_2O_2$ requires *M*, 322.1681); ν_{max}(film)/cm^{-1} 1695 (C=O), 1596 (C_6H_4OMe and Ph), 1579 (C_6H_4OMe and Ph) and 1504 (C_6H_4OMe and Ph); δ_H(200 MHz, $CDCl_3$) 8.08 (2 H, m, *J* 7.8, *o*-PhCO), 7.64–7.27 (3 H, m, C_6H_4OMe and Ph), 6.97–6.85 (1 H, m, C_6H_4OMe and Ph), 6.77–6.22 (3 H, m, C_6H_4OMe and Ph), 6.22 (1 H, s, H^2), 3.94–3.75 (2 H, m, H^5 and $H^{4'}$), 3.46 (1 H, m, $H^{8'}$), 3.33 (3 H, s, MeO), 3.30 (1 H, dd, *J* 6.5 and 7.6, H^4), 2.91 (1 H, q, *J* 8.5, H^8), 2.21–1.83 (4 H, m, CH_2CH_2); δ_C(50 MHz, $CDCl_3$) 194.2$^-$ (C=O), 147.4$^-$ (*ipso*-NC_6H_4OMe), 136.9$^-$ (*o*-NC_6H_4OMe), 135.6$^-$ (*ipso*-PhCO), 132.4$^+$, 128.4$^+$, 121.7$^+$, 117.7$^+$, 114.8$^+$, 111.6$^+$, 82.5$^+$ (C^2), 60.4$^+$ (C^5), 55.1$^+$ (OMe), 54.8$^-$ (C^4 or C^8), 54.4$^-$ (C^4 or C^8), 29.9$^-$ (C^6 or C^7) and 24.5$^-$ (C^6 or C^7); *m*/*z* 322 (60%, M^+), 217 (100, M – PhCO), 174 (40), 105 (50, PhCO) and 77 (70, Ph).

3-Diphenylphosphinoyl-2-hydroxy-2-phenylpropanal 4

Butyllithium (0.7 cm^3 of a 1.3 M solution in hexane, 0.9 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (198 mg, 0.9 mmol) in THF (15 cm^3) under argon at −78 °C to give an orange coloured solution. After 30 min at −78 °C, a solution of phenyl ketone **13** (275 mg, 0.85 mmol) in THF (5 cm^3) was added dropwise and the resulting solution was stirred at −78 °C for 45 min. Saturated aqueous ammonium chloride (1 cm^3) was added and the mixture allowed to warm to room temperature. Hydrochloric acid (2%; 10 cm^3) was then added and the resulting solution was stirred vigorously for 3 h. The THF was evaporated under reduced pressure and the residue was dissolved in CH_2Cl_2–water (1:1; 20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a yellow oil. Purification by chromatography on silica with EtOAc–hexane (1:1) as eluent gave aldehyde (*S*)-**4** (160 mg, 54%) as cubes, mp 88–90 °C (from EtOAc) identical (TLC and ^{1}H NMR) to that obtained previously, R_f(EtOAc) 0.55; $[\alpha]_D^{20}$ −71.6 (*c* 1.1 in $CHCl_3$; 88% ee).

In a separate experiment, the crude reaction mixture obtained after the first step was analysed by ^{1}H NMR: a 94:6 ratio of alcohols *anti*-**14** and *syn*-**14** had been generated.

(*S*)-3-Diphenylphosphinoyl-2-phenylpropane-1,2-diol 6
Sodium borohydride (10 mg, 0.26 mmol) was added to a stirred solution of aldehyde (*S*)-**4** (20 mg, 0.06 mmol; 88% ee) in MeOH (3 cm^3) at room temperature. After 2 h at room temperature, CH_2Cl_2–water (1:1; 20 cm^3) was added. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a white solid. Purification by chromatography on silica with EtOAc as eluent gave 1,2-diol (*S*)-**6** (15 mg, 75%) identical (TLC and ^1H NMR) to that obtained previously, R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ +24.2 (*c* 1.5 in $CHCl_3$).

2-Phenylprop-2-en-1-ol 17
Using Gassman and Harrington's method,[17] 2-phenylprop-2-en-1-ol **17** was prepared in 55% yield as a colourless liquid, bp 70–72 °C/0.1 mmHg (lit.,[17] 77–79 °C/0.25 mmHg); R_f(1:1 Et_2O–hexane) 0.3 (Found: M^+, 134.0725. $C_9H_{10}O$ requires *M*, 134.0732); ν_{max}(film)/cm^{-1} 3356 (OH), 1631 (C=C), 1599 (Ph), 1574 (Ph) and 1495 (Ph); δ_H(200 MHz, $CDCl_3$) 7.48–7.30 (5 H, m, Ph), 5.48 (1 H, d, *J* 0.9, C=CH_AH_B), 5.35 (1 H, q, *J* 1.2, C=CH_AH_B), 4.55 (2 H, br d, *J* 6.0, CH_2OH and 1 H, t, *J* 6.2, CH_2OH); δ_C(50 MHz, $CDCl_3$) 147.2$^-$ (*ipso*-Ph), 138.5$^-$ (*C*=CH_2), 128.4$^+$, 127.8$^+$ (*p*-Ph), 126.0$^+$, 112.4$^-$ (C=CH_2) and 64.8$^-$ (CH_2OH); *m*/*z* 134 (100%, M^+), 103 (100, M − CH_2OH), 92 (80) and 77 (75, Ph).

3-Diphenylphosphinoyl-2-methylpropene 15
Pyridine (4.5 cm^3, 55.6 mmol) was added dropwise to a stirred solution of 2-methylprop-2-en-1-ol (4.7 cm^3, 55.9 mmol) in Et_2O (75 cm^3) under argon at −78 °C. After 15 min at −78 °C, a solution of chlorodiphenylphosphine (10.0 cm^3, 55.8 mmol) in Et_2O (50 cm^3) was added dropwise and then stirred at −78 °C for 30 min to give a white precipitate. The mixture was allowed to warm to room temperature and filtered under argon using a Schlenk tube. The Et_2O was evaporated under reduced pressure to give a colourless oil which was dissolved in toluene (100 cm^3) and heated under reflux. After 21 h, the resulting brown solution was cooled and the toluene evaporated under reduced pressure to give the crude product as a pale yellow solid. Recrystallisation from EtOAc gave allylic phosphine oxide **15** (6.83 g, 48%) and purification of the mother liquors by chromatography on silica with EtOAc as eluent gave allylic phosphine oxide **15** (797 mg, 6%) as plates, mp 149–151 °C (from EtOAc) (lit.,[15] 144–145 °C); R_f(EtOAc) 0.35 (Found: C, 75.1; H, 6.7; P, 12.0%; M^+, 256.1018. $C_{16}H_{17}OP$ requires C, 75.0; H, 6.7; P, 12.1%; *M*, 256.1017); ν_{max}(Nujol)/cm^{-1} 1642 (C=C), 1591 (Ph), 1438 (P–Ph) and 1187 (P=O); δ_H(250 MHz, $CDCl_3$) 7.83–7.58 (4 H, m, *o*-Ph_2PO), 7.51–7.38 (6 H, m, *m*- and *p*-Ph_2PO), 4.82 (1 H, td, *J* 1.4 and 4.1, C=CH_AH_B), 4.64 (1 H, br d, *J* 4.3, C=CH_AH_B), 3.09 (2 H, d, *J* 14.0, PCH_2) and 1.76 (3 H, s, Me); δ_C(63 MHz, $CDCl_3$) 136.2$^-$ (d, *J* 9.5, *C*=CH_2), 133.6–127.9 (Ph_2PO), 116.2$^-$ (d, *J* 9.7, C=CH_2), 39.6$^-$ (d, *J* 67.3, PCH_2) and 24.5$^+$ (d, *J* 1.9, Me); *m*/*z* 256 (50%, M^+), 201 (100, Ph_2PO) and 77 (20, Ph).

3-Diphenylphosphinoyl-2-phenylpropene 16
In the same way, pyridine (1.2 cm^3, 14.8 mmol), allylic alcohol **17** (1.98 g, 14.7 mmol) and chlorodiphenylphosphine (2.65 cm^3, 14.8 mmol) in Et_2O (35 cm^3) followed by refluxing in toluene (30 cm^3) gave the crude product as an oil. Purification by chromatography on silica with EtOAc–hexane (4:1) as eluent gave *allylic phosphine oxide* **16** (3.59 g, 77%) as needles, mp 89–91 °C (from EtOAc); R_f(EtOAc) 0.4 (Found: M^+, 318.1179. $C_{21}H_{19}OP$ requires *M*, 318.1174); ν_{max}(Nujol)/cm^{-1} 1624 (C=C), 1591 (Ph), 1496 (Ph), 1437 (P–Ph) and 1225 (P=O); δ_H(200 MHz, $CDCl_3$) 7.75–7.64 (4 H, m, *o*-Ph_2PO), 7.49–7.15 (11 H, m, *m*- and *p*-Ph_2PO and Ph), 5.38 (1 H, td, *J* 0.5 and 4.5, C=CH_AH_B), 5.24 (1 H, d, *J* 4.5, C=CH_AH_B) and 3.54 (2 H, dd, *J* 0.6 and 14.2, PCH_2); δ_C(50 MHz, $CDCl_3$) 141.5$^-$ (*ipso*-Ph), 138.6$^-$ (d, *J* 9.5, *C*=CH_2), 131.7–126.4 (Ph_2PO and Ph), 118.1$^-$ (d, *J* 8.8, C=CH_2) and 36.9$^-$ (d, *J* 67.1, PCH_2); *m*/*z* 318 (70%, M^+), 201 (40, Ph_2PO), 84 (85), 77 (30, Ph) and 49 (100).

(*R*)-3-Diphenylphosphinoyl-2-methylpropane-1,2-diol 5
Allylic phosphine oxide **15** (207 mg, 0.8 mmol) was added in one portion to a stirred solution of AD-mix-β (1.13 g) in *tert*-butyl alcohol–water (1:1; 10 cm^3) at 0 °C. The resulting orange slurry was stirred vigorously at 0 °C for 72 h. Sodium sulfite (1.4 g) was then added and the mixture allowed to warm to room temperature. After stirring at room temperature for 1 h, CH_2Cl_2 (20 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 20 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product. Purification by chromatography on silica with EtOAc as eluent gave 1,2-diol (*R*)-**5** (174 mg, 74%) as fine needles identical (TLC and ^1H NMR) to that obtained previously, mp 119–121 °C (from 100:1 EtOAc–MeOH); R_f(EtOAc) 0.15; $[\alpha]_D^{20}$ +7.9 (*c* 1.05 in $CHCl_3$; 55% ee by Pirkle) (Found: C, 66.4; H, 6.4; P, 10.7%; M^+, 290.1055. $C_{16}H_{19}O_3P$ requires C, 66.2; H, 6.6; P, 10.7%; *M*, 290.1072).

(*R*)-3-Diphenylphosphinoyl-2-phenylpropane-1,2-diol 6
In the same way, allylic phosphine oxide **16** (633 mg, 2.0 mmol) and AD-mix-β (2.92 g) in *tert*-butyl alcohol–water (1:1; 20 cm^3) gave the crude product as an oil after 72 h at 0 °C. Purification by chromatography on silica with EtOAc as eluent gave 1,2-diol (*R*)-**6** (526 mg, 75%) as fine needles identical (TLC and ^1H NMR) to that obtained previously, mp 205–207 °C (from EtOAc); R_f(EtOAc) 0.4; $[\alpha]_D^{20}$ −28.2 (*c* 1.4 in $CHCl_3$; 86% ee by Pirkle) (Found: C, 71.6; H, 6.0; P, 8.85%; M^+, 352.1230. $C_{21}H_{21}O_3P$ requires C, 71.6; H, 6.0; P, 8.8%; *M*, 352.1228).

3-Diphenylphosphinoyl-2-methylpropane-1,2-diol *rac*-5
Osmium(III) chloride (1 mg, 0.003 mmol) was added to a stirred solution of allylic phosphine oxide **15** (209 mg, 0.73 mmol), potassium ferricyanide (766 mg, 2.3 mmol), potassium carbonate (296 mg, 2.14 mmol) and quinuclidine (4 mg, 0.04 mmol) in *tert*-butyl alcohol–water (1:1; 10 cm^3) at room temperature. The resulting orange slurry was stirred vigorously at room temperature for 72 h and sodium sulfite (1.5 g) was added. After stirring at room temperature for 1 h, CH_2Cl_2 (20 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (5 × 20 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave 1,2-diol *rac*-**5** (220 mg, 94%) as cubes identical (TLC and ^1H NMR) to that obtained previously, mp 116–118 °C (from EtOAc); R_f(EtOAc) 0.15 (Found: C, 65.7; H, 6.6; P, 10.6%. $C_{16}H_{19}O_3P$ requires C, 66.2; H, 6.6; P, 10.7%).

3-Diphenylphosphinoyl-2-phenylpropane-1,2-diol *rac*-6
In the same way, osmium(III) chloride (1 mg, 0.003 mmol), allylic phosphine oxide **16** (252 mg, 0.73 mmol), potassium ferricyanide (805 mg, 2.4 mmol), potassium carbonate (329 mg, 2.4 mmol) and quinuclidine (5 mg, 0.04 mmol) in *tert*-butyl alcohol–water (1:1; 10 cm^3) gave the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave 1,2-diol *rac*-**6** (253 mg, 91%) as fine needles identical (TLC and ^1H NMR) to that obtained previously, mp 182–184 °C (from EtOAc) after 72 h at room temperature; R_f(EtOAc) 0.4 (Found: C, 71.3; H, 6.0; P, 8.85%. $C_{21}H_{21}O_3P$ requires C, 71.6; H, 6.0; P, 8.8%).

Swern oxidation of 1,2-diol (*R*)-5
DMSO (20 mm^3, 0.3 mmol) was added dropwise to a stirred

solution of oxalyl chloride (15 mm^3, 0.2 mmol) in CH_2Cl_2 (2 cm^3) under argon at −78 °C. After 5 min, a solution of 1,2-diol (*R*)-**5** (45 mg, 0.15 mmol) in CH_2Cl_2 (2 cm^3) was added dropwise. After a further 10 min at −78 °C, triethylamine (100 mm^3, 0.7 mmol) was added dropwise and the resulting solution was allowed to warm to room temperature. Water (5 cm^3) was added, the layers separated and the aqueous layer extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were washed with hydrochloric acid (3 M; 3 × 10 cm^3) and water (15 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave aldehyde (*R*)-**3** (34 mg, 35%) as an oil which contained only aldehyde (*R*)-**3** (by ^1H NMR).

Swern oxidation of 1,2-diol (*R*)-6

In the same way, oxalyl chloride (40 mm^3, 0.5 mmol), DMSO (40 mm^3, 0.6 mmol) and 1,2-diol (*R*)-**5** (95 mg, 0.3 mmol) in CH_2Cl_2 (2 cm^3) followed by the addition of triethylamine (190 mm^3, 1.3 mmol) gave the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave aldehyde (*R*)-**4** (34 mg, 35%) as an oil identical (TLC and ^1H NMR) to that obtained previously, R_f(EtOAc) 0.55; $[\alpha]_D^{20}$ +82.5 (*c* 1.8 in $CHCl_3$; 86% ee).

Addition of methylmagnesium bromide to aldehyde (*S*)-3

Methylmagnesium bromide (100 mm^3 of a 3 M solution in Et_2O, 0.3 mmol) was added dropwise to a stirred solution of aldehyde (*S*)-**3** (24 mg, 0.1 mmol) in THF (2 cm^3) under argon at −78 °C. After 2 h at −78 °C, water (0.5 cm^3) was added and the mixture allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue worked up to give the crude product as an oil which contained 53:31:16 ratio (by ^1H NMR) of aldehyde (*S*)-**3** and 1,2-*diols* **19** *i.e.* a 65:35 ratio of 1,2 diols **18**; δ_H(200 MHz, $CDCl_3$) 4.90 (1 H, s, COH^{major}); 4.54 (1 H, s, COH^{minor}).

Addition of methylmagnesium bromide to aldehyde (*R*)-4

In the same way, methylmagnesium bromide (40 mm^3 of a 3 M solution in Et_2O, 0.12 mmol) and aldehyde (*R*)-**4** (18 mg, 0.05 mmol) in THF (1 cm^3) gave the crude product as an oil which contained a 55:45 ratio (by ^1H NMR) of 1,2-*diols* **19**, δ_H(200 MHz, $CDCl_3$) 7.81–7.05 (30 H, m, 2 × Ph_2PO and 2 × Ph), 5.91 (1 H, s, COH^{minor}), 5.83 (1 H, s, COH^{major}), 3.95–3.85 (1 H, m, $CHOH^{major}$), 3.80–3.75 (1 H, m, $CHOH^{minor}$), 3.42 (1 H, dd, *J* 13.7 and 15.1, $PCH_AH_B^{major}$), 3.20 (1 H, dd, *J* 14.0 and 15.1, $PCH_AH_B^{minor}$), 2.98 (1 H, dd, *J* 7.2 and 15.0, $PCH_AH_B^{minor}$), 2.79 (1 H, dd, *J* 6.7 and 15.1, $PCH_AH_B^{major}$), 1.09 (3 H, d, *J* 6.5, $CHMe^{minor}$) and 0.82 (3 H, d, *J* 6.4, $CHMe^{major}$).

(*R*)-3-Diphenylphosphinoyl-2-hydroxy-2-methylpropyl methanesulfonate 20

Triethylamine (30 mm^3, 0.2 mmol) was added dropwise to a stirred solution of 1,2-diol (*R*)-**5** (28 mg, 0.1 mmol) and methanesulfonyl chloride (12 mm^3, 0.15 mmol) in CH_2Cl_2 (2 cm^3) under argon at room temperature. After 12 h at room temperature, water (5 cm^3) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3). The combined organic extracts were washed with hydrochloric acid (3 M; 3 × 10 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a white solid. Purification by chromatography on silica with EtOAc as eluent gave *methanesulfonate* (*R*)-**20** (25 mg, 70%) as a white solid, R_f(EtOAc) 0.25; δ_H(200 MHz, $CDCl_3$) 7.82–7.71 (4 H, m, *o*-Ph_2PO), 7.56–7.42 (6 H, m, *m*- and *p*-Ph_2PO), 5.48 (1 H, br s, OH), 4.08 (1 H, dd, *J* 0.9 and 10.3, $CH_AH_BOSO_2$), 4.03 (1 H, d, *J* 10.2, $CH_AH_BOSO_2$), 2.87 (3 H, s, $MeSO_2O$), 2.78 (1 H, dd, *J* 10.5 and 15.2, PCH_AH_B), 2.52 (1 H, dd, *J* 10.0 and 15.2, PCH_AH_B) and 1.28 (3 H, s, *Me*COH); δ_C(50 MHz, $CDCl_3$) 134.1–128.6 (Ph_2PO), 76.0$^-$ (d, *J* 8.15, CH_2OSO_2), 71.7$^-$ (d, *J* 4.7, COH), 37.1$^+$ ($MeSO_2$), 36.0$^-$ (d, *J* 70.0, PCH_2) and 26.6$^+$ (d, *J* 7.0, *Me*COH).

(*R*)-3-Diphenylphosphinoyl-2-hydroxy-2-phenylpropyl methanesulfonate 22

In the same way, triethylamine (40 mm^3, 0.3 mmol), 1,2-diol (*R*)-**6** (53 mg, 0.15 mmol) and methanesulfonyl chloride (20 mm^3, 0.25 mmol) in CH_2Cl_2 (3 cm^3) gave the crude *methanesulfonate* (*R*)-**22** (65 mg, 100%) as a white solid, R_f(EtOAc) 0.4; δ_H(200 MHz, $CDCl_3$) 7.78–7.67 (2 H, m, *o*-Ph_2PO), 7.57–7.46 (4 H, m, *o*-Ph_2PO and Ph), 7.31–7.15 (6 H, m, Ph and Ph_2PO), 7.04–7.01 (3 H, m, Ph), 4.26 (1 H, d, *J* 10.9, $CH_AH_BOSO_2$), 4.20 (1 H, dd, *J* 2.5 and 11.0, $CH_AH_BOSO_2$), 3.25 (1 H, dd, *J* 12.9 and 14.9, PCH_AH_B), 3.00 (3 H, s, $MeSO_2O$) and 2.89 (1 H, dd, *J* 7.45 and 14.9, PCH_AH_B); δ_C(50 MHz, $CDCl_3$) 140.2$^-$ (*ipso*-Ph), 132.4–125.9 (Ph and Ph_2PO), 76.7$^-$ (d, *J* 11.6, CH_2OSO_2), 75.3$^-$ (d, *J* 4.7, COH), 37.7$^+$ ($MeSO_2$) and 35.7$^-$ (d, *J* 70.5, PCH_2).

(*R*)-3-Diphenylphosphinoyl-1,2-epoxy-2-methylpropane 21

Potassium carbonate (16 mg, 0.12 mmol) was added in one portion to a stirred solution of methanesulfonate (*R*)-**20** (20 mg, 0.05 mmol) in MeOH (2 cm^3) at room temperature. After 3 h at room temperature, water (10 cm^3) and CH_2Cl_2 (10 cm^3) were added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude *epoxide* (*R*)-**21** (14 mg, 100%) as a white solid, R_f(EtOAc) 0.25; $[\alpha]_D^{20}$ −0.8 (*c* 1.4 in $CHCl_3$; 55% ee); ν_{max}(Nujol)/cm^{-1} 1593 (Ph), 1438 (P–Ph) and 1166 (P=O); δ_H(200 MHz, $CDCl_3$) 7.82–7.67 (4 H, m, *o*-Ph_2PO), 7.54–7.41 (6 H, m, *m*- and *p*-Ph_2PO), 2.87 (1 H, ddd, *J* 1.2, 11.6 and 14.9, PCH_AH_B), 2.58 (1 H, d, *J* 4.5, CH_AH_BO), 2.53 (1 H, td, *J* 1.2 and 4.4, CH_AH_BO), 2.35 (1 H, dd, *J* 12.2 and 14.8, PCH_AH_B) and 1.41 (3 H, s, Me); δ_C(50 MHz, $CDCl_3$) 133.9–128.4 (Ph_2PO), 53.9$^-$ ($COCH_2$ or $COCH_2$), 53.8$^-$ ($COCH_2$ or $COCH_2$), 38.5$^-$ (d, *J* 67.8, PCH_2) and 23.2$^+$ (Me); *m*/*z* 272 (40%, M^+), 202 (100, Ph_2POH), 201 (80, Ph_2PO) and 77 (30, Ph) (Found: M^+, 272.0965. $C_{16}H_{17}O_2P$ requires *M*, 272.0966).

Reaction of methanesulfonate (*R*)-22 with potassium carbonate in MeOH

In the same way, potassium carbonate (62 mg, 0.45 mmol) and methanesulfonate (*R*)-**22** (65 mg, 0.15 mmol) in MeOH (10 cm^3) gave the crude reaction mixture (54 mg, 100%) after 2 h at room temperature as an oil which contained a 40:60 ratio (by ^1H NMR) of the *epoxide* (*R*)-**23** and the vinylphosphine oxides (*E*)-**24** and (*Z*)-**24**. (The vinyl phosphine oxides were formed in a ratio of 67:33 but were not assigned.) Diagnostic signals for epoxide (*R*)-**23**: δ_H(200 MHz, $CDCl_3$) 3.40 (1 H, d, *J* 5.1, CH_AH_BO), 3.26 (1 H, ddd, *J* 1.0, 12.0 and 15.3, PCH_AH_B), 2.93 (1 H, dd, *J* 11.9 and 15.4, PCH_AH_B) and 2.82 (1 H, dd, *J* 1.0 and 5.0, CH_AH_BO). Diagnostic signals for major vinylphosphine oxide **24**: δ_H(200 MHz, $CDCl_3$) 6.32 (1 H, d, *J* 23.4, PCH=C), 5.79 (1 H, br s, CH_2OH) and 4.74 (2 H, br m, CH_2OH); δ_C(50 MHz, $CDCl_3$) 164.2$^-$ (*ipso*-Ph), 140.8$^-$ (d, *J* 17.0, PCH=*C*), 119.3$^+$ (d, *J* 100.5, P*C*H=C) and 63.4$^-$ (d, *J* 6.7, CH_2OH). Diagnostic signals for minor vinylphosphine oxide **24**: δ_H(200 MHz, $CDCl_3$) 6.85 (1 H, td, *J* 1.0 and 20.0, PCH=C), 5.65 (1 H, br s, CH_2OH) and 4.37 (2 H, t, *J* 1.0, CH_2OH); δ_C(50 MHz, $CDCl_3$) 165.7$^-$ (*ipso*-Ph), 136.3$^-$ (d, *J* 7.4, PCH=*C*), 116.1$^+$ (d, *J* 106.7, P*C*H=C) and 66.8$^-$ (d, *J* 14.2, CH_2OH).

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