Diastereoselective nucleophilic additions to vinyl phosphine oxides

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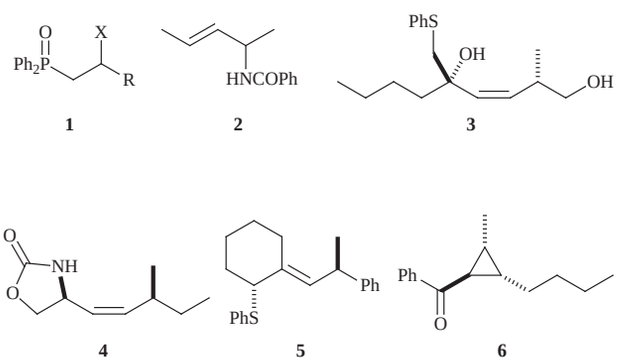
Some hydrogen, carbon, silicon, sulfur, nitrogen and oxygen nucleophiles react diastereoselectively with γ-oxygenated chiral vinyl phosphine oxides to give β-substituted phosphine oxides. Lithium *N*-benzyl-α-methylbenzylamide adds to prochiral vinyl phosphine oxides in the presence of trimethylsilyl chloride to provide, after protodesilylation, β-amino phosphine oxides as single diastereoisomers.

The diphenylphosphinoyl group is a powerful stereodirecting group which can be used to control relative and absolute stereochemistry as well as double-bond geometry.[1] As part of a continuing programme of research, we have shown that β-amido phosphine oxides **1** (X = PhCONH) are precursors of allylic amides[2] (*e.g.* **2**) and that methyl-substituted phosphine oxides **1** (X = Me) are valuable intermediates in the synthesis of allylic alcohols[3] (*e.g.* **3**), alkenyl oxazolidinones[4] (*e.g.* **4**) and allylic sulfides[5] (*e.g.* **5**) with 1,4-related chiral centres across double bonds of controlled geometry. Phosphine oxides **1** (X = Me) have also been established as intermediates in the synthesis of optically active cyclopropyl ketones[6] (*e.g.* **6**). In this paper,

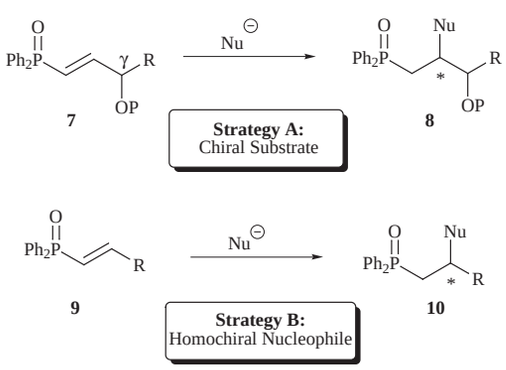


1 **2** **3** **4** **5** **6**

we describe how β-functionalised phosphine oxides can be synthesised by adding nucleophiles to vinyl phosphine oxides (Scheme 1).

In contrast to vinyl phosphonates,[7] vinyl phosphine oxides have not been widely exploited as synthetic intermediates. Early studies have shown that amines,[8] amides,[2] organocuprates[9] and silyl cuprates[10] add to the electrophilic double bond of achiral vinyl phosphine oxides. Vinyl phosphine oxides are also known to undergo cycloaddition reactions with dipolarophiles[11] and dienes[12] under thermal conditions. In this paper, we describe the first study to focus on the diastereoselectivity of nucleophilic additions to vinyl phosphine oxides. Previously, nucleophiles have been added to vinyl phosphine oxides with a chiral phosphorus atom but these reactions did not result in the formation of any new chiral centres.[9]

Our syntheses of β-functionalised phosphine oxides **8** and **10** are based on two different strategies. To start with, we describe some nucleophilic additions which are controlled by the γ chiral centre of vinyl phosphine oxides **7** (Strategy A, Scheme 1). Then, we describe the reactions of some prochiral phosphine oxides **9** with a homochiral nucleophile (Strategy B, Scheme 1). We describe the diastereoselectivity of the reactions involved and propose models to explain the sense of the asymmetric induction.



7 **8** **9** **10**

Scheme 1

Synthesis of vinyl phosphine oxides

We synthesised the prochiral vinyl phosphine oxides **9** by activation and elimination of the β-hydroxy phosphine oxides **11** (Scheme 2). Treatment of the silyl ethers **12** with sodium hydride[12] and the mesylate **13** (synthesised *in situ* from the β-hydroxy phosphine oxide **11d**) with butyllithium gave the vinyl phosphine oxides **9** in moderate to excellent yield and with complete *E* stereoselectivity.[13]

The optically active γ-hydroxy vinyl phosphine oxides **18** were produced using a two-step sequence which had been previously used to synthesise the unsaturated amides **14**.[14] Diphenylphosphinoyl diols **16**, synthesised by asymmetric dihydroxylation of the allylic phosphine oxides **15**,[15] were converted into mixtures of diastereomeric cyclic sulfites **17** and eliminated using DBU to give the γ-hydroxy vinyl phosphine oxides **18** (Scheme 3 and Table 1). The elimination of *anti*- and *syn*-**16b** to give the same enantiomer of the vinyl phosphine oxide **18b** (entries 2, 3, Table 1 and Scheme 4) allowed us to determine the absolute configuration of the diol *anti*-**16b**.[15]

The eliminations of diphenylphosphinoyl diols **16** were highly *E* selective.[13] With the simple diols **16a**–**d** (R^2 = H, entries 1–5, Table 1), the elimination proceeds through the transition state **19** in which the diphenylphosphinoyl group and R^1 are

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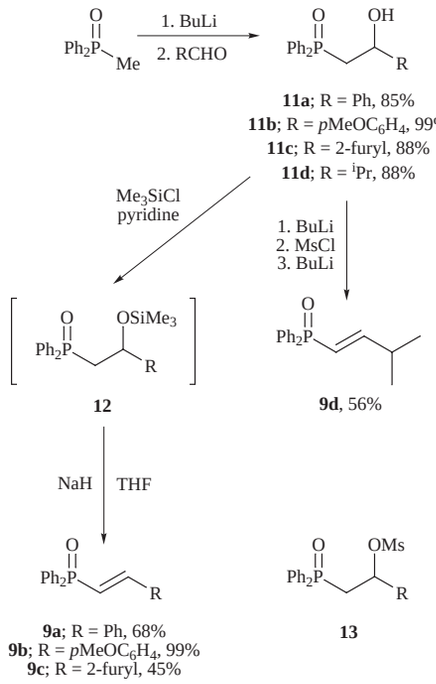
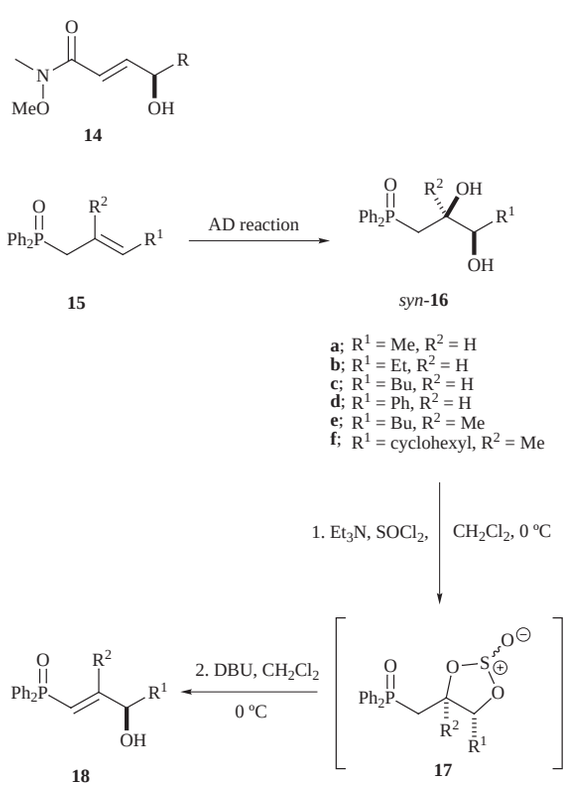
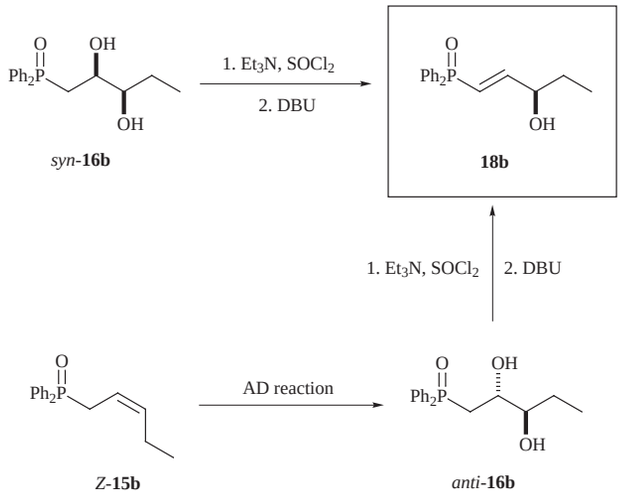


Scheme 2



Scheme 3



Scheme 4

trans on the forming double bond. When $R^2 \neq H$ (entries 6, 7, Table 1), elimination *via* the alternative transition state **20** (in which the diphenylphosphinoyl group sits above the sulfite ring) becomes significant and the *E* stereoselectivity of the reaction is lowered.

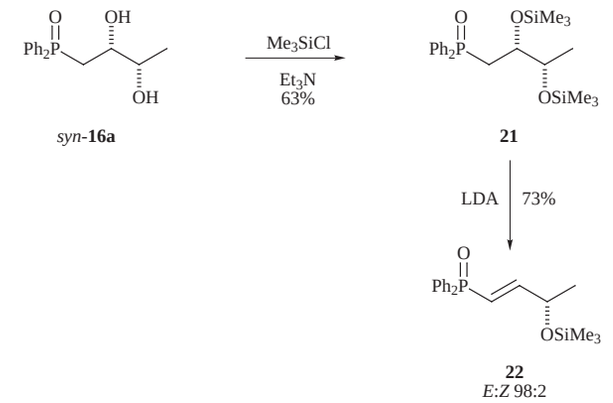
The diphenylphosphinoyl diol *syn*-**16a** was activated as the bis-trimethylsilyl ether **21**. Treatment of **21** with two equivalents of LDA gave the vinyl phosphine oxide **22** as a 98 : 2 mixture of geometric isomers (Scheme 5). Asymmetric epoxidation of the δ-hydroxy allylic phosphine oxide[16] **23** and work-up with 30% sodium hydroxide solution gave the optically active diol **24**, which was protected as the silyl ether **25**. Similarly, treatment of the diphenylphosphinoyl epoxide **27** (prepared from the allylic phosphine oxide **26**) with LDA gave the vinyl phosphine oxide **28** as a single geometric isomer.

Alcohols **18c**,**d** were protected as silyl ethers using *tert*-butyldimethylsilyl trifluoromethanesulfonate (triflate) and 2,6-lutidine (2,6-dimethylpyridine) (Scheme 6). In this way, it was possible to isolate an excellent yield of the silyl ether **29a**. Unfortunately, the yield of **29b** was much lower (32%) because the basic conditions of the reaction promoted isomerisation to the conjugated silyl enol ether **31**, which was obtained in 58% yield. The use of milder reaction conditions (imidazole and *tert*-butyldimethylsilyl chloride) provided a solution to this problem and allowed silyl ether **29b** to be isolated in quantitative yield. Vinyl phosphine oxides **18c**,**d** were easily protected

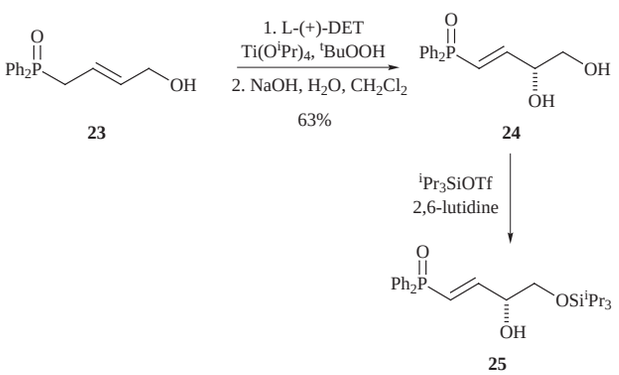
Table 1 Synthesis of γ-hydroxy vinyl phosphine oxides **18**

Entry	Starting material	R^1	R^2	Product	Ee (%)	Ratio[a] *E*:*Z*	Yield[b] (%)
1	*syn*-**16a**	Me	H	(*R*)-**18a**	46	>95:5	58
2	*syn*-**16b**	Et	H	(*R*)-**18b**	76	>95:5	65
3	*anti*-**16b**	Et	H	(*R*)-**18b**	22	>95:5	78
4	*syn*-**16c**	Bu	H	(*R*)-**18c**	76	>95:5	99
5	*syn*-**16d**	Ph	H	(*S*)-**18d**	86	>95:5	89
6	*syn*-**16e**	Bu	Me	(*R*)-**18e**	74	83:17	81
7	*syn*-**16f**	c-Hex	Me	(*R*)-**18f**	84	88:12	91

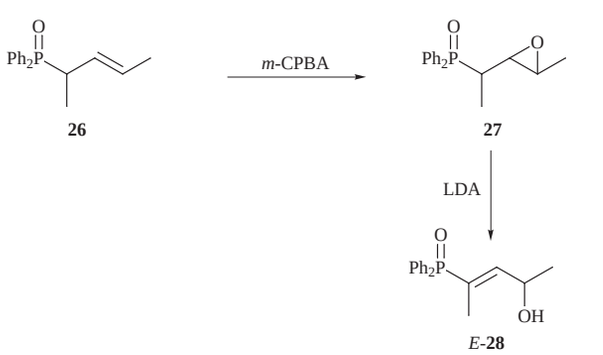
[a] By 400 MHz ^{1}H NMR. [b] Yield of mixture of geometric isomers.



syn-**16a** **21** **22**
E:*Z* 98:2

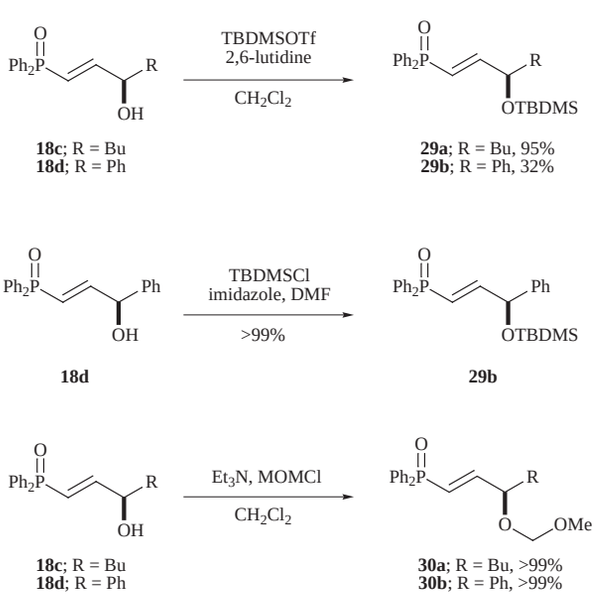


23 **24** **25**



26 **27** *E*-**28**

Scheme 5



18c; R = Bu
18d; R = Ph
29a; R = Bu, 95%
29b; R = Ph, 32%

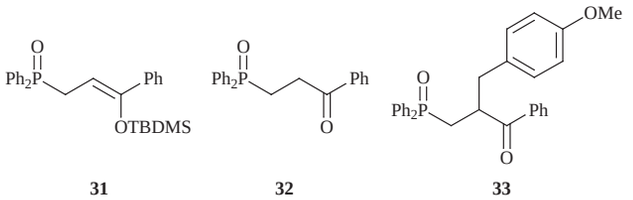
18d **29b**

18c; R = Bu
18d; R = Ph
30a; R = Bu, >99%
30b; R = Ph, >99%

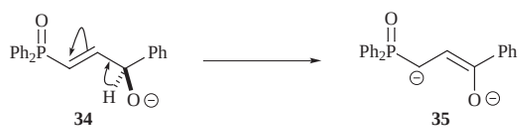
Scheme 6

as MOM acetals by treating the alcohols with methoxymethyl chloride and triethylamine (Scheme 6).

Attempted benzylation of the alcohol **18d** using sodium hydride, *p*-methoxybenzyl chloride and tetrabutylammonium iodide gave the ketones **32** and **33** in 28% and 52% yield respectively. Presumably, sodium hydride is basic enough to remove the benzylic proton from anion **34** to give the dianion **35** which is stabilised both by the diphenylphosphinoyl group and by extensive conjugation (Scheme 7). Protonation or alkylation of **35**



31 **32** **33**



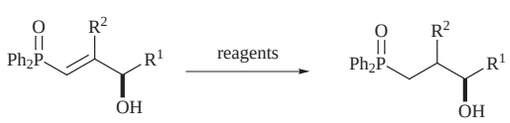
34 **35**

Scheme 7

would give the observed ketones **32** and **33**. An alternative mechanism for the direct formation of the ketone **32** may involve 1,2-migration of the marked hydrogen in the anion **34** (Scheme 7). Though disappointing, this observation did provide some evidence for a mechanism which has been proposed to explain the formation of ketones like **32** as by-products of Horner–Wittig eliminations of diphenylphosphinoyl diols **16**.[15]

Addition of hydrogen, carbon and silicon nucleophiles to γ-substituted vinyl phosphine oxides

Initially, we studied the reduction[17] of vinyl phosphine oxides **18** because these reactions are not always complicated by the issue of diastereoselectivity (Scheme 8 and Table 2).[18] Sodium



18

36a; R^1 = Bu, R^2 = H
36b; R^1 = Ph, R^2 = H
37; R^1 = Bu, R^2 = Me

Scheme 8

borohydride was not sufficiently reactive to reduce the vinyl phosphine oxide **18c** (entry 1, Table 2); in fact, later studies revealed that vinyl phosphine oxides are remarkably resistant to attack by other nucleophiles including organocuprates. In contrast, treatment of the unprotected vinyl phosphine oxides **18c**,**d** (R^2 = H) with lithium aluminium hydride gave γ-hydroxy phosphine oxides **36a**,**b** in very good yield. Similar phosphine oxides have been synthesised by classical resolution and are useful intermediates in the synthesis of homoallylic alcohols.[19,20] Treatment of the vinyl phosphine oxides **18e**,**f** (R^2 = Me) with lithium aluminium hydride gave the corresponding γ-hydroxy phosphine oxides **37** in high yield, though the reaction was not very diastereoselective (entries 4, 5, Table 2).

An alternative approach to alcohols **37** would involve the addition of methylmetal reagents to vinyl phosphine oxides **18** (R^2 = H) (Scheme 9). In contrast to reactions of similar sulfones,[21] phosphine oxides **18** reacted sluggishly with Me_3CuLi_2 (entries 1a, b, Table 3), reflecting the large size and less electron-withdrawing nature of the diphenylphosphinoyl group compared to the phenylsulfonyl group. The reactions did, however, reach completion after 7 days in refluxing ether. The sense of the stereoselectivity of our reactions was the same as the additions to the corresponding sulfones;[21] the *anti* selectivity was 2 : 1 (with **18a**, R = Me, entry 1, Table 3) and 4 : 1 (with

Table 2 Reduction of γ-hydroxy vinyl phosphine oxide **18**

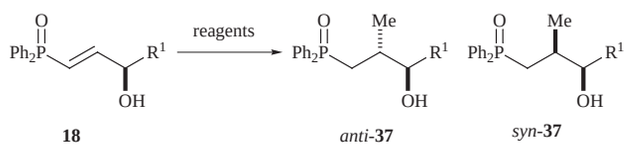
Entry	Starting material	R^1	R^2	Reagents[a]	Product	Ratio[b] *anti*:*syn*	Yield[b] (%)
1	**18c**	Bu	H	A	—	—	[c]
2	**18c**	Bu	H	B	**36a**	—	88
3	**18d**	Ph	H	B	**36b**	—	87
4	**18e**	Bu	Me	B	**37b**	59:41	83
5	**18f**	c-Hex	Me	B	**37b**	61:39	85

[a] *Reagents*: A. $NaBH_4$, EtOH; B. $LiAlH_4$, THF. [b] Isolated ratio of diastereomers. [c] No reaction by NMR.

Table 3 Addition of organocuprates to vinyl phosphine oxides **18**

Entry	Starting material	R^1	Conditions	Ratio *anti*:*syn*	Products (Yield, %)
1a	**18a**	Me	Me_3CuLi_2, ether, 35 °C, 7 days	63:37[a]	**37a** (60%[b])
1b	**18c**	Bu	Me_3CuLi_2, ether, 35 °C, 7 days	78:22[c]	*anti*-**37b** (41%); *syn*-**37b** (22%)
1c	**18d**	Ph	Me_3CuLi_2, ether, 35 °C, 7 days	74:26[c,d]	*anti*-**37c** (22%); *syn*-**37c** (10%)
2	**18d**	Ph	Me_3CuLi_2, ether, 35 °C, 7 days	—	[e]
3	**18c**	Bu	$Me_2(CN)CuLi_2$, ether, 35 °C, 3 days	77:23[c]	[f]

[a] Ratio of isolated products. [b] *anti*:*syn* 63:37. [c] Determined by analysis of the crude reaction mixture by 400 MHz NMR. [d] 30:52:18 mixture of **32**, *anti*- and *syn*-**37c**. [e] Mainly ketone **32** by NMR. [f] 19:63:18 mixture of starting material, *anti*- and *syn*-**37b**.



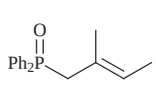
37a; R^1 = Me
37b; R^1 = Bu
37c; R^1 = Ph
37d; R^1 = cyclohexyl

Scheme 9

18c, R = Bu, entry 1, Table 3). Addition of a cyanocuprate to **18c** was also successful and, unlike the corresponding reactions of vinyl sulfones,[21] the ratio of β-hydroxy phosphine oxides **37b** obtained was similar to that observed with the higher-order cuprate Me_3CuLi_2 (compare entries 1b and 3, Table 3).

The reaction of the vinyl phosphine oxide **18d** with Me_3CuLi_2 was lower yielding than those of **18a** and **18c** (compare entry 1c with entries 1a, b, Table 3). In this case, phenyl ketone **32**, a familiar[15b] by-product from some attempted protection reactions was also isolated. Changing the solvent from ether to THF served only to promote the formation of the phenyl ketone **32** (compare entry 2 with entry 1c, Table 3).

The *anti* stereoselectivity of these cuprate addition reactions was established in two independent ways. The phosphine oxide *anti*-**37a** was spectroscopically identical with material previously synthesised by stereospecific hydroboration[22] of the allylic phosphine oxide **38** and the phosphine oxides **37b**,**c** were converted into cyclic derivatives **39** whose structure could be determined by NMR.[6,22] The *anti* and *syn* diastereomers of hydroxy phosphine oxides **37b**,**c** were readily separable by preparative HPLC.



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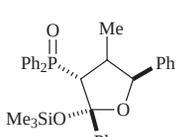
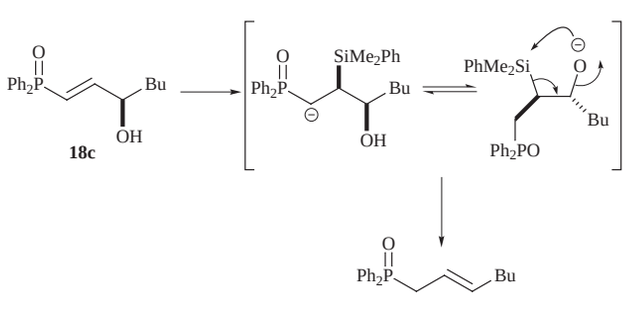


39

We tried to develop a complementary route to hydroxy phosphine oxides *syn*-**37** along the lines reported by Carretero for similar vinyl sulfones.[21] Treatment of the acetal **30b** with LDA in the presence[23] of chlorotrimethylsilane gave the α-silyl vinyl phosphine oxide **40** (Scheme 10). Unfortunately, **40** was resistant to attack by methylmagnesium bromide.

Scheme 10

The addition of the phenyldimethylsilyl group (a masked hydroxy group[10]) to vinyl phosphine oxides was also investigated. Treatment of the unprotected vinyl phosphine oxide **18c** with four equivalents of the phenyldimethylsilyl cuprate reagent[24] at −78 °C gave a 83:17 *E*:*Z* mixture of the allylic phosphine oxides[15] **41** (Scheme 11). These compounds are



Scheme 11

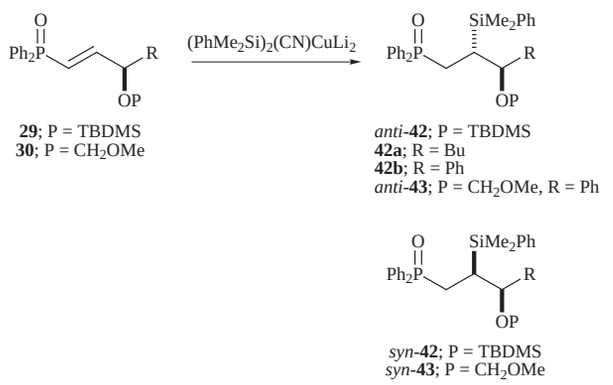
presumably the products of a tandem addition–Peterson elimination reaction, confirming that silyl cuprates do add to vinyl phosphine oxides at a much lower temperature than methyl cuprates.[25]

In the light of this result, the phenyldimethylsilyl cuprate reagent was added to some protected γ-hydroxy phosphine oxides to give the diphenylphosphinoyl silanes **42** and **43** in high yield and often with high stereoselectivity (Table 4 and Scheme 12). The stereoselectivity of this addition reaction was remarkably dependent on the exact stoichiometry of the cuprate reagent (compare entries 3 and 4; Table 4). The *anti* selectivity of the addition of the silyl cuprate reagent to the vinyl phosphine oxide **30b** was deduced from the acid-catalysed Peterson elimination[26] (which is known to be *anti* stereospecific) of the product; treatment of a 88:12 mixture of *anti*- and *syn*-**30b** with acidic methanol gave a 86:14 mixture of *E*- and *Z*-**44** (Scheme 13). Silyl ether *anti*-**42b** was even less

Table 4 Addition of silyl cuprates to vinyl phosphine oxides **29** and **30**

Entry	Starting material	R	P	Ratio[a] *anti*:*syn*	Product	Yield[b] (%)
1	**29a**	Bu	TBDMS	70:30	**42a**	84
2	**29b**	Ph	TBDMS	>95:5	**42b**	58
3	**30b**	Ph	CH_2OMe	88:12	**43**[c]	71
4[d]	**30b**	Ph	CH_2OMe	66:34	**43**	41

[a] Determined by analysis of the crude reaction mixture by 400 MHz NMR. [b] Isolated yield. [c] Decomposed to **44** on standing. [d] Ratio of silyllithium : CuCN 3 : 2.



Scheme 12

stable and decomposed to the allylic phosphine oxide (*E*)-**44** on standing in deuterochloroform.

Proposed origin of the factors which underlie the stereoselectivity of reactions of vinyl phosphine oxides with cuprate reagents

The factors (double bond geometry, substrate electrophilicity, nature of the cuprate reagent) which control the diastereoselectivity of Michael reactions of α,β-unsaturated carbonyl compounds are very complex indeed.[27] In view of the small coupling constants (3.5–4.7 Hz) between the protons β and γ to phosphorus, we suggest that phosphine oxides **18**, **29** and **30** (R′ = H, TBDMS, CH_2OMe) mainly populate the conformation in which the C–O bond more or less eclipses the carbon–carbon double bond (Fig. 1). We have shown that the addition of methyl cuprates to unprotected vinyl phosphine oxides **18** and of silyl cuprates to protected phosphine oxides were *anti* selective. The diastereoselectivity of these reactions increased with the size of the R substituent (compare entries 1a–c, Table 3, R = Me, Bu, Ph; entries 2 and 3, Table 4, R = Bu and Ph), suggesting that R may shield the top face of **45**, forcing the cuprate reagent to attack from below. A similar argument has been proposed to explain the diastereoselectivity of cuprate additions to chiral vinyl sulfones.[21] Alternatively, the observed diastereoselectivity may stem from addition of the cuprate reagents to the lower face of a reactive conformation **46** in which π*(C=C) overlaps with σ*(C–O) (Fig. 2).

Diastereoselective additions of nitrogen, sulfur and oxygen nucleophiles to chiral γ-substituted vinyl phosphine oxides

We also studied the addition of heteroatomic nucleophiles to chiral vinyl phosphine oxides. For example, sodium thiophenolate added cleanly, though not very diastereoselectively to silyl ether **22** (Scheme 14). The sense of the diastereoselectivity of this transformation was not determined.

The addition of sodium benzamide (which has been added to vinyldiphenylphosphine oxide[2]) to the silyl ether **22** was less successful: only starting material and the hydroxy vinyl phosphine oxide **18a** were isolated. We felt that the energetic barrier to nucleophilic attack might be overcome by making the reaction intramolecular. With this in mind, urethane **48** was

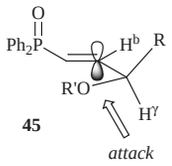


Fig. 1

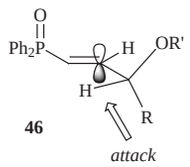
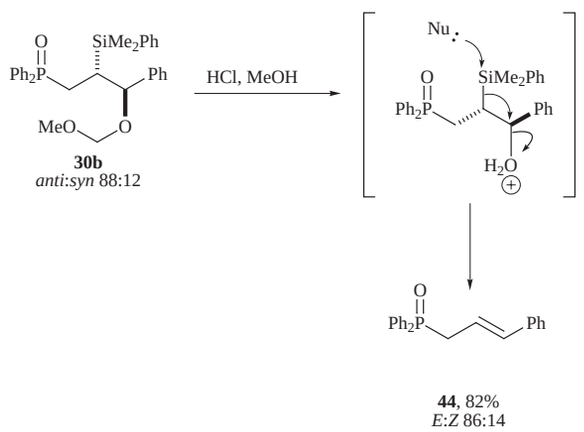
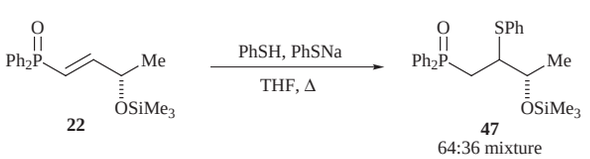


Fig. 2

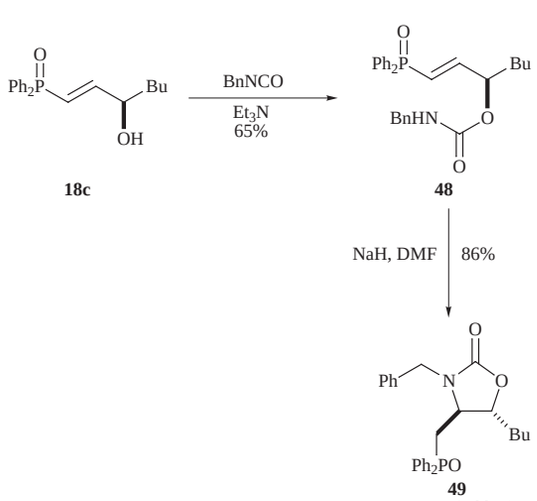


Scheme 13



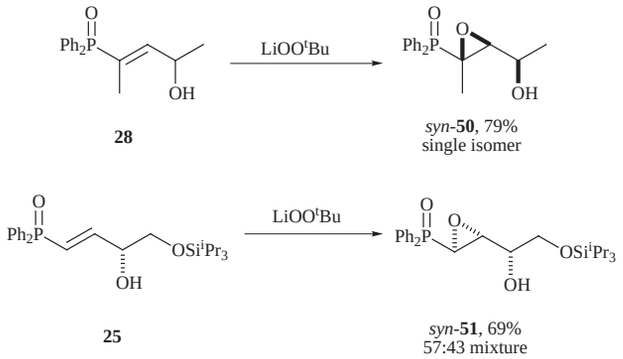
Scheme 14

synthesised by treating the alcohol **18c** with benzyl isocyanate and triethylamine; cyclisation of **48**, triggered by treatment with sodium hydride in DMF, gave the oxazolidinone **49** in 86% yield as a 88 : 12 mixture of diastereoisomers (Scheme 15). Similar reactions of vinyl sulfones suggest that the *trans* isomer was the major product.[28]



Scheme 15

Treatment of the hydroxy vinyl phosphine oxides **28** and **25** with the nucleophilic epoxidation reagent lithium *tert*-butyl hydroperoxide gave the epoxides **50** and **51** respectively (Scheme



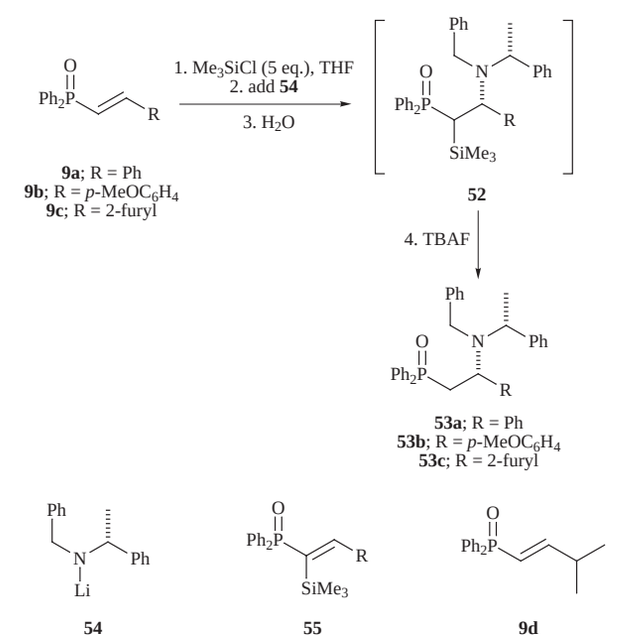
Scheme 16

16). The epoxidation of **25** was not very stereoselective. The conformationally-locked allylic alcohol **28** was, however, epoxidised with high diastereoselectivity; by analogy with similar reactions of vinyl sulfones, the transformation is thought to be *syn* selective.[29]

Asymmetric addition of Davies's chiral lithium amide to prochiral vinyl phosphine oxides

We have studied the nucleophilic addition of a chiral nucleophile, Davies's lithium amide **54**, to prochiral vinyl phosphine oxides (Strategy B, Scheme 1). The lithium amide **54** has previously been added with high diastereoselectivity to α,β-unsaturated Weinreb amides (which can be transformed into aldehydes and ketones) and α,β-unsaturated esters.[30,31] Lithium amide **54** has not, however, been added successfully to other unsaturated electrophiles; for example, no addition products were isolated when **54** was added even to non-enolisable ketones such as chalcone.[31]

Treatment of the vinyl phosphine oxides **9a**–**c** with the lithium amide[32] **54** in the presence of chlorotrimethylsilane[23] gave mixtures of the α-silyl phosphine oxides **52** (as single diastereomers) and α-silyl vinyl phosphine oxides **55**.[33] The α-silyl phosphine oxides **52a**–**c** were protodesilylated by treatment of the crude reaction mixture with tetra-*n*-butylammonium fluoride in THF to give the β-amino phosphine oxides as single diastereomers (Scheme 17 and Table 5). The



Scheme 17

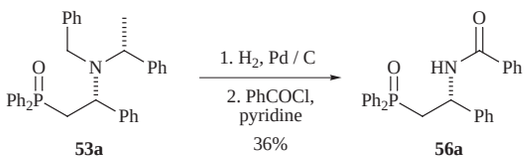
reaction appears to be limited to aryl-substituted vinyl phosphine oxides such as **9a**–**c** (entries 1–3, Table 5); **9d** (R = ^{i}Pr; entry 4) was recovered unchanged after being subjected to the same reaction conditions.

Table 5 Addition of the lithium amide **54** to prochiral vinyl phosphine oxides **9**

Entry	Starting material	R	Product	Yield[a] (%)	Diastereomeric ratio[b]
1	**9a**	Ph	**53a**	65	98:2
2	**9b**	*p*-MeOC$_6$H$_4$	**53b**	76	>99:1
3	**9c**	2-Furyl	**53c**	34	>99:1
4	**9d**	^{i}Pr	—	0[c]	—

[a] Yield of purified amine. [b] By ^{1}H NMR. [c] **9d** was recovered.

The β-amino phosphine oxide **53a** was converted into the amide **56a** by hydrogenolytic cleavage of the benzyl groups and acylation with benzoyl chloride (Scheme 18). Similar (racemic) amides have been used as intermediates in the synthesis of allylic amides.[2]



Scheme 18

We showed that the amine **57** (synthesised by hydrogenolysis of the β-amino phosphine oxide **53b**) had >98% ee (Scheme 19). Crucially, the amide *syn*-**58** obtained from coupling the homochiral amine **57** with (*S*)-mandelic acid [(*S*)-**59**] could clearly be distinguished from one of the amides (*anti*-**58**) obtained when **57** was coupled with racemic mandelic acid (*rac*-**59**). The stereochemistry drawn, which is analogous to that observed with similar reactions of α,β-unsaturated esters,[30] has been established by X-ray crystallographic analysis of the benzamide **56b**.[34]

Proposed mechanism of the addition of Davies's lithium amide to prochiral vinyl phosphine oxides

Our proposed mechanism for the reaction between Davies's lithium amide **54** and vinyl phosphine oxides **9** (Scheme 17 and Table 5) is shown in Scheme 20. We believe that the addition of **54** to phosphine oxides **9** is reversible and that the equilibrium lies towards the starting materials.§ The chlorotrimethylsilane internal trapping agent¶ removes material from this equilibrium process by reacting with the lithiated phosphine oxide **60**. This model has been proposed on the basis of three pieces of evidence.

(1) In the absence of the chlorotrimethylsilane trap, no reaction was observed between Davies's lithium amide **54** and the vinyl phosphine oxide **53a** (R = Ph); starting materials were recovered in *ca.* 90% yield.

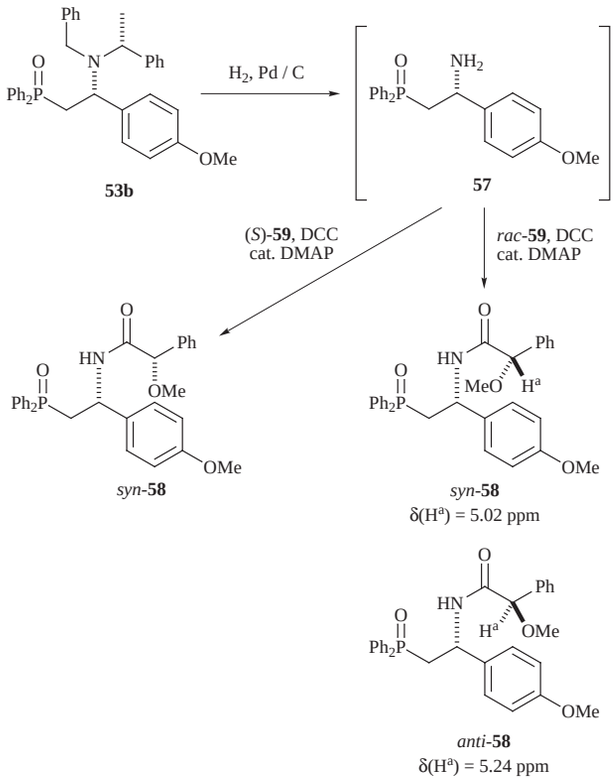
(2) The lithiated phosphine oxide **60b** (R = *p*-MeOC$_6$H$_4$–), generated by treatment of **53b** with butyllithium at −78 °C, decomposed to give the vinyl phosphine oxide **9b** and the amine derived from protonation of **54**.

(3) The α-silyl phosphine oxide **55** is not an intermediate in the reaction **9** + **54**→**52**; **55** does not react with the lithium amide **54** under our usual reaction conditions.

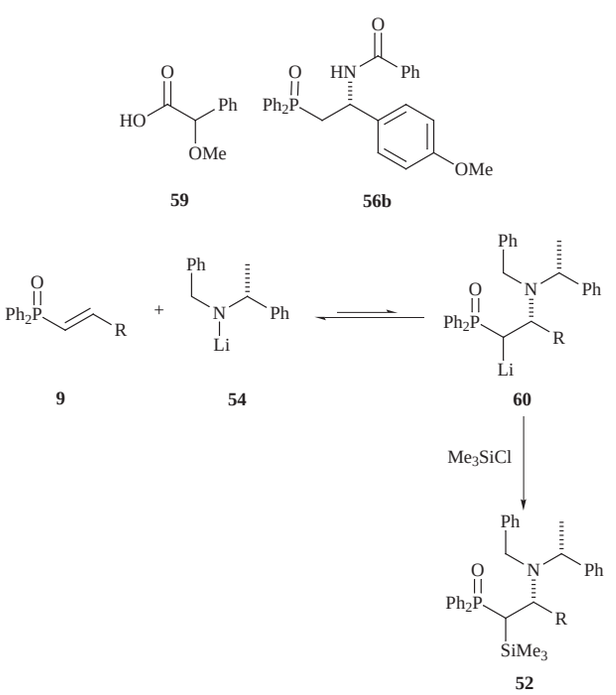
Davies has proposed a model which explains the high stereoselectivity observed in the conjugate additions of the lithium amide **54** to α,β-unsaturated esters.[37] In an analogous manner, we propose that the lithium amide **54** approaches the vinyl phosphine oxides **9** in the "butterfly"-like conformation shown in Fig. 3. Under this scenario, nucleophilic attack of the lithium

§ For another β-elimination of a β-amino organolithium, see reference 35.

¶ Lithium amides react slowly with chlorotrimethylsilane at −78 °C.[36]



Scheme 19



Scheme 20

amide **54** on the carbon–carbon double bond, with concomitant formation of the P–C–O–Li ring of lithiated phosphine oxides,[38] leads to the stereochemistry observed in our reactions.

Summary

In this paper, we have reported two strategies for controlling the stereochemistry of β-functionalised phosphine oxides by adding nucleophiles to vinyl phosphine oxides. β-Substituted phosphine oxides have already been established as key intermediates in the synthesis of allylically functionalised compounds with control over double bond geometry.[1] To start with, we studied the addition of hydrogen, carbon and heteroatomic nucleophiles to vinyl phosphine oxides with a chiral

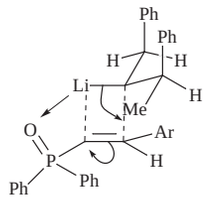


Fig. 3

centre γ to phosphorus. Then, the diastereoselective addition of Davies's chiral lithium amide to prochiral vinyl phosphine oxides in the presence of chlorotrimethylsilane was described. The products of this reaction, β-amino phosphine oxides are potential precursors of ligands for asymmetric catalysis[39] and chiral auxiliaries.[40] The use of internal traps in asymmetric conjugate additions may allow Davies's reaction to be extended to other electrophiles which do not react with lithium amide **54** alone.[31]

Experimental

All solvents were distilled before use. THF and Et_2O were freshly distilled from lithium aluminium hydride whilst CH_2Cl_2 and toluene were freshly distilled from calcium hydride. Triphenylmethane was used as indicator for THF. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine was dried by stirring over and distilling from calcium hydride and was then stored over activated 4 Å molecular sieves. *n*-Butyllithium was titrated against diphenylacetic acid before use. All non-aqueous reactions were carried out under argon using oven-dried glassware.

Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh) according to the method of Still, Kahn and Mitra.[41] Thin layer chromatography was carried out on commercially available pre-coated plates (Merck silica Kieselgel $60F_{254}$). Proton and carbon NMR spectra were recorded on Bruker WM 200, WM 250, WM 400 or AMX 500 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in ppm downfield of tetramethylsilane and values of coupling constants (*J*) are given in Hz. The symbol * after the proton NMR chemical shift indicates that the signal disappears after a D_2O "shake". Carbon NMR spectra were recorded with broad band proton decoupling and attached proton test. The symbols $^+$ and $^-$ after the carbon NMR chemical shift indicate odd and even numbers of attached protons respectively.

Melting points were measured on a Reichart hot stage microscope or a Buchi 510 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1600 (FT-IR) spectrophotometer. Mass spectra were recorded on a Kratos double-beam mass spectrometer using a DS503 data system for high resolution analysis. Microanalyses were carried out by the staff of the University Chemical Laboratory using Carlo Erba 1106 or Perkin-Elmer 240 automatic analysers. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter (using the sodium D line; 589 nm) and $[\alpha]_D^{20}$ are given in units of 10^{-1} deg cm^2 g^{-1}. (*R*)-Pirkle's reagent is (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.

2-Diphenylphosphinoyl-1-(*p*-methoxyphenyl)ethanol 11b

n-Butyllithium (1.3 mol dm^{-3} solution in hexanes, 84.6 cm^3, 0.11 mol) was added to a stirred solution of methyldiphenylphosphine oxide (21.6 g, 0.1 mol) in 400 ml dry THF at −78 °C. After stirring for 15 min, *p*-anisaldehyde (14.6 cm^3, 0.12 mol was added and the reaction was stirred for a further 30 min at −78 °C. The solution was allowed to warm up to room temperature, stirred for 1 h, quenched with saturated aqueous ammonium chloride solution (200 cm^3), extracted with dichloromethane (3 × 200 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product, which was

purified by flash chromatography (eluting with 2:1 EtOAc–hexane) or by recrystallization from EtOAc to give *the β-hydroxyphosphine oxide* **11b** (34.4 g, 99%) as white needles, mp 133 °C; R_F (EtOAc) 0.29; $\nu_{max}(CHCl_3)/cm^{-1}$ 1173 (P=O), 1438 (P–Ph) and 3756 (OH); δ_H(200 MHz, $CDCl_3$) 7.41–7.82 (10 H, m, Ph_2PO), 7.25 (2 H, d, *J* 8.6, MeOPh), 6.82 (2 H, d, *J* 8.6, MeOPh), 5.11 (1 H, t, *J* 9.5, C*H*OH), 4.92 (1 H, s, OH), 3.76 (3 H, s, OMe), 2.75 (1 H, td, *J* 10.9 and 15.0, CH_2) and 2.55 (1 H, ddd, *J* 2.1, 6.9 and 15.0, CH_2); δ_C(100 MHz, $CDCl_3$) 159.1$^-$ (C-OMe), 136.1$^-$ (d, *J* 10.4, *ipso*-Ph), 126.8–133.7 (m, Ph, MeOPh), 113.9$^+$ (MeOPh), 68.9$^+$ (CHOH), 55.3$^+$ (OMe) and 39.2$^-$ (d, *J* 67.9, CH_2); *m*/*z* (EI) 352 (4%, M^+), 334 (20, $M - H_2O$), 215 (79, $Ph_2P(O)CH_3$) and 201 (100, $Ph_2P(O)H$) (Found: M^+, 352.1222. $C_{21}H_{21}O_3P$ requires *M*, 352.1228) (Found: C, 71.3; H, 6.0; P, 8.7. $C_{21}H_{21}O_3P$ requires C, 71.6; H, 6.0; P, 8.8%).

1-Diphenylphosphinoyl-3-methylbutan-2-ol 11d

By the general method described above, methyldiphenylphosphine oxide (21.6 g, 0.1 mol) and 2-methylpropanal gave the β-hydroxyphosphine oxide[42] **11d** (25.3 g, 88%) as a colourless oil, R_F (EtOAc) 0.38; $\nu_{max}(CHCl_3)/cm^{-1}$ 1173 (P=O), 1437 (P–Ph) and 3761 (OH); δ_H(400 MHz, $CDCl_3$) 7.65–7.80 (4 H, m, Ph_2PO), 7.40–7.57 (6 H, m, Ph_2PO), 4.42 (1 H, s, OH), 3.82 (1 H, m, C*H*OH), 2.32–2.42 (2 H, m, CH_2), 1.75 (1 H, dq, *J* 6.8, 12.1, C*H*Me_2) and 0.89 (6 H, dd, *J* 1.6, 6.8, Me); *m*/*z* (EI) 288 (13%, M^+), 270 (34, $M - H_2O$), 215 (76, Ph_2POCH_3) and 201 (100, Ph_2PO).

2-Diphenylphosphinoyl-1-furan-2′-ylethanol 11c

By the general method described above, methyldiphenylphosphine oxide (21.6 g, 0.1 mol) gave the *β-hydroxyphosphine oxide* **11c** (27.4 g, 88%) as white needles, mp 151 °C; R_F (EtOAc) 0.46, $\nu_{max}(CHCl_3)/cm^{-1}$ 1175 (P=O), 1438 (P-Ph) and 3517 (OH); δ_H(400 MHz, $CDCl_3$) 7.66–7.80 (4 H, m, Ph_2PO), 7.42–7.57 (6 H, m, Ph_2PO), 7.25 (1 H, s, 4′-H), 6.24 (2 H, s, 2′-H and 3′-H), 5.19 (1 H, dt, *J* 2.3 and 10.4, C*H*OH), 4.96 (1 H, d, *J* 2.3, OH), 2.92 (1 H, ddd, *J* 10.1, 10.9 and 15.0, CH_2) and 2.73 (1 H, ddd, *J* 2.6, 7.9 and 15.0, CH_2); δ_C(100 MHz, $CDCl_3$) 155.4$^-$ (d, *J* 14.1, C-1′), 141.9$^-$, 128.7–133.4 (m, Ph, C-4′), 110.3$^+$, 106.2$^+$, 63.6$^+$ (d, *J* 3.9, CHOH) and 35.3$^-$ (d, *J* 69.7, CH_2); *m*/*z* (EI) 312 (11%, M^+), 215 (53, Ph_2POCH_3) and 202 (100, Ph_2POH) (Found: M^+, 312.0902. $C_{18}H_{17}O_3P$ requires *M*, 312.0915) (Found: C, 68.3; H, 5.5; P, 9.3. $C_{18}H_{17}O_3P$ requires C, 68.2; H, 5.5; P, 9.9%).

(*E*)-1-Diphenylphosphinoyl-3-methylbutene 9d

n-Butyllithium (1.3 mol dm^{-3} solution in hexanes; 0.85 ml, 1.1 mmol) and methanesulfonyl chloride (75 μl, 1.2 mmol) were added to a stirred solution of the β-hydroxyphosphine oxide **11d** (288 mg, 1.00 mmol) in 5 ml THF at −10 °C. The reaction mixture was stirred for 1 h at −10 °C, *n*-butyllithium (1.3 mol dm^{-3} solution in hexanes; 0.77 ml, 1.00 mmol) was added and the mixture was stirred for a further 24 h at −10 °C. The reaction was quenched by addition of aqueous hydrochloric acid solution (3.0 mol dm^{-3}, 35 cm^{-3}), extracted with dichloromethane (3 × 30 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product which was recrystallised from EtOAc–hexane 1:1 to give the vinyl phosphine oxide[43] **9d** (151 mg, 56%) as colourless needles, mp 141–143 °C; R_F (EtOAc) 0.33; $\nu_{max}(CHCl_3)/cm^{-1}$ 1176 (P=O) and 1441 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.65–7.72 (4 H, m, Ph_2PO), 7.40–7.55 (6 H, m, Ph_2PO), 6.73 (1 H, ddd, *J* 6.1, 17.1 and 19.9, C*H*CHMe_2), 6.15 (1 H, ddd, *J* 1.5, 17.1 and 24.4, Ph_2POCH), 2.53 (1 H, m, C*H*Me_2) and 1.08 (6 H, d, *J* 6.8, Me); *m*/*z* (EI) 270 (62%, M^+), 227 (47, M − ^{i}Pr), 202 (100, Ph_2POH) and 77 (73, C_7H_7).

(*E*)-1-Diphenylphosphinoyl-2-(*p*-methoxyphenyl)ethene 9b

Pyridine (105 μl, 1.3 mmol) and chlorotrimethylsilane (140 μl, 1.1 mmol) were added to a stirred solution of the β-hydroxyphosphine oxide **11b** (352 mg, 1.0 mmol) in dry dichloromethane (5 cm^3) at 0 °C. The reaction mixture was stirred for 4 h at 0 °C, the solvent was removed by evaporation under reduced pressure, water (5 cm^3) was added, and the reaction mixture was extracted with dichloromethane (3 × 30 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product, which was dissolved in dry THF (3 cm^3), and added slowly to a stirred suspension of sodium hydride (60% suspension in mineral oil, 44 mg, 1.1 mmol) in dry THF (2 cm^3) at 70 °C. The reaction mixture was stirred for 2 h at 70 °C, quenched by addition of ice, extracted with dichloromethane (3 × 30 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product, which was purified by flash chromatography (EtOAc–hexane 2:1) and by recrystallization (EtOAc–hexane 1:1) to give the *vinyl phosphine oxide* (330 mg, 99%) as colourless needles, mp 174 °C; R_F (EtOAc) 0.30; ν_{max}(Nujol)/cm^{-1} 1176 (P=O) and 1439 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.71–7.78 (4 H, m, Ph_2PO), 7.40–7.55 (9 H, m, Ph_2PO, Ar and POCH=C*H*), 6.88 (2 H, d, *J* 8.8, Ar), 6.65 (1 H, dd, *J* 17.3 and 22.3, POC*H*) and 3.82 (3 H, s, OMe); δ_C(100 MHz, $CDCl_3$) 161.2$^-$ (C-OMe), 147$^-$ (d, *J* 4, *ipso*-PhOMe), 127.9–133.8 (m, Ph, PhOMe, *C*HPhOMe), 116.2$^+$ (d, *J* 105.9, Ph_2POCH), 114.2$^+$ (*C*HPhOMe) and 55.4$^+$ (OMe) *m*/*z* (EI) 334 (93%, M^+), 202 (100, Ph_2POH) and 77 (37, C_7H_7) (Found: M^+, 334.1117. $C_{21}H_{19}O_2P$ requires *M*, 334.1122) (Found: C, 75.4; H, 5.75; P, 9.2. $C_{21}H_{19}O_2P$ requires C, 75.4; H, 5.7; P, 9.3%).

(*E*)-1-Diphenylphosphinoyl-2-furan-2′-ylethene 9c

By the general method described above, the β-hydroxy phosphine oxide **11c** (312 mg, 1.00 mmol) gave the *vinyl phosphine oxide* (130 mg, 45%) as colourless needles, mp 151 °C; R_F (EtOAc) 0.38; $\nu_{max}(CHCl_3)/cm^{-1}$ 1174 (P=O) and 1438 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.68–7.75 (4 H, m, Ph_2PO), 7.41–7.52 (7 H, m, Ph_2PO and 4′-H), 7.26 (1 H, dd, *J* 17.1 and 19.4, C*H*Ar), 6.70 (1 H, d, *J* 17.1 and 23.0, POC*H*), 6.50 (1 H, d, *J* 3.4, 2′-H) and 6.42 (1 H, dd, *J* 1.8 and 3.4, 3′-H); δ_C(100 MHz, $CDCl_3$) 151.5$^-$ (d, *J* 20, C-1′), 144.4$^-$, 128.5–134.0 (m, Ph, C-4′ and *C*HAr), 116.6$^+$ (d, *J* 105.5, Ph_2POCH), 113.7$^+$ and 112.2$^+$ (C-2′ and C-3′); *m*/*z* (EI) 294 (100%, M^+) and 202 (64, Ph_2POH) (Found: M^+, 294.0808. $C_{18}H_{15}O_2P$ requires *M*, 294.0809) (Found: C, 73.5; H, 5.15; P, 10.5. $C_{18}H_{15}O_2P$ requires C, 73.5; H, 5.1; P, 10.5%).

(*R*)-(*E*)-4-Diphenylphosphinoylbut-3-en-2-ol 18a

By the method of Sharpless *et al*,[14] triethylamine (1.15 g, 10.6 mmol) and thionyl chloride (0.63 g, 5.35 mmol) were added dropwise to a stirred solution of (2*S*,3*R*)-1-diphenylphosphinoylbutane-2,3-diol **16a** (1.35 g, 4.66 mmol) in dry dichloromethane (25 cm^3) at 0 °C. After 1 h, the reaction mixture was evaporated under reduced pressure and dry dichloromethane (25 cm^3) added. DBU (3.54 g, 23.3 mmol) was added dropwise to this solution at 0 °C. After 1 h, dichloromethane (50 cm^3) was added, the reaction mixture washed with hydrochloric acid (2 × 50 cm^3) and brine (50 cm^3), and evaporated under reduced pressure to give a crude product, which was purified by flash chromatography, eluting with 5% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18a** (733 mg, 58%) as an oil, R_f 0.44 (10% methanol in EtOAc); $[\alpha]_D^{20}$ −10.8 (*c* 1.14 in $CHCl_3$) (Found: M^+, 272.0966. $C_{16}H_{17}PO_2$ requires *M*, 272.0966); $\nu_{max}(CHCl_3)/cm^{-1}$ 3332 (OH), 1624 (C=C), 1438 (P–Ph) and 1169 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.35 (10 H, m, Ph_2PO), 6.74 (1 H, ddd, *J* 4.7, 17.0 and $^3J_{PH}$ 18.9, PCH=C*H*), 6.51 (1 H, ddd, *J* 1.5, 17.0 and $^2J_{PH}$ 24.4, PCH), 4.44 (1 H, br s, OH), 4.08 (1 H, m, C*H*OH) and 1.29 (3 H, d, *J* 6.7, Me); δ_C(100 MHz, $CDCl_3$) 155.8$^+$ (PCH=*C*H), 133–128 (m, Ph_2PO), 119.0$^+$ (d, $^1J_{PC}$ 102.4, PCH), 67.9$^+$ (d, $^3J_{PC}$ 16.6, CHOH) and 21.0$^+$ (Me); *m*/*z* 272.1 (10%, M^+), 229.1 (100) and 202.1 (95, Ph_2POH). Integration of the 500 MHz ^{1}H NMR

spectrum of the Mosher's ester of this material showed it to have 46% ee.

(*R*)-(*E*)-1-Diphenylphosphinoylpent-1-en-3-ol 18b

By the general method described above, (2*S*,3*R*)-1-diphenylphosphinoylpentane-2,3-diol *syn*-**16b** (635 mg, 2.22 mmol) gave a crude product, which was purified by flash chromatography, eluting with 8% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18b** (414 mg, 65%) as an oil, R_f 0.34 (10% methanol in EtOAc); $[\alpha]_D^{20}$ −19.9 (*c* 1.41 in $CHCl_3$) (Found: $M^+ - Et$, 257.0743. $C_{17}H_{19}PO_2$ requires $M - Et$, 257.0731); $\nu_{max}(CHCl_3)/cm^{-1}$ 3339 (OH), 1621 (C=C), 1438 (P–Ph) and 1172 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.35 (10 H, m, Ph_2PO), 6.74 (1 H, ddd, *J* 3.9, 17.0 and $^3J_{PH}$ 19.9, PCH=C*H*), 6.54 (1 H, ddd, *J* 1.6, 17.0 and $^2J_{PH}$ 24.7, PCH), 4.26 (1 H, m, C*H*OH), 3.57 (1 H, br s, OH), 1.58 (2 H, m) and 0.93 (3 H, d, *J* 7.4, Me); δ_C(100 MHz, $CDCl_3$) 154.5$^+$ (PCH=*C*H), 133–128 (m, Ph_2PO), 120.1$^+$ (d, $^1J_{PC}$ 102.0, PCH), 73.1$^+$ (d, $^3J_{PC}$ 16.1, CHOH), 29.5$^-$ (CH_2Me) and 9.7$^+$ (Me); *m*/*z* 257.1 (30%, $M^+ - Et$), 229.1 (100) and 202.1 (Ph_2POH). Integration of the 500 MHz ^{1}H NMR spectrum of the Mosher's ester of this material showed it to have 76% ee.

(*R*)-(*E*)-1-Diphenylphosphinoylpent-1-en-3-ol 18b

By the general method described above, (2*R*,3*R*)-1-diphenylphosphinoylpentane-2,3-diol *anti*-**16b** (95 mg, 0.31 mmol) gave a crude product, which was purified by flash chromatography, eluting with 8% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18b** (62 mg, 78%) as an oil, $[\alpha]_D^{20}$ −1.5 (*c* 0.69 in $CHCl_3$), spectroscopically identical to that obtained previously. Integration of the 500 MHz ^{1}H NMR spectrum of the Mosher's ester of this material showed it to have 22% ee.

(*R*)-(*E*)-1-Diphenylphosphinoylhept-1-en-3-ol 18c

By the general method described above, (2*S*,3*R*)-1-diphenylphosphinoylheptane-2,3-diol **16c** (3.63 g, 10.9 mmol) gave a crude product, which was purified by flash chromatography, eluting with 2% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18c** (3.48 g, 99%) as prisms, mp 94–95 °C (from EtOAc–hexane); R_f 0.28 (EtOAc); $[\alpha]_D^{20}$ −22.0 (*c* 0.44 in $CHCl_3$; 76% ee) (Found: C, 72.6; H, 7.35; P, 9.9%; M^+, 314.1435. $C_{19}H_{23}PO_2$ requires C, 72.6; H, 7.35; P, 9.9%; *M*, 314.1436); $\nu_{max}(CHCl_3)/cm^{-1}$ 3333 (OH), 1618 (C=C), 1437 (P–Ph) and 1173 (P=O); δ_H(400 MHz, $CDCl_3$) 7.8–7.3 (10 H, m, Ph_2PO), 6.75 (1 H, ddd, *J* 3.9, 17.0 and $^3J_{PH}$ 19.8, PCH=C*H*), 6.52 (1 H, ddd, *J* 1.3, 17.0 and $^2J_{PH}$ 24.6, PCH), 4.31 (1 H, br m, C*H*OH), 3.05 (1 H, br s, OH), 1.6–1.3 (6 H, m) and 0.86 (3 H, t, *J* 7.0, Me); δ_C(100 MHz, $CDCl_3$) 154.5$^+$ (PCH=*C*H), 134–127 (m, Ph_2PO), 119.9$^+$ (d, $^1J_{PC}$ 102, PCH), 72.0$^+$ (d, $^3J_{PC}$ 15, CHOH), 36.3$^-$, 33.1$^-$, 22.5$^-$, and 14.0$^+$ (Me); *m*/*z* 314.1 (10%, M^+), 245.1 (90), 229.1 (100) and 202.1 (100, Ph_2POH).

(*S*)-(*E*)-3-Diphenylphosphinoyl-1-phenylprop-2-en-1-ol 18d

By the general method described above, (1*S*,2*S*)-3-diphenylphosphinoyl-1-phenylpropane-1,2-diol **16d** (1.37 g, 4.1 mmol) and DBU (1.26 g, 8.2 mmol) gave a crude product, which was purified by flash chromatography, eluting with 2% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18d** (1.16 g, 89%) as an oil, R_f 0.28 (EtOAc); $[\alpha]_D^{20}$ −73.4 (*c* 0.46 in $CHCl_3$; 86% ee) (Found: M^+, 334.1146. $C_{21}H_{19}PO_2$ requires *M*, 334.1122); $\nu_{max}(CHCl_3)/cm^{-1}$ 3300 (OH), 1619 (C=C), 1437 (P–Ph) and 1170 (P=O); δ_H(400 MHz, $CDCl_3$) 7.6–7.2 (15 H, m, Ph_2PO and Ph), 6.82 (1 H, ddd, *J* 3.9, 16.9 and $^3J_{PH}$ 19.5, PCH=C*H*), 6.65 (1 H, ddd, $^4J_{HH}$ 1.5, *J* 16.9 and $^2J_{PH}$ 24.1, PCH), 5.29 (1 H, m, C*H*OH) and 4.50 (1 H, br s, OH); δ_C(100 MHz, $CDCl_3$) 153.2$^+$ (PCH=*C*H), 141.3$^-$ (*ipso*-Ph), 133–126 (m, Ph_2PO and remaining Ph), 119.9$^+$ (d, $^1J_{PC}$ 101, PCH) and 74.2$^+$ (d, $^3J_{PC}$ 17, CHOH); *m*/*z* 334.1 (10%, M^+), 306.1 (100) and 215.1 (100, $Ph_2P(OH)CH$).

(*R*)-(*E*)-1-Diphenylphosphinoyl-2-methylhept-1-en-3-ol 18e

By the general method described above, (2*S*,3*R*)-1-diphenylphosphinoyl-2-methylheptane-2,3-diol **16e** (812 mg, 2.35 mmol) gave a crude product, which was purified by flash chromatography, eluting with 2% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18e** (590 mg, 81%, 83:17 *E*:*Z* mixture) as an oil, R_f 0.50 (10% methanol in EtOAc); $[\alpha]_D^{20}$ −1.9 (*c* 0.76 in $CHCl_3$) (Found: M^+, 328.1595. $C_{20}H_{25}PO_2$ requires *M*, 328.1592); $\nu_{max}(CHCl_3)/cm^{-1}$ 3308 (OH), 1624 (C=C), 1438 (P–Ph) and 1170 (P=O); δ_H(400 MHz, $CDCl_3$) 7.75–7.3 (10 H, m, Ph_2PO), 6.28 (1 H, d, $^2J_{PH}$ 25.8, PCH^E), 6.25 (1 H, d, $^2J_{PH}$ 25.1, PCH^Z), 4.41 (1 H, s, OH), 4.09 (1 H, m, $CHOH^{E+Z}$), 1.99 (3 H, br s, $C{=}CMe^Z$), 1.92 (3 H, s, $C{=}CMe^E$), 1.7–1.1 (6H, m), 0.89 (3 H, t, *J* 7.0, Me^E) and 0.79 (3 H, t, *J* 7.2, Me^Z); δ_C(100 MHz, $CDCl_3$) 167.4$^-$ (PCH=C^Z), 166.4$^-$ (PCH=C^E), 135–128 (m, Ph_2PO), 116.0$^+$ (d, $^1J_{PC}$ 102.4, PCH^Z), 114.3$^+$ (d, $^1J_{PC}$ 104.6, PCH^E), 76.2$^+$ (d, $^3J_{PC}$ 15.7, $CHOH^E$), 73.2$^+$ ($CHOH^Z$), 35.5$^-$ (*Z*), 34.8$^-$ (*E*), 28.2$^-$ (*Z*), 27.8$^-$ (*E*), 22.7$^-$ (*E*), 22.5$^-$ (*Z*), 14.1$^+$ (Me^E) and 14.0$^+$ (Me^Z); *m*/*z* 328.2 (25%, M^+), 310.2 (80, $M^+ - H_2O$), 271.1 (90, $M^+ - Bu$) and 201.1 (100, Ph_2PO). Integration of the 500 MHz ^{1}H NMR spectrum of the Mosher's ester of this material showed it to have 74% ee.

(*R*)-(*E*)-1-Cyclohexyl-3-diphenylphosphinoyl-2-methylprop-2-en-1-ol 18f

By the general method described above, (2*R*,3*S*)-1-cyclohexyl-3-diphenylphosphinoyl-2-methylpropane-1,2-diol **16f** (1.41 g, 3.79 mmol) gave a crude product, which was purified by flash chromatography, eluting with 5% methanol in EtOAc, to yield the *vinyl phosphine oxide* **18f** (1.21 mg, 91%, 88:12 *E*:*Z* mixture) as an oil, R_f 0.32 (5% methanol in EtOAc); $[\alpha]_D^{20}$ −7.4 (*c* 3.54 in $CHCl_3$) (Found: C, 74.1; H, 7.60; P, 8.7%; M^+, 354.1750. $C_{22}H_{27}PO_2$ requires C, 74.5; H, 7.70; P, 8.7%; *M*, 354.1748); $\nu_{max}(CHCl_3)/cm^{-1}$ 3331 (OH), 1621 (C=C), 1438 (P–Ph) and 1171 (P=O); δ_H(400 MHz, $CDCl_3$) 7.8–7.6 (4 H, m), 7.5–7.3 (6 H, m, Ph_2PO), 6.22 (1 H, d, $^2J_{PH}$ 25.7, PCH), 3.88 (1 H, d, *J* 3.9, C*H*OH), 3.29 (1 H, br s, OH) and 2.0–1.0 (14 H, m); δ_C(100 MHz, $CDCl_3$) 164.5$^-$ (PCH=C^Z), 135–128 (m, Ph_2PO), 116.3$^+$ (d, $^1J_{PC}$ 103.7, PCH), 81.3$^+$ (d, $^3J_{PC}$ 15.9, CHOH), 40.8$^+$, 30.2$^-$, 27.0$^-$, 26.3$^-$, 26.2$^-$, 25.9$^-$ and 16.7$^+$ (d, $^3J_{PC}$ 7.6, Me); *m*/*z* 354.2 (50%, MH^+) and 202.1 (100, Ph_2POH). Integration of the 500 MHz ^{1}H NMR spectrum of the Mosher's ester of this material showed it to have 84% ee.

(2*R*,3*S*)-1-Diphenylphosphinoyl-2,3-bis(trimethylsilyloxy)butane 21

Triethylamine (72 μl, 0.53 mmol) and chlorotrimethylsilane (0.10, 0.38 mmol) were added dropwise to a stirred solution of (2*R*,3*S*)-1-diphenylphosphinoylbutane-2,3-diol **16a** (156 mg, 0.53 mmol) in dry THF (3 cm^3) at 20 °C. The reaction was stirred for 1 h under argon and was quenched with saturated aqueous ammonium chloride solution (5 cm^3). The layers were separated and were extracted with dichloromethane (3 × 5 cm^3), washed with brine (5 cm^3), dried ($MgSO_4$) and were evaporated under reduced pressure to give a crude product. Flash chromatography, eluting with 2:1 EtOAc–hexane, gave the *disilyl ether* **21** (147 mg, 63%) as needles, mp 85–87 °C (from hexane–EtOAc); R_f 0.61 (EtOAc); $[\alpha]_D^{20}$ −3.7 (*c* 1.0 in $CHCl_3$) (Found: M^+, 434.1861. $C_{22}H_{35}PO_3Si_2$ requires *M*, 434.1870); $\nu_{max}(CHCl_3)/cm^{-1}$ 1437 (P–Ph) and 1179 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.3 (10 H, m, Ph_2PO), 4.2 (1 H, dddd, *J* 3, 5, 8 and $^3J_{PH}$ 12, PCH_2CH), 3.8 (1 H, ddq, $^4J_{PH}$ 2, *J* 5 and 6, $MeCHOSiMe_3$), 2.65 (1 H, ddd, *J* 3, $^2J_{PH}$ 13 and $^2J_{HH}$ 15, PCH_AH_B), 2.4 (1 H, ddd, *J* 8, $^2J_{PH}$ 9 and $^2J_{HH}$ 15, PCH_AH_B), 1.1 (3 H, d, *J* 6, Me), 0.1 (9 H, s, $SiMe_3$) and −0.1 (9 H, s, $SiMe_3$);

δ_C(63 MHz, $CDCl_3$) 135–128 (m, Ph_2PO), 70.3–70.1 (m, 2 × $COSiMe_3$), 30.3$^-$ (d, $^1J_{PC}$ 73, PCH_2), 16.5$^+$ (Me), 0.2$^+$ ($SiMe_3$) and 0.1$^+$ ($SiMe_3$); *m*/*z* 434 (15%, M^+), 317.1 (100, M − $MeCHOSiMe_3$) and 73.0 (95, $OSiMe_3$). Integration of the 400 MHz ^{1}H NMR spectrum of this material in the presence of Pirkle's shift reagent showed it to have 18% ee.

(*S*)-(*E*)-4-Diphenylphosphinoylbut-3-en-2-yl trimethylsilyl ether 22

n-Butyllithium (3.6 cm^3 of a 1.35 mol dm^{-3} solution in hexanes, 4.8 mmol) was added to a stirred solution of diisopropylamine (490 mg, 4.8 mmol) in dry THF (5 cm^3) at 0 °C. After 30 min, this solution was added by cannula to a stirred solution of (2*R*,3*S*)-1-diphenylphosphinoyl-2,3-bis(trimethylsilyloxy)-butane **21** (1.0 g, 2.3 mmol) in dry THF (15 cm^3) at −78 °C. After 1 h, the reaction mixture was quenched with water, extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 2:1 EtOAc–hexane, to give the *vinyl phosphine oxide* **22** (575 mg, 73%, 98:2 *E*:*Z*) as an oil, R_f 0.73 (EtOAc); $[\alpha]_D^{20}$ +1.4 (*c* 0.7 in $CHCl_3$; 18% ee) (Found: M^+, 344.1345. $C_{19}H_{25}O_2PSi$ requires *M*, 344.1355); ν_{max}($CHCl_3$)/cm^{-1} 1636 (C=C), 1438 (P–Ph) and 1186 (P=O); δ_H(250 MHz, $CDCl_3$) 7.7–7.4 (10 H, m, Ph_2PO), 6.75 (1 H, ddd, *J* 3.0, 16.5 and $^3J_{PH}$ 20.0, PCH=C*H*), 6.45 (1 H, ddd, *J* 2.0, 16.5 and $^2J_{PH}$ 25.0, PCH), 4.5 (1 H, m, CHOSi), 1.25 (3 H, d, *J* 7.0, Me) and 0.10 (9 H, s, $SiMe_3$); δ_C(63 MHz, $CDCl_3$) 154.9$^+$ (PCH=*C*H), 133–128 (m, Ph_2PO), 119.3$^+$ (d, $^1J_{PC}$ 102, PCH), 68.7$^+$ (d, $^3J_{PC}$ 16, CHOSi), 23.4$^+$ (Me) and 0.0$^+$ ($SiMe_3$); *m*/*z* 344.1 (44%, M^+), 229.1 (100, M − $MeCHOSiMe_3CH_2$), 201.0 (95, Ph_2PO) and 77 (68, Ph).

(*R*)-(*E*)-4-Diphenylphosphinoyl-1-triisopropylsilyloxybut-3-en-2-ol 25

2,6-Lutidine (0.29 cm^3, 1.60 mmol) and triisopropylsilyl trifluoromethanesulfonate (0.21 cm^3, 0.80 mmol) were added dropwise to a stirred solution of the alcohol **24** (164.55 mg, 0.57 mmol) in dry dichloromethane (1 cm^3) at 0 °C under nitrogen. After 2 h at 0 °C, the solution was allowed to warm to room temperature, and was stirred for a further 18 h. Water (10 cm^3) and dichloromethane were added, the layers separated, and the aqueous layer extracted into dichloromethane (×3). The combined organic fractions were dried ($MgSO_4$), evaporated under reduced pressure, and purifed by flash chromatography, eluting with 3:1 hexane–EtOAc and then EtOAc, to yield the *silyl ether* **25** (99.5 mg, 77%) as an oil, R_F (EtOAc) 0.42; ν_{max}($CDCl_3$)/cm^{-1} 3550 (OH), 1435 (PPh) and 1175 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.4 (10 H, m, Ph_2PO), 6.9–6.6 (2 H, m, CH=CH), 4.42 (1 H, m, C*H*OH), 3.85 (1 H, dd, *J* 9.8 and 4.1, CH_AH_B-OSi), 3.59 (1 H, dd, *J* 9.8 and 6.9, CH_AH_BOSi), 3.7 (1 H, br s, OH) and 1.2–1.0 (21 H, m, Me_2CH × 3); δ_C(100 MHz, $CDCl_3$) 149.7$^+$ ($^2J_{PC}$ 8.0, PC=*C*H), 132–128 (Ph_2PO), 126.7$^+$ ($^1J_{PC}$ 114, PC), 72.5$^+$ ($^3J_{PC}$ 15.5, CHOH), 66.3$^-$ (CH_2OSi), 17.9$^+$ (CHMe_2 × 3), 13.0$^+$ ($^2J_{PC}$ 9.6, PC*Me*) and 11.8$^+$ (Me_2CH × 3); *m*/*z* 401 (100%, M − Me_2CH), 202 (20, Ph_2POH) and 201 (49, Ph_2PO).

(*R*)-(*E*)-1-Diphenylphosphinoylhept-1-en-3-yl *tert*-butyldimethylsilyl ether 29a

2,6-Lutidine (206 mg, 1.93 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (338 mg, 1.28 mmol) were added dropwise to a stirred solution of (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-ol **18c** in dry dichloromethane (3 cm^3) at 0 °C. After 16 h, the reaction mixture was diluted with water, extracted with dichloromethane (3 × 10 cm^3), and the combined organics were washed with hydrochloric acid (1.0 mol dm^{-3}, 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 1:1 EtOAc–hexane, to yield the *silyl ether* **29a** (261 mg, 95%) as an oil, R_f 0.49 (EtOAc); $[\alpha]_D^{20}$ −1.0 (*c* 0.38 in $CHCl_3$; 76% ee) (Found: M^+, 428.2301. $C_{25}H_{37}O_2PSi$ requires *M*, 428.2300); ν_{max}($CHCl_3$)/cm^{-1} 1653 (C=C), 1437 (P–Ph) and 1156 (P=O); δ_H(250 MHz, $CDCl_3$) 7.8–7.4 (10 H, m, Ph_2PO), 6.76 (1 H, ddd, *J* 3.7, 16.7 and $^3J_{PH}$ 20.5, PCH=C*H*), 6.47 (1 H, ddd, *J* 1.6, 16.7 and $^2J_{PH}$ 25.8, PCH), 4.34 (1 H, m, CHOSi), 1.7–1.3 (6 H, m), 0.88 (9 H, s, t-Bu), 0.87 (3 H, t, *J* 7.0, Me), 0.04 (3 H, s, SiMe) and −0.03 (3 H, s, SiMe); δ_C(63 MHz, $CDCl_3$) 154.4$^+$ (PCH=*C*H), 134–129 (m, Ph_2PO), 119.9$^+$ (d, $^1J_{PC}$ 103, PCH), 72.7$^+$ (d, $^3J_{PC}$ 15.8, CHOSi), 36.9$^-$, 27.1$^-$, 25.8$^+$ (t-Bu), 22.6$^-$, 18.2$^-$ (t-Bu), 14.0$^+$ (Me), −4.7$^+$ (s, SiMe) and −4.9$^+$ (s, SiMe); *m*/*z* 428.1 (30%, M^+) and 371 (M − Bu).

(*S*)-(*E*)-3-Diphenylphosphinoyl-1-phenylprop-2-en-1-yl *tert*-butyldimethylsilyl ether 29b

By the general method described above, 2,6-lutidine (410 mg, 3.88 mmol), *tert*-butyldimethylsilyl trifluoromethanesulfonate (683 mg, 2.59 mmol) and (*S*)-(*E*)-1-phenyl-3-diphenylphosphinoylprop-2-en-1-ol **18d** gave a crude product which was purified by flash chromatography, eluting with 1:1 EtOAc–hexane and EtOAc, to yield the *silyl ether* **29b** (189 mg, 32%) as minute needles, mp 125–127 °C (from EtOAc–hexane); R_f 0.49 (EtOAc); $[\alpha]_D^{20}$ −62.5 (*c* 0.5 in $CHCl_3$; 86% ee) (Found: C, 72.0; H, 7.15; P, 6.9%; M^+, 448.1974. $C_{27}H_{33}O_2PSi$ requires C, 72.3; H, 7.40; P, 6.9%; *M*, 448.1987); ν_{max}($CHCl_3$)/cm^{-1} 1625 (C=C), 1437 (P–Ph) and 1174 (P=O); δ_H(250 MHz, $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 6.82 (1 H, ddd, *J* 3.5, 16.7 and $^3J_{PH}$ 19.2, PCH=C*H*), 6.67 (1 H, ddd, *J* 2.6, 16.7 and $^2J_{PH}$ 24.4, PCH), 5.36 (1 H, m, CHOSi), 0.87 (9 H, s, ^{t}Bu), 0.03 (3 H, s, SiMe) and −0.08 (3 H, s, SiMe); δ_C(63 MHz, $CDCl_3$) 153.5$^+$ (PCH=*C*H), 141.4$^-$ (*ipso*-Ph), 134-129 (m, Ph_2PO and remaining Ph), 119.5$^+$ (d, $^1J_{PC}$ 102, PCH), 75.2$^+$ (d, $^3J_{PC}$ 17.0, CHOSi), 25.7$^+$ (^{t}Bu), 18.2$^-$ (^{t}Bu), −4.9$^+$ (SiMe) and −5.0$^+$ (SiMe); *m*/*z* 448.2 (35%, M^+) and 391.1 (100, M − Bu).

Also obtained was the *silyl enol ether* **31** (340 mg, 58%) as an oil, R_f 0.35 (EtOAc) (Found: M^+, 448.1974. $C_{27}H_{33}O_2PSi$ requires *M*, 448.1987); ν_{max}($CHCl_3$)/cm^{-1} 1646 (C=C), 1437 (P–Ph) and 1173 (P=O); δ_H(250 MHz, $CDCl_3$) 8.0–7.2 (15 H, m, Ph_2PO and Ph), 5.19 (1 H, q, *J* 7.5, CH=C), 3.26 (2 H, dd, *J* 7.5 and $^2J_{PH}$ 15.5, PCH_2), 0.93 (9 H, s, ^{t}Bu) and −0.11 (6 H, s, $SiMe_2$); δ_C(63 MHz, $CDCl_3$) 152.7$^+$ (d, $^3J_{PC}$ 12.6, CH=*C*), 138–126 (m, Ph_2PO and Ph), 99.8$^+$ (d, $^2J_{PC}$ 7.6, C*H*=C), 30.1$^-$ (d, $^1J_{PC}$ 67, PCH_2), 25.8$^+$ (^{t}Bu), 18.2$^-$ (^{t}Bu) and −4.0$^+$ ($SiMe_2$); *m*/*z* 448.2 (2%, M^+) and 201.0 (65, Ph_2PO).

(*S*)-(*E*)-3-Diphenylphosphinoyl-1-phenylprop-2-en-1-yl *tert*-butyldimethylsilyl ether 29b

(*S*)-(*E*)-1-Phenyl-3-diphenylphosphinoylprop-2-en-1-ol **18d** (321 mg, 0.96 mmol), *tert*-butyldimethylsilyl chloride (171 mg, 1.14 mmol) and imidazole (113 mg, 2.4 mmol) were stirred in dimethylformamide (2 cm^3) for 48 h. The reaction mixture was quenched with water (10 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product which was purified by flash chromatography, eluting with 1:1 EtOAc–hexane, to give the *silyl ether* **29b** (445 mg, >99%) as minute needles, mp 125–127 °C (from EtOAc–hexane), spectroscopically identical to that obtained previously.

(*S*)-(*E*)-3-Diphenylphosphinoyl-1-phenylprop-2-en-1-yl methoxymethyl ether 30b

Methoxymethyl chloride (1.41 ml of a 4.2 mol dm^{-3} solution, 5.90 mmol) and Hünig's base (775 mg, 6.83 mmol) were added dropwise to a solution of (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-ol **18d** (500 mg, 1.50 mmol) in dry dichloromethane (40 cm^3) at 0 °C. The solution was stirred for 1 h,

allowed to warm to room temperature, stirred for a further 15 h, quenched with saturated sodium carbonate (50 cm^3), extracted with dichloromethane (3 × 50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with EtOAc, to give the *methoxymethyl ether* **30b** (580 mg, >99%) as an oil, R_f 0.41 (EtOAc); $[\alpha]_D^{20}$ −72.4 (*c* 0.50 in $CHCl_3$; 86% ee) (Found: M^+, 378.1386. $C_{23}H_{23}O_3P$ requires *M*, 378.1385); $\nu_{max}(CHCl_3)/cm^{-1}$ 1635 (C=C), 1437 (P–Ph) and 1174 (P=O); δ_H(200 MHz, $CDCl_3$) 7.6–7.2 (15 H, m, Ph_2PO and Ph), 6.81 (1 H, ddd, *J* 4.3, 16.9 and $^3J_{PH}$ 19.5, PCH=C*H*), 6.62 (1 H, ddd, *J* 1.5, 16.9 and $^2J_{PH}$ 24.4, PCH), 5.29 (1 H, m, PhC*H*), 4.63 (2 H, AB quartet, OCH_2O) and 3.33 (3 H, s, OMe); δ_C(50 MHz, $CDCl_3$) 150.5^+ (PCH=*C*H), 138.5^- (*ipso*-Ph), 132–127 (m, Ph_2PO), 124.4^+ (d, $^1J_{PC}$ 100, PCH), 94.1^- (OCH_2O), 77.6^+ (d, $^3J_{PC}$ 16, PhC*H*) and 55.7^+ (OMe); *m*/*z* 378.1 (40, M^+) and 201.0 (100, Ph_2PO).

(*R*)-(*E*)-1-Diphenylphosphinoylhept-1-en-3-yl methoxymethyl ether 30a

By the general method described above, (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-ol **18c** (634 mg, 2.0 mmol) gave a crude product. Flash chromatography, eluting with EtOAc, gave the *methoxymethyl ether* **30a** (729 mg, >99%) as a waxy unrecrystallisable solid, R_f 0.47 (EtOAc); $[\alpha]_D^{20}$ +2.8 (*c* 0.43 in $CHCl_3$; 76% ee) (Found: M^+, 358.1690. $C_{21}H_{27}O_3P$ requires *M*, 358.1698); $\nu_{max}(CHCl_3)/cm^{-1}$ 1602 (C=C), 1437 (P–Ph) and 1171 (P=O); δ_H(200 MHz, $CDCl_3$) 7.8–7.3 (10 H, m, Ph_2PO), 6.66 (1 H, ddd, *J* 5.2, 14.5 and $^3J_{PH}$ 17.0, PCH=C*H*), 6.43 (1 H, dd, *J* 17.1 and $^2J_{PH}$ 24.1, PCH), 4.70 (2 H, AB quartet, OCH_2O), 4.23 (1 H, m, BuC*H*), 3.32 (3 H, s, OMe), 1.58 (2 H, m), 1.32 (4 H, m) and 0.88 (3 H, t, *J* 7.0, Me); δ_C(50 MHz, $CDCl_3$) 151.6^+ (PCH=*C*H), 133–127 (m, Ph_2PO), 122.3^+ (d, $^1J_{PC}$ 101, PCH), 95.0^- (OCH_2O), 77.0^+ (d, $^3J_{PC}$ 16.8, BuC*H*), 55.7^+ (OMe), 34.6^-, 27.3^-, 22.5^- and 13.9^+ (Me); *m*/*z* 358.1 (10%, M^+), 329.2 (60, M − Et), 313.1 (55, M − CH_2OMe) and 201.0 (100, Ph_2PO).

Attempted benzylation of alcohol 18d

p-Methoxybenzyl chloride (231 mg, 1.5 mmol) was added dropwise to a solution of, (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-ol **18d** (323 mg, 0.97 mmol), sodium hydride (47 mg, 60% dispersion in oil, 1.2 mmol) and tetrabutylammonium iodide (10 mg) in dry THF (15 cm^3). The reaction mixture was stirred for 30 min, quenched with water (15 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 3:1 EtOAc–hexane to EtOAc, to give the *ketone* **32** (119 mg, 28%) as an oil, R_f 0.50 (EtOAc) (Found: M^+, 454.1700. $C_{29}H_{27}PO_3$ requires *M*, 454.1697); $\nu_{max}(CHCl_3)/cm^{-1}$ 1679 (C=O) and 1438 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.2 (15 H, m, Ph_2PO and Ph), 6.98 (2 H, d, *J* 8.5, Ar), 6.71 (2 H, d, *J* 8.5, Ar), 4.21 (1 H, m, PCH_2CH), 3.71 (3 H, MeO), 3.05 (1 H, dd, *J* 7.0 and 13.6, $ArCH_AH_B$), 2.94 (1 H, td, 8.3 and 17.1, PCH_AH_B), 2.77 (1 H, dd, *J* 7.0 and 13.6, $ArCH_AH_B$) and 2.44 (1 H, ddd, *J* 4.4, 12.3 and 15.2, PCH_AH_B); δ_C(100 MHz, $CDCl_3$) 201.7^- (d, $^3J_{PC}$ 4.9, C=O), 158.3^- (*ipso*-Ph), 136–128 (m, Ph_2PO and remaining Ph and Ar), 113.9^+ (Ar), 55.2^+ (OMe), 41.5^+ (d, $^2J_{PC}$ 1.4, PCH_2CH), 39.2^- (d, $^3J_{PC}$ 9.5, $ArCH_2$) and 31.7^- (d, $^1J_{PC}$ 70.4, PCH_2); *m*/*z* 454.2 (40%, M^+), 349.1 (95, PhCO) and 216.1 (100, Ph_2POMe).

Also obtained was the *phenyl ketone* **33** (169 mg, 52%) as an oil, R_f 0.21 (EtOAc) (Found: M^+, 334.1123. $C_{21}H_{19}O_2P$ requires *M*, 334.1123); $\nu_{max}(CHCl_3)/cm^{-1}$ 1685 (C=O), 1435 (P–Ph) and 1176 (P=O); δ_H(400 MHz, $CDCl_3$) 8.0–7.4 (15 H, m, Ph_2PO and Ph), 3.28 (2 H, *AA′*BB′ m) and 2.78 (2 H, AA′*BB′* m); δ_C(63 MHz, $CDCl_3$) 197.8^- (C=O), 135–127 (m, Ph_2PO and Ph), 30.7^- (CH_2CO) and 23.7^- (d, $^1J_{PC}$ 74, PCH_2); *m*/*z* 334.1 (80%, M^+), 306.1 (90), 201.1 (90, Ph_2PO), 105 (100, PhCO) and 77 (90, Ph).

(*R*)-1-Diphenylphosphinoylheptan-3-ol 36a

(*R*)-(*E*)-1-Diphenylphosphinoylhept-1-en-3-ol **18c** (734 mg, 2.32 mmol) in dry THF (5 cm^3) was added by cannula to a stirred suspension of lithium aluminium hydride (208 mg, 5.5 mmol) in dry THF (20 cm^3) at 0 °C. The reaction was stirred for 5 min, quenched carefully with water, extracted with dichloromethane (3 × 10 cm^3), and the combined organic extracts dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 5% methanol in EtOAc, to give the γ-*hydroxyphosphine oxide* **36a** (650 mg, 88%) as needles, mp 111–113 °C (from EtOAc–hexane); R_f 0.15 (EtOAc); $[\alpha]_D^{20}$ −9.8 (*c* 0.25 in $CHCl_3$; 76% ee) (Found: C, 72.4; H, 7.80; P, 9.7%; M^+ − H, 315.1498. $C_{29}H_{25}O_2P$ requires C, 72.1; H, 7.95; P, 9.8%; *M* − H, 315.1514); $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (OH), 1438 (P–Ph) and 1171 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.4 (10 H, m, Ph_2PO), 3.65 (1 H, m, C*H*OH), 2.6–2.3 (2 H, m, PCH_2), 2.2–1.2 (8 H, m) and 0.86 (3 H, t, *J* 7.3, Me); δ_C(100 MHz, $CDCl_3$) 134–127 (m, Ph_2PO), 71.4^+ (d, $^3J_{PC}$ 9.5, CHOH), 37.0^-, 29.5^-, 27.9^-, 26.3^- (d, $^1J_{PC}$ 72, PCH_2), 22.6^- and 14.1^+ (Me); *m*/*z* 315.1 (10%, M^+ − H), 298.1 (55, M − H_2O), 259 (100, M − Bu) and 202.0 (80, Ph_2POH).

(*S*)-3-Diphenylphosphinoyl-1-phenylpropan-1-ol 36b

By the general method described above, (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-ol **18d** (498 mg, 1.49 mmol) gave a crude product which was purified by flash chromatography, eluting with 6% methanol in EtOAc, to give the *hydroxyphosphine oxide* **36b** (434 mg, 87%) as needles, mp 127–129 °C (from EtOAc–hexane); R_f 0.13 (EtOAc); $[\alpha]_D^{20}$ −11.7 (*c* 0.71 in $CHCl_3$; 86% ee) (Found: C, 75.3; H, 6.30; P, 9.1%; M^+ − H, 336.1275. $C_{21}H_{31}O_2P$ requires C, 75.0; H, 6.30; P, 9.2%; *M* − H, 336.1279); ν_{max}(Nujol)/cm^{-1} 3301 (OH), 1438 (P–Ph) and 1171 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.7–7.0 (15 H, m, Ph_2PO and Ph), 4.97 (1 H, d, *J* 6, OH), 4.58 (1 H, m, C*H*OH), 2.23 (2H, m, PCH_2) and 1.85 (2 H, m, CH_2); δ_C(100 MHz, $CDCl_3$) 144.2^- (*ipso*-Ph), 134–127 (m, Ph_2PO and remaining Ph), 73.0^+ (d, $^3J_{PC}$ 12.4, CHOH), 30.9^- (d, $^2J_{PC}$ 2.5, CH_2) and 25.5^- (d, $^1J_{PC}$ 71.8, PCH_2); *m*/*z* 336.1 (50%, M^+) and 202.0 (100, Ph_2POH).

(2*R*,3*R*)- and (2*S*,3*R*)-1-Diphenylphosphinoyl-2-methylheptan-3-ol *anti*- and *syn*-37b

By the general method described above, (*R*)-(*E*)-1-diphenylphosphinoyl-2-methylhept-1-en-3-ol **18e** (407 mg, 1.24 mmol) gave a crude product which was purified by flash chromatography, eluting with 8% methanol in EtOAc, to give the *hydroxy phosphine oxides* **37b** (337 mg, 83%, *anti*:*syn* 59:41 mixture) as an oil, $[\alpha]_D^{20}$ +0.3 (*c* 1.13 in $CHCl_3$; 74% ee), spectroscopically identical to those obtained previously.

(1*R*,2*R*)- and (1*R*,2*S*)-1-Cyclohexyl-3-diphenylphosphinoyl-2-methylpropan-1-ol *anti*- and *syn*-37d

By the general method described above, (*R*)-(*E*)-1-cyclohexyl-3-diphenylphosphinoyl-2-methylprop-2-en-1-ol **18f** (348 mg, 0.98 mmol) gave a crude product which was purified by flash chromatography, eluting with 2% methanol in EtOAc, to give the *hydroxy phosphine oxides* **37d** (294 mg, 85%, *anti*:*syn* 61:39 mixture) as an oil, R_f 0.38 (8% methanol in EtOAc); $[\alpha]_D^{20}$ −4.1 (*c* 1.49 in $CHCl_3$; 84% ee) (Found: M^+ − H, 355.1833. $C_{22}H_{29}PO_2$ requires *M* − H, 355.1827); $\nu_{max}(CHCl_3)/cm^{-1}$ 3348 (OH), 1438 (P–Ph) and 1159 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.7 (4 H, m), 7.55–7.35 (6 H, m, Ph_2PO), 3.79 (1 H, d, *J* 6.1, OH^{maj}), 3.35 (1 H, m, C*H*OH^{maj} and OH^{min}), 3.06 (1 H, q, *J* 5.0, C*H*OH^{min}), 2.65–1.0 (14 H, m), 0.99 (3 H, d, *J* 6.8, Me^{min}) and

0.90 (3 H, d, *J* 6.1, Me^{maj}); δ_C(100 MHz, $CDCl_3$) 134.5–128.5 (m, Ph_2PO), 80.4$^+$ (d, $^3J_{PC}$ 6.9, $CHOH^{maj}$), 77.4$^+$ (d, $^3J_{PC}$ 7.0, $CHOH^{min}$), 40.5$^+$ (min), 40.3$^+$ (maj), 34.5$^-$ (d, $^1J_{PC}$ 69.8, PCH_2^{maj}), 32.8$^-$ (d, $^1J_{PC}$ 70.5, PCH_2^{min}), 32–25 (m), 19.9$^+$ (d, $^3J_{PC}$ 4.4, Me^{min}) and 14.2$^+$ (d, $^3J_{PC}$ 10.2, Me^{maj}); *m*/*z* 355.2 (2%, $M^+ - H$), 338.2 ($M^+ - H_2O$) and 202.1 (Ph_2PO).

(2*R*,3*R*)- and (2*R*,3*S*)-4-Diphenylphosphinoyl-3-methylbutan-2-ol *anti*- and *syn*-37a

Methyllithium (14.3 cm^3 of a 1.4 mol dm^{-3} solution in ether, 20 mmol) was added to a stirred suspension of copper(I) iodide (1.27 g, 6.7 mmol) in dry ether (30 cm^3) at 20 °C. (*R*)-(*E*)-4-Diphenylphosphinoylbut-3-en-2-ol **18a** (397 mg, 1.45 mmol) was added to the reaction which was refluxed for 7 days, quenched with saturated ammonia solution (20 cm^3) and saturated ammonium chloride solution (20 cm^3), extracted with dichloromethane (4 × 20 cm^3), and the combined organic extracts washed with brine (2 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product. Analysis of the 400 MHz ^{1}H NMR spectrum of the crude product revealed it to be a 62:38 mixture of *anti*- and *syn*-**37a**. Purification by flash chromatography, eluting with EtOAc, gave the hydroxyphosphine oxides *anti*- and *syn*-**37a** (250 mg, 60%, *anti*:*syn* 63:37) as an oil, R_f 0.22 (EtOAc); $[\alpha]_D^{20}$ −1.6 (*c* 0.25 in $CHCl_3$; 46% ee); ν_{max}($CHCl_3$)/cm^{-1} 3348 (OH), 1438 (P–Ph) and 1162 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.4 (10 H, m, Ph_2PO), 4.10 (1 H, br s, $OH^{anti\ +\ syn}$), 3.82 (1 H, m, C*H*OH^{syn}), 3.58 (1 H, quintet, *J* 6.2, C*H*OH^{anti}), 2.6–1.2 (3 H, m), 1.15 (3 H, d, *J* 6.2, Me^{anti}), 1.13 (3 H, d, *J* 6.3, Me^{syn}), 0.95 (3 H, t, *J* 6.8, Me^{anti}) and 0.93 (3 H, t, *J* 6.8, Me^{syn}); δ_C(100 MHz, $CDCl_3$) 134–128 (m, Ph_2PO), 72.2$^+$ (d, $^3J_{PC}$ 6.7, $CHOH^{anti}$), 69.9$^+$ (d, $^3J_{PC}$ 6.0, $CHOH^{syn}$), 36.5$^+$ (d, $^2J_{PC}$ 3.7, *C*HMe^{anti}), 35.1$^+$ (d, $^2J_{PC}$ 3.7, *C*HMe^{syn}), 34.2$^-$ (d, $^1J_{PC}$ 70.0, PCH_2^{anti}), 32.1$^-$ (d, $^1J_{PC}$ 70.1, PCH_2^{syn}), 21.2$^+$ (Me^{anti}), 19.3$^+$ (d, $^3J_{PC}$ 7.6, Me^{anti}), 18.1$^+$ (Me^{syn}) and 17.8$^+$ (d, $^3J_{PC}$ 10.3, Me^{syn}); *m*/*z* 289.1 (40%, MH^+), 288.1 (10, M^+), 215.1 (70, $M^+ - C_4H_9O$) and 202.1 (100, Ph_2POH).

(1*S*,2*R*)-3-Diphenylphosphinoyl-2-methyl-1-phenylpropan-1-ol *anti*-37c

By the general method described above, copper(I) iodide (12.1 g, 64 mmol), methyllithium (136 cm^3 of a 1.4 mol dm^{-3} solution in ether, 190 mmol) and (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-ol **18d** (4.05 g, 12.1 mmol) gave a crude product after 3 days. Analysis of the 400 MHz ^{1}H NMR spectrum of the crude product revealed it to be a 30:52:18 mixture of ketone **32**, *anti*- and *syn*-**37c**. Purification by flash chromatography, eluting with EtOAc, recrystallisation from EtOAc, and HPLC separation, eluting with 1.5% methanol in chloroform gave the *hydroxy phosphine oxide anti*-**37c** (0.89 g, 22%), t_r 21 min; R_f 0.27 (EtOAc); $[\alpha]_D^{20}$ −17.1 (*c* 0.82 in $CHCl_3$; 86% ee) (Found: C, 75.3; H, 6.60; P, 8.9%; M^+, 350.1434. $C_{22}H_{23}O_2P$ requires C, 75.4; H, 6.65; P, 8.8%; *M*, 350.1436); ν_{max}($CHCl_3$)/cm^{-1} 3447 (OH) and 1423 (P–Ph); δ_H(200 MHz, $CDCl_3$) 7.8–7.1 (15 H, m, Ph_2PO and Ph), 4.67 (1 H, br s, OH), 4.42 (1 H, d, *J* 6.7, C*H*OH), 2.68 (1 H, m, C*H*Me), 2.05 (2 H, m, PCH_2) and 0.88 (3 H, d, *J* 6.7, Me); δ_C(50 MHz, $CDCl_3$) 143.6$^-$ (*ipso*-Ph), 136–126 (m, Ph_2PO and remaining Ph), 78.9$^+$ (d, $^3J_{PC}$ 7.8, CHOH), 36.4$^+$ (*C*HMe), 32.5$^-$ (d, $^1J_{PC}$ 70.2, PCH_2), and 19.3$^+$ (d, $^3J_{PC}$ 5.1, Me); *m*/*z* 350.1 (10%, M^+) and 202.0 (100, Ph_2POH).

Also obtained was (1*S*,2*S*)-3-diphenylphosphinoyl-2-methyl-1-phenylpropan-1-ol *syn*-**37c** (378 mg, 10%) as an oil, t_r 20 min; R_f 0.27 (EtOAc); $[\alpha]_D^{20}$ −12.3 (*c* 0.83 in $CHCl_3$; 86% ee) (Found: M^+, 350.1425. $C_{22}H_{23}O_2P$ requires *M*, 350.1436); ν_{max}($CHCl_3$)/cm^{-1} 3450 (OH) and 1423 (P–Ph); δ_H(200 MHz, $CDCl_3$) 7.9–7.1 (15 H, m, Ph_2PO and Ph), 4.81 (1 H, dd, *J* 3.6 and 5.3, C*H*OH), 4.67 (1 H, d, *J* 5.3, OH), 2.51 (1 H, ddd, *J* 7.4, $^2J_{PH}$ 13.0 and $^2J_{HH}$ 15.2, PCH_AH_B), 2.37 (1 H, m, C*H*Me), 2.09 (1 H, ddd, *J* 7.4, 9.7 and $^2J_{HH}$ 15.2, PCH_AH_B) and 0.89 (3 H, d, *J* 6.8, Me); δ_C(50 MHz, $CDCl_3$) 142.3$^-$ (*ipso*-Ph), 136–126 (m, Ph_2PO and remaining Ph), 76.2$^+$ (d, $^3J_{PC}$ 9.5, CHOH), 35.6$^+$ (d, $^2J_{PC}$ 2.6, *C*HMe), 32.6$^-$ (d, $^1J_{PC}$ 69.5, PCH_2), and 17.2$^+$ (d, $^3J_{PC}$ 9.1, Me); *m*/*z* 350.1 (40%, M^+), 332.1 (50, $M - H_2O$) and 202.0 (100, Ph_2POH).

(2*R*,3*R*)-1-Diphenylphosphinoyl-2-methylheptan-3-ol *anti*-37b

By the general method described above, copper(I) iodide (6.0 g, 32 mmol), methyllithium (68 cm^3 of a 1.4 mol dm^{-3} solution in ether, 95 mmol) and (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-ol **18c** (2.14 g, 6.8 mmol) with preparation of the reagent at 20 °C and reaction for 7 days in refluxing ether gave a crude product. Analysis of the 400 MHz ^{1}H NMR spectrum of the crude product revealed it to be a 78:22 mixture of *anti*- and *syn*-**37b**. Purification by flash chromatography, eluting with 2% methanol in EtOAc, and by HPLC, eluting with 1.5% methanol in chloroform, gave the *hydroxy phosphine oxide anti*-**37b** (868 mg, 41%) as an oil, t_r 17 min; R_f 0.32 (EtOAc); $[\alpha]_D^{20}$ +7.4 (*c* 0.73 in $CHCl_3$; 76% ee) (Found: MH^+, 331.1825. $C_{20}H_{27}O_2P$ requires *M*H, 331.1824); ν_{max}($CHCl_3$)/cm^{-1} 3442 (OH), 1422 (P–Ph) and 1217 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.4 (10 H, m, Ph_2PO), 3.81 (1 H, br s, OH), 3.34 (1 H, m, C*H*OH), 2.55 (1 H, ddd, *J* 5.5, $^2J_{PH}$ 12.2 and $^2J_{HH}$ 15.4, PCH_AH_B), 2.20 (1 H, ddd, *J* 6.3, $^2J_{PH}$ 10.7 and $^2J_{HH}$ 15.4, PCH_AH_B), 1.96 (1 H, m, C*H*Me), 1.6–1.3 (6 H, m), 0.95 (3 H, d, *J* 6.8, Me) and 0.85 (3 H, t, *J* 6.8, Me); δ_C(100 MHz, $CDCl_3$) 134–128 (m, Ph_2PO), 75.9$^+$ (d, $^3J_{PC}$ 6.9, CHOH), 34.8$^+$ (d, $^2J_{PC}$ 3.5, *C*HMe), 34.5$^-$, 33.4$^-$ (d, $^1J_{PC}$ 70.2, PCH_2), 28.6$^-$, 22.8$^-$, 19.4$^+$ (d, $^3J_{PC}$ 6.7, Me) and 14.1$^+$ (Me); *m*/*z* 331.1 (35%, MH^+), 273 (85, M − Bu) and 202.0 (100, Ph_2POH).

Also obtained was (2*S*,3*R*)-1-diphenylphosphinoyl-2-methylheptan-3-ol *syn*-**37b** (370 mg, 22%) as an oil, t_r 16 min; R_f 0.32 (EtOAc); $[\alpha]_D^{20}$ −1.2 (*c* 0.89 in $CHCl_3$; 76% ee) (Found: $M^+ - H$, 329.1693. $C_{20}H_{27}O_2P$ requires $M - H$, 329.1671); ν_{max}($CHCl_3$)/cm^{-1} 3450 (OH), 1423 (P–Ph) and 1208 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.8–7.4 (10 H, m, Ph_2PO), 3.87 (1 H, br s, OH), 3.58 (1 H, m, C*H*OH), 2.53 (1 H, ddd, *J* 7.8, $^2J_{PH}$ 14.0 and $^2J_{HH}$ 15.0, PCH_AH_B), 2.22 (1 H, ddd, *J* 5.8, $^2J_{PH}$ 9.1 and $^2J_{HH}$ 15.0, PCH_AH_B), 2.09 (1 H, m, C*H*Me), 1.5–1.2 (6 H, m), 0.91 (3 H, d, *J* 6.8, Me) and 0.82 (3 H, t, *J* 6.8, Me); δ_C(100 MHz, $CDCl_3$) 134–128 (m, Ph_2PO), 73.8$^+$ (d, $^3J_{PC}$ 5.0, CHOH), 34.4$^+$ (d, $^2J_{PC}$ 3.3, *C*HMe), 33.2$^-$ (d, $^1J_{PC}$ 70.0, PCH_2), 32.5$^-$, 28.6$^-$, 22.7$^-$, 17.0$^+$ (d, $^3J_{PC}$ 10.7, Me) and 14.1$^+$ (Me); *m*/*z* 329.1 (10%, $M^+ - H$), 312.2 (50, $M - H_2O$) and 202.0 (100, Ph_2POH).

Addition of $Me_2(CN)CuLi_2$ to vinyl phosphine oxide 18c in ether

By the general method described above, copper(I) cyanide (1.51 g, 7.9 mmol), methyllithium (17.1 cm^3 of a 1.4 mol dm^{-3} solution in ether, 23.9 mmol) and (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-ol **18c** (500 mg, 1.59 mmol) with preparation of the reagent at 20 °C and reaction for 3 days in refluxing ether gave a crude product. Analysis of the 400 MHz ^{1}H NMR spectrum of the crude product revealed it to be a 19:63:18 mixture of starting material, *anti*- and *syn*-**37b**.

(*R*)-(*E*)-1-Diphenylphosphinoyl-1-(trimethylsilyl)hept-1-en-3-yl methoxymethyl ether 40

LDA (6.0 cm^3 of a 0.2 mol dm^{-3} solution in THF, 1.2 mmol) was added dropwise to a solution of (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-yl methoxymethyl ether **30a** (363 mg, 1.01 mmol) and chlorotrimethylsilane (437 mg, 4.0 mmol) in dry THF (10 cm^3) at −78 °C. The reaction mixture was stirred for 2 h, quenched with water (10 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated to give a crude product which was purified by flash chromatography, eluting with 3:1 EtOAc–hexane, to give the *α-silyl vinyl phosphine oxide* **40** (310 mg, 71%) as an oil, R_f 0.55 (EtOAc); $[\alpha]_D^{20}$

+5.1 (*c* 0.51 in $CHCl_3$; 76% ee); $\nu_{max}(CHCl_3)/cm^{-1}$ 1440 (P–Ph) and 1177 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.4 (10 H, m, Ph_2PO), 6.22 (1 H, dd, *J* 9.1 and $^3J_{PH}$ 33.0, PC=CH), 4.61 (1 H, d, *J* 6.9, OCH_AH_BO), 4.55 (1 H, *J* 6.9, OCH_AH_BO), 4.41 (1 H, m, BuC*H*), 1.5–1.2 (6 H, m), 0.89 (3 H, t, *J* 6.9, Me) and 0.18 (9 H, s, $SiMe_3$); δ_C(100 MHz, $CDCl_3$) 161.8^+ (PC=*C*H), 132–128 (m, Ph_2PO), 116^- (d, $^1J_{PC}$ 101, PC), 94.8^- (OCH_2O), 76.7^+ (Bu*C*H), 55.5^+ (OMe), 34.9^-, 27.6^-, 22.6^-, 14.0^+ (Me) and 1.3^+ ($SiMe_3$).

Attempted addition of Fleming's silyl cuprate to vinyl phosphine oxide 18c

Dimethylphenylsilyllithium[10] (2.3 cm^3 of a 1.3 mol dm^{-3} solution in THF, 3.07 mmol) was added dropwise to a stirred suspension of copper(I) cyanide (138 mg, 1.53 mmol) in dry THF (10 cm^3) at 0 °C and the reaction stirred for 40 min. (*R*)-(*E*)-1-Diphenylphosphinoylhept-1-en-3-ol **18c** was added to the reaction mixture which was stirred overnight at room temperature, diluted with saturated ammonia solution (20 cm^3) and saturated ammonium chloride solution (20 cm^3), extracted with dichloromethane (4 × 20 cm^3), the combined organic extracts washed with brine (20 cm^3) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 2:1 EtOAc–hexane, to yield the allylic phosphine oxides (*E*)- and (*Z*)-**41** (71 mg, 76%, 83:27 mixture) as an oil, δ_H(400 MHz, $CDCl_3$) 7.9–7.3 (10 H, m, Ph_2PO), 5.5 (2H, m, $CH{=}CH^{E+Z}$), 3.30 (2 H, dd, *J* 7.6 and $^2J_{PH}$ 14.7, PCH_2^Z), 3.05 (2 H, dd, *J* 6 and $^2J_{PH}$ 14.0, PCH_2^E), 1.95 (2 H, m), 1.25 (4 H, m) and 0.85 (3 H, t, *J* 7.0, Me). The *E* isomer was spectroscopically identical to that reported previously.[15b]

(2*R*,3*R*)- and (2*S*,3*R*)-2-(Dimethylphenylsilyl)-1-diphenylphosphinoylheptan-3-yl *tert*-butyldimethylsilyl ether *anti*- and *syn*-42a

By the general method described above, (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-yl *tert*-butyldimethylsilyl ether **29a** (106 mg, 0.25 mmol), copper(I) cyanide (100 mg, 1.16 mmol) and dimethylphenylsilyllithium (1.7 cm^3 of a 1.3 mol dm^{-3} solution in THF, 2.2 mmol) gave a crude product which was purified by flash chromatography, eluting with 3:1 hexane–EtOAc, to yield the *silyl phosphine oxides anti*- and *syn*-**42a** (117 mg, 84%, 70:30 mixture) as an oil, R_f 0.13 (4:1 hexane–EtOAc); $[\alpha]_D^{20}$ +0.6 (*c* 0.36 in $CHCl_3$; 76% ee) (Found: M^+, 564.3020. $C_{33}H_{49}O_2PSi_2$ requires *M*, 564.3009); $\nu_{max}(CHCl_3)/cm^{-1}$ 1437 (P–Ph) and 1169 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.6–7.2 (15 H, m, Ph_2PO and SiPh), 4.36 (1 H, m, $CHOSi^{anti}$), 3.61 (1 H, t, *J* 4.5, $CHOSi^{syn}$), 2.44 (1 H, td, *J* 11.6 and 14.4, H^{anti}), 2.12–1.0 (m), 0.90 (9 H, s, $^tBu^{syn}$), 0.84 (9 H, s, $^tBu^{anti}$), 0.40, 0.39, 0.38, 0.26 (SiMe), 0.04 (2 × SiMe), 0.02 and −0.16 (SiMe); *m*/*z* 564.3 (20%, M^+) 507.2 (100, M − ^{t}Bu) and 135.1 (100, $PhMe_2Si$).

(1*R*,2*R*)-2-(Dimethylphenylsilyl)-3-diphenylphosphinoyl-1-phenylprop-1-yl *tert*-butyldimethylsilyl ether *anti*-42b

By the general method described above, (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-yl *tert*-butyldimethylsilyl ether **29b** (117 mg, 0.26 mmol), copper(I) cyanide (100 mg, 1.12 mmol) and dimethylphenylsilyllithium (1.7 cm^3 of a 1.3 mol dm^{-3} solution in THF, 2.2 mmol), with addition of **29b** at −78 °C and stirring for 2 h gradually warming to room temperature gave a crude product which was purified by flash chromatography, eluting with 3:1 hexane–EtOAc, to yield the *silyl phosphine oxide anti*-**42b** (88 mg, 58%) as an oil, R_f 0.39 (3:2 hexane–EtOAc); δ_H(400 MHz, $CDCl_3$) 7.6–7.0 (20 H, m, Ph_2PO, Ph and SiPh), 5.84 (d, *J* 4.7, CHOSi), 2.25 (1 H, ddd, *J* 12.1, 13.0 and $^2J_{HH}$ 15.7, PCH_AH_B), 2.08 (1 H, ddd, *J* 2.6, 7.9 and $^2J_{HH}$ 15.7, PCH_AH_B), 1.73 (1 H, dddd, *J* 2.6, 4.7, 11.9 and 16.2, CHSi), 0.85 (9 H, s, ^{t}Bu), 0.55, −0.09, −0.11 and −0.26 (4 × SiMe). This compound decomposed on standing to the (*E*)-allylic phosphine oxide **44**.[15b]

(1*R*,2*R*)-2-(Dimethylphenylsilyl)-3-Diphenylphosphinoyl-1-phenylpropyl methoxymethyl ether *anti*-43

By the general method described above, (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-yl methoxymethyl ether **30b** (2.25 g, 5.8 mmol), copper(I) cyanide (1.92 mg, 21.5 mmol) and dimethylphenylsilyllithium (23.6 cm^3 of a 1.7 mol dm^{-3} solution in THF, 42.5 mmol), with addition of **30b** at −78 °C and stirring for 16 h gradually warming to room temperature, gave a crude product which was purified by flash chromatography, eluting with 1:1 hexane–EtOAc, to yield the *silyl phosphine oxide anti*-**43** (2.18 g, 71%; *anti*:*syn* 88:12) as an oil, R_f 0.58 (EtOAc); $[\alpha]_D^{20}$ −15.9 (*c* 1.54 in $CHCl_3$) (Found: M^+, 514.2096. $C_{31}H_{35}O_3PSi$ requires *M*, 514.2093); $\nu_{max}(CHCl_3)/cm^{-1}$ 1437 (P–Ph) and 1176 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.1 (20 H, m, Ph_2PO, Ph and SiPh), 5.41 (1 H, br s, $CHOMOM^{syn}$), 4.88 (1 H, d, *J* 6.3, $CHOMOM^{anti}$), 4.63 (1 H, d, $^2J_{HH}$ 6.2, $OCH_AH_BO^{syn}$), 4.52 (1 H, d, $^2J_{HH}$ 6.2, $OCH_AH_BO^{syn}$), 4.22 (2 H, s, OCH_2O^{anti}), 3.37 (3 H, s, OMe^{syn}), 3.16 (3 H, s, OMe^{anti}), 2.7–1.8 (2 H, $m^{syn\,+\,anti}$), 0.38 (3 H, s, $SiMe_AMe_B^{syn}$), 0.32 (3 H, s, $SiMe_AMe_B^{anti}$), 0.09 (3 H, s, $SiMe_AMe_B^{anti}$) and −0.04 (3 H, s, $SiMe_AMe_B^{syn}$); δ_C(100 MHz, $CDCl_3$) 142.6^- (*ipso*-Ph^{syn}), 140.9^- (*ipso*-Ph^{anti}), 138.9^- (*ipso*-Ph^{syn}), 138.4^- (*ipso*-Ph^{anti}), 132–126 (m, Ph_2PO, Ph and SiPh), 96.3^- (OCH_2O^{syn}), 94.7^- (OCH_2O^{anti}), 81.5^+ ($CHOMOM^{syn}$), 79.5^+ ($CHOMOM^{anti}$), 56.4^+ (OMe^{syn}), 56.0^+ (OMe^{anti}), 29.8^+ ($CHSi^{syn}$), 28.1^+ ($CHSi^{anti}$), 27.5^- (d, $^1J_{PC}$ 67, PCH_2^{syn}), 26.4^- (d, $^1J_{PC}$ 67, PCH_2^{anti}), -1.9^+ ($SiMe_AMe_B^{syn}$), -2.3^+ ($SiMe_AMe_B^{anti}$), -1.9^+ ($SiMe_AMe_B^{syn}$) and -4.2^+ ($SiMe_AMe_B^{anti}$); *m*/*z* 514.2 (2%, M^+), 469.2 (70, M − $MeOCH_2$) and 201 (100, Ph_2PO).

(1*R*,2*R*)-2-Dimethylphenylsilyl-3-diphenylphosphinoyl-1-phenylpropyl methoxymethyl ether *anti*-43

By the general method described above, (*S*)-(*E*)-3-diphenylphosphinoyl-1-phenylprop-2-en-1-yl methoxymethyl ether **30b** (200 mg, 0.53 mmol), copper(I) cyanide (196 mg, 2.2 mmol) and dimethylphenylsilyllithium (1.8 cm^3 of a 1.3 mol dm^{-3} solution in THF, 3.3 mmol), with addition of **30b** at −78 °C and stirring for 3 h then gradually warming to room temperature gave a crude product which was purified by flash chromatography, eluting with 1:1 hexane–EtOAc, to yield the *silyl phosphine oxides anti*- and *syn*-**43** (110 mg, 41%; 66:34 mixture) as an oil, spectroscopically identical to that obtained previously.

Treatment of silyl ether *anti*-43 with acidic methanol

Concentrated hydrochloric acid (9 drops) was added to a solution of *anti*-**43** (401 mg, 0.77 mmol, *anti*:*syn* 88:12) in dry methanol (8 cm^3). The reaction mixture was refluxed for 1.5 h, quenched with water (10 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 5% methanol in EtOAc, to give the allylic phosphine oxides **44** (201 mg, 82%, *E*:*Z* 86:14 mixture) as needles, mp 171–172 °C (from EtOAc–hexane), spectroscopically identical to that obtained previously.[15b]

(2*S*,3*S*)- and (2*S*,3*R*)-4-Diphenylphosphinoyl-3-phenylsulfanylbutan-2-yl trimethylsilyl ether *anti*- and *syn*-47

A solution of thiophenol (33 mg, 0.30 mmol) and sodium hydride (6 mg, 60% dispersion in oil, 0.15 mmol) in dry THF (2 cm^3) was added by cannula to a stirred solution of (*S*)-(*E*)-4-diphenylphosphinoylbut-3-en-2-yl trimethylsilyl ether **22** (52 mg, 0.15 mmol) in dry THF (3 cm^3) at room temperature. The reaction mixture was refluxed for 14 h, quenched with water (5 cm^3), extracted with dichloromethane (3 × 5 cm^3), and the combined organic extracts washed with saturated sodium

bicarbonate (5 cm^3), saturated ammonium chloride (5 cm^3) and brine (5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to yield the *sulfides anti-* and *syn*-**47** (34 mg, 45%; 64:36 mixture of diastereomers) as an oil, R_f 0.50 (EtOAc); $[\alpha]_D^{20}$ +2.3 (*c* 0.35 in $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1438 (P–Ph) and 1171 (P=O); δ_H(400 MHz, $CDCl_3$) 7.8–7.1 (15 H, m, Ph_2PO and SPh), 4.25 (1 H, m, $CHOSi^{maj+min}$), 3.50 (1 H, dtd, $^3J_{PH}$ 2.5, *J* 7 and 11.4, PhSCH^{min}), 3.41 (1 H, dtd, $^3J_{PH}$ 4.0, *J* 7.0 and 11.4, PhSCH^{maj}), 2.96 (1 H, ddd, *J* 7.0, $^2J_{PH}$ 12.9 and $^2J_{HH}$ 15.5, PC$H_AH_B^{maj}$), 2.67 (1 H, ddd, *J* 7, $^2J_{PH}$ 12.9 and $^2J_{HH}$ 15.5, PC$H_AH_B^{min}$), 2.54 (1 H, ddd, *J* 7, $^2J_{PH}$ 8.6 and $^2J_{HH}$ 15.5, PC$H_AH_B^{min}$), 2.41 (1 H, ddd, *J* 7, $^2J_{PH}$ 9.4 and $^2J_{HH}$ 15.5, PC$H_AH_B^{maj}$), 1.27 (3 H, d, *J* 6.2, Me^{maj}), 1.27 (3 H, d, 6.3, Me^{min}), 0.03 (9 H, s, $SiMe_3^{min}$) and 0.00 (9 H, s, $SiMe_3^{maj}$).

(*R*)-(*E*)-1-Diphenylphosphinoyl-3-[(*N*-benzylcarbamoyl)oxy]-hept-1-ene 48

Triethylamine (130 mg, 1.28 mmol) and benzyl isocyanate (128 mg, 0.96 mmol) were added dropwise to a stirred solution of (*R*)-(*E*)-1-diphenylphosphinoylhept-1-en-3-ol **18c** (100 mg, 0.32 mmol) in dry dichloromethane (3 cm^3). After stirring for 2 days, the reaction was quenched with saturated ammonium chloride (5 cm^3), the aqueous suspension extracted with dichloromethane (3 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 3:2 EtOAc–hexane, to yield the *urethane* **48** (96 mg, 65%) as needles, mp 110–111 °C (from EtOAc–hexane); R_f 0.51 (EtOAc); $[\alpha]_D^{20}$ −25.3 (*c* 0.26 in $CHCl_3$; 76% ee); $\nu_{max}(CHCl_3)/cm^{-1}$ 3448 (NH), 1720 (C=O), 1437 (P–Ph) and 1176 (P=O); δ_H(400 MHz, $CDCl_3$) 7.9–7.1 (15 H, m, Ph_2PO and Ph), 6.67 (1 H, ddd, *J* 4.6, 17.1 and $^3J_{PH}$ 21.6, PCH=C*H*), 6.39 (1 H, dd, *J* 17.1 and $^2J_{PH}$ 23.5, PC*H*), 5.36 (2 H, m, NH and CHO), 4.37 (2 H, s, PhCH_AH_B), 1.61 (2 H, m), 1.31 (4 H, m) and 0.86 (3 H, t, *J* 6.8, Me); δ_C(100 MHz, $CDCl_3$) 155.7$^-$ (C=O), 149.7$^+$ (PCH=*C*H), 138.4$^-$ (*ipso*-Ph), 133–126 (15 H, m, Ph_2PO and Ph), 121.7$^+$ (d, $^1J_{PC}$ 101, P*C*H), 74.2$^+$ (d, $^3J_{PC}$ 16.8, *C*HOCO), 44.9$^-$ (Ph*C*H_2), 33.6$^-$, 27.0$^-$, 22.3$^-$ and 13.8$^+$ (Me); *m*/*z* 447.2 (5%, M^+), 313 (70, BnNHCO) and 106 (100, BnNH) (Found: C, 72.5; H, 6.75; N, 3.1%; M^+, 447.1976. $C_{27}H_{30}NO_3P$ requires C, 72.3; H, 6.95; N, 3.1%; *M*, 447.1963).

(4*S*,5*R*)-3-Benzyl-5-butyl-4-(diphenylphosphinoylmethyl)oxazolidin-2-one *anti*-49

Sodium hydride (7 mg, 60% dispersion in oil, 0.17 mmol) and (*R*)-(*E*)-1-diphenylphosphinoyl-3-[(*N*-benzylcarbamoyl)oxy]-hept-1-ene **48** (62 mg, 0.14 mmol) were dissolved in dimethylformamide (1 cm^3) at 0 °C. The reaction mixture was stirred for 3 h, the DMF removed using an oil pump, the residue diluted with saturated ammonium chloride (5 cm^3) and the aqueous suspension extracted with dichloromethane (3 × 5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product. Flash chromatography, eluting with 3:1 EtOAc–hexane gave the oxazolidinone **49** (53 mg, 86%, 88:12 mixture of diasteromers) as an oil, R_f 0.58 (EtOAc); $[\alpha]_D^{20}$ +7.0 (*c* 0.81 in $CHCl_3$; 76% ee) (Found: M^+, 447.1974. $C_{27}H_{30}NO_3P$ requires *M*, 447.1963); $\nu_{max}(CHCl_3)/cm^{-1}$ 1739 (C=O), 1423 (P–Ph) and 1176 (P=O); δ_H(400 MHz, $CDCl_3$) 7.7–7.0 (15 H, m, Ph_2PO and Ph), 4.72 (1 H, d, $^2J_{HH}$ 15.1, CH_AH_BN), 4.47 (1 H, dt, *J* 3.6 and 7.6, CHO), 4.07 (1 H, d, $^2J_{HH}$ 15.1, CH_AH_BN), 3.45 (1 H, m, CHN), 2.57 (1 H, dt, *J* 1.8 and 13.6, PCH_AH_B), 2.38 (1 H, td, *J* 9.9 and 14.6, PCH_AH_B), 1.48 (1 H, m), 1.37 (1 H, m), 1.16 (4 H, m) and 0.79 (3 H, t, *J* 6.6, Me); δ_C(100 MHz, $CDCl_3$) 154.4$^-$ (C=O), 135.7$^-$ (*ipso*-Ph), 133–126 (m, Ph_2PO and remaining Ph), 79.9$^+$ (s, CHO), 55.1$^+$ (CHN), 46.0$^-$ ($PhCH_2$), 34.1$^-$, 32.6$^-$ (d, $^1J_{PC}$ 67, PCH_2), 26.4$^-$, 22.2$^-$ and 13.9$^+$ (Me); *m*/*z* 447.2 (60%, M^+) and 202 (100, Ph_2POH).

(2*RS*,3*SR*,4*SR*)-4-Diphenylphosphinoyl-3,4-epoxypentan-2-ol *syn*-50

Lithium *tert*-butyl peroxide (1.61 cm^3 of a 0.23 M solution in THF, 0.37 mmol) was added to a stirred solution of the vinyl phosphine oxide **28** (71.0 mg, 0.248 mmol) in dry THF (2 cm^3) at 0 °C under nitrogen. The mixture was cooled to −10 °C and stirred for 18 h. Water and dichloromethane were added, and the layers were separated. The aqueous layer was extracted into dichloromethane (2 × 3 cm^3), and the combined organic fractions were dried ($MgSO_4$), evaporated under reduced pressure and purifed by flash chromatography, eluting with 3:1 EtOAc–hexane, to yield the *epoxide syn*-**50** (59.6 mg, 79%) as an oil (Found: M − Me, 287.0838. $C_{17}H_{19}O_3P$ requires *M* − Me, 287.0838); R_F (EtOAc) 0.19; ν_{max}(film)/cm^{-1} 3100–3600 (OH), 1440 (PPh) and 1130 (P=O); δ_H(250 MHz, $CDCl_3$) 8.0–7.3 (10 H, m, Ph_2PO), 3.71 (1 H, dq, *J* 7.6 and 5.2, C*H*OH), 2.68 (1 H, dd, *J* 7.7 and 6.4), 2.2 (1 H, br s, OH), 1.54 (3 H, d, *J* 10.6, PCMe) and 1.24 (3 H, d, *J* 6.4, *Me*CHOH); δ_C(100 MHz, $CDCl_3$) 132–127 (Ph_2PO), 66.5$^+$ (CHOH), 62.7$^+$ (HOCH-*C*HO), 58.3$^-$ ($^1J_{PC}$ 101.6, PC), 19.3$^+$ (*Me*CHOH) and 13.1$^+$ ($^2J_{PC}$ 13.6, PC*Me*); *m*/*z* 287 (1%, M − Me), 257 (38, M − MeCHOH), 219 (40, $Ph_2PO_2H_2$), 202 (86, Ph_2POH) and 201 (100, Ph_2PO).

(2*S*,3*R*,4*R*)- and (2*S*,3*S*,4*S*)-4-Diphenylphosphinoyl-3,4-epoxy-1-triisopropylsilyloxybutan-2-ol 51

By the general method described above, the vinyl phosphine oxide **25** (87.4 mg, 0.197 mmol) gave, after 18 h at −10 °C, and after purifcation by flash chromatography, eluting with 3:1 EtOAc−hexane, a 57:43 (by ^{1}H NMR) mixture of two diastereomers *(2S,3R,4R)- and (2S,3S,4S)-4-diphenylphosphinoyl-3,4-epoxy-1-triisopropylsilyloxybutan-2-ol syn-* and *anti*-**51** (63.4 mg, 69%) as an oil, R_F (EtOAc) 0.49; δ_H(250 MHz, $CDCl_3$) 7.9–7.3 (10 H, m, Ph_2PO), 3.9–3.6 (4 H, m, CH_2O, PCHO and C*H*OH), 3.21 (1 H, m, OCH_2CHO) and 1.0–0.9 (21 H, m, $^iPr_3Si$).

(1′*R*)-*N*-Benzyl-*N*-(1′-phenylethyl)-2-diphenylphosphinoyl-1-phenylethylamine 53a

Chlorotrimethylsilane (0.63 cm^3, 5.0 mmol) was added to a stirred solution of the vinyl phosphine oxide **9a** (304 mg, 1.0 mmol) in dry THF (15 cm^3) at −78 °C. In a separate vessel, butyllithium (1.4 mol dm^{-3} solution in hexanes; 2.5 cm^3, 3.5 mmol) was added to a stirred solution of Davies's amine (738 mg, 3.5 mmol) in dry THF (6 cm^3) and the solution of the amide was added slowly to the phosphine oxide at −78 °C by cannula. The reaction was stirred at −78 °C, warmed up to room temperature over 17 h, quenched by addition of water (15 cm^3), extracted with dichloromethane (3 × 15 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product. The crude product was dissolved in dry THF (5 cm^3) and tetra-*n*-butylammonium fluoride (1.0 mol dm^{-3}; 6 cm^3, 6 mmol) was added, the reaction stirred for 1 h, quenched with water (10 cm^3), extracted with dichloromethane (3 × 10 cm^3), dried ($MgSO_4$) and evaporated to give a crude product which was purified by column chromatography, eluting with 1:1 hexane–EtOAc, to give the *amine* **53a** (334 mg, 65%) as a colourless oil, R_F (EtOAc) 0.53; $[\alpha]_D^{20}$ +43.0 (*c* 1.4 in $CHCl_3$) (Found: C, 80.1; H, 7.0; N, 3.1%; MH^+, 516.2488. $C_{35}H_{35}NOP$ requires C, 81.5; H, 6.6; N, 2.7%; MH^+, 516.2456); $\nu_{max}(CHCl_3)/cm^{-1}$ 1179 (P=O) and 1438 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.01–7.42 (25 H, m, Ph), 4.45 (1 H, ddd, *J* 2.9, 8.8 and 10.9, CHN), 3.96 (1 H, q, *J* 6.8, C*H*Me), 3.80 (1 H, d, *J* 15.0, NCH_2), 3.68 (1 H, d, *J* 15.0, NCH_2), 2.78 (1 H, dt, *J* 3.0 and 14.9, Ph_2POCH_2), 2.56 (1 H, ddd, *J* 8.9, 11.0 and 14.9, Ph_2POCH_2), 1.22 (3 H, d, *J* 6.8, Me); δ_C(100 MHz, $CDCl_3$) 150.0$^-$, 144.5$^-$, 142.5$^-$ (Ph), 121.4–134.3 (m, Ph), 59.0$^+$, 56.6$^+$ (*C*HMePh, *C*HPh), 50.9$^-$ (CH_2), 34.5$^-$ (d, *J* 69.0, Ph_2POCH_2), 14.2$^+$ (Me); *m*/*z* (+ve

FAB) 516 (27%, MH^+), 410 (18, M − CHMePh) and 201 (100, Ph_2PO).

(1′*R*)-*N*-Benzyl-*N*-(1′-phenylethyl)-2-diphenylphosphinoyl-1-(4-methoxyphenyl)ethylamine 53b

By the general method described above, the vinyl phosphine oxide **9b** (334 mg, 1.0 mmol) gave the *amine* **53b** (415 mg, 76%) as a colourless oil, R_F (EtOAc) 0.47; $[a]_D^{20}$ +35 (*c* 1.1 in $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1179 (P=O), 1438 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.11–7.42 (22 H, m, Ph and Ar), 6.59 (2 H, d, *J* 8.7, Ar), 4.39 (1 H, ddd, *J* 2.9, 8.0 and 11.2, CHN), 3.97 (1 H, q, *J* 6.8, C*H*Me), 3.79 (1 H, d, *J* 15.0, NCH_2), 3.71 (3 H, s, OMe), 3.64 (1 H, d, *J* 15.0, NCH_2), 2.75 (1 H, dt, *J* 3.0 and 14.9, Ph_2POCH_2), 2.48 (1 H, ddd, *J* 9.0, 11.3 and 14.9, Ph_2POCH_2), 1.23 (3 H, d, *J* 6.8, Me); δ_C(100 MHz, $CDCl_3$) 158.6$^-$ (*C*-OMe), 144.6$^-$, 142.7$^-$ (Ph), 126.4–134.9 (m, Ph, MeOPh), 113.4$^+$ (MeOPh), 58.6$^+$, 56.4$^+$ (*C*HMePh, *C*HPhOMe), 55.1$^+$ (OMe), 50.9$^-$ (CH_2), 35.1$^-$ (d, *J* 69.5, Ph_2POCH_2), 13.8$^+$ (Me); *m*/*z* (+ve FAB) 546 (11%, MH^+), 440 (9, M − CHMePh), 335 (33, M − NR_2) and 201 (100, Ph_2PO) (Found: C, 78.1; H, 6.7; N, 2.4%; MH^+, 546.2561. $C_{36}H_{37}NO_2P$ requires C, 78.4; H, 6.4; N, 2.7%; MH^+, 546.2561).

(1″*R*)-*N*-Benzyl-*N*-(1″-phenylethyl)-2-diphenylphosphinoyl-1-furan-2′-ylethylamine 53c

By the general method described above, the vinyl phosphine oxide **9c** (322 mg, 1.0 mmol) gave the *amine* **53c** (172 mg, 34%) as a colourless oil, R_F (EtOAc) 0.54; $[a]_D^{20}$ −16 (*c* 1.0 in $CHCl_3$) (Found: C, 78.2; H, 6.7; N, 3.0%; MH^+, 506.22. $C_{33}H_{33}NO_2P$ requires C, 78.4; H, 6.4; N, 2.8%; MH^+, 506.2249); $\nu_{max}(CHCl_3)/cm^{-1}$ 1187 (P=O) and 1438 (P–Ph); δ_H(400 MHz, $CDCl_3$) 7.14–7.47 (21 H, m, Ph, 4′-H), 6.14 (1 H, dd, *J* 1.8 and 3.1, 3′-H), 5.98 (1 H, d, *J* 3.1, 2′-H), 4.43 (1 H, dt, *J* 2.6 and 11.0, CHN), 4.07 (1 H, q, *J* 6.7, C*H*Me), 3.72 (1 H, d, *J* 14.4, NCH_2), 3.64 (1 H, d, *J* 14.4, NCH_2), 3.07 (1 H, td, *J* 11.2 and 14.6, Ph_2POCH_2), 2.61 (1 H, dt, *J* 2.7 and 14.6, Ph_2POCH_2) and 1.07 (3 H, d, *J* 6.7, Me); δ_C(100 MHz, $CDCl_3$) 152.9$^-$ (C-1′), 144.6$^-$, 141.4$^-$ (Ph), 126.7–133.7 (m, Ph, C-4′), 110.3$^+$, 108.6$^+$ (C-2′ and C-3′), 56.6$^+$, 50.0$^+$ (*C*HMePh, *C*HPhOMe), 50.8$^-$ (CH_2), 33.6$^-$ (d, *J* 67.5, Ph_2POCH_2) and 16.0$^+$ (Me); *m*/*z* (+ve FAB) 506 (11%, MH^+), 400 (6, M − CHMePh), 335 (8, M − NR_2) and 201 (100, Ph_2PO).

1-Benzoylamido-2-diphenylphosphinoyl-1-phenylethane 56a

The amine **53a** (515 mg, 1.0 mmol) was dissolved in glacial acetic acid (5 ml), 10% palladium on charcoal (10%) was added and the reaction was stirred vigorously under a hydrogen atmosphere (4 atm) at 50 °C for 24 h. The reaction mixture was filtered through Celite, washing with methanol, and the solution was basified with saturated sodium bicarbonate solution until the pH was greater than 8. The washings were extracted with dichloromethane (4 × 100 ml), dried over $MgSO_4$ and evaporated to give a crude product as a yellow oil, which was used for the next step without further purification. The crude product was dissolved in dry dichloromethane (2 ml), cooled to 0 °C, pyridine (89 µl, 1.1 mmol) and benzoyl chloride (139 µl, 1.2 mmol) added and the reaction mixture was stirred for 2 h at 0 °C, quenched with 3 M hydrochloric acid, extracted with dichloromethane (3 × 10 ml), dried ($MgSO_4$) and evaporated to give a crude product, which was purified by column chromatography, eluting with 1 : 1 hexane–EtOAc, to give amide **56a** (153 mg, 36%) as colourless needles, R_F (EtOAc) 0.41; $[a]_D^{20}$ +17 (*c* 1.1 in $CHCl_3$) (Found: C, 76.1; H, 5.9; N, 2.5; P, 7.6%; MH^+, 426.1623. $C_{27}H_{25}NO_2P$ requires C, 76.2; H, 5.7; N, 3.3; P, 7.3%; MH^+, 426.1623); $\nu_{max}(CHCl_3)/cm^{-1}$ 1178 (P=O), 1438 (P–Ph) and 1658 (C=O); δ_H(400 MHz, $CDCl_3$) 8.95 (1 H, d, *J* 5.6, NH), 7.98 (2 H, m, COPh), 7.06–7.79 (18 H, m, Ph), 6.40 (1 H, m, CHN) and 2.88 (2 H, m, PCH_2); δ_C(100 MHz, $CDCl_3$) 166.5$^-$ (CON), 141.9$^-$, 141.8$^-$, 125.8–133.9 (Ph), 51.1$^+$ (CHN) and 35.9$^-$ (d, *J* 66.8, CH_2); *m*/*z* (+ve FAB) 426 (45%, MH^+), 307 (65, M − NCOPh) and 201 (100, Ph_2PO).

(1*S*)-1-[(*S*)-2-Methoxy-2-phenylacetamido]-2-diphenylphosphinoyl-1-(4-methoxyphenyl)ethane *syn*-58 and (1*S*)-1-[(*R*)-2-methoxy-2-phenylacetamido]-2-diphenylphosphinoyl-1-(4-methoxyphenyl)ethane *anti*-58

The amine **53b** (350 mg, 0.64 mmol) was dissolved in 5 ml glacial acetic acid, 10% palladium on charcoal (105 mg) was added, and the solution was stirred vigorously under a hydrogen atmosphere (4 atm) at 50 °C for 30 h. The reaction mixture was filtered through Celite, washed with methanol, and was basified with saturated sodium bicarbonate solution until the pH was greater than 8. The aqueous fraction was extracted with dichloromethane (4 × 100 ml), dried over $MgSO_4$ and evaporated to give a crude product which was used for the next step without further purification. The crude product was dissolved in dichloromethane (8 ml), racemic *O*-methylmandelic acid (110 mg, 0.66 mmol) and DCC (187 mg, 0.9 mmol) were added and the reaction was stirred at room temperature for 24 h, filtered through Celite and evaporated under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 1 : 1 hexane–EtOAc to give the *amide syn*-**58** (130 mg, 30%) as a colourless oil, R_F (EtOAc) 0.38; $[a]_D$ +8.8 (*c* 3.8 in $CHCl_3$) (Found: C, 72.3; H, 6.2; N, 2.5. $C_{29}H_{30}NO_4P$ requires C, 72.1; H, 6.1; N, 2.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3404 (NH), 1673 (C=O), 1438 (P–Ph) and 1178 (P=O); δ_H(400 MHz, $CDCl_3$) 8.34 (1 H, d, *J* 6.4, NH), 7.62–7.31 (15 H, m), 7.14 (2 H, d, *J* 8.7), 6.69 (2 H, d, *J* 8.7), 5.03 (1 H, apparent qd, *J* 6 and 12, CHN), 4.5 (1H, s, C*H*OMe), 3.71 (3 H, s, OMe), 3.35 (3H, s, OMe), 2.93 (1 H, ddd, *J* 8.4, 10.4 and 19.3, CH_AH_B) and 2.68 (1 H, ddd, *J* 5.4, 10.4 and 15.2, CH_AH_B); δ_C(100 MHz, $CDCl_3$) 170.3 (C=O), 158.8, 137.2, 133.6–127.1 (m), 113.9, 83.8 (CHN), 57.3 (OMe), 55.2 (OMe), 49.6 (*C*HOMe), 36.4 and 35.7 (CH_2); *m*/*z* (EI) 499 (5%, M^+), 378 (30), 335 (90), 298 (M^+ − Ph_2PO) and 201 (100, Ph_2PO).

Also obtained was the *amide anti*-**58** (125 mg, 27%) as a colourless oil, R_F (EtOAc) 0.25; $[a]_D$ −30 (*c* 1.9 in $CHCl_3$) (Found: C, 72.3; H, 6.4; N, 2.1. $C_{29}H_{30}NO_4P$ requires C, 72.1; H, 6.1; N, 2.8%); $\nu_{max}(CHCl_3)/cm^{-1}$ 3407 (NH), 1672 (C=O), 1438 (P–Ph), 1178 (P=O); δ_H(400 MHz, $CDCl_3$) 8.30 (1 H, d, *J* 6.8, NH), 7.62–7.31 (15 H, m), 7.01 (2 H, d, *J* 8.7), 6.60 (2H, d, *J* 8.7), 5.25 (1 H, apparent qd, *J* 6 and 12, CHN), 4.53 (1 H, s, C*H*OMe), 3.77 (3 H, s, OMe), 3.41 (3 H, s, OMe), 2.93 (1 H, ddd, *J* 7.6, 10.4 and 18.0, CH_AH_B), 2.68 (1 H, ddd, *J* 5.6, 10.4 and 15.8, CH_AH_B); δ_C(100 MHz, $CDCl_3$) 170.1 (C=O), 158.7, 137.2, 133.6–127.1 (m), 113.8, 83.9 (CHN), 57.6 (OMe), 55.2 (OMe), 49.1 (*C*HOMe), 36.1 and 35.9 (CH_2); *m*/*z* (EI) 499 (5%, M^+), 378 (25), 335 (90), 298 (M^+ − Ph_2PO) and 201 (100, Ph_2PO).

(1*S*)-1-[(*S*)-2-Methoxy-2-phenylacetamido]-2-diphenylphosphinoyl-1-(4-methoxyphenyl)ethane *syn*-58

By the same method, the amine **53b** (166 mg, 0.33 mmol) and (*S*)-mandelic acid gave the amide *syn*-**58** (130 mg, 58%), spectroscopically identical to that obtained previously.

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