# Preparation of Enantiomerically Pure Phosphine Oxides by Nucleophilic Displacement Chemistry using Oxazaphospholidines

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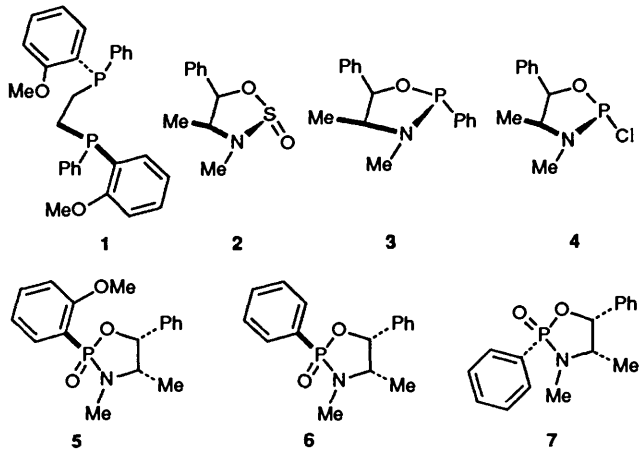
The synthesis of enantiomerically pure triaryl- and diarylvinyl-phosphine oxides from $PCl_3$ by three sequential nucleophilic displacements at phosphorus is demonstrated. A single diastereoisomer of the *P*-chlorooxazaphospholidine **4** is treated with an arylmagnesium halide to effect displacement of chloride. The major stereoisomer is formed with retention of configuration. After oxidation to the phosphine oxide with *tert*-butyl hydroperoxide, a second Grignard reaction leads to regiospecific and stereospecific P–O ring cleavage so that a second aryl group is introduced with retention of configuration. For the final step, the P–N bond is subjected to acid-catalysed methanolysis, previously shown to occur with inversion of configuration, followed by P–OMe displacement with a third arylmagnesium halide. The overall yield of triarylphosphine oxide is up to 29% for the cited five steps. Simple methoxyaryl or 2-naphthyl residues are employed to demonstrate the methodology, which permits the multigram-scale preparation of this class of compound in ⩾94% e.e. The stereochemical course of the nucleophilic displacements with arylmagnesium halides is consistent with a model in which the organomagnesium reagent is complexed to the oxo-group and attacks phosphorus *cis*-to it in a direction defined by both electronic and steric factors.

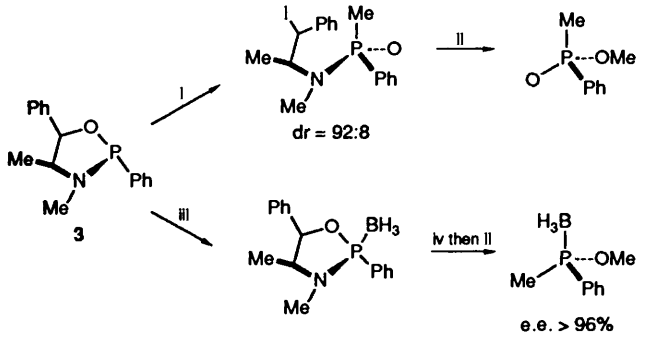
In the development of asymmetric homogeneous catalysis, the single most successful class of ligands has been *cis*-chelating diphosphines.[1] Within this class the majority of members possess a stereogenic centre, plane or axis as an intrinsic component of the P–P linking backbone. Normally the two remaining substituents at phosphorus are aryl residues (commonly $PPh_2$) although other combinations including alkylphosphines,[2] alkyl(aryl)phosphines[3] and phospholanes[4] have been utilised to good effect. The alternative approach based on phosphorus chirality is much rarer, in no small part due to the synthetic difficulty of controlling stereogenicity at phosphorus. The first effective solution to the problem of preparing enantiomerically pure phosphines was due to Mislow and coworkers;[5] the method was based on the fractional crystallisation of the diastereoisomers of *O*-menthyl methylphenylphosphinate followed by stereospecific displacement and reduction. This work led directly to the synthesis of the ligand DIPAMP {(*R*,*R*)-1,2-bis-[*o*-methoxyphenyl(phenyl)phosphino]ethane} **1** by the Monsanto group, which has on balance been the most successful of all diphosphines in its application to rhodium-complex-based asymmetric hydrogenation.[6] There have been several improvements in the overall synthesis since 1974, when the Monsanto work was first reported, the most recent method (closely related to the present work) making it easily accessible.[7] Similar routes have been utilised in the preparation of analogues[8] and homologues.[9] In other cases where *P*-chiral ligands have been utilised, the procedure has been based on resolution rather than asymmetric synthesis.[10]

At the outset of work in this area, we defined our goal as the preparation of any triaryl- or diarylalkyl-phosphine by a general procedure starting with $PCl_3$ or some other readily available reactant; this definition encompassed chelate ligands. There were already good precedents for the selected approach, which was based on the use of ephedrine as an asymmetric template for the sequential formation of three P–C bonds. In 1973 Wudl and Lee illustrated the basic principle by synthesizing enantiomerically pure sulfoxides—reaction of ephedrine with $SOCl_2$ to give the oxathiazolidines **2** which were subjected to two successive nucleophilic displacements by alkylmagnesium halides or organolithium reagents.[11] This method has




recently been refined into a practical and rather general synthesis, the main modification being the activation of the S–N bond to nucleophilic displacement by $AlMe_3$.[12] The original paper suggested (but did not test the idea) that this approach could be used to form, *inter alia*, chiral phosphine oxides—to some extent this had been anticipated by the work of Devilliers and Navech in 1970 (not cited in ref. 11)[13] whereby ephedrine and $POCl_3$ or $PSCl_3$ were shown to react, giving both the $S_P$ and $R_P$ diastereoisomers of the ensuing oxazaphospholidine oxide or sulfide. This work was further refined by Inch and coworkers[14] through a series of papers in which the stereochemistry of this family of compounds and the stereochemical course of their displacement and ring-opening reactions was established. The potential for synthesizing *P*-chiral phosphines by a route involving a diastereoisomerically pure P=O derivative was recognised early although the monosaccharide template utilised in the first example[15] gave poor chemical yields of the final product. Application of the ring-opening of oxazaphospholidines to synthesis of chiral phosphines was first developed by Jugé,[16] who utilised the chemistry outlined in Scheme 1. In the key step a diastereoisomerically pure $P^{III}$ oxazaphospholidine **3** is prepared directly from ephedrine and

undergoes stereoselective ring-opening through Arbuzov reaction with an alkyl halide; the P–O bond is regiospecifically cleaved whilst the P–N bond remains intact. Further work from the same laboratory demonstrated that phosphine–boranes[8,17] could be utilised as electrophiles in a stereospecific sequence through which one aryl and one alkyl group were introduced sequentially (Scheme 1).[7]This route provides the best practical source of the *P*-chiral diphosphine DIPAMP.




**Scheme 1** *Reagents and conditions:* i, MeI, $C_6H_6$; ii, HCl, MeOH; iii, $H_3B$-$SMe_2$; iv, MeLi, −78 °C

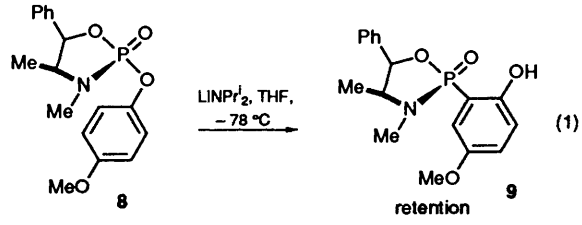
A distinctive feature of work described here is the use of three sequential nucleophilic displacements to provide the three new P–C bonds of a chiral triarylphosphine, following on from our earlier discovery of the stereospecific P–O cleavage of oxazaphospholidines with arylmagnesium halides.[18] The ultimate objective was to provide access to *P*-chiral phosphines of relevance to asymmetric catalysis, but this present paper is limited to simple syntheses which demonstrate the feasibility of a route which formally commences with $PCl_3$.

## Results and Discussion

*Formation of the First P–C Bond.*—Inch and co-workers[14] had reported that ephedrine reacts directly with $PCl_3$ to give the expected oxazaphospholidine. Thus, diastereoisomerically pure (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine **4** was prepared from $PCl_3$ and (1*R*,2*S*)-ephedrine by a modification of this method. The reaction was monitored by $^{31}P$ NMR spectroscopy which initially showed the presence of two diastereoisomers; after four hours the lower-field signal essentially disappeared, however. The isolated, reactive, low melting solid, [b.p. 160 °C (bath), 0.1 mmHg; $\delta_P$ 171] is > 98% a single diastereoisomer, assigned the structure drawn. It is stable for reasonable periods below 0 °C, but deteriorates on storage in tetrahydrofuran (THF) solution at ambient temperature.*

The reaction of compound **4** with organometallic reagents was investigated. Since the *ortho*-methoxy group plays a critical role in the functioning of the asymmetric ligand DIPAMP,[19] *o*-methoxyphenylmagnesium bromide was examined first. Reaction occurred readily in THF at low temperature. The $^{31}P$ NMR spectrum of the crude reaction mixture indicated that there were two diastereoisomers present, and on a preparative scale these were allowed to equilibrate at ambient temperature in the presence of residual magnesium halide salts before work-up, following precedent.[18,20] The product formed by this protocol was ~ 90% one compound and rather than isolate the air-sensitive material, we oxidised it directly with Bu$^t$OOH, to give *P*-oxide **5**, which was purified by flash chromatography to yield a single diastereoisomer (61%). Some traces of the second diastereoisomer were observed in the last eluted fractions. The stereochemistry was established by spectroscopic comparison with the *P*-phenyl analogue, available in both diastereoisomeric forms **6** and **7** of known absolute configuration.[21] The best guide to defining the stereochemistry by $^1H$ NMR spectroscopy lies in the 5-H signal which is consistently a *P*-coupled double doublet (*J* 3.5–5.0 Hz) in the minor diastereoisomer **7** but ostensibly a doublet lacking $^{31}P$ coupling in the major diastereoisomer. This observation is common to other related oxazaphospholidines.[21] In like manner, the reaction of compound **4** with PhMgCl proceeded to give, after oxidation, mainly the product **6** formed with retention of configuration.

It appears that the initial displacement reaction of the Grignard reagent on the phosphorus halide is selective but not stereospecific, but the isomeric products can equilibrate under the reaction conditions. A possible mechanism by which this can occur is by reversible ring-opening and reclosure induced by the halide ion present. In any event, the overall process leads to useful selectivity in a practical sense. An alternative method for introducing an *ortho*-*O*-substituted aryl group into an oxazaphospholidine has been demonstrated through the Wittig-like conversion of amidophosphate **8** into phosphonamidate **9** promoted by strong base[22] [equation (1)].



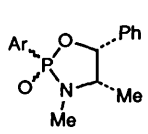
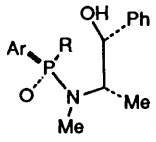
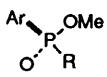

(1)

*Formation of the Second P–C Bond.*—In prior work[18] it had been demonstrated that the oxazaphospholidine **6** undergoes stereospecific ring opening on reaction with *o*-methoxyphenylmagnesium bromide in THF; the stereochemistry of the product **10** (Table 1) was established by X-ray crystallography of both reactant and product. The availability of further compounds in the series afforded an opportunity to examine the generality of this result. The *P*-epimer of **6**, compound **7**, again reacted smoothly under mild conditions with *o*-methoxyphenylmagnesium bromide in THF (−78 to 0 °C) to give a single product **11**, evidently isomeric with compound **10**. Furthermore, the *o*-methoxyphenyloxazaphospholidine oxide prepared as described above (compound **5**) reacted nearly quantitatively with PhMgCl under similar conditions to give only the diastereoisomer **11**, with no detectable quantity of diastereoisomer **10**. Compounds **10** and **11** have similar but nevertheless quite distinguishable $^1H$ NMR spectra at 500 MHz which renders their identification straightforward. The most distinctive feature is the CHN ring proton, which sits directly under the OMe-signal in the $R_P$ diastereoisomer but is upfield of it in the $S_P$-diastereoisomer. All three ring-opening reactions above must therefore proceed with retention of configuration, as had been previously noted for compound **6**.[18,20] The results are in contrast with the observations of Hall and Inch[23] who had earlier looked at the ring-opening reactions of compound **6** with MeLi or MeMgBr, and of its *P*-methyl analogue with PhLi or PhMgBr. They had failed to find a consistent pattern of selectivity, both inversion and retention being observed, with variable diastereoselectivity. The near-perfect retention of configuration in the present case is serendipitous, and provides a fortunate basis for attaining the overall goal.

A combination of the two nucleophilic displacement reactions reported here gives rapid and ready access to diastereoisomerically pure di(aryl)phosphonamides derived from ephedrine. Several analogues of compounds **8** and **9** were prepared starting either with the *o*-methoxyphenyl or phenyl precursor, as indicated in Table 1. These reactions proceeded

* See note added in proof on page 839.

**Table 1**

| Entry |  |  |  |  |
|---|---|---|---|---|
| 1 | **5** Ar = *o*-$MeOC_6H_4$; m.p. 156–157 °C $[\alpha]_D^{20}$ −44.1 (*c* 1, $CHCl_3$) | **11** R = Ph; 48%; m.p. 153 °C; $[\alpha]_D^{20}$ −30.6 (*c* 1, $CHCl_3$) | | |
| 2 | **5** | **13** R = *p*-$MeOC_6H_4$; 82%; m.p. 190–191 °C; $[\alpha]_D^{21}$ −26.1 (*c* 1.4, $CHCl_3$) | **18** 95%; m.p. 68 °C; $[\alpha]_D^{24}$ 31.0 (*c* 1.1, $CHCl_3$) | **23** 90%; oil; $[\alpha]_D^{23}$ −2.1 (*c* 1.2, $CHCl_3$) |
| 3 | **5** | **14** R = *m*-$MeOC_6H_4$; 76%; m.p. 129 °C; $[\alpha]_D^{21}$ −34.9 (*c* 1.3, $CHCl_3$) | **19** 100%; oil; $[\alpha]_D^{20}$ 8.8 (*c* 0.4, $CHCl_3$) | **24** 97%; solid; $[\alpha]_D^{24}$ −9.5 (*c* 1, $CHCl_3$) |
| 4 | **5** | **15** R = 2-naphthyl; 81%; m.p. 120 °C; $[\alpha]_D^{19}$ −18.8 (*c* 1, $CHCl_3$) | **20** 77%; m.p. 150 °C; $[\alpha]_D^{19}$ 59.7 (*c* 1.1, $CHCl_3$) | **25** 90%; oil; $[\alpha]_D^{23}$ −7.5 (*c* 0.9, $CHCl_3$) |
| 5 | **5** | **16** R = vinyl; 80%; m.p. 188–189 °C; $[\alpha]_D^{21}$ −113.5 (*c* 0.4, $CHCl_3$) | **21** 98%; oil; $[\alpha]_D^{21}$ 135.4 (*c* 1, $CHCl_3$) | |
| 6 | **6** Ar = Ph; m.p. 169–170 °C; | **10**[17,b] R = *o*-$MeOC_6H_4$; 70%, m.p. 195–197 °C; $[\alpha]_D^{20}$ −14.8 (*c* 1, $CHCl_3$) | **17**[17] 93%; oil; $[\alpha]_D^{21}$ −23.0 (*c* 1, $CHCl_3$) | |
| 7 | $[\alpha]_D^{20}$ −37.5 (*c* 1, $CHCl_3$) **6** | **12** R = vinyl; 88%, m.p. 128 °C; $[\alpha]_D^{22}$ −68.9 (*c* 1, $CHCl_3$) | **22** 93%; oil; $[\alpha]_D^{21}$ 46.8 (*c* 1, $CHCl_3$) | |
| 8 | **7**[a] Ar = Ph; m.p. 146–147 °C; $[\alpha]_D^{21}$ −54 (*c* 1, $CHCl_3$) | **11** (*o*-$MeOC_6H_4MgBr$ as reactant) | | |

[a] **7** is a $S_p$-diastereoisomer of **6**. [b] **10** is a $R_p$ diastereoisomer of **11**.

smoothly and in good yield; as far as could be ascertained by NMR examination of the crude reaction mixture, a single diastereoisomer strongly predominated in all cases. All the products are solids easily purified by crystallisation, and have chemical and spectroscopic properties consistent with the defined structure. As a corollary to the work with aryl nucleophiles, it was shown that vinylmagnesium bromide reacted readily with the oxazaphospholidines **5** and **6** to give related ring-opened products. The stereoselectivity was rather lower here (diastereoisomer ratio > 90 : < 10) and, although not proved, correspondence with the direction of arylmagnesium halide opening was assumed in the absence of further evidence.

*Formation of the Third P–C Bond.*—Further reaction to introduce a third aryl group followed literature precedent.[15,18] The phosphinamide P–N residue in the ring-opened intermediate is not easily displaced by organometallic reagents and hence has to be converted into the corresponding methylphosphinate by HCl in MeOH, before a third C–P bond can be formed. This well precedented reaction occurs with inversion of configuration, with 2–4% loss of stereochemical integrity.[18] Displacement of OMe in compound **17** by organometallic reagents occurs under significantly more forcing conditions than does the previous two *P*-alkylation steps, but is still acceptably mild and high yielding, at least when PhMgCl in THF is the reagent. In this way the examples indicated in the final column of Table 1 were obtained. The only failures observed here were with the vinylphosphonate esters, for which it is presumed that Michael addition of the Grignard reagent to the β-carbon of the vinyl group competes with the displacement step. Hence it did not prove possible to make enantiomerically pure vinyldiarylphosphine oxides, irrespective of the stage of introduction of the vinyl group. An important constraint is that organolithium reagents are much less effective than organomagnesium reagents in this methoxide-displacement step, indicating that the Lewis acidity of the nucleophilic entity is important. The reaction is envisaged as occurring *via* an intermediate in which P=O–Mg co-ordination enhances the electrophilic character of phosphorus.

The enantiomeric purity of the methylphosphinites and the phosphine oxides was estimated by using the NMR method of Kagan and co-workers[24] which exploits the diastereoisomeric complexation of chiral P=O compounds with an enantiomerically pure amide. This had been used successfully before[18] but in some of those cases the racemates were also accessible to check the method. Here it was observed for both classes of compound that addition of the shift reagent and monitoring of the OMe resonances showed the appearance of traces of a second component (2–3% in the cited cases) and often other contaminants at the same level. Where the shift experiment was checked by using the opposite hand of addend, the results were consistent with the presence of the unwanted enantiomer at that relative concentration.

## Stereochemistry of Grignard Displacement Reactions at Phosphorus

Ring-opening of oxazaphospholidines **5**–**7** reported here occurs with a consistently high degree of retention of configuration. The worst case is that of entry 5 in Table 1, where vinylmagnesium bromide effects this reaction to give the requisite

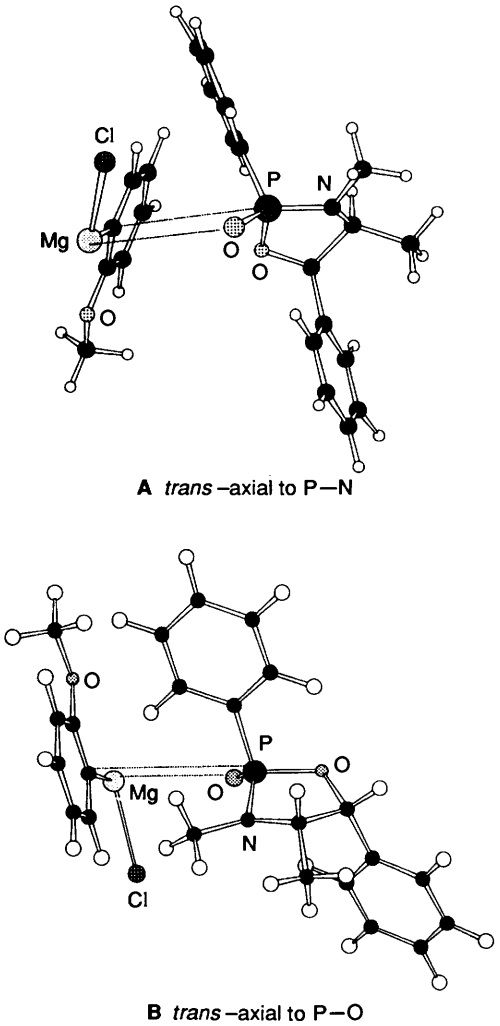


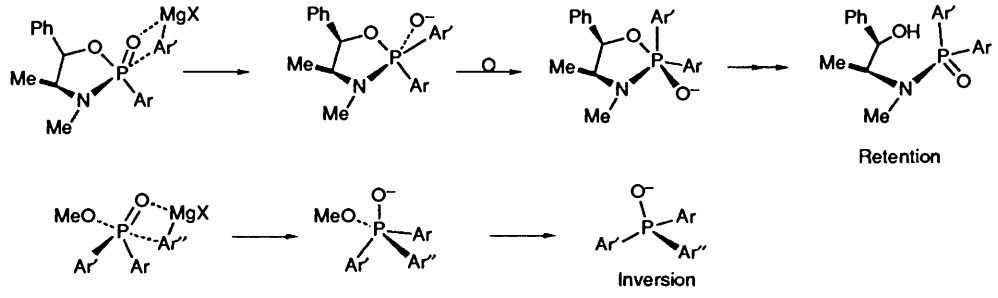

**Fig. 1** Favoured (A) and disfavoured (B) approaches of Grignard reagent to P=O, incorporating complexation of Mg to the P=O group

diastereoisomer in the ratio 91:9 to the product of inversion. In the best cases the second diastereoisomer is not detected by NMR spectroscopy (d.r. >98: <2). The displacement of methoxide by arylmagnesium halides in open-chain arylphosphinates **18–20** is in complete contrast since it occurs with essentially complete inversion of configuration, albeit under more forcing conditions than the oxazaphospholidine ring opening.

Nucleophilic displacements of X in O=PXYZ compounds have been widely discussed, particularly for phosphate esters.[25] In cases where X, Y and Z are oxygen, or there are two oxygens and a carbon, the results can be nicely rationalised in terms of stereochemical analysis of trigonal bipyramidal (TBP) 5-co-ordinate phosphorus intermediates. The experimental observations are then explained if groups enter and leave from apical positions, if the rules of apicophilicity are observed, and if 5-rings are exclusively apical–equatorial at phosphorus. Although previously discussed by ourselves and others in terms of these precepts,[18,23] we now consider that one significant factor was omitted from the previous discussion; when included, a general explanation can be offered. Under the likely reaction conditions, the P=O group is strongly co-ordinated to magnesium, evidenced by chemical-shift changes in the $^{31}P$ NMR spectrum of phosphine oxides in the presence of Grignard reagents.[26] This encourages a 4-centre mechanism, with formation of the new P–C bond along one of the three possible vectors *syn* to the P=O bond. Inspection of molecular models (Fig. 1) based on the X-ray structure of compound **6**[21] then makes the stereochemical result quite clear. Approach of the organomagnesium reagent *trans* to the existing P–aryl bond will be disfavoured because it produces an unfavourable initial intermediate with two apical P–C bonds. Approach along the stereoelectronically favourable path *trans* to endocyclic P–O is inhibited by the steric clash between the NMe group and the incoming reagent. This leaves the approach *trans* to P–N, which dominates by default as the only accessible path with acceptable stereoelectronics (Scheme 2). Once the pentaco-ordinate intermediate is formed, it must then undergo a single pseudorotation in order to place the endocyclic oxygen in an apical position prior to its cleavage. The strain inherent in the 5-membered ring (O–P–N angle 96°) ensures that only the productive pseudorotation (to the apical/equatorial [90°] rather than diequatorial [120°] 5-ring isomer) occurs, giving the product of overall retention of configuration.

The interpretation fits other observations concerning the ring opening of oxazaphospholidines with carbon nucleophiles. When the counterion is the less Lewis-acidic $Li^+$, stereochemical control is lower (according to the observations of Inch, Hall and co-workers), because the requirement for a 4-centre mechanism is not so pronounced. Likewise, when the nucleophile is smaller (MeMgBr) or the exocyclic substituent on phosphorus less bulky, the barrier to direct attack *trans* to the P–O vector leading to inversion of configuration is correspondingly less. This explains the lower diastereoselectivity of vinyl compared with arylmagnesium halides in oxazaphospholidine ring opening. In the analogous phosphine–borane ring-openings of Jugé and co-workers, the stereochemical control is high and retention of configuration is observed when organolithium reagents are used. Either there is significant association between the lithium ion and the negative end of the B–H dipole, or the stereoselectivity is governed purely by steric factors and augmented by the low reaction temperature.

For the final stage of the synthesis, displacement of methoxide from the phosphinate esters **17–21** occurs with retention of configuration, in accord with many similar observations. This has not been explained satisfactorily previously since pseudorotation pathways in 5-co-ordinate acyclic intermediates seem to permit free access to either enantiomer of the product. If the principles described above are applied here, then inversion of configuration is clearly predicted. In a 4-centre transition state,




**Scheme 2** Reaction of arylmagnesium halides with P=O compounds leading to retention in step II and inversion in step III

the oxygen of the P=O group is constrained to occupy an equatorial position in the resulting TBP intermediate. With only one electronegative group, -OR, available to reside in the apical site *trans* to the developing P–C bond, the choice is unambiguous. Loss of the OR group without any intervening pseudorotation leads to the product with inversion of configuration. This pathway is indicated in Scheme 2. Again, the necessity for employing the strongly Lewis acidic RMgX (and the chloride is more effective than the bromide in many cases) rather than RLi is apparent. Other nucleophilic displacement reactions of tetraco-ordinate phosphorus compounds involving Grignard reagents may be explained similarly, using the combination of steric and stereoelectronic arguments.[27]

*Conclusions.*—This series of reactions, which is summarised in Table 1, illustrates the ease of synthesis of triarylphosphine oxides with control of the stereochemistry at phosphorus. The chemistry requires a series of three nucleophilic displacements on an ephedrine derivative prepared directly from $PCl_3$. Future papers will extend this work to the preparation of enantiomerically pure *P*-chiral phosphines and diphosphines for their applications in homogeneous catalysis.

## Experimental

Microanalyses were performed by Mrs. V. Lambourn within the Dyson Perrins Laboratory using a Carlo Erba 1106 elemental analyser. $^1$H NMR spectra were recorded on a Varian Gemini 200 (200 MHz) or a Bruker AM 500 (500 MHz) spectrometer. $^{13}$C NMR spectra were recorded on a Bruker AM 500 (126 MHz) or a Bruker AM 250 (62.9 MHz) spectrometer as were $^{31}$P NMR and $^{11}$B NMR spectra. IR spectra were recorded on a Perkin-Elmer 781 spectrometer. *J* Values are given in Hz.

Mass spectra (*m*/*z*) were recorded by Dr. R. T. Aplin or Mr. R. Procter on a Varian MAT CH7, V.G. Micromass 16F or ZAB-1F/16F spectrometer with ammonia used as the ionising source for C.I. determination. Optical rotations were measured on a thermostatted Perkin-Elmer 241 polarimeter using the 589.3 nm D line of sodium; $[\alpha]_D$-values are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$.

M.p.s were recorded on a Köfler block and are uncorrected. All manipulations involving phosphines, Grignard and organolithium reagents were carried out under argon, using standard vacuum-line techniques, and all solvents were deoxygenated prior to use.

Flash chromatography was performed on Merck silica gel 60H, 230–300 mesh supplied by B.D.H. Solvents were purified according to standard procedures. Toluene, triethylamine and *N*-methylmorpholine were freshly distilled from $CaH_2$. Methanol was freshly distilled from magnesium, dichloromethane from $P_2O_5$; THF and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen prior to use. All solvents were obtained from either B.D.H. or Aldrich Chemical Co. Dichlorophenylphosphine, (1*R*,2*S*)-(−)-α-(1-methylaminoethyl)benzyl alcohol [(−)-ephedrine], (*S*)-(+)- or (*R*)-(−)-*N*-(3,5-dinitrobenzoyl)-α-methylbenzylamine, *tert*-butyl hydroperoxide [3.0 mol dm$^{-3}$ in 'isooctane' (2,2,4-trimethylpentane)], phenylmagnesium chloride (3.0 mol dm$^{-3}$ in THF), borane–dimethyl sulfide complex, *tert*-butyllithium (1.7 mol dm$^{-3}$ in pentane) and butyllithium (1.4 mol dm$^{-3}$ in hexane) were supplied by Aldrich. Other Grignard reagents were prepared with magnesium which had been activated by the dry-stir technique.[28] $CDCl_3$ and $C_6D_6$ were dried over 4 Å molecular sieves.

Determination of the enantiomeric purity of phosphine oxides and precursors was carried out according to the method described by Kagan[24] thus: (*R*)-(−)- or (*S*)-(+)-*N*-(3,5-dinitrobenzoyl)-α-methylbenzylamine (0.5 cm$^3$, 0.032 mmol; 0.064 mol dm$^{-3}$) in $CDCl_3$ was added to the phosphine oxide (typically 0.25 cm$^3$, 0.019 mmol; 0.076 mol dm$^{-3}$) in $CDCl_3$ contained in a 5 mm NMR tube. Its $^1$H NMR spectrum (500 MHz) was then recorded and the procedure was repeated for the opposite antipode of the chiral shift reagent.

(2R,4S,5R)-2-*Chloro*-3,4-*dimethyl*-5-*phenyl*-1,3,2-*oxazaphospholidine* **4**.—(2*R*,4*S*,5*R*)-2-Chloro-3,4-dimethyl-5-phenyl-1,3,-2-oxazaphospholidine **4** was prepared by modification of a literature procedure.[29] A solution of trichlorophosphine (4.30 cm$^3$, 47.3 mmol) in dry toluene (10 cm$^3$) was added slowly (15 min) *via* cannula to a cooled and vigorously stirred solution of (1*R*,*S*)-(−)-ephedrine (8.14 g, 47.3 mmol) and *N*-methylmorpholine (10.4 cm$^3$, 94.5 mmol) in dry toluene (250 cm$^3$) under argon. The mixture was stirred at this temperature for 1 h after which it was allowed to equilibrate to ambient temperature and was stirred overnight. The solid *N*-methylmorpholine hydrochloride was removed by standard Schlenk filtration and the solid was washed with aliquots (3 × 20 cm$^3$) of dry toluene. The combined filtrate was stripped of toluene under reduced pressure to yield (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine **4** as an oil, which was purified by Kugelrohr distillation (0.1 mmHg; 160 °C) and isolated as a solid (7.34 g, 68%) and stored under argon; $\delta_H$(500 MHz; $CDCl_3$) 0.74 (3 H, d, $J_{HH}$ 6.6, CMe), 2.73 (3 H, d, $J_{HP}$ 16.2, NMe), 3.74–3.80 (1 H, ddq, $J_{PH}$ 7.9, $J_{HH}$ 7.9, $J_{HH}$ 6.5, 4-H), 5.92 (1 H, dd, $J_{PH}$ 1.7, $J_{HH}$ 7.9, 5-H) and 7.34–7.43 (5 H, m, Ph); $\delta_P$(101 MHz; toluene) 170.3.

(2R,4S,5R)-2-(2-*Methoxyphenyl*)-3,4-*dimethyl*-5-*phenyl*-1,3,2-*oxazaphospholidine* 2-*Oxide* **5**.—To a solution of (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine **4** (7.34 g, 32.0 mmol) in vigorously stirred THF (200 cm$^3$) at −78 °C was added a solution of 2-methoxyphenylmagnesium bromide (116 cm$^3$, 35.4 mmol; 0.305 mol dm$^{-3}$ in THF) *via* cannula. The reaction mixture was allowed to equilibrate to ambient temperature over a period of 5 h, after which a portion (2 cm$^3$) was removed and stripped of solvent under reduced pressure to yield (2*R*,4*S*,5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine deoxo- **5** as an off-white solid; $\delta_H$(200 MHz; $CDCl_3$) 0.7 (3 H, d, $J_{HH}$ 6.6, CMe), 2.65 (3 H, d, $J_{HP}$ 16, NMe), 3.75 (1 H, m, 4-H), 3.9 (3 H, s, OMe), 5.52 (1 H, d, $J_{HH}$ 6.6, 5-H) and 7.2–7.5 (9 H, m); $\delta_P$(101 MHz; toluene) 138.5.

To the remaining, vigorously stirred solution was added *tert*-butyl hydroperoxide (10.7 cm$^3$, 32.0 mmol) at 0 °C and the mixture was allowed to equilibrate to ambient temperature and was stirred for 2 h, then quenched with water (100 cm$^3$) and extracted into dichloromethane (3 × 150 cm$^3$). The organics were combined, dried ($MgSO_4$), and the solvent was removed by rotary evaporation to yield (2R,4S,5R)-2-(2-*methoxyphenyl*)-3,4-*dimethyl*-5-*phenyl*-1,3,2-*oxazaphospholidine* 2-*oxide* **5** as an off-white solid. Purification by flash column chromatography ($CH_2Cl_2$–$Et_2O$; 1:1 v/v) afforded (2*R*,4*S*,5*R*)-**5** ($R_f$ 0.6) as a solid, which was recrystallised further from hot toluene to afford crystals (6.1 g, 60.2%), m.p. 156–157 °C (Found: C, 64.4; H, 6.4; N, 4.1; P, 10.0%; M$^+$, 318. $C_{17}H_{20}NO_3P$ requires C, 64.35; H, 6.35; N, 4.41; P. 9.76%; M, 317); $[\alpha]_D^{21}$ −44.1 (*c* 1, in $CHCl_3$); $\nu_{max}$(Nujol)/cm$^{-1}$ 1440s (P–Ph), 1045s (POC) and 1300s (P=O); $\delta_H$(500 MHz; $CDCl_3$) 0.85 (3 H, d, $J_{HH}$ 6.6, CMe), 2.62 (3 H, d, $J_{HP}$ 10.2, NMe), 3.85 (1 H, ddq, $J_{PH}$ 9.7, $J_{HH}$ 7.1, $J_{HH}$ 6.6, 4-H), 3.94 (3 H, s, OMe), 5.63 (1 H, dd, $J_{PH}$ = $J_{HH}$ = 7.1, 5-H), 6.96 (1 H, dd, $J_{PH}$ = $J_{3,4}$ 7.1, An, 3-H),* 7.04 (1 H, dt, $J_{PH}$ 3.0, $J_{5,6}$ 7.5, An, 5-H), 7.3–7.50 (6 H, m, Ph + An, 4-H) and 8.0 (1 H, ddd, $J_{PH}$ 14.7, $J_{5,6}$ 7.5, $J_{4,6}$ 1.8, An, 6-H); $\delta_C$(126 MHz; $CDCl_3$)

* Here, and elsewhere, An refers to the methoxyphenyl ring.

15.30 (s, 4-Me), 28.60 (d, $J_{PC}$ 6.0, NMe), 55.70 (s, OMe), 58.60 (d, $J_{PC}$ 12.0, C-4), 82.2 (s, C-5), 110.9 (d, $J_{PC}$ 8.1, An, C-5), 118.0 (d, $J_{PC}$ 120.0, An, C-1), 120.7 (d, $J_{PC}$ 13.8, An, C-6), 126.7 (s, PhC-3, -5), 128.0 (s, PhC-4), 128.2 (s, PhC-2, -6), 133.9 (s, AnC-4), 136.3 (d, $J_{PC}$ 6.1, AnC-3), 137.1 (s, PPhC-1) and 160.9 (s, AnC-2); $\delta_P$(101 MHz; $CDCl_3$) 31.0; *m/z* (C.I.) 318 (M + 1, 100%).

($S_P$)-(−)-N-[(1S,2R)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*-N-*methyl*-P-(2-*methoxyphenyl*)-P-*phenylphosphinamide* **11**.—(i) *From* (2R,4S,5R)-2-(2-*methoxyphenyl*)-3,4-*dimethyl*-5-*phenyl*-1,3,2-*oxazaphospholidine* 2-*oxide* **5**. To a cooled (−78 °C) and stirred solution of (2*R*,4*S*,5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine 2-oxide **5** (0.5 g, 1.57 mmol) in dry THF (15 $cm^3$) was added, by syringe under argon, a solution of phenylmagnesium chloride (2.0 $cm^3$, 4.0 mmol; 2.0 mol $dm^{-3}$ in THF). The mixture was stirred at this temperature for 1 h, and for 18 h at ambient temperature. The excess of Grignard reagent was quenched with water (20 $cm^3$) and the mixture was extracted with dichloromethane (3 × 20 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield ($S_P$)-(−)-N-[(1S,2R)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-P-*phenylphosphinamide* **11** as a solid. Crystallisation from toluene gave crops of needles (0.3 g, 48%), m.p. 153 °C; further crystals were deposited in a second crop (Found: C, 70.0; H, 6.6; N, 3.5; $C_{23}H_{26}NO_3P$ requires C, 69.86; H, 6.63; N, 3.54%); $[\alpha]_D^{20}$ −30.65 (*c* 1.08, $CHCl_3$); $\delta_H$(500 MHz; $CDCl_3$) 1.21 (3 H, d, $J_{HH}$ 7.1, CHMe), 2.38 (3 H, d, $J_{PH}$ 10.5, NMe), 3.70 (1 H, ddq, $J_{PH}$ 12, $J_{HH}$ 7.1, $J_{HH}$ 2.9, C*H*Me), 3.77 (3 H, s, OMe), 4.8 (1 H, dd, $J_{HH}$ 4.8, $J_{HH}$ 2.9, CHO*H*), 5.66 (1 H, d, $J_{HH}$ 3.3, C*H*Ph), 6.92 (1 H, dd, $J_{PH}$ 5.5, $J_{HH}$ 8.3, An, 3-H), 7.01 (1 H, td, $J_{5,6}$ 7.5, $J_{PH}$ 2.26, $J_{3,5}$ 1.0, An, 5-H), 7.22 (1 H, tt, $J_{4,5}$ 7.3, $J_{4,6}$ 2.0, Ph 4-H), 7.31 (4 H, m), 7.41 (2 H, td, $J_{4,5}$ 7.7, $J_{PH}$ 3.3, PPh, 3-, 5-H), 7.47 (1 H, dd, $J_{4,6}$ 1.8, $J_{4,5}$ 7.5, An 4-H), 7.51 (1 H, tt, $J_{4,5}$ 8.3, $J_{PH}$ 1.0, $J_{4,6}$ 1.8, PPh 4-H), 7.76 (2 H, ddt, $J_{PH}$ 12.1, $J_{5,6}$ 7.9, $J_{4,6}$ 1.5, PPh, 2-, 6-H) and 7.86 (1 H, ddd, $J_{PH}$ 13.6, $J_{5,6}$ 7.6, $J_{4,6}$ 1.8, An, 6-H); $\delta_C$(125 MHz; $CDCl_3$) 13.2 (s, C*Me*), 33.3 (d, $J_{PC}$ 5.4, NMe), 55.3 (s, OMe), 60.2 (s, *C*Me), ~77 (s, *C*HPh), 111.0 (d, $J_{PC}$ 7.15, An, C-5), 118.9 (d, $J_{PC}$ 122, An, C-1), 121.0 (d, $J_{PC}$ 11.6, An, C-6), 126.8 (s, Ph C-3, -5), 126.9 (s, Ph C-4), 127.8 (s, Ph C-2, -6), 128.1 (d, $J_{PC}$ 13.6, PPh C-2, -6), 132.1 (d, $J_{PC}$ 10.7, PPh C-3, -5), 133.6 (d, $J_{PC}$ 132, PPh C-1), 134.0 (s, An C-4), 135.6 (d, $J_{PC}$ 6.62, An C-3), 142.6 (s, Ph C-1) and 160.8 (s, An C-2); $\delta_P$(101 MHz; $CDCl_3$) 34.31; *m/z* (CI, $NH_3$) 396 (M + 1, 100%)$^+$, 378 (35), 288 (75), 249 (50), 231 (35), 199 (35) and 148 (50).

(ii) *From* (2S,4S,5R)-3,4-*Dimethyl*-2,5-*diphenyl*-1,3,2-*oxazaphospholidine* 2-*oxide* **7**. As above, by use of minor diastereoisomer **7** (1.0 g, 3.5 mmol) and 2-methoxyphenylmagnesium bromide (5.0 $cm^3$, 4.35 mmol; 0.87 mol $dm^{-3}$) in THF (50 $cm^3$), mixing at −78 °C, and allowing the mixture to come to 0 °C overnight.

($S_P$)-(−)-N-[(1S,2R)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*]-N-*methyl*-P-*phenyl*-P-*vinylphosphinamide* **12**.—To a cooled (−10 °C) and stirred solution of (2*R*,4*S*,5*R*)-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphospholidine 2-oxide **6** (11.34 g, 39.5 mmol) in dry THF (250 $cm^3$) was added a solution of vinylmagnesium bromide (47 $cm^3$, 47 mmol; 1.0 mol $dm^{-3}$ in THF). The mixture was stirred at this temperature for 1 h, and then at ambient temperature for 2 h. The excess of Grignard reagent was destroyed by quenching with water (100 $cm^3$) and the mixture was extracted with dichloromethane (3 × 100 $cm^3$). The organics were combined and concentrated to yield ($S_P$)-(−)-N-[(1S,2R)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-N-*methyl*-P-*phenyl*-P-*vinylphosphinamide* **12** as a solid. Crystallisation from hot THF afforded crystals (10.97 g; 88%), m.p. 128 °C (Found: C, 68.5; H, 7.3; N, 4.3; P, 10.1%. $C_{18}H_{22}NO_2P$ requires C, 68.55; H, 7.03; N, 4.44; P, 9.82%); $[\alpha]_D^{22}$ −68.9 (*c* 1, $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3284br (OH), 1603 (C=C) and 1138s (P=O); $\delta_H$(500 MHz; $CDCl_3$) 1.18 (3 H, d, $J_{HH}$ 7.0, CMe), 2.48 (3 H, d, $J_{HP}$ 10.96, NMe), 3.67–3.71 (1 H, ddq, $J_{PH}$ 4.3, $J_{HH}$ 7.0, $J_{HH}$ 3.8, C*H*Me), 5.63 (1 H, d, $J_{HH}$ 4.6, C*H*Ph), 4.86 (1 H, dd, $J_{HH}$ = $J_{HH}$ = 4.3, CHO*H*), 6.12 (1 H, ddd, $J_{PH\ trans}$ 40.8, $J_{cis}$ 11.97, $J_{HH}$ 2.47, H *trans* to P), 6.19 (1 H, ddd, $J_{PH}$ 23.0, $J_{trans}$ 18.5, $J_{HH}$ 2.47, H *cis* to P), 6.30 (1 H, ddd, $J_{PH}$ 23.0, $J_{trans}$ 18.5, $J_{cis}$ 11.9, $CH_2$=CH), 7.22–7.29 (5 H, m, Ph), 7.39 (2 H, dt, $J_{5,6}$ 7.7, $J_{PH}$ 3.2, 3-, 5-H), 7.48 (1 H, dt, $J_{4,5}$ 7.4, 4-H) and 7.57 (2 H, ddt, $J_{PH}$ 12.2, $J_{5,6}$ 7.7, $J_{4,6}$ 1.4, 2-, 6-H); $\delta_C$(126 MHz; $CDCl_3$) 13.2 (s, CMe), 30.8 (s, NMe), 58.4 (s, *C*Me), 76.9, (s, *C*Ph), 126.4 (s, Ph C-3, -5), 128.0 (s, Ph C-2, -6), 128.4 (d, $J_{PC}$ 12.6, PPh C-2, -6), 130.2 (d, $J_{PC}$ 121, P*C*H=$CH_2$), 130.0 (d, $J_{PC}$ 121, PPh C-1), 131.7 (s, PPh C-3, -5), 131.7 (s, PPh C-4), 134.7 (s, PCH=*C*$H_2$) and 142.8 (s, Ph C-1); $\delta_P$(101 MHz; $CDCl_3$) 33.8; *m/z* (C.I.) 316 (M + 1, 100%)$^+$, 298 (M − OH, 25), 288 (M − $C_2H_3$, 15) 208 (M − $C_8H_{11}$, 95).

($S_P$)-(−)-N-[(1S,2R)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-P-(4-*methoxyphenyl*)-N-*methylphosphinamide* **13**.—To a cooled (−78 °C) and stirred solution of (2*R*,4*S*,5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine 2-oxide **5** (2.0 g, 6.3 mmol) in dry THF (100 $cm^3$) was added a solution of 4-methoxyphenylmagnesium bromide (12.5 $cm^3$, 7.6 mmol; 0.6 mol $dm^{-3}$ in THF). The mixture was stirred at this temperature for 1 h, and then at ambient temperature overnight. The excess of Grignard reagent was quenched with water (100 $cm^3$) and the mixture was extracted with dichloromethane (3 × 100 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield a solid. Crystallisation from hot THF afforded crystals of ($S_P$)-(−)-N-[(1S,2R)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-P-(4-*methoxyphenyl*)-N-*methylphosphinamide* **13** (2.2 g, 82%), m.p. 190–191 °C (Found: C, 67.4; H, 6.7; N, 3.0%; M$^+$, 293. $C_{24}H_{28}NO_4P$ requires C, 67.55; H, 6.63; N, 3.39%; M, 292); $[\alpha]_D^{21}$ −26.1 (*c* 13.8, $CHCl_3$); $\nu_{max}$(Nujol)/$cm^{-1}$ 3220br (OH), 1155m (P=O) and 960m (P–O–CPh); $\delta_H$(500 MHz; $CDCl_3$) 1.19 (3 H, d, $J_{HH}$ 7.2, CH*Me*), 2.34 (3 H, d, $J_{PH}$ 10.5, NMe), 2.67 (1 H, m, C*H*Me), 3.81 (3 H, s, *o*-An OMe), 3.84 (3 H, s, *p*-An OMe), 4.84 (1 H, dd, $J_{HH}$ 5.0, $J_{HH}$ 2.7, CHO*H*), 5.85 (1 H, d, $J_{HH}$ 5.0, C*H*Ph), 6.90 (1 H, dd, $J_{HH}$ 8.7, $J_{PH}$ 5.8, *o*-An 3-H), 6.93 (2 H, dd, $J_{2,3}$ 8.9, $J_{PH}$ 2.5, *p*-An 3-, 5-H), 7.05 (1 H, ddt, $J_{5,6}$ 7.5, $J_{HP}$ 2.3, $J_{3,5}$ 0.7, *o*-An 5-H), 7.20 (1 H, tt, $J_{3,4}$ 7.3, $J_{2,4}$ 1.34, Ph-4-H), 7.28 (2 H, t, $J_{3,4}$ 7.3, Ph 3-, 5-H), 7.39 (2 H, t, $J_{2,3}$ 8.76, Ph 2-, 6-H), 7.49 (1 H, ddt, $J_{4,5}$ 8.3, $J_{4,6}$ 1.8, $J_{PH}$ 0.9, *o*-An 4-H), 7.67 (2 H, dd, $J_{PH}$ 12.1, $J_{5,6}$ 8.8, *p*-An 2-, 6-H), 7.83 (1 H, ddd, $J_{PH}$ 13.9, $J_{5,6}$ 7.6, $J_{4,6}$ 1.8, *o*-An 6-H); $\delta_C$(126 MHz; $CDCl_3$) 13.1 (s, C*Me*), 33.1 (d, $J_{PC}$ 5.4, NMe), 55.2 (s, 2 × AnOMe), 60.0 (s, *C*Me), 76.6 (s, *C*HPh), 110.9 (d, $J_{PC}$ 7.0, *o*-An C-5), 113.7 (d, $J_{PC}$ 14.2, *p*-An C-2, -6), 120.0 (d, $J_{PC}$ ~122.0, *o*-An C-1), 120.9 (d, $J_{PC}$ 12.5, *o*-An C-6), 124.0 (d, $J_{PC}$ 138.5, *p*-An C-1), 126.5 (s, Ph C-3, -5), 126.8 (s, Ph C-4), 126.8 (s, Ph C-2, -6), 133.8 (s, *o*-An C-4), 134.1 (d, $J_{PC}$ 11.8, *p*-An C-3, -5), 135.5 (d, $J_{PC}$ 6.7, *o*-An C-3), 142.7 (s, Ph C-1), 160.6 (s, *o*-An C-2) and 162.3 (s, *p*-An C-4); $\delta_P$(101 MHz; $CDCl_3$) 34.0; *m/z* (C.I.) 426 (M + 1, 55%)$^+$, 408 (M − $H_2O_5$), 318 (100), 278 (12), 261 (40) and 229 (20).

($S_P$)-(−)-N-[(1S,2R)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-P-(3-*methoxyphenyl*)-N-*methylphosphinamide* **14**.—To a cooled (−78 °C) and stirred solution of (2*R*,-4*S*, 5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine 2-oxide **5** (11.0 g, 34.8 mmol) in dry THF (350 $cm^3$) was added, *via* cannula, a solution of 3-methoxyphenylmagnesium bromide (60 $cm^3$, 38.4 mmol; 0.64 mol $dm^{-3}$ in THF) during 20 min. The mixture was stirred at this temperature for 1 h, and then was stirred at ambient

temperature overnight. The excess of Grignard reagent was quenched with water (200 $cm^3$) and the mixture was extracted with dichloromethane (3 × 200 $cm^3$). The organics were combined and concentrated to yield a solid, crystallisation of which from hot THF afforded ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-P-(3-*methoxyphenyl*)-*N*-*methylphosphinamide* **14** as crystals (11.2 g, 76%), m.p. 129 °C (Found: C, 68.0; H, 6,7; N, 3.35; P, 7.1. $C_{24}H_{28}NO_4P$ requires C, 67.55; H, 6.63; N, 3.29; P, 7.28%); $[\alpha]_D^{21}$ −34.9 (*c* 1.25, $CHCl_3$); $\nu_{max}$(Nujol)/$cm^{-1}$ 3250br (OH), 1140m (P=O) and 1035; $\delta_H$(500 MHz; $CDCl_3$) 1.21 (3 H, d, $J_{HH}$ 7.1, CH*Me*), 2.37 (3 H, d, $J_{PH}$ 10.6, NMe), 3.66–3.77 (1 H, m, C*H*Me), 3.80 (3 H, s, OMe), 3.81 (3 H, s, OMe), 4.86 (1 H, dd, $J_{HH}$ 4.9, $J_{HH}$ 2.8, CHO*H*), 5.63 (1 H, d, $J_{HH}$ 4.9, C*H*Ph), 6.91 (1 H, dd, $J_{PH}$ 5.5, $J_{HH}$ 8.3, *o*-An 3-H), 7.00–7.4 (m, 10 H), 7.50 (1 H, ddt, $J_{4,6}$ 1.6, $J_{PH}$ 0.6, $J_{4,5}$ 8.3, *o*-An 4-H) and 7.79 (1 H, ddd, $J_{PH}$ 13.9, $J_{5,6}$ 7.6, $J_{4,6}$ 1.6, *o*-An 6-H); $\delta_C$(126 MHz; $CDCl_3$) 13.24 (s, C*Me*), 33.5 (s, NMe), 55.3 (s, An OMe), 55.4 (s, An OMe), 60.0 (s, *C*Me), 77.04 (s, *C*HPh [$C_6D_6$]), 111.1 (s, *o*-An C-5), 117.2 (d, $J_{PC}$ 11.0, *m*-An C-6), 117.8 (s, *m*-An C-4), 118.5 (d, $J_{PC}$ ~ 130, *o*-An C-1), 121.0 (d, $J_{PC}$ 12.1, *o*-An C-6), 124.4 (s, *m*-An C-5), 126.6 (s, Ph C-3, -5), 126.9 (s, Ph C-4), 127.9 (s, Ph C-2, -6), 129.3 (d, $J_{PC}$ 14.5, *m*-An C-2), 134.1 (s, *o*-An C-4), 135.6 (s, *o*-An C-3), 142.6 (s, Ph C-1), 159.6 (s, *o*-An C-2) and 160.2 (s, *m*-An C-3); $\delta_P$(101 MHz; $CHCl_3$) 34.2; *m*/*z* (C.I.) 426 (M + 1, 75%)$^+$, 408 (M − $H_2O$, 10), 318 (72), 278 (12), 261 (15) and 148 (100).

($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-*N*-*methyl*-P-(2-*naphthyl*)*phosphinamide* **15**.—To a cooled (−78 °C) and stirred solution of (2*R*,4*S*,5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine 2-oxide **5** (2.0 g, 6.3 mmol) in dry THF (100 $cm^3$) was added, under argon, a solution of 2-naphthylmagnesium bromide (20 $cm^3$, 14.0 mmol; 0.7 mol $dm^{-3}$ in THF). The mixture was stirred at this temperature for 1 h, and then at ambient temperature overnight. The excess of Grignard reagent was quenched with water (100 $cm^3$) and the mixture was extracted with dichloromethane (3 × 100 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield a solid. Crystallisation from hot THF afforded crystals of ($S_P$)-(−)-*N*-[(1*S*,*SR*)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-*N*-*methyl*-P-(2-*naphthyl*)*phosphinamide* **15** (2.26 g, 81%), m.p. 120 °C (Found: C, 72.55; H, 6.8; N, 2.8; P, 6.7. $C_{27}H_{28}NO_3P$ requires C, 72.79; H, 6.33; N, 3.14; P, 6.95%); $[\alpha]_D^{19.5}$ −18.8 (*c* 1.01, $CHCl_3$); $\delta_H$(500 MHz; $CDCl_3$) 1.25 (3 H, d, $J_{HH}$ 7.1, CH*Me*), 2.40 (3 H, d, $J_{PH}$ 10.6, NMe), 3.75 (1 H, m, C*H*Me), 3.79 (3 H, s, An OMe), 4.87 (1 H, s, CHO*H*), 5.74 (1 H, s, C*H*Ph), 6.93 (1 H, dd, $J_{HH}$ 8.3, $J_{PH}$ 5.7, An 3-H), 7.06 (1 H, ddt, $J_{5,6}$ 7.5, $J_{PH}$ 2.3, $J_{3,5}$ 1.0, An 5-H), 7.21–7.69 (12 H, m, Ar) and 8.34 (1 H, d, $J_{PH}$ 14.6, Np 7-H); $\delta_P$(101 Hz; $CDCl_3$) 30.7 (1 P, s); *m*/*z* (C.I.) 446 (M + 1, 100%)$^+$, 338 (95), 298 (15) and 148 (50).

($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-*Hydroxy*-1-*methyl*-2-*phenylethyl*]-P-(2-*methoxyphenyl*)-*N*-*methyl*-P-*vinylphosphinamide* **16**.—To a vigorously stirred and cooled (−78 °C) solution of (2*R*,4*S*,5*R*)-2-(2-methoxyphenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine 2-oxide **5** (2.2 g, 6.93 mmol) in dry THF (150 $cm^3$) was added a solution of vinylmagnesium bromide (8.5 cm, 8.5 mmol; 1.0 mol $dm^{-3}$ in THF) over a period of 10 min. The mixture was stirred at this temperature for 1 h, and then overnight at ambient temperature. The excess of Grignard was quenched with water (100 $cm^3$) and extracted into dichloromethane (3 × 100 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-*hydroxy*-1-*methyl*-2-*phenyl*)-*ethyl*]-P-(2-*methoxyphenyl*)-*N*-*methyl*-P-*vinylphosphinamide* **16** as a solid. Crystallisation from hot THF yielded crystals (1.9 g, 80%), m.p. 188–189 °C (Found: C, 66.35; H, 7.2; N, 4.0; P, 8.95%; $M^+$, 346. $C_{19}H_{24}NO_3P$ requires C, 66.07; H, 7.00; N, 4.05; P, 8.97%; M, 345); $[\alpha]_D^{22}$ −113.5 (*c* 1.0, $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3250br (OH) and 1140s (P=O); $\delta_H$(500 MHz; $CDCl_3$) 1.08 (3 H, d, $J_{HH}$ 7.1, CMe), 2.44 (3 H, d, $J_{PH}$ 10.6, NMe), 3.63 (1 H, ddq, $J_{PH}$ 4.4, $J_{HH}$ 7.1, $J_{HH}$ 2.8, C*H*Me), 5.06 (1 H, d, $J_{HH}$ 5.1, C*H*Ph), 4.82 (1 H, dd, $J_{HH}$ 5.1, $J_{HH}$ 2.8, CHO*H*), 6.11 (1 H, ddd, $J_{PH\text{-}trans}$ 43.7, $J_{cis}$ 12.4, $J_{HH}$ 2.14, CH*H*=CH$_{trans}$ to P), 6.35 (1 H, ddd, $J_{PH}$ 23.0, $J_{trans}$ 18.7, $J_{HH}$ 2.14, CH*H*=CH, *cis* to P), 6.57 (1 H, ddd, $J_{PH}$ 24.5, $J_{trans}$ 18.7, $J_{cis}$ 12.6, $CH_2$=C*H*), 6.89 (1 H, dd, $J_{PH}$ 5.7, $J_{3,4}$ 8.4, An 3-H), 7.07 (1 H, ddt, $J_{PH}$ 0.6, $J_{3,5}$ 0.75, $J_{5,6}$ 7.5, An 5-H), 7.18–7.3 (5 H, m, Ph), 7.50 (1 H, dt, $J_{4,5}$ 8.1, $J_{4,6}$ 1.8, $J_{PH}$ 0.7, An 4-H) and 7.97 (1 H, ddd, $J_{PH}$ 13.4, $J_{5,6}$ 7.5, $J_{4,6}$ 1.8, An 6-H); $\delta_C$(126 MHz; $CDCl_3$) 12.4 (s, C*Me*), 31.51 (s, NMe), 31.5 (s, OMe), 59.48 (s, *C*Me), 76.5 (s, *C*HPh), 110.5 (s, *o*-An C-5), 120.0 (d, $J_{PC}$ 127.1, *o*-An C-1), 121.0 (d, $J_{PC}$ 11.5, *o*-An C-6), 126.2 (s, Ph C-3, -5), 126.8 (s, Ph C-4), 127.8 (s, Ph C-2, -6), 130.5 (d, $J_{PC}$ 124.1, PCH=$CH_2$), 133.7 (s, *o*-An C-4), 134.4 (s, *C*H=$CH_2$), 135.1 (s, *o*-An C-3), 142.6 (s, Ph C-1) and 160.2 (s, *o*-An C-2); $\delta_P$(101 MHz; $CDCl_3$) 31.0; *m*/*z* (C.I.) 346 (M + 1, 100%)$^+$, 328 (M − OH, 12), 238 (M − $C_{10}H_{14}$, 100).

(S)-(+)-*Methyl* 2-*Methoxyphenyl*-(4-*methoxyphenyl*) *phosphinate* **18**.—A standardised methanolic solution of dry HCl (4.65 $cm^3$, 4.7 mmol; 1.01 mol $dm^{-3}$ in methanol) was added dropwise to a vigorously stirred solution of ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*P*-(2-methoxyphenyl)-*P*-(4-methoxyphenyl)-*N*-methylphosphinamide (1.0 g, 2.35 mmol) in dry methanol (10 $cm^3$) at −3 °C under argon. The reaction mixture was stirred for 18 h after which it was poured into HCl (51 $cm^3$; 0.1 mol $dm^{-3}$) and extracted with dichloromethane (3 × 20 $cm^3$). The organics were combined, and washed with NaOH (15 $cm^3$; 0.1 mol $dm^{-3}$), then they were separated, and the solution was dried ($MgSO_4$) and concentrated to yield (R)-(+)-*methyl* 2-*methoxyphenyl*-(4-*methoxyphenyl*)*phosphinate* **18** as a solid (0.65 g, 95%), which was dried *in vacuo*, m.p. 68 °C (Found: C, 61.5; H, 6.1; P, 10.0. $C_{15}H_{17}NO_4P$ requires C, 61.64; H, 5.86; P, 10.60%); $[\alpha]_D^{24}$ +31.0 (*c* 1.12, $CHCl_3$); $\delta_H$(500 MHz; $C_6D_6$) 3.15 (3 H, s, *p*-An OMe), 3.17 (3 H, s, *o*-An OMe), 3.49 (3 H, d, $J_{PH}$ 11.4, POMe), 6.34 (1 H, dd, $J_{PH}$ 5.7, $J_{3,4}$ 8.3, *o*-An 3-H), 6.69 (2 H, ddt, $J_{5,6}$ 8.8, $J_{PH}$ 2.7, *J* 2.0, *p*-An 3-, 5-H), 6.85 (1 H, ddt, $J_{4,5}$ 7.5, $J_{HP}$ 2.5, $J_{3,5}$ 0.9, *o*-An 5-H), 7.09 (1 H, ddt, $J_{3,4}$ 8.2, $J_{4,6}$ 1.8, $J_{PH}$ 0.7, *o*-An 4-H), 8.02 (2 H, ddt, $J_{PH}$ 12.0, $J_{2,3}$ 8.8, *J* 2.0, *p*-An 2-, 6-H) and 8.40 (1 H, ddd, $J_{PH}$ 13.2, $J_{5,6}$ 7.5, $J_{4,6}$ 1.8, *o*-An 6-H); $\delta_C$(126 MHz; $C_5D_6$) 50.6 (s, POMe), 54.7 (s, AnOMe), 55.1 (s, An OMe), 111.5 (s, *o*-An C-5), 113.8 (d, $J_{PC}$ 14.2, *p*-An C-2, -6), 120.8 (d, $J_{PC}$ 11.9, *o*-An C-6), 121.5 (d, $J_{PC}$ 133.9, *o*-An C-1), 125.0 (d, $J_{PC}$ 148.5, *p*-An C-1), 133.9 (s, *o*-An C-4), 134.4 (d, $J_{PC}$ 11.6, *p*-An C-3, -5), 135.5 (s, *o*-An C-3), 161.3 (s, *o*-An C-2) and 162.8 (s, *p*-An C-4); $\delta_P$(101 MHz; $CDCl_3$) 32.5 (1 P, s); *m*/*z* (C.I.) 293 (M + 1, 100)$^+$.

(S)-(+)-*Methyl* 2-*Methoxyphenyl*-(3-*methoxyphenyl*)*phosphinate* **19**.—A standardised methanolic solution of dry HCl (51.6 $cm^3$, 52.8 mmol; 1.02 mol $dm^{-3}$ in methanol) was added dropwise to a vigorously stirred solution of ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*P*-(2-methoxyphenyl)-*P*-(3-methoxyphenyl)-*N*-methylphosphinamide **14** (11.2 g, 26.4 mmol) in dry methanol (150 $cm^3$) at −3 °C under argon. The reaction mixture was stirred for 18 h after which it was poured into HCl (50 $cm^3$; 0.1 mol $dm^{-3}$) and extracted with dichloromethane (3 × 20 $cm^3$). The organics were combined, and washed with NaOH (50 $cm^3$, 0.1 mol $dm^{-3}$); they were then separated, dried ($MgSO_4$), and concentrated to yield (R)-(+)-*methyl* 2-*methoxyphenyl*-3-(*methoxyphenyl*)*phosphinate* **19** as a yellow oil (8 g, 100%) which was dried *in vacuo* (Found: C, 61.8;

H, 5.75. $C_{15}H_{17}PO_4$ requires: C, 61.64; H, 5.86%); $[\alpha]_D^{20}$ +8.75 (*c* 0.41, $CHCl_3$); $\delta_H$(500 MHz; $C_6D_6$) 3.71 (3 H, s, *m*-An OMe), 3.73 (3 H, d, $J_{PH}$ 11.4, POMe), 3.80 (3 H, s, *o*-An OMe), 6.86 (1 H, dd, $J_{3,4}$ 8.3, $J_{PH}$ 6.0, *o*-An 3-H), 7.01 (1 H, m, $J_{3,4}$ 8.3, $J_{2,4}$ 2.6, *m*-An 4-H), 7.04 (1 H, m, $J_{5,6}$ 7.6, $J_{PH}$ 2.6, *o*-An 5-H), 7.31 (1 H, dt, $J_{2,3}$ 8.0, $J_{PH}$ 4.6, *m*-An 5-H), 7.38 (2 H, dt, $J_{PH}$ 13.0, $J_{2,3}$ 8.0, $J_{2,4}$ 2.7, *m*-An 2-, 6-H), 7.47 (1 H, dt, $J_{3,4}$ 8.3, $J_{4,6}$ 1.8, *o*-An 4-H) and 7.93 (1 H, ddd, $J_{PH}$ 13.3, $J_{5,6}$ 7.6, $J_{4,6}$ 1.8 o-An 6-H); $\delta_C$(126 MHz; $CDCl_3$) 51.2 (d, $J_{PC}$ 5.3, POMe), 55.3 (s, An OMe), 55.5 (s, An OMe), 111.4 (d, $J_{PC}$ 7.4, *o*-An C-5), 116.5 (d, $J_{PC}$ 11.7, *m*-An C-6), 118.1 (s, *m*-An C-4), 118.7 (d, $J_{PC}$ ~ 130, *o*-An C-1), 120.6 (d, $J_{PC}$ 12.3, *o*-An C-6), 124.0 (d, $J_{PC}$ 10.3, *m*-An C-5) 129.1 (d, $J_{PC}$ 16.0, *m*-An C-2), 133.0 (d, $J_{PC}$ 141.1, *m*-An C-1), 134.3 (s, *o*-An C-4), 134.73 (d, $J_{PC}$ 6.2, *o*-An C-3), 159.25 (d, $J_{PC}$ 16.9, *m*-An C-3), 161.08 (s, *o*-An C-2); $\delta_P$(101 MHz; $CHCl_3$) 32.75 (1 P, s); *m*/*z* (C.I.); 293 (M + 1, 100)$^+$, 274 (15), 261 (10), 242 (12), 229 (5), 214 (17).

(S)-(+)-*Methyl 2-Methoxyphenyl-(2-naphthyl)phosphinate* **20**.—A standardised methanolic solution of dry HCl (5.95 $cm^3$, 8.53 mmol; 1.43 mol $dm^{-3}$ in methanol) was added dropwise to a vigorously stirred solution of ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-*hydroxy*-1-*methyl*-2-*phenylethyl*]-*P*-(2-methoxyphenyl)-*N*-methyl-*P*-2-naphthylphosphinamide **15** (1.90 g, 4.3 mmol) in dry methanol (10 $cm^3$) at 0 °C under argon. The reaction mixture was stirred for 18 h after which it was poured into HCl (50 $cm^3$; 0.5 mol $dm^{-3}$) and extracted with dichloromethane (3 × 100 $cm^3$). The organics were combined, and washed with NaOH (30 $cm^3$; 0.1 mol $dm^{-3}$); they were then separated, dried ($MgSO_4$), and concentrated to yield (R)-*methyl* 2-*methoxyphenyl*-(2-*naphthyl*)-*phosphinate* **20** as a solid (1.03 g, 77.3%), which was further purified by recrystallisation from hot toluene and dried *in vacuo*, m.p. 150 °C (Found: C, 69.4; H, 5.6; P, 9.9. $C_{18}H_{17}O_3P$ requires C, 69.22; H, 5.48; P, 9.92%); $[\alpha]_D^{19.5}$ +59.7 (*c* 1.06, $CHCl_3$); $\delta_H$(500 MHz; $C_6D_6$) 3.70 (3 H, s, An OMe), 3.80 (3 H, d, $J_{PH}$ 11.4, POMe), 6.27 (1 H, dd, $J_{3,4}$ 8.3, $J_{PH}$ 5.8, An 3-H), 6.84 (1 H, ddt, $J_{4,5}$ 7.5, $J_{PH}$ 2.5, $J_{3,5}$ 0.9, An 5-H), 7.07 (1 H, ddt, $J_{4,5}$ 7.5, $J_{4,6}$ 2.5, $J_{PH}$ 0.9, An 4-H), 7.13 (2 H, dt, *J* 6.8, $J_{4,6}$ 1.3, Np), 7.18 (2 H, dt, *J* 6.8, *J* 1.4, Np), 7.55 (1 H, dd, $J_{PH}$ 3.7, Np 4-H), 8.06 (1 H, ddd, $J_{PH}$ 12.1, $J_{3,4}$ 8.5, $J_{1,3}$ 1.5, Np 3-H), 8.45 (1 H, ddd, $J_{PH}$ 12.1, $J_{5,6}$ 7.5, $J_{4,6}$ 1.5, An 6-H) and 8.74 (1 H, d, $J_{PH}$ 14.5, Np 1-H); $\delta_C$(126 MHz; $C_6D_6$) 51.4 (s, An OMe), 55.5 (s, POMe), 111.4 (d, $J_{PC}$ 7.4, An C-3), 119.2 (d, $J_{PC}$ 136.3, An C-1), 120.6 (d, $J_{PC}$ 12.3, An C-6), 126.5 (s, Np), 126.9 (d, $J_{PC}$ 11.0, Np), 127.5 (s, Np), 127.7 (d, $J_{PC}$ 17.6, Np C), 128.9 (s, Np), 129.5 (d, $J_{PC}$ 135.0, Np C-1), 132.4 (d, $J_{PC}$ 14.6, Np C), 133.7 (d, $J_{PC}$ 9.7, Np), 134.3 (An C-4), 134.7 (d, $J_{PC}$ 6.2, An C-5) and 161.1 (s, An C-2); $\delta_P$(101 MHz; $CHCl_3$) 32.5; *m*/*z* (C.I.) 313 (M + 1, 100)$^+$.

(S)-(+)-*Methyl 2-Methoxyphenyl(vinyl)phosphinate* **21**.—A standardised methanolic solution of dry HCl (44.3 $cm^3$, 12.18 mmol; 0.275 mol $dm^{-3}$ in methanol) was added dropwise to a vigorously stirred solution of ($S_P$)-(−)-*N*-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*-methyl-*P*-(2-methoxyphenyl)-*P*-vinylphosphinamide **16** (2.10 g, 6.09 mmol) in dry methanol (50 $cm^3$). After 1 h the mixture was quenched with dil. HCl (50 $cm^3$; 0.1 mol $dm^{-1}$) and extracted into dichloromethane (3 × 100 $cm^3$). The organics were separated, and washed successively with dil. NaOH (50 $cm^3$; 0.1 mol $dm^{-3}$) and water. The organics were separated, then dried ($MgSO_4$), and the solvent was removed by rotary evaporation to yield ($R_P$)-(+)-methyl 2-methoxyphenyl(vinyl)phosphinate **21** as an oil (1.4 g, 99%), which was dried *in vacuo*; $[\alpha]_D^{21}$ +135.4 (*c* 1.0, $CHCl_3$); $\nu_{max}$(neat)/$cm^{-1}$ 1235s (P=O); $\delta_H$(500 MHz; $CDCl_3$) 3.64 (3 H, d, $J_{PH}$ 11.6, POMe), 3.88 (s, OMe), 6.13 (1 H, ddd, $J_{PH\text{-}trans}$ 46.3, $J_{cis}$ 12.3, $J_{HH}$ 2.3 C*H*H=CH *trans* to P), 6.36 (1 H, ddd, $J_{PH}$ 24.0, $J_{trans}$ 18.8, $J_{HH}$ 2.3 CH*H*=CH *cis* to P), 6.48 (1 H, ddd, $J_{PH}$ 24.0, $J_{trans}$ 18.8, $J_{cis}$ 12.8, $CH_2$=C*H*), 6.93 (1 H, ddt, $J_{PH}$ 5.9, $J_{3,4}$ 8.4, 3-H), 7.06 (1 H, dt, $J_{PH}$ 2.5, $J_{3,5}$ 0.7, $J_{5,6}$ 7.5, 5-H), 7.52 (1 H, ddt, $J_{4,6}$ 1.8, $J_{4,5}$ 7.9, 4-H) and 7.95 (1 H, ddd, $J_{4,6}$ 1.8, $J_{5,6}$ 7.5, $J_{PH}$ 13.4, 6-H); $\delta_C$(126 MHz; $CDCl_3$) 51.1 (s, An OMe), 55.7 (s, POMe), 110.9 (s, C-5), 118.0 (d, $J_{PC}$ 120.0, C-1), 120.8 (d, $J_{PC}$ 12, C-6), 130.0 (d, $J_{PC}$ 134, PCH=$CH_2$), 134.5 (s, P*C*H=$CH_2$), 134.6 (s, C-4), 134.9 (s, C-3) and 160.9 (s, C-2); *m*/*z* (C.I.) 213 (M + 1, 100)$^+$.

(S)-(+)-*Methyl Phenyl(vinyl)phosphinate* **22**.—A standardised methanolic solution of dry HCl (6.25 $cm^3$, 6.64 mmol; 1.06 mol $dm^{-3}$ in methanol) was added dropwise to a vigorously stirred solution of ($R_P$)-(−)-*N*-[(1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl]-*N*-methyl-*P*-phenyl-*P*-vinylphosphinamide **12** (1.05 g, 3.32 mmol) in dry methanol (50 $cm^3$). After 1 h the mixture was quenched with dil. HCl (50 $cm^3$; 0.1 mol $dm^{-3}$) and extracted into dichloromethane (3 × 100 $cm^3$). The organics were separated, and washed successively with dil. NaOH (50 $cm^3$; 0.1 mol $dm^{-3}$) and water. The organics were separated, and then dried ($MgSO_4$), and the solvent was removed by rotary evaporation to yield ($S_P$)-(+)-*methyl phenyl(vinyl)phosphinate* **22** as an oil (3.8 g, 93%), which was dried *in vacuo* (Found: C, 58.9; H, 6.45; P, 17.0%; $M^+$, 183. $C_9H_{11}O_2P$ requires C, 59.34; H, 6.08; P, 17.00%; M, 182); $[\alpha]_D^{21}$ +46.8 (*c* 1.0, $CHCl_3$); $\nu_{max}$(neat)/ $cm^{-1}$ 1224s (P=O); $\delta_H$(500 MHz; $CDCl_3$) 3.68 (3 H, d, $J_{PH}$ 11.2, POMe), 6.14 (1 H, ddd, $J_{PH\text{-}trans}$ 45.1, $J_{cis}$ 9.8, $J_{HH}$ 4.8 C*H* H=CH *trans* to P), 6.29 (1 H, ddd, $J_{PH}$ 24.0, $J_{trans}$ 18.0, $J_{cis}$ 9.8 CH*H*=CH *cis* to P), 6.27 (1 H, ddd, $J_{PH}$ 23.5, $J_{trans}$ 18.0, $J_{HH}$ 4.87, $CH_2$=C*H*), 7.46 (2 H, ddt, $J_{5,6}$ 8.4, $J_{4,5}$ 7.6, $J_{PH}$ 3.5, 3-, 5-H), 7.54 (1 H, dt, $J_{4,5}$ 7.4, $J_{4,6}$ 1.5, 4-H) and 7.77 (2 H, ddt, $J_{PH}$ 12.2, $J_{5,6}$ 8.4, $J_{4,6}$ 1.5, 2-, 6-H); $\delta_C$(126 MHz; $CDCl_3$) 50.9 (d, $J_{PC}$ 6.4, P-OMe), 128.4 (d, $J_{PC}$ 13, C-2, -6), 128.9 (d, $J_{PC}$ 133, CH=$CH_2$), 130.0 (d, $J_{PC}$ 100, C-1), 131.4 (d, $J_{PC}$ 11.0, C-3, -5), 132.2 (s, *C*H=$CH_2$) and 134.6 (s, C-4); $\delta_P$(101 MHz; $CDCl_3$) 30.1; *m*/*z* (C.I.) 183 (M + 1, 100%)$^+$ and 155 (M − $C_2H_3$).

(S)-2-*Methoxyphenyl*(4-*methoxyphenyl*)*phenylphosphine Oxide* **23**.—To a vigorously stirred, cooled (−78 °C) solution of (*R*)-methyl 2-methoxyphenyl-(4-methoxyphenyl)phosphinate **18** (0.9 g, 3.1 mmol) in THF (10 $cm^3$ was added phenylmagnesium chloride (12.5 $cm^3$, 25 mmol; 2.0 mol $dm^{-3}$ in THF) during 30 min, under argon. The mixture was stirred overnight and allowed to attain ambient temperature unaided. The mixture was then quenched with water (30 $cm^3$) and extracted into dichloromethane (3 × 30 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield an oil, which was purified by dry column chromatography and elution with diethyl ether–dichloromethane (1:1) ($R_f$ 0.6). (S)-2-*methoxyphenyl*-(3-*methoxyphenyl*)*phenylphosphine oxide* **23** was obtained as an oil (0.95 g, 90%) (Found: C, 71.1; H, 5.6. $C_{20}H_{19}O_3P$ requires C, 70.99; H, 5.66%); $[\alpha]_D^{23}$ −2.07 (*c* 1.16, $CHCl_3$).

(S)-(−)-2-*Methoxyphenyl*-(3-*methoxyphenyl*)*phenylphosphine Oxide* **24**.—To a vigorously stirred, cooled (−78 °C) solution of (*R*)-methyl 2-methoxyphenyl-(3-methoxyphenyl)-phosphinate **19** (8.1 g, 27.71 mmol) in THF (150 $cm^3$) was added phenylmagnesium chloride (45 $cm^3$, 90.0 mmol; 2.0 mol $dm^{-3}$ in THF) during 30 min, under argon. The mixture was stirred overnight and allowed to attain ambient temperature unaided. The mixture was then quenched with water (100 $cm^3$) and extracted into dichloromethane (3 × 100 $cm^3$). The organics were combined, dried ($MgSO_4$), and concentrated to yield an oil, which was purified by flash column chromatography and elution with diethyl ether–THF (1:1). An oil was obtained ($R_f$ = 0.4), which was crystallised from diethyl ether to yield (S)-(−)-2-*methoxyphenyl*-(3-*methoxyphenyl*)*phenylphosphine oxide* **24** as a solid (9.1 g, 97%) (Found: C, 70.9; H, 5.6; P, 9.2. $C_{20}H_{19}O_3P$ requires C, 70.99; H, 5.38; P, 9.18%); $[\alpha]_D^{24}$ −9.5

(*c* 0.98, $CHCl_3$); $\delta_H$(500 MHz; $C_6D_6$) 2.93 (3 H, s, *m*-An OMe), 3.17 (3 H, s, *o*-An OMe), 6.32 (1 H, dd, $J_{HH}$ 8.3, $J_{PH}$ 5.2, *o*-An 3-H), 6.81 (2 H, m), 6.99–7.11 (5 H, m), 7.46 (1 H, ddt, $J_{PH}$ 12.0, $J_{2,3}$ 7.5, $J_{2,6}$ 1.2, *m*-An 2-H), 7.71 (1 H, ddd, $J_{PH}$ 13.5, $J_{2,6}$ 1.3, $J_{4,6}$ 1.23, *m*-An 6-H), 7.90 (2 H, ddd, $J_{PH}$ 12.3, $J_{5,6}$ 7.6, $J_{4,6}$ 1.5, Ph 2-, 6-H) and 8.29 (1 H, ddd, $J_{PH}$ 13.2, $J_{5,6}$ 7.6, $J_{4,6}$ 1.8, *o*-An 6-H); $\delta_C$(126 MHz; $CDCl_3$) 55.3 (s, An OMe), 55.4 (s, An OMe), 111.5 (d, $J_{PC}$ 6.0, *o*-An C-5), 116.5, (d, $J_{PC}$ 10.5, *m*-An C-6), 117.6 (s, *m*-An C-4), 118.9 (d, $J_{PC}$ ~ 140, *o*-An C-1), 120.9 (d, $J_{PC}$ 11.2, *o*-An C-6), 124.1 (d, $J_{PC}$ 9.6, *m*-An C-3), 128.1 (d, $J_{PC}$ 12.2, Ph C-2, -6), 129.1 (d, $J_{PC}$ 14.4, *m*-An C-2), 131.3 (d, $J_{PC}$ 9.7, Ph C-3, -5), 133.9 (d, $J_{PC}$ 107.3, Ph C-1), 134.1 (s, *o*-An C-4), 134.5 (d, $J_{PC}$ 107, *m*-An C-1), 134.9 (s, *o*-An C-3), 159.4 (s, *m*-An C-5) and 161.0 (s, *o*-An C-2); $\delta_P$(101 MHz; $CHCl_3$) 27.9; *m*/*z* (C.I.) 339 (M + 1, 100%), 320 (12), 217 (15), 168 (35), 154 (30) and 94 (55).

(S)-(−)-2-*Methoxyphenyl*-(2-*naphthyl*)*phenylphosphine Oxide* **25**.—To a vigorously stirred, cooled (−78 °C) solution of (*R*)-methyl 2-methoxyphenyl-(2-naphthyl)phosphinate **20** (0.2 g, 0.64 mmol) in THF (10 $cm^3$) was added phenylmagnesium chloride (2.6 $cm^3$, 5.2 mmol; 2.0 mol $dm^{-3}$ in THF) during 30 min, under argon. The mixture was stirred overnight and allowed to attain ambient temperature unaided. The mixture was then quenched with water (30 $cm^3$) and extracted into dichloromethane (3 × 20 $cm^3$). The organics were combined, dried ($MgSO_4$) and concentrated to yield (S)-(−)-2-methoxyphenyl-(2-naphthyl)phenylphosphine oxide **25** as an oil (0.21 g, 90%) (Found: C, 71.1; H, 5.6; $C_{23}H_{19}O_2P$ requires C, 77.10; H, 5.34%; $[\alpha]_D^{23}$ −7.46 (*c* 0.93, $CHCl_3$) {lit.,[5b] $[\alpha]_D$ −1.8 (MeOH) for 44% enantiomer excess}; $\delta_H$(500 MHz; $C_6D_6$) 2.9 (3 H, s, An O*Me*), 6.34 (1 H, dd, $J_{3,4}$ 8.3, $J_{PH}$ 5.3, An 3-H), 6.80 (1 H, ddt, $J_{4,5}$ 7.4, $J_{PH}$ 2.6, $J_{3,5}$ 0.6, An 5-H), 6.90–7.73 (9 H, m), 7.77 (2 H, ddt, $J_{PH}$ 12.1, $J_{5,6}$ 8.0, $J_{4,6}$ 1.5, Ph 2-, 6-H), 7.84 (1 H, ddd, $J_{PH}$ 12.5, $J_{1,2}$ 7.6, $J_{1,7}$ 1.5, Np 1-H), 8.09 (1 H, ddd, $J_{PH}$ 13.4, $J_{5,6}$ 7.6, $J_{4,6}$ 1.8, An 6-H) and 8.49 (1 H, d, $J_{PH}$ 14.1, Np 7-H); *m*/*z* (E.I.) 358 (M + 1, 100%), 340 (30), 327 (60) and 267 (45).

*Note added in proof*. In a recent paper, Kee and co-workers (V. Sum, A. J. Davies and T. P. Kee, *J. Chem. Soc., Chem. Commun.*, 1992, 1771) report the synthesis of compound **4**, observe dynamic NMR behaviour and assign the opposite configuration at phosphorus. Further experiments (P. J. Guiry and J. C. P. Laing, unpublished work) lead us to agree that a second diastereoisomer is observable in $C_7D_8$ at low temperatures ($^{31}P$ $\delta_{major}$ 170.3, $\delta_{minor}$ 171.6 at 253 K; 16:1 ratio with broadening above 235 K, and similar observations by $^1H$ NMR spectroscopy). In $CDCl_3$, however, there is a single diastereoisomer as reported above. In view of the close similarity between our observed $^3J_{HP}$ coupling and that reported for the P-phenyl analogue **3** (W. J. Richer, *Chem. Ber.*, 1984, **117**, 2328), which was assigned the same configuration as we have suggested for **4**, we currently prefer the stereochemistry presented.

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