Chiral phosphinamides: new catalysts for the asymmetric reduction of ketones by borane

Barry Burns,[a] N. Paul King,[a] Heather Tye,[a] John R. Studley,[a] Mark Gamble[b] and Martin Wills*,[b]

[a] *School of Chemistry, University of Bath, Claverton Down, Bath, UK BA2 7AY*
[b] *Department of Chemistry, University of Warwick, Coventry, UK CV4 7AL*

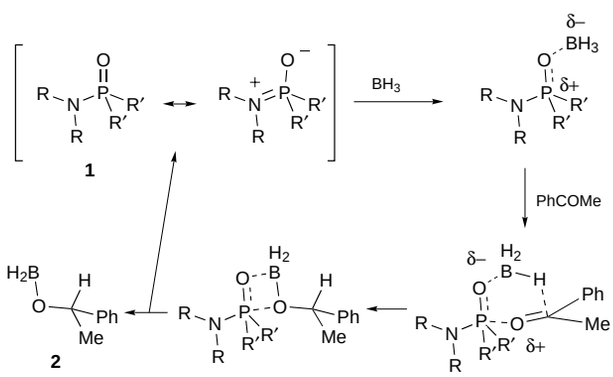
We have identified a new class of catalysts for the asymmetric reduction of prochiral ketones by borane. Key to the architecture of effective catalysts is an N–P=O structural unit which may be part of a phosphinamide, phosphonamide or a related structure. Such catalysts are simple to prepare, are often crystalline solids and may be recovered from reduction reactions and reused. The catalysts act essentially as Lewis bases, serving to increase the reactivity of borane by electron donation. The incorporation of a hydroxy group into the catalyst provides an adjacent Lewis acid site upon reaction with borane and thus affords a superior catalyst capable of asymmetric inductions of up to 92% ee.

Introduction

Asymmetric catalysis of the reduction of ketones to enantiomerically enriched alcohols remains a fundamental asymmetric transformation.[1] Many methods have been reported for this process, most of which involve either asymmetric hydrogenation using an organometallic complex,[2] or modified hydride transfer reagents and close relatives thereof.[3] In the latter class we broadly include oxazaborolidines and transfer hydrogenation methodology. Many of these methods give excellent ee values and often have wide substrate scope, however few are without some limitation or practical disadvantage. In the case of hydrogenation, a nearby directing group in the substrate is frequently required for optimum results, whilst organometallic and boron-based reducing agents are known to be sensitive to moisture and air. There is still a need for continued studies into the development of new robust and versatile catalytic methods for the asymmetric reductions of ketones.

Consideration of the structure and properties of phosphinamides of general structure **1** † suggested that they would act as catalysts of the reduction of ketones by borane.[4] The key to the structure is the N–P=O structural unit which, like a carbonyl amide, exists partially in the dipolar form in which the lone pair on nitrogen donates electron density to the P=O bond (Scheme 1). Structures of this type are known to be good electron donors and coordinate to metal ions and other counterions through the oxygen atom.

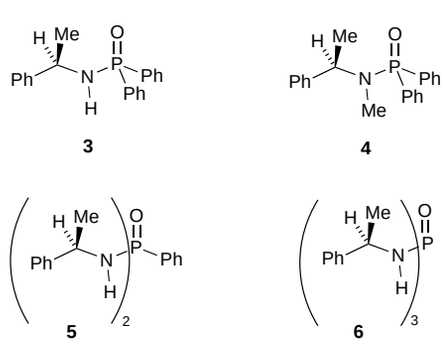
Several X-ray crystal structures of relevant complexes have been published, featuring both neutral and anionic phosphinamide groups.[5] It therefore appeared that a compound of this type could effectively donate electron density to an electron deficient reducing agent such as borane, thereby modifying its reactivity through the increase of partial negative electron density at the boron atom. In return the phosphinamide will gain a partially positive charge and may act as an effective Lewis acid (as a 'relay' from the borane) and coordinate to a ketone. The overall result of these interactions would result in activation of both borane and ketone and their alignment in an ideal position for hydride transfer. Following this reaction the reduced alkoxyborane complex **2** has the opportunity to dissociate from the catalyst thereby allowing the latter to reenter the catalytic cycle (Scheme 1). Through the incorporation of asymmetry in the catalyst, the process should be capable of modification towards a catalytic asymmetric reduction.



Scheme 1 Proposed catalytic cycle for phosphinamide mediated ketone reduction

Phosphinamides, and related reagents, are generally easy to prepare, are robust, usually crystalline, materials which we anticipated could be recovered and reused after the reactions to which they were applied.

In order to examine the potential for catalysis by phosphinamides we first prepared a sample of the *R*-(+)-(1-phenylethyl)-amine derivative **3**, as a crystalline solid in 89% yield, by the reaction of (*R*)-(+)-α-methylbenzylamine with diphenylphosphinic chloride [triethylamine, dichloromethane (DCM), rt]. Compound **3** appeared to be stable to the reaction conditions and substoichiometric quantities of this compound were found

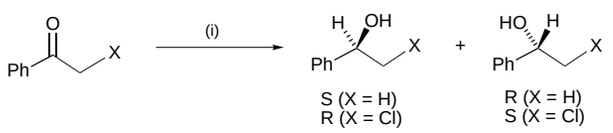


† Phosphinamides are strictly of the formula, $R_2NP(O)R_2$, although in this discussion this term will be broadly used for closely related systems containing an N–P=O structural unit such as phosphonamides $(R_2N)_2P(O)R$ and phosphoramides $(R_2N)_3P(O)$.

Table 1 Asymmetric reductions of acetophenone by phosphinamide catalysts lacking a hydroxy group (THF, rt)

Catalyst	% Catalyst	Reaction time/min (>98% reduction)	Yield alcohol (%)	Enantiomeric excess (%)
None	—	720	75	—
3	2	90	75	23 (*S*)
3	10	<60	82	26 (*S*)
4	10	<120	90	12 (*S*)
5	10	<120	83	30 (*S*)
6	10	<60	70	20 (*S*)
14	5	15	90	24 (*S*)
15	10	>300	92	2 (*S*)
16	10	>300	88	0
18	10	180	90	4 (*S*)
19	10	240	85	35 (*R*)
20	10	60	82	8 (*R*)
21	10	<10	84	46 (*R*)
22	10	30	88	19 (*R*)

to catalyse the reduction of acetophenone by borane–dimethyl sulfide complex (BMS) (Scheme 2, Table 1).



Scheme 2 *Reagents and conditions*: (i) 10 mol% catalyst, 0.6–1.0 equiv. $BH_3{\cdot}SMe_2$, see Tables 1 and 2

Addition of 10 mol% of **3** together with 0.6 equivalents of BMS resulted in >99.95% reduction of acetophenone in less than 60 minutes at room temperature. The progress of the reaction was followed using HPLC with a UV detection system. Since the molar extinction coefficient of the ketone is some 50 times that of the alcohol (our calibration), a 1 : 1 ratio of ketone to alcohol represents a conversion of >98%. This acts as a convenient marker for the qualitative comparison of catalyst performance and was used to compare the examples described throughout this study, although in all cases where the time was less than 1 hour, *no acetophenone* could be detected in the reaction mixture after this time. In contrast the uncatalysed reduction required some 12 hours under the same conditions to proceed to *just* 98% completion (at which point the ketone and alcohol signals are of the same intensity). The resulting alcohol from the first run consisted of a 1.7 : 1 mixture of enantiomers [26% ee (*S*)-major, 82% yield] as assessed by both comparison of the specific rotation with reported literature values and chiral HLPC.

Encouraged by the dramatic acceleration of the reaction obtained on adding the phosphinamide, the utility of **3** was then further investigated by varying catalyst concentration and reaction conditions. Variation of reaction solvent appeared to have little effect on reduction rate and a marginal effect on selectivity, with DCM and toluene giving very inferior results. Increasing the temperature appeared to have a detrimental effect on selectivity, whilst at 0 °C partial precipitation of catalyst occurred resulting in both reduced rate of catalysis and reduced enantioselectivity. In all cases the enantiomeric excesses were modest, but the relatively small difference in selectivity obtained when the catalyst concentration was reduced to 2 mol% suggested that virtually all the reduction was proceeding through the catalyst mediated pathway even at the lower concentration.

Since alkoxyborane complexes such as **2** could reduce further ketone to give alcohol of opposite configuration to that produced by the catalyst, we replaced BMS with catecholborane, which has only one transferable hydride, and obtained a similar enantiomeric excess [24%, (*S*)-major, 83% yield]. The use of borane–THF as the hydride source resulted in the formation of products of very low ee, suggestive that the rate of release of borane from the complex with dimethyl sulfide is at an appropriate level for the catalyst to compete effectively with the uncatalysed pathway.

The use of monochloroborane (a more reactive source of hydride) gave, as expected, considerably lower selectivity [3% ee, (*S*)-major, 71% yield] presumably due to competitive background reduction (10 mol% **3**, THF, rt). Slow addition of ketone to a solution of phosphinamide and BMS in THF resulted in no change in selectivity. Both addition of BMS to a solution of catalyst and ketone (the mode of addition used previously and throughout) and the reverse addition of ketone to a solution of catalyst and borane gave the same selectivity.

In all cases quantitative recovery of catalyst was possible *via* column chromatography and the recovered compound, which appeared spectroscopically identical to the original material, could be reused with no loss in catalytic activity, enantioselectivity or chemical yield of alcohol. It was not necessary to purify the recovered starting material by recrystallisation to obtain reproducible results. An encouraging observation was the apparent insensitivity of the catalyst to moisture. In an experiment in which one equivalent of water (relative to catalyst **3**) was added to a mixture of acetophenone and **3** prior to borane addition, the rate of reduction appeared unaffected, and a product of identical ee [26%, (*S*)-major, 85% yield] was obtained. Phosphinamide **3** appeared to be indefinitely stable to an excess of borane. Stirring a solution of **3** in THF in the presence of a tenfold excess of BMS for 24 hours did not lead to any detectable decomposition and after quenching and extraction the catalyst was recovered in >95% yield. This result clearly underlines the robust and practical nature of these catalytic materials.

In order to confirm that a hydrogen bonding interaction involving the N–H bond between two molecules of **3** (giving a dimeric species), or between catalyst and substrate, was not a prerequisite for catalysis, we prepared compound **4**. The presence of the methyl group appeared to have very little effect on the rate of catalysis (>98% reduction in <2 hours at rt), and gave a product of 12% ee in favour of the (*S*)-enantiomer (90% yield) at the 10 mol% catalyst loading level.

We next examined the effect of increasing the number of α-methylbenzylamine groups bonded to phosphorus. Phosphonamide **5** was prepared from (*R*)-(+)-α-methylbenzylamine and phenylphosphonic dichloride (triethylamine, DCM, rt) in 65% yield and the corresponding triamide **6** was prepared from phosphorus oxychloride under the same conditions in 80% yield. The results obtained using **5** and **6** were very similar to those obtained with **3** again suggesting a dominant catalyst mediated reduction pathway. The use of triphenylphosphine oxide in the reaction gave no noticeable acceleration, confirming that the full 'N–P=O' structural unit is a requirement in these catalysts.

The reduction of a series of ketones was then examined using 10 mol% of phosphinamide **3** (Fig. 1). Reduction of ketones closely related in structure to acetophenone gave the corresponding alcohols **7**–**10** with similar levels of enantiomeric induction. An α-bromo enone gave a product **11** of slightly higher ee but in disappointing yield, whilst an α-keto ester (ethyl pyruvate) was reduced to the corresponding diol in only 5% ee (*S*).

Our proposed catalyst cycle (Scheme 1) requires an electron rich P=O bond for initial donation and activation of the borane reagent. The nitrogen lone pair, though less involved in π-bonding to phosphorus than the corresponding carboxylic amides, is important in that it increases electron density in the P=O bond sufficiently to allow coordination to electrophilic borane. The importance of nitrogen π-bonding to phosphorus was next examined by introduction of an electron withdrawing group on the nitrogen atom. To this end we prepared com-

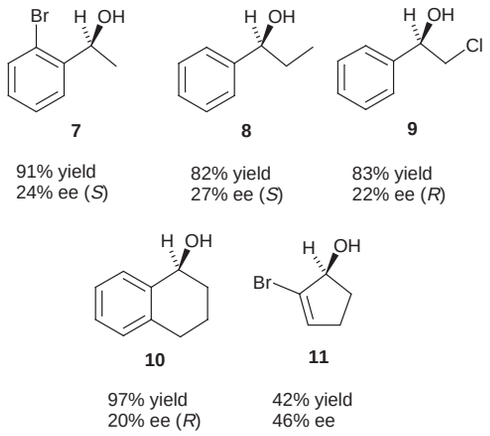
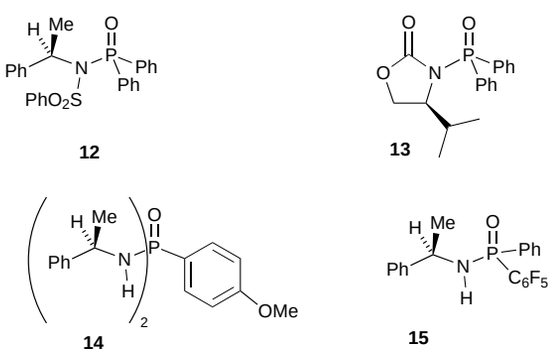


Fig. 1 Asymmetric reductions of ketones using 10 mol% **3**, BMS, THF, rt

pounds **12** and **13**. The nitrogen lone pair in these compounds should be less involved in π-bonding to phosphorus due to electron-withdrawing conjugation effects.

The *N*-sulfonyl phosphinamide **12** was prepared from the



corresponding *N*-sulfonyl amine and diphenylphosphinic chloride (sodium hydride, THF) in 38% yield. Gratifyingly, this compound appeared to show no catalytic activity; reduction of acetophenone required 10 hours at rt for completion and was only slightly above the background reduction rate. The resulting alcohol was racemic.

Compound **13** was prepared from the corresponding amino alcohol *via* the oxazolidinone. Addition of diphenylphosphinic chloride to the deprotonated oxazolidinone (sodium hydride, THF, rt) gave the phosphinamide as a white crystalline solid in good yield. Phosphinamide **13** again appeared to show reduced catalytic activity; 10 mol% of this compound promoted >98% reduction of acetophenone in 3 hours at rt and gave an alcohol of only 7% ee [(*R*) major, 84% yield].

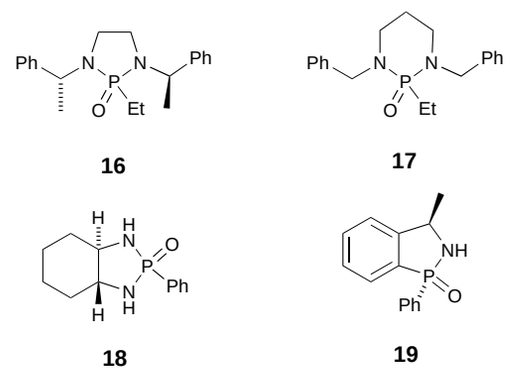
We next examined the effect of an electron donating substituent on phosphorus, an expedient which should increase electron density in the P=O bond. Phosphonamide **14** was prepared by reaction of phosphorus oxychloride with two equivalents of (*R*)-(+)-α-methylbenzylamine (triethylamine, DCM), followed by reaction of the resulting crude chloride with *p*-methoxyphenylmagnesium bromide, in 41% yield. Remarkably, in the presence of 5 mol% of this compound, no acetophenone could be detected in the reaction mixture (by TLC) after only 15 minutes at room temperature, suggesting a very high level of acceleration. Addition of BMS to a solution of phosphonamide and ketone produced a noticeable exothermic effect and gave the alcohol in 24% ee [(*S*) major, 90% yield, Table 1].

We reasoned that the methoxy group significantly increases electron density in the P=O bond through conjugation effects resulting in increased donation and hence activation of borane. It appeared that donation of electron density to borane was important for catalysis and this suggested that the donor properties of the phosphonamides were more significant than their acceptor properties.

To corroborate this idea we next investigated the effect of an electron withdrawing substituent on phosphorus, which should have an adverse effect on catalysis. Phosphinamide **15** was prepared as a single diastereomer in 28% yield by reaction of phenylphosphonic dichloride with one equivalent of (*R*)-(+)-α-methylbenzylamine (1 equivalent of triethylamine, DCM) followed by reaction of crude chloride with 2.5 equivalents of pentafluorophenylmagnesium bromide. The absolute configuration at phosphorus was not determined. This compound did not appear to catalyse the reduction reaction; acetophenone was still present in the reaction mixture after stirring overnight at room temperature. In summary, electron withdrawing substituents on the nitrogen atom of the N–P=O unit appeared to decrease both the rate of catalysis and reduction selectivity.

Having established the electronic requirements for effective catalysis, we turned our attention to the control of reduction selectivity. The acyclic compound so far examined had given modest asymmetric induction due in part, we believed, to the conformational flexibility of these molecules. In order to probe the importance of the conformation of the R_2N–P=O unit in the catalytic process and improve asymmetric induction we prepared a series of compounds in which the conformational freedom of this subunit was restricted by 'locking' the phosphorus atom into a ring.

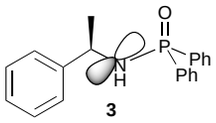
Cyclic phosphonamides **16** and **17** were prepared from the



corresponding diamines.‡ Reaction of (*R*)-(+)-α-methylbenzylamine with oxalyl chloride (2 equivalents of triethylamine, DCM, rt) gave the bis-amide in 84% yield. Reduction of a refluxing THF solution of the amide using $LiAlH_4$ gave the diamine which was then cyclised using ethylphosphonic dichloride (2 equivalents of triethylamine, DCM, rt) to give the phosphonamide **16** in 50% yield. Similarly, reaction of benzoyl chloride with 1,3-diaminopropane gave a crude bis-amide which was reduced under the same conditions as above to give the diamine in 68% yield which was cyclised with the dichloride to **17**. Remarkably, both compounds **16** and **17** proved to be poor catalysts for the reduction of acetophenone by borane, reaction times in excess of 5 hours being required for reduction. The results are summarised in Table 1. The selectivities achieved using **16** and **17** were poor, again presumably due to competing background reduction.

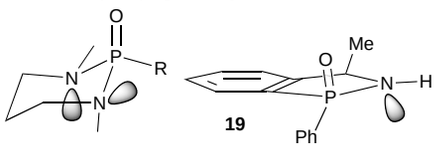
We next examined the fused bicyclic phosphoramide **22** prepared from the (*R*,*R*)-diamine and phenylphosphonic dichloride (2 equivalents of triethylamine, DCM) in 84% yield. This compound again appeared to be a poor catalyst, a reaction

‡ We also prepared a large number of oxazaphospholidines (*i.e.* through cyclisation of amino alcohols) but found that they were consistently unstable to borane. Although other workers[6a,b] have since found that the decomposition products of these reagents are effective catalysts (but cannot be recovered) we chose to concentrate only on recoverable stable catalysts in our work.



3

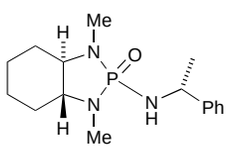
Nitrogen lone pair can donate to P=O in a good catalyst: nitrogen adopts sp^3 geometry.



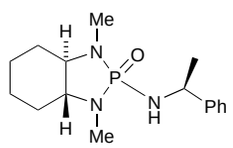
19

Nitrogen lone pair cannot donate to P=O bond in a poor catalyst. Nitrogens atoms retain sp^3 geometry

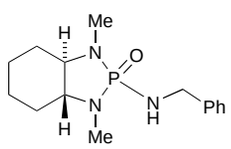
Fig. 2 The significance of orbital overlap



20



21

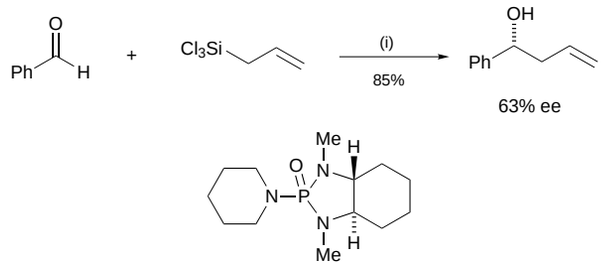


22

time in excess of 3 hours being required for >98% reduction and low enantioselectivity (Table 1). Similar results were obtained using cyclic catalyst **19** in which the phosphonamide R_2N–P=O unit is 'locked' in a five membered ring.[7] This compound again appeared to be less effective at catalysis than the acyclic series of compounds (*cf.* phosphinamide **3**) though surprisingly gave an improved level of asymmetric induction (Table 1).

These observations suggested that the optimum geometry for catalytic activity is that in which the 'R_2N–P=O' system can lie in a single plane, thus maximising electron donation from the nitrogen lone pair to the P=O bond. This suggestion is supported by a number of X-ray structures in which nitrogen is shown to be sp^2 hybridised when this condition is satisfied, which implies a high degree of overlap[5] (Fig. 2), allowing activation of borane followed by initiation of catalysis (Scheme 1). In contrast X-ray studies of compounds structurally related to **19**, in which coplanarity cannot be attained, contain essentially sp^3 hybridised nitrogen atoms, suggesting that electron donation to the P=O bond is a minimum (Fig. 2). This interaction is, however, much weaker than the corresponding effect in carboxylic amides, and the energetic benefit can be outweighed by crystal packing effects in some cases. We reasoned that in compounds such as **16**–**19**, which are poor catalysts, the coplanar geometry cannot be achieved, whilst in contrast the corresponding acyclic series of compounds, which generate the highest acceleration in reduction rate, may readily achieve this conformation.

We believed that a conformationally restricted system was important for generation of a well defined chiral environment around the phosphorus atom, but needed to combine with this the characteristics of an effective catalyst, *i.e.* R_2N–P=O coplanarity. Shortly after the initiation of this part of the project an encouraging report from Denmark,[8] who found that of a series of phosphoramides, derivative **23** was the most effective at the asymmetric mediation of the addition of allyltrichlorosilane to aldehydes (Scheme 3). This is believed to be the result of Lewis base catalysis by the phosphoramide, which donates electron density to the silicon atom in the allyl transfer transition state, and has features in common with our proposed mechanism.



23

Scheme 3 *Reagents and conditions*: (i) 1.0 equiv. **23**, CH_2Cl_2, −78 °C, 6 h

The conformationally locked C_2 symmetric component thus creates a steric environment which can direct the orientation of ketone approach to phosphorus and hence facilitate enantiofacial differentiation. Compounds of this type could be prepared by the reaction of the appropriate diamine precursor with phosphorus oxychloride, followed by displacement of the final halide using a lithiated amine. Using this method, Alexakis has prepared a number of cyclic and bicyclic phosphoramidic chlorides from C_2 symmetric diamines which have been employed as derivatising agents for the determination of the enantiomeric purity of both alcohols and amines.[9]

We prepared compounds **20** and **21**, using this approach. Triamide **20** appeared to give considerably lower selectivity and required a longer reaction time than **3** [1 h, 8% ee, (*R*) major, 82% yield]. Assuming that this contained 'mismatched' directing groups the diastereomer **21** was examined. As predicted 10 mol% of this compound catalysed the reduction of acetophenone, with complete reduction occurring in less than 10 minutes at room temperature, and gave an alcohol of 46% ee [(*R*) major, 84% yield] (Table 1).

In order to confirm that the exocyclic amide side chain was having a controlling effect, phosphoramide **22** was prepared for comparison. Repeating the reduction reaction using this material as catalyst resulted in complete reduction of ketone in 30 minutes at room temperature and gave an alcohol product of 19% ee [(*R*) major, 88% yield] (Table 1). This result also demonstrated that the diamine component favoured the product of (*R*)-configuration in the reduction reaction.

In conclusion, we have demonstrated that phosphinamides, and related materials, are effective catalysts for the asymmetric reduction of ketones by borane. The evidence which we have obtained leads us to believe that they operate in this capacity through a *Lewis base* activation of the borane. A secondary action of the phosphorus atom to act as a *Lewis acid* is of much lower significance, and therefore the rigidity of the transition state for reduction, and the ee values obtained, are compromised. Molecular modelling studies, unreported to date, support this.[10]

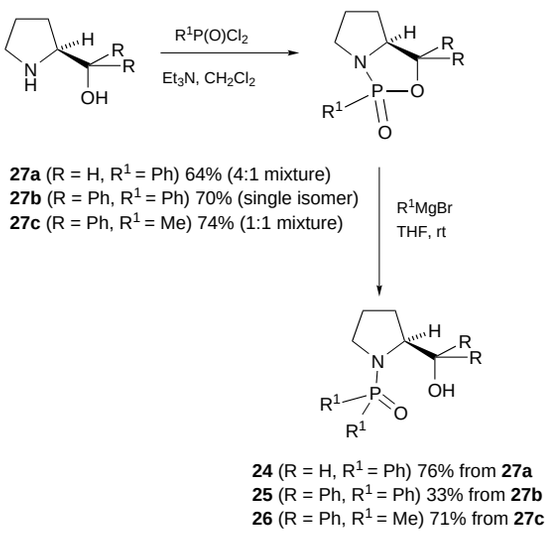
This led us to the conclusion that an effective catalyst might be constructed by combining the phosphinamide with a second functional group capable of providing an alternative electrophilic site for ketone coordination (*i.e.* a Lewis acid).[4c] We chose to study phosphinamide derivatives of L-prolinol, and closely related compounds **24**–**26** in this regard.

Phosphinamides **24**–**26** were prepared from commercially available L-proline derivatives *via* the oxazaphospholidine oxide intermediates **27**[11] as illustrated in Scheme 4. This sequence avoids the problem of competing *O*-phosphinylation when direct preparation from prolinol was attempted.[12,13] The oxazaphospholidine intermediates were generally formed as a

Table 2 Asymmetric reductions of acetophenone by phosphinamide catalysts bearing a hydroxy group (1 molar equivalent $BH_3{\cdot}SMe_2$ unless stated). The best results for each substrate are highlighted in bold.

Entry	Substrate	Catalyst	% Catalyst	Solvent	*T*/°C	Yield alcohol (%)	Enantiomeric excess (%)
1	PhCOMe	**24**	10	THF	rt	75	8 (*R*)
2	PhCOMe	**24**	100	THF	rt	79	19 (*R*)
3	PhCOMe	**24**	10	Toluene	110	84	24 (*R*)
4	PhCOMe	**24**	100	Toluene	110	81	48 (*R*)
5	PhCOMe	**26**	10	Toluene	110	**90**	**62** (***R***)
6	$PhCOCH_2Cl$	**24**	10	Toluene	110	70	32 (*S*)
7	$PhCOCH_2Cl$	**24**	100	Toluene	110	72	70 (*S*)
8	$PhCOCH_2Cl$	**24**	100	Toluene	rt	50	1 (*S*)
9	$PhCOCH_2Cl$	**24**	100	THF	55	75	53 (*S*)
10	$PhCOCH_2Cl$	**25**	100	Toluene	110	69	24 (*S*)
11	$PhCOCH_2Cl$	**25**	10	Toluene	110	75	84 (*S*)
12	$PhCOCH_2Cl$	**25**	100	Toluene	110	70	80 (*S*)[a]
13	$PhCOCH_2Cl$	**26**	10	Toluene	110	**81**	**92** (***S***)

[a] Two molar equivalents of $BH_3{\cdot}SMe_2$ were employed.



27a (R = H, R^1 = Ph) 64% (4:1 mixture)
27b (R = Ph, R^1 = Ph) 70% (single isomer)
27c (R = Ph, R^1 = Me) 74% (1:1 mixture)

24 (R = H, R^1 = Ph) 76% from **27a**
25 (R = Ph, R^1 = Ph) 33% from **27b**
26 (R = Ph, R^1 = Me) 71% from **27c**

Scheme 4

mixture of diastereoisomers and the relative configuration of the major product was not determined. Oxazaphospholidine oxides **24**–**26** are stable crystalline compounds and effective catalysts for ketone reduction by borane (Scheme 2, Table 2). Each compound was fully stable to the reaction conditions and could be recovered and reused after the reaction. Using catalyst **24** and acetophenone as substrate we initially carried out reductions at room temperature in THF solution, however under these conditions the enantiomeric excess of the product remained low, even when a stoichiometric amount of catalyst was employed. Buono has recently shown that reductions of ketones with certain catalysts[14,15] at 110 °C in toluene gives higher asymmetric inductions than the room temperature reaction. After some experimentation we found a similar trend with catalyst **24**, which gave ee values of up to 48% when one full equivalent of catalyst was employed (entries 1–4). Using chloroacetophenone as the substrate further improvements to the ee values were observed, peaking at 72% ee with catalyst **24**, although there was little difference between the results obtained at the 10 or 100 mol% level. Reducing the temperature of the reduction in toluene gave an inferior result, as did the use of THF at reflux.

A further unexpected observation was the superior ee obtained when 10 mol% of **25** was used in the reduction (only chloroacetophenone was studied with this catalyst) rather than one mole equivalent (entries 10 and 11). This is in contrast to **24** and may be because the stoichiometric system generates one mole of a borate complex which in itself is a poor reducing agent. In contrast the presence of excess borane presumably

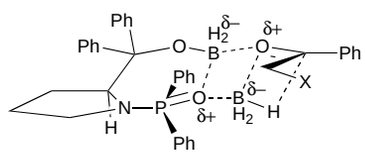
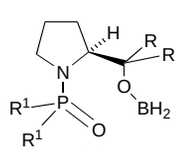


Fig. 3 Stereochemical control in the asymmetric reduction

'breaks up' this complex to form the true active catalytic species (see below). This was confirmed in part through the addition of 2 full equivalents of borane to the reaction, a procedure which returned a high selectivity (entry 12). Catalyst **26** proved to be the best of the series, with ee values peaking at 92% for chloroacetophenone and 62% for acetophenone when 10 mol% of catalyst was employed. Presumably this catalyst benefits from low levels of steric hindrance.

Although the full course of the mechanism requires further study, it is likely that the initial reaction of the above catalysts with borane leads to formation of a complex such as **28**, and



28

that the subsequent reduction transition state involves interactions of both donor and acceptor groups in this complex with the corresponding complementary reagents, as illustrated in Fig. 3. In recent reports[6a,b] on the use of cyclic oxazaphospholidine oxides for carbonyl reduction, it has been suggested that the actual catalytic species may be a closely related species to **28** in which the P–O bond is cleaved but the P–N bond is preserved.

In conclusion we have demonstrated that phosphinamides containing the appropriate functionality are capable of the catalysis of the asymmetric reduction of ketones by borane in high yield and selectivity. The best results have been obtained using catalysts which incorporate both *Lewis base and Lewis acid* sites for interaction with borane and ketone respectively. We shall report further details of our ongoing investigations in this area in due course.

Experimental

General

General experimental conditions and instruments have been described in a previous paper.[16] All NMR couplings are given in Hz.

Preparation of (*R*)-(+)-*N*-(1-phenylethyl)-*p*,*p*-diphenylphosphinamide 3

To a solution of (*R*)-(+)-α-methylbenzylamine (0.54 cm^3, 4.2 mmol) and triethylamine (1.2 cm^3, 8.4 mmol) in dichloromethane (DCM) (20 cm^3) was added diphenylphosphinic chloride (0.81 cm^3, 4.2 mmol) dropwise at 0 °C. The resulting mixture was stirred at room temperature overnight. It was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 10 cm^3). The combined organic extracts were dried (sodium sulfate) and concentrated *in vacuo* to give phosphinamide **3** as a colourless solid which was purified by recrystallisation from DCM–hexane (1.20 g, 89%), mp 158–162 °C (decomp.) (Found: C, 74.7; H, 6.2; N, 4.3. $C_{20}H_{20}NPO$ requires C, 74.77; H, 6.23; N, 4.36%); $[\alpha]_D^{22}$ +40.2 (*c* 1.0, methanol); ν_{max}(Nujol)/cm^{-1} 1961, 1902, 1671, 1307, 1204, 1172, 1108, 1034, 968, 742, 542; δ_H(400 MHz, $CDCl_3$) 1.53 (3 H, d, *J* 6.7, CHCH_3), 3.23 (1 H, br m, NH), 4.35 (1 H, br q, *J* 6.7, C*H*CH_3), 7.18–7.84 (11 H, m, aryl H), 7.76–7.90 (4 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 25.9 (dq, J_{PC} 3.3), 51.0 (d), 125.9, 127.0, 128.2, 128.3, 128.4, 128.5, 131.8, 131.9, 132.3, 132.4, 145.0 (dd, J_{PC} 6.6); δ_P(162 MHz, $CDCl_3$) 22.4 (1 P, s); *m*/*z* (EI) 321 (M^+, 4%), 306 (30), 201 (70), 120 (100), 106 (60), 77 (50), 57 (50), 43 (50).

General ketone reduction procedure using phosphinamides lacking hydroxy group

The following procedure describes the initial activity screen for phosphinamide **3** and is typical (reaction times, yields and selectivities for related systems are described in the text). The same general procedure was adopted for all ketone substrates. To a stirred solution of phosphinamide **3** (10 mol%, 82 mg, 0.257 mmol) and acetophenone (0.3 cm^3, 2.57 mmol) in anhydrous THF (2.5 cm^3) was added BMS (10 M dimethyl sulfide complex, 0.15 cm^3, 1.54 mmol) dropwise over 2 min. Vigorous effervescence was observed. The mixture was then stirred at rt for 1 h (or until all of the ketone was consumed as judged by TLC). The mixture was then diluted with diethyl ether, and saturated aqueous ammonium chloride (1 cm^3) added dropwise. The organic phase was then separated and the aqueous layer extracted with diethyl ether (3 × 5 cm^3). The combined extracts were then dried (sodium sulfate) and concentrated *in vacuo*. At this point HPLC could be employed to assess the extent of reaction.

Separation of acetophenone and 1-phenylethanol. Column: Techospere 5 ODS C18. Eluent: 37% acetonitrile–water. Flow rate: 2 cm^3 min^{-1}. Injection: 5 μl. Temperature: ambient. Detection: UV at λ 254 nm. Retention times: acetophenone, 2.7 min; 1-phenylethanol, 2.05 min. The catalyst was then removed by chromatography on silica, eluting with 20% v/v ethyl acetate–petrol. This gave 1-phenylethanol as a colourless oil which was further purified by distillation under reduced pressure (257 mg, 82%), bp 44 °C/0.5 mmHg (lit.,[3c] 98 °C/20 mmHg); $[\alpha]_D^{23}$ −11.5 (*c* 1, methanol), 26% ee (*S*)-enantiomer; δ_H(270 MHz, $CDCl_3$) 1.47 (3 H, d, *J* 6, CHCH_3), 2.15 (1 H, br s, OH), 4.85 (1 H, q, *J* 6, C*H*CH_3), 7.22–7.37 (5 H, m, aryl H). The enantiomeric excess was confirmed by chiral HPLC analysis.

Separation of (*R*)- and (*S*)-1-phenylethanol enantiomers. Column: CHIRALCEL OD. Eluent: 8% isopropyl alcohol–hexane, 0.1% diethylamine. Flow rate: 0.5 cm^3 min^{-1}. Injection: 10 μl. Temperature: ambient. Detection: UV at λ 254 nm. Retention times: (*R*)-(+)-1-phenylethanol, 10.9 min; (*S*)-(−)-1-phenylethanol, 11.9 min.

^{1}H NMR, optical rotations and Chiral-HPLC data for compounds **7**–**10** have already been reported by this group.[3c,4e,17a] Alcohol **11** has been reported by Corey[17b] in a reduction by oxazaborolidines. In this case the absolute configuration and ee were calculated by comparison of the sign and magnitude of the optical rotation; $[\alpha]_D^{22}$ −13.4 (*c* 2.5, methanol), lit.,[17b] $[\alpha]_D^{22}$ +25.8 (*c* 2.4, methanol) for a sample of *R* configuration alcohol of 90% ee. An HPLC method was not established.

Preparation of (*R*)-(+)-*N*-methyl-*N*-(1-phenylethyl)-*p*,*p*-diphenylphosphinamide 4

To a stirred solution of (*R*)-(+)-*N*-(1-phenylethyl)diphenylphosphinamide **3** (0.5 g, 1.56 mmol) in anhydrous THF (25 cm^3) at 0 °C was added *n*-butyllithium (1.6 M hexane solution, 1.08 cm^3, 1.73 mmol) dropwise. The resulting pale yellow solution was stirred at 0 °C for a further 45 min. Methyl iodide (0.1 cm^3, 1.56 mmol) was then added and the mixture allowed to warm to rt overnight. It was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 10 cm^3). The combined organic extracts were dried (sodium sulfate) and concentrated *in vacuo* to afford phosphinamide **4** as a pale yellow oil. This was then purified on silica eluting with 0→30% v/v ethyl acetate–petrol (303 mg, 58%), mp 114–117 °C (from DCM–hexane) (Found: C, 75.5; H, 6.3; N, 4.2. $C_{21}H_{22}NOP$ requires C, 75.22; H, 6.67; N, 4.18%); $[\alpha]_D^{22}$ +49.9 (*c* 1.0, methanol); ν_{max}(Nujol)/cm^{-1} 3014, 1539, 1493, 1438, 1179, 1122, 982, 932, 698, 666; δ_H(400 MHz, $CDCl_3$) 1.52 (3 H, d, *J* 7, CHCH_3), 2.28 (3 H, d, *J* 10.7, NMe), 4.65 (1 H, dq, *J* 8.9 and 7.8, C*H*CH_3), 7.27–7.42 (10 H, m, aryl H), 7.8–7.85 (5 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 16.9 (q), 27.7 (dq, J_{PC} 4.4), 53.1 (dd, J_{PC} 3.3), 126.9, 127.6, 128.1, 128.3, 128.5, 131.6, 132.16, 132.2, 132.3, 132.8, 133.1, 141.0 (dd, J_{PC} 5.5); δ_P(162 MHz, $CDCl_3$) 30.7 (1 P, s); *m*/*z* (CI) 336 (M^+ + 1, 100%), 320 (4), 232 (5), 203 (15), 134 (35).

Preparation of (*R*,*R*)-(+)-*N*,*N*′-Bis(1-phenylethyl)-*p*-phenylphosphonamide 5

To a stirred solution of (*R*)-(+)-α-methylbenzylamine (5.3 cm^3, 41 mmol) and triethylamine (6.4 cm^3, 46 mmol) in DCM (80 cm^3) at 0 °C was added phenylphosphonic dichloride (2.91 cm^3, 21 mmol) dropwise over 10 min. The cloudy solution was allowed to warm to rt and stirred overnight. The mixture was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 15 cm^3). The combined organic extracts were dried (magnesium sulfate) and concentrated *in vacuo*. The residue was then purified on silica eluting with 0→50% v/v ethyl acetate–petrol. This afforded phosphonamide **5** as a white foam (6.71 g, 45%), mp 65–67 °C (from DCM–hexane) (Found: C, 71.7; H, 7.0; N, 7.4. $C_{22}H_{25}N_2OP$ requires C, 72.52; H, 6.87; N, 7.68%); $[\alpha]_D^{20}$ +41.1 (*c* 1.0, methanol); ν_{max}(Nujol)/cm^{-1} 1376, 1208, 1180, 1126; δ_H(400 MHz, $CDCl_3$) 1.33 (3 H, d, *J* 6.7, CHCH_3), 1.41 (3 H, d, *J* 6.7, CHCH_3), 2.69 (1 H, br t, *J* 8.5, NH), 2.83 (1 H, br t, *J* 9.5, NH), 4.31 (1 H, m, C*H*CH_3), 4.56 (1 H, m, C*H*CH_3), 7.05–7.44 (13 H, m, aryl H), 7.71 (2 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 25.5 (dq, J_{PC} 4.4), 25.9 (q), 50.2 (d), 50.8 (d), 125.8, 126.8, 127.0, 128.1, 128.3, 128.35, 128.6, 131.7, 131.8, 145.1, 145.2 (d, J_{PC} 5.6), 145.8 (d, J_{PC} 5.5); δ_P(162 MHz, $CDCl_3$) 19.0 (1 P, s); *m*/*z* (CI) 365 (M^+ + 1, 100%), 349 (10), 120 (25), 105 (15), 89 (52).

(*R*,*R*,*R*)-(+)-*N*,*N*′,*N*″-Tris(1-phenylethyl)phosphoramide 6

This compound was prepared according to the above general procedure for **5** using (*R*)-(+)-α-methylbenzylamine (1.25 cm^3, 9.72 mmol), triethylamine (1.35 cm^3, 9.72 mmol) and phosphorus oxychloride (0.3 cm^3, 3.24 mmol) in DCM (15 cm^3). Phosphoramide **6** was isolated as a colourless solid (1.05 g, 80%), mp 104–107 °C (from DCM–hexane) (Found: C, 70.4; H, 7.4; N, 10.3. $C_{24}H_{30}N_3OP$ requires C, 70.76; H, 7.37; N, 10.32%); $[\alpha]_D^{19}$ +23.1 (*c* 1.74, chloroform); ν_{max}(Nujol)/cm^{-1} 3215, 1601, 1455, 1375, 1204, 1170, 1108, 1072, 980, 878, 744, 699; δ_H(400 MHz, $CDCl_3$) 1.31 (9 H, d, *J* 6.8, CHCH_3), 2.45 (3 H, br t, *J* 8, NH), 4.31 (3 H, m, C*H*CH_3), 7.12–7.27 (15 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 25.6 (dq, J_{PC} 5.6), 51.0 (d), 125.8 (d), 126.9 (d), 128.5 (d), 145.7 (d, J_{PC} 3.3); δ_P(162 MHz, $CDCl_3$) 11.9 (1 P, s); *m*/*z* (EI) 407 (m^+, 40%), 392 (40), 302 (31), 287 (10), 120 (40), 106 (100).

Preparation of (*R*)-(+)-*N*-phenylsulfonyl-α-methylbenzylamine

To a stirred solution of (*R*)-(+)-α-methylbenzylamine (6 cm^3,

46.5 mmol) and triethylamine (16.2 cm^3, 116.3 mmol) in acetonitrile (30 cm^3) at 0 °C was added benzenesulfonyl chloride (6.5 cm^3, 51.2 mmol) dropwise over 5 min. The resulting white slurry was warmed to rt and stirred for 2 h. It was then poured into saturated aqueous ammonium chloride (30 cm^3) and extracted with diethyl ether (3 × 10 cm^3). The combined organic extracts were dried (sodium sulfate) and concentred *in vacuo* to afford the sulfonyl amine as a white solid which was purified by recrystallisation from DCM–hexane to give white needles (10.8 g, 89%), mp 95–97 °C (from DCM–hexane) (Found: C, 64.1; H, 5.7; N, 5.35. $C_{14}H_{15}NO_2S$ requires C, 64.37; H, 5.75; N, 5.36%); $[a]_D^{19}$ +62.2 (*c* 2.14, chloroform); ν_{max}(Nujol)/cm^{-1} 3241, 1440, 1322, 1161, 1087, 871, 719; δ_H(270 MHz, $CDCl_3$) 1.43 (3 H, d, *J* 7, $CHCH_3$), 4.49 (1 H, p, *J* 7, $CHCH_3$), 5.14 (1 H, br d, *J* 7, NH), 7.06–7.1 (2 H, m, aryl H), 7.12–7.21 (3 H, m, aryl H), 7.36–7.51 (3 H, m, aryl H), 7.71–7.75 (2 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 23.4 (q), 53.5 (d), 125.9 (d), 126.8 (d), 127.1 (d), 128.2 (d), 128.6 (d), 132.1 (d), 140.5 (s), 141.9 (s); *m*/*z* (CI) 262 (M^+ + 1, 100%), 246 (22), 184 (26), 158 (10), 120 (20), 105 (37).

Preparation of (*R*)-(−)-*N*-phenylsulfonyl-*N*-(1-phenylethyl)-*p*,*p*-diphenylphosphinamide 12

Sodium hydride (60% suspension in oil, 114 mg, 2.85 mmol) was washed with dry petrol (3 × 1 cm^3) then slurried in anhydrous THF (10 cm^3). (*R*)-(+)-*N*-Phenylsulfonyl-α-methylbenzylamine (prepared as described above) (0.5 g, 1.9 mmol) was then added portionwise under a rapid stream of nitrogen. The resulting white slurry was stirred at rt for 1 h. Diphenylphosphinic chloride (0.4 cm^3, 2.09 mmol) was added and the mixture stirred at rt for 8 h. The mixture was then poured into saturated aqueous ammonium chloride (5 cm^3) and extracted with ethyl acetate (3 × 5 cm^3). The combined organic extracts were dried (magnesium sulfate) and concentrated *in vacuo*. The residue was purified on silica eluting with 0→40% v/v ethyl acetate–petrol. This afforded phosphinamide **12** as a white solid (328 mg, 38%), mp 63–65 °C (from DCM–hexane) (Found: C, 67.3; H, 5.42; N, 2.9. $C_{26}H_{24}NO_3S$ requires C, 67.68; H, 5.21; N, 3.04%); $[a]_D^{26}$ −2.2 (*c* 0.74, chloroform); ν_{max}(Nujol)/cm^{-1} 1377, 1214, 1164, 1121, 903, 249, 726, 690; δ_H(270 MHz, $CDCl_3$) 1.84 (3 H, d, *J* 7, $CHCH_3$), 5.56 (1 H, dq, *J* 12.7 and 6.8, $CHCH_3$), 6.89 (2 H, m, aryl H), 7.1–7.27 (5 H, m, aryl H), 7.37–7.59 (9 H, m, aryl H), 7.61–7.89 (4 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 19.2 (q), 58.0 (d), 127.4, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 128.9, 132.2, 132.5, 132.8, 133.0, 133.2, 138.6 (s), 140.2 (s); δ_P(162 MHz, $CDCl_3$) 32.6 (1 P, s); *m*/*z* (CI) 462 (M^+ + 1, 5%), 398 (10), 358 (100), 320 (45), 274 (60), 232 (38), 218 (22), 201 (12), 143 (15), 105 (29), 89 (57).

(*S*)-4-Isopropyloxazolidin-2-one

This compound was prepared according to the published procedure[18] using (*S*)-valinol (1.51 g, 15 mmol), diethyl carbonate (3.6 cm^3, 30 mmol) and anhydrous potassium carbonate (200 mg, 1.5 mmol). (*S*)-4-Isopropyloxazolidin-2-one was isolated as a white solid which was further purified by recrystallisation from ethyl acetate–hexane (1.53 g, 79%), mp 70–71 °C (lit.,[18] 70–73 °C); $[a]_D^{20}$ −16.5 (*c* 6, ethanol) {lit.,[18] $[a]_D^{20}$ −17 (*c* 6, ethanol)}; δ_H(270 MHz, $CDCl_3$) 0.77 [3 H, d, *J* 6.8, $(CH_3)_2CH$], 0.83 [3 H, d, *J* 6.6, $(CH_3)_2CH$], 1.61 [1 H, m, $(CH_3)_2CH$], 3.51 (1 H, m, $CHCH_2$), 3.97 (1 H, dd, *J* 9.8 and 6.2, $CHCH_2$), 4.31 (1 H, t, *J* 8.6, $CHCH_2$), 7.11 (1 H, br s, NH).

(*S*)-*N*-Diphenylphosphinoyl-4-isopropyloxazolidin-2-one 13

Sodium hydride (60% suspension in oil, 340 mg, 8.53 mmol) then slurried in anhydrous THF (20 cm^3). (*S*)-4-Isopropyloxazolidin-2-one (1.0 g, 7.75 mmol) was then added portionwise under a rapid stream of nitrogen. The resulting mixture was then stirred for 1 h at rt. Diphenylphosphinic chloride (1.48 cm^3, 7.75 mmol) in anhydrous THF (20 cm^3) was added dropwise and the mixture stirred at rt for 6 h (or until all of the oxazolidinone was consumed by TLC). The mixture was then poured into saturated aqueous ammonium chloride (10 cm^3) and extracted with ethyl acetate (3 × 10 cm^3). The combined organic extracts were dried (magnesium sulfate) and concentrated *in vacuo*. Phosphinamide **13** was obtained as a white solid which was further purified by recrystallisation from DCM–hexane. Obtained as white needles (2.18 g, 85%), mp 147–149 °C (from DCM–hexane) (Found: C, 65.3; H, 6.1; N, 3.9. $C_{18}H_{20}NO_3P$ requires C, 65.65; H, 6.08; N, 4.26%); $[a]_D^{26}$ +120.2 (*c* 1.58, chloroform); ν_{max}(Nujol)/cm^{-1} 1747, 1439, 1393, 1327, 1205, 1126, 1052, 971, 752, 726, 698; δ_H(270 MHz, $CDCl_3$) 0.68 [3 H, d, *J* 7 $(CH_3)_2CH$], 0.8 [3 H, d, *J* 7, $(CH_3)_2CH$], 2.21 [1 H, m, $(CH_3)_2CH$], 4.19 (1 H, dd, *J* 7.3 and 3, $CHCH_2$), 4.34 (1 H, t, *J* 8.6, $CHCH_2$), 4.44–4.47 (1 H, m, $CHCH_2$), 7.25–7.81 (8 H, m, aryl H), 8.04 (2 H, dd, *J* 13.2 and 7.4, aryl H); δ_C(68 MHz, $CDCl_3$) 14.2 (q), 17.8 (q), 30.8 (d), 60.6 (dd, J_{PC} 3.3), 65.0 (dt, J_{PC} 7.7), 128.2 (dd, J_{PC} 2.2), 128.4, 131.2 (dd, J_{PC} 7.7), 131.4 (dd, J_{PC} 11), 132.0 (dd, J_{PC} 11), 132.6, 132.8 (dd, J_{PC} 2.2), 156.6 (d, J_{PC} 7.7), 203.6 (s); δ_P(162 MHz, $CDCl_3$) 27.0 (1 P, s); *m*/*z* (CI) 330 (M^+ + 1, 100%), 286 (10), 201 (15), 158 (32), 130 (36).

(*R*,*R*)-(+)-*N*,*N*′-Bis(1-phenylethyl)-*P*-(*p*-methoxyphenyl)phosphonamide 14

To a stirred solution of (*R*)-(+)-α-methylbenzylamine (1.7 cm^3, 13 mmol) and triethylamine (1.81 cm^3, 13 mmol) in DCM (20 cm^3) at 0 °C was added phosphorous oxychloride (0.61 cm^3, 6.5 mmol) dropwise over 5 min. The resulting cloudy mixture was allowed to warm slowly to rt and stirred for a further 8 h. The solvent was then removed *in vacuo* and the residue extracted with anhydrous ethyl acetate. The solution was filtered to remove hydrochloride salts and again concentrated *in vacuo* to give *R*,*R*-(+)-*N*,*N*′-*bis*(1-*phenylethyl*)*chlorophosphoramide* as a viscous pale yellow oil which decomposed slowly at rt: δ_H(270 MHz, $CDCl_3$) 1.33 (3 H, d, *J* 6.8, $CHCH_3$), 1.42 (3 H, d, *J* 6.6, $CHCH_3$), 3.41–3.69 (2 H, br s, NH), 4.37 (2 H, m, $CHCH_3$), 7.08–7.29 (10 H, m, aryl H); *m*/*z* (CI) 325 (M^+ + 1, 0.3%), 323 (M^+ + 1, 1%), 147 (5), 105 (100). The chloride (1.0 g, 3.1 mmol) was immediately redissolved in anhydrous diethyl ether (12 cm^3) and the solution cooled to 0 °C. To this solution was added *p*-methoxyphenylmagnesium bromide (0.25 M diethyl ether solution, 3 equiv., 37.2 cm^3, 9.3 mmol) in anhydrous diethyl ether (50 cm^3). The cloudy mixture was stirred at 0 °C for 1 h, then warmed slowly to rt and stirred for a further 3 h (or until all chloride was consumed by TLC). The mixture was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 10 cm^3). The combined organic extracts were dried (magnesium sulfate) and concentrated *in vacuo*. The residue was then purified on silica eluting with 0→5% v/v methanol–DCM to give phosphonamide **14** as a colourless oil (500 mg, 41%), $[a]_D^{12}$ +29.5 (*c* 1.3, chloroform); ν_{max}(film)/cm^{-1} 3212, 3028, 2970, 1598, 1494, 1454, 1382, 1294, 1205, 1120, 967, 831, 760, 899; δ_H(270 MHz, $CDCl_3$) 1.53 (3 H, d, *J* 7, $CHCH_3$), 1.61 (3 H, d, *J* 6.8, $CHCH_3$), 2.84 (1 H, m, NH), 2.94 (1 H, m, NH), 4.02 (3 H, s, MeO), 4.4–4.62 (2 H, m, $CHCH_3$), 7.05 (2 H, dd, *J* 9 and 3, aryl H), 7.25–7.53 (10 H, m, aryl H), 7.85 (2 H, dd, *J* 12.8 and 8, aryl H); δ_C(68 MHz, $CDCl_3$) 25.2 (q), 25.3 (q), 49.8 (d), 50.3 (d), 54.8 (q), 113.2 (dd, J_{PC} 14.3), 125.5 (d), 125.54 (d), 126.4 (d), 126.5 (d), 127.9 (d), 128.0 (d), 128.1 (d), 133.3 (dd, J_{PC} 10.9), 145.5 (s), 145.6 (d, J_{PC} 3.3), 161.6 (d, J_{PC} 3.4); δ_P(162 MHz, $CDCl_3$) 18.7 (1 P, s); *m*/*z* [(−) FAB] 393 (M^+ − 1, 100%), 331 (54), 303 (50), 182 (21) (Found: $[M - H]^+$, 393.1725. $C_{23}H_{26}N_2O_2P$ requires *m*/*z*, 393.1732).

(1*R*)-*N*-(1-Phenylethyl)-*P*-phenyl-*P*-pentafluorophenylphosphinamide 15

To a stirred solution of phenylphosphonic dichloride (1.1 cm^3, 7.76 mmol) in DCM (15 cm^3) at −78 °C was added a solution of (*R*)-(+)-α-methylbenzylamine (1.0 cm^3, 7.76 mmol) and triethylamine (1.08 cm^3, 7.76 mmol) in DCM (6 cm^3) dropwise

over 10 min. The resulting solution was allowed to warm slowly to rt and stirred for 10 h. The mixture was then concentrated *in vacuo* and the residue extracted with anhydrous diethyl ether. The combined extracts were filtered to remove hydrochloride salts and again concentrated *in vacuo* to give the intermediate chloride as a viscous pale yellow oil. This was then redissolved in anhydrous ether (20 cm^3) and the solution cooled to 0 °C. Pentafluorophenylmagnesium bromide (2 M diethyl ether solution, 9 cm^3, 18 mmol) in anhydrous diethyl ether (100 cm^3) was added to this solution and was stirred for 3 h. The mixture was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 7 ml). The combined extracts were dried (magnesium sulfate) and concentrated *in vacuo* to give an oil which was further purified by flash chromatography. Phosphinamide **15** was obtained as a colourless solid (824 mg, 28%). The compound was isolated as a single diastereomer (configuration at phosphorus was not determined), mp 208–210 °C (from DCM–hexane) (Found: C, 58.0; H, 3.6; N, 3.2. $C_{20}H_{15}F_5NOP$ requires C, 58.39; H, 3.65; N, 3.41%); $[a]_D^{22}$ −20.5 (*c* 0.2, methanol); ν_{max}(Nujol)/cm^{-1} 3262, 1523, 1468, 1377, 1293, 1215, 1120, 1101, 1086, 1018, 976, 958; δ_H(270 MHz, $CDCl_3$) 1.61 (3 H, d, *J* 7, CHCH_3), 3.59 (1 H, br t, *J* 8, NH), 4.68 (1 H, m, C*H*CH_3), 7.15–7.28 (5 H, m, aryl H), 7.45–7.61 (3 H, m, aryl H), 7.83 (2 H, dd, *J* 13.7 and 7.1, aryl H); δ_C(68 MHz, $CDCl_3$) 24.8 (dq, J_{PC} 7.7), 51.0 (d), 126.1, 127.5, 128.4, 128.8, 128.9, 130.8, 131.0, 133.0, 133.1, 143.5; δ_P(162 MHz, $CDCl_3$) 13.8 (1 p, s); *m*/*z* (CI) 412 (M^+ + 1, 100%), 392 (29), 308 (8), 120 (40).

Preparation of (*R*,*R*)-*N*,*N*′-bis(1-phenylethyl)oxamide

To a stirred solution of (*R*)-(+)-α-methylbenzylamine (2 cm^3, 15.5 mmol) and triethylamine (6.5 cm^3, 46.5 mmol) in DCM (40 cm^3) at 0 °C was added oxalyl chloride (0.7 cm^3, 7.8 mmol) dropwise over 5 min. The resulting thick white slurry was warmed to rt and stirred for 3 h. Saturated aqueous ammonium chloride (20 cm^3) was then added and the mixture extracted with DCM (3 × 10 cm^3). The combined organic extracts were dried (sodium sulfate) and concentrated *in vacuo* to give the bis-amide as a pale yellow solid which was further purified by recrystallisation from DCM–hexane to give white needles (1.95 g, 84%), mp 195–199 °C (from DCM–hexane); $[a]_D^{19}$ +97.1 (*c* 0.42, chloroform); ν_{max}(Nujol)/cm^{-1} 3301, 1650, 1511, 1224, 1126; δ_H(270 MHz, $CDCl_3$) 1.54 (6 H, d, *J* 7, CHCH_3), 5.06 (2 H, dq, *J* 7.6 and 7.5, C*H*CH_3), 7.23–7.36 (10 H, m, aryl H), 7.71 (2 H, br d, *J* 7.5, NH); δ_C(68 MHz, $CDCl_3$) 21.7 (q), 49.5 (d), 126.2 (d), 127.7 (d), 128.8 (d), 141.95 (s), 158.9 (s); *m*/*z* (CI) 297 (M^+ + 1, 13%), 193 (54), 145 (6), 105 (100) (Found: $[M + H]^+$, 297.1603. $C_{18}H_{21}N_2O_2$ requires *m*/*z*, 297.1602).

Preparation of (*R*,*R*)-*N*,*N*′-bis(1-phenylethyl)ethylenediamine

To a refluxing solution of (*R*,*R*)-*N*,*N*′-bis(1-phenylethyl)-oxamide (1.51 g, 5.1 mmol) in anhydrous THF (50 cm^3) was added lithium aluminium hydride (4 equiv., 0.77 g, 20.4 mmol) portionwise [**CARE!** vigorous effervescence]. The stirred mixture was heated at reflux for 48 h. It was then cooled to rt and water (1 cm^3) was then added dropwise followed by 15% w/v aqueous sodium hydroxide (5 cm^3). The resulting mixture was stirred at rt for 1 h. It was then filtered through Celite and the residues washed with DCM (3 × 50 cm^3). The filtrate was dried (magnesium sulfate) and concentrated *in vacuo*. The residue was a brown oil which was further purified by distillation under reduced pressure bp 145–148 °C/0.5 mmHg (lit.,[9c] 110 °C/0.02 mmHg). The product was a colourless oil (1.31 g, 95%), $[a]_D^{26}$ +69.9 (*c* 1, chloroform) (lit.,[9c] *ent*-$[a]_D^{20}$ −69.4 (*c* 1.1, chloroform); δ_H(270 MHz, $CDCl_3$) 1.35 (6 H, d, *J* 6.6, CHCH_3), 2.53 (4 H, s, CH_2), 3.4 (2 H, br s, NH), 3.65 (2 H, q, *J* 6.8, C*H*CH_3), 7.2–7.41 (10 H, m, aryl H).

Preparation of *N*,*N*′-dibenzylpropane-1,3-diamine

To a stirred solution of 1,3-diaminopropane (5 cm^3, 59.9 mmol) and triethylamine (20.8 cm^3, 149.7 mmol) in DCM (160 cm^3) at 0 °C was added benzoyl chloride (13.9 cm^3, 119.8 mmol) dropwise over 10 min. This resulted in the formation of a heavy white precipitate. The mixture was then allowed to warm to rt. It was then quenched by addition of saturated aqueous ammonium chloride (60 cm^3) and extracted with DCM (3 × 50 cm^3). The combined organic extracts were then washed with brine (30 cm^3), dried (sodium sulfate) and concentrated *in vacuo* to give a white solid. The crude bis-amide was redissolved in anhydrous THF (300 cm^3) and heated to reflux. Lithium aluminimum hydride (5.36 g, 141.8 mmol) was then added portionwise [**CARE!** vigorous effervescence] and the mixture heated at reflux for 36 h. It was then cooled to rt and water (10 cm^3) was then added dropwise with external cooling. 15% w/v aqueous sodium hydroxide (6 cm^3) was then added dropwise followed by a further 15 cm^3 of water. The resulting mixture was stirred at rt for 2 h. It was then filtered through Celite and the residue washed with diethyl ether (3 × 75 cm^3). The organic phase of the filtrate was separated, dried (magnesium sulfate) and concentrated *in vacuo* to give the diamine as a yellow oil which was further purified by distillation under reduced pressure bp 187–188 °C/0.5 mmHg (lit.,[9c] 189 °C/0.6 mmHg). The product was a colourless oil (10.35 g, 68%), δ_H(270 MHz, $CDCl_3$) 1.43 (2 H, br s, NH), 1.68 (2 H, p, *J* 6.8, 2-CH_2), 2.69 (4 H, t, *J* 6.8, 1- and 3-CH_2), 3.76 (4 H, s, CH_2Ph), 7.29 (10 H, m, aryl H).

Preparation of (*R*,*R*)-1,3-bis(1-phenylethyl)-2-ethyl-1,3,2-diazaphospholidine 2-oxide 16

To a stirred solution of (*R*,*R*)-*N*,*N*′-bis(1-phenylethyl)ethylenediamine (0.52 g, 1.92 mmol) and triethylamine (0.53 cm^3, 3.84 mmol) in DCM (20 cm^3) at 0 °C was added ethylphosphonic dichloride (0.21 cm^3, 1.92 mmol) dropwise. The resulting mixture was warmed to rt and stirred for 18 h. It was then poured into an equal volume of saturated aqueous ammonium chloride and extracted with DCM (3 × 10 cm^3). The combined organic extracts were dried (sodium sulfate) and concentrated *in vacuo*. The residue was purified on silica eluting with 0→10% v/v methanol–DCM. This afforded phosphonamide **16** as a colourless oil (328 mg, 50%), $[a]_D^{19}$ +31.8 (*c* 0.11, chloroform); ν_{max}(film)/cm^{-1} 3059, 2973, 2875, 1378, 1278, 1209; δ_H(270 MHz, $CDCl_3$) 1.05 (3 H, dt, *J* 19.8 and 7.7, CH_2CH_3), 1.61 (3 H, d, *J* 6.8, CHCH_3), 1.63 (3 H, d, *J* 7, CHCH_3), 1.94 (2 H, dq, *J* 16.1 and 7.7, C$H_2$$CH_3$), 2.76–2.93 (3 H, m, CH_2), 3.01–3.1 (1 H, m, CH_2), 4.42–4.62 (2 H, m, C*H*CH_3), 7.24–7.48 (10 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 7.8 (dq, J_{PC} 5.5), 19.2 (q), 20.1 (q), 23.1 (dt, J_{PC} 119.9), 41.9 (t), 42.0 (t), 53.0 (dd, J_{PC} 6.6), 53.8 (dd, J_{PC} 5.5), 128.6 (d), 127.1 (d), 127.15 (d), 127.3 (d), 128.3 (d), 128.4 (d), 142.1 (d, J_{PC} 4.3), 143.0 (d, J_{PC} 4.3); δ_P(162 MHz, $CDCl_3$) 40.8 (1 P, s); *m*/*z* (EI) 342 (M^+, 18%), 327 (90), 313 (21), 265 (10), 237 (13), 223 (25), 105 (100) (Found: $[M]^+$, 342.1853. $C_{20}H_{27}N_2OP$ requires *m*/*z*, 342.1861).

1,3-Dibenzyl-2-ethyl-1,3,2-diazaphosphinane 2-oxide 17

This compound was prepared according to the above procedure for **16** using *N*,*N*′-dibenzylpropane-1,3-diamine (1.5 g, 5.9 mmol), triethylamine (1.64 cm^3, 11.8 mmol) and ethylphosphonic dichloride (0.63 cm^3, 5.9 mmol) in DCM (50 cm^3). Phosphonamide **17** was isolated as a white solid (1.31 g, 68%), mp 79–82 °C (from DCM–hexane) (Found: C, 69.4; H, 7.7; N, 8.5. $C_{19}H_{25}N_2OP$ requires C, 69.51; H, 7.62; N, 8.54%); ν_{max}(Nujol)/cm^{-1} 1378, 1285, 1202, 1049, 920, 721; δ_H(270 MHz, $CDCl_3$) 1.19 (3 H, dt, *J* 18.5 and 7.7, CH_2CH_3), 1.53–1.61 (1 H, m, 5-CH_2), 1.71–1.85 (1 H, m, 5-CH_2), 1.93 (2 H, dq, *J* 14.6 and 7.5, C$H_2$$CH_3$), 2.93–3.02 (4 H, m, 4- and 6-CH_2), 4.09 (2 H, dd, *J* 14.9 and 7, CH_2Ph), 4.35 (2 H, dd, *J* 14.9 and 6.4, CH_2Ph), 7.23–7.41 (10 H, m, aryl H); δ_C(100 MHz, $CDCl_3$) 7.3 (dq, J_{PC} 5.5), 19.2 (dt, J_{PC} 115.2), 24.7 (t), 46.3 (t), 50.4 (t), 126.7 (d), 127.5 (d), 127.8 (d), 127.9 (d), 128.6 (d), 128.7 (d),

138.4 (d, J_{PC} 5.5); δ_P(162 MHz, $CDCl_3$) 34.1 (1 P, s); *m*/*z* (EI) 328 (M^+, 100%), 299 (14), 148 (35), 91 (14).

(*R*,*R*)-(+)-2-Phenylperhydro-1,3,2-benzodiazaphosphole 2-oxide 18

This compound was prepared according to the above method for **16** using (*R*,*R*)-(−)-1,2-diaminocyclohexane (400 mg, 3.51 mmol), triethylamine (0.98 cm^3, 7.02 mmol) and phenylphosphonic dichloride (0.51 cm^3, 3.51 mmol) in DCM (10 cm^3). Phosphonamide **18** was isolated as a white solid (696 mg, 84%), mp 186–188 °C (decomp.) (from DCM–petrol) (Found: C, 60.6; H, 7.4; N, 11.6. $C_{12}H_{17}N_2OP$ requires C, 61.02; H, 7.20; N, 11.86%); $[a]_D^{12}$ +4.3 (*c* 0.51, methanol); ν_{max}(Nujol)/cm^{-1} 3215, 1312, 1201, 1183, 1108, 1075, 951, 897, 744; δ_H(270 MHz, $CDCl_3$) 1.21–1.52 (4 H, m, CH_2), 1.64–1.98 (4 H, m, CH_2), 2.77–3.04 (3 H, m, C*H* and 2 × NH), 3.22 (1 H, m, C*H*), 7.31–7.49 (3 H, m, aryl H), 7.83 (2 H, m, aryl H); δ_C(68 MHz, CD_3OD) 26.2 (t), 26.8 (dt, J_{PC} 4.4), 34.8 (t), 36.2 (t), 57.1 (dd, J_{PC} 5.5), 59.1 (dd, J_{PC} 18), 129.8, 129.9, 130.0, 130.1, 132.6, 132.8, 132.9, 133.6; δ_P(162 MHz, $CDCl_3$) 25.8 (1 P, s); *m*/*z* (EI) 236 (M^+, 100%), 194 (7), 101 (77), 86 (47) (Found: $[M]^+$, 236.1037. $C_{12}H_{17}N_2OP$ requires *m*/*z*, 236.1078).

Preparation of (1*S*,2*R*)-(−)-3-methyl-1-phenyl-2,3-dihydro-1*H*-2,1-benzazaphosphole 1-oxide 19

This compound was obtained by desilylation of a sample of the corresponding TBDPS protected phosphinamide. The synthesis and X-ray structure of this precursor has been reported.[7] The deprotection was effected as follows. To a stirred solution of (1*S*,2*R*)-(−)-2-(*tert*-butyldiphenylsilyl)-3-methyl-1-phenyl-2,3-dihydro-1*H*-benzazaphosphole 1-oxide (1.0 g, 2.07 mmol) in THF (17 cm^3) was added TBAF (1 M THF solution, 4.1 cm^3, 4.15 mmol) dropwise. The resulting solution was stirred at rt for 3 h. It was then poured into saturated aqueous ammonium chloride (10 cm^3) and extracted with ethyl acetate (3 × 5 cm^3). The combined organic extracts were dried (sodium sulfate) and concentrated *in vacuo*. The residue was purified on silica eluting with 0→70% v/v ethyl acetate–petrol. This afforded **19** as a white solid (457 mg, 91%), mp 232–234 °C (decomp.) (from DCM–hexane) (Found: C, 69.0; H, 5.8; N, 5.6. $C_{14}H_{14}NOP$ requires C, 69.13; H, 5.80; N, 5.76%); $[a]_D^{20}$ −131.2 (*c* 0.87, methanol); ν_{max}(Nujol)/cm^{-1} 3195, 2971, 1446, 1209, 1182, 1115, 754, 730, 694; δ_H(400 MHz, $CDCl_3$) 1.64 (3 H, d, *J* 6.4, CHCH_3), 3.71 (1 H, br d, *J* 11.6, NH), 4.82 (1 H, m, C*H*CH_3), 7.37–7.41 (4 H, m, aryl H), 7.42–7.49 (1 H, m, aryl H), 7.52–7.64 (2 H, m, aryl H), 7.67–7.72 (2 H, m, aryl H); δ_C(100 MHz, $CDCl_3$) 25.7 (q), 56.1 (dd, J_{PC} 7.3), 123.9, 124.0, 128.6, 128.8, 128.9, 130.4 (s), 132.2 (dd, J_{PC} 23.8), 132.6 (dd, J_{PC} 11.4), 134.0 (s), 149.0 (d, J_{PC} 20.1); δ_P(162 MHz, $CDCl_3$) 34.0 (1 P, s); *m*/*z* (CI) 244 (M^+, 100%), 228 (20).

(*R*,*R*)-(−)-1,3-Dimethyl-2-chloroperhydro-1,3,2-benzodiazaphosphole 2-oxide

To a stirred solution of (*R*,*R*)-(−)-*N*,*N*′-dimethylcyclohexane-1,2-diamine (1.36 g, 9.58 mmol) and triethylamine (3.3 cm^3, 23.95 mmol) in DCM (30 cm^3) at 0 °C was added phosphorus oxychloride (0.9 cm^3, 9.58 mmol) dropwise over 5 min. The resulting solution was then warmed to rt and stirred for 12 h. It was then concentrated *in vacuo* and the residue purified on silica eluting with 0→30% v/v ethyl acetate–petrol. This afforded the chloride as a white solid which was further purified by recrystallisation from toluene in DCM (50 cm^3). The chloride was obtained as white needles (1.92 g, 90%), mp 68–69 °C (from DCM–hexane) (lit.,[9a] 70 °C); $[a]_D^{21}$ −55.4 (*c* 5.5, DCM) (lit.,[9a] $[a]_D^{20}$ −57.5 (*c* 5.7, DCM); δ_H(270 MHz, $CDCl_3$) 1.09–1.32 (4 H, m, CH_2), 1.79–1.96 (4 H, m, CH_2), 2.45–2.52 (4 H, m, C*H* and NMe), 2.59 (3 H, d, *J* 11.9, NMe), 2.78 (1 H, m, C*H*).

(*R*,*R*,*R*)-2-(1-Phenylethyl)aminoperhydro-1,3,2-benzodiazaphosphole 2-oxide 20

To a stirred solution of (*R*)-(+)-α-methylbenzylamine (0.07 cm^3, 0.54 mmol) in anhydrous THF (15 cm^3) at 0 °C was added *n*-butyllithium (1.43 M hexane solution, 0.32 cm^3, 0.45 mmol) dropwise. The solution was then stirred for 20 min at 0 °C, warmed to rt and stirred for a further 10 min. It was then again cooled to 0 °C and a solution of (*R*,*R*)-1,3-dimethyl-2-chloroperhydro-1,3,2-benzodiazaphosphole 2-oxide (100 mg, 0.45 mmol) in anhydrous THF (2 cm^3) was added dropwise. The mixture was allowed to warm slowly to rt and stirred for 12 h. It was then poured into saturated aqueous ammonium chloride (10 cm^3) and extracted with ethyl acetate (3 × 7 cm^3). The combined organic extracts were dried (magnesium sulfate) and concentrated *in vacuo*. The residue was purified on silica eluting with 0→10% v/v methanol–DCM. Phosphoramide **20** was obtained as a white solid (61 mg, 44%), mp 138–142 °C (from DCM–hexane); $[a]_D^{22}$ −11.0 (*c* 0.72, chloroform); ν_{max}(Nujol)/cm^{-1} 3239, 2993, 2958, 1641, 1451, 1296, 1193, 1132, 1092, 1040, 978, 950, 899, 761, 702; δ_H(270 MHz, $CDCl_3$) 1.19–1.31 (4 H, m, CH_2), 1.42 (3 H, d, *J* 6.8, CHCH_3), 1.81–1.95 (4 H, m, CH_2), 2.13 (3 H, d, *J* 10.4, NMe), 2.39 (1 H, m, C*H*), 2.53 (3 H, d, *J* 11.5, NMe), 2.56–2.66 (1 H, m, C*H*), 3.01 (1 H, br m, NH), 4.16 (1 H, m, C*H*CH_3), 7.28–7.34 (5 H, m, aryl H); δ_C(100 MHz, $CDCl_3$) 24.3 (t), 25.8 (q), 26.3 (q), 27.9 (q), 28.5 (dt, J_{PC} 8), 51.3 (d), 63.1 (dd, J_{PC} 8.8), 62.8 (dd, J_{PC} 8.8), 125.8 (d), 126.9 (d), 128.5 (d), 146.1 (s); δ_P(162 MHz, $CDCl_3$) 27.3 (1 P, s); *m*/*z* (CI) 308 (M^+ + 1, 100%), 292 (10), 233 (7), 120 (21) (Found: $[M + H]^+$, 308.1883. $C_{16}H_{27}N_3OP$ requires *m*/*z*, 308.1892).

Phosphoramide 21 (*R*,*R*,*S*-diastereomer)

This compound was prepared according to the above procedure using (*S*)-(−)-α-methylbenzylamine (0.07 cm^3, 0.54 mmol), *n*-butyllithium (1.43 M hexane solution, 0.32 cm^3, 0.45 mmol) and *R*,*R*-1,3-dimethyl-2-chloroperhydro-1,3,2-benzodiazaphosphole 2-oxide (100 mg, 0.45 mmol) in anhydrous THF (2 cm^3). Phosphoramide **21** was obtained as a white solid (50 mg, 36%), mp 144–145 °C (from DCM–hexane); $[a]_D^{26}$ −143.5 (*c* 0.37, chloroform); ν_{max}(Nujol)/cm^{-1} 3239, 2993, 2956, 1450, 1297, 1192, 1132, 1072, 1040, 978, 701; δ_H(270 MHz, $CDCl_3$) 1.17–1.27 (4 H, m, CH_2), 1.41 (3 H, d, *J* 6.6, CHCH_3), 1.64–1.79 (3 H, m, CH_2), 1.97 (1 H, m, CH_2), 2.06 (3 H, d, *J* 11.4, NMe), 2.54–2.56 (5 H, d overlapping m, *J* 10.6, NMe and C*H*), 3.08 (1 H, br m, NH), 4.02–4.08 (1 H, m, C*H*CH_3), 7.21–7.27 (5 H, m, aryl H); δ_C(68 MHz, $CDCl_3$) 24.2 (t), 26.2 (q), 27.8 (q), 28.2 (dt, J_{PC} 8.8), 28.3 (q), 51.0 (d), 64.0 (dd, J_{PC} 8.7), 65.1 (dd, J_{PC} 9.9), 126.0 (d), 128.2 (d), 128.4 (d), 146.1 (s); δ_P(162 MHz, $CDCl_3$) 28.1 (1 P, s); *m*/*z* (EI) 307 (M^+, 5%), 232 (50), 204 (40), 189 (23), 120 (30), 42 (50) (Found: $[M + H]^+$, 308.1883. $C_{16}H_{27}N_3OP$ requires *m*/*z*, 308.1892).

(*R*,*R*)-2-Benzylaminoperhydro-1,3,2-benzodiazaphosphole 2-oxide 22

This compound was prepared according to the above general procedure using benzylamine (0.06 cm^3, 0.54 mmol), *n*-butyllithium (1.56 M hexane solution, 0.29 cm^3, 0.45 mmol) and (*R*,*R*)-(−)-1,3-dimethyl-2-chloroperhydro-1,3,2-benzodiazaphosphole 2-oxide (100 mg, 0.45 mmol) in anhydrous THF (2 cm^3). Phosphoramide **22** was obtained as a viscous oil (72 mg, 55%), $[a]_D^{19}$ −61.4 (*c* 0.96, chloroform); ν_{max}(film)/cm^{-1} 3229, 2933, 2858, 1602, 1449, 1372, 1296, 1194, 1132, 1073, 977, 899, 759, 702; δ_H(270 MHz, $CDCl_3$) 1.11–1.25 (4 H, m, CH_2), 1.75 (2 H, m, CH_2), 1.95 (2 H, m, CH_2), 2.45 (3 H, d, *J* 8.2, NMe), 2.48 (3 H, d, *J* 7.7, NMe), 2.55–2.72 (2 H, m, C*H*), 3.21 (1 H, br s, NH), 3.98 (2 H, br d, *J* 7, CH_2Ph), 7.22–7.31 (5 H, m, aryl H); δ_C(100 MHz, $CDCl_3$) 24.2 (t), 28.2 (q), 28.3 (q), 28.4 (t), 44.9 (t), 63.0 (dd, J_{PC} 9.1), 64.6 (dd, J_{PC} 9.1), 127.0 (d), 127.1 (d), 128.4 (d), 140.3 (dd, J_{PC} 5.5); δ_P(162 MHz, $CDCl_3$) 28.9 (1 P, s); *m*/*z* (EI) 293 (M^+, 100%), 188 (5), 106 (19) (Found: $[M + H]^+$, 294.1725. $C_{15}H_{25}N_3OP$ requires *m*/*z*, 294.1735).

General procedure for the formation of (5*S*)-2-alkyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octanes[19]

Alkylphosphonic dichloride (11 mmol) was added dropwise to an ice cold stirred solution of (*S*)-(+)-pyrrolidine-2-methanol (10 mmol) and triethylamine (22 mmol) in anhydrous DCM (20 cm^3). The resulting solution was allowed to warm to rt over a 3 h period and then stirred at this temperature for a further 12 h. The reaction mixture was filtered and the solvent removed *in vacuo*. The residue was purified by column chromatography.

(5*S*)-2-Phenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane 27a

Following the general procedure for bicyclooctane formation, phenylphosphonic dichloride (6.36 g, 4.63 cm^3, 32.6 mmol) was added dropwise to an ice cold stirred solution of (*S*)-(+)-pyrrolidine-2-methanol (3.00 g, 2.93 cm^3, 29.7 mmol) and triethylamine (6.60 g, 9.09 cm^3, 65.3 mmol) in anhydrous DCM (60 cm^3). After standard work-up, the crude ^{1}H NMR spectrum showed a (3:1) mixture of diastereomers. This was purified by column chromatography using MeOH–DCM–NEt_3 (2:98:0.1) as the eluent to give (5*S*)-2-phenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane **27a** (4.57 g, 69%) as a single diastereomer. This was further purified by recrystallisation from *n*-hexane–DCM (4:1); mp 115–117 °C (from *n*-hexane–DCM); $[\alpha]_D$ +94.4° (*c* 1.025, DCM) (Found: C, 59.2; H, 6.4; N, 6.3. Calc. for $C_{11}H_{14}NO_2P$: C, 59.19; H, 6.32; N, 6.28%); ν_{max}/cm^{-1} 1438 (Ph–P), 1235 (P=O), 1007 ($POCH_2$); δ_H(270 MHz; $CDCl_3$) 1.75–2.11 (4 H, m, CH_2CH_2), 2.86–3.00 (1 H, m, CH_2N), 3.70–3.81 (1 H, m, CH_2N), 3.90 (1 H, dt, *J* 2.3 and 8.6, CH_2O), 4.08–4.18 (1 H, m, CH_2O), 4.33 (1 H, ddd, *J* 6.5, 8.6 and 20.4, 5-CH), 7.41–7.56 (3 H, m, Ph), 7.78–7.87 (2 H, m, Ph); δ_C(62.9 MHz, $CDCl_3$) 27.4 and 29.8 (CH_2), 45.2 (CH_2N), 63.01 (CH, d, *J* 7.6), 69.5 (CH_2, *J* 1.9, CH_2OH), 127.8, 128.1, 128.3, 131.1, 131.4, 131.5, 131.8 (Ph); *m*/*z* (CI) 241 (M + NH_4^+, 7%), 224 (100), 146 (10), 120 (57); δ_P(162 MHz, $CDCl_3$) 39.6. The minor diastereomer gave peaks in the ^{1}H NMR spectrum at 3.02–3.15 (1 H, m), 4.05 (1 H, sextet, *J* 4.2), 4.73 (1 H, ddd, *J* 6.1, 8.8 and 14.7, 5-CH).

Standard procedure for the formation of *N*-(dialkylphosphoryl)-(*S*)-pyrrolidine-2-methanols

Alkylmagnesium bromide (1.2 mmol) was added dropwise to a stirred solution of (5*S*)-2-alkyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane (1.0 mmol) in anhydrous THF (10 cm^3) at −78 °C under a nitrogen atmosphere. The resulting solution was allowed to slowly warm to rt over a 2 h period and then stirred at this temperature for a further 6 h. The reaction was quenched with water and acidified with sat. aq. NH_4Cl. The aqueous phase was extracted with EtOAc (3 × 20 cm^3) the combined organic layers washed with water and brine, dried ($MgSO_4$) and the solvent removed *in vacuo*.

(*S*)-*N*-(Diphenylphosphoryl)pyrrolidine-2-methanol 24

Following the general procedure for ring opening the bicyclooctane, phenylmagnesium bromide (1 M in THF; 2.13 cm^3, 2.13 mmol) was added to a stirred solution of **27a** (432 mg, 1.94 mmol) in anhydrous THF (20 cm^3) under a nitrogen atmosphere at −78 °C. After allowing the mixture to warm to rt and standard work-up, the crude product was purified by column chromatography using MeOH–DCM–NEt_3 (5:95:0.1) as the eluent. This gave **24** (441 mg, 76%) as a colourless oil, which gave a white solid on standing. This was further purified by recrystallisation from *n*-hexane–DCM (4:1); mp 119–121 °C (from *n*-hexane–DCM); $[\alpha]_D$ +62° (*c* 0.5, DCM) (Found: C, 67.5; H, 6.7; N, 4.65. $C_{17}H_{20}NO_2P$ requires C, 67.76; H, 6.69; N, 4.65%); ν_{max}/cm^{-1} 3373 (OH), 1438 (P–Ph), 1172 (P=O); δ_H(270 MHz, $CDCl_3$) 1.68–2.00 (2 H, m, CH_2), 2.03–2.09 (2 H, m, CH_2), 3.07–3.15 (2 H, m, CH_2N), 3.45–3.53 (2 H, m, CH_2O), 3.70–3.73 (1 H, m, 2-CH), 5.01 (1 H, br s, exchangeable, OH), 7.41–7.57 (6 H, m, Ph), 7.75–7.91 (4 H, m, Ph); δ_C(67.8 MHz, $CDCl_3$) 25.4 (d, *J* 8.8, CH_2), 29.5 (d, *J* 6.6, CH_2), 48.6 (d, *J* 3.3, CH_2), 61.5 (CH), 65.4 (CH_2OH), 128.6, 128.7, 128.8 (Ph), 130.2, 130.8 (C_{quat} Ph), 131.8, 131.9, 132.1, 132.3, 132.4, 132.7 (Ph); δ_P(162 MHz, $CDCl_3$) 28.4; *m*/*z* (CI) 302 (M + H^+, 100%), 270 (25), 223 (11), 205 (64), 149 (95).

(2S_P5*S*)-2,4,4-Triphenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo-[3.3.0]octane 27b

Following the general procedure for bicyclooctane formation, phenylphosphonic dichloride (2.01 g, 1.46 cm^3, 10.3 mmol) was added dropwise to an ice cold stirred solution of (*S*)-(−)-α,α-diphenylpyrrolidine-2-methanol (2.38 g, 9.39 mmol) and triethylamine (2.09 g, 2.88 cm^3, 20.7 mmol) in anhydrous DCM (20 cm^3). After standard work-up the crude ^{1}H NMR spectrum showed a 7:1 mixture of diastereomers which was purified by column chromatography using DCM–NEt_3 (99.9:0.1) then EtOAc–DCM–NEt_3 (10:90:0.1) as the eluents. This gave **27b** (2.48 g, 70%) as a white powder. This was further purified by recrystallisation from *n*-hexane–DCM (4:1); mp 158–161 °C (from *n*-hexane–DCM); $[\alpha]_D$ −236.4 (*c* 0.55, $CHCl_3$) {lit.,[6b] $[\alpha]_D$ −235.6 (*c* 1.15, $CHCl_3$)} (Found: C, 73.4; H, 5.8; N, 3.7; $C_{23}H_{22}NO_2P$ requires C, 73.58; H, 5.91; N, 3.73%); ν_{max}/cm^{-1} 1447 (Ph–P), 1241 (P=O); δ_H(270 MHz, $CDCl_3$) 1.56–1.84 (4 H, m, CH_2CH_2), 2.95–3.03 (1 H, m, CH_2N), 3.67–3.79 (1 H, m, CH_2N), 4.70 (1 H, q, *J* 6.4, 5-CH), 7.24–7.61 (15 H, m, Ph); δ_C(67.8 MHz; $CDCl_3$) 26.3 (CH_2), 30.2 (CH_2), 44.8 (CH_2), 71.3 (5-CH), 88.7 (C_{quat}), 126.5, 126.7, 127.4, 128.0, 128.2, 128.3 (CH, Ph), 129.9 (C_{quat} Ph), 131.6, 131.7 (CH Ph), 132.5 (C_{quat} Ph), 141.2 (C_{quat} Ph), 143.6 (d, *J* 4.4 Hz, C_{quat} Ph); δ_P(162 MHz, $CDCl_3$) 36.09; *m*/*z* (CI) 376 (M + H^+, 100%), 278 (7), 236 (36), 205 (8), 193 (11), 149 (10), 109 (12), 97 (22), 85 (72). Characterisation for the minor diastereomer; mp 157–160 °C; $[\alpha]_D$ −64.6 (*c* 0.28, DCM); δ_H(250 MHz, $CDCl_3$) 1.20–1.40 (1 H, m, CH_2), 1.53–2.00 (3 H, m, CH_2), 2.99–3.24 (2 H, m, NCH_2), 4.76 (1 H, ddd, *J* 5.2, 11.0 and 16.5, 5-CH), 7.24–7.87 (15 H, m, Ph); δ_C(62.9 MHz, $CDCl_3$) 24.6 (CH_2), 30.6 (d, *J* 27.6, CH_2), 44.4 (d, *J* 3.9, CH_2), 72.6 (d, *J* 8.9, 5-CH), 89.7 (C_{quat}), 125.3, 126.3, 126.5, 127.3, 128.0, 128.1, 128.4, 128.6, 129.1, 132.4 (Ph), 133.1 (d, *J* 10.8), 142.0, 144.7 (Ph); δ_P(162 MHz, $CDCl_3$) 34.5; *m*/*z* (CI) 376 (M + H^+, 55%), 236 (100), 193 (38), 165 (35), 116 (15), 91 (21), 78 (16) and 70 (51).

(*S*)-*N*-(Diphenylphosphoryl)-α,α-diphenylpyrrolidine-2-methanol 25

Following the general procedure for ring opening the bicyclooctane phenylmagnesium bromide (1 M in THF; 1.47 cm^3, 1.47 mmol) was added to a stirred solution of (2S_P5*S*)-2,4,4-triphenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane (**27b**) (500 mg, 1.33 mmol) in anhydrous THF (20 cm^3) under a nitrogen atmosphere at −78 °C. After allowing the mixture to warm to rt and standard work-up the crude product was purified by column chromatography using EtOAc–DCM–NEt_3 (5:95:0.1) then EtOAc–DCM–NEt_3 (10:90:0.1) as the eluents. This gave **25** (197 mg, 33%) as a white solid.

Alternative method for the formation of (*S*)-*N*-(diphenylphosphoryl)-α,α-diphenylpyrrolidine-2-methanol 25

Diphenylphosphinic chloride (1.01 g, 815 cm^3, 4.28 mmol) was added dropwise to an ice cold stirred solution of (*S*)-(−)-α,α-diphenylpyrrolidine-2-methanol (986 mg, 3.89 mmol) and triethylamine (433 mg, 596 cm^3, 4.28 mmol) in anhydrous DCM (20 cm^3). The resulting suspension was allowed to slowly warm to rt over a 2 h period and then stirred at rt for a further 4 h. After this period the reaction was diluted with water (10 cm^3), acidified with sat. aq. NH_4Cl (10 cm^3) and the organic layer separated. The aqueous layer was extracted with DCM (3 × 20 cm^3). The combined organic layers were washed with water and brine, dried ($MgSO_4$) and the solvent removed *in vacuo*. The residue was purified by column chromatography using EtOAc–DCM–NEt_3 (5:95:0.1) then EtOAc–DCM–NEt_3 (10:90:0.1)

as the eluents. This gave **25** (1.09 g, 62%) as a white solid which was further purified by recrystallisation from *n*-hexane–DCM (4:1); mp 164–166 °C (from *n*-hexane–DCM); $[\alpha]_D$ −66.3 (*c* 1.55, DCM) (Found: C, 76.4; H, 6.3; N, 3.1. $C_{29}H_{28}NO_2P$ requires C, 76.80; H, 6.22; N, 3.09%); ν_{max}/cm^{-1} 3252 (OH), 1437 (P–Ph), 1174 (P=O); δ_H(270 MHz, $CDCl_3$) 1.14–1.41 (2 H, m, CH_2CH_2), 2.02–2.19 (2 H, m, CH_2CH_2), 2.38 (1 H, dt, *J* 7.7 and 17.1, NCH_2), 2.91 (1 H, ddd, *J* 4.1, 8.6 and 18.9, NCH_2), 4.80 (1 H, dd, *J* 8.2 and 13.6, 2-CH), 7.04 (1 H, br s, exchangeable, OH), 7.22–7.58 (18 H, m, Ph), 7.69–7.76 (2 H, m, Ph); δ_C(62.9 MHz, $CDCl_3$) 25.0 (d, *J* 4.4, CH_2), 31.0 (CH_2), 49.9 (CH_2), 67.6 (2-CH), 80.1 (C_{quat}), 126.7, 126.9, 127.2, 127.8, 128.0, 128.3, 128.5, 128.6, 129.9, 130.5, 131.6, 131.8, 131.9, 132.0 and 132.4 (Ph), 144.4 and 146.1 (C_{quat} Ph); δ_P(162 MHz, $CDCl_3$) 34.4; *m/z* (CI) 454 ($M + H^+$, 1%), 436 (26), 279 (41), 205 (70), 149 (100).

(5*S*)-2-Methyl-4,4-diphenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane 27c

Following the general procedure for bicyclooctane formation, methylphosphonic dichloride (848 mg, 6.38 mmol) in anhydrous DCM (5 cm^3) was added dropwise to an ice cold stirred solution of (*S*)-(−)-α,α-diphenylpyrrolidine-2-methanol (1.47 g, 5.80 mmol) and triethylamine (1.47 g, 2.02 cm^3, 14.5 mmol) in anhydrous DCM (20 cm^3). After standard work-up the crude ^1H NMR spectrum showed a 3:2 mixture of diastereomers. This was purified by column chromatography using EtOAc–DCM–Et_3N (25:75:0.1) then EtOAc–DCM–NEt_3 (50:50:0.1) as the eluents to give **27c** (1.35 g, 74%) as 2 separate diastereomers. Characterisation for the less polar diastereomer; mp 143–145 °C; $[\alpha]_D$ 289.5 (*c* 0.42, DCM) (Found: C, 68.7; H, 6.2; N, 4.5. $C_{18}H_{20}NO_2P$ requires C, 69.00; H, 6.43; N, 4.47%); ν_{max}/cm^{-1} 2973 and 2888 (CH), 1448 (P–alkyl), 1240 (P=O); δ_H(250 MHz, $CDCl_3$) 1.32 (3 H, d, *J* 17.2, CH_3), 1.41–1.77 (4 H, m, CH_2CH_2), 2.98–3.14 (1 H, m, NCH_2), 3.68–3.83 (1 H, m, NCH_2), 4.50 (1 H, ddd, *J* 6.1, 8.5 and 19.0, 5-CH), 7.20–7.50 (10 H, m, Ph); δ_C(62.9 MHz, $CDCl_3$) 15.9 (d, *J* 134.9, CH_3), 25.4 (CH_2), 30.1 (CH_2), 45.0 (CH_2), 70.0 (d, *J* 5.9, 5-CH), 87.0 (C_{quat}), 125.8, 126.6, 127.3, 127.9, 128.1 and 128.3 (Ph), 141.6 (d, *J* 5.9, C_{quat} Ph); δ_P(162 MHz, $CDCl_3$) 50.2; *m/z* (CI) 314 ($M + H^+$, 48%), 236 (100), 206 (9), 167 (28) and 131 (28). Characterisation of the more polar diastereomer; mp 154–156 °C; $[\alpha]_D$ −209.5 (*c* 0.53, DCM) (Found: C, 68.7; H, 6.2; N, 4.3; $C_{18}H_{20}NO_2P$ requires C, 69.00; H, 6.43; N, 4.47%); ν_{max}/cm^{-1} 1449 (P–alkyl), 1237 (P=O); δ_H(250 MHz, $CDCl_3$) 1.06–1.29 (1 H, m, CH_2), 1.62–1.83 (1 H, m, CH_2), 1.74 (3 H, d, *J* 15.4, CH_3), 1.84–2.00 (2 H, m, CH_2), 3.21–3.49 (2 H, m, NCH_2), 4.59 (1 H, ddd, *J* 5.5, 11.0 and 17.5, 5-CH), 7.22–7.38 (8 H, m, Ph), 7.56–7.61 (2 H, m, Ph); δ_C(250 MHz, $CDCl_3$) 13.1 (d, *J* 118, CH_3), 24.8 (CH_2), 29.7 (CH_2), 44.1 (d, *J* 3.9, CH_2), 72.3 (d, *J* 8.9, 5-CH), 89.2 (C_{quat}), 125.1, 126.2, 127.3, 127.9, 128.0 and 128.3 (Ph), 141.8 (d, *J* 6.9, C_{quat} Ph), 144.1 (C_{quat} Ph); δ_P(162 MHz, $CDCl_3$) 44.3; *m/z* (CI) 314 ($M + H^+$, 100%), 236 (93), 183 (21), 167 (33) and 131 (50).

(*S*)-*N*-(Dimethylphosphoryl)-α,α-diphenylpyrrolidine-2-methanol 26

Following the general procedure for ring opening the bicyclooctane methylmagnesium bromide (1.4 M in THF; 1.31 cm^3 1.83 mmol) was added to a stirred solution of (5*S*)-2-methyl-4,4-diphenyl-2-oxo-3-oxa-1-aza-2-phosphabicyclo[3.3.0]octane **27c** (479 mg, 1.53 mmol) in anhydrous THF (15 cm^3) under a nitrogen atmosphere at −78 °C. After allowing the mixture to warm to rt and standard work-up the crude product was purified by column chromatography using MeOH–DCM–Et_3N (1:99:0.1) then MeOH–DCM–Et_3N (1.5:98.5:0.1) as the eluents. This gave **26** (375 mg, 74%) as a white solid. This was further purified by recrystallisation from *n*-hexane–DCM (4:1); mp 139–141 °C (from *n*-hexane–DCM); $[\alpha]_D$ −93.3 (*c* 0.15, DCM) (Found: C, 69.1; H, 7.2; N, 4.2. $C_{19}H_{24}NO_2P$ requires C, 69.28; H, 7.34; N, 4.25%); ν_{max}/cm^{-1} 3242 (OH), 1449 (P–Ph), 1164 (P=O); δ_H(250 MHz, $CDCl_3$) 0.83–0.99 (1 H, m, CH_2), 1.35 (3 H, d, *J* 12.8, CH_3), 1.44–1.59 (1 H, m, CH_2), 1.93–2.18 (2 H, m, CH_2), 2.50–2.65 (1 H, m, NCH_2), 2.88 (1 H, ddd, *J* 6.1, 9.3 and 17.2, NCH_2), 4.69 (1 H, dt, *J* 4.2 and 8.6, 2-CH), 7.20–7.44 (10 H, m, Ph); δ_C(MHz, $CDCl_3$) 13.4 (d, *J* 80.7, CH_3), 16.6 (d, *J* 90.6, CH_3), 24.8 (d, *J* 4.9, CH_2), 30.6 (d, *J* 4.9, CH_2), 47.6 (d, *J* 4.9, CH_2), 65.9 (d, *J* 2.0, 2-CH), 79.7 (C_{quat}), 126.7, 126.9, 127.0, 127.7, 127.8, 128.6 (Ph), 144.3 and 146.4 (C_{quat} Ph); δ_P(162 MHz, $CDCl_3$) 48.3; *m/z* 330 ($M + H^+$, 7%), 312 (91), 254 (20), 238 (79), 183 (37), 146 (46), 112 (42), 95 (100).

General ketone reduction procedure using phosphinamides 24–26

A sample of (*S*)-*N*-(dimethylphosphoryl)-α,α-diphenylpyrrolidine-2-methanol **26** (16 mg, 0.05 mmol) was azeotroped *in situ* under a nitrogen atmosphere with anhydrous toluene (3 × 2 cm^3). The catalyst was dissolved in toluene (2 cm^3) to which was added borane–methyl sulfide (2 M in toluene; 255 cm^3, 0.51 mmol). The resulting solution was heated to 110 °C and once the temperature had stabilised chloroacetophenone (75 mg, 0.49 mmol) in anhydrous toluene (2 cm^3) was added dropwise over a 10 minute period. After a further 20 min the reaction was complete as assayed by thin layer chromatography and worked up as described above. This gave (*S*)-(+)-2-chloro-1-phenylethanol (61 mg, 80%) as a colourless oil in 92% ee. Unreacted catalyst could be recovered by flash chromatography.

Acknowledgements

We thank the EPSRC for funding of this project (earmarked studentship to J. R. S. and research grant to B. B. and M. P. G.), Bath University for support of final year project students (H. T., N. P. K.) and Dr J. Ballantine (EPSRC MS service, Swansea) for HRMS analyses of certain compounds. Dr R. V. H. Jones and Dr N. Wallis (Zeneca FCMO) are thanked for assistance with the development of chiral HPLC assays.

References

1 For excellent recent surveys in asymmetric catalysis see (*a*) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, John Wiley and Sons Ltd., New York, 1994; (*b*) *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH Press, Berlin, 1993; (*c*) V. K. Singh, *Synthesis*, 1992, 605.

2 *Hydrogenation of compounds containing C=C, C=O and C=N bonds*, by M. Wills, in the series *Chemistry of the Functional Groups*, edited by S. Patai, Supplement A3: The Chemistry of Double-Bonded Functional Groups Part 1, ch. 15, pp. 781–842.

3 (*a*) S. Wallbaum and J. Martens, *Tetrahedron*: *Asymmetry*, 1992, **3**, 1481; (*b*) L. Deloux and M. Srebnik, *Chem. Rev.*, 1993, **93**, 763; (*c*) M. Palmer, T. Walsgrove and M. Wills, *J. Org. Chem.*, 1997, **62**, 5226 and references therein.

4 (*a*) B. Burns, J. R. Studley and M. Wills, *Tetrahedron Lett.*, 1993, **34**, 7105; (*b*) B. Burns, N. P. King, J. R. Studley, H. Tye and M. Wills, *Tetrahedron*: *Asymmetry*, 1994, **5**, 801; (*c*) M. P. Gamble, J. R. Studley and M. Wills, *Tetrahedron Lett.*, 1996, **37**, 2853; (*d*) M. P. Gamble, J. R. Studley and M. Wills, *Tetrahedron*: *Asymmetry*, 1996, **7**, 3071; (*e*) B. Burns, M. P. Gamble, A. R. C. Simm, J. R. Studley, N. W. Alcock and M. Wills, *Tetrahedron*: *Asymmetry*, 1997, **8**, 73.

5 D. Barr, W. Clegg, R. E. Mulvey and R. Snaith, *J. Chem. Soc., Chem. Commun.*, 1984, 79; (*b*) S. E. Denmark and R. L. Dorow, *J. Am. Chem. Soc.*, 1990, **112**, 864; (*c*) S. E. Denmark, P. C. Miller and S. R. Wilson, *J. Am. Chem. Soc.*, 1991, **113**, 1468.

6 (*a*) O. Chiodi, F. Fotiadu, M. Sylvestre and G. Buono, *Tetrahedron Lett.*, 1996, **37**, 39; (*b*) V. Peper and J. Martens, *Tetrahedron*: *Asymmetry*, 1996, **37**, 8351. Closely related reagents; (*c*) R. Hulst, H. Heres, N. C. M. W. Peper and R. M. Kellogg, *Tetrahedron*: *Asymmetry*, 1996, **7**, 1373; (*d*) I. A. O'Neil, C. D. Turner and S. B. Kalindjian, *Synlett*, 1997, 777.

7 B. Burns, E. Merifield, M. F. Mahon, K. C. Molloy and M. Wills, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2243.

8 (*a*) S. E. Denmark, D. M. Coe, N. E. Pratt, B. D. Griedel, *J. Org. Chem.*, 1994, **59**, 6161; (*b*) K. Iseki, Y. Kuroki, M. Takahashi and Y. Kobayashi, *Tetrahedron Lett.*, 1996, **37**, 5149; (*c*) S. E. Denmark and S. B. D. Winter, *Synlett*, 1997, 1087.

9 (*a*) A. Alexakis, S. Mutti and P. Mangeney, *J. Org. Chem.*, 1992, **57**, 1224; (*b*) A. Alexakis, S. Mutti, J. F. Normant and P. Mangeney, *Tetrahedron*: *Asymmetry*, 1990, **1**, 437; (*c*) R. Hulst, N. K. de Vries and B. L. Feringa, *Tetrahedron*: *Asymmetry*, 1994, **5**, 699.
10 I. H. Williams and L. Linney, unpublished results.
11 The oxazaphospholidine ring opening reaction of related compounds has been reported to proceed with retention of configuration at phosphorus, for example: J. M. Brown, J. V. Carey and M. J. H. Russell, *Tetrahedron*, 1990, **46**, 4877.
12 (*a*) H. M. I. Osborn, J. B. Sweeney and B. Howson, *Synlett*, 1994, 145; (*b*) H. M. I. Osborn, A. A. Cantrill, J. B. Sweeney and B. Howson, *Tetrahedron Lett.*, 1994, **35**, 3159.
13 The reaction between prolinol and diphenylphosphine chloride, in the presence of triethylamine and in dichloromethane solvent gave a large quantity of *O*-phosphinylated material. However the same reaction using diphenylprolinol gave mainly the *N*-phosphinylated product in 56% yield.
14 (*a*) J.-M. Brunel, O. Pardigon, B. Faure and G. Buono, *J. Chem. Soc.*, *Chem. Commun.*, 1992, 287; (*b*) G. Buono, J.-M. Brunel, B. Faure and O. Pardigon, *Phosphorus*, *Sulfur Silicon*, 1993, **93**, 43.
15 J.-M. Brunel, M. Maffei and G. Buono, *Tetrahedron*: *Asymmetry*, 1993, **4**, 2255.
16 H. Tye, C. Eldred and M. Wills, *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, 457.
17 (*a*) G. Brenchley, M. Fedouloff, E. Merifield and M. Wills, *Tetrahedron*: *Asymmetry*, 1996, **7**, 2809; (*b*) E. J. Corey, C. P. Chen and G. A. Reichard, *Tetrahedron Lett.*, 1989, **30**, 5547.
18 (*a*) R. E. Gawley, G. C. Hart and L. J. Bartolli, *J. Org. Chem.*, 1989, **54**, 175; (*b*) J. R. Gage and D. A. Evans, *Org. Synth.*, 1990, **68**, 77.
19 (*a*) T. Koizumi, R. Yanada, H. Takagi, H. Hirai and E. Yoshii, *Tetrahedron Lett.*, 1981, **22**, 477; (*b*) T. Koizumi, R. Yanada, H. Takagi, H. Hirai and E. Yoshii, *Tetrahedron Lett.*, 1981, **22**, 571.

Paper 7/09174E
Received 22*nd December* 1997
Accepted 27*th January* 1998