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(*S*)-Serine derived N–O and N–P oxazoline ligands for asymmetric catalysis

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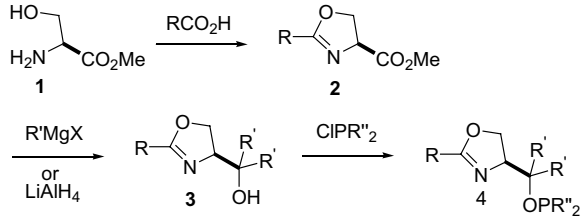
Abstract—(*S*)-Serine methyl ester and a range of carboxylic acids RCO_2H (**a** R = (η^5-C_5H_4)Fe(η^5-C_5Ph_5), **b** (η^5-C_5H_4)Co(η^4-C_4Ph_4), **c** (η^5-C_5H_4)Fe(η^5-C_5H_5), **d** 1-adamantyl, **e** C_6H_5) were readily transformed in three steps into (*R*)-4-hydroxymethyloxazoline N–O ligands **3a**–**e** containing the R substituent at position 2. Two further N–O ligands (*S*)-4-(1-hydroxy-1-methylethyl)-oxazoline **3f** and (*S*)-4-(1-hydroxy-1,1-diphenylmethyl)oxazoline **3g** both containing (η^5-C_5H_4)Co(η^4-C_4Ph_4) as a 2-substituent were also generated. Use of 5 mol% of **3a**–**f** promoted the synthesis of (*R*)-1-phenylpropan-1-ol from benzaldehyde and diethylzinc, **3a** resulting in a highest ee of 75%. In a two step synthesis via an intermediate mesylate, **3b** was converted into the corresponding (*S*)-4-(diphenylphosphinomethyl)oxazoline N–P ligand **19**, and an X-ray crystal structure analysis was obtained of the palladium dichloride adduct. Treatment of **3a**–**e** with Ph_2PCl under basic conditions resulted in the corresponding phosphinite–oxazoline N–P ligands **4a**–**e**. All the N–P ligands were screened to determine the most selective for the palladium-catalysed allylic alkylation with dimethyl malonate of the following racemic substrates: (i) 1,3-diphenylprop-2-enyl acetate [96% ee (*S*) with **4e**], (ii) 1,3-dimethylprop-2-enyl pivalate [70% ee (*S*) with **4b**] and (iii) 3-cyclohexenyl acetate [48% ee (*R*) with **4c**].

1. Introduction

Oxazolines are now firmly established as one of the most popular and successful classes of ligand for application in metal-catalysed asymmetric transformations.[1] This is at least in part to their ease of synthesis from readily available amino acids, with (*S*)-valine in particular being utilised as the basis of many highly enantioseletive metal–ligand systems. Another recent approach to catalyst discovery is the synthesis and analysis of ligand libraries as an aid to the optimisation of enantioselectivity for a specific application.[2] Ideally many diverse structures are obtainable from one or more readily available starting materials. For oxazoline ligands, an attractive building block in this context is (*S*)-serine methyl ester **1** due to the presence of three contrasting functionalities. Herein we report on the use of this enantiopure starting material for the synthesis of oxazolines **2**, precursors to N–O ligands **3** and N–P ligands **4** potentially incorporating up to three points of diversity (R, R′ and R″) (Scheme 1). In particular, use is made of air stable bulky metallocenes (R = **a**, **b**) and we report in detail on the application of ligands **3** and **4** to aldehyde alkylation and allylic alkylation, respectively. Parts of this study have been the subject of previous communications.[3,4]



Scheme 1.

2. Results and discussion

2.1. (*S*)-Serine derived N–O ligands

A range of carboxylic acids **5a**–**e** were first converted to their corresponding acid chlorides by reaction with oxalyl chloride, followed by addition of (*S*)-serine methyl ester **1** in the presence of triethylamine. Although various methods have been reported for the dehydrative

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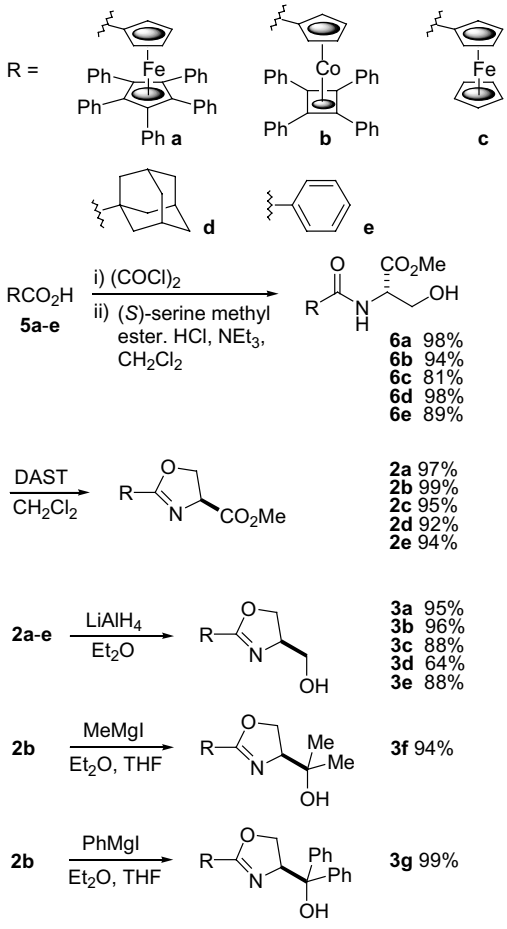
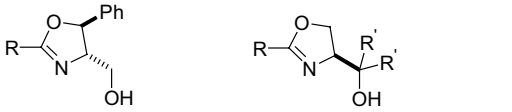
cyclisation of β-hydroxy amides, many are not compatible with serine derived systems because of competitive formation of dehydroamino esters.[5] A mild and effective method for the cyclisation of serine derived β-hydroxy amides has been reported using diethylaminosulfur trifluoride (DAST).[6] Application of this procedure to amides **6a**–**e** resulted in clean transformation into oxazolines **2a**–**e**. Subsequent reduction with $LiAlH_4$ gave new N–O ligands **3a**–**e**, also in good yield. Alternatively, Grignard reagents may be added to the intermediate oxazoline esters. This was exemplified with the synthesis of ligands **3f** and **3g** from the addition of methyl- and phenylmagnesium bromide, respectively, to ester **2b** (Scheme 2). The stereochemical integrity of **3e** was determined as >95% ee by examination of the 400 MHz ^1H NMR spectra of the esters obtained with (*S*)- and (*R*)-Mosher's acid chloride. From the former a methyl singlet at 3.41 ppm was observed, from the latter the corresponding peak was found at 3.40 ppm, and in each case none of the other possible diastereoisomer was observed.



Scheme 2.

Chiral non-racemic ligands containing a β-hydroxy nitrogen have been very widely applied to the asymmetric alkylation of aldehydes with dialkylzincs.[7] In most cases the nitrogen based functionality is a tertiary amine although 2-(hydroxymethyl)pyridines have also been widely explored. To the best of our knowledge there are only two reports on the application of 4-(hydroxymethyl)oxazolines to this reaction with ligands **7a**–**c** and **8a**–**c** (Fig. 1).[8,9] With compounds **3a**–**g** available we sought to investigate further and ideally optimise the influence of substituents R and R′ on the asymmetric catalysis of aldehyde alkylation.

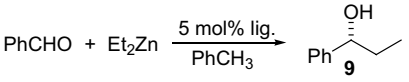


7a R = Me[8a]
7b R = Ph[8a]
7c R = 2-thiophenyl[8a]

8a R = Me, R' = Me[8a]
8b R = Me, R' = Ph[8a]
8c R = 2-biphenyl, R' = Me[8b]

Figure 1. Related 4-hydroxymethyloxazoline ligands.

Addition of 5 mol % of ligand **3a** to a toluene solution of benzaldehyde containing 1.5 equiv of diethylzinc, and stirring at room temperature for 24 h, resulted in clean conversion to (*R*)-1-phenylpropan-1-ol **9** in 75% ee (Scheme 3, Table 1, entry 1). Changing the solvent to 1:1 toluene/hexane (entry 2), the reaction temperature (entry 3), or both (entry 4), did not lead to an improvement of enantioselectivity. Thus ligands **3b**–**g** were also employed at room temperature in toluene, all of which proved inferior to the pentaphenylferrocene derivative **3a** (entries 5–8). Increasing the size of the R′ substituent results in a severe decrease in enantioselectivity (entries 9 and 10). This trend, summarised in Figure 2, is also apparent in the results obtained with ligands **7a**–**c** and **8a**–**c** for this same reaction. (*S*)-1-Phenylpropan-1-ol **9** is



Scheme 3.

Table 1. Addition of diethylzinc to benzaldehyde[a]

Entry	Catalyst[b]	Solvent	Temperature (°C)	Ee **9** (config)[c] (%)
1	**3a**	Toluene	rt	75 (*R*)
2	**3a**	50% Toluene/ hexanes	rt	61 (*R*)
3	**3a**	Toluene	0 °C	69 (*R*)
4	**3a**	50% Toluene/ hexanes	0 °C	75 (*R*)
5	**3b**	Toluene	rt	68 (*R*)
6	**3c**	Toluene	rt	36 (*R*)
7	**3d**	Toluene	rt	22 (*R*)
8	**3e**	Toluene	rt	52 (*R*)
9	**3f**	Toluene	rt	54 (*R*)
10	**3g**	Toluene	rt	8 (*R*)

[a] Reactions had proceeded to >95% conversion after 24 h.
[b] 5 mol %.
[c] Determined by GC with a Chrompack CP-Chirasil-DEX CB column. Absolute configuration determined by comparison to commercial (*R*)-1-phenylpropan-1-ol.

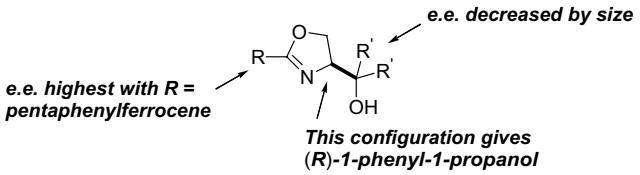


Figure 2. Ligand influences on the enantioselectivity of diethylzinc addition to benzaldehyde promoted by **3**.

obtained with **7a** (50% ee) and **7b/c** (both 57% ee); (*R*)-**9** is obtained with **8a** (30% ee), **8b** (7% ee) and **8c** (37% ee).

Calculations on the β-amino alcohol promoted alkylation of aldehydes by diethylzinc have revealed a preference for the tricyclic *anti-trans* transition state.[10] Accordingly, the hydroxymethyl oxazolines of this study can give rise to the two *anti-trans* transition states **10** and **11**, with the former leading to the observed (*R*)-1-phenylpropan-1-ol (Fig. 3).

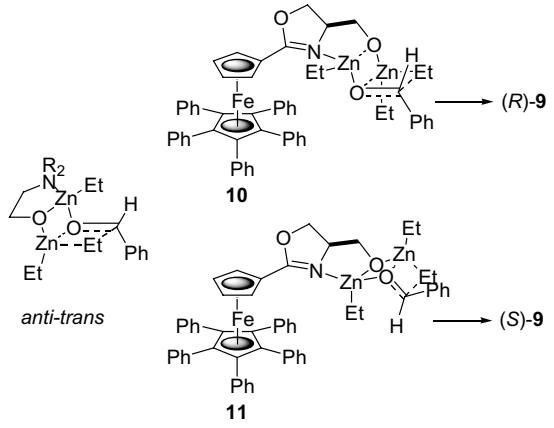


Figure 3. The two possible *anti-trans* transition states available from ligand **3a**.

β-Hydroxynitrogen functionalities are also present in the planar chiral ligands **12** and **13**, which give (*S*)-**9** (58% ee)[11] and (*R*)-**9** (64% ee),[12] respectively, from the reaction between diethylzinc and benzaldehyde (Fig. 4). The correlation between the sense of planar chirality and the configuration of **9** may be extended to **3a** with one side of the 4-(hydroxymethyl)oxazoline covered by the pentaphenylcyclopentadienyl moiety. This is consistent with the orientation of this bulky group away from the larger 4-oxazoline substituent. Thus the heterocycle is mimicking the related planar chiral systems **12** and **13**, such that the oxazoline is in an environment of *virtual* planar chirality. Related conformational preferences in complexes **14**[13] and **15**[14] have been used to account for their highly diastereoselective palladation at the positions indicated (Fig. 5).

2.2. (*S*)-Serine derived N–P ligands

Nitrogen–phosphorus ligands **17** have been previously reported by Burgess et al.[15] These are also synthesised

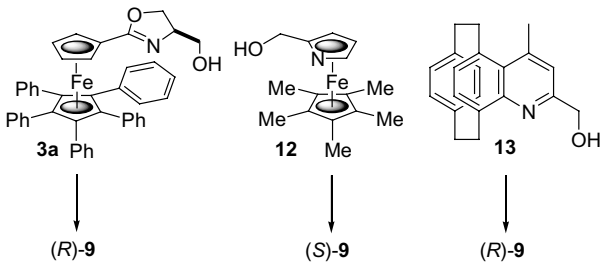


Figure 4. The correlation between ligand stereochemistry and the configuration of 1-phenyl-1-propanol **7**.

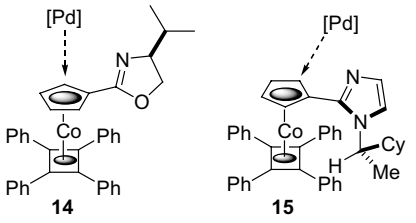
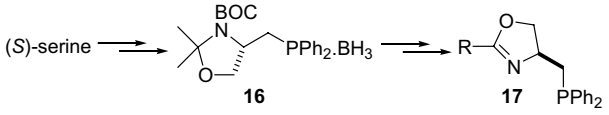


Figure 5. Metallocenes **14** and **15** and the positions of palladation on heating with $Pd(OAc)_2$.[13,14]

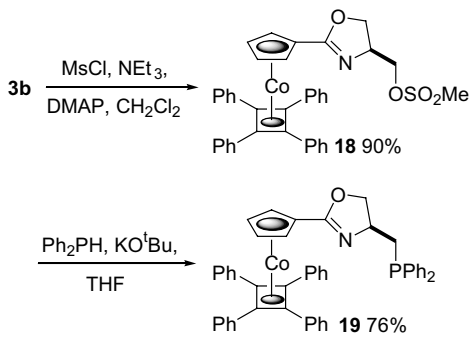
from (*S*)-serine via a common intermediate **16**, with the variable R substituent being introduced in the final steps of the synthesis (Scheme 4).



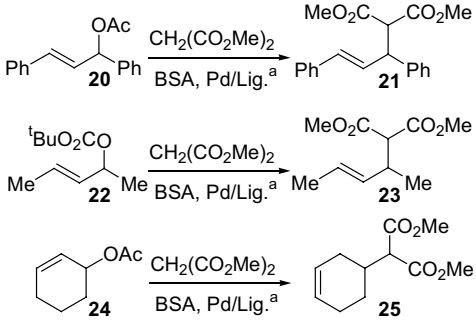
Scheme 4.

These ligands have been applied to palladium-catalysed allylic alkylation of 1,3-diphenylpropenyl acetate (up to 94% ee with R = adamantyl)[15b] and dimethylpropenyl pivalate (up to 75% ee with R = 3,5-^{t}Bu–C_6H_3).[15a] In light of the relative success of bulky metallocenes as R substituents in the diethylzinc alkylation chemistry described above, we sought to synthesis a related example of ligand **17** and test it in palladium-catalysed allylic alkylation chemistry. Thus **3b** was first converted to intermediate mesylate **18** and subsequent treatment with potassium diphenylphosphine, generated in situ, resulted in N–P ligand **19** in good overall yield (Scheme 5). This was then applied to the palladium-catalysed allylic alkylation of three representative substrates **20**, **22** and **24** (Scheme 6, Table 2).

The enantioselectivities obtained were modest and varied significantly on changing the solvent from THF to CH_2Cl_2. A feature previously observed with ligands **17** is the strong dependency of enantioselectivity on the ligand/palladium ratio employed. For example, a 1:1 ratio of **17** (R = 4-$MeOC_6H_4$) to palladium in CH_2Cl_2 is reported to give (*S*)-**21** in ~82% ee, which dropped to ~20% ee of (*R*)-**21** when a 2:1 ligand/metal ratio was employed.[15b] These differences are suggested to arise



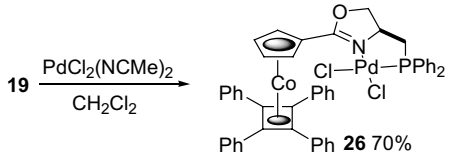
Scheme 5.



Scheme 6.

from a change in coordination mode from a P–N chelate with a 1:1 ligand/metal ratio to a bisphosphine adduct with a 2:1 ligand/metal ratio. It is possible that the solvent also has a significant effect on the coordination mode of the key π-allyl intermediate in the catalytic cycle. It is of note that use of a 1:1 ratio of **17** (R = 4-$MeOC_6H_4$)/Pd in THF gives (*S*)-**21** in only ~18% ee.[15b] The changes we observed on changing from CH_2Cl_2 to THF with ligand **19** [(*R*)-**21** to (*S*)-**21**] are opposite to the changes reported for ligands **17** [(*S*)-**21** to (*R*)-**21**]. We are unsure of the significance of this though we note that the order of elution of the two enantiomers of **21** on the same type of HPLC column is opposite to that previously reported.

To investigate the coordination geometry of ligand **19**, the palladium dichloride complex **26** was synthesised as outlined in Scheme 7 and an X-ray crystal structure obtained (Fig. 6).[19] Three points are noteworthy. Firstly, the five-membered chelate results in a distortion in the square–planar geometry about palladium, with the N(1)–Pd(1)–P(1) angle only 83.1°. Secondly, the ring formed by chelation is in an envelope conformation and the phenyl substituents at phosphorus are not in distinctively axial or equatorial orientations (N(1)–Pd(1)–P(1)–C(38) = 113.9° and N(1)–Pd(1)–P(1)–C(44) = 121.1°), and they display only a partial edge-to-face orientation (30°). This contrasts markedly with the structure of the palladium complex of phosphinoaryloxazoline **27**[20] with which (*S*)-**21** is obtained in 98.5% ee from palladium-catalysed alkylation of substrate **20**.[21]



Scheme 7.

Table 2. Pd-catalysed reaction of allylic substrates **20**, **22** and **24** with dimethyl malonate mediated by ligand **19**[a,b]

Ligand	Solvent	Ee **21** (config)[c] (%)	Ee **23** (config)[d] (%)	Ee **25** (config)[e] (%)
19	THF	43 (*S*)	36 (*S*)	5 (*R*)
19	CH_2Cl_2	24 (*R*)	6 (*S*)	25 (*R*)

[a] 6 mol% **19**, 2.5 mol% [(η^3-C_3H_5)PdCl]$_2$.
[b] Reactions had proceeded to >95% conversion after 24 h.
[c] Determined by HPLC with a Diacel Chiralcel OD column (99:1 hexanes/propan-2-ol). Absolute configuration determined by comparison to (*S*)-**21** obtained with (*S*)-2-[(*S*)-2-diphenylphosphino)ferrocenyl]-4-(1-methylethyl)oxazoline (94% ee).[16]
[d] Determined by GC with a Chrompack CP-Chirasil-DEX CB column. Absolute configuration determined by comparison to (*S*)-**23** obtained with (*S*)-2-[(*S*)-2-diphenylphosphino)ferrocenyl]-4-(1-methylethyl)-oxazoline (12% ee).[17]
[e] Determined by GC with a Chrompack CP-Chirasil-DEX CB column. Absolute configuration determined by comparison of retention times to reported literature values.[18]

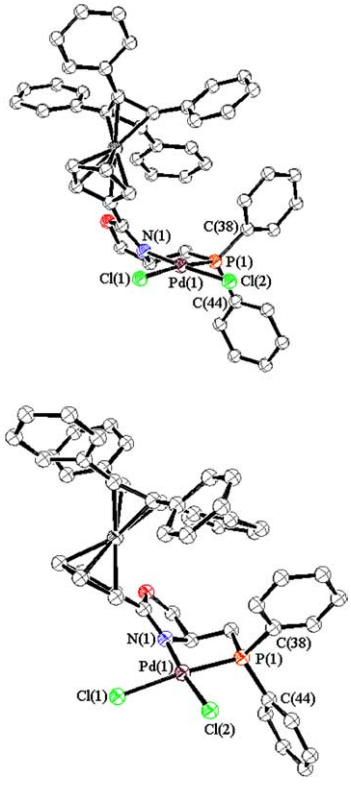


Figure 6. Representations of the crystal structures of **26**. Selected bond distances (Å) and angles (deg) are as follows: Pd(1)–N(1) = 2.018(5), Pd(1)–P(1) 2.221(2), Pd(1)–Cl(1) 2.370(2), Pd(1)–Cl(2) 2.290(2), N(1)–Pd(1)–P(1) 83.1(2), P(1)–Pd(1)–Cl(2) 90.56, N(1)–Pd(1)–Cl(1) 96.1(2), Cl(1)–Pd(1)–Cl(2) 90.41(6).

Here the axial and equatorial orientations of the two phosphorus phenyl substituents are pronounced, with selective interaction between the latter and the π-allyl intermediate accounting, in part, for the high selectivity observed with this ligand. Thirdly, the position of ligand Cl(1), resulting from the square–planar geometry about palladium, forces the cobalt metallocene to lie on the same side as the larger 4-oxazoline substituent. The C=N bond of the oxazoline is at an angle of 25° to the plane of the cyclopentadienyl ring so that one side of the heterocycle is shielded by the large cyclobutadiene moiety. Here the sense of virtual planar chirality is opposite to that speculated to arise from the reaction between **3a/b** and diethylzinc.

The results obtained with ligand **19**, taken together with the earlier work of Burgess, reveal that five-membered chelates of this type are not well suited as P–N ligands for allylic alkylation due to: (i) the instability of the chelate itself, and (ii) the lack of differentiation in the orientation of the two phosphorus aryl substituents. As already discussed, six-membered P–N derived chelates such as **27** have been applied with success to metal-catalysed allylic alkylation, as have related 2-ferrocenyl and 2-alkyl substituted ligands **28**[22] and **29**.[23] Structures **30**, homologues of ligands **17**, have been synthesised from (*S*)-aspartic acid and have been applied to palladium-catalysed allylic alkylation and iridium-catalysed hydrogenation.[24] With N–O ligands **3a–e** available we sought to generate new N–P ligands in one step with the formation of phosphinite–oxazolines **4**.[25] Structurally related phosphinite–oxazolines **31** have been previously reported derived from D-glucosamine (Fig. 7).[26]

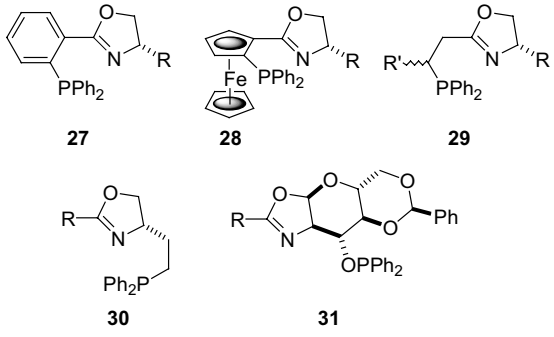
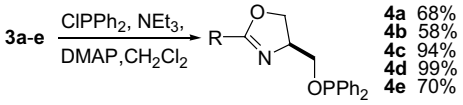


Figure 7. Oxazoline based N–P ligands.

Phosphinites **4a–e** were synthesised by simply adding chlorodiphenylphosphine to alcohols **3a–e** in the presence of triethylamine and a catalytic amount of DMAP, followed by filtration through a plug of Al_2O_3 (Scheme 8). In all cases a single peak was observed in the ^{31}P NMR spectra of the product at ~115 ppm indicating that the phosphinites had been successfully synthesised. They are however moderately air sensitive and in this study were prepared shortly before use, in the first instance as ligands for the allylic alkylation of **20** (Scheme 6, Table 3).



Scheme 8.

Table 3. Pd-catalysed reaction of **20** into **21** mediated by ligands **4a–e**[a,b]

Entry	Ligand	Solvent	Temperature (°C)	Ee of **21** (config)[c] (%)
1	**4a**	THF	20	53 (*S*)
2	**4a**	CH_2Cl_2	20	80 (*S*)
3	**4b**	CH_2Cl_2	20	52 (*S*)
4	**4c**	CH_2Cl_2	20	90 (*S*)
5	**4d**	CH_2Cl_2	20	67 (*S*)
6	**4e**	CH_2Cl_2	20	90 (*S*)
7	**4e**	CH_2Cl_2	0	96 (*S*)

[a] 6 mol% **4**, 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$.
[b] Reactions had proceeded to >95% conversion after 24 h.
[c] Determined by HPLC with a Diacel Chiralcel OD column (99:1 hexanes/propan-2-ol). Absolute configuration determined by comparison to (*S*)-**15** obtained with (*S*)-2-[(*S*)-2-diphenylphosphino)ferrocenyl]-4-(1-methylethyl)oxazoline (94% ee).[16]

Again the choice of solvent was found to be important with CH_2Cl_2 resulting in a significantly higher ee than THF (entry 2 vs 1). Thus continuing with CH_2Cl_2, the other ligands were tested under the same conditions with the smaller R substituents of ligands **4c** and **4e** both resulting in 90% ee (entries 4 and 6), the larger R substituents leading to reduced enantioselectivies (entries 3 and 5). Use of **4e** at 0 °C improved the ee further to 96% (entry 7). This result is very similar to those obtained with **30** (R = Ph) and **31** (R = Ph), also obtained at 0 °C. The former led to the generation of (*R*)-**21** in 98% ee,[24a,b] the latter gave (*S*)-**21** in 94% enantiomeric excess.[26a,b] As orientation of the oxazoline 4-substituents are opposite in ligands **30** and **4e** (as a consequence of the CIP rules their configurations are both *S*), changing from a alkyldiarylphosphine (i.e., **30**) to a diarylphosphinite does not change the sense of asymmetric induction. It also has very little effect on the selectivity, which is high. Furthermore, the conformationally locked phosphinite **31** is not required for high enantioselectivity.

In view of the similarity of the results obtained with **30** (R = Ph) and **4e**, the X-ray crystal structure analysis of **32**[24b] may also be used to account for the observed selectivity of the phosphinite–oxazoline ligands. Further to the discussion of structure **26** above two points are noteworthy. Firstly, the N–Pd–P bond angle of 90.5° is close to ideal for a square–planar complex, thus these six-membered ring chelates are expected to be significantly more stable than those arising from **19** and related structures. Secondly, as the chelate gives rise to a chair conformation, the two phosphorus phenyl substituents adopt distinctively axial and equatorial orientations. This environment, which is very similar to that arising from phosphinoaryloxazoline **27**, favours *exo*-**33** over the alternative *syn–syn* arrangement *endo*-**33**, as the latter displays an unfavourable interaction between the

equatorial phenyl and an allyl phenyl substituent. Attack *trans* to phosphorus in *exo*-**33** rather than *trans* to nitrogen then leads to (*S*)-**21**. This selectivity is determined by the relative *trans* effect of these heteroatom containing substituents, with the phosphinite expected to be similar to a phosphine in its superior ability to labilise a *trans* substituent compared to the nitrogen of an oxazoline. Finally, this model accounts for the erosion of enantioselectivity observed with larger R substituents, these resulting either a greater abundance of *endo*-**33** or the alternative *exo-anti*-configuration at the carbon *trans* to phosphorus, both of which lead to (*R*)-**21** (Fig. 8).

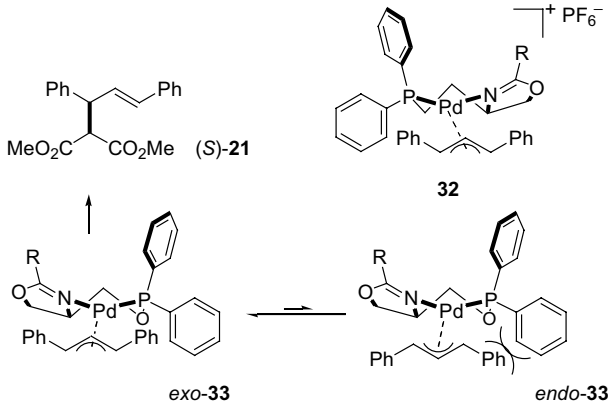


Figure 8. The origin of enantioselection in allylic alkylation of **20** with N–P ligand **4e**.

We next examined the more demanding substrates **22** and **24** (Scheme 6) and in both cases CH_2Cl_2 again proved superior to THF (entry 3 vs 2, Tables 4 and 5). Encouraging results were obtained for **4b** with dimethylpropenyl pivalate **22** (85:15 selectivity—Table 4, entry 3), and for **4c** with cyclohexenyl acetate **24** (74:26 selectivity—Table 5, entry 4). However, in both sets of results no clear correlation emerged between ee and the nature of the R substituent. Unlike 1,3-diphenylprop-2-enyl acetate **20** few ligands have been successfully applied (i.e., >90% ee) to the palladium-catalysed transformation of **22** and **24**.[27]

Table 4. Pd-catalysed reaction of **22** into **23** mediated by ligands **4a**–**e**[a,b]

Entry	Ligand	Solvent	Temperature (°C)	Ee of **23** (config)[c] (%)
1	**4a**	CH_2Cl_2	20	0
2	**4b**	THF	20	30 (*S*)
3	**4b**	CH_2Cl_2	20	70 (*S*)
4	**4c**	CH_2Cl_2	20	50 (*S*)
5	**4d**	CH_2Cl_2	20	11 (*S*)
6	**4e**	CH_2Cl_2	20	43 (*S*)

[a] 6 mol% **4**, 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$.
[b] Reactions had proceeded to >95% conversion after 24 h.
[c] Determined by GC with a Chrompack CP-Chirasil-DEX CB column. Absolute configuration determined by comparison to (*S*)-**21** obtained with (*S*)-2-[(*S*)-2-diphenylphosphino)ferrocenyl]-4-(1-methylethyl)oxazoline (12% ee).[17]

Table 5. Pd-catalysed reaction of **24** into **25** mediated by ligands **4a**–**e**[a,b]

Entry	Ligand	Solvent	Temperature (°C)	Ee of **25** (config)[c] (%)
1	**4a**	CH_2Cl_2	20	3 (*R*)
2	**4b**	THF	20	0
3	**4b**	CH_2Cl_2	20	7 (*R*)
4	**4c**	CH_2Cl_2	20	48 (*R*)
5	**4d**	CH_2Cl_2	20	6 (*R*)
6	**4e**	CH_2Cl_2	20	5 (*R*)

[a] 6 mol% **4**, 2.5 mol% $[(\eta^3\text{-}C_3H_5)PdCl]_2$.
[b] Reactions had proceeded to >95% conversion after 24 h.
[c] Determined by GC with a Chrompack CP-Chirasil-DEX CB column. Absolute configuration determined by comparison of retention times to reported literature values.[18]

3. Conclusions

In conclusion, we have demonstrated that (*S*)-serine may be readily transformed into N–O ligands **3** and N–P ligands **4** containing, respectively, up to two and three points of diversity. This methodology may of course be applied to (*R*)-serine, which is also readily available and relatively inexpensive. Using a small library of N–O ligands we quickly identified the influences of R and R′ leading to enhanced enantioselectivity for the diethylzinc addition to benzaldehyde. The synthetic methodology was extended to the synthesis of an alkyldiarylphosphine oxazoline based upon a bulky cobalt metallocene R substituent. The limitations of the resulting five-membered palladium chelate in asymmetric allylic alkylation resulted in the synthesis of phosphinite–oxazoline ligands. Analysis of a small library of these quickly lead to the identification of a highly enantioselective catalyst for the allylic alkylation of 1,3-diphenylprop-2-enyl acetate (96% ee). In view of the very large number of structures **3** and **4** potentially available, we anticipate the methodology described in this work will be applicable to the discovery of ligands for a large number of metal-catalysed asymmetric transformations.[25]

4. Experimental

4.1. General considerations

Dichloromethane was distilled from calcium hydride, THF and Et_2O were distilled from sodium benzophenone ketyl and toluene was distilled from sodium, all under an atmosphere of nitrogen. Petroleum ether refers to that fraction boiling in the range 40–60 °C. Column chromatography was performed on SiO_2 (40–63 μm).

4.2. General procedure A

Oxalyl chloride (2 equiv) was added to a solution of the acid **5** (1 equiv) in CH_2Cl_2 (20 mL/g of acid) and the resulting solution stirred at room temperature for 20 min. The solvent and excess oxalyl chloride were

removed in vacuo and the crude acid chloride was dissolved in CH_2Cl_2 (30 mL/g) and serine methyl ester hydrochloride (1 equiv) added in one portion to this solution. Triethylamine (2 equiv) and additional CH_2Cl_2 (10 mL/g) were added with ice bath cooling of the reaction mixture. This was then stirred at room temperature for 3 h, the solvent removed in vacuo, and the residue column chromatographed to give the appropriate amide **6**.

4.2.1. (η^5-(*S*)-*N*-1-(1-Carbomethoxy-2-hydroxyethyl)carboxamidecyclopentadienyl)(η^5-pentaphenylcyclopentadienyl)-iron 6a. General procedure A used—**5a** (1.073 g, 1.76 mmol) gave **6a** as a red solid (1.226 g, 98%). Mp 137–139 °C; $[\alpha]_D^{20} = +98$ (*c* 0.23, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1658 (amide), 1738 (ester); δ_H (CD_2Cl_2) 2.12 (1H, br s, O*H*), 3.61–3.68 (5H, m, OCH_2+CO_2CH_3), 4.29 (1H, dt, *J* 6.3, 3.4, C*H*N), 4.34 (2H, br s, Cp), 4.63 (2H, br s, Cp), 6.48 (1H, d, *J* 6.2, N*H*), 6.92–6.99 (20H, m, Ph), 7.03–7.10 (5H, m, Ph); δ_C (CD_2Cl_2){^{1}H} 53.5 (*C*H_3), 56.3 (*C*HN), 64.0 (*C*H_2), 74.2 (Cp), 74.9 (Cp), 78.5 (Cp), 78.8 (Cp), 81.4 (*ipso*-Cp), 89.0 (*C*$_5$Ph$_5$), 127.2 (*para*-Ph), 127.9 (*meta*-Ph), 133.0 (*ortho*-Ph), 135.8 (*ipso*-Ph), 168.9 (*C*=O), 171.8 (*C*=O); *m*/*z* (APCI) 712 (MH^+, 100). HRMS (FAB) *m*/*z* found for M^+, 711.2060; calcd for $C_{45}H_{37}FeNO_4$, 711.2067.

4.2.2. (η^5-(*S*)-*N*-1-(1-Carbomethoxy-2-hydroxyethyl)carboxamidecyclopentadienyl)(η^4-tetraphenylcyclobutadiene)-cobalt 6b. General procedure A used—**5b** (0.560 g, 1.07 mmol) gave **6b** as an orange crystalline solid (0.628 g, 94%). Mp 207–209 °C; $[\alpha]_D^{20} = -14$ (*c* 0.25, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1643 (amide), 1744 (ester); δ_H ($CDCl_3$) 2.71 (1H, br s, O*H*), 3.51–3.69 (2H, br m, OCH_2), 3.70 (3H, s, CO_2CH_3), 3.96–3.98 (1H, m, C*H*N), 4.68 (1H, br s, Cp), 4.71 (1H, br s, Cp), 4.99 (1H, br s, Cp), 5.04 (1H, br s, Cp), 6.15 (1H, d, *J* 5.7, N*H*), 7.12–7.21 (12H, m, Ph), 7.36–7.38 (8H, m, Ph); δ_C ($CDCl_3$){^{1}H} 53.1 (*C*H_3), 56.0 (*C*HN), 64.3 (*C*H_2), 76.7 (*C*$_4$Ph$_4$), 82.0 (Cp), 83.8 (Cp), 86.3 (Cp), 87.2 (Cp), 89.6 (*ipso*-Cp), 126.3 (*para*-Ph), 127.1 (*meta*-Ph), 129.2 (*ortho*-Ph), 135.5 (*ipso*-Ph), 166.2 (*C*=O), 171.1 (*C*=O); *m*/*z* (APCI) 626 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 626.1740; calcd for $C_{38}H_{33}CoNO_4$, 626.1741.

4.2.3. (*S*)-*N*-1-(1-Carbomethoxy-2-hydroxyethyl)ferrocenecarboxamide 6c. General procedure A used—**5c** (1.459 g, 6.34 mmol) gave **6c** as an orange crystalline solid (1.699 g, 81%). Mp 131–133 °C; $[\alpha]_D^{20} = -15$ (*c* 0.25, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1657 (amide), 1742 (ester); δ_H ($CDCl_3$) 3.23 (1H, br s, O*H*), 3.57 (3H, s, CO_2CH_3), 3.90–4.01 (2H, br m, OCH_2), 4.30 (5H, s, Cp), 4.31 (2H, br s, Cp), 4.65 (1H, br s, Cp), 4.65 (1H, br s, Cp), 4.74–4.78 (1H, m, C*H*N), 6.70 (1H, d, *J* 7.5, N*H*); δ_C ($CDCl_3$){^{1}H} 51.8 (*C*H_3), 53.6 (*C*HN), 62.5 (*C*H_2), 67.1 (Cp), 67.6 (Cp), 68.9 (Cp×5), 69.8 (Cp), 69.9 (Cp), 73.6 (*ipso*-Cp), 170.2 (*C*=O), 170.3 (*C*=O); *m*/*z* (ES) 331 (MH^+, 100), 213 (45) 147 (33). HRMS (ES) *m*/*z* found for MH^+, 332.0585; calcd for $C_{15}H_{18}FeNO_4$, 332.0585.

4.2.4. (*S*)-*N*-1-(1-Carbomethoxy-2-hydroxyethyl)adamantyl-1-carboxamide 6d. General procedure A used—**5d** (1.278 g, 7.09 mmol) gave **6d** as a colourless crystalline solid (1.96 g, 98%). δ_H ($CDCl_3$) 1.64–1.81 (6H, m), 1.85–1.92 (6H, m), 2.00–2.09 (3H, m), 3.76 (3H, s, CH_3), 3.83 (1H, dd, *J* 11.0, 3.3, C*H*HO), 3.98 (1H, dd, *J* 11.0, 3.8, CH*H*O), 4.61 (1H, dt, *J* 7.7, 3.3, C*H*N), 6.74 (1H, d, *J* 7.4, N*H*); δ_C ($CDCl_3$){^{1}H} 28.00 (*C*H), 36.39 (*C*H_2), 38.91 (*C*H_2), 40.63 (*C*CO), 52.51 (*C*H_3), 54.42 (*C*HN), 62.82 (O*C*H_2), 171.23 (*C*=O), 178.76 (*C*=O).

4.2.5. (*S*)-*N*-1-(1-Carbomethoxy-2-hydroxyethyl)benzenecarboxamide 6e. Benzoyl chloride (0.72 mL, 6.2 mmol) was reacted with (*S*)-serine methyl ester hydrochloride as described in general procedure A to give **6e** as a colourless crystalline solid (1.24 g, 90%). δ_H ($CDCl_3$) 3.60 (1H, br s, N*H*), 3.75 (1H, s, CH_3), 3.96 (1H, dd, *J* 11.6, 3.2, C*H*HO), 4.05 (1H, dd, *J* 11.1, 3.7, CH*H*O), 4.82 (1H, dt, *J* 7.7, 3.2, C*H*N), 7.37 (2H, t, *J* 7.9, Ph), 7.48 (1H, t, *J* 7.4, Ph), 7.81 (2H, d, *J* 7.8, Ph); δ_C ($CDCl_3$){^{1}H} 52.87 (*C*H_3), 55.27 (*C*HN), 63.20 (*C*H_2), 127.35 (Ph), 128.71 (Ph), 132.08 (*para*-Ph), 133.57 (*ipso*-Ph), 167.99 (*C*=O), 171.23 (*C*=O).

4.3. General procedure B

Diethylaminosulfur trifluoride (1.1 equiv) was added drop wise to a solution of **6** (1 equiv) in CH_2Cl_2 (20 mL/g of amide) cooled to −78 °C. This solution was then stirred at this temperature for 1 h. Anhydrous K_2CO_3 (1.5 equiv) was added in one portion and the reaction mixture allowed to warm to room temperature. Saturated $NaHCO_{3(aq)}$ (40 mL/g) was then added and the organic layer separated, dried (Na_2SO_4), filtered and the solvent removed in vacuo. The residue was column chromatographed to give the desired oxazoline **2**.

4.3.1. (η^5-(*S*)-2-(4-Carbomethoxy)oxazolinylcyclopentadienyl)(η^5-pentaphenylcyclopentadienyl) iron 2a. General procedure B used—**6a** (0.758 g, 1.07 mmol) gave **2a** as a red solid (0.713 g, 97%). Mp 132–134 °C; $[\alpha]_D^{20} = +18$ (*c* 0.26, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1645 (C=N), 1738 (C=O); δ_H (CD_2Cl_2) 3.53 (3H, s, CO_2CH_3), 3.90 (1H, dd, *J* 10.6, 8.4, 1H, OC*H*H), 4.21 (1H, t, *J* 8.2, C*H*N), 4.27–4.37 (3H, m, Cp×2+OCH*H*), 4.69 (2H, br s, Cp), 6.94–6.99 (20H, m, Ph) 7.01–7.09 (5H, m, Ph); δ_C (CD_2Cl_2){^{1}H} 51.5 (*C*H_3), 67.8 (*C*HN), 68.0 (*C*H_2), 73.6 (Cp), 74.0 (Cp), 74.2 (Cp), 76.7 (Cp), 77.2 (Cp), 87.5 (*C*$_5$Ph$_5$), 125.1 (Ph), 126.3 (Ph), 131.6 (Ph), 134.3 (*ipso*-Ph), 165.1 (*C*=N), 170.5 (*C*=O); *m*/*z* (ES) 694 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 694.2041; calcd for $C_{45}H_{36}FeNO_3$, 694.2044.

4.3.2. (η^5-(*S*)-2-(4-Carbomethoxy)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 2b. General procedure B used—**6b** (0.382 g, 0.61 mmol) gave **2b** as an orange crystalline solid (0.367 g, 99%). Mp 83–85 °C; $[\alpha]_D^{20} = -6$ (*c* 0.31, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1646 (C=N), 1740 (C=O); δ_H ($CDCl_3$) 3.48 (1H, dd, *J* 10.6,

8.1, OC*H*H), 3.66 (3H, s, CO_2CH_3), 4.02 (1H, t, *J* 8.1, C*H*N), 4.15 (1H, dd, *J* 10.6, 8.1, OCH*H*), 4.69 (1H, br s, Cp), 4.75 (1H, br s, Cp), 5.02 (1H, br s, Cp), 5.18 (1H, br s, Cp), 7.10–7.16 (8H, m, *meta*-Ph), 7.17–7.24 (4H, m, *para*-Ph), 7.31–7.38 (8H, m, *ortho*-Ph); δ_C ($CDCl_3$){^{1}H} 51.5 (*C*H_3), 67.3 (*C*H_2), 67.4 (*C*HN), 75.1 (C_4Ph_4), 81.7 (Cp), 83.0 (*ipso*-Cp), 83.7 (Cp), 84.1 (Cp), 85.1 (Cp), 125.5 (*para*-Ph), 126.9 (*meta*-Ph), 127.8 (*ortho*-Ph), 134.1 (*ipso*-Ph), 161.9 (*C*=N), 170.8 (*C*=O); *m*/*z* (APCI) 608 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 608.1637; calcd for $C_{38}H_{31}CoNO_3$, 608.1636.

4.3.3. (*S*)-4-Carbomethoxy-2-ferrocenyloxazoline 2c. General procedure B used—**6c** (1.046 g, 3.16 mmol) gave **2c** as an orange crystalline solid (0.940 g, 95%). Mp 93–95 °C; $[\alpha]_D^{20} = +224$ (*c* 0.05, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1646 (C=N), 1741 (C=O); δ_H ($CDCl_3$) 3.75 (3H, s, CO_2CH_3), 4.15 (5H, s, Cp), 4.30 (2H, br s, Cp), 4.40 (1H, dd, *J* 10.0, 8.8, OC*H*H), 4.53 (1H, t, *J* 7.3, C*H*N), 4.70–4.74 (2H, m, OCH*H*+Cp), 4.77 (1H, br s, Cp); δ_C ($CDCl_3$){^{1}H} 51.7 (*C*H_3), 67.4 (*C*HN), 67.6 (*ipso*-Cp), 68.27 (*C*H_2), 68.35 (Cp×2), 68.8 (Cp×5), 69.6 (Cp), 69.8 (Cp), 168.6 (*C*=N), 170.9 (*C*=O); *m*/*z* (ES) 313 (MH^+, 100), 254 (14). HRMS (FAB) *m*/*z* found for MH^+, 314.0485; calcd for $C_{15}H_{16}FeNO_3$, 314.0479.

4.3.4. (*S*)-4-Carbomethoxy-2-(1-adamantyl)oxazoline 2d. General procedure B used—**6d** (1.75 g, 6.2 mmol) gave **2d** as a colourless crystalline solid (1.50 g, 92%). δ_H ($CDCl_3$) 1.63–1.80 (6H, m), 1.80–1.95 (6H, m), 1.95–2.10 (3H, m), 3.79 (3H, s, C*H*$_3$), 3.94 (1H, d, *J* 4.2, C*H*N), 4.23–4.42 (2H, m, OC*H*$_2$); δ_C ($CDCl_3$){^{1}H} 28.03 (*C*H), 36.62 (*C*H_2), 38.81 (*C*H_2), 39.23 (*C*C=N), 52.94 (–*C*H_3), 54.86 (*C*HN), 63.75 (O*C*H_2), (*C*=O and *C*=N not observed).

4.3.5. (*S*)-4-Carbomethoxy-2-phenyloxazoline 2e. General procedure B used—**6e** (1.020 g, 4.57 mmol) gave **2e** as a colourless crystalline solid (0.88 g, 94%). δ_H ($CDCl_3$) 3.82 (3H, s, *C*H$_3$), 4.59 (1H, t, *J* 10, OC*H*H), 4.69 (1H, t, *J* 8, C*H*N), 4.95 (1H, dd, *J* 11, 8, OCH*H*), 7.38–7.52 (3H, m, Ph), 7.98 (2H, d, *J* 8, *ortho*-Ph); δ_C ($CDCl_3$){^{1}H} 52.87 (*C*H_3), 68.78 (*C*HN or O*C*H_2), 69.71 (*C*HN or O*C*H_2), 127.09 (*ipso*-Ph), 128.51 (Ph), 128.75 (Ph), 132.04 (*para*-Ph), 166.46 (*C*=N), 171.80 (*C*=O).

4.4. General procedure C

$LiAlH_4$ (1.1 equiv) was added in five portions over 10 min to a solution of **2** (1 equiv) in Et_2O (30 mL/g) cooled to 0 °C. After stirring for 15 min, EtOAc (50 mL/g) was added then H_2O (75 mL/g), the organic layer was then separated, dried ($MgSO_4$), filtered and the solvent removed in vacuo to give alcohols **3**.

4.4.1. (η^5-(*R*)-2-(4-Hydroxymethyl)oxazolinylcyclopentadienyl)(η^5-pentaphenylcyclopentadienyl) iron 3a. General procedure C used—**2a** (2.278 g, 3.28 mmol) gave **3a** as a red solid (2.077 g, 95%). Mp 119–120 °C; $[\alpha]_D^{20} = +96$ (*c* 0.31, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1649 (C=N); δ_H ($CDCl_3$) 3.30 (1H, dd, *J* 11.2, 4.2, OC*H*H), 3.43–3.49 (1H, m, OCH*H*), 3.92–3.99 (3H, m, OC*H*$_2$+C*H*N), 4.37 (1H, br s, Cp), 4.40 (1H, br s, Cp), 4.71 (1H, br s, Cp), 4.78 (1H, br s, Cp), 7.08–7.12 (20H, m, Ph), 7.15–7.20 (5H, m, Ph); δ_C ($CDCl_3$){^{1}H} 64.2 (*C*H_2), 68.7 (*C*HN), 68.9 (*C*H_2), 74.8 (Cp), 75.0 (Cp), 75.8 (*ipso*-Cp), 77.6 (Cp), 78.0 (Cp), 88.6 (C_5Ph_5), 126.7 (Ph), 127.4 (Ph), 132.7 (Ph), 135.6 (Ph), 165.4 (*C*=N); *m*/*z* (APCI) 666 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 666.2099; calcd for $C_{44}H_{36}FeNO_2$, 666.2095.

4.4.2. (η^5-(*R*)-2-(4-Hydroxymethyl)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene) cobalt 3b. General procedure C used—**2b** (0.495 g, 0.81 mmol) gave **3b** as an orange crystalline solid (0.453 g, 96%). Mp 109–110 °C; $[\alpha]_D^{20} = -192$ (*c* 0.36, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1650 (C=N); δ_H ($CDCl_3$) 3.39 (1H, dd, *J* 12.4, 4.3, OC*H*H), 3.56–3.73 (2H, m, OC*H*$_2$+C*H*N), 3.77 (1H, t, *J* 9.1, OCH*H*), 4.82 (1H, br s, Cp), 4.90 (1H, br s, Cp), 5.18 (1H, br s, Cp), 5.64 (1H, br s, Cp), 7.02–7.24 (12H, m, *meta*-Ph+*para*-Ph), 7.27–7.36 (8H, m, *ortho*-Ph); δ_C ($CDCl_3$){^{1}H} 62.3 (*C*H_2), 68.4 (*C*HN), 71.9 (*C*H_2), 78.0 (C_4Ph_4), 78.4 (*ipso*-Cp), 84.2 (Cp), 85.7 (Cp), 88.6 (Cp), 89.3 (Cp), 127.6 (*para*-Ph), 128.7 (*meta*-Ph), 129.2 (*ortho*-Ph), 134.6 (*ipso*-Ph), 167.2 (*C*=N); *m*/*z* (APCI) 580 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 580.1681; calcd for $C_{37}H_{31}CoNO_2$, 580.1687.

4.4.3. (*R*)-4-Hydroxymethyl-2-ferrocenyloxazoline 3c. General procedure C used—**2c** (0.366 g, 1.17 mmol) gave **3c** as an orange crystalline solid (0.293 g, 88%). Mp 117–119 °C; $[\alpha]_D^{20} = +96$ (*c* 0.05, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1650 (C=N); δ_H ($CDCl_3$) 3.55 (1H, dd, *J* 11.6, 3.4, OC*H*H), 3.84 (1H, dd, *J* 11.6, 2.5, OCH*H*), 4.09 (5H, s, Cp), 4.12–4.38 (5H, m, OC*H*$_2$+C*H*N+Cp×2), 4.56 (1H, br s, Cp), 4.70 (1H, br s, Cp); δ_C ($CDCl_3$){^{1}H} 62.6 (*C*H_2) 66.8 (*C*HN), 67.9 (Cp), 67.9 (*C*H_2), 68.2 (Cp), 68.3 (*ipso*-Cp), 68.6 (Cp×5), 69.4 (Cp), 69.5 (Cp), 167.5 (*C*=N); *m*/*z* (ES) 286 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 286.0528; calcd for $C_{14}H_{16}FeNO_2$, 286.0530.

4.4.4. (*R*)-4-Hydroxymethyl-2-(1-adamantyl)oxazoline 3d. General procedure C used—**2d** (1.43 g, 5.4 mmol) gave **3d** as a colourless crystalline solid that was recrystallised from EtOAc/petroleum ether 40:60 (0.82 g, 64%). Mp 81–83 °C; $[\alpha]_D^{20} = +100$ (*c* 0.1, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1651 (C=N); δ_H ($CDCl_3$) 1.65–1.80 (6H, m), 1.85–1.92 (6H, m), 1.95–2.08 (3H, m), 3.54 (1H, dd, *J* 11.4, 4.5, OC*H*H), 3.78 (1H, br d, *J* 12, OCH*H*), 4.06 (1H, t, *J* 6, C*H*N), 4.15–4.32 (2H, m, OC*H*$_2$); δ_C ($CDCl_3$){^{1}H} 28.07 (*C*H), 35.64 (*C*C=N), 36.71 (*C*H_2), 39.81 (*C*H_2), 64.53 (*C*H_2), 67.24 (*C*HN), 69.22 (*C*H_2), (*C*=N not observed). HRMS (ES) *m*/*z* found for MH^+, 236.1645; calcd for $C_{14}H_{22}NO_2$, 236.1651.

4.4.5. (*R*)-4-Hydroxymethyl-2-phenyloxazoline 3e. General procedure C used—**2e** (0.84 g, 4.1 mmol) gave **3e** as a colourless crystalline solid (0.64 g, 88%) that was recrystallised from EtOAc/petroleum ether 40:60 (0.41 g, 57%). Mp 97–99 °C; $[\alpha]_D^{20} = +82$ (*c* 0.1, CH_2Cl_2); ν_{max}/cm^{-1} (CH_2Cl_2) 1643 (C=N); δ_H ($CDCl_3$) 3.66 (1H, br d, *J* 12, C*H*HOH), 4.00 (1H, br d, *J* 12, CH*H*OH), 4.31–4.50 (3H, m, C*H*N and OCH_2), 7.28 (2H, t, *J* 8, Ph), 7.40 (1H, t, *J* 8, Ph), 7.74, (2H, d, *J* 8, Ph); δ_C ($CDCl_3$){^{1}H} 63.63 (*C*H$_2$), 68.26 (*C*HN), 69.28 (*C*H$_2$), 127.20 (*ipso*-Ph), 128.33 (Ph), 128.39 (Ph), 131.55 (*para*-Ph), 165.69 (*C*=N). HRMS (ES) *m*/*z* found for MH$^+$, 178.0865; calcd for $C_{10}H_{12}NO_2$, 178.0863.

4.5. General procedure D

A solution of Grignard reagent in THF (3 equiv) was added dropwise to **2b** in Et_2O (20 mL/g) and THF (20 mL/g) cooled to 0 °C. The mixture was then stirred for 3 h, allowed to warm to room temperature and stirred overnight. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ and followed by the addition of additional Et_2O and H_2O. The organic layer was separated, washed with H_2O, dried ($MgSO_4$), filtered and the solvent removed in vacuo. Column chromatography gave the desired tertiary alcohol.

4.5.1. (η^5-(*S*)-2-(4-Dimethylhydroxymethyl)oxazolinylcyclopentadienyl)(η^4- tetraphenylcyclobutadiene)cobalt 3f. General procedure D used—**2b** (1.021 g, 1.68 mmol) and 3 M MeMgI (1.68 mL, 5.04 mmol) gave **3f** as an orange solid (0.960 g, 94%). Mp 160–162 °C; $[\alpha]_D^{20} = -2$ (*c* 0.13, $CHCl_3$); δ_H ($CDCl_3$) 0.95 (3H, s, C*H*$_3$), 1.13 (3H, s, C*H*$_3$), 3.38 (1H, dd, *J* 10.0, 7.6, OC*H*H), 3.46 (1H, dd, *J* 10.0, 7.8, C*H*N), 3.80 (1H, t, *J* 7.7, OCH*H*), 4.68 (1H, br s, Cp), 4.71 (1H, br s, Cp), 5.00 (1H, br s, Cp), 5.12 (1H, br s, Cp), 7.12–7.22 (12H, m, *meta*-Ph+*para*-Ph), 7.35–7.37 (8H, m, *ortho*-Ph); δ_C ($CDCl_3$){^{1}H} 23.9 (C*H*$_3$), 25.9 (C*H*$_3$), 66.8 (*C*H$_2$), 70.1 (*C*Me$_2$), 74.4 (*C*HN), 75.0 (*C*$_4$Ph$_4$), 81.4 (Cp), 83.4 (Cp), 83.6 (*ipso*-Cp), 84.0 (Cp), 85.1 (Cp), 125.5 (*para*-Ph), 126.9 (*meta*-Ph), 127.8 (*ortho*-Ph), 134.2 (*ipso*-Ph), 161.1 (*C*=N); *m*/*z* (APCI) 608 (MH$^+$, 100). HRMS (FAB) *m*/*z* found for MH$^+$, 608.1995; calcd for $C_{39}H_{35}CoNO_2$, 608.2000.

4.5.2. (η^5-(*S*)-2-(4-Diphenylhydroxymethyl)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 3g. General procedure D used—**2b** (0.264 g, 0.43 mmol) and 3 M PhMgBr (0.43 mL, 1.29 mmol) gave **3g** as an orange solid (0.315 g, 99%). Mp >220 °C; $[\alpha]_D^{20} = -166$ (*c* 0.39, $CHCl_3$); ν_{max}/cm^{-1} (CH_2Cl_2) 1644 (C=N); δ_H ($CDCl_3$) 3.27 (1H, dd, *J* 9.7, 8.4, OC*H*H), 3.67 (1H, dd, *J* 9.4, 8.6, OCH*H*), 4.36 (1H, t, *J* 9.9, C*H*N), 4.66 (1H, br s, Cp), 4.69 (1H, br s, Cp), 4.98 (1H, br s, Cp), 5.07 (1H, br s, Cp), 7.11–7.46 (30H, m, Ph); δ_C (CH_2Cl_2){^{1}H} 68.5 (*C*H$_2$), 73.0 (*C*HN), 76.4 (*C*$_4$Ph$_4$), 83.4 (Cp), 85.0 (*ipso*-Cp), 85.1 (Cp), 85.5 (Cp), 86.4 (Cp), 125.8 (Ph), 126.9 (*para*-Ph), 127.0 (Ph), 127.3 (Ph), 127.7 (Ph), 128.4 (*meta*-Ph), 128.4 (Ph), 128.6 (Ph), 129.3 (*ortho*-Ph), 135.7 (*ipso*-Ph), 146.9 (*C*=N); *m*/*z* (APCI) 732 (MH$^+$, 100). HRMS (FAB) *m*/*z* found for MH$^+$, 732.2320; calcd for $C_{49}H_{39}CoNO_2$, 732.2313.

4.6. General procedure E

The alkylation of benzaldehyde by Et_2Zn. To a solution of diethylzinc in hexanes (1.0 M, 1.5 equiv) was added to a solution of ligand (5 mol%) in toluene (5 mL/25 mg) and the mixture stirred for 20 min. Benzaldehyde was then added (1 equiv) and this solution allowed to stir for 24 h. After this time, 0.5 mL of the reaction mixture was removed and diluted with 1 mL of CH_2Cl_2. Following filtration through a small pad of SiO_2, this was then analysed by GC (Chrompack CP-Chirasil-DEX CB analytical column; 80 °C, isothermal 30 min, ramp 8 °C/min, $t_1 = 44.41$ min for *R*-**9**, $t_2 = 46.13$ min for *S*-**9**).

4.6.1. (η^5-(*S*)-2-(4-Methylsulfonylatomethyl)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 18. Methanesulfonyl chloride (0.65 mL, 8.4 mmol) was added drop wise to a solution of **3b** (4.41 g, 7.6 mmol), triethylamine (1.27 mL, 9.1 mmol) and DMAP (5 mol%) in CH_2Cl_2 (50 mL) cooled to 0 °C. The solution was then warmed to room temperature and stirred for 3 h. The solvent was removed in vacuo and the residue column chromatographed (75% EtOAc/40–60) to give **18** as an orange solid (4.51 g, 90%). Mp 102–104 °C; $[\alpha]_D^{20} = -29$ (*c* 0.28, $CHCl_3$); δ_H ($CDCl_3$) 2.92 (1H, t, *J* 8.8, OC*H*H), 3.73 (1H, d, *J* 6.1, OCH*H*), 3.85–3.88 (2H, m, OC*H*H+C*H*N), 4.02–4.08 (1H, m, OCH*H*), 4.71 (1H, br s, Cp), 4.76 (1H, br s, Cp), 5.02 (1H, br s, Cp), 5.10 (1H, m, br s, Cp), 6.92–7.23 (14H, m, Ph), 7.34–7.36 (16H, m, Ph); δ_C ($CDCl_3$){^{1}H} 36.5 (*C*H$_3$), 64.0 (*C*HN), 68.1 (O*C*H$_2$), 69.6 (O*C*H$_2$), 75.1 (*C*$_4$Ph$_4$), 81.4 (Cp), 82.8 (*ipso*-Cp), 83.9 (2×Cp), 85.3 (Cp), 125.6 (*para*-Ph), 127.0 (*meta*-Ph), 127.8 (*ortho*-Ph), 134.0 (*ipso*-Ph), 162.8 (*C*=N); *m*/*z* (APCI) 658 (MH$^+$, 100). HRMS (FAB) *m*/*z* found for M$^+$, 657.1388; calcd for $C_{38}H_{32}CoNO_4S$, 657.1379.

4.6.2. (η^5-(*S*)-2-(4-Diphenylphosphinylmethyl)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 19. Potassium *tert*-butoxide (0.216 g, 1.92 mmol) was added in one portion to a solution of diphenylphosphine (0.134 mL, 0.77 mmol) in THF (5 mL) cooled to −10 °C. The mixture was then stirred at this temperature for 30 min to give a deep orange/red solution and added to a solution of **19** (0.506 g, 0.77 mmol) in THF (20 mL) cooled to −10 °C. The orange reaction mixture was then allowed to warm to room temperature and then heated under reflux overnight. On cooling to room temperature the reaction was quenched with H_2O (50 mL) and quickly separated, dried ($MgSO_4$), filtered and solvent removed in vacuo. The residue was then flash chromatographed (75% EtOAc/40–60) to give **19** as an air sensitive orange solid, which was immediately stored under nitrogen (0.437 g, 76%). Mp 89-90 °C; $[\alpha]_D^{20} = +17$ (*c* 0.29, $CHCl_3$); δ_H ($CDCl_3$) 1.45–1.63 (1H, m, OC*H*H), 2.43 (1H, d, *J* 13.0, OCH*H*), 3.40–3.54 (3H, m,

OCH_2+CHN), 4.46 (1H, br s, Cp), 4.57 (1H, br s, Cp), 4.94 (1H, br s, Cp), 4.99 (1H, br s, Cp), 6.94–7.12 (14H, m, Ph), 7.13–7.31 (16H, m, Ph); δ_C ($CDCl_3$){^{1}H} 35.5, 64.1 (d, *J* 17), 72.5 (d, *J* 10), 76.3 (C_4Ph_4), 82.2 (*ipso*-Cp), 82.6 (Cp), 85.0 (Cp), 85.1 (Cp), 86.7 (Cp), 126.8 (*para*-Ph), 128.4 (*meta*-Ph), 128.8 (Ph), 128.9 (Ph), 129.0 (Ph), 129.2 (Ph), 129.3 (Ph), 129.5 (Ph), 132.9 (d, *J* 18, Ph), 133.6 (d, *J* 19, Ph), 135.6 (*ipso*-Ph), 161.4 (*C*=N); *m*/*z* (APCI) 748 (MH^+, 100). HRMS (FAB) *m*/*z* found for MH^+, 748.2189; calcd for $C_{49}H_{40}CoNOP$, 748.2179.

4.7. General procedure F

The allylic alkylation of 1,3-diphenylprop-2-enyl acetate **20**. A solution of the appropriate ligand (6 mol %) in the reaction solvent (1 mL/10 mg) was added to allyl palladium chloride dimer (2.5 mol %) and the resulting solution stirred for 20 min. A solution of 1,3-diphenylprop-2-enyl acetate in the reaction solvent (1 equiv, 1 mL/100 mg) was then added and the mixture stirred for an additional 5 min followed by the addition in the following order of dimethylmalonate (2 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (2 equiv) and potassium acetate (5 mol %). The reaction mixture was stirred for 24 h after which time a 0.5 mL portion was removed and filtered through a pipette containing cotton wool and a pad of silica (diethyl ether as eluent). The solvent was removed in vacuo and a solution of the resultant oil analysed via HPLC (Chiralcel OD analytical column cooled to 11 °C using a column jacket; eluting with 99:1 hexanes/2-propanol, flow rate 0.5 mL/min, 254 nm $t_1 = 36.8$ min for *R*-**21**, $t_2 = 39.6$ min for *S*-**21**).

4.8. General procedure G

The allylic alkylation of 1,3-dimethylprop-2-enyl pivalate **22**. A solution of appropriate ligand (6 mol %) in the reaction solvent (1 mL/10 mg) was added to allyl palladium chloride dimer (2.5 mol %) and the solution stirred for 20 min. A solution of 1,3-dimethylprop-2-enyl pivalate in the reaction solvent (1 equiv, 1 mL/100 mg) was then added and stirred for an additional 5 min. Dimethylmalonate (2 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (2 equiv) and potassium acetate (5 mol %) were then added in this order. The reaction mixture was stirred for 24 h after which time a 0.5 mL portion was removed and filtered through a pipette containing cotton wool and a pad of silica (diethyl ether as eluent). The solvent was removed in vacuo and a solution of the resultant oil analysed via GC (Chrompack CP-Chirasil-DEX CB analytical column; 90 °C isothermal, $t_1 = 16.62$ min for *S*-**23**, $t_2 = 17.00$ min for *R*-**23**).

4.9. General procedure H

The allylic alkylation of 3-cyclohexenyl acetate **24**. A solution of appropriate ligand (6 mol %) in the reaction solvent (1 mL/10 mg) was added to allyl palladium chloride dimer (2.5 mol %) and the solution stirred for 20 min. A solution of cyclohexenyl acetate in the reaction solvent (1 equiv, 1 mL/100 mg) was then added and stirred for an additional 5 min. Dimethylmalonate (2 equiv), *N*,*O*-bis(trimethylsilyl)acetamide (2 equiv) and potassium acetate (5 mol %) were then added in this order. The reaction mixture was stirred for 24 h after which time 0.5 mL of the reaction mixture was removed and filtered through a pipette containing cotton wool and a pad of silica (diethyl ether as eluent). The solvent was removed in vacuo and a solution of the resultant oil analysed via GC (Chrompack CP-Chirasil-DEX CB analytical column; 110 °C isothermal, $t_1 = 29.91$ min for *S*-**25**, $t_2 = 30.57$ min for *R*-**25**).

4.9.1. $PdCl_2$ complex of (η^5-(*S*)-2-(4-diphenylphosphinylmethyl)-oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 26. $PdCl_2$ $(CH_3CN)_2$ (0.098 g, 0.38 mmol) was added in one portion to a solution of **19** (0.281 g, 0.38 mmol) in CH_2Cl_2 (10 mL). This solution was stirred for 1 h then the solvent was removed in vacuo to give an orange solid. This sample was recrystallised from hexanes/CH_2Cl_2 to give an orange crystalline solid (0.243 g, 70%). Mp >220 °C; ν_{max}/cm^{-1} (CH_2Cl_2) 1604 (C=N); δ_H ($CDCl_3$) 1.92–2.06 (br m), 3.39–3.47 (br m), 4.36 (br s), 4.74 (br s), 4.76 (br s), 5.23 (br s), 6.43 (br s), 6.84–7.84 (br m); δ_P ($CDCl_3$){^{1}H} 35.8 (PPh$_2$). HRMS (ES) *m*/*z* found for $(M-Cl)^+$, 888.0828; calcd for $C_{49}H_{39}ClCoNOPPd$, 888.0825.

4.10. General Procedure I

Chlorodiphenylphosphine (1.1 equiv) was added to a solution of alcohol **3** (1 equiv), triethylamine (1.2 equiv) and DMAP (0.1 equiv) in CH_2Cl_2 (5 mL/100mg of alcohol) cooled to −10 °C. The resulting solution was stirred for 30 min, allowed to warm to room temperature and stirred for a further 10 min. The reaction mixture was then filtered through a plug of alumina (2.5 cm × 5 cm) using 50% EtOAc/40–60 as eluent and the solvent removed in vacuo to give **4**.

4.10.1. (η^5-(*S*)-2-(4-Diphenylphosphinoxymethyl)oxazolinylcyclopentadienyl)(η^5-pentaphenylcyclopentadienyl)iron 4a. General procedure I used—**3a** (0.104 g, 0.16 mmol) gave **4a** as an air sensitive red/orange waxy solid (0.090 g, 68%). ν_{max}/cm^{-1} (CH_2Cl_2) 1648 (C=N); δ_H ($CDCl_3$) 3.11 (1H, q, *J* 8.90, OCHH), 3.69–3.78 (1H, m, OCHH), 3.82 (1H, t, *J* 8.93, OCHH), 3.89–4.07 (2H, m, OCHH and CHN), 4.28 (2H, s, Cp), 4.63 (1H, s, Cp), 4.66 (1H, s, Cp), 6.87–7.09 (25H, m, Ph), 7.12–7.29 (6H, m, Ph), 7.30–7.39 (4H, m, Ph); δ_C ($CDCl_3$){^{1}H} 66.8 (d, *J* 8, CHN), 69.1 (OCH$_2$), 70.8 (d, *J* 18.2, O CH$_2$), 73.5 (Cp), 73.9 (Cp), 74.9 (*ipso*-Cp), 76.4 (Cp), 76.8 (Cp), 87.4 (C_5Ph_5), 125.5 (*para*-Ph), 126.3 (*meta*-Ph), 127.40 (Ph), 127.45 (Ph), 127.50 (Ph), 127.55 (Ph), 128.5 (d, *J* 4, Ph), 129.2 (d, *J* 6, Ph), 129.4 (d, *J* 6, Ph), 131.6 (*ortho*-Ph), 134.4 (*ipso*-Ph), 164.0 (*C*=N); δ_P {^{1}H} 115.5 (OPPh$_2$); *m*/*z* (FAB) 850 (MH^+, 100%). HRMS (ES) *m*/*z* found for MH^+, 850.2527; calcd for $C_{56}H_{45}FeNO_2P$, 850.2537.

4.10.2. (η^5-(*S*)-2-(4-Diphenylphosphinoxymethyl)oxazolinylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt 4b. General procedure I used—**3b** (0.204 g, 0.35 mmol) gave **4b** as an air sensitive orange solid (0.156 g, 58%). Mp 130–132 °C; δ_H ($CDCl_3$) 3.41 (2H, t, *J* 9.01, OC*H*-H+OCH*H*), 3.70–3.76 (1H, m, 1H, OC*H*H), 3.80–3.99 (2H, m, OCH *H* and C*H*N), 4.65 (1H, br s, Cp), 4.72 (1H, br s, Cp), 4.96 (1H, br s, Cp), 5.08 (1H, br s, Cp), 7.01–7.41 (30H, m, Ph); δ_C ($CDCl_3$){^{1}H} 66.0 (*C*HN), 68.8 (O*C*H_2), 70.9 (O*C*H_2), 75.0 (C_4Ph_4), 81.4 (Cp), 83.8 (2×Cp), 85.0 (Cp), 125.5 (*para*-Ph), 126.9 (*meta*-Ph), 127.2, 127.3 (Ph), 127.6 (Ph), 127.8 (*ortho*-Ph), 128.3 (d, *J* 7, Ph), 129.2 (d, *J* 4, Ph), 129.4 (d, *J* 3, Ph), 134.2 (*ipso*-Ph); δ_P {^{1}H} 115.7 (O*P*Ph_2); *m*/*z* (FAB) 764 (MH^+, 53%). HRMS (EI) *m*/*z* found for M^+, 763.2041; calcd for $C_{49}H_{39}CoNO_2P$, 763.2050.

4.10.3. (*S*)-2-(4-Diphenylphosphinoxymethyl)oxazolinylferrocene 4c. General procedure I used—**3c** (0.128 g, 0.45 mmol) gave **4c** as an air sensitive orange oil (0.198 g, 94%). δ_H ($CDCl_3$) 3.77–3.82 (1H, m, OC*H*H), 3.95–4.00 (m, 1H, OCH*H*), 4.06 (5H, s, C_5H_5), 4.22–4.34 (3H, m, O*C*H_2 and C*H*N), 4.24 (2H, s, Cp), 4.64 (2H, s, Cp), 7.20–7.30 (6H, m, Ph), 7.37–7.43 (4H, m, Ph); δ_C ($CDCl_3$){^{1}H} 66.2 (d, *J* 8, *C*HN), 68.0 (2×Cp), 68.7 (5×Cp), 69.3 (2×Cp), 70.2 (d, *J* 17, O*C*H_2), 127.26 (Ph), 127.29 (Ph), 127.33 (Ph), 127.36 (Ph), 128.4 (d, *J* 5, Ph), 129.3 (d, *J* 6, Ph), 129.6 (d, *J* 6, Ph), 166.8 (*C*=N); δ_P ($CDCl_3$){^{1}H} 115.3 (O*P*Ph_2).

4.10.4. (*S*)-2-(4-Diphenylphosphinoxymethyl)oxazolinyladamantane 4d. General procedure I used—**3d** (0.106 g, 0.45 mmol) gave **4d** as an air sensitive colourless oil (0.187 g, 99%). δ_H ($CDCl_3$) 1.59 (6H, br s, 3×CH_2), 1.78 (6H, br s, 3×CH_2), 1.97 (3H, br s, 3×C*H*), 3.76–3.80 (1H, m, OC*H*H), 3.86–4.25 (4H, m, 3×OCH *H*+C*H*N), 7.21–7.33 (4H, m, Ph), 7.34–7.50 (4H, m, Ph), 7.61–7.78 (2H, m, Ph); δ_C ($CDCl_3$){^{1}H} 26.9 (3×*C*H), 35.5 (3×*C*H_2), 38.5 (3×*C*H_2), 65.4 (O*C*H_2), 68.4 (*C*HN), 70.0 (d, *J* 18, O*C*H_2), 127.25 (Ph), 127.3 (Ph), 127.45 (Ph), 127.5 (Ph), 128.3 (d, *J* 11, Ph), 129.2 (d, *J* 10, Ph), 129.4 (d, *J* 11, Ph), 174.0 (*C*=N); δ_P ($CDCl_3$){^{1}H} 115.0 (O*P*Ph_2).

4.10.5. (*S*)-2-(4-Diphenylphosphinoxymethyl)oxazolinylbenzene 4e. General procedure I used—**3e** (0.109 g, 0.62 mmol) gave **4e** as an air sensitive colourless oil, which solidified on standing (0.156 g, 70%). Mp 68–70 °C; δ_H ($CDCl_3$) 3.87–3.93 (1H, m, OC*H*H), 4.05 (1H, m, OCH*H*), 4.36 (2H, dd, *J* 7.93 3.05, O*C*H_2), 4.43–4.51 (1H, m, C*H*N), 7.15–7.42 (13H, m, Ph), 7.82–7.84 (2H, m, Ph); δ_C ($CDCl_3$){^{1}H} 67.7 (O*C*H_2), 70.6 (*C*HN), 71.8 (d, *J* 18, O*C*H_2), 126.3 (Ph), 128.6 (Ph), 128.7 (Ph), 128.8 (Ph), 129.7 (d, *J* 12, Ph), 130.6 (d, *J* 7, Ph) 130.8 (d, *J* 7, Ph), 131.8 (Ph), 165.6 (*C*=N); δ_P ($CDCl_3$){^{1}H} 116.4 (–O*P*Ph_2).

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CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.com.ac.uk).
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