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Examining the origin of selectivity in the reaction of racemic alcohols with chiral *N*-phosphoryl oxazolidinones

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ABSTRACT

A range of known and novel *N*-phosphoryl oxazolidinones and imidazolidinones were prepared and screened in the kinetic resolution of a range of racemic magnesium chloroalkoxides. Models are proposed to account for the enantioselectivity achieved based on a combination of chiral relay effects, generation of transient stereochemistry and the structure of the intermediate magnesium alkoxide.

1. Introduction

Many biochemical processes are mediated by the selective formation or cleavage of a phosphate monoester bond.[1] Pioneering work by Whitesides demonstrated that these specific biological phosphorylation events can also be replicated in the laboratory at preparative scale using isolated enzymes and appropriate cofactors.[2] Whilst the substrate specificity of many of these systems has been explored, they are still limited to key interactions of structural features of the substrate molecule within the enzyme active site. A radical solution to solving this problem has been presented by Miller et al., generating bespoke short-peptide catalysts that are tuned to the appropriate substrate and reaction class. The first demonstration of this strategy was applied to the kinetic resolution of racemic secondary alcohols employing histidine containing peptides,[3] and a related strategy was then used for the asymmetric phosphorylation of a protected *myo*-inositol.[4] This desymmetrisation could afford either enantiomer of the corresponding monophosphate, by employing different peptide catalysts. The monophosphates that were obtained were elaborated to afford a range of inositol phosphate-derived natural products.[5] Although this approach afforded the desired phosphate esters in high yield and enantioselectivity, it was only reported to be useful in the phosphorylation of protected *myo*-inositols.

Within this arena of chemistry, smaller reagent based solutions to this problem have been presented, albeit in the context of conducting much simpler kinetic resolution processes. Chiral oxazolidinones have been shown to be useful in a wide variety of transformations, mainly acting as chiral auxiliaries. Work by Evans and Anderson showed that they could be used as enantioselective acyl transfer reagents for affecting the kinetic solution of a small family of racemic secondary alcohols.[6] This study was extended by Davies et al. using 5,5-disubstituted oxazolidinones.[7]

Based on these reports, research from these laboratories has been examining the potential of the use of chiral oxazolidinones to develop an enantioselective phosphorylation procedure. In stark contrast to acylation reactions, it was found that the kinetic resolution of 1-phenylethanol gave very poor selectivity, with mechanistic data indicating this to be a consequence of the reaction proceeding via an $S_N2(P)$ pathway.[8] This work presents further studies in this area with an aim to better understand the origins of the selectivity and hence develop more selective reagents.

2. Results

The impact of making structural and electronic variations was first examined by preparing a range of chiral *N*-phosphoryl oxazolidinones as described previously or using analogous methods.[9] In addition to these, a serine-derived *N*-phosphoryl oxazolidinone **4** was also considered that may facilitate additional elements of coordinative control via the C4 hydroxymethyl group to the incoming alkoxide nucleophile. Attempts to access this started by transformation of *N*-Boc-L-TBDMS serine methyl ester **1** into the oxazolidinone **2** by a double Grignard addition, followed by immediate cyclisation (Scheme 1).

Deprotonation of oxazolidinone **2** with *n*-BuLi, followed by trapping with diethyl chlorophosphate afforded *N*-phosphoryl oxazolidinone **3**. However, treatment with TBAF led to migration of the phosphoryl group to give phosphate ester **5** as evidenced from the ^{1}H NMR spectrum of the unpurified reaction mixture. Attempted purification by flash column chromatography resulted

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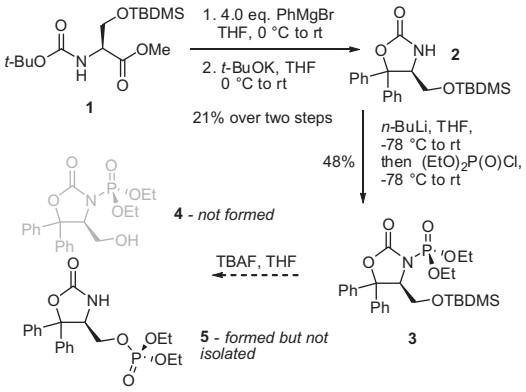
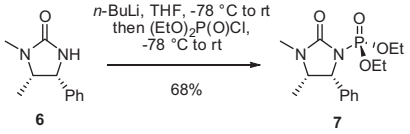


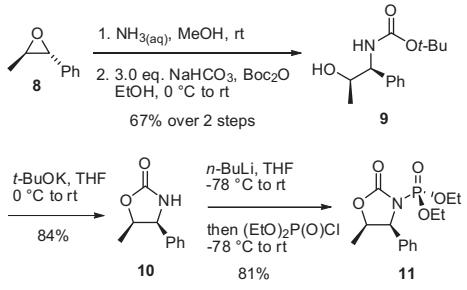
Scheme 1. Attempted synthesis of hydroxy-serine oxazolidinone **4**.



Scheme 2. Formation of *N*-phosphoryl imidazolidinone **7**.

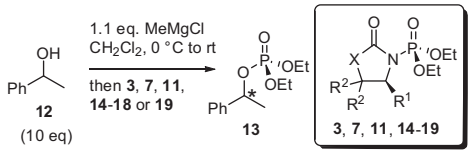
in decomposition. However, the silyl ether protected *N*-phosphoryl oxazolidinone **3** was added to the selection of phosphorylating reagents to be screened. Commercially available imidazolidinone **6** was also used. Deprotonation by treatment with *n*-BuLi, followed by the addition of diethyl chlorophosphate, provided *N*-phosphoryl imidazolidinone **7** in good yield (Scheme 2).

Since this imidazolidinone had a different substitution pattern to the other oxazolidinones used, an analogue was required to directly compare the reactivity and selectivity. The opposite enantiomer of the analogous oxazolidinone was targeted due to the ready availability of epoxide **8** starting material. This was ring-opened with ammonia to afford a 1,2-amino alcohol and immediately treated with Boc_2O to afford the *t*-butyl carbamate **9** in good yield over both steps. Treatment with *t*-BuOK gave the oxazolidinone **10**, which was phosphorylated under standard conditions to provide the target *N*-phosphoryl oxazolidinone **11** in good yield (Scheme 3).



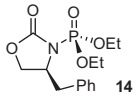
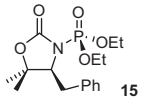
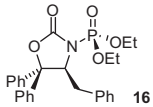
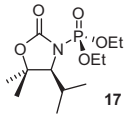
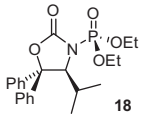
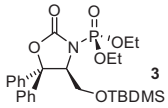
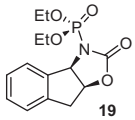
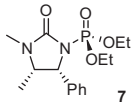
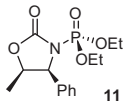
Scheme 3. Synthesis of *N*-phosphoryl oxazolidinone **11**.

As in earlier studies, the possibility of obtaining higher levels of enantioselectivity was increased by adopting the conditions set out by Evans and Davies which employed a large excess of racemic alcohol, but this did require a protocol to directly determine the selectivity of the phosphate ester product by chiral phase HPLC analysis. The use of 10 equiv of 1-phenylethanol **12** allowed each of the reactions to proceed to completion, but the selectivity remained low in each case (Scheme 4, Table 1).



Scheme 4. Screening selectivity of reagents **3**, **7**, **11** and **14**–**19**.

Table 1
Initial screening of reagents **3**, **7**, **11** and **14**–**19** as described in Scheme 4[a]

Entry	Reagent	Yield[b,c] (%)	ee[b,d] (%)
1	 **14**	57 (50)	0 (2)
2	 **15**	67 (36)	3 (4)
3	 **16**	91 (74)	14 (15)
4	 **17**	69 (57)	8 (5)
5	 **18**	88 (87)	15 (15)
6	 **3**	62 (58)	11 (10)
7	 **19**	68 (59)	5 (5)
8		0 (0)	—
9[e]	 **7**	85 (66)	−7 (−8)
10		50 (40)	4 (4)
11[e]	 **11**	75 (75)	5 (4)

[a] Reactions performed by addition of MeMgCl (0.15 mL, 3.0 M in THF, 0.45 mmol) to a solution of 1-phenyl ethanol **12** (0.50 g, 4.1 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After warming to room temperature for 1 h, the reaction was recooled to 0 °C, and phosphorylating agent **3**, **7**, **11**, **14**–**18** or **19** (0.43 mmol) was added as a solution in CH_2Cl_2 (10 mL). The reaction was left to warm to room temperature overnight, quenched with aqueous ammonium chloride, followed by standard work-up procedures.

[b] Values in parentheses represent the results of duplicate reactions.

[c] Refers to isolated product.

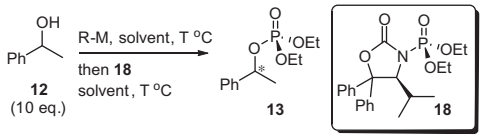
[d] Determined by chiral phase HPLC analysis.

[e] THF used as solvent and *n*-BuLi as base.

Although the selectivities were low, a clear pattern emerged, with an increase in the steric bulk of the substituents at the 5-position on the oxazolidinone leading to an increase in selectivity (entries 1–5). The TBDMS-serine derived *N*-phosphoryl oxazolidinone **3** (entry 6) gave the phosphate ester **13** in 11% ee, comparable

to the benzyl system (compare entries 3 and 6). Both of these systems have a methylene linker providing torsional freedom, allowing the group to be orientated away from the reacting centre. Use of the rigid aminoindanol derived *N*-phosphoryl oxazolidinone **19** (entry 7) afforded the phosphate ester **13** with only 5% ee. *N*-Phosphoryl imidazolidinone **7** did not react under standard conditions. However, when the reaction was carried out with *n*-BuLi in THF (entry 9) it proceeded to complete conversion with 7% ee. The use of *N*-phosphoryl oxazolidinone **11** under standard conditions led to complete conversion to phosphate ester **13**, which was obtained with 4% ee (entry 10). A switch of the conditions to *n*-BuLi in THF gave a similar result (entry 11). The selectivity and reactivity of the imidazolidone system compared favorably to the oxazolidinone (entries 8–11), but did not offer any substantial benefit. These latter results also confirmed that better selectivity was provided with oxazolidinones that are doubly substituted at the 5-position.

The benzyl and isopropyl oxazolidinones **16** and **18** were the most selective phosphorylating agents of those tested. *N*-Phosphoryl oxazolidinone **18** is a solid and so was easier to handle and purify and was therefore used in an attempt to optimize the reaction conditions (Scheme 5, Table 2). The standard reaction conditions involved initially cooling the reaction mixture to 0 °C whilst the reagents were combined, before being allowed to warm to rt (entry 1). Maintaining the reaction at −78 °C (entry 2) or 0 °C led to essentially no reaction, whilst increasing the temperature to 40 °C (entry 4) caused a drop in selectivity from 15% ee to 8% ee. Interestingly, the yield also dropped in this case which may be due to the phosphate product decomposing at elevated temperature.

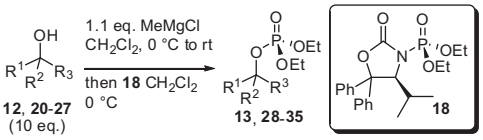


Scheme 5. Optimisation with reagent **18**.

Switching from CH_2Cl_2 to a coordinating solvent THF had little effect on the reaction (entry 5), but changing the base used did. When *n*-BuLi was used (entry 6) to form a lithium alkoxide, the selectivity of the reaction decreased to 8% ee. Performing the same reaction with *n*-BuLi in THF (entry 7) led to essentially racemic material. The use of NaH and KH (entries 8 and 9) led to a reversal in selectivity, giving the opposite enantiomer of phosphate **13** with 9% and 6% ee, respectively. If the origin of these results lies in the ability of the phosphoryl oxazolidinone to chelate with the cation of the base, then pre-treatment with a Lewis acidic additive could prove to be a useful strategy. Addition of $MgCl_2$ to the phosphoryl oxazolidinone for an hour prior to addition to the solution of alkoxide (entry 10) led to a slight decrease in ee (entry 1 vs entry 10). However, the reactivity was shut-off entirely when LiCl was used as the additive in conjunction with *n*-BuLi as the base and only starting materials were recovered (entry 11); this was also the case using $ZnCl_2$ (entries 12 and 13). The final reaction parameter investigated was the effect of varying the concentration of the reaction mixture (entries 14 and 15). Phosphate ester **13** was obtained with 15% ee, regardless of the concentration.

With the optimisation studies complete, a range of racemic alcohol substrates were investigated which were selected based on variations of the 1-phenylethanol skeleton to help glean more mechanistic information. The substrates were either commercially available, prepared by sodium borohydride reduction of the parent ketone, or Grignard addition to the parent carbonyl compound or epoxide. The corresponding racemic phosphate esters were prepared for analysis by treating the racemic alcohols with *n*-BuLi and quenching with diethyl chlorophosphate.

Each of the alcohol substrates were screened under the optimised reaction conditions (Scheme 6) and the results are summarised below (Table 3). Variation of the structure of the substrate had a considerable effect on the reactivity and selectivity of the procedure. The absolute stereochemistry of the major stereoisomer of phosphate ester obtained in the reaction with 1-phenylethanol was determined to be (*S*) by preparation of the phosphate ester from commercially available enantiomerically pure alcohol and comparison of the specific rotation and HPLC retention times.



Scheme 6. Substrate scope of reagent **18**.

Table 2
Reaction optimisation of reagent **18** as described in Scheme 5[a]

Entry	*T* (°C)	R-M	Solvent	Additive	Concentration (mmol dm^{-3})	Yield[b] (%)	ee[c] (%)
1	0 to rt	MeMgCl	CH_2Cl_2	—	13.6	88	15
2	−78	MeMgCl	CH_2Cl_2	—	13.6	0	—
3	0	MeMgCl	CH_2Cl_2	—	13.6	0	—
4	40	MeMgCl	CH_2Cl_2	—	13.6	37	8
5	0 to rt	MeMgCl	THF	—	13.6	66	14
6	0 to rt	*n*-BuLi	CH_2Cl_2	—	13.6	56	8
7	0 to rt	*n*-BuLi	THF	—	13.6	65	2
8	0 to rt	NaH	THF	—	13.6	56	−9
9	0 to rt	KH	THF	—	13.6	57	−6
10	0 to rt	MeMgCl	CH_2Cl_2	$MgCl_2$	13.6	43	10
11	0 to rt	*n*-BuLi	THF	LiCl	13.6	0	—
12	0 to rt	MeMgCl	CH_2Cl_2	$ZnCl_2$	13.6	0	—
13	0 to rt	*n*-BuLi	THF	$ZnCl_2$	13.6	0	—
14	0 to rt	MeMgCl	CH_2Cl_2	—	4.5	56	15
15	0 to rt	MeMgCl	CH_2Cl_2	—	40.9	47	15

[a] Reactions performed by addition of a solution of organometallic reagent to a solution of 1-phenyl ethanol **12** (0.50 g, 4.1 mmol) in solvent at the specified temperature. After warming to room temperature for 1 h, the reaction was re-cooled to 0 °C, and phosphorylating agent **18** (0.43 mmol) was added as a solution in solvent. The reaction was left to warm to room temperature overnight, quenched with aqueous ammonium chloride, followed by standard work-up procedures.
[b] Refers to isolated product.
[c] Determined by chiral phase HPLC analysis.

As the size of the R^2 substituent was increased, the selectivity of the phosphorylation increased. Changing the R^2 methyl group of substrate **12** to the R^2 cyclohexyl group of substrate **20** led to an increase from 15% ee to 19% ee (entries 1 and 2). A similar level of selectivity, 20% ee, was achieved when the R^2 substituent was an isopropyl group in alcohol **21** (entry 3). However, when the size of the R^2 substituent was increased to a *t*-butyl group in alcohol **22**, conversion to the corresponding phosphate ester proceeded in less than 5% (entry 4). Increasing the size of the R^1 substituent from the phenyl group of 1-phenylethanol **12** to the *ortho*-tolyl group of alcohol **23** again caused a large decrease in reactivity (entry 5). Surprisingly, when the size of the R^1 substituent was decreased to a benzyl group in substrate **24**, the corresponding phosphate ester **32** was obtained with an increased 28% ee (entry 6). Changing the isopropyl group of this substrate to a *t*-butyl group **25** again shut off the reactivity (entry 7), whilst extending the benzyl chain by an additional methylene unit **26**, led to a decrease in reactivity (entry 8). Tertiary alcohol **27** was subjected to the standard conditions but was left to deprotonate with MeMgCl for 3 h at rt prior to the addition of *N*-phosphoryl oxazolidinone **18**. However, only starting materials were recovered upon work-up (entry 9).

Based on these studies a model can start to be constructed for the changes in reactivity and selectivity observed in these processes. The more promising selectivities observed came from reactions conducted in the presence of magnesium salts, whilst low and opposite selectivities were obtained when potassium and sodium salts were used. The structures of magnesium alkoxides and magnesium chloro-alkoxides have been well studied, being shown to adopt dimeric tetrahedral species in the solid state and when dissolved.[10–12] However, magnesium complexes formed by reaction of alcohols with magnesium chloride tend to give octahedral complexes.[13] The reactions performed in this current study used 10 equiv of alcohol and 1 equiv of MeMgCl. Thus, because of the excess of alcohol present, it was unclear whether the reactive species would exist in an octahedral or tetrahedral form. In order to probe this, reactions were conducted with diminishing quantities of alcohol in THF to ensure the presence of a coordinating solvent, akin to the previously reported structural studies (Table 3). All reactions proceeded to completion based on the number of equivalents of oxazolidinone **18** with a little change in the enantioselectivity. Given that the species present when the alcohol is completely deprotonated must be the dimeric tetrahedral based system (Table 4, entry 3), it seems reasonable to assume that this is the reactive species observed in all cases.

Thus, upon addition of the phosphoryl oxazolidinone, displacement of the superfluous solvent ligands would occur, leading to complex **36**, positioning the alkoxide nucleophile in the correct trajectory for an intramolecular $S_N2(P)$ attack at the phosphorus centre. This is in accordance with previous studies indicating inversion of stereochemistry at the phosphorus centre[8] (Fig. 1a).

The drop in selectivity for the lithium, sodium and potassium alkoxides might then be attributed to the different solution structure leading to a competitive reaction pathway that is either non-selective or leads to the opposite enantiomer of product. In these cases, formation of a phosphoryl oxazolidinone–magnesium alkoxide complex may not occur due to unfavorable disruption of the alkoxide cubic cluster arrangement,[14] thus leading to an intermolecular reaction (Fig. 1b). As a consequence, since no chelation control of the phosphoryl oxazolidinone exists, the reactive conformation is likely to be different (e.g., by dipole minimisation), leading to significantly different interactions between the stereogenic elements. A related study by Eames et al. provides support for this, demonstrating that kinetic resolution of *N*-acyl oxazolidinones with the lithium alkoxide of 1-phenylethanol proceeded in poor selectivity, but when $ZnCl_2$ was employed as an additive a drastic improvement in selectivity was observed.[15] However, the reason for failure of $ZnCl_2$ in the case of the phosphoryl oxazolidinones is not clear.

Based on these assumptions of reactive intermediates, models can then be proposed that accounts for the crucial role that the 5,5-*gem*-disubstitution pattern plays in attenuating the selectivity. The substituents at the 5-position have a steric clash with the stereodirecting group at the 4-position, forcing it towards the phosphoryl group, in an analogous manner to that suggested by Davies.[7] The stereochemical relay possibly perturbs the conformation of one of the ethoxy groups whilst leaving the other undisturbed, with this conformational bias setting up a transient chiral

Table 3
Demonstration of substrate scope of reagent **18** as described in Scheme 6[a]

Entry	R^1	R^2	R^3	Alcohol	Product	Yield[b,c] (%)	ee[b,d] (%)
1	Ph	Me	H	**12**	**13**	88 (87)	15 (15)
2	Ph	Cy	H	**20**	**28**	92 (92)	19 (18)
3	Ph	*i*-Pr	H	**21**	**29**	83 (24)	20 (21)
4	Ph	*t*-Bu	H	**22**	**30**	0 (0)	—
5	*o*-Tolyl	Me	H	**23**	**31**	0 (0)	—
6	Bn	*i*-Pr	H	**24**	**32**	76 (75)	28 (28)
7	Bn	*t*-Bu	H	**25**	**33**	0 (0)	—
8	$Ph(CH_2)_2$	*i*-Pr	H	**26**	**34**	66 (66)	14 (13)
9	Ph	*i*-Pr	Me	**27**	**35**	0 (0)	—

[a] Reactions performed by addition of MeMgCl (0.15 mL, 3.0 M in THF, 0.45 mmol) to a solution of alcohol **12**, **20**–**27** (4.1 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After warming to room temperature for 1 h, the reaction was re-cooled to 0 °C, and phosphorylating agent **18** (0.43 mmol) was added as a solution in CH_2Cl_2 (10 mL). The reaction was left to warm to room temperature overnight, quenched with aqueous ammonium chloride, followed by standard work-up procedures.
[b] Values in parentheses represent the results of duplicate reactions.
[c] Refers to isolated product.
[d] Determined by chiral phase HPLC analysis.

Table 4
Examination of the effect of the number of equivalents of alcohol **12** on the reactivity and selectivity under the optimal conditions described in Scheme 6[a]

Entry	Reagent equivalencies			ee[b,c] (%)
	12	MeMgCl	**18**	**13**
1	10	1	1	12 (12)
2	10	10	1	11 (13)
3	2	2	1	10 (10)

[a] Reactions performed by addition of MeMgCl (3.0 M in THF) to a solution of alcohol **12** in THF (20 mL) at 0 °C. After warming to room temperature for 1 h, the reaction was re-cooled to 0 °C, and phosphorylating agent **18** (0.43 mmol) was added as a solution in THF (10 mL). The reaction was left to warm to room temperature overnight, quenched with aqueous ammonium chloride, followed by standard work-up procedures.
[b] Values in parentheses represent the results of duplicate reactions.
[c] Determined by chiral phase HPLC analysis.

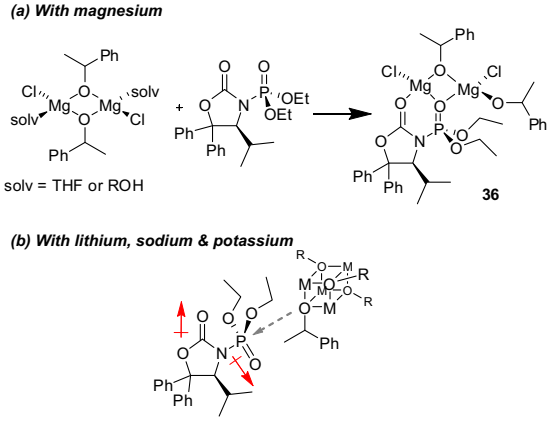


Figure 1. Possible reactive intermediates.

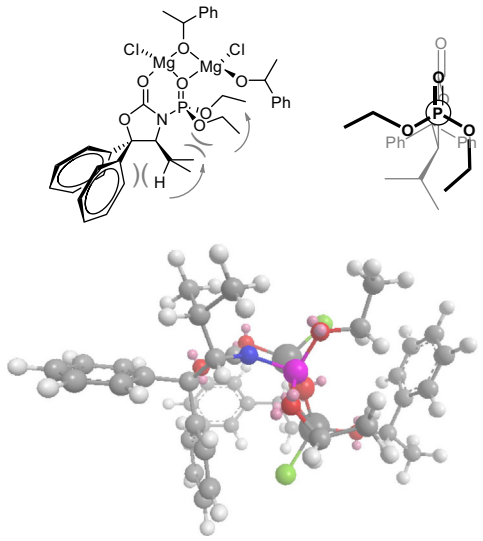


Figure 2. Possible model for the observed selectivity based upon a conformational enforced transient chiral environment.

environment around the phosphorus atom that contributes towards the selectivity of the reaction (Fig. 2).

Additionally, the dimeric magnesium alkoxide reactive complexes contain two chiral alkoxide moieties, leading to the intriguing possibility of forming diastereomeric reactive complexes, one of which may have enhanced or reduced reactivity or selectivity (Fig. 3a). Also, interactions between the two alkoxide groups might explain why some of the better selectivities were observed with alcohol **24**, since in this case, the increased size of the alcohol allows for better interaction between the two alkoxide moieties (Fig. 3b). Further experimental work is underway to probe each of these factors. Naturally, it is possible that a combination of all of these models operate either in a cooperative or non-cooperative manner. Of course, if the reaction proceeds through a pentagonal bipyramidal intermediate, then similar arguments to these exist. However, in this case, these interactions now lead to differences in energies of the ensuing intermediates, or the activation energies for pseudorotation.

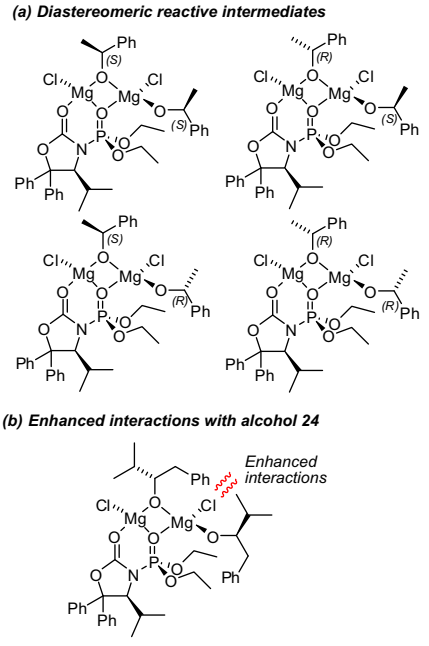


Figure 3. Possible reactive intermediates.

3. Conclusion

Further experimental evidence has been collated to help better explain the stereoselectivity of the reactions of *N*-phosphoryl oxazolidinones with magnesium chloroalkoxides. Models for the selectivity have been proposed based upon the structure of the reactive species, generation of a transient chiral environment about the phosphorus centre, formation of diastereomeric reactive species, and steric interactions between adjacent alkoxide moieties. Work is now underway to explore these concepts further and develop reagents that can both help substantiate the proposed theories and additionally provide enhanced levels of stereoselectivity.

4. Experimental

4.1. General information

Dry solvents were obtained either from the Grubbs dry solvent system or by distillation. Triethylamine was distilled from KOH, at atmospheric pressure and all other reagents were used as supplied without purification, unless specified. Glassware was flame dried and cooled under vacuum before use. Thin layer chromatography was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F_{254}). Plates were visualised using UV light or by dipping in $KMnO_4$ solution, followed by exposure to heat. Flash column chromatography was performed on silica gel (Merck Kieselgel 60 F_{254} 230–400 mesh), unless otherwise stated. ^1H and ^{13}C NMR spectra were measured using $CDCl_3$ as solvent unless otherwise stated, on a Bruker AV-250 or AV-400 MHz machine with an automated sample changer. Chemical shifts for carbon and hydrogen are given, on the δ scale. Coupling constants were measured in Hertz (Hz). ^{13}C NMR spectra were recorded using the JMOD method. Specific rotations were performed on an Optical Activity Ltd. AA-10 automatic polarimeter at 589 nm (Na line) and measured at 22 °C. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded on either a Perkin Elmer 1600 FTIR machine using 0.5 mm NaCl cells or a Perkin 100 Spectrometer fitted with an ATR accessory. Peaks between 1600 and 4000 cm^{-1} with an absorbance of >10% were quoted. Low resolution mass spectra (m/z) were recorded on a Kratos MS 25 or MS 80 spectrometer supported by a DS 55 data system, operating in either EI or ES mode. High resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on either a MicroMass LCT operating in Electrospray mode (TOF ES), or a MicroMass Prospec operating in EI mode. HPLC was carried out on a Gilson analytical system using chiral phase analytical columns (4.8 mm × 250 mm). The flow rate was 1.00 mL/min and the detector was set at 254 nm. Melting points (mp) were measured on a Gallenkamp melting point apparatus and are uncorrected. Elemental analysis was performed using a Perkin–Elmer 2400 CHN elemental analyser.

Unless otherwise stated, all reagents and substrates were used as supplied. *N*-Phosphoryl oxazolidinones **14**, **16**, **17** and **19** were prepared as previously described.[8]

4.2. (4*S*)-4-*tert*-Butyldimethylsilyloxymethyl-2-oxazolidinone 2

Magnesium turnings (1.46 g, 60.1 mmol) were stirred in THF (15 mL). Bromobenzene (6.3 mL, 59.8 mmol) was added drop-wise to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining bromobenzene was diluted with THF (30 mL) and the resulting solution was added to the reaction vessel at a rate as to ensure a steady reflux. The reaction mixture was cooled to 0 °C. *N*-Boc-*O*-*t*-Butyldimethylsilyl-L-serine methyl ester[16] **1** (5.01 g, 15.0 mmol) was dissolved in THF (15 mL) and

the resulting solution was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 48 h, before being quenched by addition of $NH_4Cl_{(aq)}$ (30 mL). The resulting mixture was extracted with EtOAc (3 × 30 mL), washed with brine (20 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was dissolved in THF (100 mL) and cooled to 0 °C. *t*-BuOK (1.25 g, 11.1 mmol) was added as a single portion and the reaction was left stirring at this temperature for 3 h, before being allowed to warm to rt and left stirring overnight. The reaction was quenched with $NH_4Cl_{(aq)}$ (30 mL) and the resulting mixture was extracted with EtOAc (3 × 40 mL). The combined organic extracts were washed with $NaHCO_{3(aq)}$ (20 mL) and brine (20 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure. The title compound **2** (1.19 g, 21%) was obtained as a white solid, following recrystallisation from EtOAc; mp 166.0–168.0 °C; $[\alpha]_D^{22} = -324.0$ (*c* 0.25, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 3297, 2954, 2932, 2857, 1761, 1730; ^1H NMR (400 MHz; $CDCl_3$) δ_H −0.05 (3H, s, SiC*H*$_3$), −0.04 (3H, s, SiC*H*$_3$), 0.87 [9H, s, SiC(C*H*$_3$)$_3$], 3.22 (1H, dd, *J* 10.3, 8.0, C*H*HO), 3.33 (1H, dd, *J* 10.3, 4.8, C*H*HO), 4.60 (1H, dd, *J* 8.0, 4.8, *CH*NH), 5.87 (1H, s, N*H*), 7.27–7.43 (8H, m, ArC*H*), 7.54–7.58 (2H, d, *J* 7.1, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C −5.7 (SiCH$_3$), −5.6 (SiCH$_3$), 18.1 [SiC(CH$_3$)$_3$], 25.8 [3× SiC(CH$_3$)$_3$], 61.6 (CHNH), 63.7 (CH$_2$), 87.8 [C(Ph)$_2$], 126.1 (2× ArCH), 126.2 (2× ArCH), 128.1 (2× ArCH), 128.5 (2× ArCH), 128.6 (2× ArCH), 138.6 (ArC), 142.3 (ArC), 158.0 (C=O); *m*/*z* (ES^+) 384.2001 (100%, MH^+ $C_{22}H_{30}NO_3Si$ requires 384.1995), 354 (55), 208 (33).

4.3. General procedure A for the phosphorylation of oxazolidinones and imidazolidinones

Oxazolidinone or imidazolidinone (1 equiv) was dissolved in THF (10 mL $mmol^{-1}$) and cooled to −78 °C. *n*-BuLi (2.5 M in hexanes, 1.1 equiv) was added drop-wise and the solution was allowed to warm to rt. The reaction mixture was left stirring for 1 h, before being cooled to −78 °C. Diethyl chlorophosphate (1 equiv) was added drop-wise and the solution was allowed to warm to rt. The reaction mixture was left stirring overnight, before being quenched by the addition of $NH_4Cl_{(aq)}$ (10 mL $mmol^{-1}$). The resulting mixture was extracted with EtOAc (3 × 15 mL), and the combined organic extracts were washed with $NaHCO_{3(aq)}$ (10 mL), brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the title compound purified as described in the individual experiments.

4.4. (4*S*)-3-Diethyl phosphoryl 4-*t*-butyldimethylsilyloxymethyl-2-oxazolidinone 3

Prepared by general procedure A using (4*S*)-4-*t*-butyldimethylsilyloxymethyl-2-oxazolidinone **2** (0.35 g, 0.91 mmol) providing the title compound **3** (0.23 g, 48%) as a white solid, following purification by flash column chromatography on silica gel, eluting with a petroleum ether/ethyl acetate mixture (4:1); mp 110.0–122.5 °C; $[\alpha]_D^{22} = -105.5$ (*c* 0.55, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 2929, 2857, 1758; Found: C, 60.32; H, 7.50; N, 2.48. $C_{26}H_{38}NO_6PSi$ requires C, 60.09; H, 7.37; N, 2.70; ^1H NMR (400 MHz; $CDCl_3$) δ_H −0.41 (3H, s, SiC*H*$_3$), −0.15 (3H, s, SiC*H*$_3$), 0.82 [9H, s, SiC(C*H*$_3$)$_3$], 1.01 (3H, td, *J* 7.1, J_{H-P} 1.0, OCH$_2$C*H*$_3$), 1.37 (3H, td, *J* 7.1, J_{H-P} 1.1, OCH$_2$C*H*$_3$), 3.44–3.54 (1H, m, OC*H*HCH$_3$), 3.70 (1H, dd, *J* 11.3, 1.5, C*H*HOTBDMS), 3.73–3.82 (1H, m, OC*H*HCH$_3$), 3.90 (1H, dd, *J* 11.3, 3.2, C*H*HOTBDMS), 4.30 (2H, pent, *J* 7.3, OC*H*$_2$CH$_3$), 5.00 (1H, br s, C*H*N), 7.23–7.38 (6H, m, ArC*H*), 7.41–7.44 (2H, d, *J* 6.9, ArC*H*), 7.61–7.64 (2H, d, *J* 7.0, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C −6.5 (SiCH$_3$), −6.1 (SiCH$_3$), 15.6 (d, J_{C-P} 6.1, OCH$_2$CH$_3$), 16.1 (d, J_{C-P} 7.7, OCH$_2$CH$_3$), 17.9 [SiC(CH$_3$)$_3$], 25.7 [3× SiC(CH$_3$)$_3$], 61.3 (CH$_2$O), 63.8 (d, J_{C-P} 5.4, OCH$_2$CH$_3$), 64.9 (d, J_{C-P} 6.1, OCH$_2$CH$_3$), 65.5 (CHN), 88.5 [d, J_{C-P} 7.7, C(Ph)$_2$], 125.4 (2× ArCH), 125.8 (2× ArCH), 127.7 (ArCH), 128.2 (2× ArCH), 128.4 (ArCH), 128.7 (2× ArCH), 138.2 (ArC), 143.1 (ArC), 154.0 (d, J_{C-P} 7.7, C=O); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −5.51; *m*/*z* (EI^+) 519.2205 (<1%, M^+ $C_{26}H_{38}NO_6SiP$ requires 519.2206), 462 (100), 418 (15), 390 (10), 234 (22), 167 (61).

4.5. (4*S*,5*S*)-3-Diethyl phosphoryl 1,5-dimethyl-4-phenyl-2-imidazolidinone 7

Prepared by general procedure A using (4*S*,5*S*)-1,5-dimethyl-4-phenyl-2-imidazolidinone **6** (0.49 g, 2.58 mmol) providing the title compound **7** (0.57 g, 68%) as a white solid, following purification by flash column chromatography on silica gel, eluting with ethyl acetate; mp 95.0–96.0 °C; $[\alpha]_D^{22} = -19.0$ (*c* 1.0, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 2981, 1698; Found: C, 55.11; H, 7.02; N, 8.51; $C_{15}H_{23}N_2O_4P$ requires C, 55.21; H, 7.10; N, 8.58; ^1H NMR (400 MHz; $CDCl_3$) δ_H 0.82 (3H, d, *J* 6.6, CHC*H*$_3$), 1.17 (3H, td, *J* 7.1, J_{P-H} 1.0, OCH$_2$C*H*$_3$), 1.33 (3H, td, *J* 7.1, J_{P-H} 1.0, OCH$_2$C*H*$_3$), 2.79 (3H, s, NC*H*$_3$), 3.82–3.95 (2H, m, OC*H*$_2$CH$_3$), 3.95–4.02 (1H, m, C*H*CH$_3$), 4.06–4.16 (1H, m, OC*H*HCH$_3$), 4.17–4.27 (1H, m, OC*H*HCH$_3$), 5.01 (1H, dd, *J* 8.3, J_{P-H} 2.2, C*H*Ph), 7.21–7.39 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 14.9 (CHCH$_3$), 16.0–16.1 (2× OCH$_2$CH$_3$), 28.2 (NCH$_3$), 56.5 (d, J_{C-P} 6.9, CHCH$_3$), 62.0 (d, J_{C-P} 3.0, CHPh), 63.6 (d, J_{C-P} 5.0, OCH$_2$CH$_3$), 63.9 (d, J_{C-P} 6.0, OCH$_2$CH$_3$), 127.8 (2× ArCH), 128.3 (3× ArCH), 137.4 (ArC), 158.3 (d, J_{C-P} 7.7, CO); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −2.32; *m*/*z* (EI^+) 326.1399 (36%, M^+ $C_{15}H_{23}N_2O_4P$ requires 326.1395), 311 (56), 255 (25), 189 (53), 147 (100), 138 (30), 132 (47).

4.6. (1*R*,2*S*)-*N*-Boc-2-amino-1-methyl-2-phenyl-1-ethanol 9[17]

(1*R*,2*R*)-(+)-1-Phenylpropylene oxide **8** (1.80 g, 13.4 mmol) was dissolved in 33% $NH_{3(aq)}$ (20 mL) to form a cloudy mixture. MeOH (30 mL) was added until the solution became clear and left to stir at rt for 48 h. The reaction mixture was extracted with EtOAc (50 mL), washed with H_2O (30 mL), dried over $MgSO_4$, filtered and solvent removed under reduced pressure. The residue was dissolved in EtOH (100 mL) with stirring and cooled to 0 °C. $NaHCO_3$ (2.60 g, 30.9 mmol) was added as a single portion, immediately followed by Boc_2O (2.39 g, 11.0 mmol). The resulting mixture was allowed to warm to rt and left to stir for 48 h, before being filtered through Hyflo SuperCel® and washed with Et_2O (50 mL). The solvent was removed under reduced pressure, the residue was re-dissolved in Et_2O (50 mL), filtered through Hyflo SuperCel® and solvent removed under reduced pressure. The title compound **9** (2.25 g, 67%) was obtained as a clear oil that did not require any further purification; $[\alpha]_D^{22} = +24.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz; $CDCl_3$) δ_H 1.06 (3H, d, *J* 6.4, C*H*$_3$), 1.43 [9H, s, C(C*H*$_3$)$_3$], 2.48 (1H, d, *J* 5.4, O*H*), 4.05–4.07 (1H, m, C*H*OH), 4.38 (0.2H, br s, rotamer A, C*H*NH), 4.62 (0.8H, br s, rotamer B, C*H*NH), 5.60 (0.8H, br s, 1H, rotamer B N*H*), 5.98 (0.2H, br s, 1H, rotamer A N*H*), 7.26–7.36 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 19.6 (CHCH$_3$), 28.4 [C(CH$_3$)$_3$], 60.0 (CHPh), 70.2 (CHCH$_3$), 79.7 [C(CH$_3$)$_3$], 127.5 (ArCH), 127.7 (3× ArCH), 128.4 (ArCH), 138.5 (ArC), 155.7 (C=O). No $[\alpha]_D$ or ^{13}C NMR were previously reported, all other data were in accordance with the literature.

4.7. (4*S*,5*R*)-4-Phenyl-5-methyl-2-oxazolidinone 10[18]

(1*R*,2*S*)-*N*-Boc-2-amino-1-methyl-2-phenyl-1-ethanol **9** (1.91 g, 7.60 mmol) was dissolved in THF (100 mL) and cooled to 0 °C. *t*-BuOK (1.05 g, 9.36 mmol) was added as a single portion and the reaction was left stirring at this temperature for 3 h, before being allowed to warm to rt overnight. The reaction was quenched with $NH_4Cl_{(aq)}$ (20 mL) and the resulting mixture was extracted with EtOAc (3 × 30 mL). The combined organic extracts were

washed with brine (40 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The title compound **10** (1.12 g, 84%) was obtained as a clear crystalline solid, following recrystallisation from EtOAc/petroleum ether 40–60 °C; mp 106.5–108.0 °C; $[\alpha]_D^{22}$ = +144.0 (*c* 0.25, $CHCl_3$); ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.97 (3H, d, *J* 6.6, C*H*$_3$), 4.93 (1H, d, *J* 6.6, C*H*Ph), 5.03 (1H, quint, *J* 6.6, C*H*CH$_3$), 5.83 (1H, s, N*H*), 7.23–7.28 (2H, m, ArC*H*), 7.31–7.46 (3H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 16.6 (*C*H$_3$), 59.9 (*C*HPh), 77.2 (*C*HCH$_3$), 126.9 (2× ArCH), 128.7 (ArCH), 128.8 (2× ArCH), 136.6 (Ar*C*), 159.7 (C=O). No mp, $[\alpha]_D$ or ^{13}C NMR data were previously reported, all other data were in accordance with the literature.

4.8. (4*S*,5*R*)-3-Diethyl phosphoryl 4-phenyl-5-methyl-2-oxazolidinone 11

Prepared by general procedure A using (4*S*,5*R*)-4-phenyl-5-methyl-2-oxazolidinone **10** (0.48 g, 2.71 mmol) providing the title compound **11** (0.68 g, 81%) as a clear oil, following purification by flash column chromatography on silica gel, eluting with a petroleum ether/ethyl acetate mixture (2:1); $[\alpha]_D^{22}$ = +62.1 (*c* 0.95, $CHCl_3$); ν_{max} (Solution)/cm^{-1} 3673, 2989, 2913, 1778, 1606; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.02 (3H, dd, *J* 6.3, J_{P-H} 0.6, CHC*H*$_3$), 1.18 (3H, td, *J* 7.2, J_{P-H} 1.3, OCH$_2$C*H*$_3$), 1.35 (3H, td, *J* 7.2, J_{P-H} 0.9, OCH$_2$C*H*$_3$), 3.79–4.02 (2H, m, OC*H*$_2$CH$_3$), 4.08–4.35 (2H, m, OC*H*$_2$CH$_3$), 5.02 (1H, pent, *J* 6.6, C*H*CH$_3$), 5.11 (1H, dd, *J* 7.2, J_{P-H} 1.6, C*H*Ph), 7.25–7.29 (2H, m, ArC*H*), 7.34–7.45 (3H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 15.8 (*C*H$_3$CH), 15.9, (d, J_{C-P} 7.3, *C*H$_3$), 16.0, (d, J_{C-P} 7.3, *C*H$_3$), 64.3 (d, J_{C-P} 5.9, O*C*H$_2$CH$_3$), 64.6 (d, J_{C-P} 6.0, OCH$_2$*C*H$_3$), 64.7 (d, J_{C-P} 4.1, *C*HPh), 76.9 (d, J_{C-P} 8.6, *C*HCH$_3$), 127.6 (2× ArCH), 128.7 (2× ArCH), 128.9 (ArCH), 135.8 (Ar*C*), 155.6 (d, J_{C-P} 8.7, *C*=O); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −4.56; *m*/*z* (EI$^+$) 313.1074 (6%, M$^+$ $C_{14}H_{20}NO_5P$ requires 313.1079), 269 (100), 240 (32), 212 (42), 138 (69), 132 (86), 104 (45), 77 (56).

4.9. (4*S*)-3-Diethyl phosphoryl 4-benzyl-5,5-dimethyl-2-oxazolidinone 15

Prepared by general procedure A using (*S*)-4-benzyl-5,5-dimethyl-2-oxazolidinone[19] (0.66 g, 3.2 mmol) providing the title compound **15** (0.81 g, 74%) as a white solid, following purification by flash column chromatography on silica gel, eluting with a petroleum ether/ethyl acetate mixture (2:1); mp 49.0–50.5 °C; $[\alpha]_D^{22}$ = −20.0 (*c* 0.5, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 2991, 1760, 1719; Found: C, 56.34; H, 7.15; N, 3.91. $C_{16}H_{24}NO_5P$ requires C, 56.30; H, 7.09; N, 4.10; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.28 [3H, s, 1× C(C*H*$_3$)$_2$], 1.33–1.41 [9H, m, 1× C(C*H*$_3$)$_2$ and 2× OCH$_2$C*H*$_3$], 2.96 (1H, dd, *J* 14.4, 10.4, C*H*$_2$Ph), 3.35 (1H, dd, *J* 14.4, 3.5, C*H*$_2$Ph), 4.11–4.36 (5H, m, C*H*N and 2× OC*H*$_2$CH$_3$), 7.17–7.32 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 16.0 (d, J_{C-P} 2.9, OCH$_2$*C*H$_3$), 16.2 (d, J_{C-P} 2.9, OCH$_2$*C*H$_3$), 22.5 [1× C(*C*H$_3$)$_2$], 28.5 [1× C(*C*H$_3$)$_2$], 37.4 (*C*H$_2$Ph), 64.5 (d, J_{C-P} 6.7, 2× OCH$_2$*C*H$_3$), 66.6 (d, J_{C-P} 3.8, *C*HN), 83.4 [d, J_{C-P} 8.6, [*C*(CH$_3$)$_2$], 126.7 (ArCH), 128.6 (2× ArCH), 129.1 (2× ArCH), 136.9 (Ar*C*), 154.3 (d, J_{C-P} 8.6, C=O); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −3.12; *m*/*z* (EI$^+$) 341.1407 (29%, M$^+$ $C_{16}H_{24}NO_5P$ requires 341.1392), 250 (53), 150 (49), 91 (100), 81 (42), 69 (52).

4.10. (4*S*)-3-Diethyl phosphoryl 4-isopropyl-5,5-diphenyl-2-oxazolidinone 18

Prepared by general procedure A using (*S*)-4-isopropyl-5,5-diphenyl-2-oxazolidinone[20] (3.72 g, 13.2 mmol) providing the title compound **18** (4.15 g, 75%) as a white solid, following purification by flash column chromatography on silica gel, eluting with a petroleum ether/ethyl acetate mixture (2:1); mp 107.0–109.0 °C; $[\alpha]_D^{22}$ = −170.0 (*c* 0.5, $CHCl_3$); ν_{max} (ATR)/cm^{-1} 2981, 2967, 1758, 1720; Found: C, 63.38; H, 6.88; N, 3.18. $C_{22}H_{28}NO_5P$ requires C, 63.30; H, 6.76; N, 3.36; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 0.82 [3H, d, *J* 6.6, CH(C*H*$_3$)$_2$], 0.95 (3H, td, *J* 7.2, J_{P-H} 1.0, OCH$_2$C*H*$_3$), 1.08 [3H, d, *J* 7.2, CH(C*H*$_3$)$_2$], 1.38 [3H, td, *J* 7.2, J_{P-H} 1.3, CH(C*H*$_3$)$_2$], 1.91–2.03 [1H, m, C*H*(CH$_3$)$_2$], 3.00–3.16 (1H, m, OC*H*HCH$_3$), 3.43–3.58 (1H, m, OC*H*HCH$_3$), 4.32 (2H, pent, *J* 7.0, OC$_2$CH$_3$), 5.01 (1H, dd, *J* 3.1, J_{H-P} 2.2, C*H*NP), 7.23–7.47 (8H, m, ArC*H*), 7.66–7.71 (2H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 15.6 [CH(CH$_3$)$_2$], 15.7 (d, J_{C-P} 6.3, OCH$_2$C*H*$_3$), 16.1 (d, J_{C-P} 6.9, OCH$_2$C*H*$_3$), 21.1 [1× CH(CH$_3$)$_2$], 30.0 [1× CH(CH$_3$)$_2$], 63.3 (d, J_{C-P} 5.8, OCH$_2$CH$_3$), 65.0 (d, J_{C-P} 6.7, OCH$_2$CH$_3$), 69.4 (d, J_{C-P} 3.1, *C*HN), 90.6 [*C*(Ph)$_2$], 125.5 (2× ArCH), 125.6 (2× ArCH), 127.8 (ArCH), 128.3 (ArCH), 128.4 (2× ArCH), 128.8 (2× ArCH), 138.3 (2× Ar*C*), 143.4 (*C*=O); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −4.31; *m*/*z* (EI$^+$) 417.1717 (3%, M$^+$ $C_{22}H_{28}NO_5P$ requires 417.1705), 374 (75), 274 (25), 207 (26), 195 (100), 167 (50), 138 (27).

4.11. Phenyl cyclohexyl methanol 20[21]

Magnesium turnings (4.35 g, 0.179 mol) were stirred in dry THF (25 mL). A few drops of bromobenzene (18.8 mL, 0.179 mol) were added to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining aryl bromide was diluted with dry THF (50 mL) and the resulting solution was added to the reaction vessel at a rate as to ensure heating at a steady reflux. The reaction mixture was cooled to 0 °C. Cyclohexane carboxaldehyde (10.5 mL, 0.087 mol) was dissolved in dry THF (25 mL) and the resulting solution was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 24 h, before being quenched by addition of $NH_4Cl_{(aq)}$ (50 mL). The resulting mixture was extracted with EtOAc (3 × 80 mL), washed with brine (40 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The title compound **20** (2.88 g, 17%) was obtained as a white solid after purification by flash column chromatography on silica gel, eluting with a hexane/ethyl acetate mixture (9:1); mp 48.0–49.0 °C (lit.[22] 46–48 °C); ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.90–1.31 (5H, m, C*H*$_2$), 1.37–1.42 (1H, m, C*H*H), 1.59–1.71 (3H, m, C*H*$_2$), 1.77–1.83 (1H, m, C*H*H), 1.88 (1H, d, *J* 3.1, O*H*), 1.99–2.04 (1H, m, C*H*H), 4.39 (1H, dd, *J* 7.1, 3.1, C*H*OH), 7.27–7.39 (5H, m, ArC*H*). All data were in accordance with the literature.

4.12. 2-Methyl-1-phenyl-1-propanol 21[23]

Isobutyrophenone (5.00 mL, 33.3 mmol) was dissolved in EtOH/CH_2Cl_2 (5:1, 120 mL) with stirring. $NaBH_4$ (2.42 g, 64.0 mmol) was added as a single portion and the resulting mixture was left to stir for 24 h. The reaction was quenched by addition of $NH_4Cl_{(aq)}$ (100 mL) and the organic solvents were removed under reduced pressure. The residue was extracted with EtOAc (3 × 40 mL), washed with brine (30 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the title compound **21** (4.46 g, 89%) was obtained as a clear oil; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 0.82 (3H, d, *J* 6.6, C*H*$_3$), 1.03 (3H, d, *J* 6.9, C*H*$_3$), 1.88–2.07 [2H, m, C*H*(CH$_3$)$_2$ and O*H*], 4.37 (1H, d, *J* 6.6, C*H*OH), 7.25–7.40 (5H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 18.2 (*C*H$_3$), 19.0 (*C*H$_3$), 35.3 [*C*H(CH$_3$)$_2$], 80.0 (*C*HOH), 126.6 (2× ArCH), 127.4 (ArCH), 128.2 (2× ArCH), 143.7 (Ar*C*). All data were in accordance with the literature.

4.13. 1-Phenyl 2,2-dimethyl propanol 22[24]

Magnesium turnings (2.41 g, 99.1 mmol) were stirred in THF (20 mL). 2-Bromo-2-methylpropane (11 mL, 98.0 mmol) was added drop-wise to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining alkyl bromide was diluted with THF (40 mL) and the resulting solution was added to

the reaction vessel at a rate as to ensure heating at a steady reflux. The reaction mixture was cooled to 0 °C. Benzaldehyde (5.00 mL, 49.2 mmol) was dissolved in THF (20 mL) and the resulting solution was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 24 h, before being quenched by addition of $NH_4Cl_{(aq)}$ (30 mL). The resulting mixture was extracted with EtOAc (3 × 40 mL), washed with brine (30 mL), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The title compound **22** (3.39 g, 42%) was obtained as a white solid, following purification by flash column chromatography on silica gel, eluting with a petroleum ether (40–60)/ethyl acetate mixture (9:1); mp 44.0–45.0 °C (lit.,[25] 44–45 °C); ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.95 [9H, s, C(C*H*$_3$)$_3$], 1.85 (1 h, d, *J* 1.9, O*H*), 4.42 (1H, d, *J* 1.9, C*H*OH), 7.24–7.35 (5H, m, ArC*H*). All data were in accordance with the literature.

4.14. 1-(*o*-Methylphenyl)ethanol 23[26]

2′-Methylacetophenone (1.00 mL, 7.65 mmol) was dissolved in EtOH/CH_2Cl_2 (6:1, 35 mL) with stirring. $NaBH_4$ (0.46 g, 12.16 mmol) was added as a single portion and the resulting mixture was left to stir for 24 h. The reaction was quenched upon addition of $NH_4Cl_{(aq)}$ (40 mL) and organic solvents were removed under reduced pressure. The product was extracted into EtOAc (3 × 20 mL), washed with brine (20 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the title compound **23** (0.83 g, 79%) was obtained as a clear oil. ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.49 (3H, d, *J* 6.4, CHC*H*$_3$), 1.90 (1H, s, O*H*), 2.37 (3H, s, ArC*H*$_3$), 5.15 (1H, q, *J* 6.4, C*H*CH$_3$), 7.13–7.30 (3H, m, ArC*H*), 7.53 (1H, dd, *J* 6.8, 1.0, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 18.9 (*C*H$_3$), 23.9 (*C*H$_3$), 66.8 (*C*HCH$_3$), 124.5 (Ar*C*H), 126.4 (Ar*C*H), 127.2 (Ar*C*H), 130.4 (Ar*C*H), 134.2 (Ar*C*), 143.9 (Ar*C*). All data were in accordance with the literature.

4.15. 3-Methyl-1-phenyl-2-butanol 24[27]

Magnesium turnings (0.80 g, 32.9 mmol) were stirred in THF (10 mL). Benzyl bromide (3.9 mL, 32.8 mmol) was added drop-wise to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining benzyl bromide was diluted with THF (20 mL) and the resulting solution was added to the reaction vessel at a rate as to ensure heating at a steady reflux. The reaction mixture was cooled to 0 °C. Isobutyraldehyde (2.50 mL, 27.5 mmol) was dissolved in THF (10 mL) and the resulting solution was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 24 h, before being quenched by the addition of $NH_4Cl_{(aq)}$ (20 mL). The resulting mixture was extracted with EtOAc (3 × 30 mL), washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the title compound **24** (2.94 g, 65%) was obtained as a clear oil, following purification by flash column chromatography on silica gel, eluting with a petroleum ether (40–60)/ethyl acetate mixture (7:3); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.03 [6H, d, *J* 6.6, CH(C*H*$_3$)$_2$], 1.58 (1H, s, O*H*), 1.69–1.88 [1H, m, C*H*(CH$_3$)$_2$], 2.62 (1H, dd, *J* 13.5, 9.4, C*H*HPh), 2.89 (1H, dd, *J* 13.5, 3.5, C*H*HPh), 3.57–3.65 (1H, m, C*H*OH), 7.23–7.38 (5H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 17.4 (*C*H$_3$), 18.9 (*C*H$_3$), 33.1 [*C*H(CH$_3$)$_2$], 40.8 (*C*H$_2$), 77.5 (*C*HOH), 126.4 (Ar*C*H), 128.6 (2× Ar*C*H), 129.4 (2× Ar*C*H), 139.2 (Ar*C*). All data were in accordance with the literature.

4.16. 1-Phenyl-3,3-dimethylbutan-2-ol 25[28]

Magnesium turnings (4.86 g, 200 mmol) were stirred in dry THF (35 mL) under an atmosphere of nitrogen. Bromobenzene (31.40 g, 21 mL, 200 mmol) was added drop-wise to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining bromobenzene was diluted with THF (125 mL) and the resulting solution was added to the reaction vessel at a rate as to ensure heating at reflux. The reaction mixture was cooled to 0 °C and copper(I) bromide (3.81 g, 20 mmol) was added portion-wise. The reaction was left to stir for 30 min at below 7 °C, before being cooled to 0 °C and 3,3-dimethyl-1,2-epoxybutane (1.00 g, 1.22 mL, 10 mmol) was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 12 h, then quenched by addition of HCl (1 M, 50 mL). The resulting mixture was extracted with EtOAc (3 × 30 mL), washed with $NaHCO_3$ (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, followed by purification by flash column chromatography on silica gel, eluting with petroleum ether 40–60 °C/EtOAC (9:1) to yield the title compound as a yellow oil (1.05 g, 59%); ν_{max} (ATR)/cm^{-1} 3457, 2953, 1604, 1494, 1478; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 1.04 [9H, s, C(C*H*$_3$)$_3$], 1.54 (1H, s, CHO*H*), 2.50 (1H, dd, *J* 13.6, 10.7, C*H*H), 2.95 (1H, dd, *J* 13.6, 2.0, C*H*H), 3.47 (1H, dd, *J* 10.7, 2.0, C*H*OH), 7.24–7.28 (3H, m, ArC*H*), 7.33–7.37 (2H, m, ArC*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ_H 25.9 (*C*H$_3$), 34.8, [(CH$_3$)$_3$*C*], 38.4 (*C*H$_2$), 80.6 (*C*HOH), 126.3 (Ar*C*H), 128.6 (Ar*C*H), 129.4 (Ar*C*H), 139.9 (Ar*C*); *m*/*z* (EI$^+$) 178.1355 (<1%, M$^+$, $C_{12}H_{18}O$ requires 178.1358), 160 (10), 145 (15), 121 (10), 103 (10), 92 (100). Data were in accordance with the literature.

4.17. 5-Phenyl-2-methyl pentan-3-ol 26[29]

Magnesium turnings (2.72 g, 112 mmol) were stirred in dry THF (20 mL) under an atmosphere of nitrogen. 2-Bromopropane (13.8 g, 10.5 mL, 112 mmol) was added drop-wise to the reaction mixture, which was heated to initiate an exothermic reaction. The remaining 2-bromopropane was diluted with THF (150 mL) and the resulting solution was added to the reaction vessel at a rate as to ensure heating at reflux. The reaction mixture was cooled to 0 °C. 3-Phenylpropionaldehyde (5.00 g, 37.3 mmol) was dissolved in THF (35 mL) and the resulting solution was added drop-wise to the reaction vessel. The reaction mixture was allowed to warm to rt and left stirring for 48 h, and quenched by addition of NH_4Cl(aq) (50 mL). The resulting mixture was extracted with EtOAc (3 × 40 mL), washed with brine (25 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the title compound (5.20 g, 78%) was obtained as faint yellow oil, after purification by flash column chromatography on silica gel, eluting with petroleum ether 40–60 °C/EtOAc (8:1); ν_{max} (ATR)/cm^{-1} 3364, 2956, 2870, 1604, 1496, 1454; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.94 [3H, dd, *J* 6.8, CH(C*H*$_3$)$_2$], 0.95 [3H, dd, *J* 6.8, CH(C*H*$_3$)$_2$], 1.41 (1H, br s, O*H*), 1.67–1.87 [3H, m, C*H*(CH$_3$)$_2$ and C*H*$_2$], 2.68 (1H, ddd, *J* 13.7, 9.4, 6.8, C*H*H), 2.88 (1H, ddd, *J* 13.7, 9.9, 5.2, C*H*H), 3.43 (1H, ddd, *J* 9.4, 5.2, 3.5, C*H*OH), 7.20–7.34 (3H, m, ArCH), 7.25–7.35 (2H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 17.2 (*C*H$_3$), 18.8 (*C*H$_3$), 32.5 (*C*H$_2$), 33.7 [(CH$_3$)$_2$*C*H], 36.0 (*C*H$_2$), 76.2 (*C*HOH), 125.8 (Ar*C*H), 128.4 (Ar*C*H), 128.5 (Ar*C*H), 142.4 (Ar*C*); *m*/*z* (EI$^+$) 178.1365 (5%, M$^+$, $C_{12}H_{18}O$ requires 178.1358), 160 (17), 117 (43), 104 (53), 91 (100). Data were in accordance with the literature.

4.18. 1,2-Dimethyl-1-phenyl-1-propanol 27[23]

Isobutyrophenone (5.00 g, 33.7 mmol) was dissolved in THF (35 mL) and the resulting solution was cooled to −78 °C. MeMgCl (13 mL, 3.0 M in THF, 39.0 mmol) was added drop-wise and the resulting mixture was allowed to warm to rt and left to stir for 24 h. The reaction was quenched upon addition of $NH_4Cl_{(aq)}$ (10 mL), extracted into EtOAc (3 × 30 mL), washed with brine (20 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure and the title compound **27**

(5.31 g, 96%) was obtained as a pale yellow oil that did not require any further purification. ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.86 [3H, d, *J* 6.9 CH(CH_3)$_2$], 0.94 [3H, d, *J* 6.9 CH(CH_3)$_2$], 1.57 (3H, s, CCH_3), 1.82 (1H, s, O*H*), 2.06 [1H, sept, *J* 6.9, *CH*(CH_3)$_2$], 7.25–7.29 (1H, m, ArC*H*), 7.35–7.39 (2H, m, ArC*H*), 7.45–7.48 (2H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 17.2 [CH(CH_3)$_2$], 17.5 [CH(CH_3)$_2$], 26.7 (CCH_3), 38.6 [*CH*(CH_3)$_2$], 76.8 (*C*OH), 125.3 (2× ArCH), 126.4 (ArCH), 127.9 (2× ArCH), 147.9 (Ar*C*). All data were in accordance with the literature.

4.19. General procedure B for the phosphorylation of authentic samples of racemic alcohols

Alcohol (1 equiv) was dissolved in dry THF (20 mL mmol^{-1}) with stirring and the solution was cooled to −78 °C. *n*-BuLi (0.40 mL, 2.5 M in hexanes, 1.05 equiv) was added drop-wise and the solution was allowed to warm to rt. The reaction mixture was left stirring for 1 h, then cooled to −78 °C. Diethyl chlorophosphate (1.1 equiv) was added drop-wise and the solution was allowed to warm to rt. The reaction mixture was left stirring for 2 h, quenched by the addition of $NH_4Cl_{(aq)}$ (10 mL) and the resulting mixture extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with $NaHCO_{3(aq)}$ (10 mL), brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure, and the target compound purified as noted in the individual experiments.

4.20. General procedure C for the asymmetric phosphorylation of alcohol substrates using reagent 18

Alcohol (0.50 g, 10 equiv) was dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. MeMgCl (1.1 equiv, 3.0 M in THF) was added drop-wise and the reaction mixture was allowed to warm to rt. After 1 h the resulting solution was cooled to 0 °C and *N*-phosphoryl oxazolidinone **18** (1 equiv) was added drop-wise as a solution in CH_2Cl_2 (10 mL). After 1 h, the reaction vessel was allowed to warm to rt and left to stir overnight. The reaction was quenched upon addition of $NH_4Cl_{(aq)}$ (10 mL), extracted into CH_2Cl_2 (3 × 30 mL) and washed with $NaHCO_{3(aq)}$ (10 mL) and brine (10 mL). The organic layer was separated, dried over $MgSO_4$, filtered and solvent removed under reduced pressure. The residue was purified by column chromatography and the ee of the resulting phosphate ester was analysed via chiral HPLC.

4.21. Diethyl 1-phenylethyl phosphate 13[8]

Obtained from general procedure B using 1-phenylethanol **12** (0.12 g, 0.98 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:1) as a clear oil (0.14 g, 53%); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.20 (3H, td, *J* 7.2, J_{P-H} 0.9, OCH$_2$CH_3), 1.30 (3H, td, *J* 7.2, J_{P-H} 0.9, OCH$_2$CH_3), 1.65 (3H, d, *J* 6.6, CHCH_3), 3.88–4.19 (4H, m, OCH_2CH$_3$), 5.49 (1H, pent, *J* 6.6, C*H*CH$_3$), 7.28–7.42 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) 16.0 (d, J_{C-P} 7.7, 2× CH$_2$*C*H$_3$), 24.2 (d, J_{C-P} 4.6, CHCH$_3$), 63.6 (2× O*C*H$_2$), 76.6 (*C*HCH$_3$), 125.9 (2× ArCH), 128.1 (ArCH), 128.5 (2× ArCH), 141.8 (Ar*C*); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −0.01. All data were in accordance with the literature.

Employing general procedure C, alcohol **12** (0.50 g, 4.09 mmol) was treated with MeMgCl (0.15 mL, 3.0 M in THF, 0.45 mmol) and *N*-phosphoryl oxazolidinone **18** (0.18 g, 0.43 mmol) to afford phosphate ester **13** (0.11 g, 88%) in 15% ee; $[\alpha]_D^{22}$ = −7.9 (*c* 0.9, $CHCl_3$) for the (*S*) enantiomer; HPLC, Chiralcel OJ, 8% *i*-PrOH in hexane; 1 mL min^{-1}; t_r 8.7 min (major) and 13.3 min (minor).

4.22. Diethyl (phenyl cyclohexylcarbinyl) phosphate 28

Obtained from general procedure B using phenyl cyclohexylcarbinyl **20** (0.12 g, 0.98 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:1) as a clear oil (0.56 g, 86%); ν_{max} (film)/cm^{-1} 2985, 2928, 2854, 1452; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 0.83–1.28 (11H, m, 2× OCH$_2$CH_3 and cyclohexyl), 1.30–1.39 (1H, m, C*H*H), 1.60–1.87 (4H, m, cyclohexyl), 2.01–2.08 (1H, m, *CH*CHO), 3.73–4.15 (4H, m, OCH_2CH$_3$), 4.97 (1H, t, *J* 7.9, *CH*O), 7.26–7.39 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 15.9 (d, J_{C-P} 6.9, CH$_2$*C*H$_3$), 16.0 (d, J_{C-P} 6.9, CH$_2$*C*H$_3$), 25.8 (d, J_{C-P} 7.7, CH$_2$), 26.2 (*C*H$_2$), 28.7 (*C*H$_2$), 29.0 (*C*H$_2$), 44.2 (d, J_{C-P} 6.9, *C*HCHO), 63.3 (d, J_{C-P} 5.4, OCH$_2$-*C*H$_3$), 63.5 (d, J_{C-P} 5.4, O*C*H$_2$CH$_3$), 85.1 (d, J_{C-P} 6.1, *C*HO), 127.2 (2× ArCH), 128.0 (ArCH), 128.1 (2× ArCH), 139.6 (Ar*C*); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −0.01; *m*/*z* (EI$^+$) 326.1643 (22%, M$^+$ $C_{17}H_{27}O_4P$ requires 326.1647), 243 (100), 172 (33), 155 (27), 91 (55), 81 (33).

Employing general procedure C, alcohol **20** (0.50 g, 2.63 mmol) was treated with MeMgCl (0.10 mL, 3.0 M in THF, 0.30 mmol) and *N*-phosphoryl oxazolidinone **18** (0.11 g, 0.26 mmol) to afford phosphate ester **28** (0.08 g, 92%) in 19% ee; $[\alpha]_D^{22}$ = −10.0 (*c* 1.0, $CHCl_3$); HPLC, Chiralcel OJ, 3% *i*-PrOH in hexane; 0.5 mL min^{-1}; t_r 11.1 min (major) and 15.5 min (minor).

4.23. Diethyl 2-methyl-1-phenyl-1-propyl phosphate 29[30]

Obtained from general procedure B using 2-methyl-1-phenyl-1-propanol **21** (0.25 g, 1.66 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:2) as a clear oil **29** (0.28 g, 58%); ν_{max} (film)/cm^{-1} 2980, 2966, 2934, 1455; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 0.81 [3H, d, *J* 6.9, CH(CH_3)$_2$], 1.05–1.13 [6H, m, CH(CH_3)$_2$ and OCH$_2$CH_3), 1.24 (3H, td, *J* 7.2, J_{P-H} 1.3), 2.07–2.21 [1H, m, C*H*(CH$_3$)$_2$], 3.75–4.16 (4H, m, OCH_2), 4.98 (1H, t, *J* 7.5, *CH*O), 7.26–7.37 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 15.9 (d, J_{C-P} 6.9, CH$_2$*C*H$_3$), 16.0 (d, J_{C-P} 7.7, CH$_2$*C*H$_3$), 18.4 [CH(*C*H$_3$)$_2$], 18.5 [CH(*C*H$_3$)$_2$], 34.8 [d, J_{C-P} 6.9, *C*H(CH$_3$)$_2$], 63.4 (d, J_{C-P} 5.4, 2× O*C*H$_2$), 85.8 (d, J_{C-P} 6.1, *C*HO), 127.1 (2× ArCH), 128.0 (ArCH), 128.1 (2× ArCH), 139.6 (C═O); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −0.01; *m*/*z* (EI$^+$) 286.1348 (27%, M$^+$ $C_{14}H_{23}O_4P$ requires 286.1334), 243 (100), 132 (39), 109 (44), 91 (55). No analytical data are reported in the literature.

Employing general procedure C, alcohol **21** (0.50 g, 3.33 mmol) was treated with MeMgCl (0.13 mL, 3.0 M in THF, 0.39 mmol) and *N*-phosphoryl oxazolidinone **18** (0.14 g, 0.33 mmol) to afford phosphate ester **29** (0.07 g, 83%) in 20% ee; $[\alpha]_D^{22}$ = −6.6 (*c* 1.5, $CHCl_3$); HPLC, Chiralcel OJ, 0.5% *i*-PrOH in hexane; 1.0 mL min^{-1}; t_r 17.9 min (major) and 24.9 min (minor).

4.24. Diethyl (1-phenyl-2,2-dimethylpropyl) phosphate 30[31]

Obtained from general procedure B using 1-phenyl-2,2-dimethylpropanol **22** (0.50 g, 3.04 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:1) as a clear oil **30** (0.69 g, 76%); ν_{max} (film)/cm^{-1} 2978, 2959, 2909, 1481, 1454; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 0.97 [9H, s, C(CH_3)$_3$], 1.09 (3H, td, *J* 7.2, J_{P-H} 1.2, CH$_2$CH_3), 1.20 (3H, td, *J* 6.9, J_{P-H} 1.0, CH$_2$CH_3), 3.72–4.14 (4H, m, 2× O*C*H$_2$), 5.00 (1H, d, J_{P-H} 8.5, C*H*), 7.30–7.36 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 15.8 (d, J_{C-P} 7.7, CH$_2$CH$_3$), 16.0 (d, J_{C-P} 6.9, CH$_2$CH$_3$), 25.9 [3× C(*C*H$_3$)$_3$], 36.0 [d, J_{C-P} 6.9, *C*(CH$_3$)$_3$], 63.4 (d, J_{C-P} 5.4, OCH$_2$), 63.5 (d, J_{C-P} 5.4, OCH$_2$), 87.8 (d, J_{C-P} 6.1, *C*HO), 127.5 (2× ArCH), 127.7 (ArCH), 127.9 (2× ArCH), 138.3 (Ar*C*); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −0.01; *m*/*z* (EI$^+$) 300.1496 (3%, M$^+$ $C_{15}H_{25}O_4P$ requires 300.1490), 244 (100), 215 (33), 107 (46), 91 (58). Only ^{31}P and selected ^{1}H NMR signals are reported in the literature.

Employing general procedure C, alcohol **22** (0.50 g, 3.05 mmol) was treated with MeMgCl (0.11 mL, 3.0 M in THF, 0.33 mmol) and *N*-phosphoryl oxazolidinone **18** (0.13 g, 0.31 mmol) to failed to provide any phosphate ester **30** and thus no chiral phase HPLC data were obtained.

4.25. Diethyl 1-[1-(*o*-methylphenyl)ethyl] phosphate 31

Obtained from general procedure B using 1-(*o*-methylphenyl)ethanol **23** (0.20 g, 1.47 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:1) as a clear oil 31 (0.32 g, 79%); ν_{max} (film)/cm^{-1} 2983, 2932, 1480,1463; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H 1.20 (3H, td, *J* 7.2, J_{P-H} 1.3, CH_2CH_3), 1.29 (3H, td, *J* 6.9, J_{P-H} 0.9, CH_2CH_3), 1.61 (3H, d, *J* 6.9, $CHCH_3$), 2.39 (3H, s, ArCH_3), 3.87–4.18 (4H, m, 2× OCH_2), 5.71 (1H, app pent, *J* 6.9, $CHCH_3$), 7.13–7.27 (3H, m, ArC*H*), 7.47–7.50 (1H, m, ArC*H*); ^{13}C NMR (62.5 MHz; $CDCl_3$) δ_C 15.9 (d, J_{C-P} 7.5, CH_2CH_3), 16.0 (d, J_{C-P} 6.9, CH_2CH_3), 19.0 (ArCCH_3), 23.6 (d, J_{C-P} 5.0, $CHCH_3$), 63.6 (d, J_{C-P} 5.7, 2× OCH_2), 73.6 (d, J_{C-P} 4.8, $CHCH_3$), 125.5 (ArCH), 126.3 (ArCH), 127.8 (ArCH), 130.4 (ArCH), 134.0 (ArCCH_3), 140.1 (Ar$CCHCH_3$); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −1.73; *m*/*z* (EI$^+$) 272.1170 (<1%, M$^+$ $C_{13}H_{21}O_4P$ requires 272.1177), 155 (57), 118 (100), 99 (32), 91 (31).

Employing general procedure C, alcohol **23** (0.50 g, 3.68 mmol) was treated with MeMgCl (0.13 mL, 3.0 M in THF, 0.40 mmol) and *N*-phosphoryl oxazolidinone **18** (0.15 g, 0.31 mmol) to failed to provide any phosphate ester **31** and thus no chiral phase HPLC data were obtained.

4.26. Diethyl 3-methyl-1-phenyl-2-butyl phosphate 32

Obtained from general procedure B using 1-(*o*-methylphenyl)ethanol **24** (0.30 g, 1.83 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (1:1) as a clear oil **32** (0.48 g, 86%); ν_{max} (film)/cm^{-1} 2968, 2935, 1497, 1455; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.98 [3H, dd, *J* 6.9, J_{P-H} 2.0, $CH(CH_3)_2$], 1.01 [3H, dd, *J* 6.9, J_{P-H} 2.0, $CH(CH_3)_2$], 1.21 (3H, td, *J* 7.1, J_{P-H} 1.0, CH_2CH_3), 1.31 (3H, td, *J* 7.1, J_{P-H} 1.0, CH_2CH_3), 1.90–2.01 [1H, m, $CH(CH_3)_2$], 2.88–2.99 (2H, m, CH_2Ph), 3.74–3.90 (2H, m, OCH_2), 3.95–4.11 (2H, m, OCH_2), 4.48–4.54 (1H, m, C*H*O), 7.21–7.33 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 16.0 (d, J_{C-P} 7.0, CH_2CH_3), 16.1 (d, J_{C-P} 7.0, CH_2CH_3), 16.8 [$CH(CH_3)_2$], 18.2 [$CH(CH_3)_2$], 31.0 [d, J_{C-P} 4.0, $CH(CH_3)_2$], 37.9 (d, J_{C-P} 4.0, CH_2Ph), 63.3 (d, J_{C-P} 6.0, OCH_2), 63.4 (d, J_{C-P} 5.0, OCH_2), 84.4 (d, J_{C-P} 6.1, CHO), 126.4 (ArCH), 128.4 (2× ArCH), 129.6 (2× ArCH), 137.8 (ArC); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −0.01; *m*/*z* (ES$^+$) 324 (64%, M$^+$+Na), 301.1576 (100, MH$^+$ $C_{15}H_{26}O_4P$ requires 301.1569).

Employing general procedure C, alcohol **24** (0.50 g, 3.04 mmol) was treated with MeMgCl (0.11 mL, 3.0 M in THF, 0.33 mmol) and *N*-phosphoryl oxazolidinone **18** (0.13 g, 0.31 mmol) to afford phosphate ester **32** (0.07 g, 76%) in 28% ee; $[\alpha]_D^{22}$ = −10.0 (*c* 1.0, $CHCl_3$); HPLC, Chiralpak AD, 2% *i*-PrOH in hexane; 1.0 mL min^{-1}; t_r 18.0 min (major) and 20.8 min (minor).

4.27. Diethyl 2-[1-phenyl-2,2-dimethylbutyl] phosphate 33

Obtained from general procedure B using 3-methyl-1-phenyl-2-butanol **24** (0.50 g, 2.8 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (5:2) as a clear oil **33** (0.07 g, 80%); ν_{max} (ATR)/cm^{-1} 2963, 1479, 1455; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 1.02 [9H, s, $C(CH_3)_3$], 1.06 (3H, td, *J* 7.1, 1.1, CH_2CH_3), 1.26 (3H, td, *J* 7.1, 1.1, CH_2CH_3), 2.80 (1H, dd, 1H, *J* 14.5, 8.8, PhC*H*H), 3.02 (1H, ddd, 1H, *J* 14.5, 3.4, 2.1, PhC*H*H), 3.42 (1H, dpent, *J* 10.1, 7.0, OC*H*H), 3.62 (1H, dpent, *J* 10.1, 7.0, OC*H*H), 3.97 (2H, m, OCH_2), 4.50 (1H, td, *J* 8.8, 3.4, C*H*O), 7.19–7.29 (5H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 16.0 (d, J_{C-P} 8.0, CH_3CH_2), 16.1 (d, J_{C-P} 8.0, CH_3CH_2), 26.2 [$(CH_3)_3C$], 35.8 [d, J_{C-P} 4.0, $(CH_3)_3C$], 37.9 PhCH_2), 62.9 (d, J_{C-P} 6.0, OCH_2), 63.3 (d, J_{C-P} 6.0, OCH_2), 88.1 (d, J_{C-P} 8.0, OCH), 126.3 (ArCH), 128.3 (2× ArCH), 129.6 (2× ArCH), 138.7 (ArC); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −1.60; *m*/*z* (ESI$^+$) 315.1726 (100%, MH$^+$, $C_{16}H_{28}O_4P$ requires 315.1725).

Employing general procedure C alcohol **24** (0.50 g, 2.81 mmol) was treated with MeMgCl (0.10 mL, 3.0 M in THF, 0.31 mmol) and *N*-phosphoryl oxazolidinone **18** (0.12 g, 0.28 mmol) only returned starting material. HPLC, Lux 3 μm Cellulose-1, 1% *i*-PrOH in hexane; 1.0 mL min^{-1}; t_r 17.3 min and 19.7 min.

4.28. Diethyl 3-[5-phenyl-2-methylpentyl] phosphate 34

Obtained from general procedure B using 5-phenyl-2-methyl pentan-3-ol **26** (0.5 g, 2.8 mmol) after purification by flash column chromatography on silica gel eluting with petroleum ether 40–60 °C/EtOAc (3:2) as a clear oil **34** (0.08 g, 91%); ν_{max} (ATR)/cm^{-1} 2963, 1496, 1454; ^{1}H NMR (400 MHz; $CDCl_3$) δ_H 0.92 [3H, d, *J* 6.8, 1× $CH(CH_3)_2$], 0.98 [3H, d, *J* 6.8, 1× $CH(CH_3)_2$], 1.37 (6H, td, *J* 7.1, 0.5, CH_2CH_3), 1.88–2.05 [3H, m, $CH(CH_3)_2$ and CH_2], 2.69 (1H, ddd, *J* 13.8, 10.8, 5.9, C*H*H), 2.81 (1H, ddd, *J* 13.8, 11.0, 5.5, C*H*H), 4.15 (4H, app dtd, *J* 14.6, 7.1, 0.8, 2× OCH_2), 4.31 (1H, ddd, *J* 12.1, 7.8, 4.4, C*H*O), 7.19–7.25 (3H, m, ArC*H*), 7.28–7.34 (2H, m, ArC*H*); ^{13}C NMR (100 MHz; $CDCl_3$) δ_C 16.2 (d, J_{C-P} 6.0, CH_3CH_2), 17.5 (CH_3), 17.7 (CH_3), 31.7 (CH_2), 31.8 [d, J_{C-P} 3.0, $(CH_3)_2CH$], 33.4 (d, J_{C-P} 4.0, CH_2), 63.5 (d, J_{C-P} 6.0, 2× OCH_2), 83.8 (d, J_{C-P} 6.0, CHO), 125.9 (ArCH), 128.4 (2× ArCH), 128.4 (2× ArCH), 141.9 (ArC); ^{31}P NMR (101 MHz; $CDCl_3$) δ_P −1.30; *m*/*z* (ES$^+$) 315.1714 (100%, MH$^+$ $C_{16}H_{28}O_4P$ requires 315.1725).

Employing general procedure C alcohol **26** (0.50 g, 2.81 mmol) was treated with MeMgCl (0.10 mL, 3.0 M in THF, 0.31 mmol) and *N*-phosphoryl oxazolidinone **18** (0.12 g, 0.28 mmol) to afford phosphate ester **34** (0.06 g, 66%) in 14% ee; $[\alpha]_D^{22}$ = −8.3 (*c* 1.2, $CHCl_3$); HPLC, Lux 3 μm Cellulose-1, 2% *i*-PrOH in hexane; 1.0 mL min^{-1}; t_r 9.6 min (minor) and 12.3 min (major).

4.29. Diethyl 2-[2-phenyl-3-methylbutyl] phosphate 35

Attempted phosphorylation using procedure B or C resulted in the return of the alcohol starting material in both cases.

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