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Stereochemical consequences of the use of chiral *N*-phosphoryl oxazolidinones in the attempted kinetic resolution of bromomagnesium alkoxides

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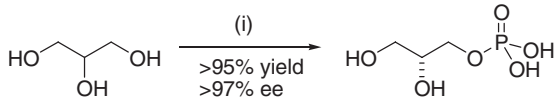
Abstract—A number of chiral *N*-phosphoryl oxazolidinones have been prepared and evaluated as asymmetric phosphoryl transfer agents with the magnesium alkoxide of 1-phenyl ethanol. The reaction proceeded with little stereoselection, which was shown to be a consequence of the reaction mechanism that occurs with inversion of configuration at phosphorus consistent with in-line attack opposite the leaving group.

1. Introduction

Phosphate esters play an important role in many biochemical pathways, from regulating immune response, host–pathogen interactions and tumour metathesis as part of cell wall polysaccharides,[1] to regulating transmembrane signalling, in the form of inositol phosphates.[2] Aside from their biological significance, phosphate esters are useful synthetic intermediates that can be used as a source of organolithium compounds,[3] be dehydrated to yield alkenes[4] or act as substrates for stereoselective displacement with Grignard reagents.[5] As a result phosphate esters are important synthetic targets.

In spite of the abundant examples of chemical phosphorylation,[6] enantioselective chemical phosphorylation is relatively underdeveloped. The only method that is widely used for the enantioselective phosphorylation of alcohols utilises enzyme systems, either isolated or as whole cells, which allow the stereo- and often enantioselective introduction of phosphate groups in generally good yields.[7] Such enzyme systems comprise of the enzyme, which catalyses the transfer of the phosphate group to the substrate and a source of the phosphate group or cofactor. For example, glycerol kinase from *Escherichia coli* or *Saccharomyces cerevisiae* readily phosphorylates glycerol, L-glyceraldehyde or dihydroxyacetone (Scheme 1).[8] As a cofactor, ATP is most commonly used, although different glycerol kinases can also utilise GTP, UTP or CTP, in addition to employing phosphoenol pyruvate (PEP) as a source of phosphate and pyruvate kinase to recycle the ADP to ATP.



Scheme 1. Reagents: Glycerol kinase, pyruvate kinase, ATP, PEP, $MgCl_2$.

The only non-enzymatic development in this area has used a histidine-containing oligopeptide capable of phosphorylating the D-*myo*-inositol-1-phosphate precursor **1** in good yield and excellent enantioselectivity (Scheme 2).[9] The peptide was obtained via combinatorial methods that has the advantage of only requiring the use of an oligopeptide rather than a whole enzyme, essentially mimicking the enzyme active site. Consequently, in principle it can be optimised for any other molecule aside from D-*myo*-inositol by the use of combinatorial methods.

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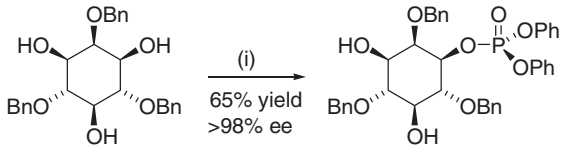


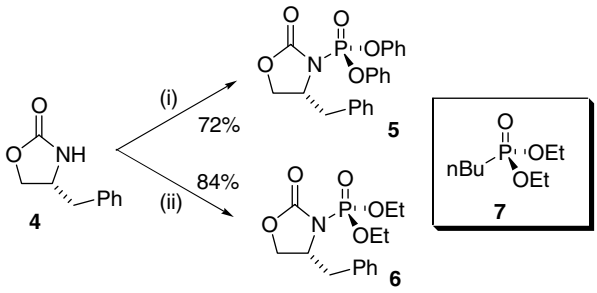
Scheme 2. Reagents: (i) 2 mol % pentapeptide, $(PhO)_2P(O)Cl$, Et_3N, toluene, 0 °C.

Previous work from our group has described the synthesis and application of *N*-phosphoryl oxazolidinones.[10] We have demonstrated that such reagents act as efficient phosphorylation agents for a wide range of alcohol substrates. Moreover, the structures of these reagents make them ideal for modification into chiral reagents of the type **2** that would be suitable for evaluation in phosphoryl transfer. Chiral oxazolidinones are amongst the most widely used auxiliaries and have been successfully used in acyl chemistry.[11] It is not surprising then that a related application of the proposed reagent **2** has been previously reported. The *N*-benzoyl *tert*-leucinol derived reagent **3** has been used in the asymmetric acylation of the magnesium alkoxide of 1-phenyl ethanol (Scheme 3).[12] An excess of alkoxide was used in this work, however the yield and ee of the ester product were excellent. Herein, we describe the synthesis and preliminary evaluation of chiral *N*-phosphoryl oxazolidinones **2** as a chemical reagent to effect the kinetic resolution of racemic alcohols via phosphorylation.

2. Results and discussion

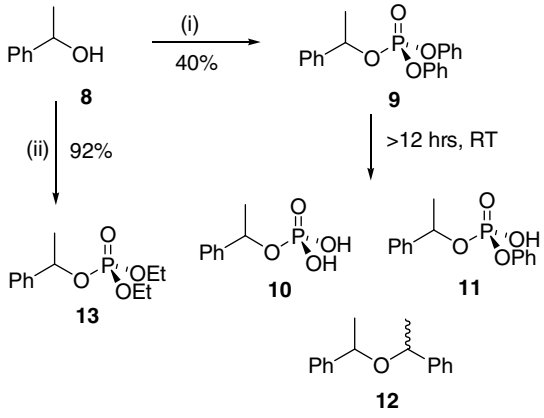
Initial trials were carried out using the (4*R*)-benzyloxazolidinone **4**, which was phosphorylated using both diphenyl and diethyl chlorophosphate (Scheme 4). While purification of the diphenyloxazolidinone **5** posed no problem, purification of the diethyl analogue **6** proved to be very difficult with a small amount of impurity present even after a series of silica and Sephadex® columns. Subsequent work (see phosphonamides **19** and **20**) suggested the by-product to be the phosphonate **7** formed from the reaction between *n*-butyl lithium and diethyl chlorophosphate.

The expected products of the kinetic resolution were also prepared. Treatment of the lithium alkoxide of 1-phenyl ethanol **8** with diphenyl chlorophosphate gave product **9**, however decomposition with loss of the phenoxy groups was found to occur within 24 h at room temperature, giving a number of products amongst

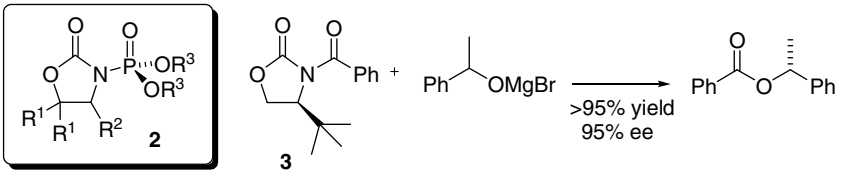


Scheme 4. Reagents: (i) *n*-BuLi, THF then $(PhO)_2P(O)Cl$; (ii) *n*-BuLi, THF then $(EtO)_2P(O)Cl$.

which were the phosphates **10** and **11** and ether **12**. The instability of the triester **9** has been previously noted, and the desired product **9** was finally prepared in 40% yield by treatment with 1.1 equiv DMAP, followed by immediate purification via column chromatography (Scheme 5).[13] This was stored in the freezer, where it was stable for a few days. In contrast, the diethyl phosphate product **13** was prepared from the lithium alkoxide of racemic 1-phenyl ethanol **8** and diethyl chlorophosphate in 92% yield and found to be significantly more stable compared to the corresponding diphenyl phosphate over a period of several months. This is not surprising since the rate of hydrolysis of phosphate esters depends on the pK_a values of the substituents,[13] with lower pK_a values resulting in higher hydrolysis rates. Since the pK_a of ethanol is 16 compared to a pK_a of 9.95 for phenol, the diethyl phosphate **13** is expected to be less prone to hydrolysis compared to the diphenyl phosphate **9**.



Scheme 5. Reagents: (i) 1.1 equiv DMAP, $(PhO)_2P(O)Cl$, THF; (ii) *n*-BuLi, THF, then $(EtO)_2P(O)Cl$.



Scheme 3.

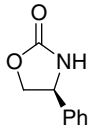
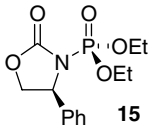
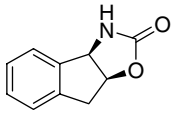
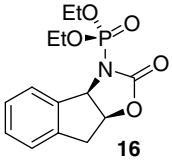
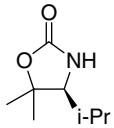
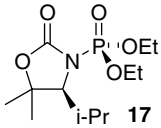
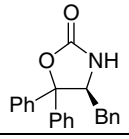
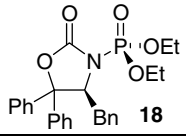
With authentic products in hand, the diphenyl phosphonamide **5** was reacted with 1 equiv of the bromomagnesium alkoxide of racemic 1-phenyl ethanol. Deprotonation of the alcohol with methyl magnesium bromide was initially carried out in ether and subsequently reacted with phosphonamide **5**, which gave unreacted starting material due to the insolubility of the magnesium alkoxide in ether. This was overcome by forming the alkoxide in ether and then solubilising it by adding dichloromethane (dichloromethane/ether 3:2, Scheme 6). However, analysis of the enantiomeric excess of unreacted alcohol **8** by chiral GC indicated no selectivity, while the ^{1}H NMR spectrum of the crude reaction mixture indicated cleavage of the P–N bond (30% cleavage after 150 min) and presence of the ether **12**. However, when the reaction was left stirring for 19 h at room temperature, although complete consumption of reagent **5** was observed, the main product observed was the bromide **14**, while the ether **12** was also present.

Since the diethyl phosphate ester **13** appeared to be considerably more stable, the phosphonamide **6** was treated under identical conditions to those described above. Once again a reaction took place, this time generating only the desired diethyl phosphate ester **13** (75% conversion after 150 min). However, chiral GC analysis of the residual alcohol **8** indicated that there was no enantiomeric excess.

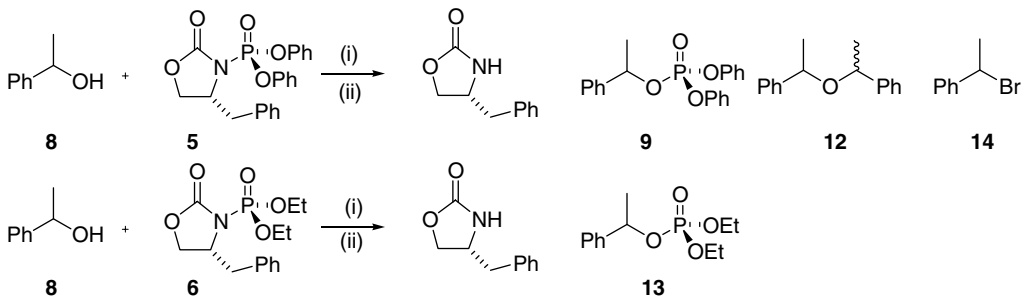
Somewhat surprised by this in view of the work previously described by Evans et al.,[12] several chiral diethyl *N*-phosphoryl oxazolidinones were prepared as previously described by deprotonation of the parent oxazolidinone followed by quench with diethyl chlorophosphate (Table 1). Diethyl phosphonamides were chosen to limit the by-products observed during the reaction. All of the reactions proceeded with quantitative conversion to the crude phosphonamide product. However purification was problematic in some cases, particularly the oxazolidinones **15** and **16** where, as in the case of the oxazolidinone **6**, repeated column chromatography failed to give analytically pure product. On the other hand, the 5,5-disubstituted phosphonamides **17** and **18** were easier to purify, possessing different R_f values to that of the phosphonate impurity.

Kinetic resolution of the bromomagnesium alkoxide of 1-phenyl ethanol was attempted with these phosphonamides by stirring for 30 min at various reaction temperatures. Samples were removed and analysed, the results are shown in Table 2. Since the enantiomers of the diethyl phosphate product **13** could not be separated by chiral HPLC, the enantioselectivity of these reactions was directly determined by the use of a chiral solvating reagent, (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl) ethanol, which facilitated the separation of the methyl groups of the two enantiomers by ^{1}H NMR spectroscopy. A sample of enantiomerically enriched phosphate of known stereochemistry was independently prepared by treatment of enantiomerically pure (*S*)-1-phenyl ethanol with *n*-BuLi in THF and subsequent reaction with diethyl chlorophosphate. In all cases, the enantioselectivities were very low, corresponding to selectivity factors (s) of less than 1. The best selectivities were observed for the sterically demanding 5,5-disubstituted oxazolidinones, which may be a consequence of the propensity of these reagents to locate the 4-substituent close to the reactive centre.[14] Given the success of the Evans system for acyl transfer it at first appeared strange that

Table 1. Preparation of *N*-phosphoryl oxazolidinones[a]

Oxazolidinone	Phosphonamide	Yield (%)[b]
	 **15**	63
	 **16**	44
	 **17**	78
	 **18**	81

[a] Reactions performed according to conditions in Scheme 4.
[b] Refers to the amount of contaminant free material obtained.

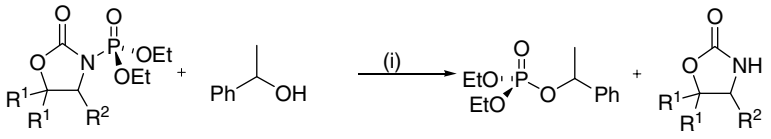


8 **5** **9** **12** **14**

8 **6** **13**

Scheme 6. Reagents: (i) alcohol **8**, Et_2O, then MeMgBr; (ii) CH_2Cl_2, reagents **5** or **6**.

Table 2. Reactivity and selectivity of *N*-phosphoryl oxazolidinones



6, **15-18** **8** **13**

Reagents: (i) Alcohol **8**, Et_2O, then MeMgBr; (ii) CH_2Cl_2, reagent **6** or **15-18**

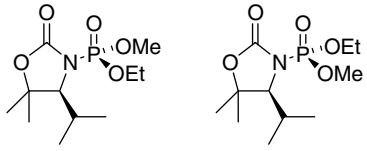
Reagent	Temperature (°C)	Conversion (%)	ee (%) of phosphate **13**[a]	Major enantiomer of phosphate **13**[b]
6	−16	25	<5	*R*
6	2	41	<5	*R*
6	20	75	<5	*R*
15	−16	20	<5	*S*
15	2	35	<5	*S*
15	20	59	<5	*S*
16	−16	15	7	*S*
16	2	47	<5	*S*
16	20	66	7	*S*
17	−16	6	<5	*S*
17	2	20	7	*S*
17	20	67	12	*S*
18	−16	21	<5	*S*
18	2	45	6	*S*
18	20	88	10	*S*

[a] Determined by ^1H NMR using (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl) ethanol.
[b] Determined by comparison with a sample of authentic product.

such poor results were obtained with the analogous phosphate one.

The lack of selectivity could be attributed to the site of attack of the alkoxide. Nucleophilic attack at a phosphorus atom is known to proceed with in-line attack, opposite to the leaving group, with inversion of configuration at phosphorus (Fig. 1).[15] As a result, the stereochemical information is probably too far away for the selectivity of the reaction to be affected.

This in-line attack of the alkoxide with inversion of configuration at phosphorus could be directly observed if a *P*-chiral phosphonamide was used instead. The product of a reaction of such a phosphonamide with an alkoxide should yield a *P*-chiral phosphate, the absolute configuration of which could be determined by comparing the $[\alpha]_D$ values or the retention times from chiral GC or HPLC with the literature values. However, since there was no literature precedence of such phosphonamides, the stereochemistry at phosphorus would be determined directly from the crystal structure of the phosphonamide. For this reason, the phosphonamides **19** and **20** were selected due to the crystallinity of the corresponding diethyl phosphonamide **17** and the very similar nature of the *O*-alkyl groups, which should not influence the outcome of the reaction (Fig. 2).



19 **20**

Figure 2. Target *P*-chiral phosphonamides.

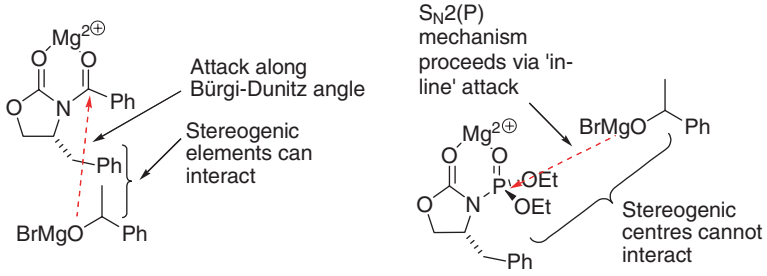
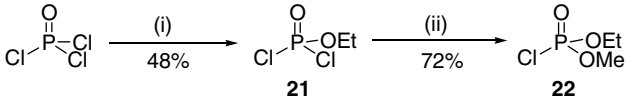


Figure 1. Trajectory of attack at *N*-acyl and *N*-phosphoryl oxazolidinones.

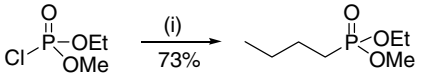
The racemic ethyl methyl chlorophosphate **22** required to access these targets was prepared as colourless oil in two steps from phosphorus oxychloride by treatment of 1 equiv of ethanol and triethylamine and purification of the dichloride **21** by distillation, followed by the same procedure using methanol (Scheme 7).



Scheme 7. Reagents: (i) EtOH, Et_3N, petrol; MeOH, Et_3N, petrol.

The phosphonamides **19** and **20** with a stereogenic phosphorus centre were then prepared by treating the lithium salt of the 5,5-dimethyl oxazolidinone **23** with ethyl methyl chlorophosphate **22** and separating the two diastereoisomers by column chromatography (Scheme 8). The ^{1}H NMR spectrum of the crude product indicated complete conversion of starting material and that some degree of selectivity in this process was evident, giving the phosphonamide in 8% de in favour of the phosphonamide **20**. This indicated possible dynamic kinetic resolution since chlorophosphates such as **22** are known to undergo racemisation, although the rate of this reaction has not been studied.[16]

The ^{1}H NMR spectrum of the crude product also suggested the presence of a by-product, which was found to have a very similar R_f value to the two diastereoisomers, thus making their separation and purification very difficult. This by-product was found to be the phosphonate **24**, formed from the reaction between *n*-butyl lithium and the chlorophosphate **22**. This was proven by treating the chlorophosphate with *n*-butyl lithium in THF, yielding the pure phosphonate in 73% yield after distillation of the crude product (Scheme 9).



Scheme 9. Reagents: (i) *n*-BuLi, THF.

Separation and crystallisation of these diastereoisomers was very difficult, however, a crystal structure of the (S_P)-enantiomer **19** was eventually obtained (Fig. 3)[17] that clearly shows the phosphate group adopting an antiperiplanar geometry to the carbonyl group, similar to that of the carbonyl group in Evans' chemistry.[18]

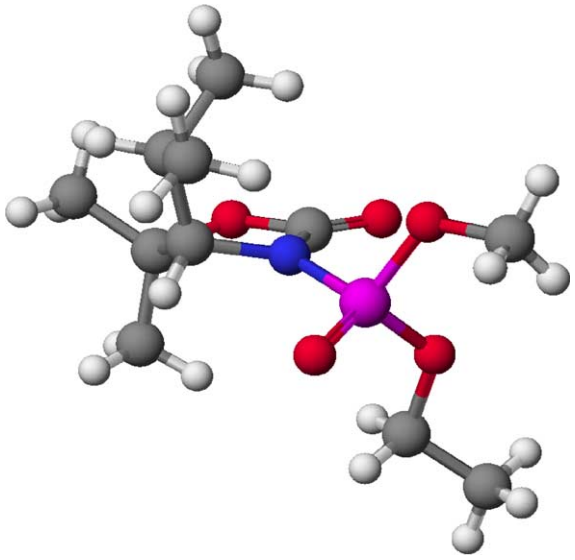
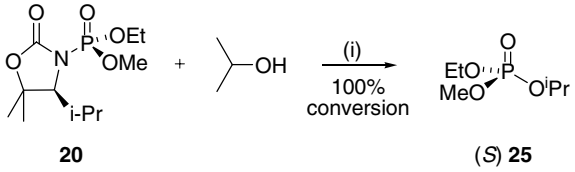


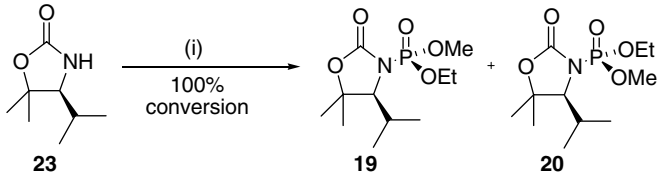
Figure 3. Crystal structure of phosphonamide **19**.

Phosphonamide **20**, which was available in larger quantities of high purity material than diastereoisomer **19**, was then treated with the magnesium alkoxide of isopropanol giving quantitative conversion to ethyl isopropyl methyl phosphate (*S*)-**25** in >95% ee according to chiral GC (Scheme 10). Attempts to purify this triester led to loss of material due to the scale of reaction and visualisation difficulties on TLC.



Scheme 10. Reagents: (i) *i*-PrOH, Et_2O, then MeMgBr; (ii) CH_2Cl_2, reagent **20**.

The phosphate (*S*)-**25** had a very small $[\alpha]_D$ value, which could not be accurately compared to the literature value,[19] and there was no literature data to compare the GC conditions. Furthermore, attempts to determine the ratio of the two enantiomers by ^{1}H NMR spectroscopy with the use of Eu[(+)-(hfc)]$_3$, for which there was literature precedence also proved unsuccessful, since the peaks corresponding to the two enantiomers could not be adequately separated from each other.[19a] For this



Scheme 8. Reagents: (i) *n*-BuLi, THF, then **22**.

reason, triester (*R*)-**25** was prepared in >95% ee by an established independent route,[19a] in order for a chiral GC of the new sample to be obtained and for the stereochemistry of the phosphorylation product to be conclusively established. Additionally, a sample of racemic triester **25** was also prepared in 75% yield by the action of the lithium alkoxide of isopropyl alcohol with chlorophosphate **22**.

Gas chromatography using a chiral stationary phase was then performed on the triester products from these different routes. It was shown that the triester derived from the phosphonamide **20** had the opposite stereochemistry to the sample of (*R*)-**25** that was prepared by established literature methods. As a consequence, the reaction of magnesium alkoxides with these phosphonamides proceeds via a typical $S_N2(P)$ reaction with apical attack of the nucleophile opposite to the leaving group and inversion of configuration. This result is in accordance with Westheimer's guidelines and all known literature data, since they all support an apical attack of the nucleophile opposite to the leaving group.[15]

3. Conclusion

We have found that the attempted kinetic resolution of *N*-phosphoryl oxazolidinones with racemic alkoxides proceeds with little or no stereoselection unlike the analogous acylation developed by Evans. This is due to the change in geometry at the reactive centre, since moving from a trigonal planar arrangement for acyl transfer to a tetrahedral one for phosphoryl transfer changes the trajectory of attack of any incoming nucleophile.

4. Experimental

4.1. General

All experiments that were carried out under a nitrogen atmosphere were performed using Schlenk line techniques. Glassware was routinely flame-dried and cooled in vacuo, followed by introduction of nitrogen. Reactions performed at −78 °C were cooled by means of an acetone/dry ice bath, at −16 °C by an ice/salt bath, while those at 0 °C by an ice bath.

4.2. Reagents

All amines used were previously dried by distilling them under a nitrogen atmosphere from potassium hydroxide pellets. *n*-Butyl lithium was used as a solution in hexanes and was titrated against 1,3-diphenyl-2-propanone tosyl hydrazone,[20] while methylmagnesium bromide was used as supplied as a solution in diethyl ether (Aldrich). Samples of authentic materials for identification purposes were prepared according to the following established literature methods; bis-(1-phenylethyl)ether **12**,[21] 1-phenylethyl bromide **14**,[22] (4*S*)-isopropyl-5,5-dimethyloxazolidin-2-one **23**;[14a] (4*S*)-4-benzyl-5,5-diphenyloxazolidin-2-one.[23]

4.3. Chromatography

Flash column chromatography was carried out with BDH silica gel (product number 153325P; particle size 40–63 μm), or Fluorochem Limited Silica Gel 60A (particle size 40–63 μm), while particle column chromatography was performed with Sephadex® LH-20 and ionic column chromatography with diethylaminoethyl cellulose DE22 purchased from Whatman. Thin layer chromatography was carried out with Merck aluminium TLC (Silica gel F_{254}). Unless otherwise noted, visualisation of TLC plates was performed with alkaline potassium permanganate or phosphomolybdic acid and heating.

4.4. Solvents

Dichloromethane and petroleum ether 40–60 were distilled under a nitrogen atmosphere from lithium aluminium hydride. THF and diethyl ether were distilled under nitrogen atmosphere from metallic sodium and benzophenone.

4.5. Instrumentation

^1H (200 MHz), and 50 MHz ^{13}C NMR spectroscopy was performed on a Bruker AC 200 spectrometer, 121 MHz ^{31}P NMR spectroscopy on a Bruker Aspect 3000 spectrometer, 300 MHz ^1H, and 75 MHz ^{13}C NMR spectroscopy on a Bruker WM300, while 500 MHz ^1H, 125 MHz ^{13}C and 202 MHz ^{31}P NMR spectroscopy on a JEOL (Japan Electron Optical Ltd) λ 500 MHz system. Residual proton signals from the deuteriated solvents were used as references (^1H 7.25 ppm, ^{13}C 77 ppm for chloroform), while coupling constants were measured in hertz. Mass spectroscopy was carried out on a Micromass Autospec M system, IR spectroscopy on a Nicklet 5 PC FT-IR Spectrometer, while elemental analysis was performed using a Carlo Erba 1106. Gas chromatography was carried out on a Hewlett Packard Model 427 instrument with a fused silica capillary and β-cyclodextrin as the stationery phase and a flame ionisation detector as the means of detection. Hydrogen was used as a carrier gas. Optical rotations were measured on a Polaar 2001 automatic polarimeter at 589 nm at 20 °C unless otherwise stated. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Melting points were determined using a Gallenkamp melting point apparatus (registered design 889339) and are uncorrected.

4.6. (±)-1-Phenylethanol diphenyl phosphate 9[13]

A solution of diphenyl chlorophosphate (0.66 g, 0.51 cm^3, 2.46 mmol) in dichloromethane (2 cm^3) was added to a solution of 1-phenyl ethanol **8** (0.30 g, 0.30 cm^3, 2.46 mmol) and DMAP (0.33 g; 2.70 mmol) in dichloromethane (3 cm^3) at ~18 °C and the solution was allowed to stir for 20 h. Aqueous satd ammonium chloride (5 cm^3) was added, the aqueous layer extracted with dichloromethane (3 × 10 cm^3) and the combined organic extracts washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3) and dried over magnesium sulfate. The solution was filtered, the solvent

was removed using rotary evaporation and the residue was purified by flash column chromatography (diethyl ether/petroleum ether 40–60, 2:1) to afford a colourless oil (0.35 g, 40% yield); δ_H (200 MHz; $CDCl_3$) 1.63 (3H, d, J 6.4 CHCH_3), 5.69 (1H, quintet, J 6.4, CHCH$_3$), 6.99–7.36 (15H, m, ArH); δ_P (121 MHz; $CDCl_3$) −11.54.

4.7. (±)-1-Phenylethanol diethyl phosphate 13[24]

n-Butyl lithium (0.57 cm^3, 0.82 mmol) was added to a solution of 1-phenyl ethanol **8** (0.10 g, 0.82 mmol) in THF (5 cm^3) at −78 °C and left to react for 15 min, then diethyl chlorophosphate (0.17 g, 0.14 cm^3, 0.98 mmol) was added. The solution was warmed to ~18 °C and left stirring for 2 h. Aqueous satd ammonium chloride (5 cm^3) was added, the aqueous layer was extracted with ethyl acetate (3 × 10 cm^3) and the combined organic extracts were washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3) and dried over magnesium sulfate. The solution was filtered, the solvent was removed using rotary evaporation and the residue purified by flash column chromatography (gradient column, 20–50% ethyl acetate in petroleum ether 40–60) to give a colourless slightly yellow oil (0.20 g, 92% yield); δ_H (200 MHz; $CDCl_3$) 1.12 (3H, td, J 7.1 and J_{P-H} 0.9, CH_3CH$_2$), 1.21 (3H, td, J 7.1 and J_{P-H} 0.9, CH_3CH$_2$), 1.62 (3H, d, J 6.4, CH_3CH), 3.84–4.18 (4H, m, CH_2CH$_3$), 5.46 (1H, quintet, J 6.4, CH$_3$CH), 7.30–7.42 (5H, m, ArH); δ_P (121 MHz; $CDCl_3$) −0.68.

4.8. (1*S*)-1-Phenylethanol diethyl phosphate (*S*)-13[25]

n-Butyl lithium (0.52 cm^3, 0.74 mmol) was added to a solution of (1*S*)-1-phenyl ethanol (>99% ee, 0.09 g, 0.74 mmol) in THF (5 cm^3) at −78 °C and left to react for 15 min before diethyl chlorophosphate (0.15 g, 0.13 cm^3, 0.89 mmol) was added. The solution was warmed to ~18 °C and stirred for 2 h. Aqueous satd ammonium chloride (5 cm^3) was added, the aqueous layer extracted with ethyl acetate (3 × 10 cm^3) and the combined organic extracts washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3) and dried over magnesium sulfate. The solution was filtered, the solvent removed using rotary evaporation and the residue purified by flash column chromatography (gradient column, 20–50% ethyl acetate in petroleum ether 40–60) to give a pale yellow oil (0.17 g, 67% yield); $[\alpha]_D = -20.2$ (c 1, $CHCl_3$) (lit.[25] −46.6, c 2.32, $CHCl_3$); δ_H (200 MHz; $CDCl_3$) 1.16 (3H, td, J 7.1 and J_{P-H} 0.8, CH_3CH$_2$), 1.26 (3H, td, J 7.0 and J_{P-H} 0.9, CH_3CH$_2$), 1.62 (3H, d, J 6.4, CH_3CH), 3.84–4.14 (4H, m, CH_2CH$_3$), 5.46 (1H, quintet, J 6.4, CH$_3$CH), 7.24–7.39 (5H, m, ArH); δ_C (75 MHz; $CDCl_3$) 16.3 (d, J_{P-C} 6.8, CH$_3$CH$_2$), 16.5 (d, J_{P-C} 6.8, CH$_3$CH$_2$), 24.6 (d, J_{P-C} 5.3, CH$_3$CH), 64.0 (d, J_{P-C} 4.6, CH$_3$$CH_2$), 77.1 (CH$_3$$C$H), 126.3 (Ar$C$H), 128.5 (Ar$C$H), 128.9 (Ar$C$H), 142.1 (Ar$C$); δ_P (202 MHz; $CDCl_3$) −1.44.

4.9. (4*R*,5*S*)-Indano[1,2-*d*]oxazolidin-2-one[26]

Potassium *tert*-butoxide (0.41 g, 3.60 mmol) was added to a solution of *tert*-butyl [(1*R*,2*S*)-2-hydroxy-2,3-dihydro-1*H*-inden-1-yl]carbamate[27] (0.90 g, 3.60 mmol) in THF (20 cm^3) at ~18 °C. The solution was allowed to stir for 30 min, water (5 cm^3) was added and the solution extracted with ethyl acetate (3 × 10 cm^3). The combined organic extracts were washed with sodium hydroxide (1.0 M, 10 cm^3), dried over magnesium sulfate, filtered and the solvent was removed using rotary evaporation. The residue was recrystallised from ethyl acetate to afford white needles (0.44 g, 70 % yield); mp 195–196 °C (lit.[26] 203–205 °C); $[\alpha]_D = +73.0$ (c 1, $CHCl_3$) (lit.[26] +76.9; c 1.2, $CHCl_3$); δ_H (300 MHz; $CDCl_3$) 3.37–3.41 (2H, m, CH_2CH), 5.19 (1H, d, J 7.3, CHN), 5.41–5.46 (1H, m, CH$_2$CH), 6.84 (1H, s, NH), 7.23–7.35 (4H, m, ArH); δ_C (75 MHz; $CDCl_3$) 39.2 (CH$_2$CH), 61.6 (CHN), 81.0 (CH$_2$$C$H), 125.2 (Ar$C$H), 126.0 (Ar$C$H), 128.3 (Ar$C$H), 129.8 (Ar$C$H), 140.1 (Ar$C$), 140.6 (Ar$C$), 160.0 ($C$=O).

4.10. General procedure A for the preparation of the *N*-phosphoryl oxazolidinones

n-Butyl lithium (1 equiv) was added to a solution of the oxazolidinone (1 equiv) in THF (10 cm^3) at −78 °C and left to react for 15 min, followed by addition of diethyl or diphenyl chlorophosphate (1 equiv). The solution was warmed to ~18 °C and allowed to stir for 120 min. Aqueous satd ammonium chloride (5 cm^3) was added and the aqueous layer was extracted with diethyl ether (3 × 10 cm^3). The combined organic extracts were washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3), dried over magnesium sulfate, filtered and the solvent was removed using rotary evaporation.

4.11. [(4*R*)-4-Benzyl-2-oxo-oxazolidin-3-yl]-phosphonic acid diphenyl ester 5

Using general procedure A, a white solid was obtained, which was purified by recrystallisation from dichloromethane/petroleum ether 60:80 (0.5 g, 72% yield); mp 118–119 °C; $[\alpha]_D = +58.1$ (c 1, $CHCl_3$); (found: C, 64.8; H, 4.8; N, 3.40. $C_{22}H_{20}O_5NP$ requires C, 64.55; H, 4.9; N, 3.4); ν_{max} (KBr disk)/cm^{-1} 1785, and 1288; δ_H (200 MHz; $CDCl_3$) 2.38 (1H, dd, J 13.3 and J 10.7, CH_2Ph), 3.07 (1H, dd, J 13.3 and 3.5, CH_2Ph), 3.97–4.08 (2H, m, OCH_2CH), 4.26 (1H, m, CHN), 7.04–7.09 (2H, m, ArH), 7.20–7.31 (6H, m, ArH), 7.34–7.39 (7H, m, ArH); δ_C (125 MHz; $CDCl_3$) 40.0 (CH$_2$Ph), 58.1 (d, J_{P-C} 5.2, CHN), 67.5 (d, J_{P-C} 9.3, OCH$_2$CH), 120.5 (d, J_{P-C} 4.2, ArCH), 121.1 (d, J_{P-C} 5.2, ArCH), 126.2 (ArCH), 127.3 (ArCH), 128.9 (ArCH), 129.3 (ArCH), 129.9 (d, J_{P-C} 10.4, ArCH), 135.0 (ArC), 149.5 (d, J_{P-C} 7.3, ArC), 149.7 (d, J_{P-C} 6.3, ArC), 154.6 (d, J_{P-C} 8.2, OCON); δ_P (121 MHz; $CDCl_3$) −11.22; m/z (EI) 409.1079 (77%, $M^+ \cdot C_{22}H_{20}NO_5P$ requires 409.1079), 318 (100), 276 (43), 233 (20), 91 (19), 77 (28).

4.12. [(4*R*)-4-Benzyl-2-oxo-oxazolidin-3-yl]-phosphonic acid diethyl ester 6

Using the general procedure A, a crude oil was obtained, which was purified by flash column chromatography

(gradient silica column, 20–60% ethyl acetate in petroleum ether 40–60) giving the title compound as a viscous colourless oil (0.99 g, 84% yield); $[\alpha]_D = -33.7$ (*c* 1, $CHCl_3$); ν_{max} (film)/cm^{-1} 1772 and 1272; δ_H (300 MHz; $CDCl_3$) 1.31–1.38 (6H, m, CH_2CH_3), 2.77 (1H, dd, *J* 10.4 and 13.2, CH_2Ph), 3.44 (1H, dd, *J* 3.5 and 13.2, CH_2Ph), 4.07–4.43 (7H, m, CH_2CH_3, $CHCH_2O$ and CHN), 7.13–7.29 (5H, m, ArH); δ_C (125 MHz; $CDCl_3$) 16.2 (d, J_{P-C} 7.2, CH_3CH_2), 40.4 (CH_2Ph), 58.1 (d, J_{P-C} 5.2, CHN), 64.8 (d, J_{P-C} 6.1, CH_3CH_2), 67.6 (d, J_{P-C} 9.3, CH_2O), 127.4 (ArCH), 129.0 (ArCH), 129.5 (ArCH), 135.4 (ArC), 155.5 (C=O); δ_P (121 MHz; $CDCl_3$) −3.61; *m*/*z* (EI) 313.1090 (38%, $M^+ \cdot C_{14}H_{20}NO_5P$ requires 313.1079), 222 (100), 194 (22), 166 (30), 109 (36), 91 (31), 86 (29).

4.13. [(4*S*)-4-Phenyl-2-oxo-oxazolidin-3-yl]-phosphonic acid diethyl ester 15

Using the general procedure A, a crude oil was obtained, which was purified by flash column chromatography (50% ethyl acetate in petroleum ether 40–60) to give the title compound as a viscous colourless oil (0.10 g, 63% yield); $[\alpha]_D = -45.3$ (*c* 1, $CHCl_3$); ν_{max} (film)/cm^{-1} 1779 and 1263; δ_H (200 MHz; $CDCl_3$) 1.05 (3H, td, *J* 7.1 and J_{P-H} 0.9, CH_3CH_2), 1.26 (3H, td, *J* 7.1 and J_{P-H} 1.0, CH_3CH_2), 3.61–3.76 (2H, m, CH_3CH_2), 3.94–4.24 (2H, m, CH_3CH_2), 4.29 (1H, ddd, *J* 8.6, 1.4 and 1.9, OCH_2CH), 4.48 (1H, t, *J* 8.6, OCH_2CH), 5.11 (1H, ddd, *J* 8.6, 1.9 and J_{P-H} 1.1, CHN), 7.19–7.35 (5H, m, ArH); δ_C (125 MHz; $CDCl_3$) 15.8 (CH_3CH_2), 15.9 (CH_3CH_2), 60.2 (CHN), 64.0 (CH_3CH_2), 64.7 (CH_3CH_2), 71.4 (OCH_2CH), 126.6 (ArCH), 128.5 (ArCH), 129.0 (ArCH), 129.0 (ArCH), 139.9 (ArC), 155.5 (d, J_{P-C} 9.3, C=O); δ_P (121 MHz; $CDCl_3$) −3.39; *m*/*z* (EI) 300.1002 (9%, $MH^+ \cdot C_{13}H_{19}NO_5P$ requires 300.1001), 255 (100), 146 (77), 104 (76), 91 (52), 77 (47).

4.14. [(4*R*,5*S*)-Indano[1,2-*d*]-2-oxo-oxazolidin-3-yl]-phosphonic acid diethyl ester 16

Using general procedure A, a crude oil was obtained, which was purified by flash column chromatography (50% ethyl acetate in petroleum ether 40–60) to give the title compound as a viscous colourless oil (0.31 g, 44% yield); $[\alpha]_D = -13.5$ (*c* 1, $CHCl_3$); ν_{max} (film)/cm^{-1} 1783 and 1279; δ_H (200 MHz; $CDCl_3$) 1.20 (3H, td, *J* 7.1 and J_{P-H} 1.0, CH_3CH_2), 1.34 (3H, td, *J* 7.1 and J_{P-H} 1.0, CH_3CH_2), 3.30 (2H, d, *J* 3.6, CH_2CHO), 3.96–4.14 (2H, m, CH_3CH_2), 4.14–4.32 (2H, m, CH_3CH_2), 5.30 (1H, dt, *J* 3.6 and *J* 7.1, CH_2CHO), 5.57 (1H, d, *J* 7.1, CHN), 7.20–7.31 (3H, m, ArH), 7.84 (1H, d, *J* 6.8, ArH); δ_C (125 MHz; $CDCl_3$) 16.0 (d, J_{P-C} 7.2, CH_3CH_2), 16.2 (d, J_{P-C} 6.2, CH_3CH_2), 38.1 (CCH_2CH), 64.5 (d, J_{P-C} 6.2, CH_3CH_2), 64.9 (d, J_{P-C} 6.3, CH_3CH_2), 65.5 (d, J_{P-C} 5.2, CH_2CHO), 79.8 (d, J_{P-C} 8.2, CHN), 125.4 (ArCH), 126.9 (ArCH), 128.0 (ArCH), 129.9 (ArCH), 139.2 (ArC), 139.5 (ArC), 155.1 (d, J_{P-C} 8.3, C=O); δ_P (121 MHz; $CDCl_3$) −3.28; *m*/*z* (EI) 311.0918 (8%, $M^+ \cdot C_{14}H_{18}NO_5P$ requires 311.0923), 267 (100), 238 (29), 210 (38), 130 (46), 115 (31).

4.15. [(4*S*)-4-Isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid diethyl ester 17

Using general procedure A, a white solid was obtained, which was purified by flash column chromatography (60% ethyl acetate in petroleum ether 40–60) to give the title compound as a white crystalline solid (0.37 g, 78% yield); mp 41–42 °C; $[\alpha]_D = -29.4$ (*c* 1, $CHCl_3$); (found: C, 49.2; H, 8.3; N, 4.7. $C_{12}H_{24}NO_5P$ requires C, 49.1; H, 8.25; N, 4.8); ν_{max} (KBr disk)/cm^{-1} 1764 and 1267; δ_H (300 MHz; $CDCl_3$) 1.03 [3H, d, *J* 7.0, $(CH_3)_2CH$], 1.13 [3H, d, *J* 7.0, $(CH_3)_2CH$], 1.37–1.43 (6H, m, CH_3CH_2), 1.47 [3H, s, $(CH_3)_2C$], 1.50 [3H, s, $(CH_3)_2C$], 2.12 [1H, heptet d, *J* 7.0 and J_{P-H} 2.0, $(CH_3)_2CH$], 3.79 (1H, dd, *J* 5.2 and *J* 2.0, CHN), 4.11–4.38 (4H, m, CH_3CH_2); δ_C (75 MHz; $CDCl_3$) 16.5 (d, J_{P-C} 7.1, CH_3CH_2), 16.6 (d, J_{P-C} 7.0, CH_3CH_2), 20.9, [$(CH_3)_2CH$], 21.9 [$(CH_3)_2CH$], 29.2 [$(CH_3)_2C$], 30.5 [$(CH_3)_2C$], 64.5 (d, J_{P-C} 6.1, CH_3CH_2), 65.1 (d, J_{P-C} 6.6, CH_3CH_2), 70.7 (d, J_{P-C} 3.0, CHN), 77.6 [$(CH_3)_2CH$], 84.4 [d, J_{P-C} 8.0, $(CH_3)_2C$], 155.7 (d, J_{P-C} 7.9, C=O); δ_P (121 MHz; $CDCl_3$) −1.88; *m*/*z* (EI) 293.1387 (3%, $M^+ \cdot C_{12}H_{24}NO_5P$ requires 293.1392), 250 (100), 206 (15), 178 (14).

4.16. [(4*S*)-4-Benzyl-2-oxo-5,5-diphenyl-oxazolidin-3-yl]-phosphonic acid diethyl ester 18

Using the general procedure A, a slightly yellow gum was obtained, which was purified by flash column chromatography (60% ethyl acetate in petroleum ether 40–60) to give the title compound as a viscous semi-solid (0.17 g, 81% yield); $[\alpha]_D = -35.0$ (*c* 1, $CHCl_3$); ν_{max} (film)/cm^{-1} 1779 and 1273; δ_H (500 MHz; $CDCl_3$) 0.90 (3H, td, *J* 7.0 and J_{P-H} 0.9, CH_3CH_2), 1.25 (3H, td, *J* 7.0 and J_{P-H} 1.1, CH_3CH_2), 2.81 (1H, dd, *J* 8.5 and 14.3, CH_2CH), 2.96 (1H, dd, *J* 4.8 and 14.3, CH_2CH), 3.27–3.32 (1H, m, CH_3CH_2), 3.58–3.63 (1H, m, CH_3CH_2), 4.05–4.12 (2H, m, CH_3CH_2), 5.24–5.27 (1H, m, CHN), 6.66–6.67 (2H, m, ArH), 6.98–7.01 (3H, m, ArH), 7.07–7.14 (5H, m, ArH), 7.19–7.25 (1H, m, ArH), 7.28–7.31 (2H, m, ArH), 7.52–7.54 (2H, m, ArH); δ_C (75 MHz; $CDCl_3$) 16.0 (d, J_{P-C} 6.9, CH_3CH_2), 16.5 (d, J_{P-C} 7.3, CH_3CH_2), 38.7 (CH_2CH), 64.1 (d, J_{P-C} 5.8, CH_3CH_2), 65.3 (d, J_{P-C} 6.6, CH_3CH_2), 66.5 (CHN), 90.3 [d, J_{P-C} 7.4, $CHC(Ph)_2O$], 126.3 (ArCH), 126.7 (ArCH), 126.7 (ArCH), 128.5 (ArCH), 128.5 (ArCH), 129.0 (ArCH), 129.1 (ArCH), 129.4 (ArCH), 136.4 (ArC), 137.7 (ArC), 142.4 (ArC), 154.2 (d, J_{P-C} 7.3, C=O); δ_P (121 MHz; $CDCl_3$) −4.27; *m*/*z* (EI) 465.1701 (1%, $M^+ \cdot C_{26}H_{28}NO_5P$ requires 465.1705), 421 (65), 268 (83), 195 (100), 167 (73), 84 (78).

4.17. General procedure B for the reaction of the 1-phenyl ethanol with the phosphoryl oxazolidinones

Methyl magnesium bromide (0.48 cm^3, 1.43 mmol) was added to a solution of 1-phenyl ethanol (175 mg, 1.43 mmol) in diethyl ether (4.5 cm^3) at −78 °C and the solution was allowed to stir for 15 min. The solution was warmed to ~20 °C, dichloromethane (3 cm^3) was added and the solution was made up to 10 cm^3 with a diethyl ether/dichloromethane 3:2 solution. From the

above solution, 1 cm^3 was added to a solution of the *N*-phosphoryl oxazolidinone (0.143 mmol) in diethyl ether (2 cm^3) and dichloromethane (1 cm^3) at the required temperature (−16, 2 or 17 °C) and allowed to stir for 30 min. Aqueous satd ammonium chloride (5 cm^3) was added, the solution extracted with ethyl acetate (3 × 10 cm^3) and the combined organic layer washed with aqueous satd sodium bicarbonate (10 cm^3) and brine (10 cm^3). The solution was dried over magnesium sulfate, filtered and the solvent was removed using a water pump and a cold trap. The residue was dried on the water pump, and the ^1H NMR spectrum of the crude product was obtained from which the enantiomeric excess of the phosphate was determined by the addition of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl) ethanol (~4 mg per sample). The enantiomeric excess of the unreacted 1-phenyl ethanol **8** was also determined by chiral GC (β-cyclodextrin column, hydrogen as the carrier gas and temperature from 105 to 140 °C by 2 °C/min; $t_1 = 10.7$ min, $t_2 = 11.2$ min).

4.18. Ethyl dichlorophosphate 21[28]

A solution of triethylamine (9.07 cm^3, 65.1 mmol) and ethanol (3.80 cm^3, 65.1 mmol) in petroleum ether (100 cm^3) was added over 1 h to a solution of phosphorus oxychloride (6.07 cm^3, 65.1 mmol) in dry petroleum ether 40–60 (50 cm^3) at −30 °C. The solution was warmed to ~18 °C and allowed to stir for 2 h, filtered under nitrogen and the solvent removed under reduced pressure using a water pump. The remaining colourless oil was purified by distillation (28 °C, 0.35 mmHg) (lit.[28] 117 °C, 760 mmHg) to give the title compound as a colourless oil (7.86 g, 48% yield); δ_H (200 MHz; $CDCl_3$) 1.43 (3H, td, *J* 7.0, J_{P-H} 0.9, CH_3CH$_2$), 4.36 (2H, qd, *J* 7.0, J_{P-H} 11.0, CH$_3$CH_2).

4.19. (±)-Ethyl methyl chlorophosphate 22[28]

A solution of triethylamine (2.88 cm^3, 20.7 mmol) and methanol (0.84 cm^3, 20.7 mmol) in petroleum ether (50 cm^3) was added over 1 h to a solution of ethyl dichlorophosphate **21** (3.37 g, 20.7 mmol) in dry petroleum ether 40–60 (30 cm^3) at −30 °C. The solution was warmed to ~18 °C and allowed to stir for 3 h, filtered under nitrogen and the solvent removed from the filtrate under reduced pressure. The remaining colourless oil was purified by distillation (22 °C at 0.03 mmHg) to give the title compound as a colourless oil (2.37 g, 72% yield); δ_H (200 MHz; $CDCl_3$) 1.35 (3H, td, *J* 7.0 and J_{P-H} 1.2, CH_3CH$_2$), 3.84 (3H, d, J_{P-H} 13.7, CH_3O), 4.14–4.37 (2H, m, CH$_3$CH_2); δ_C (125 MHz; $CDCl_3$) 15.8 (d, J_{P-C} 7.3, *C*H$_3$CH$_2$), 55.5 (d, J_{P-C} 7.2, *C*H$_3$O), 66.2 (d, J_{P-C} 7.2, CH$_3$*C*H$_2$).

4.20. [(S_P,4*S*)-4-Isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid ethyl methyl ester 19 and [(R_P,4*S*)-4-isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid ethyl methyl ester 20

Using general procedure B, except using ethyl methyl chlorophosphate **22** in THF (5 cm^3), a colourless oil was obtained (0.96 g, 86 % crude yield). The crude product contained a mixture of diastereoisomers (6:7, **19**:**20**), which were separated by repeated flash column chromatography (50% ethyl acetate in petroleum ether 40–60).

[(S_P,4*S*)-4-Isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid ethyl methyl ester **19**. $[\alpha]_D = -7.0$ (*c* 1, $CHCl_3$); ν_{max} (KBr disk)/cm^{-1} 1772 and 1273; δ_H (300 MHz; $CDCl_3$) 0.96 [3H, td, *J* 7.0 and J_{P-H} 0.9, CH(CH_3)$_2$], 1.05 [3H, d, *J* 7.0, CH(CH_3)$_2$], 1.32 (3H, t, *J* 7.1, CH$_2$CH_3), 1.39 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.06 [1H, heptet d, *J* 7.0 and 2.2, (CH$_3$)$_2$C*H*], 3.67 (1H, dd, *J* 2.2 and 5.2, NC*H*), 3.87 (3H, d, J_{P-H} 11.7, OCH_3), 4.04–4.28 (2H, m, OCH_2CH$_3$); δ_C (125 MHz; $CDCl_3$) 16.3 (*C*H$_3$CH$_2$), 20.4 [(*C*H$_3$)$_2$CH], 21.4 [(CH$_3$)$_2$*C*H], 28.7 [(*C*H$_3$)$_2$C], 30.1 [(*C*H$_3$)$_2$C], 54.9 (d, J_{P-C} 4.6, *C*H$_3$O), 64.3 (d, J_{P-C} 4.5, CH$_3$*C*H$_2$O), 70.2 (d, J_{P-C} 2.1, *C*HN), 84.1 [d, J_{P-C} 5.7, (CH$_3$)$_2$*C*], 155.3 (d, J_{P-C} 6.0, C=O); δ_P (202 MHz; $CDCl_3$) −1.02; *m*/*z* (ES) 316 (32), 302 (100, M^++Na), 294 (15), 280.1314 (67%, $MH^+ \cdot C_{11}H_{23}NO_5P$ requires 280.1324).

[(R_P,4*S*)-4-Isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid ethyl methyl ester **20**. $[\alpha]_D = -33.7$ (*c* 1, $CHCl_3$); ν_{max} (KBr disk)/cm^{-1} 1768 and 1259; δ_H (300 MHz; $CDCl_3$) 0.96 [3H, d, *J* 7.0, CH(CH_3)$_2$], 1.05 [3H, d, *J* 7.0, CH(CH_3)$_2$], 1.33 (3H, dt, *J* 7.1 and J_{P-H} 7.1, CH$_2$CH_3), 1.40 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.04 [1H, heptet d, *J* 7.0 and 2.2, (CH$_3$)$_2$C*H*], 3.71 (1H, dd, *J* 2.2 and 5.1, NC*H*), 3.79 (3H, d, J_{P-H} 11.7, OCH_3), 4.26 (2H, quintet, *J* 7.1, OCH_2CH$_3$); δ_C (125 MHz; $CDCl_3$) 16.2 (*C*H$_3$CH$_2$), 20.5 [(*C*H$_3$)$_2$CH], 21.5 [(CH$_3$)$_2$*C*H], 28.8 [(*C*H$_3$)$_2$C], 30.1 [(*C*H$_3$)$_2$C], 54.9 (d, J_{P-C} 6.6, *C*H$_3$O), 64.3 (d, J_{P-C} 5.9, CH$_3$*C*H$_2$O), 70.2 (d, J_{P-C} 2.1, *C*HN), 84.1 [d, J_{P-C} 5.7, (CH$_3$)$_2$*C*], 155.3 (d, J_{P-C} 6.0, C=O); δ_P (202 MHz; $CDCl_3$) −1.10; *m*/*z* (EI) 280.1313 (5%, $MH^+ \cdot C_{11}H_{23}NO_5P$ requires 280.1314), 236 (51), 192 (44), 164 (100).

4.21. *n*-Butyl-phosphonic acid ethyl methyl ester 24[29]

n-Butyl lithium (1.6 cm^3, 2.57 mmol) was added to a solution of ethyl methyl chlorophosphate **22** (0.41 g, 2.57 mmol) in THF (10 cm^3) at −78 °C and left to react for 15 min before the solution was warmed to ~18 °C and allowed to stir for 2 h. Aqueous satd ammonium chloride (5 cm^3) was added and the solution extracted with ethyl acetate (3 × 10 cm^3). The combined organic layer was washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3), dried over magnesium sulfate and filtered. The solvent was removed using rotary evaporation to afford a slightly yellow oil, which was purified via flash column chromatography (gradient column, 40–80% ethyl acetate in petroleum ether 40–60) to give a colourless oil (0.47 g, 73% yield); δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3, CH_3CH$_2$), 1.30–1.43 (5H, m, CH_3CH$_2$O and CH$_3$CH_2), 1.55–1.59 (2H, m, CH$_3$CH_2), 1.67–1.73 (2H, m, CH$_3$CH_2), 3.72 (3H, d, *J* 10.78, CH_3O), 4.06–4.13 (2H, m, CH$_3$CH_2); δ_C (75 MHz; $CDCl_3$) 13.9 (*C*H$_3$CH$_2$), 16.9 (d, J_{P-C} 5.8, *C*H$_3$CH$_2$), 24.1 (d, J_{P-C} 17.3, *C*H$_2$), 24.4 (*C*H$_2$), 24.8 (d, J_{P-C} 5.2, *C*H$_2$), 26.2 (*C*H$_2$), 52.4 (d, J_{P-C} 6.6, *C*H$_3$O), 62.0 (d, J_{P-C} 6.5, CH$_3$*C*H$_2$); δ_P (202 MHz;

$CDCl_3$) 34.34; *m/z* (EI) 181.0990 (27%, $M^{+}\cdot C_{11}H_{23}NO_5P$ requires 181.0993), 138 (83), 124 (49), 111 (100), 96 (45).

4.22. (*S*)-Ethyl methyl isopropyl phosphate (*S*)-25[19b]

Methyl magnesium chloride (0.55 cm^3, 1.65 mmol) was added to a solution of 2-propanol (99 mg, 1.65 mmol) in diethyl ether (4.5 cm^3) at −78 °C and the solution was allowed to stir for 15 min. The solution was warmed to ~20 °C, dichloromethane (3 cm^3) was added and the solution was made up to 10 cm^3 with a diethyl ether/dichloromethane 3:2 solution. From the above solution, 1 cm^3 was added to a solution of [(R_P,4*S*) 4-isopropyl-5,5-dimethyl-2-oxo-oxazolidin-3-yl]-phosphonic acid ethyl methyl ester **20** (47 mg, 0.165 mmol) in diethyl ether (2 cm^3) and dichloromethane (1 cm^3) at ~18 °C and allowed to stir for 24 h. Aqueous satd ammonium chloride (5 cm^3) was added, the solution extracted with ethyl acetate (3 × 10 cm^3), the combined organic layer washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3), dried over magnesium sulfate, filtered and the solvent was removed using rotary evaporation to afford a colourless oil (22 mg, 100% conversion). Further purification using flash column chromatography (20% ethyl acetate in petroleum ether 40–60) led to the loss of the product. Selected NMR signals of crude material: δ_H (500 MHz; $CDCl_3$) 1.26–1.29 [9H, m, CH_3CH_2 and $(CH_3)_2CH$], 3.70 (3H, d, J_{P-H} 8.2, CH_3O), 4.04 (2H, q, *J* 7.0, CH_3CH_2), 4.59 [1H, octet, *J* 6.4, $(CH_3)_2CH$]; δ_C (125 MHz; $CDCl_3$) 16.2 (d, J_{P-C} 6.2, CH_3CH_2), 23.7 [d, J_{P-C} 5.2, $(CH_3)_2CH$], 54.0 (d, J_{P-C} 6.2, CH_3CH_2), 63.7 [d, J_{P-C} 5.2, $(CH_3)_2CH$], 72.7 (d, J_{P-C} 6.3, CH_3O). For GC, a β-cyclodextrin column was used with hydrogen as the carrier gas, and temperature from 65 to 120 °C by 0.3 °C/min; t_R = 52.95 min.

4.23. (±)-Ethyl methyl isopropyl phosphate 25[16]

n-Butyl lithium (1 cm^3, 1.6 mmol) was added to a solution of 2-propanol (0.10 g, 1.6 mmol) in THF (5 cm^3) at −78 °C and the solution was allowed to stir for 15 min. A solution of *rac*-ethyl methyl chlorophosphate **22** (0.29 g, 1.6 mmol) in THF (2 cm^3) was added at −78 °C and the solution was warmed to ~18 °C and allowed to stir for 13 h. Aqueous satd ammonium chloride (5 cm^3) was added and the solution extracted with ethyl acetate (3 × 10 cm^3). The combined organic layer was washed with aqueous satd sodium bicarbonate (10 cm^3), brine (10 cm^3), dried over magnesium sulfate and filtered. The solvent was removed using rotary evaporation to afford a colourless oil (0.22 g, 75% yield); δ_H (300 MHz; $CDCl_3$) 1.22–1.27 [9H, m, CH_3CH_2 and $(CH_3)_2CH$], 3.65 (3H, d, J_{P-H} 11.1, CH_3O), 4.04 (2H, quintet, *J* 7.1, CH_3CH_2), 4.55 [1H, octet, *J* 6.3, $(CH_3)_2CH$]; δ_C (125 MHz; $CDCl_3$) 16.1 (d, J_{P-C} 6.2, CH_3CH_2), 23.6 [d, J_{P-C} 5.2, $(CH_3)_2CH$], 53.8 (d, J_{P-C} 6.2, CH_3CH_2), 63.4 [d, J_{P-C} 6.2, $(CH_3)_2CH$], 72.5 (d, J_{P-C} 6.3, CH_3O). For GC, a β-cyclodextrin column was used with hydrogen as the carrier gas, and temperature from 65 to 120 °C by 0.3 °C/min; t_1 = 52.95 min, t_2 = 53.83 min.

4.24. (*R*)-Ethyl isopropyl methyl phosphate (*R*)-25[30]

The title compound was prepared in accordance with an established literature procedure[30] to afford a colourless oil (0.04 g); δ_H (300 MHz; $CDCl_3$) 1.29–1.70 [9H, m, CH_3CH_2 and $(CH_3)_2CH$], 3.72 (3H, d, J_{P-H} 11.0, CH_3O), 4.09 (2H, quintet, *J* 7.3, CH_3CH_2), 4.63 [1H, octet, *J* 6.3, $(CH_3)CH$]; δ_C (75 MHz; $CDCl_3$) 16.1 [d, J_{P-C} 6.7, $(CH_3)_2CH$], 23.5 (d, J_{P-C} 5.0, CH_3CH_2), 53.9 (d, J_{P-C} 6.0, CH_3O), 63.5 (d, J_{P-C} 5.8, CH_3CH_2), 72.6 [d, J_{P-C} 5.8, $(CH_3)_2CH$]; δ_P (202 MHz; $CDCl_3$) −0.26. For GC, a β-cyclodextrin column was used with hydrogen as the carrier gas, and temperature from 65 to 120 °C by 0.3 °C/min; t_R = 53.82 min.

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CCDC, 12 Union Road, Cambridge CB2 1EX, UK [fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
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