Control of stereochemistry with phosphine oxides: asymmetric synthesis of 4-alkenyloxazolidin-2-ones with 1,4-related stereogenic centres across a double bond

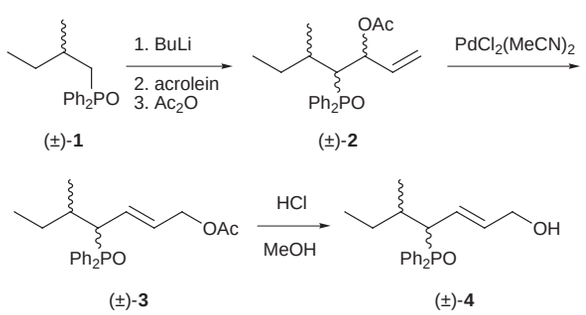
Jonathan Clayden † and Stuart Warren *

University Chemical Laboratory, Lensfield Road, Cambridge, UK CB2 1EW

Treatment of optically active epoxyurethanes with four contiguous stereogenic centres [derived from a kinetic resolution during Sharpless epoxidation of diphenylphosphinoyl (Ph_2PO) allylic alcohols] with base leads to sequential regioselective intramolecular nucleophilic attack (on the epoxide) and Horner–Wittig elimination to give single geometrical isomers of alkenyl oxazolidinones. Any stereoisomer of 4-alkenyloxazolidin-2-ones containing 1,4-related stereogenic centres spanning a double bond of either geometry can be produced with control over geometrical (*E*,*Z*), relative (*syn*,*anti*) and absolute (*R*,*S*) stereochemistry.

Introduction

We have used the diphenylphosphinoyl group[1] to control the stereochemistry of double bonds, the diastereoselectivity of carbon–carbon bond forming reactions and more recently, by using Sharpless asymmetric epoxidation[2] or dihydroxylation, the absolute stereochemistry of cyclopropanes (using the Sharpless AD reaction)[3] and a variety of allylically functionalised alkenes, among them a series of unsaturated α-amino acids (using the Sharpless AE reaction).[4] In this paper we report[5] the culmination of our Sharpless epoxidation work in the synthesis of enantiomerically enriched samples of any diastereoisomer (including geometrical isomer) of the alkenyl oxazolidinone **5** by the strategy outlined in Schemes 1 and 2.



Scheme 1 Synthesis of racemic δ-hydroxy allylic phosphine oxides **4**

The starting materials were prepared by the reactions shown in Scheme 1. We have previously described[6] the stereospecific palladium-catalysed rearrangements used to convert the easily prepared Horner–Wittig intermediates **2** into the δ-hydroxy allylic phosphine oxides **4**. The racemic mixture of diastereoisomers of **4** formed by this route was separated into *syn* and *anti*-**4** by HPLC.

Each racemic allylic alcohol **4** was subjected to Sharpless epoxidation[2] to give, by kinetic resolution at about 50% completion, enantiomerically enriched epoxides **5** and remaining enantiomerically enriched allylic alcohols **4** (Scheme 2).[7] Epoxidation of the enantiomerically enriched allylic alcohols with MCPBA gave the remaining two diastereoisomers of the epoxide **5**. The enantiomer of **5** produced in these reactions is determined by the enantiomer of diisopropyl tartrate used in the Sharpless epoxidation but the diastereoisomer is determined by the fortunately different diastereoselectivities of the Sharpless (*anti* to Ph_2PO) and MCPBA (*syn* to Ph_2PO) epoxidations.[8]

The remainder of this paper describes the development of these epoxides **5** by nucleophilic opening and Horner–Wittig elimination to give the alkenyloxazolidinones **7**. Because our final step was to be a Horner–Wittig elimination, the ring opening of the epoxides **5** had to be regioselective, with attack at C-2‡ in order to reveal a hydroxy group β to the Ph_2PO group. We have previously found that an efficient way to achieve this regioselectivity was to oxidise the epoxy alcohol to an epoxy ketone or an epoxy acid before ring opening. We now describe[5] an alternative—the attachment of the nucleophile to the C-1 hydroxy group with a tether short enough to force *exo*-intramolecular attack on the epoxide. Nitrogen,[1,9–11] sulfur,[12] carbon[13] and oxygen[14–16] nucleophiles can be introduced highly regioselectively and in good yield in this manner. Under certain conditions the resulting oxyanion collapses immediately to give an alkene by stereospecific Horner–Wittig elimination.

Results and discussion

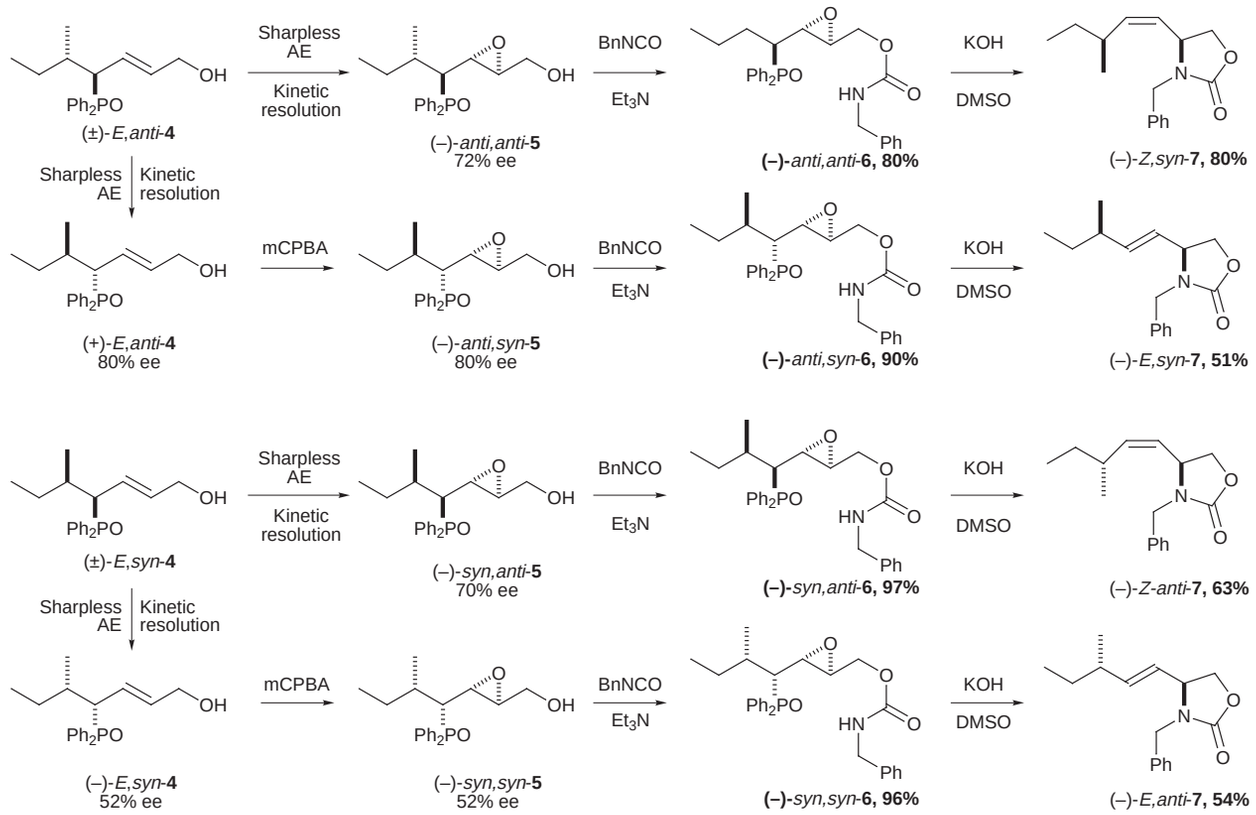
In view of potential applications (in peptide and nucleoside chemistry) of nitrogen-containing compounds of the type we intended to make, we decided to use a urethane as an intramolecular nucleophile, drawing on the methods introduced by Roush[9] and by Kishi.[10] The enantiomerically enriched§ epoxy alcohols[7,8] **5**, **8**, **10**, **12** and **14** listed in Table 1 and shown in Scheme 3 were therefore treated with benzyl isocyanate and triethylamine[8] to give urethanes **6**, **9**, **11**, **13** and **15**. Excellent yields were obtained in nearly all cases.

These various compounds were chosen to provide models for the most important series **5**. The epoxide **10** is the simplest straight chain system lacking any stereogenic centre other than the three required by the chemistry. The isopropyl series **8** is a better model as it has a branch where the fourth stereogenic

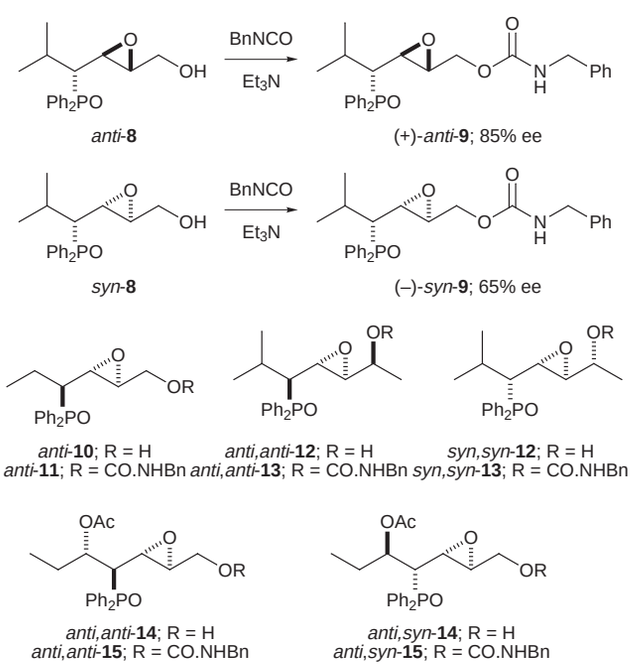
† *Present address*: Department of Chemistry, University of Manchester, Oxford Rd, Manchester, UK M13 9PL.

‡ Sharpless's numbering system for epoxy alcohols assigns C-1 to the carbon atom bearing the hydroxy group and C-2 and C-3 sequentially to the carbon atoms bearing the epoxide (C. H. Behrens, S. Y. Ko, K. B. Sharpless and F. J. Walker, *J. Org. Chem.*, 1985, **50**, 5687; C. H. Behrens and K. B. Sharpless, *J. Org. Chem.*, 1985, **50**, 5696).

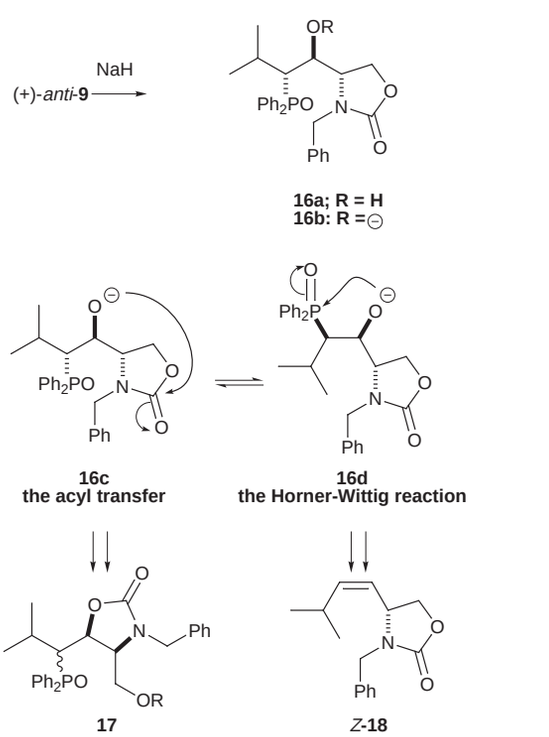
§ Enantiomeric excesses were determined by proton NMR in the presence of (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol (W. H. Pirkle, D. L. Sikkenga and M. J. Parkin, *J. Org. Chem.*, 1977, **42**, 384) and varied from 52 to >99% ee, depending on the efficiency of the kinetic resolution by which they were made.[3]



Scheme 2 Synthesis of all stereoisomers of 4-alkenyloxazolidin-2-ones



Scheme 3 Model epoxy alcohols and the urethanes derived from them



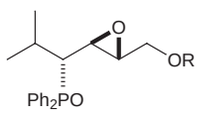
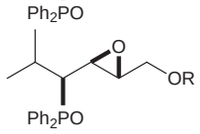
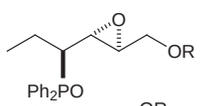
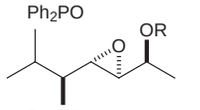
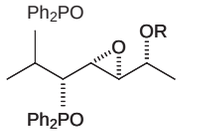
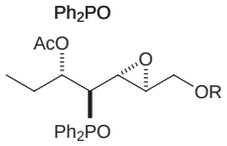
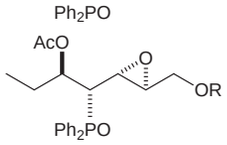
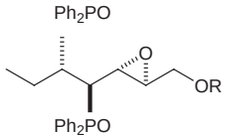
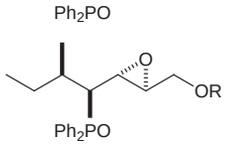
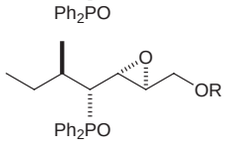
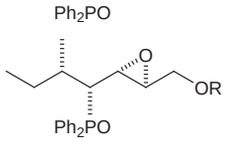
Scheme 4 Acyl transfer and Horner–Wittig reactions from base-catalysed ring closure of epoxyurethanes

centre will be required. Series **12** retains this branch and has an easily inserted extra stereogenic centre while series **14** with an extra stereogenic centre at the required position was our first attempt to produce 1,4-related centres. The acetoxy group in compounds **14** proved to be a bad choice and it was only with series **5** that we attained our goal.

Attempted epoxide opening to give β-hydroxy phosphine oxides

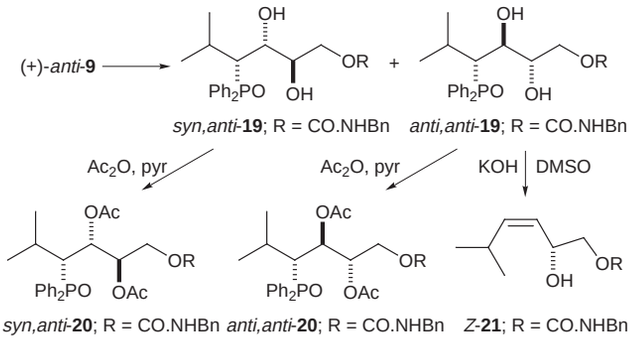
Roush's conditions for epoxide opening of the epoxyurethanes to give the oxazolidinones, sodium hydride in THF,[9] in fact release the oxyanion **16b** of the adduct **16a**. Two further reactions are possible under these conditions (Scheme 4): an acyl transfer shown as the mechanism on structure **16c**, also observed by Roush,[9] and the Horner–Wittig reaction shown as a mechanism on structure **16d**. We initially hoped to isolate the β-hydroxy phosphine oxide from protonation of **16b**, and therefore followed the closure reaction of (+)-*anti*-**9** carefully by TLC. Treatment with sodium hydride (4 equiv.) in THF gave, after 2 h, two products, both of which were isolated, one after

Table 1 Synthesis of urethanes

Entry	Structure	Starting material (R = H)	Product (R = CONHBn)	Yield (%)
1		*anti*-**8**	*anti*-**9**	92
2		*syn*-**8**	*syn*-**9**	86
3		*anti*-**10**	*anti*-**11**	71
4		*anti*,*anti*-**12**	*anti*,*anti*-**13**	88
5		*syn*,*syn*-**12**	*syn*,*syn*-**13**	100
6		*anti*,*anti*-**14**	*anti*,*anti*-**15**	99
7		*anti*,*syn*-**14**	*anti*,*syn*-**15**	95
8		*anti*,*anti*-**5**	*anti*,*anti*-**6**	80
9		*syn*,*anti*-**5**	*syn*,*anti*-**6**	97
10		*anti*,*syn*-**5**	*anti*,*syn*-**6**	90
11		*syn*,*syn*-**5**	*syn*,*syn*-**6**	96

acetylation. They were both primary alcohols, and probably were epimers (at *C*HPOPh$_2$) of the acyl transfer product **17**. The NMR spectra were similar except for a spectacular difference between the coupling constants $^3J_{P–CHO}$ but we were unable to assign their stereochemistries with certainty.

Attempted Lewis acid-catalysed cyclisation of the same urethane (+)-*anti*-**9** gave a quite different but equally useless result (Scheme 5). Treatment with boron trifluoride–diethyl ether in either dichloromethane or THF–ether,[15] followed by aqueous or acidic work up, gave mixtures of two compounds, both of which were clearly still uncyclised urethanes. Comparisons of their NMR spectra with those of similar compounds, and bis-acetylation to give **20**, enabled us to assign their structures as *syn*,*anti*-**19** and *anti*,*anti*-**19**. The low value of $^3J_{P–CHOH}$ in *anti*,*anti*-**19** (10.4 Hz) indicated that it was an *anti* β-hydroxy phosphine oxide:[17] this was confirmed by Horner–Wittig elimination to give the *Z* alkene **21**, with $^3J_{CH–CH}$ = 10.4 Hz, albeit in very low yield. These products may be produced by addition of

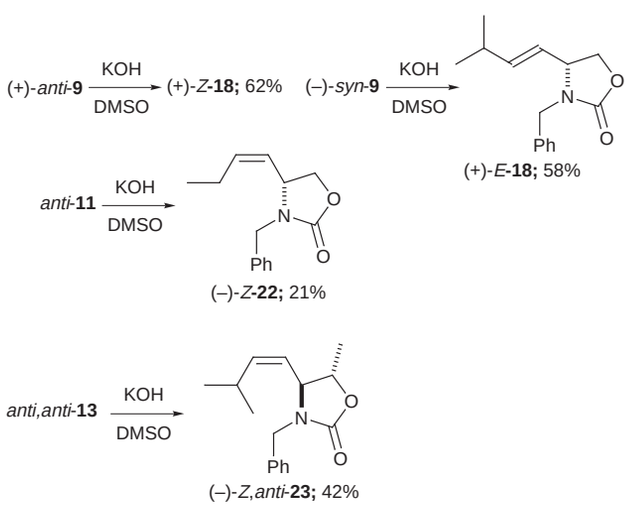


Scheme 5 Attempted Horner–Wittig reactions from Lewis acid-catalysed ring closure of epoxyurethanes

water as in early studies on nucleophilic openings of similar systems, Roush[15] noted that boron trifluoride–diethyl ether promotes attack of water on acylated epoxy alcohols to give diols.

Sequential epoxide opening—Horner–Wittig elimination

We therefore returned to the base-catalysed nitrogen ring closures, this time attempting to achieve what we wanted to avoid before: direct Horner–Wittig elimination of the β-hydroxy phosphine oxide oxyanion **16b** formed by the ring closure. Treating (+)-*anti*-**9** with sodium hydride in DMF gave several products in very low yield, none of which was recognisable as an oxazolidinone. However, adding powdered potassium hydroxide (3 equiv.) instead of NaH to (+)-*anti*-**9** in DMSO gave, after several hours at 60 °C, the desired *Z* alkenyl oxazolidinone *Z*-**18** in surprisingly high yield (62%), with no trace of the *E* isomer (Scheme 6). Clearly, under these conditions ring



Scheme 6 Horner–Wittig reactions on model compounds

closure to **16b** is being followed by Horner–Wittig elimination to give *Z*-**18** before acyl transfer can take place. The same conditions gave the *E* isomer (+)-*E*-**18** from the *syn* epoxyurethane (−)-*syn*-**9**, and the *Z* compound (−)-*Z*-**22** in poor yield from the ethyl-substituted *anti* epoxyurethane *anti*-**11**. Compounds **18** and **22** are protected amino alcohols with potential applications in amino acid and carbohydrate chemistry.[18]

Synthesis of compounds with 1,4-related stereogenic centres across a double bond

This reaction, applied to compounds containing further stereogenic centres, allowed us to make compounds with control over relative, absolute and geometrical stereochemistry. *anti*,*anti*-**13** gave (−)-*Z*,*anti*-**23**, while *syn*,*syn*-**13** gave (−)-*E*,*syn*-**23** in good yield (76%). The latter reaction was also possible using just 1.2 equivalents of the more easily measured

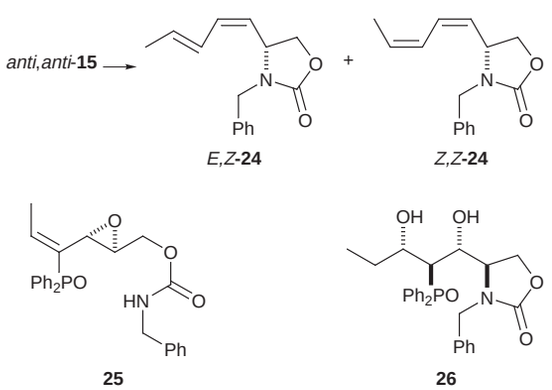
Table 2 Attempted Horner–Wittig eliminations of *anti*,*anti*-**15**

Entry	Conditions	Product	Yield (%)
1	KOH (3 equiv.), DMSO, 60 °C	4:1 *E*,*Z*-**24** and *Z*,*Z*-**24**	24 11
2	KOH (3 equiv.), DMSO, r.t.	*E*,*Z*-**24** and *Z*,*Z*-**24**	19 *a*
3	KHDMS (1 equiv.), DMSO, 60 °C	1:1 *E*,*Z*-**24** and *Z*,*Z*-**24**	49
4	KHDMS (1 equiv.), DMSO, r.t.	**25**	
5	NaH, THF	**26**	

[a] Yield not determined

and handled potassium hexamethyldisilazide but the yield (36%) was lower.

Attempts to induce epoxide opening and Horner–Wittig elimination of *anti*,*anti*-**15**, and so generate 1,4-stereogenic centres across a controlled geometry double bond were unsuccessful (Table 2). In most cases (entries 1–3), a low yield of a mixture of the two dienes *E*,*Z*- and *Z*,*Z*-**24** was formed (Scheme 7). This unwanted elimination of acetic acid happened



Scheme 7 Attempted Horner–Wittig reactions on model compounds **15** with an acetoxy group

even when the reaction was carried out at room temperature (entry 2). Potassium hexamethyldisilazide at room temperature gave a vinyl phosphine oxide **25** by elimination of acetic acid with the epoxide intact (entry 4).

Treatment of *anti*,*anti*-**15** with sodium hydride in THF gave diol **26** in 49% yield, without accompanying acyl transfer or epimerisation, but with concomitant hydrolysis of the acyl group. Although Horner–Wittig elimination of **26** could now choose to take place either to the left or to the right of the Ph_2PO group, it chose to do neither. Reaction with sodium hydride in DMF returned starting material, and reaction with potassium hydroxide in DMSO gave several products in very low yield, none of which was identifiable as an allylic alcohol.

Nonetheless, by turning to the more stable methyl-substituted epoxides **6** we were able to achieve our goal: the synthesis of a complete set of four isomers of **7** with 1,4-related stereogenic centres of either relative stereochemistry across either geometry of the double bond. Treatment of each of the four diastereomers *anti*,*anti*-, *anti*,*syn*-, *syn*,*anti*- and *syn*,*syn*-**6** with KOH in DMSO gave the stereoisomeric compounds (−)-*Z*,*syn*-**7**, (−)-*E*,*syn*-**7**, (−)-*Z*,*anti*-**7** and (−)-*E*,*syn*-**7** in reasonable yield (Scheme 1). The other four stereoisomers, the (+)-enantiomers of this four, would clearly be available by using D-(−)-dialkyl tartrate in the asymmetric epoxidations and kinetic resolutions used to make the epoxides **5**.[4] The four stereoisomers have distinct ^{1}H NMR spectra (see Experimental section). The enantiomeric excesses of the compounds were not improved from those originally found in the kinetic resolution even by crystallisation of intermediates and so the final products have ees varying from a disappointing 52% to a reasonable 80%.

Conclusion

Compounds **7** are similar to those used by Ibuka[19] in his synthesis of dipeptide isosteres, and similar compounds, bearing 1,4-related stereogenic centres separated by a double bond, have been the subject of considerable interest both as dipeptide isosteres[20,21] and because of their value as synthetic intermediates.[22] The synthetic strategy we employ here is similar to ones we[23] and others[22] have used before, namely the stereospecific conversion to a controlled-geometry double bond of the middle two of a string of four stereogenic centres. Few published syntheses of this type of compound allow formation of a *Z* double bond,[21,23] and, to our knowledge, this was the first allowing all four stereoisomers of either enantiomeric series to be made.¶ Our strategy is quite different from those involving stereospecific rearrangements,[24] which invariably lead to the thermodynamically more stable (usually[25] *trans*) double bond. We have continued work in this area by investigating the diastereoselective alkylation of diphenylphosphinoyl lactones as a strategy for 1,4-stereocontrol across a double bond.[26]

Experimental

Flash chromatography refers to chromatography performed on silica by the method of Still, Kahn and Mitra.[27] The suffixes $^+$ and $^-$ to peaks in the ^{13}C NMR spectra indicate the sign of the peak generated by an Attached Proton Test. Enantiomeric excesses were determined by proton NMR of the starting epoxy alcohols in the presence of (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol.

(2*R*,3*S*,4*R*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylhexane *anti*-9

Triethylamine (0.42 ml, 3.4 mmol, 2 equiv.) and benzyl isocyanate (0.32 ml, 2.6 mmol, 1.5 equiv.) were added to a stirred solution of the epoxy alcohol *anti*-**8**[7,8] (558.7 mg, 1.69 mmol) in dry dichloromethane (17 ml) at room temperature under nitrogen. After 18 h, saturated aqueous ammonium chloride (10 ml) and water (20 ml) were added. The layers were separated, and the aqueous layer extracted with dichloromethane (× 2). The combined organic fractions were dried ($MgSO_4$), evaporated under reduced pressure and purified by flash chromatography, eluting with 3:1 EtOAc–hexane, to give the *urethane anti*-**9** (723.5 mg, 92%) as needles, mp 156.5–158.5 °C (from EtOAc), $[\alpha]_D^{25}$ +51.7 (*c* 0.76 in $CHCl_3$; 85% ee) (Found: C, 70.05; H, 6.39; N, 2.95; P, 6.50; M + H, 464.1979. $C_{27}H_{30}NO_4P$ requires C, 69.97; H, 6.52; N, 3.02; P, 6.68; *M* + H, 464.1991); R_F (EtOAc) 0.41; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1705 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(250 MHz; $CDCl_3$) 8.0–7.3 (15 H, m, Ph_2PO and Ph), 5.07 (1 H, br t, NH), 4.39 (2 H, ABX m, CH_2N), 3.87 (1 H, dd, *J* 12.2 and 2.1, CH_AH_BO), 3.50 (1 H, dd, *J* 12.3 and 6.2, CH_AH_BO), 3.39 (1 H, d × fine m, *J* 9.6, PCHC*H*O), 2.5–2.3 (2 H, m, OCH_2CHO and $CHMe_2$), 2.04 (1 H, dt, *J* 2.5 and 9.4, CHP), 1.30 (3 H, d, *J* 6.9, $CHMe_AMe_B$) and 1.17 (3 H, d, *J* 6.9, $CHMe_AMe_B$); δ_C(100 MHz; $CDCl_3$) 155.6$^-$ (C=O), 138.2$^-$ (CH_2Ph *ipso*), 133–128 (Ph_2PO and Ph), 64.0$^-$ (CH_2O), 55.5$^+$ (OCH_2CHO), 52.9$^+$ (PCHCHO), 47.0$^+$ ($^1J_{PC}$ 65.5, PCH), 45.1$^-$ (CH_2N), 27.9$^+$ ($CHMe_2$), 24.1$^+$ ($^3J_{PC}$ 12.4, $CHMe_AMe_B$) and 19.1$^+$ ($CHMe_AMe_B$); *m*/*z* (+FAB) 464 (100%, M + H), 219 (40, $Ph_2PO_2H_2$) and 201 (95, Ph_2PO).

¶ Since publication of our preliminary communication,[5] Rich[21] has published a synthesis of all four stereoisomers in one enantiomeric series of a dipeptide isostere containing 1,4-related chiral centres separated by an *E* or a *Z* double bond.

(2*R*,3*S*,4*S*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylhexane *syn*-9

In the same way, epoxy alcohol *syn*-**8**[7,8] (38.2 mg, 0.116 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane and then EtOAc, the *urethane syn*-**9** (46.2 mg, 86%) as a wax, $[\alpha]_D^{25}$ −1.6 (*c* 2.31 in $CHCl_3$; 65% ee) (Found: M + H, 464.1948. $C_{27}H_{30}NO_4P$ requires *M* + H, 464.1991); R_F (EtOAc) 0.35; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1705 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 8.0–7.3 (15 H, m, Ph_2PO and Ph), 5.34 (1 H, br t, NH), 4.32 (2 H, ABX m, CH_2N), 4.26 (1 H, dd, *J* 12.3 and 3.6, CH_AH_BO), 3.98 (1 H, dd, *J* 12.3 and 5.6, CH_AH_BO), 3.19 (1 H, m, PCHC*H*O), 3.12 (1 H, fine m, OCH_2CHO), 2.31 (1 H, m, $CHMe_2$), 2.00 (1 H, dt, *J* 2.7 and 7.6, CHP), 1.09 (3 H, d, *J* 7.0, $CHMe_AMe_B$) and 1.12 (3 H, d, *J* 7.0, $CHMe_AMe_B$); δ_C(63 MHz; $CDCl_3$) 155.8$^-$ (C=O), 138.1$^-$ (CH_2Ph *ipso*), 133–128 (Ph_2PO and Ph), 64.3$^-$ (CH_2O), 56.2$^+$ ($^3J_{PC}$ 13.6, OCH_2CHO), 52.2$^+$ (PCH*C*HO), 46.9$^+$ ($^1J_{PC}$ 68.4, PCH), 44.9$^-$ (CH_2N), 27.0$^+$ ($^2J_{PC}$ 1.5, $CHMe_2$), 23.6$^+$ ($^3J_{PC}$ 12.1, $CHMe_AMe_B$) and 18.9$^+$ ($^3J_{PC}$ 1.8, $CHMe_AMe_B$); *m*/*z* (+FAB) 464 (100%, M + H), 219 (23, $Ph_2PO_2H_2$) and 201 (65, Ph_2PO).

(2*S*,3*R*,4*S*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxyhexane *anti*-11

In the same way, epoxy alcohol *anti*-**10** (468.2 mg, 0.146 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane and then EtOAc, the *urethane anti*-**11** (46.4 mg, 71%) as a wax, mp 149–152 °C, $[\alpha]_D^{25}$ −41.0 (*c* 2.32 in $CHCl_3$; >95% ee) (Found: M + H, 450.1881. $C_{26}H_{28}NO_4P$ requires *M* + H, 450.1834); R_F (EtOAc) 0.30; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1705 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(250 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.15 (1 H, br t, NH), 4.30 (2 H, ABX m, CH_2N), 3.87 (1 H, dd, *J* 12.2 and 2.1, CH_AH_BO), 3.48 (1 H, dd, *J* 12.3 and 6.1, CH_AH_BO), 3.12 (1 H, d × fine m, *J* 8.8, PCHC*H*O), 2.46 (1 H, fine m, OCH_2CHO), 2.1–1.8 (3 H, m, PCH and $CHMe_2$) and 1.07 (3 H, t, *J* 7.4, Me); δ_C(62.9 MHz; $CDCl_3$) 155.6$^-$ (C=O), 138.1$^-$ (CH_2Ph *ipso*), 133–128 (Ph_2PO and Ph), 63.7$^-$ (CH_2O), 55.3$^+$ (OCH_2CHO and PCH*C*HO), 45.0$^-$ (CH_2N), 43.5$^+$ ($^1J_{PC}$ 66.0, PCH), 21.0$^-$ (CH_2Me) and 12.7$^+$ ($^3J_{PC}$ 11.2, Me); *m*/*z* (+FAB) 450 (100%, M + H), 219 (21, $Ph_2PO_2H_2$), 202 (16, Ph_2PO) and 201 (56, Ph_2PO).

(2*S*,3*R*,4*R*,5*R*)-2-[(*N*-Benzylcarbamoyl)oxy]-5-diphenylphosphinoyl-3,4-epoxy-6-methylheptane *anti*,*anti*-13

In the same way, epoxy alcohol *anti*,*anti*-**12**[7,8] (96.8 mg, 0.281 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane, the *urethane anti*,*anti*-**13** (117.6 mg, 88%) as fibrous needles, mp 169.5–170.5 °C (from EtOAc), $[\alpha]_D^{25}$ −51.8 (*c* 1.97 in $CHCl_3$; >99% ee) (Found: C, 60.30; H, 6.73; N, 2.82; P, 6.49%; M + H, 478.2151. $C_{28}H_{32}NO_4P$ requires C, 60.4; H, 6.75; N, 2.93; P, 6.49%; *M* + H, 478.2147); R_F (EtOAc) 0.42; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 4.80 (1 H, br t, NH), 4.42 (1 H, dq, *J* 1.9 and 6.5, MeC*H*O), 4.26 (2 H, ABX m, CH_2N), 3.26 (1 H, d × fine m, *J* 9.5, PCHC*H*O), 2.44 (1 H, t, *J* 2.4, MeCHC*H*O), 2.22 (1 H, dd × septet, *J* 13.3, 2.2 and 6.7, $CHMe_2$), 2.01 (1 H, dt, *J* 2.4 and 9.4, CHP), 1.18 (3 H, d, *J* 6.9, $CHMe_AMe_B$), 1.05 (3 H, d, *J* 7.0, $CHMe_AMe_B$) and 0.75 (3 H, d, *J* 6.6 *Me*CHO); δ_C(100 MHz; $CDCl_3$) 155.5$^-$ (C=O), 138.8$^-$ (CH_2Ph *ipso*), 133–128 (Ph_2PO and Ph), 66.2$^+$ (Me*C*HO), 58.9$^+$ (MeCHO*C*HO), 52.4$^+$ (PCH*C*HO), 46.3$^+$ ($^1J_{PC}$ 65.3, PCH), 44.9$^-$ (CH_2N), 27.9$^+$ (*Me*CHO), 24.0$^+$ ($^2J_{PC}$ 7.8, $CHMe_2$), 18.9$^+$ ($CHMe_AMe_B$) and 15.0$^+$ ($CHMe_AMe_B$); *m*/*z* (+FAB) 478 (100%, M + H), 219 (24, $Ph_2PO_2H_2$), 202 (20, Ph_2POH) and 201 (70, Ph_2PO).

(2*R*,3*R*,4*R*,5*S*)-2-[(*N*-Benzylcarbamoyl)oxy]-5-diphenylphosphinoyl-3,4-epoxy-6-methylheptane *syn*,*syn*-13

In the same way, epoxy alcohol *syn*,*syn*-**12**[7,8] (88.1 mg, 0.256 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane, the *urethane syn*,*syn*-**13** (122.2 mg, 100%) as an oil, $[\alpha]_D^{25}$ +7.3 (*c* 0.93 in $CHCl_3$; 89% ee) (Found: M + H, 478.2124. $C_{28}H_{32}NO_4P$ requires *M* + H, 478.2147); R_F (EtOAc) 0.45; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1695 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 8.0–7.3 (15 H, m, Ph_2PO and Ph), 5.20 (1 H, t, *J* 5.8, NH), 4.81 (1 H, quintet, *J* 6.3, MeC*H*O), 4.30 (2 H, ABX m, CH_2N), 3.21 (1 H, ddd, *J* 7.6, 5.3 and 1.7, PCHC*H*O), 3.02 (1 H, dd, *J* 4.3 and 1.7, MeCHC*H*O), 2.32 (1 H, m, $CHMe_2$), 2.02 (1 H, ddd, *J* 9.3, 8.1 and 2.5, CHP), 1.23 (3 H, d, *J* 6.5, *Me*CHO), 1.07 (3 H, d, *J* 7.0, $CHMe_AMe_B$) and 1.04 (3 H, d, *J* 7.0 $CHMe_AMe_B$); δ_C(100 MHz; $CDCl_3$) 155.5$^-$ (C=O), 138.2$^-$ (CH_2Ph *ipso*), 133–128 (Ph_2PO and Ph), 69.8$^+$ (Me*C*HO), 60.2$^+$ ($^3J_{PC}$ 13.1, MeCHO-*C*HO), 51.5$^+$ (PCH*C*HO), 46.7$^+$ ($^1J_{PC}$ 67.5, PCH), 44.9$^-$ (CH_2N), 27.1$^+$ (*Me*CHO), 23.6$^+$ ($^2J_{PC}$ 12.5, $CHMe_2$), 18.9$^+$ ($CHMe_AMe_B$) and 16.5$^+$ ($CHMe_AMe_B$); *m*/*z* (CI) 478 (100%, M + H).

(2*R*,3*R*,4*R*,5*S*)-5-Acetoxy-1-[(*N*-benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxyheptane *anti*,*anti*-15

In the same way, epoxy alcohol *anti*,*anti*-**14**[7,8] (106.9 mg, 0.275 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane, the *urethane anti*,*anti*-**15** (142.7 mg, 99%) as a wax, mp 152–153 °C, $[\alpha]_D^{25}$ −67.6 (*c* 0.80 in $CHCl_3$; 83% ee) (Found: C, 66.78; H, 6.21; N, 2.48; P, 5.88%; M + H, 522.2046. $C_{29}H_{32}NO_6P$ requires C, 66.79; H, 6.18; N, 2.69; P, 5.94; *M* + H, 522.2045); R_F (EtOAc) 0.39; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.35–5.2 (2 H, m, NH and C*H*OAc), 4.29 (2 H, ABX m, CH_2N), 3.82 (1 H, dd, *J* 12.3 and 2.2, CH_AH_BO), 3.47 (1 H, dd, *J* 12.3 and 6.2, CH_AH_BO), 3.36 (1 H, d × fine m, *J* 9.3, C*H*OCHCH$_2$O), 2.48 (1 H, fine m, OCH_2CHO), 2.36 (1 H, dt, *J* 2.3 and 9.8, CHP), 2.0–1.7 (2 H, m, CH_2Me), 1.75 (3 H, s, OAc) and 0.82 (3 H, t, *J* 7.4 *Me*CH$_2$); δ_C(62.9 MHz; $CDCl_3$) 169.9$^-$ (Me*C*=O), 155.6$^-$ (HNC=O), 138.1$^-$ (CH_2Ph *ipso*), 133–127 (Ph_2PO and Ph), 72.5$^+$ ($^2J_{PC}$ 3.3, *C*HOAc), 63.7$^-$ (CH_2O), 55.6$^+$ (MeCHO*C*HO), 52.1$^+$ ($^2J_{PC}$ 5.5, PCH*C*HO), 45.3$^+$ ($^1J_{PC}$ 65.3, PCH), 44.9$^-$ (CH_2N), 26.1$^-$ ($^3J_{PC}$ 8.0, CH_2Me), 20.6$^+$ (*Me*C=O) and 10.1$^+$ (CH_2Me); *m*/*z* (+FAB) 522 (100%, M + H), 219 (22, $Ph_2PO_2H_2$) and 201 (48, Ph_2PO).

(2*R*,3*R*,4*S*,5*R*)-5-Acetoxy-1-[(*N*-benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxyheptane *anti*,*syn*-15

In the same way, epoxy alcohol *anti*,*syn*-**14**[7,8] (70.8 mg, 0.182 mmol) gave, after purification by flash chromatography, eluting with 3:1 EtOAc–hexane and then EtOAc, the *urethane anti*,*syn*-**15** (90.4 mg, 95%) as a foam, $[\alpha]_D^{25}$ +3.7 (*c* 0.70 in $CHCl_3$; ee unknown); R_F (EtOAc) 0.35; $\nu_{max}(CHCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.33 (1 H, m, *CH*OAc), 5.12 (1 H, br t, NH), 4.30 (3 H, m, CH_2N and CH_AH_BO), 3.89 (1 H, dd, *J* 12.4 and 5.8, CH_AH_BO), 3.17 (2 H, m, C*H*C*H*CH$_2$O), 2.45 (1 H, dt, *J* 3.8 and 9.0, CHP), 2.0–1.6 (2 H, m, CH_2Me), 1.76 (3 H, s, OAc) and 0.82 (3 H, t, *J* 7.3, *Me*CH$_2$); δ_C(62.9 MHz; $CDCl_3$) 169.9$^-$ (Me*C*=O), 155.8$^-$ (HNC=O), 138.0$^-$ (CH_2Ph *ipso*), 133–127 (Ph_2PO and Ph), 72.8$^+$ (*C*HOAc), 64.5$^-$ (CH_2O), 56.4$^+$ ($^3J_{PC}$ 11.5, OCH_2CHO), 52.3$^+$ (PCH*C*HO), 45.1$^+$ ($^1J_{PC}$ 67.0, PCH), 45.1$^-$ (CH_2N), 28.3$^-$ ($^3J_{PC}$ 8.0, CH_2Me), 20.7$^+$ (*Me*C=O) and 10.3$^+$ (CH_2Me); *m*/*z* 521 (0.5%, M$^+$), 219 (10, $Ph_2PO_2H_2$), 202 (35, Ph_2POH), 201 (45, Ph_2PO) and 60 (100, AcOH).

(2*R*,3*R*,4*S*,5*S*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylheptane *anti*,*anti*-6

In the same way, epoxy alcohol *anti*,*anti*-**5**[7,8] (120.6 mg, 0.350 mmol) gave, after purification by flash chromatography, eluting with 2:1 EtOAc–hexane, the *urethane anti*,*anti*-**6** (132.8 mg, 80%) as needles, mp 154.5–156 °C (from EtOAc), $[\alpha]_D^{25}$ −61.3 (*c*

1.51 in $CDCl_3$; 70% ee) (Found: C, 70.25; H, 6.86; N, 3.04; P, 6.36%; M + H, 478.2108. $C_{28}H_{32}NO_4P$ requires C, 70.4; H, 6.75; N, 2.93; P, 6.49%; *M* + H, 478.2147); R_F (EtOAc) 0.55; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(250 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.03 (1 H, br t, NH), 4.30 (2 H, ABX m, CH_2N), 3.80 (1 H, dd, *J* 12.1 and 2.1, CH_AH_BO), 3.41 (1 H, dd, *J* 12.3 and 6.2, CH_AH_BO), 3.29 (1 H, d × fine m, *J* 9.5, PCHC*H*O), 2.37 (1 H, fine m, OCH_2CHO), 2.2–1.9 (3 H, m, CHP, C*H*Me and CH_AH_BMe), 1.39 (1 H, m, CH_AH_BMe), 1.08 (3 H, d, *J* 6.8, CH*Me*) and 0.82 (3 H, t, *J* 7.3, CH_2Me); δ_C(62.9 MHz; $CDCl_3$) 155.7$^-$ (C=O), 138.2$^-$ (CH_2Ph *ipso*), 134–127 (Ph_2PO and Ph), 63.9$^-$ (CH_2O), 55.8$^+$ (OCH_2CHO), 53.4$^+$ (PCH*C*HO), 47.5$^+$ ($^1J_{PC}$ 65.5, PCH), 45.1$^-$ (CH_2N), 34.9$^+$ (*C*HMe), 25.8$^-$ (CH_2Me), 19.8$^+$ ($^3J_{PC}$ 12.1, CH*Me*) and 12.3$^+$ (CH_2Me); *m/z* (+FAB) 478 (100%, M + H), 219 (24, $Ph_2PO_2H_2$), 202 (20, Ph_2POH) and 201 (68, Ph_2PO).

(2*R*,3*R*,4*S*,5*R*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylheptane *syn*,*anti*-6

In the same way, epoxy alcohol *syn*,*anti*-**5**[4] (73.6 mg, 0.214 mmol) gave, after purification by flash chromatography, eluting with 2:1 EtOAc–hexane, the *urethane syn*,*anti*-**6** (102.2 mg, 97%) as needles, mp 156–158 °C (from EtOAc), $[\alpha]_D^{25}$ −43.0 (*c* 1.08 in $CDCl_3$; 72% ee) (Found: C, 70.67; H, 6.80; N, 3.09; P, 6.40%; M + H, 478.2115. $C_{28}H_{32}NO_4P$ requires C, 70.4; H, 6.75; N, 2.93; P, 6.49%; *M* + H, 478.2147); R_F (EtOAc) 0.53; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(250 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.01 (1 H, br t, NH), 4.31 (2 H, ABX m, CH_2N), 3.82 (1 H, dd, *J* 12.2 and 2.2, CH_AH_BO), 3.44 (1 H, dd, *J* 12.2 and 6.2, CH_AH_BO), 3.32 (1 H, d × fine m, *J* 9.5, PCHC*H*O), 2.37 (1 H, fine m, OCH_2CHO), 2.12 (1 H, dt, *J* 1.7 and 9.5, CHP), 1.96 (1 H, m, C*H*Me), 1.48 (2 H, m, CH_2Me), 1.26 (3 H, d, *J* 6.9, CH*Me*) and 0.81 (3 H, t, *J* 7.3, CH_2Me); δ_C(62.9 MHz; $CDCl_3$) 155.7$^-$ (C=O), 138.2$^-$ (CH_2Ph *ipso*), 134–127 (Ph_2PO and Ph), 64.0$^-$ (CH_2O), 55.6$^+$ (OCH_2CHO), 52.6$^+$ (PCH*C*HO), 45.1$^-$ (CH_2N), 44.8$^+$ ($^1J_{PC}$ 67.0, PCH), 34.4$^+$ (*C*HMe), 10.3$^-$ ($^3J_{PC}$ 12.1, *C*H_2Me), 16.4$^+$ (CH*Me*) and 12.1$^+$ (CH_2Me); *m/z* (+FAB) 478 (76%, M + H), 219 (40, $Ph_2PO_2H_2$), 202 (22, Ph_2POH) and 201 (100, Ph_2PO).

(2*R*,3*R*,4*R*,5*R*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylheptane *anti*,*syn*-6

In the same way, epoxy alcohol *anti*,*syn*-**5**[7,8] (71.1 mg, 0.206 mmol) gave, after purification by flash chromatography, eluting with 2:1 EtOAc–hexane, the *urethane anti*,*syn*-**6** (88.4 mg, 90%) as an oil, $[\alpha]_D^{25}$ −1.9 (*c* 2.21 in $CDCl_3$; 52% ee) (Found: M + H, 478.2140. $C_{28}H_3NO_4P$ requires *M* + H, 478.2147); R_F (EtOAc) 0.51; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(250 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.29 (1 H, br t, NH), 4.35–4.2 (3 H, m, CH_2N and CH_AH_BO), 3.91 (1 H, dd, *J* 12.3 and 5.5, CH_AH_BO), 3.15 (2 H, m, C*H*C*H*CH_2O), 2.00 (1 H, dt, *J* 2.5 and 9.9, CHP), 1.95 (2 H, m, C*H*Me and CH_AH_BMe), 1.05 (1 H, m, CH_AH_BMe), 0.97 (3 H, d, *J* 6.8, CH*Me*) and 0.72 (3 H, t, *J* 7.2, CH_2Me); δ_C(62.9 MHz; $CDCl_3$) 155.9$^-$ (C=O), 138.2$^-$ (CH_2Ph *ipso*), 132–127 (Ph_2PO and Ph), 64.2$^-$ (CH_2O), 57.3$^+$ ($^3J_{PC}$ 13.0, OCH_2CHO), 52.5$^+$ (PCH*C*HO), 47.5$^+$ ($^1J_{PC}$ 67.9, PCH), 45.0$^-$ (CH_2N), 34.2$^+$ (*C*HMe), 25.8$^-$ (*C*H_2Me), 19.6$^+$ ($^3J_{PC}$ 12.2, CH*Me*) and 12.5$^+$ (CH_2Me); *m/z* (+FAB) 478 (100%, M + H), 219 (20, $Ph_2PO_2H_2$), 202 (15, Ph_2POH) and 201 (60, Ph_2PO).

(2*R*,3*R*,4*R*,5*S*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-2,3-epoxy-5-methylheptane *syn*,*syn*-6

In the same way, epoxy alcohol *syn*,*syn*-**5**[7,8] (26.9 mg, 0.0781 mmol) gave, after purification by flash chromatography, eluting with 2:1 EtOAc–hexane, the *urethane syn*,*syn*-**6** (37.3 mg, 96%) as an oil, $[\alpha]_D^{25}$ −11.8 (*c* 0.90 in $CDCl_3$; 80% ee) (Found: M + H, 478.2122. $C_{28}H_{32}NO_4P$ requires *M* + H, 478.2147); R_F (EtOAc) 0.50; $\nu_{max}(CDCl_3)/cm^{-1}$ 3450 (NH), 1700 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.17 (1 H, br t, NH), 4.33 (3 H, m, CH_2N), 4.27 (1 H, dd, *J* 12.2 and 3.3, CH_AH_BO), 3.98 (1 H, dd, *J* 12.2 and 5.1, CH_AH_BO), 3.23 (1 H, ddd, *J* 9.6, 6.9 and 1.9, PCHC*H*O), 3.10 (1 H, fine m, OCH_2CHO), 2.12 (1 H, dt, *J* 1.9 and 9.6, CHP), 1.96 (1 H, m, C*H*Me), 1.36 (2 H, quintet, *J* 7.3, CH_2Me), 1.11 (3 H, d, *J* 7.0, CH*Me*) and 0.79 (3 H, t, *J* 7.3, CH_2Me); δ_C(62.9 MHz; $CDCl_3$) 155.9$^-$ (C=O), 138.1$^-$ (CH_2Ph *ipso*), 134–127 (Ph_2PO and Ph), 64.3$^-$ (CH_2O), 56.0$^+$ ($^3J_{PC}$ 14.0, OCH_2CHO), 52.2$^+$ (PCH*C*HO), 45.0$^-$ (CH_2N), 44.7$^+$ ($^1J_{PC}$ 67.8, PCH), 33.7$^+$ (*C*HMe), 30.1$^-$ ($^3J_{PC}$ 12.1, *C*H_2Me), 16.5$^+$ (CH*Me*) and 12.1$^+$ (CH_2Me); *m/z* (+FAB) 478 (100%, M + H), 219 (24, $Ph_2PO_2H_2$), 202 (20, Ph_2POH) and 201 (90, Ph_2PO).

Ring closure of *anti*-9 with sodium hydride in THF

Sodium hydride (15 mg of a 60% suspension, 0.375 mmol, 4.3 equiv.) was added to a stirred solution of the urethane *anti*-**9** (40.35 mg, 0.0871 mmol) in dry THF (1.5 ml). After 2 h, saturated aqueous ammonium chloride and water were added, and the mixture extracted with dichloromethane (× 3). The combined organic fractions were dried (Na_2SO_4) and evaporated under reduced pressure, and purified by PTLC, eluting with EtOAc, to give (4S,5S,1′S or R)-3-*benzyl*-4-*hydroxymethyl*-5-(1′-*diphenylphosphinoyl*-2′-*methylpropyl*)*oxazolidin*-2-*one* **17**; **R** = **H** (11.8 mg, 29%) as a solid, $[\alpha]_D^{25}$ +16.7 (*c* 1.18 in $CDCl_3$; 85% ee) (Found: M + H, 464.1973. $C_{27}H_{30}NO_4P$ requires *M* + H, 464.1990); R_F (EtOAc) 0.32; $\nu_{max}(CDCl_3)/cm^{-1}$ 3330 (OH), 1730 (C=O), 1440 (PPh) and 1150 (P=O); δ_H(400 MHz; $CDCl_3$) 7.8–7.1 (15 H, Ph_2PO and Ph), 5.16 (1 H, dt, *J* 5.9 and 3.9, CHN), 4.90 (1 H, d, *J* 15.5, PhCH_AH_BN), 4.07 (1 H, d, *J* 15.5, PhCH_AH_BN), 3.90 (1 H, dt, *J* 2.6 and 4.1, CHO), 3.66 (1 H, dd, *J* 11.6 and 3.6, CH_AH_BOH), 3.52 (1 H, dd, *J* 11.6 and 5.9, CH_AH_BOH), 3.2 (1 H, br s, OH), 2.59 (1 H, dt, *J* 12.0 and 2.1, CHP), 2.20 (1 H, m, C*H*Me_2), 1.16 (3 H, d, *J* 7.0, CHMe_AMe_B) and 0.82 (3 H, d, *J* 7.2, CHMe_AMe_B); δ_C(400 MHz; $CDCl_3$) 157.9$^-$ (C=O), 135–127 (Ph_2PO and Ph), 75.4$^+$ (CHO), 63.6$^-$ (CH_2OH), 57.0$^+$ ($^3J_{PC}$ 5.0, CHN), 46.4$^-$ (Ph*C*H_2N), 42.3$^+$ ($^1J_{PC}$ 65.3, PCH), 25.3$^+$ (*C*HMe_2), 24.5$^+$ (CHMe_AMe_B) and 21.6$^+$ ($^3J_{PC}$ 8.5, CHMe_AMe_B); *m/z* (+FAB) 464 (100%, M + H) and 201 (30, Ph_2PO).

Also obtained was (4S,5S,1′R or S)-3-*benzyl*-4-*hydroxymethyl*-5-(1′-*diphenylphosphinoyl*-2′-*methylpropyl*)*oxazolidin*-2-*one* **17**; **R** = **H** (22.4 mg, 56%) as a solid, $[\alpha]_D^{25}$ +14.96 (*c* 2.24 in $CDCl_3$; 85% ee) (Found: M + H, 464.1966. $C_{27}H_{30}NO_4P$ requires *M* + H, 464.1990); R_F (EtOAc) 0.21; $\nu_{max}(CDCl_3)/cm^{-1}$ 3300 (OH), 1740 (C=O), 1430 (PPh) and 1160 (P=O); δ_H(400 MHz; $CDCl_3$) 7.8–7.2 (15 H, Ph_2PO and Ph), 5.46 (1 H, fine m, CHN), 4.49 (1 H, d, *J* 15.3, PhCH_AH_BN), 3.95 (1 H, d, *J* 15.4, PhCH_AH_BN), 3.88 (1 H, dd, *J* 24.0 and 2.8, CHO), 3.62 (1 H, dd, *J* 12.5 and 3.4, CH_AH_BOH), 3.53 (1 H, dd, *J* 12.5 and 3.9, CH_AH_BOH), 2.49 (1 H, d × fine m, *J* 9.0, CHP), 2.20 (1 H, m, C*H*Me_2), 1.01 (3 H, d, *J* 7.0, CHMe_AMe_B) and 0.85 (3 H, d, *J* 7.2, CHMe_AMe_B); δ_C(400 MHz; $CDCl_3$) 157.1$^-$ (C=O), 135–128 (Ph_2PO and Ph), 77.2$^+$ (CHO), 63.1$^-$ (CH_2OH), 53.5$^+$ (CHN), 46.2$^-$ (Ph*C*H_2N), 42.7$^+$ ($^1J_{PC}$ 66.0, PCH), 22.3$^+$ (*C*HMe_2), 22.8$^+$ ($^3J_{PC}$ 12.5, CHMe_AMe_B) and 19.6$^+$ ($^3J_{PC}$ 8.5, CHMe_AMe_B); *m/z* (+FAB) 464 (100%, M + H) and 201 (30, Ph_2PO).

Acetylation (excess acetic anhydride–pyridine) of oxazolidinone **9** (14.9 mg, 0.032 mmol) gave, after 18 h, and without further purification, the *acetate* (4S,5S,1′R or S)-4-*acetoxymethyl*-3-*benzyl*-5-(1′-*diphenylphosphinoyl*-2′-*methylpropyl*)-*oxazolidin*-2-*one* **17**; **R** = **Ac** (11.2 mg, 69%) as an oil; R_F (EtOAc) 0.48; δ_H(400 MHz; $CDCl_3$) 8.0–7.3 (15 H, Ph_2PO and Ph), 5.74 (1 H, q, *J* 3.4, CHN), 4.57 (1 H, d, *J* 15.2, PhCH_AH_BN), 4.16 (1 H, dd, *J* 12.5 and 2.9, CH_AH_BOAc), 4.07 (1 H, dd, *J* 12.5 and 4.2, CH_AH_BOAc), 3.95 (1 H, d, *J* 15.1, PhCH_AH_BN), 3.86 (1 H, dd, *J* 23.7 and 3.5, CHO), 2.59 (1 H, d × fine m, *J* 9.1, CHP), 2.35 (1 H, m, C*H*Me_2), 1.88 (3 H, s,

OAc), 1.09 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 0.98 (3 H, d, *J* 7.2, CHMe$_A$*Me*$_B$).

Attempted ring closure of *anti*-9 with boron trifluoride–diethyl ether in dichloromethane

Boron trifluoride–diethyl ether (15 μl, 0.122 mmol, 1.3 equiv.) was added to a stirred solution of the urethane *anti*-**9** (43.8 mg, 0.0945 mmol) in dry dichloromethane (2 ml) at room temperature under nitrogen. After 44 h, 0.5 M sulfuric acid (2 ml) was added, and the mixture rapidly stirred for 75 min. TLC showed no change in the constituents of the mixture during this period. Ethyl actetate was added, and the mixture washed with 0.5 M sulfuric acid. The aqueous fractions were extracted with ethyl actetate (× 3). The combined organic fractions were dried (Na_2SO_4) and evaporated under reduced pressure to give a crude product. This was purifed by PTLC, eluting with EtOAc, to give the *diol* (2S,3S,4R)-1-[(N-*benzylcarbamoyl*)*oxy*]-4-*diphenylphosphinoyl*-5-*methylhexane*-2,3-*diol syn*,*anti*-**19** (15.6 mg, 36%) as a solid, $[\alpha]_D^{25}$ −8.1 (*c* 1.35 in $CDCl_3$; 88% ee); R_F (EtOAc) 0.44; $\nu_{max}(CHCl_3)/cm^{-1}$ 3300 (OH), 1705 (C=O), 1140 (P=O) and 1120 (P–Ph); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.25 (1 H, t, *J* 5.8, NH), 4.37 (1 H, d, *J* 1.8, OH), 4.33 (1 H, d, *J* 12.2, C*H*$_A$H$_B$O), 4.30 (2 H, AB m, CH_2N), 4.24 (1 H, dd, *J* 12.3 and 5.2, CH$_A$*H*$_B$O), 4.01 (1 H, t, *J* 10.6, PCHC*H*OH), 3.88 (1 H, m, OCH$_2$C*H*OH), 2.93 (1 H, d × fine m, *J* 9.3, CHP), 2.30 (1 H, m, C*H*Me$_2$), 1.16 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 0.97 (3 H, d, *J* 7.2, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 158.2$^-$ (C=O), 138.0$^-$ (Ph *ipso*), 133–127 (Ph_2PO and Ph), 71.1$^+$ (PCH*C*HOH), 70.8$^+$ ($^3J_{PC}$ 11.0, OCH$_2$-*C*HOH), 68.1$^-$ (CH_2O), 45.1$^-$ (NCH_2), 42.7$^+$ ($^1J_{PC}$ 67.7, PCH), 26.0$^+$ (*C*HMe$_2$), 23.5$^+$ (CH*Me*$_A$Me$_B$) and 22.5$^+$ ($^3J_{PC}$ 10.37, CHMe$_A$*Me*$_B$).

Also obtained was *diol* (2R,3R,4R)-1-[(N-*benzylcarbamoyl*)-*oxy*]-4-*diphenylphosphinoyl*-5-*methylhexane*-2,3-*diol anti*,*anti*-**19** (10.9 mg, 25%) as a solid, $[\alpha]_D^{25}$ −38.0 (*c* 0.71 in $CDCl_3$; 85% ee); R_F (EtOAc) 0.33; $\nu_{max}(CHCl_3)/cm^{-1}$ 3300 (OH), 1705 (C=O), 1140 (P=O) and 1180 (P–Ph); δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.02 (1 H, t, *J* 5.6, NH), 4.95 (1 H, d, *J* 3.3, OH), 4.34 (1 H, d, *J* 5.8, NCH_2), 4.30 (1 H, m, OCH$_2$-C*H*OH), 4.17 (1 H, dd, *J* 11.3 and 4.9, C*H*$_A$H$_{BO}$), 4.11 (1 H, d × m, *J* 27.8, PCHC*H*OH), 4.08 (1 H, dd, *J* 11.6 and 6.5, CH$_A$*H*$_B$O), 3.28 (1 H, d, *J* 7.4, OH), 2.69 (1 H, dt, *J* 10.2 and 2.8, CHP), 2.10 (1 H, m, C*H*Me$_2$), 1.08 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 1.01 (3 H, d, *J* 7.1, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 156.3$^-$ (C=O), 138–127 (Ph_2PO and Ph), 70.4$^+$ (PCH*C*HOH), 69.4$^+$ ($^3J_{PC}$ 7.1, OCH$_2$*C*HOH), 65.6$^-$ (CH_2O), 47.1$^+$ ($^1J_{PC}$ 65.2, PCH), 45.1$^-$ (NCH_2), 26.9$^+$ (*C*HMe$_2$), 23.1$^+$ ($^3J_{PC}$ 11.6, CH*Me*$_A$Me$_B$) and 21.2$^+$ (CHMe$_A$*Me*$_B$).

(2*S*,3*S*,4*R*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-5-methylhexane-2,3-diyl diacetate *syn*,*anti*-20

Acetylation (excess acetic anhydride–pyridine) of diol *syn*,*anti*-**19** (15.6 mg, 0.034 mmol) gave the *bisacetate syn*,*anti*-**20** (19.0 mg, 98%) as an oil, δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.55 (1 H, ddd, *J* 12.2, 7.2 and 1.5, PCH-C*H*OAc), 5.31 (1 H, m, OH$_2$C*H*OAc), 4.90 (1 H, br t, NH), 4.3 (3 H, m, PhCH$_2$ and C*H*$_A$H$_B$O), 3.94 (1 H, dd, *J* 12.3 and 5.6, CH$_A$*H*$_B$O), 2.65 (1 H, d × fine m, *J* 9.7, CHP), 2.4 (1 H, m, C*H*Me$_2$), 2.08 (3 H, s), 2.04 (3 H, s) (OAc × 2), 1.17 (3 H, d, *J* 7.0) and 0.91 (3 H, d, *J* 7.0).

(2*R*,3*R*,4*R*)-1-[(*N*-Benzylcarbamoyl)oxy]-4-diphenylphosphinoyl-5-methylhexane-2,3-diyl diacetate *anti*,*anti*-20

Acetylation (excess acetic anhydride–pyridine) of diol *anti*,*anti*-**19** (10.9 mg, 0.022 mmol) gave the *bisacetate anti*,*anti*-**20** (10.2 mg, 82%) as an oil, R_F (EtOAc) 0.37; δ_H(400 MHz; $CDCl_3$) 7.9–7.2 (15 H, m, Ph_2PO and Ph), 5.57 (1 H, ddd, *J* 12.3, 7.7 and 1.5, PCHC*H*OAc), 5.30 (1 H, dt, *J* 7.7 and 4.0, OH$_2$C*H*OAc), 4.85 (1 H, br t, *J* 5.7, NH), 4.33 (2 H, d, *J* 5.9, PhCH$_2$N), 4.27 (1 H, dd, *J* 12.4 and 3.3, C*H*$_A$H$_B$OCO), 4.02 (1 H, dd, *J* 12.3 and 4.5, CH$_A$*H*$_B$OCO), 2.54 (1 H, d × fine m, *J* 10.9, CHP), 2.40 (1 H, m, C*H*Me$_2$), 2.05 (3 H, s), 1.97 (3 H, s) (OAc × 2), 1.20 (3 H, d, *J* 7.0) and 1.02 (3 H, d, *J* 7.0).

Horner–Wittig elimination of diol *anti*,*anti*-19

Powdered potassium hydroxide (85%, 18 mg, 0.32 mmol, 6.3 equiv.) was added to a stirred solution of diol *anti*,*anti*-**19** (24.7 mg, 0.0513 mmol) in dry DMSO (1.2 ml) under nitrogen. The mixture was heated at 60 °C for 3 h, cooled to room temperature, and quenched with saturated aqueous ammonium chloride and water. The mixture was extracted with ether (× 3), and the combined organic fractions were washed with brine, dried (Na_2SO_4), evaporated under reduced pressure, and purifed by PTLC, eluting with EtOAc, to yield material (2.0 mg, 15%) tentatively identifed as the *allylic alcohol* (R)-(Z)-1-[(N-*benzylcarbamoyl*)*oxy*]-5-*methylhex*-3-*en*-2-*ol Z*-**21**, R_F (EtOAc) 0.65; δ_H(400 MHz; $CDCl_3$) (distinctive signals) 5.54 (1 H, t, *J* 10.7) and 5.16 (1 H, t, *J* 10.7) (CH=CH).

(*R*)-(*Z*)-3-Benzyl-4-(3′-methylbut-1′-enyl)oxazolidin-2-one *Z*-18

Powdered potassium hydroxide (85%, 20 mg, 0.30 mmol, 3 equiv.) was added to a stirred solution of the urethane *anti*-**9** (44.3 mg, 0.095 mmol) in dry DMSO (3 ml) at room temperature under nitrogen. The mixture was heated at 60 °C for 16 h. The mixture was cooled to room temperature, and saturated aqueous ammonium chloride and water were added. The aqueous suspension was extracted with ether (× 3). The combined organic fractions were washed with water, dried (Na_2SO_4), evaporated under reduced pressure and purified by PTLC, eluting with 3:2 hexane–EtOAc, to give the *oxazolidinone Z*-**18** (14.4 mg, 62%) as an oil, $[\alpha]_D^{25}$ +47.4 (*c* 1.44 in $CDCl_3$; 85% ee) (Found: M$^+$, 245.1396. $C_{15}H_{19}NO_2$ requires *M*, 245.1416); R_F (3:2 hexane–EtOAc) 0.48; ν_{max}(film)/cm^{-1} 1740 (C=O); δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.55 (1 H, t, *J* 10.4, C*H*=CHCHN), 5.15 (1 H, t, *J* 10.4, CH=C*H*CHN), 4.69 (1 H, d, *J* 15.0, NC*H*$_A$H$_B$), 4.37 (2 H, m, NCH and C*H*$_A$-H$_B$O), 3.93 (1 H, d, *J* 15.0, NCH$_A$*H*$_B$), 3.86 (1 H, t, *J* 6.5, CH$_A$*H*$_B$O), 2.19 (1 H, d × septet, *J* 10.4 and 7.0, C*H*Me$_2$), 0.86 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 0.83 (3 H, d, *J* 7.0, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 158.4$^-$ (C=O), 144.6$^+$ (CH=*C*HCHN), 136.1$^-$ (Ph *ipso*), 128.8$^+$, 128.4$^+$ (Ph *ortho* and *meta*), 128.0$^+$ (Ph *para*), 123.4$^+$ (*C*H=CHCHN), 67.6$^-$ (CH_2O), 52.1$^+$ (CHN), 45.9$^-$ (CH_2N), 27.0$^+$ (*C*HMe$_2$), 23.7$^+$ (CH*Me*$_A$-Me$_B$) and 22.7$^+$ (CHMe$_A$*Me*$_B$); *m*/*z* 246 (100%, M + H), 245 (90, M$^+$), 178 (45, M − C_5H_7), 165 (15, M − Ph) and 104 (85, BnNH).

(*R*)-(*E*)-3-Benzyl-4-(3′-methylbut-1′-enyl)oxazolidin-2-one *E*-18

In the same way, the urethane *syn*-**9** (28.8 mg, 0.062 mmol) gave, after 4 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone E*-**18** (8.8 mg, 58%) as an oil, $[\alpha]_D^{25}$ +19.1 (*c* 0.88 in $CDCl_3$; 65% ee) (Found: M$^+$, 245.1410. $C_{15}H_{19}NO_2$ requires *M*, 245.1416); R_F (1:1 Et_2O–hexane) 0.29; $\nu_{max}(CDCl_3)/cm^{-1}$ 1740 (C=O); δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.59 (1 H, dd, *J* 15.4 and 6.6, C*H*=CHCHN), 5.17 (1 H, dd, *J* 15.3 and 8.7, CH=C*H*CHN), 4.68 (1 H, d, *J* 14.9, NC*H*$_A$H$_B$), 4.35 (1 H, t, *J* 8.4, C*H*$_A$H$_B$O), 4.00 (1 H, d, *J* 14.9, NCH$_A$*H*$_B$), 3.95 (2 H, m, NCH and CH$_A$*H*$_B$O), 2.30 (1 H, octet, *J* 6.7, C*H*Me$_2$), 0.98 (3 H, d, *J* 7.0, CH*Me*$_A$Me$_B$) and 0.96 (3 H, d, *J* 7.0, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 158.3$^-$ (C=O), 139.0$^+$ (CH=*C*HCHN), 136.0$^-$ (Ph *ipso*), 128.6$^+$, 128.4$^+$ (Ph *ortho* and *meta*), 127.8$^+$ (Ph *para*), 125.0$^+$ (*C*H=CHCHN), 67.4$^-$ (CH_2O), 51.6$^+$ (CHN), 45.8$^-$ (CH_2N), 20.7$^-$ (*C*H$_2$Me) and 14.1$^+$ (CH$_2$*Me*); *m*/*z* 245 (100%, M$^+$), 178 (52, M − C_5H_7), 165 (10, M − Ph) and 104 (95, BnNH).

(*S*)-(*Z*)-3-Benzyl-4-(but-1′-enyl)oxazolidin-2-one *Z*-22

In the same way, the urethane *anti*-**11** (45.7 mg, 0.101 mmol) gave, after 14 h, and after purification by PTLC, eluting with 3:1 hexane–EtOAc, the *oxazolidinone Z*-**22** (4.90 mg, 21%) as

an oil, $[\alpha]_D^{25}$ −66.1 (*c* 0.57 in $CHCl_3$; >95% ee) (Found: M + H, 232.1335. $C_{14}H_{17}NO_2$ requires *M* + H, 232.1337); R_F (3:1 hexane–EtOAc) 0.23; $\nu_{max}(CHCl_3)/cm^{-1}$ 1740 (C=O); δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.72 (1 H, dt, *J* 10.8 and 7.7, CH_2CH=CH), 5.24 (1 H, tt, *J* 10.9 and 1.3, CH=C*H*CHN), 4.79 (1 H, d, *J* 15.0, NCH_AH_B), 4.37 (2 H, m, NCH and CH_A-H_BO), 3.92 (1 H, d, *J* 15.1, NCH_AH_B), 3.87 (1 H, t, *J* 6.4, CH_A-H_BO), 1.80 (1 H, d of quintets, *J* 1.7 and 7.5, CH_2Me) and 0.88 (3 H, t, *J* 7.5, Me); δ_C(62.9 MHz; $CDCl_3$) 158.4$^-$ (C=O), 144.6$^+$ (CH=*C*HCHN), 136.1$^-$ (Ph *ipso*), 128.8$^+$, 128.4$^+$ (Ph *ortho* and *meta*), 123.4$^+$ (Ph *para*), 123.4$^+$ (*C*H=CHCHN), 67.6$^-$ (CH_2O), 52.1$^+$ (CHN), 45.9$^-$ (CH_2N), 27.0$^+$ (*C*HMe$_2$), 23.7$^+$ (CH*Me*$_A$-Me$_B$) and 22.7$^+$ (CHMe$_A$*Me*$_B$); *m*/*z* 246 (100%, M + H), 245 (90, M$^+$), 178 (45, M − C_5H_7), 165 (15, M − Ph) and 104 (85, BnNH); *m*/*z* (CI) 232 (100%, M + H).

(4*S*,5*S*)-(*Z*)-3-Benzyl-4-(3′-methylbut-1′-enyl)-5-methyloxazolidin-2-one *Z*,*anti*-23

In the same way, the urethane *anti*,*anti*-**13** (25.3 mg, 0.053 mmol) gave, after 15 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone Z*,*anti*-**23** (5.7 mg, 42%) as an oil, $[\alpha]_D^{25}$ −84.2 (*c* 0.57 in $CDCl_3$; >99% ee) (Found: M + H, 260.1645. $C_{16}H_{21}NO_2$ requires *M* + H, 260.1650); R_F (1:1 Et_2O–hexane) 0.33; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.54 (1 H, t, *J* 10.6, C*H*=CHCHN), 5.09 (1 H, t, *J* 10.4, CH=C*H*CHN), 4.77 (1 H, d, *J* 15.1, NCH_AH_B), 4.14 (1 H, dq, *J* 7.9 and 6.2, OC*H*Me), 3.92 (1 H, d, *J* 15.0, NCH$_A$$H_B$), 3.91 (1 H, m, CHN), 2.20 (1 H, m, C*H*Me$_2$), 1.33 (3 H, d, *J* 6.2, OCH*Me*) and 0.85 (6 H, d, *J* 6.6, CH*Me*$_2$); δ_C(100 MHz; $CDCl_3$) 158.0$^-$ (C=O), 144.9$^+$ (CH=*C*HCHN), 136.0$^-$ (Ph *ipso*), 128.6$^+$, 128.2$^+$ (Ph *ortho* and *meta*), 127.7$^+$ (Ph *para*), 122.8$^+$ (*C*H=CHCHN), 76.1$^-$ (CHO), 59.2$^+$ (CHN), 45.8$^-$ (CH_2N), 26.8$^+$ (O*C*HMe), 23.4$^+$ (*C*HMe$_2$), 22.5$^+$ (CH*Me*$_A$Me$_B$) and 18.7$^+$ (CHMe$_A$*Me*$_B$); *m*/*z* (+FAB) 260 (100%, M + H).

(4*S*,5*R*)-(*E*)-3-Benzyl-4-(3′-methylbut-1′-enyl)-5-methyloxazolidin-2-one *E*,*syn*-23

In the same way, the urethane *syn*,*syn*-**13** (24.8 mg, 0.051 mmol) gave, after 7 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone E*,*syn*-**23** (10.5 mg, 78%) as an oil, $[\alpha]_D^{25}$ −1.7 (*c* 1.05 in $CDCl_3$; 89% ee) (Found: M + H, 260.1665. $C_{16}H_{21}NO_2$ requires *M* + H, 260.1650); R_F (1:1 Et_2O–hexane) 0.31; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(400 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.56 (1 H, dd, *J* 15.4 and 6.6, C*H*=CHCHN), 5.21 (1 H, dd, *J* 15.6 and 9.6, CH=C*H*-CHN), 4.72 (1 H, d, *J* 15.0, NCH_AH_B), 4.60 (1 H, dq, *J* 8.0 and 6.5, OC*H*Me), 3.92 (1 H, d, *J* 14.8, NCH$_A$$H_B$), 3.91 (1 H, dd, *J* 9.6 and 8.0, CHN), 2.33 (1 H, octet, *J* 6.6, C*H*Me$_2$), 1.24 (3 H, d, *J* 6.5, OCH*Me*), 1.00 (3 H, d, *J* 7.1, CH*Me*$_A$Me$_B$) and 0.98 (3 H, d, *J* 7.1, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 158.0$^-$ (C=O), 145.9$^+$ (CH=*C*HCHN), 136.4$^-$ (Ph *ipso*), 128.6$^+$, 128.4$^+$ (Ph *ortho* and *meta*), 127.7$^+$ (Ph *para*), 120.1$^+$ (*C*H=CHCHN), 73.7$^-$ (CHO), 61.1$^+$ (CHN), 45.9$^-$ (CH_2N), 30.1$^+$ (O*C*HMe), 22.14$^+$, 22.09$^+$ (*C*HMe$_2$ and CH*Me*$_A$Me$_B$) and 16.1$^+$ (CHMe$_A$-*Me*$_B$); *m*/*z* (+FAB) 260 (100%, M + H).

(5*S*,3′*S*)-(*Z*)-3-Benzyl-4-(3′-methylpent-1′-enyl)oxazolidin-2-one *Z*,*syn*-7

In the same way, the urethane *anti*,*anti*-**6** (35.9 mg, 0.0752 mmol) gave, after 2 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone Z*,*syn*-**7** (15.6 mg, 80%) as an oil, $[\alpha]_D^{25}$ −79.1 (*c* 1.56 in $CDCl_3$; 70% ee) (Found: M + H, 260.1645. $C_{16}H_{20}NO_2$ requires *M* + H, 260.1650); R_F (1:1 Et_2O–hexane) 0.31; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.53 (1 H, t, *J* 10.7, C*H*=CHCHN), 5.24 (1 H, dd, *J* 10.8 and 8.4, CH=C*H*CHN), 4.78 (1 H, d, *J* 15.1, NCH_AH_B), 4.42 (1 H, q, *J* 8.5, CHN), 4.35 (1 H, t, *J* 8.6, CH_AH_BO), 3.96 (1 H, d, *J* 15.0, NCH$_A$$H_B$), 3.83 (1 H, dd, *J* 7.7 and 8.9, CH$_A$$H_B$O), 1.96 (1 H, d × sextet, *J* 9.9 and 6.7, C*H*Me), 1.21 (2 H, m, CH_2Me), 0.81 (3 H, d, *J* 6.7, CH*Me*$_A$Me$_B$) and 0.74 (3 H, t, *J* 7.4, CHMe$_A$*Me*$_B$); δ_C(100 MHz; $CDCl_3$) 158.3$^-$ (C=O), 143.4$^+$ (CH=*C*HCHN), 135.9$^-$ (Ph *ipso*), 128.8$^+$, 128.1$^+$ (Ph *ortho* and *meta*), 127.7$^+$ (Ph *para*), 124.5$^+$ (*C*H=CHCHN), 67.5$^-$ (CH_2O), 52.1$^+$ (CHN), 45.7$^-$ (CH_2N), 33.7$^+$ (*C*HCH$_2$), 29.7$^-$ (CH*C*H$_2$), 21.2$^+$ (CH*Me*) and 11.7$^+$ (CH$_2$*Me*); *m*/*z* (+FAB) 260 (100%, M + H).

Irradiation of the double sextet at δ 1.96 in the ^{1}H NMR spectrum reduced the triplet at δ 5.53 to a doublet.

(5*S*,3′*R*)-(*Z*)-3-Benzyl-4-(3′-methylpent-1′-enyl)oxazolidin-2-one *Z*,*anti*-7

In the same way, the urethane *syn*,*anti*-**6** (28.7 mg, 0.0661 mmol) gave, after 75 min, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone Z*,*anti*-**7** (9.9 mg, 63%) as an oil, $[\alpha]_D^{25}$ −40.7 (*c* 0.99 in $CDCl_3$; 72% ee) (Found: M + H, 260.1627. $C_{16}H_{20}NO_2$ requires *M* + H, 260.1650); R_F (1:1 Et_2O–hexane) 0.31; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.44 (1 H, t, *J* 10.6, C*H*=CHCHN), 5.26 (1 H, t, *J* 10.7, CH=C*H*CHN), 4.80 (1 H, d, *J* 15.0, NCH_AH_B), 4.35 (2 H, m, CHN and CH_AH_BO), 3.96 (1 H, d, *J* 15.0, NCH$_A$$H_B$), 3.85 (1 H, t, *J* 8.2, CH$_A$$H_B$O), 1.93 (1 H, m, C*H*Me), 1.28 (1 H, m, CH_AH_BMe), 1.06 (1 H, m, CH$_A$$H_B$Me), 0.87 (3 H, d, *J* 6.5, CH*Me*) and 0.67 (3 H, t, *J* 7.4, CH$_2$*Me*); δ_C(100 MHz; $CDCl_3$) 158.3$^-$ (C=O), 143.0$^+$ (CH=*C*H-CHN), 135.9$^-$ (Ph *ipso*), 128.6$^+$, 128.3$^+$ (Ph *ortho* and *meta*), 127.8$^+$ (Ph *para*), 124.6$^+$ (*C*H=CHCHN), 67.4$^-$ (CH_2O), 52.0$^+$ (CHN), 45.8$^-$ (CH_2N), 33.9$^+$ (*C*HCH$_2$), 29.6$^-$ (CH*C*H$_2$), 20.7$^+$ (CH*Me*) and 11.8$^+$ (CH$_2$*Me*); *m*/*z* (+FAB) 260 (100%, M + H).

(5*S*,3′*R*)-(*E*)-3-Benzyl-4-(3′-methylpent-1′-enyl)oxazolidin-2-one *E*,*syn*-7

In the same way, the urethane *anti*,*syn*-**6** (26.9 mg, 0.0619 mmol) gave, after 2 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone E*,*syn*-**7** (8.15 mg, 51%) as an oil, $[\alpha]_D^{25}$ −0.8 (*c* 1.60 in $CDCl_3$; 52% ee) (Found: M + H, 260.1667. $C_{16}H_{20}NO_2$ requires *M* + H, 260.1650); R_F (1:1 Et_2O–hexane) 0.30; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.50 (1 H, dd, *J* 15.3 and 7.7, C*H*=CHCHN), 5.21 (1 H, dd, *J* 15.3 and 8.0, CH=C*H*-CHN), 4.74 (1 H, d, *J* 15.0, NCH_AH_B), 4.36 (1 H, t, *J* 7.7, CH_AH_BO), 4.01 (1 H, q, *J* 7.9, CHN), 3.98 (1 H, d, *J* 15.0, NCH$_A$$H_B$), 3.92 (1 H, t, *J* 7.5, CH$_A$$H_B$O), 2.07 (1 H, septet, *J* 6.9, C*H*Me), 1.34 (2 H, qn, *J* 7.6, CH_2Me), 0.94 (3 H, d, *J* 6.7, CH*Me*) and 0.88 (3 H, t, *J* 7.3, CH$_2$*Me*); δ_C(62.9 MHz; $CDCl_3$) 158.1$^-$ (C=O), 144.2$^+$ (CH=*C*HCHN), 136.0$^-$ (Ph *ipso*), 128.7$^+$, 128.5$^+$ (Ph *ortho* and *meta*), 127.6$^+$ (Ph *para*), 124.6$^+$ (*C*H=CH-CHN), 67.6$^-$ (CH_2O), 57.9$^+$ (CHN), 45.7$^-$ (CH_2N), 37.9$^+$ (*C*HCH$_2$), 29.2$^-$ (CH*C*H$_2$), 19.7$^+$ (CH*Me*) and 11.6$^+$ (CH$_2$*Me*); *m*/*z* (+FAB) 260 (100%, M + H).

Irradiation of the septet at δ 2.07 in the ^{1}H NMR spectrum simplifed the double doublet at δ 5.50 to a doublet.

(5*S*,3′*S*)-(*E*)-3-Benzyl-4-(3′-methylpent-1′-enyl)oxazolidin-2-one *E*,*anti*-7

In the same way, the urethane *syn*,*syn*-**6** (18.0 mg, 0.0377 mmol) gave, after 4 h, and after purification by PTLC, eluting with 3:2 Et_2O–hexane, the *oxazolidinone E*,*anti*-**7** (5.3 mg, 54%) as an oil, $[\alpha]_D^{25}$ −22.2 (*c* 0.98 in $CDCl_3$; 80% ee) (Found: M + H, 260.1661. $C_{16}H_{21}NO_2$ requires *M*, 260.1650); R_F (1:1 Et_2O–hexane) 0.30; $\nu_{max}(CDCl_3)/cm^{-1}$ 1730 (C=O); δ_H(250 MHz; $CDCl_3$) 7.4–7.2 (5 H, m, Ph), 5.51 (1 H, dd, *J* 15.3 and 7.5, C*H*=CHCHN), 5.20 (1 H, dd, *J* 15.3 and 8.5, CH=C*H*CHN), 4.71 (1 H, d, *J* 14.9, NCH_AH_B), 4.36 (1 H, t, *J* 7.1, CH_AH_BO), 4.01 (1 H, t, *J* 7.1, CH$_A$$H_B$O), 4.00 (1 H, d, *J* 14.9, NCH$_A$$H_B$), 3.93 (1 H, q, *J* 7.8, CHN), 2.06 (1 H, septet, *J* 6.9, C*H*Me), 1.28 (2 H, m, CH_2Me), 0.99 (3 H, d, *J* 6.7, CH*Me*) and 0.83 (3 H, t, *J* 7.4, CH$_2$*Me*); δ_C(62.9 MHz; $CDCl_3$) 158.1$^-$ (C=O), 144.3$^+$

(CH=*C*HCHN), 136.0$^-$ (Ph *ipso*), 128.7$^+$, 128.4$^+$ (Ph *ortho* and *meta*), 127.8$^+$ (Ph *para*), 124.5$^+$ (*C*H=CHCHN), 67.6$^-$ (CH_2O), 57.8$^+$ (CHN), 45.6$^-$ (CH_2N), 38.1$^+$ (*C*HCH_2), 29.2$^-$ (CH*C*H$_2$), 19.8$^+$ (CH*Me*) and 11.7$^+$ (CH_2*Me*); *m*/*z* (+FAB) 260 (100%, M + H).

Attempted ring closure of *anti*,*anti*-15

In the same way, *anti*,*anti*-**14** (43 mg, 0.0825 mmol) gave, after 14 h, and after purification by PTLC, eluting with 3:1 hexane–EtOAc, a 4:1 mixture of two compounds (4.85 mg, 24%) tentatively identifed by their ^{1}H NMR spectrum as Z,E- and Z,Z-*dienes* (Z,E)- and (Z,Z)-3-*benzyl*-4-(*penta*-1′,3′-*dienyl*)*oxazolidin*-2-*one* **24** (Found: M − H, 242.1158. $C_{15}H_{17}NO_2$ requires *M* − H, 242.1180); R_F (3:1 hexane–EtOAc) 0.23; δ_H(400 MHz; $CDCl_3$) distinctive signals for *Z*,*E*-**24**: 7.4–7.2 (5 H, m, Ph), 6.10 (1 H, t, *J* ≈ 10.2), 6.05 (1 H, t, *J* ≈ 10.2) (C*H*=C*H*–CHN), 5.78 (1 H, dq, *J* 14.0 and 7.0, MeC*H*=CH), 5.33 (1 H, dd, *J* 14.2 and 9.0, MeCH=C*H*), 4.75 (1 H, d, *J* 15.0, PhCH_AH_BN), 4.35 (1H, t, *J* 8.5, CH_AH_BO), 4.1–3.8 (3 H, m, PhCH$_A$$H_BN, CH_A$$H_B$O and CHN) and 1.78 (3 H, dd, *J* 6.5 and 1.3, CH=CH*Me*), distinctive signals for *Z*,*Z*-**24**: 5.11 (1 H, t, *J* 9.9, MeCH=C*H*), 1.71 (3 H, d, *J* 6.5, CH*Me*); *m*/*z* 243 (0.25%, M$^+$), 176 (16, M − Ph) and 91 (100).

In another experiment, using potassium hexamethyldisilazide (1 equiv.), and stirring for 16 h at room temperature, a crude product was obtained which ^{1}H NMR showed contained mainly a compound tentatively identifed as the *vinyl phosphine oxide* (4R,5R)-(E)-6-[(N-*benzylcarbamoyl*)*oxy*]-3-*diphenylphosphinoyl*-4,5-*epoxyhex*-2-*ene* **25** δ_H(400 MHz; $CDCl_3$) (distinctive signal) 6.02 (1 H, dt, *J* 24.0 and 6.9, PC=CH).

Ring closure of *anti*,*anti*-15 with sodium hydride in THF

Sodium hydride (47 mg of a 60% suspension, 1.18 mmol, 4.3 equiv.) was added to a stirred solution of the urethane *anti*,*anti*-**15** (142.7 mg, 0.274 mmol) in dry THF (5 ml). After 2 h, saturated aqueous ammonium chloride and water were added, and the mixture extracted with dichloromethane (× 3). The combined organic fractions were dried (Na_2SO_4) and evaporated under reduced pressure, and purifed by flash chromatography, eluting with 4:1 EtOAc–hexane, to give (4R,1′R,2′S,3′S)-3-*benzyl*-4-(2′-*diphenylphosphinoyl*-1′,3′-*dihydroxypentyl*)*oxazolidin*-2-*one* **26** (64.3 mg, 49%) as a foam, $[a]_D^{25}$ −9.2 (*c* 0.93 in $CDCl_3$; 85% ee) (Found: M − H_2O + Na, 484.1640. $C_{27}H_{30}NO_5P$ requires *M* − H_2O + Na, 484.1654); R_F (EtOAc) 0.50; ν_{max}(film)/cm^{-1} 3300 (OH), 1720 (C=O), 1140 (P=O) and 1180 (P–Ph); δ_H(400 MHz; $CDCl_3$) 7.7–6.8 (15 H, m, Ph_2PO and Ph), 4.75 (1 H, d, *J* 15.8, NCH_AH_B), 4.68 (1 H, dd, *J* 9.6 and 1.8, C*H*OHCHN), 4.12 (2 H, m, CH_2C*H*OH and CH_AH_BO), 3.97 (1 H, d, *J* 15.8, NCH$_A$$H_B$), 3.89 (1 H, d, *J* 13.2, CH$_A$$H_B$O), 3.75 (1 H, ddt, *J* 16.4, 9.3 and 3.5, CHN), 2.63 (1 H, dd, *J* 11.3 and 3.2, CHP), 1.5 (1 H, m, CH_AH_BMe), 1.1 (1 H, m, CH$_A$$H_B$Me) and 0.64 (3 H, t, *J* 7.0, Me); δ_C(62.9 MHz; $CDCl_3$) 158.3$^-$ (C=O), 135.1$^-$ (Ph *ipso*), 133–127 (Ph_2PO and Ph), 73.9$^+$ (CHN*C*HOH), 71.1$^+$ (CH_2*C*HOH), 67.5$^-$ (CH_2O), 50.6$^+$ ($^3J_{PC}$ 3.0, CHN), 45.8$^-$ (CH_2N), 36.2$^+$ ($^1J_{PC}$ 67.4, CHP), 31.9$^-$ ($^3J_{PC}$ 7.8, *C*H$_2$Me) and 10.3$^+$ (Me); *m*/*z* (+FAB) 484 (10%, M − H_2O + Na), 462 (100, M − OH), 257 (20, $Ph_2POC_3H_4O$), 202 (32, Ph_2POH) and 201 (80, Ph_2PO).

Acknowledgements

We thank the EPSRC and Glaxo Wellcome for a CASE award (to J. C.) and Dr Eric Collington for many helpful discussions.

References

1 J. Clayden and S. Warren, *Angew. Chem.*, *Int. Ed. Engl.*, 1996, **35**, 241.
2 M. G. Finn and K. B. Sharpless in *Asymmetric Synthesis*, Academic Press, Orlando (1985), ed. J. D. Morrison, vol. 5, ch. 8; Y. Gao, R. M. Hanson, J. M. Klunder, S. Y. Ko, H. Masamune and K. B. Sharpless, *J. Am. Chem. Soc.*, 1987, **109**, 5765.
3 A. Nelson and S. Warren, *Tetrahedron Lett.*, 1996, **37**, 1501.
4 J. Clayden, A. B. McElroy and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1995, 1913.
5 Preliminary communication: J. Clayden, E. W. Collington, R. B. Lamont and S. Warren, *Tetrahedron Lett.*, 1993, **34**, 2203.
6 J. Clayden and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 2913; J. Clayden and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1994, 1529.
7 J. Clayden and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1994, 2811.
8 J. Clayden, E. Egert, A. B. McElroy and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1994, 2801.
9 W. R. Roush and M. A. Adam, *J. Org. Chem.*, 1985, **50**, 3752.
10 N. Minami, S. S. Ko and Y. Kishi, *J. Am. Chem. Soc.*, 1982, **104**, 1109.
11 V. Jäger, U. Stahl and W. Hümmer, *Synthesis*, 1991, 776; J. C. Schmidhauser and K. L. Longley, *Tetrahedron Lett.*, 1991, **32**, 7155.
12 T. W. Hart and B. Vacher, *Tetrahedron Lett.*, 1992, **33**, 3009.
13 S. W. McCombie, B. B. Shankar and A. K. Ganguly, *Tetrahedron Lett.*, 1985, **26**, 6301.
14 S. W. McCombie and W. A. Metz, *Tetrahedron Lett.*, 1987, **28**, 383.
15 W. R. Roush, R. J. Brown and M. DiMare, *J. Org. Chem.*, 1983, **48**, 5083.
16 E. J. Corey, P. B. Hopkins, J. E. Munroe, A. Marfat and S.-I. Hashimoto, *J. Am. Chem. Soc.*, 1980, **102**, 7987.
17 A. D. Buss, W. B. Cruse, O. Kennard and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1984, 243.
18 D. Xu and K. B. Sharpless, *Tetrahedron Lett.*, 1993, **34**, 951; M. P. Sibi and P. A. Renhowe, *Tetrahedron Lett.*, 1990, **31**, 7407; M. P. Sibi and B. Li, *Tetrahedron Lett.*, 1992, **33**, 4115; P. L. Beaulieu, J.-L. Duceppe and C. Johnson, *J. Org. Chem.*, 1991, **56**, 4196.
19 T. Ibuka, H. Habashita, S. Funakoshi, N. Fujii, Y. Oguchi, T. Uyehara and Y. Yamamoto, *Angew. Chem.*, *Int. Ed. Engl.*, 1990, **29**, 801.
20 T. Ibuka, K. Nakai, H. Habashita, Y. Hotta, N. Fujii, N. Mimura, Y. Miwa, T. Taga and Y. Yamamoto, *Angew. Chem.*, *Int. Ed. Engl.*, 1994, **33**, 652 and references therein.
21 A. C. Bohrstedt, J. V. N. V. Prasad and D. Rich, *Tetrahedron Lett.*, 1993, **34**, 5217.
22 P. J. Murphy and G. Procter, *Tetrahedron Lett.*, 1990, **31**, 1059.
23 D. Hall, A.-F. Sévin and S. Warren, *Tetrahedron Lett.*, 1991, **32**, 7123.
24 See, for example, V. K. Aggarwal, I. Coldham, S. McIntyre and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1991, 451; R. C. Hartley, I. C. Richards and S. Warren, *J. Chem. Soc.*, *Perkin Trans. 1*, 1994, 508.
25 For an exception, see M. A. M. Fuhry, A. B. Holmes and D. R. Marshall, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 2743.
26 H. J. Mitchell and S. Warren, *Tetrahedron Lett.*, 1996, **37**, 2105.
27 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.

Paper 8/02577K
Received 3*rd April* 1998
Accepted 10*th July* 1998