# Allene synthesis by an asymmetric Baylis–Hillman style reaction on vinylphosphine oxides

**David J. Fox, Jonathan A. Medlock, Richard Vosser and Stuart Warren***

*University Chemical Laboratory, Lensfield Road, Cambridge, UK CB2 1EW.*
*E-mail: sw134@cam.ac.uk*

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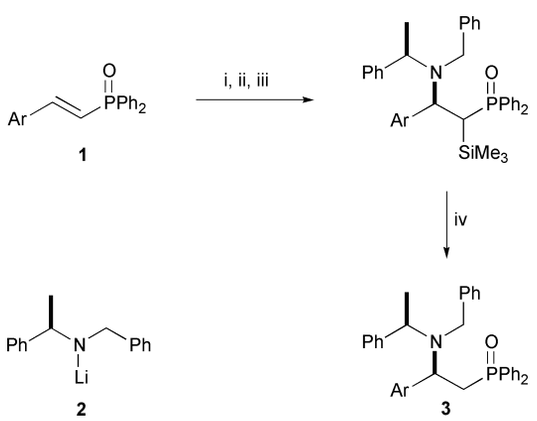
A novel reaction has been discovered with a mechanism similar to the Baylis–Hillman reaction. Reaction of a vinylic phosphine oxide with (*R*)-*N*-lithio-α-methylbenzylbenzylamine **2** in the presence of an aldehyde gave hydroxyphosphine oxides in good to moderate yields and moderate to poor enantioselectivities. The hydroxyphosphine oxides undergo the Horner–Wittig elimination reaction to produce allenes. Baylis–Hillman reactions of vinylic phosphine oxides with tertiary amines were also investigated.

## Introduction

The Baylis–Hillman reaction is a method for the α-alkylation of an α,β-unsaturated carbonyl compound. The reaction is catalysed by a nucleophilic catalyst, usually a tertiary amine; the accepted mechanism is conjugate addition of the nucleophilic catalyst, quenching of the enolate with an electrophile and then elimination of the catalyst.[1,2] The standard Baylis–Hillman reaction suffers from very slow reaction rates and much recent attention has focused on improving the rate using a wide variety of nucleophilic catalysts and Lewis acids,[3,4] high pressure[5] and microwave irradiation.[6] Asymmetric Baylis–Hillman reactions have been reported using a variety of strategies, and enantiomeric excesses of up to 99% have been reported for the use of a chiral catalyst.[7]

We have recently reported the synthesis of enantiomerically enriched aminophosphine oxides **3** by the application of the asymmetric conjugate addition reaction developed by Davies[8] to vinylic phosphine oxides **1** (Scheme 1).[9,10] The reaction

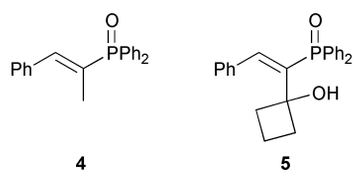



**Scheme 1** *Reagents and conditions*: i, $Me_3SiCl$, THF, −78 °C; ii, **2**; iii, $H_2O$; iv, TBAF, THF.

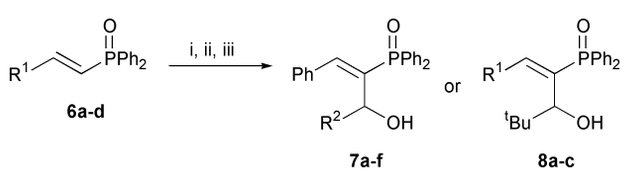
proceeded only in the presence of trimethylsilyl chloride as an internal quench. We now report a modestly asymmetric Baylis–Hillman style reaction which has been used to synthesise enantiomerically enriched allenes.

## Results and discussion

During further investigation of the conjugate addition reaction (Scheme 1), we found that the use of other internal electrophiles resulted in Baylis–Hillman like products. Reaction of **1** (Ar = Ph) with methyl iodide gave a 76% yield of the phosphine oxide **4** and reaction with cyclobutanone, which we have used previously as an internal quench,[11] gave a 50% yield of the hydroxyphosphine oxide **5**.




Reaction with a prochiral electrophile, pivalaldehyde, gave enantiomerically enriched products, albeit with poor selectivity. A range of aldehydes was investigated (Scheme 2, Table 1,




**Scheme 2** *Reagents and conditions*: i, $R^2CHO$, THF, −78 °C; ii, **2**; iii, $H_2O$.

entries 1–5), and all the products were (*E*)-vinyl phosphine oxides. An α-quaternary centre is required on the aldehyde for any enantioselectivity to be observed. Yields were decreased for aldehydes bearing an α-secondary centre (entry 5), presumably due to competing deprotonation of the aldehyde by the lithium amide. No reaction was observed with benzaldehyde (entry 6); benzaldehyde may have been reduced by the lithium amide. No reaction was observed with acetone or diisopropyl ketone. The former is presumably rapidly deprotonated and the latter is probably too hindered to react. Other vinylic phosphine oxides were investigated (Table 1, entries 7–9). The highest enantiomeric excess was observed for the vinylic phosphine oxide **6b** bearing a *tert*-butyl substituent (entry 7).

When the reaction was performed on the vinylic phosphine oxide **6e**, the hydroxyphosphine oxide **9** was isolated as a mixture of diastereoisomers, as well as the expected product **8d** (Scheme 3). This suggests that the reaction is proceeding by an addition–elimination mechanism (Scheme 4), similar to the Baylis–Hillman reaction, rather than by an α-lithiation

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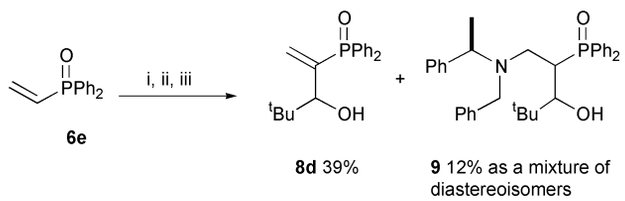
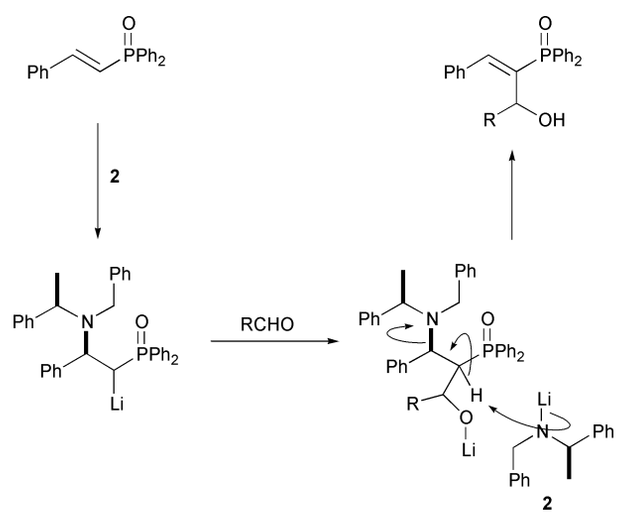
**Table 1** Synthesis of compounds **7** and **8** from **6a–d**

| Entry | Starting material | $R^1$ | $R^2$ | Product | Yield (%) | Ee (%) |
|---|---|---|---|---|---|---|
| 1 | **6a** | Ph | $^t$Bu | **7a** | 87 | 28 |
| 2 | **6a** | Ph | 1-SPh$^{cy}$Hex [a] | **7b** | 55 | 13 |
| 3 | **6a** | Ph | $CMe_2CH_2CH{=}CH_2$ | **7c** | 67 | 23 |
| 4 | **6a** | Ph | $^i$Pr | **7d** | 62 | 0 |
| 5 | **6a** | Ph | $(CH_2)_6Me$ | **7e** | 33 | 0 |
| 6 | **6a** | Ph | Ph | **7f** | 0 | — |
| 7 | **6b** | $^t$Bu | $^t$Bu | **8a** | 58 | 51 |
| 8 | **6c** | $^i$Pr | $^t$Bu | **8b** | 53 | 12 |
| 9 | **6d** | Me | $^t$Bu | **8c** | 47 | 11 |

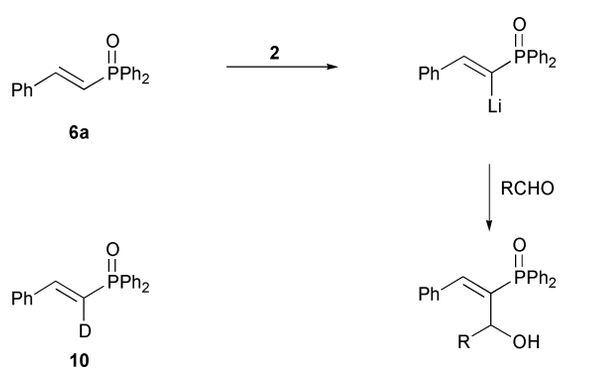
[a] 1-Phenylsulfanylcyclohexyl.




**Scheme 3** *Reagents and conditions*: i, $^t$BuCHO, THF, −78 °C; ii, **2**; iii, $H_2O$.




**Scheme 4**



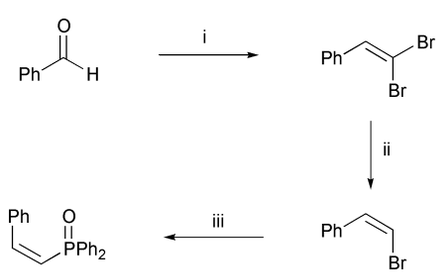

**Scheme 5**

mechanism (Scheme 5). Nagaoka and Tomioka have reported a similar reaction of vinylic phosphonates catalysed by LDA and suggest a Baylis–Hillman style reaction.[12] Such a mechanism has also been reported by Harrowven and Poon[13] for the reaction of lithium tetramethylpiperidine with diethyl maleate and a range of ketones.

## Mechanistic investigations

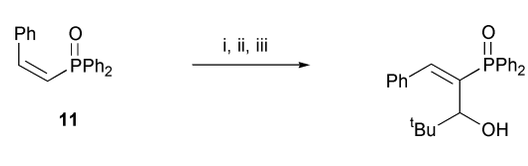
In order to determine the mechanism of formation of the hydroxyphosphine oxides **7** and **8**, the vinylic phosphine oxide **6a** was treated with the lithium amide **2** in the absence of an electrophile and quenched with deuterated methanol after 30 minutes. The recovered starting material showed no deuteration of the α-position. The analogous reaction involving the deuterated vinyl phosphine oxide **10** (prepared with 80% deuterium incorporation at the α-position in an analogous way to the preparation[14] of **6a**), and quenching with methanol, showed no loss of deuteration. Although this suggests that deprotonation is not occurring, Seebach and co-workers have shown that the deprotonation of carbonyl compounds with lithium amides and quenching with $D_2O$ or deuterated alcohols do not always result in deuteration at the α-position.[15,16] Seebach achieved deuteration by treatment of the enolate–amine complex with *n*-butyllithium after deprotonation by the lithium amide and then quenching with a deuterium source. Repeating this with the vinylphosphine oxide **6a** resulted in complete deuteration of the α-position. Although this suggests that deprotonation may be occurring, it is far from conclusive as deprotonation may be due to the *n*-butyllithium rather than the lithium amide.

Evidence for the Baylis–Hillman style reaction also comes from reaction of the (*Z*)-vinylic phosphine oxide **11**. The phosphine oxide **11** was synthesised in three steps from benzaldehyde (Scheme 6), using literature methods.[17–19] Reaction




**Scheme 6** *Reagents and conditions*: i, $PPh_3$, $CBr_4$, $CH_2Cl_2$, 84%; ii, $Pd(PPh_3)_4$, $Bu_3SnH$, PhH, 29%; iii, $Pd(PPh_3)_4$, $Et_3N$, $Ph_2P(O)H$, PhMe, 90 °C, 77%.

of **11** under the standard reaction conditions gave the (*E*)-hydroxyphosphine oxide **7a** with an enantiomeric excess of 31% in *exactly the same sense* as observed previously (Scheme 7). In

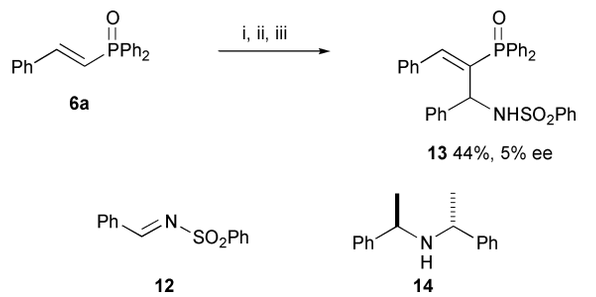



**Scheme 7** *Reagents and conditions*: i, $^t$BuCHO, THF, −78 °C; ii, **2**; iii, $H_2O$.

the absence of an electrophile, complete isomerisation of the (*Z*)-phosphine oxide **11** to the (*E*)-isomer **6a** is observed with either 1 or 0.2 equivalents of the lithium amide **2**. Thus, in the reaction illustrated in Scheme 7, the (*Z*)-phosphine oxide **11**

is presumably isomerising to the (*E*)-isomer **6a**, which subsequently reacts. We believe that the results above and the isolation of the aminophosphine oxide **9** show that this novel reaction has an addition–elimination mechanism (Scheme 4), that is, a *Baylis–Hillman style* reaction.

The Baylis–Hillman style reaction has also been performed with the sulfonamide imine **12**, producing the aminophosphine oxide **13** in moderate yield but poor enantioselectivity (Scheme 8). Various reaction conditions were investigated to attempt

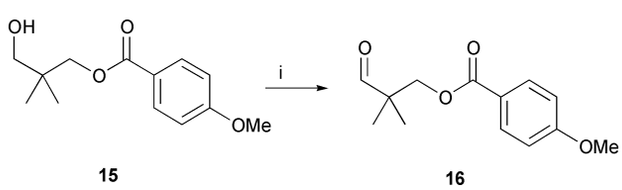



**Scheme 8** *Reagents and conditions*: i, **12**, THF, −78 °C; ii, **2**; iii, $H_2O$.

to improve the enantioselectivity. Use of the lithium amide derived from the $C_2$ symmetric amine[20] **14** resulted in a lower yield (53%) of the hydroxyphosphine oxide **7a** and only a 12% enantiomeric excess. If external quench conditions were used (addition of the aldehyde after the addition of the lithium amide), the resulting hydroxyphosphine oxides were racemic. Quenching the reaction at −78 °C gave the hydroxyphosphine oxide **7a** in 19% ee. Changing the order of addition of the reagents had a slight effect. Addition of a solution of the hydroxyphosphine oxide and aldehyde to the solution of lithium amide **2** gave the hydroxyphosphine oxide **7a** in 35% ee and the hydroxyphosphine oxide **8a** in 43% ee.

### Determination of the stereochemistry

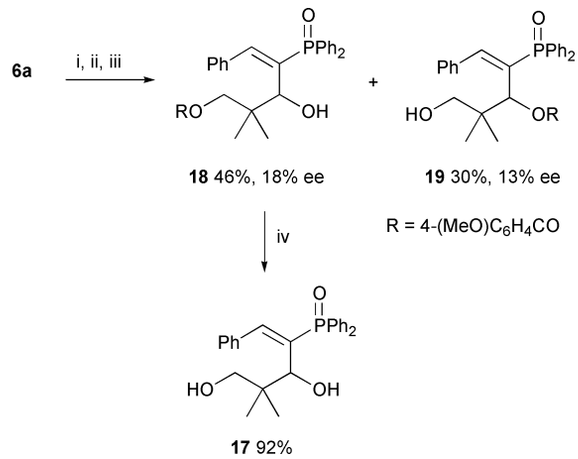
In the above discussion, the major isomer of product has not been indicated. Attempts were made to derivatise the hydroxyphosphine oxides **7a** and **8a** with enantiomerically pure derivatising groups without success, presumably due to the bulky *tert*-butyl and diphenylphosphinoyl groups. In order to derivatise hydroxyphosphine oxides such as **7** and **8**, we envisaged synthesising a hydroxyphosphine oxide such as **17**. The protected aldehyde **16** was synthesised in excellent yield from the known mono-protected diol[21] **15** (Scheme 9). The



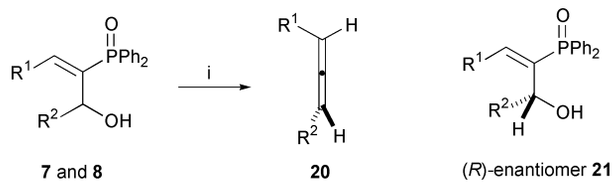

**Scheme 9** *Reagents and conditions*: i, oxalyl chloride, DMSO, $Et_3N$, $CH_2Cl_2$, −78 °C, 98%.

Baylis–Hillman style reaction of vinylphosphine oxide **6a** and the aldehyde **16** resulted in a mixture of the two hydroxyphosphine oxides **18** and **19** (Scheme 10). Hydrolysis of the ester was achieved with lithium hydroxide. The diol **17** was successfully derivatised with (1*S*)-(+)-camphor-10-sulfonyl chloride, but we were unable to separate the resulting diastereoisomers.

The absolute stereochemistry of the hydroxyphosphine oxides was determined from the corresponding allenes **20**, synthesised *via* the Horner–Wittig elimination reaction of the hydroxyphosphine oxides (Scheme 11, Table 2). The Horner–Wittig elimination proceeds in good yield except in the case where $R^1 = {}^iPr$ (entry 2), due to the allene's high volatility. Comparing the specific rotation of the resulting allenes with literature values[22] and assuming the stereospecific *syn*




**Scheme 10** *Reagents and conditions*: i, **16**, THF, −78 °C; ii, **2**; iii, $H_2O$; iv, LiOH, MeOH.

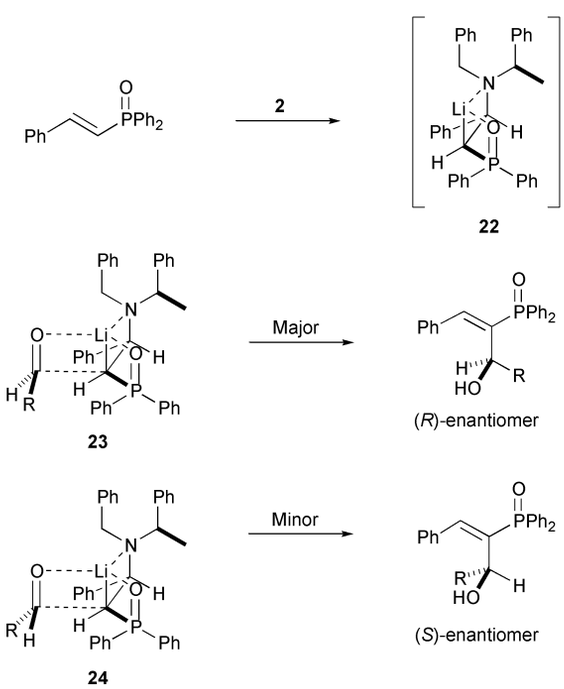



**Scheme 11** *Reagents and conditions*: i, NaH, DMF, 60 °C.

Horner–Wittig elimination,[23] we can assign the stereochemistry of the major enantiomer of the hydroxyphosphine oxides as the (*R*)-enantiomer **21**. Wang and co-workers [24,25] have previously reported the synthesis of allenes by addition of a lithiated vinyl phosphine oxide (generated by iodide–lithium exchange) to aldehydes and ketones and spontaneous Horner–Wittig elimination on warming to room temperature.

### Origins of the selectivity

To account for the observed selectivity, two stereochemical defining steps have to be considered. The first, the asymmetric conjugate addition of the lithium amide, is accounted for by an extension of the model proposed by Davies and co-workers,[26] where the lithium amide approaches the top face of the double bond, as drawn (Scheme 12), with the methyl group pointing




**Scheme 12**

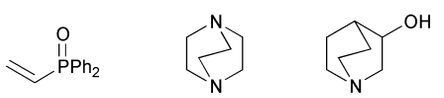
**Table 2** Synthesis of allenes **20** from compounds **7** and **8**

| Entry | $R^1$ | $R^2$ | Yield (%) | $[\alpha]_D/10^{-1}$ deg dm$^2$ g$^{-1}$ | Lit.[22] $[\alpha]_D/10^{-1}$ deg dm$^2$ g$^{-1}$ |
|---|---|---|---|---|---|
| 1 | Ph | $^t$Bu | 89 | +46 | +370 |
| 2 | $^i$Pr | $^t$Bu | 5 | +5 | +110 |
| 3 | $^t$Bu | $^t$Bu | 74 | +28 | +124 |

forward. We believe that the lithiated phosphine oxide **22** is the product of the conjugate addition as lithiated phosphine oxides have been shown to have an $sp^3$ configuration.[27,28] The aldehyde then approaches the carbon–lithium bond of the lithiated species **22**. The oxygen atom of the aldehyde is chelated to the lithium atom and the R group of the aldehyde can adopt one of two possible positions **23** or **24**. The R group has a steric interaction with one of the two phenyl rings, attached either to the phosphine oxide or to the end of the alkyl chain. These two groups are very similar; hence, the observed enantioselectivity is low. The interaction between the R group and the phenyl ring on the phosphine oxide is less than the corresponding interaction with the other phenyl ring because the P–C bond between the phenyl ring and phosphorus is longer, as is the P–C bond between the reacting centre and phosphorus. This suggests that conformation **23** is preferred, leading to the (*R*)-enantiomer. This explanation is consistent with the observation that when the phenyl group on the alkyl chain is replaced with a *tert*-butyl group, the selectivity increases (Table 1, entries 1 and 7).

### Baylis–Hillman reactions

A similar route to *racemic* hydroxyphosphine oxides such as **7** and **8** would be to perform a Baylis–Hillman reaction, using a tertiary amine, on vinylic phosphine oxides. Baylis–Hillman reactions of vinyl diethylphosphonate have been reported by Villiéras and co-workers, although reaction times are 7–29 days.[29] We started our investigation with vinyldiphenylphosphine oxide **6e**, butanal and a range of nucleophilic catalysts: DABCO **25**, 3-hydroxyquinuclidine **26**, DBU, DMAP, tri-




**6e** **25** **26**

phenylphosphine and tricyclohexylphosphine. It was not possible to repeat the solvent-free reaction conditions of Villiéras as the phosphine oxide is a crystalline solid and so the reaction was attempted in dichloromethane. In all cases the starting material was recovered after 2–4 days. Use of high pressure (80 bar) and lanthanide Lewis acids, which have previously been used to accelerate the Baylis–Hillman reaction,[3,4,30] also resulted in no reaction. A change of solvent to the more polar deuterated DMSO and deuterated methanol also gave recovered starting material after three days, although in the case of deuterated methanol, partial deuteration of the α-position was observed. This observation suggests that nucleophilic addition of 3-hydroxyquinuclidine **26** to the vinylphosphine oxide **6e** was occurring. The reaction was repeated at 50 °C, recording an NMR spectrum every 30 minutes. Fig. 1 shows a graph of the integration value of the signal corresponding to the α-proton against time, showing pseudo first-order kinetics with a half-life of approximately 10 hours (at 50 °C). This confirms that conjugate addition of the nucleophile is occurring, forming **27**, but nothing can be said about the position of any of the equilibria in Scheme 13. We expect that reaction of the zwitterion **27** with an aldehyde to be even slower than deuteration. Thus, this could be the reason that no reaction is observed.

In conclusion, we have demonstrated that vinylic phosphine oxides undergo a Baylis–Hillman style reaction producing

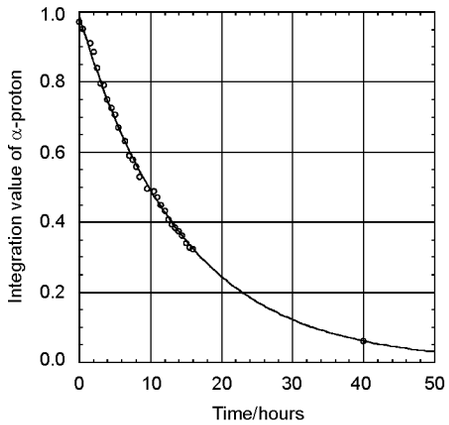
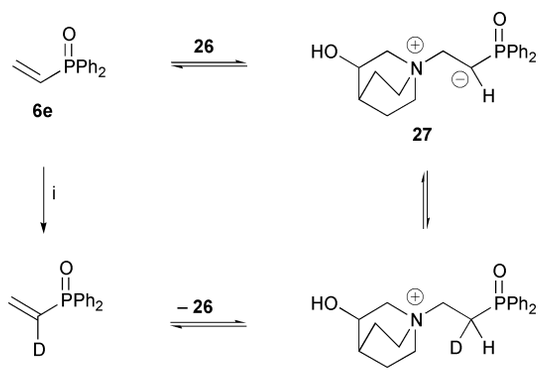



**Fig. 1** Graph showing integration of the α-proton of **6e** against time.




**Scheme 13** *Reagents and conditions*: i, **26**, $CD_3OD$, 50 °C.

hydroxyphosphine oxides, which can undergo Horner–Wittig elimination to produce enantiomerically enriched allenes. Baylis–Hillman reactions of vinylphosphine oxides are not observed due to the slow reaction of the intermediate **27** with aldehydes.

## Experimental

All solvents were distilled before use. THF was freshly distilled from lithium aluminium hydride with triphenylmethane as the indicator. Dichloromethane, diethyl ether and methanol were distilled from calcium hydride. Pyridine was dried by stirring over and distilling from calcium and was stored over 4 Å molecular sieves. Triethylamine was dried in the same way but stored over calcium hydride. Anhydrous dimethyl sulfoxide was bought from Aldrich and stored over 4 Å molecular sieves. *n*-Butyllithium was titrated against diphenylacetic acid before use. All non-aqueous reactions were carried out under argon using oven- and vacuum-dried glassware. Column chromatography was performed with Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography was carried out on pre-coated plates (Merck Kieselgel $60F_{254}$).

Analytical chiral HPLC was carried out using a Daicel Chiralpak AD column and guard column with a Spectra-Physics SP8800 pump, a Spectra-Physics SP8450 UV detection system and a ChromJet single channel integrator. Proton and carbon NMR spectra were recorded on Bruker DPX250, DPX400, DRX400, DRX500 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million (ppm) downfield from tetramethylsilane. The

symbol "*" after a proton NMR signal indicates that the signal disappears after a $D_2O$ shake. Carbon NMR were recorded with broadband proton decoupling, the symbol "+" after a carbon NMR chemical shift indicates an odd number of attached protons, whereas the symbol "−" indicates an even number, as determined by APT or DEPT analysis. Coupling constants for proton and carbon NMR signals are quoted in Hz, rounded to the nearest 0.5 Hz and are reported as observed. Electron impact (EI) mass spectra were recorded on a Kratos double focusing magnetic sector instrument using a DS503 data system for high-resolution analysis or a MSI double focusing magnetic sector Concept IH instrument. Fast atom bombardment (FAB) mass spectra were obtained from a Kratos MS 890 instrument. Electrospray (ESI) mass spectra were recorded using a Brucker Bio-Apex II FT-ICR instrument or a Micromass Q-Tof machine. Liquid secondary ion mass spectra (LSIMS) were recorded on an MSI double focusing Concept IH instrument. Microanalyses were carried out by the staff of the University Chemical Laboratory using a Leeman Labs CE440 Elemental Analyzer (C, H and N) and LBK Biochrom Ultrospec 4050 (P). Melting points were measured on a Stuart Scientific SMP1 melting point apparatus and are uncorrected. Infra-red spectra were recorded using a Perkin Elmer 1600 (FT-IR) spectrometer and optical rotations were recorded on a Perkin Elmer 241 polarimeter using to the sodium D line (589 nm) at room temperature and are given in units of $10^{-1}$ deg dm$^2$ g$^{-1}$.

### (*E*)-2-Diphenylphosphinoyl-1-phenylprop-1-ene 4

A solution of freshly prepared (*R*)-*N*-benzyl-*N*-lithio-1-phenylethylamine at −78 °C [prepared by the addition of *n*-butyllithium (1.4 M in hexane, 250 µl, 0.39 mmol) to a solution of (*R*)-*N*-benzyl-1-phenylethylamine (83 mg, 0.39 mmol), in dry THF (10 cm$^3$)] was added by cannula to a solution of (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (100 mg, 0.33 mmol) and methyl iodide (47 mg, 21 µl, 0.66 mmol) in dry THF (7 cm$^3$) at −78 °C. The reaction mixture was stirred at −78 °C for 30 minutes and allowed to warm to room temperature over 30 minutes. The reaction was quenched by addition of saturated aqueous ammonium chloride solution (15 cm$^3$) and water (30 cm$^3$). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 100 cm$^3$). The combined organic extracts were evaporated under reduced pressure and dissolved in dichloromethane (100 cm$^3$). This solution was washed with 10% citric acid solution (100 cm$^3$), water (100 cm$^3$), brine (100 cm$^3$), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product. The residue was chromatographed ($SiO_2$, EtOAc) to give a 8 : 92 mixture of starting material–vinylphosphine oxide[31] **4** (87 mg) as a colourless gum which we were unable to separate. Yield of product 80 mg (76%).

### (*E*)-1-Diphenylphosphinoyl-1-(1′-hydroxycyclobutyl)-2-phenylethene 5

In a similar way, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (100 mg, 0.33 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (82 mg, 0.39 mmol), *n*-butyllithium (1.4 M in hexane, 260 µl, 0.36 mmol) and cyclobutanone (28 mg, 30 µl, 0.66 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc) to give the *hydroxyphosphine oxide* **5** (60 mg, 50%) as a colourless gum; $R_f$(EtOAc) 0.29; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3500–3200 (br, OH), 1438 (P–Ph) and 1158 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.80–7.70 (4H, m, $Ph_2PO$), 7.60–7.25 (11H, m, Ph and $Ph_2PO$), 6.67 (1H, d, *J* 23, CHPh), 4.43* (1H, br s, OH), 2.05–1.80 (5H, m, $CH_2$) and 1.43–1.32 (1H, m, $CH_2$); $\delta_C$(100 MHz; $CDCl_3$) 143.3$^+$ (d, *J*, 13, CHPh), 136–127 (m, Ph, $Ph_2PO$ and $Ph_2PO$-*C*), 77.6$^+$ (CHOH), 36.7$^-$ ($CH_2$), 36.6$^-$ ($CH_2$) and 16.2$^-$ ($CH_2$); *m*/*z* (FAB) 375 (53%, MH$^+$), 357 (88, M − OH), 201 (80, $Ph_2PO$) and 154 (100, M − OH − $Ph_2PO$) (Found: MH$^+$, 375.1515. $C_{24}H_{24}O_2P$ requires *M*, 375.1514).

### General method for asymmetric Baylis–Hillman style reactions

A solution of freshly prepared (*R*)-*N*-benzyl-*N*-lithio-1-phenylethylamine at −78 °C [prepared by the addition of *n*-butyllithium (1.1 mmol) to a solution of (*R*)-*N*-benzyl-1-phenylethylamine[32] (1.2 mmol), in dry THF (15 cm$^3$)] was added by cannula to a solution of the phosphine oxide (1 mmol) and the electrophile (2 mmol) in dry THF (25 cm$^3$) at −78 °C. The reaction mixture was stirred at −78 °C for 30 minutes and allowed to warm to room temperature over 30 minutes. The reaction was quenched by addition of saturated aqueous ammonium chloride solution (15 cm$^3$) and water (30 cm$^3$). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 100 cm$^3$). The combined organic extracts were evaporated under reduced pressure and dissolved in dichloromethane (100 cm$^3$). This solution was washed with 10% citric acid solution (100 cm$^3$), water (100 cm$^3$), brine (100 cm$^3$), dried ($MgSO_4$) and evaporated under reduced pressure to yield a crude product.

### (*E*)-4,4-Dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpent-1-ene 7a

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (1.20 g, 4 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (1.00 g, 4.7 mmol), *n*-butyllithium (1.4 M in hexane, 3.1 cm$^3$, 4.3 mmol) and pivalaldehyde (0.680 g, 860 µl, 8 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 1 : 0) to give the *hydroxyphosphine oxide* **7a** (1.34 g, 87%) as needles, mp 174–175 °C (from EtOAc); $[\alpha]_D$ −75 (*c*. 1.0 in $CHCl_3$); $R_f$(EtOAc) 0.60; $\nu_{max}$(Nujol)/cm$^{-1}$ 3500–3000 (br, OH), 1440 (P–Ph) and 1153 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.95–7.85 (2H, m, $Ph_2PO$), 7.70–7.20 (13H, m, Ph and $Ph_2PO$), 6.88 (1H, d, *J* 23.5, CHPh), 5.53* (1H, d, *J* 11, OH), 4.92 (1H, dd, *J* 23.5 and 11, C*H*OH) and 0.77 (9H, s, $CMe_3$); $\delta_C$(100 MHz; $CDCl_3$) 145.6$^+$ (d, *J* 12.5, *C*HPh), 136–127 (m, Ph, $Ph_2PO$ and $Ph_2PO$-*C*), 79.2$^+$ (d, *J* 4.5, CHOH), 36.9$^-$ (*C*Me$_3$) and 26.1$^+$ (C*Me*$_3$); *m*/*z* (FAB) 391 (100%, MH$^+$), 373 (87, M − OH), 333 (44, M − $^t$Bu) and 201 (58, $Ph_2PO$) (Found: MH$^+$, 391.1806. $C_{25}H_{28}O_2P$ requires *M*, 391.1827) (Found: C, 76.6; H, 7.1; P, 7.9. $C_{25}H_{27}O_2P$ requires C, 76.9; H, 7.0; P, 7.9%). Chiral HPLC analysis (70 : 30 isohexane–propan-2-ol (IPA), $\tau_{major}$ 7.4 min, $\tau_{minor}$ 15.0 min) of this material showed an enantiomeric excess of 28%.

### (*E*)-2-Diphenylphosphinoyl-3-phenyl-1-(1′-phenylsulfanylcyclohexyl)prop-2-en-1-ol 7b

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (200 mg, 0.65 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (164 mg, 0.73 mmol), *n*-butyllithium (1.4 M in hexane, 517 µl, 0.79 mmol) and 1-(phenylsulfanyl)-cyclohexanecarbaldehyde[33] (290 mg, 1.32 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 2 : 1) to give the *hydroxyphosphine oxide* **7b** (188 mg, 55%) as prisms, mp 174–175 °C (from EtOAc–hexane); $[\alpha]_D$ −23 (*c*. 0.72 in $CHCl_3$); $R_f$(EtOAc) 0.57; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3500–3100 (br, OH), 1438 (P–Ph) and 1158 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.93–7.83 (2H, m, $Ph_2PO$), 7.70–6.80 (19H, m, Ph, SPh, $Ph_2PO$ and C*H*Ph), 5.71* (1H, d, *J* 8, OH), 5.11 (1H, dd, *J* 23 and 8, C*H*OH) and 1.90–0.90 (10H, m, 5 × $CH_2$); $\delta_C$(100 MHz; $CDCl_3$) 148.5$^+$ (d, *J* 12.5, CHPh), 140–128 (m, Ph, SPh, $Ph_2PO$ and $Ph_2PO$-*C*), 76.4$^+$ (d, *J* 4, CHOH), 62.6$^-$ (CSPh), 31.3$^-$, 31.1$^-$, 26.0$^-$, 22.2$^-$ and 21.8$^-$ (5 × $CH_2$); *m*/*z* (FAB) 525 (71%, MH$^+$), 415 (31, M − SPh), 397 (54, M − SPh − OH), 201 (100, $Ph_2PO$) and 191 (54, $C_6H_{10}SPh$) (Found: MH$^+$, 525.2009. $C_{33}H_{34}O_2PS$ requires *M*, 525.2017) (Found: C, 75.2; H, 6.5; P, 5.7. $C_{33}H_{33}O_2PS$ requires C, 75.5; H, 6.3; P, 5.9%). Chiral HPLC analysis (70 : 30 isohexane–IPA, $\tau_{major}$ 10.7 min, $\tau_{minor}$ 20.6 min) of this material showed an enantiomeric excess of 13%.

**(*E*)-4,4-Dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylhepta-1,6-diene 7c**

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (200 mg, 0.66 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (164 mg, 0.73 mmol), *n*-butyllithium (1.4 M in hexane, 517 µl, 0.79 mmol) and 2,2-dimethylpent-4-enal (164 mg, 200 µl, 1.32 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 2 : 1) to give the *hydroxyphosphine oxide* **7c** (184 mg, 67%) as a colourless gum; $[\alpha]_D$ −48 (*c*. 1.9 in $CHCl_3$); $R_f$(EtOAc) 0.64; $\nu_{max}(CHCl_3)/cm^{-1}$ 3400–3200 (br, OH), 1436 (P–Ph) and 1160 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.95–7.85 (2H, m, $Ph_2PO$), 7.70–7.20 (13H, m, Ph and $Ph_2PO$), 6.88 (1H, d, *J* 23.5, CHPh), 5.80–5.30 (2H, m, C*H*$CH_2$ and OH), 5.03 (1H, d, *J* 23.5, C*H*OH), 4.86 (1H, dd, *J* 10 and 2.5 $CH_{cis}H_{trans}$), 4.77 (1H, dd, *J* 17 and 2.5, $CH_{cis}H_{trans}$), 2.10 (1H, dd, *J* 13.5 and 7.5, $CH_AH_B$), 1.81 (1H, dd, *J* 13.5 and 7, $CH_AH_B$), 0.79 (3H, s, Me) and 0.59 (3H, s, Me); $\delta_C$(100 MHz; $CDCl_3$) 146.1$^+$ (d, *J* 12.5, *C*HPh), 135–127 (m, *C*H=$CH_2$, $Ph_2PO$-*C*, Ph and $Ph_2PO$), 116.6$^-$ (CH=*C*$H_2$), 78.0$^+$ (d, *J* 4.5, CHOH), 43.2$^-$ ($CH_2$), 22.8$^+$ (Me) and 22.7$^+$(Me); *m*/*z* (FAB) 417 (100%, $MH^+$), 399 (83, M − OH), 333 (67, M − $C_6H_{11}$) and 201 (72, $Ph_2PO$) (Found: $MH^+$, 417.1986. $C_{27}H_{30}O_2P$ requires *M*, 417.1983). Chiral HPLC analysis (70 : 30 isohexane–IPA, $\tau_{major}$ 6.9 min, $\tau_{minor}$ 16.0 min) of this material showed an enantiomeric excess of 23%.

**(*E*)-2-Diphenylphosphinoyl-3-hydroxy-4-methyl-1-phenylpent-1-ene 7d**

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (100 mg, 0.33 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (83 mg, 0.39 mmol), *n*-butyllithium (1.4 M in hexane, 250 µl, 0.39 mmol) and isobutyraldehyde (48 mg, 60 µl, 0.66 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 2 : 3 to 3 : 2) to give the *hydroxyphosphine oxide* **7d** (77 mg, 62%) as a colourless gum; $R_f$(EtOAc) 0.55; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500–3200 (br, OH), 1437 (P–Ph) and 1159 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.95–7.85 (2H, m, $Ph_2PO$), 7.75–7.65 (2H, m, $Ph_2PO$), 7.65–7.40 (6H, m, $Ph_2PO$ and Ph), 7.37–7.23 (5H, m, $Ph_2PO$ and Ph), 6.83 (1H, d, *J* 23, CHPh), 4.65* (1H, d, *J* 10.5, OH), 4.46 (1H, dt, *J* 23 and 10.5, C*H*OH), 2.10–2.00 (1H, m, C*H*$Me_2$), 0.98 (3H, d, *J* 6.5, Me) and 0.46 (3H, d, *J* 6.5, Me); $\delta_C$(100 MHz; $CDCl_3$) 144.5$^+$ (d, *J* 12.5, *C*HPh), 139–128 ($Ph_2PO$, Ph and $Ph_2PO$-*C*), 78.0$^+$ (d, *J* 5.5, CHOH), 34.0$^+$ (*C*H$Me_2$), 19.9$^+$ (Me) and 19.8$^+$ (Me); *m*/*z* (EI) 376 (1%, $M^+$), 333 (100, M − $^iPr$) and 201 (43, $Ph_2PO$) (Found: $M^+$, 376.1579. $C_{24}H_{24}O_2P$ requires *M*, 376.1592). Chiral HPLC analysis (70 : 30 isohexane–IPA, $\tau_1$ 7.5 min, $\tau_2$ 10.0 min) of this material showed an enantiomeric excess of 0%.

**(*E*)-2-Diphenylphosphinoyl-3-hydroxy-1-phenyldec-1-ene 7e**

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethylene[14] **6a** (100 mg, 0.33 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (83 mg, 0.39 mmol), *n*-butyllithium (1.4 M in hexane, 250 µl, 0.39 mmol) and octanal (84 mg, 103 µl, 0.66 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 2 : 3 to 2 : 1) to give the *hydroxyphosphine oxide* **7e** (47 mg, 33%) as a colourless gum; $R_f$(EtOAc) 0.60; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500–3200 (br, OH), 1437 (P–Ph) and 1158 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.90–7.80 (2H, m, $Ph_2PO$), 7.73–7.65 (2H, m, $Ph_2PO$), 7.63–7.43 (6H, m, $Ph_2PO$ and Ph), 7.37–7.18 (5H, m, $Ph_2PO$ and Ph), 6.69 (1H, d, *J* 22.5, CHPh), 4.95–4.80 (1H, m, C*H*OH), 4.60* (1H, d, *J* 10.5, OH), 1.95–1.80 (1H, m, $CH_2$), 1.61–1.50 (1H, m, $CH_2$), 1.44–1.32 (1H, m, $CH_2$), 1.25–0.95 (9H, m, $CH_2$) and 0.83 (3H, t, *J* 7, Me); $\delta_C$(100 MHz; $CDCl_3$) 140.8$^+$ (d, *J* 12.5, *C*HPh), 136–126 ($Ph_2PO$, Ph and $Ph_2PO$-*C*), 69.9 (d, *J* 5, CHOH), 51.4$^-$, 35.7$^-$, 29.8$^-$, 27.1$^-$, 24.1$^-$, 20.6$^-$ (6 × $CH_2$) and 12.1$^+$ (Me); *m*/*z* (EI) 432 (1%, $M^+$), 333 (100, M − $C_7H_{15}$) and 201 (31, $Ph_2PO$) (Found: $M^+$, 432.2225. $C_{28}H_{33}O_2P$ requires *M*, 432.2218). Chiral HPLC analysis (85 : 15 isohexane–EtOH, $\tau_1$ 24.2 min, $\tau_2$ 32.4 min) of this material showed an enantiomeric excess of 0%.

**3,3-Dimethyl-1-diphenylphosphinoylbutan-2-ol**

*n*-Butyllithium (1.4 M in hexane, 50.9 $cm^3$) was added to a stirred solution of the methyldiphenylphosphine oxide (14.0 g, 65 mmol) in dry THF (400 $cm^3$) at −78 °C. The orange solution was stirred for 30 minutes and pivalaldehyde (6.69 g, 8.5 $cm^3$, 77 mmol) was added. The reaction mixture was stirred at −78 °C for 30 minutes and allowed to warm to room temperature over 1 hour. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (20 $cm^3$). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 30 $cm^3$). The combined organic extracts were washed with brine (50 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude β-hydroxyphosphine oxide. The crude product was recrystallised from EtOAc–hexane to give the hydroxyphosphine oxide (17.25 g, 88%) as needles, mp 142–143 °C (from EtOAc–hexane) (lit.,[34] 137–138 °C from toluene–petroleum ether), which has previously been reported[34] with incomplete data; $R_f$(EtOAc) 0.37; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500–3200 (br, OH), 1438 (P–Ph) and 1151 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.80–7.66 (4H, m, $Ph_2PO$), 7.57–7.42 (6H, m, $Ph_2PO$), 4.36* (1H, s, OH), 3.67 (1H, br t, *J* 10.5, C*H*OH), 2.44–2.23 (2H, m, $CH_2$) and 0.88 (9H, s, $CMe_3$); $\delta_C$(100 MHz; $CDCl_3$) 134.1$^-$ (d, *J* 100, *ipso*-$Ph_2PO$), 132.4$^+$ (*para*-$Ph_2PO$), 132.4$^+$ (*para*-$Ph_2PO$), 132.0$^-$ (d, *J* 97, *ipso*-$Ph_2PO$), 131.4$^+$ (d, *J* 9, *ortho*-$Ph_2PO$), 130.8$^+$ (d, *J* 9.5, *ortho*-$Ph_2PO$), 129.2$^+$ (d, *J* 11.5, *meta*-$Ph_2PO$), 129.1$^+$ (d, *J* 12, *meta*-$Ph_2PO$), 74.6$^+$ (d, *J* 5, CHOH), 35.5$^-$ (d, *J* 12, *C*$Me_3$), 31.5$^-$ (d, *J* 72, $CH_2$) and 28.8$^+$ (C*Me*$_3$); *m*/*z* (LSIMS) 303 (92%, $MH^+$), 285 (45, M − OH) and 201 (100, $Ph_2PO$) (Found: $MH^+$, 303.1488. $C_{18}H_{24}O_2P$ requires *M*, 303.1498).

**(*E*)-3,3-Dimethyl-1-diphenylphosphinoylbut-1-ene 6b**

By method of Santelli-Rouvier,[14] 3,3-dimethyl-1-diphenylphosphinoylbutan-2-ol (15.0 g, 50 mmol), pyridine (5.10 g, 5.4 $cm^3$, 65 mmol), trimethylsilyl chloride (5.94 g, 6.9 $cm^3$, 55 mmol) and sodium hydride (60% dispersion in mineral oil, 2.19 g, 55 mmol) gave a crude product that was recrystallised (EtOAc–hexane) to give the *unsaturated phosphine oxide* **6b** (9.25 g, 65%) as prisms, mp 161–162 °C (from EtOAc–hexane); $R_f$(EtOAc) 0.33; $\nu_{max}(CHCl_3)/cm^{-1}$ 1438 (P–Ph) and 1176 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.72–7.63 (4H, m, $Ph_2PO$), 7.53–7.40 (6H, m, $Ph_2PO$), 6.74 (1H, dd, *J* 20.5 and 17.5, $CHCMe_3$), 6.09 (1H, dd, *J* 24.5 and 17.5, PCH) and 1.01 (9H, s, $CMe_3$); $\delta_C$(100 MHz; $CDCl_3$) 160.4$^+$ *C*H$CMe_3$), 131.6$^-$ (d, *J* 104, *ipso*-Ph), 129.7$^+$ (d, *J* 1.5, *para*-Ph), 129.4$^+$ (d, *J* 10, *ortho*-Ph), 126.6$^+$ (d, *J* 12, *meta*-Ph), 114.6$^+$ (d, *J* 103.5, $Ph_2PO$-*C*), 33.4$^-$ (d, *J* 15, *C*$Me_3$) and 26.8$^+$ (C*Me*$_3$); *m*/*z* (FAB) 285 (100%, $MH^+$), 201 (6, $Ph_2PO$) (Found: $MH^+$, 285.1390. $C_{18}H_{22}OP$ requires *M*, 285.1403) (Found: C, 75.8; H, 7.5; P, 11.0. $C_{18}H_{21}OP$ requires C, 76.0; H, 7.4; P, 10.9%).

**(*E*)-4-Diphenylphosphinoyl-3-hydroxy-2,2,6,6-tetramethylhept-4-ene 8a**

By the general method, (*E*)-3,3-dimethyl-1-diphenylphosphinoylbut-1-ene **6b** (1.42 g, 5.0 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (1.27 g, 6.0 mmol), *n*-butyllithium (1.4 M in hexane, 3.9 $cm^3$, 5.5 mmol) and pivalaldehyde (0.86 g, 1.1 $cm^3$, 10 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 2 : 3 to 3 : 2) to give the *vinyl phosphine oxide* **8a** (1.08 g, 58%) as needles, mp 142–144 °C (from dichloromethane–hexane); $[\alpha]_D$ −79 (*c*. 0.86 in $CHCl_3$); $R_f$(EtOAc) 0.63; $\nu_{max}(CHCl_3)/cm^{-1}$ 3550–3200 (br, OH), 1437 (P–Ph) and 1156 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.87–7.80 (2H, m, $Ph_2PO$), 7.64–7.32 (8H, m, $Ph_2PO$), 5.74* (1H, d, *J* 1.5, OH), 5.72 (1H, d,

*J* 37, C=C*H*), 4.96 (1H, dd, *J* 27.5 and 10.5, C*H*OH), 1.12 (9H, s, $CMe_3$) and 0.90 (9H, s, $CMe_3$); $\delta_C$(125 MHz; $CDCl_3$) 157.9$^+$ (d, *J* 10.5, $Ph_2PO$-C*C*H), 136.7$^-$ (d, *J* 104, *ipso*-$Ph_2PO$), 131.9$^+$ (*para*-$Ph_2PO$), 131.8$^+$ (d, *J* 9, *ortho*-$Ph_2PO$), 131.6$^+$ (d, *J* 9.5, *ortho*-$Ph_2PO$), 131.5$^+$ (*para*-$Ph_2PO$), 131.1$^-$ (d, *J* 99, $Ph_2PO$-*C*), 130.4$^-$ (d, *J* 103, *ipso*-$Ph_2PO$), 128.5$^+$ (d, *J* 11.5, *meta*-$Ph_2PO$), 128.2$^+$ (d, *J* 12, *meta*-$Ph_2PO$), 77.9$^+$ (d, *J* 5.5, CHOH), 36.5$^+$ (d, *J* 17, C=CH*C*$Me_3$), 36.3$^-$ (*C*$Me_3$), 30.7$^+$ and 27.6$^+$ (C*Me*$_3$); *m*/*z* (LSIMS) 271 (42%, MH$^+$), 353 (100, M − OH), 313 (15, M − $CMe_3$) and 201 (79, $Ph_2PO$) (Found: MH$^+$, 371.2149. $C_{23}H_{32}O_2P$ requires *M*, 371.2124) (Found: C, 74.5; H, 8.5; P, 8.5. $C_{23}H_{31}O_2P$ requires C, 74.6; H, 8.4; P, 8.4%). Chiral HPLC analysis (90 : 10 isohexane–IPA, $\tau_{major}$ 9.1 min, $\tau_{minor}$ 19.6 min) of this material showed an enantiomeric excess of 51%.

### (*E*)-4-Diphenylphosphinoyl-3-hydroxy-2,2,6-trimethylhept-4-ene 8b

By the general method, (*E*)-1-diphenylphosphinoyl-3-methylbutene[10] (100 mg, 0.37 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (94 mg, 0.44 mmol), *n*-butyllithium (1.4 M in hexane, 290 µl, 0.41 mmol) and pivalaldehyde (63 mg, 81 µl, 0.74 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 2 : 1) to give the *hydroxyphosphine oxide* **8b** (70 mg, 53%) as a colourless gum; $[\alpha]_D$ −15 (*c*. 0.84 in $CHCl_3$); $R_f$(EtOAc) 0.50; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3500–3100 (br, OH), 1614 (C=C), 1437 (P–Ph) and 1155 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.82–7.74 (2H, m, $Ph_2PO$), 7.62–7.43 (6H, m, $Ph_2PO$), 7.40–7.34 (2H, m, $Ph_2PO$), 5.73* (1H, br d, *J* 10, OH), 5.61 (1H, ddd, *J* 24, 10.5 and 0.5, C=CH), 4.53 (1H, dd, *J* 23 and 10, C*H*OH), 2.89–2.75 (1H, m, $CHMe_2$), 0.97 (3H, d, *J* 6.5, Me), 0.90 (3H, d, *J* 6.5, Me) and 0.88 (9H, s, $CMe_3$); $\delta_C$(100 MHz; $CDCl_3$) 154.9$^+$ (d, *J*, C=*C*H), 134.4$^-$ (d, *J* 103.5, *ipso*-Ph), 131–130 (m, *ortho*- and *para*-Ph), 130.1$^-$ (d, *J* 98.5, *ipso*-Ph), 127.9$^-$ (d, *J* 91, $Ph_2PO$-*C*), 127.1$^+$ (d, *J* 12, *meta*-Ph), 126.8$^+$ (d, *J* 12, *meta*-Ph), 79.6$^+$ (d, *J* 5.5, CHOH), 35.2$^-$ (*C*$Me_3$), 27.2$^+$ (*C*H$Me_2$), 25.4$^+$ (C*Me*$_3$), 20.3$^+$ (Me) and 20.0$^+$ (Me); *m*/*z* (LSIMS) 357 (100%, MH$^+$), 339 (8, M − OH) (Found: MH$^+$, 357.1983. $C_{22}H_{30}O_2P$ requires *M*, 357.1978). Chiral HPLC analysis (90 : 10 isohexane : IPA, $\tau_{major}$ 8.1 min, $\tau_{minor}$ 6.7 min) of this material showed an enantiomeric excess of 12%.

### (*E*)-5,5-Dimethyl-3-diphenylphosphinoyl-4-hydroxyhex-2-ene 8c

By the general method, (*E*)-1-diphenylphosphinoylprop-1-ene **6d** (300 mg, 1.23 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (253 mg, 1.2 mmol), *n*-butyllithium (1.4 M in hexane, 785 µl, 1.1 mmol) and pivalaldehyde (172 mg, 220 µl, 2 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1) to give the *hydroxyphosphine oxide* **8c** (1.99 mg, 47.5%) as white plates, mp 174–176 °C (from EtOAc–hexane); $R_f$(EtOAc) 0.56; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3600–3200 (br, OH), 1437 (Ph-P), 1218 (P=O); $\delta_H$(500 MHz; $CDCl_3$) 7.77 (2H, ddt, *J* 11.5, 7 and 1.5, Ph), 7.58 (1H, tq, *J* 7.5 and 1.5, Ph), 7.54–7.45 (5H, m, Ph), 7.39 (2H, dtd, *J* 7.5, 3 and 1.5, Ph), 6.03 (1H, dqd, *J* 23.5, 7 and 1, C*H*$CH_3$), 5.69* (1H, d, *J* 10, OH), 4.55 (1H, ddd, *J* 22.5, 10 and 1, C*H*OH), 1.85 (3H, dd, *J* 7 and 3.3, Me), 0.90 (9H, s, $Me_3$); $\delta_C$(125 MHz; $CDCl_3$) 144.2$^+$ (d, *J* 12, *C*HMe), 135.5$^-$ (d, *J* 103, *ipso*-Ph), 134.2$^-$ (d, *J* 93, *ipso*-Ph), 131.9–131.6$^+$ (m, *ortho*- and *para*-Ph), 131.7$^-$ (d, *J* 99, $Ph_2PO$-*C*), 128.4$^+$ (d, *J* 25.5, *meta*-Ph), 128.4$^+$ (d, *J* 25.8, *meta*-Ph), 80.4$^+$ (d, *J* 5.4, COH), 37.7$^-$ (*C*$Me_3$), 26.8$^+$ (C*Me*$_3$), 16.0$^+$ (d, *J* 16.5, Me). Chiral HPLC analysis (80 : 20 isohexane–IPA, $\tau_{major}$ 21.7 min, $\tau_{minor}$ 14.3 min) of this material showed an enantiomeric excess of 11%.

### 4,4-Dimethyl-2-diphenylphosphinoyl-3-hydroxypent-1-ene 8d

By the general method, vinyldiphenylphosphine oxide[35] **6e** (228 mg, 1 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (253 mg, 1.2 mmol), *n*-butyllithium (1.4 M in hexane, 785 µl, 1.1 mmol) and pivalaldehyde (172 mg, 220 µl, 2 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 2 : 3 to 3 : 2) to give the *hydroxyphosphine oxide* **8d** (122 mg, 39%) as prisms, mp 179–180 °C (from EtOAc–hexane); $R_f$(EtOAc) 0.35; $\tau_{max}$($CHCl_3$)/cm$^{-1}$ 3600–3100 (br, OH), 1438 (P–Ph) and 1166 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.77–7.70 (2H, m, $Ph_2PO$), 7.68–7.60 (2H, m, $Ph_2PO$), 7.60–7.40 (6H, m, $Ph_2PO$), 6.08 (1H, d, *J* 43.5, $CH_{cis}H_{trans}$), 5.51 (1H, d, *J* 21, $CH_{cis}H_{trans}$), 4.34* (1H, d, *J* 8, OH), 4.20 (1H, dd, *J* 15 and 8, C*H*OH) and 0.91 (9H, s, $CMe_3$); $\delta_C$(100 MHz; $CDCl_3$) 151.4$^-$ (d, *J* 89.5, $Ph_2PO$-*C*), 141–136 (m, $Ph_2PO$ and $CH_2$), 91.0$^+$ (CHOH), 44.0$^-$ (*C*$Me_3$) and 34.1$^+$ (C*Me*$_3$); *m*/*z* (FAB) 315 (15%, MH$^+$) (Found: MH$^+$, 315.1518. $C_{19}H_{24}O_2P$ requires *M*, 315.1514) (Found: C, 72.5; H, 7.3; P, 10.1. $C_{19}H_{23}O_2P$ requires C, 72.6; H, 7.4; P, 9.9%). Chiral HPLC analysis (90 : 10 isohexane–IPA, $\tau_{major}$ 16.5 min, $\tau_{minor}$ 14.2 min) of this material showed an enantiomeric excess of 5%.

**(1′*R*)-*N*-Benzyl-*N*-(1′-methylbenzyl)-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxypentylamine 9.** Compound **9** was also isolated (as a 1.9 : 1 mixture of diastereoisomers). Colourless gum (64 mg, 12%), 1.9 : 1 mixture of diastereoisomers, $R_f$(EtOAc) 0.57; $\nu_{max}$($CHCl_3$)/cm$^{-1}$ 3500–3300 (br, OH), 1438 (P–Ph), 1158 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.83–7.07 (18H$_{major}$ and 18H$_{minor}$, m, Ph), 7.05 (2H$_{minor}$, br d, *J* 7.5, Ph), 7.00 (2H$_{major}$, br d, *J* 7, Ph), 3.76–3.60 (2H$_{major}$ and 2H$_{minor}$, m, C*H*Me and C*H*OH), 3.49 (1H$_{minor}$, d, *J* 15, $NCH_2$), 3.39 (1H$_{major}$, d, *J* 15, $NCH_2$), 3.31–3.15 (3H$_{major}$ and 2H$_{minor}$, m, $NCH_2$), 3.00–2.90 (1H$_{minor}$, m, $NCH_2$), 2.77–2.57 (1H$_{major}$ and 1H$_{minor}$, m, PCH), 1.12 (3H$_{minor}$, d, *J* 7, CH*Me*), 0.98 (3H$_{major}$, d, *J* 7, CH*Me*), 0.80 (9H$_{minor}$, s, C*Me*$_3$) and 0.71 (9H$_{major}$, s, C*Me*$_3$), no OH peaks observed; $\delta_C$(100 MHz; $CDCl_3$) 138.8$^-$ ($Ph_{major}$), 138.7$^-$ ($Ph_{minor}$), 138.2$^-$ ($Ph_{major}$), 137.4$^-$ ($Ph_{minor}$) and 132–122 (m, $Ph_{major}$ and $Ph_{minor}$), 75.3$^+$ ($C_{minor}$HOH), 74.8$^+$ ($C_{major}$HOH), 58.4$^+$ (N*C*$_{minor}$HMe), 57.2$^+$ (N*C*$_{major}$HMe), 52.4$^-$ (N*C*$_{major}$-$H_2$Ph), 51.8 (N*C*$_{minor}H_2$Ph), 44.6$^-$ (CH*C*$_{minor}H_2$N), 42.7$^-$ (CH*C*$_{major}H_2$N), 35.8$^+$ (d, *J* 68.5, PC$_{minor}$H), 35.5$^+$ (d, *J* 68.5, PC$_{major}$H), 34.3$^+$ and 34.3$^+$ (*C*$_{major}$Me$_3$ and *C*$_{minor}$Me$_3$), 24.9$^+$ and 24.9$^+$ (C*Me*$_{3\ major}$ and C*Me*$_{3\ minor}$), 17.2$^+$ (Me$_{minor}$) and 11.5$^+$ (Me$_{major}$); *m*/*z* (LSIMS) 526 (73%, MH$^+$), 422 (44, M − CHMePh), 340 (100, M − $CH_2$Ph − Ph − OH), 303 (41, M − $CH_2$NBn(CHMePh)) and 201 (46, $Ph_2PO$) (Found: MH$^+$, 526.2858. $C_{34}H_{41}NO_2P$ requires *M*, 526.2859).

### [$^2H_3$]Methyldiphenylphosphine oxide

Chlorodiphenylphosphine (11.03g, 50 mmol) in dry ether (25 cm$^3$) was added slowly to a solution of [$^2H_3$]methylmagnesium iodide (1.0 M in ether, 50 cm$^3$, 50 mmol), at 0 °C. The reaction mixture was stirred for 2h, warming to room temperature. Water (40 cm$^3$) was slowly added and the layers were separated. The aqueous layer was washed with dichloromethane (3 × 30 cm$^3$), the combined organic extracts were washed with brine (100 cm$^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was dissolved in dichloromethane (40 cm$^3$) and aqueous hydrogen peroxide was added dropwise until no further temperature rise was observed. Water (20 cm$^3$) was added, the layers were separated and the aqueous layer was washed with dichloromethane (3 × 30 cm$^3$). The combined organic extracts were washed with brine (50 cm$^3$), dried ($MgSO_4$) and evaporated under reduced pressure to give the deuterated phosphine oxide (9.90 g, 90%) as needles, mp 111–112 °C (from EtOAc–hexane) whose data matched those previously reported.[36]

### 2,2-Dideuterio-2-diphenylphosphinoyl-1-phenylethanol

In a similar way to the synthesis of 3,3-dimethyl-1-diphenylphosphinoylbutan-2-ol, [$^2H_3$]methyldiphenylphosphine oxide (6.60 g, 30 mmol), benzaldehyde (3.82g, 3.6 cm$^3$, 36 mmol) and *n*-butyllithium (1.4 M in hexane, 23.6 cm$^3$, 33 mmol) gave

a crude product that was recrystallised from dichloromethane–hexane to give the *hydroxyphosphine oxide* (6.16 g, 63%) as prisms, mp 142–143 °C (from dichloromethane–hexane); $R_f$(EtOAc) 0.35; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 3600–3200 (br, OH), 1437 (P–Ph) and 1168 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.80–7.75 (2H, m, $Ph_2PO$), 7.70–7.65 (2H, m, $Ph_2PO$), 7.54–7.42 (6H, $Ph_2PO$ and Ph), 7.34–7.20 (5H, m, $Ph_2PO$ and Ph), 5.16 (1H, d, *J* 9, C*H*OH) and 5.02* (1H, d, *J* 1.5, OH); $\delta_C$(100 MHz; $CDCl_3$) $143.8^-$ (d, *J* 13.5, *ipso*-Ph), 134–125 ($Ph_2PO$ and Ph), $69.1^+$ (d, *J* 4, CHOH) and $38.7^-$ (m, $CD_2$); *m*/*z* (LSIMS) 325 (42%, $MH^+$), 307 (35, M − OH), 201 (100, $Ph_2PO$) (Found: $MH^+$, 325.1313. $C_{20}H_{18}D_2O_2P$ requires *M*, 325.1310).

### (*E*)-1-Deuterio-1-diphenylphosphinoyl-2-phenylethene 10

By the method of Santelli-Rouvier,[14] 2,2-dideuterio-2-diphenylphosphinoyl-1-phenylethanol (4.1 g, 12.7 mmol), pyridine (1.30 g, 1.4 $cm^3$, 16.5 mmol), trimethylsilyl chloride (1.51 g, 1.7 $cm^3$, 14.0 mmol) and sodium hydride (60% dispersion in mineral oil, 335 mg, 13.9 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc) to give the *unsaturated phosphine oxide* **10** (10.10 g, 71%) as needles. The deuterium content on the α-position was approximately 80% by NMR; $R_f$(EtOAc) 0.36; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1439 (P–Ph) and 1175, (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.80–7.70 (4H, m, $Ph_2PO$), 7.60–7.30 (12H, m, Ph, $Ph_2PO$ and C*H*Ph) and 6.83 (0.2H, dd, *J* 22.5 and 17.5, PCH); $\delta_C$(100 MHz; $CDCl_3$) $147.5^+$ (d, *J* 3.5, *C*HPh), $135.1^-$ (d, *J* 17.5, *ipso*-Ph), $133.0^-$ (d, *J* 105, *ipso*-$Ph_2PO$), $131.9^+$ (d, *J* 2.5, *para*-$Ph_2PO$), $131.4^+$ (d, *J* 10, *ortho*-$Ph_2PO$), $130.1^+$ (Ph), $128.9^+$ (Ph), $128.6^+$ (d, *J* 12, *meta*-$Ph_2PO$), $127.8^+$ (Ph), $119.3^+$ (d, *J* 104, PCD); *m*/*z* (EI) 305 (100%, $M^+$), 228 (19, M − Ph), 202 (58, $Ph_2PO$), 153 (74, M − 2 × Ph), 136 (47, PCDCHPh) (Found: $MH^+$, 305.1072. $C_{20}H_{18}D_2O_2P$ requires *M*, 305.1079).

### (*E*)-1,3-Diphenyl-2-diphenylphosphinoyl-1-phenylsulfonylaminoprop-1-ene 13

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene[14] **6a** (200 mg, 0.66 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (164 mg, 0.79 mmol), *n*-butyllithium (1.4 M in hexane, 520 μl, 0.72 mmol) and *N*-benzylidenebenzenesulfonamide[37] **12** (322 mg, 1.32 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 1 : 0) to give the *aminophosphine oxide* **13** (160 mg, 44%) as needles, mp 162–164 °C (from EtOAc–hexane); $R_f$(EtOAc) 0.65; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 3233 (NH), 1437 (P–Ph), 1331 ($SO_2$) and 1162 (P=O and $SO_2$); $\delta_H$(400 MHz; $CDCl_3$) 8.20* (1H, d, *J*, 9.5, NH), 7.65–6.80 (25H, m, $PhSO_2$, 2 × Ph and $Ph_2PO$), 6.74 (1H, d, 20.5, C=CH) and 6.33 (1H, dd, *J* 22.6 and 9.5, CHN); $\delta_C$(100 MHz; $CDCl_3$) 143–125 (m, $PhSO_2$, 2 × Ph, $Ph_2PO$, CHPh and $Ph_2PO$-*C*) and $55.9^+$ (d, *J* 6, CHN); *m*/*z* (FAB) 550 (29%, $MH^+$) 408 (15, M − $PhSO_2$), 393 (35, M − $PhSO_2NH$), 201 (55, $Ph_2PO$), 154 (100, PhCHNHSO) and 136 (81, PhCHNHS) (Found: $MH^+$, 550.1610. $C_{33}H_{29}O_3NPS$ requires *M*, 550.1606). Chiral HPLC analysis (50 : 50 isohexane–IPA, $\tau_{major}$ 9.5 min, $\tau_{minor}$ 11.7 min) of this material showed an enantiomeric excess of 5%.

### 2,2-Dimethyl-3-(4-methoxybenzoyloxy)propanal 16

Oxalyl chloride (0.83 g, 570 μl, 6.5 mmol) in dry dichloromethane (5 $cm^3$) was added to a solution of dry dimethyl sulfoxide (1.2 g, 5 mmol) in dry dichloromethane (30 $cm^3$) at −78 °C. After 30 minutes 2,2-dimethyl-3-hydroxypropyl 4-methoxybenzoate[21] **15** (1.2 g, 5 mmol) in dry dichloromethane (15 $cm^3$) was added and the reaction was stirred for a further 30 minutes. Triethylamine (3.06 g, 4.2 $cm^3$, 30 mmol) was added and the reaction was allowed to warm to room temperature over 22 hours. Water (100 $cm^3$) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 50 $cm^3$), the combined organic extracts were washed with water (100 $cm^3$), brine (100 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by Kugelrohr distillation (oven temperature 145 °C, 0.1 mmHg) to give the *aldehyde* **16** (1.17 g, 98%) as a pale yellow oil; $\nu_{max}$(liquid film)/$cm^{-1}$ 2971, 2839, 2713 (CH), 1713 (br, 2 × C=O), 1607 and 1512 ($C_6H_4OMe$); $\delta_H$(400 MHz; $CDCl_3$) 9.59 (1H, s, CHO), 7.89 (2H, br d, *J* 9, *meta*-$C_6H_4OMe$), 6.86 (2H, br d, *J* 9, *ortho*-$C_6H_4OMe$), 4.29 (2H, s, $CH_2$), 3.75 (3H, s, OMe) and 1.16 (6H, s, 2 × Me); $\delta_C$(100 MHz; $CDCl_3$) $201^+$ (CHO), $163.8^-$ and $161.5^-$ (*para*-$C_6H_4OMe$ and C=O), $129.5^+$ (*ortho*-$C_6H_4OMe$), $119.9^-$ (*ipso*-$C_6H_4OMe$), $111.6^+$ (*meta*-$C_6H_4OMe$), $66.0^-$ ($CH_2$), $53.3^+$ (OMe), $44.5^-$ (*C*$Me_2$) and $16.8^+$ (C*Me*$_2$); *m*/*z* (ESI) 259 (95%, $MNa^+$) (Found: $MNa^+$, 259.0936. $C_{13}H_{16}O_4Na$ requires *M*, 259.0946).

### (*E*)-4,4-Dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpent-1-en-5-yl 4-methoxybenzoate 18

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene **6a** (575 mg, 1.9 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (480 mg, 2.3 mmol), *n*-butyllithium (1.4 M in hexane, 1.5 $cm^3$, 2.1 mmol) and 2,2-dimethyl-3-(4-methoxybenzoyloxy)propanal **16** (670 mg, 2.83 mmol) gave a crude product that was chromatographed ($SiO_2$, EtOAc–hexane, 1 : 1 to 1 : 0) to give the *hydroxyphosphine oxide* **18** (470 mg, 46%) as needles, mp 153–154 °C (from dichloromethane–hexane); $[\alpha]_D$ −22 (*c*. 0.73 in $CHCl_3$); $R_f$(EtOAc) 0.54; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 3200–3500 (br, OH), 1707 (C=O), 1437 (P–Ph), 1168 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.97–7.88 (2H, m, $Ph_2PO$), 7.70–7.61 (7H, m, $Ph_2PO$, Ph and *meta*-$C_6H_4OMe$), 7.53–7.40 (3H, m, $Ph_2PO$ and Ph), 7.30–7.19 (5H, m, $Ph_2PO$ and Ph), 6.95 (1H, d, *J* 23.5, C*H*Ph), 6.82 (2H, br d, *J* 9, *ortho*-$C_6H_4OMe$), 5.74* (1H, d, *J* 10.5, OH), 5.39 (1H, ddd, *J* 23.5, 10.5 and 1, C*H*OH), 4.19 (1H, d, *J* 11, C$H_{AH}$B), 3.85 (3H, s, OMe), 3.83 (1H, d, *J* 11, $CH_AH_B$), 0.94 (3H, s, Me) and 0.70 (3H, s, Me); $\delta_C$(100 MHz; $CDCl_3$) $165.6^-$ and $162.7^-$ (*para*-$C_6H_4OMe$ and C=O), $147.0^+$ (d, *J* 12.5, *C*HPh), 136–127 (m, $Ph_2PO$, Ph, *ortho*-$C_6H_4OMe$ and $Ph_2PO$-*C*), $122.5^-$ (*ipso*-$C_6H_4OMe$), $113.0^+$ (*meta*-$C_6H_4OMe$), $74.7^+$ (d, *J* 4.5, CHOH), $70.1^-$ ($CH_2$), $55.0^+$ (OMe), $40.5^-$ (*C*$Me_2$), $22.3^+$ (Me) and $20.9^+$ (Me); *m*/*z* (LSIMS) 541 (57%, $MH^+$), 523 (100, M − OH), 333 (57, M − $CMe_2CH_2O$-COAr), 201 (95, $Ph_2PO$) (Found: $MH^+$, 541.2137. $C_{33}H_{34}O_5P$ requires *M*, 541.2128) (Found: C, 73.1; H, 6.2; P, 5.9. $C_{33}H_{33}O_5P$ requires C, 73.3; H, 6.15; P, 5.9%). Chiral HPLC analysis (70 : 30 isohexane–IPA, $\tau_{major}$ 14.4 min, $\tau_{minor}$ 44.9 min) of this material showed an enantiomeric excess of 18%.

**(*E*)-4,4-Dimethyl-5-hydroxy-2-diphenylphosphinoyl-1-phenylpent-1-en-3-yl 4-methoxybenzoate 19.** Compound **19** was also isolated. Amorphous white solid (300 mg, 30%), $[\alpha]_D$ −36 (*c*. 1.0 in $CHCl_3$); $R_f$(EtOAc) 0.42; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 3100–3500 (br, OH), 1712 (C=O), 1438 (P–Ph) and 1166 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.70–7.07 (17H, m, $Ph_2PO$, Ph and *meta*-$C_6H_4OMe$), 6.85 (1H, d, *J* 23.5, C*H*Ph), 6.73 (2H, br d, *J* 9, *ortho*-$C_6H_4OMe$), 6.72 (1H, d, *J* 17.1, C*H*OCOAr), 6.51* (t, *J* 7.5, $CH_2OH$), 3.82 (3H, s, OMe), 3.67 (2H, d, *J* 7.5, $CH_2OH$), 0.84 (3H, s, Me) and 0.55 (3H, s, Me); $\delta_C$(100 MHz; $CDCl_3$) $166.0^-$ and $163.6^-$ (*para*-$C_6H_4OMe$ and C=O), $147.8^+$ (d, *J* 12.5, *C*HPh), 137–128 (m, $Ph_2PO$, Ph, *ortho*-$C_6H_4OMe$ and $Ph_2PO$-*C*), $121.8^-$ (*ipso*-$C_6H_4OMe$), $113.4^+$ (*meta*-$C_6H_4OMe$), $77.7^+$ (*C*HOC=O), $68.0^-$ ($CH_2$), $55.8^+$ (OMe), $44.1^-$ (*C*$Me_2$), $24.0^+$ (Me) and $23.0^+$ (Me); *m*/*z* (LSIMS) 541 (68%, $MH^+$), 389 (55, M − OCOAr), 201 (100, $Ph_2PO$) (Found: $MH^+$, 541.2127. $C_{33}H_{34}O_5P$ requires *M*, 541.2128). Chiral HPLC analysis (50 : 50 isohexane–IPA, $\tau_{major}$ 6.8 min, $\tau_{minor}$ 18.2 min) of this material showed an enantiomeric excess of 13%.

### (*E*)-4,4-Dimethyl-3,5-dihydroxy-2-diphenylphosphinoyl-1-phenylpent-1-ene 17

Lithium hydroxide (135 mg, 3.1 mmol) was added to a solution

of (*E*)-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpent-1-en-5-yl 4-methoxybenzoate **18** (830 mg, 1.5 mmol, 18% ee) in methanol (20 $cm^3$). The reaction was stirred for 23 hours and the solvent was evaporated under reduced pressure. The residue was dissolved in dichloromethane–water (1 : 1, 40 $cm^3$) and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 $cm^3$), the combined organic extracts were washed with brine (50 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure to give *diol* **17** (582 mg, 92%) as prisms, mp 157–158 °C (from EtOAc–hexane); $[\alpha]_D$ −35 (*c*. 0.96 in $CHCl_3$); $R_f$(EtOAc) 0.41; $\nu_{max}(CHCl_3)/cm^{-1}$ 3600–3000 (br, OH), 1437 (P–Ph) and 1153 (P=O); $\delta_H$(400 MHz; $CDCl_3$) 7.87–7.80 (2H, m, $Ph_2PO$), 7.73–7.67 (2H, m, $Ph_2PO$), 7.60–7.48 (6H, m, $Ph_2PO$ and Ph), 7.36–7.20 (5H, m, $Ph_2PO$ and Ph), 6.85 (1H, d, *J* 24.5, C*H*Ph), 5.72* (1H, t, *J* 6.5, $CH_2OH$), 5.22 (1H, dd, *J* 20.5 and 9.5, C*H*OH), 4.61* (1H, br d, *J* 9.5, CHO*H*), 3.82 (1H, dd, *J* 12 and 7, $CH_AH_B$), 3.32 (1H, dd, *J* 12 and 6, $CH_AH_B$), 0.97 (3H, s, Me) and 0.48 (3H, s, Me); $\delta_C$(100 MHz; $CDCl_3$) 145.8$^+$ (d, *J* 12.5, *C*HPh), 138–127 (m, $Ph_2PO$, Ph and $Ph_2PO$-*C*), 78.2$^+$ (CHOH), 69.3$^-$ ($CH_2OH$), 41.4$^-$ ($CMe_2$), 23.1$^+$ (Me) and 22.0$^+$ (Me); *m*/*z* (ESI) 429 (100%, $MNa^+$), 407 (92, $MH^+$) (Found: $MH^+$, 407.1777. $C_{25}H_{28}O_3P$ requires *M*, 407.1776) (Found: C, 73.9; H, 6.7; P, 7.7. $C_{25}H_{28}O_3P$ requires C, 73.9; H, 6.7; P, 7.6%).

### Derivatisation of diol 17; (*E*)-5-[(*S*)-(camphor-10-sulfonyl)oxy]-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpent-1-ene

Triethylamine (5 drops) and catalytic DMAP were added to a solution of (*E*)-4,4-dimethyl-3,5-dihydroxy-2-diphenylphosphinoyl-1-phenylpent-1-ene **17** (100 mg, 0.25 mmol, 10% ee) in dichloromethane (10 $cm^3$). (1*S*)-(+)-Camphor-10-sulfonyl chloride (74 mg, 0.30 mmol) was added and the reaction mixture was stirred for 20 hours. Water (20 $cm^3$) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 $cm^3$), the combined organic extracts were washed with brine (50 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product. The residue was chromatographed ($SiO_2$, EtOAc–dichloromethane, 1 : 1) to give a mixture of diastereoisomers of the *camphor derived phosphine oxide* (128 mg, 84%) as a colourless gum. $R_f$(EtOAc) 0.63; $\nu_{max}(CDCl_3)/cm^{-1}$ 3500–3100 (br, OH and NH), 1745 (C=O), 1438 (P–Ph), 1356 ($SO_2$) and 1163 (P=O and $SO_2$); $\delta_H$(500 MHz; $CDCl_3$) 7.97–7.90 ($2H_{major}$ and $2H_{minor}$, m, $Ph_2PO$), 7.66–7.23 ($13H_{major}$ and $13H_{minor}$, m, $Ph_2PO$ and Ph), 6.92 ($1H_{major}$, d, *J* 23.5, CHPh), 6.91 ($1H_{minor}$, d, *J* 23.5, CHPh), 5.76 ($1H_{major}$ and $1H_{minor}$, br d, *J* 10.5, OH), 5.30–5.20 ($1H_{major}$ and $1H_{minor}$, m, C*H*OH), 4.22 ($1H_{major}$ and $1H_{minor}$, d, *J* 9.5, $CH_AH_BO$), 3.81 ($1H_{minor}$, d, *J* 9.5, $CH_AH_BO$), 3.78 ($1H_{major}$, d, *J* 9.5, $CH_AH_BO$), 3.47 ($1H_{minor}$, d, *J* 15, $CH_AH_BSO_2$), 3.43 ($1H_{major}$, d, *J* 15, $CH_AH_BSO_2$), 2.92 ($1H_{major}$, d, *J* 15, $CH_AH_BSO_2$), 2.84 ($1H_{minor}$, d, *J* 15, $CH_AH_BSO_2$), 2.44–2.31 ($2H_{major}$ and $2H_{minor}$, m, camphor), 2.09–1.86 ($5H_{major}$ and $5H_{minor}$, m, camphor), 1.57 ($1H_{major}$, dd, *J* 9.5 and 4.5, camphor), 1.55 ($1H_{minor}$, dd, *J* 9.5 and 5, camphor), 1.42–1.35 ($1H_{major}$ and $1H_{minor}$, m, camphor), 1.07 ($3H_{major}$, s, $Me_AMe_BCCH_2O$), 1.06 ($3H_{minor}$, s, $Me_AMe_BCCH_2O$), 0.87 ($3H_{minor}$, s, $Me_AMe_B$ on camphor), 0.86 ($3H_{major}$, s, $Me_AMe_B$ on camphor), 0.84 ($3H_{major}$, s, $Me_AMe_B$ on camphor), 0.83 ($3H_{minor}$, s, $Me_AMe_B$ on camphor), 0.67 ($3H_{major}$, s, $Me_AMe_BCCH_2O$) and 0.66 ($3H_{minor}$, s, $Me_AMe_BCCH_2O$); $\delta_C$(125 MHz; $CDCl_3$) 214.2$^-$$_{major}$ (C=O), 214.1$^-$$_{minor}$ (C=O), 147.6$^+$$_{major}$ (d, *J* 12.5, *C*HPh), 147.5$^+$$_{minor}$ (d, *J* 12.5, *C*HPh), 136–128 (m, $Ph_2PO$, Ph and $Ph_2PO$-*C*), 76.0$^-$$_{major}$ ($CH_2O$), 76.0$^-$$_{minor}$ ($CH_2O$), 74.6$^+$$_{major}$ (CHOH), 74.6$^+$$_{minor}$ (CHOH), 57.7$^-$$_{major}$ ($CH_2SO_2$), 57.6$^-$$_{minor}$ ($CH_2SO_2$), 47.8$^-$ ($CCH_2SO_2$ $_{major}$ and $CCH_2SO_2$ $_{minor}$), 46.4$^-$$_{major}$ ($CH_2C$=O), 46.4$^-$$_{minor}$ ($CH_2$-C=O), 42.8$^+$$_{major}$ (CH on camphor), 42.7$^+$$_{minor}$ (CH on camphor), 42.4$^-$ ($CMe_2$ $_{major}$ and $CMe_2$ $_{minor}$), 41.2$^-$$_{major}$ ($CH_2$ on camphor), 41.2$^-$$_{minor}$ ($CH_2$ on camphor), 26.8$^-$ ($CH_2$ $_{major}$ and $CH_2$ $_{minor}$), 24.7$^-$$_{major}$ ($CMe_2$), 24.6$^-$$_{minor}$ ($CMe_2$), 21.5$^+$, 21.4$^+$, 19.6$^+$, 19.6$^+$, 19.5$^+$ and 19.4$^+$ ($4 \times Me_{major}$ and $4 \times Me_{minor}$); *m*/*z* (ESI) 643 (100%, $MNa^+$) (Found: $MNa^+$, 643.2268. $C_{35}H_{41}NaO_6PS$ requires *M*, 643.2259).

### General procedure for the synthesis of allenes

The hydroxyphosphine oxide (1 mmol) in dry DMF (12 $cm^3$) was added to a stirred suspension of sodium hydride (2 mmol) in dry DMF (5 $cm^3$) at 20 °C. The reaction mixture was stirred at 60 °C for 30 minutes, allowed to cool to room temperature and poured into saturated ammonium chloride solution (25 $cm^3$). The aqueous layer was extracted with ether (3 × 25 $cm^3$) and the combined organic extracts were washed with water (30 $cm^3$), brine (30 $cm^3$), dried ($MgSO_4$) and evaporated under reduced pressure at 0 °C to give the crude allene.

#### 4,4-Dimethyl-1-phenylpenta-1,2-diene 20a

By the general method, (*E*)-4,4-dimethyl-2-diphenylphosphinoyl-3-hydroxy-1-phenylpent-1-ene **7a** (150 mg, 0.38 mmol) and sodium hydride (60% dispersion in mineral oil, 31 mg, 0.77 mmol) gave a crude product that was purified by Kugelrohr distillation (9 mmHg, oven temperature 110 °C) to give the allene **20a** (59 mg, 89%) as a colourless oil; $[\alpha]_D$ +46.0 (*c*. 1.65 in EtOH) (lit.,[22] +370 (in EtOH)) whose data matched those previously reported.[22]

#### 2,2,6,6-Tetramethylhepta-3,4-diene 20b

By the general method, (*E*)-4-diphenylphosphinoyl-3-hydroxy-2,2,6,6-tetramethylhept-4-ene **8a** (150 mg, 0.40 mmol) and sodium hydride (60% dispersion in mineral oil, 32 mg, 0.81 mmol) gave a crude product that was purified by Kugelrohr distillation (8 mmHg, oven temperature 60 °C) to give the allene **20b** (47 mg, 74%) as a colourless oil; $[\alpha]_D$ +28 (*c*. 1.4 in EtOH) (lit.,[22] +124 (in EtOH)) whose data matched those previously reported.[22]

#### 2,2,6-Trimethylhepta-3,4-diene 20c

By the general method, (*E*)-4-diphenylphosphinoyl-3-hydroxy-2,2,6-trimethylhept-4-ene **8b** (250 mg, 0.70 mmol) and sodium hydride (60% dispersion in mineral oil, 37 mg, 0.91 mmol) gave a crude product that was purified by Kugelrohr distillation (105 mmHg, oven temperature 80 °C) to give the allene **20c** (5 mg, 5%) as a colourless oil; $[\alpha]_D$ +4.5 (*c*. 0.25 in $CDCl_3$) (lit.,[22] +110 (in EtOH)) whose data matched those previously reported.[22]

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