

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

Received (in Cambridge, UK) 21st May 2001, Accepted 18th July 2001

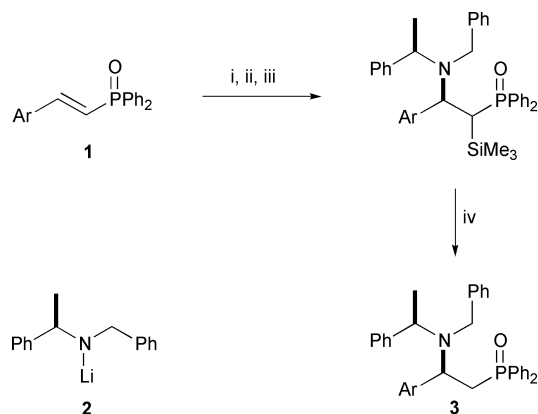
First published as an Advance Article on the web 15th August 2001

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 pressure⁵ 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 Davies⁸ to vinylic phosphine oxides **1** (Scheme 1).^{9,10} The reaction



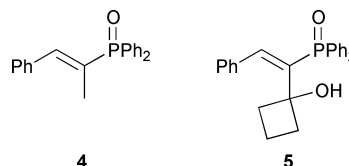
Scheme 1 Reagents and conditions: i, Me_3SiCl , THF, -78°C ; ii, **2**; iii, H_2O ; iv, TBAF, THF.

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.

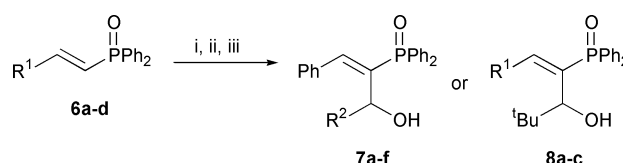
Results and discussion

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** ($\text{Ar} = \text{Ph}$) 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,



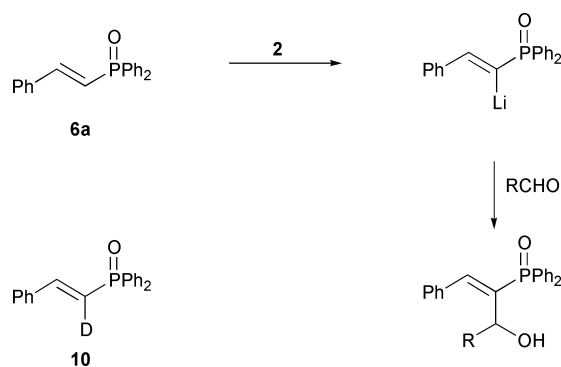
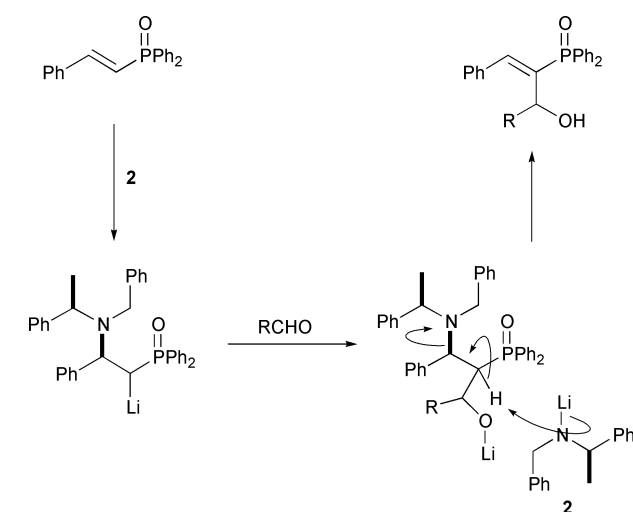
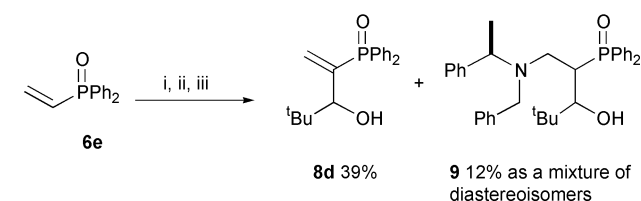
Scheme 2 Reagents and conditions: i, R^2CHO , THF, -78°C ; ii, **2**; iii, H_2O .

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

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 ^c Hex ^a	7b	55	13
3	6a	Ph	CMe ₂ CH ₂ CH=CH ₂	7c	67	23
4	6a	Ph	ⁱ Pr	7d	62	0
5	6a	Ph	(CH ₂) ₆ Me	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.

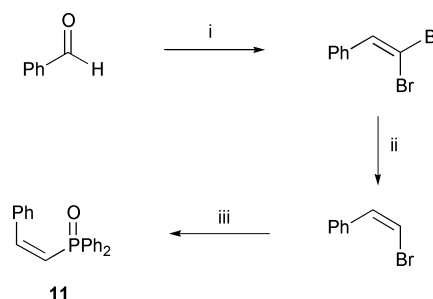
mechanism (Scheme 5). Nagaoka and Tomioka have reported a similar reaction of vinylic phosphonates catalysed by LDA and suggest a Baylis–Hillman style reaction.¹² Such a mechanism has also been reported by Harrowven and Poon¹³ for the reaction of lithium tetramethylpiperidine with diethyl maleate and 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

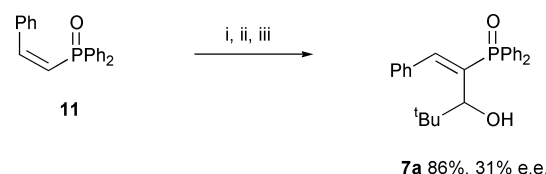
6a was treated with the lithium amide **2** in the absence of an electrophile and quenched with deuterated methanol after 30 minutes. The recovered starting material showed no deuteration of the α -position. The analogous reaction involving the deuterated vinyl phosphine oxide **10** (prepared with 80% deuterium incorporation at the α -position in an analogous way to the preparation¹⁴ 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 D₂O 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, PPh₃, CBr₄, CH₂Cl₂, 84%; ii, Pd(PPh₃)₄, Bu₃SnH, PhH, 29%; iii, Pd(PPh₃)₄, Et₃N, Ph₂P(O)H, PhMe, 90 °C, 77%.

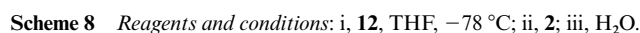
of **11** under the standard reaction conditions gave the (*E*)-hydroxyphosphine oxide **7a** with an enantiomeric excess of 31% in exactly the same sense as observed previously (Scheme 7). In



Scheme 7 Reagents and conditions: i, ^tBuCHO, THF, −78 °C; ii, **2**; iii, H₂O.

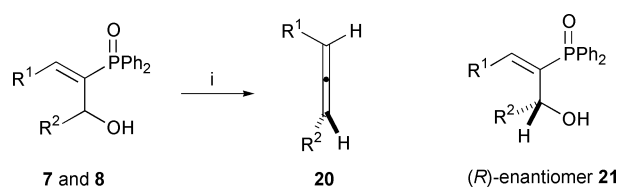
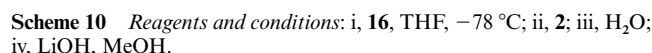
the absence of an electrophile, complete isomerisation of the (*Z*)-phosphine oxide **11** to the (*E*)-isomer **6a** is observed with either 1 or 0.2 equivalents of the lithium amide **2**. Thus, in the reaction illustrated in Scheme 7, the (*Z*)-phosphine oxide **11**

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



Determination of the stereochemistry

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 R¹ = ⁱPr (entry 2), due to the allene's high volatility. Comparing the specific rotation of the resulting allenes with literature values²² and assuming the stereospecific *syn*



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.

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

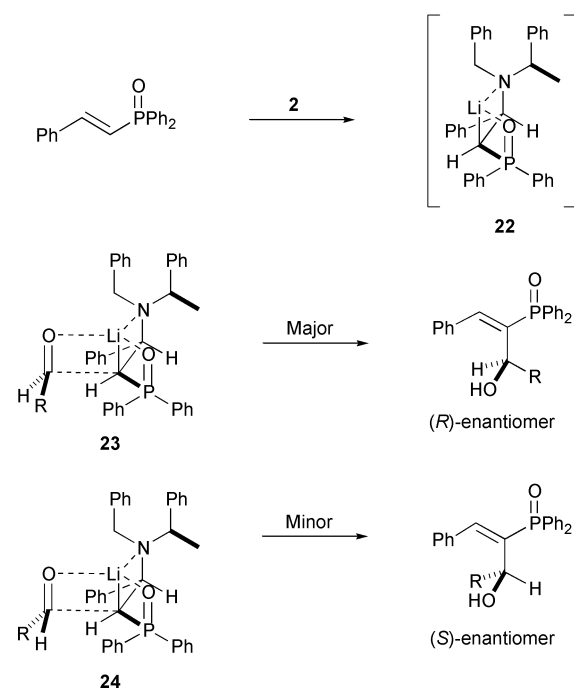
2242 *J. Chem. Soc., Perkin Trans. 1*, 2001, 2240–2249

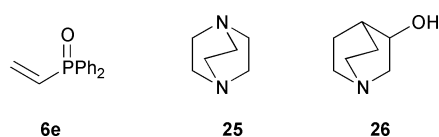
Table 2 Synthesis of allenes **20** from compounds **7** and **8**

Entry	R ¹	R ²	Yield (%)	[α] _D /10 ⁻¹ deg dm ² g ⁻¹	Lit. ²² [α] _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 sp³ 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).

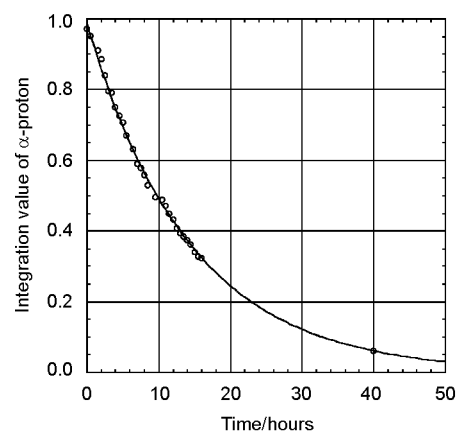
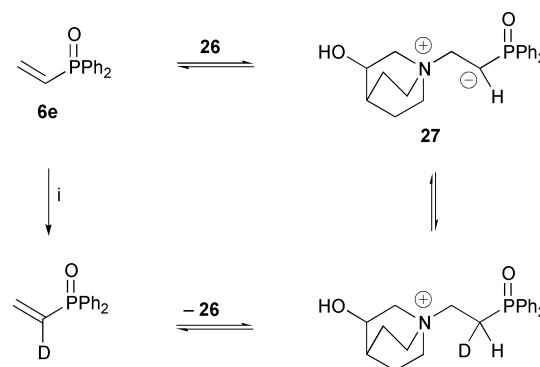
Baylis–Hillman reactions

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 Villieras and co-workers, although reaction times are 7–29 days.²⁹ We started our investigation with vinyl diphenylphosphine oxide **6e**, butanal and a range of nucleophilic catalysts: DABCO **25**, 3-hydroxyquinuclidine **26**, DBU, DMAP, tri-



phenylphosphine and tricyclohexylphosphine. It was not possible to repeat the solvent-free reaction conditions of Villieras 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**, CD₃OD, 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 60F₂₅₄).

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 D₂O 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 Bruker 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 Ultraspec 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 the sodium D line (589 nm) at room temperature and are given in units of 10^{−1} deg dm² 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 cm³)] was added by cannula to a solution of (*E*)-1-diphenylphosphinoyl-2-phenylethene¹⁴ **6a** (100 mg, 0.33 mmol) and methyl iodide (47 mg, 21 µl, 0.66 mmol) in dry THF (7 cm³) 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 cm³) and water (30 cm³). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 100 cm³). The combined organic extracts were evaporated under reduced pressure and dissolved in dichloromethane (100 cm³). This solution was washed with 10% citric acid solution (100 cm³), water (100 cm³), brine (100 cm³), dried (MgSO₄) and evaporated under reduced pressure to yield a crude product. The residue was chromatographed (SiO₂, EtOAc) to give a 8 : 92 mixture of starting material–vinylphosphine oxide³¹ **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-phenylethene¹⁴ **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 (SiO₂, EtOAc) to give the *hydroxyphosphine oxide* **5** (60 mg, 50%) as a colourless gum; *R*_f(EtOAc) 0.29; *v*_{max}(CHCl₃)/cm^{−1} 3500–3200 (br, OH), 1438 (P–Ph) and 1158 (P=O); *δ*_H(400 MHz; CDCl₃) 7.80–7.70 (4H, m, Ph₂PO), 7.60–7.25 (11H, m, Ph and Ph₂PO), 6.67 (1H, d, *J* 23, CHPh), 4.43* (1H, br s, OH), 2.05–1.80 (5H, m, CH₂) and 1.43–1.32 (1H, m, CH₂); *δ*_C(100 MHz; CDCl₃) 143.3⁺ (d, *J*, 13, CHPh), 136–127 (m, Ph, Ph₂PO and Ph₂PO-C), 77.6⁺ (CHOH), 36.7[−] (CH₂), 36.6[−] (CH₂) and 16.2[−] (CH₂); *m/z* (FAB) 375 (53%, MH⁺), 357 (88, M – OH), 201 (80, Ph₂PO) and 154 (100, M – OH – Ph₂PO) (Found: MH⁺, 375.1515. C₂₄H₂₄O₂P 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-phenylethylamine³² (1.2 mmol), in dry THF (15 cm³)] was added by cannula to a solution of the phosphine oxide (1 mmol) and the electrophile (2 mmol) in dry THF (25 cm³) 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 cm³) and water (30 cm³). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 100 cm³). The combined organic extracts were evaporated under reduced pressure and dissolved in dichloromethane (100 cm³). This solution was washed with 10% citric acid solution (100 cm³), water (100 cm³), brine (100 cm³), dried (MgSO₄) 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-phenylethene¹⁴ **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 cm³, 4.3 mmol) and pivalaldehyde (0.680 g, 860 µl, 8 mmol) gave a crude product that was chromatographed (SiO₂, 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); [*α*]_D −75 (c. 1.0 in CHCl₃); *R*_f(EtOAc) 0.60; *v*_{max}(Nujol)/cm^{−1} 3500–3000 (br, OH), 1440 (P–Ph) and 1153 (P=O); *δ*_H(400 MHz; CDCl₃) 7.95–7.85 (2H, m, Ph₂PO), 7.70–7.20 (13H, m, Ph and Ph₂PO), 6.88 (1H, d, *J* 23.5, CHPh), 5.53* (1H, d, *J* 11, OH), 4.92 (1H, dd, *J* 23.5 and 11, CHOH) and 0.77 (9H, s, CMe₃); *δ*_C(100 MHz; CDCl₃) 145.6⁺ (d, *J* 12.5, CHPh), 136–127 (m, Ph, Ph₂PO and Ph₂PO-C), 79.2⁺ (d, *J* 4.5, CHOH), 36.9[−] (CMe₃) and 26.1⁺ (CMe₃); *m/z* (FAB) 391 (100%, MH⁺), 373 (87, M – OH), 333 (44, M – 'Bu) and 201 (58, Ph₂PO) (Found: MH⁺, 391.1806. C₂₅H₂₈O₂P requires *M*, 391.1827) (Found: C, 76.6; H, 7.1; P, 7.9. C₂₅H₂₇O₂P requires C, 76.9; H, 7.0; P, 7.9%). Chiral HPLC analysis (70 : 30 isohexane–propan-2-ol (IPA), *τ*_{major} 7.4 min, *τ*_{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-phenylethene¹⁴ **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)cyclohexanecarbaldehyde³³ (290 mg, 1.32 mmol) gave a crude product that was chromatographed (SiO₂, 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); [*α*]_D −23 (c. 0.72 in CHCl₃); *R*_f(EtOAc) 0.57; *v*_{max}(CHCl₃)/cm^{−1} 3500–3100 (br, OH), 1438 (P–Ph) and 1158 (P=O); *δ*_H(400 MHz; CDCl₃) 7.93–7.83 (2H, m, Ph₂PO), 7.70–6.80 (19H, m, Ph, SPh, Ph₂PO and CHPh), 5.71* (1H, d, *J* 8, OH), 5.11 (1H, dd, *J* 23 and 8, CHOH) and 1.90–0.90 (10H, m, 5 × CH₂); *δ*_C(100 MHz; CDCl₃) 148.5⁺ (d, *J* 12.5, CHPh), 140–128 (m, Ph, SPh, Ph₂PO and Ph₂PO-C), 76.4⁺ (d, *J* 4, CHOH), 62.6[−] (CSPH), 31.3[−], 31.1[−], 26.0[−], 22.2[−] and 21.8[−] (5 × CH₂); *m/z* (FAB) 525 (71%, MH⁺), 415 (31, M – SPh), 397 (54, M – SPh – OH), 201 (100, Ph₂PO) and 191 (54, C₆H₁₀SPh) (Found: MH⁺, 525.2009. C₃₃H₃₄O₂PS requires *M*, 525.2017) (Found: C, 75.2; H, 6.5; P, 5.7. C₃₃H₃₃O₂PS requires C, 75.5; H, 6.3; P, 5.9%). Chiral HPLC analysis (70 : 30 isohexane–IPA, *τ*_{major} 10.7 min, *τ*_{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-phenylethene¹⁴ **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 μ l, 0.79 mmol) and 2,2-dimethylpent-4-enal (164 mg, 200 μ l, 1.32 mmol) gave a crude product that was chromatographed (SiO₂, EtOAc–hexane, 1 : 1 to 2 : 1) to give the *hydroxyphosphine oxide* **7c** (184 mg, 67%) as a colourless gum; $[a]_D^{25}$ –48 (c. 1.9 in CHCl₃); R_f (EtOAc) 0.64; ν_{\max} (CHCl₃)/cm^{–1} 3400–3200 (br, OH), 1436 (P–Ph) and 1160 (P=O); δ_H (400 MHz; CDCl₃) 7.95–7.85 (2H, m, Ph₂PO), 7.70–7.20 (13H, m, Ph and Ph₂PO), 6.88 (1H, d, *J* 23.5, CHPh), 5.80–5.30 (2H, m, CHCH₂ and OH), 5.03 (1H, d, *J* 23.5, CHOH), 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); δ_C (100 MHz; CDCl₃) 146.1⁺ (d, *J* 12.5, CHPh), 135–127 (m, CH=CH₂, Ph₂PO–C, Ph and Ph₂PO), 116.6[–] (CH=CH₂), 78.0⁺ (d, *J* 4.5, CHOH), 43.2[–] (CH₂), 22.8⁺ (Me) and 22.7⁺ (Me); *m/z* (FAB) 417 (100%, MH⁺), 399 (83, M – OH), 333 (67, M – C₆H₁₁) and 201 (72, Ph₂PO) (Found: MH⁺, 417.1986. C₂₇H₃₀O₂P requires *M*, 417.1983). Chiral HPLC analysis (70 : 30 isohexane–IPA, τ_{major} 6.9 min, τ_{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-phenylethene¹⁴ **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 μ l, 0.39 mmol) and isobutyraldehyde (48 mg, 60 μ l, 0.66 mmol) gave a crude product that was chromatographed (SiO₂, 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; ν_{\max} (CHCl₃)/cm^{–1} 3500–3200 (br, OH), 1437 (P–Ph) and 1159 (P=O); δ_H (400 MHz; CDCl₃) 7.95–7.85 (2H, m, Ph₂PO), 7.75–7.65 (2H, m, Ph₂PO), 7.65–7.40 (6H, m, Ph₂PO and Ph), 7.37–7.23 (5H, m, Ph₂PO 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, CHOH), 2.10–2.00 (1H, m, CHMe₂), 0.98 (3H, d, *J* 6.5, Me) and 0.46 (3H, d, *J* 6.5, Me); δ_C (100 MHz; CDCl₃) 144.5⁺ (d, *J* 12.5, CHPh), 139–128 (Ph₂PO, Ph and Ph₂PO–C), 78.0⁺ (d, *J* 5.5, CHOH), 34.0⁺ (CHMe₂), 19.9⁺ (Me) and 19.8⁺ (Me); *m/z* (EI) 376 (1%, M⁺), 333 (100, M – ⁱPr) and 201 (43, Ph₂PO) (Found: M⁺, 376.1579. C₂₄H₂₄O₂P requires *M*, 376.1592). Chiral HPLC analysis (70 : 30 isohexane–IPA, τ_1 7.5 min, τ_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-phenylethene¹⁴ **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 μ l, 0.39 mmol) and octanal (84 mg, 103 μ l, 0.66 mmol) gave a crude product that was chromatographed (SiO₂, 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; ν_{\max} (CHCl₃)/cm^{–1} 3500–3200 (br, OH), 1437 (P–Ph) and 1158 (P=O); δ_H (400 MHz; CDCl₃) 7.90–7.80 (2H, m, Ph₂PO), 7.73–7.65 (2H, m, Ph₂PO), 7.63–7.43 (6H, m, Ph₂PO and Ph), 7.37–7.18 (5H, m, Ph₂PO and Ph), 6.69 (1H, d, *J* 22.5, CHPh), 4.95–4.80 (1H, m, CHOH), 4.60* (1H, d, *J* 10.5, OH), 1.95–1.80 (1H, m, CH₂), 1.61–1.50 (1H, m, CH₂), 1.44–1.32 (1H, m, CH₂), 1.25–0.95 (9H, m, CH₂) and 0.83 (3H, t, *J* 7, Me); δ_C (100 MHz; CDCl₃) 140.8⁺ (d, *J* 12.5, CHPh), 136–126 (Ph₂PO, Ph and Ph₂PO–C), 69.9 (d, *J* 5, CHOH), 51.4[–], 35.7[–], 29.8[–], 27.1[–], 24.1[–], 20.6[–] (6 \times CH₂) and 12.1⁺ (Me); *m/z* (EI) 432 (1%, M⁺), 333 (100, M – C₇H₁₅) and 201 (31, Ph₂PO) (Found: M⁺,

432.2225. C₂₈H₃₃O₂P requires *M*, 432.2218). Chiral HPLC analysis (85 : 15 isohexane–EtOH, τ_1 24.2 min, τ_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 cm³) was added to a stirred solution of the methylidiphenylphosphine oxide (14.0 g, 65 mmol) in dry THF (400 cm³) at –78 °C. The orange solution was stirred for 30 minutes and pivalaldehyde (6.69 g, 8.5 cm³, 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 cm³). The layers were separated and the aqueous layer was extracted with dichloromethane (3 \times 30 cm³). The combined organic extracts were washed with brine (50 cm³), dried (MgSO₄) 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 reported³⁴ with incomplete data; R_f (EtOAc) 0.37; ν_{\max} (CHCl₃)/cm^{–1} 3500–3200 (br, OH), 1438 (P–Ph) and 1151 (P=O); δ_H (400 MHz; CDCl₃) 7.80–7.66 (4H, m, Ph₂PO), 7.57–7.42 (6H, m, Ph₂PO), 4.36* (1H, s, OH), 3.67 (1H, br t, *J* 10.5, CHOH), 2.44–2.23 (2H, m, CH₂) and 0.88 (9H, s, CMe₃); δ_C (100 MHz; CDCl₃) 134.1[–] (d, *J* 100, *ipso*-Ph₂PO), 132.4⁺ (*para*-Ph₂PO), 132.4⁺ (*para*-Ph₂PO), 132.0[–] (d, *J* 97, *ipso*-Ph₂PO), 131.4⁺ (d, *J* 9, *ortho*-Ph₂PO), 130.8⁺ (d, *J* 9.5, *ortho*-Ph₂PO), 129.2⁺ (d, *J* 11.5, *meta*-Ph₂PO), 129.1⁺ (d, *J* 12, *meta*-Ph₂PO), 74.6⁺ (d, *J* 5, CHOH), 35.5[–] (d, *J* 12, CMe₃), 31.5[–] (d, *J* 72, CH₂) and 28.8⁺ (CMe₃); *m/z* (LSIMS) 303 (92%, MH⁺), 285 (45, M – OH) and 201 (100, Ph₂PO) (Found: MH⁺, 303.1488. C₁₈H₂₄O₂P 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 cm³, 65 mmol), trimethylsilyl chloride (5.94 g, 6.9 cm³, 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; ν_{\max} (CHCl₃)/cm^{–1} 1438 (P–Ph) and 1176 (P=O); δ_H (400 MHz; CDCl₃) 7.72–7.63 (4H, m, Ph₂PO), 7.53–7.40 (6H, m, Ph₂PO), 6.74 (1H, dd, *J* 20.5 and 17.5, CHCMe₃), 6.09 (1H, dd, *J* 24.5 and 17.5, PCH) and 1.01 (9H, s, CMe₃); δ_C (100 MHz; CDCl₃) 160.4⁺ (CHCMe₃), 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, Ph₂PO–C), 33.4[–] (d, *J* 15, CMe₃) and 26.8⁺ (CMe₃); *m/z* (FAB) 285 (100%, MH⁺), 201 (6, Ph₂PO) (Found: MH⁺, 285.1390. C₁₈H₂₂OP requires *M*, 285.1403) (Found: C, 75.8; H, 7.5; P, 11.0. C₁₈H₂₁OP 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 cm³, 5.5 mmol) and pivalaldehyde (0.86 g, 1.1 cm³, 10 mmol) gave a crude product that was chromatographed (SiO₂, 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); $[a]_D^{25}$ –79 (c. 0.86 in CHCl₃); R_f (EtOAc) 0.63; ν_{\max} (CHCl₃)/cm^{–1} 3550–3200 (br, OH), 1437 (P–Ph) and 1156 (P=O); δ_H (400 MHz; CDCl₃) 7.87–7.80 (2H, m, Ph₂PO), 7.64–7.32 (8H, m, Ph₂PO), 5.74* (1H, d, *J* 1.5, OH), 5.72 (1H, d,

J 37, C=CH), 4.96 (1H, dd, J 27.5 and 10.5, CHOH), 1.12 (9H, s, CMe₃) and 0.90 (9H, s, CMe₃); δ_{C} (125 MHz; CDCl₃) 157.9⁺ (d, J 10.5, Ph₂PO-CCH), 136.7⁻ (d, J 104, *ipso*-Ph₂PO), 131.9⁺ (*para*-Ph₂PO), 131.8⁺ (d, J 9, *ortho*-Ph₂PO), 131.6⁺ (d, J 9.5, *ortho*-Ph₂PO), 131.5⁺ (*para*-Ph₂PO), 131.1⁻ (d, J 99, Ph₂PO-C), 130.4⁻ (d, J 103, *ipso*-Ph₂PO), 128.5⁺ (d, J 11.5, *meta*-Ph₂PO), 128.2⁺ (d, J 12, *meta*-Ph₂PO), 77.9⁺ (d, J 5.5, CHOH), 36.5⁺ (d, J 17, C=CHCMe₃), 36.3⁻ (CMe₃), 30.7⁺ and 27.6⁺ (CMe₃); m/z (LSIMS) 271 (42%, MH⁺), 353 (100, M - OH), 313 (15, M - CMe₃) and 201 (79, Ph₂PO) (Found: MH⁺, 371.2149. C₂₃H₃₂O₂P requires M , 371.2124) (Found: C, 74.5; H, 8.5; P, 8.5. C₂₃H₃₁O₂P requires C, 74.6; H, 8.4; P, 8.4%). Chiral HPLC analysis (90 : 10 isohexane-IPA, τ_{major} 9.1 min, τ_{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-methylbutene¹⁰ (100 mg, 0.37 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (94 mg, 0.44 mmol), *n*-butyllithium (1.4 M in hexane, 290 μ l, 0.41 mmol) and pivalaldehyde (63 mg, 81 μ l, 0.74 mmol) gave a crude product that was chromatographed (SiO₂, EtOAc-hexane, 1 : 1 to 2 : 1) to give the *hydroxyphosphine oxide* **8b** (70 mg, 53%) as a colourless gum; $[a]_{\text{D}}^{25}$ -15 (c. 0.84 in CHCl₃); R_{f} (EtOAc) 0.50; ν_{max} (CHCl₃)/cm⁻¹ 3500-3100 (br, OH), 1614 (C=C), 1437 (P-Ph) and 1155 (P=O); δ_{H} (400 MHz; CDCl₃) 7.82-7.74 (2H, m, Ph₂PO), 7.62-7.43 (6H, m, Ph₂PO), 7.40-7.34 (2H, m, Ph₂PO), 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, CHOH), 2.89-2.75 (1H, m, CHMe₂), 0.97 (3H, d, J 6.5, Me), 0.90 (3H, d, J 6.5, Me) and 0.88 (9H, s, CMe₃); δ_{C} (100 MHz; CDCl₃) 154.9⁺ (d, J , C=CH), 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, Ph₂PO-C), 127.1⁺ (d, J 12, *meta*-Ph), 126.8⁺ (d, J 12, *meta*-Ph), 79.6⁺ (d, J 5.5, CHOH), 35.2⁻ (CMe₃), 27.2⁺ (CHMe₂), 25.4⁺ (CMe₃), 20.3⁺ (Me) and 20.0⁺ (Me); m/z (LSIMS) 357 (100%, MH⁺), 339 (8, M - OH) (Found: MH⁺, 357.1983. C₂₂H₃₀O₂P requires M , 357.1978). Chiral HPLC analysis (90 : 10 isohexane : IPA, τ_{major} 8.1 min, τ_{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 μ l, 1.1 mmol) and pivalaldehyde (172 mg, 220 μ l, 2 mmol) gave a crude product that was chromatographed (SiO₂, 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; ν_{max} (CHCl₃)/cm⁻¹ 3600-3200 (br, OH), 1437 (Ph-P), 1218 (P=O); δ_{H} (500 MHz; CDCl₃) 7.77 (2H, dtd, 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, CHCH₃), 5.69* (1H, d, J 10, OH), 4.55 (1H, ddd, J 22.5, 10 and 1, CHOH), 1.85 (3H, dd, J 7 and 3.3, Me), 0.90 (9H, s, Me₃); δ_{C} (125 MHz; CDCl₃) 144.2⁺ (d, J 12, CHMe), 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, Ph₂PO-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⁻ (CMe₃), 26.8⁺ (CMe₃), 16.0⁺ (d, J 16.5, Me). Chiral HPLC analysis (80 : 20 isohexane-IPA, τ_{major} 21.7 min, τ_{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, vinylidiphenylphosphine oxide³⁵ **6e** (228 mg, 1 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (253 mg, 1.2 mmol), *n*-butyllithium (1.4 M in hexane, 785 μ l, 1.1 mmol) and

pivalaldehyde (172 mg, 220 μ l, 2 mmol) gave a crude product that was chromatographed (SiO₂, 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; τ_{max} (CHCl₃)/cm⁻¹ 3600-3100 (br, OH), 1438 (P-Ph) and 1166 (P=O); δ_{H} (400 MHz; CDCl₃) 7.77-7.70 (2H, m, Ph₂PO), 7.68-7.60 (2H, m, Ph₂PO), 7.60-7.40 (6H, m, Ph₂PO), 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, CHOH) and 0.91 (9H, s, CMe₃); δ_{C} (100 MHz; CDCl₃) 151.4⁻ (d, J 89.5, Ph₂PO-C), 141-136 (m, Ph₂PO and CH₂), 91.0⁺ (CHOH), 44.0⁻ (CMe₃) and 34.1⁺ (CMe₃); m/z (FAB) 315 (15%, MH⁺) (Found: MH⁺, 315.1518. C₁₉H₂₄O₂P requires M , 315.1514) (Found: C, 72.5; H, 7.3; P, 10.1. C₁₉H₂₃O₂P requires C, 72.6; H, 7.4; P, 9.9%). Chiral HPLC analysis (90 : 10 isohexane-IPA, τ_{major} 16.5 min, τ_{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; ν_{max} (CHCl₃)/cm⁻¹ 3500-3300 (br, OH), 1438 (P-Ph), 1158 (P=O); δ_{H} (400 MHz; CDCl₃) 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, CHMe and CHOH), 3.49 (1H_{minor}, d, J 15, NCH₂), 3.39 (1H_{major}, d, J 15, NCH₂), 3.31-3.15 (3H_{major} and 2H_{minor}, m, NCH₂), 3.00-2.90 (1H_{minor}, m, NCH₂), 2.77-2.57 (1H_{major} and 1H_{minor}, m, PCH), 1.12 (3H_{minor}, d, J 7, CHMe), 0.98 (3H_{major}, d, J 7, CHMe), 0.80 (9H_{minor}, s, CMe₃) and 0.71 (9H_{major}, s, CMe₃), no OH peaks observed; δ_{C} (100 MHz; CDCl₃) 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⁺ (NC_{minor}HMe), 57.2⁺ (NC_{major}HMe), 52.4⁻ (NC_{major}H₂Ph), 51.8 (NC_{minor}H₂Ph), 44.6⁻ (CHC_{minor}H₂N), 42.7⁻ (CHC_{major}H₂N), 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}Me₃ and C_{minor}Me₃), 24.9⁺ and 24.9⁺ (CMe₃ major and CMe₃ minor), 17.2⁺ (Me_{minor}) and 11.5⁺ (Me_{major}); m/z (LSIMS) 526 (73%, MH⁺), 422 (44, M - CHMePh), 340 (100, M - CH₂Ph - Ph - OH), 303 (41, M - CH₂NBn(CHMePh)) and 201 (46, Ph₂PO) (Found: MH⁺, 526.2858. C₃₄H₄₁NO₂P requires M , 526.2859).

[²H₃]Methyldiphenylphosphine oxide

Chlorodiphenylphosphine (11.03g, 50 mmol) in dry ether (25 cm³) was added slowly to a solution of [²H₃]methylmagnesium iodide (1.0 M in ether, 50 cm³, 50 mmol), at 0 °C. The reaction mixture was stirred for 2h, warming to room temperature. Water (40 cm³) was slowly added and the layers were separated. The aqueous layer was washed with dichloromethane (3 \times 30 cm³), the combined organic extracts were washed with brine (100 cm³), dried (MgSO₄) and evaporated under reduced pressure. The residue was dissolved in dichloromethane (40 cm³) and aqueous hydrogen peroxide was added dropwise until no further temperature rise was observed. Water (20 cm³) was added, the layers were separated and the aqueous layer was washed with dichloromethane (3 \times 30 cm³). The combined organic extracts were washed with brine (50 cm³), dried (MgSO₄) 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, [²H₃]methyldiphenylphosphine oxide (6.60 g, 30 mmol), benzaldehyde (3.82g, 3.6 cm³, 36 mmol) and *n*-butyllithium (1.4 M in hexane, 23.6 cm³, 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; ν_{\max} (CHCl₃)/cm⁻¹ 3600–3200 (br, OH), 1437 (P–Ph) and 1168 (P=O); δ_H (400 MHz; CDCl₃) 7.80–7.75 (2H, m, Ph₂PO), 7.70–7.65 (2H, m, Ph₂PO), 7.54–7.42 (6H, Ph₂PO and Ph), 7.34–7.20 (5H, m, Ph₂PO and Ph), 5.16 (1H, d, *J* 9, CHOH) and 5.02* (1H, d, *J* 1.5, OH); δ_C (100 MHz; CDCl₃) 143.8⁻ (d, *J* 13.5, *ipso*-Ph), 134–125 (Ph₂PO and Ph), 69.1⁺ (d, *J* 4, CHOH) and 38.7⁻ (m, CD₂); m/z (LSIMS) 325 (42%, MH⁺), 307 (35, M – OH), 201 (100, Ph₂PO) (Found: MH⁺, 325.1313. C₂₀H₁₈D₂O₂P 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 cm³, 16.5 mmol), trimethylsilyl chloride (1.51 g, 1.7 cm³, 14.0 mmol) and sodium hydride (60% dispersion in mineral oil, 335 mg, 13.9 mmol) gave a crude product that was chromatographed (SiO₂, 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; ν_{\max} (CHCl₃)/cm⁻¹ 1439 (P–Ph) and 1175 (P=O); δ_H (400 MHz; CDCl₃) 7.80–7.70 (4H, m, Ph₂PO), 7.60–7.30 (12H, m, Ph, Ph₂PO and CHPh) and 6.83 (0.2H, dd, *J* 22.5 and 17.5, PCH); δ_C (100 MHz; CDCl₃) 147.5⁺ (d, *J* 3.5, CHPh), 135.1⁻ (d, *J* 17.5, *ipso*-Ph), 133.0⁻ (d, *J* 10.5, *ipso*-Ph₂PO), 131.9⁺ (d, *J* 2.5, *para*-Ph₂PO), 131.4⁺ (d, *J* 10, *ortho*-Ph₂PO), 130.1⁺ (Ph), 128.9⁺ (Ph), 128.6⁺ (d, *J* 12, *meta*-Ph₂PO), 127.8⁺ (Ph), 119.3⁺ (d, *J* 10.4, PCD); m/z (EI) 305 (100%, M⁺), 228 (19, M – Ph), 202 (58, Ph₂PO), 153 (74, M – 2 × Ph), 136 (47, PCDCHPh) (Found: MH⁺, 305.1072. C₂₀H₁₈D₂O₂P requires *M*, 305.1079).

(*E*)-1,3-Diphenyl-2-diphenylphosphinoyl-1-phenylsulfonyl-aminoprop-1-ene 13

By the general method, (*E*)-1-diphenylphosphinoyl-2-phenylethene **14** (200 mg, 0.66 mmol), (*R*)-*N*-benzyl-1-phenylethylamine **2** (164 mg, 0.79 mmol), *n*-butyllithium (1.4 M in hexane, 520 μ l, 0.72 mmol) and *N*-benzylidenebenzenesulfonamide³⁷ **12** (322 mg, 1.32 mmol) gave a crude product that was chromatographed (SiO₂, 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; ν_{\max} (CHCl₃)/cm⁻¹ 3233 (NH), 1437 (P–Ph), 1331 (SO₂) and 1162 (P=O and SO₂); δ_H (400 MHz; CDCl₃) 8.20* (1H, d, *J* 9.5, NH), 7.65–6.80 (25H, m, PhSO₂, 2 × Ph and Ph₂PO), 6.74 (1H, d, 20.5, C=CH) and 6.33 (1H, dd, *J* 22.6 and 9.5, CHN); δ_C (100 MHz; CDCl₃) 143–125 (m, PhSO₂, 2 × Ph, Ph₂PO, CHPh and Ph₂PO-*C*) and 55.9⁺ (d, *J* 6, CHN); m/z (FAB) 550 (29%, MH⁺) 408 (15, M – PhSO₂), 393 (35, M – PhSO₂NH), 201 (55, Ph₂PO), 154 (100, PhCHNH₂SO) and 136 (81, PhCHNH₂SO) (Found: MH⁺, 550.1610. C₃₃H₂₉O₃NPS requires *M*, 550.1606). Chiral HPLC analysis (50 : 50 isohexane–IPA, τ_{major} 9.5 min, τ_{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 μ l, 6.5 mmol) in dry dichloromethane (5 cm³) was added to a solution of dry dimethyl sulfoxide (1.2 g, 5 mmol) in dry dichloromethane (30 cm³) at –78 °C. After 30 minutes 2,2-dimethyl-3-hydroxypropyl 4-methoxybenzoate²¹ **15** (1.2 g, 5 mmol) in dry dichloromethane (15 cm³) was added and the reaction was stirred for a further 30 minutes. Triethylamine (3.06 g, 4.2 cm³, 30 mmol) was added and the reaction was allowed to warm to room temperature over 22 hours. Water (100 cm³) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 50 cm³), the combined organic extracts were washed with water

(100 cm³), brine (100 cm³), dried (MgSO₄) 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; ν_{\max} (liquid film)/cm⁻¹ 2971, 2839, 2713 (CH), 1713 (br, 2 × C=O), 1607 and 1512 (C₆H₄OMe); δ_H (400 MHz; CDCl₃) 9.59 (1H, s, CHO), 7.89 (2H, br d, *J* 9, *meta*-C₆H₄OMe), 6.86 (2H, br d, *J* 9, *ortho*-C₆H₄OMe), 4.29 (2H, s, CH₂), 3.75 (3H, s, OMe) and 1.16 (6H, s, 2 × Me); δ_C (100 MHz; CDCl₃) 201⁺ (CHO), 163.8⁻ and 161.5⁻ (*para*-C₆H₄OMe and C=O), 129.5⁺ (*ortho*-C₆H₄OMe), 119.9⁻ (*ipso*-C₆H₄OMe), 111.6⁺ (*meta*-C₆H₄OMe), 66.0⁻ (CH₂), 53.3⁺ (OMe), 44.5⁻ (CMe₂) and 16.8⁺ (CMe₂); m/z (ESI) 259 (95%, MNa⁺) (Found: MNa⁺, 259.0936. C₁₃H₁₆O₄Na 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 cm³, 2.1 mmol) and 2,2-dimethyl-3-(4-methoxybenzoyloxy)propanal **16** (670 mg, 2.83 mmol) gave a crude product that was chromatographed (SiO₂, 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 CHCl₃); R_f (EtOAc) 0.54; ν_{\max} (CHCl₃)/cm⁻¹ 3200–3500 (br, OH), 1707 (C=O), 1437 (P–Ph), 1168 (P=O); δ_H (400 MHz; CDCl₃) 7.97–7.88 (2H, m, Ph₂PO), 7.70–7.61 (7H, m, Ph₂PO, Ph and *meta*-C₆H₄OMe), 7.53–7.40 (3H, m, Ph₂PO and Ph), 7.30–7.19 (5H, m, Ph₂PO and Ph), 6.95 (1H, d, *J* 23.5, CHPh), 6.82 (2H, br d, *J* 9, *ortho*-C₆H₄OMe), 5.74* (1H, d, *J* 10.5, OH), 5.39 (1H, ddd, *J* 23.5, 10.5 and 1, CHOH), 4.19 (1H, d, *J* 11, CH_{AB}), 3.85 (3H, s, OMe), 3.83 (1H, d, *J* 11, CH_{AH}), 0.94 (3H, s, Me) and 0.70 (3H, s, Me); δ_C (100 MHz; CDCl₃) 165.6⁻ and 162.7⁻ (*para*-C₆H₄OMe and C=O), 147.0⁺ (d, *J* 12.5, CHPh), 136–127 (m, Ph₂PO, Ph, *ortho*-C₆H₄OMe and Ph₂PO-*C*), 122.5⁻ (*ipso*-C₆H₄OMe), 113.0⁺ (*meta*-C₆H₄OMe), 74.7⁺ (d, *J* 4.5, CHOH), 70.1⁻ (CH₂), 55.0⁺ (OMe), 40.5⁻ (CMe₂), 22.3⁺ (Me) and 20.9⁺ (Me); m/z (LSIMS) 541 (57%, MH⁺), 523 (100, M – OH), 333 (57, M – CMe₂CH₂OCOAr), 201 (95, Ph₂PO) (Found: MH⁺, 541.2137. C₃₃H₃₄O₅P requires *M*, 541.2128) (Found: C, 73.1; H, 6.2; P, 5.9. C₃₃H₃₃O₅P requires C, 73.3; H, 6.15; P, 5.9%). Chiral HPLC analysis (70 : 30 isohexane–IPA, τ_{major} 14.4 min, τ_{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 CHCl₃); R_f (EtOAc) 0.42; ν_{\max} (CHCl₃)/cm⁻¹ 3100–3500 (br, OH), 1712 (C=O), 1438 (P–Ph) and 1166 (P=O); δ_H (400 MHz; CDCl₃) 7.70–7.07 (17H, m, Ph₂PO, Ph and *meta*-C₆H₄OMe), 6.85 (1H, d, *J* 23.5, CHPh), 6.73 (2H, br d, *J* 9, *ortho*-C₆H₄OMe), 6.72 (1H, d, *J* 17.1, CHOCOAr), 6.51* (t, *J* 7.5, CH₂OH), 3.82 (3H, s, OMe), 3.67 (2H, d, *J* 7.5, CH₂OH), 0.84 (3H, s, Me) and 0.55 (3H, s, Me); δ_C (100 MHz; CDCl₃) 166.0⁻ and 163.6⁻ (*para*-C₆H₄OMe and C=O), 147.8⁺ (d, *J* 12.5, CHPh), 137–128 (m, Ph₂PO, Ph, *ortho*-C₆H₄OMe and Ph₂PO-*C*), 121.8⁻ (*ipso*-C₆H₄OMe), 113.4⁺ (*meta*-C₆H₄OMe), 77.7⁺ (CHOC=O), 68.0⁻ (CH₂), 55.8⁺ (OMe), 44.1⁻ (CMe₂), 24.0⁺ (Me) and 23.0⁺ (Me); m/z (LSIMS) 541 (68%, MH⁺), 389 (55, M – OCOAr), 201 (100, Ph₂PO) (Found: MH⁺, 541.2127. C₃₃H₃₄O₅P requires *M*, 541.2128). Chiral HPLC analysis (50 : 50 isohexane–IPA, τ_{major} 6.8 min, τ_{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 cm³). 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 cm³) and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 cm³), the combined organic extracts were washed with brine (50 cm³), dried (MgSO₄) and evaporated under reduced pressure to give *diol* **17** (582 mg, 92%) as prisms, mp 157–158 °C (from EtOAc–hexane); [α]_D –35 (c. 0.96 in CHCl₃); R_f (EtOAc) 0.41; ν_{\max} (CHCl₃)/cm^{–1} 3600–3000 (br, OH), 1437 (P–Ph) and 1153 (P=O); δ_H (400 MHz; CDCl₃) 7.87–7.80 (2H, m, Ph₂PO), 7.73–7.67 (2H, m, Ph₂PO), 7.60–7.48 (6H, m, Ph₂PO and Ph), 7.36–7.20 (5H, m, Ph₂PO and Ph), 6.85 (1H, d, *J* 24.5, *CH*Ph), 5.72* (1H, t, *J* 6.5, CH₂OH), 5.22 (1H, dd, *J* 20.5 and 9.5, CHOH), 4.61* (1H, br d, *J* 9.5, CHOH), 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); δ_C (100 MHz; CDCl₃) 145.8⁺ (d, *J* 12.5, CHPh), 138–127 (m, Ph₂PO, Ph and Ph₂PO–C), 78.2⁺ (CHOH), 69.3[–] (CH₂OH), 41.4[–] (CMe₂), 23.1⁺ (Me) and 22.0⁺ (Me); *m/z* (ESI) 429 (100%, MNa⁺), 407 (92, MH⁺) (Found: MH⁺, 407.1777. C₂₅H₂₈O₃P requires *M*, 407.1776) (Found: C, 73.9; H, 6.7; P, 7.7. C₂₅H₂₈O₃P 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 cm³). (1*S*)-(+)-Camphor-10-sulfonyl chloride (74 mg, 0.30 mmol) was added and the reaction mixture was stirred for 20 hours. Water (20 cm³) was added and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 cm³), the combined organic extracts were washed with brine (50 cm³), dried (MgSO₄) and evaporated under reduced pressure to give the crude product. The residue was chromatographed (SiO₂, 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; ν_{\max} (CDCl₃)/cm^{–1} 3500–3100 (br, OH and NH), 1745 (C=O), 1438 (P–Ph), 1356 (SO₂) and 1163 (P=O and SO₂); δ_H (500 MHz; CDCl₃) 7.97–7.90 (2H_{major} and 2H_{minor}, m, Ph₂PO), 7.66–7.23 (13H_{major} and 13H_{minor}, m, Ph₂PO 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, CHOH), 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_BSO₂), 3.43 (1H_{major}, d, *J* 15, CH_AH_BSO₂), 2.92 (1H_{major}, d, *J* 15, CH_AH_BSO₂), 2.84 (1H_{minor}, d, *J* 15, CH_AH_BSO₂), 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_BCCH₂O), 1.06 (3H_{minor}, s, Me_AMe_BCCH₂O), 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_BCCH₂O) and 0.66 (3H_{minor}, s, Me_AMe_BCCH₂O); δ_C (125 MHz; CDCl₃) 214.2[–] (C=O), 214.1[–] (C=O), 147.6⁺ (d, *J* 12.5, CHPh), 147.5⁺ (d, *J* 12.5, CHPh), 136–128 (m, Ph₂PO, Ph and Ph₂PO–C), 76.0[–] (CH₂O), 76.0[–] (CH₂O), 74.6⁺ (CHOH), 74.6⁺ (CHOH), 57.7[–] (CH₂SO₂), 57.6[–] (CH₂SO₂), 47.8[–] (CCH₂SO₂ major and CCH₂SO₂ minor), 46.4⁺ (CH₂C=O), 46.4[–] (CH₂C=O), 42.8⁺ (CH on camphor), 42.7⁺ (CH on camphor), 42.4[–] (CMe₂ major and CMe₂ minor), 41.2[–] (CH₂ on camphor), 41.2[–] (CH₂ on camphor), 26.8[–] (CH₂ major and

CH₂ minor), 24.7[–] (CMe₂), 24.6[–] (CMe₂), 21.5⁺, 21.4⁺, 19.6⁺, 19.6⁺, 19.5⁺ and 19.4⁺ (4 × Me_{major} and 4 × Me_{minor}); *m/z* (ESI) 643 (100%, MNa⁺) (Found: MNa⁺, 643.2268. C₃₅H₄₁NaO₆PS requires *M*, 643.2259).

General procedure for the synthesis of allenes

The hydroxyphosphine oxide (1 mmol) in dry DMF (12 cm³) was added to a stirred suspension of sodium hydride (2 mmol) in dry DMF (5 cm³) 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 cm³). The aqueous layer was extracted with ether (3 × 25 cm³) and the combined organic extracts were washed with water (30 cm³), brine (30 cm³), dried (MgSO₄) 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; [α]_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; [α]_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; [α]_D +4.5 (c. 0.25 in CDCl₃) (lit.,²² +110 (in EtOH)) whose data matched those previously reported.²²

Acknowledgements

We thank Fraser Kerr and Fiona Bell of AstraZeneca for assistance with chiral HPLC and the EPSRC for a grant to JAM.

References

- 1 E. Ciganek, *Org. React. (N. Y.)*, 1997, **51**, 201.
- 2 S. E. Drewes and G. H. P. Roos, *Tetrahedron*, 1988, **44**, 4653.
- 3 V. K. Aggarwal, G. J. Tarver and R. McCague, *Chem. Commun.*, 1996, 2713.
- 4 V. K. Aggarwal, A. Mereu, G. J. Tarver and R. McCague, *J. Org. Chem.*, 1998, **63**, 7183.
- 5 G. H. P. Roos and P. Rampersadh, *Synth. Commun.*, 1993, **23**, 1261.
- 6 M. K. Kundu, S. B. Mukherjee, N. Balu, R. Padmakumar and S. V. Bhat, *Synlett*, 1994, 444.
- 7 A. G. M. Barrett, A. S. Cook and A. Kamimura, *Chem. Commun.*, 1998, 2533; Y. Iwabuchi, M. Nakatani, N. Yokoyama and S. Hatakeyama, *J. Am. Chem. Soc.*, 1999, **121**, 10219; K.-S. Yang and K. Chen, *Org. Lett.*, 2000, **2**, 729.
- 8 S. G. Davies and O. Ichihara, *Tetrahedron: Asymmetry*, 1991, **2**, 183.
- 9 B. Bartels, C. G. Martin, A. Nelson, M. G. Russell and S. Warren, *Tetrahedron Lett.*, 1998, **39**, 1637.

- 10 B. Bartels, J. Clayden, C. G. Martin, A. Nelson, M. G. Russell and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1807.
- 11 C. Guéguen, P. O'Brien, S. Warren and P. Wyatt, *J. Organomet. Chem.*, 1997, **529**, 279.
- 12 Y. Nagaoka and K. Tomioka, *J. Org. Chem.*, 1998, **63**, 6428.
- 13 D. C. Harrowven and H. S. Poon, *Tetrahedron*, 1996, **52**, 1389.
- 14 C. Santelli-Rouvier, *Synthesis*, 1988, 64.
- 15 T. Laube, J. D. Dunitz and D. Seebach, *Helv. Chim. Acta*, 1985, **68**, 1373.
- 16 D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1624.
- 17 F. Ramirez, N. B. Desai and N. McKelvie, *J. Am. Chem. Soc.*, 1962, **84**, 1745.
- 18 J. Uenishi, R. Kawahama, Y. Shiga, O. Yonemitsu and J. Tsuji, *Tetrahedron Lett.*, 1996, **37**, 6759.
- 19 Y. Xu, J. Xia and H. Guo, *Synthesis*, 1986, 691.
- 20 M. B. Eleveld, H. Hogeveen and E. P. Schudde, *J. Org. Chem.*, 1986, **51**, 3635.
- 21 Y. Oikawa, T. Yoshioka and O. Yonemitsu, *Tetrahedron Lett.*, 1982, **23**, 889.
- 22 C. J. Elsevier and P. Vermeer, *J. Org. Chem.*, 1989, **54**, 3726.
- 23 A. D. Buss, W. B. Cruse, O. Kennard and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1984, 243.
- 24 B. Liu, K. K. Wang and J. L. Peterson, *J. Org. Chem.*, 1996, **61**, 8503.
- 25 K. K. Wang, H. R. Zhang and J. L. Peterson, *J. Org. Chem.*, 1999, **64**, 1650.
- 26 J. F. Costello, S. G. Davies and O. Ichihara, *Tetrahedron: Asymmetry*, 1994, **5**, 1999.
- 27 J. E. Davies, R. P. Davies, L. Dunbar, P. R. Raithby, M. G. Russell, R. Snaithe, S. Warren and A. E. H. Wheatley, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2334.
- 28 D. R. Armstrong, D. Barr, M. G. Davidson, G. Hutton, P. O'Brien, R. Snaithe and S. Warren, *J. Organomet. Chem.*, 1997, **529**, 29.
- 29 H. Amri, M. M. Elgaied and J. Villiéras, *Synth. Commun.*, 1990, **20**, 659.
- 30 R. J. W. Schuurman, A. van der Linden, R. P. F. Grimbergen, R. J. M. Nolte and H. W. Scheeren, *Tetrahedron*, 1996, **52**, 8307.
- 31 A. H. Davidson, I. Fleming, J. I. Grayson, A. Pearce, R. L. Snowden and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1977, 550.
- 32 C. M. Cain, R. P. C. Cousins, G. Coumbarides and N. S. Simpkins, *Tetrahedron*, 1990, **46**, 523.
- 33 D. House and S. Warren, unpublished results.
- 34 Y. G. Shermolovich, A. V. Solov'ev, N. P. Kolesnik and L. N. Markovskii, *J. Gen. Chem. USSR (Engl. Transl.)*, 1989, **59**, 464.
- 35 D. J. Collins, L. E. Rowley and J. M. Swan, *Aust. J. Chem.*, 1974, **27**, 841.
- 36 A. L. Baumstark and P. C. Vasquez, *J. Org. Chem.*, 1984, **49**, 793.
- 37 R. Albrecht, G. Kresze and B. Mlakar, *Chem. Ber.*, 1964, 483.