The chemistry of lithiated phosphine oxides: the stereoselective synthesis of alkene-4,5-diols

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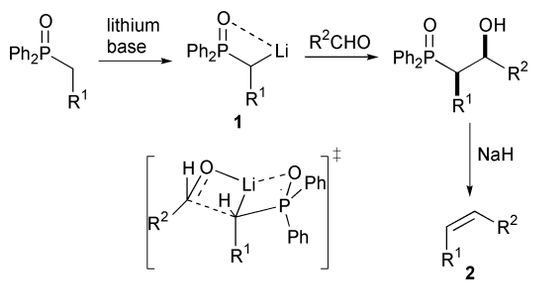
Received (in Cambridge, UK) 20th October 2000, Accepted 27th October 2000
First published as an Advance Article on the web 14th December 2000

Single enantiomers of (*E*)-1,5-diarylpentene-4,5-diols have been synthesised by Horner–Wittig elimination. The stereochemistry is controlled by an asymmetric dihydroxylation, and a stereoselective reduction of a β-keto phosphine oxide.

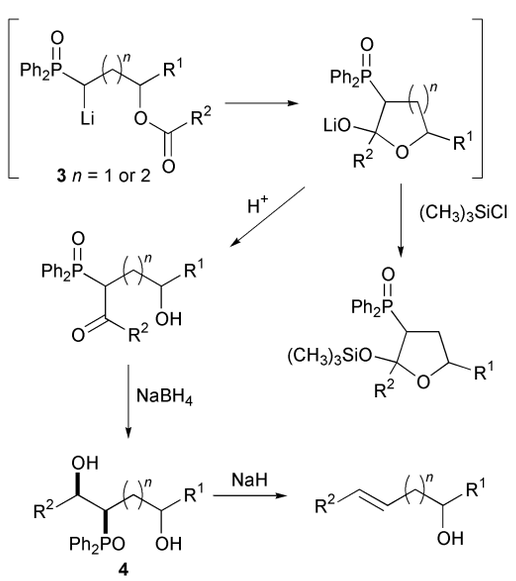
Phosphine oxides are useful intermediates in the synthesis of phosphines and other organic molecules.[1] Much of this chemistry relies on the reactions of α-lithiated phosphine oxides **1**, for instance their addition to carbonyl compounds in the Horner–Wittig synthesis of alkenes **2** (Scheme 1),[2] or their



Scheme 1

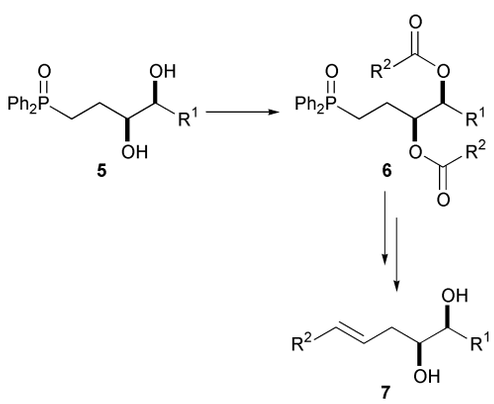
oxidative dimerisation in the synthesis of homochiral bisphosphine 1,2-bis[(*o*-methoxyphenyl)phenyl phosphino]ethane (DIPAMP).[3] Pioneering work by Snaith and others has provided both evidence for the structures of lithiated phosphine oxides[4] and a greater mechanistic understanding of stereoselectivity in Horner–Wittig additions with aldehydes.[5]

Phosphine oxides with γ- or δ-acyloxy groups, once lithiated **3**, react intramolecularly to give the products of acyl transfer



Scheme 2

(Scheme 2).[6] The tetrahedral intermediate formed in the initial addition to the ester functionality can be trapped by the trimethylsilyl chloride within the reaction.[7] Ketones formed by the acyl-transfer process can be reduced diastereoselectively to *syn*-β-hydroxy phosphine oxides **4**, which in turn give (*E*)-alkenes stereospecifically by base mediated elimination. A phosphine oxide containing both γ- and δ-acyloxy groups could transfer either of the two acyl-groups, and we report the selectivity of this process. We made the bis-ester **6** required for the acyl-transfer process from a vicinal diol **5**, and this was made in enantiomerically pure form by asymmetric dihydroxylation of an alkene. The acyl-transfer product was reduced and converted into an (*E*)-alkene, as with other β-keto phosphine oxides (Scheme 3). Such an alkene **7** is an enantiomerically pure 1,2-

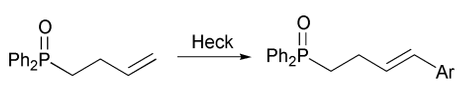


Scheme 3

dihydroxypent-4-ene, the product of the imaginary regio- and stereoselective dihydroxylation of a 1,4-diene.

Synthesis

(*E*)-β-Substituted styrenes tend to be dihydroxylated with high enantioselectivity using the commercial AD-mix reagents.[8] It was envisaged that such a substrate containing an appropriately positioned phosphinoyl group could be synthesised by a Heck coupling onto (but-3-enyl)diphenylphosphine oxide **8** (Scheme 4). This reaction however, using either iodobenzene or 4-iodoanisole, gave inseparable mixtures of products, despite



Scheme 4

 DOI: 10.1039/b008500f

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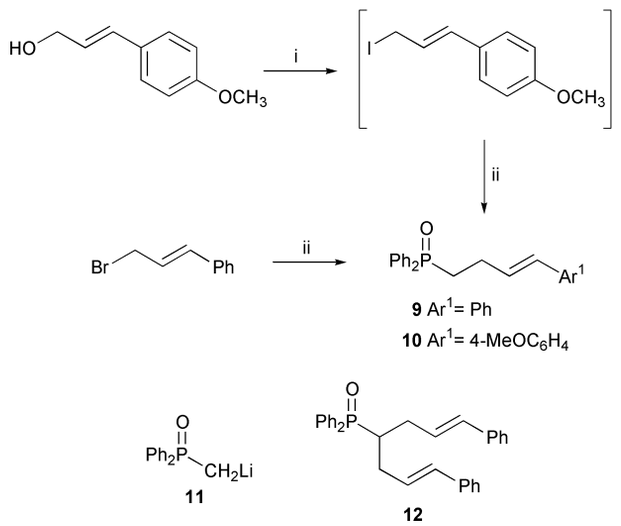
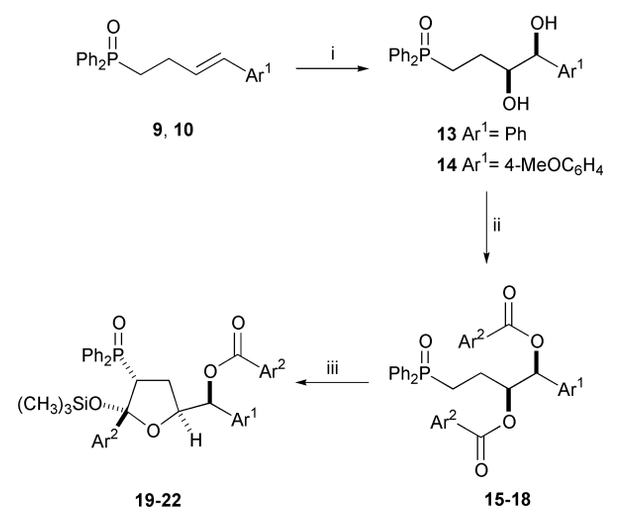
many attempts at varying the reagents and reaction conditions. This area is a matter of continuing interest within this group.

An alternative synthesis of these alkenes was possible by alkylation of lithiated (diphenyl)methylphosphine oxide **11** (Scheme 5). In the case of product **10** the electrophile was



Scheme 5 *Reagents and conditions*: i, Me_3SiCl, NaI, THF, −78 °C; ii, **11**, THF, −78 °C, 39% (**9**), 44% (**10**, 2 steps).

made *in situ* from 4-methoxycinnamyl alcohol. Asymmetric dihydroxylation was then achieved with excellent enantioselectivity to give diols **13** and **14**, followed by acylation producing four bis-esters **15** to **18**. Lithiation of these compounds with lithium diisopropylamide in the presence of trimethylsilyl chloride (−78 °C to room temperature) gave cyclic ketals **19** to **22** with high stereoselectivity (Scheme 6 and Table 1). In the



Scheme 6 *Reagents and conditions*: i, AD-α-mix, $MeSO_2NH_2$, *t*-BuOH, H_2O, 98% (**13**), 58% (**14**); ii, Ar^2COCl, Et_3N, DMAP, CH_2Cl_2; iii, LDA, Me_3SiCl, THF, −78 °C to rt, SiO_2.

case of bis-esters **15** and **17** simple acyl-transfer of the proximal benzoate group could be achieved at −78 °C without the use of trimethylsilyl chloride. The similar ketone **24** was synthesised by treatment of ketal **20** with tetra-*n*-butylammonium fluoride (TBAF). These ketones were reduced to give mono-benzoates **26** to **28** or triols **29** to **31** (Scheme 7 and Table 2), which were treated with sodium hydride to produce alkenediols **32** to **34** as single geometric isomers (Scheme 8).

Discussion

The synthesis of dihydroxylation substrate **9** by alkylation can also produce dialkylation product **12** as a by-product.

Table 1 Bis-esters from the benzoylation of diols **13** and **14**, and cyclic ketals formed by lithiation and *in situ* trapping with trimethylsilyl chloride

Ar^1	Ar^2	Compound	Yield (%)	Compound	Yield (%)
Ph	Ph	**15**	98	**19**	81
Ph	4-$MeOC_6H_4$	**16**	95	**20**	89
4-$MeOC_6H_4$	Ph	**17**	57	**21**	51
4-$MeOC_6H_4$	4-$MeOC_6H_4$	**18**	73	**22**	30

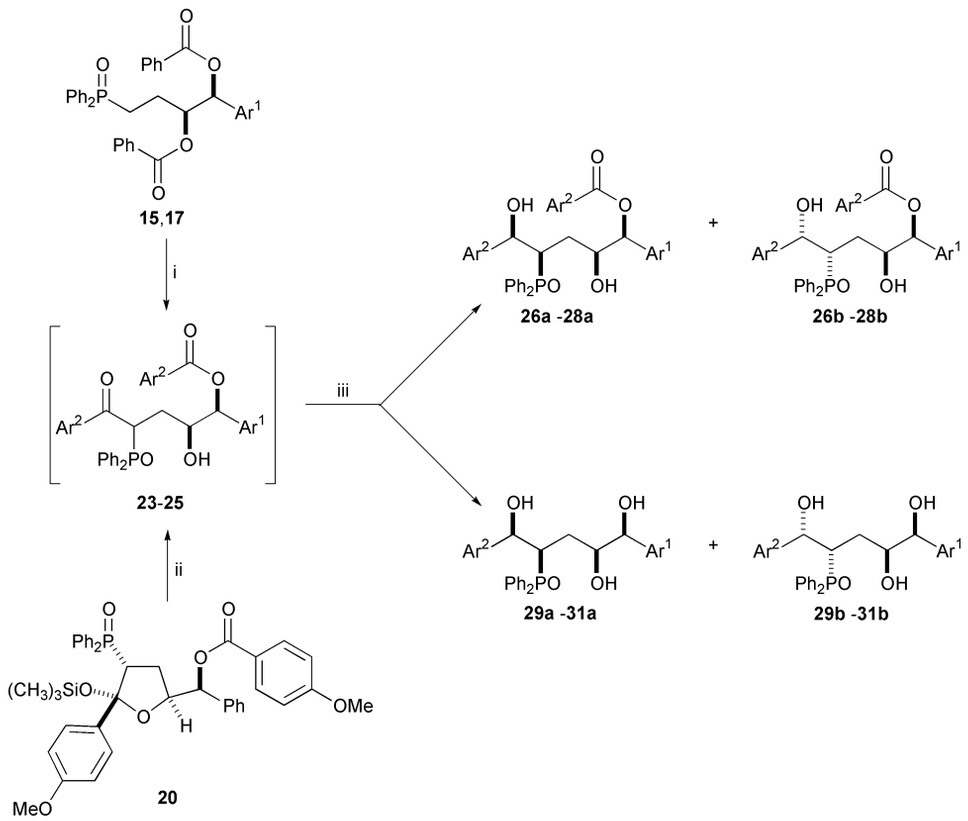
Table 2 *In situ* reduction of phosphoryl ketones to give mono-benzoates (yields of isolated major diastereoisomers) and triols (combined yields of both diastereoisomers)

Ar^1	Ar^2	Ketone	Mono-benzoate	Yield (%)	Triol	Yield (%)
Ph	Ph	**23**	**26**	28	**29**	60
Ph	4-$MeOC_6H_4$	**24**	**27**	34	**30**	—
4-$MeOC_6H_4$	Ph	**25**	**28**	—	**31**	50

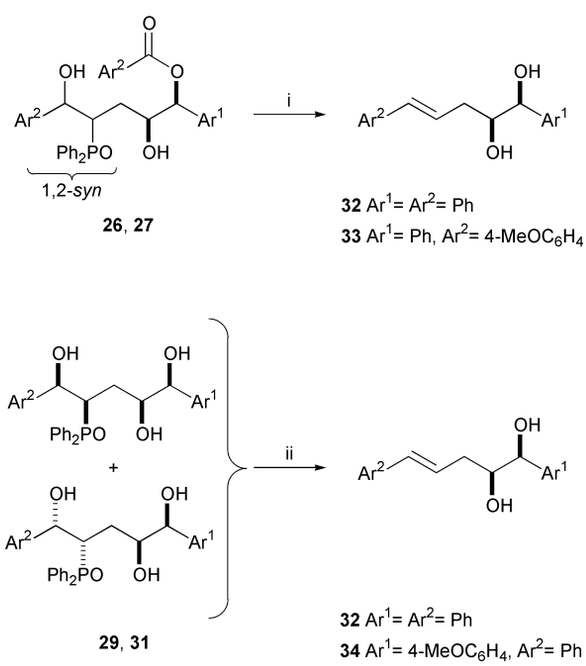
Generally, if lithiated (diphenyl)methylphosphine oxide **11** is added very slowly to an excess of the electrophile then the formation of this by-product can be reduced. It is interesting to note that the formation of diene **12** is accompanied by the appearance of a dark green colour in the reaction mixture. The cause of this unusual colouration was established by the independent treatment of alkene **9** with lithium diisopropylamide to give a dark green solution of the lithiated phosphine oxide, which could be reprotonated to give starting material. The enantioselectivity of the asymmetric dihydroxylation was established by chiral HPLC in comparison with authentic racemic samples of diols **13** and **14** synthesised using the non-asymmetric variant of the dihydroxylation procedure.[9] The stereoselectivities are very high (>95% ee) for these 4-phosphinoylalkenes using the standard AD-mix. This is not the case for similar 3-phosphinoylalkenes, where the enantioselectivities are lower, possibly due to unfavourable interactions between the phosphine oxide group and the osmium or the ligand in the transition structure.[10]

Acyl transfer from oxygen to carbon has been observed for both γ- and δ-acyloxy phosphine oxides.[6] Before this study it was unknown whether there would be any selectivity in the reaction of a lithiated phosphine oxide containing both ester groups. Here however substrates **15** to **18** did react only by addition to the proximal ester group, as seen by *in situ* trapping to form the 5-membered-ring ketals **19** to **22**. This can be explained by assuming that the (4,5)-bicyclic transition structure **34** would form significantly faster than the (4,6) alternative **35** (Scheme 9). The structure of the 5-membered-ring ketals has been established for a similar compound by X-ray crystallography, by which it was also shown that the trimethylsilyloxy and phosphinoyl groups adopt a *syn*-relationship in the product.[7] This stereochemistry is possibly a result of the chelation of the lithium to both the phosphine oxide and carbonyl groups in the transition structure **34**, similar to that proposed by Snaith *et al.* for similar reactions with aldehydes.[5] The C(5)-stereochemistry in the ring may be due to the preferred pseudo-equatorial orientation of the side chain in the transition structure.

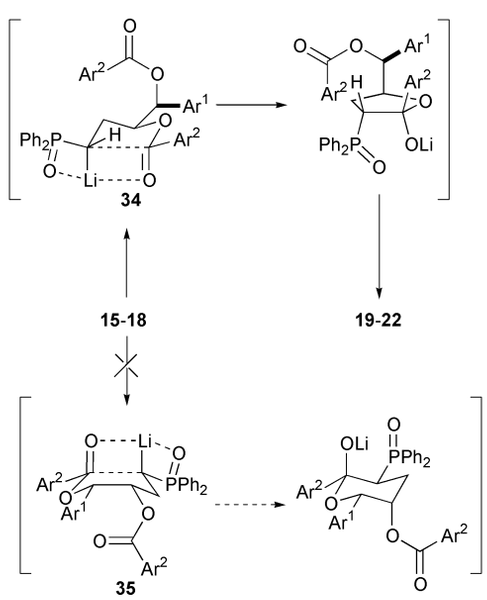
The best yields of ketals **19** to **22** were obtained when the reactions were allowed to warm slowly from −78 °C to ambient temperature, and by quenching the reaction with silica gel instead of an aqueous work-up. This is especially true for the 4-methoxybenzoate esters **16** and **18** which, once lithiated at −78 °C, do not react to any measurable extent at this temperature. Lithiated versions of benzoate esters **15** and **17** do however react at −78 °C and the non-silylated acyl-transfer products **23** and **25** can be obtained by quenching the reactions



Scheme 7 *Reagents and conditions*: LDA, THF, −78 °C; ii, TBAF, THF; iii, $NaBH_4$, EtOH.



Scheme 8 *Reagents and conditions*: i, NaH (2 eq.), DMF, 20 to 60 °C, 71% (**32**), 35% (**33**); ii, NaH (3 eq.), DMF, 20 to 60 °C, 60% (**32**), 60% (**34**).

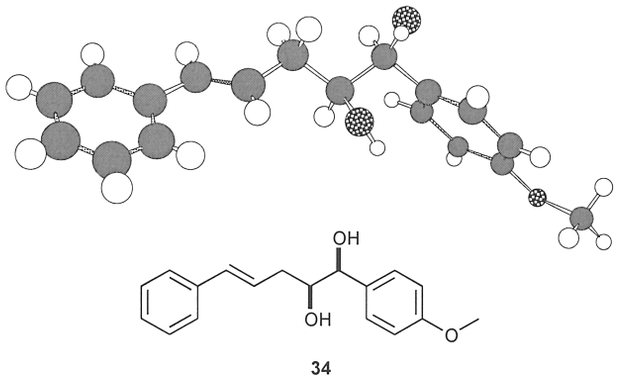


Scheme 9

at low temperature with ammonium chloride. The difference in behaviour between the benzoate and 4-methoxybenzoate esters is possibly due to the deactivation of the ester by the electron-donating methoxy substituent.

The β-keto phosphine oxides, produced either by low temperature acyl transfer or by treatment of a silyl ketal with TBAF, were reduced with sodium borohydride to give mixtures of diols **26** to **28** and triols **29** to **31**, the result of reductive cleavage of the second benzoate group. Benzoate cleavage seems to be time- and temperature-dependent, but is slower than the ketone reductions. The reduction of ketone **23** produced a mixture of two diastereoisomers of a triols **29a** and **29b**, and their mono-benzoates **26a** and **26b**. It seems that the diastereomeric ratio of mono-benzoates and triols is similar, indicating that the benzoate cleavage either does not affect the ketone reduction selectivity, or occurs subsequently. The major diastereoisomer of the mono-benzoate could be isolated by chromatography, but the two diastereoisomers of the triol were isolated as a 3.4 to 1 mixture.

The absolute stereochemistry of the major diastereoisomer of mono-benzoate **26** was not determined, but it was eliminated by treatment with sodium hydride to give the (*E*)-alkene **32** (Scheme 8), showing that structure has a C(1)–C(2) *syn*-stereochemistry and is either compound **26a** or **26b** (Scheme 7).



34

Fig. 1

It should be noted that these conditions also lead to the removal of the remaining benzoate group. Similarly, the mixture of triols **29a** and **29b** also gave the same alkenediol **32** as a single geometric isomer, indicating that they both also have C(1)–C(2) *syn*-stereochemistry. While the high 1,2-*syn*-selectivity for the reduction of β-keto phosphine oxides is well known, the 1,3-selectivity for this reduction is not well understood.[11] Reduction of ketone **25** produced triols **31a** and **31b** as a mixture (mono-benzoate **28** was not detected), and reduction of ketone **24** produced a major diastereoisomer of mono-benzoate **27** without any triol **30**. Treatment with sodium hydride gave the corresponding (*E*)-alkenediols **33** and **34**. The structure of alkene **34** was confirmed by X-ray crystallography (Fig. 1).

The alkenediols **32**–**34** are the products of a formal regio- and enantioselective dihydroxylation of 1,5-diarylpenta-1,4-dienes. While selective dihydroxylations of dienes are known, they are usually performed on substrates containing two or more alkene groups with distinctly different steric or electronic properties. For instance, Sharpless and co-workers have studied the asymmetric dihydroxylation of a range of conjugated systems,[12] and Evans *et al*. have reported a selective dihydroxylation of a non-conjugated diene as part of a synthesis of Zaragozic acid C.[13] The selective asymmetric dihydroxylation of (*E*)-hexa-1,4-diene has been reported by Sharpless and co-workers. In this case the more substituted double bond reacted with a 13 : 1 selectivity.[12] Diols such as **32**–**34** have not been obtained by simple selective dihydroxylation of symmetrical or near-symmetrical dienes, and the methodology presented here represents a simple and extremely adaptable method of synthesising such compounds.

Conclusion

The synthesis of enantiomerically pure (*E*)-1,5-diaryl-1,2-dihydroxypent-4-enes can be performed using a combination of the stereochemically reliable asymmetric dihydroxylation reaction and phosphine oxide mediated olefin synthesis. Along with these reactions it has been shown that the addition of a lithiated phosphine oxide to a γ-acyloxy substituent occurs selectively in the presence of a similar δ-substituent, and that these acyl-transfer products can be reduced with both 1,2- and 1,3-stereoselectivity, *en route* to diastereo- and enantiomerically pure alkenediols.

Experimental

General

All solvents were distilled before use. THF was freshly distilled from lithium aluminium hydride whilst CH_2Cl_2 was freshly distilled from calcium hydride. Triphenylmethane was used as an indicator for THF. Methanol was freshly distilled from sodium methoxide. Diisopropylamine, DMF, and DMSO were dried by stirring over and distilling from calcium hydride (at reduced pressure when necessary) and were stored over activated 4 Å molecular sieves. *n*-Butyllithium was titrated against diphenylacetic acid before use. All reactions were carried out with oven-dried glassware and all reactions in non-aqueous solutions were carried out under an atmosphere of argon.

Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography was carried out on commercially available pre-coated plates (Merck Kieselgel $60F_{254}$). Proton, carbon and phosphorus NMR spectra were recorded on Bruker DPX250, AM400, DRX400 or DRX500 Fourier Transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million down field of tetramethylsilane and values of coupling constants (*J*) are given in Hz. Carbon NMR spectra were recorded with broad band proton decoupling and Attached Proton Test or DEPT. Where indicated the symbols $^+$ and $^-$ after the carbon NMR chemical shift indicate odd and even numbers of attached protons respectively. Signals marked with * in proton NMR disappear when a D_2O shake is performed.

Melting points were measured on a Stuart Scientific melting point apparatus (SMP 1) and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 1600 (FT-IR) spectrophotometer. Mass spectra were recorded on a Kratos (MS890) single beam spectrometer or a micromass platform with an HP1050 LC system. Microanalyses were carried out by the staff of the University Chemical Laboratory using Carlo Erba 1106 or Perkin-Elmer 240 automatic analysers.

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter (using the sodium D line; 589 nm). Specific rotations are given in units of 10^{-1} deg dm^2 g^{-1}.

[(*E*)-4-Phenylbut-3-enyl]diphenylphosphine oxide 9 and (*E*,*E*)-1,7-diphenyl-4-diphenylphosphinoyl-hepta-1,6-diene 12

By the method of Nelson and co-workers,[10] *n*-butyllithium (19.5 cm^3 of a 2 M solution in hexane; 23.31 mmol) was added dropwise to a stirred solution of methyldiphenylphosphine oxide (5.00 g, 23.31 mmol) in dry THF (100 cm^3) under argon at 0 °C and the deep red solution was cooled to −78 °C. After 1 hour, the lithiated phosphine oxide solution was added by cannula over a period of 15 minutes to a stirred solution of cinnamyl bromide (5.2 g, 3.95 cm^3, 26.5 mmol) in dry THF (60 cm^3) under argon at −78 °C and stirred for 3 h. The resulting dark green solution was allowed to warm to 10 °C overnight (colour changed to red). Saturated ammonium chloride solution (50 cm^3) was added and the mixture was filtered. The aqueous layer was extracted with dichloromethane (4 × 100 cm^3). The combined organic extracts were washed with brine (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product as an orange oil. Purification by flash chromatography on silica with EtOAc as eluent gave the alkene product[10] **9** (3.68 g, 39%) and *diene* **12** (834 mg, 8%) as white amorphous solids. The *diene* product: mp 134–136 °C (from EtOAc); R_f (EtOAc) 0.44; $\nu_{max}(CDCl_3)/cm^{-1}$ 1817 (C=C), 1597 (Ph), 1437 (P-Ph) and 1177 (P=O); δ_H(400 MHz; $CDCl_3$) 8.22–7.81 (4 H, m, *o*-Ph_2PO), 7.53–7.45 (6 H, m, *o*-Ph_2PO, *m*-Ph_2PO), 7.37–7.15 (10 H, m, Ph), 6.29 (2 H, d, *J* 15.5, PhC*H*), 6.10 (1 H, dt, *J* 15.5, 6.5, C*H*CH_2), 3.12–2.47 (5 H, m, CH_2 and C*H*); δ_C(100 MHz; $CDCl_3$) 137.2$^-$ (*i*-Ph), 132.6$^-$ (d, *J* 94, *i*-Ph_2PO), 132.2$^+$ (PhCH), 131.6$^+$ (*p*-Ph_2PO), 131.0$^+$ (d, *J* 8.6, *o*-Ph_2PO), 128.7$^+$ (d, *J* 11.3, *m*-Ph_2PO), 128.4$^+$, 126.1$^+$ (*o*-Ph, *m*-Ph), 127.7$^+$ (d, *J* 10.3, PhCH*C*H), 126.1$^+$, (*p*-Ph), 38.4$^+$ (d, *J* 69, PCH), 31.3$^-$ (PCH*C*H$_2$); *m*/*z* (EI+) 448 (65%, M$^+$), 331 (95, Ph_2P=OCH_2CH_2CHCHPh) and 201 (100, Ph_2PO) (Found: M$^+$, 448.19665. $C_{31}H_{29}OP$ requires *M*, 448.19560).

[(*E*)-4-(4-Methoxyphenyl)but-3-enyl]diphenylphosphine oxide 10

(*E*)-3-(4-Methoxyphenyl)prop-2-enol[14] (0.200 g, 1.22 mmol) and sodium iodide (0.183 g, 1.22 mmol) were dissolved in dry

THF (10 cm^3) under argon and shaded from light by tin foil. The clear solution was degassed and subsequently trimethylsilyl chloride (0.33 g, 3.04 mmol) was added slowly at room temperature over a period of 2 min. The resulting solution was stirred for a further 1 h. In a separate flask *n*-butyllithium (1.7 cm^3 of a 1.44 M solution in hexane, 2.44 mmol) was added at 0 °C to a stirred solution of methyldiphenylphosphine oxide (0.53 g, 2.44 mmol) in dry THF (10 cm^3), stirred for 1 h, subsequently cooled to −78 °C and stirred for a further 15 min. The resulting orange solution was added by cannula over a period of 10 min at −78 °C to a stirred solution of the iodide. The resulting yellow solution was stirred at −78 °C in the dark for 9 h. Saturated ammonium chloride (5 cm^3), water (10 cm^3) and ethyl acetate (30 cm^3) were added and the mixture was allowed to warm to room temperature. The organic layer was separated from the aqueous layer, washed with 10% sodium thiosulfate solution (2 × 25 cm^3), brine (10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product as a yellow oil. Purification by column chromatography on silica with EtOAc as eluent gave the *phosphine oxide* (0.195 g, 44%) as a white solid; R_f (EtOAc) 0.32; a sample was recrystallized (EtOAc–hexane) as long needles, mp 94–96 °C (EtOAc–hexane); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1607 (Ar) and 1175 (P=O); δ_H(400 MHz; $CDCl_3$) 7.78–7.72 (4 H, m, *o*-Ph_2P), 7.52–7.43 (6 H, m, *p*-Ph_2P), 7.17 (2 H, d, *J* 8.5, *o*-$MeOC_6H_4$), 6.80 (2 H, d, *J* 8.5, *m*-$MeOC_6H_4$), 6.31 (1 H, d, *J* 16.0, ArC*H*=CH), 6.02 (1 H, dt, *J* 16.0, 6.5, C*H*CH_2), 3.76 (3 H, s, CH_3O), 2.55–2.47 (2 H, m, PCH_2), 2.45–2.38 (2 H, m, CHCH_2); δ_C(100 MHz; $CDCl_3$) 159.3 (CH_3OC), 133.4 (d, *J* 98, *i*-Ph_2PO), 132.1 (d, *J* 2, *p*-Ph_2PO), 131.2 (d, *J* 9, *o*-Ph_2PO), 130.5 (Ar*C*H), 130.4 (*i*-$MeOC_6H_4$), 129.1 (d, *J* 12, *m*-Ph_2PO), 127.5 (*m*-$MeOC_6H_4$), 127.3 (d, *J* 15, *C*HCH_2), 55.7 (OCH_3), 30.2 (d, *J* 71, PCH_2) and 25.4 (d, *J* 3, CH*C*H_2); δ_P(162 MHz; $CDCl_3$) 34.4; *m*/*z* (EI+) 362 (100%, M^+) and 201 (55, Ph_2PO) (Found: M^+, 362.1413. $C_{23}H_{23}O_2P$ requires *M*, 362.1435).

(1*S*,2*S*)-4-Diphenylphosphinoyl-1–(4-methoxyphenyl)butane-1,2-diol 14

By the method of Nelson and co-workers,[10] AD-mix-α (6.18 g), methanesulfonamide (0.420 g, 4.41 mmol) and [(*E*)-4-(4-methoxyphenyl)but-3-enyl]diphenylphosphine oxide **10** (1.60 g, 4.41 mmol) in 1:1 *tert*-butyl alcohol–water (88 cm^3) (shaded from the light) were stirred for 5 days to give a crude product as a white amorphous solid. Purification by flash chromatography on silica with 1:19 MeOH–EtOAc and then 1:9 MeOH–EtOAc as eluent gave the *diol* (1.02 g, 58%) as white needles, mp 130–132 °C (from EtOAc); R_f (MeOH–EtOAc 1:19) 0.32; HPLC: Chiralpak AD, 13.4 min (isopropyl alcohol–isohexane 30:70, 1 cm^3 min^{-1}) >99% ee; $[\alpha]_D^{19}$ −12.9 (*c* 0.17, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3269 (OH), 3069 (OH), 1608 (Ar), 1514 (Ar), 1437 (P–Ph) and 1174 (P=O); δ_H(400 MHz; $CDCl_3$) 7.68–7.61 (4 H, m, *o*-Ph_2PO), 7.51–7.38 (6 H, m, *m*-Ph_2PO, *p*-Ph_2PO), 7.17 (2 H, d, *J* 8.5, *o*-$MeOC_6H_4$), 6.69 (2 H, d, *J* 8.5, *m*-$MeOC_6H_4$), 4.89 (1 H, d, *J* 4.0, OH), 4.31 (1 H, dd, *J* 7.0, 2.5, ArC*H*OH), 3.83 (1 H, d, *J* 2.5, OH), 3.75 (3 H, s, OCH_3), 3.73–3.67 (1 H, m, C*H*(OH)CH_2), 2.45–2.25 (2 H, m, PCH_2), 1.73–1.55 (2 H, m, PCH_2CH_2); δ_C(100 MHz; $CDCl_3$) 159.3 (MeO*C*), 133.5 (*i*-$MeOC_6H_4$), 132.5 (d, *J* 98, *i*-Ph_2PO), 132.3$^+$ (*p*-Ph_2PO), 132.0$^+$ (d, *J* 9, *o*-Ph_2PO), 129.2$^+$ (d, *J* 12, *m*-Ph_2PO), 128.6$^+$ (*o*-$MeOC_6H_4$), 114.2$^+$ (*m*-$MeOC_6H_4$), 77.5$^+$ (Ar*C*HOH), 76.2$^+$ (d, *J* 10, CH_2-*C*HOH), 55.7$^+$ (OCH_3), 27.1$^-$ (*C*H_2CH) and 26.2$^-$ (d, *J* 72, PCH_2); δ_P(162 MHz; $CDCl_3$) 36.8; *m*/*z* (EI+) 378 (28%, M − H_2O), 259 (100, Ph_2P=OCH_2CH_2CHOH) and 201 (55, Ph_2PO) (Found: M − H_2O, 378.1384. $C_{23}H_{23}O_3P$ requires *M*, 378.1385).

General procedure for the preparation of benzoic and methoxybenzoic acid esters

Triethylamine and the chosen acid chloride were added dropwise to a stirred solution of the diol and 4-(dimethylamino)-pyridine in dry dichloromethane at room temperature. The reaction was stirred for 18 h, quenched with water, extracted with dichloromethane, dried and evaporated under reduced pressure to give the crude product.

(1*S*,2*S*)-1,2-Bis(benzoyloxy)-4-diphenylphosphinoyl-1-phenylbutane 15

Using the general procedure, triethylamine (4.3 g, 42.5 mmol), benzoyl chloride (5.3 g, 37.7 mmol), diol **13**[10] (3.00 g, 8.16 mmol) and 4-(dimethylamino)pyridine (1.70 g, 14.2 mmol) in dry dichloromethane (70 cm^3) gave a crude product. Purification by flash chromatography on silica with 2:1 EtOAc–hexane as eluent gave the *diester* (4.20 g, 98%) as white needles, mp 159–161 °C; R_f (EtOAc–hexane, 2:1) 0.14; $[\alpha]_D^{23}$ −2.0 (*c* 1.61, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 1720 (C=O), 1438 (P–Ph) and 1178 (P=O); δ_H(400 MHz; $CDCl_3$) 8.02–7.85 (4 H, m, $PhCO_2$), 7.70–7.22 (21 H, m, Ph_2PO, Ph and $PhCO_2$), 6.10 (1 H, d, *J* 7.5, PhCH), 5.70 (1 H, q, *J* 6.5, CH_2CH), 2.40–2.20 (2 H, m, PCH_2) and 2.00–1.90 (2 H, m, PCH_2CH_2); δ_C(100.6 MHz; DMSO-d_6) 165.0$^-$ (C=O), 164.5$^-$ (C=O), 137–126 (m, Ph_2PO and Ph), 75.7$^+$ (Ph*C*H), 75.0$^+$ (d, *J* 15.0, CH_2CH), 24.1$^-$ (d, *J* 72.5, PCH_2) and 22.5$^-$ (PCH_2CH_2); *m*/*z* (ES+) 597 (35%, MNa^+), 576 (100, M^+), 453 (22, M − $PhCO_2H$), 316 (54, M − Ph_2P=OMe, $-CO_2$), 261 (30, Ph_2P=O$MeCO_2$) and 217 (49, Ph_2P=OMe) (Found: MNa^+, 597.1809. $C_{36}H_{31}ONaP$ requires *M*, 597.1807).

(1*S*,2*S*)-Bis(4-methoxybenzoyloxy)-4-diphenylphosphinoyl-1-phenylbutane 16

Using the general procedure, triethylamine (0.80 cm^3, 5.73 mmol), 4-methoxybenzoyl chloride (847 mg, 4.97 mmol), diol **13**[10] (700 mg, 1.91 mmol) and 4-(dimethylamino)pyridine (397 mg, 3.25 mmol) gave a crude product. Purification by flash chromatography on silica with 1:9 MeOH–EtOAc as eluent gave the *diester* (1.21 g, >95%) as a white solid, mp 150–152 °C (EtOAc); R_f (MeOH–EtOAc 1:9) 0.34; $[\alpha]_D^{23}$ +3.99 (*c* 0.60, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1712 (C=O), 1606 (Ar), 1511 (Ar), 1437 (P–Ph) and 1169 (P=O); δ_H(400 MHz; $CDCl_3$) 7.91 (2 H, d, *J* 9, *o*-$MeOC_6H_4$), 7.88 (2 H, d, *J* 9.0, $MeOC_6H_4$), 7.65–7.57 (4 H, m, Ph_2PO), 7.51–7.32 (7 H, m, Ph_2PO and Ph), 7.30–7.26 (4 H, m, Ph), 6.819 (2 H, d, *J* 9, *m*-$MeOC_6H_4$), 6.86 (2 H, d, *J* 9 *m*-$MeOC_6H_4$), 6.05 (1 H, d, *J* 7.5, PhC*H*OH), 5.69–5.64 (1 H, m, CH_2CHO), 3.82 (3 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 2.38–2.27 (2 H, m, PCH_2), 2.00–1.92 (2 H, m, PCH_2CH_2); δ_C(100 MHz; $CDCl_3$) 167.8 (C=O), 167.3 (C=O), 165.7 (MeO*C*), 165.6 (MeO*C*), 138.6 (*i*-Ph), 134.5 (d, *J* 99, *i*-Ph_2PO), 134.0–130.0 (m, Ar), 129.5$^+$ (*o*-$MeOC_6H_4$), 124.2 (*C*CO_2), 124.0 (*C*CO_2), 114.1$^+$ (*m*-$MeOC_6H_4$), 114.0$^+$ (*m*-$MeOC_6H_4$), 78.5$^+$ (Ph*C*HOH), 78.0$^+$ (d, *J* 15, CH_2CHO), 57.5$^+$ (2 × OCH_3), 27.8$^-$ (d, *J* 72, PCH_2) and 25.7$^-$ (br s, PCH_2CH_2); *m*/*z* (EI+) 482 (40%, M − $MeOC_6H_4OH$), 393 (55, M − Ph_2P=OCH_2-CH_3), 347 (55, Ph_2P=O$CH_2CHCHCHOHPh$), 201 (30, Ph_2PO) and 135 (100, $MeOC_6H_4CO$) (Found: M − $MeOC_6H_4OH$, 482.16424. $C_{30}H_{27}O_4P$ requires *M*, 482.16470).

(1*S*,2*S*)-Bis(benzoyloxy)-4-diphenylphosphinoyl-1-(4-methoxyphenyl)butane 17

Using the general procedure, triethylamine (0.35 cm^3, 2.57 mmol), benzoyl chloride (0.27 cm^3, 2.33 mmol), the diol **14** (370 mg, 0.93 mmol), and 4-(dimethylamino)pyridine (171 mg, 1.40 mmol) in dry dichloromethane (10 cm^3) were stirred for 8 h to give a crude product. Purification by flash chromatography on silica with 2:1 EtOAc–hexane as eluent gave the *diester* (323 mg, 57%) as a white solid, mp 160–161 °C (from EtOAc); R_f (EtOAc) 0.33; $[\alpha]_D^{23}$ +3.1 (*c* 0.71, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1721 (C=O); δ_H(400 MHz; $CDCl_3$) 7.96 (2 H, d, *J* 7.0, *o*-$PhCO_2$), 7.90 (2 H, d, *J* 7.0, *o*-$PhCO_2$), 7.65–7.57 (4 H, m, Ph_2PO), 7.53–7.29 (14 H, m, Ph_2PO and Ar), 6.82 (2 H, d, *J* 9.0,

$MeOC_6H_4$), 6.06 (1 H, d, *J* 8.0, ArC*H*OH), 5.73–5.68 (1 H, m, CH_2CHO), 3.76 (3 H, s, OCH_3), 2.41–2.25 (2 H, m, CH_2P), 2.03–1.90 (2 H, m, $CHCH_2$); δ_C(100 MHz; $CDCl_3$) 168.5 (C=O), 167.9 (C=O), 162.4 (CH_3OC), 133–128 (m, Ar), 114.7$^+$ (*m*-$MeOC_6H_4$), 76.9$^+$ (Ar*C*HOH), 75.6$^+$ (d, *J* 15, *C*HOH), 55.7$^+$ (CH_3O), 26.6$^-$ (d, *J* 72, PCH_2), 25.7$^-$ (PCH_2CH_2); δ_P(162 MHz; $CDCl_3$) 32.2; *m*/*z* (ES+) 627 (100%, MNa^+), 576 (20, M − CH_2CH_3) and 483 (45, M − $PhCO_2$) (Found: MNa^+, 627.1949. $C_{37}H_{33}O_6NaP$ requires *M*, 627.1912).

(1*S*,2*S*)-1,2-Bis(4-methoxybenzoyloxy)-4-diphenylphosphinoyl-1-(4-methoxyphenyl)butane 18

Using the general procedure, triethylamine (0.21 cm^3, 1.48 mmol), 4-methoxybenzoyl chloride (225 mg, 4.97 mmol), diol **14** (195 mg, 0.49 mmol) and 4-(dimethylamino)pyridine (128 mg, 1.06 mmol) gave a crude product. Purification by flash chromatography on silica with EtOAc as eluent gave the *diester* (239 mg, 73%) as a white solid, mp 171–172 °C (EtOAc); R_f (EtOAc) 0.26; $[\alpha]_D^{23}$ +14.2 (*c* 0.52, $CHCl_3$); $\nu_{max}(CH_2Cl_2)$/cm^{-1} 1714 (C=O), 1599 (Ar), 1436 (P–Ph) and 1169 (P=O); δ_H(250 MHz; $CDCl_3$) 7.93 (2 H, d, *J* 9.0, $MeOC_6H_4CO_2$), 7.87 (2 H, d, *J* 9.0, $MeOC_6H_4CO_2$), 7.69–7.55 (4 H, m, Ph_2PO), 7.53–7.32 (6 H, m, Ph_2PO), 7.33 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.87 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.82 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.81 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.01 (1 H, d, *J* 8.0, CH_2CHCH), 5.72–5.61 (1 H, m, CH_2CH), 3.84 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3), 2.39–2.24 (2 H, m, PCH_2), 2.02–1.87 (2 H, m, PCH_2CH_2); δ_C(100 MHz; $CDCl_3$) 165.8 (C=O), 165.2 (C=O), 163.6, 163.4, 159.4 (CH_3OC), 139–113 (m, Ar), 76.2 (Ar*C*HOH), 74.9 (d, *J* 15, CH_2CHO), 57.5, 57.5, 55.3 (3 × OCH_3), 25.6 (d, *J* 72, PCH_2) and 23.2 (d, *J* 2, PCH_2CH_2); *m*/*z* (EI+) 512 (10%, M − $MeOC_6H_4CO_2H$), 201 (30, Ph_2PO) and 135 (100, $MeOC_6H_4CO$) (Found: M$^+$, 512.17471. $C_{31}H_{29}O_5P$ requires *M*, 512.17526).

General procedure for the preparation of ketals

By the method of Hutton and co-workers,[7] a solution of LDA was prepared by the dropwise addition of *n*-butyllithium (1.5 M solution in hexane, 2.55 mmol) to a stirred solution of diisopropylamine (3.48 mmol) in dry THF (10 cm^3) at 0 °C. The prepared LDA was added dropwise to a solution of the diester (1.74 mmol) and chlorotrimethylsilane (6.97 mmol) in dry THF (25 cm^3) at −78 °C. The reaction mixture was stirred for 4 h and warmed to room temperature. The reaction was quenched by the addition of silica (4 g) and evaporated under reduced pressure to give a silica absorbed residue.

(1′*S*,2*R*,3*R*,5*S*)-3-Diphenylphosphinoyl-5-[phenyl(benzoyloxy)-methyl]-2-phenyl-2-trimethylsilyloxytetrahydrofuran 19

Using the general procedure, *n*-butyllithium (1.7 cm^3 of a 1.5 M solution in hexane, 2.55 mmol), diisopropylamine (352 mg, 3.48 mmol), diester **15** (1.00 g, 1.74 mmol) and chlorotrimethylsilane (757 mg, 6.97 mmol) gave the silica adsorbed residue. Purification by flash chromatography on silica with 2:1 EtOAc–hexane as eluent gave the *tetrahydrofuran* (920 mg, 81%) as colourless needles, mp 77–79 °C; R_f (EtOAc–hexane 2:1) 0.68; $[\alpha]_D^{23}$ +9.8 (*c* 1.04, $CHCl_3$); $\nu_{max}(CDCl_3)$ 1720 (C=O), 1438 (PhP) and 1177 (P=O); δ_H(400 MHz; $CDCl_3$) 8.20–7.10 (25 H, m, Ph), 6.20 (1 H, d, *J* 5.5, PhC*H*CH), 5.10 (1 H, dt, *J* 10.0 and 5.5, PhCHC*H*), 3.25 (1 H, dt, *J* 10.5 and 3.5, Ph_2POCH), 2.43 (1 H, dddd, *J* 19.0, 13.0, 5.5 and 4.5, CH_ACH_B), 2.26 (1 H, ddt, *J* 29.0, 19.5 and 10.5, CH_ACH_B) and −0.20 (9 H, Me_3Si); δ_C(100.6 MHz; $CDCl_3$) 165.0 (C=O), 132–124 (m, Ph), 79.9$^+$ (Ph*C*HOBz), 76.0$^+$ (CH_2CHO), 59.6 (COSi), 51.3$^+$ (d, *J* 80.0, PCH) 29.7$^-$ (CH_2) and 0.0$^+$ ($SiMe_3$); *m*/*z* (EI+) 435 (18%, M − $PhCO_2CHPh$), 345 (100, M − $PhCO_2CHPh$, −Me_3SiO) and 201 (38, Ph_2PO) (Found MNa^+, 669.2181. $C_{39}H_{39}O_5SiPNa$ requires *M*, 669.2202).

(1′*S*,2*R*,3*R*,5*S*)-3-Diphenylphosphinoyl-2-(4-methoxyphenyl)-5-[phenyl(4-methoxybenzoyloxy)methyl]-2-trimethylsilyloxy-tetrahydrofuran 20

Using the general procedure, *n*-butyllithium (0.80 cm^3 of a 2.5 M solution in hexane, 2 mmol) diisopropylamine (202 mg, 2 mmol), diester **16** (639 mg, 1.01 mmol), chlorotrimethylsilane (438 mg, 4.03 mmol) were stirred for 48 h to give the silica adsorbed residue. Purification by flash chromatography on silica with ethyl acetate as eluent gave the *tetrahydrofuran* (638 mg, 89%) as an amorphous solid, mp 88–90 °C (from EtOAc); R_f (EtOAc) 0.55; $[\alpha]_D^{19}$ −5.8 (*c* 0.53, $CHCl_3$); $\nu_{max}(CH_2Cl_2)$/cm^{-1} 1710 (C=O), 1606 (Ar), 1511 (Ar), 1438 (P–Ph) and 1168 (P=O); δ_H(250 MHz; $CDCl_3$) 8.11 (2 H, d, *J* 9.0, $MeOC_6H_4$), 7.67–7.28 (15 H, m, Ph_2PO, Ph), 7.18 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.94 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.72 (2 H, d, *J* 9.0, $MeOC_6H_4$), 6.18 (1 H, d, *J* 4.0, PhC*H*O), 5.04 (1 H, dt, *J* 10.0 and 5.5, CH_2CHO), 3.87 (3 H, s, OCH_3), 3.80 (3 H, s, OCH_3), 3.25 (1 H, dt, *J* 10.0 and 4.5, PCH), 2.49–2.18 (2 H, m, $CHCH_2$) and −0.19 ($SiMe_3$); δ_C(100 MHz; $CDCl_3$) 165.4$^-$ (C=O), 163.5$^-$ (MeO*C*), 159.0$^-$ (MeO*C*), 137.0$^-$, 136.0$^-$ (*i*-Ar), 133.8$^-$ (d, *J* 97, *i*-PhP), 133.2$^-$ (d, *J* 102, *i*-PhP), 130–126 (Ar), 122.5$^-$ (*i*-Ar), 113.7$^+$ (*m*-$MeOC_6H_4$), 112.9$^+$ (*m*-$MeOC_6H_4$), 108.3$^-$ (SiO*C*O), 80.4$^+$ (CH_2CHO), 76.8$^+$ (Ph*C*HOC$_6$H$_4$OMe), 55.5$^+$ (CH_3O), 55.2$^+$ (CH_3O), 52.0$^+$ (d, *J* 73, CHP), 30.4$^-$ (CH_2) and 0.8$^+$ ($SiMe_3$); *m*/*z* (EI+) 706 (6%, M), 555 (43, M − $MeOC_6H_4CO_2$), 465 (60, M − $MeOC_6H_4CO_2H$, −Me_3SiOH), 201 (40, Ph_2P=O) and 135 (100, $MeOC_6H_4CO$) (Found: M$^+$, 706.25078. $C_{41}H_{43}O_7PSi$ requires *M*, 706.25157).

(1′*S*,2*R*,3*R*,5*S*)-3-Diphenylphosphinoyl-5-[4-methoxyphenyl-(benzoyloxy)methyl]-2-phenyl-2-trimethylsilyloxytetrahydro-furan 21

Using the general procedure, *n*-butyllithium (0.42 cm^3 of a 1.44 M solution in hexane, 0.6 mmol) diisopropylamine (65 mg, 0.6 mmol), diester **17** (245 mg, 0.41 mmol) and chlorotrimethylsilane (176 mg, 1.62 mmol) gave the silica adsorbed residue. Purification by flash chromatography on silica with ethyl acetate as eluent gave the *tetrahydrofuran* (140 mg, 51%) as a white solid, mp 73–74 °C (from EtOAc); R_f (EtOAc) 0.55; $[\alpha]_D^{19}$ +10.6 (*c* 0.53, $CHCl_3$); $\nu_{max}(CH_2Cl_2)$/cm^{-1} 1714 (C=O), 1605 (Ar), 1437 (P–Ph) and 1169 (P=O); δ_H(250 MHz; $CDCl_3$) 8.13 (2 H, d, *J* 7.5, *o*-$PhCO_2$), 7.69–7.16 (20 H, m, Ph_2PO, Ph, and $MeOC_6H_4$), 6.86 (2 H, d, *J* 8.5, *m*-$MeOC_6H_4$), 6.16 (1 H, d, *J* 5.0, $MeOC_6H_4CHO$), 5.15–5.05 (1 H, m, C*H*O), 3.78 (3 H, s, OCH_3), 3.28 (1 H, dt, *J* 10.0 and 4.0, PCH), 2.49–2.10 (2 H, m, $CHCH_2$) and −0.16 (9 H, $SiMe_3$); δ_C(100 MHz; $CDCl_3$) 165.8 (C=O), 159.7 (CH_3OC), 145.5 (*i*-Ar), 135.5–125.7 (m, Ar), 113.9 (*m*-$MeOC_6H_4$), 108.5 (d, *J* 4, OCO), 80.7 (CH_2CHO), 77.2 (Ar*C*HOBz), 55.3 (CH_3O), 52.1 (d, *J* 73, PCH), 30.6 (CH_2) and 0.9 ($SiMe_3$); *m*/*z* (EI+) 661 (15%, M − Me), 554 (20, M − $MeOC_6H_4$, −Me), 435 (100, M − $MeOC_6H_4CO_2CHPh$) and 201 (55, Ph_2PO) (Found: M − Me$^+$, 661.21857. $C_{39}H_{38}O_6PSi$ requires *M*, 661.21753).

(1′*S*,2*R*,3*R*,5*S*)-3-Diphenylphosphinoyl-5-[4-methoxyphenyl(4-methoxybenzoyloxy)methyl]-2-(4-methoxyphenyl)-2-trimethyl-silyloxytetrahydrofuran 22

Using the general procedure, *n*-butyllithium (0.4 cm^3 of a 2.5 M solution in hexane, 1 mmol) diisopropylamine (101 mg, 1 mmol), diester **18** (150 mg, 0.23 mmol) and chlorotrimethylsilane (101 mg, 0.90 mmol) were stirred at 0 °C for 24 h to give the silica adsorbed residue. Purification by flash chromatography on silica with ethyl acetate as eluent gave the *tetrahydrofuran* (50 mg, 30%) as an amorphous solid; R_f (EtOAc) 0.48; $\nu_{max}(CDCl_3)$/cm^{-1} 1725 (C=O), 1605 (Ar), 1441 (P–Ph) and 1176 (P=O); δ_H(400 MHz; $CDCl_3$) 8.07 (2 H, d, *J* 9.0, *o*-$MeOC_6H_4CO_2$), 7.64–7.59 (4 H, m, Ph_2PO), 7.46 (2 H, d, *J* 9.0, *o*-$MeOC_6H_4$), 7.44–7.27 (6 H, m, Ph_2PO), 7.16 (2 H, d,

J 9.0, *o*-$MeOC_6H_4$), 6.90 (2 H, d, *J* 9.0, *m*-$MeOC_6H_4$), 6.84 (2 H, d, *J* 9.0, *m*-$MeOC_6H_4$), 6.70 (2 H, d, *J* 9.0, *m*-$MeOC_6H_4$), 6.11 (1 H, d, *J* 5.5, $MeOC_6H_4CHO$), 5.02 (1 H, dt, *J* 10.0 and 5.5, CH_2CHO), 3.84 (3 H, s, OCH_3), 3.78 (3 H, s, OCH_3), 3.76 (3 H, s, OCH_3), 3.24 (1 H, dt, *J* 10.0 and 4.5, PC*H*), 2.49–2.35 (2 H, m, $CHCH_2$) and −0.17 ($SiMe_3$); δ_C(100 MHz; $CDCl_3$) 165.5 (C=O), 163.5 (CH_3OC), 160.9 (CH_3OC), 159.0 (CH_3OC), 137.8 (*i*-Ar), 134.7 (d, *J* 97, *i*-PhP), 134.0 (d, *J* 102, *i*-PhP), 131.8–127.0 (m, Ar), 122.6 (*i*-Ar), 113.8, 113.6, 113.0 (*m*-Ar), 108.5 (OCOSi), 80.5 (CH_2CHO), 77.2 ($MeOC_6H_4CHO$), 55.4 (CH_3O), 55.2 (CH_3O), 55.2 (CH_3O), 52.1 (d, *J* 73, PCH), 30.6 (CH_2) and 0.7 ($SiMe_3$); *m*/*z* (ES+) 759 (100%, MNa^+) and 735 (5, M^+) (Found: MNa^+, 759.25330. $C_{38}H_{37}O_7NaP$ requires *M*, 759.25190).

General procedure for the preparation of triols and mono-benzoates by acyl transfer

A solution of LDA was prepared by the dropwise addition of *n*-butyllithium (1.25 M solution in hexane, 0.44 mmol) to a stirred solution of diisopropylamine (0.44 mmol) in dry THF (10 cm^3) at 0 °C. The prepared LDA was added dropwise to a solution of the diester (0.83 mmol) in dry THF (10 cm^3) at −78 °C and stirred for 5 h. The reaction mixture was quenched with saturated ammonium chloride and subsequently warmed to room temperature. Ethyl acetate (50 cm^3) was added and the mixture filtered. The aqueous layer was separated from the organic layer and extracted with ethyl acetate (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude product which was dissolved in refluxing ethanol (12 cm^3) and sodium borohydride (1 to 5 eq.) added. The mixture was heated under reflux for 4 h and then cooled to room temperature. Saturated ammonium chloride (6 cm^3) was added and the ethanol removed under reduced pressure. The aqueous residue was acidified by the addition of dilute HCl, diluted with brine (10 cm^3) and extracted with dichloromethane (3 × 40 cm^3). The organic layers were pooled, dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product.

(1*R*,2*R*,4*S*,5*S*)- or (1*S*,2*S*,4*S*,5*S*)-5-Benzoyloxy-2-diphenylphosphinoyl-1,5-diphenylpentane-1,4-diol 26(a or b) and (1*R*,2*R*,4*S*,5*S*)- and (1*S*,2*S*,4*S*,5*S*)-2-diphenylphosphinoyl-1,5-diphenylpentane-1,4,5-triol 29(a and b)

A solution of LDA was prepared by the dropwise addition of *n*-butyllithium (0.6 cm^3 of a 2 M solution in hexane, 1.2 mmol) to a stirred solution of diisopropylamine (0.168 cm^3, 1.2 mmol) in dry THF (10 cm^3) at 0 °C. The prepared LDA was added dropwise to a solution of the diester **15** (0.460 g, 1 mmol) in dry THF (10 cm^3) at −78 °C and stirred for 5 h. The reaction mixture was quenched with saturated ammonium chloride (10 cm^3) and subsequently warmed to room temperature. Ethyl acetate (50 cm^3) was added and the mixture filtered. The aqueous layer was separated from the organic layer and extracted with ethyl acetate (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an off-white solid which was dissolved in ethanol (14 cm^3) and sodium borohydride (25 mg, 5 mmol, 5 eq.) added. The mixture was heated under reflux for 4 h and then cooled to room temperature. Saturated ammonium chloride (10 cm^3) was added and the ethanol was removed under reduced pressure. The aqueous residue was acidified by the addition of dilute HCl, diluted with brine (10 cm^3) and extracted with dichloromethane (3 × 40 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an amorphous white solid. Purification by flash chromatography on silica with 1:1 EtOAc–hexane as eluent gave the *triols* **29** and *mono-benzoate* **26** as a colourless oil. The *triol* (232 mg, 60%) was an inseparable 3.4:1 mixture of diastereoisomers which has the following data: R_f (EtOAc–hexane 1:1) 0.03; $\nu_{max}(CDCl_3)/cm^{-1}$ 3586 (OH), 3316 (br, OH) and 1438 (P–Ph); *m*/*z* 495 (100%, MNa^+) and 473 (3, M^+) (Found MNa^+ 495.1699. *M*, requires 495.1803).

Compound 29. Major diastereoisomer: δ_H(400 MHz; $CDCl_3$) 7.64–7.56 (4 H, m, Ph_2PO), 7.50–7.05 (14 H, m, Ph_2PO and 2 × Ph), 7.01–6.96 (2 H, m, Ph), 5.04 (1 H, td, *J* 5.7 and 15.6, PCHC*H*OH), 4.56 (1 H, d, *J* 6.0, OH), 4.13 (1 H, dd, *J* 3.4 and 6.5, PhC*H*OHCHOH), 4.02 (1 H, d, *J* 3.9, OH), 3.43–3.35 (1 H, m, CH_2CHOH), 3.17 (1 H, d, *J* 3.2, OH), 3.15–3.07 (1 H, m, PCH), 1.80–1.60 (2 H, m, CH_2); δ_C(100 MHz; $CDCl_3$) 140.5$^-$ (Ar), 132–126 (m, Ar), 77.3$^+$, 74.9$^+$, 73.9$^+$ (3 × CHOH), 42.4$^+$ (d, *J* 67.1, CHP) and 30.1$^-$ (CH_2).

Compound 29. Minor diastereoisomer: δ_H(400 MHz; $CDCl_3$) 7.78–7.72 (2 H, m, Ph_2PO), 7.54–7.05 (16 H, m, Ph_2PO and 2 × Ph), 6.95–6.90 (2 H, m, Ph), 4.77 (1 H, ddd, *J* 4.4, 7.8 and 12.3, PCHC*H*OH), 4.52 (1 H, d, *J* 4.5, OH), 4.06 (1 H, dd, *J* 4.7 and 7.1, PhC*H*OHCHOH), 3.77 (1 H, d, *J* 4.4, OH), 3.28–3.20 (1 H, m, CH_2CHOH), 3.15–3.07 (1 H, m, PCH), 2.84 (1 H, d, *J* 3.6, OH), 1.80–1.60 (2 H, m, CH_2); δ_C(100 MHz; $CDCl_3$) 141.8$^-$ (Ar), 132–126 (m, Ar), 78.0$^+$, 74.6$^+$, 73.7$^+$ (3 × CHOH), 42.4$^+$ (d, *J* 67.1, *C*HP) and 30.1$^-$ (CH_2).

Compound 26(a or b). Major diastereoisomer: (130 mg, 28%) has the following data: R_f (EtOAc–hexane) 0.11; $[a]_D^{23}$ −24.8 (*c* 0.139, CH_2Cl_2); $\nu_{max}(CDCl_3)/cm^{-1}$ 3589 (OH), 3316 (br, OH), 1437 (P–Ph) and 1177 (P=O); δ_H(400 MHz; $CDCl_3$) 7.92 (2 H, d, *J* 7.1 Ar), 7.74–7.62 (4 H, m, Ph_2PO), 7.55 (1 H, br t, *J* 6.2, Ar), 7.47–7.28 (8 H, m, Ph_2PO and Ar), 7.26–7.20 (5 H, m, Ar), 7.15–7.11 (3 H, m, Ar), 7.07–7.03 (2 H, m, Ar), 5.51 (1 H, d, *J* 4.9, PhC*H*OCOPh), 5.13 (1 H, dd, 2.4 and 4.5, OH), 4.87 (1 H, ddd, *J* 4.3, 7.2 and 15.0, PhCHOH), 3.35–3.25 (2 H, m, PCH and C*H*OH), 2.63 (1 H, dd, *J* 4.8 and 8.6, OH), 1.65 (1 H, br q, *J* 11.0, CH_AH_B) and 1.42–1.34 (1 H, m, CH_AH_B); δ_C(100 MHz, $CDCl_3$) 165.5$^-$ (C=O), 142.1$^-$ (Ar), 136.8$^-$ (Ar), 134–126 (m, Ar), 79.2$^+$ (Ph*C*HOCOPh), 74.5$^+$ (CHOH), 71.2$^+$ (d, *J* 10.3, Ph*C*HOH), 40.4$^+$ (d, *J* 67.3, PCH) and 29.9$^-$ (CH_2); *m*/*z* (ES^+) 599.2 (48%, MNa^+), 576.4 (M) and 558.4 (M − H_2O); *m*/*z* (EI+) 201 (100%, Ph_2PO) (Found MNa^+ 599.1989. *M*, requires 599.1963).

(1*R*,2*R*,4*S*,5*S*)- or (1*S*,2*S*,4*S*,5*S*)-5-(4-Methoxybenzoyloxy)-2-diphenylphosphinoyl-1-(4-methoxyphenyl)-5-phenylpentane-1,4-diol 27(a or b)

A solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (1 M, 0.29 cm^3, 0.29 mmol, 1.0 eq.) was added at room temperature to a solution of tetrahydrofuran **20** (204 mg, 0.29 mmol, 1.0 eq.) in tetrahydrofuran (8 cm^3). The resulting yellow solution was stirred for 30 min and became brown. The solvent was evaporated under reduced pressure and the residue (brown oil) was filtered through a pad of silica gel (1 cm) eluting with ethyl acetate (250 cm^3) and evaporated to give an off-white foam. This was dissolved in absolute ethanol (15 cm^3), sodium borohydride was added in intervals of approximately 3 h (110 mg, 2.9 mmol) and the resulting solution was stirred overnight. Saturated ammonium chloride (5 cm^3) was added and the ethanol was removed under reduced pressure. The aqueous residue was diluted with brine (5 cm^3), acidified with dilute hydrochloric acid and extracted with dichloromethane (3 × 75 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Purification by flash chromatography on silica with 1:19 MeOH–CH_2Cl_2 as eluent gave the *diol* (59 mg, 34%) as a single diastereoisomer as a thick oil; R_f (MeOH–CH_2Cl_2 1:19) 0.28; $[a]_D^{19}$ −23.7 (*c* 0.9, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 3690 (OH), 3603 (br OH), 1712 (C=O), 1438 (P–Ph) and 1168 (P=O); δ_H(400 MHz; $CDCl_3$) 7.87 (2 H, d, *J* 9.0, *o*-$MeOC_6H_4$), 7.73–7.04 (17 H, m, Ph_2PO, Ph and *o*-$MeOC_6H_4$), 6.87 (2 H, d, *J* 9.0, *m*-$MeOC_6H_4$), 6.67 (2 H, d, *J* 9.0, *m*-$MeOC_6H_4$), 5.48 (1 H, d, *J* 5.0, PhC*H*), 4.99 (d, 1H,

J 4.0, OH), 4.82 (1 H, ddd, *J* 12.0, 8.0 and 4.0, $MeOC_6H_4CHO$), 3.87 (3 H, s, OCH_3), 3.74 (3 H, s, OCH_3), 3.26–3.23 (2 H, m, PCH and C*H*OH), 2.65 (1 H, br s, OH) and 1.70–1.24 (2 H, m, $CHCH_2$); δ_C(100 MHz; $CDCl_3$) 165.5 (C=O), 163.5 (CH_3OC), 159.2 (CH_3OC), 137.1 (*i*-Ar), 134.1 (*i*-Ar), 132.0–126.4 (m, Ar), 122.1 (*i*-Ar), 113.6, 113.4 (*m*-$MeOC_6H_4$), 78.8, 74.1, (CHO), 71.4 (d, *J* 9, CH_2CHO), 55.5 (OCH_3), 55.2 (OCH_3), 40.7 (d, *J* 68, CHP) and 29.9 (CH_2); *m*/*z* (ES+) 659 (20%, MNa^+), 637 (40, MH^+), 467 (100, M − $MeOC_6H_4CO_2$, $-H_2O$) and 265 (60, $MeOC_6H_4CHOHCHCHCHCHPh$) (Found: MNa^+, 659.21440. $C_{38}H_{37}O_7NaP$ requires *M*, 659.21746).

(1*R*,2*R*,4*S*,5*S*)- and (1*S*,2*S*,4*S*,5*S*)-2-Diphenylphosphinoyl-5-(4-methoxyphenyl)-1-phenylpentane-1,4,5-triol 31(a and b)

A solution of LDA was prepared by the dropwise addition of *n*-butyllithium (0.79 cm^3 of a 1.25 M solution in hexane, 1.0 mmol) to a stirred solution of diisopropylamine (0.1 g, 1.0 mmol) in dry THF (10 cm^3) at 0 °C. The prepared LDA was added dropwise to a solution of the diester **17** (500 mg, 0.83 mmol) in dry THF (10 cm^3) at −78 °C and stirred for 5 h. The reaction mixture was quenched with saturated ammonium chloride (10 cm^3) and subsequently warmed to room temperature. Ethyl acetate (50 cm^3) was added and the mixture filtered. The aqueous layer was separated from the organic layer and extracted with ethyl acetate (2 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an off-white solid (405 mg) which was dissolved in ethanol (12 cm^3) and sodium borohydride (25 mg, 0.67 mmol, 1 eq.) was added. The mixture heated at reflux for 4 h and then cooled to room temperature. Saturated ammonium chloride (6 cm^3) was added and the ethanol was removed under reduced pressure. The aqueous residue was acidified by the addition of dilute HCl, diluted with brine (10 cm^3) and extracted with dichloromethane (3 × 40 cm^3). The organic layers were pooled, dried ($MgSO_4$) and evaporated under reduced pressure to give an amorphous solid. Purification by flash chromatography on silica with 1:9 MeOH–EtOAc as eluent gave the *triol* (209 mg, 50%) as a white amorphous solid, an inseparable 3:2 mixture of diastereoisomers which has the following data; R_f (EtOAc) 0.30; $\nu_{max}(CDCl_3)/cm^{-1}$ 3684 (OH), 3592 (OH), 3339 (br OH), 1438 (P–Ph) and 1174 (P=O); *m*/*z* (ESI) 503 (100%, MH^+), 467 (75, M − 2 × OH) and 265 (79, M − 2 × OH, $-Ph_2PO$) (Found: $(M - MeOC_6H_4CHOH)^+$, 365.1292. $C_{22}H_{22}O_3P$ requires *M*, 365.1307).

Major diastereoisomer: δ_H(500 MHz; DMSO-d_6) 7.76–7.68 (3 H, m, Ph_2PO), 7.64–7.60 (1 H, m, Ph_2PO), 7.54–7.35 (6 H, m, Ph_2PO), 7.27–7.08 (5 H, m, Ph), 6.85 (2 H, d, *J* 8.5, $MeOC_6H_4$), 6.72 (2 H, d, *J* 8.5, $MeOC_6H_4$), 5.50 (1 H, d *J* 4.5, OH), 4.86 (1 H, d, *J* 4.5, $MeOC_6H_4CH$), 4.83–4.75 (1 H, m, PhC*H*), 4.71 (1 H, d, *J* 4.5, OH), 3.85–3.83 (1 H, m, C*H*(OH)CH_2), 3.70 (3 H, s, OCH_3), 3.33–3.19 (2 H, m, PC*H* and OH) and 1.42–1.17 (2 H, m, CH_2); δ_C(100 MHz; DMSO-d_6) 159.3 (MeO*C*), 143.2–126.9 (m, Ar), 113.2 (*m*-$MeOC_6H_4$), 76.7 (CHO), 73.2 (d, *J* 9, CHO), 72.8 (CHO), 41.2 (d, *J* 69, CHPO) and 29.0 (CH_2).

Minor diastereoisomer: δ_H(500 MHz; DMSO-d_6) 7.76–7.68 (3 H, m, Ph_2PO), 7.64–7.60 (1 H, m, Ph_2PO), 7.54–7.35 (6 H, m, Ph_2PO), 7.27–7.08 (5 H, m, Ph), 6.85 (2 H, d, *J* 8.5, $MeOC_6H_4$), 6.70 (2 H, d, *J* 8.5, $MeOC_6H_4$), 5.68 (1 H, d, *J* 4.5, OH), 4.88 (1 H, d, *J* 4.5, $MeOC_6H_4CH$), 4.83–4.75 (1 H, m, PhC*H*), 4.80 (1 H, d, *J* 4.5, OH), 4.02–4.00 (1 H, m, C*H*(OH)CH_2), 3.70 (3 H, s, OCH_3), 3.33–3.19 (2 H, m, PC*H* and OH), 1.42–1.17 (2 H, m, CH_2); δ_C(100 MHz; DMSO-d_6) 159.2 (MeO*C*), 143.2–126.9 (m, Ar), 113.2 (*m*-$MeOC_6H_4$), 75.6 (CHO), 72.5 (d, *J* 9, CHO), 73.2 (CHO), 41.2 (d, *J* 69, CHPO), 29.0 (CH_2).

General procedure for the preparation of diol containing alkenes

Sodium hydride (0.75 mmol) was added under argon to a solution of the triol (0.26 mmol) in dry DMF (7 cm^3). The resulting suspension was heated to 50 °C over 10 min during which a white precipitate was formed. The reaction mixture was stirred for a further 30 min until the diphenylphosphine oxide was consumed according to TLC and subsequently cooled to room temperature. Water (7 cm^3) was added and the white precipitate dissolved. The mixture was diluted with brine (7 cm^3) and extracted with EtOAc (3 × 30 cm^3). The combined organic extracts were washed with dilute HCl (0.1 M, 3 × 10 cm^3), brine (5 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product.

(*E*,1*S*,2*S*)-1,2-Dihydroxy-1,5–diphenylpent-4-ene 32

Using the general procedure, sodium hydride (27 mg, 0.68 mmol), triol **29** (109 mg, 0.23 mmol) in dry DMF (7 cm^3) gave a crude product. Purification by flash chromatography on silica with 1:1 EtOAc–hexane as eluent gave the *alkene* (35 mg, 60%) as a colourless oil; R_f (EtOAc–hexane 1:1) 0.33; $[a]_D^{23}$ −12.6 (*c* 0.3, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 3682 (OH), 3618 (OH) and 1521 (C=C); δ_H(400 MHz; $CDCl_3$) 7.38–7.22 (10 H, m, 2 × Ph), 6.41 (1 H, d, *J* 15.9, PhC*H*CH), 6.20 (1 H, ddd, *J* 6.9, 8.2 and 15.9, PhCHC*H*), 4.54 (1 H, d, *J* 6.8, PhC*H*OH), 3.84 (1 H, ddd, *J* 4.3, 7.0 and 7.5, CH_2CHOH), 2.35–2.25 (2 H, m, CH_2) (no OH peaks observed); δ_C(100 MHz; $CDCl_3$) 140.8^- (*i*-Ph), 137.2^- (*i*-Ph), 133.2^+, 130.2^+, 128.6^+, 128.5^+, 128.4^+, 128.2^+, 127.3^+, 126.9^+, 126.1^+, 125.7^+ (2 × Ph and C=C), 75.4^+ (2 × CHOH), 36.5^- (CH_2); *m*/*z* (ES+) 277 (100%, M^+) (Found MNa^+, 277.11990. $C_{17}H_{18}O_2Na$ requires *M*, 277.1204).

Alternative synthesis of (*E*,1*S*,2*S*)-1,2-dihydroxy-1,5-diphenylpent-4-ene 32

Sodium hydride (15 mg, 0.4 mmol), diol **26** (70 mg, 0.12 mmol) in dry DMF (3 cm^3) gave by the same general procedure as for compound **32** above a crude product. Purification by flash chromatography on silica with 1:1 EtOAc–hexane as eluent gave the *alkene* (50 mg, 71%) as a colourless oil (Data identical to that above).

(*E*,1*S*,2*S*)-1,2-Dihydroxy-1-phenyl-5-(4-methoxyphenyl)pent-4-ene 33

By the general procedure for compound **26**: sodium hydride (5.9 mg, 0.15 mmol) and diol **27** (47 mg, 0.07 mmol) gave the crude product. Purification by flash chromatography on silica with 1:1 EtOAc–hexane as eluent gave the *alkene* (7 mg, 35%) as a yellow oil; R_f (EtOAc–hexane 1:1) 0.43; $[a]_D^{23}$ −3.6 (*c* 0.2, $CHCl_3$); δ_H(500 MHz; $CDCl_3$) 7.38–7.34 (4 H, m, Ar and Ph), 7.33–7.27 (1 H, m, Ph), 7.26–7.24 (2H, m, Ph), 6.82 (2 H, d, *J* 8.5, *m*-$MeOC_6H_4$), 6.37 (1 H, d, *J* 16.0, $MeOC_6H_4CHCH$), 6.04 (1 H, ddd, *J* 16.0, 8.0, and 7.0, $MeOC_6H_4CHCH$), 4.54 (1 H, d, *J* 6.5, PhC*H*OH), 3.84–3.80 (1 H, m, CH_2CHOH), 3.79 (3H, s, OCH_3), 2.69 (1 H, br s, OH), 2.38 (1 H, br s, OH) and 2.36–2.15 (2 H, m, CH_2); δ_C(100 MHz; $CDCl_3$) 159.0^- (CH_3OC), 140.8^- (*i*-Ar), 132.7^+ (ArCH), 129.9^- (*i*-Ar), 128.5^+, 127.2^+, 126.9^+ (*o*-Ar, *m*-Ar), 128.1^+, 123.2^+ (*p*-Ph, ArCH*C*H), 113.9^+ (*m*-$MeOC_6H_4$), 77.5^+ (Ph*C*HOH), 75.4^+ (CH_2CHOH), 55.2^+ (CH_3O) and 36.5^- (CH_2); *m*/*z* (EI+) 284 (20%, M^+), 147 (100, $MeOC_6H_4CHCHCH_2$), 134 (50, $MeOC_6H_4CHCH$) and 121 (70, $MeOC_6H_4CH$) (Found: M^+, 284.14006. $C_{18}H_{20}O_3$ requires *M*, 284.14125).

(*E*,1*S*,2*S*)-1,2-Dihydroxy-1-(4-methoxyphenyl)-5-phenylpent-4-ene 34

Using the general procedure, sodium hydride (30 mg, 0.75 mmol), triol **31** (132 mg, 0.26 mmol) in dry DMF (7 cm^3) gave a crude product. Purification by flash chromatography on silica with 1:1 EtOAc–hexane as eluent gave the *alkene* (45 mg, 60%) which was recrystallised from diethyl ether–petroleum ether (40–60 °C) (1:1) to give needles, mp 66–67 °C (diethyl ether);

R_f (EtOAc–hexane 1:1) 0.29; $[a]_D^{23}$ −20.7 (*c* 0.61, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 3686 (OH), 3603 (br, OH) and 1612 (C=C); δ_H(400 MHz; $CDCl_3$) 7.35–7.28 (6 H, m, Ar-H), 7.22 (1 H, t, *J* 7.0, Ar-H), 6.91 (2 H, d, *J* 8.5, Ar-H), 6.41 (1 H, d, *J* 16.0, PhC*H*CH), 6.20 (1 H, ddd, *J* 16.0, 8.0 and 7.0, PhCHC*H*), 4.49 (1 H, br d, *J* 7.0, C*H*(OH)Ar), 3.85–3.79 (4 H, m, CH_2CHOH and OMe), 2.76 (1 H, d, *J* 2.5, O*H*), 2.59 (1 H, d, *J* 2.8, O*H*), 2.33 (1 H, dddd, *J* 14.5, 7.0, 4.0 and 1.2, CH_AH_B) and 2.25 (1 H, dtd, *J* 14.5, 8.0 and 1.2, CH_AH_B); δ_C(100 MHz; $CDCl_3$) 157.5$^-$ (MeO*C*), 135.2$^-$ (*i*-Ar), 131.0$^+$ (Ph*C*H), 130.8$^-$ (*i*-Ar), 126.4$^+$, 126.1$^+$, 124.0$^+$ (*o*-Ar, *m*-Ar), 125.2$^+$, 123.7$^+$ (*p*-Ph, PhCH*C*H), 111.9$^+$ (*m*-$MeOC_6H_4$), 74.9$^+$ ($MeOC_6H_4$-*C*HOH), 73.4$^+$ (CH_2CHOH), 53.2$^+$ (CH_3O) and 34.5$^-$ (CH_2); *m*/*z* (EI+) 284 (23%, M^+), 137 (100, MeOPhCHOH), 121 (37, $MeOC_6H_4CH$) (Found: M^+, 284.14010. $C_{18}H_{20}O_3$ requires *M*, 284.14125).

Single crystals of **34** were recrystallised from EtOAc–hexanes, mounted in inert oil and transferred to the cold gas stream of the diffractometer.

Crystal structure determination of alkenediol 34

Crystal data.† $C_{18}H_{20}O_3$, $M = 284.34$, monoclinic, $a = 11.3620(10)$, $b = 4.8730(5)$, $c = 13.9800(8)$ Å, $\beta = 100.937(6)°$, $U = 759.97(11)$ Å^3, $T = 180(2)$ K, space group $P2_1$, $Z = 2$, μ(Mo-Kα) = 0.083 mm^{-1}, 4628 reflections measured, 2306 unique ($R_{int} = 0.0441$) which were used in all calculations. The final $wR(F^2)$ was 0.1003 (all data). The absolute stereochemical configuration was not determined.

Acknowledgements

We thank the EPSRC for a studentship (J. A. M.), BBSRC and British Biotech for a CASE award (M. D. E.), the Danish Natural Science Research Council and the Danish Technical Research Council (T. B.), Pfizer and the Newton Trust (C. R. T.) for financial support. Most particularly we acknowledge the influence of the late Ron Snaith on our work. He taught us to see organo-lithium compounds as they really are as well as contributing the skills essential for the isolation and characterisation of these vital intermediates. Such confidence as we have in interpreting the reactions in this paper come from our long association with Ron. We all miss him very much.

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† CCDC reference number 152854. See http://www.rsc.org/suppdata/p1/b0/b008500f/ for crystallographic data in CIF or other electronic format.