Investigation of the configurational stability of lithiated phosphine oxides using diastereomerically pure and enantiomerically enriched phosphine oxides

PERKIN 1

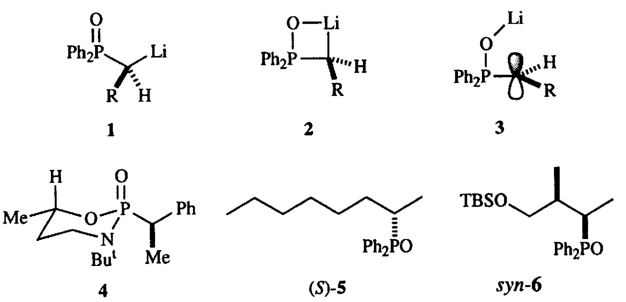
Peter O'Brien and Stuart Warren *

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

Lithiation of racemic but diastereomerically pure phosphine oxides followed by electrophilic quench indicates that lithiated phosphine oxides are not configurationally stable over a period of minutes in THF at −78 °C. These results have been verified using an optically active phosphine oxide: lithiation and *in situ* quench experiments with Me_3SiCl and cyclobutanone indicate that the lithium derivatives are not configurationally stable even on the timescale of their reaction with these electrophiles.

Even though we have been carrying out a range of synthetic transformations using lithium derivatives of diphenylphosphine oxide for quite some time,[1] very little is known about the exact nature and properties of the organolithiums which are typically generated in THF solution at −78 °C. In particular, we had never previously needed to consider whether our lithiated phosphine oxides were configurationally stable or not. However, because we had started to use some chiral phosphine oxides in synthesis, we needed to know the fate of a chiral centre α to phosphorus when the phosphine oxides were lithiated. We now report in full[2] an investigation of the configurational stability of lithiated phosphine oxides.

As well as being of fundamental importance, we imagined that a study into configurational stability might well shed some light on the likely solution structures of the lithiated phosphine oxides. Three possible structures for the organolithiums are **1**, **2** and **3** (Scheme 1). Both structures **1** and **2** have a sp^3 hybridised



Scheme 1

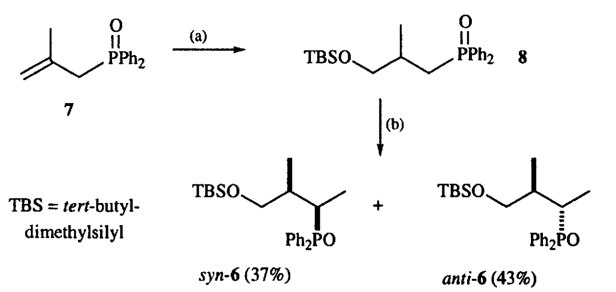
carbon α to phosphorus whilst structure **3** is sp^2 hybridised with no carbon–lithium contact whatsoever. Using X-ray crystallography and NMR methods, Denmark[3] and Boche[4] have shown that lithium derivatives of some phosphonates and phosphonamides exist with sp^2 hybridised structures (equivalent to **3**). In contrast, recent work (X-ray crystallography and *ab initio* calculations) has suggested that some lithiated phosphazenes and phosphonates have four-membered ring structures (equivalent to **2**).[5] Our own[6] *ab initio* calculations have suggested that the four-membered ring structure **2** is the most likely[7] for our lithiated phosphine oxides..

At the outset of our study, virtually nothing was known about the configurational stability of phosphorus-stabilised organolithiums. Previously, Denmark had noted that phosphonamide **4**, upon lithiation, did not maintain its configuration at the carbon α to phosphorus—this was believed to be due to the intermediacy of an organolithium derivative with a sp^2 hybridised carbon (equivalent to **3**) and rapid rotation about the carbon–phosphorus bond.[8] The only result of relevance to our diphenylphosphine oxides was described by Cram[9,10] back in 1963: phosphine oxide (*S*)-**5** was used to demonstrate that the free carbanion generated using potassium *tert*-butoxide in refluxing polar solvents (*e.g. tert*-butylalcohol, methanol and DMSO) underwent racemisation faster than proton–deuterium exchange. Perhaps surprisingly, the corresponding sulfones are actually configurationally stable under essentially the same conditions.[11]

Configurational stability is most often determined using either enantiomerically enriched or diastereomerically pure† compounds.[10] We have actually used both of these approaches to investigate the configurational stability of lithiated phosphine oxides. We chose to assess the configurational stability (or instability) in THF at −78 °C as these are precisely the reaction conditions under which lithiated phosphine oxides are used in synthesis.[1] Phosphine oxides (*S*)- and (*R*)-**5** (originally used by Cram in his study[9,10]) as well as phosphine oxides *syn*- and *anti*-**6** (Scheme 1) were selected for our investigation and we begin by describing their synthesis.

Background synthetic work: synthesis of phosphine oxides 5 and 6

Phosphine oxides *syn*- and *anti*-**6** were synthesised as outlined in Scheme 2. Hydroboration of the known[13,14] allylic phosphine



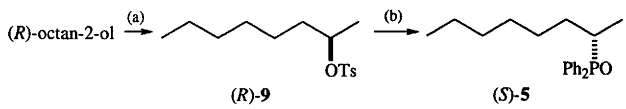
Scheme 2 *Reagents:* (a) i $BF_3 \cdot Et_2O$, $NaBH_4$, THF, RT, 2 h then H_2O_2, NaOH, RT, 1.5 h (89%); ii, TBSCl, DMF, imidazole, RT, 18 h (91%); (b) i, BuLi, THF, −78 °C; ii, MeI (100%)

oxide **7** followed by silyl protection of the resulting hydroxy functionality generated silyl ether **8** which was subjected to a stereorandom methylation.[15] Phosphine oxides *syn*- and *anti*-**6**

† This was the approach used by Demmark when he showed that the organolithium derived from phosphonamide **4** was not configurationally stable in THF at −60 °C.[8]

(45:55) were obtained in quantitative yield and were easily separated by flash chromatography. The relative stereochemistry was assigned on the basis of a ^{13}C NMR coupling constant correlation:‡ *syn*-**6** has $^3J_{PC}$ (Me) = 11.5 Hz and $^3J_{PC}$ (CH_2) = 0 Hz; *anti*-**6** has $^3J_{PC}$ (Me) = 1.8 Hz and $^3J_{PC}$ (CH_2) = 14.0 Hz. However, as we shall see, the actual assignment of stereochemistry is of no consequence in the present study.

We have synthesised phosphine oxide (*S*)-**5** using a two-step route (Scheme 3) which is slightly modified from the approach

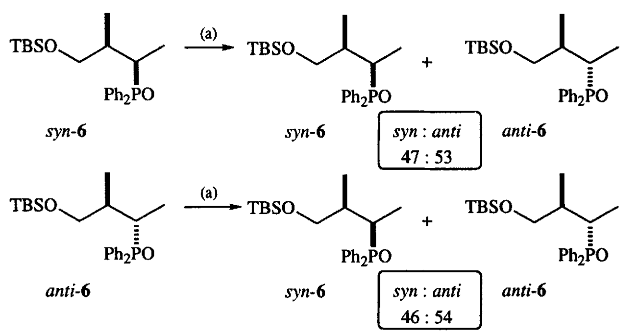


Scheme 3 *Reagents:* (a) Pyridine, *p*-TsCl, RT, 20 h (75%); (b) i, Ph_2PLi, THF, 0 °C, 30 min; ii, H_2O_2 (88%)

previously reported by Cram.[9] Simple tosylation of commercially available (*R*)-octan-2-ol gave tosylate (*R*)-**9** in 75% yield. Then, a solution of lithium diphenylphosphide was generated using the method of Ashby[16] and reacted with tosylate (*R*)-**9** in THF at 0 °C to give a crude phosphine product which was not isolated; oxidation with hydrogen peroxide afforded phosphine oxide (*S*)-**5** in 88% yield. Phosphine oxides (*R*)-**5** and *rac*-**5** were prepared in the same way. Using 400 MHz ^1H NMR spectroscopy in the presence of Pirkle's chiral solvating agent, (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol,[17] we demonstrated that phosphine oxide (*S*)-**5** had ≥95% ee.

Investigation of configurational stability using diastereomerically pure compounds

We began our configurational stability investigation by lithiating phosphine oxide *syn*-**6** using butyllithium in THF at −78 °C to give the usual deep-red solution. Quenching with methanol after 45 min generated a 47:53 mixture of *syn*- and *anti*-**6** (Scheme 4). Essentially the same ratio of *syn*- and *anti*-**6**

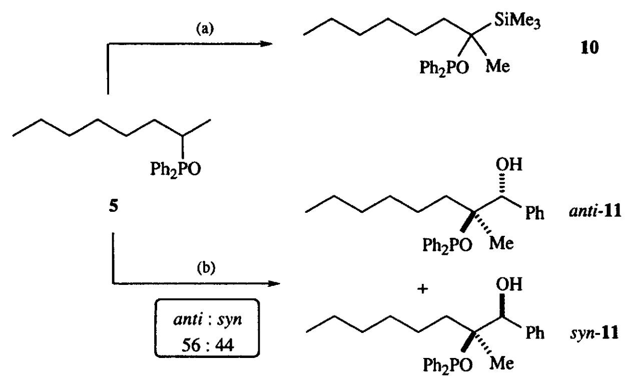


Scheme 4 *Reagents:* (a) i, BuLi, THF, −78 °C, 45 min; ii, MeOH (100%)

(46:54) was obtained when we started with the diastereomeric phosphine oxide *anti*-**6** (Scheme 4). These results clearly indicate that lithiated phosphine oxides are not configurationally stable under these conditions: after 45 min at −78 °C in THF, the initially diastereomerically pure lithiated phosphine oxide had epimerised completely.

Investigation of configurational stability using enantiomerically enriched compounds

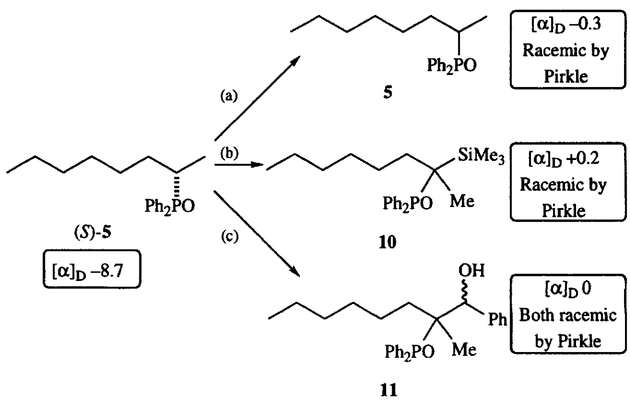
Before we carried out the key configurational stability experiments, we treated phosphine oxide *rac*-**5** with Me_3SiCl and with benzaldehyde (Scheme 5) in order to prepare silyl phosphine oxide *rac*-**10** and alcohol *rac*-**11** (mixture of *syn* and *anti* diastereoisomers) for chiral analysis. With benzaldehyde, a 56:44



Scheme 5 *Reagents:* (a) i, BuLi, THF, −78 °C; ii, Me_3SiCl (49%); (b) i, BuLi, THF, −78 °C; ii, PhCHO; iii, NH_4Cl (77%)

ratio of alcohols *anti*- and *syn*-**11** was obtained although the assignment of stereochemistry is only tentative.§

Next, phosphine oxide (*S*)-**5** was lithiated by treatment with butyllithium in THF at −78 °C and then quenched with methanol after 1 h. Recovered phosphine oxide **5** was isolated in quantitative yield and had, as expected, racemised (Scheme 6).



Scheme 6 *Reagents:* (a) i, BuLi, THF, −78 °C, 1 h; ii, MeOH (100%); (b) i, BuLi, THF, −78 °C, 30 min; ii, PhCHO; iii, NH_4Cl (74%); (c) i, BuLi, THF, −78 °C, 1 h; ii, Me_3SiCl, −78 °C, 9 h (74%)

We then lithiated (*S*)-**5** in the same way but left it at −78 °C for a shorter period of time and treated it with a different electrophile. Thus, after 30 min, benzaldehyde was added to give a 56:44 ratio of racemic alcohols *anti*- and *syn*-**11** in 74% yield. Exactly the same result was obtained when we quenched with Me_3SiCl: racemic silyl phosphine oxide **10** was generated in 74% yield (Scheme 6).

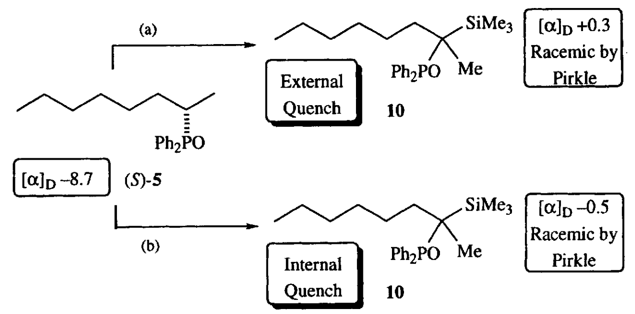
What was needed was a shorter timescale of investigation and, in an attempt to do this, we decided to make use of *in situ* (or internal) electrophilic quenches. The most frequently employed internal quench system involves the use of LDA and Me_3SiCl, a method that was originally introduced by Corey[18] and takes advantage of the fact that LDA and Me_3SiCl can coexist[19] at low temperature.

First of all, we repeated the externally quenched reaction between phosphine oxide (*S*)-**5** and Me_3SiCl using LDA as the base. As expected, racemic silyl phosphine oxide **10** was obtained. However, even when we added a solution of LDA to a solution of phosphine oxide (*S*)-**5** and an excess of Me_3SiCl in THF at −78 °C (internal quench conditions), we still obtained

‡ By comparing X-ray crystal structures of four such alkyl phosphine oxides with their ^{13}C NMR spectra, we have noticed that $^3J_{PC}$ coupling constants are consistently dependent on the relative stereochemistry.

§ The two compounds were inseparable by chromatography but, fortunately, ^1H NMR analysis of the mixture in the presence of Pirkle's reagent did show adequate splitting of the signals due to *each* enantiomer for *both* diastereoisomers.

racemic silyl phosphine oxide **10** (Scheme 7). This result enables us to establish a more accurate timescale for our configurational instability: lithiated phosphine oxides lose their configuration α to phosphorus *before* they react with Me_3SiCl.

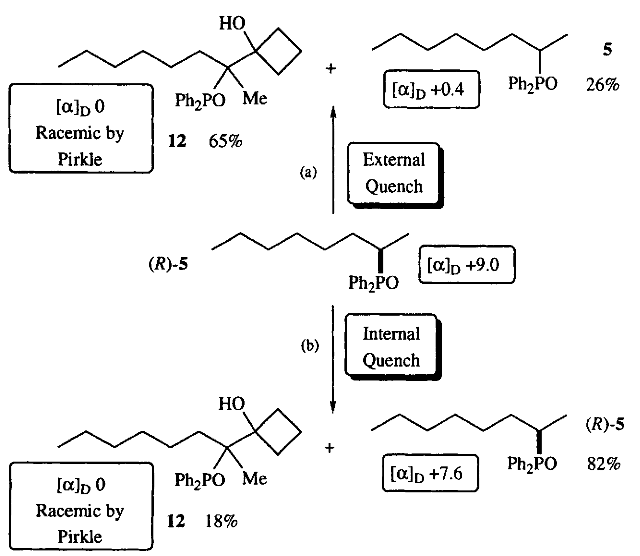


Scheme 7 *Reagents:* (a) i, LDA, THF, −78 °C, 1 h; ii, Me_3SiCl, −78 °C, 8 h (41%); (b) i, LDA added to (*S*)-**5** and Me_3SiCl, THF, −78 °C; ii, −78 °C, 8 h (50%)

At this point, we wondered whether it would be possible to shorten the timescale of our investigation still further. We reasoned that a carbonyl electrophile would react faster than Me_3SiCl with our lithiated phosphine oxides (carbon–lithium species). In addition, a carbonyl electrophile would be a far more 'realistic' trapping agent as carbonyl electrophiles (and not Me_3SiCl) are most commonly combined with lithiated phosphine oxides.[1] However, when we attempted to react a simple phosphine oxide (butyldiphenylphosphine oxide) with LDA and benzaldehyde¶ under internal quench conditions, no addition product was obtained.

Because of the failure with benzaldehyde, we turned our attention to a different carbonyl electrophile—cyclobutanone.[21] Cyclobutanone was chosen with three things in mind: (i) it is a particularly reactive ketone because the carbonyl group is in a four membered ring; (ii) its enolisation by LDA would be less likely to occur than in other ketones because the enolate would be in a four membered ring; (iii) it is an achiral electrophile[22] and would not generate a mixture of diastereomeric alcohols (unlike benzaldehyde).

Initially, we carried out an externally quenched reaction with cyclobutanone and a 65% yield of racemic alcohol **12** was obtained (Scheme 8). In addition, a 26% yield of *racemic* starting phosphine oxide **5** $\{[\alpha]_D^{20}$ +0.4 (*c* 1.3 in $CHCl_3$)$\}$ was recovered. Hence, under these conditions, the starting phosphine oxide (*R*)-**5** is fully lithiated; presumably, enolisation of cyclobutanone by the lithiated phosphine oxide is a competing reaction giving the 26% yield of racemic phosphine oxide **5**.



Scheme 8 *Reagents:* (a) i, LDA, THF, −78 °C, 30 min; ii, cyclobutanone, −78 °C, 2 h; iii, NH_4Cl; (b) i, LDA added to (*R*)-**5** and cyclobutanone, THF, −78 °C; ii, −78 °C, 3 h; iii, NH_4Cl

Using an internal quench procedure, LDA was added to a THF solution (−78 °C) of phosphine oxide (*R*)-**5** in the presence of cyclobutanone. A low yield (18%) of racemic alcohol **12** was obtained. However, in this case, we were also able to recover *optically active* phosphine oxide (*R*)-**5** $\{[\alpha]_D^{20}$ +7.6 (*c* 3.0 in $CHCl_3$)$\}$ in 82% yield. Under the internal quench conditions, it appears as though phosphine (*R*)-**5** is incompletely lithiated by the LDA; enolisation of cyclobutanone by LDA[23] is clearly competing with lithiation of phosphine oxide (*R*)-**5** by LDA. Despite this, all of the lithiated phosphine oxide that does form racemises completely before it reacts with the cyclobutanone.

Summary

Using diastereomerically pure and enantiomerically enriched phosphine oxides, we have demonstrated that lithiated diphenylphosphine oxides are not configurationally stable in THF at −78 °C on the timescale of their reaction with Me_3SiCl or cyclobutanone.‖ Because these are the exact reaction conditions that lithiated phosphine oxides are used in synthesis,[1] we did not try to vary the temperature, solvent or metal counter-ion in an attempt to discover configurationally stable lithiated phosphine oxides—we were only really interested in what was happening under our usual reaction conditions. In any case, configurationally unstable lithiated phosphine oxides are still synthetically useful as the intramolecular acylation developed in our laboratory adequately demonstrates. The high stereoselectivity observed in this reaction is a consequence of many cooperating factors but the formation of a single diastereomeric product can only really be rationalised if the intermediate organolithium derivatives are not configurationally stable.[26]

Finally, we still do not know exactly how these configurational stability results correlate with the solution structure of the lithiated phosphine oxides.[6] For example, configurational instability could result from rapid pyramidal inversion in structures **1** or **2** (Scheme 1) or it could result from rapid rotation about the carbon–phosphorus bond in the sp^2 hybridised structure **2** (Scheme 1). Alternatively, the sp^2 hybridised structure **2** could exist in an achiral conformation in which the p-orbital is perpendicular to the phosphorus–oxygen bond—in this case, the concept of configuration is, of course, meaningless.

Experimental

General methods have been described previously.[27] Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh) according to the method of Still, Kahn and Mitra.[28] The symbols + and − after the carbon NMR chemical shift indicate odd and even numbers of attached protons respectively. Enantiomeric excesses were determined by measuring the integration of the 400 MHz ^{1}H NMR spectrum in the presence of (*R*)-Pirkle's chiral shift reagent. (*R*)-Pirkle's reagent is (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.[17] The general method used for determining enantiomeric excesses has been described previously[14] and is referred to in the experimental section as 'by Pirkle'.

[1-(1,1-Dimethylethyl)dimethylsiloxy]-3-diphenylphosphinoyl-2-methylpropane 8

A solution of allylic phosphine oxide **7**[13,14] (3.16 g, 12.35 mmol) in THF (50 cm^3) was added dropwise to a stirred suspension of

¶ Seebach has successfully used benzaldehyde as part of an *in situ* quench to trap a lithium enolate derived from an amino acid.[20]

‖ More recently, we have used the 'Hoffmann test'[24] to demonstrate that lithiated phosphine oxides are not configurationally stable on the timescale of their reaction with an aldehyde.[25] Our results will be reported in full in due course.

sodium borohydride (997 mg, 26.2 mmol) in THF (15 cm^3) under argon at 0 °C. Then, boron trifluoride–diethyl ether (2.3 cm^3, 18.7 mmol) was added dropwise and the resulting solution was allowed to warm to room temperature. After 2 h at room temperature, water (10 cm^3) was added dropwise (care—vigorous reaction) followed by the addition of sodium hydroxide (3 M; 10 cm^3) and hydrogen peroxide (100 vol; 4 cm^3). The resulting solution was stirred at room temperature for 1.5 h and then EtOAc (150 cm^3) was added. The layers were separated and the aqueous layer was extracted with EtOAc (2 × 150 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc and then EtOAc–MeOH (15:1) as eluent gave the alcohol (3.0 g, 89%) as rectangular plates, mp 135–137 °C (from EtOAc). This alcohol (1.05 g, 3.8 mmol) was added in one portion to a stirred solution of imidazole (786 mg, 11.55 mmol) and TBDMSCl (873 mg, 5.8 mmol) in DMF (5 cm^3) under argon at room temperature. After 18 h at room temperature, CH_2Cl_2 (50 cm^3) was added and the layers separated. The aqueous layer was then extracted with CH_2Cl_2 (2 × 50 cm^3). The combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave *silylated alcohol* **8** (1.35 g, 91%) as needles, mp 101–104 °C (from EtOAc); R_F(EtOAc) 0.4 (Found: C, 68.05; H, 8.8; P, 8.1%; M^+, 388.2000. $C_{22}H_{33}O_2PSi$ requires C, 68.0; H, 8.8; P, 8.0%; *M*, 388.1983); $\nu_{max}(CHCl_3)/cm^{-1}$ 1592 (Ph), 1438 (P–Ph), 1252 ($SiBu^tMe_2$), 1171 (P=O) and 839 ($SiBu^tMe_2$); δ_H(200 MHz, $CDCl_3$) 7.81–7.66 (4 H, m, *o*-Ph_2PO), 7.48–7.35 (6 H, m, *m*- and *p*-Ph_2PO), 3.46 (1 H, ddd, *J* 1.8, 5.2 and 9.8, CH_AH_BOSi), 3.35 (1 H, dd, *J* 6.7 and 9.7, CH_AH_BOSi), 2.65 (1 H, ddd, *J* 3.3, 9.0 and 13.0, PCH_AH_B), 2.20–2.05 (1 H, br m, *CH*Me), 1.94 (1 H, ddd, *J* 8.8, 12.7 and 14.9, PCH_AH_B), 1.01 (3 H, d, *J* 6.6, CH*Me*), 0.85 (9 H, s, CMe_3), −0.28 (3 H, s, $SiMe_AMe_B$) and −0.38 (3 H, s, $SiMe_AMe_B$); δ_C(50 MHz, $CDCl_3$) 135.6–128.4 (Ph_2PO), 68.4^- (d, *J* 12.3, CH_2OSi), 32.5^- (d, *J* 72.4, PCH_2), 31.1^+ (d, *J* 2.9, CHMe), 25.9^+ (CMe_3), 18.2^- (CMe_3), 18.1^+ (d, *J* 4.2, CHMe), -5.4^+ ($SiMe_AMe_B$) and -5.5^+ ($SiMe_AMe_B$); *m/z* 388 (10%, M^+), 373 (50, M − Me), 331 (100, M − CMe_3), 215 [10, $Ph_2P(O)CH_2$] and 201 (10, Ph_2PO).

(2*R**,2*S**)-2,3-Dimethyl-1-[(1,1-dimethylethyl)dimethylsiloxy]-3-diphenylphosphinoylpropane *anti*-6 and (2*R**,3*R**)-2,3-dimethyl-1-[(1,1-dimethylethyl)dimethylsiloxy]-3-diphenylphosphinoylpropane *syn*-6

Butyllithium (1.5 M solution in hexane; 0.7 cm^3, 1.05 mmol) was added dropwise to a stirred solution of phosphine oxide **8** (406 mg, 1.05 mmol) in THF (10 cm^3) under argon at −78 °C. The resulting orange solution was stirred at −78 °C for 30 min and then methyl iodide (60 µl, 1.2 mmol) was added dropwise. After 1 h at −78 °C, saturated aqueous ammonium chloride (2 cm^3) was added and the solution was allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (30 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a white solid which contained a 55:45 ratio (by ^1H NMR) of phosphine oxides *anti*- and *syn*-**6** (444 mg, 100%). Purification by chromatography on silica with EtOAc as eluent gave *phosphine oxide syn*-**6** (156 mg, 37%) as plates, mp 170–172 °C (from EtOAc); R_F(EtOAc) 0.55 (Found: C, 68.5; H, 8.85; P, 7.8%; M^+, 402.2142. $C_{23}H_{35}O_2PSi$ requires C, 68.6; H, 8.8; P, 7.7%; *M*, 402.2144); $\nu_{max}(CHCl_3)/cm^{-1}$ 1592 (Ph), 1438 (P–Ph), 1253 ($SiBu^tMe_2$), 1174 (P=O) and 840 ($SiBu^tMe_2$); δ_H(400 MHz, $CDCl_3$) 7.84–7.75 (4 H, m, *o*-Ph_2PO), 7.48–7.39 (6 H, m, *m*- and *p*-Ph_2PO), 3.87 (1 H, dd, *J* 4.1 and 10.1, CH_AH_BOSi), 3.43 (1 H, dd, *J* 8.3 and 10.0, CH_AH_BOSi), 2.44 (1 H, dqd, *J* 3.5, 7.5 and 11.0, PCH), 2.06–1.98 (1 H, m, *CH*Me), 1.10 (3 H, dd, *J* 7.5 and 16.8, PCH*Me*), 1.02 (3 H, d, *J* 6.9, CH*Me*), 0.82 (9 H, s, CMe_3), −0.04 (3 H, s, $SiMe_AMe_B$) and −0.08 (3 H, s, $SiMe_AMe_B$); δ_C(100 MHz, $CDCl_3$) 133.8–128.5 (Ph_2PO), 64.8^- (CH_2OSi), 35.6^+ (*C*HMe), 35.4^+ (d, *J* 71.2, PCH), 25.9^+ (CMe_3), 18.2^- (CMe_3), 17.6^+ (d, *J* 11.5, CH*Me*), 8.95^+ (PCH*Me*) and -5.4^+ ($SiMe_2$); *m/z* 402 (5%, M^+), 387 (70, M − Me), 345 (100, M − CMe_3) and 201 (50, Ph_2PO) and *phosphine oxide anti*-**6** (181 mg, 43%) as plates, mp 153–155 °C (from EtOAc); R_F(EtOAc) 0.4 (Found: C, 68.4; H, 8.9; P, 7.8%; M^+, 402.2145. $C_{23}H_{35}O_2PSi$ requires C, 68.6; H, 8.8; P, 7.7%; *M*, 402.2144); $\nu_{max}(CHCl_3)/cm^{-1}$ 1592 (Ph), 1438 (P–Ph), 1253 ($SiBu^tMe_2$), 1174 (P=O) and 840 ($SiBu^tMe_2$); δ_H(400 MHz, $CDCl_3$) 7.87–7.82 (2 H, m, *o*-Ph_2PO), 7.77–7.72 (2 H, m, *o*-Ph_2PO), 7.45–7.39 (6 H, *m*- and *p*-Ph_2PO), 3.38 (1 H, ddd, *J* 1.5, 5.4 and 10.1, CH_AH_BOSi), 3.34 (1 H, t, *J* 9.9, CH_AH_BOSi), 2.90 (1 H, dqd, *J* 1.4, 7.4 and 14.9, PCH), 2.19–2.14 (1 H, m, *CH*Me), 1.02 (3 H, dd, *J* 7.3 and 17.0, PCH*Me*), 0.93 (3 H, d, *J* 7.0, CH*Me*), 0.91 (9 H, s, CMe_3), 0.01 (3 H, s, $SiMe_AMe_B$) and 0.005 (3 H, s, $SiMe_AMe_B$); δ_C(100 MHz, $CDCl_3$) 134.2–128.5 (Ph_2PO), 65.5^- (d, *J* 14.0, CH_2OSi), 34.0^+ (*C*HMe), 30.0^+ (d, *J* 73.75, PCH), 26.0^+ (CMe_3), 18.3^- (CMe_3), 8.95^+ (PCH*Me*), 5.5^+ (d, *J* 1.8, CH*Me*), -5.3^+ ($SiMe_AMe_B$) and -5.5^+ ($SiMe_AMe_B$); *m/z* 402 (5%, M^+), 387 (30, M − Me), 345 (100, M − CMe_3) and 201 (60, Ph_2PO).

(*R*)-(−)-Octan-2-yl tosylate 9

(*R*)-(−)-Octan-2-ol (1.0 cm^3, 6.4 mmol) was added dropwise to a stirred solution of toluene-*p*-sulfonyl chloride (1.2 g, 6.3 mmol) in pyridine (4 cm^3) under argon at 0 °C. The resulting solution was allowed to warm to room temperature and stirred at room temperature for 20 h. The mixture was poured onto ice–water (20 cm^3) and extracted with Et_2O (3 × 20 cm^3). The combined organic extracts were washed successively with hydrochloric acid (3 M; 3 × 20 cm^3) and saturated aqueous sodium hydrogen carbonate (30 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with hexane–EtOAc (7:3) as eluent gave tosylate (*R*)-**9** (1.34 g, 75%) as a colourless liquid, R_F(1:1 EtOAc–hexane) 0.6; $[\alpha]_D^{20}$ −3.1 (*c* 1.4 in $CHCl_3$); $\nu_{max}(film)/cm^{-1}$ 1598 (C_6H_4), 1496 (C_6H_4), 1363 (SO_2) and 1177 (SO_2); δ_H(200 MHz, $CDCl_3$) 7.78 (1 H, d, *J* 8.3, *o*-$C_6H_4SO_2$), 7.32 (1 H, d, *J* 8.4, *m*-$C_6H_4SO_2$), 4.58 (1 H, sex, *J* 6.2, CHOTs), 2.42 (3 H, s, C_6H_4Me), 1.60–1.35 (2 H, m, CH_2CHOTs), 1.24 (3 H, d, *J* 6.2, CH*Me*), 1.15 (8 H, br s, 4 × CH_2) and 0.83 (3 H, t, *J* 6.2, CH_2Me); δ_C(100 MHz, $CDCl_3$) 144.3^- (*ipso*-$C_6H_4SO_2$), 134.6^- (*ipso*-C_6H_4Me), 129.6^+ (*o*-$C_6H_4SO_2$), 127.7^+ (*m*-$C_6H_4SO_2$), 80.7^+ (CHOTs), 36.5^- (CH_2), 31.5^- (CH_2), 28.7^- (CH_2), 24.8^- (CH_2), 22.4^- (CH_2), 21.5^+ (Me), 20.8^+ (Me) and 14.0^+ ($MeCH_2$); *m/z* 284 (70%, M^+), 172 (80), 154 (80), 113 (100, M − OTs) and 91 (80, C_6H_4Me) (Found: M^+, 284.1449. $C_{15}H_{24}O_3S$ requires *M*, 284.1446).

In the same way, tosylate *rac*-**9**[29] was prepared in 80% yield and tosylate (*S*)-**9** {$[\alpha]_D^{20}$ +2.8 (*c* 1.3 in $CHCl_3$)} was prepared in 87% yield.

(*S*)-(−)-2-Diphenylphosphinoyloctane 5

A solution of lithium diphenylphosphide in THF was prepared according to the method of Ashby:[16] butyllithium (1.6 M solution in hexane; 2.2 cm^3, 3.5 mmol) was added dropwise to a stirred solution of diphenylphosphine (0.6 cm^3, 3.4 mmol) in THF (5 cm^3) under argon at −30 °C to give a deep orange solution. After 4 h, a solution of tosylate (*R*)-**9** (645 mg, 2.3 mmol) in THF (2 cm^3) was added dropwise and the resulting bright red solution was allowed to warm to 0 °C. After a further 30 min, hydrogen peroxide (100 vol, 3 cm^3) was added dropwise (care—vigorous reaction) to give a colourless solution. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (30 cm^3) and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave phosphine oxide (*S*)-**5**†† (626 mg, 88%) as needles, mp 95–97 °C (from 1:1 EtOAc–hexane) (lit.,[9] 94–95 °C); R_F(EtOAc) 0.5; $[\alpha]_D^{20}$ −8.7 (*c* 1.6 in $CHCl_3$; ≥95% ee by Pirkle) and $[\alpha]_D^{20}$ −10.6 (*c* 1.2 in CCl_4) [lit.,[9] $[\alpha]_{546}^{25}$ −14.7 (*c* 6.4 in CCl_4)] (Found: C, 76.2; H, 8.6; P, 9.8%; M$^+$, 314.1807. $C_{20}H_{27}OP$ requires C, 76.4; H, 8.7; P, 9.9%; *M*, 314.1780); ν_{max}(Nujol)/cm^{-1} 1590 (Ph), 1436 (P–Ph) and 1178 (P=O); δ_H(400 MHz, $CDCl_3$) 7.78–7.72 (4 H, m, *o*-Ph_2PO), 7.47–7.37 (6 H, m, *m*- and *p*-Ph_2PO), 2.34–2.26 (1 H, m, PCH), 1.63–1.54 (1 H, m), 1.45–1.35 (1 H, m), 1.21–0.98 (7 H, m), 1.12 (3 H, dd, *J* 7.1 and 17.0, CH*Me*) and 0.79 (3 H, t, *J* 6.7, CH_2*Me*); δ_C(100 MHz, $CDCl_3$) 133.0–128.5 (Ph_2PO), 32.0$^+$ (d, *J* 72.1, PCH), 31.5$^-$ (CH_2), 28.9$^-$ (CH_2), 28.7$^-$ (CH_2), 27.35$^-$ (d, *J* 12.4, PCHCH_2), 22.5$^-$ (CH_2), 14.0$^+$ (CH_2*Me*) and 12.0$^+$ (d, *J* 2.1, CH*Me*); *m/z* 314 (20%, M$^+$), 230 (100), 229 (75, M − C_6H_{13}), 202 (100, Ph_2POH), 201 (100, Ph_2PO) and 77 (50, Ph).

In the same way, phosphine oxide *rac*-**5** {mp 96–98 °C (from 1:1 EtOAc–hexane) (Found: C, 76.4; H, 8.7; P, 9.8%; M$^+$, 314.1807. $C_{20}H_{20}OP$ requires C, 76.4; H, 8.7; P, 9.9%; *M*, 314.1780)} was prepared in 74% yield and phosphine oxide (*R*)-**5** {mp 92–94 °C (from EtOAc); $[\alpha]_D^{20}$ +9.0 (*c* 1.3 in $CHCl_3$) (Found: C, 76.5; H, 8.8; P, 9.85%; M$^+$, 314.1779. $C_{20}H_{27}OP$ requires C, 76.4; H, 8.7; P, 9.9%; *M*, 314.1780)} was prepared in 82% yield.

Lithiation (butyllithium) and external quench of *syn*-6 with methanol

Butyllithium (1.5 M solution in hexane; 100 µl, 0.15 mmol) was added dropwise to a stirred solution of phosphine oxide *syn*-**6** (48 mg, 0.12 mmol) in THF (2 cm^3) under argon at −78 °C. The resulting red solution was stirred at −78 °C for 45 min and then MeOH (0.5 cm^3) was added. The resulting colourless solution was allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil (50 mg, 100%) which contained a 53:47 ratio of phosphine oxides *anti*- and *syn*-**6** (by ^{1}H NMR).

Lithiation (butyllithium) and external quench of *anti*-6 with methanol

In the same way, butyllithium (1.5 M solution in hexane; 90 µl, 0.14 mmol) and phosphine oxide *anti*-**6** (40 mg, 0.1 mmol) in THF (2 cm^3) followed by the addition of MeOH (0.5 cm^3) gave the crude product (40 mg, 100%) as an oil which contained a 54:46 ratio of phosphine oxides *anti*- and *syn*-**6** (by ^{1}H NMR).

2-Diphenylphosphinoyl-2-trimethylsilyloctane 10

Butyllithium (1.3 M solution in hexane; 0.35 cm^3, 0.46 mmol) was added dropwise to a stirred solution of phosphine oxide *rac*-**5** (109 mg, 0.35 mmol) in THF (4 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at −78 °C for 1 h and then Me_3SiCl (100 µl, 0.79 mmol) was added dropwise. After 4 h at −78 °C, the colourless solution was allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a colourless oil. Purification by chromatography on silica with EtOAc as eluent gave *silyl phosphine oxide* **10** (66 mg, 49%) as a colourless oil, R_F(EtOAc) 0.6; ν_{max}(Nujol)/cm^{-1} 1436 (P–Ph), 1178 (P=O) and 845 ($SiMe_3$); δ_H(200 MHz, $CDCl_3$) 8.07–8.00 (4 H, m, *o*-Ph_2PO), 7.48–7.43 (6 H, m, *m*- and *p*-Ph_2PO), 1.80–1.13 (10 H, m, 5 × CH_2), 1.40 (3 H, d, *J* 17.8, PCMe), 0.83 (3 H, t, *J* 6.3, CH_2*Me*) and −0.03 (9 H, s, $SiMe_3$); δ_C(50 MHz, $CDCl_3$) 135.0–127.8 (Ph_2PO), 34.2$^-$ (CH_2), 31.4$^-$ (CH_2), 30.2$^-$ (CH_2), 29.8$^-$ (d, *J* 56.3, PC), 25.6$^-$ (d, *J* 6.9, PCHCH_2), 22.5$^-$ (CH_2), 16.9$^+$ (Me), 13.9$^+$ (Me) and −0.9$^+$ ($SiMe_3$); *m/z* 386 (10%, M$^+$), 371 (80, M − Me), 230 (100), 202 (80, Ph_2POH) and 201 (60, Ph_2PO) (Found: M$^+$, 386.2212. $C_{23}H_{35}OPSi$ requires *M*, 386.2195).

(1*R,2*S**)-2-Diphenylphosphinoyl-2-methyl-1-phenyloctan-1-ol *anti*-11 and (1*R**,2*R**)-2-diphenylphosphinoyl-2-methyl-1-phenyloctan-1-ol *syn*-11**

Butyllithium (1.6 M solution in hexane; 0.3 cm^3, 0.48 mmol) was added dropwise to a stirred solution of phosphine oxide *rac*-**5** (124 mg, 0.4 mmol) in THF (5 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at −78 °C for 30 min and then benzaldehyde (50 µl, 0.5 mmol) was added dropwise. After 1 h at −78 °C, saturated aqueous ammonium chloride (0.5 cm^3) was added and the colourless solution allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a white solid. Purification by chromatography on silica with EtOAc–hexane (1:1) as eluent gave a 56:44 ratio (by ^{1}H NMR) of *alcohols anti*- and *syn*-**11**‡‡ (127 mg, 77%) as fine needles, mp 186–189 °C (from EtOAc); R_F(EtOAc) 0.5 (Found: C, 77.2; H, 8.0; P, 7.6%; M$^+$, 420.2215. $C_{27}H_{33}O_2P$ requires C, 77.1; H, 7.9; P, 7.4%; *M*, 420.2218); ν_{max}(Nujol)/cm^{-1} 3150 (OH), 1436 (P–Ph) and 1148 (P=O); δ_H(400 MHz, $CDCl_3$) 8.05–7.88 (8 H, m, 2 × *o*-Ph_2PO), 7.56–7.43 (12 H, m, 2 × *m*- and *p*-Ph_2PO), 7.27–7.19 (10 H, m, 2 × Ph), 6.07 (1 H, s, OH^{anti}), 5.69 (1 H, d, *J* 2.3, OH^{syn}), 5.04 (1 H, dd, *J* 2.4 and 11.8, PhC*H*OH^{syn}), 4.95 (1 H, d, *J* 9.4, PhC*H*OH^{anti}), 1.87–1.80 (2 H, m, CH_2), 1.59–1.52 (2 H, m, CH_2), 1.34–0.82 (16 H, m, 8 × CH_2), 1.31 (3 H, d, *J* 16.7, PCMe^{syn}), 1.00 (3 H, d, *J* 17.3, PCMe^{anti}), 0.76 (3 H, t, *J* 7.1, CH_2*Me*^{syn}) and 0.75 (3 H, t, *J* 7.1, CH_2*Me*^{anti}); δ_C(100 MHz, $CDCl_3$) 139.9–125.6 (Ph_2PO), 78.2$^+$ (PhCHOH), 76.9$^+$ (PhCHOH), 44.7$^-$ (d, *J* 65.3, PC), 44.2$^-$ (d, *J* 65.4, PC), 33.4–20.5$^-$ (CH_2), 20.5$^+$ (Me), 14.0$^+$ (Me) and 13.5$^+$ (Me); *m/z* 420 (20%, M$^+$), 402 (80, M − H_2O), 314 (60, M − PhCHO), 243 (100), 202 (90, Ph_2POH), 201 (60, Ph_2PO) and 77 (50, Ph).

Lithiation (butyllithium) and external quench of (*S*)-5 with methanol

Butyllithium (1.6 M solution in hexane; 0.15 cm^3, 0.24 mmol) was added dropwise to a stirred solution of phosphine oxide (*S*)-**5** (45 mg, 0.14 mmol) in THF (2 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at −78 °C for 1 h and then MeOH (0.2 cm^3) was added. After 30 min at −78 °C, the colourless solution was allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1:1 CH_2Cl_2–water (30 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give racemic phosphine oxide **5** (45 mg, 100%) as needles identical (TLC and ^{1}H NMR) with that obtained previously, $[\alpha]_D^{20}$ − 0.3 (*c* 1.5 in $CHCl_3$; racemic by Pirkle).

†† Phosphine oxide (*S*)-**5** has been synthesised before[9] but full characterisation has not been described.

‡‡ Alcohols *syn*- and *anti*-**11** were inseparable by flash chromatography. We have tentatively assigned the diastereoisomers using a ^{1}H NMR coupling constant rule.

Lithiation (butyllithium) and external quench of (*S*)-5 with Me_3SiCl

Butyllithium (1.6 M solution in hexane; 0.4 cm^3, 0.64 mmol) was added dropwise to a stirred solution of phosphine oxide (*S*)-**5** (98 mg, 0.31 mmol) in THF (5 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at 78 °C for 1 h and then Me_3SiCl (200 μl, 1.58 mmol) was added dropwise. After 9 h at −78 °C, the colourless solution was allowed to warm to room temperature and the THF then evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc–hexane (1 : 1) as eluent gave racemic silyl phosphine oxide **10** (86 mg, 74%) as a colourless oil identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ +0.2 (*c* 1.5 in $CHCl_3$; racemic by Pirkle) and racemic phosphine oxide **5** (15 mg, 15%) as needles identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ −0.1 (*c* 1.5 in $CHCl_3$).

Lithiation (butyllithium) and external quench of (*S*)-5 with benzaldehyde

Butyllithium (1.6 M solution in hexane; 0.4 cm^3, 0.64 mmol) was added dropwise to a stirred solution of phosphine oxide (*S*)-**5** (100 mg, 0.3 mmol) in THF (5 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at −78 °C for 30 min and then benzaldehyde (100 μl, 1.0 mmol) was added dropwise. After 1 h at −78 °C, saturated aqueous ammonium chloride (0.5 cm^3) was added and the colourless solution allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1 : 1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as a white solid. Purification by chromatography on silica with EtOAc–hexane (1 : 1) as eluent gave a 56 : 44 ratio (by ^1H NMR) of alcohols *anti*- and *syn*-**11** (93 mg, 74%) as plates identical (TLC and ^1H NMR) with those obtained previously, mp 175–177 °C (from EtOAc); $[\alpha]_D^{20}$ 0 (*c* 0.9 in $CHCl_3$; both diastereoisomers racemic by Pirkle).

Lithiation (LDA) and external quench of (*S*)-5 with Me_3SiCl

A solution of LDA (prepared from 90 μl of Pr^i_2NH, 0.64 mmol and 0.4 cm^3 of a 1.6 M solution of butyllithium in hexane, 0.64 mmol) in THF (2 cm^2) was added dropwise to a stirred solution of phosphine oxide (*S*)-**5** (90 mg, 0.29 mmol) in THF (3 cm^3) under argon at −78 °C. The resulting dark-red solution was stirred at −78 °C for 1 h and then Me_3SiCl (200 μl, 1.58 mmol) was added dropwise. After 8 h at −78 °C, the colourless solution was allowed to warm to room temperature and the THF evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with 1 : 1 EtOAc–hexane as eluent gave racemic silyl phosphine oxide **10** (45 mg, 41%) as a colourless oil identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ +0.3 (*c* 2.0 in $CHCl_3$; racemic by Pirkle).

Lithiation (LDA) and internal quench of (*S*)-5 with Me_3SiCl

A solution of LDA (prepared from 90 μl of $^iPr_2NH$, 0.64 mmol and 0.4 cm^3 of a 1.6 M solution of butyllithium in hexane, 0.64 mmol) in THF (2 cm^3) was added dropwise to a stirred solution of phosphine oxide (*S*)-**5** (98 mg, 0.31 mmol) and Me_3SiCl (200 μl, 1.58 mmol) in THF (3 cm^3) under argon at −78 °C. After 8 h at -78 °C, the colourless solution was allowed to warm to room temperature and the THF evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc–hexane (1 : 1) as eluent gave racemic silyl phosphine oxide **10** (60 mg, 50%) as a colourless oil identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ −0.5 (*c* 2.5 in $CHCl_3$; racemic by Pirkle).

Attempted lithiation (LDA) and internal quench of butyldiphenylphosphine oxide with benzaldehyde

A solution of LDA (prepared from 110 μl of Pr^i_2NH, 0.8 mmol and 0.5 cm^3 of a 1.6 M solution of butyllithium in hexane, 0.8 mmol) in THF (1 cm^3) was added dropwise to a stirred solution of butyldiphenylphosphine oxide (104 mg, 0.4 mmol) and benzaldehyde (200 μl, 2.5 mmol) in THF (3 cm^3) under argon at −78 °C. After 3 h at −78 °C, saturated aqueous ammonium chloride (0.5 cm^3) was added and the colourless solution allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1 : 1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil which contained only starting butyldiphenylphosphine oxide and benzaldehyde (by TLC).

Lithiation (LDA) and external quench of (*S*)-5 with cyclobutanone: 1-1′-diphenylphosphinoyl-1′-methylheptylcyclobutanol 12

A solution of LDA (0.3 M solution in THF; 2.5 cm^3, 0.75 mmol) was added dropwise to a stirred solution of phosphine oxide (*R*)-**5** (208 mg, 0.7 mmol) in THF (5 cm^3) under argon at −78 °C. The resulting dark red solution was stirred at −78 °C for 30 min and then cyclobutanone (75 μl, 1.0 mmol) was added dropwise. After 2 h at −78 °C, saturated aqueous ammonium chloride (0.5 cm^3) was added and the colourless solution allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1 : 1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc as eluent gave racemic *alcohol* **12** (165 mg, 65%) as plates, mp 110–112 °C (from EtOAc); R_F(EtOAc) 0.6; $[\alpha]_D^{20}$ 0 (*c* 3.8 in $CHCl_3$; racemic by Pirkle) (Found: C, 74.9; H, 8.8; P, 8.2%; M^+, 384.2216. $C_{24}H_{33}O_2P$ requires C, 75.0; H, 8.7; P, 8.1%; *M*, 384.2218); $\nu_{max}(CHCl_3)/cm^{-1}$ 3348 (OH), 1591 (Ph), 1438 (P–Ph) and 1169 (P=O); δ_H(400 MHz, $CDCl_3$) 8.07–8.03 (2 H, m, *o*-Ph_2PO), 7.99–7.94 (2 H, m, *o*-Ph_2PO), 7.51–7.43 (6 H, m, *m*- and *p*-Ph_2PO), 5.92 (1 H, s, OH), 2.31–2.27 (1 H, m), 2.08–1.99 (4 H, m), 1.80–1.75 (2 H, m), 1.65–1.55 (1 H, m), 1.48 (3 H, d, *J* 17.7, PCMe), 1.26–0.97 (8 H, m) and 0.78 (3 H, t, *J* 7.1, CH_2*Me*); δ_C(100 MHz, $CDCl_3$) 133.2–128.3 (Ph_2PO), 82.8$^-$ (d, *J* 3.0, COH), 45.8$^-$ (d, *J* 63.9, PC), 35.0$^-$ (d, *J* 20.8, CH_2), 34.2$^-$ (CH_2), 34.15$^-$ (CH_2), 31.7$^-$ (CH_2), 30.2$^-$ (CH_2), 24.2$^-$ (d, *J* 9.3, CH_2), 22.5$^-$ (CH_2), 14.0$^+$ (Me), 17.6$^-$ (CH_2) and 14.1$^+$ (Me); *m/z* 384 (10%, M^+), 366 (20, M − H_2O), 313 (10, M − C_4H_7O) and 202 (100, Ph_2POH) and racemic phosphine oxide **5** (67 mg, 26%), as needles, identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ +0.4 (*c* 1.3 in $CHCl_3$).

Lithiation (LDA) and internal quench of (*S*)-5 with cyclobutanone

A solution of LDA (0.3 M solution in THF; 2.5 cm^3, 0.75 mmol) was added dropwise to a stirred solution of phosphine oxide (*R*)-**5** (98 mg, 0.31 mmol) and cyclobutanone (65 μl, 0.8 mmol) in THF (5 cm^3) under argon at −78 °C. After 3 h at −78 °C, saturated aqueous ammonium chloride (0.5 cm^3) was added and the colourless solution allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was dissolved in 1 : 1 CH_2Cl_2–water (20 cm^3) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 cm^3) and the combined organic extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the crude product as an oil. Purification by chromatography on silica with EtOAc–hexane (2 : 1) and then EtOAc as eluent gave racemic alcohol **12** (44 mg, 18%) as an oil, $[\alpha]_D^{20}$ 0 (*c* 2.0 in $CHCl_3$; racemic by Pirkle) and phosphine oxide (*R*)-**5** (169 mg, 82%), as needles, identical (TLC and ^1H NMR) with that obtained previously, $[\alpha]_D^{20}$ +7.6 (*c* 3.0 in $CHCl_3$).

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