Synthesis, X-ray structures and chemistry of enantiomerically pure 10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxides

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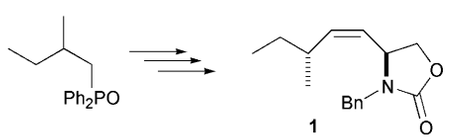
Several phosphepine oxides were synthesised in optically pure form. Sharpless asymmetric dihydroxylation was used to introduce the chiral centres in all cases. Ring closure was achieved using either $PhPCl_2$ or $PrPCl_2$ together with a double nucleophile generated by either a double *ortho*-lithiation or double bromine–lithium exchange. The X-ray crystal structures of three phosphepine oxides illustrate their different conformations. The NMR spectra of several phosphepine oxides are described as is the chemistry which is shown to differ from that of acyclic phosphine oxides.

Introduction

For some time we have been interested in phosphine oxides and the Horner–Wittig reaction.[1] Particularly we are interested in stereocontrol that may be achieved by the diphenylphosphinoyl group in a molecule *before* the Horner–Wittig reaction is initiated. Hence a β-hydroxyphosphine oxide may be reacted to introduce extra stereocentres with stereocontrol relative to the Ph_2PO group before elimination. And since the elimination is stereospecific, a diastereomerically pure β-hydroxyphosphine oxide leads to a geometrically pure olefin.[1] Clayden combined this introduction of additional chiral centres followed by stereospecific elimination to synthesise all four diastereomers of the oxazolidinone **1** (Scheme 1).[2]



Scheme 1

We have previously reported[3] achiral seven-membered phosphorus heterocycles—phosphepines. We have reported some optically pure phosphepine oxides in preliminary communications[4,5] and now give full details of the synthesis, structure, conformation and chemistry of these compounds including X-ray crystal structures, NMR experiments and the more interesting reactions that did not proceed as planned.

Optically pure phosphine oxides with chirality at the phosphorus atom have been reported[6–8] (Fig. 1) but because chirality at the phosphorus atom is destroyed in the elimination step of the Horner–Wittig reaction we preferred to build the chirality into the carbon framework by joining a C_2 symmetrical unit, such as **17**, and the phosphorus atom in a seven-membered ring. Although the phosphepine oxide in Fig. 1 is not C_2 symmetric it is derived from C_2-symmetric precursors. The phosphorus atom is thus not chiral and could be described either as a pseudo-asymmetric centre or as chirotopic and non-stereogenic.[9]

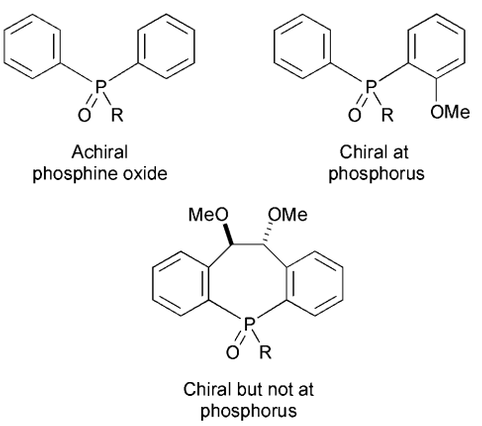


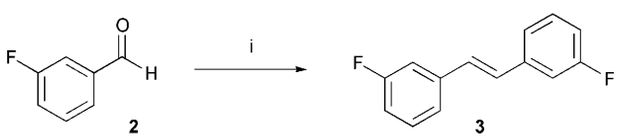
Fig. 1

Results and discussion

Synthesis

There are two key steps in the synthesis of all of our phosphepine oxides. The first is the Sharpless asymmetric dihydroxylation of a stilbene which enantioselectively installs the two chiral centres.[10] The second is the ring closure reaction itself which has two components: (i) the formation of a double nucleophile by dilithiation and (ii) reaction with a phosphorus electrophile ($RPCl_2$). The dilithiation was achieved using either *ortho*-lithiation or bromine–lithium exchange.

Stilbenes **3**, **5** and **6** were prepared with *ortho*-lithiation in mind and dibromostilbene **4** and dichlorostilbene **7** with a view to halogen–lithium exchange. Starting from the corresponding aldehydes, stilbenes **3**–**6** were synthesised using the McMurry coupling reaction.[11] Lithium metal was used to reduce the $TiCl_3$ (rather than the more modern method using a Zn/Cu couple).[12] Hence 3-fluorobenzaldehyde was transformed into (*E*)-3,3′-difluorostilbene **3** in 95% yield (Scheme 2). This synthesis of



Scheme 2 *Reagents and conditions*: i $TiCl_3$, Li, DME, reflux 18 h.

stilbenes was extremely *E*-selective—the difluorostilbene was isolated in a 99.92:0.08 *E*:*Z* ratio. Though dibromostilbene **4** could be synthesised using the usual McMurry conditions, higher yields (71%) were obtained with a shorter reaction time (6 instead of 18 hours). Presumably the bromide of both the starting material and product reacted slowly with the excess

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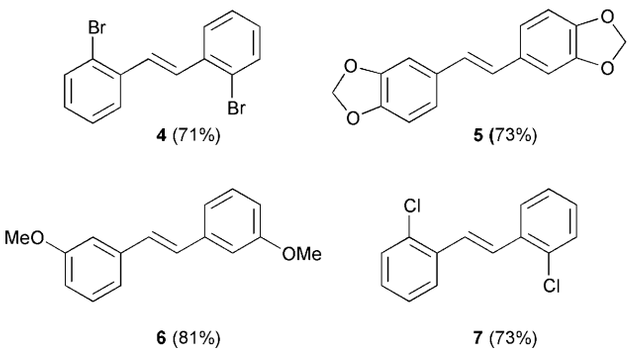
Table 1 Asymmetric dihydroxylation of stilbenes

Stilbene	Substitution	Product	Yield (%)	Ee (%)	$[\alpha]_D$
3	3-F	**8**	89	≥99	+98.8
4	2-Br	**9**	94	≥99	−38.8
6	3-OMe	**10**	96	≥99	+97.9
7	2-Cl	**11**	65[a]	—	—
5	3,4-OCH_2O	**12**	84	≥99	+167

[a] Yield obtained in a racemic dihydroxylation.



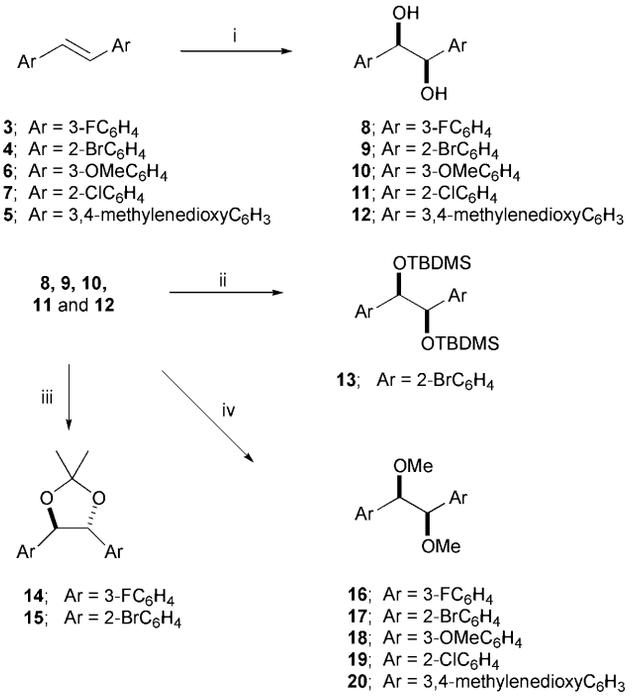
lithium metal. It is worth noting that bis(methylenedioxy)-stilbene **5** was very difficult to extract from the McMurry reaction mixture due to its insolubility in hexane. There are other methods available for the synthesis of this compound.[13] Dichlorostilbene **7** was synthesised from 2,α-dichlorotoluene by the method of Hoeg and Lusk.[14]

The stilbenes were dihydroxylated using the commercially available AD-β-mix. The enantiomeric excesses of the diols were determined in comparison with racemic samples by NMR using Pirkle's chiral shift reagent and were excellent (≥99%) in all cases.[15] The signals of the two enantiomers of diol **9** were not separated by Pirkle's chiral shift reagent but the diether **17** was successfully analysed instead. In all cases, determination of ee was performed before recrystallisation or any other process that might enhance enantiopurity (Table 1).

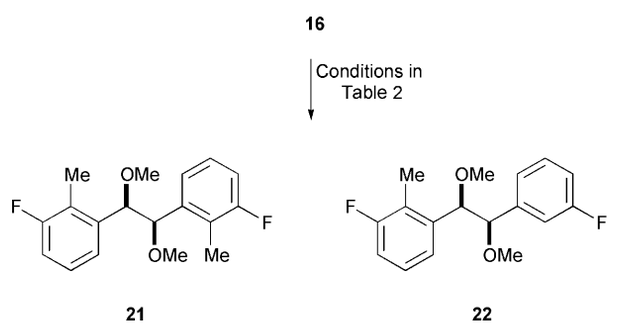
The diols were protected in three different ways. Methylation was achieved using NaH followed by MeI (Scheme 3). Both the difluoride **16** and dibromide **17** could thus be formed in 98% yield. The method of silylation we chose was that of Corey *et al.*[16] Four equivalents of 2,6-lutidine and three equivalents of TBDMSOTf gave the dibromide **13** in 98% yield. Some literature methods for the formation of acetals call for refluxing conditions in which, with 2,2-dimethoxypropane, the methanol resulting from the reaction is removed.[17] In contrast we found that warming our diols for a couple of hours with 2,2-dimethoxypropane was sufficient to form the acetals **14** and **15** in yields of up to 98%. The transformation was effected much more cleanly at the lower temperature.

Lithiation reactions

For successful ring formation effective double lithiation of the precursors was paramount. The optimum lithiation conditions for ring precursors **16**, **17** and **20** were probed using different lithiating reagents and methyl iodide as the electrophile (Table 2, Scheme 4). We attempted to lithiate difluoride **16** with *n*-butyllithium and with *sec*-butyllithium with and without TMEDA. The best results were obtained with *sec*-butyllithium without TMEDA. The dimethylated product **21** was isolated in an 84% yield. Attempts to improve the reaction further through the use of *tert*-butyllithium resulted only in the destruction of starting material. It is interesting to note that the fluorine and oxygen atoms collaborate so that, of the two positions *ortho* to the fluorine atom (Fig. 2), only position-2 was methylated. Attempts to lithiate the difluoro acetal **14** were not successful.



Scheme 3 Preparation of precursors. *Reagents and conditions*: i AD-β-mix; ii 2,6-lutidine, TBDMSOTf, CH_2Cl_2; iii 2,2-dimethoxypropane, toluene-*p*-sulfonic acid, CH_2Cl_2, 50 °C; iv NaH, THF then MeI.



Scheme 4 Investigating *ortho*-lithiation of **16**.

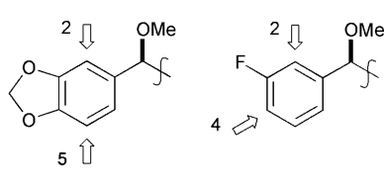
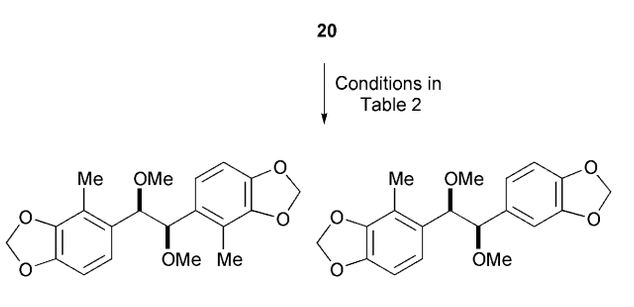


Fig. 2 Regioselectivity of *ortho*-lithiation.

We were also able to dimethylate **20** in an 84% yield and *sec*-butyllithium was again superior to *n*-butyllithium (Table 2, Scheme 5). Once again, regioselectivity was very good and no methylation at position-5 was detected.

The studies with **16** and **20** indicate that the extent of double lithiation is *at least* 84% since there is the possibility of sites that



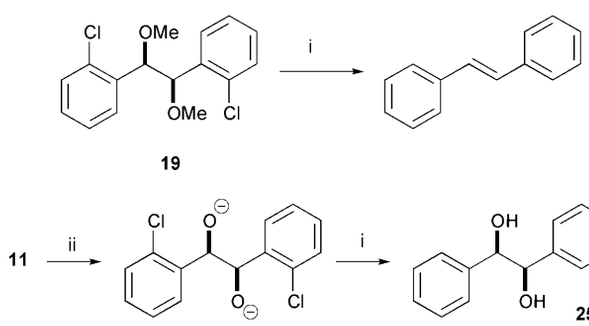
Scheme 5 Investigating *ortho*-lithiation of **20**.

Table 2 Lithiation and methylation of precursors **16** and **20**

Substrate	Conditions	Time	Starting material (%)	Monomethylated product, yield (%)	Dimethylated product, yield (%)
16	*n*-BuLi–TMEDA	1 h 40 min	8	**22**, 52	**21**, 39
16	*n*-BuLi	4 h	21	**22**, 60	**21**, 19
16	*sec*-BuLi–TMEDA	3 h	20	**22**, 34	**21**, 46
16	*sec*-BuLi	3 h	0	**22**, 16	**21**, 84
16	*tert*-BuLi–Et_2O	1 h	—	—	—
20	*n*-BuLi–THF −78 °C–0 °C	55 min	60	**24**, 25	**23**, 15
20	*sec*-BuLi, −78 °C	1 h 20 min	2	**24**, 14	**23**, 84

are lithiated but not alkylated. These sites are reprotonated and appear as either starting material or monolithiated material. Although we could make the acetal **20** react cleanly and at low temperature, we were surprised that the analogous anisole **18** resisted all our methylation attempts. The reactivity difference between the two substrates is, however, in line with the results of Rodrigo *et al*.[18] and sadly we had to abandon **18** as a substrate for ring formation.

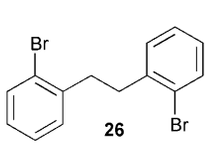
Although chlorobenzene is difficult to lithiate directly—the chlorine atom would rather direct a lithiation than undergo a halogen–lithium exchange itself[19]—it may be lithiated through the use of lithium naphthalenide.[20] However, our attempts to lithiate the chlorinated substrate **19** in this way gave stilbene as the major product (Scheme 6). Clearly, in addition to reduction



Scheme 6 *Reagents and conditions*: i Li Naphthalenide −98 °C, THF then MeOH; ii BuLi, 0 °C, THF.

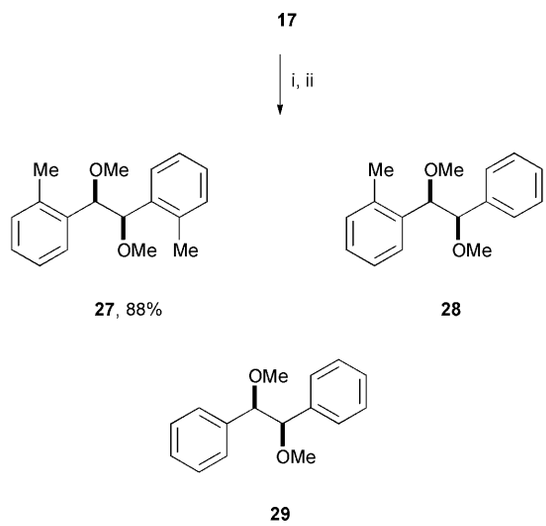
of the C–Cl bonds, the benzylic C–O bonds were easily reduced. The non-chlorinated diether **29** was also converted to stilbene with lithium naphthalenide as was dichlorostilbene **7**. Though we were able to inhibit benzylic reduction by using the dianion of diol **11**, this unprotected diol was not suitable as a precursor for formation of a phosphepine. We abandoned **19** as a potential phosphepine precursor.

Although *n*-butyllithium is effective at lithiating dibromobibenzyl **26**,[3] it is less effective in the lithiation of dibromide **17**



and several products were formed. To our surprise, the reaction with the more reactive *tert*-butyllithium proceeded very smoothly.[21] The fraction of dibromide **17** that becomes lithiated but is not then alkylated *is* detectable (unlike that of compounds **16** and **20**), since protonation of these sites does not give starting material but the debrominated materials **28** and **29** (Scheme 7). Hence ^{1}H NMR indicated an 88% yield of the dimethylated product **27** but 96% lithiation.

Three aromatic substitution patterns were thus suitable for phosphepine synthesis. Two of these—the fluoro and the acetal substrates—rely on an *ortho*-lithiation strategy and require the assistance of the benzylic OMe group for the formation of

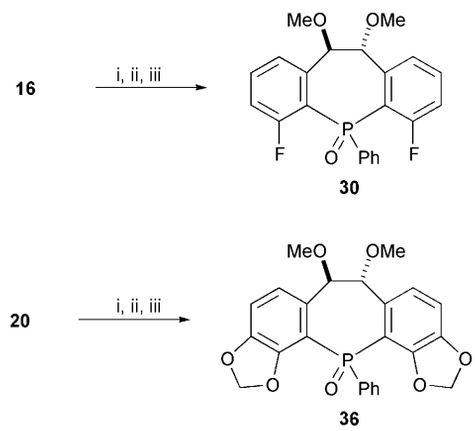


Scheme 7 *Reagents and conditions*: i *tert*-BuLi (4.1 equivalents), −78 to −23 °C; ii MeI, −78 °C to rt.

phosphepines. Changing the group on the oxygen can have a deleterious effect on *ortho*-lithiation (we were unable to lithiate fluoroacetal **14**). But the third pattern (bromo substitution) affords us additional flexibility. With this halogen–lithium exchange strategy the bromine atom does all the work and we are at liberty to protect the benzylic oxygen in alternative ways.

Ring closure reactions

In general, the yields of the seven membered rings do not reflect the high levels of lithiation that we know are achieved with the precursors. Reaction of difluoro compound **16** with *sec*-butyllithium followed by $PhPCl_2$ and then H_2O_2 gave the phosphepine **30** (Scheme 8) in reproducible yield of 51% and in a similar way phosphepine oxide **36** (Table 3) was formed from **20** in a 41% yield. The quality of *sec*-butyllithium turned out to be crucial and using *sec*-butyllithium which had deteriorated from 1.3 M to 0.9 M (and taking this change into account in the



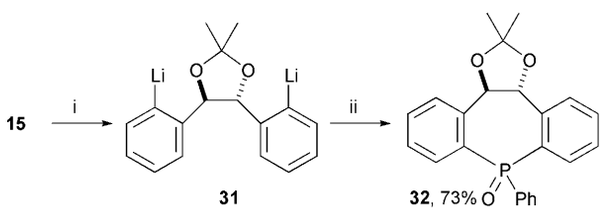
Scheme 8 *Reagents and conditions*: i *sec*-BuLi; ii $PhPCl_2$; iii H_2O_2.

Table 3 Summary of phosphepine oxides prepared. General structure in Scheme 11

R^1	X	Conditions	R^2	Y	Yield (%)	Compound
Me	2-Br	4.1 eq. *tert*-BuLi–Et_2O	Ph	H	25	**33**
Me	2-Br	2.35 eq. *tert*-BuLi–Et_2O	Pr	H	5	**34**
Me	3-F	2.2 eq. *sec*-BuLi–THF	Ph	4, 6-F	51	**30**
Me	3-F	2.36 eq. *sec*-BuLi–THF	Pr	4, 6-F	30	**35**
Me	3,4-OCH_2O	2.35 eq. *sec*-BuLi–THF	Ph	3,4:6,7-OCH_2O	41	**36**
Me	3,4-OCH_2O	2.5 eq. *sec*-BuLi–THF	Pr	3,4:6,7-OCH_2O	8	**37**
$SiMe_2{}^tBu$	2-Br	2.4 eq. *tert*-BuLi–Et_2O	Ph	H	31	**38**
$SiMe_2{}^tBu$	2-Br	2.34 eq. *tert*-BuLi–Et_2O	Pr	H	24	**39**
CMe_2	2-Br	2.4 eq. *tert*-BuLi–THF	Ph	H	73	**32**
CMe_2	2-Br	2.34 eq. *tert*-BuLi–THF	Pr	H	37	**40**

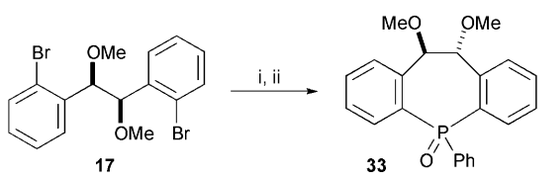
reactions) could reduce the yield of phosphepine oxide **30** to 12%.

When *tert*-butyllithium was used to generate lithiated species by halogen–lithium exchange, either two equivalents (that is, one equivalent per bromine atom) or four equivalents (two equivalents per bromine atom) may be used. In the former case the temperature of the lithiated species needs to be kept at −78 °C while in the latter it needs to be increased to allow isobutane and isobutene to form.[21] The method and solvent used often had a profound influence on the yield. Acetal **15** was lithiated to give **31** before ring closure then gave phosphepine **32** (Scheme 9). If species **31** were generated with 2.4 equivalents of



Scheme 9 *Reagents and conditions*: i 2.4 equivalents *tert*-BuLi THF; ii $PhPCl_2$; iii H_2O_2.

tert-butyllithium in THF then the yield of phosphepine **32** was 73% but 4.1 equivalents in Et_2O gave only a trace of product. Conversely, a better yield (25%) of **33** from **17** was obtained using 4.1 equivalents of *tert*-butyllithium in Et_2O than with 2.3 equivalents in THF (18%) (Scheme 10). We speculate that

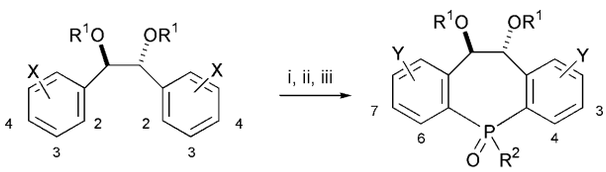


Scheme 10 *Reagents and conditions*: i *tert*-BuLi; ii $PhPCl_2$; iii H_2O_2.

LiBr may be partly responsible for the changes in yield in these reactions.

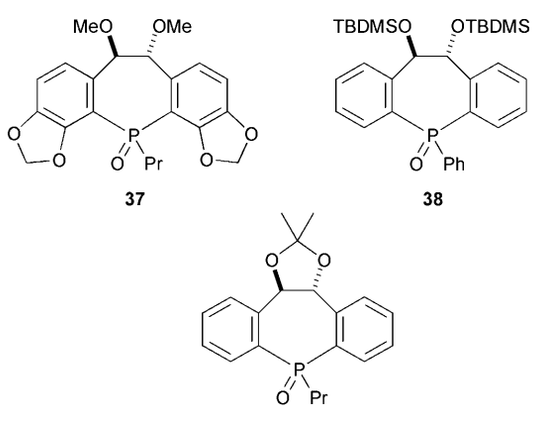
Phosphepines were also constructed using $PrPCl_2$ as the electrophile rather than $PhPCl_2$. We synthesised $PrPCl_2$ following the method of Weil *et al*.[22] The yields of these propyl derivatives were always lower than their phenyl analogues. All the phosphepines synthesised are summarised below (Table 3, Scheme 11).

Although in several cases hydrogen peroxide was used to form the phosphepine oxide from the corresponding phosphepine *in situ* this was not always the best method. In many cases several impurites and the phosphine oxide product coeluted. This was particularly the case with the phosphepine oxides having a *P*-propyl substituent. And so a more elaborate procedure was developed which enabled the isolation of purer material. The reaction was quenched at the phosphine stage (that is, before addition of any hydrogen peroxide) by the addition of a few microlitres of water followed by silica (or sometimes just silica was added) to minimise oxidation. The



Scheme 11 *Reagents and conditions*: i conditions in Table 3; ii R^2PCl_2; iii H_2O_2.

phosphine was purified by column chromatography.† Oxidation of the phosphine in the normal way (H_2O_2) followed by chromatography thus gave phosphepine oxides **34**, **35**, **36**, **37**, **39** and **40**.



Symmetry

We have previously shown how symmetry—and its destruction—are illustrated in NMR spectra. The C_2 symmetry of diether **16** is perfectly illustrated in the proton-decoupled ^{19}F NMR spectrum.[4] Although the C_2 symmetry itself is destroyed it has done its job—the phosphorus atom is not a stereogenic centre. With two fluorine atoms and a phosphorus atom, signals in the carbon NMR spectra displayed splitting and the splitting patterns of diastereotopic carbon atoms could overlap. Comparison of spectra run at two different field strengths allowed us to determine coupling constants and chemical shifts (Fig. 3) unambiguously.

X-Ray structures

Diol **41** was made by the hydrolysis of the acetal function of **32** (Scheme 12). The X-ray crystal structures of phosphepine oxides **30**, **35** and **41** were determined.‡

† In the region of the TLC plate where the phosphine oxide *would* have been, there ran a streaky continuum of impurities.

‡ All three crystals diffracted poorly resulting in rather high final *R* values. Nevertheless, the gross structural features in which we are interested are well established. All structures are solved in a chiral space group but the absolute configuration was not determined crystallographically. CCDC reference number 207/501. See http://www.rsc.org/suppdata/p1/b0/b006883g/ for crystallographic files in .cif format.

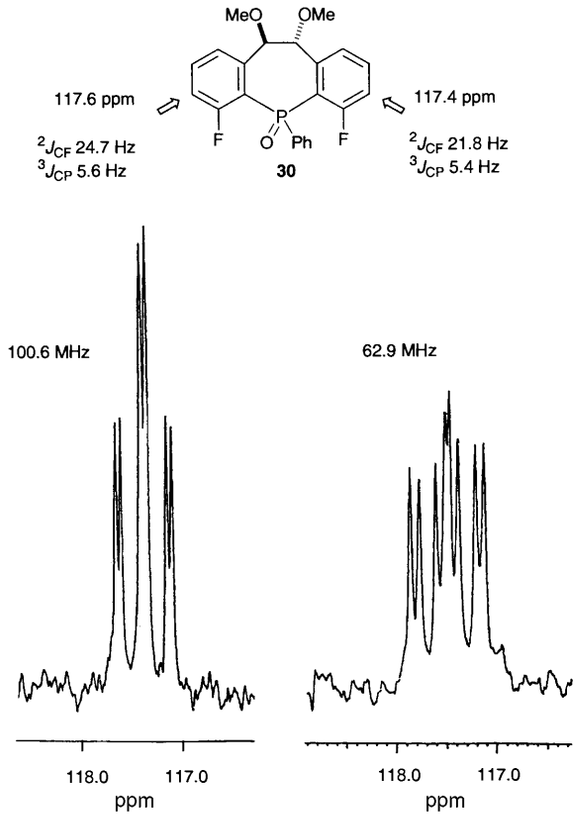


Fig. 3 Detail of ^{13}C NMR spectra of **30** at 100.6 MHz and 62.9 MHz.

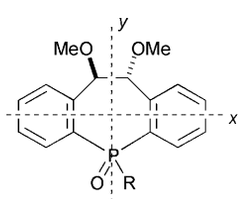
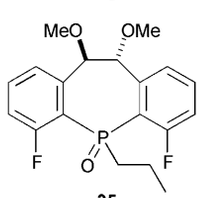
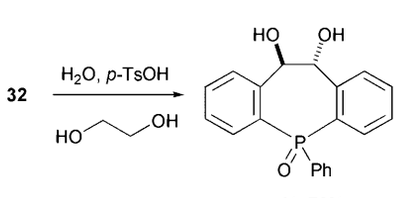


Fig. 4





Scheme 12

For the three X-ray structures it is interesting to note the conformation of the seven-membered ring and instructive to imagine a plane that contains both benzene rings and then consider the structures' perturbation from this starting point.

With diol **41** the two benzene rings are bent down from the imaginary plane about axis *y* (Fig. 4) like the wings of a butterfly.§ They are also slightly twisted relative to each other so that the view from the two chiral centres towards the phosphorus atom contains the underside of one ring and the topside of the other. The seven-membered ring of diol **41** adopts a twist boat arrangement (evident in Fig. 5). The exocyclic phenyl group adopts a pseudoaxial position. Fig. 6 shows an orthogonal view of **41**.

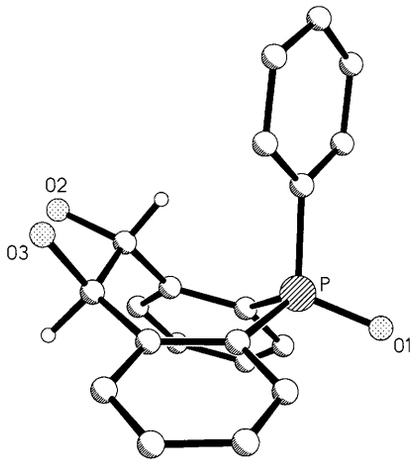


Fig. 5 Side view of **41**.

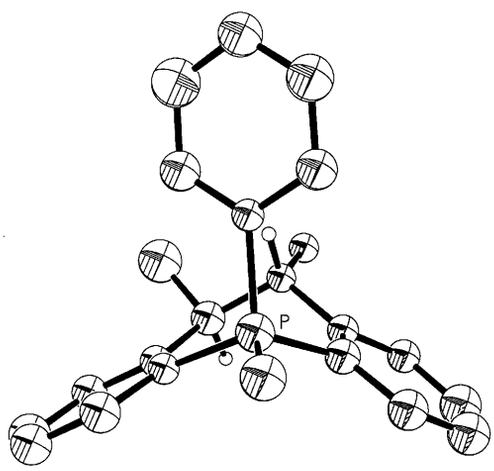


Fig. 6 P-to-backbone view of **41**.

This conformation contrasts with the other two compounds in which the twist of the seven-membered rings is completely different. Returning to our imaginary plane with phosphepine oxide **35**,¶ the deviation this time involves a twist about axis *x* (Fig. 4). The fluorine atom of one ring moves above the plane while the fluorine atom of the other ring moves below the plane. Hence the two phenyl rings resemble the blades of a propeller. In this manner, the twisted seven membered ring adopts a C_2 symmetrical arrangement. A view from the phosphorus atom to the back of the ring in both cases (Figs. 8 and 10) clearly shows how the two rings are twisted about the axis *x* (Fig. 4). The propyl chain is in a pseudo-axial position with the α-protons pointing away from the seven-membered ring and the β-protons pointing into this chiral environment. Orthogonal views are shown in Figs. 7 and 9.

In phosphepine oxide **30** the arrangement of the two phenyl groups and the twist of the seven-membered ring is very similar to the arrangement in **35**.‖ The plane of the exocyclic phenyl

§ Crystal data for **41**—$C_{21}H_{18}Cl_3O_3P$, $M = 455.67$, orthorhombic, $a = 12.60(2)$, $b = 17.44(4)$, $c = 9.36(2)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90°$, $V = 2057(7)$ Å^3, $T = 293(2)$ K, space group $P2_12_12_1$, $Z = 4$, $\mu = 0.543$ mm^{-1}; 1290 reflections collected, $R_1 = 0.0804$ [$I > 2\sigma(I)$], $wR_2 = 0.1543$.

¶ Crystal data for **30**—$C_{22}H_{19}F_2O_3P$, $M = 400.34$, orthorhombic, $a = 13.68(3)$, $b = 29.41(6)$, $c = 9.49(2)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90°$, $V = 3819(14)$ Å^3, $T = 293(2)$ K, space group $P2_12_12_1$, $Z = 8$, $\mu = 0.183$ mm^{-1}; 2345 reflections collected, $R_1 = 0.0840$ [$I > 2\sigma(I)$], $wR_2 = 0.1517$.

‖ Crystal data for **35**—$C_{19}H_{21}F_2O_3P$, $M = 366.33$, orthorhombic, $a = 7.96(2)$, $b = 30.20(6)$, $c = 15.10(3)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90°$, $V = 3631(14)$ Å^3, $T = 293(2)$ K, space group $P2_12_12_1$, $Z = 8$, $\mu = 0.186$ mm^{-1}; 2240 reflections collected, $R_1 = 0.0802$ [$I > 2\sigma(I)$], $wR_2 = 0.1878$.

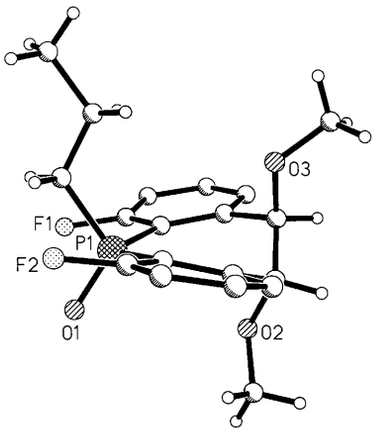


Fig. 7 Side view of **35**.

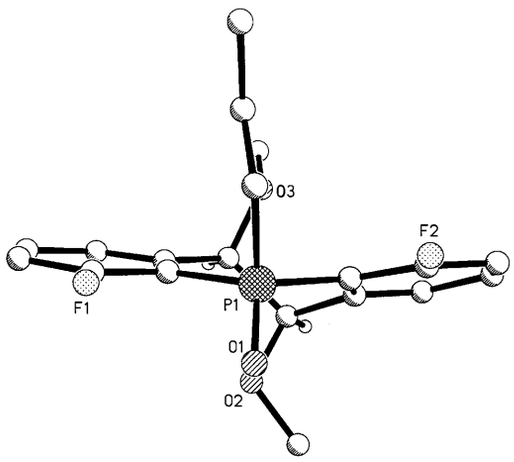


Fig. 8 P-to-backbone view of **35**.

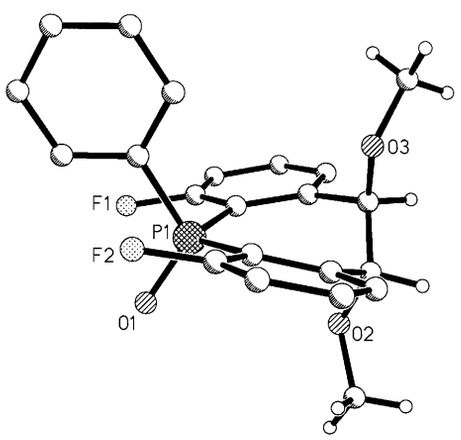


Fig. 9 Side view of **30**.

group is at an angle that virtually bisects the seven-membered ring.

^{1}H NMR of propyl chain and benzylic protons

The two benzylic protons (the backbone protons) of the phosphepine oxides give signals which appear as AB systems and the ^2J coupling constant is 8.4 ± 0.7 Hz. Phosphepine oxide **35** displayed an unusual feature in the 400 MHz ^{1}H spectrum. The usual AB system in the benzylic region was not observed. Instead, although one of the protons displayed the normal doublet, the other appeared as broad singlet. That broad singlet became an only slightly broad doublet at 200 MHz and a ^{1}H NMR spectrum (at 400 MHz) of a sample run in DMSO-d_6

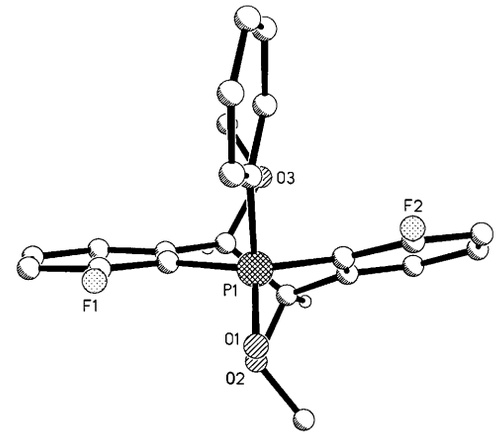


Fig. 10 P-to-backbone view of **30**.

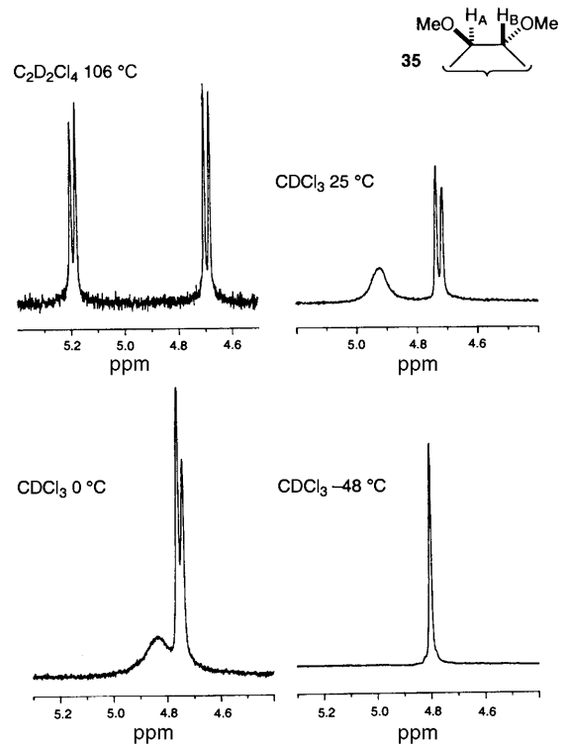


Fig. 11 Temperature dependence of the benzylic signals of **35**.

looked perfectly normal with the usual AB quartet corresponding to the benzylic protons. To investigate the broad signal, we cooled a sample of the phosphepine (Fig. 11). In $CDCl_3$, cooling to just 0 °C, we notice that the two signals begin to coalesce and at −48 °C become a singlet. The sample was cooled even further in a mixture of trichlorofluoromethane (Freon 11®) and CD_2Cl_2 to −100 °C but this had no effect on the singlet. When the sample was warmed up in a solution of 1,1,2,2-tetrachloroethane-d_2, the broad singlet gradually sharpened into a doublet and at the same time the A and B signals separated.

It is not an uncommon situation for the single signal of two—chemically different—protons in fast exchange to separate, as the sample is cooled, into the two component signals so characteristic of slow exchange. Although at first sight it looks as though the opposite is occurring with our compound—with two doublets at elevated temperatures and a singlet at low temperatures—this is, of course, not the case.

The signal at lower temperatures is a singlet because the coupling is not observed—the two diastereotopic protons just happen to have the same chemical shift at that temperature. At no temperature are the two diastereotopic protons interconverting to one another's environments in any way. Obviously, when

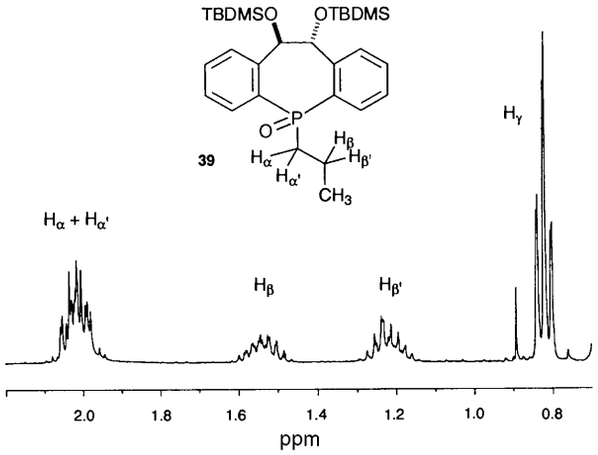


Fig. 12 Typical propyl signals. Signals of **39**.

the signals are doublets they are so simply because they couple to one another.

Suppose that the propyl group is rotating past one of the benzylic protons. It is important to bear in mind that it can rotate past only *one* of the benzylic protons because the other one is on the other side of the ring (Fig. 7). If the propyl group is spinning round very fast, then the benzylic proton will experience a range of environments very quickly—it will be in fast exchange and we will see a sharp signal. If the propyl group is moving very slowly, and it populates one rotamer much more than the others then we would also see a sharp signal. The intensity for the signal or signals corresponding to the other rotamers could be so small as not to be seen.

In between these two states is the state where the movement of the propyl group is close to the NMR timescale. Here we see a broad signal. This hypothesis is consistent with the results at 200 MHz. The signal is sharper at this field. The separation between the frequencies of the two benzylic environments will be smaller in hertz and so it is much easier for the process to be in fast exchange.** In a different solvent, or indeed in a different compound, the propyl group would rotate at a different rate. So long as this rate were not too close to the NMR timescale, we would expect to see a sharp signal.

The propyl chain

With propyl-substituted phosphepines, the two protons on the carbon α to phosphorus are diastereotopic as are those on the β-position carbon. Fig. 12 shows the signals from the propyl chain of **39**. A curious feature of the phosphepine oxides is that the two protons on the β-carbon are always, when there is a split at all, separated by a greater chemical shift difference than those on the α-carbon (Fig. 12). They must experience a greater difference in chemical environment than those on the α-carbon. And indeed, inspection of the X-ray crystal structure of **35** shows that while the α-protons point away from the ring, the β-protons point directly into this chiral environment which must affect the degree to which their diastereotopicity is apparent in the ^{1}H NMR spectrum.

Phosphepine oxide **35** was one of those propylphosphepines which did not illustrate the diastereotopicity of its α- *or* β-protons in the ^{1}H NMR spectrum at room temperature. As the compound was cooled down, so the two two-proton multiplets separated into four one-proton multiplets (Fig. 13). The cooling must enhance the difference between the environments experienced by diastereotopic protons.

** Another way to look at this is to see the 200 MHz machine as having a slower timescale so that, as far as the machine is concerned, the process is happening quickly.

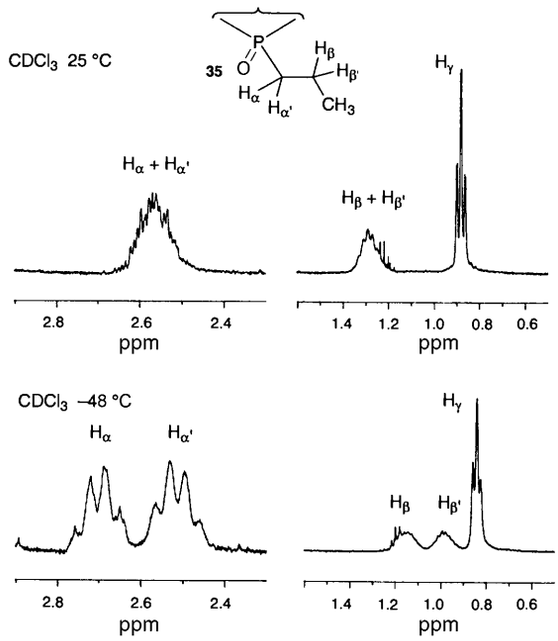
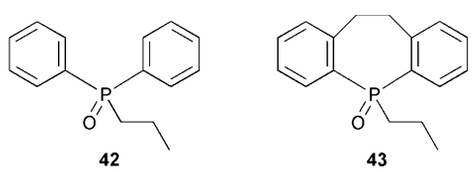


Fig. 13 Temperature dependence of the propyl signals of **35**.

Reactions of phosphepine oxides

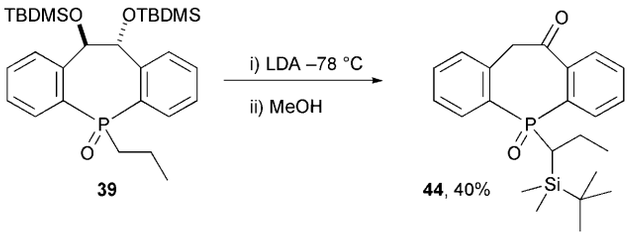
Simple alkyl(diphenyl)phosphine oxides such as **42** may be lithiated and then reacted with a range of electrophiles.[1] A large variety of electrophiles including silyl electrophiles may be employed though, because a Horner–Wittig elimination is often wanted later, the electrophiles are commonly ketones or aldehydes.[23] Achiral phosphepine oxides such as **43** have been shown to undergo reactions similar to these acyclic compounds.[3]



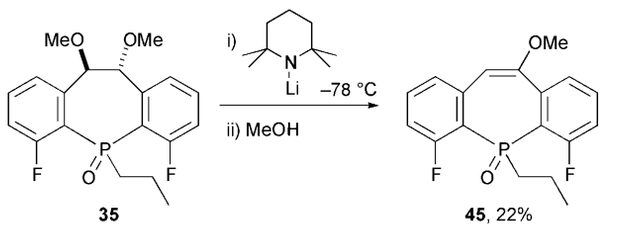
Unfortunately, chiral phosphepine oxides **35**, **39** and **40** are not nearly as robust as their achiral conterparts. Following difficulties we encountered with what should have been a straightforward lithiation followed by an electrophilic quench, we investigated the phosphepine oxides to see if they were stable to the basic conditions we typically use. They were not.

Butyllithium was added to phosphepine oxide **39** at −78 °C. The deep red colour characteristic of lithiated phosphine oxides[24] developed as soon as the base was added. The reaction mixture was warmed to 0 °C and quenched with MeOH. TLC analysis indicated many products. However, when the reaction was repeated using LDA instead of butyllithium and was maintained at −78 °C throughout, TLC indicated that only one new compound had formed (Scheme 13). One of the TBDMS groups had been removed from the molecule altogether and the other had migrated to give ketone **44**. Starting material was also recovered in a 15% yield. This ketone **44** had formed as a single diastereomer and was optically active. A similar result was obtained when phosphine oxide **39** was reacted with LDA for 15 min at −78 °C before cyclohexanone was added. No adduct was detected and ketone **44** was isolated once more.

Silyl groups were perhaps the least secure protecting groups and experiments were performed with the methyl-protected difluorophosphepine oxide **35**. With this compound we used



Scheme 13

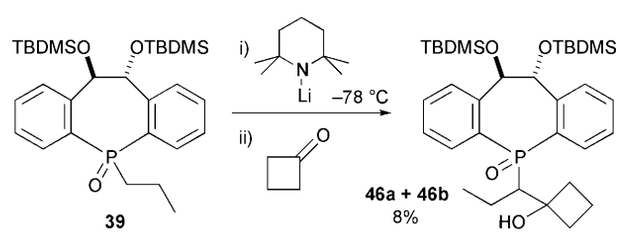


Scheme 14

the more hindered base, LiTMP (Scheme 14). Once again, the red colour developed as soon as the base was added. The reaction was quenched after just 15 minutes and kept at −78 °C throughout. Starting material was recovered in 47% yield together with a material whose NMR spectrum was consistent with the enol ether **45**.

The phenyl analogue, **30**, of propylphosphepine oxide **35** cannot be deprotonated next to phosphorus and **30** was perfectly stable to base—no elimination occurred and the starting material was recovered in 90% yield. Clearly deprotonation of the propyl group is a prerequisite for destabilisation of the phosphepine oxide.††

We used cyclobutanone as an "internal quench"[25] with phosphepine oxide **35** in an attempt to trap the lithiated derivative before it rearranged but only starting material was recovered. Cyclobutanone was used as an external quench with phosphepine oxide **39** but it was allowed only 90 seconds with base before the addition of cyclobutanone (Scheme 15).



Scheme 15

Together with starting material and the rearranged product **44**, two other products were identified in a 37 : 63 ratio and combined yield of 8% which were consistent with the desired adduct diastereomers (**46a** + **46b**).

Even with reactive electrophiles and "internal quench" conditions we were unable to achieve anything like acceptable yields of phosphine oxide adducts. We were forced to conclude that our phosphepine oxides would not be suitable as chiral auxiliaries due to their instability under the basic conditions typically employed.

Formation and reactions of phosphepinium salts

Allen *et al.*[26] studied the hydrolysis of phosphepinium salts in aqueous base (Fig. 14). Upon hydrolysis, the phosphorus–carbon bond that cleaves could be an endo- or exo-cyclic bond.

†† There seems to be no other difference between the two substrates. The nature of the backbone of the two phosphepines would be very similar.

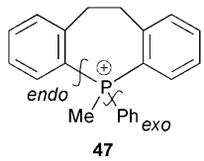
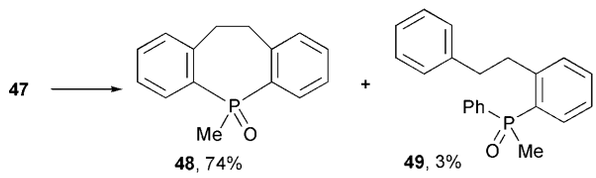


Fig. 14 Endo- *vs.* exo-cyclic cleavage.

They found that an exocyclic phenyl group leaves in preference to an endocyclic aryl group. Phosphepinium salt **47** gave a 74% yield of phosphine oxide **48** (Scheme 16)[26] together with only

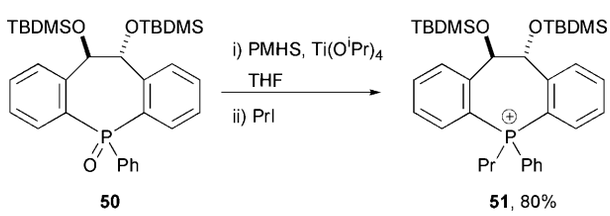


Scheme 16 Phosphepinium salt hydrolysis.[26]

3% of the non-cyclic phosphine oxide **49** resulting from endocyclic cleavage.

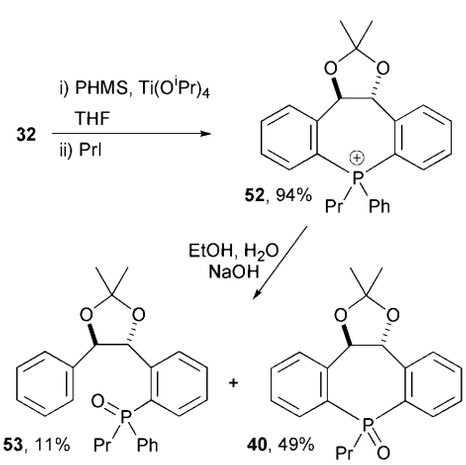
We saw this reaction as a potentially useful way to convert a *P*-phenylphosphepine oxide into its corresponding *P*-alkylphosphepine oxide. This was attractive because the phenyl-substituted phosphepine oxides were available in higher yields than their alkyl analogues *and* because $PhPCl_2$ is commercially available but, in many cases, $AlkylPCl_2$ is not.

Phosphine oxides are readily reduced to phosphines using silanes: trichlorosilane is the most commonly employed.[27] After reduction with trichlorosilane a basic aqueous workup is required to liberate the phosphine but we preferred the alternative reduction method of Lawrence *et al.*[28] which allows for the reduction of the phosphine oxide followed by quaternisation in one pot. By this method, which uses poly(methylhydrosiloxane) (PMHS) and $Ti(^iPrO)_4$, **50** was converted into **51** in an 80% yield (Scheme 17).



Scheme 17 Reduction and *in situ* quaternisation of **50**.

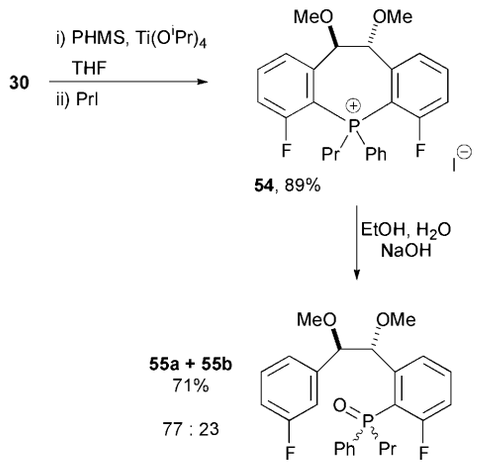
Acetal **32** was thus transformed into its phosphonium salt in a 94% yield (Scheme 18). Hydrolysis gave the propyl-



Scheme 18

substituted phosphepine oxide **40** as the major product in 49% yield from exocyclic cleavage) and 11% of the alternative non-cyclic product **53**.

When the phosphonium salt **54** was hydrolysed (Scheme 19)



Scheme 19

two new products were detected by TLC but these did not correspond to the endocyclic and exocyclic cleavage products. Rather, they *both* resulted from endocyclic cleavage. The two products **55a** and **55b** were isolated in a 71% yield and in a ratio of 23 : 77. There are two possible diastereomeric products because the two aryl rings of phosphepinium **54** are diastereotopic and at 23 : 77 the hydrolysis is modestly diastereoselective.

This endocyclic result was not wholly unexpected as fluorine substituents might enhance the degree of endocyclic cleavage by making the endocyclic aryl rings better leaving groups. Fluorine, the very atom that allowed us to close the ring in the first place—by facilitating *ortho*-lithiation—caused it to open up again in this subsequent reaction.

In conclusion, the combination of either an *ortho*-lithiation or halogen–lithium exchange strategy to give an enantiomerically pure doubly lithiated species that is reacted with a doubly electrophilic phosphorus has allowed the construction of ten new and unusual phosphepine oxides. Though the phosphepine oxides were not in the event useful in asymmetric synthesis the strategy used for their synthesis is potentially applicable to other hetero- and carbocyclic compounds.

Experimental

Flash chromatography[29] was performed using Merck 9385 Kieselgel 60. Thin layer chromatography (TLC) was performed using commercially available glass plates coated with Merck silica Kieselgel 60F_{254}. High performance liquid chromatography (HPLC) was performed using a Dynamax prepacked silica column (25 cm × 21.4 mm internal diameter) using a Gilson model 303 pump and a Cecil Instruments CE212A UV detector at 254 nm. All solvents were distilled before use. Anhydrous solvents were distilled from $LiAlH_4$ in the case of Et_2O and THF, from CaH_2 in the case of CH_2Cl_2, MeOH, hexane and toluene, and from $CaCl_2$ in the case of CCl_4. Triphenylmethane was used as indicator for THF.

Melting points were determined on a Reichert hot stage microscope and are uncorrected. Infra red spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrometer. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter (using the sodium D line; 589 nm) and $[a]_D$ given in units of 10^{-1} deg cm^2 g^{-1}.

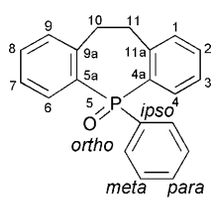
All NMR instuments used were made by Bruker. Proton, carbon, phosphorus and fluorine NMR spectra were recorded using the AC 250, WM 250 or AM 400 Fourier transform spectrometers, using an internal deuterium lock. Carbon spectra were determined with broad band decoupling and an attached proton test (APT). Signals from carbon atoms with an odd number of attached protons are designated ($^+$) while those with an even number are designated ($^-$).

All mass spectra were determined by electron impact (EI) unless otherwise stated. Other methods used were chemical ionisation (CI) and fast atom bombardment (FAB). All three methods were performed on a Kratos MS890 spectrometer by technical staff. Microanalyses were performed by technical staff using either the Carlo Erba 1106 or Perkin-Elmer 240 automatic analysers.

When using *n*-butyllithium, and especially when using *sec*-butyl or *tert*-butyllithium, best results were obtained using Hamilton 1700 series gas-tight Teflon tipped microsyringes (<1000 μl) which did not require lubrication, and Hamilton 1000 series gas-tight Teflon tipped syringes (>1 ml) lubricated with poly(dimethylsiloxane) 200® fluid with a viscosity of 100 centistokes.

Key to NMR assignments

Aromatic protons are referred to by their ring position followed by "-ArH". The "C" in "ArC" is the numbered carbon within that ring and not a carbon attached to the ring. Carbons outside the ring are italicised when "Ar" is included in the assignment *e.g.* 129.0$^+$ ($^4J_{CF}$ 2.3, Ar*C*H). When a carbon nucleus is observed to couple to only one other nucleus then it is not referred to as a doublet. Any greater multiplicity, such as a double doublet, is noted.



Protons and carbons that form part of a phosphepine system are numbered according to the numbering system indicated above. The exocyclic portion is assigned using the labels *ipso*, *ortho*, *meta* and *para*. When two *ortho* positions are non-equivalent, *ortho′* is also used and their positions illustrated. When coupling constants refer to the coupling between two protons, or between two unassigned nuclei, then no subscripts follow "*J*".

Stilbenes

(*E*)-3,3′-Difluorostilbene 3. Titanium(III) chloride (97 g, 0.628 mol, 4 eq.) was added to a dry 2 litre three neck flask under an argon atmosphere. Anhydrous 1,2-dimethoxyethane (900 ml) was added *via* cannula followed by lithium wire (13.1 g, 1.87 mol, 12 eq.) prepared according to the method of Fleming and McMurry.[30] The mixture was stirred with a mechanical stirrer and refluxed for 1.5 h and then allowed to cool until refluxing had just stopped. Then 3-fluorobenzaldehyde (19.4 g, 0.156 mol) was added and the mixture refluxed for 18 h before being allowed to cool for 24 h. The reaction mixture was diluted with light petroleum (bp 40–60 °C) (700 ml) and filtered through a pad of Florisil. The remaining slurry was extracted with light petroleum (bp 40–60 °C) (2 × 150 ml). 1,2-Dimethoxyethane (500 ml) was added to the remaining slurry, refluxed for 1 h, cooled, diluted with light petroleum (bp 40–60 °C) (400 ml) and the extraction repeated.‡‡ The organic extracts were combined and evaporated under reduced pressure. The solid residue was

‡‡ This second extraction was in addition to that suggested in the procedure by Fleming and McMurray, but extracted a further 0.9 g of crude material from the reaction slurry.

dissolved in dichloromethane and passed through silica to remove insoluble resinous material. The solid was recrystallised from light petroleum (bp 40–60 °C) and then from ethanol to give the (*E*)-stilbene **3** (14.7 g). The mother liquors were purified by flash chromatography, eluting with light petroleum (bp 40–60 °C), to give the (*Z*)-stilbene (13.4 mg, 0.084%) and additional (*E*)-stilbene **3** (1.32 g). Total (*E*)-stilbene **3** (16.0 g, 94.8%) was isolated as hexagonal plates, mp 86–87 °C [from light petroleum (bp 40–60 °C)]; R_f^E(hexane) 0.26; ν_{max} ($CDCl_3$)/cm^{-1} 1611 (Ar), 1586 (Ar) and 1487 (Ar); δ_H(400 MHz; $CDCl_3$) 7.32 (2 H, td, *J* 7.8 and $^4J_{HF}$ 5.9, 5-ArH), 7.26 (2 H, dt, *J* 7.8 and 1.2, 6-ArH), 7.21 (2 H, ddd, $^3J_{HF}$ 10.2, *J* 2.4 and 1.2, 2-ArH), 7.05 (2 H, s, ArC*H*) and 6.98 (2 H, tdd, $^3J_{HF}$ 7.8, $^3J_{HH}$ 7.8, *J* 2.4 and 1.2, 4-ArH); δ_C(100.6 MHz; $CDCl_3$) (lit.,[31] ^{13}C data virtually identical) 163.4$^-$ ($^1J_{CF}$ 245.4, 3-ArC), 139.4$^-$ ($^3J_{CF}$ 7.5, 1-ArC), 130.4$^+$ ($^3J_{CF}$ 8.3, 5-ArC), 129.0$^+$ ($^4J_{CF}$ 2.3, Ar*C*H), 122.8$^+$ ($^4J_{CF}$ 2.4, 6-ArC), 115.0$^+$ ($^2J_{CF}$ 21.4, 2-ArC) and 113.1$^+$ ($^2J_{CF}$ 21.8, 4-ArC). The (*Z*)-stilbene was isolated as an oil, R_f^Z(hexane) 0.33; δ_C(100.6 MHz; $CDCl_3$) 162.8$^-$ ($^1J_{CF}$ 245.6, 3-ArC), 139.0$^-$ ($^3J_{CF}$ 7.6, 1-ArC), 130.2$^+$ (Ar*C*H), 130.0$^+$ ($^3J_{CF}$ 8.3, 5-ArC), 124.7$^+$ (6-ArC), 115.6$^+$ ($^2J_{CF}$ 21.6, 2-ArC) and 114.4$^+$ ($^2J_{CF}$ 21.1, 4-ArC).

(*E*)-2,2′-Dibromostilbene 4. 2-Bromobenzaldehyde (11.7 g, 63.2 mmol) was reacted in a method similar to that used in the synthesis of the stilbene **3**. The reaction mixture was refluxed for 6 h. The product was recrystallised from light petroleum (bp 40–60 °C) and then from ethanol to give the stilbene (7.58 g, 71%) as rectangular plates, mp 112–114 °C (from EtOH) (lit.,[32] 108.0–108.5 °C); R_f(hexane) 0.32; δ_H(250 MHz; $CDCl_3$) 7.72 (2 H, dd, *J* 7.8 and 1.6, 3-ArH), 7.59 (2 H, dd, *J* 8.0 and 1.2, 6-ArH), 7.40 (2 H, s, ArC*H*), 7.34 (2 H, td, *J* 7.6 and 1.2, 4-ArH) and 7.15 (2 H, td, *J* 7.7 and 1.6, 5-ArH); δ_C(62.9 MHz; $CDCl_3$) 136.8$^-$ (1-ArC), 133.1$^+$, 130.1$^+$, 129.3$^+$, 127.7$^+$, 127.2$^+$ and 124.3$^-$ (2-ArC). In another experiment, in which the reaction mixture was refluxed for 18 h, the isolated yield was 44%.

(*E*)-3,3′-Dimethoxystilbene 6. 3-Methoxybenzaldehyde (5.54 g, 40.7 mmol) was reacted in a method similar to that used in the synthesis of the stilbene **3** to give the stilbene (3.97 g, recryst. 81%) as rectangular prisms, mp 100–101 °C [from light petroleum bp (40–60 °C)–CH_2Cl_2] (lit.,[33] 99–100 °C, from EtOH); R_f(ether–hexane, 1:4) 0.36; δ_H(400 MHz; $CDCl_3$) 7.29 (2 H, t, *J* 7.9, 5-ArH), 7.13 (2 H, br d, *J* 7.7, 6-ArH), 7.09 (2 H, s, ArC*H*), 7.06 (2 H, br s, 2-ArH), 6.84 (2 H, dd, *J* 8.2 and 2.4, 4-ArH) and 3.86 (6 H, s, OMe); δ_C(62.9 MHz; $CDCl_3$) 160.0$^-$ (3-ArC), 138.8$^-$ (1-ArC), 129.8$^+$, 129.0$^+$, 119.4$^+$, 113.5$^+$, 111.9$^+$ and 55.4$^+$ (Me).

(*E*)-3,4:3′,4′-Bis(methylenedioxy)stilbene 5. Piperonal (5.40 g, 36.0 mmol) was reacted in a method similar to that used in the synthesis of the stilbene **3**. After the reaction mixture had cooled, light petroleum (bp 40–60 °C) (100 ml) was added before filtering.§§ The residue was further extracted with dichloromethane (4 × 250 ml). Silica (100 g) was added to the combined extracts which were then concentrated by evaporation under reduced pressure. The resulting solid was eluted with dichloromethane and the resulting material was washed with refluxing dichloromethane (15 ml) to give the stilbene (3.52 g, 73%) as prisms, mp 214–215 °C (from CH_2Cl_2) (lit.,[34] 206 °C from AcOH); R_f(ether–hexane, 1:4) 0.35; δ_H(250 MHz; $CDCl_3$) 7.02 (2 H, d, *J* 1.6, 2-ArH), 6.90 (2 H, dd, *J* 8.0 and 1.6, 6-ArH), 6.84 (2 H, s, ArC*H*), 6.78 (2 H, d, *J* 8.0, 5-ArH) and 5.96 (4 H, s, OCH_2O); δ_C(100.6 MHz; $CDCl_3$) 148.1$^-$ (3 or 4-ArC), 147.1$^-$ (3 or 4-ArC), 132.0$^-$ (1-ArC), 126.7$^+$, 121.2$^+$, 108.4$^+$, 105.4$^+$ and 101.1$^-$ (CH_2).

(*E*)-2,2′-Dichlorostilbene 7. 1,2-Bis(2-chlorophenyl)-1-chloroethane[14] (4.45 g, 15.6 mmol) was thermally dehydrochlorinated by heating to reflux in the absence of solvent, according to the method of Hoeg and Lusk.[14] HCl fumes were evolved. The resulting brown solid was purified by flash chromatography, eluting with hexane, and recrystallised from hexane to yield the stilbene (3.07 g, 79%) as needles, mp 98–99 °C (from hexane) (lit.,[14] 98.5–99 °C); R_f(Et_2O–hexane, 1:4) 0.57; ν_{max} ($CDCl_3$)/cm^{-1} 3070 (C=C–H), 1592 (Ar) and 1566 (Ar); δ_H(250 MHz; $CDCl_3$) 7.74 (2 H, dd, *J* 7.8 and 1.7, 3-ArH), 7.48 (2 H, s, ArC*H*), 7.39 (2 H, dd, *J* 7.8 and 1.3, 6-ArH), 7.29 (2 H, td, *J* 7.8 and 1.3, 4-ArH) and 7.22 (2 H, td, *J* 7.8 and 1.6, 5-ArH); δ_C($CDCl_3$) 135.1$^-$, 133.5$^-$, 129.7$^+$, 128.8$^+$, 127.2$^+$, 126.9$^+$ and 126.8$^+$ (Found: M^+, 248.0151. $C_{14}H_{10}Cl_2$ requires *M*, 248.0160) (Found: C, 67.4; H, 4.00; Cl, 28.3. $C_{14}H_{10}Cl_2$ requires C, 67.5; H, 4.05; Cl, 28.5%).

Diols

(1*RS*,2*RS*)-1,2-Bis(3,4-methylenedioxyphenyl)ethane-1,2-diol 12. Potassium ferricyanide (1.98 g, 6.01 mmol, 3 eq.), potassium carbonate (0.84 g, 6.08 mmol), osmium(III) chloride hydrate (8.5 mg, 0.027 mmol, 0.0135 eq.), quinuclidine (62.0 mg, 0.558 mmol) and methanesulfonamide (190 mg, 2.00 mmol) were added to water (12 ml) and 2-methylpropan-2-ol (12 ml). The mixture was warmed slightly and stirred until all the solids had dissolved and then allowed to cool to room temperature. 3,4:3′,4′-Bis(methylenedioxy)stilbene **5** (553 mg, 2.06 mmol, 1.03 eq.) was added to the solution, the flask lightly stoppered with a glass stopper, and the mixture stirred vigorously for over 42 h. Anhydrous sodium sulfite (3.0 g, 23.8 mmol) was then added and stirring continued for 1 h before the addition of dichloromethane (20 ml). The layers were separated and the aqueous phase was further extracted with dichloromethane (3 × 10 ml). The combined organic extracts were washed with 2 M KOH (5 ml) and dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography, eluting with Et_2O–hexane, 3:7) to give the racemic diol (221 mg, 36%), mp 143–144 °C (from Et_2O–hexane) (lit.,[35] 132 °C, from benzene); R_f(Et_2O–hexane, 2:1) 0.17; ν_{max} (KBr)/cm^{-1} 3469 (OH), 3315 (OH) and 1503 (Ar); δ_H(400 MHz; $CDCl_3$) 6.71 (2 H, d, *J* 1.6, 2-ArH), 6.65 (2 H, d, *J* 8.0, 5-ArH), 6.53 (2 H, dd, *J* 8.0 and 1.6, 6-ArH), 5.93 (2 H, d, *J* 1.4, OCH_AH_BO), 5.92 (2 H, d, *J* 1.4, OCH_AH_BO), 4.56 (2 H, s, ArC*H*) and 2.79 (2 H, s, OH); δ_C(100.6 MHz; $CDCl_3$) 147.7$^-$ (3 or 4-ArC), 147.4$^-$ (3 or 4-ArC), 134.0$^-$ (1-ArC), 120.8$^+$ (6-ArC), 108.1$^+$ (5 or 2-ArC), 107.4$^+$ (5 or 2-ArC), 101.2$^-$ (OCO) and 79.1$^+$ (Ar*C*OH); *m*/*z* 303 (57%, MH^+), 285 (61, MH − H_2O), 151 (60, ArCHOH) and 133 (100, ArCHOH − H_2O) (Found: MH^+, 303.08810. $C_{16}H_{14}O_6$ requires *M* + H, 303.08687).

(1*R*,2*R*)-1,2-Bis(3,4-methylenedioxyphenyl)ethane-1,2-diol 12. Methanesulfonamide (447 mg, 4.70 mmol) and AD-mix-β (6.36 g, 4.54 mmol olefin capacity) were added to water (22 ml) and 2-methylpropan-2-ol (22 ml). The mixture was warmed slightly and stirred until all the solids had dissolved and then cooled to 2 °C. 3,4:3′,4′-Bis(methylenedioxy)stilbene **5** (1.20 g, 4.48 mmol) was added to the solution and the mixture stirred vigorously for 96 h. The temperature was not allowed to exceed 7 °C. The cold bath was removed and anhydrous sodium sulfite (7.1 g, 56.3 mmol) was added and stirring continued for 1 h before the addition of dichloromethane (40 ml). The layers were separated and the aqueous phase was further extracted with dichloromethane (3 × 20 ml). The combined organic extracts were washed with 2 M KOH (10 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by

§§ The insolubility of the product required that only 100 ml of light petroleum (bp 40–60 °C) were added to the 1,2-dimethoxyethane and that further extractions with dichloromethane were necessary. Dichloromethane extracts undesired materials form the reaction residue. This, coupled with the low solubility of the product, made purification difficult. Other methods are available.[13]

flash chromatography, eluting with Et_2O–hexane, 3:7 to give the *enantiomerically pure diol* (1.14g, 84%). Characterisation data were identical to the racemic compound except: mp 163–164 °C (from CH_2Cl_2–MeOH); $[a]_D^{24}$ +167 (*c* 0.635 in MeOH). The 400 MHz ^{1}H NMR spectrum of the unrecrystallised diol, in comparison with a racemic sample, in the presence of Pirkle's chiral shift reagent, indicated an enantiomeric excess of ≥99%.

(1*RS*,2*RS*)-1,2-Bis(2-bromophenyl)ethane-1,2-diol 9. 2,2′-Dibromostilbene **4** (2.00 g, 5.90 mmol) was reacted in a method similar to that used in the synthesis of the diol **12**. The crude product was purified by flash chromatography, eluting with Et_2O–hexane, to give the racemic diol (1.98 g, 90%) as rectangular prisms, mp 123–124 °C (from hexane–dichloromethane) (lit.,[32] 118.5–119.0 °C); R_f(Et_2O–hexane, 1:1) 0.23; ν_{max} (KBr)/cm^{-1} 3600–2500 (OH), 1592 (Ar) and 1568 (Ar); δ_H(400 MHz; $CDCl_3$) 7.69 (2 H, dd, *J* 1.6 and 7.8, 3-ArH), 7.45 (2 H, dd, *J* 8.1 and 1.1, 6-ArH), 7.35 (2 H, td, *J* 7.6 and 1.1, 4-ArH), 7.14 (2 H, td, *J* 7.9 and 1.7, 5-ArH), 5.31 (2 H, dd, *J* 2.5 and 1.1, ArC*H*) and 2.77 (2 H, dd, *J* 2.6 and 1.3, OH); δ_C(62.9 MHz; $CDCl_3$) 138.7$^-$ (1-ArC), 132.8$^+$ (3-ArC), 129.7$^+$, 129.6$^+$, 127.5$^+$ (5-ArC), 123.0$^-$ (2-ArC) and 75.2$^+$ (Ar*C*OH).

(1*R*,2*R*)-1,2-Bis(2-bromophenyl)ethane-1,2-diol 9. Methanesulfonamide (3.39 g, 0.0419 mol) and AD-mix-β (50.2 g) were added to a three neck 1 litre flask containing water (180 ml) and 2-methylpropan-2-ol (180 ml). The mixture was stirred with a mechanical stirrer until all the solids had dissolved. The flask was then cooled to 0 °C and dibromostilbene **4** (12.0 g, 32.3 mmol) added. The reaction mixture was stirred vigorously for 72 h and maintained between 0 and 3 °C. Then anhydrous sodium sulfite (54.0 g, 0.439 mol) was added and the mixture stirred overnight. Dichloromethane (350 ml) was added and the phases separated. The aqueous layer was further extracted with dichloromethane (3 × 175 ml) and the combined organic layers were washed with 2 M KOH (30 ml), dried ($MgSO_4$) and volatile materials evaporated under reduced pressure. The residue was purified by flash chromatography, eluting with Et_2O–hexane, and then recrystallised (hexane–dichloromethane, 1.1:1, 92 ml) to give the diol (12.5 g, 94%) as needles. Characterisation data were identical to the racemic compound except: mp 110–110.5 (from hexane–dichloromethane) (lit.,[32] 105.5–106.0 °C); $[a]_D^{25}$ −38.3 (*c* 1.28 in EtOH) {lit.,[32] $[a]_D^{23}$ +39.9 (*c* 1.0 in EtOH) for (*S*,*S*) enantiomer}. The 400 MHz ^{1}H NMR spectrum of the dimethyl ether of the unrecrystallised diol, in comparison with a racemic sample, in the presence of Pirkle's chiral shift reagent, indicated an enantiomeric excess of ≥99%.

(1*RS*,2*RS*)-1,2-Bis(3-methoxyphenyl)ethane-1,2-diol 10. 3,3′-Dimethoxystilbene **6** (488 mg, 1.78 mmol, 1.02 eq.) was reacted in a method similar to that used in the synthesis of the diol **12**. The crude product was purified by flash chromatography, eluting with 4:1 Et_2O–hexane, to give the *racemic diol* (468 mg, 85%) as prisms, mp 52–54 °C (from Et_2O–hexane); R_f(Et_2O–hexane, 4:1) 0.23; ν_{max} ($CHCl_3$)/cm^{-1} 3564 (OH), 3452 (OH), 1598 (Ar) and 1493 (Ar); δ_H(400 MHz; $CDCl_3$) 7.13 (2 H, t, *J* 8.1, 4-ArH), 6.76 (2 H, dd, *J* 8.1 and 2.5, 3 or 5-ArH), 6.70–6.68 (4 H, m), 4.63 (2 H, s, ArC*H*), 3.69 (6 H, s, OMe) and 3.01 (2 H, s, OH); δ_C(100.6 MHz; $CDCl_3$) 159.6$^-$ (3-ArC), 141.7$^-$ (1-ArC), 129.3$^+$ (5-ArC), 119.4$^+$ (6-ArC), 113.9$^+$ (2-ArC), 112.4$^+$ (4-ArC), 79.0$^+$ (Ar*C*H) and 55.4$^+$ (OMe); *m*/*z* 274 (0.4%, M$^+$), 256 (0.5, M − H_2O) and 138 (100, ArCH_2OH) (Found: M$^+$, 274.1200. $C_{16}H_{18}O_4$ requires *M,* 274.1205).

(1*R*,2*R*)-1,2-Bis(3-methoxyphenyl)ethane-1,2-diol 10. 3,3′-Dimethoxystilbene **6** (1.15 g, 4.79 mmol) was reacted in a method similar to that used in the synthesis of diol **12** to yield the *enantiomerically pure diol* (1.26 g, 96%) as needles. Characterisation data were identical to the racemic compound except: mp 74–75 °C (from EtOAc–hexane); $[a]_D^{24}$ +97.9 (*c* 1.05 in CH_2Cl_2). The 400 MHz ^{1}H NMR spectrum of the unrecrystallised diol, in comparison with a racemic sample, in the presence of Pirkle's chiral shift reagent, indicated an enantiomeric excess of ≥99%.

(1*RS*,2*RS*)-1,2-Bis(2-chlorophenyl)ethane-1,2-diol 11. 2,2′-Dichlorostilbene **7** (513 mg, 2.06 mmol, 1.03 eq.) was reacted in a method similar to that used in the synthesis of diol **12**. The crude product was purified by flash chromatography, eluting with Et_2O–hexane, to give the racemic diol (367 mg, 64.6%), as needles, mp 107–108 °C (from Et_2O–hexane) (lit.,[36] 105–106 °C from Et_2O–pentane); R_f(Et_2O) 0.62; ν_{max} (Nujol)/cm^{-1} 3426 (OH), 3299 (OH) and 1573 (Ar); δ_H(250 MHz; $CDCl_3$) 7.68 (2 H, dd, *J* 1.4 and 6.8, 2-ArH), 7.36–7.32 (6 H, m), 5.35 (2 H, s, ArC*H*) and 3.14 (2 H, s, OH); δ_C(62.9 MHz; $CDCl_3$) 137.1$^-$ (1-ArC), 132.5$^-$ (2-ArC), 129.4$^+$, 129.0$^+$, 128.99$^+$, 126.7$^+$ and 72.9$^+$ (Ar*C*OH). In another similar experiment, performed in the absence of methanesulfonamide, the yield, after a reaction time of 43 h, was 46%. Starting material (41%) was also recovered.

(1*RS*,2*RS*)-1,2-Bis(3-fluorophenyl)ethane-1,2-diol 8. Potassium ferricyanide (18.1 g, 55.1 mmol), potassium carbonate (7.59 g, 55 mmol), osmium(III) chloride hydrate (40.8 mg, 0.130 mmol), quinuclidine (72.0 mg, 0.648 mmol) and methanesulfonamide (1.76 g, 18.5 mmol) were added to water (95 ml) and 2-methylpropan-2-ol (95 ml). The mixture was stirred vigorously with a mechanical stirrer until all solids had dissolved. 3,3′-Difluorostilbene **3** (4.02 g, 18.6 mmol) was added and the suspension stirred vigorously for 96 h at room temperature. Anhydrous sodium sulfite (28 g, 0.22 mol) was then added and stirring was continued for 1 h before the addition of dichloromethane (175 ml). The layers were separated and the aqueous phase was further extracted with dichloromethane (3 × 100 ml). The combined organic extracts were washed with 2 M KOH (15 ml), dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography, eluting with Et_2O–hexane, and then recrystallised (CH_2Cl_2–hexane, 57:43) to give the diol (3.74 g, 81.5%) as needles, mp 128–130.5 °C (from CH_2Cl_2–hexane) (lit.,[37] 118–119 °C, from petrol–toluene); R_f(Et_2O–hexane, 2:1) 0.17; ν_{max} (KBr)/cm^{-1} 3471 (OH), 3275 (OH) and 1594 (Ar); δ_H(400 MHz; $CDCl_3$) 7.19 (2 H, td, *J* 7.9 and $^4J_{HF}$ 6.0, 5-ArH), 6.96–6.89 (4 H, m, 4 and 6-ArH), 6.83 (2 H, d, $^3J_{HF}$ 7.7, 2-ArH), 4.67 (2 H, s, ArC*H*) and 2.84 (2 H, s, OH); δ_C(100.6 MHz; $CDCl_3$) 162.6$^-$ ($^1J_{CF}$ 246.2, 3-ArC), 142.1$^-$ ($^3J_{CF}$ 78.4, 1-ArC), 129.7$^+$ ($^3J_{CF}$ 8.1, 5-ArC), 122.6$^+$ ($^4J_{CF}$ 2.3, 6-ArC), 115.0$^+$ ($^2J_{CF}$ 21.1, 4-ArC), 113.8$^+$ ($^2J_{CF}$ 22.0, 2-ArC) and 78.4$^+$ (Ar*C*OH); *m*/*z* 250 (0.1%, M$^+$) and 125 (95, ArCHOH) (Found: M$^+$, 250.0808. $C_{14}H_{12}F_2O_2$ requires *M*, 250.0805).

(1*R*,2*R*)-1,2-Bis(3-fluorophenyl)ethane-1,2-diol 8. 3,3′-Difluorostilbene **3** (7.91 g, 36.6 mmol) was reacted in a method similar to that used in the synthesis of enantiomerically pure diol **9**. The crude product was purified by flash chromatography, eluting with 1:1 Et_2O–hexane, and then recrystallised (CH_2Cl_2–hexane, 1:2) to give the *enantiomerically pure diol* (8.14 g, 88.9%) as fine needles. Characterisation data were identical to the racemic compound except: mp 79–80 °C (from CH_2Cl_2–hexane, 1:2); $[a]_D^{21.5}$ +112 (*c* 0.99 in $CHCl_3$). The 400 MHz ^{1}H NMR spectrum of the unrecrystallised diol {$[a]_D^{21.5}$ +98.8 (*c* 1.01 in $CHCl_3$)}, in comparison with a racemic sample, in the presence of Pirkle's chiral shift reagent, indicated an enantiomeric excess of ≥99%.

Protected diols

(1*R*,2*R*)-1,2-Bis(3-fluorophenyl)-1,2-dimethoxyethane 16. (1*R*,2*R*)-1,2-Bis(3-fluorophenyl)ethane-1,2-diol **8** (4.31 g, 17.2 mmol) was dissolved in dry THF (20 ml) and added *via* cannula to a stirred suspension of sodium hydride 60% w/w (2.36 g, 59.0

mmol) in dry THF (200 ml) at 2 °C under argon. Residual diol was added with more THF (20 ml). The reaction mixture was stirred and allowed to reach room temperature. It was stirred for 1 h, cooled to 2 °C, and methyl iodide (2.3 ml, 36.9 mmol) was added dropwise. The mixture was allowed to reach room temperature and stirred overnight before sodium hydroxide solution (45 ml, 2.9 M) was added. The mixture was vigorously stirred for 3 h. The layers were separated and the aqueous layer extracted with Et_2O (3 × 100 ml). The combined organic extracts were evaporated and water removed as an azeotrope with toluene (2 × 200 ml). The residue was purified by flash chromatography, eluting with 1:1 Et_2O–hexane, to give the *diether* (4.71 g, 98.3%), mp 88–88.5 °C (from Et_2O–hexane); R_f(Et_2O–hexane, 1:1) 0.50; ν_{max} ($CHCl_3$)/cm^{-1} 2828 (OC–H), 1614 (Ar) and 1592 (Ar); δ_H(400 MHz; $CDCl_3$) 7.12 (2 H, td, *J* 8.0 and $^4J_{HF}$ 5.9, 5-ArH), 6.88 (2 H, tdd, $^3J_{HF}$ 8.6, $^3J_{HH}$ 8.6, *J* 2.5 and 0.8, 4-ArH), 6.79–6.73 (4 H, m, 2 and 6-ArH), 4.27 (2 H, s, ArC*H*) and 3.27 (6 H, s, OMe); δ_C(100.6 MHz; $CDCl_3$) 163.0$^-$ ($^1J_{HF}$ 204.6, 3-ArC), 140.9$^-$ (1-ArC), 129.6$^+$ ($^3J_{HF}$ 7.8, 5-ArC), 123.7$^+$ (6-ArC), 114.9$^+$ ($^2J_{HF}$ 21.2), 114.6$^+$ ($^2J_{HF}$ 21.9), 86.9$^+$ (Ar*C*H) and 57.5$^+$ (Me); δ_F(235.4 MHz; $CDCl_3$; ^{1}H decoupled) −113.9; *m*/*z* 247 (4.5%, M − OMe) and 139 (100, ArCHOMe) (Found: C, 69.11; H, 5.81. $C_{16}H_{16}F_2O_2$ requires C, 69.05; H, 5.80); [*a*]$_D^{24}$ −50.8 (*c* 0.985 in CH_2Cl_2).

(1*RS*,2*RS*)-1,2-Bis(3-fluorophenyl)-1,2-dimethoxyethane 16. Dry (1*RS*,2*RS*)-1,2-bis(3-fluorophenyl)ethane-1,2-diol **8** (0.982 g, 3.93 mmol) was dissolved in dry THF (20 ml). The diol solution was added to sodium hydride (550 mg of 60% w/w, 13.8 mmol) contained in a flask at 0 °C *via* cannula with continuous stirring. The suspension was allowed to reach room temperature and stirred for 1 h. It was then cooled to 0 °C and methyl iodide (0.504 ml, 8.06 mmol) was added dropwise. The suspension was allowed to reach room temperature overnight. NaOH (20 ml of 3.5 M) was added and the mixture was stirred vigorously for 24 h. The layers were separated and the aqueous layer extracted with Et_2O (3 × 80 ml). The extracts were evaporated under reduced pressure and any water removed as an azeotrope with toluene (80 ml). The residue was purified by flash chromatography, eluting with Et_2O–hexane, to give the *diether* (0.833 g, 76%) after recrystallisation (3 × hexane) as rectangular prisms. Characterisation data were exactly the same as the enantiomerically pure compound except: mp 80–81 °C (from hexane).

(1*RS*,2*RS*)-1,2-Bis(2-bromophenyl)-1,2-dimethoxyethane 17. Dry (1*RS*,2*RS*)-1,2-bis(2-bromophenyl)ethane-1,2-diol **9** (571 mg, 1.53 mmol) was dissolved in dry THF (7.5 ml). The diol solution was added to sodium hydride¶¶ (214 mg of 60% w/w, 5.36 mmol) contained in a flask at 0 °C *via* cannula with continuous stirring. The suspension was allowed to reach room temperature and stirred for 1 h. It was then cooled to 0 °C and methyl iodide (0.38 ml, 6.12 mmol) was added dropwise. The suspension was allowed to reach room temperature overnight. NaOH (7.5 ml of 3.5 M) was added and the mixture was stirred vigorously for 24 h. The layers were separated and the aqueous layer extracted with Et_2O (3 × 30 ml). The extracts were evaporated under reduced pressure and any water removed as an azeotrope with toluene (30 ml). The residue was purified by flash chromatography, eluting with Et_2O–hexane, to give the diether (603 mg, 98%), mp 115.5–116 °C (from hexane); R_f(Et_2O–hexane, 1:4) 0.31; ν_{max} (KBr)/cm^{-1} 2821 (OC–H), 1589 (Ar) and 1566 (Ar); δ_H(400 MHz; $CDCl_3$) (lit.||||) 7.65 (2 H, dd, *J* 7.8 and 1.6, 3-ArH), 7.40 (2 H, dd, *J* 8.0 and 0.8, 6-ArH), 7.31 (2 H, td, *J* 7.6 and 0.8, 4-ArH), 7.09 (2 H, td, *J* 7.7 and 1.6, 5-ArH), 4.94 (2 H, s, ArC*H*) and 3.18 (6 H, s, OMe); δ_C(62.9 MHz; $CDCl_3$) 137.2$^-$ (1-ArC), 132.3$^+$, 130.5$^+$, 129.3$^+$, 127.2$^+$, 124.1$^-$ (2-ArC), 83.8$^+$ (Ar*C*HOMe) and 57.3$^+$ (OMe); *m*/*z* 399 (M$^+$ − 1, 9%), 367 (M − OMe, 80), 201 (ArCHOMe, 100) and 199 (ArCHOMe, 100) (Found: M$^+$ − 1, 398.94090. $C_{16}H_{16}Br_2O_2$ requires *M* − 1, 398.94190).

(1*R*,2*R*)-1,2-Bis(2-bromophenyl)-1,2-dimethoxyethane 17. (1*R*,2*R*)-1,2-Bis(2-bromophenyl)ethane-1,2-diol **9** (4.43 g, 11.9 mmol) was reacted in a method similar to that used in the synthesis of the diether **16** to yield the *enantiomerically pure diether* (4.31 g, 91%) as rectangular prisms. Characterisation data identical to the racemic compound except: mp 89–91 °C (from hexane); [*a*]$_D^{23.5}$ −109 (*c* 1.17 in CH_2Cl_2).

(1*R*,2*R*)-1,2-Bis(3-methoxyphenyl)-1,2-dimethoxyethane 18. (1*R*,2*R*)-1,2-Bis(3-methoxyphenyl)ethane-1,2-diol **10** (370 mg, 1.35 mmol) was reacted in a method similar to that used in the synthesis of diether **2** to give the *enantiomerically pure diether* (390 mg, 96%) as an oil, R_f(Et_2O–hexane, 2:1) 0.39; ν_{max} ($CHCl_3$)/cm^{-1} 2828 (OC–H), 1601 (Ar) and 1489 (Ar); δ_H(250 MHz; $CDCl_3$) 7.08 (2 H, t, *J* 7.8, 5-ArH), 6.71 (2 H, ddd, *J* 8.2, 2.7 and 0.9, 4 or 6-ArH), 6.61 (2 H, br d, *J* 7.5, 4 or 6-ArH), 6.57 (2 H, unresolved dd, 2-ArH), 4.25 (2 H, s, ArC*H*), 3.67 (6 H, s, ArOCH_3) and 3.27 (6 H, s, CHOCH_3) (lit.***); δ_C(100.6 MHz; $CDCl_3$) 159.5$^-$ (3-ArC), 140.1$^-$ (1-ArC), 129.0$^+$ (5-ArC), 120.5$^+$ (6-ArC), 113.8$^+$, 113.0$^+$, 87.7$^+$ (Ar*C*H), 57.4$^+$ (CHO*C*H$_3$) and 55.3$^+$ (ArO*C*H$_3$); *m*/*z* 302 (2%, M$^+$), 271 (24, M − OMe) and 151 (100, ArCHOMe) (Found: M$^+$, 302.1529. $C_{18}H_{22}O_4$ requires *M*, 302.1518); [*a*]$_D^{24}$ −7.4 (*c* 0.85 in CH_2Cl_2).

(1*RS*,2*RS*)-1,2-Bis(3,4-methylenedioxyphenyl)-1,2-dimethoxyethane 20. In the same way but with a reaction time of only 2 h with the methyl iodide, (1*RS*,2*RS*)-1,2-bis(3,4-methylenedioxyphenyl)ethane-1,2-diol **12** (114 mg, 0.377 mmol) gave the racemic diether (96.5 mg, 78%) as prisms, mp 120–122 °C (from Et_2O–hexane); R_f(hexane–ether, 1:1) 0.30; ν_{max} (KBr)/cm^{-1} 2826 (OCH_3), 1609 (Ar) and 1505 (Ar); δ_H(250 MHz; $CDCl_3$) (lit.†††[38]) 6.63 (2 H, d, *J* 1.6, 2-ArH), 6.60 (2 H, d, *J* 8.0, 5-ArH), 6.42 (2 H, dd, *J* 8.0 and 1.6, 6-ArH), 5.91 (2 H, d, *J* 1.4, OCH_AH$_B$O), 5.90 (2 H, d, *J* 1.4, OCH$_A$$H_B$O), 4.16 (2 H, s, ArC*H*) and 3.24 (6 H, s, OMe); δ_C(100.6 MHz; $CDCl_3$) 147.4$^-$ (3 or 4-ArC), 147.0$^-$ (3 or 4-ArC), 132.2$^-$ (1-ArC), 121.7$^+$ (6-ArC), 107.73$^+$ (2 or 5-ArC), 107.67$^+$ (2 or 5-ArC), 100.9$^-$ (OCH_2O), 87.3$^+$ (Ar*C*H) and 56.9$^+$ (OMe); *m*/*z* 331 (10.5%, MH$^+$), 299 (40, MH$^+$ − OMe) and 165 (100, ArCHOMe) (Found: MH$^+$, 331.11900. $C_{18}H_{18}O_6$ requires *M* + H, 331.11817).

(1*R*,2*R*)-1,2-Bis(3,4-methylenedioxyphenyl)-1,2-dimethoxyethane 20. In the same way, (1*R*,2*R*)-1,2-bis(3,4-methylenedioxyphenyl)ethane-1,2-diol **12** (325 mg, 1.08 mmol) gave the *enantiomerically pure diether* (344 mg, 97%) as rectangular plates. Characterisation data were identical to the racemic compound except: mp 79–80 °C (from hexane–CH_2Cl_2); [*a*]$_D^{25}$ +39.2 (*c* 1.30 in CH_2Cl_2).

(1*RS*,2*RS*)-1,2-Bis(2-chlorophenyl)-1,2-dimethoxyethane 19. In the same way with a reaction time of only 2 h with the methyl iodide, (1*RS*,2*RS*)-1,2-bis(2-chlorophenyl)ethane-1,2-diol **11** (233 mg, 0.823 mmol) gave the *diether* (209 mg, 82%) as prisms,

¶¶ No attempt was made to remove the mineral oil from the sodium hydride. Prveious attempts to do so led to lower yields.

|||| Dhimane *et al.*[38] quote values of: 7.93–7.00 (8 H, m, Ar), 5.14 (2 H, s, CH–O) and 3.34 (6 H, s, CH_3–O) for this compound and 7.90–7.06 (8 H, m, Ar), 5.01 (2 H, s, CH–O) and 3.21 (6 H, s, CH_3–O) for the *meso* compound. It may be that their assignments are mistaken since our signals are in better agreement with those of the reported *meso* compound.

*** Dhimane *et al.*[38] quote values of: 7.30–6.61 (8 H, m, Ar), 4.30 (2 H, s, CH–O), 3.70 (6 H, s, CH_3–OAr) and 3.30 (6 H, s, CH_3–O) for this compound and 7.41–6.76 (8 H, m, Ar), 4.30 (2 H, s, CH–O), 4.76 (6 H, s, CH_3–OAr) and 3.18 (6 H, s, CH_3–O) for the *meso* compound.

††† Dhimane *et al.*[38] quote values of: 6.88–6.30 (6 H, m, Ar), 5.90 (4 H, s, CH_2), 4.10 (2 H, s, CH–O) and 3.38 (6 H, s, CH_3–O) for this compound and 6.73–6.68 (6 H, m, Ar), 5.96 (4 H, s, CH_2), 4.08 (2 H, s, CH–O) and 3.18 (6 H, s, CH_3–O) for the *meso* compound.

mp 107–108 °C (from Et_2O–hexane); R_f(Et_2O–hexane, 1:4) 0.28; ν_{max} ($CHCl_3$)/cm^{-1} 2829 (OCH_3), 1595 (Ar) and 1573 (Ar); δ_H(400 MHz; $CDCl_3$) 7.63 (2 H, dd, *J* 7.7 and 1.6, 3-ArH), 7.27 (2 H, td, *J* 7.4 and 1.6, 4-ArH), 7.22 (2 H, dd, *J* 7.9 and 1.5, 6-ArH), 7.16 (2 H, td, *J* 7.5 and 1.6, 5-ArH), 4.95 (2 H, s, ArC*H*) and 3.17 (6 H, s, OMe); δ_C(62.9 MHz; $CDCl_3$) 135.7$^-$ (1-ArC), 133.7$^-$ (2-ArC), 130.0$^+$, 129.0$^+$ (2 signals), 126.7$^+$, 81.5$^+$ (Ar*C*HOMe) and 57.6$^+$ (OCH_3); *m*/*z* 279 (0.4%, M − MeO), 248 (0.3, M − 2MeO), 178 (30, M − 2MeOCl) and 155 (100, ArCHOMe) (Found: M$^+$ − MeO, 279.0349. $C_{16}H_{16}Cl_2O_2$ requires *M* − MeO, 279.0344).

(1*RS*,2*RS*)-1,2-Bis(2-bromophenyl)-1,2-bis[(1,1-dimethylethyl)dimethylsiloxy]ethane 13. Dry (1*RS*,2*RS*)-1,2-bis(2-bromophenyl)ethane-1,2-diol **9** (170 mg, 0.269 mmol) was dissolved in dry dichloromethane (0.5 ml). 2,6-Lutidine ((2,6-dimethylpyridine) 125 µl, 1.08 mmol, 4 eq.) was added and the mixture was cooled to 0 °C. (1,1-Dimethylethyl)dimethylsilyl trifluoromethanesulfonate (183 µl, 0.807 mmol, 3 eq.) was added to the stirring solution dropwise and the reaction mixture was allowed to reach room temperature and stirred for 2.5 h. HCl (2 ml of a 2 M solution) was added to the reaction mixture which was then extracted with CH_2Cl_2 (3 × 10 ml). The combined organic extracts were dried ($MgSO_4$) and purified by flash chromatography, eluting with hexane, to yield the *diether* (243 mg, 89%) as rectangular prisms, mp 144–145 °C (from EtOH); R_f(hexane) 0.28; ν_{max} ($CHCl_3$)/cm^{-1} 2956 (SiC–H_3), 2929 (SiC–H_3), 1590 (Ar) and 1362 (CMe_3); δ_H(250 MHz; $CDCl_3$) 7.73 (2 H, dd, *J* 7.8 and 1.8, 3-ArH), 7.48 (2 H, dd, *J* 8.0 and 1.2, 6-ArH), 7.29 (2 H, td, *J* 7.6 and 1.2, 4-ArH), 7.10 (2 H, td, *J* 7.7 and 1.8, 5-ArH), 5.20 (2 H, s, ArC*H*O), 0.70 (18 H, s, CMe_3), −0.45 (6 H, s, Si*Me*$_A$Me$_B$) and −0.51 (6 H, s, SiMe$_A$*Me*$_B$); δ_C(62.9 MHz; $CDCl_3$) 141.1$^-$ (1-ArC), 132.5$^+$ (3-ArC), 131.8$^+$ (4-ArC), 128.6$^+$ (6-ArC), 126.4$^+$ (5-ArC), 121.3$^-$ (2-ArC), 74.4$^+$ (Ar*C*H), 25.8$^+$ (C*Me*), 18.0$^-$ (*C*Me), −5.8$^+$ (Si*Me*$_A$Me$_B$) and −6.1$^+$ (SiMe$_A$*Me*$_B$); *m*/*z* 585 (0.16%, M − Me), 543 (19, M − ^{t}Bu), 301 (98, ArCHOSi^{t}BuMe$_2$) and 299 (100, ArCHOSi^{t}BuMe$_2$) (Found: M$^+$ − Me, 583.0699. $C_{26}H_{40}Br_2O_2Si_2$ requires *M* − Me, 583.0705).

(1*R*,2*R*)-1,2-Bis(2-bromophenyl)-1,2-bis[(1,1-dimethylethyl)-dimethylsiloxy]ethane 13. In the same way, but reacting overnight, (1*R*,2*R*)-1,2-bis(2-bromophenyl)ethane-1,2-diol **9** (1.86 g, 5 mmol) gave the *diether* (2.93 g, 98%) as rectangular prisms. Characterisation data were identical to the racemic compound except: mp 140–141 °C (from EtOH); $[a]_D^{23.5}$ −39.5 (*c* 1.04 in CH_2Cl_2).

(4*RS*,5*RS*)-2,2-Dimethyl-4,5-bis(3-fluorophenyl)-1,3-dioxolane 14. (1*RS*,2*RS*)-1,2-Bis(3-fluorophenyl)ethane-1,2-diol **8** (1.05 g, 4.20 mmol), 1,2-dimethoxypropane (2.50 ml, 20.4 mmol) and toluene-*p*-sulfonic acid (30 mg, 0.174 mmol) were stirred in anhydrous cyclohexane (25 ml). After stirring for 1 h at 50 °C. Sodium hydroxide solution (15 ml, 1.25 M) was added and stirring continued for 30 min before the mixture was left to stand overnight. The mixture was extracted with ether (3 × 20 ml) and the extract dried ($MgSO_4$) and evaporated under reduced pressure. The solid was purified by flash chromatography, eluting with hexane–ether, 19:1, to give the *dioxolane* (1.14 g, 93%) as an oil, R_f(Et_2O–hexane, 1:19) 0.29; ν_{max} (liquid film)/cm^{-1} 1593 (Ar), 1489 (Ar), 1374 (CMe_2) and 1142 (CO); δ_H(400 MHz; $CDCl_3$) 7.28 (2 H, ddd, *J* 8.9, 7.8 and $^4J_{HF}$ 5.8, 5-ArH), 7.03–6.99 (4 H, m, 4 and 6-ArH), 6.91 (2 H, dt, $^3J_{HF}$ 7.7 and *J* 1.1, 2-ArH), 4.68 (2 H, s, ArC*H*) and 1.66 (6 H, s, Me); δ_C(100.6 MHz; $CDCl_3$) 163.0$^-$ ($^1J_{CF}$ 246.3, 3-ArC), 139.2$^-$ ($^3J_{CF}$ 7.1, 1-ArC), 130.1$^+$ ($^3J_{CF}$ 8.3, 5-ArC), 122.4$^+$ ($^4J_{CF}$ 2.6, 6-ArC), 115.4$^+$ ($^2J_{CF}$ 21.1, 2 or 4-ArC), 113.5$^+$ ($^2J_{CF}$ 22.2, 2 or 4-ArC), 109.9$^-$ (OCO), 84.7$^+$ (Ar*C*H) and 27.1$^+$ (CH_3); δ_F(235.4 MHz; $CDCl_3$) −113.0 (td, J_{HF} 9.5 and 5.9); *m*/*z* 275 (2%, M$^+$ − Me) and 166 (100, M − ArCHO) (Found: M$^+$ − Me, 275.0872. $C_{17}H_{16}F_2O_2$ requires *M* − Me, 275.0884).

(4*R*,5*R*)-2,2-Dimethyl-4,5-bis(2-bromophenyl)-1,3-dioxolane 15. (1*R*,2*R*)-1,2-Bis(2-bromophenyl)ethane-1,2-diol **9** (1.00 g, 2.69 mmol), 1,2-dimethoxypropane (1.37 ml, 11.2 mmol) and toluene-*p*-sulfonic acid (17 mg, 0.098 mmol) were stirred in anhydrous cyclohexane (14 ml). After stirring for 10 min at 50 °C, the mixture was brought to 40 °C for 1 h 50 min. Sodium hydroxide solution (10 ml, 1.13 M) was added and stirring continued before the mixture was left to stand overnight. The mixture was extracted with ether (3 × 20 ml) and the extract dried ($MgSO_4$) and evaporated under reduced pressure. The solid was purified by flash chromatography, eluting with 9:1 hexane–ether, to give the *dioxolane* (1.09 g, 98%) as rectangular prisms, mp 114–115 °C (from hexane); R_f(hexane–ether, 2:1) 0.31; ν_{max} ($CHCl_3$)/cm^{-1} 1594 (Ar), 1570 (Ar), 1068 (CO); δ_H(250 MHz; $CDCl_3$) 7.72 (2 H, dd, *J* 7.7 and 1.7, 3-ArH), 7.41 (2 H, dd, *J* 7.9 and 1.3, 6-ArH), 7.38 (2H, td, *J* 7.6 and 1.3, 4-ArH), 7.14 (2 H, td, *J* 7.7 and 1.7, 5-ArH), 5.21 (2 H, s, ArC*H*) and 1.71 (6 H, s, CH_3); δ_C(100 MHz; $CDCl_3$) 135.5$^-$ (1-ArC), 132.7$^+$, 129.6$^+$, 128.6$^+$, 127.7$^+$, 123.2$^-$ (2-ArC), 109.5$^-$ (OCO), 83.3$^+$ (Ar*C*H) and 27.2$^+$ (Me); *m*/*z* 412 (4%, M$^+$), 397 (8, M − Me), 228 (99, M − ArCHO) and 226 (100, M − ArCHO) (Found: M$^+$, 411.9498. $C_{17}H_{16}Br_2O_2$ requires *M*, 411.9497); $[a]_D^{20.5}$ −11.4 (*c* 0.916 in $CHCl_3$).

Lithiation experiments

Lithiation and dimethylation of the acetal 20 with *sec*-butyllithium. *sec*-Butyllithium (150 µl of a 1.3 M solution in cyclohexane, 0.20 mmol) was added dropwise to a stirred solution of the diether **20** (29 mg, 0.088 mmol) in THF (1 ml) under argon at −78 °C. After stirring at −78 °C for 80 min, methyl iodide (25 µl, 0.40 mmol) was added dropwise. After 1 h at −78 °C, the reaction mixture was allowed to come to room temperature and stirred overnight. The reaction mixture was diluted with Et_2O (10 ml), washed with KOH (2 ml of a 2 M solution), brine and dried ($MgSO_4$). ^{1}H NMR indicated the formation of the dimethylated species **23** (83%), δ_H(200 MHz; $CDCl_3$) 6.85 (2 H, d, *J* 8.2, 5 or 6-ArH), 6.60 (2 H, d, *J* 8.2, 5 or 6-ArH), 5.89 (2 H, d, *J* 1.4, OC*H*$_A$H$_B$O), 5.87 (2 H, d, *J* 1.4, OCH$_A$*H*$_B$O), 4.54 (2 H, s, ArC*H*), 3.21 (6 H, s, OMe) and 1.80 (6 H, s, Ar*Me*); δ_C(100.6 MHz; $CDCl_3$) 145.8$^-$ (3 or 4-ArC), 145.6$^-$ (3 or 4-ArC), 130.4$^-$ (1-ArC), 121.5$^+$ (6-ArC), 119.1$^-$ (2-ArC), 105.8$^+$ (5-ArC), 100.6$^-$ (OCH_2O), 83.2$^+$ (Ar*C*H), 56.4$^+$ (OMe) and 11.1$^+$ (Ar*Me*), the monomethylated species **24** (14%) and starting material (2%).

Lithiation and dimethylation of dimethyl ether 20 with *n*-butyllithium. *n*-Butyllithium (150 µl of a 1.5 M solution in hexane, 0.23 mmol) was added dropwise to a stirred solution of the diether **20** (35 mg, 0.11 mmol) in THF (2 ml) under argon at −78 °C. After stirring at −78 °C for 35 min and at 0 °C for 20 min, methyl iodide (22 µl, 0.35 mmol) was added dropwise. After 30 min at −78 °C and 10 min at room temperature, methanol (300 µl) was added. The reaction mixture was diluted with Et_2O (10 ml), washed with KOH (2 ml of a 2 M solution), brine and dried ($MgSO_4$). ^{1}H NMR indicated the formation of the dimethylated species **23** (15%), the monomethylated species (25%) and starting material (60%).

Lithiation of the dimethyl ether 16 with *sec*-butyllithium. *sec*-Butyllithium (150 µl of a 1.3 M solution in cyclohexane, 0.20 mmol) was added dropwise to a stirred solution of the diether **16** (24 mg, 0.086 mmol) and TMEDA (20 ml, 0.26 mmol) in dry THF (1 ml) under argon at −78 °C. After 3 h, methyl iodide (15 µl, 0.24 mmol) was added and the mixture stirred for 45 min at −78 °C and overnight at room temperature before adding KOH (1 ml of a 2 M solution). The mixture was stirred for 4 h and

then diluted with Et_2O, washed with brine and dried ($MgSO_4$). ^1H NMR indicated the dimethylated species **21** (46%), the monomethylated species **22** (34%) and starting material (20%).

In a similar experiment, performed in the absence of TMEDA, ^1H NMR indicated the dimethylated species **21** (84%), R_f(Et_2O–hexane, 1:1) 0.38; δ_H(250 MHz; $CDCl_3$) 7.17 (2 H, dd, *J* 7.9 and 1.3, 6-ArH), 7.08 (2 H, td, *J* 7.9 and $^4J_{HF}$ 5.5, 5-ArH), 6.86 (2 H, ddd, $^3J_{HF}$ 9.6, *J* 7.9 and 1.3, 4-ArH), 4.64 (2 H, s, ArC*H*), 3.22 (6 H, s, OMe) and 1.74 (6 H, d, $^4J_{HF}$ 2.3, Ar*Me*); the mono methylated species (16%), δ_H(250 MHz; $CDCl_3$) 7.19–7.04 (3 H, m), 6.94–6.69 (4 H, m), 4.56 (1 H, d, *J* 7.5, MeArC*H*), 4.33 (1 H, d, *J* 7.5, ArC*H*), 3.29 (3 H, s), 3.26 (3 H, s) and 1.81 (3 H, d, $^4J_{HF}$ 2.3) and no starting material.

Lithiation of the dimethyl ether 16 with *n*-butyllithium. *n*-Butyllithium (170 μl of a 1.5 M solution in hexane, 0.26 mmol) was added dropwise to a stirred solution of the diether **16** (34 mg, 0.12 mmol) and TMEDA (39 ml, 0.26 mmol) in dry THF (1 ml) under argon at −78 °C. After 1 h 40 min, methyl iodide (20 μl, 0.32 mmol) was added and the mixture stirred for 20 min at −78 °C and for 10 min at room temperature before being quenched with methanol. The reaction mixture was diluted with Et_2O (10 ml), washed with KOH, brine and dried ($MgSO_4$). ^1H NMR indicated the formation of the dimethylated species **21** (39%), the monomethylated species **22** (52%) and starting material (8%).

Method A. General procedure for the lithiation and methylation of protected dibromodiols. The protected dibromodiol (0.080 mmol) was dried under vacuum (0.01 mmHg) and dissolved in dry THF (1 ml). Butyllithium (120 μl of a 1.5 M solution in hexane, 0.180 mmol) was added dropwise to the stirred solution of the dibromodiol under an atmosphere of argon at −78 °C and stirring continued for 20 min. Methyl iodide (13 μl, 0.209 mmol) was added dropwise to the mixture which was stirred for 15 min before being allowed to warm to room temperature. Either KOH (2 ml of a 1 M solution) or ammonium chloride (2 ml of a saturated solution) were added to the reaction mixture which was extracted with Et_2O (2 × 5 ml). The extract was dried ($MgSO_4$) and evaporated under reduced pressure to yield the reaction products.

*Attempted lithiation of dibromo dimethyl ether **17**.* By method A with TMEDA for 25 min, diether **17** gave (by ^1H NMR) a 50% yield of the dimethylated product **27**, 15% yield of the diprotonated species **29** and a 93% degree of lithiation.‡‡‡ In another experiment, the diether **17** was reacted by method A but with *tert*-butyllithium (2.2 eq.) and TMEDA. ^1H NMR indicated a 73% yield of the dimethylated product **27**, a 6% yield of the diprotonated species **29** and an 86% degree of lithiation. In another experiment, the diether **17** was reacted by method A but in hexane solution at 0 °C and with TMEDA. A reaction time of 25 min was allowed with the methyl iodide at room temperature. ^1H NMR indicated a 46% yield of the dimethylated product **27**, a 17% yield of the diprotonated species **29** and a 78% degree of lithiation. In another experiment, the diether **17** was reacted by method A but with *tert*-butyllithium (4.1 eq.). The butyllithium was added at −98 °C and stirred for 1.5 h before the mixture was warmed to −23 °C for 25 min and recooled to −78 °C. The electrophile was added and the reaction mixture allowed to warm to room temperature and react overnight. ^1H NMR indicated a 96% degree of lithiation and an 88% yield of the dimethylated product **27**, δ_H(250 MHz; $CDCl_3$) 7.44 (2 H, dd, *J* 7.6 and 1.7, 6-ArH), 7.18–7.02 (4 H, m, 4 and 5-ArH), 6.87 (2 H, d, *J* 7.3, 3-ArH), 4.66 (2 H, s, ArC*H*), 3.21 (6 H, s, ArCO*Me*) and 1.76 (6 H, s, Ar*Me*); δ_C(62.9 MHz; $CDCl_3$) 137.2^- (1-ArC), 136.3^- (2-ArC), 130.1^+, 128.2^+, 127.7^+, 125.8^+, 83.4^+ (Ar*C*HOMe), 56.7^+ (OMe) and 19.1^+ (Ar*Me*).

‡‡‡ By ^1H NMR it is possible to detect, in addition to starting material and the desired product, the diprotonated species **29** and a product which is monomethylated and monoprotonated.

Synthesis of *P*-phenyl substituted phosphepine oxides

Method B. General procedure for the preparation of phosphepine oxides from protected dibromodiols using *tert*-butyllithium. Dry protected diol (1.95 mmol) was dissolved in dry Et_2O (45 ml) under argon and cooled to −78 °C. *tert*-Butyllithium (2.75 ml of a 1.7 M solution, 4.66 mmol, 2.4 eq.) was added dropwise to the stirred solution. Stirring was continued for 2.5 h before freshly distilled dichloro(phenyl)phosphine (425 μl in 9.4 ml of THF solution, 3.13 mmol) was added dropwise. After 2 h at −78 °C, the reaction mixture was allowed to warm to room temperature and stirred overnight. A solution of saturated $NaHCO_3$ (5 ml) was added to the reaction mixture and the Et_2O removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (50 ml) and stirred vigorously as H_2O_2 (2 ml of approx. 100 vol. solution, 18 mmol) was added dropwise. After 30 min, the layers were separated and the aqueous layer further extracted with CH_2Cl_2 (2 × 20 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography to yield the phosphine oxide.

Method C. General elaborated procedure for the preparation of phosphepine oxides from protected dibromodiols using *tert*-butyllithium. Dry protected diol (1.02 mmol) was dissolved in dry Et_2O (25 ml) under argon and cooled to −78 °C. *tert*-Butyllithium (1.26 ml of a 1.9 M solution, 2.39 mmol) was added dropwise to the stirred solution. Stirring was continued for 3 h before freshly distilled dichloro(phenyl)phosphine (200 μl in 5 ml of THF solution, 1.47 mmol) was added dropwise. After 2 h at −78 °C, the reaction mixture was allowed to warm to room temperature and stirred overnight. Water (40 μl) was added followed by silica (approx. 1 g) and the solvent was evaporated under reduced pressure. Flash chromatography gave the phosphine which was dissolved in CH_2Cl_2 (25 ml). Water (10 ml) was added and the mixture stirred vigorously as H_2O_2 (3 ml of 100 vol. solution in water, 26 mmol) was added dropwise. After 30 min, the layers were separated and the aqueous layer further extracted with CH_2Cl_2 (2 × 15 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography to yield the phosphine oxide.

Method D. General procedure for the preparation of phosphepine oxides using *sec*-butyllithium. Dry protected diol (0.44 mmol) was dissolved in dry THF (5 ml) under argon and cooled to −78 °C. *sec*-Butyllithium (690 μl of a 1.4 M solution,§§§ 0.966 mmol, 2.2 eq.) was added dropwise to the stirred solution. Stirring was continued for 3.5 h before freshly distilled dichloro(phenyl)phosphine (77 μl, 0.57 mmol) was added dropwise. After 6 h at −78 °C, the reaction mixture was allowed to warm to room temperature slowly and stirred overnight. Water (200 μl) was added and THF evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 ml), cooled to 0 °C and stirred vigorously as H_2O_2 (1.5 ml of an approx. 100 vol. solution, 13 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 2 h before water (10 ml) was added. The layers were separated and the aqueous layer further extracted with CH_2Cl_2 (3 × 10 ml). The combined extracts were dried ($MgSO_4$) and purified by flash chromatography to yield the phosphine oxide.

§§§ Determined using butan-2-ol and 2,2′-biquinoline.[39]

Method E. General elaborated procedure for the preparation of phosphepine oxides using *sec*-butyllithium. Dry protected diol (0.759 mmol) was dissolved in dry THF (15 ml) under argon and cooled to −78 °C. *sec*-Butyllithium (1.38 ml of a 1.3 M solution in cyclohexane,§§§ 1.79 mmol, 2.35 eq.) was added dropwise to the stirred solution. Stirring was continued for 2 h before freshly distilled dichloro(phenyl)phosphine (150 μl in 2.5 ml of THF, 1.11 mmol) was added dropwise. After 3.5 h at −78 °C, the reaction mixture was allowed to warm to room temperature slowly and stirred for 1 h at room temperature. Water (200 μl) was added followed by silica (approx. 1 g). The remaining procedure of method C was followed to yield the phosphine oxide.

(10*R*,11*R*)-3,4:6,7-Bis(methylenedioxy)-10,11-dimethoxy-10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 36. (1*R*,2*R*)-1,2-Bis(3,4-methylenedioxyphenyl)-1,2-dimethoxyethane **20** (104 mg, 0.315 mmol) was reacted by a modified method E; no water was added. A solution of 1:1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 1:1) 0.33. Flash chromatography, eluting with 5% methanol in EtOAc yielded the *phosphine oxide* (25 mg, 18%) as plates, mp 184–187 °C (from hexane–EtOAc), R_f(methanol–EtOAc, 1:19) 0.32; ν_{max} ($CHCl_3$)/cm^{-1} 2825 (OC–H_3), 2781 (OC–H_2O), 1602 (Ar), 1500 (Ar), 1435 (P–Ph), 1240 (P=O) and 1093 (C–O); δ_H(400 MHz; $CDCl_3$) 7.83 (2 H, ddd, $^3J_{PH}$ 13.4, *J* 7.6 and 1.4, *o*-PhH), 7.40–7.36 (1 H, m, *p*-PhH), 7.33–7.28 (2 H, m, *m*-PhH), 6.86–6.81 (2 H, m), 6.79–6.75 (2 H, m), 6.11 (1 H, d, *J* 1.3, $OC_AH_AH_BO$), 5.88 (1 H, d, *J* 1.3, $OC_BH_AH_BO$), 5.76 (1 H, d, *J* 1.3, $OC_AH_AH_BO$), 5.49 (1 H, d, *J* 1.3,$OC_BH_AH_BO$), 4.75 (1 H, d, *J* 8.3, $ArCH_ACH_BAr$), 4.71 (1 H, d, *J* 8.3, $ArCH_ACH_BAr$), 3.20 (3 H, s, OMe_A) and 3.14 (3 H, s, OMe_B); δ_C(100.6 MHz; $CDCl_3$) 151.8$^-$ (br), 148.4$^-$ (J_{PC} 9.3), 148.2$^-$ (J_{PC} 9.1), 136.0$^-$ ($^1J_{PC}$, 110.1, *ipso*-PhC), 132.3$^-$ (J_{PC} 4.8), 131.1$^+$ (J_{PC} 11.2, *o* or *m*-PhC), 130.5$^+$ (*p*-PhC), 129.1$^-$ (J_{PC} 5.4), 127.3$^+$ (*o* or *m*-PhC), 125.6$^+$ ($^3J_{PC}$ 11.4, 1 or 9-ArC), 124.9$^+$ ($^3J_{PC}$ 11.3, 1 or 9-ArC), 117.1$^-$ ($^1J_{PC}$ 103.0, 4a or 5a-ArC), 115.1$^-$ ($^1J_{PC}$ 104.7, 4a or 5a-ArC), 110.1$^+$ (2 or 8-ArC), 109.7$^+$ (2 or 8-ArC), 102.0$^-$ (OC_AO), 101.8$^-$ (OC_BO), 85.3$^+$ (ArC_AHC_BHAr), 84.5 (ArC_AHC_BHAr), 56.6$^+$ (OMe_A) and 56.4$^+$ (OMe_B); *m*/*z* 452 (6%, M^+) (Found: M^+, 452.1041. $C_{24}H_{21}O_7P$ requires *M*, 452.1025); $[a]_D^{17}$ −239 (*c* 1.06 in $CHCl_3$). In another experiment by method D but using 3.0 equivalents of *sec*-butyllithium, the phosphepine oxide was isolated in a slightly less pure form than the above, in a 41% yield.

(10*R*,11*R*)-4,6-Difluoro-10,11-dimethoxy-10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 30. (1*R*,2*R*)-1,2-Bis(3-fluorophenyl)-1,2-dimethoxyethane **16** (122 mg, 0.439 mmol) was reacted by method D. Purification by flash chromatography, eluting with 1:19 methanol–EtOAc gave the *phosphine oxide* (89 mg, 51%) as prisms, mp > 270 °C (from EtOAc–EtOH); R_f(methanol–EtOAc, 1:19) 0.26; ν_{max} (KBr)/cm^{-1} 2825 (OC–H_3), 1603 (Ar), 1574 (Ar), 1446 (P–Ph), 1261 (P=O) and 1094 (C–O); δ_H(400 MHz; $CDCl_3$) 7.83 (2 H, dd, $^3J_{PH}$ 13.7 and *J* 8.0, *o*-PhH), 7.49–7.33 (5 H, m), 7.18 (1 H, dd, *J* 7.1 and 2.4, 1- or 9-ArH), 7.13 (1 H, dd, *J* 7.3 and 2.9, 1- or 9-ArH), 7.03–6.94 (2 H, m, looks like 2 × tdd, 3 and 7-ArH), 4.89 (1 H, d, *J* 8.8, $ArCH_ACH_BAr$), 4.87 (1 H, d, *J* 8.8, $ArCH_ACH_BAr$), 3.22 (3 H, s, OMe_A) and 3.21 (3 H, s, OMe_B); δ_C(100.6 MHz; $CDCl_3$)¶¶¶ 165.3$^-$ ($^1J_{CF}$ 254.1, 4 or 6-ArC), 165.0$^-$ ($^1J_{CF}$ 254.6, 4 or 6-ArC), (141–135)$^-$ (4 lines visible, 9a and 11a), 133.2$^+$ ($^3J_{PC}$ 9.8, 1 or 9-ArC), 132.7$^+$ ($^3J_{PC}$ 10.5, 1 or 9-ArC), 130.6$^+$ ($^4J_{PC}$ 2.4, *p*-PhC), 130.2$^+$ (J_{PC} 11.3, *o* or *m*-PhC), 127.8$^+$ (dd, $^3J_{CF}$ 13.8 and $^4J_{PC}$ 2.8, 2 or 8-ArC), 127.7$^+$ (J_{PC} 13.5, *o* or *m*-PhC), 127.3$^+$ (dd, $^3J_{CF}$ 10.6 and $^4J_{PC}$ 3.1, 2 or 8-ArC), 124.6$^-$ (dd, $^1J_{PC}$ 101.0 and $^3J_{CF}$ 11.3, 4a or 5a-ArC), 122.6$^-$ (dd, $^1J_{PC}$ 104.2 and $^3J_{CF}$ 12.2, 4a or 5a-ArC), 117.6$^+$ (dd, $^2J_{CF}$ 24.7 and $^3J_{PC}$ 5.6, 3 or 7-ArC), 117.4$^+$ (dd, $^2J_{CF}$ 21.8 and $^3J_{PC}$ 5.4, 3 or 7-ArC), 85.1$^+$ (ArC_AHC_BHAr), 84.2$^+$ (ArC_AHC_BHAr), 57.0$^+$ (OMe_A) and 56.9$^+$ (OMe_B); δ_F(235.4 MHz; $CDCl_3$; ^{1}H decoupled) −97.07 ($^3J_{FP}$ 7.5) and −97.73 ($^3J_{FP}$ 12.7); δ_F(235.4 MHz; $CDCl_3$; ^{1}H coupled) −97.08 (m) and −97.73 (td, $^3J_{FP}$ 11.6, $^3J_{HF}$ 11.6 and $^4J_{HF}$ 5.1); *m*/*z* 400 (1.1%, M^+) and 385 (4, M − Me) (Found: M^+, 400.1041. $C_{22}H_{19}F_2O_3P$ requires *M*, 400.1040); $[a]_D^{17.5}$ −163 (*c* 1.06 in $CHCl_3$).

Other variations led to lower yields. In experiments in which THF was not removed before the oxidation step, the yields were 35 and 39%. When lower quality *sec*-butyllithium was used (0.93 M)‖‖‖‖‖ the isolated yield was 12%. When 2.4 equivalents of *n*-butyllithium were used and the reaction mixture stirred for only 1.5 h before addition of electrophile, the yield was 19%. Three other experiments with *n*-butyllithium at 0 °C or *tert*-butyllithium in Et_2O gave no product.

(10*R*,11*R*)-10,11-Dimethoxy-10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 33. (1*R*,2*R*)-1,2-Bis(2-bromophenyl)-1,2-dimethoxyethane **17** (125 mg, 0.313 mmol) was reacted by a modified method B; 4.1 equivalents of *tert*-butyllithium were used and after 1 h 15 min at −78 °C, the solution was allowed to stir at −23 °C for 30 min. It was then recooled to −78 °C and the dichloro(phenyl)phosphine was added in a solution of Et_2O. Flash chromatography, eluting with 9:1 EtOAc–CH_2Cl_2 gave the *phosphine oxide* (29 mg, 25%) as an oil, R_f(EtOAc) 0.16; ν_{max} ($CHCl_3$)/cm^{-1}1602 (Ar), 1437 (P–Ph), 1242 (P=O) and 1106 (C–O); δ_H(400 MHz; $CDCl_3$) 8.39 (1 H, ddd, $^3J_{PH}$ 12.8, *J* 6.7 and 1.5, 4 or 6-ArH), 8.14 (1 H, ddd, $^3J_{PH}$ 12.9, *J* 7.6 and 0.9, 4 or 6-ArH), 7.60–7.39 (9 H, m), 7.35–7.30 (2 H, m), 4.79 (1 H, d, *J* 8.7, $ArCH_ACH_BAr$), 4.68 (1 H, d, *J* 8.7, $ArCH_ACH_BAr$), 3.09 (3 H, OMe_A) and 2.88 (3 H, OMe_B); δ_C(100.6 MHz; $CDCl_3$) 139.7$^-$ ($^2J_{PC}$ 10.3, 9a or 11a-ArC), 139.5$^-$ ($^2J_{PC}$ 10.1, 9a or 11a-ArC), 136.5$^-$ ($^1J_{PC}$ 106.5, *ipso*-PhC), 134.2$^+$ (J_{PC} 7.3), 133.8$^+$ (J_{PC} 6.4), 132.0$^+$ (J_{PC} 2.4), 131.9$^+$ (J_{PC} 12.1), 131.7$^+$ (J_{PC} 2.5), 131.2$^+$ (J_{PC} 2.3), 131.0–127.9 (several lines), 84.7$^+$ (ArC_AHC_BHAr), 82.5$^+$ (ArC_AHC_BHAr), 57.1$^+$ (OMe_A) and 56.2$^+$ (OMe_B); *m*/*z* 364 (42%, M^+) and 349 (100, M − Me) (Found: M^+, 364.1237. $C_{22}H_{21}O_3P$ requires *M*, 364.1228); $[a]_D^{25}$ −148 (*c* 0.707 in CH_2Cl_2).

(10*R*,11*R*)-10,11-Isopropylidenedioxy-10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 32. (4*R*,5*R*)-2,2-Dimethyl-4,5-bis(2-bromophenyl)-1,3-dioxolane **15** (200 mg, 0.485 mmol) was reacted by a modified method B; THF (20 ml) was used as the solvent. After 1 h at −78 °C following the addition of the dichloro(phenyl)phosphine, TLC indicated that the reaction to form the phosphine was complete. The reaction was continued at 0 °C for 15 min before quenching and oxidation was performed according to method B. Flash chromatography, eluting with EtOAc, gave the *phosphine oxide* (133 mg, 73%) as plates, mp 141–142 °C (from EtOAc–hexane), R_f (EtOAc) 0.33; ν_{max} (KBr)/cm^{-1} 1590 (Ar), 1436 (P–Ph), 1241 (P=O) and 1132 (C–O); δ_H(400 MHz; $CDCl_3$) 8.36 (1 H, ddd, $^3J_{PH}$ 12.4, *J* 7.6 and 1.1, 4 or 6-ArH), 8.24 (1 H, ddd, $^3J_{PH}$ 12.6, *J* 7.8 and 1.1, 4 or 6-ArH), 7.81–7.75 (2 H, m, 1 and 9-ArH), 7.63 (2 H, br t, *J* 7.6), 7.53 (br t, *J* 7.6), 7.44–7.38 (1 H, m), 7.34–7.26 (4 H, m), 5.09 (1 H, d, *J* 9.1, $ArCH_ACH_BAr$), 5.01 (1 H, d, *J* 9.1, $ArCH_ACH_BAr$), 1.57 (3 H, s, OMe_A) and 1.46 (3 H, s, OMe_B); δ_C(100.6 MHz; $CDCl_3$) 140.5$^-$ ($^2J_{PC}$ 10.9, 9a or 11a-ArC), 140.3$^-$ ($^2J_{PC}$ 10.1, 9a or 11a-ArC), 135.8$^-$ ($^1J_{PC}$ 104.3, *ipso*-PhC), 133.7$^+$ (J_{PC} 6.4), 133.4$^+$ (J_{PC} 6.2), 132.9$^+$ ($^4J_{PC}$ 2.3, 2 or 8-ArC), 132.6$^+$ ($^4J_{PC}$ 2.3, 2 or 8-ArC), 131.7 ($^4J_{PC}$ 2.4, *p*-PhC), 130.9 (J_{PC} 10.6, *o* or *m*-PhC), 128.61$^+$ (J_{PC} 12.3, *o* or *m*-PhC), 128.60$^-$ ($^1J_{PC}$ 92.9, 4a or 5a-ArC),**** 127.9$^+$ (J_{PC} 8.6), 127.8$^+$ (J_{PC} 8.8), 127.6$^-$ ($^1J_{PC}$ 92.2, 4a or 5a-ArC),**** 127.3$^+$

¶¶¶ The signals in this spectrum were compared to those in a 62.9 MHz spectrum to establish unambiguously coupling constants in pairs of diastereotopic carbon signals.

‖‖‖‖‖ As determined by butan-2-ol and 1,10-phenanthroline.[39]

**** Or 128.58$^-$ ($^1J_{PC}$ 97.8, 4a or 5a-ArC) and 127.7$^-$ ($^1J_{PC}$ 97.1, 4a or 5a-ArC).

(J_{PC} 11.0), 123.7$^+$ (J_{PC} 10.8), 109.6$^-$ (OCO), 80.6$^+$ (ArC_AC$_B$Ar), 78.5 ($^3J_{PC}$ 3.5, ArC$_A$$C_B$Ar), 27.0$^+$ (CMe_A) and 26.6$^+$ (CMe_B); *m*/*z* 376 (2%, M$^+$) and 318 (100, M − Me_2CO) (Found: M$^+$, 376.1224. $C_{23}H_{21}O_3P$ requires *M*, 376.1228); $[a]_D^{18.5}$ +114 (*c* 1.00 in CH_2Cl_2).

In another similar experiment in which the dichloro(phenyl)-phosphine was mixed with TMEDA (4 equivalents relative to starting material) in THF before addition, the product was isolated in a 73% yield. In another similar experiment which was conducted in Et_2O instead of THF and where 2.5 equivalents of TMEDA were added immediately after the dichloro-(phenyl)phosphine, the product was isolated in a 55% yield. In another experiment using Et_2O instead of THF, 4.1 equivalents of *tert*-butyllithium with warming to −23 °C for 45 min before recooling to −78 °C and adding the electrophile, the product was isolated in 28% yield.

(10*R*,11*R*)-10,11-Bis[(1,1-dimethylethyl)dimethylsiloxy]-10,11-dihydro-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 38. By method B, except that the dichloro(phenyl)phosphine was mixed with TMEDA (1.17 ml, 7.77 mmol) before addition, (1*R*,2*R*)-1,2-bis(2-bromophenyl)-1,2-bis[(1,1-dimethylethyl)-dimethylsiloxy]ethane **13** (1.17 g, 1.95 mmol) gave the *phosphine oxide* (355 mg, 30.5%) as an oil, R_f(hexane–EtOAc, 1:1) 0.23; ν_{max} ($CHCl_3$)/cm^{-1} 1601 (Ar), 1438 (Ph–P) and 1252 (P=O); δ_H(400 MHz; $CDCl_3$) 8.00 (1 H, ddd, J_{PH} 13.4, *J* 7.6 and 1.0, 4 or 6-ArH), 7.69 (2 H, ddd, $^3J_{PH}$ 12.2, *J* 7.8 and 1.4, *o*-PhH), 7.65–7.60 (1 H, m), 7.42–7.27 (9 H, m), 5.15 (1 H, d, *J* 7.9, ArCH_ACH$_B$Ar), 5.11 (1 H, d, *J* 7.9, ArCH$_A$CH_BAr), 0.63 (9 H, s, Si$_A$^{t}Bu), 0.56 (9H, s, Si$_B$^{t}Bu), 0.00 (3 H, s, SiMe$_A$), −0.06 (3 H, s, SiMe$_B$), −0.09 (3 H, s, SiMe$_C$) and −0.24 (3 H, s, SiMe$_D$); δ_C(100.6 MHz; $CDCl_3$) 143.5$^-$ (J_{PC}, 9.5), 141.2$^-$, 137.3$^-$ (J_{PC} 105.5), 135.2$^+$ (J_{PC} 9.3), 134.6$^+$ (J_{PC} 7.9), 134.0–127.5$^+$, 132.9$^-$ (J_{PC} 100.2), 78.9$^+$ (ArC_AHC$_B$HAr), 77.7$^+$ (ArC$_A$HC_BHAr), 25.6$^+$ (C$_A$$Me_3$), 25.4$^+$ (C$_B$$Me_3$), 18.0$^-$ (C_AMe$_3$), 17.8$^-$ (C_BMe$_3$), −4.5$^-$ (SiMe$_A$), −4.62$^-$ (SiMe$_B$), –4.65$^-$ (SiMe$_C$) and −5.1$^-$ (SiMe$_D$); *m*/*z* 564 (9.2%, M$^+$) and 507 (100, M − ^{t}Bu) (Found: M$^+$, 564.2666. $C_{32}H_{45}O_3PSi_2$ requires *M*, 564.26449); $[a]_D^{25.5}$ −107 (*c* 1.48 in CH_2Cl_2) and another unidentified compound (245 mg) as plates, mp 147–148 °C (hexane); R_f(hexane–EtOAc) 0.35; ν_{max} ($CHCl_3$)/cm^{-1} 1593, 1440 and 1232; δ_H(400 MHz; $CDCl_3$) 8.18 (2 H, ddd, *J* 13.3, 8.1 and 1.2), 7.80 (2 H, m like d AB quartet), 7.55–7.42 (6 H, m), 7.37 (1 H, td, *J* 7.5 and 1.3), 7.31–7.27 (2 H, m), 6.06 (1 H, d, *J* 4.8), 4.71 (1 H, s), 0.83 (9 H, s), 0.76 (9 H, s), 0.35 (3 H, s), 0.22 (3 H, s), −0.22 (3 H, s) and −0.46 (3 H, s); δ_C(100.6 MHz; $CDCl_3$) 143.1$^-$ (J_{PC} 8.2), 142.0$^-$ (J_{PC} 7.1), 135.8$^+$, 133.7$^-$, 133.2–127.3 (several lines), 79.6$^+$ (J_{PC} 6.4), 73.2$^+$ (J_{PC} 2.8), 26.8$^+$, 25.9$^+$, 18.2$^-$, 17.8$^-$, −1.0$^+$, −3.5$^+$, −4.0$^+$ and −5.3$^+$; *m*/*z* 564, (0.2%, M$^+$), 549 (3, M − Me) and 507 (100, M − ^{t}Bu) (Found: M$^+$, 564.2636. $C_{32}H_{45}O_3PSi_2$ requires *M*, 564.26449); $[a]_D^{20.5}$ +50.8 (*c* 1.07 in CH_2Cl_2).

Synthesis of *P*-propyl substituted phosphepine oxides

Dichloro(propyl)phosphine. Anhydrous $ZnCl_2$ (100 ml of a 1 M solution in Et_2O, 0.1 mol) was added dropwise to a stirred solution of propylmagnesium chloride (100 ml of a 1 M solution in Et_2O, 0.1 mol) at 0 °C. After the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred for 30 min. The resulting suspension was added *via* thick Teflon cannula to a solution stirred with an overhead stirrer of freshly distilled PCl_3 (23.4 ml, 0.268 mol) in refluxing Et_2O (30 ml). Additional Et_2O (15 ml) was used to rinse the suspension into the refluxing ether. Refluxing was continued for 1 h 10 min and the mixture left to stand overnight before being filtered *via* thick Teflon cannula through a Schlenk tube under argon and the precipitate was washed with ether (2 × 50 ml). The ether was removed by evaporation under reduced pressure. Fractional distillation of the resulting residue gave the phosphine (4.78 g, 33%), bp 134–136 °C (lit.,[40] 134.5 °C).

(10*R*,11*R*)-3,4:6,7-Bis(methylenedioxy)-10,11-dimethoxy-10,11-dihydro-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 37. (1*R*,2*R*)-1,2-Bis(3,4-methylenedioxyphenyl)-1,2-dimethoxy-ethane **20** (123 mg, 0.372 mmol) was reacted by a modified method E; 2.5 equivalents of *sec*-butyllithium were used and no water was added to the reaction mixture before silica. A solution of 1:1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 1:1) 0.39. Flash chromatography, eluting with 5% methanol in EtOAc yielded the *phosphine oxide* (12.8 mg, 8%) as an oil, R_f(methanol–EtOAc, 1:19) 0.23; ν_{max} ($CHCl_3$)/cm^{-1} 2825 (COC–H$_3$), 2782 (OC–H$_2$O), 1589 (Ar), 1501 (Ar), 1241 (P=O) and 1093 (C–O); δ_H(400 MHz; $CDCl_3$) 6.86 (1 H, dd, *J* 7.7 and $^4J_{PH}$ 0.7, 1 or 9-ArH), 6.85 (1 H, dd, *J* 7.8 and $^4J_{PH}$ 1.0, 1 or 9-ArH), 6.78 (1 H, d, *J* 7.8, 2 or 8-ArH), 6.76 (1 H, d, *J* 7.7, 2 or 8-ArH), 6.16 (1 H, d, *J* 1.2, OC$_A$$H_AH_B$O), 6.14 (1 H, d, *J* 1.4, OC$_B$$H_AH_B$O), 6.08 (1 H, d, *J* 1.3, OC$_A$H$_A$$H_B$O), 6.07 (1 H, d, *J* 1.4, OC$_B$H$_A$$H_B$O), 4.67 (1 H, d, *J* 8.3, ArCH_ACH$_B$Ar), 4.62 (1 H, d, *J* 8.3, ArCH$_A$CH_BAr), 3.11 (3 H, s, OMe$_A$), 3.10 (3 H, s, OMe$_B$), 2.62–2.45 (2 H, m, PCH$_2$), 1.38–1.22 (2 H, m, PCH$_2$CH_2) and 0.87 (3 H, td, ^4J 7.2 and J_{PH} 1.3, CH$_2$$Me$); δ_C(100.6 MHz; $CDCl_3$) 151.1$^-$, 148.3$^-$, 148.1$^-$, 131.8$^-$ (J_{PC} 4.2),†††† 130.2$^-$ (J_{PC} 4.7),†††† 125.8$^+$ (J_{PC} 10.3, 1 or 9-ArC),†††† 125.5$^+$ (J_{PC} 10.7, 1 or 9-ArC),†††† 110.0$^+$ (2 or 8-ArC), 109.7$^+$ (2 or 8-ArC), 102.0$^-$ (OC$_A$H$_2$O), 101.8$^-$ (OC$_B$H$_2$O), 85.1$^+$ (ArC_AHC$_B$HAr), 84.5$^+$ (ArC$_A$HC_BHAr), 56.4$^+$ (OMe$_A$), 56.3$^+$ (OMe$_B$), 33.8$^-$ ($^1J_{PC}$ 73.4, PCH$_2$), 16.0$^-$ (PCH$_2$$CH_2$), 15.8$^+$ ($^3J_{PC}$ 18.8, CH$_2$$Me$); *m*/*z* 418 (33%, M$^+$) and 403 (72, M − Me) (Found: M$^+$, 418.1183. $C_{21}H_{23}O_7P$ requires *M*, 418.1181); $[a]_D^{17}$ −297 (*c* 0.92 in $CHCl_3$).

(10*R*,11*R*)-4,6-Difluoro-10,11-dimethoxy-10,11-dihydro-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 35. (1*R*,2*R*)-1,2-Bis(3-fluorophenyl)-1,2-dimethoxyethane **16** (211 mg, 0.759 mmol) was reacted by a modified method E. 2.36 equivalents of *sec*-butyllithium were used. A solution of 1:1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 1:1) 0.33. Flash chromatography, eluting with 5% methanol in EtOAc yielded the *phosphine oxide* (84 mg, 30%) as prisms, mp 181–184 °C (from methanol–EtOAc); R_f(methanol–EtOAc, 1:19) 0.18; ν_{max} (KBr)/cm^{-1} 2825 (OC–H$_3$), 1602 (Ar), 1574 (Ar), 1260 (P=O) and 1087 (C–O); δ_H(400 MHz; $CDCl_3$) 7.47 (1 H, t, *J* 7.7), 7.45 (1 H, t, *J* 7.7), 7.18–7.12 (4 H, m), 4.92 (1 H, br s, ArCH_ACH$_B$Ar), 4.72 (1 H, d, *J* 8.2, ArCH$_A$CH_BAr), 3.13 (3 H, s, OMe$_A$), 3.12 (3 H, s, OMe$_B$), 2.61–2.50 (2 H, m, PCH$_2$), 1.31–1.22 (2 H, m, PCH$_2$CH_2) and 0.87 (td, *J* 7.2 and $^4J_{PH}$ 1.2, CH$_2$$Me$); δ_C(50.3 MHz; $CDCl_3$)‡‡‡‡ 165.2$^-$ ($^1J_{CF}$ 253.2, 4 or 6-ArC), 164.7$^-$ ($^1J_{CF}$ 250.1, 4 or 6-ArC), 141.0$^-$ (9a or 11a-ArC), 140.0$^-$ (9a or 11a-ArC), 132.6$^+$ ($^3J_{CF}$ 10.3, 2 or 8-ArC),§§§§ 132.5$^+$ ($^3J_{CF}$ 10.0, 2 or 8-ArC),§§§§ 128.0$^+$ ($^3J_{PC}$ 8.7, 1 or 9-ArC),§§§§ 127.1$^+$ ($^3J_{PC}$ 8.3, 1 or 9-ArC),§§§§ 117.2$^+$ (dd, $^2J_{CF}$ 26.1 and $^3J_{PC}$ 5.2, 3 or 7-ArC), 116.9$^+$ (dd, $^2J_{CF}$ 25.9 and $^3J_{PC}$ 5.2, 3 or 7-ArC), 84.4$^+$ (10 or 11-ArC), 84.3$^+$ (10 or 11-ArC), 56.8$^+$ (OMe$_A$), 56.7$^+$ (OMe$_B$), 35.8$^-$ (dd, $^1J_{PC}$ 73.5 and $^4J_{CF}$ 6.2, PCH$_2$), 16.2$^+$ (PCH$_2$$CH_2$), 15.7$^+$ ($^3J_{PC}$ 19.2, CH$_2$$Me$); *m*/*z* 366 (30%, M$^+$) and 351 (100, M − Me) (Found: M$^+$, 366.1192. $C_{19}H_{21}F_2O_3P$ requires *M*, 366.1196); $[a]_D^{26}$ −193 (*c* 1.04 in $CHCl_3$).

†††† Signal established in conjunction with a 50.3 MHz spectrum.

‡‡‡‡ The signals in this spectrum were compared to those in a 100.6 MHz spectrum to establish unambiguously coupling constants in pairs of diastereotopic carbon signals.

§§§§ Tentative assignment. On the magnitude of the coupling constant alone, the assignment of these four signals could be transposed. That is, (1 or 9) swapped with (2 or 8) and *vice versa* and coupling to fluorine swapped with coupling to phosphorus. When the substituent constants[41] for fluorine are applied to the signals of the analogous non-fluorinated compound **34**, chemical shifts of 132.2 and 138.2 ppm are predicted for the 2- and 8-aromatic carbons.

(10*R*,11*R*)-10,11-Dimethoxy-10,11-dihydro-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 34. (1*R*,2*R*)-1,2-Bis(2-bromophenyl)-1,2-dimethoxyethane **17** (408 mg, 1.02 mmol) was reacted by method C. A solution of 1 : 1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 1 : 1) 0.49. Flash chromatography, eluting with 5% methanol in EtOAc yielded the *phosphine oxide* (15.1 mg, 5%) as an oil, R_f(methanol–EtOAc, 1 : 19) 0.37; ν_{max} ($CHCl_3$)/cm^{-1} 2826 (O–Me), 1602 (Ar), 1158 (P=O) and 1101 (C–O); δ_H(400 MHz; $CDCl_3$) 8.36 (1 H, ddd, $^3J_{PH}$ 12.2, *J* 5.2 and 3.8, 4 or 6-ArH), 8.31–8.26 (1 H, m, 4 or 6-ArH), 7.54–7.48 (4 H, m), 7.41–7.34 (2 H, m), 4.76 (d, *J* 7.7, ArCH_ACH$_B$Ar), 4.73 (d, *J* 7.7, ArCH$_A$CH_BAr), 3.23 (3 H, s, OMe$_A$), 3.04 (3 H, s, OMe$_B$), 2.07–1.97 (2 H, m, PCH$_2$), 1.63–1.59 (1 H, m, PCH$_2$CH_A), 1.30–1.24 (1 H, m, PCH$_2$CH_B) and 0.86 (3 H, td, *J* 7.2 and $^4J_{PH}$ 1.1, CH$_2$*Me*); δ_C(100.6 MHz; $CDCl_3$) 138.4$^-$ ($^2J_{PC}$ 10.4, 9a or 11a-ArC), 137.3$^-$ ($^2J_{PC}$ 9.7, 9a or 11a-ArC), 134.3$^+$ (J_{PC} 5.7), 133.7$^+$ (J_{PC} 6.6), 133.5$^-$ ($^1J_{PC}$ 94.1, 4a or 5a-ArC), 132.48$^-$ ($^1J_{PC}$ 95.4, 4a or 5a-ArC), 132.45$^+$ (J_{PC} 11.7), 131.9$^+$ (J_{PC} 12.0), 131.3$^+$ ($^4J_{PC}$ 2.3, 2 or 8-ArC), 131.1$^+$ ($^4J_{PC}$ 2.3, 2 or 8-ArC), 128.4$^+$ (J_{PC} 10.8), 128.2$^+$ (J_{PC} 10.7), 86.3$^+$ (ArC_AHC$_B$HAr), 84.1$^+$ (ArC$_A$HC_BHAr), 56.78$^+$ (OMe$_A$), 56.74$^+$ (OMe$_B$), 37.7$^-$ ($^1J_{PC}$ 72.7, PCH$_2$), 15.9$^-$ ($^2J_{PC}$ 3.9, PCH$_2$*C*H$_2$) and 15.6$^+$ ($^3J_{PC}$ 16.8, CH$_2$*Me*); *m*/*z* 330 (35%, M$^+$), 315 (100, M − Me) and 287 (13, M − Pr) (Found: M$^+$, 330.1385. $C_{19}H_{23}O_3P$ requires *M*, 330.1385); $[a]_D^{17}$ −195 (*c* 1.01 in $CHCl_3$).

(10*R*,11*R*)-10,11-Isopropylidenedioxy-10,11-dihydro-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 40. (4*R*,5*R*)-2,2-Dimethyl-4,5-bis(2-bromophenyl)-1,3-dioxolane **15** (274 mg, 0.665 mmol) was reacted by a modified method C; THF (25 ml) was used as solvent. A solution of 9 : 1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 9 : 1) 0.49. Flash chromatography, eluting with EtOAc, gave the *phosphine oxide* (84 mg, 37%) as an oil, R_f(EtOAc) 0.25; ν_{max} ($CHCl_3$)/cm^{-1} 1593 (Ar), 1166 (P=O) and 1133 (C–O); δ_H(400 MHz; $CDCl_3$) 8.27–8.20 (2 H, m, 4 and 6-ArH), 7.81 (1 H, dd, *J* 7.6 and 4.4, 1 or 9-ArH), 7.71 (1 H, dd, *J* 7.7 and 4.7, 1 or 9-ArH), 7.60 (1 H, tt, *J* 7.6, J_{HH} 1.2 and J_{PH} 1.2), 7.53 (1 H, tt, *J* 7.5, J_{HH} 1.4 and J_{PH} 1.4), 7.48 (2 H, td, *J* 7.6 and 1.4), 5.29 (1 H, d, *J* 8.8, ArCH_ACH$_B$Ar), 4.84 (1 H, d, *J* 8.8, ArCH$_A$CH_BAr), 2.04–1.86 (2 H, m, PCH$_2$), 1.58 (3 H, s, OMe$_A$), 1.57 (3 H, s, OMe$_B$), 1.58–1.48 (1 H, m, PCH$_2$CH_A), 1.34–1.26 (1 H, m, PCH$_2$CH_B), 0.85 (3 H, td, *J* 7.2 and $^4J_{PH}$ 0.9, CH$_2$*Me*); δ_C(62.9 MHz; $CDCl_3$) 140.2$^-$ ($^2J_{PC}$ 11.1, 9a or 11a-ArC), 139.3$^-$ ($^2J_{PC}$ 9.9, 9a or 11a-ArC), 133.6$^+$ (J_{PC} 5.5), 132.70$^+$ (J_{PC} 6.7), 132.68$^+$ (2 or 8-ArC), 131.9$^+$ (J_{PC} 2.3, 2 or 8-ArC), 130.1$^-$ ($^1J_{PC}$ 90.1, 4a or 5a-ArC), 128.0$^-$ ($^1J_{PC}$ 89.8, 4a or 5a-ArC), 127.8$^+$ (J_{PC} 10.5), 127.7$^+$ (J_{PC} 10.5), 126.8$^+$ (J_{PC} 10.5), 123.2$^+$ (J_{PC} 10.6), 109.9$^-$ (OCO), 80.7$^+$ ($^3J_{PC}$ 0.9, 10 or 11-ArC), 79.5 ($^3J_{PC}$ 2.3, 10 or 11-ArC), 37.6$^-$ ($^1J_{PC}$ 71.8, PCH$_2$), 27.1$^+$ (C*Me*$_A$), 26.5$^+$ (C*Me*$_B$), 15.6$^-$ ($^2J_{PC}$ 4.1, PCH$_2$*C*H$_2$) and 15.3$^+$ ($^3J_{PC}$ 15.9, CH$_2$*Me*); *m*/*z* 342 (2%, M$^+$), 300 (10, M − MeCH=CH), 299 (11, M − Pr), 284 (47, M − Me_2CO) and 242 (100, M − MeCH=CH − Me_2CO) (Found: M$^+$, 342.1396. $C_{20}H_{23}O_3P$ requires *M*, 342.1385); $[a]_D^{26}$ +90.8 (*c* 0.85 in $CHCl_3$).

Phosphepine oxide **40** was also prepared by hydrolysis of the corresponding phosphonium salt **52**. Sodium hydroxide (1 ml of a 2 M solution) was added to phosphepinium iodide **52** (126 mg, 0.238 mmol) suspended in EtOH (2 ml). The mixture was refluxed for 18 h. Ethanol was evaporated under reduced pressure, water (5 ml) added and the mixture extracted with CH_2Cl_2 (3 × 15 ml). The combined extracts were dried ($MgSO_4$), evaporated under reduced pressure and the products separated by flash chromatography, eluting with EtOAc, to give the desired phosphine oxide **40** (40 mg, 49%) and, from endocyclic cleavage, phosphine oxide **53** (10 mg, 11%), R_f(EtOAc) 0.31; δ_C(62.9 MHz; $CDCl_3$) 138.9$^-$, 136.1$^-$, 133.4–126.5 ($^+$, several lines), 109.1$^-$ (OCO), 85.2$^+$ (ArC_AHC$_B$HAr), 79.7$^+$ (ArC$_A$HC_BHAr), 31.8$^-$ ($^1J_{PC}$ 72.0), 27.4$^+$ (C*Me*$_A$), 26.7$^+$ (C*Me*$_B$), 15.5$^+$ ($^3J_{PC}$ 15.6, PCH$_2$CH$_2$*Me*) and 15.0$^-$ (PCH$_2$*C*H$_2$).

(10*R*,11*R*)-10,11-Bis[(1,1-dimethylethyl)dimethylsiloxy]-10,11-dihydro-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 39. (1*R*,2*R*)-1,2-Bis(2-bromophenyl)-1,2-bis[(1,1-dimethylethyl)-dimethylsiloxy]ethane **13** (587 mg, 0.978 mmol) was reacted by method C. A solution of 9 : 1 hexane–Et_2O was used as eluent for purification of the phosphine, R_f(hexane–Et_2O, 9 : 1) 0.61. Flash chromatography, eluting with EtOAc yielded the *phosphine oxide* (127 mg, 24%) as waxy plates, mp 103–105 °C (from hexane), R_f(EtOAc) 0.51; ν_{max} ($CHCl_3$)/cm^{-1} 1592 (Ar), 1578 (Ar), 1256 (P=O) and 1094 (C–O); δ_H(400 MHz; $CDCl_3$) 8.32 (1 H, ddd, J_{PH} 12.3, *J* 6.4 and 2.6, 4 or 6-ArH), 8.25 (1 H, ddd, J_{PH} 12.2, *J* 6.5 and 2.5), 7.50–7.42 (4 H, m), 7.28–7.22 (2 H, m), 5.07 (1 H, d, *J* 7.7, ArCH_ACH$_B$Ar), 5.04 (1 H, d, *J* 7.7, ArCH$_A$CH_BAr), 2.08–1.95 (2 H, m, PCH$_2$), 1.60–1.47 (1 H, m, PCH$_2$CH_AH$_B$), 1.29–1.14 (1 H, m, PCH$_2$CH$_A$$H_B$), 0.82 (3 H, td, *J* 7.3 and J_{PH} 1.1, CH$_2$*Me*), 0.69 (9 H, s, Si$_A$C*Me*$_3$), 0.42 (9 H, s, Si$_B$C*Me*$_3$), −0.02 (3 H, s, SiMe$_A$), −0.04 (3 H, s, SiMe$_B$), −0.05 (3 H, s, SiMe$_C$) and −0.40 (3 H, s, SiMe$_D$); δ_C(100.6 MHz; $CDCl_3$) 141.0$^-$ (J_{PC} 9.8, 9a or 11a-ArC), 140.8$^-$ (J_{PC} 10.6, 9a or 11a-ArC), 134.1$^+$ (J_{PC} 5.9), 133.8$^+$ (J_{PC} 6.9), 133.1$^-$ (J_{PC} 94.5, 4a or 5a-ArC), 132.7$^-$ (J_{PC} 91.9, 4a or 5a-ArC), 131.9$^+$ (J_{PC} 11.9), 131.3$^+$ (J_{PC} 2.4, 2 or 8-ArC), 131.2$^+$ (J_{PC} 2.2, 2 or 8-ArC), 131.0$^+$ (J_{PC} 12.4), 127.8$^+$ (J_{PC} 11.0), 127.3$^+$ (J_{PC} 10.8), 80.1$^+$ (ArC_AHC$_B$HAr), 78.0$^+$ (ArC$_A$HC_BHAr), 38.4$^-$ ($^1J_{PC}$ 72.5, PCH$_2$), 25.7$^+$ (Si$_A$C*Me*$_3$), 25.2$^+$ (Si$_B$C*Me*$_3$), 18.2$^-$ (Si$_A$*C*Me$_3$), 17.6$^-$ (Si$_B$*C*Me$_3$), 15.6$^-$ ($^2J_{PC}$ 4.2, PCH$_2$*C*H$_2$), 15.3$^+$ ($^3J_{PC}$ 16.8, PCH$_2$CH$_2$*Me*), −4.5 (SiMe$_A$), −4.6 (SiMe$_B$) and −4.9 (SiMe$_C$ + SiMe$_D$, 2 × intensity implies 2 signals); *m*/*z* 530 (6.6%, M$^+$) and 473 (79, M − ^{t}Bu) (Found: M$^+$, 530.2780. $C_{29}H_{47}O_3PSi_2$ requires *M*, 530.2801); $[a]_D^{17}$ −165 (*c* 1.00 in $CHCl_3$).

Reactions of phosphepine oxides

(10*R*,11*R*)-10,11-Dihydro-10,11-dihydroxy-5-phenyl-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxide 41. The acetal **32** (155 mg, 0.412 mmol) and toluene-*p*-sulfonic acid (156 mg, 0.907 mmol) were stirred together overnight in water (1 ml) and ethylene glycol (5 ml) at 82 °C in a flask fitted with an air condenser. Water (5 ml) was added and the mixture extracted with dichloromethane (5 × 5 ml). Methanol (5 ml) was added to the extract which was dried ($MgSO_4$) and evaporated under reduced pressure. The solid was purified by flash chromatography, eluting with EtOAc to give the *diol* as prisms (97 mg, 70%), mp >130 °C (dec.) (from EtOH); R_f(EtOAc) 0.18; ν_{max} (KBr)/cm^{-1} 3288 (O–H), 1590 (Ar), 1437 (Ph–P) and 1159 (P=O); δ_H(400MHz; $CDCl_3$) 8.16 (1 H, td, *J* 7.8 and 1.3, 4 or 6-ArH), 8.13 (1 H, td, *J* 7.6 and 1.2, 4 or 6-ArH), 7.85 (1 H, dd, *J* 7.8 and 4.7, 1 or 9-ArH), 7.77 (1 H, dd, 7.8 and 4.8, 1 or 9-ArH), 7.63–7.56 (2 H, m), 7.51–7.43 (3 H, m), 7.38–7.35 (2 H, m), 5.00 (1 H, dd, *J* 9.7 and 3.1, HOCH_ACH$_B$OH), 4.84 (1 H, dd, *J* 9.7 and 4.6, HOCH$_A$CH_BOH), 3.54 (1 H, d, *J* 4.7, HOCH$_A$CH$_B$O*H*) and 3.49 (1 H, d, *J* 3.3, *H*OCH$_A$CH$_B$OH); δ_C(100.6 MHz; CD_3OD)¶¶¶¶ 145.1$^-$ (J_{PC} 11.3), 144.9$^-$ (J_{PC} 11.8), 135.8$^-$ ($^1J_{PC}$ 106.1), 134.2$^+$ (J_{PC} 1.7), 133.9$^+$ (J_{PC} 2.1), (133.5–133.4)$^+$, 133.2$^+$ (J_{PC} 12.2), 132.9$^+$ (J_{PC} 12.2), 131.8$^+$ (J_{PC} 11.0), 130.1$^-$ ($^1J_{PC}$ 102.2), 130.0$^+$ (J_{PC} 12.6), 129.1$^-$ ($^1J_{PC}$ 98.9), 128.8$^+$ (J_{PC} 10.6), 128.6$^+$ (J_{PC} 11.1), 128.2$^+$ (J_{PC} 11.5), 77.3$^+$ (C$_A$OH) and 73.2$^+$ ($^3J_{PC}$ 2.8, C$_B$OH); *m*/*z* 336 (11%, M$^+$), 318 (95, M − H_2O), 165 (100) and 77 (36, $C_6H_5^+$) (Found: M$^+$, 336.0913. $C_{20}H_{17}O_3P$ requires *M*, 336.0915); $[a]_D^{20.5}$ +87.4 (*c* 0.835 in MeOH).

In another experiment, the diol **41** was prepared by the desilylation of bis(silyl ether) **50**. Tetrabutylammonium fluoride

¶¶¶¶ Data compared with 50.3 MHz spectrum to determine coupling constants.

(800 μl of a 1 M solution in THF, 0.80 mmol) was added dropwise to solid bis(silyl ether) **50** (75 mg, 0.13 mmol). The mixture was stirred at room temperature for 30 min before H_2O (5 ml) was added and the mixture extracted with CH_2Cl_2 (5 × 5 ml). The combined extracts were dried ($MgSO_4$), evaporated under reduced pressure and the residue purified by flash chromatography, eluting with EtOAc followed by 1:19 MeOH–EtOAc, to give diol **41** (37 mg, 83%).

One diastereomer of 10,11-dihydro-5-{1-[(1,1-dimethylethyl)-dimethylsilyl]propyl}-5*H*-dibenzo[*b*,*f*]phosphepin-11-one-5-oxide 44

A solution of LDA was added dropwise to a solution of phosphine oxide **39** (13.6 mg, 0.0257 mmol) in dry THF under argon at −78 °C until a red colour persisted (15 μl of a 0.20 M solution in THF) followed by more LDA (128 μl of a 0.20 M solution in THF, 0.0256 mmol). After 15 min at −78 °C, methanol (100 ml) was added to the reaction mixture which was allowed to warm to 0 °C. Saturated NH_4Cl solution (1 ml) was added and THF was removed under reduced pressure. The remaining mixture was extracted with dichloromethane (3 × 5 ml), dried ($MgSO_4$) and purified by flash chromatography, eluting with 1:1 hexane–EtOAc, to give starting material (2 mg, 15%) and an oil which was tentatively identified as the title phosphine oxide (4 mg, 40%), R_f(EtOAc–hexane, 1:1) 0.32; δ_H(400 MHz; $CDCl_3$) 7.96 (1 H, ddd, $^3J_{PH}$ 12.2, *J* 7.4 and 1.5, 4 or 6-ArH), 7.66 (1 H, dd, *J* 10.4 and 7.2), 7.58 (1 H, dd, *J* 7.7 and 3.1), 7.45 (1 H, tt, *J* 7.5 and 1.3), 7.37–7.28 (3 H, m), 7.04 (1 H, dd, *J* 6.7 and 5.4), 3.28 (1 H, dd, *J* 17.5 and $^3J_{PH}$ 2.2, ArCH_A-H_BCO), 2.95 (1 H, d, *J* 17.5, ArCH$_A$$H_B$CO), 2.71 (1 H, ddd, $^2J_{PH}$ 19.3, *J* 11.7 and 1.4, PCH), 2.00–1.83 (1 H, m like ddqd, PCHCH_AH$_B$), 1.56–1.43 (1 H, m, PCHCH$_A$$H_B$), 1.20 (3 H, t, *J* 10.0), 1.05 (9 H, s, CMe_3), 0.18 (3 H, s, $SiMe_A$) and −0.08 (3 H, s, $SiMe_B$); δ_C(100.6 MHz; $CDCl_3$) 208.8$^-$ (CO), 149.4$^+$ ($^2J_{PC}$ 18.0, 9a or 11a-ArC), 138.5$^+$ ($^2J_{PC}$ 12.0, 9a or 11a-ArC), 135.2–123.3 ($^+$ and $^-$, several lines), 54.7$^+$ ($^1J_{PC}$ 62.0, PCH), 42.8$^-$ (Ar*C*H$_2$), 25.9$^+$ (C*Me*$_3$), 18.5$^-$ (*C*Me$_3$), 16.3$^-$ (PCH*C*H$_2$), 13.0$^+$ (PCHCH$_2$*Me*), −2.0$^-$ ($SiMe_A$) and −2.1 ($SiMe_B$); $[a]_D^{19}$ −118 (*c*. 0.12 in CH_2Cl_2).

In another experiment, LDA (165 μl of a 0.20 M solution in THF) was added to phosphine oxide **39** (15.8 mg, 0.0299 mmol) and, after 15 min at −78 °C, cyclohexanone (8.0 μl, 0.077 mmol) was added. The red colour of the solution persisted for 1.5 h after which time the reaction mixture was allowed to warm. When the reaction temperature reached −15 °C, the colour faded. The reaction was maintained at this temperature for 5 min, warmed to 0 °C and quenched with saturated NH_4Cl. The reaction mixture gave, after flash chromatography, starting material in a 23% yield and phosphine oxide **39** in a 43% yield.

4,6-Difluoro-10-methoxy-5-propyl-5*H*-dibenzo[*b*,*f*]phosphine 5-oxide 45. Lithium 2,2,6,6-tetramethylpiperidinide (LiTMP, 410 μl of a 0.20 M solution in THF, 0.082 mmol) was added dropwise to a solution of phosphine oxide **35** (30 mg, 0.082 mmol) in dry THF at −78 °C under argon. A red colour developed on addition of base. After stirring for 15 min at −78 °C, methanol (50 μl, 1.2 mmol) was added followed immediately by saturated NH_4Cl (1 ml). The THF was removed under reduced pressure and the resulting mixture extracted with CH_2Cl_2 (3 × 5 ml). The combined extracts were dried and purified by flash chromatography, eluting with 1:19 methanol–EtOAc, to give starting material (14 mg, 47%), and an oil which was tentatively identified as the title phosphine oxide (6 mg, 22%), R_f(MeOH-EtOAc, 1:19) 0.37; δ_H(400 MHz; $CDCl_3$) 7.65 (1 H, ddd, *J* 7.9, 2.5 and 1.1), 7.46 (1 H, td, *J* 10.2 and 5.5), 7.36 (1 H, tdd, *J* 7.9, 5.6 and 0.6), 7.19–7.13 (2 H, m), 7.02–6.96 (1 H, m), 6.43 (1 H, s, C*H*COMe), 3.93 (3 H, s, CHCO*Me*), 2.65–2.55 (2 H, m, PCH_2), 1.95–1.80 (2 H, m , PCH_2CH_2) and 1.13 (3 H, t, *J* 6.7, CH_2Me).

(10*R*,11*R*)-10,11-Bis[(1,1-dimethylethyl)dimethylsiloxy]-10,11-dihydro-5-[(1*RS*)-1-(1-hydroxycyclobutyl)propyl]-5*H*-dibenzo[*b*,*f*]phosphepine 5-oxides 46a and 46b. A solution of 2,2,6,6-lithium tetramethylpiperidinide (535 μl of a 0.2 M solution in THF, 0.107 mmol) was added dropwise to a solution of phosphine oxide **39** (56 mg, 0.106 mmol) in dry THF (1.5 ml) under argon at −78 °C. After 90 seconds at −78 °C, cyclobutanone (12 μl, 0.16 mmol) was added. The deep red colour which had developed with the addition of base, disappeared upon the addition of cyclobutanone. After 15 min at −78 °C, methanol (0.5 ml) was added followed by saturated NH_4Cl (0.5 ml). The THF was removed under reduced pressure and the remaining mixture extracted with dichloromethane (3 × 5 ml), dried ($MgSO_4$) and purified by flash chromatography, eluting with 1:1 hexane–EtOAc, to give starting material (36 mg, 64%) and a mixture of mostly silyl transfer product **44** (7.9 mg, 19%) with two products which were tentatively identified as the title compounds in the ratio 37:63 (5.1 mg, 8%). The latter two products were identified by characteristic ^{1}H NMR signals of δ_H(400 MHz; $CDCl_3$) 5.18 (1 H^{37}, d, *J* 7.3, ArCH_ACH$_B$Ar), 5.16 (1 H,^{63} d, *J* 6.7, ArCH_ACH$_B$Ar), 5.07 (1 H^{63}, d, *J* 6.7, ArCH$_A$-CH_BAr) and 4.98 (1 H,^{37} d, *J* 7.3, ArCH$_A$CH_BAr). Attempts to further purify this mixture led to the isolation of one compound, δ_H(400 MHz; $CDCl_3$) 8.31 (1 H, dd, $^3J_{PH}$ 12.8 and *J* 7.3, 4 or 6-ArH), 8.22 (1 H, dd, $^3J_{PH}$ 11.5 and *J* 7.5, 4 or 6-ArH), 7.72–7.69 (1 H, m), 7.53–7.38 (5 H, m), 5.57 (1 H, s, OH), 5.16 (1 H, d, *J* 6.7, ArCH_ACH$_B$Ar), 5.07 (1 H, d, *J* 6.7, ArCH$_A$CH_B-Ar), 2.81 (1 H, dt, *J* 8.0 and 6.3, PCH), 1.80–1.20 (8 H, m), 0.90 (9 H, s, C$_A$Me$_3$), 0.64 (3 H, t, *J* 7.5, CH_2Me), 0.58 (9 H, s, C$_B$Me$_3$), 0.14 (3 H, s, $SiMe_A$), 0.06 (6 H, s, $SiMe_B$ and $SiMe_C$) and −0.37 (3 H, s, $SiMe_D$).

Formation of phosphepinium salts

(10*R*,11*R*)-4,6-Difluoro-10,11-dimethoxy-10,11-dihydro-5-phenyl-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepin-5-ium iodide 54. Phosphine oxide **30** (98 mg, 0.245 mmol), PMHS (110 μl, 1.84 mmol of hydride) and titanium(IV) tetraisopropoxide (75 μl, 0.252 mmol) were refluxed together in dry THF (1 ml) for 2.5 h. Propyl iodide (1 ml, 10.3 mmol) was added and the reaction mixture was refluxed overnight, cooled and hexane (2 ml) was added. The precipitate was filtered from the supernatant and washed with hexane to give the *phosphonium salt* (121 mg, 89%) as a yellow powder, δ_H(400 MHz; $CDCl_3$) 7.90–7.85 (1 H, m), 7.82–7.77 (4 H, m), 7.71–7.64 (2 H, m), 7.57–7.53 (2 H, m), 7.30–7.20 (2 H, m), 5.47 (2 H, AB signal—singlet with side bands, *J* 9.9, ArCH_ACH_BAr), 3.44–3.32 (1 H, m, PCH_A), 3.27 (3 H, s, OMe_A), 3.26 (3 H, s, OMe_B), 3.02–2.95 (1 H, m, PCH_B), 1.61–1.45 (2 H, m, PCH_2CH_2) and 1.08 (3 H, td, *J* 7.2 and $^4J_{PH}$ 1.6, CH_2Me); δ_C(100.6 MHz; $CDCl_3$) 163.84$^-$ ($^1J_{CF}$ 252.8, 4 or 6-ArC), 163.79$^-$ ($^1J_{CF}$ 243.2, 4 or 6-ArC), 144.9$^-$ (9a or 11a-ArC), 143.7$^-$ (9a or 11a-ArC), 137.6$^+$ (*J* 9.3), 137.2$^+$ (*J* 9.7), 134.1$^+$, 131.0$^+$ (*J* 11.0), 130.4–129.8 ($^+$, 6 lines), 117.8–117.3 ($^+$, 5 lines), 82.6$^+$ (Ar*C*$_A$HC$_B$HAr), 82.4$^+$ (ArC$_A$H*C*$_B$-HAr), 57.71$^+$ (OMe_A), 57.66$^+$ (OMe_B), 26.5$^-$ ($^1J_{PC}$ 72.3, PCH_2), 16.4$^-$ ($^2J_{PC}$ 3.4, PCH_2CH_2) and 15.5$^+$ ($^3J_{PC}$ 18.5, PCH_2CH_2Me); *m*/*z* 427 (100%, M$^+$) (Found by +FAB: M$^+$, 427.16410. Cation $C_{25}H_{26}F_2O_2P$ requires *M*, 427.16384).

(10*R*,11*R*)-10,11-Isopropylidenedioxy-10,11-dihydro-5-phenyl-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepin-5-ium iodide 52. Phosphine oxide **32** (200 mg, 0.532 mmol) was dissolved in THF (1 ml). Titanium(IV) tetraisopropoxide (220 μl, 0.740 mmol) and PMHS (325 μl, 5.44 mmol of hydride) were added to the phosphine oxide solution and the mixture was refluxed for 1 h 45 min after which time TLC indicated that there was no remaining phosphine oxide. Propyl iodide (1 ml, 10.3 mmol) was added and the mixture refluxed for 4 h. Hexane (3 ml) was added and the mixture allowed to cool, filtered, and the filter cake washed with hexane to give the *phosphonium salt* (219 mg,

78%) as a brown powder, δ_H(400 MHz; $CDCl_3$) 8.48 (1 H, ddd, $^3J_{PH}$ 14.3, *J* 7.7 and 0.9, 4 or 6-ArH), 8.03 (1 H, dd, *J* 7.7 and $^4J_{PH}$, 1 or 9-ArH), 7.98–7.56 (11 H, m), 5.16 (2 H, AB m, $ArCH_ACH_BAr$), 4.05 (1 H, dtd, *J* 15.8, 11.1 and 4.7, PCH_A-CH_B), 3.50 (1 H, dtd, *J* 16.0, 11.4 and 4.7, PCH_ACH_B), 1.61 (3 H, s, $OCMe_A$), 1.57 (3 H, s, $OCMe_B$), 1.55–1.42 (2 H, m, PCH_2CH_2) and 1.18 (3 H, td, *J* 7.2 and $^4J_{PH}$ 1.6, CH_2Me) (Found by +FAB: M^+, 403.18270. Cation $C_{26}H_{28}O_2P$ requires *M*, 403.18268).

(10*R*,11*R*)-10,11-Bis[(1,1-dimethylethyl)dimethylsiloxy]-10,11-dihydro-5-phenyl-5-propyl-5*H*-dibenzo[*b*,*f*]phosphepin-5-ium iodide 51. Phosphine oxide **50** (203 mg, 0.360 mmol) was dried by removing any residual water as an azeotrope with toluene and dissolved in dry THF (1 ml). Titanium(IV) tetraisopropoxide (110 μl, 0.370 mmol) and PMHS (215 μl, 3.60 mmol of hydride) were added to the phosphine oxide solution which was refluxed for 2 h. Propyl iodide (500 μl, 5.1 mmol) was added and the reaction mixture was refluxed overnight. The mixture was cooled and hexane was added. Volatile materials were removed under reduced pressure and hexane was added to the residue. The resulting precipitate was filtered from the supernatant and washed with hexane to give a yellow solid (408 mg). Water was added to the solid and the mixture extracted with CH_2Cl_2 (×3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the pure *phosphonium salt* (212 mg, 80%) identified by ^{1}H NMR, δ_H(400MHz; $CDCl_3$); 8.25 (1 H, ddd, $^3J_{PH}$ 15.2, *J* 5.7 and 3.4, 4 or 6-ArH), 8.13 (2 H, ddd, $^3J_{PH}$ 12.8, *J* 7.8 and 1.5, *o*-PhH), 7.71–7.51 (8 H, m, ArH), 7.44 (1 H, dd, *J* 7.4 and $^4J_{PH}$ 4.5, 1 or 9-ArH), 7.36 (1 H, dd, *J* 9.3 and $^4J_{PH}$ 5.0, 1 or 9-ArH), 5.25 (2 H, AB q, *J* 8.2, $ArCH_ACH_BAr$), 3.66 (1 H, dtd, *J* 15.5, 11.8 and 4.3, PCH_A-CH_B), 3.26 (1 H, dtd, *J* 15.5, 12.6 and 4.5, PCH_ACH_B), 1.66–1.52 (1 H, m, $PCH_2CH_ACH_B$), 1.42–1.27 (1 H, m, PCH_2CH_A-CH_B), 1.13 (3 H, td, *J* 7.2 and $^4J_{PH}$ 1.7, $PCH_2CH_2CH_3$), 0.63 (9 H, s, $Si_A{}^tBu$), 0.54 (9 H, s, $Si_B{}^tBu$), −0.02 (3 H, s, $SiMe_A$), −0.05 (3 H, s, $SiMe_B$), −0.08 (3 H, s, $SiMe_C$) and −0.16 (3 H, s, $SiMe_D$).

Attempt to make phosphepine oxide 35 by hydrolysis of phosphonium iodide 54. Phosphonium iodide **54** was stirred in a solution of ethanol (1.5 ml) and NaOH (1 ml of a 2 M solution) at 86 °C overnight and then refluxed for 5 h. Ethanol was removed under reduced pressure. Water (2 ml) was added and the mixture was extracted with CH_2Cl_2 (4 × 2 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The products in the resulting residue were separated by flash chromatography, eluting with 1:1 hexane–EtOAc to yield phosphine oxide **55a** (9 mg, 17%), R_f(EtOAc–hexane, 1:1) 0.42; δ_H(250 MHz; $CDCl_3$) 7.73–7.63 (3 H, m), 7.56–7.26 (7 H, m), 7.10–6.90 (2 H, m), 5.57 (1 H, slightly br s, $ArCH_ACH_BAr$), 4.68 (1 H, d, *J* 2.2, $ArCH_ACH_BAr$), 3.15 (3 H, s, OMe_A), 2.67 (3 H, s, OMe_B), 2.50–2.20 (2 H, m, PCH_2), 1.81–1.65 (2 H, m, PCH_2CH_2), 1.06 (3 H, td, *J* 7.2 and $^4J_{PH}$ 1.0, PCH_2CH_2Me) and phosphine oxide **55b** (28 mg, 54%), R_f(EtOAc–hexane, 1:1) 0.31; δ_H(400 MHz; $CDCl_3$) 7.73–7.68 (3 H, m), 7.57–7.41 (4 H, m), 7.32 (1 H, d, *J* 7.7), 7.24–7.18 (2 H, m), 7.01 (1 H, ddd, *J* 10.6, 8.2 and 4.2), 6.87 (1 H, td, *J* 8.6 and 2.5), 6.20 (1 H, d, *J* 2.6, $ArCH_ACH_BAr$), 4.42 (1 H, d, *J* 2.6, $ArCH_ACH_BAr$), 3.16 (3 H, s, OMe_A), 2.90 (3 H, s, OMe_B), 2.48–2.29 (2 H, m, PCH_2), 1.87–1.73 (1 H, br m, PCH_2CH_A), 1.66–1.51 (1 H, br m, PCH_2CH_B) and 1.03 (3 H, t, *J* 7.3, PCH_2-CH_2Me); δ_F(235 MHz; $CDCl_3$; ^{1}H coupled) −98.9 to −98.9 (1 F, m) and −114.2 to −114.4 (1 F, m).

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