Reaction of Metallated *tert*-Butyl(phenyl)phosphane Oxide with Electrophiles as a Route to Functionalized Tertiary Phosphane Oxides: Alkylation Reactions

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P-Chiral tertiary phosphane oxides have been prepared from each of the secondary phosphane oxides racemic **1**, (S_P)-(–)-**4** and (R_P)-(+)-*tert*-butylphenylphosphane oxide (**5**) by lithiation with LDA or *n*BuLi, or sodiation with sodium hydride, in THF, and then by treatment with a series of primary alkyl halides. Doubly *P*-chiral ditertiary bis(phosphane oxides) are also obtained from these metallated secondary phosphane oxides by treatment with electrophiles based on straight-chain, tartrate-derived, and bishalomethylarene dihalides. In general, the bis-phosphane oxides are obtained in good yields. However, when the α,ω-dihalide bears an embedded heteroatom (O or Si), yields are diminished. The enantiomeric purity of each of the products was assessed through admixture with (R_P)- and (S_P)-*tert*-butyl(phenyl)phosphanylthioic acids and measurement of the *tert*-butyl resonances in the ^{1}H-NMR spectra. In all cases, the act of metallation of the enantiomerically pure secondary phosphane oxide followed by its alkylation is not accompanied by detectable racemization. This method for preparing *P*-chiral tertiary phosphane oxides is therefore more straightforward than those described previously.

Introduction

Asymmetric catalysis has a vital role in pharmaceutical and chemical industries in providing enantiomerically pure compounds.[1] Chiral phosphanes, which constitute the main family of ligands for catalysis, have chirality that is normally resident in the backbone[2–5] or, less commonly, at the phosphorus atom.[6] The classic method to prepare the latter, potentially more valuable class, is based on the method of Mislow.[6] This method, involving resolution of diastereoisomeric menthyl phosphinates and displacement of the menthyl group by an organometallic nucleophile, has grown into a general method for the preparation of *P*-chiral phosphane oxides.[7,8] Stereoselective reduction of the tertiary phosphane oxides with silane-based or other reagents then provides the phosphane.[7,9] However, nucleophilic displacements involving phosphinates are sensitive to the structural variation of groups both attached to the phosphorus atom and within the organometallic nucleophile, to the nature of the metal counterion in the organometallic nucleophile, and to the nature of the ester leaving group.[7,10]

Because of these problems, attention has been focussed on converting menthyl phosphinates into nucleophilic phosphorus equivalents, such as secondary phosphane oxides, by reductive removal of the menthyl group. Whilst the use of hydride from LAH to displace the menthyl group from the menthyl phosphinate results in substantial racemization,[11,12] the use of lithium 4,4′-di-*tert*-butylbiphenylide in THF provides a lithiated secondary phosphane oxide whose treatment in situ with alkylating agents gives enantiomerically pure tertiary phosphane oxides with retention of configuration at the phosphorus atom.[13] In related fashion, selenium–lithium exchange on a chiral selenophosphinate precursor provides a lithiated secondary phosphane oxide whose alkylation proceeds with retention of configuration.[14] *O*-Alkyl groups are also reductively cleaved in stereoselective fashion from phosphane–borane complexes of menthyl phosphinites.[15] The resulting secondary phosphane–boranes can be alkylated in situ and then deprotected by triethylamine to provide the tertiary phosphanes. Secondary *O*-alkyl phosphinites, on the other hand, do not maintain their configuration during metallation with sodium hydride and alkylation.[16]

Whilst optically active secondary phosphane oxides appear to be stable in basic neutral protic solutions, they have been reported to be racemized by mineral acids.[12] Nevertheless, based on the literature precedents described above involving generation in situ and stereoselective alkylation of lithiated secondary phosphane oxides,[13,14] we were confident of developing a general approach to *P*-chiral tertiary phosphane oxides from secondary phosphane oxides by simple deprotonation of the latter under aprotic conditions,

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and treatment of the metallated reagent with the appropriate electrophile. In other words, we considered that the general application of the methodology involving aprotic conditions for generation and reaction of metallated reagents, which has so revolutionized enolate and aldol chemistry over the past three decades, to organophosphorus chemistry should provide substantially improved routes to functionalized tertiary phosphane oxides, with abundant opportunity for stereocontrol in appropriate circumstances.

We now describe in detail the preparation of tertiary phosphane oxides by alkylation of the metallated secondary phosphane oxides. In succeeding papers, we describe the reactions of the metallated secondary phosphane oxides with carbonyl compounds and imines, and of metallated tertiary alkyl phosphane oxides derived from the metallated secondary phosphane oxides with carbonyl compounds. Preliminary communications involving early aspects of these works have appeared.[17,18]

Results and Discussion

Racemic *tert*-butyl(phenyl)phosphanylthioic acid was prepared from racemic *tert*-butyl(phenyl)phosphane oxide (**1**),[19] and resolved on a 100-g scale. The enantiomeric phosphanylthioic acids **2** and **3** were desulfurized by means of Raney nickel under ultrasound irradiation at room temperature to provide the secondary phosphane oxides **4** and **5** (Scheme 1). Desulfurization in the absence of ultrasound irradiation resulted in substantial racemization, as previously noted.[17] Related desulfurisation in the absence of ultrasound was reported some time ago.[20] An assay of the enantiomeric purity of the secondary phosphane oxides through admixture with the phosphanylthioic acids **2** and **3** was carried out as previously described.[17,21,22] It should be pointed out here that a promising, more direct method of resolving racemic *tert*-butyl(phenyl)phosphane oxide (**1**), which does not require derivatisation of the racemic secondary phosphane oxide, has recently been reported, but the method has to be developed further so that it may deliver resolved material with high enantiomeric purities; such a method has not been used here.[23]

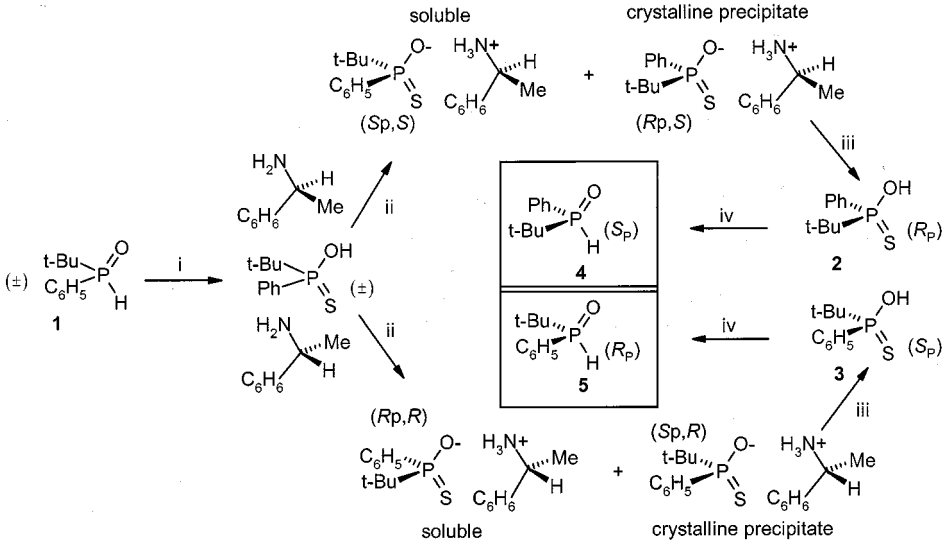
Alkylation of the Metallated Secondary Phosphane Oxides

Preparation of Tertiary Phosphane Oxides

As indicated above, the use of groups with a nucleophilic phosphorus atom to prepare *P*-chiral tertiary phosphane oxides relies on reductive or transmetallation methods to generate the metallated secondary phosphane oxide. We show here that *P*-chiral tertiary phosphane oxides are readily accessible through direct deprotonation of (S_P)- and (R_P)-*tert*-butyl(phenyl)phosphane oxide (**4** and **5**) and nucleophilic substitution of the metallated reagents with primary alkyl halides under aprotic conditions.

Lithiation of each of **1**, **4**, and **5** with LDA in THF at −78 °C and treatment with primary alkyl bromides and iodides furnished the alkylation products without loss of optical purities, as indicated by the NMR assay method[17,21] (Table 1). Whilst most alkylations proceeded smoothly, reaction with benzyl bromide was complicated by formation of diastereomers of the dialkylation product **9** (10−20%) arising through deprotonation and alkylation of the product **8** in the reaction mixture. The configurational integrity of the secondary phosphane oxides **4** and **5** is strictly maintained during the alkylation reactions, as illustrated by direct comparison of the data for compounds **15** and **22** with literature data (Table 1).

We also found that NaH in THF may be used to deprotonate the secondary phosphane oxides, and the products are obtained without detectable racemization. Thus, treatment of the (*S*)-phosphane oxide **4** with NaH at 0 °C in THF followed by treatment with methyl iodide gave the (*S*)-*tert*-butyl(methyl)phenylphosphane oxide **15** in very good



Scheme 1

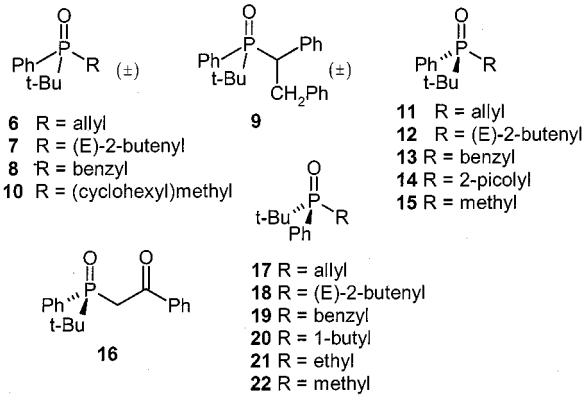
Table 1. Tertiary phosphane oxides from the reactions of metallated *tert*-butyl(phenyl)phosphane oxides **1**, **4**, and **5** with alkyl halides

Entry	**1**-, **4**-, or **5**-M	Alkyl halide	Product[a]	Yield (%)	M.p. [°C]	$[\alpha]_D^{20}$
1	**1**-Li	3-bromo-1-propene	**6**	57	71−73	−
2	**1**-Li	(*E*)-1-bromo-2-butene	**7**	81	95−97	−
3	**1**-Li	benzyl bromide	**8**	70	193−195	−
			9	9	162−165[b]	−
4	**1**-Li	(bromomethyl)cyclohexane	**10**	82	114−115	−
5	**4**-Li	3-bromo-1-propene	**11**	57	71−73	+30.5 (c = 1.47, MeOH)
6	**4**-Li	(*E*)-1-bromo-2-butene	**12**	78	102−103	+39.5 (c = 1.10, $CHCl_3$)
7	**4**-Li	benzyl bromide	**13**	68	182−184	+110.5 (c = 1.08, $CHCl_3$)
8	**4**-Li	2-(chloromethyl)pyridine	**14**	75	178−179	−40.4 (c = 0.88, $CHCl_3$)
9	**4**-Li	iodomethane	**15**	54	99−100	−23.5 (c = 1.17, MeOH)[c]
10	**4**-Na	iodomethane	**15**	95	99−100	−23.2 (c = 0.82, MeOH)
11	**4**-Na	α-chloroacetophenone	**16**	72	118−119	+104 (c = 4.41, $CHCl_3$)
12	**5**-Li	3-bromo-1-propene	**17**	56	71−73	−31.8 (c = 1.53, MeOH)
13	**5**-Li	(*E*)-1-bromo-2-butene	**18**	80	102−103	−39.6 (c = 1.15, $CHCl_3$)
14	**5**-Li	benzyl bromide	**19**	59	180−184	−111.7 (c = 1.17, $CHCl_3$)
15	**5**-Li	1-bromobutane	**20**	68	108−109	+32.4 (c = 1.32, MeOH)
16	**5**-Li	iodoethane	**21**	72	103−104	+28.1 (c = 1.32, MeOH)
17	**5**-Li	iodomethane	**22**	52	99−100	+23.1 (c = 1.57, MeOH)[d]

[a] Where appropriate, phosphane oxides were assayed by ^{1}H NMR spectroscopy at 300 MHz for enantiomeric purity; in each case the other enantiomer could not be detected, indicating a content of the major enantiomer of ca. 99.6%.[17] − [b] Crystalline compound is a single diastereomer obtained from a mixture of diastereomers. − [c] Ref.[22] $[\alpha]_D^{20} = -21.8$ (c = 1.0, MeOH). − [d] Ref.[22] $[\alpha]_D^{20} = +22.7$ (c = 1.0, MeOH).

yield (95%). The reaction with α-chloroacetophenone is particularly noteworthy in that it provides in good yield the chiral analogue **16** of dibenzoylmethane, a well-known ligand capable of forming anionic complexes with main-group and transition metals.

Some limitations to the use of alkylating agents were apparent. Reactions of the lithiated phosphane oxides with secondary halides such as cyclohexyl bromide or 2-bromobutane were unsuccessful and the starting secondary phosphane oxide (62−68%) was recovered, together with alkenes (12−14%) resulting from elimination. Equally, the lithiated phosphane oxides displayed no tendency to react with S_N1-active, hindered electrophiles such as fluorenyl chloride or mesylate.



Preparation of Ditertiary Bis(phosphane oxides)

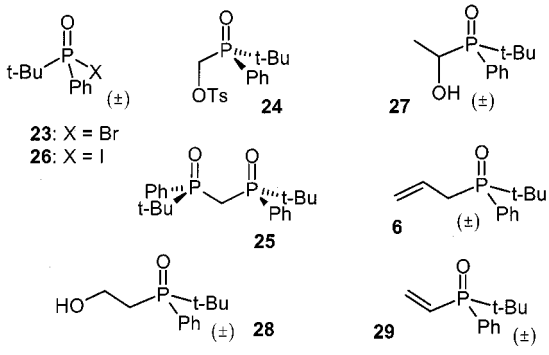
The potential value of bis(phosphane oxides) is underscored by the widespread use of the corresponding bis(phosphanes) as ligands in asymmetric catalysis, and the ability of the bis(phosphane oxides) to form stable complexes with metal ions.[24] We therefore probed reactions of metallated **1**, **4**, and **5** with primary α,ω-alkanediyl dihalides and vinylphosphane oxides as a means of obtaining these compounds.

A solution of **1**-Li in THF at −78 °C with dibromoethane gave only compound **23** (78%). In addition, we were not able to induce reactions of the metallated secondary phosphane oxides with (α-tosyloxymethyl)phosphane oxides such as compound **24**.[25] Thus, the putative doubly *P*-chiral analogues such as compound **25** of the anionic acac ligands could not be obtained in this way, although the compound has been prepared by a different approach, as will be described in a later paper.[25] In this case, a reaction analogy with the normally unsuccessful S_N2 displacement on neopentyl systems is apparent.

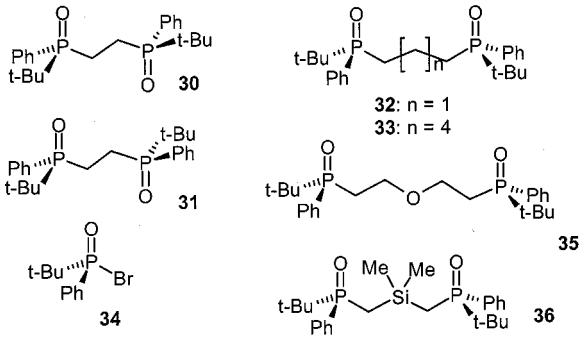
Initial attempts to prepare the bis(phosphane oxide) **30**[24] by reaction of **1**-Li in THF at −78 °C with diiodoethane resulted in the formation of compound **26** (78%). No reaction took place with ethane-1,2-diyl ditosylate. Thus, conjugate addition of **4**-Li to the racemic vinylphosphane oxide **29** was employed. It is noted that a complementary reaction has been reported previously − that of the thermal addition of a racemic neutral secondary phosphane oxide to (S_P)-methyl(phenyl)vinylphosphane oxide in toluene to generate mixtures of diastereomers that are separable by chromatography.[26] Although neutral **4** and **5** are stable during routine manipulation at room temperature, they do undergo oxidation upon chromatography or upon protracted storage in contact with the atmosphere. We were therefore anxious to conduct the conjugate addition under the mildest conditions possible by using the lithiated reagents.

Whilst attempted thermal elimination of the *S*-methylthionothio- or *S*-phenylthionocarbonate derivatives of the racemic α-hydroxyphosphane oxide **27**[27] did not succeed in providing **29**, the latter was prepared from the β-hydroxyphosphane **28**. Although it was not possible to prepare **28** from **1**-Li and ethylene oxide,[27] it was obtained from the

allylphosphane oxide **6** either by dihydroxylation followed by glycol cleavage and reduction of the resulting aldehyde with sodium tetrahydroboroate (42%), or by ozonolysis/reduction (86%). Tosylation of **28** and elimination of tosylate with DBU gave **29** (64% from **28**), whose treatment with **4**-Li in THF at −78 °C resulted in clean conversion into the (S_P,S_P)-bis(phosphane oxide) **30** (39%) and the *meso* compound **31** (39%), which were separated by chromatography. As noted elsewhere,[24] crystallization and melting of **30** is sensitive to traces of water, and optical rotation data were taken on a sample dried under vacuum. It is to be noted that initial data reported in our preliminary communications[18] did not take into account the effect of hydration on melting points and optical rotations.



In contrast to the reactions with dihaloethanes, longer chain dihalides reacted with **5**-Li in THF at −78 °C to give the bis(phosphane oxides) **32** and **33** in acceptable yields (52−58%), together with varying amounts of compound **34** (Table 2, below). Use of bis(2-chloroethyl) ether and bis(chloromethyl)dimethylsilane as electrophiles provided products **35** (23%) and **36** (36%) (Table 2).



However, formation of the methylated phosphane oxide **22** (Table 1) competed in the case of 1,3-bis(chloromethyl)-dimethylsilane, and was the only product identified from 1,3-bis(chloromethyl)tetramethyldisiloxane.[28]

The lithiated secondary phosphane oxides failed to react with secondary dihalides such as 1,2-diiodocyclohexane and 2,5-dibromopentane. In the latter case, the starting phosphane oxide (76%) and a small amount of compound **23** (9%) were recovered when **1**-Li was used.

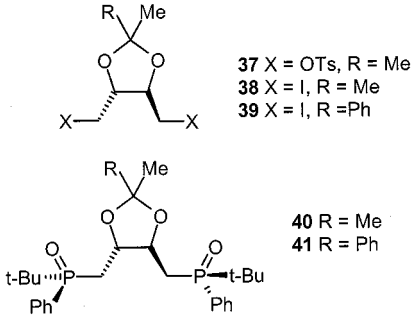
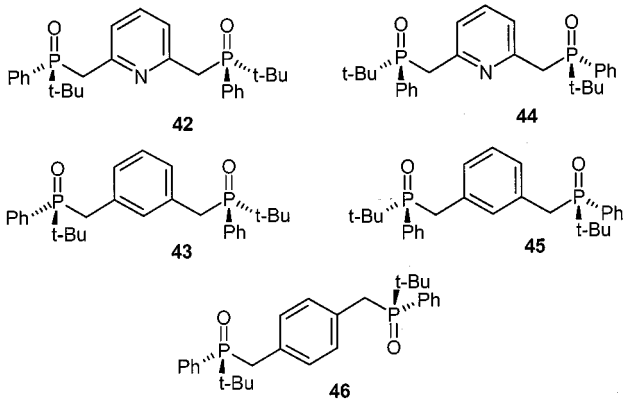


Table 2. Bis(phosphane oxides) from the reactions of lithiated *tert*-butyl(phenyl)phosphane oxides **1**, **4**, and **5** with alkyl dihalides and vinylphosphane oxide

Entry	**1**-, **4**-, or **5**-Li	Electrophile	Products	Yield (%)	M.p. [°C]	$[\alpha]_D^{20}$
1	**1**	1,2-dibromoethane	**23**	78	71−73	−
2	**1**	1,2-diiodoethane	**26**	78	decomp.	−
3	**4**	(±)-*tert*-butyl(phenyl)vinylphosphane oxide (**29**)	**30**	39	121−122	−62.4 (c = 1.12, $CHCl_3$)[a]
			31	39	133−134	−
4	**5**	1,3-dibromopropane	**32**	52	114−117	+60.0 (c = 1.01, $CHCl_3$)
			34	16		
5	**5**	1,6-dibromohexane	**33**	58	118−119	+65.0 (c = 1.3, $CHCl_3$)
			34	11		
6	**5**	bis(2-chloroethyl) ether	**35**	23	112−113	+58.2 (c = 1.03, $CHCl_3$)
7	**5**	bis(chloromethyl)dimethylsilane	**36**[b]	ca. 36[c]	103−104	+62.5 (c = 1.28, $CHCl_3$)
			22[b] [c]	ca. 36[c]	−[d]	−[d]
8	**5**	1,3-bis(chloromethyl)tetramethyldisiloxane	**22**[b]	76	−[d]	−[d]
9	**5**	**38**	**40**	8	140−141	+18.7 (c = 1.96, $CHCl_3$)
10	**5**	**39**	**41**	71	153−154	−9.2 (c = 2.38, $CHCl_3$)
11	**4**	2,6-bis(chloromethyl)pyridine	**42**	77	169−170	−30.6 (c = 1.08, $CHCl_3$)
12	**5**	2,6-bis(chloromethyl)pyridine	**44**	78	167−168	+30.8 (c = 1.05, $CHCl_3$)
13	**4**	1,3-bis(bromomethyl)benzene	**43**	81	70−71	−103.3 (c = 1.35, $CHCl_3$)
14	**5**	1,3-bis(bromomethyl)benzene	**45**	89	70−71	+102.0 (c = 1.25, $CHCl_3$)
15	**4**	1,4-bis(bromomethyl)benzene	**46**	54	277−278	−75 (c = 0.46, $CHCl_3$)

[a] Ref.[24] for anhydrous (R_PR_P) enantiomer: m.p. 192−193 °C, $[\alpha]_D^{20}$ = +36.8 (c = 0.98, MeOH). − [b] Product isolated by HPLC. − [c] Yields estimated by NMR spectroscopy. − [d] Not determined.

Chiral bis(phosphanes) with achiral phosphorus atoms but with a chiral carbon backbone are the easiest to prepare. One of the most useful is DIOP, which is prepared commercially by the reaction of lithium diphenylphosphide with tartrate-based ditosylate **37**.[4] The insertion of *P*-chirality into such ligands is of considerable interest, and has been addressed previously with rather limited success.[29] We thus examined the behaviour of **4**-Li and **5**-Li with tartrate-derived electrophiles. However, whilst the ditosylate **37** did not react with **5**-Li, the diiodide **38** gave the bis(phosphane oxide) **40**, albeit in low yield (8%). Competing decomposition of the diiodide was apparent. However, use of the diiodo methyl phenyl ketonide **39** instead of the acetonide **38** gave the diphosphane dioxide **41** in good yield (71%). Notably, the enantiomer of the lithiated (R_P) reagent, **5**-Li, namely the lithiated (S_P) reagent **4**-Li, did not react with **39**. In an attempt to exploit the lack of reactivity of **4**-Li with **39** in a kinetic resolution experiment with **1**-Li, it was found that reaction of 1 equiv. of **1**-Li with 0.5 equiv. of diiodide **39** in THF at −78 °C under nitrogen gave recovered secondary phosphane oxide with 54% *ee* with respect to **4**, while reaction with 0.4 equiv. of diiodide provided secondary phosphane oxide with 66% *ee* with respect to **4**.



Treatment of **4**-Li and **5**-Li with bis(halomethyl)arene electrophiles in THF at −78 °C afforded the bis(phosphane oxides) **42**−**46** (54−81%, Table 2). All enantiomers were assayed by ^{1}H-NMR spectroscopy at 300 MHz for enantiomeric purity by admixture with each of the (R_P)- and (S_P)-phosphanylthioic acids **2** and **3**. It was difficult to obtain crystalline samples of the pyridinediylbis(methylphosphane oxides) **42** and **44**. Whilst initial crops of crystals could be obtained from EtOAc, solutions had to be protected from the atmosphere in order to prevent uptake of water and formation of a second phase, apparently due to hydrated phosphane oxide, in concentrated solutions. If crystals were obtained, these rapidly lost crystal shape, but did not deliquesce. A ^{1}H-NMR spectrum of these crystals obtained after exposure to the atmosphere indicated the presence of water. Thus, specific rotations were taken on crystalline samples dried under vacuum. Here also, initial data were reported that did not take the hydration into account.[18]

Conclusion

The alkylation of lithiated *P*-chiral secondary phosphane oxides is demonstrated to be straightforward, and does not cause identifiable racemization. Whilst it was initially thought that the presence of the lithium counterion is important in ensuring that racemization of the secondary phosphane oxides does not take place during metallation and alkylation, the successful experiments in which NaH is used as the metallating agent illustrates that this is not the case. As we will report in detail shortly, stereoselective reactions with carbonyl compounds may also be carried out with the sodiated secondary phosphane oxides; we defer discussion on the nature of the metallated species as either a P^{III}-metallated phosphinite or the P^{V}-metallated phosphane oxide to the later publication. Suffice to say here that the corresponding intermediates obtained by reductive lithiation of phosphinates and selenophosphinates are depicted as P^{III}-metallated phosphinates.[13,14]

The current methodology represents an advance over the use of specialized techniques such as reductive deoxygenation or deselenylation of the phosphinate or selenophosphinate precursors to provide the metallated secondary phosphane oxide. Whilst limitations are apparent with respect to the alkyl halide in that only S_N2-reactive halides react, the variety of enantiomerically pure *P*-chiral phosphane oxides accessible by direct alkylation does compensate. The methodology described here is clearly generally applicable, although we have worked exclusively with secondary phosphane oxides bearing *tert*-butyl and phenyl substituents. Of particular note in relation to work involving conjugate addition of the lithiated reagents derived from allylic phosphane oxides to cyclic conjugated enones, the *P*-chiral allylic and butenylphosphane oxides **11**, **12**, **17**, and **18**, previously relatively inaccessible,[30] are now readily available. The lithiated *P*-chiral compounds undergo completely enantioselective addition to prochiral cyclic enones.[30,31] The utility of the bis(phosphane oxides) as ligands in asymmetric catalysis will be reported elsewhere.

Experimental Section

General: All solvents were purified by standard procedures. THF and Et_2O were predried over type 4-Å molecular sieves and distilled prior to use from sodium/benzophenone ketyl under nitrogen. Diisopropylamine, pyridine, and triethylamine were predried and distilled from sodium hydroxide under nitrogen and stored over type 4-Å molecular sieves. CH_2Cl_2 was distilled prior to use from calcium hydride under nitrogen. − Thin layer chromatography was carried out on Merck silica gel 60 F 254, unless otherwise stated and visualised under ultraviolet light (254 nm), or through spraying with acidic ammonium molybdate(IV), basic potassium permanganate, 7% dodecaphosphomolybdic acid in EtOH, or by placing in iodine vapour. − Flash chromatography was carried out on Merck silica gel 60 (230−400 mesh ASTM), RDH neutral alumina (70−230 mesh) or Aldrich Florisil® (200 mesh). − Melting points were determined in a capillary tube and are uncorrected. − IR spectra were recorded as thin films on NaCl plates by using a Perkin−Elmer 16 PC FTIR spectrophotometer. − ^{1}H- (400 MHz),

^{13}C- (100 MHz), and ^{31}P-NMR (161 MHz) spectra were recorded with a JOEL FX-400 spectrometer, and ^{1}H (300 MHz), ^{13}C (75 MHz), and ^{31}P NMR (121 MHz) spectra were recorded with a Bruker ARX-300 spectrometer, with $CDCl_3$ unless otherwise stated. As reference for ^{31}P NMR spectra, trimethyl phosphite (δ_P = 140.0, s) was used. − Optical rotations were recorded with a Perkin−Elmer 241 polarimeter. − Analytical high performance liquid chromatography (HPLC) was performed with a Waters 600 Controller, and Waters 717 plus Autosampler equipped with 486 Tunable Absorbance Detector. Analytical runs were performed with a flow rate of 1 mL/min on an HP Si 5μ column (4.6 mm ID × 25 cm).

Preparation of Secondary Phosphane Oxides

(±)-*tert*-Butyl(phenyl)phosphane Oxide (1): A solution of *t*BuCl (120 mL, 1.1 mol) in dry Et_2O (500 mL) was added dropwise to Mg turnings (26.0 g) in dry Et_2O (250 mL) under nitrogen at a rate so as to maintain a gentle reflux. After the addition, the mixture was stirred under reflux (50 °C bath temperature) for 4 h. The resulting grey suspension was cooled to 0 °C and a solution of $PPhCl_2$ (50 mL, 0.37 mol) in dry Et_2O (500 mL) was added dropwise. The mixture was heated under reflux for about 18 h. The mixture was cooled to 0 °C, poured into ice (100 g) and treated with HCl (5 M). The ether layer was separated and the aqueous layer was extracted with CH_2Cl_2 (10 × 150 mL). The combined organic layers were washed with brine (300 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give a pale yellow viscous oil, which was purified by vacuum distillation to give **1** as a colourless oil that on cooling transformed into a white amorphous solid (40.4 g, 60%); b.p. 110 °C/0.8 Torr (ref.[19] b.p. 40−41 °C/0.05 Torr). − ^{1}H NMR (400 MHz): δ = 1.15 (d, *J* = 16.6 Hz, 9 H, Me_3C), 7.03 (d, *J* = 453.1 Hz, 1 H, PH), 7.56−7.60 (m, 3 H, ArH), 7.65−7.70 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 46.4 (s).

(±)-*tert*-Butyl(phenyl)phosphanylthioic Acid: A mixture of **1** (40.5 g, 0.223 mol) in dry toluene (200 mL) containing sulfur (7.27 g, 0.224 gatom) under nitrogen was heated overnight (about 10 h) under reflux at 130 °C (bath temperature). After cooling to room temperature, the product was partitioned between toluene and NaOH solution (0.7 M, 8 × 100 mL). The aqueous solution was acidified and then extracted with CH_2Cl_2 (12 × 100 mL). The organic layers were washed with brine, dried ($MgSO_4$), and then concentrated under reduced pressure to give the phosphanylthioic acid as a cream solid (44.2 g, 93%), which was used without further purification. − ^{1}H NMR (400 MHz): δ = 1.02 (d, *J* = 16.11 Hz, 9 H, Me_3C), 7.27−7.34 (m, 3 H, ArH), 7.77−7.83 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 96.8 (s).

Resolution of (±)-*tert*-Butyl(phenyl)phosphanylthioic Acid: The racemic acid (44.15 g, 0.206 mol) in dry Et_2O (800 mL) at room temperature under nitrogen was treated with a solution of (*S*)-(−)-methylbenzylamine (25.0 mL, 0.206 mol) in dry Et_2O (250 mL) and the mixture was stirred overnight. The precipitate of the crude (R_P,*S*) salt was collected by filtration and washed with a little cold ether. The salt was dissolved in hot $CHCl_3$ (300 mL) and after the solution was cooled slightly, dry Et_2O (300 mL) was added to reprecipitate the salt. The salt was collected by filtration and the filtrate concentrated to half of its volume to gain a second crop of the salt. The combined filtrates were retained for recovery of the (S_P) acid (see below). The optical purity of the (R_P,*S*) salt was checked by NMR spectroscopy, and the above process repeated until > 99.4% optical purity was achieved; that is, the other diastereomer could not be detected at 400 MHz. The salt was dissolved in NaOH solution (0.7 M, 70 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give (*S*)-(−)-α-methylbenzylamine, which was distilled and reused. The aqueous portion was acidified with 6 M HCl and extracted with CH_2Cl_2 (5 × 70 mL). The combined extracts were dried ($MgSO_4$) and concentrated to leave the (R_P)-(+) acid **2**. Recrystallization from light petroleum yielded white needles (15.9 g, 72%), m.p. 95−96 °C. − $[\alpha]_D^{20}$ = +30.1 (*c* = 2.36, MeOH) {ref.[32] m.p. 96 °C, $[\alpha]_D^{20}$ = +25.62 (*c* = 0.9, MeOH)}. − ^{1}H NMR (200 MHz): δ = 1.140 (d, *J* = 17.7 Hz, 9 H, Me_3C), 7.25−7.48 (m, 3 H, *m*- and *p*-ArH), 7.64−7.84 (m, 2 H, *o*-ArH). − ^{31}P NMR (161 MHz): δ = 96.8 (s). − MS; *m*/*z* (%): 215 (6) [M + 1], 214 (58) [M], 159 (9), 158 (98), 157 (12), 126 (8), 125 (95), 110 (6), 77 (7), 63 (9), 57 (58), 51 (15), 47 (28), 41 (23), 32 (27), 29 (20), 28 (100). − IR (KBr): $\tilde{\nu}$ = 2975s, 2868s, 1477w, 1435w, 1361w, 111m, 913s, 817w, 718m, 696m, 668s, 588w cm^{-1}. − The combined filtrates were concentrated to give the optically impure (S_P,*S*) salt. This was partitioned as described above to give (*S*)-(−)-α-methylbenzylamine. The crude (S_P) acid obtained on acidification was treated according to the above procedure with (*R*)-(+)-α-methylbenzylamine in ether. The resulting (S_P,*R*) salt was fractionally recrystallized as described above, and processed to provide (S_P)-(−) acid **3**. Recrystallization from light petroleum gave white needles (17.40 g, 79%), m.p. 95−96 °C. − $[\alpha]_D^{20}$ = −29.2 (*c* = 1.65, MeOH) {ref.[32] m.p. 93−94 °C, $[\alpha]_D^{20}$ = −19.5 (*c* = 1.5, MeOH); ref.[32] $[\alpha]_D^{20}$ = −23.84 (*c* = 1.1, MeOH)}.

(S_P)-(−)-*tert*-Butyl(phenyl)phosphane Oxide (4): The (R_P) acid **2** (10.3 g, 0.048 mol) in dry EtOH (300 mL) under dry nitrogen was degassed in an ultrasonic bath at 15 °C for 20 min. Raney nickel in dry degassed absolute EtOH was stirred until evenly dispersed and then the resulting suspension (10 mL) was transferred by syringe to the reaction vessel. The reaction mixture was mechanically stirred and sonicated in an Elma T840DH ultrasonic bath under nitrogen, with further lots of Raney nickel suspension (each 10 mL) being added at 1 h and 2 h after commencement. The progress of the reaction was monitored by TLC (EtOH/EtOAc, 10:90), and was generally complete after 3 h. The mixture was filtered under nitrogen through Celite. The residue was washed with EtOH, the washings filtered through the Celite, and the total filtrates were combined and concentrated under reduced pressure to yield **4** as a white solid that was sufficiently pure for subsequent reactions (7.60 g, 87%), m.p. 71−73 °C. − $[\alpha]_D^{20}$ = −32.45 (*c* = 1.20, $CHCl_3$) {ref.[33] m.p. 72−74 °C, $[\alpha]_D^{20}$ = −28.8 (*c* = 2.0, benzene)}. − ^{1}H NMR (400 MHz): δ = 1.15 (d, *J* = 16.6 Hz, 9 H, Me_3C), 7.03 (d, *J* = 453.1 Hz, 1 H, PH), 7.56−7.60 (m, 3 H, ArH), 7.65−7.70 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 46.4 (s).

(R_P)-(+)-*tert*-Butyl(phenyl)phosphane Oxide (5): According to the above procedure, the (S_P)-(−) acid **3** (10.0 g, 0.047 mmol) was converted into **5**, which was obtained as a white solid (6.76 g, 79%). − $[\alpha]_D^{20}$ = +33.2 (*c* = 1.29, $CHCl_3$) {ref.[33] m.p. 72−74 °C, $[\alpha]_D^{20}$ = +27.9 (*c* = 2.0, benzene)}. − ^{31}P NMR (161 MHz): δ = 46.4 (s).

Reaction of Metallated Secondary Phosphane Oxides with Alkyl Halides − Preparation of Tertiary Phosphane Oxides

From Lithiated Secondary Phosphane Oxides. − General Procedure: LDA was prepared by the addition of *n*BuLi (1.1−1.2 equiv., 2.5 M in hexanes) with 2,2′-bipyridine as indicator, to a solution of diisopropylamine (1.1−1.2 equiv.) in THF (ca. 15 mL per 2 mmol of LDA) at 0 °C under nitrogen. The resulting deep red solution was cooled to −78 °C and then added dropwise to a solution of the secondary phosphane oxide (1.1 equiv.) in THF (ca. 15 mL per 2 mmol) at −78 °C. The solution was stirred for 15 min, and then a solution of the halide (1.0 mmol) in THF (15 mL per 1 mmol)

was added dropwise. The colour of the mixture changed from red to yellow immediately. The progress of the reaction was monitored by TLC. The reaction mixture was quenched on completion, usually after 1 h with warming to −50 °C or as indicated, with saturated aqueous NH_4Cl. The reaction mixture was extracted with Et_2O (3 × 30 mL). The combined extracts were washed with water (3 × 30 mL), brine (50 mL), dried with $MgSO_4$, and concentrated under reduced pressure to leave the residue, which was further purified by chromatography to give the product. Crystalline products were dried thoroughly under vacuum prior to recording of melting point and optical rotation.

3-Bromo-1-propene (Allyl Bromide): From LDA (3.74 mmol), **1** (572 mg, 3.14 mmol) and allyl bromide (380 mg, 3.14 mmol) in THF was obtained a yellow oil, which after chromatography (EtOH/EtOAc, 5:95) gave **6** as needles (397 mg, 57%), m.p. 71−73 °C, from EtOAc. − ^{1}H NMR (400 MHz): δ = 1.12 (d, J = 14.65 Hz, 9 H, Me_3C), 2.87−3.02 (m, 2 H, 3-H), 5.10−5.20 (m, 2 H, 1-H), 5.74−5.86 (m, 1 H, 2-H), 7.46−7.51 (m, 3 H, ArH), 7.68−7.74 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 46.4. − MS (EI); *m*/*z* (%): 222 (6) [M^+], 181 [$M^+ - C_3H_5$], 165 [$M^+ - Me_3C$], 91 [C_7H_7]. − $C_{13}H_{19}OP$ (222.3): calcd. C 70.25, H 8.63; found C 69.96, H 8.35. − Similarly, from each of **4** and **5** (0.61 mmol) and LDA (0.73 mmol) were obtained, respectively, the (S_P) product **11** (77 mg, 57%), needles, m.p. 71−73 °C, $[\alpha]_D^{20}$ = +30.5 (c = 1.47, MeOH), and the (R_P) product **17** (76 mg, 56%), needles, m.p. 72−73 °C, $[\alpha]_D^{20}$ = −31.8 (c = 1.53, MeOH).

(*E*)-1-Bromo-2-butene (Crotyl Bromide): In order to obtain crotyl bromide containing minimal quantities of the (*Z*) isomer, the following method had to be used. Crotonaldehyde (74 g, 1.05 mol) in dry Et_2O (150 mL) was added to a stirred suspension of LAH (14 g, 0.38 mol) in dry Et_2O (460 mL) at such a rate as to maintain a gentle reflux. The mixture was stirred for 24 h at room temperature and heated gently for 1 h prior to quenching with gradual addition of saturated aqueous Na_2SO_4. The resulting mixture was filtered through Celite. The residue was washed with dry ether (3 × 30 mL) and the combined filtrates were dried (Na_2SO_4). Evaporation of the solvent at atmospheric pressure left the crude alcohol, distillation of which at reduced pressure afforded (*E*)-2-butenol as a colourless liquid (27.1 g, 37%), b.p. 45−48 °C, 30−40 Torr (ref.[34] 121−122 °C, 760 Torr). The alcohol (5.0 g, 0.07 mol) in dry Et_2O (25 mL) at 0 °C under nitrogen was treated dropwise with freshly distilled phosphorus tribromide (3.35 mL, 0.035 mol). The mixture was stirred for 3 h at 10 °C before being poured onto ice (75 g). The organic phase was washed successively with water, saturated aqueous K_2CO_3, and brine, and then dried (Na_2SO_4). Ether was removed by distillation at atmospheric pressure to give the crude product as a pale orange liquid (6.12 g, 65%), which was used as such; distillation induces isomerisation to give mixtures containing ca. 10% of the (*Z*) isomer. − A mixture of **1** (14.2 g, 0.079 mol) and crotyl bromide (0.198 mol, 2.5 equiv.) in THF (150 mL) was added by cannula during 1 h to a solution of LDA (0.094 mmol) in THF (180 mL) at −78 °C. The resulting solution was stirred at −78 °C for a further 1.25 h with warming to −20 °C, and then quenched with saturated aqueous NH_4Cl (30 mL). The mixture was concentrated under vacuum at room temperature to remove excess THF, and the residual aqueous solution was extracted with CH_2Cl_2 (4 × 150 mL). The combined extracts were washed with water (150 mL), brine (50 mL), and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure at room temperature left the crude product as a yellow oil, which was submitted to flash chromatography (EtOH/EtOAc, 3:97) to afford **7** as a cream microcrystalline solid (14.8 g, 81%), m.p. 95−97 °C (ref.[30] m.p. 52−54 °C). − ^{1}H NMR (400 MHz): δ = 1.12 (d, ^2J = 14.65 Hz, 9 H, Me_3C), 1.57−1.60 (m, 3 H, 4-H), 2.80−2.95 (m, 2 H, 1-H), 5.36−5.45 (m, 1 H, 2-H), 5.54−5.61 (m, 1 H, 3-H), 7.43−7.53 (m, 3 H, ArH), 7.67−7.72 (m, 2 H, ArH). − ^{13}C NMR (100 MHz): δ = 18.13 (s, Me), 24.61 (s, *Me*$_3$C), 28.26 (d, J = 62.5 Hz, Me_3C), 33.02 (d, J = 66.2 Hz, C1′), 119.78 (s, C3′), 128.06 (d, J = 11.0 Hz, C2′), 131.10 (d, J = 11.0 Hz, *o*-C), 131.32 (s, *p*-C), 131.99 (d, J = 7.3 Hz, *m*-C). − ^{31}P NMR (161 MHz): δ = 46.1. − MS (EI); *m*/*z* (%): 237 (5) [MH^+], 236 [M^+], 182 [$Me_3CPhP(O)H$], 91 [$C_7H_7^+$]. − $C_{14}H_{21}OP$ (236.3): calcd. C 71.16, H 8.96; found C 71.15, H 8.98. − A solution of the bromoalkene (324 mg, 2.4 mmol) and **4** (364 mg, 2.0 mmol) in THF (10 mL) was added by cannula to a solution of LDA (2.1 mmol) in THF (14 mL) at −78 °C. The resulting solution was stirred at −78 °C for a further 1 h and then quenched with saturated aqueous NH_4Cl. The mixture was extracted with Et_2O (3 × 20 mL), and the combined extracts were processed in the usual way to give the (S_P)-phosphane oxide **12** as prisms (368 mg, 78%), m.p. 96−98 °C, $[\alpha]_D^{20}$ = +39.5 (c = 1.01, $CHCl_3$) (ref.[30] m.p. 52−54 °C, $[\alpha]_D^{20}$ = +16.0, c = 0.79 $CHCl_3$), from hexane/EtOAc. − For a larger scale preparation that obviates the use of chromatography, the following is representative. Compound **5** (6.70 g, 0.028 mol) and the freshly prepared bromide (0.084 mol, 3.0 equiv.) in THF (15 mL) was added to LDA (0.056 mol, 1.2 equiv.) in THF (150 mL) at −78 °C. After 1 h, the reaction mixture was worked up as above to give a white crystalline solid admixed with a yellow oil. This was partially dissolved in boiling pentane, the supernatant liquid was decanted with filtering and then the filtrate was concentrated until a cloudiness developed. Upon cooling the filtered solution to room temperature over 2 h, large colourless crystals (2.9 g, 34%) were obtained. The mother liquor and the yellow residue remaining after decanting were combined and heated to dissolve the residue. Decanting of the liquid, followed by concentration and cooling as above afforded a further crystalline fraction (3.80 g, 44%), which consisted solely of (R_P)-phosphane oxide **18** according to NMR analysis. The combined yield of the (R_P)-phosphane oxide **18** was 6.7 g (78%). A small portion recrystallized from pentane gave large clear prisms, m.p. 95−98 °C, $[\alpha]_D^{20}$ = −39.6 (c = 1.15, $CHCl_3$) {ref.[30] m.p. 52−54 °C, $[\alpha]_D^{20}$ = −16.0 (c = 1.045, $CHCl_3$)}.

Benzyl Bromide: LDA (1.2 equiv., 3.74 mmol) in THF (15 mL) at −78 °C was added dropwise by cannula to **1** (572 mg, 3.14 mmol) in THF (15 mL). The resulting solution was stirred for 15 min and benzyl bromide (537 mg, 3.14 mmol) was added dropwise. The solution was stirred for a further 1 h with warming to room temperature, and worked up in the usual way to give a yellow oil, which after chromatography (EtOH/EtOAc, 5:95) gave firstly *tert*-butyl(1,2-diphenylethyl)phenylphosphane oxide (**9**) (104 mg, 9%) as a 70:30 mixture of diastereomers, from which the major (R_PS_PRS) isomer was separated by recrystallization from EtOAc, as needles, m.p. 162−165 °C. − ^{1}H NMR (400 MHz): δ = 1.31 (d, J = 14.2 Hz, 9 H, Me_3C), 3.26 (ddd, J = 4.9, 11.7, 13.7 Hz, 1 H, 2′-H), 3.63 (ddd, J = 2.9, 6.35, 11.7 Hz, 1 H, 2′-H), 3.72 (ddd, J = 2.9, 5.9, 14.2 Hz, 1 H, 1′-H), 6.87−7.30 (m, 6 H, ArH), 7.44−7.49 (m, 2 H, ArH), 7.90−8.05 (brm, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 48.3. − MS (CI); *m*/*z* (%): 363 (100) [M^+ + 1]. − $C_{24}H_{27}OP$ (362.4): calcd. C 79.53, H 7.51; found C 79.65, H 7.54. − The mother liquors contained primarily the minor (R_PS_PSR) isomer: ^{1}H NMR (400 MHz): δ = 0.83 (d, J = 14.65 Hz, 9 H, Me_3C), 2.93 (ddd, J = 2.4, 8.3, 13.7 Hz, 1 H, 2′-H), 3.12 (ddd, J = 4.4, 11.7, 14.2 Hz, 1 H, 2′-H), 3.48 (ddd, J = 2.4, 4.8, 11.7 Hz, 1 H, 1′-H), 6.65−6.69 (m, 2 H, ArH), 7.05−7.14 (m, 5 H, ArH), 7.57−7.60 (m, 3 H, ArH). − ^{31}P NMR (161 MHz): δ = 47.4. − The next product was the benzylphosphane oxide **8** (600 mg, 70%),

as needles, m.p. 194−195 °C, from EtOAc. − ^{1}H NMR (400 MHz): δ = 1.15 (d, *J* = 14.65 Hz, 9 H, Me_3C), 3.45 (dd, *J* = 14.65, 27.8 Hz, 1 H, 1-H), 3.47 (dd, *J* = 14.65, 42.3 Hz, 1 H, 1-H), 7.11−7.20 (m, 3 H, ArH), 7.27−7.29 (m, 2 H, ArH), 7.39−7.49 (m, 3 H, *m*-ArH and *p*-ArH), 7.70−7.75 (m, 2 H, *o*-ArH). − ^{13}C NMR (100 MHz): δ = 24.72 (s, Me_3C), 31.32 (d, *J* = 58.8 Hz, C1′), 33.37 (d, *J* = 68.0 Hz, Me_3C), 126.52 (s), 128.00 (d, *J* = 9.2 Hz, *o*-C), 128.33 (s), 129.34 (s), 130.14, (d, *J* = 5.5 Hz), 131.37 (s, *p*-C), 131.88 (s), 132.03 (d, *J* = 7.4 Hz, *m*-C). − ^{31}P NMR (161 MHz): δ = 45.0. MS (EI); *m*/*z* (%): 272 (32) [M^+], 216 [$MH^+ - Me_3C$], 182 [$Me_3CPhP(O)H$], 125 [$MH^+ - PhCH_2 - Me_3C$], 91 [$C_7H_7^+$]. − $C_{17}H_{21}OP$ (272.3): calcd. C 74.98, H 7.77, P 11.37; found C 75.08, H 7.94, P 11.36. − From each of **4** and **5** (each 100 mg, 0.55 mmol), LDA (1.2 equiv.) and benzyl bromide (94.1 mg, 0.55 mmol, 1.0 equiv.) in THF (10 mL) at −60 °C was obtained, according to the above conditions, the dialkylation product (10−20%) and, respectively, the (S_P) product **13**, (100 mg, 68%), as needles, m.p. 187−189 °C, $[\alpha]_D^{20}$ = +110.5 (*c* = 1.08, MeOH), and the (R_P) product **19** (87 mg, 59%), as needles, m.p. 187−189 °C, $[\alpha]_D^{20}$ = −111.7 (*c* = 1.17, MeOH).

(Bromomethyl)cyclohexane: Treatment of **1** (572 mg, 3.14 mmol) in THF (15 mL) with LDA (3.74 mmol) and then with (bromomethyl)-cyclohexane (556 mg, 3.14 mmol) at −78 °C followed by warming of the reaction mixture to room temperature during 1 h gave a yellow oil. This was submitted to chromatography (EtOH/EtOAc, 5:95) to give **10** (718 mg, 82%) as needles, m.p. 114−115 °C, from EtOAc/hexane. − ^{1}H NMR (400 MHz): δ = 0.98−1.24 (m, 2 × 4-H, 2 × 6-H), 0.81−0.96 (m, 1 × 5-H), 1.05 (d, *J* = 14.2 Hz, 9 H, Me_3C), 1.48−1.78 (m, 2 × 3-H, 1 × 5-H, 2 × 7-H), 1.83−2.71 (m, 2 × 1-H, 1 × 2-H), 7.40−7.50 (m, 3 H, ArH), 7.66−7.71 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 50.6. − MS (CI); *m*/*z* (%): 279 (69) [M^+ + 1]. − $C_{17}H_{27}OP$ (278.3734): calcd. C 73.35, H 9.78; found C 73.39, H, 9.79.

2-(Chloromethyl)pyridine: Compound **4** (186 mg, 1.02 mmol) in THF (5 mL) was treated with LDA (1.07 mmol) in THF (5 mL) at −78 °C, and then with 2-(chloromethyl)pyridine (130 mg, 1.02 mmol) in THF (5 mL). The mixture was stirred for 0.5 h and worked up in the usual way to give **14** after chromatography (MeOH/EtOAc, 10:90) (210 mg, 75%) as needles, m.p. 173.0−174.7 °C. − $[\alpha]_D^{20}$ = −40.4 (*c* = 0.88, $CHCl_3$) from EtOAc. − ^{1}H NMR (400 MHz): δ = 1.15 (d, *J* = 14.7 Hz, 9 H, Me_3C), 3.74 (dd, *J* = 12.8, 14.6 Hz, 1 H, CH_2), 3.75 (apq, *J* = 14.6, 17.0 Hz, 1 H, CH_2), 7.04−7.08 (m, 1 H, py-5-H), 7.37−7.48 (m, 5 H, ArH, py-4-H and py-3-H), 7.73−7.80 (m, 2 H, ArH), 8.41 (d, *J* = 4.9 Hz, 1 H, py-6-H). − ^{31}P NMR (161 MHz): δ = 45.8. − MS (CI); *m*/*z* (%): 274 (100) [M^+], 216 [$M^+ - Me_3C$]. − $C_{16}H_{20}NOP$ (273.3): calcd. C 70.31, H 7.38; found C 70.52, H 7.39.

Methyl Iodide: Compound **4** (572 mg, 3.14 mmol) in THF (15 mL) was treated with LDA (3.74 mmol, 1.2 equiv.) in THF (15 mL) at −78 °C and then with methyl iodide (446 mg, 3.14 mmol, 1 equiv.). The solution was stirred for 1 h with warming to room temperature. The reaction mixture was quenched and worked up to provide **15** after chromatography (EtOH/EtOAc 5:95) (328 mg, 52%) as needles, m.p. 99−100 °C, $[\alpha]_D^{20}$ = −23.5 (*c* = 1.17, MeOH) {ref.[22] m.p. 99−100 °C, $[\alpha]_D^{20}$ = −21.8 (*c* = 1.0, MeOH)}. − ^{1}H NMR (400 MHz): δ = 1.03 (d, *J* = 14.65 Hz, 9 H, Me_3C), 1.62 (d, *J* = 12.2 Hz, 3 H, Me), 7.35−7.42 (m, 3 H, *m*-ArH and *p*-ArH), 7.60−7.65 (m, 2 H, *o*-ArH). − ^{13}C NMR (100 MHz): δ = 15.57 (d, *J* = 66.2 Hz, Me), 24.44 (s, Me_3C), 32.47 (d, *J* = 69.8 Hz, Me_3C), 128.12 (d, *J* = 7.4 Hz, *o*-C), 129.50 (d, *J* = 86.4 Hz, *ipso*-C), 131.25 (s, *p*-C), 131.85 (d, *J* = 7.4 Hz, *m*-C). − ^{31}P NMR (161 MHz): δ = 50.4. − MS (EI); *m*/*z* (%): 196 (2) [M^+], 140 [$MH^+ - Me_3C$], 91 [$C_7H_7^+$]. − (R_P)-Phosphane oxide **22** (340 mg, 54%) was prepared according to the above procedure from **5** (572 mg, 3.14 mmol) and methyl iodide (446 mg, 3.14 mmol), as needles, m.p. 99−100 °C. − $[\alpha]_D^{20}$ = +23.1 (*c* = 1.57, MeOH) {ref.[22] $[\alpha]_D^{20}$ = +22.7 (*c* = 1.0, MeOH)}, from EtOAc.

1-Bromobutane: Treatment of **5** (546 mg, 3 mmol) in THF (10 mL) with LDA (3.2 mmol) and then with 1-bromobutane (282 μL, 3.3 mmol) at −78 °C followed by warming, and then quenching of the reaction mixture at room temperature after 1.5 h gave a semi-crystalline residue. This was submitted to chromatography (EtOH/EtOAc, 5:95) to give **20** (432 mg, 68%), as needles, m.p. 108−109 °C. − $[\alpha]_D^{20}$ +32.4 (*c* = 1.32, MeOH), from EtOAc. − ^{1}H NMR (300 MHz): δ = 1.10 (9 H, d, *J* = 14.2 Hz, Me_3C), 1.21 (brdd, *J* = 16.1, 7.5 Hz, 3 H, Me), 1.62−1.95 (m, 4 H, CH_2), 2.00−2.12 (m, 2 H, CH_2), 7.47−7.51 (m, 3 H, ArH), 7.68−7.73 (m, 2 H, ArH). − ^{31}P NMR (121 MHz): δ = 50.3 (s). − MS (EI); *m*/*z* (%): 238 (66) [M^+]. − $C_{14}H_{23}OP$ (238.3): calcd. C 70.56, H 9.73; found C 70.71, H 9.76.

Ethyl Bromide: Treatment of **5** (546 mg, 3 mmol) in THF (10 mL) with LDA (3.2 mmol) and then with ethyl bromide (246 μL, 3.3 mmol) at −78 °C followed by warming, and then quenching of the reaction mixture at room temperature after 1.5 h gave a semi-crystalline residue. Chromatography (EtOH/EtOAc, 5:95) gave **21** (454 mg, 72%) from EtOAc, as needles, m.p. 103−104 °C. − $[\alpha]_D^{20}$ = +28.1 (*c* = 1.32, MeOH). − ^{1}H NMR (300 MHz): δ = 1.12 (d, *J* = 14.2 Hz, 9 H, Me_3C), 1.22 (dd, *J* = 15.6, 7.5 Hz, 3 H, Me), 2.00−2.12 (m, 2 H, CH_2), 7.47−7.51 (m, 3 H, ArH), 7.68−7.73 (m, 2 H, ArH). − ^{13}C NMR (75 MHz): δ = 5.33 (d, *J* = 5.6 Hz, Me), 15.58 (d, *J* = 64.7 Hz, CH_2), 24.39 (s, Me_3C), 32.63 (d, *J* = 66.2 Hz, Me_3C), 127.99 (d, *J* = 5.1 Hz, *o*-C), 131.09 (s, *p*-C), 131.79 (d, *J* = 7.7 Hz, *m*-C). − ^{31}P NMR (121 MHz): δ = 50.2 (s). − MS (EI); *m*/*z* (%): 210 (26) [M^+] . − $C_{12}H_{19}OP$ (210.3): calcd. C 68.55, H 9.11; found C 68.73, H 9.14.

From Sodiated Secondary Phosphane Oxides

Methyl Iodide: The (S_P)-phosphane oxide **4** (3.64 g, 20 mmol) in THF (30 mL) was added dropwise to NaH (60%, 0.88 g, 22 mmol) at 0 °C by cannula under nitrogen. Evolution of hydrogen commenced immediately. The yellow sodiated phosphane oxide solution was stirred for 15 min and then treated with methyl iodide (24 mmol) in THF (30 mL) at 0 °C. The mixture was stirred for 0.5 h at room temperature, and then quenched with saturated aqueous NH_4Cl (30 mL). The organic layer and the aqueous layer were separated and the latter was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were shaken with saturated aqueous $NaHSO_3$. The colourless organic solution was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure to give (S_P)-*tert*-butyl(methyl)phenylphosphane oxide (3.84 g, 98%) as a white solid, which was sufficiently pure for use in further reactions. Further purification by chromatography (ethanol/ethyl acetate, 5:95) gave the methylphosphane oxide **15** (3.73 g, 95%), as colourless needles, m.p. 99−100 °C. − $[\alpha]_D^{20}$ = −23.2 (*c* = 0.82, MeOH), from EtOAc, data that are in agreement with those obtained for **15** above.

Chloroacetophenone: The (S_P)-phosphane oxide **4** (261 mg, 1.43 mmol) in THF (5 mL) was sodiated as described above. The resulting yellow mixture was cooled to −78 °C, and then treated with chloroacetophenone (265 mg, 1.72 mmol) in THF (5 mL). The mixture was stirred overnight with concomitant warming to room temperature, and then quenched with saturated aqueous NH_4Cl (5 mL). The organic layer and the aqueous layer were separated and the latter was extracted with EtOAc (2 × 5 mL). The combined

organic extracts were dried ($MgSO_4$) and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography (ethyl acetate/hexanes, 80:20) to give the product **16** (309 mg, 72%) as colourless needles, m.p. 118−119 °C. − $[\alpha]_D^{23}$ = +104 (*c* = 4.41, $CHCl_3$), from dichloromethane/hexanes. − ^{1}H NMR (300 MHz): δ = 1.21 (d, *J* = 15.5 Hz, 9 H, Me_3C), 3.72 (dd, *J* = 11.6, 13.05 Hz, 1 H, CH_2), 4.07 (dd, *J* = 15.3, 13.05 Hz, 1 H, CH_2), 7.39−7.57 (m, 6 H, ArH), 7.75−7.83 (m, 2 H, ArH), 8.05−8.06 (m, 2 H, ArH). − ^{13}C NMR (75.5 MHz): δ = 24.8, 34.7 (d, *J* = 70.0 Hz), 38.5 (d, *J* = 47.1 Hz), 128.5 (d, *J* = 11.3 Hz), 128.8, 129.3 (d, *J* = 90.9 Hz), 129.9, 132.3 (d, *J* = 2.8 Hz), 132.6 (d, *J* = 8.3 Hz), 133.9, 137.5, 194.1 (d, *J* = 6 Hz). − ^{31}P NMR (121 MHz): δ = 43.8. − MS (CI); *m*/*z* (%): 301 (100) [MH^+]. − $C_{18}H_{21}O_2P$ (300.3): calcd. C 71.99, H 7.05; found C 72.02, H 7.12. − Small amounts of other uncharacterized products were also formed.

Preparation of Ditertiary Bis(phosphane oxides)

Exploratory Approaches from Dihaloethanes and 1: Treatment of a mixture of **1** (364 mg, 2.00 mmol) and 1,2-dibromoethane (188 mg, 1.00 mmol) in THF (10 mL) at −78 °C with LDA (1.35 mL, 2.00 mmol) followed by quenching after 1 h with saturated aqueous NH_4Cl and the usual workup gave a yellow residue, chromatography (EtOAc/hexanes, 30:70) of which gave **23** (407 mg, 78%) as needles, m.p. 82−83 °C (ref.[35] 81−83 °C) from EtOAc/hexanes. − Similarly, from **1** (364 mg, 2.00 mmol), 1,2-diiodoethane (282 mg, 1.00 mmol) and LDA (1.35 mL, 2.00 mmol) was obtained a yellow residue, chromatography (EtOAc/hexanes, 30:70) of which gave **26** as needles (320 mg, 52%) from EtOAc/hexanes. − ^{1}H NMR (400 MHz): δ = 1.29 (d, *J* = 19.5 Hz, 9 H, Me_3C), 7.49−7.75 (m, 2 H, ArH), 7.57−7.61 (m, 1 H, ArH), 7.86−7.91 (m, 2 H, ArH). − ^{31}P NMR (161 MHz): δ = 75.6. − MS (CI); *m*/*z* (%): 309 (42) [M^+]. − $C_{10}H_{14}IOP$ (308.1): calcd. C 38.98, H 4.58; found C 39.26, H 4.61.

From (±)-*tert*-Butyl(phenyl)vinylphosphane Oxide 29: To a solution of phosphane oxide **6** (442 mg, 2.0 mmol) in *t*BuOH/water (1:1, 30 mL) was added $K_3Fe(CN)_6$ (1.98 g, 6.0 mmol), K_2CO_3 (83 mg, 6.0 mmol), and OsO_4 (2 drops, 100 mg in 2 mL of *t*BuOH) at 0 °C. The reaction mixture was stirred first at 0 °C for 6 h and then at room temperature for 12 h. Sodium sulfite was then added to the yellow solution until the colour changed to brown. The mixture was then stirred for a further 1 h. The solvent was removed under reduced pressure and the residue was extracted with Et_2O (3 × 15 mL). The organic extracts was dried ($MgSO_4$) and concentrated under reduced pressure to give a colourless oil, which was purified by flash chromatography (EtOH/CH_2Cl_2, 16:84) to give (±)-*tert*-butyl-(2,3-dihydroxypropyl)phenylphosphane oxide as an inseparable mixture of diastereomers (55:45) as a colourless oil (465 mg, 90%). − ^{1}H NMR (400 MHz): δ (both isomers) = 7.45−7.58 (m, 3 H, ArH), 7.66−7.72 (m, 2 H, ArH); δ (major) = 1.12 (d, *J* = 15.1 Hz, 9 H, Me_3C), 2.13 (ddd, *J* = 2.4, 5.4, 15.1 Hz, 1 H, 1′-H), 2.28−2.41 (m, 1 H, 1′-H), 3.45−3.62 (m, 2 H, 3′-H), 4.05−4.13 (m, 1 H, 2′-H); δ (minor) = 1.11 (d, *J* = 15.1 Hz, 9 H, Me_3C), 2.28−2.41 (m, 2 H, 1′-H), 3.45−3.62 (m, 2 H, 3′-H), 3.89−3.96 (m, 1 H, 2′-H). − MS (CI); *m*/*z* (%): 257 (100) [M^+ + 1], 239 [M^+ − OH]. − $C_{13}H_{21}O_3P$ (256.3): calcd. C 60.93, H 8.26; found C 61.12, H 8.30. − A solution of the dihydroxy phosphane oxide (256 mg, 1 mmol) in *t*BuOH/water (1:1, 16 mL) was treated with $NaIO_4$ (426 mg, 2 mmol) at room temperature. The mixture was stirred at room temperature overnight after which it was cooled to 0 °C and treated with solid sodium tetrahydroborate (30 mg). The resulting mixture was stirred at 0 °C for 45 min. It was then diluted with Et_2O (25 mL) and quenched by the dropwise addition of water (8 mL). The ether layer was separated and aqueous layer was extracted with Et_2O (2 × 10 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give a white solid, which was purified by flash chromatography (MeOH/EtOAc, 1:9) to give **28** as an oil (198 mg, 88%). ^{1}H NMR (400 MHz): δ = 1.14 (d, *J* = 14.65 Hz, 9 H, Me_3C), 2.18−2.26 (m, 1 H, 1′-H), 3.87−3.98 (m, 2 H, 2′-H), 2.40−2.50 (m, 1 H, 1′-H), 7.49−7.58 (m, 3 H, ArH), 7.68−7.74 (m, 2 H, ArH). − ^{13}C NMR (100 MHz): δ = 23.93 (s, Me), 25.58 (d, *J* = 64.3 Hz, C1), 32.75 (d, *J* = 68.0 Hz, Me_3C), 57.19 (d, *J* = 3.7 Hz, C2), 128.32 (d, *J* = 10.9 Hz, *o*-C), 129.40 (d, *J* = 88.2 Hz, *ipso*-C), 131.70 (d, *J* = 7.4 Hz, *m*-C). − ^{31}P NMR (161 MHz): δ = 51.5. − IR (film) $\tilde{\nu}_{max}$ = 4050, 3360, 3058, 2962, 2904, 2870, 1658, 1642, 1590, 1548, 1476, 1438, 1396, 1368, 1210, 1144, 1106, 1072, 1042, 998, 942, 818, 784, 752, 700, 632 cm^{-1}. − MS (EI); *m*/*z* (%): 227 (16) [M + H^+], 196 [MH^+ −CH_2OH], 165 [MH^+ − Me_3C], 91 [$C_7H_7^+$]; (CI); 227 (100) [M + 1], 196 [MH^+ − CH_2OH]. − $C_{12}H_{19}O_2P$ (226.3): calcd. C 63.70, H 8.46; found C 63.91, H 8.46. − Alternatively, ozone (1 mL/min) was bubbled through a solution of **6** (125 mg, 0.563 mmol) in CH_2Cl_2/MeOH (1:5, 12 mL) at −78 °C until the solution became pale blue in colour (ca. 30 min). The solution was warmed to 0 °C and sodium tetrahydroborate (100 mg) was added. The resulting mixture was stirred at 0 °C for 45 min, diluted with Et_2O (20 mL) and treated with water (5 mL). The ether layer was separated and the aqueous layer was extracted with Et_2O (2 × 5 mL). The combined ether extracts were processed as described above to give **28** as an oil (73.2 mg, 58%). − Compound **28** (45.2 mg, 0.2 mmol) and triethylamine (31 μL, 0.22 mmol) in CH_2Cl_2 (5 mL) was treated with tosyl chloride (41.9 mg, 0.22 mmol) at 0 °C under nitrogen. The resulting mixture was stirred at room temperature under nitrogen for 12 h. It was then diluted with CH_2Cl_2 (5 mL), washed with water (3 × 4 mL), and dried ($MgSO_4$) and concentrated under reduced pressure to give a yellow oil. Chromatography (EtOAc/hexanes, 5:95) gave the tosylate as a white microcrystalline solid (48.2 mg, 63%), m.p. 144−145 °C. − ^{1}H NMR (400 MHz): δ = 1.09 (d, *J* = 15.1 Hz, 9 H, Me_3C), 2.53−2.60 (m, 2 H, 2′-H), 4.06−4.14 (m, 1 H, 1′-H), 4.28−4.36 (m, 1 H, 1′-H), 7.27 (d, *J* = 7.81 Hz, 2 H, *m*-ArH), 7.46−7.50 (m, 2 H, ArH), 7.53−7.57 (m, 1 H, ArH), 7.64−7.69 (m, 2 H, ArH), 7.65 (d, *J* = 8.3 Hz, 2 H, *o*-ArH). − ^{13}C NMR (100 MHz): δ = 21.92 (s, MePh), 23.33 (s, Me_3C), 24.38 (d, *J* = 60.7 Hz, C1′), 33.29 (d, *J* = 69.9 Hz, Me_3C), 65.52 (C2′), 128.23 (s), 128.81 (d, *J* = 11.1 Hz, *o*-C), 129.60 (s), 130.20 (*p*-C), 131.96 (d, *J* = 7.3 Hz, *m*-C), 132.32 (s), 132.76 (s), 145.31 (s). − ^{31}P NMR (161 MHz): δ = 44.6. − IR (KBr): $\tilde{\nu}_{max}$ = 3426, 2966, 1654, 1598, 1476, 1438, 1358, 1214, 1190, 1176, 1110, 1046, 1012, 958, 816, 744, 700, 664, 630 cm^{-1}. − MS (EI); *m*/*z* (%): 380 (2) [M^+], 323 [M^+ − Me_3C], 209 [M^+ − OTs], 91 [$C_7H_7^+$]. − $C_{19}H_{25}O_4PS$ (380.4): calcd. C 59.99, H 6.62; found C 60.22, H 6.66. − A solution of DBU (17 μL, 0.2 mmol) and the tosylate (38.0 mg, 0.2 mmol) in CH_2Cl_2 (2 mL) was stirred at room temperature under nitrogen for 1 h. It was then concentrated under reduced pressure. Chromatography (EtOH/EtOAc, 5:95) of the residue afforded the vinylphosphane oxide **29** as an oil (19.8 mg, 48%). − ^{1}H NMR (400 MHz): δ = 1.12 (d, *J* = 14.65 Hz, 9 H, Me_3C), 6.34 (ddd, 1 H, *J* = 1.95, 12.7, 36.65 Hz, 2-H), 6.47 (ddd, *J* = 1.95, 18.55, 19.5 Hz, 2-H), 6.73 (ddd, *J* = 12.7, 18.55, 27.8 Hz, 1 H, 1-H), 7.43−7.53 (m, 3 H, ArH), 7.71−7.76 (m, 2 H, ArH). − ^{13}C NMR (100 MHz): δ = 24.06 (s, Me_3C), 32.46 (d, *J* = 71.7 Hz, Me_3C), 127.02 (d, *J* = 88.2 Hz, C2′), 128.12 (d, *J* = 11.0 Hz, *o*-C), 130.66 (d, *J* = 91.9 Hz, *ipso*-C), 131.44 (C1′), 131.70 (d, *J* = 7.3 Hz, *m*-C), 136.09 (s, *p*-C). − ^{31}P NMR (161 MHz): δ = 36.5. − IR (film): $\tilde{\nu}_{max}$ = 3056, 2960, 2902, 2868, 1716, 1644, 1600, 1476, 1462, 1436, 1392, 1366, 1258, 1214, 1168, 1110, 1072, 988, 940, 838, 816, 778, 734, 708, 638 cm^{-1}. − MS

(CI); *m/z* (%): 209 (1) [MH^+], 1152 [$MH^+ - Me_3C$], 91 [$C_7H_7^+$]. − $C_{12}H_{17}OP$ (208.2): calcd. C 69.21, H 8.23; found C 69.45, H 8.25. − A solution of **29** (208 mg, 1.0 mmol) in THF (5 mL) at −78 °C under nitrogen was added dropwise by cannula to a solution of lithiated **4** (218 mg, 1.2 mmol) in THF (5 mL). The mixture was stirred for 4 h after which the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL). The reaction mixture was extracted with ether (2 × 30 mL) and the extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by chromatography (EtOH/EtOAc, 5:95) to give firstly the (S_P,S_P) diastereomer **30** (152 mg, 39%) of the bis(phosphanyl)ethane, as needles, m.p. 121−122 °C. − $[\alpha]_D^{20}$ = +62.4 (*c* = 1.12, $CHCl_3$). − ^{1}H NMR (400 MHz): δ = 1.08 (d, *J* = 14.65 Hz, 18 H, Me_3C); 2.34−2.41 (m, 2 H, 1-H, 3-H), 2.68−2.73 (m, 2 H, 1-H, 3-H), 7.24−7.44 (m, 6 H, ArH), 7.52−7.58 (m, 4 H, ArH). − ^{31}P NMR (161 MHz): δ = 51.2. − MS (EI); *m/z* (%): 390 (100) [M^+]. − $C_{22}H_{32}O_2P_2$ (390.4): calcd. C 67.68, H 8.26; found C 67.86, H 8.28. − The *meso* isomer **31** (152 mg, 39%), needles, m.p. 133−134 °C, was eluted next. − ^{1}H NMR (400 MHz): δ = 1.05 (d, *J* = 15.1 Hz, 18 H, Me_3C), 2.38−2.48 (m, 2 H, 1-H, 3-H), 2.62−2.68 (m, 2 H, 1-H, 3-H), 7.38−7.48 (m, 6 H, ArH), 7.58−7.62 (m, 4 H, ArH). − ^{31}P NMR (161 MHz): δ = 51.5. − MS (EI); *m/z* (%): 390 (100) [M^+]. − $C_{22}H_{32}O_2P_2$ (390.4): calcd. C 67.68, H 8.26; found C 67.88, H 8.27.

1,3-Dibromopropane: Compound **5** (364 mg, 2.00 mmol) and the dihalide (202 mg, 1.00 mmol) in THF (8 mL) at −78 °C under nitrogen were treated dropwise with LDA (2.00 mmol, 1.48 M). After 1 h, the reaction mixture was worked up in the usual way. Chromatography (MeOH/EtOAc, 15:85) of the residue gave **32** (284 mg, 70%) as needles, m.p. 114−117 °C. − $[\alpha]_D^{20}$ = +60.0 (*c* = 1.01, $CHCl_3$), from MeOH/EtOAc. − ^{1}H NMR (400 MHz): δ = 1.06 (d, *J* = 14.65 Hz, 18 H, Me_3C), 1.71−1.81 (m, 2 H, 2-H), 2.00−2.18 (m, 2 H, 1-H, 3-H), 2.42−2.50 (m, 2 H, 1-H, 3-H), 7.26−7.42 (m, 6 H, ArH), 7.54−7.59 (m, 4 H, ArH). − ^{31}P NMR (161 MHz): δ = 50.2. − MS (CI); *m/z* (%): 406 (28) [M^+ + 1]. − $C_{23}H_{36}O_2P_2$ (406.5): calcd. C 67.99, H 8.95; found C 67.96, H 8.93.

1,6-Dibromohexane: Compound **5** (364 mg, 2.00 mmol) and the dihalide (244 mg, 1.00 mmol) in THF (8 mL) and LDA (2.00 mmol, 1.48 M) at −78 °C according to the above conditions gave a crystalline residue, chromatography (MeOH/EtOAc 15:85) of which gave **33** (379 mg, 83%) as needles, m.p. 118−119 °C. − $[\alpha]_D^{20}$ = +65.0 (*c* = 1.30, $CHCl_3$), from MeOH/EtOAc. − ^{1}H NMR (400 MHz): δ = 1.08 (d, *J* = 14.2 Hz, 18 H, Me_3C), 1.65−1.89 (m, 8 H, 2-H, 3-H, 4-H, 5-H), 2.02−2.20 (m, 2 H, 1-H, 6-H), 2.41−2.50 (m, 2 H, 1-H, 6-H), 7.27−7.41 (m, 6 H, ArH), 7.52−7.60 (m, 4 H, ArH). − ^{31}P NMR (161 MHz): δ = 50.5. − MS (CI); *m/z* (%): 448 (32) [M^+ + 1]. − $C_{26}H_{40}O_2P_2$ (446.5): calcd. C 69.89, H 9.19; found C 69.83, H 9.17.

Bis(2-chloroethyl) Ether: From **5** (364 mg, 2.00 mmol), bis(2-chloroethyl) ether (120 μL, 1.00 mmol) and LDA (1.35 mL of 1.48 M solution, 2.00 mmol) in THF according to the above procedure was obtained a viscous gum. Chromatography (MeOH/EtOAc, 15:85) gave **35** as a white microcrystalline solid (98 mg, 23%), m.p. 112−113 °C. − $[\alpha]_D^{20}$ = +58.2 (*c* = 1.03, $CHCl_3$). − ^{1}H NMR (400 MHz): δ = 1.10 (d, *J* = 15.1 Hz, 18 H, Me_3C), 3.38−3.47 (m, 2 H, 1-H, 5-H), 2.25−2.35 (m, 4 H, 2-H, 4-H), 3.68−3.77 (m, 2 H, 1-H, 5-H), 7.30−7.53 (m, 6 H, ArH), 7.65−7.72 (m, 4 H, ArH). − ^{13}C NMR (100 MHz): δ = 23.95 (d, *J* = 62.5 Hz, PCH_2), 24.11 (s, Me_3C), 32.67 (d, *J* = 69.9 Hz, Me_3C), 64.27 (s, CH_2O), 128.14 (d, *J* = 9.2 Hz, *m*-C), 130.47 (d, *J* = 62.5 Hz, *ipso*-C), 131.46 (s, *p*-C), 131.61 (d, *J* = 7.3 Hz, *o*-C). − ^{31}P NMR (161 MHz): δ = 45.4. MS (CI); *m/z* (%): 435 (33) [M^+ + 1]. − $C_{24}H_{36}O_3P_2$ (434.5): calcd. C 66.34, H 8.35; found C 66.51, H 8.36.

Bis(chloromethyl)dimethylsilane: From **5** (364 mg, 2.00 mmol), LDA (2.0 mmol, 1.48 M) and the dihalide (146 μL, 1.00 mmol) in THF (8.0 mL) at −78 °C according to the above procedure was obtained a colourless gum. Chromatography (MeOH/EtOAc, 10:90) gave an inseparable mixture of two products (305 mg, 72%). Analytically pure samples were obtained by separation with HPLC (*i*PrOH/EtOAc, 3:97, flow rate 1 mL/min, UV detection at 254 nm) to give firstly **36**, t_R = 15.6 min, which crystallized as needles, m.p. 103−104 °C. − $[\alpha]_D^{20}$ = +62.5 (*c* = 1.28, $CHCl_3$) from EtOAc. − ^{1}H NMR (400 MHz): δ = −0.26 (s, 6 H, $SiMe_2$), 1.08 (d, *J* = 14.6 Hz, 18 H, Me_3C), 1.47 (dd, *J* = 8.3, 14.6 Hz, 2 H, CH_2), 1.97 (dd, *J* = 14.6, 17.1 Hz, 2 H, CH_2), 7.37−7.45 (m, 6 H, ArH), 7.64−7.68 (m, 4 H, ArH). − ^{13}C NMR (100 MHz): δ = 0.04 (d, *J* = 5.50 Hz, Me), 10.92 (d, *J* = 57.0 Hz, CH_2), 24.13 (s, Me_3C), 33.47 (d, *J* = 69.9 Hz, Me_3C), 127.86 (d, *J* = 11.0 Hz, *m*-C), 130.91 (s, *p*-C), 131.74 (d, *J* = 7.40 Hz, *o*-C), 132.71 (d, *J* = 86.4 Hz, *ipso*-C). − ^{31}P NMR (121 MHz): δ = 48.2. − MS (CI); *m/z* (%): 449 (100) [M^+ + 1], 433 [M^+ − Me]. − $C_{24}H_{38}O_2P_2Si$ (448.6): calcd. C 64.26, H 8.54; found C 64.39, H 8.55. − The more polar product, t_R = 16.2 min, was identified as the (R_P)-methylphosphane oxide **22**. Spectroscopic data are identical with those of an authentic sample.

Attempted Preparation from Bis(chloromethyl)tetramethyldisiloxane: From **5** (364 mg, 2.00 mmol), the dihalide (220 μL, 1.00 mmol) and LDA (2.0 mmol) in THF at −78 °C according to the above procedure was obtained a colourless gum. Chromatography (MeOH/EtOAc, 10:90) gave **22** (297 mg, 76%).

Diiodide 38: The diiodide was prepared as a colourless viscous oil via the ditosylate **37** from diethyl tartrate according to a literature procedure.[36] An LDA solution (2.00 mmol, 1.48 M) was added dropwise to a solution of **5** (364 mg, 2.00 mmol) and **38** (381 mg, 1.00 mmol) in THF (15 mL) at −78 °C under nitrogen. The mixture was stirred for 1 h at −78 °C, and then quenched with saturated aqueous NH_4Cl (5 mL) and extracted with Et_2O (3 × 15 mL). The extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated under reduced pressure to leave a colourless viscous residue. Chromatography (MeOH/EtOAc, 15:85) gave **40** (39.1 mg, 8%), as needles, m.p. 140−141 °C. − $[\alpha]_D^{27}$ = +18.7 (*c* = 1.96, EtOH), from EtOAc. − ^{1}H NMR (400 MHz): δ = 1.14 (d, *J* = 15.6 Hz, 18 H, Me_3C), 1.18 (s, 6 H, Me), 2.00−2.02 (m, 1 H, CH_2), 2.26−2.28 (m, 1 H, CH_2), 2.34−2.37 (m, 1 H, CH_2), 2.42−2.44 (m, 1 H, CH_2), 3.74−3.79 (m, 1 H, 5-H), 4.12−4.14 (m, 1 H, 4-H), 7.70−7.80 (m, 4 H, ArH), 7.45−7.56 (m, 6 H, ArH). − ^{31}P NMR (161 MHz): δ = 45.3. − MS (CI); *m/z* (%): 489 (2) [M^+ − 1]. − $C_{27}H_{40}O_4P_2$ (490.6): calcd. C 66.11, H 8.22; found C 66.15, H 8.24.

Diiodide 39: The diiodide was obtained from the corresponding ditosylate according to the literature procedure.[36] A solution of compound **5** (364 mg, 2.00 mmol) and **39** (443 mg, 1.00 mmol) in THF (15 mL) at −78 °C under nitrogen was treated dropwise with LDA (1.35 mL of 1.48 M solution, 2.00 mmol). The mixture was stirred for 1 h, and then worked up and submitted to chromatography according to the experiment described above to give **41** (391 mg, 71%), as needles, m.p. 153−154 °C. − $[\alpha]_D^{27}$ = −9.2 (*c* = 2.38, EtOH), from EtOAc. − ^{1}H NMR (400 MHz): δ = 1.06 (d, *J* = 14.65 Hz, 9 H, Me_3C), 1.15 (d, *J* = 15.1 Hz, 9 H, Me_3C), 1.24 (s, 3 H, Me), 2.03 (1 H, ddd, *J* = 3.4, 8.8, 15.1 Hz, CH_2), 2.41 (ddd, *J* = 3.4, 15.1, 15.1 Hz, 1 H, CH_2), 2.47 (ddd, *J* = 3.9, 7.3, 15.1 Hz, 1 H, CH_2), 2.62 (ddd, *J* = 4.40, 15.2, 15.1 Hz, 1 H, CH_2),

3.86−3.93 (m, 1 H, 5-H), 7.44−7.56 (m, 6 H, ArH), 4.24−4.31 (m, 1 H, 4-H), 6.75−6.77 (d, J = 6.8 Hz, 2 H, ArH), 7.07−7.15 (m, 3 H, ArH), 7.70−7.81 (m, 4 H, ArH). − ^{31}P NMR (161 MHz): δ = 46.3, 46.7. − MS (CI); *m*/*z* (%): 551 (5) [M^+ − 1]. − $C_{32}H_{42}O_4P_2$ (552.6): calcd. C 69.55, H 7.66; found C 69.59, H 7.67.

Preparation of Bis(phosphinylmethyl)arenes 42−46 from Bis(halomethyl)arenes. − General Procedure: LDA was prepared by the addition of *n*BuLi (2.2 equiv., 1.0 mL, 2.2 mmol, 2.5 M in hexanes), with 2,2′-bipyridine as indicator, to a solution of diisopropylamine (2.2 equiv., 0.34 mL, 2.2 mmol) in THF (15 mL) at 0 °C under nitrogen. The resulting deep red solution was stirred for 30 min, then cooled to −78 °C. It was then added dropwise to a solution of the (S_p)- or (R_p)-phenylphosphane oxides **4** or **5** (382 mg, 2.1 mmol, 2.1 equiv.) in THF (15 mL). The solution was stirred for 15 min, and then a solution of the dihalides (1.0 equiv., 1.0 mmol) in THF (15 mL) was added dropwise. The colour of the mixture changed from red to yellow immediately. The completion of the reaction was evaluated by TLC analysis. The reaction mixture was quenched with saturated aqueous NH_4Cl. The reaction mixture was extracted with Et_2O (3 × 30 mL). The combined extracts were washed with water (3 × 30 mL), brine (50 mL), dried with $MgSO_4$, and concentrated under reduced pressure to leave the crude product, which was purified by chromatography.

2,6-Bis(chloromethyl)pyridine: From **5** and the dihalide (176 mg, 1.0 mmol) in THF at −78 °C during 2 h was obtained a semicrystalline residue, chromatography (MeOH/EtOAc, 15:85) of which gave **44** (175 mg, 75%), as needles, m.p. 167−168 °C. − $[\alpha]_D^{22}$ = +30.8 (c = 1.05, $CHCl_3$), from CH_2Cl_2/hexane. − ^{1}H NMR (300 MHz): δ = 1.05 (d, J = 15.0 Hz, 18 H, Me_3C), 3.52−3.71 (m, 4 H, CH_2), 7.05−7.46 (m, 9 H, ArH), 7.72−7.75 (m, 4 H, ArH). − ^{13}C NMR (100 MHz): δ = 24.35 (s, Me_3C), 33.36 (d, J = 69.8 Hz, Me_3C), 33.81 (d, J = 56.9 Hz, C1′), 123.29 (s), 128.10 (d, J = 11.0 Hz, *o*-C), 131.66 (s, *p*-C), 132.03 (d, J = 7.4 Hz, *m*-C), 137.11 (s), 152.75 (d, J = 7.3 Hz). − ^{31}P NMR (121 MHz): δ = 45.7. − MS (EI); *m*/*z* (%): 467 (12) [M^+], 410 [M^+ − Me_3C], 354 [M^+ + 1 − 2 × Me_3C], 287 [M^+ − $PhMe_3CP(O)$]. − MS (CI); *m*/*z* (%): 468 (100) [M^+ + 1]. − IR (KBr): $\tilde{\nu}_{max}$ = 3424, 3049, 2971, 2940, 2917, 2867, 1594, 1578, 1457, 1436, 1389, 1367, 1224, 1173, 1105, 1057, 1003, 942 cm^{-1}. − $C_{27}H_{35}NO_2P_2$ (467.5): calcd. C 69.35, H 7.55, N 3.00; found C 69.15, H 7.55, N 2.92. − From **4** and the dihalide (176 mg, 1.0 mmol) in THF (10 mL) according to the general procedure was obtained, after chromatography (MeOH/EtOAc, 15:85), **42** (180 mg, 77%) as needles, m.p. 169−170 °C. − $[\alpha]_D^{23}$ = −30.6 (c =1.08, $CHCl_3$).

1,3-Bis(bromomethyl)benzene: The reaction mixture from the lithiated **4** and the dibromide (264 mg, 1.0 mmol) in THF (10 mL) was quenched with saturated aqueous NH_4Cl (10 mL) and extracted with EtOAc (3 × 15 mL). The extracts were washed with brine (10 mL), dried with $MgSO_4$ and concentrated under reduced pressure to leave a residue, chromatography (MeOH/EtOAc, 15:85) of which gave **43** (377 mg, 81%), as needles, m.p. 70−71 °C. − $[\alpha]_D^{23}$ = −103.3 (c = 1.35, $CHCl_3$), from CH_2Cl_2/hexane. − ^{1}H NMR (300 MHz): δ = 1.10 (d, J = 14.6 Hz, 18 H, Me_3C), 3.28−3.52 (m, 4 H, CH_2), 6.99−7.07 (m, 4 H, ArH), 7.38−7.42 (m, 6 H, ArH), 7.63−7.69 (m, 4 H, ArH). − ^{13}C NMR (75 MHz): δ = 24.67 (s, Me_3C), 31.16 (d, J = 58.9 Hz, Me_3C), 33.33 (d, J = 67.9 Hz, C1′), 127.96 (d, J = 10.9 Hz), 128.32 (s), 129.10 (s), 130.26 (s), 131.21 (s), 131.93 (d, J = 7.9 Hz), 132.14 (d, J = 8.4 Hz). − ^{31}P NMR (121 MHz): δ = 45.5. − IR (KBr): $\tilde{\nu}_{max}$ = 3057, 2968, 2937, 2898, 2871, 1438, 1397, 1362, 1216, 1171, 1109 cm^{-1}. − MS (EI); *m*/*z* (%): 466 (8) [M^+]; (CI); 467 (100) [M^+ + 1]. − $C_{28}H_{36}P_2O_2$ (466.5): calcd. C 72.07, H 7.78; found C 72.08, H 7.75. − Compound **5** and the dibromide (264 mg, 1.0 mmol) according to the above procedure gave **45** (374 mg, 80%), as needles, m.p. 70−71 °C. − $[\alpha]_D^{23}$ = +102 (c = 1.25, $CHCl_3$), from CH_2Cl_2/hexane. − ^{1}H NMR (300 MHz): δ = 1.10 (d, J = 14.6 Hz, 18 H, Me_3C), 3.28−3.52 (m, 4 H, CH_2), 6.99−7.07 (m, 4 H, ArH), 7.38−7.42 (m, 6 H, ArH), 7.63−7.69 (m, 4 H, ArH). − ^{13}C NMR (75 MHz): δ = 24.67 (s, Me_3C), 31.16 (d, J = 58.9 Hz, Me_3C), 33.33 (d, J = 67.9 Hz, C1′), 127.96 (d, J = 10.9 Hz), 128.32 (s), 129.10 (s), 130.26 (s), 131.21 (s), 131.93 (d, J = 7.9 Hz), 132.14 (d, J = 8.4 Hz). − ^{31}P NMR (121 MHz): δ = 45.5 (s). − IR (KBr): $\tilde{\nu}_{max}$ = 3057, 2968, 2937, 2898, 2871, 1438, 1397, 1362, 1216, 1171, 1109 cm^{-1}. − MS (CI); *m*/*z* (%): 467 (100) [M^+ + 1]. − $C_{28}H_{36}P_2O_2$ (466.5): calcd. C 72.07, H 7.78; found C 72.08, H 7.75.

1,4-Bis(bromomethyl)benzene: Lithiated **4** and the dibromide (263.8 mg, 1.0 mmol) in THF (10 mL) were stirred during 2 h. Chromatography (MeOH/EtOAc, 15:85) gave **46** (252 mg, 54%), from hexane, as a fine microcrystalline solid, m.p. 277−278 °C. − $[\alpha]_D^{20.5}$ = −75 (c = 0.46, $CHCl_3$). − ^{1}H NMR (300 mhz) δ = 1.08 (d, J = 14.4 Hz, 18 H, Me_3C), 3.25−3.48 (dd, J = 27.2, 9.8 Hz, 4 H, CH_2), 7.13 (m, 4 H, ArH), 7.37−7.68 (m, 10 H, ArH). − ^{13}C NMR (75 MHz): δ = 24.73 (s, Me_3C), 31.20 (d, J = 59.0 Hz), 33.42 (d, J = 68.2 Hz), 127.93 (d, J = 11.1 Hz), 130.13 (s), 131.26 (s), 131.92 (d, J = 7.9 Hz). − ^{31}P NMR (121 mhz): δ = 45.2. − MS (CI); *m*/*z* (%): 467 (100) [M^+ + 1]. − IR (KBr): $\tilde{\nu}_{max}$ = 3052, 2944, 2900, 2868, 1638, 1514, 1476, 1436, 1349, 1366,1324, 1246, 1168, 1136, 1108, 1072, 938 cm^{-1}. − $C_{28}H_{36}P_2O_2$ (466.5): calcd. C 72.07, H 7.78; found C 72.01, H 7.73.

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