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P-Stereogenic Compounds

Stereospecific Synthesis of α- and β-Hydroxyalkyl P-Stereogenic Phosphine–Boranes and Functionalized Derivatives: Evidence of the P=O Activation in the BH_3-Mediated Reduction

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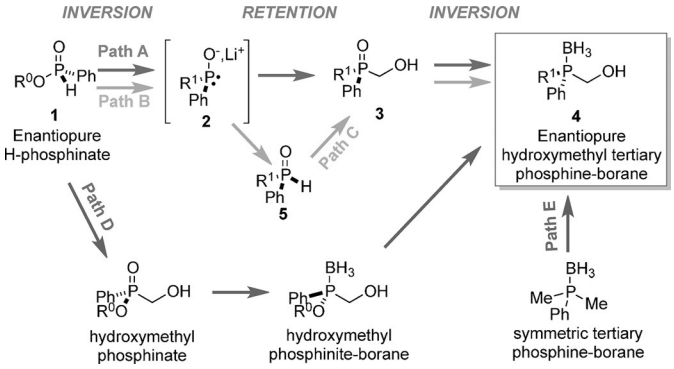
Abstract: Access to hydroxy-functionalized P-chiral phosphine–boranes has become an important field in the synthesis of P-stereogenic compounds used as ligands in asymmetric catalysis. A family of optically pure α and β-hydroxyalkyl tertiary phosphine–boranes has been prepared by using a three-step procedure from readily accessible enantiopure adamantylphosphinate, obtained by semi-preparative HPLC on multigram scale. Firstly, a two-step one-pot transformation affords the enantiopure hydroxyalkyl tertiary phosphine oxides in good yields and enantioselectivities. The third step, BH_3-mediated reduction, allows the formation of the desired phosphine–boranes with excellent stereospecifity. The mechanistic study of this reduction provides new evidence to elucidate the crucial role of the pendant hydroxy group and the subsequent activation of the P=O bond by the boron atom.

Introduction

Chiral phosphorus ligands are the most popular chiral ligands used in asymmetric organometallic catalysis, due to their tunable steric and electronic properties,[1] and therefore, play an important role in industrial processes.[2] Among these chiral ligands, bidendate or bifunctional phosphorus compounds are more appreciated, due to their potential to offer opportunities to construct well-defined and structurally rigid organometallic complexes. Moreover, P-stereogenic compounds bearing the chiral center closely bound to the active metal center could offer better enantioselectivity. For this reason the preparation of stable P-stereogenic compounds remains a challenge in asymmetric catalysis as organocatalysts[3] or as ligands.[4] The first synthesis of enantioenriched α-hydroxymethyl tertiary phosphine–borane by direct desymmetrization of the dimethylphenylphosphine–borane was initially reported by Evans and co-workers,[5] and pursued by others[6] (Scheme 1, path E). This class of compounds very recently gained more attention as they were used as key intermediates during the synthesis of hybrid phosphine–phosphite bidendate chiral ligands, which have been well developed in the past five years and found to be active for different catalytic enantioselective transformations.[7]



Scheme 1. Comparative pathways to prepare optically pure functionalized tertiary phosphine–boranes **4** (path A: this work; path B: ref. [16], [17]; path C: ref. [11]; path D: ref. [12]; path E: ref. [5], [6].

Access to enantioenriched hydroxyalkyl tertiary phosphine–boranes (TPB) is possible by reduction of the corresponding tertiary phosphine oxides (TPO). Many reagents can reduce the P=O bond with inversion or retention of configuration at phosphorus atom.[8] However, the relatively high temperature required to obtain the phosphine in high yield is a major drawback in terms of chemo- and stereoselectivity. This can be easily circumvented when the P=O bond bears an alcohol functionality controlling the reduction achieved by a mixture of $HSiCl_3$ and BH_3·THF complex.[9] Interestingly Kiełbasiński and

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co-workers[10] reported that enantioenriched hydroxyalkyl-TPOs could be reduced stereoselectively to the corresponding TPBs at room temperature by using BH_3·THF alone. Very recently, by using this reducing reagent, Pietrusiewicz and co-workers published the preparation of a large family of functionalized TPBs (Scheme 1, path C).[11] At the same time, our group developed a new methodology for the synthesis of these important molecules throughout three stereoselective steps (Scheme 1, path D).[12] Starting from optically pure H-adamantylphenylphosphinate **1**, we were able to prepare enantiopure hydroxymethyl-TPBs. First, optically pure H-adamantyl (hydroxymethyl)-phosphinates (e.r. > 97.5:2.5) were prepared, then reduced by stereospecific reduction with BH_3·THF to obtain the corresponding H-adamantyl(hydroxymethyl)phosphinites boranes (e.r. > 97.5:2.5). The latter afforded by alkylation the hydroxymethyl-TPBs (e.r. > 99.5:0.5).

Herein we report a practical synthesis of functionalized TPBs **4**, combining the two-step one-pot synthesis of optically pure α and β-hydroxyalkyl-TPO **3** followed by their stereospecific BH_3-mediated reduction (Scheme 1, path A). We aim to study the stereochemistry of the reactions by assigning precisely the absolute configuration of the P=O **3** and P-BH_3 **4** compounds by vibrational circular dichroism (VCD) and X-ray diffraction (XRD) of the obtained crystals. The dynamic stereochemistry of the chiral compounds and the NMR studies support the intermediates involving in the borane reduction reaction.

Results and Discussion

Two-step one-pot synthesis of α- and β-hydroxy-functionalized phosphine oxides

The preparation of functionalized TPOs **3** was developed first by Haynes and co-workers.[13] The reaction of the configurationally stable lithiated P-chiral *tert*-butylphenylphosphine oxide with aldehydes and α,β-unsaturated carbonyl compounds takes place at −78 °C, resulting in high yields with moderate to good diastereoselectivities. These phosphinylation reactions proceed with retention of configuration at the phosphorous atom. From ethylphenylphosphinate, other TPOs have been prepared by reaction with *tert*-butyllithium, followed by addition of propylene oxide.[9,14] Recently, first-rank studies on crystallization-induced asymmetric transformations developed by Minnaard and co-workers showed the importance of obtaining hydroxy-functionalized TPO **3**.[15] Starting from racemic secondary phosphine oxide (SPO), a family of optically pure α-hydroxymethyl TPOs was obtained with good yield and diastereoselectivities, thanks to the consecutive crystallization-induced asymmetric transformations.

According to these studies, enantioenriched compounds **3** were prepared from SPO or from the lithiated phosphinite **2**, which can be obtained from phosphinates (Scheme 1, path B). Indeed P-stereogenic SPOs have been synthesized with an excellent enantioselectivity from diastereoisomerically pure (R_P)-H-menthylphenylphosphinate and organolithium or Grignard reagents. The nucleophilic substitution of the menthyloxy leaving group of the H-phosphinate proceeds stereospecifically with inversion of configurations at phosphorus. Others[16] and our group[17] have shown that substitution reaction results from a two-step reaction path involving first a deprotonation of H-phosphinates followed by a substitution of the menthyloxy group. Depending on the reactivity of the organometallic reagent, we have demonstrated a competitive reaction between the H-menthylphenylphosphinate and the leaving menthylate anion. This degenerate process, whereby the nucleophile and leaving group are the same, causes epimerization of the phosphorus chiral center and a subsequent decrease in the enantioselectivity of the SPOs. Therefore we underwent recently the preparation of a more stable phosphinate, the H-adamantylphenylphosphinate **1**.[18] 25 g of each enantiomer can be prepared by semipreparative chiral HPLC. We demonstrated its significant reactivity, affording a large variety of P-stereogenic compounds through a divergent strategy.[12] Among these compounds, enantioenriched SPOs were obtained in good yields and enantioselectivities.

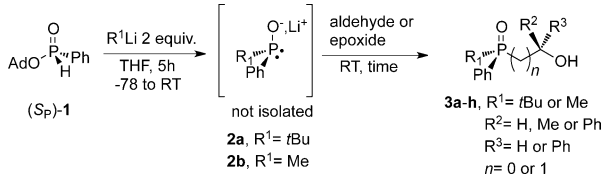
We applied herein this strategy to develop the synthesis of optically pure phosphine oxides **3**. Enantiopure (S_P)- or (R_P)-**1** reacts with 2 equivalent of *tert*-butyllithium or methyllithium to form the phosphinito intermediate **2**, which then reacts in situ with various aldehydes or epoxides as electrophiles to afford the chiral TPO **3** in moderate to good yields (Table 1). This one-pot synthesis is very convenient, as it avoids the nontrivial purification of the SPO from 1-adamantanol (derived from the hydrolysis of **2**). Moreover, the reaction is divergent, as it allows the introduction of two different alkyl groups (*t*Bu or Me) on the phosphorus atom, as well as various pendant hydroxyalkyl chains. Remarkably, no erosion of the enantiomeric excess was observed (although a very slight erosion was noted in the case of the formation of **3b**). All compounds were obtained with high enantioselectivity. When using paraformaldehyde as an electrophile, the alkylations were completed in only 2 h (Table 1, entries 1–3), regardless of the alkyl groups on the phosphorus atom. For the other aldehydes and epoxides, the alkylations were slower (completed in 15 h). For acetaldehyde, we observed a low diastereoselectivity (1.4:1) in favor of the like (S_PS)-diastereoisomer **3d** (according to XRD; see the Supporting Information). For benzaldehyde, a better diastereoselectivity was obtained (3:1). The addition of 2,2-diphenylepoxide (Table 1, entry 11) afforded the phosphine oxide **3h** in low yield.

We also carried out the preparation of analogues of the phosphine oxide **3a** in which the OH group is replaced by various functions: ether **6** (Scheme 2), tertiary amine **7**, secondary amine **8**, alkene **9**, ketone **10** and amide **11** (Table 2).

Synthesis of phosphine–boranes through stereospecific BH_3-mediated reduction

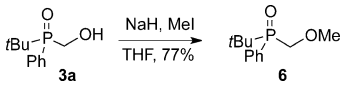
With a family of optically pure α- or β-hydroxyalkyl TPOs **3** and α-functionalized TPOs **6**–**10** in hand, we studied their reduction with borane complexes. In contrast with the mechanism proposed by Kiełbasiński,[10b] who did not consider the participation of the hydroxy group in the reduction (Scheme 3, path A), Pietrusiewicz and co-workers[11] suggested that the re-

Table 1. One-pot preparation of optically enriched tertiary phosphine oxides (TPO) **3** from enantiopure phosphinate **1**.



Entry	**1**	R^1	Electrophile	*n*	R^2	R^3	*t* [h]	Yield [%]	d.r.	**3** (e.r.)
1	S_P	*t*Bu		0	H	H	2	66	n.a.	(R_P)-**3a** (99:1)
2	R_P	*t*Bu		0	H	H	2	67	n.a.	(S_P)-**3a** (99.5:0.5)
3	R_P	Me		0	H	H	2[a]	48	n.a.	(S_P)-**3b** (96:4)
4	S_P	*t*Bu		1	H	H	15	67	n.a.	(R_P)-**3c** (99.5:0.5)
5	R_P	*t*Bu		1	H	H	15	66	n.a.	(S_P)-**3c** (99.5:0.5)
6	R_P	*t*Bu		0	Me	H	15	58	1.4:1	(S_P,*S*)-**3d** (>99.5:0.5[b])
7	S_P	*t*Bu		1	Me	H	15	61	>20:1[c]	(R_P,*R*)-**3e** (99.5:0.5)
8	S_P	*t*Bu		1	H	Me	15	64	>20:1[c]	(R_P,*S*)-**3e** (99.5:0.5)
9	S_P	*t*Bu		0	H	Ph	15	67	3:1	(R_P,*R*)-**3f** (99.5:0.5[d])
10	S_P	*t*Bu		1	Ph	H	15	54	>20:1[e]	(R_P,*R*)-**3g** (99.5:0.5)
11	R_P	*t*Bu		1	Ph	Ph	15	20	n.a.	(S_P)-**3h** (99.5:0.5)

Equation depicts absolute configuration S_P for compound **1**. [a] Addition of phosphinate was carried out at −20 °C; [b] absolute configurations of the major diastereoisomer determined by DRX analysis; e.r. of minor diastereoisomer = 98.5:1.5; [c] reaction with racemic phosphinate and epoxide gave a 1.4:1 diastereoisomeric ratio; [d] absolute configuration assigned by analogy with the compound **3d**; e.r. of minor diastereoisomer = 98:2; [e] reaction with racemic phosphinate and epoxide gave a 1.2:1 diastereoisomeric ratio.



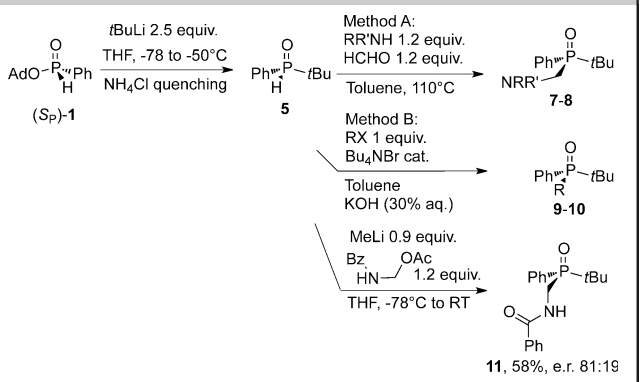
Scheme 2. Synthesis of α-methoxyether tertiary phosphine oxide **6**.

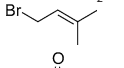
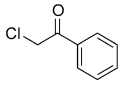
duction of the phosphine oxides **3** is promoted by the presence of the OH group, which reacts first with BH_3 to afford the 5-membered ring key intermediate **A**. The latter evolves for further reduction, providing the reduced compound **B** (Scheme 3, path B). Recently, we employed this convenient method to obtain optically pure hydroxymethylphosphinite–boranes.[12] Interestingly, this reduction led to the selective reduction of the P=O bond with limited reduction of the POAd bond (Scheme 4).

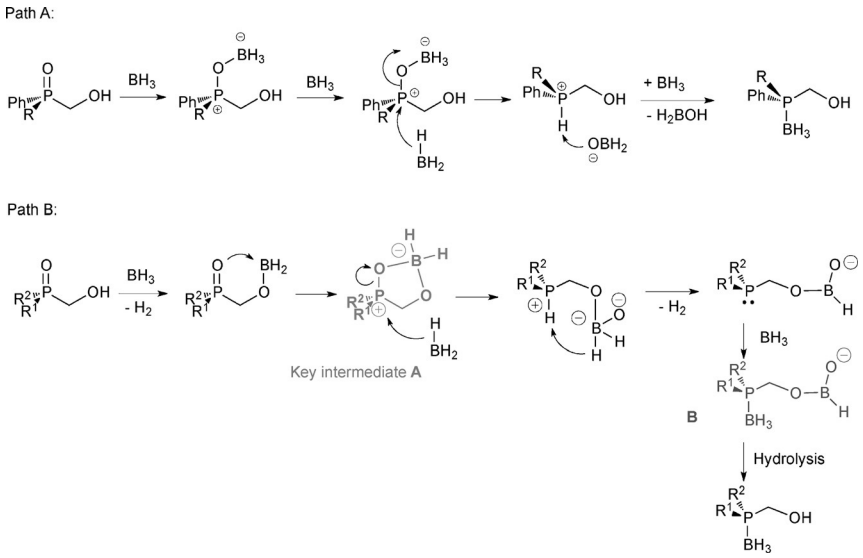
To gain more information on the mechanism of this reduction, we examined the influence of the amount of BH_3·THF complex on the conversion of **3a** into **B** (in situ ^{31}P NMR analysis) and on the yield of **4a** after 2 h at room temperature (Table 3 and Figure 1). When using 0.33 equivalents of BH_3·THF, **3a** was fully converted but no reduction of the P=O bond occurred (Table 3, entry 1). When increasing the amount to 0.66 equiv, a small amount of **4a** was detected but not isolated (Table 3, entry 2). Increasing the amount of borane allowed the formation of **4a** regularly. With 2 equivalents of BH_3·THF, the reduction went almost to completion (Table 3, entry 5) but the system reached the maximum conversion when using 3 equivalents of borane. After hydrolysis, compound **4a** was obtained in 94% yield (Table 3, entry 7).

To better understand the nature of different species involved during the reduction process, we monitored the reduction by ^{31}P NMR spectroscopy. This allowed the observation of the disappearance of starting material **3a** and the appearance of the supposed intermediates **A** and **B** (Scheme 3). However, it appears that the reaction mixture is more complex due to the formation of the compounds $\mathbf{A}_n$ and $\mathbf{B}_n$ by the disproportionation equilibria (Scheme 5). As previously mentioned, when using 0.33 equivalents of BH_3·THF, no reduction of the P=O bond occurred, even if **3a** disappeared completely (Table 3, entry 1). Notably, after 90 h, only one narrow peak at $\delta = 41$ ppm (^{31}P NMR) was observed, as well as a broad peak at $\delta = 20$ ppm (^{11}B NMR).

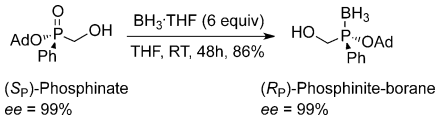
Table 2. Preparation of optically enriched functionalized tertiary phosphine oxides (TPO) from enantiopure SPO **5**.



Entry	RR′NH or RX	Method	Yield [%]	TPO (e.r.)
1	Et_2NH	A	62	(R_P)-**7** (99:1)
2	$BnNH_2$	A	66	(R_P)-**8** (95.5:4.5)
3		B	81	(R_P)-**9** (99.5:0.5)
4		B	53	**10**



Scheme 3. Proposed mechanism by Kiełbasiński (path A) and Pietrusiewicz (path B) for the BH_3-mediated reduction of α-hydroxymethyl TPO. Molecules of THF that stabilize the boron species are omitted for clarity.



Scheme 4. Stereospecific reduction of α-hydroxymethylphosphinate to α-hydroxymethylphosphinite–borane.

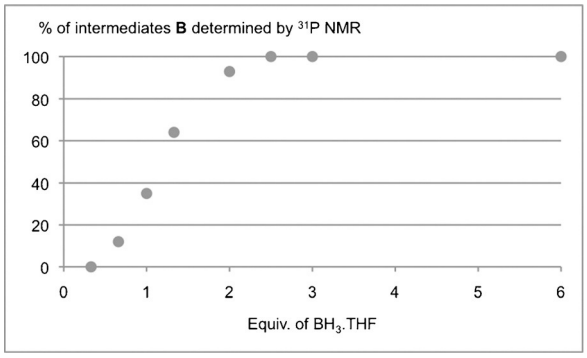
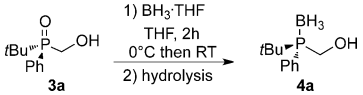


Figure 1. Influence of the amount of BH_3·THF on the formation of intermediates **B**.

Table 3. Influence of the amount of BH_3·THF on the conversion of phosphine oxide **3a** into phosphine–borane **4a**.



3a **4a**

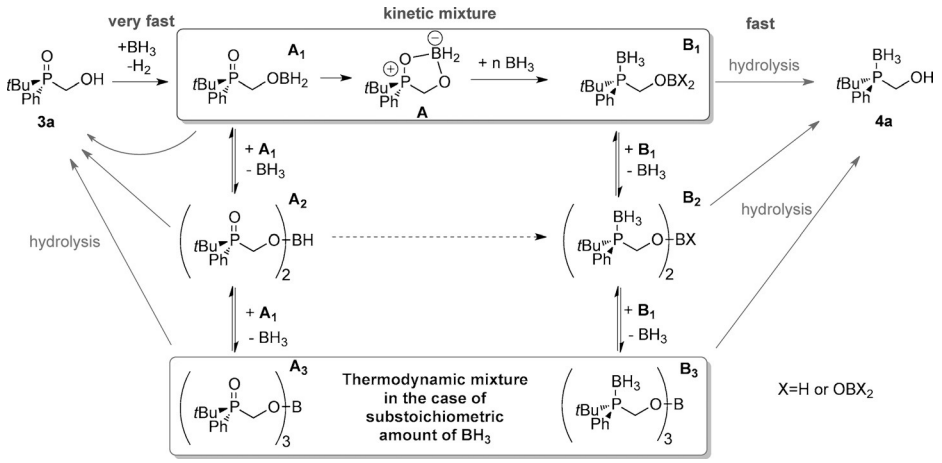
Entry	e.r. of **3a**	Equiv. of BH_3·THF	Conv. [%][a]	**B** [%][b]	Yield [%][c]	e.r. of **4a**
1	*rac*	0.33	100	0	–[d]	–
2	*rac*	0.66	100	12	–	–
3	*rac*	1	100	35	31	*rac*
4	*rac*	1.33	100	64	59	*rac*
5	*rac*	2	100	93	88	*rac*
6	*rac*	2.5	100	100	91	*rac*
7	*rac*	3	100	100	94	*rac*
8	*rac*	6	100	100	96	*rac*
9	97:3 (R_P)	2.5	n.d.	100	91	98:2 (R_P)
10	99:1 (R_P)	1.33	n.d.	64	59	97:3 (R_P)
11	97:3 (S_P)	6	n.d.	100	87	95:5 (S_P)
12	99:1 (R_P)	6	n.d.	100	97	96:4 (R_P)

Equation depicts absolute configuration R_P for compound **3a**. [a] After 2 h, determined by ^{31}P NMR spectroscopy; [b] after 2 h, presence of the intermediates **B** determined by ^{31}P NMR spectroscopy; [c] isolated product; [d] 70% of starting material recovered.

This suggests the presence of the P=O species alone without interaction (due to steric hindrance) with the formed $B(OR)_3$ unit. According to this data, we supposed that the compound $\mathbf{A_3}$ had been formed (see NMR spectra in the Supporting Information). When **3a** reacts with 0.66 equivalents of borane, the intermediates **B** were formed after 2 h, according to the ^{31}P NMR spectrum (Figure 2).

The broad peaks detected at $\delta = 27$–33 ppm were attributed to P–BH_3 species indeed the signals correspond to the one obtained when the compound **4a** is in presence of 0.5 equivalents of BH_3·THF in [D_8]THF (see NMR spectra in the Supporting Information). After 24 h, we detected a broad and intense peak at $\delta = 43$–44 ppm, corresponding to a mixture of compounds **A**. This chemical shift corresponds to that of P–O species with a weak interaction with the neighboring boron atom. After 70 h, the thermodynamic mixture presents two major peaks, one at $\delta = 41$ ppm that corresponds to the one attributed to $\mathbf{A_3}$ and the other at $\delta = 27$–28 ppm inherent to one of the compounds **B**.

We have considered the dynamic stereochemistry of the borane reduction from enantiopure starting compounds. The reaction is stereospecific, as the reductions on enantiopure (R_P)- and (S_P)-**3a** occurred with inversion of the configuration at the phosphorus atom and led only to the enantiomers (R_P)- and (S_P)-**4a**, respectively (Table 3, entries 9-12). The inversion and the absolute configuration of the P-stereogenic centers were determined by XRD (Figure 3) and confirmed by VCD spectroscopy (Figure 4), the efficiency of which has been proven in solving the absolute configurations of numerous chiral molecules.[19]



Scheme 5. Disproportionation during the reduction of **3a** with BH_3. Only the homodimers or trimers of the P=O ($\mathbf{A_2}$ and $\mathbf{A_3}$) and P–BH_3 ($\mathbf{B_2}$ and $\mathbf{B_3}$) species were drawn for clarity but heterodimers or trimers should be also present.

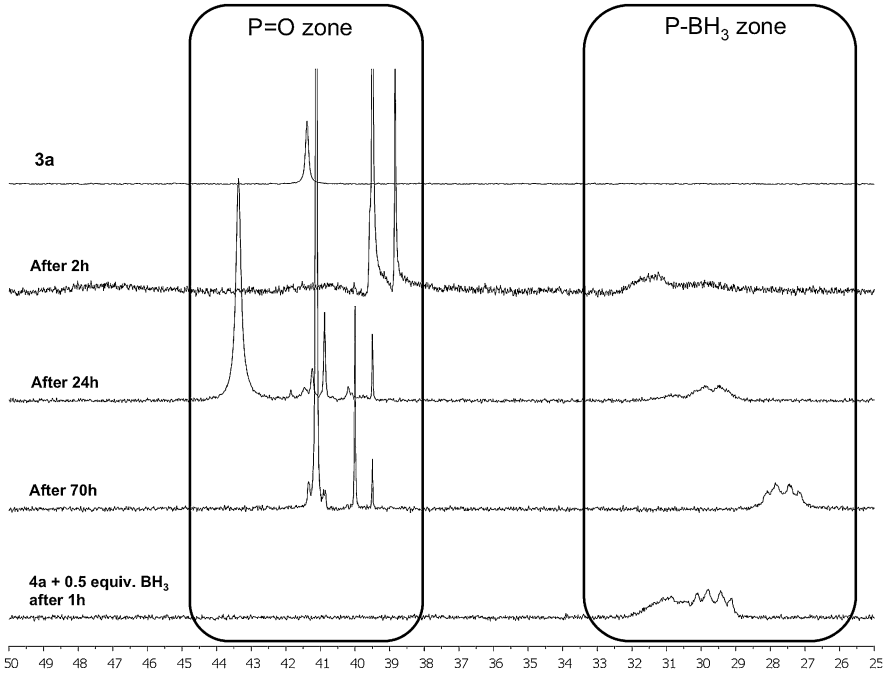


Figure 2. ^{31}P NMR spectra from the reaction of **3a** with 0.66 equivalents of BH_3·THF in [D_8]THF at 25 °C.

The absolute configurations of pure enantiomers (−)-**3a** and (−)-**4a** were obtained by comparing their experimental IR and VCD spectra with the corresponding average spectra calculated for (R_P)-**3a** and (S_P)-**4a** enantiomers, respectively. A very interesting couplet at 2400 cm^{-1} can be observed on the spectrum of **4a**, which is associated to the stretching vibrational modes of the B–H bonds of the borane moiety. These bands, relatively intense and isolated on the spectra, are very good chirality indicators that have, to our knowledge, not to date been used for this series of molecules. Indeed the sign of the couplet (− or +) can be related to the absolute configuration (S_P) of the molecule. The band associated to the stretching vibrational mode of the O–H bond (3600 cm^{-1}) is also remarkable. Although less intense, like B–H stretching bands it is isolated on the VCD spectra and its negative sign can be related to the (S_P) absolute configuration. Thus, by analysing the IR and VCD spectra in the spectral range 3800–1800 cm^{-1}, but also between 1800 and 1050 cm^{-1} (see the Supporting Information), we established unambiguously the absolute configurations (S_P) of enantiomer (−)-**4a**. Considering that a majority of calculated bands of (R_P)-**3a** have the same signs and intensities as the measured bands of (−)-**3a**, we were also able to establish its absolute configuration.

The optimized conditions (3 equivalents of BH_3·THF) were applied to the reduction of the enantiopure α- or β-hydroxyalkyl TPO **3** (Table 4). The main point of this study is the stereospecificity of the reaction as observed in the case of **3a**. Here again, the reactions occurred with inversion of configuration at the phosphorus atom, as confirmed for the products **4c** and **4d** by XRD (see the Supporting Information) and VCD (Figure 5). Thanks to the couplet at 2400 cm^{-1}, we established the absolute configuration (S_P) of (−)-**4c** and (S_P,S) of (−)-**4d**.

The reduction of the compounds **3** probably proceeds according to the same mechanism. However, β-hydroxyalkyl TPO ($n=1$; Table 4, entries 2, 3, 5, 6, 8, and 9) were much less reactive than α-hydroxyalkyl TPO ($n=0$; Table 4, entries 1, 4, and 7). Indeed, a higher temperature (50 °C) and more borane (6 equiv) were necessary to obtain the TPB with moderate yields (34–57%). The difference in the length of the alkyl chain is probably responsible of this difference of reactivity. The first step of the reduction is supposed to be the formation of a P–O–B key intermediate **A** (see Scheme 3, path B). Compounds **3a**,**b**,**d**,**f** would form a 5-membered ring intermediate whereas compounds **3c**,**e**,**g**,**h** would form a 6-membered ring intermediate. It is interesting to compare this difference in reactivity to that observed during the hydrolysis of cyclic phosphonium species, which is 1300 times faster for the 5-membered ring than for the 6-membered ring.[20]

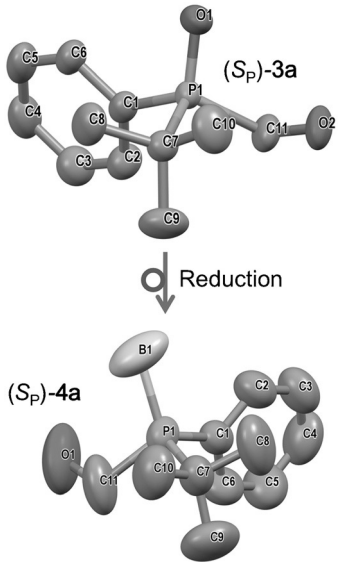


Figure 3. Single crystal X-Ray structures of phosphine oxides **3a** and corresponding phosphine–boranes **4a**. Thermal ellipsoids are set at 50% probability. Hydrogen atoms are omitted for clarity.

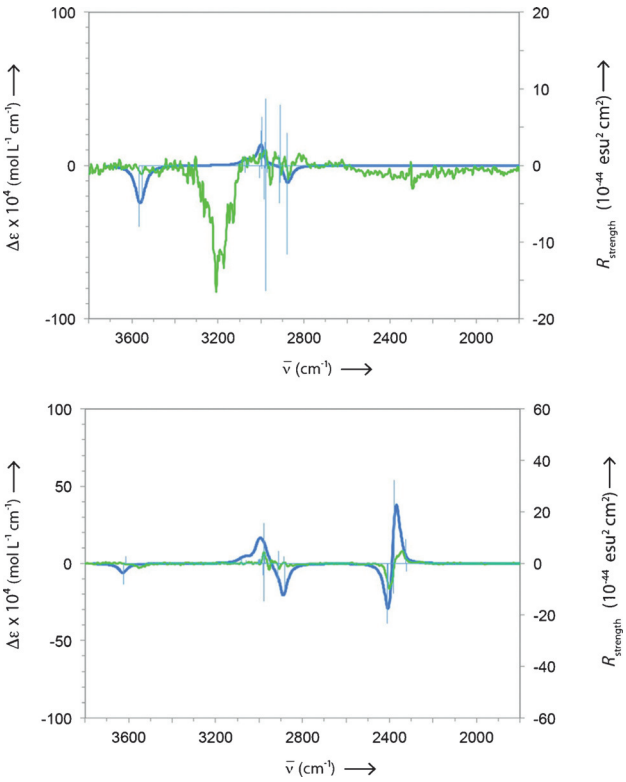
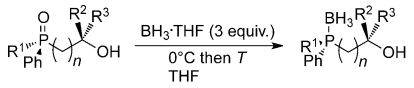


Figure 4. VCD spectra of **3a** [top; green: measured for (−)-**3a**; blue: calculated for (R_P)-**3a**] and **4a** [bottom; green: measured for (−)-**4a**; blue: calculated for (S_P)-**4a**]

In the case of the reductions of **3d** and **3f** ($n=0$, $R^3 \neq H$), racemic secondary phosphine–borane (SPB) *t*BuPhP(BH_3)H was obtained in 12 and 11% yields, respectively (Table 4, entries 4 and 7), and the amount does not increase for the prolonged reaction time. Moreover, **4d** does not undergo the retro-phosphinylation in the presence of excess BH_3, even under heating conditions, which shows the stability of the protected phosphine. Nevertheless, a loss of d.r. was observed during the formation of **4d** and **4f** (respectively from >20:1 to 15:1 and from 3:1 to 2.5:1), and the e.r. of the minor diastereoisomer of **4f** was 87:13 (Table 4, entry 7). These results can be attributed to the instability of the free α-hydroxyphosphines, which give achiral *tert*-butylphenyphosphide according to a retro-phosphinylation.

To study the BH_3 reduction chemoselectivity, different attempts were made to reduce the various α- or β-functionalized phosphines (ether **6**, tertiary amine **7**, secondary amine **8**, alkene **9**, ketone **10**, and amide **11**; Scheme 6).

Table 4. Reduction of TPO **3** to TPB **4**.



3a-h, R^1= *t*-Bu or Me, R^2= H, Me or Ph, R^3= H or Ph, *n*= 0 or 1 → **4a-h**, R^1= *t*-Bu or Me, R^2= H, Me or Ph, R^3= H or Ph, *n*= 0 or 1

Entry	**3** (e.r./d.r.)	*n*	R^1	R^2	R^3	*t* [h]	*T* [°C]	Yield [%]	d.r.[a]	**4** (e.r.)[b]
1	(S_P)-**3b** (96:4)	0	Me	H	H	2[c]	25	87	n.a.	(S_P)-**4b** (96.5:3.5)
2	(R_P)-**3c** (99:1)	1	*t*Bu	H	H	72[d]	50	56	n.a.	(R_P)-**4c** (99.5:0.5)
3	(S_P)-**3c** (99.5:0.5)	1	*t*Bu	H	H	72[d]	50	59	n.a.	(S_P)-**4c** (99.5:0.5)
4	($S_P S$)-**3d** (98.8:1.2/>20:1 d.r.)	0	*t*Bu	Me	H	5	25	73[e]	15:1	($S_P S$)-**4d** (99:1)
5	($R_P R$)-**3e** (99.5:0.5/>20:1 d.r.)	1	*t*Bu	Me	H	84[d]	50	51	>20:1	($S_P R$)-**4e** (99.5:0.5)
6	($R_P S$)-**3e** (99.5:0.5/>20:1 d.r.)	1	*t*Bu	H	Me	84[d]	50	54	>20:1	($R_P S$)-**4e** (99.5:0.5)
7	($R_P R$)-**3f** (99.5:0.5/3:1 d.r.)	0	*t*Bu	Ph	H	2	25	63[f]	2.5:1	($R_P R$)-**4f** (98.5:1.5[g])
8	($R_P R$)-**3g** (99.5/:0.5/>20:1 d.r.)	1	*t*Bu	Ph	H	72	50	57	>20:1	($R_P R$)-**4g** (>99.5:0.5)
9	(S_P)-**3h** (99.5:0.5)	1	*t*Bu	Ph	Ph	72	50	41	n.a.	(S_P)-**4h** (98.5:1.5)

Equation depicts absolute configuration R_P for compound **3a–h**. [a] Determined by ^{31}P NMR spectroscopy before the workup; [b] e.r. of the major diastereoisomer; [c] with 4 equivalents of BH_3·THF; [d] with 6 equivalents of BH_3·THF; [e] 12% of racemic SPB was also isolated; [f] 11% of racemic SPB was also isolated; [g] e.r. of minor diastereoisomer was 87:13.

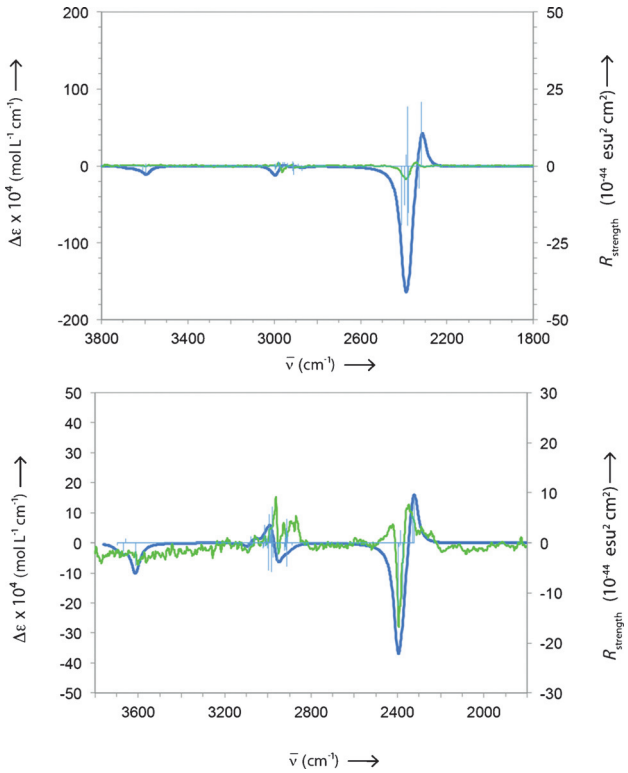
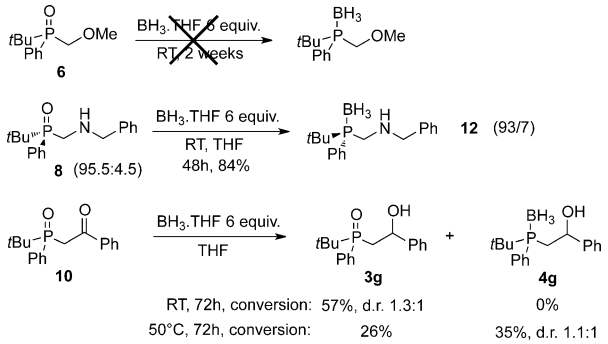


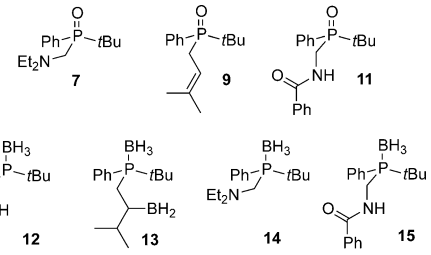
Figure 5. VCD spectra of **4c** [top; green: measured for (−)-**4c**; blue: calculated for (S_P)-**4c**] and **4d** [bottom; green: measured for (−)-**4d**; blue: calculated for (S_PS)-**4d**]



Scheme 6. Attempts at reduction of ether **6**, amine **8**, and ketone **10**.

All reactions were carried out with 6 equivalents of BH_3·THF complex. As expected, no reaction occurred with the α-ether/phosphine oxide **6**. This result accounts for the implication of the hydroxy group in the mechanism of the P=O reduction. The α-secondary amino phosphine oxide **8** was transformed into the α-amino phosphine–borane **12** in 84% yield. Starting from enantioenriched **8** (e.r. = 95.5:4.5), the reduction occurred with a very slight erosion of the enantiomeric excess (e.r. = 93:7). The prior formation of R^1R^2NH–BH_3 complex could lead to the formation of the dehydrogenated $R^1R^2N^+{=}BH_2^-$ with the assistance of the neighboring P=O bond.[21] This species could give rise to a 5-membered ring **A**-type intermediate, as in the favorable enantioselective reduction of **3a**.

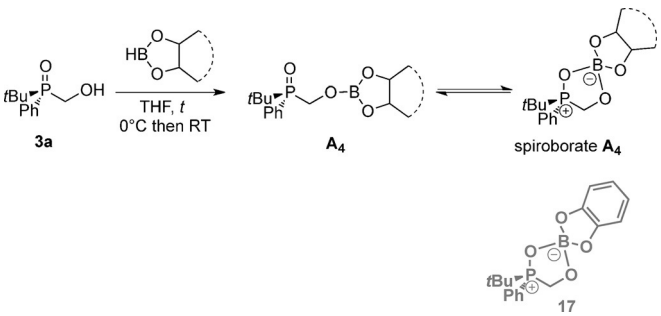
The reduction of the β-ketone/phosphine oxide **10** was also interesting (Scheme 6). At room temperature, only the ketone function was reduced after 72 h to give the secondary alcohol **3g** (57% conversion determined by ^{31}P NMR spectroscopy) in 1.3:1 d.r. At 50 °C, the reaction went further, affording the phosphine–borane **4g** (35% conversion). This corroborates the result obtained during the reduction of **3g**, which forms the less reactive 6-membered ring intermediate (Table 4, entry 8). In the case of α-amide/phosphine oxide **11**, the α-secondary amino phosphine–borane **12** and the α-amide/phosphine–borane **15** were obtained in 53 and 10% yield, respectively, after 2 h (Scheme 7 and the Supporting Information). The reduction of the other functionalized phosphine oxides **7** and **9** was also examined. Surprisingly the α-tertiary amino phosphine oxide **7** was reduced to the non-stable α-tertiary amino phosphine–borane **14** (29% conv. after 60 h). This reactivity could be explained by the BH_3–NR_3 interaction, which could be sufficient to activate the neighboring P=O group. The β,γ-alkenyl phosphine oxide **9** was converted by action of BH_3 into the phosphine–borane **13**, as a mixture of disproportionation products (based on ^{31}P NMR of the crude; attempted derivatization with H_2O_2/$NaOH_{(aq)}$ led only to trace amount of alcohol; see the Supporting Information).



Scheme 7. α-Functionalized phosphine oxides **7**, **9**, and **11** and their reduced derivatives **12**, **13**, **14**, and **15**.

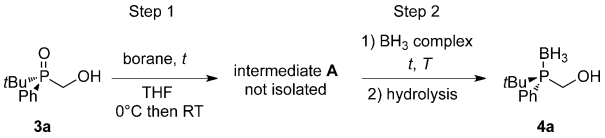
Isolation of the key intermediate A

To establish the presence of a 5-membered ring intermediate during the reduction, we undertook the preparation of the spiroborate $\mathbf{A_4}$, by addition of 1.05 equivalents of pinacolborane or catecholborane to **3a** (Scheme 8). No cyclic intermediate was isolated with pinacolborane. However, with catecholbor-



Scheme 8. Isolation of the spiroborate $\mathbf{A_4}$ during reduction of **3a** with various types of borane.

Table 5. Effect of the nature of the borane on enantioselectivity.

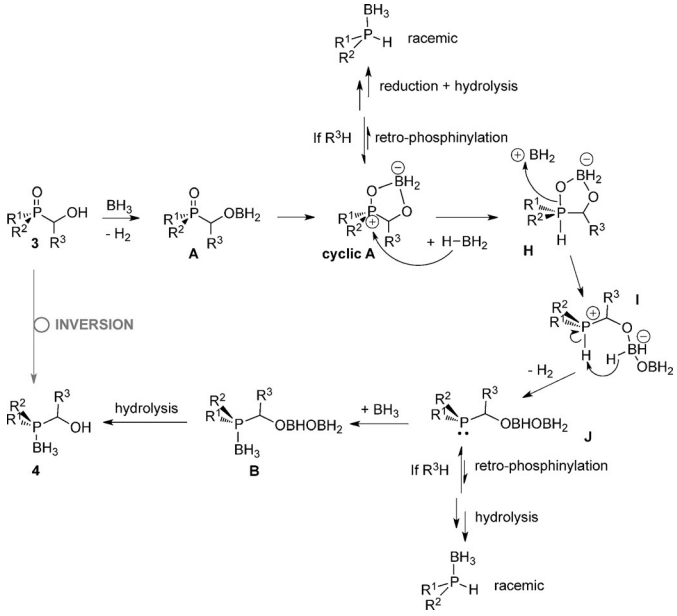


Entry	e.r. of **3a**	Step 1	Step 2	Yield [%]	e.r. of **4a**
1	99.5:0.5 (S_P)	2 equivalents of BH_3·SMe_2, 6 h	–	87	97:3 (S_P)
2	99:1 (R_P)	4 equivalents of catecholborane, 2 h[a]	3 equivalents of BH_3·SMe_2, 0 °C, 1 h	91	51:49
3	99:1 (R_P)	1.05 equivalents of catecholborane, 1 h	1.33 equivalents of BH_3·THF, RT, 2 h	69	82:18 (R_P)
4	98.9:1.1 (R_P)	4 equivalents of pinacolborane, 6 h	–	0	n.d.

Equation depicts absolute configuration R_P for compound **3a**. [a] The reduced products were detected by ^{31}P NMR before the Step 2 which resulted in their protection (see the Supporting Information).

ane, the cyclic intermediate **17** was isolated in 68% yield (see the Supporting Information). The $^{31}P\{^1H\}$ NMR spectrum displays a broad signal at $\delta = 68$ ppm, which is shifted to lower field with respect to **3a**, thus evidencing the interaction between P=O and $B(OR)_3$.[22] Moreover, the ^{11}B NMR spectrum showed a more shielded shift ($\delta = +12.7$ ppm) compared to that of catechol–B(OR) ($\delta = +23$ ppm).[23] Similarly, reaction of **3c** with catecholborane afforded the corresponding 6-membered ring intermediate as confirmed by the $^{31}P\{^1H\}$ and ^{11}B NMR at $\delta = 67.9$ and 13.3 ppm, respectively. Unfortunately, crystallization attempts were not successful due to the high moisture sensitivity.

Further experiments were carried out to study the effect of the nature of borane on the reduction of the P=O bond (Table 5). As expected, reduction with BH_3·SMe_2 required longer reaction time to be completed, although the enantiopurity was not extensively affected (e.r. = 97:3; Table 5, entry 1). Surprisingly, the catecholborane reduced **3a**, also but led to complete racemization (Table 5, entry 2). In contrast, pinacolborane failed to reduce P=O (Table 5, entry 4). Reducing **3a** stepwise with 1.05 equivalents of catecholborane followed by 1.33 equivalents of BH_3·THF afforded compound **4a** with a reduction of enantiopurity to e.r. = 82:18 (Table 5, entry 3). The racemization process with catecholborane is evident. Although the exact mechanismrequires further study, we believe that the free phosphine *t*BuPhPCH$_2$O–catecholborane, formed under BH_3-deficient conditions, can reversibly undergo the retroaddition reaction to form the symmetrical *t*BuPhP$^-$ phosphide anion.



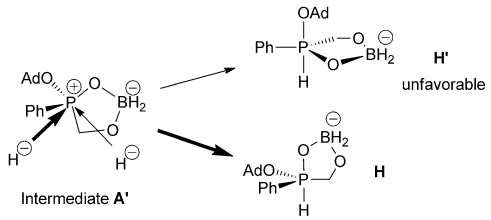
Scheme 9. Proposed mechanism for the stereospecific BH_3-mediated reduction of **3**. Molecules of THF that stabilize the borane species are omitted for clarity

Mechanistic aspects of BH_3-mediated reduction

The above experimental data demonstrates the implication of one molecule of BH_3 in the formation of the 5-membered ring intermediate "cyclic **A**," which activates the P=O bond to allow its reduction, as suggested by Pietrusiewicz and co-workers.[11] Therefore, we proposed a mechanism whereby the participation of the hydroxymethylene chain is a determining factor in the reduction of the P=O bond (Scheme 9).

In a first step, fast deprotonation of the alcohol group with borane leads to the formation of an alkoxyborane $R^1R^2P(O)CH_2OBH_2$ **A** and hydrogen gas. A favorable intramolecular acid–base Lewis interaction between the alkoxyborane and the oxygen of the P=O bond affords a 5-membered cyclic zwitterionic phosphonium intermediate "cyclic **A**." The latter reacts with the BH_3·THF in the position *anti* to the P–O bond to give a pentacoordinated oxyphosphorane **H** with an anionic five membered ring bound at one apical position (through O) and one equatorial position (through C) of the trigonal bipyramidal (TBP) structure and the hydrogen at the other apical position. The R^1 and R^2 substituents and the ring carbon are positioned in favorable equatorial positions with respect to the apicophilicity rule.[24] This mechanism involves an inversion of configuration at phosphorus affording the H–phosphonium intermediate **I**. Ring strain imposed on the intermediate "cyclic **A**" may lower the energy difference between the latter and transition state, if that strain is partly relieved along the reaction coordinate. Indeed the borane reduction rate depends on the ring size of the intermediate; for $n = 0$, the phosphine oxide is

reduced very fast compared with the phosphine oxide with $n=1$, for which the reduction is very slow (see Table 4). The deprotonation of the phosphonium **I** with the pendant alkoxy–BH_2 anion leads to the free phosphine **J**, which has to be quickly protected by BH_3 to retain its enantiopurity. The final hydrolysis releases the desired compound **4**. In the case of the reduction of **3 d** or **3 f** we observed the partial formation of racemic SPB (Table 4, entries 4 and 7). This could be explained by the cleavage of the P–C bond (retro-phosphinylation), which could occur during the different steps of the reduction, probably from intermediates **A** or **J**. This borane reduction mechanism, based on the P^V phosphorane intermediate, could also be applied to interpret the reduction of the adamantyl(hydroxymethyl)phenylphosphinate ($R^1=$AdO; $R^2=$Ph; $R^3=$H), in which the departure of AdO was limited. The apical attack of the hydride on the cyclic phosphonium **A′**, in line with the AdO substituent, leads an unfavorable diequatorial positioning of the five-membered ring, with the hydride and AdO substituents in the apical positions of the trigonal bipyramid **H′**. This unfavorable process is high in energy with respect to a hydride attack, leading to a privileged phosphorane **H** (Scheme 10).



Scheme 10. Extension of the mechanism to adamantyl(hydroxymethyl)phenylphosphinate.

Conclusion

In summary, we have developed a stereospecific efficient synthesis of α- and β-hydroxy-functionalized P-chiral tertiary phosphine–borane complexes from enantiopure H-adamantylphenylphosphinate. We have shown that the α- and β-hydroxy chain bound to the phosphorus plays a major role in the reduction of P=O. This chain controls the stereochemistry of the reduction by formation of a pentacoordinated P^V intermediate. Indeed the BH_3 play three roles: activating, reducing and protecting agent. We are convinced that this synthetic method will be used to prepare different functionalized stereogenic P^{III} compounds.

Experimental Section

General considerations are found in the Supporting Information.

Syntheses

General procedure A: One-pot nucleophilic addition/aldehyde trapping of adamantyl phosphinate for the preparation of 3a, b, d, and f

A flame-dried 250 mL two-necked round bottom flask was charged with dry THF (65 mL), then the flask was cooled to −78 °C and organolithium reagent (2.4 equiv) was added slowly. The resulting yellow mixture was stirred for 15 min at around −75 °C. Then, a solution of adamantylphosphinate in THF (1 equiv) (0.5 M in THF) was added dropwise at −78 °C and the reaction mixture was maintained at a temperature below −75 °C for 1 hour. The mixture was allowed to warm to −30 °C over 3 h and at that temperature, distilled water (15 mL) was added and then the reaction was warmed to room temperature. Then, corresponding aldehyde (1.6 equiv) was added and the mixture was stirred for 1 h. The reaction mixture was cooled to 0–5 °C and quenched with saturated aqueous NH_4Cl (30 mL). The aqueous layer was extracted with EtOAc (3× 50 mL), and the organic solutions were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel using a combination of petroleum ether and acetone.

(R_P)-*tert*-Butyl(hydroxymethyl)(phenyl)phosphine oxide [(R_P)-**3 a**] was obtained according to procedure A as a white solid (obtained by washing the crude several times with cold ether instead of column chromatography) with a 66% yield (405 mg). $[\alpha]_D^{20}=-16.8$ ($c=$ 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.70$ (ddd, $J=8.4$, 7.5, 1.5 Hz, 2H), 7.59–7.36 (m, 3H), 5.51 (td, $J=6.7$, 3.1 Hz, 1H), 4.43 (dd, $J=14.4$, 6.6 Hz, 1H), 4.25 (dd, $J=14.3$, 6.4 Hz, 1H), 1.14 ppm (d, $J=14.4$ Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): $\delta=46.42$; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=131.93$ (d, J(C,P)=7.3 Hz), 131.93, 128.88 (d, J(C,P)=85.3 Hz), 128.48 (d, J(C,P)=10.3 Hz), 57.59 (d, J(C,P)= 72.2 Hz), 32.71 (d, J(C,P)=65.6 Hz), 24.80; HPLC separation (Lux-Cellulose-2, hexane/isopropanol 50:50, 1 mL min^{-1}, UV 254 nm); t_R (S_P)=5.24 min, t_R (R_P)=8.60 min), e.r.=99:1; these data are consistent with those in the literature.[10b]

(S_P)-*tert*-Butyl(hydroxymethyl)(phenyl)phosphine oxide [(S_P)-**3 a**]: $[\alpha]_D^{20}=+20.3$ ($c=0.48$, $CHCl_3$); e.r.>99.5:0.5; Single crystal growth for X-ray molecular structure determination was carried out into Et_2O/*n*-hexane at −20 °C. The absolute configuration of the crystallized molecule is S_P.

(S_P)-(Hydroxymethyl)(methyl)(phenyl)phosphine oxide [(S_P)-**3 b**) was obtained according to procedure A as a white solid with a 48% overall yield (147 mg) using methyllithium at −20 °C as nucleophile. $[\alpha]_D^{20}=-17.3$ ($c=1.00$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=$ 7.77–7.65 (m, 2H), 7.58–7.50 (m, 1H), 7.50–7.43 (m, 2H), 5.78 (d, $J=3.6$ Hz, 1H), 4.08 (ddd, $J=14.4$, 5.4, 4.0 Hz, 1H), 3.99 (dd, $J=$ 14.3, 7.1 Hz, 1H), 1.77 ppm (d, $J=12.9$ Hz, 3H);^{31}P NMR (121 MHz, $CDCl_3$): $\delta=37.59$; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=132.10$ (d, J(C,P)= 2.7 Hz), 131.28 (d, J(C,P)=93.6 Hz), 130.40 (d, J(C,P)=9.1 Hz), 128.74 (d, J(C,P)=11.4 Hz), 62.27 (d, J(C,P)=81.9 Hz), 12.73 ppm (d, J(C,P)=68.9 Hz); these data are consistent with those in the literature;[11] $R_f=0.25$ (3:1 petroleum ether/acetone); HPLC separation (Chiralpak AS-H, heptane/ethanol 80:20, 1 mL min^{-1}, UV 254 nm; t_R (R_P)=6.29 min, t_R (S_P)=7.61 min), e.r.=96:4.

(S_P)-*tert*-Butyl-((S_C)-1-hydroxyethyl)phenyl)phosphine oxide [(S_P,S)-**3 d**] was obtained according to procedure A as a white solid with a 58% yield. ^{1}H and ^{31}P{^{1}H} NMR shows d.r. of 1.4:1.0. Major diastereoisomer was isolated by crystallization in CH_2Cl_2/*n*-hexane at −20 °C. (Yield 0.17 g, 13%); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.69$ (m, 2H), 7.51 (m, 1H), 7.45 (m, 2H), 4.82 (br s, 1H, -OH), 4.57 (qd, $J=$ 6.8, 6.8 Hz, 1H), 1.33 (dd, $J=6.8$, 14.0 Hz, 3H), 1.23 ppm (d, $J=$ 14.4 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): $\delta=48.12$.^{13}C NMR (101 MHz, $CDCl_3$): $\delta=131.78$ (d, J(C,P)=2.2 Hz), 131.70 (d, J(C,P)= 7.3 Hz), 130.09 (d, J(C,P)=80.0 Hz), 128.51 (d, J(C,P)=10.3 Hz), 64.73 (d, J(C,P)=72.6 Hz), 33.42 (d, J(C,P)=64.2 Hz), 25.56, 18.25 ppm; minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=$ 7.94 (m, 2H), 7.51 (m, 1H), 7.45 (m, 2H), 4.60 (qd, $J=7.2$ Hz, 3.2 Hz, 1H), 4.40 (br s, 1H, -OH), 1.50 (dd, $J=6.8$ Hz, 14.0 Hz, 3H), 1.23 ppm (d, $J=14.4$ Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): $\delta=47.56$; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=132.81$ (d, J(C,P)=7.3 Hz), 131.67 (d,

J(C,P) = 2.9 Hz), 128.96, 128.08 (d, J(C,P) = 10.3 Hz), 65.65 (d, J(C,P) = 79.3 Hz), 33.16 (d, J(C,P) = 62.9 Hz), 25.28, 18.78 ppm (d, J(C,P) = 1.4 Hz).

Major diastereoisomer (d.r. = 50.0:1.0) was isolated by preferential crystallization for three times in CH_2Cl_2/*n*-hexane at −20 °C. $[\alpha]_D^{20}$ = +1.7 (c = 0.48, $CHCl_3$); The absolute configuration of the crystallized molecule is ($S_P S$); HPLC separation (Chiralpak IE, hexane/ethanol 95:5, 1 mL min^{-1}, UV 254 nm; t_R ($S_P S$) = 11.33 min, t_R ($R_P R$) = 12.48 min), e.r. = 98.8:1.2.

(R_P)-*tert*-Butyl((R_C)-hydroxy(phenyl)methyl)phenylphosphine oxide [($R_P R$)-**3 f**] was obtained according to procedure A as a white solid (700 mg, 67% yield). ^{1}H and ^{31}P NMR show a d.r. of 3:1.

Major diastereoisomer: ^{1}H NMR (400 MHz, [D$_6$]DMSO, ppm): δ = 7.74 (m, 2H), 7.75 (m, 1H), 7.4 (m, 2H), 7.34 (m, 2H), 7.18–7.08 (m, 3H), 6.24 (dd, J = 5.6 Hz, 16.0 Hz, 1H), 3.33 (brs, 1H, -OH), 1.13 ppm (d, J = 14.4 Hz, 9H);^{31}P NMR (162 MHz, [D$_6$]DMSO): δ = 47.97; ^{13}C NMR (101 MHz, [D$_4$]MeOH): δ = 139.33 (d, J(C,P) = 1.8 Hz), 133.21 (d, J(C,P) = 7.3 Hz), 133.05 (d, J(C,P) = 2.2 Hz), 130.79 (d, J(C,P) = 84.7 Hz), 129.56 (d, J(C,P) = 5.1 Hz), 129.36 (d, J(C,P) = 10.3 Hz), 128.93, 128.90, 73.78 (d, J(C,P) = 78.2 Hz), 35.30 (d, J(C,P) = 63.9 Hz), 26.08 ppm; minor diastereoisomer: ^{1}H NMR (400 MHz, [D$_4$]MeOH): δ = 7.92 (m, 2H), 7.54 (m, 1H), 7.45 (m, 2H), 7.32 (m, 2H), 7.20-7.12 (m, 3H), 5.55 (d, J = 9.6 Hz, 1H), 1.27 ppm (d, 9H, J = 14.4 Hz); ^{31}P NMR (162 MHz, [D$_4$]MeOH): δ = 51 ppm; ^{13}C NMR (101 MHz, [D$_4$]MeOH): δ = 139.57 (d, 1C, J(C,P) = 2.2 Hz), 134.10 (d, J(C,P) = 8.4 Hz), 133.21 (d, J(C,P) = 2.9 Hz), 128.18, 129.03 (d, J(C,P) = 10.3 Hz), 128.94, 128.91, 128.86 (d, J(C,P) = 3.0 Hz), 73.36 (d, J(C,P) = 81.5 Hz), 34.73 (d, J(C,P) = 63.1 Hz), 25.62 ppm; these data are consistent with those in the literature[2]. $[\alpha]_D^{20}$ n.d. (d.r. = 3:1); R_f = 0.25(1:1 petroleum ether/acetone) HPLC separation (Lux-Cellulose-4, heptane/ethanol 95:5, 1 mL min^{-1}, UV 220 nm; major diastereoisomer: t_R ($R_P R$) = 12.01 min; t_R ($S_P S$) = 15.28 min, e.r. = 99.5:0.5; minor diastereoisomer: t_R ($R_P S$) = 18.45 min; t_R ($S_P R$) = 13.49 min, e.r. = 98:2.

General procedure B: One-pot nucleophilic addition/epoxide trapping of adamantylphosphinate for the preparation of 3c, e, g and h

A 100 mL round-bottom flask was charged with dry THF (25 mL) under argon, and the flask was cooled to −78 °C. Then, *t*BuLi (2.5 equiv) was added dropwise and the orange-yellow mixture was stirred for 15 min at around −75 °C. Then, a solution of adamantylphosphinate (1 equiv) in THF (5 mL) was added dropwise at −78 °C and the reaction mixture was maintained at a temperature below −75 °C for 1 hour. The mixture was allowed to warm to −30 °C over 3 h and, at that temperature, the given epoxide (4 equiv) was added in one portion. The mixture was warmed to room temperature and was stirred overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl (15 mL), the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated under vacuum. The crude mixture was separated by column chromatography on silica gel using a combination of petroleum ether and acetone.

(R_P)-*tert*-Butyl(2-hydroxyethyl)(phenyl)phosphine oxide [(R_P)-**3 c**] was obtained according to procedure B as a white solid (70% yield). $[\alpha]_D^{20}$ = −51.7 (c = 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (m, J = 1.6, 7.6 Hz, 8.4 Hz, 2H), 7.54 (m, J = 6.8 Hz, J = 1.2 Hz, 1H), 7.47 (m, J = 7.6 Hz, J = 2.4 Hz, 2H), 3.98–3.82 (m, 2H), 3.10 (br, 1H, -OH), 2.50–2.36 (m, J(H,H) = 15.2, 8.4, 6.0 Hz, J(H,P) = 10.4 Hz, 1H), 2.26–2.15 (m,1H), 1.12 ppm (d, J = 14.8 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 53.14 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 132.05 (d, J(C,P) = 2.2 Hz), 132.00 (d, J(C,P) = 8.1 Hz), 119.70 (d, J(C,P) = 87.3 Hz), 118.64 (d, J(C,P) = 11.0 Hz), 47.74 (d, J(C,P) = 5.9 Hz), 23.09 (d, J(C,P) = 69.0 Hz), 15.71 (d, J(C,P) = 63.9 Hz), 14.24 ppm; these data are consistent with those in the literature;[11] R_f = 0.2 (1:1 petroleum ether/acetone); HPLC separation (Lux-Cellulose-2, hexane/isopropanol 50:50, 1 mL min^{-1}, UV 254 nm; t_R (R_P) = 6.67 min, t_R (S_P) = 9.42 min), e.r. = 99.5:0.5.

(S_P)-*tert*-Butyl(2-hydroxyethyl)(phenyl)phosphine oxide [(S_P)-**3 c**] was obtained according to procedure B as a white solid (440 mg, 66%); $[\alpha]_D^{20}$ = +61.7 (c = 0.50, $CHCl_3$) e.r. = 99.5:0.5. Single crystal growth for X-ray molecular structure determination was carried out into Et_2O/*n*-hexane at −20 °C. The absolute configuration of the crystallized molecule is S_P.

(R_P)-*tert*-Butyl((R_C)-2-hydroxypropyl)(phenyl)phosphine oxide [($R_P R_C$)-**3 e**] was obtained according to procedure B as a white solid with a 61% overall yield (400 mg). M.p. 135–137.4 °C. $[\alpha]_D^{20}$ = −58.0 (c = 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.66 (m, 2H), 7.61–7.44 (m, 3H), 4.95 (s, 1H), 4.09–3.88 (m, 1H), 2.18 (dt, J = 14.8, 10.4 Hz, 1H), 2.09 (ddd, J = 14.8, 5.0, 1.7 Hz, 1H), 1.24 (dd, J = 6.1, 1.4 Hz, 3H), 1.12 ppm (d, J = 15.0 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 52.93 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.84, 131.83 (d, J(C,P) = 7.8 Hz), 129.33 (d, J(C,P) = 86.5 Hz), 128.45 (d, J(C,P) = 10.7 Hz), 63.25 (d, J(C,P) = 5.4 Hz), 32.69 (d, J(C,P) = 68.4 Hz), 31.14 (d, J(C,P) = 63.6 Hz), 24.87 (d, J(C,P) = 14.2 Hz), 23.90 ppm; HRMS (ESI) calcd for [M−H]$^+$: 241.1352; found: 241.1353; R_f = 0.2 (2:1 petroleum ether/acetone); these data are consistent to those in the literature;[11] HPLC separation (Lux-Amylose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R ($S_P S$) = 10.34 min, t_R ($R_P R$) = 11.58 min), e.r. > 99.5:0.5.

(R_P)-*tert*-Butyl((S_C)-2-hydroxypropyl)(phenyl)phosphine oxide [($R_P S_C$)-**3 e**] was obtained according to procedure B as a white solid with a 64% overall yield (415 mg). M.p. 123.9-126 °C. $[\alpha]_D^{20}$ = +3.6 (c = 1.055, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.62 (m, 2H), 7.57–7.41 (m, 3H), 4.51–4.30 (m, 2H *OH* + *CHMe*), 2.40 (ddd, J = 15.0, 8.7, 2.9 Hz, 1H), 2.16 (dt, J = 15.0, 8.6 Hz, 1H), 1.26 (d, J = 6.2 Hz, 3H), 1.13 ppm (d, J = 14.7 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 49.32; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.62 (d, J(C,P) = 2.7 Hz), 131.57 (d, J(C,P) = 87.6 Hz), 131.30 (d, J(C,P) = 8.2 Hz), 128.24 (d, J(C,P) = 10.8 Hz), 64.80 (d, J(C,P) = 5.5 Hz), 33.21 (d, J(C,P) = 68.1 Hz), 32.46 (d, J(C,P) = 62.9 Hz), 24.88 (d, J(C,P) = 10.8 Hz), 24.14 ppm; HRMS (ESI) calcd for [M−H]$^+$: 241.1352; found: 241.1353; R_f = 0.2 (2:1 petroleum ether/acetone); HPLC separation (Lux-Amylose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm t_R ($S_P R$) = 8.91 min, t_R ($R_P S$) = 9.86 min), e.r. > 99.5:0.5.

(R_P)-*tert*-Butyl((R_C)-2-hydroxy-2-phenylethyl)(phenyl)phosphine oxide [($R_P R_C$)-**3 g**] was obtained according to procedure B as a white solid with a 54% overall yield (297 mg). M.p. 93.5–96.1 °C; $[\alpha]_D^{20}$ = −83.0 (c = 0.73, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65–7.58 (m, 2H), 7.54–7.46 (m, 1H), 7.46–7.40 (m, 2H), 7.40–7.34 (m, 2H), 7.29 (dd, J = 8.1, 6.8 Hz, 2H), 7.22 (ddd, J = 8.5, 2.6, 1.3 Hz, 1H), 5.42 (tt, J = 9.8, 2.6 Hz, 1H), 5.03 (d, J = 3.0 Hz, 1H), 2.62 (ddd, J = 15.1, 7.5, 2.5 Hz, 1H), 2.43 (ddd, J = 15.1, 10.0, 8.7 Hz, 1H), 1.19 ppm (d, J = 14.8 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 49.32; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.01 (d, J(C,P) = 10.9 Hz), 131.56 (d, J(C,P) = 2.7 Hz), 131.34 (d, J(C,P) = 88.5 Hz), 131.22 (d, J(C,P) = 8.3 Hz), 128.44, 128.13 (d, J(C,P) = 11.0 Hz), 127.54, 125.43, 70.61 (d, J(C,P) = 5.3 Hz), 34.00 (d, J(C,P) = 41.1 Hz), 33.37 (d, J(C,P) = 48.8 Hz), 24.24 ppm; IR (ATR): $\tilde{\nu}$ = 445, 473, 494, 517, 538, 602, 642, 698, 746, 818, 1053, 1107, 1149, 1437, 2869, 2904, 2962, 3035, 3061, 3281 cm^{-1}; HRMS (ESI) calcd for [M−Na]$^+$:325.1328; found: 325.1325; R_f = 0.15 (3:1 petroleum ether/acetone); HPLC separation (Chiralpak IC, heptane/ethanol 80:20, 1 mL min^{-1}, UV 254 nm; t_R ($S_P S$) = 6.47 min, t_R ($R_P R$) = 10.42 min), e.r. > 99.5:0.5.

(S_P)-*tert*-Butyl(2-hydroxy-2,2-diphenylethyl)(phenyl)phosphine oxide [(S_P)-**3 h**] was obtained according to procedure B as a white solid with a 20% yield (111 mg). M.p. 199.2–205.7 °C; $[\alpha]_D^{20} = +6.2$ (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.43 (m, 2H), 7.43–7.12 (m, 10H), 6.95 (br s, 1H, -OH), 6.87–6.73 (m, 3H), 3.13 (dd, J = 14.6, 5.8 Hz, 1H), 3.04 (dd, J = 14.6, 10.3 Hz, 1H), 1.12 ppm (d, J = 14.9 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 50.26; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.05 (d, J(C,P) = 10.6 Hz), 144.66 (d, J(C,P) = 2.3 Hz), 131.11 (d, J(C,P) = 8.3 Hz), 130.98 (d, J(C,P) = 2.8 Hz), 130.03 (d, J(C,P) = 88.7 Hz), 128.22, 127.80 (d, J(C,P) = 11.2 Hz), 127.26, 127.01, 126.36, 126.28, 125.35, 77.46 (d, J(C,P) = 5.4 Hz), 34.14 (d, J(C,P) = 61.2 Hz), 33.38 (d, J(C,P) = 68.9 Hz), 23.80 ppm; IR (ATR): $\tilde{\nu}$ = 476, 512, 595, 614, 653, 691, 719, 745, 780, 818, 915, 979, 1101, 1136, 1436, 2855, 2924, 2962, 3058, 3228 cm^{-1}; HRMS (ESI) calcd for $[M-H]^+$: 379.1821; found: 379.1820; R_f = 0.25 (100% EtOAc); HPLC separation (Chiralpak AZ-H, heptane/ethanol 80:20, 1 mL min^{-1}, UV 254 nm; t_R (S_P) = 9.70 min, t_R (R_P) = 12.16 min), e.r. = 99:1.

tert-Butyl(1-methoxymethyl)(phenyl)phosphine oxide (**6**): To a suspension of NaH (60%, 40 mg) in THF (10 mL) was slowly added the solution of (+/−)-**3 a** (100 mg) in THF (10 mL, 10 mg mL^{-1}) at −10 °C. The reaction mixture was allowed to warm to 0 °C and stirred for a further 1 h and the resulting mixture was quenched with excess MeI while maintaining the temperature at 0 °C. The solvent was removed under reduced pressure to give the solids which were dissolved in water (20 mL). The product was extracted with CH_2Cl_2 (3×20 mL), and the combined organic layers were dried over $MgSO_4$. After solvent removal, the product was chromatographed through a silica gel column. Yield (82 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (m, 2H), 7.51 (m, 1H), 7.45 (m, 2H), 4.12 (m, 1H), 4.08 (m, 1H), 3.47 (d, 3H, J = 0.8 Hz), 1.17 ppm (d, 9H, J = 9.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 41.88 (s); HRMS (ESI) calcd for $[M+H]^+$ 227.1195; found 227.1194; these data are consistent to those in the literature.[11]

Procedure C: Phase-transfer catalyzed addition of SPO to alkylhalides for the preparation of 9 and 10

Under argon, a 25 mL round bottom flask was charged with a solution of phosphine oxide (1 equiv, 0.2 M) in technical grade toluene. Then, the same volume of 30% aqueous KOH solution was added at room temperature, followed by tetrabutylammonium bromide (TBAB, 10 mol%) and the electrophile (1 equiv). After the required amount of time, the reaction mixture was dissolved in water, the organic layer is separated and the pH of the aqueous layer was adjusted around 7–8 using aqueous saturated NH_4Cl, and extracted with CH_2Cl_2. The organic layers were combined and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a combination of petroleum ether and acetone.

(R_P)-*tert*-Butyl(3-methylbut-2-en-1-yl)(phenyl)phosphine oxide [(R_P)-**9**] was obtained according to procedure C as a white solid with a 81% overall yield (166 mg). M.p. 96.6–98.1 °C; $[\alpha]_D^{20} = -34.9$ (c = 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.65 (m, 2H), 7.53–7.43 (m, 3H), 5.19 (qd, J = 6.2, 1.3 Hz, 1H), 3.10–2.70 (m, 2H), 1.65 (m, 6H), 1.14 (d, J = 14.4 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 48.00; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.37 (d, J(C,P) = 10.9 Hz), 131.93 (d, J(C,P) = 7.8 Hz), 131.28 (d, J(C,P) = 2.6 Hz), 130.51 (d, J(C,P) = 86.5 Hz), 128.03 (d, J(C,P) = 10.6 Hz), 112.89 (d, J(C,P) = 8.2 Hz), 33.04 (d, J(C,P) = 67.4 Hz), 25.84 (d, J(C,P) = 2.2 Hz), 24.65, 24.18 (d, J(C,P) = 63.3 Hz), 18.32 ppm(d, J(C,P) = 1.8 Hz); IR (ATR): $\tilde{\nu}$ = 434, 474, 511, 540, 627, 698, 744, 766, 818, 1107, 1165, 1437, 1475, 1634, 1662, 2862, 2904, 2970, 3059 cm^{-1}; HRMS (ESI) calcd for $[M-H]^+$: 251.1559; found: 251.1558; R_f = 0.3 (3:1 petroleum ether/acetone); HPLC separation (Lux-Amylose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R (S_P) = 7.23 min, t_R (R_P) = 8.75 min, e.r. = 99.5:0.5.

(+/−)-2-(*tert*-Butyl(phenyl)phosphoryl)-1-phenylethanone (**10**) was obtained according to procedure C as a white solid in a 63% yield (188 mg). R_f = 0.5 (2:1 petroleum ether/acetone); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20–7.98 (m, 1H), 7.91–7.69 (m, 2H), 7.55–7.49 (m, 2H), 7.49–7.38 (m, 4H), 4.06 (dd, J = 15.3, 13.1 Hz, 1H), 3.71 (dd, J = 13.0, 11.7 Hz, 1H), 1.21 ppm (d, J = 15.5 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 44.25 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.75 (d, J(C,P) = 6.0 Hz), 137.07, 133.49, 132.25 (d, J(C,P) = 8.3 Hz), 131.89 (d, J(C,P) = 2.7 Hz), 129.59, 128.84 (d, J(C,P) = 90.4 Hz), 128.42, 128.06 (d, J(C,P) = 11.2 Hz), 38.25 (d, J(C,P) = 46.7 Hz), 34.34 (d, J(C,P) = 70.1 Hz), 24.36 ppm; HRMS (ESI) calcd for $[M-H]^+$: 301.1352; found: 301.1352; these data are consistent with those in the literature.[13b]

Procedure D: Synthesis of phosphine oxides 7 and 8

A 10 mL Schlenk tube was charged with paraformaldehyde (1.5 equiv, 0.5 M) in CH_2Cl_2. To the suspension of paraformaldehyde was added the amine (1.5 equiv) and the reaction was stirred for 2 h at room temperature. Then, the solvent was removed from the clear solution under reduced pressure and secondary phosphine oxide were successively added (0.15 M in toluene). The reaction was heated to 110 °C for 15 h. The crude mixture was reduced in volume by solvent removal under reduced pressure and purified by column chromatography on silica gel using a combination of petroleum ether and acetone as eluent.

(R_P)-*tert*-Butyl[(diethylamino)methyl](phenyl)phosphine oxide (**7**) was obtained according to procedure D as a pale-yellow solid with a 62% overall yield (177 mg). M.p. 67.8–70.2 °C; $[\alpha]_D^{20} = +11.7$ (c = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.66 (m, 2H), 7.57–7.37 (m, 3H), 3.27 (dd, J = 15.0, 6.1 Hz, 1H), 3.11 (dd, J = 15.0, 4.6 Hz, 1H), 2.79 (dq, J = 14.2, 7.1 Hz, 2H), 2.64 (dq, J = 13.8, 7.0 Hz, 2H), 1.16 (d, J = 14.2 Hz, 9H), 0.97 (t, J = 7.1 Hz, 6H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 44.48 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 131.92 (d, J(C,P) = 7.4 Hz), 131.23 (d, J(C,P) = 2.6 Hz), 130.77 (d, J(C,P) = 84.9 Hz), 127.93 (d, J(C,P) = 10.4 Hz), 49.11 (d, J(C,P) = 78.8 Hz), 48.44 (d, J(C,P) = 7.2 Hz), 33.23 (d, J(C,P) = 66.2 Hz), 24.81, 11.23 ppm; IR (ATR): $\tilde{\nu}$ = 474, 503, 517, 544, 600, 629, 698, 710, 733, 750, 779, 818, 839, 1068, 1105, 1148, 1167, 1250, 1385, 1391, 1437, 1466, 1475, 2800, 2870, 2968, 3055, 3419 cm^{-1}; HRMS (ESI) calcd for $[M-H]^+$:268.1825; found: 268.1828; R_f = 0.2 (3:1 petroleum ether/acetone); HPLC separation (Chiralpak AZ-H, heptane/ethanol 95:5, 1 mL min^{-1}, UV 220 nm; t_R (S_P) = 10.31 min, t_R (R_P) = 12.41 min), e.r. = 99:1.

(R_P)-[(Benzylamino)methyl](*tert*-butyl)(phenyl)phosphine oxide (**8**) was obtained according to procedure D as a pale yellow viscous oil with a 66% overall yield (109 mg). $[\alpha]_D^{20} = +17.5$ (c = 0.99, $CHCl_3$, > 99.5:0.5 e.r.); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.60 (m, 2H), 7.57–7.40 (m, 3H), 7.36–7.17 (m, 5H), 3.85 (s, 2H), 3.31 (dd, J = 13.9, 7.0 Hz, 1H), 3.19 (dd, J = 13.9, 5.3 Hz, 1H), 1.96 (s, N-H), 1.12 ppm (d, J = 14.5 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 46.50 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.52, 131.79 (d, J(C,P) = 7.9 Hz), 131.69 (d, J(C,P) = 2.7 Hz), 130.01 (d, J(C,P) = 86.8 Hz), 128.48, 128.37, 128.35 (d, J(C,P) = 10.6 Hz), 127.23, 55.43 (d, J(C,P) = 13.1 Hz), 42.96 (d, J(C,P) = 71.1 Hz), 32.79 (d, J(C,P) = 67.1 Hz), 24.80 ppm; IR (ATR): $\tilde{\nu}$ = 480, 519, 544, 596, 613, 634, 744, 818, 1109, 1161, 1437, 1462, 2867, 2928, 2970, 3043, 3080, 3348, 3446 cm^{-1}; HRMS (ESI) calcd for $[M-H]^+$: 302.1668; found: 302.1668; R_f = 0.3(2:1 petroleum ether/acetone); HPLC separation (Lux-Cellulose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R (S_P) = 10.40 min, t_R (R_P) = 13.02 min), e.r. = 95.5:4.5.

(R_P)-*N*-{[*tert*-Butyl(phenyl)phosphoryl]methyl}benzamide (**11**): A 10 mL Schlenk tube was charged with enantiopure *tert*-butyl phenyl secondary phosphine oxide (120 mg) and the tube was subjected to several vaccum/argon cycles to give an inert atmosphere. Then, anhydrous THF (3.5 mL) was added and the reaction mixture was cooled to −78 °C. At this temperature, MeLi solution (370 μL, 1.6 M in Et_2O, 0.9 equiv) was added slowly, and the reaction mixture was stirred 30 min at −78 °C. Then, a solution of benzamidomethyl acetate (0.5 g mL^{-1}, 300 μL, 1.2 equiv; see the Supporting Information) at −40 °C was added and the mixture was allowed to warm to room temperature overnight. Then, the reaction was quenched with saturated $NaHCO_3$ solution and water, and the water layer was extracted with EtOAc (2×25 mL). The organic layers were combined, dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of 3:1 to 1:1 petroleum ether/acetone to give a white solid with a 58% overall yield (120 mg). M.p. 192.1–200.6 °C; $[\alpha]_D^{20} = -6.6$ (c = 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (dd, J = 9.4, 7.8 Hz, 2H), 7.69 (d, J = 7.3 Hz, 2H), 7.57–7.41 (m, 4H), 7.36 (t, J = 7.6 Hz, 2H), 6.96 (N-H,brs, 1H), 4.47–4.35 (m, 1H), 4.25–4.12 (m, 1H), 1.19 ppm (d, J = 15.0 Hz, 9H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 47.69 ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.60 (d, J = 4.8 Hz), 133.77, 132.13 (d, J = 2.6 Hz), 131.73 (d, J = 4.2 Hz), 131.69 (d, J = 4.1 Hz), 128.53, 128.43 (d, J = 11.0 Hz), 128.22 (d, J = 89.2 Hz), 127.06, 34.20 (d, J = 67.4 Hz), 32.87 (d, J = 67.6 Hz), 24.26 ppm; IR (ATR): $\tilde{\nu}$ = 472, 206, 633, 697, 748, 817, 1109, 1163, 1313, 1437, 1490, 1540, 1651, 2870, 2904, 2966, 3059, 3237 cm^{-1}; HRMS (ESI) calcd for $[M-H]^+$: 316.1461; found: 316.1461; HPLC separation (Lux-Amylose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R (S_P) = 13.59 min, t_R (R_P) = 11.86 min), e.r. = 79:21.

General procedure E for the borane-mediated reduction

A 10 mL Schlenk tube equipped with magnetic stirring bar was charged with phosphine oxide (1 equiv), and the tube was subjected to several vaccum/argon cycles to give an inert atmosphere. Then, an adjusted volume of anhydrous THF (concentration in phosphine oxide = 0.16 M) was added if necessary and the reaction mixture was cooled to 0 °C. At this temperature, a solution of BH_3·THF (1 M in THF) was added dropwise, and the clear mixture was stirred for 5 min at 0 °C. It was then allowed to warm to given temperature, and stirred for the given time. Then, the reaction mixture was cooled to 0 °C and quenched with distilled water. A saturated $NaHCO_3$ aqueous solution was then added, and the aqueous layer was extracted with CH_2Cl_2 (3×5 mL) The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (using a combination of petroleum ether/ethyl acetate) to yield the desired product.

(R_P)-*tert*-Butyl(hydroxymethyl)(phenyl)phosphine–borane [(R_P)-**4a**] was obtained according to general procedure E (2 h at 20 °C) as a white solid with a 91% overall yield (90 mg). $[\alpha]_D^{20} = +8.4$ (c = 0.51, $CHCl_3$,); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (m, J(H,H) = 8.0 Hz, J(H,P) = 8.4 Hz, 2H, Ph), 7.51 (m J(H,H) = 7.2 Hz, J(H,P) = 1.2 Hz, 1H, Ph), 7.44 (m, J(H,H) = 8.0 Hz, J(H,P) = 2.0 Hz, 2H, Ph), 4.54 (d, J(H,H) = 13.6 Hz, 1H, >CH_2, -CH_2OH), 4.27 (dd, J(H,H) = 13.6 Hz, J(H,P) = 2.4 Hz, 1H, >CH_2, -CH_2OH), n.d. (-OH), 1.15 (d, J(H,P) = 13.6 Hz; 9H, *t*Bu), 0.69 ppm (q, J(H,B) = 93.6 Hz, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 31.26 ppm (bq, J(B,P) = 53.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.69 (d, J(C,P) = 7.6 Hz, 2C, =CH-, Ph), 131.79 (d, J(C,P) = 1.9 Hz, 1C, =CH-, Ph), 128.70 (d, J(C,P) = 9.2 Hz, 2C, =CH-, Ph), 125.10 (d, J(C,P) = 49.5 Hz, 1C, >C=, Ph), 56.13 (d, J(C,P) = 38.8 Hz, 1C, >CH_2OH), 29.42 (d, J(C,P) = 30.1 Hz, 1C, >C<, *t*Bu), 26.07 ppm (brd, 3C, J(C,P) = 1.1 Hz, -CH_3, *t*Bu); ^{11}B NMR (128 MHz, CDCl): δ = −43.68 ppm (d, J(B,P) = 58.4 Hz); R_f = 0.2 (5:1 petroleum ether/EtOAc); HRMS (EI^+) calcd. for $C_{11}H_{20}BOP$ $[M+Na]^+$ 233.1239; found 247.1233; HPLC separation (Lux-Cellulose-2, Hexane/isopropanol 70:30, 1 mL min^{-1}, UV 254 nm; t_R (R_P) = 3.79 min, t_R (S_P) = 4.25 min), e.r. = 98:2.

(S_P)-*tert*-Butyl(hydroxymethyl)(phenyl)phosphine–borane [(S_P)-**4a**]: e.r. = 95:5. $[\alpha]_D^{20} = -7.1$ (c = 0.51, $CHCl_3$,). Single crystal growth for X-ray molecular structure determination was carried out into Et_2O/*n*-hexane at −20 °C. The absolute configuration of the crystallized molecule is S_P.

(S_P)-(Hydroxymethyl)(methyl)(phenyl)phosphine–borane (**4b**) was obtained according to general procedure E (2 h at 20 °C) as a white solid with a 87% overall yield (55 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.67 (m, 2H), 7.51 (m, 3H), 4.08 (s, 2H), 2.12 (O-H, brs, 1H), 1.65 (d, J = 10.5 Hz, 3H), 1.28–0.18 ppm (m, BH_3, 3H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 10.94 ppm (m); R_f = 0.2 (5:1 petroleum ether/EtOAc) These data are consistent with the literature.[12] HPLC separation (Chiralpak AD-H, heptane/ethanol 70:30 1 mL min^{-1} UV 254 nm; t_R (S_P) = 5.08 min, t_R (R_P) = 6.95 min), e.r. = 96.5:3.5.

(R_P)-*tert*-Butyl(2-hydroxyethyl)(phenyl)phosphine–borane [(R_P)-**4c**] was obtained according to general procedure E (72 h at 50 °C) as a white solid with a 56% yield (80 mg, R_F = 0.2; 3:1 EP/EtOAc). $[\alpha]_D^{20} = +22.7$ (c = 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (m, 2H), 7.50 (m, 1H), 7.45 (m, 2H), 3.91-3.75 (m, 2H), 2.47 (m, 1H,), 2.24 (brs, 1H, -OH), 2.16 (m, 1H), 1.09 (d, J = 14.0 Hz, 9H), 0.74 ppm (m, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.64 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.53 (d, J(C,P) = 8.1 Hz), 131.62 (d, J(C,P) = 2.9 Hz), 128.66 (d, J(C,P) = 9.6 Hz), 125.99 (d, J(C,P) = 49.2 Hz), 58.1 (d, J(C,P) = 1.4 Hz), 29.30 (d, J(C,P) = 33.7 Hz), 25.5 (d, J(C,P) = 2.2 Hz), 22.68 ppm (d, J(C,P) = 32.3 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): δ = −41.75 ppm (d, J(B,P) = 59.2 Hz); HRMS (EI^+) calcd for $C_{12}H_{22}BOP$ $[M+Na]^+$ 247.1396; found 247.1395; HPLC separation (Lux-Cellulose 2, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R (R_P) = 9.94 min, t_R (S_P) = 11.25 min), e.r. = 99:1.

(S_P)-*tert*-Butyl(2-hydroxyethyl)(phenyl)phosphine–borane [(S_P)-**4c**]: 59% yield (89 mg). $[\alpha]_D^{20} = -22.7$ (c = 1.0, $CHCl_3$); e.r. = 99:1. Single crystal growth for X-ray molecular structure determination was carried out into Et_2O/*n*-hexane at −20 °C. The absolute configuration of the crystallized molecule is S_P.

(S_P)-*tert*-Butyl((S_C)-1-hydroxyethyl)(phenyl)phosphine–borane (**4d**) was obtained according to general procedure E (2 h at 20 °C) as a white solid with a 73% yield.

Major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (m, 2H), 7.50 (m, 1H), 7.43 (m, 2H), (q, J = 6.4 Hz, 1H), 1.85 (br s, 1H, -OH), 1.52 (dd, J = 6.8 Hz, J = 14.0 Hz, 3H), 1.20 (d, J = 13.6 Hz, 9H), 0.60 ppm (m, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 38.85 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 134.91 (d, J(C,P) = 7.3 Hz), 131.57 (d, J(C,P) = 1.8 Hz), 128.43 (d, J(C,P) = 9.2 Hz), 125.07 (d, J(C,P) = 48.1 Hz), 65.20 (d, J(C,P) = 36.8 Hz), 30.40 (d, J(C,P) = 29.7 Hz), 26.91, 20.80 ppm (d, J(C,P) = 4.8 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): δ = −43.06 ppm (d, J(B,P) = 58.0 Hz); $[\alpha]_D^{20} = -28.6$ (c = 0.99, $CHCl_3$,); HPLC separation [(*S*,*S*)-Whelk-O1 heptane/isopropanol 95:5 1 mL min^{-1} UV 254 nm; t_R (S_P,*S*) = 8.06 min, t_R (R_P,*R*) = 10.86 min], e.r. = 99:1. The major diastereoisomer was isolated by crystallization into Et_2O/*n*-hexane at −20 °C. The absolute configuration of the crystallized molecule is (S_P,*S*).

Minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (m, 2H), 7.52–7.48 (m, 1H), 7.45–7.39 (m, 2H), 4.84 (m, 1H), 2.15 (br d, J = 11.2 Hz, 1H, -OH), 1.29 (dd, J = 6.8 Hz, J = 13.2 Hz, 3H), 1.18 (d, J = 13.6 Hz, 9H), 0.62 ppm (m, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 36.70 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.81 (d, J(C,P) =

7.3 Hz,), 131.65 (d, J(C,P) = 2.2 Hz), 128.66 (d, J(C,P) = 9.6 Hz), 126.51 (d, J(C,P) = 47.0 Hz), 62.90 (d, J(C,P) = 39.6 Hz), 30.08 (d, J(C,P) = 30.1 Hz), 26.51 (d, J(C,P) = 2.2 Hz), 20.23 ppm (d, J(C,P) = 6.0 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -45.61$ ppm (d, J(B,P) = 58.4 Hz); these data are consistent with those in the literature.[11]

(R_P)-*tert*-Butyl[(R_C)hydroxy(phenyl)methyl](phenyl)phosphine–borane (**4 f**) was obtained according to general procedure E (2 h at 20 °C) as a white solid with a 63% (2.6:1 d.r.) overall yield (186 mg).

Major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.99$ (m, 2H), 7.50 (m, 1H), 7.42 (m, 2H,), 7.37–7.32 (m, 2H), 7.26–7.20 (m, 3H), 5.60 (d, J = 4.8 Hz, 1H), 2.59 (br s, 1H, -OH), 1.11 (d, J = 13.6 Hz, 9H), 0.59 ppm (m, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 39.81 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.45 (d, J(C,P) = 2.2 Hz), 135.16 (d, J(C,P) = 7.3 Hz), 131.76 (d, J(C,P) = 2.9 Hz), 128.96 (d, J(C,P) = 2.2 Hz), 128.55 (d, J(C,P) = 3.6 Hz), 128.39 (d, J(C,P) = 7.5 Hz), 128.35 (d, J(C,P) = 2.9 Hz), 124.87 (d, J(C,P) = 46.2 Hz), 71.92 (d, J(C,P) = 33.8 Hz), 31.28 (d, J(C,P) = 27.9 Hz), 26.87 ppm (d, J(C,P) = 1.5 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -43.07$ ppm (d, J(B,P) = 56.1 Hz);

Minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.57$ (t, J = 8.0 Hz, J = 8.4 Hz, 2H), 7.35–7.29 (m, 4H), 7.3–7.20 (m, 2H), 7.13–7.08 (m, 2H), 5.62 (1H), 3.04 (t, J = 9.2 Hz, J = 9.2 Hz, 1H, -OH), 1.26 (d, J = 13.6 Hz, 9H), 0.59 ppm (m, 3H, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 39.35 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.08 (d, J(C,P) = 3.7 Hz), 134.39 (d, J(C,P) = 7.3 Hz), 131.54 (d, J(C,P) = 2.2 Hz), 128.36 (d, J(C,P) = 4.3 Hz), 128.24, 128.15, 125.47 (d, J(C,P) = 48.5 Hz), 70.02 (d, J(C,P) = 36.1 Hz), 31.16 (d, J(C,P) = 28.8 Hz), 26.81 ppm (d, J(C,P) = 2.2 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): δ = −44.27 ppm (d, J(B,P) = 57.4 Hz); these data are consistent with those in the literature;[11] R_f = 0.28 (9:1 *n*-hexane/EtOAc).

$[\alpha]_D^{20}$ = nd (d.r. = 2.6:1); HPLC separation (Lux-Amylose 2, heptane/ethanol 80:20, 1 mL min^{-1}, UV 254 nm; major diastereoisomer: t_R ($S_P S$) = 4.90 min, t_R ($R_P R$) = 5.49 min), e.r. = 98.5:1.5; minor diastereoisomer: t_R ($R_P S$) = 4.30 min, t_R ($S_P R$) = 5.95 min), e.r. = 87:13.

(R_P)-*tert*-Butyl(((R_C)-2-hydroxypropyl)(phenyl)phosphine–borane [($R_P R_C$)-**4 e**] was obtained according to general procedure E (72 h at 50 °C) as a white solid with a 51% overall yield (101 mg). M.p. 79.1–81.3 °C; $[\alpha]_D^{20} = -22$ (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.69 (m, 2H), 7.57–7.40 (m, 3H), 4.47–4.21 (m, 1H), 2.35 (ddd, J = 14.7, 12.7, 9.1 Hz, 1H), 2.27 (br s, OH), 2.09 (ddd, J = 14.8, 8.6, 2.7 Hz, 1H), 1.32 (dd, J = 6.2, 1.6 Hz, 3H), 1.09 (d, J = 13.9 Hz, 9H), 1.09–0.27 ppm (m, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 25.26 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.34 (d, J(C,P) = 8.0 Hz), 131.26 (d, J(C,P) = 2.5 Hz), 128.27 (d, J(C,P) = 9.5 Hz), 126.95 (d, J(C,P) = 50.0 Hz), 64.46, 29.36 (d, J(C,P) = 20.4 Hz), 29.03 (d, J(C,P) = 19.2 Hz), 25.36 (d, J(C,P) = 2.3 Hz), 25.04 ppm (d, J(C,P) = 10.7 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -41.96$ ppm (d, J(B,P) = 56.8 Hz); HRMS (ESI) calcd for $[M-Na]^+$: 261.1553; found: 261.1553; R_f = 0.2 (5:1 petroleum ether/EtOAc); HPLC separation (Lux-Cellulose 3, heptane/ethanol 95:5, 1 mL min^{-1}, UV 254 nm; t_R ($S_P S$) = 9.93 min, t_R ($R_P R$) = 8.90 min), e.r. = 99.5:0.5.

(R_P)-*tert*-Butyl[(S_C)-2-hydroxypropyl](phenyl)phosphine–borane [($R_P S_C$)-**4 e**] was obtained according to general procedure E (72 h at 50 °C) as a colorless viscous oil with a 54% overall yield (107 mg). $[\alpha]_D^{20} = +31.3$ (c = 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.61 (m, 2H), 7.59–7.40 (m, 3H), 4.04–3.80 (m, 1H), 3.20 (s, 1H, OH), 2.38 (t, J = 15.1 Hz, 1H), 2.03 (ddd, J = 14.8, 9.1, 3.8 Hz, 1H), 1.25 (d, J = 6.0 Hz, 3H), 1.10 (d, J = 14.1 Hz, 9H), 1.11–0.18 ppm (m, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 26.29 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 133.33 (d, J(C,P) = 7.9 Hz), 131.48 (d, J(C,P) = 2.5 Hz), 128.55 (d, J(C,P) = 9.4 Hz), 125.67 (d, J(C,P) = 49.8 Hz), 63.33, 29.09 (d, J(C,P) = 33.7 Hz), 28.69 (d, J(C,P) = 32.3 Hz), 25.29 (d, J(C,P) = 2.3 Hz), 24.95 ppm (d, J(C,P) = 11.5 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -41.62$ ppm (d, J(B,P) = 56.2 Hz); HRMS (ESI) calcd for $[M-Na]^+$: 261.1553; found: 261.1553; R_f = 0.2 (10:1 petroleum ether/EtOAc; HPLC separation (Lux-Cellulose 3, heptane/ethanol 95:5, 1 mL min^{-1}, UV 254 nm; t_R (minor) = 18.43 min, t_R (major) = 13.21 min), e.r. = 99.5:0.5.

(R_P)-*tert*-Butyl[(R_C)-2-hydroxy-2-phenylethyl](phenyl)phosphine–borane [($R_P R_C$)-**4 g**] was obtained according to general procedure E (72 h at 50 °C) as a white solid with a 57% overall yield (68 mg). M.p. 113.1–115.2 °C; $[\alpha]_D^{20} = +12.7$ (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.67 (m, 2H), 7.60–7.45 (m, 3H), 7.35–7.24 (m, 5H), 4.79 (td, J = 9.7, 1.7 Hz, 1H), 3.58 (br s, 1H-OH), 2.60 (t, J = 14.6 Hz, 1H), 2.33 (ddd, J = 14.9, 9.6, 3.2 Hz, 1H), 1.11 (d, J = 14.2 Hz, 9H), 1.11–0.33 ppm (m, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 27.14 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 144.17 (d, J(C,P) = 11.0 Hz), 133.49 (d, J(C,P) = 7.9 Hz), 131.60 (d, J(C,P) = 2.4 Hz), 128.62, 128.62 (d, J(C,P) = 9.5 Hz), 127.75, 125.39, 125.27 (d, J(C,P) = 49.7 Hz), 69.24, 30.49 (d, J(C,P) = 30.2 Hz), 29.26 (d, J(C,P) = 33.3 Hz), 25.32 ppm (d, J(C,P) = 2.4 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -41.40$ ppm (d, J(B,P) = 51.2 Hz); IR (ATR): $\tilde{\nu}$ = 424, 440, 486, 530, 565, 617, 629, 696, 743, 750, 814, 976, 1018, 1047, 1067, 1107, 1367, 1437, 2380, 2872, 2906, 2960, 2974, 3028, 3063, 3502 cm^{-1}; HRMS (ESI) calcd for $[M-Na]^+$: 323.1710; found: 323.1714; R_f = 0.2 (10:1 petroleum ether/EtOAc); HPLC separation (Chiralpak IC, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R ($S_P S$) = 6.90 min, t_R ($R_P R$) = 8.33 min), e.r. > 99.5:0.5.

(S_P)-*tert*-Butyl(2-hydroxy-2,2-diphenylethyl)(phenyl)phosphine–borane (**4 h**) was obtained according to general procedure E (72 h at 50 °C) as a white solid with a 41% overall yield (33 mg). M.p. 147.1–149.5 °C; $[\alpha]_D^{20} = -28.3$ (c = 0.72, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (dd, J = 9.3, 7.9 Hz, 2H), 7.47 (d, J = 7.5 Hz, 2H), 7.45–7.38 (m, 1H), 7.31 (t, J = 7.6 Hz, 4H), 7.23 (t, J = 7.3 Hz, 1H), 7.14 (dd, J = 7.6, 1.9 Hz, 2H), 6.95–6.85 (m, 3H), 4.68 (s, 1H-OH), 3.44 (t, J = 14.3 Hz, 1H), 2.86 (dd, J = 14.9, 6.5 Hz, 1H), 1.14 (d, J = 14.0 Hz, 5H), 1.14–0.24 ppm (m, BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 21.62 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 148.01 (d, J(C,P) = 8.9 Hz), 144.42 (d, J(C,P) = 2.1 Hz), 133.34 (d, J(C,P) = 8.0 Hz), 131.02 (d, J(C,P) = 2.5 Hz), 128.27, 128.09 (d, J(C,P) = 9.7 Hz), 127.43, 127.14, 126.70, 126.51 (d, J(C,P) = 50.7 Hz), 126.37, 125.47, 77.67, 33.41 (d, J(C,P) = 28.4 Hz), 30.27 (d, J(C,P) = 34.5 Hz), 25.46 ppm (d, J(C,P) = 2.1 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -41.20$ ppm (d, J(B,P) = 47.8 Hz); IR (ATR): $\tilde{\nu}$ = 428, 491, 564, 591, 635, 693, 739, 793, 989, 1061, 1105, 1168, 1364, 1448, 1491, 2324, 2397, 2869, 2927, 2958, 2977, 3057, 3476 cm^{-1}; HRMS (ESI) calcd for $[M-Na]^+$: 399.2024; found: 399.2031; R_f = 0.5 (5:1 petroleum ether/EtOAc); HPLC separation (Chiralpak AZ-H, heptane/ethanol 80:20, 1 mL min^{-1}, UV 254 nm; t_R (R_P) = 4.72 min, t_R (S_P) = 5.38 min), e.r. = 98.5:1.5.

(R_P)-[(Benzylamino)methyl](*tert*-butyl)(phenyl)phosphine–borane (**12**) was obtained according to general procedure E (24 h at 20 °C) as a white solid with a 84% overall yield (75 mg). M.p. 103.9-106 °C; $[\alpha]_D^{20} = -23.4$ (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.60 (m, 2H), 7.57–7.47 (m, 1H), 7.48–7.39 (m, 2H), 7.36–7.23 (m, 5H), 3.84 (s, 2H), 3.41–3.20 (m, 2H), 1.10 (d, J = 13.6 Hz, 9H), 1.09–0.23 ppm (m, BH_3, 3H); ^{31}P NMR (162 MHz, $CDCl_3$): δ = 29.46 ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 139.33, 133.36 (d, J(C,P) = 7.7 Hz), 131.27 (d, J(C,P) = 2.4 Hz), 128.32 (d, J(C,P) = 16.4 Hz), 128.32 (d, J(C,P) = 9.4 Hz), 127.16, 126.15, 125.66, 55.34 (d, J(C,P) = 12.3 Hz), 39.87 (d, J(C,P) = 41.0 Hz), 29.12 (d, J(C,P) = 31.3 Hz), 25.82 ppm (d, J(C,P) = 1.9 Hz); ^{11}B NMR (128 MHz, $CDCl_3$): $\delta = -42.81$ ppm (d, J(B,P) = 52.3 Hz); IR (ATR): $\tilde{\nu}$ = 430, 460, 488, 490, 563, 590, 617, 629, 694, 739, 785, 816, 1001, 1018, 1026, 1067, 1108, 1134, 1184, 1365, 1394, 1437, 1454, 1462, 1475, 2260, 2341,

2375, 2804, 2868, 2943, 2972, 3028, 3061, 3333 cm^{-1}; HRMS (ESI) calcd for $[M-Ag]^+$: 406.1023; found: 406.1019; $R_f = 0.2$ (10:1 petroleum ether/EtOAc); HPLC separation (Chiralcel OD-3, heptane/ethanol 90:10, 1 mL min^{-1}, UV 254 nm; t_R (S_P) = 4.93 min, t_R (R_P) = 4.59 min), e.r. = 93:7.

(+/−)-*N*-{[*tert*-Butyl(phenyl)phosphine–borane]methyl}benzamide (**15**) was obtained according to general procedure E (24 h at 20 °C) as a white solid with a 10% yield (5 mg). M.p. 144.7–152.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.76$ (t, $J = 8.3$ Hz, 2H), 7.68 (d, $J = 7.2$ Hz, 2H), 7.54–7.43 (m, 4H), 7.39 (t, $J = 7.5$ Hz, 2H), 6.64 (br s, 1H, -NH), 4.49 (ddd, $J = 15.0$, 8.4, 6.9 Hz, 1H), 4.18–4.07 (m, 1H), 1.18 (d, $J = 14.1$ Hz, 9H), 1.10–0.60 ppm (m, 3H, -BH_3); ^{31}P NMR (162 MHz, $CDCl_3$): $\delta = 32.92$ ppm (m); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 167.28$ (d, J(C,P) = 4.4 Hz), 133.62, 133.43 (d, J(C,P) = 8.1 Hz), 131.85, 128.68, 128.58, 126.92, 124.04 (d, J(C,P) = 50.5 Hz), 30.92 (d, J(C,P) = 40.7 Hz), 29.38 (d, J(C,P) = 30.6 Hz), 25.56 ppm (d, J(C,P) = 2.1 Hz); $R_f = 0.4$ (5:1 petroleum ether/EtOAc); IR (ATR): $\tilde{\nu} = 487$, 703, 742, 921, 1067, 1263, 1309, 1436, 1487, 1520, 1654, 2343, 2374, 2869, 2928, 2961, 3060, 3335, 3421 cm^{-1}; HRMS (ESI) calcd for $[M-Na]^+$: 336.1659; found: 336.1657.

(S_P)-{(Benzo[*d*][1,3,2]dioxaborol-2-yloxy)methyl}(*tert*-butyl)(phenyl) phosphine oxide (**17**): To a solution of (S_P)-**3a** (207 mg) in CH_2Cl_2 (3 mL) was added dropwise a solution of catecholborane in THF (1.0 M, 1.03 mL, 1.05 equiv) at 0 °C. The resulting mixture was allowed to warm slowly to room temperature and the solution was further stirred for 2 h at room temperature. The reaction mixture was then evaporated under reduced pressure to give the residual solid which was washed with Et_2O (4×3 mL) and then dried under vacuum. Yield (219 mg, 68%); ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 7.61$ (m, 2H, Ph), 7.58 (m, 1H, Ph), 7.46 (m, 2H, Ph), 6.62 (brd, 4H, $BO_2C_6H_4$), 4.66 (dd, $J = 14.0$ Hz, 1H), 4.48 (dd, $J = 14.0$ Hz, 1H), 1.17 ppm (d, $J = 16.4$ Hz, 9H); ^{31}P NMR (162 MHz, CD_2Cl_2): $\delta = 67.98$ ppm (br s); ^{13}C NMR (101 MHz, CD_2Cl_2): $\delta = 133.91$, 132.04 (d, J(C,P) = 8.8 Hz), 129.36 (d, J(C,P) = 12.3 Hz), 119.81 (br s, $BO_2C_6H_4$), 110.70 (br s, $BO_2C_6H_4$), 58.07 (d, J(C,P) = 60.1 Hz), 32.49 (d, J(C,P) = 61.6 Hz), 23.92 ppm; ^{11}B NMR (128 MHz, CD_2Cl_2): $\delta = 13.20$ ppm (s).

Crystal data

(S_P)-**3a**, $C_{11}H_{17}O_2P$, Mw = 212.22 from CH_2Cl_2/hexane at −20 °C; orthorhombic; space group $P2_12_12_1$; $a = 6.1924(1)$, $b = 9.7370(2)$, $c = 19.0102(4)$; $\alpha = \beta = \gamma = 90°$; $V = 1146.23(4)$ Å^3; $Z = 4$; $\rho_{calc} = 1.230$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 456.0$; $\mu = 0.214$ mm^{-1}; $T = 293$ K.

(S_P)-**3c**, $C_{12}H_{19}O_2P$, Mw = 226.24 from CH_2Cl_2/hexane at −20 °C; orthorhombic; space group $P2_12_12_1$; $a = 6.1383(1)$, $b = 10.4646(2)$, $c = 19.3716(4)$; $\alpha = \beta = \gamma = 90°$; $V = 1244.33(4)$ Å^3; $Z = 4$; $\rho_{calc} = 1.208$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 488.0$; $\mu = 0.201$ mm^{-1}; $T = 293$ K.

($S_P S$)-**3d**, $C_{12}H_{19}O_2P$, Mw = 226.24 from CH_2Cl_2/hexane at −20 °C; orthorhombic; space group $P2_12_12_1$; $a = 6.5659(1)$, $b = 10.2859(2)$, $c = 18.3189(5)$; $\alpha = \beta = \gamma = 90°$; $V = 1237.19(5)$ Å^3; $Z = 4$; $\rho_{calc} = 1.215$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 488.0$; $\mu = 0.202$ mm^{-1}; $T = 293$ K.

(S_P)-**4a**, $C_{11}H_{20}BOP$, Mw = 210.05 from diethyl ether at 4 °C; orthorhombic; space group $P2_12_12_1$; $a = 9.3013(2)$, $b = 21.2793(3)$, $c = 27.0260(5)$; $\alpha = \beta = \gamma = 90°$; $V = 5349.13(17)$ Å^3; $Z = 16$; $\rho_{calc} = 1.043$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 1824.0$; $\mu = 0.176$ mm^{-1}; $T = 293$ K.

(S_P)-**4c**, $C_{12}H_{22}BOP$, Mw = 224.08 from diethyl ether at 4 °C; orthorhombic; space group $P2_12_12_1$; $a = 7.4049(1)$, $b = 15.1152(2)$, $c = 25.7220(5)$; $\alpha = \beta = \gamma = 90°$; $V = 2878.98(8)$ Å^3; $Z = 8$; $\rho_{calc} = 1.034$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 976.0$; $\mu = 0.167$ mm^{-1}; $T = 293$ K.

($S_P S$)-**4d**, $C_{12}H_{22}BOP$, Mw = 224.08 from diethyl ether at 4 °C; orthorhombic; space group $P2_12_12_1$; $a = 7.2910(1)$, $b = 12.9893(2)$, $c = 14.6934(3)$; $\alpha = \beta = \gamma = 90°$; $V = 1391.54(4)$ Å^3; $Z = 4$; $\rho_{calc} = 1.070$ g cm^{-3}; λ ($Mo_{K\alpha1}$) = 0.71073 Å; $F(000) = 488.0$; $\mu = 0.173$ mm^{-1}; $T = 293$ K.

CCDC 1053124, 1053119, 1053122, 1053123, 1053121 and 1053120 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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