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H-adamantylphosphinates as universal precursors of P-stereogenic compounds

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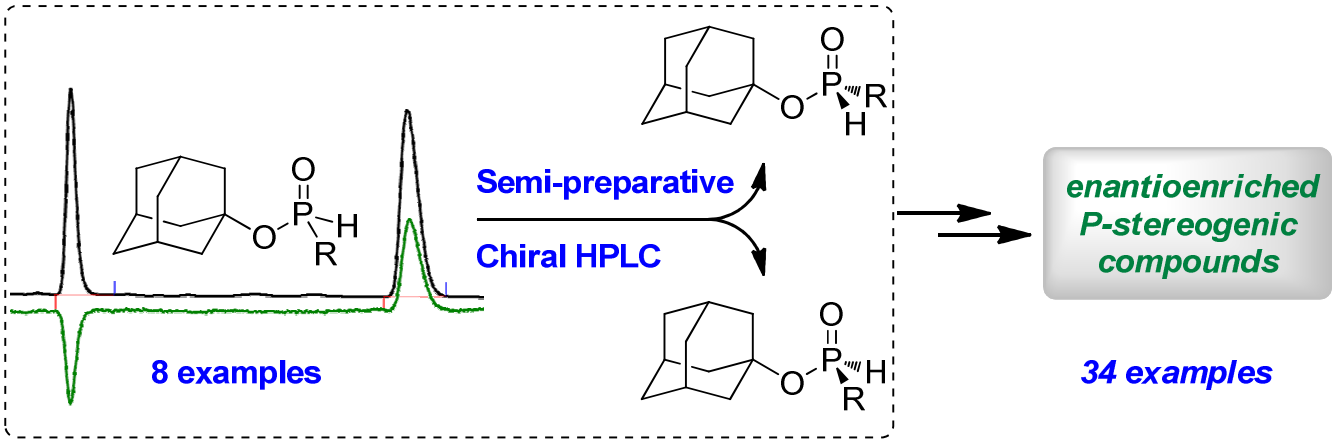


ABSTRACT: A new family of H-adamantylphosphinates as universal precursors of P-stereogenic ligands was obtained in one step from commercial chlorophosphines. Both enantiomers of these air and moisture stable intermediates can easily be separated by semi-preparative chiral HPLC in gram scale and individually undergo stereoselective transformations to afford each enantiomers of a set of P-stereogenic compounds such as secondary phosphine oxides and boron-protected monophosphines.

INTRODUCTION

Phosphorus donor species undoubtedly represent one of the major classes of transition metal ligands, which have largely contributed to the evolution of catalysis into an indispensable tool in organic synthesis and the industrial production of chemicals. In contrast to the lighter pictogen element nitrogen, the inversion barrier of tricoordinated phosphorus is high, allowing for the obtention of P-stereogenic trivalent phosphorus ligands, which may thereby bring the chiral center in close proximity to the metal in subsequent complexes. While this perspective potentially holds great promises in

asymmetric catalysis, mastering the substitution pattern on trivalent phosphorus centers represents a major synthetic challenge. A conventional route to trivalent P-stereogenic architectures consists in stereoselectively producing pentavalent P-stereogenic precursors. While the reactive center displays a tetrahedral geometry reminiscent of carbon, substitution reactions generally do not follow the same routes and the control of their stereoselectivity remains an arduous task.[1]

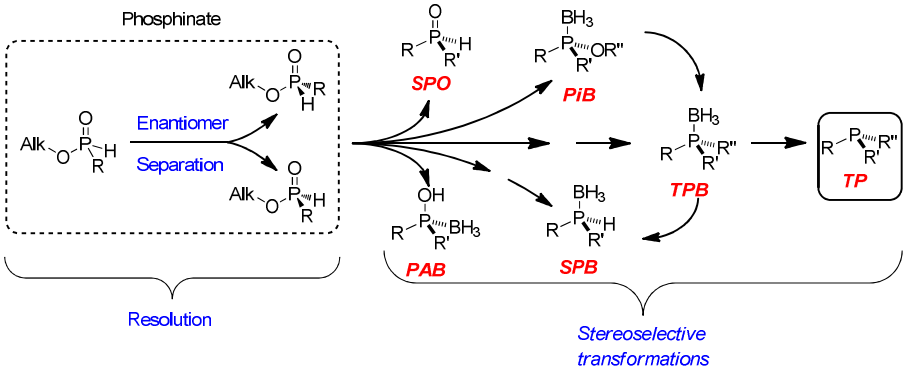
Despite these synthetic difficulties, methods for the preparation of optically active P-stereogenic compounds have recently received considerable attention. In particular, a number of procedures have been proposed with an intention to offer to the community a general and convenient synthetic strategy.[2] In such a perspective, phosphine oxides represent a potential class of precursors with attractive features: they can lead to chiral phosphine ligands through a few well established stereoselective step as well as be powerful trivalent ligands themselves. In contrast to most trivalent species, phosphine oxides are air- and moisture-stable and can be prepared on the large scale in racemic form. Still, the main synthetic challenge relies in the synthetic accessibility of both enantiomers individually with high yields, high purities and through straightforward procedures.[3] Elegant works based on the chiral pool[4] or stereospecific reduction of optically enriched P-stereogenic phosphine oxides[5] have been reported during the last few decades but generally allowed for the construction of only one stereoisomer. In the last few months, significant breakthroughs in this area were reported by Minnaard and co-workers, Berger and Monchamp, and Gilheany and co-workers.[6] While these new methodologies still rely on the use of enantiopure auxiliaries from the chiral pool to covalently or non-covalently transfer chiral information to the phosphorus center through the formation of diastereoisomers, dynamic kinetic resolution and controlled inversion of the diastereoselectivity of key steps provided an access to both configurations of several pentavalent species with high isolated yields.

We herein report the synthesis of a family of universal precursors of P-stereogenic phosphine oxides and of their trivalent derivatives. In complement to the approaches previously mentioned, this strategy relies on the straightforward multigram scale chromatographic separation of both enantiomers of these phosphinates. These universal precursors do not only display exceptional configurational and chemical stability but can also be converted into key P-stereogenic species with high stereospecificities (Scheme 1).[7]

In previous studies, we have investigated (R_P)-H-menthylphosphinates obtained by resolution as potential precursors leading through straightforward procedures to optically active P-stereogenic phosphine oxides[8] and phosphine-boranes.[9] We therefore decided to evaluate the viability and versatility of an alternative yet unexplored strategy: accessing enantiopure P-stereogenic ligands from alkylphosphinates through preparative chiral chromatography in a perspective of process development.[10]

Preparative chiral chromatography has recently become a preferred method for rapidly acquiring enantiopure compounds in the pharmaceutical and fine chemical industry.[11] This technology has drawn an increasingly widespread interest due to its cost effectiveness. In many instances, developing and executing a chromatographic enantioseparation is faster and less labor-intensive than more traditional approaches for accessing enantiopurity. Additionally, solvent recycling and effluent/side product reduction render this approach economically attractive and greener than alternative separation techniques.

Scheme 1. From P-stereogenic phosphinates to the galaxy of enantiopure P-stereogenic monodentate ligands.



SPO: secondary phosphine oxide; PiB: phosphinite borane; TPB: tertiary phosphine borane; TP: tertiary phosphine; SPB: secondary phosphine borane; PAB: phosphinous acid-borane.

RESULTS AND DISCUSSION

We began our study by the preparation of a series of H-alkoxyphenylphosphinates and screened the impact of the alkoxy moiety on the chemical and configurational stability as well as the chromatographic resolution. Synthesis was conducted from aryl-dichlorophosphine **1** with one equivalent of the alcohol in the presence of pyridine as a base followed by gentle hydrolysis. The objective was to identify a low-cost alkoxy group, which, coupled to a readily available family of trivalent chlorophosphine substrates bearing a broad range of side chains would lead to a family of air-, moisture- configurationally stable phosphinates that could be easily separated by chromatography on most usual chiral stationary phases. In this field, it is considered that useful preparative HPLC separation typically have alpha of at least 1.2, and hopefully 1.5 or better.[11]

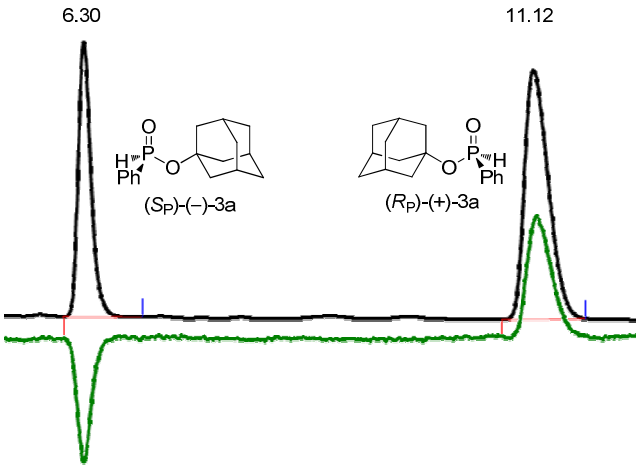
1. From a lead to a family and an ultimate precursor

Ethanol and isopropanol in the presence of pyridine afforded the desired primary and secondary alkoxyphosphinates in 95% yield, while the reaction failed with *tert*-butanol.[12] While these P-stereogenic precursors could easily be separated by chiral chromatography with selectivity ratio and resolution factors up to 1.5 and 7 respectively, they failed the tests in

terms of configurational stability. In fact, analyses by chiral chromatography revealed a racemization process occurring on a timescale of several minutes for the former and hours for the latter. This epimerization process, which was previously observed and reported on menthol derivatives, seems symptomatic of primary and secondary alcohols (*vide infra*). *Tert*-butylphenylphosphinate could be obtained from phenylphosphinic acid following the methodology developed by Yiotakis[13] and separated into stable individual enantiomers with a good purity. This candidate was also eliminated as a possible universal precursor regarding the cost of the synthetic starting material and the poor versatility in terms of variants of the N,N-dimethylformamide di-*tert*-butyl acetal reactant.

This preliminary round leads us to focus our efforts on tertiary alcohols. Following the synthetic pathway described previously, 1-adamantanol afforded the desired H-adamantylphosphinate (±)-**3a** and (±)-**3b** from commercially available dichlorophenylphosphine and *o*-tolyldichlorophosphine with 95% and 90% yield respectively (Table 1, entries 1 and 2). These P-stereogenic adamantane-based model compounds appeared to fulfil the required criteria expected for universal precursors. Pure and configurationally stable enantiomers (R_P)-(+)-**3a** and (S_P)-(−)-**3a**[14] could easily be obtained by semi-preparative chiral HPLC with separation and resolution factors up to 2.3 and 13 respectively (Chart 1)(See supporting information for detail).[15]

Chart 1. Chiral HPLC of H-adamantylphenylphosphinate (±)-3a



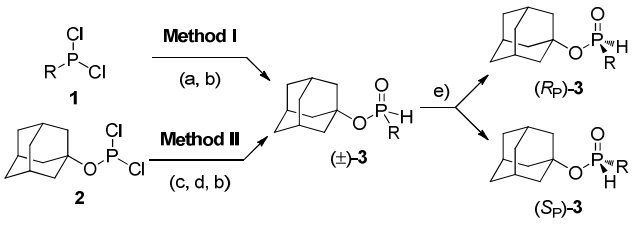
Analytical separation on Lux Cellulose-2 in hexane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm (black line) and polarimeter (green line).

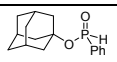
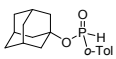
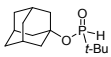
The remarkable and unusual ease to separate the enantiomers on most commercial chiral phases appeared to be specific to the 1-adamantyl substituent. In fact, while resolution factors of the ethylphenylphosphinate remained below 1.5 and around 1 on most chiral phases, the values for the adamantylphenylphosphinate analogues were comprised between 1.2 and 2.3. Still, the versatility of this new family appeared to be restricted by the lack of available dichlorophosphine precur-

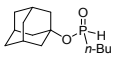
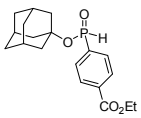
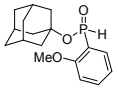
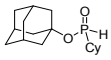
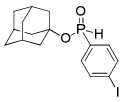
sors. We therefore considered the synthesis of dichloro-adamantyloxyphosphine **2** as the universal precursor of this family, by treating trichlorophosphine with 1-adamantanol. The desired product **2** was easily obtained in 75% yield and indeed provided access to a large panel of H-adamantylalkyl- and H-adamantylarylphosphinates bearing functional groups **3a-h**. An extensive range of phosphinates **3** can be synthesized using both methodologies. Phosphinate **3d** bearing *n*-butyl substituent was obtained with 29% yield due to difficult purification on silica gel (Table 1, entry 4) but secondary and tertiary alkyl groups could be introduced with good yield (Table 1, entries 7 and 3). Arylphosphinates **3e,f,h** were obtained with moderate yield (Table 1, entries 5, 6 and 8) but the aryl substitution with electron withdrawing or donating group in *ortho* or *para* position did not affect the formation of these phosphinates. Remarkably this whole series of H-adamantylphosphinates **3a-h** displayed excellent separation ratio and resolution factor on a broad range of stationary phases.

In addition to the parameters describing the separation, preparative chromatography is mostly concerned with productivity, which measures how much purified material can be prepared with a given quantity of stationary phase per unit time. Semi-preparative equipment (1 cm diameter column) allowed the separation of 25 g of racemic mixture in 56 hours, into 12 g of each enantiomers with excellent purity (**3a** : 25 g leading to S_P-(–)-**3a** 12 g (45% yield), ee >99%, and R_P-(+)-**3a** 12.4 g (47% yield), ee =98%). Similarly, the enantiomers (+)-**3b-h** and (–)-**3b-h** could be separated on the same scale as straightforwardly with semi-preparative equipment.

Table 1. Synthetic pathways leading to H-adamantylphosphinates [a]



Entry	Reactant	Method	Product	Yield[b]
1	**1a**	**I** R = Ph	 **(±) 3a**	95%[c]
2	**1b**	**I** R =*o*-Tolyl	 **(±) 3b**	90%
3	**2**	**II**		75%

		R = *t*-Bu	(±) **3c**	
4	**2**	**II** R = *n*-Bu	 (±) **3d**	29%
5	**2**	**II** R = *p*-$CO_2Et(C_6H_4)$	 (±) **3e**	54%
6	**2**	**II** R = *o*-$OMe(C_6H_4)$	 (±) **3f**	57%
7	**2**	**II** R = Cy	 (±) **3g**	66%
8	**2**	**II** R = *p*-$I(C_6H_4)$	 (±) **3h**	57%

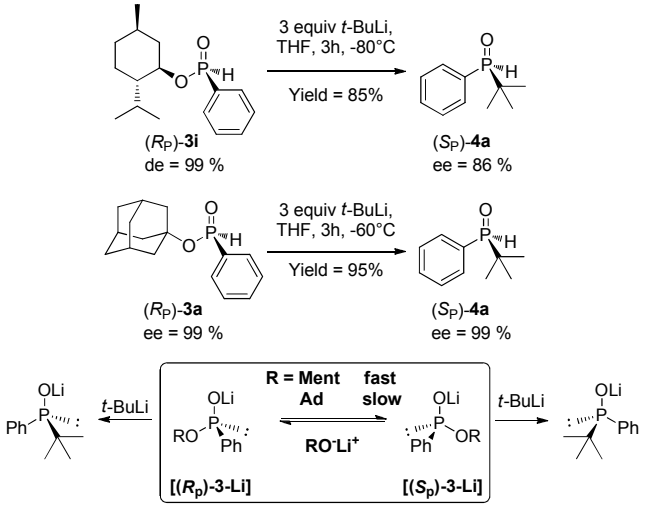
[a] Reaction conditions: a) Adamantanol (1 equiv.), pyridine (1 equiv.), CH_2Cl_2, 0 °C to r.t., 12 h; b) H_2O, 0 °C, 3 h; c) RMgX THF, -60 °C to r.t., 12 h; d) EtOH (1 equiv.), r.t., 1 h; e) Semi-preparative chiral HPLC separation. [b] chemical yield after purification. [c] **3a** was obtained in 49% yield using method **II** without optimization.

Having in hand a series of pure enantiomers with various electronic and steric properties, we examined their reactivity in terms of straightforward conversion into P-stereogenic stable preligands such as SPO or protected monophosphines

2. Conversion of H-adamantylphosphinates into secondary phosphine oxides

Nucleophilic addition of organolithium reagent to enantiopure P-stereogenic phosphinate have been reported to lead to enantioenriched SPO, an air and moisture stable family of pre-ligands displaying catalytic activity in cross-coupling reactions.[16] We were pleased to find that (R_P)-**3a** with 3 equivalents of *tert*-BuLi at – 78 °C afforded *tert*-butylphenylphosphine oxide (S_P)-**4a** in 95% yield without racemization at the phosphorus atom in contrast to the reaction carried out with pure (R_P)-H-menthylphosphinate (R_P)-**3i** (Scheme 2).

Scheme 2. Comparative conversion of H-alkylphosphinates into secondary phosphine oxides using secondary or tertiary alcohol



These results suggest that the substitution of adamantyloxy group on the deprotonated phosphinate [(R_P)-**3a**-Li] proceeds more rapidly than its racemization. Thus, in the case of pure (R_P)-**3i**, the loss of optical purity at low temperature may be imputed to the presence of significant levels of lithium menthylate in the medium through competitive nucleophilic substitution on the phosphinate intermediate [(R_P)-**3i**-Li]. The use of tertiary alcoholate as a leaving group excludes this competitive substitution process (Scheme 2).

This assumption was supported by the slow racemization process observed at low temperature on pure (R_P)-**3i** which was deliberately triggered by introduction of catalytic amounts of sodium menthylate.[17] As for the performance of the chromatographic enantioseparation, the nature of alkoxy group borne by phosphinates **3** appears to have a dramatic impact on the stereoselectivity of subsequent nucleophilic substitutions on the phosphorus center leading to P-stereogenic pre-ligands.

To confirm the robustness of this pathway leading to SPOs with reduced concomitant racemization, enantiomers (R_P)-**3a** and (S_P)-**3a** were used as general substrates for substitution of the alkoxy moiety by a set of alkyl groups. As expected, both enantiomers **4a-c** were obtained with enantiomeric excesses > 90% (Table 2).

Table 2. Stereospecific synthesis of optically active SPO

Entry	Phosphinate, ee (%), R_1Li	T°C, time[a]	Yield [**4**] (%)[b]	ee (%)[c]
1	(R_P)-(+)-**3a**, 99 *t*-BuLi	-50, 2h	(S_P)-(-)-**4a**, 80	99
2	(S_P)-(-)-**3a**, 99	-50, 2h	(R_P)-(+)-**4a**,	99

	t-BuLi		80	
3	(R_P)-(+)-**3a**, 99	-50, 14h	(S_P)-(-)-**4b**,	92
	n-BuLi		80	
4	(S_P)-(-)-**3a**, 99	-50, 14h	(R_P)-(+)-**4b**,	92
	n-BuLi		80	
5	(R_P)-(+)-**3a**, 99	-20, 3h	(S_P)-(-)-**4c**,	91
	MeLi		76	
6	(S_P)-(-)-**3a**, 99	-20, 3h	(R_P)-(+)-**4c**,	90
	MeLi		78	

[a] See supporting information for details; [b] Yield after purification; [c] Enantiomeric excess was determined by HPLC analysis (see Supporting Information).

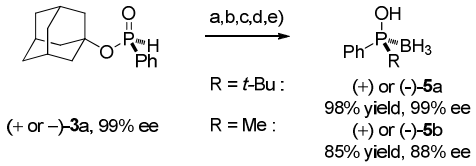
Substitution with *tert*-BuLi gave the best yields and enantiomeric excesses (Table 2, entries 1 and 2). However, when enantiomerically pure **3a** was treated with *n*-BuLi in THF at –78 °C, the reaction proceeds smoothly and the conversion appeared to be complete at –50 °C after 14h. Under these conditions, the substitution of adamantyloxy group occurs with a slight racemization yielding each enantiomer with 92% of ee (Table 2, entries 3 and 4). Same results were obtained with MeLi at –20 °C (Table 2, entries 5 and 6). Unlike pathways based on resolution through formation of matching/mismatching diastereoisomeric pairs, this strategy provides a straightforward access of both enantiomers of various SPO and may thereby facilitate their use in asymmetric catalysis.

3. An entry to P-stereogenic monophosphines

To confirm the status of universal precursors of phosphinate **3**, two reaction pathways leading to precursors of P-stereogenic monophosphines were explored.

Taking advantage of the exceptionally slow rate of racemization of precursors **3** in basic conditions, phosphinous acid-boranes **5** could be obtained with excellent ee from enantiopure **3a**. To exemplify the potency of this convenient pathway, phosphinous acid-boranes **5a** and **5b** bearing substituents with contrasted stereoelectronic features such as *tert*-butyl and methyl groups were obtained with 99% and 88% ee respectively (Scheme 3). We, among others, have shown in previous work[18] that these compounds can be converted in two successive steps with excellent yields and enantiomeric excesses to protected forms of secondary phosphine (secondary phosphine boranes), pre-ligands of widespread interest.[19]

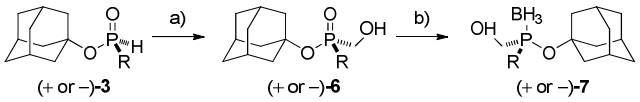
Scheme 3. One pot synthesis of phosphinous acid-boranes (+) or (–)-5a and (+) or (–)-5b[a]



[a] Reagents and conditions: a) *tert*-BuLi (3 equiv.), –50°C, THF, 3 h or MeLi (3 equiv.), –20°C, THF, 3 h; b) TMSCl, –50°C or –20°C to rt, THF; c) BH_3•SMe_2, THF, 3 h; d) H_2O, H^+; e) TBAF, THF.

To access trivalent P-stereogenic compounds, an alternative pathway consisting in the non-racemizing cleavage of the PO double bond, a major challenge in phosphorus chemistry,[20] was designed. The strategy relies on the introduction of a hydroxymethyl handle on the phosphorus center of phosphinates **3** in order to control the stereoselectivity of subsequent PO reduction on resulting adducts with borane (Table 3).[21] In that perspective, compounds **3a**, **3c**, **3f**, and **3g** were reacted with formaldehyde to form optically pure phosphinates **6a**, **6c**, **6f** and **6g**. These P-stereogenic compounds indeed proved to be excellent intermediates in the synthesis of highly optically enriched (ee > 95 %) phosphinite-boranes **7a**, **7c**, **7f** and **7g** by simple exposure to borane (Table 3).

Table 3. Conversion of optically pure 3 into hydroxymethylphosphinite-boranes 7[a]



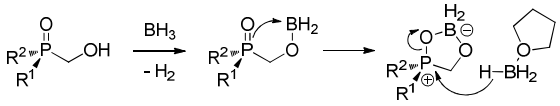
Entry	Phosphinate, ee (%)[b]	Yield [**6**], ee (%)[c]	Yield [**7**], ee (%)
1	(R_P)-(+)-**3a**, 99	84 [(S_P)-(+)-**6a**], 99	86 [(R_P)-(-)-**7a**], 99
2	(S_P)-(-)-**3a**, 99	96 [(R_P)-(-)-**6a**], 99	84 [(S_P)-(+)-**7a**], 96
3	(R_P)-(+)-**3c**, >95	75 [(S_P)-(-)-**6c**], >95	51 [(R_P)-(+)-**7c**],[d] >95
4	(S_P)-(-)-**3c**, >95	72 [(R_P)-(+)-**6c**], >95	48 [(S_P)-(-)-**7c**],[d] >95
5	(R_P)-(+)-**3e**, 99	90 [(S_P)-(+)-**6e**], >99	/[e]
6	(S_P)-(-)-**3e**, 99	65 [(R_P)-(-)-**6e**], >99	/[e]
7	(+)-**3f**, 99	70 [(+)-**6f**], 99	81 [(-)-**7f**], 99
8	(-)-**3f**, 99	72 [(-)-**6f**], 98	77 [(+)-**7f**], 99
9	(+)-**3g**, >95	94 [(-)-**6g**], >95	73 [(+)-**7g**], >95

10	(-)-**3g**, >95	85 [(+)-**6g**], >95	78 [(-)-**7g**], >95

[a] Reagents and conditions: a) $(CH_2O)_n$ (1.5 equiv.), LiOH, THF/H_2O, r.t., 3h; b) BH_3•THF (6 equiv.), THF, r.t., 48h. [b] Yield after purification. [c] Enantiomeric excess was determined by HPLC analysis. [d] Reaction time after the addition of BH_3•THF was 96h. [e] Due to the presence of the ester group in R, the attempted borane reduction of **6e** led to extensive ester reduction of starting material.

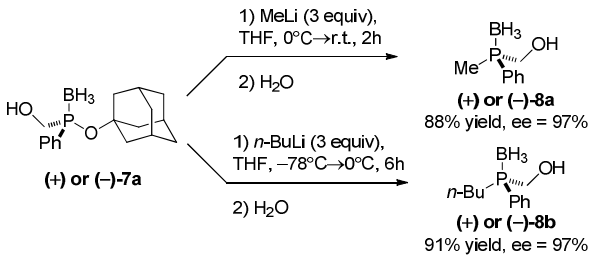
The reaction is compatible with a wide variety of H-adamantylphosphinates and is stereoselective for all phosphinates **6a**, **6c**, **6f** and **6g** and phosphinite-boranes **7a**, **7c**, **7f** and **7g** (Table 3, entries 1-8). Phosphinate-borane **6c** bearing a *tert*-Bu substituent was the only member of the series to afford the expected **7c** with moderate yield (Table 3, entry 3) due to the competitive formation of secondary phosphine-borane.[22] To our knowledge, this represents one of the very few example of phosphinate P=O bond reduction with stereochemical control at phosphorus center.[21] This reduction is controlled by the presence of hydroxymethyl bound to phosphorus atom. A five-membered cyclic phosphonium intermediate was proposed by Pietrusiewicz which further undergo hydride attack at phosphorus atom to deliver the phosphine-borane with inversion of the configuration (Scheme 4).[23]

Scheme 4. Proposed mechanism for PO bond reduction with BH_3.



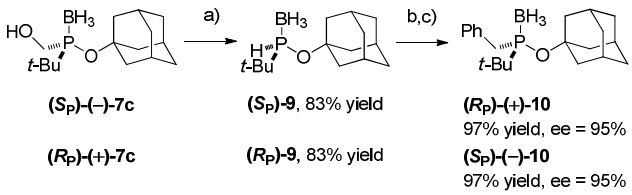
Beyond the fundamental challenge that stereoselective PO cleavage represents, phosphinite-boranes **7** stand as key intermediates towards protected P-stereogenic monophosphines. To take advantage of the hydroxymethyl moiety introduced we firstly examined the reactivity of phosphinite-borane **7a** towards the substitution of the adamantyloxy group, leading to a new family of hydroxymethyl phosphine-boranes with potential chelating features (Scheme 5). The utility of the hydroxymethyl group both during the synthesis of phosphine or diphosphine ligand and for the coordination of the resulting ligands with transition metal has been well established before.[24]

Scheme 5. Preparation of optically active hydroxymethylphosphine-boranes 8



Confirming the advantage of the adamantyloxy as a leaving group affording substitutions without loss of the enantiomeric excess, compound **7a** reacted smoothly with primary alkyllithiums to give the corresponding phosphine-borane **8a** and **8b** with inversion of configuration at the phosphorus atom (Scheme 5).[25] However, as a consequence of the steric hindrance of the substrate, *tert*-BuLi was not suitable for this reaction and only starting material was recovered after hydrolysis of the reaction medium.[26]

Scheme 6. Substitution of the hydroxymethyl group on optically active phosphinite-boranes through oxidation-substitution[a]



[a] Reagents and conditions: a) $RuCl_3$ (20 mol%), $K_2S_2O_8$ (3 equiv.), KOH (10 equiv.) CH_3CN/H_2O, 10h; b) *n*-BuLi (1.5 equiv.), THF, −78 °C, 20 min; c) BnBr (4 equiv), −78 °C→0 °C, 4h.

Still, the versatility of the methodology based on adamantyloxy phosphinate precursors allowed to introduce the bulky *tert*-Bu group directly on compound **3,** which leads to **7c** after hydroxymethylation and P=O cleavage. To further achieve introduction of substituents of the phosphorus center, nucleophilic substitution must be replaced by oxidation into secondary phosphinite-borane **9**[27] followed by nucleophilic substitution (Scheme 6). During these two steps, the hydroxymethyl handle is the leaving group while the adamantyloxy is a spectator. **7c** is therefore a key compound which displays dual reactivity and leads through alternative pathways to new bulky P-stereogenic stable compounds that can be used in asymmetric catalysis.

SUMMARY

In conclusion, semi-preparative chiral HPLC can lead to the straightforward multi-gram scale separation of H-adamantylphosphinates as universal precursors bearing various substituents. These new objects provide an unprecedented access, through various types of substitution on the phosphorus center to both enantiomers of phosphine oxides and boranes protected P-stereogenic ligands. Both enantiomers of optically enriched phosphine-boranes can be accessed through a well-established route involving phosphinous-borane intermediates. Additionally, the same universal precursor can lead to a new family of phosphinite-boranes **7,** which display dual reactivity: the alkoxy or the hydroxymethyl substituents can alternatively be replaced on demand by tailored substituents leading to new protected P-stereogenic phos-

phines/phosphinites. We believe that these new classes of easily accessible enantioenriched precursors will contribute to the current *renaissance* of P-stereogenic ligands.

EXPERIMENTAL SECTION

General Experimental Details.

All solvents were purified by standard procedures or obtained from a Solvent Purification System. Unless otherwise mentioned, all reactions were carried out under an atmosphere of dry argon. Thin Layer Chromatography (TLC) was carried out on silica gel 60 F_{254} and visualized under ultraviolet light (254 and 366 nm), or through spraying with 5% phosphomolybdic acid in EtOH, or by placing in iodine vapor. Flash chromatography was performed with silica gel 60 (230-400 mesh). Solvents for chiral chromatography (*n*-hexane, *n*-heptane, 2-PrOH, EtOH, MeOH) are HPLC grade, degassed and filtered on membrane 0.45µm before use. Lux Cellulose-2, Lux Amylose-2, (*S*,*S*)-Whelk-O1 and Chiralpak IA columns (250*10mm) were used for semi-preparative separation. Lux Cellulose-2, Lux Cellulose-4, Lux Amylose-2, (*S*,*S*)-Whelk-O1, Chiralcel OD-3 and Chiralpak AS-H, AZ-H, AD-H, IA columns (250*4.6mm) were used for the analytical separation. Chiral HPLC analyses were performed with UV detector and polarimetric or circular dichroism (CD) detector. Retention times Rt are given in minutes, retention factor $k_i = (Rt_i - Rt_o)/Rt_o$ and enantioselectivity factor $\alpha = k_2/k_1$. The sign given by the chiroptical detector is the sign of the enantiomer in the mobile phase used, at the specified wavelength.[28] ^1H, ^{13}C, ^{31}P and ^{11}B NMR spectra were recorded on spectrometers operating at 400 and 300 MHz for ^1H. ^{13}C and ^{31}P nuclei were observed with ^1H decoupling. Unless otherwise specified NMR spectra have been made in $CDCl_3$. As external reference for ^{31}P NMR spectra, 85% phosphoric acid was used. Chemical shifts (δ) of ^1H and ^{13}C are reported in ppm relative to $CHCl_3$ (δ = 7.26 for ^1H and δ = 77.0 for ^{13}C) and C_6D_6 (δ = 7.15 for ^1H and δ = 128.02 for ^{13}C). *J* values are given in Hz. Proton (^1H) NMR information is given in the following format: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; sept; septet; m, multiplet), coupling constant *J*, number of protons). The prefix broad or b indicates the signal in question is broadened. Melting points (uncorrected) were determined in a capillary tube. $[\alpha]_D^{25}$ values were determined with a Polarimeter, using a 10 cm length double jacketed cell: the sign (+) or (–) given for the described chiral compounds is the sign obtained at 589 nm in chloroform. High-resolution MS experiments were performed with an orthogonal acceleration time-of-flight (oa-TOF) mass analyzer equipped with an electrospray ionisation (ESI) source. In the positive ion mode, the capillary voltage was set at +5500 V and the cone voltage was set between 10-55 V. In MS, accurate mass measurements were performed using two reference ions from a poly(ethylene glycol) or poly(propylene glycol) internal standard, according to a procedure described elsewhere. Intensity data were collected on a diffractometer using graphitemonochromated MoKα radiation (λ = 0.71073 Å) at 293 K. The collected frames were processed with the software HKL-2000, structures were solved by

the direct methods, and refined using the SHELXL-97 software package. Compounds **4a-c**,[8] **5a-b**,[9a] **8a**[27] and **8b**[29] were known and characterizations data were in accordance with the literature.

Main reason for the epimerization of (R_P)-3i

a) Reaction without sodium menthylate

A dry Schlenk tube is charged under argon atmosphere with a solution of phosphinate **(R_P)-3i** (de > 99%) (1 mmol) and cooled down to –80°C in THF (5 mL). A solution of Lithium diisopropylamide (1 mmol, 2M in THF) in THF (2 mL) was added dropwise, the reaction mixture was stirred at –80°C for 2h and the solution was hydrolyzed with THF/acetic acid; 9/1 at –80°C. The solution was allowed to warm to room temperature and water was added. A diastereomeric excess of 88% was determined by ^{31}P NMR after extraction with diethyl ether.

b) Reaction with sodium menthylate

A dry Schlenk tube is charged under argon atmosphere with a solution of phosphinate **(R_P)-3i** (de > 99%) (1 mmol) and cooled down to –80°C in THF (5 mL). A solution of Lithium diisopropylamide (1 mmol, 2M in THF) in THF (2 mL) was added dropwise and after 5 min at this temperature, a solution of lithium menthylate (1 mmol in THF) (1mL), was also added. The reaction mixture was stirred at –80°C for 2h and the solution was hydrolyzed with THF/acetic acid; 9/1 at –80°C. The solution was allowed to warm to room temperature and water was added. A diastereomeric excess of 68% was determined by ^{31}P NMR after extraction with diethyl ether.

Synthesis of dichloro-adamantyloxyphosphine 2

A solution of 1-adamantanol (3.04 g, 20 mmol) in THF (15 mL) was added dropwise at -78°C to trichlorophosphine (1.75 mL, 20 mmol) in THF (15 mL). The solution was allowed to warm to room temperature and stirred overnight. Dichloro-adamantyloxyphosphine **2** was isolated after bulb to bulb distillation (bp 110°C/0.08 mbar) in 75% yield (3.8 g). Air and moisture sensitive white solid at 4°C: ^{1}H NMR (400 MHz, C_6D_6): δ 1.22 (bs, 6H), 1.75 (bs, 3H), 1.89 (bs, 6H); ^{31}P NMR (162 MHz, C_6D_6): δ 191.50 (s).

General procedure for the synthesis of racemic adamantylhydrogenophosphinate (Method I)

A solution of adamantanol (8.5 g, 56 mmol) and pyridine (4.5 mL, 56 mmol) in dichloromethane (100 mL) was added dropwise at 0°C to a solution of dichloroarylphosphine (56 mmol) in dichloromethane (20 mL). After 15h at room temperature, water (40 mL) was added slowly at 0°C. The two layers were separated and the aqueous phase was extracted with hexane (3 x 20 mL). The organic layers were collected and concentrated under reduced pressure. Hexane (100 mL) was added to the resulting crude and the organic phase was washed with aqueous sodium bicarbonate solution 10% (100 mL). The aqueous phase was extracted with hexane (3 x 30 mL). The organic layers were collected, dried over $MgSO_4$, filtrated,

and concentrated under reduced pressure to give adamantylhydrogenophenylphosphinate **3a** and **3b** in 95 % and 90% yield respectively.

Adamantylhydrogenophenylphosphinate **3a**. White solid, 14.7 g (95% yield), S_P-(–)-**3a** $[\alpha]_D^{25}$ –44.2 (*c* = 1.045, $CHCl_3$), R_P-(+)-**3a** $[\alpha]_D^{25}$ +44.3 (*c* = 1.07, $CHCl_3$) : ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.65 (bs, 6H), 2.13 (bs, 6H), 2.21 (bs, 3H), 7.44-7.56 (m, 3H), 7.79 (d, *J* = 553.3 Hz, 1H), 7.71-7.82 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 30.7 (3C), 35.3 (3C), 43.7 (d, *J* = 4.9 Hz, 3C), 82.1 (d, *J* = 8.8 Hz), 128.1 (d, *J* = 13.8 Hz, 2C), 130.4 (d, *J* = 11.6 Hz, 2C), 131.3 (d, *J* = 137.5 Hz), 132.1 (d, *J* = 2.8 Hz); ^{31}P NMR (81 MHz, $CDCl_3$) : δ 15.2 (s). HRMS (ESI-MS) [M+H]+: found 277.1352; calculated for $C_{16}H_{22}O_2P^+$: 277.1351. Chiral HPLC: analytical separation on Lux Cellulose-2 in hexane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimetric: Rt_1 = 6.30 (S_P)-(–), Rt_2 = 11.12(R_P)-(+), k_1 = 1.1 (S_P)-(–), k_2 = 2.7 (R_P)-(+), α = 2.46, Rs = 13.3. Semi-preparative separation on Lux-Cellulose-2 (250 x 10 mm) in methanol at 5 mL/min and 30°C with UV detection 235 nm, 0.1 mL of a 175 mg/mL racemic solution were injected every 2.4 min. After 700 injections, 6.0 g of (S_P)-(–)-**3a** (ee >99%) and 6.2 g of (R_P)-(+)-**3a** (ee = 98%).

Adamantylhydrogeno-o-tolylphosphinate **3b**. White solid, 14.6 g (90% yield), (–)-**3b** $[\alpha]_D^{25}$ –24.5 (*c* = 0.94, $CHCl_3$), ee = 99%; (+)-**3b** $[\alpha]_D^{25}$ +25.1 (*c* = 1.02, $CHCl_3$), ee = 99%: ^{1}H NMR (300 mHz, $CDCl_3$): *δ* 1.65-1.67.(m, 6H), 2.14-2.15 (bs, 6H), 2.22 (bs, 3H), 2.57 (s, 3H), 7.21 – 7.25 (m, 1H), 7.30 (td, *J* = 7.4, 2.8 Hz, 1H), 7.44 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.79 (ddd, *J*=16.1, 7.5, 1.3 Hz, 1H), 7.84 (d, *J* = 547.3 Hz, 1H); ^{13}C NMR (100.6 MHz,$CDCl_3$): *δ* 19.8 (d, *J* = 6.6 Hz), 30.8 (3C), 35.4 (3C), 43.7 (d, *J* = 4.9 Hz, 3C), 82.4 (d, *J* = 8.8 Hz), 125.4 (d, *J* = 14.3 Hz), 129.4 (d, *J* = 137 Hz), 130.7 (d, *J* = 11.5 Hz), 131.3 (d, *J* = 12.7 Hz), 132.1 (d, *J* = 2.7 Hz), 140.4 (d, *J* = 10.5 Hz); ^{31}P NMR (121.5 MHz, $CDCl_3$): *δ* 15.2 (s). HRMS (ESI-MS) [M+H]+: found 291.1508; calculated for $C_{17}H_{24}O_2P^+$: 291.1512. Chiral HPLC: analytical separation on Lux Amylose-2 in hexane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 220 nm and polarimetric: Rt_1 = 5.60 (–), Rt_2 = 8.94 (+), k_1 = 0.87 (–), k_2 = 1.98, α = 2.29, Rs = 8.38. Semi-preparative separation on Lux-Amylose-2 (250 x 10 mm) in hexane/ethanol (1/1) at 5 mL/min and 30°C with UV detection 220 nm, 0.6 mL of a 22 mg/mL racemic solution were injected every 12 min. After 100 injections, 670 mg of (–)-**3b** (ee > 99%) and 660 mg of (+)-**3b** (ee > 99%).

General procedure for the synthesis of racemic adamantylhydrogenophosphinate (Method II)

A solution of aryl or alkyl magnesium bromide (8 mmol) in THF (2 mL) was added dropwise at –50°C to dichloroadamantyloxyphosphine **2** (8 mmol) in hexane (2 mL) and the solution was allowed to warm to room temperature. After 15h at room temperature, water (2 mL) was added slowly at 0°C. The two layers were separated and the aqueous phase was extracted with hexane (3 x 5 mL). The organic layers were collected and concentrated under reduced pressure. Hexane (5 mL) was added to the resulting crude and the organic phase was washed with aqueous sodium bicarbonate solu-

tion 10% (5 mL). The aqueous phase was extracted with hexane (3 x 5 mL). The organic layers were collected, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure to give adamantylhydrogenophosphinate **3c-h**.

Adamantylhydrogeno-*tert*-butylphosphinate **3c**. White solid, 1.54 g (75% yield): (S_P)-(–)-**3c** $[\alpha]_D^{25}$ –19.4 (*c* = 1.03, $CHCl_3$), ee = 99%; (R_P)-(+)-**3c** $[\alpha]_D^{25}$ +19.6 (*c* = 1.1, $CHCl_3$), ee = 99%: ^{1}H RMN (400 MHz, $CDCl_3$), δ 1.06 (d, *J* = 17.7 Hz, 9H), 1.62 (bm, 6H), 2.01 (bm, 6H), 2.17 (bs, 3H), 6.86 (d, *J* = 509.5 Hz, *P*-H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 23.1 (3C), 30.9 (d, *J* = 99.9 Hz), 31.2 (3C), 36.0 (3C), 44.0 (d, *J* = 4.4 Hz, 3C), 81.6 (d, *J* = 10.5 Hz); ^{31}P NMR (161 MHz, $CDCl_3$): δ 37.5 (s). HRMS (ESI-MS) [M+H]+: found 257.1665; calculated for $C_{14}H_{26}O_2P^+$: 257.1666. Chiral HPLC: analytical separation on (*S*,*S*)-Whelk-O1 in hexane/isopropanol (7/3) at 1 ml/min and 25°C with polarimetric detection: Rt_1 = 7.32 (S_P)-(–), Rt_2 = 10.89 (R_P)-(+), k_1 = 1.29 (S_P)-(–), k_2 = 2.4 (R_P)-(+), α = 1.87, Rs = 7.79. Semi-preparative separation on (*S*,*S*)-Whelk-O1 (250 x 10 mm) in hexane/isopropanol (7/3) at 5 mL/min with polarimetric detection, 0.15 mL of a 384 mg/mL racemic solution were injected every 5 min. After 26 injections, 720 mg of (–)-**3c** (ee > 95%) and 735 mg of (+)-**3c** (ee > 95%).

Adamantylhydrogeno-*n*-butylphosphinate **3d**. Colorless oil, 743 mg (29% yield), (–)-**3d** $[\alpha]_D^{25}$ –1.7 (*c* = 1.105, $CHCl_3$) ee = 99%, (+)-**3d** $[\alpha]_D^{25}$ +1.8 (*c* = 1.05, $CHCl_3$) ee = 99%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.1 Hz, 3H), 1.35 (dq, *J* = 14.6, 7.1 Hz, 2H), 1.41-1.53 (m, 2H), 1.58 (t, *J* = 3.0 Hz, 6H), 1.60-1.70 (m, 2H), 1.96-2.02 (m, 6H), 2.13 (bs, 3H), 7.23 (d, *J* = 521 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.5, 23.0 (d, *J* = 2.2 Hz), 23.4 (d, *J* = 16.1 Hz), 29.1 (d, *J* = 97.6 Hz), 30.9 (3C), 35.6 (3C), 43.8 (d, *J* = 4.4 Hz, 3C), 81.2 (d, *J* = 8.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.5 (s). HRMS (ESI-MS) [M+H]+: found 257.1665; calculated for $C_{14}H_{26}O_2P^+$: 257.1665. Chiral HPLC: analytical separation on (*S*,*S*)-Whelk-O1 in hexane/isopropanol (7/3) at 1 ml/min and 25°C with polarimetric detection: Rt_1 = 10.87 (–), Rt_2 = 12.57 (+), k_1 = 2.62 (–), k_2 = 3.19, α = 1.22, Rs = 4.18. Semi-preparative separation on (*S*,*S*)-Whelk-O1 (250 x 10 mm) in hexane/isopropanol (7/3) at 5 mL/min with polarimetric detection, 0.11 mL of a 105 mg/mL racemic solution were injected every 4 min. After 35 injections, 166 mg of (–)-**3d** (ee > 95%) and 198 mg of (+)-**3d** (ee > 95%).

Adamantylhydrogeno-4-(ethyloxycarbonyl)phenylphosphinate **3e**. White solid, 752 mg (54% yield): (S_P)-(–)-**3e** $[\alpha]_D^{25}$ –21.7 (*c* = 1.065, $CHCl_3$) (R_P)-(+)-**3e** $[\alpha]_D^{25}$ +22.2 (*c* = 1.11, $CHCl_3$) White solid : ^{31}P NMR (162 MHz, $CDCl_3$) δ 13.1 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (t, *J* = 7.1 Hz, 3H), 1.65 (t, *J* = 3.0 Hz, 6H), 2.12 (d, *J* = 3.0 Hz, 6H), 2.21 (bs, 3H), 4.39 (q, *J* = 7.3 Hz, 2H), 7.82 (d, *J* = 560 Hz, 1H), 7.84 (dd, *J* = 13.3, 8.0 Hz, 2H), 8.13 (dd, *J* = 8.1, 2.9 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.2, 31.1 (3C), 35.6 (3C), 44.2 (d, *J* = 4.4 Hz, 3C), 61.4, 83.4 (d, *J* = 8.8 Hz), 129.4 (d, *J* = 13.9 Hz, 2C), 130.9 (d, *J* = 11.7 Hz, 2C), 134.0 (d, *J* = 2.9 Hz), 136.3 (d *J* = 135.0 Hz), 165.7; HRMS (ESI-MS) [M+H]+: found 349.1563; calculated for $C_{19}H_{26}O_4P^+$: 349.1565. Chiral HPLC: analytical separation on Chiralpak AD-H in hexane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 7.91 (R_P)-(+), Rt_2 = 9.38 (S_P)-(–), k_1 = 1.64 (R_P)-(+), k_2 = 2.13 (S_P)-(–), α = 1.30, Rs = 2.39. Semi-preparative separation on Chiralpak IA (250 x 10 mm) in hexane/ethanol (1/1) at 5 mL/min and 30°C with UV detection

280 nm, 0.19 mL of a 42.5 mg/mL racemic solution were injected every 4 min. After 45 injections, 152 mg of (S_P)-(–)-**3e** (ee > 99%) and 179 mg of (R_P)-(+)-**3e** (ee > 99%).

Adamantylhydrogeno-o-anisylphosphinate **3f**. White solid 1.75 g (57% yield): (–)-**3f** $[\alpha]_D^{25}$ –57.1 (*c* = 0.925, $CHCl_3$) ee = 99%, (+)-**3f** $[\alpha]_D^{25}$ +57.0 (*c* = 0.95, $CHCl_3$) ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58 (t, *J* = 3.14 Hz, 6H), 2.04 (d, *J* = 3.01 Hz, 6H), 2.13 (bs, 3H), 3.81 (s, 3H), 6.85 (dd, *J* = 8.03, 6.78 Hz, 1H), 6.99 (td, *J* = 7.40, 2.51 Hz, 1H), 7.39 (d, *J* = 573 Hz, 1H), 7.41-7.47 (m, 1H), 7.75 (ddd, *J* = 14.49, 7.47, 1.63 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.1 (3C), 35.8 (3C), 44.1 (d, *J* = 4.4 Hz, 3C), 55.6, 81.9 (d, *J* = 8.8 Hz), 110.8 (d, *J* = 6.6 Hz), 119.6 (d, *J* = 138.6 Hz), 120.7 (d, *J* = 13.2 Hz), 133.1 (d, *J* = 6.6 Hz), 134.2 (d, *J* = 1.5 Hz), 161.1 (d, *J* = 4.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.30 (s). HRMS (ESI-MS) [M+H]+: found 307.1458; calculated for $C_{17}H_{24}O_3P^+$: 307.1458. Chiral HPLC: analytical separation on Lux-Cellulose-2 in heptane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 7.20 (–), Rt_2 = 10.83 (+), k_1 = 1.40 (–), k_2 = 2.61, α = 1.86, Rs = 9.01. Semi-preparative separation on Lux-Cellulose-2 (250 x 10 mm) in hexane/ethanol (1/1) at 5 mL/min and 30°C with polarimetric detection, 0.4 mL of a 50 mg/mL racemic solution were injected every 6 min. After 70 injections, 752 mg of (–)-**3f** (ee > 99%) and 726 mg of (+)-**3f** (ee > 98%).

Adamantylhydrogeno-cyclohexylphosphinate **3g**. White solid, 1.49 g (66% yield): (–)-**3g** $[\alpha]_D^{25}$ –20.3 (*c* = 0.92, $CHCl_3$), ee = 99%, (+)-**3g** $[\alpha]_D^{25}$ +19.4 (*c* = 1.01, $CHCl_3$) ee =99%: ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.9 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18-1.34 (m, 5H), 1.63 (bs, 6H), 1.65-1.74 (m, 2H), 1.78-1.99 (m, 4H), 2.01-2.07 (m, 6H), 2.18 (bs, 3H), 7.01 (dd, *J* = 513, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.4 (d, *J* = 2.2 Hz), 24.6 (d, *J* = 1.5 Hz), 25.3, 25.8 (d, *J* = 2.2 Hz), 25.9 (d, *J* = 2.2 Hz), 31.0 (3C), 35.8 (3C), 37.4 (d, *J* = 100 Hz) 43.9 (d, *J* = 4.4 Hz, 3C) 80.9 (d, *J* = 9.5 Hz). HRMS (ESI-MS) [M+H]+: found 283.1821; calculated for $C_{16}H_{28}O_2P^+$: 283.1822. Chiral HPLC: analytical separation on (*S*,*S*)-Whelk-O1 in hexane/isopropanol (7/3) at 1 ml/min and 25°C with polarimetric detection: Rt_1 = 9.93 (–), Rt_2 = 12.01 (+), k_1 = 2.31 (–), k_2 = 3.00, α = 1.30, Rs = 2.67. Semi-preparative separation on (*S*,*S*)-Whelk-O1 (250 x 10 mm) in hexane/isopropanol (7/3) at 5 mL/min with polarimetric detection, 0.18 mL of a 88 mg/mL racemic solution were injected every 3.5 min. After 75 injections, 583 mg of (–)-**3g** (ee > 95%) and 508 mg of (+)-**3g** (ee > 95%).

Adamantylhydrogeno-4-iodophenylphosphinate **3h**. White solid 917 mg (57% yield): (–)-**3h** $[\alpha]_D^{25}$ –28.5 (*c* = 0.965, $CHCl_3$) ee = 99%, (+)-**3h** $[\alpha]_D^{25}$ +28.4 (*c* = 1.00, $CHCl_3$) ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68 (t, *J* = 3.0 Hz, 6H), 2.14 (d, *J* = 3.3 Hz, 6H), 2.24 (bs, 3H), 7.46-7.55 (m, 2H), 7.77 (d, *J* = 559 Hz, 1H), 7.85-7.90 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.1 (3C), 35.7 (3C), 44.2 (d, *J* = 4.4 Hz, 3C), 83.2 (d, *J* = 8.8 Hz), 100.3 (d, *J* = 3.7 Hz), 131.3 (d, *J* = 137.9 Hz), 132.3 (d, *J* = 11.7 Hz, 2C), 137.8 (d, *J* = 13.9 Hz, 2C); ^{31}P NMR (162 MHz, $CDCl_3$) δ 13.3 (s). HRMS (ESI-MS) [M+H]+: found 403.0315; calculated for $C_{16}H_{21}O_2PI^+$: 403,0318. Chiral HPLC: analytical separation on Lux-Amylose-2 in heptane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 8.00 (–), Rt_2 = 15.79 (+), k_1 = 1.67 (–), k_2 = 4.26 (+), α = 2.55, Rs =

13.05 or on Chiralpak AD-H in hexane/ethanol (1/1) at 1 mL/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 7.13 (+), Rt_2 = 8.61 (–), k_1 = 1.38 (+), k_2 = 1.87 (–), α = 1.35, Rs = 3.17. Semi-preparative separation on Lux-Amylose-2 (250 x 10 mm) in ethanol at 3 mL/min and 30°C with UV detection 254 nm, 0.95 mL of a 27.5 mg/mL racemic solution were injected every 35 min. After 21 injections, 248 mg of (–)-**3h** (ee > 99%) and 269 mg of (+)-**3h** (ee = 99%).

General procedure for the synthesis of optically active SPO 4a-c

A dry Schlenk tube is charged under argon atmosphere with a solution of alkyllithium (2.2 mmol) in THF (5 mL) and cooled down to –50°C. A solution of phosphinate **3a** (1 mmol) in THF (2 mL) was added dropwise, the reaction mixture was stirred at –50°C for 2h and the solution was allowed to warm to –20°C. The reaction mixture was stirred at this temperature for 3h. The reaction mixture is then diluted with Et_2O (5 mL) and NH_4Cl saturated aqueous solution (5 mL). The organic phase was separated off, and the aqueous phase was extracted with AcOEt (2 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated under vacuum. Purification of the crude by chromatography on a short plug of deactivated silica gel (10 % H_2O) using Et_2O/light petroleum/MeOH 4/1/0.05 as eluent, afforded SPO **4**.

General procedure for synthesis of phosphinous acid-boranes 5a,b

A dry Schlenk tube is charged under argon atmosphere with a solution of alkyllithium (2.2 mmol) in THF (5 mL) and cooled down to –50°C. A solution of phosphinate **3a** (1 mmol) in THF (2 mL) was added dropwise, the reaction mixture was stirred at –50°C for 2h and the solution was allowed to warm to –20°C. After stirring the reaction mixture 2h at this temperature, trimethylsilyl chloride (279 µL, 2.2 mmol) was added and the solution was allowed to warm to room temperature. The reaction was monitoring by ^{31}P NMR. Then, $BH_3.SMe_2$ (208 µL, 2.2 mmol) was added at room temperature. After 3 hours, the completion of the reaction was confirmed by ^{31}P NMR. Aqueous HCl (5 %) was added under vigorous stirring. The aqueous layer was washed with dichloromethane (3 x 10 mL). The organic layers were combined and volatiles were removed under vacuum. The residue was dissolved in THF and tetra-*n*-butylammonium fluoride (1 M solution in THF, 0.6 mmol) was added under vigorous stirring. The residue was dissolved in diethyl ether. Aqueous NaOH (10 %) was added under vigorous stirring until pH>10. The organic layer was extracted with water and the combined aqueous layers were washed twice with diethyl ether. Aqueous HCl (5 %) was added dropwise until pH<1. The product was extracted with diethyl ether (3 x 10 mL). The organic layers were washed with brine, dried over Na_2SO_4 and volatiles were removed under vacuum. Phosphinous acid-boranes **5a,c** proved to be stable to air and moisture. However, neat compound proved to lose their BH_3 moieties to afford the corresponding secondary phosphine oxide. This undesirable transformation also occurred upon prolonged exposition to high vacuum. Thus **5a,c** were preferentially stored in solution and "neat" samples usually featured trace amounts of solvents.

General procedure for the synthesis of optically active phosphinates 6

To a suspension of (adamantyl)(hydrogeno)phosphinate **3a,c,e,f,g** (0.5 mmol) and paraformaldehyde (1.5 equiv., 23 mg, 0.75 mmol) in THF (20mL) was added dropwise the solution of $LiOH.H_2O$ (30 mol%) in water (0.5 mL) under stirring conditions. The mixture was further stirred for 3h at room temperature. The obtaining solution was diluted with water (20 mL) and was neutralized with saturated NH_4Cl aqueous solution. The product was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4 and were evaporated to dryness under reduced pressure. The residue was purified by column chromatography on deactivated silica gel (10 wt% H_2O) with Et_2O, CH_2Cl_2 or AcOEt as eluent or by slow crystallization into CH_2Cl_2/Et_2O mixture at –20°C.

Adamantyl(hydroxymethyl)phenylphosphinate **6a**. Single crystal growth for X-ray molecular structure determination was carried out into CH_2Cl_2/*n*-hexane solution at low temperature (–20°C). White solide, 0.147 g (96% yield). (R_P)-(–)-**6a** $[\alpha]_D^{25}$ –23.7 (*c* = 0.55, $CHCl_3$), ee = 99%; (S_P)-(+)-**6a** $[\alpha]_D^{25}$ +22.8 (*c* = 0.6, $CHCl_3$), ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60 (bs, 6H), 1.99-2.10 (m, 6H), 2.13 (bs, 3H), 3.91 (bd, *J* = 14.5 Hz, 1H), 3.99 (dd, *J* = 14.5 Hz, *J* = 6.3 Hz, 1H), 4.4 (bs, 1H), 7.43-7.51 (m, 2H), 7.51-7.59 (m, 1H), 7.79-7.88 (m, 2H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 30.9 (3C), 35.4 (3C), 44.1 (d, *J* = 3.30 Hz, 3C), 61.2 (d, *J* = 118.5 Hz), 82.8 (d, *J* = 9.9 Hz), 128.0 (d, *J* = 12.1 Hz, 2C), 131.5 (d, *J* = 9.9 Hz, 2C), 131.7 (d, *J* = 2.7 Hz), 131.8 (d, *J* = 123.3 Hz); ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$) δ 33.1 (s); HRMS (ESI-MS) [M+H]+: found 307.1456; calculated for $C_{17}H_{24}PO_3^+$ 307.1458. Chiral HPLC: analytical separation on Lux-Cellulose-2 in hexane/ethanol (1/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 5.91 (R_P)-(–), Rt_2 = 9.11 (S_P)-(+), k_1 = 0.97 (–), k_2 = 2.04 (+), α = 2.10, Rs = 7.81.

Adamantyl-*t*-butyl(hydroxymethyl)phosphinate **6c**. Purification by column chromatography using AcOEt as eluent (Rf = 0.3) or recrystallization in Et_2O at -18°C. White solid, 0.449 g (82% yield). (S_P)-(–)-**6c** $[\alpha]_D^{25}$ –3.0 (*c* = 0.51, $CHCl_3$), ee = 99%; (R_P)-(+)-**6c** $[\alpha]_D^{25}$ +3.1 (*c* = 0.52, $CHCl_3$), ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (d, *J* = 15.2 Hz, 9H), 1.63 (bs, 6H), 2.07 (bs, 6H) 2.17 (bs, 3H), 3.57 (bs, 1H), 3.83 (dd, *J* = 14.3 Hz, *J* = 7.0 Hz, 1 H), 3.97 (d, *J* = 14.3 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.20, 31.2 (3C), 32.5 (d, J = 93.9 Hz), 35.8 (3C), 44.4 (d, J = 2.9 Hz, 3C), 58.1 (d, J = 91.7 Hz), 81.9 (d, *J* = 11.00 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 53.5 (s); HRMS (ESI-MS) [M+Na]+: found 309.1591; calculated for $C_{15}H_{27}O_3PNa^+$ 309.1590. Chiral HPLC: analytical separation on Chiralcel OD-3 in hexane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 205 nm and polarimeter: Rt_1 = 4.96 (R_P)-(+), Rt_2 = 5.59 (S_P)-(–), k_1 = 0.65 (R_P)-(+), k_2 = 0.86 (S_P)-(–), α = 1.32, Rs = 1.92.

Adamantyl(hydroxymethyl)4-(ethyloxycarbonyl)phenylphosphinate **6e**. Purification by column chromatography using Et_2O as eluent (Rf = 0.25). White solid 176 mg (90% yield). (R_P)-(–)-**6e** $[\alpha]_D^{25}$ –33.6 (*c* = 0.81, $CHCl_3$), ee = 99%; (S_P)-(+)-**6e** $[\alpha]_D^{25}$ +33.4 (*c* = 0.82, $CHCl_3$), ee = 99%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (t, *J* = 7.15 Hz, 3H), 1.59 (bs, 6H), 1.97 - 2.10 (m,

6H), 2.14 (bs, 3H), 2.76 - 2.85 (m, 1H), 3.87 - 4.04 (m, 2H), 4.42 (q, *J* = 7.15 Hz, 2H), 7.93 (dd, *J* = 11.19, 8.25 Hz, 2H), 8.14 (dd, *J* = 8.25, 3.12 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3, 31.2 (3C), 35.6 (3C), 44.5 (d, *J* = 3.7 Hz, 3C), 61.4, 61.5 (d, *J* = 117.4 Hz), 84.1 (d, *J* = 9.5 Hz), 129.3 (d, *J* = 12.5 Hz, 2C), 131.8 (d, *J* = 9.5 Hz, 2C), 133.8 (d, *J* = 2.9 Hz), 136.8 (d, *J* = 121.7 Hz), 165.9; ^{31}P NMR (121 MHz, $CDCl_3$) δ 31.5; HRMS (ESI-MS) [M+H]+: found 379.1669; calculated for $C_{20}H_{28}O_5P^+$ 379.1669. Chiral HPLC: analytical separation on Chiralcel OD-3 in hexane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 205 nm and polarimeter: Rt_1 = 6.89 (–), Rt_2 = 8.96 (+), k_1 = 1.30 (–), k_2 = 1.99 (+), α = 1.53, Rs = 4.89.

Adamantyl-o-anisyl(hydroxymethyl)phosphinate **6f**. Purification by column chromatography using Et_2O as eluent (Rf = 0.12). White solid 0.405 g (72% yield).). (–)-**6f** $[\alpha]_D^{25}$ –71.2 (*c* = 1.07, $CHCl_3$), ee = 99%; (+)-**6f** $[\alpha]_D^{25}$ +71.0 (*c* = 1.10, $CHCl_3$), ee = 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (bs, 6H), 1.93-2.03 (m, 6H), 2.09 (bs, 3H), 3.89 (s, 3H), 4.03 (dd, *J* = 14.3 Hz, *J* = 6.4 Hz, 1H), 4.08 (dd, *J* = 14.3, 3.8 Hz, 1H), 6.93 (dd, *J* = 7.90, 6.15 Hz, 1H) 7.07 (bt, *J* = 7.1, 1 H), 7.2 (bt, *J* = 7.5 Hz, 1H), 7.96 (ddd, *J* = 12.91, 7.50, 1.54 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.1 (3C), 35.7 (3C), 44.3 (d, *J* = 3.7 Hz, 3C), 55.5, 61.6 (d, *J* = 116.6 Hz), 82.69 (d, *J* = 10.3 Hz), 110.8 (d, *J* = 7.3 Hz), 120 (d, *J* = 121 Hz), 120.9 (d, *J* = 11.7 Hz), 134.2 (d, *J* = 2.2 Hz), 135.3 (d, *J* = 6.6 Hz), 160.7 (d, *J* = 5.14 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 31.4 (s); HRMS (ESI-MS) [M+H]+: found 337.1563; calculated for $C_{18}H_{26}O_4P^+$ 337.1563. Chiral HPLC: analytical separation on Chiralpak AZ-H in heptane/ethanol (8/2) at 1 ml/min and 25°C with UV detection at 254 nm and CD at 254 nm: Rt_1 = 9.22 (+), Rt_2 = 10.18 (–), k_1 = 2.07 (+), k_2 = 2.39 (–), α = 1.15, Rs = 1.81.

Adamantyl(cyclohexyl)(hydroxymethyl)phosphinate **6g**. Purification by column chromatography using Et_2O as eluent (Rf = 0.12). White solid 0.353 g (94% yield). (–)-**6g** $[\alpha]_D^{25}$ –2.01 (*c* = 0.7, $CHCl_3$), ee > 95%; (+)-**6g** $[\alpha]_D^{25}$ +1.6 (*c* = 0.87, $CHCl_3$), ee > 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17-1.45 (m, 5H), 1.63 (bs, 6H), 1.67-2.03 (m, 6H), 2.05 (bs, 6 H), 2.17 (bs, 3H), 3.77-3.88 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.9 (d, *J* = 2.9 Hz), 25.4 (d, *J* = 3. 7 Hz), 25.9 (d, *J* = 1.5 Hz), 26.2 (d, *J* = 3.7 Hz), 26.3 (d, *J* = 3.7 Hz), 31.1 (3C), 35.7 (3C), 37.1 (d, *J* = 93.9 Hz), 44.5 (d, *J* = 2.9 Hz, 3C), 59.1 (d, *J* = 98.3 Hz), 81.7 (d, *J* = 10.3 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 49.5 (s); HRMS (ESI-MS) [M+H]+: found 313.1927; calculated for $C_{17}H_{30}O_3P^+$ 313.1927. Chiral HPLC: analytical separation on Chiralpak AD-H in heptane/ethanol (95/5) at 1 ml/min and 25°C with UV detection at 220 nm and polarimeter: Rt_1 = 12.16 (+), Rt_2 = 14.59 (–), k_1 = 3.05 (+), k_2 = 3.86 (–), α = 1.27, Rs = 3.51.

General procedure for the synthesis of tertiary optically pure phosphinite-boranes 7

To a solution of **6a,c,e,g** (0.6 mmol) in THF (3 mL) was slowly added the solution of BH_3 (1M in THF) (3.6 mmol, 6 equiv., 3.6mL) at room temperature under stirring conditions. The mixture was further stirred for 48h-96h at room temperature. The resulting solution was evaporated under reduced pressure to give the oil liquids which were quenched with saturated $NaHCO_3$ aqueous solution at 0°C. The products were extracted with CH_2Cl_2 (10mL x 3). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. ^{31}P NMR analysis of the

crude mixture had shown the presence of secondary phosphine-borane as by-product (Table S1). The residue was purified by the silica gel chromatography using AcOEt/*n*-hexane or CH_2Cl_2 as eluent.

Adamantyl(hydroxymethyl)phenylphosphinite borane **7a**. Purification by column chromatography using hexane/AcOEt (9/1) as eluent (Rf = 0.1). White solid 1.57 g (86% yield). (R_P)-(–)-**7a** $[\alpha]_D^{25}$ –112.6 (*c* = 0.5, $CHCl_3$), ee = 99%; (S_P)-(+)-**7a** $[\alpha]_D^{25}$ +132.1 (*c* = 0.5, $CHCl_3$), ee = 96%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.51 - 1.41 (bm, 3H), 1.58 (t, *J* = 3.0 Hz, 6H), 2.00 (d, *J* = 3.0 Hz, 6H), 2.14 (bs, 3H), 3.92 - 4.02 (m, 2H), 7.46 - 7.52 (m, 2H), 7.52 - 7.58 (m, 1H), 7.83 - 7.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.0 (3C), 35.4 (3C), 43.7 (d, *J* = 3.8 Hz, 3C), 63.8 (d, *J* = 55.0 Hz), 82.5 (d, *J* = 6.6 Hz), 128.3 (d, *J* = 9.9 Hz, 2C), 131.1 (d, *J*=10.45 Hz, 2C), 131.6 (d, *J* = 55.0 Hz), 131.8 (d, *J*=2.20 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 93.8 - 95.6 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -39.1 (bd, *J* = 62.3 Hz); HRMS (ESI-MS) [M-H]$^-$: found 289.1539; calculated for $C_{16}H_{23}BO_2P^-$ 289.1537. Chiral HPLC: analytical separation on Chiralcel OD-3 in hexane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 6.58 (R_P)-(–), Rt_2 = 7,52 (S_P)-(+), k_1 = 1.19 (R_P)-(–), k_2 = 1.51 (S_P)-(+), α = 1.26, Rs = 2.38.

Adamantyl-*t*-butyl(hydroxymethyl)phosphinite borane **7c**. Purification by column chromatography using hexane/AcOEt (9/1) as eluent (Rf = 0.4). White solid 0.29 g (51% yield). (S_P)-(–)-**7c** $[\alpha]_D^{25}$ –4.3 (*c* = 0.99, $CHCl_3$), ee > 95%; (R_P)-(+)-**7c** $[\alpha]_D^{25}$ +4.2 (*c* = 0.93, $CHCl_3$), ee > 95%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.21 – 1.09 (bm, 3H), 1.19 (d, *J* = 13.90 Hz, 9H), 1.63 (t, *J* = 3.07 Hz, 6H), 1.97 – 2.08 (m, 6 H), 2.19 (bs, 3H), 3.91 (dd, J = 13.9, 2.3 Hz ,1H), 4.01 (dd, J = 13.9, 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.7 (d, J = 2.2 Hz, 3C), 31.23 (3C), 31.8 (d, J = 42.5 Hz), 35.72 (3C), 43.93 (d, *J* = 2.93 Hz, 3C), 60.2 (d, J = 37.4 Hz), 81.7 (d, J = 8.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 116.8 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -41.3 (d, *J* = 61.5 Hz); HRMS (ESI-MS) [M+Na]+: found 307.1969; calculated for $C_{15}H_{30}BO_2PNa^+$ 307.1972. Chiral HPLC: analytical separation on Lux-Cellulose-4 in heptane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 220 nm and polarimeter: Rt_1 = 5.50 (S_P)-(–), Rt_2 = 6.80 (R_P)-(+), k_1 = 0.83 (S_P)-(–), k_2 = 1.27 (R_P)-(+), α = 1.53, Rs = 5.08.

Adamantyl-o-anisyl(hydroxymethyl)phosphinite borane **7f**. Purification by column chromatography using hexane/AcOEt (6/4) as eluent (Rf = 0.23). White solid 124 mg (81% yield). (–)-**7f** $[\alpha]_D^{25}$ –99.2 (*c* = 0.95, $CHCl_3$), ee = 99%; (+)-**7f** $[\alpha]_D^{25}$ +98.5 (*c* = 0.95, $CHCl_3$), ee = 99%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.5-1.37 (m, 3H), 1.52-1.61 (m, 6H), 1.91-1.99 (m, 6H), 2.11 (bs, 3H), 3.92 (s, 3H), 4.21-4.30 (m, 2H), 6.96 (dd, *J* = 8.34, 3.22 Hz, 1H), 7.07 (tdd, *J* = 7.46, 7.46, 2.20, 0.88 Hz, 1 H), 7.53 (dddd, *J* = 8.34, 7.46, 1.61, 0.88 Hz, 1H), 7.96 (ddd, *J* = 13.54, 7.54, 1.61 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 31.2 (3C), 35.7 (3C), 43.9 (d, *J* = 3.67 Hz, 3C), 55.6 (3C), 62.7 (d, *J* = 55.7 Hz), 82.2 (d, *J* = 7.3 Hz), 111.1 (d, *J* = 4.40 Hz), 119.5 (d, *J* = 51.3 Hz), 121.2 (d, *J* = 11.7 Hz), 134.3 (d, *J* = 2.2 Hz), 135.7 (d, *J* = 16.1 Hz), 161.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 96.9–98.7 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -38.3 (bd, *J* = 65.4 Hz); HRMS (ESI-MS) [M+Na]+: found 357.1768; calculated for

$C_{18}H_{28}BO_3PNa^+$ 357.1765. Chiral HPLC: analytical separation on Chiralpak AS-H in heptane/ethanol (9/1) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 6.17 (–), Rt_2 = 8.37 (+), k_1 = 1.06 (–), k_2 = 1.79 (+), α = 1.69, Rs = 4.

Adamantyl(cyclohexyl)(hydroxymethyl)phosphinite borane **7g**. Purification by column chromatography using CH_2Cl_2 as eluent (Rf = 0.5). White solid 114 mg (78% yield). (–)-**7g** $[\alpha]_D^{25}$ –4.1 (*c* = 0.99, $CHCl_3$), ee > 95%; (+)-**7g** $[\alpha]_D^{25}$ +4.0 (*c* = 0.98, $CHCl_3$), ee > 95%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.14-1.06 (m, 3 H), 1.14-1.47 (m, 5 H), 1.61 (bs, 6 H), 1.67-1.94 (m, 6 H), 1.94-2.05 (m, 6 H), 2.17 (bs, 3 H), 3.87 (d, *J* = 13.9 Hz, 1H), 3.94 (d, *J* = 13.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 25.2 (d, *J* = 2.20 Hz) 25.6, 25.8 (d, *J* = 1.5 Hz), 26.3 (d, *J* = 3.7 Hz), 26.5 (d, *J* = 3.7 Hz), 31.1 (3C), 35.6 (3C), 36.1 (d, *J* = 43.3 Hz), 43.9 (d, *J* = 2.93 Hz, 3C), 60.4 (d, *J* = 41.1 Hz), 81.3 (d, *J* = 6.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 109.3-111.2 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -40.3 (bd, *J* = 61.5 Hz); HRMS (ESI-MS) [M+Na]+: found 333.2126; calculated for $C_{17}H_{32}BO_2PNa^+$ 333.2128. Chiral HPLC: analytical separation on Chiralpak AS-H in heptane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 220 nm and polarimeter: Rt_1 = 6.80 (–), Rt_2 = 7.80 (+), k_1 = 1.27 (–), k_2 = 1.60 (+), α = 1.26, Rs = 2.02.

General procedure for the synthesis of hydroxymethylphosphine-boranes 8

To a solution of adamantyl(hydroxymethyl)phenyl-phosphine borane (0.28 mmol, 86 mg) in THF (3 mL) was added at 0°C the solution of RLi (3equiv). The resulting mixture was allowed to warm to room temperature and stirred further for 2h. The obtaining solution was subsequently quenched with water (2 mL), and then neutralized with the saturated NH_4Cl aqueous solution (5 mL). The product was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure to give residue which was purified by silica gel chromatography.

(Hydroxymethyl)methylphenylphosphine borane **8a**. Hexane/AcOEt: 3/1 Rf = 0.4. Clear oil, 42 mg (88% yield) (R_P)-(–)-**8a** $[\alpha]_D^{25}$ –9.3 (*c* = 1.2, $CHCl_3$), ee = 97%; (S_P)-(+)-**8a** $[\alpha]_D^{25}$ +9.2 (*c* = 1.51, $CHCl_3$), ee = 98%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.22-1.15 (m, 3H), 1.65 (d, *J* = 10.54 Hz, 3H), 2.1 (bs, 1H), 4.07 (s, 2H), 7.46-7.58 (m, 3H), 7.72-7.80 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 6.9 (d, *J* = 38.9 Hz), 61.05 (d, *J* = 41.1 Hz), 127.0 (d, *J* = 52.8 Hz, 1 C), 128.9 (d, *J* = 10.3 Hz, 2C), 131.8 (d, *J* = 2.2 Hz), 131.9 (d, *J* = 8.8 Hz, 2C); ^{31}P NMR (162 MHz, $CDCl_3$) δ 10.05-11.61 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -41.1 (bd, *J* = 56.8 Hz); HRMS (ESI-MS) [M+Na]+: found 191.0773; calculated for $C_8H_{14}BOPNa^+$ 191.0769. Chiral HPLC: analytical separation on Chiralpak AD-H in hexane/ethanol (7/3) at 1 ml/min and 25°C with UV detection at 254 nm and polarimeter: Rt_1 = 5.09 (R_P)-(–), Rt_2 = 7.03 (S_P)-(+), k_1 = 0.7 (R_P)-(–), k_2 = 1.34 (S_P)-(+), α = 1.93, Rs = 5.29.

n-Butyl(hydroxymethyl)phenylphosphine borane **8b**. Purification by column chromatography using CH_2Cl_2 as eluent (Rf = 0.29). Clear oil, 64 mg (91% yield). (R_P)-(–)-**8b** $[\alpha]_D^{25}$ –18.4 (*c* = 0.8, $CHCl_3$), ee = 97%; (S_P)-(+)-**8b** $[\alpha]_D^{25}$ +17.6 (*c* = 1.01, $CHCl_3$), ee = 98%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.23 – 1.10 (bm, 3H), 0.90 (t, *J*=7.02 Hz, 3H), 1.33 - 1.65 (m, 4H), 1.93 (bs,

1H), 1.95 - 2.08 (m, 2H), 4.12 (s, 2 H), 7.45 - 7.59 (m, 3H), 7.72 - 7.81 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.5, 21.4 (d, J = 35.2 Hz), 24.2 (d, J = 13.2 Hz), 24.7, 59.9 (d, J = 41.1 Hz), 126.2 (d, J = 52.08 Hz), 128.9 (d, J = 9.54 Hz, 2C), 131.7 (d, J=2.9 Hz), 132.3 (d, J = 8.07 Hz, 2C); ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.7 - 17.5 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -42.8 (bd, J = 59.2 Hz); HRMS (ESI-MS) [M+Na]+: found 233.1241; calculated for $C_{11}H_{20}BOPNa^+$ 233.1239. Chiral HPLC: analytical separation on Chiralpak AZ-H in heptane/ethanol (8/2) at 1 ml/min and 25°C with UV detection at 254 nm and polarimetric: Rt_1 = 4.64 (R_P)-(–), Rt_2 = 5.24 (S_P)-(+), k_1 = 0.55 (R_P)-(–), k_2 = 0.75 (S_P)-(+), α = 1.36, Rs = 2.04.

Oxidative One-Carbon Degradation of (adamantyl)(*t*-butyl)(hydroxymethyl)phosphinite-borane

Adamantylhydrogeno-*t*-butylphosphinite-borane **9**. To a solution of KOH (2.2 mmol, 10 equiv., 128 mg) and $K_2S_2O_8$ (0.66 mmol, 3 equiv., 185 mg) in water (2.0 mL) was added the solution of $RuCl_3.xH_2O$ (10 mg, 20-30% molar) in water (1 mL) at 0°C. The resulting mixture was allowed to be stirred at 0°C for 20 min and then the solution of (adamantyl)(hydroxymethyl)(*t*-butyl)phosphinite-borane (0.22 mmol, 0.065g) in acetonitrile (1 mL) was slowly added. The reaction solution was allowed to be further stirred for 10h at RT. The obtaining solution was diluted with water and neutralized with HCl aqueous solution (2M). The product was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4. The solvents were removed under reduced pressure to give residue which was purified by silica gel chromatography using CH_2Cl_2/petroleum ether (1/9) as eluent (R_F = 0.17). Solid 48 mg, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.20 - 1.05 (m, 3H), 1.18 (d, J = 15.22 Hz, 9H), 1.63 (bs, 6H), 1.99 (bs, 6H), 2.20 (bs, 3H), 6.20 (d, J = 355.47 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.9 (d, J = 2.93 Hz), 30.0 (d, J = 45.48 Hz), 31.1 (3C), 35.7 (3C), 43.2 (d, J = 3.67 Hz, 3C), 80.3 (d, J = 8.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 102.7-104.2 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -39.7 (bd, J=60.0 Hz); HRMS (ESI-MS) [M+Na]+: found 277.1866; calculated for $C_{14}H_{28}BOPNa^+$ 277.1866.

Alkylation of secondary phosphinite-borane

Adamantylbenzyl-*t*-butylphosphinite-borane **10**. To a solution of (adamantyl)hydrogeno-*t*-butylphosphinite-borane (0.22 mmol, 0.055g) in THF (2mL) was added slowly at -78°C the solution of *n*-BuLi (1.6M in *n*-hexane) (0.33 mmol, 1.5 equiv., 0.2mL). The mixture was stirred for 20 min while maintaining the reaction temperature at -78°C. Benzyl bromide (0.88 mmol, 4 equiv., 0.102 mL) was added and the obtaining solution was maintained at -78°C for further 2h and then was allowed to warm to 0°C during 2h. The reaction was quenched with the saturated NH_4Cl aqueous solution. The product was extracted with CH_2Cl_2 (3 x 10 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure to give oily residue which was purified by column chromatography on silica gel with CH_2Cl_2/petroleum ether in ratio of 1:9 as eluent (Rf = 0.13). White solid, 72 mg, 97% yield. (S_P)-(–)-**10** $[\alpha]_D^{25}$ –36.2 (c = 0.97, $CHCl_3$), ee = 95%; (R_P)-(+)-**10** $[\alpha]_D^{25}$ +37.6 (c = 0.95, $CHCl_3$), ee = 95%: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.31 – 1.12

(bm, 3H), 1.18 (d, *J* = 13.80 Hz, 9H), 1.44 - 1.54 (m, 6H), 1.55 - 1.62 (m, 3H), 1.79 (bd, *J* = 11.04 Hz, 3H), 2.02 (bs, 3H), 3.01 (d, *J* = 13.60 Hz, 1H), 3.15 (t, *J* = 13.60 Hz, 1H), 7.21 - 7.35 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.8 (d, *J* = 2.93 Hz), 31.2 (3C), 32.8 (d, *J* = 44.0 Hz), 34.7 (d, *J* = 31.5 Hz), 35.7 (3C), 43.6 (d, *J* = 2.93 Hz, 3C), 81.5 (d, *J* = 7.3 Hz), 126.6 (d, *J* = 2.9 Hz) 128.0 (d, *J* = 2.20 Hz, 2C), 130.9 (d, *J* = 4.40 Hz, 2C), 133.22 (d, *J* = 7.34 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 118.14 - 119.89 (bm); ^{11}B NMR (128 MHz, $CDCl_3$) δ -39.41 (bd, *J* = 60.7 Hz); HRMS (ESI-MS) $[M+NH_4]+$: found 362.2785; calculated for $C_{21}H_{38}BNOP^+$ 362.2783. Chiral HPLC: analytical separation on Chiralcel OD-3 in heptane/isopropanol (95/5) at 1 ml/min and 25°C with UV detection at 220 nm and polarimeter: Rt_1 = 4.01 (S_P)-(–), Rt_2 = 5.16 (R_P)-(+), k_1 = 0.34 (S_P)-(–), k_2 = 0.72 (R_P)-(+), α = 2.13, Rs = 3.4.

ASSOCIATED CONTENT

Supporting information: the crystal structure of (+)-(R_P)-**3e**; (-)-(R_P)-**6a**; (+)-(R_P)-**6c**; (-)-(S_P)-**7c** and (+)-(R_P)-**10**, NMR spectra of all new compounds and HPLC data for the determination of enantiomeric excesses. This material is available free of charge via the Internet at http://pubs.acs.org/.

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