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Versatile synthesis of P-chiral (ephedrine) AMPP ligands via their borane complexes. Structural consequences in Rh-catalyzed hydrogenation of methyl α-acetamidocinnamate

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Abstract

An efficient and versatile synthesis of aminophosphine phosphinite (AMPP) ligands derived from ephedrine, with possible stereogenic P(III)-center(s) is described, using the borane complex methodology. The reaction of oxazaphospholidine borane with an organolithium reagent, leads to the formation of the ring-opened product, which is trapped by a chlorophosphine (borane), to afford the corresponding aminophosphine phosphinite boranes in good yields. Treatment of the borane complexes with dabco, gives the corresponding aminophosphine phosphinite ligands in 70–90% yield. These ligands are used for the preparation of Rh catalysts applied to the asymmetric hydrogenation of methyl α-acetamidocinnamate yielding the phenylalanine derivative with (*R*) 22% to (*S*) 99% e.e. These results show the importance of the structural modification at the P-stereogenic center(s), which could either amplify or cancel out the asymmetric induction resulting from the ephedrine backbone, for enantioselective catalysis.

1. Introduction

C_2-Symmetric diphosphines or chelating monophosphines bearing chirality on the carbon backbone are today the most currently used chiral ligands in asymmetric reactions catalyzed by transition metals.[1] Nevertheless, other classes of phosphorus ligands, in which the chirality is induced by planar chirality,[2] by an aminoalcohol[3] or glucose,[4] also provide highly stereoselective catalysts, particularly for hydroformylation, hydrocyanation or cycloaddition reactions.

In spite of the pioneering work of Horner[5] and Knowles,[6] phosphines bearing chirality on the phosphorus atom have not been used extensively to date in asymmetric catalysis, mainly due to the difficulty of their stereoselective preparation. Nevertheless, as their asymmetric synthesis has made some important progress due to the use of borane complexes,[7–9] these ligands again receive particular interest in

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catalysis;[10] the stereogenic phosphorus atom being close to the metal center allows a better asymmetric induction to be expected. It may also be pointed out that the P-chirality allows new classes of chiral ligand, such as bulky[11] or chelating monophosphines, to be studied.[12] Moreover, it is now possible to develop ligands with both stereogenic carbon and phosphorus groups, and therefore to increase the number of possible stereoisomers of a designed ligand, for the optimization of an asymmetric catalyst.

The asymmetric induction of diphosphine rhodium or ruthenium complexes has been attributed to the conformational chirality of the P-phenyl substituents, oriented in axial or equatorial directions, which results from the distorted conformation of the ring containing the chelated metal and the bidentate ligand[13] (Fig. 1a). If the substituents at phosphorus atom(s) are different, with R_1 larger than R_2, we can observe that the dissymmetry may amplify the influence of the backbone on the conformation of such a ring, thus favoring one geometry for the catalytic complex and, therefore, a better stereoselectivity (Fig. 1b).

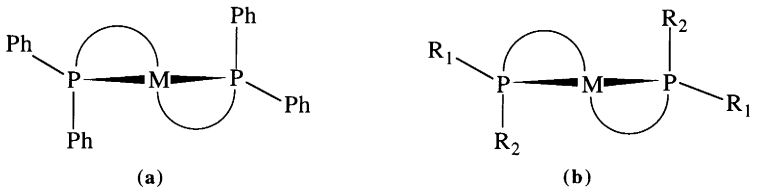
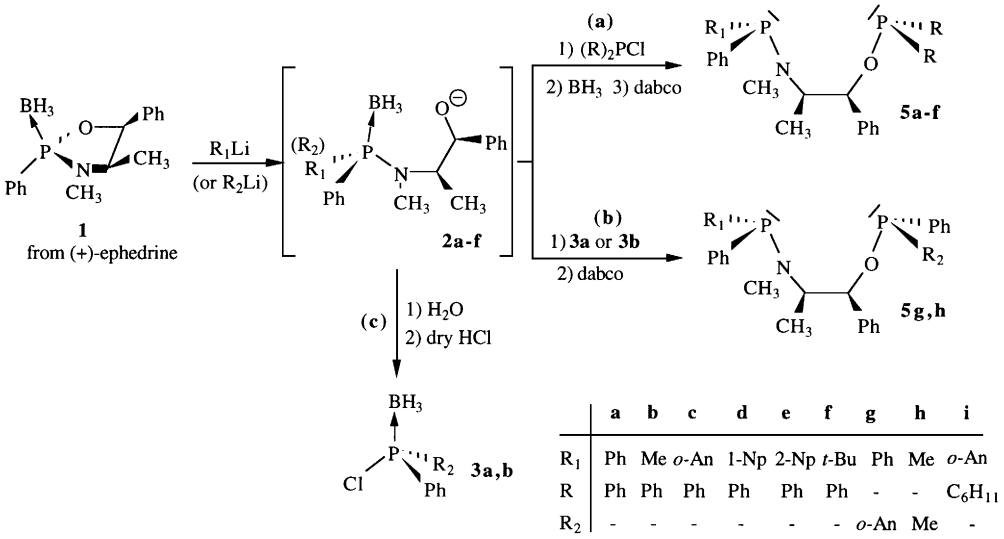


Fig. 1.

During the last decade, our group has studied the asymmetric synthesis of P-chiral mono and diphosphines based on the stereoselective ring opening of the oxazaphospholidine, derived from ephedrine.[14] On this basis we report herein a versatile methodology starting from oxazaphospholidine borane complex **1**, affording various aminophosphine phosphinite **5** derivatives of the EPHOS ligand **5a**,[3a,b] bearing one or two stereogenic phosphorus atom(s)[15] (Scheme 1). The consequences in asymmetric catalysis of the structural modifications of these ligands derived from ephedrine, are studied on homogeneous rhodium-catalytic hydrogenation of methyl α-acetamidocinnamate **6**.



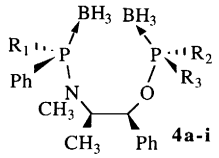
	a	b	c	d	e	f	g	h	i
R_1	Ph	Me	*o*-An	1-Np	2-Np	*t*-Bu	Ph	Me	*o*-An
R	Ph	Ph	Ph	Ph	Ph	Ph	-	-	C_6H_{11}
R_2	-	-	-	-	-	-	*o*-An	Me	-

Scheme 1.

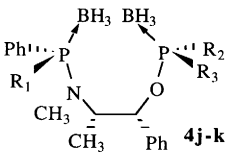
2. Results and discussion

The starting complex **1**, or its enantiomer **1′**, are prepared by condensation of $PhP(NMe_2)_2$ with (+)- or (−)-ephedrine followed by complexation with boranedimethylsulfide (BMS).[7f] The synthesis of these aminophosphine phosphinites, obtained as stable diborane complexes **4**, is based on the reaction of the complex **1** (or **1′**) with an organolithium reagent to give the ring opening product **2**, which is trapped with a chlorophosphine borane **3** (Scheme 1b), or a chlorophosphine $(R)_2PCl$ and then a borane (Scheme 1a). Aminophosphine phosphinite complexes **4** are isolated by chromatography; then the borane can be easily removed by exchange with dabco to yield the corresponding ligand **5**. The structure of the aminophosphine phosphinite borane complexes **4a**–**k** prepared from both (+)- and (−)-ephedrine, are reported in Table 1.

Table 1
Aminophosphine phosphinite diborane complexes **4** prepared



4a-i



4j-k

entry	starting complex	R_1	R_2	R_3	AMPP$(BH_3)_2$	yield (%)
1	**1**	Ph	Ph	Ph	**4a**	63
2	**1**	Me	Ph	Ph	**4b**	79
3	**1**	*o*-An	Ph	Ph	**4c**	62
4	**1**	1-Np	Ph	Ph	**4d**	62
5	**1**	2-Np	Ph	Ph	**4e**	78
6	**1**	*t*-Bu	Ph	Ph	**4f**	64
7	**1**	Ph	Ph	*o*-An	**4g**	44
8	**1**	Me	Ph	Me	**4h**	18
9	**1**	*o*-An	C_6H_{11}	C_6H_{11}	**4i**	67
10	**1'**	Ph	Ph	*o*-An	**4j**	73
11	**1'**	*o*-An	Ph	*o*-An	**4k**	40

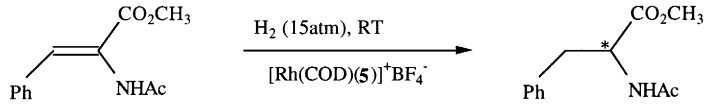
The reaction of phenyllithium with the complex **1** leads after P–O bond cleavage to the ring opening product **2a** (R_1=Ph), which is trapped with chlorodiphenylphosphine Ph_2PCl then with borane, to afford the (−)-EPHOS in 63% yield, as a diborane complex **4a** (Scheme 1a; Table 1, entry 1). In the same way, other organolithium reagents (R_1=methyl, *o*-anisyl, 1- or 2-naphthyl, *t*-butyl) lead in 62–78% yield to the corresponding diborane complexes **4b**–**f**, with a stereogenic aminophosphine group and complete retention of configuration at the phosphorus atom[7e] (entries 2–6). When the *o*-anisyl ring opening product **2c** is trapped with chlorodicyclohexylphosphine, the resulting derivative **4i** obtained after reaction with borane, has a more sterically hindered phosphinite group (entry 9).

On the other hand, aminophosphine phosphinites bearing a chiral phosphinite group are prepared by trapping the ring opening intermediate **2** with P-chiral chlorophosphine boranes **3a** or **3b**, which are previously prepared by acidolysis of the corresponding aminophosphine borane **2**[7f,16] (Scheme 1c). This

is illustrated by the preparation of the aminophosphine P-chiral phosphinite complexes **4g**, **4j** (Scheme 1b; entries 7, 10), or **4h**, **4k** bearing stereogenicity at both phosphorus centers (entries 8, 11).

Decomplexation of borane complexes **4** is achieved with retention of the configuration, by heating with dabco[17] (Scheme 1a,b); then the free aminophosphine phosphinites **5** are purified by filtration through neutral alumina. The diastereomeric purity of the ligands **5** is controlled by ^{31}P NMR analysis, showing two signals at around 60 and 110 ppm, which are characteristic of the P–N and P–O groups, respectively.

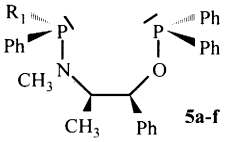
In order to study the structural modification of aminophosphine phosphinite ligands **5** relative to the EPHOS ligand **5a**, the asymmetric hydrogenation of methyl α-acetamidocinnamate **6** has been investigated using a cationic rhodium complex (Scheme 2). The results are summarized in Table 2.



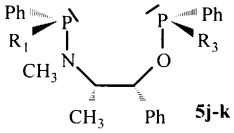
6 **7**

Scheme 2.

Table 2
Asymmetric hydrogenation of substrate **6**, catalyzed by Rh/AMPP **5** complexes



5a-f



5j-k

entry	R_1	R_3	AMPP	solvant	time[b] (h)	yield[a] (%)	e.e (%)[c]	abs.conf.
1	Ph	-	(-)-EPHOS **5a**	CH_2Cl_2	18	98	11	*S*
2	Ph	-	(-)-EPHOS **5a**	C_6H_6	22	95	46	*S*
3	Me	-	**5b**	CH_2Cl_2	3	95	22	*R*
4	*o*- An	-	**5c**	CH_2Cl_2	10.5	99	89	*S*
5	*o*- An	-	**5c**	C_6H_6	20	98	99	*S*
6	1-Np	-	**5d**	CH_2Cl_2	4	99	88	*S*
7	1-Np	-	**5d**	C_6H_6	17	98	95	*S*
8	2-Np	-	**5e**	CH_2Cl_2	4.5	96	16	*S*
9	*t* -Bu	-	**5f**	CH_2Cl_2	4	95	2	*S*
10	Ph	*o*- An	**5j**	CH_2Cl_2	13	98	80	*S*
11	*o*- An	*o*- An	**5k**	CH_2Cl_2	12	94	1	*S*

[a] Isolated yield [b] Reaction time [c] Determined by HPLC with Chiracel OD

In dichloromethane, the structural modifications at the phosphorus center are of great influence on the asymmetric induction. Thus, changing the pro-*R* phenyl of the (−)-EPHOS **5a** aminophosphine group, by a methyl (ligand **5b**), the hydrogenation gives the phenylalanine derivative **7** with the opposite absolute configuration (e.e. 22% (*R*), against 11% (*S*)) for the former **5a** (Table 2, entries 1, 3). On the other hand, when *o*-anisyl replaces the pro-*R* phenyl of **5a**, the resulting ligand **5c** considerably increases the asymmetric induction for the hydrogenation, since (*S*)-aminoester **7** is obtained with an enantiomeric

excess of 89% (entry 4). Similar results are obtained with the ligand **5d** bearing a (*R*)-1-naphthyl-aminophosphine group (entry 5), which leads to the (*S*)-aminoester **7** with 88% e.e. If the hydrogenation is carried out in benzene, the *o*-anisyl and the 1-naphthyl ligand provides the (*S*)-aminoester **7** with 99 and 95% e.e., respectively, compared to 46% e.e. obtained for the (−)-EPHOS[18] (entries 2, 5, 7). However, when the 2-naphthyl substitutes the pro-*R* phenyl of the (−)-EPHOS aminophosphine part (ligand **5e**), the (*S*)-aminoester **7** is obtained with an enantiomeric excess comparable to **5a** (e.e. 16% and 11%, respectively, entries 1, 8). Surprisingly, the introduction of a *t*-butyl substituent on the aminophosphine part of **5a** leads to the quasi-racemic product **7** (entry 9).

In the case of the ligand **5j** bearing an (*R*)-*o*-anisyl phenyl phosphinite group, the hydrogenation catalysis of **6** also leads to the phenylalanine derivative **7** with (*S*)-absolute configuration and 80% e.e. (entry 10). The fact that the *o*-anisyl ligands **5c** and **5j**, derived from the (+) and (−)-ephedrine, respectively, both afford the aminoester **7** with the same (*S*)-absolute configuration and high e.e. (entries 4, 10), clearly shows the predominance of the P-center's chirality over the carbon backbone effect. It is likely that these two ligands have similar structures resulting from the relative configuration of the larger substituents, borne by each stereogenic center of the chelated seven-membered ring (Fig. 2a, b). The key importance of the configuration of the phosphorus center is also shown from the ligand **5k**, bearing *o*-anisyl aminophosphine and phosphinite groups with opposite absolute configuration (entry 11). The (*S*)- and (*R*)-configurations of the two phosphorus groups imply a quasi-meso structure for the ligand **5k**, which in this case does not give any asymmetric induction (Fig. 2c).

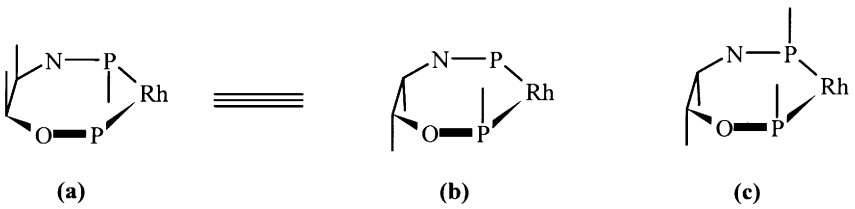


Fig. 2.

Although the mechanism and the origin of the asymmetric induction must be carefully claimed, we suggest the following model to explain the structure of AMPP–rhodium complexes in the initial catalytic step (Fig. 3).

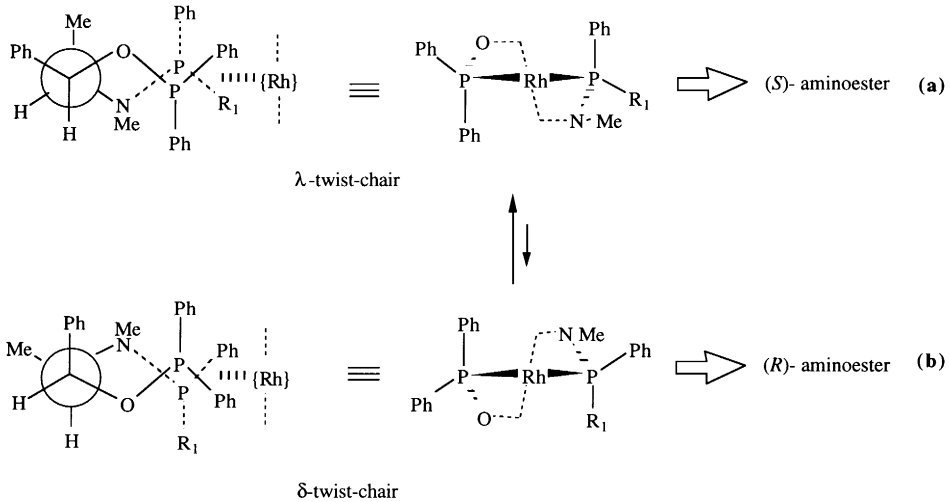


Fig. 3.

As the phenyl substituent entails higher 1,3-diaxial interaction in cycloalkane than methyl,[19] it should be reasonable to consider that the (−)-EPHOS **5a**–rhodium complex adopts the λ-twist-chair conformation, with the phenyl group of the (+)-ephedrine backbone in an equatorial position (Fig. 3a). The formation of a λ-conformation is in good agreement with the asymmetric hydrogenation of the substrate **6** yielding the phenylalanine derivative **7** with (*S*)-configuration, which can be predicted from the well-known empirical correlation established in the case of the rhodium diphosphine[13a] or diphosphinite complex.[13c] The presence of a sterically hindered substituent R_1 on the aminophosphine moiety, requires an equatorial position, and consequently favors the λ-conformation of the chelated ring (Fig. 3a). This is illustrated by the ligands **5c**–**e** bearing *o*-anisyl, 1-naphthyl or 2-naphthyl as R_1 substituents, respectively, which lead, by catalyzed hydrogenation, to the (*S*)-phenylalanine derivative **7** (entries 4–8). When R_1 is a methyl (ligand **5b**), the δ-twist-chair conformation is then favored by a lower interaction of this substituent in an axial position with the other axial group of the chelate–rhodium ring complex (Fig. 3b), affording the product **7** in major absolute configuration (*R*) (entry 2). The poor results obtained in the case of the *t*-butyl ligand **5f** (entry 6), show the limitation to increase the steric hindrance of the aminophosphine moiety of the ligand, which must change the conformation of the ring of the rhodium–chelate and the arrangement of the ligands around the metal center, affording a weak stereoselective precatalyst species.

3. Conclusion

We have described herein a general and efficient synthesis of chiral aminophosphine phosphinite ligands **5** derived from (+) and (−)-ephedrine; the key step was the regio- and stereoselective ring opening of the oxazaphospholidine borane complex **1** by an organolithium reagent, followed by the trapping of the alcoholate intermediate **2** with a chlorophosphine. The aminophosphine phosphinites obtained can be easily isolated as stable borane complexes; when necessary the borane protective group can be removed by an exchange with dabco, to provide the corresponding P(III) ligands, well fitted to be used in catalysis. The interest of this synthetic method is demonstrated by the possibility of preparing numerous aminophosphine phosphinites with stereogenic phosphorus atoms. The aminophosphine phosphinite ligands **5**, used for asymmetric catalyzed hydrogenation of methyl α-acetamidocinnamate **6** by rhodium complexes, reveals the importance of the stereogenic P-center, compared to the effect induced by the ephedrine backbone. Introducing the *o*-anisyl or 1-naphthyl groups on the aminophosphine part leads to the phenylalanine derivative **7** with the e.e. reaching 99%, while the (−)-EPHOS ligand gives 46% e.e. under the same conditions. Taking into account this new powerful and convenient synthetic method, it is now possible to prepare numerous P-chiral AMPP derivatives from the same skeletal backbone (i.e. ephedrine), for the optimization of asymmetric catalysis.

4. Experimental

4.1. General

All reactions were carried out under an argon atmosphere in dried glassware. Solvents were dried and freshly distilled under a nitrogen atmosphere over sodium/benzophenone for THF, toluene and benzene, P_2O_5 for CH_2Cl_2 and sodium ethylate for EtOH. Hexane and isopropanol for HPLC were of chromatographic grade and used without further purification. Methyllithium, *s*-butyllithium, *t*-butyllithium and chlorodicyclohexylphosphine were purchased from Aldrich, Acros and Avocado. Commercially available

2-bromoanisole, 1-bromonaphthalene and bromobenzene were distilled before use. The toluene HCl solution was obtained by bubbling HCl gas and titration of the resulting solution. HPLC analyses were performed on a Gilson 116 UV detector. Flash chromatography was performed on silica gel (60ACC, 6–35 microns; SDS) or neutral aluminium oxide (Carlo Erba; ref. 417241). All NMR spectral data were obtained on a Bruker DPX 250 spectrometer using TMS as internal reference for ^{1}H and ^{13}C NMR and 85% phosphoric acid as external reference for ^{31}P NMR. Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotation values were determined at 20°C on a Perkin–Elmer 241 polarimeter. Infrared spectra were recorded on a Bruker Equinox 55. Mass spectral analyses were performed on a NERMAG R10-10C and a JEOL MS 700 for exact mass, at the Mass Spectroscopy Laboratories of ENSCP and ENS, Paris. The major peak *m/z* is mentioned with the intensity as a percentage of the base peak in brackets. Elemental analyses were measured with a precision superior to 0.3% at the Microanalysis Laboratories of the Pierre and Marie Curie University, Paris.

*4.2. Synthesis of aminophosphine phosphinite diborane **4a–k***

4.2.1. Preparation of aryllithium reagents

In a two-necked flask equipped with a magnetic stirrer, 1 equivalent of *s*-butyllithium was added. The mixture was allowed to cool to 0°C and 1 equivalent of 1-bromoanisole (1-bromonaphthalene or bromobenzene) was slowly added with a syringe and under stirring. After formation of a white precipitate, the mixture was stirred for 1 h at 0°C. The organolithium reagent was solubilized with a minimum of dry THF before use.

In the case of the solid 2-bromonaphthalene, 1 equivalent of arylhalide was introduced into a flask, then 1 equivalent of *s*-butyllithium was slowly added with a syringe and under stirring at 0°C. The rest of the procedure was performed as described above.

*4.2.2. Typical procedure for **4a–k***

A 100 mL round-bottomed flask equipped with a magnetic stirrer and an argon inlet was charged with a solution of 1 g of the oxazaphospholidine borane **1** (3.5 mmol) in 6 mL of THF. Then two equivalents of an organolithium reagent (7 mmol) were added slowly at −78°C under stirring, and the reaction temperature was slowly warmed to 0°C until complex **1** had completely disappeared. The reaction could be monitored by TLC over silica (toluene:AcOEt, 9:1). Then 2 equivalents of chlorodiphenylphosphine (or chlorodicyclohexylphosphine) (7 mmol) were added, and the mixture was stirred for 2 h and warmed to room temperature. Boranedimethylsulfide (BMS; 10 equivalents) was added and the mixture stirred overnight. The THF and excess of borane were removed under reduced pressure and the residue was hydrolyzed at room temperature, then extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and the solvent removed. The residue was purified by chromatography on silica gel using toluene:petroleum ether, 1:1, as eluent, yielding the AMPP diborane complex **4** in 62–79% yield.

*4.2.3. (−)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}aminodiphenylphosphine borane **4a** ((−)-EPHOS diborane complex)*

Yield=63%; white solid; mp: 175°C; $[\alpha]_D^{20}=-76.3$ (*c* 1.035, $CHCl_3$); R_f=0.45 (toluene:petroleum ether, 1:1); IR (neat, ν cm^{-1}): 3054 (w), 2983 (w), 2375 (vs), 2342 (m), 1589 (m), 1483 (w), 1457 (w), 1436 (vs), 1222 (m); ^{1}H NMR ($CDCl_3$): δ 1.28 (3H, d, $^{3}J_{HH}$=6.5, C*H*$_3$), 2.24 (3H, d, $^{3}J_{PNCH}$=7.6, NC*H*$_3$), 4.56 (1H, m, NC*H*), 5.33 (1H, dd, $^{3}J_{HH}=^{3}J_{POCH}$=9.3, OC*H*), 6.6 (2H, m, *H* arom), 7.0–7.8 (23H, m, *H* arom), 7.9 (1H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 72.5 (q, $^{1}J_{PB}$=56.7, *P*–N), 108.0 (q, $^{1}J_{PB}$=66.3, *P*–O); ^{13}C NMR ($CDCl_3$): δ 16.1 (*C*H$_3$), 29.4 (d, $^{2}J_{PNC}$=4.8, NC*H*$_3$), 57.4 (dd, $^{2}J_{PNC}$=8.8, $^{3}J_{POCC}$=11.0, N*C*H), 83.2 (dd, $^{2}J_{POC}$=3.0, $^{3}J_{PNCC}$=9.0, O*C*H), 127.0–132.6 (*C* arom), 138.0 (*C* arom); MS (DCI; CH_4)

m/z (relative intensity): 560 (M^+-H; 30), 547 (M^+-BH_3; 11), 362 (20), 346 (70), 334 (65), 256 (25), 231 (25), 203 (100), 187 (80), 148 (30); HRMS (DCI, CH_4) calcd for $C_{34}H_{38}B_2NOP_2$ [M^+-H]: 560.2615; found: 560.2627; anal. calcd for $C_{34}H_{39}B_2NOP_2$ (561.2605): C 72.76, H 7.00, N 2.50; Found: C 72.76, H 6.88, N 2.27.

*4.2.4. (*S*p)-(−)*-N-*Methyl*-N-*{(1*R,*2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}-aminomethylphenylphosphine borane* ***4b***

Yield=79%; white solid; mp=130–132°C (*i*-PrOH); $[\alpha]_D^{20}=-55.3$ (*c* 1.09, $CHCl_3$); R_f=0.6 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2387 (vs, B–H), 2343 (vs), 1454 (s), 1436 (vs), 1222 (s), 1165 (s); ^{1}H NMR ($CDCl_3$): δ 1.34 (3H, d, $^2J_{PCH}$=6.6, PC*H*$_3$), 1.51 (3H, d, $^3J_{HH}$=8.8, C*H*$_3$), 2.30 (3H, d, $^3J_{PNCH}$=8.1, NC*H*$_3$), 4.39 (1H, m, NC*H*), 5.33 (1H, dd, $^3J_{POCH}=^3J_{HH}$=9.4, OC*H*), 6.6 (2H, m, *H* arom), 7.0–7.6 (16H, m, *H* arom), 7.73 (2H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 68.7 (q, $^1J_{PB}$=87, *P*–N), 108.3 (q, $^1J_{PB}$=74.3, *P*–O); ^{13}C NMR ($CDCl_3$): δ 11.3 (d, $^1J_{PC}$=39.4, P*C*H$_3$), 16.3 (*C*H$_3$), 28 (d, $^2J_{PNC}$=3.3, N*C*H$_3$), 57.1 (dd, $^2J_{PNC}=^3J_{POCC}$=10.0, N*C*H), 82.5 (dd, O*C*H), 127.8–132.8 (*C* arom), 138.3 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 498 (M^+-H; 35), 484 (M^+-H-BH_3; 10), 362 (5), 298 (5), 284 (50), 272 (30), 231 (15), 203 (100), 194 (20), 148 (25), 125 (50), 109 (15); HRMS (DCI, CH_4) calcd for $C_{29}H_{36}B_2NOP_2$ [M^+-H]: 498.2457; found: *m/z* 498.2469; anal. calcd for $C_{29}H_{37}B_2NOP_2$ (499.1849): C 69.78, H 7.47, N 2.81; found: C 69.79, H 7.40, N 2.64.

*4.2.5. (*R*p)-(−)*-N-*Methyl*-N-*{(1*R,*2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}-amino*-o-*anisylphenylphosphine borane* ***4c***

Yield=62%; white solid; mp=183–184°C; $[\alpha]_D^{20}=-64.7$ (*c* 1.32, $CHCl_3$); R_f=0.5 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2392 (vs, B–H), 1587 (s), 1570 (s), 1477 (s), 1456 (s), 1436 (s), 1429 (s), 1276 (s), 1249 (s), 1222 (s), 1160 (s); ^{1}H NMR ($CDCl_3$): δ 1.35 (3H, d, $^3J_{HH}$=6.5, C*H*$_3$), 2.38 (3H, d, $^3J_{PNCH}$=7.9, NC*H*$_3$), 3.5 (3H, s, OC*H*$_3$), 4.6 (1H, m, NC*H*), 5.40 (1H, dd, $^3J_{POCH}=^3J_{HH}$=9.5, OC*H*), 6.6 (2H, m, *H* arom), 6.9 (1H, m, *H* arom), 6.95–7.65 (19H, m, *H* arom), 7.7 (2H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 70.2 (br, *P*–N), 107.6 (q, $^1J_{PB}$=72.2, *P*–O); ^{13}C NMR ($CDCl_3$): δ 15.6 (*C*H$_3$), 29.75 (d, $^2J_{PNC}$=4.6, N*C*H$_3$), 54.9 (O*C*H$_3$), 57.4 (dd, $^2J_{PNC}$=8.7, $^3J_{POCC}$=11.9, N*C*H), 83.4 (dd, $^2J_{POC}$=3.2, $^3J_{PNCC}$=9.5, O*C*H), 111.4 (d, J_{PC}=4.5, *C* arom), 118.4 (d, J_{PC}=54.2, *C* arom), 120.8 (d, J_{PC}=10.9, *C* arom), 127.5–138 (*C* arom), 160.9 (*C* arom), MS (DCI, CH_4) *m/z* (relative intensity): 590 (M^+-H; 20), 576 (M^+-H-BH_3; 24), 364 (60), 272 (15), 217 (30), 203 (100), 148 (35); HRMS (DCI, CH_4), calcd for $C_{35}H_{40}B_2NO_2P_2$ [M^+-H]: 590.2721; found: *m/z* 590.2733; anal. calcd for $C_{35}H_{41}B_2NO_2P_2$ (591.2819): C 71.10, H 6.99, N 2.37; Found: C 70.94, H 7.07, N 2.23.

*4.2.6. (*R*p)-(−)*-N-*Methyl*-N-*{(1*R,*2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}-amino-1-naphthylphenylphosphine borane* ***4d***

Yield=62%; white solid; mp=160–162°C; $[\alpha]_D^{20}=-96.9$ (*c* 1.22, $CHCl_3$); R_f=0.65 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2383 (s, B–H), 1436 (s), 1111 (s), 1064 (s), 1010 (s), 980 (s), 953 (m); ^{1}H NMR ($CDCl_3$): δ 1.54 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.40 (3H, d, $^3J_{PNCH}$=7.2, NC*H*$_3$), 4.8 (1H, m, C*H*N), 5.42 (1H, dd, $^3J_{POCH}$=8.9, OC*H*), 6.85 (2H, m, *H* arom), 7.0–8.0 (25H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 72.9 (br, *P*–N), 115 (br, *P*–O); ^{13}C NMR ($CDCl_3$): δ 15.9 (*C*H$_3$), 29.8 (d, $^2J_{PNC}$=3.9, N*C*H$_3$), 57.5 (dd, $^3J_{POCC}$=11, $^2J_{PNC}$=8.5, N*C*H), 83.4 (dd, $^2J_{POC}$=2.6, $^3J_{PNCC}$=9.3, O*C*H), 124.5–137.8 (*C* arom); MS (DCI, CH_4) 610 (M^+-H; 15), 596 (M^+-H-BH_3; 25), 412 (15), 396 (50), 384 (100), 327 (25), 292 (15), 237 (45), 203 (100), 148 (20); HRMS (DCI, CH_4) calcd for $C_{38}H_{40}ONP_2B_2$ [M^+-H]: 610.2771; found: 610.2789; anal. calcd for $C_{38}H_{41}B_2NOP_2$: C 74.66, H 6.76, N 2.29; found: C 74.61, H 6.69, N 2.27.

*4.2.7. (*R*p)-(−)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}-amino-2-naphthylphenylphosphine borane **4e***

Yield=78%; white solid; mp=71–75°C; $[\alpha]_D^{20}=-65.3$ (*c* 1.04, $CHCl_3$); R_f=0.65 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2362 (vs, B–H), 2339 (m, B–H), 1457 (m), 1159 (m), 1109 (m), 1062 (m), 1012 (m), 983 (m); ^{1}H NMR ($CDCl_3$): δ 1.44 (3H, d, $^3J_{HH}$=6.50, C*H*$_3$), 2.43 (3H, d, $^3J_{PNCH}$=7.7, NC*H*$_3$), 4.73 (1H, m, NC*H*), 5.49 (1H, dd, $^3J_{POCH}=^3J_{HH}$=9.3, OC*H*), 6.75 (2H, m, *H* arom), 7.0–7.65 (19H, m, *H* arom), 7.85 (5H, m, *H* arom), 8.15 (1H, d, *J*=16.5, *H* arom); ^{31}P NMR ($CDCl_3$): δ 72.0 (br, *P*–N), 107.6 (br, *P*–O); ^{13}C NMR ($CDCl_3$): δ 16.16 (*C*H$_3$), 29.4 (d, $^2J_{PNC}$=4.5, NC*H*$_3$), 57.4 (dd, $^2J_{PNC}$=8.8, $^3J_{POCC}$=11.3, NC*H*), 83.4 (dd, $^2J_{POC}$=2.4, $^3J_{PNCC}$=8.9, OC*H*), 124.6–137.9 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 610 (M^+-H; 15), 596 (M^+-H-BH_3; 12), 396 (40), 384 (95), 364 (10), 306 (15), 276 (25), 237 (95), 203 (100), 187 (75), 148 (40); HRMS (DCI, CH_4) calcd for $C_{38}H_{40}ONP_2B_2$ [M^+-H]: 610.2771; found: 610.2783.

*4.2.8. (*S*p)-(−)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito borane)-1-methyl-2-phenyl]ethyl}-amino-*tert*-butylphenylphosphine borane **4f***

Yield=64%; white solid; mp=137–138°C; $[\alpha]_D^{20}=-86.1$ (*c* 1.19, $CHCl_3$); R_f=0.75 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (m, C–H), 2382 (s), 1436 (s), 1109 (s), 1067 (s), 1015 (s), 978 (s), 949 (s); ^{1}H NMR ($CDCl_3$): δ 1.11 (9H, d, $^3J_{PCCH}$=13.8, C(C*H*$_3$)$_3$), 1.33 (3H, d, $^3J_{HH}$=5.5, C*H*$_3$), 2.62 (3H, d, $^3J_{PNCH}$=5.5, NC*H*$_3$), 4.38 (1H, m, NC*H*), 5.40 (1H, dd, $^3J_{POCH}=^3J_{HH}$=10.6, OC*H*), 6.66–7.8 (20H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 87.8 (q, $^1J_{PB}$=72.3, *P*–N), 107.32 (q, $^1J_{PB}$=77.6, *P*–O); ^{13}C NMR ($CDCl_3$): δ 14.8 (*C*H$_3$), 28.1 (d, $^2J_{PCC}$=2.8, C(*C*H$_3$)$_3$), 31.9 (d, $^2J_{PNC}$=4.3, NC*H*$_3$), 34.29 (d, $^1J_{PC}$=35.2, *C*(CH$_3$)$_3$), 58.0 (dd, $^2J_{PNC}=^3J_{PNCC}$=8.8, NC*H*), 83.4 (dd, $^2J_{POC}$=3, $^3J_{PNCC}$=5.3, OC*H*), 127.7–136.6 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 540 (M^+-H; 10), 526 (M^+-H-BH_3; 10), 326 (100), 314 (90), 236 (45), 203 (90), 187 (25), 146 (15); HRMS (DCI, CH_4) calcd for $C_{32}H_{42}ONP_2B_2$ [M^+-H]: 540.2928; found: 540.2944; anal. calcd for $C_{32}H_{43}B_2NOP_2$ (541.2594): C 71.01, H 8.01, N 2.59; found: C 71.00, H 8.04, N 2.41.

*4.2.9. (*R*p)-(−)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(dicyclohexylphosphinito borane)-1-methyl-2-phenyl]ethyl}-amino-*o*-anisylphenylphosphine borane **4i***

Yield=67%; white solid; mp=178–181°C; $[\alpha]_D^{20}=-37.8$ (*c* 1.02, $CHCl_3$); R_f=0.5 (toluene); IR (neat, ν cm^{-1}): 2931 (s), 2850 (s), 2364 (s), 2336 (s), 1456 (m), 1275 (m), 1250 (m), 1065 (s), 1013 (s); ^{1}H NMR ($CDCl_3$): δ 0.4–2.1 (22H, m, C*H*$_2$ (cyclohexyl)) 1.35 (3H, d, $^3J_{HH}$=6.4, C*H*$_3$), 2.34 (3H, d, $^3J_{PNCH}$=8.0, NC*H*$_3$), 3.41 (3H, s, OC*H*$_3$), 4.5 (1H, m, NC*H*), 5.07 (1H, dd, $^3J_{POCH}=^3J_{HH}$=9.0, OC*H*), 6.53 (2H, m, *H* arom), 6.6–7.7 (12H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 69.7 (br, *P*–N), 135.6 (br, *P*–O); ^{13}C NMR ($CDCl_3$): δ 16.2 (*C*H$_3$), 25.4–26.9 (*C*H$_2$), 29.7 (d, $^2J_{PNC}$=4.8, NC*H*$_3$), 35.7 (d, $^1J_{PC}$=41.6, PC*H*), 37.3 (d, $^1J_{PC}$=31.4, PC*H*), 54.9 (s, OC*H*$_3$), 57.8 (dd, $^2J_{PNC}$=8.1, $^3J_{POCC}$=11.5, NC*H*), 82.3 (dd, $^2J_{POC}$=4.8, $^3J_{PNCC}$=9.7, OC*H*), 111.4 (d, J_{PC}=4.3, *C* arom), 118.6–139 (*C* arom), 160.8 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 602 (M^+-H; 15), 588 (M^+-H-BH_3, 15), 376 (60), 364 (85), 272 (15), 243 (35), 215 (100), 148 (35); HRMS (DCI, CH_4) calcd for $C_{35}H_{52}B_2NO_2P_2$ [M^+-H]: 602.3660; found: 602.3661; anal. calcd for $C_{35}H_{53}B_2NO_2P_2$ (603.3767): C 69.67, H 8.85, N 2.32; found: C 69.51, H 8.76, N 2.14.

*4.3. Synthesis of the aminophosphine phosphinite diborane **4g**, **4j**–**k***

*4.3.1. Preparation of (*S*p)-*o*-anisylchlorophenylphosphine borane **3b***

A 100 mL two-necked flask equipped with a magnetic stirrer, an argon inlet and a rubber septum was charged with 600 mg of the aminophosphine borane **2b**[7c] (1.52 mmol) and a solution of HCl in toluene

(0.26 M, 35 mL, 9.12 mmol) was directly added (without previous solubilization of the aminophosphine) at room temperature under strirring. After 1 h, the ephedrine hydrochloride was filtered off on a millipore 4 μm filter, and the solution was rapidly used without further purification.

Colorless viscous oil; R_f=0.8 (toluene); IR (neat, ν cm^{-1}): 3058, 3010, 2941, 2839 (C−H), 2394 (B−H), 1589, 1575, 1478, 1433, 1280, 1252, 1181, 1165, 1055; ^{1}H NMR ($CDCl_3$): δ 0.7–3.2 (3H, br, B*H*$_3$), 3.06 (3H, s, OC*H*$_3$), 6.3–6.4 (1H, m, *H* arom), 6.72–6.83 (1H, m, *H* arom), 6.95–7.22 (4H, m, *H* arom), 7.67–7.8 (2H, m, *H* arom), 8.0–8.1 (1H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 81 (q, $^1J_{PB}$=57.8); ^{13}C NMR ($CDCl_3$): δ 55.7 (O*C*H$_3$), 111.9–161.1 (*C* arom).

*4.3.2. Typical procedure for **4g**, **4j**–**k***

A 250 mL round-bottomed flask equipped with a magnetic stirrer was charged with 4.28 g of oxazaphospholidine borane **1** (or **1′**; 15 mmol) and 23 mL of dry THF. To this solution cooled at −78°C, 1 equivalent of *o*-AnLi (or PhLi; 15 mmol) were added, and the reaction stirred during 1 h 30 min. Then the mixture was warmed to 0°C, and added to *o*-anisylphenylchlorophosphine borane **3b** (1.5 mmol), previously prepared according to the procedure described in Section 4.5.1. After one night under stirring, the reaction was hydrolyzed at room temperature, then the THF was removed under reduced pressure, and the residue extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and the solvent was removed under vacuum to give a crude product, which was purified by chromatography on silica gel using toluene:petroleum ether, 1:1, as eluent. The AMPP diborane complexes were isolated in 40–73% yield, whereas the excess of aminophosphine **2** was recovered in 60% yield after recrystallization in a hexane:*i*-PrOH, 7:3, mixture.

*4.3.3. (−)-*N-*Methyl*-N-*{(1*R,*2*S)-*[2-((*R*p)*-*o*-*anisylphenylphosphinito borane)-1-methyl-2-phenyl]-ethyl}aminodiphenylphosphine borane **4g***

Yield=44%; white solid; mp=147–148°C; $[\alpha]_D^{20}$ −72.5 (*c* 1.01, $CHCl_3$); R_f=0.4 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2383 (s, B–H), 2341 (m, B–H), 1589 (m), 1574 (m), 1476 (s), 1454 (s), 1434 (s), 1279 (s), 1252 (s); ^{1}H NMR ($CDCl_3$): δ 1.33 (3H, d, $^3J_{HH}$=6.5, C*H*$_3$), 2.28 (3H, d, $^3J_{PNCH}$=7.6, NC*H*$_3$), 3.55 (3H, s, OC*H*$_3$), 4.58 (1H, m, NC*H*), 5.40 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=9.5, OC*H*), 6.6 (2H, m, *H* arom), 6.9 (1H, m, *H* arom), 7.0–7.6 (20H, m, *H* arom), 7.9 (1H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 72.4 (br, *P*–N), 106.4 (q, $^1J_{PB}$=75.1, *P*–O); ^{13}C NMR ($CDCl_3$): δ 16 (*C*H$_3$), 29.3 (d, $^2J_{PNC}$=4.5, NC*H*$_3$), 55.4 (O*C*H$_3$), 57.5 (m, $^2J_{PNC}$=9.6, $^3J_{POCC}$=10.9, N*C*H), 82.2 (m, O*C*H), 111.7 (d, J_{PC}=5.4, *C* arom), 119.4–138.3 (*C* arom), 160.75 (d, J_{PC}=4.3, *C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 590 (M^+−H; 25), 576 (M^+−H−BH_3; 70), 417 (50), 346 (15), 332 (65), 233 (100), 187 (20), 148 (35); HRMS (DCI, CH_4) calcd for $C_{35}H_{40}B_2NO_2P_2$ [M^+−H]: 590.2721; found: 590.2733.

*4.3.4. (+)-*N-*Methyl*-N-*{(1*S,*2*R)-*[2-((*R*p)*-*o*-*anisylphenylphosphinito borane)-1-methyl-2-phenyl]-ethyl}aminodiphenylphosphine borane **4j***

Yield=73%; white solid; mp=162°C; $[\alpha]_D^{20}$=+104.5 (*c* 1.07, $CHCl_3$); R_f=0.45 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (m, C–H), 2382 (s, B–H), 2350 (m, B–H), 1592 (s), 1570 (m), 1479 (s), 1455 (s), 1437 (s), 1282 (s), 1256 (s), 1136 (s), 1105 (s); ^{1}H NMR ($CDCl_3$): δ 1.30 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.2 (3H, d, $^3J_{PNCH}$=7.5, NC*H*$_3$), 3.27 (3H, s, OC*H*$_3$), 4.55 (1H, m, NC*H*), 5.27 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=9.1, OC*H*), 6.32 (1H, m, *H* arom), 6.51 (2H, m, *H* arom), 6.72 (1H, m, *H* arom), 6.8–7.7 (20H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 72.6 (br, *P*–N), 105 (br, *P*–O); ^{13}C NMR ($CDCl_3$): δ 16.2 (*C*H$_3$), 29.3 (d, $^2J_{PNC}$=4.8, NC*H*$_3$), 54.6 (O*C*H$_3$), 57.4 (dd, $^2J_{PNCH}$=8.5, $^3J_{POCC}$=10.9, N*C*H), 82.0 (dd, O*C*H), 110 (d, J_{PC}=3.6, *C* arom), 118.5–137 (*C* arom), 160.4 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 590 (M^+−H; 100), 576 (M^+−H−BH_3; 70), 346 (40), 334 (40), 242 (25), 233 (50), 157 (20), 185 (20); HRMS (DCI,

CH_4) calcd for $C_{35}H_{40}B_2NO_2P_2$ [M^+-H]: 590.2720; found: 590.2739; anal. calcd for $C_{35}H_{41}B_2NO_2P_2$ (591.2819): C 71.10, H 6.99, N 2.37; found: C 70.95, H 7.10, N 2.19.

*4.3.5. (*S*p)-(+)*-N-*Methyl*-N-*{(1*S*,2*R*)-[2-((*R*p)*-o-*anisylphenylphosphinito borane)-1-methyl-2-phenyl]-ethyl}amino*-o-*anisylphenylphosphine borane* ***4k***

Yield=40%; white solid; mp=192–193°C; $[\alpha]_D^{20}$=+92.6 (*c* 0.84, $CHCl_3$); R_f=0.5 (toluene); IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2389 (s, B–H), 2340 (w, B–H), 1589 (s), 1573 (m), 1477 (s), 1462 (m), 1435 (m), 1427 (m), 1280 (s), 1252 (m), 1010 (m), 983 (s); ^{1}H NMR ($CDCl_3$): δ 1.43 (3H, d, $^3J_{HH}$=6.5, C*H*$_3$), 2.41 (3H, d, $^3J_{PNCH}$=7.9, NC*H*$_3$), 3.37 (3H, s, OC*H*$_3$), 3.53 (3H, s, OC*H*$_3$), 4.66 (1H, m, NC*H*), 5.4 (1H, dd, ^3J=9.2, OC*H*), 6.45 (1H, m, *H* arom), 6.6 (2H, m, *H* arom), 6.7–7.9 (20H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 70.0 (br, *P*–N), 104.6 (q, $^1J_{P-B}$=66, *P*–O); ^{13}C NMR ($CDCl_3$): δ 15.7 (*C*H$_3$), 29.7 (d, $^2J_{PNC}$=4.8, NCH$_3$), 54.6 (OCH$_3$), 54.9 (OCH$_3$), 57.5 (dd, $^2J_{PNC}$=9.6, $^3J_{POCC}$=11.5, NCH), 82.3 (dd, $^2J_{POC}$=2.9, $^3J_{PNCC}$=9.6, OCH), 110.3 (d, J_{PC}=4.1, *C* arom), 111.4 (d, J_{PC}=4.5, *C* arom), 118.3 (d, J_{PC}=16.3, *C* arom), 119.7 (d, J_{PC}=12.8) 119.1 (d, J_{PC}=15.2, *C* arom), 120.8 (d, J_{PC} =10.9, *C* arom), 127.5–137.8 (*C* arom), 160.4 (*C* arom), 161 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 620 (M^+-H; 40), 606 (M^+-H-BH_3; 20), 392 (15), 376 (90), 364 (55), 307 (10), 272 (20), 233 (100), 217 (50), 148 (15); HRMS (DCI, CH_4) calcd for $C_{36}H_{42}B_2NO_3P_2$ [M^+-H]: 620.2826; found: 620.2827; anal. calcd for $C_{36}H_{43}B_2NO_3P_2$ (621.3081): C 69.59; H 6.98, N 2.25; found: C 69.45, H 7.07, N 2.08.

*4.4. (*S*p)-(−)*-N-*Methyl*-N-*{(1*R*,2*S*)-[2-((*S*p)-methylphenylphosphinito borane)-1-methyl-2-phenyl]-ethyl}aminomethylphenylphosphine borane* ***4h***

*4.4.1. Preparation of (*R*p)-chloromethylphenylphosphine borane* ***3a***[7f]

A 250 mL two-necked flask equipped with a magnetic stirrer, an argon inlet and a rubber septum was charged with 1.2 g (4 mmol) of the aminophosphine borane **2a**[7c,f] and 178 mL of toluene. A solution of HCl in toluene (0.38 M, 22.1 mL, 8.4 mmol, 2.1 equivalents) was added at room temperature under stirring (the final concentration of aminophosphine borane had to be about 20 mM). After 1 h, the ephedrine hydrochloride was filtered off with a millipore 4 μm filter, and the solution rapidly used without further purification. After removal of the solvent, the chlorophosphine borane can be purified in poor yield by chromatography on a short column of silica gel, previously dried overnight at 80°C and washed with acetone then cyclohexane, yielding compound **3a**.

Colorless viscous oil; R_f=0.8 (toluene); IR (neat, ν cm^{-1}): 3080, 3000, 2933, 2940 (C–H), 2383 (B–H), 1437, 1119, 1062, 949, 909, 745, 690; ^{1}H NMR ($CDCl_3$): δ 0.5–2.0 (3H, br, B*H*$_3$), 1.2 (3H, d, $^2J_{PCH}$=11, C*H*$_3$), 7.3–7.7 (3H, m, *H* arom), 7.8–8.0 (2H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 96.8 (q, $^1J_{PB}$=47); ^{13}C NMR ($CDCl_3$): δ 19.9 (d, ^{1} J_{PC}=31, P*C*H$_3$), 129.1 (d, J_{PC}=2, *C* arom), 130.8 (d, J_{PC}=12, *C* arom), 133.1 (d, J_{PC}=2, *C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 173 (M^+; 1), 140 (20), 125 (100), 109 (64).

4.4.2. Synthesis of ***4h***

A 100 mL round-bottomed flask equipped with a magnetic stirrer and an argon inlet was charged with 1 equivalent of oxazaphospholidine borane **1** (3.5 mmol) and 3 mL of THF. CH_3Li (4.9 mmol, 1.4 equivalents) was added at −78°C and the reaction stirred during 1 h and allowed to warm to 0°C. The crude product is transferred at −78°C with a syringe to 4.9 mmol of methylphenylchlorophosphine borane **3a** previously prepared as described in Section 4.4.1. The reaction was stirred for 1 h 50 min then hydrolyzed at room temperature. THF was removed under reduced pressure. After extraction of the crude product with CH_2Cl_2, the organic extracts were dried over anhydrous magnesium sulfate and the solvent

removed. The residue was purified by chromatography on silica gel using toluene:petroleum ether, 1:1, as eluent yielding the AMPP in 18% unoptimized yield.

Yield=18%; white solid; $[\alpha]_D^{20}=-22.1$ (*c* 1.03, $CHCl_3$); R_f=0.4 (toluene); mp=124°C; IR (neat, ν cm^{-1}): 3050–2900 (w, C–H), 2396 (s, B–H), 2368 (s, B–H), 1455 (m), 1292 (m), 1063 (m); ^{1}H NMR ($CDCl_3$): δ 1.35 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 1.45 (3H, d, $^2J_{PCH}$=8.8, NPC*H*$_3$), 1.64 (3H, d, $^2J_{PCH}$=9.2, OPC*H*$_3$), 2.22 (3H, d, $^3J_{PNCH}$=8.2, NC*H*$_3$), 4.25 (1H, m, C*H*N), 5.04 (1H, dd, ^3J=7.3, OC*H*), 6.5–6.65 (2H, m, *H* arom), 6.9–7.3 (11H, m, *H* arom), 7.3–7.45 (2H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 68.6 (q, $^1J_{PB}$=68.7, *P*–N), 113.1 (q, $^1J_{PB}$=80, *P*–O); ^{13}C NMR (62.9 MHz): δ 11.2 (d, $^1J_{PC}$=39.4, NP*C*H$_3$), 15.8 (*C*H$_3$), 16.4 (d, $^1J_{PC}$=50, OP*C*H$_3$), 28 (d, $^2J_{PC}$=3.3, N*C*H$_3$), 57 (dd, $^2J_{PNC}$=$^3J_{POCC}$=9.6, N*C*H), 82.1 (dd, $^2J_{POC}$=3.5, $^3J_{POCC}$=9, O*C*H), 127.8–132.6 (*C* arom), 138.1 (*C* arom); MS (DCI, CH_4) *m/z* (relative intensity): 436 (M^+-H; 100), 422 (M^+-H-BH_3; 35), 298 (25), 270 (25), 194 (15), 180 (20), 141 (40), 125 (15), 107 (5); HRMS (DCI, CH_4) calcd for $C_{24}H_{34}B_2NOP_2$ [M^+-H]: 436.2302; found: 436.2313; anal. calcd for $C_{24}H_{35}B_2NOP_2$ (437.1141): C 65.95, H 8.07, N 3.20; found: C 65.96, H 8.14, N 3.14.

*4.5. Typical procedure for the decomplexation of aminophosphineborane phosphinite borane **4a**–**k**.*

In a three-necked flask equipped with a reflux condenser, a magnetic stirrer and an argon inlet, 1 equivalent (0.5 mmol) of AMPP borane **4** was charged. Diazabicyclooctane (2 mmol, 4 equivalents) was added, the flask purged with three cycles of argon and 3 mL of dry toluene added. The mixture was heated at 70°C for 12 h. The crude product was rapidly filtered off on a neutral alumina column (15 cm height, 2 cm diameter) using toluene:AcOEt, 9:1, as eluent. AMPP **5** was recovered in isolated yields varying between 70 and 90%.

*4.5.1. (−)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}aminodiphenylphosphine **5a** ((−)-EPHOS)*

$[\alpha]_D^{20}=-57.7$ (*c* 0.75, toluene); ^{1}H NMR ($CDCl_3$): δ 1.36 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.19 (3H, d, $^3J_{PNCH}$=3.1, NC*H*$_3$), 4.00 (1H, m, NC*H*), 4.80 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=8.8, OC*H*), 6.66 (m, 2H), 7.0–7.6 (23H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 66.0 (*P*–N), 111.7 (*P*–O).

*4.5.2. (*S*p)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}aminomethylphenylphosphine **5b***

^{1}H NMR ($CDCl_3$): δ 1.15 (3H, d, $^2J_{PCH}$=6, PC*H*$_3$), 1.29 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.09 (3H, d, $^3J_{PNCH}$=3.8, NC*H*$_3$), 3.9 (1H, m, NC*H*), 4.85 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=10.0, OC*H*), 6.55 (2H, m, *H* arom), 7.0–7.9 (18H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 52.4 (*P*–N), 111.9 (*P*–O).

*4.5.3. (*R*p)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}amino-o-anisylphenylphosphine **5c***

^{1}H NMR ($CDCl_3$): δ 1.45 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.19 (3H, NC*H*$_3$), 3.65 (3H, s, OC*H*$_3$), 4.0 (1H, m, NC*H*), 4.8 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=8.8, OC*H*), 6.6 (2H, m, *H* arom), 6.75–7.65 (22H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 56 (*P*–N), 111 (*P*–O).

*4.5.4. (*R*p)-*N*-Methyl-*N*-{(1*R*,2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}amino-1-naphthylphenylphosphine **5d***

^{1}H NMR ($CDCl_3$): δ 1.30 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.15 (3H, d, $^3J_{PNCH}$=3, NC*H*$_3$), 4.0 (1H, m, NC*H*), 4.72 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=8.7, OC*H*), 6.5 (2H, m, *H* arom), 6.8–7.8 (24H, m, *H* arom), 8.1 (1H, m, *H* arom); ^{31}P NMR ($CDCl_3$): δ 57.7 (*P*–N), 112.1 (*P*–O); ^{13}C NMR ($CDCl_3$): δ 16.85 (d, $^3J_{PNCC}$=3.8,

*C*H$_3$), 31.6 (d, $^2J_{PNC}$=9.8, NC*H*$_3$), 65.5 (dd, $^2J_{PNC}$=7.5, $^3J_{POCC}$=39.8, NC*H*), 86.4 (dd, $^2J_{POC}$=10.3, $^3J_{PNCC}$=17.9, OC*H*), 125–142.1 (*C* arom).

*4.5.5. (*R*p)*-N-*Methyl*-N-*{(1*R,*2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}amino-2-naphthylphenylphosphine* ***5e***

^{1}H NMR (CDCl$_3$): δ 1.37 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.24 (3H, d, $^3J_{PNCH}$=3, NC*H*$_3$), 3.97 (1H, m, NC*H*), 4.84 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=9.0, OC*H*), 6.72–6.75 (2H, m, *H* arom), 7.1–7.8 (25H, m, *H* arom); ^{31}P NMR (CDCl$_3$): δ 63.6 (*P*–N), 111.2 (*P*–O).

*4.5.6. (*S*p)-(−)-*N-*Methyl*-N-*{(1*R,*2*S*)-[2-(diphenylphosphinito)-1-methyl-2-phenyl]ethyl}amino-*tert-*butylphenylphosphine* ***5f***

^{1}H NMR (CDCl$_3$): δ 0.9 (9H, d, $^3J_{PCCH}$=12.7, C(C*H*$_3$)$_3$), 1.3 (3H, d, $^3J_{HH}$=6.7, C*H*$_3$), 2.5 (3H, d, $^3J_{PNCH}$=3, NC*H*$_3$), 3.85 (1H, m, NC*H*), 4.7 (1H, dd, $^3J_{HH}$=$^3J_{POCH}$=8, OC*H*), 6.7–7.6 (20H, m, *H* arom); ^{31}P NMR (CDCl$_3$): δ 89.5 (*P*–N), 110.8 (*P*–O).

*4.5.7. (*R*p)-*N-*Methyl*-N-*{(1*R,*2*S*)-[2-(dicyclohexylphosphinito)-1-methyl-2-phenyl]ethyl}amino-*o-*anisylphenylphosphine* ***5i***

^{31}P NMR (CDCl$_3$): δ 56.6 (*P*–N), 102.7 (*P*–O).

*4.5.8. (*S*p)-*N-*Methyl*-N-*{(1*S,*2*R*)-[2-(*R*p)-*o-*anisylphenylphosphinito)-1-methyl-2-phenyl]ethyl}amino-*o-*anisylphenylphosphine* ***5k***

^{31}P NMR (CDCl$_3$): δ 56.6 (*P*–N), 102.7 (*P*–O).

4.5.9. N-*Methyl*-N-*{(1*R,*2*S*)-[2-(*R*p)-*o-*anisylphenylphosphinito)-1-methyl-2-phenyl]ethyl}aminodiphenylphosphine* ***5g***

^{1}H NMR (CDCl$_3$): δ 1.5 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.25 (3H, d, $^3J_{PNCH}$=3.2, NC*H*$_3$), 3.75 (3H, s, OC*H*$_3$), 4.05 (1H, m, NC*H*), 4.9 (1H, dd, $^3J_{POCH}$=$^3J_{HH}$=9.1, OC*H*), 6.5–7.8 (24H, m, *H* arom); ^{31}P NMR (CDCl$_3$): δ 66.1 (*P*–N), 102.5 (*P*–O).

4.5.10. N-*Methyl*-N-*{(1*S,*2*R*)-[2-(*R*p)-*o-*anisylphenylphosphinito)-1-methyl-2-phenyl]ethyl}aminodiphenylphosphine* ***5j***

^{1}H NMR (CDCl$_3$): δ 1.35 (3H, d, $^3J_{HH}$=6.6, C*H*$_3$), 2.28 (3H, d, $^3J_{PNCH}$=3.1, NC*H*$_3$), 3.6 (3H, s, OC*H*$_3$), 4.1 (1H, m, NC*H*), 4.9 (1H, dd, $^3J_{POCH}$=$^3J_{HH}$=9, OC*H*), 6.6 (2H, m, *H* arom), 6.9 (1H, *H* arom), 7–7.7 (24H, m, *H* arom); ^{31}P NMR (CDCl$_3$): δ 66.4 (*P*–N), 103.2 (*P*–O).

4.6. Preparation of the precatalyst Rh-complexes

4.6.1. Preparation of the cationic [Rh(COD)$_2$]$^+$BF$_4^-$

This precatalyst complex was prepared following a modified procedure of Schrock and Osborn.[20] In a Schlenk tube, under argon atmosphere, 200 mg (0.406 mmol) of [Rh(COD)Cl]$_2$[21] and 0.40 mL of 1,5-cyclooctadiene were dissolved in 4 mL of dry and degassed CH_2Cl_2. In the dark, $AgBF_4$ (0.81 mmol) was added in one portion, and the mixture was stirred for 15–20 min. The solution was filtered through a bed of Celite which was washed with dry CH_2Cl_2. The filtrate was carefully concentrated to 1 mL and 1.5 mL of ether was added to precipitate (COD)$_2$Rh$^+$BF$_4^-$ as a brown solid. This complex was used for generating the chiral Rh-complexes.

*4.6.2. General procedure for the preparation of [Rh(COD)(AMPP **5**)]$^+BF_4^-$ catalysts*

In a Schlenk tube, under an argon atmosphere, a solution of 0.020 mmol of AMPP **5** in 1 mL of dry and degassed CH_2Cl_2 was added to 0.0197 mmol (8 mg) of $Rh(COD)_2{}^+BF_4^-$ in 1 mL of dry and degassed CH_2Cl_2 at room temperature. The mixture was stirred for 1–2 h and used without further purification for the asymmetric hydrogenation.

*4.6.3. [Rh(COD)(**5a**)]$^+BF_4^-$*

^{31}P NMR ($CDCl_3$): δ 94.4 (dd, $^1J_{PRh}$=163.2, $^2J_{PP}$=21.6, *P*–N), 120.9 (dd, $^1J_{PRh}$=170.6, $^2J_{PP}$=22.6, *P*–O).

*4.6.4. [Rh(COD)(**5d**)]$^+BF_4^-$*

^{31}P NMR ($CDCl_3$): δ 94.3 (dd, $^1J_{PRh}$=161.6, $^2J_{PP}$=19.8, *P*–N), 119.2 (dd, $^1J_{PRh}$=168.6, $^2J_{PP}$=19.2, *P*–O).

*4.7. Hydrogenation of methyl α-acetamidocinnamate using Rh(COD)(AMPP **5**) catalysts*

4.7.1. Typical procedure

In a 100 mL autoclave, under an argon atmosphere, was introduced 130 mg (0.59 mmol) of *Z*-methyl α-acetamidocinnamate, 3% mol (0.0197 mmol) of catalyst (prepared according to the above-mentioned procedure) and 8 mL of degassed dry CH_2Cl_2. When the hydrogenation was performed with benzene as the solvent, CH_2Cl_2 was removed under vacuum before use. The reactor was then connected to a hydrogen cylinder, and subjected to six vacuum/H_2 cycles, before pressurizing to an initial pressure of 15 bars of H_2. The reaction mixture was allowed to stir for 3 to 13 h at room temperature. Once the reaction was finished, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel using toluene:AcOEt, 3:1, as eluent.

*4.7.2. Methyl α-N-acetylphenylalaninate **7**[22]*

The enantiomeric excesses and the absolute configuration of compound **7** were determined on a Chiracel OD column (Daicel), with a hexane:*i*PrOH, 95:5, mixture as eluent, flow rate 1 mL min^{-1} and UV detection λ=254 nm: (*S*)-enantiomer t_R=21.9 min, (*R*)-enantiomer 26.3 min.

^1H NMR ($CDCl_3$): δ 1.90 (3H, s, COC*H*$_3$), 3.04 (2H, m, C*H*$_2$Ph), 3.64 (3H, s, CO_2CH_3), 4.81 (1H, m, C*H*CO_2CH_3), 5.90 (1H, br, N*H*$COCH_3$), 6.90–7.3 (5H, m, *H* arom); ^{13}C NMR ($CDCl_3$): δ 22.9 (CO*C*H_3), 37.7 (*C*H_2Ph), 52.1 (*C*HCO_2CH_3), 53.1 (CO_2*C*H_3), 127 (*C* arom), 128.4 (*C* arom), 129.1 (*C* arom), 135.8 (*C* arom), 169.6 (*C*OCH_3), 172.0 (*C*O_2CH_3).

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