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Enantiodivergent synthesis of P-chirogenic phosphines

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This paper is dedicated to Pascal Le Floch.

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ABSTRACT

Several approaches for the enantiodivergent synthesis of P-chirogenic mono- and diphosphines are described, using ephedrine methodology and phosphine borane chemistry. Firstly, both enantiomers of a tertiary phosphine can be obtained starting from the same oxazaphospholidine borane complex, prepared from (+)-ephedrine, when changing the order of addition of the organolithium reagents during the synthetic pathway. The second approach is based on the chlorophosphine boranes, which react with an organolithium reagent, to afford the corresponding phosphines with inversion of configuration. In the case where the chlorophosphine borane reacts with the *t*-butyl lithium reagent, a metal-halogen exchange occurs to afford the corresponding phosphide borane with retention of the configuration. The reaction of the phosphide borane with an alkyl halide leads to the same phosphine, but with the opposite configuration. Another approach depends on the diastereoselective preparation of the starting oxazaphospholidine borane complex from (−)-ephedrine, which leads according the case, to either one or the other enantiomer of a phosphine. Finally, the synthesis of (*R*,*R*)- and (*S*,*S*)-1,2-bis(methylphenylphosphino)ethane is also demonstrated using both enantiomers of the P-chirogenic diphosphinite diborane, which simultaneously allows the introduction of alkyl- or aryl substituents on the phosphorus atoms. In summary, these approaches show the great efficiency of the "ephedrine methodology" for the enantiodivergent synthesis of P-chirogenic mono- and diphosphines, and bearing alkyl or aryl substituents.

Mots clés :
Synthèse asymétrique
Énantiomères
Phosphines chirales
Complexes borane

RÉSUMÉ

La synthèse énantiodivergente de mono- et diphosphines P-chirogéniques utilisant la « méthode éphédrine » et la chimie des phosphines borane, est décrite selon plusieurs approches. La première est basée sur le principe que les deux énantiomères d'une phosphine tertiaire peuvent être obtenus à partir du même complexe d'oxazaphospholidine borane, préparé à partir de (+)-éphédrine, par simple changement de l'ordre

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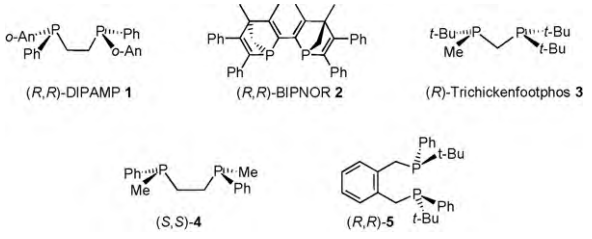
d'introduction des substituants du phosphore au cours de la synthèse. Une seconde approche repose sur l'utilisation des chlorophosphines borane qui réagissent avec un organolithien pour donner les phosphines correspondantes avec inversion de configuration. Dans le cas où la chlorophosphine borane réagit avec le *t*-butyllithium, un échange halogène-métal se produit pour donner un phosphure borane chiral avec rétention de la configuration ; la réaction du phosphure borane avec un halogénure d'alkyle permet alors d'obtenir une même phosphine, mais de configuration opposée. Une autre approche repose sur la synthèse diastéréosélective du complexe d'oxazaphospholidine borane de départ à partir de (−)-ephedrine, qui conduit selon le cas, à l'un ou l'autre énantiomère d'une phosphine. Enfin, la synthèse de (*R*,*R*)- et (*S*,*S*)-1,2-diphosphine P-chirogénique à pont éthano est décrite en utilisant les deux énantiomères d'un diphosphinite diborane, qui permet l'introduction simultanée de substituants alkyles ou aryles sur les deux atomes de phosphore. En résumé, ces différentes approches montrent la très grande efficacité de la « méthode éphédrine » pour la synthèse énantiodivergente de mono- et diphosphines P-chirogéniques, porteuses de groupements alkyles ou aryles.

1. Introduction

Numerous asymmetric catalyzed reactions were developed with transition metal complexes using chiral phosphorus ligands [1,2]. This class of ligands is widely used because their structure can be easily modified on the phosphorus center, or in its α- or β-position, owing to numerous electrophilic or nucleophilic reactions of their P(III)- or P(IV)-precursors [2–4]. Noteworthy, over the last decade, the chemistry of phosphorus ligands has made significant breakthroughs due to the borane used as protecting group, giving stable complexes, often crystallized, and affording clean reactions [4–6]. In addition, the chirality of the phosphorus ligands can stem either from the carbon backbone or from the phosphorus center, increasing thus the number of possible stereoisomers to improve asymmetric catalysis results [7].

As the asymmetric catalysis requires the selective formation of a single enantiomer, the availability of chiral ligands in both enantiomeric forms is essential to afford the desired stereoisomer. In most cases, both enantiomers of the phosphorus ligands are obtained by chemical resolution (For resolution of BINAP, MeO-BIPHEP or SYNPHOS, see [8]), or from their chiral original backbone scaffold (For the synthesis of JOSIPHOS and MonoPHOS from chiral backbone scaffolds, see [9]). In other cases, the enantiomers are obtained by stereoselective synthesis starting from the chiral pool (For representative synthesis of DIOP and PHOX starting from the pool chiral, see [10]), or from prochiral precursors (For the asymmetric synthesis of DuPHOS, see [11]).



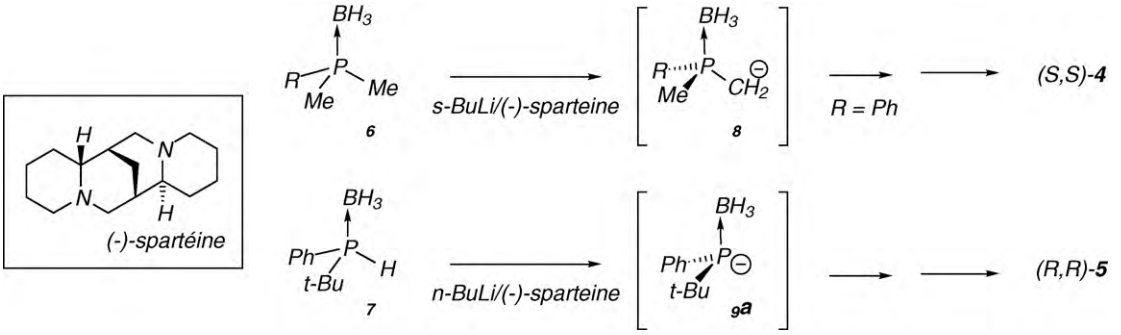
In the case of the DIPAMP **1**, BIPNOR **2** and Trichickenfootphos **3**, the P-chirogenic phosphines were obtained enantiomerically pure by chemical resolution or by chromatography on a chiral column, respectively [12]. However, most of the time, this class of ligands are prepared by efficient stereoselective synthesis using the phosphorus borane chemistry [4,6,13–17]. The principle of these syntheses is based on the preparation of enantiomerically enriched P-chirogenic organophosphorus borane building blocks **8**–**10**, acting either as nucleophilic or electrophilic reagents.

In the first case, the nucleophilic reagents **8** and **9a** are prepared in the presence of (−)-sparteine, by enantioselective deprotonation of the dimethylphosphine borane **6**, or by dynamic thermodynamic resolution of the secondary phosphine borane **7**, respectively (Scheme 1). The homocoupling of the anion **8** in the presence of $CuCl_2$ under air, or the reaction of **9a** with an electrophile, leads to the preparation of P-chirogenic ligands by C-C or P-C bond formation, such as in (*S*,*S*)-**4** or (*R*,*R*)-**5** (Scheme 1) [13,14]. Noteworthy, these nucleophilic methodologies have been successfully applied by T. Imamoto and coll. for the synthesis of several efficient chiral ligands in asymmetric catalysis, which are currently commercially available (MiniPHOS, BisP*, Quinox P*) [4,15].

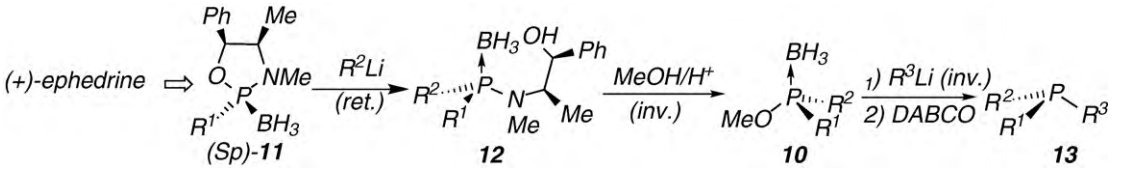
Unfortunately both nucleophilic methodologies are restricted to bulky alkyl or methyl substituents on the phosphorus atom. Furthermore, as only (−)-sparteine is commercially avalaible, only one enantiomer is accessible. The stereoselective synthesis of the other enantiomer is still possible, but using in this case, demanding strategies [16] or the (+)-sparteine surrogate [17].

In the case of the P-chirogenic electrophilic building blocks **10**, the synthesis is based on subsequent stereoselective reactions starting from the oxazaphospholidine borane complex **11**, prepared from (+)-ephedrine (Scheme 2) [6(a,c),18]. After reaction with an organolithium reagent the starting complex (*Sp*)-**11** affords the ring-opening product **12**, which leads to the P-chirogenic phosphinite borane **10** by P-N bond cleavage under acidic methanolysis conditions [6(a,c),18]. The reaction of the phosphinite borane **10** with an organolithium reagent, leads to the corresponding P-chirogenic phosphines **13**, after decomplexation with DABCO (Scheme 2).

As ephedrine is available in both antipodal forms (+) or (−), the stereoselective synthesis of both enantiomeric



Scheme 1.



Scheme 2.

mono- or diphosphines can be achieved. In addition, we previously reported the enantiodivergent synthesis of both enantiomers starting from the same complex **11**, by simply changing the order of addition of the organolithium reagents (i.e. R^3Li then R^2Li vs R^2Li then R^3Li) (Scheme 2) [6(a,c), 18]. However, this method was mainly examplified using aryl substituents on the phosphorus atom, because in the case of alkyl group, side reactions can occur by deprotonation in α-position of the phosphine borane.

We now wish to report some new efficient routes for the enantiodivergent synthesis of P-chirogenic mono- and diphosphines using the ephedrine methodology, giving easy access to both enantiomers, notably for derivatives bearing alkyl groups.

2. Results and discussion

2.1. Enantiodivergent synthesis using P-chirogenic chlorophosphine boranes as electrophilic reagents (Route A)

In connection with our on-going work on the asymmetric synthesis of P-chirogenic phosphorus compounds, we developed earlier the facile preparation of chlorophosphine boranes **14** as new P-chirogenic electrophilic building blocks [19]. The chlorophosphine boranes **14** are readily obtained by acidolysis of the aminophosphine boranes **12** with a toluene solution of HCl, leading to the P-N bond cleavage with inversion of configuration on the phosphorus atom (Scheme 3) [19].

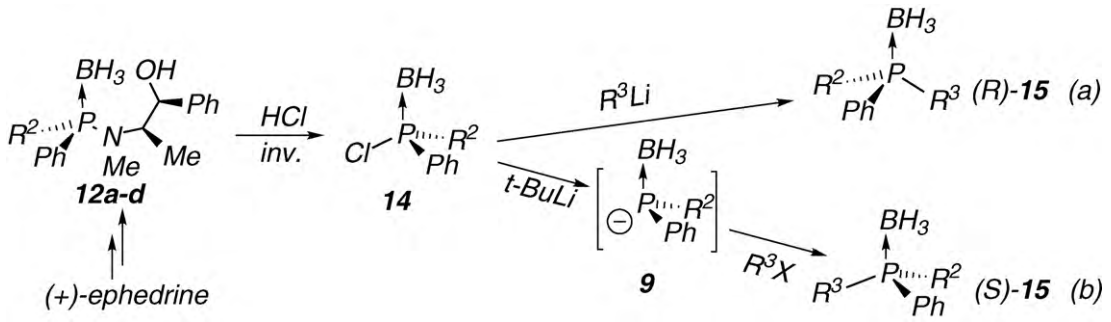
The reaction of the chlorophosphine boranes **14** with organolithium reagents stereospecifically provides the corresponding P-chirogenic phosphine boranes **15**, with inversion of configuration on the phosphorus atom (Scheme 3a). The route (A) was successfully applied to the enantioselective synthesis of both (*R*) and (*S*)-enantiomers of the di- or triaryl-phosphine boranes **15a-d**, reported in Table 1.

Thus, inverting the introduction order of the substituents during the synthesis, i.e. methyl as former group then *o*-anisyl, or reversely, can afford either the (*S*)- or the (*R*)-PAMP borane **15a** respectively, with e.e. up to 98% (entries 1,2; Table 1). Both enantiomers of the tertiary phosphine boranes **15b** and **15c**, were separately prepared using the same procedure starting respectively from *o*-anisyl-, ferrocenyl- or *m*-xylyl-aminophosphine boranes **12b**, **12c** or **12d**, which are derived from the (+)-ephedrine (Table 1, entries 3–6).[4] The X-ray structures of the phosphine boranes (*R*)-**15b** and (*S*)-**15b** were obtained and their ORTEP views are given in Figs. 1 and 2, with selected structural parameters.

2.2. Enantiodivergent synthesis using P-chirogenic phosphide borane reagents (Route B)

Recently, the investigation of the reaction between the *t*-butyllithium reagent and the chlorophosphine boranes **14**, led to the discovery of an unexpected new metal-halide exchange affording the corresponding P-chirogenic phosphide boranes **9** with retention of the configuration at the phosphorus atom (Scheme 3b). Following the subsequent addition of alkyl halide in excess, the corresponding phosphine boranes **15** were obtained in good to excellent yields and with e.e. up to 99% (Scheme 3b, Table 2). The route (B) was also successfully applied for the enantioselective preparation of the phosphine borane (*S*)-**15a** (PAMP.borane). The latter is obtained by acidolysis with HCl of the

[4] The *o*-anisylphenyl-*m*-xylylphosphine **12d** is referred as the Chou-Phos in the laboratory.



Scheme 3.

Table 1
Enantiodivergent synthesis of phosphine boranes **15** using chlorophosphine boranes **14**.

Entry	Aminophosphine boranes			Chlorophosphine boranes			Phosphine boranes			
	R^1	R^2		HCl (equiv)	Time (h)		R^3	Yields (%)[a]	e.e. (%)[b]	Conf.
1	Ph	Me	**12a**	2.1	1	**14a**	*o*-An	80	90[b]	(*S*)-**15a**
2	Ph	*o*-An	**12b**	4	1	**14b**	Me	90	98[b]	(*R*)-**15a**
3	Ph	*o*-An	**12b**	4	1	**14b**	Fc	71	95[b]	(*R*)-**15b**
4	Ph	*o*-An	**12b**	4	1	**14b**	*m*-Xyl	79	99[b]	(*S*)-**15c**
5	Ph	Fc	**12c**	15	48	**14c**	*o*-An	79	98[b]	(*S*)-**15b**
6	Ph	*m*-Xyl	**12d**	6	1	**14d**	*o*-An	82	99[b]	(*R*)-**15c**
7	Ph	*i*-Pr	**12e**[c]	5	12	**14e**	Me	68	89[d]	(*R*)-**15d**
8	*i*-Pr	Ph	**12f**[c]	5	12	**14e**	Me	86	96[d]	(*S*)-**15d**

[a] Isolated yields.
[b] Determined by HPLC on a chiral column of the borane complex.
[c] Prepared from (−)-ephedrine (see Scheme 4).
[d] Determined by ^{31}P NMR of the phosphine oxide derivative in presence of reagent **21**.

aminophosphine borane **12b**, then metal-halide exchange with *t*-BuLi reagent, and finally, trapping with methyl iodide (Table 2, entry 1). Noteworthy, the phosphine borane (*S*)-**15a**, obtained in this case, is the enantiomer of that prepared following the route (A) starting from aminophosphine borane **12b** (Table 1, entry 2).

Interestingly, route (B) offers a versatile and efficient pathway for the enantiodivergent synthesis of P-chiro-

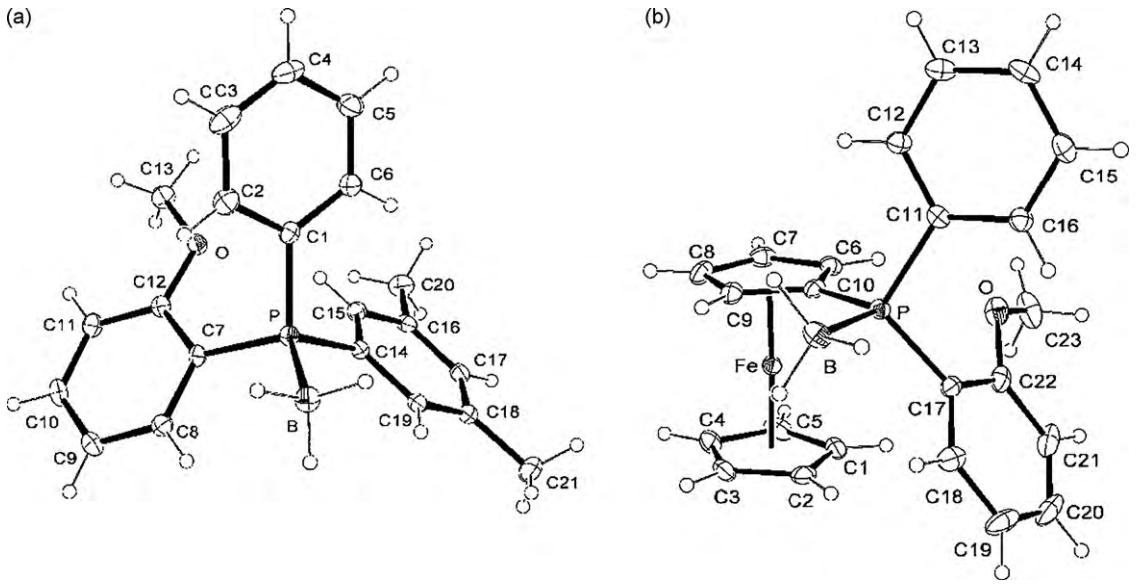


Fig. 1. Crystal structures: (a) Phosphine borane (*R*)-**15c**. Selected bond lengths (Å), angles (°): P-B 1.917(2), P-C(1) 1.8138(18), P-C(7) 1.8170(17), P-C(14) 1.8165(16); C(1)-P-B 109.53(9); C(7)-P-B 111.37(8), C(14)-P-B 113.43(9). (b) Phosphine borane (*R*)-**15b**. Selected bond lengths (Å), angles (°): P-B 1.913(3), P-C(10) 1.793(2), P-C(11) 1.815(2), P-C(17) 1.810(2), Cp(1)-Fe 1.659(2), Cp(2)-Fe 1.645(2); C(10)-P-B 109.87(12), C(11)-P-B 107.82(11), C(17)-P-B 112.83(13), Cp(1)-Fe-Cp(2) 176.86 (12).

Table 2
Enantiodivergent synthesis of phosphine boranes **15** using chlorophosphine boranes **14** as phosphide borane **9** precursors.

Entry	Aminophosphine boranes			Chlorophosphine boranes			Phosphine boranes			
	R^1	R^2		HCl (equiv)	Time (h)		R^3X	Yields (%)[a]	e.e. (%)	Conf.
1	Ph	*o*-An	**12b**	4	1	**14b**	MeI	75	92[b]	(*S*)-**15a**
2	Ph	*i*-Pr	**12e**[c]	5	12	**14e**	MeI	73	96[d]	(*S*)-**15d**
3	*i*-Pr	Ph	**12f**[c]	5	12	**14e**	MeI	71	96[d]	(*R*)-**15d**

[a] Isolated yields.
[b] Determined by HPLC on a chiral column of the borane complex.
[c] Prepared from (−)-ephedrine.
[d] Determined by ^{31}P NMR of the phosphine oxide derivative in presence of reagent **21**.

genic phosphines. Thus, the *i*-propylaminophosphine borane **12e**, which was prepared from the oxazaphospholidine complex (R_p)-**11a**, leads to both enantiomers of the phosphine borane **15d** (Scheme 4a). On the one hand, the acidolysis of **12e** with HCl, which affords the corresponding chlorophosphine-borane intermediate, provides the (*S*)-methylphenyl-*i*-propylphosphine borane **15d** after a metal-halogen exchange using *t*-BuLi reagent, and then trapping with methyl iodide (Scheme 4a; Table 2, entry 2). On the other hand, the (*R*)-methylphenyl-*i*-propylphosphine borane **15d** was obtained according to route (A), after HCl acidolysis of the aminophosphine borane **12e** then reaction with MeLi (Scheme 4; Table 1, entry 7).

The synthesis of both enantiomers of the phosphine borane **15d** was also achieved starting from the phenyl-*i*-propylaminophosphine borane **12f**, readily obtained from the 2-*i*-propyloxazaphospholidine borane **16a**. This new starting complex **16a** was prepared in a diastereomerically pure form by subsequent reactions of PCl_3 with (−)-ephedrine [21], then with *i*-propylmagnesium reagent and finally with BH_3·DMS (Scheme 4b). The relative configuration of the complex **16a** was determined by comparison with the X-Ray structure of the 2-ethyloxazaphospholidine borane **16b** (R^1 = Et). This latter compound was prepared by a similar procedure from (−)-ephedrine, but using ethylmagnesium chloride instead of *i*-propylmagnesium reagent.[5] The reaction of the oxazaphospholidine borane **16a** with the phenyllithium reagent affords the phenyl-*i*-propylaminophosphine borane **12f** by P-O bond cleavage of the heterocycle (Scheme 4b). The X-ray structure of compound **12f** (Fig. 2) proves the stereochemistry of ring-opening process with inversion of configuration on the phosphorus centre (Scheme 4b). After acidolysis with HCl of the epimer **12f**, then metal-halide exchange with *t*-BuLi reagent of the chlorophosphine-borane intermediate, and finally trapping with MeI, the (*R*)-methylphenyl-*i*-propylphosphine borane **15d** was obtained in 71% yield and with 97% e.e. (Scheme 4b; Table 2, entry 3).

Finally, the (*S*)-methylphenyl-*i*-propylphosphine borane **15d** was also obtained from the *i*-propylaminophosphine borane **12f** using route (A), by acidolysis with HCl followed by a reaction with MeLi (Scheme 4; Table 1, entry 8).

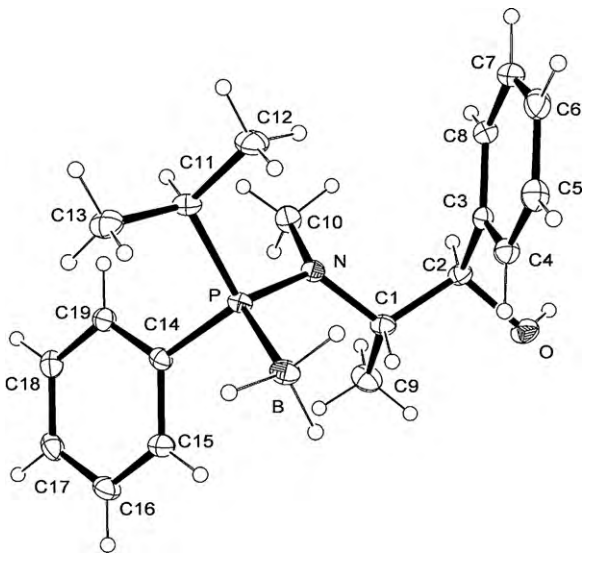


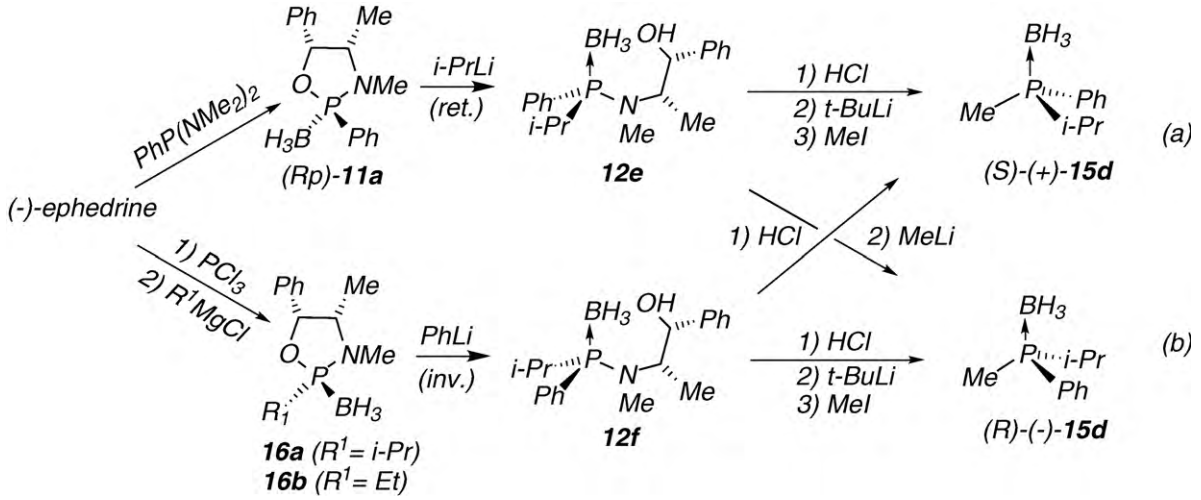
Fig. 2. Crystal structure of aminophosphine borane **12f** with selected bond lengths (Å), angles (°): P-B 1.9206(19); P-N 1.6755(13), P-C(11) 1.8285(16, P-C(14) 1.8263(16; N-P-B 114.47(8); C(11)-P-B 112.31(8), C(14)-P-B 110.93(8), C(1)-N-P 118.35(10), C(1)-N-C(10) 116.03(13), C(10)-N-P 118.84(11).

2.3. Enantiodivergent synthesis of the P-chirogenic 1,2-bis(methylphenylphosphino)ethane **4**

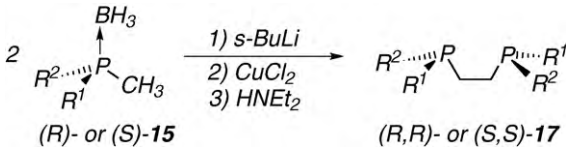
The synthesis of both enantiomers of the P-chirogenic 1,2-bis(diphosphino)ethane **17** can be achieved by a Knowles' like coupling of the corresponding (*R*)- or (*S*)-methylphosphine borane **15**, which are prepared according to one of the approaches described above (Scheme 5) [12a,18].

Preliminary results indicate that the C-C bond coupling can also be achieved with the (*R*)-methylphenylphosphinite borane **10a** affording the corresponding (*R*,*R*)-1,2-bis(phenylphosphinito borane)ethane **18** (Scheme 6a) [21,22]. Interestingly, the reaction of two equivalents of methyl lithium reagent with the compound **18** leads to the (*S*,*S*)-diphosphine diborane **19** and then, to the (*S*,*S*)-(+)-diphosphine **4** after decomplexation of the borane protecting group (Scheme 6a, Table 3, entry 6). The other enantiomer of the diphosphine (*R*,*R*)-(−)-**4** was then prepared using the same pathway, but starting from (−)-ephedrine (Scheme 6b, Table 3, entry 7).

[5] To be published.



Scheme 4.

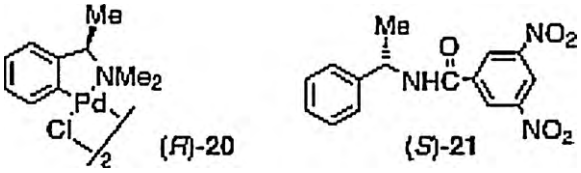


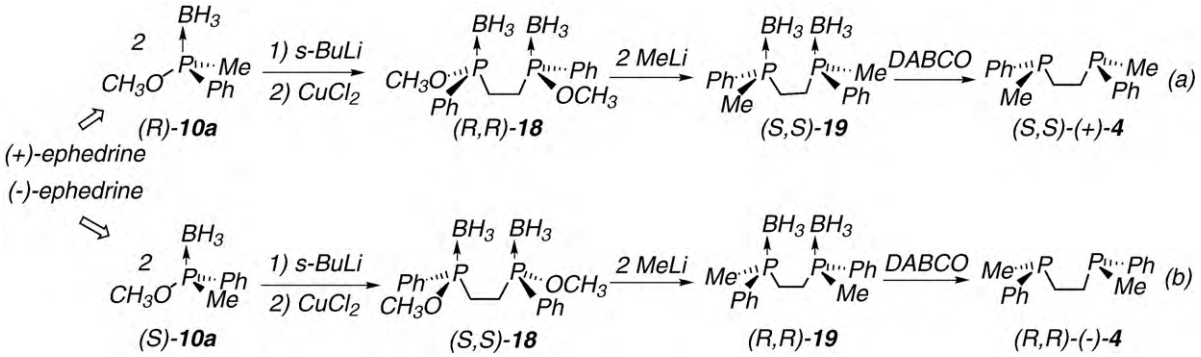
Scheme 5.

The X-ray structure of the (*S,S*)-1,2-bis(phenylphosphinito borane)ethane **18** (Fig. 3), exhibits an unfolded conformation with the substituents disposed anti relative each other. Moreover, the (*S*) absolute configuration of the phosphinite borane fragments is consistent with the retention of the configuration during the C-C bond coupling of the anion resulting from **10a** (Scheme 6).

2.4. Decomplexation of the borane complexes into P-chirogenic mono- and diphosphines

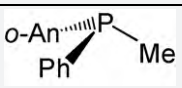
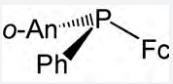
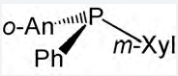
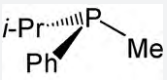
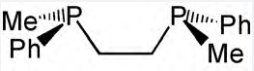
The phosphine borane complexes can directly be used without decomplexation, for the synthesis of quaternary phosphonium salts [23], (thio)phosphorylated derivatives [24], and chiral complexes or catalysts derived from transition metals [25,26b]. When the uncoordinated phosphines are required, the borane decomplexation can be achieved from a reaction with an amine [26], a strong acid [27], EtOH [28] or an olefin [24b,29], to quantitatively lead to the corresponding P(III)-compound with complete retention of configuration on the phosphorus atom. The uncoordinated P-chirogenic mono- **13** and the diphosphine **4** were obtained by heating at 50 °C either in pure diethyl amine, or in toluene in the presence of DABCO. Subsequently, the purification is achieved by fast filtration through neutral alumina (Scheme 2, Table 3). The enantiomeric excesses of the phosphines were determined either by HPLC on a chiral column after an additional complexation with BH_3.DMS, or by ^{31}P NMR in presence of the chiral palladium complex **20** (For the preparation of the chiral palladium complex **19**, see [30a]; For the preparation of N,N-dimethyl-1-phenylethylamine, see [30b]; For the 31P NMR, see [30c]), or by ^{31} P NMR of the phosphine oxide derivatives in presence of the resolving Kagan's reagent **21** [31].





Scheme 6.

Table 3
Preparation of free mono- and diphosphines from their borane complexes.

Entry	Borane complex	Conditions	Mono- and diphosphine				
					$[\alpha]_{D^{20}}$	δ^{31}P NMR	e.e. (%)
1	(*R*)-**15a**	$HNEt_2$ 50 °C/10h		(*R*)-**13a**	+46[a]	−36	98[d]
2	(*S*)-**15b**	DABCO 50 °C/10h		(*S*)-**13b**	−4.8[b]	−28.3	98[d]
3	(*S*)-**15c**	DABCO 50 °C/10h		(*S*)-**13c**	−3.8[b]	−16.9	99[d]
4	(*S*)-**15d**	DABCO 50 °C/10h		(*S*)-**13d**	−10[b]	−19.3	93[e]
5	(*R*)-**15d**	DABCO 50 °C/10h		(*R*)-**13d**	–	–	96[e]
6	(*S,S*)-**18**	DABCO 50 °C/10h		(*S,S*)-**4**	+24.5[b]	–	99[f]
7	(*R,R*)-**18**	DABCO 50 °C/10h		(*R,R*)-**4**	−23.5[c]	−32	99[f]

[a] In MeOH.
[b] In $CHCl_3$.
[c] In CH_2Cl_2.
[d] Determined by HPLC on a chiral column of the borane complex derivative.
[e] Determined by ^{31}P NMR of the phosphine oxide derivative in presence of reagent **21**.
[f] Determined by ^{31}P NMR in presence of chiral palladium complex **20**.

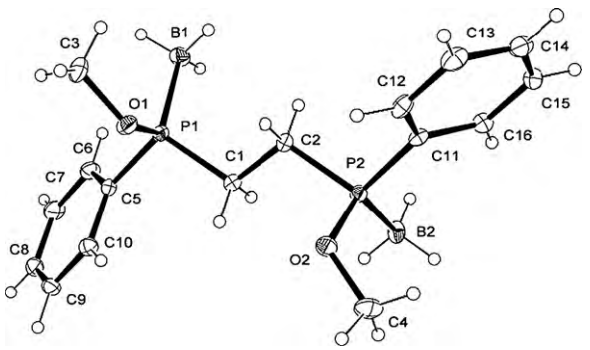


Fig. 3. Crystal structure of the (*S,S*)-diphosphinite diborane **18**. Selected bond lengths (Å), angles (°): (a) P(1)-C(1) 1.806(3), P(2)-C(2) 1.804(3), P(1)-C(5) 1.803(3), P(2)-C(11) 1.805(3), P(1)-O(1) 1.607(3), P(2)-O(2) 1.600(2), P(1)-B(1) 1.895(3), P(2)-B(2) 1.889(4); O(1)-P(1)-C(1) 99.90(14), O(2)-P(2)-C(2) 99.42(13), O(1)-P(1)-C(5) 106.13(13), O(2)-P(2)-C(11) 105.77(14), O(1)-P(1)-B(1) 116.66(17), O(2)-P(2)-B(2) 116.19(16).

3. Conclusion

Several approaches for the enantiodivergent syntheses of P-chirogenic mono- and diphosphines were described, using the convenient ephedrine methodology and the borane complex chemistry.

Since the two enantiomers of ephedrine are available, the stereoselective synthesis of both enantiomers of mono- or diphosphine is easily performed. Furthermore, both enantiomers of a phosphine ligand can also be obtained, starting from the same oxazaphospholidine borane complex derived from (+)-ephedrine, when changing the order of addition of the organolithium reagents during the synthetic pathway.

An alternate approach is based on the P-chirogenic chlorophosphine boranes, which afford one enantiomer of a phosphine borane with inversion of configuration, by a reaction with an organolithium reagent. On the other hand, the chlorophosphine boranes also provide the corresponding P-chirogenic phosphide boranes **9** with retention of configuration on the phosphorus atom, by an unexpected metal-halogen exchange using the *t*-butyllithium reagent. The addition of alkyl halide to the resulting phosphide boranes then affords the corresponding phosphine boranes, but with opposite configuration.

A third approach is based on the stereoselective synthesis of the starting oxazaphospholidine borane complex derived from (−)-ephedrine. In the case where this complex is prepared using the bis(dimethylamino)-phosphine, the absolute configuration of phosphorus centre is (*R*). When it is prepared by subsequent reactions of (−)-ephedrine with PCl_3, and then with a Grignard

reagent, the configuration of the phosphorus centre is (*S*). Consequently, depending on the method for the preparation of the starting oxazaphospholidine borane, the convenient synthesis can provide either phosphine enantiomers.

Finally, the synthesis of (*R*,*R*)- and (*S*,*S*)-1,2-bis(methylphenylphosphino)ethane **4** was also described, using both P-chirogenic diphosphinite diborane **18** enantiomers prepared from (+)- or (−)-ephedrine.

In summary, the efficiency of the ephedrine methodology is again highlighted by offering several approaches for the synthesis of both enantiomeric P-chirogenic mono- and diphosphines in the desired absolute configuration, notably bearing alkyl substituents.

4. Experimental section

All reactions were carried out under an Ar atmosphere in dried glassware. Solvents were dried and freshly distilled under an Ar atmosphere over sodium/benzophenone for THF, diethylether, toluene and benzene, CaH_2 for CH_2Cl_2. Hexane and isopropanol for HPLC were of chromatography grade and used without further purification. Methyllithium (1.6 M in Et_2O), *s*-butyllithium (1.4 M in cyclohexane), *t*-butyllithium (1.6 M in pentane), phenyllithium (1.8 M in Bu_2O), isopropyllithium (0.7 M in pentane), isopropylmagnesium chloride (2 M in THF), ethylmagnesium chloride (2 M in THF), ferrocene, 2-bromoanisole, 5-bromo-*m*-xylene, methyl iodide, $BH_3.SMe_2$, *N*-methyl morpholine and 1,4-diazabicyclo[2.2.2]octane (DABCO) were purchased from Aldrich, Acros or Alfa Aesar, and used as received. (+)- and (−)-ephedrine were purchased from Aldrich and dried by azeotropic shift of toluene on rotary evaporator. Phosphorus trichloride was distilled and $CuCl_2$ dried at 100 °C for 12 h, before use. The solution of HCl in toluene (0.2–0.4 M) was obtained by bubling HCl gas in toluene and titrated by acidimetry before use. The (2*S*, 4*R*, 5*S*)-(−)-3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphospholidine-2-borane **11a** and its enantiomer (2*R*, 4*S*, 5*R*)-(+)-**11a**, were prepared from the appropriate (+)- or (−)-ephedrine, as previously described [19a].

The (S_p)-(+)-*N*-methyl-*N*-[(1*S*,2*R*)(1-hydroxy-2-methyl-1-phenyl-2-propyl)]aminomethylphenyl phosphine borane **12a** and (R_p)-(+)-*N*-methyl-*N*-[(1*S*,2*R*)(1-hydroxy-2-methyl-1-phenyl-2-propyl)] amino-*o*-anisylphenylphosphine borane **12b** were prepared from the (+)-ephedrine according to the published procedure [19c]. (*R*)-(+) and (*S*)-(−)-[(O-methyl)-methylphenylphosphinite]borane **10a** were obtained as previously described, starting from the (+)- and (−)-ephedrine respectively [18(a,b),26c,32]. Chiral HPLC analysis were performed on SHIMADZU 10-series apparatus, using chiral columns (Chiralcel OK, Chiralcel OD, Chiralcel OD-H, Chiralpack AD, Chiralcel OJ, Lux 5 μ-cellulose-2), and with hexane/propan-2-ol mixtures as the mobile phase (Flow rate 1 mL min^{-1}; UV detection λ = 254 nm). Thin layer chromatography (TLC) was performed on 0.25 mm E. Merck precoated silica gel plates and exposed by UV, potassium permanganate or iodine treatment. Flash chromatography was performed with the indicated solvents using silica gel 60 A, (35–70 μm; Acros) or aluminium oxide 90 standardized (Merck). All NMR spectra data were recorded on BRUKER AM 250, 300 AVANCE, 500 AVANCE DRX and 600 AVANCE II spectrometers at ambient temperature. Data are reported as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, brd = broad doublet, dhept = - doublet of heptuplet, coupling constant(s) in Hertz. Melting points were measured on a Kofler bench melting point apparatus and are uncorrected. Optical rotations values were recorded at 20 °C on a Perkin-Elmer 341 polarimeter, using a 10 cm quartz vessel. Infrared spectra were recorded on a Bruker Vector 22 apparatus. Mass and HRMS spectra were recorded on Mass, Bruker ESI micro TOF-Q apparatus, at the Université de Bourgogne (Dijon). The major peak m/z was 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 Universités P. & M. Curie (Paris) and Bourgogne (EA 1108 CHNS-O FISONS Instrument). X-Ray analyses were performed at the Université de Bourgogne, and the data were collected at 115 K on a Bruker Nonius Apex II CCD system using graphite-monochromated Mo-Kα radiation. The structures were solved by direct methods (SIR92)[33] and refined with full-matrix least-squares methods based on F^2 (SHELXL-97)[34] with the aid of the WINGX program [35]. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were either included in theirs calculated positions or found in Fourier difference maps (CH_3 and BH_3). Crystallographic data and structures refinement details for **12f**, **15c**, **15d** and **18** are summarized in Table 4.

CCDC 768724, 768725, 768726 and 768727 contain the supplementary crystallographic data for **15d**, **15c**, **18**, **12f**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

4.1. Synthesis of (2S,4S,5R)-(−)-2-isopropyl-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine borane *16a*

A 250 mL Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with 50 mL of toluene and 2.8 mL (25.8 mmol) of *N*-methylmorpholine. Addition of PCl_3 (1.12 mL, 12.9 mmol) was smoky and the resulting solution was cooled to −78 °C. Then (−)-ephedrine (2.1 g, 12.9 mmol) in 10 mL of toluene was added dropwise via syringe. The reaction was allowed to reach room temperature overnight and *N*-methylmorpholine hydrochloride was filtered under argon. The resulting crude solution (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine was used further without purification. ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 168.6 ([20] + 172.4).

A 250 mL Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with crude solution of (2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine in toluene. The mixture was cooled to −60 °C and 8 mL of isopropylmagnesium chloride (2 M in THF; 16.1 mmol) was added. Reaction was stirred at this

Table 4
Crystallographic data and structures refinement details for **12f**, **15c**, **15d** and **18**.

Compounds	**12f**	**15c**	**15d**	**18**
Empirical formula	$C_{19}H_{29}BNOP$	$C_{21}H_{24}BOP$	$C_{23}H_{24}BFeOP$	$C_{16}H_{26}B_2O_2P_2$
Formula weight	329.21	334.18	414.05	333.93
Temperature (K)	115(2)	115(2)	110(2)	115(2)
Crystal system	Orthorhombic	Orthorhombic	Monoclinic	Monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P2_1$
a (Å)	8.2195(4)	10.0720(2)	8.5691(3)	10.9431(5)
b (Å)	14.5616(6)	12.8584(3)	10.4833(3)	8.6606(6)
c (Å)	16.1165(8)	14.5612(3)	11.6417(4)	10.8797(8)
α (°)	90	90	90	90
β (°)	90	90	106.7440(10)	90.906(4)
γ (°)	90	90	90	90
Volume (Å^3)	1928.97(16)	1885.82(7)	1001.46(6)	946.19(11)
Z	4	4	2	2
$\rho_{calc.}$ (g/cm^3)	1.134	1.177	1.373	1.172
μ (mm^{-1})	0.146	0.150	0.842	0.232
Size (mm^3)	0.32 × 0.30 × 0.12	0.20 × 0.20 × 0.18	0.40 × 0.30 × 0.20	0.25 × 0.05 × 0.05
F(000)	712	712	432	356
λ	0.71073	0.71073	0.71073	0.71073
sin(θ)/ λ max; Å^{-1}	0.65	0.65	0.65	0.65
Index ranges	h: −10; 10 k: −18; 18 l: −20; 20	h: −13; 13 k: −16; 16 l: −18; 18	h: −11; 10 k: −13; 13 l: −15; 14	h: −12; 13 k: −8; 11 l: −14; 14
Reflection collected	4310	4307	6351	3302
R_{int}	0.017	0.023	0.024	0.026
Reflection with $I \geq 2\sigma$ (I)	4180	3796	3950	3132
Data/restraints/parameters	4310/0/214	4307/0/223	4472/1/248	3302/1/200
R indices ($I \geq 2\sigma$ [I])	$R1$ = 0.0341[a] $wR2$ = 0.0773[b]	$R1$ = 0.0364[a] $wR2$ = 0.0816[b]	$R1$ = 0.0329[a] $wR2$ = 0.0614[b]	$R1$ = 0.0439[a] $wR2$ = 0.0939[b]
R indices (all data)	$R1$ = 0.0362[a] $wR2$ = 0.0792[b]	$R1$ = 0.0464[a] $wR2$ = 0.0855[b]	$R1$ = 0.0427[a] $wR2$ = 0.0644[b]	$R1$ = 0.0481[a] $wR2$ = 0.0981[b]
Goodness-of-fit[c] on F^2	1.082	1.045	1.046	1.082
Absolute structure parameters	0.04(8)	0.04(8)	0.000(13)	0.00(14)
$\Delta\rho$ (e Å^{-3})	0.200 and −0.180	0.181 and −0.311	0.217 and −0.286	0.291 and −0.242
CCDC deposition No.	768 727	768 725	768 724	768 726

[a] $R1 = \Sigma(||F_o|-|F_c||)/\Sigma|F_o|$.
[b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2 / \Sigma[w(F_o^2)^2]^{1/2}$ where $w = 1/[\sigma^2(F_o^2 + (0.0228P)^2 + 0.85P]$ for **12f**, $w = 1/[\sigma^2(F_o^2 + (0.0387P)^2 + 0.39P]$ for **15c**, $w = 1/[\sigma^2(F_o^2 + (0.0182P)^2 + 0.11P]$ for **15d** and $w = 1/[\sigma^2(F_o^2 + (0.0149P)^2 + 0.12P]$ for**18**.
[c] $S = [\Sigma w(F_o{}^2\text{-}F_c{}^2)^2/(n\text{-}p)]^{1/2}$ (n = number of reflections, p = number of parameters).

temperature for 1 h and then 2 mL of BH_3·BMS complex were added. After 1 h under stirring, the mixture was hydrolyzed at −60 °C, and the aqueous layer was extracted with CH_2Cl_2. Combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel with a mixture hexane/CH_2Cl_2 (15:10) as eluent to afford the oxazaphospholidine borane complex **16a** as a mixture of epimers in a 20:1 ratio (1.76 g, 55% yield). Crystallisation from hexane gives 1.4 g (43%) of the major isomer **16a**.

$[\alpha]_{D^{20}} = -12.3$ (c 1.9, $CHCl_3$); mp = 50 °C; IR (ν cm^{-1}): 3035, 2978, 2859, 2402, 2372, 2344, 1460, 1385, 1290, 1226, 1190, 965, 875, 836, 739; ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.0–0.90 (m, 3H), 0.59 (d, J = 6.7 Hz, 3H), 1.03 (dd, J = 15.4 and 7.2 Hz, 3H), 1.05 (dd, J = 15.4 and 7.2 Hz, 3H), 1.82 (dhept, J = 9.0 and 7.2 Hz, 1H), 2.58 (d, J = 9.4 Hz, 3H), 3.55 (dq, J = 17.1 and 6.5 Hz, 1H), 5.35 (dd, J = 5.8 and 1.6 Hz, 1H), 7.10- 7.23 (m, 5H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 156.1 (q, J = 75.8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.9 (d, J = 1.8 Hz), 15.8 (d, J = 2.2 Hz), 16.2, 30.5 (d, J = 8.1 Hz), 31.7 (d, J = 29.1 Hz), 60.0 (d, J = 2.4 Hz), 84.2 (d, J = 7.4 Hz), 126.3, 126.2, 128.4, 136.5 (d, J = 5.9 Hz); HRMS (ESI) calcd for $C_{13}H_{23}BNNaOP$ [M + Na]$^+$: 274.1505; found: 274.1470.

4.2. Synthesis of the aminophosphine boranes **12**

4.2.1. Preparation of organolithium reagents

4.2.1.1. Aryllithium reagents by metal-halogen exchange. In a two necked-flask equipped with a magnetic stirrer and an argon inlet, 1 equiv. of *sec*-butyllithium is added. The mixture is cooled to 0 °C and 1 equiv. of 1-bromoanisole (1-bromonaphthalene or bromobenzene) is slowly added with a syringe while stirring. After the formation of a white precipitate, the mixture is stirred for 1 h at 0 °C. The organolithium reagent is dissolved with a minimum of dry THF before use.

4.2.1.2. Preparation of ferrocenyllithium by deprotonation of the ferrocene. A 250 mL three-necked flask equipped with a magnetic stirrer under an argon atmosphere was charged with ferrocene (0.74 g, 4 mmol) and THF (10 mL). At 0 °C, *t*-BuLi (2.75 mL, 1.6 M in hexane, 4.4 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 1 h, before use.

4.2.2. General procedure

In a 100 mL three-necked flask, equipped with a magnetic stirrer and an argon inlet, 5 mmol of the oxazaphospholidine

borane complex **11a** were dissolved in 5 mL of anhydrous THF. The mixture was cooled at −78 °C and 2 equiv. (10 mmol) of the organolithium reagent were slowly added. The resulting mixture was stirred and warmed to 0 °C (or RT) until the starting material had completely reacted. The reaction was monitored by TLC over silica (CH_2Cl_2 as eluent), and was finally hydrolyzed at 0 °C with 2 mL of water. The THF was removed under reduced pressure and the aqueous layer was extracted several times with dichloromethane. The combined organic phases were dried over $MgSO_4$ and the solvent was removed. The residue was purified on a short column of silica gel, using a mixture of toluene/AcOEt 95:5 as eluent, to afford the aminophosphine boranes **12**. The aminophosphine boranes can be recrystallized using a mixture hexane/isopropanol 7:3.

*4.2.3. (R_p)-(+)-N-methyl-N-[(1S,2R)(1-hydroxy-1-phenyl-prop-2-yl]aminoferrocenylphenyl phosphine borane **12c** (from (S_p)-**11a**)*

Yield = 80%; Orange crystals; $[\alpha]_{D^{20}} = +113.9$ (*c* 1.0, $CHCl_3$); R_f = 0.62 (toluene/EtOAc [9:1]); IR (KBr, ν cm^{-1}): 3500 (O-H), 2372 (B-H), 1455, 1437, 1386, 1367, 1217, 1163, 1106, 1063, 1022, 998, 956, 884, 822, 763, 746, 721, 698, 646, 614; ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.20–2.00 (m, 3H), 0.91 (d, *J* = 6.3 Hz, 3H), 2.05 (brs, 1H), 2.38 (d, *J* = 8.4 Hz, 3H), 4.16–4.25 (m, 1H), 4.23–4.27 (m, 1H), 4.30 (brs, 5H), 4.51 (d, *J* = 11.7 Hz, 2H), 4.58–4.62 (m, 1H), 4.87 (d, *J* = 5.7 Hz, 1H), 7.28–7.46 (m, 10H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 70.7 (m); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 13.7, 31.3, 40.3, 58.4 (d, *J* = 10.6 Hz), 70.9, 71.9, 73.0, 79.6, 127.3, 128.4, 128.8, 128.9, 129.1, 131.1, 132.2 (d, *J* = 9.8 Hz), 143.3; Anal. calcd for $C_{26}H_{31}BFeNOP$ (471.17): C 66.28, H 6.63, N 2.97; found: C 66.33, H 6.83, N 3.02.

*4.2.4. (R_p)-(−)-N-methyl-N-[(1S,2R)(1-hydroxy-1-phenyl-prop-2-yl]aminophenyl-m-xylylphosphine borane **12d** (from (S_p)-**11a**)*

Yield = 70%; White crystals; $[\alpha]_{D^{20}} = -47$ (*c* 0.6, $CHCl_3$); mp = 124 °C; R_f = 0.12 (toluene); IR (KBr, ν cm^{-1}): 3549 (O-H), 3055–2796 (C–H), 2394 (B–H), 1596, 1455, 1438, 1270, 1160, 1065, 1037; ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.20–2.00 (m, 3H), 1.27 (d, *J* = 6.5 Hz, 3H), 1.90 (bs, 1H), 2.33 (s, 6H), 2.51 (d, *J* = 7.8 Hz, 3H), 4.30 (m, 1H), 4.83 (brs, 1H), 7.13 (brs, 1H), 7.17–7.24 (m, 3H), 7.28 (brs, 1H), 7.30–7.36 (m, 4H), 7.38–7.40 (m, 1H,), 7.42–7.48 (m, 3H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 70.5 (brd, *J* = 82.7 Hz); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 13.4, 21.4, 30.4 (d, *J* = 3.6 Hz), 58.1 (d, *J* = 9.9 Hz), 78.8 (d, *J* = 5.6 Hz), 126.7, 127.9, 128.2 (d, *J* = 10.2 Hz), 128.5, 129.9 (d, *J* = 10.2 Hz), 130.5 (d, *J* = 2.1 Hz), 131.2 (d, *J* = 31.5 Hz), 132.0 (d, *J* = 10.7 Hz), 138.0 (d, *J* = 10.7 Hz), 142.5; MS (EI) *m/z* (relative intensity) 805 (2 M^+ + Na; 15), 414 (M^+ + Na; 100), 392 (M^+ + H; 13); HRMS (ESI) calcd for $C_{24}H_{31}BNNaOP$ [M + Na^+]: 392.23091; found: 392.23095; Anal. calcd for $C_{24}H_{31}BNOP$ (391.302): C 73.67, H 7.99, N 3.58; found: C 73.90, H 8.02, N 3.56.

*4.2.5. (R_p)-(+)-N-methyl-N-[(1R,2S)(1-hydroxy-1-phenyl-prop-2-yl]aminophenyl-i-propyl phosphine borane **12e** (from (R_p)-**11a**)*

Yield = 80%; Colorless oil; $[\alpha]_{D^{20}} = +31.7$ (*c* 0.6, $CHCl_3$); R_f = 0.25 (CH_2Cl_2); IR (ν cm^{-1}): 3510 (O-H), 2974–2874 (C-H), 2380 (B-H), 1453, 1436, 1386, 1220, 1173, 1107, 1071, 1023, 1005, 955, 914, 884, 742, 727, 698, 645, 619, 582; ^{1} H NMR ($CDCl_3$, 300.13 MHz) δ 0.10–0.90 (m, 3H), 0.96 (dd, *J* = 17.1 and 7.2 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 1.09 (dd, *J* = 15.3 and 7.2 Hz, 3H), 2.50 (d, *J* = 7.2 Hz, 3H), 2.47–2.61 (m, 1H), 3.97-–4.09 (m, 1H), 4.68 (d, *J* = 4.8 Hz, 1H), 7.07–7.19 (m, 3H), 7.23–7.37 (m, 5H), 7.46 (m, 2H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 76.4; ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 12.9 (d, *J* = 3.8 Hz), 17.5 (d, *J* = 5.3 Hz), 22.8 (d, *J* = 44.5 Hz), 29.9 (d, *J* = 3.0 Hz), 59.1 (d, *J* = 7.6 Hz), 79.2 (d, *J* = 2.3 Hz), 126.7, 128.1, 128.9, 129.0 (d, *J* = 2.3 Hz), 131,7 (d, *J* = 55.9 Hz), 131.8 (d, *J* = 9.1 Hz), 143.2; MS (EI) *m/z* (relative intensity) 352 (M^+ + Na; 100), 338 (M^+ - BH_3 + Na; 95); HRMS (ESI) calcd for $C_{19}H_{29}BNNaOP$ [M + Na]$^+$ 352.1962; found: 352.1976.

*4.2.6. (S_p)-(+)-N-methyl-N-[(1R,2S)(1-hydroxy-1-phenyl-prop-2-yl]aminophenyl-i-propyl phosphine borane **12f***

A 50 mL Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with 15 mL of THF and 0.75 g (3 mmol) of (2*S*,4*S*,5*R*)-(−)-*2-isopropyl-3,4-dimethyl-5-phenyl-1,3,2-oxaza phospholidine borane* **16a** (major isomer). The mixture was cooled to −78 °C and 3.33 mL (6 mmol) of phenyllithium was added and stirred overnight at ambient temperature. After hydrolysis at 0 °C, the aqueous layer was extracted with CH_2Cl_2 and the organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using CH_2Cl_2 as eluent, to afford the aminophosphine borane **12f** as a mixture of epimers in a 9:1 ratio (0.81 g, 82% yield). Crystallisation from hexane:isopropanol (7:3) affords 0.51 g (52%) of major isomer **12f**.

$[\alpha]_{D^{20}} = -14.8$ (*c* 1.1, $CHCl_3$); mp 130 °C; IR (ν cm^{-1}): 3510 (OH), 2417 (BH), 2375 (BH), 2343 (BH), 1387, 1103, 1018, 999, 743, 723, 698, 585. ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.1- 0.90 (m, 3H), 0.99 (dd, *J* = 15.4 and 7.3 Hz, 3H), 1.03 (dd, *J* = 15.4 and 7.3 Hz, 3H), 1.88 (bs, 1H), 2.53 (d, *J* = 8.4 Hz, 3H), 2.63 (dhept, *J* = 16.3 and 7.1 Hz, 1H), 4.11 (dhept, *J* = 6.8 and 1.2 Hz, 1H), 4.78 (d, *J* = 5.2 Hz, 1H), 7.24- 7.52 (m, 8H), 7.70–7.76 (m, 2H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 76.3 (brd, *J* = 88 Hz); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 12.1, 15.6, 16.8 (d, *J* = 5.4 Hz), 21.5 (d, *J* = 47.4 Hz), 29.1 (d, *J* = 3.5 Hz), 58.0 (d, *J* = 7.0 Hz), 78.7 (d, *J* = 6.3 Hz), 126.4, 127.6, 128.3, 128.4, 128.5, 130.5 (d, *J* = 47.8 Hz), 130.9 (d, *J* = 2.3 Hz), 131.4 (d, *J* = 7.1 Hz), 142. HRMS (ESI) calc. for $C_{19}H_{29}BNNaOP$ [M^+ + Na] 352.19755; found 352.19823.

*4.3. Preparation of the chlorophenylphosphine borane **14***

4.3.1. General procedure

In a 50 mL two-necked flask equipped with a magnetic stirrer, an argon inlet and a septum was introduced 2 mmol of the aminophosphine borane **12**. A solution of HCl in toluene was then added under stirring at room temperature, without previous dissolution of the compound **12** (see conditions, Table 1). After reaction (Table 1), the precipitate of ephedrine hydrochloride was filtred off on Millipore 4 μm filter, and the excess of HCl was removed by several vacuum/argon cycles. The toluene solution of chlorophosphine borane **14** obtained was immediately used without

further purification in highly stereoselective synthesis. For their analyses, the chlorophosphine boranes **14** were obtained after evaporation of toluene and purification by filtration on a short column of silica gel.

*4.3.2. (R)-(+)-Chloromethylphenylphosphine borane **14a***

14a was prepared from the aminophosphine borane **12a** derived from the (+)-ephedrine, according to the literature [19c].

*4.3.3. (S)-o-Anisylchlorophenylphosphine borane **14b** (from **12b** derived from the (+)-ephedrine)*

Yield = 99%; colorless oil; R_f = 0.80 (toluene); ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.40–2.20 (m, 3H), 3.63 (s, 3H), 6.91 (dd, J = 8.3 and 4.6 Hz, 1H), 7.11 (td, J = 7.6 and 2.6 Hz, 1H), 7.39–7.61 (m, 4H), 7.72–7.82 (m, 2H), 7.95 (ddd, J = 14.9, 7.7 and 1.6 Hz, 1H); ^{31}P NMR ($CDCl_3$, + 121.5 MHz) δ + 91.9 (brd, J = 51.4 Hz); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 55.7, 112.0 (d, J = 4.4 Hz), 117.6 (d, J = 47.7 Hz), 121.1 (d, J = 12.3 Hz), 128.5 (d, J = 11.5 Hz), 128.7 (d, J = 50.8 Hz), 131.1 (d, J = 12.9 Hz), 132.0 (d, J = 2.6 Hz), 134.6 (d, J = 14.3 Hz), 135.5 (d, J = 1.8 Hz), 161.1 (d, J = 2.4 Hz); MS (EI) *m/z* (relative intensity): 263 (M-H$^+$; 9), 250 (M$^+$-BH_3; 100), 215 (40), 183 (35), 107 (20), 91 (40), 77 (10); HRMS (ESI) calcd for $C_{13}H_{12}ClOP$ [M$^+$-BH_3]: 250.0314; found: 250.0298.

*4.3.4. (S)-Chloroferrocenylphenylphosphine borane **14c** (from **12c** derived from the (+)-ephedrine)*

Yield = 80%; orange oil; R_f = 0.50 (petroleum ether/AcOEt [3:1]); ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.60–1.80 (m, 3H), 4.20 (s, 5H), 4.44–4.49 (m, 2H), 4.54–4.55 (m, 1H), 4.56–4.64 (m, 1H), 7.41–7.48 (m, 3H), 7.77–7.84 (m, 2H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 93.3 (brs); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 70.6, 71.3 (d, J = 60.0 Hz), 71.4 (d, J = 10.2 Hz), 72.7 (d, J = 9.0 Hz), 72.8 (d, J = 8.6 Hz), 73.1 (d, J = 15.3 Hz), 128.7 (d, J = 11.0 Hz), 131.2 (d, J = 12.2 Hz), 132.4 (d, J = 2.4 Hz), 132.4 (d, J = 50.7 Hz); MS (EI) *m/z* (relative intensity): 346 (M-Cl + O + Na$^+$; 15), 333 (M-BH_3-Cl + O + Na$^+$; 100); HRMS (ESI) calcd for $C_{16}H_{17}BClNaFeP$ [M$^+$ + Na]: 365.0095; found: 365.0090.

*4.3.5. (S)-Chlorophenyl-m-xylylphosphine borane **14d** (from **12d** derived from the (+)-ephedrine)*

The resulting crude solution of chlorophosphine borane **14d** was used without further purification. ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 93.5 (brs).

*4.3.6. (S)-Chlorophenyl-i-propylphosphine borane **14e** (from **12e** derived from the (−)-ephedrine)*

Yield = 78%; colorless oil; R_f = 0.60 (petroleum ether/AcOEt [3:1]); ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.50–1.60 (m, 3H), 1.12 (dd, J = 19.1 and 7.1 Hz, 3H), 1.28 (dd, J = 17.7 and 7.0 Hz, 3H), 2.39–2.51 (m, 1H), 7.49–7.62 (m, 3H), 7.83–7.90 (m, 2H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 113.4 (brs); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 16.8, 17.2 (d, J = 3.0 Hz), 33.2 (d, J = 24.9 Hz), 129.5 (d, J = 10.6 Hz), 132.3 (d, J = 11.3 Hz), 133.3 (d, J = 2.3 Hz), 133.6 (d, J = 51 Hz); MS (EI) *m/z* (relative intensity): 191 (M-Cl-BH_3 + O + Na$^+$; 100).

The *(R)-Chlorophenyl-i-propylphosphine borane* **14e**, which was prepared from **12f** and the (−)-ephedrine, exhibits satisfactory analytical data in agreement with the (*S*)-enantiomer described before.

*4.4. Preparation of phosphine boranes **15** from chlorophosphine boranes **14** (Route A)*

4.4.1. General procedure

To a solution of chlorophosphine borane **14** in toluene cooled at −78 °C was added the organolithium reagent (2.5 equiv). The reaction mixture was let to warm to RT during 1 h, then hydrolysed with water (20 mL). The organic phase was removed and the aqueous layer was extracted with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$, then concentrated. The residue was purified by chromatography on a short column of silica gel with toluene/petroleum ether: 7/3 as eluent, to afford the phosphine boranes **15**. Their recrystallisation in a mixture hexane/*i*-PrOH, affords the enantiomerically pure phosphine boranes **15**.

*4.4.2. (S)-(+)- and (R)-(−)-o-Anisylmethylphenylphosphine borane **15a***

15a were prepared from **14a** and **14b** respectively, according to the literature [19a]. This compound exhibit satisfactory analytical data in agreement with the recent ones reported in § 4.5.2.

*4.4.3. (S)-(−)-o-Anisylferrocenylphenylphosphine borane **15b** (from **12c** derived from the (+)-ephedrine)*

Yield = 79%; orange solid; $[\alpha]_D^{25} = -70.3$ (c 1.0, $CHCl_3$) for 98% e.e.; mp = 140 °C; R_f = 0.46 (toluene); ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.50–1.60 (m, 3H), 3.47 (s, 3H), 4.02 (s, 5H), 4.47–4.54 (m, 3H), 4.67–4.70 (m, 1H), 6.86–6.89 (m, 1H), 7.03–7.09 (m, 1H), 7.31–7.39 (m, 3H), 7.46–7.56 (m, 3H), 7.75–7.82 (m, 1H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 14.9 (brs); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 55.9, 69.1 (d, J = 70.3 Hz), 70.4, 72.0 (d, J = 8.2 Hz), 72.3 (d, J = 7.6 Hz), 74.0 (d, J = 8.4 Hz), 74.5 (d, J = 11.9 Hz), 111.3 (d, J = 63.4 Hz), 112.4 (d, J = 4.4 Hz), 120.8 (d, J = 25.9 Hz), 121.5 (d, J = 11.5 Hz), 128.5 (d, J = 10.5 Hz), 129.1 (d, J = 28.4 Hz), 130.5 (d, J = 2.4 Hz), 131.9 (d, J = 9.9 Hz), 133.2 (d, J = 62.8 Hz), 134.1 (d, J = 10.7 Hz), 136.1 (d, J = 12.3 Hz), 161.5; Anal, calcd for $C_{23}H_{24}FeBOP$ (414.075): C 66.72, H 5.84; found: C 66.96, H 6.01.

The enantiomeric excess of *o*-anisylferrocenylphenylphosphine borane **15b** was determined by HPLC analysis on a Chiralcel AD column, eluent: hexane/*i*-PrOH (98:2), 1 mL/min, λ = 254 nm: (*R*)-**15b**, t_R = 11.6 min; (*S*)-**15b**, t_R = 12.3 min.

The *(R)-(+)-o-anisylferrocenylphenylphosphine borane* **15b**, prepared from **12b** derived from the (+)-ephedrine, exhibits satisfactory analytical data in agreement with the (*S*)-enantiomer: Yield = 71%; $[\alpha]_{D^{25}} = +67.2$ (*c* 0.6, $CHCl_3$) for 95% e.e.

*4.4.4. (R)-(−)-o-Anisylphenyl-m-xylylphosphine borane **15c** (from **12d** derived from the (+)-ephedrine)*

Yield = 82%; white solid; $[\alpha]_{D^{20}} = -9.6$ (*c* 1.0, $CHCl_3$) for 99% e.e.; mp: 174–176 °C; R_f = 0.46 (toluene); ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.60–1.80 (m, 3H), 2.32 (s, 6H), 3.57 (s, 3H), 6.92–6.96 (m, 1H), 7.05–7.22 (m, 2H), 7.26–7.28

(m, 2H), 7.41–7.67 (m, 7H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 18.1 (brs); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 22.0, 55.9, 112.4 (d, J = 4.6 Hz), 117.8 (d, J = 56.5 Hz), 121.8 (d, J = 11.3 Hz), 128.9 (d, J = 10.4 Hz), 129.5 (d, J = 59.9 Hz), 130.6 (d, J = 60.3 Hz), 131.1 (d, J = 9.9 Hz), 131.2 (d, J = 2.4 Hz), 133.2 (d, J = 2.5 Hz), 133.5 (d, J = 9.8 Hz), 134.3 (d, J = 1.9 Hz), 136.7 (d, J = 11.5 Hz), 138.5 (d, J = 11.0 Hz), 162.1; HRMS (ESI) calcd for $C_{21}H_{24}BOP$: 334.1733; found: 334.1746. Anal, calcd for $C_{21}H_{24}BOP$ (334.166): C 75.45, H 7.19; found: C 75.50, H 7.41.

The enantiomeric excess of *o*-anisylphenyl-*m*-xylylphosphine borane **15c** was determined by HPLC analysis on a Chiralcel OK column, eluent: hexane/*i*-PrOH 80:20, 40 °C, 0.5 mL/min, λ = 254 nm: (*R*)-**15c**, t_R = 9.00 min; (*S*)-**15c**, t_R = 17.35 min.

The *(S)-(+)-o-anisylphenyl-m-xylylphosphine borane* **15c**, prepared from **12b** derived from the (+)-ephedrine, exhibits satisfactory analytical data in agreement with the (*R*)-enantiomer: Yield = 79%; $[\alpha]_D^{20} = +10.0$ (*c* 1.0, $CHCl_3$) for 99% e.e..

4.4.5. (S)-(+)-Methylphenyl-i-propylphosphine borane **15d** (from **12f** derived from the (−)-ephedrine)

Yield = 86%; colorless oil; $[\alpha]_{D^{20}} = +17.6$ (c 1.4, $CHCl_3$) for 96% e.e.; R_f = 0.75 (petroleum ether/ ethyl acetate [10:1]); IR (ν cm^{-1}) 3207, 2963, 2925, 2873, 2374 (BH), 1463, 1437, 1416, 1262, 1096, 1020, 799, 553, 540, 530; ^{1}H NMR ($CDCl_3$, 300.13 MHz) δ 0.10–0.90 (m, 3H), 1.02 (dd, J = 15.9 and 7.2 Hz, 3H), 1.15 (dd, J = 15.6 and 7.2 Hz, 3H), 1.54 (d, J = 10.2 Hz, 3H), 2.02–2.11 (m, 1H), 7.46–7.48 (m, 3H), 7.68–7.73 (m, 2H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 16.4 (q, J_{PB} = 59.5 Hz); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 8.7 (d, J = 38.2 Hz), 17.2, 26.7 (d, J = 36.1 Hz), 129.3 (d, J = 9.4 Hz), 129.5 (d, J = 52.4 Hz), 131.8 (d, J = 2.4 Hz), 132.6 (d, J = 8.6 Hz); MS (EI) *m/z* (relative intensity): 203 (M + Na$^+$; 100); HRMS (ESI) calcd for $C_{10}H_{18}BNaP$: 203.1133; found: 203.1120.

The enantiomeric excess of the phosphine borane **15d** was determined by ^{31}P NMR ($CDCl_3$, 121.5 MHz) of the phosphine oxide derivative prepared according reference [24b], in presence of the Kagan's reagent (*S*)-**21** [31]: δ + 44.37 for (*S*)-**15d** and + 44.26 for (*R*)-**15d**.

The *(R)-(−)-methylphenyl-i-propylphosphine borane* **15d**, prepared from **12e** derived from the (−)-ephedrine, exhibits satisfactory analytical data in agreement with the (*S*)-enantiomer: Yield = 68%; 89% e.e.

4.5. Preparation of phosphine boranes **15** from phosphide boranes **9** (Route B)

4.5.1. General procedure

The solution of chlorophosphine borane **14**, prepared according to the procedure described on § 4.3, was cooled at −85 °C and *t*-butyllithium (0.75 mmol, 3 equiv.) was added dropwise over 2 minutes. After stirring for 5 min at −85 °C, dry THF (0.5 mL) was added dropwise over 30 seconds and the reaction mixture turns deep yellow. An excess of methyl iodide (0.75 mmol, 3 equiv.) was finally added in once. The white mixture was stirred for 10 minutes at low temperature before being hydrolyzed (5 mL of water). The aqueous phase was extracted with ethyl acetate (1 × 10 mL) and with dichloromethane (2 × 10 mL), the combined organic layers were dried over $MgSO_4$ and the solvent was removed.

4.5.2. (S)-(+)-o-Anisylmethylphenylphosphine borane **15a** (from **12b** derived from the (+)-ephedrine)[19a]

Yield = 75%; white crystals (hexane/dichloromethane); $[\alpha]^{25}$ = + 25.8 (c 1.3, MeOH) for 92% e.e.; mp = 76–77 °C; R_f = 0.55 (toluene); ^{1} H NMR ($CDCl_3$, 300.13 MHz) δ 0.40–1.50 (m, 3H), 1.94 (d, J = 10.6 Hz, 3H), 3.67 (s, 3H), 6.88 (dd, J = 8.3 and 3.5 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 7.33–7.56 (m, 4H), 7.56–7.69 (m, 2H), 7.87 (ddd, J = 13.8, 7.6 and 1.6 Hz, 1H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 9.2 (q, J = 66.1 Hz). The enantiomeric excess of *o*-anisylmethylphenylphosphine borane **15a** was determined by HPLC analysis on a Chiralcel OK column, eluent: hexane/*i*-PrOH 80:20, 1 mL/min, 40 °C, λ = 210 nm: (R)-15a, t_R = 11 min; (*S*)-enantiomer, t_R = 21 min.

4.5.3. (S)-(+)-or (R)-(−)-Methylphenyl-i-propylphosphine borane **15d**

15d, prepared from **12e** or **12f**, respectively, exhibits satisfactory analytical data in agreement with the ones described in § 4.4.5. *S)-(+)*-**15d**: yield = 73%; 96% e.e.; *(R)-(−)*-**15d**: Yield = 71%; $[\alpha]_{D^{20}} = -17.0$ (c 1.2, $CHCl_3$) for 97% e.e.

4.6. Preparation of phosphines from their borane complexes

General procedure: In a 50 mL two-necked flask equipped with a magnetic stirrer and an argon inlet, 1 mmol of phosphine borane **15** and 3 equiv. of DABCO were dissolved in 2 mL of toluene. The reaction mixture was heated at 45 °C overnight. After cooling, the crude mixture was purified by chromatography on neutral alumina, using toluene as eluent.

4.6.1. (R)-(+)-o-Anisylmethylphenylphosphine **13a**

Oil; $[\alpha]_D$ + 45.7 (*c* 1.7, MeOH); R_f = 0.54 (toluene/hexane 8:2); IR (ν cm^{-1}) 3068, 3001, 2964, 2906, 1584, 1574, 1474, 1462, 1295, 1268, 1241, 1179, 1073, 1043, 882, 753, 696. ^{1}H NMR ($CDCl_3$, 250 MHz), δ 1.55 (d, J = 4.8, 3H), 3.64 (s, 3H), 6.70–6.80 (dd, 1H), 6.81 (t, J = 9 Hz, 1H), 7.00–7.10 (m, 1H), 7.15–7.30 (m, 4H), 7.35–7.47 (m, 2H); ^{31}P NMR ($CDCl_3$, 101 MHz) δ −36 (s); ^{13}C NMR ($CDCl_3$, 63 MHz), δ 10.8 (d, J = 13.3). 55.1 (s), 110.0 (s), 120.6 (s), 127.9 (d, J = 6.7 Hz), 129.5 (s), 131.1 (s), 131.8 (d, 9.5 Hz), 139.0 (brs), 160.6 (d, J = 2.8 Hz).

4.6.2. (S)-(−)-o-Anisylferrocenylphenylphosphine **13b**

Oil; $[\alpha]_D$ −4.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 3.63 (s, 3H), 3.75–3.76 (m, 1H), 4.03 (s, 5H), 4.19–4.20 (m, 1H), 4.24–4.25 (m, 1H), 4.31–4.32 (m, 1H), 6.73–6.84 (m, 3H), 7.16–7.26 (m, 4H), 7.36–7.40 (m, 2H). ^{31}P NMR ($CDCl_3$,125 MHz) δ −23.3 (s).

4.6.3. (S)-(−)-o-Anisylphenyl-m-xylylphosphine **13c**

Oil; $[\alpha]_D$ −3.8 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 2.28 (s, 6H), 3.78 (s, 3H), 6.62–6.71 (m, 1H), 6.84–6.97 (m, 5H), 7.24–7.36 (m, 6H); ^{31}P NMR ($CDCl_3$, 125 MHz) δ −16.9 (s); ^{13}C NMR ($CDCl_3$, 75.5 MHz), δ 21.3, 55.7, 110.2 (d,

J = 1.8 Hz), 121.0, 125.8 (d, J = 11.4 Hz), 128.3 (d, J = 6.9 Hz), 128.4, 130.3 (d, J = 22.8 Hz), 130.6 (d, J = 21.7 Hz), 133.7, 133.8 (d, J = 19.4 Hz), 136.1 (d, J = 9.1 Hz), 137.0 (d, J = 10.2 Hz), 137.7 (d, J = 8 Hz), 161.2 (d, J = 15.3 Hz).

4.6.4. (S)-(−)- Methylphenyl-i-propylphosphine ***13d***,

Oil; $[\alpha]_D$ −10 (c 0.3, $CHCl_3$) for 93% e.e.; ^1H NMR ($CDCl_3$, 300 MHz), δ 0.93 (dd, 3H, J = 7 and 14.8 Hz), 1.05 (dd, 3H, J = 7 and 13.7 Hz), 1.30 (d, 3H, J = 13.7 Hz), 1.78 (dhept, 1H, J = 7 and 4.3 Hz), 7.31–7.38 (m, 3H), 7.45–7.53 (m, 2H); ^{31}P NMR ($CDCl_3$, 125 MHz) δ −19.3 (s); ^{13}C NMR ($CDCl_3$, 75.5 MHz), δ 8.6 (d, J = 15.1 Hz), 18.7 (d, J = 14 Hz), 19.4 (d, J = 15.3 Hz), 28.5 (d, J = 8.2 Hz), 128.1 (d, J = 7.6 Hz), 128.6, 132.3 (d, J = 18.1 Hz), 139.1 (d, J = 15.1 Hz).

4.7. Preparation of 1,2-bis(methylphenylphosphino)ethane ***4***

4.7.1. Synthesis of 1,2-bis(methoxyphenylphosphino borane)ethane ***18***

The diphosphinite diborane **18** was prepared by coupling the α-carbanion derived from the (O-methyl)-methylphenylphosphinite borane **10a**, in presence of $CuCl_2$ under air, according to the procedure described in reference [23].

In a 50 mL two-necked flask equipped with a magnetic stirrer and an argon inlet, 1 mmol of **10a** was dissolved in 2 mL of dry THF at −78 °C. Then, 1 mmol of *s*-butyllithium was slowly added under stirring. The temperature of the mixture was kept at −78 °C for 15 min, then allowed to warm at −30 °C. After 1 hour in these conditions, dry $CuCl_2$ (1.1 mmol) was added and the temperature was brought to 0 °C and allowed under air. After 12 hours, the mixture was hydrolyzed by HCl 10%, and extracted with CH_2Cl_2. The solvent was removed and the residue purified by chromatography on silica gel using hexane/CH_2Cl_2 (6:4) as eluent.

The *(S,S)-(−)-***18** was prepared as previously described starting from (−)-ephedrine [22].

The *(R,R)-(+)-1,2-Bis(methoxyphenylphosphino borane)ethane* **18** was prepared starting from (+)-ephedrine: yield = 80%; solid; $[\alpha]_{D^{20}} = +115.0$ (c 1.3, $CHCl_3$); mp = 115 °C; R_f = 0.48 (hexane/CH_2Cl_2 [55:45]); ^1H NMR ($CDCl_3$, 300.13 MHz) δ 0.00–1.50 (m, 6H), 1.91–2.07 (m, 2H), 2.07–2.24 (m, 2H), 3.58 (dd, J = 6.0 and 6.0 Hz, 6H), 7.45–7.59 (m, 6H), 7.59–7.73 (m, 4H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 118.1 (brd, J = 58.0 Hz); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 23.3 (d, J = 43.0 Hz), 54.1, 128.2–132.4.

4.7.2. Synthesis of 1,2-bis(methylphenylphosphino borane)ethane ***19*** *[13a]*

In a 50 mL two-necked flask equipped with a magnetic stirrer and an argon inlet, 1 mmol of diphosphinite borane **18** was dissolved in 2 mL of dry THF at −78 °C. Then, 2 mmol of the methyl lithium reagent was added dropwise under stirring. The temperature of the mixture was kept at −78 °C for 15 min, then allowed to warm at 0 °C. The mixture was hydrolyzed and extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$ and the solvent evaporated. The residue was purified by flash chromatography on silica gel using hexane/dichloromethane as eluent.

The *(S,S)-(+)-***19** was prepared starting from *(R,R)-(+)-***18** derived from (+)-ephedrine: yield = 95%; solid; mp = 167 °C (*i*-PrOH); R_f = 0.44 (hexane/CH_2Cl_2 [55:45]); $[\alpha]_{D^{20}} = +33.8$ (c 1, $CHCl_3$); IR (KBr, ν cm^{-1}): 3056, 2909 (C-H), 2378 (B-H), 1457, 1420, 1063, 739, 693; ^1H NMR ($CDCl_3$, 300.13 MHz) δ 0.00–1.40 (m, 6H), 1.53 (brd, J = 9.8 Hz, 6H), 1.80–1.88 (m, 2H), 1.96–2.04 (m, 2H), 7.39–7.51 (m, 6H), 7.54–7.64 (m, 4H); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 12.9 (brs); ^{13}C NMR ($CDCl_3$, 75.0 MHz) δ 10.9 (d, J = 38.0 Hz), 20.7 (d, J = 35.0 Hz), 128.9–131.7; MS (DCI, CH_4) m/z (relative intensity): 287 (60), 104 (100), 91 (80), 77 (60); Anal. calcd for $C_{16}H_{26}B_2P_2$ (312.17): C 63.54, H 8.67; found: C 63.58, H 8.61.

The *(R,R)-(−)-***19** was prepared starting from *(S,S)-(−)-***18** derived from the (−)-ephedrine: yield = 76%; mp = 162 °C (Hexane); $[\alpha]_D^{20} = -33.4$ (c 0.3, $CHCl_3$); ^{31}P NMR ($CDCl_3$, 121.5 MHz) δ + 12.2 (brd, J = 64 Hz).

4.7.3. 1,2-bis(Methylphenylphosphino borane)ethane ***4*** *[13a]*

In a 50 mL two-necked flask, with a magnetic stirrer and an argon inlet, 1 mmol of diphosphine diborane **19** and 3 equiv. of DABCO were dissolved in 2 mL of toluene. The reaction mixture was heated at 45 °C overnight. After cooling, the crude mixture was purified by chromatography on neutral alumina, using toluene as eluent.

(S,S)-(+)-1,2-bis(Methylphenylphosphino)ethane **4**: yield = 95%; oil; $[\alpha]_{D^{25}} = +24.5$ (c 0.9, $CHCl_3$); R_f = 0.85 (hexane/toluene/ethyl acetate [20:70:10]); IR (KBr, ν cm^{-1}): 3071, 2961 (C-H), 2899, 1485, 1433, 1096, 1069, 1027, 879, 748, 695; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (d, J = 2.0 Hz, 6H), 1.53 (q, J = 3 Hz, 4H), 7.17–7.51 (m, 10H); ^{31}P NMR ($CDCl_3$, 125 MHz) δ – 32.0; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.3, 25.8, 128.3–131.6; MS (DCI, CH_4) m/z (relative intensity): 274 (35), 259 (65), 244 (50), 227 (65), 200 (40), 185 (30), 121 (100), 91 (50), 75 (55); HRMS (ESI) calcd for $C_{16}H_{20}P_2$: 274.1040; found: 274.1041. Anal. calcd for $C_{16}H_{20}P_2$ (274.10): C 70.04, H 7.35; found: C 70.03, H 7.44.

(R,R)-(−)-1,2-bis(Methylphenylphosphino)ethane **4**: yield = 95%; $[\alpha]_D^{25} = -23.5$ (c 0.9, $CHCl_3$); ^{31}P NMR ($CDCl_3$, 125 MHz) δ – 32 (s). ^1H –NMR ($CDCl_3$, 300 MHz), δ 1.28 (d, J = 2 Hz, 6H), 1.67 (q, J = 4 Hz, 4 H), 7.30–7.35 (m, 6 H), 7.37–7.43 (m, 4 H); ^{13} C NMR ($CDCl_3$, 75.5 MHz), δ (11.4, 25.9, 128.3, 128.4, 131.4, 139.6.

The enantiomeric purity was checked by ^{31}P NMR in presence of the chiral palladium complex **20**. ^{31}P –NMR ($CDCl_3$, 125 MHz) δ (ppm) −32 (s),

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