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Efficient Synthesis of (P-Chirogenic) *o*-Boronated Phosphines from *sec*-Phosphine Boranes

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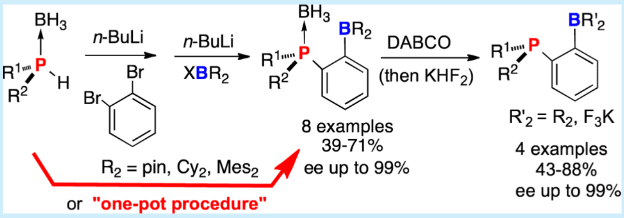
S *Supporting Information*

ABSTRACT: An efficient synthesis of boronated phosphines with an *o*-phenylene-bridge prepared from *sec*-phosphine boranes and using benzyne chemistry is reported. Successive reactions of *sec*-phosphine boranes with *n*-BuLi and 1,2-dibromobenzene, and then with boron reagents, afford the *o*-boronatophenylphosphine derivatives in 71% yields. The use of P-chirogenic *sec*-phosphine boranes leads to the free boronated phosphines with retention of configuration at the P-center after decomplexation. The reaction of P-chirogenic *o*-boronatophenylphosphine with KHF_2 affords the corresponding trifluoroborated phosphine with ee >98%.



Recently, boronated phosphines $R'_2P(Y)BR_2$ have received particular attention due to their unusual reactivity arising from the presence of a Lewis acid and base pair without a donor–acceptor bond.[1] These compounds are also called "Frustrated Lewis Pairs" (FLPs) and have demonstrated their utility for the activation of dihydrogen and binding of small molecules such as CO_2, alkene, alkynes, enals, NO, SO_2, etc.[1,2]

Interestingly, boronated phosphines have shown promising properties in coordination chemistry,[3] transition-metal catalysis,[4] organocatalysis,[5] and also for anion binding.[6] To date, few chiral boronated phosphines such as **1**–**3** were described and used in asymmetric reactions (Figure 1).[7]

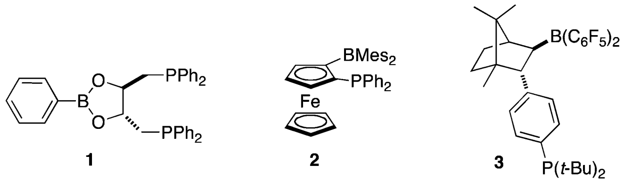
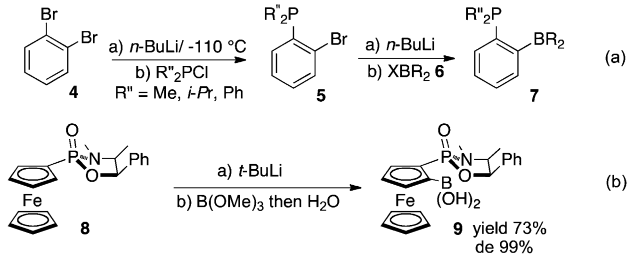


Figure 1. Examples of chiral boronated phosphines.

Despite the abundant organophosphorus chemistry, relatively few versatile methods exist allowing the borylation of arylphosphines at the *ortho* position. Usually, the preparation of *o*-phenylene-bridged boron-phosphines such as **7** is achieved by borylation of the *o*-bromophenyl phosphine **5**, previously prepared from 1,2-dibromobenzene **4** (Scheme 1a). However, this method is highly dependent on the unstable *o*-lithiated bromobenzene and its reactivity at very low temperature with chlorophosphine R''_2PCl (Scheme 1a).[2b,3a,4e,5b,c]

So far, the nature of the substituents at the P-center in boronated phosphines such as **7** remained limited, and no example of chiral derivatives has been described. To the best of our knowledge, only the ferrocenyl derivatives **2** and **9** were reported as chiral *o*-boronated organophosphorus derivatives.[7c,8] As an example, compound **9** was prepared via a diastereoselective *o*-lithiation of the chiral ferrocenyl precursor **8** (Scheme 1b).[8]

Scheme 1. Synthesis of *o*-Boron-arylphosphine Derivatives



Our group recently described a powerful method for the stereoselective synthesis of P-chirogenic *o*-bromo- or *o*-iodophenylphosphines from secondary phosphine boranes, using aryne chemistry.[9,10] We then extended this method to the synthesis of P-chirogenic *o*-boronatophenylphosphine borane complexes and their corresponding free phosphines.[10]

Chiral and achiral *o*-boronatophenylphosphine boranes **12** were synthesized in two steps from the *sec*-phosphine boranes **10** by successive reaction with 1,2-dibromobenzene **4** and borylation (Table 1). Thus, the *o*-bromophenylphosphine boranes **11a**, **11b** and **11c** were first prepared in 75%, 63%, and 55% yields, respectively, from the reaction of the corresponding *sec*-phosphine boranes **10a**–**c** with *n*-butyllithium (1.2 equiv) and 1,2-dibromobenzene **4**, following a procedure reported in the literature (entries 1,3,9).[9] Under similar conditions, when P-chirogenic (*S*)-ferrocenylphenylphosphine

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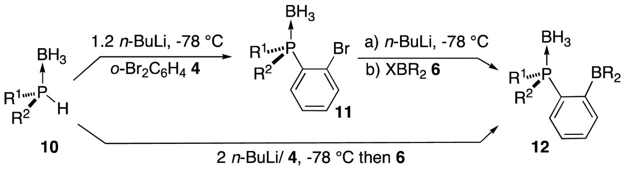
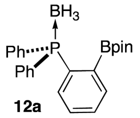
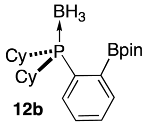
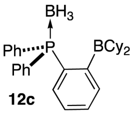
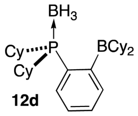
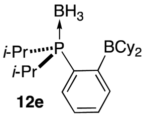
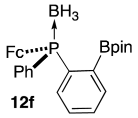
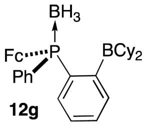
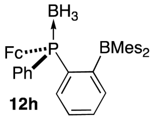
Table 1. Synthesis of the *o*-Boronated Phosphine Boranes 12



entry	phosphine boranes				boron reagent **6**	*o*-boronatophenyl phosphine.BH$_3$ **12**	yield[c] (%)
	R^1	R^2	*sec*-[a]	*o*-Br[b]			
1	Ph	Ph	**10a**	**11a**	*i*-PrOBpin **6a**	 **12a**	51
2	Ph	Ph	**10a**	-	**6a**	**12a**	54[d]
3	Cy	Cy	**10b**	**11b**	*i*-PrOBpin **6a**	 **12b**	66
4	Cy	Cy	**10b**	-	**6a**	**12b**	54[d]
5	Ph	Ph	**10a**	**11a**	ClBCy$_2$ **6b**	 **12c**	71
6	Ph	Ph	**10a**	-	**6b**	**12c**	58[d]
7	Cy	Cy	**10b**	**11b**	ClBCy$_2$ **6b**	 **12d**	55
8	Cy	Cy	**10b**	-	**6b**	**12d**	54[d]
9	*i*-Pr	*i*-Pr	**10c**	**11c**	ClBCy$_2$ **6b**	 **12e**	53
10	Fc	Ph	**10d**[a]	**11d**	*i*-PrOBpin **6a**	 **12f**	43[e]
11	Fc	Ph	**10d**	-	**6a**	**12f**	39[d,e]
12	Fc	Ph	**10d**[a]	**11d**	ClBCy$_2$ **6b**	 **12g**	60[e]
13	Fc	Ph	**10d**[a]	**11d**	FBMes$_2$ **6c**	 **12h**	48[e]
14	Fc	Ph	**10d**[a]	-	**6c**	**12h**	48[d,e]

[a] Prepared according to a procedure outlined in ref 10. [b] Prepared according to a procedure outlined in ref 9. [c] Isolated yields. [d] Yield using a one-pot procedure starting from **10**. [e] 99% ee; determined by HPLC on chiral column.

borane **10d**,[10] previously prepared from (*R*)-chloroferrocenylphenylphosphine borane, was used, (*S*)-*o*-bromophenylphosphine borane **11d** was stereoselectively obtained in 47% yield with complete retention of the configuration at the P-center (99% ee, entry 10).[9] After metal–halide exchange with *n*-butyllithium, *o*-bromophenylphosphine borane **11a** led to the corresponding *o*-lithiated derivative. It was then trapped by isopropyl pinacolatoborate **6a** to afford the *o*-boronatophenyl diphenylphosphine borane **12a** in 51% isolated yield (entry 1). In the case of dicyclohexyl(*o*-bromophenyl)phosphine borane **11b**, the reaction with the boron reagent **6a** led to the *o*-boronatophenylphosphine borane **12b** in 66% yield (entry 3).

Crystals of **12b** were obtained from methylene chloride/methanol and analyzed by X-ray diffraction (Figure 2). This structure consists of a distorted tetrahedral geometry at the P atom (typical for phosphine borane adducts). The boronato substituents are in staggered conformation with respect to both cyclohexyl substituents, and the B atoms are in a trigonal planar environment (Figure 2).

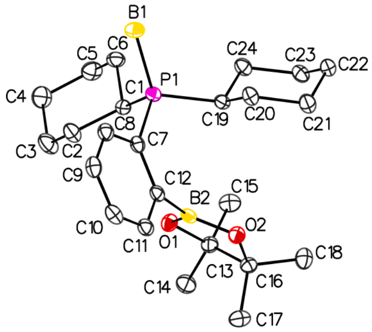


Figure 2. View of *o*-boronatophenylphosphine borane **12b**. The thermal ellipsoids are drawn at the 50% probability level. H atoms are omitted for clarity. Selected bond lengths [Å], angles [deg], and dihedral angles [deg]: P1–C19 1.846(1), P1–B1 1.893(2), C1–P1–C19 104.80(6), C1–P1–C7 111.05(6), C19–P1–B1 114.57(8), B1–P1–C1–C6 34.24(14), B1–P1–C19–C24 −66.78(12).

In addition, when the borylation reaction is performed with the chloro(dicyclohexyl)boron reagent **6b**, the *o*-bromophenylphosphine boranes **11a–c** provide the corresponding dicyclohexylboronatophenylphosphine boranes **12c–e** in yields ranging from 53% to 71% (entries 5, 7, 9). Finally, the reaction of (*S*)-ferrocenylphosphine borane **11d** with butyllithium and then with reagents **6a–c** affords the corresponding (*S*)-*o*-boronatophenylphosphine boranes **12f–h** without racemization in 43% to 60% yields (entries 10, 12, 13).

The recrystallization of **12f** and **12h** in hexane and a dichloromethane/hexane mixture, respectively, provided crystals suitable for X-ray diffraction analyses. The ORTEP views of their structures are shown in the Supporting Information and Figure 3, respectively.

The B atom is in a trigonal planar environnement in the pinacolatoboronatophosphine borane **12f** and in a fac-trivacant octahedron for the P-chirogenic *bis*(mesityl)boronatophosphine borane **12h** (Figure 3). The ferrocenyl Cp rings are parallel within 3.34(17)° or 1.61(19)° for **12f** and **12h**, respectively, and the (*S*)-configuration of the P atom in both cases is deduced from the refinement of the Flack parameter. Bond lengths and angles are availaible in the Supporting Information.

It should be noted that both boron atoms B1 and B2 are very closed in the compound **12h** (B1–B2 = 2.865(4) Å) (Figure 3). The quality of the data obtained by X-ray diffraction analysis made it possible to locate the protons in the Fourier difference map and to show that proton H1B is taken in an agostic interaction (B1–H1B = 1.21(3) Å, B2···H1B = 1.80(3) Å, B1–

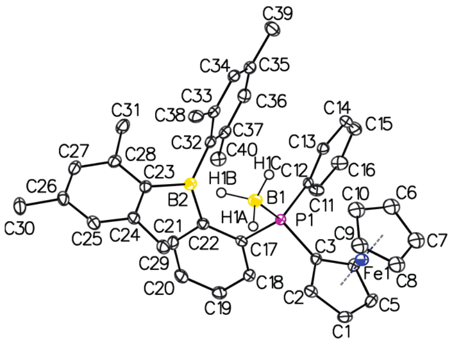
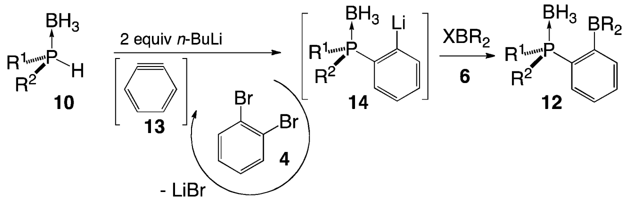


Figure 3. View of *o*-boronated phosphine borane **12h**. The thermal ellipsoids are drawn at the 50% probability level. H atoms are omitted for clarity. Selected bond lengths [Å], angles [deg], and dihedral angles [deg]: B1−P1 1.918(1), C3−P1 1.790(2), C17−P1 1.816(2), C3−P1−B1 114.51(11), C3−P1−C17 105.51(10), C17−P1−B1 106.76(11), C17−P1−C12 108.75(10), C4−C3−P1−B1 −141.8(2), C13−C12−P1−B1 24.0(2).

H1B···B2 = 143(2)°) (see Supporting Information). Moreover B2 is almost in a tetrahedral environment with angles of C32−B2−C23 = 121.7(2)°, C23−B2−C22 = 112.6(2)°, and C22−B2−C32 = 120.4(2)° (Figure 3).

Interestingly, when the synthesis is performed according to a one-pot procedure by successive reactions of **10a−d** with 1,2-dibromobenzene **4** and 2 equiv of *n*-BuLi, then, with the boron reagents **6**, the *o*-boronated phosphine boranes **12** are obtained in similar yields to those obtained via the *o*-bromo intermediate **11**, ranging from 39% to 71% (entries 2, 4, 6, 8, 11, 14). The synthesis of *o*-boronated phosphine borane **12** by this one-pot procedure is likely to occur via a mechanism involving the benzyne intermediate **13** (Scheme 2). Thus, the reaction begins with the deprotonation of the secondary phosphine borane **10**, giving the corresponding phosphide, while the excess of *n*-BuLi promotes the formation of benzyne **13** by LiBr elimination. Reaction of phosphide borane with benzyne **13** leads to the *o*-lithiated phosphine borane **14**, which is trapped by the boron reagent **6** to afford the corresponding *o*-boronated phosphine borane **12** (Scheme 2).

Scheme 2. Proposed Mechanism for the Formation of *o*-Boronatophenylphosphine Boranes 12



On the other hand, the free chiral or achiral *o*-boronatophenylphosphines **16** can be obtained by either decomplexation of their borane complexes **12** using DABCO (Scheme 3, method **A**) or direct borylation of *o*-bromophenylphosphines **15** (Scheme 3, method **B**). The results are summarized in Table 2.

According to the former case, the *o*-boronatophenyl phosphine boranes **12a** and **12f** were deprotected with DABCO at rt to afford the corresponding free phosphines **16a**, **16b** in 88% and 80% yields, respectively (Table 2, entries 1, 2). It should be noted that the borane decomplexation of **12f** was achieved stereospecifically, because the HPLC analysis on the chiral column did not show any racemization for **16b** (entry 2).

Scheme 3. Preparation of Free *o*-Boronatophenylphosphines 16

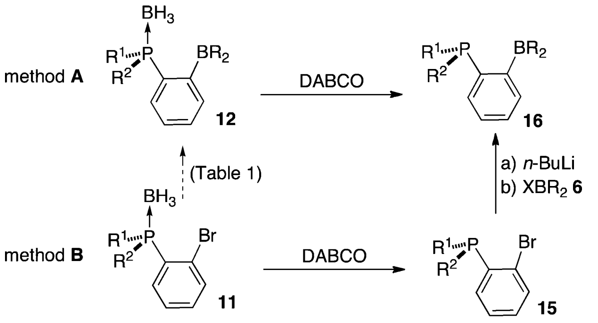
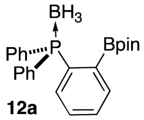
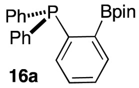
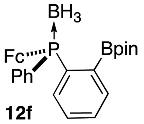
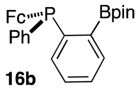
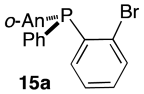
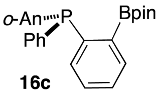


Table 2. Preparation of Free *o*-Boronatophenylphosphines 16

entry	phosphine(borane)	conditions[a]	*o*-boronato phenylphosphine	yield[b] (%)
1	 **12a**	**A**	 **16a**	88
2	 **12f**	**A**	 **16b**	80[c]
3	 **15a**	**B**	 **16c**	58[c]

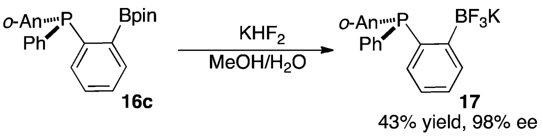
[a] Method **A**: decomplexation using DABCO; Method **B**: reaction with *n*-BuLi and then the boron reagent **6a**. [b] Isolated yields. [c] 99% ee by HPLC on chiral column.

In the second case, *o*-bromophenylphosphine **15** was previously prepared by decomplexation of its borane complex **11** with DABCO according to a described procedure[9] (Scheme 3). Thus, the reaction of the enantiomerically pure P-chirogenic *o*-bromophenyl phosphine **15a**[9] with *n*-butyllithium at −78 °C led to the *o*-lithiated anion by metal−halide exchange, which subsequently was trapped with the boron reagent **6a**, to afford the corresponding *o*-boronatophenyl phosphine **16c** in 58% yield and 99% ee (Scheme 3, method **B**; Table 2, entry 3).

As the boronate compounds could be easily converted into their trifluoroborate derivatives, also useful in transition metal catalyzed cross-coupling reactions,[11] the preparation of P-chirogenic *o*-trifluoroboratophenyl phosphines was made. Thus, treatment of **16c** with KHF_2 leads to the P-chirogenic phosphine **17** in 43% yield (ee >98%) (Scheme 4).

In conclusion, the synthesis of chiral and achiral *o*-boronated phosphine borane complexes was achieved in good to high isolated yields, starting from *sec*-phosphine boranes and using aryne chemistry. This methodology is based on two key steps by

Scheme 4. Preparation of the P-Chirogenic *o*-Trifluoroboratophenylphosphine 17



successive reactions of the *sec*-phosphine boranes, first with 1,2-dibromobenzene and then with a boron reagent. When the synthesis is performed using P-chirogenic *sec*-phosphine boranes, the *o*-boronatophenyl derivatives are obtained without racemization and with complete retention of the configuration at the P-center, as established by X-ray analysis. The decomplexation of the borane adducts under basic conditions provides the corresponding free *o*-boronatophenylphosphine in yields up to 88%. The use of this new and efficient method for the preparation of achiral or P-chirogenic *o*-boronated phosphines appears to be promising for the development and the applications of this interesting class of ambiphilic compounds.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental data, selected spectral data for all new compounds, and X-ray data for compounds **12b**, **12f**, and **12h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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