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# Synthesis and reactivity of 1,1-diborylalkanes towards C-C bond formation and related mechanisms

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**Abstract.** *Gem*-diborylalkanes have emerged as efficient reagents for synthesizing organoboron compounds through selective C-C bond-forming reactions. Activation of the 1,1-diborylalkanes, generate carbanions with enhanced stability that are able to react with a series of electrophiles, carbonyl compounds, imines and epoxides to promote the new C-C bond. These new set of reactions become general for a wide range of substrates and they can be understood by alternative mechanisms that justify the potential use of these reagents. The formation of the C-C(B) bond can be afforded with chemo- diastereo- and enantioselectivity, because the nucleophilc α-boryl or α-diboryl carbanions attack in a stereoselective manner, by means of the catalyst involved. The synthesis of *gem*-diborylalkanes has also been launched by innovative methods and facilitates the access to multiborylated reagents with different substituents and properties.



**Keywords:** 1,1-diborylalkanes; borylmethalation; diborylmethane; cross-coupling; mechanism

## 1 Introduction

1,1-Diborylalkanes have emerged as efficient reagents for C-C bond formation through selective transformations (see Figure 1 for representative *gem*-diborylalkanes).[1] Depending on the activation mode of the 1,1-diborylalkanes, two main strategies can be considered for the new C-C bond formation: a) deprotonation-alkylation and b) deborylation-alkylation (Scheme 1), giving access to organodiboryl and organomonoboryl compounds, respectively. The main advantage on using 1,1-diborylalkanes over organoboron reagents is that cross-coupling reaction can take place between multisubstituted $sp^3$-carbons, preventing eventual side reactions, even at room temperature.

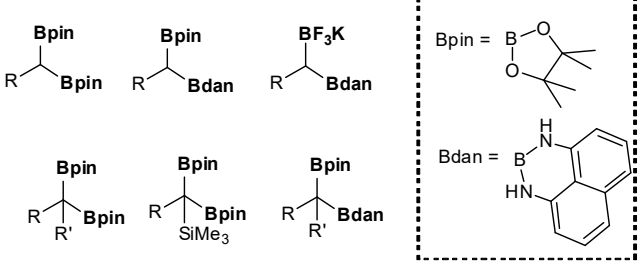
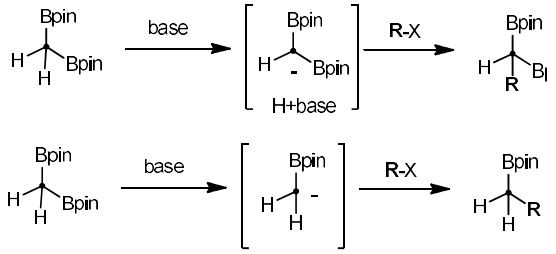


**Figure 1.** Selected 1,1-diborylalkanes

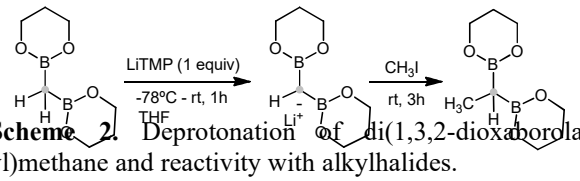



**Scheme 1.** C-C bond formation through 1,1-diborylalkanes: a) deprotonation-alkylation and b) deborylation-alkylation.

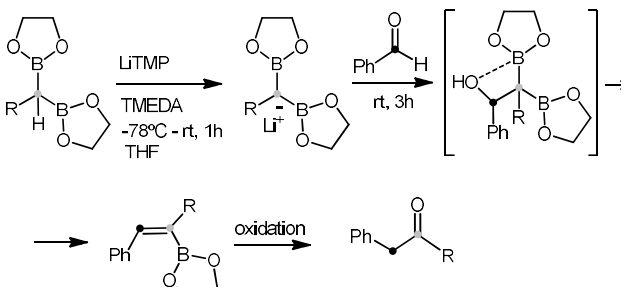
In both approaches, the key step is the carbanion formation by addition of a base which interacts with the H or alternatively with the Bpin moiety. The carbanions formed seem to have a relative stabilization with the remaining boryl unit[2] while they can be trapped by diverse carbon electrophiles, in a selective manner, to generate specific C-C bonds.

## 2 Activation of *gem*-diborylalkanes with bases

The efficient deprotonation of di(1,3,2-dioxaborolan-2-yl)methane and di(1,3,2-dioxaborinan-2-yl)methane with lithium 2,2,6,6-tetramethylpiperidide (LiTMP), in tetrahydrofuran at room temperature, was originally accomplished by Matteson and co-workers.[3,4] The resulting diborylmethide salt, conducted a straightforward cross-coupling with alkyl halides (Scheme 2), which in turn could be deprotonated again and alkylated with a second alkyl halide to form fully substituted *gem*-diboronic esters.[3] The authors also observed that the diborylmethide salt can react with esters or aldehydes, to produce ketones via cross-coupling / B-O elimination to form alkene boronic esters, that are eventually oxidized (Scheme 3).[4]

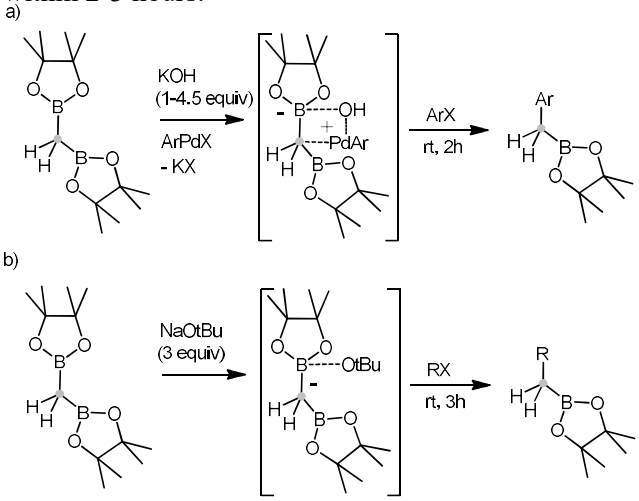



**Scheme 2.** Deprotonation of di(1,3,2-dioxaborolan-2-yl)methane and reactivity with alkylhalides.




**Scheme 3.** Deprotonation of di(1,3,2-dioxaborinan-2-yl)methane and reactivity with aldehydes

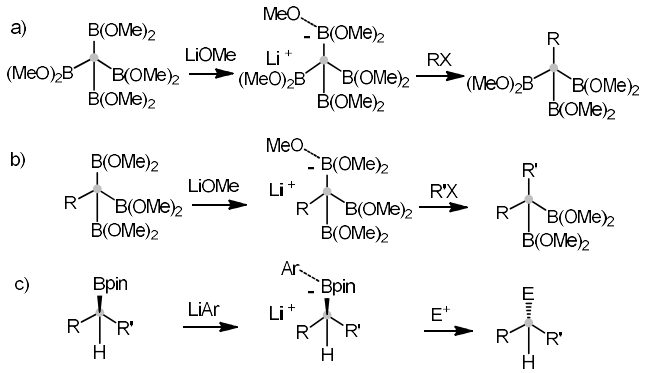
While the reactivity of the boron substituted carbanions was efficiently proved, the unhindered organoboron groups contributed to hydrolytically sensitive intermediates,[5] requiring alternative substituents on B, such as 1,1-dimesitylborylalkanes. The condensation of aliphatic aldehydes with dimesitylboron stabilized carbanions, resulting in a straightforward access to homologated ketones via cross-coupling / B-O elimination / oxidation.[6] However, the establishment of pinacolboryl units in 1,1-diborylalkanes has consolidated the use of stable and readily accessible *gem*-diborylalkanes, launching their increasing application in cross-coupling reactions. The commercially available bis[(pinacolato)boryl]methane can alternatively be activated via borate formation with specific bases, and the reactivity of the α-boryl anion with carbon electrophiles can take place both in the presence or absence of transition metal complexes, (Scheme 4). Shibata and co-workers' pioneer work, in 2010, showed the formation of a borate intermediate ("ate" complex) that can easily transmetalate with Pd(II) species (Scheme 4a).[7-10] Morken and co-workers observed in 2014, that bis[(pinacolato)boryl]methane can be activated throughout borate intermediate, via interaction with an alkoxide, to conduct a cross-coupling with alkyl halides (Scheme 4b).[11] However, in both examples, large amount of base is required, and the cross-coupling takes place at room temperature within 2-3 hours.




**Scheme 4.** α-Boryl anion formation via borate intermediate ("ate" complex).

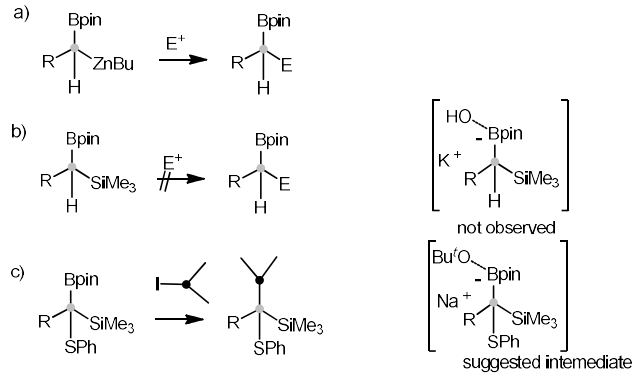
The base-assisted deborylative alkylation of tri- and tetra(alkoxyboronates) was already observed by Matteson and co-workers in 1970, and it was also proved that the poliboryl"ate" complexes were trapped by carbon electrophiles (Scheme 5a,b).[12] Aggarwal and co-workers have demonstrated that secondary and tertiary boronic esters can be activated to form the "ate"

complex that react with a broad range of electrophiles with inversion of the stereochemistry (Scheme 5c).[13] The strong influence of adding organolithium on the reactivity of the 1,1-diborylalkanes with electrophiles was already studied by NMR suggesting that the "ate" complex is only slightly dissociated into the boron stabilized carbanions and the corresponding organoborane.[14]



**Scheme 5.** C-C bond formation through borate intermediate in tetra- tri- and mono(alkoxyboronates).

For comparison, B/Zn or B/Cu organodimetallic intermediates can be trapped by various carbon electrophiles in a selective manner, to form a new C-C bond (Scheme 6a).[15] In that case, the formation of a stable "ate" complex is excluded and zincio-ene intermediates are considered instead. The addition of the copper salt $CuCN_2LiCI$ converts the zinc compounds to the more reactive copper derivatives. The congener 1,1-borylsilylalkane does not react with carbon electrophiles, probably due to the fact that the Si atom does not favor the generation of a borate intermediate at room temperature, resulting inactive in the C-C bond formation (Scheme 6b),[7] unless a $RS^-$ substituent is present in the reagent. In the later case, the deborylative alkylation can be performed, at room temperature, with primary and secondary alkyl halides (Scheme 6c).[16]



**Scheme 6.** C-C bond formation through *gem*-zincio/boryl species, *gem*-silicio/boryl and *gem*-zincio/sulphyl/boryl species.

When the 1,1-diborylalkane has two different *gem*-boryl groups, as in the case of Bpin/Bdan in $CH_3(H)C(Bpin)(Bdan)$, the activation towards the "ate" complex depends on the relative Lewis acidity of the boryl groups involved. An experimental and theoretical study has revealed that a methoxy group ineracts preferentially with the Bpin moiety in $CH_3(H)C(Bpin)(Bdan)$ forming a stable Lewis acid-base adduct. From this adduct, the deborylation to generate the carbanion occurs with a moderate free energy barrier (21.9 kcal $mol^{-1}$). Moreover, the stabilization of the carbanion using the α-Bdan moiety is reflected in the HOMO orbital, which shows strong delocalization of the carbanion p-type electron density into the π-channel of the Bdan moiety. For comparison, the Bdan could also be activated but the reaction path is shifted up in energy by 4 kcal $mol^{-1}$, and the resulting α-(pinacolato)boronate carbanion is less stable than the α-(1,8-naphthalenediaminato)boronate by 12.3 kcal $mol^{-1}$. According to NBO analysis, the Bpin fragment supports a less negative charge (−0.14e) than the Bdan fragment (−0.21e), as inferred from the corresponding HOMO orbitals (Scheme 7). Thus, selective functionalization of the Bpin position is expected, via "ate" complex formation.

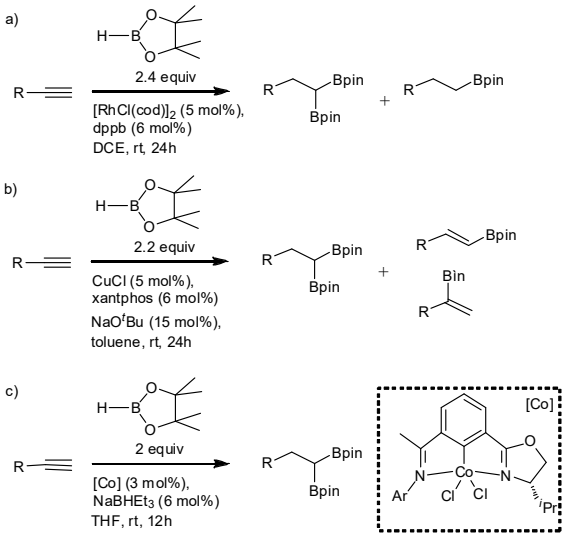
**Scheme 7.** Representation of HOMO orbitals, formally corresponding to the carbanion lone pair, for α-(1,8-naphthalenediaminato)boronate anion (left) and α-(pinacolato)boronate (right).

# 3 Synthesis of *gem*-diborylalkane

## 3.1 Hydroboration of alkynes and borylalkenes

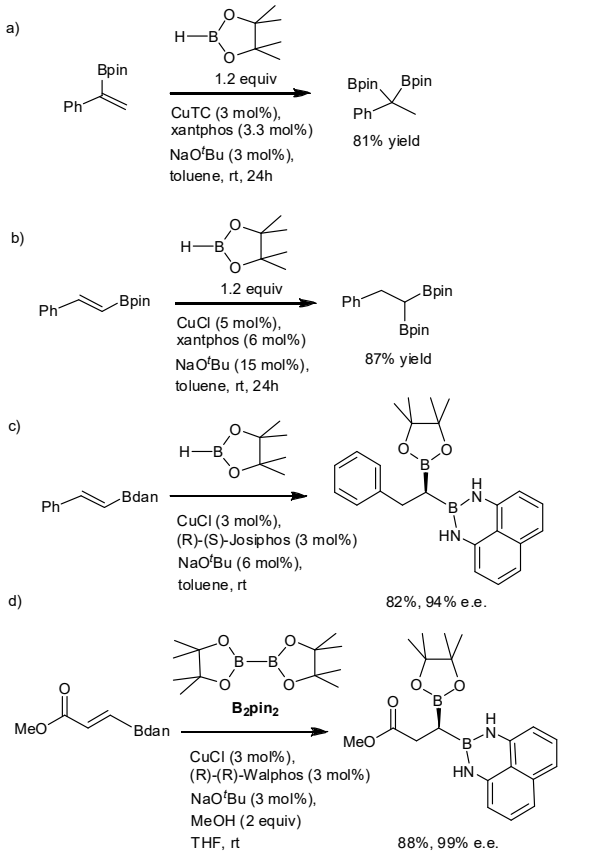
Original synthetic approaches to obtain 1,1-diborylalkanes are based on non-catalytic and catalytic sequential hydroboration of terminal alkynes, with high regioselectivity in the terminal carbon for the addition of the two boryl moieties.[17] Current protocols use Rh, Cu and Co complexes involving high atom economy, easy access of starting materials and mild

reaction conditions, although relative formation of by-products, through reduction and β-hydride elimination respectively, can be observed (Scheme 8).[18] Huang and co-workers[18d] described a selective methodology where the cobalt complex of iminopyridine-oxazoline catalyzes the sequential hydroboration with pinacolborane at room temperature with high yields, high regioselectivity, and wide functional group tolerance (Scheme 8c).




**Scheme 8.** Transition metal catalyzed sequential hydroboration of terminal alkynes.

Also the copper catalyzed hydroboration of vinylboronates provides a direct access to 1,1-diborylalkanes,[19] with high regioselectivity towards terminal and internal *gem*-diborylalkanes (Scheme 9). Yun and co-workers developed this methodology suggesting that the copper catalyzed hydroboration of vinylboronates is more energetically favorable than the hydroboration of terminal alkynes. The addition of pinacolborane to vinylboronates containing the pinacolboryl moiety, gives the corresponding 1,1-diborylalkane while the addition of pinacolborane to vinylboronates containing the Bdan moiety, generate 1,1-diborylalkane with two different boryl groups.[18c,20] In the latter case, when the ligand is chiral, the catalytic system gives access to enantiomerically enriched 1,1-diboryl derivatives (Scheme 9c). A variety of Bdan-substituted alkene compounds could be hydroborated with high levels of enantioselectivity when the copper (I)/(R,S)-Josiphos catalysts were used. The enantiomeric ratio values were similar for all the substituted alkenes (R=aryl or primary or secondary alkyl), thus indicating the minimal influence of the R substituent (remote from the Bdan group) on enantioselectivity with the copper catalyst system. Hall and co-workers also described that a catalytic asymmetric conjugate borylation of β-boronylacrylates (containing Bdan moiety) with bis(pinacolato)diboron ($B_2pin_2$) provided geminal diboronate products that feature two distinct boronyl units, up to 99% enantiomeric excess (Scheme 9d).[21a] Despite the fact that $B_2pin_2$ is used as boron source, the presence of MeOH favors the hydroborated product, resulting in a less atom economic reaction. This work represents the first syntheses of enantiomerically pure 3,3-diboronyl carboxyesters. The X-ray crystallographic structure of the product in Scheme 9d revealed that the boron pinacolate is slightly distorted from planarity, probably because of the coordination with the carbonyl oxygen (distance O-B in Bpin = 2.94 Å, distance O-B in Bdan = 4.41 Å). Also the weaker π-overlap between the oxygens and the B of the Bpin supports the idea of this coordination.



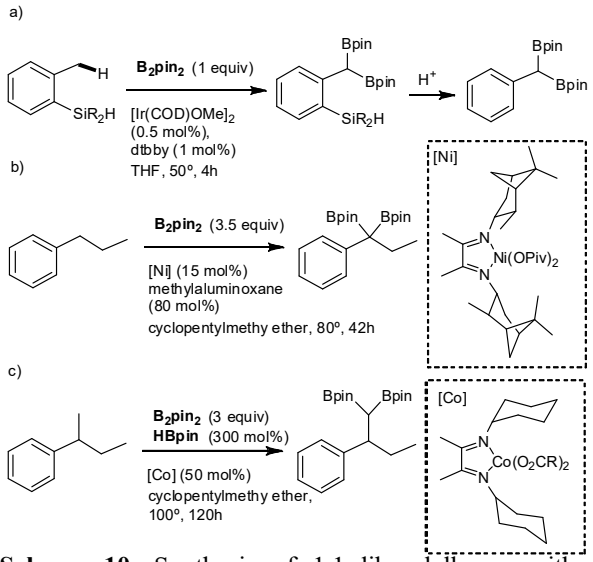

**Scheme 9.** Copper (I) catalyzed hydroboration of vinylboronates.

## 3.2 C-H activation / borylation

Diborylation of primary benzylic C–H bonds in 2-methyl hydrosilylarenes can be catalyzed by $[Ir(COD)OMe]_2$ in the presence of 4,4'-di-tert-butyl-2,2'-bipyridine (dtbpy), as reported by Hartwig and co-workers.[22] The hydrosilylane acts as a directing group, independently on the nature of the Si substitutents, being easily removed to generate the 1,1-benzyldiboronate esters (Scheme 10a). The method is general since various substituted arenes underwent selective diborylation reactions exclusively at the benzylic position, irrespective of the electronic nature of the substituents or functional groups. The diborylation also occurred at the benzylic position of a

naphthyl moiety although higher temperatures were required.

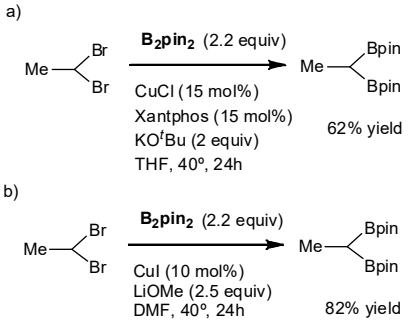
Chirik and co-workers, have demonstrated that an α-diimine nickel catalyst is effective for the diborylation of benzylic C(sp3)−H bonds of methyl- and alkylarenes (Scheme 10b).[23] Similarly, the same group has developed cobalt complexes bearing α-diimine ligands that are active for the C($sp^3$)-H diborylation of a range of substituted alkyl arenes using $B_2pin_2$ as the boron source. In addition to benzylic C-H borylation, this method provide the possibility to remote unactivated C($sp^3$)-H diborylation, in the absence of directing groups (Scheme 10c).[24] Both Ni and Co complexes have launched an unprecedented reactivity although large amounts of boron source, catalyst loading and high temperatures are needed.




**Scheme 10.** Synthesis of 1,1-diborylalkanes with C-H activation.

## 3.3 Substitution of 1,1-dihalides with diboron reagents

Ito and co-workers have demonstrated the transformation of 1,1-dibromo compounds with $B_2pin_2$, in the presence of copper /Xantphos catalyst and KO$^t$Bu as base. This represents the first practical procedure for boryl substitution of unactivated alkyl halides, and double substitution can take place efficiently at 40ºC, from 1,1-dibromo ethane (Scheme 11a).[25] Similar procedure has been further developed by Fu and co-workers,[26] to prepare several 1,1-diborylalkanes from 1,1-dibromoalkanes (Scheme 11b), introducing substituents via a slightly improved method to that of Matteson and Moody, based on deprotonation/alkylation. Despite the simplicity of the substitution of 1,1-dihalides, the limitation of a suitable 1,1-diborylalkanes, decreases the applicability of this method for multisubstituted compounds.

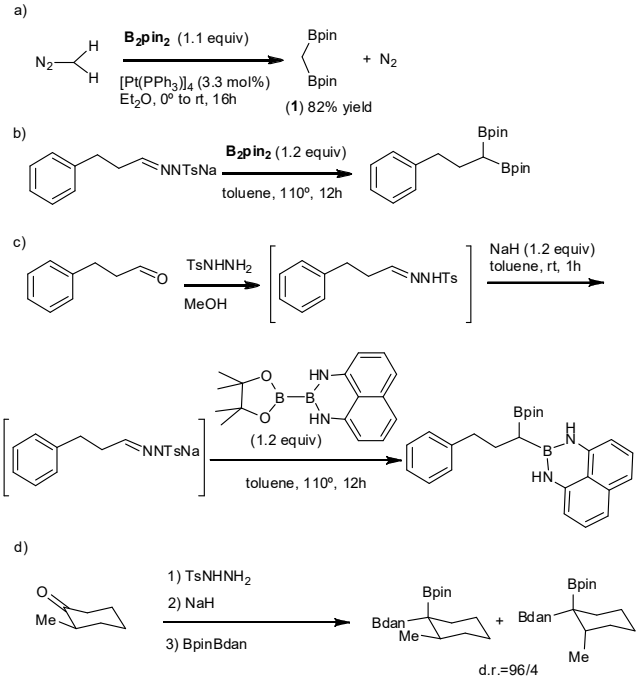



**Scheme 11.** Synthesis of 1,1-diborylalkanes via substitution of 1,1-dibromoalkanes with $B_2pin_2$.

## 3.4 Carbene insertion into diboron compounds

1,1-Diborylalkanes can also be achieved by diazoalkyl insertion into diboron reagents. The pioneer proof of concept was carried out by Srebnik and co-workers,[27] via treatment of $B_2pin_2$ with an ethereal solution of diazomethane, in the presence of $Pt(PPh_3)_4$, resulting in the high-yield synthesis of bis[(pinacolato)boryl]methane (**1**), (Scheme 12a). Substituted diazomethanes, such as diphenyl diazomethane, 1-diazo-1,2,3,4-tetrahydronaphthalene, methyl phenyl diazomethane and 2-methoxyphenyl methyl diazomethane, can be efficiently transformed into substituted *geminal* diborons in toluene, requiring temperatures around 110°C overnight for quantitative conversions.[28] Further optimization of reaction conditions has permitted the reaction to work a lower temperature (80ºC) and shorter reaction times (6 h, >98% conversion of $B_2pin_2$).[29] The method tolerates both electron-donating and electron-withdrawing substituents at the *para* position of p-phenyl methyl diazomethanes and insertion of p-chlorophenyl methyl diazomethane is chemoselective. Internal and terminal alkyl diazoalkanes provided complete conversion into the corresponding 1,1-diborylalkanes in 6 h at just 40ºC. An alternative insertion of N-tosylhydrazone to diboron reagents has also been launched in a transition metal-free context by Wang and co-workers.[30] The pioneer example was carried out on the transformation of the tosylhydrazone sodium salt, sodium 2-(3-phenylpropylidene)-1-tosylhydrazin-1-ide, which was easily transformed into the 1,1-diborated product in toluene at 110ºC, for 12 h (Scheme 12b). In order to avoid the isolation of tosylhydrazone sodium salts, it has been installed a preparative procedure to *in situ* generate tosylhydrazone sodium salts, by using sodium hydride on the accessible tosylhidrazones.[31] N-tosylhydrazones derived from ketones, were less reactive probably due to the steric hindrance and poor solubility.

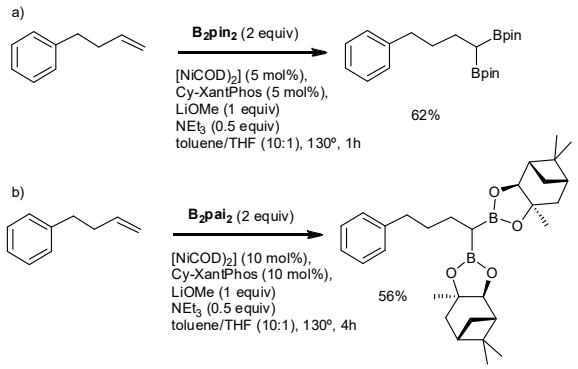
The insertion of diazocompounds into the non-symmetric Bpin-Bdan reagent, was performed by Cuenca et al., and has allowed to prepare 1,1-diborylalkanes including two different *gem*-boryl groups in RR'C(Bpin)(Bdan). In addition, in this work, it has been able to transform, in a one-pot protocol, aldehydes and cyclic and non-cyclic ketones into the 1,1-diborylalkane without intermediate isolation of N-tosylhydrazones (Scheme 12c).[32] The suggested mechanism has been rationalized by DFT calculations and might occur via a concerted-asynchronous mechanism. Diastereoselection is attained on substituted cyclohexanones with values up to d.r.= 96/4 for the 1,1-diboration of 2-methyl-cyclohexanone (Scheme 12d).




**Scheme 12.** Synthesis of 1,1-diborylalkanes via insertion of diazomethanes into diboron reagents.

## 3.5 1,1-Diboration of terminal alkenes

A variety of nonactivated terminal aliphatic alkenes can be readily converted to 1,1-diborylalkanes when reacted with $B_2pin_2$ in the presence of $[Ni(COD)_2]$ modified with Cy-XantPhos as the optimized ligand. This methodology has recently been developed by Fu and co-workers.[33] The presence and nature of the base is also crucial for this transformation, as a mixture of LiOMe/$NEt_3$ seems to be the most beneficial in a toluene/THF mixture of solvents (Scheme 13a). The limit of this reaction is that 1,1-disubstituted alkenes and internal alkenes are ineffective substrates. Vinylarenes resulted also efficient in the 1,1-diboration but $PCy_3$ was used as ligand, for the $[Ni(COD)_2]$ precursor of catalyst. Besides, $B_2pai_2$ (bis[(+)-pinanediolato]diboron) could also be used as boron source and the desired 1,1-diborylalkane products can be obtained in moderate yields (Scheme 13b).



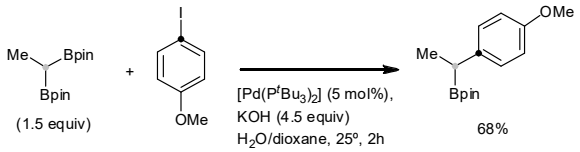

**Scheme 13.** Synthesis of 1,1-diborylalkanes via 1,1-diboration of terminal alkenes with diboron reagents.

# 4. C-C bond formation with 1,1-diborylalkanes

Cross-coupling reactions of alkylboron compounds generally suffer from a slow transmetallation step, secondary reactions such as β-hydride elimination or protodeboronation. In addition, the C-C bond formation requires high reaction temperatures as well as excess of alkylboron compounds. The use of 1,1-diborylalkanes provides a new strategy towards the cross-coupling, facilitated by the easy activation of the *gem*-diboranes, and the straightforward reactivity with diverse carbon electrophiles, in a selective manner, even at room temperature. As Shibata and co-workers described in the first observation of a chemoselective and regioselective cross-coupling on a multisubstituted $sp^3$-carbon in 1,1-diborylalkanes,[7] the boryl group plays a pivotal role in promoting the coupling. In the following section, it is described the different application of 1,1-diborylalkanes to form C-C bonds, highlighting the presence or absence of transition metal involved, as well as the reaction conditions. The substrate scope and limitations are also discussed.

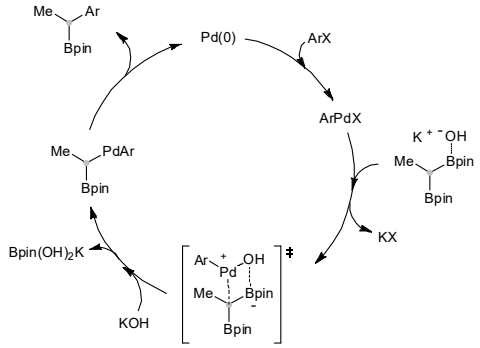
## 4.1 Coupling with aryl electrophiles

The reaction of 1,1-di(pinacol)borylethane with 4-iodoanisole in the presence of 5 mol% of $[Pd(P^tBu_3)_2]$ resulted in an unprecedented coupling of the aryl electrophile with the "ate" complex formed with the aid of 4.5 equiv of KOH. Shibata and co-workers[7] observed this phenomenon for the first time in 2010 and since then, an increased interest in this reaction has been detected. The cross-coupling can take place at room temperature without byproducts, and the retained boryl unit do not participate in any further coupling, under the same reaction conditions.



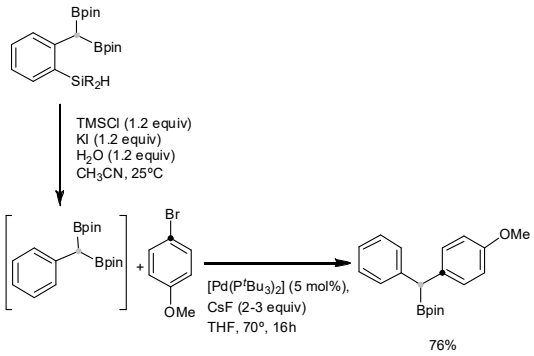

**Scheme 14.** Catalyzed coupling of 1,1-di(pinacol)borylethane with 4-iodoanisole, assisted by KOH.

The source of the base was crucial, as strong bases such as LiOH, NaOH and KOH resulted effective, while other bases, such as $K_3PO_4$, $Cs_2CO_3$, $Na_2CO_3$ and $Ag_2O$ did not provide the coupled product. The amount of base could be optimized further to equimolar amount with respect to the diborylmethane.[8] The scope of haloarenes is wide as well as the diversity of 1,1-diborylalkanes used efficiently in that reaction. An interesting feature of this reaction is the chemoselectivity during the cross-coupling on an $sp^3$-carbon derived from 1,1-diborylalkane with an aryl bromide bearing a primary alkyl-Bpin moiety. The authors explain that the cross-coupling reaction could be considered as a transmetallation of ArPdX with the "ate" complex,[7,8] generating the σ-alkylPdAr intermediate, which undergoes reductive elimination to give the coupled product (Scheme 15). Since the vacant orbital of boron can stabilize a C-metal bond, the relatively stabilized α-Pd/B intermediate would prevent the β-hydride elimination.



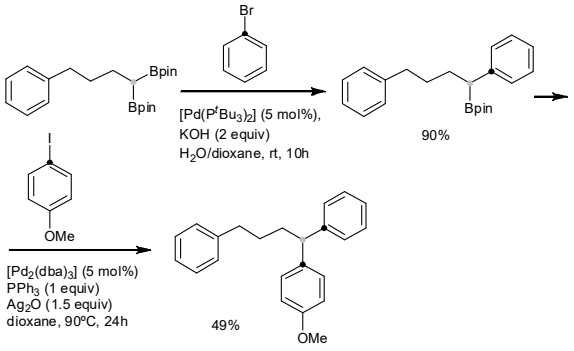

**Scheme 15.** Plausible mechanism for coupling of 1,1-di(pinacol)borylethane with 4-iodoanisole, assisted by KOH.

A group of 1,1-benzyldiboronate esters could be prepared by Hartwig and co-workers via diboration of benzylic C-H bonds. Those products contain the directing hydrosilyl group that can be essentially cleaved without affecting the benzyl-(bis)Bpin linkage, (Scheme 16).[22] Further approach to develop a cross-coupling reaction between the 1,1-benzyldiboronate esters and aryl bromides, employed [Pd(P$^t$Bu$_3$)$_2$] (5 mol%) as catalytic system and CsF (2 equiv) as base in THF at 70ºC. The need to heat in the cross-coupling for this particular class of 1,1-diborylalkanes might be related to the influence of the aryl group, both in the formation of the "ate"complex and the carbanion stabilization. The desilylation and chemoselective coupling sequence could be conducted in one-pot process (Scheme 16).[22]




**Scheme 16.** Desilylation of 1,1-benzyldiboronate esters and consecutive cross-coupling .

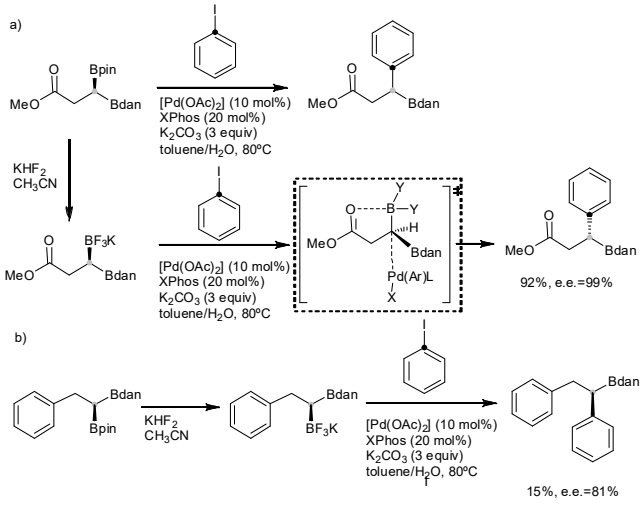
Originally, Wang and co-workers,[31] and later on Huang and co-workers, have explored the chemoselective monoarylation and stepwise diarylation through two different palladium complexes.[18d] Using [Pd(P$^t$Bu$_3$)$_2$] as the catalytic system and KOH as the base, the monoarylation is carried out at room temperature as Shibata and co-workers described previously.[7] *O*- and *S*-containing benzoheterocyclic and heterocyclic bromides are also favorable substrates under these reaction conditions. However, the coupling with *p*-$CF_3$-substituted aryl bromide and 4-bromo-2-methyl pyridine gave the cross-coupled product but protodeborylation of the resting boryl moiety took place. The second cross-coupling from the secondary benzylic boronate esters was carried out with aryl iodides and $Pd_2(dba)_2$/$PPh_3$ in the presence of $Ag_2O$, to generate the diarylated products (Scheme 17). A method for enantioselective desymmetrization of 1,1-diborylalkanes through a stereoselective Pd-catalyzed Suzuki–Miyaura cross-coupling has been thoroughly optimized.[21b]




**Scheme 17.** Double cross-coupling of 1,1-dialkylboranes from reference [18d].

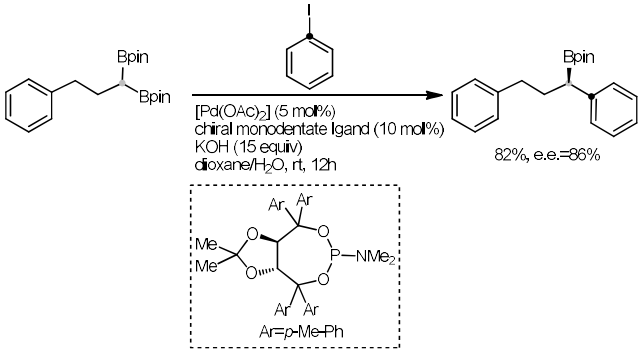
The groups of Hall and Yun,[20,21] independently carried out studies to react the highly optically enriched 1,1-diboron compounds with aryl halides. Interestingly since the two boryl groups are different (Bpin and

Bdan) the crossscoupling reaction becomes chemoselective facilitating the reactivity of Bpin versus Bdan (as it results inert in cross-coupling reactions). The initial experiments carried out towards this objective mixed the enantio enriched 1,1-diboron with phenyl iodide in the presence of $Pd(OAc)_2$ (10 mol%), XPhos as ligand (20 mol%) and $K_2CO_3$ as base (3 equiv), but the desired cross-coupled product appeared as a racemate, by means of a plausible intermediate that lost the stereochemical integrity (Scheme 18a).[21] However, the transformation of the Bpin unit into its corresponding trifluoroborate salt, and subsequent cross-coupling reaction, under the same conditions, resulted in the desired product with complete inversion of the stereochemistry, as the teams of Suginome and Molander observed previously.[34,35] The unique by-product observed was the protodeborated product, so a slight excess of the 1,1-diboron compounds is required. This approach demonstrates that a strong cooperative effect is at play, facilitating the transmetallation step through both the coordination of the methyl ester to the boron atom as well as the stabilization of the α-borylated, Pd(II) intermediate, (Scheme 18a). The Bdan unit seems to stabilizes the α-B-Pd(II) intermediate since 1,8-diaminonaphthalene protecting group accommodates the carbanion. A second cross-coupling reaction was also explored by Hall and co-workers from the chiral monoboronate, although a transformation of the Bdan moiety to the trifluoroborate salt was required first. In contrast, when Yun and co-workers conducted the cross-coupling of 1,1-diboryl-2-phenylethane (containing the Bpin and Bdan moieties) with phenyl iodide in presence of $Pd(OAc)_2$ (10 mol%), XPhos as ligand (20 mol%) and $K_2CO_3$ as base (3 equiv), the resulted cross-coupled product retained the configuration, although with a decrease of e.e. and low yield (Scheme 18b).[20]




**Scheme 18.** Cross-coupling of highly optically enriched 1,1-diboron compounds with aryl halides.

The selection of an appropriate chiral catalyst, based on Pd complex and a chiral ligand, can catalyze the enantiotopic-group-selective cross-coupling of achiral 1,1-diborylalkanes, to be transformed into nonracemic organoboronate derivatives. Morken and co-workers have found that $Pd(OAc)_2$ (5 mol%) modified with monodentate phosphoramidites (10 mol%) and a large excess of KOH as base (15 equiv), catalyzed the cross-coupling of 1,1-diboron compounds with aryl iodides, with concomitant enantioenriched C-C formation (Scheme 19).[36] It has been observed that an excess of monodentate ligand is critical for highest enantioselection, presumably as a result of competing backround nonligated pathways at lower ligand loading. Aryl bromides can also be used as electrophiles in the desymmetric coupling but the addition of NaI is required for high selectivity.



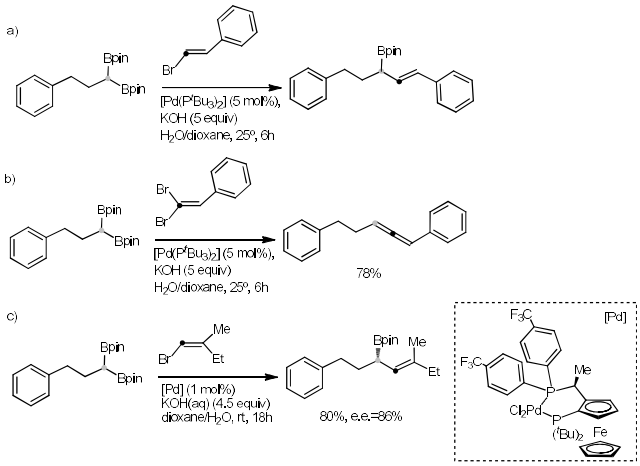

**Scheme 19.** Enantiotopic-group-selective cross-coupling of achiral 1,1-diborylalkanes.

## 4.2 Coupling with vinyl electrophiles

The reactivity of vinyl bromides in the coupling reactions with 1,1-diborylalkanes, was studied by Wang and co-workers,[37] in the presence of $[Pd(P^tBu_3)_2]$ as the catalyst and aqueous KOH (10 M) as the base. Although the coupling reaction proceeded efficiently, the allyl boronate product could not be isolated, instead it was further coupled with extra vinyl bromide to form 1,4-dienes as the main product, togeher with protodeboronated by-product (Scheme 20a). Alternativelly, the same authors decribed the palladium-catalyzed coupling of 1,1-dibromoalkenes with 1,1-diborylalkanes. The allene product could be isolated in good yield (Scheme 20b).[37]

It has been described by Morken and-coworkers,[38] the reactivity between vinyl electrophiles and geminal boronates allowing efficient access to enantiomerically enriched allylic boronates. The reaction requires $Pd(OAc)_2$ (5 mol%), and a specific Josiphos type ligand L (5.5 mol%), or alternatively the preformed catalyst $LPdCl_2$ in lower loading (1 mol%) (Scheme 20c). Base KOH (4.5 equiv) is required and the transformation takes place at room temperature, for 18 h, giving access to the cross-coupled product with enantioselection from 68% to 88%. Other substituents on the 1,1-disubstituted vinyl halide were compatible with the reaction but monosubstituted vinyl bromides

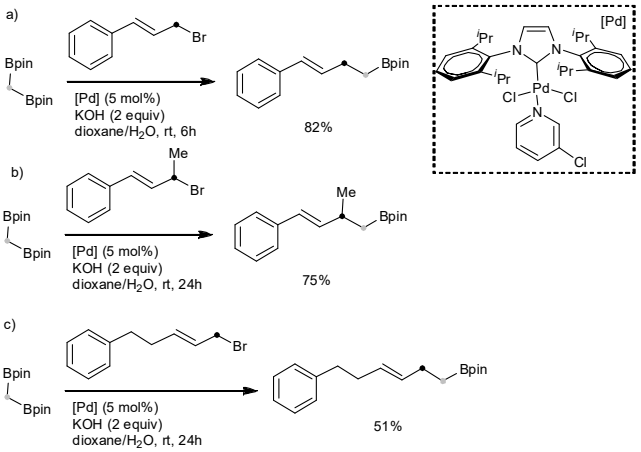
afforded significant amounts of biscoupling products. Under the influence of the chiral palladium complex, the 1,1-diborylalkanes explored undergo asymmetric cross-coupling with the bromoalkenes to generate nonracemic allyl boronates. Mechanistic experiments suggest the operation of a pathway involving outer-sphere stereoinvertive transmetallation.




**Scheme 20.** Cross-coupling of vinyl halides with 1,1-diboron compounds in the presence of Pd complexes.

## 4.3 Coupling with allyl electrophiles

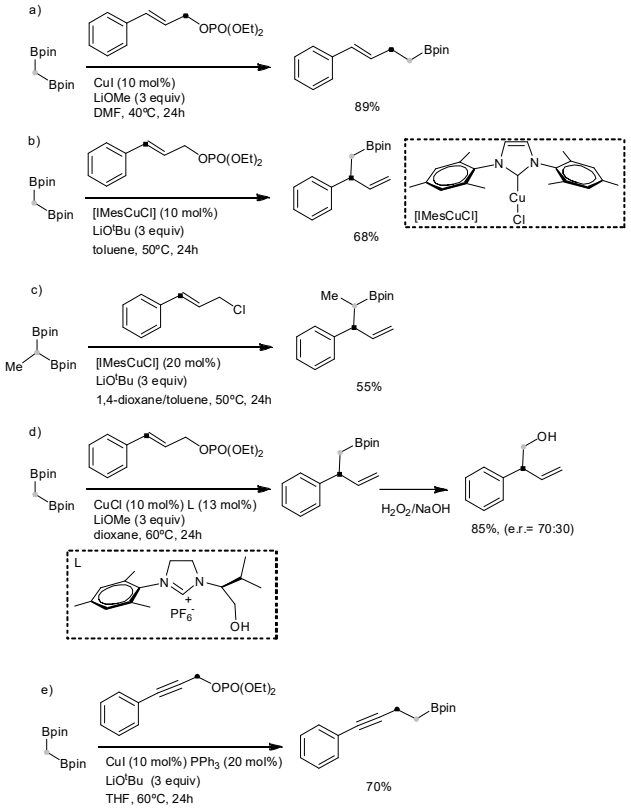
Cross-coupling reaction between sp$^3$-carbon of bis[(pinacolato)boryl]methane and sp$^3$-carbon in allyl halides, has been efficinetly performed by Shibata and co-workers,[9] with palladium complexes such as [Pd(P$^t$Bu$_3$)$_2$] at room temperature, providing the homoallylboronate in moderate to high yields. The base KOH (2 equiv) is required to assits the carbanion formation and transmetallation from the 1,1-diborylalkanes to the Pd complex. This reaction takes place providing mainly the (*E*)-isomer at the α-carbon of the allylic position. In order to generalize high yields for this coupling, the Pd-PEPPSI-IPr catalyst seems to favor quantitative conversions (Scheme 21a), presumably because monodentate ligands contribute to form the π-allylpalladium intermediate, which undergoes subsequent transmetallation. As far as the leaving group is concerned, while allyl bromides provided good reactivity, the corresponding cinnamyl chloride of cinnamyl diethyl phosphates afforded cross-coupled products in low yield. Other leaving groups, such as hydroxide, alkoxide, acetate and triflate did not give the desired product. Using substituted (*E*)-cinnamyl bromides as coupling reagents, it has been observed that electron donating groups are compatible with the reaction, while electron withdrawing groups diminished the yield and heteroatomic substituents retarded the reaction. The reaction is also beneficial for secondary allyl halides (Scheme 21b) as well as aliphatic allylhalides (Scheme 21c).[9]



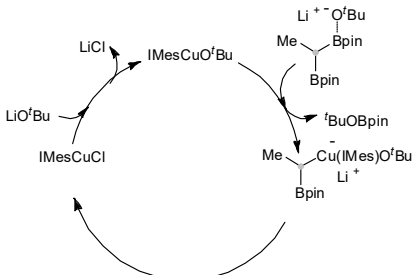

**Scheme 21.** Cross-coupling of primary and secondary allyl halides with bis[(pinacolato)boryl]methane

Bis[(pinacolato)boryl]methane has also been coupled with cinnamyl ethyl phosphate following a substitution pattern, in the presence of copper (I) catalyst, CuI (10 mol%) with 3 equiv of LiOMe, with DMF as solvent, during 24 h, at 40ºC (Scheme 22a).[26] The reaction was observed first by Fu and co-workers and a S$_N$2 mechanism seems to operate in the C-C bond formation of the new homoallylboronate product. Contrarily to the previous study, the catalytic system based on [(IMes)CuCl] (Imes = 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene) catalyzes the S$_N$2'-selective allylic alkylation of cinnamyl ethyl phosphate with 1,1-diborylalkanes in the presence of 3 equiv of LiOtBu, in toluene at 50ºC, for 24 h (Scheme 22b). Cho and co-workers[39a] have developed this new strategic synthesis of homoallylboronate product that results efficient for a wide substrate scope. The bis[(pinacolato)boryl]methane do not react with cinnamyl acetate or *tert*-butyl cinnamyl carbamate, although the reactivity with methyl cinnamyl carbamate afforded 17% of product as a mixture of S$_N$2 / S$_N$2'homoallylboronates. However, the cinnamyl chloride resulted the most reactive substrate towards the selective formation of the S$_N$2'homoallylboronate, opening a strategic application to cross-coupling of bis[(pinacolato)boryl]methane with aromatic and aliphatic allylic chlorides. Substituted 1,1-diborylalkanes also performed well the cross coupling with allyl chlorides but higher catalyst loading was required (20 mol%) as well as a 5:1 mixture of 1,4-dioxane and toluene as the solvent (Scheme 22c). This new approach indicated that S$_N$2'selectivity is highly favored by the presence of a NHC ligand.[39a] A plausible mechanism to justify the S$_N$2'selectivity suggest that [(IMes)CuCl] reacts with LiO$^t$Bu to form

[(IMes)CuO$^t$Bu] that undergoes transmetallation with the "ate" complex delivered by the *gem*-diboron compounds and the alkoxyde. The monoalkylalkoxycuprate(III) interacts with the allyl chloride via $S_N2$'substitution (Scheme 23). Fu and co-workers,[39b] have also performed a strategic copper-catalyzed $S_N2$'selective allylic substitution reaction of 1,1-diborylakanes. The catalytic system in this case is based on copper (I) modified with chiral N-heterocyclic carbene ligand, being able to perform the reaction with enantioselectivity (Scheme 22d). Alternative catalysts have also been described for asymmetric allylation with 1,1-diborylalkanes.[39c,d] Fu and co-workers have described that Cu/$PPh_3$ catalyzes the propargylic substitution reaction with bis[(pinacolato)boryl]methane. The reaction seems to be general for primary and secondary propargyl compopunds with high tolerance to diverse functional groups (Scheme 22e).[39e]

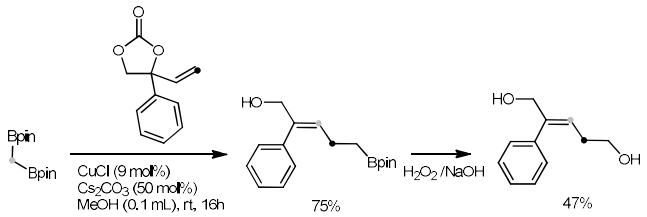



**Scheme 22.** Cross-coupling reaction of allyl phosphates and allyl chlorides with *gem*-diboron reagents.



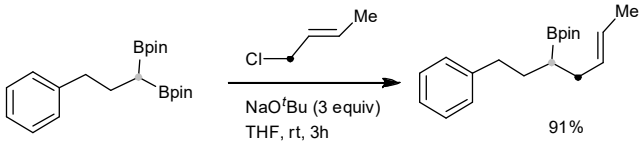

**Scheme 23.** Plausible mechanism for cross-coupling of allyl chlorides with *gem*-diboron reagents.

From the above mentioned method to prepare branched alkylboronates by [(IMes)CuCl]-catalyzed allylic substitution reactions of allylic chlorides with 1,1-diborylalkanes, it was reported that *tert*-butyl cinnamyl carbamate or methyl cinnamyl carbamate, were not transformed into the corresponding products. However, the ligandless CuCl catalytic system is able to catalyze the $S_N2$'allyl-alkyl coupling of vinyl cyclic carbonates, with concomitant ring opening of the cyclic carbonate, via extrusion of $CO_2$. Since the product retain the OH functioanlity, the products can be *in situ* converted to 1,5-diols as part of a efficient applicability (Scheme 24). In this methodology reported by Fernández and Kleij,[40] the (E)-isomer is predominantly formed, and remarkably this method only need 50 mol% of base ($Cs_2CO_3$) and the reac tions can be undertaken at rt.




**Scheme 24.** Allyl-alkyl coupling between diborylmethane and vinyl cyclic carbonates.

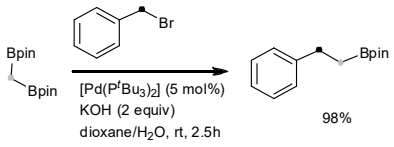
An alkoxide-promoted deborylative alkylation of geminal boronates has also been developed in a transition metal-free context. The presence of the base guarantees the alkoxyde interaction with one boryl moiety of the *gem*-diboronate, generating the "ate" complex, with the concomitant formation of a highly reactive α-boryl carbanion (Scheme 25). This reactivity has been launched by Morken and co-workers,[11] showing that allylic chlorides can be trapped with the transient α-boryl carbanion following a $S_N2$ mechanism, enabling a single-carbon homologation/borylation of the allyl halides.



**Scheme 25.** Cross-coupling of allyl chlorides with *gem*-diboron reagents via "ate" complex formation.

## 4.4 Coupling with benzyl electrophiles

The reactivity of bis[(pinacolato)boryl]methane with benzyl bromide has been studied by Shibata and co-workers,[9] in the presence of [Pd($P^tBu_3$)$_2$] catalyst (5 mol%) and KOH (2 equiv), at room temperature. The phenethylboronate is quantitatively formed within 2.5 h (Scheme 26). The formation of a $\eta^3$-benzylpalladium complex is suggested to be involved. Interestingly, the benzyl chloride also peformed well in the cross-coupling reaction, but other leaving groups, such as hydroxide, alkoxyde, acetate, carbonate, triflate, phsophate were not suitable. The reaction is general for a variety of benzyl bromides with substituents in the aryl group, both electron-donating or electron-withdrawing groups.




**Scheme 26.** Cross-coupling of benzyl bromides with *gem*-diboron reagents.

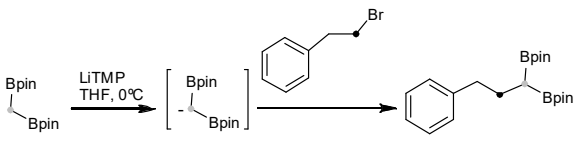
## 4.5 Coupling with alkyl electrophiles

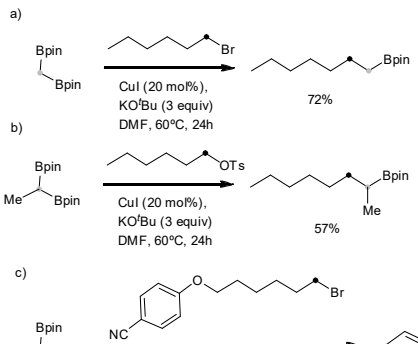
The cross-coupling between $sp^3$-carbon of 1,1-diborylalkanes and $sp^3$-carbon of alkyl electrophiles represents an efficient method to construct selective C-C bonds giving access to primary, secondary and tertiary alkylboronic esters. Morken and co-workers have demonstrated that alkylation of bis[(pinacolato)boryl]methane can be conducted by deprotonation with LiTMP and subsequent treatment with (2-bromoethyl)benzene (Scheme 27).[38]

**Scheme 27.** Cross-coupling of (2-bromoethyl)benzene with bis[(pinacolato)boryl]methane, via deprotonation with LiTMP.

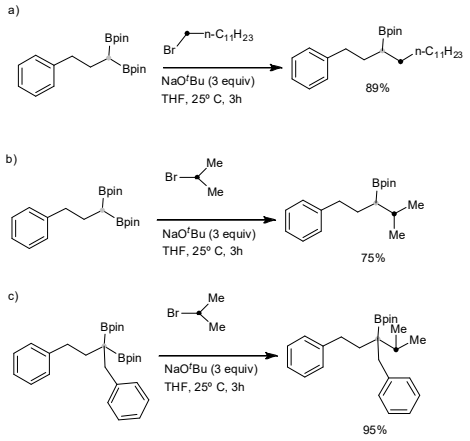
The cross-coupling of bis[(pinacolato)boryl]methane and mono- or disubstituted 1,1-diborylalkanes with primary alkyl halides, has been studied by Fu and co-workers,[26] in the presence of CuI (20 mol%) LiOtBu (3 equiv) and DMF as solvent, The reaction becomes efficient working at 60ºC for 24h (Scheme 28). Many functional groups, such as acetal, terminal olefin, TBS-protected alcohol are tolerated within this methodology. Aryl and alkyl esters are good substrates. Moderate transformation into the coupled products takes place for aryl cyanide, phthalic imide, or heterocyclic compounds.

Morken and co-workers[11] developed the transition-metal free cross-coupling of 1,1-diborylalkanes with alkyl halides, by "ate" complex activation of the *gem*-diboryl compounds and *in situ* trapping of the electrophile. The scope of the alkoxide-promoted deborylative alkylation was explored in the presence of 3 equiv of NaO$^t$Bu in THF. Bis[(pinacolato)boryl]methane and monosubstituted geminal boronates react with primary halides to furnish the secondary organoboronates in good yield (Scheme 29a). The reactivity with secondary halides is also efficent (Scheme 29b). The construction of tertiary organoboronates, is possible via reacion of disubstituted *gem*-diboronates and alkyl halides, via alkoxide-promoted deborylative alkylation, but higher reaction temperatures (40ºC – 60ºC) are required.



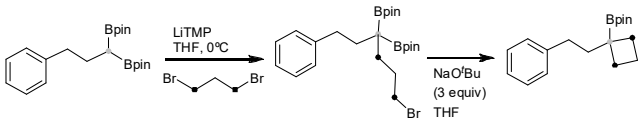



**Scheme 28.** Copper (I) catalyzed cross-coupling of alkyl halides with substituted 1,1-diborylalkanes.



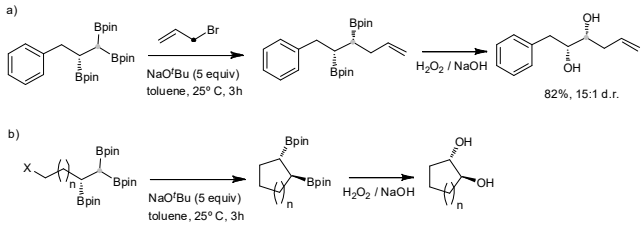

**Scheme 29.** Alkoxide-promoted deborylative alkylation of substituted 1,1-diborylalkanes with alkyl halides.

When 1,n-dihalides are used in the alkoxide-promoted deborylative alkylation, it is possible to conduct intramolecular ring forming, giving access to cyclic organoboronates (Scheme 30), that are not readily available by other methods.[11]




**Scheme 30.** Alkoxide-promoted deborylative cyclization of substituted 1,1-diborylalkanes with 1,n-dihalides.

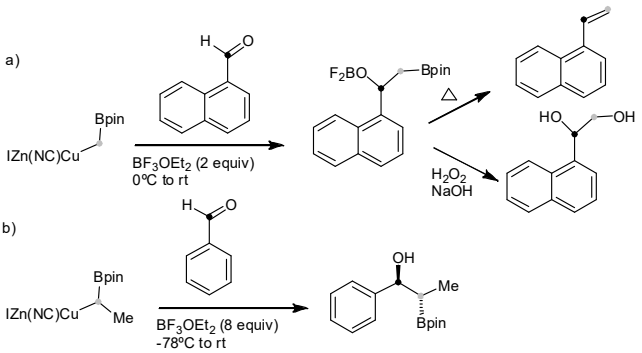
Deborylative alkylation reactions with chiral 1,1,2-organo-tris(boronates), has been conducted by Morken and co-workers,[41] with NaO$^t$Bu (5 equiv) in toluene at rt. The reaction is efficient for both primary and secondary aliphatic bromides (Scheme 31a). The *syn*-diastereoisomer seems to be the favored product, which after in situ oxidation, generates 1,2-diols. When 1,n-dihalides are involved, the intramolecular alkylative coupling is expected generating *anti*-1,2-diol, in high levels of diastereoselectivity (Scheme 31b).



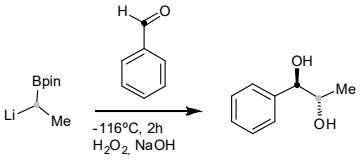

**Scheme 31.** Alkoxide-promoted deborylative cyclization of chiral 1,1,2-organo-tris(boronates) with alkyl halides.

## 4.6 Nucleophilic addition of 1,1-organodiboronates to carbonyl compounds

The boron-Wittig olefination using α-boryl carbanions was originally studied by the teams of Pelter and Matteson. While Pelter and co-workers[42] observed the condensation of dimesitylboryl carbanions with carbonyl compounds giving either *E*- or *Z*-alkenes, Matteson and co-workers[43] determined that the addition of lithiated bis(dialkoxyboryl)methane to aldehydes or ketones provided a convenient procedure for producing l-alkenylboronates. The probe of the 1,2-oxaboretaninide intermediate in the boron-Wittig reaction was isolated and fully characterized by Okazaki and co-workers.[44] After the establishment of the methodology, the Knochel's copper (I) boryl carbanions,[15] formed from the corresponding Zn boryl carbanions, were efficiently added to diverse types of electrophiles. However, it was Miyaura and co-workers[45] who first observed the copper (I) boryl carbanions addition to aldehydes in the presence of boron trifluoride etherate yielding stable β-hydroxyalkylboronates (Scheme 32a). The thermal dehydroxyboronation or the alkaline hydrogen peroxide oxidation provide the corresponding alkenes or 1,2-alkanediol (Scheme 32a). When a secondary alkyl boronate ester was added to benzaldehyde, it was possible to obtain the 1,2-hydroxyboronate in 6:1 d.r. (*anti/syn* selectivity).[45] Pelter and co-workers reported excellent levels of *anti* selectivity for the addition on alehydes of dimesityl-boron stabilized carbanions with Li. In that case, strong Li bases and cryogenic conditions (-116ºC) were required for the carbanion generation (Scheme 33).[46]

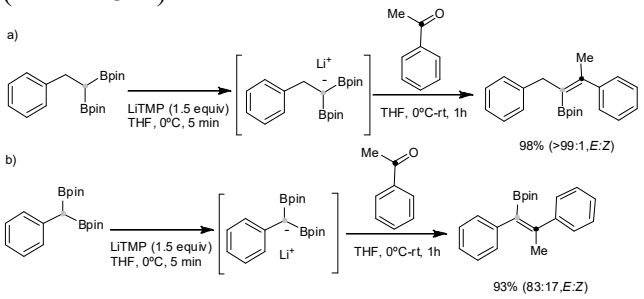



**Scheme 32.** Alkylation of aldehydes with α-boron nucleophiles stabilized with copper.



**Scheme 33.** Alkylation of aldehydes with α-boron nucleophiles stabilized with Li.

Endo, Shibata and co-workers,[47] based on the previous methods, underlined a stereoselective synthesis of tetrasubstituted alkenylboronates via lithiation/nucleophilic addition reaction of 1,1-diborylalkanes to ketones. The corresponding product was selectively formed on the (*E*)-isomer (Scheme 34a). It seems that the aryl group present in the ketones might regulate the stereoselectivity. Hartwig and co-workers,[22] also probed that 1,1-benzyldiboronate esters could react with ketones to form the corresponding tetrasubstituted alkene favoring the *E* product, conducting the reaction at 0ºC, in THF (Scheme 34b)

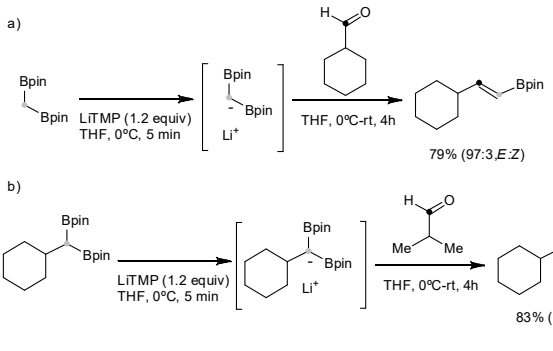


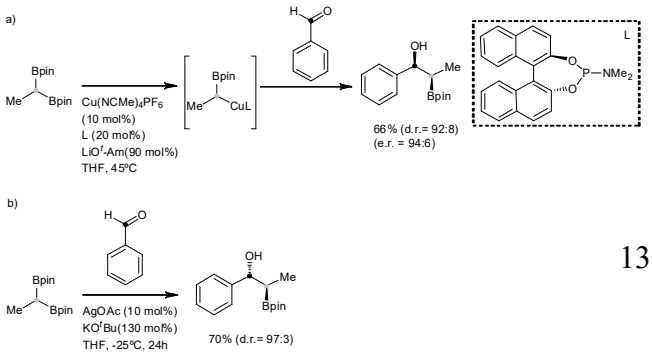

**Scheme 34.** Alkylation of aldehydes with 1,1-diborylalkanes, followed by B-O elimination towards stereoselective tetrasubstituted alkenes.

Morken and co-workers,[48] applied the same synthetic methodology to prepare di- and trisubstituted alkenylboronates, by adding the diboron stabilized carbanions with Li, to aldehydes. *Trans*-vinyl boronate esters were efficiently formed from deprotonation of bis[(pinacolato)boryl]methane with LiTMP and subsequent treatment with aldehydes (Scheme 35a). Yields and stereoselectivity towards the *trans* isomer can be considered high but depends on the aldehyde involved. Interestingly, dienyl and enynyl boronate esters could be synthetized by using the corresponding unsaturated aldehydes. When substituted 1,1-diorganoboranes were involved, the trisubstituted alkenylboronates could be prepared but with lower diastereoselection (Scheme 35b). The substituents on the boron can also influence in the diastereoselection ratio.

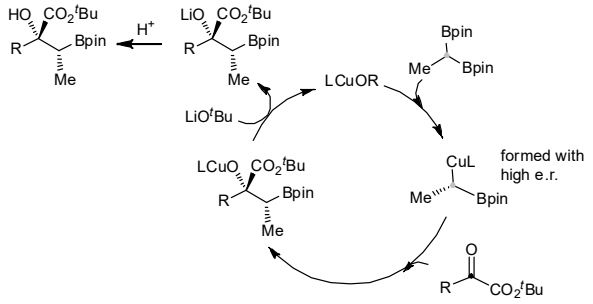
**Scheme 35.** Alkylation of aldehydes with 1,1-diborylalkanes, followed by B-O elimination towards stereoselective di- and trisubstituted alkenes

Meek and co-workers[49a] explored the copper-catalyzed addition of 1,1-diborylalkanes to aldehydes. By using chiral ligands, modifying the copper (I) complex, it was possible to generate 1,2-hydroxyboronate products containing two contiguous stereogenic centers, with high diastereo- and enantioselectivity on the *syn*-product (Scheme 36a). The reaction most likely proceeds via a chiral α-boron copper (I)/alkyl intermediate that adds to the aldehyde, with concomitant formation of the C-C bond, and resulted tolerant to aryl and vinyl aldehydes. They extended the study to enantioselective substituted 1,1-diborylalkanes to α-ketoesters, with high d.r. values and up to 99:1 e.r.[49b] Mechanistic experiments suggested an absolute stereocontrol at the α-boryl component, even in cases of low aldehyde facial selectivity (Scheme 37). The same authors[50] have developed a close methodology towards the diastereoselective synthesis of *anti*-1,2-hydroxyboronates through silver-catalyzed reaction of 1,1-diborylalkanes to aryl and alkyl aldehydes. The catalyst involved is AgOAc, without the addition of any ligand, that interacts with 130 mol% of KO$^t$Bu or nBuLi, to favor the *anti* products (Scheme 36b). It has been proposed a mechanism that justify the *anti*-selectivity of 1,2-addition reaction, involving an "ate" complex formation between the *gem*-diboron compound and the base, followed by interaction with AgOAc to produce the α-boryl alkyl silver species. The later intermediate reacts with excess of aldehyde to generate 1,2-hydroxyboronate that eventually undergoes a salt metathesis to release the product and regenerate the catalyst (Scheme 38).[50]

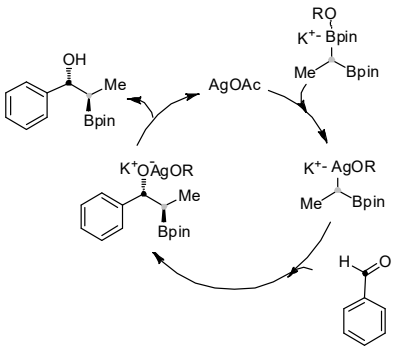


**Scheme 36.** Diastereoselective synthesis of *syn*- and *anti*-1,2-hydroxyboronates via alkylation of 1,1-diborylalkanes with aldehydes, catalyzed by copper (I) or silver (I), respectively.



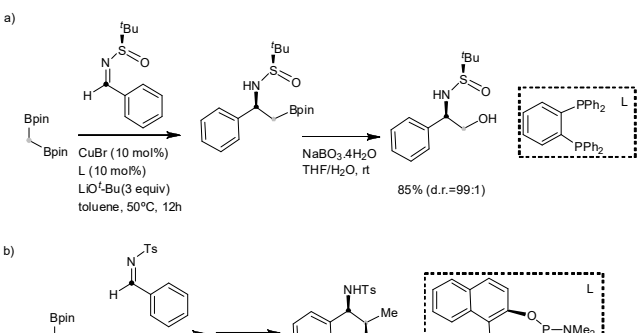

**Scheme 37.** Proposed mechanism of the copper (I)-catalyzed reaction of 1,1-diborylalkanes with α-ketoesters.




**Scheme 38.** Proposed mechanism of the silver(I)-catalyzed reaction of 1,1-diborylalkanes with aldehydes.

## 4.7 Nucleophilic addition of 1,1-organodiboronates to aldimines

The copper-catalyzed chemo- and diastereoselective addition of 1,1-diborylalkanes to N-tert-butanesulfinyl aldimines, has been launched by Cho and co-workers,[51a] and proved to be an efficient method towards the synthesis of β-aminoboronates with good yields and high diastereoselectivity. The *in situ* oxidation, also produces diastereoselective access to β-amino alcohols (Scheme 39a). The authors suggest that the reaction proceeds via a chairlike six-membered cyclic transition state, in which the boron might be coordinated to oxygen atom of the sulfinyl moiety. Valuable enantioenriched β-aminoboron compounds, bearing contiguous stereogenic centers, can also be carried out within this methodology but using a chiral ligand (Scheme 39b).[51b]

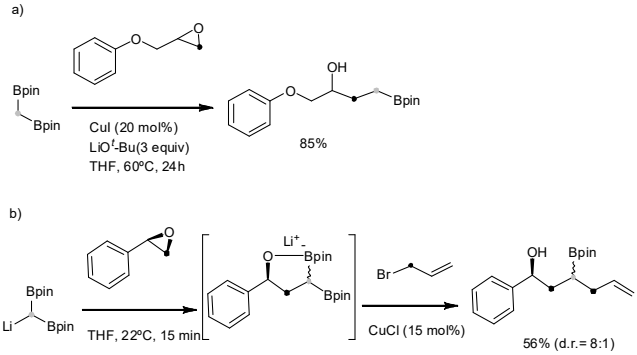



**Scheme 39.** Proposed mechanism of the silver(I)-catalyzed reaction of 1,1-diborylalkanes with aldehydes.

## 4.8 Nucleophilic addition of 1,1-organodiboronates to epoxides and aziridines

Xiao, Fu and co-workers[52] have demonstrated that copper can catalyze epoxide opening reaction with *gem*-diborylmethane. Aliphatic and aromatic epoxides are converted to the corresponding γ-pinacolboronate alcohols in moderate to excellent yields. The reaction requires CuI (20 mol%), LiO$^t$Bu (3 equiv) and 60ºC in THF as solvent (Scheme 40a). It also applied to react with N-sulfonyl aziridine, giving access to γ-pinacolboronate amines.

Bis[(pinacolato)boryl]methane can also act as a conjunctive reagent, as Meek and co-workers[53] have observed, enabling the coupling of epoxides and allylic electrophiles. The global reaction affords 1,3-hydroxy-organoborons with high stereoselectivity, using available chiral epoxides. A Li base deprotonates the 1,1-diborylalkane followed by nucleophilic attack to the epoxide with concomitant ring opening. The resulting boronate might form a cyclic species that progress through deborylative transmetallation with copper (I), to end up with trapping of an electrophile. Scheme 40b illustrates the tandem bis-electrophile coupling of the diborylmethane.

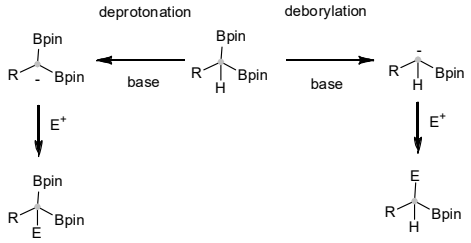



**Scheme 40.** Stereoselective linchpin coupling method between 1,1-diborylalnakes and chiral epoxides and allyl electrophiles, catalyzed by copper (I).

## 5. Concluding remarks and future orientations

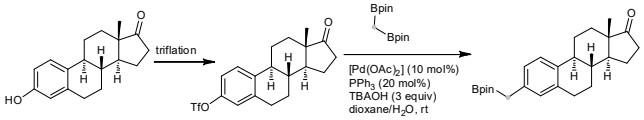
The increased use of 1,1-diborylalkanes as novel nucleophiles is due to the inherent characteristics of the boron atom, that stabilizes the carbanion formation after activation via deprotonation of deborylation (Scheme 41). The synthetic application of 1,1-

diborylalkanes as nucleophile in C-C bond formation has exceeded the expectations.



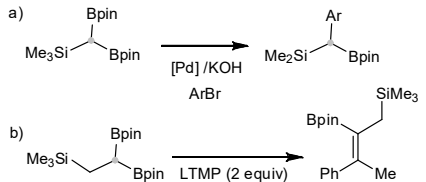

**Scheme 41.** Scenario for activation of 1,1-diborylalkanes and electrophilic trapping.

From the Shibata and co-workers's pioneer work in this area, the synthesis of benzylboronate derivatives by cross coupling of 1,1-diborylalkanes and aryl halides, has been extrapolated to the utilization of $sp^2$ C–O electrophiles. Therefore palladium complexes efficiently catalyze cross-coupling reaction of aryl triflates with 1,1-diborylalkanes in the presence of organic ionic bases. Chemoselective methylboration of the natural product estrone illustrates this new application and highlights the possibility to transform phenols into the desired benzylboronate as a simple strategy (Scheme 42).[54]



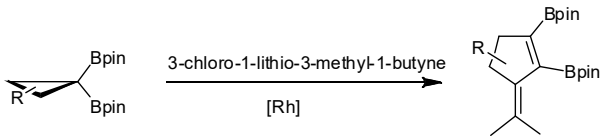

**Scheme 42.** Cross coupling of trifalte derivative of estrone with 1,1-diborylalkanes.

The generation of selective C-C bond involving 1,1-diborylalkanes open the possibility to include alternative substituents in the reagent since the protocol is respectful with heteroatoms and other functional groups. 1,1-Diboryl(methyl)trimethylsilane cross couples with aryl halides at room temperature, when a silver salt and KOH were added to the palladium catalyst. The reaction, described by Yutaka and co-workers, gave benzylboronate derivatives bearing a suitable trimethylsilyl group at the benzylic position (Scheme 43a).[55a] Shibata and co-workers also found that 2,2-diboryl(ethyl)trimethylsilane can be deprotonated with LTMP facilitating a nucleophilic addition to ketones that gives access to the synthesis of allylsilanes with excelent stereoselectivity (Scheme 43b).[55b] Fernández and co-workers established that $HC(Bpin)_2(SiMe_3)$ represents
a new olefination reagent, providing a modular synthesis of all carbon tetra-substituted alkenes by silicon or boron-based selective transformations. This novel protocol opens the door to the stereoselective preparation of tetra-substituted olefins, exemplified by the synthesis of Tamoxifen (Scheme 43c).[55c]



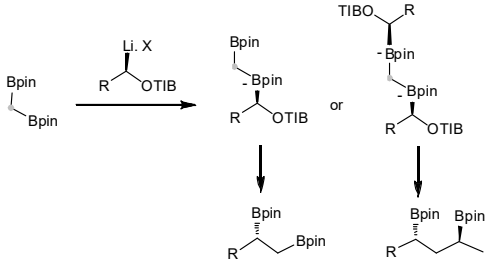

**Scheme 43.** Chemoselective cross coupling of *gem*-diboryl(trimethylsilanes)

It is important to note that 1,1-diborylalkanes, are also important synthons towards ring-expansion systems, as it has been described by Hiyama and co-workers. The easy preparation of 1,1-diborylated cyclopropanes, from 1,1-dibrominated cyclopropanes, facilitates the synthesis of allenylcyclopropanes, that undergo ring-expansion in the presence of Rh catalyst to give 1,2-diborylated methylenecyclopentenes, in an straightforward method (Scheme 44).[56]



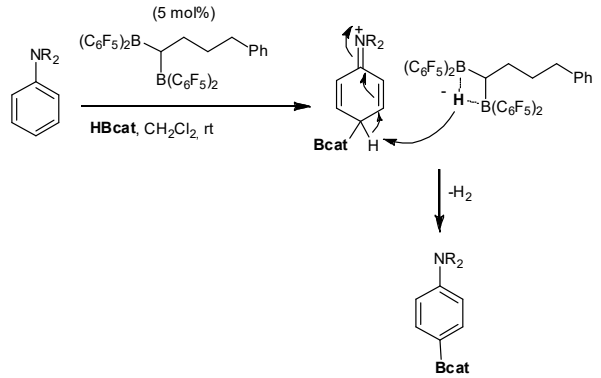

**Scheme 44.** Trasformation of 1,1-diborylated cyclopropanes into 1,2-diborated olefins, via ring exansion.

1,1-Diborylalkanes can also be homologated uni- and bidirectionally by using enantiomerically pure Li-stabilized carbenoids to give 1,2- and 1,3-bis(boronic esters), respectively. The selection of the type of carbeniod is responsable for the reaction selectivity, thus hindered chiral carbenoids such as (+) sparteine, infuence the selective single homologation of diborylmethane, while primary chiral carbenoids enable the exclusive double homologation of diborylmethane (Scheme 45). Aggarwal and co-workers have developed this regiodivergent strategy representing a formal carbenoid-carbenoid coupling reaction.[57] Interestingly, for these transformation to be successful, the acidic methylene group of diborylmethane must not undergo deprotonation but also the fragmentation of the intermediate boron"ate" complex, to form stabilized α-boryl carabnions, must not occur.



**Scheme 45.** Homologation of geminal diboryl compounds via carbenoid-carbenoid coupling reaction

1,1-Diborylalkanes can also be used as catalyst in the borylation of electron rich arenes and heteroarenes. It has been postulated that strongly electrophilic 1,1-diborylalkanes can interact with hydrides forming a chelating system, that further supply the hydride to interact with a proton and form hydrogen, acting as specific catalyst in the hydroboration of arenes and heteroarenes (Scheme 46).




**Scheme 46.** Arene and heteroarene borylation catalyzed by strongly electrophilic 1,1-diborylalkanes.

1,1-Diborylalkanes have emerged from the last decade as good candidates for C-C bond formation as nucleophilic reagents, as electrophilic reagents but also as catalysts. The stability and easy handle of those compounds justify the increasing demand of 1,1-diborylalkanes and the design of new strategic reactions.

## Acknowledgements

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REVIEW

Synthesis and reactivity of 1,1-diborylalkanes towards C-C bond formation and related mechanisms

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