CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS

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Catalytic access to (poly)borylated compounds by coupling unsaturated substrates and diboron or methyldiboron reagents

PhD Thesis

Supervised by Dr. Maria Elena Fernández Gutiérrez

Departament de Química Física i Inorgànica

UNIVERSITAT ROVIRA i VIRGILI

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Dr. Maria Elena Fernández Gutiérrez, professora titular del Departament de Química Física i Inorgànica de la Universitat Rovira i Virgili,

FAIG CONSTAR que aquest treball, titulat:

"Catalytic access to (poly)borylated compounds by coupling unsaturated substrates and diboron or methyldiboron reagents",

que presenta Núria Miralles Prat per a l'obtenció del títol de Doctor i que acompleix els requeriments per a poder optar a Menció Internacional, ha estat realizat sota la meva direcció al Departament de Química Física i Inorgànica de la Universitat Rovira i Virgili.

Tarragona, 3 de gener de 2018

La directora de la tesi doctoral

Dr. Maria Elena Fernández Gutiérrez

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"Nadie es tan pobre que no
pueda regalar una sonrisa,
ni tan rico que no la necesite"

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Chapter 1

Introduction and Objectives

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1.1. Organoborane reagents

In the last two decades, the chemistry of organoborane compounds has broadly been explored giving many interesting target compounds and reaction patterns because they are of great interest in synthetic organic chemistry, as well as in biomedical science. The main reason for the tremendous impact of organoboron chemistry in organic synthesis is due to its versatility since the C-B bond can be easily transformed into C-O, C-N and C-C bonds, among others. Their popularity lies not only from their diverse reactivity profile but also from their non-toxic nature and excellent functional group tolerance. Now, organoboron reagents offer prominent transformations in both metal-catalyzed[1] and transition metal-free[2] methodologies for the formation of selective C-B bonds.

Organodiboron compounds can be mainly divided in two groups: diboron and *gem*-diborylalkane reagents. Diboron compounds formed with a B-B σ-bond are the most recurrent borane reagents, including symmetrical ones, such as bis(pinacolato)diboron [B_2pin_2 (**1**)], bis(neopentylglycolato)diboron [B_2neop_2 (**2**)], bis(hexyleneglycolato)diboron [B_2hex_2 (**3**)], and non-symmetrical diboron reagents such as BpinBdan (**4**) (dan = 1,8-diaminonaphthalene) (Figure 1.1). Among them, B_2pin_2 reagent is the most frequently used because is commercially available, and easy to handle and store. In another group, there are *gem*-diborylalkane reagents which have a carbon atom between both boryl units. The possible substitution on the sp^3 carbon atom, apart from the variety on the boron moieties, offers a large range of 1,1-diborylalkanes. The commercially available and most commonly used *gem*-diborylalkane is 1,1-diborylmethane (**5**) (Figure 1.1).

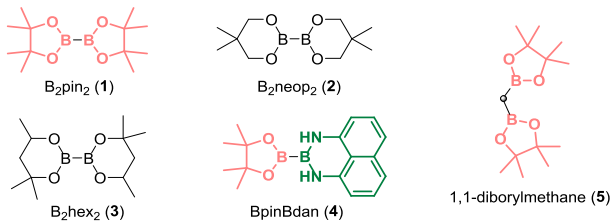
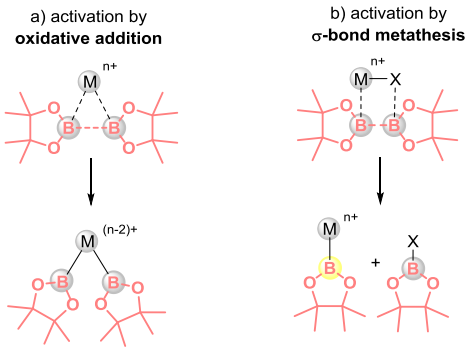


Figure 1. 1 Common diboron and *gem*-diborylalkane reagents.

The main advantages on using 1,1-diborylalkanes instead of diboron reagents are: 1) cross-coupling reaction can take place between multisubstituted sp^3 carbons, and 2) one-pot homologation with the CH_2Bpin fragment.

1.2. Activation of organoborane reagents

The activation of organoborane reagents has been considered of great importance due to the ability to cleavage the B-B σ-bond in a homo- and heterolytic manner. The nature of the organoborane reagents justifies their activation either *via* organocatalytic methods or with transition metal complexes, which essentially generate boryl units with electrophilic or nucleophilic character. Traditionally, the activation of diboron reagents and its addition to C-C bonds have been mediated by transition metal catalysts. The first time that the B-B bond of B_2pin_2 reagent (**1**) was cleavage to be added in a terminal alkyne providing 1,2-diborated products was handled by Miyaura and co-workers using a platinum complex $[Pt(PPh_3)_4]$.[3] In this case, the cleavage is supposed to take place homolytically due to the oxidative addition, followed by coordination of the substrate, insertion and reductive elimination that allows the regeneration of the Pt catalyst and delivers the diboronated product. This mechanism proceeds through a *syn* addition and is characterized to generate an electrophilic trivalent boryl unit when it is bonded to the Pt metal center (Scheme 1.1a). When the diboron reagent is cleavaged heterolytically, the two boryl units are separated and become electronically different. Copper(I) salts react with diboron reagents to generate Cu-boryl species where the boryl moiety has a nucleophilic character (Scheme 1.1b).

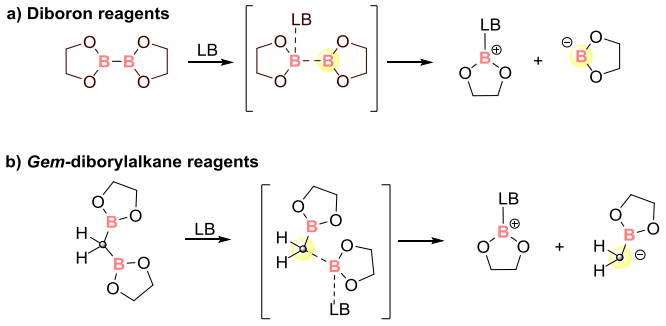


Scheme 1. 1 Possible activation modes of B_2pin_2 with transition metal complexes.

Normally, organoboron compounds have been seen as Lewis acids preferring to accept electrons rather than donate them, due to the empty *p* orbital of boron atom. However, it is important to note that subtle changes on the boron substituents make a huge impact on the boron electronic properties. This can be

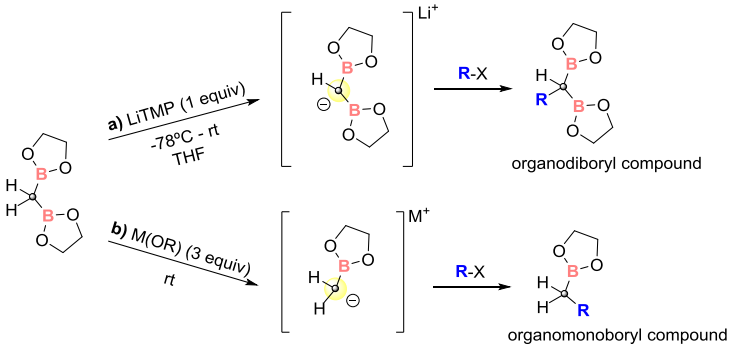
easy exemplified with the work of Bertrand and co-workers, who synthesized a neutral tricoordinate boron derivative and they studied the effect of its substituents.[4]

Despite the widespread use of organoborane reagents in organic synthesis and catalysis, their application as boron-centered nucleophiles for the direct construction of C-B bonds still remains quite bare. A very promising option to full fill the lack of nucleophilic boron reactivity is the use of B(sp^3)-B(sp^2) diboron adducts, in which one boron atom of the diboron reagent is quaternized without the presence of transition metals. These B(sp^3)-B(sp^2) diboron adducts have been considered as plausible intermediates in many borylation reactions.[5] DFT studies have demonstrated that, in the B(sp^3)-B(sp^2) diboron adducts, the B-B bond is polarized towards the non-quaternized boron atom turning it into a potential nucleophile (Scheme 1.2a). Something similar happens with the diborylmethane reagent, when one of the boryl units is quaternized and polarizes the C-B σ-bond, enhancing the carbon atom with nucleophilic character (Scheme 1.2b).



Scheme 1. 2 Comparative activation of organoborane reagents through the addition of Lewis bases.

Gem-diborylalkane reagents can be activated and further reacted following two main strategies: a) deprotonation-alkylation, and b) deborylation-alkylation, giving access to organodiboryl and organomonoboryl compounds, respectively (Scheme 1.3). In both cases the key step is the carbanion formation by addition of a base which interacts whether with the acidic proton or with one boryl moiety. The formed carbanion seems to have some relative stabilization with the remaining boryl unit[6] while they can be trapped by various electrophiles.



Scheme 1. 3 Modes of activation of 1,1-diborylalkanes and further reactivity.

Remarkably, the quaternization of one boron atom of organoborane reagents can invert completely its reactivity, transforming a conventional electrophile into a potential nucleophilic reagent.

1.3. Reactivity of trivalent boron species

Carbó and Fernández designed a map that correlates the charge of the boryl fragment with the boron p/s-population ratio in the M-B or B(sp^3)-B(sp^2) σ-bond (Figure 1.2).[7] This trending map helps to predict the nucleophilicity of trivalent boron compounds which can be useful for synthetic chemists to select the appropriate conditions to activate organoborane reagents. It is important to highlight that the overall charge on the boryl fragment provides an indication of the nucleophilic character that is induced by its counterpart, whereas the boron p/s ratio gives a measure of the intrinsic nucleophilicity of the boryl fragment and, reflects the polarization in the M-B or B(sp^3)-B(sp^2) σ-bond (Figure 1.2). The map includes three types of boryl moieties: 1) bonded to main-group metals; 2) coordinated to transition metals and rare-earth metals; 3) bonded to an sp^3 boryl moiety.

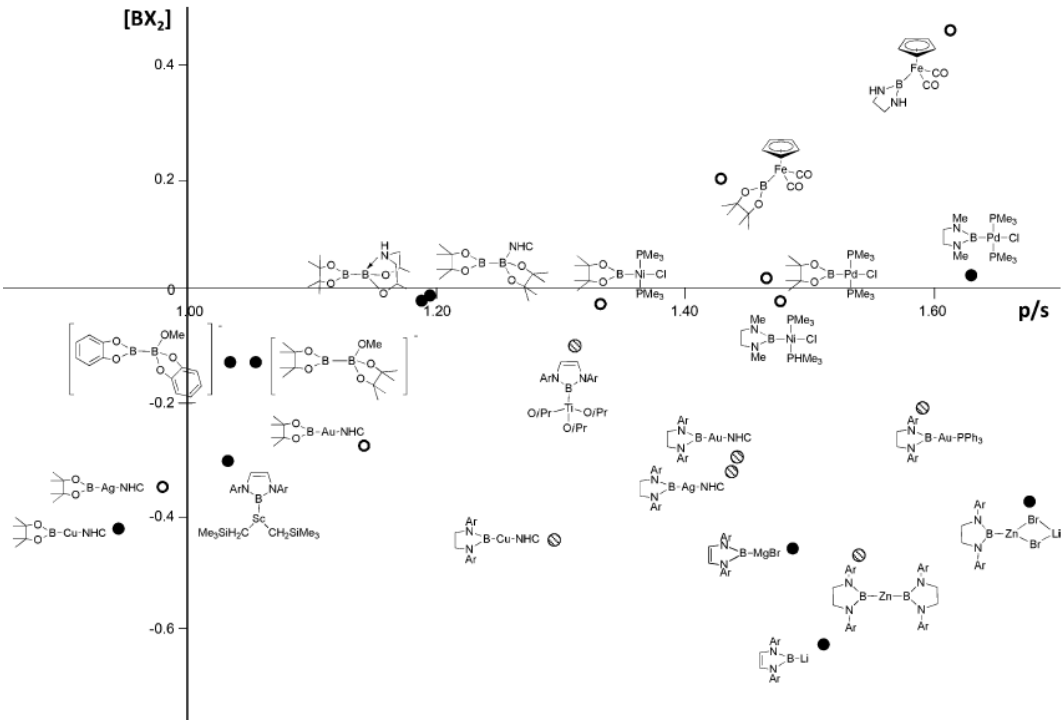


Figure 1. 2 Map correlation between the charge on the [BX2] fragment and the boron p/s-population ratio.

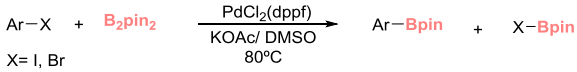
Diboron reagents activated with Lewis bases have a modest negative charge on the B(sp^2) fragment, but the boron p/s-population ratios are very low. Their position on the map (Figure 1.2) indicates that the B(sp^3)-B(sp^2) σ-bond is weakly polarized being the MeO^- ion the one that induces the greatest polarization.
In the case of *gem*-diborylalkane reagents, when they are activated by the addition of a Lewis base, their reactivity through nucleophilic character can be comparable with the [MeO--Bpin-Bpin]$^-$ adduct.

1.4. Substitution of aryl halides

Arylboronic acids and esters are key components for modern cross-coupling reactions and advanced synthetic transformations.[8] Classical preparation of aryl boronic acids or boronate esters was usually achieved *via* halogen-metal exchange or aryl bromides or iodides with arylmagnesium or –lithium reagents and

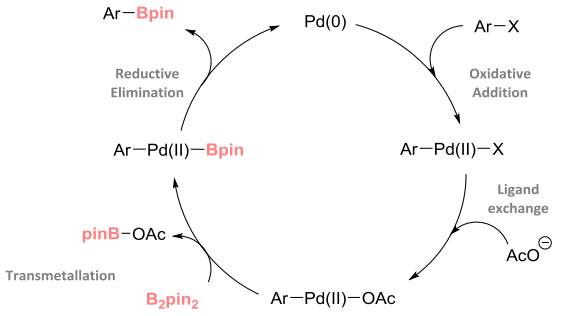
subsequent trapping with trialkylborates. However, this direct approach is incompatible with base-sensitive functional groups.

Since 1995 when Miyaura disclosed the first example of palladium-catalyzed borylation of aryl halides with bis(pinacolato)diboron (Scheme 1.4),[9] a large number of metal-catalyzed processes by palladium, and other metals, have emerged.[10]



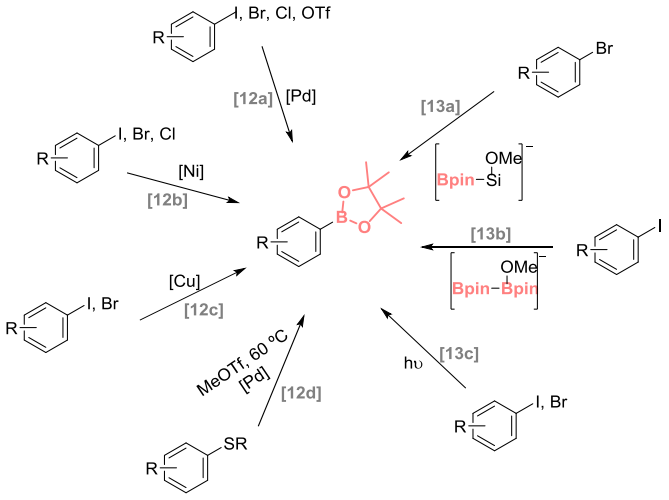
Scheme 1. 4 First palladium-catalyzed borylation of aryl halides with B_2pin_2.

The proposed catalytic cycle starts with the oxidative addition of the aryl halide to a Pd(0) complex to afford a *trans*-palladium(II) complex, Ar-Pd(II)-X (Scheme 1.5). Then, ligand exchange generates an acetoxopalladium intermediate with high reactivity towards the transmetallation with diboron reagent. Subsequently, reductive elimination of the arylboronate (Ar-Bpin) takes place along with the catalyst regeneration. Later on, Sakaki supported this mechanism with DFT calculations, stressing that the heterolytic cleavage of B-B bond is facilitated due to the polarization induced by the AcO-Bpin interaction.[11] It is also observed that the strenghthening of the AcO-Bpin bonding interaction compensates the weakening of the Pd-OAc and B-B bonds, to accelerate the transmetallation step.



Scheme 1. 5 Proposed catalytic cycle for the Pd-catalyzed borylation of aryl halides with B_2pin_2.

Nowadays, a common pathway to prepare these type of reagents employ the original Miyaura borylation reaction between aryl halides and B_2pin_2 (**1**) in the presence of catalytic amounts of transition metal complexes,[12] and more recently the transition metal-free version[13] (Scheme 1.6).



Scheme 1. 6 Borylation of aryl halides

Within the last decade, greener chemical transformations have become a hot issue in organic synthesis. Thus, the synthesis of arylboronates without transition-metal catalysts has received continuous attention and represents a challenge for organic chemists. The work of Zhang and co-workers where they reported that the activation of B_2pin_2 with Cs_2CO_3 and MeOH can promote the nucleophilic boryl substitution of a wide range of funcionalized aryl iodides towards the synthesis of valuable aryl boronic esters,[13b] was the beginning of new methodologies on borylation of aryl halides in a transition metal-free context (Scheme 1.6).[2]

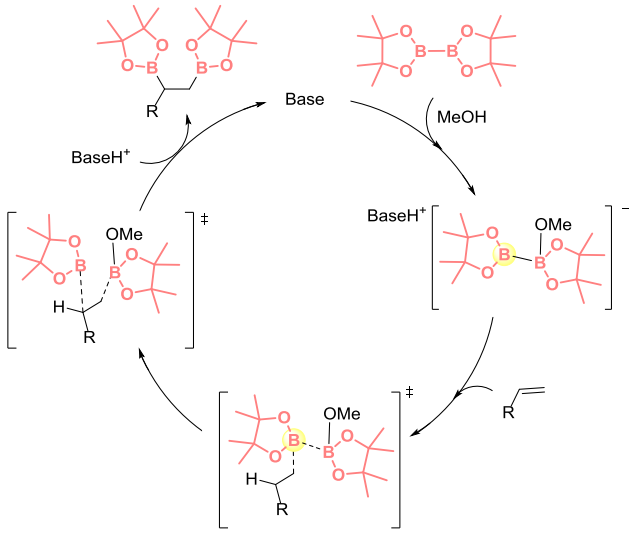
1.5. Catalytic diboration of unsaturated substrates

The olefin diboration reaction is a useful strategy for the conversion of alkenes into a range of important building blocks where both boryl units of the diboron reagent are added to the substrate. In this context, many strategies have been developed to efficiently promote the 1,2-addition by means of transition metal

complexes, and more recently, the metal-free version has also achieved a significant impact in the synthetic community. The success of catalytic diboration depends on the B-B bond activation by low-valent metal centers, but also on the kinetic lability of the key intermediate borylmetal complex when reacts with unsaturated organic substrates.

Diboration of alkenes is a very complicated process due to the possibility of β-hydride elimination with subsequent hydroborated product formation, resulting in a complex mixture of products.[14] Oxidative addition of diboron reagents in transition metal complexes, leads to diborylmetal intermediates which determine the chemoselectivity (diboration *versus* hydroboration) when react with alkenes. Thus, the design of a proper catalyst, that selectively provides 1,2-bis(boronate) esters, is one of the main challenges in this catalytic reaction. Since the discovery of the Pt-catalyzed diboration reaction of alkynes,[3] several other transition metal complexes have been object of study.[15] Another mechanism was suggested to describe the diboration reaction when the transition metal catalyst involved has lower *d* orbital energies, such as Cu(I) complexes. In that case, the σ-bond metathesis between the diboron reagent and the M-X unit is the key step.[16]

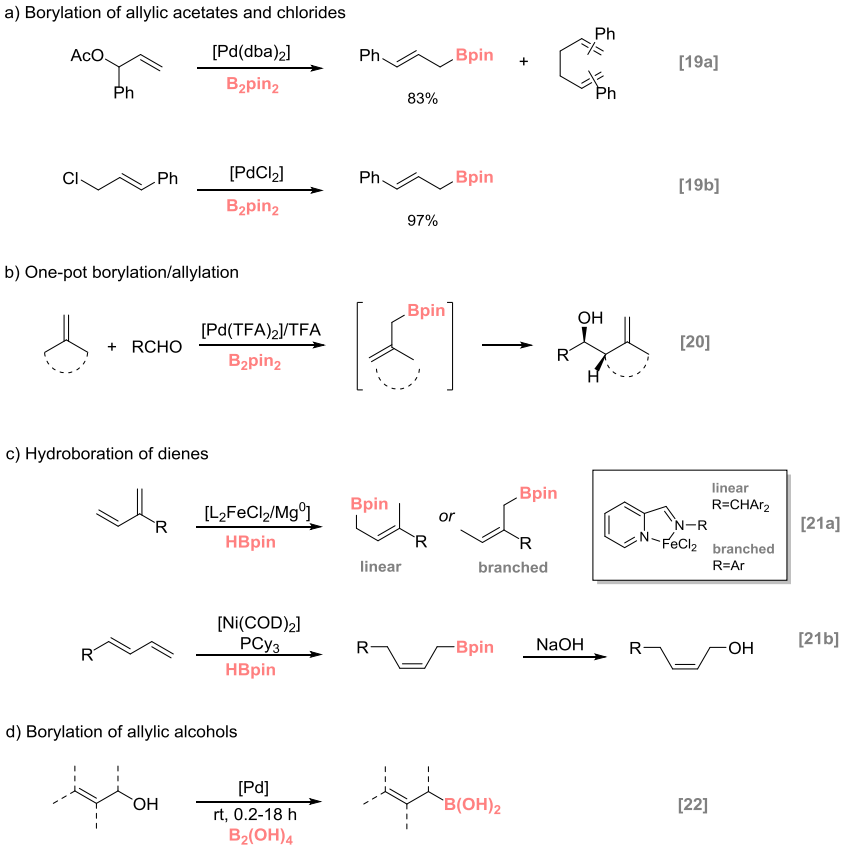
Some years ago, our group reported the discovery of diboration of diverse unsaturated substrates with B_2pin_2 in the absence of transition metal catalysts.[17] It was demonstrated that a nucleophilic sp^2 boryl moiety, formed upon interaction of tetraalkoxydiboranes and a Lewis base (methoxide), can attack non-activated C=C bonds (Scheme 1.7). A combination of Cs_2CO_3 and MeOH provides a synthetically useful methoxide source that reacts with B_2pin_2 to form *in situ* the corresponding acid-base Lewis adduct $[MeO\text{--}Bpin\text{-}Bpin]^-$. The sp^2 boryl moiety becomes nucleophilic and attacks the terminal carbon of the alkene, forming a carbanion in the internal carbon of the olefin. That carbanion eventually reacts with the sp^2-boryl and provokes the B-B cleavage (Scheme 1.7).



Scheme 1. 7 Proposed catalytic cycle for the transition metal-free diboration of alkenes.

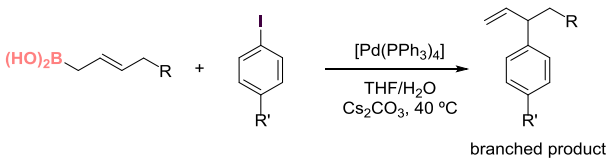
1.6. Nucleophilic allylic substitution

Over the past few years, organoboron chemistry has raised an explosion in the number of methods for the installation and manipulation of organoboron functional groups as well as the understanding of their mechanistic study. Within this broad area, allyl boronic acids and their esters represent a unique class of reagents due to their ability to react with electrophiles. The most dominant reactions are allylboration of carbonyl and imine functionalities because it leads to synthetically useful products with high and predictable selectivity.[18] Allylboronates can be prepared by reacting allylic organometallic reagents with boron reagents followed by treatment with aqueous acid, diols or KHF_2 in order to obtain the corresponding boronic acid, cyclic boronate ester, or potassium trifluoroborate compound. There also exist borylation reactions of specific substrates to generate the desired allylboronate compounds, such as, borylation of allylic acetates,[19] borylation of alkenes,[20] hydroboration of dienes[21] or borylation of alcohols using the boronic acid as boron source[22] (Scheme 1.8).



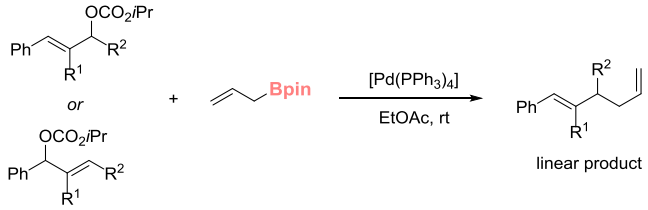
Scheme 1. 8 Selected examples of allylic borylation reactions

Another important and growing area for the synthesis of macromolecules are cross-coupling reactions of substituted allylboronates for the formation of new C-C bonds. This transformation normally suffers from the lack of regio-, diastereo-, and enantioselectivity due to the difficulty of transferring an allyl group to an electrophile in a stereospecific manner. Studies to control the regiochemistry of this reaction were separately disclosed by the group of Miyaura[23] and the group of Szabó.[24] The group of Szabó demonstrated that the commonly used $Pd(PPh_3)_4$ catalyst facilitates the cross-coupling of iodoarenes and allylboronic acids with high regioselectivity towards the branched allylic product (Scheme 1.9).[24]



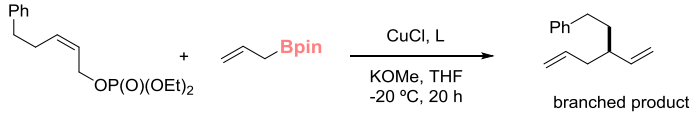
Scheme 1. 9 Cross-coupling between allylboronic acids and iodoarenes.

Allyl-allyl cross-coupling reactions of allylboronates have been reported by the group of Kobayashi.[25] They claimed that palladium(0)-catalyzed intermolecular C-C cross-coupling reactions between allylic carbonates and allyl, allenyl, or propargyl boronates which proceed with certain selectivity towards the linear product (Scheme 1.10).



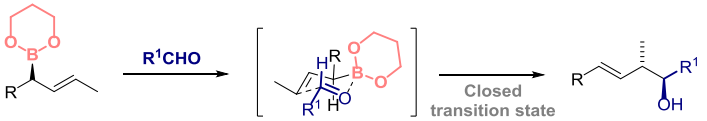
Scheme 1. 10 Cross-coupling reaction between allylboronates and allylic carbonates.

Another more recent report by Sawamura and co-workers[26] showed an enantioselective copper-catalyzed allyl-allyl coupling between allylboronates and (*Z*)-allylic phosphates, using a chiral *N*-heterocyclic carbene ligand. It has been suggested to proceed *via* S_N2'-type regioselectivity to deliver the corresponding branched isomer (Scheme 1.11).



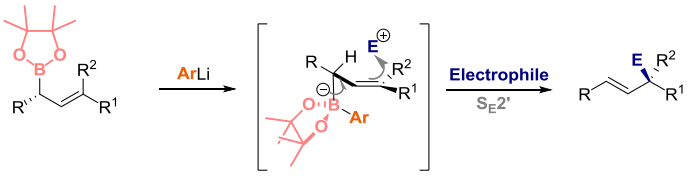
Scheme 1. 11 Cross-coupling between allylboronates and allylic phosphates.

Some other examples about applications of allylboronate compounds can be found in the literature.[27] However, reactions of allylboronate compounds with other types of electrophiles are indeed rare, because π-electrophiles allow the simultaneous activation of both the boron atom and the carbonyl group in a closed transition state (Scheme 1.12).



Scheme 1. 12 Allylborylation reaction with aldehydes.

The group of Aggarwal has very recently published the reactivity of allylboronate complexes with electrophiles.[28] They observed that the addition of an aryllithium to an allylboronic ester creates a stable and potent nucleophilic allylboronate complex that reacts with much more diverse array of electrophiles through S_E2' pathway (Scheme 1.13).



Scheme 1. 13 Reactivity of allylboronate complexes with electrophiles.

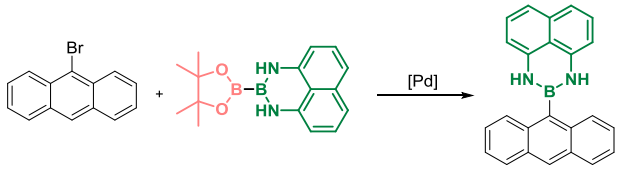
In this context, this thesis focuses on the use of both B_2pin_2 diboron and 1,1-diborylmethane reagents to be added to unsaturated substrates, by means of metal-catalyzed or transition metal-free methodologies, to obtain mono-, di- and triborylated compounds. In the following sections, we describe the importance of those synthesized molecules containing one or more C-B bonds.

1.7. Objectives

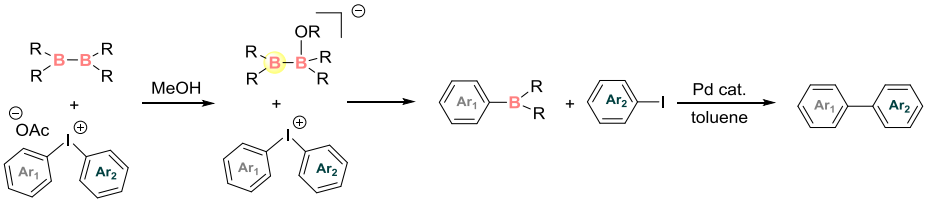
The **specific objectives** of the thesis are:

1 The study of two new strategies to conduct the borylation of aryl halides:

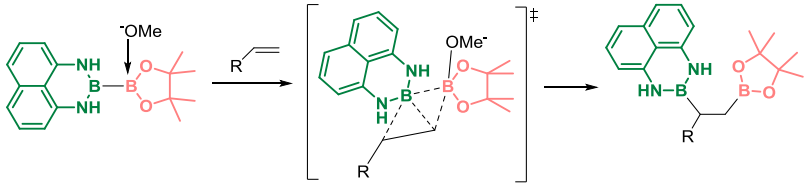
1.1 Conduct a palladium catalyzed borylation of a sterically hindered haloarene with BpinBdan reagent, and its imaging by AFM.



1.2 Perform the first approach on the borylation of diaryliodonium salts, and concomitant cross-coupling.

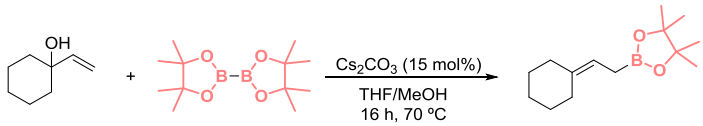


2 The development of selective diboration of alkenes, with BpinBdan, in the absence of transition metal catalysts.

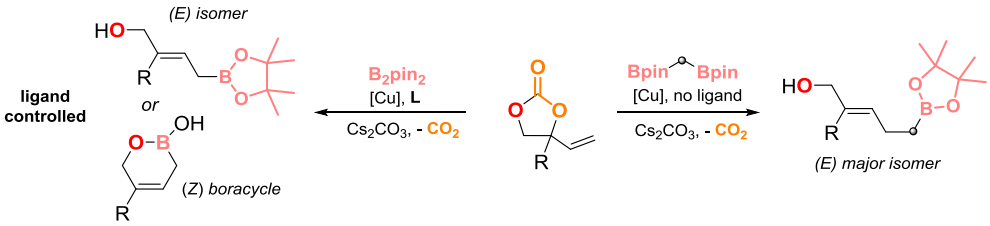


3 The study of unprecedented allylic borylation reactions:

3.1 Transformation of allylic and propargylic alcohols into allylboronate compounds under transition metal-free conditions.



3.2 Copper catalyzed methylborylation and borylation of vinyl cyclic carbonates.



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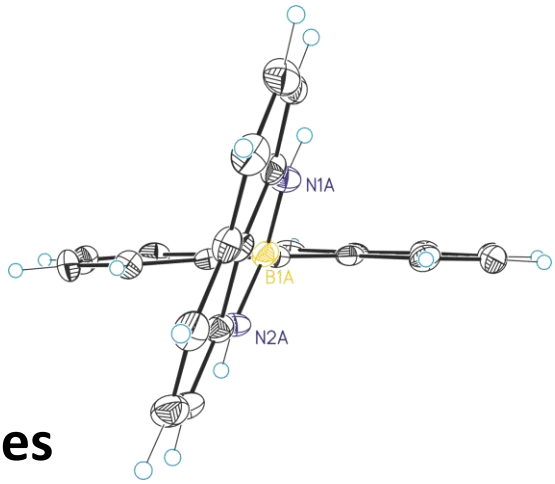


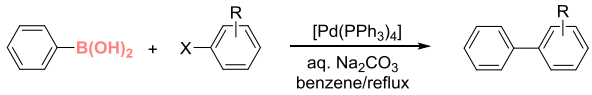
Chapter 2

Borylation of aryl halides

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat

2.1. Focus of the chapter

Aryl boronic acids and their esters have been considered essential synthetic blocks to easily prepare carbon-carbon bonds, principally in Suzuki-Miyaura cross-coupling reactions.[1] The palladium catalyzed cross-coupling reaction between different types of organoboron compounds and various electrophiles, in the presence of a base, provides a powerful and general methodology for the formation of C-C bonds. The aryl- or vinylboronic esters readily cross-couple with organic electrophiles to give selectively coupled products in high yields. Among such reactions, the most commonly used coupling is between aryl boronic esters and aromatic electrophiles to provide symmetrical and non-symmetrical biaryls. The first method to prepare biaryls by the coupling between aryl boronic acids and haloarenes was presented in 1981 by the group of Suzuki (Scheme 2.1).[2] Since then, a large number of improved methodologies have been reported making special emphasis on the organoboron counterpart.[3]



Scheme 2. 1 First reported cross-coupling of haloarenes with aryl boronic acids.

The borylation reaction becomes an essential pathway in preparing the aryl boronic esters. In this chapter we will focus on two main strategies for the borylation of aryl halides:

On the first part, we study a palladium catalyzed activation of the non-symmetrical diboron reagent BpinBdan (pin = pinacolato, dan = 1,8-diaminonaphthalene) to selectively transfer the Bdan moiety to 9-bromoanthracene. A careful study of the new organoboron compound is performed using imaging techniques.

On the second part of this chapter, we study the transition metal-free approach to conduct the borylation of diaryliodonium salts, to give access to aryl boronic esters in a selective way, as well as the intrinsic C-C bond formation.

2.2. Synthesis of 9-anthracene naphthodiazaborinine and its imaging by AFM.

2.2.1. Context of the work

The key factor governing the reactivity of organoboron compounds is the Lewis acidity of the boron atom. The vacant *p* orbital can be partially filled with the lone electron pair of adjacent atoms, tuning the Lewis acid property. Since nitrogen atoms efficiently donate their lone pair of electrons, the Lewis acidity of Bdan moieties are significantly lowered in comparison with that of Bpin moieties (Figure 2.1). Hence, in chemical synthesis, the Bdan unit has been defined as a protecting group and is principally introduced to unsaturated compounds from the non-symmetrical diboron compound BpinBdan (**4**) by means of metal-catalyzed[4] and organocatalyzed borylations reactions.[5]

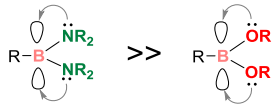
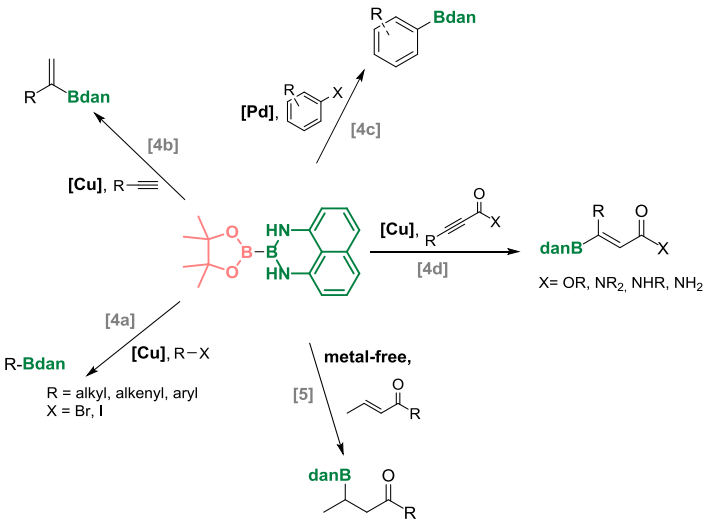


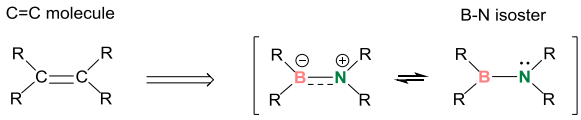
Figure 2. 1 Relative Lewis acidity of $B(NR_2)_2$ and $B(OR_2)_2$ fragments.

In Scheme 2.2 there are some examples of selective Bdan transfer from BpinBdan reagent to different organic scaffolds. For instance, the group of Li reported the direct introduction of the Bdan unit through a formal nucleophilic substitution of aryl bromides employing a Pd-catalyzed Miyaura-type reaction.[4c] Mechanistically, in all cases, the cause of such selectivity was proposed to be the preferred interaction between the more Lewis acidic Bpin moiety with basic promoting reagents or catalyst, generating *in situ* a nucleophilic Bdan unit. Then, the Bdan unit reacts with electrophilic carbons to form the corresponding organoboronates with selective C-B bond formation.
Less explored is the direct introduction of Bdan boryl unit from HBdan.[6]



Scheme 2. 2 Selective boryl transfer of Bdan from the non-symmetrical diboron BpinBdan.

The B-N/C-C isosterism, that consist on the replacement of a C=C unit with the isoelectronic and isosteric B-N unit (Scheme 2.3), represents a viable strategy to expand the chemical diversity of polycyclic aromatic hydrocarbons (PAHs). That leads to compounds with minimal geometric disruption but with some different electronic structures.[7] Since Dewar's pioneering work,[8] new methods for the preparation of original BN isosteres of PAHs have been developed.[9]



Scheme 2. 3 B-N isosterism and comparison with the carbonaceous counterpart.

In the context of the synthesis of new conjugated molecules that contain B-N units, the Bdan moiety is an example of isoelectronic and isosteric correlations to the corresponding C-C system. The substitution of the N-B-N unit into the aromatic carbonaceous phenalenyl anion system changes the topology type of the aromatic system. Therefore, we planned to synthesize the 9-anthracene naphthodiazaborinine (**6**) to illustrate the isosteric partner as a potential functional material (Figure 2.2).

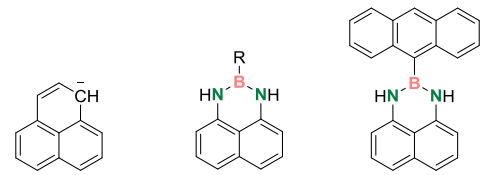
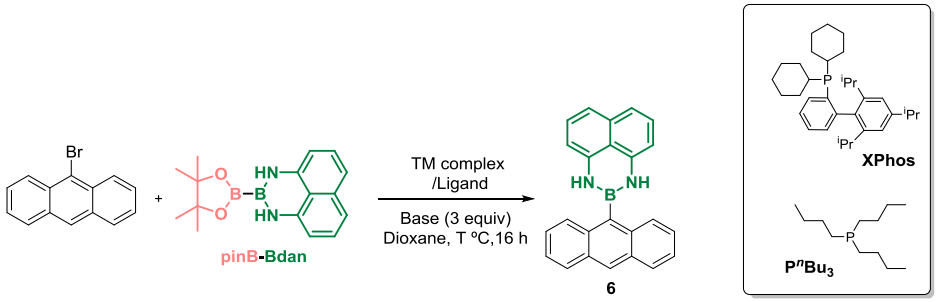


Figure 2. 2 Comparative perspective between R-Bdan species and the corresponding phenalenyl anion. Representation of 9-anthracene naphthodiazaborinine (**6**).

2.2.2. Results and discussion

The lack of examples based on the chemoselective transfer of Bdan moieties to bulky di-*ortho*-substituted aryl halides, prompted us to study the borylation of 9-bromoanthracene with BpinBdan through a series of metal-catalyzed reactions to prepare 9-anthracene naphthodiazaborinine (**6**). Initial catalytic conditions were examined with 3 mol% of $Pd_2(dba)_3$, 9 mol% of the Buchwald ligand XPhos and KOAc as the base (Table 2.1, entry 1). This catalytic system promoted a complete consumption of the diboron reagent and the formation of **6** in 66% NMR yield. The reaction also produced anthracene as hydrogenated side product. Attempts to decrease the formation of anthracene involved lower temperatures, 70°C (Table 2.1, entry 2) or lower proportion of ary halide, Ar-X (Table 2.1, entry 3), but none of these changes were beneficial. However, adjusting the Ar-X/BpinBdan ratio to 1/1.5 led to an improved NMR yield of **6** (82%), with 76% isolated yield (Table 2.1, entry 4). Remarkably, the well-established conditions, CuI/P^nBu_3/KO^tBu, for the borylation reaction of aryl halides,[10] did not show significant catalytic activity even when the more reactive 9-iodoanthracene was used (Table 2.1, entries 5 and 6). Meaningfully, **6** is the first Bdan-borylated compound arising from a di-*ortho*-substituted aryl halide.

Table 2. 1 Conditions for the metal-catalyzed Bdan transfer to 9-bromoanthracene.[a]



Entry	TM complex	Ligand	Base	T(°C)	Conv. (%)	ArX/BpinBdan (equiv)	**6** NMR Yield (%)[b]
1	$Pd_2(dba)_3$	XPhos	KOAc	100	100	1.2/1	66
2	$Pd_2(dba)_3$	XPhos	KOAc	70	70	1.2/1	51
3	$Pd_2(dba)_3$	XPhos	KOAc	100	82	1/1	48
4	**$Pd_2(dba)_3$**	**XPhos**	**KOAc**	**100**	**100**	**1/1.5**	**82[76][c]**
5	CuI	P^{n}Bu$_3$	KO^{t}Bu	r.t.	78	1/1.5	8
6[d]	CuI	P^{n}Bu$_3$	KO^{t}Bu	r.t.	99	1/1.5	9

[a]Conditions: 9-bromoanthracene (0.2 mmol), BpinBdan, TM complex (3 mol%), Ligand (9 mol%), base (3 equiv), 1,4-dioxane (0.86 mL), 16 h. [b]Yields were determined by ^{1}H NMR analysis of the crude reaction mixture using ferrocene as an internal standard. [c]Value in brackets refers to isolated yield. [d]In this case 9-iodoanthracene was used as Ar-X.

Several studies were conducted to purify 9-anthracene naphthodiazaborinine (**6**). Nice yellow crystals of **6** grew at room temperature from a mixture of pentane:ethyl acetate (30:1), and the solid state featured a 70.2° dihedral angle between the anthracenyl and the naphthodiazaborinine planes (Figure 2.3), obtained in the X-ray diffraction data.

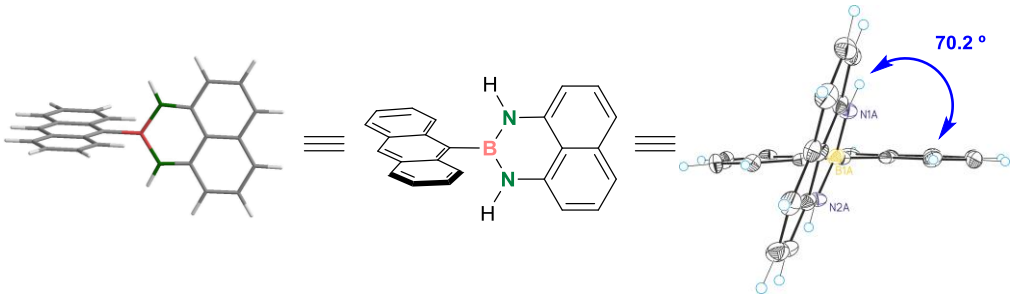


Figure 2. 3 A side-on view of molecular structure of **6** that highlights the non-planarity of the core.

The group of Gross, at the IBM Research in Zurich, has a recognized expertise on imaging techniques, principally with atomic force microscopy (AFM).[11] In collaboration with this group, we submited product **6** to the AFM analysis and it was deposited onto a Cu (111) single crystal, which was partially covered by a doble-layer NaCl islands. The AFM image was recorded in constant-height mode with a CO-functionalized tip. In Figure 2.4a, the felt edge of the anthracenyl head and the right part of the naphthodiazaborinine unit appear with bright contrast. This indicates the presence of repulsive interactions caused by an increased adsorption height of these parts of the molecule. Due to the steric hindrance between the H atoms bound to the N atoms and the closest hydrogens of the anthracenyl unit, the molecule is non-planar. These results are in total agreement with the previously observed structure by X-ray analysis (Figure 2.3). Because of the 3D shape of the molecule, this structure could not be determined unambiguously from the image presented in Figure 2.4b alone.

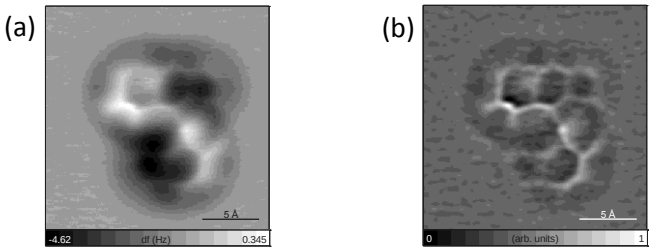
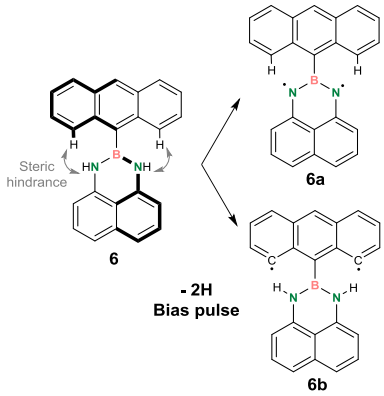


Figure 2. 4 a) AFM frequency shift map recorded with the CO tip. b) Laplace-filtered image of (a).

In order to know more about the influence of the H bonded to N atoms on the global structure **6**, we decided to eliminate those H atoms that cause steric hindrance on molecule **6**. There are two possibilities that are summarized in

Scheme 2.4: removing the hydrogens either from the N atoms (**6a**) or from the closest C atoms of the anthracenyl unit (**6b**).



Scheme 2. 4 Dehydrogenation of **6** with bias pulse and formation of two possible radical intermediates **6a** and **6b**.

Dehydrogenation was induced by increasing the bias voltage in constant-height mode until a sudden change in the tunneling current occurred. After the tip-induced reaction, constant-height AFM imaging with a CO tip was performed. As a result of the manipulation, the entire molecule could be imaged with atomic resolution and the symmetric appearances of the anthracenyl and the naphthodiazaborinine groups indicate planar adsorption geometry.
However, the exact location of the dehydrogenated points could not be exactly determined from imaging by AFM in the dehydrogenated molecule **6** (Figure 2.5).

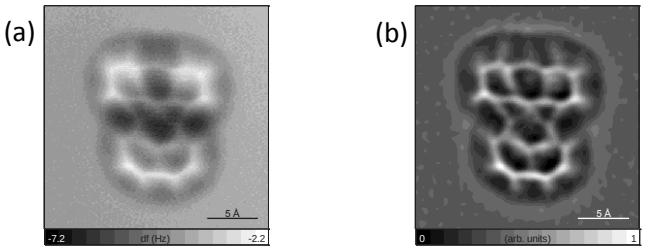


Figure 2. 5 a) AFM image with the CO tip taken after tip-induced of **6** on Cu (111). b) Laplace-filtered image of (a).

To clarify the mechanism of the planarization, by dehydrogenation, the orbital structure of the manipulated molecule was studied. Scanning-tunneling

microscopy (STM) is particularly suited to study the structural environment of an adsorbed molecule on the atomic length scale and to probe the electronic properties of this individual and well-characterized structure. A two-monolayer-thick NaCl film was used to electronically decouple the molecule from the metal substrate to avoid undesirable disturbances.[12]

On NaCl, the molecule could also be dehydrogenated at a similar bias as on Cu (111). It was also possible to image the manipulated molecule at its first negative ion resonance. In the measurement, the highest orbital density is observed above the naphthodiazaborinine part, whereas the anthracenyl head of the molecule exhibits only a faint contrast. Moreover, density functional theory calculations show that the orbitals with the lowest unoccupied character are located at the naphthodiazaborinine in the case of **6a** (see Figure 2.6b), when in fact they shift to the anthracenyl head in the case of **6b** (see Figure 2.6c).

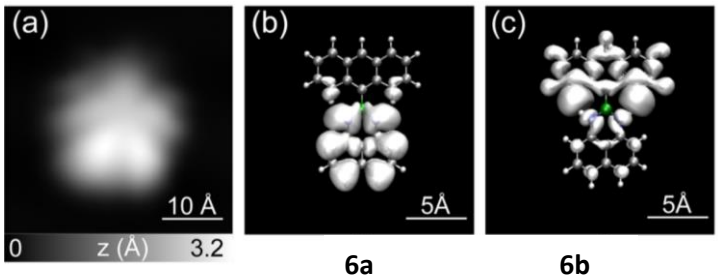


Figure 2. 6 a) STM measurement of product after dehydrogenation of **6** on NaCl. (b, c) Calculated density of the lowest unoccupied orbitals of the dehydrogenated molecules **6a** and **6b,** respectively.

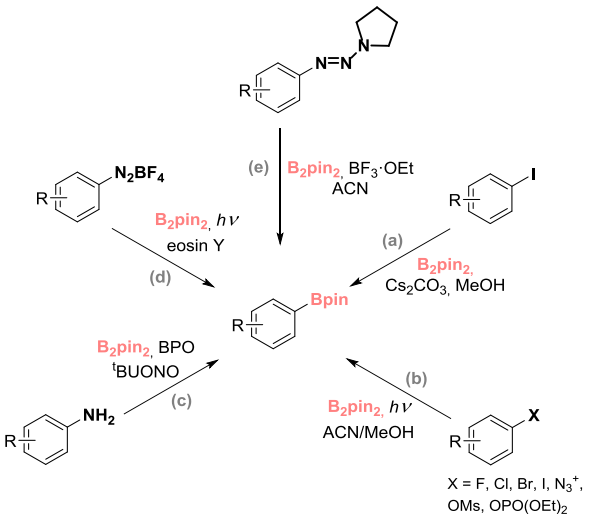
Therefore, the dehydrogenation took place at the N sites. Finally, it could unambiguously be assigned the compound imaged in Figure 2.5 as **6a** and the compound imaged in Figure 2.4 as **6**.

2.3. Transition metal-free borylation of diaryliodonium salts

2.3.1. Context of the work

Although many metal catalyzed processes have contributed with meaningful advances in the field of aryl borylation, all of them rely on the use of transition metal catalyst.[13] Processes enabling borylation of aryl halides under transition metal-free conditions have just emerged.[14]

Initially, Zhang and co-workers observed that the B_2pin_2 could be activated by the methoxide formed from the combination of Cs_2CO_3 and methanol. This seemed to be enough to promote the nucleophilic boryl substitution of a wide range of functionalized aryl iodide compounds towards the synthesis of relevant arylboronic esters (Scheme 2.5a).[15] Alternatively, an efficient photolytic borylation reaction between aryl iodides or aryl bromides, with B_2pin_2 in aqueous solution and at low temperatures, was presented to complement the aryl boronate preparation methods in transition metal-free context. The postulated adduct to be involved in the activation of the diboron reagent is $[B_2pin_2{\cdot}OH]^-$.[16] Additionally, this reaction is susceptible to work in batch and continuous flow conditions. Related work has already extended the photochemistry on borylation reactions of haloarenes, including electron-rich fluoroarenes and quaternary arylammonium salts (Scheme 2.5b).[17]



Scheme 2. 5 Transition metal-free borylation of aryl electrophiles.

A fully novel access to the synthesis of arylboronates, without the need of transition metals, is taking advantage from readily available arylamines which under Sandmeyer reaction conditions replace the aromatic amino group with a boryl moiety. To this end, Wang and co-workers developed ideal conditions that consist on the use of *tert*-butyl nitrite (^{t}BuONO) and benzoyl peroxide (BPO, as additive) at room temperature to quantitatively form arylboronate compounds (Scheme 2.5c).[18] Similarly, the borylation of aryldiazonium salts under irradiation with visible light provides another route to achieve the synthesis of arylboronates with excellent functional group tolerance (Scheme 2.5d).[19] The use of aryltriazenes as substrates for deaminoborylation has also been explored as a facile transition metal-free procedure (Scheme 2.5e).[20]

Hypervalent iodine compounds have recently received considerable attention as mild, non-toxic, and selective reagents in organic synthesis, being their main and classical use as oxidant reagents.[21] The novel, facile and efficient synthetic routes to prepare diaryliodonium salts have encouraged the development of more applications of them. In recent years, impressive improvement on their chemistry is reflected by the growing number of publications and reviews (Figure 2.7).[22]

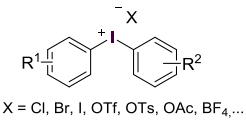
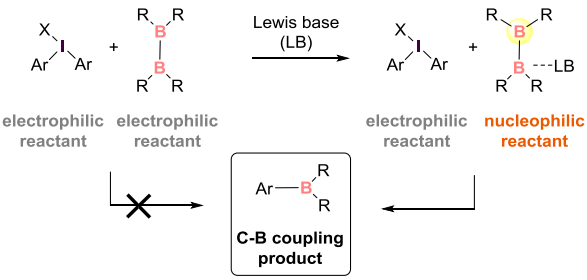


Figure 2. 7 General structure of diaryliodonium salts.

Iodine (III) reagents with two carbon ligands have properties resembling those of Pd complexes, and can be employed in reaction pathways that are similar to metal-catalyzed reactions. Diaryliodonium salts readily undergo various efficient metal-catalyzed cross-coupling reactions[23] since the excellent leaving group ability of the PhI moiety, turn them into more reactive reagents than aryl halides.[24] It is believed that palladium catalyzed cross-coupling reaction with I(III) compounds most commonly involves oxidative addition of $[Ph_2I]X$ to the Pd(0) center, and then release PhI and afford a Pd(II)-phenyl complex. From there, transmetallation between boron and Pd(II) followed by C-C bond formation and, reductive elimination would liberate the biaryl product and regenerate Pd(0) catalyst.[23a]

Diaryliodonium salts are among the oldest, most common, stable and best investigated polyvalent iodine compounds.

The direct C-B bond formation of aryl boronic esters through an effective coupling reaction between diaryliodonium salts and bis(pinacolato)diboron (**1**), appears unconventional at first sight as it involves the combination of two apparently electrophilic reactants (Scheme 2.6).



Scheme 2. 6 Conceptual approach to carbon-boron bond formation using diaryliodonium salts and B_2pin_2.

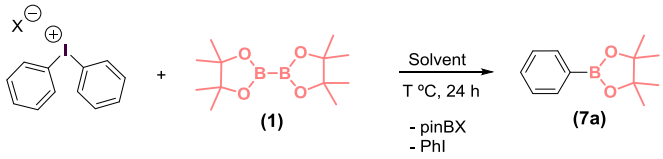
Regarding the formation of the target carbon-boron bond, we contemplated that a Lewis base could be employed for the activation of the diboron reactant. This interaction should provide a quaternized boron atom that enhances the nucleophilic character in the B(sp^2) to attack the electrophilic iodine (III) and, to form the desired C-B bond. This approach is reminiscent of previous alkoxide base mediated reactions developed.[14] This strategic work has been carried out in collaboration with the group of Prof. K. Muñiz, preparing the diaryliodonium salts for the present study.

2.3.2. Results and discussion

To validate the work hypothesis (Scheme 2.6), a subsequent screening of various diphenyliodonium salts and bis(pinacolato)diboron (**1**) was carried out. In that context, the reaction was explored in methanol at room temperature, without any additive or base. We consider the possibility to use the counter ion (OAc, OTf, PF_6, Cl) as the activator of the B_2pin_2 (Table 2.2, entries 1-4). The acetate derivative gave the best results for the borylation reaction of the model substrate

diphenyliodonium salt (Ph_2IX) with B_2pin_2. The expected borylated product **7a** was isolated in high yield, 77% (Table 2.2, entry 3). Screening of the borylation on the diaryliodonium salts Ph_2IPF_6, Ph_2IOTf and Ph_2ICl did not afford any borylated product (Table 2.2, entries 1, 2 and 4). When the reaction between Ph_2IOAc and B_2pin_2 was carried out at room temperature, the conversion diminished to 59% (Table 2.2, entry 5). The use of alternatives alcohols to MeOH, as solvent, did not offered better results, but it clearly showed that the methoxide formed from the interaction between methanol and acetate, is the best alkoxide to activate **1** (Table 2.2, entries 6 and 7). It is noteworthy to say that the lack of alcohol as solvent also produced some borylation, presumably as a consequence of the OAc interaction with B_2pin_2 (Table 2.2, entry 8).

Table 2. 2 Optimization of conditions in the borylation of diphenyliodonium salts.[a]



Entry	Counter ion (X^-)	Solvent	T°C	Yield (%)[b]
1	PF_6	MeOH	50	-
2	OTf	MeOH	50	-
3	**OAc**	**MeOH**	**50**	**83 [77][c]**
4	Cl	MeOH	50	-
5	OAc	MeOH	RT	59
6	OAc	EtOH	50	52
7	OAc	iPrOH	50	13
8	OAc	THF	50	39

[a]Conditions: $Ph_2I^+X^-$ (0.2 mmol), B_2pin_2 (0.3 mmol), solvent (1.25 mL), 24 h. [b]Average yield from two independent runs calculated by GC-MS with mesitylene as internal standard. [c]Value in brackets refers to isolated yield of the borylated product.

This successful transformation leads to two important conclusions: First, the solvent methanol plays a crucial role in the activation of diboron reagent through an intermediate such as **A** (Figure 2.8A). Secondly, the pronounced dependence of the reaction on the counter ion of the diphenyliodonium reagent suggests an essential participation of this anion as well in the activation step. This may include assistance of its negative charge throughout the hydrogen-bonding network of the protic solvent (Figure 2.8B).

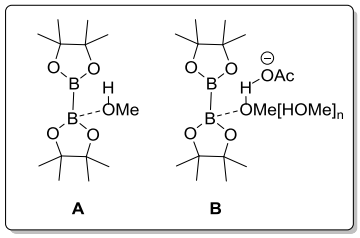
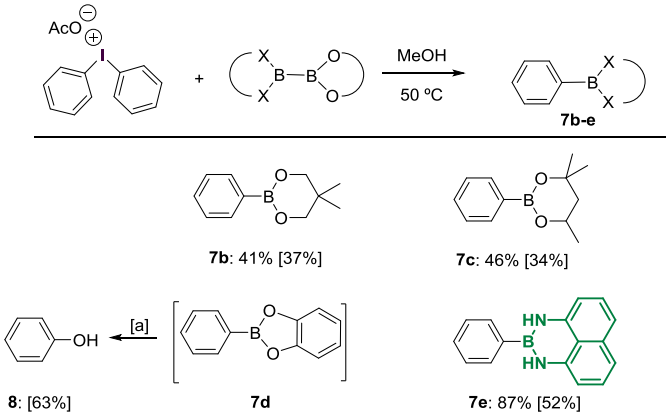


Figure 2. 8 Possible scenarios of the methanol and counter ion participation on the activation of diboron reagent.

The reaction was further extended to various diboron compounds (Scheme 2.7). The symmetrical diboron reagents B_2neop_2 (**2**) and B_2hex_2 (**3**) react with the diphenyliodonium acetate providing moderate yields for the corresponding borylated products **7b** and **7c**. The same protocol was also applied to the B_2cat_2 to furnish the coupling product **7d**. Due to the low stability of the catecholboryl derivative, it was transformed into phenol (**8**) upon oxidative work-up. Interestingly, when the non-symmetrical diboron reagent BpinBdan (**4**) was used, a selective activation at the more acidic Bpin center occurred. This promotes the transfer of the Bdan unit to selectively generate C-B coupling product **7e** in 87% yield. It represents the first borylation with Bdan moiety in a transition metal-free context.



Scheme 2. 7 Influence of the diboron reagent on the borylation of diphenyliodonium salts. Conditions: Ph_2IOAc (0.2 mmol), B_2pin_2 (1.5 equiv), methanol (1.25 mL), 50°C, 24 h. Average yield from two independent runs calculated by GC-MS with mesitylene as internal standard. Values in brackets refer to isolated yields. [a] Isolated yield of the corresponding alcohol after oxidative work up with $NaOH/H_2O_2$.

The extension of the reaction has been evaluated for 15 symmetric diaryliodonium salts, which include *ortho*-, *meta*- and *para*-substitution patterns, as well as higher substituted aromatic entities (Figure 2.9).

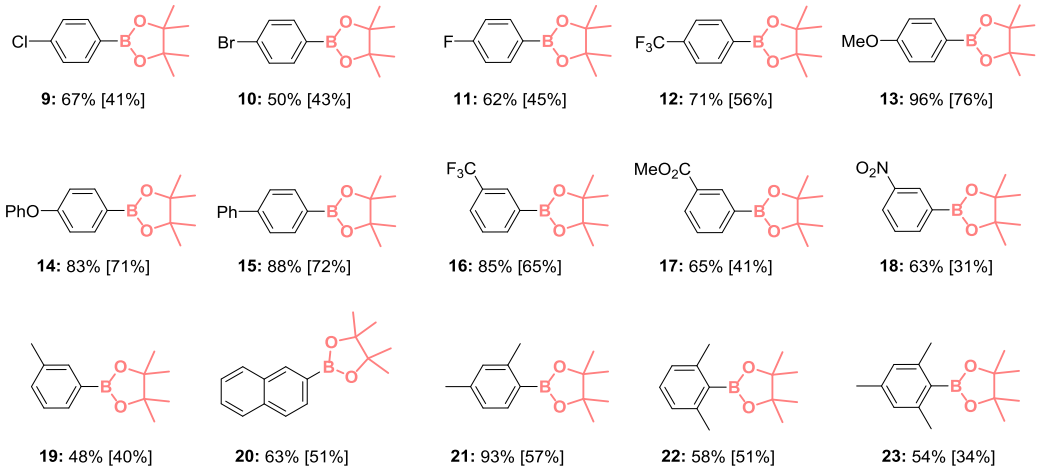


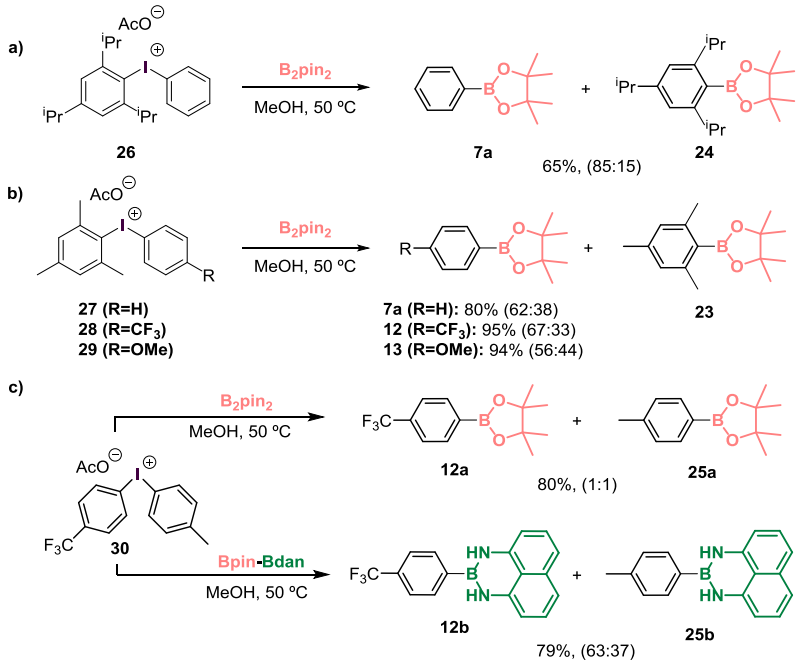
Figure 2. 9 Substrate scope of the borylation of diaryliodonium salts with B_2pin_2. Conditions: Ar_2IOAc (0.2 mmol), B_2pin_2 (1.5 equiv), methanol (1.25 mL), 50°C, 24 h. Average yield from two independent runs calculated by GC-MS with mesitylene as internal standard. Values in brackets refer to isolated yields.

In general, electron donating groups on the *p*-substituted aryls of the diaryliodonium salts, contribute to higher amount of borylated product formation (**13**-**15**) in comparison with the less electron rich functional groups (**9**-**12**). In contrast, *m*-substituted aryl(pinacolboronate) products, which bear electron withdrawing substituents (**16**-**18**) are favored in front of the *m*-tolyl borylated product (**19**). As generally noted in arylboronates, yields can diminish during the purification step.
Appealingly, the present method could also be handled with highly substituted diaryliodonium salts (Ar_2IOAc) demonstrating the tolerance towards the formation of sterically encumbered arylboronate compounds (**20**-**23**).

In order to explore the selectivity of this methodology, two different strategies were conducted using novel non-symmetric diaryliodonium salts (**26**-**30**): (i) Their reactivity with the already well-studied B_2pin_2 and (ii) their reactivity with the non-symmetrical diboron reagent BpinBdan. In Scheme 2.8 is showed how the sterically hindrance of the diaryliodonium salt exerts a huge degree of selectivity with B_2pin_2. Clearly, the reaction of **26** with B_2pin_2 is conducted towards the

formation of **7a/24** in 85:15 ratio, emphasizing that the steric factors are predominant (Scheme 2.8a). Similar trend is observed when the non-symmetrical diaryliodonium salts **27** and **28** are transformed into the corresponding borylated products with B_2pin_2 in favor of the less sterically hindered product **13/23** (Scheme 2.8b). However, substrate **29** generated nearly equimolar mixtures of the hindered and unhindered borylated products (Scheme 2.8b).

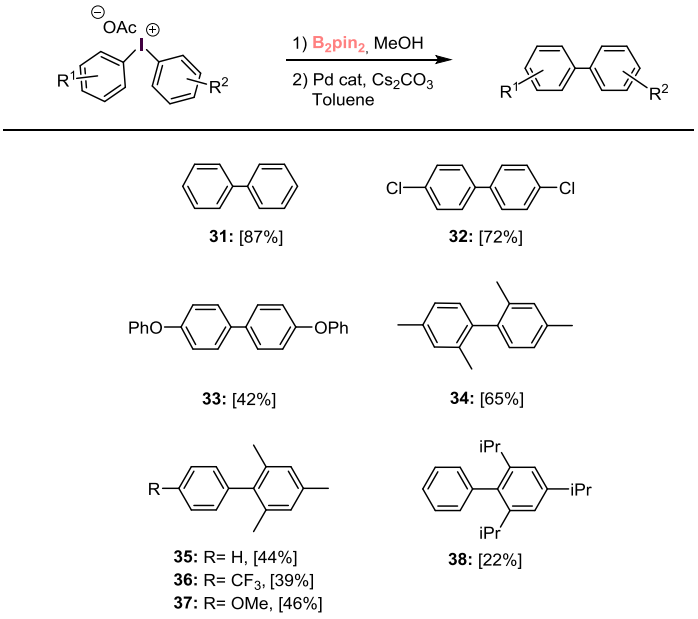
Alternatively, the difference on electronic nature between both aryl substituents on the Ar_2IOAc seems to do not discriminate on the borylative reaction. This is easily exemplified when the diaryliodonium salt **30** was reacted with B_2pin_2 and provided a ratio about 1:1 of the two arylboronate products **12a** and **25a** (Scheme 2.8c). A slightly difference was observed with the reaction between substrate **30** and BpinBdan reagent, which gives a ratio 63:37 in favor of the electronwithdrawing arylboronate **12b** (Scheme 2.8c).



Scheme 2. 8 Borylation of non-symmetrical diaryliodonium salts.

Transformations which involve the use of both aryl groups from the diaryliodonium precursor are indeed rare.[25] In our specific case, we could develop a protocol in order to make use of both aryl groups from Ar_2IOAc, turning this

borylation into an atom economical reaction. To this end, after the borylation reaction of the diaryliodonium salt, that generates an equimolar amount of free aryl iodide, the solvent was changed from methanol to toluene, followed by addition of palladium catalyst $Pd(PPh_3)_4$ and carbonate base (Scheme 2.9).



Scheme 2. 9 One pot cross coupling from diaryliodonium salts *via* B_2pin_2. Conditions for cross-coupling: $Pd(PPh_3)_4$ (10 mol%), Cs_2CO_3 (2 equiv), toluene (2 mL), 80°C, 16 h. Yields in brackets refer to isolated yields based on Ar_2IOAc.

The direct Suzuki-Miyaura coupling provides the corresponding diaryl compounds.[26] The one pot borylation/cross-coupling reaction was efficiently performed to obtain the diphenyl products **31** and **32** (Scheme 2.9). Moderate conversion was achieved for the isolation of **33** and **34** where electronic and steric challenging substrates where involved. Even more interestingly, when the non-symmetrical diaryliodonium salts were employed, the hetero cross-coupled products (**35**-**38**) were isolated as unique coupled products without the presence of homo coupled products.

2.4. Conclusions

We have been able to synthesize 9-anthracene naphthodiazaborinine (**6**) from the borylation of a di-*ortho*-substituted aryl halide with BpinBdan. The reaction has been performed in the presence of a Pd complex and the yield has been maximized by adjusting the aryl halide/BpinBdan ratio. The structure of the synthesized molecule was verified to be non-planar by X-ray analysis and atomic force microscopy (AFM). It was also demonstrated the easy dehydrogenation of **6** within the AFM pulse, and the 3D compound became planar with a precise analysis of the delocalized electronic charge.

A new protocol for the formation of aryl-boron bonds has been developed *via* transition metal-free borylation of diaryliodonium salts. The use of readily available diaryliodonium acetates become an attractive alternative C-B bond formation when B_2pin_2 is activated by MeOH/OAc and reacted with Ar_2IOAc at 50°C. The reaction does not work with $^-PF_6$, ^-OTf or ^-Cl as counter ions in the diaryliodonium salts and become selective when the non-symmetrical diboron reagent BpinBdan is involved, with the exclusive Bdan moiety transfer. The borylation reaction was extended to a series of symmetrical diaryliodonium salts with B_2pin_2 which offer the corresponding arylboronates from moderate to good yields. The use of non-symmetrical diaryliodonium salts also highlights the influence of steric and electronic properties along the transition metal-free borylation reaction.
Furthermore, the reactivity has been extended to an unprecedented C-C coupling of both aryl groups of the initial hypervalent diaryliodonium reagent *via* one pot borylation/cross-coupling reaction. This appealing transformation, applied to non-symmetrical diaryliodonium salts, gives selective access to hetero cross-coupling synthesis by the assistance of B_2pin_2.

2.5. References chapter 2

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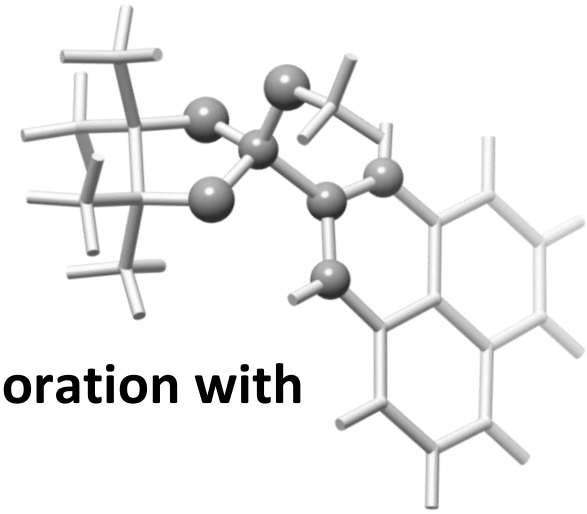
UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat



Chapter 3

Organocatalytic diboration with BpinBdan

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
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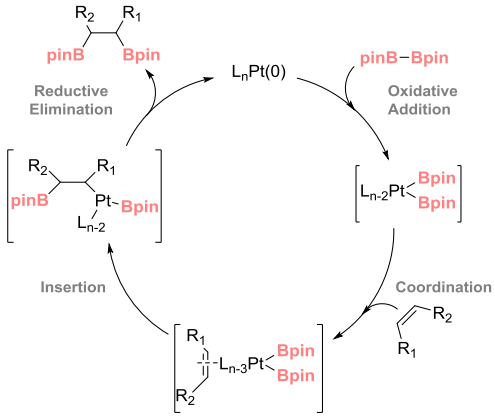
3.1. Focus of the chapter

The catalytic addition of B_2pin_2 to alkenes has been the most widespread 1,2-diboration process, since several transition metal complexes have been deeply studied to activate the diboron reagent and transfer the two boryl units to unsaturated substrates promoting the 1,2-addition.[1] In 1997, Miyaura et al. reported the first use of B_2pin_2 as reagent in diboration of terminal and cyclic alkenes developing a new route to provide bis(boryl)alkanes.[2] They found that $Pt(dba)_2$ was an excellent catalyst to activate the B-B bond generating intermediate [Pt-$(Bpin)_2$] that participates in the substrate coordination, and subsequent insertion into Pt-B bond (Scheme 3.1).[3] Then, the reductive elimination step provides the diborated product and regenerates the catalyst with the original oxidation state. The characteristic *syn*-addition of B-B bonds, enables stereoselective synthesis of bis(boronate) compounds which retain the stereoselectivity in further functionalizations.



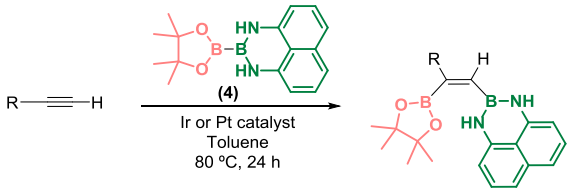
Scheme 3. 1 Catalytic cycle of platinum-mediated diboration of alkenes with B_2pin_2.

Within last decade, the transition metal-free version has also gained a significant impact in the synthetic community.[4] In this context, our group was pioneer to develop the first alkoxide activation of B_2pin_2 towards the concomintant 1,2-addition to a wide range of alkenes.[5] In this chapter we study the transition metal-free approach to conduct 1,2-diboration of cyclic and non-cyclic alkenes with the non-symmetrical diboron reagent BpinBdan (pin = pinacolato, dan = 1,8-diaminonaphthalene).

3.2. Context of the work

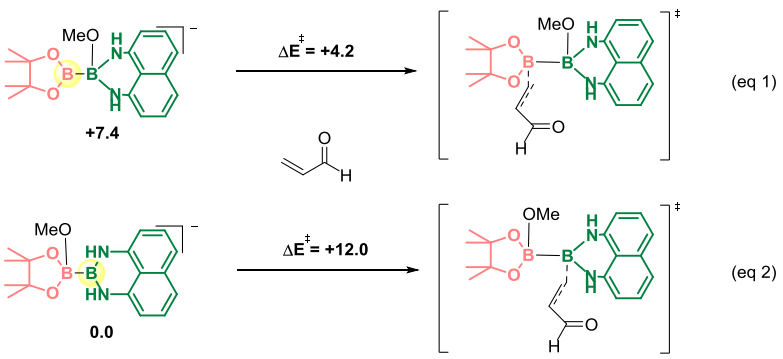
An alkoxide can activate the diboron reagent B_2pin_2 by quaternization of one boryl unit and enhancing the nucleophilic character of the B(sp^2) boryl unit. The adduct [MeO--Bpin-Bpin]$^-$ reacts with alkenes and force the olefin to act as an electrophile.[6] The combination of base and methanol are required to form the alkoxide that acts as the real catalyst. This innovative pull-push effect of diboron compounds has been found nowadays in many applications, even in the enantioselective and diastereoselective C-B bond formation.[7]

The use of non-symmetrical diboron reagent is another interesting feature towards the possible difunctionalization of target compounds. Despite the fact that several efforts have been pursued to perform non-symmetrical diboration reactions, only few examples can be found in the literature. Suginome and co-workers have successfully achieved the diboration of alkynes with BpinBdan (**4**) catalyzed by Ir and Pt complexes.[8] They observed that the major regioisomer obtained was the 1-alkene-1,2-diboronate with the Bdan moiety installed at the terminal position (Scheme 3.2).



Scheme 3. 2 Metal-catalyzed diboration of unactivated alkynes with BpinBdan.

Detailed DFT calculations have been performed in order to have more insights about the potential reactivity of BpinBdan reagent in a transition metal-free context. Our group in collaboration with Carbó and Cid, evaluated the nucleophilic potential of Bdan(sp^2) moiety in the [MeO--Bpin-Bdan]$^-$ adduct with respect to the corresponding adduct of B_2pin_2 (Scheme 3.3).[9] It concluded that due to the π donation from nitrogen lone pair to the boron empty orbital of the Bdan moiety, the acidity of that boron unit is weakened and has less tendency to accommodate the alkoxide (Scheme 3.3, eq 1). The most energetically favored adduct [MeO--Bpin-Bdan]$^-$ (Scheme 3.3, eq 2) is even though less reactive in the presence of activated alkenes.



Scheme 3. 3 Comparative adduct formation between [MeO--Bdan-Bpin]$^-$ and [MeO--Bpin-Bdan]$^-$, and relative reactivity with CH_2CHCHO. Electronic energies in kcal mol^{-1}.[9]

With all those precedents in mind, our next challenge is to perform the selective activation of BpinBdan and the addition to non-activated alkenes, in order to promote the regioselective 1,2-diboration reaction.

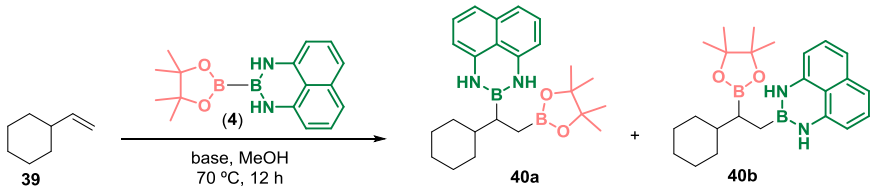
3.3. Results and discussion

To conduct a mixed diboration of simple alkenes with the non-symmetrical diboron reagent BpinBdan (**4**) in the absence of metals or additives, a short optimization was carried out using vinyl cyclohexane (**39**) as model susbtrate (Table 3.1).

First of all, we used the same reaction conditions employed on the organocatalytic diboration of alkenes with B_2pin_2,[5] but now using the BpinBdan reagent. Consequently, we mixed 0.5 mmol of **39**, 1.1 equiv of BpinBdan, 30 mol% of Cs_2CO_3 and 2 mL of THF as solvent, stirring 16 h at 70^{o}C but we didn't observe the desired diborated product. This fact was not surprising since it was previously claimed by the group[9] that the nucleophilic character of the (sp^2)Bdan moiety in the [MeO--Bpin-Bdan]$^-$ adduct is lower than the corresponding to the (sp^2)Bpin moiety in the [MeO--Bpin-Bpin]$^-$. In order to push the Bdan unit to initiate the nucleophilic attack to the alkene, methanol was introduced as solvent. That promoted the reaction outcome and moderate conversion towards the diborated product was achieved (Table 3.1, entry 1). According to our hypothesis, the major isomer formed was the one with the Bdan unit at the internal position. Next, we conducted a systematic

study to determine the influence of the amount of base (Table 3.1, entries 1-3). We concluded that the higher amount of base did not improve the reaction outcome and we selected 30 mol% as the optimized one. Other bases (NaO^{t}Bu, NaOMe and LiO^{t}Bu) were tested without any improvement in neither conversions or selectivities (Table 3.1, entries 4-6).

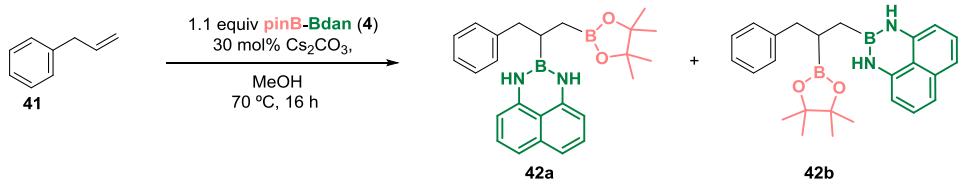
Table 3. 1 Optimization of reaction conditions for the organocatalytic diboration of vinyl cyclohexane with BpinBdan.[a]



Entry	Base	Base (mol%)	Conv. (%)[b]	**40a /40b** (%[b]
1	**Cs_2CO_3**	**30**	**81**	**97[38%][c]/3**
2	Cs_2CO_3	50	88	94[40%][c]/6
3	Cs_2CO_3	75	74	95/5
4	NaO^{t}Bu	30	52	94/6
5	NaOMe	30	60	81/19
6	LiO^{t}Bu	30	44	92/8

[a]Conditions: Substrate **39** (0.5 mmol), BpinBdan (1.1 equiv), base, MeOH (2 mL), 70°C, 16 h. [b]Conversions and selectivities calculated by GC/MS from two independent runs. [c]Values in brackets refer to isolated yield of the product **40a**.

In order to confirm the hypothesized regioselectivity, we moved to allylbenzene substrate (**41**) which has more diagnostic signals and we applied the optimized reaction conditions (Scheme 3.4).



Scheme 3. 4 Organocatalytic diboration of allylbenzene (**41**) with BpinBdan reagent.

Allylbenzene was chosen due to the diastereotopic protons on the benzylic position of the corresponding diborated product that could be diagnostic for the

characterization of the major regioisomer. The ^{1}H NMR spectrum of the crude showed two different groups of signals that belongs to two different diborated products (**42a**) and (**42b**) in a ratio of 4:1. In the isolated diborated products (**42a**) and (**42b**) it could be observed the diastereotopic protons of the benzylic position, H_a and $H_{a'}$ (multiplets 2.5-3 ppm, Figure 3.1).

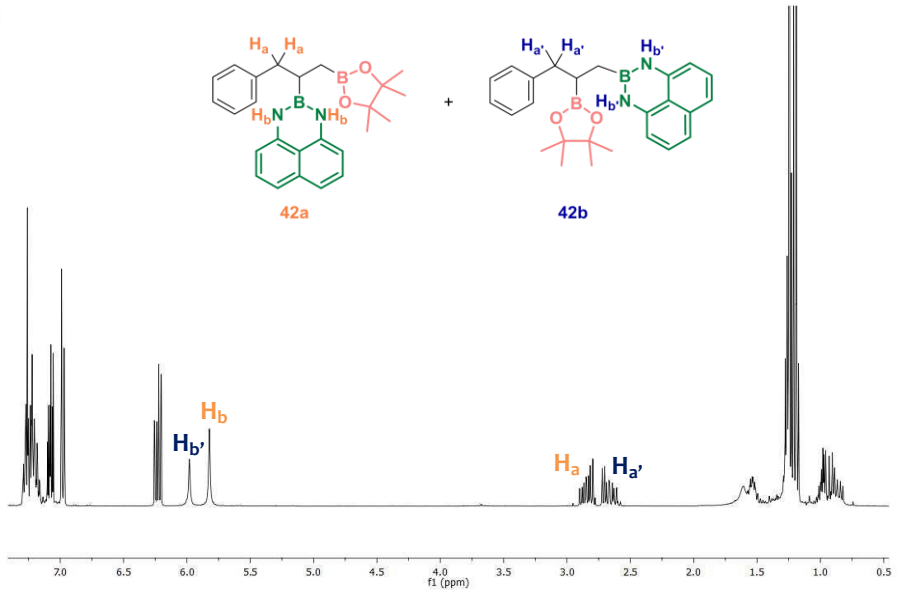


Figure 3. 1 ^{1}H NMR spectrum of isolated diborated products (**42a**) and (**42b**) in a ratio of 4:1.

The NOESY 1D experiment on the diborated products provides information about the spatial distribution of the molecule giving positive NOE when protons are close enough to be correlated. Selective irradiation on the amine protons of the Bdan moiety (broad singlet around 6 ppm in Figure 3.1) of each isomer ($H_{b'}$ and H_b) was applied. When the most abundant amine proton was irradiated (H_b) a positive NOE with the diastereotopic protons (H_a) was observed (Figure 3.2a), demonstrating that the major diborated isomer contained the Bdan unit in the internal position. When the less abundant amine proton was irradiated ($H_{b'}$), a negative NOE was obtained and it confirmed that the minoritary regioisomer is the one containing the Bdan unit in the terminal position (Figure 3.2b).

This result was in sharp contrast with the regioselectivity observed by Suginome and co-workers on the diboration of alkynes with BpinBdan by Pt or Ir catalysts (Scheme 3.2).[8]

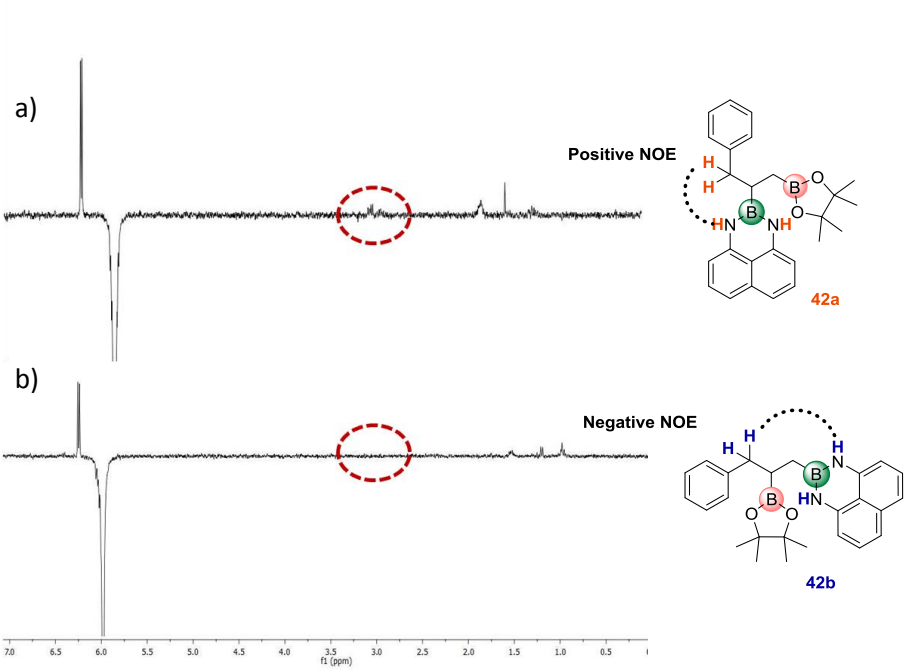
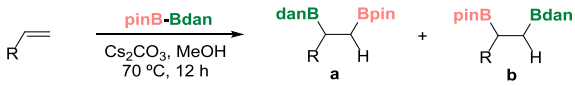
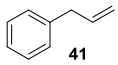
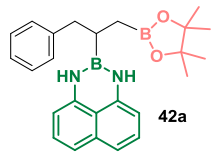
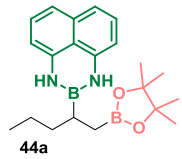
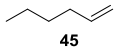
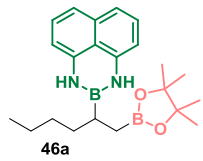
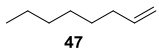
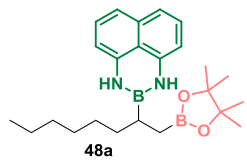
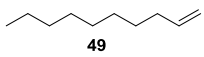
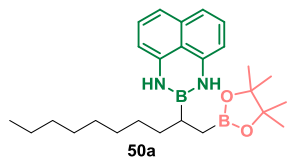


Figure 3. 2 NOESY 1D experiments of the diborated regioisomeric products.

Once the regioselectivity was validated, the metal-free diboration reaction was extended to terminal olefins with variable alkyl chain lenght (Table 3.2). In all aliphatic olefins studied, the conversion was moderate, and high for 1-decene (**49**) (Table 3.2, entry 5). However, isolated yields were low as a consequence of product manipulation during the purification step. The trend to preferentially generate the regioisomer with the Bdan unit in the internal position could be extrapolated from the previous studies.

Table 3. 2 Substrate scope of terminal alkenes for the organocatalytic diboration with BpinBdan.[a]



Entry	Substrate	Conv. (%)[b] (a/b)	Product	**a** [IY%] [c]
1	 41	56 (80/20)	 42a	30
2	 43	48 (92/8)	 44a	20
3	 45	42 (88/12)	 46a	17
4	 47	65 (92/8)	 48a	25
5	 49	85 (91/9)	 50a	70

[a]Conditions: Substrate (0.5 mmol), BpinBdan (1.1 equiv), Cs_2CO_3 (30 mol%), MeOH (2 mL), 70°C, 12 h.
[b]Conversion and regioselectivity calculated by GC-MS from an average of two independent runs.
[c]Isolated yield of regioisomer **a**.

In a second set of experiments, internal olefins were subjected to the organocatalytic mixed diboration reaction (Figure 3.3). The acyclic *cis*-3-hexene was moderately converted into the desired product **51**. The 1,2-addition of Bdan

and Bpin moieties to cyclic olefins took place in a *syn* fashion, even though in all cases conversion was moderate, and isolated yields were up to 42% (Figure 3.3).

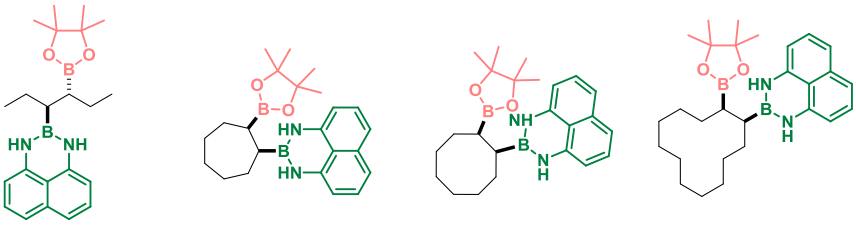
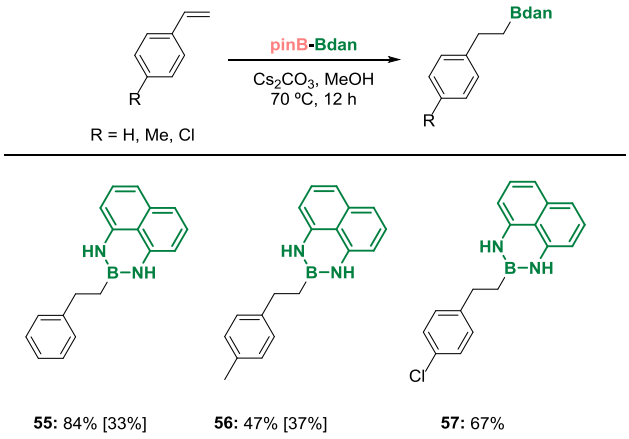


Figure 3. 3 Organocatalytic diboration of internal alkenes with BpinBdan.

However, this new methodology to obtain different protected diborated products in the absence of transition metal complexes has a substrate scope limitation. When vinylarenes were exposed to the diboration reaction with BpinBdan under the same reaction conditions, a mixture of products were obtained, being the major one the hydroborated product with the Bdan moiety in the terminal position (Scheme 3.5).



Scheme 3. 5 Reactivity of vinylarenes with BpinBdan under transition metal-free conditions.

With the objective of having more insight into the mechanism of the metal-free non-symmetrical diboration reaction, in collaboration with Carbó and Cid, DFT calculations were conducted so that the intrinsic control of the regioselectivity could be understood. The mechanism of the organocatalytic diboration of non-

activated olefins with B_2pin_2 reagent has already been computationally characterized by Bo and co-workers.[5] They proposed the nucleophilic attack of the boron reagent towards the substrate through an interaction between the strongly polarized B-B σ-bond of the activated diboron reagent and the antibonding π* orbital of the olefin. This proposal was the starting point to analyze the origin of our regioselectivity.

In Figure 3.4 is depicted the energy profile of the two possible regioisomeric pathways. From the beginning two different Lewis acid-base adducts can be formed when we work with the non-symmetrical BpinBdan diboron reagent: [MeO--Bpin-Bdan]$^-$ (**A**) and [MeO--Bdan-Bpin]$^-$ (**A'**). In a recent report from our group, it has been shown that the Bpin moiety is stronger Lewis acid than Bdan, and consequently, the former adduct **A** is lower in energy than **A'**,[9] even though the energy barrier for the interconversion between both adducts is modest.

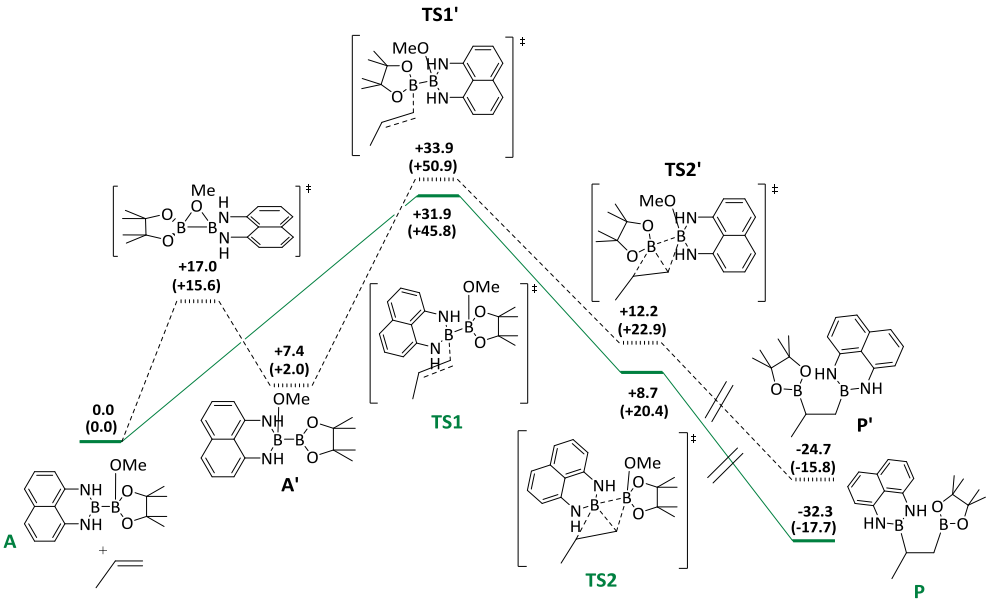
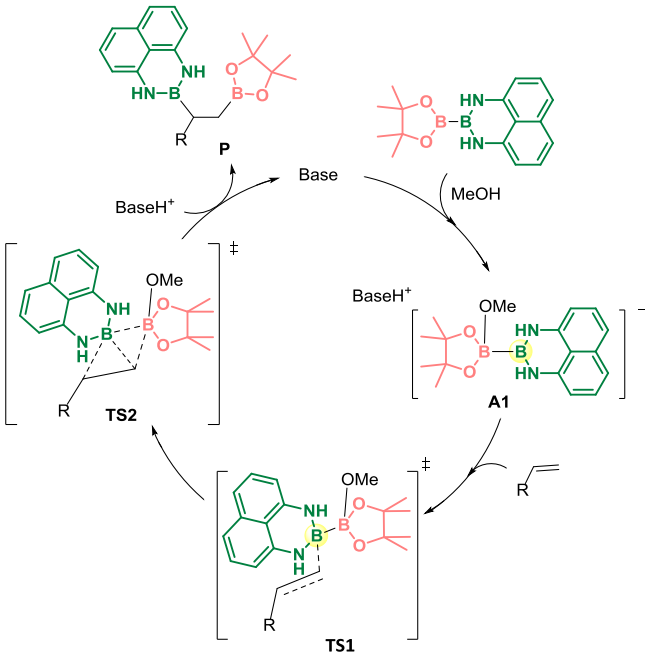


Figure 3. 4 Energetic profile of [MeO--BpinBdan]$^-$ with propene as model substrate. Electronic energies and Gibbs free energies in MeOH (in parenthesis) in kcal/mol.

The most energetically demanding step and the one that determines the regioselectivity is the nucleophilic boryl attack on the terminal carbon to reach **TS1** and **TS1'**. As expected,[9] the computed energy barrier for the attack of the Bdan group (+31.9 kcal mol^{-1}) is higher than that for the Bpin group (+26.5 kcal mol^{-1}).

However, owing to the relatively low energy barrier for interconversion of **A** and **A'**, the product distribution should be determined by the relative energy between the transition states of both paths, being **TS1** lower in energy than **TS1'**. The transition state **TS1** is followed by a lower energy-lying transition state (**TS2**), in which the Bdan moiety shifts to the internal olefinic carbon and the Bpin(OMe) moiety binds to the terminal carbon, leading to the diborated product (**P**) (Figure 3.4). These results are in total agreement with the experimentally observed selectivity for Bdan addition to the internal position, albeit small amount formation of the opposite regioisomer can be observed. Moreover, these calculations offer an explanation for the opposite regioselectivity obtained in comparison with that found for the diboration of alkynes by Ir and Pt complexes.[8]

Finally, having in mind the experimental data obtained and the DFT calculations carried out by Carbó and Cid, we suggest the following catalytic mechanism for the diboration of alkenes with the non-symmetrical diboron reagent BpinBdan (Scheme 3.6).



Scheme 3. 6 Suggested catalytic cycle for transition metal-free diboration with BpinBdan.

The catalytic cycle would consist on methoxide activation of the non-symmetrical diboron reagent BpinBdan forming the Lewis acid-base adduct (**A1**). Then, nucleophilic attack of the sp^2 Bdan unit, which has gained nucleophilic character through the polarization of the B-B σ-bond, occurs to the terminal position of the electrophilic alkene (**TS1**). Now, the boron atom of the Bdan unit becomes electrophilic and is susceptible to be attacked by the more electronegative internal carbon of the double bond, shifting the Bdan unit to the internal position of the olefin (**TS2**). At the same time, the cleavage of B-B bond and the Bpin moiety addition to the terminal position takes place, and generates the desired diborated product. All these concerted movements justify the regioselective 1,2-addition of BpinBdan to alkenes.

3.4. Conclusions

We have been able to perform an unprecedented diboration reaction of terminal and internal alkenes with the non-symmetrical BpinBdan reagent in a transition metal-free context. The reaction exhibits high control of regioselectivity, locating the Bdan unit in the internal position of the alkene. Calculations performed by Carbó and Cid on the energetic profile for the organocatalytic diboration of propene, with BpinBdan diboron reagent, supported the experimental observations and provided the basis to rationalize the reaction outcome.

The new synthetic platform opens a non-existing methodology to prepare, *via syn*-addition, the mixed 1,2-diboron compounds that selectively contain the Bdan unit in the internal position.

3.5. References chapter 3

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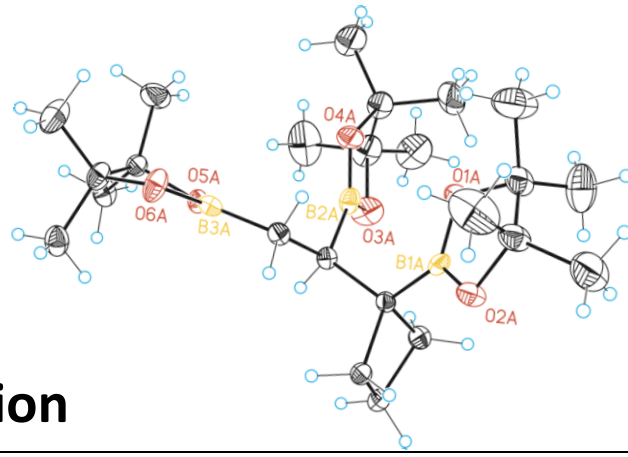
UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat



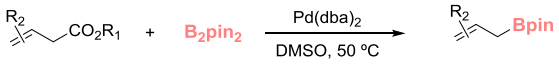
Chapter 4

Allylic Borylation

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat

4.1. Focus of the chapter

Allyl boronic esters have gained a prominent status in organic synthesis due to their relevant reactivity with carbonyls and imines, converting this reactivity in the methodology of choice for the preparation of homoallylic alcohols and amines.[1] Moreover, allylboronates are being effective partners in a range of cross-coupling reactions with aryl[2] and allyl[3] electrophiles. Recently, it has been described that by addition of aryllithium, the corresponding allylboronate complexes display enhanced nucleophilicity, enabling addition to a wide range of electrophiles, forming new C-C, C-F or C-S bonds.[4] Allylboronic esters are configurationally stable, easily accessible in high enantioselectivity and unlike most other allylmetals do not undergo 1,3-transposition. Catalytic synthesis of allylboronates has received much attention and is attractive due to the group tolerance and mild conditions offered. In this sense, Miyaura and co-workers were pioneer on the preparation of allylboronates through palladium catalyzed cross-coupling of allylic electrophiles and B_2pin_2 (Scheme 4.1),[5] although it was occasionally accompanied with dimerized side-products.



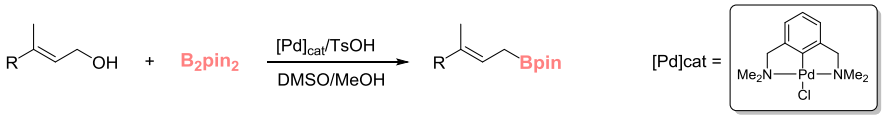
Scheme 4. 1 First palladium-catalyzed cross-coupling between allyl electrophiles and B_2pin_2.

The spotlight of this chapter is the preparation of allyl- and homoallyl-boronic esters, and towards this end we planned to adopt two different methods:
The first strategy consists on a transition metal-free borylation of tertiary allylic alcohols with B_2pin_2 (**1**) as starting materials.
On the second approach, we aimed to explore the S_N2' allyl-alkyl and allyl-boryl coupling reactions using vinyl cyclic carbonates as selected substrates, and 1,1-diborylmethane (**5**) and B_2pin_2 (**1**) as reagents. In this occasion, the activation of borane reagents is handled by copper(I). Moreover the oxidation of both homoallylboronates and allylboronates gives access to synthetically useful unsaturated 1,5-pent-2-ene and 1,4-but-2-ene diols, respectively.

4.2. Transition metal-free borylation of allylic alcohols

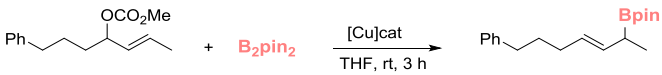
4.2.1. Context of the work

Allylic alcohols are one of the most readily available substrates in palladium-catalyzed allylic displacement reactions. Unfortunately, the hydroxyl group is one of the most unwilling leaving group in substitution reactions, and therefore, employment of metal complexes, additives and/or harsh conditions were required in these processes.[6] In 2006, the group of Szabó developed the direct conversion of allylic alcohols into allylic boronic acids through palladium-pincer complex catalysis.[6b] Soon after, this transformation was extended for the same group, to isolable pinacol boronic esters (Scheme 4.2).[6a] The mechanism of the palladium-catalyzed synthesis of allylboronates from allylic alcohols was also investigated by the group of Szabó.[7]



Scheme 4. 2 Palladium-catalyzed borylation of allylic alcohols.

Another common route to overcome the difficulty on borylation of allylic alcohols is to use activated allylic substrates such as acetates or carbonates, which are usually prepared from the corresponding allylic alcohols. Improvements on this borylation reaction appeared by using $Pd(OAc)_2$[6a] or Cu(I)[8] (Scheme 4.3) affording allylboronates with very good yields and also good enantioselectivities.[8a] More recently, it was reported the borylation of the easy accessible allylic halides accomplished by a commercially available Pd catalysts.[9]



Scheme 4. 3 Cu(I)-Xanphos catalyzed borylation of allylic carbonates with B_2pin_2.

Due to the efficient methodology of transition metal-free borylation procedures based on the quaternization of diboron reagents and their appreciable increase in reactivity in the presence of suitable bases, we propose to fill the gap of preparing allylboronate compounds in the absence of transition metal complexes. For that,

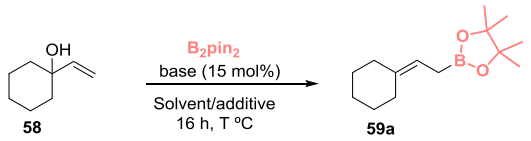
we started collaboration with Prof. Kálmán Szabó from the Stockholm University, because they are experts on the preparation and manipulation of allylboronate compounds.

4.2.2. Results and discussion

We initiated our studies on the transition metal-free borylation reaction of allylic alcohols selecting the commercially available allylic alcohol **58** as model substrate and B_2pin_2 diboron reagent. The reaction conditions chosen were 0.3 mmol of **58**, 2 equiv of B_2pin_2, base (about 15 mol%) in THF at 70°C. Under these conditions, the desired product **59a** was obtained in 15% yield (Table 4.1, entry 1). The addition of MeOH as solvent resulted beneficial as it was observed in previous studies of the group,[10] that it favors the activation of B_2pin_2 towards the nucleophilic attack. In this case, the yield of **59a** increased up to 45% (Table 4.2, entry 2). Then, we explored the combination of THF as solvent and methanol as additive, and we found that 10 equiv of MeOH were optimal (Table 4.1, entries 3-4). The influence of the temperature was also studied and 70°C were required *versus* 50°C to quantitative formation of **59a** (Table 4.1, entries 4-5). The important role of the base on the organocatalytic borylation reaction is to facilitate the formation of the Lewis acid-base adduct $[Hbase]^+[MeO\text{-}B_2pin_2]^-$.[11] We tested K_2CO_3, NaOMe and NaO^{t}Bu in comparison with Cs_2CO_3 and we found that the later resulted the most efficient base for our purpose (Table 4.1, entries 4, 6-8).

Allylic borylation

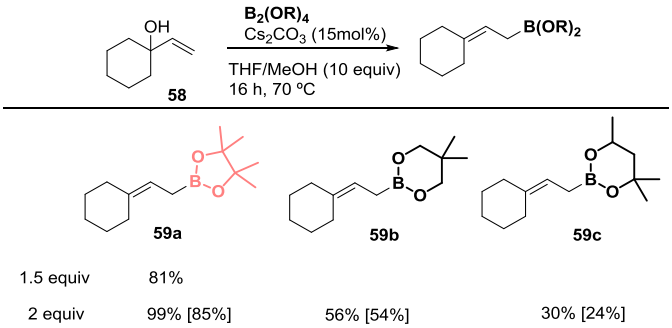
Table 4. 1 Optimization conditions for the borylation of allylic alcohols with B_2pin_2.[a]



Entry	Base	Solvent	Additive (10 equiv)	T(°C)	**59a** Yield (%)[c]
1	Cs_2CO_3	THF	-	70	15
2	Cs_2CO_3	MeOH	-	70	45
3	Cs_2CO_3	THF	MeOH[b]	70	45
4	**Cs_2CO_3**	**THF**	**MeOH**	**70**	**99 [85]**[d]
5	Cs_2CO_3	THF	MeOH	50	47
6	K_2CO_3	THF	MeOH	70	75
7	NaOMe	THF	MeOH	70	76
8	NaO^{t}Bu	THF	MeOH	70	61

[a]Conditions: Substrate **58** (0.3 mmol), B_2pin_2 (2 equiv), base (15 mol%), MeOH (10 equiv), solvent (0.5 mL), 70°C, 16 h. [b]50 equiv of additive were used. [c]Yields were determined by ^{1}H NMR analysis of the crude reaction mixture using naphthalene as internal standard. [d]Values is brackets refer to isolated yield.

The choice for the most active diboron reagent, as well as, their required quantity was subjected to study. In Scheme 4.4 is showed that 2 equiv of B_2pin_2 gave the desired allylboronate **59a** in higher yields than the analogous **59b** and **59c** using B_2neop_2 and B_2hex_2 diboron reagents, respectively.



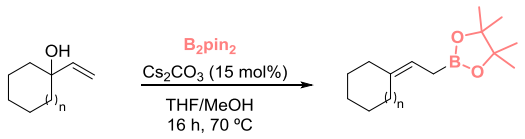
Scheme 4. 4 Influence of the diboron reagent in the transition metal-free borylation of **58.** Yields were determined by ^{1}H NMR analysis of the crude reaction mixture with naphthalene as internal standard. Values in brackets refer to isolated yields.

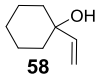
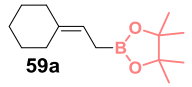
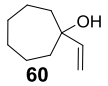
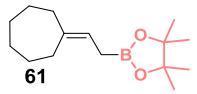
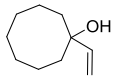
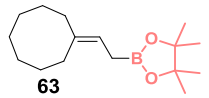
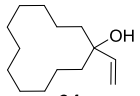
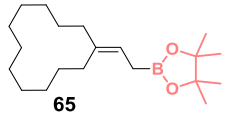
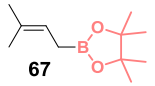
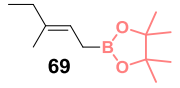
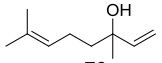
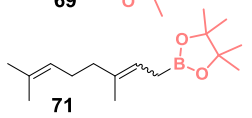
Looking for the generality of the reaction, we examined cyclic tertiary allylic alcohols with different ring sizes (**60**, **62**, **64**), which were prepared following a general procedure for the synthesis of tertiary allylic alcohols,[12] that is also described in the experimental part.

The transition metal-free borylation provided the corresponding exocyclic allylboronates **61**, **63** and **65** in quantitative yields, and high isolated yields, regardless the ring size (Table 4.2, entries 1-4). Acyclic tertiary alcohols were also well tolerated (Table 4.2, entries 5-7), although the reaction rate was lowered. This could probably be associated to the less stability of the isolated corresponding borylated compounds (**67**, **69** and **71**), considering that the NMR yields in the crude were also quantitative.

It is important to highlight that the efficiency of the organocatalytic borylation is comparable to the corresponding methods with palladium catalyst.[6b, 13] It was also studied the borylation reaction with secondary alcohol 1-octen-3-ol, which isolated yield was low (17%). Even more shocking, the primary alcohol (*E*)-2-octen-1-ol was not transformed into the desired allylboronic ester. This could be the consequence of two main problems: a) The better leaving group ability of protonated tertiary allylic alcohols (such as **58**), compared to primary or secondary ones. b) The worse stability of non-substituted allylboronates. Therefore, this transition metal-free borylation is efficient for tertiary allylic alcohols and is limited in scope with primary and secondary allylic alcohol substrates.

Table 4. 2 Substrate scope of the transition metal-free allylic borylation of tertiary allylic alcohols.[a]

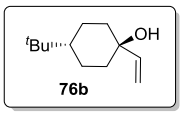


Entry	Substrate	Product	NMR yield (%)[b]	Isolated yield [%][c]
1	 58	 59a	99	85
2	 60	 61	92	84
3	 62	 63	97	79
4	 64	 65	99	79
5	 66	 67	97	55
6	 68	 69	95	60
7[d]	 70	 71	71	42

[a]Conditions: tertiary allylic alcohols (0.3 mmol), B_2pin_2 (2 equiv), Cs_2CO_3 (15 mol%), THF (0.5 mL), MeOH (10 equiv), 70°C, 16 h. [b]Yields were determined by ^1H NMR analysis of the crude reaction mixture with naphthalene as internal standard. [c]Isolated yields. [d]E/Z ratio for **71** is 1:1.

Allylic alcohols with a cyclic structure were found to be general and suitable for this borylation reaction, thus we turned our attention to study the influence of the substitution on the ring of cyclohexyl allylic alcohol (Scheme 4.5). A series of *para*-substituted cyclohexyl allylic alcohols (**72**, **74**, **76**, **78**) were prepared from the related cyclohexyl ketones[12] to analyze the electronic effect. For these substrates, the two diastereoisomeric alcohols were isolated in pure form,[14] and for the case

of **76b** we could have obtained crystal diffraction data to confirm its relative configuration (Figure 4.1).



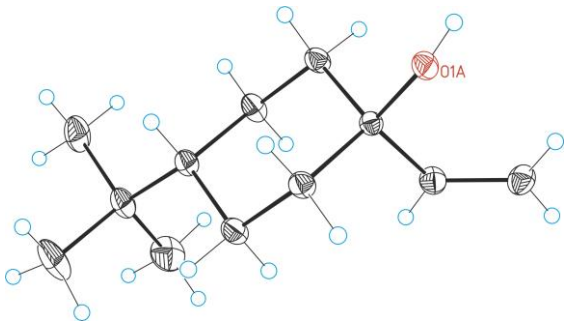
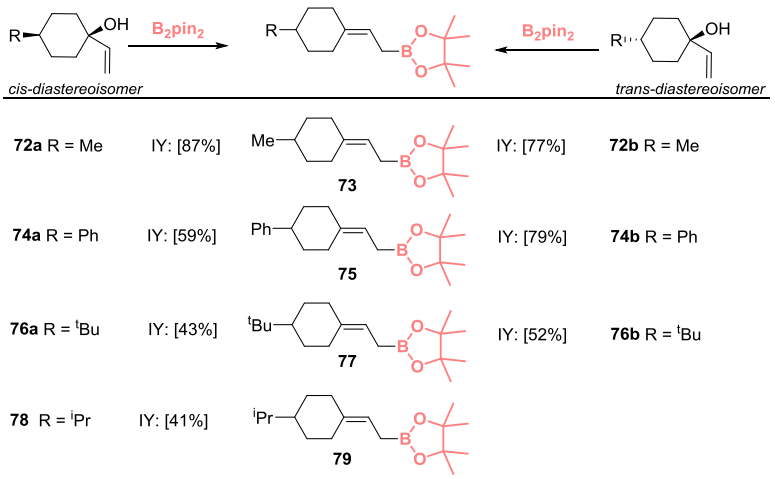


Figure 4. 1 X-ray diffraction of *trans*-4-Tertbutyl-1-vinyl-1-cyclohexanol (**76b**).

Independently, the *cis*- and *trans*-diastereoisomers (**72a,b**; **74a,b** and **76a,b**) were subjected to allylic borylation under exactly the same reaction conditions (Scheme 4.5).

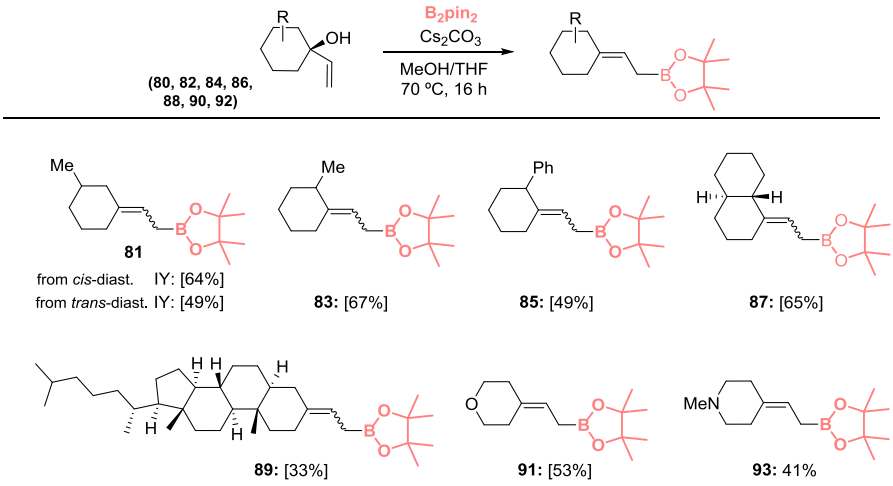


Scheme 4. 5 Scope of *p*-substituted cyclohexyl allylic alcohols on the transition metal-free allylic borylation. Conditions: allylic alcohol (0.3 mmol), B_2pin_2 (2 equiv), Cs_2CO_3 (15 mol%), THF (0.5 mL), MeOH (10 equiv), 70°C, 16 h. Values in brackets refer to isolated yields.

The same borylated product **73** was formed from both diastereoisomers **72a** and **72b** that reacted independently of their relative configuration giving similar rates. Moving from substrate **72** to **74** or **76**, we noted a lower yield. Concerning

substrate **78**, since the mixture of diastereoisomers could not be separated, then the borylation was carried out with the *cis/trans* mixture of allylic alcohol **78**, towards the corresponding allylboronate **79** in moderate yield. All these allylboronates (**73**, **75**, **77** and **79**) were reported for the first time in this work.[15]

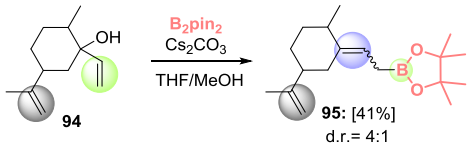
Moving to *meta*- or *ortho*-substituted cyclohexyl allylic alcohols, the transition metal-free allylic borylation provides mixtures of *cis/trans* allylboronates. In Scheme 4.6 is summarized how the two diastereoisomers of 3-methyl-1-vinyl-1-cyclohexanol (**80**) are converted into the allylboronate **81** as 1:1 mixture of isomers. Analogous trend was noticed for 2-methyl-1-vinyl-1-cyclohexanol (**82**) and 2-phenyl-1-vinyl-1-cyclohexanol (**84**) giving allylboronates **83** and **85** as mixtures of isomers. The bicyclic alcohol, synthesized from decalone in its chiral form, was also object of this study and the corresponding allylboronate **87** was isolated in 65% yield. The more challenging 5-α-cholestan-3-one was subjected to alkylation to obtain the chiral allylic alcohol (**88**) and it was subjected to the transition metal-free allylic borylation reaction affording **89** in a mixture of *cis/trans* isomers 1:1 with 80% NMR yield, despite the fact that it could only be isolated in a 33% yield (Scheme 4.6). All these boronic esters were synthesized for the first time in this work.[15]



Scheme 4. 6 Substrate scope of polysubstituted and functionalized cyclohexyl allylic alcohols. Conditions: allylic alcohol (0.3 mmol), B_2pin_2 (2 equiv), Cs_2CO_3 (15 mol%), THF (2 mL), MeOH (10 equiv), 70°C, 16 h. Values in brackets refer to isolated yields.

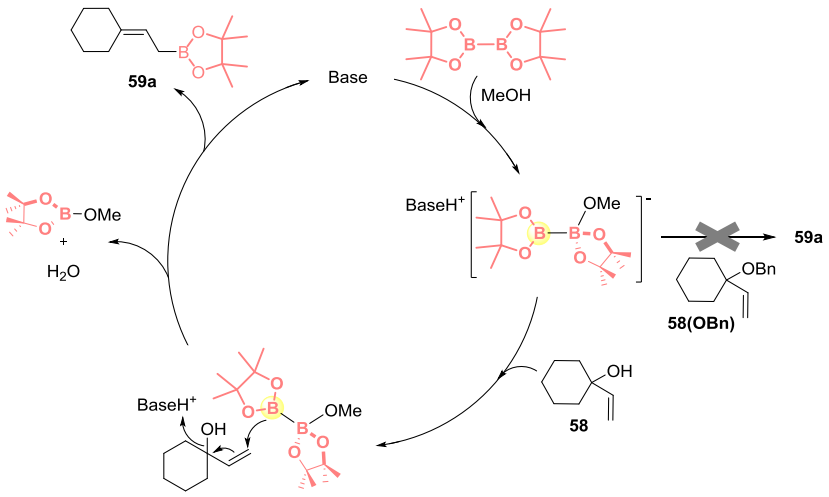
The tolerance of other functional groups was also studied. We were pleased to see that N- and O-containing cyclic tertiary alcohols can perform the transition metal-free borylation reaction providing **91** and **93** in moderate yield as single isomers (Scheme 4.6).

The selectivity of the reaction was tested with 2-methyl-5-(prop-1-en2-yl)-1-vinyl-1-cyclohexanol (**94**). We were delighted to see that allylic borylation is exclusively carried out *versus* the potential transition metal-free diboration[16] on the pendant alkene (Scheme 4.7). The reaction was performed under the same optimized reaction conditions, and in this case the *cis/trans* ratio of the borylated product **95** was 4:1.



Scheme 4. 7 Selective transition metal-free borylation. Conditions: allylic alcohol (0.3 mmol), B_2pin_2 (2 equiv), Cs_2CO_3 (15 mol%), THF (2 mL), MeOH (10 equiv), 70°C, 16 h. Value in brackets refers to isolated yield.

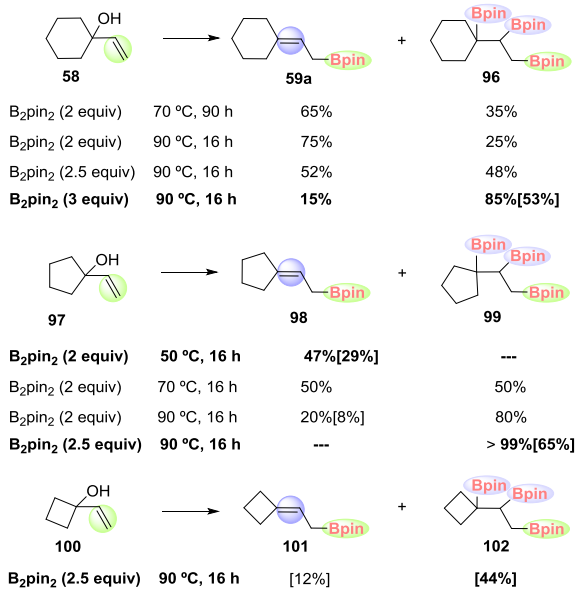
To explain a possible mechanism for this reaction a catalytic cycle has been depicted below (Scheme 4.8). We suggest that it is based in a S_N2'-type mechanism in which the initial step is a base-mediated nucleophilic attack by the methoxide group, formed *in situ* from the combination of MeOH and base, on one of the Bpin units of B_2pin_2 to give the corresponding adduct.[11] As consequence, the B(sp^2) becomes nucleophilic and might attack the terminal position of the allylic alcohol which leads to C-OH bond cleavage. Probably, the OH moiety acting as leaving group is assisted by the $[H\text{-base}]^+$ adduct, and that turned the OH_2^+ in a better leaving group. Simultaneous formation of the new carbon-boron bond provides the allylboronate compound **59a**. The presence of unprotected hydroxyl group in substrate **58** is a prerequisite. We could not observe any formation of **59a** borylated product using benzyl-protected substrate **58(OBn)** when it was subjected to the same organocatalytic conditions. A possible explanation is the necessity of a good leaving group to accomplish the allylic borylation, which is formed by the protonation of the hydroxyl group.



Scheme 4. 8 Suggested mechanism for the transition metal-free allylic borylation.

One can imagine that the double bond present in the allylboronated product **59a** might be susceptible to further borylation in similar reaction conditions. Experimentally, when the allylic borylation of model substrate **58** was carried out within 90 h at 70°C, a new product could be identified as triborated specie **96** (Scheme 4.9). We figured out the *in situ* formation of **96** *via* transition metal-free diboration of product **59a**. This fact was confirmed by a separate study in which isolated compound **59a** was submited to transition metal-free diboration with 2 equiv of B_2pin_2 and 15 mol% of Cs_sCO_3 at 70°C for 90 h. From this, product **96** was obtained in high yield. This unexpected tandem performance of Lewis acid-base adduct, $[Hbase]^+[MeO\text{--}B_2pin_2]^-$, served as the basis of a new transition metal-free tandem borylation reactions towards polyborylated compounds. An optimization of the reaction conditions allowed to transform the allylic alcohol **58** into triborated compound **96**, in one-pot protocol, within 16 h at 90°C using up to 3 equiv of B_2pin_2 (Scheme 4.9).

Appealingly, when this reactivity was explored with 1-vinyl-cyclopentol (**97**) and 1-vinyl-cyclobutanol (**100**), the triborated product was mainly formed at 90°C and milder reaction conditions were required to selectively obtain the allylboronate compound, probably as a consequence of more congested cyclobutane and cyclopentane systems (Scheme 4.9).



Scheme 4. 9 Transition metal-free tandem allylic borylation/diboration towards 1,2,3-triborylated species. Conditions: Allylic alcohol (0.3 mmol), B_2pin_2, Cs_2CO_3 (15 mol%), THF (0.5 mL), MeOH (10 equiv). Yields were determined by ^1H NMR analysis of the crude reaction mixture with naphthalene as internal standard. Values in brackets refer to isolated yields.

Fortunately, triborated species were crystalline solids, and for compound **102** we were able to obtain single crystals and the structure could be confirmed by X-ray diffraction (Figure 4.2).

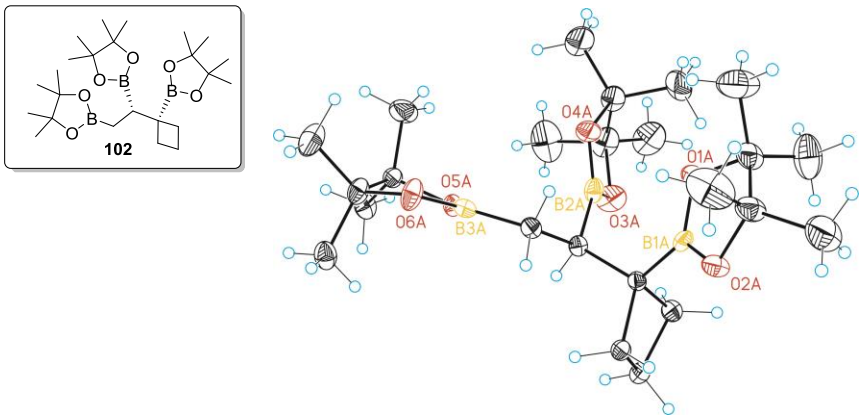
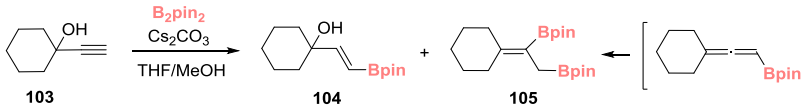


Figure 4. 2 X-ray diffraction structure of 1,2,3-polyborated product **102**.

To complement the prior investigation, we carried out the transition metal-free borylation of 1-propargylic cyclohexanol (**103**) under the previously optimized reaction conditions. In this case, we mostly obtained the product of the corresponding hydroborated triple bond (**104**) (Scheme 4.10b), but a little amount of a secondary product (**105**) was observed. Interestingly, when the temperature was slightly decreased to 50°C, product **104** was isolated in 91% yield and only traces of the second product could be detected (Scheme 4.10a). Furthermore, when the temperature was increased, the secondary product was predominantly formed. Its isolation and fully characterization allowed us to identify it as the alkenyl borane **105**. At 90°C we can selectively obtain product **105** in 68% isolated yield (Scheme 4.10c). Probably, it is formed as a consequence of the diboration of the allene intermediate, even though it could not be observed.[17]



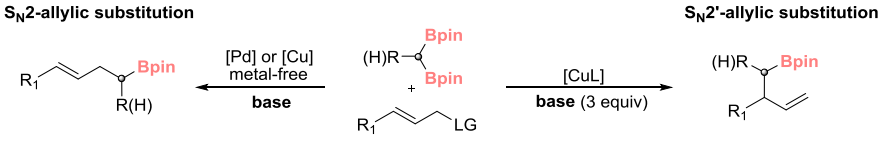
a)	50 °C	**93% [91%]**	traces
b)	70 °C	86%	10%
c)	90 °C	15%	**70%[68%]**

Scheme 4. 10 Transition metal-free borylation of 1-propargyl cyclohexanol. Conditions: substrate **103** (0.3 mmol), B_2pin_2 (2 equiv), Cs_2CO_3 (15 mol%), MeOH (10 equiv), THF (0.5 mL), 16 h. Yields were determined by ^1H NMR analysis of the crude reaction mixture using naphthalene as internal standard. Values in brackets refer to isolated yields.

4.3. Copper catalyzed S_N2' allyl-alkyl and allyl-boryl couplings of vinyl cyclic carbonates

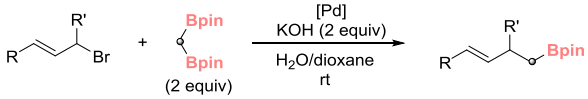
4.3.1. Context of the work

Alternatively to the direct generation of C-B bonds formed from diboron reagents, the use of 1,1-diborylalkane reagents, to conduct nucleophilic borylmethylation, has been less studied. However, the last has a tremendous interest since homologated organoboron products offer important scaffolds in organic synthesis. Previous studies have shown that *gem*-diborated compounds are useful reagents with alkyl-[18] and aryl-based electrophiles.[19] The reactivity of *gem*-diborated compounds with allyl electrophiles can be mainly divided in two groups depending on the S_N2-allylic substitution or S_N2'-allylic substitution (Scheme 4.11).



Scheme 4. 11 Allyl-alkyl couplings using allylic electrophiles and *gem*-diborated reagents.

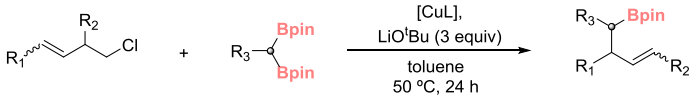
Shibata and co-workers efficiently performed the allyl-alkyl coupling using a palladium complex such as $[Pd(P^tBu_3)_2]$ at room temperature, providing the homoallylboronate compounds in moderate to high yields (Scheme 4.12).[20] The KOH base (2 equiv) is required to assist the carbanion formation and transmetallation from the 1,1-diborylalkane to the Pd complex. The reaction seems to operate in the C-C bond formation through a S_N2 mechanism. Then, the mainly product obtained is the (*E*)-isomer at the α-carbon of the allylic position.



Scheme 4. 12 Alkyl-allyl coupling between 1,1-diborylalkane and allyl bromides through palladium catalyst**.**

In a similar way, bis[(pinacolato)boryl]methane (**5**) has also been coupled with cinnamyl phosphates in the presence of copper (I) catalyst and LiOMe (3 equiv).[21]

Complementary, Cho and co-workers observed that in a copper catalyzed allylic substitution reactions of allylic chlorides with 1,1-diborylalkane reagents, the S_N2' selectivity can be highly favored by the presence of a NHC ligand (Scheme 4.13), and suggested a plausible mechanism to justify it.[18a]

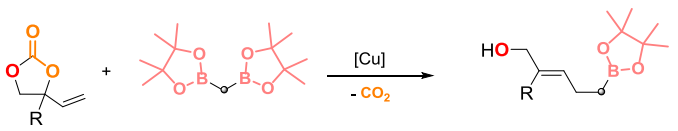


Scheme 4. 13 Preparation of branched alkylboronates by S_N2'reactions of allylic chlorides with 1,1-diborylalkanes.

This new methodology gives the opportunity to synthesize branched alkylboronates in good yields by copper catalyzed allylic substitution reactions of allylic chlorides, but it is limited to these allylic halides, since other allylic substrates, such as allylic carbonates, could not be borylated.

We were looking to expand the synthesis of linear alkylboronates, when we became inspired by the work of Kleij,[22] on their applications of stable vinyl cyclic carbonates or also named vinylethylene carbonates (VECs). The success on the use of vinyl cyclic carbonates on decarboxylative functionalizations with suitable electrophiles, such as Michael acceptors,[23] and the postulation of a switterionic Pd-intermediate structure, make them ambivalent reactants and also amenable to react with nucleophiles, such as water[22b] and amines.[22c]

Here we address the focal point on the synthesis of alkylboronic esters from vinyl-substituted cyclic carbonates facing a new conceptual reactivity towards decarboxylative borylation of readily available vinyl cyclic carbonates with 1,1-diborylmethane (**5**) as borane reagent (Scheme 4.14). This project was carried out in collaboration of the group of Prof. Arjan Kleij who were in charge to prepare all the vinyl cyclic carbonates of the present study.



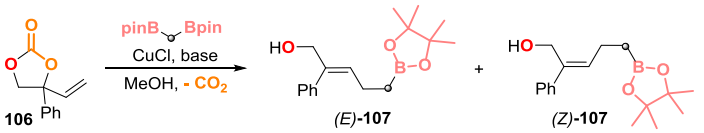
Scheme 4. 14 Proposed reactivity between vinyl cyclic carbonates and 1,1-diborylmethane.

4.3.2. Results and discussion

In order to extend the nucleophilic borylmethylation reaction, we have explored the use of CuCl as copper(I) source to catalyze the allylic alkylation of vinyl cyclic carbonates with 1,1-diborylmethane reagent. The use of these specific substrates, would allow addition functionality to be retained in the homoallylic borylated product since a hydroxyl group is generated with the concomitant loss of CO_2, providing access to scaffolds that are not easy to prepare through other routes.

To test the viability of the envisioned strategy and based on the reactivity previously reported by Cho and co-workers,[18a] we selected a lavish vinyl cyclic carbonate (**106**) for reacting with the *gem*-diborylmethane in the presence of a catalytic amount of CuCl and 15 mol% of Cs_2CO_3 as base (Table 4.3, entry 1). Initially we carried out the reaction in the presence of MeOH as solvent and base to *in situ* generate the Cu-OMe derivative from CuCl at room temperature. Neither the use of a double amount of *gem*-diborylmethane or the presence of alternative bases, such as LiO^tBu, improved the reaction outcome (Table 4.3, entries 2 and 3, respectively). The use of a carbene ligand, 3-bis(2,6-diisopropylphenyl)imidazolinium chloride, to promote the coupling reaction was unsuccessful (Table 4.3, entry 4), as well as when the ligand employed was triphenylphosphine (Table 4.3, entry 5). The use of higher Cs_2CO_3 loading (50 mol%) was optimal to afford product **107** in 75% of yield (Table 4.3, entry 6). Remarkably, the *E/Z* ratio which in all cases is about 4:1, is higher than the corresponding ratios observed in the cross-coupling of vinyl cyclic carbonates with arylboronic acids catalyzed by Pd nanoparticles.[24]

Table 4. 3 Allyl-alkyl couplings between diborylmethane and the vinyl cyclic carbonate **106.**[a]

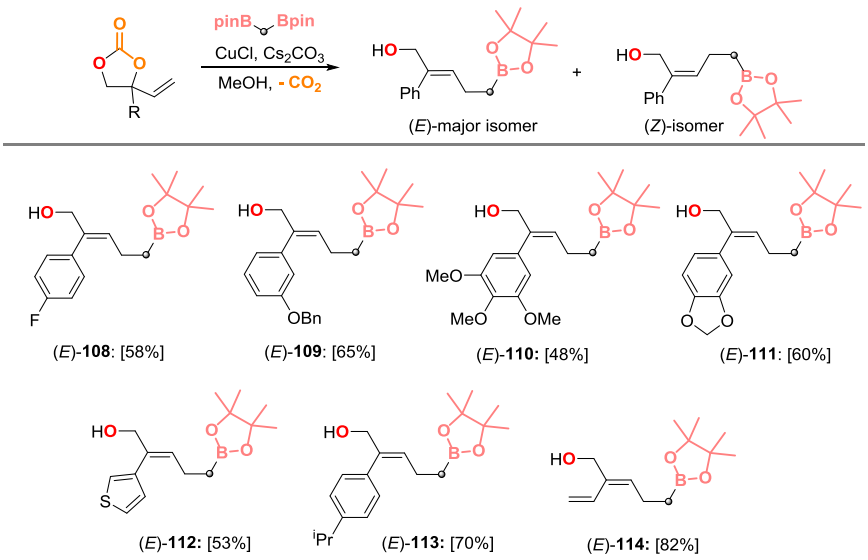


Entry	Cu/L	Base (mol%)	*E/Z*	**(*E*)-107** Yield (%)[b]
1	CuCl	Cs_2CO_3, 15	4/1	58
2[c]	CuCl	Cs_2CO_3, 15	4/1	40
3	CuCl	LiO^tBu, 15	4/1	24
4	CuCl,/SIPr	Cs_2CO_3, 15	3.9/1	35
5	CuCl/PPh_3	Cs_2CO_3, 15	4/1	13
6	**CuCl**	**Cs_2CO_3, 50**	**4/1**	**75**

[a]Conditions: carbonate (0.2 mmol), $CH_2(Bpin)_2$ (1.2 equiv), CuCl (9 mol%), ligand (13 mol%), base, MeOH (0.1 mL), rt, 16 h. [b]Yields were determined by ^1H NMR analysis of the crude reaction mixture using naphthalene as internal standard. [c]2 equiv of $CH_2(Bpin)_2$ were used.

The exclusive formation of the new C-C bond at the terminal position exemplifies the regiocontrol of the allyl-alkyl coupling reaction, but is important to highlight that the S_N2' process allows, by simple decarboxylation from the original cyclic carbonate, to keep a synthetically useful OH functionality. To the best of our knowledge, the only examples reported for Cu-catalyzed S_N2'-selective allylic substitution reaction between 1,1-diborylalkanes and allylic chlorides resulted unproductive for allylic carbonates.[18a] Therefore we opened a complementary reactivity and this methodology represents a carbonate ring opening reaction with relative high stereocontrol.

With the optimized reaction conditions in hand, the substrate scope was next explored to react with 1,1-diborylmethane (Scheme 4.15).



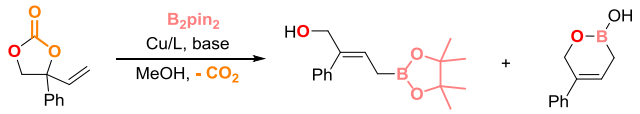
Scheme 4. 15 Substrate scope for the allyl-alkyl couplings between diborylmethane and vinyl cyclic carbonates. Conditions: carbonate (0.2 mmol), $CH_2(Bpin)_2$ (1.2 equiv), CuCl (9 mol%), Cs_2CO_3 (50 mol%), MeOH (0.1 mL), rt, 16 h. Values in brackets refer to isolated yields.

A general trend is observed on the borylated products **108-114**, being the *E*-stereoisomer favored in all cases. In those reaction crudes the *E/Z* ratio were close to 4:1 independently from the substituent present in the vinyl cyclic carbonate. Both stereoisomers could be isolated from the reaction media, the corresponding isolated yield of the *E*-isomers are shown in the Scheme 4.15 (on the experimental section, details for the *Z*-isomers can be found). The electronic differences on the substituents in the aryl group, as well as their relative position, did not show any significant effect in the formation of the homoallylboronates **(*E*)-108**, **(*E*)-109**, **(*E*)-110**, **(*E*)-111** and **(*E*)-113** with isolated yields up to 70%. The reaction also illustrated tolerance towards other functionalities present in the carbonate, including thiophenyl groups **(*E*)-112** and the interesting butadiene derivative **(*E*)-114** which was isolated in high yield (82%).

To further test the viability of the C-B bond formation from vinyl cyclic carbonates, we carried out the same reaction with substrate **106**, but changing the 1,1-dibroylmethane for B_2pin_2. We were glad to see that again the conversion of the substrate was quantitative with the principal formation of the allylboronate **(*E*)-115** in 60% isolated yield (Table 4.4, entry 1). However, a little amount of a secondary product was also formed. After isolation and fully characterization of

this secondary product, it was identified as a result of an intramolecular cyclization from the corresponding *Z*-stereoisomer, affording the boracyclic compound **(*Z*)-116**. The nucleophilic attack of the boryl moiety onto the vinyl cyclic carbonate **106** readily takes place at rt through a Cu-Bpin intermediate that is *in situ* formed in the reaction media. Nonetheless, the transition metal-free version does not allow for allylic borylation of vinyl cyclic carbonates.

Table 4. 4 Allyl-Boryl coupling between B_2pin_2 and the vinyl cyclic carbonate **106.**[a]



106 *(E)*-**115** *(Z)*-**116**

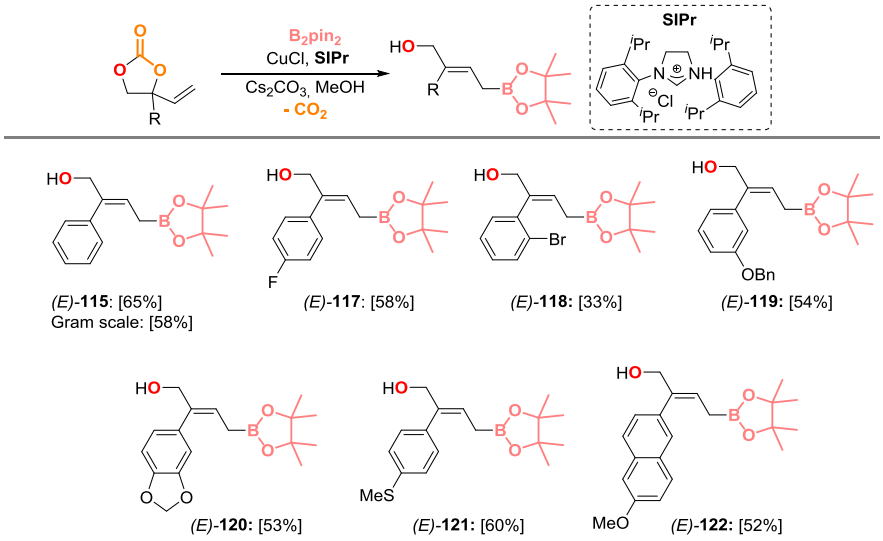
Entry	Cu/L	Base	Conv. (%)[b]	(*E*)-**115** (%)[b]	(*Z*)-**116** (%)[b]
1	CuCl	Cs_2CO_3	95	62[60]	17
2	CuCl,	KO^{t}Bu	61	41[40]	19
3	CuO^{t}Bu	Cs_2CO_3	64	47[37]	15
4	CuCl/SIPr	Cs_2CO_3	99	69[65]	31[30]
5	CuCl/PPh_3	Cs_2CO_3	99	57	35

[a]Conditions: Substrate **106** (0.2 mmol), B_2pin_2 (1.2 equiv), CuCl (9 mol%), ligand (13 mol%), base (15 mol%), MeOH (0.1 mL), rt, 16 h. [b]Conversions and yields were determined by ^{1}H NMR analysis of the crude reaction mixture using mesitylene as internal standard. Values in brackets refer to isolated yields.

Again, the copper catalyzed reaction proceeded regioselectively as the C-B bond was exclusively formed at the terminal position of the allylic intermediate confirming the S_N2' mechanism.[25] The use of alternative bases such as KO^{t}Bu, reduced both overall conversion and stereoselectivity (Table 4.4, entry 2). We also carried out the reaction with a preformed CuO^{t}Bu catalyst (Table 4.4, entry 3) and the results showed similar reactivity than the *in situ* formed catalyst derived from CuCl/KO^{t}Bu in MeOH. Therefore, we continued with the *in situ* prepared catalyst for simplicity. The amount of base was optimized to 15 mol%, which is significantly less than the amount of base used in similar copper-catalyzed allylic borylations, requiring typically 1-3 equivalents. The use of an *N*-heterocyclic carbene ligand (SIPr) exhibits a little improvement in terms of conversion towards the borylated products and enhanced yield of allylboronate **(*E*)-115** up to 69% (Table 4.4, entry 4). On the other hand, when the copper catalyst was combined with a phosphine

ligand the mixture of borylated products obtained was slightly shifted in favor to the (*Z*)-stereoisomer. It can be seen that with CuCl/PPh_3 catalyst the *E/Z* ratio obtained is 57:35 (Table 4.4, entry 5). Since the borylation reaction with B_2pin_2 seems to be ligand-controlled, we performed a series of experiments in order to find the best ligand for each stereoisomer.

Concerning the (*E*)-stereoisomer, after an exhaustive screening of different type of carbenes, we could not obtain better selectivity. Then, we proceeded to examine the borylation of a series of vinyl cyclic carbonates using CuCl/SIPr as catalyst system on the optimized conditions. The depicted (*E*)-allylboronates in Scheme 4.16 were obtained as the main product, with some minor amount of the (*Z*)-isomer (< 10%). In general, rather similar isolated yields were obtained (52-65%) independently from the substituted cyclic carbonate. The borylation of **106** towards **(*E*)-115** could also be carried out on gram-scale with a slightly lower yield (58%, Scheme 4.16). However, we found a limitation using vinyl carbonates with alkyl groups (R = Me, Cy) which were unproductive.

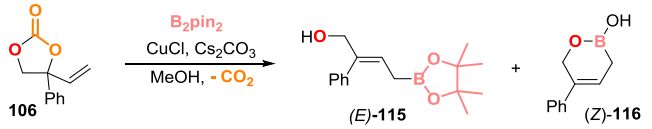


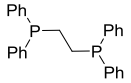
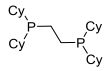
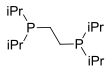
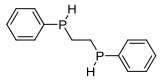
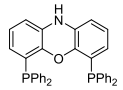
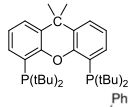
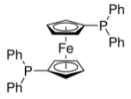
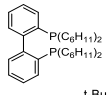
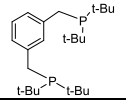
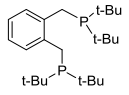
Scheme 4. 16 Substrate scope on (*E*)-selective allyl-boryl couplings between B_2pin_2 and vinyl cyclic carbonates. Conditions: Carbonate (0.2 mmol), B_2pin_2 (1.2 equiv), CuCl (9 mol%), SIPr (13 mol%), Cs_2CO_3 (15 mol%), MeOH (0.1 mL), rt, 16 h. Values in brackets refer to isolated yields.

Noteworthy, copper-mediated decarboxylative allylic borylation reactions of acyclic carbonates have already been used to obtain allenylboronates,[17b, 26] vinylboronates,[27] and allylboronates.[8, 28] Nevertheless, all those methods lose the whole OCO_2R functional group during the C-B bond formation while our new methodology permits additional functionality to be retained in the final product.

On the other hand, the borylation reaction towards the (*Z*)-boracycle product using the same carbonate **106**, was also explored testing up to 15 phosphine ligands (Table 4.5). We observed that diphosphine ligands with a small bite angle (Table 4.5, entry 3) were able to boost the **(*Z*)-116** in front of **(*E*)-115** in a ratio of 52:36 respectively. Even more interestingly, when 1,2-bis(di-*tert*-butylphosphinomethyl)benzene (P-P) was added to the reaction media, exclusive formation of (*Z*)-boracycle could be achieved (Table 4.5, entry 12).

Table 4. 5 High Throughput Experimental (HTE) studies on the phosphine ligand.[a]

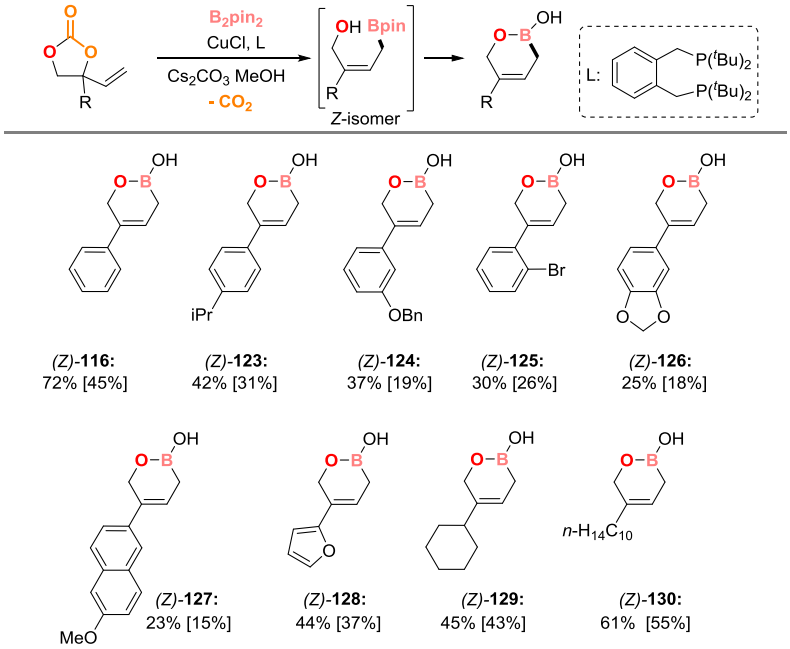


Entry	Ligand	Conv. (%)[b]	(*E*)-**115** (%)[b]	(*Z*)-**116** (%)[b]
1	PPh_3	99	57	35
2		97	46	29
3		91	36[24]	52[39][c]
4		0	---	---
5		Decomp.	---	---
6		90	44	47
7		99	38	47
8		79	21	34
9		75	17	36
10		0	---	---
11		75	29	46
12		**99**	**---**	**72[45]** [c]

[a]Conditions: Substrate **106** (0.2 mmol), B_2pin_2 (1.2 equiv), CuCl (9 mol%), phosphine (13 mol%), Cs_2CO_3 (15 mol%), MeOH (0.1 mL), rt, 16 h. [b]Conversions and yields were determined by ^1H NMR analysis of the crude reaction mixture using mesitylene as internal standard. [c]Values in brackets refer to isolated yields.

Allylic borylation

Since stereocontrol in acyclic and cyclic systems is an important synthetic challenge, we extended the scope of the decarboxylative borylation to selectively obtain (*Z*)-configured products. Thus, 1,2-bis(di-*tert*-butylhosphinomethyl)benzene was used as ligand, under the same reaction conditions, for the allylic borylation of alkyl/aryl-substituted vinyl cyclic carbonates advanced towards the (*Z*)-stereoisomer following intramolecular annulation to afford the boracyclic product (Scheme 4.17). The target borylated compounds were exclusively obtained in moderate yield although substantial loss of borylated product upon isolation by chromatography occurred.



Scheme 4. 17 Substrate scope on (*Z*)-selective allyl-boryl couplings between B_2pin_2 and vinyl cyclic carbonates. Conditions: Carbonate (0.2 mmol), B_2pin_2 (1.2 equiv), CuCl (9 mol%), phosphine (13 mol%), Cs_2CO_3 (15 mol%), MeOH (0.1 mL), rt, 16 h. Conversions and yields were determined by ^1H NMR analysis of the crude reaction mixture using mesitylene as internal standard. Values in brackets refer to isolated yields.

For the boracycle **(*Z*)-116** we were able to obtain single crystals and the structure could be also confirmed by X-ray diffraction (Figure 4.3).

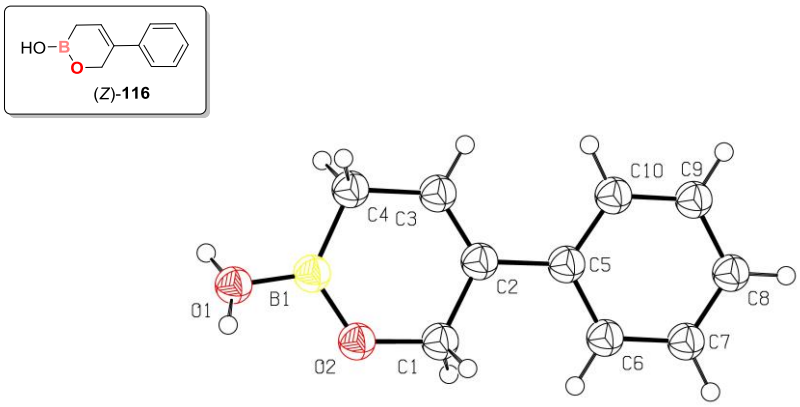
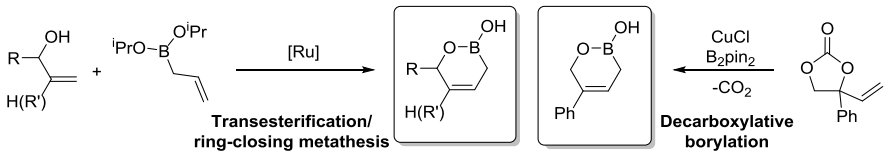


Figure 4. 3 X-ray diffraction of boracycle **(Z)-116.**

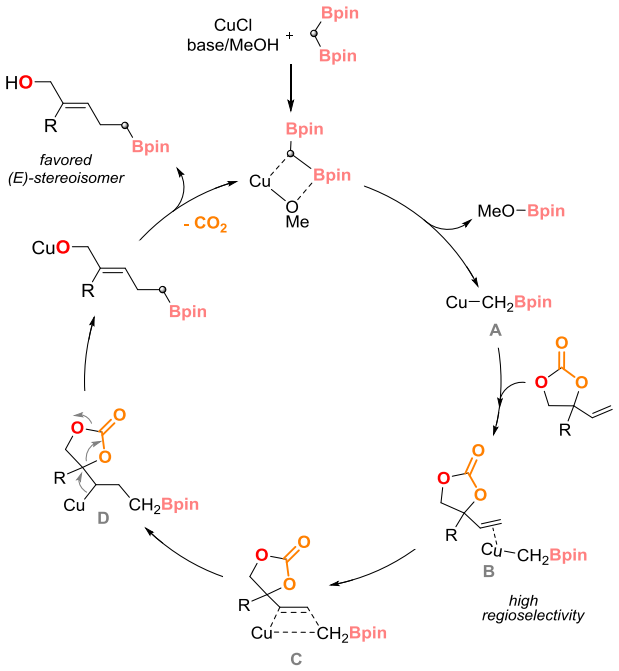
Boracycles are important in the context of diversity-oriented organic synthesis, as well as in organoboron based drug discovery.[29] Boron-containing heterocycles have previously been formed *via* reaction of unsaturated boronic esters with allylic or propargylic alcohols that would transiently provide mixed organoboronic esters which could be trapped using standard ring-closing metathesis protocols (Scheme 4.18, left).[30] Our methodology drives the synthesis of allylboracycles in a complementary way to populate the chemical functionality to a given area of biological interest (Scheme 4.18, right).



Scheme 4. 18 Alternative organic synthesis of (*Z*)-allylboracyclic compounds.

A proposed mechanism for the S_N2' allyl-alkyl coupling (Scheme 4.19) and S_N2' allyl-boryl coupling reactions may involve first activation of the *gem*-diborylmethane reagent or B_2pin_2 to form Cu-CH_2Bpin or Cu-Bpin, respectively. In Scheme 4.19 is shown the suggested catalytic cycle for the case of *gem*-diborylmethane as organoborane reagent. The Cu-CH_2Bpin intermediate **A** coordinates the terminal alkene of substrate to generate **B** followed by

regioselective addition, producing a new alkyl-Cu intermediate **C**. Hereafter, elimination of the product from **D** in a formal *anti*-S_N2' pathway releases CO_2 and regenerates the copper complex.

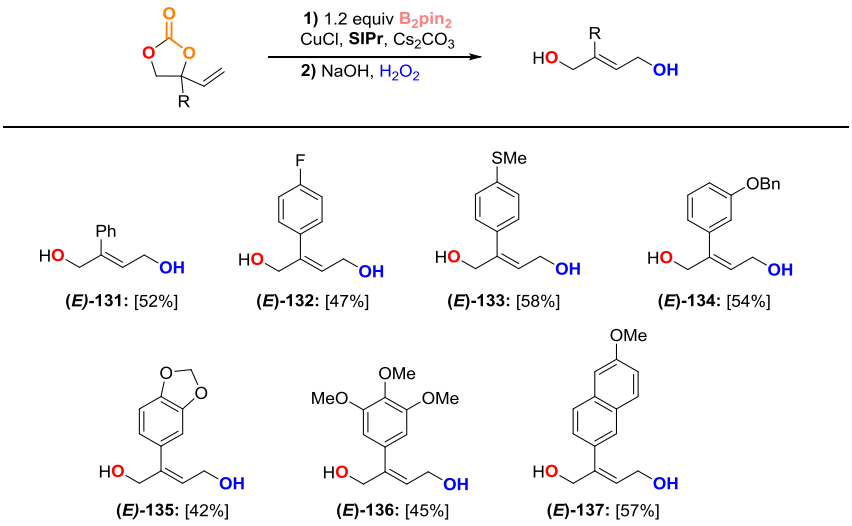


Scheme 4. 19 Proposed mechanism for SN2' allyl-alkyl coupling using *gem*-diborylmethane as organoborane reagent.

To demonstrate the versatility of the products obtained in this study, further transformations of homoallylic and allylic borylated products were investigated. Diols are among the most widespread framework in chemistry, being of eminent value for organic and polymeric synthesis. The preparation of diol scaffolds still remains a challenge to synthetic chemistry, particularly acyclic unsaturated (*E*)-configured 1,4-diols. Up to now, the limited amount of available strategies for (*E*)-1,4-but-2-ene diols synthesis have in common that they require Grignard reagents precursors with rather limited scope.[31] We found that could have synthetic interest an *in situ* borylation/oxidation sequence to obtain (substituted) (*E*)-1,4-but-2-ene diols and 1,5-pent-2-ene diols.

Thereafter, allylboronate compounds in the presence of sodium hydroxide and hydrogen peroxide in a mixture of THF/H_2O were oxidized at room temperature

and afforded the corresponding (*E*)-configured but-2-ene-1,4-diols (Scheme 4.20) which were isolated as main products.

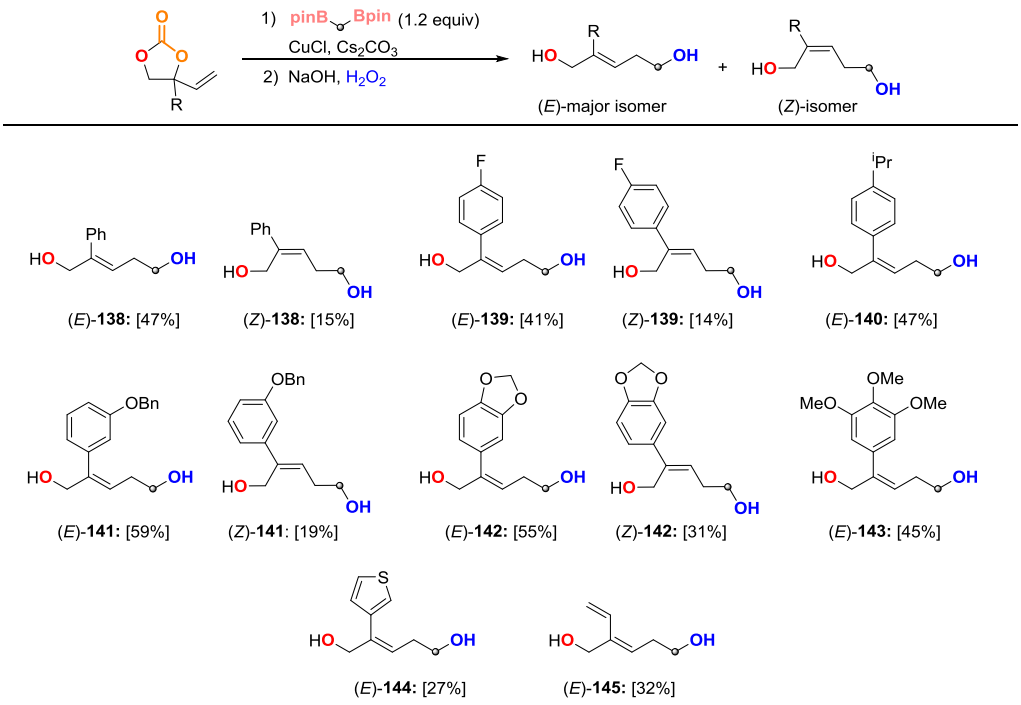


Scheme 4. 20 One-pot borylation/oxidation to prepare (*E*)-1,4-but-2-ene diols.

Interestingly, these (*E*)-isomers of such 1,4-but-2-ene diols are valuable compounds, being about 190 times more expensive than their corresponding (*Z*)-isomers.[22b, 32] Therefore, our versatile one-pot approach opens a new straightforward route toward these scaffolds, which are useful in organic synthesis.[33] Moreover, this is a complementary route to prepare 1,4-but-2-ene diol scaffolds to the one described by Kleij and co-workers starting from the same vinyl cyclic carbonates. They used water as nucleophilic reagent and through Pd catalytic complex in mild reaction conditions, they could stereoselectively end up with numerous (*Z*)- 1,4-but-2-ene diols.[22b]

By the same way, homoallylic borylated compounds were submitted under the same oxidation conditions to afford the corresponding (*E*)-1,5-pent-2-ene diols (Scheme 4.21). The related (*Z*)-isomers of the 1,5-pent-2-ene diols could also be isolated in low yield.

Allylic borylation



Scheme 4. 21 One-pot borylation/oxidation to prepare 1,5-pent-2-ene diols.

4.4. Conclusions

A singular method was described for alkoxide-catalyzed allylic borylation, using readily available tertiary allylic alcohols and B_2pin_2 as precursors, to provide access to new 1,1-disubstituted allylboronates. This methodology employs catalytic amount of Cs_2CO_3 as base and methanol to promote the formation of the Lewis acid-base adduct, $[Hbase]^+[MeO\text{--}B_2pin_2]^-$. Curiously, with an excess of diboron reagent, this adduct can also encourage the *in situ* diboration of the allylic double bond, which generates 1,2,3-polyborylated products.

The same strategy was applied to a propargylic alcohol that selectively afforded the hydroborated triple bond or the alkenyl diborane product just by tuning the temperature of the reaction.

Complementary, using a copper-catalyzed system with 1,1-diborylmethane, we were able to handle stereoselective S_N2' allylic substitutions of vinyl cyclic carbonates to form homoallylboronated products. When the same reaction was conducted with B_2pin_2 instead, the products obtained were the corresponding allylboronates. In that case, the reaction could be ligand-controlled to selectively get either (*E*)- or (*Z*)-stereoisomers. The use of an *N*-heterocyclic carbene (SIPr) favored the (*E*)-allylboronate compound whereas when the ligand of choice was a diphosphine (P-P), the allyl-boryl coupling gave a boracycle product as consequence of intramolecular annulation of the corresponding (*Z*)-stereoisomer.
If both allyl-alkyl and allyl-boryl couplings of vinyl cyclic carbonates were followed by oxidative workup, the reactions provided direct access to valuable (*E*)-configured 1,4-but-2-ene diols and 1,5pent-2-ene diols.

4.5. References chapter 4

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Chapter 5
Concluding remarks

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat

In chapter 2, we have prepared for the first time 9-anthracene naphthodiazaborinine (**6**) using BpinBdan reagent through a palladium-catalyzed borylation reaction. This molecule was fully characterized using NMR techniques and X-ray diffraction data of a single crystal obtained from the purified product. Moreover, compound **6** was subjected to AFM analysis. The non-planar molecule was imaged, and it was also planarized *via* dehydrogenation with bias pulse. The delocalized electronic charge could also be determined by AFM demonstrating the dehydrogenation of the amine groups.
In this context of borylation of aryl halides, we took advantage from the current growth of hypervalent iodine compounds by attempting to borylate diaryliodonium salts in the absence of transition metals. The successful borylation gave as a result an interesting study on the electronic and steric properties of the diaryliodonim substrates. The study culminated with a one-pot borylation/cross-coupling reaction between the borylated compound and the corresponding equimolar aryl iodide formed. In the presence of a palladium complex the related biaryl compounds (symmetrical and non-symmetrical) were obtained in moderate to good yields.

In chapter 3, the diboration reaction was performed with the non-symmetrical diboron reagent BpinBdan, in a transition metal-free context. A series of unactivated alkenes were submitted to the optimized diboration conditions. The diborated products of allylbenzene substrate offered characteristic signals to unambiguously assign the relative position of the two different boryl units by NMR experiments. These experimental results were supported by DFT calculations carried out by Carbó and Cid, which allowed us to suggest a plausible mechanism of the reaction. We have concluded that the difference on the boron atoms acidity is enough to selectively quaternize the Bpin moiety in front of the Bdan moiety, and thus, the Bdan moiety gains nucleophilic character to attack the terminal position of the olefin. The concerted mechanism allows for regioselective C-Bdan formation in the internal position.

In chapter 4, we focus on the preparation of allylboronic ester compounds. On a first approach, the borylation of allylic and propargylic alcohols were successfully carried out using B_2pin_2 as diboron reagent, and in the absence of transition metal complexes. Furthermore, the consecutive borylation/diboration reaction allowed

the formation of 1,2,3-triborated species just by increasing the amount of B_2pin_2 and the temperature.

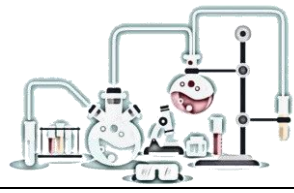
In the second approach, we pursued the allylic borylation using a copper-catalyzed system in combination with 1,1-diborylmethane as organoborane reagent. The selection of vinyl cyclic carbonates as substrates was crucial to obtain difunctionalized compounds in just one step. Under optimized borylation conditions, vinyl cyclic carbonates undergo decarboxylation of a CO_2 molecule, retaining a hydroxyl group in the final molecule. That gave as a result a series of homoallylic boronate alcohols, preferentially formed as the (*E)*-isomer.

Subsequently, the same reaction was carried out, but using the B_2pin_2 as diboron reagent. The optimized reaction conditions and the proper selection of the ligand was pivotal to selectively obtain the (*E*)- or (*Z*)-isomer. When the copper-complex was modified with an *N*-heterocyclic carbene, the (*E*)-allylboronate compounds were preferentially obtained. Whereas, if the ligand used was 1,2-bis(di-*tert*-butylhosphinomethyl)benzene the corresponding (*Z*)-isomer gave interesting (*Z*)-boracyclic compounds, after intramolecular annulation.

Moreover, all these homoallyl- and allylboronic esters could be oxidized by simple aquous work up, to end up with synthetically useful (*E*)-1,4-but-2-ene and 1,5-pent-2-ene diols.

Chapter 6

Experimental part



UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat

6.1. General considerations

All air-sensitive reactions and manipulations were conducted in an oven and flame-dried glassware under an argon atmosphere by using Schlenk-type techniques. Solvents and reagents were obtained from commercial suppliers as Sigma Aldrich Co. or Ally Chem, and dried or purified (if needed) by standard procedures, as specified in "Purification of Laboratory Chemicals".[1]

Flash chromatography was performed on standard silica gel (Merck Kieselgel 60 F_{254} 400-630 mesh) using standard visualizing agents: UV fluorescence (254 and 366 nm), potassium permanganate/Δ.

Deuterated chloroform ($CDCl_3$) was used as solvent for routine NMR measurements. NMR spectra were recorded at 300K on a Varian Goku 400 or a Varian Mercury 400 spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts (δ) are reported in ppm with the solvent (or TMS) resonance as the internal standard ($CHCl_3$: 7.26 ppm (^{1}H)) and ($CDCl_3$: 77.16 ppm (^{13}C). ^{11}B NMR chemical shifts (δ) are reported in ppm relative to $(CH_3CH_2)_2O\cdots BF_3$. Data are reported as follows: chemical shift, multiplicity (d = doublet, t = triplet, q = quartet, br s= broad signal, m = multiplet), coupling constants (Hz) and integration.

High resolution mass spectra (HRMS) were recorded using a 6210 Time of Flight (TOF) mass spectrometer from Agilent Technologies (Waldbronn, Germany) with and ESI interface and it was performed at the Servei de Recursos Científics i Tècnics (Universitat Rovira I Virgili, Tarragona) or using a BIOTOF II Time of Flight (TOF) mass spectrometer from Bruker with and APCI interface or EI interface and it was performed at the Unidade de Espectrometria de Masas e Proteómica (Universidade de Santiago de Compostela, Santiago de Compostela).
GC-MS analyses were performed on a HP6890 gas chromatograph and an Agilent Technologies 5973 Mass selective detector (Waldbronn, Germany) equipped with an achiral capillary column HP-5 (30 m, 0.25 mm, i.d., 0.25 µm thickness) using He as the carrier gas.

6.2. Experimental procedures in chapter 2

6.2.1. Synthesis of BpinBdan reagent (4)

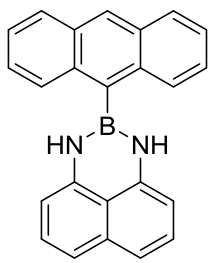
To prepare the mixed diboron reagent (pin)B-B(dan) a slightly modified version of the previously described protocol[2] was used. Thus tetrakis(dimethylamino)diboron ($B_2(NMe_2)_4$) was synthesize from B_2cat_2 instead of BCl_3SMe_2. Once prepared the $B_2(NMe_2)_4$ was sought to react with 1,8-diaminonaphthalene and pinacol in a 1:1:1 ratio in dichloromethane. The slurry was stirred at room temperature for 36 h. After evaporation of volatile materials under vacuum, the solid residue was washed with hot toluene (×3) to collect washings containing the desired product. After evaporation of toluene from the solution under vacuum, the resultant solid was washed with hexane (×3). The solid material was dried under vacuum. Following this procedure a global isolated yield of (83 %) was attained in a 26.6 mmol scale reaction.

6.2.2. Synthesis of 9-anthracene naphthodiazaborinine

An oven-dried reseable Teflon screw-cap Schlenk reaction tube was evacuated an refilled with argon; under argon counter flow, 9-bromoanthracene (0.2 mmol), BpinBdan (1.5 equiv), XPhos (9 mol%), KOAc (3 equiv) and $Pd_2(dba)_3$ (3 mol%) were added as solids. After evacuation and refill with argon for three times, dry and degassed 1,4-dioxane (0.86 mL) was added. Then, the Schlenk tube was sealed and heated at 100^{o}C in an oil bath for 16 h. After the reaction was cooled down to room temperature, the obtained mixture was filtered over a Celite® small pad and solvent was concentrated on a rotatory evaporator. After all the volatiles removed, the crude residue was purified by silica gel flash chromatography to afford the desired product **6**.

6.2.3. Characterization of 9-anthracene naphthodiazaborinine

2-(anthracen-9-yl)-2,3-dihydro-1H-naphtho[1,8-de][1,3,2]diazaborinine:



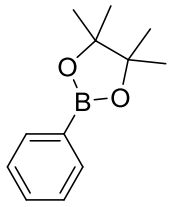
The product **6** was purified by flash column chromatography using as eluent a mixture of hexane/ethyl acetate (60:1 to 10:1). It was obtained as yellow solid (52.3mg, 76%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.49 (s, 1H), 8.24 (m, 2H), 8.03 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.46 (m, 4H), 7.16 (qd, *J* = 8.4, 1.3 Hz, 4H), 6.39 (dd, *J* = 7.0, 1.3 Hz, 2H), 6.2 (br s, 2H).**^{13}C NMR (100 MHz, $CDCl_3$)** δ = 141.2, 136.6, 134.5, 131.3, 129.8, 128.9, 128.9, 128.0, 127.8, 125.6, 125.4, 118.3, 106.3.**^{11}B NMR (128 MHz, $CDCl_3$)** δ = 30.43 (br s). **HRMS (ESI) for $C_{24}H_{17}BN_2$ $[M]^+$:** calculated: 344.1485, found: 344.1517.

6.2.4. Experimental procedure for the transition metal-free borylation of diaryl diaryliodonium salts

To an oven-dried Schlenk-type tube with a magnetic stir bar, B_2pin_2 (76.2 mg, 0.3 mmol) was added under argon. Then, the diaryliodonium salt (0.2 mmol) and the MeOH as solvent (1.25 mL) were added. The vial was sealed with a teflon septum cap and heated to 50^{o}C in an oil bath for 24 hours. The reaction mixture was then cooled to room temperature. An aliquot of 20 µL was diluted with 40 µL of a prepared solution of mesitylene as internal standard and analyzed by GC-MS to determine yield and selectivity, respectively. The reaction mixture and all the volatiles were removed under reduced pressure and the crude product was purified by column chromatography.

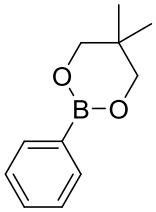
6.2.5. Characterization of aryl borylated compounds

4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane:



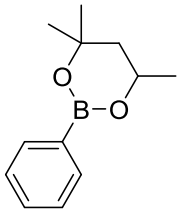
The product **7a** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was obtained as yellowish oil (77%). Data in agreement with the literature value.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 7.34-7.40 (m, 2H), 7.43-7.49 (m, 1H), 7.81 (dd, *J* = 1.4, 8.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 25.0, 83.9, 127.9, 131.4, 134.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.1 (br s). **MS (70 eV) m/z:** 204.1 [M^+].

5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane:



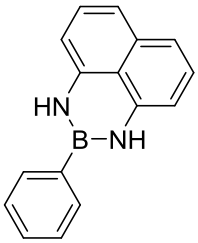
The product **7b** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was obtained as white solid (37%). Data in agreement with the literature values.[4] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.03 (s, 6H), 3.78 (s, 4H), 7.36 (ddd, *J* = 1.0, 4.3, 8.2 Hz, 2H), 7.41-7.46 (m, 1H), 7.80 (dd, *J* = 1.4, 8.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 29.8, 32.0, 72.4, 127.7, 130.8, 133.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 29.3 (br s). **MS (70 eV) m/z:** 190.1 [M^+].

4,4,6-Trimethyl-2-phenyl-1,3,2-dioxaborinane:



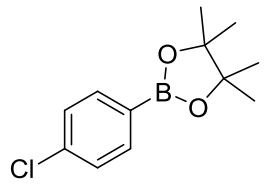
The product **7c** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was obtained as yellowish oil (34%). Data in agreement with the literature values.[5] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.35 (d, *J* = 6.2 Hz, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.56-1.63 (m, 1H), 1.87 (dd, *J* = 13.9, 2.9 Hz, 1H), 4.35 (bs, 1H), 7.32-7.36 (m, 2H), 7.38-7.82 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 23.5, 28.5, 31.6, 46.3, 65.3, 71.3, 127.8, 130.7, 134.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 27.0 (br s). **MS (70 eV) m/z:** 204.13 [M^+].

2-Phenyl-2,3-dihydro-1*H*-naphtol[1,8-*de*][1,3,2]diazaborinine:



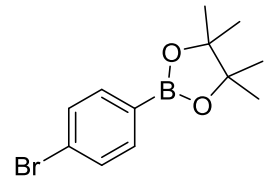
The product **7e** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was obtained as pink oil (52%). Data in agreement with the literature values.[6] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.04 (bs, 2H), 6.43 (d, *J* = 7.3 Hz, 2H), 7.08 (d, *J* = 8.3 Hz, 2H), 7.17 (dd, *J* = 1.2, 7.2, Hz, 2H), 7.44-7.50 (m, 3H), 7.66 (dd, *J* = 1.7, 7.7 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 106.2, 117.9, 119.9, 127.7, 130.4, 131.5, 136.4, 141.7. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 29.5 (br s). **MS (70 eV) m/z**: 244.1 [M^+].

4,4,5,5-Tetramethyl-2-(4-chlorophenyl)-1,3,2-dioxaborolane:



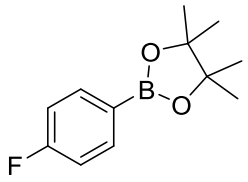
The product **9** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was obtained as colorless oil (41%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.8, 83.9, 127.9, 136.1, 137.5. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 30.8 (br s). **MS (70 eV) m/z:** 238.1 [M^+].

4,4,5,5-Tetramethyl-2-(4-bromophenyl)-1,3,2-dioxaborolane:



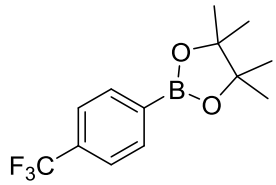
The product **10a** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was obtained as yellow oil (36.2%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H). **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.3 (br s). **MS (70 eV) m/z:** 282.0 [M^+].

4,4,5,5-Tetramethyl-2-(4-fluorophenyl)-1,3,2-dioxaborolane:



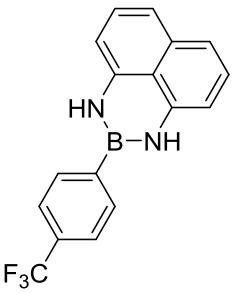
The product **11** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (15:1). It was obtained as colorless oil (45%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 7.07-702 (m, 2H), 7.81-7.77 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.8, 83.9, 114.8 (d, *J* = 20.2 Hz), 136.9 (d, *J* = 8.3 Hz), 165.1 (d, J = 150.8 Hz). **MS (70 eV) m/z:** 222.1 [M^+].

4,4,5,5-Tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane:



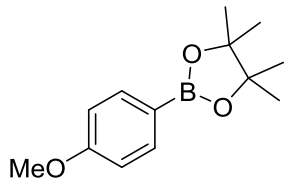
The product **12a** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (15:1). It was obtained as white solid (56%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.36 (s, 12H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.9, 84.2, 124.1 (q, *J* = 272.7 Hz), 124.3 (q, *J* = 3.8 Hz), 132.8 (q, *J* = 32.0 Hz), 135.0. **MS (70 eV) m/z:** 272.1 [M^+].

2-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-naphtol[1,8-*de*][1,3,2]diaza-borinine:



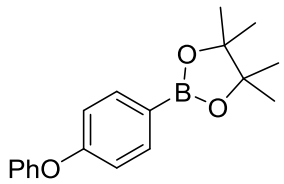
The product **12b** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was afforded as white solid. Data in agreement with the literature values.[8] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.05 (br s, 2H), 6.43 (dd, *J* = 0.9, 7.3 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.17 (dd, *J* = 1.2, 7.2, Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 106.3, 118.3, 120.1, 124.2 (q, *J* = 272 Hz), 125.1 (q, *J* = 3.8 Hz), 127.7, 131.9, 132.2 (q, *J* = 31 Hz), 136.4, 140.6. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 29.9 (br s).

4,4,5,5-Tetramethyl-2-(4-methoxyphenyl)-1,3,2-dioxaborolane:



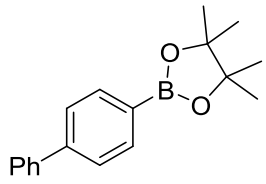
The product **13** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was obtained as colorless oil (76%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 3.83 (s, 3H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 8.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.8, 55.1, 83.5, 113.3, 136.5, 162.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.3 (br s). **MS (70 eV) m/z:** 234.2 [M^+].

4,4,5,5-Tetramethyl-2-(4-phenoxyphenyl)-1,3,2-dioxaborolane:



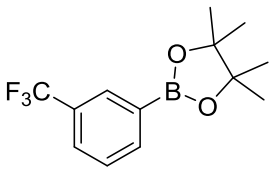
The product **14** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as yellow oil (71%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 6.95-7.00 (m, 2H), 7.00-7.06 (m, 2H), 7.13 (dd, *J* = 2.1, 8.5 Hz, 1H), 7.31-7.39 (m, 2H), 7.75-7.81 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.8, 83.7, 117.6, 119.4, 121.4, 123.6, 129.8, 136.6, 156.5, 160.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.3 (br s). **HRMS (EI):** calc. for $[C_{18}H_{22}BO_3]^+$ ($[M+H]^+$): 297.1584, Found: 297.1646.

4,4,5,5-tetramethyl-2-(4-biphenylyl)-1,3,2-dioxaborolane:



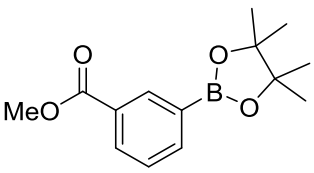
The product **15** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as white solid (72%). Data in agreement with the literature values.[9] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 7.34-7.41 (m, 1H), 7.42-7.50 (m, 2H), 7.59-7.70 (m, 4H), 7.91 (d, *J* = 7.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.9, 83.8, 126.5, 127.3, 127.6, 128.8, 135.3, 141.0, 143.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.7 (br s).

4,4,5,5-Tetramethyl-2-(2-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane:



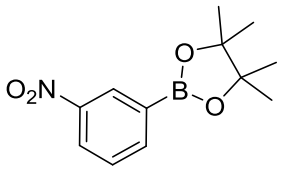
The product **16** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as colorless oil (65%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.36 (s, 12H), 7.45-7.52 (m, 1H), 7.67-7.73 (m, 1H), 7.97 (d, *J* = 7.4 Hz, 1H), 8.06 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 25.0, 84.4, 124.4 (q, *J* = 272.7 Hz), 127.9 (q, *J* = 3.8 Hz), 128.2, 130.2 (q, *J* = 31.5 Hz), 131.5 (q, *J* = 3.7 Hz), 138.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 30.8 (br s)**. ^{19}F NMR (376 MHz, $CDCl_3$)** δ = -62.2. **MS (70 eV) m/z:** 272.1 [M^+].

Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate:



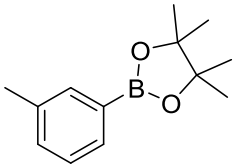
The product **17** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (10:1). It was afforded as yellowish solid (41%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.35 (s, 12H), 3.92 (s, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.98 (dt, *J* = 1.3, 7.4 Hz, 1H), 8.10-8.15 (m, 1H), 8.47 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.8, 52.0, 84.0, 127.8, 129.5, 132.8, 135.8, 139.1, 167.2. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.3 (br s). **MS (70 eV) m/z:** 262.1 [M^+].

4,4,5,5-tetramethyl-2-(3-nitrophenyl)-1,3,2-dioxaborolane:



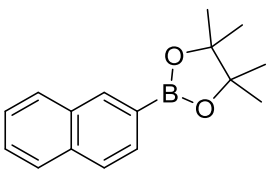
The product **18** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (50:1). It was afforded as yellow solid (31%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.36 (s, 12H), 7.54 (t, *J* = 7.8 Hz, 1H), 8.09 (d, *J* = 7.3Hz, 1H), 8.26-8.31 (m, 1H), 8.64 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.9, 84.6, 125.9, 128.8, 129.4, 140.7. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 30.4 (br s). **MS (70 eV) m/z**: 249.1 [M^+].

4,4,5,5-Tetramethyl-2-(3-methyl)-1,3,2-dioxaborolane:



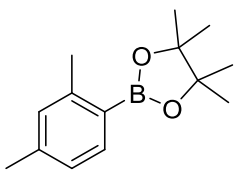
The product **19** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as colorless oil (40%). Data in agreement with the literature values.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 2.35 (s, 3H), 7.26-7.29 (m, 2H), 7.60-7.63 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.2, 24.8, 83.7, 127.7, 131.7, 132.0, 135.3, 137.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.0 (br s). **MS (70 eV) m/z:** 218.3 [M^+].

4,4,5,5-Tetramethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborolane:



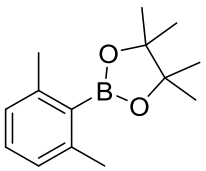
The product **20** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as yellow solid (51%). Data in agreement with the literature values.[10] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.40 (s, 12H), 7.43-7.58 (m, 3H), 7.80-7.92 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.9, 83.9, 125.8, 126.9, 127.7, 128.7, 130.3, 132.8, 134.9, 136.2. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.3 (br s). **MS (70 eV) m/z:** 254.3 [M^+].

4,4,5,5-Tetramethyl-2-(2,4-dimethylphenyl)-1,3,2-dioxaborolane:



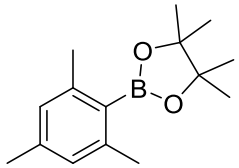
The product **21** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as colorless oil (57%). Data in agreement with the literature value.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 2.33 (s, 3H), 2.52 (s, 3H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.01 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.5, 22.1, 24.8, 83.2, 125.5, 130.7, 136.1, 140.8, 144.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.0 (br s). **MS (70 eV) m/z:** 232.2 [M^+].

4,4,5,5-Tetramethyl-2-(2,6-dimethylphenyl)-1,3,2-dioxaborolane:



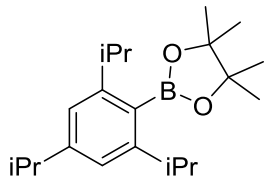
The product **22** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as colorless oil (51%). Data in agreement with the literature values.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.39 (s, 12H), 2.39 (s, 6H), 6.92-6.97 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 22.2, 24.9, 83.7, 126.4, 129.2, 141.7. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.2 (br s). **MS (70 eV) m/z:** 232.2 [M^+].

2-Mesityl-4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane:



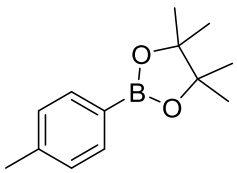
The product **23** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as yellowish oil (34%). Data in agreement with the literature values.[3] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.37 (s, 12H), 2.24 (s, 3H), 2.37 (s, 6H), 6.78 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.2, 22.2, 24.9, 83.4, 127.4, 138.9, 142.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.3 (br s). **MS (70 eV) m/z:** 246.2 [M^+].

4,4,5,5-Tetramethyl-2-(2,4,6-triisopropylphenyl)-1,3,2-dioxaborolane:



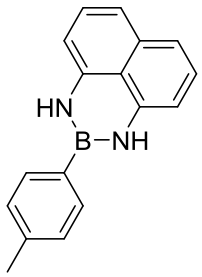
The product **24** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as white solid. Data in agreement with the literature values.[11] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.22-1.31 (m, 18H), 1.37 (s, 12H), 2.92 (hp, *J* = 6.9 Hz, 1H), 3.01 (hp, *J* = 6.9 Hz, 2H), 7.05 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.2, 22.2, 24.9, 83.4, 127.4, 138.9, 142.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.1 (br s). **MS (70 eV) m/z:** 33.30 [M^+].

4,4,5,5-Tetramethyl-2-*p*-tolyl-1,3,2-dioxaborolane:



The product **25a** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (20:1). It was afforded as white solid (22%). Data in agreement with the literature values.[7] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.34 (s, 12H), 2.36 (s, 3H), 7.19 (d, *J* = 7.9 Hz), 7.71 (d, *J* = 7.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.7, 24.9, 83.6, 128.5, 134.8, 134.9, 141.4. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.13 (br s).

2-(*p*-tolyl)-2,3-dihydro-1*H*-naphtol[1,8-*de*][1,3,2]diazaborinine:



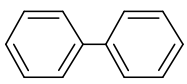
The product **25b** was purified by flash column chromatography using as eluent a mixture of petroleum ether/EtOAc (2%). It was afforded as white solid. Data in agreement with the literature values.[8] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 2.30 (s, 3H), 6.01 (br, 2H), 6.31 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 7.04 (t, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 7.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.7, 106.2, 117.9, 119.9, 127.7, 130.2, 131.5, 136.4, 140.5, 141.3. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 29.7 (br s).

6.2.6. Experimental procedure for the *in situ* cross-coupling reaction

The crude mixture from the borylation reaction as described before was dried under reduced pressure (high vacuum pump) in order to remove the methanol solvent traceless. Then, palladium catalyst $Pd(PPh_3)_4$ (10 mol%, 0.02 mmol), cesium carbonate base (2 equiv, 0.4 mmol) and 2 mL of dried toluene were added subsequently under argon atmosphere. The vial was sealed with a teflon septum cap and heated overnight to 80^{o}C in an oil bath. An aliquot of 0.2 mL was diluted in dichloromethane and analyzed by GC-MS to determine the conversion and selectivity. The sample was combined with the rest of the reaction mixture. All the volatiles were removed under reduced pressure, and the crude product was purified by flash column chromatography.

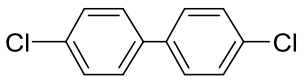
6.2.7. Characterization of cross-coupled products

Biphenyl:



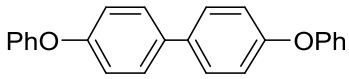
The product **31** was purified by flash column chromatography using hexane as eluent. It was obtained as a white solid (87%). Data in agreement with the literature values.[12] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.47-7.51 (m, 6H), 7.64-7.66 (m, 4H). **MS (70 eV) m/z:** 154.1 [M^+].

4,4'-Dichlorobiphenyl:



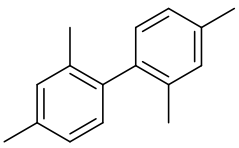
The product **32** was purified by flash column chromatography using hexane as eluent. It was obtained as a white solid (72%). Data in agreement with the literature values.[12] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.39 (d, *J* = 8.5 Hz, 4H), 7.46 (d, *J* = 8.6 Hz, 4H). **MS (70 eV) m/z:** 222.1 [M^+].

4,4'-Diphenoxybiphenyl:



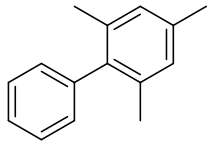
The product **33** was purified by flash column chromatography using hexane as eluent. It was obtained as a white solid (42%). Data in agreement with the literature values.[13] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.07-7.10 (m, 8H), 7.11-7.17 (m, 2H), 7.33-7.41 (m, 4H), 7.51-7.57 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 118.8, 118.9, 123.2, 128.0, 129.6, 135.4, 156.4, 156.9. **MS (70 eV) m/z:** 338.3 [M^+].

2,2',4,4'-Tetramethylbiphenyl:



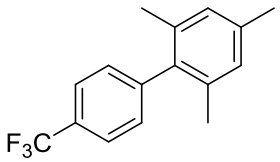
The product **34** was purified by flash column chromatography using hexane as eluent. It was obtained as colorless oil (65%). Data in agreement with the literature values.[14] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 2.06 (s, 6H), 2.39 (s, 6H), 7.00-7.07 (m, 4H), 7.11 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 19.8, 21.1, 126.2, 129.4, 130.5, 135.8, 136.5, 138.6. **MS (70 eV) m/z:** 210.2 [M^+].

2-Phenylmesitylene :



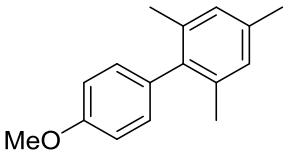
The product **35** was purified by flash column chromatography using hexane as eluent. It was obtained as white solid (44%). Data in agreement with the literature values.[15] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 2.01 (s, 6H), 2.35 (s, 3H), 6.96 (s, 2H), 7.13-7.17 (m, 2H), 7.31-7.37 (m, 1H), 7.39-7.45 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 20.7, 21.0, 126.5, 128.0, 128.3, 129.3, 135.9, 136.5, 139.0, 141.0. **MS (70 eV) m/z:** 196.2 [M^+].

1-Mesityl-4-(trifluoromethyl)benzene:



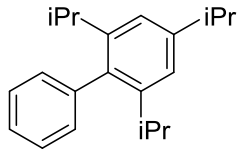
The product **36** was purified by flash column chromatography using hexane as eluent. It was obtained as a yellowish solid (39%). Data in agreement with the literature values.[16] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.99 (s, 6H), 2.34 (s, 3H), 6.96 (s, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 20.8, 21.2, 124.4 (q, *J* = 272.4 Hz), 125.5 (q, *J* = 3.7 Hz), 128.4, 129.0 (q, *J* = 32.1 Hz), 129.9, 135.8, 137.4, 137.7, 145.1. **MS (70 eV) m/z:** 264.3 [M^+].

4-Mesitylanisole:



The product **37** was purified by flash column chromatography using hexane as eluent. It was obtained as colorless oil (46%). Data in agreement with the literature values.[17] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 2.01 (s, 6H), 2.32 (s, 3H), 3.85 (s, 3H), 6.92-6.97 (m, 4H), 7.03-7.07 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 21.0, 21.1, 55.1, 113.9, 128.2, 130.4, 133.4, 136.6, 138.8, 158.3. **MS (70 eV) m/z**: 226.2 [M^+].

2,4,6-Triisopropyl-1,1'-biphenyl:



The product 38 was purified by flash column chromatography using hexane as eluent. It was obtained as a white solid (22%). Data in agreement with the literature values.[18] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.07 (d, *J* = 6.9 Hz, 12H), 1.31 (d, *J* = 6.9 Hz, 6H), 2.59 (hp, *J* = 6.8 Hz, 2H), 2.94 (hp, *J* = 6.9 Hz, 1H), 7.05 (s, 2H), 7.16-7.20 (m, 2H), 7.33-7.41 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 24.2, 24.4, 30.4, 34.4, 120.6, 126.5, 128.0, 129.9, 137.2, 141.0, 146.6, 147.9. **MS (70 eV) m/z**: 280.4 [M^+].

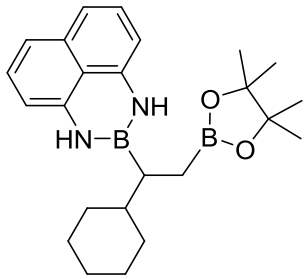
6.3. Experimental procedures in chapter 3

6.3.1. Experimental procedure for the organocatalytic diboration of olefins

To an oven-dried Schlenk tube with a magnetic stir bar, BpinBdan reagent (0.161 g, 0.55 mmol) was added under argon. Then, cesium carbonate (48.8 mg for 30 mol% or 81.4 mg for 50 mol %), MeOH (2 mL) and substrate (0.50 mmol) were added. The Schlenk tube was sealed with a teflon septum cap and heated to 70°C in an oil bath for 16 hours. The reaction mixture was allowed to cool down to room temperature and an aliquot of 0.1 mL was diluted in dichloromethane and analysed by GC-MS to determine de conversion and selectivity. The sample was combined with the rest of the reaction mixture, all the volatiles were removed in vacuum and the crude was purified by flash column chromatography.

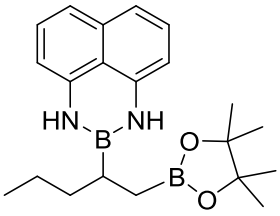
6.3.2. Characterization of non-symmetrical diborated compounds

2-(1-cyclohexyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



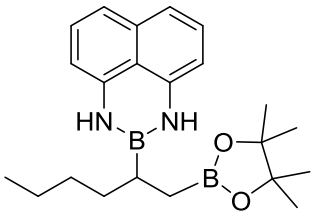
The product **40a** was purified by flash column chromatography deactivated with 10% of Et_3N (petroleum ether/EtOAc = 8:1). It was obtained as a yellow oil (40 %). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.11 (dd, *J* = 8.8, 8.0 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.35 (d, *J* = 8.0 Hz, 2H), 5.95 (br s, 2H), 1.82 (m, 1H), 1.75 (m, 11H), 1.33 (m, 2H), 1.12 (s, 6H), 1.10 (s, 6H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.5, 136.5, 127.5, 117.0, 105.3, 83.3, 41.3, 33.3, 32.3, 26.8, 25.1, 24.9. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 36.2 (br s). **MS (70 eV) m/z**: 404.6 [M^+].

2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentan-2-yl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



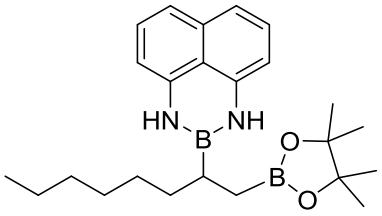
The product **44a** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a yellow pale oil (20 %). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 8.5, 8.0 Hz, 2H), 6.97 (d, *J* = 8.5Hz, 2H), 6.27 (d, *J* = 8.0 Hz, 2H), 5.94 (br s, 2H), 1.46 (m, 1H), 1.36 (m, 2H), 1.25 (s, 12H) 1.24 (m, 7H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.5, 136.3, 127.6, 117.0, 105.3, 83.3, 36.9, 31.9, 29.7, 29.1, 24.9, 22.1, 14.4. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 35.6 (br s). **MS (70 eV) m/z:** 364.3 [M^+].

2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-2-yl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



The product **46a** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a yellow pale oil (17%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.08 (dd, *J* =8.0, 7.6 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.27 (d, *J* = 7.6 Hz, 2H), 5.94 (br s, 2H), 1.31 (m, 3H), 1.25 (s, 12H), 0.87 (m, 9H).**^{13}C NM**R **(100.6 MHz, $CDCl_3$)** δ = 141.7, 136.3, 127.7, 117.0, 106.3, 105.2, 83.2, 34.3, 31.4, 24.9, 24.9, 23.1, 14.1. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 36.5 (br s). **MS (70 eV) m/z:** 378.3 [M^+].

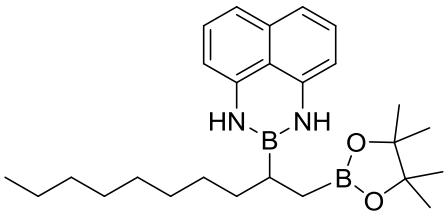
2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-yl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



The product **48a** was purified by flash column chromatography (petroleum ether/EtOAc = 15:1). It was obtained as a yellow pale oil (25%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.11 (dd, *J* = 8.0, 7.9 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.31 (d, *J* = 7.9 Hz, 2H), 5.97 (br s, 2H), 1.36 (m, 5H), 1.26 (s, 12H), 0.86 (m, 11H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.5, 136.3,

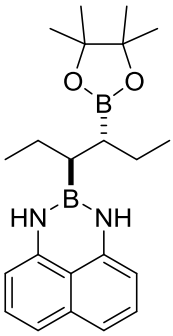
127.6, 117.0, 105.3, 105.2, 83.3, 34.6, 31.9, 29.7, 29.1, 25.0, 24.9, 22.7, 14.2. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 34.5 (br s). **MS (70 eV) m/z:** 406.3 [M^+].

2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)decan-2-yl)-2,3-dihydro1*H*-naphtho-1,8-[1,3,2]diazaborinine:



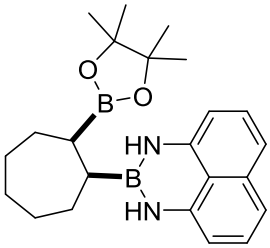
The product **50a** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a yellow oil (70%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 8.6, 8.0 Hz, 2H), 6.98 (d, *J* = 8.6 Hz, 2H), 6.28 (d, *J* = 8.0 Hz, 2H), 5.94 (br s, 2H), 1.40 (m, 5H), 1.27 (s, 12H), 0.92 (m, 15H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.6, 136.4, 127.7, 119.7, 117.2, 105.6, 83.5, 34.9, 32.2, 30.0, 29.6, 29.4, 29.1, 24.9, 24.8, 22.7 14.1. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 32.3 (br s). **MS (70 eV) m/z:** 434.4 [M^+].

2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-3-yl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



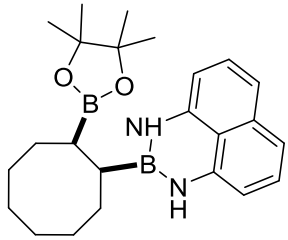
The product **51** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a yellow oil (24%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 8.2, 8.0 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.27 (d, *J* = 8.0 Hz, 2H), 5.93 (br s, 2H), 1.33 (m, 2H), 1.25 (s, 12H), 1.21 (m, 6H), 0.84 (m, 4H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.7, 136.6, 127.9, 119.8, 117.4, 105.6, 83.2, 82.8, 38.9, 34.4, 32.1, 30.1, 25.3, 24.8, 24.4, 22.7, 14.9. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 38.1 (br s). **MS (70 eV) m/z:** 378.3 [M^+].

2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptyl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



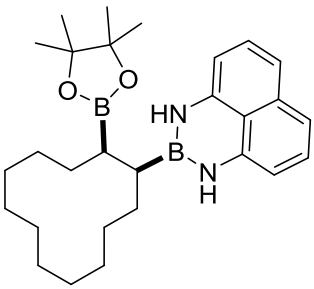
The product **52** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a colourless oil (42%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.08 (dd, *J* = 8.4, 8.0 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.29 (br s, 2H), 6.25 (d, *J* = 8.0 Hz, 2H), 1.93 (m, 1H), 1.85 (m, 1H), 1.55 (m, 6H), 1.29 (s, 12H), 0.88 (m, 4H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.8, 136.2, 127.5, 116.7, 105.1, 83.3; 31.8, 30.6, 29.7, 29.6, 28.8, 27.6, 25.1. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 39.7 (br s). **MS (70 eV) m/z :** 390.3 [M^+].

2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclooctyl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:



The product **53** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a colourless oil (32%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 7.6, 7.2 Hz, 2H), 7.01 (d, *J* = 7.6 Hz, 2H), 6.27 (d, *J* = 7.2 Hz, 2H), 6.23 (br s, 2H), 1.80-1.45 (m, 14H), 1.30 (s, 6H), 1.25 (s, 6H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.8, 136.9, 127.8, 119.5, 116.8, 105.2, 83.6, 82.6, 28.8, 27.6, 26.5, 26.0, 25., 25.0. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 34.9 (br s). **MS (70 eV) m/z:** 404.3 [M^+].

2-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclodecyl)-2,3-dihydro-1*H*-naphtho-1,8-[1,3,2]diazaborinine:

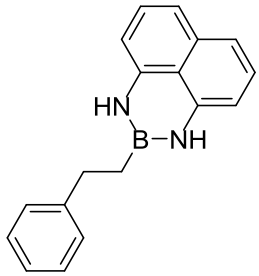


The product **54** was purified by flash column chromatography (petroleum ether/EtOAc=15:1). It was obtained as a colourless oil (21%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.09 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.02 (d, *J* = 7.2 Hz, 2H), 6.41 (d, *J* = 7.8 Hz, 2H), 5.62 (br s, 2H), 1.77-1.49 (m, 14H), 1.28 (s, 6H), 1.22 (s, 6H), 1.21 (m, 4H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.4, 136.32,

127.54, 119.49, 117.01, 105.36, 83.09, 82.72, 34.34, 29.82, 26.38, 25.64, 25.46, 24.77, 22.39, 14.06. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 38.4 (br s). **MS (70 eV) m/z** : 432.3 [M^+].

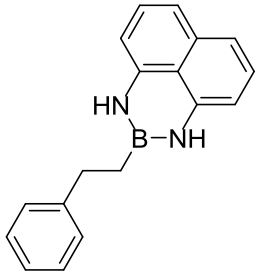
6.3.3. Characterization of hydroborated products

2-phenethyl-2,3-dihydro-1H-naphtho-1,8-[1,3,2]diazaborinine:



The product **55** was purified by flash column chromatography deactivated with 10% of Et_3N (petroleum ether/EtOAc = 20:1). It was obtained as a yellow oil (33%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29-7.17 (m, 5H), 7.05 (dd, *J* = 8.8, 8.0 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.22 (d, *J* = 8.0 Hz, 2H), 5.54 (br s, 2H), 2.76 (t, *J* = 8.0 Hz, 2H), 1.22 (t, *J* = 8.0 Hz, 2H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.2, 128.7, 128.2, 127.8, 126.1, 117.6, 105.7, 31.0, 29.9. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 32.6 (br s). **MS (70 eV) m/z:** 272.3 [M^+].

2-(4-methylphenethyl)-2,3-dihydro-1H-naphtho-1,8-[1,3,2]diazaborinine:



The product **56** was purified by flash column chromatography deactivated with 10% of Et_3N (petroleum ether/EtOAc = 20:1). It was obtained as a yellow oil (37%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.15-7.07 (m, 6H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.25 (d, *J* = 8.0 Hz, 2H), 5.56 (br s, 2H), 2.76 (t, *J* = 8.0 Hz, 2H), 2.35 (s, 3H), 1.23 (t, *J* = 8.0 Hz, 2H). **^{13}C NMR (100.6 MHz, $CDCl_3$)** δ = 141.5, 136.3, 135.3, 129.2, 127.8, 127.5, 117.4, 110.0, 105.5, 30.3, 24.8, 21.0. **^{11}B NMR (128.3 MHz, $CDCl_3$)** δ = 31.7 (br s). **MS (70 eV) m/z:** 286.3 [M^+].

6.4. Experimental procedures in chapter 4

6.4.1. General procedure for the synthesis of vinyl alcohols[19]

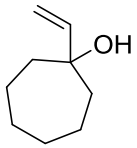
A vinyl magnesium bromide solution 1.0 M in THF (15 mmol) was added to a THF solution of the corresponding ketone (10 mmol). After stirring for 16 h at room temperature, an aqueous solution of NH_4Cl (50 mL, 1 M) was added. The organic layer was separated and it was extracted with ether (3x50 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated in *vacuo*. The residue was purified by chromatography using silica gel and petroleum ether/diethyl ether (10:1). All reactions were conducted in oven and flame-dried glassware under an inert atmosphere of argon, using Schlenk-type techniques.

Procedure followed for the alcohol protection:[20]

A solution of sodium hydride (530 mg of 60% dispersion, 13 mmol) in dry THF (8 mL) was warmed to 45°C and benzyl bromide (0.8 mL, 7 mmol) was added. 1-vinylcyclohexan-1-ol (**58**) (0.27 mL, 2 mmol) in dry THF (2.7 mL) was added dropwise during 20 min. After being heated overnight, the reaction mixture was allowed to cool down to room temperature and water was added until evolution of hydrogen ceased. The aqueous layer was separated and extracted with diethyl ether. The combined organic layers were dried with $MgSO_4$, filtered and concentrated in the rotatory evaporator. The residue was purified by chromatography using silica gel and petroleum ether/ethyl acetate mixture (15/1). Product **58(OBn)** was obtained as yellowish oil (307 mg, 71%).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38-7.25 (m, 5H), 5.84 (dd, J = 17.5, 11.2 Hz, 1H), 5.24-5.19(m, 2H), 4.33 (s, 2H), 1.90-1.86 (m, 2H), 1.71-1.48 (m, 6H), 130-125 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.5, 139.9, 128.4, 127.5, 127.1, 114.9, 76.2, 63.7, 34.4, 25.9, 21.9.

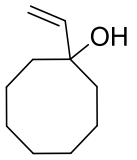
6.4.2. Spectral data of vinyl alcohols

1-Vinyl-1-cycloheptanol:



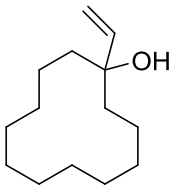
The product **60** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (57%). The characterization data is in agreement with the literature values.[19a] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.02 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.20 (dd, *J* = 17.3, 1.2 Hz, 1H), 4.98 (dd, *J* = 10.7, 1.2 Hz, 1H), 1.79-1.60 (m, 8H), 1.57-1.49 (m, 2H), 1.48-1.39 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 146.6, 110.1, 75.6, 41.2, 29.5, 22.1.

1-Vinyl-1-cyclooctanol:



The product **62** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (68%). The characterization data is in agreement with the literature values.[19a] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.02 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.22 (dd, *J* = 17.4, 1.3 Hz, 1H), 5.03 (dd, *J* = 10.8, 1.3 Hz, 1H), 1.78-1.46 (m, 14H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 145.8, 111.3, 75.3, 36.3, 28.2, 24.7, 22.0. **HRMS-(ESI+) for $C_{10}H_{18}O$ $[M]^+$:** calculated: 154.1358, found: 154.1354.

1-Vinyl-1-cyclododecanol:

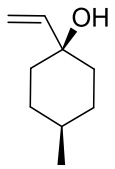


The product **64** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as yellow oil (97%). The characterization data is in agreement with the literature values.[19a] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.99 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.21 (dd, *J* = 17.4, 1.4 Hz, 1H), 5.02 (dd, *J* = 10.8, 1.4 Hz, 1H), 1.68-1.58 (m, 2H), 1.53-1.42 (m, 4H), 1.36 (s, 16H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 145.8, 111.3, 75.6, 26.6, 26.1, 22.7, 22.3, 19.7. **HRMS-(ESI+) for $C_{14}H_{26}O$ $[M]^+$:** calculated: 210.1984, found: 210.1974.

4-Methyl-1-vinyl-1-cyclohexanol:

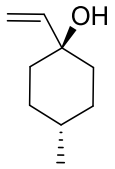
The product was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). Two diastereoisomers could be identified and separated. The overall isolated yield is 78%. The characterization data is in agreement with the literature values.[21]

cis-4-Methyl-1-vinyl-1-cyclohexanol (white solid, **72a**):



^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.94 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.23 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.00 (dd, *J* = 10.7, 1.3 Hz, 1H), 1.63-1.45 (m, 6H), 1.38-1.30 (m, 3H), 0.93 (d, *J* = 5.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.0, 111.1, 71.4, 37.2, 32.0, 30.2, 22.5.

trans-4-Methyl-1-vinyl-1-cyclohexanol (yellow oil, **72b**):

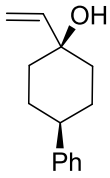


^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.07 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.30 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.13 (dd, *J* = 10.8, 1.3 Hz, 1H), 1.84-1.75 (m, 2H), 1.71-1.61 (m, 2H), 1.59-1.48 (m, 3H), 1.14-1.02 (m, 2H), 0.90 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.5, 113.5, 72.2, 37.9, 31.7, 31.5, 21.4. **HRMS-(ESI+) for $C_9H_{16}O$ $[M]^+$:** calculated: 140.1201, found: 140.1198.

4-Phenyl-1-vinyl-1-cyclohexanol:

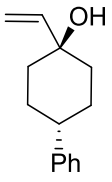
The product was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). Two diastereoisomers could be identified and separated. The overall isolated yield is 79%. The characterization data is in agreement with the literature values.[19a]

cis-4-Phenyl-1-vinyl-1-cyclohexanol (yellow solid, **74a**):



^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35-7.27 (m, 4H), 7.24-7.19 (m, 1H), 6.03 (dd, *J* = 17.2, 10.8 Hz, 1H), 5.31 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.07 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.52 (dt, *J* = 12.2, 3.3 Hz, 1H), 2.00-1.89 (m, 2H), 1.80-1.74 (m, 4H), 1.71-1.63 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.2, 146.8, 128.4, 126.9, 126.1, 111.3, 71.1, 43.8, 37.4, 29.1.

trans-4-Phenyl-1-vinyl-1-cyclohexanol (white solid, **74b**):

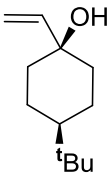


^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33-7.29 (m, 2H), 7.25-7.18 (m, 3H), 6.19 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.41 (dd, *J* = 17.5, 1.2 Hz, 1H), 5.26 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.68-2.55 (m, 1H), 2.03-1.95 (m, 2H), 1.94-1.86 (m, 2H), 1.80-1.60 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 146.5, 142.8, 128.5, 126.9, 126.2, 114.4, 71.9, 43.6, 38.9, 31.2. **HRMS-(ESI+) for $C_{14}H_{18}O$ $[M]^+$:** calculated: 202.1358, found: 202.1362.

4-Tertbutyl-1-vinyl-1-cyclohexanol:

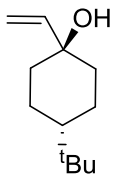
The product was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). Two diastereoisomers could be identified and separated. The overall isolated yield is 75%. The characterization data is in agreement with the literature values.[19b]

cis-4-Tertbutyl-1-vinyl-1-cyclohexanol (yellow oil, **76a**):



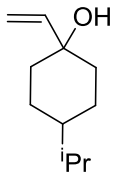
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.92 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.22 (dd, *J* = 17.4, 1.1 Hz, 1H), 4.99 (dd, *J* = 10.7, 1.1 Hz, 1H), 1.68-1.56 (m, 4H), 1.50-1.33 (m, 5H), 0.87 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.1, 111.0, 71.4, 47.9, 37.8, 32.6, 27.8, 27.7, 22.4.

trans-4-Tertbutyl-1-vinyl-1-cyclohexanol (white solid, **76b**):



^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.09 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.32 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.16 (dd, *J* = 10.8, 1.3 Hz, 1H), 1.91-1.84 (m, 2H), 1.74-1.66 (m, 2H), 1.58-1.48 (m, 3H), 1.16-1.02 (m, 2H), 0.84 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 142.9, 113.9, 72.3, 47.7, 39.3, 32.4, 27.8, 24.6. **HRMS-(ESI+) for $C_{12}H_{22}O$ $[M]^+$:** calculated: 182.1665, found: 182.1672

4-Isopropyl-1-vinyl-1-cyclohexanol (78):

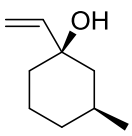


The product was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (35%). The characterization data is in agreement with the literature values.[22] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.07 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.31 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.15 (dd, *J* = 10.8, 1.3 Hz, 1H), 1.86-1.82 (m, 2H), 1.69-1.65 (m, 2H), 1.55-1.42 (m, 5H), 1.13-1.23 (m, 1H), 0.86 (s, 3H), 0.85 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.1, 133.5, 72.3, 43.1, 38.4, 31.8, 26.6, 20.1. **HRMS-(ESI+) for $C_{11}H_{20}O$ $[M]^+$:** calculated: 168.1514, found: 168.1513.

3-Methyl-1-vinyl-1-cyclohexanol:

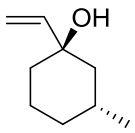
The product was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as yellow oil (94%). The characterization data is in agreement with the literature values.[21]

cis-Methyl-1-vinyl-1-cyclohexanol (colorless oil, **81a**):



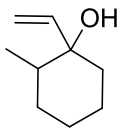
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.92 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.21 (dd, *J* = 17.3, 1.3 Hz, 1H), 4.98 (dd, *J* = 10.7, 1.3 Hz, 1H), 1.83-1.73 (m, 1H), 1.72-1.64 (m, 2H), 1.62-1.53 (m, 4H), 1.35 (td, *J* = 13.4, 4.7 Hz, 1H), 1.08 (d, *J* = 12.4 Hz, 1H), 0.88 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.1, 110.8, 72.5, 45.8, 36.8, 34.4, 27.7, 22.6, 21.5.

trans-3-Methyl-1-vinyl-1-cyclohexanol (white solid, **81b**):



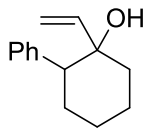
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.08 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.30 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.13 (dd, *J* = 10.8, 1.3 Hz, 1H), 1.85-1.75 (m, 2H), 1.70-1.62 (m, 2H), 1.56-1.48 (m, 1H), 1.45-1.24 (m, 3H), 1.18 (d, *J* = 12.7 Hz, 1H), 0.90 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.7, 113.6, 72.7, 47.8, 38.6, 34.4, 30.1, 23.3, 22.6. **HRMS-(ESI+) for $C_9H_{16}O$ $[M]^+$:** calculated: 140.1201, found: 140.1203.

2-Methyl-1-vinyl-1-cyclohexanol:



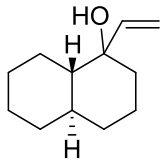
The product **82** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (70%). The characterization data is in agreement with the literature values.[19a] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.82 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.23 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.05 (dd, *J* = 10.8, 1.4 Hz, 1H), 1.77-1.65 (m, 1H), 1.61-1.23 (m, 8H), 0.80 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 146.3, 111.5, 74.3, 38.9, 38.8, 30.0, 26.1, 21.6, 15.6. **HRMS-(ESI+) for $C_9H_{16}O$ $[M]^+$:** calculated: 140.1201, found: 140.1198.

2-Phenyl-1-vinyl-1-cyclohexanol:



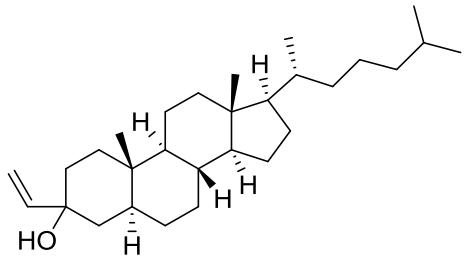
The product **84** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as yellow oil (82%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.31-7.25 (m, 2H), 7.24-7.19 (m, 3H), 5.86 (dd, *J* = 17.3, 10.8 Hz, 1H), 4.90 (dd, *J* = 17.3, 1.2 Hz, 1H), 4.84 (dd, *J* = 10.8, 1.2 Hz, 1H), 2.66 (dd, *J* = 12.9, 3.5 Hz, 1H), 2.13 (dq, *J* = 13.1, 3.6 Hz, 1H), 1.92-1.66 (m, 5H), 1.46-1.37 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 146.1, 142.3, 129.1, 128.1, 126.6, 111.5, 73.9, 52.3, 38.4, 27.9, 26.4, 21.6. **HRMS-(ESI+) for $C_{14}H_{18}O$ $[M]^+$:** calculated: 202.1358, found: 202.1360.

(4aR, 8aS)-1-vinyldecahydronaphthalen-1-ol:



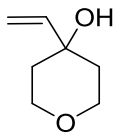
The product **86**was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as yellowish oil (96%). The characterization data is in agreement with the literature values.[23] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.78 (dd, *J* = 17.3, 10.8 Hz, 1H), 5.20 (dd, *J* = 17.3, 1.4 Hz, 1H), 5.04 (dd, *J* = 10.8, 1.4 Hz, 1H), 1.74-1.48 (m, 8H), 1.37-1.31 (m, 2H), 1.20-1.15 (m, 2H), 1.01-0.92 (m, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 146.2, 111.5, 74.4, 49.5, 39.3, 37.0, 34.7, 34.0, 26.9, 26.5, 25.9, 21.3. **HRMS-(ESI+) for $C_{12}H_{20}O$ $[M]^+$:** calculated: 180.1514, found: 180.1516.

(5S, 8R, 9S, 10S, 13R, 14S, 17R)-10, 13-dimethyl-17-((R-6-methylheptan-2-yl)-3-vinylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-3-ol:



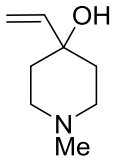
The product **88** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as white solid (92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.10 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.31 (dd, *J* = 17.5, 1.3 Hz, 1H), 5.15 (dd, *J* = 10.8, 1.2 Hz, 1H), 1.96 (dt, *J* = 12.5, 3.2 Hz, 1H), 1.85-1.75 (m, 1H), 1.73-1.61 (m, 5H), 1.56-1.42 (m, 6H), 1.38-1.22 (m, 12H), 1.15-1.05 (m, 5H), 0.91-0.88 (m, 4H), 0.87 (d, *J* = 1.9 Hz, 3H), 0.85 (d, *J* = 1.9 Hz, 3H), 0.84 (s, 3H), 0.64 (s, *J* = 4.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.7, 113.6, 72.8, 56.6, 56.4, 54.5, 43.6, 39.6, 36.3, 35.9, 35.6, 34.5, 29.8, 28.4, 28.2, 24.4, 24.0, 23.9, 23.0, 22.7, 18.8, 12.3, 12.2. **HRMS-(ESI+) for $C_{29}H_{50}O$ $[M]^+$:** calculated: 414.3862, found: 414.3869.

4-Vinyltetrahydro-2*H*-pyran-4-ol:



The product **90** was purified by flash column chromatography using as eluent a mixture of hexanes/ethyl acetate (1:1). It was obtained as colorless oil (78%). The characterization data is in agreement with the literature value.[24] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.95 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.26 (dd, *J* = 17.4, 1.0 Hz, 1H), 5.09 (dd, *J* = 10.7, 1.0 Hz, 1H), 3.88-2.69 (m, 4H), 1.88-1.74 (m, 2H), 1.67 (br s, 1H), 1.52-1.48 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 145.1, 112.5, 69.4, 63.8, 37.6.

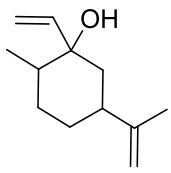
1-Methyl-4-vinylpiperidin-4-ol:



The product **92** was purified by flash column chromatography using THF as eluent. The silica gel was previously deactivated in solid by adding 0.8 mL of Et_3N to 26 cm^3 of silica. It was obtained as yellowish oil (55%). The characterization data is in agreement with the literature values.[25] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.95 (dd, *J* = 17.3, 10.7 Hz,

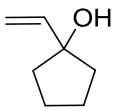
1H), 5.27 (dd, *J* = 17.3, 1.0 Hz, 1H), 5.07 (dd, *J* = 10.7, 1.0 Hz, 1H), 2.70-2.59 (m, 2H), 2.47-2.38 (m, 2H), 2.32 (s, 3H), 1.89-1.82 (m, 2H), 1.60-1.57 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ =.145.5, 112.3, 69.3, 51.3, 46.2, 36.9.

2-Methyl-5-(prop-1-en2-yl)-1-vinyl-1-cyclohexanol:



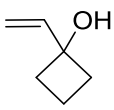
The product **94** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (80%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ =5.83 (dd, *J* = 17.3, 10.8, 1H), 5.24 (dd, *J* = 17.3, 1.3, 1H), 5.08 (dd, *J* = 10.8, 1.3, 1H), 4.70-4.67 (m, 2H), 2.31 (tt, *J* = 12.4, 3.3, 1H), 1.82-1.75 (m, 1H), 1.71 (s, 3H), 1.65 (ddd, *J* = 13.6, 3.3, 2.4 Hz, 1H), 1.60-1.54 (m, 1H), 1.48-1.42 (m, 2H), 1.41-1.33 (m, 1H), 1.27-1.17 (m, 1H), 0.82 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 150.1, 146.2, 111.7, 108.6, 74.8, 43.9, 39.9, 38.7, 31.5, 29.1, 21.1, 15.3. **HRMS-(ESI+) for $C_{12}H_{20}O$ $[M]^+$:** calculated: 180.1514, found: 180.1504.

1-Vinyl-1-cyclopentanol:



The product **97** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as colorless oil (15%). The characterization data is in agreement with the literature values.[19a] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.02 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.27 (dd, *J* = 17.3, 1.3 Hz, 1H), 5.03 (dd, *J* = 10.7, 1.3 Hz, 1H), 1.90-1.84 (m, 2H), 1.73-1.65 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 144.4, 111.1, 82.2, 40.3, 23.7.

1-Vinyl-1-cyclobutanol:



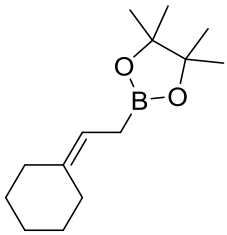
The product **100** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (10:1). It was obtained as orange oil (62%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.13 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.27 (dd, *J* = 17.3, 2.8 Hz, 1H), 5.07 (dd, *J* = 10.7, 1.3 Hz, 1H), 2.24-2.08 (m, 4H), 1.85-1.73 (m, 1H), 1.65-1.51 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 142.5, 111.3, 75.2, 36.0, 12.1. **HRMS-(ESI+) for $C_6H_{10}O$ $[M]^+$:** calculated: 98.0732, found: 98.0727.

6.4.3. General procedure for the transition metal-free borylation of allylic alcohols

To an open-air vial equipped with a magnetic stir bar, B_2pin_2 (0.1524 g, 0.6 mmol), cesium carbonate (14.7 mg, 15 mol %), THF as solvent (0.5 mL), MeOH as additive (120 µL, 10 equiv) and substrate (0.3 mmol) were added. The vial was sealed with a plastic cap and heated to 70°C in an oil bath for 16 h. The reaction mixture was cooled to room temperature. Then, a known amount of naphthalene as internal standard was added. Without further manipulations, an aliquot was taken to determine the conversion and selectivity by ^{1}H NMR analysis. The reaction mixture was purified by silica gel flash chromatography to afford the allylborylated product.

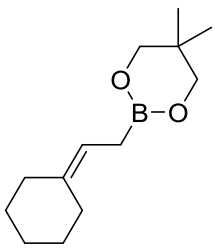
6.4.4. Characterization of allylborylated compunds

2-(2-Cyclohexylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



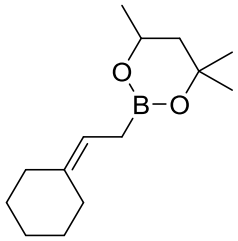
The product **59a** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (50:1). It was obtained as colorless oil (85%). This data is in agreement with the reported literature values.[26] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.17 (dd, *J* = 8.2, 7.2 Hz, 1H), 2.10-2.05 (m, 4H), 1.59 (d, *J* = 7.6 Hz, 2H), 1.51-1.46 (m, 6H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.8, 115.0, 83.2, 37.1, 28.8, 28.7, 27.7, 27.1, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.2 (br s). **HRMS-(ESI+) for $C_{14}H_{25}BO_2$ $[M]^+$:** calculated: 236.1948, found: 236.1950

2-(2-cyclohexylideneethyl)-5,5-dimethyl-1,3,2-dioxaborinane:



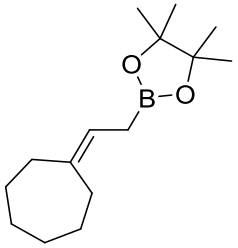
The product **59b** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). It was obtained as colorless oil (54%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.17 (dd, *J* = 7.7, 4.4 Hz, 1H), 3.59 (s, 4H), 2.15-2.02 (m, 4H), 1.54-1.41 (m, 8H), 0.95 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.1, 116.2, 72.2, 37.3, 31.8, 28.8, 28.6, 27.7, 27.1, 21.9. **^{11}B NMR (128 MHz, $CDCl_3$) δ =** 29.5 (br s). **HRMS-(ESI+) for $C_{13}H_{23}BO_2$ $[M]^+$:** calculated: 222.1791, found: 222.1789.

2-(2-cyclohexylideneethyl)-4,4,6-trimethyl-1,3,2-dioxaborinane:



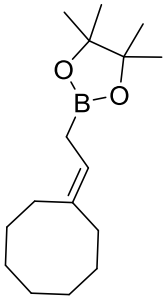
The product **59c** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). It was obtained as colorless oil (24%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.17 (t, *J* = 7.6 Hz, 1H), 4.20-4.12 (m, 1H), 2.11-2.05 (m, 4H), 1.74 (dd, *J* = 13.9, 3.0 Hz, 2H), 1.55-1.44 (m, 8H), 1.26 (s, 6H), 1.23 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 138.7, 116.8, 70.7, 64.8, 46.0, 37.3, 31.4, 28.9, 28.7, 28.2, 27.8, 27.2, 23.3. **^{11}B NMR (128 MHz, $CDCl_3$) δ =** 29.6 (br s). **HRMS-(ESI+) for $C_{14}H_{25}BO_2$ $[M]^+$:** calculated: 236.1948, found: 236.1947.

2-(2-cycloheptylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



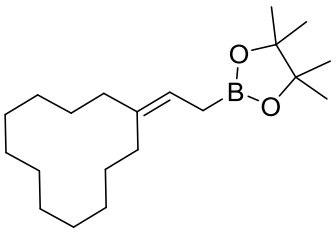
The product **61** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (50:1). It was obtained as colorless oil (84%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.24 (t, *J* = 7.8 Hz, 1H), 2.2-2.18 (m, 4H), 1.56 (d, *J* = 7.6, 2H), 1.55-1.45 (m, 8H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 141.4, 118.8, 83.1, 37.9, 30.2 30.2, 29.7, 29.3, 26.9, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.3 (br s). **HRMS-(ESI+) for $C_{15}H_{27}BO_2$ $[M]^+$:** calculated: 250.2104, found: 250.2110

2-(2-cyclooctylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



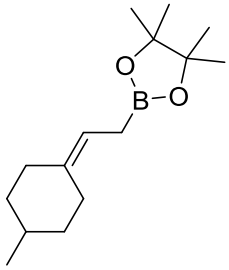
The product **63** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as colorless oil (79%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.28 (t, *J* = 8.0 Hz, 1H), 2.18-2.12 (m, 4H), 1.62-1.50 (m, 6H), 1.48 (s, 6H), 1.24 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.8, 118.3, 82.2, 36.9, 28.1, 26.5, 25.8, 25.3 (*J* = 4.3 Hz), 25.2, 23.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.2 (br s). **HRMS-(ESI+) for $C_{16}H_{29}BO_2$ $[M]^+$:** calculated: 264.2261, found: 264.2265.

2-(2-cyclododecylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



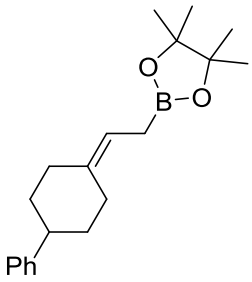
The product **65** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as yellow oil (79%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.31 (t, *J* = 8 Hz, 1H), 2.01 (m, 4H), 1.65 (d, *J* = 7.9 Hz, 2H), 1.52 (m, 2H), 1.42 (m, 2H), 1.30 (m, 14H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 137.10, 119.4, 83.1, 31.9, 28.6, 25.3, 25.1, 24.9, 24.5, 24.3, 24.2, 23.9, 23.4, 22.5. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.15 (br s). **HRMS-(ESI+) for $C_{20}H_{37}BO_2$ $[M]^+$:** calculated: 320.2887, found: 320.2903.

2-(2-(4-Methylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



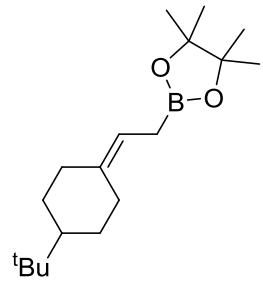
The product **73** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as yellow oil (87%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.18 (t, *J* = 7.7 Hz, 1H), 2.57-2.47 (m, 1H), 2.22-2.11 (m, 1H), 2.06-1.99 (m, 1H), 1.76-1.64 (m, 3H), 1.59 (d, *J* = 7.6 Hz, 2H), 1.54-1.43 (m, 1H), 1.23 (s, 12H), 0.97-0.89 (m, 2H), 0.87 (d, *J*= 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.4, 115.2, 83.2, 36.9, 36.4, 35.9, 33.0, 27.9, 24.9, 22.3. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.32 (br s).**HRMS-(ESI+) for $C_{15}H_{27}BO_2$ $[M]^+$:** calculated: 250.2104, found: 250.2112.

2-(2-(4-Phenaylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



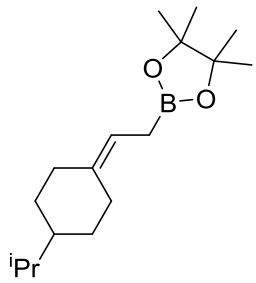
The product **75** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as colorless oil (79%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29 (m, 2H), 7.21 (m, 3H), 5.28 (t, *J* = 7.6 Hz, 1H), 2.69 (m, 2H), 2.32 (m, 1H), 2.19 (m, 1H), 1.89 (m, 2H), 1.66 (d, *J* = 7.4 Hz, 2H), 1.49 (m, 2H), 1.42 (m, 1H), 1.26 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.4, 138.4, 128.4, 126.9, 126.0, 116.0, 83.2, 44.9, 36.8, 36.0, 35.0, 28.4, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.22 (br s). **HRMS-(ESI+) for $C_{20}H_{29}BO_2$ $[M]^+$:** calculated: 312.2600, found: 312.2270.

2-(2-(4-Tertbutylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



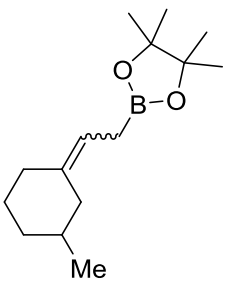
The product **77** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as yellow oil (52%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.16 (t, *J* = 7.7 Hz, 1H), 2.60 (ddd, *J* = 13.4, 5.7, 3.1 Hz, 1H), 2.28-2.18 (m, 1H), 2.04-1.91 (m, 1H), 1.87-1.74 (m, 2H), 1.69-1.54 (m, 4H), 1.23 (s, 12H), 1.04-0.93 (m, 2H), 0.83 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.8, 114.7, 83.1, 48.6, 36.9, 32.6, 29.4, 28.5, 28.3, 27.8, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.80 (br s). **HRMS-(ESI+) for $C_{18}H_{33}BO_2$ $[M]^+$:** calculated: 292.2574, found: 292.2574.

2-(2-(4-Isopropylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **79** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was obtained as colorless oil (41%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.17 (t, *J* =7.5 Hz, 1H), 2.57 (d, *J* = 11.7 Hz, 1H), 2.20 (d, *J* = 13.6 Hz, 1H), 1.98 (t, *J* = 13.1 Hz, 1H), 1.78-1.54 (m, 5H), 1.48-1.37 (m, 1H), 1.24 (s, 12H), 1.09-0.91 (m, 3H), 0.84 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.8, 114.7, 83.0, 44.3, 36.5, 32.5, 31.4, 30.4, 28.0, 24.7, 29.8 (*J* = 3.4 Hz). **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.22 (br s). **HRMS-(ESI+) for $C_{17}H_{31}BO_2$ $[M]^+$:** calculated: 278.2417, found: 278.2411.

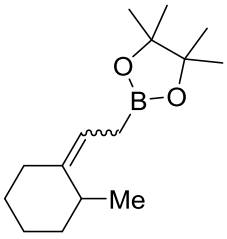
2-(2-(3-Methylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **81** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (50:1). It was isolated as a mixture of *Z*/*E* diastereoisomers (50:50) and obtained as colorless oil (64%). Spectrum data of one diastereoisomer. **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.18 (t, *J* = 8.0 Hz, 1H), 2.48-2.41 (m, 1H), 2.19-2.08 (m, 1H), 1.91 (ddd, *J* =14.1, 3.8, 1.7 Hz, 1H), 1.78-1.62 (m, 3H), 1.60 (d, *J* = 7.5 Hz, 2H), 1.48-1.36 (m, 2H),

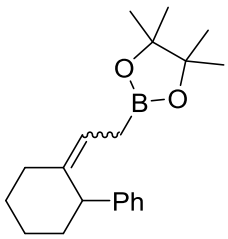
1.10-0.97 (m, 1H), 1.23 (s, 12H), 0.87 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.3, 115.3, 83.1, 45.5, 36.9, 35.5, 28.1, 26.7, 24.9, 22.5. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.29 (br s). **HRMS-(ESI+) for $C_{15}H_{27}BO_2$ $[M]^+$:** calculated: 250.2104, found: 250.2101.

2-(2-(2-Methylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



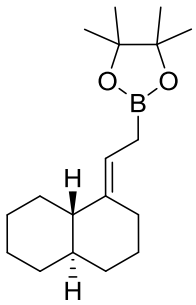
The product **83** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (50:1). It was isolated as a mixture of *Z*/*E* diastereoisomers (50:50) and obtained as colorless oil (67%). Spectrum data of one diastereoisomer. **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.18-5.10 (m, 1H), 2.52-2.38 (m, 1H), 2.13-2.02 (m, 1H), 1.98-1.94 (m, 1H), 1.60-1.56 (m, 6H), 1.52-1.47 (m, 2H), 1.23 (s, 12H), 1.00 (d, J = 7.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.3, 112.6, 83.1, 36.9, 32.5, 28.7, 28.0, 24.9, 21.2, 17.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.15 (br s). **HRMS-(ESI+) for $C_{15}H_{27}BO_2$ $[M]^+$:** calculated: 250.2104, found: 250.2100.

2-(2-(2-Phenylcyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



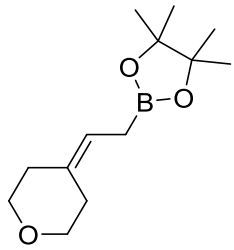
The product **85** was purified by flash column chromatography using as eluent a mixture of hexanes/diethyl ether (50:1). It was obtained as colorless oil (49%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.31-7.25 (m, 5H), 4.86 (t, *J* = 8.0 Hz, 1H), 3.33 (dd, *J* = 8.6, 4.1 Hz, 1H), 2.44-2.32 (m, 1H), 2.08-1.85 (m, 3H), 1.70-1.49 (m, 6H), 1.22 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 141.9, 128.6, 128.1, 125.8, 117.8, 83.1, 50.1, 33.4, 28.1, 27.8, 25.4, 24.8. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.04 (br s). **HRMS-(ESI+) for $C_{20}H_{29}BO_2$ $[M]^+$:** calculated: 312.2261, found: 312.2282.

2-(2-(octahydronaphthalen-1(*2H*)-ylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



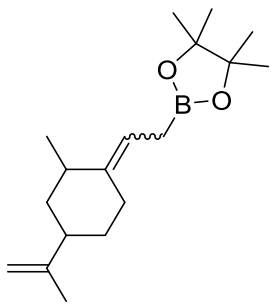
The product **87** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (50:1). It was obtained as colorless oil (65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.08 (t, *J* = 7.6 Hz, 1H), 2.65 (d, *J* = 12.9 Hz, 1H), 1.82-1.69 (m, 3H), 1.69-1.52 (m, 7H), 1.49-1.45 (m, 1H), 1.22 (s, 12H), 1.15-0.87 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.0, 111.9, 48.1, 45.1, 35.1, 35.0, 29.7, 28.9, 27.5, 26.8, 26.5, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.12 (br s). **HRMS-(ESI+) for $C_{18}H_{31}BO_2$ $[M]^+$:** calculated: 290.2417, found: 290.2414.

2-(2-(Tetrahydro-4*H*-pyran-4-ylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **91** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (9:1). It was isolated as colorless oil (53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.29 (dd, *J* = 8.4, 7.2 Hz, 1H), 3.69-3.61 (m, 4H), 2.22 (ddd, *J* = 11.8, 8.2, 3.0, 4H), 1.62 (d, *J* = 7.8 Hz, 2H), 1.24 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 134.3, 117.4, 83.3, 69.9, 68.9, 36.9, 29.7, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.4 (br s). **HRMS-(ESI+) for $C_{13}H_{23}BO_3$ $[M]^+$:** calculated: 238.1740, found: 238.1738.

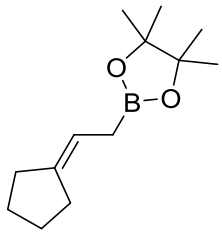
2-(2-(2-Methyl-4-(prop-1-en-2-yl)cyclohexylidene)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **95** was purified by flash column chromatography using as eluent a mixture of hexane/diethyl ether (50:1). It was isolated as a mixture of *Z*/*E* diastereoisomers (80:20) and obtained as colorless oil (41%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.20-5.12 (m, 1H), 4.72-4.66 (m, 2H), 2.72-2.68 (m, 1H), 1.93-1.76 (m, 3H), 1.74 (s, 3H), 1.70-1.51 (m, 5H), 1.44-1.32 (m, 1H), 1.23 (s, 12H), 1.02 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR**

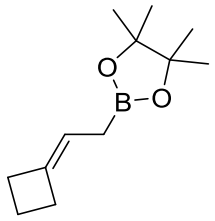
(100 MHz, $CDCl_3$) δ = 150.7, 142.8, 112.8, 108.3, 83.1, 46.6, 38.0, 37.7, 34.5, 32.2, 24.9, 24.8, 21.1, 18.4. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.09 (br s). **HRMS-(ESI+) for $C_{18}H_{31}BO_2$ $[M]^+$:** calculated: 290.2417, found: 290.2424.

2-(2-cyclopentylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



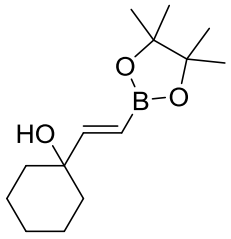
The product **98** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (50:1). It was isolated as colorless oil (27%).**^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.33 (m, 1H), 2.24-2.20 (m, 2H), 2.17-2.12 (m, 2H), 1.68-1.56 (m, 6H), 1.24 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.7, 114.0, 83.2, 33.7, 28.9, 26.8, 26.4, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.30 (br s). **HRMS-(ESI+) for $C_{13}H_{23}BO_2$ $[M]^+$:** calculated: 222.1791, found: 222.1786.

2-(2-cyclobutylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **101** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (50:1). It was isolated as colorless oil (12%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.19-5.05 (m, 1H), 2.71-2.51 (m, 4H), 1.97-1.82 (m, 2H), 1.49 (d, *J* = 7.7 Hz, 2H), 1.25 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.9, 114.7, 83.2, 30.9, 29.3, 24.9, 16.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.6 (br s). **HRMS-(ESI+) for $C_{12}H_{21}BO$ $[M]^+$:** calculated: 208.1635, found: 208.1633.

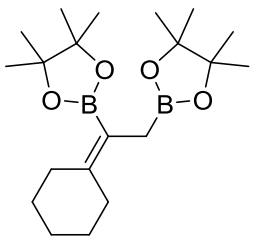
1-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)cyclohexan-ol:



The product **104** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (4:1). It was obtained as colorless oil (91%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.69 (d, *J* = 18.2 Hz, 1H), 5.65 (d, *J* = 18.2 Hz, 1H), 1.63-1.50 (m, 10H), 1.27 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 160.1, 83.4, 72.6, 37.2, 25.6, 25.2, 25.0,

24.9, 21.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 27.15 (br s). **HRMS-(ESI+) for $C_{14}H_{25}BO_3$ $[M]^+$:** calculated: 252.1897, found: 252.1895.

2,2'-(1-cyclohexylideneethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane):



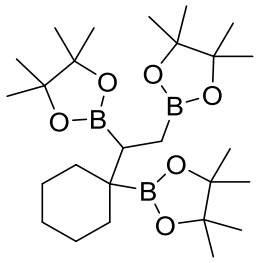
The product **105** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (50:1). It was obtained as colorless oil (68%). The characterization data is in agreement with the literature values.[27] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 2.49-2.43 (m, 2H), 2.18-2.14 (m, 2H), 1.77 (s, 2H), 1.53 (s, 6H), 1.25 (s, 12H), 1.20 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 153.5, 82.9, 82.8, 34.9, 31.4, 29.2, 28.1, 27.2, 25.0, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.7 (br s), 31.9 (br s). **HRMS-(ESI+) for $C_{20}H_{36}B_2O_4$ $[M]^+$:** calculated: 362.2800, found: 362.2800.

6.4.5. General procedure for the metal-free consecutive allyl borylation-diboration reaction

To an open-air vial equipped with a magnetic stir bar, B_2pin_2 (0.1904 g, 0.75 mmol), cesium carbonate (14.7 mg, 15 mol %), THF as solvent (0.5 mL), MeOH as additive (120 µL, 10 equiv) and substrate (0.3 mmol) were added. The vial was sealed with a plastic cap and heated to 90°C in an oil bath for 16 hours. The reaction mixture was cooled to room temperature. Then, a known amount of naphthalene as internal standard was added. Without further manipulations, an aliquot was taken to determine the conversion and selectivity by GC-MS analysis. After removing all the volatiles in a rotatory evaporator, the crude residue was purified by silica gel flash chromatography to afford the polyborylated product.

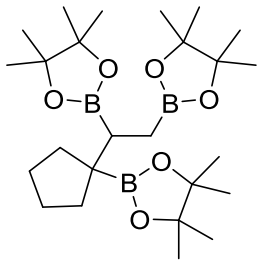
6.4.6. Characterization of polyborylated compounds

2,2'-(1-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohexyl)ethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane):



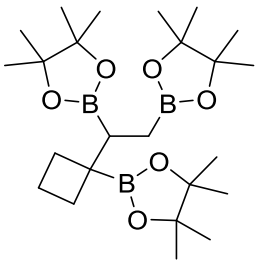
The product **96** was purified by flash column chromatography using as eluent a mixture of hexane/ethyl acetate (50:1). It was isolated as yellowish oil (53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.99 (d, J = 12.8 Hz, 1H), 1.90 (d, J = 13.1 Hz, 1H), 1.58 (t, J = 15.4 Hz, 3H), 1.22 (s, 24H), 1.18 (d, *J* = 1.7 Hz, 12H), 1.15-0.82 (m, 8H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 82.4, 82.7, 82.7, 35.5, 33.8, 26.9, 26.1, 25.7, 25.4, 25.3, 25.1, 25.1, 25.0, 24.8, 24.7, 9.1 (C-B). **^{11}B NMR (128 MHz, $CDCl_3$) δ =** 34.8, 30.9 (br s). **HRMS-(ESI+) for $C_{26}H_{49}B_3O_6$ $[M]^+$:** calculated: 490.3808, found: 490.3809.

2,2'-(1-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopentyl)ethane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane):



The product **99** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (50:1). It was isolated as colorless oil (65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 1.96-1.87 (m, 1H), 1.85-1.78 (m, 1H), 1.61-1.51 (m, 2H), 1.50-1.40 (m, 2H), 1.39-1.32 (m, 1H), 1.21 (s, 24H), 1.20 (d, *J* = 1.1 Hz, 12H), 1.15-1.03 (m, 2H), 0.98-0.91 (m, 1H), 0.85-0.80 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 83.6, 82.8, 82.7, 35.3, 35.2, 25.9, 25.6, 25.2, 25.1, 25.0, 25.0, 24.8, 24.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.6, 29.6 (br s). **HRMS-(ESI+) for $C_{24}H_{44}B_3O_6$ $[M\text{-}CH_3]^+$:** calculated: 461.3417, found: 461.3411.

2-(2-cyclopentylideneethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane:



The product **102** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). It was isolated as colorless solid (44%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 2.15-2.07 (m, 1H), 2.03-1.97 (m, 1H), 1.95-1.61 (m, 5H), 1.22 (s, 24H), 1.19 (s, *J* = 2.7 Hz, 12H), 0.90-0.79 (m, 1H), 0.68 (dd, *J* = 15.8, 3.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 82.8, 82.7, 82.6, 31.0, 30.6, 25.1, 25.0, 25.0, 24.9, 24.8, 17.8. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.9 (br s). **HRMS-(ESI+) for $C_{24}H_{45}B_3O_6$ $[M]^+$:** calculated: 462.3495, found: 462.3496.

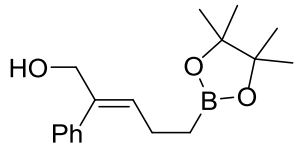
6.4.7. Allyl-alkyl couplings using vinyl cyclic carbonates and diborylmethane

An oven-dried Schlenk tube, sealed with a rubber septum and equipped with a magnetic stirring bar, was charged with 0.2 mmol (1 equiv) of compound **106** under Argon, followed by the addition of diborylmethane **(5)** (0.24 mmol, 1.2 equiv) and CuCl (0.018 mmol, 9 mol%) to the reaction mixture. Then, 0.1 mL of a previously prepared solution of dried methanol and cesium carbonate (0.1 mmol, 50 mol%) were added and the reaction was allowed to stir overnight at room temperature.

The crude was filtered through a small pad of celite® followed by a copious washing with dichloromethane. The solvent was gently concentrated at the rotatory evaporator and the NMR yield was calculated through comparison to an internal standard (naphthalene or mesitylene). Purification by flash chromatography on silica gel afforded the desired product.

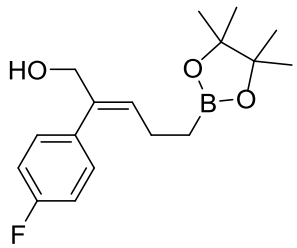
6.4.8. Characterization of homoallylboronate compounds

2-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



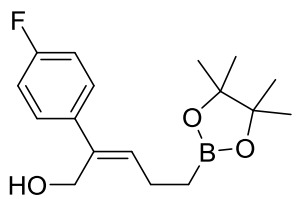
The product **(*E*)-107** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a colourless oil (43.2 mg, 75%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.31 (m, 5H), 5.76 (tt, *J* = 7.4, 1.1 Hz, 1H), 4.33 (d, *J* = 1.8Hz, 2H), 2.15 (m, 2H), 1.25 (s, 12H), 0.89 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.3, 138.6, 131.3, 128.8, 128.4, 127.2, 83.2, 68.4, 24.9, 23.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.99 (br s). **HRMS (ESI) for $C_{17}H_{25}BNaO_3$ $[M+Na]^+$:** calculated: 311.1794, found: 311.1801

(*E*)-2-(4-fluorophenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



The product **(*E*)-108** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (25.7 mg, 42%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.19 (m, 2H), 7.04 (m, 2H), 5.73 (tt, *J* = 7.4, 1.2 Hz, 1H), 4.28 (s, 2H), 2.10 (m, 2H), 1.22 (s, 12H), 0.83 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 163.2, 160.8, 138.3, 134.4 (d, *J* = 3.6 Hz), 131.9, 130.4 (d, *J* = 7.9 Hz), 127.7 (d, *J* = 7.8 Hz), 115.3 (d, *J* = 21.2 Hz), 83.2, 68.4, 24.9, 23.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.98 (br s). **HRMS (ESI) for $C_{17}H_{24}BFNaO_3$ $[M+Na]^+$:** calculated: 329.1700, found: 329.1707.

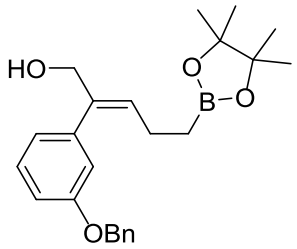
(*Z*)-2-(4-fluorophenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



The product **(*Z*)-108** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a colourless (9.8 mg, 16%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.43 (m, 2H), 7.20 (m, 2H), 5.73 (t, *J* = 7.6 Hz, 1H), 4.48 (s, 2H), 2.42 (dd, *J* = 14.1, 7.6 Hz, 2H), 1.21 (s, 12H), 1.07

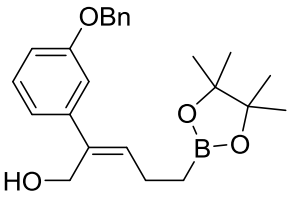
(m, 2H). **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.01 (br s).

(*E*)-2-(benzo[*d*][1,3]dioxol-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



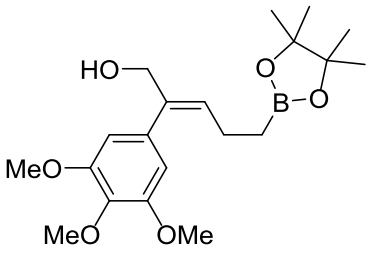
The product **(*E*)-109** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (51.2 mg, 65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.48 – 7.22 (m, 6H), 6.87 (m, 3H), 5.72 (t, *J* = 7.4 Hz, 1H), 5.06 (s, 2H), 4.28 (s, 2H), 2.13 (m, 2H), 1.23 (s, 12H), 0.84 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 158.8, 140.4, 139.1, 137.1, 131.4, 129.4, 128.7, 128.1, 127.7, 121.5, 115.4, 113.5, 83.2, 70.1, 68.3, 24.9, 23.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.91 (br s). **HRMS (ESI) for $C_{24}H_{31}BNaO_4$ $[M+Na]^+$:** calculated: 417.2213, found: 417.2220.

(*Z*)-2-(benzo[*d*][1,3]dioxol-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



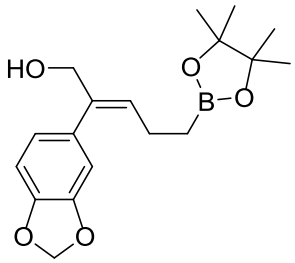
The product **(*Z*)-109** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (16.5 mg, 21%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.39 (m, 5H), 7.24 (m, 1H), 7.13 (m, 1H), 7.08 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.86 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.81 (t, *J* = 7.8 Hz, 1H), 5.07 (s, 2H), 4.50 (s, 2H), 2.43 (m, 2H), 1.22 (s, 12H), 1.06 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 158.9, 143.8, 138.4, 137.2, 134.5, 129.4, 128.7, 128.1, 127.7, 118.9, 113.3, 112.9, 83.6, 70.1, 60.4, 24.8, 22.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.43 (br s). **HRMS (ESI) for $C_{24}H_{31}BNaO_4$ $[M+Na]^+$:** calculated: 417.2213, found: 417.2222.

(*E*)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(3,4,5-trimethoxyphenyl)pent-2-en-1-ol:



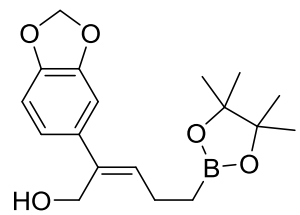
The product ***(E)*-110** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (2:1). It was obtained as colourless oil (36.3 mg, 48%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.45 (s, 2H), 5.71 (t, *J* = 7.4 Hz, 1H), 4.29 (s, 2H), 3.85 (s, 3H), 3.84 (s, 6H), 2.16 (m, 2H), 1.23 (s, 12H), 0.86 (t, *J* = 7.6 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 153.2, 139.4, 137.2, 134.2, 131.6, 105.9, 83.3, 68.4, 61.0, 56.3, 24.9, 23.3. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.06 (br s). **HRMS (ESI) for $C_{20}H_{31}BNaO_6$ $[M+Na]^+$:** calculated: 401.2111, found: 401.2107.

(*E*)-2-(benzo[*d*][1,3]dioxol-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



The product **(*E*)-111** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (39.8 mg, 60%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.79 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 1.6 Hz, 1H), 6.88 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.95 (s, 2H), 5.67 (t, *J* = 7.3 Hz, 1H), 4.25 (s, 2H), 2.13 (m, 2H), 1.22 (s, 12H), 0.83 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.6, 146.6, 138.8, 132.3, 131.4, 122.1, 109.3, 108.4, 101.1, 83.2, 68.5, 24.9, 23.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.89 (br s). **HRMS (ESI) for $C_{18}H_{25}BNaO_5$ $[Na+M]^+$:** calculated: 355.1692, found: 355.1699.

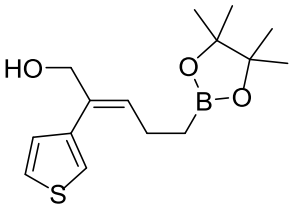
(*Z*)-2-(benzo[*d*][1,3]dioxol-5-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



The product **(*Z*)-111** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (21.2 mg, 32%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.86 (m, 2H), 6.66 (d, *J* = 8.1 Hz, 1H), 5.83 (s, 2H), 5.60 (t, *J* = 7.8 Hz, 1H), 4.36 (s, 2H), 2.30 (m, 2H), 1.12 (s,

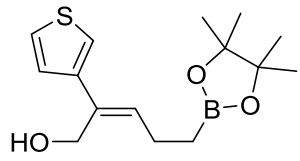
12H), 0.95 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.8, 146.6, 138.1, 136.6, 133.2, 119.6, 108.2, 106.9, 100.0, 83.6, 60.5, 24.8, 22.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.06 (br s). **HRMS (ESI) for $C_{18}H_{25}BNaO_5$ $[M+Na]^+$:** calculated: 355.1692, found: 355.1700.

(*Z*)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(thiophen-2-yl)pent-2-en-1-ol:



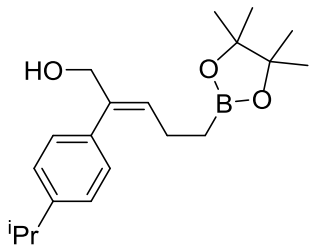
The product ***(E)*-112** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (2:1). It was obtained as colourless oil (31.1 mg, 53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.31 (dd, *J* = 5.0, 3.0, 1H), 7.22 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.10 (dd, *J* = 5.0, 1.3 Hz, 1H), 5.71 (t, *J* = 7.3 Hz, 1H), 4.30 (s, 2H), 2.27 (dd, *J* = 15.4, 7.5 Hz, 2H), 1.23 (s, 12H), 0.88 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 138.6, 133.9, 132.5, 128.2, 125.1, 122.9, 83.2, 68.5, 24.9, 23.4. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.91 (br s). **HRMS (ESI) for $C_{15}H_{23}BNaO_3S$ $[M+Na]^+$:** calculated: 317.1359, found: 317.1358.

(*E*)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(thiophen-2-yl)pent-2-en-1-ol:



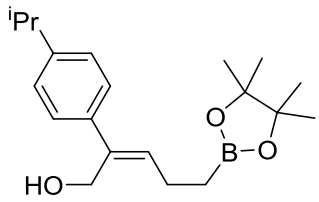
The product ***(Z)*-112** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (2:1). It was obtained as colourless oil (18.8 mg, 32%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29 (m, 1H), 7.24 (m, 2H), 5.91 (t, *J* = 9.7 Hz, 1H), 4.48 (s, 2H), 2.40 (m, 2H), 1.21 (s, 12H), 1.04 (t, *J* = 7.0 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 149.9, 133.5, 132.7, 125.8, 125.5, 119.8, 83.6, 60.1, 29.8, 24.8. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 34.16 (br s). **HRMS (ESI) for $C_{15}H_{23}BNaO_3S$ $[M+Na]^+$:** calculated: 317.1359, found: 317.1357.

(*E*)-2-(4-isopropylphenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



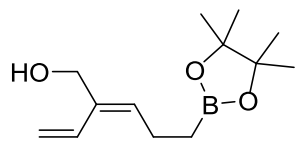
The product ***(E)*-113** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). It was obtained as yellowish oil (44.9 mg, 70%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.18 (m, 4H), 5.70 (t, *J* = 7.3 Hz, 1H), 4.30 (s, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 2.14 (m, 2H), 1.25 (d, *J* = 6.9 Hz, 6H), 1.22 (s, 12H), 0.84 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.6, 139.2, 135.8, 131.1, 128.7, 126.4, 83.2, 68.4, 33.9, 29.8, 24.9, 24.1, 23.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.74 (br s). **HRMS (ESI) for $C_{20}H_{31}BNaO_3$ $[M+Na]^+$:** calculated: 353.2263, found: 353.2258.

(*Z*)-2-(4-isopropylphenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-2-en-1-ol:



The product ***(Z)*-113** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). It was obtained as yellowish oil (15.8 mg, 24%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.38 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 5.77 (t, *J* = 7.8 Hz, 1H), 4.50 (s, 1H), 2.90 (hept, *J* = 6.9 Hz, 1H), 2.40 (m, 2H), 1.23 (d, *J* = 6.9 Hz, 2H), 1.21 (s, 12H), 1.04 (t, *J* = 6.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.6, 139.6, 138.3, 133.6, 126.5, 126.1, 83.6, 60.4, 33.9, 29.8, 24.9, 24.1, 22.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.77 (br s). **HRMS (ESI) for $C_{20}H_{31}BNaO_3$ $[M+Na]^+$:** calculated: 353.2263, found: 353.2261.

(*E*)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-vinylpent-2-en-1-ol:



The product ***(E)*-114** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as yelowish oil (39.0 mg, 82%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.68 (dd, *J* = 17.7, 11.2 Hz, 1H), 5.65 (t, *J* = 7.6 Hz, 1H), 5.33 (d, *J* = 17.7 Hz, 1H), 5.14 (d, *J* = 11.2 Hz, 1H), 4.25 (s, 2H), 2.28 (m, 2H), 1.23 (s, 12H), 0.88 (t, *J* = 7.9 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 135.1, 134.6,

131.5, 114.1, 83.3, 64.9, 24.9, 21.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.99 (br s). **HRMS (ESI) for $C_{13}H_{23}BNaO_3$ $[M+Na]^+$:** calculated: 261.1637, found: 261.1636.

6.4.9. Experimental procedure for the allyl boryl couplings between vinyl cyclic carbonates and B_2pin_2 with carbene ligand

An oven-dried Schlenk tube sealed with a rubber septum and equipped with a magnetic stir bar, was charged with 0.2 mmol (1 equiv) of compound **3** under argon, followed by the addition of bis(pinacolato)diboron (0.24 mmol, 1.2 equiv), CuCl (0.018mmol, 9 mol%), and 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride (SIPr) (0.026mmol, 13 mol%) to the reaction mixture. Then, 0.1 mL of a previously prepared solution of dried methanol and cesium carbonate (0.03 mmol, 15 mol%) were added and the reaction was allowed to stir overnight at room temperature.

The crude was filtered through a small pad of celite® followed by a copious washing with dichloromethane. The solvent was gently concentrated at the rotatory evaporator and the NMR yield was calculated through comparison to an internal standard (naphthalene or mesitylene). Purification by flash chromatography on silica gel afforded the desired product.

Scale up details:

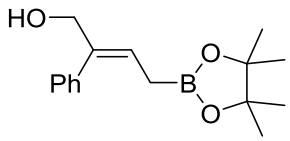
The reaction was carried out with the same protocol mentioned above, but using the following quantities:

The Schlenk tube was charged with 874 mg (4.6 mmol) of compound **3** under argon, followed by the addition of 1.403 mg of B_2pin_2 (1.2 equiv, 5.52 mmol), 41 mg of CuCl (9 mol%, 0.41 mmol), and 255 mg of **SIPr** (13 mol%, 0.6 mmol) to the reaction mixture. Then, 2.3 mL of of a previously prepared solution of dried methanol and 225 mg of cesium carbonate (15 mol%, 0.69 mmol) were added and the reaction was allowed to stir overnight at room temperature.

The (*E*)-allylboronate product ***(E)*-115** was obtained after purification by flash chromatography on silica gel as described below, in 58% isolated yield (731 mg).

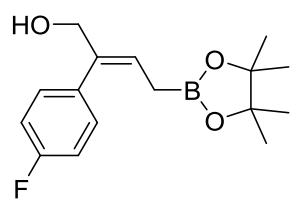
6.4.10. Characterization of (*E*)-allylboronate compounds:

(*E*)-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol:



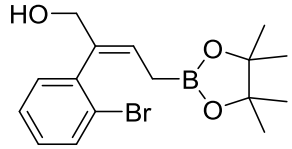
The product ***(E)*-115** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (35.6 mg, 65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.39-7.31 (m, 2H), 7.29-7.22 (m, 3H), 5.86 (tt, *J* = 8.1, 0.9 Hz, 1H), 4.34 (d, *J* = 0.9 Hz, 2H), 1.67 (d, *J* = 8.0 Hz, 2H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 140.2, 138.5, 128.9, 128.4, 127.1, 124.5, 83.5, 68.5, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.35 (br s). **HRMS (ESI) for $C_{16}H_{23}BNaO_3$ $[M+Na]^+$:** calculated: 297.1638, found: 297.1646.

(*E*)-2-(4-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol:



The product ***(E)*-117** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as pale yellow oil (32.7 mg, 58%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.25-7.18 (m, 2H), 7.07-6.99 (m, 2H), 5.86 (tt, *J* = 8.2, 1.0 Hz, 1H), 4.30 (d, *J* = 1.0 Hz, 2H), 1.64 (d, *J* = 8.2 Hz, 2H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 161.9 (d, *J* = 243.5 Hz), 139.2, 134.4, 130.5 (d, *J* = 7.7 Hz), 125.0, 115.3 (d, *J* = 20.6 Hz), 83.5, 68.5, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.22 (br s). **HRMS (ESI) for $C_{16}H_{22}BFNaO_3$ $[M+Na]^+$:** calculated: 315.1541, found: 315.1543.

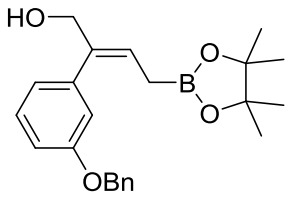
(*E*)-2-(2-bromophenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-ol:



The product ***(E)*-118** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (23.2 mg, 33%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.58 (m, 1H), 7.27 (m, 1H), 7.14 (m, 2H), 5.96 (tt, *J* = 8.1, 1.1 Hz, 1H), 4.28 (d, *J* = 7.6 Hz, 2H), 1.65 (d, *J* = 8.0 Hz, 2H), 1.22 (s,

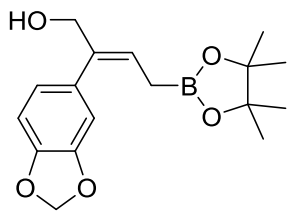
12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.5, 139.4, 132.8, 131.4, 128.9, 127.5, 126.3, 123.7, 83.5, 67.8, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.89 (br s). **HRMS (ESI) for $C_{16}H_{20}BBrNaO_3$ $[M+Na]^+$:** calculated: 375.0743, found: 375.0734.

(*E*)-2-(3-(benzyloxy)phenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-ol:



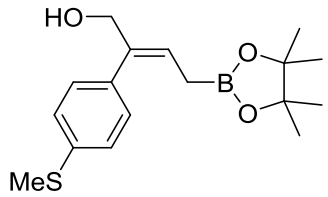
The product ***(E)*-119** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colorless oil (41.06 mg, 54%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.39 (m, 6H), 6.87 (m, 3H), 5.85 (tt, *J* = 8.0, 5.3 Hz, 1H), 5.06 (s, 2H), 4.33 (d, *J* = 5.3 Hz, 2H), 1.68 (d, *J* = 8.2 Hz, 2H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 158.9, 140.0, 139.9, 137.1, 129.5, 128.7, 128.1, 127.7, 124.6, 121.5, 115.5, 113.6, 83.5, 70.1, 68.5, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.34 (br s). **HRMS (ESI) for $C_{23}H_{29}BNaO_4$ $[M+Na]^+$:** calculated: 403.2055, found: 403.2057.

(*E*)-2-(benzo[d][1,3]dioxol-5-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-ol:



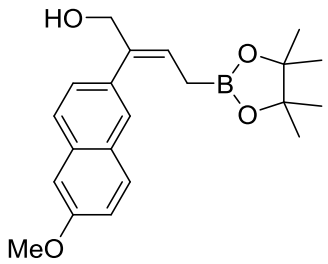
The product ***(E)*-120** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colorless oil (33.7 mg, 53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.76 (m, 3H), 5.95 (s, 2H), 5.81 (tt, *J* = 8.1, 3.9 Hz, 1H), 4.28 (d, *J* = 3.9 Hz, 2H), 1.67 (d, *J* = 8.0 Hz, 2H), 1.24 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.7, 146.6, 139.8, 132.2, 124.5, 122.2, 109.5, 108.4, 101.0, 83.5, 66.6, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.87 (br s). **HRMS (ESI) for $C_{17}H_{23}BNaO_5$ $[M+Na]^+$:** calculated: 341.1536, found: 341.1540.

(*E*)-2-(4-(methylthio)phenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-ol:



The product ***(E)*-121** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (38.4 mg, 60%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.32 (m, 4H), 5.85 (tt, *J* = 8.1, 1.0 Hz, 1H), 4.32 (d, *J* = 1.1 Hz, 2H), 2.48 (s, 3H), 1.68 (d, *J* = 8.1 Hz, 2H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 139.5, 137.1, 135.3, 129.4, 126.7, 124.8, 83.5, 68.4, 24.9, 16.0. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 33.08 (br s).

(*E*)-2-(6-methoxynaphthalen-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-en-1-ol:



The product ***(E)*-122** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (36.8 mg, 52%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.71 (m, 3H), 7.36 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.14 (m, 2H), 5.93 (tt, *J* = 8.2, 4.6 Hz, 1H), 4.42 (d, *J* = 4.6Hz, 2H), 3.93 (s, 3H), 1.72 (d, *J* = 8.1 Hz, 2H), 1.23 (s, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 157.7, 140.1, 133.7, 129.5, 128.9, 127.7, 127.6, 126.9, 124.7, 118.9, 105.7, 83.5, 55.4, 24.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 32.55 (br s). **HRMS (ESI) for $C_{21}H_{27}BNaO_4$ $[M+Na]^+$:** calculated: 377.1900, found: 377.1886.

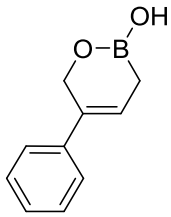
6.4.11. General procedure for the allyl-boryl couplings between B_2pin_2 and vinyl cyclic carbonates with diphosphine ligand

An oven-dried Schlenk tube sealed with a rubber septum and equipped with a magnetic stir bar, was charged with 0.2 mmol (1 equiv) of compound **3** under Argon, followed by the addition of bis(pinacolato)diboron (0.24 mmol, 1.2 equiv), CuCl (0.018 mmol, 9 mol%), and,1,2-bis(di-*tert*-butylphosphinomethyl)benzene (**P-P**) (0.026 mmol, 13 mol%) to the reaction mixture. Then, 0.1 mL of a previously

prepared solution of dried methanol and cesium carbonate (0.03 mmol, 15 mol%) were added and the reaction was allowed to stir overnight at room temperature. The crude was filtered through a small pad of celite® followed by a copious washing with dichloromethane. The solvent was gently concentrated at the rotatory evaporator and the NMR yield was calculated through comparison to an internal standard (naphthalene or mesitylene). Purification by flash chromatography on silica gel afforded the desired product.

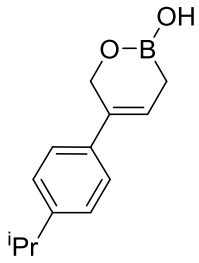
6.4.12. Characterization of (*Z*)-boracycle compounds

5-phenyl-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



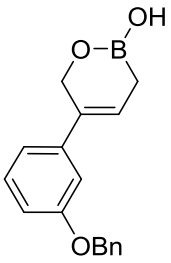
The product ***(Z)*-116** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (20:1). It was obtained as a crystalline solid (15.7 mg, 45%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29 (m, 5H), 6.13 (s, 1H), 4.94 (td, *J* = 3.6, 1.8 Hz, 2H), 1.66 (dd, *J* = 7.5, 3.7 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 138.5, 135.6, 128.6, 127.5, 125.5, 122.7, 66.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.62 (br s).

5-(4-isopropylphenyl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



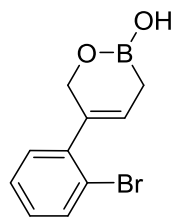
The product ***(Z)*-123** was purified by flash column chromatography using as eluent a mixture of pentane/diethyl ether (20:1). It was obtained as a crystalline solid (13.4 mg, 31%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.19 (m, 4H), 6.10 (br s, 1H), 4.92 (m, 2H), 2.89 (hept, *J* = 6.9 Hz, 1H), 1.65 (m, 2H), 1.24 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 148.2, 136.3, 135.5, 126.7, 125.4, 122.0, 67.1, 33.9, 24.1. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.56 (br s).

5-(3-(benzyloxy)phenyl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



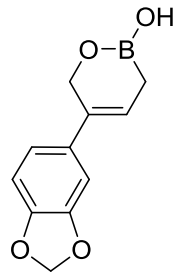
The product **(*Z*)-124** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (10.6 mg, 19%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.39 (m. 6H), 6.88 (m, 3H), 6.14 (br s, 1H), 5.06 (s, 2H), 4.90 (m, 2H), 1.65 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 159.0, 140.3, 137.0, 129.6, 128.8, 128.2, 127.7, 122.9, 118.2, 113.5, 112.5, 70.1, 66.9. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.67 (br s). **HRMS (EI) for $C_{17}H_{17}BO_3$ $[M]^+$:** calculated: 280.1271, found: 280.1277.

5-(2-bromophenyl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



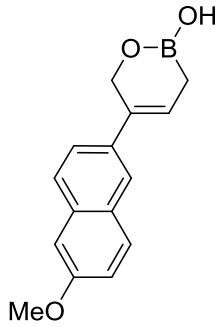
The product **(*Z*)-125** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (13.1 mg, 26%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.56 (m, 1H), 7.26 (m, 1H), 7.14 (m, 2H), 5.78 (br s, 1H), 4.73 (br s, 2H), 1.64 (br s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 140.6, 137.5, 132.9, 130.9, 129.1, 127.5, 125.4, 123.2, 67.3. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.56 (br s). **HRMS (EI) for $C_{10}H_0BO_2Br$ $[M]^+$:** calculated: 251.9957, found: 251.9949.

5-(benzo[*d*][1,3]dioxol-5-yl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



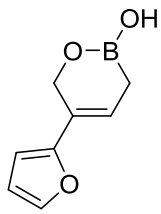
The product **(*Z*)-126** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a white solid (7.8 mg, 18%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.75 (m, 3H), 6.03 (br s, 1H), 5.95 (s, 2H), 4.85 (m, 2H), 1.63 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.9, 147.0, 133.1, 121.9, 118.8, 108.3, 106.3, 101.2, 67.1, 53.6. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.62 (br s). **HRMS (EI) for $C_{11}H_{11}BO_4$ $[M]^+$:** calculated: 218.0750 , found: 218.0755.

5-(7-methoxynaphthalen-2-yl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



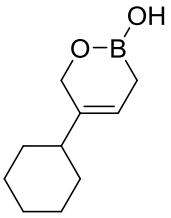
The product **(*Z*)-127** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as colourless oil (7.6 mg, 15%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.69 (dd, *J* = 8.7, 4.2 Hz, 2H), 7.58 (s, 1H), 7.45 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.13 (m, 2H), 6.26 (br s, 1H), 5.06 (m, 2H), 3.92 (s, 3H), 1.57 (m, 2H). **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.67 (br s). **HRMS (EI) for $C_{15}H_{15}BO_3$ $[M]^+$:** calculated: 254.1114, found: 254.1105.

5-(furan-2-yl)-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



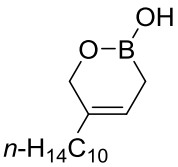
The product ***(Z)*-128** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a crystalline solid (12.4 mg, 37%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.34 (d, *J* = 1.6 Hz, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 2H), 6.12 (br s, 1H), 4.84 (m, 2H), 1.65 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 151.7, 141.6, 126.4, 120.3, 111.1, 103.8, 64.6. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.58 (br s).

5-cyclohexyl-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



The product ***(Z)*-129** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a crystalline solid (15.5 mg, 43%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.51 (br s, 1H), 4.49 (br s, 2H), 1.80-1.61 (m, 6H), 1.43 (m, 2H), 1.32-1.03 (m, 5H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 140.9, 116.7, 66.9, 41.9, 32.2, 26.7, 26.2. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.81 (br s). **HRMS (EI) for $C_{10}H_{17}BO_2$ $[M]^+$:** calculated: 180.1322, found: 180.9891.

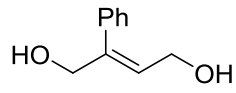
5-decyl-3,6-dihydro-2H-1,2-oxaborinin-2-ol:



The product ***(Z)*-130** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). It was obtained as a crystalline solid (26.2 mg, 55%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 5.51 (br s, 1H), 4.45 (br s, 2H), 1.88 (m, 2H), 1.25 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 135.9, 118.5, 67.9, 33.2, 32.0, 29.8, 29.7, 29.6, 29.5, 29.5, 28.1, 22.8, 14.3. **^{11}B NMR (128 MHz, $CDCl_3$)** δ = 31.55 (br s). **HRMS (EI) for $C_{14}H_{27}BO_2$ [M]$^+$:** calculated: 238.2104, found: 238.2110.

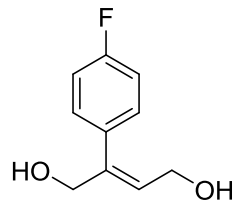
6.4.13. Characterization of (*E*)-but-2-ene-1,4-diols

(*E*)-2-phenylbut-2-ene-1,4-diol:



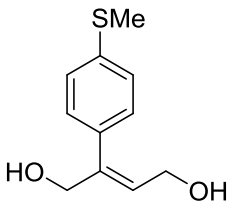
The product ***(E)*-131** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as a white solid (17.0 mg, 52%). The characterization data is in agreement with the reported values.[4] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.33 (m, 3H), 7.17 (m, 2H), 5.95 (t, *J* = 6.8 Hz, 1H), 4.36 (s, 2H), 4.12 (d, *J* = 6.6 Hz, 2H), 1.74 (br s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.3, 137.3, 128.6, 128.5, 127.9, 126.1, 67.1, 59.9.

(*E*)-2-(4-fluorophenyl)but-2-ene-1,4-diol:



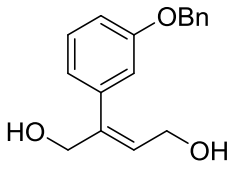
The product ***(E)*-132** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (17.1 mg, 47%). The characterization data is in agreement with the reported values.[4] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.17 (m, 2H), 7.05 (m, 2H), 5.95 (t, *J* = 6.8 Hz, 1H), 4.34 (s, 2H), 4.11 (d, *J* = 6.8 Hz, 2H), 2.01 (br s, 1H), 1.75 (br s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 162.4 (d, *J* = 247.0 Hz), 142.3, 133.2, 130.2 (d, *J* = 8.0 Hz), 126.6, 115.5 (d, *J* = 21.4 Hz), 67.1, 59.8. **HRMS (ESI) for $C_{10}H_{11}FNaO_2$ [M+Na]$^+$:** calculated: 205.0641, found: 205.0621.

(*E*)-2-(4-(methylthio)phenyl)but-2-ene-1,4-diol:



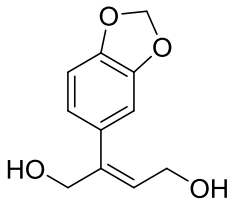
The product ***(E)*-133** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (24.3 mg, 58%). The characterization data is in agreement with the reported values.[4] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.25 (m, 2H), 7.13 (m, 2H), 5.95 (t, *J* = 6.8 Hz, 1H), 4.37 (s, 2H), 4.15 (d, *J* = 6.8 Hz, 2H), 2.49 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 142.7, 138.4, 133.8, 128.9, 126.5, 126.4, 67.8, 59.0, 15.8. **HRMS (ESI) for $C_{11}H_{14}O_2S$ $[M]^+$:** calculated: 210.0715, found: 210.0708.

(*E*)-2-(3-(benzyloxy)phenyl)but-2-ene-1,4-diol:



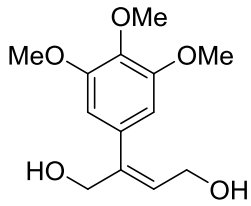
The product ***(E)*-134** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as a white solid (29.2 mg, 54%). **^{1}H NMR (400 MHz, MeOD)** δ = 7.40 (m, 2H), 7.32 (m, 2H), 7.24 (m, 2H), 6.90 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.80 (m, 1H), 6.75 (m, 1H), 5.83 (tt, *J* = 6.8, 1.5 Hz, 1H), 5.04 (s, 2H), 4.20 (d, *J* = 1.3Hz, 2H), 3.96 (d, *J* = 6.8 Hz, 2H). **^{13}C NMR (100 MHz, MeOD)** δ = 160.0, 143.9, 140.7, 138.7, 130.3, 129.5, 128.8, 128.6, 127.0, 122.1, 116.2, 115.0, 0.9, 67.0, 60.0. **HRMS (ESI) for $C_{17}H_{18}O_3$ $[M]^+$:** calculated: 270.1256, found: 270.1252.

(E)-2-(benzo[*d*][1,3]dioxol-5-yl)but-2-ene-1,4-diol:



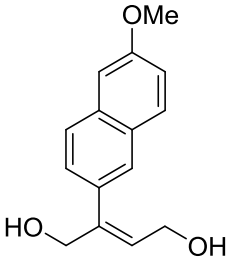
The ***(E)*-135** product was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (17.5 mg, 42%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.80 (d, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 1.6 Hz, 1H), 6.64 (dd, *J* = 7.9, 1.7 Hz, 1H), 5.97 (s, 2H), 5.90 (tt, *J* = 6.8, 1.4 Hz, 1H), 4.30 (d, *J* = 3.3 Hz, 2H), 4.14 (d, *J* = 6.6 Hz, 2H), 1.97 (br s, 1H), 1.72 (br s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.8, 147.3, 142.8, 131.0, 126.2, 122.0, 108.9, 108.4, 101.3, 67.3, 59.9. **HRMS (ESI) for $C_{11}H_{12}NaO_4$ $[M+Na]^+$:** calculated: 231.0633, found: 231.0619.

(*E*)-2-(3,4,5-trimethoxyphenyl)but-2-ene-1,4-diol:



The product ***(E)*-136** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (4:1). It was obtained as colourless oil (22.9 mg, 45%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.42 (s, 2H), 5.92 (t, *J* = 6.8 Hz, 1H), 4.34 (s, 2H), 4.15 (d, *J* = 6.8 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 153.2, 143.4, 137.6, 132.9, 126.3, 105.6, 67.2, 61.0, 59.9, 56.3. **HRMS (ESI) for $C_{13}H_{18}O_5$ $[M]^+$:** calculated: 254.1154, found: 254.1154.

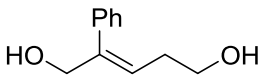
(*E*)-2-(6-methoxynaphthalen-2-yl)but-2-ene-1,4-diol:



The product ***(E)*-137** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as a white solid (20.0 mg, 41%). **^{1}H NMR (400 MHz, MeOD)** δ = 7.71 (t, *J* = 9.3 Hz, 2H), 7.57 (s, 1H), 7.28 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 7.09 (ddd, *J* = 7.3, 3.6, 2.3 Hz, 1H), 5.93 (tt, *J* = 7.5, 1.1 Hz, 1H), 4.32 (d, *J* = 1.0 Hz, 2H), 4.06 (d, *J* = 6.8 Hz, 2H), 3.87 (s, 3H). **^{13}C NMR (100 MHz, MeOD)** δ = 159.3, 144.1, 153.4, 134.3, 130.4, 128.3, 128.0, 127.7, 127.2, 120.0, 106.5, 67.2, 60.2, 55.7. **HRMS (ESI) for $C_{15}H_{16}NaO_3$ $[M+Na]^+$:** calculated: 267.0997, found: 267.0992.

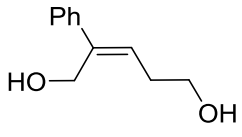
6.4.14. Characterization of pent-2-ene-1,5-diols:

(*E*)-2-phenylpent-2-ene-1,5-diol:



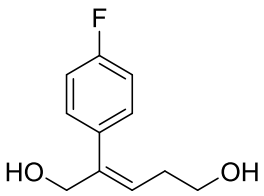
The product **(*E*)-138** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (16.7 mg, 47%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.29 (m, 5H), 5.75 (t, *J* = 7.4 Hz, 1H), 4.31 (s, 2H), 3.62 (t, J = 6.3 Hz, 2H), 2.26 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 143.1, 138.3, 128.7, 128.5, 127.4, 124.6, 67.9, 62.5, 32.0. **HRMS (ESI) for $C_{11}H_{14}O_2$ $[M]^+$:** calculated: 178.0994, found: 178.0989.

(*Z*)-2-phenylpent-2-ene-1,5-diol:



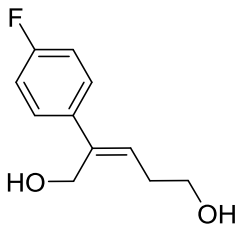
The product **(*Z*)-138** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (5.3 mg, 15%). The characterization data is in agreement with the reported values.[5] **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.49 (m, 2H), 7.35 (m, 2H), 7.26 (m, 1H), 5.75 (t, *J* = 8.2 Hz, 1H), 4.50 (s, 2H), 3.77 (t, *J* = 7.6 Hz, 2H), 2.56 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 142.7, 141.7, 128.8, 128.6, 127.3, 126.2, 60.1, 59.8, 31.6. **HRMS (ESI) for $C_{11}H_{14}O_2$ $[M]^+$:** calculated: 178.0994, found: 178.0990.

(*E*)-2-(4-fluorophenyl)pent-2-ene-1,5-diol:



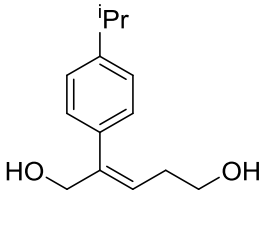
The product **(*E*)-139** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as a white solid (16.5 mg, 42%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.20 (m, 2H), 7.04 (m, 2H), 5.76 (t, *J* = 7.4 Hz, 1H), 4.29 (s, 2H), 3.64 (t, *J* = 6.3 Hz, 2H), 2.27 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 162.1 (d, *J* = 246.2 Hz), 142.1, 134.1 (d, *J* = 3.4Hz), 130.4 (d, *J* = 7.9 Hz), 125.3, 115.4 (d, *J* = 21.2 Hz), 67.9, 62.3, 31.9. **HRMS (ESI) for $C_{22}H_{26}F_2O_4$ $[2M]^+$:** calculated: 392.1799, found: 392.1806.

(*Z*)-2-(4-fluorophenyl)pent-2-ene-1,5-diol:



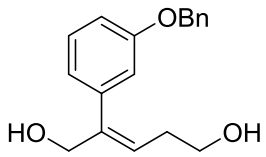
The product **(*Z*)-139** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (5.5 mg, 14%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.45 (m, 2H), 7.01 (m, 2H), 5.88 (t, *J* = 8.2Hz, 1H), 4.48 (s, 2H), 3.79 (t, *J* = 5.5 Hz, 2H), 2.55 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 162.3 (d, *J* = 245.9 Hz), 141.9, 137.8, 128.6, 127.8 (d, *J* = 7.9 Hz), 115.3 (d, *J* = 21.3 Hz), 61.1, 59.9, 31.5. **HRMS (ESI) for $C_{22}H_{26}F_2O_4$ $[2M]^+$:** calculated: 392.1799, found: 392.1806.

(*E*)-2-(4-isopropylphenyl)pent-2-ene-1,5-diol:



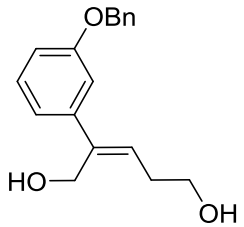
The product ***(E)*-140** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (1:1). It was obtained as colourless oil (20.7 mg, 47%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.15 (m, 4H), 5.73 (t, *J* = 7.4 Hz, 1H), 4.32 (s, 2H), 3.64 (t, *J* = 6.4 Hz, 2H), 2.89 (hept, *J* = 7.0 Hz, 1H), 2.30 (m, 2H), 1.24 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 148.0, 143.1, 135.4, 128.6, 126.7, 124.1, 68.1, 62.6, 33.9, 32.2, 24.1. **HRMS (ESI) for $C_{14}H_{20}O_2$ $[M]^+$:** calculated: 220.1463, found: 220.1464.

(*E*)-2-(3-benzyloxy)phenyl)pent-2-ene-1,5-diol:



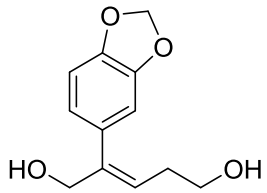
The product **(*E*)-141** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (33.5mg, 59%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.34 (m, 6H), 6.91 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.83 (m, 2H), 5.73 (t, *J* = 7.4 Hz, 1H), 5.06 (s, 2H), 4.30 (d, *J* = 1.1 Hz, 2H), 3.58 (t, *J* = 6.3 Hz, 2H), 2.25 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 158.8, 142.8, 139.7, 137.0, 129.6, 128.7, 128.1, 127.6, 124.7, 121.3, 115.4, 113.7, 70.0, 67.8, 62.4, 32.0. **HRMS (ESI) for $C_{18}H_{20}O_3$ $[M]^+$:** calculated: 287.1412, found: 287.1421.

(*Z*)- 2-(3-benzyloxy)phenyl)pent-2-ene-1,5-diol:



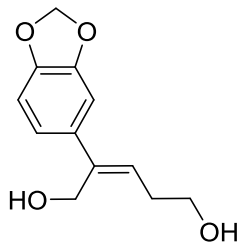
The product **(*Z*)-141** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as a white solid (10.8 mg, 19%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.37 (m, 5H), 7.25 (t, *J* = 7.9 Hz, 1H), 7.13 (m, 1H), 7.08 (m, 1H), 6.88 (ddd, *J* = 8.2, 2.5, 0.8 Hz, 1H), 5.94 (t, *J* = 8.2 Hz, 1H), 5.08 (s, 2H), 4.48 (s, 2H), 3.76 (t, *J* = 5.7 Hz, 2H), 2.55 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 159.0, 143.3, 142.6, 137.1, 129.6, 128.9, 128.7, 128.1, 127.7, 118.9, 113.6, 112.9, 70.1, 61.0, 59.8, 31.6. **HRMS (ESI) for $C_{18}H_{20}O_3$ $[M]^+$:** calculated: 287.1412, found: 287.1421.

(*E*)-2-(benzo[*d*][1,3]dioxol-5-yl)pent-2-ene-1,5-diol:



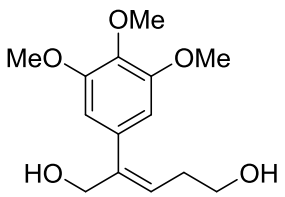
The product **(*E*)-142** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (24.4 mg, 55%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.80 (d, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 1.6 Hz, 1H), 6.68 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.95 (s, 2H), 5.71 (t, *J* = 7.4 Hz, 1H), 4.27 (d, *J* = 1.0 Hz, 2H), 3.63 (t, *J* = 6.3 Hz, 2H), 2.30 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 174.7, 146.8, 142.6, 131.9, 124.7, 122.0, 109.2, 108.4, 101.1, 68.0, 62.4, 32.0. **HRMS (ESI) for $C_{12}H_{14}O_4$ $[M]^+$:** calculated: 222.0892, found: 222.0897.

(*Z*)- 2-(benzo[*d*][1,3]dioxol-5-yl)pent-2-ene-1,5-diol:



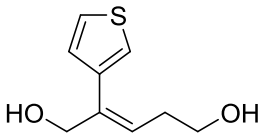
The product **(*Z*)-142** was purified by flash column chromatography using as eluent mixture hexane/ethyl acetate (1:1). It was obtained as colourless oil (13.8 mg, 31%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.98 (m, 2H), 6.76 (d, *J* = 8.0 Hz, 1H), 5.95 (s, 2H), 5.83 (t, *J* = 8.2 Hz, 1H), 4.44 (s, 2H), 3.75 (t, *J* = 5.7 Hz, 2H), 2.53 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 147.9, 146.9, 142.3, 136.0, 127.0, 119.7, 108.3, 106.9, 101.1, 61.1, 59.9, 31.5. **HRMS (ESI) for $C_{12}H_{14}O_4$ $[M]^+$:** calculated: 222.0892, found: 222.0897.

(*E*)-2-(3,4,5-trimethoxyphenyl)pent-2-ene-1,5-diol:



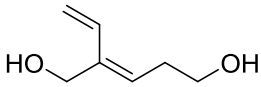
The product **(*E*)-143** was purified by flash column chromatography using as eluent ethyl acetate. It was obtained as colourless oil (24.1 mg, 45%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.44 (s, 2H), 5.72 (t, *J* = 7.4 Hz, 1H), 4.31 (s, 2H), 3.84 (s, 3H), 3.83 (s, 6H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.31 (dt, *J* = 7.2, 6.4 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 153.2, 143.2, 137.2, 133.8, 124.8, 105.8, 68.0, 62.5, 61.0, 56.3, 32.2. **HRMS (ESI) for $C_{14}H_{20}O_5$ $[M]^+$:** calculated: 268.1311, found: 268.1314.

(*Z*)-2-(thiophen-2-yl)pent-2-ene-1,5-diol:



The product ***(E)*-144** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (1:1). It was obtained as yellowish oil (9.9 mg, 27%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.33 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.24 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.09 (dd, *J* = 5.0, 1.3 Hz, 1H), 5.76 (tt, *J* = 7.3, 1.2 Hz, 1H), 4.33 (d, *J* = 1.1 Hz, 2H), 3.70 (t, *J* = 6.3 Hz, 2H), 2.43 (dt, *J* = 7.3, 6.3 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 138.3, 137.7, 128.0, 125.7, 125.5, 123.2, 68.0, 62.5, 32.4. **HRMS (ESI) for $C_9H_{12}O_2S$ $[M]^+$:** calculated: 184.0558, found: 184.0558.

(*E*)-2-vinylpent-2-ene-1,5-diol:



The product ***(E)*-145** was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (1:1). It was obtained as colourless oil (8.2 mg, 32%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 6.65 (dd, *J* = 17.7, 11.2, 1H), 5.69 (t, *J* = 7.6 Hz, 1H), 5.36 (d, *J* = 17.7 Hz, 1H), 5.20 (d, *J* = 11.3 Hz, 1H), 4.31 (s, 2H), 3.70 (t, *J* = 6.4 Hz, 2H), 2.46 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 138.3, 130.1, 127.6, 115.2, 64.5, 62.3, 29.8. **HRMS (ESI) for $C_7H_{12}O_2$ $[M]^+$:** calculated: 128.0837, found: 128.0839.

6.5. References chapter 6

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Chapter 7
Summary

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
Núria Miralles Prat

7.1. Summary

Organoboron compounds are essential tools in organic synthesis due to their tremendous versatility. That is the reason why many researchers dedicate their efforts to improve and to innovate through new methodologies to install boronate units into organic frameworks. In this thesis, we wanted to contribute to the development of catalytic organoboron chemistry by singular activation methods to activate organoborane reagents and convert them into nucleophilic reagents[1] to be added to unsaturated substrates, in a selective manner.

The first chapter is related to borylation of aryl halides and is investigated in two different lines. In the first one, a more classical palladium-catalyzed methodology is applied to the non-symmetrical diboron reagent BpinBdan to borylate the highly sterically hindered 9-bromoanthracene. The borylated product was selectively obtained with the Bdan unit incorporated on the anthracenyl synton. This greatly aromatized molecule was further analyzed by Atomic Force Molecular (AFM) techniques.[2] Since the new molecule was non-planar, dehydrogenation on the amine protons from the Bdan unit was induced, and studied in detail (Figure 7.1).

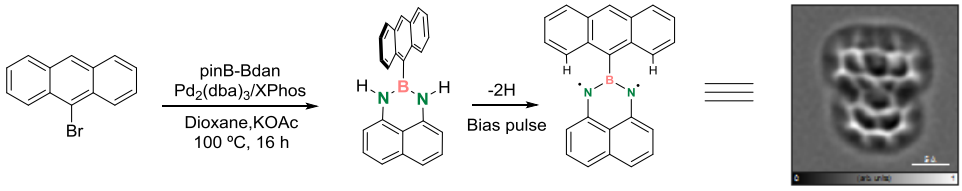
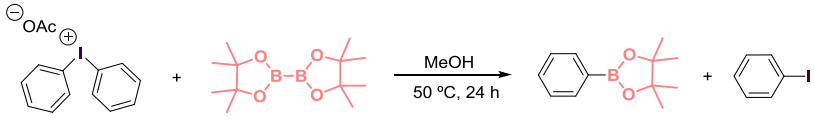


Figure 7. 1 Synthesis of 9-anthracene naphthodiazaborinine and its dehydrogenated structure imaged by AFM.

Alternatively, a transition metal-free approach on borylation of diaryliodonium salts was explored using the B_2pin_2 diboron reagent (Scheme 7.1). In this case, the counter ion of the diaryliodonium compound plays a crucial role on the activation of B_2pin_2 since the reaction proceeds in the absence of base.

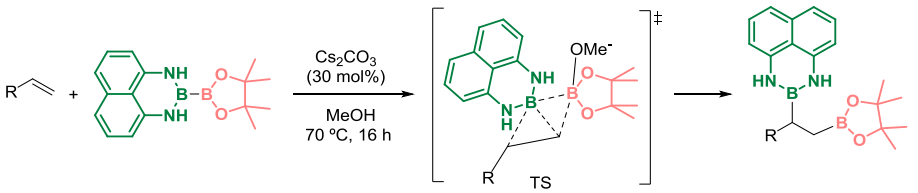


Scheme 7. 1 Transition metal-free borylation of diaryliodonium salts with B_2pin_2.

Summary

During the borylation reaction, one equivalent of aryl iodide is formed which could brightly be used as coupling partner for an *in situ* cross-coupling reaction along with the generated aryl borylated product, just by the addition of a palladium complex. Interestingly, in the case of non-symmetrical diaryliodonium salts, the borylation reaction act as a platform to selectively generate hetero cross-coupled products.

Efforts to broad the use of the non-symmetrical diboron reagent BpinBdan are presented in the second chapter. The activation of BpinBdan in the absence of any transition metal was achieved by the sole addition of base and methanol which preferentially generate the [MeO--BpinBdan]$^-$ adduct.[3] That circumstance enhances the nucleophilic character of Bdan unit to attack the olefin. The major diborated isomer formed in this context, contains the Bdan unit located in the internal position of the olefin (Scheme 7.2). This was confirmed by NMR experiments.

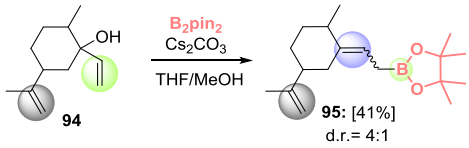


Scheme 7. 2 Transition metal-free diboration of alkenes using the non-symmetrical reagent BpinBdan.

Moreover, all these results were supported by DFT calculations carried out in collaboration with Carbó and Cid, who could find the two consecutive transition states that justifies the postulation of the suggested mechanism for the transition metal-free diboration of alkenes with BpinBdan reagent.

Probably, among all organoboron compounds, those that have more application in organic synthesis are the allylboronate compounds.[4] This is the reason why in the fourth chapter two original strategies were investigated to establish new methodologies for the preparation of those valuable compounds. In the transition metal-free context, it was carried out the borylation of allylic and propargylic tertiary alcohols using B_2pin_2 as diboron reagent. Having a hydroxyl group in the allylic position was an important issue because the organocatalytic conditions

allow to protonate it (OH_2^+) and then, turns it into a good leaving groug. Furthermore, it could also be possible to selectively borylate the allylic alkene in front of another olefin present in the same substrate, as a matter of chemoselective reaction (Scheme 7.3).



Scheme 7. 3 Selective transition metal-free allylic borylation.

The experimental results obtained prompted us to suggest a possible mechanism. This could follow an S_N2' pathway after the activation of B_2pin_2 through quaternization of one boryl unit by the methoxide.
Additionally, it was also observed that just by increasing the amount of B_2pin_2 and the temperature, the allylic double bond of the borylated product, can be further diborated generating *in situ* triborated compounds (Figure 7.2).

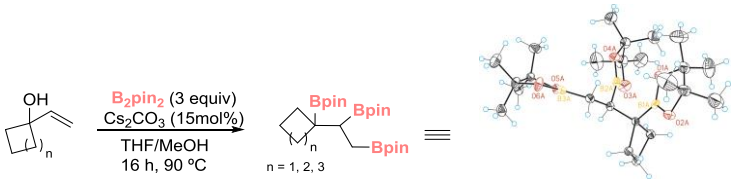
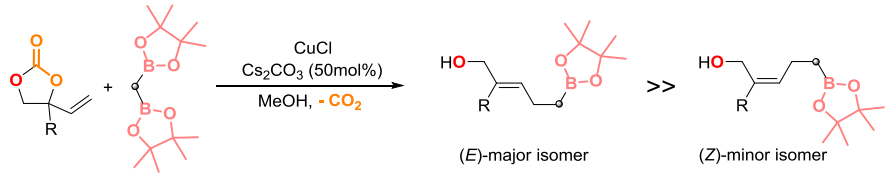


Figure 7. 2 Transition metal-free borylation/diboration tandem of tertiary allylic alcohols with B_2pin_2.

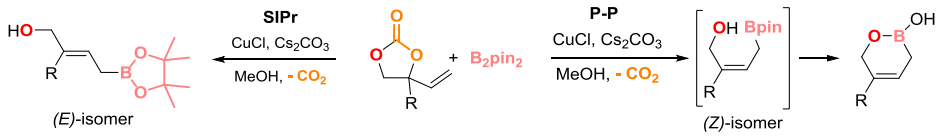
The preparation of homoallyl- and allylboronate compounds was also examined from another perspective. The use of *gem*-diborylalkanes as organoboron reagents has recently emerged as a new source of boron units with the particularity that also adds a carbon atom to the organic framework.[5] In this sense, copper chloride was used as catalyst to activate the *gem*-diborylmethane reagent and to couple it with a series of vinyl cyclic carbonates. Previous synthetic methods which describe the borylation of allylic carbonates with B_2pin_2 through decarboxylation involve the loss of CO_2 but also the OR moiety from the $–OCO_2R$ leaving group.[6] Therefore, the present reaction that proceeds under mild reaction conditions with only 50 mol% of base, and following an S_N2' allylic substitution pathway, has an

additional benefit being the hydroxyl group retained in the homoallylic boron scaffold (Scheme 7.4).



Scheme 7. 4 Allyl-alkyl coupling between *gem*-diborylmethane and vinyl cyclic carbonates.

Interestingly, when the same reaction was carried out using the B_2pin_2 diboron reagent, two different allylborylated products were obtained. When the copper catalyst was combined with an *N*-heterocyclic carbene (SIPr), the (*E*)-stereoisomer was favored giving difunctionalized (*E*)-allylboronates. Whereas when the ligand of choice was a diphosphine, particularly the 1,2-bis(di-*tert*-butylphosphinomethyl)benzene (P-P), the exclusive product formed was a (*Z*)-boracycle. This is a consequence of the intramolecular annulation of the corresponding (*Z*)-stereoisomer (Scheme 7.5).



Scheme 7. 5 Ligand controlled allyl-boryl coupling between B_2pin_2 and vinyl cyclic carbonates.

To culminate the present study, a direct application of those prepared homoallyl- and allylboronates was accomplished just by simple oxidative work up, to obtain the corresponding 1,5-pent-2-ene diols and 1,4-but-2-ene diols. Concerning the (*E*)-1,4-but-2-ene diols, they are highly valuable compounds which alternative routes to prepare them require the use of Grignard reagents precursors with rather limited scope.

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Chapter 8

List of publications, conferences and research stay

UNIVERSITAT ROVIRA I VIRGILI
CATALYTIC ACCESS TO (POLY)BORYLATED COMPOUNDS BY COUPLING UNSATURATED SUBSTRATES AND DIBORON OR METHYLDIBORON REAGENTS
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List of publications

N. Miralles, J. Cid, A.B. Cuenca, J. J. Carbó, E. Fernández "*Mixed diboration of alkenes in a metal-free context*" *Chem. Commun*. **2014**, *51*, 1693-1696.

Gerard Palau-Lluch, Xavier Sanz, Enrico La Cascia, Marc G. Civit, Núria Miralles, Ana B. Cuenca, Elena Fernández **"***Organocatalytic functionalisation through boron chemistry*" *Pure Appl. Chem.* **2015***,* 87, 181-193.

N. Miralles, R. M. Romero, K. Muñiz, E. Fernández "*A mild boron-boron bond formation from diaryliodonium salt" Chem. Commun*. **2015***, 51,* 14068-14071.

N. Miralles, R. Alam, K. J. Szabó, E. Fernández "*Transition-metal-free borylation of allylic and propargylic alcohols*" *Angew. Chem. Int. Ed*. **2016**, *55*, 4303-4306.

Z. Majzik, A. B. Cuenca, N. Pavlicek, N. Miralles, G.Meyer, L. Gross, E. Fernández, "*Synthesis of a naphthodiazaborole and its verification by planarization with AFM" ACS Nano,* **2016**, *10*, 5340-5345.

N. Miralles, J.E. Gómez, A.W. Kleij, E. Fernández *"Copper-mediated S_N2' allyl-alkyl and allyl-boryl couplings of vinyl cyclic carbonates" Org. Lett*. **2017**, *19*, 6096-6099. *****Highlighted in ***Synfacts 2018, 14(01), 0076.***

N. Miralles, R.J. Maza, E. Fernández *"Synthesis and reactivity of 1,1-diborylalkanes towards C-C bond formation and related mechanisms" Adv. Synth. Catal*. **2017**, DOI**:** 10.1002/adsc.201701390 (**VIP**).

Posters and presentations

IMEBORON XV Conference, Prague (Chez Republic), August 2014 - Poster and flash presentation.

GEQO XXXII, Tarragona (Spain), September 2014 - Poster presentation.

OMCOS 18, Sitges (Spain), July 2015 - Poster presentation
**Inorganic chemistry Frontiers* Poster Prize

ISySyCat, Évora (Portugal), September 2015 - Poster presentation

XXVI Reunión Bienal de Química Orgánica, Punta Umbría (Spain), June 2016 - Oral communication

Summer School on Molecular Boron Chemistry, Würzburg (Germany), July 2016 - poster presentation

EUROBORON VII, Suzdal (Russia), September 2016 - Oral communication

IUPAC 46th World Chemistry Congress, São Paulo (Brazil), July 2017 - Oral communication

Research abroad

Project: Synthesis of allylboronate compounds *via* transition metal-free borylation of allylic alcohols.
Center: Stockholm University, Sweden.
Supervisor: Prof. Kálmán J. Szabó
Period: September-December 2014