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Borylation of conjugated dienes with diboranes. A stereo- and chemoselective analysis

Master's Thesis

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1. Abstract

We have explored the catalytic transition metal-free borylation of 1,3-disubstituted conjugated dienes through the *in situ* formation of adduct [MeO-Bpin-Bpin]$^-$, to promote allylic borylative sequences. Surprisingly, for the model substrate (3-methylbuta-1,3-dien-1-yl)benzene we have observed a consecutive allylic borylation followed by 1,2 hydroboration. Even more remarkable, the 1,2-hydroboration locates the Bpin moiety at the more hindered position of the allylborane. Intramolecular Pd catalyzed cross-coupling with borylated products containing Ar-Br functionalities, favours the chemoselective intramolecular cross-coupling reaction, generating tetrahydronaphthalenes with a new tetrasubstituted carbon. Computational studies using DFT methods have characterized the reaction mechanism for the borylation reaction and allowed to rationalize the observed stereoselectivity. Additionally, we have explored state-of-the-art computational methodologies to analyze post-transition state bifurcations and rationalize the observed borylative pathways.

2. Introduction

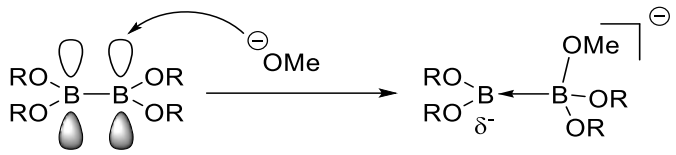
The synthesis of organoboron compounds using the tetra-alkoxy diboron reagent bis(pinacolatodiboron) (B_2pin_2) has been expanded since Miyaura and co-workers implemented its use alongside transition metal catalysts (involving Pt, Pd or Cu), focusing on the insertion of the boryl moieties into olefins. [1,2]

The borylation reactions are essentially conducted through the B-B bond cleavage from the diboron species whereas a weaker and more polarized M-B bond is formed, making the transfer of the boryl group favoured, as either electrophilic or nucleophilic synthons depending on the properties of the transition metal employed.

Within the last 20 years, a new methodology for the activation of diboron reagents has been employed, replacing the use of transition metals, and involving the use of Lewis bases. Fernández's group developed a new methodology aimed to promote borylation of enones with B_2pin_2 upon addition of MeOH, substoichiometric amounts of a phosphine and a base (Cs_2CO_3).[3]

The key for the success of this chemical transformation, was the use of MeOH as a co-solvent, that generates the corresponding MeO^- by the aid of the Cs_2CO_3 base. The MeO^-, in turn, could activate the B_2pin_2 via nucleophilic attack on the empty p orbital, forming the adduct [MeO-Bpin-Bpin]$^-$.

Computational studies have shown the structure and the nature of the B-B bond after this activation, with the non-quaternized boron atom acquiring a partial electronic charge, becoming nucleophilic, and in turn, destabilizing the B-B bond (Scheme 1).[4]



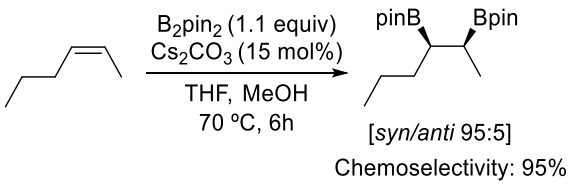
Scheme 1. General scheme for the activation of diboron reagents by a Lewis base

The discovery of this adduct, opened a new path for the generation of many organoborated products in a transition-metal-free context, which until now where synthesized by transition-metal catalysts.[5]

The chemical reactivity of the adduct [MeO-Bpin-Bpin]$^-$ was extended by testing it with many different α,β-unsaturated carbonyl compounds, where the effectiveness of different solvents

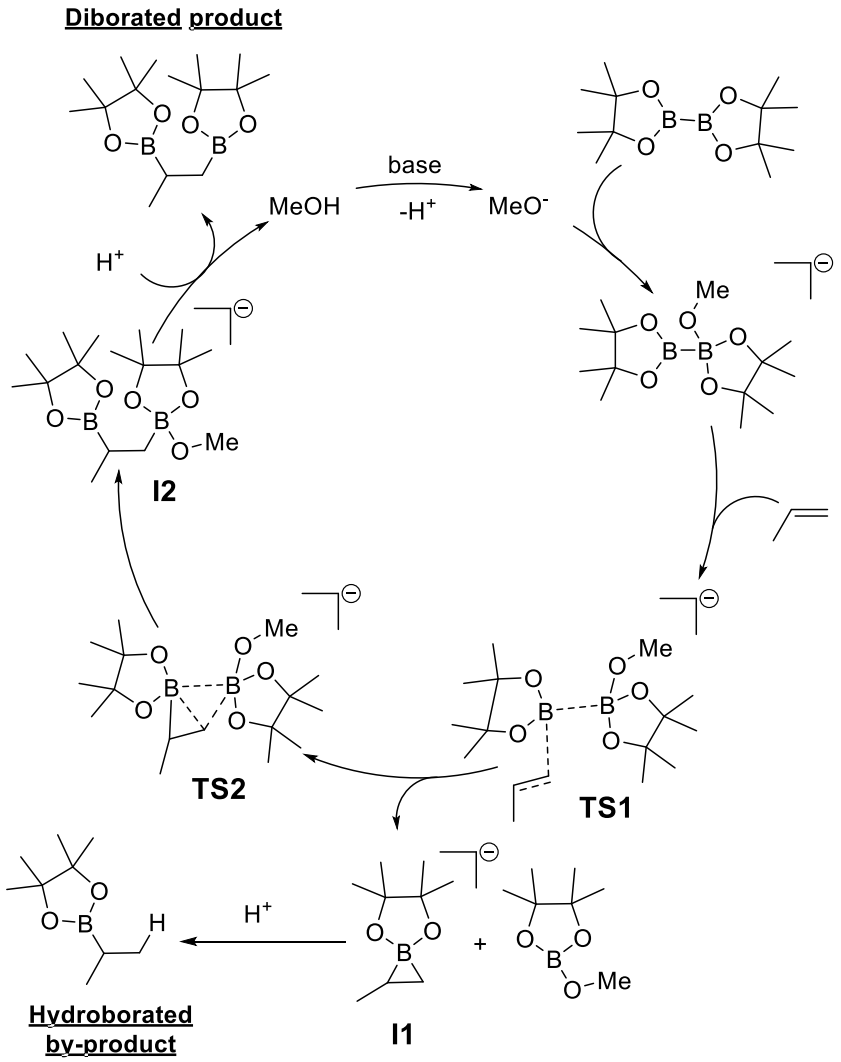
and bases were optimized even in the absence of phosphines, which were suggested to activate the substrate; but also, a large substrate scope was studied for the C-B bond formation, including non-activated alkenes.[4]

Unlike in the previous studies, when the nucleophilic adduct [MeO-Bpin-Bpin]$^-$ reacted with non-activated alkenes, the formation of two C-B bonds along the alkene took place, in a *syn* stereoselective manner, being considered a 1,2-diboration process (Scheme 2).[4]



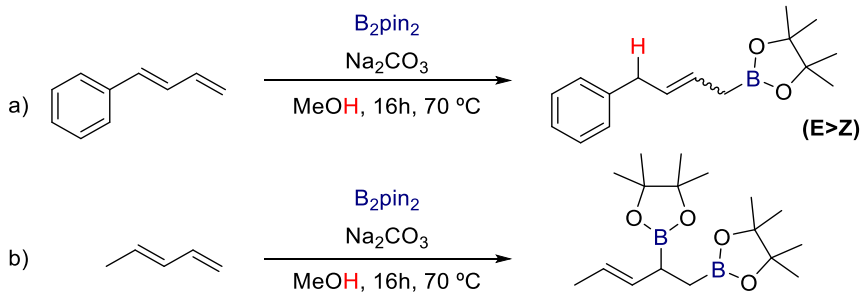
Scheme 2. Transition-metal-free diboration of non-activated alkenes.

The computational studies conducted on this system suggested that the reaction mechanism proceeded first through a TS where the adduct [MeO-Bpin-Bpin]$^-$ interacted with the olefin, which then connected to another TS where the new anionic species would react with the remaining Bpin-OMe group, providing eventually the diborated product through intermediate **I2** (Scheme 3). The first TS could also lead to a cyclic anionic intermediate (**I1**), which could be protonated to give the 1,2-hydroborated product. This type of mechanistic sequence where two TS are directly related with two intermediates resembled very much the Valley-Ridge bifurcation points, described by Houk.[6]



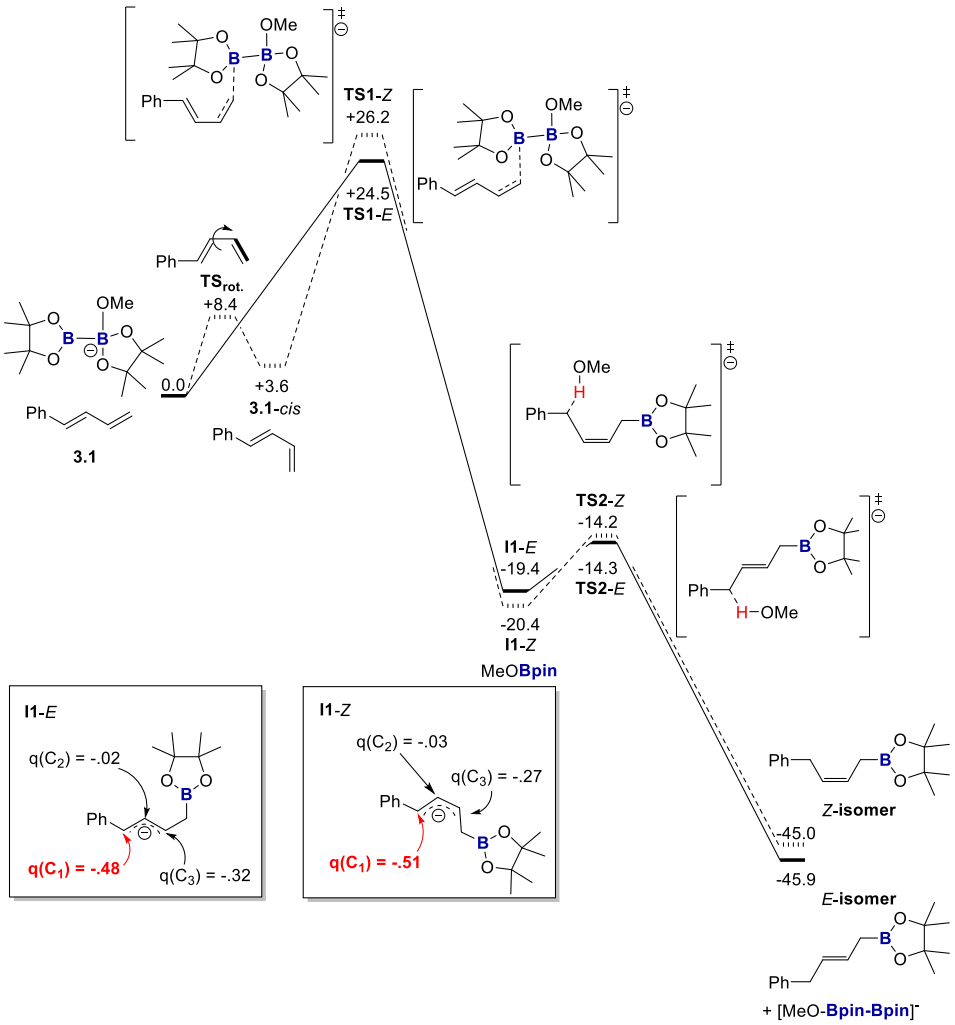
Scheme 3. Mechanistic proposal for the 1,2-diboration of alkenes, with [MeO-Bpin-Bpin]$^-$

Subsequent studies by Maza and co-workers[7] explored the reactivity of conjugated 1,3-dienes under these transition-metal-free borylation conditions, finding that depending on the nature of the diene employed, the chemoselectivity changed. They found that for polyconjugated dienes like (*E*)-buta-1,3-dien-1-ylbenzene, the electron withdrawing nature of the allylic system allowed for the borylation of the terminal carbon, followed by protonation at the internal position of the allyl anion, obtaining the named 1,4-hydroborated product (Scheme 4). However, while for non-activated conjugated dienes, such as (*E*)-penta-1,3-diene, the 1,2-diboration took place, resembling the 1,2-diboration of non-activated alkenes.



Scheme 4. Borylation reaction with [MeO-Bpin-Bpin]$^-$ of a) (*E*)-buta-1,3-dien-1-ylbenzene and b) 1,2-diboration of (*E*)-penta-1,3-diene

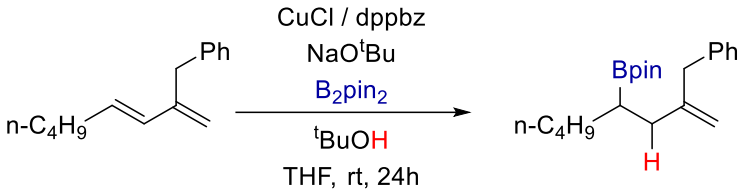
In this study, they discerned the reaction mechanism for the allylic borylation-protonation in the case of (*E*)-buta-1,3-dien-1-ylbenzene, and rationalized the observed stereoselectivity (Scheme 5).



Scheme 5. Free-energy profile (kcal·mol^{-1}) for the allylic borylation-protonation of (*E*)-buta-1,3-dien-1-ylbenzene.

Although the previous study covered representative types of dienes, many still remained unexplored, like the 1,3-disubstituted conjugated dienes.

Recently, these types of dienes have been studied under the context of Cu-catalyzed borylations using diphosphine ligands,[8] developing a regioselective 1,2-hydroboration at the internal alkene, achieving regioisomeric ratios over 20:1 (Scheme 6).



Scheme 6. Regioselective 1,2-hydroboration of 1,3-disubstituted conjugated dienes with Cu-based catalysts.

The transition-metal-free borylation of these types of dienes, however, has not been studied despite the fact of the growing interest of the polyborated compounds in polyfunctionalization strategies, such as, the *trans*-diboration of propargyl alcohols,[9] or the triborylation of terminal alkynes.[10]

3. Objectives

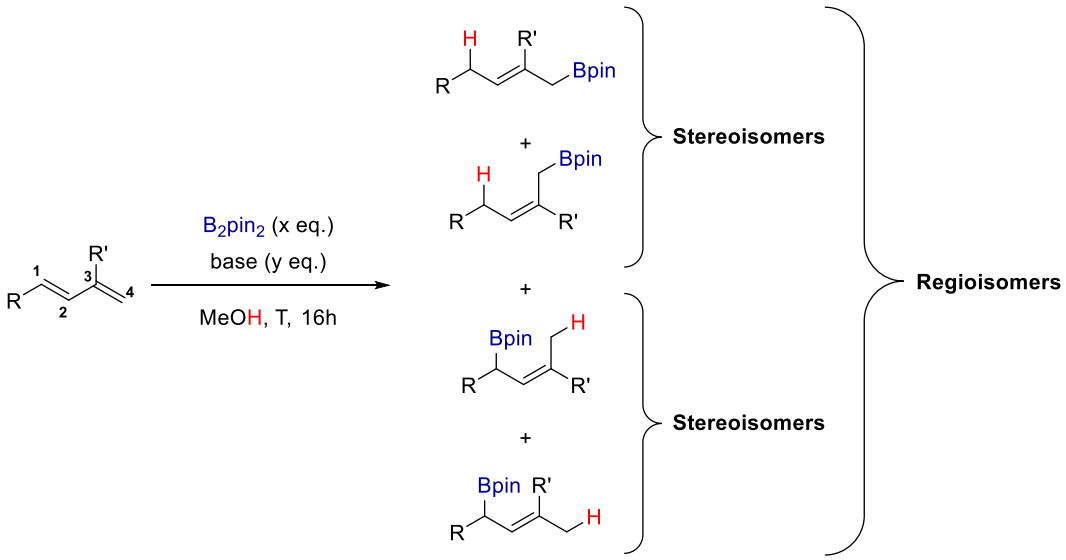
- The study of the reactivity of 1,3-disubstituted conjugated dienes toward the transition-metal-free borylation, and the optimization of the reaction conditions.
- The synthesis of functionalized tetrahydronaphthalenes, from polyborated compounds.
- The use of DFT calculations to explain of the reaction mechanisms, as well as to rationalize of the stereoselectivity.
- The use of a novel methodology for determining the selectivity on bifurcation points in the PES in order to explain the chemoselectivity of the reaction.

4. Results and discussion

4.1 Work hypothesis

In this work we aimed to explore the reactivity of 1,3-disubstituted conjugated dienes under transition-metal-free borylation conditions, in order to evaluate the feasibility of those reactions, as well as to explore the regio- and stereoselectivity of the reaction outcome, in comparison to the Cu-catalyzed borylation and the transition-metal-free borylation of other types of conjugated dienes.

Our initial work hypothesis was that the borylation might be initiated through either C^1 or C^4 of the conjugated diene followed by allylic conjugation/protonation with MeOH as the solvent, leading to the allylic borylated product. Theoretically, this reactivity can lead to four possible products depending on the four possible isomers generated by the C-Bpin formation (Scheme 7).



Scheme 7. Possible allylboranes generated by the allylic borylation-protonation of 1,3-disubstituted conjugated dienes.

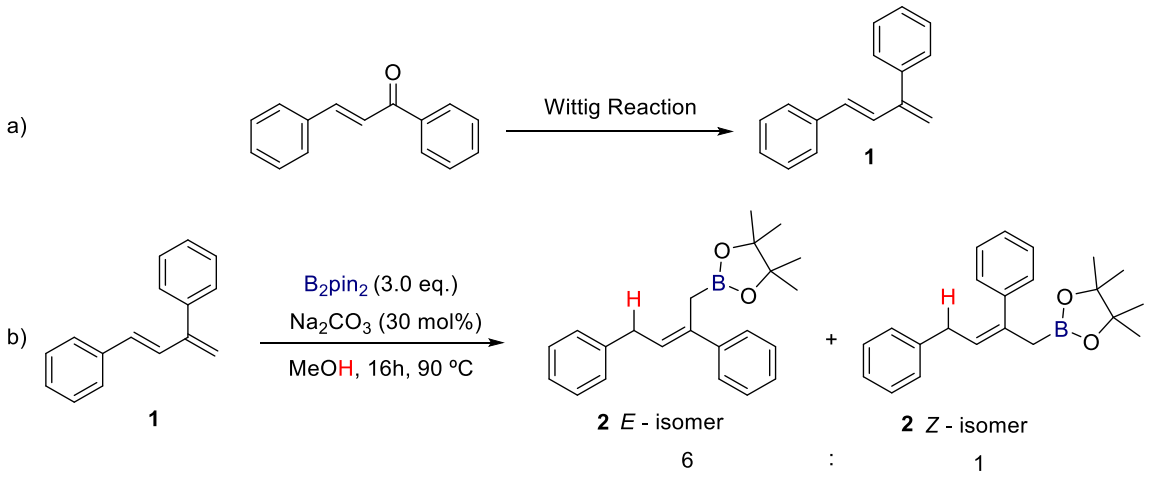
As an alternative possibility, we envisioned that depending on the nature of the **R** groups, the 1,2-hydroboration of the terminal alkene could take place, as well as the 1,2-diboration.

In order to test our hypothesis on the reactivity of 1,3-disubstituted conjugated dienes, we proposed to study the transition-metal-free borylation of the substrates with R=Ar and R'= Ph or Me.

4.2 Allylic borylation of (E)-buta-1,3-diene-1,3-diyldibenzene

In order to study the allylic borylation reaction of 1,3-disubstituted conjugated dienes, we selected the substrate (*E*)-buta-1,3-diene-1,3-diyldibenzene (**1**) as a model substrate, which was prepared via Wittig reaction from *trans*-chalcone (Scheme 8a). The borylation was carried out using the diboron reagent B_2pin_2, the base Na_2CO_3, and methanol as solvent, in order to generate the $[MeO\text{-}Bpin\text{-}Bpin]^-$ adduct, required to initiate the nucleophilic borylation.

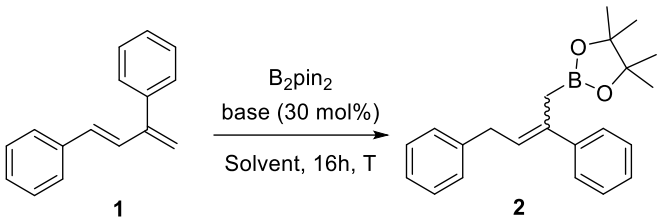
An allylic borylation reaction took place in a chemoselective manner since the C-B bond was exclusively formed on the terminal C=C (Scheme 8b).



Scheme 8. a) Synthesis of (*E*)-buta-1,3-diene-1,3-diyldibenzene (**1**) and b) metal-free allylic borylation-protonation of **1.**

The reaction produced the 1,4-hydroborated product **2** with a stereoselection *E*:*Z* = 6:1 (Scheme 8b). Under these reaction conditions, no diborated or polyborated products were observed. Next, we conducted a systematic study to optimize the reaction conditions (Table 1).

Table.1. Transition-metal-free borylation of (*E*)-buta-1,3-diene-1,3-diyldibenzene (**1**).[a]



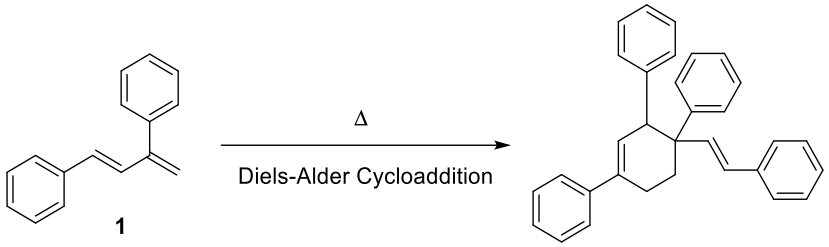
Entry	Solvent	Base	B_2pin_2 equiv.	Temperature (°C)	% NMR Yield [Isolated Yield]	Ratio *E*:*Z*
1	MeOH	Na_2CO_3	1.1	90	12	5:1
2	MeOH	Cs_2CO_3	1.1	90	9	4:1
3	MeOH-DCM (1:1)	Na_2CO_3	1.1	90	9[7]	3:1
4	MeOH-THF (1:1)	Na_2CO_3	1.1	90	9[7]	3:1
5	MeOH	Na_2CO_3	1.1	45	2	-
6	MeOH	Na_2CO_3	1.1	r.t.	2	-
7	MeOH	Na_2CO_3	3.0	90	19[13]	6:1

[a]Standard conditions: **1** (0.25 mmol), base (0.075 mmol), B_2pin_2 (0.275 – 0.75 mmol), solvent (1 mL), 16h, T (°C). Yield calculated by ^{1}H NMR using naphthalene as internal standard.

Along the optimization of the reaction conditions, we observed that the use of either Na_2CO_3 or Cs_2CO_3 at 30 mol% gave comparable results, about 12% and 9% NMR Yield (Table 1, entries 1, 2). Also, it was determined that MeOH was the ideal solvent, and the optimal temperature was 90 °C (Table 1, entries 3-6). An excess of B_2pin_2 (3.0 equiv.) slightly increased the yield.

However, although we modified the reaction conditions, the yields of the borylated product didn't exceed 20%. The reason of the low yield is due to the fact that the substrate suffers Diels-Alder cycloaddition during the borylation reaction, and therefore decomposition of the substrate competes with the borylation reaction. This particular reactivity of 1,3-disubstituted conjugated dienes has already been studied[11] and it has been shown that depending on the substituents of the diene, the kinetics of the Diels Alder reaction can be greatly accelerated, with conjugated substituents like aryl or styryl groups being some of the most activating groups. In particular, **1** has a Diels Alder reaction rate 10000 times greater than that of (*E*)-buta-1,3-dien-1-ylbenzene **1**.[11] The cycloaddition also is possible even at room temperature, producing mainly (*E*)-5'-phenyl-2'-styryl-1',2',3',4'-tetrahydro-1,1':2',1''-terphenyl (Scheme 9). Under our reaction

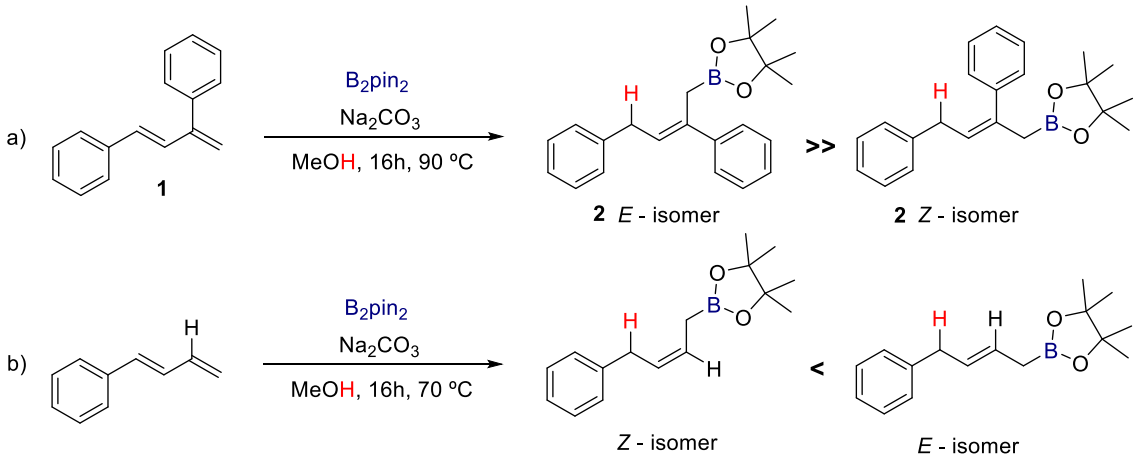
conditions for borylation of **1**, the major product was always the result of the cycloaddition, making the borylation reaction inefficient.



Scheme 9. Substrate (*E*)-buta-1,3-diene-1,3-diyldibenzene (**1**) suffers from Diels Alder reaction.

The assignment of the stereoselectivity of the allylic borylation of **1** towards the *E*-isomer, was next addressed.

The 1-D NOE experiments justifies formation of *E*-isomer (Scheme 10a). For comparison, the reported allylic borylation of (*E*)-buta-1,3-dien-1-ylbenzene, also favoured the formation of the *E*-isomer[7] (Scheme 10b).

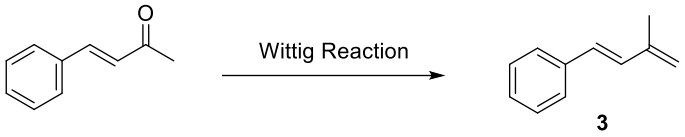


Scheme 10. Stereoselectivity on the borylation reaction of a) (*E*)-buta-1,3-diene-1,3-diyldibenzene and b) (*E*)-buta-1,3-dien-1-ylbenzene.[7]

Wanting to explore more substrates, and having into account the stability of them, we chose to move into the study of the borylation reaction of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene.

4.3 Allylic borylation of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene

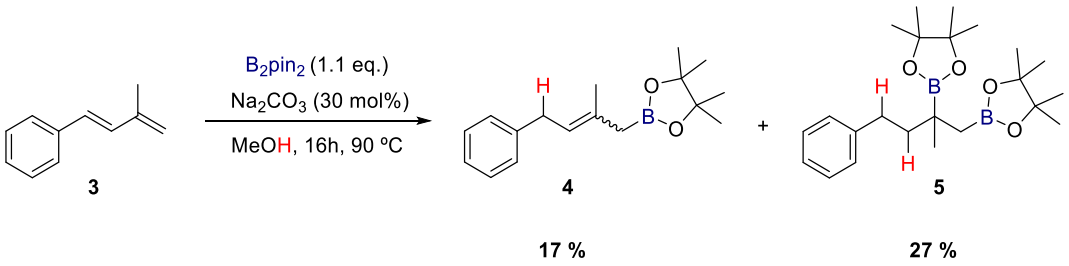
We studied next the reactivity of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene (**3**). The synthesis of **3** was performed by the Wittig reaction from the commercially available (*E*)-4-phenylbut-3-en-2-one (Scheme 11).



Scheme 11. Synthesis of substrate (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene (**3**).

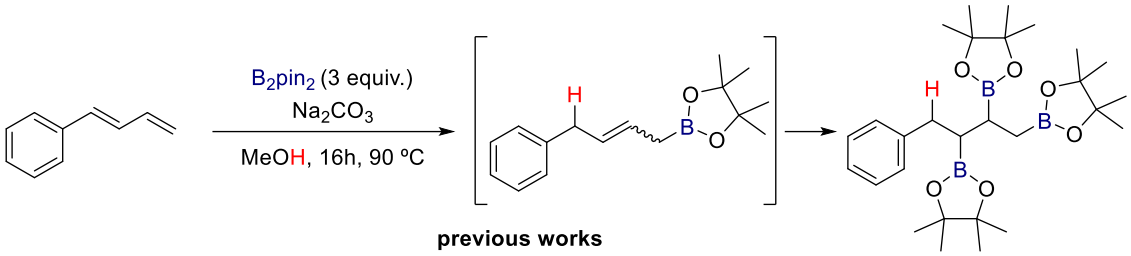
We conducted the allylic borylation of **3** with the standard borylation conditions, using 1 mL of MeOH as the solvent, 1.1 equiv. of B_2pin_2 as the borylating agent, 30 mol% of Na_2CO_3 as the base. The reaction was performed at 90 °C for 16h.

We observed that while conversion of starting material was not completed, no Diels-Alder side reaction was detected. Instead, the major product observed was the one from the allylic borylation-protonation (**4**) as a stereoisomer mixture, together with a polyborated product identified as **5** (Scheme 12).



Scheme 12. Reaction outcome through the allylic borylation of substrate **3.**

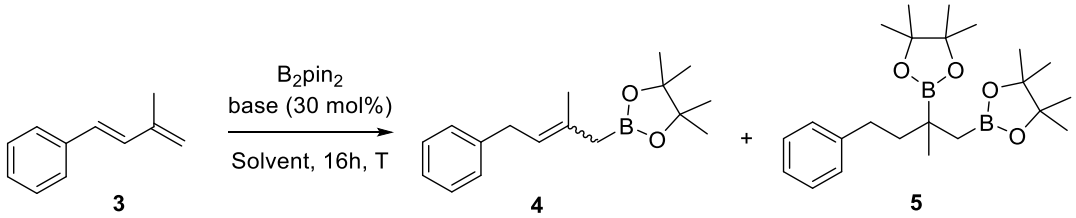
In a previous work[12] it was observed that upon treatment of conjugated dienes with excess of B_2pin_2 under borylation conditions, the triborated product was synthetized as a result of the 1,2-diboration of the allylic organoborane intermediate (Scheme 13). For comparison we postulated that product **5** might be formed from **4** via regioselective subsequent hydroboration.



Scheme 13. Triboration of (*E*)-buta-1,3-dien-1-ylbenzene.[12]

Next, we focused on the optimization of the reaction, studying the nature of the base, excess of B_2pin_2, solvent and T (Table 2), in order to obtain the diborated product 5 as the major product.

Table.2. Optimization of the reaction conditions in the transition-metal-free borylation of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene (**3**).[a]



Entry	Solvent	Base	B_2pin_2 equiv.	Temperature (°C)	%NMR Yield (4) [Isolated Yield]	% NMR Yield (5) [Isolated Yield]
1	MeOH	Na_2CO_3	1.1	90	17[5]	27[16]
2	^{i}PrOH	Na_2CO_3	1.1	90	0	0
3	MeOH	Cs_2CO_3	1.1	90	13	13
4	MeOH	KO^{t}Bu	1.1	90	7	10
5	MeOH	Na_2CO_3	1.1	70	17	17
6	MeOH	Na_2CO_3	2.2	90	26 [12]	35 [28]
7	MeOH	Na_2CO_3	2.2	110	11	60
8	MeOH	Na_2CO_3	3.0	110	9[8]	77[61]

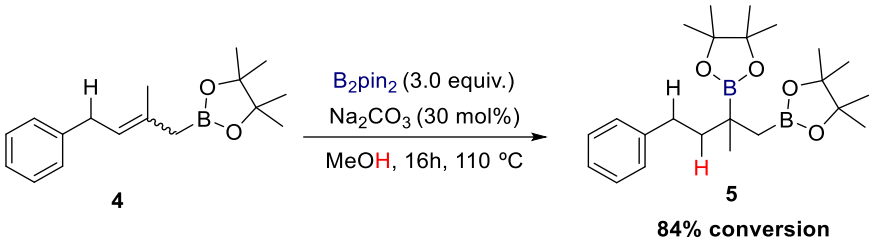
[a]Standard conditions: **3** (0.25 mmol), base (0.075 mmol), B_2pin_2 (0.275 – 0.75 mmol), solvent (1 mL), 16h, T (°C). Yield calculated by ^{1}H NMR using naphthalene as internal standard.

The use of ^{i}PrOH as solvent instead of MeOH, inhibited the reaction (Table 2, entries 1,2). Na_2CO_3 resulted to be the suitable base, since the use of Cs_2CO_3 and KO^{t}Bu provided low yields in **4** and **5** (Table 2, entries 1, 3 and 4). When the reaction temperature was 70 °C, a similar amount of both products **4** and **5** were obtained in low yield (Table 2, entry 5). However, it was found that increasing the amount of B_2pin_2, and increasing the reaction temperature, influenced not only

in the overall conversion of the substrate, but also favoured the formation of mainly the polyborated product **5** (Table 2, entries 6-8)**.** We selected 3.0 equiv. of the diborane and 110 °C as the optimal reaction conditions to obtain product **5** in 61% isolated yield (Table 2, entry 8).

The 1-D NOESY experiment to determine the major stereoisomer (from a dr = 3/1) in the allylic borylated product **4**, was not conclusive.

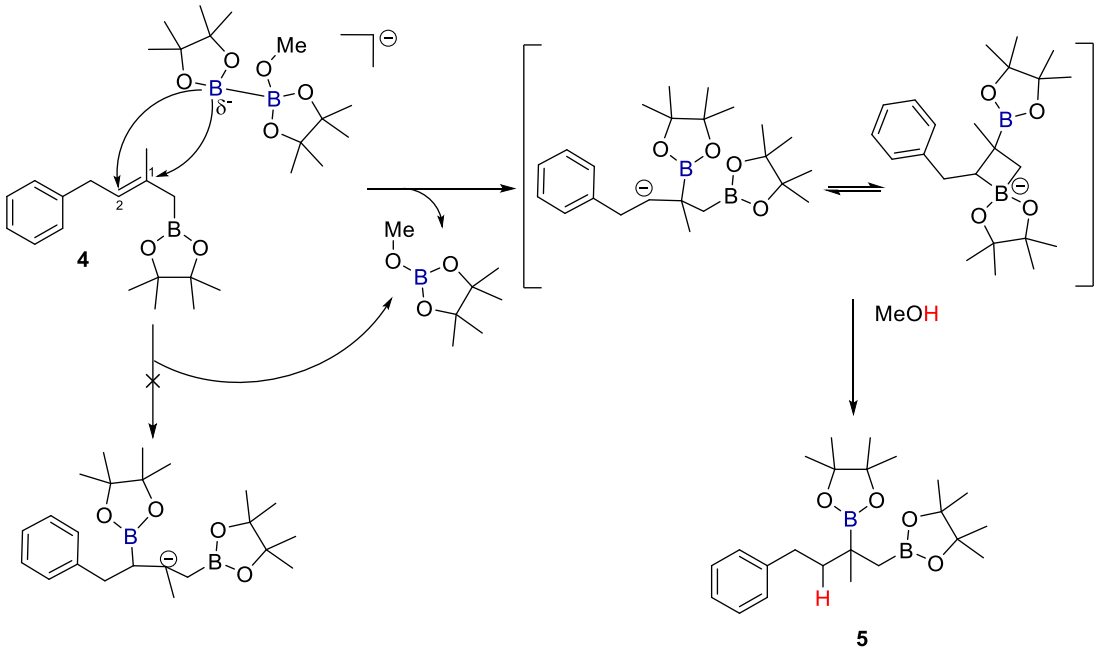
Next, in order to justify the reaction mechanism of the allylic borylation/hydroboration sequence, we performed a separate experiment where isolated product **4** was reacted with B_2pin_2 under the optimized reaction conditions and to our delight, product **5** was produced in 84% conversion (Scheme 14).



Scheme 14. Borylation reaction of **4** with B_2pin_2 under optimized reaction conditions.

Through this experiment, it was unequivocally proved that for the formation of **5**, the borylated intermediate **4** had to be formed first, thus confirming that the polyboration took place in a sequential manner.

The mechanism suggested two plausible nucleophilic attacks of the adduct [MeO-Bpin-Bpin]$^-$ in C^1 or C^2. Experimentally we have only observed that the C-Bpin new bond is formed in C^1 generating a carbanion in C^2 that might interact with the terminal Bpin to form a four membered ring boronate intermediate that eventually reacts with the MeOH toward the protonated product 5 (Scheme 15).



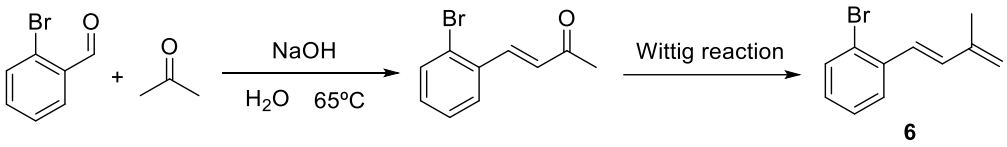
Scheme 15. Proposed mechanistic scheme for the 1,2-hydroboration.

As for a possible explanation behind the fact 1,2-diboration of **4** is not taking place here, unlike with the case with (*E*)-buta-1,3-dien-1-ylbenzene, we postulate that the presence of a methyl substituent in C^1 increases the steric hinderance around the double bond, making the process of diboration less favoured.

4.4 Allylic borylation of (*E*)-1-bromo-2-(3-methylbuta-1,3-dien-1-yl)benzene

In order to generalize the reactivity through the sequence allylic borylation/1,2-hydroboration, we selected next (*E*)-1-bromo-2-(3-methylbuta-1,3-dien-1-yl)benzene (**6**) as a substrate including C-Br functionalization, interesting for further transformations of the polyborated product.

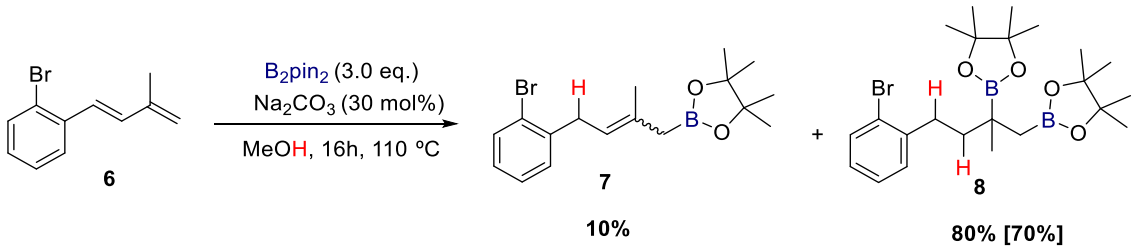
We synthesized the diene **6** via Wittig reaction of the enone which was previously prepared via aldol condensation of 2-bromobenzaldehyde and acetone (Scheme 16).



Scheme 16. Synthetic procedure for the synthesis of substrate **6**.

The borylation of **6** was carried out using the optimized reaction conditions for the polyboration of **3** (MeOH (1 mL), 30 mol% of Na_2CO_3, 3.0 equiv. of B_2pin_2, 110 °C for 16 hours).

Under these reaction conditions, the transformation of **6** into the polyborated product **8**was quantified by NMR yield (80%), and as isolated yield (70%) (Scheme 17). The allylic organoborane **7** was also detected in 10% NMR yield indicating that it was not completely consumed during the 16h (Scheme 17).



Scheme 17. Polyboration of **6**

4.5 Cross-coupling reaction of polyborated product (8)

The main objective behind the synthesis of **8**, was to study the cyclization between the C(sp^3)-B bonds present in the molecule and the C(sp^2)-Br. Although both couplings between C(sp^2)-Br and the C(sp^3)-B present in **8** could be possible, we assumed that the more reasonable transformation is the one with the less substituted C(sp^3)-B. This reaction would produce 4,4,5,5-tetramethyl-2-(2-methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3,2-dioxaborolane (**9**), a molecule of the family of tetrahydronaphthalenes, which belongs to a group of relevant compounds for the drug industry, such as Mibefradil[13] which was employed in the treatment of angina and high blood pressure, or Etoposide,[14] which is used as an anti-tumoral treatment (Figure 1).

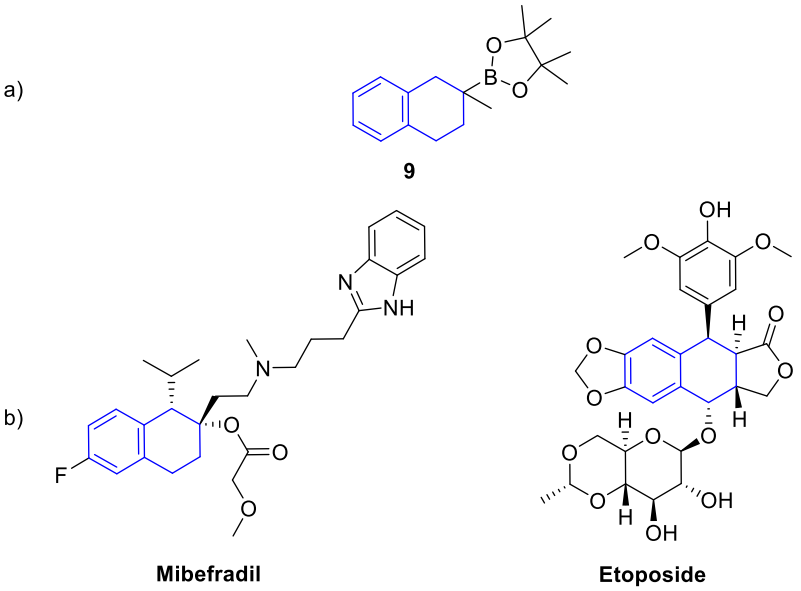
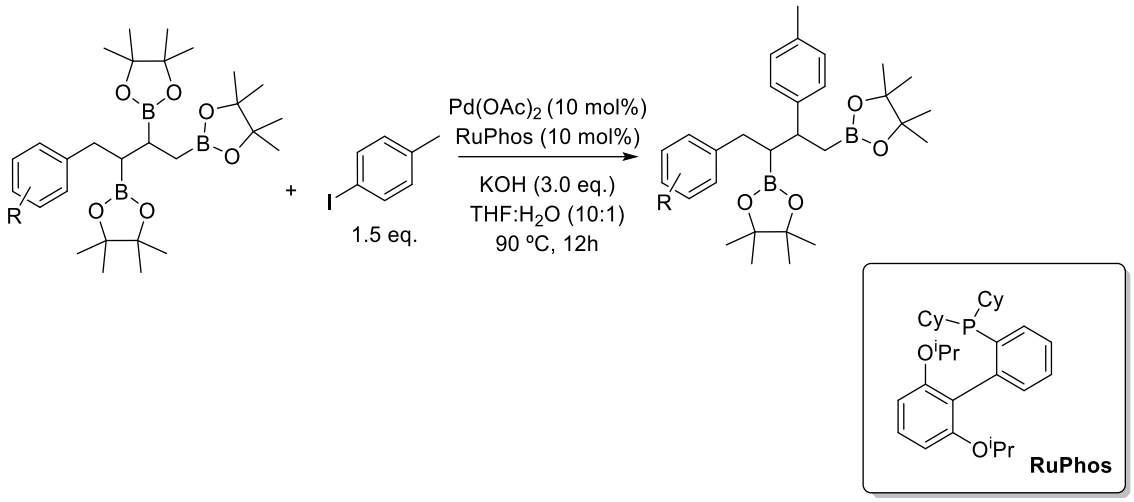


Figure 1. a) 4,4,5,5-tetramethyl-2-(2-methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3,2-dioxaborolane (**9**) and b) examples of tetrahydronaphthalene units as part of bioactive drugs.

Our final tetrahydronapthalene would still present another Bpin group, for further functionalizations, which would open many possibilities for the synthesis of functionalized tetrahydronapthalene molecules.

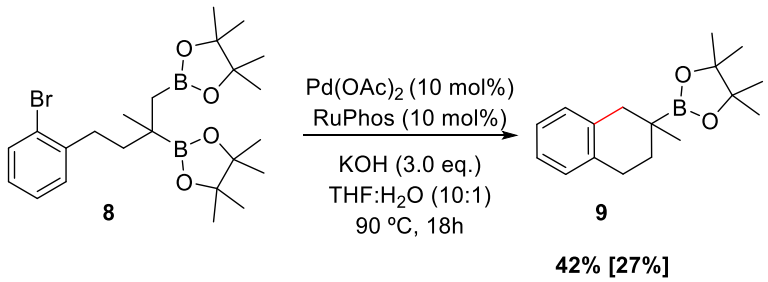
The Pd-catalyzed cross coupling reaction of aryl halides and organoboranes has been a very important method for C-C bond forming ever since its proposal by Suzuki-Miyaura[15] in 1979. Many advances have been made in this field, especially in the development of ligands for the palladium complexes, which improve the efficiancy of the reactions. Among the most powerful family of ligands, is that of dialkylaryl phosphine ligands, of which many varieties have been

synthesized and studied.[16] In our case, we had C(sp^3)-B and Ar-Br bonds, and so we had to search for a ligand that had proven effectiveness with this particular set of reagents. In the bibliographic search, we found that cross-coupling reactions had been done between 1,2,3- triborated compounds and aryl halides[12] and using $Pd(OAc)_2$ and the specific phosphine ligand RuPhos (Scheme 18).



Scheme 18. Selective C(sp^3)-B/C(sp^2)-X cross coupling reaction reported by Davenport and Fernández.[12]

Employing the $Pd(OAc)_2$/RuPhos catalytic system, the desired product **9** was synthetized in 42% NMR yield, and after purification, product **9** was isolated in 27% yield. The reaction was totally selective towards the less hindered C(sp^3)-B bond favouring the formation of the tetrahydronaphthalene **9** (Scheme 19).

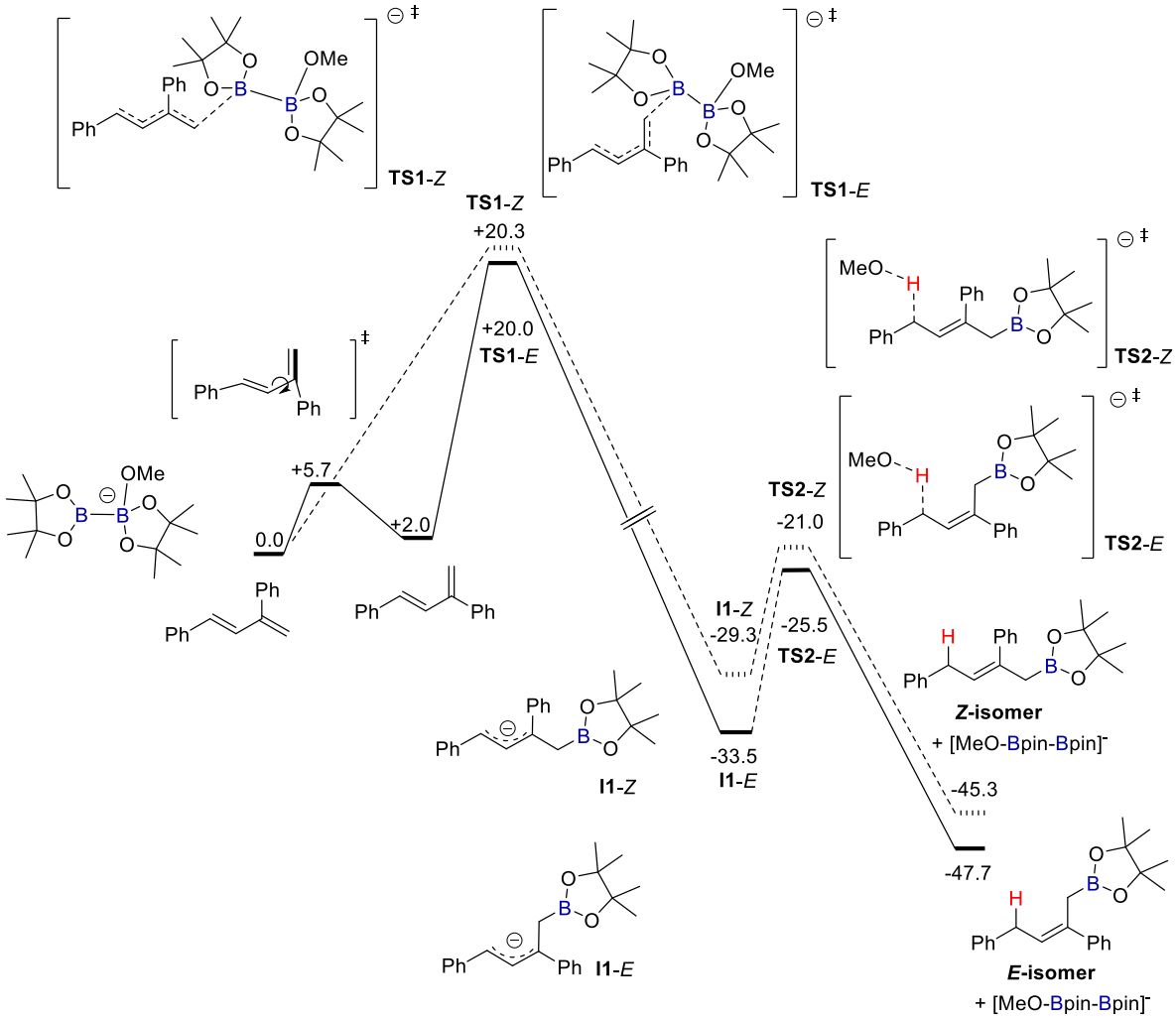


Scheme 19. Pd-catalyzed Suzuki-Miyaura cross-coupling reaction of our polyborated product **8**.

We have proved that substituted tetrahydronaphthalenes with tetrasubstituted carbons can be prepared from 1,3-disusbstituted conjugated dienes in a sequential allylic borylation/hydroboration/cross-coupling reaction. Our next challenge will be to induce asymmetry in the tetrasubstituted carbon of the tetrahydronaphthalene.

4.6 Computational study on the borylation of of (*E*)-buta-1,3-diene-1,3-diyldibenzene

In order to rationalize the activity, stereo- and regioselectivity of the reaction, we performed a computational DFT study on the previously proposed reaction mechanism.[7] Following a similar protocol to that of previous DFT study on the borylation of (*E*)-buta-1,3-diene-1,3-yldibenzene,[7] we characterized the relevant points in the potential energy surface for the reaction pathways that lead to *E* and *Z* isomers. Scheme 20 shows the computed free-energy profiles of the reaction for the *E* and *Z* paths (solid and dashed lines, respectively).



Scheme 20. Potential free-energy profiles (kcal·mol^{-1}) for the 1,4-hydroboration of (*E*)-buta-1,3-diene-1,3-diyldibenzene. Solid and dashed lines correspond to the paths yielding the *E* and *Z* stereoisomeric products respectively.

This mechanism starts with the nucleophilic attack of the [MeO-Bpin-Bpin]$^-$ to the less substituted carbon of the diene, which is the rate determining step of the catalytic cycle for both stereoisomeric paths. This attack has a moderate free-energy barrier of 20.0 kcal·mol^{-1} for *E*-path. The corresponding transition state structure (**TS1**-*E*) is shown in Figure 2.

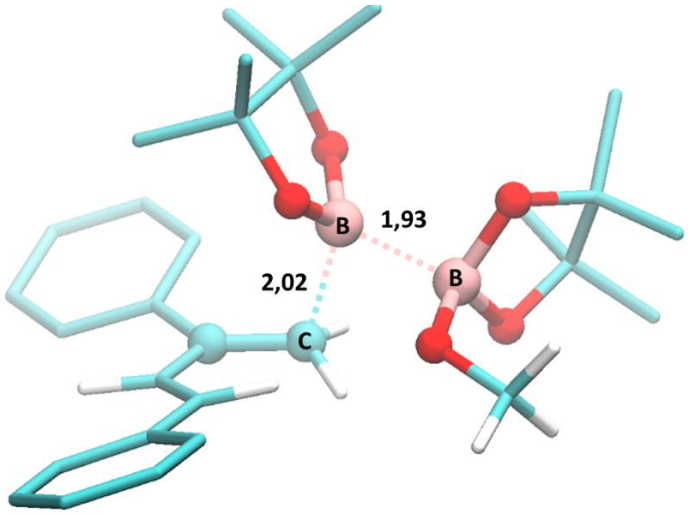


Figure 2. Molecular structure of **TS1**-*E*. Distances in Å.

The result is the formation of the stable Bpin-OMe species, as well as the anionic intermediate **I1**, whose negative charge is significantly stabilized by conjugation of the allyl system, as well as with the Ph groups, making this process thermodynamically favourable and non-reversible.

After this, a methanol molecule protonates **I1**, giving the final product, with the proton and the boryl group in a 1,4 relative positon. Protonation takes place on the allylic carbon of **I1**-*E* supporting the largest negative charge as illustrated by the calculation of electrostatic potential-based ESP atomic charges (Figure 3). In line with charge distribution, the estimated barrier for protonation at that carbon using a single MeOH solvent molecule is quite low (8.0 kcal·mol^{-1}).

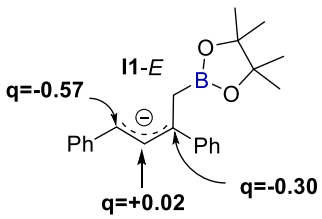


Figure 3. ESP atomic charges on **I1**-*E*.

To study the stereoselectivity of the reaction, we considered the two possible reaction pathways, the one where the more stable *trans* conformer is borylated to produce the *Z*-isomer,

and the another, in which the diene undergoes a first an isomerization *trans* to *cis*, and then, the *cis* isomer is borylated to yield the *E*-isomer of the. This isomerization process proceeds through a low free-energy barrier (5.7 kcal·mol^{-1}) that allows a fast equilibrium between the two diene isomers at the reaction temperatures. The *cis* isomer is less energetically stable than the *trans* one, although the energy difference is relatively small (2.0 kcal·mol^{-1}). The lower stability of the *cis* isomer is compensated by a lower free-energy barrier for borylation (18.0 *vs* 20.3 kcal·mol^{-1}, for *cis* and *trans* dienes, respectively). The higher reactivity of the *cis* conformer could be related to orbital interactions that could stabilize the electronic charge, as has been postulated for the case of α,β-unsaturated carbonils.[17] Overall, the transition state at the *Z* path (**TS1**-*Z*) is 0.3 kcal·mol^{-1} higher than the corresponding transition state for the *E* path (**TS1**-*E*). Since borylation step is irreversible (computed reverse free-energy barrier > 50 kcal·mol^{-1}), this results in a small preference for the *E* over the *Z* products, in full agreement with experimental observations.

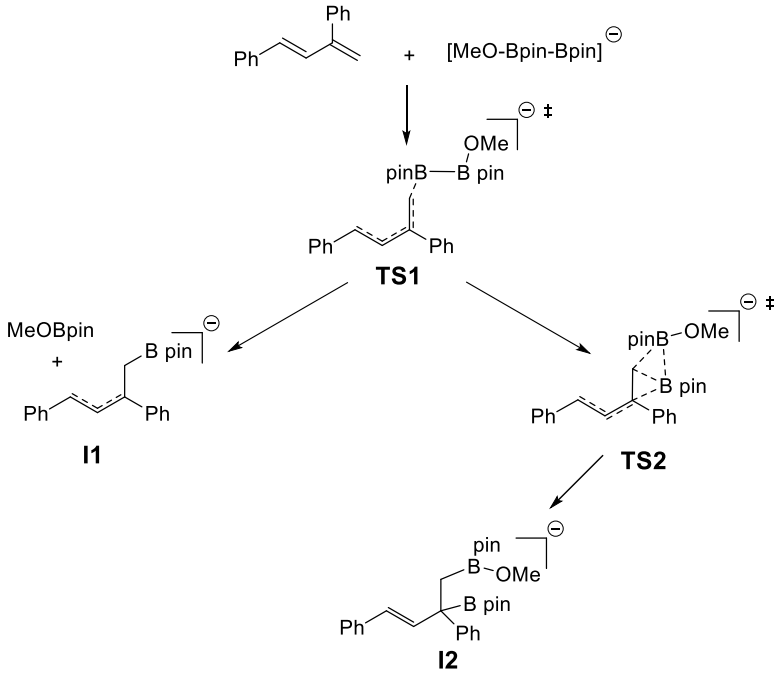
Even more interestingly, ongoing from previously studied (*E*)-buta-1,3-dien-1-ylbenzene (Scheme 5) to diene **1**, in which a phenyl group is introduced in position 3, one can observe some interesting trends: (1) adding the phenyl substituent the alkene moiety becomes more electrophilic and the borylation free-enery barrier reduces significantly (from 24.5 to 18.0 kcal·mol^{-1} for *E* paths), and (2) the energy difference between the *trans* and *cis* isomers reduces from 3.6 to 2.0 kcal·mol^{-1}, and as a consequence, the reaction through the *cis* isomer becomes energetically favoured for the **1** substrate. Although the energy difference does not correlate quantitatively with the isomer ratio found experimentally, the shift in isomer preference upon change in the substrate substituents has been computationally rationalized.

Additionally, we studied the chemoselectivity of the borylation of (*E*)-buta-1,3-diene-1,3-diyldibenzene in terms of the allylic borylation-protonation versus the 1,2-diboration. Early studies on the diboration of unactivated alkenes proposed that the attack of [MeO-Bpin-Bpin]$^-$ adduct to the double bond proceeds through a TS that can connect either with the borylation product or with another TS for diboration, via a bifurcation point in the PES (Scheme 3).[4] Bifurcation points are described in Houk and co-workers' study as points after a TS where the PES divides and leads into two different products.[6] This means that a single TS can connect to another TS without the involvement of an energy minimum. There are many examples in the literature of reactions that have been postulated to have these peculiar PES, generally involved in pericyclic reactions,[18] but also present in substitution reactions.[19] Unlike in the case of competing mechanisms, where the product ratio can be determined by comparison of the

activation free-energies of their respective pathways, in cases where bifurcations are present, selectivity is determined by the shape and contour of the PES after the TS, and thus it is no longer a simple comparison between stationary point's energy.

This is usually resolved via multiple *ab initio* MD simulations starting from the TS structure, and the selectivity is determined by the number of times a simulation reaches each one of the possible products. However, these studies are computationally expensive, and in order to determine the selectivity's of these types of reactions in an inexpensive way, the use of algorithms that extrapolate these has been proposed as an interesting alternative. In our case, we chose to use *ValleyRidge*,[20] a method able to qualitatively predict the selectivity ratio for various reactions that present bifurcation points in their PES. It does that by generating vectors connecting the different species in the PES as well as the vectors associated to the relevant vibrations of the TS.

In order to use the algorithm, we calculated the geometries of both TS involved, the ones of the products that connect to them, and finally the frequencies of the TS, all of these needed to generate the mathematical vectors necessary to determine the selectivity (Scheme 21).



Scheme 21. Mechanism of the possible borylation reactions, and structures employed with the *ValleyRidge* method.

The *ValleyRidge* method predicted, that the major product was the borylated product (**I1**), with a selectivity ratio of 91:9 (**I1**:**I2**). This result predicts that the system is selective toward the formation of the borylated intermediate, which would actually match with the experimental results, as the 1,2-diborated product was not observed.

However, in this specific case, conclusive evidence of the presence of a bifurcation point could not be found, as analysis of the Intrinsic Reaction Coordinate (IRC) of **TS1** did not show any "flat" or unusual section in the coordinate along the PES (Figure 4). This characteristic zone is an indicator of the presence of a bifurcation point nearby, and the absence of it in our IRC calculations doesn't allow us to assure that this situation is present in our case study. Further studies are ongoing in our research group to better understand the chemoselectivity in the borylation of dienes.

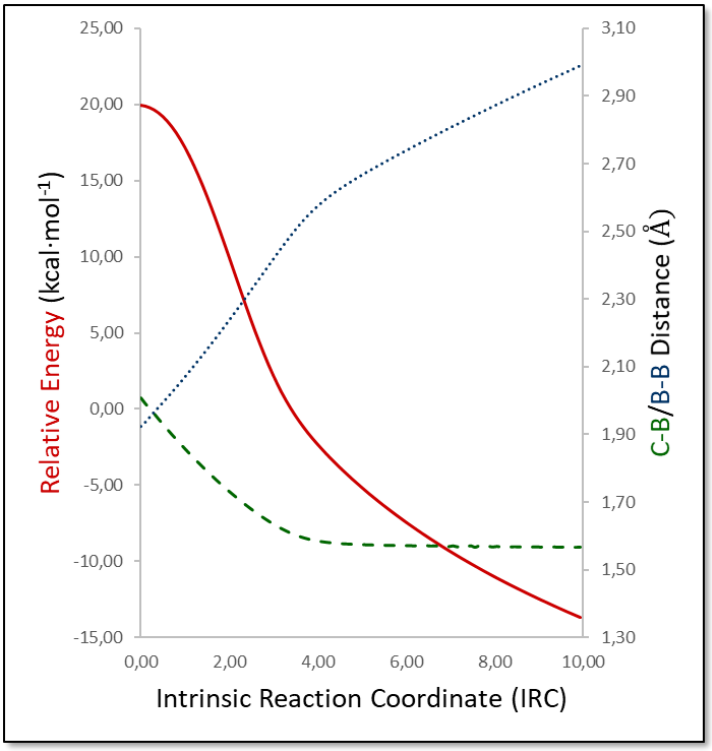
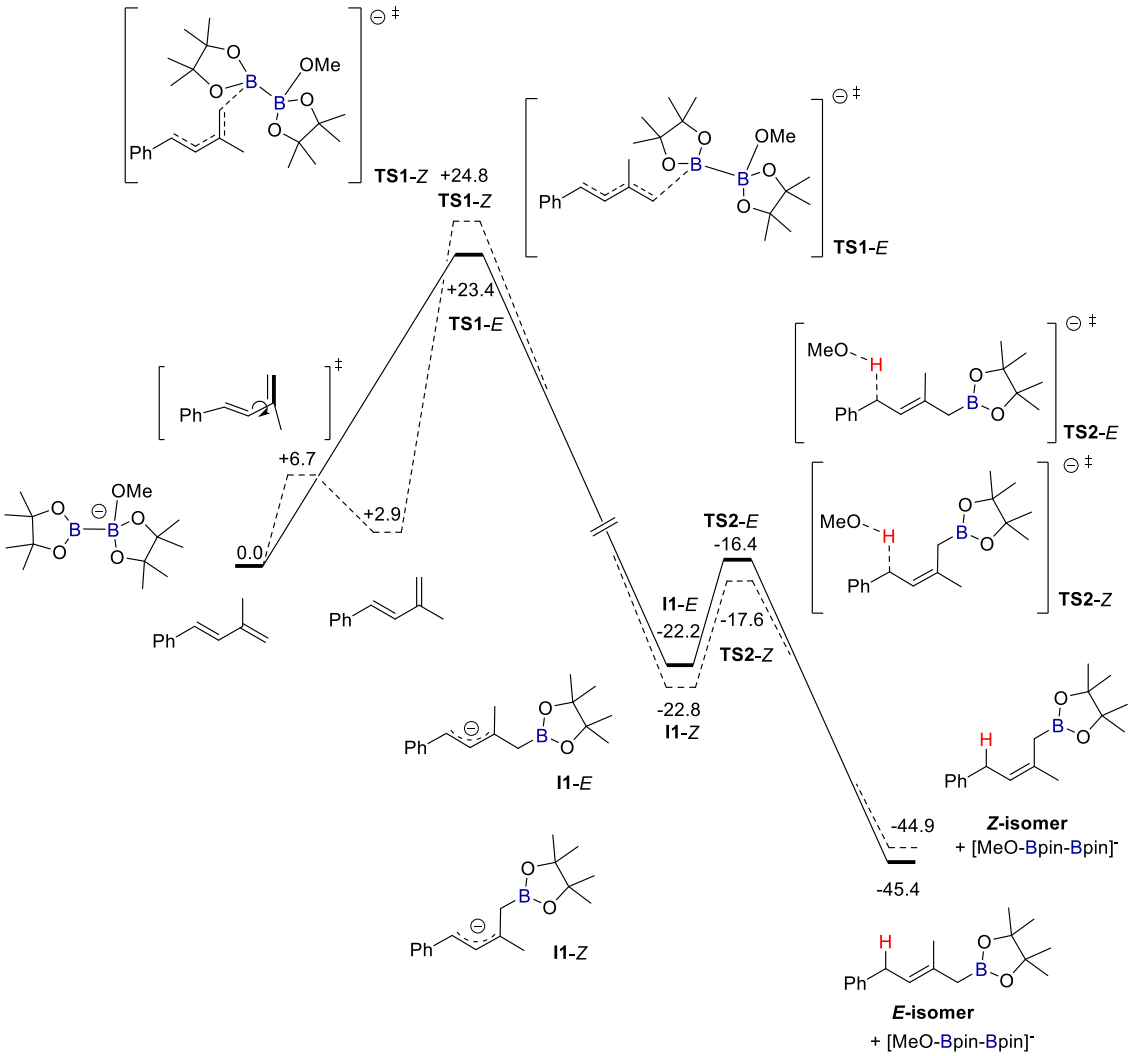


Figure 4. Section of the IRC from **TS1** into **P1**. Relative Energies (Red, solid line), C-B bond distance (Green, dashed line) and B-B bond of the diborane (Blue, dotted line) are illustrated here. No flat sections on any of the representations can be appreciated.

4.7 Computational study on the borylation of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene



Scheme 22. Potential free-energy profiles (kcal·mol^{-1}) for the 1,4-hydroboration of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene. Solid and dashed lines correspond to the paths yielding the *E* and *Z* stereoisomeric products respectively.

We also performed an analogous DFT study on the reaction mechanism of the borylation of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene (**3**), in which the phenyl substituent has been replaced by a methyl group. Scheme 22 shows the corresponding potential free-energy profile for the *E* and the *Z* paths (solid and dashed lines, respectively). Here, we can observe that *cis* isomer is energetically less stable than in the case of **1** with the phenyl group (+2.9 and +2.0 for **3** and **1**, respectively). This indicates that the methyl group of **3** *trans* isomer generates less repulsive interactions with the 1,2 double bond than the corresponding phenyl substituent of **1**. Another

consequence is that the relative rates of reaction paths through *trans* and *cis* dienes inverts again, and for **3** the reaction through *trans* diene isomer is kinetically preferred. Thus, the overall free-energy barrier through **TS1**-*E* is 1.4 kcal·mol^{-1} lower in energy than that through the **TS1**-*Z*. This would indicate that the *E*-isomer would be preferentially formed over the *Z* one, even though this could not be determined experimentally (see above). Again the carbon supporting the largest negative charge in the intermediate **I1** is the carbon at the position 4 (relative to the boryl moiety), resulting in the overall 1,4-hydroboration (Figure 5).

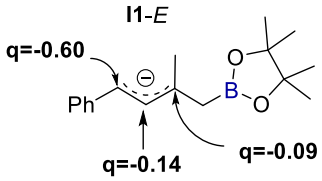


Figure 5. ESP atomic charges on intermediate **I1**-*E*.

5. Conclusions

In this work, we have explored the reactivity of selected 1,3-disubstituted conjugated dienes through borylation reactions, and for the case of 1-aryl-3-methyl substituted ones, we have determined the optimal conditions for the double borylation reaction which is able to generate useful polyborated products.

Then we were able to successfully perform an intramolecular C(sp^2)-Br/C(sp^3)-B cross-coupling reaction in a selective manner, generating synthetically useful tetrahydronaphthalenes with tetrasubstituted carbons.

Computational studies on the allylic borylation reaction have rationalized the regioselectivity for 1,4-hybroborated products and the stereoselectivity for the *E*-isomer in the reaction with (*E*)-buta-1,3-diene-1,3-diyldibenzene. Also for the allylic borylation of (*E*)-(3-methylbuta-1,3-dien-1-yl)benzene, for which stereoisomer distribution could not be determined experimentally, we computationally predict that the *E*-isomer is the major product.

Lastly, we employed novel computational methodology for determining the selectivity on bifurcation points in the PES to study the chemoselectivity of the allylic borylation against the diboration for the case of (*E*)-buta-1,3-diene-1,3-diyldibenzene, and the results agreed with the experimental outcome.

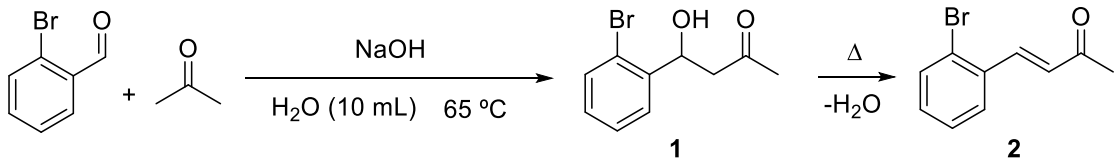
6. Experimental Section

6.1 General information (Chemicals and Instrumentation)

Solvents and reagents were obtained from commercial suppliers and dried and/or purified (if needed) by standard procedures. Diboron reagents were purchased from Ally Chem and used without further purification. All reactions were conducted in oven and flame-dried glassware under an inert atmosphere of argon, using Schlenk-type techniques. **Flash chromatography** was performed on standard silica gel (Merck Kieselgel 60 F254 400-630 mesh). **Thin layer chromatography** was performed on Merck Kieselgel 60 F254 which was developed using standard visualizing agents: UV fluorescence (254 and 366 nm) or potassium permanganate/Δ. **NMR spectra** were recorded at a Varian Goku 400 or a Varian Mercury 400 spectrometer. ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm (^{1}H) and $CDCl_3$: 77.16 ppm (^{13}C)). $^{11}B\{^{1}H\}$ NMR chemical shifts (δ) are reported in ppm relative to $(CH_3)_2O\cdots BF_3$. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, hept = heptuplet, br = broad, 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 an 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 an APCI interface or EI interface and it was performed at the Unidade de Espectrometría 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 (30m, 0.25mm i. d., 0.25µm thickness) using He as the carrier gas.

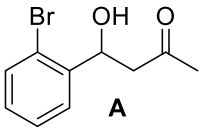
6.2 Synthesis of Substrates

Procedure for the synthesis of 4-(2-bromophenyl)but-3-en-2-one via Aldol reaction.[21,22]



To a 50 mL Schlenk-type flask with a magnetic stirrer, it was added 10 mmol of 2-bromobenzaldehyde, 27.5 mmol of acetone and 10 mL of water and the mixture was stirred until it reached 65 °C. Then 2.4 mL of a 1% (w/w) sodium hydroxide solution (0.6 mmol of NaOH) were added and the reaction was stirred at 65 °C for 1.5 hours. After that time, the crude was analyzed with TLC, and the completion of starting material was confirmed. The reaction was quenched with a saturated solution of NH_4Cl (20 mL), and the aqueous layer extracted three times with EtOAc. The organic layers were collected, washed with brine and dried with anhydrous $MgSO_4$. The crude product was purified with flash column chromatography. Assessment of products structure was done by comparison with bibliographic spectra.[21,22]

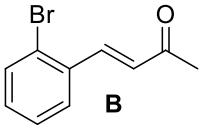
4-(2-bromophenyl)-4-hydroxybutan-2-one. (A)



The product was purified by column chromatography using as eluent pentane:Et_2O(0% → 38%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62 (dd, J = 7.7, 1.6 Hz, 1H), 7.52 (dd, J = 8.0, 1.3 Hz, 1H), 7.36 (m, 1H), 7.15 (td, J = 7.7, 1.7 Hz, 1H), 5.46 (dt, J = 9.7, 2.7 Hz, 1H), 3.51 (d, J = 3.1 Hz, 1H), 3.07 – 2.97 (dd, J = 17.8, 2.7 Hz, 1H), 2.66 (dd, J = 17.8, 9.7 Hz, 1H), 2.23 (s, 3H).

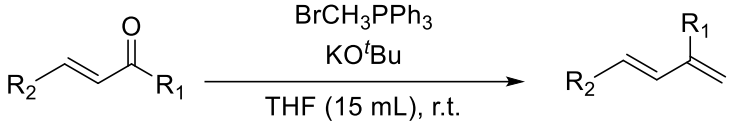
4-(2-bromophenyl)but-3-en-2-one. (B)



The product was purified by column chromatography using as eluent pentane:Et_2O(0% → 38%). It was obtained as a yellow oil (848.7 mg, 38 % yield).

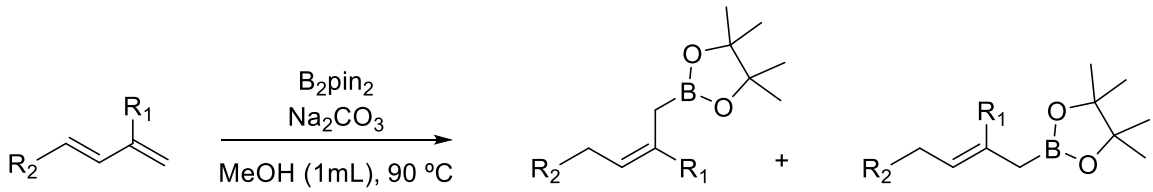
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (d, J = 16.3 Hz, 1H), 7.67 – 7.60 (m, 2H), 7.39 – 7.31 (m, 1H), 7.28 – 7.22 (m, 1H), 6.63 (dd, J = 16.3, 0.7 Hz, 1H), 2.43 (d, J = 0.7 Hz, 3H).

General procedure for the synthesis of 1,3-disubstituted conjugated dienes via Wittig reaction.



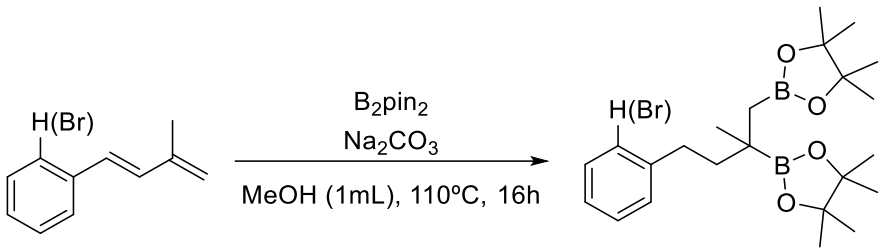
To an oven dried 100 mL Schlenk-type flask with a magnetic stirrer, 5.0 mmol of $BrCH_3PPh_3$ and 5.2 mmol of KO^tBu were added, and they were dissolved with 11 mL of THF, and stirred at room temperature for 30 minutes. The solution changed from colourless solution to vibrant yellow. Meanwhile, 4.0 mmol of the enone was dissolved in an argon purged Schlenk-type flask with 4 mL of dry THF. After the 30 minutes, the enone solution was added drop-wise to the ylide solution at 0 °C and left stirring until completion, 3 hours, at room temperature. The reaction was quenched with a saturated solution of NH_4Cl (20 mL). The aqueous layer was extracted three times with Et_2O and the combined organic layers were washed with brine and dried with anhydrous $MgSO_4$ and concentrated. The crude product was purified with flash column chromatography to afford the desired diene.

General procedure for allylic borylation of 1,3-disubstituted conjugated dienes



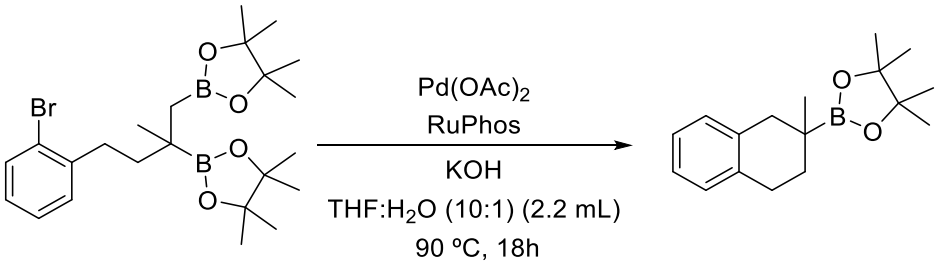
To an oven dried Schlenk-type flask with a magnetic stirrer, 0.3 mmol of buta-1,3-diene-1,3-diyldibenzene were added, alongside with 0.9 mmol of B_2pin_2 and 0.09 mmol of Na_2CO_3. Then, 1 mL of dry MeOH was added, and the solution was heated to 90 °C for 16h under stirring. Upon completion, the reaction mixture was concentrated under reduced pressure. An aliquot was taken to determine the conversion and selectivity by ^{1}HNMR analysis with naphthalene as internal standard. The crude residue was purified by flash column chromatography to afford the borylated product.

General procedure for the polyboration of 1-aryl-3-methyl conjugated dienes



To an oven dried Schlenk-type flask with a magnetic stirrer, 0.25 mmol of substrate were added, alongside with 0.75 mmol of B_2pin_2 and 0.075 mmol of Na_2CO_3. Then, 1 mL of dry MeOH was added, and the solution was heated to 110 °C for 16h under stirring. Upon completion, the reaction mixture was concentrated under reduced pressure. An aliquot was taken to determine the conversion and selectivity by ^{1}HNMR analysis with naphthalene as internal standard. The crude residue was purified by flash column chromatography.

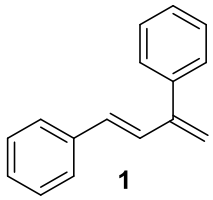
General procedure for the synthesis of 4,4,5,5-tetramethyl-2-(2-methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3,2-dioxaborolane (9) via Suzuki-Miyaura Coupling



To an oven dried Schlenk-type flask with a magnetic stirrer, 0.15 mmol of substrate were added, alongside with 0.45 mmol of KOH, 0.015 mmol of $Pd(OAc)_2$ and 0.015 mmol of RuPhos (2-dicyclohexylphosphino-2',6'-diisopropoxybiphenyl) ligand. Then, 2 mL of THF, and 0.2 mL of water, sparged with argon, were added. The solution was heated to 90 °C for 18 h under stirring. After completion the reaction was filtered through Celite, and then 10 mL of a saturated solution of NH_4Cl was added. The aqueous layer was extracted three times with Et_2O and the combined organic layers were washed with brine, dried with anhydrous $MgSO_4$ and concentrated. The crude product was purified with flash column chromatography to afford the product.

6.3 Characterization of 1,3-disubstituted conjugated dienes

(*E*)-buta-1,3-diene-1,3-diyldibenzene (1)



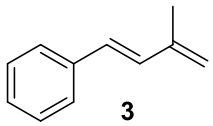
1

For the synthesis of (*E*)-buta-1,3-diene-1,3-diyldibenzene, the general procedure was followed, but with the addition taking place with **both** solutions at 0 °C, to avoid excessive heating that lead to the formation of other side products. The product was obtained by flash column chromatography using pentane as an eluent. It was obtained as a colourless liquid (334.7 mg, 41% yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 – 7.32 (m, 7H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.24 – 7.17 (m, 1H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.50 (d, *J* = 16.1 Hz, 1H), 5.41 (d, *J* = 1.7 Hz, 1H), 5.24 (d, *J* = 1.7 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.2, 140.2, 137.2, 131.9, 130.4, 128.6, 128.5, 128.2, 127.7, 127.6, 126.6, 117.4.

(*E*)-(3-methylbuta-1,3-dien-1-yl)benzene (3)



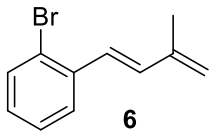
3

The product was purified with flash column chromatography using pentane as eluent. It was obtained as a colourless liquid (416.1 mg, 72 % yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47 – 7.40 (m, 2H), 7.36 – 7.28 (m, 2H), 7.25 – 7.18 (m, 1H), 6.88 (d, J = 16.1 Hz, 1H), 6.53 (d, J = 16.1 Hz, 1H), 5.12 (br, 1H), 5.08 (br, 1H), 1.98 (dd, J = 1.4, 0.7 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.1, 137.4, 131.7, 128.7, 128.6, 127.4, 126.5, 117.4, 18.6.

(*E*)-1-bromo-2-(3-methylbuta-1,3-dien-1-yl)benzene (6)



6

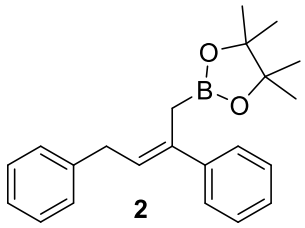
The product was obtained heating at 55 °C, and purified with flash column chromatography using pentane as eluent. It was obtained as a colourless liquid (591.4 mg, 70 % yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47 (td, J = 8.3, 1.5 Hz, 2H), 7.22 – 7.14 (m, 1H), 7.06 – 6.91 (m, 1H), 6.85 – 6.67 (m, 2H), 5.10 – 5.02 (m, 2H), 1.95 – 1.90 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.2, 137.2, 134.4, 133.1, 128.7, 127.5, 126.7, 124.2, 118.5, 18.6.

6.4 Characterization of borylated compounds

Characterization of 2-(2,4-diphenylbut-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2)



2

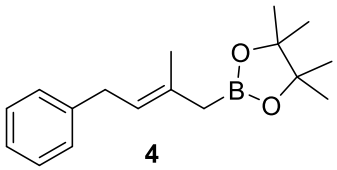
The product was purified by flash column chromatography using pentane:Et_2O(0% → 4%) as eluent. It was obtained as a colorless liquid (13.3 mg, 13% yield) (E:Z = 6:1).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 – 7.38 (m, 2H), 7.30 – 7.26 (m, 6H), 7.22 – 7.15 (m, 2H), 5.91 (t, J = 7.2 Hz, 1H), 3.56 (d, J = 7.1 Hz, 2H), 2.20 (s, 2H), 1.18 (s, 11H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.1, 141.3, 136.8, 128.7, 128.4, 128.1, 126.6, 126.1, 125.86, 83.4, 35.3, 24.7.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 32.43.

Characterization of 4,4,5,5-tetramethyl-2-(2-methyl-4-phenylbut-2-en-1-yl)-1,3,2-dioxaborolane (4)



4

The product was purified by flash column chromatography using pentane:Et_2O(0% → 9%) as eluent. It was obtained as a colourless oil (5.4 mg, 8 % yield). (E:Z = 3:1)

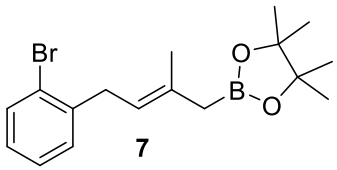
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 – 7.11 (m, 5H), 5.36 – 5.24 (m, 1H), 3.33 (d, *J* = 7.3 Hz, 2H), 1.79 (m, 5H), 1.24 (s, 12H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.0, 133.2, 128.5, 128.3, 125.6, 122.4, 83.3, 34.6, 25.8, 24.8.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 33.30.

HRMS-(ESI+) for $C_{17}H_{25}BO_2$ $[M+H^+]^+$: calculated: 273.2020; found: 273.2021.

Characterization of 2-(4-(2-bromophenyl)-2-methylbut-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (7)



7

The product was purified by flash column chromatography using pentane:Et_2O(0% → 9%) as eluent. It was obtained as a colourless oil (8.9 mg, 10 % yield).

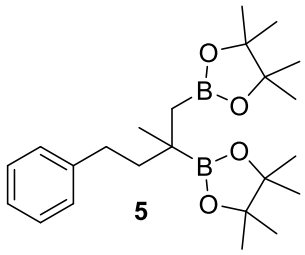
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (ddd, *J* = 7.9, 3.7, 1.3 Hz, 1H), 7.32 – 7.13 (m, 2H), 7.07 – 6.98 (m, 1H), 5.31 – 5.23 (m, 1H), 3.43 (d, *J* = 7.1 Hz, 2H), 1.82 – 1.72 (m, 5H), 1.24 (s, 12H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.1, 134.3, 132.7, 132.5, 130.3, 129.8, 127.4, 127.3, 124.6, 120.55, 83.3, 83.2, 34.9, 30.5, 25.9, 24.8, 24.8, 24.8.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 32.74.

HRMS-(ESI+) for $C_{17}H_{25}BO_2$ $[M+H^+]^+$: calculated: 351.1125, found: 351.1121.

Characterization of 2,2'-(2-methyl-4-phenylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (5)



5

The product was purified by flash column chromatography using pentane:Et_2O(0% → 9%) as eluent. It was obtained as a colourless oil (61.4 mg, 61 % yield).

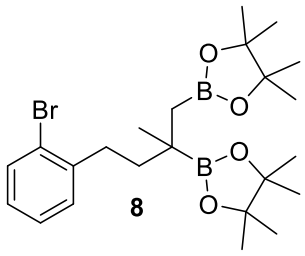
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30 – 7.21 (m, 2H), 7.21 – 7.11 (m, 3H), 2.57 (m, 2H), 1.71 – 1.56 (m, 2H), 1.27 (d, J = 1.5 Hz, 12H), 1.23 (s, 12H), 1.05 (s, 3H), 1.04 (d, J = 15.5 Hz, 1H), 0.77 (d, J = 15.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.9, 128.4, 128.2, 125.4, 83.9, 82.9, 44.3, 32.4, 25.1, 25.0, 24.8, 24.8, 24.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 34.03.

HRMS-(ESI+) for $C_{17}H_{25}BO_2$ $[M+H^+]^+$: calculated: 401.3029, found: 401.3035.

Characterization of 2,2'-(4-(2-bromophenyl)-2-methylbutane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (8)



8

The product was purified by flash column chromatography using pentane:Et_2O(0% → 9%) as eluent. It was obtained as a colourless oil (84 mg, 70 % yield).

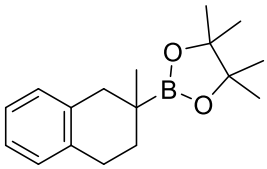
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 – 7.42 (m, 1H), 7.24 – 7.17 (m, 2H), 7.06 – 6.92 (m, 1H), 2.79 – 2.64 (m, 2H), 1.69 – 1.50 (m, 2H), 1.28 (d, *J* = 1.5 Hz, 12H), 1.23 (s, 12H), 1.08 (d, *J* = 15.5 Hz, 1H), 1.08 (s, 3H), 0.79 (d, *J* = 15.5 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.0, 132.6, 130.4, 127.4, 127.2, 124.4, 83.1, 82.9, 42.2, 34.1, 32.6, 25.1, 25.0, 24.9, 24.8, 23.9, 22.4, 15.3, 14.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 33.48.

HRMS-(ESI+) for $C_{17}H_{25}BO_2$ $[M+H^+]^+$: calculated: 479.2134, found: 479.2142.

Characterization of 4,4,5,5-tetramethyl-2-(2-methyl-1,2,3,4-tetrahydronaphthalen-2-yl)-1,3,2-dioxaborolane (9)



9

The product was purified by flash column chromatography using pentane:Et_2O(0% → 9%) as eluent. It was obtained as a white solid (11.1 mg, 27 % yield).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.04 (br, 4H), 2.94 (d, J = 16.0 Hz, 1H), 2.91 – 2.73 (m, 2H), 2.40 (d, J = 16.0 Hz, 1H), 2.02 – 1.91 (m, 1H), 1.48 (ddd, J = 13.0, 8.8, 6.4 Hz, 1H), 1.12 (d, J = 16.2 Hz, 12H), 1.05 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.0, 136.3, 129.3, 128.7, 125.3, 125.2, 83.0, 39.5, 32.2, 27.0, 24.5, 23.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz) δ 34.95.

HRMS-(ESI+) for $C_{17}H_{25}BO_2$ $[M+H^+]^+$: calculated: 295.1840, found: 295.1837.

6.5 Computational Details

All calculations were performed with the Gaussian 16 A.03 program,[23] in the framework of DFT.[24] The functional used in this work is the hybrid functional B3LYP,[25] meaning that on the exchange-correlation functional, the exact HF solution of the exchange energy is introduced to improve the functional, in this case, 20 %. In order to take into account, the long-range non-polar interactions, we included Grimme's D3 dispersion correction,[26] which has been proven to be very effective at modelling such interactions. As for the basis set (, we used the 6-311G(d,p) set,[27-30] which is a split valence triple-zeta Pople's basis set. The 6-311G(d,p) basis set uses 1 basis function for the non-valence orbitals, 3 basis functions for the valence orbitals, and one polarized function (atomic orbitals with a higher angular momentum quantum number) in the form of d-type orbitals for our non-hydrogen atoms, and p-type orbitals for the hydrogens. The choice of these parameters was so that energy comparisons between our calculations and previous calculations in the group[7] could be done.

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