BORATA ALKENE INTERMEDIATES FOR SELECTIVE C-C COUPLING REACTIONS

Sara González Morán

UNIVERSITAT ROVIRA i VIRGILI

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SARA GONZÁLEZ MORÁN

DOCTORAL THESIS
2024

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PhD Thesis

Supervised by Prof. María Elena Fernández Gutiérrez

Departamento de Química Física e Inorgánica (URV)

UNIVERSITAT ROVIRA i VIRGILI

Tarragona, March 2024

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Universitat Rovira i Virgili

Prof. María Elena Fernández Gutiérrez, profesora catedrática del Departamento de Química Física e Inorgánica de la Universitat Rovira i Virgili,

HAGO CONSTAR que este trabajo, titulado:

"**Borata Alkene Intermediates for Selective C-C Coupling Reactions**"

que presenta Sara González Morán para la obtención del título de Doctor, y que cumple los requerimientos para poder optar a la Mención Internacional, ha estado realizado bajo mi dirección en el Departamento de Química Física e Inorgánica de la Universitat Rovira i Virgili.

Tarragona, 3 de abril del 2024

La directora de la tesis doctoral

Prof. María Elena Fernández Gutiérrez

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El presente trabajo se ha desarrollado mediante una beca Joan Oró FI (2021FI_B 00308, 2022FI_B1 00082) y una beca de proyecto de la Universitat Rovira i Virgili (PID2019-109674GB). El contenido descrito en la presente tesis ha sido financiado por:

- El Ministerio de Economía, Industria y Competitividad de España (MINECO) mediante los proyectos PID2022_141693NB-I00 y PID2019-109674GB-I00.
- La Generalitat de Catalunya mediante la Ayuda Joan Oró para la contratación de personal investigador (2021FI_B 00308, 2022FI_B1 00082)
- La Universitat Rovira i Virgili mediante la contratación de personal investigador en formación PID2019-109674GB.

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Agradecimientos

Han sido muchas las personas que me han acompañado estos años de doctorado, brindándome su apoyo y ayuda. Esta tesis también es un poquito suya, y por ello, agradezco:

En primer lugar, y como no podía ser de otra manera, a Elena, porque su profesionalidad y sus sabios consejos han sido imprescindibles a lo largo de todo este trayecto. Por transmitirme la pasión por esta química del boro tan peculiar, de la cual haber formado parte me hace sentir orgullosa. Por acogerme en su grupo de investigación, y por sus esfuerzos para que todos nos sintamos a gusto en él; esfuerzos que, por lo menos en mi caso, han resultado indudablemente exitosos.

A todos mis compañeros y excompañeros de grupo, por compartir conmigo la rutina del día a día en el laboratorio y por ese sentimiento de camaradería que nos caracteriza a los 'borillos'. Especialmente, a Paula, a quien espero que esta tesis le sirva un poco de inspiración para la suya, aunque estoy convencida de que, con su capacidad y eficiencia, le espera un prometedor futuro. A Mireia, cuyos inicios como TFG ya predecían la excelente química en la que se está convirtiendo. Ha sido un placer haber estado en parte de ese recorrido, y espero poder seguir siendo testigo de él (y que no me destierre fuera de fronteras, como hace con la mesa). A Ricardo, por haberme demostrado que puedo contar con él, dentro de la química y fuera de ella. Siempre dispuesto a echar una mano, escuchar o apuntarse a unas cervezas, si es necesario. A Oriol, por haber sido el mejor mentor que podría haber pedido, por su voluntad de ayudar a todo aquél que se lo pide, por hacerme soltar carcajadas tan altas y bochornosas y por ser un aliado o rival inigualable, depende de cómo nos levantemos ese día, en juegos y debates. A Dario, quien espero que haya encontrado, al menos, un poco útil alguna de las cosas que le enseñé en el laboratorio. A Alba y a Nerea, quienes sé

que van a hacerse buen cargo del futuro del grupo, y a Stanley, que espero que esté contento con su decisión de unírsenos durante un año.

A todas las personas con quienes he compartido el despacho 229, lugar donde hemos reído (y llorado), hemos celebrado cumpleaños y publicaciones, hemos cotilleado, hemos creado una amplia cultura gastronómica y también, por qué no decirlo, hemos trabajado juntos. En particular, a Anna, por estar preparada cuando he necesitado un poco de charlita y por no dejar que me quede anticuada y enseñarme qué es lo que está a la última en Corea. A Angie, por hacerme sentir comprendida hasta cuando ninguna de las dos estamos entendiendo mucho, por ser mi legítima sustituta, pues opino que el despacho necesita, al menos, una chica con mechas rosas, y, sobre todo, por haber sido mi salvavidas cuando alguien empezaba a hablar de fútbol. A Lola, por darme la primera bienvenida al laboratorio 216 y por la paciencia cuando le demostré lo pesada y preguntona que puedo ser, y a quien voy a echar de menos tener sentada detrás de mí. A Joris, a pesar de que se adueñase de mis tijeras, mis bolis, mi permanganato, y muchas veces invadiese mi vitrina para dejar, a continuación, todo un poco desorganizado (imagino que es cosa de franceses); el tiempo que he pasado en el laboratorio y Tarragona ha sido mucho más divertido gracias a él. A Jordi, por ser un ejemplo de dedicación y por sus intensas conversaciones; a veces motivadoras, otras veces profundas, y, ocasionalmente, sobre la antigua Roma, pero, sin duda, interesantes. A Daniel, porque no me importa mi puntuación en su clasificación, y tampoco voy a hacer *rafting* para mejorarla; él, para mí, es amigo de clase A. Aunque tuvo un despacho para ella sola, a Jessica, por mejorar la estética a la hora de comer con su bonita presentación culinaria. Y, por supuesto, a Pol, quien ya debe estar comprobando que puede huir a miles de kilómetros, que yo mantengo mi amenaza de no permitir que deje de estar presente en mi vida. Como bien dijo Lenny: 'Gracias por ser mi amigo'.

A los técnicos de laboratorio, cuyo trabajo hace mucho más fácil el nuestro. Particularmente, a Raquel, que tantos desaguisados nos ha solucionado

manteniendo su buen humor; y también a Ramón, por la tranquilidad que ha tenido con mis prisas constantes en RMN.

A los científicos con quienes he convivido en vecindad dentro de la Facultad de Química: computacionales, orgánicos y analíticos, por los momentos en los que nuestros mundos paralelos han convergido, y hemos disfrutado de juntos de congresos y eventos de la URV. A Álex, que siendo del ICIQ ha sido siempre bienvenido a los planes del despacho 229, y viceversa. A David, porque entre tanto mediterráneo, a veces se agradece tener a un camarada del Xabarín Club.

A Belén, por permitirme unirme a su grupo durante tres meses y por su trato profesional y amable durante ese período en Estocolmo. A todos sus integrantes, destacando a Bea, María, y Há, porque por poquito me hacéis no echar de menos al mío. También a Aitor, por haber sido :) conmigo desde el primer día y a Miguel, que cuida de mi ex-monstera. Y, por supuesto, a quienes me hicieron sentir una más y me permitieron ser parte de planes increíbles: Laia, Sara, Juan Carlos y Antía.

A mis amigas de Ponfe, con las que hasta de vacaciones me he podido desahogar hablando de química y del laboratorio, a pesar de que a ellas este mundo de moléculas y reactivos les resulte un poco extraño. A mis amigos Marina, José y, de manera especial, a Carol, porque no nos importa mucho dónde, pero siempre tenemos un nuevo destino propuesto para poder vernos. A mis compañeros de piso, que han sido obligados a soportar mis historias y anécdotas, mientras cenábamos o merendábamos, cuando no podían huir.

Por último, a toda mi familia, y más especialmente a mi hermana, María, y a mis padres, Olga y Anselmo, por su constante apoyo, por ayudarme en todo momento en el que los necesito, aunque sea en la distancia, y por su paciencia y comprensión, incluso cuando tenemos opiniones diferentes en cuanto a la frecuencia con la que debería llamar por teléfono.

Mil gracias a todos vosotros.

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CHAPTER 1

General Introduction and Objectives

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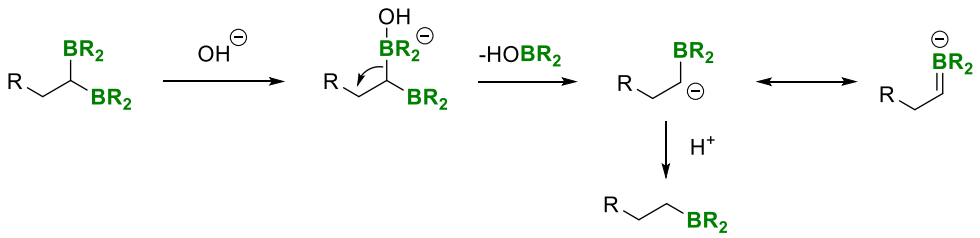
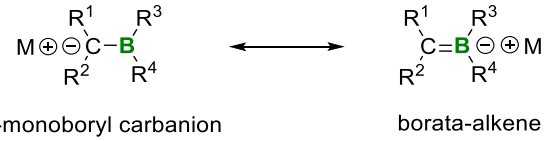
1.1 Historical background and definition of borata-alkene species

The first depiction of a C=B bond within borata-alkene species occurred in 1961 proposed by Brown and Zweifel.[1] After the observation of the hydrolytic instability of the geminal diborated products, they hypothesized the loss of one of the carbon-boron bonds through the stabilization of an α-boryl carbanion, leading to a borata-alkene intermediate (Scheme 1.1). Furthermore, in 1966, Zweifel and Arzouman offered additional insights into the stabilization of the carbanion, attributing this phenomenon to the unoccupied p orbital located in the neighboring boron atom.[2,3]



Scheme 1.1. Original proposal for the stabilized α-boryl carbanion.

Thus, the borata-alkene synthon $[CH_2{=}BR_2]^-$ is a formal expression of stabilized α-monoboryl carbanions due to the deficiency in valence of the adjacent three-coordinated boron center. Borata-alkene intermediate and α-boryl carbanion structures can be illustrated as resonance forms (Scheme 1.2).[4,5]



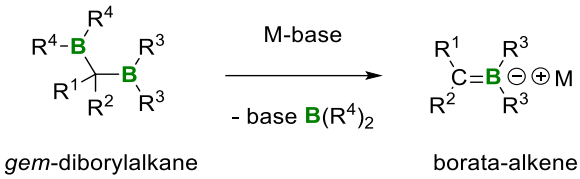
Scheme 1.2. Resonance forms of borata-alkene species.

This introduction is aimed to provide a precise view on the most relevant synthetic methods to synthesize borata-alkene species, but also to give some clues about characterization methods and application protocols.

1.2 Synthesis of borata-alkenes

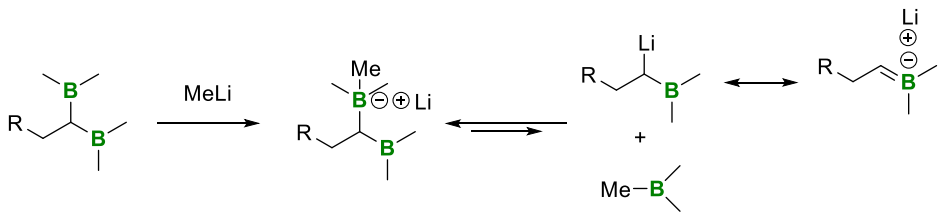
1.2.1 Monodeborylation of *gem*-diboryl alkanes

The synthesis of α-boryl carbanions, and hence their respective borata-alkene representation, can be carried out *via* deborylation of *gem*-diborylalkanes (Scheme 1.3). This is a well-established procedure in organic chemistry.[4,5]



Scheme 1.3. Mechanism for monodeborylation of *gem*-diboryl alkanes.

In agreement with their prior results, in 1971 Zweifel and co-workers conducted NMR studies which confirmed that the addition of methyllithium as a base to *gem*-diboryl alkanes gave the corresponding boron'ate' complex (Scheme 1.4).[2,3,6,7] The utilization of alkyl lithium reagents to deborylate *gem*-diboryl alkanes was also observed by Zubiani and co-workers in 1966, with the use of MeLi or BuLi.[8]

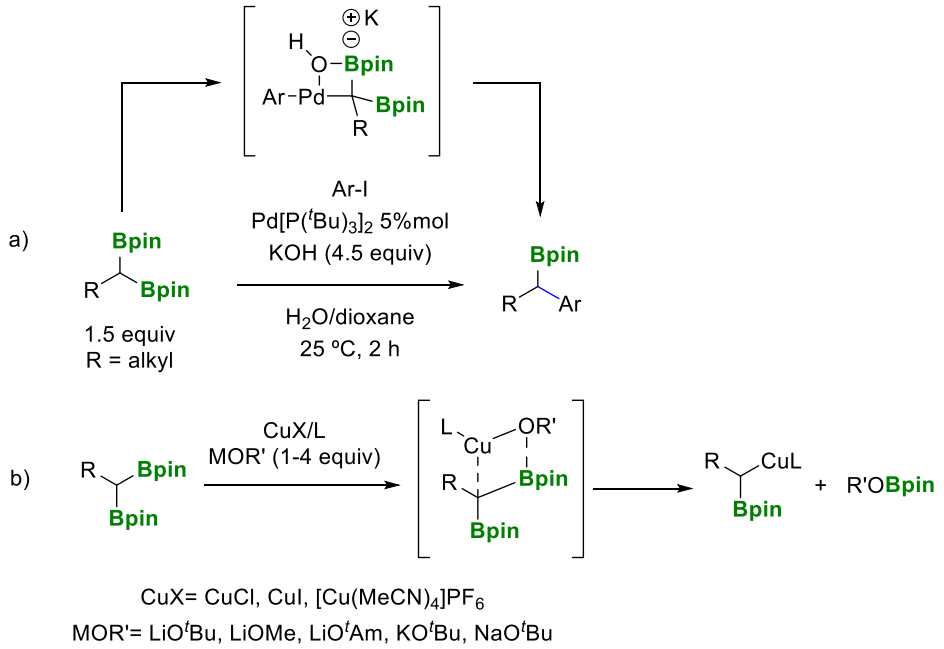


Scheme 1.4. Monodeborylation of a *gem*-diboryl alkanes with MeLi as base.

Shibata and co-workers have reported that the Pd-catalyzed deborylative arylation of *gem*-diborylalkanes afforded the corresponding benzyl borylated products through a Suzuki–Miyaura cross-coupling reaction. The key to success is the generation of a monoboron'ate' intermediate by virtue of the adjacent boron atom in 1,1-diborylalkanes, which prevents the β-hydride elimination process (Scheme 1.5a). The base played an important role in the reaction. The

utilization of strong bases such as LiOH, NaOH and KOH was crucial for promoting the reaction.[9,10]

In addition, Cu (I) salts are also involved in the deborylation of 1,1-diborylalkanes to deliver the corresponding α-boryl carbanions, essentially performed *in situ*. Alkoxy groups (-OR') and stabilizing ligands, such as mono and diphosphines, comonly promote the σ-bond metathesis pathway, involving the concurrent formation of R_2'B-OR'' as a by-product (Scheme 1.5b).[11]

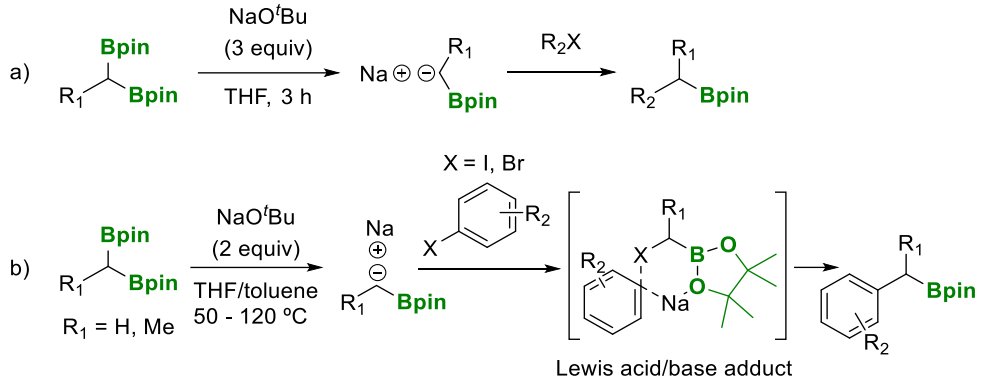


Scheme 1.5. *In situ* formation of a) borylalkyl Pd (II) species b) borylalkyl copper (I) species.

Without the use of transition metals catalysts, Morken and co-workers described an alkoxide-promoted deborylative alkylation of geminal boronates. These reactions proceed through the intermediacy of α-boryl carbanions, whose formation was examined using different MOR' bases (Scheme 1.6a).[12]

Alternatively, Cho's research group developed a new borylation method for aryl and vinyl halides using *gem*-diborylalkanes as the boron source.[13] The combination of 1,1-bis[(pinacolato)boryl]alkanes with NaO^{t}Bu, as a base,

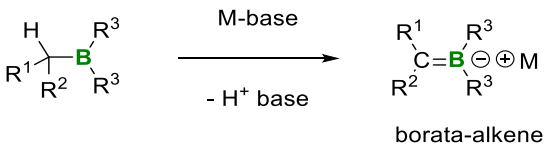
generated an α-boryl carbanion *in situ*, to form an unusual Lewis acid/base adduct with the organohalide reactant (Scheme 1.6b). [13]



Scheme 1.6. α-Boryl carbanion formation *via* alkoxide-promoted deborylative a) alkylation and b) arylation.

1.2.2 Deprotonation of the α-hydrogen from an organoborane compound

The addition of base to an organoborane normally results in the coordination of the base to the boron atom, as illustrated in the previous section. However, Rathke and Know observed that using a base with large steric requirements avoids coordination to boron, and promote the deprotonation of the acidic α-hydrogen contributing to the borata-alkene formation (Scheme 1.7).[14,15]

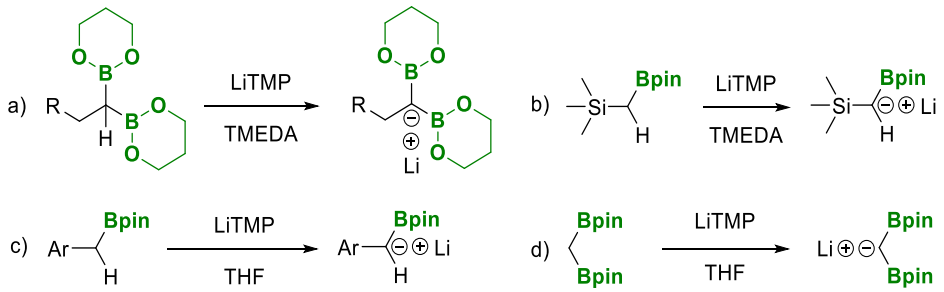


Scheme 1.7. Mechanism for deprotonation of the α-hydrogen from an organoborane compound.

In fact, Matteson and co-workers were able to successfully generate 1,1-bis(dioxaborinyl)alkyllithium reagents through the α-deprotonation of geminal bis(boronates), preserving the integrity of the geminal boryl groups.[16] The intermediate was synthesized using lithium 2,2,6,6-tetramethylpiperidide

(LiTMP) as the base, in the presence of tetramethylethylenediamine (TMEDA) as an activator (Scheme 1.8a).[16,17] Further, it was extended to the α-lithiation of α-(silyl)alkaneboronates, therefore pinacol(trimethylsilyl)borylmethane was transformed to the corresponding lithio(trimethylsilyl)borylmethane using the same procedure (Scheme 1.8b).[18]

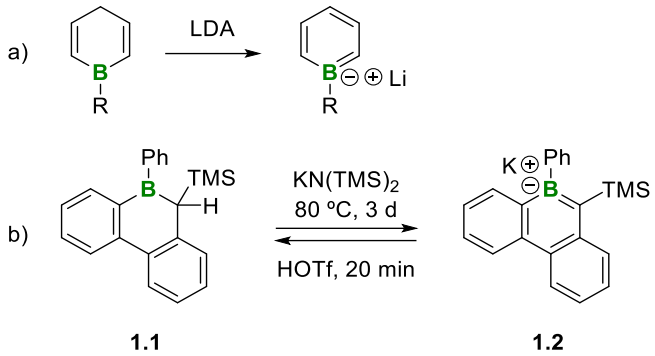
Moreover, Zhan and co-workers disclosed the generation of α-boryl anions by deprotonation of benzyl boronates with LiTMP in tetrahydrofuran (THF) (Scheme 1.8c). Benzylboronates bearing groups like halides, alkyls, naphtil or Bpin moiety were well tolerated and then, diverse electrophiles could be incorporated to the α position.[19,20] More recently, Morken and co-workers have followed a similar procedure to activate readily accessible 1,1-bis(pinacolboronates) with LiTMP, to subsequently react with aldehydes to furnish a variety of synthetically useful di- and trisubstituted alkenylboronic esters (Scheme 1.8d).[17]



Scheme 1.8. α-Deprotonation for a) *gem*-diborylalkanes, b) α-(silyl)alkaneboronates, c) benzyl boronates and d) commercially available 1,1-bis(pinacolboronate).

The removal of the α-hydrogen, adjacent to a tricoordinate boron atom, led to the synthesis of different lithium boratabenzenes (Scheme 1.9a).[21] Martin and coworkers have found that the deprotonation of compound 9-borataphenanthrene **1.1** is a viable method to prepare boratabenzene-containing species. Potassium bis(trimethylsilyl)amide $KN(TMS)_2$ proved to be a suitable base for the formation of borataphenanthrene anion **1.2** (Scheme

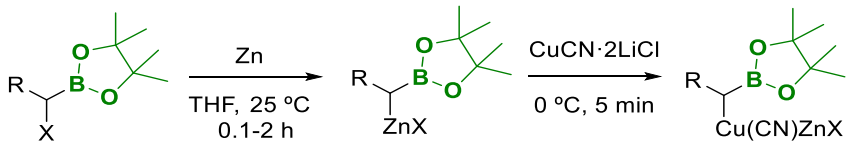
1.9b), which reveals a remarkable reactivity pattern of both boratabenzenes and borata-alkenes.[22]



Scheme 1.9. Formation of a) lithium boratabenzenes and b) 9-borataphenanthrene anion *via* α-deprotonation.

1.2.3 Metallation of α-halo boronic esters

Knochel reported a general route involving the reaction of α-halo boronic esters with Zn and Cu to produce α-(dialkoxyboryl)alkyl zinc and copper organometallic species, respectively.[23] First, zinc borata-alkene compounds are formed, which can be transformed into the more reactive copper compounds through a reaction with copper(I) cyanide dilithium chloride complex (CuCN·2LiCl) in THF (Scheme 1.10).[4,23,24]

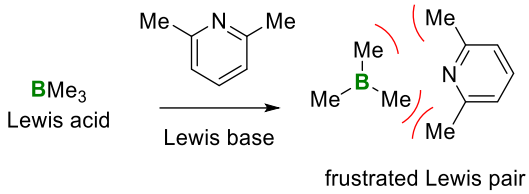


Scheme 1.10. Synthesis of zinc borata-alkene and copper borata-alkene species *via* metallation of an α-halo boronic ester.

1.2.4 Frustrated Lewis Pair

The term "frustrated" Lewis pair (FLP) describes the inherent driving force of a Lewis pair to interact through the Lewis-basic and Lewis-acidic site to form a

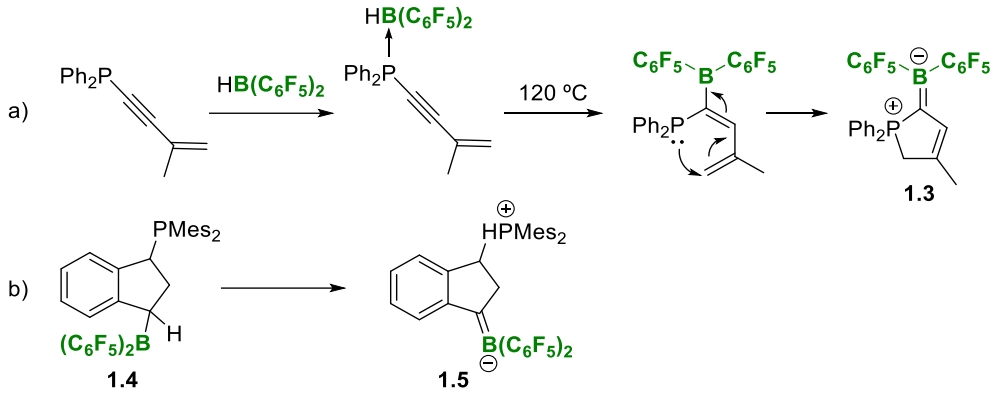
Lewis adduct, which is prevented by steric and electronic prerequisites (Scheme 1.11).[25]



Scheme 1.11. Example of the frustrated Lewis pair adduct.

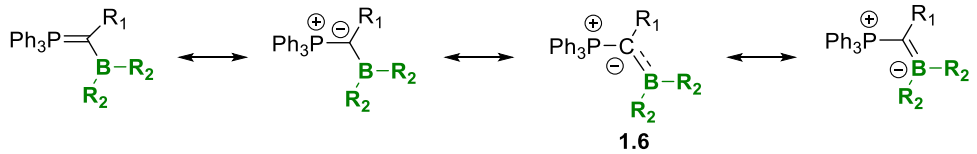
By employing this methodology, the base-free synthesis of a stable borata-alkene zwitterion **1.3** has been obtained through the ring closing of an *in situ* formed P/B system. This mechanism is postulated to occur rapidly through an intramolecular conjugate addition promoted by FLP forces (Scheme 1.12a).[14,26,27]

The attachment of strongly electron-withdrawing C_6F_5 substituents on boron has been confirmed to significantly enhance the CH acidity in the α-position, which favors the formation of the borata-alkene specie. However, the strongly enhanced Lewis acidity makes these boranes prone to facile Lewis acid/Lewis base adduct formation under conventional deprotonation conditions.[14,28] In the P/B system **1.4**, both intra or intermolecular Lewis pair adduct formation was effectively hindered. Instead, the α-deprotonation by the bulky $PMes_2$ base in the P/B system **1.4** can take place to form the zwitterionic borata-alkene/phosphonium compound **1.5** (Scheme 1.12b).[14]



Scheme 1.12. FLP forces towards zwitterionic phosphonium/borata-alkenes formation by a) intramolecular conjugate addition and b) α-deprotonation by the bulky $PMes_2$ base.

On the other hand, Breher and co-workers were able to generate α-borylated phosphorus ylide (α-BCP) with a significant borata-alkene character (Scheme 1.13). This was achieved by generating electronic frustration by competition for a lone pair of electrons, thus inducing high polarity within a C–B π-bond, as **1.6** shows.[23,29]

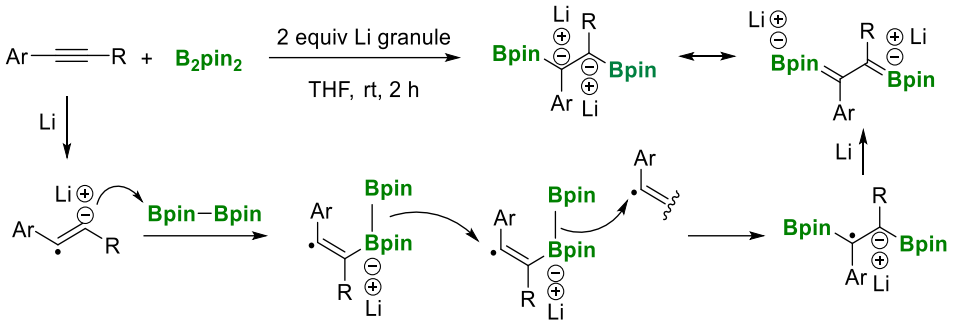


Scheme 1.13. Resonance structures of an α-borylated phosphorus ylide.

1.2.5 Nucleophilic attack on the boryl moiety

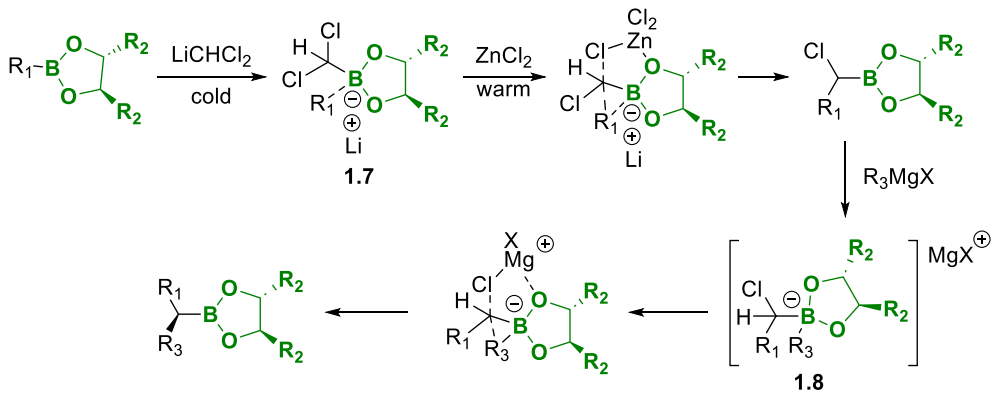
Yorimitsu and co-workers, have discovered that diborative reduction of alkynes occurred in the presence of bis(pinacolato)diboron and alkali metals to afford 1,2-diboryl-1,2-dimetalloalkanes, facilitated by vinylic radical anion intermediates.[30] This led to the simultaneous formation of two carbon–boron bonds and two carbon–alkali metal bonds in one operation. Alkoxy-substituted B_2pin_2 is resistant to reduction by alkali metals. On the other hand, because of the vacant p orbitals of the boron atom, B_2pin_2 can rapidly react with the vinylic anionic species, to suppress the undesired protonation or oligomerization.

Moreover, the vacant p orbitals of the boron atoms, in the installed 1,2-dianionic species contribute to its sufficient stability by delocalizing the negative charge (Scheme 1.14).[30]



Scheme 1.14. Diborylative reduction of alkynes.

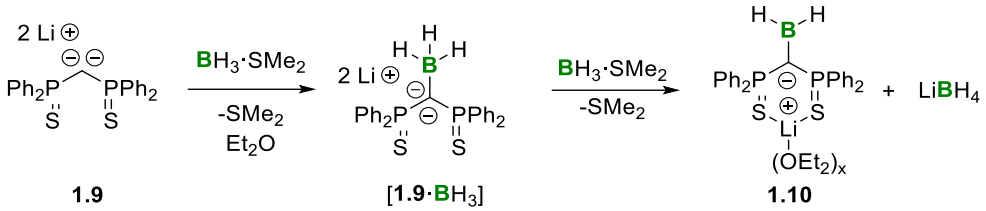
Previously, Matteson and co-workers had reported an (α-haloalkyl)boronic ester homologation that took advantage of the formation of intermediate borate complexes in an iterative two-step sequence (Scheme 1.15). It starts with the displacement of a leaving group from the α-carbon atom of an alkylboronic ester with the addition of (dichloromethyl)lithium towards the formation of the (dichloromethyl)borate complex **1.7**. To conclude the homologation, a Grignard reagent leads to the borate anion **1.8**, that evolves the substitution reaction.[31,32]



Scheme 1.15. Matteson homologation mechanism.

Additionally, in a reaction described by Mézailles and co-workers, the nucleophilic dianion **1.9** attacks to $BH_3{\cdot}SMe_2$ to result in the formation of

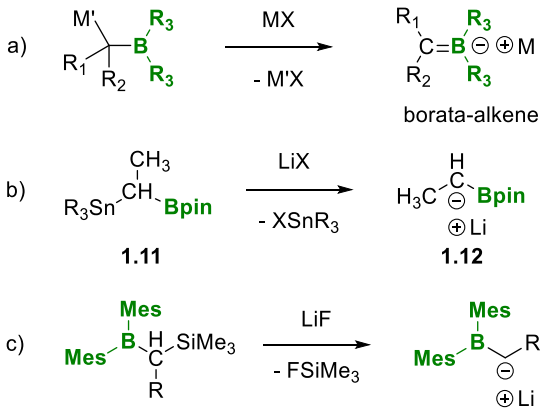
intermediate [**1.9**·BH_3], as it illustrates the Scheme 1.16. They showed that the dianion is able to stabilize BH_2^+ cation, yielding the zwitterionic organoborane **1.10**.[33]



Scheme 1.16. Formation of borata-alkene species by nucleophilic attack to BH_3 ·SMe_2.

1.2.6 Transmetallation of α-borylmethide metal salts with organometallic reagents

Boron-stabilized carbanions can also be generated by transmetallation of α-borylmethide metal salts with organometallic bases, following the mechanism illustrated in Scheme 1.17a. The α-trialkylstannyl boronic ester **1.11** reacts with LiX, resulting in the formation of (1-lithioethyl)boronic ester (**1.12**) through the exchange of Sn with Li cation (Scheme 1.17b). Notably, the interaction of LiF with dimesitylboryl (trimethylsilyl)alkanes also yields α-boryl carbanions, with the formation of $FSiMe_3$ (Scheme 1.17c).[34]



Scheme 1.17. a)Transmetallation towards borata-alkene formation, b)Li/Sn transmetallation pathway, c) Li/Si transmetallation step.

1.3 Characterization of borata-alkenes

The stabilization and reactivity of borata-alkenes are related with the electron distribution in the σ bonds between the α-carbanionic center and the adjacent boron atom, which delocalizes the electron density throughout its empty p orbital. The suggested hyperconjugation is consistent with experimental outcomes. Structural parameters such as bond lengths and angles, spectroscopic data and nuclear shielding of the nuclei involved are affected by marked changes. [5,35,36]

1.3.1 Characterization by X-ray diffraction

The first X-ray crystal structure of a boron-stabilized carbanion was described by Power in 1986.[37] The anion was made by deprotonation of $BMes_3$ with ^{n}BuLi and it was treated with a crown ether salt for its crystallization, forming the $[Li(12\text{-crown-}4)_2]$ salt **1.13** (Figure 1.1a). Comparing it with triaryl- or trialkylboranes, the C-B bond length was significantly shorter (1.522 Å), establishing the structure of the anion as shown in the Figure 1.1a. It also suggested that the stability is mainly due to delocalization of the negative charge.[37]

Following this procedure, the same authors were also able to crystallize and characterize the borata-alkene $[CH_2BMes_2]^-$ **1.14** (Figure 1.1b), where the bulky substituents on boron played a crucial role in providing the necessary stabilization.[38] When 2 equiv of 12-crown-4 were added to the THF solution of its lithium salt, crystals were obtained in a 40% yield as colorless parallelepipeds. The C-B bond exhibit a length of 1.440 Å, consistent with a boron-carbon double bond formulation.[38]

In a more recent development, an additional borata-alkene structure was successfully crystallized by employing a suitable base for deprotonation, lithium 2,2,6,6-tetramethylpiperidide (LiTMP), resulting in a borata-alkene product

1.15 isolated as a yellow solid in 67% yield (Figure 1.1c).[39] The method for obtaining single crystals suitable for the X-ray crystal structure analysis was carried out by slow evaporation of a pentane solution at −32 °C. Molecules of the composition of **1.15**[LiHTMP] were isolated in the crystal. The length of the typical borata-alkene B-C double bond linkage was determined to be 1.468 Å and the coordination geometry of the boron atom was stablished as trigonal planar. In the same work, the role of the lithium cation in influencing the typical features of the borata-alkene system was investigated. The Li^+ free salt **1.15** was synthesized through cation exchange. A comparison of the structural data of the two compounds reveals a remarkable similarity, suggesting that the cations have a marginal influence on the structural features of the borata-alkene moiety in **1.15**.[14]

On the other hand, the characteristic distance of 1.444 Å between the B-C bond in a borata-alkene specie was determined in the X-Ray diffraction analysis of the previously mentioned zwitterionic heterocyclic phosphonium borata–alkene **1.3** (Figure 1.1d). Notably, a Li^+ counter ion was not needed for the crystallization.[26]

Since the coordination chemistry of borata-alkenes as ligand motifs has attracted increasing attention in recent years, several metal borata-alkene complexes have been isolated and characterized by X-ray diffraction. Crystallographic evidence revealed a η^2-coordination in borata-alkene tantalocene complex. Species **1.16a** and **1.16b** include Ta–B distances of 2.729 and 2.739 Å, and B–C distances of 1.509 and 1.526 Å, which are intermediate between typical B–C(sp^3) bond distances (1.578 Å for BMe_3) and B=C(sp^2) (Figure 1.1e).[23,39]

The borata-alkenes application as polar alkene ligand analogues in organometallic and coordination chemistry was extended following the aforementioned seminal study.[29] To date, an example of this development was seen in the syntheses of methylene-bridged chelate phosphane/borata-alkene

Rh complexes **1.17** (Figure 1.1f) and **1.18** (Figure 1.1g),[40] or transition metal complexes including elements such as Mo (Figure 1.1h **1.19a**), W (Figure 1.1h **1.9b**),[41] Cu (Figure 1.1h **1.20a**), Zn (Figure 1.1i **1.20b**) or Au (Figure 1.1i **1.20c**).[42]

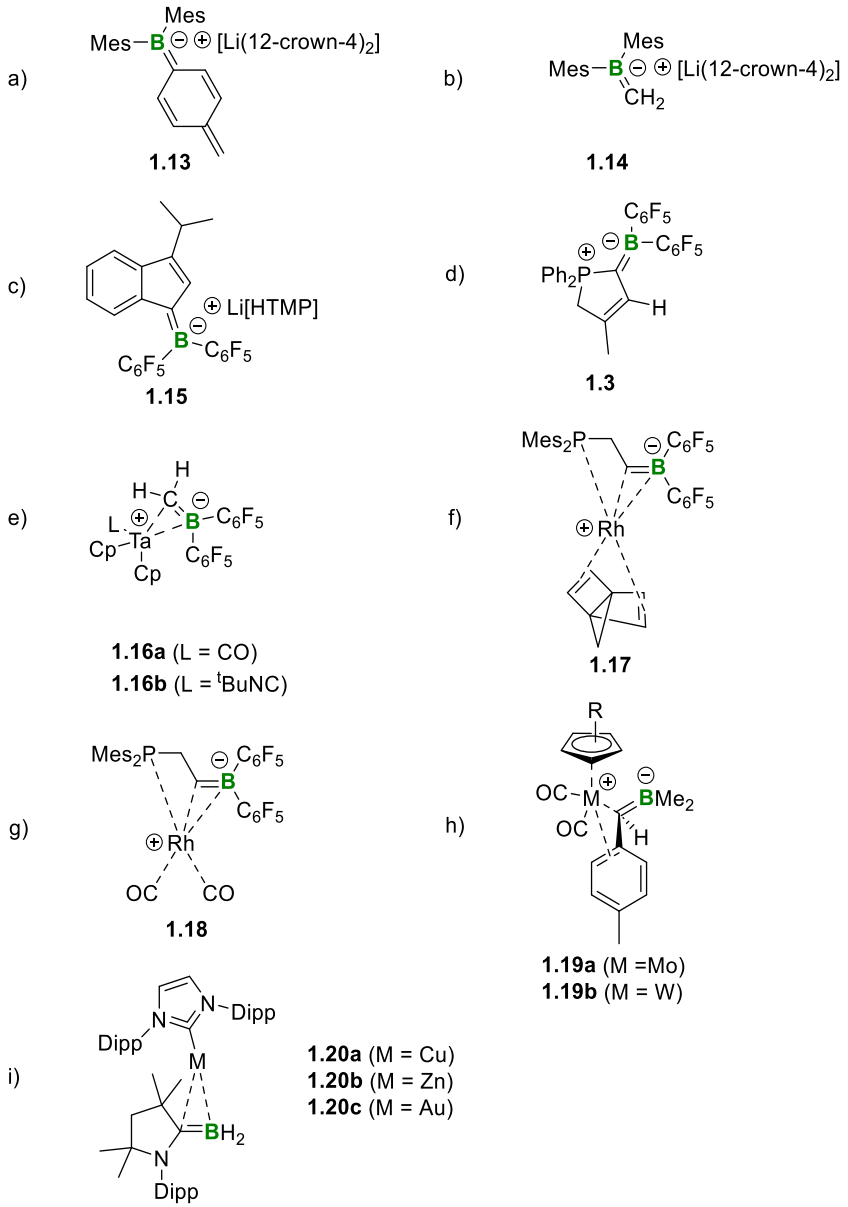


Figure 1.1. Structure of borata-alkenes complexes.

1.3.2 Characterization by Nuclear Magnetic Resonance (NMR)

Depending on the nature of the boron and carbon substituents, the Nuclear Magnetic Resonance (NMR) spectroscopy can be used as a straightforward analysis to predict the weak or strong borata-alkene character.

Regarding the ^{11}B data NMR, it is noteworthy to mention the high-field chemical shifts observed in borata-alkene motifs when compared to the corresponding α-boryl alkanes. For instance, the ^{11}B NMR spectrum of compound **1.21** (Figure 1.2a) in C_6D_6 revealed a single signal at δ=67.2 ppm, aligning with the signals observed for triarylboranes, like trimesitylborane (δ=76.8 ppm).[43] In contrast, the compound **1.22**, crystalized in a tetramethylethylenediamine (TMEDA) solution (Figure 1.2b), exhibited a peak in higher field, at δ=45.5 ppm in deuterated tetrahydrofurane (THF-d_8).[44]

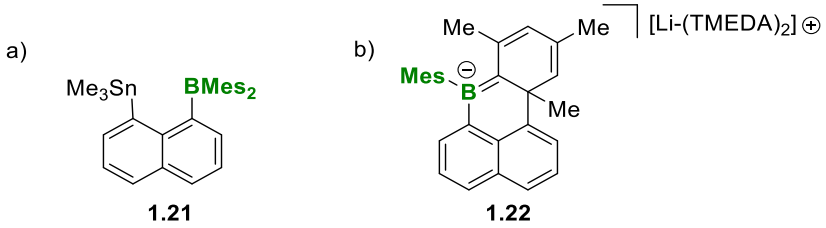
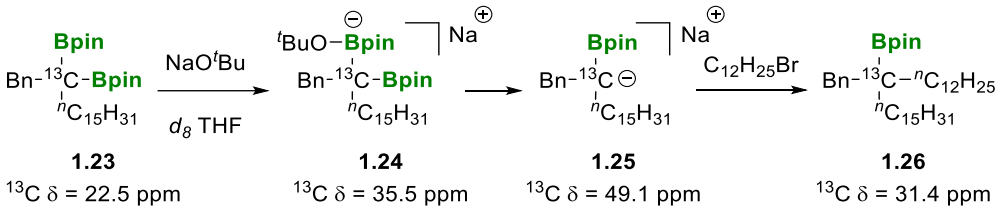


Figure 1.2. Structure of the compounds analyzed by ^{11}B NMR a) 1-(Dimesitylboron)-8-(trimethyltin)naphthalenediyl and b) borataalkene salt-Li(TMEDA)$_2$.

Another example would be the trend in ^{11}B NMR chemical shifts observed during the deprotonation of Mes_2BCH_3 to yield the $Mes_2B{=}CH_2^-$ anion **1.14** (Figure 1.1b). A THF solution of Mes_2BCH_3 exhibited a broad singlet at +83.6 ppm. Following the addition of $LiN(C_6H_{11})_2$ in THF, a new signal at +40.4 ppm emerged, presumably attributed to the solvated ions $[Li^+][Mes_2BCH_2]$. Upon introducing 12-crown-4 to this solution, a slight upfield shift to +35.0 ppm was observed. The modest, yet significant, shift observed upon the addition of 12-crown-4 suggests a potential association between [Li]+ and $[Mes_2BCH_2]^-$ ions in THF solution in the absence of 12-crown-4.[38]

On the contrary, the ^{13}C NMR data for the borata-alkene appears at downfield chemical shifts, in agreement with the acquired sp^2 character of C in the borata-alkene when it is compared with the corresponding boranes. To give an example, in the analysis of α-boryl carbanions, Morken and co-workers analyzed by ^{13}C NMR compound **1.23**, possessing a ^{13}C-labeled peak at δ=22.5 ppm (Scheme 1.18). When reacted with NaO^{t}Bu in THF, it resulted in the formation of product **1.24** (^{13}C δ=35.5 ppm), corresponding to the boron'ate' complex, and **1.25** (^{13}C δ =49.1 ppm), which was formed more slowly than **1.24**. Upon addition of bromododecane to the reaction mixture, the resonance at 49.1 ppm was immediately replaced with a resonance at 31.4 ppm, the latter of which corresponded to deborylative alkylation product **1.26**. Notably, the chemical shift of putative intermediate **1.25** is far more downfield than is typical for an alkali-metal-derived carbanion (^{13}C δ=−15.3 ppm for CH_3Li), presumably due to the delocalization of the electron density in the C═B bond.[12]



Scheme 1.18. ^{13}C NMR to identify compounds involved in deborylative alkylation.

1.3.3 Characterization by Infrared (IR)

One of the simplest examples of borata-alkene, $Me_2BCH_2^-$ anion (Figure 1.1b), has been characterized using IR multiple photon dissociation technique. Morton and co-workers reported, for the first time, the spectra of $Me_2B{=}CH_2^-$ in the gas phase. The obtained spectra were in good agreement with those predicted by DFT calculations. Consequently, IR spectra of gaseous $Me_2B{=}CH_2^-$ indicates that the B–C bonds in the anion $Me_2B{=}CH_2^-$ are weaker than the strong B–C bonds of trimethylboron, suggesting hyperconjugation in the borata-alkene fragment.[45]

1.3.4 Characterization by density functional theory (DFT)

To gain more insight into the electronic structure and the reactivity trends of α-boryl-carbanions, R. Maza et al. conducted a detailed computational study.[5] Different α-boryl carbanions were analyzed, studying their electronic structures and reactivity trends influenced by the nature of the different boryl moieties, carbanionic substituents, the numbers of boryl motifs, and the metal involved.

Overall, the study determined that the free carbanionic intermediates were better described as borata-alkene species. π-Acidic boron atoms (i. e., $BMes_2$ or $B(C_5F_5)_2$), aromatic substituents on boron (i. e., Bdan), or electron withdrawing substituents on carbon induced a larger delocalization of the carbanionic charge through the π-channel, that resulted in a more stable and less reactive intermediate. Multi-boryl species showed very polar C–B bonds, while losing some borata-alkene characteristics. Some of these trends have been displayed in Figure 1.3.[5, 46]

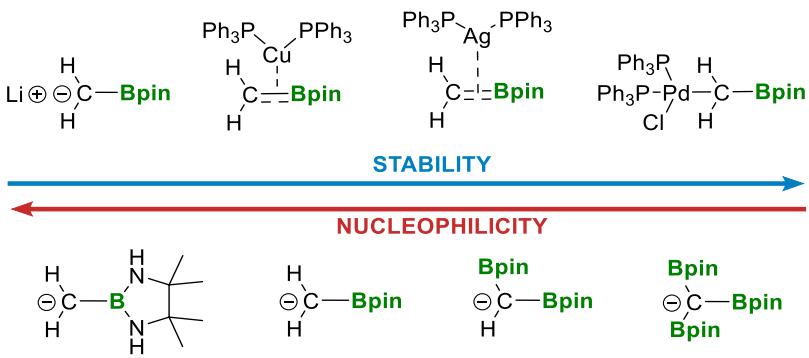


Figure 1.3. Trends towards stability and nucleophilic character on representative α-borylstabilized carbanions.

The electronic structure of borata-alkenes is highly unsymmetrical. Carbon 2p orbital has much higher contribution to the HOMO, and the boron 2p orbital has much higher contribution to the LUMO. Due to this asymmetry, when a metal is involved, M-B interactions will be favored for electron rich transition metals, and M-C interactions will be favored for electron-deficient transition metals.[24]

Thus, α-boryl carbanions can be classified in three different type of α-boryl alkylidene metal species: 1) borata-alkene salts with alkali and alkaline earth metals such as Li (Figure 1.4a), 2) η2-(C–B) borata-alkene complexes with early transition metals, Cu and Ag (Figure 1.4b), and 3) α-boryl alkyl complexes with late transition metals such as Pd (Figure 1.4c).[5]

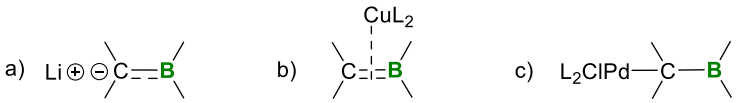


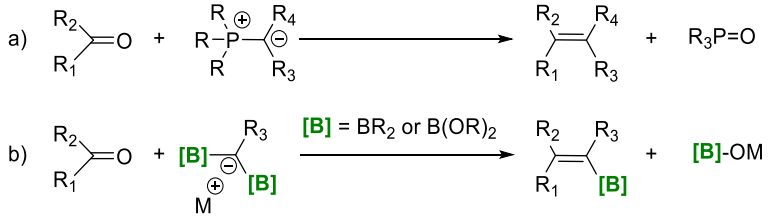
Figure 1.4. The three binding modes of borata-alkenes a)borata-alkene salt, b) η2-(C–B) borata-alkene complexes and c) σ bond with α-boryl alkyl complexes.

1.4 Application

Based on the previously mentioned propierties of borata-alkenes, and consequently the diverse types of α-boryl species, through their electronic and steric properties, it has been possible to justify the observed reactivity trends.[5]

1.4.1 Boron-Wittig reaction

One of the most extended applications of α-boryl carbanions synthons is the boron-Wittig reaction.[47] Similar to the original Wittig olefination (Scheme 1.19a), where alkenes are synthesized by the reactivity between aldehydes or ketones with ylides generated from phosphonium salts, the α-bis(boryl)carbanions can be employed in the boron-Wittig reaction (Scheme 1.19b).[47]

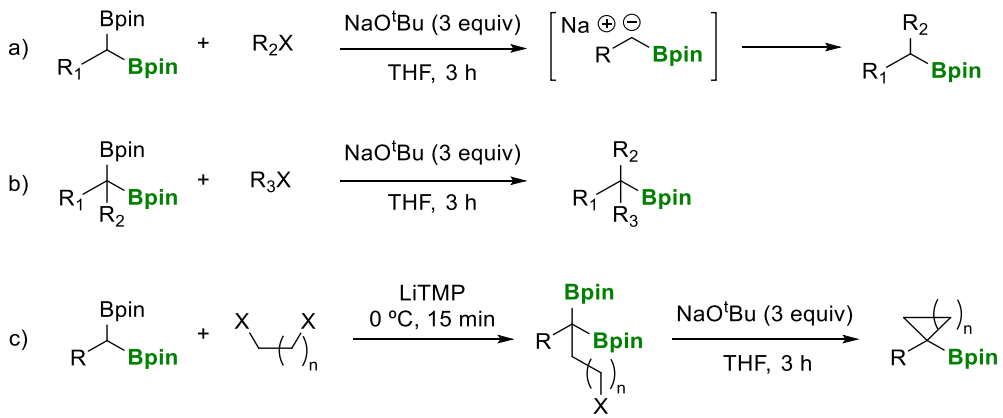


Scheme 1.19. Mechanism of a) Wittig olefination and b) boron-Wittig olefination.

1.4.2 Reactions with electrophiles

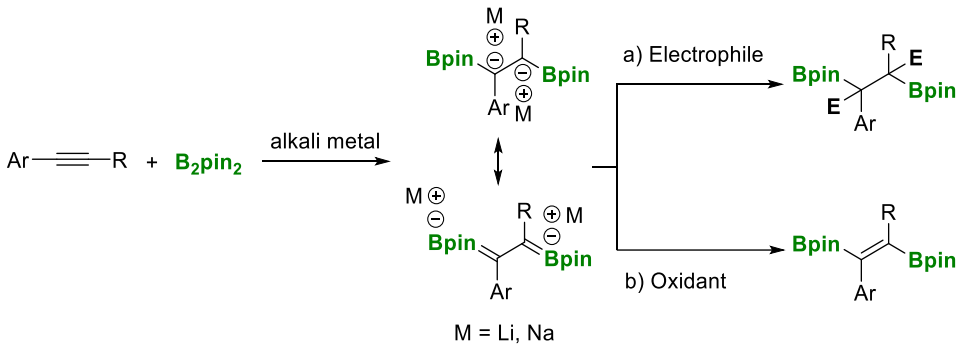
Borata-alkene salts show highly polarized metal-carbon interactions and a significant nucleophilic character, which makes them suitable for reacting with electrophiles.[5]

Morken and co-workers have successfully obtained borata-alkene species without utilizing transition metals catalysts achieved by the monodeborylation of *gem*-diboryl alkanes.[12] They also established an electrophilic trap of the α-boryl anions, synthesizing primary, secondary, and tertiary alkylboronic esters with high efficiency and simplicity. In Scheme 1.20a, the reaction between monosubstituted geminal boronates and primary halides is displayed, yielding secondary organoboronates. This method has proved a high versatility, evidenced in the substrate scope as well as the electrophiles employed for the alkylation. Moreover, it is effective with secondary alkyl bromide electrophiles and allylic chlorides, *via* an S_N2 mechanism. Deborylative alkylation of internal geminal bis(boronates) is also feasible (Scheme 1.20b), along with intramolecular deborylative alkylation for the formation of carbocyclic organoboronates (Scheme 1.20c).[12]



Scheme 1.20. Base-promoted activation of geminal diborylalkanes for a, b) alkylation with primary halides and c) intramolecular alkylation.

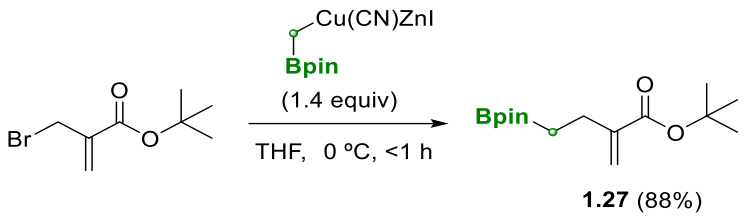
Another reaction involving electrophiling trapping with borata-alkenes salts involves the formation of 1,2-diboryl-1,2-dimetalloalkanes (Scheme 1.14). When the 1,2-dianionic species were treated with electrophiles (MeOD for deuteration, dimethyl sulfate and 1,3-dichloropropane) 1,2-diborylalkanes were formed with certain diastereoisomery (Scheme 1.21a). In addition, the oxidation of 1,2-dianionic specie with 2,3-dibromobutane furnished the corresponding 1,2-diborylalkene product with preferential *E* stereoisomery (Scheme 1.21b).[30]



Scheme 1.21. Diborative reduction of alkynes to 1,2-diboryl-1,2-dimetalloalkanes to form a) 1,2-diborylalkanes and b) 1,2-diborylalkenes.

Borata-alkene complexes with transition metals such as Cu(I), can trap several electrophilic reagents in an efficient way. Additionally, the modification of Cu(I) complexes with chiral ligands, induces asymmetric platforms towards the synthesis of enantioenriched organoboron compounds.[11]

The zinc borata-alkene and specially the more active copper borata-alkene salt, synthesized by metallation of an α-halo boronic ester performed by Knochel, has exibited excellent reactivity toward allyl halides.[11,23] This is evidenced in the model reaction involving *tert*-butyl α-(bromomethyl)-acrylate with (Bpin)CH_2Cu(CN)Znl (Scheme 1.22). Product **1.27** showed control over chemoselectivity, with the α,β–unsaturated ester remaining inert while efficient alkyl bromide substitution occurs.[11]

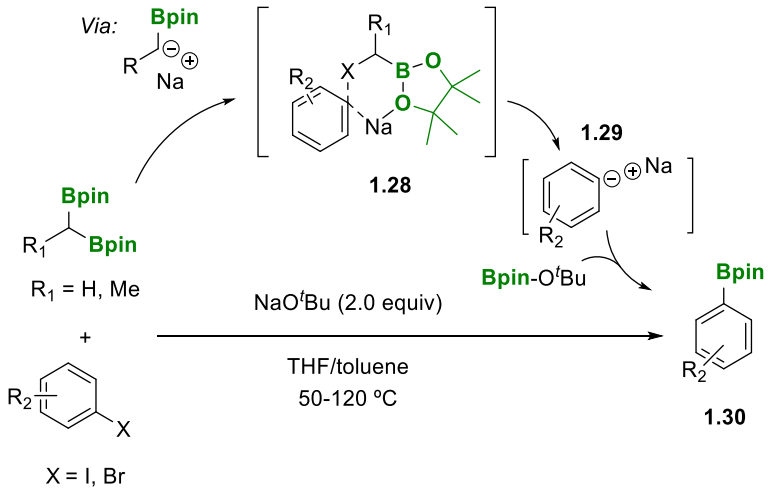


1.27 (88%)

Scheme 1.22. Copper catalyzed allylation between *tert*-butyl α-(bromomethyl)-acrylate with (Bpin)CH_2Cu(CN)ZnI.

1.4.3 C-B bond formation

The generation of carbon–boron bonds in aryl halides using *gem*-bis[(pinacolato)boryl]alkanes has been developed by Cho.[13] As illustrated in Scheme 1.6b, NaO^{t}Bu has been used as a base to generate an α-boryl carbanion that can form acid/base adducts between α-[(pinacolato)boryl]alkylanions and organohalides.[13,48] Six-membered coordinated intermediates **1.28** are formed to subsequently release sodium aryl anion species **1.29**. When [(pinacolato)boryl]iodoalkanes or *tert*-butoxyboronate ester are employed as the boron source, carbon–boron bonds are efficiently built towards aryl and alkenylboronic ester **1.30** in good yields (Scheme 1.23).[48]



Scheme 1.23. Borylation of aryl halides with *gem*-bis[(pinacolato)boryl]alkanes.

1.4.4 C-C bond formation

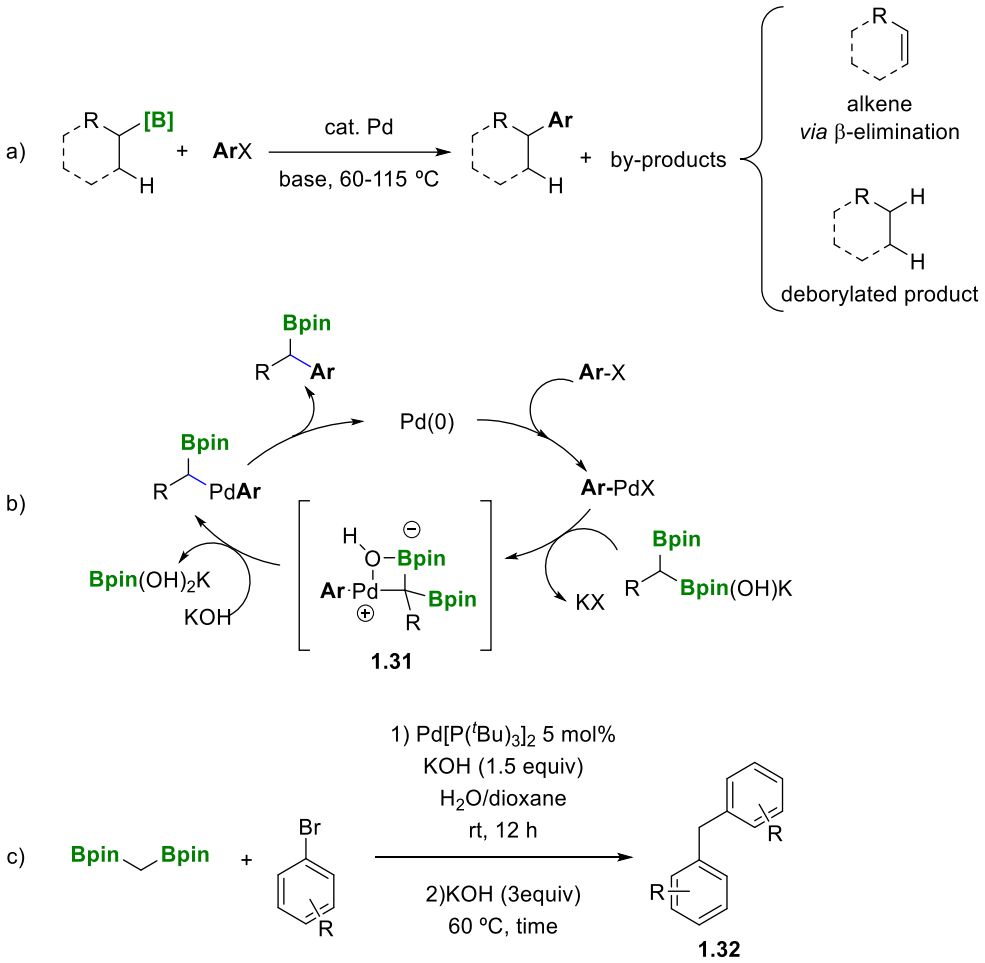
Since α-boryl alkyl complexes with late transition metals have a less polarized and stronger metal-carbon bond, they are prone to undergoing other types of C–C bond forming reactions, such as cross-coupling through transmetallation strategies.[5]

Typically, Suzuki–Miyaura cross-coupling (SMC) reactions have been a reliable method for C–C bond formation. However, when organoboronates were involved, some challenges had to be faced, including slow transmetallation, subsequent β-hydride elimination, and protodeboronation (Scheme 1.24a). Shibata and co-workers have demonstrated the usefulness of 1,1-diborylalkanes for chemoselective and regiospecific SMC at room temperature, in order to address these limitations.

The viability of the reaction is attributed to the formation of a monoborate intermediate, generated with a suitable base. Scheme 1.24b demonstrates how the transmetallation between ArPdX and potassium borate provides the σ-alkyl-PdAr intermediate **1.31**, which is sufficiently stable to prevent reductive elimination. Notably, only one boronate complex is formed, even in the presence of excess of a base. After the first catalytic coupling reaction, the mono-boronate compounds are produced but would not undergo further cross-coupling reaction under the same reaction conditions.[9,10]

Likewise, this approach has subsequently been applied to the synthesis of both symmetrical and unsymmetrical derivatives of diarylmethanes **1.32** (Scheme 1.24c)**.** The reaction conditions can be modulated by adjusting both the reaction temperature and the amount of base in a *one-pot* process. This type of cross-

coupling reactions are performed with air-stable diborylmethane.[10]



Scheme 1.24. Mechanism of cross-coupling reactions a) in typical SMC using alkylborans, b) using of 1,1-diborylalkanes with aryl halides and c) SMC reaction of *gem*-diborylmethane towards diphenyl methane products.

1.5 References

(1) Brown, H. C.; Zweifel, G. Hydroboration. XI. The Hydroboration of Acetylenes—A Convenient Conversion of Internal Acetylenes into cis-Olefins and of Terminal Acetylenes into Aldehydes. *J. Am. Chem. Soc.,* **1961**, *83* (18), 3834–3840.

(2) Zweifel, G.; Arzoumanian, H. Geminal Organometallic Compounds. I. The Synthesis and Structure of 1,1-Diborohexane. *J. Am. Chem. Soc.,* **1967**, *89*, 291–295.

(3) Zweifel, G.; Arzoumanian, H. Synthesis of Mixed Geminal Organometallic Compounds. *Tetrahedron Lett*., **1996**, *23,* 2535–2538.

(4) Maza, R. J.; Carbó, J. J.; Fernández, E. Borata-Alkene Species as Nucleophilic Reservoir. *Adv. Synth. Catal*., **2021**, *363* (9), 2274–2289.

(5) Maza, R. J.; Fernández, E.; Carbó, J. J. Mapping the Electronic Structure and the Reactivity Trends for Stabilized α-Boryl Carbanions. *Chem. - Eur. J.,* **2021**, *27* (48), 12352–12361.

(6) Marek, I.; Normant, J.-F. Synthesis and Reactivity of sp^3-Geminated Organodimetallics. *Chem. Rev.,* **1996**, *96,* 3241–3267.

(7) Zweifel, G.; Fisher, R. P.; Horng, A. A Convenient Procedure for the Synthesis of Secondary Alcohols from 1-Alkynes *via* the Alkylation of Boron-Stabilized Carbanions. *Synthesis*, **1973**, *1,* 37–38.

(8) Cainelli, G.; Dal Bello, G.; Zubiani, G. *gem*-Dimetallic Compounds; A Novel Approach to Olefins Starting from Carbonyl Compounds and Acetylenic Derivatives. *Tetrahedron Lett.,* **1966**, *36*, 4315–4318.

(9) Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. Chemoselective and Regiospecific Suzuki Coupling on a Multisubstituted sp^3-Carbon in 1,1-Diborylalkanes at Room Temperature. *J. Am. Chem. Soc.,* **2010**, *132* (32), 11033–11035.

(10) Nallagonda, R.; Padala, K.; Masarwa, A. Organic & Biomolecular Chemistry *gem*-Diborylalkanes: Recent Advances in Their Preparation, Transformation and Application. *Org. Biomol. Chem.,* **2018**, *16*, 1050–1064.

(11) Corro, M.; Salvado, O.; González, S.; Dominguez-Molano, P.; Fernández, E. Reactivity Trends with Borylalkyl Copper(I) Species. *Eur. J. Inorg. Chem.,* **2021**, *2021* (28), 2802–2813.

(12) Hong, K.; Liu, X.; Morken, J. P. Simple Access to Elusive α-Boryl Carbanions and Their Alkylation: An Umpolung Construction for Organic Synthesis. *J. Am. Chem. Soc.,* **2014**, *136* (30), 10581–10584.

(13) Lee, Y.; Baek, S. Y.; Park, J.; Kim, S. T.; Tussupbayev, S.; Kim, J.; Baik, M. H.; Cho, S. H. Chemoselective Coupling of 1,1-Bis[(Pinacolato)Boryl]Alkanes for the Transition-Metal-Free Borylation of Aryl and Vinyl Halides: A Combined Experimental and Theoretical Investigation. *J. Am. Chem. Soc.,* **2017**, *139* (2), 975–984.

(14) Kohrt, S.; Dachwitz, S.; Daniliuc, C. G.; Kehr, G.; Erker, G. Stabilized Borata-Alkene Formation: Structural Features, Reactions and the Role of the Counter Cation. *Dalton Trans.,* **2015**, *44*, 21032–21040.

(15) Rathke, M. W.; Know, R. Generation of Boron-Stabilized Carbanions. *J. Am. Chem. Soc.,* **1972**, *94*, 6854–6856.

(16) Matteson, D. S.; Moody, R. J. Carbanions from Deprotonation of *gem*-Diboronic Esters. *J. Am. Chem. Soc.,* **1977***, 99,* 3196–3197.

(17) Coombs, J. R.; Zhang, L.; Morken, J. P. Synthesis of Vinyl Boronates from Aldehydes by a Practical Boron-Wittig Reaction. *Org. Lett.,* **2015**, *17* (7), 1708–1711.

(18) He, Z.; Zajdlik, A.; Yudin, A. K. α-Borylcarbonyl Compounds: from Transient Intermediates to Robust Building Blocks. *Dalton Trans.,* **2014**, *43*, 11434–11451.

(19) Jin, H.; Han, J.; Liu, X.; Feng, C.; Zhan, M. Access to Diverse Organoborons by α-Deprotonation and Functionalization of Benzylboronates. *Org. Lett.,* **2023**, *25* (22), 4168–4172.

(20) Matteson, D. S.; Moody, R. J. Deprotonation of 1,1-Diboronic Esters and Reactions of the Carbanions with Alkyl Halides and Carbonyl Compounds. *Organometallics,* **1982**, *1* (1), 20–28.

(21) Ashe, A. J.; Al-Ahmad, S.; Fang, X. Boratabenzenes: From Chemical Curiosities to Promising Catalysts. *J. Organomet. Chem.,* **1999**, *581* (1), 92–97.

(22) Bartholome, T. A.; Kaur, A.; Wilson, D. J. D.; Dutton, J. L.; Martin, C. D. The 9-Borataphenanthrene Anion. *Angew. Chem. Int. Ed.,* **2020**, *59* (28), 11470–11476.

(23) Knochel, P. New Approach to Boron-Stabilized Organometallic. *J. Am. Chem. Soc.,* **1990**, *112*, 7431–7433.

(24) Eaton, M.; Zhang, Y.; Liu, S.-Y. Borata-alkenes, Boraalkenes, and the η^2-B,C Coordination Mode in Coordination Chemistry and Catalysis. *Chem. Soc. Rev.,* **2024**, *53*, 1915–1935.

(25) Paradies, J. From Structure to Novel Reactivity in Frustrated Lewis Pairs. *Coord. Chem. Rev.,* **2018**, *380*, 170–183.

(26) Yu, J.; Kehr, G.; Daniliuc, C. G.; Erker, G. A Unique Frustrated Lewis Pair Pathway to Remarkably Stable Borata-Alkene Systems. *Eur. J. Inorg. Chem.,* **2013**, *19*, 3312–3315.

(27) Stephan, D. W.; Erker, G. Frustrated Lewis Pair Chemistry: Development and Perspectives. *Angew. Chem. Int. Ed.,* **2015**, *54* (22), 6400–6441.

(28) Moquist, P.; Chen, G.-Q.; Muck-Lichtenfeld, C. M.; Bussmann, K.; Daniliuc, C. G.; Kehr, G.; Erker, G. α-CH Acidity of Alkyl–B(C_6F_5)$_2$ Compounds – the Role of Stabilized Borata-Alkene Formation in Frustrated Lewis Pair Chemistry. *Chem. Sci.,* **2015**, *6,* 816–825.

(29) Radius, M.; Breher, F. α-Borylated Phosphorus Ylides (α-BCPs): Electronic Frustration within a C−B π-Bond Arising from the Competition for a Lone Pair of Electrons. *Chem. - Eur. J.,* **2018**, *24* (59), 15744–15749.

(30) Takahashi, F.; Nogi, K.; Sasamori, T.; Yorimitsu, H. Diborative Reduction of Alkynes to 1,2-Diboryl-1,2-Dimetalloalkanes: Its Application for the Synthesis of Diverse 1,2-Bis(Boronate)s. *Org. Lett.,* **2019**, *21* (12), 4739–4744.

(31) Matteson, D. S. Boronic Esters in Asymmetric Synthesis. *J. Org. Chem.,* **2013**, *78* (20), 10009–10023.

(32) Thomas, S. P.; French, R. M.; Jheengut, V.; Aggarwal, V. K. Homologation and Alkylation of Boronic Esters and Boranes by 1,2-metallate Rearrangement of Boron'ate' Complexes. C*hem. Rec.,* **2009**, *9* (1), 24–39.

(33) Lafage, M.; Pujol, A.; Saffon-Merceron, N.; Mézailles, N. M. BH_3 Activation by Phosphorus-Stabilized Geminal Dianions: Synthesis of Ambiphilic Organoborane, DFT Studies, and Catalytic CO_2 Reduction into Methanol Derivatives. *ACS Catal*., **2016**, *6* (5), 3030–3035.

(34) Matteson, D. S.; Wilson, J.W. An α-Lithio Boronic Ester from an α-Trimethylstannyl Boronic Ester. *Organometallics,* **1985**, *4* (9), 1690–1692.

(35) Mesić, M.; Novak, I.; Sunko, D. E.; Vančik, H. C–H Hyperconjugation in α-Chlorocarbocations. *J. Chem. Soc., Perkin Trans. 2,* **1998**, *11*, 2371–2374.

(36) Wrackmeyer, B.; Tok, O. L. Hyperconjugation in Trialkylboranes Shown by Indirect Nuclear Spin-Spin Coupling Constants. Experimental Data and Density Functional Theory (DFT) Calculations. *J. Chem. Sci.,* **2005**, *60* (3), 259–264.

(37) Bartlett, R. A. and Power, P. P. X-ray Crystal Structure of the Boron-Stabilized Carbanion [Li(12-crown-4)$_2$][$CH_2C_6H_2$(3,5-Me_2)(4-B{2,4,6-$Me_3C_6H_2$}$_2$)]·Et_2O: Evidence for “Boron Ylide” Character. *Organometallics*, **1986**, *5*, 1916–1917.

(38) Olmstead, M. M.; Power, P. P.; Weese, K. J.; Doedens, R. J. Isolation and X-Ray Crystal Structure of the Boron Methylidenine Ion $[Mes_2BCH_2]$-(Mes = 2, 4, 6 $Me_3C_6H_2$): A Boron-Carbon Double Bonded Alkene Analogue. *J. Am. Chem. Soc.,* **1987**, *109*, 2541–2542.

(39) Cook, K. S.; Piers, W. E.; Hayes, P. G.; Parvez, M. Reactions of a Borata-alkene Ligand at Tantalocene Centers: Isonitrile Insertion into the B-C Bond of the $[CH_2B(C_6F_5)_2]$ Ligand *via* the η^1 Bonding Mode. *Organometallics*, **2002**, *21* (12) 2422–2425.

(40) Watanabe, K.; Ueno, A.; Tao, X.; Škoch, K.; Jie, X.; Vagin, S.; Rieger, B.; Daniliuc, C. G.; Letzel, M. C.; Kehr, G.; Erker, G.; Wacker, B. Reactions of an Anionic Chelate Phosphane/Borata-Alkene Ligand with $[Rh(Nbd)Cl]_2$, $[Rh(CO)_2Cl]_2$ and $[Ir(Cod)Cl]_2$. *Chem. Sci.,* **2020**, *11*, 7349–7355.

(41) Wadepohl, H.; Arnold, U.; Kohl, U.; Pritzkow, H.; Wolf, A. Hydroboration of Metal-Carbon Triple Bonds. *J. Chem. Soc.,* **2000**, 3554–3565.

(42) Phillips, N. A.; Kong, R. Y.; White, A. J. P.; Crimmin, M. R. Group 11 Borata-alkene Complexes: Models for Alkene Activation. *Angew. Chem. Int. Ed.,* **2021**, *133* (21), 12120– 12126.

(43) Schulte, M.; Gabbaï. F.P. Synthesis of B/Ga and B/In Heteronuclear Bidentate Lewis Acids: Formation of Intramolecular π-Arene-Gallium(III) and -Indium(III) Complexes *Chem. Eur. J.,* **2002**, *8*, 3802–3807.

(44) Hoefelmeyer, J. D.; Solé. S.; Gabbaï, F. P. Reactivity of the Dimesityl-1,8-Naphthalenediylborate Anion: Isolation of the Borataalkene Isomer and Synthesis of 1,8-Diborylnaphthalenes. *Dalton Trans.* **2004**, *54*(8), 1254–1258.

(45) Oomens, J.; Steill, J. D.; Morton, T. H. IR Spectra of Boron-Stabilized Anions in the Gas Phase. *Inorg. Chem.* **2010**, *49* (15), 6781–6783.

(46) Cyraniak, A.; Freza, S.; Skurski, P. An *Ab* Initio Study on the Stability of Isolated Borata-Alkene Synthons. *Chem. Phys.,* **2022**, *559*, 111543.

(47) Cuenca, A. B.; Fernández, E. Boron-Wittig Olefination with g*em*-Bis(Boryl)Alkanes. *Chem. Soc. Rev.,* **2021**, *50*, 72–86.

(48) Jo, W.; Lee, J. H.; Cho, S. H. Advances in Transition Metal-Free Deborylative Transformations of *gem*-Diborylalkanes. *Chem. Comm.,* **2021**, *57* (36), 4346–4353.

1.6 Objectives

The current doctoral thesis has been undertaken with the main purpose of enhancing the knowledge on organoboron chemistry field, developing novel synthetic methodologies, and exploring the versatile applications of borata-alkene species towards a variety of novel compounds.

The specific objectives of each chapter are outlined below:

Chapter 2 searches the innovation using Cu(I) complexes towards the activation of 1,1,1',1'-tetrapinacolborylethane to produce the corresponding α-borylalkyl copper species, followed by allylic alkylation sequences.

Chapter 3 aims to develop a straightforward intermolecular three-component assembly involving alkenylboranes. Without the use of catalysts, additives, or radical initiators, the objective was to demonstrate that borata-alkene intermediates can lead to the synthesis of tertiary boronic esters.

Chapter 4 focusses on the exploration of the intermolecular three-component assembly between alkenylboranes, ^{t}BuLi and carbonyl functional groups to synthesize tri- and tetrasubstituted alkenes and diene

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Sara González Morán

CHAPTER 2

Cu(I) Activation of 1,1,1',1'-Tetrapinacolborylethane towards Allylic Alkylation Reactions

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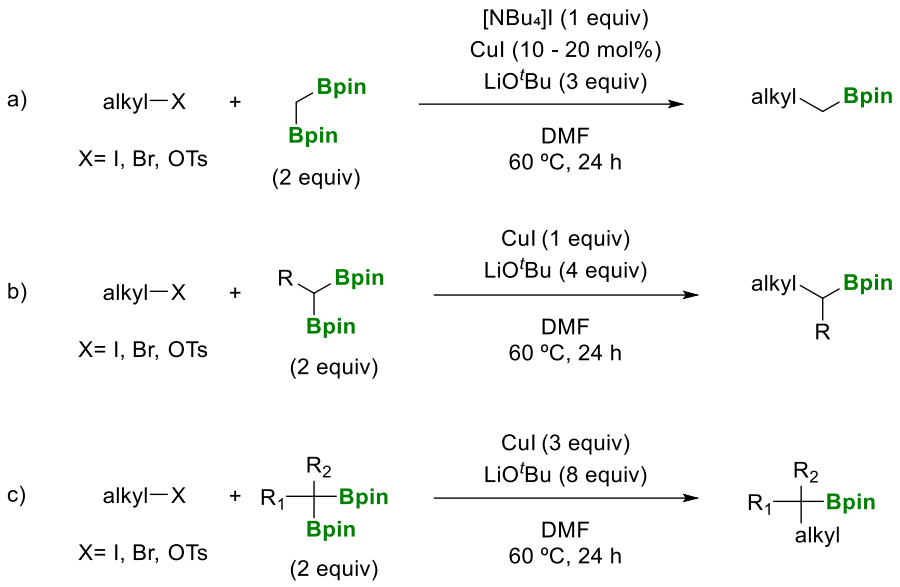
2.1 State of the art

One of the most reliable counter cation in the stabilization of borata-alkenes is copper(I). The highly polarized metal-carbon interactions in $^{2}\eta$-(C–B) borata-alkene complexes with copper(I) confers the carbanion with nucleophilic character, to enable the efficient trapping of a variety of electrophilic reagents.[1,2]

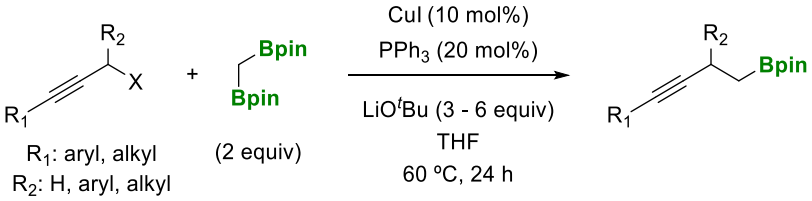
A facile access to borylalkyl copper (I) species from *gem*-diborylalkanes is due to the Cu(I) activation of B-C-B bonds. The incorporation of stabilizing ligands, such as mono and diphosphines, can be used to contribute to the steric and electronic tuning of the borylalkyl copper(I) catalyst.[1]

Fu, Marder and co-workers reported the first Cu-catalyzed cross-coupling of *gem*-diborylalkanes with nonactivated primary alkyl halides. The reaction involving diborylmethane proceeded in the presence of 10%-20% CuI and 3 equiv of LiO^{t}Bu, in dimethylformamide (DMF) (Scheme 2.1a).[3] It was observed that the reactivity of alkyl bromide and tosylate was higher than that of aryl bromide, as well as the reactivity of alkyl bromide was higher than that of aryl and alkyl chloride. Notably, functional groups such as acetal, terminal olefin and *tert*-butyldimethylsilyl ethers (TBS)-protected alcohol were well-tolerated, whereas alkyl esters, aryl esters, heterocyclic compounds or amino acid derivatives, gave only moderate yields. Furthermore, the addition of tetrabutylammonium iodide was added to enhace the yields. On the other hand, 1 equiv of CuI and 4 equiv of LiO^{t}Bu were required for the coupling of substitued 1,1-diborylalkanes (Scheme 2.1b), while tertiary alkylboronic esters could be obtained using 3 equiv of CuI and 8 equiv of LiO^{t}Bu (Scheme 2.1c). A plausible S_N2 mechanism has been suggested for this homologation of alkyl halides.[3]



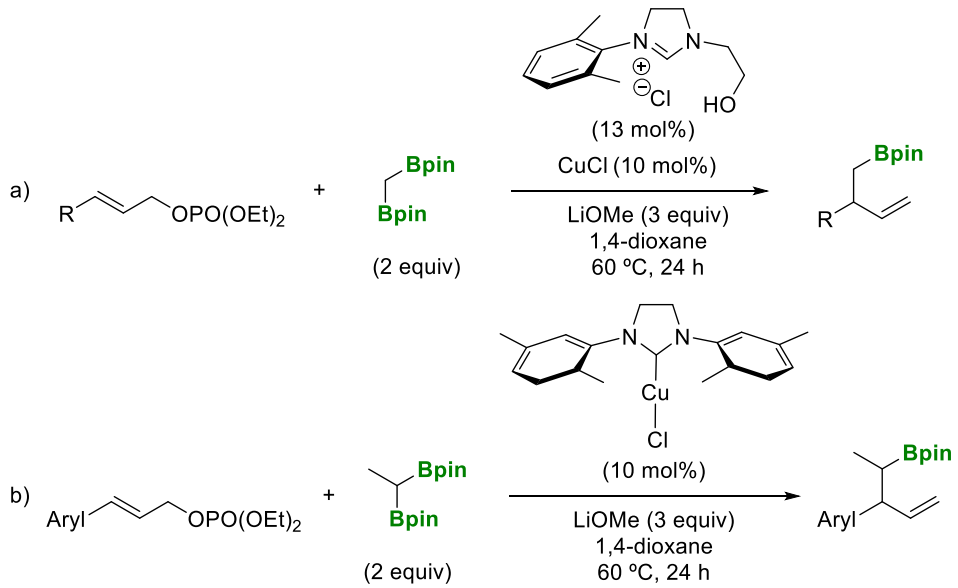
Scheme 2.1. Cu catalyzed reaction of primary electrophiles with a) diborylmethane, b) monosubstitued 1,1-diborylalkanes and c) disubstitued 1,1-diborylalkanes.

Xiao, Fu and co-workers have demonstrated the Cu/PPh_3-catalyzed cross-coupling reaction in which a propargyl derivative reacted with diborylmethane (Scheme 2.2).[4] Moderate to good yields were obtained utilizing 10 mol% of CuI modified with PPh_3 in the presence of LiO^tBu, with THF as solvent, at 60 °C. In the case of primary propargyl compounds, 3 equiv of LiO^tBu were necessary, and it showed good tolerance to diverse functional groups. When the reaction was performed with secondary propargyl systems, the base had to be incremented to 6 equiv, since authors proved the Cl leaving group resulted the most efficient, albeit the formation of by-products was significant.[4]



Scheme 2.2. Copper-catalyzed propargylation of diborylmethane.

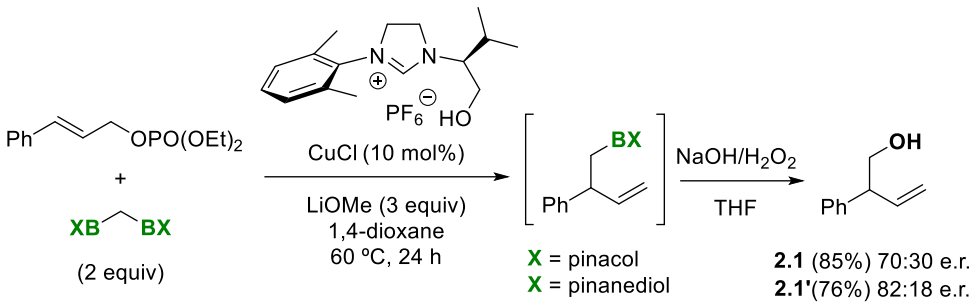
The same authors studied copper-catalyzed S_N2'-selective alkylation reactions of allylic electrophiles with 1,1-diborylalkanes, obtaining the branched γ-substitution products. The reaction was optimized with 10 mol% of the Cu/(NHC)-catalytic system (NHC: N-heterocyclic carbene) and 3 equiv of LiOMe, in 1,4-dioxane at 60 °C (Scheme 2.3a).[5] Under these conditions, a variety of synthetically important functional groups were compatible: aromatic and aliphatic allylic phosphates, NO_2, CF_3, CN, and vinyl groups could react with diborylmethane. A variety of halogen-substituted cinnamyl phosphates could successfully afford the corresponding products in good yields through S_N2' mechanism. Both (*Z*)- and (*E*)-allylic phosphates showed similar reactivity and provided the same branched product with high selectivity. Some modifications were carried out in the copper catalyst to lead improvements in yield and diastereoselectivity when 1,1-diborylethane was used as substrate (Scheme 2.3b).[5]



Scheme 2.3. Copper-catalyzed S_N2'-selective allylic substitution reaction of a) 1,1-diborylmethane and b) 1,1-diborylethane.

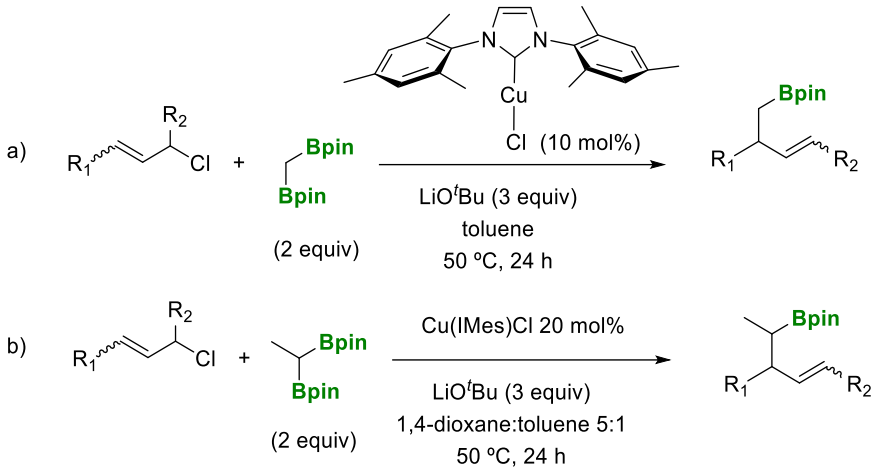
The asymmetric version of this reaction was studied with a Cu complex modified with chiral NHC ligand. The branched organoboron product was oxidized *in situ*

to provide the corresponding alcohol. The authors found that the enantiomeric excess (ee) value was controlled when diborylmethane is used with different steric hindrance at the boryl moiety; for instance, the product **2.1** using pinacolboryl was obtained in a 40% ee, whereas the product **2.1'** using pinanediolboryl was obtained in 64% ee (Scheme 2.4).[5]



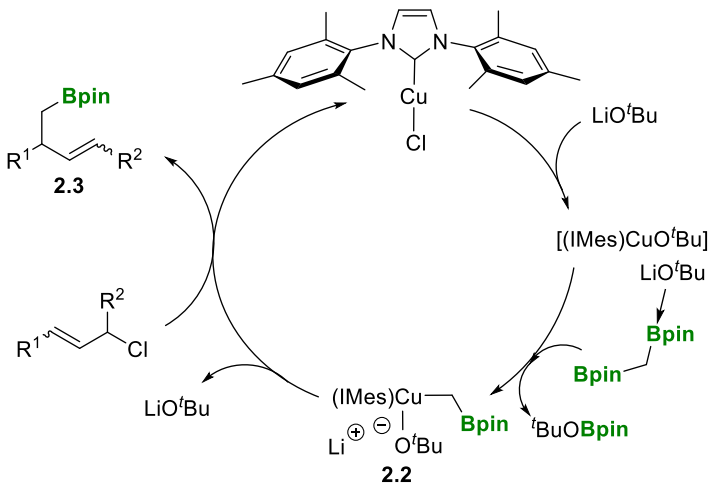
Scheme 2.4. Enantioselective Cu-NHC catalyzed S_N2' allylic alkylation reaction of allylic phosphates with diborylmethane.

Similarly, Cho and co-workers have also reported a Cu/(NHC)-catalyzed S_N2'-selective allylic alkylation reaction of allylic chlorides with 1,1-diborylalkanes. In this case, the optimized reaction was conducted in toluene at 50 °C, with 3 equiv of LiO^tBu and 10 mol% of Cu(IMes)Cl (Scheme 2.5a). This method exhibited a wide substrate scope containing both aromatic and aliphatic allylic chlorides, where S_N2' selectivity is highly favored versus the S_N2 mechanism. Various functional groups, including silyl ether, pivalate and chloride were well tolerated. The reactions of substituted 1,1-diborylalkanes were also investigated. After re-optimization it was found that the reaction required a higher catalyst loading (20 mol%) and a 5:1 mixture of 1,4-dioxane and toluene as the solvent to afford the corresponding products (Scheme 2.5b), opening the possibilities for the development of a copper-catalyzed diastereoselective allylic substitution reaction.[6]



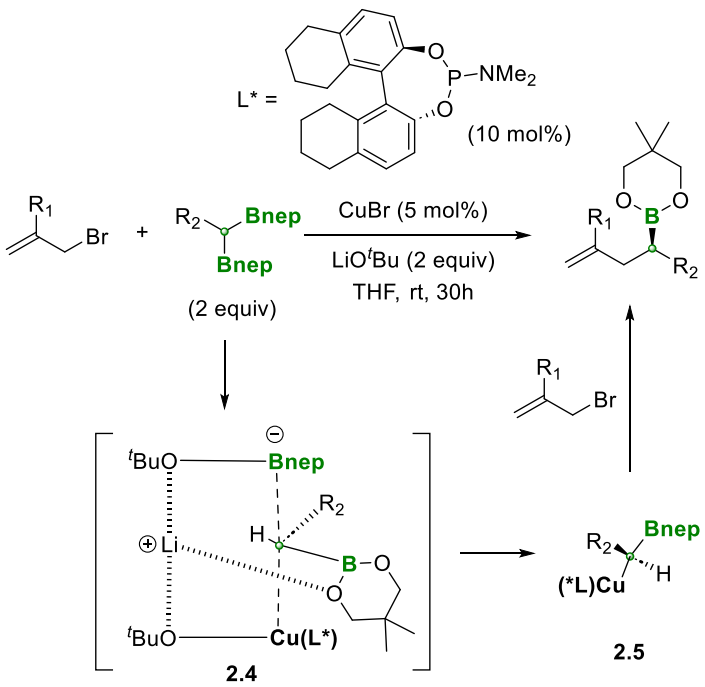
Scheme 2.5. Cu(IMes)Cl-catalyzed S_N2'-selective allylic substitution reaction of allylic chlorides with a) 1,1-diborylmethane and b) 1,1-diborylethane.

A plausible mechanism is shown in Scheme 2.6. On the basis of precedent literature,[7,8] it has been suggested that first, the copper alkoxide complex [Cu(IMes)O^{t}Bu] is generated from [Cu(IMes)Cl] in the presence of LiO^{t}Bu, to be further involved in the transmetallation towards the monoalkyl alkoxycuprate **2.2**. The resulting heterocuprate should promote the subsequent S_N2' substitution of the allylic chloride to afford the branched alkylboronates **2.3** and the regenerated copper(I) complex [Cu(IMes)Cl].[6]



Scheme 2.6. Mechanism of Cu(IMes)Cl-catalyzed S_N2'-selective allylic substitution reaction.

More recently, Sawamura and co-workers developed a copper-catalyzed enantiotopic-group selective allylation of *gem*-diborylalkanes with a series of allyl bromides.[8] The combination of copper(I) bromide and a H_8–BINOL derived phosphoramidite ligand, with 2 equiv of LiO^tBu in THF at room temperature, proved to be the most effective catalytic system to give homoallylic boronate esters that contain a boron-substituted carbon stereogenic center with high enantiomeric purity. A significant range of *gem*-diborylalkanes and allyl bromides resulted efficient for the coupling, including alkyls, cycloalkyls, protected amines, *tert*-butyldimethylsilyl (TBS)-protected ether or trimethylsilyl (TMS) groups. Mechanistic studies have revealed an enantiotopic-group selective transmetallation between *gem*-diborylalkanes and chiral copper complex (**2.4**) to generate the chiral α-borylalkyl-copper species (**2.5**), which subsequently undergoes C–C bond formation with allyl bromides (Shceme 2.7).[6]



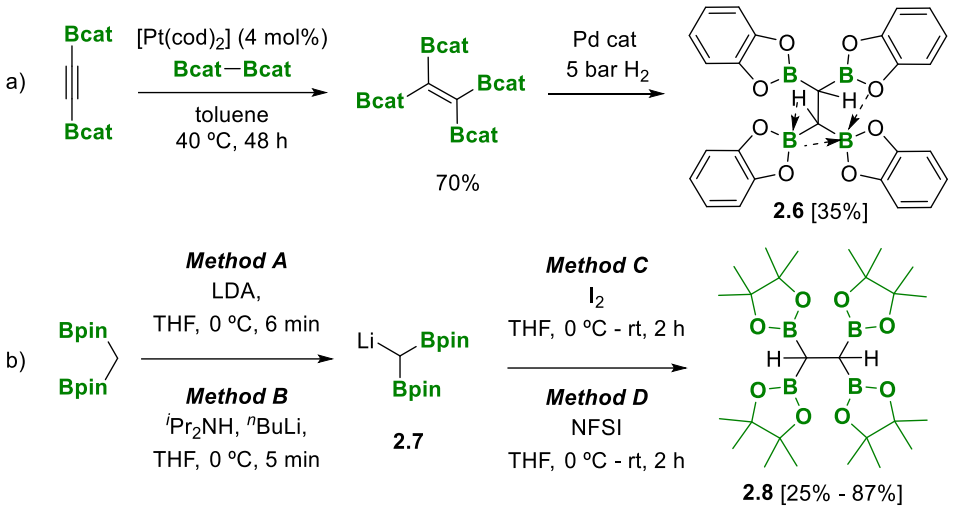
Scheme 2.7. Copper-catalyzed enantioselective coupling of *gem*-diborylalkanes with allylic electrophiles.

2.2 Context of the work

Tetraborylethane compounds are considered densely borylated small molecules with potential functionalization. Siebert, Gleiter and co-workers have conducted the synthesis of tetraborylethenes through a Pt-catalyzed diboration of bis(catecholato)diboron (B_2cat_2) with diborylacetylenes.[9] Subsequently, these compounds underwent hydrogenation facilitated by Pd catalysts leading to the formation of the tetracatecholborylethane compound **2.6** (Scheme 2.8a). Natural Bond Orbital (NBO) analyses revealed that in the structure **2.6** the geminal catechol rings were twisted to allow a B-O donor-acceptor interaction between two vicinal catechol rings. Additionally, there was a B-B interaction between the boron atoms of two geminal catechol rings and an agnostic interaction between one boron p_z orbital and the C-H bond of the ethane fragment. These interactions provided to the molecule **2.6** an enhanced stability.[9]

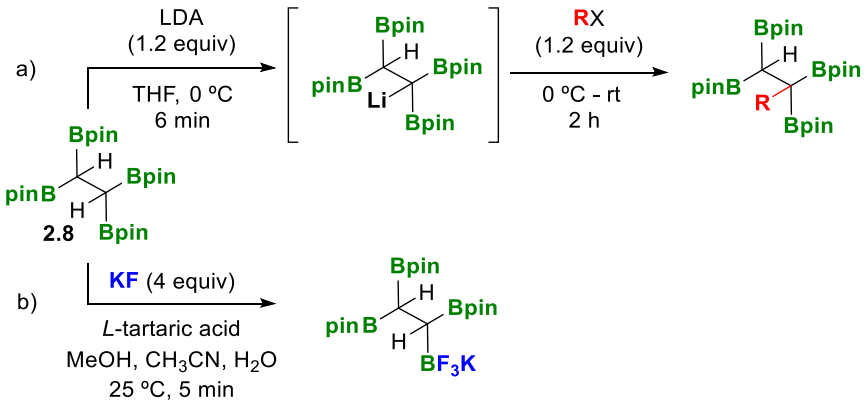
The synthesis of 1,1,1′1′-tetrapinacolborylethane (**2.8**) has been patented by Zhang et al.[10] They employed dipinacolborylmethane *via* activation with lithium diisopropylamide (LDA) to generate a dipinacolborylmethide lithium salt (**2.7**) that subsequently reacted with I_2 to form **2.8** in moderate yields (Scheme 2.8b, *Methods A and C*).

Masarwa and co-workers have established the formation of the lithium salt **2.7** following the *Method B* with $^{i}Pr_2NH$ and $^{n}BuLi$.[11] In addition, Cho and co-workers have been able to isolate **2.7**, for the first time, as a white solid.[12] Furthermore, they introduced the use of N-fluorobenzenesulfonimide (NFSI) for the halogenative step, in order to transform **2.7** into the tetraborylethane product **2.8** (Scheme 2.8b, *Method D*).[13]



Scheme 2.8. Synthetic approaches towards 1,1,1',1'-tetraborylethane.

Despite the fact that the synthesis of 1,1,1′1′-tetrapinacolborylethane (**2.8**) has been well established, its structural characterization and reactivity have received less attention. In the Scheme 2.9a, it is displayed the unique example of the formation of tetrasubstituted carbon centers through a single deprotonation with LDA followed by electrophilic trapping with RX.[10] Complementary, Masarwa and co-workers have developed the desymmetrization of **2.8** *via* nucleophilic mono trifluorination (Scheme 2.9b).[11] However, the research about copper-catalyzed allylic alkylation of molecule 1,1,1′1′-tetrapinacolborylethane has kept unexplored.



Scheme 2.9. Activation modes of 1,1,1',1'-tetraborylethane.

2.3 Specific objectives

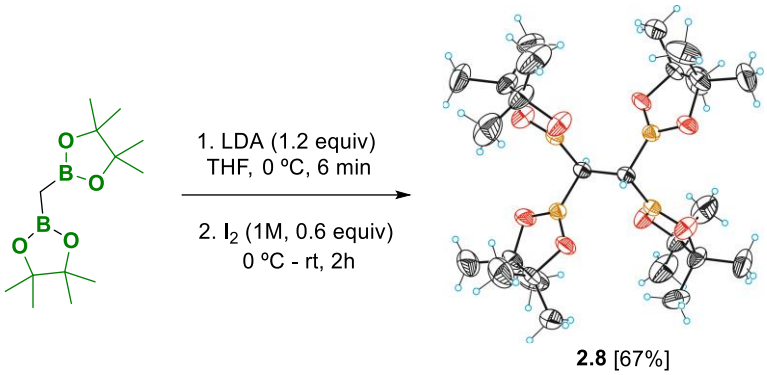
Taking into consideration the above-mentioned benefits of Cu (I) complexes in the activation of 1,1-diborylalkanes to deliver the corresponding α-borylalkyl copper species, the main goal in this chapter is the generation of new knowledge about the reactivity of 1,1,1′1′-tetrapinacolborylethane (**2.8**) throughout its activation with Cu(I) followed by allylic alkylation sequences.[14]

The specific objectives are:

1. Synthesis of the compound 1,1,1′1′-tetrapinacolborylethane and its full characterization.
2. Search of the optimization reaction conditions for the Cu-catalyzed coupling of 1,1,1′,1′-tetrapinacolborylethane with allyl bromide.
3. Study of a general scope of allyl halides in the reaction outcome.
4. Extension of the reaction through a second allylic alkylation of the homoallyl triboronate systems.
5. Synthesis of methylenecyclopentane-1,2-dipinacolboronic ester to evaluate diastereoselection through the ring closing protocol.

2.4 Results and discussion

The initial step to accomplish the objectives of this study involved the synthesis of compound 1,1,1,1′-tetrapinacolborylethane (**2.8**), which was obtained adapting the protocol by Zhang et al. (Scheme 2.10).[10] The product was achieved in 67% isolated yield and subsequently crystallized, allowing a full characterization through X-ray diffraction. Acquired data showed that the relative orientation of the "empty" boron p_z orbital does not present intramolecular B-O or B-B interactions, in contrast to the intramolecular interactions in compound **2.6**, which is consistent with the lower Lewis acid properties of Bpin moiety compared to the Bcat motif.



Scheme 2.10. Synthesis of 1,1,1',1'-tetrapinacolborylethane, and X-ray diffraction structure.

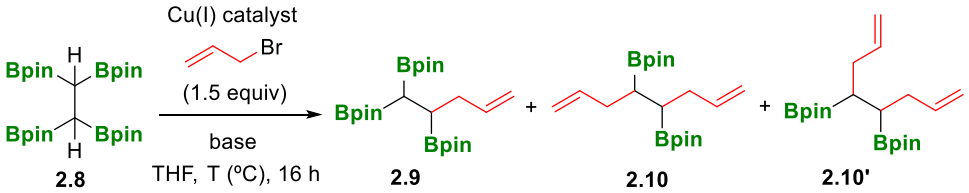
In order to explore the copper-catalyzed allylic alkylation with compound **2.8**, we launched a preliminary study of the CuCl catalyzed allylic alkylation of 1,1,1′,1′-tetrapinacolborylethane (**2.8**) with allyl bromide in the presence of LiO^{t}Bu as base, at 60 °C, in THF. Two main products were observed after the reaction: the monoalkylated compound (**2.9**) in 67% yield and the dialkylated by-product in 23% yield, as a mixture of 1:1 diastereoisomers **2.10/2.10'**, suggesting a double allylic alkylation (Table 2.1, entry 1).

To minimize the formation of the dialkylation by-products, several parameters were subjected to modifications. Firstly, the addition of ligand PPh_3 to the Cu(I) catalytic system, favored the formation of homoallyl triboronate product **2.9** (Table 2.1, entry 2). This observation can imply that, owing to the sterically hindered catalytic system Cu-PPh_3, the double allylic alkylation is less favored.

On the other hand, replacement of LiO^{t}Bu by NaO^{t}Bu decreased the percentage formation on the desired product **2.9**. Along with the by-products **2.10/2.10'**, protodeborylated by-products (**pdb**) were formed in a 29% yield (Table 2.1, entry 3). The advantages of LiO^{t}Bu in CuCl catalyzed allylic alkylation of 1,1-diborylalkanes, in contrast to other bases, had previously been reported by Cho and co-workers.[6]

When $[Cu(MeCN)_4]PF_6$ was used as Cu(I) source, product **2.9** could be isolated in 54% (Table 2.1, entry 4). Nevertheless, a higher temperature (90 °C) did not favor the formation of **2.9**, leading to the appearance of **pdb** (Table 2.1, entry 5). Finally, reduction of LiO^{t}Bu loading eliminated the formation of the by-products (Table 2.1, entry 6). The optimized reaction conditions resulted from the use of 1.5 equiv of base within the catalytic system $[Cu(MeCN)_4]PF_6/PPh_3$ at 60 °C to synthesize product **2.9** in 65% isolated yield (Table 2.1, entry 7).

Table 2.1. Optimization of the reaction conditions for Cu catalyzed coupling of 1,1,1',1'-tetrapinacolborylethane with allyl bromide.[a]



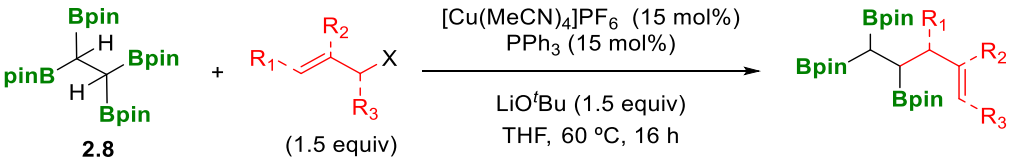
Entry	Cu(I) (mol%)	Base (equiv)	T (°C)	Conversion (%)[b]	2.9 (%)[b][%][c]	2.10/2.10' (%)[b]
1	CuCl (10)	LiO^{t}Bu (2)	60	90	67 [31]	23
2	CuCl/PPh_3 (10/10)	LiO^{t}Bu (2)	60	88	78 [51]	10
3	CuCl/PPh_3 (10/10)	NaO^{t}Bu (2)	60	85	45	11 (and 29% **pdb**)[d]
4	$[Cu(MeCN)_4]PF_6$ (10)	LiO^{t}Bu (2)	60	70	58 [54]	12
5	$[Cu(MeCN)_4]PF_6$ (10)	LiO^{t}Bu (2)	90	95	54	31(and 10% **pdb**)[d]
6	$[Cu(MeCN)_4]PF_6$ (10)	LiO^{t}Bu (1.5)	90	62	60	--
7	$[Cu(MeCN)_4]PF_6/PPh_3$ (15/15)	LiO^{t}Bu (1.5)	60	72	70 [65]	2

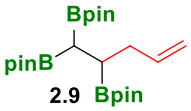
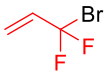
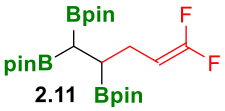
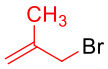
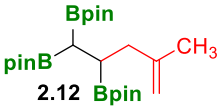
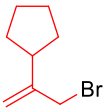
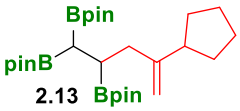
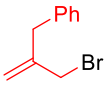
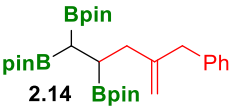
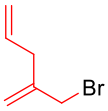
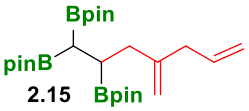
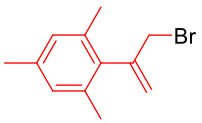
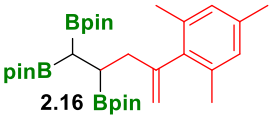
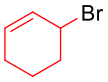
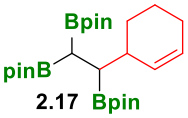
[a]Reactions performed at 0.15 mmol scale of **2.8**, allyl bromide (1.5 equiv), CuCl or $[Cu(MeCN)_4]PF_6$ (10-15 mol%), PPh_3 (10-15 mol%), LiO^{t}Bu (1.5-2 equiv), THF (2 mL), 16 h. [b]Conversion and yields determined by NMR with naphthalene as internal standard. [c]Isolated yield. [d]Protodeborylated by-products (**pdb**).

Afterwards, we selected a variety of allyl halides to explore the reactivity of compound **2.8** under the optimized reaction conditions. The allylic alkylation on 3-bromo-3,3-difluoroprop-1-ene, took place regioselectively on the γ position allowing the obtention of the corresponding 3-substituted 1,1-difluoroalkene **2.11** (Table 2.2, entry 2). Remarkably, these type of *gem*-difluoroalkene compounds are particularly interesting due to the fact that $C=CF_2$ motifs are considered beneficial for certain mechanism-based enzyme inhibitors,[15–17] while also functioning as bioisosteres for aldehydes and ketones.[18–21]

As a general trend, the allyl bromides containing the functional groups R_2 = methyl, cyclopentyl and benzyl, reacted with **2.8**, in the presence of $Cu(I)/PPh_3$ allowing the isolation of homoallyl triboronate products **2.12**, **2.13** and **2.14**, in moderate yields (Table 2.2, entries 3–5). When **2.8** reacted with 2-(bromomethyl)penta-1,4-diene enabled the formation of the polyborylated product **2.15**, tolerating the presence of alkene groups (Table 2.2, entry 6). In the case of the mesityl group, the reaction progressed efficiently towards the allylic alkylation, despite the steric hindrance, isolating compound **2.16** in 73% (Table 2.2, entry 7). Notably, the cyclic 3-bromocyclohex-1-ene was a suitable electrophile along the Cu(I) catalyzed allylic alkylation of **2.8**, since product **2.17** was effciently synthesized and isolated in 67% yield, within 1:1 dr (Table 2.2, entry 8).

Table 2.2. Scope of Cu catalyzed coupling between 1,1,1',1'-tetrapinacolborylethane and allyl halides.[a]



Entry	Allyl halide	Product	Isolated Yield [%][b]
1			[65%]
2			[74%]
3			[58%]
4			[51%]
5			[68%]
6			[31%]
7			[73%]
8			[67%] (dr=1/1)

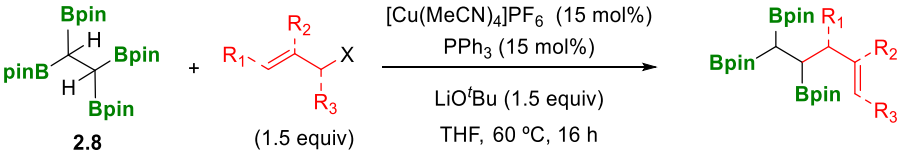
[a]Reactions performed at 0.15 mmol scale of **2.8**, allyl bromide (1.5 equiv), $[Cu(MeCN)_4]PF_6$ (15 mol%), PPh_3 (15 mol%), LiO^tBu (1.5 equiv), THF (2 mL), 60 °C, 16 h. [b]Isolated yield after flash column chromatography purification.

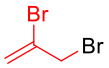
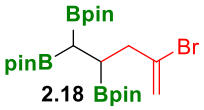
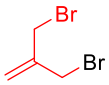
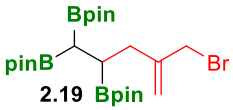
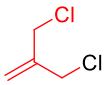
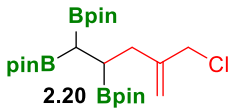
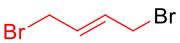
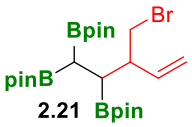
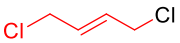
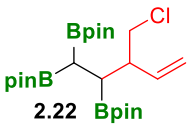
With the aim of expanding the applicability and versatility of this methodology, a series of double halogenated allyl bromides were employed with 1,1,1′,1′-tetrapinacolborylethane. Raising the temperature to 90 °C, the reagent 2,3-dibromoprop-1-ene was studied for the coupling with **2.8** in the presence of Cu/PPh_3 giving exclusively the product **2.18**, showing a chemoselectivity in the C–Br coupling (Table 2.3, entry 1) and retaining the C (sp^2)-Br, which allows further downstream transformations.[22–24] Both reagents 3-bromo-2-(bromomethyl)prop-1-ene and 3-chloro-2-(chloromethyl)prop-1-ene reacted with **2.8**, allowing the isolation of compounds **2.19** and **2.20**, in similar moderate yields (Table 2.3, entries 2 and 3).

To complete the scope, internal allyl halides were next studied. The copper catalyzed allylic alkylation between **2.8** and (*E*)-1,4-dibromo-2-butene or (*E*)-1,4-dichloro-2-butene proceeded towards the coupling exclusively at the γ position of the allyl halides, generating products **2.21** and **2.22** in 53% and 86% isolated yield, respectively, within 1:1 dr (Table 2.3, entries 4 and 5).

In view of the products generated with this approach, we suggest that the Cu catalyzed allylic alkylation between 1,1,1′,1′-tetrapinacolborylethane and the allyl halides depicted in Table 2.2 and Table 2.3 might undergo a S_N2' mechanism. This would be in agreement with reported copper-catalyzed S_N2'-selective allylic alkylation reactions involving diborylmethane,[5,6,25,26] *gem*-diborylalkanes,[27] as well as *gem*-diborylalkenes.[22]

Table 2.3. Scope of Cu catalyzed coupling between 1,1,1',1'-tetrapinacolborylethane and double halogenated allyl halides.[a]

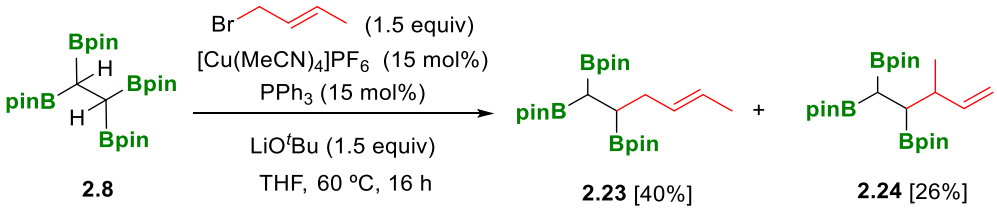


Entry	Allyl halide	Product	Isolated Yield [%][b]
1[c]			[55%]
2			[41%]
3			[43%]
4[c]			[53%] (dr=1/1)
5[c]			[86%] (dr=1/1)

[a]Reactions performed at 0.15 mmol scale of **2.8**, allyl bromide (1.5 equiv), $[Cu(MeCN)_4]PF_6$ (15 mol%), PPh_3 (15 mol%), LiO^tBu (1.5 equiv), THF (2 mL), 60 °C, 16 h. [b]Isolated yield after flash column chromatography purification. [c]90 °C, base (1.75 equiv).

A completely different reactions outcome took place in the coupling between **2.8** and (*E*)-1-bromobut-2-ene, since the reaction evolved to the formation of products **2.23** and **2.24**, in about 2:1 ratio respectively, with a favored α-selectvity versus γ-selectvity (Scheme 2.11). In this case, the S_N2 mechanism seemed to be favored, as previously suggested by Liu and Fu, indicating that the solvent could interfere in the isomerization step and affect the α/γ-regioselectivity.[26] The formation of **2.23** *via* base assisted deborylation, followed

by nucleophilic addition to the α-position of the allyl halide[28] has been discarded due to the lack of reactivity when Cu(I) is removed.



2.8 **2.23** [40%] **2.24** [26%]

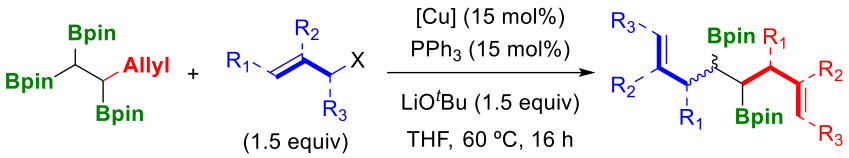
Scheme 2.11. Solvent-controlled regioselective allylic alkylation between **2.8** and (*E*)-1-bromobut-2-ene.

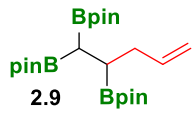
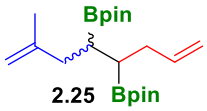
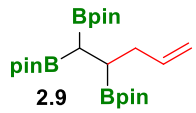
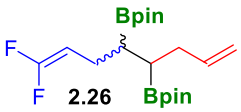
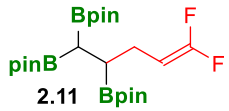
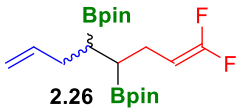
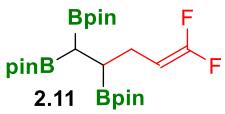
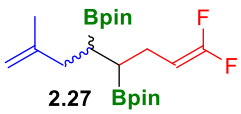
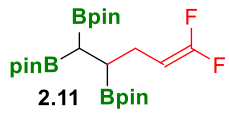
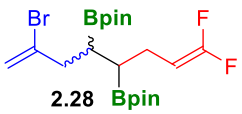
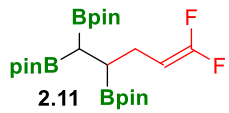
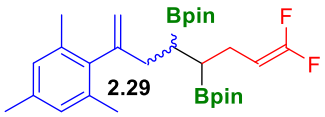
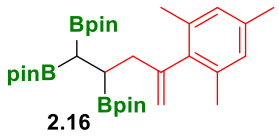
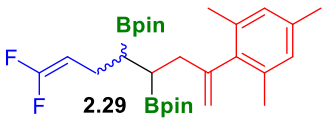
To broaden the applicability of the reaction, the homoallyl triboronate systems, prepared from Cu-catalyzed first allylic alkylation of **2.8** were subjected to a second Cu-catalyzed allylic alkylation under the previously optimized conditions to generate mixed dihomoallyl diboronates (Table 2.4). Compound **2.9** and 3-bromo-2-methylprop-1-ene, reacted in the presence of the catalytic system $[Cu(MeCN)_4]PF_6/PPh_3$, yielding the corresponding mixed dihomoallyl diboronate **2.25**, which could be isolated as both diastereoisomers within 1:1 dr (Table 2.4, entry 1). Similar trend was observed when the allylic compound **2.9** reacted with 3-bromo-3,3-difluoroprop-1-ene to generate product **2.26** (Table 2.4, entry 2).

However, when the same compound **2.26** was synthesized from the homoallyl triboronate system **2.11** by Cu-catalyzed coupling with the 3-bromoprop-1-ene, the dr slightly increased up to 1:1.5 dr (Table 2.4, entry 3). Taking this into account, we proceeded to study whether the 1,1-difluoroalkenyl polyborated compound **2.11** could influence on the diasteroselection of the second Cu-catalyzed allylic alkylation. Several allyl bromide reagents were evaluated, leading to products **2.27** and **2.28** that exhibited moderate diastereoselectivity, specially in the formation of product **2.29** (Table 2.4, entries 4–6). Interestingly, the preparation of **2.29** from the homoallyl triboronate system **2.16**, gave also the same diastereoselection but with opposite preference on the major

diasteroisomer, as a consequence of the steric hindrance of the mesityl group (Table 2.4, entry 7).

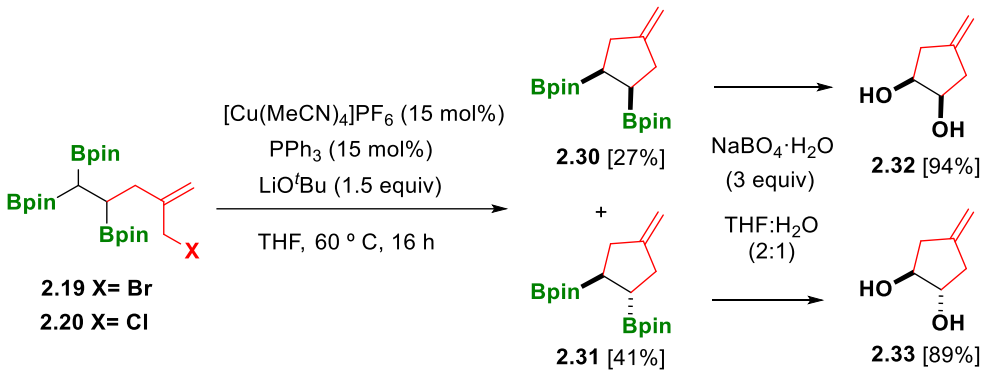
Table 2.4. Cu catalyzed second allylic alkyation of homoallyl triboronate systems.[a]



Entry	Substrate	Product	NMR Yield[b] (dr)[b] [%][c]
1			67% (dr=1/1) [25%][29%]
2			99% (dr=1/1.2) [34%][43%]
3			89% (dr=1/1.5) [33%][50%]
4			64% (dr=1/1.2) [23%][29%]
5			53% (dr=1/1.4) [19%][25%]
6			43% (dr=1/2) [11%][20%]
7			72% (dr=2/1) [44%][21%]

[a]Reactions performed at 0.2 mmol scale of homoallyl triboronate, allyl bromide (1.5 equiv), $[Cu(MeCN)_4]PF_6$ (15 mol%), PPh_3 (15mol%), LiO^{t}Bu (1.5 equiv), THF (2 mL), 60 °C, 16 h. [b]NMR yield and diastereo ratio calcultaed with naphthalene as internal standard. [c]Isolated yield for each diastereoisomer.

To conclude, we complemented this study by exploring the intramolecular Cu-catalyzed allylic alkylation of the homoallyl triboronate systems **2.19** and **2.20**, aimed to promote the synthesis of methylenecyclopentane-1,2-dipinacolboronic esters. Under the optimized reaction conditions, the conversion to the desired product remained consistent regardless of the bromide or chloride leaving group in the substrate **2.19** and **2.20** and a mixture of products were generated with a diastereomeric ratio 2/1 in favor of the *trans* diastereoisomer **2.31** (Scheme 2.12). The subsequent oxidation provided a direct pathway to the synthesis of *trans*-methylenecyclopentane-1,2-diol **2.33** in 89% isolated yield, which serves as an intermediate for the construction of cephalotaxine derivatives with antileukemic activity.[29]



Scheme 2.12. Intramolecular Cu catalyzed coupling of homoallyl triboronate systems **2.19** and **2.20**.

2.5 Conclusions

In summary, we have synthesized 1,1,1′1′-tetrapinacolborylethane (**2.8**) from dipinacolborylmethane and we conducted its full characterization through X-ray diffraction to establish the relative orientation of the "empty" boron p_z orbital within the four Bpin moieties. We launched an unexplored Cu catalyzed coupling of 1,1,1′,1′-tetrapinacolborylethane with allyl bromide identifying the optimized reaction conditions with the catalytic system $[Cu(MeCN)_4]PF_6/PPh_3$ and LiO^tBu

(1.5 equiv) minimizing the formation of double alkylation by-products. The substrate scope covered some representative examples of sterically hindered allyl halides that suggest a S_N2' mechanism for the Cu catalyzed allylic alkylation. A subsequent second allylic alkylation of the homoallyl triboronate systems, allowed the synthesis of mixed dihomoallyl diboronates. An intriguing intramolecular Cu-catalyzed allylic alkylation of the homoallyl triboronate systems **2.19** and **2.20** facilitated the synthesis of methylenecyclopentane-1,2-dipinacolboronic ester with 2:1 diastereoselection in favour of the *trans*-diastereoisomer.

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2.6 References

(1) Corro, M.; Salvado, O.; González, S.; Dominguez-Molano, P.; Fernández, E. Reactivity Trends with Borylalkyl Copper(I) Species. *Eur. J. Inorg. Chem*., **2021**, *28*, 2802–2813.

(2) Maza, R. J.; Fernández, E.; Carbó, J. J. Mapping the Electronic Structure and the Reactivity Trends for Stabilized α-Boryl Carbanions. *Chem. Eur. J.,* **2021**, *27* (48), 12352–12361.

(3) Zhang, Z. Q.; Yang, C. T.; Liang, L. J.; Xiao, B.; Lu, X.; Liu, J. H.; Sun, Y. Y.; Marder, T. B.; Fu, Y. Copper-Catalyzed/Promoted Cross-Coupling of *gem*-Diborylalkanes with Nonactivated Primary Alkyl Halides: An Alternative Route to Alkylboronic Esters. *Org. Lett.,* **2014**, *16* (24), 6342–6345.

(4) Li, F.; Zhang, Z. Q.; Lu, X.; Xiao, B.; Fu, Y. Copper-Catalyzed Propargylation of Diborylmethane. *Chem.Commun.,* **2017**, *53* (25), 3551–3554.

(5) Zhang, Z. Q.; Zhang, B.; Lu, X.; Liu, J. H.; Lu, X. Y.; Xiao, B.; Fu, Y. Copper-Catalyzed S_N2'-Selective Allylic Substitution Reaction of *gem*-Diborylalkanes. *Org. Lett.,* **2016**, *18* (5), 952–955.

(6) Kim, J.; Park, S.; Park, J.; Cho, S. H. Synthesis of Branched Alkylboronates by Copper-Catalyzed Allylic Substitution Reactions of Allylic Chlorides with 1,1-Diborylalkanes. *Angew. Chem. Int. Ed.,* **2016**, *128* (4), 1520–1523.

(7) Yamanaka, M.; Kato, S.; Nakamura, E. Mechanism and Regioselectivity of Reductive Elimination of π-Allylcopper (III) Intermediates. *J. Am. Chem. Soc.,* **2004**, *126* (20), 6287–6293.

(8) Li, D.; Ohmiya, H.; Sawamura, M. Copper-Catalyzed γ-Selective and Stereospecific Allylic Alkylation of Ketene Silyl Acetals. *J. Am. Chem. Soc.,* **2011**, *133* (15), 5672–5675.

(9) Bluhm, M.; Maderna, A.; Pritzkow, H.; Bethke, S.; Gleiter, R.; Siebert, W. Synthesis of Tetraborylethenes and 1,1,1',1'-Tetra- and Hexaborylethanes; Electronic Interactions in Tetraborylethenes and 1,1,1',1'-Tetraborylethanes, and HF-SCF Calculation. *Eur. J. Inorg. Chem.,* **1999**, 1693–1700.

(10) Zhang, Z.; Fu, Y.; Xiao B. Preparation of Tetraborate Ethane Compound. *Patent CN 2016-10726662,* **2017**.

(11) Kumar, N.; Reddy, R. R.; Masarwa, A. Stereoselective Desymmetrization of *gem*-Diborylalkanes by "Trifluorination." *Chem. Eur. J.,* **2019**, *25* (34), 8008–8012.

(12) Lee, Y.; Park, J.; Cho, S. H. Generation and Application of (Diborylmethyl)Zinc(II) Species: Access to Enantioenriched *gem*-Diborylalkanes by an Asymmetric Allylic Substitution. *Angew. Chem. Int. Ed.,* **2018**, *57* (39), 12930–12934.

(13) Han, S.; Lee, Y.; Jung, Y.; Cho, S. H. Stereoselective Access to Tetra- and Tri-Substituted Fluoro- and Chloro-Borylalkenes *via* Boron-Wittig Reaction. *Angew. Chem. Int. Ed.,* **2022**, *61* (41), e202210532.

(14) González, S.; Del Carratore, D.; Maza, R. J.; Fernández, E. The Seriatim Cu(I) Activation of 1,1,1',1'-Tetrapinacolborylethane to Prospective Ring Closing. *Tetrahedron Chem,* **2023**, *8*, 100045.

(15) Kirihara, M.; Takuwa, T.; Okumura, M.; Wakikawa, T.; Takahata, H.; Momose, T.; Takeuchi, Y.; Nemoto, H. α-Bromo-α,α-difluoroallyl Derivatives as Synthetic Intermediate: Nucleophilic Substitution of α-Bromo-α,α-difluoroallyl Derivatives in the Presence of Palladium Catalysts. *Chem. Pharm. Bull.,* **2000***, 48* (6) 885–888.

(16) Meanwell, N. A. Fluorine and Fluorinated Motifs in the Design and Application of Bioisosteres for Drug Design. *J. Med. Chem.,* **2018**, *61* (14), 5822–5880.

(17) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001–2011). *Chem. Rev.,* **2014**, *114* (4), 2432–2506.

(18) Lang, S. B.; Wiles, R. J.; Kelly, C. B.; Molander, G. A. Photoredox Generation of Carbon-Centered Radicals Enables the Construction of 1,1-Difluoroalkene Carbonyl Mimics. *Angew. Chem. Int. Ed.,* **2017**, *56* (47), 15073–15077.

(19) Hu, M.; Ni, C.; Li, L.; Han, Y.; Hu, J. *gem*-Difluoroolefination of Diazo Compounds with $TMSCF_3$ or $TMSCF_2Br$: Transition-Metal-Free Cross-Coupling of Two Carbene Precursors. *J. Am. Chem. Soc.,* **2015**, *137* (45), 14496–14501.

(20) Zhang, X.; Cao, S. Recent Advances in the Synthesis and CF Functionalization of *gem*-Difluoroalkenes. *Tetrahedron Lett.,* **2017**, *58* (5), 375–392.

(21) Chelucci, G. Synthesis and Metal-Catalyzed Reactions of *gem*-Dihalovinyl Systems. *Chem. Rev.,* **2012**, *112* (3), 1344–1462.

(22) Pujol, M.; Maza, R. J.; Salvado, O.; Carbó, J. J.; Fernández, E. Site-Selective (*Z*)-α-Borylalkenyl Copper Systems for Nucleophilic Stereodefined Allylic Coupling. *Angew. Chem.Int. Ed.,* **2022**, *61* (37), e202208495.

(23) Falciola, C. A.; Alexakis, A. High Diversity on Simple Substrates: 1,4-Dihalo-2-butenes and Other Difunctionalized Allylic Halides for Copper-Catalyzed S_N2' Reactions. *Chem. Eur. J.,* **2008**, *14* (34), 10615–10627.

(24) Falciola, C. A.; Alexakis, A. 1,4-Dichloro- and 1,4-Dibromo-2-butenes as Substrates for Cu-Catalyzed Asymmetric Allylic Substitution. *Angew. Chem. Int. Ed.,* **2007**, *46* (15), 2619–2622.

(25) Miralles, N.; Gómez, J. E.; Kleij, A. W.; Fernández, E. Copper-Mediated S_N2' Allyl-Alkyl and Allyl-Boryl Couplings of Vinyl Cyclic Carbonates. *Org. Lett.,* **2017**, *19* (22), 6096–6099.

(26) Zhang, Q.; Wang, B.; Liu, J. Q.; Fu, Y.; Wu, Y. C. Mechanistic Insights into Solvent and Ligand Dependency in Cu(I)-Catalyzed Allylic Alkylation with *gem*-Diborylalkanes. *J. Org. Chem.,* **2018**, *83* (2), 561–570.

(27) Kim, M.; Park, B.; Shin, M.; Kim, S.; Kim, J.; Baik, M. H.; Cho, S. H. Copper-Catalyzed Enantiotopic-Group-Selective Allylation of *gem*-Diborylalkanes. *J. Am. Chem. Soc.,* **2021**, *143* (2), 1069–1077.

(28) Coombs, J. R.; Zhang, L.; Morken, J. P. Enantiomerically Enriched Tris(Boronates): Readily Accessible Conjunctive Reagents for Asymmetric Synthesis. *J. Am. Chem. Soc.,* **2014**, *136* (46), 16140–16143.

(29) Taniguchi, T.; Ishibashi, H. Short Synthesis of (-)-Cephalotaxine Using a Radical Cascade. *Org. Lett*., **2008**, *10* (18), 4129–4131.

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CHAPTER 3

Lithium Borylalkyde Salt towards Alkylation Reactions

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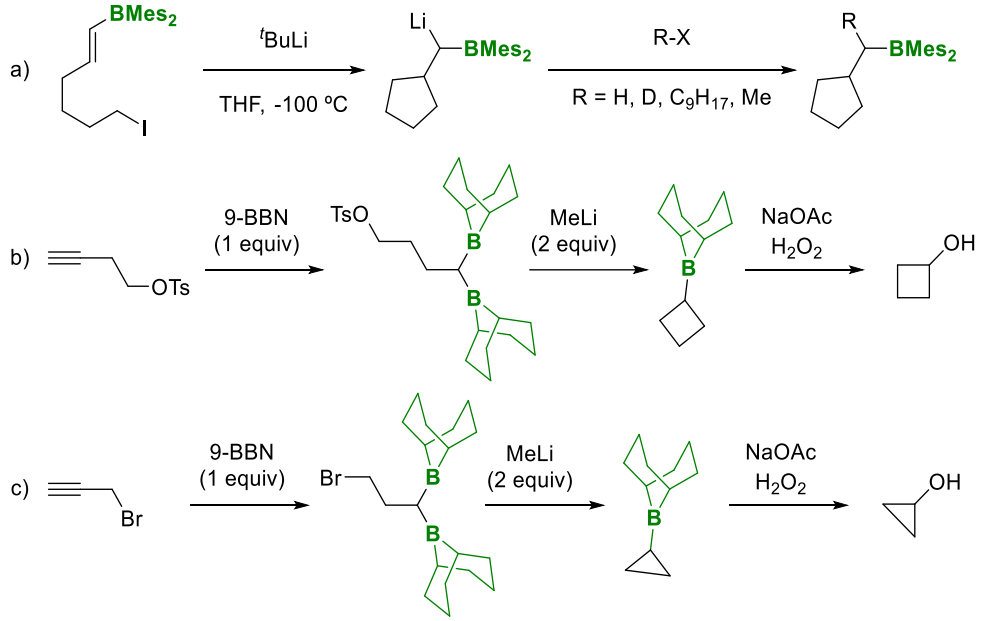
3.1 State of the art

The utilization of alkyllithium reagents for the deborylation of *gem*-diboryl alkanes has been widely extended since Zubiani and co-workers first investigated this process in 1966.[1] Sterically hindered amide bases, such as lithium diisopropylamide (LDA) and lithium 2,2,6,6-tetramethylpiperidide (LiTMP) can generate α-boryl carbanions by the deprotonation of the α-C–H bond of *gem*-diborylalkanes.[2–4] Another approach involves the use of sterically encumbered groups attached to boron, like methyldimesitylborane derivatives,[5,6] due to hindered properties on the boryl moiety. It is prevented that the bases do not coordinate to the boron, to form the corresponding boron'ate' compound. Following this methodology, the intramolecular nucleophilic addition of vinyl dimesitylboranes with hindered boryl substituents, allowed the preparation of cyclopentane products. This process has been carried out by the generation of an α-borata-alkene intermediate (Scheme 3.1a).[7]

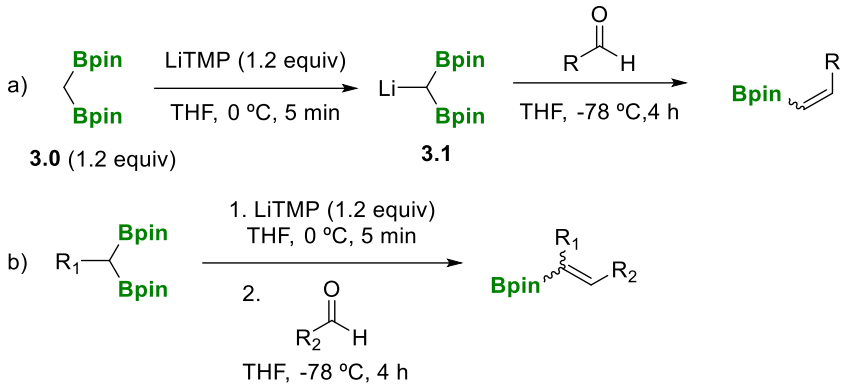
Another example of an intramolecular ring closure mechanism involving hindered boryl substituents has been demonstrated by an open-chain boron intermediate that formed a cyclobutane with a hindered boryl moiety. Initially, the dihydroboration of the tosylate of 3-butyn-1-ol with 9-borabicyclo[3.3.1]nonane (9-BBN) was performed, followed by the treatment with methyllithium to give the cyclobutane with the boryl substituent. Finally, the intermediate could be oxidized *in situ* to yield cyclobutanol (Scheme 3.1b). Cyclopropanol could also be synthesized using a similar procedure but starting from the dihydroboration of propargyl bromide (Scheme 3.1c).[8]



Scheme 3.1. Intramolecular nucleophilic addition of α-borylcarbanions towards a) borylated cyclopentanyl derivatives, b) cyclobutanol and c) cyclopropanol.

gem-(Diborylalkyl)lithium reagents have been typically generated *in situ* from *gem*-bis(boryl)alkanes with lithiated bases and have found application in numerous valuable syntheses.[9] For instance, Morken and co-workers have performed a highly stereoselective boron-Wittig reaction between bis(pinacolato)boryl methane and aldehydes (Scheme 3.2a). The intermediate (diborylmethyl)lithium salt **3.1** was formed by deprotonation using LiTMP to be subsequently reacted with a variety of linear, unsaturated and α-branched aldehydes to give the corresponding disubstituted alkenylboronic esters.

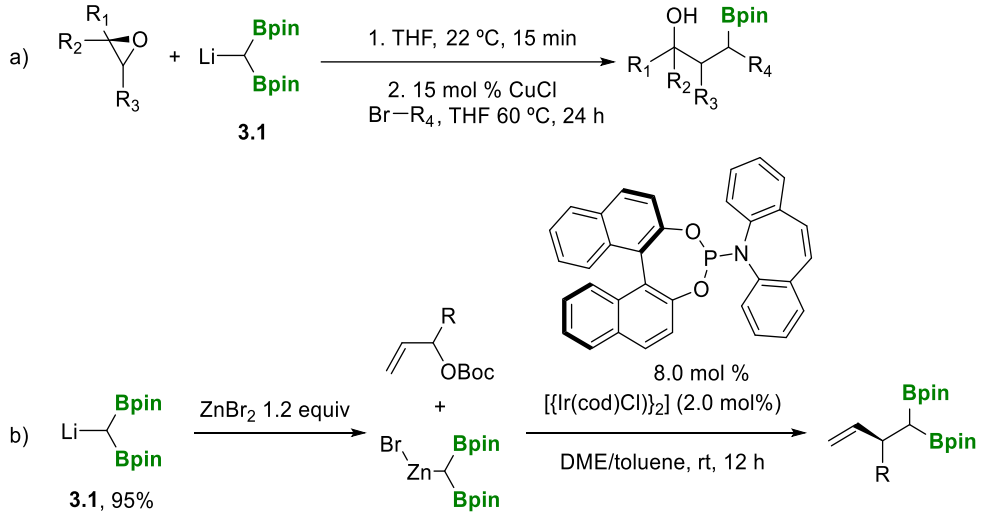
The Boron-Wittig reaction between other *gem*-(diborylalkyl)lithium reagents and aldehydes has also been studied to obtain trisubstituted alkenylboronic esters (Scheme 3.2b). Although the stereoselectivity was only achieved in moderate values for disubstituted alkenylboronic esters in certain experiments, the trisubstituted alkenylboronic esters could be prepared with high stereoselection.[10]



Scheme 3.2. *gem*-(Diborylalkyl)lithium reagents in a Boron–Wittig reaction to synthetize a) disubstituted alkenylboronic esters and b) trisubstituted alkenylboronic esters.

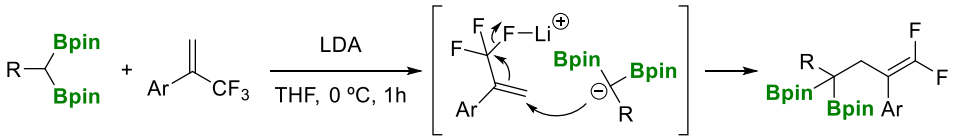
The reagent (diborylmethyl)lithium **3.1** has been used as a convenient reagent to enable the couplings of epoxides and allyl electrophiles in a stereoselective one-pot Cu-catalyzed coupling strategy, affording 1,3-hydroxy-organoborons (Scheme 3.3a). The first step involved the ring-opening of readily available chiral epoxides with the geminal species **3.1** to build C–C bonds with diastereomeric control. Subsequently, a stereospecific deborylative transmetallation with copper(I) generated the organocopper reagent, which was able to react with electrophiles forming tertiary C(sp^3) stereocenters and versatile Bpin moiety. A wide scope of terminal and internal epoxides has been tested in this three-component coupling reaction, as well as several electrophilic reagents.[11]

Remarkably, Cho and coworkers have established a method for the isolation of (diborylmethyl)lithium (**3.1**). They have employed the isolated compound **3.1** to generate (diborylmethyl)zinc(II) species by transmetallation with zinc(II) halides (X=Br, Cl) to subsequently apply them to the synthesis of enantioenriched *gem*-diborylalkanes bearing a stereogenic center at the β-position of the diboryl groups by an asymmetric allylic substitution reaction (Scheme 3.3b). The obtained *gem*-diborylalkanes can undergo appropriate stereospecific transformations, highlighting the synthetic utility of these compounds.[12]



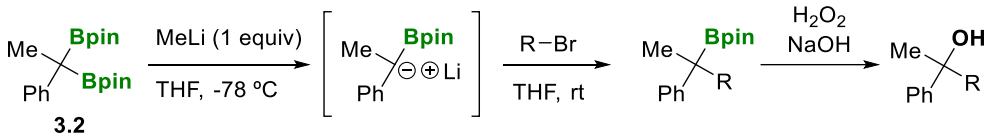
Scheme 3.3. Use of (diborylmethyl)lithium **3.1** intermediate to synthetize a) 1,3-hydroxy-organoborons and b) substituted *gem*-diborylalkanes.

The same authors have developed a synthesis of 4,4-difluoro homoallylic diboronate esters through a transition-metal-free defluorinative C–C bond-forming reaction of trifluoromethyl alkenes with *gem*-(diborylalkyl)lithiums (Scheme 3.4).[13] The resulting products, given the synthetic utility of diboron groups, can be converted into a variety of fluorine-containing organic molecules, attracting significant interest in both agrochemical and pharmaceutical industrial application. Substituted *gem*-(diborylalkyl)lithiums were generated *in situ* from *gem*-diborylalkanes, in the presence of LDA, and provided products with tetrasubstituted carbon centres. It has been proposed that the reaction proceeds *via* a concerted pathway involving the nucleophilic S_N2' attack of the α–borata-alkene intermediate to the terminal position of trifluoromethyl alkene followed by F^- displacement, forming LiF by-product.[13]



Scheme 3.4. Defluorinative C–C bond-forming reaction of trifluoromethyl alkenes with *gem*-(diborylalkyl)lithiums.

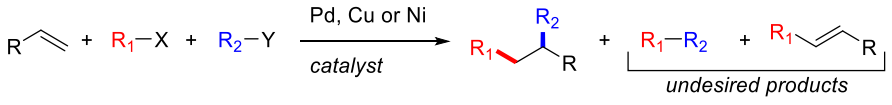
Kingsbury and Wommack serendipitously achieved the deborylative alkylation reaction of the disubstituted 1,1-diborylalkane **3.2**. Bimolecular alkylation of the α-borata-alkene, generated *in situ* from **3.2** by MeLi, reacted with several primary alkyl bromides, such as methyl bromide, n-butyl bromide, allyl bromide, and benzyl bromide (Scheme 3.5). The corresponding tertiary alkylboronate esters were oxidized to form tertiary alcohols.[14]



Scheme 3.5. Methyllithium-mediated deborylative alkylation of disubstituted *gem*-diborylalkane.

3.2 Context of the work

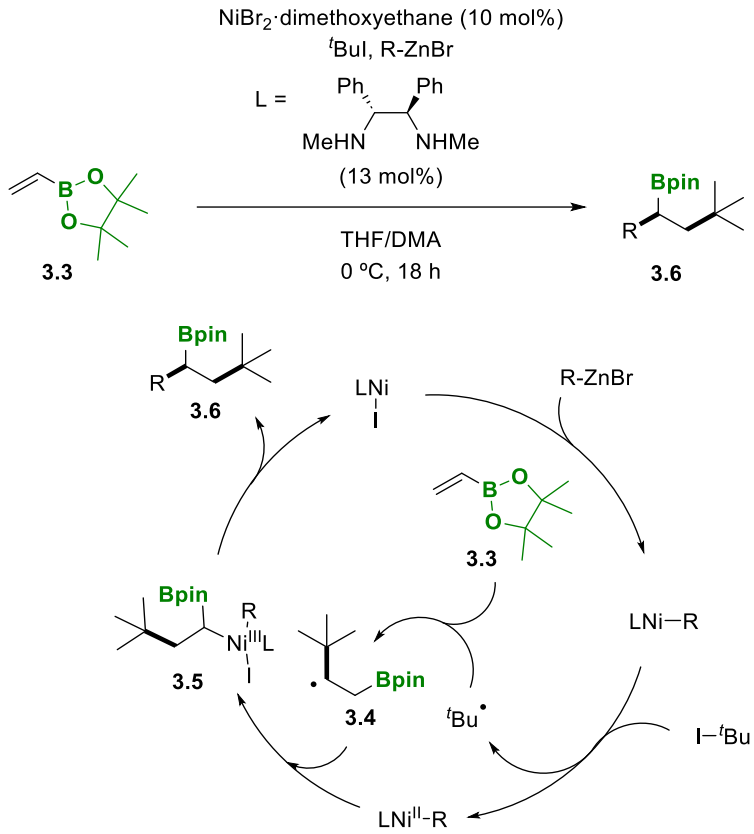
The formation of two carbon–carbon bonds across an alkene, known as dicarbofunctionalization, is an effective strategy to generate complex molecules from readily available chemicals. This method combines an alkene with two carbon electrophiles/nucleophiles and generates products with stereocenters. Alkene dicarbofunctionalization reactions have been conducted through cross-coupling with organic halides and organometallic reagents using Pd, Ni or Cu as catalysts.[15] However, the catalytic cycles might generate undesired by-products, due to the cross coupling between both reagents or Heck-type sequences through inherent β-H-elimination pathways. These drawbacks limit the application of this method to essentially C(sp^2) or C(sp) hybridized reagents (Scheme 3.6).



Scheme 3.6. General alkene dicarbofunctionalization reaction and formation of undesired by-products with R_1, R_2 = C(sp), C(sp^2) >> C(sp^3).

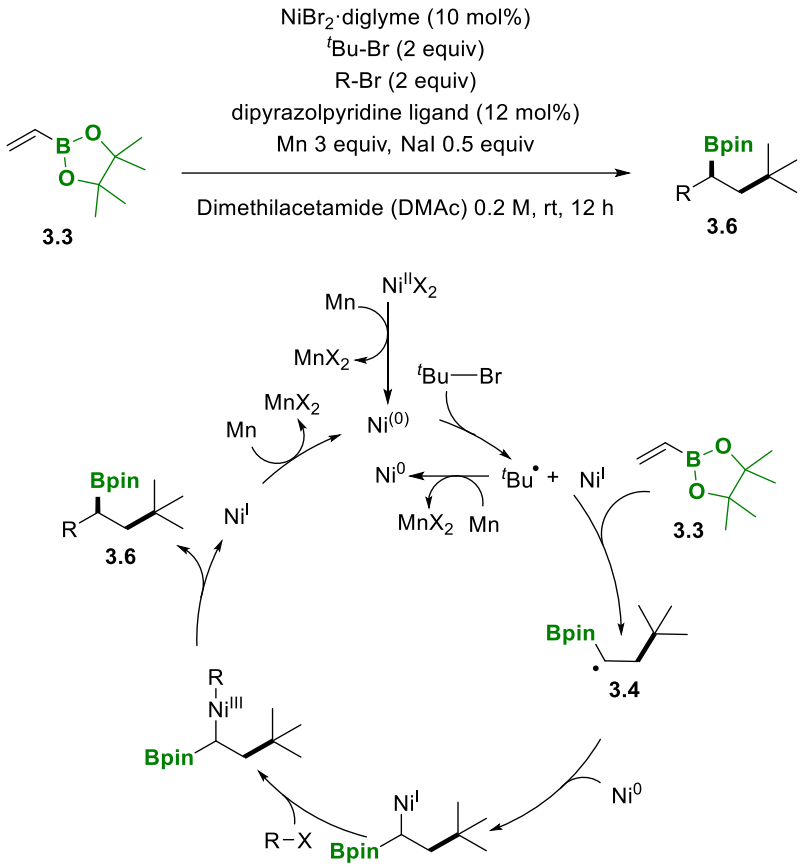
Throughout the past few years, significant progress has been made in difunctionalizing alkenes with C(sp)- and C(sp^2)-hybridized coupling partners. Nevertheless, catalytic alkene difunctionalization with two alkyl groups that creates two new C(sp^3)–C(sp^3) bonds involves more severe challenges.[16] This ambitious goal has scarcely succeeded, and the most remarkable examples are based on the use of Ni,[16,17] Ti,[18,19] Fe[20] or Co[21] catalyst.

The formation of stable α-boryl radical intermediates on the vinylboronic acid pinacol ester **3.3** can be performed *via* transition-metal/radical catalytic processes, making possible overcoming the limitation to the broad use of C(sp^3) electrophiles. Morken and co-workers have described an alternate process that involves a Ni/radical hybrid reaction, enabling the coupling of organozinc reagents, alkyl iodides, and alkenyl boron compounds in an enantioselective manner (Scheme 3.7).[22] The reaction appeared to proceed by a tandem radical addition/cross-coupling cascade, where the halide abstraction from the C(sp^3) alkyl halide with a Ni^{I} alkyl complex, furnished the radical intermediate **3.4**. Subsequently, Ni^{II} alkyl complex combined with **3.4** generated a Ni^{III} complex **3.5** along with a Ni^{I} complex iodide. Complex **3.5** then undergoes reductive elimination and delivers the product **3.6**. Transmetallation between the organozinc reagent and Ni^{I} complex iodide regenerates the starting Ni^{I} alkyl complex (Scheme 3.7).



Scheme 3.7. Mechanism of the three-component nickel/radical coupling reaction with the vinylboronic acid pincol ester **3.3** precursor.

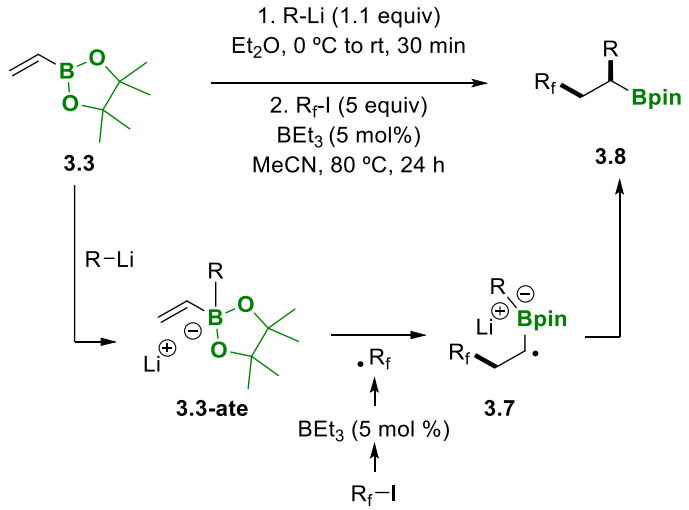
An alternative approach towards three-component Ni catalyzed difunctionalization of vinylboronic esters has been proposed by Lu, Fu and co-workers through a nickel-catalyzed reductive dialkylation of **3.3** with a variety of alkyl bromides.[23] They have avoided the use of organometallic reagents by developing a nickel/photoredox dual-catalyzed reductive cross-coupling. The reaction was initiated with the formation of a nucleophilic *tert*-alkyl radical in the presence of Ni^{II} catalyst and the Mn(0) as a reductant, to subsequently be added to the alkenylboronic ester **3.3**. The resulting *sec*-alkyl radical **3.4**, stabilized by a contiguous boron atom, was trapped by the nickel catalyst to perform an oxidative addition with the alkyl halide to accomplish the cross-coupling and obtain the product **3.6** (Scheme 3.8).



Scheme 3.8. Mechanism of the three-component nickel-catalyzed reductive dialkylation with the vinylboronic acid pincol ester **3.3** precursor.

Other three-component processes that enabled two C–C bonds have emerged by merging photocatalysis and nickel catalysis. Molander and co-workers have established a functional group tolerant procedure to form in a single step C(sp^3)–C(sp^3) and C(sp^3)–C(sp^2) bonds, which have set both quaternary and tertiary centers.[24] Martin and co-workers' strategy developed a methodology promoting a dual catalysis attaining excellent chemo- and regioselectivity in the 1,2-difunctionalization of alkenylboronic esters under mild conditions.[25] Despite the significant advancements in this field, examples on formation of two C(sp^3)–C(sp^3) bonds across the alkenylboronic ester had not been described.

Vinylboronic acid derivatives and their corresponding boron-ate complexes have proven to be highly valuable substrates in organic synthesis. Studer and co-workers have avoided transition metal catalysts by generating a vinylboronic ester 'ate' complex **3.3-ate**.[26] It has been proposed that perfluoroalkyl iodides (R_f–I) acted as carbon radical precursors with the additive BEt_3 as a radical initiator to form the adduct radical **3.3-ate**. Then, a single-electron oxidation of **3.3-ate** by the perfluoroalkyl iodide would lead in a radical-polar crossover step towards zwitterion **3.7**. Ionic 1,2-alkyl/aryl migration would eventually provide the target boronic ester **3.8** (Scheme 3.9).

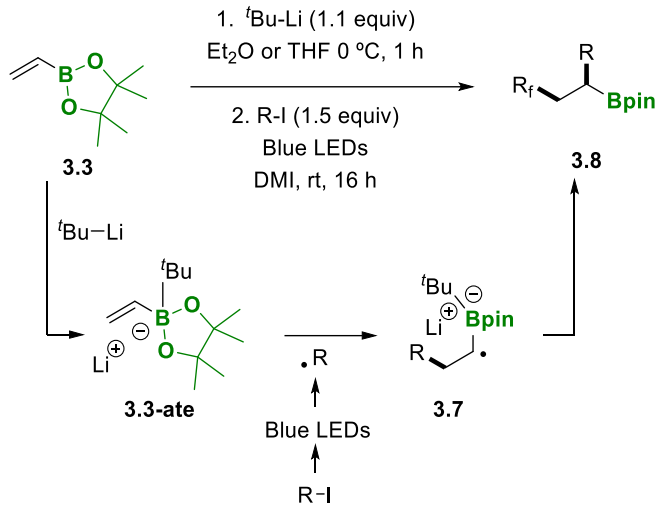


Scheme 3.9. Mechanism of the three-component radical-polar crossover reaction of the vinylboronic acid pincol ester **3.3** precursor.

Alternatively, Morken and co-workers' approach involved a palladium-induced metallate rearrangement wherein 1,2-migration of an alkyl or aryl group from boron to the vinyl α-carbon occurs concomitantly with C–Pd σ-bond formation, enabling 1,2-difunctionalized products.[27] However, these methodologies have not been reported to form two C(sp^3)–C(sp^3) bonds across the alkenyl boronates.

Eventually, Aggarwal and co-workers considered merging the features of photoredox reactions with 1,2-metalate rearrangements.[28] Specifically, they

designed the reaction of vinyl boronates **3.3-ate** type with electrophilic α-carbonyl radicals, generated by an homolytic cleavage of the alkyl iodide by visible light. The reaction led to the radical anion **3.7** that underwent single-electron oxidation and triggered a 1,2-metalate rearrangement, yielding boronic esters **3.8** (Scheme 3.10). In some particular cases, a ruthenium photocatalyst was necessary to achieve high yields. [28]



Scheme 3.10. Mechanism of the three-component photochemical alkylation of the vinylboronic acid pincol ester **3.3** precursor.

3.3 Specific objectives

The main goal of this chapter is the development of an operational simple intermolecular three-component assembly across alkenylboranes. In the absence of catalyst, additive or any type of radical initiators, we planned to accomplish the electrophilic trapping of borata-alkene intermediates led to the synthesis of tertiary boronic esters.[29]

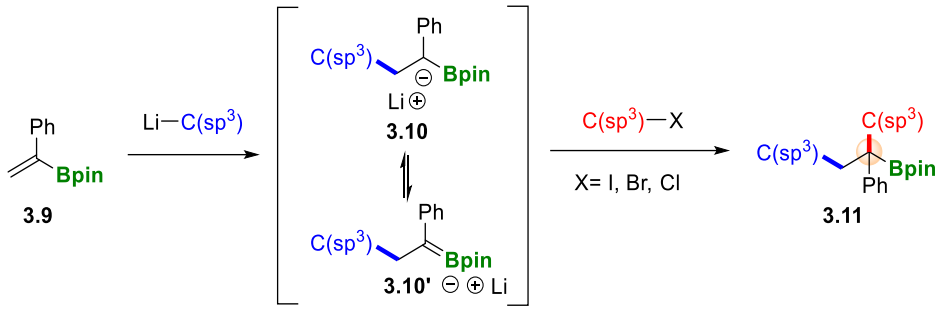
The specific objectives are:

1. Synthesis of tertiary boronic ester products by assembling Li–C(sp^3) reagents, a vinylboronic acid pincol ester, and primary or secondary alkyl halides.
2. Oxidation of the tertiary boronic esters towards novel tertiary alcohols.
3. Study of selective alkyl trapping sequences in the reaction outcome.
4. Intramolecular deborylative cyclization of one of the obtained products.
5. Extension of the reaction to transborylated 1-phenylvinylboronic acid pinacol ester to isolate chiral substrate.
6. Synthesis of diastereoisomeric tertiary boronic ester products and their corresponding enantioselective alcohols.
7. ^{11}B NMR spectroscopic studies about ^{t}BuLi addition to alkenylboronic esters, followed by alkylation with MeI or protonated with MeOH.

3.4 Results and discussion

Herein, we envisioned the polar addition of Li–C(sp^3) reagent to the terminal carbon of 1-phenylvinylboronic acid pinacol ester **3.9**, with the subsequent formation of the corresponding α-boryl carbanion. The valence deficiency of the adjacent three coordinate boron center confers high stability to the system, as it is displayed in the Scheme 3.11 with the borata-alkene resonance forms **3.10** – **3.10'**.[30,31] The reaction is planned to conclude with an electrophilic trapping with alkyl halides C(sp^3)–X v*ia* substitution pathways, forming two new C(sp^3)–C(sp^3) bonds *via* borata-alkene intermediates in a "all-C(sp^3)" cross-coupling reaction (Scheme 3.11). The work showcased here lacks the need for catalysts,

additives, or radical initiators to deliver valuable tetrasubstituted carbon centers in **3.11**.

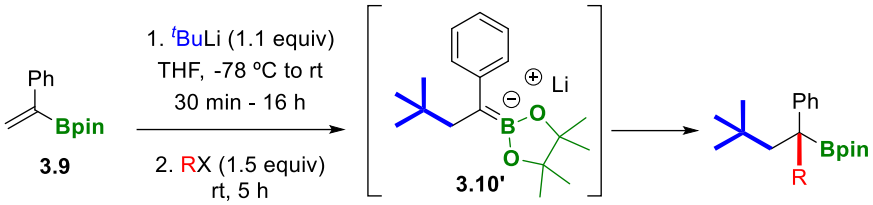


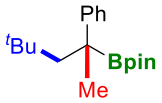
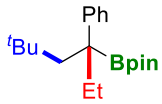
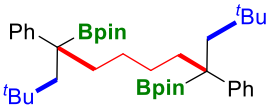
Scheme 3.11. Dicarbofunctionalization of alkenes with formation of two C(sp^3)–C(sp^3) bonds *via* borata-alkene intermediates.

As a proof of concept, we explored the addition of 1.1 equiv of ^{t}BuLi to 1-phenylvinylboronic acid pinacol ester **3.9**, at -78 °C for 30 minutes, and 16 h at room temperature, in THF as solvent. Subsequently, 1.5 equiv of MeI was added and the reaction mixture was stirred for 5 h. Substrate **3.9** was converted into product **3.12** in 85% (by NMR in comparison with internal standard naphthalene) and 75% isolated yield (Table 3.1, entry 1). The formation of two new C(sp^3)–C(sp^3) bonds across the 1,1-arylboryl alkene was conducted regioselectively placing the ^{t}Bu group at the terminal position and the Me group at the internal position.

The simplicity of the three-component assembly could be extended to other primary iodides, achieving a comparable reaction outcomes. Product **3.13** was obtained with EtI as the electrophilic reagent although with lower yield (Table 3.1, entry 2). Remarkably, a double dicarbofunctionalized product **3.14** could be isolated when using 1,4-diiodobutane reagent, since two tetrasubstituted carbon atoms were simultaneously formed (Table 3.1, entry 3). This significant increase of the molecular complexity involves five-components assembly in a simple operational step.

Table 3.1. Scope of dicarbofunctionalization with ^{t}BuLi and primary alkyl iodides.[a]



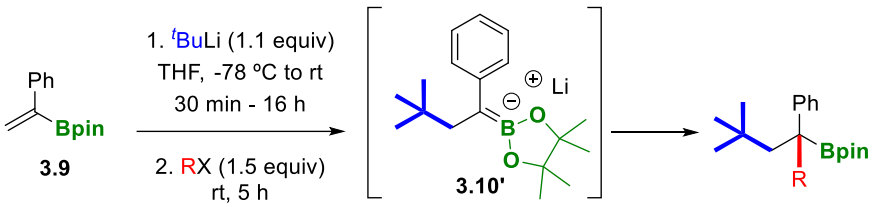
Entry	Allyl halide	Product	Conversion %[b] and Isolated Yield [%][c]
1	Me—I	 **3.12**	85 % [75 %]
2	Et—I	 **3.13**	71 % [55 %]
3		 **3.14**	83 % [79 %]

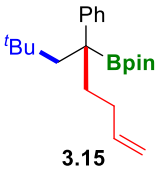
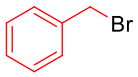
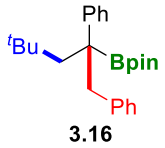
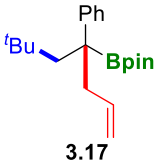
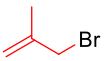
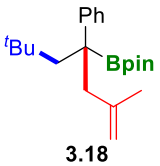
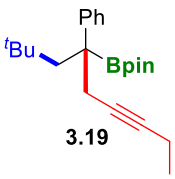
[a]Reactions performed at 0.3 mmol scale of **3.9**, ^{t}BuLi(1.1 equiv), THF (2 mL), -78 °C for 30 min., rt for 16 h. Then, RX (1.5 equiv), rt, 5 h. [b]Conversion and yields determined by NMR with naphthalene as internal standard. [c]Isolated yield after purification.

Next, we were committed to prove whether alternative functional groups were compatible with this 1,2-dicarbofunctionalization strategy and to our delight the primary alkyl bromide 4-bromobut-1-ene was efficiently trapped to generate product **3.15** in 93% isolated yield (Table 3.2, entry 1). Benzyl bromide was next assembled to **3.9**, in the presence of ^{t}BuLi, and the new C–C bond was conveniently performed to generate product **3.16** in 76% isolated yield (Table 3.2, entry 2). Allyl bromides were also explored and the tertiary homoallylic boronic esters **3.17** and **3.18** could be efficiently prepared in comparable yield (Table 3.2, entry 3-4). The tolerance of alternative functional groups along the 1,2-dicarbofunctionalization process was studied with the introduction of the

electrophile 1-bromopent-2-yne, preserving the triple bond intact since no allene group was detected at the isolated product **3.19** (Table 3.2, entry 5).

Table 3.2. Scope of dicarbofunctionalization with ^{t}BuLi and primary allyl bromides.[a]

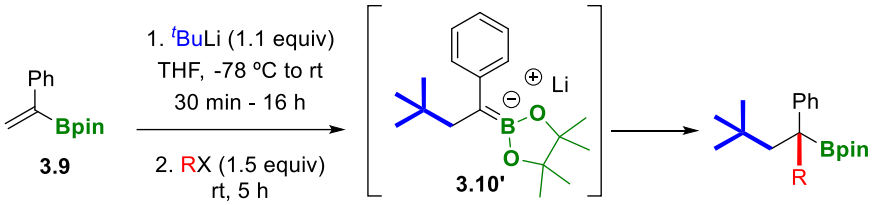


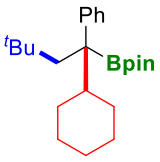
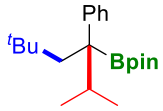
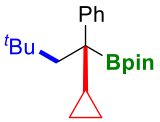
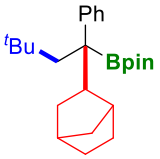
Entry	Allyl halide	Product	Conversion %[b] and Isolated Yield [%][c]
1		 **3.15**	97% [93%]
2		 **3.16**	83% [76%]
3		 **3.17**	85% [71%]
4		 **3.18**	85% [78%]
5		 **3.19**	50% [41%]

[a]Reactions performed at 0.3 mmol scale of **3.9**, ^{t}BuLi(1.1 equiv), THF (2 mL), -78 °C for 30 min., rt for 16 h. Then, RX (1.5 equiv), rt, 5 h. [b]Conversion and yields determined by NMR with naphthalene as internal standard. [c]Isolated yield after purification.

Secondary alkyl iodide CyI could also be used in the trapping sequence, resulting in the product **3.20** in 69 % isolated yield (Table 3.3, entry 1). More challenging resulted the use of secondary alkyl bromide electrophiles, which were also explored to be trapped with the borata-alkene intermediate **3.10'**, and tertiary boronic esters **3.21**–**3.22** could be prepared in modest yields (Table 3.3, entry 2-3), as well as product **3.23** with 7:3 diastereomeric ratio (Table 3.3, entry 4).

Table 3.3. Scope of dicarbofunctionalization with ^{t}BuLi and secondary alkyl halides.[a]

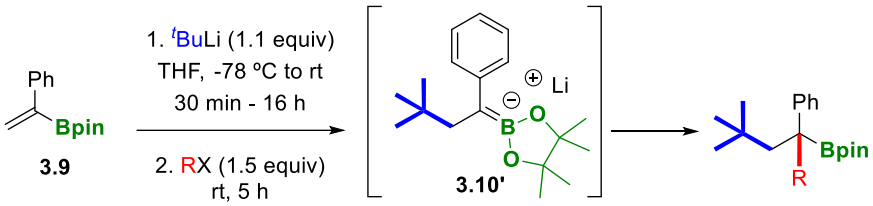


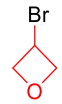
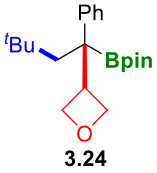
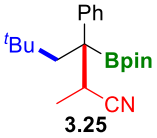
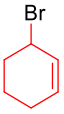
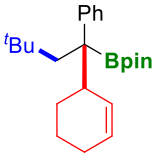
Entry	Allyl halide	Product	Conversion %[b] and Isolated Yield [%][c]
1		 **3.20**	75% [69%] (dr = 1:1)
2		 **3.21**	46% [41%]
3		 **3.22**	39% [33%]
4		 **3.23**	50% [46%] (dr = 7:3)

[a]Reactions performed at 0.3 mmol scale of **3.9**, ^{t}BuLi(1.1 equiv), THF (2 mL), -78 °C for 30 min., rt for 16 h. Then, RX (1.5 equiv), rt, 5 h. [b]Conversion and yields determined by NMR with naphthalene as internal standard. [c]Isolated yield after purification.

Not only we were able to introduce sterically hindered cyclic systems in the electrophilic trapping, but also we proved the tolerance with diverse functional groups. Table 3.4 shows the formation of products **3.24** - **3.26** in modest yields. However, it can be demonstrated the feasibility of the reaction with ether groups, cyano groups and unsaturated groups. Again, moderate yields were obtained due to the steric impediment of the secondary electrophiles.

Table 3.4. Scope of dicarbofunctionalization with ^{t}BuLi and secondary alkyl bromides with functional groups.[a]

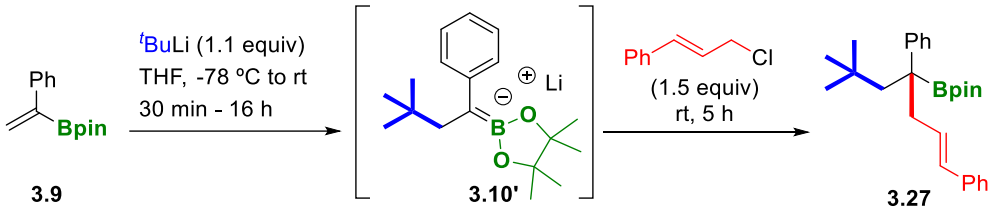


Entry	Allyl halide	Product	Conversion %[b] and Isolated Yield [%][c]
1		 **3.24**	32% [25%]
2		 **3.25**	36% [32%]
3		 **3.26**	37% [34%] (dr = 7:3)

[a]Reactions performed at 0.3 mmol scale of **3.9**, ^{t}BuLi(1.1 equiv), THF (2 mL), -78 °C for 30 min., rt for 16 h. Then, RX (1.5 equiv), rt, 5 h. [b]Conversion and yields determined by NMR with naphthalene as internal standard. [c]Isolated yield after purification.

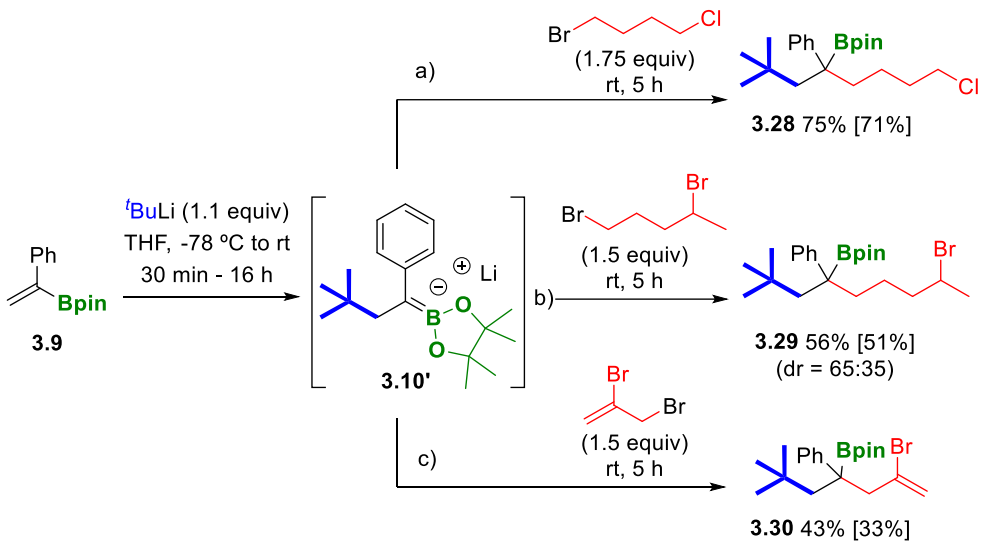
In addition, in order to check whether an allylic rearrangement is operating through the C–C bond formation, we selected cinnamyl chloride to react with

3.9, in the presence of ^{t}BuLi. However, to the light of the exclusive formation of product **3.27**, where no conjugative process was observed, we could confirm that the substitution of chloride took place preferentially (Scheme 3.12). This, along with the lack of activity observed with ^{t}BuI, PhI and vinyl-I, as alkylating agents, is consistent with a S_N2 reaction mechanism.



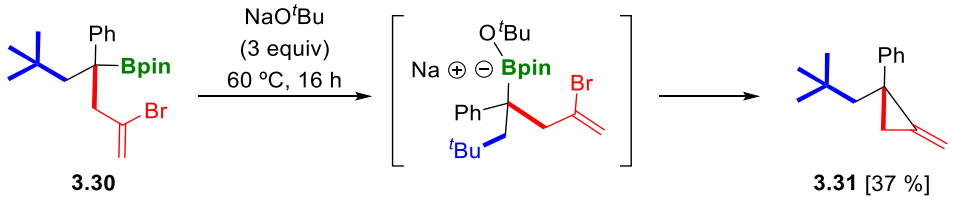
Scheme 3.12. Dicarbofunctionalization of alkene **3.9** with with ^{t}BuLi and cinnamyl chloride.

The preference in the coupling with alkyl bromides versus alkyl chlorides could be demonstrated when 1-bromo-4-chlorobutane reacted with **3.9** and ^{t}BuLi, generating only monoalkylated product **3.28**, preserving the C–Cl functionality throughout the three-component assembly (Scheme 3.13a). Interestingly, selective alkyl trapping has also been observed when the borata-alkene intermediate **3.10'** reacted with 1,4-dibromopentane or 2,3-dibromoprop-1-ene to form the tertiary boronic esters **3.29** (Scheme 3.13b) and **3.30** (Scheme 3.13c), respectively, demonstrating the preference for primary versus secondary alkyl bromides along the trapping sequence. As far as we know, compounds **3.12**-**3.30** were prepared for the first time in this work.



Scheme 3.13. Selective trapping of alkene **3.9** with with ^{t}BuLi and a) 1-bromo-4-chlorobutane, b) 1,4-dibromopentane and c) 2,3-dibromoprop-1-ene.

In the presence of an excess of NaO^{t}Bu as a base, the Bpin moiety can suffer protodeborylation.[32] Thus, when we protodeborylated the previously obtained compound **3.30** with 3 equiv of base, at 60 °C in hexane for 16 h, we could observe an intramolecular cyclization towards the product **3.31** in a moderate yield (Scheme 3.14).



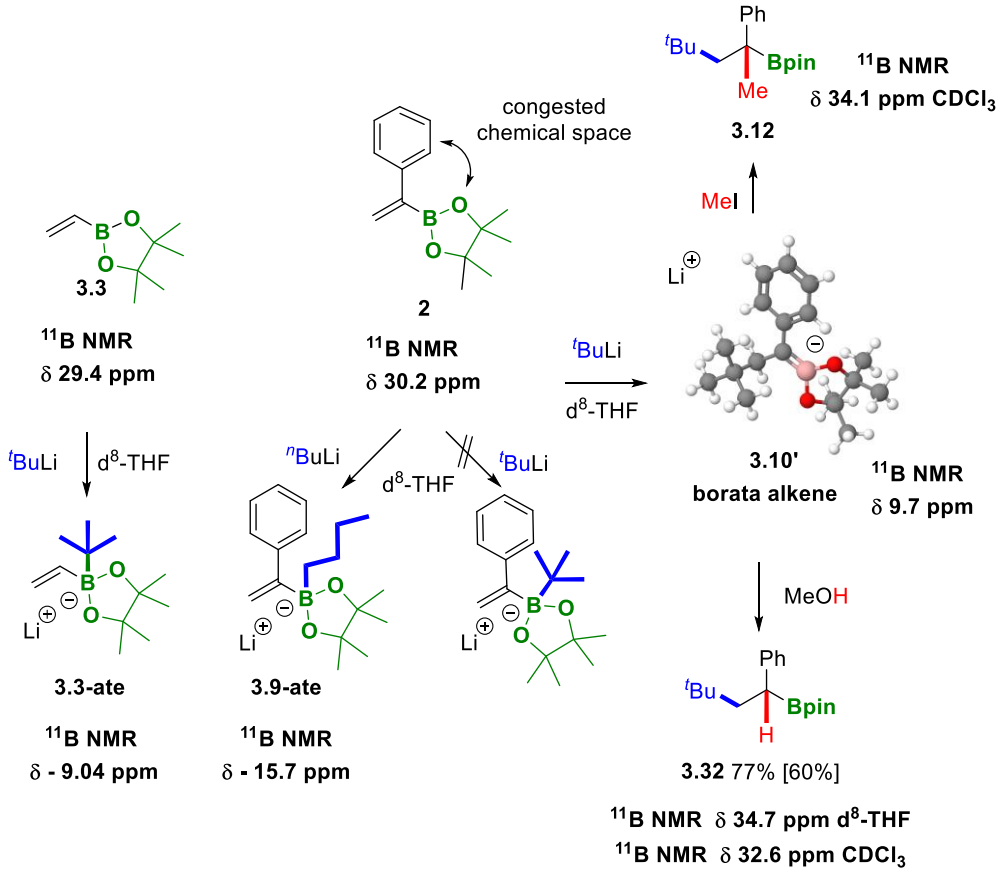
Scheme 3.14. Intramolecular deborylative cyclization of the product **3.30**.

Our nex challenge was to explain the unexpected reactivity observed on the olefin activation to nucleophilic addition of ^{t}Bu by virtue of the presence of the polarizing pinacolboryl substituent. In addition, the presence of the Ph group, in geminal position to the Bpin group, seems to be of fundamental importance, because the Ph group in alpha position suppressed the formation of the boron 'ate' complex, which led to the borata-alkene as the favoured intermediate. The

expected direct interaction of the ^{t}Bu group with the empty p orbital of boron seems to be precluded in this case due to the congested chemical space in the 1,1-disubstituted alkene **3.9** (Scheme 3.15).

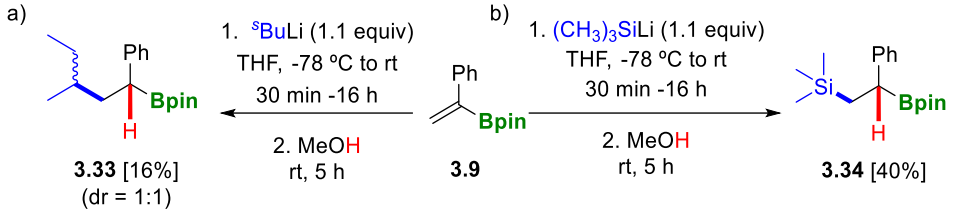
Whereas the vinylboronic ester 'ate' complex **3.3-ate** formation between unhindered vinylboronic ester **3.3** and ^{t}BuLi, or between ^{n}BuLi and **3.9** (**3.9-ate**) is favoured, to the best of our knowledge the vinylboronic ester 'ate' complex formed between **3.9** and ^{t}BuLi, is unknown. This suppression of boron 'ate' complex formation was unambiguously confirmed by ^{11}B nuclear magnetic resonance spectroscopy (in deuterated tetrahydrofuran solvent) by mixing **3.9** and ^{t}BuLi (1:1), since only one characteristic borata-alkene signal at δ=9.7 ppm was observed,[30] in contrast to the signals observed about δ=−9.0 and −15.7 ppm associated to boron'ate' species **3.3-ate** and **3.9-ate**, respectively (Scheme 3.15).

A precedent on boron-activated nucleophilic addition to olefins by steric suppression of boron'ate' complex was reported for α-trimetylsilyl substituted vinyldimesitylboranes, although attempts to alkylate the borata-alkene intermediate were only successful with MeI.[7] The trapping of the α-boryl carbanion **3.10'** with MeOH resulted in the formation of the secondary boronic ester **3.32** (Scheme 3.15), with a comparable yield to that obtained *via* iridium photoredox/nickel catalysis alkylation/arylation of **3.9**.[24]



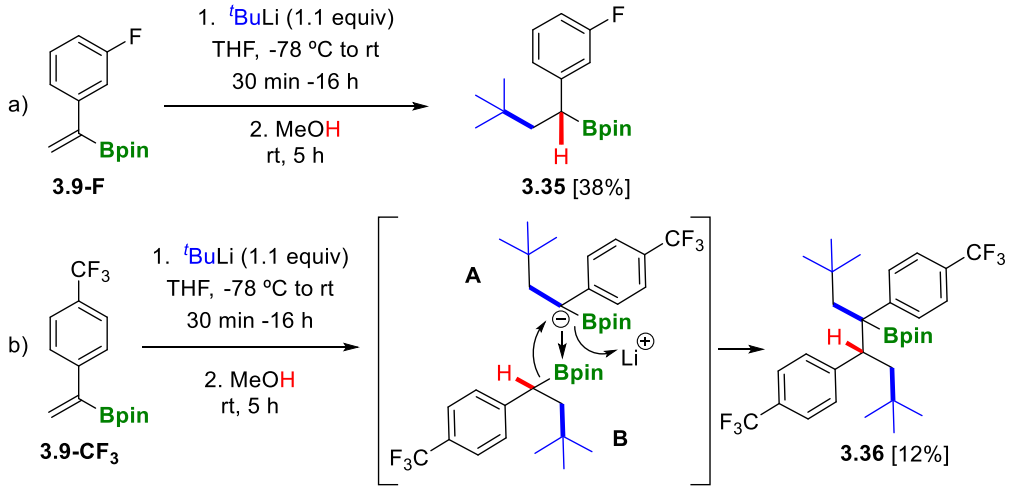
Scheme 3.15. ^{11}B NMR spectroscopic studies about ^{t}BuLi addition to alkenylboronic esters, followed by alkylation with MeI or protonated with MeOH.

When the alternative lithiated base *sec*-butyllithium (^{s}BuLi) was added to **3.9**, we were able to isolate the secondary boronic ester **3.33** (Scheme 3.16a), as a (1:1) mixture of the two diastereoisomers, by trapping the borata-alkene intermediate with MeOH. Although the conversion was quantitative,the isolated yield was very low due to inherent instability of the product during the purification protocol. For comparison, the use of $(CH_3)_3SiLi$ to activate substrate **3.9**, followed by protonation with MeOH, allowed the isolation of the silylborylated specie **3.34** (Scheme 3.16b). The use of the alternative organometallic regent *tert*-butyl-magnesium bromide was inefficient for the activation of **3.9**, and unreacted substrate was observed instead.



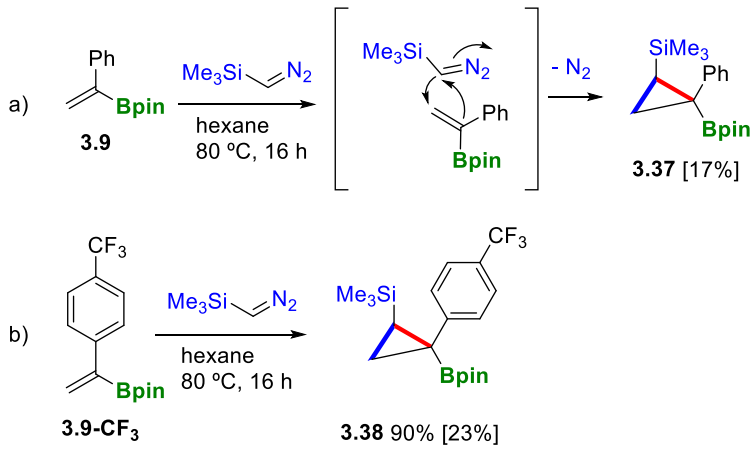
Scheme 3.16. Nucleophilic addition to the terminal carbon of 1-phenylvinylboronic acid pinacol ester **3.9** of the lithiated bases a) ^{s}BuLi and b) $(CH_3)_3SiLi$.

The introduction of electron withdrawing substituents on the aryl group in the substrates **3.9-F** and **3.9-CF$_3$** was postulated to generate an extra stabilization of the carbanion lone pair on the α-boryl carbanion. When the ^{t}BuLi was added to the vinylboronic ester **3.9-F**, followed by addition of MeOH, the corresponding secondary boronic ester **3.35** was isolated in 38% (Scheme 3.16a). However, when the ^{t}BuLi was added to **3.9-CF$_3$** the reaction produced the tertiary boronic ester as a dimer **3.36** (Scheme 3.17b), suggesting a deborylative cross coupling pathway. We postulated a plausible interaction between the α-boryl carbanion **A** with the boryl of the secondary boronic ester **B**, *via* boron "ate" formation and 1,2-shift rearrangement (Scheme 3.17b). In this case, the molecular assembling involves four components in a single operational step.



Scheme 3.17. ^{t}BuLi addition to the terminal carbon of the alternative 1,1-arylboryl alkenes a) *m*-fluoro-1-phenylvinylboronic acid pinacol ester and b) *p*-trifluoromethyl-1-phenylvinylboronic acid pinacol ester.

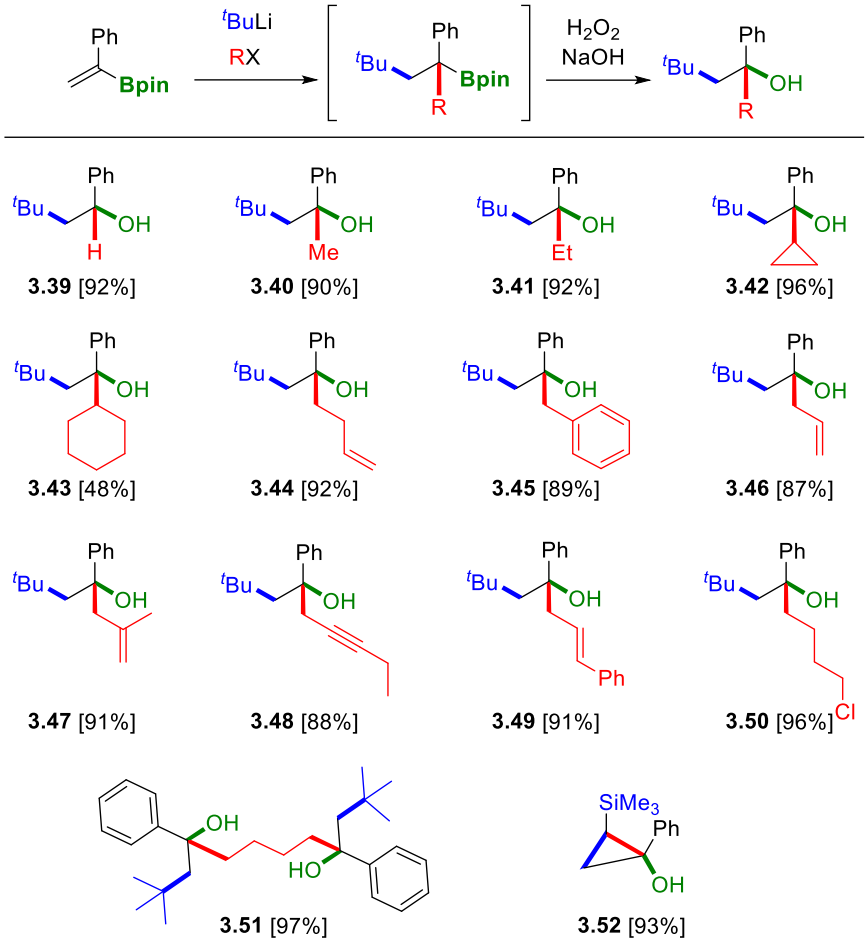
We also postulated that a carbene addition on the terminal position of the alkene might be followed by an intramolecular C–C bond formation through the borata-alkene, with the concomitant N_2 release. When **3.9** reacted with (trimethylsilyl)diazomethane (TMSDM), the polysubstituted cyclopropane **3.37** (Scheme 3.18a) was essentially formed, although isolated in low yield. Similarly, substrate **3.9-CF$_3$** could be used to yield the product **3.38** in 23% isolated yield (Scheme 3.18b). This reaction has become the first transition metal free catalyzed cyclopropanation of alkenylboranes with TMSDM.[33,34] The relative stereoselectivity shows an exclusive *trans* configuration of the $SiMe_3$ and Bpin vicinal substituents in both resulting products.



Scheme 3.18. Addition of TMSDM to a) 1-phenylvinylboronic acid pinacol ester and b) *p*-trifluoromethyl-1-phenylvinylboronic acid pinacol ester to form polysubstituted cyclopropanes.

One of the most straightforward applications of the dicarbofunctionalization of 1,1-arylboryl alkenes developed in this work is the oxidation of the prepared tertiary boronic esters to form tertiary alcohols. This procedure has been conducted with H_2O_2/NaOH and the resulting alcohols were isolated in quantitative yields (Scheme 3.19). It is worth mentioning that tertiary alcohols **3.41**–**3.51** have been synthetized for the first time through our methodology. Only 4,4-dimethyl-2-phenylpentan-2-ol (**3.40**) was earlier prepared *via* air-assisted addition of Grignard reagents to olefins[35] or *via* multicomponent oxyalkylation of styrenes enabled by hydrogen-bond-assisted photoinduced

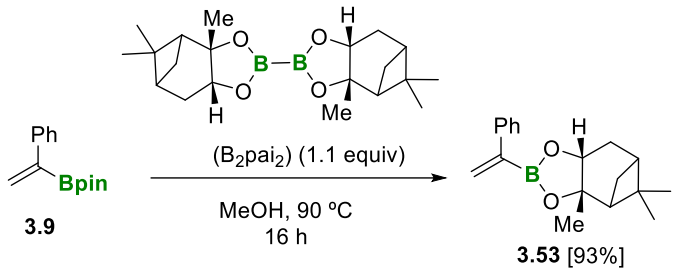
electron transfer.[36] Additionally, the polysubstituted cyclopropanol 1-phenyl-2-(trimethylsilyl)cyclopropan-1-ol (**3.52**) had been previously synthetized by coupling of vinylsilanes and esters with titanium(II) as catalyst.[37]



Scheme 3.19. Oxidation of tertiary boronic esters towards the synthesis of novel secondary and tertiary alcohols.

To conclude the scope of this 1,2-dialkylation of 1,1-arylboryl alkenes *via* borata-alkene intermediates, we aimed to induce asymmetry in the new tertiary boronic esters, and their corresponding tertiary alcohols. First, in accordance with preceding studies in the group, we transborylated the Bpin moiety in 1-phenylvinylboronic acid pinacol ester **3.9** using bis-(+)-pinanediolato diboron (B_2pai_2) to synthesize the corresponding chiral substrate 1,1-disubstituted

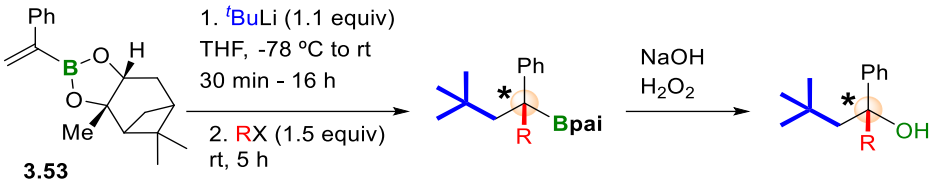
alkenyl (+)-pinanediolboronic ester (**3.53**) in a simple and direct protocol (Scheme 3.20).[38]

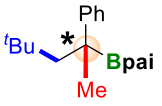
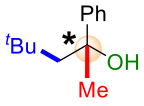
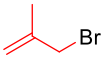
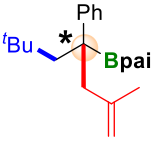
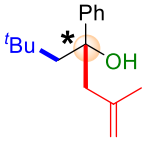
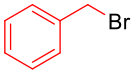
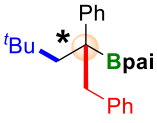
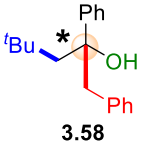


Scheme 3.20. Synthesis of chiral substrate *via* transborylation of alkenylboranes with diboranes.

The addition of ^{t}BuLi to **3.53** and the subsequent trapping with methyliodide or 2-methylallylbromide, resulted in the formation of the diastereoisomeric mixture of tertiary boronic esters **3.54** and **3.55**, respectively. The modest diastereomieric ratio was confirmed when oxidation of **3.54** and **3.55** generated the tertiary alcohols **3.56** and **3.57**, in 9% and 12% enantiomeric excess, respectively (Table 3.5, entries 1 and 2). However, when the electrophilic trapping of the chiral alkenylboronic ester **3.53** was performed with benzylbromide, the tertiary alcohol **3.58** was isolated in 44% enantiomeric excess. In this case, the oxidation was completed *in situ*, without the isolation of the corresponding tertiary boronic ester (Table 3.5, entry 3). Similar e.e. values were obtained in the enantioselective version of the radical-polar crossover reaction with commercially available chiral (+)-vinylboronic acid pinanediol ester, following the reaction above-displayed in Scheme 3.9.[26] The increased enantioselectivity for product **3.58** over **3.56** and **3.57** might be due to the increased sterically hindrance provided by the chiral boryl moiety on the trapping reagent.

Table 3.5. Dicarbofunctionalization with ^{t}BuLi of the chiral substrate 3.53 and subsequent trapping with C(sp^3)-X/oxidation.[a]



Entry	Allyl halide	Product	Isolated Yield [%][b]	Alcohol	Isolated Yield [%][b]
1	Me—I	 **3.54**	[58%] (dr= 55:45)	 **3.56**	[90 %] 9 ee[c]
2		 **3.55**	[60%] (dr= 60:40)	 **3.57**	[70%] 12 ee[c]
3		 *in situ*	-	 **3.58**	[15%] 44 ee[c]

[a]Reactions performed at 0.3 mmol scale of **3.53**, ^{t}BuLi(1.1 equiv), THF (2 mL), -78 °C for 30 min., rt for 16 h. Then, RX (1.5 equiv), rt, 5 h. [b]Isolated yield. [c]ee calculated by HPLC.

3.5 Conclusions

In conclusion, we have described here one operational simple unconventional intermolecular assembly across alkenylboranes. This methodology forms two C(sp^3)–C(sp^3) bonds through regioselective 1,2-dicarbofunctionalization of 1,1-arylboryl alkenes, generating tertiary boronic esters which are highly valuable compounds for diverse follow-up chemistry, such as oxidation towards tertiary alcohols. This methodology facilitates a rapid influx of molecular complexity throughout the ^{t}BuLi, ^{s}BuLi, Me_3SiLi or TMSDM addition to alkenylboronic esters allowing the generation of two new C(sp^3)–C(sp^3) bonds across the alkene, *via*

borata-alkene intermediates, in the absence of catalyst, additives or any type of radical initiators.

The differences in electrophilic trapping between bromides and chlorides, as well as between secondary and primary alkyl halides, have been explored. This selective alkyl trapping has enabled the cyclization of one of the functionalized products. In addition, some experiments have suggested an S_N2 mechanism in the reaction. Remarkably, ^{11}B NMR spectroscopic studies have provided further insight into this process. To finish, the reaction has been extended to synthesize stereoisomeric products and their corresponding enantioselective alcohols with a moderate enantioselectivity achieved.

3.6 References

(1) Cainelli, G.; Dal Bello, G.; Zubiani, G. *gem*-Dimetallic compounds; A novel Approach to Olefins Starting from Carbonyl Compounds and Acetylenic Derivatives. *Tetrahedron Lett.,* **1966**, *36*, 4315–4318.

(2) Matteson, D. S.; Moody, R. J. Deprotonation of 1,1-Diboronic Esters and Reactions of the Carbanions with Alkyl Halides and Carbonyl Compounds. *Organometallics,* **1982**, *1* (1), 20–28.

(3) Kohrt, S.; Dachwitz, S.; Daniliuc, C. G.; Kehr, G.; Erker, G. Stabilized Borata-Alkene Formation: Structural Features, Reactions and the Role of the Counter Cation. *Dalton Trans.,* **2015**, *44*, 21032–21040.

(4) Rathke, M. W.; Know, R. Generation of Boron-Stabilized Carbanions. *J. Am. Chem. Soc.,* **1972**, *94*, 6854–6856.

(5) Pelter, A.; Singaram, B.; Warren, L.; Wilson, J. W. Hindered Organoboron Groups in Organic Chemistry. 18. The Production of Boron Stabilised Carbanions. *Tetrahedron* **1993**, *49* (14), 2965–2978.

(6) Klis, T.; Lulinski, S.; Serwatowski, J. Formation and Synthetic Applications of Metalated Organoboranes. *Curr. Org. Chem.,* **2010**, *14* (20), 2549–2566.

(7) Cooke, M. P.; Widener, R. K. Nucleophilic Addition Reactions of Hindered Unsaturated Boranes. A New Synthesis of Organoboranes. *J. Am. Chem. Soc.,* **1987**, *109* (3), 931–933.

(8) Brown, H. C.; Rhodes, S. P. Synthesis of B-Cyclopropyl- and B-Cyclobutylbicyclo[3.3.1]Nonane *via* Ring Closure of Boron Intermediates. A Convenient Entry into Cyclopropyl and Cyclobutyl Derivatives *via* Hydroboration. *J. Am. Chem. Soc.,* **1969**, *91* (15), 4306–4307.

(9) Jo, W.; Lee, J. H.; Cho, S. H. Advances in Transition Metal-Free Deborylative Transformations of *gem*-Diborylalkanes. *Chem. Commun.,* **2021**, *57* (36), 4346–4353.

(10) Coombs, J. R.; Zhang, L.; Morken, J. P. Synthesis of Vinyl Boronates from Aldehydes by a Practical Boron-Wittig Reaction. *Org. Lett.,* **2015**, *17* (7), 1708–1711.

(11) Murray, S. A.; Liang, M. Z.; Meek, S. J. Stereoselective Tandem Bis-Electrophile Couplings of Diborylmethane. *J. Am. Chem. Soc.* **2017**, *139* (40), 14061–14064.

(12) Lee, Y.; Park, J.; Cho, S. H.; Lee, Y; Park, J.; Cho, S. H. Generation and Application of (Diborylmethyl)Zinc(II) Species: Access to Enantioenriched *gem*-Diborylalkanes by an Asymmetric Allylic Substitution. *Angew. Chem. Int. Ed.,* **2018**, *57* (39), 12930–12934.

(13) Kim, H.; Jung, Y.; Cho, S. H. Defluorinative C-C Bond-Forming Reaction of Trifluoromethyl Alkenes with *gem*-(Diborylalkyl)Lithiums. *Org. Lett.,* **2022**, *24* (14), 2705–2710.

(14) Wommack, A. J.; Kingsbury, J. S. On the Scope of the Pt-Catalyzed Srebnik Diborylation of Diazoalkanes. An Efficient Approach to Chiral Tertiary Boronic Esters and Alcohols *via* B-Stabilized Carbanions. *Tetrahedron Lett.,* **2014**, *55* (20), 3163–3166.

(15) Wickham, L. M.; Giri, R. Transition Metal (Ni, Cu, Pd)-Catalyzed Alkene Dicarbofunctionalization Reactions. *Acc. Chem. Res.,* **2021**, *54* (17), 3415–3437.

(16) Dhungana, R. K.; Sapkota, R. R.; Wickham, L. M.; Niroula, D.; Giri, R. Ni-Catalyzed Regioselective 1,2-Dialkylation of Alkenes Enabled by the Formation of Two C(sp^3)-C(sp^3) Bonds. *J. Am. Chem. Soc.,* **2020**, *142* (50), 20930–20936.

(17) Derosa, J.; van der Puyl, V. A.; Tran, V. T.; Liu, M.; Engle, K. M. Directed Nickel-Catalyzed 1,2-Dialkylation of Alkenyl Carbonyl Compounds. *Chem. Sci.,* **2018**, *9* (23), 5278–5283.

(18) Terao, J.; Kato, Y.; Kambe, N. Titanocene-Catalyzed Regioselective Alkylation of Styrenes with Grignard Reagents Using B-Bromoethyl Ethers, Thioethers, or Amines. *Chem. Asian. J.,* **2008**, *3*, 1472–1478.

(19) Terao, J.; Saito, K.; Nii, S.; Kambe, N.; Sonoda, N. Regioselective Double Alkylation of Styrenes with Alkyl Halides Using a Titanocene Catalyst. *J. Am. Chem. Soc.,* **1998**, *120* (45), 11822–11823.

(20) Ouyang, X. H.; Li, Y.; Song, R. J.; Hu, M.; Luo, S.; Li, J. H. Intermolecular Dialkylation of Alkenes with Two Distinct C(sp^3)H Bonds Enabled by Synergistic Photoredox Catalysis and Iron Catalysis. *Sci. Adv.,* **2019**, *5* (3), 9839–9868.

(21) Mizutani, K.; Shinokubo, H.; Oshima, K. Cobalt-Catalyzed Three-Component Coupling Reaction of Alkyl Halides, 1,3-Dienes, and Trimethylsilylmethylmagnesium Chloride. *Org. Lett.,* **2003**, *5* (21), 3959–3961.

(22) Chierchia, M.; Xu, P.; Lovinger, G. J.; Morken, J. P. Enantioselective Radical Addition/Cross-Coupling of Organozinc Reagents, Alkyl Iodides, and Alkenyl Boron Reagents. *Angew. Chem. Int. Ed.,* **2019**, *58* (40), 14245–14249.

(23) Wang, X.-X.; Lu, X.; He, S.-J.; Fu, Y. Nickel-Catalyzed Three-Component Olefin Reductive Dicarbofunctionalization to Access Alkylborates. *Chem. Sci.,* **2020**, *11* (30), 7950–7956.

(24) Campbell, M. W.; Compton, J. S.; Kelly, C. B.; Molander, G. A. Three-Component Olefin Dicarbofunctionalization Enabled by Nickel/Photoredox Dual Catalysis. *J. Am. Chem. Soc.,* **2019**, *141* (51), 20069–20078.

(25) Sun, S.-Z.; Duan, Y.; Mega, R. S.; Somerville, R. J.; Martin, R. Site-Selective 1,2-Dicarbofunctionalization of Vinyl Boronates through Dual Catalysis. *Angew. Chem. Int. Ed.,* **2020**, *59* (11), 4370–4374.

(26) Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. Radical-Polar Crossover Reactions of Vinylboron Ate Complexes. *Science,* **2017**, *355*, 936–938.

(27) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. Catalytic Conjunctive Cross-Coupling Enabled by Metal-Induced Metallate Rearrangement. *Science,* **2016**, *351*, 70–74.

(28) Silvi, M.; Sandford, C.; Aggarwal, V. K. Merging Photoredox with 1,2-Metallate Rearrangements: The Photochemical Alkylation of Vinyl Boronate Complexes. *J. Am. Chem. Soc.,* **2017**, *139*, 5736–5739.

(29) González, S.; Salvado, O.; Fernández, E. 1,2-Dialkylation of 1,1-Arylboryl Alkenes v*ia* Borata-Alkene Intermediate. *Adv. Synth. Catal.,* **2022**, *364*, 1701–1707.

(30) Maza, R. J.; Carbó, J. J.; Fernández, E. Borata-Alkene Species as Nucleophilic Reservoir. *Adv. Synth. Catal.,* **2021**, *363* (9), 2274–2289.

(31) Maza, R. J.; Fernández, E.; Carbó, J. J. Mapping the Electronic Structure and the Reactivity Trends for Stabilized α-Boryl Carbanions. *Chem. - Eur. J.,* **2021**, *27* (48), 12352–12361.

(32) Hong, K.; Liu, X.; Morken, J. P. Simple Access to Elusive α-Boryl Carbanions and Their Alkylation: An Umpolung Construction for Organic Synthesis. *J. Am. Chem. Soc.,* **2014**, *136* (30), 10581–10584.

(33) Fontani, P.; Carboni, B.; Vaultier, M.; Carrie, R.; Maas, G. Synthesis of Cyclopropylboronic Acid Esters by Carbene Transfer to 1-Alkenylboronic Acid Esters. *Synthesis,* **1991**, *8*, 605–609.

(34) Zhang, Y.; Wang, J. Recent Developments in Pd-Catalyzed Reactions of Diazo Compounds. *Eur. J. Org. Chem.* **2011**, *2011*, 1015–1026.

(35) Nobe, Y.; Arayama, K.; Urabe, H. Air-Assisted Addition of Grignard Reagents to Olefins. A Simple Protocol for a Three-Component Coupling Process Yielding Alcohols. *J. Am. Chem. Soc.,* **2005**, *127* (51), 18006–18007.

(36) Tlahuext-Aca, A.; Garza-Sanchez, R. A.; Glorius, F. Multicomponent Oxyalkylation of Styrenes Enabled by Hydrogen-Bond-Assisted Photoinduced Electron Transfer. *Angew. Chem. Int. Ed.* **2017**, *56* (13), 3708–3711.

(37) Mizojiri, R.; Urabe, H.; Sato, F. New Synthesis of Silylcyclopropanols *via* Titanium(II)-Mediated Coupling of Vinylsilanes and Esters. *Tetrahedron Lett.,* **1999**, *40* (13), 2557–2560.

(38) Dominguez-Molano, P.; Bru, G.; Salvado, O.; Maza, R. J.; Carbó, J. J.; Fernández, E. Transborylation of Alkenylboranes with Diboranes. *Chem. Commun.,* **2021**, *57* (98), 13361–13364.

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BORATA ALKENE INTERMEDIATES FOR SELECTIVE C-C COUPLING REACTIONS
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CHAPTER 4

Lithium Borylalkyde Salt Reacting with Carbonyl Compounds and α,β-Unsaturated Carbonyl Compounds

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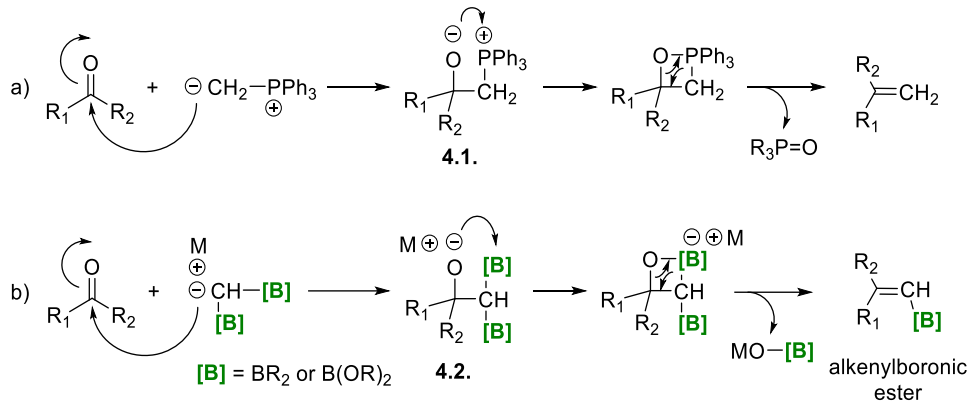
Sara González Morán

4.1 State of the art

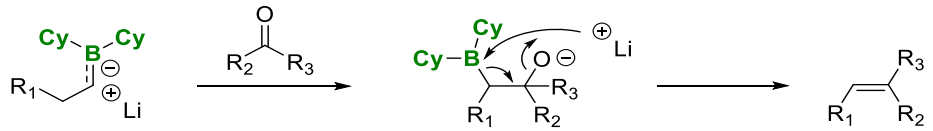
Stereoselective synthesis of substituted alkenes and dienes can be accomplished by efficient alkenylboronic ester, taking advantage of the functionalization of C-B bonds.[1] Boron-Wittig reaction allows the preparation of alkenylboronic esters as a consequence of the nucleophilic attack of α-boryl carbanions to carbonyl compounds. Formally, this reaction resembles the original Wittig olefination, reported in 1954, that is based on the reactivity of aldehydes or ketones with ylides generated from phosphonium salts.[2] While the driving force of the Wittig reaction is the formation of a stable phosphine oxide, in the boron-Wittig reaction it is due the stability associated to B–O bonds of the boronate by-products.[3]

Both types of condensations share similar elementary steps. In the Wittig reaction (Scheme 4.1a), the process begins with the attack of the ylide carbon on the carbonyl group, forming the betaine intermediate **4.1**. Subsequently, the attack of oxygen on phosphorous towards oxaphosphetane and reverse [2+2] cycloaddition delivers the phosphine oxide and the alkene. Similarly, the boron-Wittig reaction initiates with the attack of an α-boryl carbanion on the carbonyl derivative (Scheme 4.1b) to form **4.2**. Following this step, the attack of oxygen to Lewis acid B forms the corresponding tetrasubstituted borylated intermediate and finally, a B–O elimination leads to the formation of the corresponding alkene. Depending on the use of α-monoboryl carbanions, α-bisboryl carbanions or α-trisboryl carbanions, the olefination produces alkenes, 1-borylalkenes or 1,1-diborylalkenes, respectively.[3]



Scheme 4.1. Mechanism of a) Wittig reaction and b) boron-Wittig reaction.

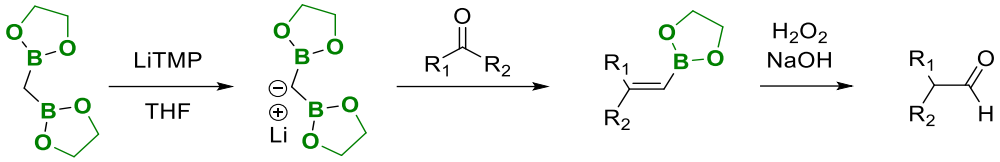
The first example of the condensation of *gem*-bis(boryl)alkanes with aldehydes and ketones to yield olefins was observed by Zubiani and co-workers in 1966.[4] These authors observed that benzaldehyde and a series of aliphatic, aromatic and cyclic ketones could efficiently be converted to the corresponding olefin by reaction with α-boryl carbanion lithium salt, through nucleophilic attack of the borata-alkene intermediate followed by B–O elimination (Scheme 4.2).[5]



Scheme 4.2. First condensation of borata-alkenes with aldehydes and ketones *via* B–O elimination observed by Zubiani and co-workers.

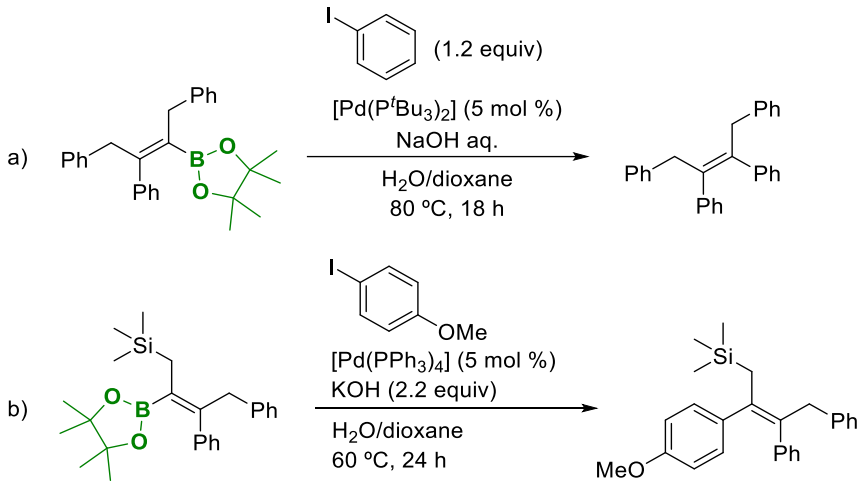
Rathke and Kow were the first to use lithium 2,2,6,6-tetramethylpiperidide (LiTMP) as a base to form the borata-alkene syntons, by deprotonation instead of monodeborylation of *gem*-diboryl alkanes.[6] This was feasible due to the large steric requirements, which made coordination to boron less feasible.[7] Taking advantage of this, Matteson and co-workers' investigations extended this boron-Wittig olefination towards the use of more stable pinacol-based boronic esters, as well as the employment of polyboronic esters, which led to the formation of vinylboronic ester derivatives that could be used for further functionalization at the C(sp^2)–B bond. For instance, these alkenylboronic esters could undergo an

oxidation to afford aldehyde homologation products with good yields (Scheme 4.3).[8–11]



Scheme 4.3. Condensation of lithium bis(ethylenedioxyboryl)methide with ketones followed by *in situ* oxidation.

Later, Endo, Shibata and co-workers defined the conditions for C–C coupling of tetrasubstituted alkenylboronic esters containing a stable Bpin moiety, with the aid of catalytic amounts of [Pd(P^tBu_3)$_2$] and NaOH (Scheme 4.4a).[12] Alternatively, they also demonstrated the compatibility of a trimethyl silyl moiety, for the Suzuki–Miyaura cross-coupling, switching to [Pd(PPh_3)$_4$] and KOH as catalyst and base(Scheme 4.4b).[13]

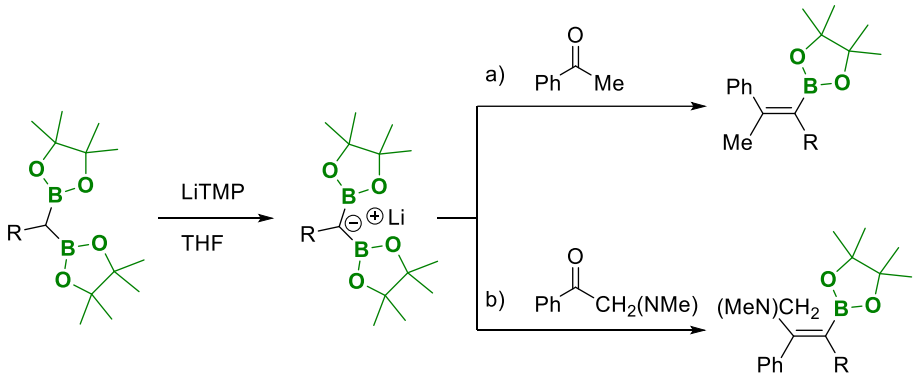


Scheme 4.4. Suzuki–Miyaura cross-coupling of a) tetrasubstituted alkenylboronic esters and b) alkenyl(silylmethyl)boronic esters.

Stereoselectivity of the resulting alkenylboronic esters was first studied by Pelter and co-workers in 1987 through boron-Wittig reactions with aromatic aldehydes. They postulated a stereoselective control throughout the borylated intermediates before the B-O elimination. These intermediates were proposed

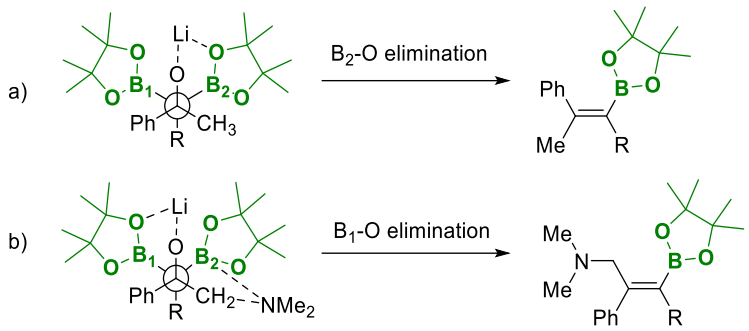
to play a crucial role in directing the stereochemistry principally by steric issues, leading to trisubstituted products with *E*- or *Z*-stereoselectivity.[14]

In 2015, Endo and Shibata also stablished the stereoselective control on the synthesis of tetrasubstituted alkenylboronic esters. They explored the *in-situ* deprotonation of *gem*-diborylalkanes, with LiTMP to obtain the borata-alkene intermediates. The subsequent nucleophilic attack to a series of ketones afforded a favored Bpin moiety positioned *syn* with respect to the aryl groups from the ketone (Scheme 4.5a). However, the introduction of coordinating groups in the ketone favored the inversion on the stereoselectivity. Thus, in this case the main product is a tetrasubstituted alkenylboronic ster with Bpin moiety *anti* to the aryl groups (Scheme 4.5b).[12]



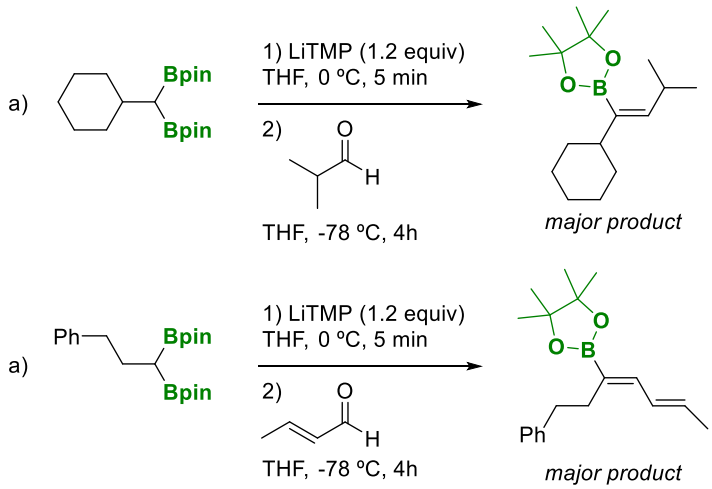
Scheme 4.5. Stereoselectivity on boron-Wittig reaction with aryl ketones.

A plausible mechanism according to these observations, and DFT computational studies, could involve the intramolecular coordination of heteroatoms to lithium. Scheme 4.6a shows that *syn*-elimination proceeds *via* LiO–C–C–Bpin intramolecular interaction. The inversion of stereoselectivity in Figure 4.1b indicated that the coordination of the nitrogen atom on the B_2 at in the pinacolboryl group, could inhibit the coordination of LiO moiety on the B_2. Thus, the product could have been synthetized through LiO–C–C–B_1 *syn*-elimination.[2,15]



Scheme 4.6. Hypothesis on the origin of the stereoselective for boron-Wittig reaction with aryl ketones.

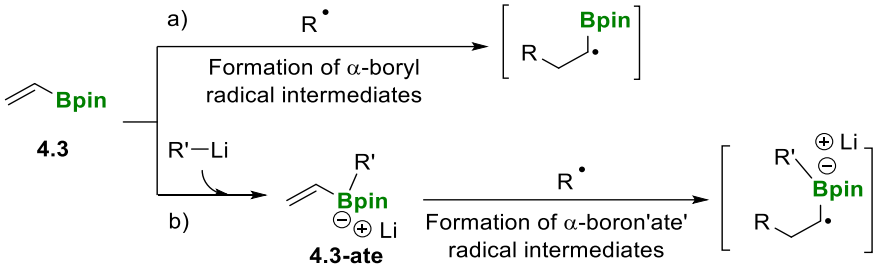
Morken and co-workers have performed a highly stereoselective boron-Wittig procedure between 1,1-bis(pinacolboryl)alkanes and aldehydes, resulting in the synthesis of a variety of di- and trisubstituted alkenylboronic esters.[16] They have found that steric hindrance influences in the stereoselectivity of the E/Z products. In cases where either large boryl substituents or large aldehyde substituents were used, the synthesis of the E isomer was favored (Scheme 4.7a). On the other hand, when small aldehyde and small boryl moieties were employed, the Z product was favored, as it is showed in Scheme 4.7b with an α,β-unsaturated aldehyde.[16]



Scheme 4.5. Stereoselectivity on boron-Wittig reaction with aryl ketones.

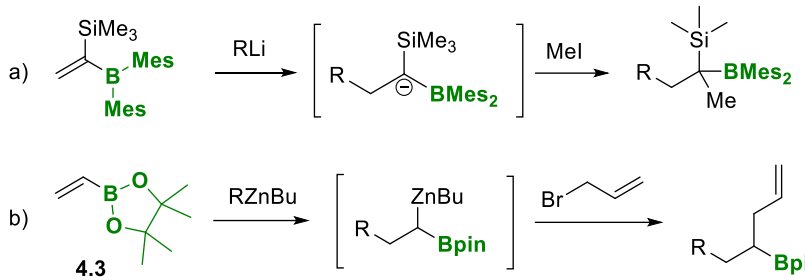
4.2 Context of the work

Vinylborane functional group represents a highly valuable synthetic opportunity to react through the alkene π-system due to the adjacent empty p orbital on boron atom. 1,2-Difunctionalization of alkenylboronic esters can be performed through the formation of α-boryl radical intermediates on the vinylboronic acid pinacol ester **4.3** (Scheme 4.8a)[17–20] or α- boron'ate' radical intermediates after the formation of boron'ate' **4.3-ate** (Scheme 4.8b).[21–23]



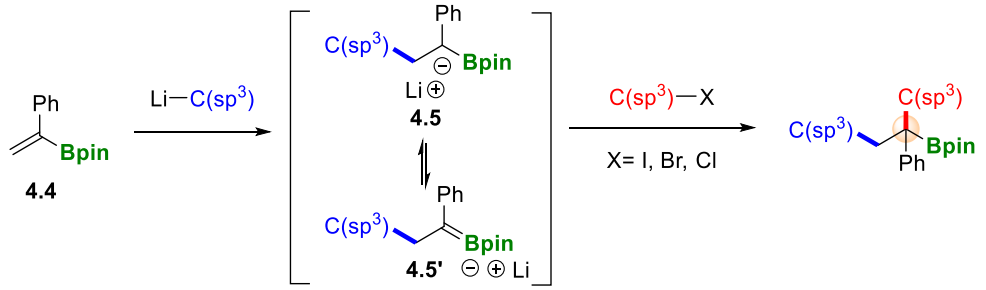
Scheme 4.8. Activation of alkenylboronic ester **4.3** as electron acceptor motif through a) α-boryl radical intermediates and b) α- boron'ate' radical.

Because of the competitive formation of boron'ate' species, examples of nucleophilic addition to the alkene π-system in vinylboranes are limited. Hindered arylboranes, such as dimesitylboranes have been used to prevent the boron'ate' formation due to steric effects.[24,25] Cooke and co-workers have demonstrated the feasible nucleophilic addition of organolithium reagents to α-substituted vinyldimesitylborane, followed by electrophilic trapping with MeI (Scheme 4.9a).[26] Another approach has been developed by Nakamura and co-workers, who extended this concept towards the organozinc nucleophilic addition to the vinylpinacolborane **4.3**, with subsequent electrophilic trapping *via gem*-zincio/boryl intermediates (Scheme 4.9b). Experiments and theoretical calculations suggested that the formation of a stable boron'ate' complex could be avoided by the combined use of an allylic zinc reagent and the bulky pinacol borane substituent.[27]



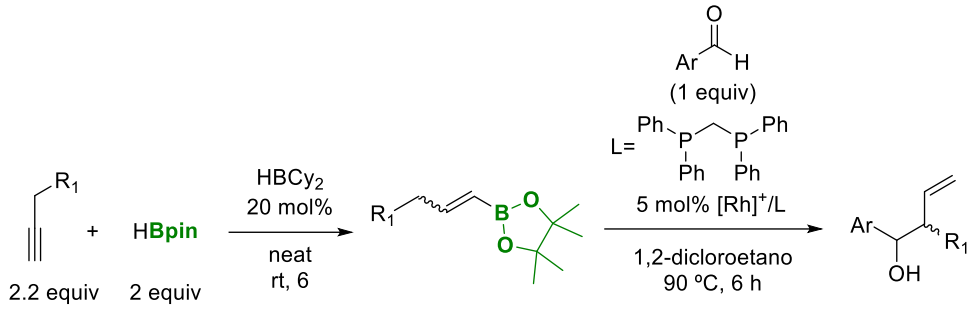
Scheme 4.9. Nucleophilic addition to vinylboranes with a) organolithium reagents and b) addition of an organozinc reagent.

We have been able to disclose the polar addition of alkyllithium reagents to the terminal carbon of 1-arylvinylboronic acid pinacol ester **4.4** followed by electrophilic trapping with a series of C(sp³)X allowed the formation of two new C(sp³)–C(sp³) bonds across the alkene (Scheme 4.10).[28] This reactivity is permitted by the remarkable stability of the α-arylboryl carbanion due to the valence deficiency of the adjacent three coordinated boron center, also represented with the borata-alkene resonance form.



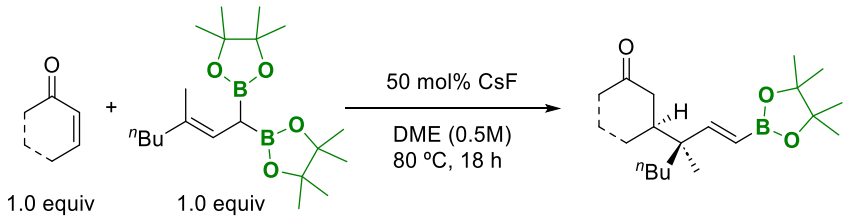
Scheme 4.10. Dicarbofunctionalization of alkenes with formation of two C(sp³)–C(sp³) bonds *via* borata-alkene intermediates.

Murakami and co-workers were pioneers to study the one-pot allylation reaction of aldehydes with alkenylboronic esters, which acted as the synthetic equivalent to γ-substituted allylboronates. In the presence of cationic rhodium(I) catalysts, they could synthetize stereodefined homoallylic alcohols from terminal alkynes and aldehydes (Scheme 4.11).[29]



Scheme 4.11. Rhodium-catalyzed reaction of alkenylboronic esters with aldehydes leading to allylation products.

1,4-Addition of allylic nucleophiles to electron-deficient alkenes provides an effective strategy for the generation of complex molecular structures. Meek and co-workers detailed a practical and efficient method for the diastereoselective synthesis of γ-quaternary carbon stereogenic centers through intermolecular 1,4-allyl additions. Boron-stabilized allylic nucleophiles, formed through Lewis base boron activation, reacted selectively and stereospecifically to deliver versatile 1,6-ketoalkenylboronate products (Scheme 4.12).[30]



Scheme 4.12. Synthesis of stereogenic quaternary carbons by diastereoselective conjugate addition of boron-stabilized allylic nucleophiles to enones.

4.3 Specific objectives

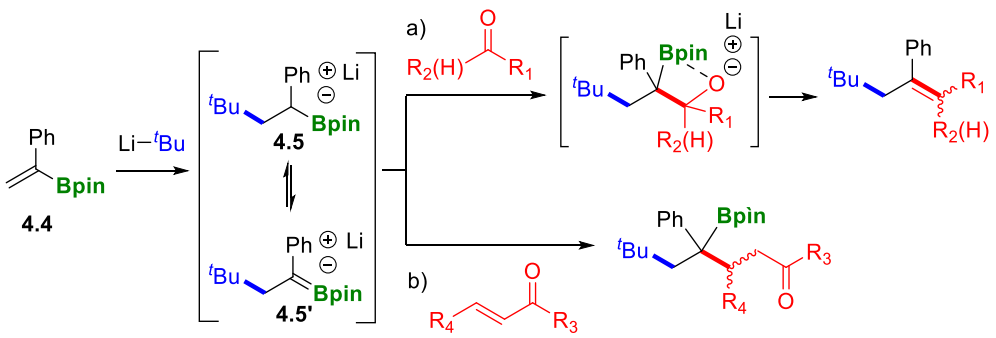
Considering the research conducted by our group, in this chapter we explored the nucleophilic addition to 1-phenylvinylboronic acid pinacol ester **4.4** by ^{t}BuLi, followed by electrophilic trapping with carbonyl functional groups, aldehydes and ketones.[31]

The specific objectives are:

1. Synthesis of trisubstituted alkenes, assembling Li–C(sp^3) reagent with vinylboronic acid pincol ester **4.4** and aldehydes, *via* boron-Wittig sequence.
2. Synthesis of tetrasubstituted alkenes and dienes employing ketones through boron-Wittig reaction.
3. 1,4-Addition of α,β-unsaturated carbonyl compounds to generate new tetrasubstituted carbon centers.
4. Functionalization of the obtained products through Suzuki-Miyaura cross coupling.

4.4 Results and discussion

We describe here the polar addition of ^{t}BuLi reagent to the terminal carbon of 1-phenylvinylboronic acid pinacol ester **4.4**, followed by the trapping of the formed α-boryl carbanion **4.5** with carbonyl groups. When aldehyde or ketones were used, boron-Wittig reaction proceeded through a B-O elimination to generate tri- or tetrasubstituted alkenes (Scheme 4.13a). However, electrophilic trapping can chemoselectively be performed through 1,4-addition on α,β-unsaturated carbonyl compounds (Scheme 4.13b).

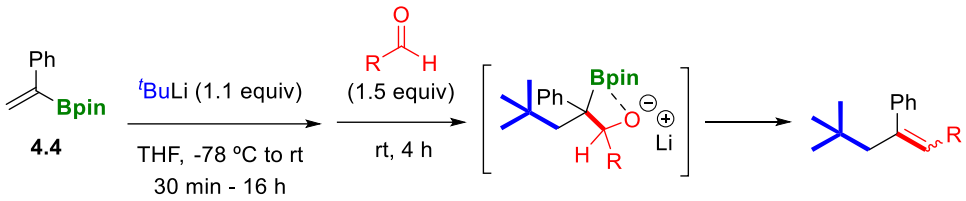


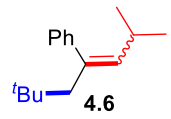
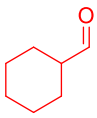
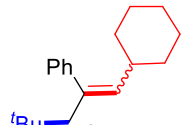
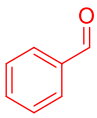
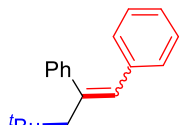
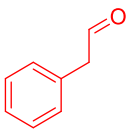
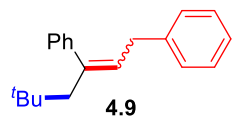
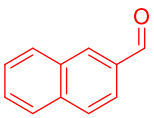
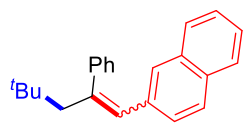
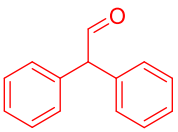
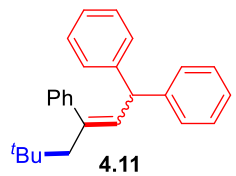
Scheme 4.13. Nucleophilic addition of ^{t}BuLi to 1-phenylvinylboronic acid pinacol ester **4.4** followed by electrophilic trapping with a) aldehydes and ketones and b) α,β-unsaturated carbonyl compounds.

In the initial experiments, we prepared the borata-alkene intermediate **4.5** by addition of 1.1 equiv of ^{t}BuLi to 1-phenylvinylboronic acid pinacol ester **4.4**, at -78 °C for 30 minutes, followed by stirring the solution at room temperature for 16 hours in THF as the solvent. Subsequently, 1.5 equiv of isobutyraldehyde were added and the reaction mixture was stirred for 4 hours at room temperature. Substrate **4.4** was converted into product **4.6** in 74% (calculated by NMR in comparison with naphthalene as internal standard) and 70% isolated yield (Table 4.1, entry 1). We observed the formation of both stereoisomers in 1:1 ratio, that were purified together since they resulted impossible to separate by flash chromatography purification. Similar results were obtained when cyclohexanal was the electrophilic partner involved (Table 4.1, entry 2).

We next explored aromatic aldehydes towards the formation of trisubstituted alkenes. Notably, benzaldehyde and 2-phenylacetaldehyde exhibited lower conversion, although a comparable stereoselection, to give products **4.8** and **4.9** in 1:1 ratio (Table 4.1, entres 3 and 4). Bulkier aromatic aldehydes were explored, such as 2-naphthaldehyde and 2,2-diphenylacetaldehyde, which led to the formation of **4.10** and **4.11** with moderate yields, preserving the same stereoselection 1/1 (Table 4.1, entries 4 and 5). Remarkably, both stereoisomers of products **4.9** and **4.11** could be isolated and characterized separately accordingly to 1D-NMR NOE experiments.

Table 4.1. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with aldehydes.[a]

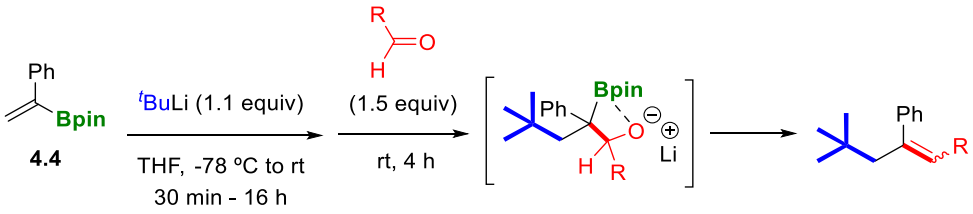


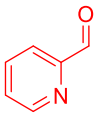
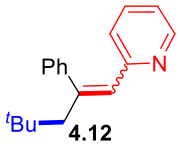
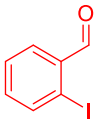
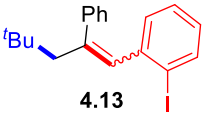
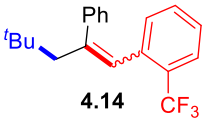
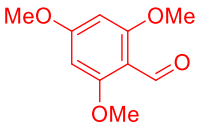
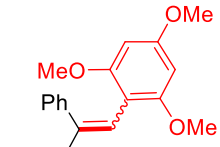
Entry	Aldehyde	Product	Conversion %[b] and Isolated Yield [%]	*E/Z* stereoselectivity[b]
1		 **4.6**	74% [70%]	1/1[c]
2		 **4.7**	73% [69%]	1/1[c]
3		 **4.8**	35% [33%]	1/1[c]
4		 **4.9**	42% [38%]	1/1[d]
5		 **4.10**	49% [48%]	1/1[c]
6		 **4.11**	65% [58%]	1/1[d]

[a]Reaction conditions: 1) **4.4** (0.3 mmol), *t*BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16h; 2) aldehyde (0.45 mmol), rt, 4h, and MeOH (2mL). [b]Conversion and *E/Z* stereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers. [d]Isolated as pure *E* or *Z* stereoisomers.

To expand the aldehyde scope, we studied the reactivity with other aromatic aldehydes containing different functional groups. Interestingly, picolinaldehyde showed a remarkably enhanced reactivity, affording alkene **4.12** in a NMR conversion of 90% and 84% isolated yield (Table 4.2, entry 1). This suggested a marked influence of electronic issues during the electrophilic trapping. However, although we speculated about a plausible interaction of nitrogen with the Bpin moiety to favour the formation of one specific stereoisomer, based on previous studies about the boron-Wittig reaction between picolinealdehyde and $LiC(Bpin)_2(SiMe_3)$,[32] in our case no stereopreference was observed. Product **4.12** was generated in 1:1 ratio, but both stereoisomers could be separated and identified. When steric hindrance on the *ortho* position of the benzaldehyde was introduced with *o*-iodobenzaldehyde, we obtained alkene **4.13** in a moderate yield with stereoisomers (*E/Z*)=1/1 (Table 4.2, entry 2). Notably, alkene **4.14** was synthesized using *o*-(trifluoromethyl)benzaldehyde, showing a modest stereoselectivity of (*E/Z*)=4/5 (Table 4.2, entry 3). Nevertheless, stereoselection of up to dr=1:3 of the trisubstituted alkene **4.15** was achieved when the sterically hindered aldehyde 2,4,6-$(OMe)_3$-C_6H_2CHO was involved in the electrophilic trapping (Table 4.2, entry 4). Major diastereoisomer of product **4.15** was isolated and subsequently unambiguously characterized by 1D-NMR NOE experiments, resulting in *Z*-stereoisomer.

Table 4.2. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with functionalized aromatic aldehydes.[a]



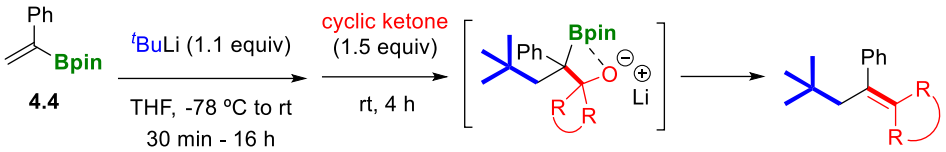
Entry	Aldehyde	Product	Conversion %[b] and Isolated Yield [%]	*E/Z* stereoselectivity[b]
1		 **4.12**	90% [84%]	1/1[d]
2		 **4.13**	59% [56%]	1/1[c]
3		 **4.14**	74% [69%]	4/5[c]
4		 **4.15**	96% [92%]	1/3[c,d]

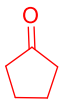
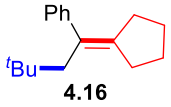
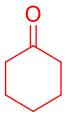
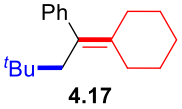
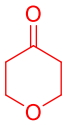
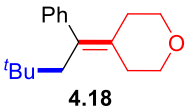
[a]Reaction conditions: 1) **4.4** (0.3 mmol), [t]BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16h; 2) aldehyde (0.45 mmol), rt, 4h, and MeOH (2mL). [b]Conversion and *E/Z* stereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers. [d]Isolated as pure *E* or *Z* diastereoisomers.

The scope of cyclic ketones was next examined to analyze the electrophilic trapping after [t]BuLi activation of **4.4** (Table 4.3). Cyclopentanone, cyclohexanone and tetrahydro-4H-pyran-4-one reacted with the borata-alkene intermediate **4.5** to give the corresponding tetrasubstituted alkenes **4.16**-**4.18**, (Table 4.3, entries 1-3). From moderate to high yields, the transformation of

cyclohexanone towards **4.17** was the most efficient with 81% isolated yield (Table 4.3, entry 2).

Table 4.3. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with cyclic ketones.[a]

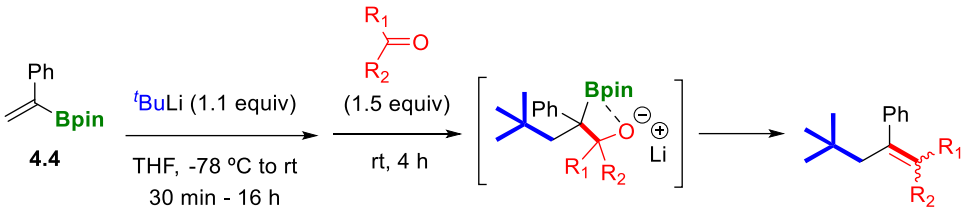


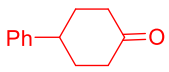
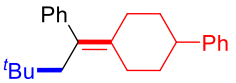
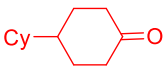
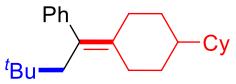
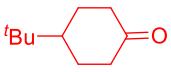
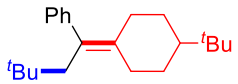
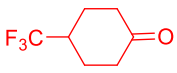
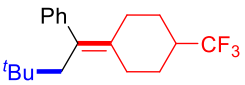
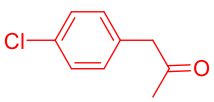
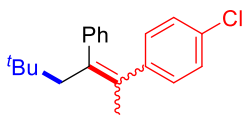
Entry	Ketone	Product	Conversion %[b] and Isolated Yield [%]
1		 **4.16**	72% [68%]
2		 **4.17**	87% [81%]
3		 **4.18**	66% [59%]

[a]Reaction conditions: 1) **4.4** (0.3 mmol), ^{t}BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16h; 2) aldehyde (0.45 mmol), rt, 4h, and MeOH (2mL). [b]Conversion calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard.

Next, an electronically and sterically diverse array of 4-substituted cyclohexanones was studied (Table 4.4, entries 1-4). Consistent with the aforementioned results, moderate to high yields were afforded, being alkene **4.21** isolated with the higher yield in 83% (Table 4.4, entry 3). When the acyclic ketone 1-(4-chlorophenyl)propan-2-one was explored for the electrophilic trapping, the tetrasubstituted alkene **4.23** could be isolated in 52% yield, with E/Z = 1/1 ratio (Table 4.4, entry 5).

Table 4.4. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with sterically diverse ketones.[a]



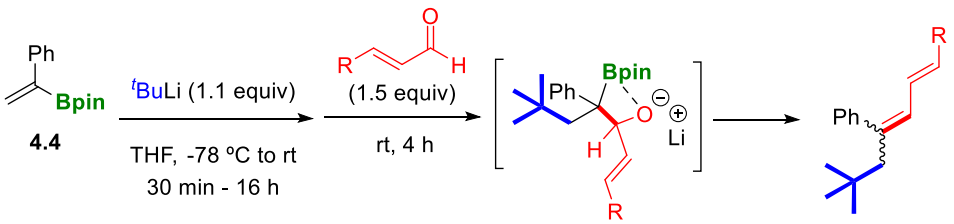
Entry	Ketone	Product	Conversion %[b] and Isolated Yield [%]	*E/Z* stereoselectivity[b]
1		 **4.19**	85% [77%]	---
2		 **4.20**	77% [70%]	---
3		 **4.21**	85% [83%]	---
4		 **4.22**	78% [73%]	---
5		 **4.23**	54% [52%]	1/1[c]

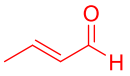
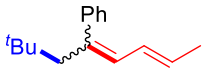
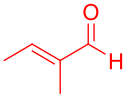
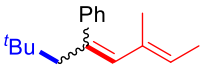
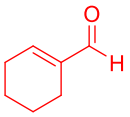
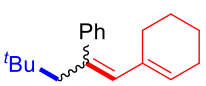
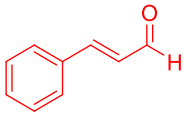
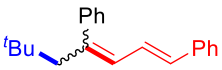
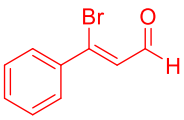
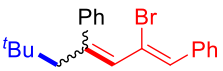
[a]Reaction conditions: 1) **4.4** (0.3 mmol), [t]BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16 h; 2) aldehyde (0.45 mmol), rt, 4 h, and MeOH (2 mL). [b]Conversion and *E/Z* stereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of stereosiomers.

Our subsequent study involved α,β-unsaturated aldehydes, with the aim to explore the chemoselectivity of the electrophilic trapping sequence. When (*E*)-but-2-enal, (*E*)-2-methylbut-2-enal and (*E*)-2-methylbut-2-enal were added to react with the borata-alkene intermediate **4.5**, the trapping of the aldehyde functionality took place chemoselectively, to give the corresponding conjugated

dienes **4.24**-**4.26**, although in low yield and stereoselectivity (*E*/*Z*=1/1) (Table 4.5, entries 1-3). With the aim to facilitate the conjugate addition through the electrophilic trapping sequence, we hypothesized about the use of cinnamaldehyde and (*Z*)-2-bromo-3-phenylacrylaldehyde. However, in both cases the boron-Wittig reaction took place chemoselectivity, in moderate yield towards dienes **4.27** and **4.28**, respectively (Table 4.5, entries 4,5).

Table 4.5. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with α,β-unsaturated aldehydes.[a]

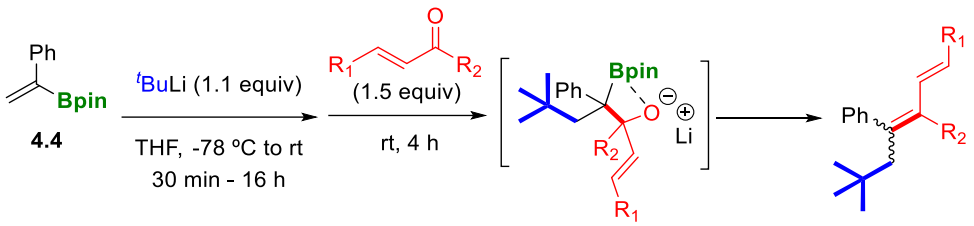


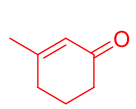
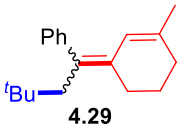
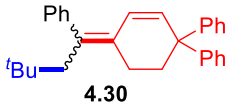
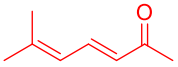
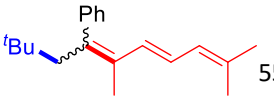
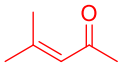
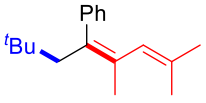
Entry	α,β-unsaturated aldehyde	Product	Conversion %[b] and Isolated Yield [%]	*E*/*Z* stereoselectivity[b]
1		 **4.24**	19% [17%]	1/1[c]
2		 **4.25**	49% [47%]	1/1[c]
3		 **4.26**	39% [31%]	1/1[c]
4		 **4.27**	61% [59%]	1/1[c]
5		 **4.28**	45% [43%]	1/1[c]

[a]Reaction conditions: 1) **4.4** (0.3 mmol), *t*BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16 h; 2) aldehyde (0.45 mmol), rt, 4 h, and MeOH (2 mL). [b]Conversion and *E*/*Z* stereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers.

Cyclic and acyclic α,β-unsaturated ketones allowed the formation of chemoselective dienes and trienes. Thus, dienes **4.29** and **4.30** were synthesized in moderate yields with *E*/*Z*=1/1 ratio (Table 4.6, entries 1 and 2). (*E*)-6-Methylhepta-3,5-dien-2-one reacted towards the triene **4.31** formation with a 48% isolated yield (Table 4.6, entry 3). It is worth mentioning that the polysubstituted diene **4.32** was obtained with total *Z*-diastereoselectivity, probably due to the enhanced steric hindrance around the enolate intermediate (Table 4.6, entry 4).

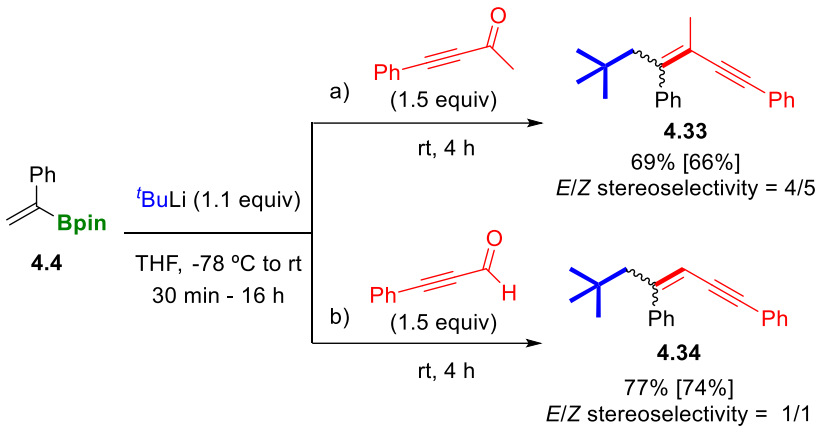
Table 4.6. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by trapping with α,β–unsaturated ketones.[a]



Entry	α,β-unsaturated ketone	Product	Conversion %[b] and Isolated Yield [%]	*E*/*Z* stereoselectivity[b]
1		 **4.29**	67% [62%]	1/1[c]
2		 **4.30**	77% [76%]	1/1[c]
3		 **4.31**	55% [48%]	1/1[c]
4		 **4.32**	24% [21%]	0/1[d]

[a]Reaction conditions: 1) **4.4** (0.3 mmol), [t]BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16 h; 2) aldehyde (0.45 mmol), rt, 4 h, and MeOH (2 mL). [b]Conversion and *E*/*Z* stereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers. [d]Isolated as diastereoisomer.

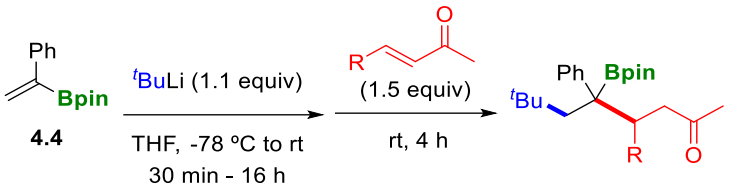
In addition, triple bonds were also tolerated in the 1,2-dicarbofunctionalization of **4.4**. The formation of substituted enynes **4.33** and **4.34** was achieved involving in the electrophilic trapping sequence with 4-phenylbut-3-yn-2-one (Scheme 4.11a) and 3-phenylpropiolaldehyde (Scheme 4.11b), although with dr= 5/4 and 1/1, respectively. Both stereoisomers of **4.33** and **4.34** could be isolated as pure stereoisomer. The reaction proceeded chemoselectively though boron-Wittig sequence, although with moderate yields.

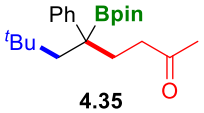
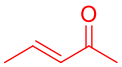
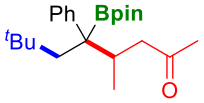
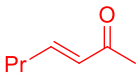
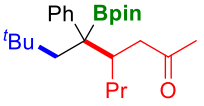
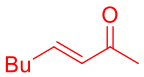
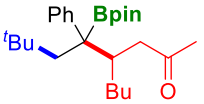


Scheme 4.11. Formation of substituted enynes with a) 4-phenylbut-3-yn-2-one and b) 3-phenylpropiolaldehyde.

Contrary to the results obtained in Table 4.6, when the α,β-unsaturated ketone but-3-en-2-one was studied for the electrophilic trapping of the borata-alkene intermediate **4.5**, we observed the exclusive formation of 7,7-dimethyl-5-phenyl-5-(pinacolboryl)octan-2-one **4.35** as a consequence of the 1,4-addition (Table 4.7, entry 1). This remarkable observation gave us the opportunity to explore a related substrate scope of unhindered α,β-unsaturated ketones. In that context, (*E*)-pent-3-en-2-one, (*E*)-hept-3-en-2-one and (*E*)-oct-3-en-2-one reacted with the borata-alkene intermediate **4.5** *via* chemoselective conjugated addition giving access to products **4.36-4.38**, in moderate yields, (Table 4.7, entries 2-4).

Table 4.7. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by conjugated addition to α,β–unsaturated ketones.[a]



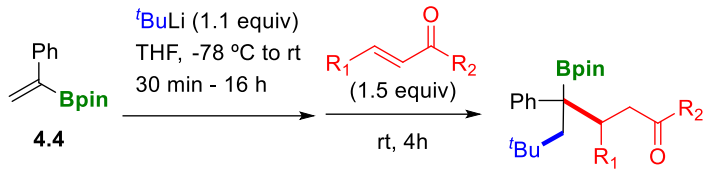
Entry	α,β-unsaturated ketone	Product	Conversion %[b] and Isolated Yield [%]	dr[b]
1		 **4.35**	43% [39%]	---
2		 **4.36**	41% [35%]	4/3[c]
3		 **4.37**	54% [50%]	3/2[c,d]
4		 **4.38**	63% [59%]	10/7[c]

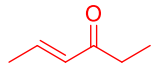
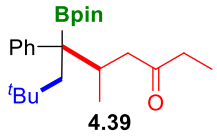
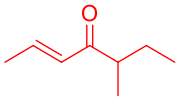
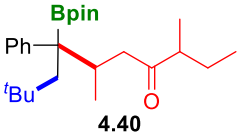
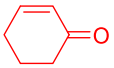
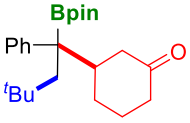
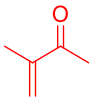
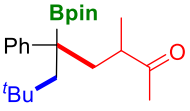
[a]Reaction conditions: 1) **4.4** (0.3 mmol), *t*BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16 h; 2) aldehyde (0.45 mmol), rt, 4 h, and MeOH (2mL). [b]Conversion and diastereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers. [d]Isolated as diastereoisomer.

Subsequently, we investigated if larger substituents on the ketone substrate were compatible with this 1,4-addition sequence. (*E*)-hex-4-en-3-one and (*E*)-5-methylhept-2-en-4-one were employed to achieve products **4.39** and **4.40** with isolated yields up to 73% or 72% (Table 4.8, entries 1 and 2). The diastereoselectivity was not fully controlled, being slightly increased when bulky substituents were involved, as it is displayed in the dr = 10:7 of product **4.38**, (Table 4.7, entry 4). *tert*-Butyllithium activation of **4.4** followed by trapping with cyclohex-2-en-1-one allowed the efficient conjugated addition

towards product **4.41**, although with dr= 1:1 (Table 4.8, entry 3). Notably, product **4.42** could be isolated as a single diastereoisomer, although in low yield (Table 4.8, entry 4).

Table 4.8. *tert*-Butyllithium activation of 1-phenylvinylboronic acid pinacol ester 4.4, followed by by conjugated addition to large substituted α,β-unsaturated ketones.[a]

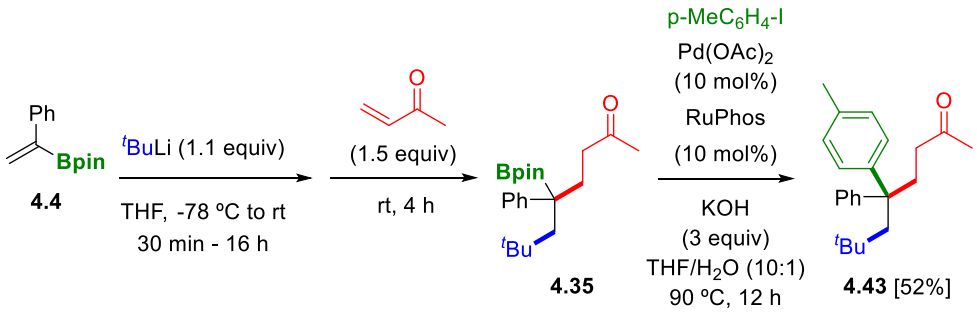


Entry	α,β-unsaturated ketone	Product	Conversion %[b] and Isolated Yield [%]	dr[b]
1		 **4.39**	79% [73%]	5/3[c]
2		 **4.40**	75% [72%]	nd
3		 **4.41**	70% [65%]	1/1[c,d]
4		 **4.42**	53% [27%]	---

[a]Reaction conditions: 1) **4.4** (0.3 mmol), [t]BuLi (0.33 mmol), THF (2 mL), -78 °C, 30 min, and then rt, 16 h; 2) aldehyde (0.45 mmol), rt, 4 h, and MeOH (2 mL). [b]Conversion and diastereoselectivity calculated by ^{1}H NMR spectroscopy with naphthalene as internal standard. [c]Isolated as mixture of diastereosiomers. [d]Isolated as diastereoisomer.

In all the examples described in Table 4.7 and 4.8, a new tetrasubstituted carbon center has been formed from 1-phenylvinylboronic acid pinacol ester substrate **4.4**. This approach to form tetrasubstituted carbon center with the α,β-unsaturated ketones becomes potentially useful since the quaternary center can

be easily achieved by cross coupling reaction of the tetrasubstituted carbon center. We illustrated the straightforward transformation of **4.35** into product **4.43** *via* Suzuki-Miyaura cross coupling with *p*-MeC_6H_4I, in the presence of $Pd(OAc)_2$ (Scheme 4.12).



Scheme 4.12. Functionalization of **4.35** towards the generation of a quaternary centre through Suzuki-Miyaura cross coupling.

4.5 Conclusions

In conclusion, we have described that 1-phenylvinylboronic acid pinacol ester **4.4** can be activated by nucleophilic attack of ^{t}BuLi, by suppression of any boron'ate' by-product formation. The corresponing α-arylboryl carbanion is stabilized as a borata-alkene, accumulating the nucleophilic character to react with aldehydes and ketones. The resulting α-arylboryl enolate intermediates evolve through B-O elimination to generate tri- or tetrasubstituted alkenes and dienes, *via* boron-Wittig sequence, with little control on the diastereoselectivity. In addition, the feasibility of conjugate addition of α-boryl carbanion represents an emerging area and our approach becomes potentially useful since the α-arylboryl carbanion intermediate **4.5** is formed *in situ* and eventually reacts with unhindered α,β-unsaturated ketones to generate the tetrasubstituted carbon center through 1,4-addition.

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4.6 References

(1) Carreras, J.; Caballero, A.; Pérez, P. J. Alkenyl Boronates: Synthesis and Applications. *Chem. Asian J.,* **2019**, *14* (3), 329–343.

(2) Wittig, G.; Merkle, W. Über die Bildung von Diphenyl aus Halogenbenzolen und Phenyl-lithium; gleichzeitig ein Beitrag zur Klärung der wechselnden Haftfestigkeit von Liganden. *Chem. Eur. J.,* **1942**, *75* (12), 1491–1500.

(3) Cuenca, A. B.; Fernández, E. Boron-Wittig Olefination with *gem*-Bis(Boryl)Alkanes. *Chem. Soc. Rev.,* **2021**, *50*, 72–86.

(4) Cainelli, G.; Dal Bello, G.; Zubiani, G. *gem*-Dimetallic compounds; A novel approach to olefins starting from carbonyl compounds and acetylenic derivatives. *Tetrahedron Lett.,* **1966**, *36*, 4315–4318.

(5) Maza, R. J.; Carbó, J. J.; Fernández, E. Borata-Alkene Species as Nucleophilic Reservoir. *Adv. Synth. Catal.,* **2021**, *363* (9), 2274–2289.

(6) Rathke, M. W.; Kow, R. Generation of Boron-Stabilized Carbanions. *J. Am. Chem. Soc.,* **1972**, *94*, 6854–6856.

(7) Kohrt, S.; Dachwitz, S.; Daniliuc, C. G.; Kehr, G.; Erker, G. Stabilized Borata-Alkene Formation: Structural Features, Reactions and the Role of the Counter Cation. *Dalton Trans.,* **2015**, *44*, 21032–21040.

(8) Matteson, D.S. Methanetetraboronic and Methanetriboronic Esters as Synthetic Intermediates. *Synthesis*, **1975**, *3*, 147–158.

(9) Matteson, D. S.; Moody, R. J. Carbanions from Deprotonation of *gem*-Diboronic Esters. .*J. Am. Chem. Soc.,* **1977***, 99,* 3196–3197.

(10) Matteson, D. S.; Tripathy, P. B. Alkene-1,1-Diboronic Esters from the Condensation of Triborylmethide Anions with Ketones or Aldehydes. *J. Organomet. Chem.,* **1974**, *69* (1), 53–62.

(11) Nallagonda, R.; Padala, K.; Masarwa, A. Organic & Biomolecular Chemistry g*em*-Diborylalkanes: Recent Advances in Their Preparation, Transformation and Application. *Org. Biomol. Chem.,* **2018**, *16*, 1050–1064.

(12) Endo, K.; Hirokami, M.; Shibata, T. Stereoselective Synthesis of Tetrasubstituted Alkenylboronates *via* 1,1-Organodiboronates. *J. Org. Chem.,* **2010**, *75* (10), 3469–3472.

(13) Endo, K.; Sakamoto, A.; Ohkubo, T.; Shibata, T. Stereoselective Synthesis of Allylsilanes Bearing Tetrasubstituted Olefin *via* 2,2-Diborylethylsilane. *Chem. Lett.,* **2011**, *40* (12), 1440–1442.

(14) Pelter, A.; Buss, E.; Colclough, *E*. Stereoselective Synthesis of *E*-and *Z*-Alkenes by the Boron-Wittig Reaction. *Chem. Commun.,* **1987,** *14***,** 297–299.

(15) Itami, K.; Nokami, T.; Yoshida, J. I. [Bis(2-Pyridyldimethylsilyl)Methyl]Lithium. New Reagent for the Stereoselective Synthesis of Vinylsilanes. *Org. Lett.,* **2000**, *2* (9), 1299–1302.

(16) Coombs, J. R.; Zhang, L.; Morken, J. P. Synthesis of Vinyl Boronates from Aldehydes by a Practical Boron-Wittig Reaction. *Org. Lett.,* **2015**, *17* (7), 1708–1711.

(17) Chierchia, M.; Xu, P.; Lovinger, G. J.; Morken, J. P. Enantioselective Radical Addition/Cross-Coupling of Organozinc Reagents, Alkyl Iodides, and Alkenyl Boron Reagents. *Angew. Chem. Int. Ed.,* **2019**, *58* (40), 14245–14249.

(18) Wang, X.-X.; Lu, X.; He, S.-J.; Fu, Y. Nickel-Catalyzed Three-Component Olefin Reductive Dicarbofunctionalization to Access Alkylborates. *Chem. Sci.,* **2020**, *11* (30), 7950–7956.

(19) Campbell, M. W.; Compton, J. S.; Kelly, C. B.; Molander, G. A. Three-Component Olefin Dicarbofunctionalization Enabled by Nickel/Photoredox Dual Catalysis. *J. Am. Chem. Soc.,* **2019**, *141* (51), 20069–20078.

(20) Sun, S.-Z.; Duan, Y.; Mega, R. S.; Somerville, R. J.; Martin, R. Site-Selective 1,2-Dicarbofunctionalization of Vinyl Boronates through Dual Catalysis. *Angew. Chem. Int. Ed.,* **2020**, *59* (11), 4370–4374.

(21) Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. Radical-Polar Crossover Reactions of Vinylboron Ate Complexes. *Science,* **2017**, *355*, 936–938.

(22) Silvi, M.; Sandford, C.; Aggarwal, V. K. Merging Photoredox with 1,2-Metallate Rearrangements: The Photochemical Alkylation of Vinyl Boronate Complexes. *J. Am. Chem. Soc.,* **2017**, *139*, 5736–5739.

(23) Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. Catalytic Conjunctive Cross-Coupling Enabled by Metal-Induced Metallate Rearrangement. *Science,* **2016**, *351*, 70–74.

(24) Blount, J. F.; Finocchiaro, P.; Gust, D.; Mislow, K. Conformational Analysis of Triarylboranes. *J. Am. Chem. Soc.,* **1973**, *95* (21), 7019–7029.

(25) Glogowski, M. E.; Zumbulyadis, N.; Williams, J. L. R. Boron Photochemistry XVI. Base Stabilization of Dimesitylboryl-Containing Dyes and Related ^{11}B NMR Studies. *J. Organomet. Chem.,* **1982**, *231* (2), 97–107.

(26) Cooke, M. P.; Widener, R. K. Nucleophilic Addition Reactions of Hindered Unsaturated Boranes. A New Synthesis of Organoboranes. *J. Am. Chem. Soc.,* **1987**, *109* (3), 931–933.

(27) Nakamura, M.; Hara, K.; Hatakeyama, T.; Nakamura, E. Regioselective Allylzincation of Alkenylboronate. *Org. Lett.,* **2001**, *3* (20), 3137–3140.

(28) González, S.; Salvado, O.; Fernández, E. 1,2-Dialkylation of 1,1-Arylboryl Alkenes v*ia* Borata-Alkene Intermediate. *Adv. Synth. Catal.,* **2022**, *364* (10), 1701–1707.

(29) Shimizu, H.; Igarashi, T.; Miura, T.; Murakami, M. Rhodium-Catalyzed Reaction of 1-Alkenylboronates with Aldehydes Leading to Allylation Products. *Angew. Chem. Int. Ed.,* **2011**, *50* (48), 11465–1469.

(30) Liang, M. Z.; Meek, S. J. Synthesis of Quaternary Carbon Stereogenic Centers by Diastereoselective Conjugate Addition of Boron-Stabilized Allylic Nucleophiles to Enones. *J. Am. Chem. Soc.,* **2020**, *142* (22), 9925–9931.

(31) González, S.; Fernández, E. Alkenylboronic Ester Activation to Nucleophilic Addition and Electrophilic Trapping with Carbonyl Groups. *Synlett,* **2022**, *34* (12), 1409–1414.

(32) Salvado, O.; Fernández, E. A Modular Olefination Reaction between Aldehydes and Diborylsilylmethide Lithium Salts. *Chem. Comm.,* **2021**, *57* (51), 6300–6303.

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CHAPTER 5

Concluding Remarks

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The present doctoral thesis has succeeded in developing synthetic methodologies to enhance the formation of borata-alkene species. Moreover, we explore the versatile applications of this species into the formation of a wide array of unprecedent organoboron compounds.

In Chapter 2, the substrate 1,1,1′,1′-tetrapinacolborylethane has been synthesized with 67% isolated yield, and its structure was analyzed by X-ray diffraction, gaining insight into the relative orientation of the "empty" boron pz orbital within the four Bpin moieties. Subsequently, we optimized the reaction conditions for coupling this substrate with allyl bromide through Cu catalysis ,to maximize the formation of the monoalkylated product, while minimizing by-products. Next, the substrate scope covered representative examples of sterically hindered allyl halides, suggesting an S_N2' mechanism for the Cu-catalyzed allylic alkylation. A second allylic alkylation reaction of the homoallyl triboronate systems was performed to form dihomoallyl diboronates. Finally, a Cu-catalyzed intramolecular cyclation with homoallyl triboronate systems resulted in cyclopentane derivatives with 2:1 diastereoselection in favor of the *trans*-diastereoisomer.

In Chapter 3, a straightforward intermolecular three-component assembly across alkenylboranes has been developed, forming two $C(sp^3)–C(sp^3)$ bonds through regioselective 1,2-dicarbofunctionalization of 1,1-arylboryl alkenes. A wide variety of tertiary boronic esters have been synthesized, including products with halides, alkenes, alkynes, aromatic compounds, esters, and cyanide groups. These tertiary boronic esters have also been converted into tertiary alcohols. Differences in electrophilic trapping between bromides and chlorides, as well as between secondary and primary alkyl halides, have been explored, demonstrating selectivity, and suggesting an S_N2 mechanism in the trapping reaction. This selective alkyl trapping has enabled the cyclization of one of the functionalized products. The reaction mechanism has been studied using ^{11}B NMR spectroscopy, confirming the involvement of borata-alkene

intermediates. The addition of various lithiated bases to alkenylboronic esters has been attemped, with ^{t}BuLi, ^{s}BuLi, Me_3SiLi, or TMSDM succeeding in the formation of the previously mentioned intermediate. To finish, the reaction has been extended to synthesize stereoisomeric products and their corresponding enantioselective alcohols with a moderate enantioselectivity achieved.

In Chapter 4, the intermolecular three-component assembly utilizing alkenylboranes, *via* borata-alkene intermediates, has been further extended by incorporating carbonyl functional groups for electrophilic trapping, thereby synthesizing tri- and tetrasubstituted alkenes and dienes. Borata-alkene intermediates that react with aldehydes and ketones evolve through B-O elimination in a boron-Wittig sequence to form alkenes and dienes. However, unhindered α,β-unsaturated ketones have reacted through 1,4-addition to generate products with a tetrasubstituted carbon center products and an untouched Bpin moiety. To conclude, an example of functionalization has been performed through a Suzuki-Miyaura cross-coupling.

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CHAPTER 6

Experimental Section

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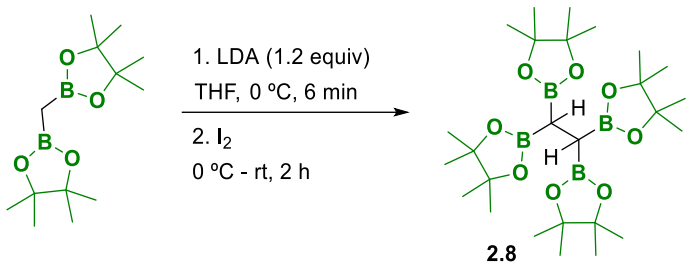
6.1 General considerations

Solvents and reagents were obtained from commercial suppliers, such as Sigma-Aldrich Inc., Apollo Scientific, Fluorochem, Alfa Aesar, TCI Chemicals, ThermoFisher, Abcr, etc.; and dried and/or purified (if needed) by standard procedures.[1] Allyl halides, other than those commercially available, were prepared accordingly to reported methods.[2] Bis(pinacolato)diboron (B_2pin_2) and bis(hexyleneglycolato)diboron (B_2hex_2) were obtained as a generous donation from Dalian Allychem Co. ,and were 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 purification procedures were performed on standard silica gel (Merck Kieselgel 60 F254 400-630 mesh). Thin Layer Chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} 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) were reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm (1 H)) and ($CDCl_3$: 77.16 ppm (^{13}C). $^{11}B\{^{1}H\}$ NMR chemical shifts (δ) were 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. Melting points were conducted in a Digital Melting Point IA 9100.

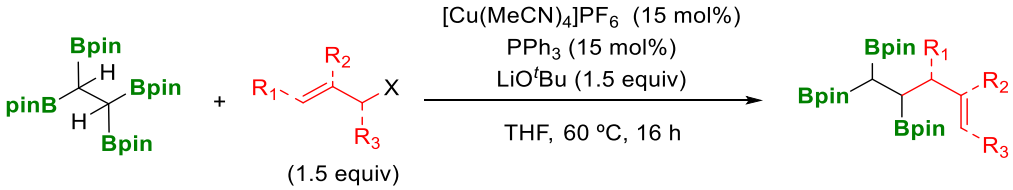
6.2 Experimental section for Chapter 2

6.2.1 General procedure for the synthesis of 1,1,1',1'-tetrapinacolborylethane[3]



Dipinacolborylmethane (1.0 equiv, 20 mmol) was dissolved in dried THF (100 mL) in a rounded-bottom Schlenk flask and cooled to 0 °C. A lithium diisopropylamide (LDA) solution (1.2 equiv, 24 mmol) in THF, was added dropwise and the reaction mixture was stirred for 6 minutes at 0 °C. Then, an iodine solution in THF (1M, 0.6 equiv, 12 mmol) was added slowly and the resulting mixture was warmed from 0 °C to room temperature and stirred for 2 h. The resulting reaction crude was extracted with 50 mL of Et_2O, 50 mL of $Na_2S_2O_3$ (1M), 50 mL of NH_4Cl (1M) and 50 mL of a saturated solution of NaCl and dried over $MgSO_4$. The crude product was purified by flash column chromatography with pentane/ethyl acetate (5:1).

6.2.2 General procedure for the Cu catalyzed coupling between 1,1,1',1'-tetrapinacolborylethane and allyl halides

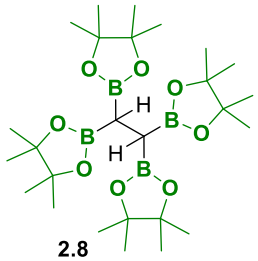


In a flamed Schlenk-tube equipped with a magnetic stir bar, 1,1,1',1'-tetrapinacolborylethane (80 mg, 0.15 mol%), $[Cu(MeCN)_4]PF_6$ (8 mg, 15 mmol%), PPh_3 (6 mg, 15 mol%) and LiO^tBu (18 mg, 1.5 equiv) were added in THF (2 mL) under argon atmosphere. The reaction mixture was stirred at 60 °C for 10 min and then the allyl bromide (1.5 equiv) was introduced into the reaction mixture. After being stirred at 60 °C for 16 h, the reaction was concentrated under a vacuum and the NMR yield was calculated through comparison to an internal standard (toluene). The crude residue was purified by silica gel flash chromatography to afford the desired product.

6.2.3 General procedure for the oxidation of methylenecyclopentane-1,2-dipinacolboronic esters

In an opened-air flask, charged with a magnetic stir bar, were added methylenecyclopentane-1,2-dipinacolboronic ester (0.1 mmol, 1 equiv), $NaBO_3 \cdot H_2O$ (0.3 mmol, 3 equiv), THF (2 mL) and distilled water (1 mL). The reaction was closed with a septum with a needle to avoid over pressures and was stirred for 16 h at room temperature. After this period of time, the mixture was extracted with Et_2O (3 x 15 mL), the organic layer was dried with anhydrous magnesium sulphate, filtered and the solvents were evaporated. The resulting crude was purified by silica gel chromatography to obtain the corresponding alcohol.

6.2.4 Characterization data for 1,1,1',1'-tetrapinacolborylethane



2.8

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (5:1). The product **2.8** was obtained as a white solid (7.15 g, 67%).

^{1}H NMR(400 MHz, $CDCl_3$) δ = 1.19 (s, 24H), 1.18 (s, 24H), 0.99 (s, 2H).

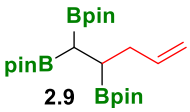
^{13}C NMR (100 MHz, $CDCl_3$) δ = 82.7, 24.9, 24.4, 5.4(C-B).

^{11}B NMR (128 MHz, $CDCl_3$) δ = 34.6.

HRMS-(ESI$^+$) for $C_{26}H_{51}B_4O_8$ [M-H]$^+$: calculated: 535.3956, found: 535.3961.

6.2.5 Characterization data for products

2,2',2''-(pent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.9)



2.9

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.9** was obtained as colourless oil (43.7 mg, 65%).

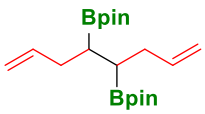
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.79 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H), 5.00-4.85 (m, 2H), 2.21 (t, J = 6.8 Hz, 2H), 1.44 (dt, J = 9.8, 6.8 Hz, 1H), 1.21 (s, 12H), 1.20 (s, 24H), 0.88 (d, J = 9.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.9, 115.1, 83.0, 82.9, 82.8, 37.6, 25.1, 25.0, 24.9, 24.8, 24.8, 24.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.8.

HRMS-(ESI$^+$) for $C_{23}H_{44}B_3O_6$ [M-H]$^+$: calculated: 449.3417, found: 449.3426.

2,2'-(octa-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.10)



2.10

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1).

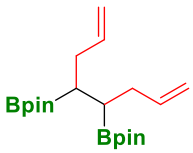
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.76 (ddt, J = 17.1, 10.1, 6.9 Hz, 2H), 4.98 – 4.88 (m, 2H), 4.84 (ddt, J = 10.1, 2.3, 1.1 Hz, 2H), 2.21 – 2.03 (m, 4H), 1.19 – 1.24 (26H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.1, 114.8, 34.7, 31.0, 25.2, 25.1, 25.0, 24.8.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.6.

HRMS (ESI) for $C_{23}H_{37}B_2O_4$ $[M+H^+]^+$: calculated: 363.2872, found: 363.2883.

2,2'-(octa-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.10')



2.10'

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1).

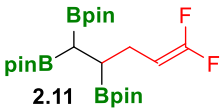
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.74 (ddt, J = 17.0, 10.2, 6.9 Hz, 2H), 4.98 – 4.90 (m, 2H), 4.84 (ddt, J = 10.1, 2.4, 1.2 Hz, 2H), 2.28 – 2.14 (m, 2H), 1.16 (m, 26H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.1, 114.9, 83.0, 34.3, 25.2, 24.8.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.9.

HRMS (ESI) for $C_{23}H_{37}B_2O_4$ $[M+H^+]^+$: calculated: 363.2872, found: 363.2885.

2,2',2''-(5,5-difluoropent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.11)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.11** was obtained as a white solid (53.7 mg, 74%).

^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.16 (dt, J = 25.7, 8.0, 7.9 Hz, 1H), 2.11 (dd, J = 8.0, 7.0 Hz, 2H), 1.39 (t, J = 9.7, 7.0 Hz, 1H), 1.21 (s, 12H), 1.20 (s, 24H), 0.84 (d, J = 9.7 Hz, 1H).

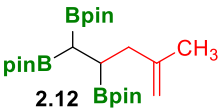
^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.0 (t, $^{1}J_{C\text{-}F}$ = 287.706), 83.1, 83.1, 83.0, 78.1 (t, $^{2}J_{C\text{-}F}$ = 20.6 Hz), 25.7 (d, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 25.1, 25.0, 24.9, 24.8, 24.8, 19.8, 10.6.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.4.

^{19}F NMR (377 MHz, $CDCl_3$) δ = -89.61 (dd, J = 48.7, 7.9 Hz), -91.79 (dd, J = 49.2, 25.7 Hz).

HRMS-(ESI^{+}) for $C_{23}H_{42}B_3F_2O_6$ $[M+H]^{+}$: calculated: 485.3223, found: 485.3238.

2,2',2''-(4-methylpent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.12)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.12** was obtained as colourless oil (40.2 mg, 58%).

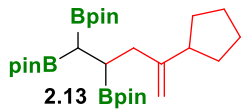
^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.66 (bs, 2H), 2.31 – 2.01 (m, 2H), 1.69 (s, 3H), 1.53 (td, J = 8.6, 7.2 Hz, 1H), 1.21 (s, 12H), 1.21 (s, 12H), 1.21(s (12H) 0.81 (d, J = 8.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.1, 110.6, 83.0, 83.0, 82.9, 38.3, 25.1, 25.0, 25.0, 24.9, 22.5.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.7.

HRMS-(ESI+) for $C_{26}H_{48}B_3O_6$ $[M-H]^{+}$: calculated: 461.3417, found: 461.3414.

2,2',2''-(4-cyclopentylpent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.13)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.13** was obtained as a colourless oil (39.5 mg, 51%).

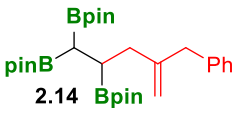
^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.70 – 4.66 (bs, 2H), 2.47 – 2.37 (m, 1H), 2.20 – 2.14 (m, 2H), 1.88 – 1.71 (m, 3H), 1.65 – 1.50 (m, 5H), 1.37 – 1.33 (m, 1H), 1.20 (s, 24H), 1.19 (s, 6H), 1.19 (s, 6H), 0.83 (d, J = 9.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.3, 107.3, 82.9, 82.8, 82.8, 45.2, 40.2, 31.6, 31.3, 25.1, 25.0, 25.0, 25.0, 24.9, 24.8, 24.8, 24.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.4.

HRMS-(ESI$^+$) for $C_{28}H_{50}B_3O_6$ $[M-H]^+$: calculated: 515.3886, found: 515.3882.

2,2',2''-(4-benzylpent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.14)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.14** was obtained as white solid (54.9 mg, 68%).

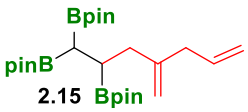
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.33 – 7.07 (m, 5H), 4.83 (s, 1H), 4.60 (s, 1H), 3.33 (s, 2H), 2.14 (d, J = 8.2 Hz, 2H), 1.62 (dt, J = 8.7, 8.4 Hz, 1H), 1.22 (s, 12H), 1.20 (s, 12H), 1.17 (s, 6H), 1.14 (s, 6H), 0.84 (d, J = 9.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.2, 140.4, 129.3, 128.1, 125.7, 112.0, 82.9, 82.9, 82.8, 42.5, 39.7, 25.1, 25.1, 24.9, 24.9, 24.8, 24.6.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.2.

HRMS-(ESI+) for $C_{30}H_{50}B_3O_6$ $[M+H]^+$: calculated: 539.3881, found: 539.3891.

2,2',2''-(4-methylenehept-6-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.15)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (15:1). The product **2.15** was obtained as a colourless liquid (17.1 mg, 31%).

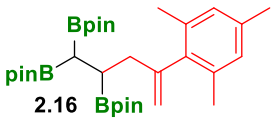
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.77 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H), 5.02 – 4.87 (m, 2H), 4.74 (s, 1H), 4.66 (s, 1H), 2.69 (d, J = 7.0 Hz, 2H), 2.11 (d, J = 7.0 Hz, 2H), 1.52 – 1.44 (m, 1H), 1.14 (s, 24H), 1.13 (s, 12H), 0.76 (d, J = 10.5 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.4, 137.0, 115.7, 110.8, 83.0, 82.9, 82.8, 40.3, 40.1, 25.1, 25.1, 24.9, 24.9, 24.8, 24.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.5.

HRMS (ESI) for $C_{26}H_{48}B_3O_6$ $[M+H^+]^+$: calculated: 489.3725, found: 489.3727.

2,2',2''-(4-mesitylpent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.16)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.16** was obtained as colourless oil (62.0 mg, 73%).

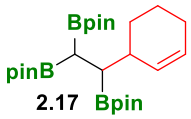
^{1}H NMR(400 MHz, $CDCl_3$) δ = 6.81 (s, 2H), 5.25 (s, 1H) , 4.75 (s, 1H), 2.37 – 2.27 (m, 2H), 2.25 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H), 1.68 (td, J = 8.8, 5.7 Hz, 1H) , 1.23 (s, 12H), 1.22 (s, 12H), 1.20 (s, 6H), 1.19 (s, 6H), 1.00 (d, J = 8.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 149.2, 141.3, 135.4, 135.4, 135.1, 128.0, 127.9, 112.3, 83.0, 82.9, 82.9, 39.9, 25.2, 25.1, 25.0, 24.8, 24.7, 24.6, 21.0, 19.8, 19.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.1.

HRMS-(ESI+) for $C_{32}H_{54}B_3O_6$ $[M+H]^+$: calculated: 567.4194, found: 567.4213.

2,2',2''-(2-(cyclohex-2-en-1-yl)ethane-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.17)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.17** was obtained as colourless oil in a mixture of diastereoisomers 1:1 (49 mg, 67%).

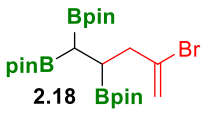
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.71 – 5.54 (m, 4H), 2.34 – 2.27 (m, 1H), 2.21 – 2.14 (m, 1H), 1.90 (dd, J = 6.9, 3.6 Hz, 4H), 1.74 (ddt, J = 10.3, 7.5, 2.8 Hz, 5H), 1.58 – 1.38 (m, 5H), 1.19 (s, 72H), 1.10 (d, J = 11.4 Hz, 1H), 1.03 (d, J = 11.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.6, 131.4, 127.0, 126.1, 82.9, 82.9, 82.9, 82.8, 82.8, 40.1, 38.7, 29.3, 26.8, 25.6, 25.6, 25.4, 25.2, 25.2, 25.2, 25.1, 24.9, 24.8, 24.8, 24.7, 24.6, 24.5, 24.5, 22.9, 22.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.8.

HRMS (ESI) for $C_{26}H_{48}B_3O_6$ $[M-H]^+$: calculated: 489.3730, found: 489.3738.

2,2',2''-(4-bromopent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.18)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.18** was obtained as colourless oil (41.8 mg, 55%).

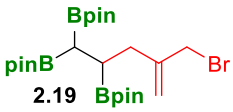
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.53 (d, J = 1.4 Hz, 1H), 5.36 (d, J = 1.5 Hz, 1H), 2.65 (ddd, J = 15.0, 7.3, 1.2 Hz, 1H), 2.55 (dd, J = 7.5, 1.1 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.21 (s, J = 2.0 Hz, 37H), 0.85 (d, J = 7.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.3, 116.9, 83.0, 82.9, 82.8, 44.2, 25.0, 24.9, 24.8, 24.8, 24.6, 24.5.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 34.1.

HRMS (ESI) for $C_{23}H_{42}B_3BrO_6$ $[M-H]^+$: calculated: 527.2522, found: 257.2533.

2,2',2''-(4-(bromomethyl)pent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.19)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.19** was obtained as white solid (33.2 mg, 41%).

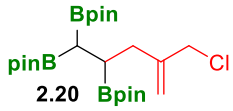
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.12 (s, 1H), 4.97 (s, 1H), 4.07-3.90 (m, 2H), 2.39-2.25 (m, 2H), 1.50 (q, J = 8.5 Hz, 1H), 1.22 (s, 12H), 1.21 (s, 12H), 1.20 (s, 12H), 0.80 (d, J = 8.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.4, 117.0, 83.2, 83.0, 82.9, 44.4, 25.2, 25.1, 25.0, 24.9, 24.8, 24.7, 18.1, 11.9.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.9.

HRMS (ESI) for $C_{24}H_{45}B_3BrO_6$ $[M+H]^+$: calculated: 541.2673, found: 541.2689.

2,2',2''-(4-(chloromethyl)pent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.20)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product **2.20** was obtained as colourless oil (32.0 mg, 43%).

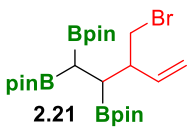
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.02 (s, 1H), 4.96 (s, 1H), 4.12 – 3.98 (m, 2H), 2.33 – 2.23 (m, 2H), 1.51 (dt, J = 6.7 Hz, 7.0 Hz, 1H), 1.21 (s, 12H), 1.21 (s, 12H), 1.19 (s, 12H), 0.82 (d, J = 7.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.5, 115.1, 83.0, 83.0, 82.9, 29.1, 27.7, 25.1, 25.0, 24.9, 24.9, 24.8, 24.7.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.4.

HRMS (ESI) for $C_{24}H_{45}B_3ClO_6$ $[M+H]^+$: calculated: 497.3178, found: 497.3197.

2,2',2''-(3-(bromomethyl)pent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.21)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product was was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.21A** was obtained as colourless oil (21 mg, 26%). The product **2.21B** was obtained as colourless oil (22 mg, 27%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.21A** δ = 5.70 (ddd, J = 17.0, 10.3, 8.9 Hz, 1H), 5.16 – 4.98 (m, 2H), 3.70 (dd, J = 9.8, 3.2 Hz, 1H), 3.37 (t, J = 10.0 Hz, 1H), 2.64 (tdd, J = 9.7, 6.8, 3.1 Hz, 1H), 1.53 (dd, J = 9.1, 7.0 Hz, 1H), 1.24 (s, 12H), 1.23 (s, 12H), 1.20 (s, 12H), 0.92 (d, J = 9.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.21A** δ = 139.9, 120.2, 85.2, 85.0, 84.9, 53.6, 50.4, 27.3, 27.1, 27.0, 26.7, 26.7, 26.6.

^{11}B NMR (128 MHz, $CDCl_3$) **2.21A** δ = 34.1.

HRMS (ESI) for $C_{24}H_{45}B_3BrO_6$ $[M+H]^+$: calculated: 541.2673, found: 541.2691.

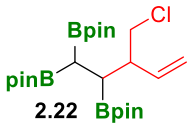
^{1}H NMR(400 MHz, $CDCl_3$) **2.21B** δ = 5.57 (ddd, J = 17.0, 10.3, 8.9 Hz, 1H), 5.55 (m, 2H), 3.52 (m, 2H), 2.51 (tt, J = 9.3, 4.6 Hz, 1H), 1.64 (dd, J = 11.3, 3.9 Hz, 1H), 1.23 (s, 12H), 1.21 (s, 12H), 1.20 (s, 12H), 0.99 (d, J = 11.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.21B** δ = 138.7, 115.3, 81.6, 81.5, 47.0, 46.0, 23.6, 23.5, 23.3, 23.3, 23.2.

^{11}B NMR (128 MHz, $CDCl_3$) **2.21B** δ = 33.9.

HRMS (ESI) for $C_{24}H_{45}B_3BrO_6$ $[M+H]^+$: calculated:541.2673, found: 541.2678.

2,2',2''-(3-(chloromethyl)pent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.22)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (10:1). The product was was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.22A** was obtained as colourless oil (33.5 mg, 45%). The product **2.22B** was obtained as colourless oil (31.3 mg, 42%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.22A** δ = 5.58 (ddd, J = 16.9, 10.4, 9.3 Hz, 1H), 5.17 – 5.02 (m, 2H), 3.70 – 3.58 (m, 2H), 2.46 (m, 1H), 1.62 (dd, J = 11.4, 3.9 Hz, 1H), 1.23 (s, 12H), 1.21 – 1.20 (s, 24H), 0.99 (d, J = 11.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.22A** δ = 140.3, 116.8, 83.2, 83.1, 49.6, 47.5, 25.2, 25.1, 24.9, 24.8, 24.8.

^{11}B NMR (128 MHz, $CDCl_3$) **2.22A** δ = 34.5.

HRMS (ESI) for $C_{24}H_{45}B_3ClO_6$ $[M+H]^+$: calculated: 497.3178, found: 497.3186.

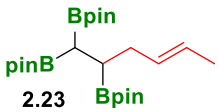
^{1}H NMR(400 MHz, $CDCl_3$) **2.22B** δ = 5.57 (ddd, J = 16.9, 10.4, 9.3 Hz, 1H), 5.24 – 4.98 (m, 2H), 3.80 – 3.58 (m, 2H), 2.46 (m, 1H), 1.61 (dd, J = 11.4, 3.9 Hz, 1H), 1.25 (s, 12H) 1.23 (s, 12H), 1.20 (s, 12H) 0.99 (d, J = 11.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.22B** δ = 138.2, 118.5, 83.5, 83.3, 83.2, 51.8, 48.7, 25.6, 25.4, 25.3, 25.0, 24.9, 24.9.

^{11}B NMR (128 MHz, $CDCl_3$) **2.22B** δ = 34.8.

HRMS (ESI) for $C_{24}H_{45}B_3ClO_6$ $[M+H]^+$: calculated: 497.3178, found: 497.3186.

(*E*)-2,2',2''-(hex-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.23)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). The product **2.23** was obtained as a colourless liquid (27.7 mg, 40%).

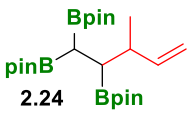
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.47 – 5.30 (m, 2H), 2.21 – 2.07 (m, 2H), 1.59 (d, J = 5.0 Hz, 3H), 1.44 – 1.39 (m, 1H), 1.21 (s, 12H), 1.20 (s, 24H), 0.89 (d, J = 10.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 131.3, 125.4, 82.9, 36.2, 25.1, 25.0, 24.9, 24.8, 24.8, 18.0.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 34.5

HRMS (ESI) for $C_{24}H_{46}B_3O_6$ $[M+H^+]^+$: calculated: 463.3568, found: 463.3583.

2,2',2''-(3-methylpent-4-ene-1,1,2-triyl)tris(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)(2.24)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). The product **2.24** was obtained as a colourless liquid (17.9 mg, 26%).

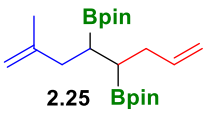
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.85 (ddd, J = 17.6, 10.2, 7.7 Hz, 1H), 4.98 – 4.82 (m, 2H), 3.76 – 3.58 (m, 1H), 2.39 – 2.26 (m, 1H), 1.44 – 1.36 (m, 1H), 1.22 (s, 24H), 1.21 (s, 12H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 10.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.7, 112.3, 82.9, 82.8, 41.1, 29.8, 25.4, 25.1, 25.0, 24.8, 24.8, 24.7, 17.9.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 33.7

HRMS (ESI) for $C_{24}H_{45}B_3NaO_6$ $[M+Na^+]^+$: calculated: 485.3388, found: 485.3385.

2,2'-(2-methylocta-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.25)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.25A** was obtained as colourless oil (25%). The product **2.25B** was obtained as colourless oil (29%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.25A** δ = 5.80 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H), 5.03 – 4.97 (m, 2H), 4.94 – 4.87 (m, 2H), 4.68 (br s, 2H), 2.34 – 2.23 (m, 1H), 2.20 – 2.13 (m, 3H), 1.68 (s, 3H), 1.39 – 1.29 (m, 1H), 1.23 (s, 6H), 1.22 (s, 12H), 1.22 (s, 6H), 1.14 (dt, *J* = 8.7, 6.3 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.25A** δ = 145.9, 139.2, 114.7, 110.5, 82.9, 82.8, 38.2, 34.5, 25.0, 24.9, 24.8, 24.7, 22.4.

^{11}B NMR (128 MHz, $CDCl_3$) **2.25A** δ = 34.3.

HRMS (ESI) for $C_{21}H_{39}B_2O_4$ $[M-H]^+$: calculated: 377.3034, found: 377.3035.

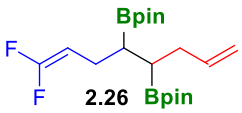
^{1}H NMR(400 MHz, $CDCl_3$) **2.25B** δ = 5.76 (ddt, J = 17.1, 10.1, 6.9 Hz, 1H), 4.98 – 4.88 (m, 1H), 4.87 – 4.79 (m, 1H), 4.66 – 4.57 (m, 2H), 2.16 – 2.07 (m, 3H), 2.01 (dd, J = 14.0, 5.6 Hz, 1H), 1.64 (s, 3H), 1.36 – 1.29 (m, 1H), 1.22 – 1.09 (m, 1H), 1.16 (s, 12H), 1.15 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.25B** δ = 146.0, 139.0, 114.6, 110.4, 82.9, 38.6, 34.6, 24.9, 24.94 22.6.

^{11}B NMR (128 MHz, $CDCl_3$) **2.25B** δ = 34.2.

HRMS (ESI) for $C_{21}H_{39}B_2O_4$ $[M-H]^+$: calculated: 377.3034, found: 377.3037.

2,2'-(1,1-difluoroocta-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane)(2.26)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.26A** was obtained as colourless oil (33%). The product **2.26B** was obtained as colourless oil (50%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.26A** δ = 5.79 (ddt, J = 17.0, 10.1, 6.9 Hz, 1H), 5.05 – 4.87 (m, 2H), 4.16 (dtd, J = 25.6, 7.9, 2.9 Hz, 1H), 2.35 – 2.22 (m, 1H), 2.20 – 2.06 (m, 3H), 1.28 – 1.20 (m, 26H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.26A** δ = 156.2 (t, $^{1}J_{C\text{-}F}$ = 284.5 Hz), 138.9, 115.1, 83.2, 83.2, 78.2 (t, $^{2}J_{C\text{-}F}$ = 20.7 Hz), 34.2, 25.1, 24.8, 24.8, 24.7, 22.6 (d, $^{3}J_{C\text{-}F}$ = 4.1 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) **2.26A** δ = -89.6 (d, J = 48.4 Hz), -91.5 (dd, J = 48.4, 25.6 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.26A** δ = 33.7

HRMS (ESI) for $C_{20}H_{35}B_2F_2O_4$ $[M+H^+]^+$: calculated: 399.2684, found: 399.2695.

^{1}H NMR(400 MHz, $CDCl_3$) **2.26B (major)** δ = 5.79 – 5.68 (m, 1H), 4.98 – 4.81 (m, 2H), 4.12 (dtd, J = 25.6, 8.0, 2.8 Hz, 1H), 2.23 – 2.11 (m, 1H), 2.11 – 1.97 (m, 3H), 1.19 – 1.13 (m, 2H), 1.16 (s, 12H), 1.16 (s, 12H).

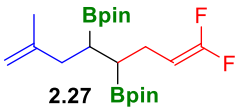
^{13}C NMR (100 MHz, $CDCl_3$) **2.26B (major)** δ = 156.0 (t, $^{1}J_{C\text{-}F}$ = 284.0 Hz), 138.8, 114.9, 83.0, 83.0, 78.1 (t, $^{2}J_{C\text{-}F}$ = 20.7 Hz), 34.1, 24.7, 25.0, 24.6, 22.5 (d, $^{3}J_{C\text{-}F}$ = 4.2 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.26B (major)** δ = 33.6.

^{19}F NMR (377 MHz, $CDCl_3$) **2.26B (major)** δ = -89.5 (d, *J* = 48.8 Hz), -91.6 (dd, *J* = 48.8, 25.6 Hz).

HRMS (ESI) for $C_{20}H_{35}B_2F_2O_4$ $[M+H^+]^+$: calculated: 399.2684, found: 399.2687.

2,2'-(1,1-difluoro-7-methylocta-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.27)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.27A** was obtained as colourless oil (23%). The product **2.27B** was obtained as colourless oil (29%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.27A** δ = 4.69 (s, 1H), 4.68 (s, 1H), 4.20 (dtd, J = 25.6, 7.9, 2.8 Hz, 1H), 2.25 – 2.16 (m, 1H), 2.13 – 2.03 (m, 3H), 1.70 (s, 3H), 1.40 (dt, J = 10.0, 6.4 Hz, 1H), 1.23 (s, 12H), 1.21 (s, 12H), 1.17 – 1.10 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.27A** δ = 145.8, 110.7, 83.2, 83.1, 78.4 (t, $^{1}J_{C\text{-}F}$ = 22.4 Hz), 38.4, 25.0, 25.0, 25.0, 24.9 (d, $^{2}J_{C\text{-}F}$ = 4.0 Hz), 22.6.

^{19}F NMR (377 MHz, $CDCl_3$) **2.27A** δ = -89.72 (d, *J* = 47.4 Hz), -91.47 (dd, J = 47.4, 25.5 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.27A** δ = 33.6.

HRMS (ESI) for $C_{21}H_{37}B_2F_2O_4$ $[M+H]^+$: calculated: 413.2841, found: 413.2840.

^{1}H NMR(400 MHz, $CDCl_3$) **2.27B (major)** δ = 4.62 (s, 2H), 4.10 (dtd, J = 25.6, 8.0, 2.8 Hz, 1H), 2.20 – 2.00 (m, 4H), 1.62 (s, 3H), 1.28 – 1.23 (m, 1H), 1.16 (s, 12H), 1.15 (s, 12H), 1.06 – 1.01 (m, 1H).

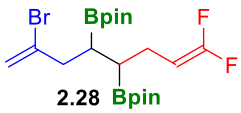
^{13}C NMR (100 MHz, $CDCl_3$) **2.27B (major)** δ = 145.8, 110.9, 83.1, 83.1, 78.4 (t, $^{1}J_{C\text{-}F}$ = 20.7 Hz), 38.2, 25.1, 25.0, 24.9, 24.8, 23.1 (d, $^{2}J_{C\text{-}F}$ = 4.0 Hz), 22.4.

^{19}F NMR (377 MHz, $CDCl_3$) **2.27B (major)** δ = -89.68 (d, J = 48.9 Hz), -91.74 (dd, J = 48.9, 25.5 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.27B (major)** δ = 33.5.

HRMS (ESI) for $C_{21}H_{37}B_2F_2O_4$ $[M+H]^+$: calculated: 413.2841, found: 413.2846.

2,2'-(7-bromo-1,1-difluoroocta-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.28)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.28A** was obtained as colourless oil (19%). The product **2.28B** was obtained as colourless oil (25%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.28A** δ = 5.59 (br s, 1H), 5.38 (d, J = 1.6 Hz, 1H), 4.23 (dtd, J = 25.6, 8.0, 2.8 Hz, 1H), 2.64 (ddd, J = 15.0, 9.1, 1.2 Hz, 1H), 2.48 (ddd, *J* = 14.9, 6.3, 1.2 Hz, 1H), 2.15 – 2.03 (m, 2H), 1.65 – 1.52 (m, 1H), 1.24 – 1.21 (m, 25H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.28A** = 135.08, 117.07, 82.94, 82.83, 78.0 (t, $^{2}J_{C-F}$ = 22.0 Hz), 41.53, 24.61, 24.54, 24.52, 22.8 (d, $^{2}J_{C-F}$ = 4.8 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) **2.28A** δ = -89.42 (d, *J* = 49.3 Hz), -91.33 (dd, J = 49.3, 25.4 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.28A** δ = 34.4.

HRMS (ESI) for $C_{20}H_{33}B_2BrF_2NaO_4$ $[M+Na^+]^+$: calculated: 499.1609, found: 499.1605.

^{1}H NMR(400 MHz, $CDCl_3$) **2.28B (major)** δ = 5.58 (br s, 1H), 5.38 (d, J = 1.4 Hz, 1H), 4.18 (dtd, *J* = 25.6, 8.5, 7.4, 2.8 Hz, 1H), 2.66 – 2.54 (m, 2H), 2.27 – 2.06 (m, 2H), 1.49 (td, J = 7.8, 5.0 Hz, 1H), 1.23 (s, 12H), 1.23 (s, 12H), 1.09 (td, J = 7.7, 4.8 Hz, 1H).

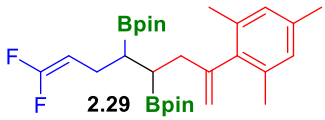
^{13}C NMR (100 MHz, $CDCl_3$) **2.28B (major)** δ = 135.5, 117.4, 83.3, 83.2, 78.4 (t, $^{2}J_{C-F}$ = 21.2 Hz), 41.95, 25.03, 24.97, 24.95, 24.93, 23.23 (d, $^{3}J_{C-F}$ = 4.1 Hz).

^{19}F NMR (377 MHz, $CDCl_3$) **2.28B (major)** δ = -89.48 (d, *J* = 48.8 Hz)-91.62 (dd, J = 48.8, 25.3 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.28B (major)** δ = 34.4

HRMS (ESI) for $C_{20}H_{33}B_2BrF_2NaO_4$ $[M+Na^+]^+$: calculated: 499.1609, found: 499.1603.

2,2'-(1,1-difluoro-7-mesitylocta-1,7-diene-4,5-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.29)



The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (20:1). The product **2.29A** was obtained as colourless oil (44%). The product **2.29B** was obtained as colourless oil (21%).

^{1}H NMR(400 MHz, $CDCl_3$) **2.29A (major)** δ = 6.83 (s, 2H), 5.20 (d, J = 1.9 Hz, 1H), 4.76 (d, J = 1.7 Hz, 1H), 4.19 (dtd, J = 25.5, 8.0, 2.8 Hz, 1H), 2.42 – 2.10 (m, 4H), 2.26 (s, 3H), 2.22 (s, 3H), 2.19 (s, 3H), 1.49 (dt, J = 9.9, 5.0 Hz, 1H), 1.29 – 1.18 (m, 1H), 1.24 (s, 6H), 1.23 (s, 6H), 1.21 (s, 6H), 1.19 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) **2.29A (major)** δ = 149.2, 141.0, 135.4 (t, $^{1}J_{C-F}$ = 30.8 Hz), 128.1, 128.0, 112.2, 83.3, 83.2, 78.5 (t, $^{2}J_{C-F}$ = 20.8 Hz), 36.8, 25.2, 25.0, 25.0, 24.6, 23.1 (d, $^{3}J_{C-F}$ = 4.1 Hz), 21.1, 19.8, 19.8.

^{19}F NMR (377 MHz, $CDCl_3$) **2.29A (major)** δ = -89.66 (d, *J* = 48.7 Hz), -91.57 (dd, J = 48.7, 25.6 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.29A (major)** δ = 34.4.

HRMS (ESI) for $C_{29}H_{45}B_2F_2O_4$ $[M+H]^+$: calculated:517.3467, found: 517.3467.

^{1}H NMR(400 MHz, $CDCl_3$) **2.29B** δ = 6.82 (s, 2H), 5.22 (d, J = 1.8 Hz, 1H), 4.76 (d, J = 1.6 Hz, 1H), 4.17 (dtd, J = 25.4, 7.9, 2.8 Hz, 1H), 2.40 – 2.30 (m, 1H), 2.26 (s, 3H), 2.22 (s, 3H), 2.20 – 2.07 (m, 6H), 1.54 (td, J = 7.0, 3.4 Hz, 1H), 1.26 – 1.17 (m, 1H), 1.24 (s, 12H), 1.20 (s, 12H).

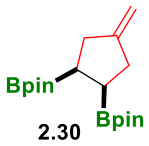
^{13}C NMR (100 MHz, $CDCl_3$) **2.29B** δ = 149.2, 140.8, 135.2 (t, $^{1}J_{C-F}$ = 30.8 Hz), 128.0, 127.8, 112.2, 83.1, 78.1 (t, $^{2}J_{C-F}$ = 21.4 Hz), 37.0, 25.1, 24.8, 24.8, 24.7, 22.9 (d, $^{3}J_{C-F}$ = 4.2 Hz), 20.9, 19.6, 19.6.

^{19}F NMR (377 MHz, $CDCl_3$) **2.29B** δ = -89.55 (d, *J* = 47.8 Hz), -91.19 (dd, J = 47.8, 25.4 Hz).

^{11}B NMR (128 MHz, $CDCl_3$) **2.29B** δ = 34.4.

HRMS (ESI) for $C_{29}H_{45}B_2F_2O_4$ $[M+H]^+$: calculated:517.3467, found: 517.3465.

2,2'-((1R,2S)-4-methylenecyclopentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.30)



2.30

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). The product **2.30** was obtained as a white solid (13.5 mg, 27%).

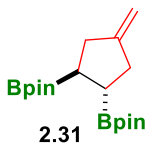
^{1}H NMR(400 MHz, $CDCl_3$) δ = 5.01 – 4.60 (m, 2H), 2.45 – 2.33 (m, 4H), 1.56 (td, J = 5.5, 2.9 Hz, 2H), 1.23 (s, 12H), 1.22 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.9, 104.1, 83.1, 36.0, 25.0, 24.8.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 34.5.

HRMS (ESI) for $C_{18}H_{33}B_2O_4$ $[M+H]^+$: calculated: 335.2564, found: 335.2561.

2,2'-((1R,2R)-4-methylenecyclopentane-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (2.31)



2.31

The product was purified by flash column chromatography using as eluent a mixture of pentane/ethyl acetate (30:1). The product **2.31** was obtained as a white solid (20.6 mg, 41%).

^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.73 (tt, J = 2.7, 1.7 Hz, 2H), 2.45 – 2.34 (m, 2H), 1.30 – 1.22 (m, 2H), 1.16 (s, 24H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 155.1, 103.7, 83.0, 36.7, 24.8.

^{11}B NMR (128 MHz, $CDCl_3$) δ = 34.7.

HRMS (ESI) for $C_{18}H_{33}B_2O_4$ $[M+H]^+$: calculated: 335.2559, found: 335.2560.

(1R,2S)-4-methylenecyclopentane-1,2-diol (2.32)

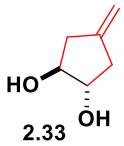
2.32

The product was purified by flash column chromatography using as eluent a mixture of dichloromethane /methanol (20:1). The product **2.32** was obtained as a colourless liquid (10.7 mg, 94%).

^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.93 (s, 2H), 4.05 (s, 2H), 2.50 (dd, J = 191.8, 15.0 Hz, 4H), 2.45 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.9, 108.9, 78.0, 38.7.

(1R,2R)-4-methylenecyclopentane-1,2-diol (2.33)



2.33

The product was purified by flash column chromatography using as eluent a mixture of dichloromethane /methanol (20:1). The product **2.33** was obtained as a colourless liquid (15.2 mg, 89%).

^{1}H NMR(400 MHz, $CDCl_3$) δ = 4.93 (p, J = 2.3 Hz, 2H), 4.48 – 3.52 (m, 2H), 3.45 – 1.87 (m, 4H), 2.60 (br s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.8, 105.0, 74.0, 34.7.

6.2.6 X-Ray single-crystal diffraction analysis for 2.8

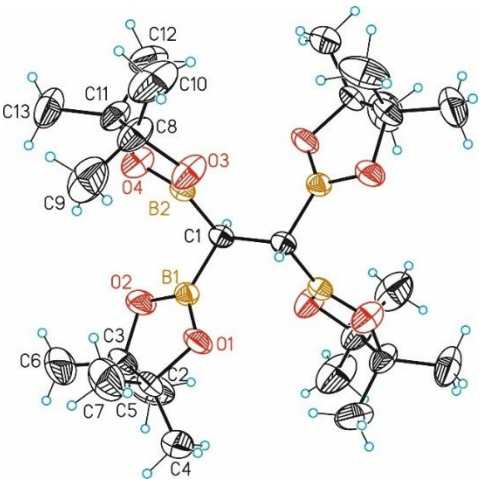


Figure 6.1. X-ray diffraction structure of 1,1,1',1'-tetrapinacolborylethane.

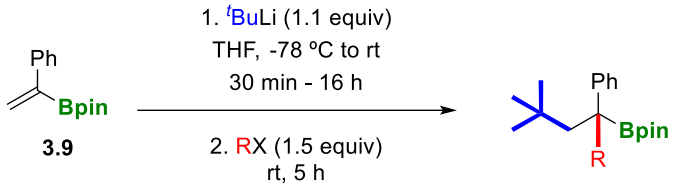
This compound crystallizes in the monoclinic space group $P2_1/n$. The asymmetric unit contains one molecule of the expected compound which shows highly disordered five membered rings (pseudo-rotation). The structure is of acceptable quality (no A- or B-alerts) and publishable with a R1 value of 8.67 %. CCDC number 2284601.

Table 6.1. Crystal data and structure refinement for mo_RJ578RT_0m_5.

Identification code	mo_RJ578RT_0m_5	
Empirical formula	C13 H25 B2 O4	
Formula weight	266.95	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 11.713(3) Å	α= 90°.
	b = 13.154(3) Å	β= 117.689(8)°.
	c = 12.284(3) Å	γ = 90°.
Volume	1675.9(8) $Å^3$	
Z	4	
Density (calculated)	1.058 Mg/m^3	
Absorption coefficient	0.074 mm^{-1}	
F(000)	580	
Crystal size	0.200 x 0.150 x 0.100 mm^3	
Theta range for data collection	1.986 to 27.535°.	
Index ranges	-15<=h<=13, 0<=k<=16, 0<=l<=15	
Reflections collected	7243	
Independent reflections	7243 [R(int) = ?]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7243 / 284 / 334	
Goodness-of-fit on F^2	1.108	
Final R indices [I>2sigma(I)]	R1 = 0.0867, wR2 = 0.2556	
R indices (all data)	R1 = 0.1699, wR2 = 0.3042	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.315 and -0.220 $e.Å^{-3}$	

6.3 Experimental section for Chapter 3

6.3.1 General procedure for 1,2-dialkylation



A flame dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**3.9**) (69.5 mg, 0.3 mmol, 1.0 equiv.) in dried THF (2 mL), then sealed with a rubber septum and put under a nitrogen atmosphere at −78 °C. A solution of *tert*-butyllithium reagent (0.19 mL, 0.33 mmol, 1.1 equiv.) in hexane (1.7 M) was added dropwise and the reaction mixture was stirred for 30 minutes at −78 °C and then stirred at room temperature for 16 h. The reagent RX (0.45 mmol, 1.5 equiv.) was added dropwise, and the reaction mixture was stirred for 5 h at room temperature. Finally, the reaction was quenched by addition of MeOH (5 mL) and extracted with Et_2O three times. The combined organic layers were dried by addition of $MgSO_4$ filtered through Celite and concentrated under reduced pressure. The NMR yield was calculated by comparison to an internal standard (naphthalene). The crude product was purified by flash column chromatography.

6.3.2 General procedure for alkylation/protonation

A flame dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**3.9**) (69.5 mg, 0.3 mmol, 1.0 equiv.) in dried THF (2 mL), then sealed with a rubber septum and put under a nitrogen atmosphere at −78 °C. A solution of *tert*-butyllithium reagent (0.19 mL, 0.33 mmol, 1.1 equiv.) in hexane (1.7 M) was added dropwise and the reaction mixture was stirred for 30 minutes at −78 °C and then stirred at room temperature for 16 h. The reaction mixture was

quenched by addition of MeOH (5 mL) and extracted with Et_2O three times. The combined organic layers were dried by addition of $MgSO_4$ filtered through Celite and concentrated under reduced pressure. The NMR yield was calculated by comparison to an internal standard (naphthalene). The crude product was purified by flash column chromatography.

6.3.3 General procedure for cyclopropanation

A flame dried Schlenk tube equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**3.9**) (69.5 mg, 0.3 mmol, 1.0 equiv.) in dried hexane (0.5 mL), then sealed with a rubber septum and put under a nitrogen atmosphere. A solution of (trimethylsilyl)diazomethane (1.05 mL, 2.1 mmol, 7 equiv.) in hexane (2 M) was added dropwise and the reaction mixture was stirred for 16 h at 80 °C. After the reaction time, the solvent was evaporated in a rotatory evaporator and the NMR yield was calculated by comparison to an internal standard (naphthalene). The crude mixture was purified by silica gel chromatography.

6.3.4 General procedure for oxidation of boronic esters

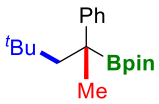
A 50 mL round-bottom flask equipped with a magnetic stir bar was charged with the boronic ester (0.2 mmol) in THF (2 mL). A solution of NaOH (1.00 mL, 3 M) was added and the reaction mixture was stirred for 5 min. A solution of H_2O_2 (2.00 mL, 33% v/v) was added dropwise and the reaction mixture was stirred for 12 h. The crude was quenched with 2 mL of a saturated solution of $Na_2S_2O_3$ and extracted with diethyl ether. The organic phases were dried over $MgSO_4$ and concentrated in a rotatory evaporator. The oxidized product was purified by silica gel chromatography.

6.3.5 General procedure for transborylation of alkenylboranes

A flame dried Schlenk tube equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**3.9**) (69.5 mg, 0.3 mmol, 1.0 equiv.) and bis-(+)-pinanediolato diboron (0.33 mmol, 1.1 equiv.) in dried MeOH (2 mL), then sealed with a rubber septum and put under a nitrogen atmosphere. The reaction mixture was stirred for 16 h at 90 °C. After the reaction time, the solvent was evaporated in a rotatory evaporator and the NMR yield was calculated by comparison to an internal standard (naphthalene). The crude mixture was purified by silica gel chromatography.

6.3.6 Characterization of tertiary boronic esters

2-(4,4-dimethyl-2-phenylpentan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.12)



3.12

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.12** (68.2 mg, 75% yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.46 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.26 (t, *J* = 7.8 Hz, 2H), 7.16 -7.07 (m, 1H), 1.94 (d, *J* = 14.2 Hz, 1H), 1.72 (d, *J* = 14.2 Hz, 1H), 1.47 (s, 3H), 1.18 (s, 6H), 1.17 (s, 6H), 0.86 (s, 9H).

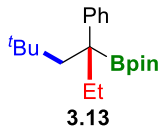
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 148.1, 128.0, 127.5, 125.2, 83.4, 52.7 32.4, 31.8, 24.9, 24.7, 23.2.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.1.

HRMS (ESI) for $C_{19}H_{31}BO_2$ $[M+NH_4]^+$: calculated: 320.2768, found: 320.2761.

M.p. = 69.8 °C.

2-(5,5-dimethyl-3-phenylhexan-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.13)



3.13

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.13** (52.2 mg, 55% yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.49 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.29-7.21 (m, 2H), 7.13-7.08 (m, 1H), 1.99 (d, *J* = 14.2 Hz, 1H),1.80 (m, 2H), 1.74 (d, *J* = 14.2 Hz, 1H), 1.24 (2, 6H), 1.22 (2, 6H), 0.73 (s, 9H), 0.72 (t, *J* = 7.4 Hz, 3H).

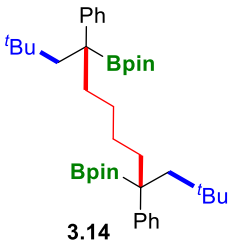
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.9, 129.2, 127.9, 125.2, 83.0, 48.9, 33.3, 31.7, 30.8, 25.3, 25.0, 11.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.7.

HRMS (ESI) for $C_{20}H_{33}BO_2$ $[M+NH_4]^+$: calculated: 334.2924, found: 334.2917.

M.p. = 73.1 °C.

2,2'-(2,2,11,11-tetramethyl-4,9-diphenyldodecane-4,9-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.14)



3.14

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.14** (74.63 mg, 79 % yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.50-7.42 (m, 4H), 7.23 (t, *J* = 7.6 Hz, 4H), 7.10 (t, *J* = 7.3 Hz, 2H), 1.96 (d, *J* = 14.2 Hz, 2H), 1.98-1.77 (m, 4H), 1.72 (d, *J* = 14.2 Hz, 1H), 1.70 (d, J = 14.2 Hz, 1H), 1.25-1.18 (m, 24H), 1.15-0.97 (m, 4H), 0.70 (s, 9H), 0.69 (s, 9H).

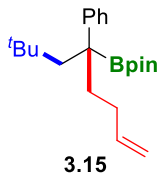
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.0, 146.0, 128.4, 128.3, 127.8, 127.8, 125.0, 83.2, 50.3, 49.9, 38.5, 38.1, 32.2, 32.2, 31.5, 31.5, 26.3, 26.2, 25.3, 25.2, 24.9.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.8.

HRMS (ESI) for $C_{40}H_{64}B_2O_4$ $[M+NH_4]^+$: calculated: 648.5334, found: 648.5349.

M.p. = 70.2 °C.

2-(2,2-dimethyl-4-phenyloct-7-en-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.15)



3.15

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.15** (93.42 mg, 93 % yield) as colourless oil.

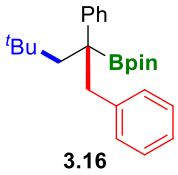
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.45-7.39 (m, 2H), 7.20-7.14 (m, 2H), 7.09-6.98 (m, 1H), 5.69 (ddt, *J* = 16.7, 10.2, 6.5 Hz, 1H), 4.90-4.75 (m, 2H), 1.99 (d, *J* = 14.3 Hz, 1H), 1.88 (m, 2H), 1.79-1.74 (m, 2H), 1.71 (d, J = 14.3 Hz, 1H), 1.16 (s, 6H), 1.14 (s, 6H), 0.68 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.5, 139.4, 128.2, 127.8, 125.1, 113.7, 83.2, 49.7, 37.3, 32.1, 31.4, 30.9, 29.6, 25.1, 24.8.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.3.

HRMS (ESI) for $C_{22}H_{36}BO_2$ $[M+NH_4]^+$: calculated: 396.2845, found: 396.2841.

2-(4,4-dimethyl-1,2-diphenylpentan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.16)



3.16

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.16** (86.18 mg, 76 % yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.67 (d, *J* = 9.9 Hz, 2H), 7.25 (t, *J* = 7.9 Hz, 2H), 7.17-7.12 (m, 1H), 7.05 (d, *J* = 2.1 Hz, 3H), 6.89 (t, *J* = 3.3 Hz, 2H), 3.35 (d, *J* = 14.5 Hz, 1H), 3.15 (d, *J* = 14.9 Hz, 1H), 2.10 (d, *J* = 14.3 Hz, 1H), 1.95 (d, *J* = 14.2 Hz, 1H), 1.16 (s, 6H), 1.08(s, 6H), 0.71 (s, 9H).

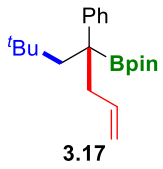
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 207.0, 145.6, 140.0, 130.2, 129.4, 127.8, 127.5, 125.8, 125.4, 83.4, 52.5, 46.5, 32.3, 31.6, 31.1, 25.4, 25.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.1.

HRMS (ESI) for $C_{25}H_{35}BO_2$ $[M+NH_4]^+$: calculated: 396.3068, found: 396.3083.

M.p. = 67.9 °C.

2-(6,6-dimethyl-4-phenylhept-1-en-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.17)



3.17

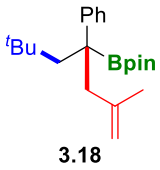
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.17** (69.8 mg, 71 % yield) as colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.53-7.46 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.15-7.07 (m, 1H), 5.62 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 4.99 (m, 1H), 4.91 (m, 1H), 2.73 (d, *J* = 6.9 Hz, 2H), 2.00 (d, *J* = 14.3 Hz, 1H), 1.78 (d, *J* = 14.3 Hz, 1H), 1.24 (s, 6H), 1.22 (s, 6H), 0.72 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.4, 136.4, 128.6, 127.9, 125.3, 116.6, 83.5, 50.0, 42.5,32.4, 31.7, 25.3, 25.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.5.

HRMS (ESI) for $C_{21}H_{33}BO_2$ $[M+NH_4]^+$: calculated: 346.2917, found: 346.2931.

4,4,5,5-tetramethyl-2-(2,6,6-trimethyl-4-phenylhept-1-en-4-yl)-1,3,2-dioxaborolane (3.18)



3.18

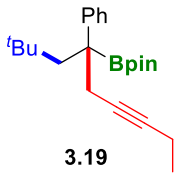
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.18** (80.09 mg, 78 % yield) as colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.65-7.63 (m, 2H), 7.25-7.20 (m, 3H), 7.10 (tt, J = 7.2, 1.7 Hz, 1H), 4.64 (m, 1H), 4.55 (m, 1H), 2.74 (d, J = 16.6 Hz, 1H), 2.62 (d, J = 16.4 Hz, 1H), 2.03 (d, J = 14.2 Hz, 1H), 1.80 (d, J = 14.2 Hz, 1H), 1.52 (s, 3H), 1.23 (s, 6H), 1.22 (s, 6H), 0.67 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.9, 143.7, 128.8, 127.7, 125.1, 112.7, 83.4, 52.5, 46.5, 32.3, 31.4, 31.1, 25.5, 25.2, 24.9.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.3.

HRMS (ESI) for $C_{22}H_{35}BO_2$ $[M+NH_4]^+$: calculated: 360.3088, found: 360.3064.

2-(2,2-dimethyl-4-phenylnon-6-yn-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.19)



3.19

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.19** (43.55 mg, 41 % yield) as colourless oil.

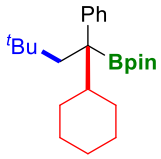
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.39-7.36 (m, 2H), 7.25-7.21 (m, 2H), 7.14-7.09 (m, 1H), 2.89 (dt, *J* = 16.4, 2.4 Hz, 1H), 2.78 (dt, *J* = 16.4, 2.4 Hz, 1H), 2.15-1.97 (m, 4H), 1.19 (s, 6H), 1.18 (s, 6H), 1.04 (t, *J* = 7.5 Hz, 3H), 0.79 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.2, 127.9, 127.6, 125.2, 84.1. 83.5, 78.5, 46.8, 32.6, 31.8, 29.8, 25.6, 24.9, 24.6, 14.4, 12.6.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.7.

HRMS (ESI) for $C_{23}H_{35}BO_2$ $[M+NH_4]^+$: calculated: 372.3074, found: 372.3088.

2-(1-cyclohexyl-3,3-dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.20)



3.20

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.20** (79.4 mg, 69 % yield) as white solid. The product appeared as a mixture of diastereoisomers 1:1.

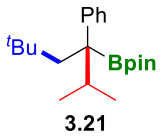
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.60 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.24-7.18 (m, 2H), 7.14-7.09 (m, 1H), 2.22 (d, *J* = 13.9 Hz, 1H), 2.04 (d, *J* = 12.0 Hz, 1H), 1.86-1.75 (m, 2H), 1.62-1.58 (m, 2H), 1.53 (d, *J* = 13.9 Hz, 1H), 1.45 (d, J = 12.9 Hz, 1H), 1.35 (2, 6H), 1,34 (s, 6H), 1.32 (m, 1H), 1.27 (m, 4H), 1.25 (m, 1H), 10.57 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 130.1, 127.5, 125.2, 83.4, 50.4, 50.0, 31.8, 31.6, 29.9, 29.5, 27.8, 27.6, 27.2, 26.0, 25.3.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.9.

HRMS (ESI) for $C_{24}H_{39}BO_2$ $[M+NH_4]^+$: calculated: 388.3384, found: 388.3387. M.p. = 64.2 °C.

4,4,5,5-tetramethyl-2-(2,5,5-trimethyl-3-phenylhexan-3-yl)-1,3,2-dioxaborolane (3.21)



3.21

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.21** (40.6 mg, 41 % yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.62-7.55 (m, 2H), 7.22 (dd, J = 8.3, 6.9 Hz, 2H), 7.15-7.08 (m, 1H), 2.23-2.16 (m, 1H), 2.20 (d, J = 14 Hz, 1H), 1.52 (d, J = 13.9 Hz, 1H), 1.35 (s, 6H), 1.33 (s, 6H), 1.06 (d, J = 7.0 Hz, 3H), 0.72 (d, J = 7.0 Hz, 3H), 0.57 (s, 9H).

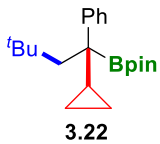
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 130.0, 127.5, 125.2, 83.4, 51.0, 38.9, 31.8, 31.5, 25.9, 25.2, 19.9, 19.7.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.1.

HRMS (ESI) for $C_{21}H_{35}BO_2$ $[M+NH_4]^+$: calculated: 331.2809, found: 331.2807.

M.p. = 59.2 °C.

2-(1-cyclopropyl-3,3-dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.22)



3.22

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.22** (32.3 mg, 33 % yield) as colourless oil.

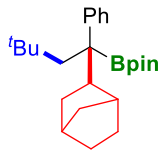
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.55 (dd, J = 8.3, 1.3 Hz, 2H), 7.26-7.22 (m, 2H), 7.16-7.07 (m, 1H), 1.83 (s, 2H), 1.24 (s, 12H), 1.23-1.24 (m, 1H), 0.79 (s, 9H), 0.66-0.50 (m, 4H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.4, 128.7, 127.7, 125.1, 83.3, 49.5, 32.4, 32.0, 24.9, 24.8, 18.3, 4.3, 4.3.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.6.

HRMS (ESI) for $C_{21}H_{33}BO_2$ $[M+NH_4]^+$: calculated: 329.2648, found: 329.2650.

2-(1-(bicy.clo[2.2.1]heptan-2-yl)-3,3-dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.23)



3.23

Flash column chromatography (pentane:EtOAc 400:1) yielded the product **3.23** (53.0 mg, 46 % yield as a mixture of two diastereoisomers 70:30) as white solid.

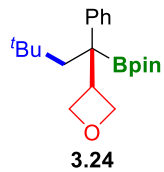
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.75-7.68 (m, 2H), 7.24-7.18 (m, 2H), 7.13-7.06 (m, 1H), 2.22-2.18 (m, 2H), 2.14 (d, J = 14.5 Hz, 1H), 1.75 (d, J = 14.5 Hz, 1H), 1.73-1.64 (m, 2H), 1.56-1.49 (m, 2H), 1.39 (s, 6H), 1.37 (s, 6H), 1.21 (m, 2H), 1.08 (m, 2H), 1.00-0.79 (m, 1H), 0.69 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.7, 129.8, 127.3, 124.9, 83.3, 57.1, 52.6, 40.6, 39.9, 37.7, 32.1, 31.9, 31.1, 30.6, 29.9, 26.6, 25.8, 23.5.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.3.

HRMS (ESI) for $C_{25}H_{40}BO_2$ $[M+H^+]^+$: calculated: 383.3121, found: 383.3116. M.p. = 97.2 °C.

2-(3,3-dimethyl-1-(oxetan-3-yl)-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.24)



3.24

Flash column chromatography (pentane:EtOAc 400:1) yielded the product **3.24** (25.80 mg, 25 % yield) as colourless oil.

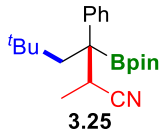
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.25-7.17 (m, 4H), 7.15-7.10 (m, 1H), 4.88-4.69 (m, 3H), 4.69-4.64 (m, 1H), 1.95 (d, J = 14.8 Hz, 1H), 1.65 (d, J = 14.8 Hz, 1H), 1.32 (s, 6H), 1.32 (s, 6H), 0.65 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.5, 128.3, 128.0, 125.6, 83.9, 75.5, 74.9, 47.6, 40.6, 31.8, 25.1, 25.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.6.

HRMS (ESI) for $C_{21}H_{34}BO_3$ $[M+H^+]^+$: calculated: 345.2601, found: 345.2605.

2,5,5-trimethyl-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanenitrile (3.25)



3.25

Flash column chromatography (pentane:EtOAc 400:1 .to 20:1) yielded the product **3.25** (32.75 mg, 32 % yield, as a mixture of two diastereoisomers 60:40) as colourless oil.

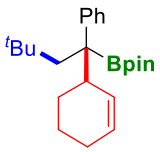
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.79-7.72 (m, 2H), 7.33-7.27 (m, 2H), 7.24-7.18 (m, 1H), 3.21 (q, J = 7.1 Hz, 1H), 2.27 (d, J = 14.3 Hz, 1H), 2.05 (d, J = 14.3 Hz, 1H), 1.35 (s, 6H), 1.33 (s, 6H), 1.07 (d, J = 7.1 Hz, 3H), 0.79 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 140.8, 129.5, 128.0, 126.7, 84.3, 49.9, 35.7, 31.7, 25.6, 25.5, 16.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.0.

HRMS (ESI) for $C_{21}H_{33}BNO_2$ $[M+H^+]^+$: calculated: 342.2608, found: 342.2599.

2-(1-(cyclohex-2-en-1-yl)-3,3-dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.26)



3.26

Flash column chromatography (pentane:EtOAc 400:1) yielded the product **3.26** (37.5 mg, 34 % yield as a mixture of two diastereoisomers 70:30) as colourless oil.

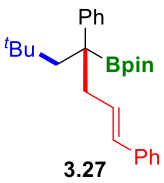
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.69-7.63 (m, $2H_M$), 7.58-7.51 (m, $2H_m$), 7.28-7.18 (m, 2.H_M, $2H_m$), 7.17-7.08 (m, $1H_M$, $1H_m$), 6.06 (dt, J = 10.6, 2.1Hz, $1H_m$), 5.70-5.62 (m,$1H_m$), 5.54-5.46 (m, $1H_M$), 5.35 (dt, J = 10.2, 1.9 Hz, $1H_M$), 2.86-2.79 (m, $1H_M$), 2.70-2.59 (m, $1H_m$), 2.48 (d, J = 13.8 Hz, $1H_m$), 2.18 (d, J = 13.9 Hz, $1H_M$), 2.09-2.00 (m, 2HM, $2H_m$), 1.93-1.78 (m, $1H_M$), 1.67-1.43 (m, $3H_M$,$3H_m$), 1.34 (s, $6H_M$), 1.33 (s, $6H_m$), 1.28 (s, $6H_m$), 1.26 (s, $6H_M$), 0.58 (s, $9H_m$), 0.56 (s, $9H_M$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.6, 130.7, 130.4, 127.7, 127.7, 126.9, 125.5, 125.4, 83.6, 83.5, 50.9, 50.0, 47.8, 46.9, 31.9, 31.6, 31.4, 31.0, 26.0, 25.8, 25.7, 25.6, 25.6, 25.2, 25.2, 24.7, 23.4, 23.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.8.

HRMS (ESI) for $C_{24}H_{37}BO_2$ $[M+NH_4]^+$: calculated: 369.2970, found: 369.2964.

(*Z*)-2-(6,6-dimethyl-1,4-diphenylhept-1-en-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.27)



3.27

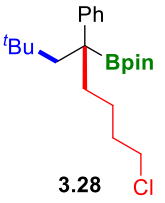
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.27** (111.1 mg, 91 % yield) as colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.63-7.56 (m, 2H), 7.33-7.23 (m, 6H), 7.22-7.13 (m, 2H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.08 (dt, *J* = 15.7, 7.0 Hz, 1H), 2.94 (dt, J = 7.3, 1.6 Hz, 2H), 2.10 (d, *J* = 14.4 Hz, 1H), 1.90 (d, *J* = 14.4 Hz, 1H), 1.26 (s, 6H), 1.24 (s, 6H), 0.79 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.5, 138.1, 131.8, 128.7, 128.6, 128.5, 127.9, 126.8, 126.1, 125.3, 83.5, 50.0, 41.7, 32.5, 31.7, 29.8, 25.3, 25.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.8.

HRMS (ESI) for $C_{27}H_{37}BO_2$ $[M+NH_4]^+$: calculated: 422.3225, found: 422.3247.

2-(8-chloro-2,2-dimethyl-4-phenyloctan-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.28)



3.28

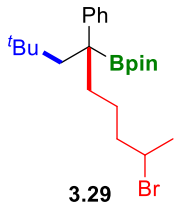
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product 3.28 (80.50 mg, 71 % yield) as colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.50-7.47 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 2H), 7.11 (tt, *J* = 7.3, 1.2 Hz, 1H), 3.44 (td, *J* = 6.8, 2.9 Hz, 2H), 1.98 (d, *J* = 14.2 Hz, 1H), 1.91 (m 2H), 1.75 (d, *J* = 14.2 Hz, 1H), 1.77-1.66 (m, 2H), 1.30-1.19 (m, 2H), 1.24 (s, 6H), 1.22 (s, 6H), 0.73 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 128.3, 128.0, 125.2, 83.4, 50.0, 45.1, 37.8, 33.6, 32.2, 31.5, 25.2, 25.0, 24.7, 23.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.8.

HRMS (ESI) for $C_{22}H_{36}BClO_2$ $[M+NH_4]^+$: calculated: 393.2841, found: 393.2845.

2-(8-bromo-2,2-dimethyl-4-phenylnonan-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.29)



3.29

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.29** (66.7 mg, 51% yield as a mixture of two diastereoisomers M:m=65:35) as colourless solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.53-7.43 (m, $2H_M$, $2H_m$), 7.25-7.20 (m, $2H_M$, $2H_m$), 7.15-7.07 (m, $1H_M$, $1H_m$), 4.1-3.98 (m, $1H_M$, $1H_m$), 2.03-1.64 (m, $6H_M$, $6H_m$), 1.63-1.60 (m, $3H_M$, $3H_m$), 1.42-1.27 (m, $1H_M$, $1H_m$), 1.26-1.19 (m, $12H_M$, $12H_m$), 1.19-1.10 (m, $1H_M$, $1H_m$), 0.74 (s, $9H_m$), 0.71 (s, $9H_M$).

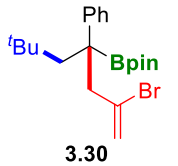
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 145.6, 128.3, 128.2, 127.9, 127.9, 125.2, 125.2, 83.4, 52.0, 51.7, 50.3, 49.3, 42.2, 42.0, 38.0, 37.1, 32.2, 32.2, 31.5, 31.5, 26.6, 26.4, 25.3, 25.1, 24.9, 24.9, 24.0, 23.6.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.4.

HRMS (ESI) for $C_{23}H_{39}BBrO_2$ $[M+H^+]^+$: calculated: 437.2221, found: 437.2225.

M.p. = 48.6 °C.

2-(2-bromo-5,5-dimethyl-3-phenylhex-1-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.30)



3.30

Flash column chromatography (pentane:EtOAc 400:1) yielded the product **3.30** (40.1 mg, 33 % yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.59-7.55 (m, 2H), 7.31-7.19 (m, 2H), 7.17-7.09 (m, 1H), 5.32 (m, 1H), 5.25 (m, 1H), 3.21 (dt, J = 3.1, 1.7 Hz, 2H), 2.02 (d, J = 14.1 Hz, 1H), 1.88 (d, J = 14.1 Hz, 1H), 1.21 (s, 6H), 1.17 (s, 6H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.1, 131.5, 128.0, 125.4, 118.7, 83.6, 50.4, 48.7, 32.1, 31.2, 25.0, 24.8.

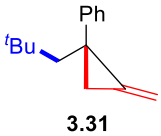
^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.9.

HRMS (ESI) for $C_{21}H_{33}BBrO_2$ $[M+H^+]^+$: calculated: 407.1756, found: 407.1757.

M.p. = 83.9 °C.

6.3.7 Characterization of cyclopropane

2-methylene-1-neopentylcyclopropyl)benzene (3.31)



3.31

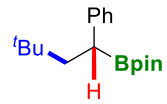
Flash column chromatography (pentane) yielded the product **3.31** (22.2 mg, 37 % yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.43-7.38 (m, 2H), 7.28-7.22 (m, 2H), 7.19-7.13 (m, 1H), 5.72-5.66 (m, 1H), 5.55-5.50 (m, 1H), 2.19 (d, J = 14.3 Hz, 1H), 1.45 (d, J = 14.3 Hz, 1H), 1.33-1.26 (m, 2H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.2, 140.2, 128.4, 128.1, 126.1, 105.0, 52.3, 32.6, 30.6, 27.9, 20.0.

6.3.8 Characterization of secondary boronic esters

2-(3,3-Dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.32)



3.32

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.32** (115.1 mg, 60% yield) as white sòlid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.23 (d, J = 4.4 Hz, 4H), 7.13 - 7.08 (m, 1H), 2.39 (dd, J = 10.0, 3.7 Hz, 1H), 2.02 (dd, J = 13.3, 10.0 Hz, 1H), 1.50 (dd, J = 13.3, 3.8 Hz, 1H), 1.14 (d, J = 2.5 Hz, 12H), 0.90 (s, 9H).

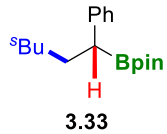
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 143.6, 128.5, 128.4, 125.2, 83.4, 46.7, 31.6, 29.9, 24.8, 24.6.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 32.6.

HRMS (ESI) for $C_{18}H_{29}BO_2$ $[M+NH_4]^+$: calculated: 306.2604, found: 306.2613.

M.p. = 63.4 °C.

4,4,5,5-Tetramethyl-2-(3-methyl-1-phenylpentyl)-1,3,2-dioxaborolane (3.33)



3.33

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.33** (20.0 mg, 16% yield as a mixture of diastereosiomers 1:1) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.24-7.21 (m, 8H), 7.14 - 7.10 (m, 2H), 2.43 (dt, J = 9.3, 7.2 Hz, 2H), 1.87 (ddd, J = 13.2, 9.2, 6.0 Hz, 1H), 1.74 (ddd, J = 14.0, 9.0, 5.2 Hz, 1H), 1.58 (ddd, J = 13.5, 8.4, 7.2 Hz, 2H), 1.43-1.37 (m, 1H), 1.36-1.30 (m, 2H), 1.44-1.38 (m, 1H), 1.19 (d, J = 2.5 Hz, 12H), 1.17 (s, 12H), 1.16-1.08 (m, 2H), 0.89-0.83 (m, 10H), 0.81 (t, J = 7.3 Hz, 3H).

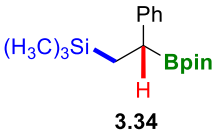
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.0, 143.7, 128.6, 128.6, 128.5, 128.4, 128.4, 125.2, 125.2, 83.4, 39.9, 39.2, 33.9, 33.3, 29.9, 29.4, 24.8, 24.8, 24.8, 19.7, 19.0, 11.5, 11.5.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.5.

HRMS (ESI) for $C_{18}H_{29}BO_2$ $[M+NH_4]^+$: calculated: 306.2604 , found: 306.2608.

M.p. = 62.6 °C.

Trimethyl(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)silane (3.34)



3.34

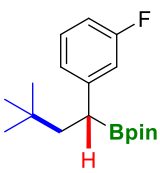
Flash column chromatography (pentane:EtOAc 200:1) yielded the product **3.34** (36.49 mg, 40% yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.25-7.22 (m, 4H), 7.16-7.06 (m, 1H), 2.48-2.28 (m, 1H), 1.25-1.19 (m, 1H), 1.17 (s, 6H), 1.16 (s, 6H), 0.90 (dd, J = 14.6, 6.8 Hz, 1H), -0.09 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.8, 128.3, 128.2, 125.1, 83.4, 24.8, 24.7, 19.4, -1.11.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.3.

2-(1-(3-fluorophenyl)-3,3-dimethylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.35)



3.35

Flash column chromatography (pentane:EtOAc 200:1) yielded the product **3.35** (34.87 mg, 38% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.23-7.13 (m, 1H), 7.03-6.91 (m, 2H), 6.85-6.75 (m, 1H), 2.40 (dd, J = 9.7, 4.0 Hz, 1H), 1.99 (dd, J = 13.4, 9.7 Hz, 1H), 1.48 (dd, J = 13.4, 4.0 Hz, 1H), 1.15 (s, 6H), 1.15 (s,6H), 0.89 (s, 9H).

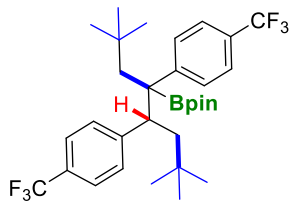
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 163.0 (d, J = 244.6 Hz), 147.7 (d, J = 7.1 Hz), 129.6 (d, J = 8.3 Hz), 124.0 (d, J = 2.8 Hz), 115.0 (d, J = 21.1 Hz), 112.0 (d, J = 21.1 Hz), 83.5, 46.4, 31.5, 29.8, 24.7, 24.6.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.17.

^{19}F NMR ($CDCl_3$, 376 MHz, δ ppm): -114.0.

HRMS (ESI) for $C_{18}H_{29}BFO_2$ $[M+H^+]^+$: calculated: 307.2239, found: 307.2242

4,4,5,5-tetramethyl-2-(2,2,7,7-tetramethyl-4,5-bis(4-(trifluoromethyl)phenyl)octan-4-yl)-1,3,2-dioxaborolane (3.36)



3.36

Flash column chromatography (pentane:EtOAc 400:2) yielded the product **3.36** (10.52 mg, 12% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.38 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.03 (d, J = 8.2 Hz, 2H), 6.95 (d, J = 8.2 Hz, 2H), 2.68-2.54 (m, 2H), 2.34 (dd, J = 9.8, 4.1 Hz, 1H), 1.94 (dd, J = 13.3, 9.8 Hz, 1H), 1.45 (dd, J = 13.3, 4.1 Hz, 1H), 1.10 (s, 12H), 0.86 (s,9H), 0.83 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.8, 130.2, 130.2, 129.0, 129.0, 128.3, 128.1, 127.8, 126.4, 125.1, 125.1, 118.4, 118.2, 83.5, 83.4, 48.4, 45.9, 44.2, 33.3, 31.5, 30.3, 30.3, 30.1, 29.8, 29.7, 24.7, 24.5, 24.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 32.6.

^{19}F NMR ($CDCl_3$, 376 MHz, δ ppm): -62.38.

6.3.9 Characterization of silylpinacolborylcyclopropanes

2,2'-(3-Phenylprop-1-ene-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (3.37)

3.37

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **3.37** (16 mg, 17% yield) as pale yelowish oil.

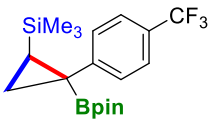
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.25 – 7.18 (m, 4H), 7.17 – 7.06 (m, 1H), 1.24 (dd, J = 9.9, 2.9 Hz, 1H), 1.20 (s, 6H), 1.19 (s, 6H), 1.05 (dd, J = 8.0, 2.9 Hz, 1H), 0.10 (s, 9H), 0.08 – 0.03 (m, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.4, 129.2, 127.9, 125.2, 83.4, 25.3, 24.6, 16.9, 15.7, -0.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.7.

HRMS (ESI) for $C_{18}H_{30}BO_2Si^+[M+H^+]^+$: calculated: 317.2106, found: 317.2106.

Trimethyl((1S,2S)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)silane (3.38)



3.38

Flash column chromatography (pentane:EtOAc 100:3) yielded the product **3.38** (27 mg, 23% yield) as pale yelowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.46 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 1.28 (dd, J = 10.1, 3.1 Hz, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 1.12 (dd, J = 8.1, 3.1 Hz, 1H), 0.12 (s, 9H), 0.09 – 0.06 (m, 1H).

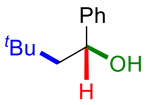
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 151.6, 130.0, 129.4, 128.5, 124.9 (q, J = 3.6 Hz), 83.7, 25.3, 24.6, 17.2, 16.4, -0.4.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.4.

HRMS (ESI) for $C_{19}H_{29}BF_3O_2Si^+[M+H^+]^+$: calculated: 385.1982, found: 385.1986.

6.3.10 Characterization of tertiary and secondary alcohols

3,3-Dimethyl-1-phenylbutan-1-ol (3.39)



3.39

Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.39** (32.81 mg, 92% yield) as white solid.

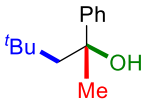
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.40-7.30 (m, 4H), 7.28-7.23 (m, 1H), 4.84 (dd, J = 8.4, 3.6 Hz, 1H), 1.77 (dd, J = 14.5, 8.4 Hz, 1H), 1.68 (s, 1H), 1.62 (dd, J = 14.5, 3.6 Hz, 1H), 1.00 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.6, 128.7, 127.5, 125.9, 72.7, 53.1, 30.3.

HRMS (ESI) for $C_{12}H_{17}$ $[M\text{-}H^+]^-$: calculated: 161.1330, found: 161.1324.

M.p. = 65.5 °C.

4,4-Dimethyl-2-phenylpentan-2-ol (3.40)



3.40

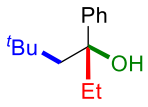
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.40** (34.56 mg, 90% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.49-7.42 (m, 2H), 7.34-7.30 (m, 2H), 7.24-7.17 (m, 1H), 1.95 (d, J = 14.8 Hz, 1H), 1.84 (d, J = 14.8 Hz, 1H), 1.58 (s, 2H), 0.81 (s, 5H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 148.8, 128.1, 126.4, 125.1, 75.9, 56.2, 34.1, 31.5.

HRMS (ESI) for $C_{12}H_{19}O$ $[M\text{-}H^+]^+$: calculated: 191.1514, found: 192.1420.

5,5-Dimethyl-3-phenylhexan-3-ol (3.41)



3.41

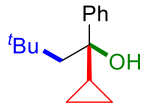
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.41** (38.09 mg, 92% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.41-7.36 (m, 2H), 7.33-7.29 (m, 2H), 7.23-7.16 (m, 1H), 1.95 (d, J = 14.8 Hz, 1H), 1.89-1.74 (m, 3H), 1.66 (s, 1H), 0.77 (s, 9H), 0.66 (t, J = 7.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.4, 127.9, 126.1, 125.8, 78.14, 6.21, 38.9, 31.9, 31.7, 7.4.

HRMS (ESI) for $C_{14}H_{21}O$ $[M\text{-}H^+]^-$: calculated: 205.1592, found: 205.1594.

1-Cyclopropyl-3,3-dimethyl-1-phenylbutan-1-ol (3.42)



3.42

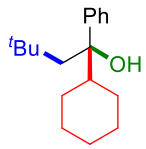
Flash column chromatography (pentane:EtOAc 10:1) yielded the product **3.42** (42.01 mg, 96% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.50 – 7.44 (m, 2H), 7.35 – 7.27 (m, 2H), 7.26 – 7.17 (m, 1H), 2.04 (d, J = 14.9 Hz, 1H), 1.85 (d, J = 14.9 Hz, 1H), 1.39 (s, 1H), 1.36 – 1.27 (m, 1H), 0.80 (s, 9H), 0.51 – 0.42 (m, 2H), 0.36 – 0.24 (m, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.5, 127.8, 126.3, 125.6, 75.5, 54.6, 31.7, 31.6, 24.7, 2.0, 1.2.

HRMS (ESI) for $C_{15}H_{21}O$ $[M\text{-}H^+]^-$: calculated: 217.1592, found: 231.1741.

1-Cyclohexyl-3,3-dimethyl-1-phenylbutan-1-ol (3.43)



3.43

Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.43** (24.94 mg, 48% yield) as white solid.

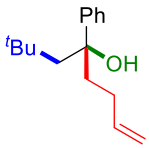
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.41-7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.22-7.15 (m, 1H), 2.06-1.98 (m, 1H), 1.95 (d, J = 14.8 Hz, 1H), 1.89 (d, J = 14.8 Hz, 1H), 1.83-1.75 (m, 1H), 1.64-1.60 (m, 3H), 1.26-1.21 (m, 4H), 1.11-1.03 (m, 2H), 0.9-0.83 (m, 2H), 0.72 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.1, 127.6, 126.2, 126.0, 79.5, 51.3, 51.1, 31.9, 31.7, 27.0, 26.9, 26.9, 26.8, 26.6.

HRMS (ESI) for $C_{18}H_{27}O$ $[M\text{-}H^+]^-$: calculated: 259.2061, found: 259.2040.

M.p. = 70.9 °C.

2,2-Dimethyl-4-phenyloct-7-en-4-ol (3.44)



3.44

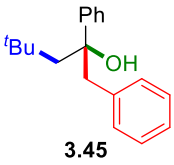
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.44** (42.72 mg, 92% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.40-7.37 (m, 2H), 7.34-7.27 (m, 2H), 7.23-7.18 (m, 1H), 5.81-5.71 (m, 1H), 4.98-4.85 (m, 2H), 2.00-1.77 (m, 6H), 1.26 (s, 1H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.3, 139.1, 128.0, 126.2, 125.7, 114.7, 78.2, 55.6, 45.3, 31.9, 31.7, 27.8.

HRMS (ESI) for $C_{16}H_{23}O$ $[M\text{-}H^+]^-$: calculated: 231.1749, found: 231.1741.

4,4-dimethyl-1,2-diphenylpentan-2-ol (3.45)



3.45

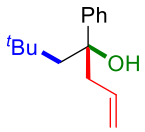
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.45** (47.75 mg, 89% yield) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.36-7.32 (m, 2H), 7.30-7.26 (m, 2H), 7.22-7.19 (m, 1H), 7.18-7.12 (m, 3H), 6.87-6.85 (m, 2H), 3.14 (d, J = 13.2 Hz, 1H), 2.99 (d, J = 13.2 Hz, 1H), 2.11 (dd, J = 14.7, 1.0 Hz, 1H), 1.88 (d, J = 14.7 Hz, 1H), 1.79 (d, J = 1.0 Hz, 1H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.2, 136.1, 130.9, 128.2, 127.8, 126.8, 126.3, 126.1, 54.4, 52.9, 32.0, 31.7.

HRMS (ESI) for $C_{19}H_{28}NO$ $[M+NH_4^+]^+$: calculated: 286.1827, found: 286.2181. M.p. = 73.5 °C.

6,6-Dimethyl-4-phenylhept-1-en-4-ol (3.46)



3.46

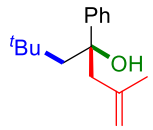
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.46** (37.90 mg, 87% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.44-7.37 (m, 2H), 7.34-7.28 (m, 2H), 7.23-7.17 (m, 1H), 5.47-5.36 (m, 1H), 5.17-5.05 (m, 2H), 2.69 (dd, J = 13.5, 5.7 Hz, 1H), 2.44 (dd, J = 13.5, 9.1 Hz, 1H), 2.07 (d, J = 1.0 Hz, 1H), 1.95 (d, J = 14.7 Hz, 1H), 1.83 (d, J = 14.7 Hz, 1H), 0.76 (s, 8H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.7, 133.5, 128.0, 126.3, 125.7, 120.2, 76.5, 54.8, 51.0, 31.9, 31.6.

HRMS (ESI) for $C_{15}H_{22}O$ $[M+NH_4]^+$: calculated: 200.1565, found: 200.1569.

2,6,6-trimethyl-4-phenylhept-1-en-4-ol (3.47)



3.47

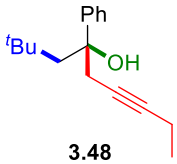
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.47** (42.24 mg, 92% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.46-7.38 (m, 2H), 7.33-7.26 (m, 2H), 7.22-7.14 (m, 1H), 4.92-4.83 (m, 1H), 4.76-4.70 (m, 1H), 2.62 (d, J = 12.6 Hz, 1H), 2.49 (d, J = 13.0 Hz, 1H), 2.42 (s, 1H), 2.00 (d, J = 14.6 Hz, 1H), 1.80 (d, J = 14.6 Hz, 1H), 1.16 (s, 3H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.7, 142.6, 127.8, 126.26, 126.0, 116.3, 75.7, 55.4, 54.7, 32.1, 31.6, 24.4.

HRMS (ESI) for $C_{16}H_{24}O$ $[M+H^+-H_2O]^+$: calculated: 214.1719, found: 214.1722.

2,2-dimethyl-4-phenylnon-6-yn-4-ol (3.48)



3.48

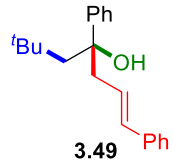
Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.48** (42.98 mg, 88% yield) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.45-7.40 (m, 2H), 7.34-7.28 (m, 2H), 7.25-7.18 (m, 1H), 2.70-2.52 (m, 2H), 2.47 (s, 1H), 2.12 (qt, J = 7.5, 2.4 Hz, 2H), 2.00 (d, J = 14.7 Hz, 1H), 1.91 (d, J = 14.7 Hz, 1H), 1.06 (t, J = 7.5 Hz, 3H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.1, 127.8, 126.4, 125.4, 86.2, 75.9, 75.0, 53.0, 37.7, 31.6, 31.3, 14.2, 12.4.

HRMS (ESI) for $C_{17}H_{23}$ $[M+H^+-H_2O]^+$: calculated: 226.1722, found: 226.1727.

(*E*)-6,6-dimethyl-1,4-diphenylhept-1-en-4-ol (3.49)



3.49

Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.49** (53.51 mg, 91% yield) as white solid.

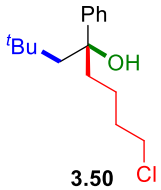
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.49-7.40 (m, 2H), 7.37-7.29 (m, 2H), 7.29-7.16 (m, 6H), 6.47 (d, J = 15.9 Hz, 1H), 5.88 – 5.75 (m, 1H), 2.82 (dd, J = 13.6, 5.9, 1H), 2.61 (dd, J = 13.6, 9.2 Hz, 1H), 2.10 (s, 1H), 2.01 (d, J = 14.7 Hz, 1H), 1.88 (d, J = 14.7 Hz, 1H), 0.77 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.7, 137.2, 135.2, 128.6, 128.1, 127.5, 126.4, 126.46, 125.7, 124.8, 77.1, 54.7, 50.4, 32.0, 31.6.

HRMS (ESI) for $C_{21}H_{25}$ $[M+H^+-H_2O]^+$: calculated: 276.1878, found: 276.1883.

M.p. = 62.5 °C.

8-chloro-2,2-dimethyl-4-phenyloctan-4-ol (3.50)



3.50

Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.50** (51.47 mg, 96% yield) as white solid.

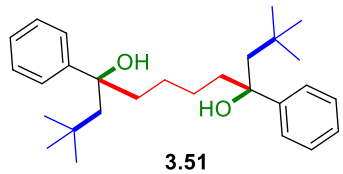
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.39-7.36 (m, 2H), 7.34-7.28 (m, 2H), 7.25-7.17 (m, 1H), 3.44-3.41 (m, 2), 1.96 (d, J = 14.8 Hz, 1H), 1.86-1.58 (m, 6H), 1.50-1.36 (m, 1H), 1.26 (s, 1H), 1.10-0.92 (m, 1H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.2, 128.0, 126.3, 125.6, 77.9, 55.4, 45.7, 44.9, 33.0, 31.9, 31.7, 20.6.

HRMS (ESI) for $C_{16}H_{24}Cl$ $[M+H^+-H_2O]^+$: calculated: 250.1488, found: 250.1503.

M.p. = 68.6 °C.

2,2,11,11-tetramethyl-4,9-diphenyldodecane-4,9-diol (3.51)



3.51

Flash column chromatography (pentane:EtOAc 100:3 to 10:1) yielded the product **3.51** (79.59 mg, 89% yield) as white solid.

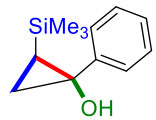
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.36-7.23 (m, 8H), 7.21-7.14 (m, 2H), 1.88 (d, J = 14.8 Hz, 2H), 1.74 (d, J = 14.8, 2H), 1.71-1.59 (m, 6H), 1.21-1.09 (m, 2H), 0.82-0.73 (m, 20H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm: 146.6, 146.5, 127.8, 127.8, 126.0, 125.6, 77.9, 77.9, 55.4, 55.4, 46.3, 46.3, 31.8, 31.6, 23.2, 23.2.

HRMS (ESI) for $C_{28}H_{41}O_2$ $[M\text{-}H^+]^-$: calculated: 409.3107, found: 409.3098.

M.p. = 93.1 °C.

(1R,2S)-1-Phenyl-2-(trimethylsilyl)cyclopropan-1-ol (3.52)



3.52

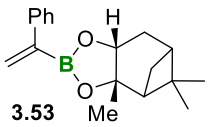
Flash column chromatography (pentane:EtOAc 10:1) yielded the product **3.52** (38 mg, 93% yield) as pale yelowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.26 – 7.22 (m, 2H), 7.18 – 7.12 (m, 1H), 7.04 – 7.00 (m, 2H), 3.86 (dd, J = 7.5, 2.4 Hz, 1H), 2.04 (dd, J = 8.1, 2.4 Hz, 1H), 1.94 (s, 1H), 0.33 (dd, J = 8.1, 7.5 Hz, 1H), 0.14 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 142.4, 128.4, 125.8, 125.7, 60.0, 29.3, 19.4, -0.2.

6.3.11 Characterization of chiral substrate

[1,3,2]dioxaborole (3.53)



3.53

Flash column chromatography (pentane:EtOAc 200:1) yielded the product **3.53** (79 mg, 93% yield) as a paleyelowish oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.53 – 7.45 (m, 2H), 7.37 – 7.29 (m, 2H), 7.28 – 7.20 (m, 2H), 6.08 (d, J = 2.0 Hz, 2H), 4.41 (dd, J = 8.8, 1.9 Hz, 1H), 2.44 – 2.34 (m, 1H), 2.32 – 2.21 (m, 1H), 2.16 – 2.09 (m, 1H), 2.01 – 1.90 (m, 2H), 1.46 (s, 3H), 1.31 (s, 3H), 1.25 (d, J = 10.9 Hz, 1H), 0.88 (s, 3H).

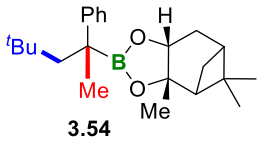
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 141.6, 131.1, 128.3, 127.3, 127.1, 86.3, 78.3, 51.5, 39.6, 38.3, 35.7, 28.8, 27.2, 26.7, 24.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 30.0.

HRMS (ESI) for $C_{18}H_{24}BO_2$ $[M+H^+]^+$: calculated: 283.1869; found: 283.1854.

6.3.12 Characterization of chiral boronic esters

2-(4,4-dimethyl-2-phenylpentan-2-yl)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborole (3.54)



3.54

Flash column chromatography (pentane:EtOAc 200:1) yielded the product **3.54** (61.64 mg, 58 % yield, , two diastereomers M:m=55:45) as colourless liquid.

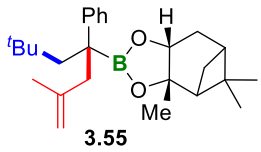
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.50-7.45 (m, $2H_M$, $2H_m$), 7.29-7.23 (m, $2H_M$, $2H_m$), 7.14-7.08 (m, $1H_M$, $1H_m$), 4.3-4.22 (m, $1H_M$, $1H_m$), 2.36-2.22 (m, $1H_M$, $1H_m$), 2.08-1.95 (m, $3H_M$, $3H_m$), 1.86-1.70 (m, $3H_M$, $3H_m$), 1.51 (s, $3H_m$), 1.51 (s, $3H_M$), 1.37-1.29 (m, $4H_M$, $4H_m$), 1.24 (s, $3H_m$), 1.24 (s, $3H_M$), 0.88 (s, $9H_m$), 0.87 (s, $9H_M$), 0.81 (s, $3H_M$, $3H_m$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 148.1, 148.0, 127.9, 127.9, 127.3, 127.3, 125.0, 86.0, 85.5, 78.0, 77.8, 52.7, 52.6, 51.5, 51.5, 51.5, 39.6, 39.4, 39.4, 38.4, 35.8, 35.6, 35.6, 32.4, 32.4, 31.7, 31.7, 28.8, 28.4, 28.4, 27.3, 27.1, 26.5, 26.1, 26.1, 24.1, 23.2, 23.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.4.

HRMS (ESI) for $C_{23}H_{39}NBO_2$ $[M+NH_4^+]^+$: calculated: 372.3074, found: 372.3079.

3a,5,5-trimethyl-2-(2,6,6-trimethyl-4-phenylhept-1-en-4-yl)hexahydro-4,6-methanobenzo[d][1,3,2]dioxaborole (3.55)



3.55

Flash column chromatography (pentane:EtOAc 200:1) yielded the product **3.55** (70.96 mg, 60 % yield, , two diastereomers M:m=60:40) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.67-7.57 (m, $2H_M$, $2H_m$), 7.25-7.19 (m, $2H_M$, $2H_m$), 7.14-7.05 (m, $1H_M$, $1H_m$), 4.71-4.51 (m, $2H_M$, $2H_m$), 4.35-4.23 (m, $1H_M$, $1H_m$), 2.79 (d, J = 16.6 Hz, $1H_m$), 2.77 (d, J = 16.6 Hz, $1H_M$), 2.68 (d, J = 16.6 Hz, $1H_m$), 2.64 (d, J = 16.6 Hz, $1H_M$), 2.38-2.27 (m, $1H_M$, $1H_m$), 2.12-2.01 (m, $3H_M$, $3H_m$), 1.92-1.77 (m, $3H_M$, $3H_m$), 1.53 (s, $3H_m$), 1.52 (s, $3H_M$), 1.36 (s, $3H_m$), 1.35 (s, $3H_M$), 1.27 (s, $3H_M$, $3H_m$), 1.24-1.19 (m, $1H_M$, $1H_m$), 0.84 (s, $3H_m$), 0.83 (s, $3H_M$), 0.70 (s, $9H_m$), 0.70 (s, $9H_M$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 143.5, 128.5, 128.5, 127.6, 125.0, 125.0, 112.9, 112.8, 86.1, 85.7, 77.9, 52.2, 52.0, 51.6, 51.4, 46.0, 45.7, 39.4, 39.3, 38.5, 38.4, 35.4, 35.3, 32.3, 32.2, 31.3, 28.6, 28.3, 28.2, 27.2, 27.1, 27.0, 25.9, 25.73, 24.9, 24.8, 24.1, 24.1, 24.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.2

HRMS (ESI) for $C_{26}H_{43}NBO_2$ $[M+NH_4^+]^+$: calculated: 412.3387, found: 412.3375.

M.p. = 55.6 °C.

6.3.13 Enantiomeric excess determined by HPLC

Racemic alcohols and enantiomerically enriched alcohols were analyzed by chiral HPLC analysis, ADH-column, 25 °C, 40-60 bar.

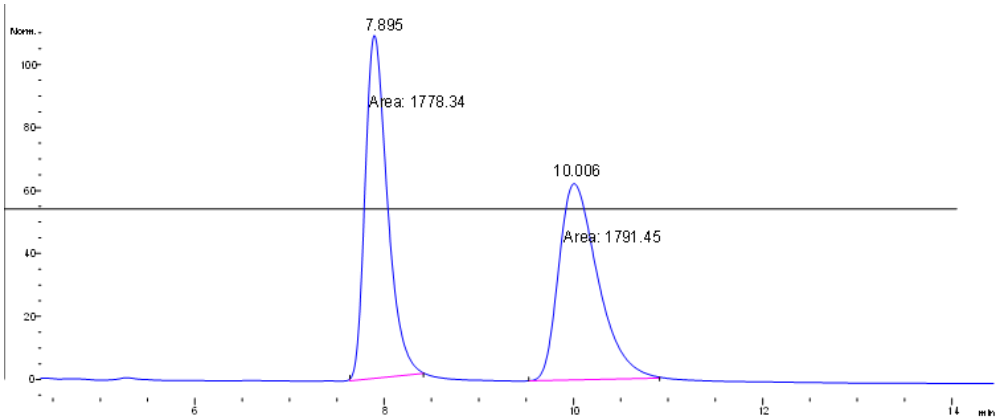


Figure 6.2. Separation of racemic species for **3.45**. Hexane: EtOH = 99:01, 1 mL/min.

Table 6.2.

Time	Area	Height	Width	Area%	Symmetry
7.895	1778.3	108.8	0.2723	49.816	0.686
10.006	1791.4	62.2	0.4796	50.184	0.629

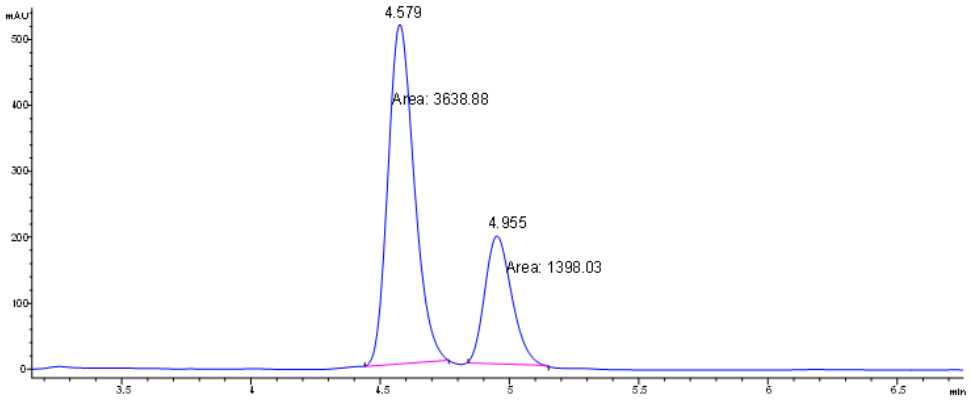


Figure 6.3. Separation of enantiomerically enriched species for **3.58**. Hexane: EtOH = 98:02, 1 mL/min.

Table 6.3.

Time	Area	Height	Width	Area%	Symmetry
4.579	3638.9	515.7	0.1176	72.244	0.798
4.955	1398	194.1	0.1201	27.756	0.788

6.3.14 ^{11}B NMR spectroscopic studies

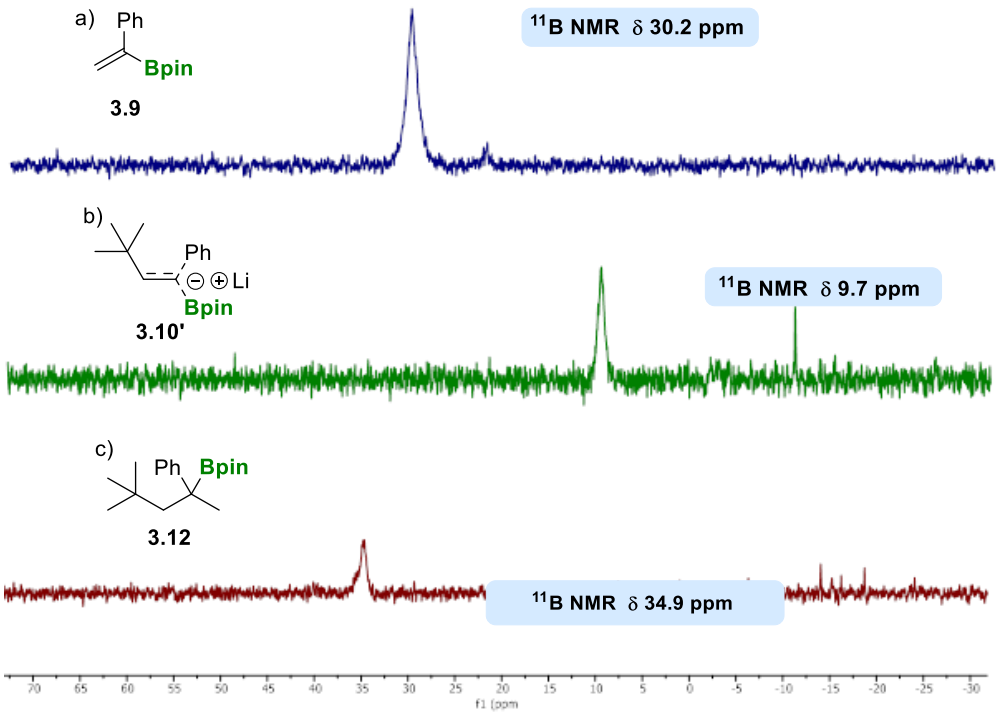


Figure 6.4. Evolution of ^{11}B NMR spectroscopic signals in experiments performed at room temperature, in d^8-THF, from a) 1-phenylvinylboronic acid pinacol ester **3.9**, b) addition of 1 equiv of ^{t}BuLi to **3.9** with concomitant formation of α-borylcarbanion **3.10'**, and c) addition of 1 equiv of MeI to α-borylcarbanion **3.10'** with subsequent formation of product tertiary boronic ester **3.12**.

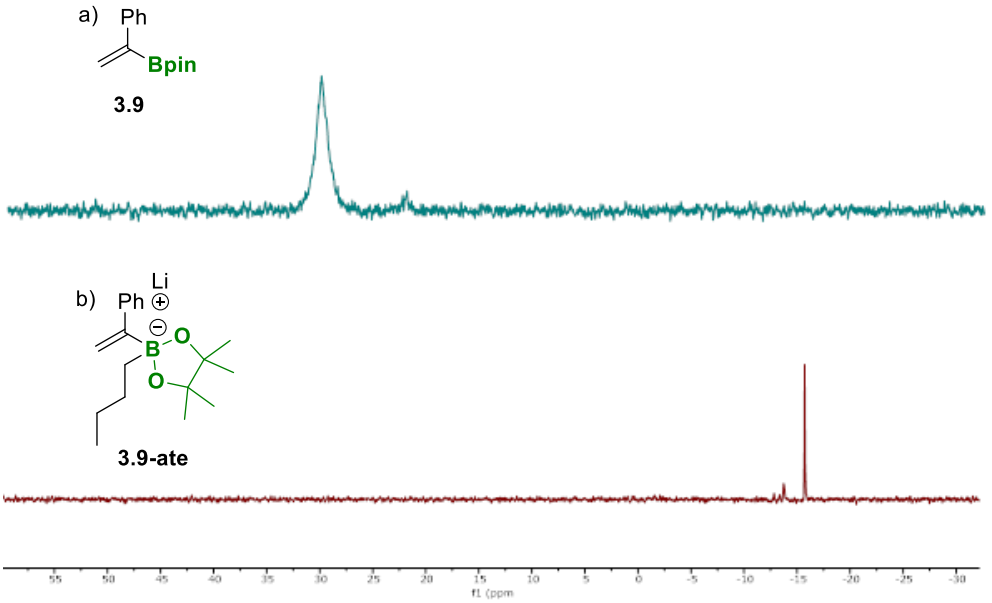


Figure 6.5. Evolution of ^{11}B NMR spectroscopic signals in experiments performed at room temperature, in d^8-THF, from a) 1-phenylvinylboronic acid pinacol ester **3.9**, b) addition of 1 equiv of ^{n}BuLi to **3.9** with concomitant formation of boron 'ate' **3.9-ate**.

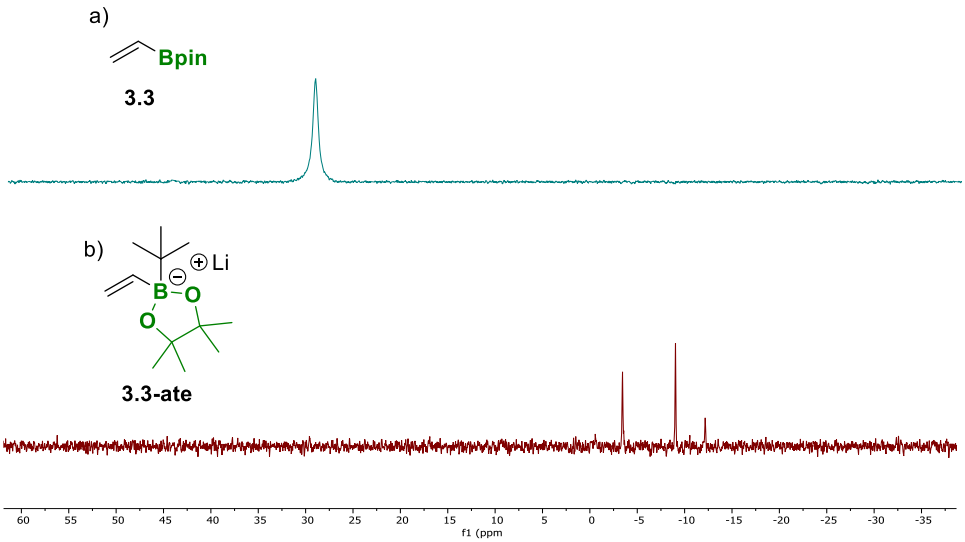
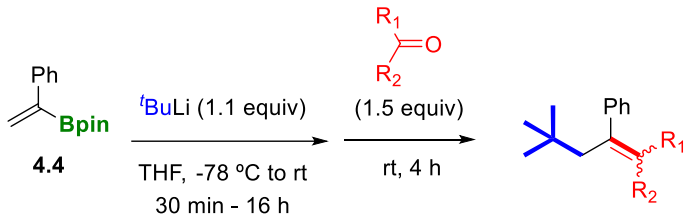


Figure 6.6. Evolution of ^{11}B NMR spectroscopic signals in experiments performed at room temperature, in d^8-THF, from a) vinylboronic acid pinacol ester **3.3**, b) addition of 1 equiv of ^{t}BuLi to **3.3** with concomitant formation of boron 'ate' **3.3-ate**.

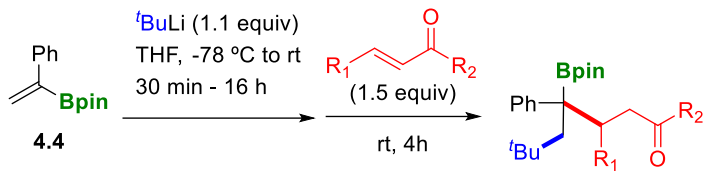
6.4 Experimental section for Chapter 4

6.4.1. General methodology for 1,2-dicarbofunctionalization through Boron-Wittig olefination with aldehydes or ketones



A flame dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**4.4**) (69.5 mg, 0.3 mmol, 1.0 equiv) in dried THF (2 mL), then sealed with a rubber septum and put under a nitrogen atmosphere at -78 °C. A solution of *tert*-butyllithium reagent (0.19 mL, 0.33 mmol, 1.1 equiv) in hexane (1.7 M) was added dropwise and the reaction mixture was stirred for 30 minutes at -78 °C and then stirred at room temperature for 16 h. The aldehyde or ketone (0.45 mmol, 1.5 equiv) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. Finally, the reaction was quenched by addition of MeOH (5 mL) and extracted with Et_2O three times. The combined organic layers were dried by addition of $MgSO_4$ filtered through Celite and concentrated under reduced pressure. The NMR yield was calculated by comparison to an internal standard (naphthalene). The crude product was purified by flash column chromatography.

6.4.2 General methodology for 1,2- dicarbofunctionalization through conjugated addition to α,β-unsaturated ketones



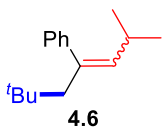
A flame dried 100 mL round-bottom flask equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane **(4.4)** (69.5 mg, 0.3 mmol, 1.0 equiv) in dried THF (2 mL), then sealed with a rubber septum and put under a nitrogen atmosphere at -78 °C. A solution of *tert*-butyllithium reagent (0.19 mL, 0.33 mmol, 1.1 equiv) in hexane (1.7M) was added dropwise and the reaction mixture was stirred for 30 minutes at -78 °C and then stirred at room temperature for 16 h. The α,β–unsaturated ketone (0.45 mmol, 1.5 equiv) was added dropwise and the reaction mixture was stirred for 4 h at room temperature. Finally, the reaction was quenched by addition of MeOH (5 mL) and extracted with Et_2O three times. The combined organic layers were dried by addition of $MgSO_4$ filtered through Celite and concentrated under reduced pressure. The NMR yield was calculated by comparison to an internal standard (naphthalene). The crude product was purified by flash column chromatography.

6.4.3 General methodology for cross-coupling reaction

To a Schlenk flask equipped with a stirrer bar was added the substrate **4.35** (1 equiv, 0.3 mmol), 4-iodotoluene (1.5 equiv, 0.45 mmol) and solid potassium hydroxide (3 equiv, 0.9 mmol). The flask was then sealed and flushed three times with argon before being taken to the glovebox where palladium acetate (10 mol%) and Ruphos (10 mol%) were added. The flask was once again sealed. The sealed flask was taken from the glovebox and dry THF (3.5 mL) and water, sparged for thirty minutes with argon (0.35 mL), were added. The reaction was heated to 90 °C and left to stir for 12 h.

6.4.4 Characterization of products isolated from Boron-Wittig olefination

(*E/Z*)-(2,6,6-trimethylhept-3-en-4-yl)benzene (4.6)



4.6

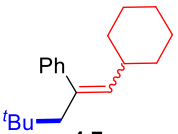
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.6** (45.3 mg, 70% yield. *E/Z*=1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.34-7.25 (m, 6H), 7.25-7.17 (m, 4H) , 5.41 (d, J = 10.0 Hz, 1H), 5.24 (d, J = 10.1 Hz, 1H), 2.68 (m, 1H), 2.50 (s, 2H), 2.43 (m, 1H), 2.31 (s, 2H), 1.03 (d, J = 6.5 Hz, 6H), 0.95 (d, J = 6.6 Hz, 6H), 0.79 (s, 9H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.7, 142.4, 139.5, 138.1, 135.7, 135.5, 128.1, 127.4, 127.2, 126.3, 125.5, 125.5, 52.6, 41.9, 31.8, 31.4, 29.9, 29.5, 27.7, 27.2, 23.0, 22.5.

HRMS (ESI) for $C_{16}H_{25}$ $[M+H]^+$: calculated: 217.1956 , found: 217.1953.

(*E/Z*)-(1-cyclohexyl-4,4-dimethylpent-1-en-2-yl)benzene (4.7)



4.7

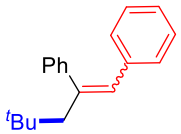
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.7** (53.1 mg, 69% yield. *E/Z* =1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.34-7.16 (m, 10H), 5.43 (d, J = 10.0 Hz, 1H), 5.25 (d, J = 10.1 Hz, 1H), 2.50 (s, 2H), 2.38-2.26 (m, 1H), 2.25 (s, 2H), 2.17-2.05 (m, 1H), 1.83-1.55 (m, 8H), 1.43-1.05 (m, 12H), 0.79 (s, 9H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.4, 143.1, 138.7, 137.5, 136.8, 136.6, 128.8, 128.1, 127.9, 127.0, 126.2, 126.1, 53.3, 42.6, 38.3, 37.5, 33.9, 33.3, 32.5, 32.0, 30.5, 30.1, 26.3, 26.2, 26.2, 25.8.

HRMS (ESI) for $C_{19}H_{29}$ $[M+H]^+$: calculated: 257.2269, found: 257.2272.

(*E/Z*)-(4,4-dimethylpent-1-ene-1,2-diyl)dibenzene (4.8)



4.8

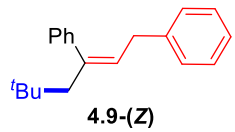
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.8** (24.8 mg, 33% yield. *E/Z* = 1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.49-7.43 (m, 2H), 7.40-7.32 (m, 6H), 7.31-7.17 (m, 7H), 7.15-7.03 (m, 3H), 6.96-6.90 (m, 2H), 6.70 (s, 1H), 6.44 (s, 1H), 2.75 (s, 2H), 2.51 (s, 2H), 0.84 (s, 9H), 0.71 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.0, 142.6, 142.4, 141.6, 138.9, 137.9, 131.6, 129.6, 129.3, 129.2, 129.1, 128.3, 128.3, 127.9, 127.2, 126.9, 126.8, 126.4, 126.1, 125.6, 54.0, 42.1, 33.0, 32.6, 30.7, 30.3.

HRMS (ESI) for $C_{19}H_{23}$ $[M+H]^+$: calculated: 251.1790, found: 251.1794.

(*Z*)-(5,5-dimethylhex-2-ene-1,3-diyl)dibenzene (4.9-*Z*)



4.9-(*Z*)

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.9-*Z*** (15.1 mg, 19% yield) as white solid.

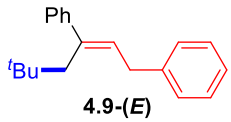
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm 7.36-7.14 (m, 10H), 5.64 (t, J = 7.6 Hz, 1H), 3.38 (d, J = 7.6 Hz, 2H), 2.41 (s, 2H), 0.78 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 142.2, 141.8, 140.4, 128.9, 128.7, 128.5, 128.4, 128.1, 126.6, 125.9, 53.3, 35.4, 32.2, 30.3.

HRMS (ESI) for $C_{20}H_{25}$ $[M+H]^+$: calculated: 265.1956, found: 265.1951

M.p.: 76.4 °C

(*E*)-(5,5-dimethylhex-2-ene-1,3-diyl)dibenzene (4.9-*E*)



4.9-(*E*)

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.9-*E*** (14 mg, 18% yield) as white solid.

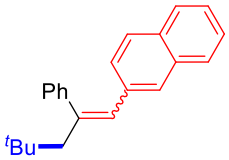
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm 7.36-7.27 (m, 5H), 7.26-7.16 (m, 5H), 5.81 (t, J = 7.3 Hz, 1H), 3.56 (d, J = 7.3 Hz, 2H), 2.60 (s, 2H), 0.82 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.0, 141.3, 140.2, 130.8, 128.6, 128.6, 128.2, 127.0, 126.5, 126.1, 42.8, 35.8, 33.3, 30.6.

HRMS (ESI) for $C_{20}H_{25}$ $[M+H]^+$: calculated: 265.1956, found: 265.1953

M.p.: 76.4 °C

(*E/Z*)-1-(4,4-dimethyl-2-phenylpent-1-en-1-yl)naphthalene (4.10)



4.10

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.10** (43.2 mg, 48% yield. *E/Z*=1/1) as white solid.

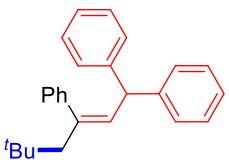
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.87-7.80 (m, 4H), 7.72-7.59 (m, 2H), 7.53-7.45 (m, 7H), 7.41-7.34 (m, 4H), 7.32-7.27 (m, 1H), 7.25-7.21 (m, 5H), 6.96 (dd, J = 8.5, 1.8 Hz, 1H), 6.85 (s, 1H), 6.60 (s, 1H), 2.84 (s, 2H), 2.57 (s, 2H), 0.86 (s, 9H), 0.71 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.9, 143.0, 142.4, 142.1, 136.5, 135.5, 133.5, 133.5, 132.2, 132.1, 131.5, 129.6, 129.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.6, 127.4, 127.2, 127.0, 127.0, 127.0, 126.1, 125.9, 125.8, 125.6, 54.0, 42.3, 33.1, 32.6, 30.7, 30.3.

HRMS (ESI) for $C_{23}H_{25}$ $[M+H]^+$: calculated: 301.1953, found: 301.1951.

M.p.: 73.6 °C

(*Z*)-(5,5-dimethylhex-2-ene-1,1,3-triyl)tribenzene (4.11-*Z*)



4.11-(*Z*)

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.11-*Z*** (29 mg, 29% yield) as white solid.

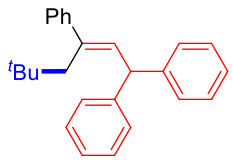
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.27-7.21 (m, 8H), 7.18-7.08 (m, 7H), 5.90 (d, J = 10.1 Hz, 1H), 4.74 (d, J = 10.1 Hz, 1H), 2.41 (s, 2H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 207.2, 145.4, 142.0, 139.6, 132.4, 128.7, 128.5, 128.4, 128.1, 126.7, 126.2, 53.4, 50.3, 32.4, 31.1, 30.3.

HRMS (ESI) for $C_{26}H_{29}$ $[M+H]^+$: calculated: 341.2269, found: 341.2258

M.p.: 96.7 °C

(*E*)-(5,5-dimethylhex-2-ene-1,1,3-triyl)tribenzene (4.11-*E*)



4.11-(*E*)

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.11-*E*** (27.8 mg, 28.6% yield) as white solid.

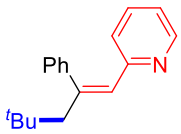
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.38-7.34 (m, 2H), 7.31-7.27 (m, 6H), 7.25-7.17 (m, 7H), 6.10 (d, J = 10.1 Hz, 1H), 5.07 (d, J = 10.1 Hz, 1H), 2.61 (s, 2H), 0.77 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.8, 144.9, 140.0, 134.3, 128.6, 128.5, 128.5, 128.4, 128.2, 127.2, 126.7, 126.3, 45.0, 42.8, 33.0, 30.8.

HRMS (ESI) for $C_{26}H_{29}$ $[M+H]^+$: calculated: 341.2269, found: 341.2266.

M.p.: 96.7 °C

(*Z*)-2-(4,4-dimethyl-2-phenylpent-1-en-1-yl)pyridine (4.12-*Z*)



4.12-(*Z*)

Flash column chromatography (pentane:EtOAc 100:50 to 100:100) yielded the product **4.12-(*Z*)** (28.3 mg, 44% yield) as white solid.

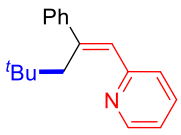
^{1}H NMR (CDCl3, 400 MHz, δ ppm): 8.53-8.47 (m, 1H), 7.28-7.21 (m, 4H), 7.21-7.16 (m, 2H), 6.93 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.58 (s, 1H), 6.59-6.54 (m, 1H), 2.54 (s, 2H), 0.84 (s, 9H).

^{13}C NMR (CDCl3, 100 MHz, δ ppm): 145.8, 144.9, 140.0, 134.3, 128.6, 128.5, 128.2, 127.2, 126.7, 126.3, 50.0, 42.8, 33.0, 30.8.

HRMS (ESI) for C18H22N $[M+H]^+$: calculated: 252.1748, found: 252.1747

M.p.: 123.2 °C

(*E*)-2-(4,4-dimethyl-2-phenylpent-1-en-1-yl)pyridine (4.12-*E*)



4.12-(*E*)

Flash column chromatography (pentane:EtOAc 100:50 to 100:100) yielded the product **4.12-(*E*)** (28.7 mg, 44% yield) as white solid.

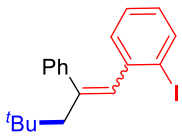
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 8.66-8.59 (m, 1H), 7.64 (td, J = 7.7, 1.9 Hz, 1H), 7.52-7.45 (m, 2H), 7.38-7.32 (m, 2H), 7.33-7.23 (m, 2H), 7.09 (ddd, J = 7.7, 4.8, 1.2 Hz, 1H), 6.68 (s, 1H), 3.24 (s, 2H), 0.72 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 157.7, 149.1, 146.7, 146.1, 136.1, 130.0, 128.3, 127.2, 127.2, 124.8, 121.1, 41.7, 33.3, 30.5.

HRMS (ESI) for $C_{18}H_{22}N$ $[M+H]^+$: calculated: 252.1740, found: 252.1747

M.p.: 123.2 °C

(*E/Z*)-1-(4,4-dimethyl-2-phenylpent-1-en-1-yl)-2-iodobenzene (4.13)



4.13

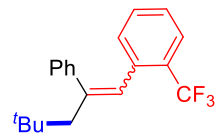
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.13** (63.2 mg, 56% yield. *E/Z*=1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.92-7.87 (m, 1H), 7.79-7.83 (m, 1H), 7.59-7.54 (m, 2H), 7.41-7.33 (m, 4H), 7.32-7.27 (m, 1H), 7.19-7.12 (m, 3H), 7.11-7.06 (m, 2H), 7.00-6.89 (m, 2H), 6.76 (td, J = 7.6, 1.7 Hz, 1H), 6.64 (dd, J = 7.8, 1.7 Hz, 1H), 6.57 (s, 1H), 6.38 (s, 1H), 2.64 (s, 2H), 2.56 (s, 2H), 0.89 (s, 9H), 0.63 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.1, 142.6, 142.6, 142.4, 142.3, 141.5, 138.9, 138.6, 135.2, 133.7, 131.3, 130.4, 129.3, 128.4, 128.2, 128.1, 127.9, 127.7, 127.4, 127.2, 127.2, 126.8, 101.3, 100.7, 52.7, 42.0, 33.3, 32.9, 30.6.

HRMS (ESI) for $C_{19}H_{22}I$ $[M+H]^+$: calculated: 377.0756, found: 377.0761.

(*E/Z*)-1-(4,4-dimethyl-2-phenylpent-1-en-1-yl)-2-(trifluoromethyl)benzene (4.14)



4.14

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.14** (65.9 mg, 69% yield. *E/Z*=4/5) as a white solid.

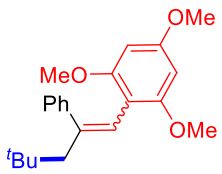
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.70-7.65 (m, $1H_E$), 7.60-7.56 (m, $1H_Z$), 7.54-7.48 (m, $1H_E$), 7.48-7.42 (m, $3H_E$), 7.39-7.30 (m, $3H_E$) , 7.30-7.24 (m, $1H_E$), 7.17-7.02 (m, $7H_Z$), 6.78-82 (q, J = 2.8 Hz, $1H_E$), 6.73 (d, J = 8.0 Hz, $1H_Z$), 6.71-6.66 (m, $1H_Z$), 2.64 (s, $2H_E$), 2.55 (s, $2H_Z$), 0.82 (s, $9H_Z$), 0.60 (s, $8H_E$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.4, 144.1, 143.9, 141.6, 137.5, 137.5, 137.5, 137.5, 132.5, 131.5, 131.4, 131.0, 129.5, 128.1, 128.0, 127.3, 127.2, 126.9 126.7, 126.3, 126.1, 126.0, 125.5, 125.4, 53.2, 42.5, 33.0, 32.9, 30.6, 30.3.

HRMS (ESI) for $C_{20}H_{22}F_3$ $[M+H]^+$: calculated: 319.1673, found: 319.1669.

M.p.: 62.7 °C

(*E/Z*)-2-(4,4-dimethyl-2-phenylpent-1-en-1-yl)-1,3,5-trimethoxybenzene (4.15)



4.15

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.15** (93.8 mg, 92% yield. *E/Z*= 1/3) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.53-7.47 (m, $2H_E$), 7.33-7.27 (m, $2H_E$), 7.23-7.18 (m, $1H_E$), 7.12-7.00 (m, $5H_Z$), 6.31 (s, $1H_E$), 6.19 (s, $1H_Z$), 6.16 (s, $2H_E$), 5.97 (s, $2H_Z$), 3.84 (s, $3H_E$), 3.80 (s, $6H_E$), 3.76 (s, $3H_Z$), 3.45 (s, $6H_Z$), 2.55 (s, $2H_Z$), 2.38 (s, $2H_E$), 0.82 (s, $9H_Z$), 0.58 (s, $9H_E$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 160.3, 160.1, 158.4, 158.3, 146.0, 144.2, 143.2, 141.6, 128.0, 127.9, 127.3, 127.3, 126.4, 125.8, 122.8, 121.1, 109.6, 109.4, 90.8, 90.6, 55.9, 55.4, 55.3, 52.8, 43.8, 32.8, 32.4, 31.1, 30.3, 30.2.

HRMS (ESI) for $C_{22}H_{29}O_3$ $[M+H]^+$: calculated: 341.2111, found: 341.2113.

M.p.: 88.3 °C

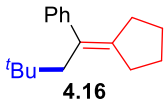
(*Z*)-2-(4,4-dimethyl-2-phenylpent-1-en-1-yl)-1,3,5-trimethoxybenzene (4.15-*Z*)

^{1}H NMR (CDCl3, 400 MHz, δ ppm): 7.16-6.98 (m, 5H), 6.19 (s, 1H), 5.97 (s, 2H), 3.76 (s, 3H), 3.45 (s, 6H), 2.55 (s, 2H), 0.82 (s, 9H).

^{13}C NMR (CDCl3, 100 MHz, δ ppm): 160.1, 158.3, 144.2, 141.6, 127.9, 127.32, 125.8, 121.1, 109.4, 90.6, 55.4, 55.3, 52.4, 32.4, 31.1, 30.2.

M. p.: 88.3 °C

(1-cyclopentylidene-3,3-dimethylbutyl)benzene (4.16)



4.16

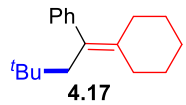
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.16** (46.5 mg, 68% yield) as a colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.29-7.23 (m, 2H), 7.22-7.18 (m, 2H), 7.17-7.12 (m, 1H), 2.44-2.34 (m, 4H), 2.23-2.15 (m, 2H), 1.74-1.64 (m, 2H), 1.60-1.50 (m, 2H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.8, 142.8, 130.8, 128.8, 127.7, 125.6, 48.3, 33.5, 32.8, 31.8, 30.5, 26.9, 26.6.

HRMS (ESI) for $C_{17}H_{25}$ $[M+H]^+$: calculated: 229.1956, found: 229.1951 .

(1-cyclohexylidene-3,3-dimethylbutyl)benzene (4.17)



4.17

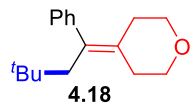
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.17** (58.9 mg, 81% yield) as a colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.28-7.23 (m, 2H), 7.19-7.11 (m, 3H), 2.42 (s, 2H), 2.33-2.30 (m, 2H), 2.08-2.01 (m, 2H), 1.64-1.55 (m, 4H), 1.49-1.43 (m, 2H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.5, 138.2, 131.0, 129.7, 127.7, 125.6, 46.6, 33.0, 32.4, 31.7, 30.5, 28.9, 28.3, 27.1.

HRMS (ESI) for $C_{18}H_{27}$ $[M+H]^+$: calculated: 241.1955, found: 241.1951.

4-(3,3-dimethyl-1-phenylbutylidene)tetrahydro-2H-pyran (4.18)



4.18

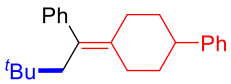
Flash column chromatography (pentane:EtOAc 100:0 to 100:1) yielded the product **4.18** (43.2 mg, 59% yield) as a colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.30-7.25 (m, 2H), 7.21-7.15 (m, 1H), 7.14-7.11 (m, 2H), 3.79-3.70 (m, 2H), 3.63-3.56 (m, 2H), 2.50-2.43 (m, 2H), 2.43 (s, 2H), 2.25-2.20 (m, 2H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.3, 133.2, 132.9, 129.7, 127.9, 126.1, 69.6, 69.1, 46.5, 33.2, 32.0, 32.4, 30.5.

HRMS (ESI) for $C_{17}H_{25}O$ $[M+H]^+$: calculated: 245.1901, found: 245.1900.

(3,3-dimethyl-1-(4-phenylcyclohexylidene)butyl)benzene (4.19)



4.19

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.19** (73.5 mg, 77% yield) as a white solid.

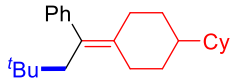
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.32-7.27 (m, 4H), 7.25-7.15 (m, 6H), 3.00-2.90 (m, 1H), 2.79-2.68 (m, 1H), 2.65-2.56 (m, 1H), 2.52-2.40 (m, 2H), 2.11-1.99 (m, 2H), 1.92-1.81 (m, 2H), 1.66-1.54 (m, 1H), 1.55-1.42 (m, 1H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.1, 147.2, 136.9, 131.9, 129.7, 128.5, 127.8, 127.0, 126.1, 125.8, 46.8, 44.8, 36.0, 35.6, 33.1, 32.1, 31.5, 30.5.

HRMS (ESI) for $C_{24}H_{29}$ $[M-H]^-$: calculated: 317.2253, found: 317.2264.

M.p.: 88.9 °C

4-(3,3-dimethyl-1-phenylbutylidene)-1,1'-bi(cyclohexane) (4.20)



4.20

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.20** (68.1 mg, 70% yield) as a white solid.

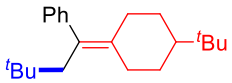
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.29-7.22 (m, 2H), 7.18-7.11 (m, 3H), 2.87-2.75 (m, 1H), 2.55-2.34 (m, 3H), 1.90-1.81 (m, 2H), 1.75-1.62 (m, 5H), 1.31-1.05 (m, 8H), 1.03-0.91 (m, 3H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.5, 138.3, 130.7, 129.7, 127.7, 125.6, 46.6, 43.6, 43.1, 33.1, 32.0, 31.9, 31.5, 31.3, 30.5, 30.5, 30.5, 27.0.

HRMS (ESI) for $C_{24}H_{37}$ $[M+H]^+$: calculated: 325.2895, found: 325.2899.

M.p.: 66.3 °C

(1-(4-(tert-butyl)cyclohexylidene)-3,3-dimethylbutyl)benzene (4.21)



4.21

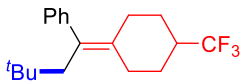
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.21** (62.7 mg, 83% yield) as a colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.30-7.24 (m, 2H), 7.20-7.12 (m, 3H), 2.87 (dq, J = 13.4, 3.1 Hz, 1H), 2.53 (dq, J = 13.4, 3.1 Hz, 1H), 2.48-2.37 (m, 2H), 1.96-1.78 (m, 2H), 1.78-1.61 (m, 2H), 1.26-1.06 (m, 2H), 1.04-0.92 (m, 1H), 0.86 (s, 9H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.4, 138.1, 130.7, 129.8, 127.7, 125.6, 48.5, 46.6, 33.1, 32.9, 32.6, 32.1, 31.6, 31.1, 30.5, 29.9, 29.5, 28.9, 27.8.

HRMS (ESI) for $C_{22}H_{34}$ $[M+H]^+$: calculated: 298.2648, found: 298.2655.

(3,3-dimethyl-1-(4-(trifluoromethyl)cyclohexylidene)butyl)benzene (4.22)



4.22

Flash column chromatography (pentane:EtOAc 100:0 to 100:1) yielded the product **18** (68.8 mg, 73% yield) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.31-7.26 (m, 2H), 7.22-7.16 (m, 1H), 7.14-7.10 (m, 2H), 2.93 (dq, J = 13.9, 3.3 Hz, 1H), 2.58 (dq, J = 13.9, 3.3 Hz, 1H), 2.43 (s, 2H), 2.31-2.13 (m, 1H), 2.12-2.01 (m, 1H), 1.96-1.82 (m, 2H), 1.77-1.67 (m, 1H), 1.50-1.39 (m, 1H), 1.35-1.25 (m, 1H), 0.75 (s, 9H).

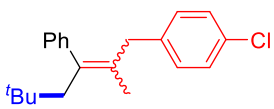
^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.0, 128.4, 128.3, 125.1, 83.4, 46.7, 31.5, 30.2, 29.8, 24.7, 24.7, 24.6.

^{19}F NMR ($CDCl_3$, 376 MHz, δ ppm): -73.5.

HRMS (ESI) for $C_{19}H_{26}F_3$ $[M+H]^+$: calculated: 311.1987, found: 311.1991.

M.p.: 68.3 °C

(*E*/*Z*)-1-chloro-4-(2,5,5-trimethyl-3-phenylhex-2-en-1-yl)benzene (4.23)



4.23

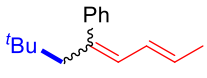
Flash column chromatography (pentane:EtOAc 100:0 to 100:1) yielded the product **4.23** (48.7 mg, 52% yield. *E*/*Z*=1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.33-7.11 (m, 16H), 7.05-7.00 (m, 2H), 3.56 (s, 2H), 3.32 (s, 2H), 2.53 (s, 2H), 2.49 (s, 2H), 1.72 (s, 3H), 1.48 (s, 3H), 0.80 (s, 9H), 0.77 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.0, 144.8, 139.8, 138.9, 137.1, 136.6, 131.7, 131.6, 131.6, 131.5, 130.0, 129.6, 129.2, 128.6, 128.45 128.02, 128.0, 127.9, 126.1, 126.1, 126.0, 47.7, 47.2, 41.0, 39.8, 33.4, 33.1, 30.6, 30.6, 20.1, 19.1.

HRMS (ESI) for $C_{21}H_{26}Cl$ $[M+H]^+$: calculated: 313.1723, found: 313.1617.

((4*E*/*Z*,6*E*)-2,2-dimethylocta-4,6-dien-4-yl)benzene (4.24)



4.24

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.24** (11.0 mg, 17% yield. *E*/*Z*= 1/1) as white solid.

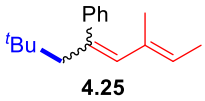
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.42-7.27 (m, $2H_E$,$4H_Z$), 7.25-7.16 (m, $3H_E$, 1 H_Z), 6.47-6.35 (m, $1H_Z$), 6.28 (d, J = 11.0 Hz, $1H_Z$), 6.17-6.10 (m, $1H_E$), 6.04 (d, J = 11.0 Hz, $1H_E$), 5.79 (dq, J = 15.0, 6.8 Hz, $1H_Z$), 5.75-5.66 (m, $1H_E$), 2.59 (s, $2H_Z$), 2.37 (s, $2H_E$), 1.83 (d, J = 6.8 Hz, $3H_Z$), 1.69 (d, J = 6.7 Hz, $3H_E$), 0.79 (s, $9H_Z$), 0.75 (s, $9H_E$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.9, 138.3, 131.2, 130.4, 130.1, 129.3, 129.2, 129.1, 129.0, 128.81, 128.3, 128.2, 128.0, 126.9, 126.8, 126.5, 53.0, 42.7, 34.3, 32.6, 30.6, 30.2, 22.5, 18.7

HRMS (ESI) for $C_{16}H_{21}$ $[M-H]^-$: calculated: 213.1633, found: 213.1638.

M.p.: 97.0 °C

((4*Z*/*E*,6*E*)-2,2,6-trimethylocta-4,6-dien-4-yl)benzene (4.25)



4.25

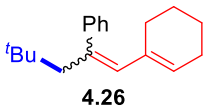
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.25** (32.18 mg, 47% yield. *E*/*Z*= 1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.37-7.16 (m, 10H), 6.07(s, 1H), 6.03 (s, 1H), 5.55-5.47 (m, 1H), 5.46-5.38 (m, 1H), 2.69 (s, 2H), 2.36 (s, 2H), 1.81 (s, 3H), 1.74-1.69 (m, 3H), 1.60-1.56 (m, 3H), 1.33-1.30 (m, 3H), 0.77 (s, 9H), 0.74 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.6, 143.6, 138.9, 137.6, 135.9, 134.5, 134.2, 133.9, 131.4, 129.4, 128.1, 127.8, 127.6, 127.2, 126.4, 126.4, 124.1, 54.0, 42.1, 32.6, 32.5, 30.7, 30.2, 16.9, 15.9, 13.8, 13.8.

HRMS (ESI) for $C_{17}H_{25}$ $[M+H]^+$: calculated: 228.1878, found: 228.1881.

(*E*/*Z*)-(1-(cyclohex-1-en-1-yl)-4,4-dimethylpent-1-en-2-yl)benzene (4.26)



4.26

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.26** (23.7 mg, 31% yield. *E*/*Z*= 1/1) as white solid.

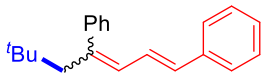
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.43-7.23 (m, 10H), 6.08-6.05 (m, 1H), 6.04-6.02 (m, 1H), 5.83-5.74 (m, 1H), 5.67-5.59 (m, 1H), 2.77 (s, 2H), 2.43 (s, 2H), 2.27-2.18 (m, 4H), 2.15-2.04 (m, 2H), 1.84-1.62 (m, 6H), 1.59-1.52 (m, 2H), 1.52-1.43 (m, 2H), 0.84 (s, 9H), 0.83 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 146.8, 143.7, 139.2, 137.9, 136.1, 136.0, 134.8, 133.6, 129.5, 129.0, 128.2, 127.6, 127.3, 126.7, 126.5, 126.4, 54.5, 42.4, 34.4, 32.7, 32.6, 30.8, 30.3, 29.6, 28.6, 26.1, 25.9, 23.2, 22.6, 22.5, 22.4, 14.3.

HRMS (ESI) for $C_{19}H_{25}$ $[M+H]^{\cdot}$: calculated: 253.1943, found: 253.1941.

M.p.: 71.2 °C

((1*E*,3*E*/3*Z*)-6,6-dimethylhepta-1,3-diene-1,4-diyl)dibenzene (4.27)



4.27

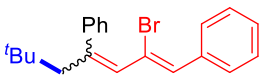
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.27** (48.1 mg, 58% yield. *E/Z*= 1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.48-7.13 (m, 21H), 6.90 (dd, J = 15.6, 11.0 Hz, 1H), 6.70-6.51 (m, 3H), 6.29 (d, J = 11.0 Hz, 1H), 2.75 (s, 2H), 2.50 (s, 2H), 0.86 (s, 9H), 0.81 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.5, 142.7, 142.1, 141.7, 138.0, 137.1, 132.2, 131.3, 131.2, 130.3, 129.3, 128.8, 128.6, 128.4, 128.1, 127.5, 127.2, 127.0, 126.8, 126.7, 126.6, 126.5, 126.4, 53.1, 43.0, 33.4, 32.8, 30.7, 30.3.

HRMS (ESI) for $C_{21}H_{23}$ $[M-H]^-$: calculated: 275.1789, found: 275.1794.

((1*Z*,3*Z*/*E*)-2-bromo-6,6-dimethylhepta-1,3-diene-1,4-diyl)dibenzene (4.28)



4.28

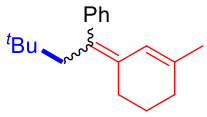
Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.28** (45.7 mg, 43% yield. *E/Z*= 1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.69-7.64 (m, 2H), 7.45-7.17 (m, 18H), 6.95 (s, 1H), 6.35 (s, 1H), 6.32 (s, 1H), 6.19 (s, 1H), 2.81 (s, 2H), 2.45 (s, 2H), 0.83 (s, 9H), 0.80 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 144.2, 143.9, 143.7, 141.3, 136.2, 136.0, 132.0, 131.2, 131.2, 130.3, 129.2, 128.8, 128.8, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 127.6, 127.2, 127.2, 121.1, 120.9, 52.2, 42.3, 33.2, 32.8, 30.8, 30.4, 30.3

HRMS (ESI) for $C_{21}H_{24}Br$ $[M+H]^+$: calculated: 355.1061, found: 355.0903.

(*E,Z*)-(3,3-dimethyl-1-(3-methylcyclohex-2-en-1-ylidene)butyl)benzene (4.29)



4.29

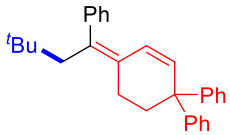
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.29** (47.2 mg, 62% yield, *E/Z*= 1/1) as a colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.32-7.26 (m, 4H), 7.21-6.37 (m, 6H), 6.40-6.37 (m, 1H), 5.93-5.90 (m, 1H), 2.54 (s, 2H), 2.48 (s, 2H), 2.45-2.39 (m, 2H), 2.24-2.18 (m, 2H), 2.09-2.02 (m, 4H), 1.86-1.84 (m, 3H), 1.82-1.74 (m, 2H), 1.66-1.64 (m, 3H), 1.63-1.54 (m, 2H), 0.76 (s, 9H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.2, 144.5, 138.6, 137.1, 133.0, 132.9, 132.8, 132.3, 130.3, 129.8, 128.4, 127.7, 125.9, 125.8, 123.5, 122.66, 46.8, 45.8, 33.5, 33.3, 31.1, 31.0, 30.9, 30.6, 30.5, 29.5, 28.4, 27.4, 24.8, 24.4, 23.7, 23.3.

HRMS (ESI) for $C_{19}H_{27}$ $[M+H]^+$: calculated: 255.2103, found: 255.2107.

(*E,Z*)-4'-(3,3-dimethyl-1-phenylbutylidene)-3',4'-dihydro-2'H-1,1':1',1''-terphenyl (4.30)



4.30

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.30** (89.4 mg, 76% yield, *E/Z*= 1/1) as a white solid.

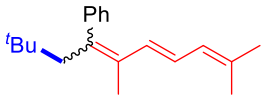
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.36-7.13 (m, 30H), 6.85 (d, J = 10.3 Hz, 1H), 6.39 (d, J = 10.1 Hz, 1H), 6.23 (d, J = 10.3 Hz, 1H), 6.00 (d, J = 10.1 Hz, 1H), 2.61 (s, 2H), 2.50-2.43 (m, 6H), 2.32-2.20 (m, 4H), 0.80 (s, 9H), 0.75 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 148.6, 148.6, 144.5, 143.7, 136.9, 136.2, 136.2, 134.9, 131.9, 131.6, 130.2, 129.5, 128.2, 128.2, 128.1, 128.0, 127.8, 127.8, 127.0, 126.4, 126.2, 126.0, 49.1, 49.0, 46.8, 46.0, 36.6, 36.4, 33.5, 33.3, 30.6, 30.5, 25.7, 24.7.

HRMS (ESI) for $C_{30}H_{33}$ $[M+H]^+$: calculated: 393.2583, found: 393.2577.

M.p.: 86.5 °C

((4*Z*/*E*,6*E*)-2,2,5,9-tetramethyldeca-4,6,8-trien-4-yl)benzene (4.31)



4.31

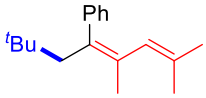
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.31** (38.6 mg, 48% yield, *E/Z*= 1/1) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.33-7.28 (m, 5H), 7.24-7.16 (m, 5H), 6.77 (d, J = 15.1 Hz, 1H), 6.54 (dd, J = 15.1, 10.9 Hz, 1H), 6.42 (dd, J = 15.3, 10.7 Hz, 1H), 6.27 (d, J = 15.3 Hz, 1H), 6.09-5.98 (m, 1H), 5.77-5.72 (m, 1H), 2.62 (s, 2H), 2.57 (s, 2H), 2.02 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.81 (s, 3H), 1.80 (s, 3H), 1.75 (s, 3H), 0.77 (s, 9H), 0.77 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 194.9, 154.6, 144.6, 142.71, 139.4, 134.7, 132.0, 131.0, 130.3, 130.1, 129.9, 129.7, 129.1, 128.2, 128.1, 127.7, 126.5, 126.4, 126.2, 125.6, 124.6, 48.9, 48.3, 46.7, 33.9, 33.5, 30.7, 30.6, 30.3, 26.4, 26.3, 18.6, 16.0.

HRMS (ESI) for $C_{20}H_{27}$ $[M-H]^-$: calculated: 267.2096, found: 267.2107.

(*Z*)-(2,2,5,7-tetramethylocta-4,6-dien-4-yl)benzene (4.32-*Z*)



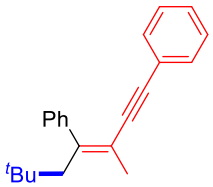
4.32-(*Z*)

Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.32-*Z*** (15.3 mg, 21% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.25 (s, 1H), 7.22-7.16 (m, 2H), 7.14-7.07 (m, 3H), 2.48 (s, 2H), 1.89 (s, 3H), 1.53 (s, 3H), 1.43 (s, 3H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 145.6, 136.6, 132.3, 131.7, 129.8, 129.6, 128.5, 127.2, 125.5, 46.6, 33.5, 30.5, 25.6, 20.8, 19.8

(*Z*)-(3,6,6-trimethylhept-3-en-1-yne-1,4-diyl)dibenzene (4.33-*Z*)



4.33-(*Z*)

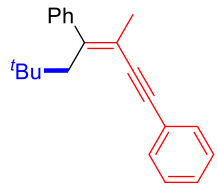
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.33-*Z*** (32 mg, 36% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.48-7.43 (m, 2H), 7.36-7.30 (m, 2H), 7.28-7.18 (m, 4H), 7.17-7.13 (m, 2H), 2.57 (s, 2H), 2.11 (s, 3H), 0.81 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.2, 144.3, 131.3, 129.2, 128.2, 127.6, 127.5, 126.8, 124.2, 116.9, 93.0, 90.5, 46.5, 34.0, 30.5, 20.8.

HRMS (ESI) for $C_{22}H_{25}$ $[M+H]^+$: calculated: 289.1946, found: 289.1951.

(*E*)-(3,6,6-trimethylhept-3-en-1-yne-1,4-diyl)dibenzene (4.33-*E*)



4.33-(*E*)

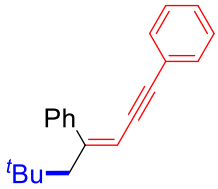
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.33-*E*** (26 mg, 29% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.50-7.45 (m, 2H), 7.37-7.30 (m, 5H), 7.27-7.19 (m, 3H), 2.84 (s, 2H), 1.91 (s, 3H), 0.83 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 147.4, 142.5, 131.4, 128.9, 128.5, 128.0, 128.0, 126.9, 126.0, 124.2, 116.9, 92.8, 92.4, 50.6, 33.6, 30.5, 20.7.

HRMS (ESI) for $C_{22}H_{25}$ $[M+H]^+$: calculated: 289.1946, found: 289.1949.

(*Z*)-(6,6-dimethylhept-3-en-1-yne-1,4-diyl)dibenzene (4.34-*Z*)



4.34-(*Z*)

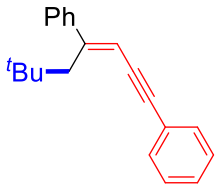
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.34-*Z*** (30.2 mg, 37% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.62-7.56 (m, 2H), 7.43-7.33 (m, 2H), 7.33-7.22 (m, 6H), 5.77 (s, 1H), 2.52 (s, 2H), 0.82 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 152.3, 141.1, 131.4, 128.6, 128.3, 127.9, 127.8, 127.7, 124.0, 108.9, 91.2, 88.8, 51.6, 30.2, 22.5.

HRMS (ESI) for $C_{21}H_{23}$ $[M+H]^+$: calculated: 275.1796, found: 275.1794.

(*E*)-(6,6-dimethylhept-3-en-1-yne-1,4-diyl)dibenzene (4.34-*E*)



4.34-(*E*)

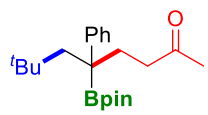
Flash column chromatography (pentane:EtOAc 100:0) yielded the product **4.34-*E*** (30 mg, 37% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.49-7.45 (m, 2H), 7.42-7.38 (m, 2H), 7.37-7.28 (m, 6H), 5.96 (s, 1H), 2.87 (s, 2H), 0.88 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 153.3, 143.2, 131.4, 128.5, 128.5, 128.1, 127.9, 126.6, 124.0, 110.2, 94.3, 89.2, 45.5, 33.7, 30.6

HRMS (ESI) for $C_{21}H_{23}$ $[M+H]^+$: calculated: 275.1796, found: 275.1792.

7,7-dimethyl-5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-one (4.35)



4.35

Flash column chromatography (pentane:EtOAc 100:0 to 100:20) yielded the product **4.35** (41.9 mg, 39% yield) as a white solid.

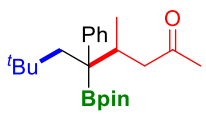
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.49-7.44 (m, 2H), 7.29-7.21 (m, 2H), 7.16-7.10 (m, 1H), 2.23-2.14 (m, 4H), 2.00 (s, 3H), 1.94 (d, J = 14.2 Hz, 1H), 1.77 (d, J = 14.2 Hz, 1H), 1.24 (s, 6H), 1.20 (s, 6H), 0.76 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.5, 145.1, 128.3, 128.2, 125.5, 83.5, 50.1, 40.0, 32.0, 31.7, 31.5, 30.1, 25.2, 24.9.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.5.

HRMS (ESI) for $C_{22}H_{36}BO_3$ $[M+H]^+$: calculated: 359.2757, found:359.2752.

4,7,7-trimethyl-5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-one (4.36)



4.36

Flash column chromatography (pentane:EtOAc 100:0 to 100:20) yielded the product **4.36** (39.1 mg, 35% yield, two diastereomers M:m=4:3) as colourless liquid.

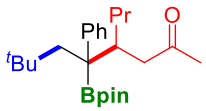
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.67-7.61 (m, $2H_M$), 7.55-7.50 (m, $2H_m$), 7.30-7.18 (m, $2H_M$, $2H_m$), 7.16-7.10 (m, $1H_M$, $1H_m$), 2.95 (dd, J = 16.4, 2.8 Hz, $1H_M$), 2.73-2.58 (m, $1H_M$), 2.23-2.13 (m, $1H_M$, $1H_m$), 2.17 (s, $3H_M$), 2.13-2.05 (m, $1H_M$, $1H_m$), 1.92 (s, $3H_m$), 1.74-1.64 (m, $1H_M$, $1H_m$), 1.58-1.36 (m, $1H_M$, $2H_m$), 1.37 (s, $6H_M$), 1.36 (s, $6H_M$), 1.34 (s, $12H_m$), 1.05 (d, J = 6.9,Hz, $3H_m$), 0.68 (d, *J* = 6.9 Hz, $3H_M$), 0.58 (s, $9H_M$), 0.56 (s, $9H_m$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.6, 209.6, 145.0, 144.6, 130.0, 128.6, 127.7, 127.5, 125.9, 125.6, 83.7, 83.6, 50.7, 50.5, 48.7, 48.3, 39.4, 39.2, 31.8, 31.8, 31.4, 31.4, 30.8, 30.3, 26.0, 25.8, 25.3, 25.2, 17.3, 17.0.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.6.

HRMS (ESI) for $C_{23}H_{38}BO_3$ $[M+H]^+$: calculated: 373.2914, found: 373.2917.

7,7-dimethyl-5-phenyl-4-propyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-one (4.37)



4.37

Flash column chromatography (pentane:EtOAc 100:0 to 100:20) yielded the product **4.37** (60.1 mg, 50% yield, two diastereomers M:m=3:2) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.70-7.66 (m, $2H_M$), 7.52-7.44 (m, $2H_m$), 7.26-7.07 (m, $3H_M$, $3H_m$), 3.15 (dd, J = 18.1, 4.7 Hz, $1H_M$), 2.77-2.66 (m, $1H_M$), 2.44 (dd, J = 17.8, 2.4 Hz, $1H_m$), 2.28-2.15 (m, $4H_M$), 2.08 (dd, J = 17.8, 7.9 Hz, $1H_m$), 1.92 (d, J = 13.6 Hz, $1H_M$), 1.89-1.73 (m, $4H_m$), 1.63-1.57 (m, $1H_m$), 1.51-1.42 (m, $1H_M$, $1H_m$), 1.36 (s, $6H_M$), 1.35 (s, $6H_m$), 1.33 (s, $6H_M$), 1.33 (s, $6H_m$), 1.26- 0.80 (m, $4H_M$, $7H_m$), 0.66 (t, J = 7.1 Hz, $3H_M$), 0.55 (s, $9H_m$), 0.51 (s, $9H_M$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.3, 145.5, 130.4, 130.0, 128.7, 127.8, 127.5, 125.9, 125.7, 125.6, 83.6, 83.5, 53.1, 50.9, 50.7, 48.6, 47.0, 43.7, 43.5, 36.2, 35.7, 32.0, 31.8, 31.5, 31.3, 30.5, 30.3, 30.2, 26.1, 25.6, 25.4, 25.0, 22.5, 21.6, 14.8, 14.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.6.

Major diasteroisomer 4.37

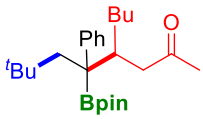
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.70-7.66 (m, 2H), 7.26-7.20 (m, 2H), 7.15-7.10 (m, 1H), 3.15 (dd, J = 18.1, 4.7 Hz, 1H), 2.77-2.66 (m, 1H), 2.29-2.13 (m, 4H), 1.92 (d, J = 13.6 Hz, 1H), 1.45 (d, J = 13.6 Hz, 1H), 1.36 (s, 6H), 1.33 (s, 6H), 1.16-1.03 (m, 2H), 0.98-0.82 (m, 3H), 0.66 (t, J = 7.1 Hz, 3H), 0.51 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.3, 145.5, 130.0, 127.8, 125.6, 83.5, 50.7, 47.0, 43.5, 35.7, 31.8, 31.3, 30.5, 30.5, 26.1, 25.0, 21.6, 14.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.4.

HRMS (ESI) for $C_{25}H_{42}BO_3$ $[M+H]^+$: calculated: 401.3227, found: 401.3222.

4-butyl-7,7-dimethyl-5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-one (4.38)



4.38

Flash column chromatography (pentane:EtOAc 100:0 to 100:20) yielded the product **4.38** (73.3 mg, 59% yield, two diastereomers M:m=10:7) as colourless liquid.

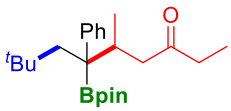
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm):7.69-6.67 (m, $2H_M$), 7.50-7.44 (m, $2H_m$), 7.25-7.16 (m, $2H_M$, $2H_m$), 7.16-7.06 (m, $1H_M$, $1H_m$), 3.16 (dd, J = 18.1, 4.8 Hz, $1H_M$), 2.75-2.62 (m, $1H_M$, $1H_m$), 2.29-2.14 (m, $4H_M$, $1H_m$), 2.11-2.03 (m, $1H_m$), 1.91 (d, J = 13.6 Hz, $1H_M$), 1.90-1.86 (m, $1H_m$), 1.83 (s, $3H_m$), 1.64-1.62 (m, $1H_m$), 1.45 (d, J = 13.6 Hz, $1H_M$), 1.35 (s, $6H_M$), 1.34 (s, $6H_m$), 1.33 (s, $6H_M$), 1.32 (s, $6H_m$), 1.27-0.93 (m, $6H_M$, $5H_m$), 0.88 (t, J = 7.1 Hz, $3H_m$), 0.77- 0.71 (m, $1H_m$), 0.68 (t, J = 6.9 Hz, $3H_M$), 0.55 (s, $9H_m$), 0.51 (s, $9H_M$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.3, 209.1, 145.6, 145.2, 130.4, 128.0, 127.8, 125.7, 125.6, 83.6, 83.5, 50.9, 50.7, 48.5, 46.9, 43.8, 43.7, 33.5, 33.1, 32.0, 31.8, 31.4, 31.4, 31.2, 30.8, 30.5, 30.2, 30.2, 30.0, 26.03, 25.6, 25.4, 25.3, 25.0, 23.4, 22.6, 14.2, 14.1.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.1.

HRMS (ESI) for $C_{26}H_{44}BO_3$ $[M+H]^+$: calculated: 415.3383, found: 415.3379.

5,8,8-trimethyl-6-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)nonan-3-one (4.39)



4.39

Flash column chromatography (pentane:EtOAc 100:0 to 100:20) yielded the product **35** (84.6 mg, 73% yield, two diastereomers M:m=5:3) as colourless liquid.

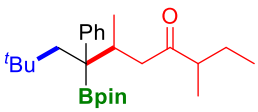
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.69-7.60 (m, $2H_M$), 7.57-7.47 (m, $1H_m$), 7.27-7.17 (m, $2H_m$, $2H_m$), 7.16-7.08 (m, $1H_M$, $1H_m$), 2.91 (dd, J = 16.2, 3.1 Hz, $1H_M$), 2.74-2.62 (m, $1H_M$, $1H_m$), 2.56-2.04 (m, $5H_M$, $5H_m$), 1.55 (d, J = 13.9 Hz, $1H_M$), 1.47 (d, J = 13.9 Hz, $1H_m$), 1.37 (s, $6H_M$), 1.36 (s, $6H_M$), 1.34 (s, $12H_m$), 1.07 (t, J = 7.4 Hz, $3H_M$), 1.04 (d, J = 6.8 Hz, $3H_m$), 0.91 (t, J = 7.4 Hz, $3H_m$), 0.66 (d, J = 6.8 Hz, $3H_M$), 0.57 (s, $9H_M$), 0.55 (s, $6H_m$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 212.2, 212.1, 145.1, 144.8, 130.0, 127.9, 127.7, 125.8, 125.6, 83.7, 83.6, 50.7, 50.6, 47.2, 46.9, 39.6, 39.2, 36.9, 36.4, 31.9, 31.8, 31.4, 31.4, 26.0, 25.8, 25.3, 25.2, 17.4, 17.1, 8.1, 7.9.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 34.6.

HRMS (ESI) for $C_{24}H_{40}BO_3$ $[M+H]^+$: calculated: 387.3070, found: 387.3076.

3,6,9,9-tetramethyl-7-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)decan-4-one (4.40)



4.40

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.40** (89.4 mg, 72% yield, three diastereomers A:B:C=2:2:1) as a white solid.

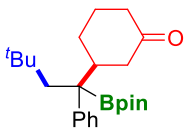
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm: 7.67-7.62 (m, 2H), 7.25-7.21 (m, 2H), 7.16-7.10 (m, 1H), 2.96-2.86 (m, 1H), 2.75-2.65 (m, 1H), 2.46 (dq, J = 13.7, 6.8 Hz, 1H), 2.31 (ddd, J = 17.0, 10.2, 8.3 Hz, 1H), 2.09 (dd, J = 13.7, 2.3 Hz, 1H), 1.76-1.63 (m, 1H), 1.53 (dd, J = 13.7, 4.9 Hz, 1H), 1.37 (s, 6H), 1.34 (s, 6H), (t, J = 6.8 Hz, 3H), 0.91-0.87 (m, 3H), 0.67-0.64 (m, 3H), 0.56 (s, $9H_A$), 0.56 (s, $9H_B$), 0.55 (s, $9H_C$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 215.1, 215.0, 214.9, 214.9, 145.1, 144.9, 144.8, 130.0, 129.6, 128.0, 127.8, 127.7, 125.7, 125.5, 83.6, 83.5, 50.7, 50.6, 50.6, 48.75, 48.5, 48.0, 47.7, 46.4, 45.8, 45.7, 39.0, 38.9, 38.6, 38.4, 31.9, 31.8, 31.4, 31.4, 26.2, 26.2, 26.0, 25.8, 25.7, 25.6, 25.6, 25.4, 25.3, 25.2, 17.6, 17.5, 17.2, 17.1, 16.2, 16.1, 15.9, 15.6, 11.9, 11.8, 11.7, 11.7.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.3.

HRMS (ESI) for $C_{26}H_{44}BO_3$ $[M+H]^+$: calculated: 415.3375, found: 415.3378.

3-(3,3-dimethyl-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)cyclohexan-1-one (4.41)



4.41

Flash column chromatography (pentane:EtOAc 100:0 to 100:3) yielded the product **4.41** (74.9 mg, 65% yield, two diastereomers A:B=1:1) as white solid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.65-7.58 (m, $2H_B$), 7.54-7.47 (m, $2H_A$), 7.25-7.19 (m, $2H_A$, $2H_B$), 7.18-7.09 (m, $1H_A$, $1H_B$), 2.78-2.68 (m, $1H_B$), 2.37-1.97 (m, 7HA, $5H_B$), 1.96-1.85 (m, $1H_B$), 1.70-1.49 (m, $2H_A$, $2H_B$), 1.40-1.31 (m, $12H_A$, $12H_B$), 1.30-1.12 (m, $1H_A$, $1H_B$), 0.96-0.80 (m, $1H_A$, $1H_B$), 0.61 (s, H_A), 0.58 (s, $9H_B$).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 212.8, 212.4, 144.4, 143.1, 129.9, 129.8, 127.8, 127.8, 125.8, 125.8, 83.8, 83.7, 49.9, 49.8, 49.8, 49.5, 45.7, 44.7, 41.9, 41.8, 31.8, 31.7, 31.7, 31.5, 31.1, 28.6, 27.8, 26.1, 25.9, 25.8, 25.7, 3.5, 25.2.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.1.

HRMS (ESI) for $C_{24}H_{38}BO_3$ $[M+H^+]^+$: calculated: 385.2909, found: 385.2915.

Diastereoisomer A

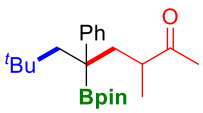
^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.54-7.46 (m, 2H), 7.25-7.18 (m, 2H), 7.16-7.09 (m, 1H), 2.33-2.14 (m, 5H), 2.10-1.98 (m, 2H), 1.65 (d, J = 14.0 Hz, 1H), 1.60-1.52 (m, 2H), 1.37 (s, 6H), 1.35 (s, 6H), 1.27-1.12 (m, 1H), 0.94-0.81 (m, 1H), 0.61 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 212.4, 143.1, 129.9, 127.8, 125.8, 83.8, 49.8, 49.5, 44.7, 41.8, 31.8, 31.7, 28.6, 25.9, 25.8, 25.5.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.1.

HRMS (ESI) for $C_{24}H_{38}BO_3$ $[M+H]^+$: calculated: 385.2909, found: 385.2915.

3,7,7-trimethyl-5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octan-2-one (4.42)



4.42

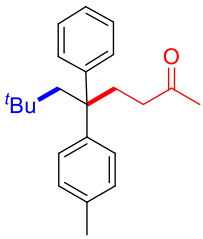
Flash column chromatography (pentane:EtOAc 100:0 to 10:3) yielded the product **4.42** (30.2 mg, 27% yield) as a colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.58-7.53 (m, 2H), 7.20-7.18 (m, 2H), 7.13-7.08 (m, 1H), 2.54-2.40 (m, 2H), 1.97 (d, J = 14.2 Hz, 1H), 1.76-1.68 (m, 2H), 1.47 (s, 3H), 1.33 (s, 6H), 1.32 (s, 6H), 0.92 (d, J = 6.8 Hz, 3H), 0.64 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 214.2, 144.4, 130.1, 127.7, 83.5, 45.4, 44.4, 32.0, 31.5, 29.0, 25.8, 25.3, 22.8, 19.7.

^{11}B NMR ($CDCl_3$, 128.3 MHz, δ ppm): 33.2.

7,7-dimethyl-5-phenyl-5-(p-tolyl)octan-2-one (4.43)



4.43

Flash column chromatography (pentane:EtOAc 100:0 to 10:3) yielded the product **4.43** (7 mg, 52% yield.) as colourless liquid.

^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 7.23-7.18 (m, 2H), 7.15 – 7.00 (m, 7H), 2.59-2.50 (m, 1H), 2.37-2.31 (m, 4H), 2.30-2.20 (m, 4H), 1.99-1.86 (m, 1H), 1.71-1.62 (m, 2H), 1.47 (dd, J = 14.0, 3.7 Hz, 1H), 0.73 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz, δ ppm): 209.1, 146.8, 136.9, 136.7, 135.9, 135.7, 129.5, 129.4, 128.9, 128.8, 128.4, 128.0, 126.0, 63.5, 51.0, 41.8, 41.0, 33.6, 31.4, 30.2, 21.2, 21.2.

6.5 References

(1) Douglas D.; *Armarego, W.L.F.; Perrin, D.D.; Purification of Laboratory Chemicals. Pergamin Press.* ***1988****.*

(2) Kim, M.; Park, B.; Shin, M.; Kim, S.; Kim, J.; Baik, M. H.; Cho, S. H. Copper-Catalyzed Enantiotopic-Group-Selective Allylation of *gem*-Diborylalkanes. *J. Am. Chem. Soc.,* **2021**, *143* (2), 1069–1077.

(3) Zhang, Z.; Fu, Y.; Xiao B. Preparation of Tetraborate Ethane Compound *Patent CN 2016-10726662,* **2017***.*

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CHAPTER 7

Summary

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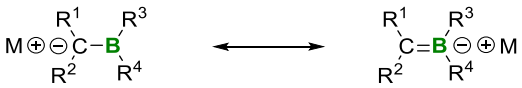
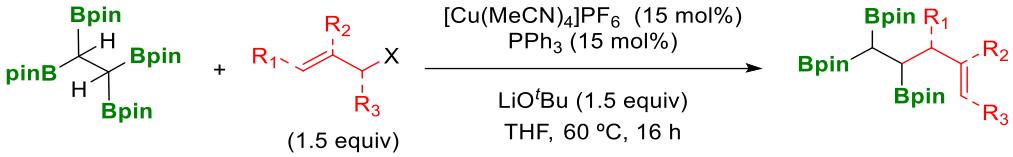
The borata-alkene unit $[CH_2=BR_2]^-$ represents a formal depiction of stabilized α-monoboryl carbanions, arising from the deficient valence of the nearby three-coordinate boron center (Scheme 9.1). Not only strategic advanced synthetic methodologies for the production of borata-alkenes have been reported, but also the development of characterization techniques of borata-alkenes has allowed the understanding of their properties. In this doctoral thesis, borata-alkenes have played a pivotal role in enabling new reactions and thereby expanding our understanding and utilization of these intermediates, in order to explore the wide range of applications of borata-alkene species in producing different novel compounds.



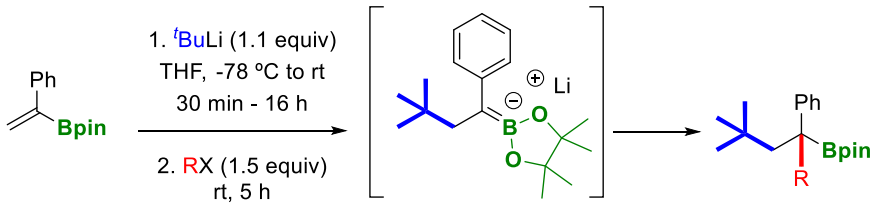
Scheme 9.1. Resonance forms of borata-alkene species.

In Chapter 2, we studied the use of Cu(I) complexes to catalytically activate 1,1,1',1'-tetrapinacolborylethane, Cu-catalyzed producing the corresponding α-borylalkyl copper species, followed by allylic alkylation sequences. The structure of 1,1,1',1'-tetrapinacolborylethane has been revealed through X-ray diffraction, contributing to a better understanding of its reactivity. Additionally, this chapter outlines reaction conditions suitable to react the α-borylalkyl copper species with a wide range of allyl bromide reagents in mono allylic alkylation *via* an S_N2' mechanism (Scheme 9.2). Furthermore, a second allylic alkylation of homoallyl triboronate systems was carried out to obtain dihomoallyl diboronates. Finally, a Cu-catalyzed intramolecular cyclization involving homoallyl triboronate systems yielded cyclization products exhibiting a 2:1 diastereoselectivity favoring the *trans*-diastereoisomer.



Scheme 9.2. Cu(I) activation of 1,1,1',1'-tetrapinacolborylethane towards allylic alkylation reactions.

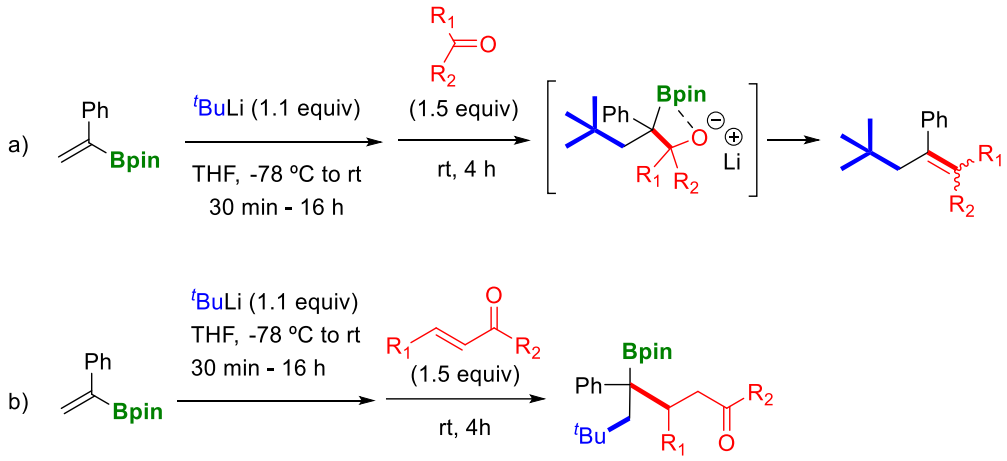
In Chapter 3 we have revealed the regioselective nucleophilic addition of sterically hindered C(sp^3) to 1,1-arylboryl alkenes, by stabilization of borata-alkene intermediates, followed by electrophilic trapping of the α-boryl carbanionic species with C(sp^3) electrophiles, at room temperature. This goal has been envisioned through engaged C(sp^3) chemical entities avoiding metal catalysts, additives, radical initiators or specific irradiation. This multicomponent reaction guarantees that the new tetrasubstituted carbons formed retains all the C atoms from the three starting materials involved in the assembly (Scheme 9.3). The resulting tertiary boronic esters could potentially be oxidized to yield novel tertiary alcohols. In addition, when employing a chiral substrate, moderate diastereoisomeric ratio was achieved. The significance of the borata-alkene intermediate in the reaction has been investigated through ^{11}B NMR spectroscopic studies, and experiments have been conducted to confirm the S_N2 mechanism in the electrophilic trapping.



Scheme 9.3. Dicarbofunctionalization of alkenes with formation of two C(sp^3)–C(sp^3) bonds *via* borata-alkene intermediates.

Chapter 4 outlines the exploration of this intermolecular three-component assembly using alkenylboranes as substrate to show that borata-alkene intermediates can react with carbonyl functional groups to synthesize tri- and tetrasubstituted alkenes and dienes. When the borata-alkene interacts with

ketones and aldehydes, the resulting α–arylboryl enolates evolve through B-O elimination to generate tri or tetrasubstituted alkenes and dienes, *via* Boron Wittig sequence (Scheme 9.4a). When unhindered α,β-unsaturated carbonyl compounds react with the borata-alkenes, the electrophilic trapping is chemoselectively performed through 1,4-addition generating new tetrasubstituted carbon centers (Scheme 9.4b).



Scheme 9.4. Nucleophilic addition of ^{t}BuLi to 1-phenylvinylboronic acid pinacol ester followed by electrophilic trapping with a) aldehydes and ketones and b) α,β–unsaturated carbonyl compounds.

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