A new context for palladium mediated B-addition reaction: an open door to consecutive functionalization

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Palladium metal-catalyzed boron addition to unsaturated carbon–carbon bonds provides an efficient and convenient route for the preparation of organoboranes, which are versatile intermediates for organic synthesis. Palladium complexes are responsible for the exclusive catalytic performance and eventually allow access to selectively functionalized molecules by catalytic consecutive tandem sequences. The final objective is to find suitable palladium complexes that make it possible to perform a one-pot sequential reaction (B-addition/functionalization) by means of a multifaceted palladium catalyst. Mechanistic insights into the concatenated reactions through B chemistry are required if one wants to understand the experimental results.

1 Introduction

Metal mediated catalytic B-addition reactions to unsaturated bonds[1–7] are useful methods for the synthesis of valuable organoboranes, with an inherent control over the selectivity of the C–B bond formation, even at a nanosize level.[8] Alternative metal-free protocols[9] are considered to be advanced strategies, but stereoselective versions are still required.

Organoboranes[10] are highly versatile intermediates. They can be transformed into new functionalities, with retention of the configuration throughout subsequent stoichiometric and catalytic reactions. Thus for example, the C–B bond can be converted into C–O,[11] C–N[12] and C–F[13] bonds by oxidation, amination and fluorination protocols, respectively. Organoboranes can also be regarded as a platform to introduce C–C functionality into target products, not only through homologation reactions,[14] but also through catalytic cross-coupling reactions with a variety of organic electrophiles.[15] A convenient one-pot, two-step procedure requires a common catalyst for both reactions to be found (Scheme 1). To this end, we started to investigate Pt[16] catalysts, then we became interested in highlighting the potential of palladium for consecutive catalytic reactions, because of its multifaceted catalytic properties and efficiency.

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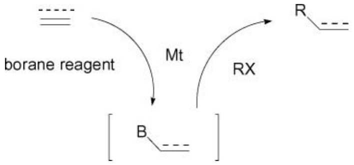
Cristina Pubill-Ulldemolins

Cristina Pubill-Ulldemolins received her B. S. in chemistry from University Rovira i Virgili in 2008. During the last course she experienced an interesting research project on synthesis of a bis(3,5-dimethyl-4-vinylpyrazol-1-yl)acetic acid and metal complexes thereof, carried out at the Friedrich-Alexandre-University of Erlangen-Nürnberg in Germany. She obtained an ICIQ grant from December 2008 to develop an interdisciplinary Ph.D studies with Dr Carles Bo exploring theoretical design of catalytic systems to be used in catalytic diboration reactions. The later experimental part is being developed at the University Rovira i Virgili in the Catalytic Organoborane Chemistry research line under the supervision of Dr Elena Fernández. Her research interests cover the catalytic diboration of alkenes with Rh, Ir, Pd and Pt complexes and the mechanistic insights of the processes.

Amadeu Bonet

Amadeu Bonet received his B. S. in chemistry from University Rovira i Virgili in 2007. In 2008 he experienced an interesting research project concerned with the catalytic hydroboration reaction under the supervision of Dr Cathy Crudden at Queen's University in Canada. In January 2009 he obtained a FI grant from the Generalitat de Catalunya and he is currently pursuing a Ph.D at the University Rovira i Virgili in the Catalytic Organoborane Chemistry research line. His research interests cover the asymmetric β-boration of α,β-unsaturated carbonyl compounds.

2 Palladium complexes catalyze B-addition reaction



Scheme 1

In their pioneering paper,[2] Männig and Nöth showed that Wilkinson's complex was more active than any other Rh complex in catalytic hydroboration. Complexes of Pd were inactive under the reaction conditions used, but in 1989 Suzuki and Miyaura reported that catecholborane (HBcat) hydroborated a variety of conjugated dienes in a 1,4-fashion in the presence of $Pd(PPh_3)_4$ as precatalyst (Scheme 2).[17] The allylborane intermediates were converted to the alcohols by aldehyde insertion.

Similarly, Pd complexes modified with PPh_3 ligands mediated the 1,4-addition of HBcat to 1,3-enynes, forming the allenic borane intermediate, which reacted with benzaldehyde to provide the corresponding homopropargyl alcohol, (Scheme 3).[18] As the ratio of the phosphine to the palladium increased, the 1,2-addition on the triple bond favoured the formation of the dienylborane product.

Since catalytic hydroboration is a useful tool for the synthesis of vinyl boron compounds,[19] Kang and Ko[20] used this transformation to prepare polymers or oligomers containing alternate vinylene units (Scheme 4). Although Rh and Ir complexes were more efficient at catalyzing the pinacolborane addition to 1,3,5-triethynylbenzene, palladium was considered to be an interesting alternative, in particular for the further cross-coupling of the tris(borylvinyl)benzene with arylbromides.

Phosphine-based palladium complexes, such as $Pd(PPh_3)_4$ and $PdCl_2(dppf)$, are good catalysts for the hydroboration of thioacetylenes,[21] (Scheme 5), except for terminal alkynes (R = H). These palladium catalytic systems seem to be effective enough

Carles Bo

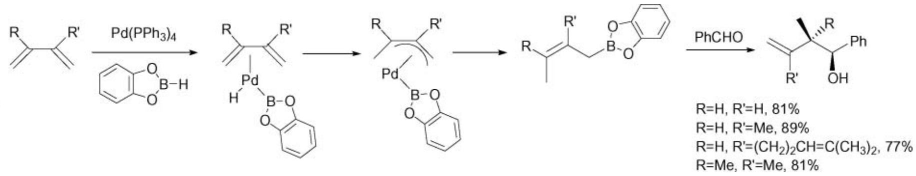
Carles Bo was born in El Vendrell (Baix Penedès) in 1963, graduated in Chemistry in 1986 at the University of Barcelona, and obtained an M.Sc. degree in 1988 for studies on homogeneous catalysis. He continued research in chemistry (but computationally) and obtained a Ph.D. degree in 1992 under the supervision of Prof. J. M. Poblet. The thesis dealt with the topological analysis of the electronic charge density function in transition metal compounds. During the thesis he visited the Laboratoire de Chimie Quantique (Strasbourg) several times and carried out research work under the guidance of Profs. Dedieu and Bénard, and later he spent a short post-doctoral stay at Prof. Baerends' group in Amsterdam. He holds an Assistant Professor position in Physical Chemistry at the University Rovira i Virgili (Tarragona) since 1995. His research activities concern the application of computational methods to the study of systems containing transition metal atoms, putting special attention in solving chemical problems in close collaboration with experimentalists. Topics studied include a variety of transition metal complexes, metallo-carbohedrenes, metallofullerenes and polyoxoanions. He is currently working at the ICIQ (Tarragona) as a group leader

Henrik Gulyás

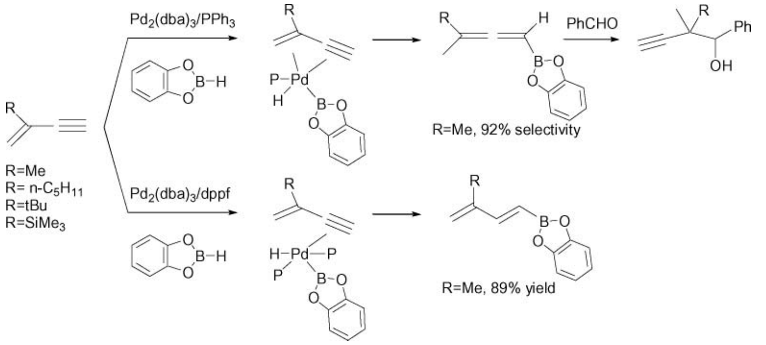
Henrik Gulyás was born in 1971 in Hungary. He did his Ph.D. studies at University of Veszprém (now Pannon University, Veszprém, Hungary) under the supervision of Prof. József Bakos, in the area of aqueous-phase homogenous catalysis. He earned his degree in 2005. In 2005–2007 he was working on a post-doctoral research project for BASF under the supervision of Prof. Piet van Leeuwen at the Institute of Chemical Research of Catalonia (ICIQ), Tarragona, Spain. During this period he developed new supramolecular strategies to assemble bidentate phosphorus ligands for transition metal catalyzed reactions. In 2007 he received a Torres Quevedo fellowship, and continued his research at ICIQ, working on the synthesis and catalytic applications of chiral non-racemizing secondary phosphine-oxide ligands. From 2009 he has been an assistant professor at the University Rovira i Virgili, working in the research group of Dr Elena Fernandez. His research interest is the development of new catalytic synthetic routes towards organoboron reagents.

Elena Fernández

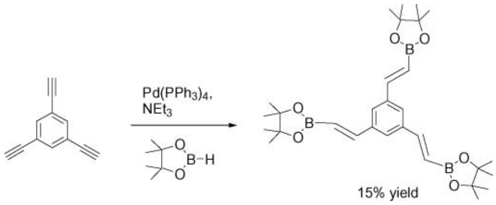
Elena Fernández was born in 1968 in Spain. She received her undergraduate degree in chemistry at the University of Barcelona in 1991. She subsequently did graduate work in catalytic hydroformylation of sugars with Prof. Sergio Castillón and Dr A. Ruiz at the University Rovira i Virgili, from which she earned her Ph.D. in 1995. The following two years, she moved at the University of Oxford (UK) to a postdoctoral position with Prof. John M. Brown where her studies culminated with an approach towards the first catalytic asymmetric hydroboration–amination reaction. Elena returned to Tarragona and accepted a lecturer position working in collaboration with Prof. Carmen Claver at the University Rovira i Virgili, becoming part of the permanent staff in 2000. Her group's research interests are centred on the application of transition metal complexes in selective organic purposes. More particularly, she has initiated a research programme aimed at developing catalytic tandem organic sequences through selective boron addition chemistry.



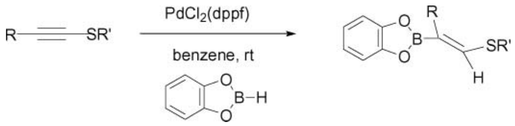
Scheme 2



Scheme 3



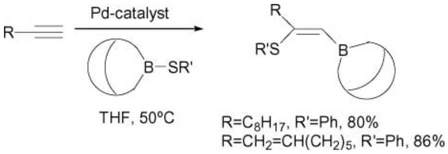
Scheme 4



Scheme 5

to permit the preparation of *trans*-catecholboryl vinyl sulfide in quantitative yields. We will come back to this work later on because it was the first example of palladium catalyzing consecutive hydroboration–cross coupling reaction, within the same catalytic system.

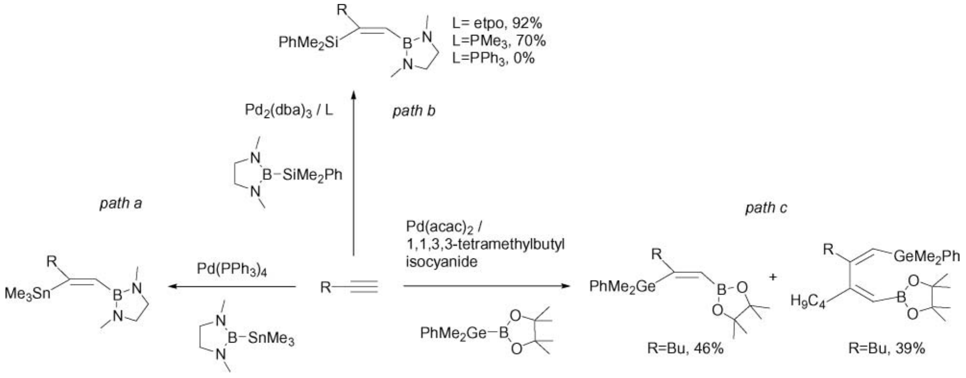
To solve the problem of catalytic B–H addition to terminal thioacetylenes, the same authors proposed the alternative palladium(0) catalyzed thioboration of terminal alkynes with 9-(alkylthio)-9-borabicyclo[3.3.1]nonane, (9-(phenylthio)-9-BBN) (Scheme 6).[22] $Pd(PPh_3)_4$ was the catalytic system chosen to favour the chemoselective thioboration of terminal alkynes in the presence of double bonds in the substrate. Interestingly, neither Rh-, Cu- nor Co-based catalytic systems were active in this transformation. The reaction was rather sensitive to the steric hindrance of the alkynes, such as cyclohexylethyne, but the use of an alternative catalytic system, $(Pd(dba)_2$ and diphenyl(2,4,6-trimethoxyphenyl)phosphine), significantly increased the thioboration for these hindered substrates. These are also good examples of reactions where the products are susceptible to further transformation in the same one-pot system by consecutive palladium cross coupling. This will be discussed in detail in the last part of the article.



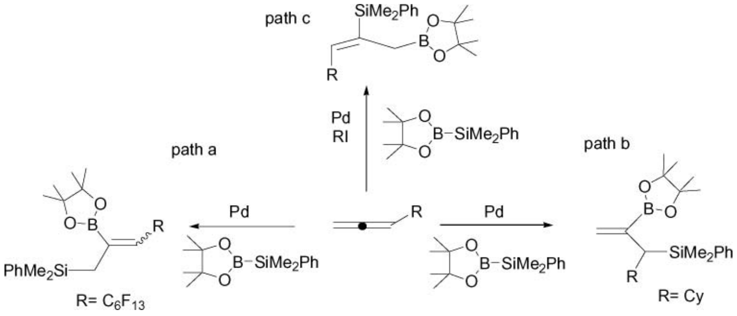
Scheme 6

Continuing with the palladium-mediated B addition to alkynes through inter-heteroatom reactions, we will focus on some well established methods for borylstannylation, borylsilylation and germaboration. *cis* Addition of borylstannanes to alkynes has been catalyzed by $Pd(PPh_3)_4$, $Pd(dba)_2$, $Cl_2Pd(PPh_3)_2$ or $Me_2Pd(PMe_2(CH_2CH_2)PMe_2)$ to give β-(stannylalkenyl)boranes in high yield (Scheme 7, *path a*).[23] A silicon–boron bond can be regio- and stereoselectively added to alkynes in the presence of the catalytic system palladium(0)-*tert*-alkyl isocyanide but less efficiently with $Pd(PPh_3)_4$.[24] Similarly, Ito extended the reaction to other B–Si reagents such as $PhMe_2Si–B(pin)_2$ and $PhMe_2Si–B(NMe_2)_2$[25] and more recently cyclic silylboranes have also been efficiently used.[26] A clear ligand effect was noted by Tanaka *et al.*,[27] who showed that the catalytic performance of palladium tended to decrease by changing the ligands, (etpo (etpo = $[P(OCH_2)_3CEt]$) > PMe_3 > PPh_3) (Scheme 7, *path b*). The regio- and stereoselective formation of the alkenyl-silicon and boron moiety had considerable synthetic potential, particularly in carbon–carbon bond forming reactions, as we will discuss in the last part of the manuscript. In contrast, germaboration proceeded with lower chemoselectivity when palladium complexes catalysed the Ge–B addition to alkynes: in addition to the expected regioisomer obtained by the normal addition protocol, the dimerized byproduct was also observed (Scheme 7, *path c*).[28]

Ever since the early report by Suzuki and Miyaura that demonstrated the capability of $Pd(PPh_3)_4$ to catalyze the addition of catecholborane (HBcat) to conjugated dienes,[17] further efforts



Scheme 7

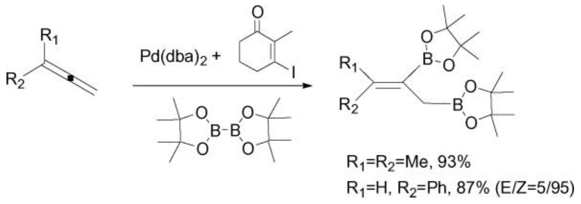


Scheme 8

have been devoted directly to adding interelement linkages to both 1,3-dienes and 1,2-dienes. However, despite the great success of palladium in the silaboration of alkynes, similar palladium complexes were not efficient in the silaboration of 1,3-dienes.[29] Some theoretical studies, to be discussed below, try to explain this behaviour. On the other hand, silaboration of allenes catalyzed by palladium proceeded through regioselective addition of boron to the central carbon of 1,2-diene, but whether it is on the internal or terminal double bond depends on the nature of the substituents of the substrate, the nature of catalyst, and the reaction conditions (Scheme 8, *path a* and *b*).[30] The enantioface-selective palladium silaboration of allenes *via* double asymmetric induction has also been explored. The addition of a catalytic amount of an organic iodide, iodine or silyl iodide could initiate the silaboration reaction of allenes in the presence of phosphine-free palladium complexes, (Scheme 8, *path c*). It is important to note that the reaction proceeded with unexpected regioselectivity when the B atom was placed on the terminal carbon of the allene substrate. Further related studies justified this behaviour with the formation of $PhMe_2SiI$ and its participation in the catalytic cycle.[31]

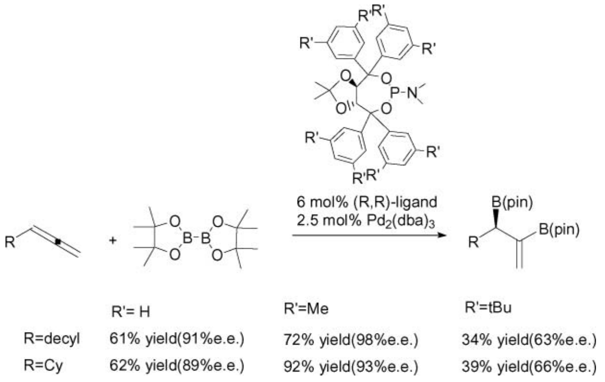
Alternatively, palladium catalyzed the 1,4-stannaboration of 1,3-dienes to obtain (*Z*)-1-boryl-4-stannyl-2-butenes in quantitative yields,[32] and borostannylation of 1,2-dienes with consecutive cyclization in the case of allenynes,[33] as we will discuss later on.

In contrast to the relatively successful palladium-mediated B addition to alkynes, 1,3-dienes and 1,2-dienes through H–B, Si–B, Sn–B and Ge–B moieties, the diboration reaction was less efficient under standard conditions. Diboration of 1,2-dienes is of great interest because the diborated product contains allylboronate and vinylboronate functionalities. We have found the first example in Cheng's work where $Pd(dba)_2$ was assumed to catalyze the diboration of allenes using an aryl or alkenyl iodide as cocatalyst (Scheme 9).[34] The catalytic reaction was completely regioselective with one boryl group added to the middle carbon and the other to the nonsubstituted terminal carbon of the allene moiety. The authors also demonstrated that several other phosphine-free Pd(II) complexes showed the same high activity, but the reaction was sensitive to the presence of phosphines, (1 eq. of PPh_3 to $Pd(dba)_2$ significantly reduced the conversion while 2 eq. completely inhibited the reaction).



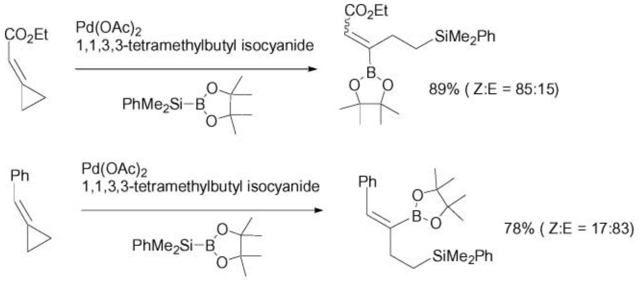
Scheme 9

Morken has reported another palladium approach to the diboration of allenes, where he uses $Pd_2(dba)_3$ modified with Lewis basic ligands. While monodentate alkyl phosphines, phosphites and phosphorous triamides were convenient for the reaction, diphosphines such as dppe were completely ineffective. Further work demonstrated that Pd(0)-phosphoramidite complexes catalyze the enantioselective diboration of prochiral allenes and provides new opportunities for asymmetric synthesis through tandem reaction sequences[35] (Scheme 10). Recent advances have demonstrated that Taddol-derived phosphoramidite ligands, fine-tuned by subtle modifications in the aryl rings, have a significant positive impact on asymmetric induction.[36]



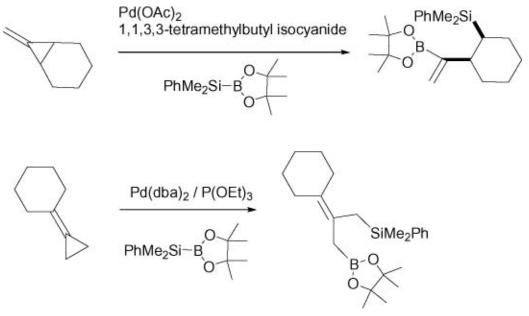
Scheme 10

The last part of this section discusses the palladium-mediated B addition to alkenes. The first example we have found is the silaboration of methylenecyclopropanes by $Pd(OAc)_2$/1,1,3,3-tetramethylbutyl isocyanide to afford α,β-unsaturated ester as a 85 : 15 mixture of *Z* and *E* isomers (Scheme 11).[37] The product is interesting because it contains a vinyl boryl group as well as a homoallylic silyl group in the same molecule. This reaction can be regarded as a "proximal" C–C/Si–B metathesis and proceeds with remarkably high regioselectivity. The stereoselectivity seemed to depend on the steric bulk of the substrate.



Scheme 11

The same palladium–isonitrile catalytic system effectively induced silaborative "proximal" C–C bond cleavage when the substrate had substituents on the cyclopropane ring (Scheme 12). However, when the palladium catalytic system was formed from $Pd(dba)_2$ as precursor and $P(OEt)_3$ as ligand, the silaboration proceeded differently in cycloalkylidenecyclopropanes: the regioselectivity was derived from the "distal" cleavage (Scheme 12).



Scheme 12

Most recently, our research group has been able to find a catalytic system capable of adding a diboron reagent to alkenes. Palladium(II)–NHC complexes (NHC = N-heterocyclic carbene ligands, Fig. 1) turned out to be very efficient catalysts for the 1,2 diboration of alkenes, and were the first examples of Pd-catalysts capable of mediating this B–B addition (Scheme 13). The reaction is completely chemoselective in the presence of a mild base (NaOAc) and an excess of diboron reagent. The scope of the catalytic reaction is quite broad, as it has been demonstrated that both terminal and internal alkenes can be functionalized.

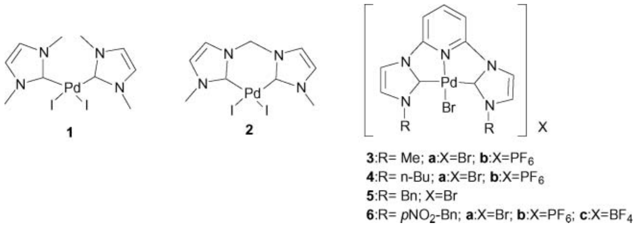
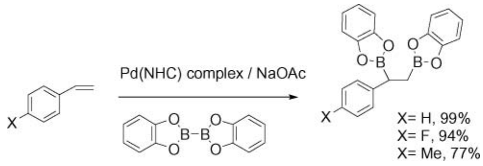
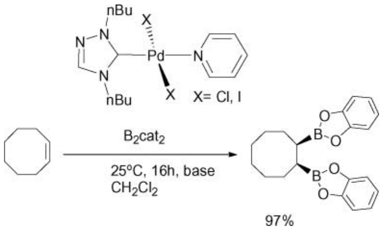


Fig. 1



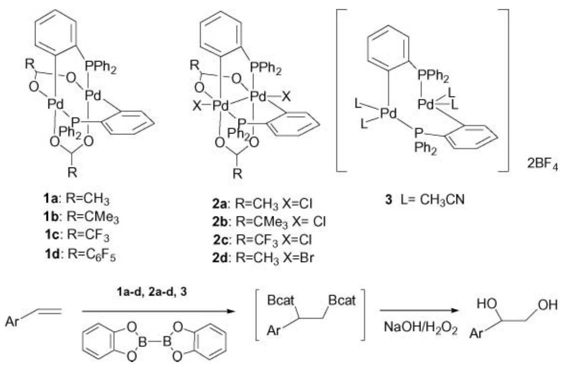
Scheme 13

More recently our group has observed a perceptible influence of metal heterocyclic carbene–pyridyl mixed-ligand complexes on the catalytic diboration of cyclic alkenes. Palladium modified with NHC and pyridine ligands proved to be efficient in the chemoselective diboration of such hindered cyclic alkenes as cyclooctene, cyclohexene and cyclopentene, in the presence of a base, at room temperature (Scheme 14).[39]



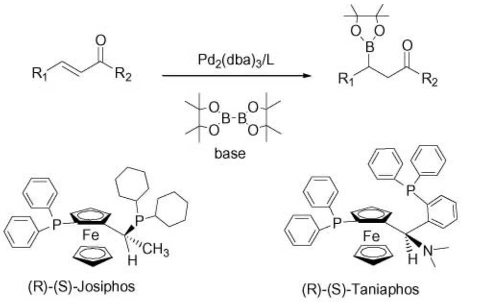
Scheme 14

In collaboration with Prof. Lahuerta and Dr M. A. Ubeda, our group has also contributed to the application of novel Pd_2^{6+} compounds and their Pd_2^{4+} counterparts to efficiently mediate the diboration of vinylarenes and aliphatic 1-alkenes, under mild and basic reaction conditions. A variety of 1,2-diboronate esters were produced in excellent conversions and chemoselectivities (Scheme 15).[40] The presence of bis(catecholato)diboron (B_2cat_2) induced the reduction of Pd(III) to Pd(II), while the catalytic precursor of Pd(II) was transformed into Pd(0)-nanoparticles. An *in situ* catalytic tandem reaction was designed to transform the diboronate intermediates into the monoarylated product which after oxidative work-up provided the carbohydroxylated adduct (see the last section of this perspective).



Scheme 15

We are particularly interested in finding new catalytic systems which are able to perform β-boration on α,β-unsaturated carbonyl compounds and, when it is possible, to induce asymmetry in the new C_β–B bond. Therefore, we were very pleased to observe that catalyst precursor $Pd_2(dba)_3/L$ (L = (*R*)-(*S*)-Taniaphos, (*R*)-(*S*)-Josiphos) performed this reaction and became the first example of palladium-mediated β-boration of α,β-unsaturated esters,[41] (Scheme 16). When the palladium source was modified with the chiral ligands (*R*)-(*S*)-Taniaphos and (*R*)-(*S*)-Josiphos, enantiomeric excesses were as high as 91%. The enantioselectivities strongly depended on the ester moiety of the substrate ('R_2', Scheme 16).



R_1=Me, R_2= OiBu, 60% conv, 86% e.e.
R_1=Me, R_2= OEt, 99% conv, 91% e.e.
R_1=Me, R_2= OMe, 99% conv, 87% e.e.

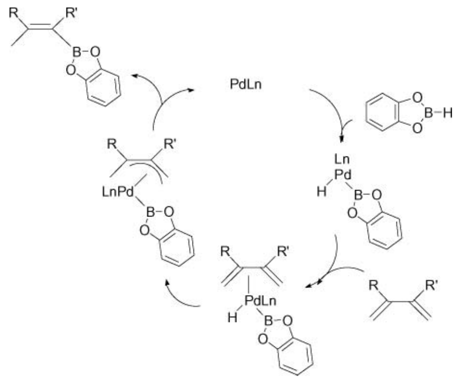
R_1=Me, R_2= OiBu, 30% conv, 90% e.e.

Scheme 16

3 Mechanistic insights

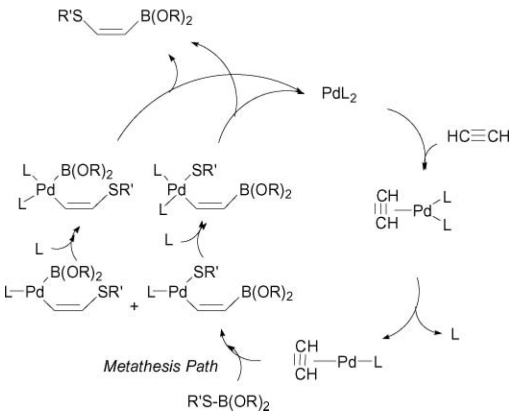
It has been suggested that the most general catalytic cycle for B additions to unsaturated substrates proceeds through oxidative addition of the borane reagent to the transition metal complex, followed by the expected coordination of the substrate and insertion into the metal boryl unit, and eventual reductive elimination. However, the reason why some of the palladium mediated catalytic B-addition reactions are not conducted in a similar way to Pt- or Rh-based catalytic systems requires a deep understanding, so that new and more efficient routes can be designed to allow further functionalization of the substrate through consecutive palladium-mediated reactions

In the first reported palladium-mediated hydroboration of catecholborane to 1,3-dienes, the oxidative addition of the B–H unit was assumed to be an early step in the catalytic cycle, which was followed by coordination of the diene and insertion into the Pd–H bond, to generate the desired product by reductive elimination as the final step (Scheme 17).[17] The mechanism was postulated to resemble palladium-catalyzed hydrosilylation,[42] in which the hydride transfer from the oxidative adduct might be the regioselective step. Hayashi *et al.*[18] also supported the idea of oxidative addition of catecholborane to Pd(0) species, in view of the proposed intermediates to explain the different chemoselectivity in hydroboration of 1-buten-3-ynes.



Scheme 17

The same authors postulated that there was a similar trend in the B–S addition to alkynes by $Pd(PPh_3)_4$. After oxidative addition of the B–S unit to Pd(0), the coordination of the alkyne to the metal and further insertion through the Pd–S bond could explain the high regioselectivity in the product with the S atom bonded to the internal carbon.[22] However, a few years later Musaev and Morokuma explored[43] the mechanism of the palladium(0)-catalyzed thioboration of acetylene from a theoretical point of view. Some of their main findings were that the oxidative addition of the S–B bond to $Pd(PH_3)_2$ was not possible, so the oxidative addition mechanism proposed by Suzuki *et al.*[22] could not be theoretically justified. Musaev and Morokuma proposed a new mechanism involving alternative steps: acetylene coordination to $Pd(PH_3)_2$ followed by dissociation of a phosphine ligand and addition of the S–B bond to the metal centre *via* a metathesis-like transition state. The last step in the catalytic cycle could involve isomerization of the resulting complex, accompanied by recoordination of the phosphine ligand and reductive elimination of the alkenyl-thioboron product (Scheme 18). They also found

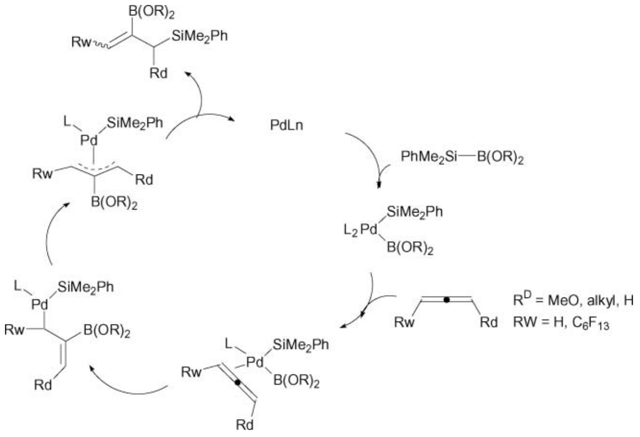


Scheme 18

that the rate-determining stage was the addition of the S–B bond to the metal center (with 18.6 kcal mol^{-1} barrier), *via* a metathesis-like transition state in which R′S–B(OR)$_2$ simultaneously attacks Pd and one of the C atoms in the Pd(PH$_3$)(C$_2$H$_2$) intermediate. Another interesting fact is that throughout the reaction, the *Z*-isomer around the double C–C bond was kept. However, the high control of regioselectivity in the reaction outcome was not completely explained by the mechanistic proposal.

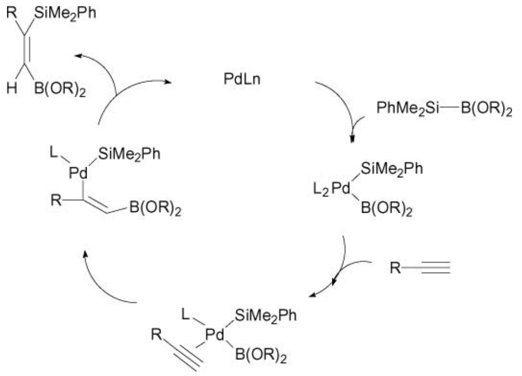
Alternatively, Sakaki *et al.*[44] theoretically explored the σ-bond activation of (HO)$_2$B–XH$_3$ (where X= C, Si, Ge and Sn) by palladium complexes. Interestingly, they found that (HO)$_2$B–SiH$_3$, (HO)$_2$BGeH$_3$ and (HO)$_2$B–SnH$_3$ undergo oxidative addition to Pd(PH$_3$)$_2$ with either a very small barrier or no barrier. Only the oxidative addition of (HO)$_2$B–CH$_3$ to Pd(PH$_3$)$_2$ could not take place, but the reductive elimination of (HO)$_2$B–CH$_3$ from Pd(CH$_3$)[B(OH)$_2$](PH$_3$)$_2$ occurs with no barrier. They also found that the Pd–B(OH)$_2$ bond is much stronger than Pd–XH$_3$ bonds. This is because the Pd–B(OH)$_2$ bond order increases due to the π-back-donation to the empty pπ orbital of B from the doubly occupied dπ orbital of Pd. They pointed out that the *trans* influence of the boryl group is even stronger than the very strong *trans* influence of the silyl group.

The permissible oxidative addition of (HO)$_2$B–SiH$_3$ to Pd(0) complexes calculated by Sakaki *et al.*[44] made it possible for Suginome and Ito[45] to postulate a mechanism for the silaboration of 1,2-dienes following the classical catalytic cycle that involves a (boryl)(silyl)palladium(II) complex formed by oxidative addition of the Si–B bond to the Pd(0) complex, (Scheme 19). The activation of the Si–B bond might be followed by the coordination of the allene and the subsequent migratory insertion of a more electron-deficient C–C double bond. They suggested that the C=C bond may preferentially be inserted into the Pd–B bond rather than the Pd–Si bond. Thus, selective B–C bond formation may proceed at the *sp* carbon of allene to give a σ-allylic palladium intermediate in which the silyl group and the allylic carbon are located in a *trans* fashion. From this intermediate a rapid conversion to the corresponding π-allylic palladium complex is expected, which then undergoes facile reductive elimination of the silicon and the carbon atom located in *cis* to the silyl group.



Scheme 19

A similar mechanism was postulated by Ito *et al.*[25] for the palladium-catalyzed silaboration of terminal alkynes, involving oxidative addition of the Si–B bond to the palladium complex, followed by regioselective insertion of the carbon–carbon triple bond and a subsequent reductive elimination of the product (Scheme 20). It is notable that the (boryl)(silyl)palladium(II) complex may undergo a regioselective and *cis*-insertion of alkynes at the Pd–B bond with regioselective B–C bond formation at the terminal *sp* carbon to give the (β-borylvinyl)silylpalladium(II) intermediate (Scheme 20).



Scheme 20

However, when we take into account the palladium-mediated diboration reaction, we can theoretically justify why it cannot proceed through the assumed catalytic cycle that involves the oxidative addition of diboron to the Pd(0), and then the coordination and migratory insertion of the substrate into the Pd–B bond, ending with the reductive elimination step that provides the diborated product. What Musaev and Morokuma[46] found was that the B–B oxidative addition step to Pd(0) was endothermic by 5.0 kcal mol^{-1} with a reverse barrier of only 0.1 kcal mol^{-1} for Pd(0). They considered that the oxidative addition was unfavourable in this case both thermodynamically and kinetically for Pd(0) complexes. The main reason for this behaviour has been explained in terms of the large promotion energy from the d^{10} to the s^{1}d^9 configuration of the Pd(0) atom. But at this point we need to ask why palladium catalyzes the thioboration reaction of alkynes[22] but not the diboration reaction, if neither of the reactions proceeds *via* pathways involving the oxidative addition of B–S or B–B to the metal center, since the oxidative-addition products do not exist in any of the cases. Musaev and Morokuma found an explanation involving the five-centred “metathesis” transition state in which the Pd–S and C–B bonds are formed, and the B–S and one of the π bonds of the acetylene are broken simultaneously. It seems that while the d^{10} to s^{1}d^9 the promotion energy of Pd(0) still has to be paid to form Pd–S and Pd–C bonds, the resultant complex is very stable due to the strong C–B bond and, therefore, provides the thermodynamic driving force for the process. However, the same kind of “metathesis-like” transition state located for the Pd(0)-catalyzed alkyne diboration reaction with (CH$_2$O)$_2$B–B(OCH$_2$)$_2$ lies about 34.1 kcal mol^{-1} higher than that for (CH$_2$O)$_2$B–B(OCH$_2$)$_2$ + Pd(PH$_3$)(C$_2$H$_2$) (Fig. 2). Therefore the metathesis pathway seems to be more favoured for the alkyne thioboration than the analogous diboration reaction. Musaev and Morokuma also mentioned that the fundamental difference between the alkyne thioboration and diboration of alkynes can be explained in terms of the hypervalent characters of the third-row atoms (sulfur)

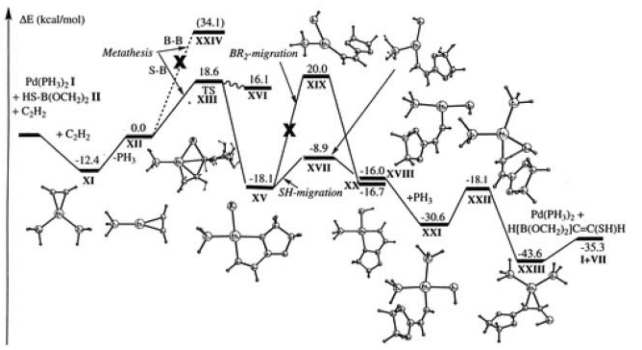
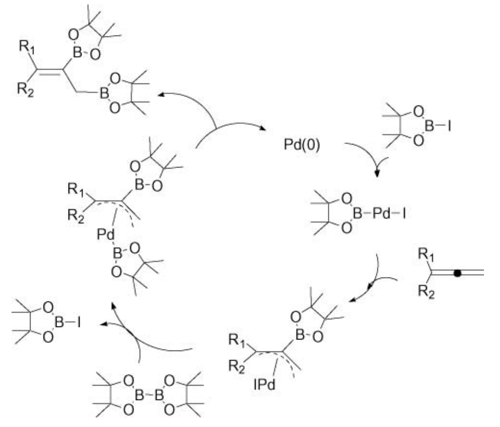


Fig. 2 Potental-energy profile of the catalytic cycle of the acetylene thioboration reaction catalyzed by $Pd(PH_3)_2$, taken from reference 43. The number given in parentheses corresponds to the acetylene diboration reaction catalyzed by $Pd(PH_3)_2$.

compared to the second-row elements (boron). The hypervalent character of the sulfur atom allows it to simultaneously interact with the $B(OR)_2$ group and the Pd, which consequently stabilizes the transition state.

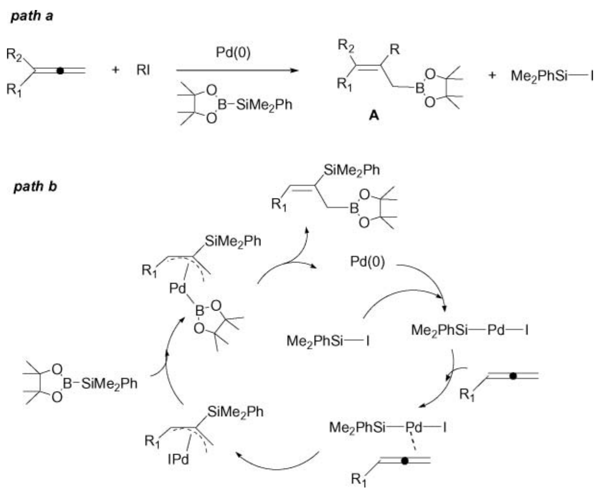
Simultaneously, Sakaki,[47] also theoretically, explored the insertion of $Pd(PH_3)_2$ into $X_2B–BX_2$ (X = H, OH). They demonstrated that the insertion into $(HO)_2B–B(OH)_2$ is difficult, unlike the insertion into the Si–Si bond, and the $Pd–B(OH)_2$ bond energy (49 kcal mol^{-1}) was calculated to be much smaller than the analogous $Pt–B(OH)_2$ bond energy, (about 60 kcal mol^{-1}).

Taking into account the work of Musaev, Morokuma[46] and Sakaki,[47] the unusual diboration of allenes catalyzed by palladium complexes and organic iodides described by Cheng *et al.*[34] (Scheme 9) required an alternative explanation for the mechanism involved. The authors postulated a new catalytic cycle based on the observation that an aryl, alkenyl iodide or I_2 was required to initiate the catalytic reaction. A key intermediate seemed to be the iodo(pinacolato)boron generated from the Pd-mediated three-component assembly of organic iodide, allene and diboron B_2pin_2. Therefore, the iodo(pinacolato)boron was added to Pd(0) by oxidative addition and the adduct reacted with the allene to provide the Pd–allyl species with the boryl unit attached to the central carbon of the π-allyl group. Transmetallation of the later intermediate with the diboron reagent gave a new Pd–(allyl)boryl species and regenerated the iodo(pinacolato)boron. Final reductive elimination produced the desired citoronic product and regenerated the Pd(0) species (Scheme 21).



Scheme 21

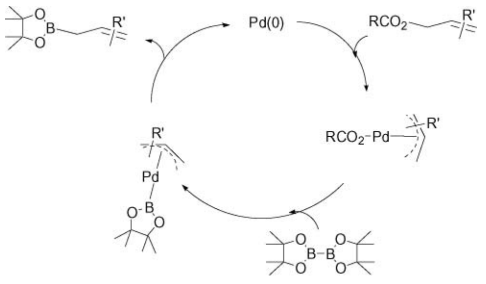
The same authors have extended the postulated catalytic cycle to the silaboration reaction of allenes in the presence of phosphine-free palladium complexes (Scheme 8),[31] where the organic iodide probably acts as an initiator undergoing oxidative addition with Pd(0) to give a palladium(II) intermediate that reacts with allene and borylsilane to afford the 1,2-trisubstituted boryl compound A and the silyl iodide (Scheme 22, path a). The role of the silyl iodide in the catalytic cycle has also been supported by the fact that Me_3SiI is an effective initiator for the catalytic cycle. The observation that phosphine retards the catalytic reaction may be explained by the competition between the phosphine and the allene substrate for coordination to the palladium intermediate. The observed regioselectivity might be determined at the transmetallation step between the Pd–allyl species and the borylsilane. The regioselectivity for the product would be completely different if a boryl iodide was generated instead of silyl iodide (Scheme 22b). The extension of this postulated mechanism from that of palladium diboration reaction seems reasonable, despite the fact that Sakaki[44] has demonstrated the permissible oxidative addition of $(HO)_2B–SiH_3$ to Pd(0) complexes.



Scheme 22

Transmetallation between π-allylpalladium(II) species with bis(pinacolato)diboron was first reported by Miyaura *et al.*[48] in the context of allylboronate synthesis from allylic acetates. The high reactivity of the oxopalladium complex toward the transmetallation with organoboron compounds can be attributed not only to the high reactivity of the Pd–O bond, which consists of a soft acid and a hard base combination, but also to the high oxophilicity of the boron centre (Scheme 23).

Using the input by Cheng *et al.*[34] on the palladium diboration of allenes, we developed the novel catalytic activation of the B–B bond by palladium(II)–NHC complexes in the presence of a mild base (NaOAc) and an excess of diboron reagent, which led to the chemoselective 1,2-diboration of alkenes.[38] We suggested that this reaction could be explained by the heterolytic cleavage of the diboron reagent rather than oxidative addition of a B–B bond to the metal. As we mentioned above, previous theoretical studies[46,47] on Pd(0) phosphine model complexes concluded that the oxidative addition of B–B cannot take place since it is an endothermic process with an extremely low reverse barrier. More



Scheme 23

recently, and in the framework of the diboration of styrene by Cu(I)–NHC catalysts, we reported a DFT study[49] suggesting that the oxidative addition of B_2cat_2 to afford a Cu(III)–NHC–diboryl complex would be highly endothermic (Fig. 3, OA-BB) so a Cu(I)–NHC–(σ-B_2cat_2) intermediate would be formed instead, (Fig. 3, SA-BB).

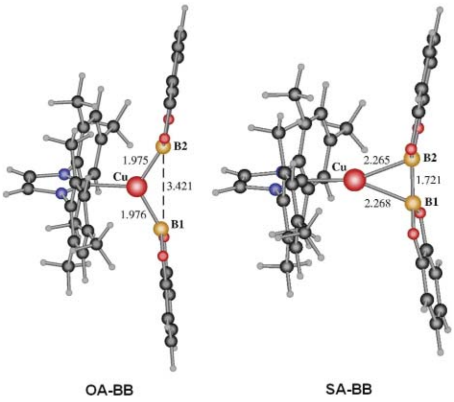


Fig. 3 B3LYP optimized structures of **OA-BB** (oxidative addition) and **SA-BB** (sigma adduct) for $[(NHC)Cu(CatB–Bcat)]^+$. Selected distances are in Å.

In this case, a mechanism involving transmetallation sequences was suggested. Consequently, we wondered whether the observation that an excess of B_2cat_2 is required for total conversion of alkenes suggests an alternative mechanism. First we explored the direct oxidative addition of B_2cat_2 to [Pd(II)–NHC–Br]+ (3a). As *path A* in Fig. 4 indicates, the oxidative addition of B_2cat_2 to the cationic complex 4a is an endothermic process by 22.0 kcal mol^{-1}, while the barrier of the reverse process is extremely low. These results are in agreement with previous studies.[46,47] It should be pointed out that the product of this process is a saturated hexacoordinated Pd(IV) complex which requires a vacant site to be created so that the reaction can proceed. Decoordination of the bromide followed by coordination of the substrate, alkene insertion and reductive elimination would follow the "classical" reaction pathway. Alternatively, reductive elimination of a B(cat)Br adduct produces a [Pd(II)–(NHC)–B(cat)]+ (3a-B) cationic complex intermediate which inserts the alkene into the Pd–B bond to form the Pd–alkylboronate species. We calculated that the formation of 3a-B is 3.4 kcal mol^{-1} above the reactants, as Fig. 4 shows. It is conceivable that there is another possible active species which results from the preliminary decoordination of bromide to give a dicationic $[Pd(II)–NHC]^{2+}$ complex. This intermediate could form a very stable sigma complex with B_2cat_2, 3a9-sB2 (see *path B* in Fig. 4) which is 32.9 kcal mol^{-1} below the two isolated reagents. In contrast to the case of Cu(I)–NHC in which the oxidative addition was discounted,[49] here the oxidative addition process is only slightly endothermic (by 9.6 kcal mol^{-1}) and has a moderate energy barrier. Since this product is coordinatively unsaturated, alkene coordination would be the following step. In view of these results, we do not rule out the possibility that Pd(IV) species participated in the mechanism, probably stabilised by the strong sigma donor NHC ligand. In this regard, when weaker donor ligands were used, the reaction did not proceed.

However, when the base is added, the mechanism could switch towards transmetallation, since this would explain the increase not only in selectivity but also in conversion when an excess of B_2cat_2 is used. It is accepted that the role of the base is to accelerate the rate of the transmetalation, as it does in the related cross-coupling reaction of organoboron compounds.[50] However, we cannot rule out the possibility that the base participates in the halide displacement at the palladium species and facilitates the transmetalation.[51] The treatment of (NHC)Pd(II)–Br, with NaOAc and B_2cat_2 in d_8-THF resulted in the formation of a new signal at 13.6 ppm in ^{11}B NMR from the original 28 ppm of B_2cat_2. The shift of the ^{11}B signal to higher fields from the original B_2cat_2 could be explained by the increasing diboron nucleophilicity because of interaction with NaOAc. This is also supported by the fact that when the catalytic diboration was carried out in the presence of (NHC)Pd(II)–Br and bis(pinacolato)diboron, (B_2pin_2), no diboronate ester was observed, in accordance with the absence of new signals in ^{11}B and ^1H NMR from the mixture of (NHC)Pd(II)–Br with NaOAc and B_2pin_2.

We also explored the role of the base by using OH^- as a model and characterizing the intermediate shown in Fig. 5, in which one of the boron atoms directly interacts with the base. This adduct could explain the ^{11}B NMR data and it is analogous to the one proposed in the Suzuki–Miyaura reaction. Moreover, the interaction of the B_2cat_2 with the base weakens and polarizes the B–B bond as is shown by the data in Fig. 4. We also investigated the effect of the base when B_2cat_2 is coordinated to the palladium dicationic complex. The approach of the OH^- base to the sigma complex **3a′-σB2** was found to be highly dependent on the initial geometry, and led either to the new intermediate shown in Fig. 6, or to the formation of the BcatOH species and the cationic complex **3a′-B**, which are considered to be the intermediates of the transmetallation process. In order to evaluate the thermodynamics of this transformation (avoiding charge separation *in vacuo*), we considered B_2cat_2 and $[Pd(II)–NHC–OH]^+$ as the starting point. In this way, the overall process is favourable by −39.7 kcal mol^{-1}. Note that this result contrasts with the bromide-mediated transmetallation which was computed to be slightly endothermic by a few kcal mol^{-1}. Therefore, the interaction of the base with the diboron reagent together with the strong exothermicity of the transmetallation step in the presence of the base, could very well drive the reaction to completion.

Finally, on the basis of the experimental observations and the computational results presented, we suggested the following mechanism: first, a base-assisted transmetallation step which activates the catalyst; second, alkene coordination and insertion into the Pd–B bond; and third, a new transmetallation with B_2cat_2

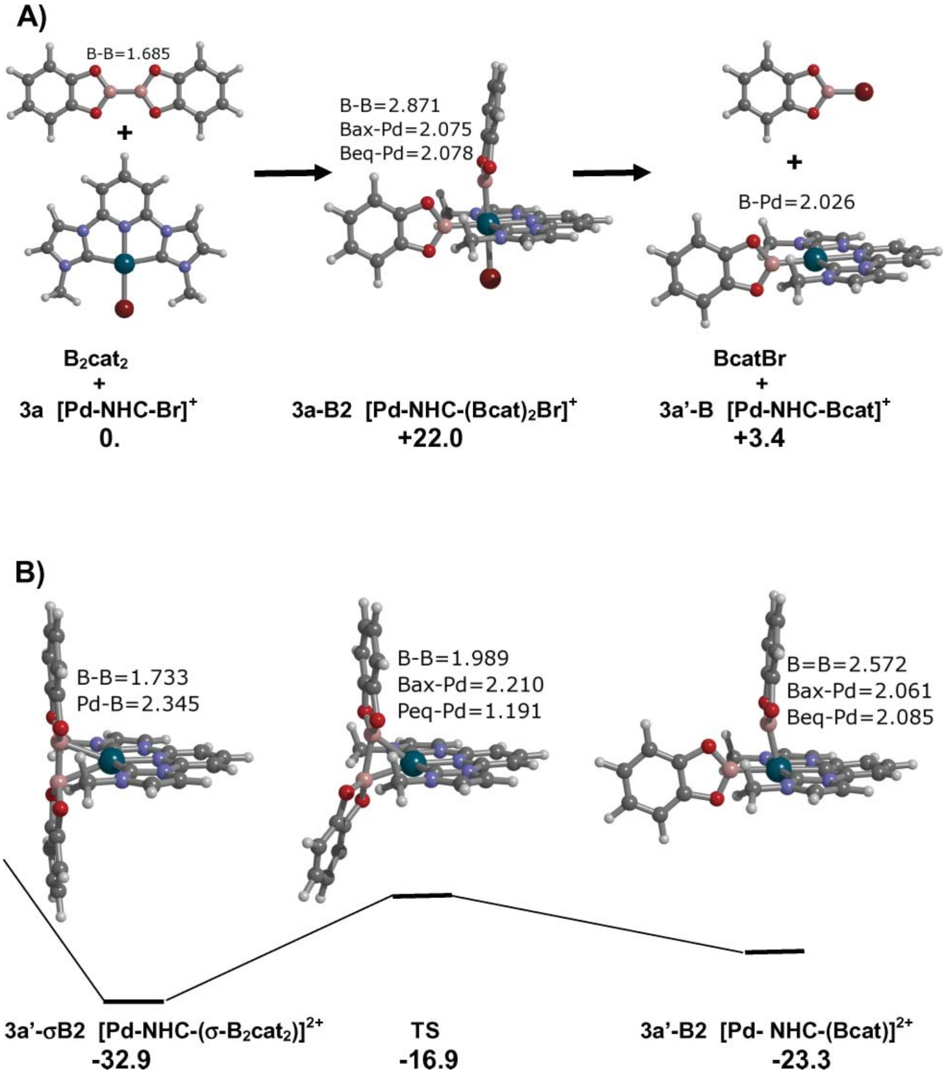


Fig. 4 Molecular structures, selected geometrical parameters (in Å) and reaction energies (in kcal mol^{-1}) for direct oxidative addition processes.

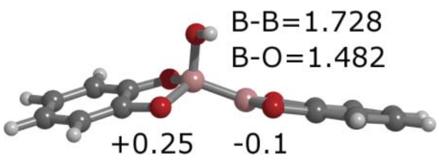
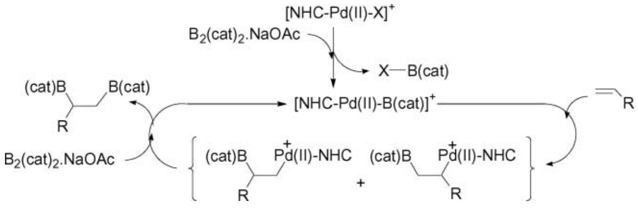


Fig. 5 [B_2cat_2–OH]$^-$ adduct. Selected geometrical parameters (in Å) and variation in the atomic charges of boron atoms with respect to free B_2cat_2.

provides the diborated final product and regenerates the active species (Scheme 24).



Scheme 24

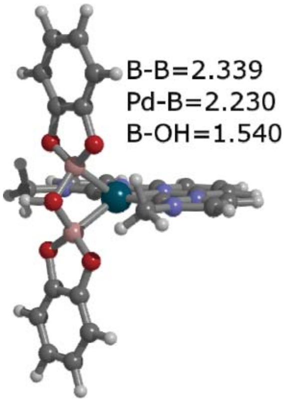
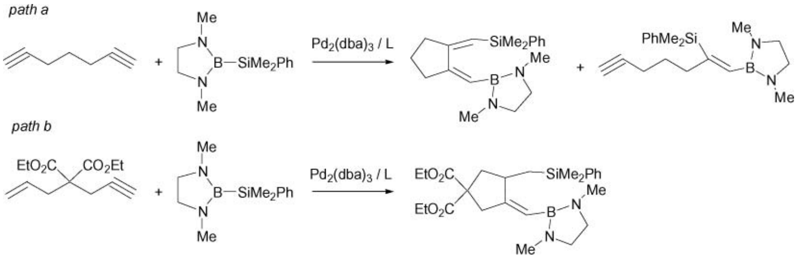


Fig. 6 Molecular structure of the [Pd–NHC–B_2cat_2–OH]$^+$ intermediate.

The suggested participation of transmetallation steps in the palladium-mediated B addition reaction opens up new perspectives in the application of the palladium complex in subsequent catalytic steps, such as cross coupling and cyclization reactions.



Scheme 25

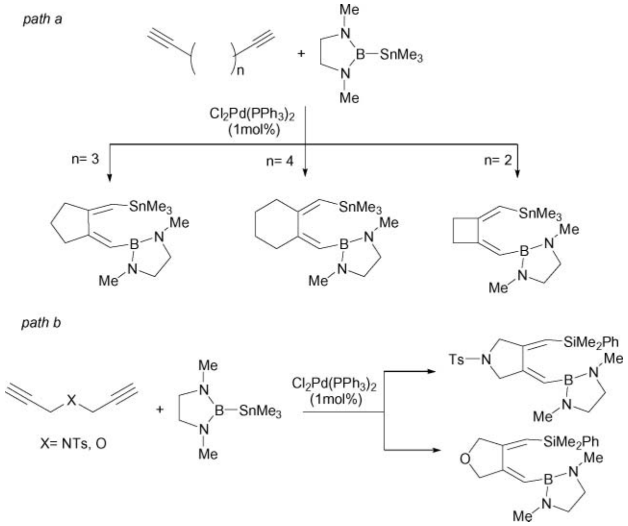
4 Organoboranes in palladium-catalyzed functionalization of unsaturated organic molecules

This section considers two of the most interesting functionalizations *via* organoboranes, through consecutive palladium-catalyzed reactions: the tandem sequence boron addition/cyclization, and the boron addition/cross coupling reactions. We only describe examples where the two subsequent Pd-catalyzed reactions are carried out in "one pot", without the isolation of the organoborane intermediate, and we put particular emphasis on the enormous interest in using one single Pd-catalyst for the two different reactions.

Despite the efforts that have been made to perform transition metal-catalyzed cyclizations of unsaturated organic compounds,[52] the alternative tandem sequence boron addition/cyclization reaction is extremely useful, because the resulting boron-containing cyclic compounds allow numerous synthetic applications.

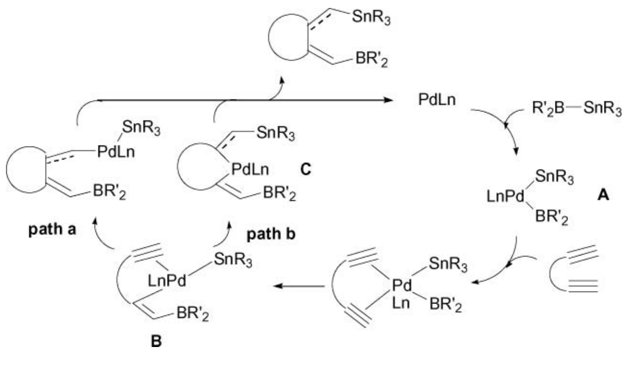
Palladium–catalyzed boron addition/cyclization reactions were first described in the presence of B–Si and B–Sn reagents. Borylsilylative carbocyclization[27] of hepta-1,6-diyne and 1,3-dimethyl-2-dimethylphenylsilyl-2-bora-1,3-diazacyclopentane with the $Pd_2(dba)_2$-etpo system afforded the cyclic compound in 87% yield. The byproduct from the simple addition of the B–Si reagent to one of the two acetylenic bonds without carbocyclization was also formed in 13% yield (Scheme 25, *path a*). However, the reaction of octa-1,7-diyne turned out to be less selective for the cyclization product. The broad scope of the reaction was demonstrated when the enyne 4,4-bis(ethoxycarbonyl)hept-6-en-1-yne was cyclo-functionalized, and the boron atom was added regioselectively to the terminal carbon of the acetylene (Scheme 25, *path b*).

Even more selective catalytic borylstannylative carbocyclization of diynes has also been successfully achieved by palladium complexes under mild conditions, affording 1-(borylmethylidene)-2-(stannylmethylidene)cycloalkanes.[53] With regard to the catalyst, besides $Cl_2Pd(PPh_3)_2$, a series of palladium complexes such as $Cl_2Pd(P(o\text{-tolyl})_3)_2$, $Pd(PPh_3)_4$ and $Pd(dba)_2$, exhibited equally excellent catalytic activity. The undesired byproduct arising from the simple addition of the borylsilane to one of the two acetylenic bonds of the diynes, was not observed. The substrate scope was quite broad, the reaction could be carried out with numerous symmetrical and unsymmetrical diynes, in order to generate the corresponding six-, five- and, most surprisingly, four-membered rings (Scheme 26 *path a*). A facile route to 1,2-dimethylidene heterocyclic compounds was described by the borylstannylative carbocyclization of nitrogen- and oxygen-containing 1,6-diynes (Scheme 26 *path b*).

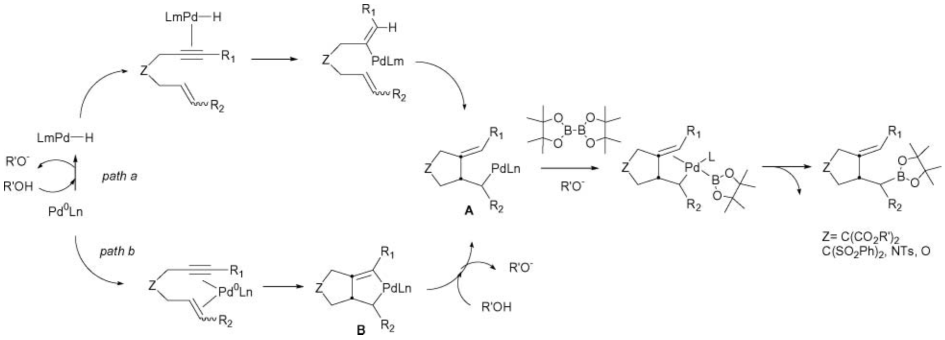


Scheme 26

The enyne hept-6-en-1-yne also undergoes the palladium-borylstannylative carbocyclization with complete regioselectivity, and the boryl group is exclusively introduced into the acetylenic bond. On the basis of the selectivity observed, Tanaka *et al.*[53] suggested a catalytic cycle with a mechanistic pathway in which the oxidative addition of the B–Sn bond to a palladium(0) species generates the corresponding *cis*-boryl(stannyl)palladium(II) species **A** (Scheme 27). Further coordination of the diyne (or enyne) and *cis* insertion of an acetylenic moiety into the Pd–B bond could provide the intermediate **B**. The preferential insertion into the Pd–B bond rather than the Pd–Sn bond is strongly supported by the regioselective introduction of the boryl group into the more reactive terminal acetylene. Subsequent *cis* insertion



Scheme 27

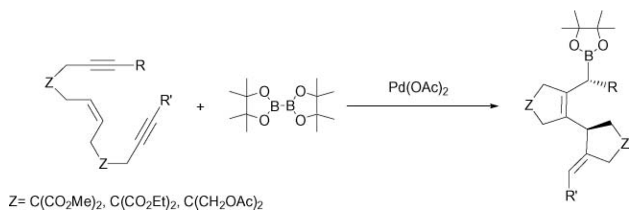


Scheme 28

of the other acetylenic (or olefinic) moiety into the resulting Pd–alkenyl bond and reductive elimination give the cyclized product and regenerates the palladium(0) species (Scheme 27, path a). An alternative mechanistic pathway involving the palladacycle intermediate **C** could not be excluded (Scheme 27, path b).

More recently, a novel Pd-catalyzed cyclization reaction of 1,6-enynes has been described in the presence of bis(pinacolato)-diboron that provides homoallylic alkylboronates.[54] The authors carried out the synthesis of homoallylic alkylboronates with a broad range of substrates, under mild conditions. The reaction is compatible with a wide variety of functional groups. However, some cycloisomerization derivatives can also be formed as by-products. A plausible mechanism for this borylative cyclization of 1,6-enynes involves the reduction of the precatalyst to afford catalytically active Pd(0) species. Further formation of a Pd hydride species by protonation with the alcohol followed by insertion of the alkyne into the Pd–H bond seems to account for the observed alkene stereochemistry[55] (Scheme 28, path a). Alternatively, it has been postulated that intermediate **A** could be formed by sequential coordination of the enyne to Pd(0), oxidative cyclometallation to give metallacycle **B**, and subsequent protonolysis of the Pd–C (sp^2) bond[56] (Scheme 28, path b). A common final sequence could involve transmetallation of **A** with bis(pinacolato)diboron promoted by an alkoxide reagent and followed by reductive elimination to give the final product and regenerate the Pd(0) catalyst.

Cárdenas *et al.* have also described the palladium-catalyzed dicyclization of 6-ene-1,11-diynes with bis(pinacolato)diboron to give synthetically useful allylboranes under mild conditions. With this new route, two new C–C bonds and one C–B bond are stereospecifically formed in a single operation (Scheme 29). The stereochemical outcome depends on the starting alkene configuration. The reaction is general and has been applied to differently substituted enediynes. Isolation of intermediate 1,3-dienes suggests a regioselective β-hydrogen elimination along the reaction pathway.[57]



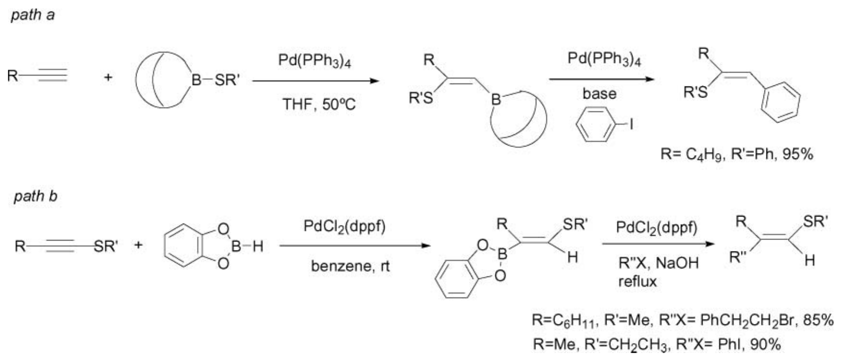
Scheme 29

The palladium-catalyzed cross-coupling reaction has been widely and successfully carried out *via* transmetallation between organoborane reagents and organopalladium complexes. Therefore, the carbon–carbon bond forming reaction that uses the Suzuki–Miyaura protocols has found numerous applications in both industrial processes and small scale laboratory syntheses,[15] because it has several advantages. It is largely unaffected by the presence of water, it tolerates a broad range of functional groups, and generally proceeds in regio- and stereoselectively. Moreover, the inorganic by-product of the reaction is non-toxic and can be easily removed from the reaction mixture.

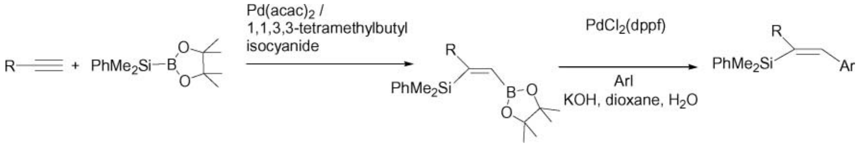
Miyaura and Suzuki[22] were the first to demonstrate the usefulness of the one-pot synthesis of vinylic sulfides by sequential thioboration and cross-coupling reactions, both of which were catalyzed by a common palladium(0) catalyst. Therefore the β-(alkylthio)alkenylborane obtained from the thioboration of 1-hexene were directly subjected to the next cross-coupling with iodobenzene, which proceeded smoothly in THF at 50 °C in the presence of aqueous NaOH and Pd(PPh$_3$)$_4$ (Scheme 30, *path a*). Interestingly, the regio- and stereochemical integrity of the boron intermediates was completely maintained during the cross-coupling reaction. Simultaneously, the same authors reported the use of phosphine-based palladium complexes for a convenient one-pot synthesis of vinylic sulfides from thioalkynes *via* a catalytic hydroboration–coupling sequence.[21] The catalytic hydroboration of thioacetylenes with catecholborane proceeds regio- and stereospecifically through *syn*-addition. This configuration is conserved during the cross-coupling reaction with aryl, alkynyl, or vinylic halides. The stereochemistry of the vinylic halides is also retained during this stage (Scheme 30, *path b*).

Ito *et al.*[24,25] also developed an interesting synthetic application of the Pd-catalyzed silaboration of alkynes followed by palladium cross coupling reactions. It has to be noted that ligands are different for each Pd complex, so compatibility of complexes fails in this example. The reaction of organic halides with alkenylboranes that contain a silyl group β and are *cis* to the boryl group produces the corresponding vinylsilane stereoselectively (Scheme 31).

Catalytic access to allene diboration products provides another opportunity for synthesis through such tandem reaction sequences as catalytic allylation/cross-coupling reactions. Therefore, the Suzuki–Miyaura coupling reaction can also terminate a single-pot cascade reaction sequence by the simple addition of iodobenzene and KOH to the diboration/allylboration mixture to afford the



Scheme 30



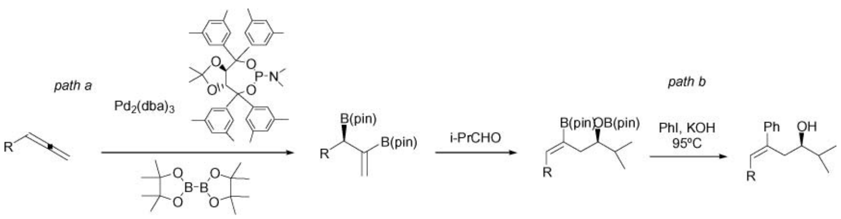
Scheme 31

coupling product in 79% yield after heating to 95 °C for 6 h (Scheme 32, *path b*). The palladium complex that catalyzes the allene diboration is also active for the Suzuki–Miyaura coupling and is not destroyed during the allylation reaction.[36] Interestingly, the aforementioned tandem functionalization protocol does not involve any erosion of enantiomeric excess from the asymmetric allene diboration/allylboration process (Scheme 32, *path a*).

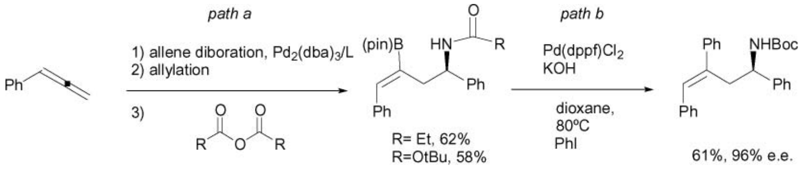
Transforming diboron adducts that contain both allylboronate and vinylboronate functional groups in concatenated reaction sequences has another significant application in the one-pot synthesis of β-amidoketones. Morken *et al.*[58] have recently carried out the allene diboration/imine allylation tandem process by performing allene diboration followed by the addition of silylimine to methanol. Alternatively, upon executing the allene diboration, the authors mixed the reaction mixture with a methanolic solution of an aldehyde and solid ammonium acetate. As well as preparing the β-amidoketone products, the allylation intermediate was also subjected to Boc protection conditions, and the vinyl boronate was then treated with iodobenzene under Suzuki–Miyaura cross-coupling conditions (Scheme 33, *path b*). Ligands are different for each Pd complex, so compatibility of complexes fails in this example.

Alternatively, chiral allyl vinyl boronates generated by catalytic enantioselective diboration of prochiral allenes can react *in situ* with a hydroborating reagent to form a novel triboron intermediate which can be used in the cross-Suzuki–Miyaura coupling reaction (Scheme 34). However, only the primary C–B bond is transformed into the new C–C bond, while the remaining C–B bonds can be oxidized in the reaction work up to provide internal chiral diols in a concise single-pot fashion.[59] Interestingly, the second step of the reaction sequence, the hydroboration reaction of the organodiboron,[60] proceeds stereoselectively. The origin of diastereoselection has been rationalized with a transition structure that involves aligning the electron-rich allylic C–B bond with the reacting π-system.

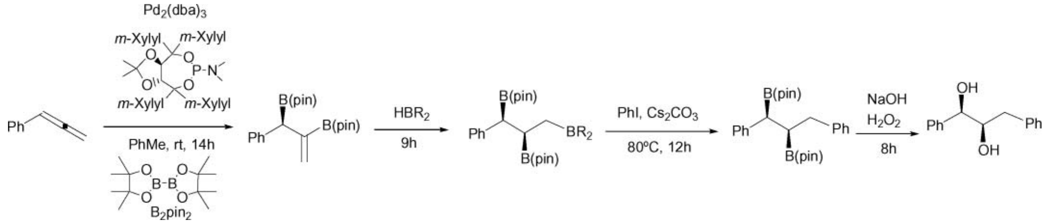
Since the silaboration of allenes is highly regioselective, one can take advantage of the reactivity of the allylsilane moiety to prepare functionalized alkenylboranes (Scheme 35). A cascade



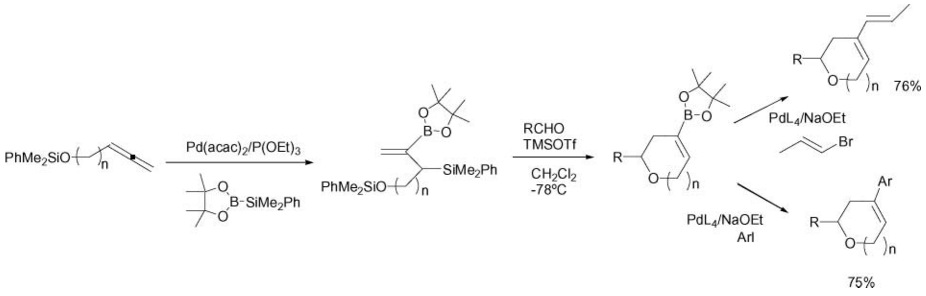
Scheme 32



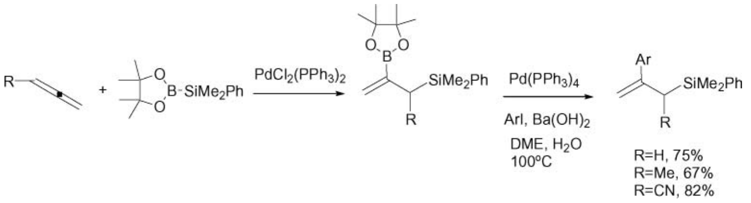
Scheme 33



Scheme 34



Scheme 35

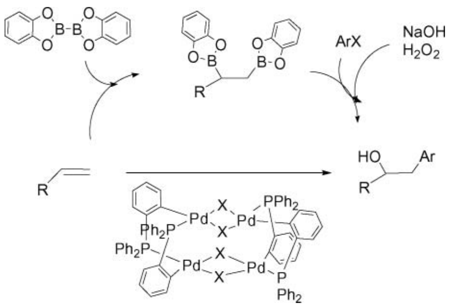


Scheme 36

cyclization giving *trans*-1,2-benzodecaline skeletons *via* the sequential reaction of α-phenethyl-β-borylallylsilane with aldehydes has been reported. Further vinylation or arylation transformations were successfully carried out through consecutive palladium cross coupling reactions, despite the fact that the ligands are different for each palladium complex.[61,62]

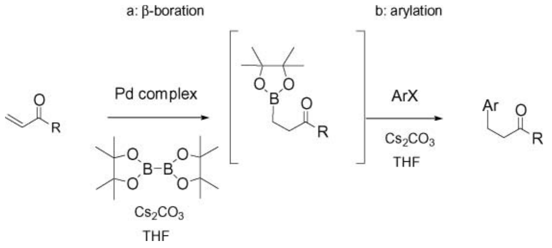
Another series of silaboration products generated by the palladium-catalyzed regioselective silaboration of 1,2-dienes served as useful precursors for the synthesis of 2-arylallylsilanes. For instance, the selective replacement of the boryl group by a phenyl group gives dimethylphenyl(2-phenylallyl)silane in high yields[45] (Scheme 36). However, two different types of palladium complexes were required.

An interesting catalytic carbohydroxylation of alkenes by a tandem diboration/Suzuki–Miyaura cross-coupling/oxidation reaction has been carried out by our group with Pd_2^{6+} complexes and their Pd_2^{4+} counterparts. An *in situ* catalytic tandem reaction was designed to transform vinylarenes and aliphatic 1-alkenes into the monoarylated product which, after oxidative work up, provides the carbohydroxylated adduct (Scheme 37). Remarkably, the same catalyst performs both reactions with total conversion of the alkene.[40] Once the diboration of 3,3-dimethyl-1-butene with B_2cat_2 had been properly completed (after 4 h at room temperature in the presence of $[Pd(C_6H_4PPh_2)Br]_4$, and the base NaOAc), the addition of aryl halides and aryl triflates provided total monoarylation of the primary alkylboronic ester. Further oxidative work-up led to total conversion of the alkene into the carbohydroxylated adduct. Similar results were achieved when the complex *cis*-$Pd_2(C_6H_4PPh_2)_2(O_2CCH_3)_2Cl_2$ was used as catalyst precursor. We observed that aryl halides are more active reagents than the aryl triflates when the catalytic conditions for the cross-coupling reaction were optimized, and that 10% H_2O was required to complete the monoarylation process. The absence of H_2O only provided the desired product in 50% yield. The efficiency of the base Cs_2CO_3 guaranteed the sequence of arylation, despite the presence of NaOAc in the reaction. Similarly to 3,3-dimethyl-1-butene, the substrate vinylcyclohexane was transformed in the tandem reaction with identical success.



Scheme 37

We also examined whether palladium-based complexes could perform the tandem single-pot diboration/Suzuki–Miyaura cross coupling by using only 2.5 mol% of palladium dimer complexes throughout the tandem reaction (Scheme 38). We were very pleased to observe that complex $Pd_2(\mu\text{-}((C_6H_4)PPh_2)_2(\mu\text{-}C_9H_7NPPh_2)(\mu\text{-}O_2CCH_3)$ catalyzed the β-boration of ethyl acrylate and methyl vinyl ketone followed by cross coupling with a range of arylbromides, although moderate conversions were observed after 24 h of reaction. However, the β-boration of dimethyl acrylamide with B_2pin_2 was properly completed after the addition of 3-bromoanisole, in the presence of 2 eq of Cs_2CO_3 and H_2O, to provide total β-arylation. THF was the solvent of choice for the two consecutive reactions, since the use of toluene diminished the cross-coupling transformation. Taking into account the recent report by Crudden *et al.*,[63] about the positive influence of Ag_2O in palladium coupling reactions of secondary organoboronic esters with retention of configuration, we are planning to explore this method for the tandem single-pot diboration/Suzuki–Miyaura cross coupling of alkenes, catalyzed by palladium complexes. Molander *et al.*,[64] have reviewed recently the field of monocoordinated palladium complexes as catalysts for cross-coupling reactions with organotrifluoroborates, providing new important perspectives.



Scheme 38

5 Conclusions

The catalytic boron addition to unsaturated substrates is by itself an important reaction because it provides useful organoboranes that can be functionalized. The versatility of these organoboranes through the formation of new C–C bonds involves the presence of alternative catalytic systems. However, when the two steps are designed to be carried out under the same catalytic system, the synthetic usefulness of this methodology becomes real and palladium has a crucial role in these transformations. In addition, the palladium complexes control the regio- and stereochemistry in the boron addition reaction and guarantee the integrity of the C–B intermediates during the C–C bond formation steps. Work on developing catalytic systems based on multifaceted palladium complexes has only just started. In this regard, understanding the mechanism and the intrinsic catalytic performance throughout the tandem reaction is essential if the catalysis is to be improved.

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